Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Synthesis and Biological Evaluation of New Paclitaxel and Discovery of Potent Antitumor Agents

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Supplementary Information

I. Experimental Section

General Information: All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), methanol (MeOH), triethylamine (Et_3N), toluene, benzene, diethyl ether (Et_2O), acetonitrile (MeCN), *N*,*N*-dimethylformamide (DMF), and methylene chloride (CH_2Cl_2) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated.

Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as a visualizing agent and an aqueous solution of phosphomolybdic acid and cerium sulfate and heat as developing agents (Hanessian's stain). Acros Organics silica gel (60, particle size 0.035–0.070 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker DRX-600, DRX-500, or AMX-400 instruments and calibrated using residual undeuterated solvent (^{1}H NMR; $CDCl_3$: δ_H = 7.26 ppm and ^{13}C NMR; $CDCl_3$: δ_C = 77.16 ppm) as an internal reference. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

IR spectra (infrared) were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. High-resolution mass spectra (HR-MS) were recorded on a VG ZAB-ZSE mass spectrometer using MALDI (matrix-assisted laser-desorption ionization) or ESI (electrospray ionization).

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Optical rotations were recorded on a Perkin-Elmer Model 343 polarimeter at 589 nm and are reported in units of 10^{-1} (deg cm^2 g^{-1}). Melting points are uncorrected. Chemical nomenclature was generated using ChemBioDraw Ultra, Version 12.0.

Purity over 95 % was established by TCL analysis and integration of high field proton NMR spectra of tested compounds.

Reaction of 10-deacetylbaccatin III (III) with DAST. Synthesis of compounds 1a−4a and 1b−3b.

General procedure A: 10-Deacetylbaccatin III (**III**) (100 mg, 0.184 mmol, 1.0 equiv) was dissolved in dry THF (3 mL), 4 Å granular molecular sieves (MS) were added and the resulting solution was cooled to −78 ºC. DAST reagent (0.05 mL, 0.378 mmol, 2.0 equiv) was added dropwise over the period of 5 min and the resulting mixture was stirred at −78 ºC for 3 h. After the reaction was completed (monitored by TLC) it was slowly quenched with sat. aq. NH_4Cl (5 mL) at −78 ºC. The biphasic mixture was extracted with CH_2Cl_2 (2 × 5 mL), the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (silica gel, EtOAc/hexanes 1:1) or PTLC (silica gel, EtOAc/hexanes 1:1) yielded pure products. Note: 1) Due to the inconsistent quality of DAST it is recommended to "titrate" the reaction mixture with 0.5 equiv aliquots of the reagent until most of the starting material is consumed; 3) products **1a−3a** tend to slowly rearrange to **1b−3b** upon longer exposure to silica gel.

General procedure B: III (313 mg, 0.575 mmol, 1.0 equiv) was dissolved in dry THF (5 mL), 4 Å granular molecular sieves (MS) were added and the resulting solution was cooled to −78 ºC. DAST reagent (0.15 mL, 1.15 mmol, 2.0 equiv) was added dropwise over the period of 5 min

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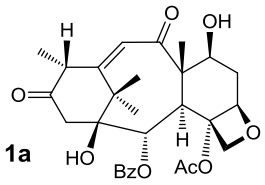
and the resulting mixture was stirred at −78 ºC. After 2−3 h, CH_2Cl_2 (2 mL) was added, followed by another 2.0 equiv of DAST (0.15 mL, 1.15 mmol). The resulting reaction mixture was allowed to warm up to room temperature over 16 h, and then it was quenched with sat. aq. NH_4Cl, (5 mL) and the biphasic mixture extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (silica gel, EtOAc/hexanes 1:1) or PTLC (silica gel, EtOAc/hexanes 1:1) yielded pure products. NOTE: Excess of DAST, moisture and/or higher temperatures resulted in formation of alkene **4a**.

General procedure C: 1a (270 mg, 0.513 mmol, 1.0 equiv) was dissolved in dry THF (5 mL), 4 Å granular molecular sieves (MS) were added and the resulting solution was cooled to 0 ºC. After the addition of Et_3SiCl (0.43 mL, 2.56 mmol, 5.0 equiv), Et_3N (0.36 mL, 2.58 mmol, 5.0 equiv) and 4-DMAP (31 mg, 0.254 mmol, 0.5 equiv) the resulting mixture was stirred for 1.5 h. Standard workup followed by flash column chromatography (silica gel, EtOAc/hexanes 1:2) yielded pure product.

General procedure D: A solution of **1a−3a** (20–102 mg, 0.038–0.193 mmol, 1.0 equiv) in dry THF (1–3 mL) was placed in a flask containing 4 Å granular molecular sieves, 4-DMAP (12–59 mg, 0.098–0.483 mmol, 2.5 equiv) and was stirred for 20−24 h. Then it was quenched with sat. aq. NH_4Cl (5 mL) and the biphasic mixture extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (silica gel, EtOAc/hexanes 1:1 or 1:2) or PTLC (silica gel, EtOAc/hexanes 1:1 or 1:2) yielded pure products **1b−3b** (in some cases the purification was not required).

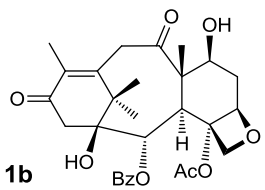
(*2aR,4S,4aS,8R,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-4,11-dihydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**1a**): Compound **1a** was obtained in



1a

93% yield (90 mg) from 100 mg of **III** (0.184 mmol) and 0.05 mL of DAST (0.378 mmol) (procedure A). **1a**: R_f = 0.20 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{32}$ = −149.5 (*c* = 1.05 in CH_2Cl_2); IR (film) ν_{max} = 3465, 2982, 1703, 1451, 1370, 1315, 1240, 1177, 1106, 1068, 1026, 982, 946, 911, 878, 849, 805, 772, 730, 710 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 5.90 (d, *J* = 1.2 Hz, 1H), 5.82 (d, *J* = 7.4 Hz, 1H), 4.90 (dd, *J* = 9.5, 2.6 Hz, 1H), 4.33 (d, *J* = 8.5 Hz, 1H), 4.20 (d, *J* = 8.5 Hz, 1H), 3.93 (ddd, *J* = 11.2, 6.3, 5.0 Hz, 1H), 3.62 (q, *J* = 6.4 Hz, 1H), 3.05 (d, *J* = 6.9 Hz, 1H), 3.03 (d, *J* = 18.3 Hz, 1H), 2.55 (ddd, *J* = 14.6, 9.6, 6.6 Hz, 1H), 2.52 (d, *J* = 18.3 Hz, 1H), 2.36 (s, 3H), 1.93 (s, OH), 1.84−1.79 (m, 1H) overlaps with 1.82 (br s, OH), 1.65 (s, 3H), 1.37 (s, 3H), 1.33 (s, 3H), 1.23 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 210.15, 205.19, 170.47, 167.36, 146.80, 134.15, 130.25, 128.98, 128.93, 122.42, 84.23, 80.32, 79.24, 76.38, 73.86, 69.62, 59.12, 49.03, 46.76, 45.57, 44.52, 35.90, 26.95, 24.22, 22.20, 11.28, 8.60 ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{34}O_9$ [M + H^+] 527.2275, found 527.2282.

(*2aR,4S,4aS,11S,12S,12aR,12bS*)-12b-Acetoxy-4,11-dihydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**1b**): Compound **1b** was obtained in



1b

98% yield (19.6 mg) from 20 mg of **1a** (0.038 mmol) and 12 mg of 4-DMAP (0.098 mmol) (procedure D). **1b**: R_f = 0.22 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −45.8 (*c* = 0.88 in $CHCl_3$); IR (film) ν_{max} =

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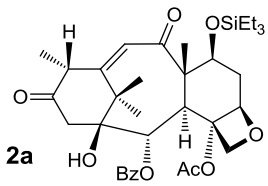
3448, 2939, 1707, 1664, 1602, 1451, 1371, 1315, 1272, 1242, 1178, 1107, 1070, 1026, 983, 916, 731, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 5.72 (d, *J* = 6.5 Hz, 1H), 4.94 (d, *J* = 9.3 Hz, 1H), 4.36 (dd, *J* = 10.8, 7.0 Hz, 1H), 4.33 (d, *J* = 8.5 Hz, 1H), 4.16 (d, *J* = 6.5 Hz, 1H), 4.13 (d, *J* = 8.5 Hz, 1H), 4.04 (d, *J* = 15.0 Hz, 1H), 3.73 (d, *J* = 15.0 Hz, 1H), 2.96 (d, *J* = 19.4 Hz, 1H), 2.65 (d, *J* = 19.4 Hz, 1H) overlaps with 2.63 (ddd, *J* = 14.6, 9.4, 7.0 Hz, 1H), 2.20 (s, 3H), 1.98 (s, 3H), 1.82 (br s, OH), 1.79 (ddd, *J* = 14.5, 11.0, 2.0 Hz, 1H), 1.62 (s, 3H), 1.43 (br s, OH), 1.23 (s, 3H), 1.22 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 206.39, 197.65, 170.25, 166.98, 156.68, 136.65, 134.15, 130.21, 128.94, 128.93, 84.10, 80.62, 78.81, 76.47, 73.26, 71.22, 60.90, 47.02, 45.71, 44.56, 42.84, 37.23, 32.39, 21.94, 20.80, 13.71, 9.64 ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{34}O_9$ [M + H^+] 527.2276, found 527.2260.

(*2aR,4S,4aS,8R,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**2a**): Compound **2a** was obtained in



2a

74% yield (243 mg) from 270 mg of **1a** (0.513 mmol), 0.43 mL of Et_3SiCl (2.56 mmol), 0.36 mL of Et_3N (2.58 mmol) and 31 mg of 4-DMAP (0.254 mmol) (procedure C). NOTE: Compound **2a** can be alternatively made in 70% yield (157 mg) using procedure A from 231 mg (0.351 mmol) of 7-triethylsilyl-10-deacetylbaccatin III (**IV**) and DAST (0.185 mL, 1.4 mmol, 4.0 equiv were needed to drive the reaction to completion presumably due to DAST's diminished quality). **2a**: R_f = 0.42 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −94.7 (*c* = 1.25 in CH_2Cl_2); IR (film) ν_{max} = 3496, 2957, 2878, 1708, 1452, 1368, 1269, 1240, 1177, 1096, 1069, 1026, 990, 946, 911, 884, 825, 729, 710 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.8 Hz, 2H), 7.62 (t, *J* = 7.5

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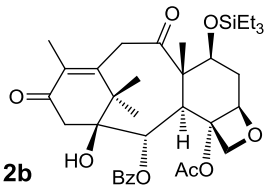
Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 5.95 (d, *J* = 1.1 Hz, 1H), 5.78 (d, *J* = 7.2 Hz, 1H), 4.90 (dd, *J* = 9.6, 2.3 Hz, 1H), 4.33 (d, *J* = 8.5 Hz, 1H), 4.16 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.14 (dd, *J* = 10.9, 6.6 Hz, 1H), 3.63 (q, *J* = 6.3 Hz, 1H), 3.00 (d, *J* = 18.4 Hz, 1H), 2.94 (d, *J* = 7.3 Hz, 1H), 2.51 (d, *J* = 18.4 Hz, 1H), 2.41 (ddd, *J* = 14.4, 9.6, 6.6 Hz, 1H), 2.37 (s, 3H), 1.88−1.83 (ddd, *J* = 14.3, 11.0, 2.6 Hz, 1H) overlaps with 1.86 (s, OH), 1.63 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.58−0.51 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 206.92, 205.49, 170.45, 167.40, 145.73, 134.06, 130.26, 129.06, 128.87, 123.46, 84.48, 80.26, 79.39, 76.38, 73.76, 71.08, 59.17, 49.07, 47.52, 45.57, 44.59, 37.03, 27.14, 23.90, 22.22, 11.24, 8.39, 6.94, 5.32 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{48}O_9Si$ [M + H^+] 641.3140, found 641.3143.

(*2aR,4S,4aS,11S,12S,12aR,12bS*)-12b-Acetoxy-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**2b**): Compound **2b** was obtained in



2b

96% yield (98 mg) from 102 mg of **2a** (0.159 mmol) and 50 mg of 4-DMAP (0.410 mmol) (procedure D). **2b**: R_f = 0.47 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −37.2 (*c* = 0.957 in $CHCl_3$); IR (film) ν_{max} = 3502, 2956, 2878, 1728, 1667, 1605, 1452, 1414, 1371, 1315, 1269, 1242, 1178, 1106, 1046, 1026, 987, 947, 826, 730, 711 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 5.67 (dd, *J* = 6.6, 1.1 Hz, 1H), 4.92 (dd, *J* = 9.4, 1.7 Hz, 1H), 4.49 (dd, *J* = 10.5, 6.8 Hz, 1H), 4.32 (d, *J* = 8.5 Hz, 1H), 4.11 (d, *J* = 8.5 Hz, 1H), 4.08 (d, *J* = 6.5 Hz, 1H), 3.97 (d, *J* = 14.3 Hz, 1H), 3.68 (dd, *J* = 14.3, 1.4 Hz, 1H), 2.94 (d, *J* = 19.6 Hz, 1H), 2.64 (dd, *J* = 19.6, 1.1 Hz, 1H), 2.50 (ddd, *J* = 14.4, 9.5, 6.8 Hz, 1H), 2.19 (s, 3H), 1.99 (d, *J* = 1.2 Hz, 3H), 1.86 (ddd, *J* = 14.3, 10.6, 2.1 Hz, 1H), 1.80 (br s, OH), 1.60 (s, 3H),

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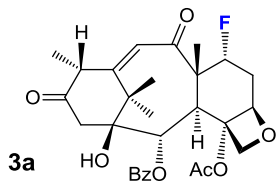
1.23 (s, 3H), 1.20 (s, 3H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.64−0.52 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 204.74, 197.78, 170.28, 167.00, 157.00, 136.48, 134.06, 130.21, 129.02, 128.87, 84.26, 80.65, 78.84, 76.46, 73.32, 72.17, 61.19, 46.99, 45.77, 44.69, 42.79, 37.42, 32.69, 21.96, 20.56, 13.71, 9.90, 6.93, 5.46 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{48}O_9Si$ [M + H^+] 641.3140, found 641.3138.

(*2aR,4R,4aR,8R,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**3a**): Compound **3a** was obtained in



3a

63% yield (192 mg) from 313 mg of **III** (0.575 mmol) and 0.3 mL of DAST (2.29 mmol) (procedure B). **3a**: R_f = 0.47 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −106.6 (*c* = 1.275 in $CHCl_3$); IR (film) ν_{max} = 3458, 2984, 1703, 1451, 1420, 1366, 1270, 1233, 1178, 1106, 1068, 1041, 999, 948, 911, 878, 841, 730, 711 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 5.85 (d, *J* = 7.5 Hz, 1H), 5.77 (d, *J* = 7.3 Hz, 1H), 5.00 (dd, *J* = 8.8, 2.1 Hz, 1H), 4.59 (ddd, *J* = 46.3, 4.8, 1.3 Hz, 1H−CF), 4.36 (d, *J* = 8.3 Hz, 1H), 4.27 (d, *J* = 8.3 Hz, 1H), 3.58 (q, *J* = 6.4 Hz, 1H), 3.26 (d, *J* = 7.5 Hz, 1H), 3.08 (d, *J* = 18.0 Hz, 1H), 2.62−2.53 (m, 1H) overlaps with 2.52 (d, *J* = 18.0 Hz, 1H), 2.38 (s, 3H), 2.27−2.15 (dddd, *J* = 46.0, 16.8, 5.0, 2.5 Hz, 1H), 1.88 (s, OH), 1.70 (d, *J* = 1.0 Hz, 3H), 1.36 (s, 3H), 1.28 (s, 3H), 1.22 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 211.05, 205.02, 169.16, 167.46, 144.15 (d, *J* = 2.0 Hz), 134.14, 130.28, 129.11, 128.93, 125.61 (d, *J* = 8.0 Hz), 95.25 (d, *J* = 179.7 Hz, C−F), 81.96, 80.61, 79.45, 76.81, 74.19, 57.26 (d, *J* = 15.7 Hz), 48.73, 45.67, 43.90, 41.05, 33.99 (d, *J* = 24.1 Hz), 26.72, 24.01, 22.06, 13.72 (d, *J* = 7.0 Hz), 11.24 ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{33}FO_8$ [M + H^+] 529.2232, found 529.2257.

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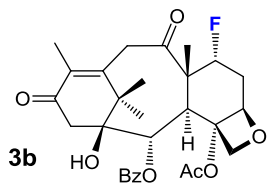
(*2aR,4R,4aR,11S,12S,12aR,12bS*)-12b-Acetoxy-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**3b**): Compound **3b** was obtained in



78% yield (79.4 mg) from 102 mg of **3a** (0.193 mmol) and 59 mg of 4-DMAP (0.483 mmol) (procedure D). **3b**: R_f = 0.55 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −18.5 (*c* = 0.433 in $CHCl_3$); IR (film) ν_{max} = 3483, 2929, 1740, 1723, 1696, 1666, 1612, 1452, 1414, 1370, 1315, 1271, 1238, 1179, 1139, 1096, 1070, 1039, 989, 949, 917, 830, 732, 712 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 5.82 (d, *J* = 6.8 Hz, 1H), 5.00 (d, *J* = 8.6 Hz, 1H), 4.62 (dd, *J* = 47.1, 5.0 Hz, 1H−CF), 4.40 (d, *J* = 6.8 Hz, 1H), 4.38 (d, *J* = 8.6 Hz, 1H), 4.24 (d, *J* = 8.6 Hz, 1H), 4.11 (dd, *J* = 15.9, 3.7 Hz, 1H), 3.75 (d, *J* = 15.9 Hz, 1H), 3.06 (d, *J* = 19.6 Hz, 1H), 2.66 (d, *J* = 19.6 Hz, 1H), 2.61−2.52 (ddd, *J* = 25.1, 16.9, 8.7 Hz, 1H), 2.26−2.15 (dddd, *J* = 45.6, 16.9, 5.3, 2.0 Hz, 1H) overlaps with 2.21 (s, 3H), 1.91 (s, 3H), 1.82 (s, OH), 1.65 (s, 3H), 1.21 (s, 3H), 1.17 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 208.75 (d, *J* = 1.6 Hz), 197.62, 169.17, 167.12, 155.53, 136.97, 134.17, 130.25, 129.07, 128.96, 95.91 (d, *J* = 178.9 Hz, C−F), 81.80, 80.58, 78.79, 77.45, 73.53, 59.66 (d, *J* = 17.6 Hz), 50.18 (d, *J* = 5.8 Hz), 43.90, 42.83, 39.21 (d, *J* = 2.0 Hz), 34.14 (d, *J* = 24.0 Hz), 31.37, 21.87, 21.12, 14.75 (d, *J* = 6.9 Hz), 13.42 (d, *J* = 5.1 Hz) ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{33}FO_8$ [M + H^+] 529.2232, found 529.2242.

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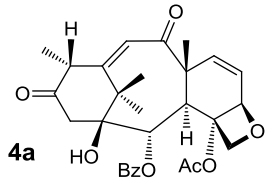
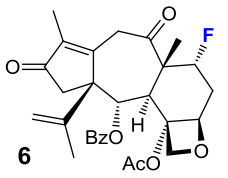
(*2aR,4aR,8R,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,4a,5,8,9,10,11,12,12a,12b-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**4a**): Compound **4a** is sometimes formed in small amounts as a by-product together with **3a**. All attempts to purify **4a** from **3a** failed; hence it was used without further purification (ratio **4a**:**3a** usually varies from 1:5 to 1:3). R_f = 0.47 (silica gel, EtOAc/hexanes 1:1); HRMS (ESI-TOF): calcd for $C_{29}H_{32}O_8$ [M + H^+] 509.2170, found 529.2169.



(*2aR,4R,4aR,9aS,10S,10aR,10bS*)-10b-Acetoxy-4-fluoro-4a,7-dimethyl-5,8-dioxo-9a-(prop-1-en-2-yl)-2a,3,4,4a,5,6,8,9,9a,10,10a,10b-dodecahydro-1*H*-azuleno[5',6':3,4]benzo[1,2-*b*]oxet-10-yl benzoate (**6**): Compound **6** was obtained in 46% yield (13 mg) from 30 mg of **III** (0.055 mmol) and 0.025 mL of DAST (0.189 mmol) in CH_2Cl_2 (2 mL). **6**: R_f = 0.55 (silica gel, EtOAc/hexanes 1:1); IR (film) ν_{max} = 2928, 1741, 1708, 1652, 1451, 1369, 1268, 1231, 1108, 1070, 1051, 914, 822, 712 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 6.25 (d, *J* = 8.0 Hz, 1H), 5.11 (s, 1H), 5.08−4.99 (dd, *J* = 46.9, 6.0 Hz, 1H−CF) overlaps with 5.02 (s, 1H) overlaps with 5.01 (d, *J* = 8.2 Hz, 1H), 4.45 (d, *J* = 8.3 Hz, 1H), 4.38 (d, *J* = 8.3 Hz, 1H), 3.82 (d, *J* = 18.0 Hz, 1H), 3.57 (d, *J* = 18.0 Hz, 1H), 3.43 (d, *J* = 8.0 Hz, 1H), 2.62 (d, *J* = 18.7 Hz, 1H), 2.55−2.46 (m, 1H) overlaps with 2.48 (d, *J* = 18.7 Hz, 1H), 2.31−2.21 (m, 1H), 1.95 (s, 3H), 1.79 (s, 3H), 1.72 (s, 3H), 1.64 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 207.05 (d, *J* = 2.0 Hz), 205.83, 169.06, 165.87, 162.30, 142.92, 141.16, 134.08, 129.89, 129.21, 128.91, 115.53, 94.13 (d, *J* = 175.2 Hz, C−F), 82.53, 79.48, 75.27, 69.88, 59.44, 56.73 (d, *J* = 18.8 Hz), 43.97, 43.91, 38.50 (d, *J* = 2.4 Hz), 33.66 (d, *J* = 24.4 Hz), 21.52, 20.63, 15.14



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(d, J = 6.7 Hz), 8.21 ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{31}FO_7$ [M + H^+] 511.2127, found 511.2127.

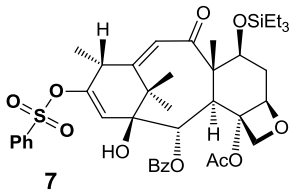
Fluorination of 2a and 3a with NFSi and Selectfluor®. Synthesis of compounds 7−9 and 10−13.

General fluorination procedure A: Compound (**2a** or **3a**) (30 mg of **2a**, 0.047 mmol, 1.0 equiv) was dissolved in anhydrous THF (0.75–1 mL), 4 Å granular molecular sieves (MS) were added and the resulting solution was cooled to −78 ºC. When KHMDS (0.21 mL, 0.103 mmol, 0.5 M solution in toluene, 2.2 equiv) was added the solution turned into a slurry gel and gained deep orange color. After 15 min, *N*-fluorobenzenesulfonimide (NFSi or NHSI) (44 mg, 0.140 mmol, 3.0 equiv) in a small amount of dry THF (0.25–0.50 mL) was added, the resulting solution was allowed to stir for 1 h at −78 ºC, and 1 h at room temperature. Then it was quenched with sat. aq. NH_4Cl, (3 mL) and the biphasic mixture extracted with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. PTLC (silica gel, EtOAc/hexanes either 1:1 and 1:2, or EtOAc/benzene 1:5) yielded pure products.

General fluorination procedure B: Compound (**2a** or **3a**) (17 mg of **3a**, 0.032 mmol, 1.0 equiv) was dissolved in anhydrous THF (0.5–0.75 mL), 4 Å granular molecular sieves (MS) were added and the resulting solution was cooled to −78 ºC. When KHMDS (0.13 mL, 0.065 mmol, 0.5 M solution in toluene, 2.0 equiv) was added the solution turned a slurry gel and gained deep orange color. After 0.3−1 h, 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectfluor®) (114 mg, 0.322 mmol, 10.0 equiv) was added in a small amount of dry DMF (0.1 mL) (or CH_3CN) (0.1–0.25 mL), the resulting pale yellow solution was allowed to stir for 0.5−1 h at −78 ºC, and 1 h at room temperature. Then it was quenched with

sat. aq. NH_4Cl (3 mL), and the biphasic mixture extracted with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. PTLC (silica gel, EtOAc/hexanes 1:1 or 1:2) yielded pure products.

(*2aR,4S,4aS,8R,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-9-((phenylsulfonyl)oxy)-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,11,12,12a,12b-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**7**): Compound **7** was



7

obtained in 33% yield (12.2 mg) from 30 mg of **2a** (0.047 mmol), 0.21 mL of KHMDS (0.103 mmol, 0.5 M solution in toluene), and 44 mg of NFSi (0.140 mmol) (procedure A). In some cases product **9** was also observed, usually in trace quantities (≤ 5%). **7**: R_f = 0.29 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = +4.9 (*c* = 0.715 in $CHCl_3$); IR (film) ν_{max} = 3441, 2955, 2878, 1718, 1450, 1375, 1270, 1244, 1193, 1178, 1092, 1070, 1009, 993, 883, 863, 848, 828, 800, 775, 753, 728, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 7.5 Hz, 2H), 7.96 (d, *J* = 7.5 Hz, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.9 Hz, 2H), 7.48 (t, *J* = 7.9 Hz, 2H), 5.89 (s, 1H), 5.82 (d, *J* = 6.8 Hz, 1H), 5.22 (d, *J* = 2.2 Hz, 1H), 4.88 (dd, *J* = 9.7, 3.0 Hz, 1H), 4.29 (dd, *J* = 8.6, 1.0 Hz, 1H), 4.22 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.19 (dd, *J* = 11.2, 6.3 Hz, 1H), 3.36−3.33 (m, 2H), 2.39 (ddd, *J* = 14.4, 9.8, 6.3 Hz, 1H), 2.17 (s, 3H), 1.89 (ddd, *J* = 14.4, 11.2, 3.2 Hz, 1H), 1.65 (s, OH), 1.59 (s, 3H), 1.21 (m, 6H), 1.10 (s, 3H), 0.93 (t, *J* = 8.0 Hz, 9H), 0.58−0.49 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 206.99, 170.35, 166.43, 153.77, 146.81, 135.80, 134.83, 133.81, 130.13, 129.57, 129.34, 128.81, 128.39, 122.55, 119.19, 84.38, 80.78, 80.30, 76.79, 73.20, 70.82, 59.65, 46.27, 43.37, 38.91, 37.12, 25.75, 23.44, 21.83, 13.28, 8.84, 6.93, 5.32 ppm; HRMS (ESI-TOF): calcd for $C_{41}H_{52}O_{11}SSi$ [M + H^+] 781.3072, found 781.3066.

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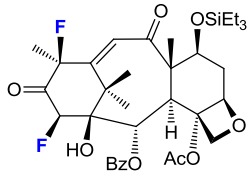
(*2aR,4S,4aS,8S,10R,11S,12S,12aR,12bS,E*)-12b-Acetoxy-8,10-difluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (8):



8

Compound **8** was obtained in 24% yield (3.8 mg) from 15 mg of **2a** (0.023 mmol), 0.094 mL of KHMDS (0.047 mmol, 0.5 M solution in toluene), and 83 mg of Selectfluor® (0.234 mmol) (procedure B). In some cases product **9** was also observed in small amounts (1−20%). **8**: R_f = 0.52 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{24}$ = −18.3 (*c* = 0.655 in $CHCl_3$); IR (film) ν_{max} = 3431, 2955, 1762, 1727, 1452, 1374, 1246, 1178, 1106, 1068, 1026, 993, 948, 922, 904, 834, 730, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 6.52 (d, *J* = 4.0 Hz, 1H), 6.06 (dd, *J* = 7.3, 2.3 Hz, 1H), 4.98 (dd, *J* = 45.6, 2.1 Hz, 1H−CF), 4.90 (dd, *J* = 9.6, 3.0 Hz, 1H), 4.39 (d, *J* = 8.5 Hz, 1H), 4.28 (d, *J* = 8.5 Hz, 1H), 4.19 (dd, *J* = 11.1, 6.3 Hz, 1H), 3.48 (d, *J* = 7.3 Hz, 1H), 2.79 (d, *J* = 10.1 Hz, OH), 2.46 (ddd, *J* = 14.5, 9.7, 6.3 Hz, 1H), 2.23 (s, 3H), 2.00 (ddd, *J* = 14.4, 11.1, 3.2 Hz, 1H), 1.74 (s, 3H), 1.67 (d, *J* = 20.6 Hz, 3H), 1.33 (s, 3H), 1.15 (d, *J* = 6.3 Hz, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.62−0.52 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 204.13, 201.04 (dd, *J* = 17.1, 16.1 Hz), 171.33, 165.46, 140.58 (d, *J* = 16.0 Hz), 134.25, 133.25 (d, *J* = 4.8 Hz), 130.23, 129.01, 128.67, 93.26 (dd, *J* = 198.0, 2.4 Hz, C−F), 88.10 (dd, *J* = 201.4, 2.9 Hz, C−F), 84.35, 81.34, 78.90 (dd, *J* = 14.7, 2.3 Hz), 76.33, 74.31, 70.65, 59.29, 46.26, 43.74 (d, *J* = 1.4 Hz), 37.15, 25.69 (d, *J* = 2.8 Hz), 25.30, 21.86 overlaps with 21.81 (d, *J* = 29.0 Hz), 9.06, 6.93, 5.31 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{46}F_2O_9Si$ [M + H^+] 677.2952, found 677.2948.

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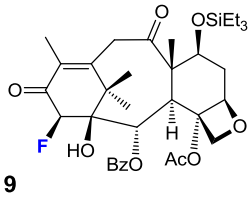
(*2aR,4S,4aS,10R,11S,12S,12aR,12bS)*-12b-Acetoxy-10-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**9**): Compound **9** was observed in some cases (together with **8**) and obtained in variable yields 1−20% (3.0 mg refers to 20%) from 15 mg of **2a** (0.023 mmol), 0.094 mL of KHMDS (0.047 mmol, 0.5 M solution in toluene), and 83 mg of Selectfluor® (0.234 mmol) (procedure B). Larger quantities of KHMDS, warmer temperatures and prolonged reaction time promote the formation of product **9**. R_f = 0.43 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{23}$ = −3.0 (*c* = 0.298 in $CHCl_3$); IR (film) ν_{max} = 3509, 2957, 2879, 1731, 1686, 1603, 1452, 1372, 1266, 1243, 1105, 1069, 1045, 1026, 992, 825, 729, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 5.87 (t, *J* = 6.3 Hz, 1H), 4.89 (dd, *J* = 10.0, 2.0 Hz, 1H) overlaps with 4.86 (d, *J* = 46.8 Hz, 1H−CF), 4.46 (dd, *J* = 10.6, 6.8 Hz, 1H), 4.30 (d, *J* = 8.6 Hz, 1H), 4.22 (d, *J* = 8.6 Hz, 1H), 3.98 (d, *J* = 6.8 Hz, 1H) overlaps with 3.96 (d, *J* = 14.2 Hz, 1H), 3.67 (dd, *J* = 14.5, 1.4 Hz, 1H), 2.76 (d, *J* = 12.1 Hz, OH), 2.48 (ddd, *J* = 14.5, 9.6, 6.7 Hz, 1H), 2.18 (s, 3H), 2.05 (s, 3H), 1.89 (ddd, *J* = 14.2, 10.7, 2.3 Hz, 1H), 1.64 (s, 3H), 1.27 (s, 3H), 1.13 (d, *J* = 2.2 Hz, 3H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.64−0.52 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 203.64, 192.76 (d, *J* = 15.1 Hz), 170.23, 165.52, 159.53, 134.43 (d, *J* = 1.2 Hz), 133.93, 130.09, 129.17, 128.90, 88.15 (d, *J* = 188.2 Hz, C−F), 84.11, 80.93, 76.27, 75.98 (d, *J* = 13.9 Hz), 72.03, 71.96 (d, *J* = 2.1 Hz), 61.39, 46.80, 45.15, 44.02 (d, *J* = 1.1 Hz), 37.33, 33.60, 21.96, 20.85, 13.88, 9.93, 6.93, 5.45 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{47}FO_9Si$ [M + H^+] 659.3046, found 659.3041.



9

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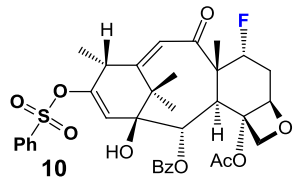
(*2aR,4R,4aR,8R,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-9-((phenylsulfonyl)oxy)-2a,3,4,4a,5,8,11,12,12a,12b-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (10):



10

Compound **10** was obtained in 24% yield (5.5 mg) from 18 mg of **3a** (0.034 mmol), 0.17 mL of KHMDS (0.085 mmol, 0.5 M solution in toluene), and 54 mg of NFSi (0.171 mmol) (procedure A). **10**: R_f = 0.52 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −30.5 (*c* = 1.04 in $CHCl_3$); IR (film) ν_{max} = 3444, 2942, 1721, 1654, 1450, 1374, 1314, 1271, 1241, 1192, 1178, 1107, 1091, 1069, 1040, 1008, 950, 914, 883, 856, 809, 777, 756, 730, 712, 687 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.7 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.68−7.63 (m, 2H), 7.57 (t, *J* = 7.7 Hz, 2H), 7.51 (t, *J* = 7.7 Hz, 2H), 5.89 (d, *J* = 7.0 Hz, 1H), 5.69 (d, *J* = 7.0 Hz, 1H), 5.31 (d, *J* = 2.3 Hz, 1H), 4.93 (dd, *J* = 8.9, 3.9 Hz, 1H), 4.56 (ddd, *J* = 46.0, 3.8, 2.5 Hz, 1H−CF), 4.39 (d, *J* = 8.5 Hz, 1H), 4.30 (d, *J* = 8.5 Hz, 1H), 3.67 (d, *J* = 6.9 Hz, 1H), 3.29 (q, *J* = 6.8 Hz, 1H), 2.63 (dddd, *J* = 19.3, 16.5, 9.0, 2.5 Hz, 1H), 2.25−2.13 (m, 1H) overlaps with 2.19 (s, 3H), 1.68 (s, OH), 1.65 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.16 (s, 3H), 1.10 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 211.24, 169.26, 166.42, 154.13, 145.53 (d, *J* = 1.8 Hz), 135.94, 134.81, 133.90, 130.17, 129.57, 129.37, 128.89, 128.35, 124.61 (d, *J* = 7.6 Hz), 118.68, 95.60 (d, *J* = 179.0 Hz, C−F), 81.95, 81.66, 79.96, 77.53, 73.64, 57.34 (d, *J* = 17.8 Hz), 42.67, 40.24, 38.51, 33.89 (d, *J* = 23.0 Hz), 25.27, 23.54, 21.82, 15.05 (d, *J* = 7.2 Hz), 13.15 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{37}FO_{10}S$ [M + H^+] 669.2164, found 669.2165.

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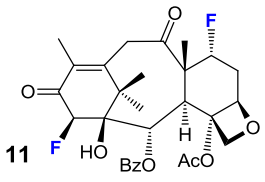
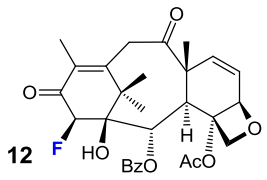
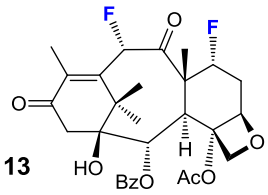
(*2aR,4R,4aR,10R,11S,12S,12aR,12bS*)-12b-Acetoxy-4,10-difluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**11**): Compound **11** was observed and obtained in small amounts ≤ 5% (1.35 mg), together with **13** (procedure B). **11**: R_f = 0.57 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −2.0 (*c* = 0.135 in $CHCl_3$); IR (film) ν_{max} = 3485, 2924, 1729, 1688, 1609, 1452, 1420, 1371, 1315, 1267, 1234, 1178, 1093, 1068, 1043, 1033, 1016, 993, 947, 916, 830, 731, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.8 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 6.00 (t, *J* = 6.5 Hz, 1H), 4.97 (dd, *J* = 9.0, 2.2 Hz, 1H) overlaps with 4.95 (d, *J* = 47.1 Hz, 1H−CF), 4.64 (dd, *J* = 47.0, 4.7 Hz, 1H−CF), 4.36 (s, 2H), 4.30 (d, *J* = 6.9 Hz, 1H), 4.10 (dd, *J* = 16.0, 3.6 Hz, 1H), 3.74 (d, *J* = 16.0 Hz, 1H), 2.87 (d, *J* = 12.8 Hz, OH), 2.57 (dddd, *J* = 24.5, 16.5, 8.8, 1.5 Hz, 1H), 2.28−2.16 (m, 1H) overlaps with 2.19 (s, 3H), 1.98 (s, 3H), 1.64 (s, 3H), 1.21 (s, 3H), 1.38 (d, *J* = 1.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 207.95 (d, *J* = 1.7 Hz), 192.79 (d, *J* = 15.1 Hz), 169.13, 165.85, 157.66, 134.91 (d, *J* = 1.1 Hz), 134.03, 130.11, 129.20, 128.98, 96.18 (d, *J* = 178.1 Hz, C−F), 88.03 (d, *J* = 188.1 Hz, C−F), 81.64, 81.00, 77.16 overlaps with $CDCl_3$, 76.06 (d, *J* = 14.1 Hz), 72.23 (d, *J* = 2.1 Hz), 59.72 (d, *J* = 17.5 Hz), 49.91 (d, *J* = 5.7 Hz), 43.22, 38.73 (d, *J* = 2.1 Hz), 34.03 (d, *J* = 23.5 Hz), 32.41, 21.92, 21.36, 14.95 (d, *J* = 6.7 Hz), 13.67 (d, *J* = 4.4 Hz) ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{32}F_2O_8$ [M + H^+] 547.2138, found 547.2134.



(*2aR,4aR,10R,11S,12S,12aR,12bS*)-12b-Acetoxy-10-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,4a,5,6,9,10,11,12,12a,12b-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**12**): Compound **12** was observed and obtained in small quantities ≤ 2% (1.07 mg), together with **13**. (Compound **12** is presumably formed from contaminant by-product **4a** produced together with **3a** from **III** and DAST, see **4a** characterization and Scheme 1). **12**: R_f = 0.66 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −23.8 (*c* = 0.107 in $CHCl_3$); IR (film) ν_{max} = 3519, 2930, 1729, 1688, 1604, 1451, 1378, 1315, 1267, 1239, 1094, 1069, 1027, 989, 917, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 7.8 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 6.11 (t, *J* = 6.3 Hz, 1H), 6.04 (dd, *J* = 10.0, 5.5 Hz, 1H), 5.79 (d, *J* = 10.0 Hz, 1H), 5.05 (d, *J* = 5.5 Hz, 1H), 4.93 (d, *J* = 47.0 Hz, 1H−CF), 4.43 (d, *J* = 8.4 Hz, 1H), 4.36 (d, *J* = 8.4 Hz, 1H), 4.25 (d, *J* = 6.5 Hz, 1H), 3.86 (d, *J* = 16.1 Hz, 1H), 3.72 (d, *J* = 16.1 Hz, 1H), 2.88 (d, *J* = 12.8 Hz, OH), 2.18 (s, 3H), 1.93 (s, 3H), 1.85 (s, 3H), 1.24 (s, 3H), 1.16 (d, *J* = 1.5 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 207.85, 192.58 (d, *J* = 15.5 Hz), 169.54, 165.69, 159.06, 139.34, 134.16 (d, *J* = 1.1 Hz), 134.00, 130.09, 129.23, 128.94, 126.59, 87.99 (d, *J* = 188.1 Hz, C−F), 81.05, 80.84, 76.27 (d, *J* = 14.7 Hz), 76.22, 72.65 (d, *J* = 2.0 Hz), 59.13, 47.47, 43.54, 40.32, 32.90, 22.08, 21.48, 21.07, 13.74 ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{31}FO_8$ $[M + H^+]$ 527.2076, found 527.2092.



(*2aR,4R,4aR,6S,11S,12S,12aR,12bS*)-12b-Acetoxy-4,6-difluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**13**): Compound **13** was obtained in 17% yield (3.0 mg) from 17 mg of **3a** (0.032 mmol), 0.13 mL of KHMDS (0.065 mmol, 0.5 M solution in



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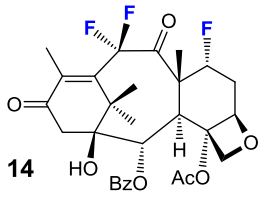
toluene), and 114 mg of Selectfluor® (0.322 mmol) (procedure B). In some cases product **11** was also observed in small amounts (≤ 5%). **13**: R_f = 0.49 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{23}$ = −58.8 (*c* = 0.405 in $CHCl_3$); IR (film) ν_{max} = 3681, 3483, 2923, 1722, 1671, 1453, 1370, 1269, 1234, 1178, 1152, 1105, 1058, 1033, 988, 946, 912, 830, 731, 712 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 7.7 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 5.81 (dd, *J* = 6.9, 1.1 Hz, 1H), 5.66 (dd, *J* = 47.2, 1.7 Hz, 1H−CF), 5.02 (dd, *J* = 8.8, 2.2 Hz, 1H), 4.72 (ddd, *J* = 46.3, 4.8, 1.6 Hz, 1H−CF), 4.51 (d, *J* = 6.8 Hz, 1H), 4.39 (d, *J* = 8.6 Hz, 1H), 4.26 (d, *J* = 8.6 Hz, 1H), 3.11 (d, *J* = 19.6 Hz, 1H), 2.69 (dd, *J* = 19.6, 1.1 Hz, 1H), 2.60 (dddd, *J* = 22.5, 16.7, 8.8, 1.9 Hz, 1H), 2.27−2.16 (dddd, *J* = 44.8, 16.7, 4.8, 2.4 Hz, 1H) overlaps with 2.21 (s, 3H), 2.07 (d, *J* = 4.9 Hz, 3H), 1.92 (s, OH), 1.71 (s, 3H), 1.27 (s, 3H), 1.14 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 205.53 (d, *J* = 16.3 Hz), 197.38, 168.93, 167.02, 149.74 (d, *J* = 11.7 Hz), 136.02 (d, *J* = 1.4 Hz), 134.31, 130.25, 129.02, 128.87, 95.51 (d, *J* = 180.6 Hz, C−F), 94.23 (d, *J* = 200.1 Hz, C−F), 81.83, 80.66, 78.05 (d, *J* = 1.1 Hz), 77.59, 73.21, 60.61 (d, *J* = 19.1 Hz), 42.98, 41.61 (d, *J* = 5.1 Hz), 39.01 (d, *J* = 2.6 Hz), 34.03 (d, *J* = 23.6 Hz), 31.75, 21.84, 19.63, 15.77 (d, *J* = 6.8 Hz), 12.41 (dd, *J* = 13.7, 5.7 Hz) ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{32}F_2O_8$ [M + H^+] 547.2139, found 547.2139.

(*2aR,4R,4aR,11S,12S,12aR,12bS*)-12b-Acetoxy-4,6,6-trifluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**14**): Compound **14** was obtained in



14

97% yield (3.0 mg) from 3.0 mg of **13** (0.0055 mmol), 0.03 mL of KHMDS (0.015 mmol, 0.5 M solution in toluene), and 12 mg of Selectfluor® (0.034 mmol) (procedure B). **14**: R_f = 0.55 (silica gel, EtOAc/hexanes 1:1); mp = 229–230 ºC (CH_3Cl/hexanes/EtOAc 10:5:1); $[\alpha]_D^{30}$ = −15.5 (*c* =

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0.067 in $CHCl_3$); IR (film) ν_{max} = 3447, 2919, 2851, 1726, 1682, 1452, 1371, 1270, 1232, 1095, 1068, 1043, 983, 928, 905, 736, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.8 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 5.83 (d, *J* = 7.0 Hz, 1H), 5.00 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.71 (ddd, *J* = 46.3, 3.4, 3.4 Hz, 1H−CF), 4.40 (d, *J* = 8.7 Hz, 1H), 4.34 (d, *J* = 8.7 Hz, 1H), 4.26 (d, *J* = 7.0 Hz, 1H), 3.12 (d, *J* = 19.9 Hz, 1H), 2.73 (d, *J* = 19.9 Hz, 1H), 2.64 (dddd, *J* = 19.3, 16.6, 8.9, 2.6 Hz, 1H), 2.28−2.16 (dddd, *J* = 46.3, 16.6, 3.7, 3.7 Hz, 1H) overlaps with 2.20 (s, 3H), 2.13 (dd, *J* = 7.7, 5.1 Hz, 3H), 1.93 (s, OH), 1.76 (s, 3H), 1.25 (s, 3H), 1.18 (d, *J* = 4.5 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 200.78 (t, *J* = 26.4 Hz), 197.70 (d, *J* = 1.1 Hz), 169.02, 167.02, 147.20 (m), 140.08 (dd, *J* = 7.1, 1.2 Hz), 134.39, 130.25, 129.06, 128.79, 95.16 (d, *J* = 182.4 Hz, C−F), 81.73, 81.09, 78.16, 77.93, 73.08, 58.75 (d, *J* = 18.6 Hz), 42.77, 40.98 (dd, *J* = 4.6, 1.1 Hz), 39.48 (d, *J* = 2.4 Hz), 33.91 (d, *J* = 23.1 Hz), 32.00 (d, *J* = 1.1 Hz), 21.89, 19.33 (d, *J* = 9.4 Hz), 16.51 (d, *J* = 6.3 Hz), 12.97 (m) and (CF_2 carbon was not observed) ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{31}F_3O_8$ [M + Na^+] 587.1863, found 587.1853.

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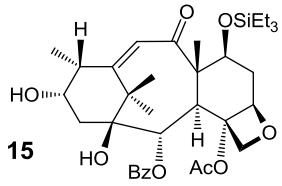
Reduction of diketones 2a, 2b, 3a, 3b, 4a, 9, 13, and 14. Synthesis of compounds 15−17, 18a−21a, 18b−21b, 22−36.

General reduction procedure A: Intermediate (**2a**, **2b**, **3a**, **3a:4a** mixture, **3b**, **8**, **13** and **14**) (4–137 mg, 0.007–0.250 mmol, 1.0 equiv) was dissolved in THF/MeOH mixture (0.5–3 mL total, 1:2) and the resulting solution was cooled to 0 ºC. Then $NaBH_4$ (from 2.5 equiv to large excess, mentioned below) was added and the solution turned into a slurry gel. After the reaction was complete (monitor by TLC, 0.5–3 h) it was quenched with sat. aq. NH_4Cl (3 mL), and the biphasic mixture was extracted with CH_2Cl_2 (or EtOAc to prevent the formation of emulsion) (2 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (silica gel, EtOAc/hexanes 1:1 or 1:2) or PTLC (silica gel, EtOAc/hexanes 1:1 or 1:2) yielded pure products. NOTE: *Luche* reduction ($NaBH_4$, $CeCl_3$•$7H_2O$) produced similar results.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (15): Compound **15** was obtained

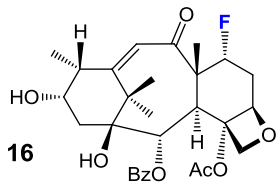


15

in 94% yield (47 mg) from 50 mg of **2a** (0.078 mmol) and 7.4 mg of $NaBH_4$ (0.195 mmol) (procedure A). **15**: R_f = 0.28 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −39.6 (*c* = 1.49 in CH_2Cl_2); IR (film) ν_{max} = 3464, 2954, 2877, 1707, 1451, 1362, 1272, 1248, 1178, 1106, 1068, 988, 874, 829, 731, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 5.76 (s, 1H), 5.70 (d, *J* = 8.0 Hz, 1H), 5.04 (d, *J* = 9.6 Hz, 1H), 4.30 (d, *J* = 8.0 Hz, 1H), 4.27 (d, *J* = 8.2 Hz, 1H), 4.21 (m, 2H), 4.08 (m, 1H), 3.04 (m, 1H), 2.45 (ddd, *J* = 14.3, 9.5, 6.8 Hz, 1H), 2.33 (d, *J* = 16.0 Hz, 1H), 2.21 (s, 3H), 1.87 (ddd, *J* = 14.2, 10.6, 1.9 Hz, 1H)

overlaps with 1.84 (m, 1H), 1.78 (d, *J* = 17.1 Hz, 1H) overlaps with 1.76 (m, 1H), 1.70 (s, 3H), 1.20 (s, 3H), 1.19 (s, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.60−0.53 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 209.24, 170.29, 167.91, 146.20, 133.64, 130.31, 129.84, 128.65, 122.28, 84.38, 84.11, 80.27, 76.19, 74.06, 71.29, 70.77, 58.76, 45.94, 44.51, 37.29, 37.01, 35.83, 26.87, 25.00, 22.74, 12.31, 8.81, 7.04, 5.36 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{50}O_9Si$ [M + H^+] 643.3297, found 643.3315.

(*2aR,4R,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-4-fluoro-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**16**): Compound **16** was obtained in



16

66% yield (38 mg) from 58 mg of **3a:4a** mixture (0.110 mmol) and 12 mg of $NaBH_4$ (0.316 mmol) together with **17** (30%, 17 mg) (procedure A). **16**: R_f = 0.41 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −93.0 (*c* = 1.14 in $CHCl_3$); IR (film) ν_{max} = 3473, 2942, 1698, 1451, 1362, 1315, 1248, 1181, 1111, 1094, 1067, 1043, 1026, 989, 947, 911, 871, 830, 795, 729, 710 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.8 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 5.76 (d, *J* = 8.2 Hz, 1H), 5.58 (d, *J* = 7.1 Hz, 1H), 5.14 (d, *J* = 8.3 Hz, 1H), 4.66 (dd, *J* = 46.5, 5.7 Hz, 1H−CF), 4.58 (d, *J* = 8.2 Hz, 1H), 4.31 (d, *J* = 8.0 Hz, 1H), 4.26 (d, *J* = 8.0 Hz, 1H), 4.06 (m, 1H), 2.98 (m, 1H), 2.52 (ddd, *J* = 27.2, 16.9, 8.5 Hz, 1H), 2.40 (d, *J* = 16.2 Hz, 1H), 2.28−2.17 (ddd, *J* = 43.3, 16.9, 5.9 Hz, 1H) overlaps with 2.22 (s, 3H), 1.81 (m, 3H), 1.76 (s, 3H), 1.18 (s, 3H), 1.14 (s, 3H), 1.03 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.81, 169.21, 167.96, 145.23 (d, *J* = 1.7 Hz), 133.69, 130.32, 129.88, 128.68, 123.99 (d, *J* = 6.3 Hz), 96.20 (d, *J* = 178.5 Hz, C−F), 84.09, 82.18, 80.14, 76.43, 74.19, 71.04, 57.31 (d, *J* = 17.8 Hz), 43.98, 39.26,

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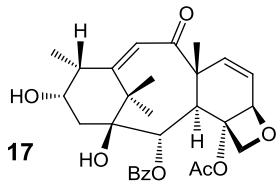
37.31, 36.01, 33.83 (d, *J* = 24.5 Hz), 26.46, 24.86, 22.47, 12.95 (d, *J* = 7.4 Hz), 12.41 ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{35}FO_8$ [M + H^+] 531.2389, found 531.2394.

(*2aR,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,4a,5,8,9,10,11,12,12a,12b-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**17**): Compound **17** was obtained in 30% yield (17 mg) from 58 mg of



17

3a:**4a** mixture (ca. 2:1) and 12 mg of $NaBH_4$ (0.316 mmol) together with **15** (66%, 38 mg) (procedure A). **17**: R_f = 0.31 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −129.6 (*c* = 1.12 in $CHCl_3$); IR (film) ν_{max} = 3463, 2975, 1717, 1699, 1451, 1357, 1316, 1251, 1177, 1150, 1112, 1091, 1067, 1026, 987, 917, 826, 805, 730, 711, 646 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.8 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 6.04 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.92 (d, *J* = 9.8 Hz, 1H), 5.88 (dd, *J* = 7.6, 1.0 Hz, 1H), 5.54 (s, 1H), 5.27 (d, *J* = 5.7 Hz, 1H), 4.38 (m, 2H), 4.28 (dd, *J* = 7.8, 1.0 Hz, 1H), 4.07 (m, 1H), 3.03 (m, 1H), 2.37 (d, *J* = 15.9 Hz, 1H), 2.21 (s, 3H), 1.93 (s, 3H), 1.88−1.84 (m, 1H) overlaps with 1.87 (s, 1H), 1.76 (t, *J* = 2.2 Hz, 1H), 1.20 (s, 3H), 1.18 (s, 3H), 1.01 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 214.50, 169.48, 167.81, 147.56, 142.12, 133.70, 130.30, 129.82, 128.66, 126.34, 121.51, 83.18, 81.10, 80.84, 75.84, 74.44, 70.71, 57.41, 44.52, 42.42, 37.53, 36.12, 26.61, 24.59, 22.90, 20.51, 12.37 ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{34}O_8$ [M + H^+] 511.2326, found 511.2324.

General coupling procedure B1: Alcohol (**15**−**17**, **24**, **25**) (11.8–26.2 mg, 0.022–0.041 mmol, 1.0 equiv) was dissolved in a flask containing anhydrous THF (0.75–1.5 mL) and dry (*3R,4S*)-3-triethylsilanyloxy-4-phenyl-*N*-Boc-2-azetidinone (**V**) (54–74 mg, 0.149–0.205 mmol, 5−10 equiv total), 4 Å granular molecular sieves (MS) were added and the resulting solution was cooled to 0 ºC. When NaHMDS (0.1–0.17 mL, 0.060–0.102 mmol, 0.6 M solution in toluene,

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2.5 equiv) was added dropwise over a period of 5−10 min the solution turned yellow. Sometimes excess of **V** was added until the reaction was complete or no further changes by TLC were observed. After 0.5 h the reaction was quenched with sat. aq. NH_4Cl (3 mL), and the resulting biphasic mixture was extracted with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. PTLC (silica gel, EtOAc/hexanes 1:1 or 1:2) yielded pure products. NOTE: Other side-products were also observed (optimized procedures for their formation are listed below, see **B2** and **B3**).

General coupling-deacetylation procedure B2: Alcohol (**15**, **16**) (12.3–23 mg, 0.019–0.043 mmol, 1.0 equiv) was dissolved in a flask containing dry THF (0.75–1.5 mL). The solution was cooled to −78 ºC and NaHMDS (0.10–0.14 mL, 0.060–0.084 mmol, 0.6 M solution in toluene, 2.0−3.0 equiv) was added dropwise. The resulting mixture turned yellow and then it was stirred for 0.5 h. The solution was allowed to reach 0 ºC and after 10 min (*3R,4S*)-3-triethylsilanyloxy-4-phenyl-*N*-Boc-2-azetidinone (**V**) (28–40 mg, 0.077–0.110 mmol, 5−8 equiv total) was added in two portions (add excess if needed in 0.75 mL of THF). When the reaction was complete (as monitored by TLC) it was quenched with sat. aq. NH_4Cl (3 mL), and the resulting biphasic mixture extracted with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. PTLC (silica gel, EtOAc/hexanes 1:2) yielded pure products.

General side-coupling procedure B3: Alcohol (**15**, **16**) (13.7–40 mg, 0.021–0.075 mmol, 1.0 equiv) was dissolved in a round bottom flask containing dry THF (0.75–1.5 mL). The solution was cooled to −78 ºC and NaHMDS (0.11–0.276 mL, 0.066–0.166 mL, 0.6 M solution in toluene, 2.0−3.0 equiv) was added dropwise. The resulting mixture turned yellow and then was stirred for 1 h. (*3R,4S*)-3-Triethylsilanyloxy-4-phenyl-*N*-Boc-2-azetidinone (**V**) (39–136 mg,

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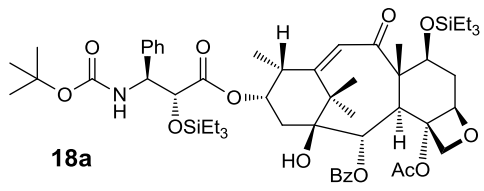
0.108–0.376 mmol, 5−10 equiv total) was added in two portions at −78 ºC, and the mixture was stirred for 0.5 h at −78 ºC and for 0.5 h at 0 ºC. Excess of **V** was added until the reaction was either complete or no obvious changes were observed (by TLC). The yellow solution was quenched with sat. aq. NH_4Cl (3 mL), and the resulting biphasic mixture extracted with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. PTLC (silica gel, EtOAc/hexanes 1:2) yielded pure products.

General deprotection procedure C: The silylated coupling product (**18a**, **18b**, **20a**, **20b**, **22**, **26**, **28**) was dissolved in THF/MeOH mixture (0.5–3 mL total, 1:2) and the solution was cooled to 0 ºC and "titrated" with 0.1 mL aliquots of HCl (1.0 M) until most of the starting material was consumed and fully deprotected product was formed (as seen by TLC, 1–3 h). The reaction mixture was quenched with sat. aq. $NaHCO_3$ (3 mL), diluted with water (1–2 mL) and the mixture extracted with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. PTLC (silica gel, EtOAc/hexanes either 1:1 and 1:2, or EtOAc/benzene 1:5) yielded pure products.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-3-phenyl-2-((triethylsilyl)oxy)propanoyl)oxy)-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (18a):

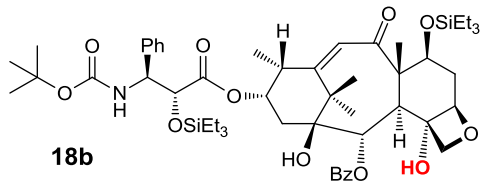


18a

Compound **18a** was obtained in 53% yield (17.6 mg) from 20.8 mg of **15** (0.032 mmol), 0.14 mL of NaHMDS (0.084 mmol, 0.6 M solution in toluene), and 70 mg of **V** (0.194 mmol) (procedure B1). NOTE: Yields for the formation of **18a** varied and rarely exceeded 30%. **18a**: R_f = 0.67 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −45.7 (*c* = 0.457 in

$CHCl_3$); IR (film) ν_{max} = 3450, 2956, 2878, 1755, 1713, 1493, 1454, 1367, 1276, 1246, 1164, 1108, 1062, 1032, 991, 945, 859, 829, 743, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.27 (m, 3H) overlaps with 7.26 ($CDCl_3$), 5.91 (s, 1H) overlaps with 5.89 (m, 1H), 5.79 (d, *J* = 7.6 Hz, 1H), 5.47 (d, *J* = 9.8 Hz, 1H), 5.29 (d, *J* = 9.8 Hz, 1H), 4.97 (dd, *J* = 9.7, 2.2 Hz, 1H), 4.48 (s, 1H), 4.31−4.24 (m, 3H), 3.67 (d, *J* = 7.5 Hz, 1H), 3.33 (m, 1H), 2.50−2.43 (m, 1H) overlaps with 2.48 (s, 3H), 2.04−1.90 (m, 3H), 1.69 (s, 3H), 1.29 (s, 3H), 1.25 (s, 1H), 1.22 (s, 3H), 1.19 (s, 9H), 0.98 (t, *J* = 7.9 Hz, 9H) overlaps with 0.97 (m, 3H), 0.74 (t, *J* = 7.9 Hz, 9H), 0.61−0.55 (m, 6H), 0.43−0.26 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 208.07, 171.02, 170.97, 167.22, 155.06, 149.94, 139.48, 133.57, 130.35, 129.43, 128.80, 128.61, 127.67, 126.44, 122.56, 84.60, 80.77, 79.82, 79.12, 76.31, 75.75, 75.71, 71.25, 70.53, 58.21, 57.03, 47.44, 43.95, 37.14, 36.21, 35.49, 28.19, 27.75, 26.42, 22.24, 12.31, 9.37, 7.00, 6.63, 5.30, 4.36 ppm; HRMS (ESI-TOF): calcd for $C_{55}H_{81}NO_{13}Si_2$ [M + H^+] 1020.5319, found 1020.5306.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-9-(((*2R,3S*)-3-((tert-Butoxycarbonyl)amino)-3-phenyl-2-((triethylsilyl)oxy)propanoyl)oxy)-11,12b-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**18b**): Compound **18b** was obtained



18b

in 60% yield (11.3 mg) from 12.3 mg of **15** (0.019 mmol), 0.1 mL of NaHMDS (0.060 mmol, 0.6 M solution in toluene), and 28 mg of **V** (0.077 mmol) (procedure B2). **18b**: R_f = 0.57 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −58.8 (*c* = 1.06 in $CHCl_3$); IR (film) ν_{max} = 3580, 3439, 2955, 2915, 2878, 1753, 1708, 1496, 1452, 1366, 1246, 1161, 1120, 1094, 1071, 1006, 975, 918, 881, 859, 831, 730, 712 cm^{-1}; ^1H NMR (600 MHz,

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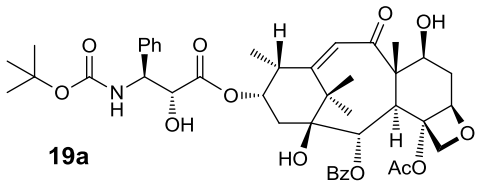
$CDCl_3$): δ = 8.14 (d, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.30−7.25 (m, 3H) overlaps with 7.26 ($CDCl_3$), 6.29 (dd, *J* = 10.6, 1.7 Hz, 1H), 5.91 (d, *J* = 8.2 Hz, 1H), 5.86 (s, 1H), 5.81 (dd, *J* = 7.9, 5.6 Hz, 1H), 5.57 (d, *J* = 10.6 Hz, 1H), 4.95 (dd, *J* = 9.7, 2.9 Hz, 1H), 4.41 (d, *J* = 2.0 Hz, 1H), 4.32 (d, *J* = 7.6 Hz, 1H), 4.31 (s, 1H), 4.06 (d, *J* = 7.6 Hz, 1H), 3.97 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.41 (d, *J* = 8.1 Hz, 1H), 3.25 (m, 1H), 2.79 (d, *J* = 17.4 Hz, 1H), 2.48 (ddd, *J* = 14.7, 9.8, 6.4 Hz, 1H), 2.12−2.05 (m, 2H), 1.75 (s, OH), 1.73 (s, 3H), 1.49 (s, 9H), 1.26 (s, 3H), 1.23 (s, 3H), 0.99−0.95 (m, 12H), 0.74 (t, *J* = 8.0 Hz, 9H), 0.63−0.57 (q, *J* = 7.8 Hz, 6H), 0.38−0.21 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 208.65, 171.27, 167.57, 156.00, 147.70, 139.51, 133.82, 130.20, 129.17, 128.99, 128.34, 127.51, 126.62, 121.70, 85.58, 83.16, 80.29, 79.83, 75.68, 74.61, 74.37, 72.69, 72.64, 59.04, 55.26, 51.44, 44.20, 37.29, 35.77, 34.61, 28.50, 27.38, 24.66, 12.45, 8.71, 7.03, 6.61, 5.36, 4.26 ppm; HRMS (ESI-TOF): calcd for $C_{53}H_{79}NO_{12}Si_2$ [M + H^+] 978.5213, found 978.5212.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**19a**): Compound **19a** was obtained in

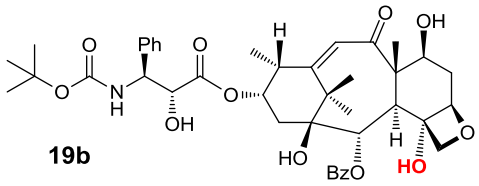


19a

83% yield (14 mg) from 21.8 mg of **18a** (0.021 mmol) (procedure C). **19a**: R_f = 0.28 (silica gel, EtOAc/hexanes 1:1); mp = 178–181 ºC (CH_3CN); $[\alpha]_D^{30}$ = −95.3 (*c* = 0.723 in $CHCl_3$); IR (film) ν_{max} = 3442, 2933, 1707, 1496, 1452, 1367, 1246, 1168, 1108, 1066, 1026, 987, 915, 732, 712 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.40−7.36 (m, 4H), 7.30 (m, 1H), 5.86 (m, 2H) overlaps with 5.85 (d, *J* = 7.8 Hz, 1H), 5.43 (d, *J* = 9.8 Hz, 1H), 5.30 (d, *J* = 9.7 Hz, 1H), 4.97

(dd, *J* = 9.4, 2.4 Hz, 1H), 4.56 (s, 1H), 4.32 (d, *J* = 8.4 Hz, 1H), 4.27 (d, *J* = 8.4 Hz, 1H), 3.94 (dd, *J* = 10.5, 7.0 Hz, 1H), 3.65 (d, *J* = 7.4 Hz, 1H), 3.45 (br s, 1H), 3.28 (m, 1H), 2.62 (ddd, *J* = 14.7, 9.4, 7.0 Hz, 1H), 2.38 (s, 3H), 2.10 (br s, OH), 2.09−1.99 (m, 2H), 1.90 (ddd, *J* = 14.7, 10.9, 2.6 Hz, 1H), 1.73 (s, 3H) overlaps with 1.71 (br s, OH), 1.28 (s, 3H), 1.26 (s, 9H), 1.23 (s, 3H), 0.93 (d, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.66, 172.68, 170.98, 167.31, 155.10, 150.35, 139.23, 133.81, 130.31, 129.29, 128.87, 128.85, 127.95, 126.72, 121.40, 84.05, 81.11, 80.01, 79.87, 76.12, 75.14, 74.19, 72.89, 69.14, 58.59, 55.91, 46.32, 43.86, 35.93, 35.68, 35.53, 28.29, 27.63, 26.02, 22.13, 12.39, 9.66 ppm; HRMS (ESI-TOF): calcd for $C_{43}H_{53}NO_{13}$ [M + H^+] 792.3589, found 792.3587.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-9-(((*2R,3S*)-3-((tert-Butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4,11,12b-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**19b**): Compound **19b** was obtained in 89% yield (18 mg) from 26.3 mg



19b

of **18b** (0.027 mmol) (procedure C). **19b**: R_f = 0.22 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −107.1 (*c* = 1.589 in $CHCl_3$); IR (film) ν_{max} = 3435, 2978, 1695, 1495, 1451, 1367, 1315, 1273, 1166, 1110, 1069, 1050, 1026, 974, 911, 875, 731, 713 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.39−7.33 (m, 4H), 7.29 (t, *J* = 7.0 Hz, 1H), 5.90 (d, *J* = 7.8 Hz, 1H), 5.74 (s, 1H), 5.62 (m, 2H), 5.31 (d, *J* = 8.8 Hz, 1H), 4.86 (br s, 1H), 4.74 (dd, *J* = 9.5, 4.1 Hz, 1H), 4.66 (s, 1H), 4.45 (d, *J* = 7.9 Hz, 1H), 4.00 (d, *J* = 7.9 Hz, 1H), 3.85 (s, 1H), 3.74 (d, *J* = 7.7 Hz, 1H), 3.69 (dd, *J* = 11.0, 5.9 Hz, 1H), 3.18 (m, 1H), 2.58 (m, 1H), 2.46 (d, *J* = 16.9 Hz, 1H), 2.20−2.09 (m, 2H), 1.98 (m, 1H), 1.73 (s, OH), 1.68 (s, 3H), 1.42 (s, 9H), 1.23 (s, 3H), 1.22 (s, 3H), 0.84 (d, *J* = 6.7 Hz, 3H)

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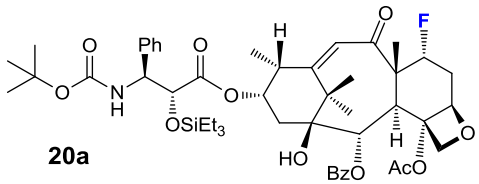
ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.18, 171.97, 166.90, 155.46, 148.43, 139.13, 134.18, 129.84, 129.19, 129.10, 128.72, 128.00, 126.87, 121.04, 85.35, 82.58, 80.52, 79.77, 75.45, 75.08, 74.48, 73.59, 69.66, 58.96, 56.37, 48.17, 44.26, 36.01, 35.46, 35.42, 28.51, 26.78, 24.92, 12.44, 9.16 ppm; HRMS (ESI-TOF): calcd for $C_{41}H_{51}NO_{12}$ [M + Na^+] 772.3303, found 772.3293.

(*2aR,4R,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-3-phenyl-2-((triethylsilyl)oxy)propanoyl)oxy)-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**20a**): Compound **20a** was obtained in



20a

53% yield (10.8 mg) from 11.8 mg of **16** (0.022 mmol), 0.1 mL of NaHMDS (0.060 mmol, 0.6 M solution in toluene), and 54 mg of **V** (0.149 mmol) (procedure B1). **20a**: R_f = 0.48 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −80.5 (*c* = 1.96 in $CHCl_3$); IR (film) ν_{max} = 3448, 2956, 2878, 1743, 1715, 1494, 1453, 1367, 1274, 1243, 1162, 1122, 1065, 1027, 979, 946, 846, 736, 711 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 7.6 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.28−7.26 (m, 3H) overlaps with 7.26 ($CDCl_3$), 5.90−5.85 (m, 1H) overlaps with 5.86 (d, *J* = 7.7 Hz, 1H), 5.71 (dd, *J* = 7.0, 1.7 Hz, 1H), 5.48 (d, *J* = 9.7 Hz, 1H), 5.30 (d, *J* = 9.8 Hz, 1H), 5.06 (d, *J* = 8.6 Hz, 1H), 4.69 (dd, *J* = 46.0, 5.0 Hz, 1H−CF), 4.45 (s, 1H), 4.36−4.32 (m, 2H), 3.91 (d, *J* = 7.7 Hz, 1H), 3.32 (m, 1H), 2.60 (dddd, *J* = 24.8, 16.9, 8.8, 1.0 Hz, 1H), 2.45 (s, 3H), 2.35−2.23 (dddd, *J* = 45.6, 16.9, 5.2, 2.1 Hz, 1H), 2.19−2.12 (m, 1H), 1.96 (dd, *J* = 15.2, 5.7 Hz, 1H), 1.77 (s, 3H), 1.28 (s, 3H), 1.25 (br s, OH), 1.20 (s, 9H), 1.17 (s, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.74 (t, *J* = 7.9 Hz, 9H), 0.41−0.24 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.90, 170.89, 169.89, 167.26, 155.09, 148.59 (d, *J* = 1.4 Hz), 139.50, 133.65, 130.37, 129.42, 128.85, 128.61, 127.64, 126.45,

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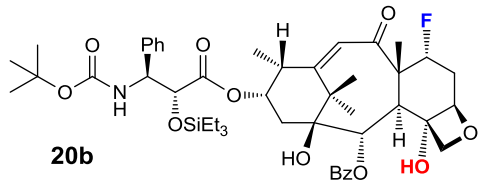
124.61 (d, *J* = 6.3 Hz), 95.99 (d, *J* = 178.5 Hz, C−F), 82.34, 80.94, 79.73, 79.01, 76.68, 75.78, 75.72, 70.93, 57.10, 56.47 (d, *J* = 17.7 Hz), 43.20, 41.06, 35.86, 35.81, 33.97 (d, *J* = 24.0 Hz), 28.21, 27.57, 26.02, 22.08, 14.39 (d, *J* = 6.8 Hz), 12.21, 6.62, 4.35 ppm; HRMS (ESI-TOF): calcd for $C_{49}H_{66}FNO_{12}Si$ [M + H^+] 908.4411, found 908.4411.

(*2aR,4R,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-9-(((*2R,3S*)-3-((tert-Butoxycarbonyl)amino)-3-phenyl-2-((triethylsilyl)oxy)propanoyl)oxy)-4-fluoro-11,12b-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**20b**): Compound **20b** was obtained



20b

in 52% yield (19.4 mg) from 23 mg of **16** (0.043 mmol), 0.14 mL of NaHMDS (0.084 mmol, 0.6 M solution in toluene), and 40 mg of **V** (0.110 mmol) (procedure B2). All attempts to purify **20b** were unsuccessful; therefore it was used without further purification. **20b**: R_f = 0.43 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −92.8 (*c* = 1.675 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.8 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.32−7.28 (m, 4H), 7.22 (m, 1H), 6.39 (d, *J* = 10.8 Hz, 1H), 5.94 (d, *J* = 8.8 Hz, 1H), 5.73 (dd, *J* = 7.0, 4.9 Hz, 1H), 5.68 (d, *J* = 5.8 Hz, 1H), 5.55 (d, *J* = 10.8 Hz, 1H), 4.98 (d, *J* = 8.7 Hz, 1H), 4.79 (dd, *J* = 3.0, 46.9 Hz, 1H−CF), 4.52 (s, 1H), 4.40 (m, 2H), 4.12 (d, *J* = 7.6 Hz, 1H), 3.97 (d, *J* = 8.8 Hz, 1H), 3.18 (m, 1H), 2.86 (d, *J* = 17.2 Hz, 1H), 2.57 (m, 1H), 2.38−2.26 (m, 1H), 2.02 (dd, *J* = 17.2, 7.4 Hz, 1H), 1.82 (s, 1H), 1.78 (s, 3H), 1.50 (s, 9H), 1.23 (s, 3H), 1.20 (s, 3H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.71 (t, *J* = 8.1 Hz, 9H), 0.33−0.17 (m, 6H) ppm;

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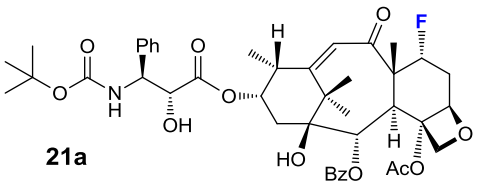
(*2aR,4R,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**21a**): Compound **21a** was obtained in



21a

96% yield (14.8 mg) from 17.7 mg of **20a** (0.0195 mmol) (procedure C). **21a**: R_f = 0.25 (silica gel, EtOAc/hexanes 1:2); mp = 233–235 °C (CH_3CN/hexanes/EtOH 10:2:5); $[\alpha]_D^{30}$ = −99.2 (*c* = 1.48 in $CHCl_3$); IR (film) ν_{max} = 3564, 3448, 2975, 2932, 1716, 1702, 1496, 1452, 1367, 1257, 1164, 1108, 1069, 1044, 1027, 991, 912, 840, 731, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.7 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.27 (m, 1H) overlaps with 7.26 ($CDCl_3$), 5.86 (d, *J* = 8.2 Hz, 1H), 5.80 (d, *J* = 6.7 Hz, 1H), 5.65 (d, *J* = 9.7 Hz, 1H), 5.59 (m, 1H), 5.36 (d, *J* = 9.6 Hz, 1H), 5.03 (d, *J* = 8.3 Hz, 1H), 4.75 (dd, *J* = 46.9, 5.5 Hz, 1H−CF), 4.64 (dd, *J* = 3.6, 2.1 Hz, 1H), 4.35 (d, *J* = 8.4 Hz, 1H), 4.29 (d, *J* = 8.4 Hz, 1H), 3.72 (d, *J* = 8.0 Hz, 1H), 3.68 (m, 1H), 3.12 (m, 1H), 2.52 (ddd, *J* = 27.2, 17.1, 8.5 Hz, 1H), 2.33−2.28 (m, 1H), 2.23 (s, 3H) overlaps with 2.23 (m, 1H), 2.12 (dd, *J* = 16.9, 7.1 Hz, 1H), 1.81 (s, 3H), 1.80 (s, OH), 1.36 (s, 9H), 1.22 (s, 3H), 1.18 (s, 3H), 0.93 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.40, 173.21, 170.09, 167.64, 154.98, 146.39, 140.32, 133.93, 130.18, 129.43, 128.79, 128.58, 127.58, 127.01, 123.77 (d, *J* = 5.2 Hz), 96.92 (d, *J* = 176.0 Hz, C−F), 82.60, 81.76, 81.35, 79.59, 76.15, 75.06, 74.66, 73.79, 57.66 (d, *J* = 17.5 Hz), 55.79, 43.46, 40.14, 36.09, 35.67, 33.85 (d, *J* = 23.8 Hz), 28.47, 27.51, 24.86, 21.84, 13.34 (d, *J* = 7.3 Hz), 12.61 ppm; HRMS (ESI-TOF): calcd for $C_{43}H_{52}FNO_{12}$ [M + H^+] 794.3546, found 794.3548.

