Electronic Supporting Information

Streamlined Total Synthesis of Trioxacarcins and Its Application to the Design, Synthesis and Biological Evaluation of Analogues Thereof. Discovery of Simpler Designed and Potent Trioxacarcin Analogues

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General Information:

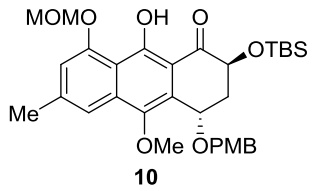
Unless otherwise noted, all reactions were performed in flame-dried or oven-dried glassware under nitrogen atmosphere. Non-aqueous reagents were transferred using syringe techniques under nitrogen atmosphere. Tetrahydrofuran (THF), *N*,*N*-dimethylformamide (DMF), acetonitrile (MeCN), dichloromethane (CH_2Cl_2), triethylamine (Et_3N), toluene, and pyridine were obtained anhydrous by degassing with argon and then passing through activated alumina columns to remove water and oxygen. Bulk grade hexanes, pentane, diethyl ether and ethyl acetate for chromatography were used without further treatment. Commercial reagents were obtained at the highest commercially available quality and used without further purification unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated.

Reactions were monitored by standard thin-layer chromatography (TLC) techniques using EMD silica gel $60F_{254}$ pre-coated plates (0.25 mm thickness). Following the run, TLC plates were visualized under UV light and/or by appropriate stains (*p*-anisaldehyde or ceric ammonium nitrate or potassium permanganate). Flash column chromatography was performed using silica gel (60, particle size 0.035–0.070 mm) obtained from Acros Organics. Preparative thin-layer chromatography (PTLC) separations were carried out using 0.25 or 0.50 mm E. Merck silica gel plates ($60F_{254}$).

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III HD 600 MHz instrument equipped with a 5 mm DCH cryoprobe and calibrated using residual undeuterated solvent for ^{1}H NMR [δ 7.26 ($CDCl_3$) or 5.32 (CD_2Cl_2) or 7.16 (C_6D_6) ppm] and ^{13}C deuterated solvent for ^{13}C NMR [δ 77.16 ($CDCl_3$) or 53.84 (CD_2Cl_2) or 128.06 (C_6D_6) ppm] as internal references at 300 K. The following abbreviations were used to indicate the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; quint: quintet; m, multiplet; br, broad. NMR coupling constants are reported as *J* values in Hz and chemical shift values δ in parts per million (ppm). High resolution mass spectrometric measurements (HRMS) were obtained on Agilent Technologies 6530 Accurate Mass QTof LC/MS (ESI) or Agilent 1200 HPLC-6130 MSD (ESI). Melting points were recorded on a Thomas-Hoover Unimelt capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Optical rotations were recorded on a Schmidt+Haensch POLARTRONIC M100 polarimeter at 589.44 nm using 100 mm cells and the solvent and concentration indicated and are reported in units of 10^{-1} (deg cm^2g^{-1}).

Experimental Procedures and Characterization Data

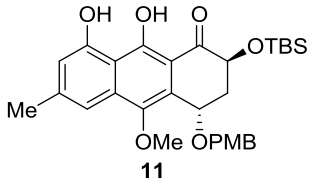
(2*S*,4*S*)-2-[(*tert*-Butyldimethylsilyl)oxy]-9-hydroxy-10-methoxy-4-[(4-methoxybenzyl)oxy]-8-(methoxymethoxy)-6-methyl-3,4-dihydroanthracen-1(2*H*)-one (10): To a stirred solution of



10

cyanophthalide **9**[1] (702 mg, 3.01 mmol, 1.0 equiv) in THF (30 ml) at −78 °C was added *t*-BuOLi (1.0 M in THF, 9.03 ml, 9.03 mmol, 3.0 equiv). After stirring at this temperature for 10 min, a solution of enone **7**[2] (1.09 g, 3.01 mmol, 1.0 equiv) in THF (10 ml) was added dropwise. The resulting reaction mixture was stirred at −78 °C for 30 min before Me_2SO_4 (3.60 g, 30.1 mmol, 10 equiv) was added dropwise. The resulting mixture was warmed to −5 °C and stirred at this temperature for 5 h before it was quenched with NH_4Cl (sat. aq., 150 ml). The resulting mixture was extracted with EtOAc (3 × 40 ml), and the combined organic phases were washed with brine (50 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:6) to give the title compound (1.26 g, 2.16 mmol, 72% yield) as a yellow foam. **10**: R_f = 0.58 (silica gel, EtOAc:hexanes 1:4); $[\alpha]_D^{25}$ = +30.2 (*c* = 0.2, CH_2Cl_2); FT-IR (film): ν_{max} = 2952, 1620, 1577, 1514, 1443, 1386, 1250, 1172, 1152, 1046, 870 cm^{-1}; ^1H NMR (600 MHz, CD_2Cl_2) δ = 14.79 (s, 1 H), 7.52 (s, 1 H), 7.27 (d, *J* = 8.6 Hz, 2 H), 6.98 (d, *J* = 1.6 Hz, 1 H), 6.88–6.65 (m, 2 H), 5.30 (s, 2 H), 5.18 (t, *J* = 2.9 Hz, 1 H), 4.97 (dd, *J* = 12.4, 5.2 Hz, 1 H), 4.67 (d, *J* = 11.1 Hz, 1 H), 4.55 (d, *J* = 11.0 Hz, 1 H), 3.84 (s, 3 H), 3.77 (s, 3 H), 3.56 (s, 3 H), 2.72 (ddd, *J* = 13.4, 5.2, 3.3 Hz, 1 H), 2.51 (s, 3 H), 2.20–2.12 (m, 1 H), 0.97 (s, 9 H), 0.23 (s, 3 H), 0.17 (s, 3 H) ppm; ^{13}C NMR (151 MHz, CD_2Cl_2) δ = 204.1, 163.0, 159.7, 157.6, 145.0, 142.7, 135.6, 131.0, 129.7, 126.7, 116.7, 116.3, 115.6, 114.1, 108.6, 96.5, 71.1, 69.8, 69.3, 63.0, 56.8, 55.6, 37.1, 26.1, 22.5, 18.8, −4.2, −5.1 ppm; HRMS (ESI-TOF) calcd for $C_{32}H_{42}O_8SiNa^+$ $[M+Na]^+$ 605.2541, found 605.2529.

(2*S*,4*S*)-2-[(*tert*-Butyldimethylsilyl)oxy]-8,9-dihydroxy-10-methoxy-4-[(4-methoxybenzyl)oxy]-6-methyl-3,4-dihydroanthracen-1(2*H*)-one (11): To a stirred solution of **10** (812 mg, 1.39 mmol,

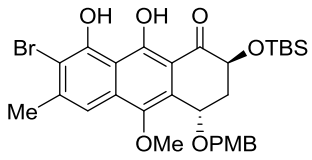


11

1.0 equiv) in THF (50 ml) at 0 °C was added $MgBr_2 \cdot Et_2O$ (1.08 g, 4.17 mmol, 3.0 equiv) in one portion. After stirring at this temperature for 2 h, the reaction was quenched with H_2O (50 ml). The resulting mixture was extracted with EtOAc (3 × 40 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:10) to give the title

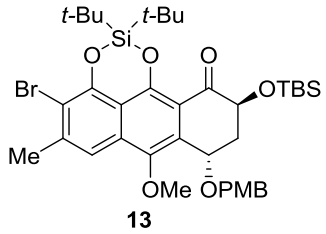
compound (594 mg, 1.08 mmol, 79% yield) as a yellow foam. **11**: $R_f = 0.55$ (silica gel, EtOAc:hexanes 1:6); $[\alpha]_D^{25} = +14.7$ ($c = 1.0$, CH_2Cl_2); FT-IR (film): $\nu_{max} = 2953$, 1634, 1613, 1514, 1443, 1389, 1249, 1155, 1045, 1005, 872 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) $\delta = 15.95$ (s, 1H), 9.78 (s, 1H), 7.30 (s, 1H), 7.28 (d, $J = 8.3$ Hz, 2H), 6.87 (d, $J = 8.2$ Hz, 2H), 6.79 (s, 1H), 5.18–5.13 (m, 1H), 5.00 (dd, $J = 12.3$, 5.2 Hz, 1H), 4.67 (d, $J = 11.1$ Hz, 1H), 4.57 (d, $J = 11.1$ Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 2.70 (ddd, $J = 13.5$, 5.2, 3.4 Hz, 1H), 2.49 (s, 3H), 2.17 (td, $J = 12.8$, 12.4, 2.5 Hz, 1H), 0.97 (s, 9H), 0.24 (s, 3H), 0.18 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) $\delta = 203.9$, 162.8, 159.4, 158.6, 145.7, 144.2, 134.6, 130.4, 129.6, 125.3, 114.2, 114.0, 114.0, 113.6, 113.0, 107.1, 70.9, 69.2, 68.8, 62.8, 55.4, 37.1, 26.0, 26.0, 22.6, 18.7, −4.3, −5.1 ppm; HRMS (ESI-TOF) calcd for $C_{30}H_{38}O_7SiNa^+$ $[M+Na]^+$ 561.2279, found 561.2265.

(2S,4S)-7-Bromo-2-[(*tert*-butyldimethylsilyl)oxy]-8,9-dihydroxy-10-methoxy-4-[(4-methoxy-benzyl)oxy]-6-methyl-3,4-dihydroanthracen-1(2*H*)-one (12): To a stirred solution of phenol **11** (560 mg, 1.04 mmol, 1.0 equiv) in THF (50 ml) at −78 °C was added a solution of NBS (185 mg, 1.04 mmol, 1.0 equiv) in THF (10 ml) dropwise. The resulting reaction mixture was stirred at −78 °C for 30 min, then warmed to room temperature and stirred at this temperature for 5 h before it was quenched with NH_4Cl (sat. aq., 50 ml). The resulting mixture was extracted with EtOAc (3 × 50 ml), and the combined organic phases were washed with brine (50 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:10) to give the title compound (525 mg, 0.85 mmol, 82% yield) as a yellow oil. **12**: $R_f = 0.50$ (silica gel, EtOAc:hexanes 1:6); $[\alpha]_D^{25} = +28.9$ ($c = 0.2$, CH_2Cl_2); FT-IR (film): $\nu_{max} = 2952$, 1622, 1514, 1443, 1316, 1249, 1171, 1055, 1004, 872 cm^{-1};^1H NMR (600 MHz, CD_2Cl_2) $\delta = 16.12$ (s, 1H), 10.54 (s, 1H), 7.46 (s, 1H), 7.30–7.16 (m, 2H), 6.94–6.73 (m, 2H), 5.18–5.15 (m, 1H), 5.01 (dd, $J = 12.3$, 5.3 Hz, 1H), 4.67 (d, $J = 11.0$ Hz, 1H), 4.55 (d, $J = 11.0$ Hz, 1H), 3.85 (s, 3H), 3.77 (s, 3H), 2.72 (ddd, $J = 13.6$, 5.4, 3.5 Hz, 1H), 2.60 (s, 3H), 2.23–2.12 (m, 1H), 0.97 (s, 9H), 0.23 (s, 3H), 0.18 (s, 3H) ppm; ^{13}C NMR (151 MHz, CD_2Cl_2) $\delta = 204.8$, 161.8, 159.7, 155.0, 145.9, 143.9, 133.0, 130.7, 129.9, 129.8, 126.4, 114.9, 114.1, 113.6, 110.1, 108.1, 71.3, 71.2, 69.4, 69.1, 69.1, 63.2, 55.6, 37.2, 26.0, 24.7, 18.8, −4.3, −5.1 ppm; HRMS (ESI-TOF) calcd for $C_{30}H_{38}BrO_7Si^+$ $[M+H]^+$ 617.1565, found 617.1554.