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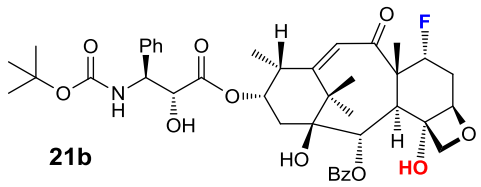
(*2aR,4R,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-9-(((*2R,3S*)-3-((tert-Butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4-fluoro-11,12b-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**21b**): Compound **21b** was obtained in 73% yield (13.5 mg) from 19.4 mg of **20b** (0.024 mmol) (procedure C). **21b**: R_f = 0.14 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −110.2 (*c* = 1.25 in $CHCl_3$); IR (film) ν_{max} = 3422, 2977, 1698, 1497, 1451, 1366, 1271, 1164, 1108, 1069, 1027, 973, 908, 869, 844, 813, 728, 712, 700 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.37 (m, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.26 (m, 1H) overlaps with 7.26 ($CDCl_3$), 5.87 (d, *J* = 8.3 Hz, 1H), 5.76 (dd, *J* = 9.5, 3.1 Hz, 1H), 5.70 (d, *J* = 6.0 Hz, 1H), 5.65 (dd, *J* = 6.3, 4.7 Hz, 1H), 5.59 (d, *J* = 9.5 Hz, 1H), 4.77 (m, 1H) overlaps with 4.74 (ddd, *J* = 46.4, 2.8, 2.8 Hz, 1H−CF), 4.62 (d, *J* = 1.5 Hz, 1H), 4.46 (d, *J* = 7.9 Hz, 1H), 4.16 (br s, 1H), 4.07 (d, *J* = 7.9 Hz, 1H) overlaps with 4.03 (br s, 1H), 3.96 (d, *J* = 8.3 Hz, 1H), 3.17 (m, 1H), 2.67 (d, *J* = 17.0 Hz, 1H), 2.57 (dddd, *J* = 19.9, 16.5, 9.1, 2.0 Hz, 1H), 2.24 (dddd, *J* = 53.0, 16.5, 3.4, 3.4 Hz, 1H), 2.07 (dd, *J* = 17.0, 7.0 Hz, 1H), 1.83 (s, 1H), 1.69 (s, 3H), 1.43 (s, 9H), 1.22 (s, 3H), 1.18 (s, 3H), 0.93 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.52, 172.44, 167.30, 155.50, 146.26, 139.41, 134.07, 130.04, 129.18, 129.11, 128.61, 127.66, 126.65, 123.69 (d, *J* = 4.0 Hz), 98.67 (d, *J* = 174.3 Hz, C−F), 84.44, 82.99, 80.45, 79.88, 75.29, 75.01, 74.62, 74.18, 57.26 (d, *J* = 17.1 Hz), 56.01, 43.74 (d, *J* = 1.8 Hz), 43.14, 36.05, 35.01, 33.58 (d, *J* = 21.7 Hz), 28.50, 26.88, 24.55, 14.41 (d, *J* = 6.7 Hz), 12.65 ppm; HRMS (ESI-TOF): calcd for $C_{41}H_{50}FNO_{11}$ [M + H^+] 752.3440, found 752.3448.



21b

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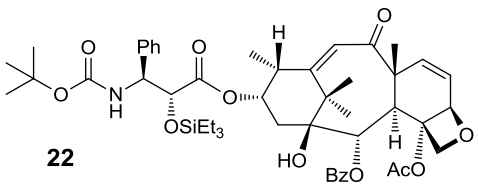
(*2aR,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-3-phenyl-2-((triethylsilyl)oxy)propanoyl)oxy)-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,4a,5,8,9,10,11,12,12a,12b-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**22**): Compound **22** was obtained in 31% yield (9.0 mg) from 16.5 mg of **17** (0.032 mmol), 0.135 mL of NaHMDS (0.081 mmol, 0.6 M solution in toluene), and 58 mg of **V** (0.160 mmol) (procedure B1).



22

22: R_f = 0.53 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −107.0 (*c* = 0.867 in $CHCl_3$); IR (film) ν_{max} = 3447, 2956, 2878, 1713, 1493, 1452, 1367, 1274, 1244, 1162, 1122, 1065, 1025, 976, 838, 733, 712 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.27 (m, 3H) overlaps with 7.26 ($CDCl_3$), 6.05 (dd, *J* = 9.9, 5.5 Hz, 1H), 5.95 (d, *J* = 7.1 Hz, 1H), 5.90 (m, 1H) overlaps with 5.88 (d, *J* = 9.9 Hz, 1H), 5.70 (d, *J* = 2.0 Hz, 1H), 5.48 (d, *J* = 9.7 Hz, 1H), 5.29 (d, *J* = 9.7 Hz, 1H), 5.09 (d, *J* = 5.5 Hz, 1H), 4.47 (s, 1H), 4.41 (d, *J* = 8.1 Hz, 1H), 4.34 (d, *J* = 8.1 Hz, 1H), 3.95 (d, *J* = 7.0 Hz, 1H), 3.34 (m, 1H), 2.48 (s, 3H), 2.09 (t, *J* = 14.1 Hz, 1H), 1.98−1.91 (m, 1H) overlaps with 1.92 (s, 3H), 1.40 (br s, 1H), 1.32 (s, 3H), 1.23 (s, 9H), 1.21 (s, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.74 (t, *J* = 8.0 Hz, 9H), 0.41−0.26 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.37, 171.02, 170.58, 166.99, 155.18, 151.16, 140.81, 139.41, 133.70, 130.33, 129.37, 128.82, 128.63, 127.68, 126.44, 125.99, 122.24, 81.57, 81.40, 79.84, 78.08, 76.36, 75.84, 75.65, 71.07, 57.09, 56.86, 43.93, 43.31, 36.31, 35.97, 28.23, 27.60, 26.02, 22.48, 21.04, 12.14, 6.62, 4.37 ppm; HRMS (ESI-TOF): calcd for $C_{49}H_{65}NO_{12}Si$ [M + H^+] 888.4349, found 888.4350.

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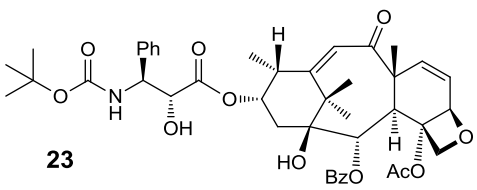
(*2aR,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,4a,5,8,9,10,11,12,12a,12b-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**23**): Compound **23** was obtained in



23

94% yield (7.1 mg) from 8.67 mg of **22** (0.0098 mmol) (procedure C). **23**: R_f = 0.20 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −107.3 (*c* = 0.710 in $CHCl_3$); IR (film) ν_{max} = 3440, 2979, 1702, 1495, 1452, 1367, 1245, 1165, 1108, 1067, 1050, 1026, 974, 914, 731, 712 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.12 (d, *J* = Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.39−7.33 (m, 4H), 7.30 (m, 1H), 6.04 (dd, *J* = 9.8, 5.6 Hz, 1H), 5.96 (d, *J* = 7.0 Hz, 1H), 5.91 (d, *J* = 9.8 Hz, 1H), 5.81 (m, 1H), 5.72 (s, 1H), 5.43 (d, *J* = 9.8 Hz, 1H), 5.26 (d, *J* = 9.5 Hz, 1H), 5.19 (d, *J* = 5.0 Hz, 1H), 4.55 (s, 1H), 4.50 (d, *J* = 8.0 Hz, 1H), 4.33 (d, *J* = 8.1 Hz, 1H), 3.84 (d, *J* = 6.5 Hz, 1H), 3.26 (m, 2H), 2.36 (s, 3H), 2.20−2.15 (m, 1H), 2.05 (dd, *J* = 15.8, 6.4 Hz, 1H), 1.93 (s, 3H), 1.76 (br s, 1H), 1.30 (s, 9H) overlaps with 1.29 (s, 3H), 1.21 (s, 3H), 0.91 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.03, 172.43, 170.32, 167.18, 155.18, 149.85, 141.17, 139.18, 133.85, 130.20, 129.36, 128.88, 128.82, 127.97, 126.73, 126.24, 122.21, 81.88, 80.94, 80.11, 79.43, 75.52, 75.47, 74.39, 73.12, 57.17, 56.06, 44.03, 43.49, 36.09, 35.94, 28.32, 27.57, 25.44, 22.41, 20.66, 12.34 ppm; HRMS (ESI-TOF): calcd for $C_{43}H_{51}NO_{12}$ $[M + H^+]$ 774.3484, found 774.3476.

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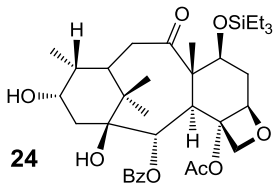
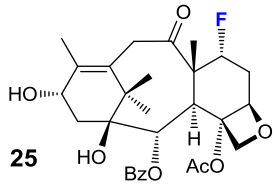
(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS*)-12b-Acetoxy-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-4-((triethylsilyl)oxy)tetradecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**24**, mixture): Reduction of enone **2b** produced a complex mixture of compounds with over-reduced alcohol **24** as a major product. Attempts to separate **24** from the reaction mixture failed and the compound was introduced into the next step without further purification. **24**: R_f = 0.53 (silica gel, EtOAc/hexanes 1:1); HRMS (ESI-TOF): calcd for $C_{35}H_{52}O_9Si$ [M + Na^+] 667.3273, found 667.3273.



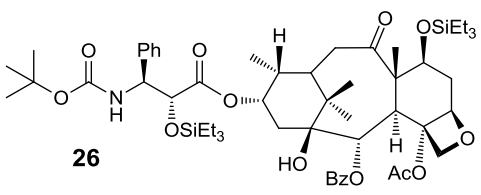
24

(*2aR,4R,4aR,9S,11S,12S,12aR,12bS*)-12b-Acetoxy-4-fluoro-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**25**, mixture): Reduction of enone **3b** produced a mixture of compounds with alcohol **25** as a major product. Multiple attempts to separate **25** from the reaction mixture failed and it was introduced into the next step without further purification. **25**: R_f = 0.36 (silica gel, EtOAc/hexanes 1:1); HRMS (ESI-TOF): calcd for $C_{29}H_{35}FO_8$ [M + H^+] 531.2389, found 531.2397.



25

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-Butoxycarbonyl)amino)-3-phenyl-2-((triethylsilyl)oxy)propanoyl)oxy)-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-((triethylsilyl)oxy)tetradecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**26**): Compound **26** was obtained in 24% yield (10 mg) from 26.2 mg of **24** (0.041 mmol, mixture obtained from **2b**), 0.17 mL of NaHMDS (0.102 mmol, 0.6 M solution in toluene), and 74 mg of **V** (0.205



26

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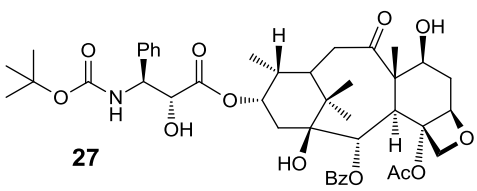
mmol) (procedure B1). **26**: R_f = 0.58 (silica gel, EtOAc/hexanes 1:2); IR (film) ν_{max} = 3447, 2956, 2878, 1753, 1713, 1493, 1454, 1366, 1268, 1245, 1162, 1110, 1069, 989, 858, 831, 742, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 7.7 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.37−7.34 (m, 4H), 7.28 (m, 1H), 5.77 (d, *J* = 8.9 Hz, 1H), 5.57 (ddd, *J* = 11.9, 9.8, 6.8 Hz, 1H), 5.50 (d, *J* = 10.0 Hz, 1H), 5.28 (dd, *J* = 9.9, 1.9 Hz, 1H), 5.00 (dd, *J* = 9.5, 1.5 Hz, 1H), 4.47 (d, *J* = 2.0 Hz, 1H), 4.34 (dd, *J* = 10.3, 6.9 Hz, 1H), 4.29 (s, 2H), 3.86 (d, *J* = 9.0 Hz, 1H), 2.95 (m, 1H), 2.76 (m, 1H), 2.53−2.47 (m, 1H), 2.42 (s, 3H), 2.36 (dd, *J* = 12.5, 15.2 Hz, 1H), 2.28−2.22 (m, 2H), 1.98 (dd, *J* = 15.6, 6.8 Hz, 1H), 1.92 (ddd, *J* = 14.5, 10.5, 2.1 Hz, 1H), 1.70 (s, 3H), 1.56 (s, OH), 1.18 (s, 9H), 1.14 (s, 3H), 1.08 (s, 3H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.84 (d, *J* = 7.3 Hz, 3H), 0.73 (t, *J* = 7.9 Hz, 9H), 0.59−0.49 (m, 6H), 0.40−0.24 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 211.91, 171.56, 171.11, 167.09, 155.10, 139.60, 133.48, 130.36, 129.52, 128.68, 128.49, 127.61, 126.75, 84.81, 80.23, 79.66, 79.05, 75.57 (2 overlapping peaks), 73.96, 69.94, 69.83, 57.29, 57.22, 46.55, 44.52, 42.44, 37.01, 36.24, 34.58, 31.81, 31.56, 28.22, 27.01, 21.99, 12.70, 9.46, 6.97, 6.62, 5.23, 4.35 ppm; HRMS (ESI-TOF): calcd for $C_{55}H_{83}NO_{13}Si_2$ [M + H^+] 1044.5295, found 1044.5234.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxotetradecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**27**): Compound **27** was obtained in 58% yield (4.5 mg) from 10 mg of **26** (0.0098



27

mmol) (procedure C). **27**: R_f = 0.22 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −125.8 (*c* = 0.065 in $CHCl_3$); IR (film) ν_{max} = 3436, 2933, 1700, 1495, 1452, 1367, 1315, 1267, 1168, 1102, 1077, 1053, 1025, 981, 914, 869, 732, 714, 701 cm^{-1}; ^1H NMR

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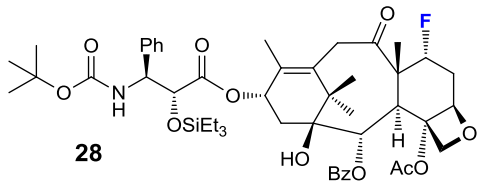
(600 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.3 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 7.3 Hz, 1H), 5.77 (d, *J* = 8.6 Hz, 1H), 5.62 (m, 2H), 5.36 (d, *J* = 9.6 Hz, 1H), 4.97 (d, *J* = 9.0 Hz, 1H), 4.57 (br s, 1H), 4.33−4.28 (m, 3H), 3.99 (dd, *J* = 10.0, 7.6 Hz, 1H), 3.58 (d, *J* = 8.5 Hz, 1H), 3.52 (dd, *J* = 12.3, 10.1 Hz, 1H), 2.61−2.53 (m, 2H), 2.41 (dd, *J* = 12.5, 10.5 Hz, 1H), 2.26 (m, 2H), 2.23 (s, 3H), 2.13 (ddd, *J* = 10.1, 10.1, 3.3 Hz, 1H), 1.83 (ddd, *J* = 14.9, 10.5, 1.7 Hz, 1H), 1.79 (s, OH), 1.72 (s, 3H), 1.65 (br s, OH), 1.38 (s, 9H), 1.11 (s, 3H), 1.10 (s, 3H), 0.89 (d, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 216.27, 172.71, 171.76, 167.54, 154.92, 140.48, 133.90, 130.15, 129.42, 128.76, 128.65, 127.71, 126.93, 83.80, 81.63, 79.75, 79.11, 75.56, 75.18, 73.39, 73.13, 69.57, 58.21, 56.32, 46.62, 43.88, 42.35, 36.06, 35.49, 34.77, 32.65, 32.31, 28.51, 25.71, 22.03, 15.11, 8.80 ppm; HRMS (ESI-TOF): calcd for $C_{43}H_{55}NO_{13}$ [M + H^+] 794.3746, found 794.3741.

(*2aR,4R,4aR,9S,11S,12S,12aR,12bS*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-3-phenyl-2-((triethylsilyl)oxy)propanoyl)oxy)-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**28**): Compound **28** was obtained



28

crude in 30% yield (6.3 mg) from 12.2 mg of **25** (0.023 mmol, mixture obtained from **3b**), 0.1 mL of NaHMDS (0.060 mmol, 0.6 M solution in toluene), and 42 mg of **V** (0.116 mmol) (procedure B1). Multiple attempts to purify **28** failed and it was introduced into the next step without further purification. **28**: R_f = 0.45 (silica gel, EtOAc/hexanes 1:2); IR (film) ν_{max} = 3451, 2956, 1745, 1717, 1493, 1453, 1367, 1271, 1242, 1164, 1121, 1069, 987, 710 cm^{-1}; HRMS (ESI-TOF): calcd for $C_{49}H_{66}FNO_{12}S$ [M + H^+] 908.4411, found 908.4411.

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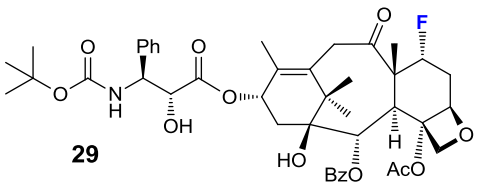
(*2aR,4R,4aR,9S,11S,12S,12aR,12bS*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**29**): Compound **29** was obtained in



29

89% yield (10.8 mg) from 13.9 mg of **28** (0.015 mmol) (procedure C). **29**: R_f = 0.47 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −72.1 (*c* = 0.315 in $CHCl_3$); IR (film) ν_{max} = 3438, 2979, 1712, 1495, 1452, 1390, 1367, 1269, 1242, 1169, 1096, 1069, 1041, 1026, 987, 911, 731, 708 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.39−7.37 (m, 4H), 7.31 (m, 1H), 6.13 (m, 1H), 5.77 (d, *J* = 7.0 Hz, 1H), 5.43 (d, *J* = 9.6 Hz, 1H), 5.29 (d, *J* = 8.8 Hz, 1H), 5.00 (d, *J* = 8.7 Hz, 1H), 4.62 (dd, *J* = 46.9, 5.1 Hz, 1H−CF) overlaps with 4.61 (br s, 1H), 4.36 (d, *J* = 8.5 Hz, 1H), 4.28 (m, 2H), 3.89 (dd, *J* = 16.8, 3.8 Hz, 1H), 3.47 (d, *J* = 16.8 Hz, 1H), 3.32 (br s, 1H), 2.52 (ddd, *J* = 25.5, 16.8, 8.8 Hz, 1H), 2.40 (m, 1H) overlaps with 2.38 (s, 3H), 2.28 (m, 1H) overlaps with 2.22 (m, 1H), 1.69 (s, OH) overlaps with 1.68 (s, 3H) overlaps with 1.67 (s, 3H), 1.36 (s, 9H), 1.18 (s, 3H), 1.10 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 211.34, 172.84, 169.36, 167.29, 155.36, 138.69, 133.83, 133.57, 132.45, 130.33, 129.44, 128.93, 128.86, 128.09, 126.87, 96.54 (d, *J* = 178.3 Hz, C−F), 82.13, 81.26, 80.20, 78.81, 77.73, 75.39, 73.78, 72.62, 58.83 (d, *J* = 18.0 Hz), 56.15, 48.39 (d, *J* = 4.6 Hz), 43.36, 39.70 (d, *J* = 2.0 Hz), 36.04, 34.15 (d, *J* = 24.0 Hz), 28.36, 24.89, 23.55, 22.69, 15.09 (d, *J* = 7.0 Hz), 14.37 (d, *J* = 3.3 Hz) ppm; HRMS (ESI-TOF): calcd for $C_{43}H_{52}FNO_{12}$ [M + H^+] 794.3546, found 794.3544.

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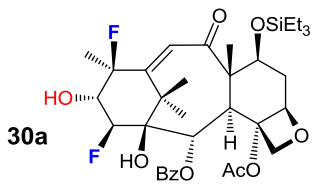
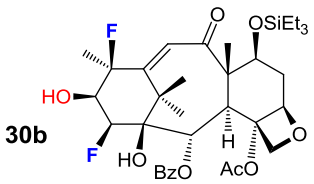
(*2aR,4S,4aS,8S,9S,10S,11S,12S,12aR,12bS,E*)-12b-Acetoxy-8,10-difluoro-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (30a):



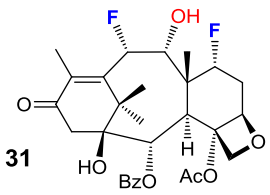
Compound **30a** was obtained in 44% yield (2.66 mg) from 6.0 mg of **8** (0.0089 mmol) and large excess of $NaBH_4$ together with **30b** (39%, 2.36 mg) (**30a**:**30b** ~ 1:2 by NMR spectroscopic analysis) (procedure A). Compounds **30a** and **30b** were separated by PTLC (silica gel, EtOAc/benzene 1:5). **30a**: R_f = 0.35 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{23}$ = −15.6 (*c* = 0.242 in $CHCl_3$); IR (film) ν_{max} = 3441, 2955, 1728, 1452, 1373, 1267, 1245, 1178, 1104, 1068, 992, 946, 903, 862, 829, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 6.29 (d, *J* = 3.7 Hz, 1H), 5.95 (dd, *J* = 7.6, 3.0 Hz, 1H), 4.96 (ddd, *J* = 22.6, 19.1, 9.2 Hz, 1H) overlaps with 4.93 (d, *J* = 9.7 Hz, 1H), 4.47 (dd, *J* = 47.8, 9.3 Hz, 1H−CF), 4.35 (dd, *J* = 8.4, 0.9 Hz, 1H), 4.27 (d, *J* = 8.5 Hz, 1H), 4.13 (dd, *J* = 11.0, 6.4 Hz, 1H), 3.31 (d, *J* = 7.6 Hz, 1H), 3.20 (br s, OH), 2.87 (d, *J* = 13.3 Hz, OH), 2.43 (ddd, *J* = 14.5, 9.7, 6.4 Hz, 1H), 2.28 (s, 3H), 1.95 (ddd, *J* = 14.2, 11.1, 3.0 Hz, 1H), 1.70 (s, 3H), 1.62 (d, *J* = 22.7 Hz, 3H), 1.34 (d, *J* = 5.5 Hz, 3H), 1.28 (s, 3H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.59−0.53 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 205.40, 170.88, 165.78, 143.39 (dd, *J* = 18.3, 1.5 Hz), 133.90, 130.26, 129.23, 129.20 (d, *J* = 5.4 Hz), 128.85, 97.44 (dd, *J* = 180.0, 9.6 Hz, C−F), 91.99 (dd, *J* = 182.3, 9.9 Hz, C−F), 84.34, 80.89, 77.16 (2 signals) overlapping with $CDCl_3$, 76.25, 74.71, 70.71, 58.45, 46.19, 42.92 (d, *J* = 1.7 Hz), 37.10, 28.04 (d, *J* = 4.6 Hz), 27.61, 21.89, 20.17 (d, *J* = 28.0 Hz), 8.89, 6.95, 5.30 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{48}F_2O_9Si$ [M + H^+] 679.3108, found 679.3119.

(*2aR,4S,4aS,8S,9R,10S,11S,12S,12aR,12bS,E*)-12b-Acetoxy-8,10-difluoro-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-4-((triethylsilyl)oxy)-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**30b**): **30b**: R_f = 0.35 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{23}$ = −27.8 (*c* = 0.235 in $CHCl_3$); IR (film) ν_{max} = 3466, 2955, 1727, 1452, 1377, 1264, 1176, 1105, 1068, 1026, 996, 826, 709 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.4 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 6.13 (d, *J* = 2.2 Hz, 1H), 6.03 (dd, *J* = 7.7, 6.7 Hz, 1H), 4.92 (dd, *J* = 48.6, 4.5 Hz, 1H−CF) overlaps with 4.92 (dd, *J* = 9.6, 2.6 Hz, 1H), 4.32 (s, 2H), 4.05 (dd, *J* = 10.9, 6.5 Hz, 1H), 3.52 (m, 1H), 3.14 (d, *J* = 7.9 Hz, 1H), 2.91 (dd, *J* = 12.0, 3.0 Hz, OH), 2.70 (d, *J* = 8.5 Hz, OH), 2.43 (ddd, *J* = 14.6, 9.6, 6.5 Hz, 1H), 2.33 (s, 3H), 1.93 (ddd, *J* = 14.4, 11.0, 2.8 Hz, 1H), 1.72 (d, *J* = 21.9 Hz, 3H), 1.69 (s, 3H), 1.33 (d, *J* = 8.1 Hz, 3H), 1.26 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.58−0.53 (m, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 204.75, 171.43, 165.94, 145.38 (d, *J* = 19.7 Hz), 133.79, 130.09, 129.50, 128.85 (d, *J* = 4.4 Hz), 128.24, 97.48 (d, *J* = 187.5 Hz, C−F), 92.10 (d, *J* = 176.6 Hz, C−F), 84.08, 81.01, 80.94 (d, *J* = 15.4 Hz), 77.16 overlapping with $CDCl_3$, 76.07, 71.00, 70.63 (d, *J* = 4.0 Hz), 59.11, 45.94, 43.29 (d, *J* = 2.2 Hz), 37.14, 27.27, 26.03 (dd, *J* = 16.0, 7.3 Hz), 21.88 (d, *J* = 28.4 Hz), 21.72, 8.31, 6.94, 5.30 ppm; HRMS (ESI-TOF): calcd for $C_{35}H_{48}F_2O_9Si$ $[M + H^+]$ 679.3108, found 679.3113.



30b

(*2aR,4R,4aR,5R,6S,11S,12S,12aR,12bS*)-12b-Acetoxy-4,6-difluoro-5,11-dihydroxy-4a,8,13,13-tetramethyl-9-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**31**): Compound **31** was obtained in 58% yield (2.36 mg) from 4.05 mg of **13** (0.0074 mmol) and large excess of $NaBH_4$ (procedure A). **31**: R_f = 0.12



31

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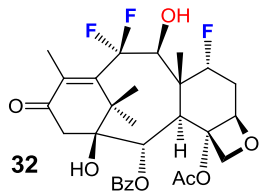
(silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{23}$ = +93.0 (*c* = 0.236 in $CHCl_3$); IR (film) ν_{max} = 3458, 2962, 1721, 1667, 1451, 1371, 1272, 1235, 1144, 1096, 1082, 1054, 978, 911, 831, 803, 730, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 5.86 (dd, *J* = 5.9, 1.1 Hz, 1H), 5.70 (d, *J* = 49.1 Hz, 1H−CF), 5.05 (dd, *J* = 48.1, 5.5 Hz, 1H−CF) overlaps with 5.03 (d, *J* = 8.5 Hz, 1H), 4.41 (d, *J* = 8.4 Hz, 1H), 4.28 (dd, *J* = 26.8, 4.4 Hz, 1H), 4.19 (dd, *J* = 8.4, 0.8 Hz, 1H), 3.85 (d, *J* = 5.8 Hz, 1H), 2.99 (d, *J* = 19.3 Hz, 1H), 2.73 (br s, OH), 2.65 (dd, *J* = 19.3, 1.0 Hz, 1H), 2.56 (ddd, *J* = 25.7, 17.0, 8.6 Hz, 1H), 2.21 (s, 3H) overlaps with 2.23−2.09 (m, 1H), 2.01 (m, 3H), 1.84 (s, OH), 1.60 (s, 3H), 1.49 (s, 3H), 1.30 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 197.80, 169.01, 167.04, 150.13 (d, *J* = 11.6 Hz), 137.59 (d, *J* = 1.7 Hz), 134.20, 130.27, 128.97, 128.95, 93.28 (d, *J* = 193.7 Hz, C−F), 87.29 (d, *J* = 176.8 Hz, C−F), 83.00, 81.56, 77.46 overlaps with 77.45, 73.93 (d, *J* = 19.8 Hz), 72.24, 49.19 (d, *J* = 20.3 Hz), 43.32, 42.24 (d, *J* = 6.0 Hz), 39.27 (d, *J* = 2.6 Hz), 34.36 (d, *J* = 25.1 Hz), 34.08, 21.95, 20.34, 16.80 (d, *J* = 8.9 Hz), 13.28 (dd, *J* = 14.4, 11.0 Hz) ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{34}F_2O_8$ [M + H^+] 549.2294, found 549.2293.

(*2aR,4R,4aR,5S,11S,12S,12aR,12bS*)-12b-Acetoxy-4,6,6-trifluoro-5,11-dihydroxy-4a,8,13,13-tetramethyl-9-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**32**): Compound **32** was obtained in

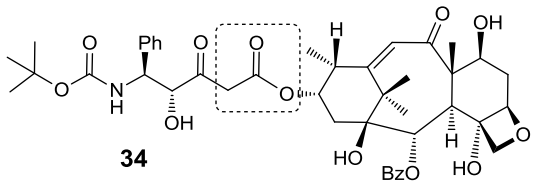


32

95% yield (2.2 mg) from 2.3 mg of **14** (0.0041 mmol) and large excess of $NaBH_4$ (procedure A under *Luche* conditions). **32**: R_f = 0.41 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{24}$ = +64.8 (*c* = 0.22 in $CHCl_3$); IR (film) ν_{max} = 3459, 2923, 2851, 1725, 1683, 1451, 1369, 1272, 1237, 1214, 1108, 1069, 1026, 963, 905, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 6.10 (d, *J* = 5.3 Hz, 1H), 5.17 (ddd, *J* = 45.3, 8.4, 2.0 Hz, 1H−CF), 4.87 (ddd, *J*

= 5.6, 5.6, 2.7 Hz, 1H), 4.51 (dd, *J* = 18.7, 8.0 Hz, 1H), 4.41 (d, *J* = 8.7 Hz, 1H), 4.27 (d, *J* = 8.7 Hz, 1H), 3.31 (d, *J* = 5.4 Hz, 1H), 3.10 (br s, OH), 2.94 (d, *J* = 19.6 Hz, 1H), 2.71 (d, *J* = 19.6 Hz, 1H), 2.58 (dddd, *J* = 14.4, 8.4, 5.9, 5.9 Hz, 1H), 2.25 (s, 3H), 2.16−2.07 (dddd, *J* = 34.6, 14.8, 5.6, 2.2 Hz, 1H) overlaps with 2.07 (d, *J* = 3.0 Hz, 3H), 1.90 (br s, OH), 1.60 (s, 3H), 1.57 (d, *J* = 11.9 Hz, 3H), 1.29 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 197.58 (t, *J* = 2.5 Hz), 170.26, 166.87, 147.57 (dd, *J* = 25.6, 16.6 Hz), 143.00 (dd, *J* = 7.9, 2.4 Hz), 134.23, 130.28, 129.07, 128.89, 96.05 (d, *J* = 178.6 Hz, C−F), 83.83 (d, *J* = 9.1 Hz), 83.60 (d, *J* = 1.2 Hz), 78.97, 78.05, 76.08 (ddd, *J* = 26.3, 22.0, 6.0 Hz), 73.49, 46.77 (dd, *J* = 13.1, 5.1 Hz), 43.90 (dd, *J* = 4.3, 2.5 Hz), 43.83 (d, *J* = 1.3 Hz), 43.05, 34.13, 30.86 (d, *J* = 21.8 Hz), 22.31, 21.06 (d, *J* = 19.6 Hz), 16.56 (t, *J* = 3.1 Hz), 15.72 (d, *J* = 6.9 Hz) and (CF_2 carbon was not observed) ppm; HRMS (ESI-TOF): calcd for $C_{29}H_{33}F_3O_8$ [M + H^+] 589.2020, found 589.2003.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-9-(((*4R,5S*)-5-((tert-Butoxycarbonyl)amino)-4-hydroxy-3-oxo-5-phenylpentanoyl)oxy)-4,11,12b-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**34**): Compound **34** was obtained in 39% yield (6.6 mg) over 2 steps



34

(coupling B3 and deprotection C) from 13.7 mg of **15** (0.021 mmol), 0.11 mL of NaHMDS (0.066 mmol, 0.6 M solution in toluene), and 39 mg of **V** (0.108 mmol) (procedures B3 and C). **34**: R_f = 0.23 (silica gel, EtOAc/hexanes 1:1); mp = 161–163 ºC (hexanes/EtOAc 10:1); $[\alpha]_D^{30}$ = −119.9 (*c* = 0.66 in $CHCl_3$); IR (film) ν_{max} = 3434, 2978, 1698, 1496, 1451, 1367, 1276, 1166, 1070, 1026, 975, 910, 731 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.45−7.40 (m, 4H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 5.87 (d, *J* = 7.6 Hz, 1H), 5.84 (s, 1H), 5.49 (d, *J* = 9.3 Hz, 1H),

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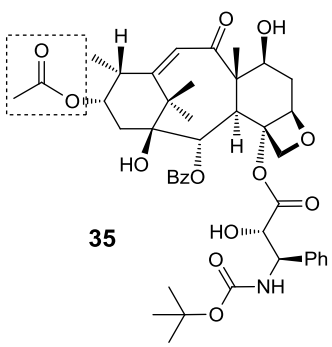
5.41 (m, 1H), 5.37 (d, *J* = 9.4 Hz, 1H), 4.74 (dd, *J* = 9.1, 4.3 Hz, 1H), 4.69 (br s, OH), 4.46 (d, *J* = 8.0 Hz, 1H), 4.07 (d, *J* = 16.7 Hz, 1H), 3.96 (d, *J* = 8.0 Hz, 1H), 3.90 (d, *J* = 16.6 Hz, 1H), 3.81 (br s, OH), 3.64 (d, *J* = 7.6 Hz, 1H), 3.54 (br m, 1H), 3.39 (br s, OH), 3.20 (m, 1H), 2.59 (d, *J* = 16.9 Hz, 1H), 2.52 (ddd, *J* = 14.6, 9.5, 5.9 Hz, 1H), 2.22 (br s, OH), 2.06 (dd, *J* = 16.9, 6.3 Hz, 1H), 1.97 (m, 1H), 1.73 (s, OH), 1.65 (s, 3H), 1.39 (s, 9H), 1.24 (s, 3H), 1.22 (s, 3H), 1.06 (d, *J* = 6.6 Hz, 3H) pm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.29, 203.10, 166.91, 166.16, 155.68, 148.62, 139.21, 134.08, 129.89, 129.14, 129.07, 128.94, 128.05, 126.90, 121.04, 85.74, 82.50, 80.70, 80.55, 79.92, 75.22, 74.33, 73.82, 69.75, 58.80, 54.94, 48.10, 45.14, 44.36, 35.98, 35.37, 35.35, 28.41, 26.69, 24.93, 12.47, 9.22 ppm; HRMS (ESI-TOF): calcd for $C_{43}H_{53}NO_{13}$ [M + H^+] 792.3590, found 792.3584.

(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-9-Acetoxy-12b-(((*2S,3R*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**35**): Compound **35** was obtained

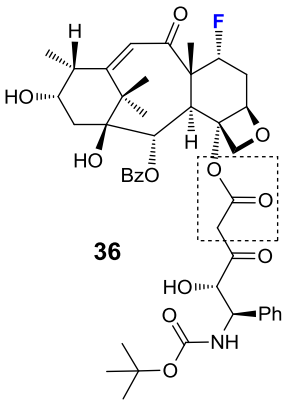


35

together with **34** in 12% yield (4.6 mg) over 2 steps (coupling B2 or B3 and deprotection C) from 30 mg of **15** (0.047 mmol), 0.17 mL of NaHMDS (0.102 mmol, 0.6 M solution in toluene), and 51 mg of **V** (0.141 mmol) (procedures B2 or B3 and C). **35**: R_f = 0.28 (silica gel, EtOAc/hexanes 1:1); $[\alpha]_D^{30}$ = −50.8 (*c* = 0.38 in $CHCl_3$); IR (film) ν_{max} = 3439, 2978, 1709, 1495, 1452, 1367, 1269, 1166, 1109, 1070, 1025, 988, 911, 732, 713 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.40−7.33 (m, 5H), 5.82 (d, *J* = 7.8 Hz, 1H), 5.78 (d, *J* = 1.0 Hz, 1H), 5.65 (q, *J* = 7.0 Hz, 1H), 5.36 (d, *J* = 6.4 Hz, 1H), 5.12 (dd, *J* = 7.0, 5.0 Hz, 1H), 4.52 (d, *J* = 8.0 Hz, 1H),

4.48 (br s, 1H), 4.28 (s, 2H), 4.22 (br s, 1H), 3.91 (dd, *J* = 10.6, 6.8 Hz, 1H), 3.59 (d, *J* = 7.8 Hz, 1H), 3.15 (m, 1H), 2.50 (m, 1H), 2.23 (m, 1H), 2.07 (s, 3H) overlaps with 2.04 (br s, 1H), 1.97 (dd, *J* = 16.4, 7.2 Hz, 1H), 1.83−1.76 (m, 2H), 1.72 (s, 3H), 1.41 (s, 9H), 1.20 (s, 3H), 1.19 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.72, 171.43, 170.11, 167.48, 156.68, 150.20, 137.72, 133.90, 130.50, 129.40, 129.24, 128.99, 128.86, 127.11, 120.79, 83.20, 82.27, 81.12, 81.07, 77.16 overlaps with $CDCl_3$, 75.87, 74.70, 71.19, 69.43, 58.75, 58.31, 46.52, 43.83, 36.00, 35.99, 35.51, 28.36, 27.53, 25.53, 21.27, 12.40, 9.53. HRMS (ESI-TOF): calcd for $C_{43}H_{53}NO_{13}$ [M + H^+] 792.3589, found 792.3579.

(*2aR,4R,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-(((*4S,5R*)-5-((tert-Butoxycarbonyl)amino)-4-hydroxy-3-oxo-5-phenylpentanoyl)oxy)-4-fluoro-9,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**36**): Compound **36** was obtained in



36

16% yield (9.4 mg) over 2 steps (coupling B3 and deprotection C) from 40 mg of **16** (0.075 mmol), 0.276 mL of NaHMDS (0.166 mmol, 0.6 M solution in toluene), and 136 mg of **V** (0.376 mmol) (procedures B3 and C). **36**: R_f = 0.35 (silica gel, EtOAc/hexanes 1:2); $[\alpha]_D^{30}$ = −48.9 (*c* = 0.94 in $CHCl_3$); IR (film) ν_{max} = 3440, 2980, 1698, 1494, 1452, 1391, 1367, 1315, 1273, 1164, 1109, 1060, 1026, 990, 911, 731, 712 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 7.7 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.49 (t *J* = 7.8 Hz, 2H), 7.42−7.38 (m, 4H), 7.32 (m, 1H), 5.78 (d, *J* = 8.1 Hz, 1H), 5.57 (d, *J* = 7.0 Hz, 1H), 5.40 (m, 2H), 5.21 (d, *J* = 8.2 Hz, 1H), 4.70 (m, 1H) overlaps with 4.70 (s, 1H), 4.63 (dd, *J* = 46.4, 5.6 Hz, 1H−CF), 4.32−4.27 (m, 2H), 4.20 (d, *J* = 17.0 Hz, 1H), 4.09 (s, 1H), 3.93 (br s, 1H), 3.82 (d, *J* = 17.0 Hz, 1H), 3.25 (s, 1H), 2.96 (m, 1H), 2.52 (ddd, *J* = 27.1, 16.6, 8.2 Hz, 1H),

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2.38 (d, *J* = 15.8 Hz, 1H), 2.28−2.16 (ddd, *J* = 43.3, 17.0, 5.9 Hz, 1H), 1.84 (dd, *J* = 15.8, 5.4 Hz, 1H), 1.77 (br s, OH), 1.75 (d, *J* = 0.9 Hz, 3H), 1.41 (s, 9H), 1.19 (s, 3H), 1.14 (s, 3H), 1.06 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 213.86, 203.50, 167.94, 164.28, 155.64, 145.50 (d, *J* = 1.3 Hz), 139.28, 133.77, 130.22, 129.83, 128.96, 128.78, 128.11, 126.83, 123.97 (d, *J* = 6.1 Hz), 95.89 (d, *J* = 179.2 Hz, C−F), 84.10, 81.90, 81.61, 80.85, 79.93, 76.40, 74.12, 70.77, 57.29 (d, *J* = 18.0 Hz), 54.73, 44.73, 43.99, 39.32, 37.58, 36.61, 33.75 (d, *J* = 24.7 Hz), 28.39, 26.44, 24.86, 13.02 (d, *J* = 7.2 Hz), 12.66 ppm; HRMS (ESI-TOF): calcd for $C_{43}H_{52}FNO_{12}$ [M + H^+] 794.3546, found 794.3546.

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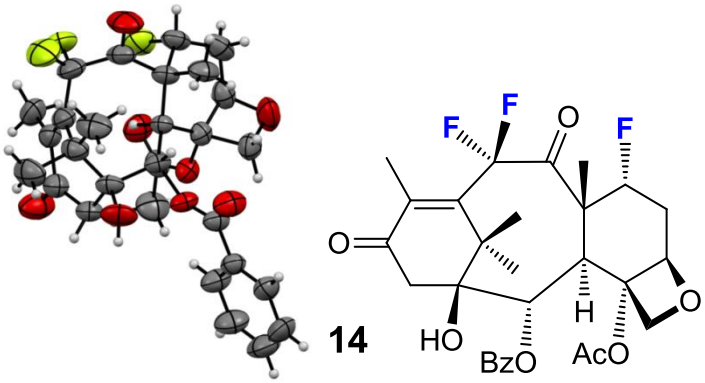
II. X-ray Structures

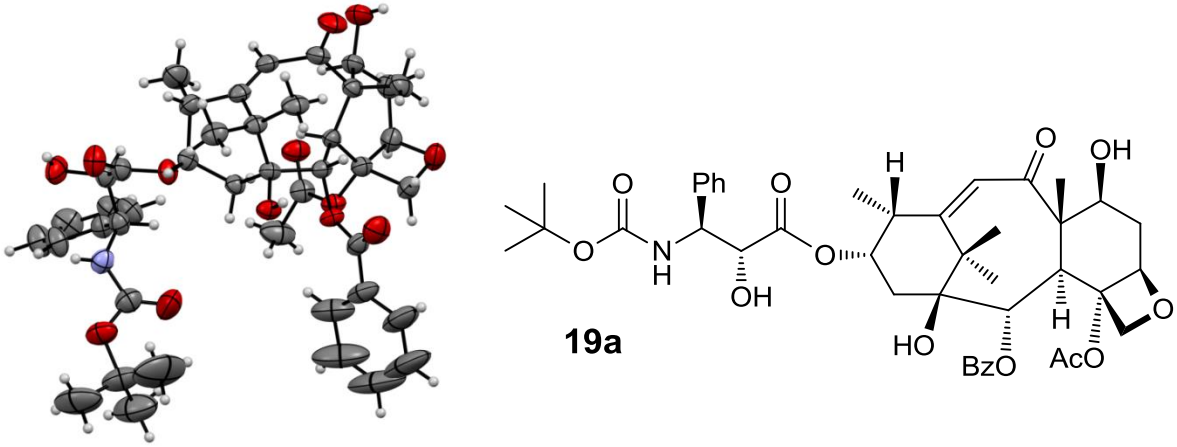
(*2aR,4R,4aR,11S,12S,12aR,12bS*)-12b-Acetoxy-4,6,6-trifluoro-11-hydroxy-4a,8,13,13-tetramethyl-5,9-dioxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**14**): mp = 229−230 ºC (CH_3Cl/hexanes/EtOAc 10:5:1).

ORTEP of **14** (CCDC-931453):



(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**19a**): mp = 178−181 ºC (CH_3CN).

ORTEP of **19a** (CCDC-931454):



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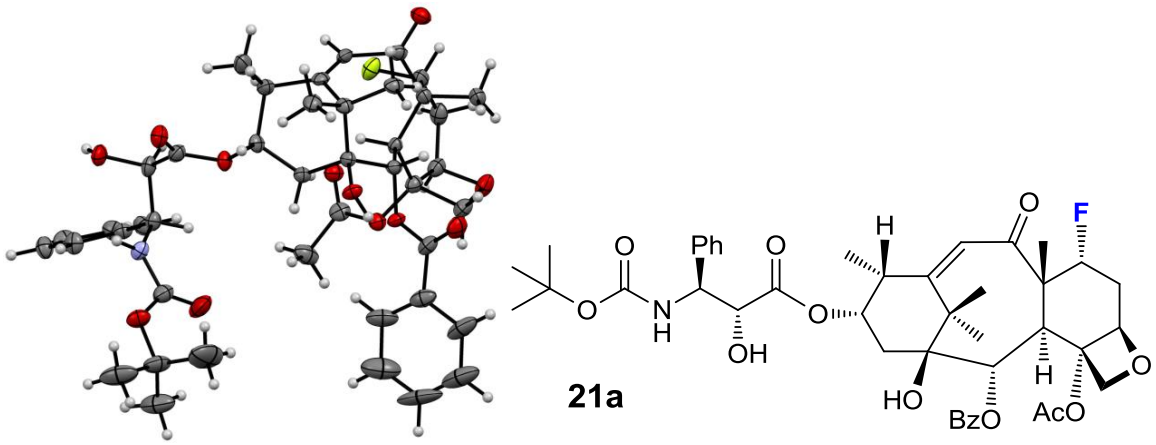
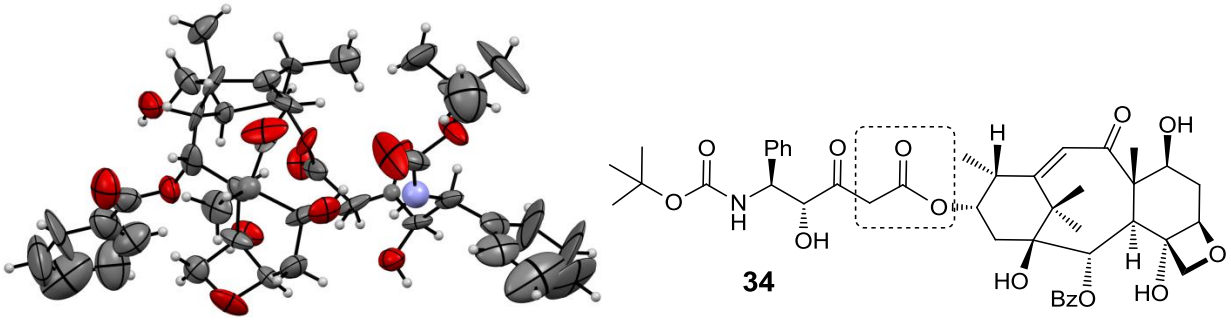
(*2aR,4R,4aR,8R,9S,11S,12S,12aR,12bS,Z*)-12b-Acetoxy-9-(((*2R,3S*)-3-((tert-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoyl)oxy)-4-fluoro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**21a**): mp = 233−235 ºC (CH_3CN/hexanes/EtOH 10:2:5).

ORTEP of **21a** (CCDC-931455):



(*2aR,4S,4aS,8R,9S,11S,12S,12aR,12bS,Z*)-9-(((*4R,5S*)-5-((tert-Butoxycarbonyl)amino)-4-hydroxy-3-oxo-5-phenylpentanoyl)oxy)-4,11,12b-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,8,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate (**34**): mp = 161−163 ºC (hexanes/EtOAc 10:1).

ORTEP of **34** (CCDC-931456):



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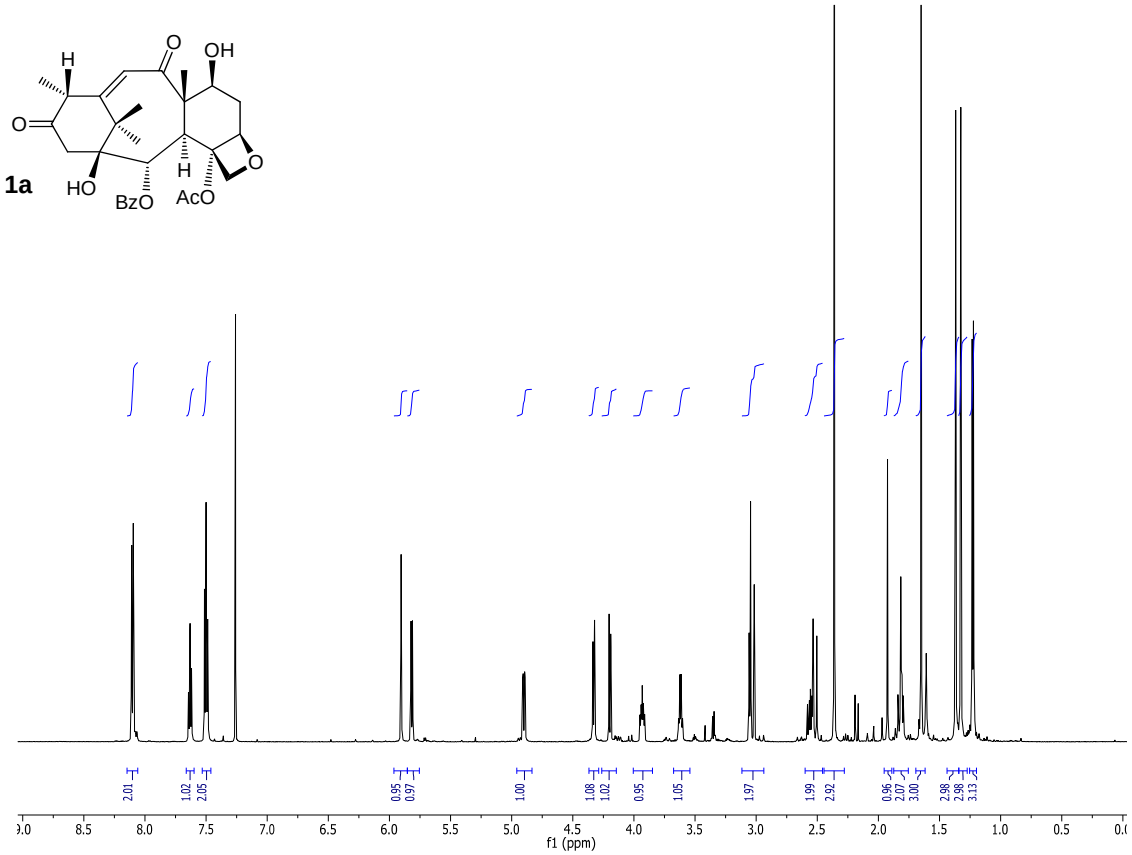
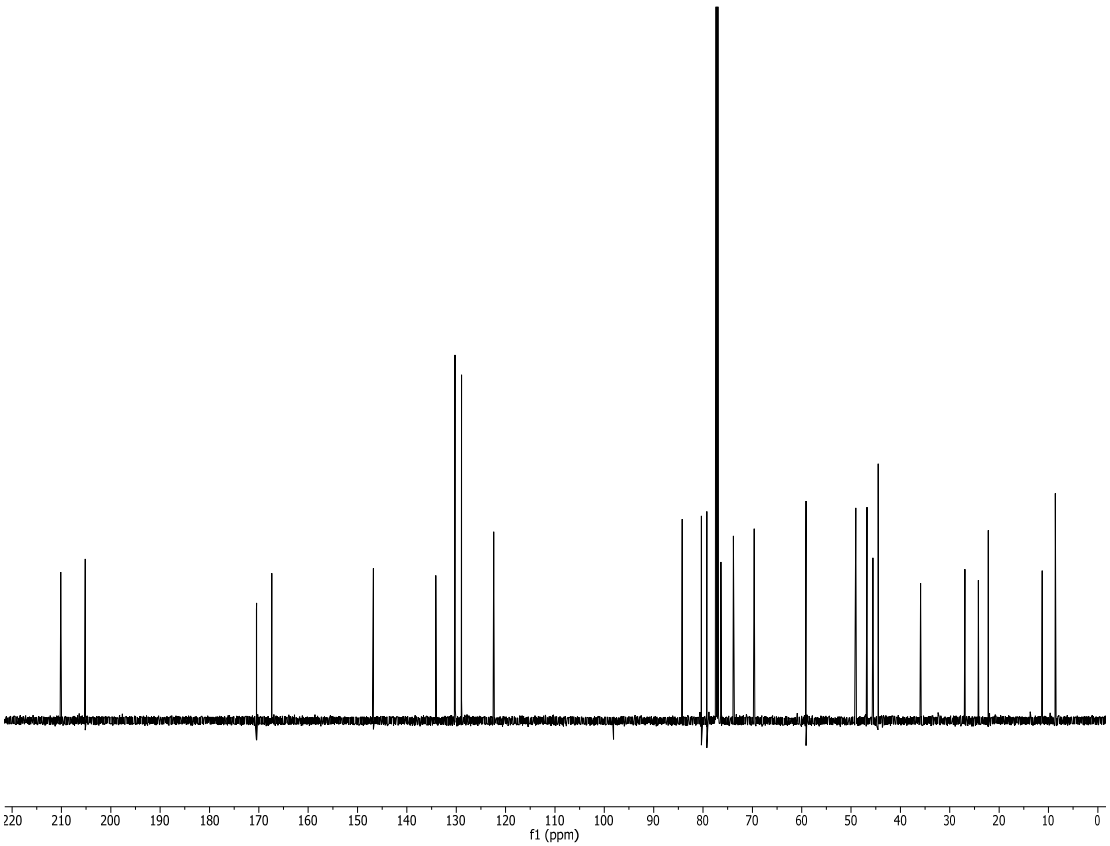
^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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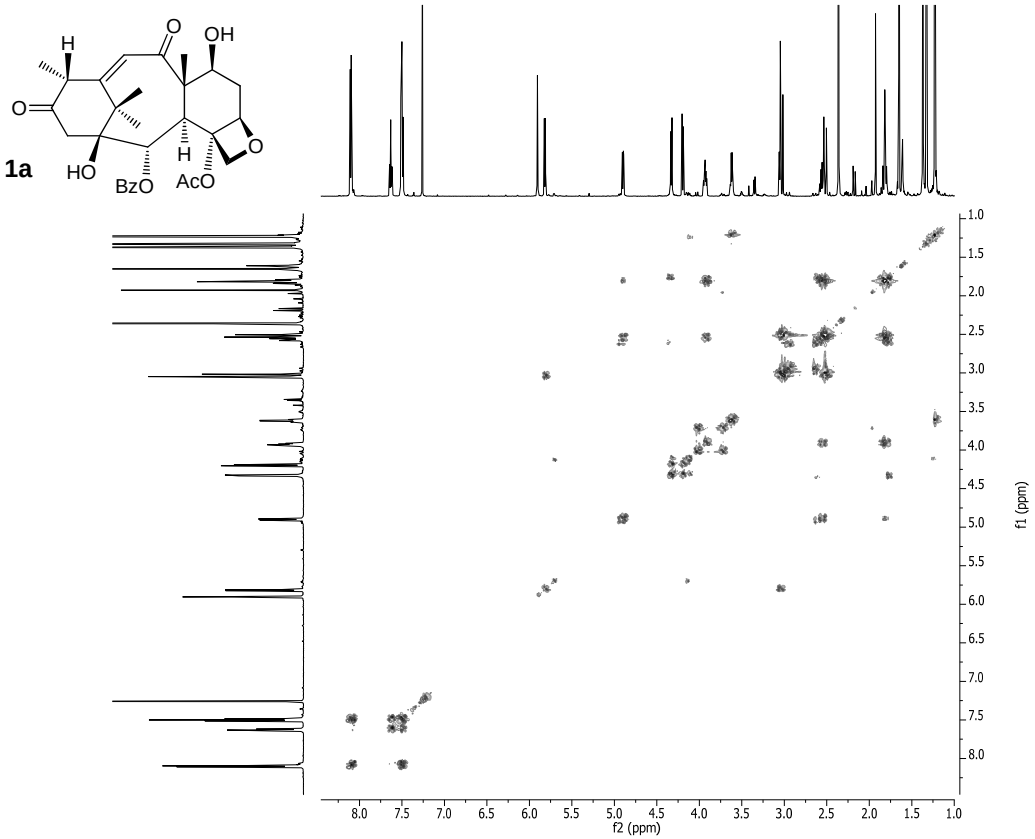
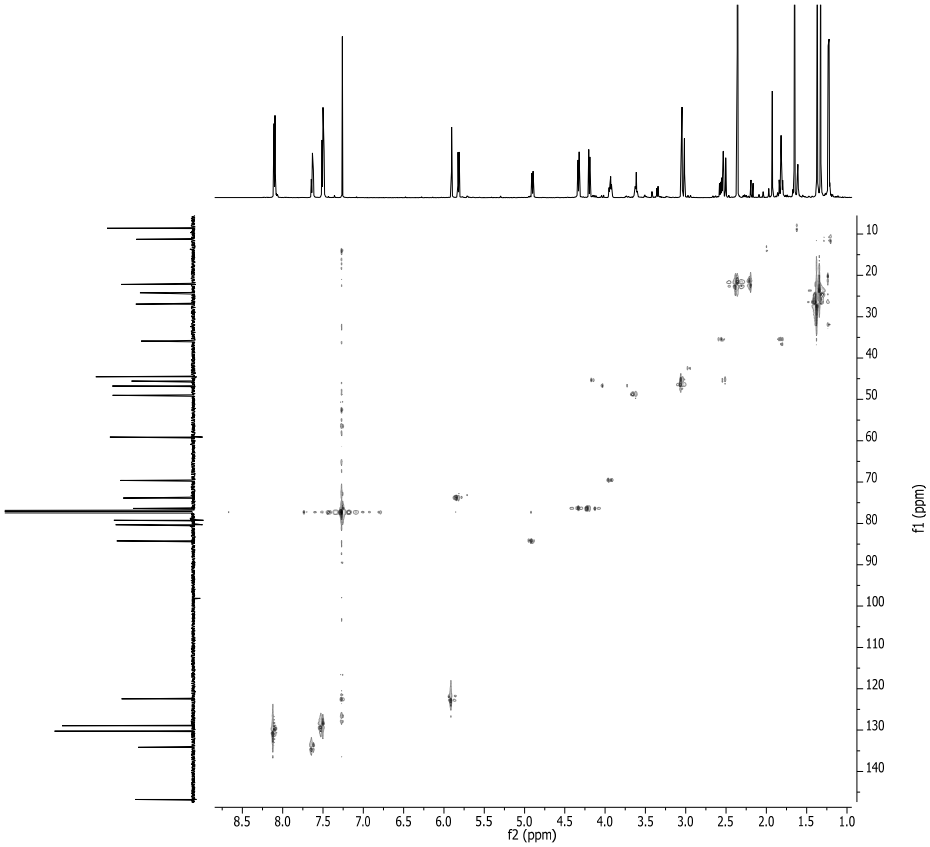
COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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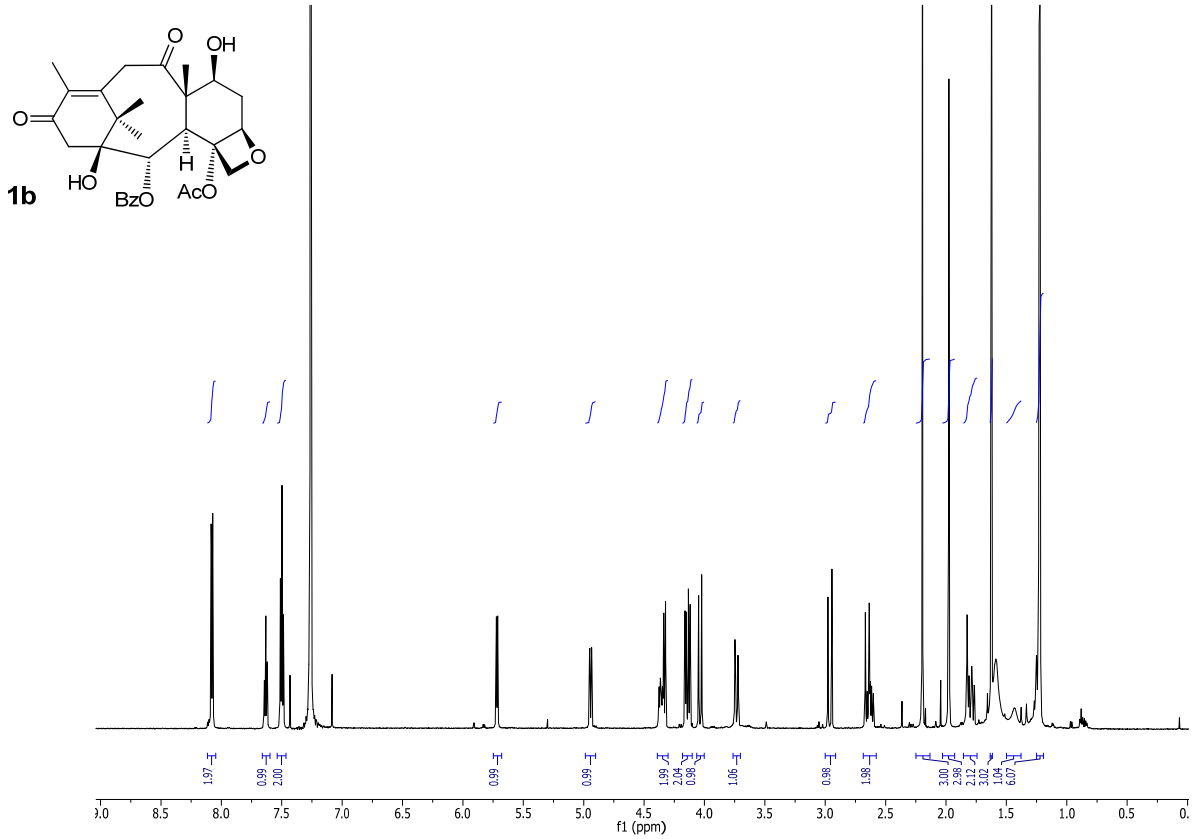
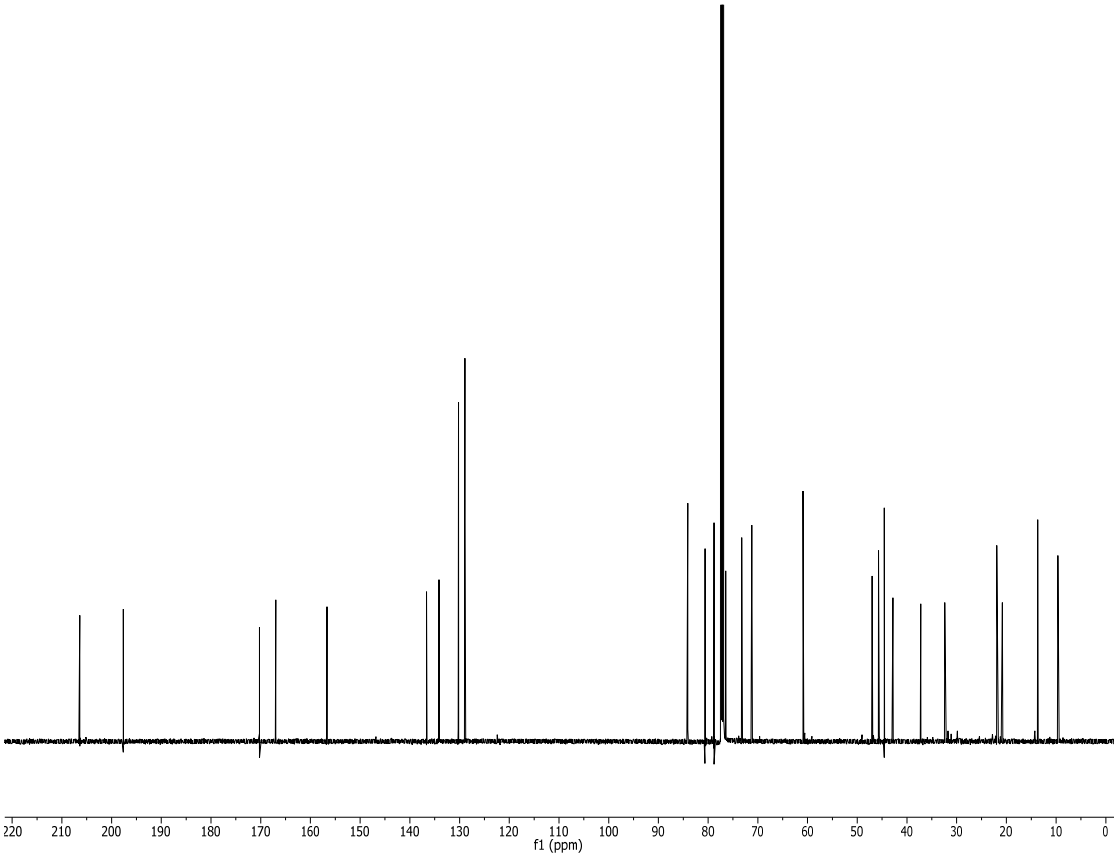
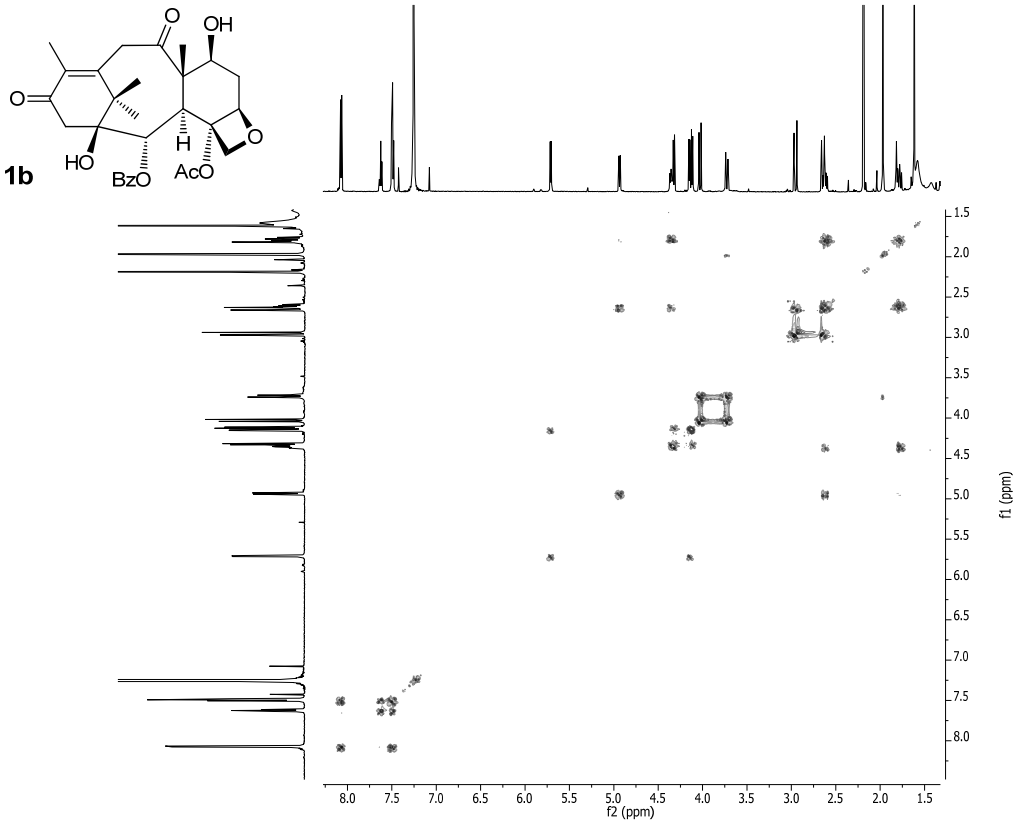
^{1}H NMR (600 MHz, $CDCl_3$):



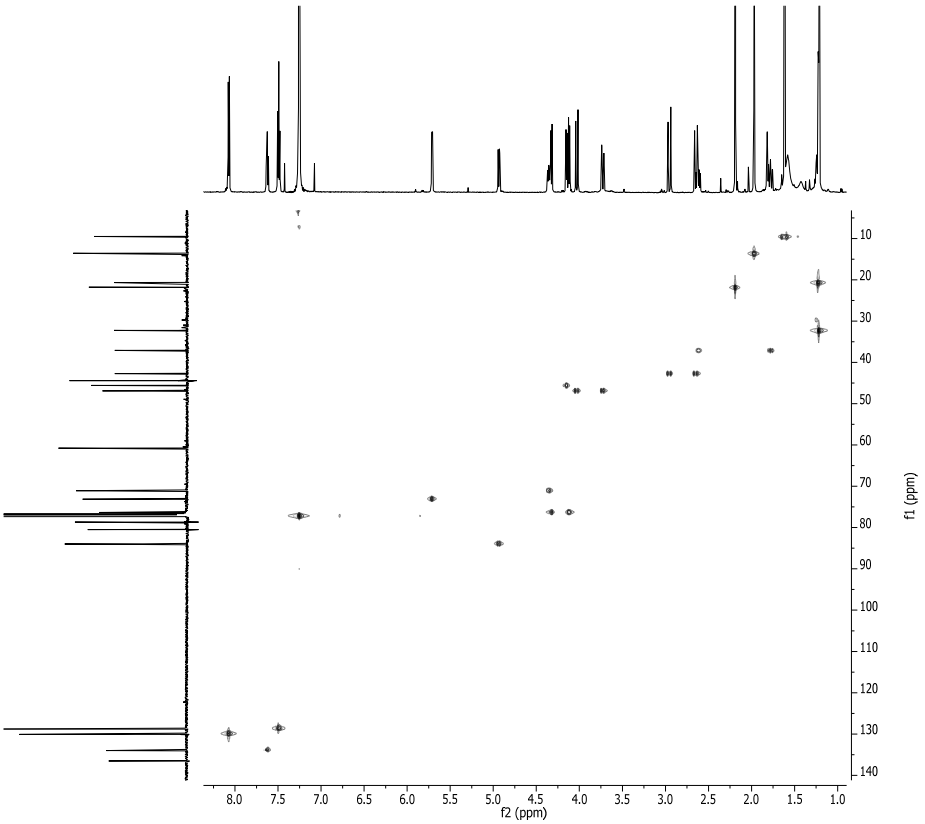
^{13}C NMR (600 MHz, $CDCl_3$):



COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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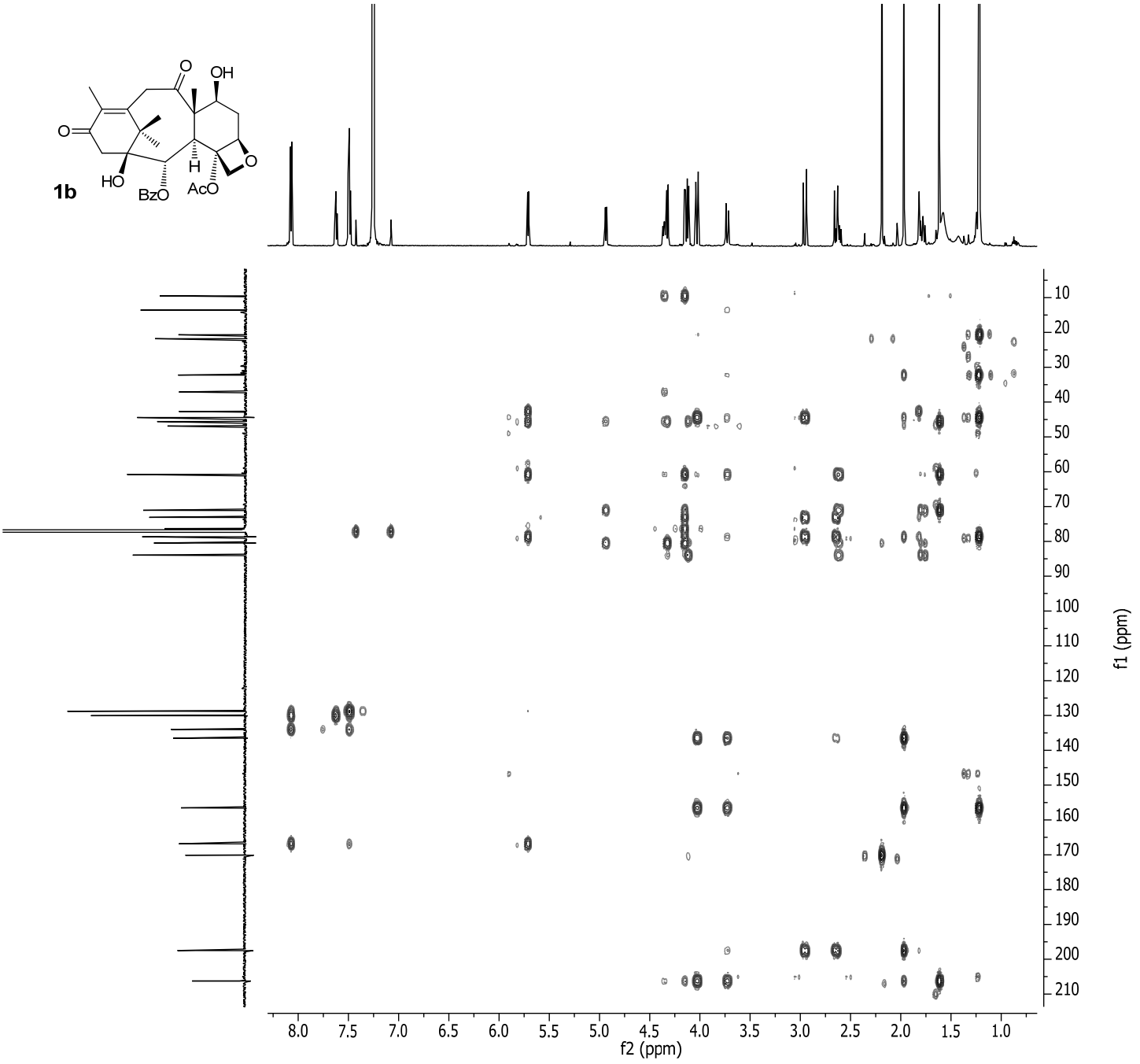
HMBC (600 MHz, $CDCl_3$):



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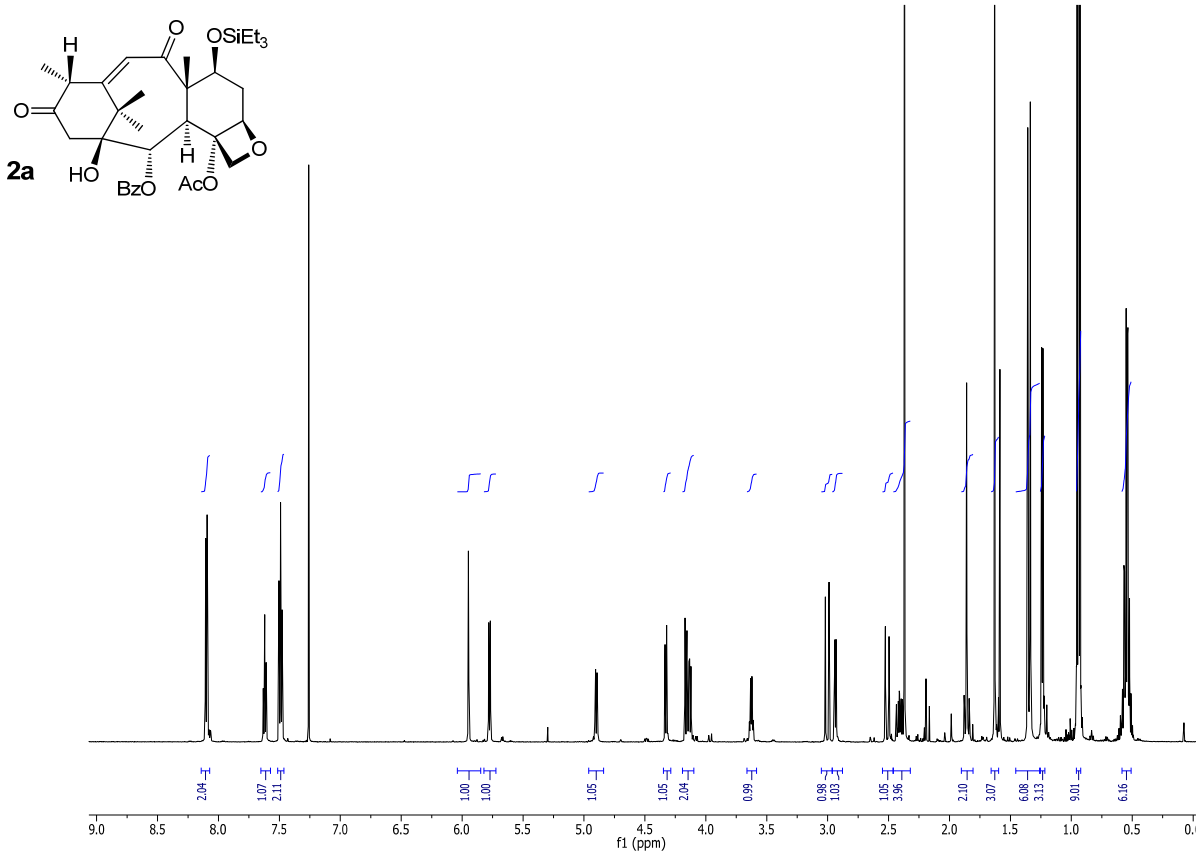
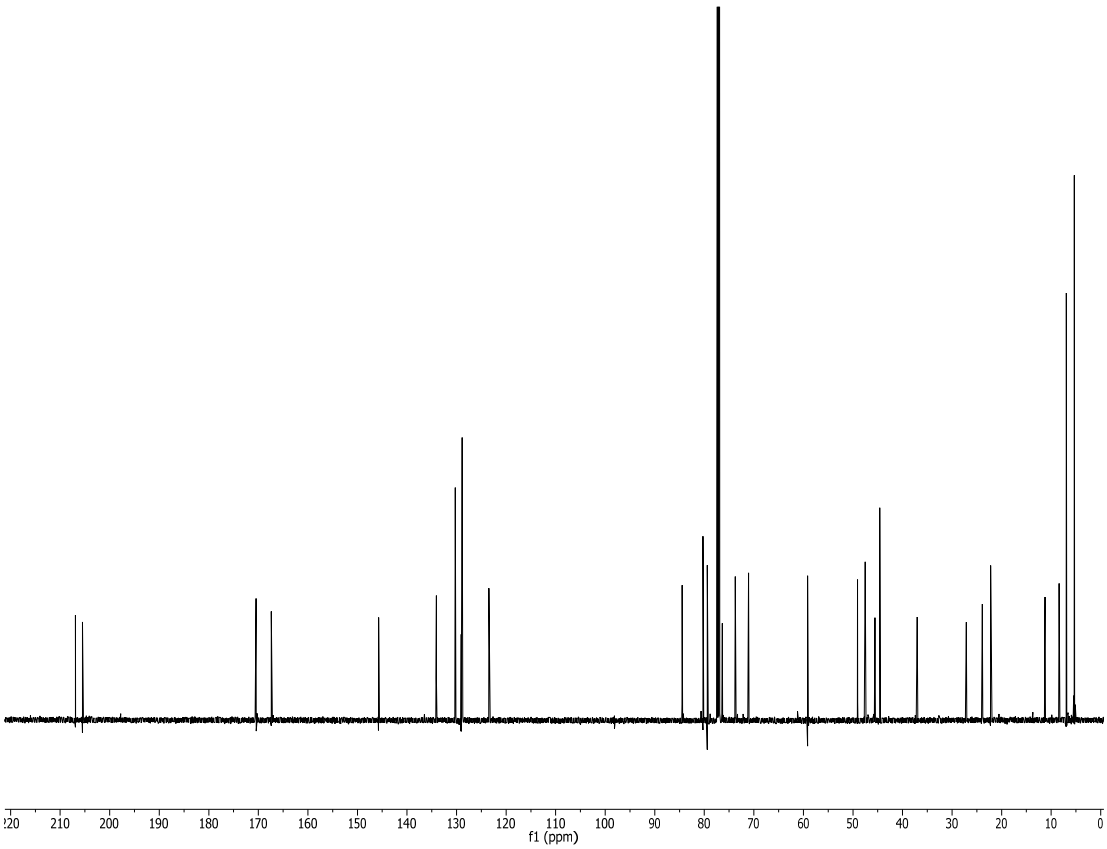
^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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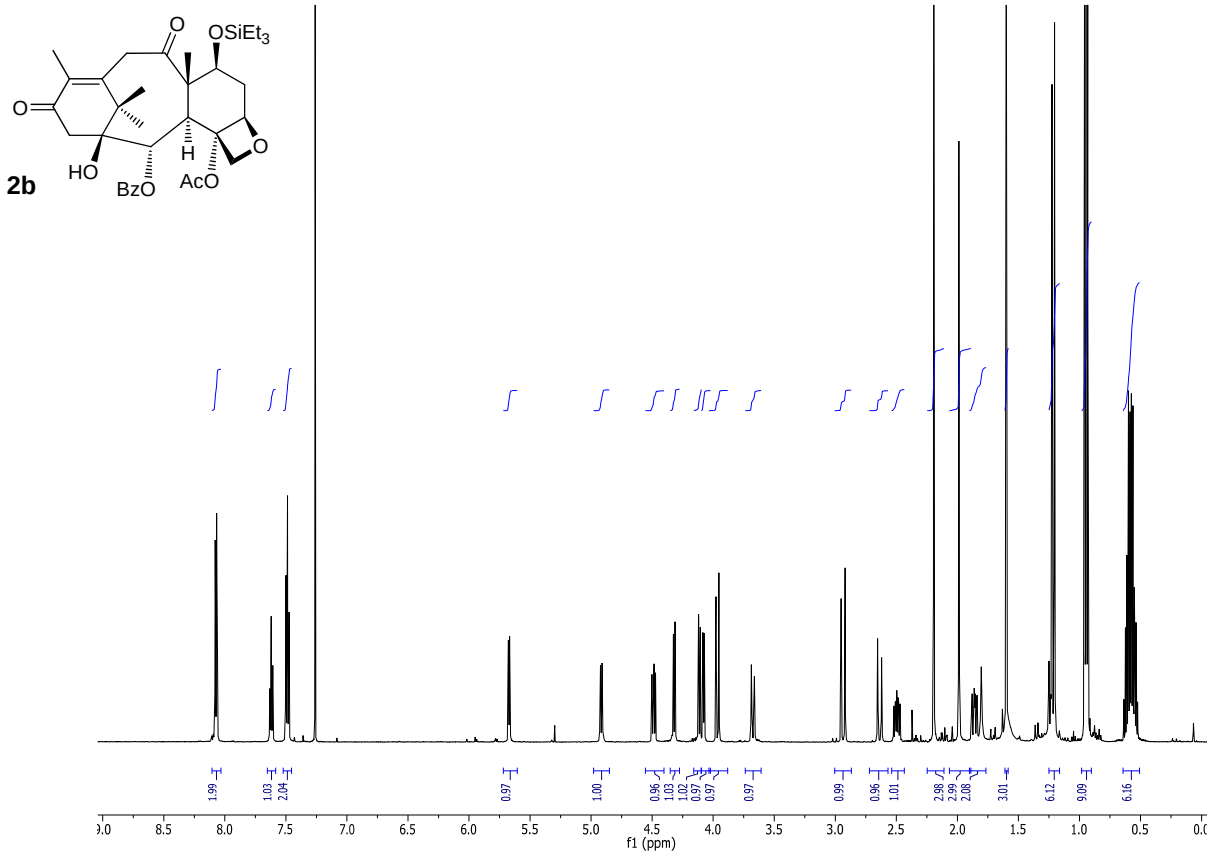
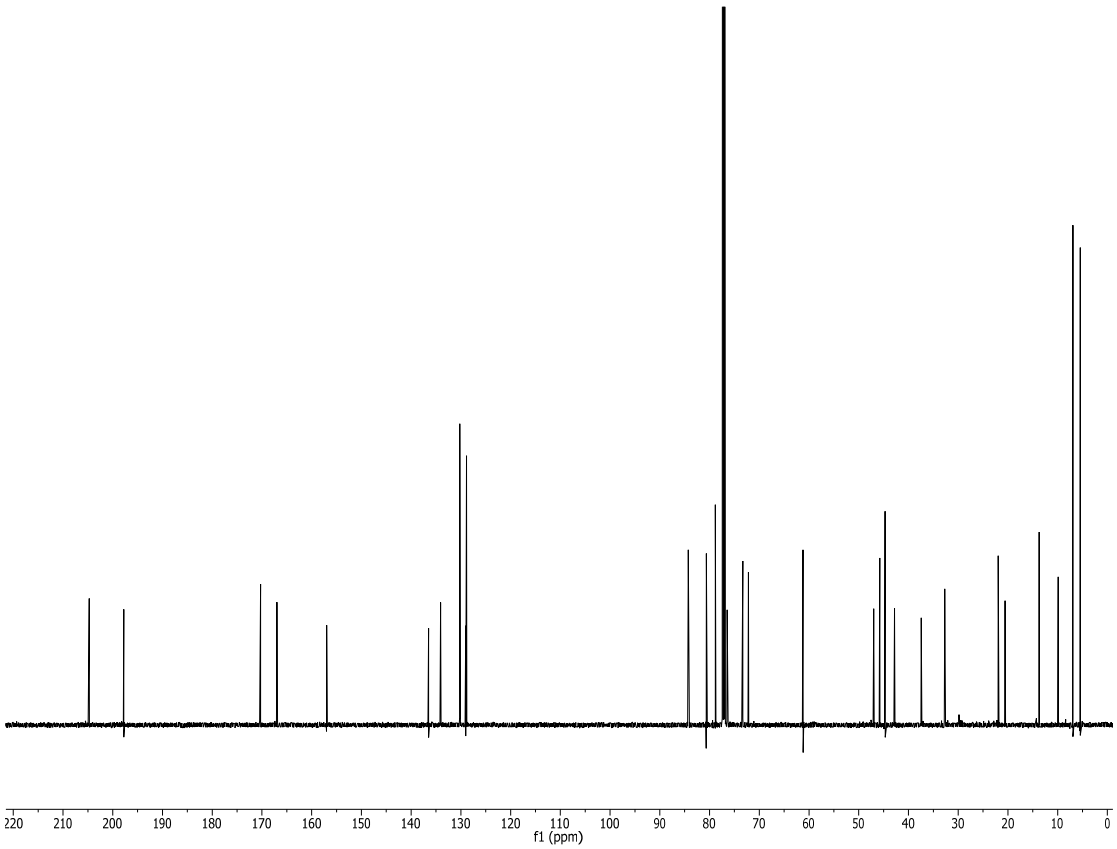
^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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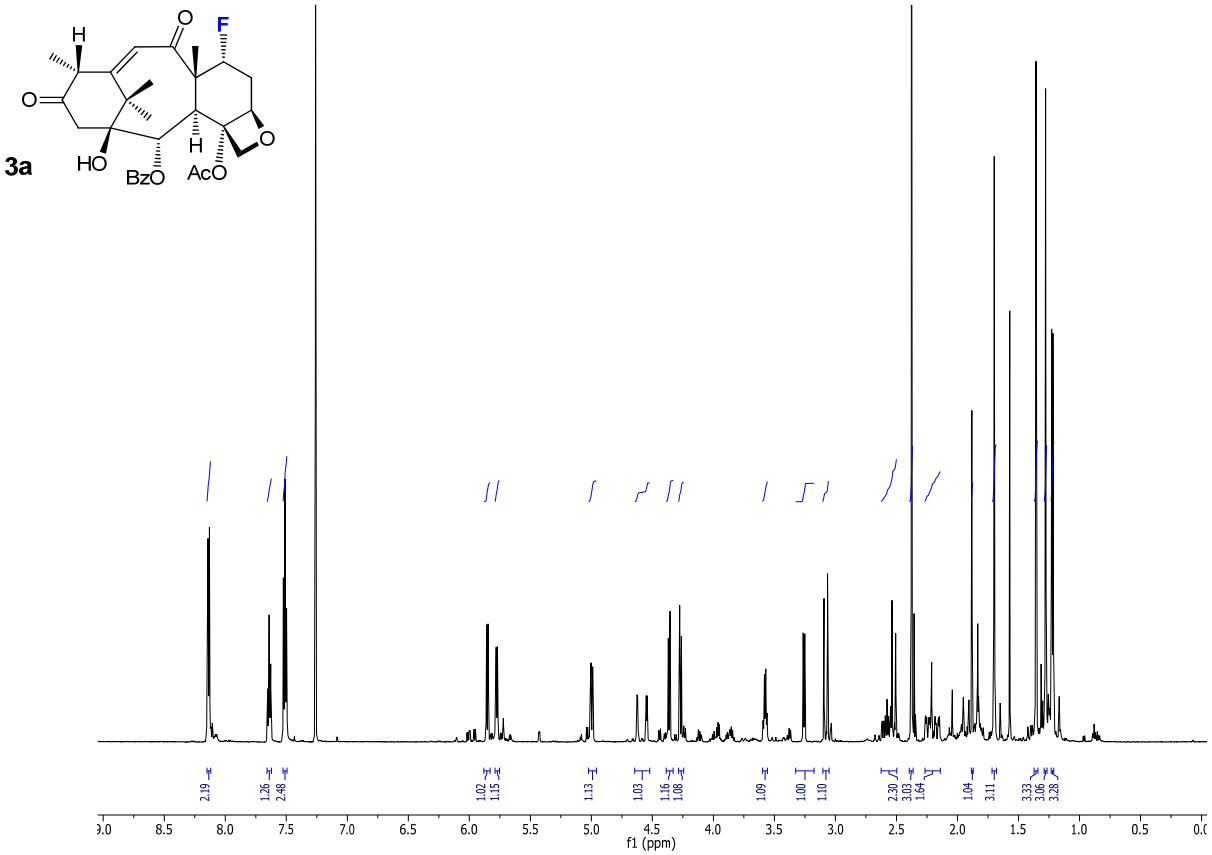
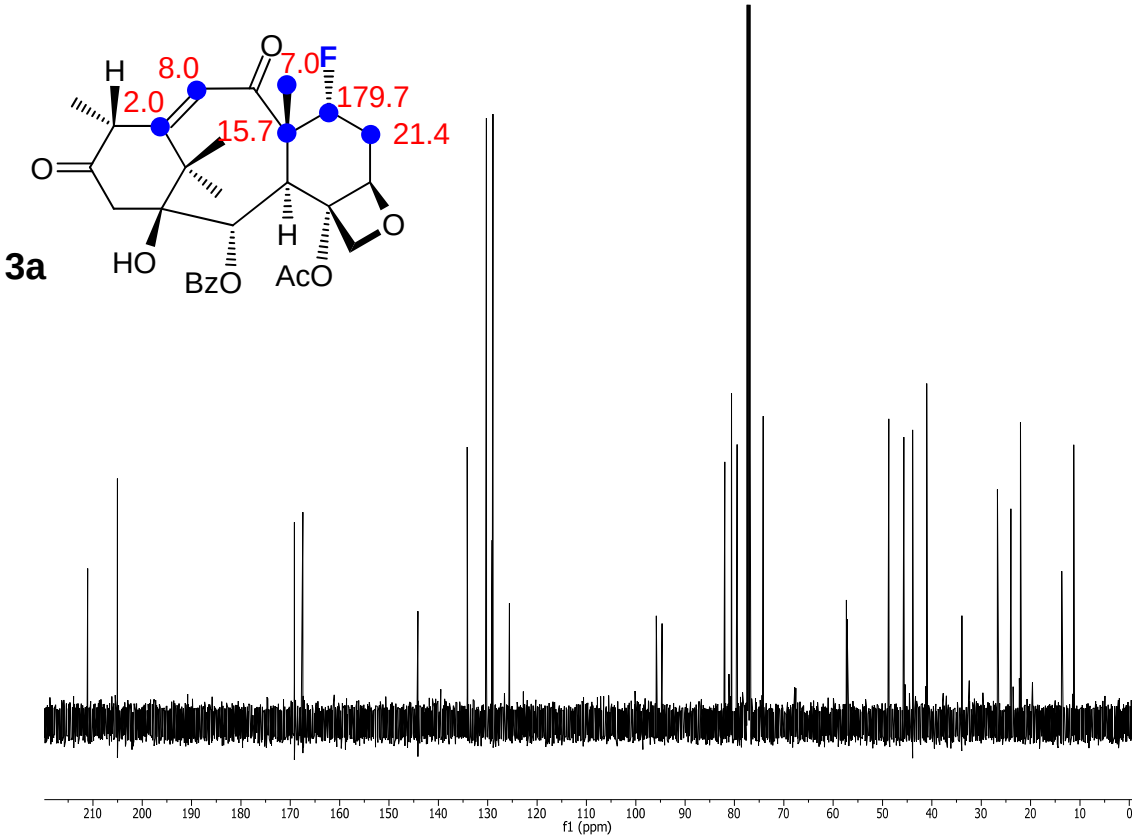
^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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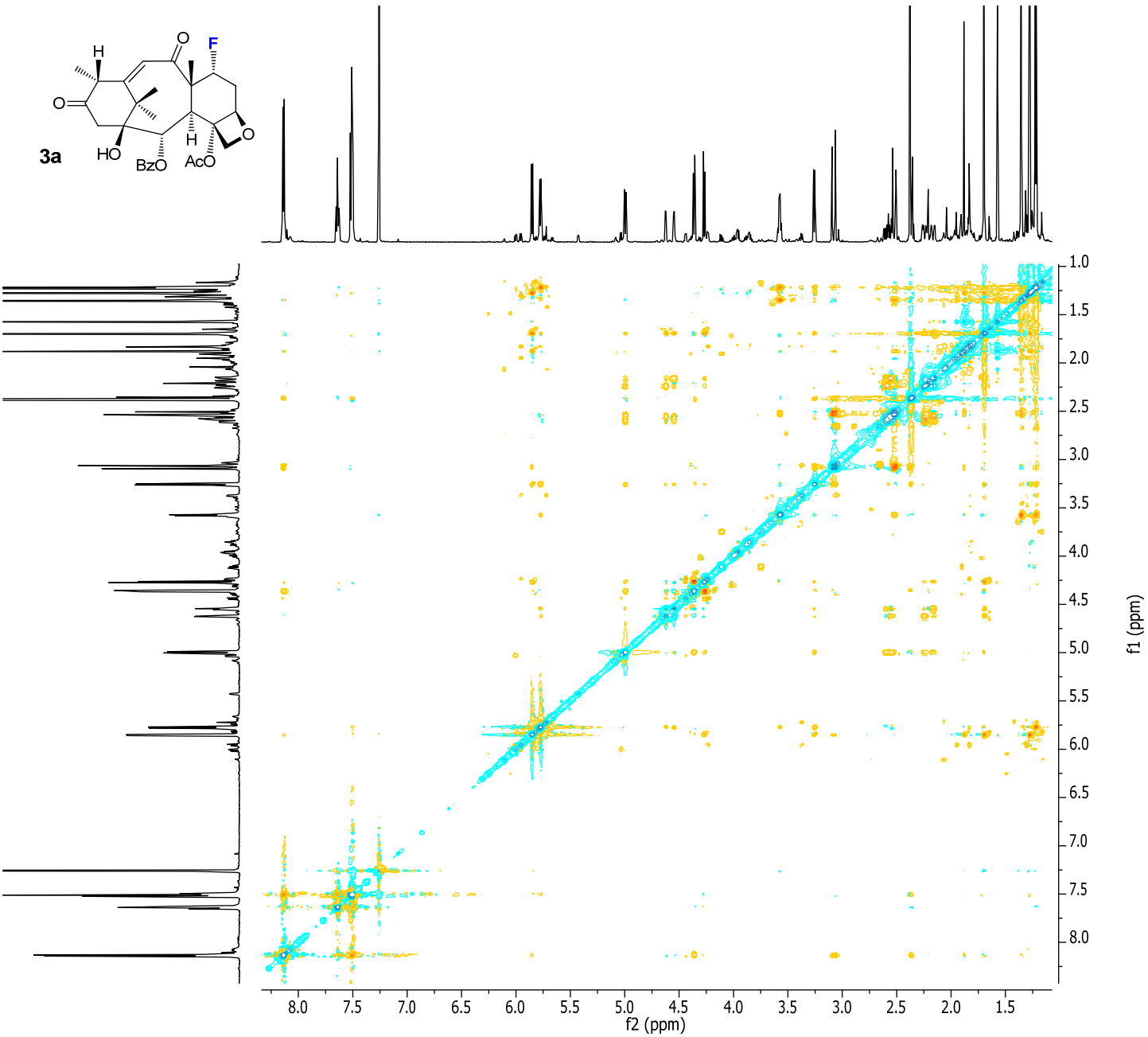
NOESY (600 MHz, $CDCl_3$):



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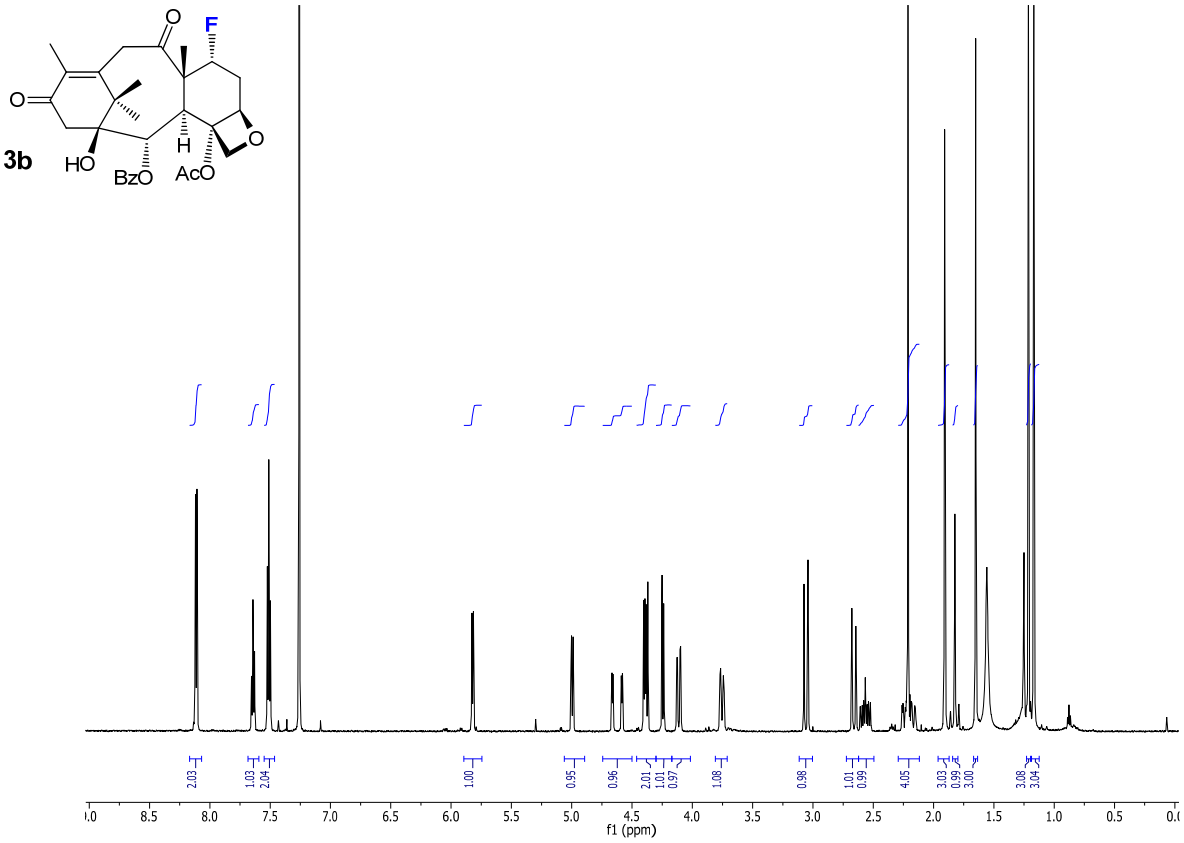
^{1}H NMR (600 MHz, $CDCl_3$):



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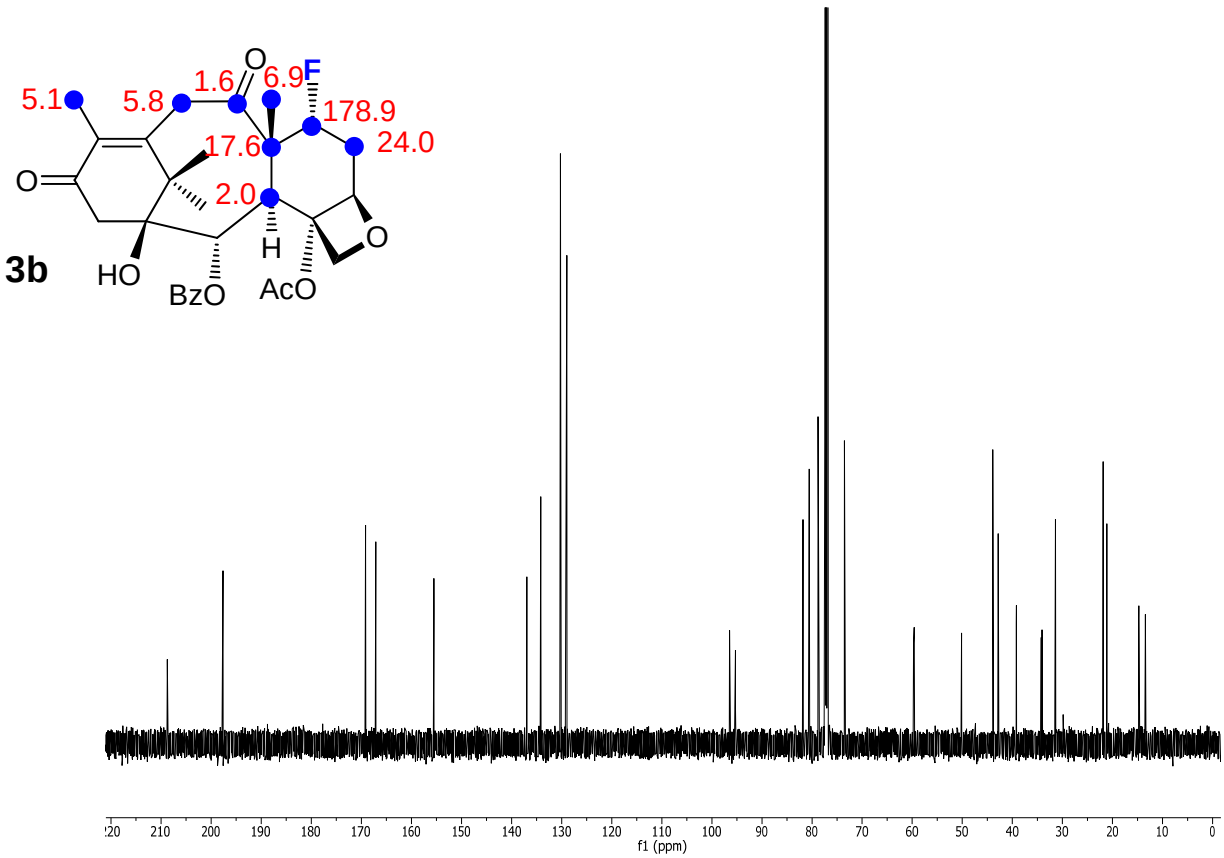

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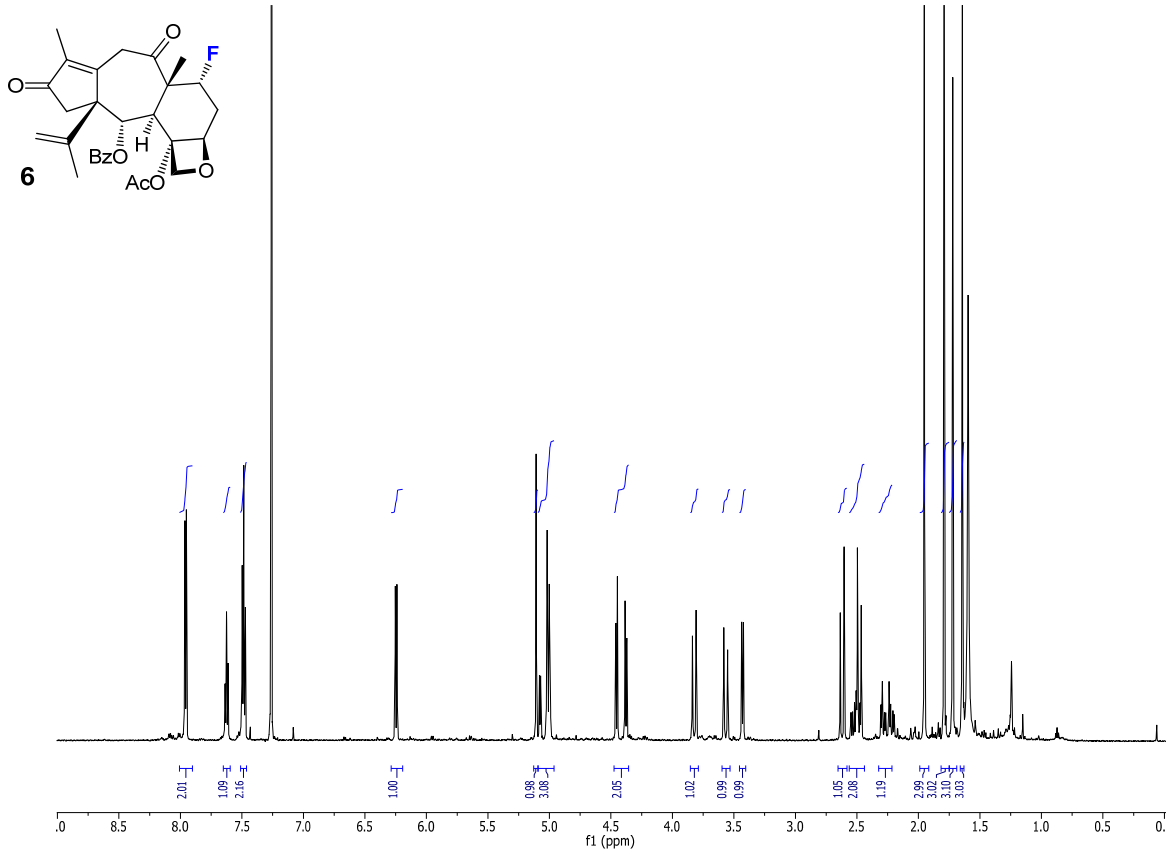
^{1}H NMR (600 MHz, $CDCl_3$):



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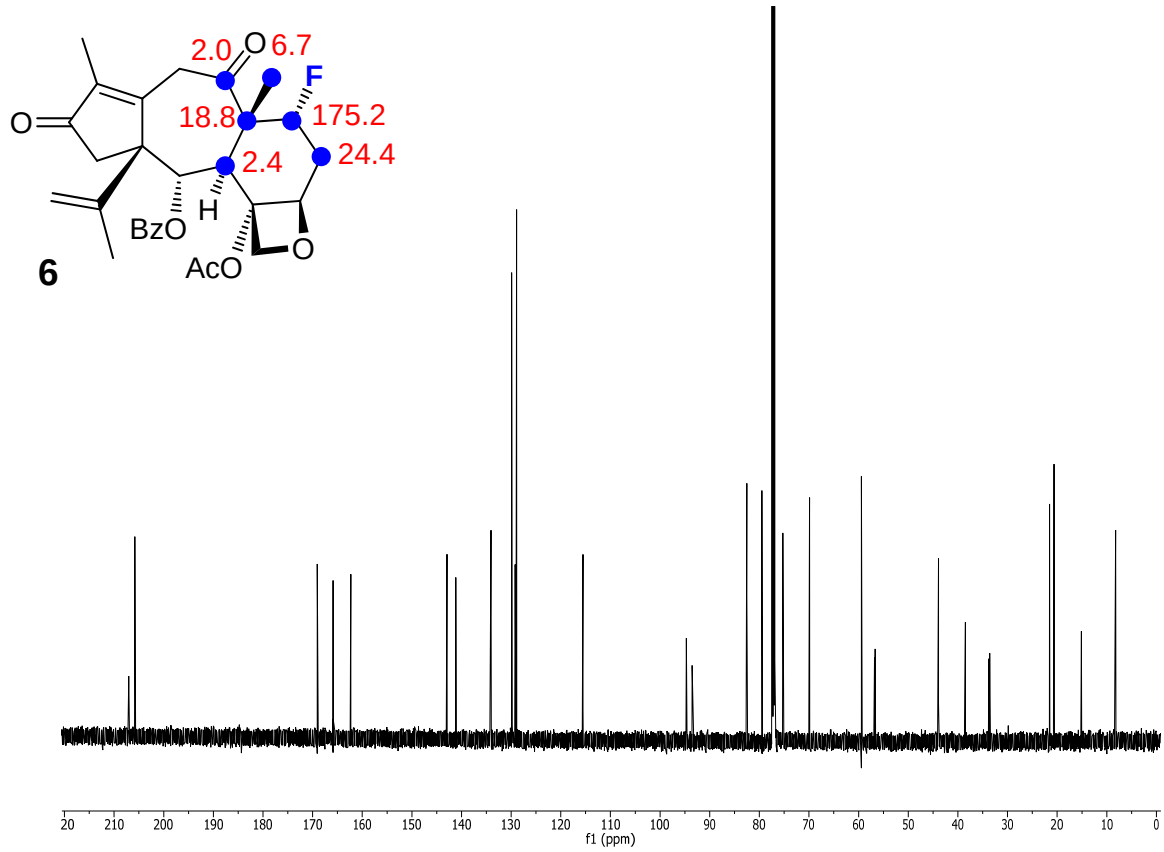

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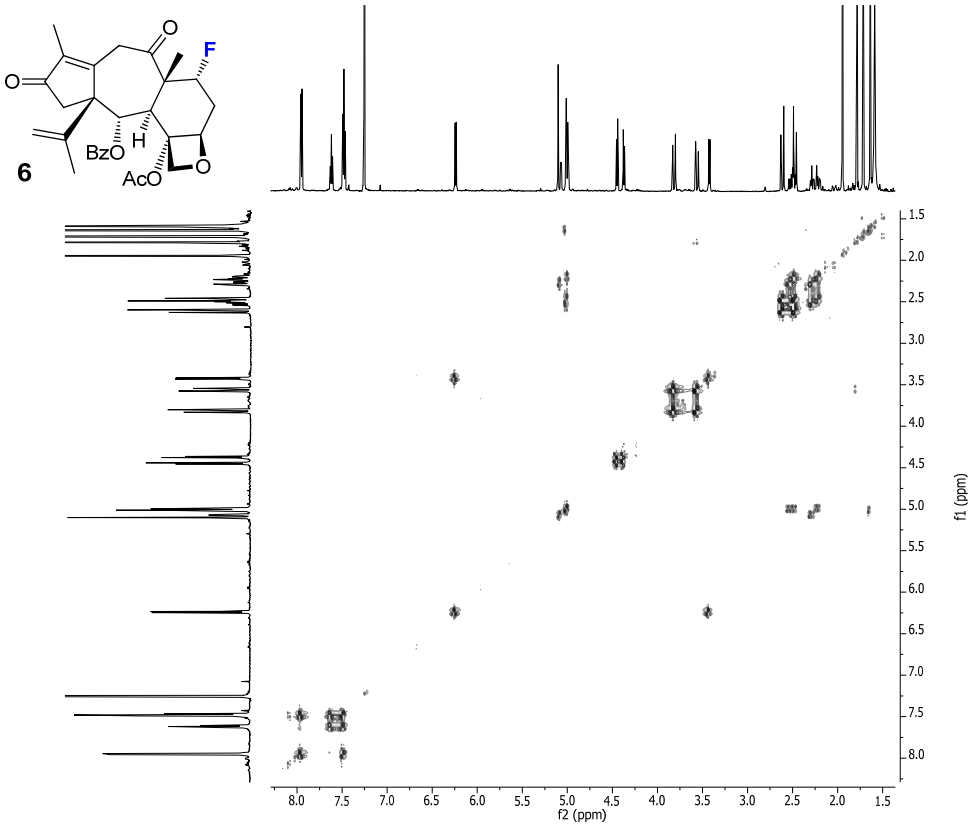
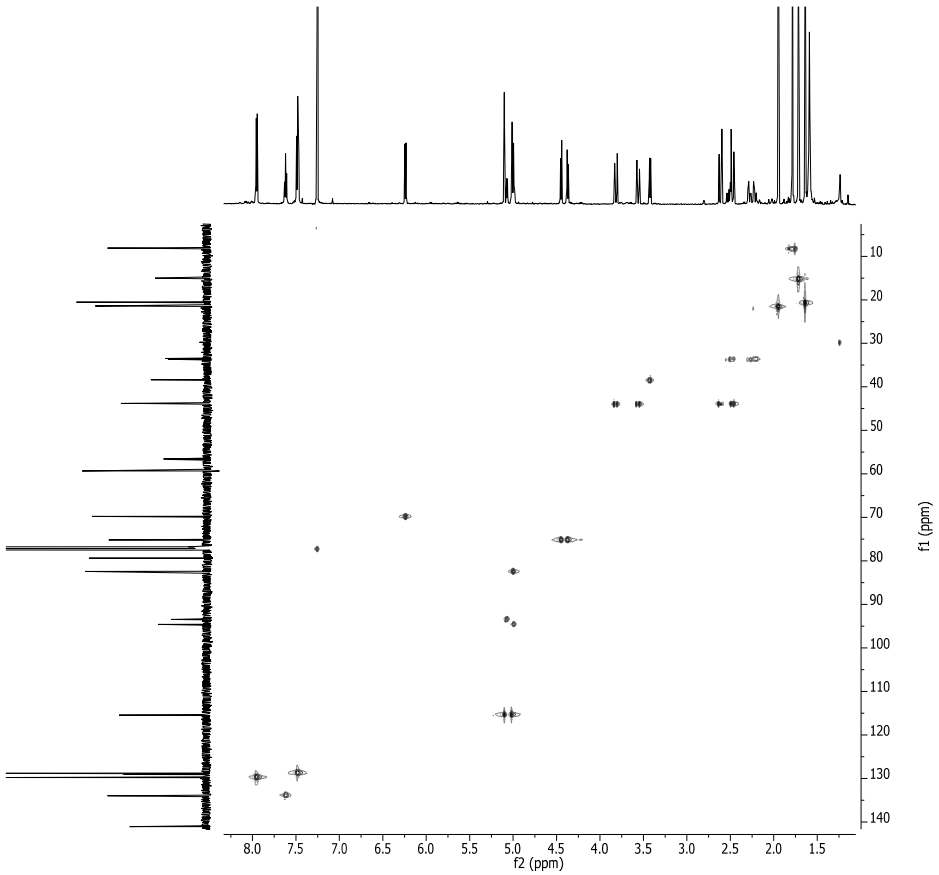
COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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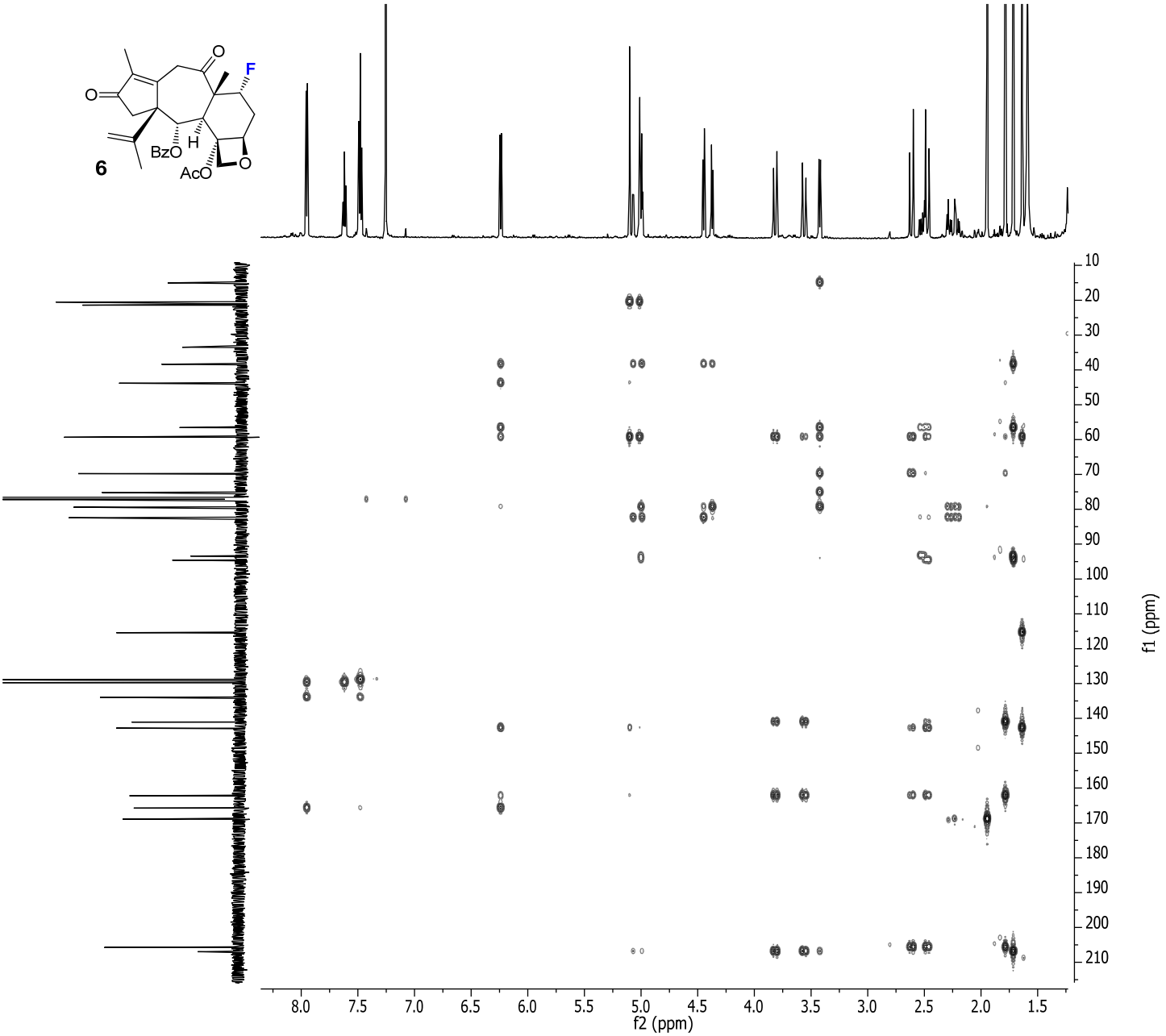

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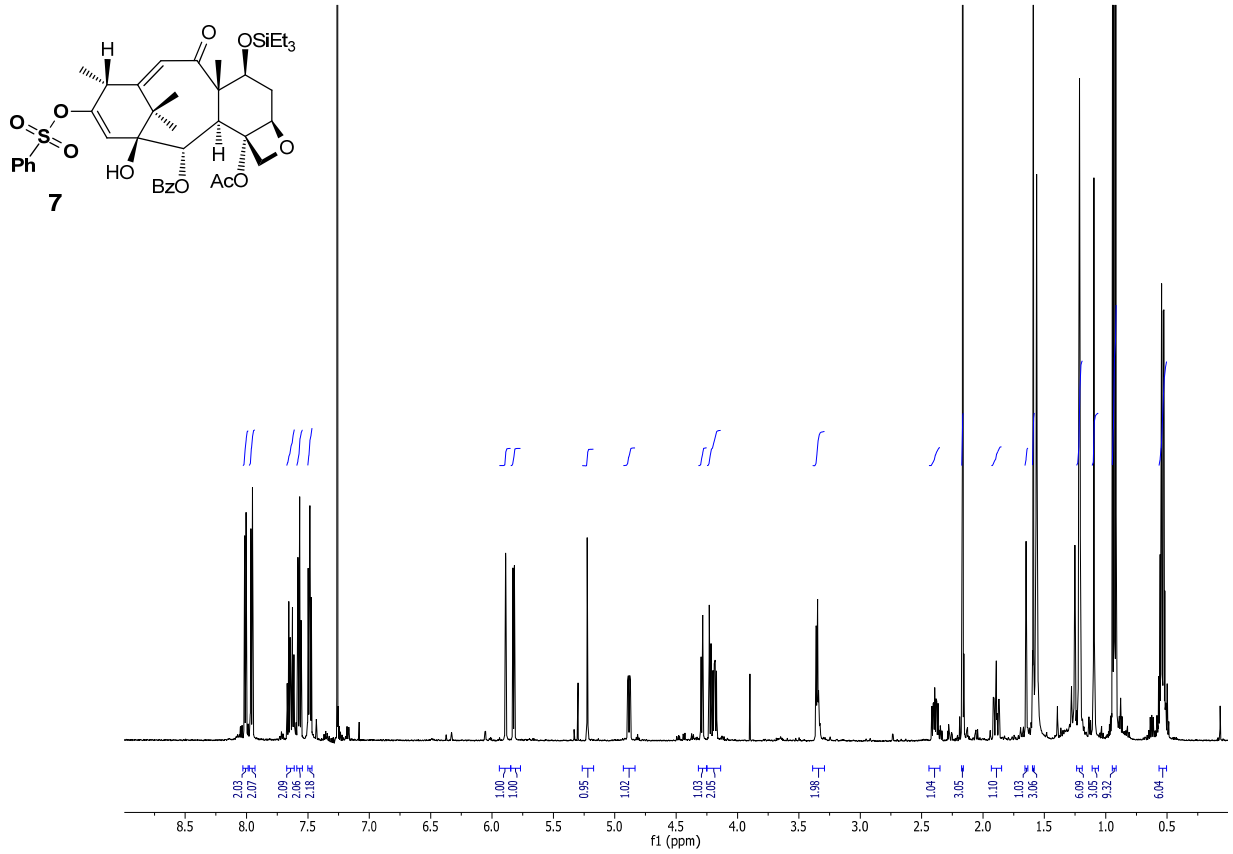

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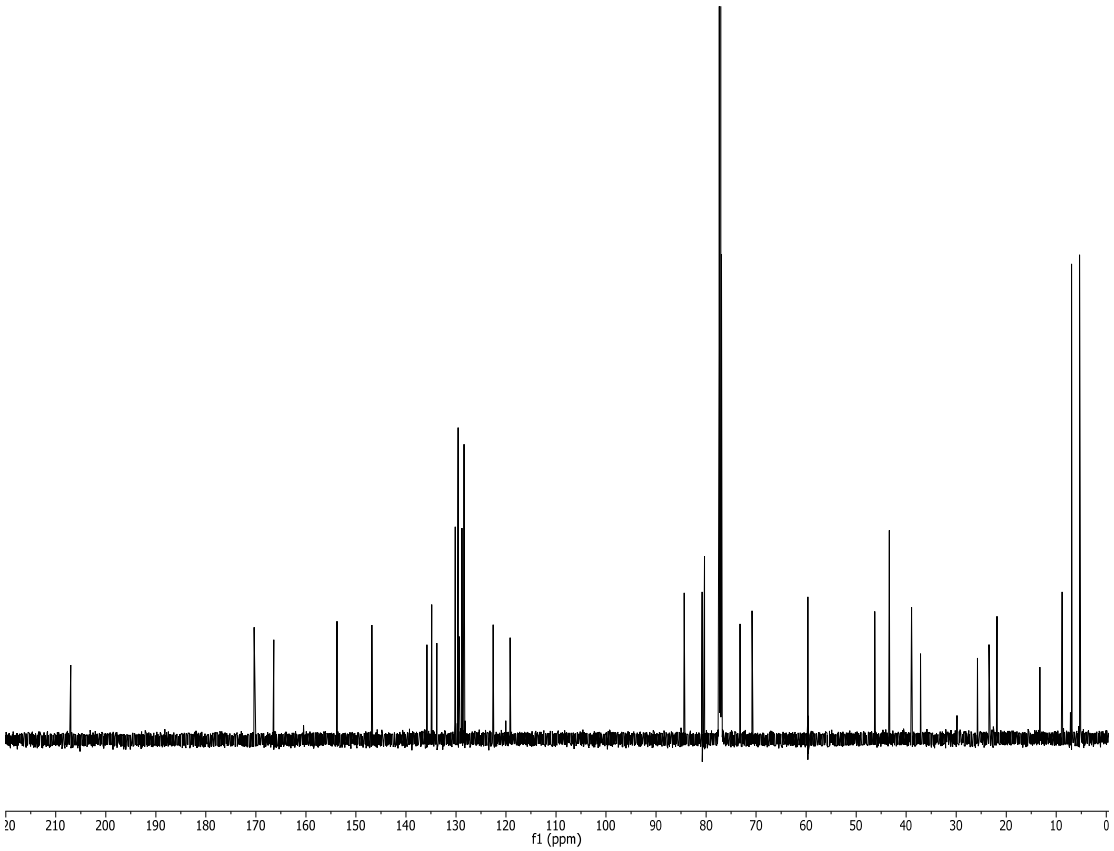

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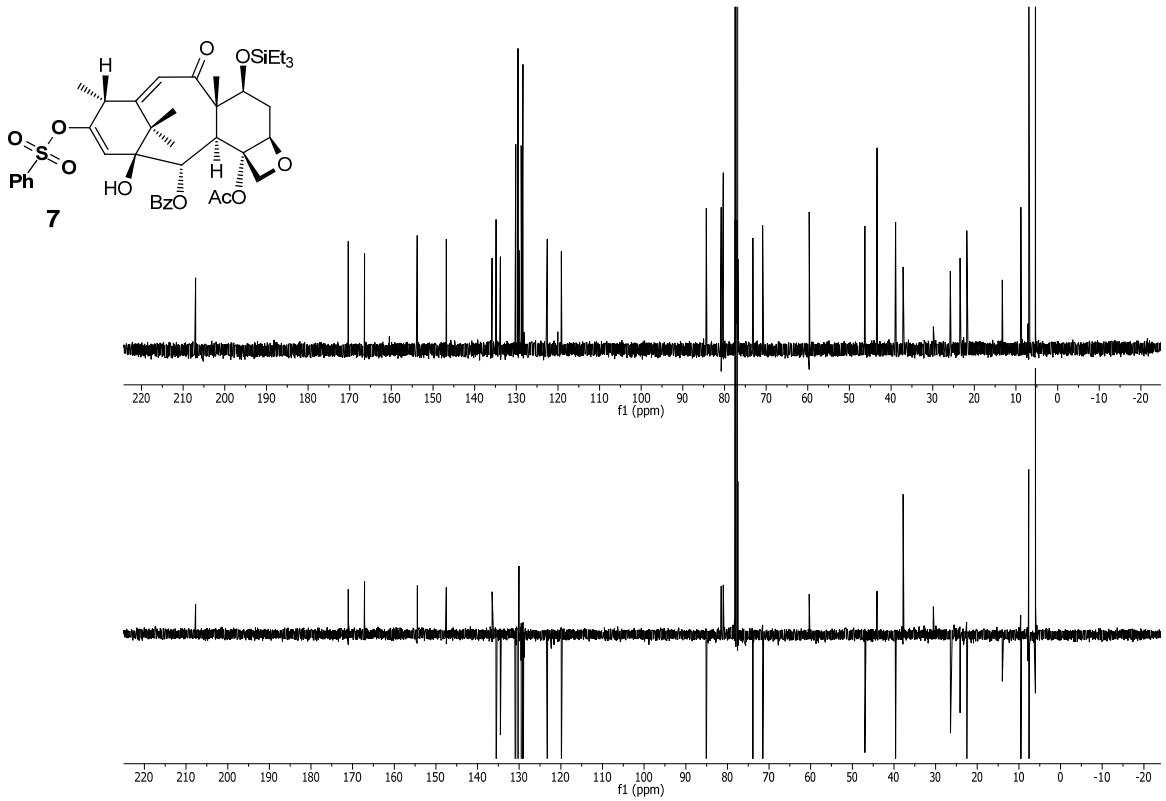

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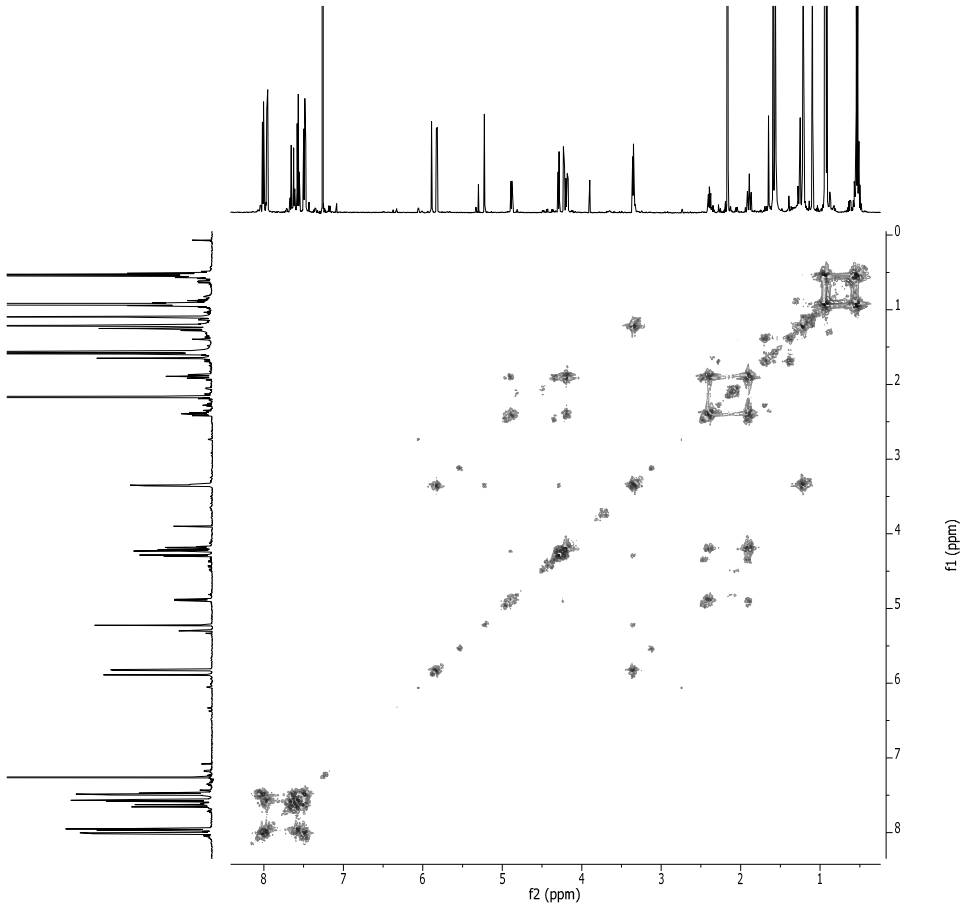

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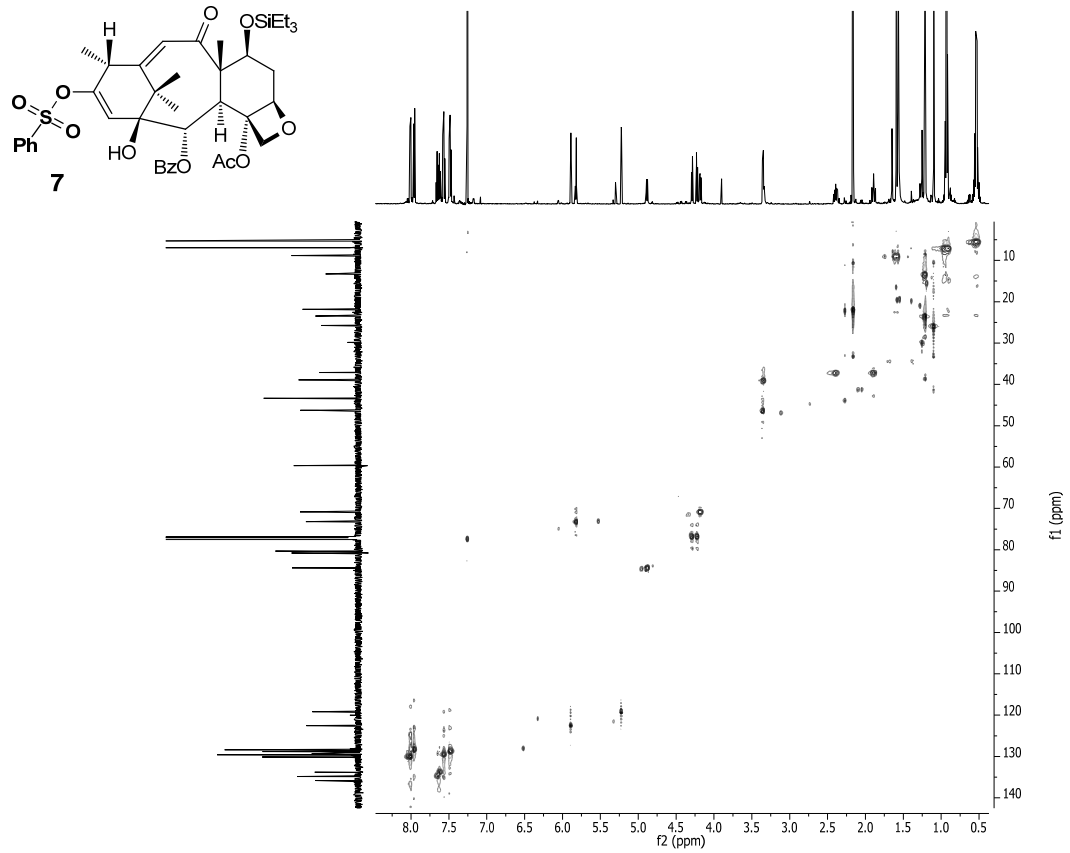
HMQC (600 MHz, $CDCl_3$):



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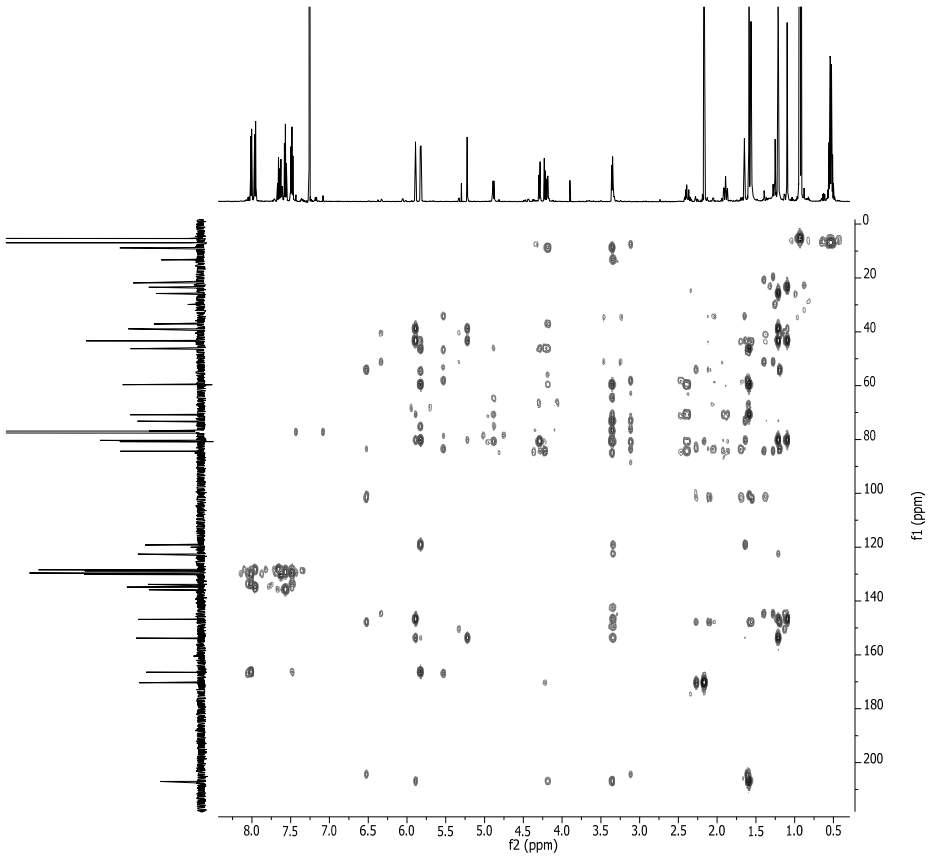

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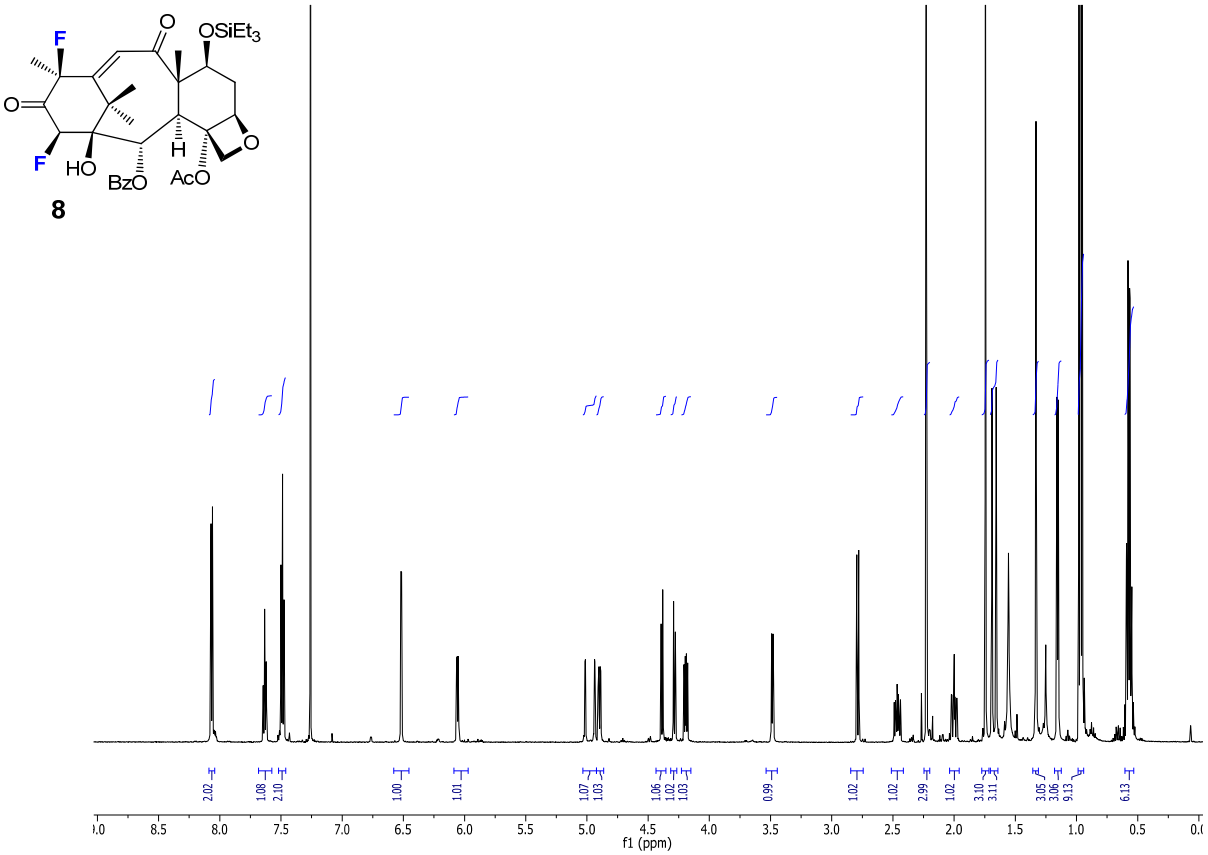
^{1}H NMR (600 MHz, $CDCl_3$):



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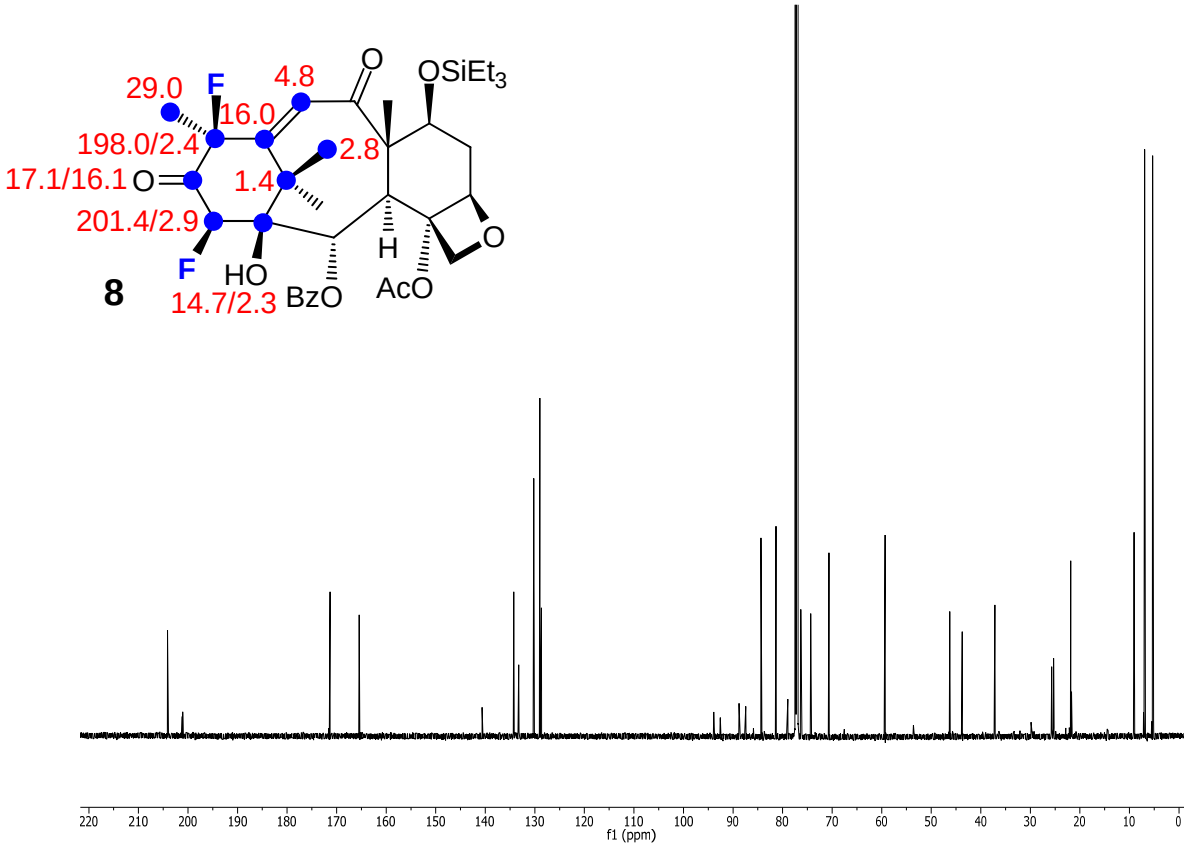

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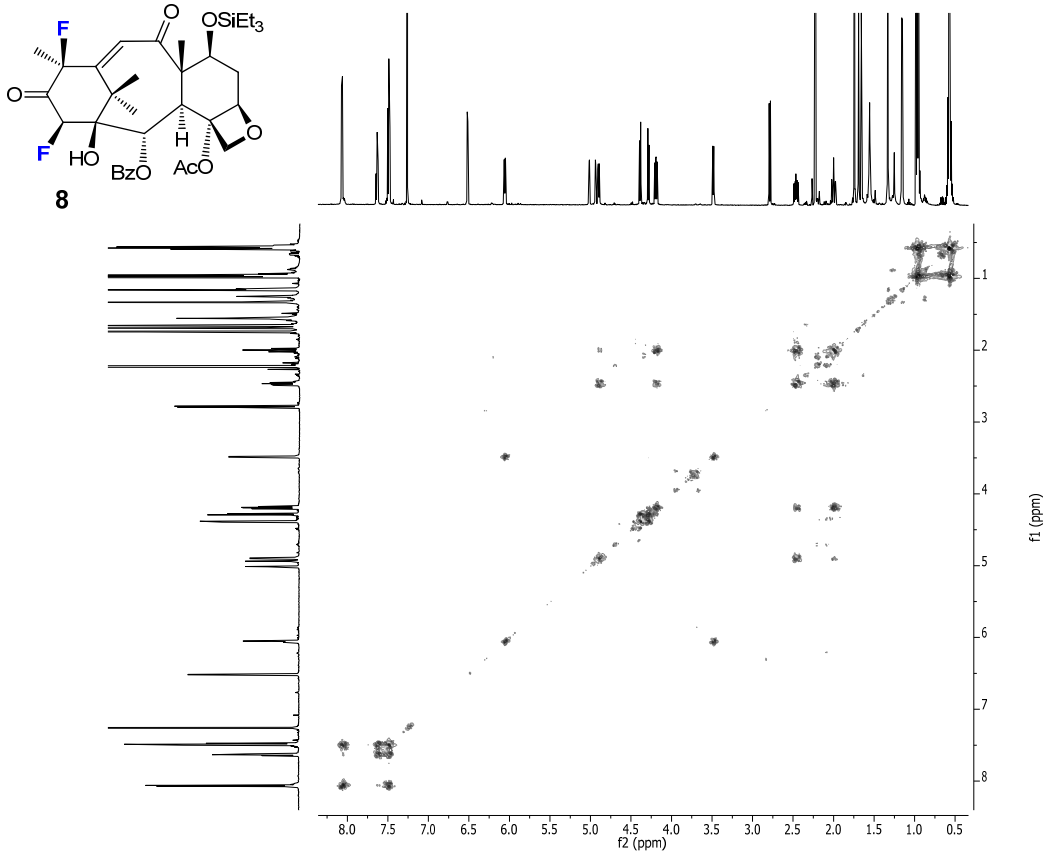