12

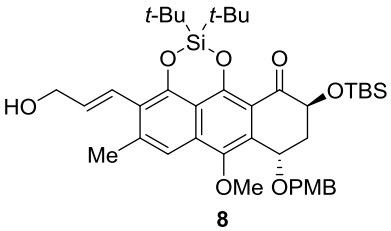
(8*S*,10*S*)-4-Bromo-2,2-di-*tert*-butyl-10-[(*tert*-butyldimethylsilyl)oxy]-7-methoxy-8-[(4-methoxybenzyl)oxy]-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (13): To



13

a stirred solution of **12** (838 mg, 1.36 mmol, 1.0 equiv) in CH_2Cl_2 (30 ml) at 0 °C was added 2,6-lutidine (437 mg, 4.08 mmol, 3.0 equiv), and then *t*-$Bu_2Si(OTf)_2$ (716 mg, 1.63 mmol, 1.2 equiv) was added dropwise over a period of 10 min. After stirring at this temperature for another 10 min, the reaction was quenched with NH_4Cl (sat. aq., 20 ml) and the resulting mixture was extracted with CH_2Cl_2 (2 × 50 ml). The combined organic phases were washed with brine (50 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc: hexanes 1:6) to give the title compound (730 mg, 0.97 mmol, 71% yield) as a yellow foam. **13**: R_f = 0.75 (silica gel, EtOAc: hexanes 1:4); $[\alpha]_D^{25}$ = +43.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2934, 2859, 1698, 1606, 1514, 1472, 1405, 1361, 1250, 1157, 1066, 829 cm^{-1}; ^1H NMR (600 MHz, CD_2Cl_2) δ = 7.51 (d, *J* = 1.2 Hz, 1 H), 7.37–7.21 (m, 2 H), 6.94–6.64 (m, 2 H), 5.18 (t, *J* = 2.9 Hz, 1 H), 4.83 (dd, *J* = 12.4, 5.2 Hz, 1 H), 4.70 (d, *J* = 10.8 Hz, 1 H), 4.58 (d, *J* = 10.8 Hz, 1 H), 3.88 (s, 3 H), 3.77 (s, 3 H), 2.73 (ddd, *J* = 13.6, 5.2, 3.1 Hz, 1 H), 2.58 (d, *J* = 0.9 Hz, 3 H), 2.12 (ddd, *J* = 13.5, 12.3, 2.7 Hz, 1 H), 1.14 (s, 9 H), 1.11 (s, 9 H), 0.95 (s, 9 H), 0.21 (s, 3 H), 0.14 (s, 3 H) ppm; ^{13}C NMR (151 MHz, CD_2Cl_2) δ = 194.9, 159.7, 150.0, 149.2, 146.8, 140.9, 130.9, 130.7, 130.1, 130.0, 119.4, 116.6, 115.7, 115.2, 114.1, 112.0, 71.6, 71.4, 70.2, 63.1, 55.6, 36.9, 26.2, 26.2, 26.2, 24.6, 21.5, 21.3, 18.9, −4.1, −5.2 ppm; HRMS (ESI-TOF) calcd for $C_{38}H_{53}BrO_7Si_2Na^+$ $[M+Na]^+$ 779.2405, found 779.2407.

(8*S*,10*S*)-2,2-Di-*tert*-butyl-10-[(*tert*-butyldimethylsilyl)oxy]-4-[(*E*)-3-hydroxyprop-1-en-1-yl]-7-methoxy-8-[(4-methoxybenzyl)oxy]-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (8): To a stirred mixture of aryl bromide **13** (553 mg, 0.730 mmol, 1.0 equiv), tri(2-

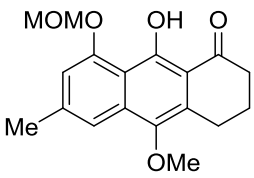


8

furyl)phosphine (33.8 mg, 0.146 mmol, 0.2 equiv) and $Pd(PPh_3)_4$ (83.8 mg, 0.0725 mmol, 0.1 equiv) in DMF (20 ml) was added stannane **14** (380 mg, 1.10 mmol, 1.5 equiv), After bubbled with argon balloon three times, *N*,*N*-diisopropylethylamine (0.253 ml, 1.46 mmol, 2.0 equiv) and LiCl (1 M in THF, 1.46 ml, 1.46 mmol, 2.0 equiv) was added. After stirring at 110 °C for 12 h, the reaction mixture was cooled to 23 °C, then was diluted with EtOAc (20 ml) and quenched with water (10 ml). The resulting mixture was washed with brine (3 × 10 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was

purified by flash column chromatography (silica gel, EtOAc:hexanes 1:4→1:2) to give the title compound (364 mg, 0.496 mmol, 68% yield) as a yellow foam. $[\alpha]_D^{25} = +28.1$ ($c = 0.1$, CH_2Cl_2). All spectroscopic data were consistent with those reported in the literature.[2]

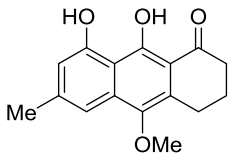
9-Hydroxy-10-methoxy-8-(methoxymethoxy)-6-methyl-3,4-dihydroanthracen-1(2*H*)-one (15):



15

To a stirred solution of cyanophthalide **9** (9.60 g, 41.2 mmol, 1.0 equiv) in THF (100 ml) at −78 °C was added *t*-BuOLi (1.0 M in THF, 123.6 ml, 123.6 mmol, 3.0 equiv). After stirring at this temperature for 10 min, a solution of cyclohexanone (4.40 ml, 45.3 mmol, 1.1 equiv) in THF (27 ml) was added dropwise. The resulting reaction mixture was stirred at −78 °C for 30 min before Me_2SO_4 (23.4 ml, 247 mmol, 6.0 equiv) was added dropwise. Then the resulting mixture was warmed to 23 °C and stirred at this temperature for 5 h before it was quenched with NH_4Cl (sat. aq., 150 ml). The resulting mixture was extracted with EtOAc (3 × 80 ml), and the combined organic phases were washed with brine (150 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:4) to give the title compound **13** (9.39 g, 29.7 mmol, 72% yield) as a yellow foam. **15**: $R_f = 0.50$ (silica gel, EtOAc:hexanes 1:3); FT-IR (film): $\nu_{max} = 3375$, 2498, 1618, 1577, 1444, 1384, 1330, 1234, 1177, 1039 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) $\delta = 15.02$ (s, 1 H), 7.46 (d, $J = 1.6$ Hz, 1 H), 6.94 (d, $J = 1.6$ Hz, 1 H), 5.35 (s, 2 H), 3.79 (s, 3 H), 3.60 (s, 3 H), 3.04 (dd, $J = 6.9$, 5.5 Hz, 2 H), 2.73 (dd, $J = 7.1$, 5.8 Hz, 2 H), 2.50 (d, $J = 0.8$ Hz, 3 H), 2.12–2.05 (m, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) $\delta = 204.6$, 162.8, 157.3, 142.9, 142.1, 135.5, 128.6, 115.3, 114.9, 114.1, 110.7, 96.0, 60.9, 56.6, 39.0, 23.7, 22.6, 22.4 ppm. HRMS (ESI) calcd for $C_{18}H_{20}O_5Na^+$ $[M+Na]^+$ 339.1203, found 339.1210.

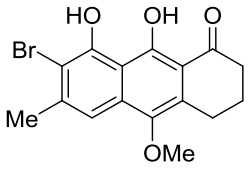
8,9-Dihydroxy-10-methoxy-6-methyl-3,4-dihydroanthracen-1(2*H*)-one (16): To a stirred solution of **15** (7.80 g, 24.7 mmol, 1.0 equiv) in THF (100 ml) at 0 °C was added $MgBr_2 \cdot Et_2O$ (12.7 g, 49.6 mmol, 2.0 equiv) in one portion. After stirring at this temperature for 3 h, the reaction was quenched with H_2O (50 ml). The resulting mixture was extracted with EtOAc (3 × 50 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:4) to give the title compound (6.07 g, 22.3 mmol, 90% yield) as a yellow foam. **16**: $R_f = 0.40$ (silica gel, EtOAc:hexanes 1:3); FT-IR (film): $\nu_{max} = 3354$, 2995, 2959, 2938, 1633, 1616, 1512, 1446, 1395, 1334, 1244, 1170,



16

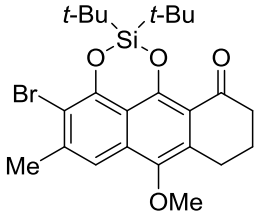
1038 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 16.14 (s, 1 H), 9.82 (s, 1 H), 7.24 (s, 1 H), 6.72 (s, 1 H), 3.80 (s, 3 H), 3.01 (t, *J* = 6.2 Hz, 2 H), 2.76–2.64 (m, 2 H), 2.47 (s, 3 H), 2.09 (quint, *J* = 6.3 Hz, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.6, 163.2, 158.6, 144.2, 143.6, 134.8, 127.5, 113.0, 112.7, 111.5, 109.2, 60.9, 38.0, 23.3, 22.6, 22.4 ppm; HRMS (ESI) calcd for $C_{16}H_{17}O_4^+$ $[M+H]^+$ 273.1121, found 273.1127.

7-Bromo-8,9-dihydroxy-10-methoxy-6-methyl-3,4-dihydroanthracen-1(2*H*)-one (17): To a stirred solution of phenol **16** (5.0 g, 18.4 mmol, 1.0 equiv) in THF (200 ml) at −78 °C was added a solution of NBS (3.27 g, 18.4 mmol, 1.0 equiv) in THF (20 ml) dropwise. The resulting reaction mixture was stirred at −78 °C for 30 min, then warmed to room temperature and stirred at this temperature for 5 h before it was quenched with NH_4Cl (sat. aq., 100 ml). The resulting mixture was extracted with EtOAc (3 × 100 ml), and the combined organic phases were washed with brine (100 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:10→1:2) to give the title compound **15** (5.47 g, 15.6 mmol, 85% yield) as a yellow foam. **17**: R_f = 0.16 (silica gel, EtOAc:hexanes 1:3); FT-IR (film): ν_{max} = 3322, 2948, 1490, 1391, 1256, 1241, 1048 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 16.30 (s, 1 H), 10.60 (s, 1 H), 7.35 (s, 1 H), 3.79 (s, 3 H), 3.02–2.99 (m, 2 H), 2.74 (t, *J* = 6.4 Hz, 2 H), 2.57 (s, 3 H), 2.10 (quint, *J* = 6.4 Hz, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.8, 162.2, 154.7, 143.6, 143.5, 132.8, 128.0, 113.8, 113.8, 120.0, 109.8, 108.7, 61.1, 37.9, 24.7, 23.3, 22.2 ppm. HRMS (ESI) calcd for $C_{16}H_{16}BrO_4^+$ $[M+H]^+$ 351.0226, found 351.0229.



17

4-Bromo-2,2-di-*tert*-butyl-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (18): To a stirred solution of **17** (4.24 g, 12.1 mmol, 1.0 equiv) in CH_2Cl_2 (150 ml) at −78 °C were added Et_3N (11.8 ml, 84.8 mmol, 7.0 equiv), and then *t*-$Bu_2Si(OTf)_2$ (4.8 ml, 14.3 mmol, 1.2 equiv) was added dropwise over a period of 5 min. The reaction mixture was allowed to warm to 0 °C and then quenched with $NaHCO_3$ (sat. aq., 50 ml) at 0 °C and stirred for 30 min at 23 °C. The resulting mixture was partitioned and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 ml). The combined organic phases were washed with brine (100 ml), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:50) to give the title compound (4.96 g, 10.1 mmol, 84% yield) as a pale

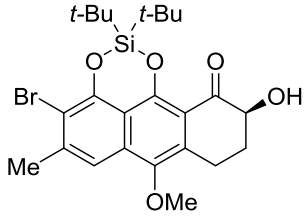


18

yellow powder. **18**: R_f = 0.35 (silica gel, EtOAc:hexanes 1:3); FT-IR (film): ν_{max} = 2936, 2861, 1681, 1622, 1605, 1561, 1472, 1402, 1361, 1229, 1063 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 1.1 Hz, 1 H), 3.83 (s, 3 H), 3.08–2.94 (m, 2 H), 2.66–2.63 (m, 2 H), 2.57 (d, *J* = 1.0 Hz, 3 H), 2.08 (quint, *J* = 6.5 Hz, 2 H), 1.14 (s, 18 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.6, 149.8, 149.6, 144.5, 140.7, 131.9, 130.5, 116.5, 114.9, 114.7, 114.6, 110.8, 61.2, 61.1, 41.4, 41.3, 41.2, 26.3, 26.3, 26.3, 26.2, 24.6, 24.5, 24.5, 24.4, 24.3, 24.2, 22.5, 21.3, 21.0 ppm; HRMS (ESI) calcd for $C_{24}H_{31}BrO_4SiNa^+$ $[M+Na]^+$ 513.1067, found 513.1077.

General procedure for *α*-hydroxylation of ketone 18: To a stirred solution of ketone **18** (0.1 mmol) in THF (1 ml) at −78 °C was added base (0.15 mmol, 1.5 equiv) dropwise. The resulting mixture was stirred at this temperature for 0.5 h and then oxaziridine (0.15 mmol, 1.5 equiv) was added in one portion. The resulting mixture was stirred at −78 °C for 0.5 h before it was quenched with NH_4Cl (sat. aq., 2 ml). The reaction mixture was extracted with EtOAc (3 × 5 ml), and the combined organic phases were washed with brine (3 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:10→1:5) to give alcohol (10*R*)- or (10*S*)-**20**. The enantiomeric ratio of **20** was determined by HPLC (Chiralcel OD-H, 25 °C, flow rate: 1 mL/min, hexanes/isopropanol: 99.5/0.5, 254 nm): 6.83 min for (10*R*)-**20**, 7.41 min for (10*S*)-**20**.

(*S*)-4-Bromo-2,2-di-*tert*-butyl-10-hydroxy-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*]-[1,3,2]dioxasilin-11(8*H*)-one [(10*S*)-20]: (10*S*)-**20** was obtained in 77% yield (38.9 mg, 0.0769 mmol, *er* 14:1) as a pale yellow foam according to the general procedure with LTMP as base and oxaziridine (−)-**19**. (10*S*)-**20**: R_f = 0.21 (silica gel, EtOAc:hexanes 1:5); $[\alpha]_D^{25}$ = −1.0 (*c* = 0.52, CHCl3); FT-IR (film): ν_{max} = 3465, 2936, 2862, 1682, 1606, 1562, 1472, 14445, 1404. 1367, 1253 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.45 (s, 1 H), 4.32 (ddd, *J* = 13.4, 5.3, 2.5 Hz, 1 H), 4.26 (d, *J* = 2.5 Hz, 1 H), 3.84 (s, 3 H), 3.41 (ddd, *J* = 17.4, 4.6, 2.5 Hz, 1 H), 2.93 (ddd, *J* = 17.8, 13.4, 4.9 Hz, 1 H), 2.58 (s, 3 H), 2.53 (dtd, *J* = 12.6, 5.1, 2.4 Hz, 1 H), 1.95 (qd, *J* = 13.2, 4.6 Hz, 1 H), 1.17 (s, 9 H), 1.12 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 197.2, 150.3, 149.8, 145.0, 141.4, 130.9, 130.8, 114.8, 114.7, 114.1, 111.1, 74.2, 60.9, 31.0, 26.3, 26.2, 24.6, 22.2, 21.5, 21.1ppm; HRMS (ESI-TOF) calcd for $C_{24}H_{31}BrO_5Si^+$ $[M+H]^+$ 507.1197, found 507.1181.



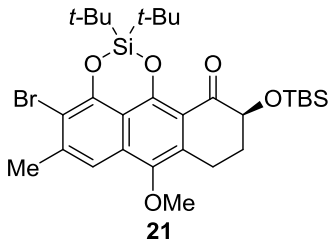
(10*S*)-20

(10*R*)-**20** was obtained in 78% yield (39.0 mg, 0.078 mmol, *er* 14:1) as a pale yellow foam according to the general procedure with LTMP as base and oxaziridine (+)-**19**. (10*R*)-**20**: $[\alpha]_D^{25}$ = +1.2 (*c* = 0.25,

$CHCl_3$). Other physical and spectral data are indentical with those of (10*S*)-**20**.

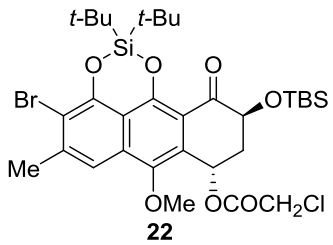
rac-**20** was prepared according to the general procedure with LTMP as base and oxaziridine *rac*-**19** for analysis purposes.

(10*S*)-4-Bromo-2,2-di-*tert*-butyl-10-{[*tert*-butyl(dimethyl)silyl]oxy}-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (21): To a stirred solution of alcohol **20** (39.6 mg, 0.0780 mmol, 1.0 equiv) in CH_2Cl_2 (1 ml) at −78 °C were sequentially added 2,6-lutidine (36 μL, 0.31 mmol, 4.0 equiv) and TBSOTf (54 mg, 0.234 mmol, 3.0 equiv). The resulting mixture was stirred at this temperature for 30 min before it was quenched with Na_2CO_3 (sat. aq., 1 ml). The reaction mixture was extracted with CH_2Cl_2 (3 ml), and the combined organic phases were washed with brine (2 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:10) to give the title compound (47.1 mg, 0.076 mmol, 97% yield) as a colorless oil. 21: R_f = 0.50 (silica gel, EtOAc:hexanes 1:5); $[\alpha]_D^{25} = -1.65$ (*c* = 0.48, $CHCl_3$); FT-IR (film): ν_{max} = 3464, 2935, 2860, 1700, 1606, 1564, 1472, 1445, 1403, 1361, 1253 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 1.1 Hz, 1 H), 4.30 (dd, *J* = 8.7, 3.8 Hz, 1 H), 3.83 (s, 3 H), 3.28 (ddd, *J* = 17.2, 7.0, 5.2 Hz, 1 H), 2.99 (ddd, *J* = 17.3, 7.8, 5.4 Hz, 1 H), 2.57 (d, *J* = 1.0 Hz, 3 H), 2.28–2.08 (m, 2 H), 1.13 (d, *J* = 1.6 Hz, 18 H), 0.87 (s, 9 H), 0.13 (s, 3 H), 0.12 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 195.3, 149.7, 149.4, 144.6, 140.4, 131.0, 130.3, 116.0, 114.8, 114.6, 110.6, 75.5, 60.8, 31.3, 26.3, 26.2, 26.0, 24.5, 21.3, 21.3, 21.0, 18.6, −4.3, −5.1 ppm; HRMS (ESI-TOF) calcd for $C_{30}H_{46}BrO_5Si_2^+$ $[M+H]^+$ 621.2062, found 621.2020.



21

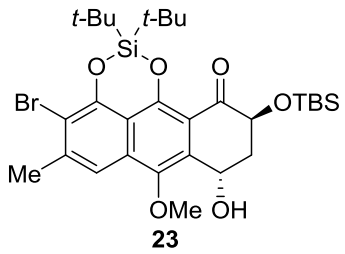
(8*S*,10*S*)-4-Bromo-2,2-di-*tert*-butyl-10-{[*tert*-butyl(dimethyl)silyl]oxy}-7-methoxy-5-methyl-11-oxo-8,9,10,11-tetrahydroanthra[1,9-*de*][1,3,2]dioxasilin-8-yl chloroacetate (22): To a stirred mixture of **21** (191 mg, 0.307 mmol, 1.0 equiv) and chloroacetic acid (577 mg, 6.14 mmol, 20.0 equiv) and 4Å molecule sieves (1.0 g) in CH_2Cl_2 (3 ml) at 0 °C was added DDQ (139 mg,0.614 mmol, 2.0 equiv). The resulting mixture was stirred at this temperature for 6 h before it was diluted with EtOAc (10 ml) and the resulting mixture was poured into $NaHCO_3$ (sat. aq., 20 ml). The reaction mixture was filtered through Celite®, then extracted with EtOAc (3 × 10 ml). The combined organic phases were washed with brine (5 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by



22

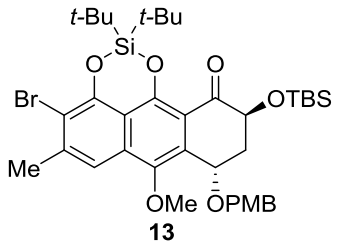
flash column chromatography (silica gel, EtOAc:hexanes 1:10) to give the title compound (**22**, 191 mg, 0.268 mmol, 87% yield) as a colorless oil. **22**: R_f = 0.39 (silica gel, EtOAc:hexanes 1:5); $[\alpha]_D^{25}$ = −43.7 (*c* = 0.58, $CHCl_3$); FT-IR (film): ν_{max} = 2935, 2897, 2861, 1742, 1705, 1605, 1566 1472, 1407, 1362 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 1.1 Hz, 1 H), 6.66 (t, *J* = 3.5 Hz, 1 H), 4.67 (dd, *J* = 12.1, 4.7 Hz, 1 H), 4.10 (d, *J* = 14.7 Hz, 1 H), 4.06 (d, *J* = 14.6 Hz, 1 H), 3.86 (s, 3 H), 2.58 (d, *J* = 0.9 Hz, 3 H), 2.52 (ddd, *J* = 14.3, 4.7, 3.3 Hz, 1 H), 2.43 (ddd, *J* = 14.3, 12.1, 3.8 Hz, 1 H), 1.15 (s, 9 H), 1.13 (s, 9 H), 0.92 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.6, 166.7, 149.9, 149.1, 147.2, 141.2, 130.3, 125.8, 116.7, 115.4, 114.6, 112.6, 71.8, 67.8, 62.6, 41.1, 37.4, 26.3, 26.2, 26.0, 24.6, 21.5, 21.1, 18.8, −4.3, −5.3 ppm; HRMS (ESI-TOF) calcd for $C_{32}H_{47}BrO_7Si_2^+$ $[M+H]^+$ 713.1727, found 713.1729.