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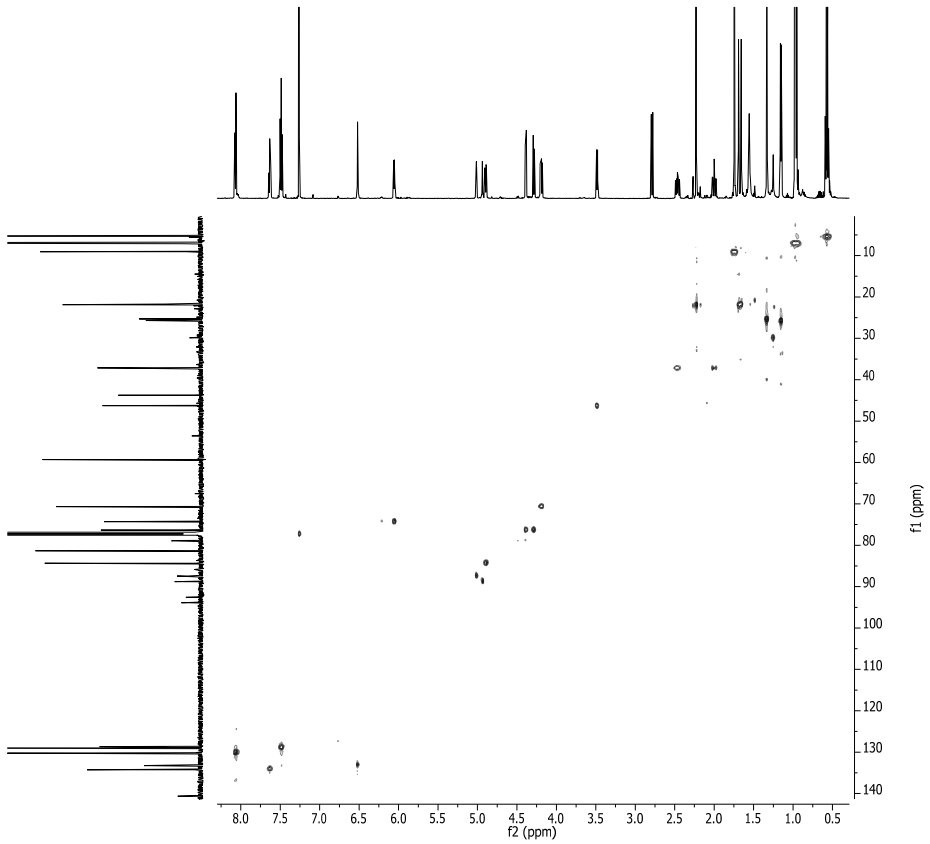

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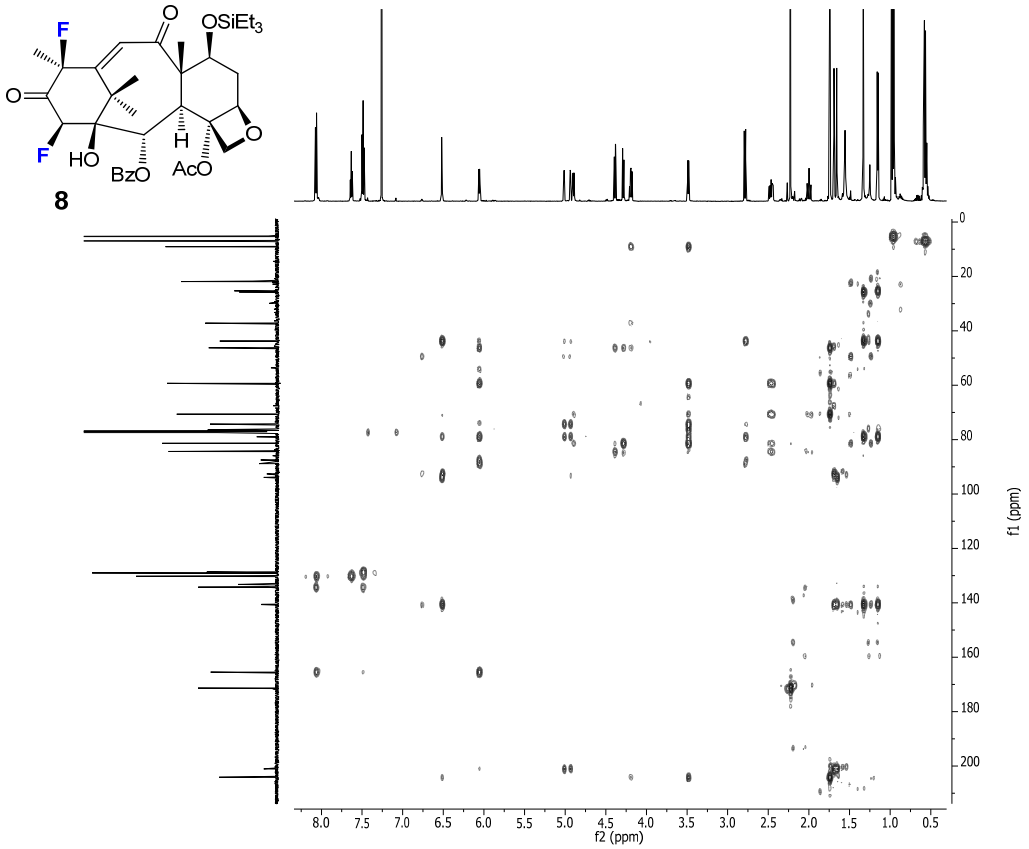
HMBC (600 MHz, $CDCl_3$):



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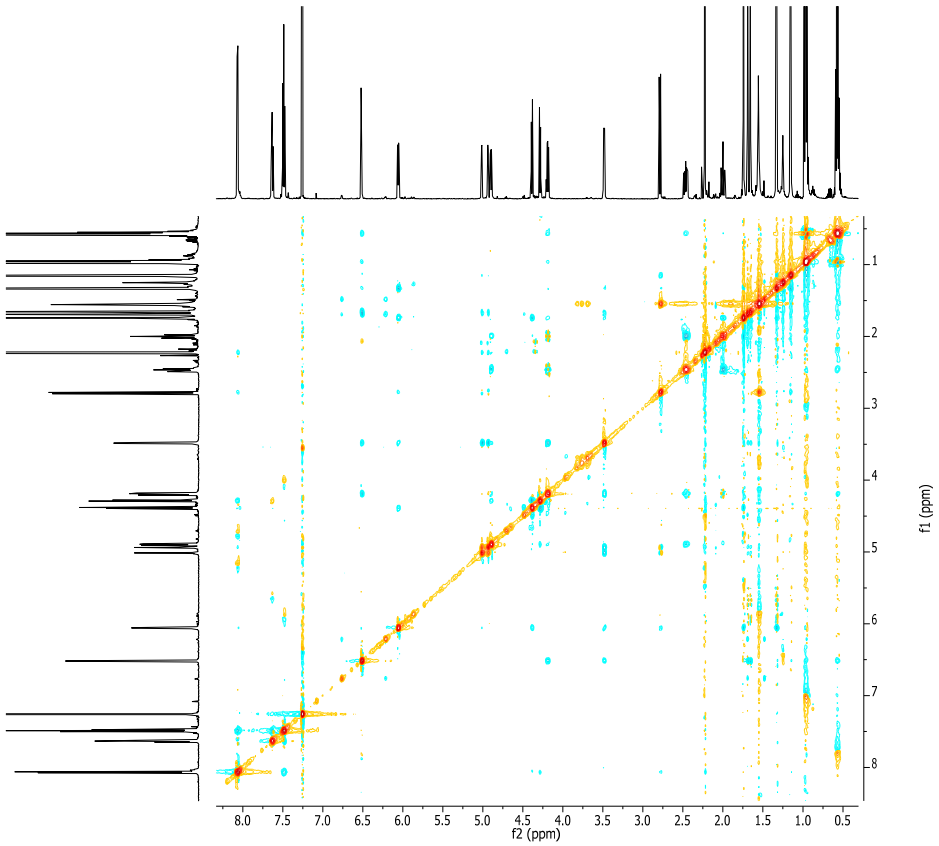

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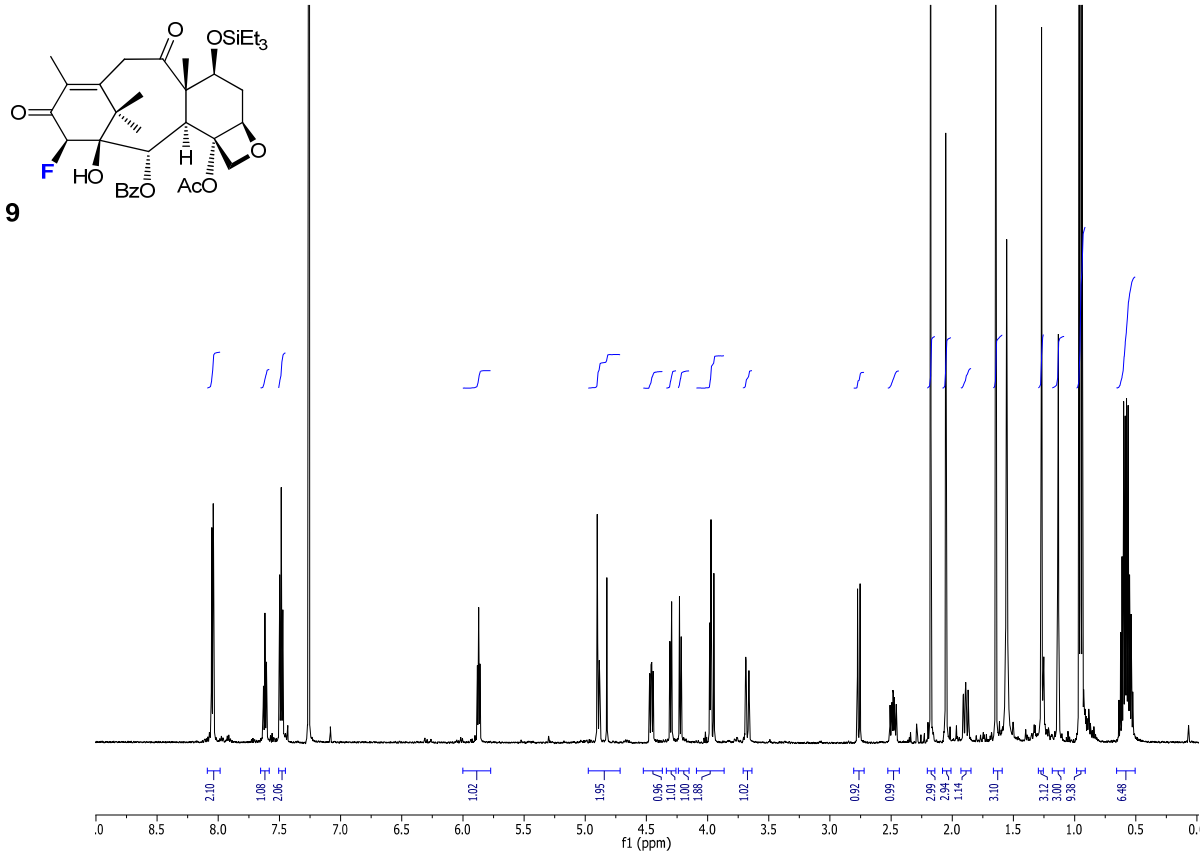
^{1}H NMR (600 MHz, $CDCl_3$):



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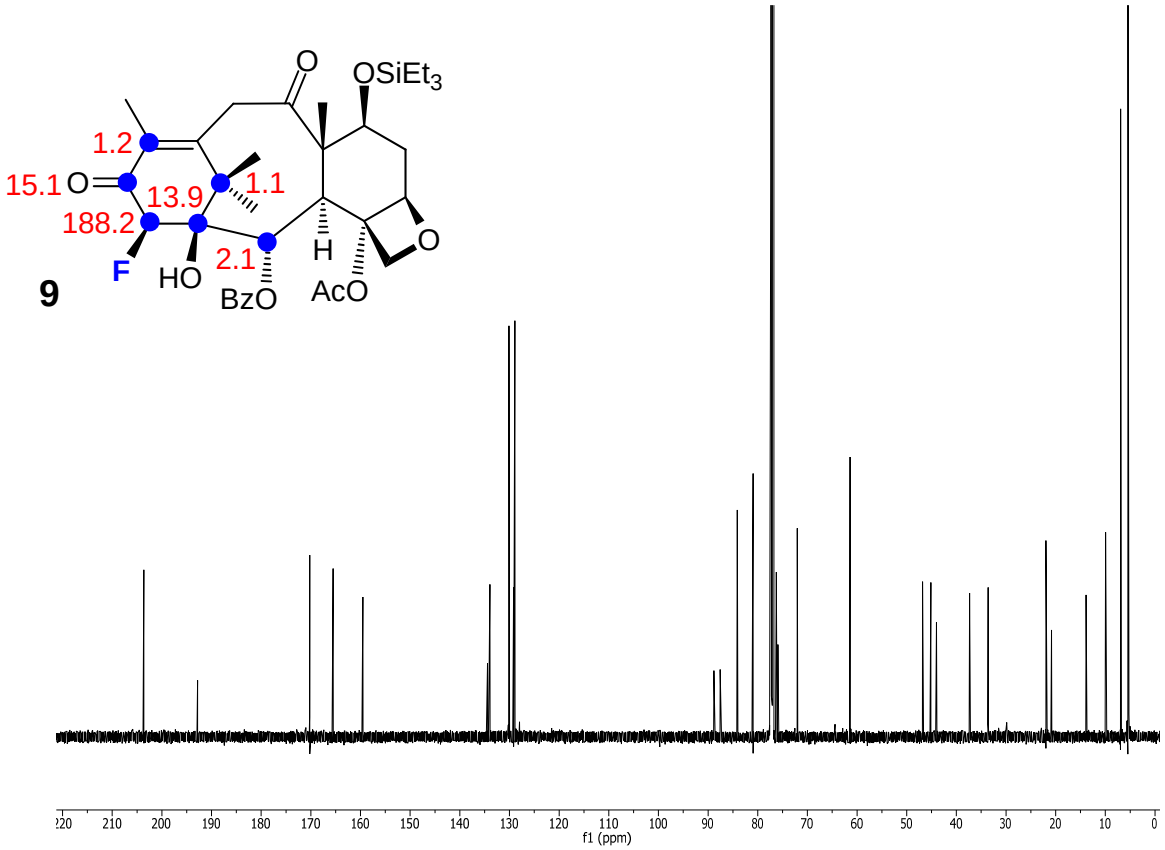

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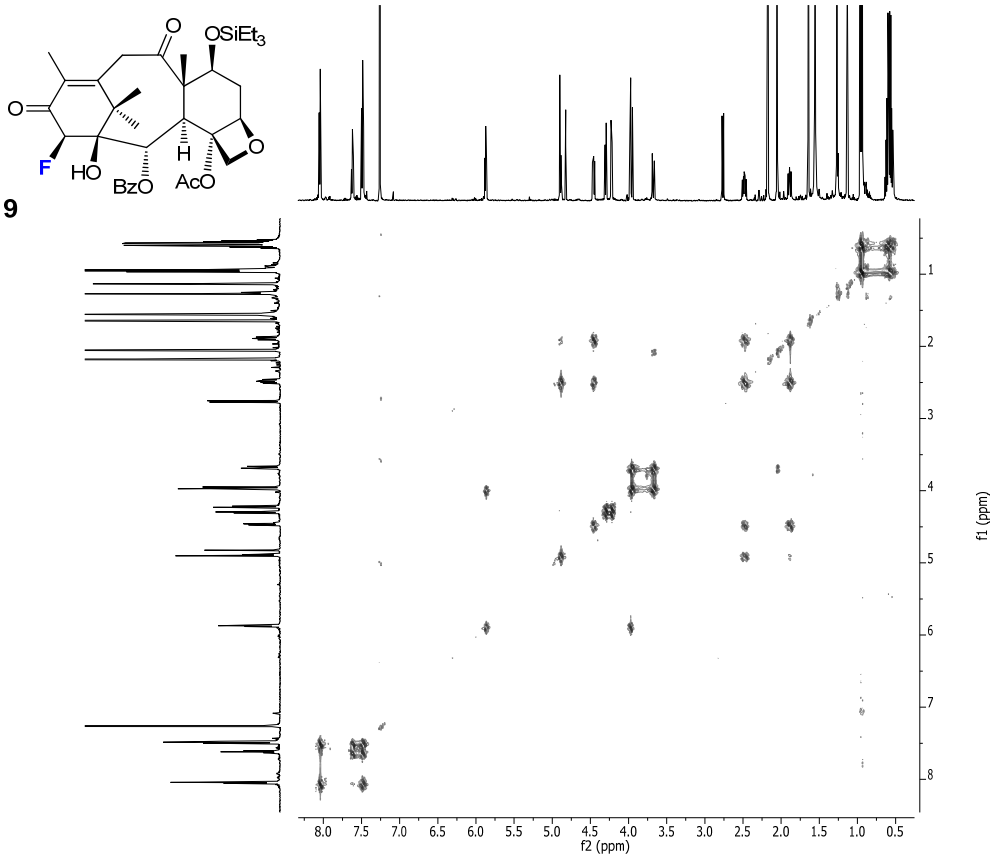

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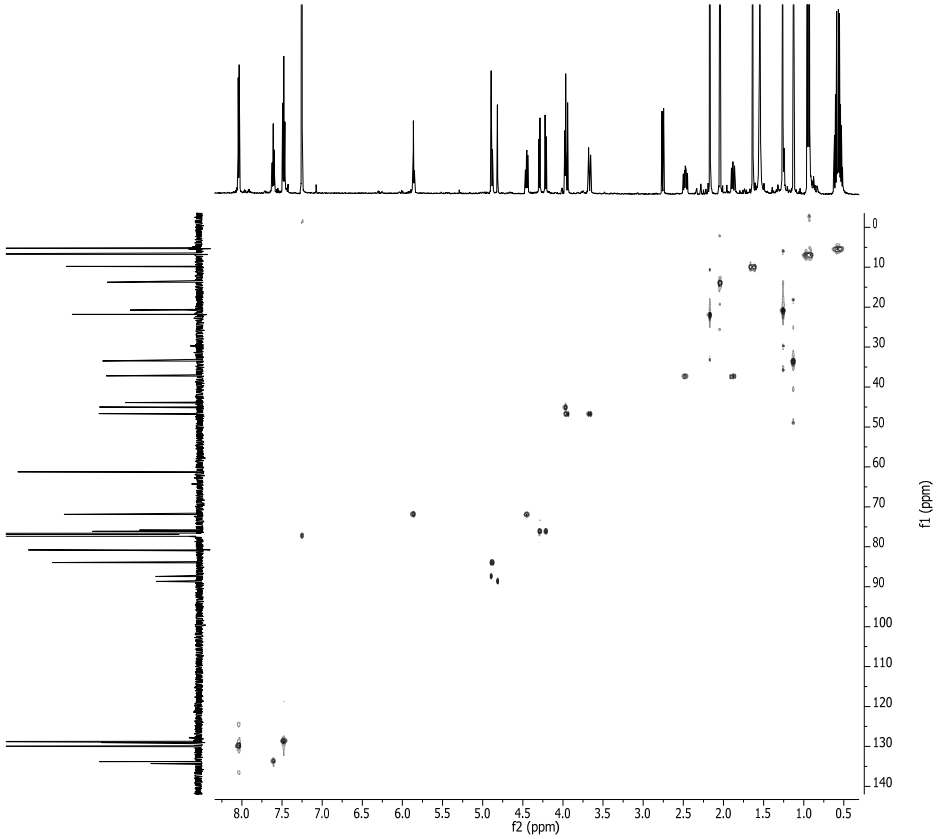
HMQC (600 MHz, $CDCl_3$):



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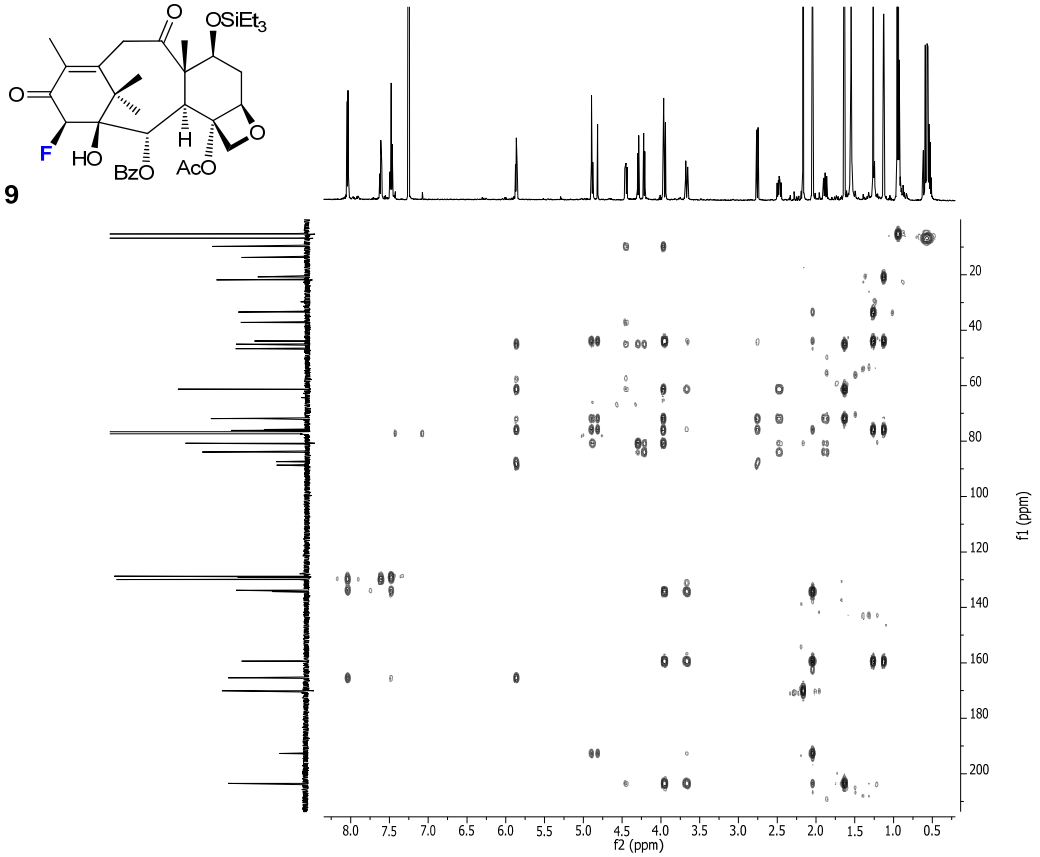
HMBC (600 MHz, $CDCl_3$):



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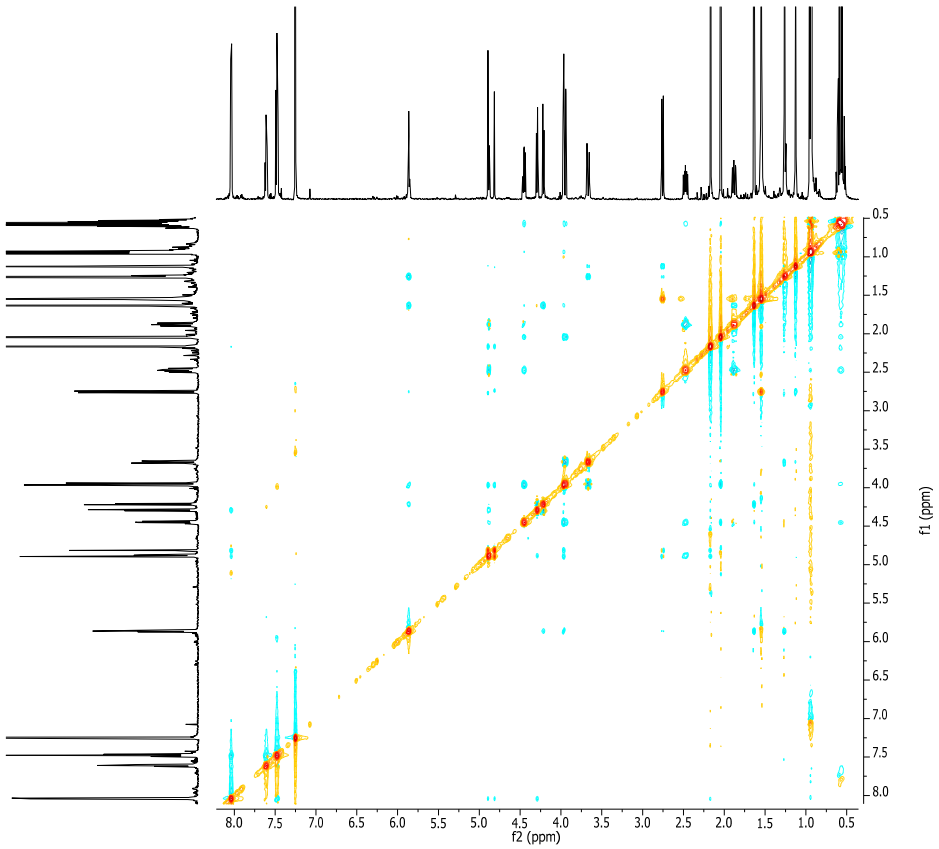

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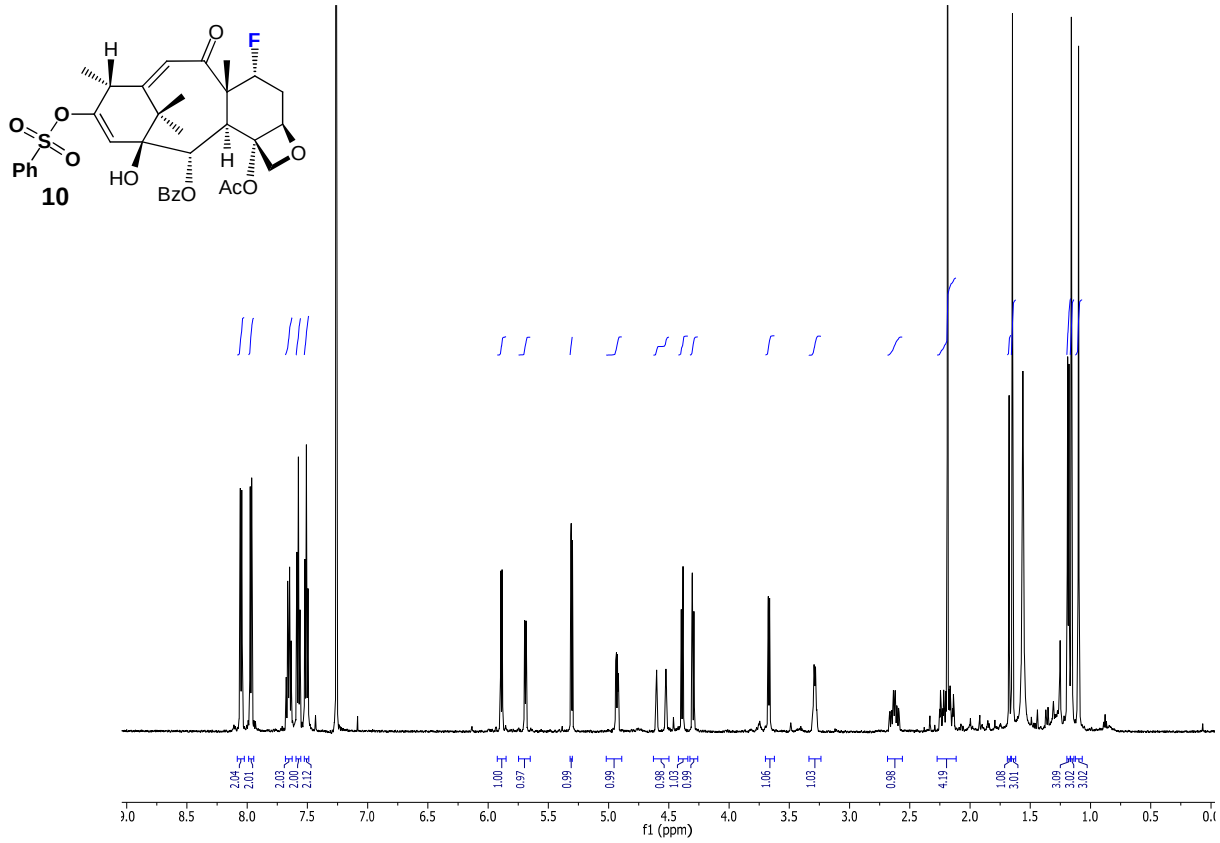
^{1}H NMR (600 MHz, $CDCl_3$):



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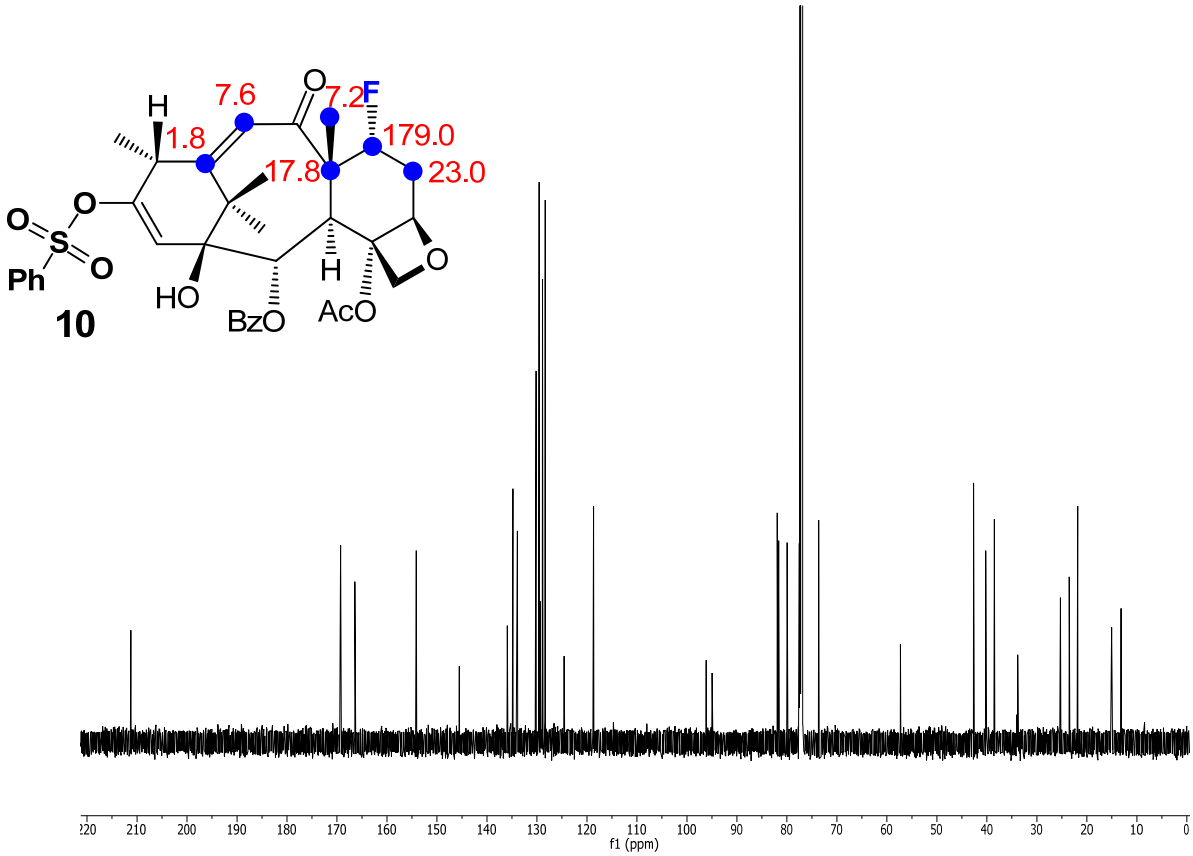

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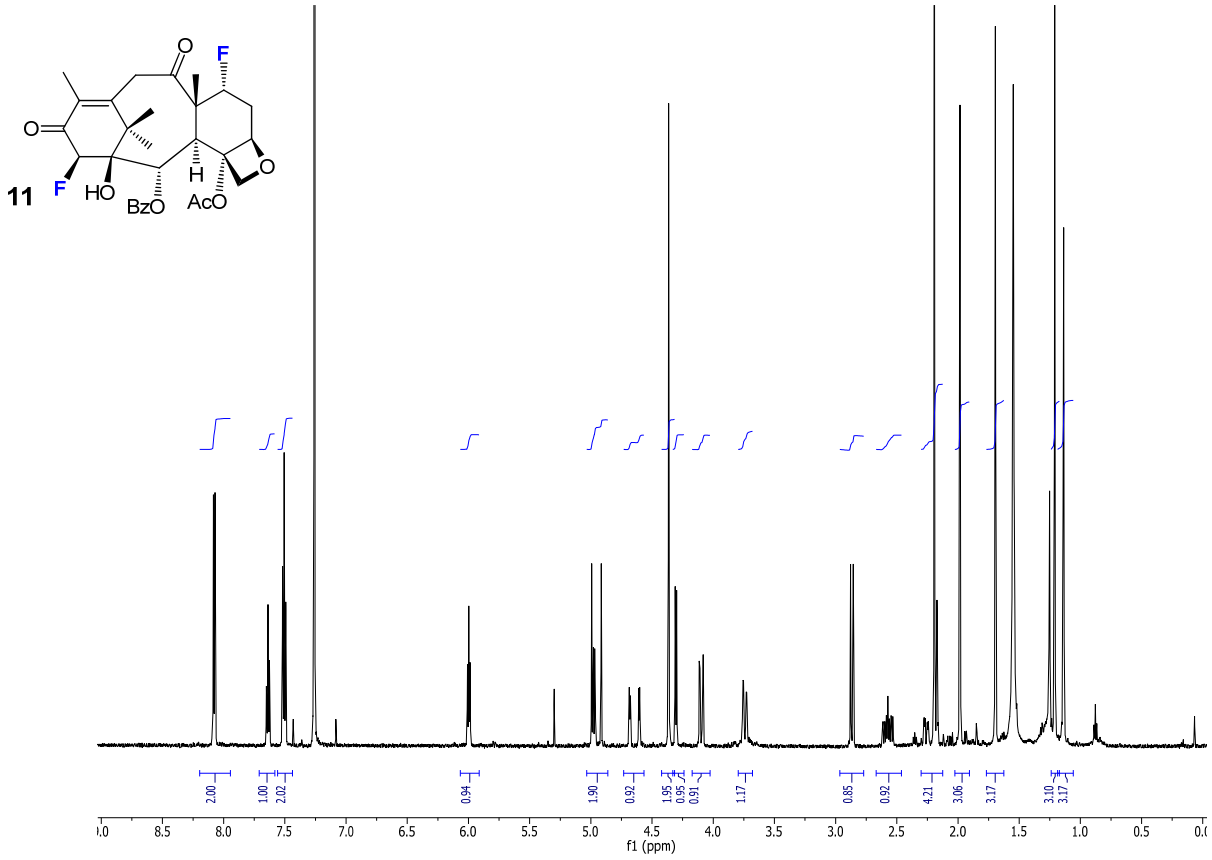

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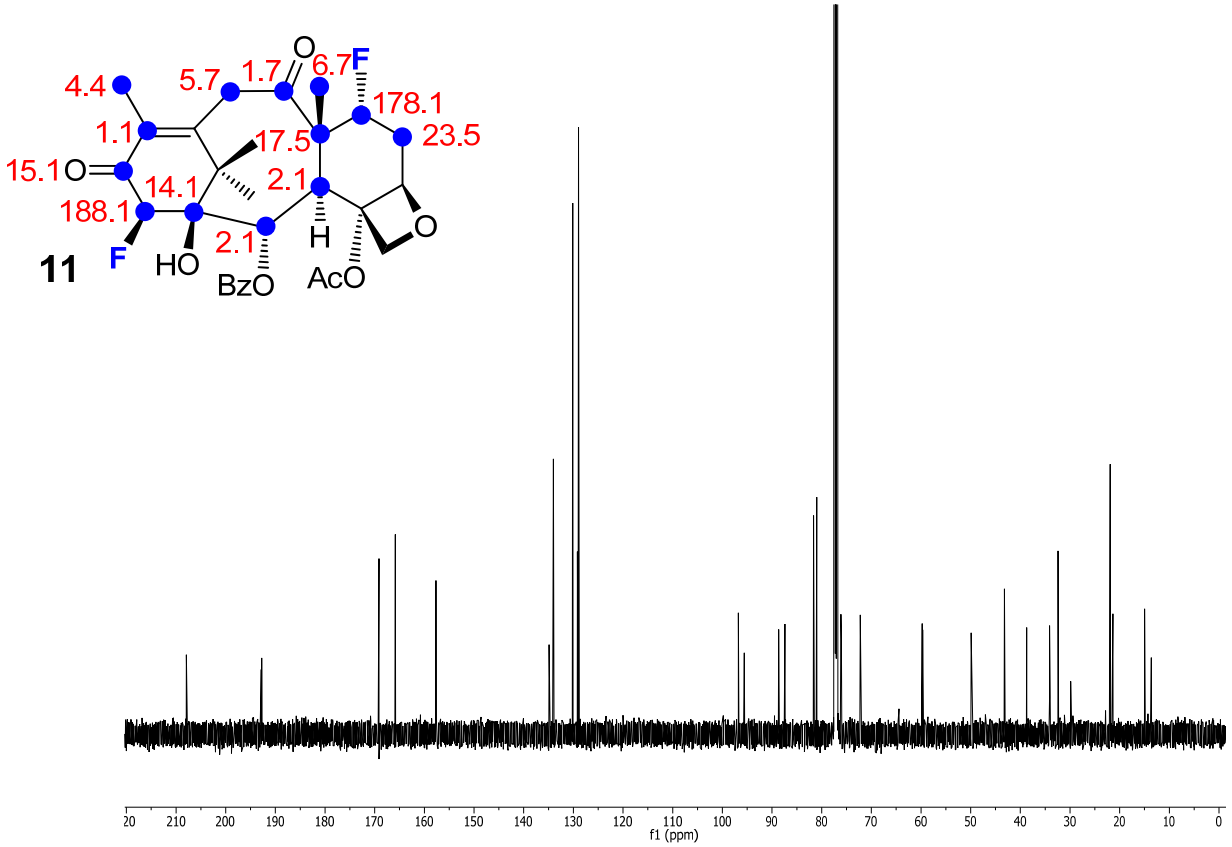

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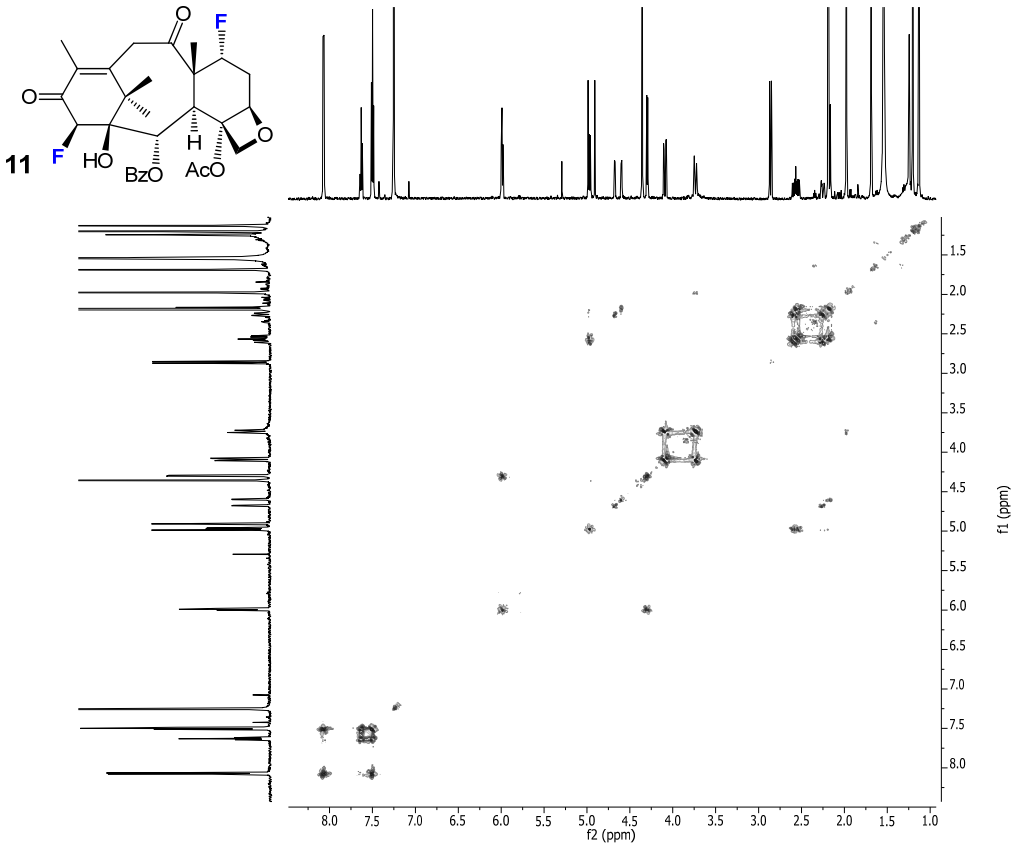
COSY (600 MHz, $CDCl_3$):



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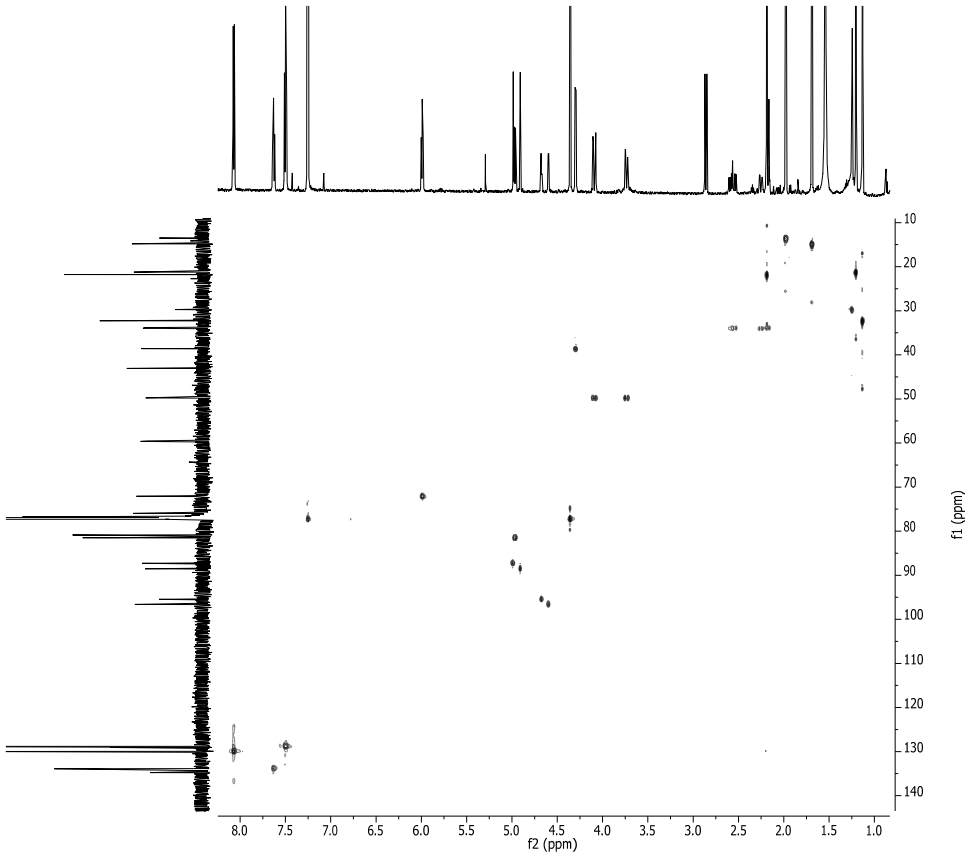

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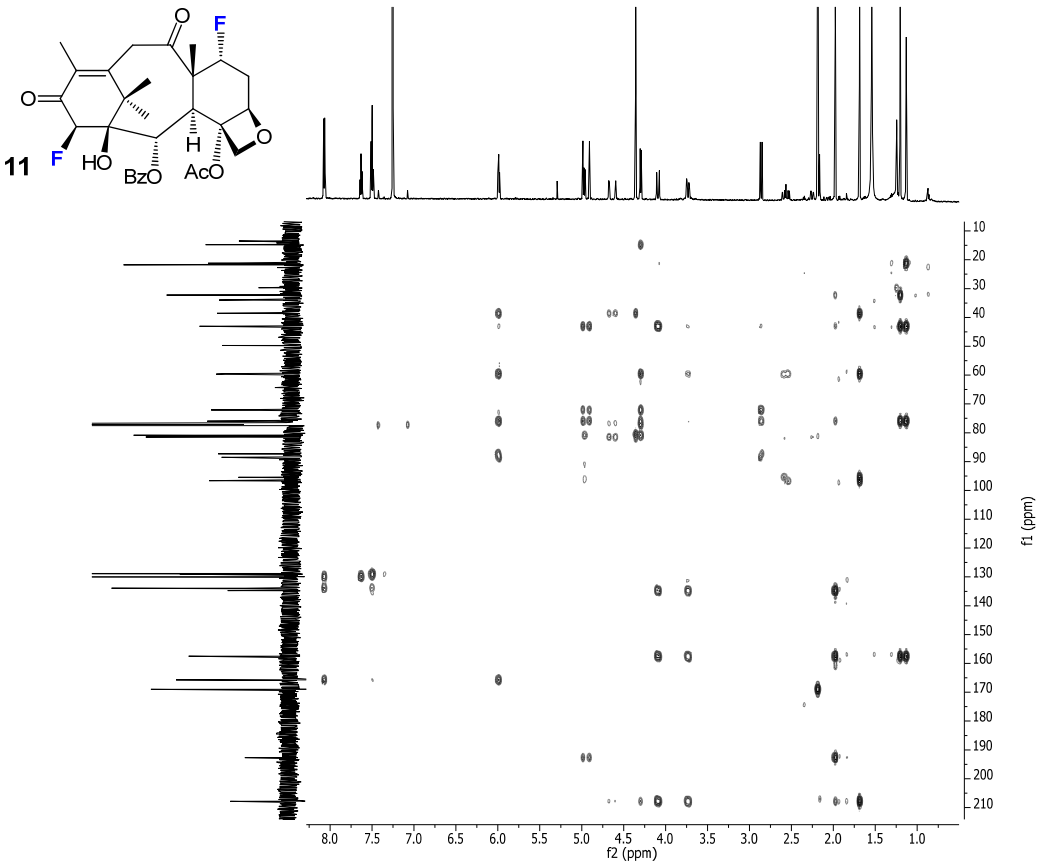
HMBC (600 MHz, $CDCl_3$):



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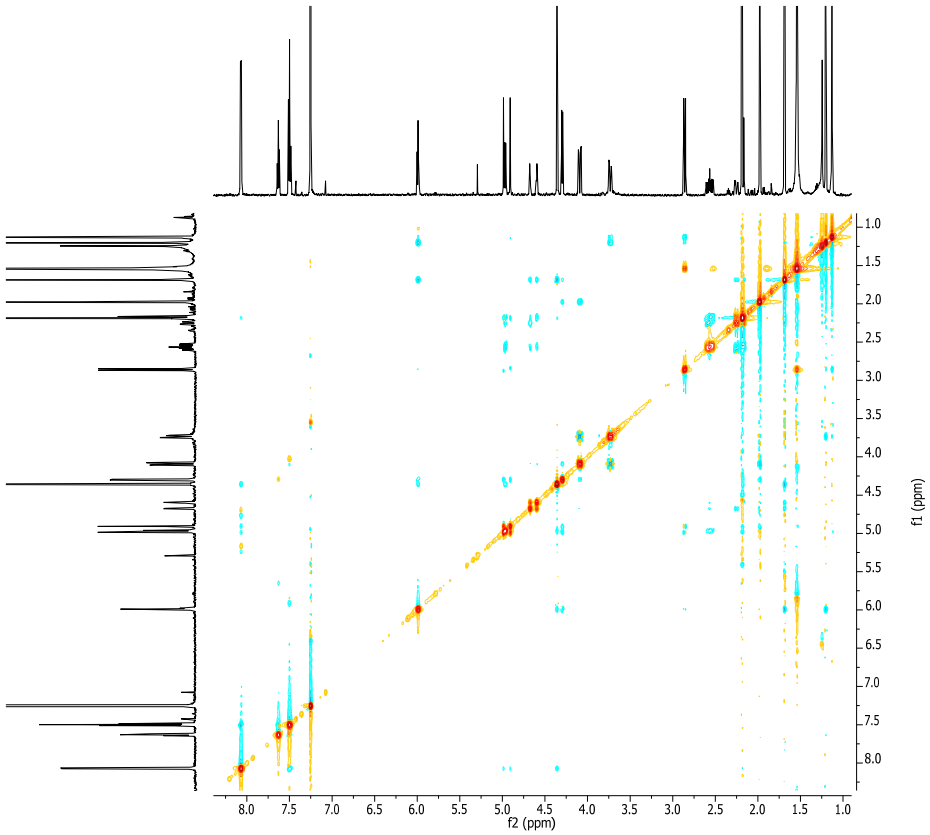

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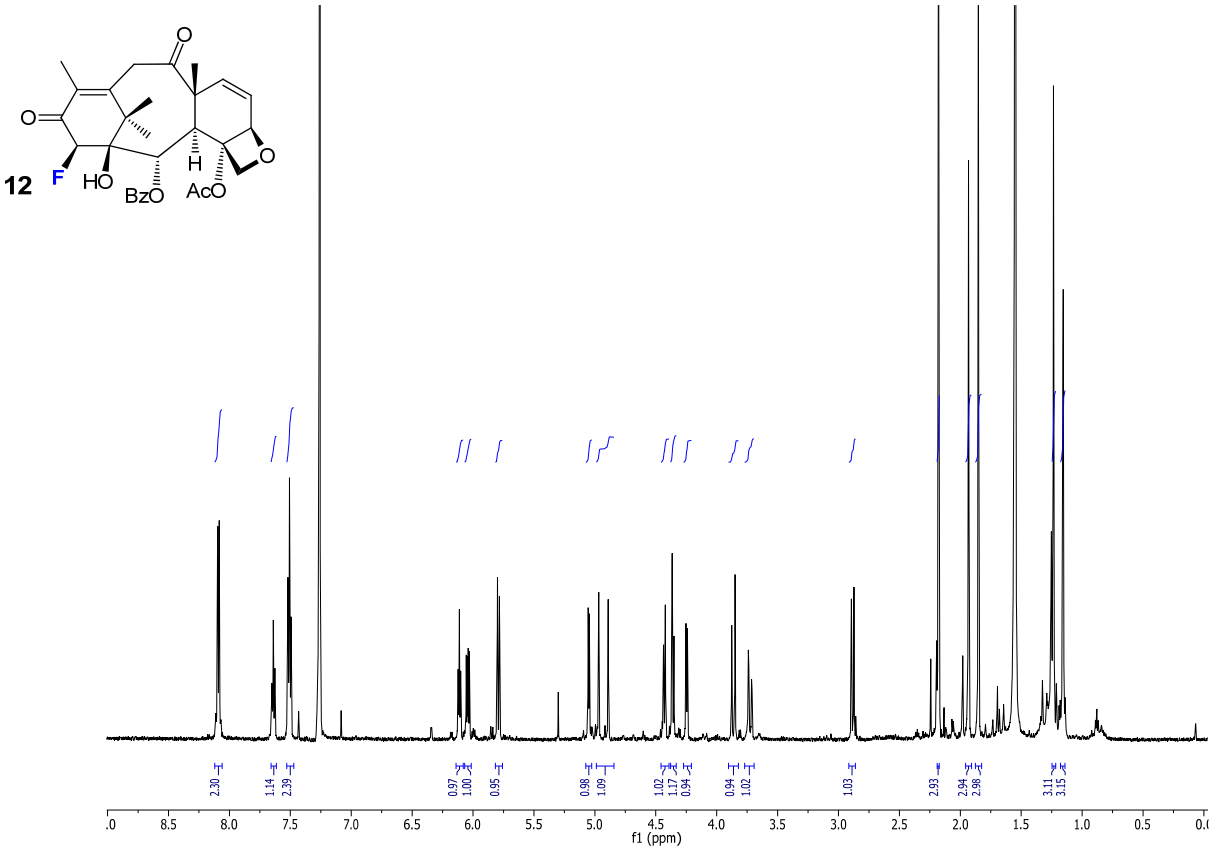
^{1}H NMR (600 MHz, $CDCl_3$):



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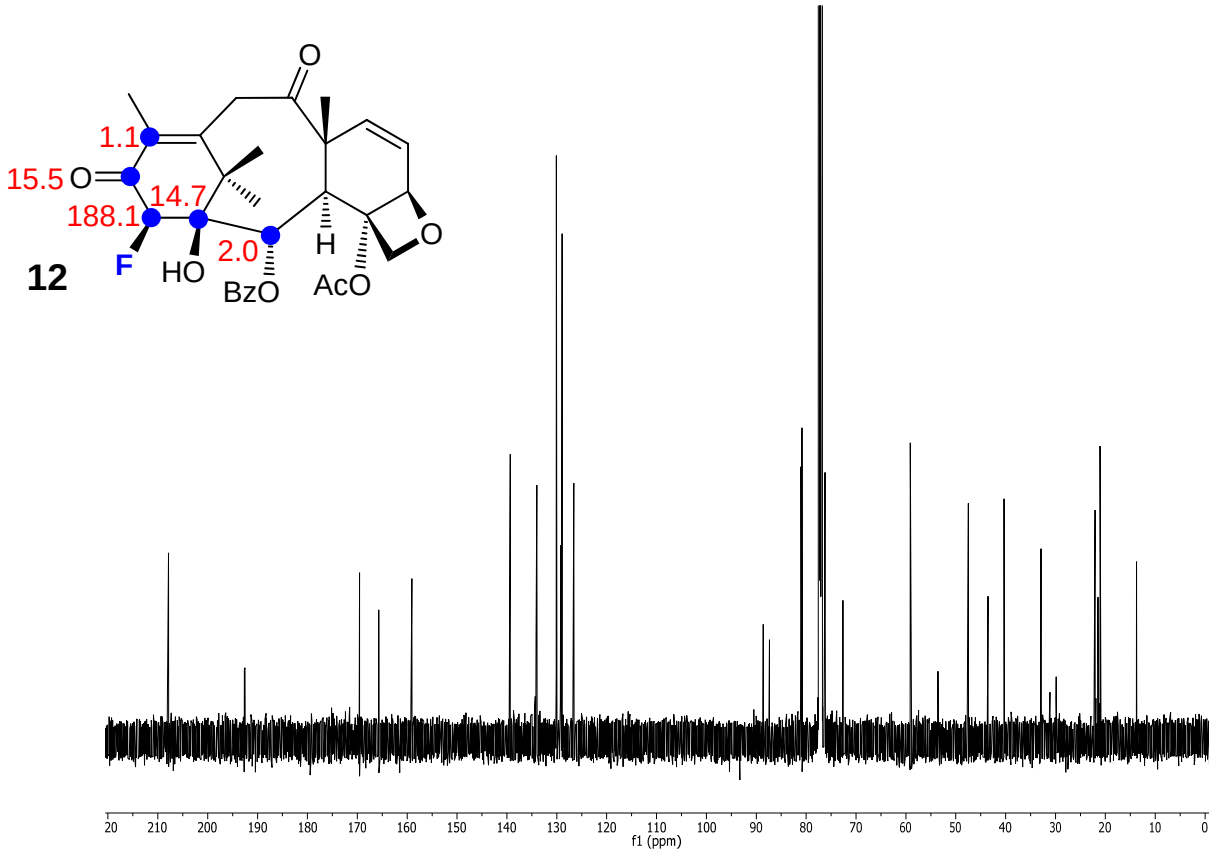

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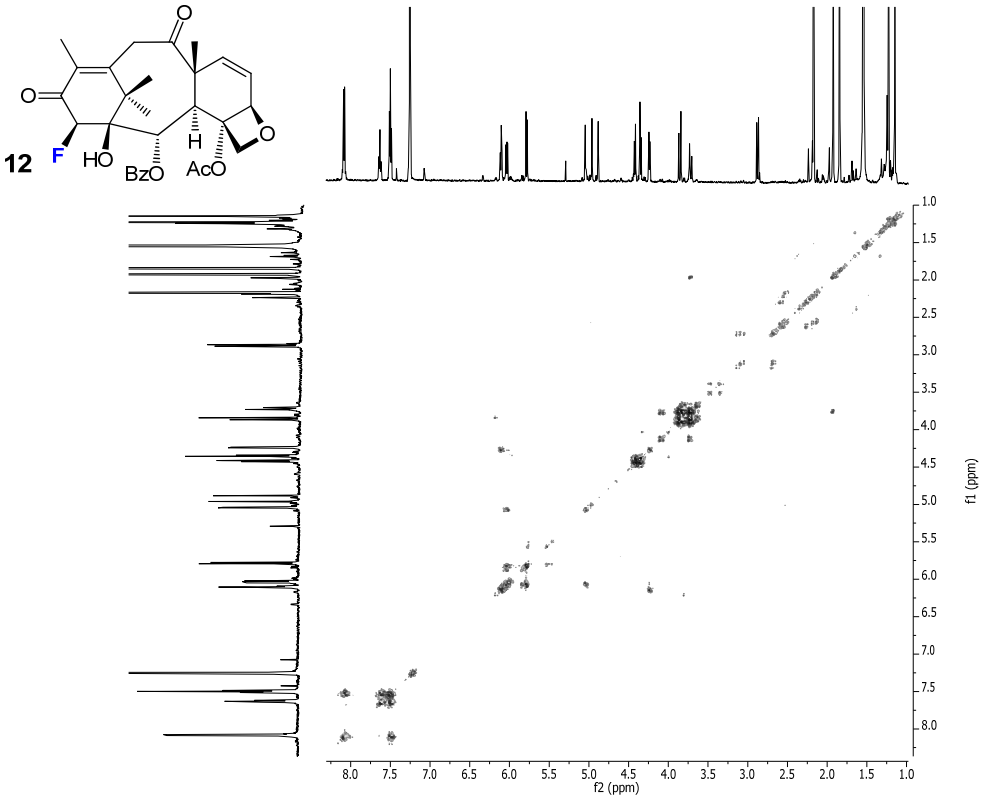
COSY (600 MHz, $CDCl_3$):



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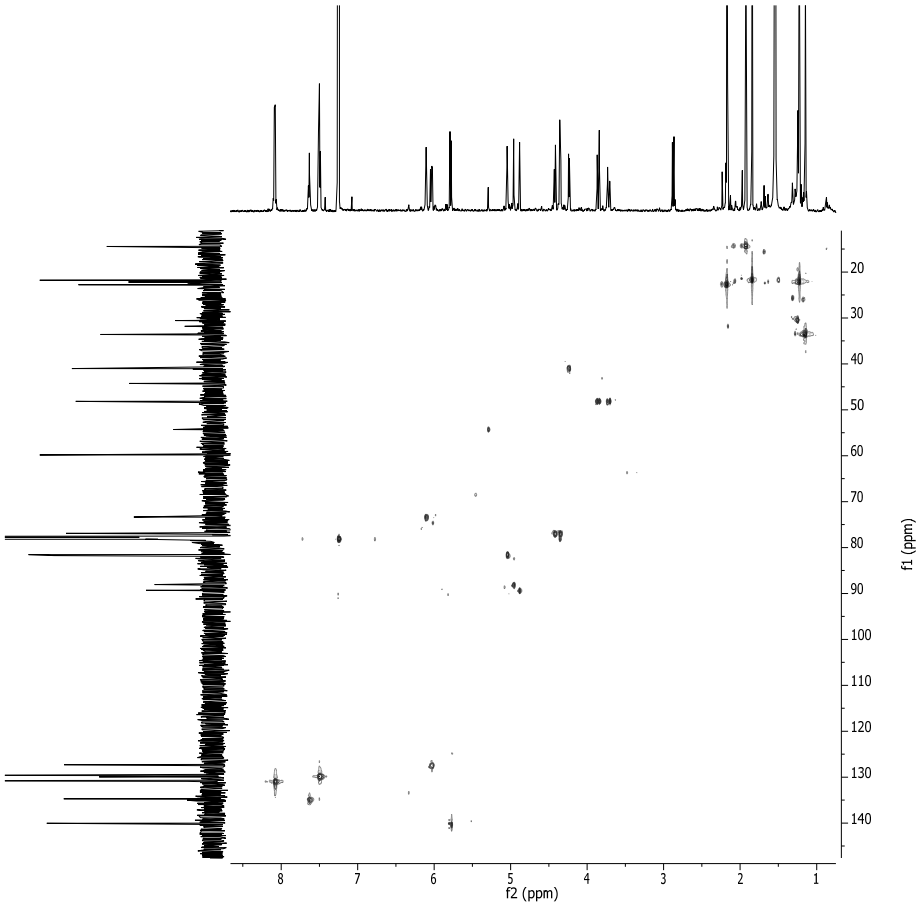

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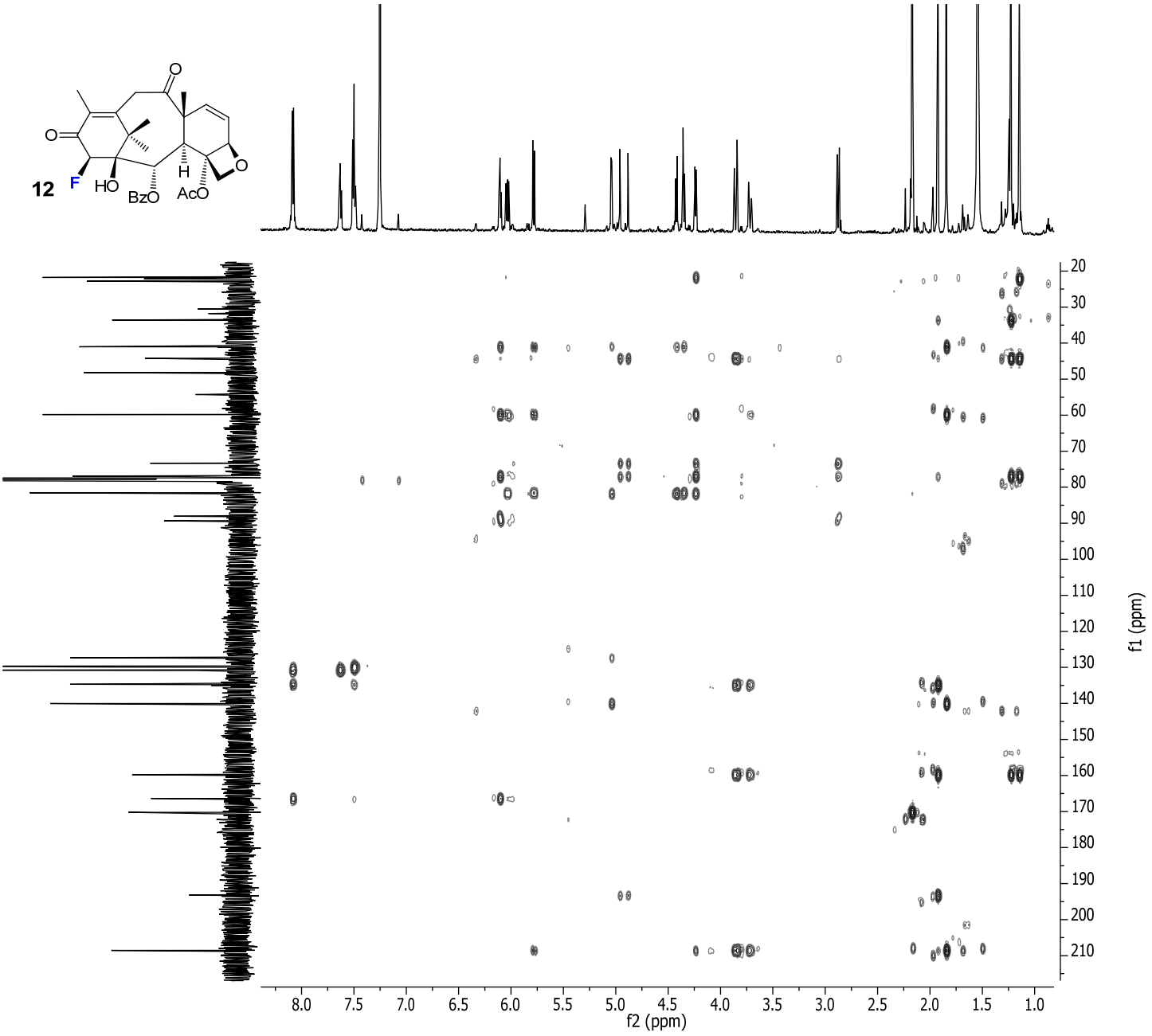

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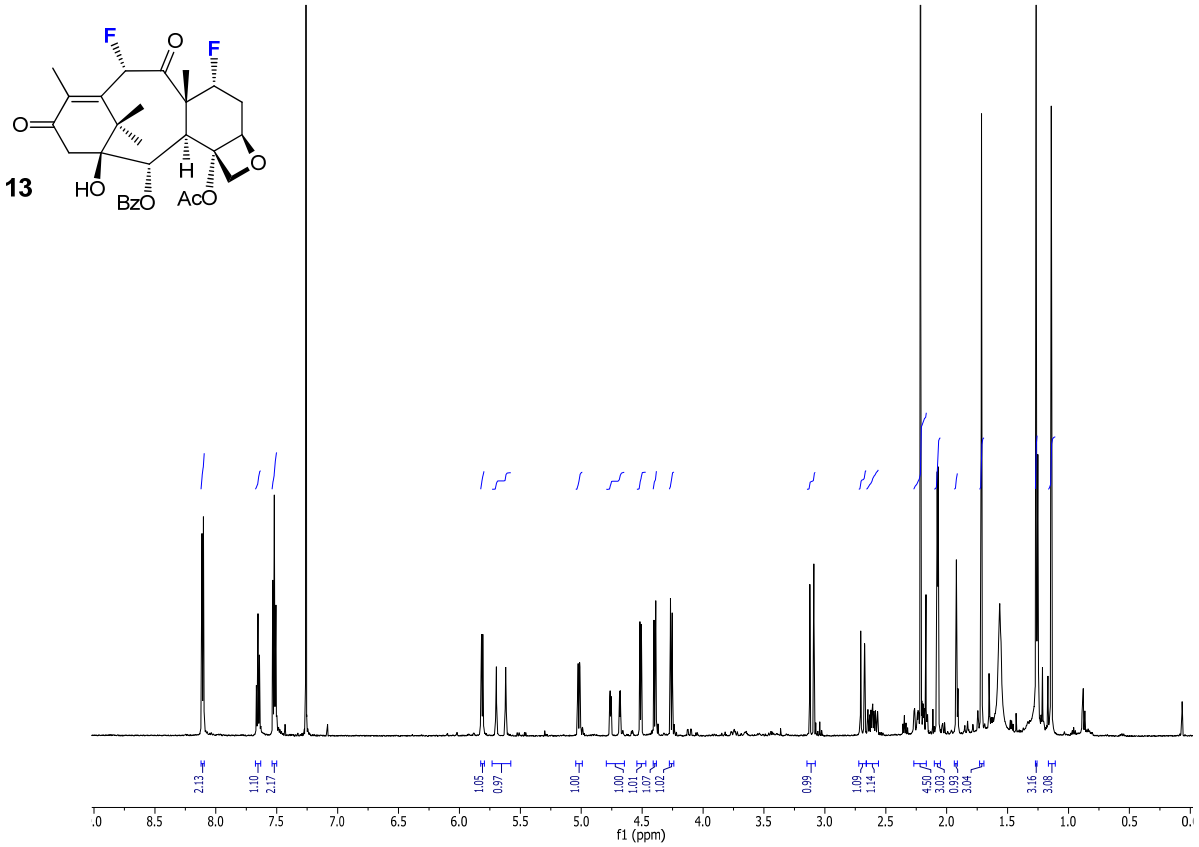
^{1}H NMR (600 MHz, $CDCl_3$):



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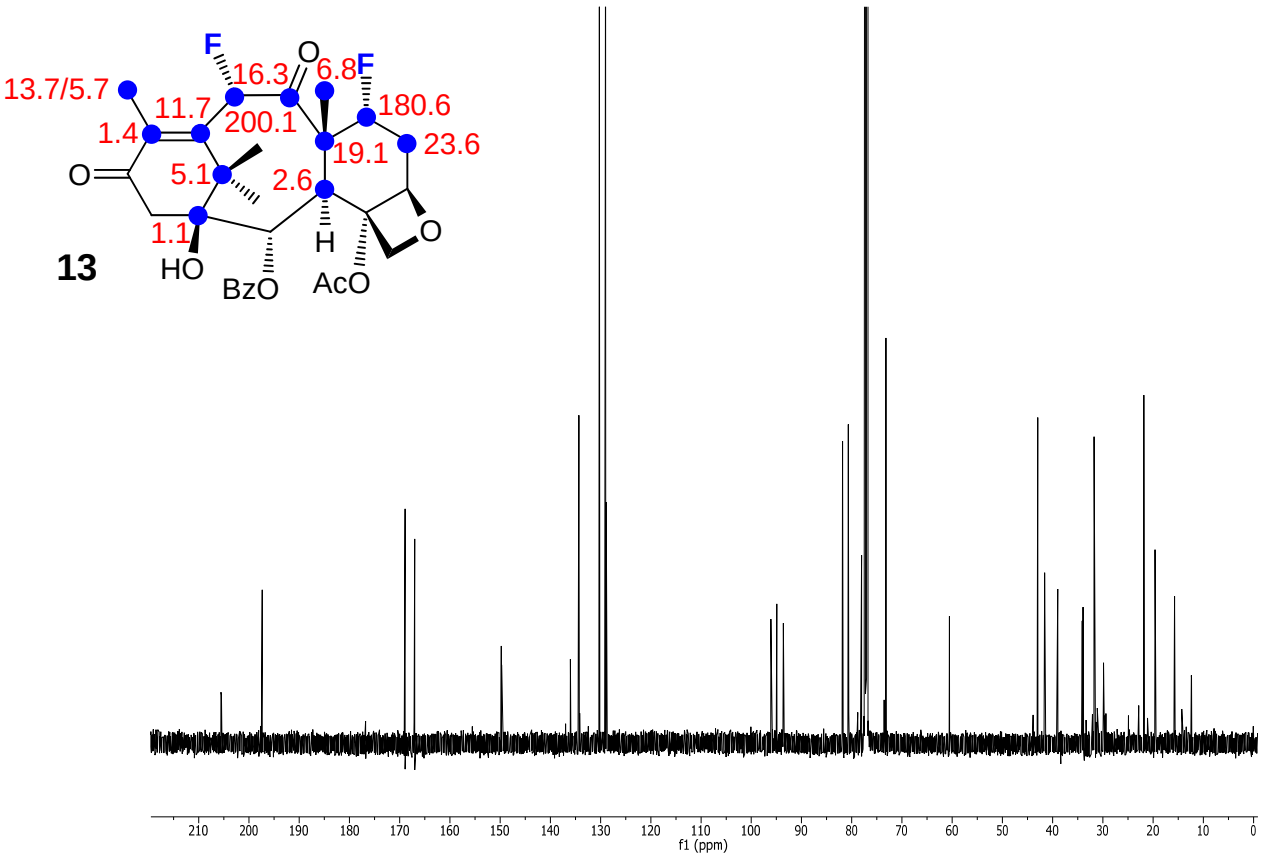

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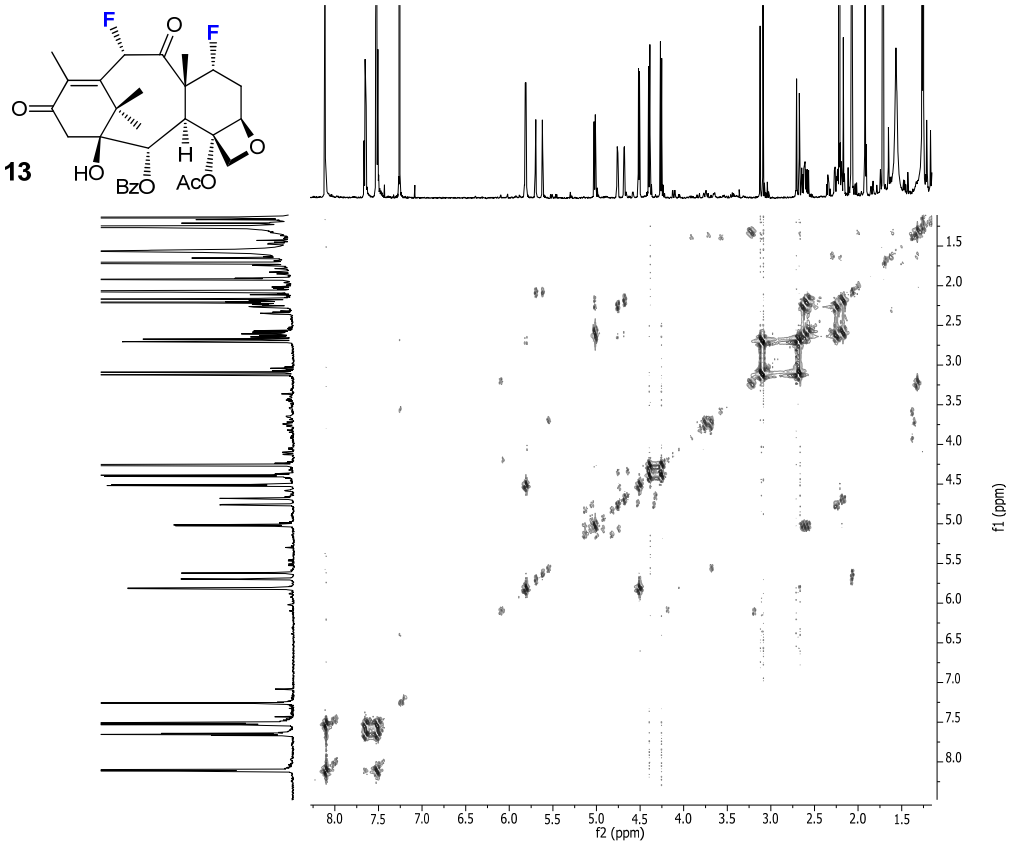

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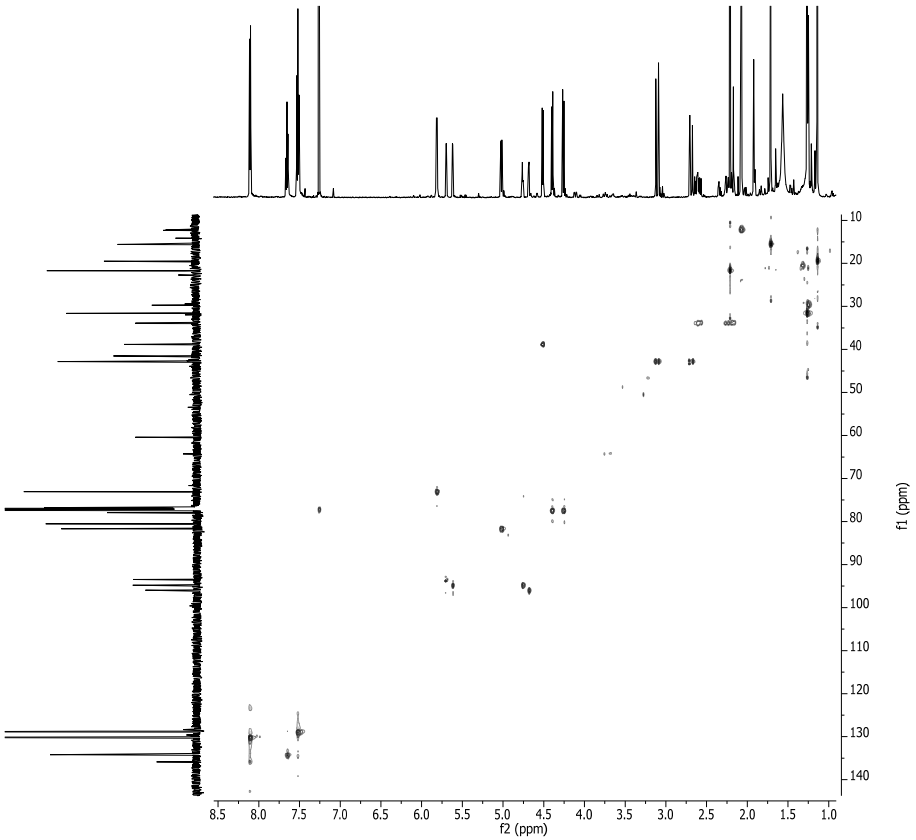

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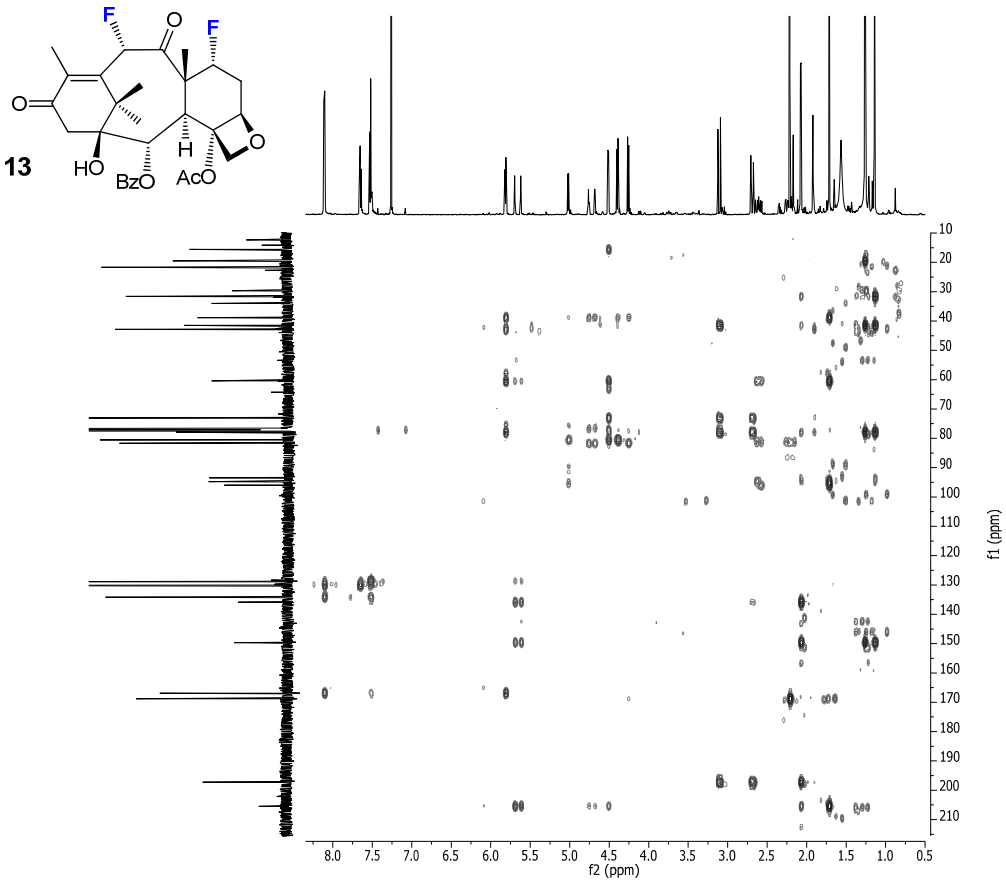
HMBC (600 MHz, $CDCl_3$):



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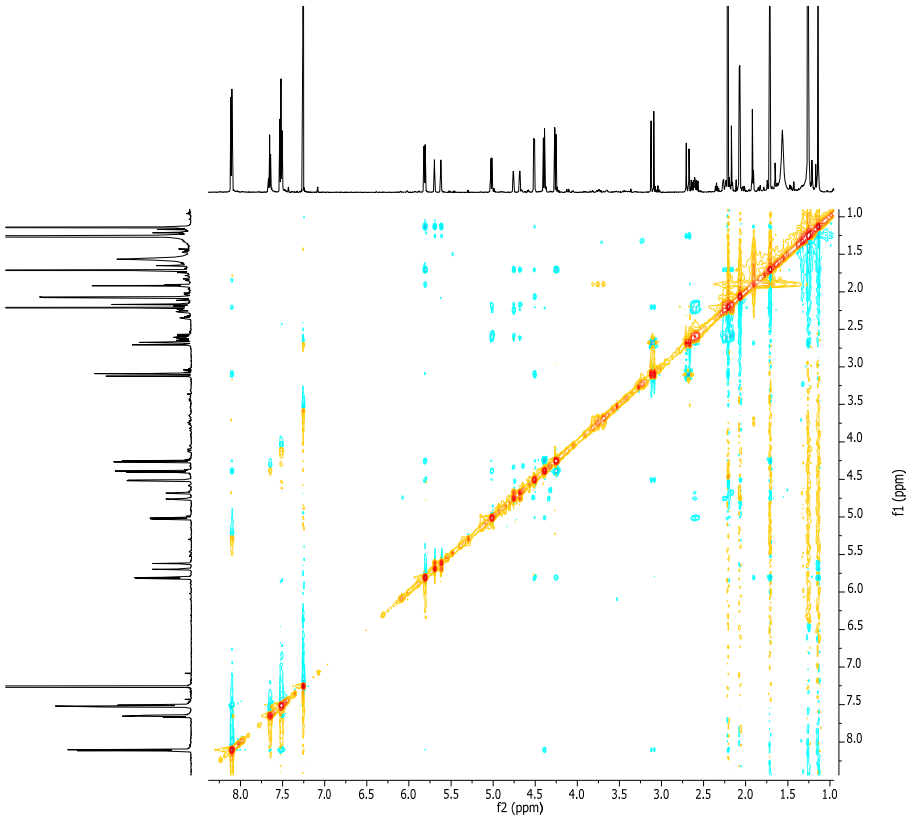

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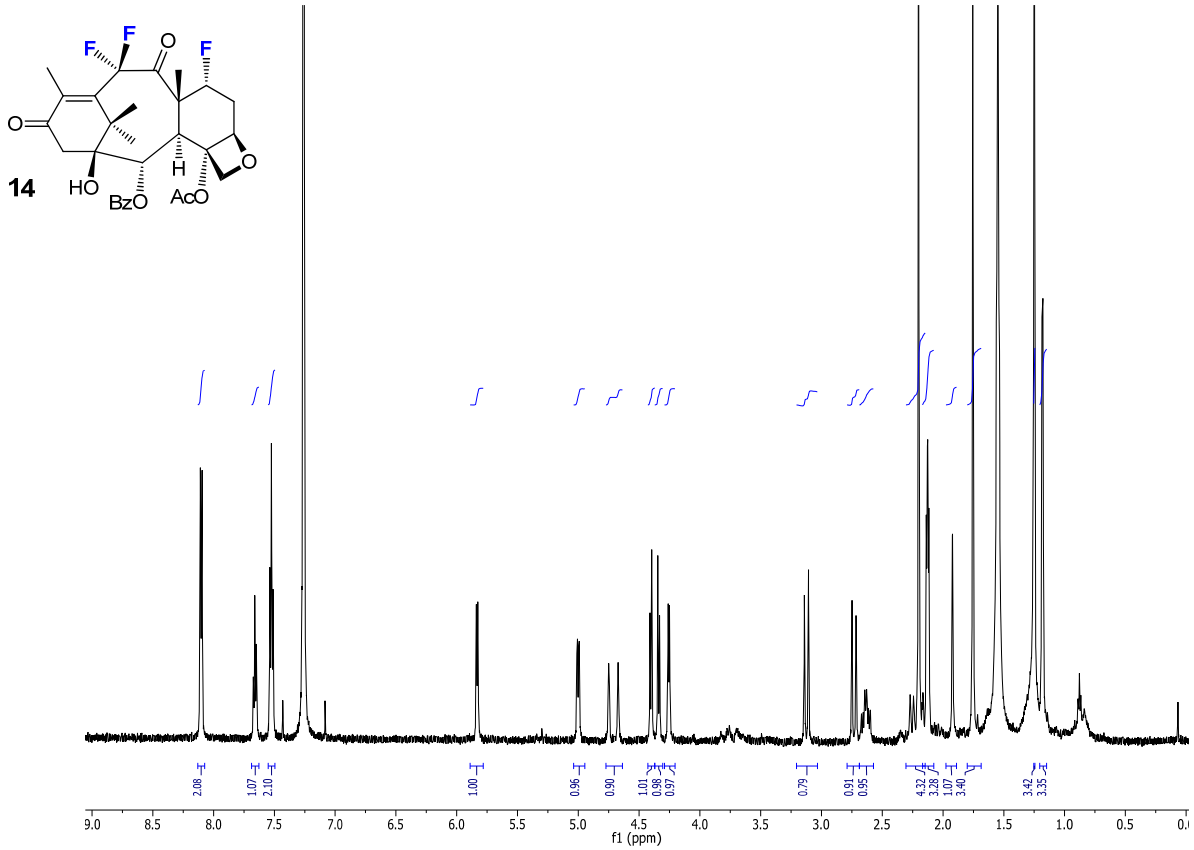
^{1}H NMR (600 MHz, $CDCl_3$):



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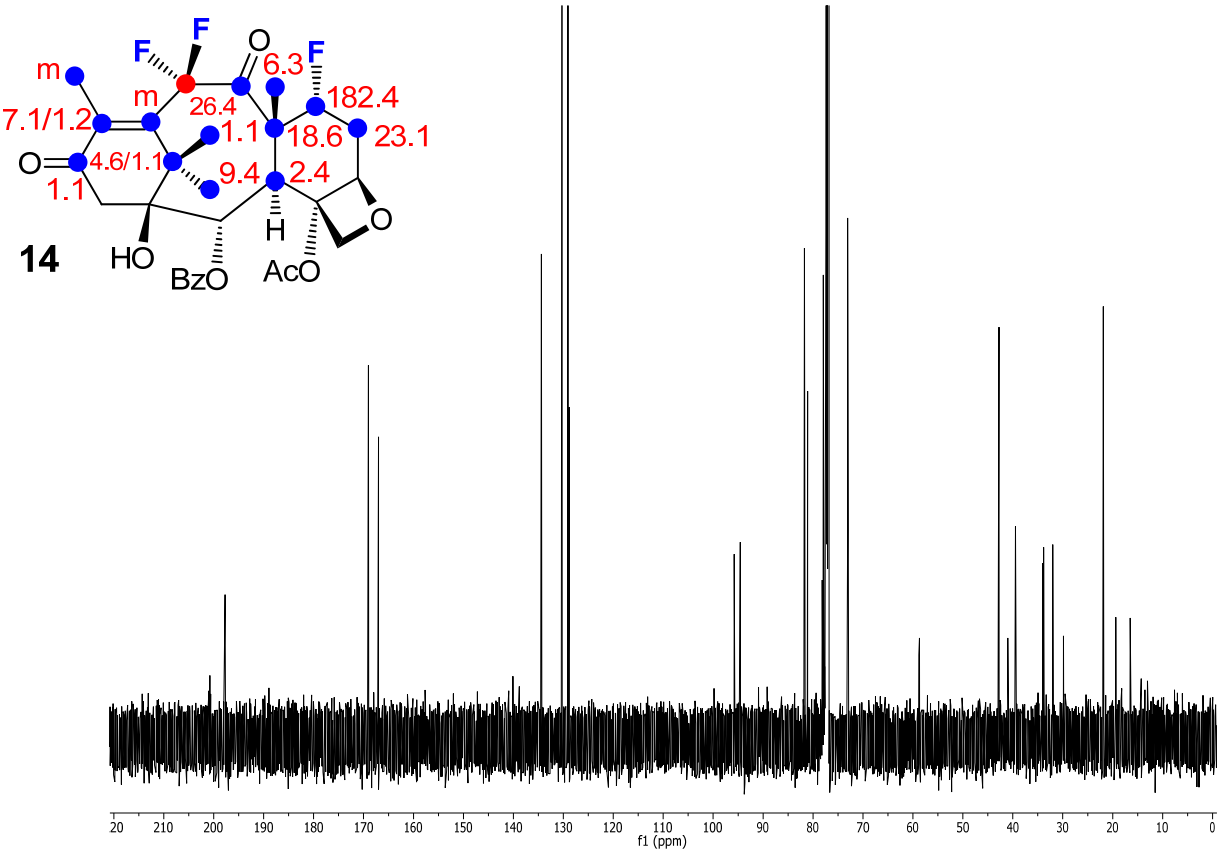

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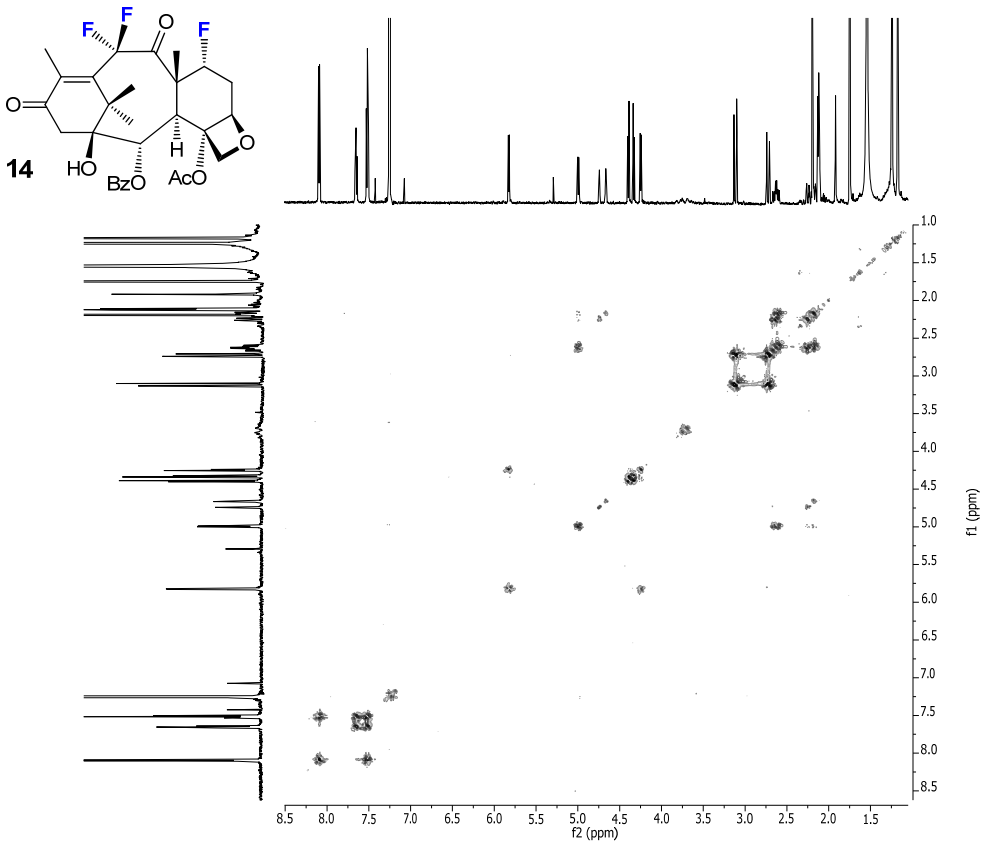

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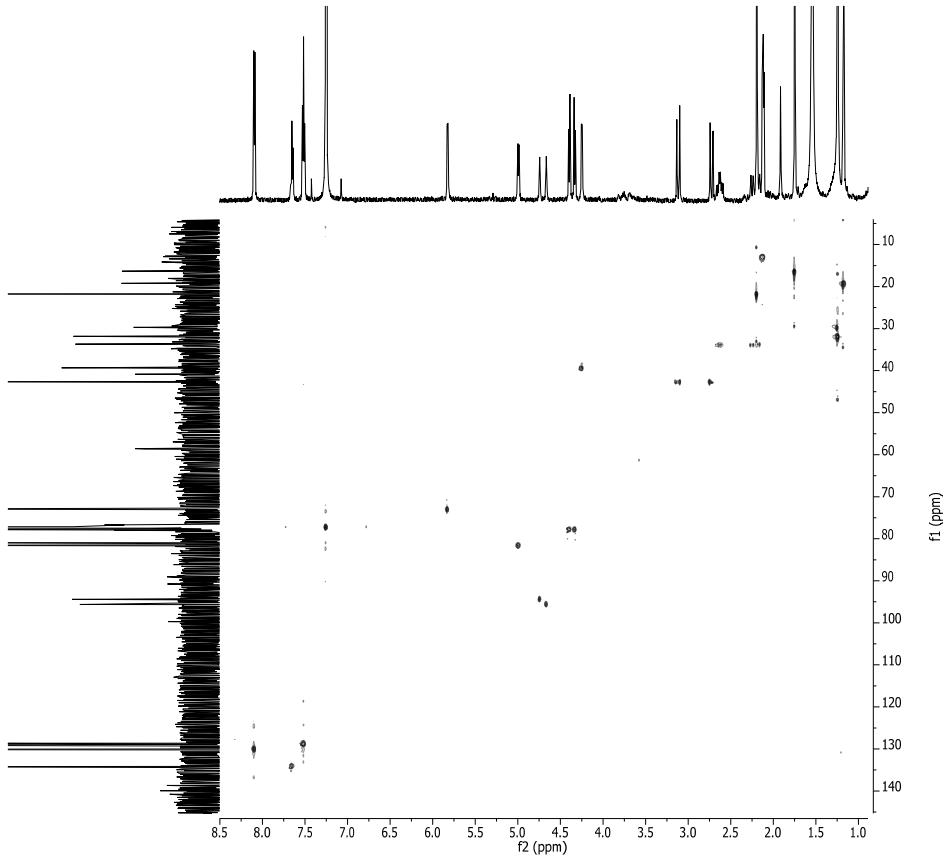

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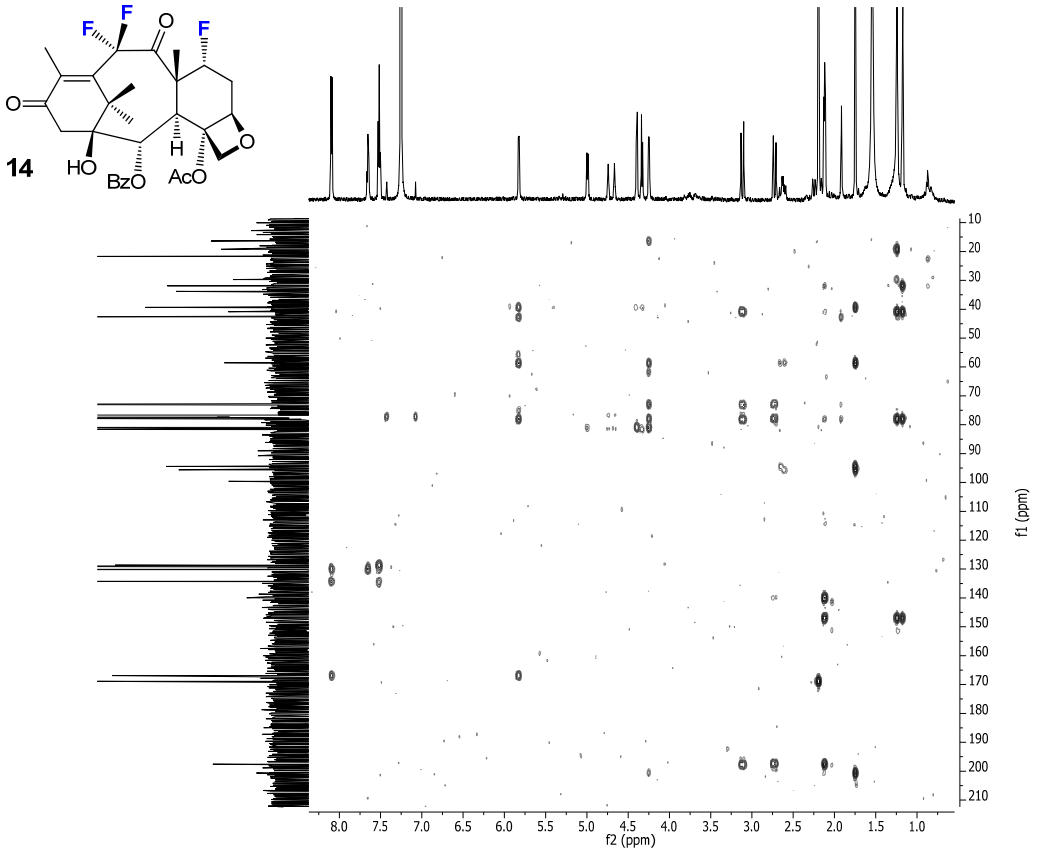

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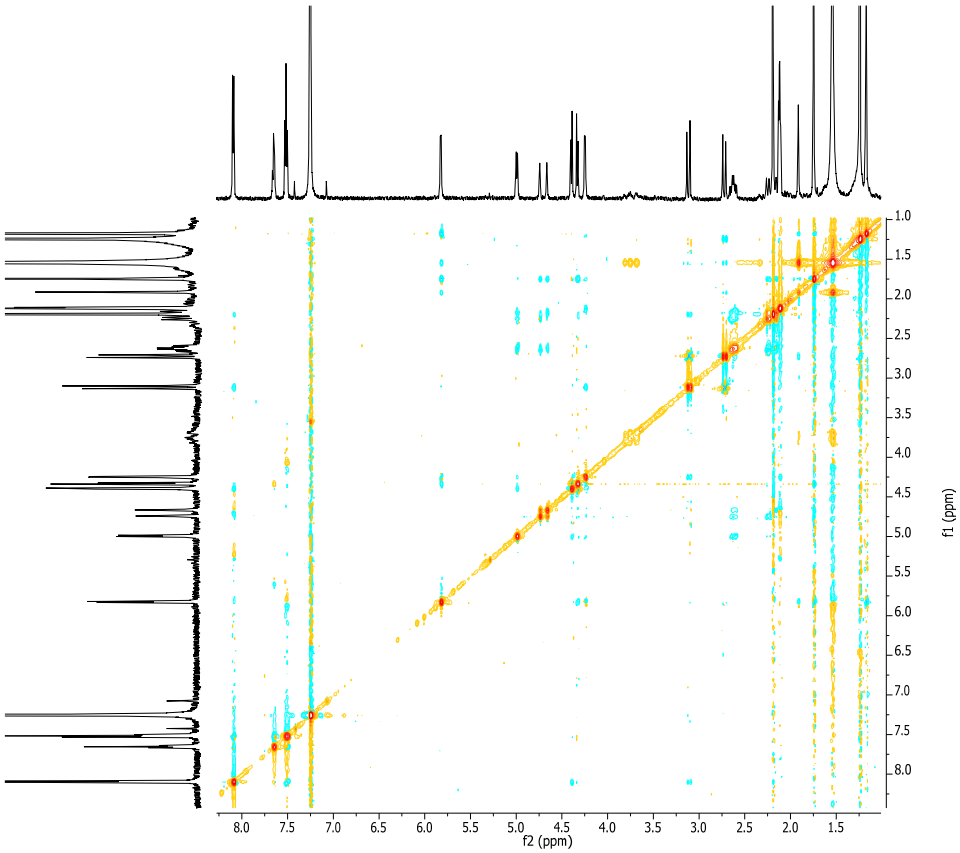
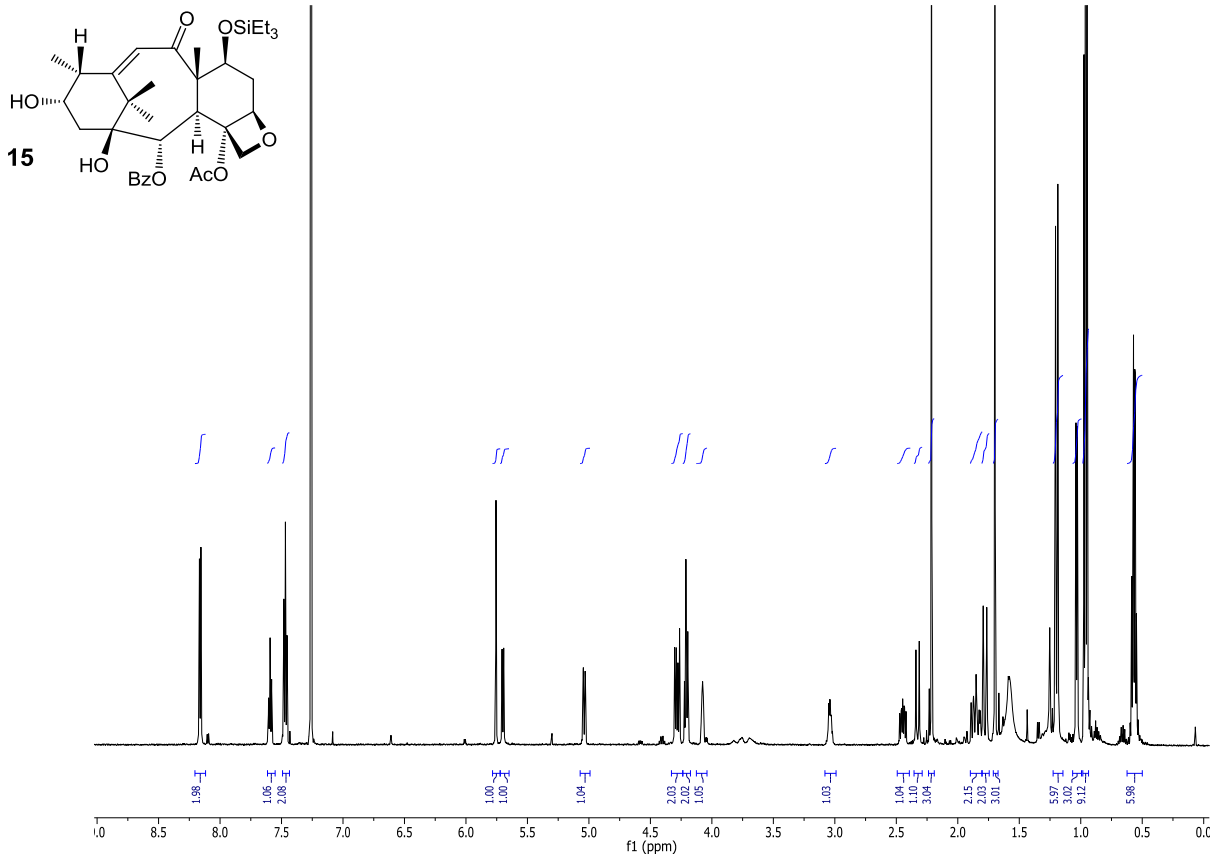
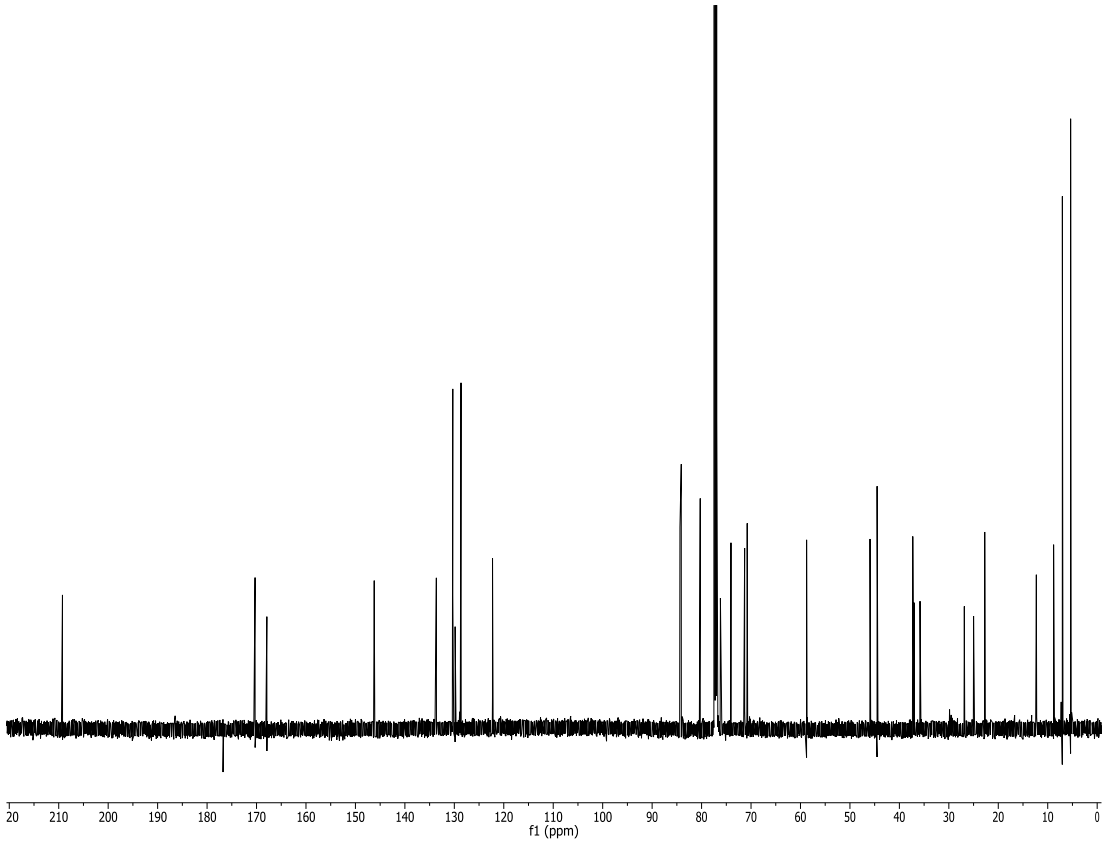


^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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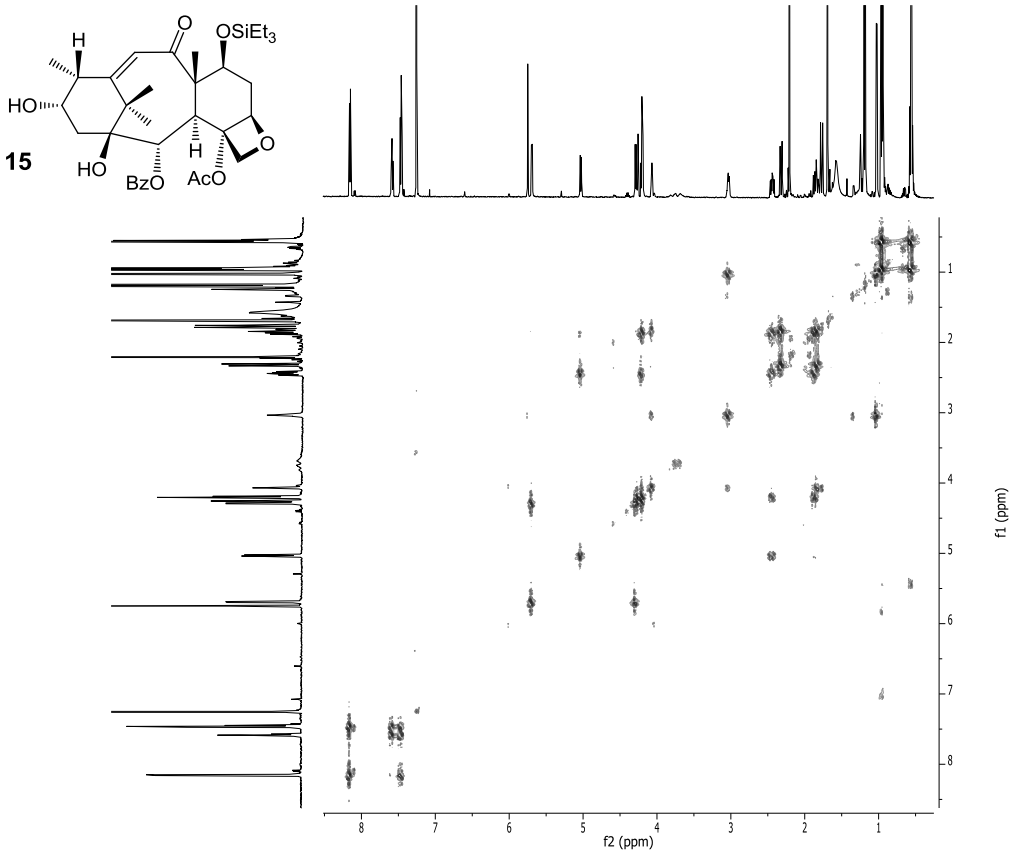
COSY (600 MHz, $CDCl_3$):



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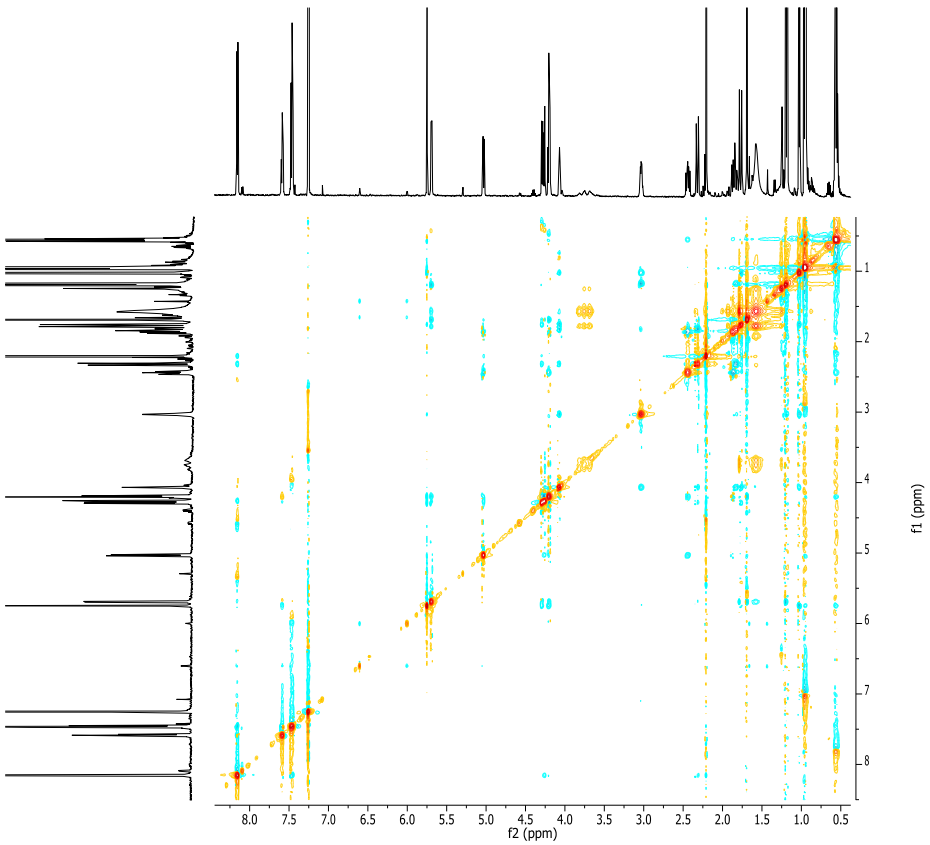

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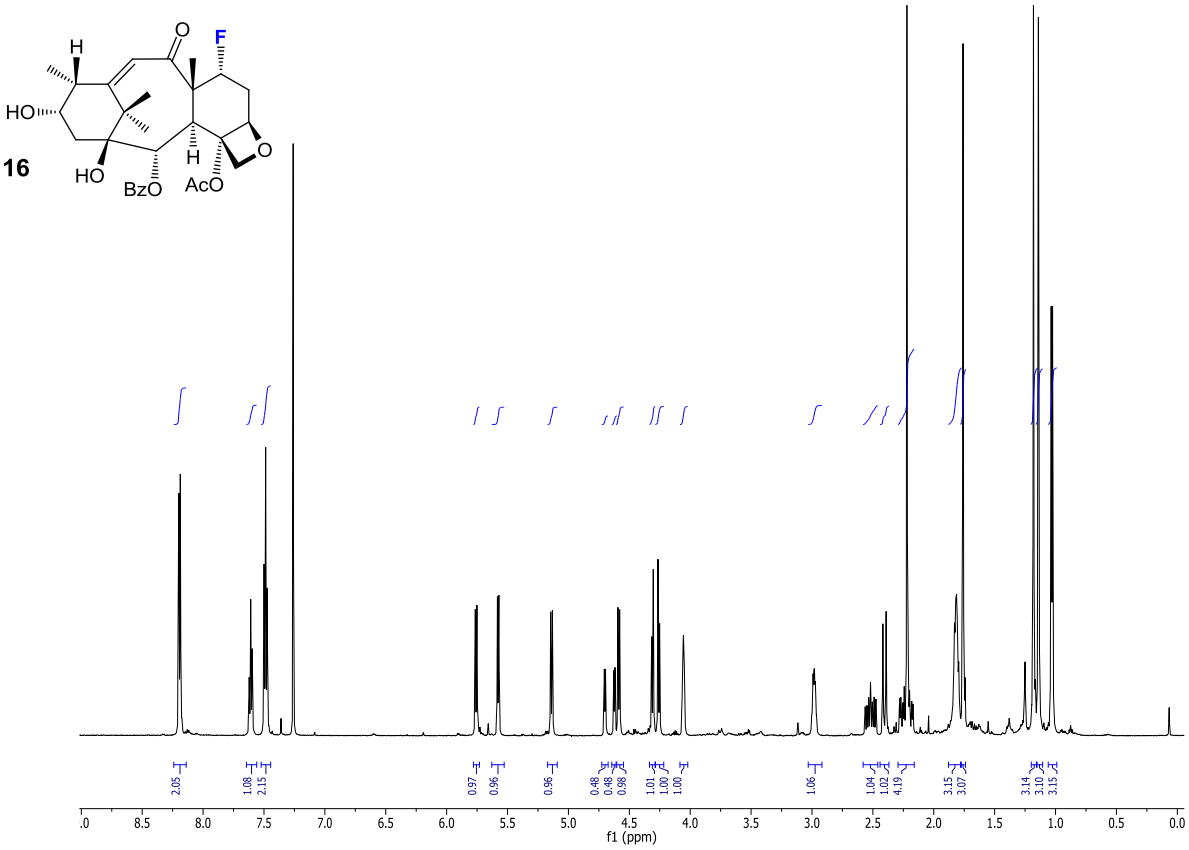

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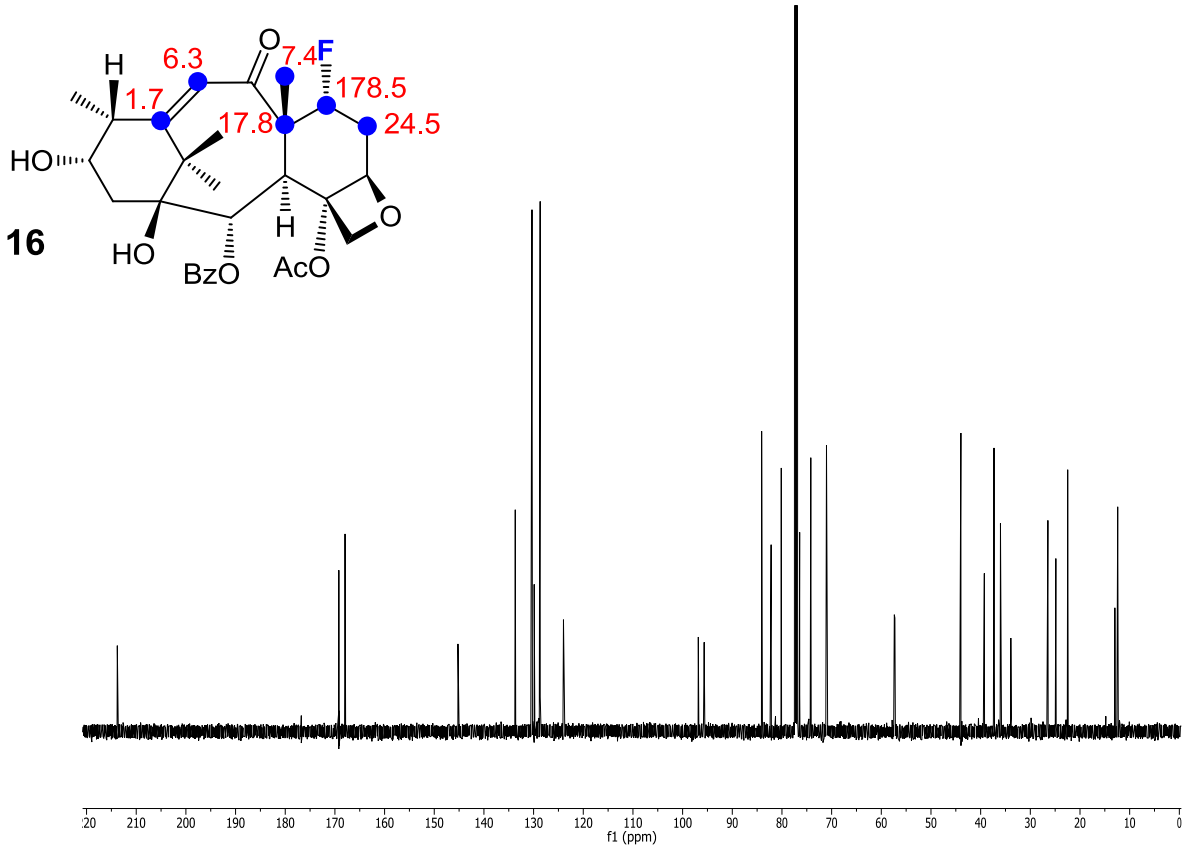

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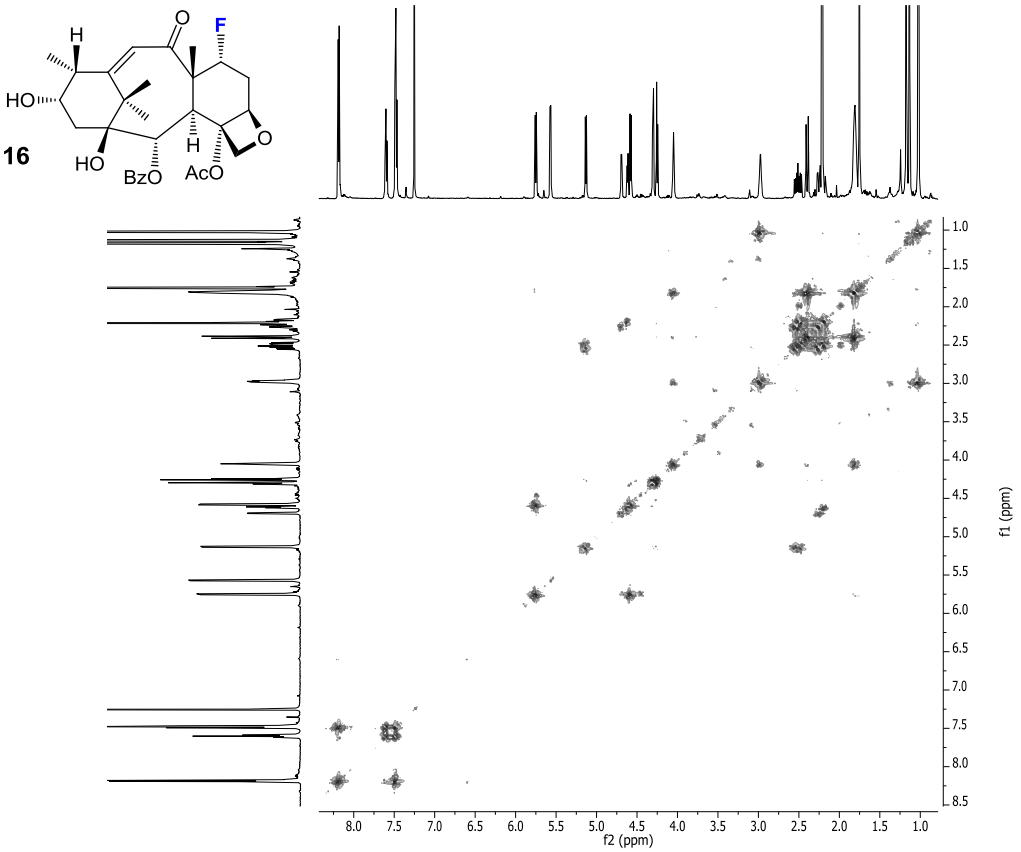

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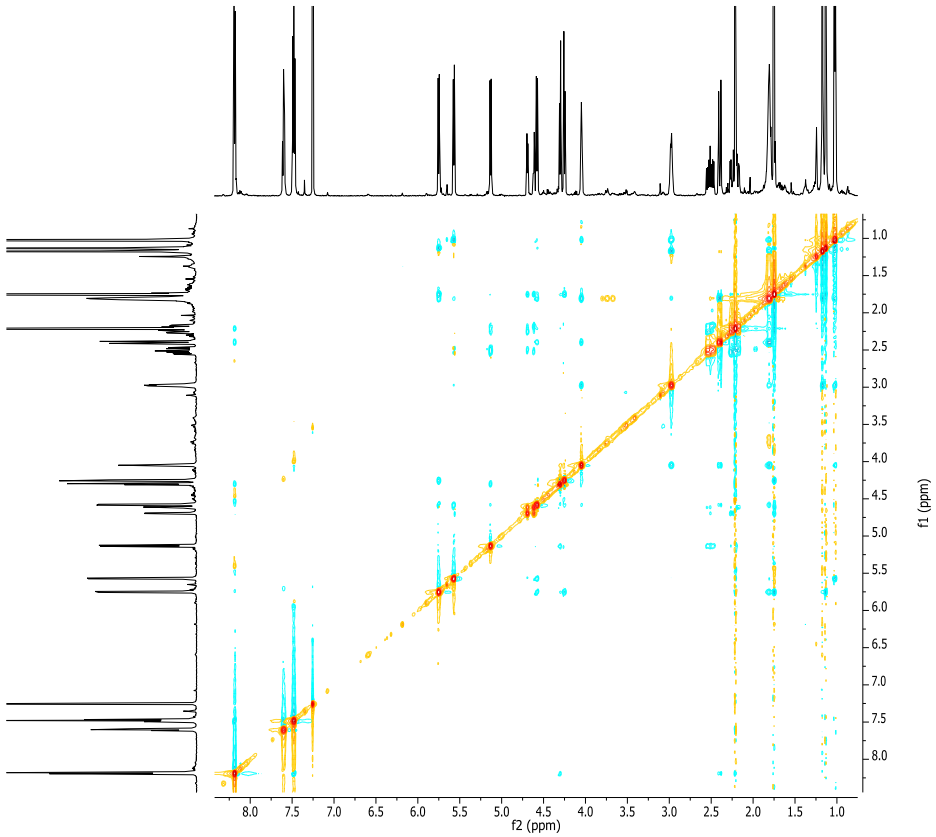

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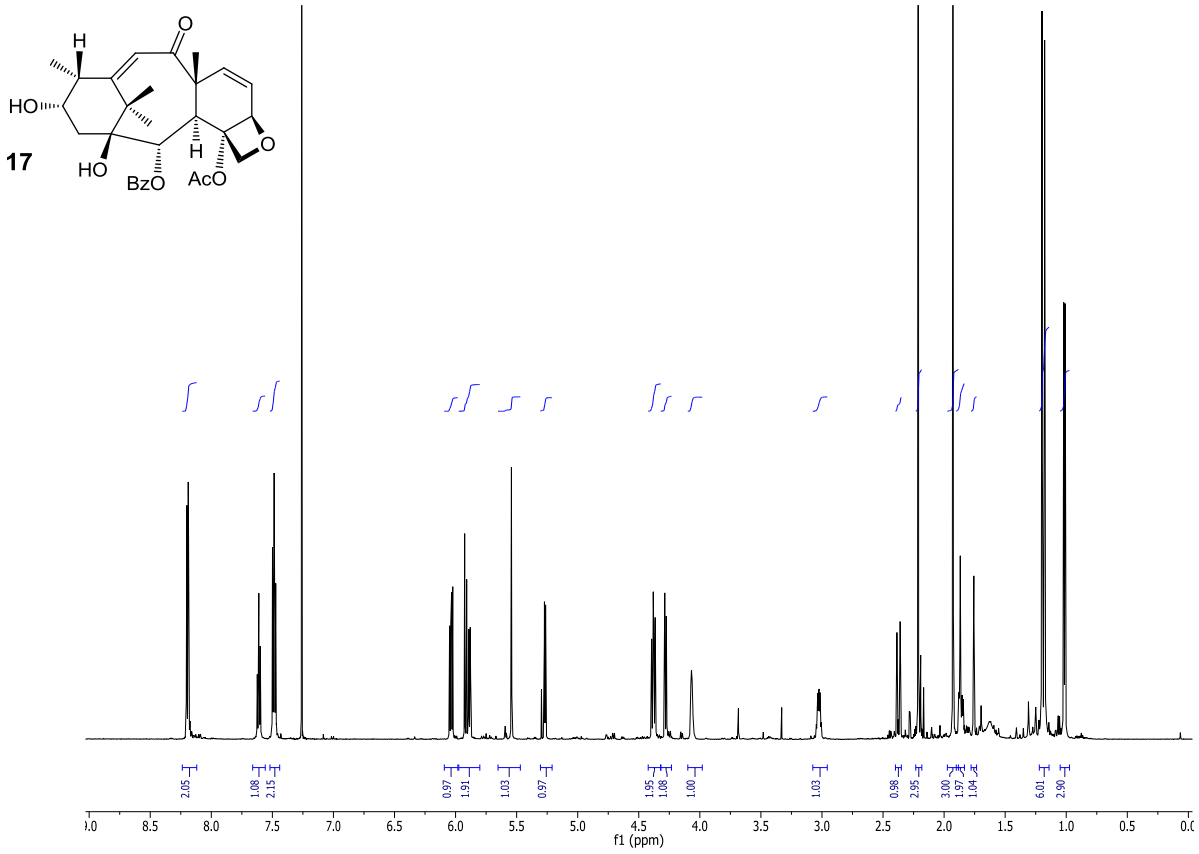

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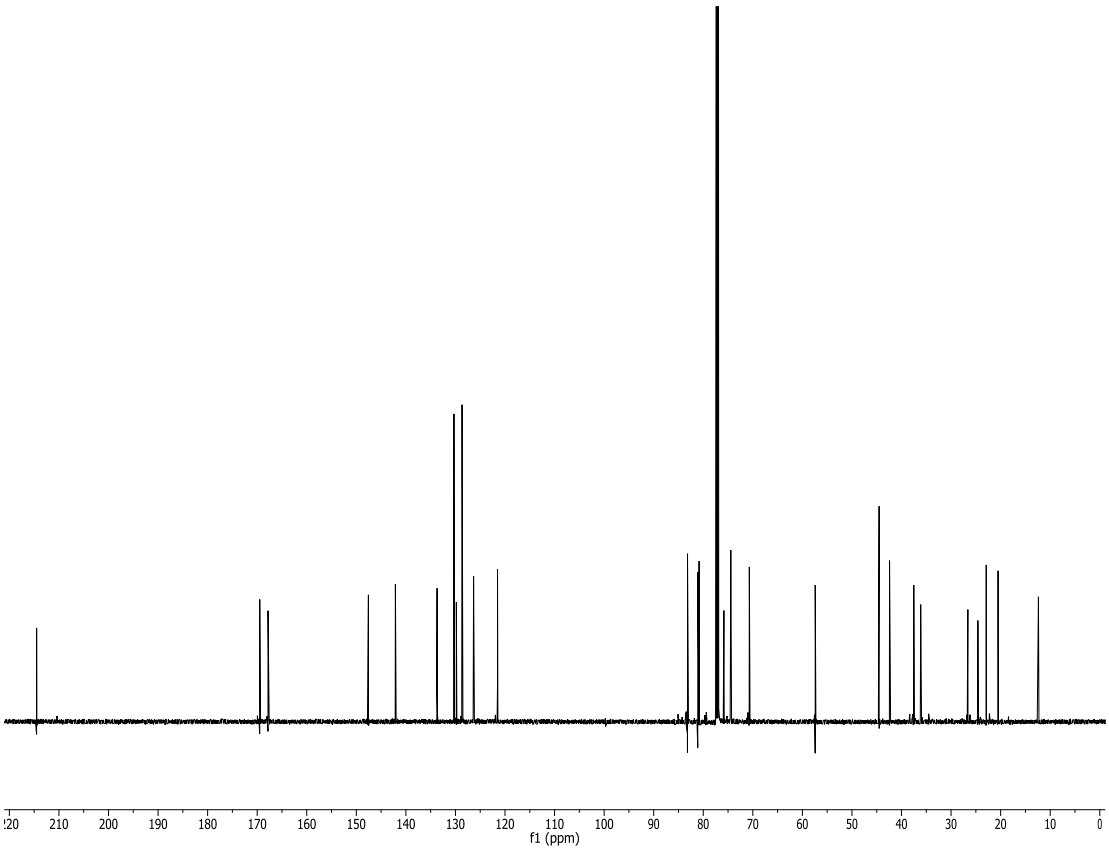

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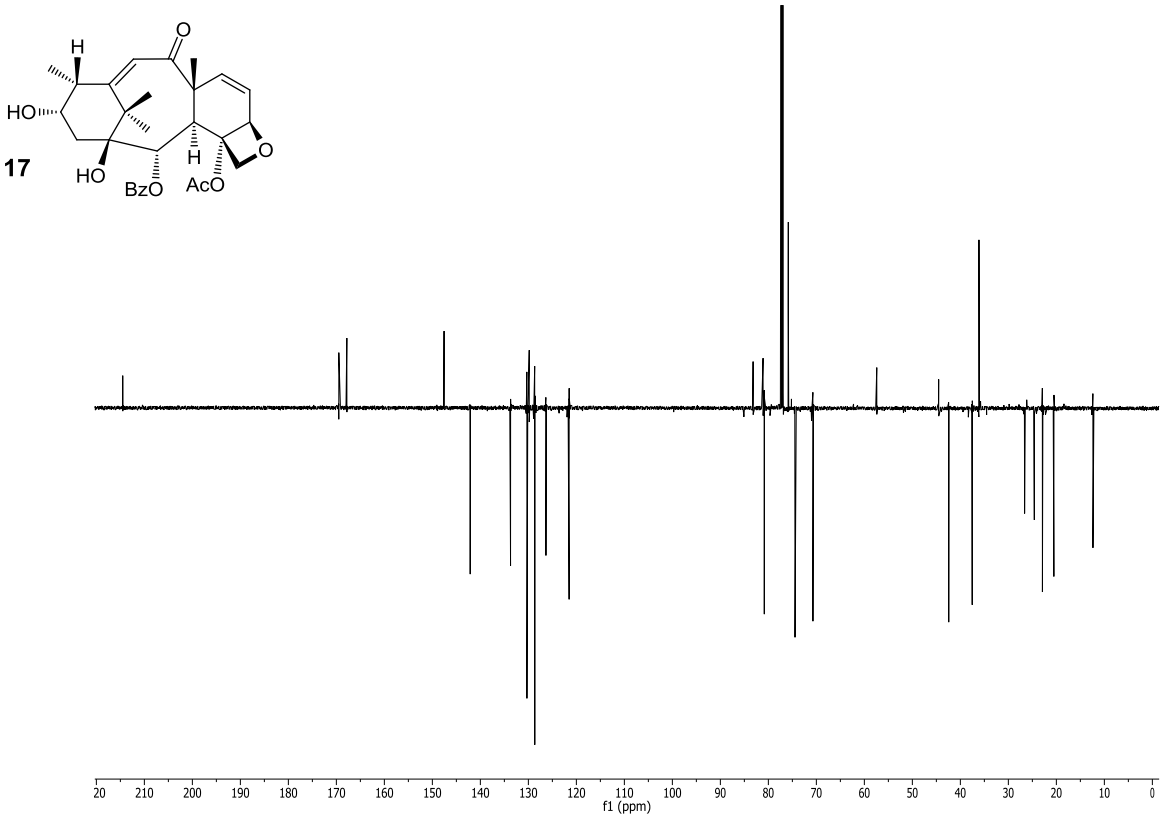
APT (600 MHz, $CDCl_3$):



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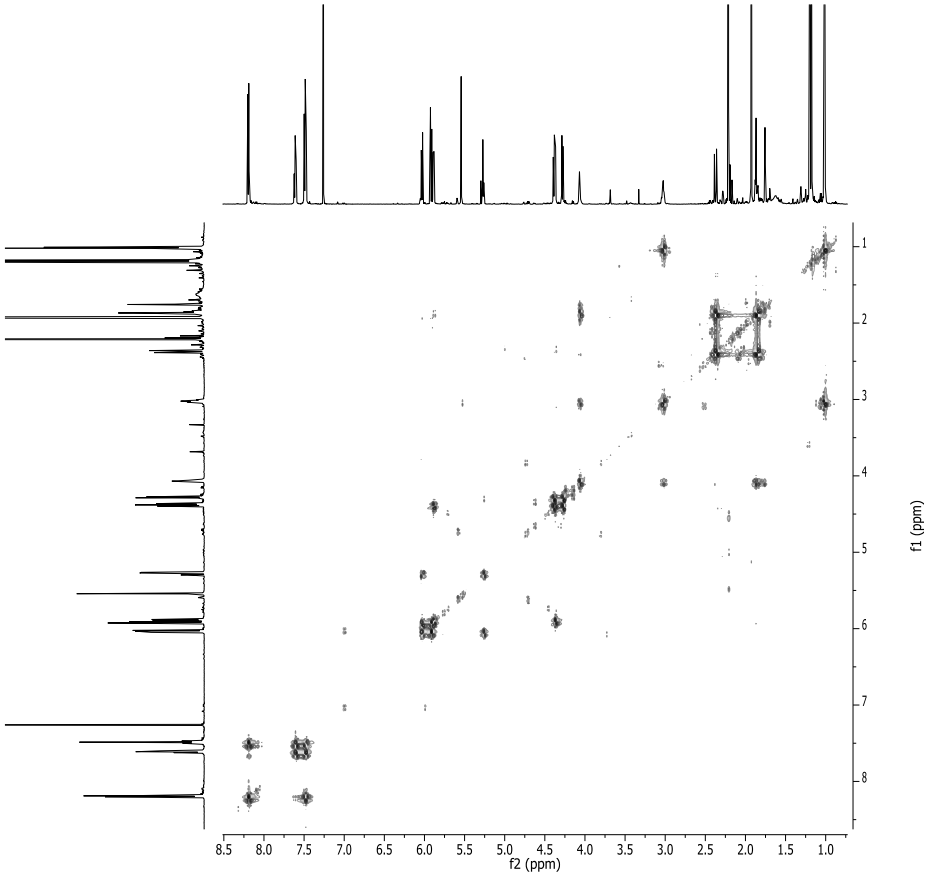

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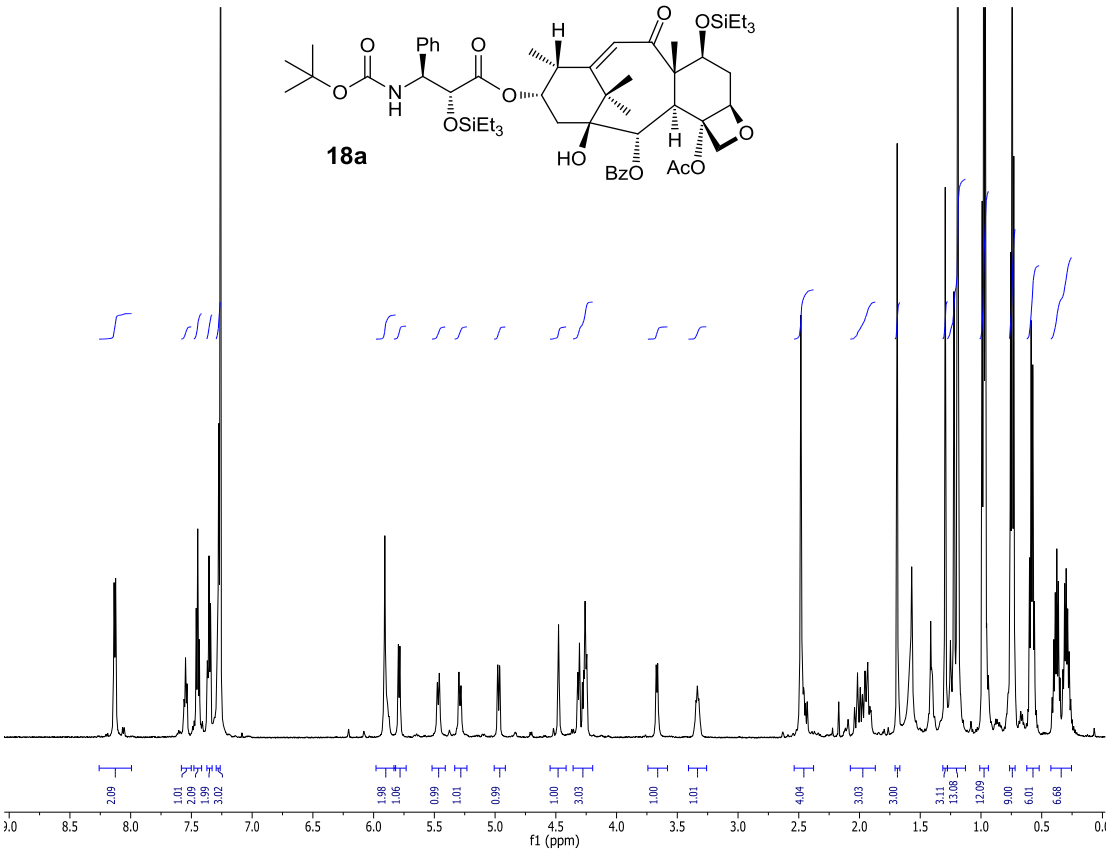

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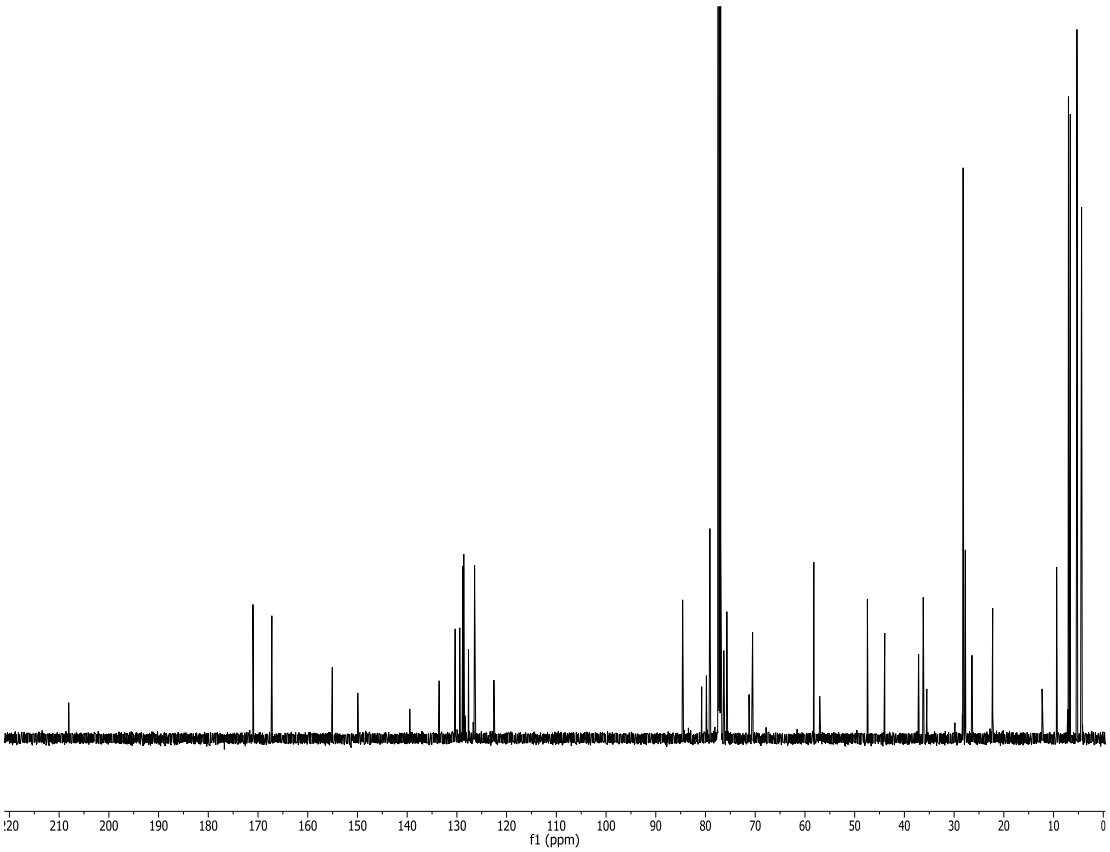

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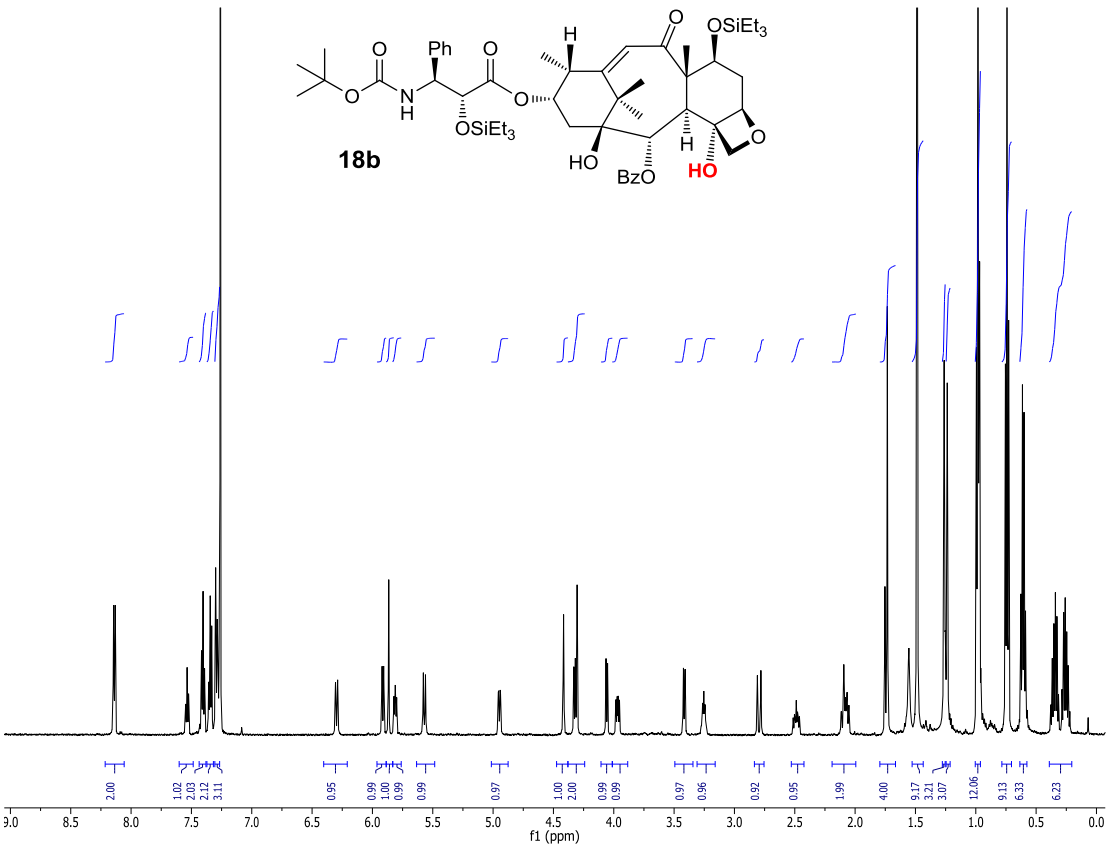

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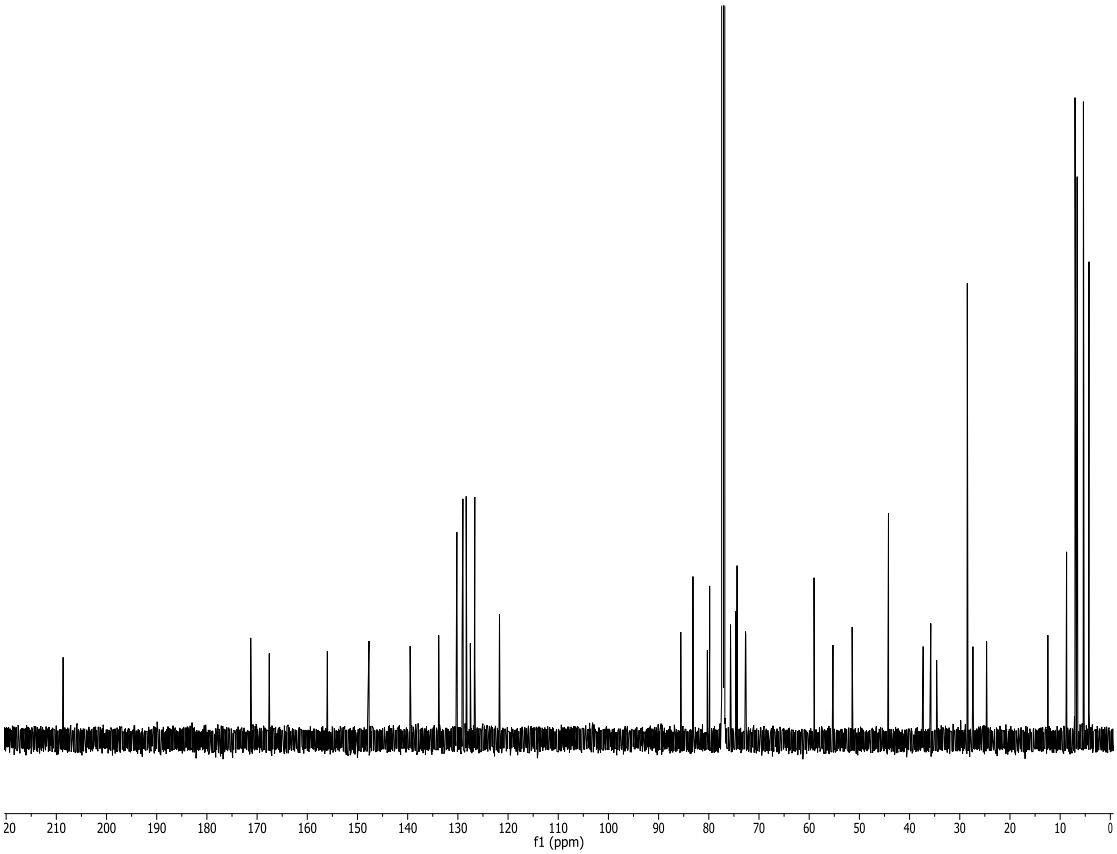