(8*S*,10*S*)-4-Bromo-2,2-di-*tert*-butyl-10-{[*tert*-butyl(dimethyl)silyl]oxy}-8-hydroxy-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (23): To a stirred solution of chloroacetate **22** (122 mg, 0.186 mmol, 1.0 equiv) in MeOH (1 ml) at 0 °C was added LiOH (0.45 M in MeOH, 413 μL, 0.186 mmol, 1.2 equiv) dropwise. The resulting mixture was stirred at this temperature for 5 min before it was diluted with EtOAc (2 ml) and quenched with NH_4Cl (sat. aq., 2 ml). The reaction mixture was extracted with EtOAc (3 × 5 ml), and the combined organic phases were washed with brine (3 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:10) to give the title compound (109 mg, 0.169 mmol, 91% yield) as a colorless oil. **23**: R_f = 0.21 (silica gel, EtOAc:hexanes 1:5); $[\alpha]_D^{25}$ = −28.9 (*c* = 1.84, $CHCl_3$); FT-IR (film): ν_{max} = 3464, 2935, 2860, 1700, 1606, 1564, 1472, 1445, 1403, 1361, 1253 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 1.0 Hz, 1 H), 5.44 (td, *J* = 4.8, 2.2 Hz, 1 H), 4.68 (dd, *J* = 10.2, 4.0 Hz, 1 H), 3.96 (s, 3 H), 3.25 – 3.17 (m, 1 H), 2.59 (s, 3 H), 2.51–2.43 (m, 1 H), 2.38 (dt, *J* = 13.7, 4.4 Hz, 1 H), 1.14 (s, 9 H), 1.11 (s, 9 H), 0.88 (s, 9 H), 0.15 (s, 3 H), 0.11 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 194.8, 149.8, 148.9, 146.0, 140.8, 132.0, 130.3, 116.1, 114.8, 114.2, 111.8, 72.7, 63.7, 62.3, 38.9, 26.2, 26.2, 26.0, 24.6, 21.3, 21.3, 18.6, −4.3, −5.2 ppm; HRMS (ESI-TOF) calcd for $C_{30}H_{46}BrO_6Si_2^+$ $[M+H]^+$ 637.2011, found 637.2009.



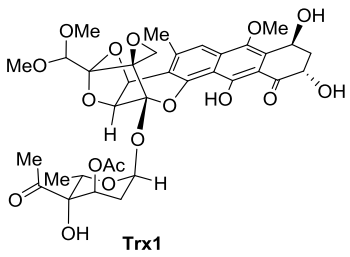
23

(8*S*,10*S*)-4-Bromo-2,2-di-*tert*-butyl-10-{[*tert*-butyl(dimethyl)silyl]oxy}-7-methoxy-8-[(4-methoxybenzyl)oxy]-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (13): To a stirred solution of **23** (21.4 mg, 0.0335 mmol, 1.0 equiv) in toluene (0.5 ml) at 23 °C were added a solution of freshly prepared 4-methoxybenzyl-2,2,2-trichloroacetimidate (22 mg, 0.077 mmol, 2.3 equiv) in toluene (0.2 ml) and $Cu(OTf)_2$ (2.0 mg, 0.0055 mmol, 0.2 equiv). The resulting mixture was stirred at this temperature for 6 h before it was directly subject to a flash column chromatography (silica gel, EtOAc:hexanes 1:10) to afford the title compound (**13**, 17.8 mg, 0.0235 mmol, 70% yield) as a colorless oil together with the recovered starting material (4.8 mg, 0.0075 mmol, 22% yield). **13**: $[\alpha]_D^{25} = +37.5$ ($c = 0.6$, CH_2Cl_2); Enantiomeric ratio of **13** was determined by HPLC (Chiralcel OD-H, 25 °C, flow rate: 1 mL/min, hexanes/isopropanol: 99/1, 254 nm) as 54:1. Other physical and spectral data are identical with those reported in the previous route.



13

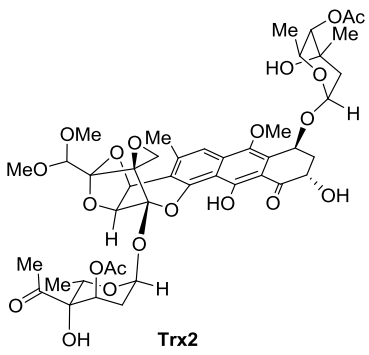
(1*S*,2*R*,8*S*,10*S*,13a*R*)-2-(Dimethoxymethyl)-8,10,12-trihydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 4-*C*-acetyl-3-*O*-acetyl-2,6-dideoxy-*α*-D-*ribo*-hexopyranoside (Trx1): To a stirred solution of **24**[3] (1.4 mg, 1.7 μmol) in CH_3CN (0.1 ml) at 23 °C in a reaction flask shielded from light using aluminum foil was added $Et_3N{\cdot}3HF$ (10.0 mg, 61.4 μmol, 36 equiv). After stirring at this temperature for 12 h, the reaction mixture was diluted with EtOAc (10 ml). The resulting mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative HPLC (Atlantis Prep T3 OBD column, 5 μm, 19 × 150 mm, UV detection at 270 nm, gradient elution with 20→80% (1→30 min), then 80→100% (30→35 min) MeCN in H_2O, flow rate: 5 mL/min, 20.0→22.0 min) to give **Trx1** (1.0 mg, 1.4 μmol, 83% yield) as an orange foam. **Trx1**: $R_f = 0.23$ (silica gel, EtOAc); $[\alpha]_D^{25} = +210.0$ ($c = 0.02$, CH_2Cl_2); FT-IR (film): $\nu_{max} = 3449, 2938, 1718, 1619, 1567, 1387, 1224, 1092, 983, 734\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$) $\delta = 13.78$ (s, 1 H), 7.46 (s, 1 H), 5.81 (t, $J = 3.0$ Hz, 1 H), 5.46 (t, $J = 2.8$ Hz, 1 H), 5.31 (d, $J = 4.2$ Hz, 1 H), 5.30 (s, 1 H), 5.20 (d, $J = 4.1$ Hz, 1 H), 5.01 (q, $J = 6.4$ Hz, 1 H), 4.92 (dd, $J = 12.8$, 5.5 Hz, 1 H),



Trx1

4.75 (t, *J* = 3.0 Hz, 1 H), 4.74 (s, 1 H), 3.92 (s, 3 H), 3.91 (s, 1 H), 3.64 (s, 3 H), 3.57 (br s, 1 H), 3.48 (s, 3 H), 2.84 (d, *J* = 5.9 Hz, 1 H), 2.75 (d, *J* = 6.0 Hz, 1 H), 2.78–2.71 (m, 1 H), 2.62 (s, 3 H), 2.36 (s, 3 H), 2.35 (t, *J* = 3.4 Hz, 2 H), 2.23 (s, 3 H), 2.17 (td, *J* = 13.1, 3.2 Hz, 1 H), 1.09 (d, *J* = 6.4 Hz, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 208.7, 203.2, 170.3, 162.4, 151.9, 144.4, 142.7, 135.7, 129.4, 116.3, 114.7, 114.7, 107.1, 104.6, 101.7, 99.4, 92.5, 78.2, 72.0, 70.7, 69.0, 68.3, 67.7, 64.5, 62.9, 61.9, 56.6, 55.9, 47.4, 37.0, 28.9, 27.0, 21.3, 20.4, 14.5 ppm; HRMS (ESI-TOF) calcd for $C_{35}H_{40}O_{17}Na^+$ $[M+Na]^+$ 755.2158, found 755.2152.

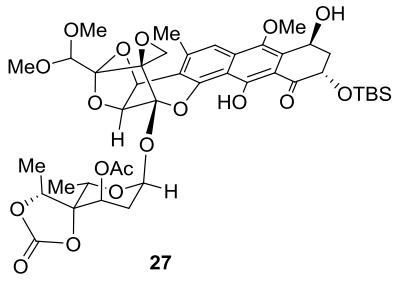
(1*S*,8*S*,10*S*,13a*S*)-8-[(4-*O*-Acetyl-2,6-dideoxy-3-*C*-methyl-*α*-L-*xylo*-hexopyranosyl)oxy]-2-(dimethoxymethyl)-10,12-dihydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 4-*C*-acetyl-3-*O*-acetyl-2,6-dideoxy-*α*-L-*xylo*-hexopyranoside (Trx2): To a stirred solution of **25**[3] (1.1 mg, 1.1 μmol, 1.0 equiv) in CH_3CN (0.1 ml) at 23 °C in a reaction flask shielded from light using aluminum foil was added $Et_3N{\cdot}3HF$ (10.0 mg, 61.4 μmol, 57 equiv). After stirring at this temperature for 12 h, the reaction mixture was diluted with EtOAc (10 ml). The resulting mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative HPLC (Atlantis Prep T3 OBD column, 5 μm, 19 × 150 mm, UV detection at 270 nm, gradient elution with 20→50% (1→5 min), then 50→90% (5→45 min) MeCN in H_2O, flow rate: 5 mL/min, 20.9→22.8 min) to give **Trx2** (0.7 mg, 0.8 μmol, 71% yield) as an orange foam. R_f = 0.58 (silica gel, EtOAc); $[\alpha]_D^{25} = -10.0$ (*c* = 0.05, CH_2Cl_2); FT-IR (film): ν_{max} = 3508. 2937, 1736, 1621, 1377, 1228, 1107, 1092, 997, 731 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 14.01 (s, 1 H), 7.48 (s, 1 H), 5.81 (t, *J* = 3.1 Hz, 1 H), 5.39 (t, *J* = 2.9 Hz, 1 H), 5.38 (d, *J* = 3.8 Hz, 1 H), 5.32 (d, *J* = 4.1 Hz, 1 H), 5.20 (d, *J* = 4.2 Hz, 1 H), 5.01 (q, *J* = 6.4 Hz, 1 H), 4.76 (dd, *J* = 17.1, 4.6 Hz, 1 H), 4.75 (d, *J* = 3.8 Hz, 2 H), 4.54 (q, *J* = 6.1 Hz, 1 H), 3.91 (s, 1 H), 3.84 (br s, 1 H), 3.84 (s, 3 H), 3.64 (s, 3 H), 3.57 (br s, 1 H), 3.48 (s, 3 H), 2.85 (d, *J* = 5.9 Hz, 1 H), 2.81 (ddd, *J* = 13.4, 5.4, 3.3 Hz, 1 H), 2.76 (d, *J* = 5.9 Hz, 1 H), 2.61 (s, 3 H), 2.36 (s, 3 H), 2.35 (t, *J* = 3.4 Hz, 2 H), 2.23 (s, 3 H), 2.24–2.17 (m, 1 H), 2.14 (s, 3 H), 1.96 (dd, *J* = 14.6, 4.1 Hz, 1 H), 1.62 (d, *J* = 14.7 Hz, 1 H), 1.24 (d, *J* = 6.6 Hz, 3 H), 1.09 (d, *J* = 6.5 Hz, 3 H), 1.07 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 208.6, 202.7, 171.1, 170.3, 170.3, 163.2, 152.0, 144.8, 143.0, 135.4, 126.5, 116.7, 115.0, 114.8, 107.3, 104.6, 101.8, 99.4, 98.0, 92.5, 78.2, 74.4, 72.0, 70.7, 69.0, 68.8, 68.3, 67.9, 67.5,



Trx2

64.5, 62.9, 62.7, 60.4, 56.5, 56.0, 47.4, 36.7, 28.9, 27.0, 25.7, 21.3, 21.0, 20.9, 20.4, 16.9, 14.5, 14.2 ppm; HRMS (ESI-TOF) calcd for $C_{44}H_{54}O_{21}Na^+$ $[M+Na]^+$ 941.3050, found 941.3026.

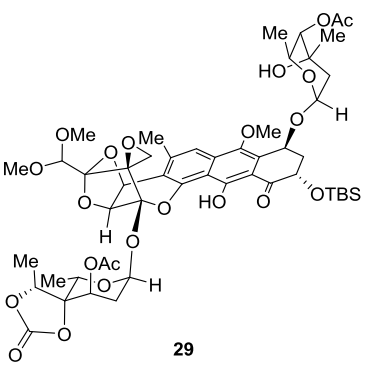
(4*R*,5*S*,6*S*,8*S*,10*R*)-8-{[(1*S*,8*S*,10*S*,13a*S*)-10-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-(dimethoxymethyl)-8,12-dihydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl]oxy}-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-10-yl acetate (27): To a stirred solution of mono-glycosylated compound **26**[3]



27

(4.1 mg, 4.1 µmol, 1.0 equiv) in CH_2Cl_2 (0.2 ml) and H_2O (0.05 ml, pH 7.0 buffer) at 23 °C in a reaction flask shielded from light using aluminum foil was added DDQ (2.7 mg, 12 µmol, 2.9 equiv). After stirring at this temperature for 3 h, the reaction was quenched with brine (2 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 2 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give **27** (3.0 mg, 3.4 µmol, 83% yield) as an orange foam. **27**: R_f = 0.30 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +6.7 (*c* = 0.15, CH_2Cl_2); FT-IR (film): ν_{max} = 2952, 2856, 1815, 1749, 1621, 1389, 1221, 1082, 1048, 1015, 868 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.43 (s, 1 H), 7.44 (d, *J* = 1.1 Hz, 1 H), 5.76 (dd, *J* = 4.3, 2.2 Hz, 1 H), 5.43 (t, *J* = 3.5 Hz, 1 H), 5.22 (d, *J* = 4.1 Hz, 1 H), 5.18 (d, *J* = 4.1 Hz, 1 H), 5.02 (t, *J* = 3.7 Hz, 1 H), 4.90 (dd, *J* = 11.8, 5.0 Hz, 1 H), 4.70 (s, 1 H), 4.64 (q, *J* = 6.3 Hz, 1 H), 4.59 (q, *J* = 6.8 Hz, 1 H), 3.91 (s, 3 H), 3.61 (s, 3 H), 3.46 (s, 3 H), 2.82 (d, *J* = 6.0 Hz, 1 H), 2.73 (d, *J* = 6.0 Hz, 1 H), 2.60 (d, *J* = 1.1 Hz, 3 H), 2.50 (ddd, *J* = 13.5, 5.0, 3.6 Hz, 1 H), 2.51 (br s, 1 H), 2.38–2.29 (m, 2 H), 2.28–2.23 (m, 1 H), 2.23 (s, 3 H), 1.60 (d, *J* = 6.8 Hz, 3 H), 1.36 (d, *J* = 6.4 Hz, 3 H), 0.96 (s, 9 H), 0.23 (s, 3 H), 0.16 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 203.2, 170.1, 162.7, 153.5, 151.8, 143.9, 142.1, 135.3, 129.9, 116.3, 114.9, 114.4, 108.2, 104.7, 101.8, 99.5, 91.4, 81.0, 80.8, 72.2, 70.7, 69.5, 69.2, 68.3, 64.2, 62.8, 62.7, 56.7, 55.8, 47.6, 38.9, 30.4, 26.0, 21.2, 20.5, 18.7, 15.3, 14.9, 2.0, −4.3, −5.2 ppm; HRMS (ESI-TOF) calcd for $C_{42}H_{54}O_{18}SiNa^+$ $[M+Na]^+$ 897.2972, found 897.2961.

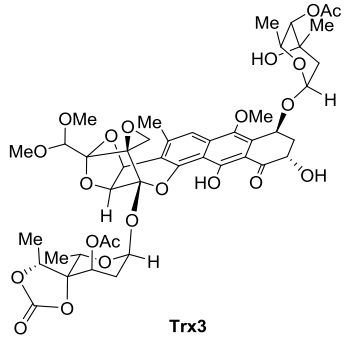
(4*R*,5*S*,6*S*,8*S*,10*R*)-8-{[(1*S*,8*S*,10*S*,13a*S*)-8-[(4-*O*-Acetyl-2,6-dideoxy-3-*C*-methyl-*α*-L-*xylo*-hexopyranosyl)oxy]-10-{[*tert*-butyl(dimethyl)silyl]oxy}-2-(dimethoxymethyl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl]oxy}-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-10-yl acetate (29):To a stirred mixture of the hydroxy mono-glycosylated product **27** (3.5 mg, 4 µmol,



29

1.0 equiv), PPh_3AuNTf_2 (0.025 M in CH_2Cl_2, 48 µL, 1.2 µmol, 0.3 equiv) and 4 Å MS (80 mg) in CH_2Cl_2 (0.4 ml) at 0 °C was added a solution of carbohydrate donor **28** (3.0 mg, 8.0 µmol, 2.0 equiv) in CH_2Cl_2 (160 µL) dropwise over 30 min. The reaction mixture was stirred at this temperature for another 15 min, and then quenched with Et_3N (5 µL). The resulting mixture was filtered through Celite® and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give the title compound (3.7 mg, 3.5 µmol, 88% yield) as an orange foam. **29**: R_f = 0.39 (silica gel, hexanes:EtOAc 2:3); $[\alpha]_D^{25}$ = −57.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 3522, 2933, 2856, 1815, 1748, 1621, 1389, 1223, 1083, 1015, 996, 866 cm^{-1}; NMR (600 MHz, $CDCl_3$) = δ 7.25–7.22 (m, 1 H), 7.20 (d, *J* = 8.6 Hz, 2 H), 6.79–6.73 (m, 2 H), 5.50 (d, *J* = 1.5 Hz, 1 H), 5.33 (d, *J* = 3.8 Hz, 1 H), 5.21 (d, *J* = 1.3 Hz, 1 H), 5.13 (d, *J* = 3.8 Hz, 1 H), 5.09 (t, *J* = 2.9 Hz, 1 H), 4.80 (s, 1 H), 4.76 (dd, *J* = 12.4, 5.1 Hz, 1 H), 4.60 (d, *J* = 10.9 Hz, 1 H), 4.50 (d, *J* = 10.9 Hz, 1 H), 3.93–3.87 (m, 1 H), 3.79 (s, 3 H), 3.69 (s, 3 H), 3.53 (d, *J* = 4.4 Hz, 6 H), 2.62 (ddd, *J* = 13.6, 5.2, 3.1 Hz, 1 H), 2.48 (s, 3 H), 2.04 (ddd, *J* = 13.6, 12.4, 2.8 Hz, 1 H), 1.70 (d, *J* = 9.8 Hz, 1 H), 1.05 (s, 9 H), 0.98 (s, 9 H), 0.85 (s, 9 H), 0.13 (s, 3 H), 0.04 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 203.0, 170.5, 170.1, 163.3, 153.4, 151.9, 144.4, 142.4, 135.1, 126.7, 116.8, 115.1, 114.7, 108.4, 104.7, 101.8, 99.5, 98.3, 91.4, 81.0, 80.8, 74.6, 72.2, 70.7, 69.4, 69.2, 68.9, 68.4, 68.3, 64.2, 62.9, 62.8, 56.6, 55.9, 47.6, 38.9, 36.8, 30.4, 25.9, 25.9, 25.9, 21.2, 21.0, 20.5, 18.6, 17.0, 15.3, 14.9, −4.2, −5.3 ppm; HRMS (ESI-TOF) calcd for $C_{51}H_{68}O_{22}SiNa^+$ $[M+Na]^+$ 1083.3864, found 1083.3849.

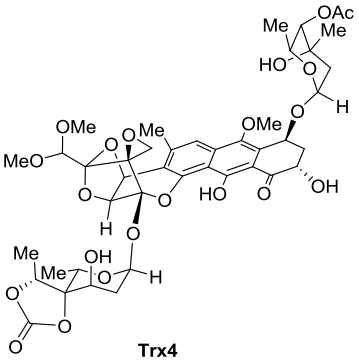
(4*R*,5*S*,6*S*,8*S*,10*R*)-8-{[(1*S*,8*S*,10*S*,13a*S*)-8-[(4-*O*-Acetyl-2,6-dideoxy-3-*C*-methyl-*α*-L-*xylo*-hexopyranosyl)oxy]-2-(dimethoxymethyl)-10,12-dihydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl]oxy}-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-10-yl acetate (Trx3): To a stirred solution of **29** (1.0 mg, 1.1 µmol, 1.0 equiv) in CH_3CN (0.1 ml) at 23 °C in a reaction flask shielded from light using aluminum foil was added $Et_3N{\cdot}3HF$ (10.0 mg, 61.4 µmol, 65 equiv). After stirring at this temperature for 12 h, the reaction mixture was diluted with EtOAc (10 ml). The resulting mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated



Trx3

under reduced pressure. The residue was purified by preparative HPLC (Atlantis Prep T3 OBD column, 5 μm, 19 × 150 mm, UV detection at 270 nm, gradient elution with 20→50% (1→5 min), then 50→90% (5→40 min) MeCN in H_2O, flow rate: 5 mL/min, 23.3→24.8 min) to give **Trx3** (0.75 mg, 0.80 μmol, 85% yield) as an orange foam. **Trx3**: R_f = 0.40 (silica gel, hexanes: EtOAc 1:2); $[\alpha]_D^{25}$ = −6.8 (*c* = 0.044, CH_2Cl_2); FT-IR (film): ν_{max} = 3525, 2932, 1814, 1747, 1621, 1378, 1224, 1083, 1047, 997 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.04 (s, 1 H), 7.49 (s, 1 H), 5.74 (dd, *J* = 3.7, 1.7 Hz, 1 H), 5.39 (t, *J* = 2.9 Hz, 1 H), 5.38 (d, *J* = 3.8 Hz, 1 H), 5.24 (d, *J* = 4.1 Hz, 1 H), 5.19 (d, *J* = 4.1 Hz, 1 H), 5.01 (t, *J* = 3.6 Hz, 1 H), 4.77 (dd, *J* = 13.2, 5.4 Hz, 1 H), 4.75 (s, 1 H), 4.70 (s, 1 H), 4.65 (q, *J* = 6.3 Hz, 1 H), 4.59 (q, *J* = 6.8 Hz, 1 H), 4.54 (q, *J* = 6.4 Hz, 1 H), 3.84 (s, 4 H), 3.61 (s, 3 H), 3.58 (s, 1 H), 3.46 (s, 3 H), 2.84 (d, *J* = 5.9 Hz, 1 H), 2.81 (ddd, *J* = 13.4, 5.3, 3.4 Hz, 1 H), 2.75 (d, *J* = 5.9 Hz, 1 H), 2.61 (s, 3 H), 2.38 (ddd, *J* = 15.0, 3.5, 2.1 Hz, 1 H), 2.23 (s, 3 H), 2.28–2.17 (m, 2 H), 2.14 (s, 3 H), 1.96 (dd, *J* = 14.6, 4.0 Hz, 1 H), 1.62 (d, *J* = 16.8 Hz, 1 H), 1.60 (d, *J* = 6.8 Hz, 3 H), 1.37 (d, *J* = 6.4 Hz, 3 H), 1.24 (d, *J* = 6.7 Hz, 3 H), 1.07 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 202.8, 170.3, 170.0, 163.1, 153.3, 151.8, 144.8, 142.9, 135.4, 126.6, 116.8, 114.9, 114.8, 107.4, 104.6, 101.7, 99.4, 98.1, 91.3, 80.8, 80.7, 74.4, 71.9, 70.6, 69.0, 68.8, 68.2, 67.9, 67.6, 64.0, 62.9, 62.7, 56.5, 55.8, 47.5, 36.7, 30.1, 25.7, 21.0, 20.9, 20.4, 16.9, 15.2, 14.7 ppm; HRMS (ESI-TOF) calcd for $C_{45}H_{54}O_{22}Na^+$ $[M+Na]^+$ 969.2999, found 969.2999.