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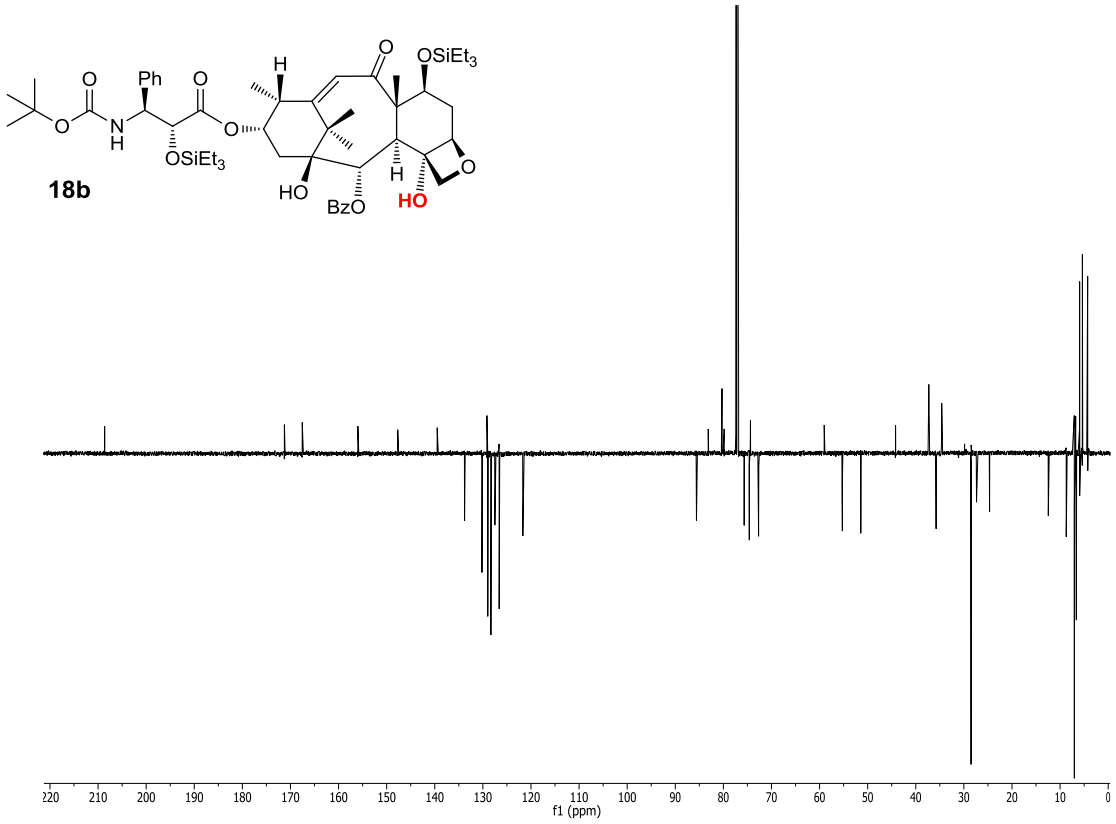

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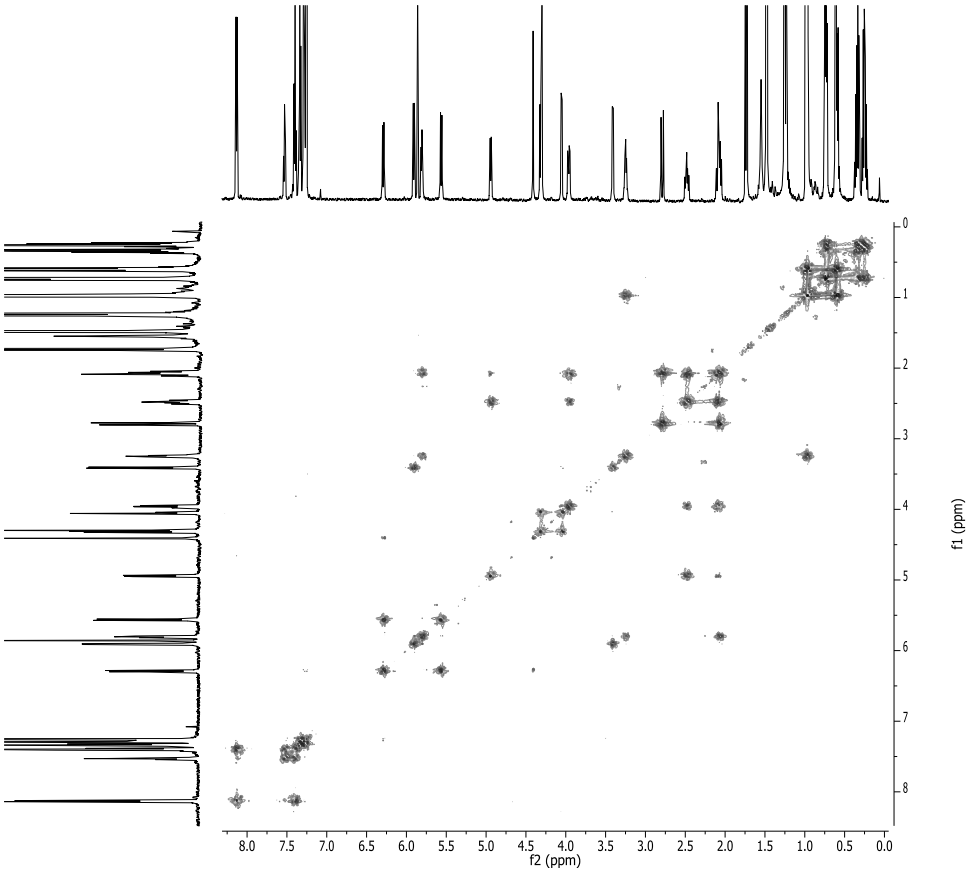

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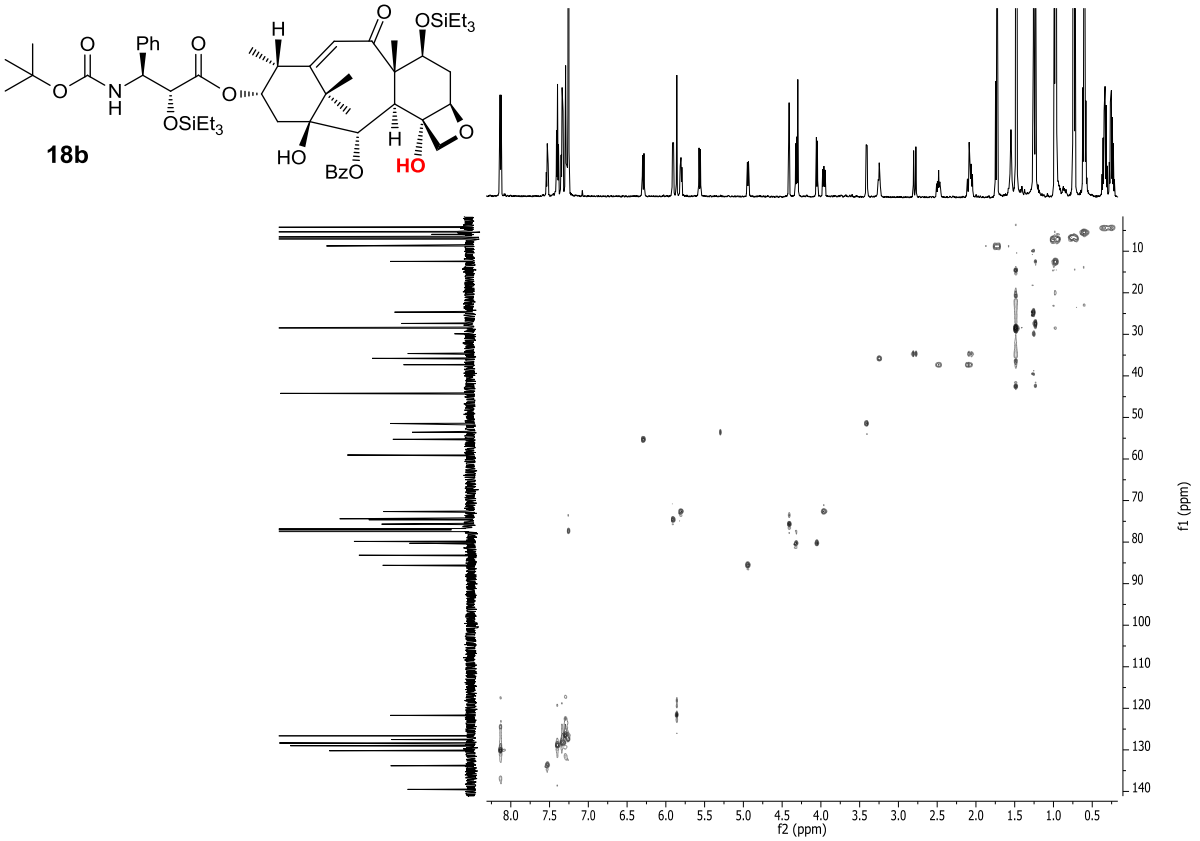
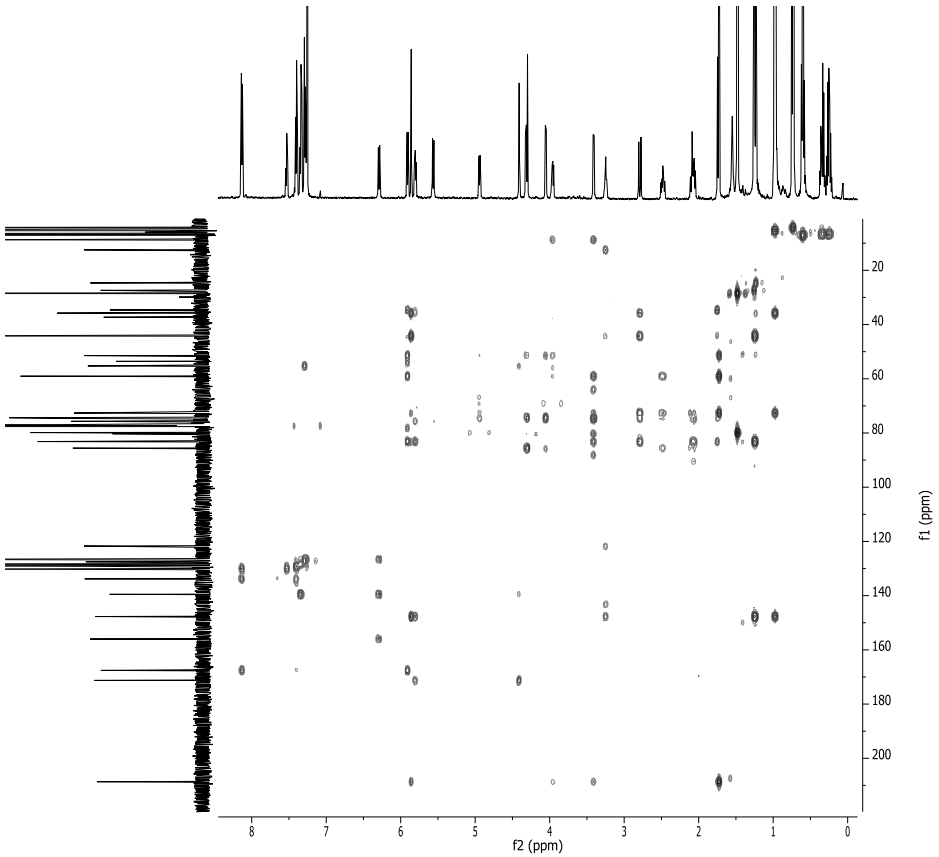
HMQC (600 MHz, $CDCl_3$):



HMBC (600 MHz, $CDCl_3$):



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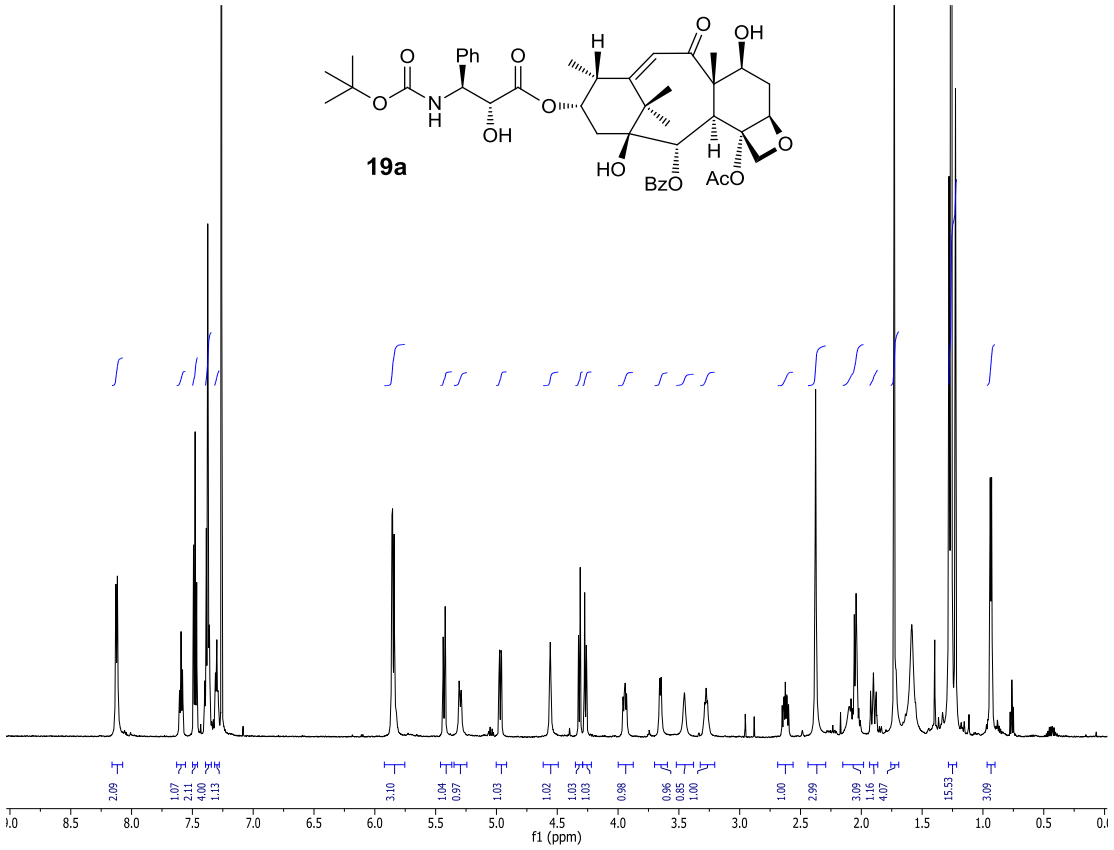

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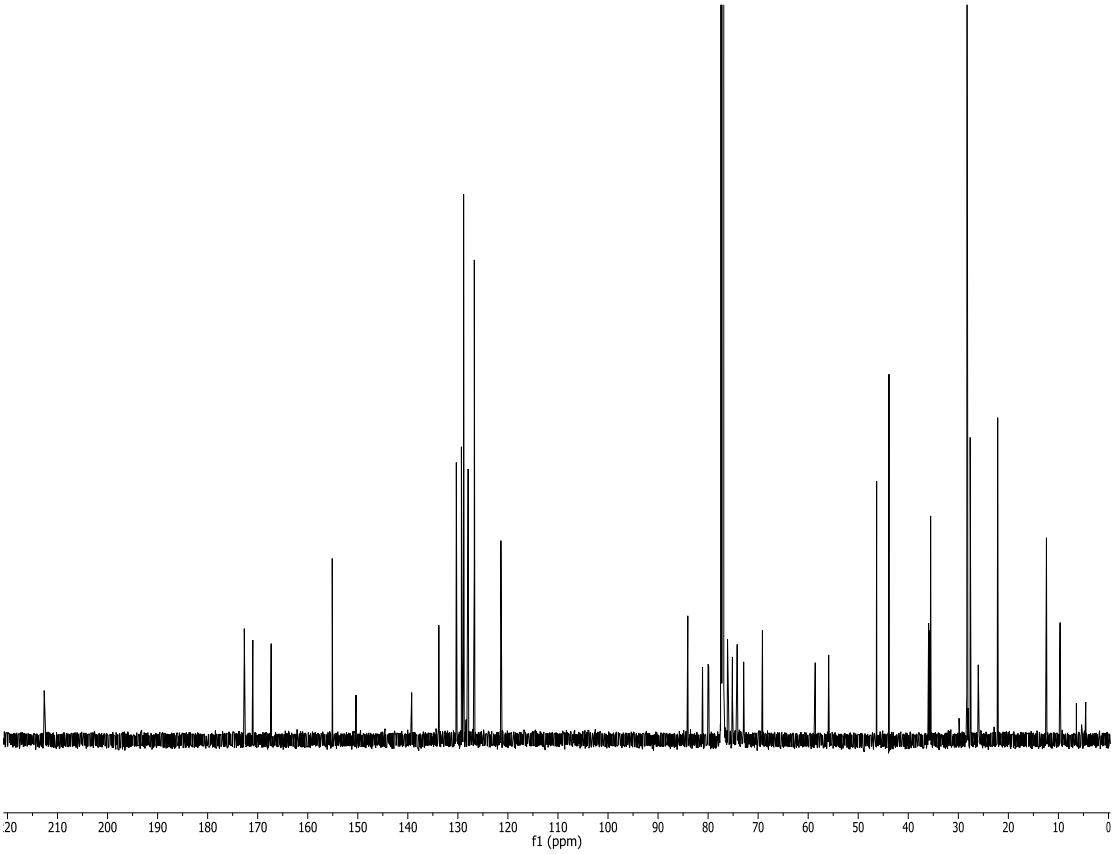

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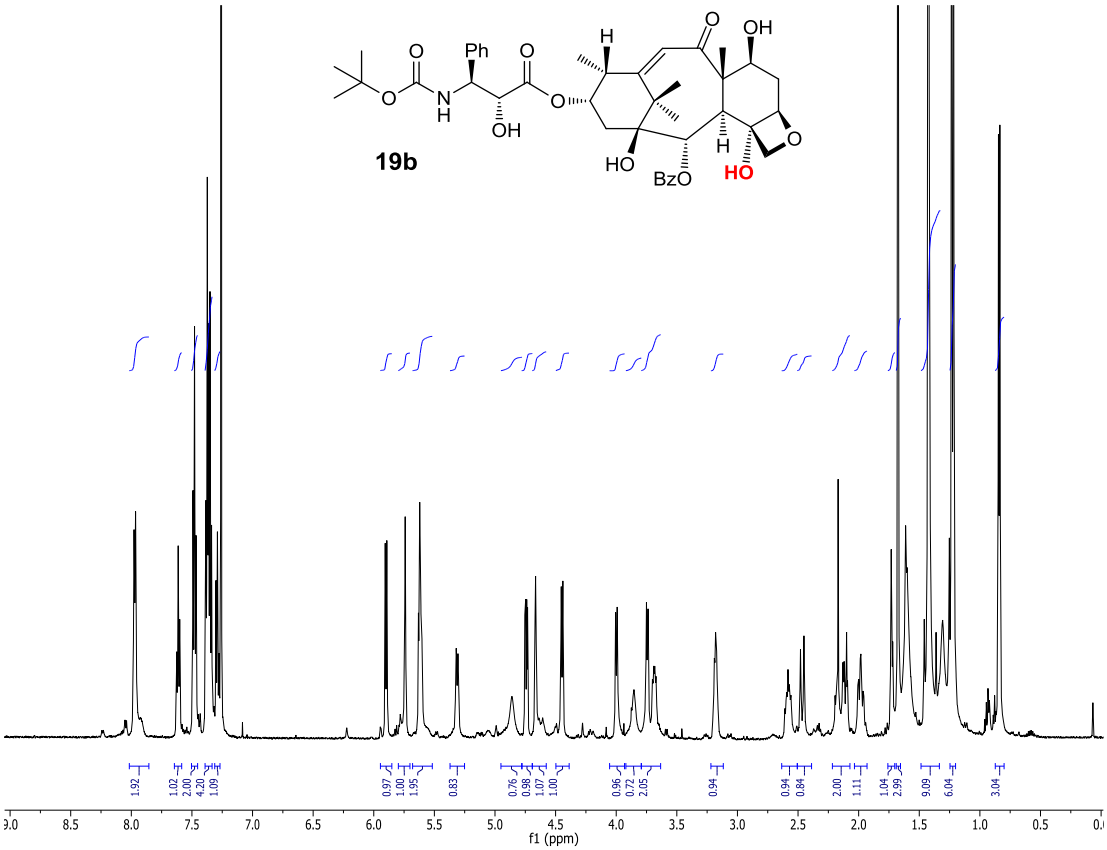

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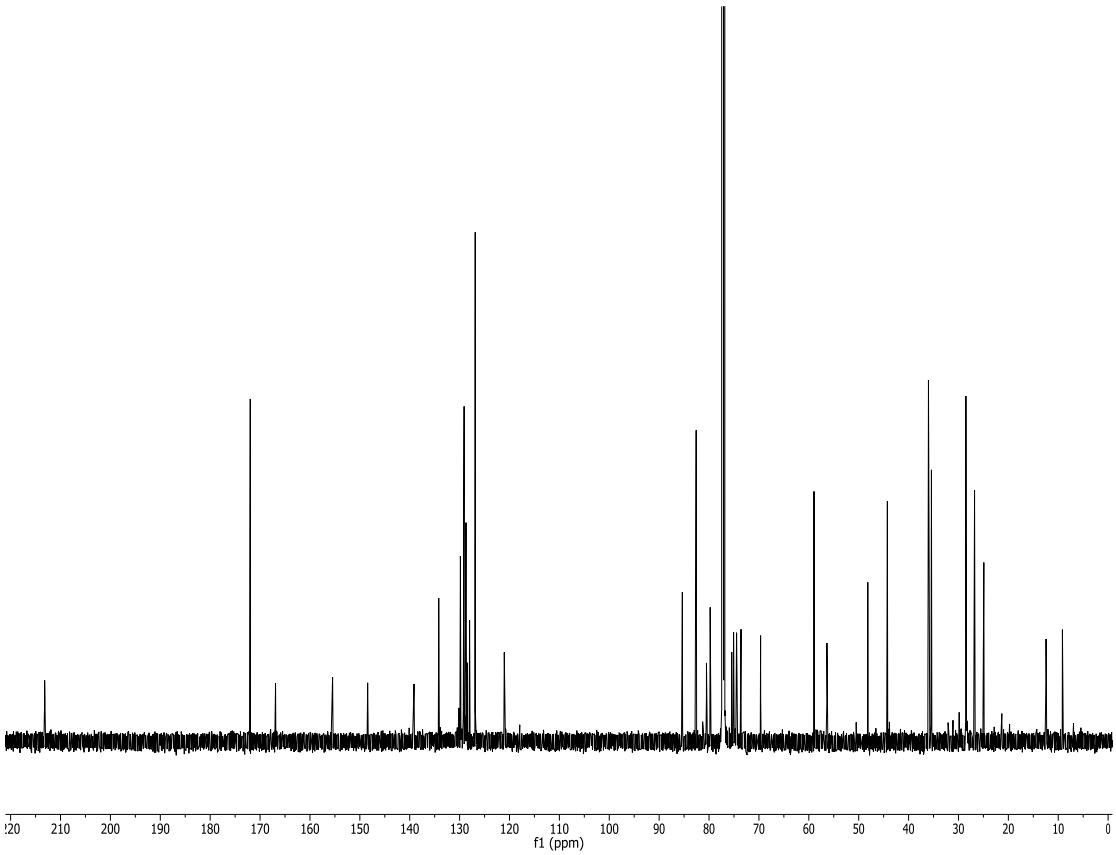

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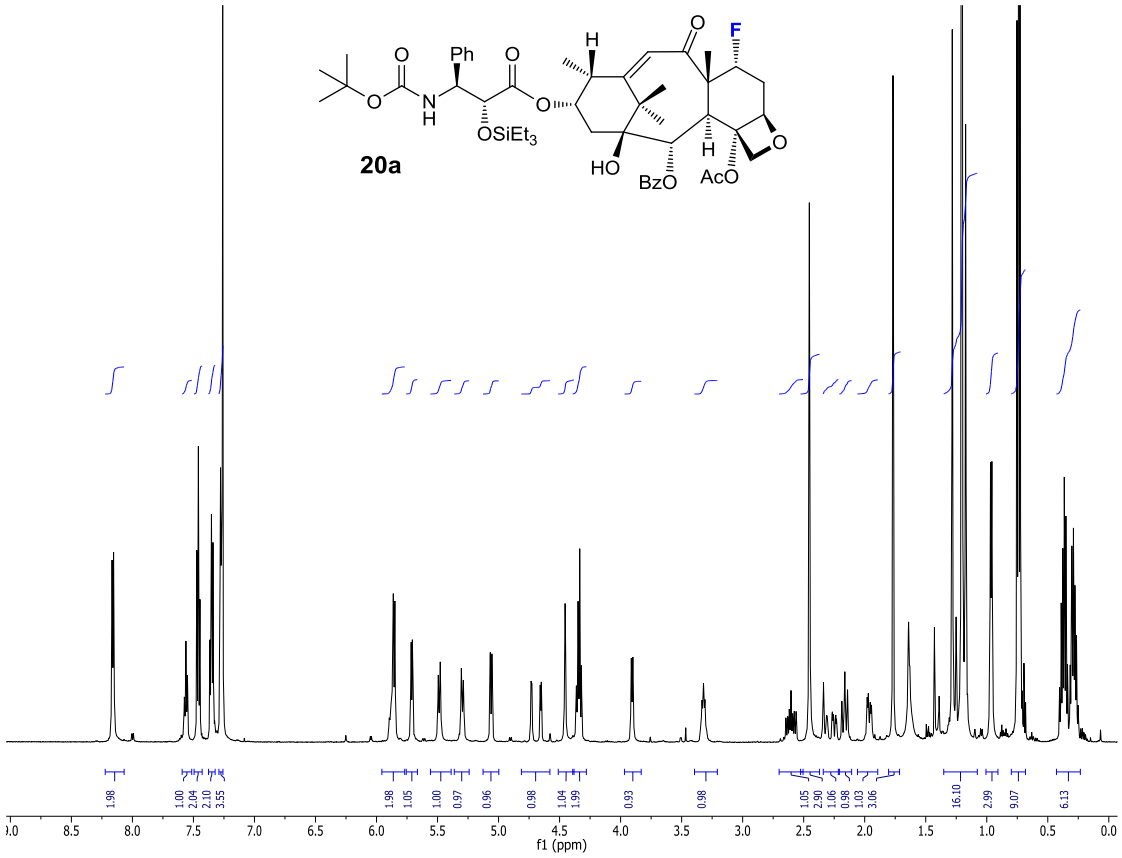

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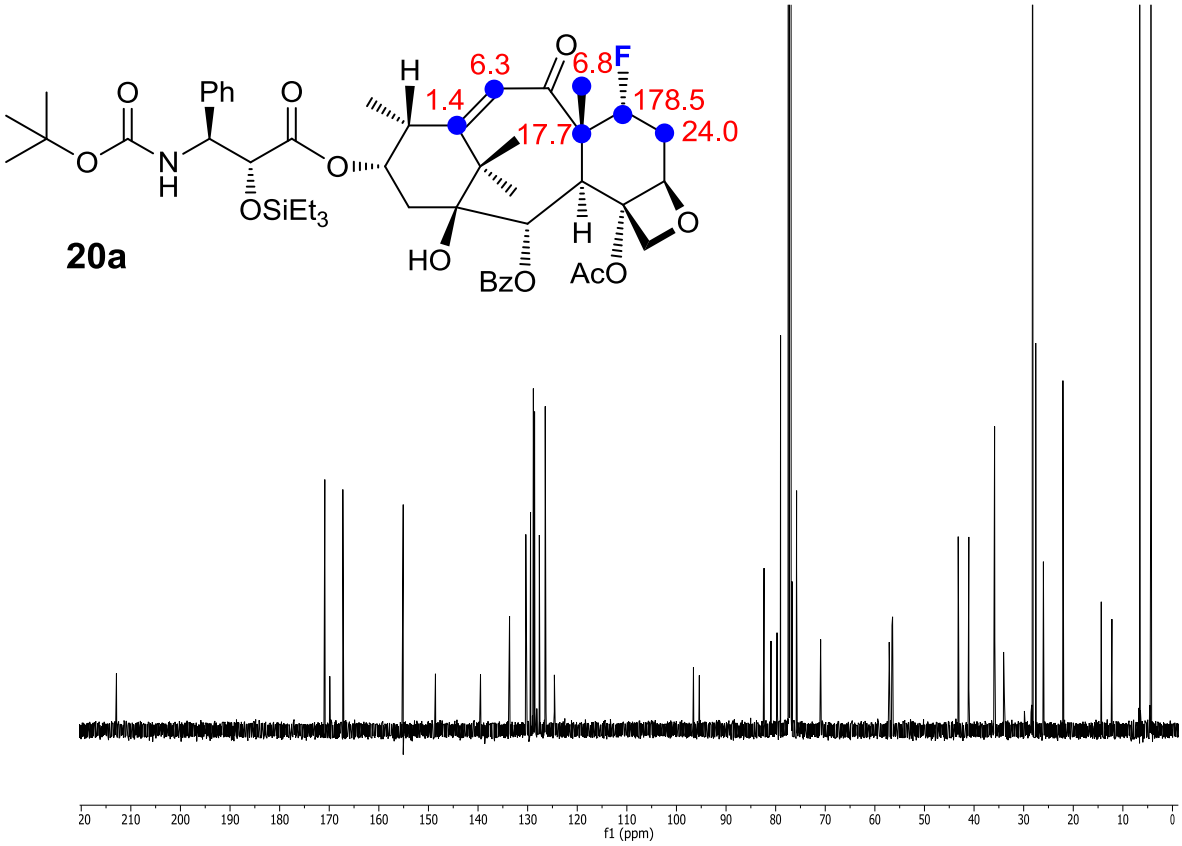

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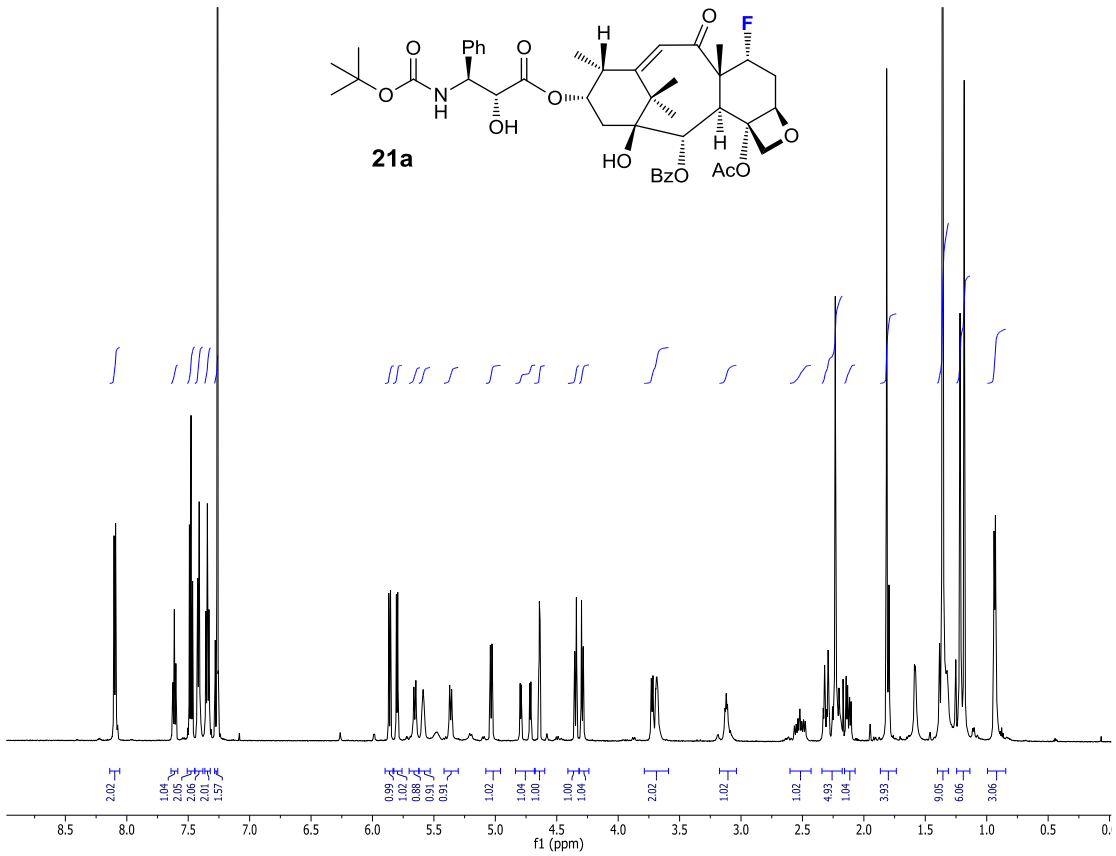

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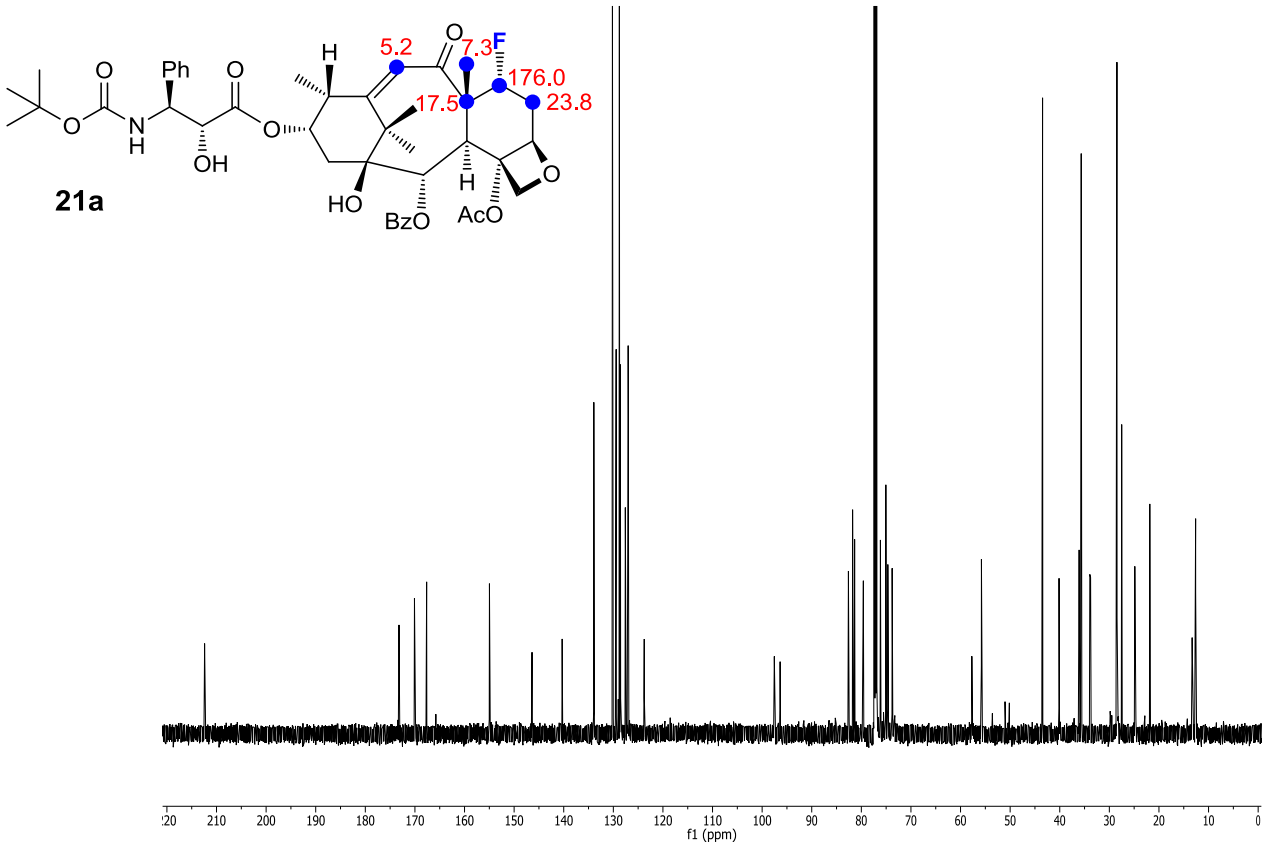

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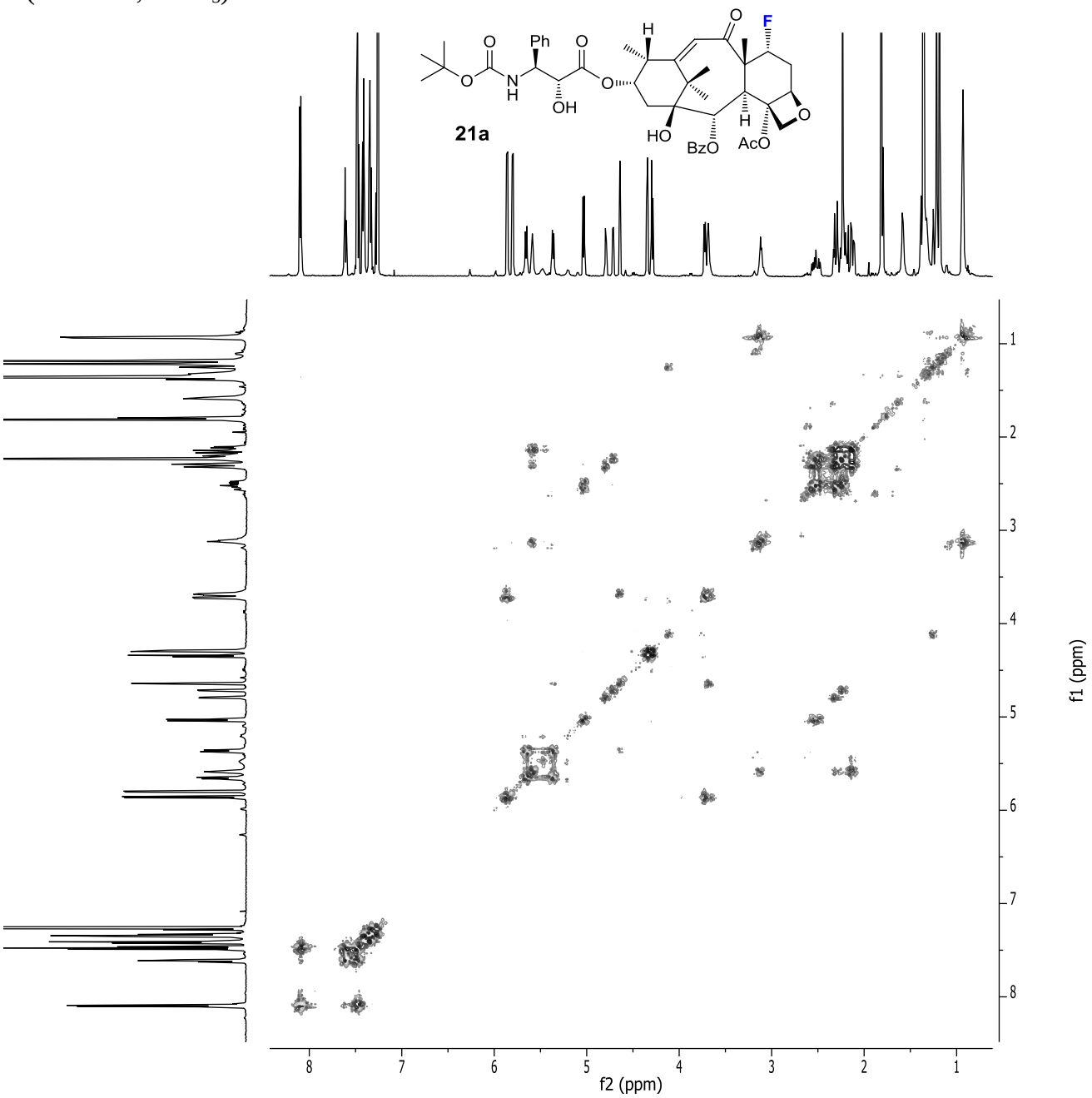
COSY (600 MHz, $CDCl_3$):



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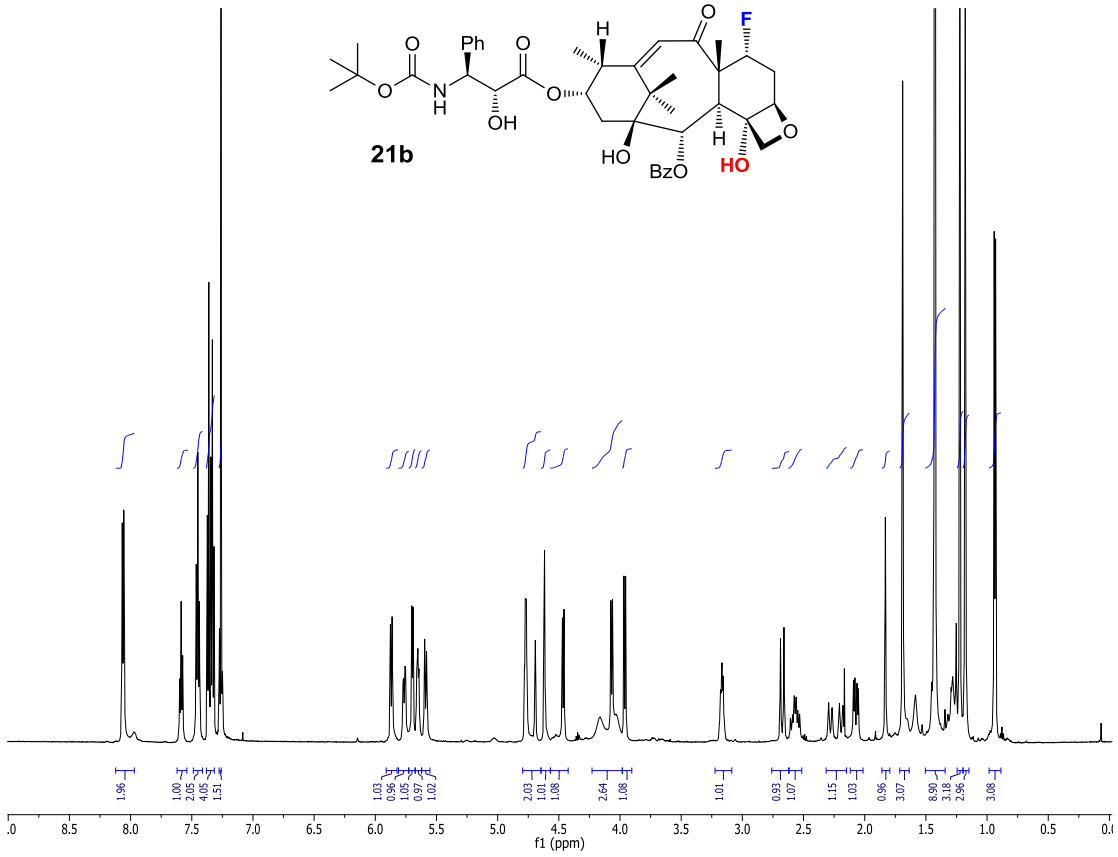

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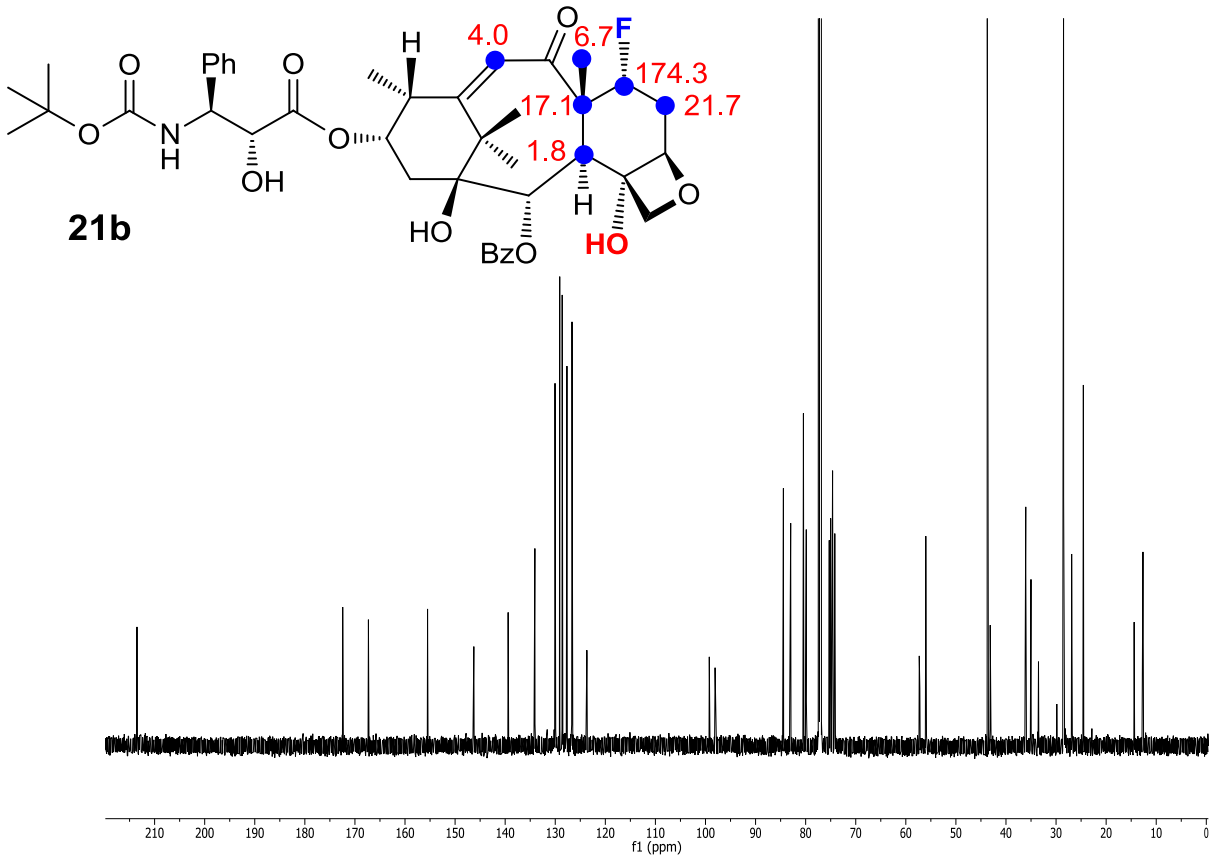

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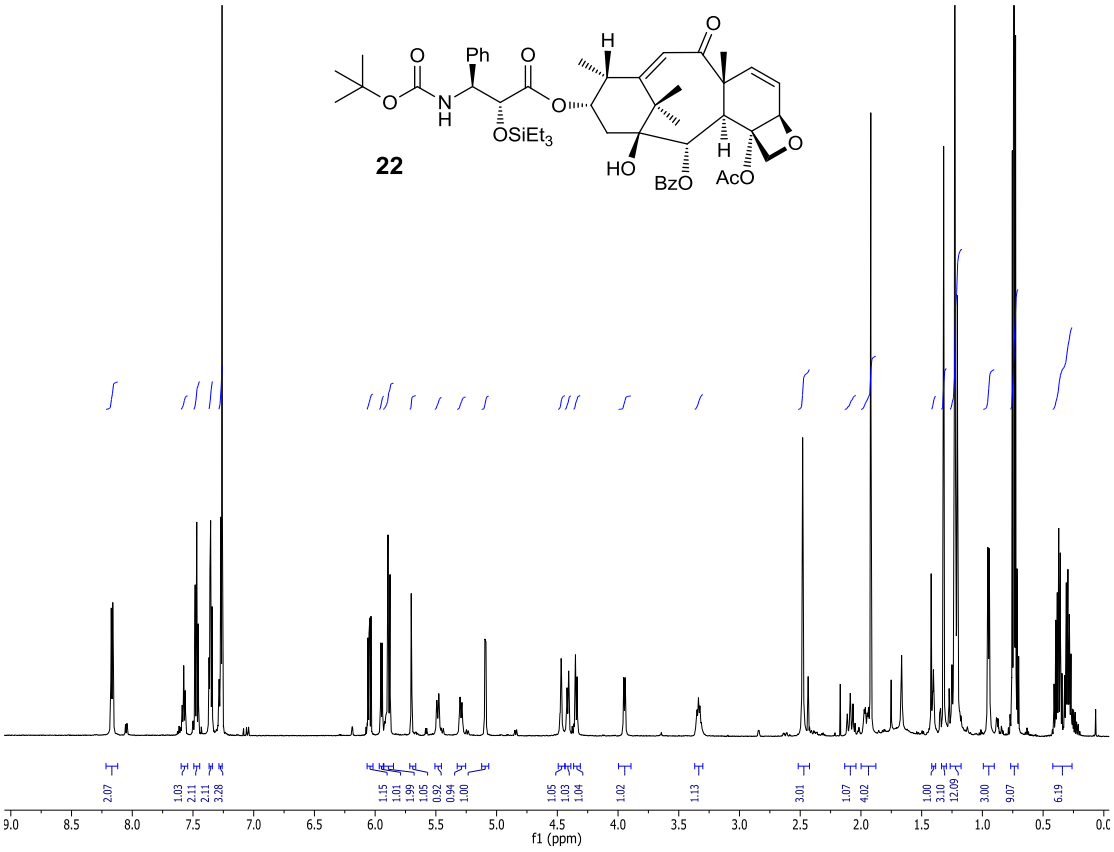

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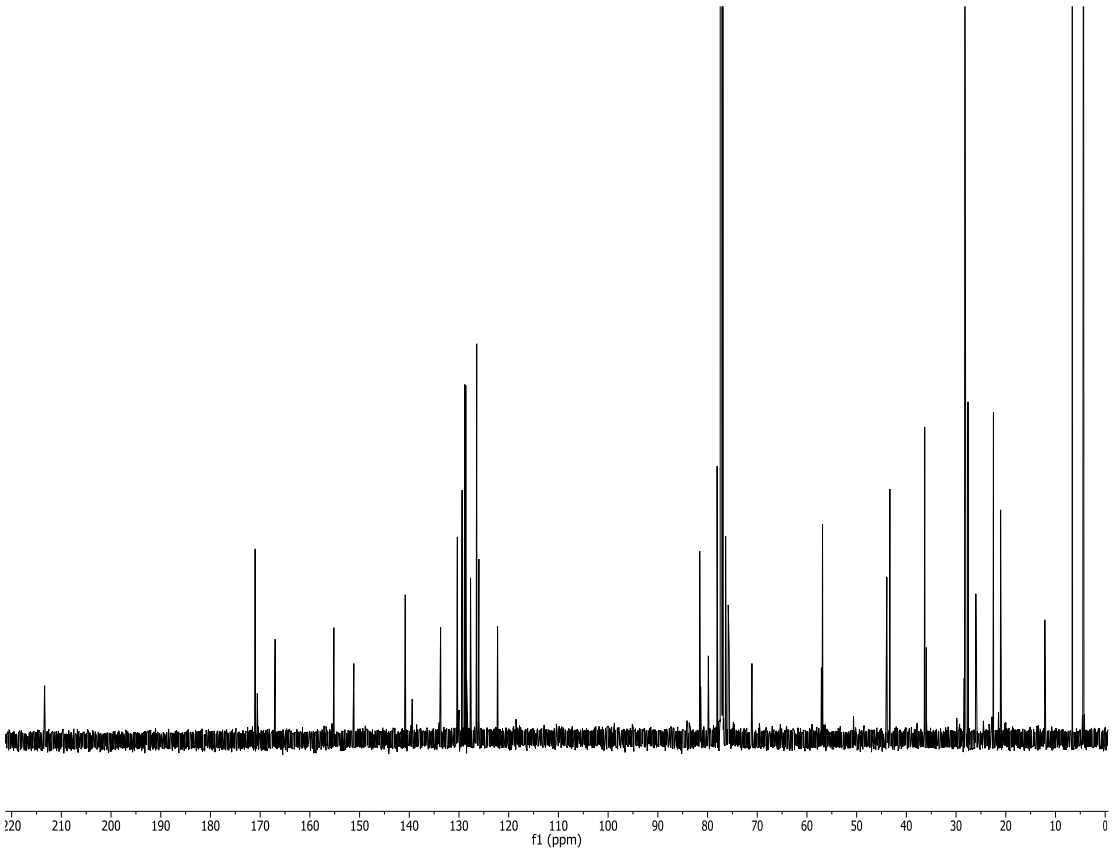

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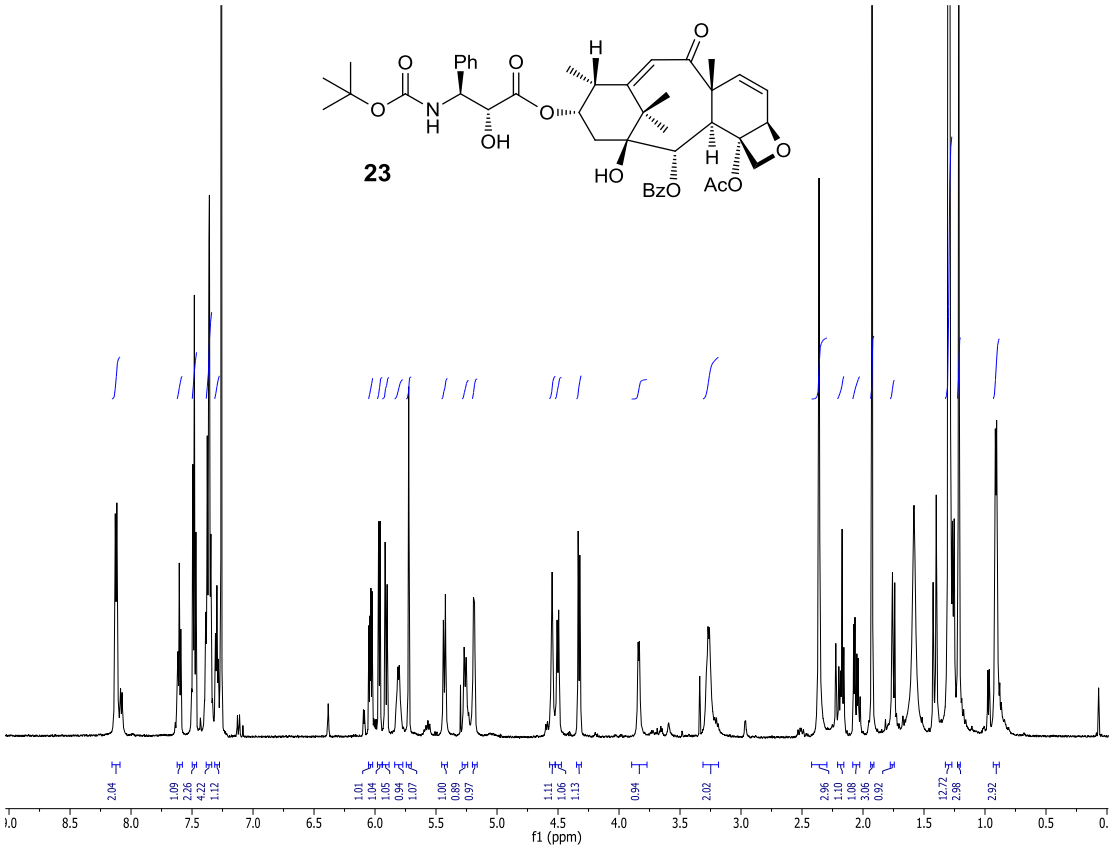

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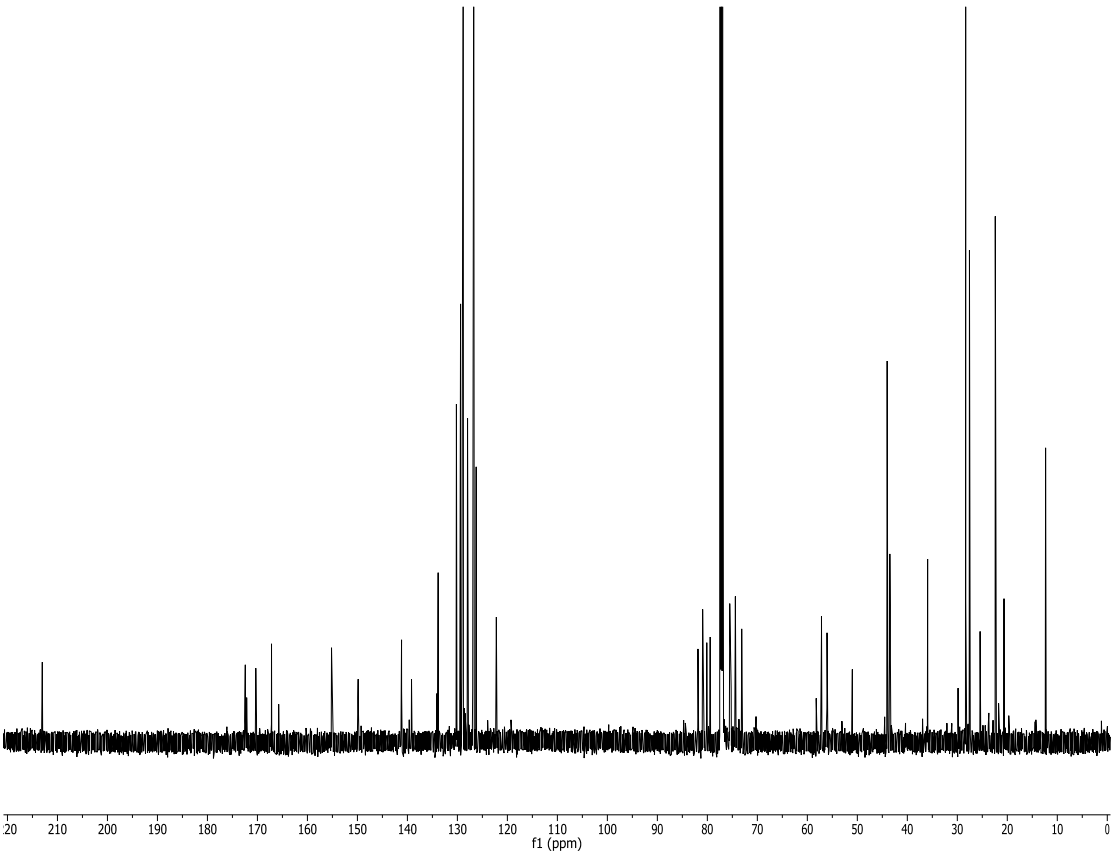

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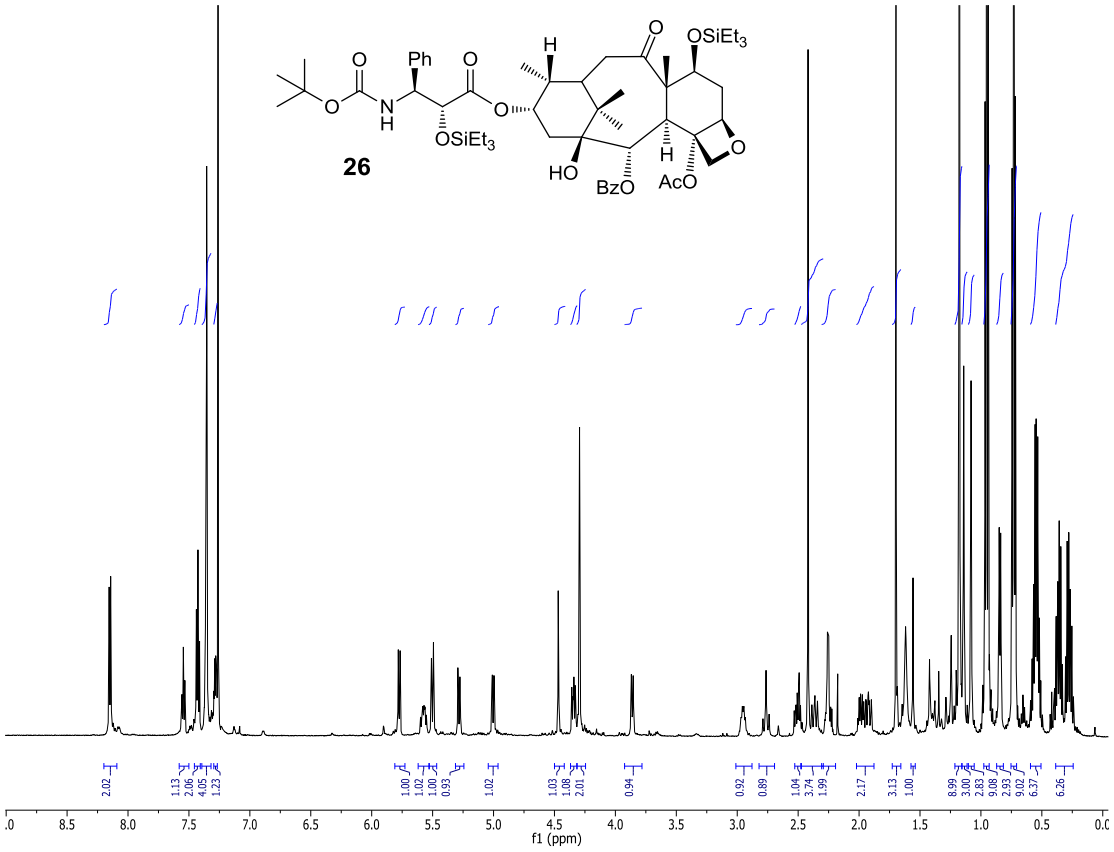

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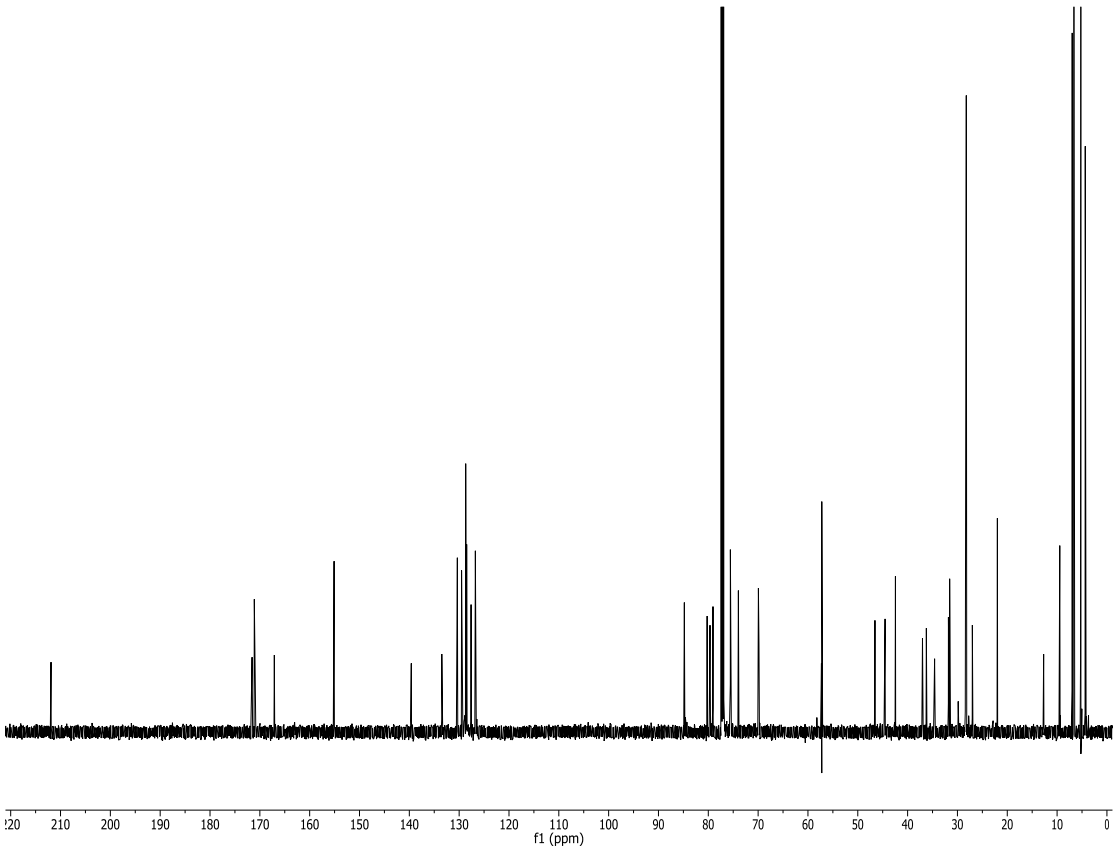

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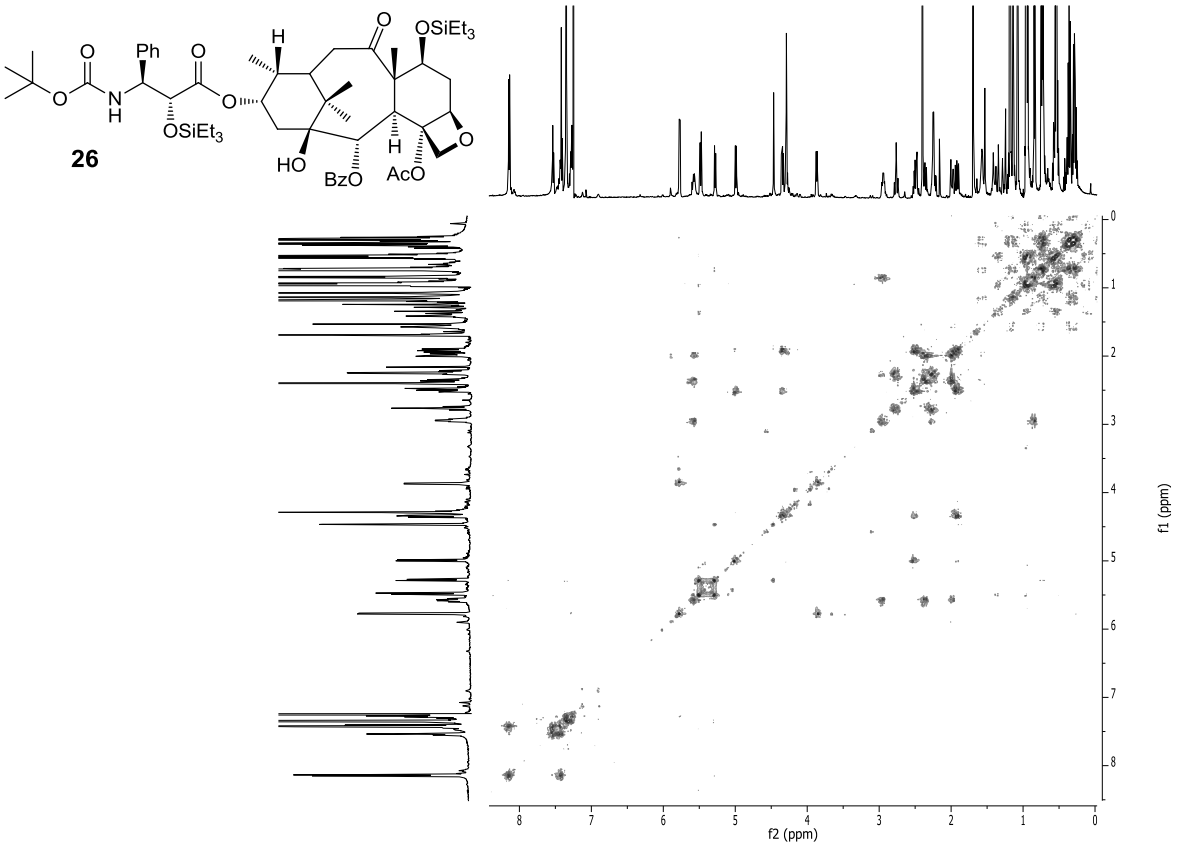
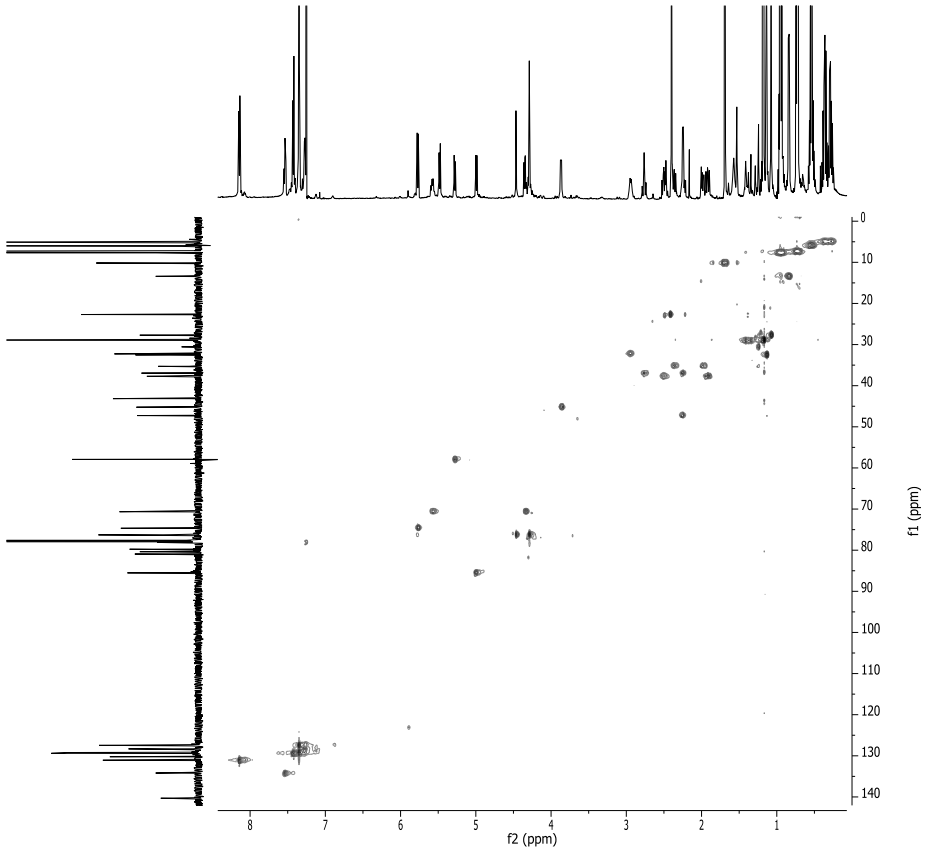
COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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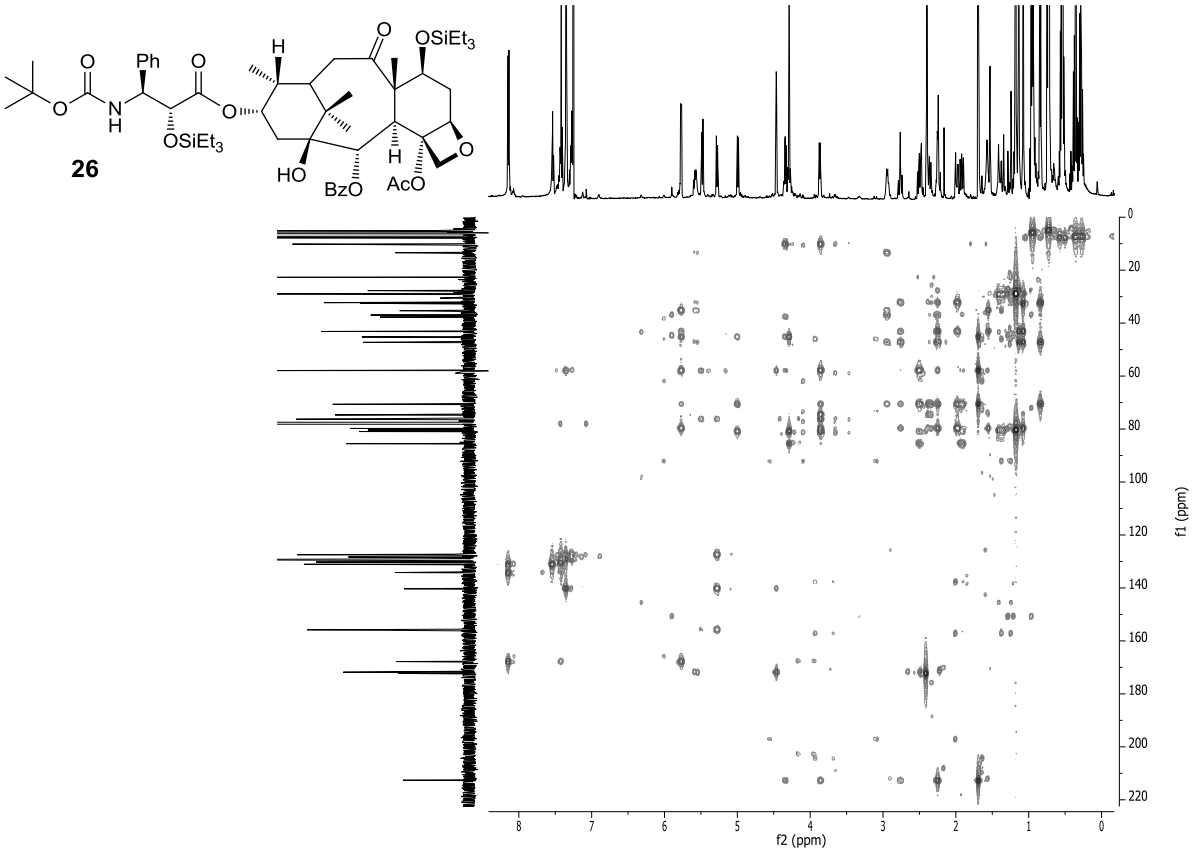
HMBC (600 MHz, $CDCl_3$):



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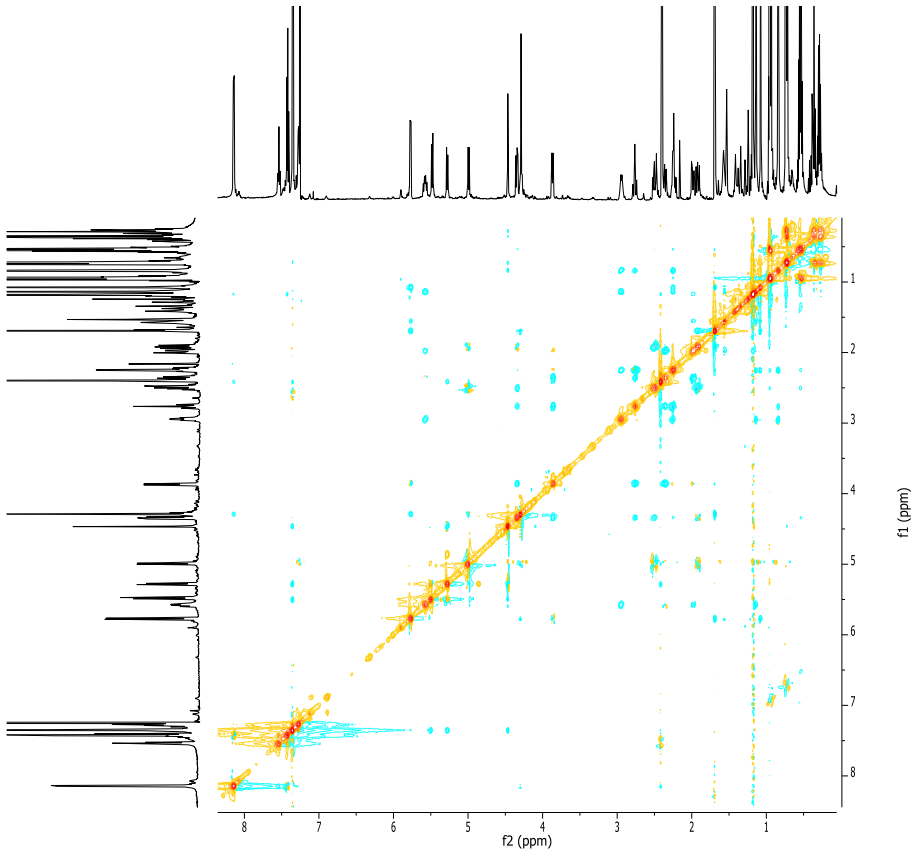