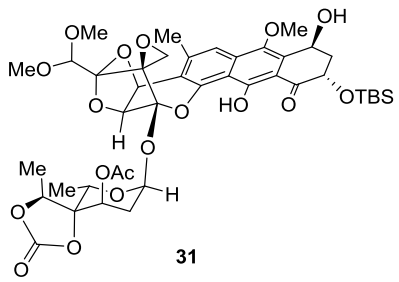
(1*S*,8*S*,10*S*,13a*S*)-2-(Dimethoxymethyl)-10,12-dihydroxy-13a-{[(4*R*,5*S*,6*S*,8*S*,10*R*)-10-hydroxy-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-8-yl]oxy}-7-methoxy-5-methyl-11-oxo-3a,8,9,10,11,13a-hexahydro-4*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-8-yl 4-*O*-acetyl-2,6-dideoxy-3-*C*-methyl-*α*-L-*xylo*-hexopyranoside (Trx4): To a stirred solution of **Trx3** (1.0 mg, 0.94 μmol, 1.0 equiv) in MeOH (0.15 ml) at 0 °C was added K_2CO_3 (1.0 mg, 7.24 μmol, 7.7 equiv). After stirring at this temperature for 45 min, the reaction was diluted with EtOAc (10 ml) and quenched with NH_4Cl (2.0 mg). The resulting mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative HPLC (Atlantis Prep T3 OBD column, 5 μm, 19 × 150 mm, UV detection at 270 nm, gradient elution with 20→50% (1→5 min), then 50→90% (5→40 min) MeCN in H_2O, flow rate: 5.0 mL/min, 23.7→24.8 min) to give **Trx4** (0.5 mg, 0.6 μmol, 59% yield) as an orange foam. **Trx4**: R_f = 0.78 (silica gel, EtOAc); $[\alpha]_D^{25}$ = −30.0



Trx4

(c = 0.06, CH_2Cl_2); FT-IR (film): ν_{max} = 3501, 2928, 1811, 1621, 1388, 1225, 1088, 996 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.06 (s, 1 H), 7.51 (s, 1 H), 5.80 (s, 1 H), 5.40 (br s, 1 H), 5.38 (d, J = 3.8 Hz, 1 H), 5.31 (d, J = 4.1 Hz, 1 H), 5.23 (d, J = 4.1 Hz, 1 H), 4.82–4.73 (m, 3 H), 4.71 (s, 1 H), 4.69 (q, J = 6.0 Hz, 1 H), 4.54 (q, J = 6.2 Hz, 1 H), 4.05–3.96 (m, 2 H), 3.85 (s, 3 H), 3.82 (s, 1 H), 3.61 (s, 3 H), 3.55 (s, 1 H), 3.48 (s, 3 H), 2.98 (d, J = 5.6 Hz, 1 H), 2.89 (d, J = 5.6 Hz, 1 H), 2.82 (ddd, J = 8.3, 4.4, 2.7 Hz, 1 H), 2.61 (s, 3 H), 2.26 (s, 2 H), 2.21 (td, J = 13.4, 2.6 Hz, 1 H), 2.14 (s, 3 H), 1.97 (dd, J = 14.6, 4.0 Hz, 1 H), 1.66–1.59 (m, 5 H), 1.39 (d, J = 6.3 Hz, 3 H), 1.24 (d, J = 6.5 Hz, 4 H), 1.07 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 203.0, 170.3, 163.1, 153.9, 151.7, 144.9, 142.8, 135.5, 126.7, 117.1, 114.8, 107.5, 104.7, 101.6, 99.8, 98.1, 93.7, 81.9, 81.7, 74.4, 71.3, 70.0, 69.2, 68.8, 68.2, 68.0, 67.5, 63.4, 62.9, 62.8, 56.8, 56.2, 48.2, 36.7, 32.2, 25.7, 20.9, 20.4, 16.9, 15.2, 14.7 ppm; HRMS (ESI-TOF) calcd for $C_{43}H_{52}O_{21}Na^+$ $[M+Na]^+$ 927.2893, found 927.2875.

(4*S*,5*S*,6*S*,8*S*,10*R*)-8-{[(1*S*,8*S*,10*S*,13a*S*)-10-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-(dimethoxymethyl)-8,12-dihydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl]oxy}-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-10-yl acetate (31): To a stirred solution of glycoside product **30**[3] (5.6 mg, 6.73 µmol, 1.0 equiv) in CH_2Cl_2 (0.3 ml) and H_2O (0.075 ml, pH 7.0 buffer) at 23 °C in a reaction flask shielded from light using aluminum foil was added DDQ (4.6 mg, 20 µmol, 3.0 equiv). After stirring at this temperature for 3 h, the reaction was quenched with brine (2 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 2 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give 31 (3.7 mg, 4.23 µmol, 75% yield) as an orange foam.

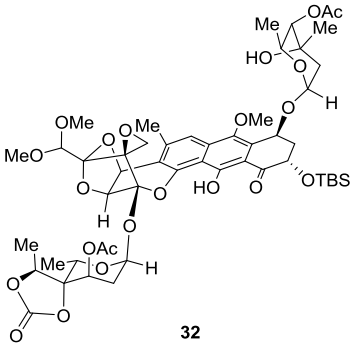


31

31: R_f = 0.29 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = −6.3 (c = 0.16, CH_2Cl_2); FT-IR (film): ν_{max} = 3505, 2930, 2856, 1815, 1749, 1621, 1389, 1222, 1112, 1080, 1048, 1002, 837 cm^{-1}; ^1H NMR (600 MHz, CDCl3) δ = 14.40 (s, 1 H), 7.43 (s, 1 H), 5.78 (d, J = 4.1 Hz, 1 H), 5.43 (t, J = 3.5 Hz, 1 H), 5.24 (d, J = 4.1 Hz, 1 H), 5.18 (d, J = 4.2 Hz, 1 H), 5.10 (s, 1 H), 4.90 (dd, J = 11.8, 5.0 Hz, 1 H), 4.70 (s, 1 H), 4.64 (q, J = 6.6 Hz, 1 H), 4.57 (q, J = 6.5 Hz, 1 H), 3.90 (s, 3 H), 3.61 (s, 3 H), 3.45 (s, 3 H), 2.80 (d, J = 5.9 Hz, 1 H), 2.72 (d, J = 5.9 Hz, 1 H), 2.59 (s, 3 H), 2.50 (ddd, J = 13.6, 5.0, 3.6 Hz, 1 H), 2.47–2.39 (m, 2 H), 2.33 (ddd, J = 13.5, 11.8, 3.6 Hz, 1 H), 2.25 (s, 3 H), 2.22–2.15 (m, 1 H), 1.39 (d, J = 6.5 Hz, 3 H), 1.28 (d, J = 6.6 Hz, 3 H), 0.96 (s, 9 H), 0.23 (s, 3 H), 0.16 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 202.9, 170.8, 170.5, 170.2, 163.4, 152.1, 145.0, 143.2,

135.6, 126.6, 116.8, 115.2, 115.0, 107.4, 104.8, 101.8, 99.8, 98.2, 92.3, 74.6, 72.0, 72.0, 71.4, 69.1, 68.9, 68.3, 68.2, 68.1, 67.7, 65.4, 63.1, 62.9, 56.7, 56.5, 47.5, 36.8, 29.9, 25.9, 21.4, 21.2, 21.0, 20.6, 17.0, 15.3, 15.0 ppm; HRMS (ESI-TOF) calcd for $C_{42}H_{54}O_{18}SiNa^+$ $[M+Na]^+$ 897.2972, found 897.2961.

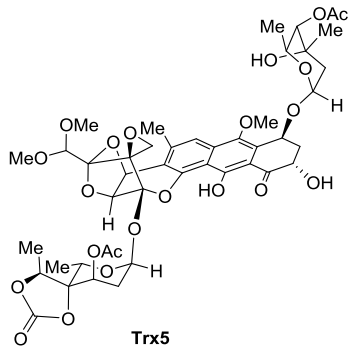
(4*S*,5*S*,6*S*,8*S*,10*R*)-8-{[(1*S*,8*S*,10*S*,13a*S*)-8-[(4-*O*-Acetyl-2,6-dideoxy-3-*C*-methyl-*α*-L-*xylo*-hexopyranosyl)oxy]-10-{[*tert*-butyl(dimethyl)silyl]oxy}-2-(dimethoxymethyl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl]oxy}-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-10-yl acetate (32): To a stirred solution of hydroxy glycoside product **31** (3.5 mg, 4.0 μmol, 1.0 equiv),



32

were added sequantially PPh_3AuNTf_2 (0.025 M in CH_2Cl_2, 48 μL, 1.2 μmol, 0.3 equiv) and 4 Å MS (80 mg) in CH_2Cl_2 (0.4 ml) at 0 °C, followed by a solution of carbohydrate donor **28** (3.0 mg, 8.0 μmol, 2.0 equiv) in CH_2Cl_2 (160 μL) dropwise over 30 min. The reaction mixture was stirred at this temperature for another 15 min, and then quenched with Et_3N (5 μL). The resulting mixture was filtered through Celite® and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give the title compound (2.6 mg, 2.5 μmol, 62% yield) as an orange foam. **32**: R_f = 0.18 (silica gel, hexanes:EtOAc 1:1); $[\alpha]_D^{25}$ = −82.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 3523, 1816, 1749, 1621, 1388, 1224, 1082, 998 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.60 (s, 1 H), 7.46 (d, *J* = 1.1 Hz, 1 H), 5.77 (d, *J* = 4.2 Hz, 1 H), 5.43–5.33 (m, 2 H), 5.25 (d, *J* = 4.2 Hz, 1 H), 5.18 (d, *J* = 4.2 Hz, 1 H), 5.15–5.08 (m, 1 H), 4.79 (dd, *J* = 12.6, 5.2 Hz, 1 H), 4.75 (s, 1 H), 4.70 (s, 1 H), 4.64 (q, *J* = 6.5 Hz, 1 H), 4.57 (q, *J* = 6.4 Hz, 1 H), 4.54–4.49 (m, 1 H), 3.82 (s, 3 H), 3.80 (s, 1 H), 3.61 (s, 3 H), 3.45 (s, 3 H), 2.82 (d, *J* = 5.9 Hz, 1 H), 2.74 (d, *J* = 5.9 Hz, 1 H), 2.63–2.53 (m, 4 H), 2.46 (dd, *J* = 14.9, 2.8 Hz, 1 H), 2.35 (td, *J* = 13.1, 2.8 Hz, 1 H), 2.25 (s, 3 H), 2.19 (dt, *J* = 15.2, 3.8 Hz, 1 H), 2.14 (s, 3 H), 1.95 (dd, *J* = 14.6, 4.1 Hz, 1 H), 1.63 (d, *J* = 14.6 Hz, 1 H), 1.39 (d, *J* = 6.5 Hz, 3 H), 1.29 (d, *J* = 6.6 Hz, 3 H), 1.23 (d, *J* = 6.6 Hz, 3 H), 1.08 (s, 3 H), 0.96 (s, 9 H), 0.26 (s, 3 H), 0.17 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 202.9, 170.5, 170.0, 163.3, 153.4, 151.9, 144.4, 142.4, 135.1, 126.7, 116.7, 115.2, 114.6, 108.4, 104.7, 101.7, 99.2, 98.2, 91.9, 80.8, 74.6, 72.1, 69.4, 69.2, 68.9, 68.4, 68.3, 66.3, 65.7, 62.9, 62.7, 56.5, 55.8, 47.6, 36.8, 29.8, 25.9, 25.9, 21.3, 21.0, 20.5, 18.6, 17.0, 15.3, 13.6, −4.2, −5.3 ppm; HRMS (ESI-TOF) calcd for $C_{51}H_{68}O_{22}SiNa^+$ $[M+Na]^+$ 1083.3864, found 1083.3839.

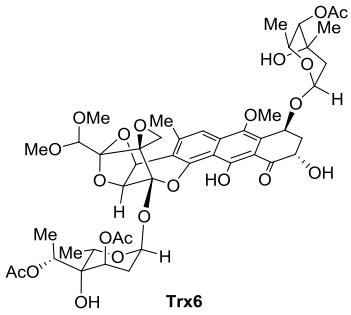
(4*S*,5*S*,6*S*,8*S*,10*R*)-8-{[(1*S*,8*S*,10*S*,13a*S*)-8-[(4-*O*-Acetyl-2,6-dideoxy-3-*C*-methyl-*α*-L-*xylo*-hexopyranosyl)oxy]-2-(dimethoxymethyl)-10,12-dihydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl]oxy}-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-10-yl acetate (Trx5): To a



Trx5

stirred solution of **32** obtained above (1.6 mg, 1.51 μmol, 1.0 equiv) in CH_3CN (0.2 ml) at 23 °C in a reaction flask shielded from light using aluminum foil was added $Et_3N{\cdot}3HF$ (10.0 mg, 61.4 μmol, 41 equiv). After stirring at this temperature for 12 h, the reaction mixture was diluted with EtOAc (10 ml). The resulting mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative HPLC (Atlantis Prep T3 OBD column, 5 μm, 19 × 150 mm, UV detection at 270 nm, gradient elution with 30→50% (1→5 min), then 50→90% (5→40 min) MeCN in H_2O, flow rate: 5 mL/min, 22.6→23.7 min) to give **Trx5** (1.3 mg, 1.3 μmol, 89% yield) as an orange foam. R_f = 0.22 (silica gel, hexanes: EtOAc 2:3); $[\alpha]_D^{25} = -45.0$ (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 3504, 2930, 1812, 1748, 1621, 1386, 1226, 1081, 998, 942 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.02 (s, 1 H), 7.49 (s, 1 H), 5.76 (d, *J* = 4.0 Hz, 1 H), 5.41–5.37 (m, 2 H), 5.26 (d, *J* = 4.1 Hz, 1 H), 5.19 (d, *J* = 4.1 Hz, 1 H), 5.11 (br s, 1 H), 4.77 (dd, *J* = 13.2, 5.4 Hz, 1 H), 4.75 (s, 1 H), 4.70 (s, 1 H), 4.65 (q, *J* = 6.5 Hz, 1 H), 4.57 (d, *J* = 6.6 Hz, 1 H), 4.54 (d, *J* = 6.6 Hz, 1 H), 3.84 (s, 4 H), 3.62 (s, 3 H), 3.58 (s, 1 H), 3.45 (s, 3 H), 2.85–2.78 (m, 2 H), 2.74 (d, *J* = 5.9 Hz, 1 H), 2.60 (s, 3 H), 2.49 (dd, *J* = 15.1, 2.1 Hz, 1 H), 2.25 (s, 3 H), 2.24–2.17 (m, 2 H), 2.14 (s, 3 H), 1.96 (dd, *J* = 14.5, 4.0 Hz, 1 H), 1.62 (d, *J* = 14.6 Hz, 1 H), 1.39 (d, *J* = 6.5 Hz, 3 H), 1.29 (d, *J* = 6.6 Hz, 3 H), 1.24 (d, *J* = 6.5 Hz, 3 H), 1.07 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 202.8, 170.3, 169.9, 163.2, 153.3, 151.9, 144.8, 142.9, 135.4, 126.6, 116.8, 114.9, 114.8, 107.3, 104.6, 101.7, 99.0, 98.0, 91.9, 80.6, 74.4, 71.8, 69.0, 68.8, 68.2, 67.9, 67.5, 66.1, 65.6, 62.9, 62.7, 60.4, 56.4, 55.7, 47.4, 36.7, 29.6, 25.7, 21.2, 21.0, 20.9, 20.4, 16.9, 15.2, 14.2, 13.5 ppm; HRMS (ESI-TOF) calcd for $C_{45}H_{54}O_{22}Na^+$ $[M+Na]^+$ 969.2999, found 969.2970.

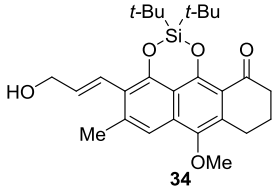
(2*S*,3*R*,4*R*,6*R*)-6-{[(2*S*,8'*S*,10'*S*,17'*S*)-17'-({(2*S*,4*R*,5*S*,6*S*)-4-Acetoxy-5-[(1*R*)-1-acetoxyethyl]-5-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl}oxy)-19'-(dimethoxymethyl)-10',13'-dihydroxy-6'-methoxy-3'-methyl-11'-oxo-17'*H*-spiro[oxirane-2,18'-[16,20,22]trioxahexacyclo-[17.2.1.$0^{2,15}$.$0^{5,14}$.$0^{7,12}$.$0^{17,21}$]docosa[2,4,6,12,14]pentaen]-8'-yl]oxy}-4-hydroxy-2,4-dimethyltetra-hydro-2*H*-pyran-3-yl acetate (Trx6): To a stirred solution of **33**[3] (1.0 mg, 0.93 μmol, 1.0 equiv) in



Trx6

CH_3CN (0.1 ml) at 23 °C in a reaction flask shielded from light using aluminum foil was added $Et_3N{\cdot}3HF$ (10.0 mg, 61.4 μmol, 66 equiv). After stirring at this temperature for 12 h, the reaction mixture was diluted with EtOAc (10 ml). The resulting mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative HPLC (Atlantis Prep T3 OBD column, 5 μm, 19 × 150 mm, UV detection at 270 nm, gradient elution with 20→50% (1→5 min), then 50→90% (5→40 min) MeCN in H_2O, flow rate: 5.0 mL/min, 26.3→27.5 min) to give **Trx6** (0.80 mg, 0.83 μmol, 89% yield) as an orange foam. **Trx6**: R_f = 0.16 (silica gel, hexanes: EtOAc 1:2); $[\alpha]_D^{25}$ = +17.5 (*c* = 0.04, CH_2Cl_2); FT-IR (film): ν_{max} = 3443, 2924, 2852, 1735, 1622, 1446, 1377, 1257, 1085, 998, 800 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.01 (s, 1 H), 7.48 (s, 1 H), 5.71 (d, *J* = 3.0 Hz, 1 H), 5.39 (t, *J* = 2.5 Hz, 1 H), 5.38 (d, *J* = 3.7 Hz, 1 H), 5.27 (d, *J* = 4.1 Hz, 1 H), 5.19 (d, *J* = 4.1 Hz, 1 H), 5.08 (br s, 1 H), 5.05 (q, *J* = 6.5 Hz, 1 H), 4.79–4.75 (m, 3 H), 4.70 (s, 1 H), 4.54 (q, *J* = 6.5 Hz, 1 H), 3.84 (s, 4 H), 3.63 (s, 3 H), 3.57 (s, 1 H), 3.46 (s, 3 H), 2.85–2.77 (m, 2 H), 2.73 (d, *J* = 5.9 Hz, 1 H), 2.61 (s, 3 H), 2.29 (s, 1 H), 2.27–2.22 (m, 2 H), 2.18 (s, 3 H), 2.14 (s, 3 H), 2.05 (s, 3 H), 1.96 (dd, *J* = 14.6, 4.1 Hz, 1 H), 1.63 (d, *J* = 14.6 Hz, 1 H), 1.31 (d, *J* = 6.4 Hz, 3 H), 1.25–1.23 (m, 4 H), 1.19 (d, *J* = 6.6 Hz, 3 H), 1.07 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 203.0, 170.7, 170.3, 170.0, 163.2, 152.0, 144.8, 143.0, 135.4, 126.5, 116.7, 115.1, 114.8, 107.3, 104.6, 101.7, 99.7, 98.0, 92.2, 74.4, 71.8, 71.8, 71.2, 69.0, 68.8, 68.1, 68.1, 67.9, 67.5, 65.2, 62.9, 62.7, 56.5, 56.4, 47.4, 36.7, 29.7, 25.7, 21.2, 21.1, 20.9, 20.4, 16.9, 15.1, 14.9 ppm; HRMS (ESI-TOF) calcd for $C_{46}H_{58}O_{22}Na^+$ $[M+Na]^+$ 985.3312, found 985.3280.

(*E*)-2,2-Di-*tert*-butyl-4-(3-Hydroxyprop-1-en-1-yl)-7-methoxy-5-methyl-9,10-dihydro-anthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (34): To a stirred mixture of aryl bromide **18** (3.60 g,

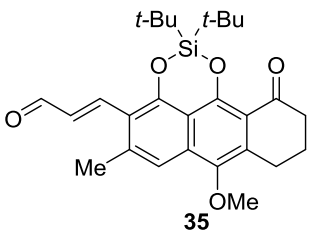


34

7.33 mmol, 1.0 equiv), tri(2-furyl)phosphine (343 mg, 1.48 mmol, 0.2 equiv) and $Pd(PPh_3)_4$ (844 mg, 0.73 mmol, 0.1 equiv) in DMF (100 ml) was added stannane **14** (3.80 g, 11.0 mmol, 1.5 equiv), then argon was bubbled through

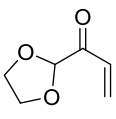
the solution before *N*,*N*-diisopropylethylamine (2.55 ml, 14.7 mmol, 2.0 equiv) and LiCl (1 M in THF, 14.7 ml, 14.7 mmol, 2.0 equiv) were added. After stirring at 100 °C for 12 h, the reaction mixture was cooled to 23 °C and then diluted with EtOAc (200 ml) and quenched with water (100 ml). The resulting mixture was washed with brine (3 × 50 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:4→1:2) to give the title compound (2.54 g, 5.42 mmol, 74% yield) as a yellow foam. **34**: R_f = 0.23 (silica gel, EtOAc:hexanes 1:4); FT-IR (film): ν_{max} = 3696, 3681, 1678, 1605, 1585, 1401, 1371, 1168, 1058, 1014 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.38 (s, 1 H), 6.75–6.67 (dt, *J* = 16.1, 1.5 Hz, 1 H), 6.58 (dt, *J* = 16.1, 5.8 Hz, 1 H), 4.39 (ddd, *J* = 6.0, 5.9, 1.5 Hz, 2 H), 3.83 (s, 3 H), 3.04 (dd, *J* = 6.9, 5.3 Hz, 2 H), 2.64 (dd, *J* = 7.2, 5.8 Hz, 2 H), 2.52 (s, 3 H), 2.08 (quint, *J* = 6.5 Hz, 2 H), 1.40 (t, *J* = 6.0 Hz, 1 H), 1.13 (s, 18 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.7, 151.2, 150.7, 144.4, 139.8, 133.9, 131.6, 130.8, 124.8, 120.1, 116.3, 114.8, 114.7, 65.2, 61.1, 41.4, 26.4, 24.3, 22.5, 22.4, 21.3 ppm; HRMS (ESI-TOF) calcd for $C_{27}H_{37}O_5Si^+$ $[M+H]^+$ 469.2405, found 469.2419.