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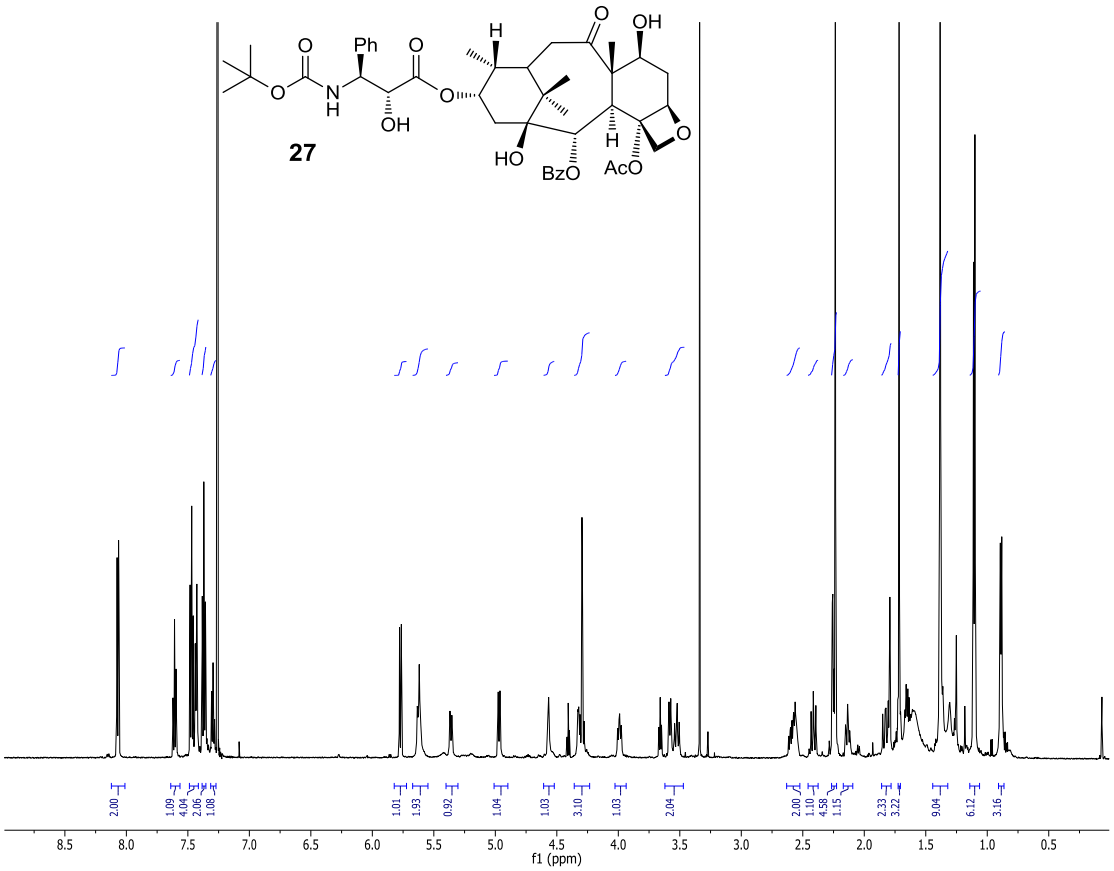
^{1}H NMR (600 MHz, $CDCl_3$):



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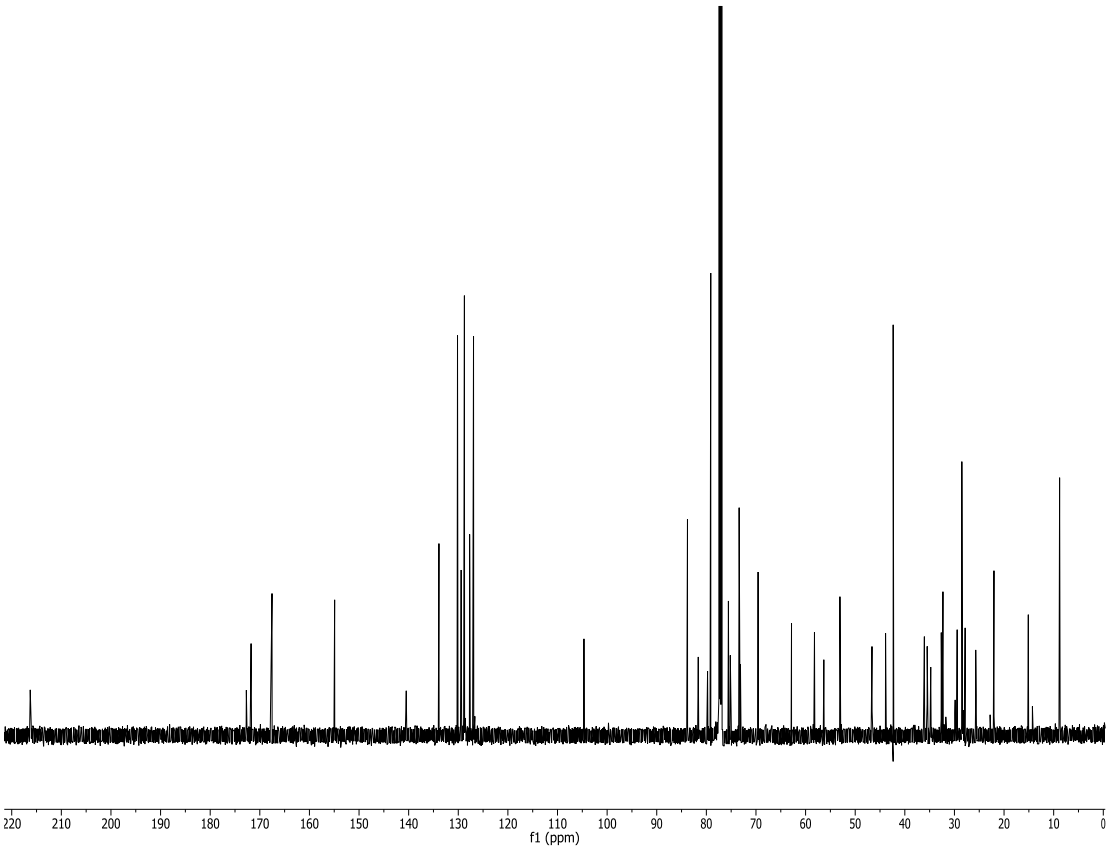

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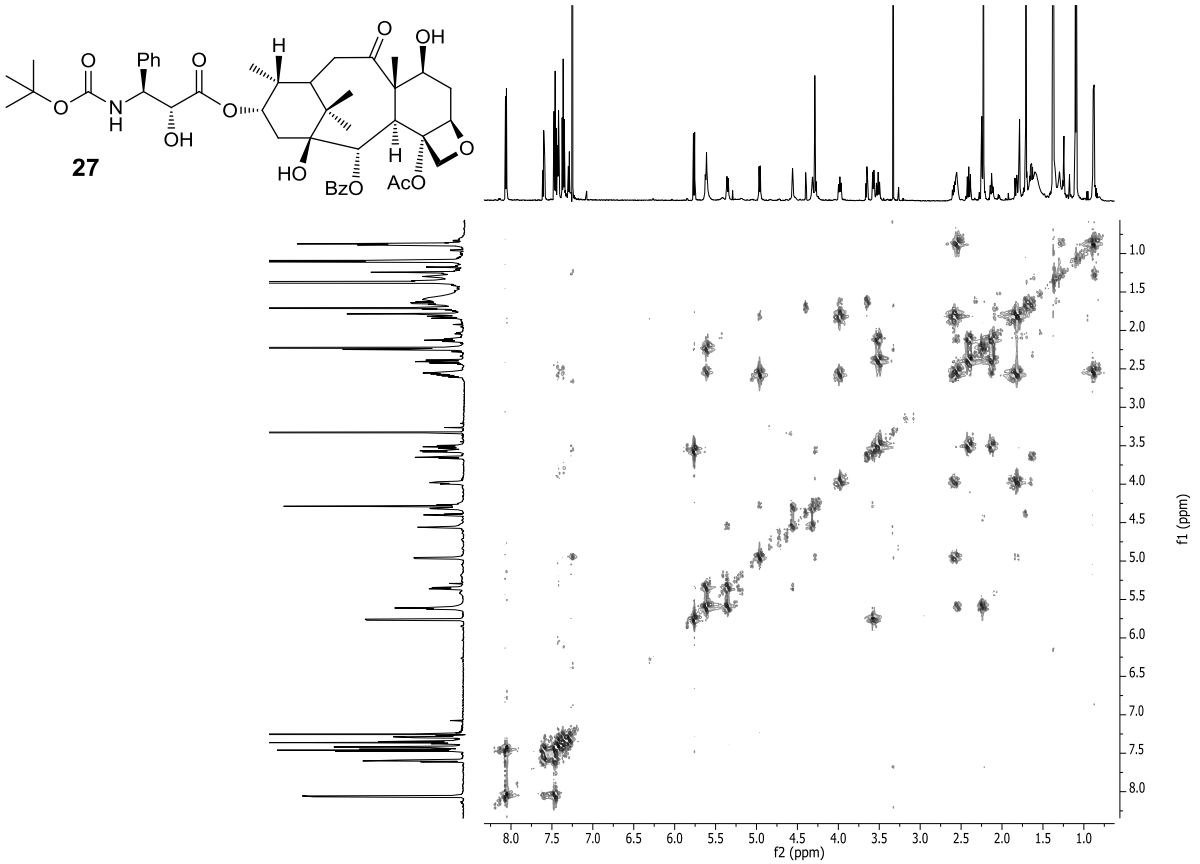
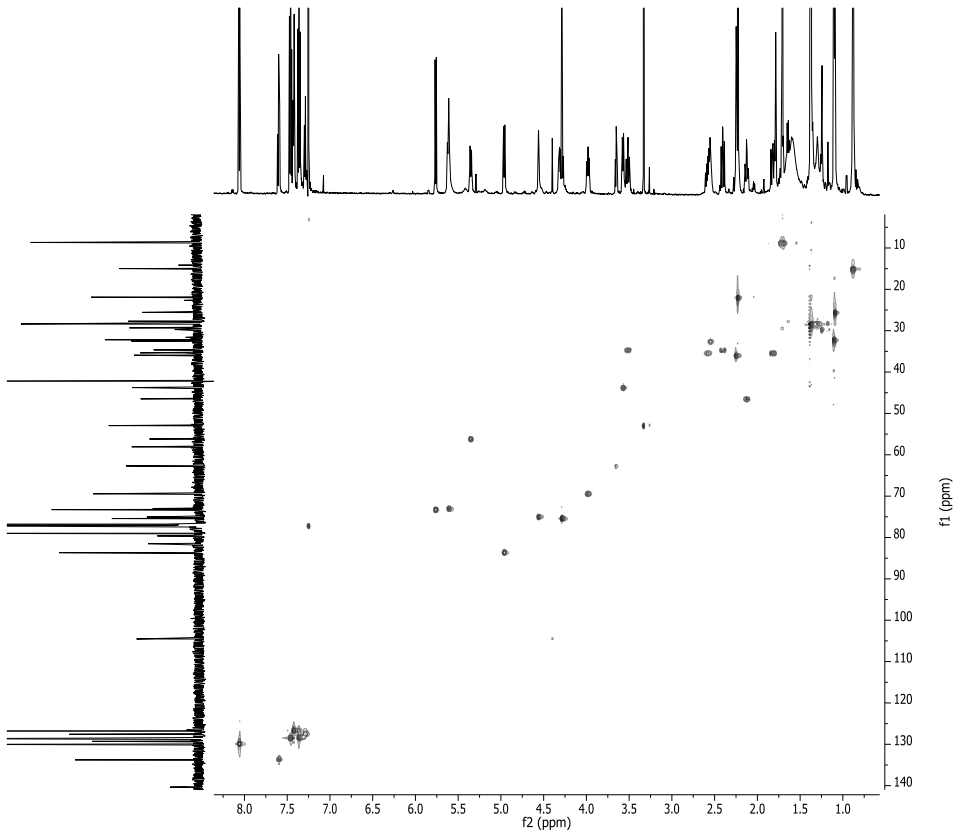
COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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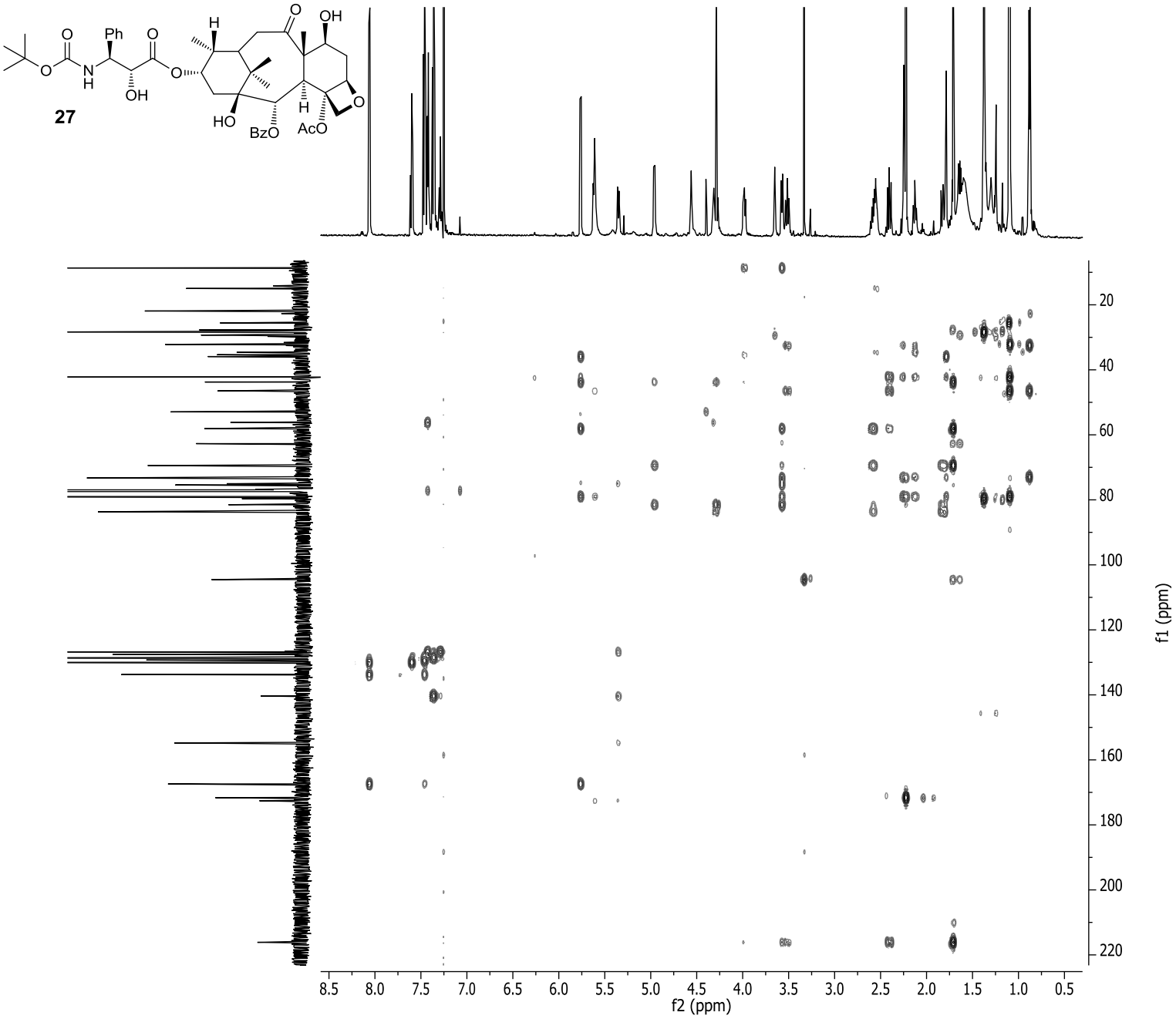
HMBC (600 MHz, $CDCl_3$):



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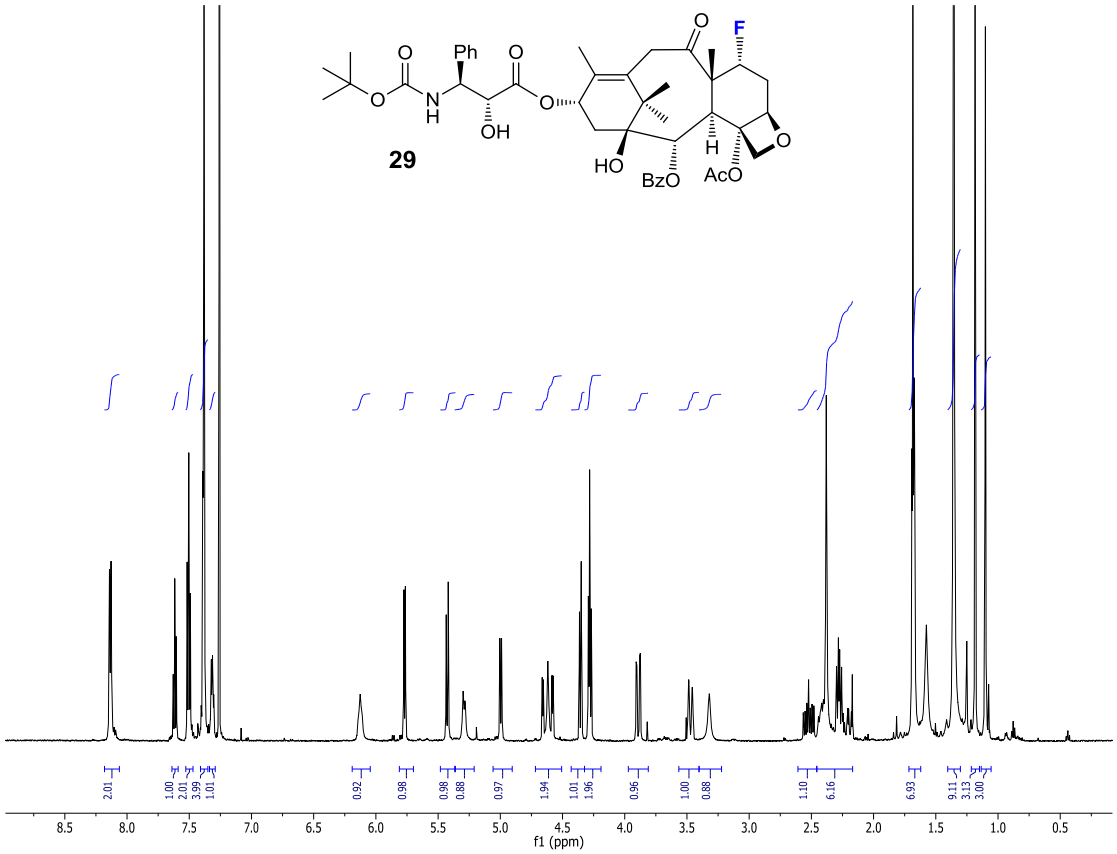

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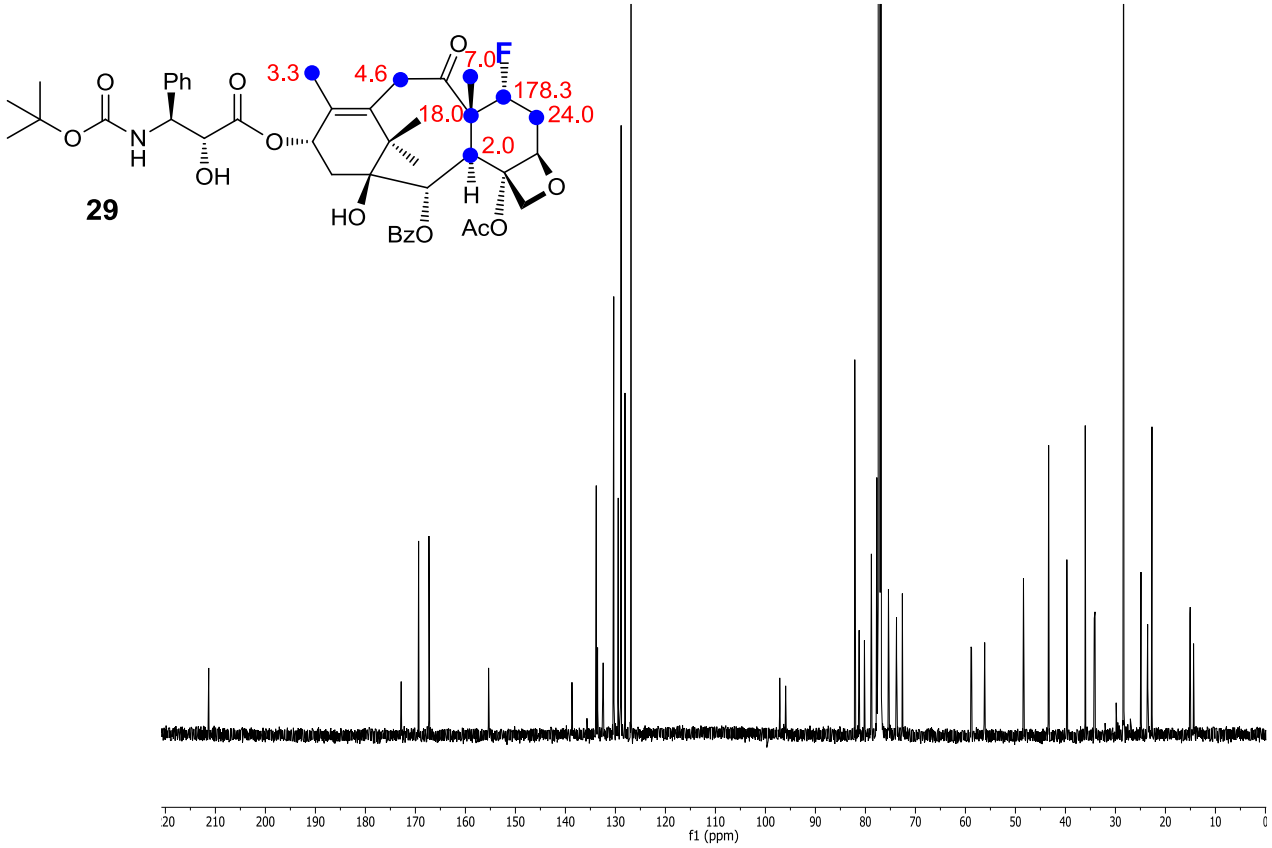

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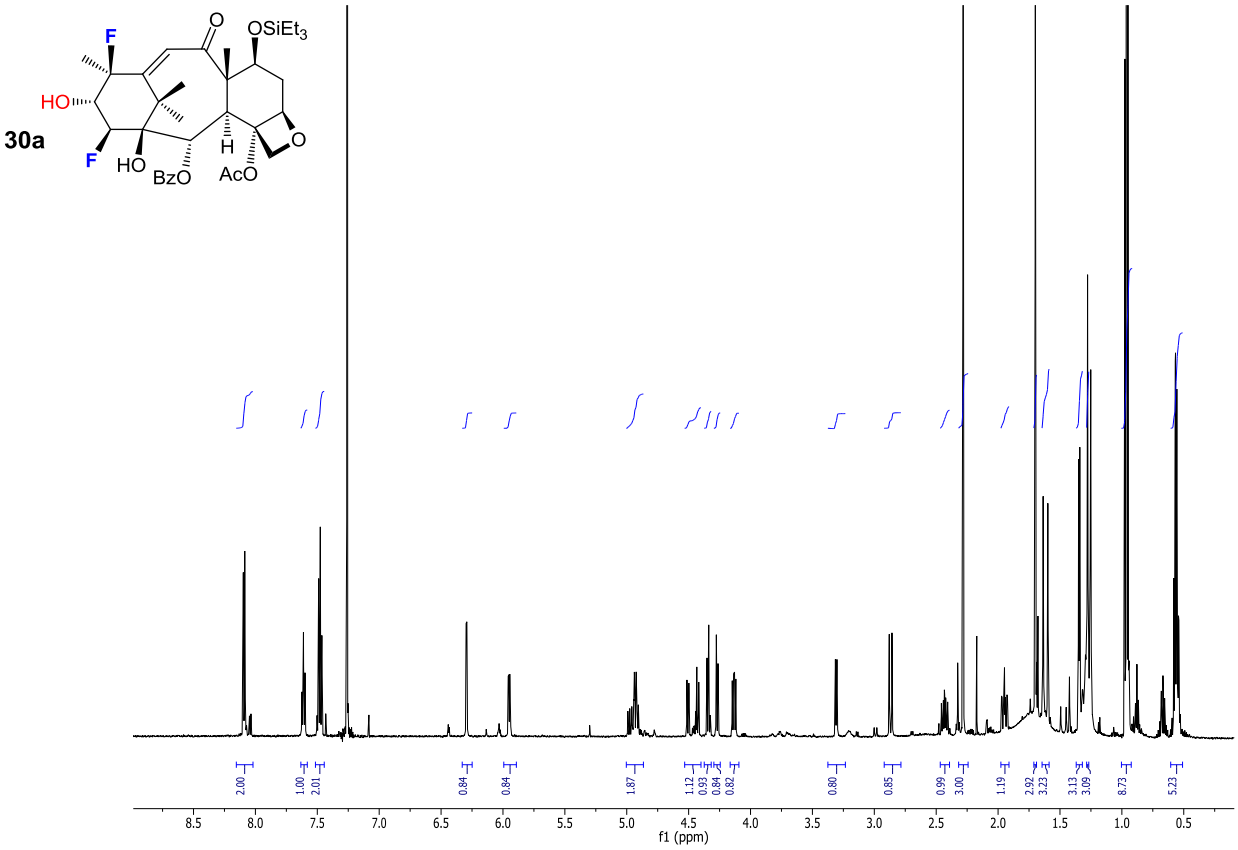

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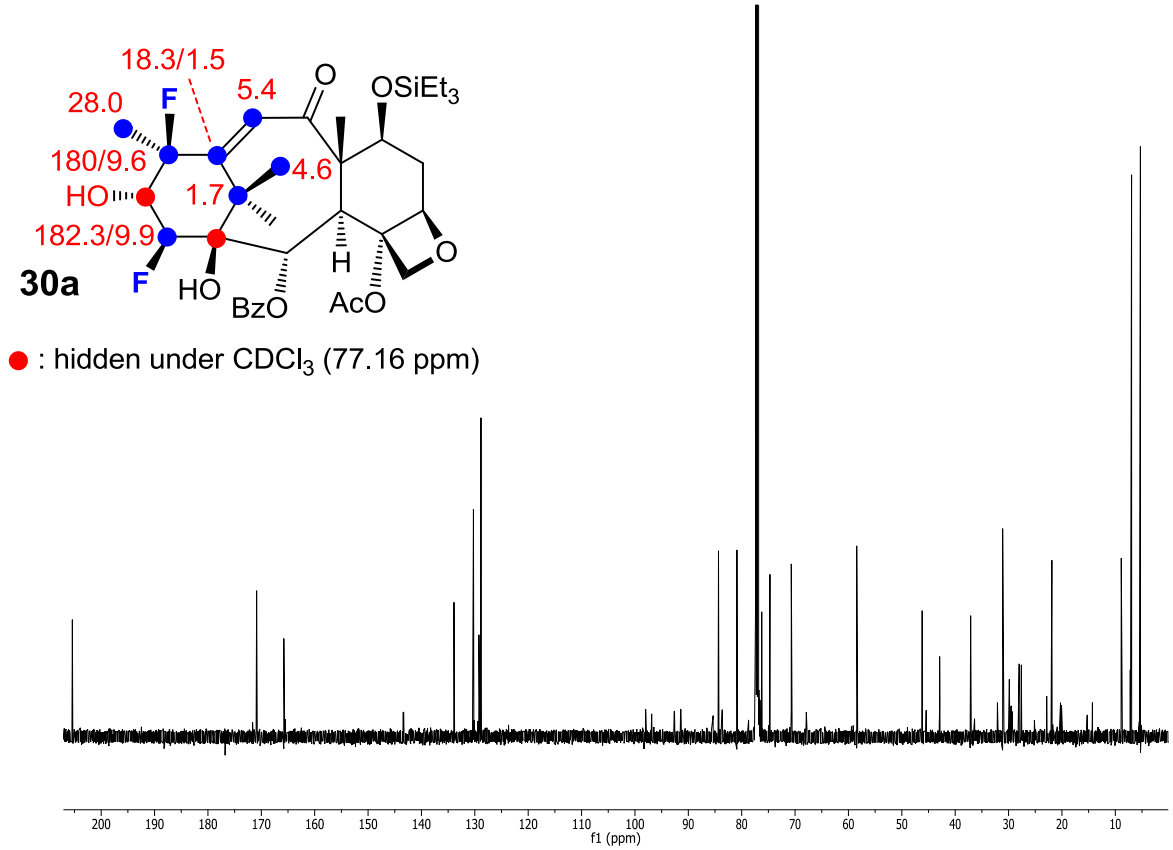

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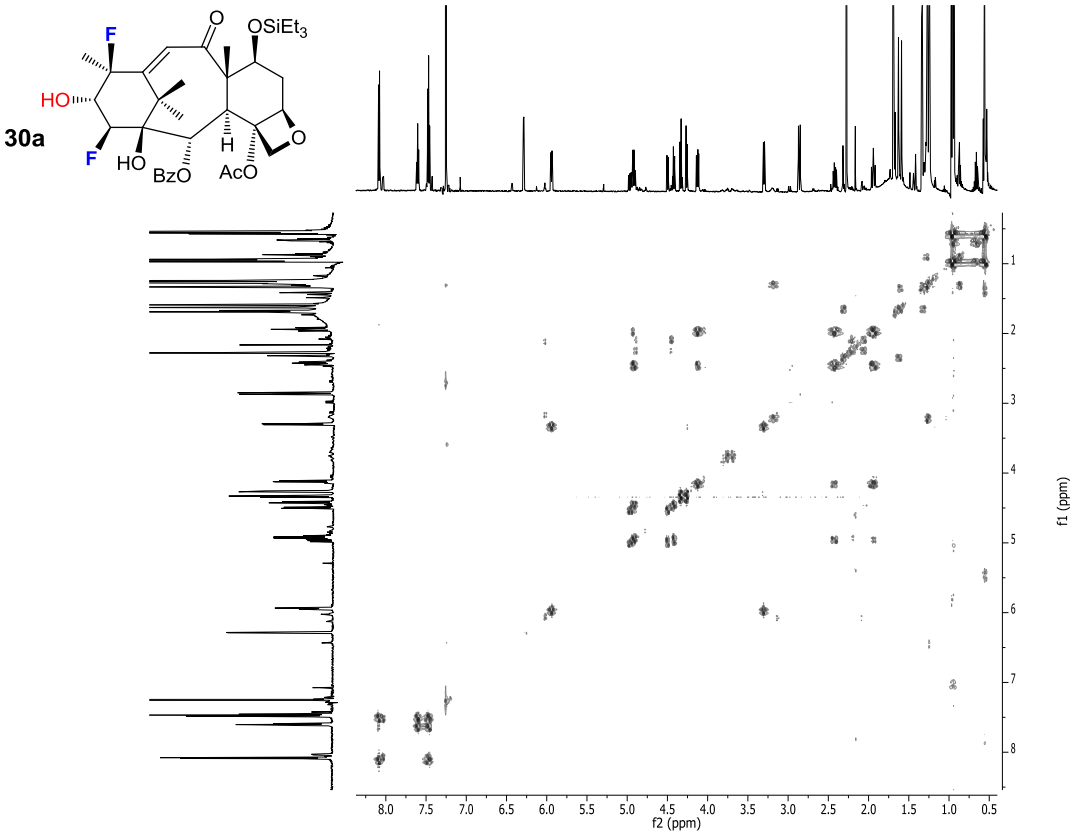

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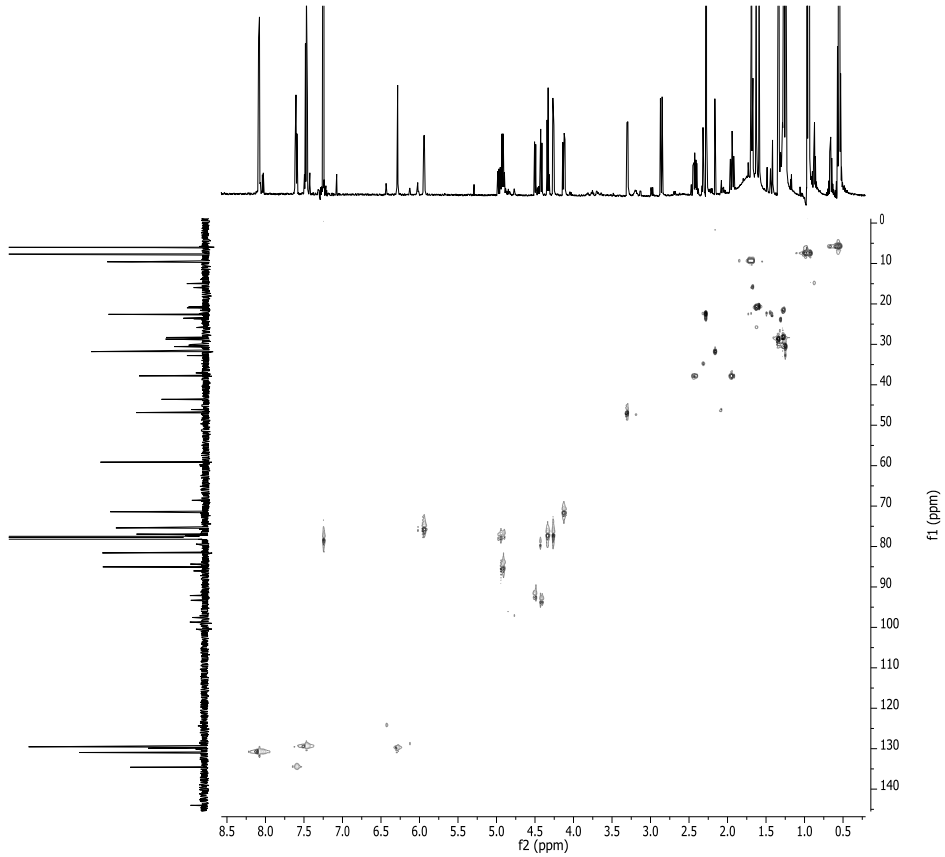

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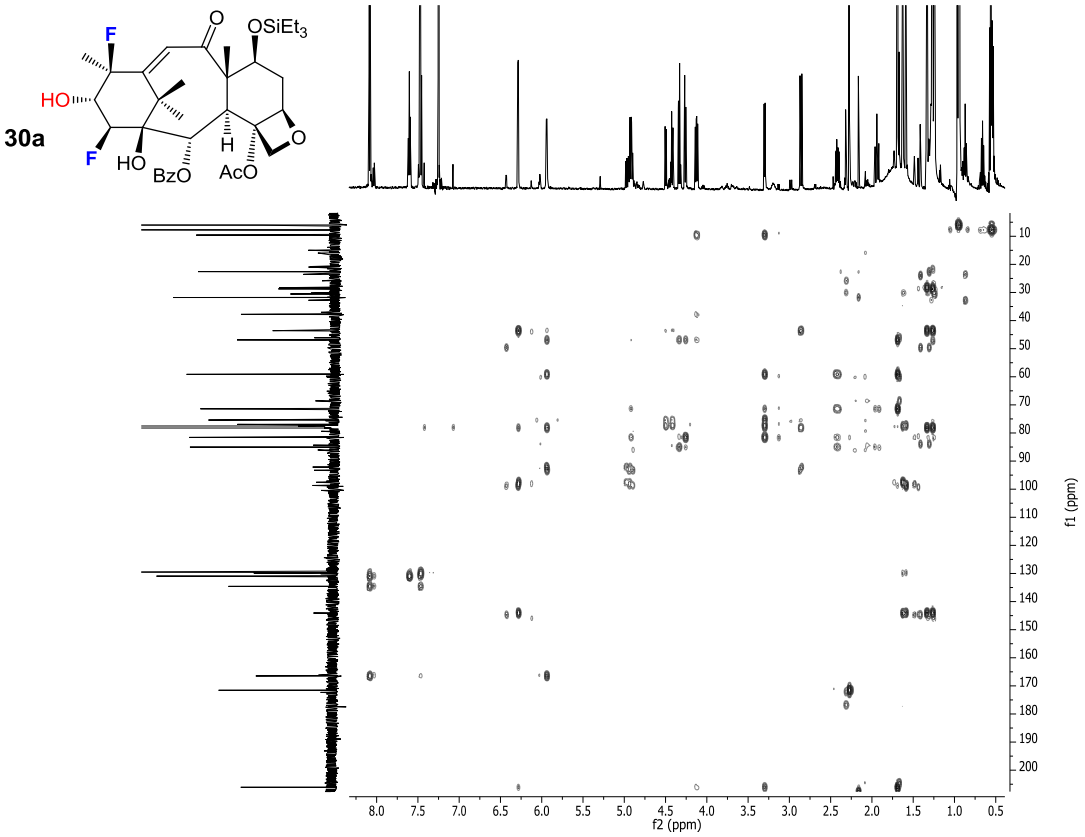
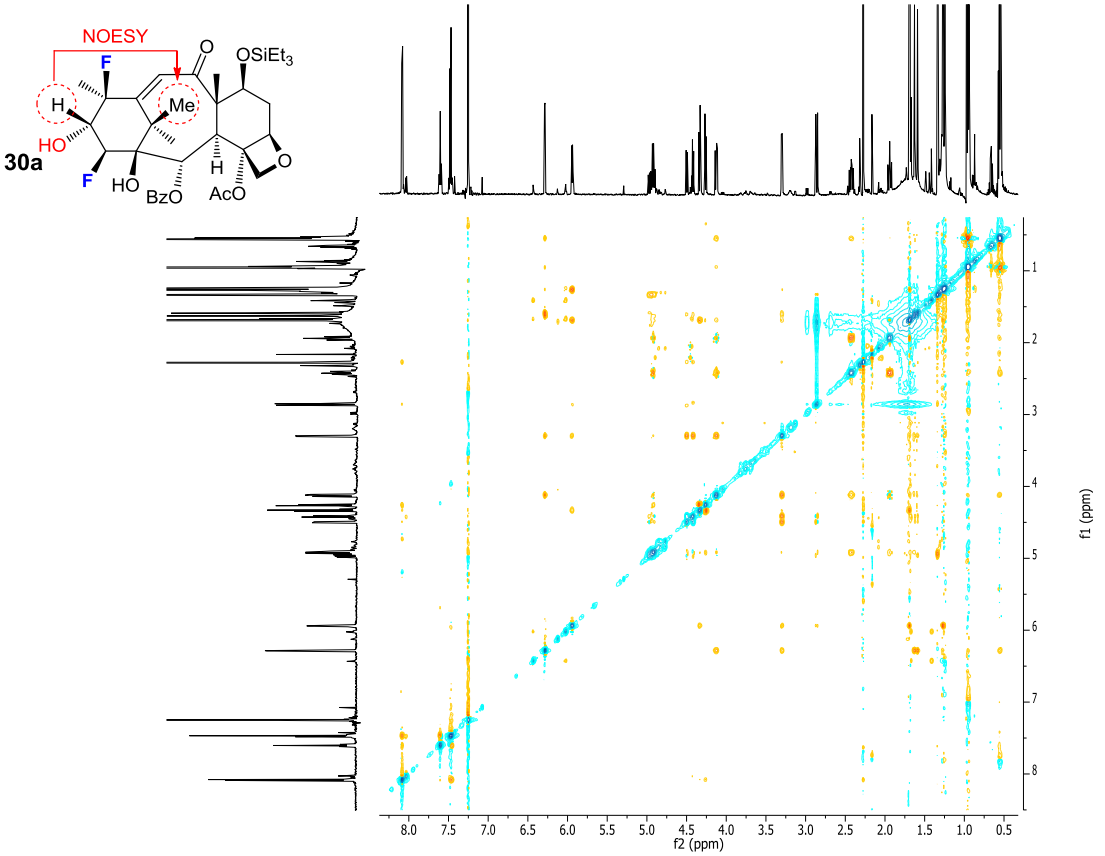
HMBC (600 MHz, $CDCl_3$):



NOESY (600 MHz, $CDCl_3$):



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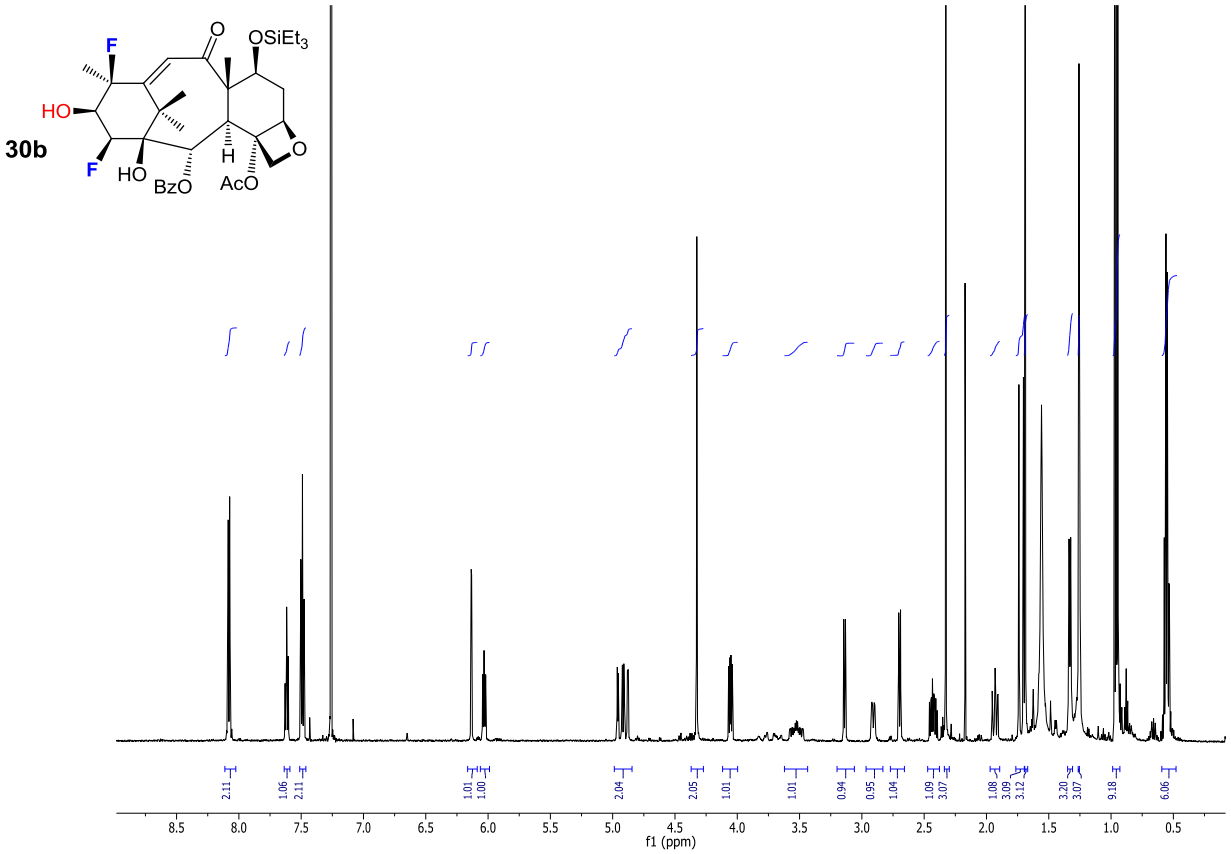
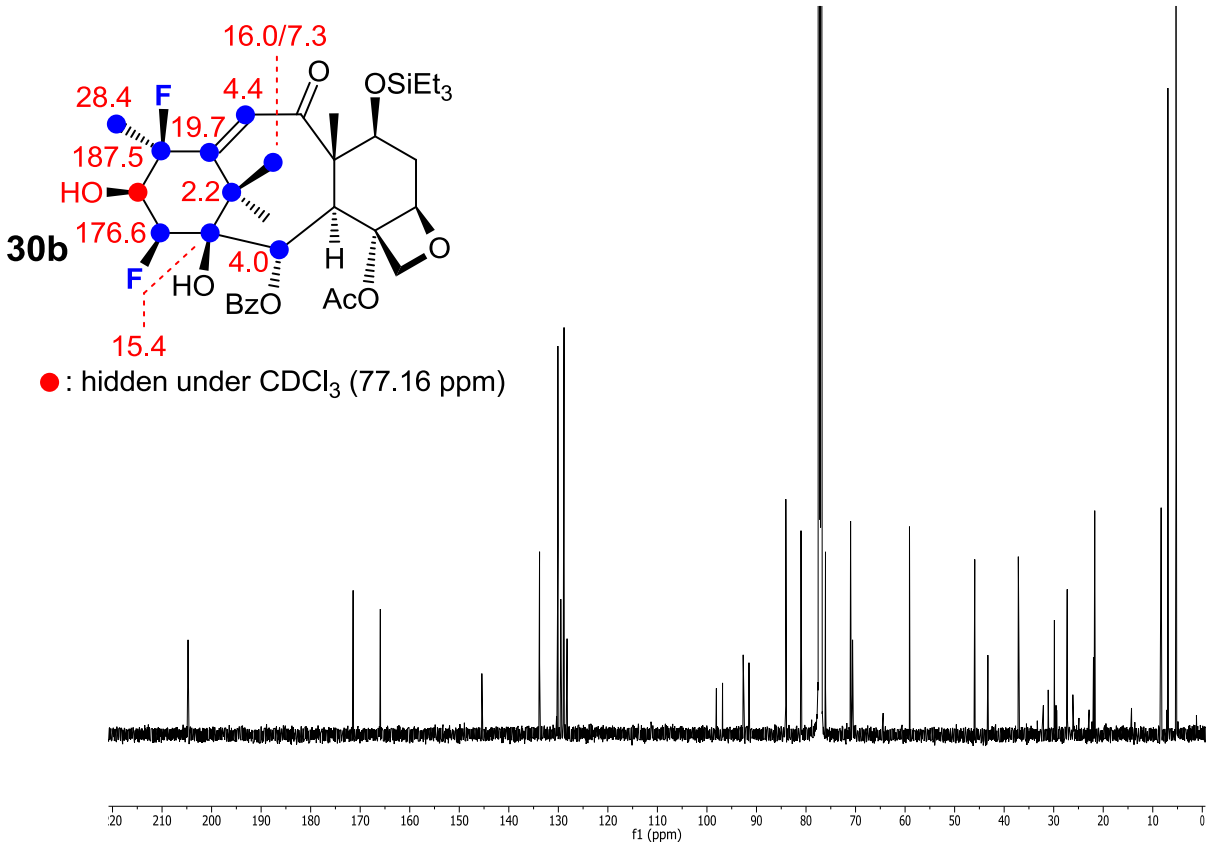
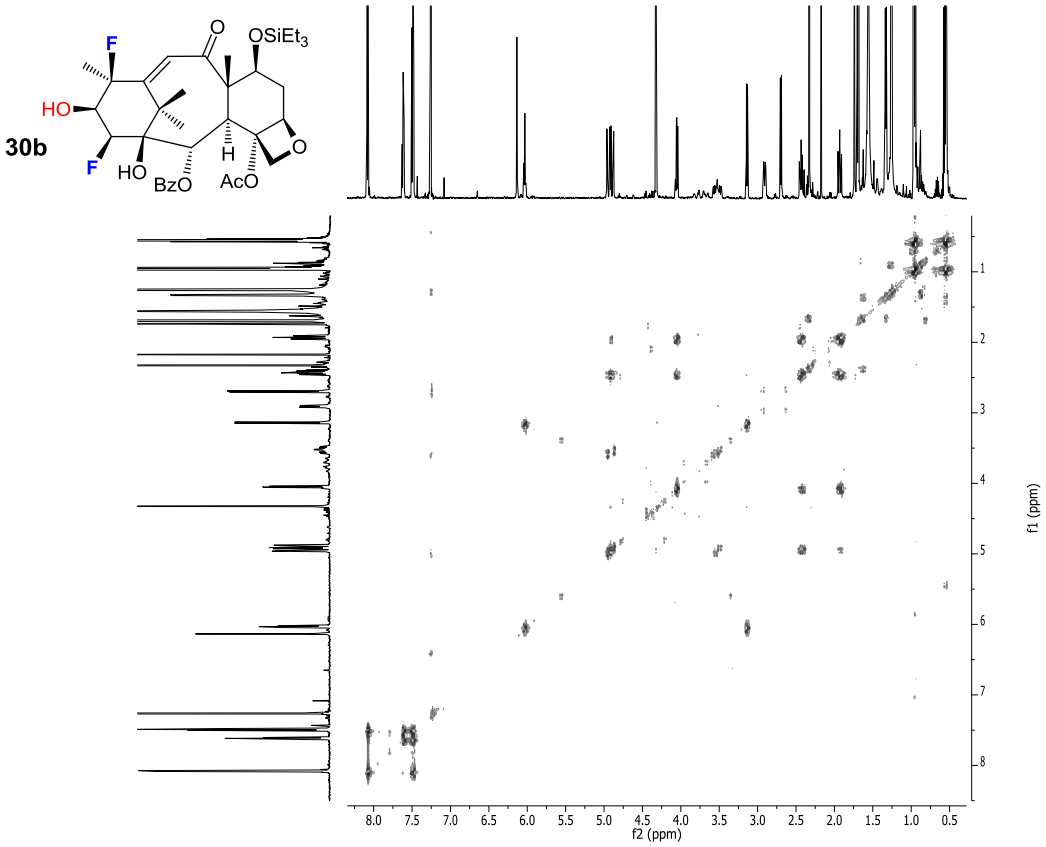
^{1}H NMR (600 MHz, $CDCl_3$):



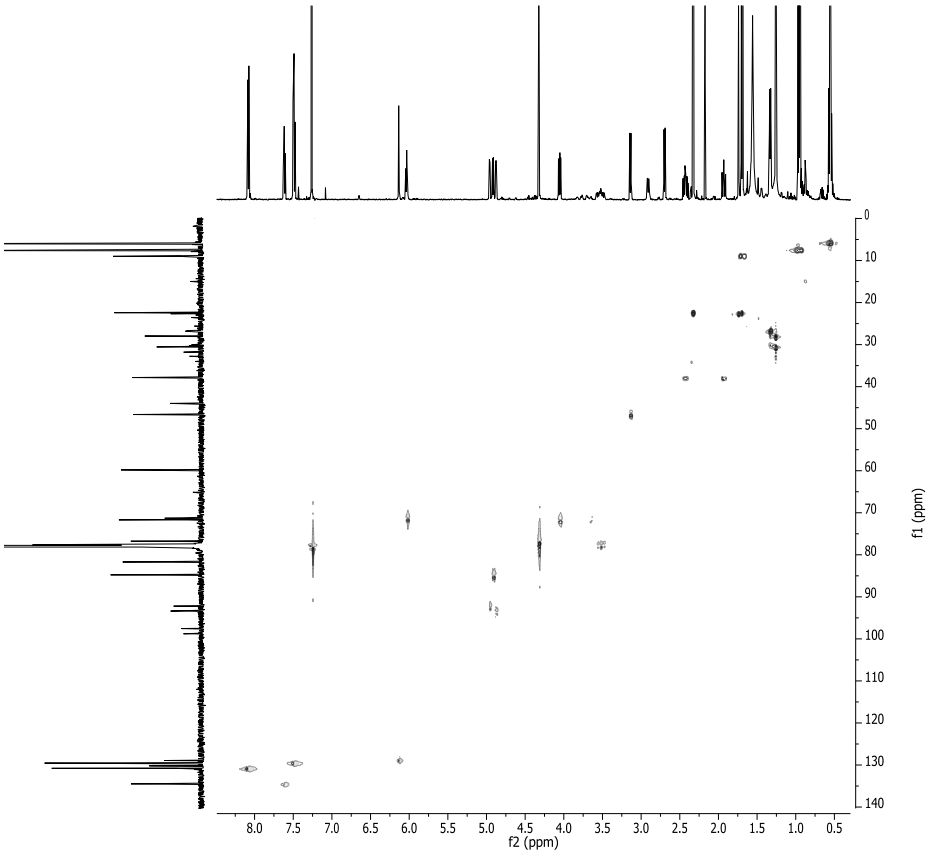
^{13}C NMR (600 MHz, $CDCl_3$):



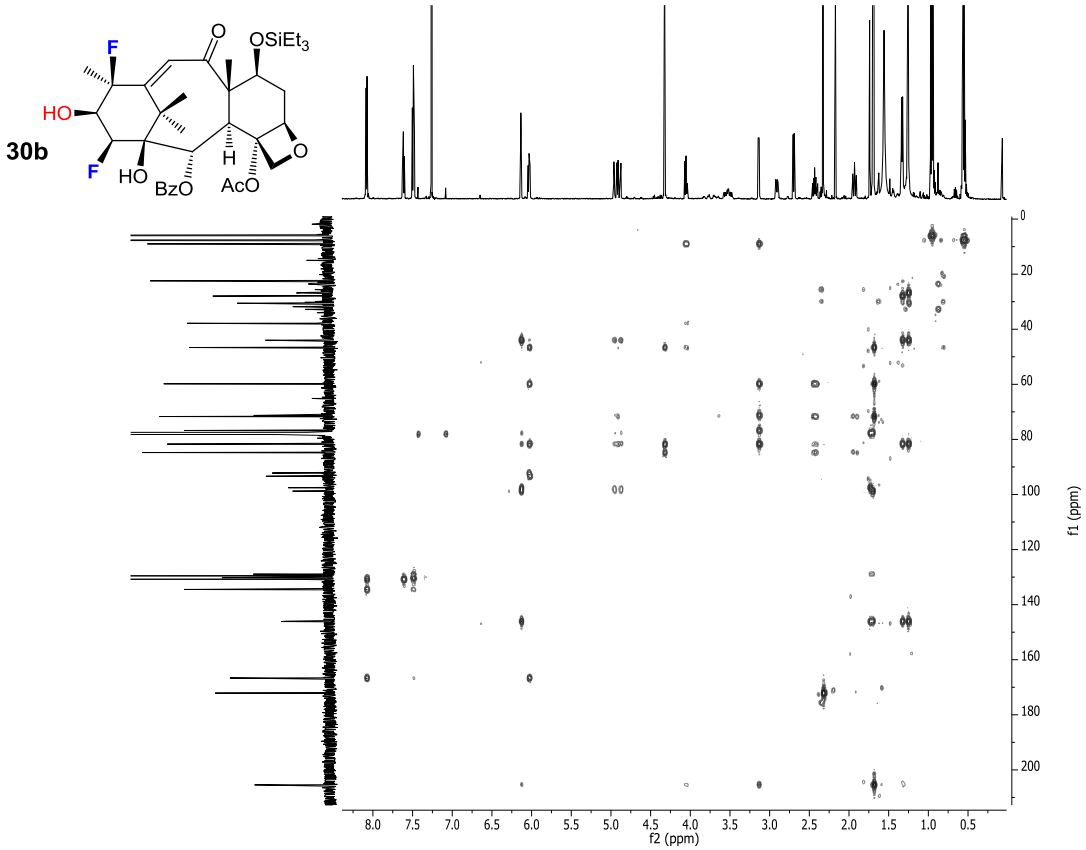
COSY (600 MHz, $CDCl_3$):



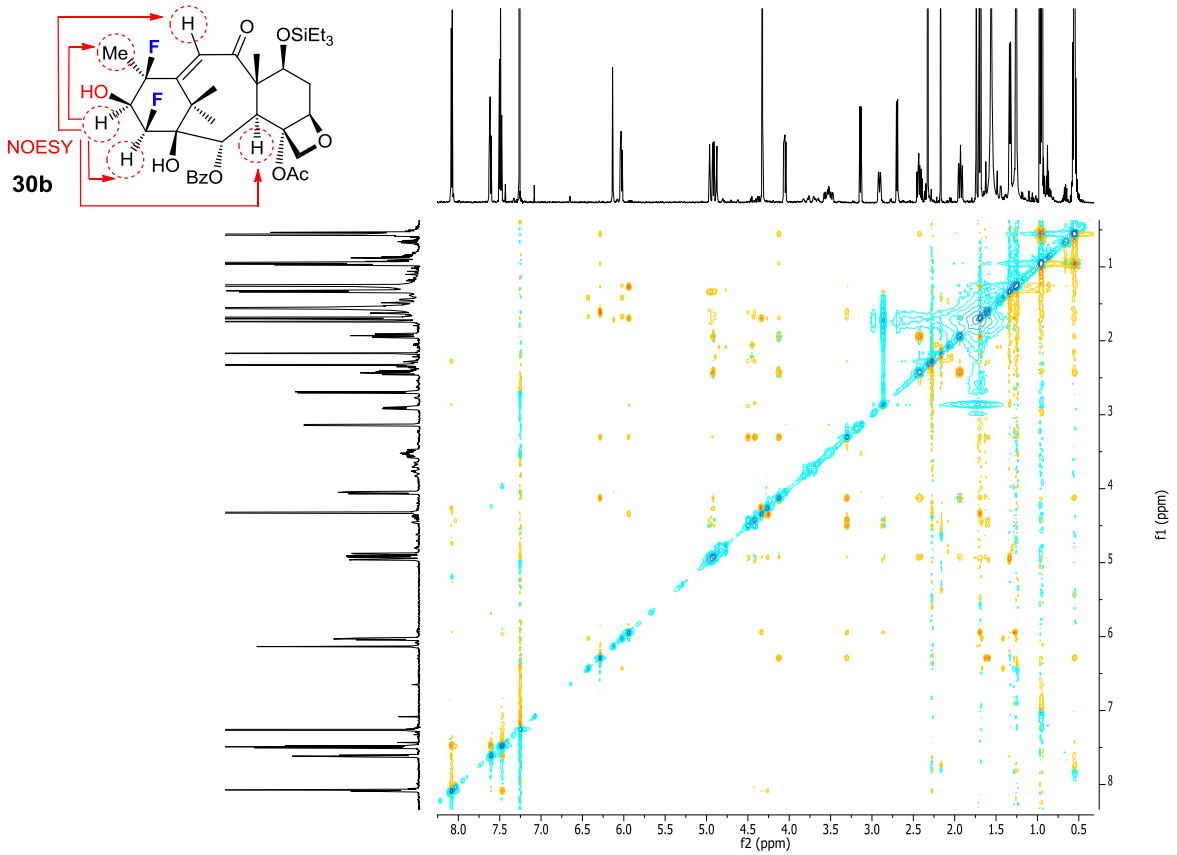
HMQC (600 MHz, $CDCl_3$):



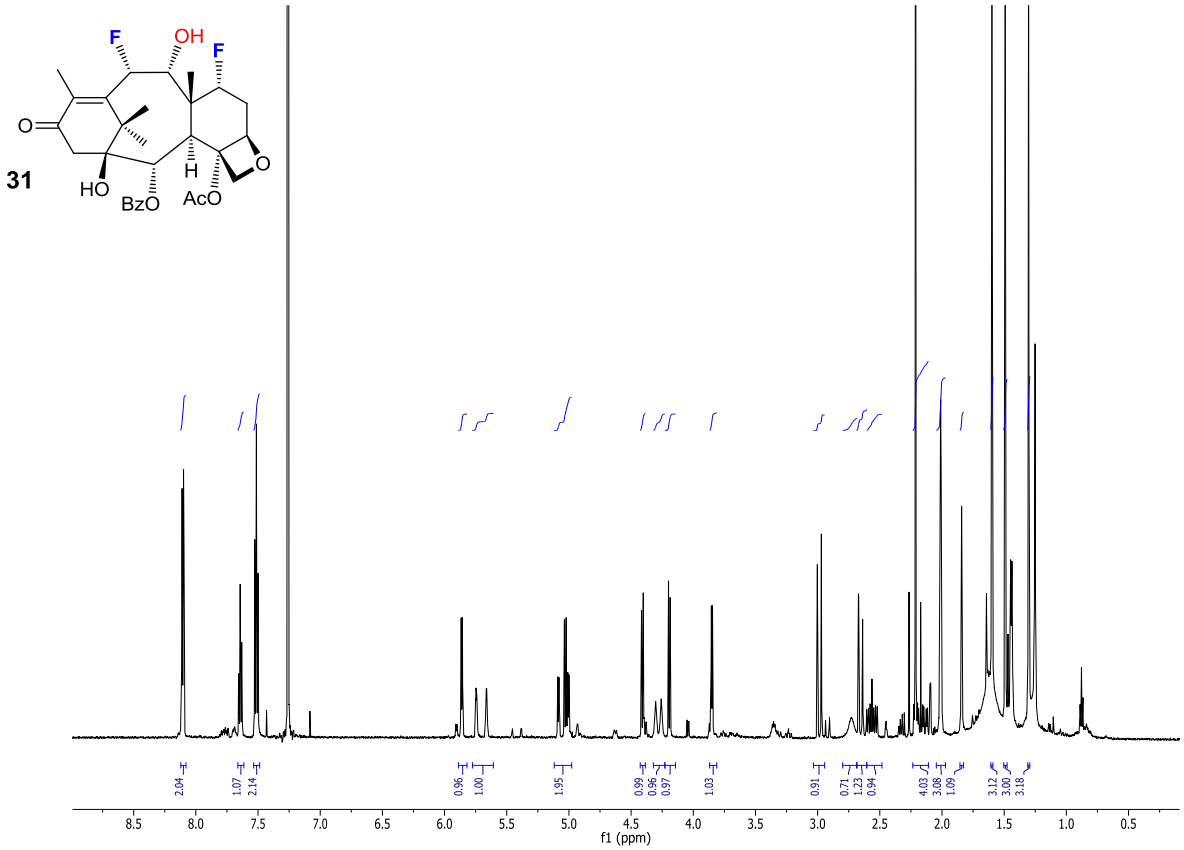
HMBC (600 MHz, $CDCl_3$):



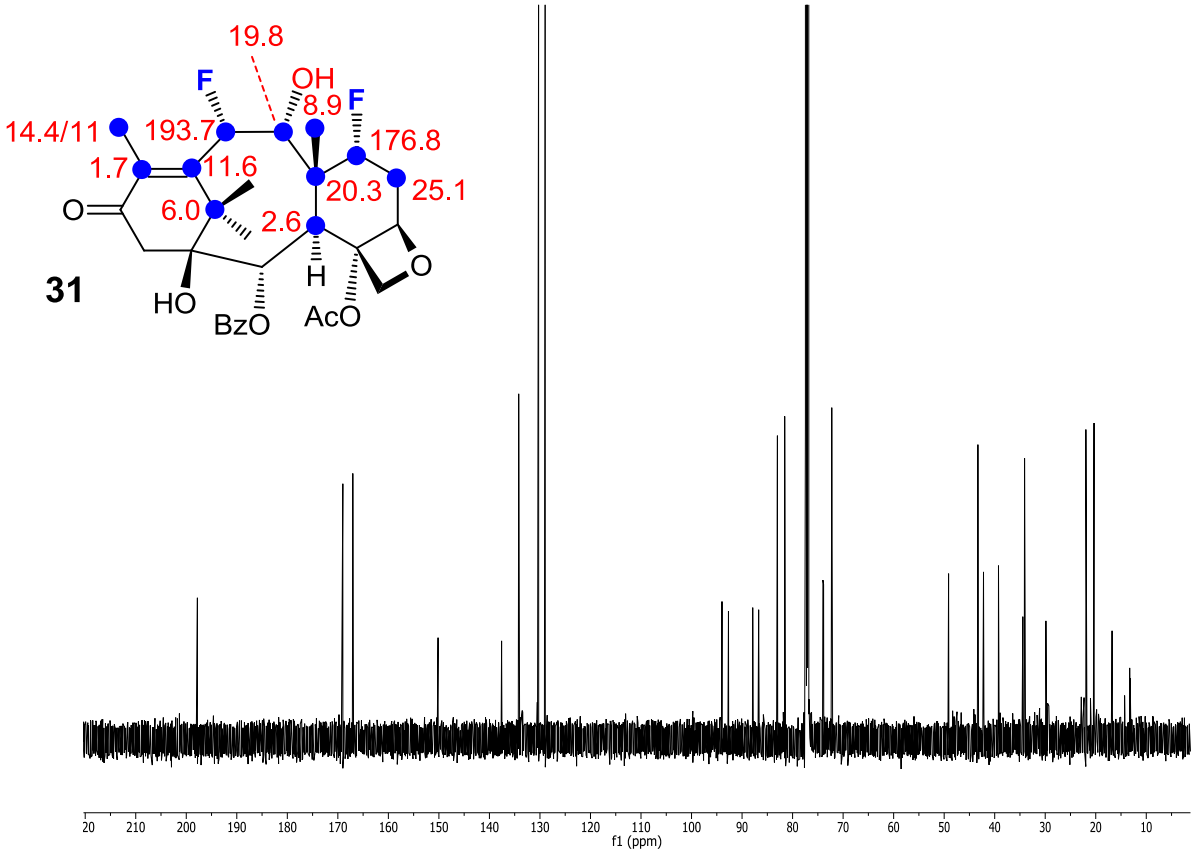
NOESY (600 MHz, $CDCl_3$):



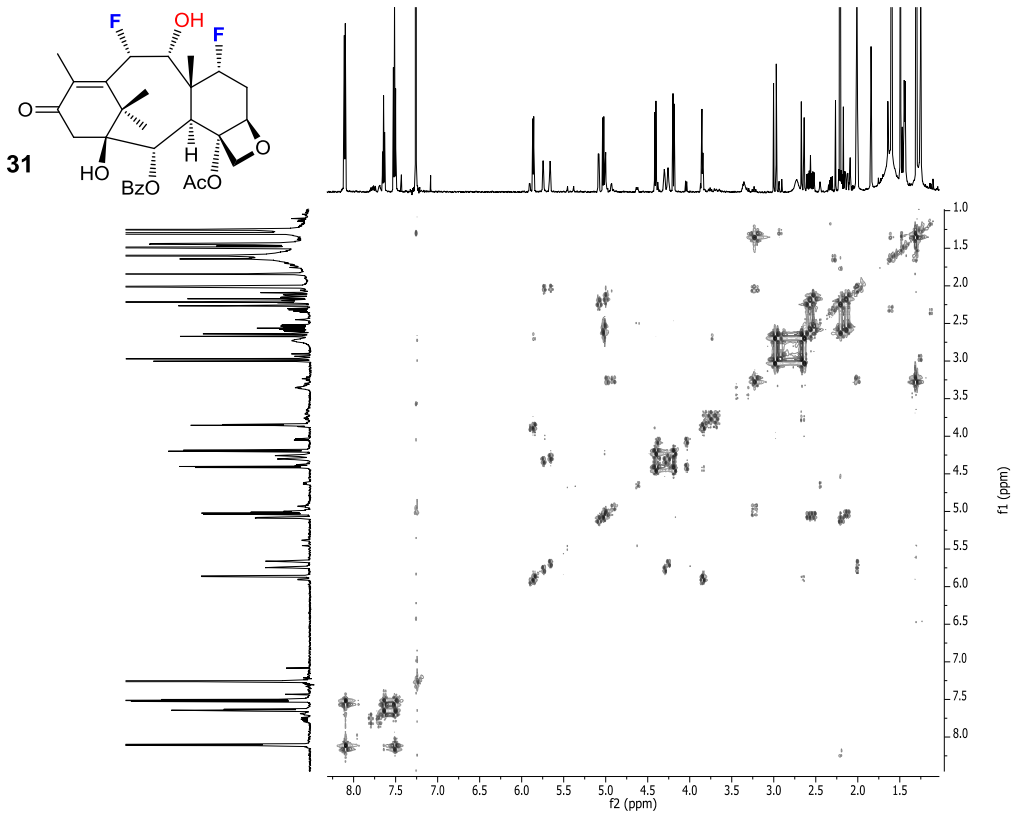
^{1}H NMR (600 MHz, $CDCl_3$):



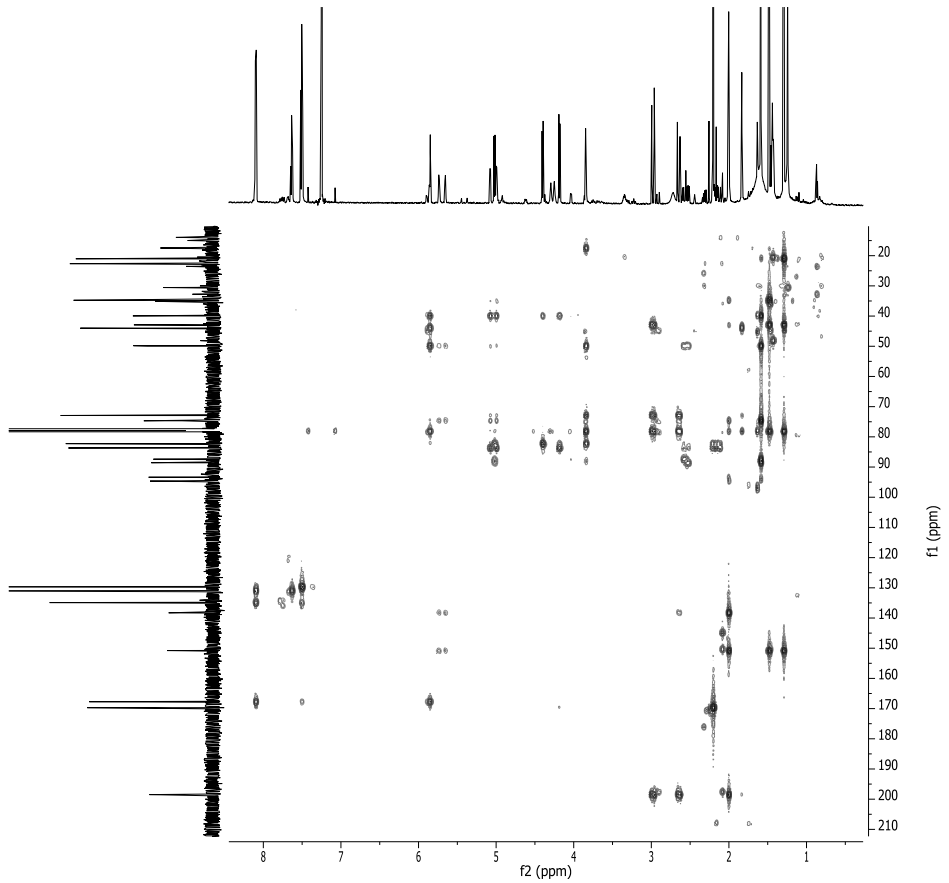
^{13}C NMR (600 MHz, $CDCl_3$):



COSY (600 MHz, $CDCl_3$):



HMBC (600 MHz, $CDCl_3$):



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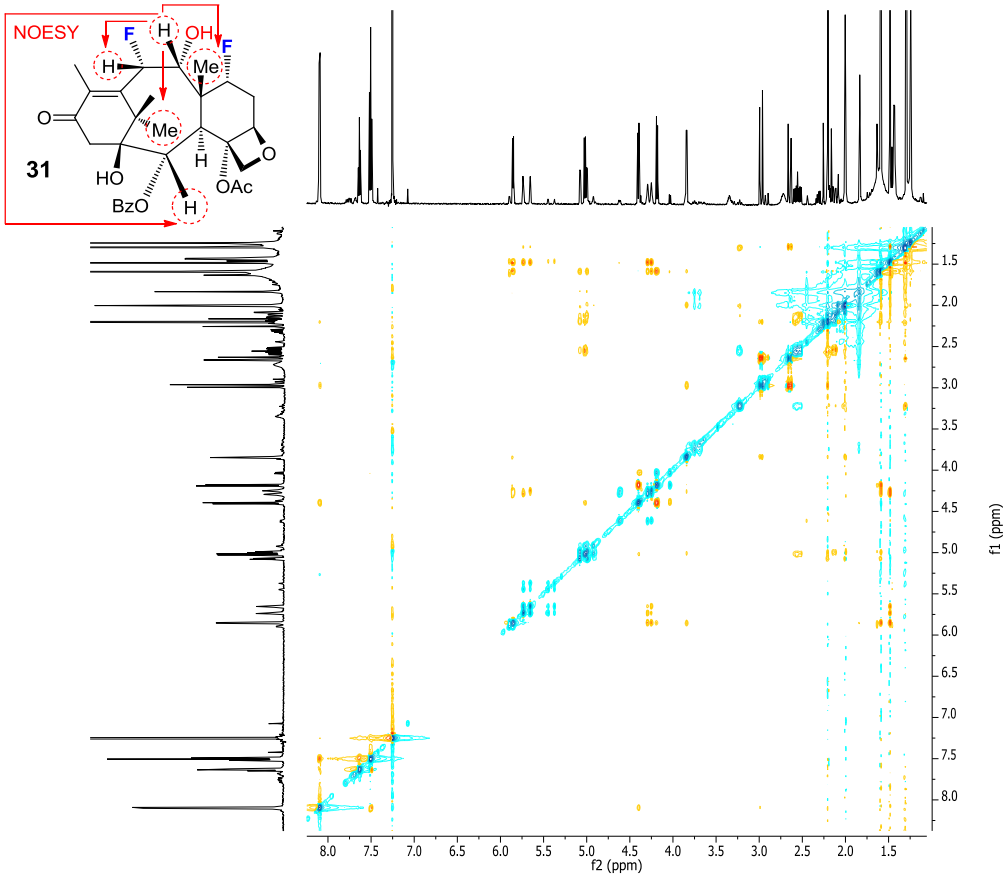
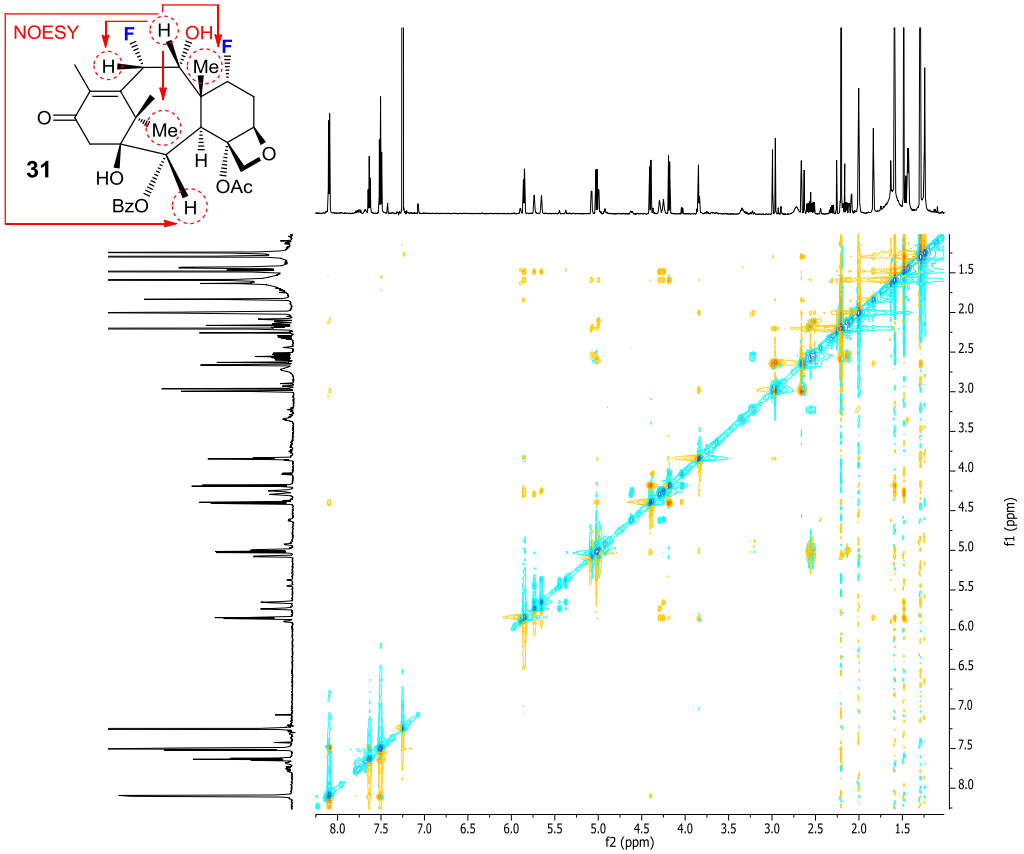
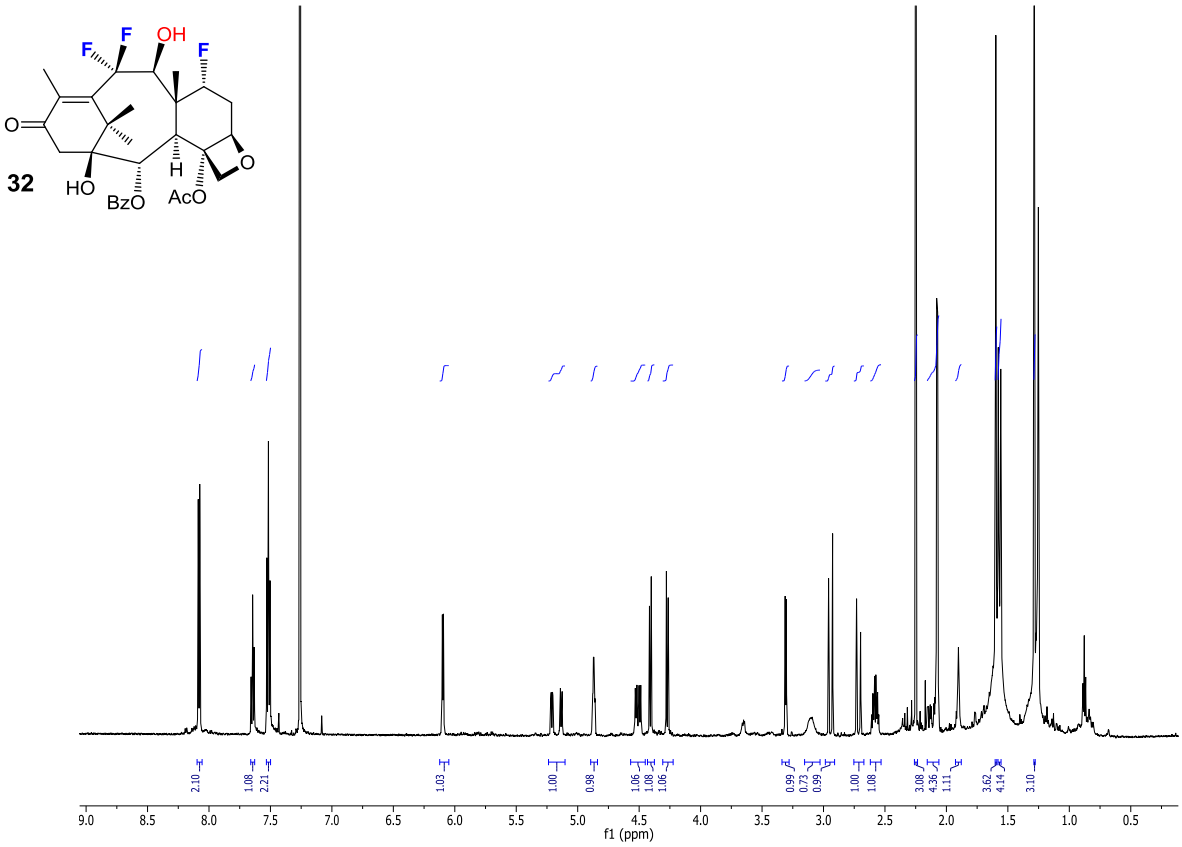
NOESY (600 MHz, $CDCl_3$):



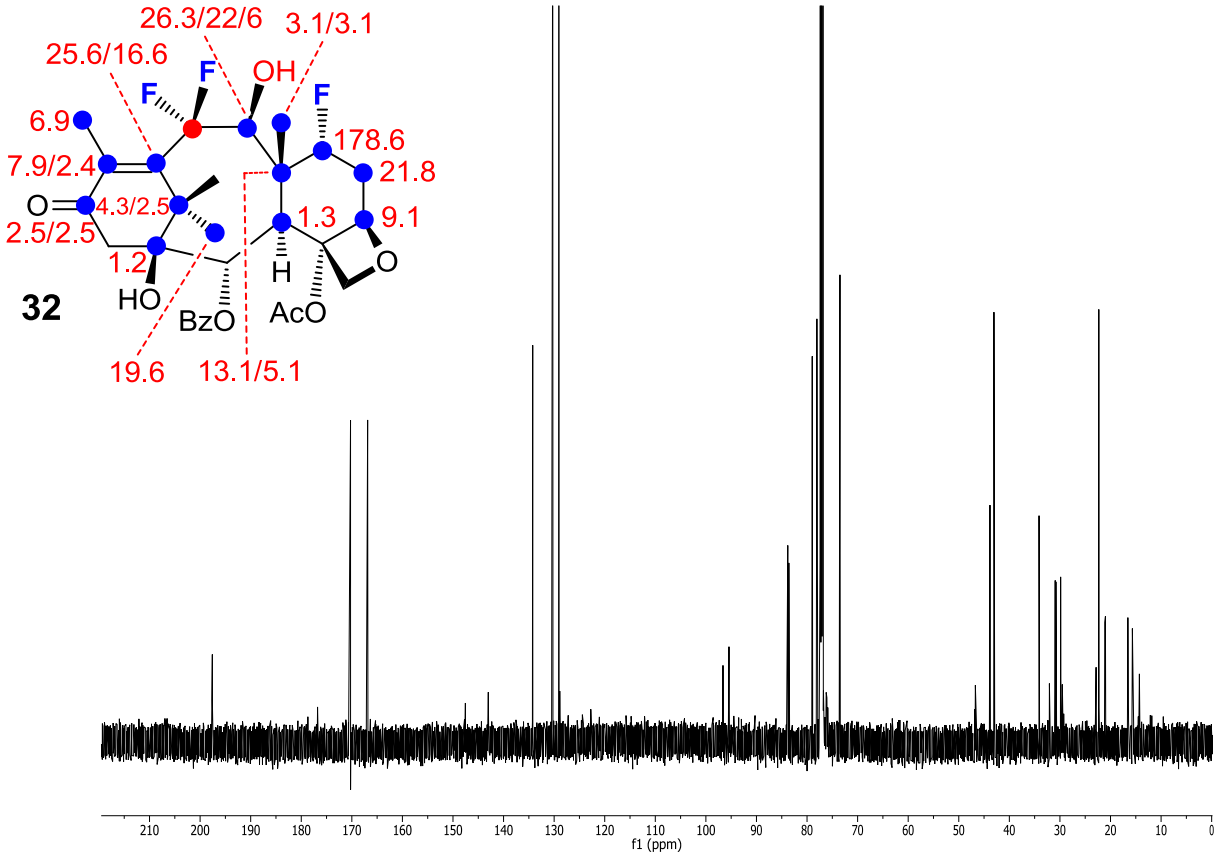
ROESY (600 MHz, $CDCl_3$):



^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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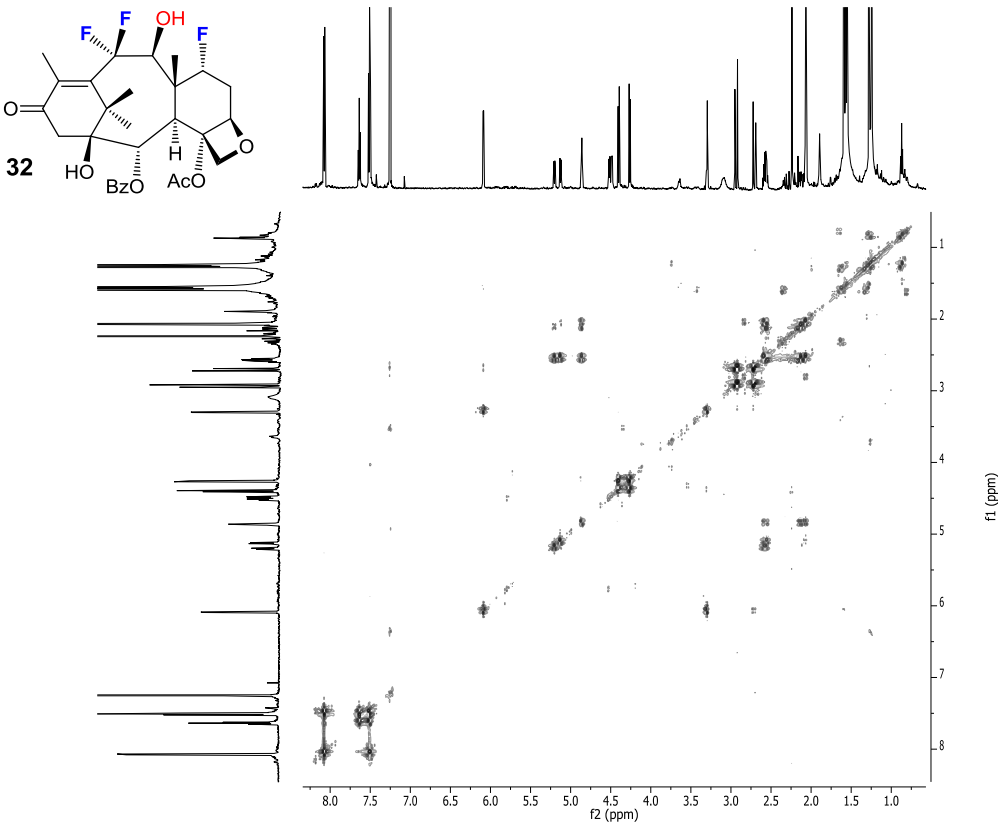
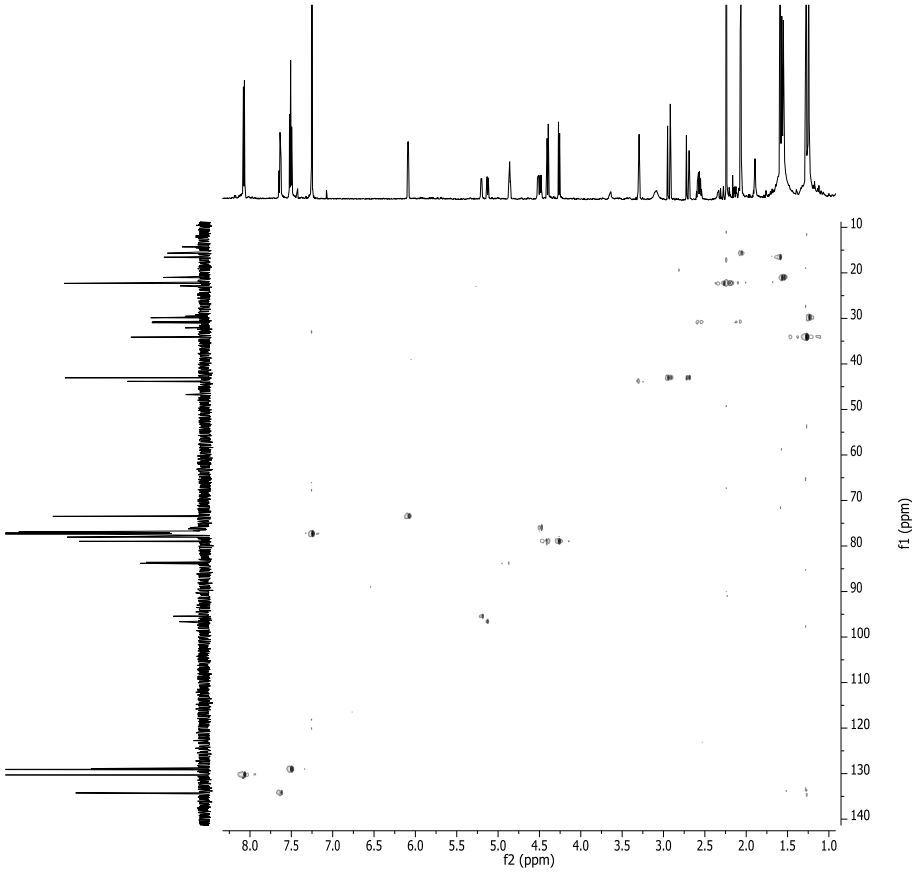
COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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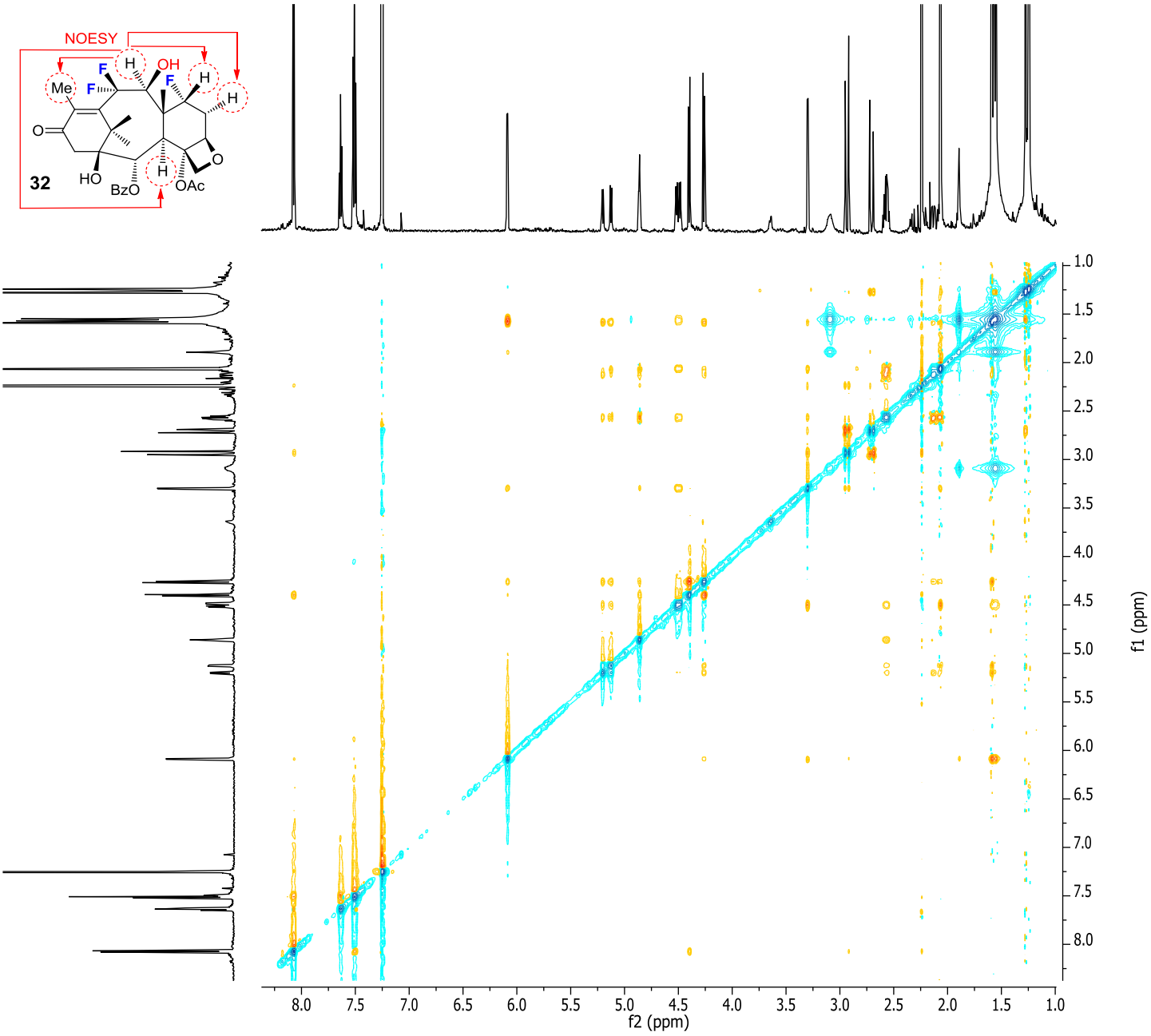
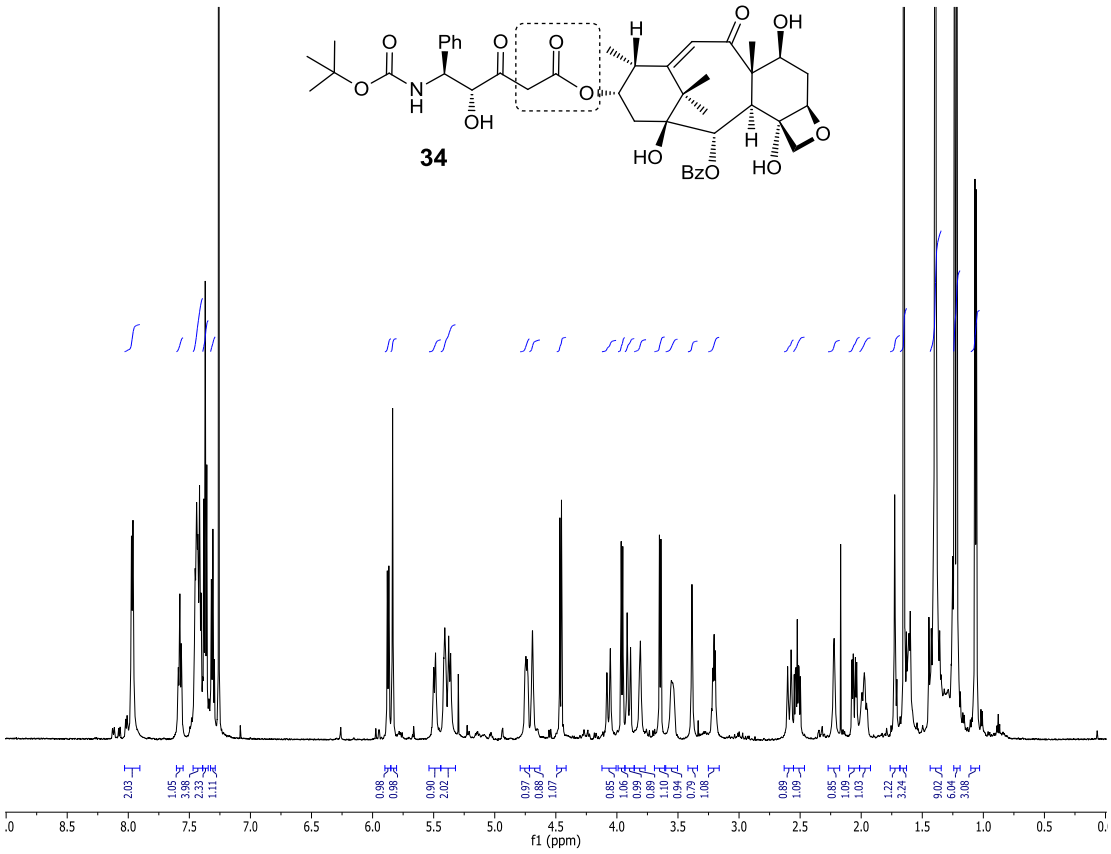
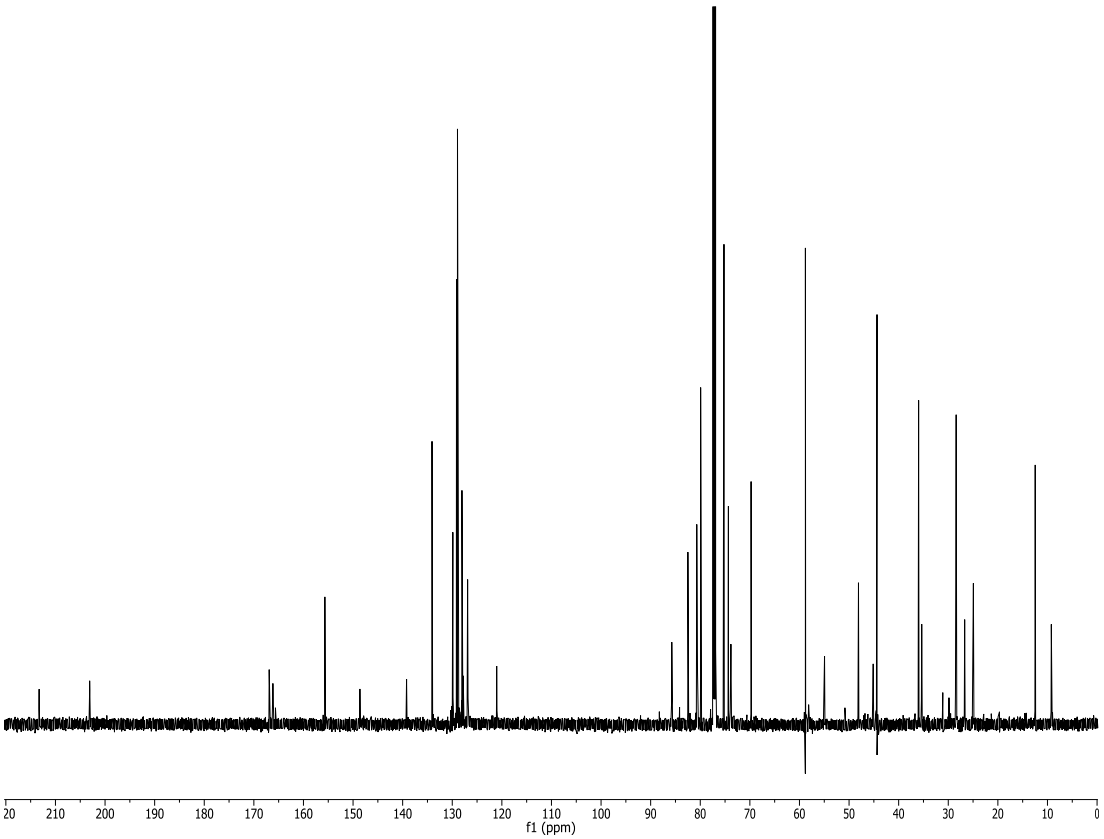
NOESY (600 MHz, $CDCl_3$):



^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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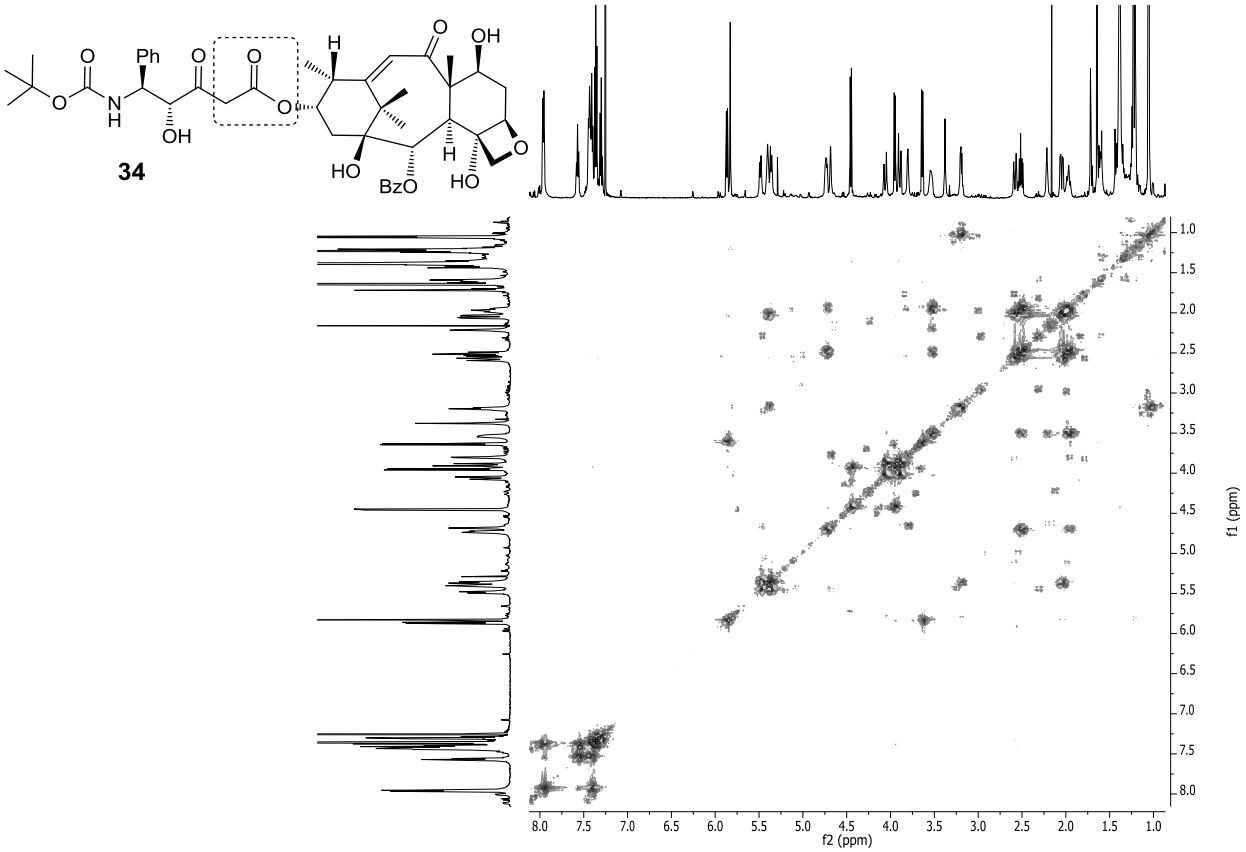
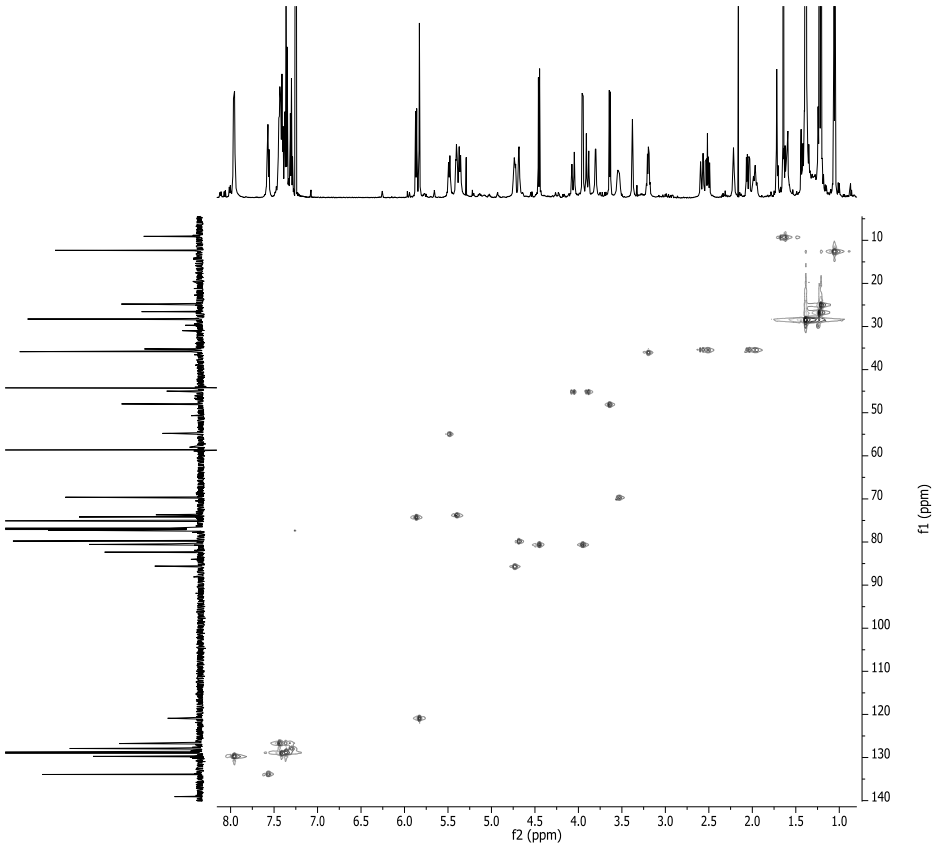
COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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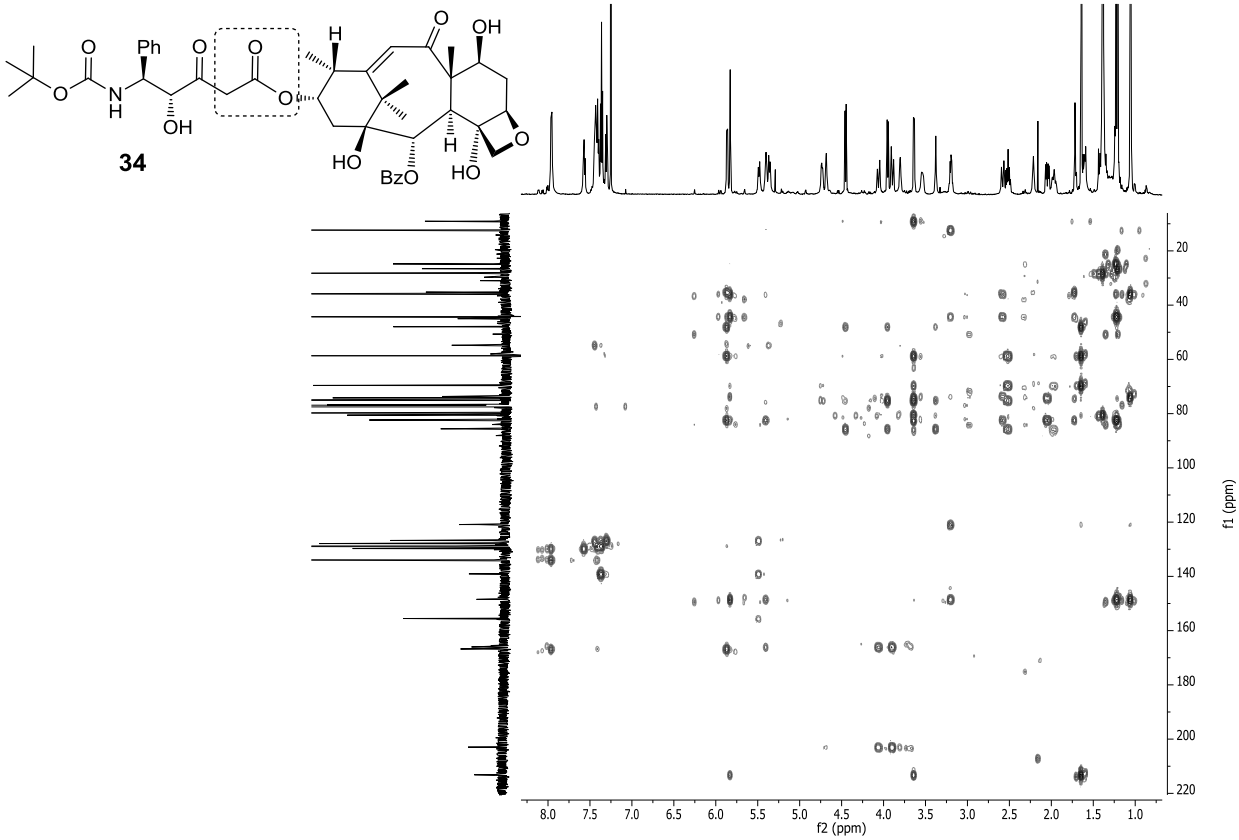
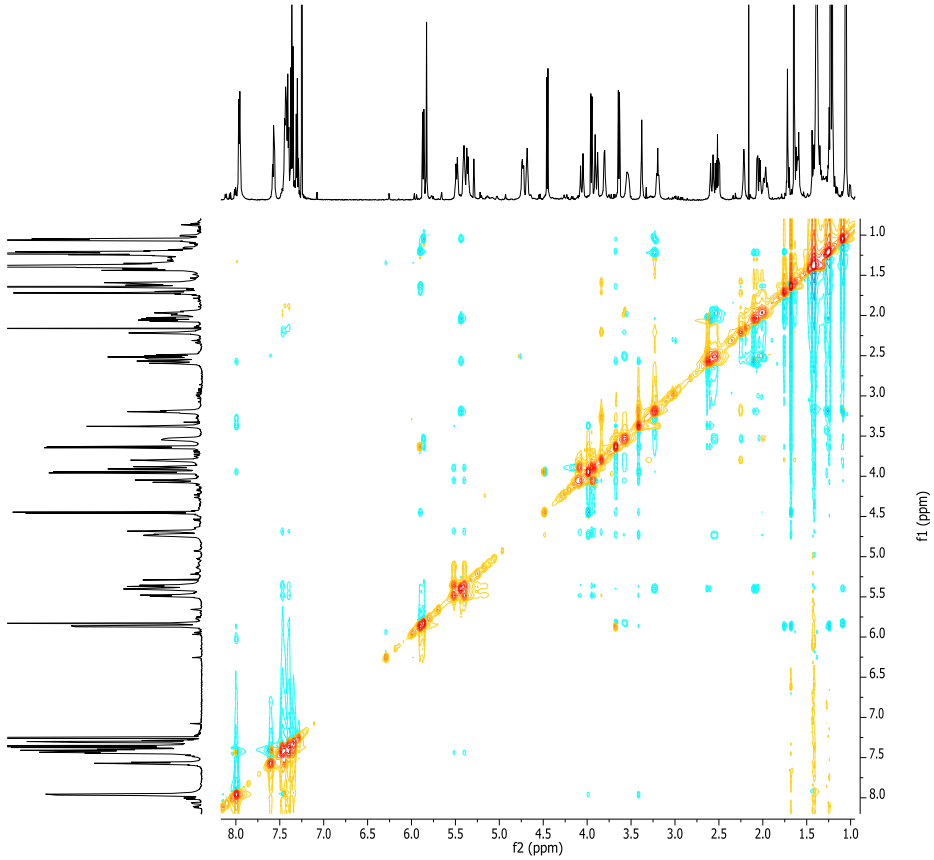
HMBC (600 MHz, $CDCl_3$):



ROESY (600 MHz, $CDCl_3$):



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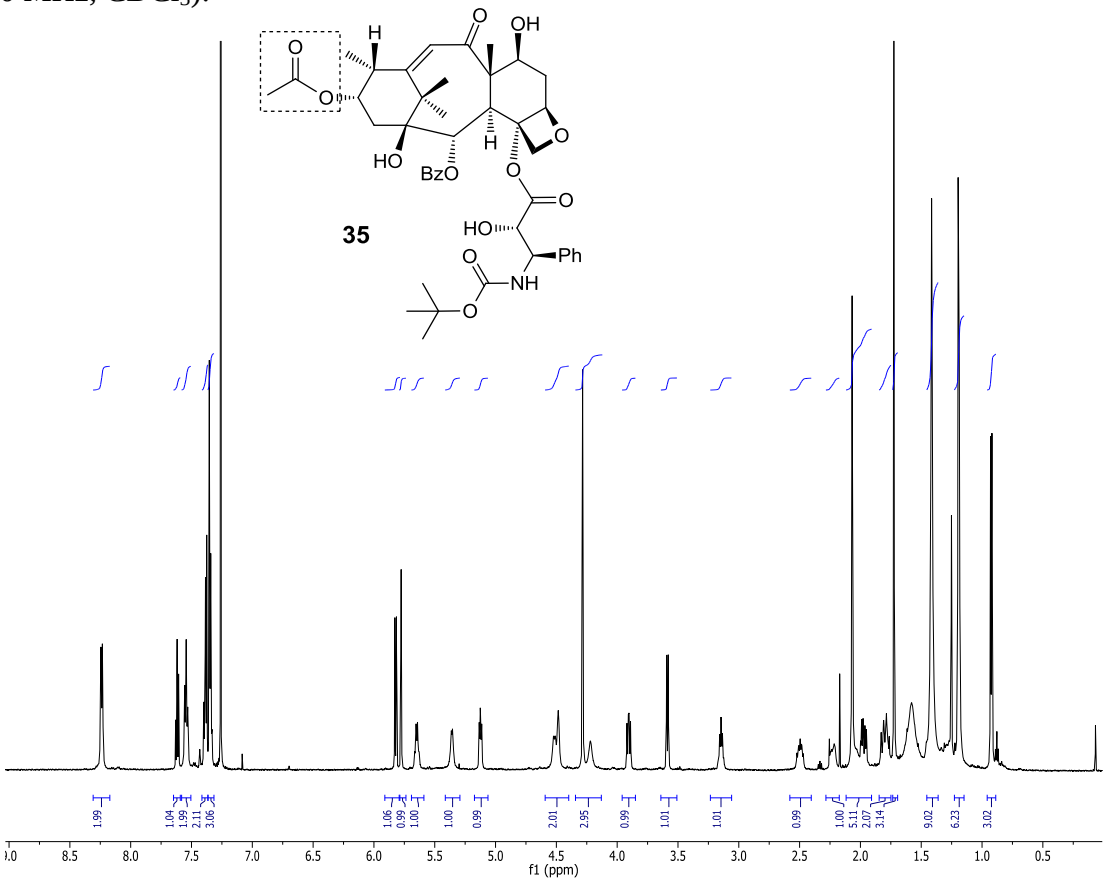
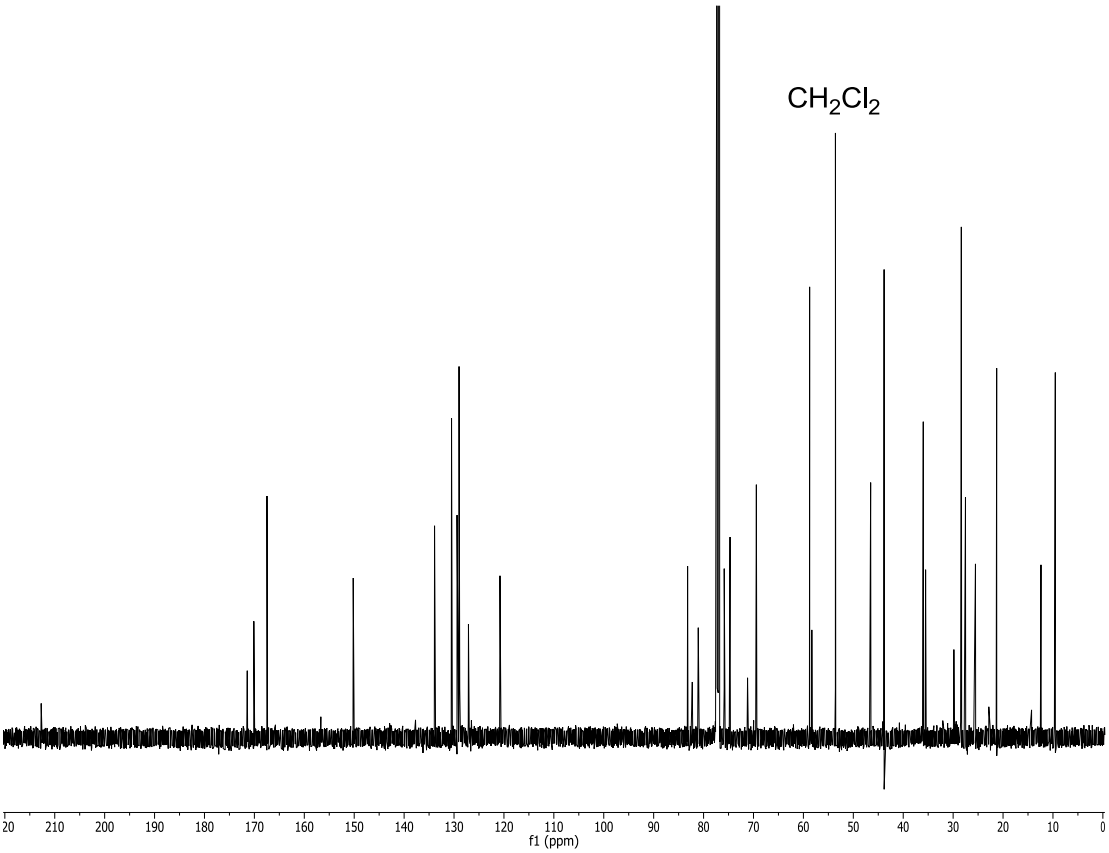
^{1}H NMR (600 MHz, $CDCl_3$):



^{13}C NMR (600 MHz, $CDCl_3$):



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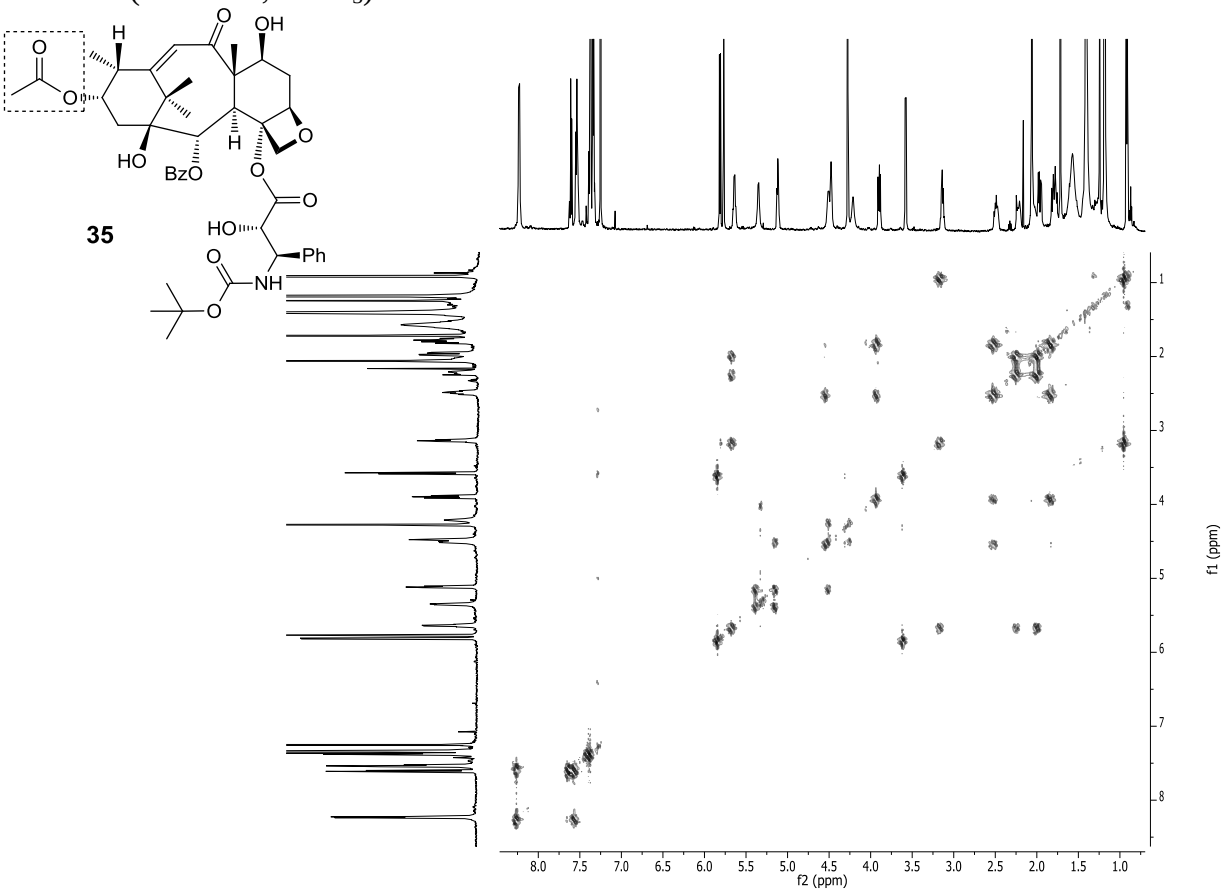
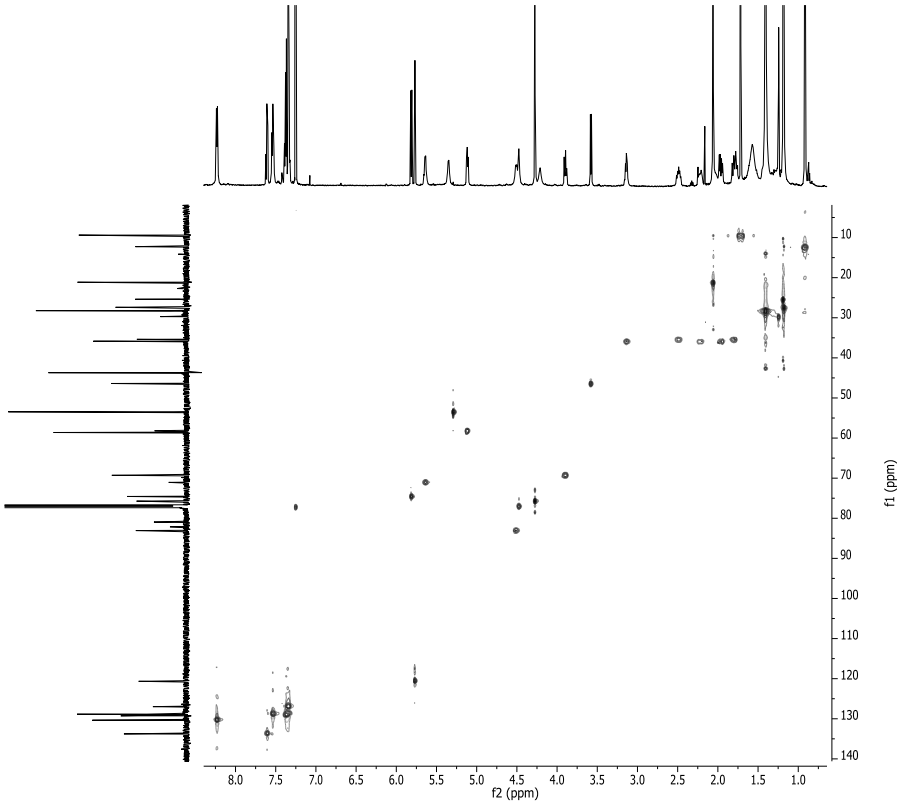
COSY (600 MHz, $CDCl_3$):



HMQC (600 MHz, $CDCl_3$):



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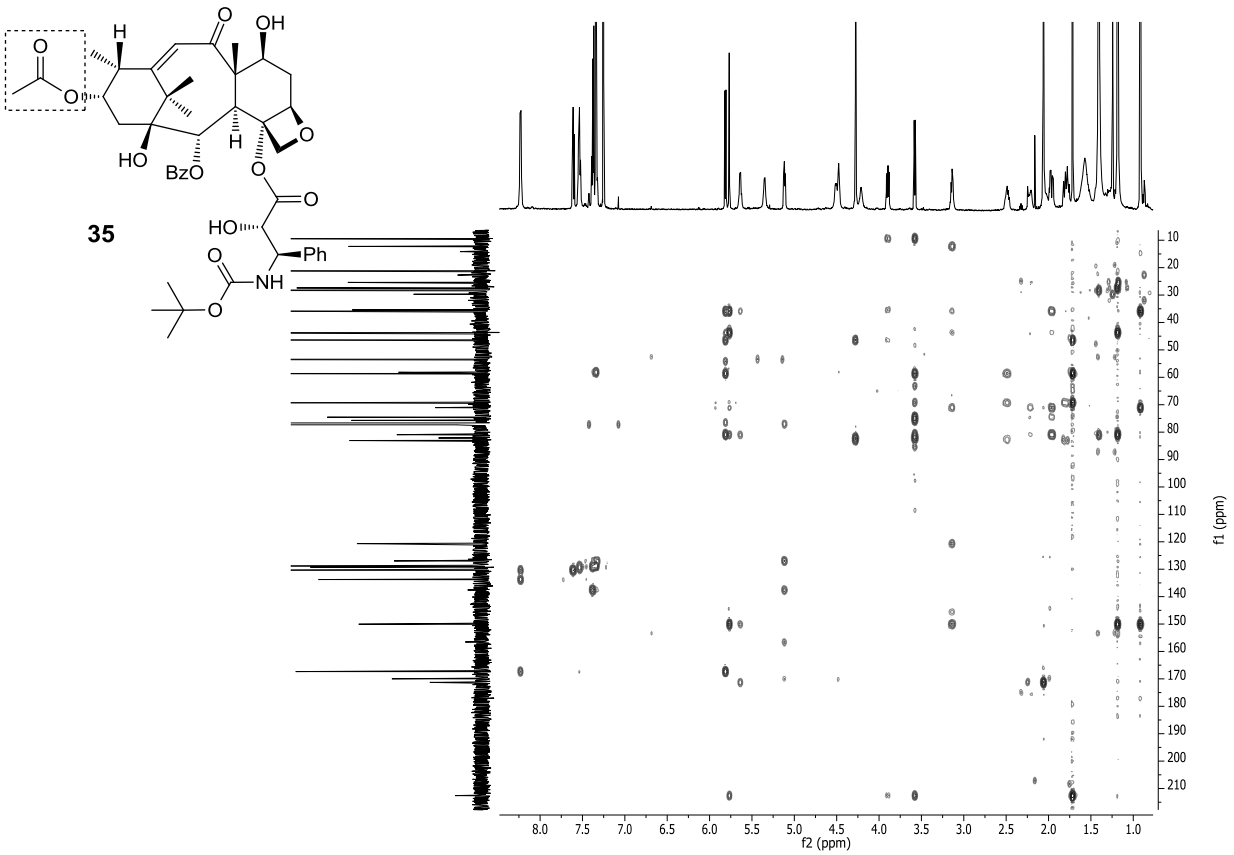
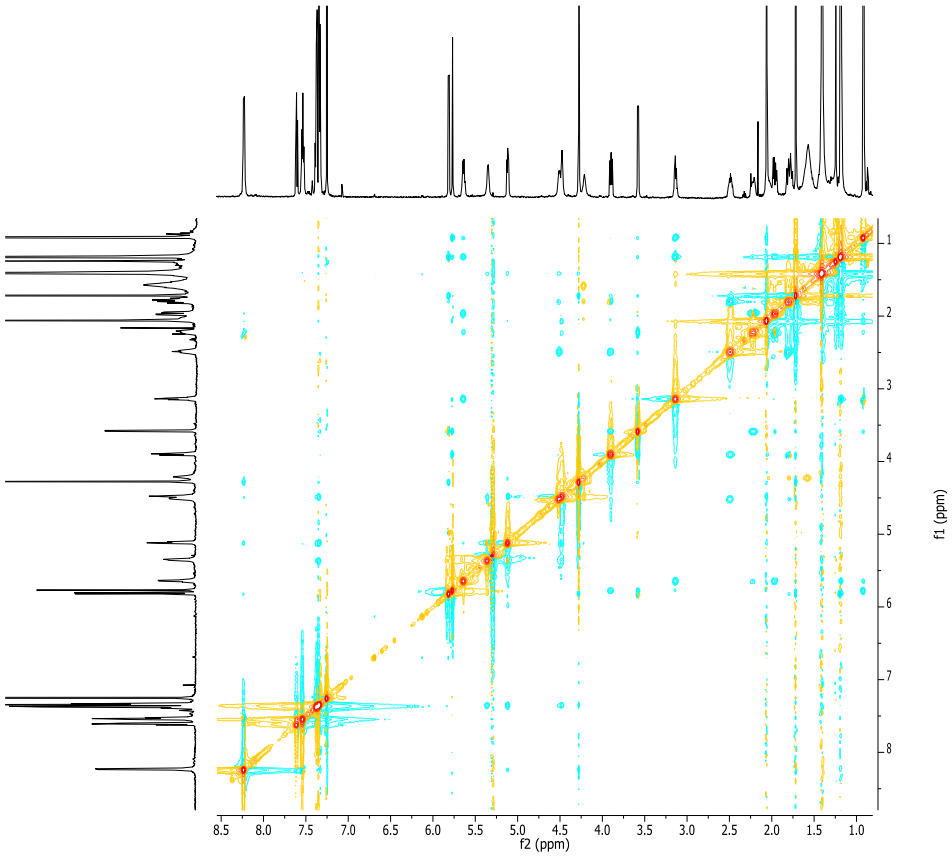
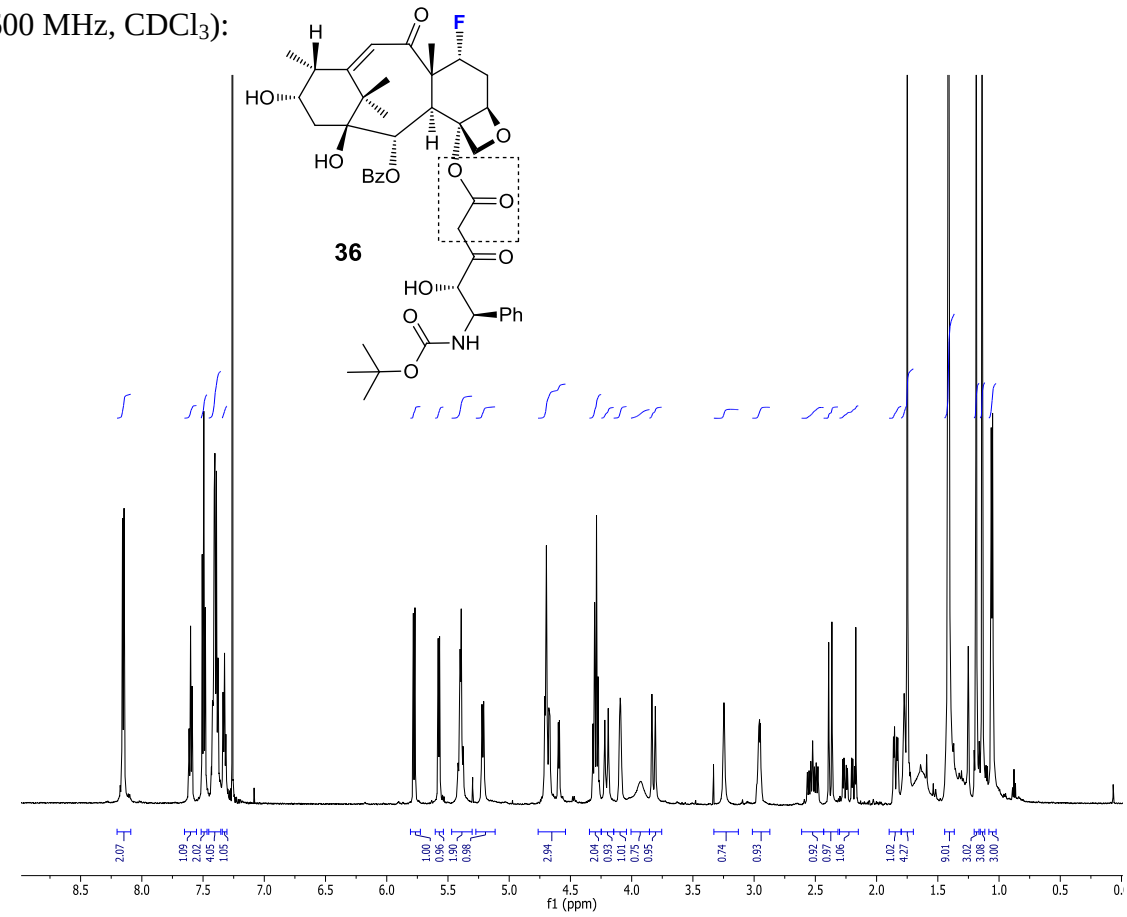
HMBC (600 MHz, $CDCl_3$):



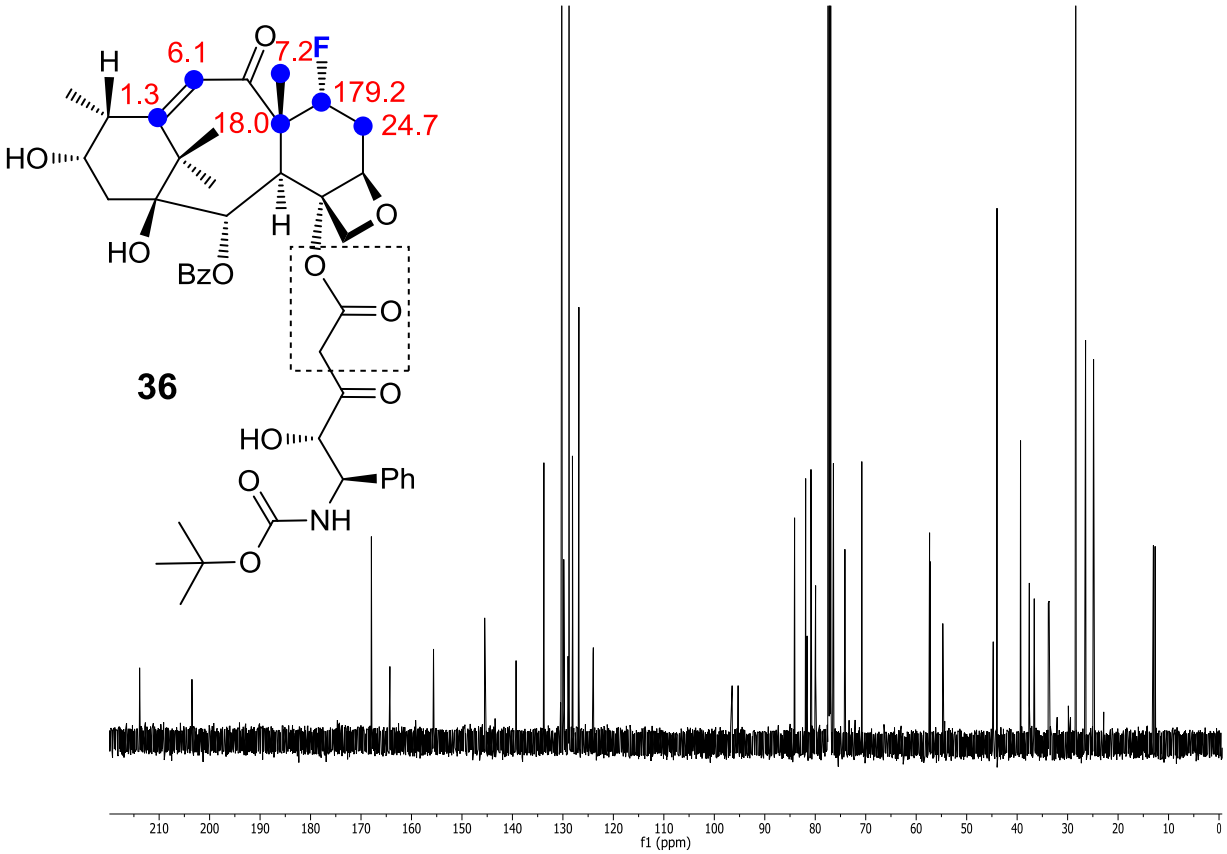
ROESY (600 MHz, $CDCl_3$):



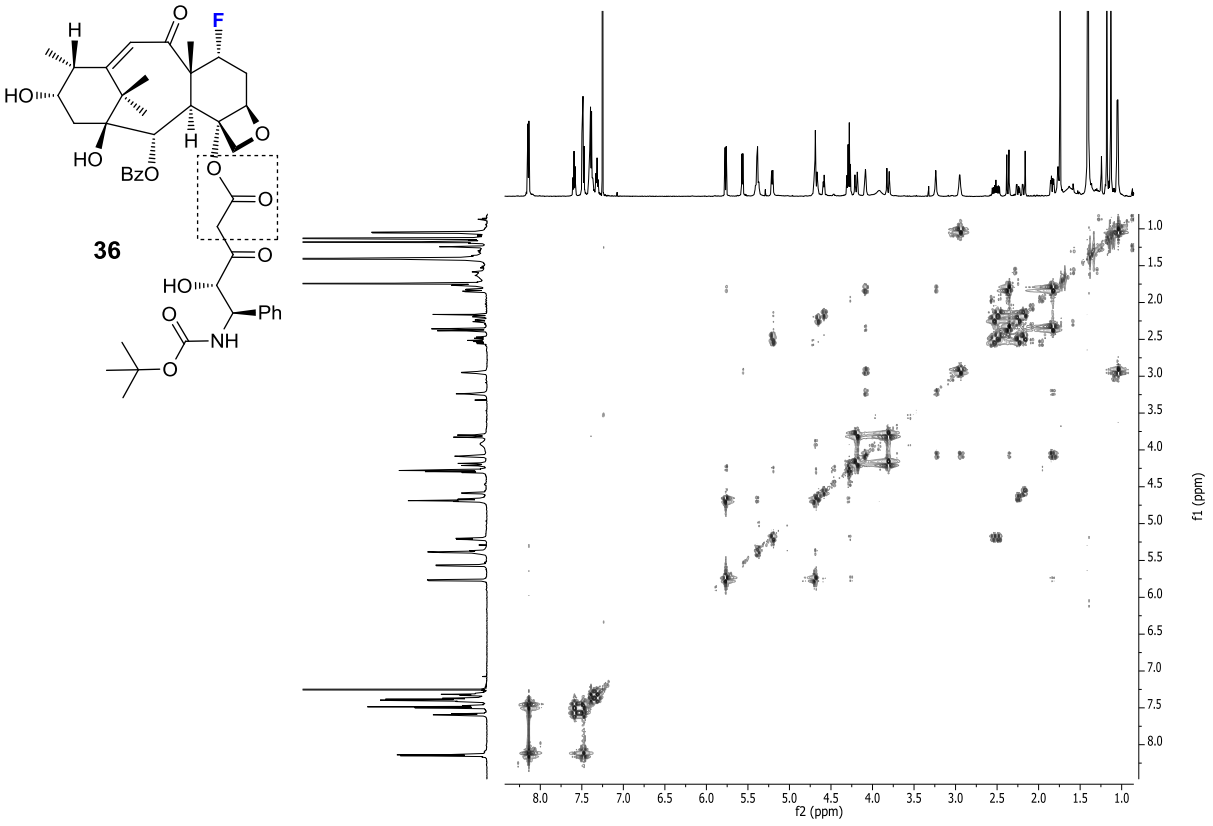
^{1}H NMR (600 MHz, $CDCl_3$):



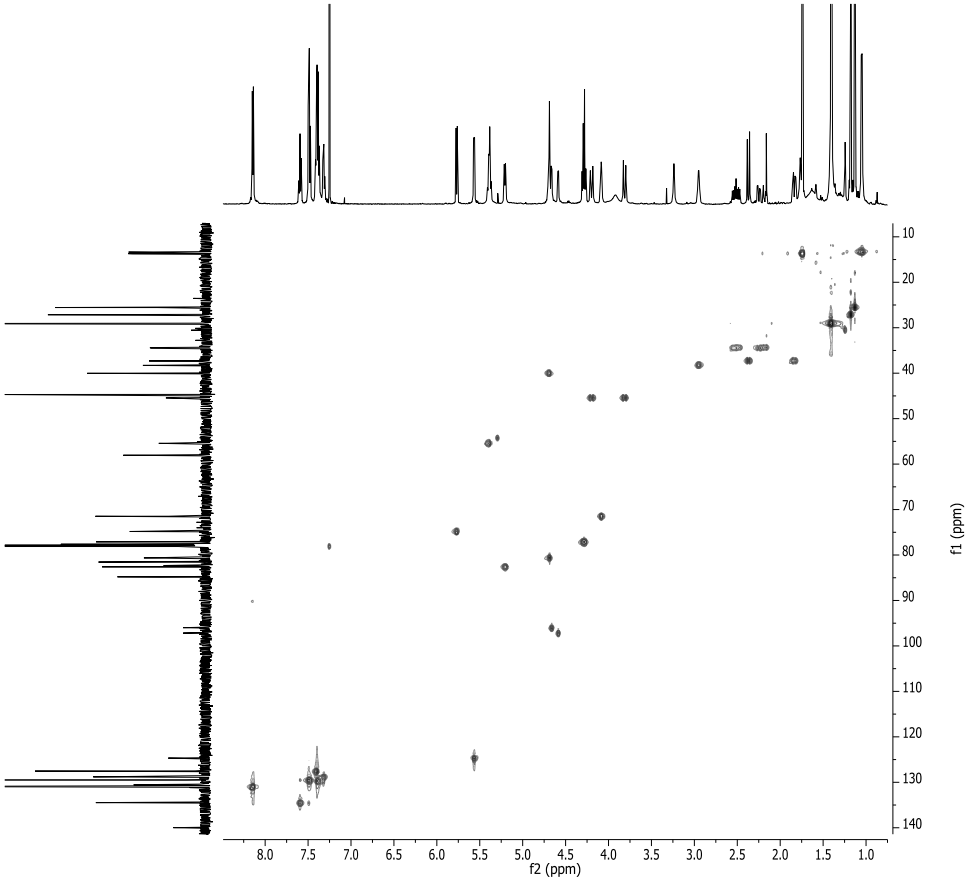
^{13}C NMR (600 MHz, $CDCl_3$):



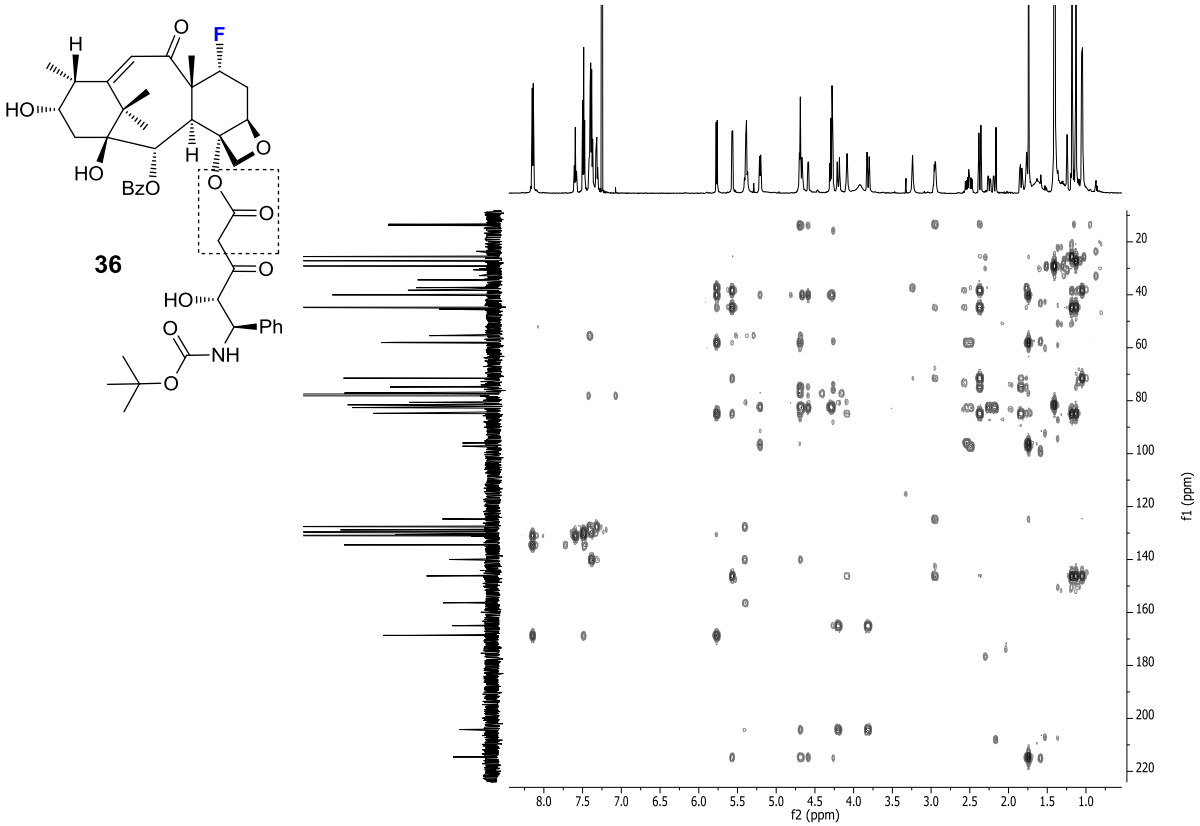
COSY (600 MHz, $CDCl_3$):



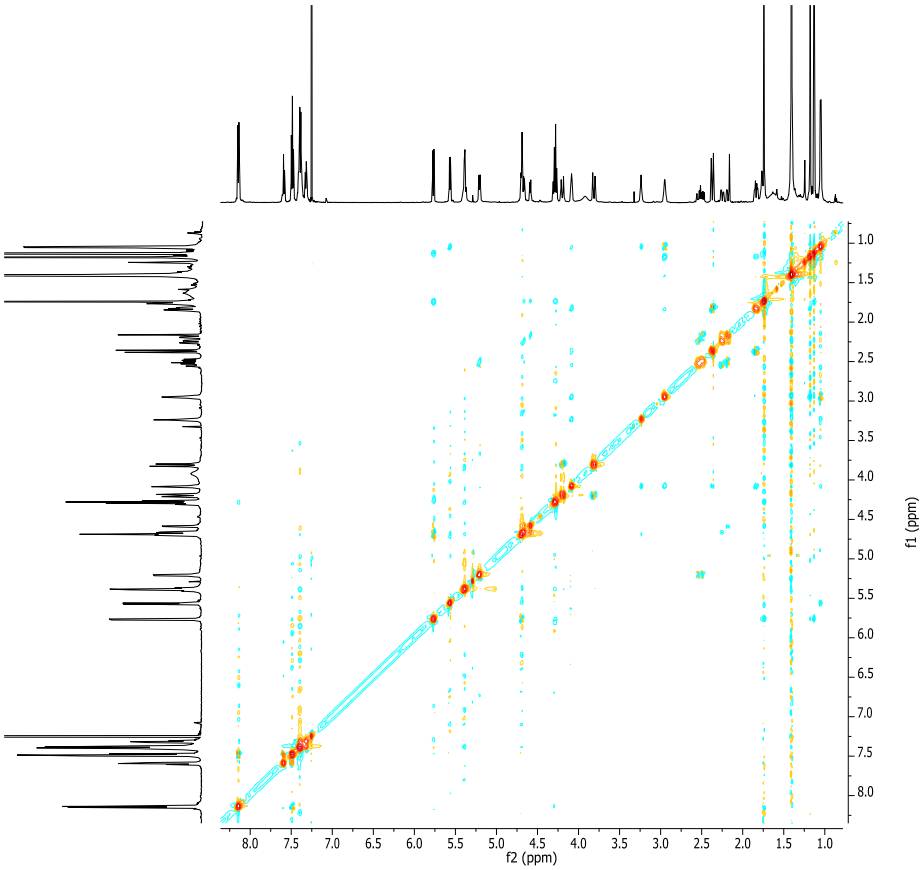
HMQC (600 MHz, $CDCl_3$):



HMBC (600 MHz, $CDCl_3$):



ROESY (600 MHz, $CDCl_3$):



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(IV) Table S1

Table S1. List for Compound Numbers and Corresponding NCI compound IDs

Compound Number	Corresponding NCI Compound ID
7	765855
10	765854
19a	765350
19b	765351
21a	765348
21b	765349
23	765856
27	765352
29	765347
34	765853
35	765852
36	765857