(*E*)-3-(2,2-Di-*tert*-butyl-7-methoxy-5-methyl-11-oxo-8,9,10,11-tetrahydroanthra[1,9-*de*]-[1,3,2]dioxasilin-4-yl)acrylaldehyde (35): To a stirred solution of allylic alcohol **34** (2.50 g, 5.34 mmol, 1.0 equiv) in CH_2Cl_2 (50 ml) at 0 °C were added TPAP (187 mg, 0.53 mmol, 0.1 equiv) and NMO (937 mg, 8.01 mmol, 1.5 equiv). After stirring at this temperature for 4 h, the reaction was quenched with $NaHCO_3$ (20 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 50 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:6→1:4) to give the title compound (2.04 g, 4.37 mmol, 82% yield) as a yellow foam. **35**: R_f = 0.55 (silica gel, EtOAc:hexanes 1:4); FT-IR (film): ν_{max} = 2937, 2862, 1682, 1583, 1472, 1372, 1167, 1130, 1015, 887 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 9.71 (d, *J* = 7.7 Hz, 1 H), 7.76 (d, *J* = 16.0 Hz, 1 H), 7.42 (d, *J* = 1.2 Hz, 1 H), 7.06 (dd, *J* = 16.0, 7.7 Hz, 1 H), 3.84 (s, 3 H), 3.06 (dd, *J* = 6.9, 5.4 Hz, 2 H), 2.65 (dd, *J* = 7.2, 5.8 Hz, 2 H), 2.62 (d, *J* = 1.0 Hz, 3 H), 2.09 (p, *J* = 6.5 Hz, 2 H), 1.14 (s, 18 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.3, 195.5, 154.6, 150.9, 147.0, 144.7, 139.8, 134.4, 132.6, 132.4, 117.5, 117.0, 115.6, 114.5, 61.2, 41.3, 26.3, 26.3, 24.4, 22.4, 22.4, 21.3 ppm; HRMS (ESI-TOF) calcd for $C_{27}H_{35}O_5Si^+$ $[M+H]^+$ 467.2248, found 467.2259.

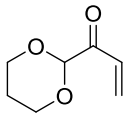


35

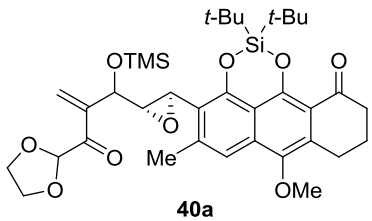
1-(1,3-Dioxolan-2-yl)prop-2-en-1-one (38a): To a stirred solution of 1-(1,3-dioxolan-2-yl) ethan-1-one (4.00 g, 34.5 mmol, 1.0 equiv), paraformaldehyde (3.10 g, 103 mmol, 3.0 equiv) and diisopropylammonium trifluoroacetate (15.5 g, 72.0 mmol, 2.1 equiv) in dry THF (30 ml), trifluoroacetic acid (0.26 ml, 3.40 mmol) was added, and the mixture was heated under reflux for 12 h, the reaction mixture was cooled to 23 °C, then was diluted with Et_2O (50 ml) and quenched with $NaHCO_3$ (sat. aq., 50 ml). The resulting mixture was extracted with Et_2O (3 × 50 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, Et_2O:pentane 1:4→1:2) to give the title compound (2.30 g, 18.0 mmol, 52% yield) as a colorless oil. R_f = 0.43 (silica gel, hexanes:EtOAc 3:1); FT-IR (film): ν_{max} = 2895, 1709, 1697, 1614, 1475, 1406, 1205, 1106, 1058, 1028, 939 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 6.71–6.46 (m, 1 H), 6.53–6.31 (m, 1 H), 6.04–5.72 (m, 1 H), 5.46–5.16 (m, 1 H), 4.12–3.74 (m, 4 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 194.0, 131.3, 101.2 (overlap), 65.7 ppm; HRMS (ESI-TOF) calcd for $C_6H_9O_3^+$ $[M+H]^+$ 129.0552, found 129.0551.


38a

1-(1,3-dioxan-2-yl)prop-2-en-1-one (38b): **38b** was prepared from the corresponding 1-(1,3-dioxan-2-yl)ethan-1-one. R_f = 0.26 (silica gel, hexanes:EtOAc 3:1); FT-IR (film) ν_{max} = 2958, 2920, 2851, 1803, 1716, 1615, 1462, 1407, 1378, 1238 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 6.73 (dd, *J* = 17.5, 10.7 Hz, 1 H), 6.50 (dd, *J* = 17.6, 1.6 Hz, 1 H), 5.88 (dd, *J* = 10.7, 1.6 Hz, 1 H), 4.98 (s, 1 H), 4.24 (ddd, *J* = 12.2, 4.9, 1.6 Hz, 2 H), 3.89 (td, *J* = 12.2, 2.4 Hz, 3 H), 2.22 – 2.14 (m, 1 H), 1.45 (dt, *J* = 14.1, 2.3 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.9, 131.4, 131.0, 100.3, 67.2, 25.8 ppm; HRMS (ESI-TOF) calcd for $C_7H_{11}O_3^+$ $[M+H]^+$ 143.0703, found 143.0705.


38b

2,2-Di-*tert*-butyl-4-[(3*S*)-3-{2-(1,3-dioxolan-2-ylcarbonyl)-1-[(trimethylsilyl)oxy]prop-2-en-1-yl}oxiran-2-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (40a): To a stirred solution of aldehyde **35** (400 mg, 0.858 mmol, 1.0 equiv) in toluene (10 ml) at 23 °C were added H_2O_2 (30 wt% in H_2O, 110 µl, 1.08 mmol, 1.3 equiv) and (*S*)-(−)-*α*,*α*-diphenyl-2-pyrrolidine methanol trimethylsilyl ether (0.05 M in toluene, 3.40 ml, 0.171 mmol, 0.2 equiv). After stirring at the same temperature for 4 h, the reaction mixture was diluted with EtOAc (50 ml). The resulting mixture was washed with H_2O (2 × 10 ml), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give



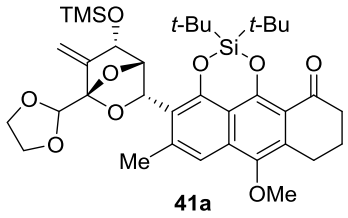
40a

the crude epoxide **37**, which was taken to the next step without further purification.

To a stirred solution of the so obtained crude epoxide **37** in THF (5 ml) at 23 °C was added DABCO (48.0 mg, 0.429 mmol, 0.5 equiv), 4-nitrophenol (59.6 mg, 0.429 mmol, 0.5 equiv) and enone **38a** (690 mg, 5.4 mmol, 6.3 equiv). After stirring at this temperature for 12 h, the reaction mixture was diluted with EtOAc (50 ml). The resulting mixture was washed with brine (2 × 10 ml) and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:4→1:2) to give the crude alcohol **39a**. To a stirred solution of crude alcohol obtained above in CH_2Cl_2 (10 ml) at −78 °C was added dropwise a solution of imidazole (116 mg, 1.67 mmol, 2.0 equiv) in CH_2Cl_2 (2 ml), followed by TMSCl (108 µl, 0.86 mmol, 1.0 equiv). The resulting reaction mixture was stirred at this temperature for 15 min before it was quenched with $NaHCO_3$ (sat. aq., 5 ml). The resulting mixture was stirred at 23 °C for 15 min, and then extracted with CH_2Cl_2 (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:4) to give the title compound (**40a**, plus **C4-*epi*-40a**) (205 mg, 0.30 mmol, *dr ca*. 5:1, 35% for the three steps) as a yellow foam. **40a** (plus **C4-*epi*-40a**): R_f = 0.20 (silica gel, EtOAc:hexanes 1:4); $[\alpha]_D^{25}$ = −66.9 (*c* = 0.2, CH_2Cl_2); FT-IR (film): ν_{max} = 2935, 2897, 1682, 1614, 1403, 1371, 1252, 1147, 1016, 888 cm^{-1}; ^1H NMR (600 MHz, C_6H_6) δ = 7.55 (s, 1 H, major), 7.52 (s, 1 H, minor), 6.46–6.43 (m, 1 H, major), 6.40–6.39 (m, 1 H, minor), 6.26 (s, 1 H, major), 6.28–6.25 (m, 1 H, minor), 5.64 (s, 1 H, minor), 5.61 (s, 1 H, major), 5.41–5.40 (m, 1 H, minor), 5.26 (dd, *J* = 3.8, 1.1 Hz, 1 H, major), 4.43 (d, *J* = 2.2 Hz, 1 H, major), 4.03 (d, *J* = 2.3 Hz, 1 H, minor), 3.80–3.79 (m, 1 H, minor), 3.69 (dd, *J* = 3.7, 2.2 Hz, 1 H, major), 3.65–3.53 (m, 4 H, major + minor), 3.49 (s, 3 H, minor), 3.49 (s, 3 H, major), 3.41–3.36 (m, 4 H, major + minor), 2.78–2.63 (m, 4 H, major + minor), 2.55 (s, 3 H, major), 2.47 (s, 3 H, minor), 2.41–2.31 (m, 4 H, major + minor), 1.54 (quint, *J* = 6.4 Hz, 4 H, major + minor), 1.30 (s, 9 H, minor), 1.28 (s, 9 H, major), 1.27 (s, 9 H, minor), 1.26 (s, 9 H, major), 0.17 (s, 9 H, minor), 0.16 (s, 9 H, major) ppm; ^{13}C NMR (151 MHz, C_6D_6) δ = 194.9 (major + minor), 194.32 (major), 194.24 (minor), 152.8 (minor), 152.3 (major), 150.4 (major + minor), 145.9 (major + minor), 145.18 (minor), 145.11 (major), 141.5 (major), 140.8 (minor), 132.40 (major), 132.35 (minor), 132.0 (major), 131.9 (minor), 129.6 (minor), 129.2 (major), 119.7 (major), 119.6 (minor), 117.08 (major), 117.07 (minor), 115.4 (major + minor), 114.92 (major), 114.91 (minor), 99.9 (major), 99.8 (minor), 69.2 (major), 68.4 (minor), 65.41 (minor), 65.39 (major), 65.33 (minor), 65.31 (major), 62.3 (major), 61.2 (minor), 60.47 (major), 60.45 (minor), 53.1 (major),

51.4 (minor), 41.4 (major + minor), 26.6 (major), 26.5 (major), 24.3 (major + minor), 22.4 (major + minor), 21.7 (minor), 21.6 (major), 21.4 (major), 21.3 (minor), 21.2 (minor), 21.1 (major), 0.2 (minor), 0.1 (major) ppm; HRMS (ESI-TOF) calcd for $C_{36}H_{50}O_9Si_2Na^+$ $[M+Na]^+$ 705.2886, found 705.2885.

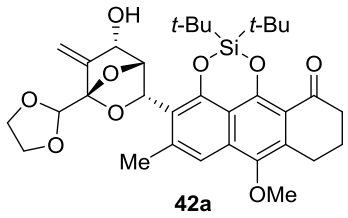
2,2-Di-*tert*-butyl-4-{(1*R*,3*S*,4*S*,5*R*)-1-(1,3-dioxolan-2-yl)-6-methylene-5-[(trimethylsilyl)oxy]-2,7-dioxabicyclo[2.2.1]hept-3-yl}-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (41a): To a flame-dried flask and 4 Å molecule sieves was added the solution of



41a

40a (160 mg, 0.234 mmol, 1.0 equiv) in CH_2Cl_2 (4 ml). To the stirred mixture at −50 °C was added a solution of $BF_3{\cdot}Et_2O$ (0.1 M in CH_2Cl_2, 704 µl, 0.0704 mmol, 0.3 equiv). The resulting mixture was allowed to warm to 0 °C and was quenched by $NaHCO_3$ (sat. aq., 5 ml) and then extracted with EtOAc (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:4) to afford **41a** (76.8 mg, 0.112 mmol, 48% yield) as a yellow foam. **41a**: R_f = 0.67 (silica gel, EtOAc:hexanes 1:2); $[\alpha]_D^{25}$ = +161.0 (*c* = 0.2, CH_2Cl_2); FT-IR (film): ν_{max} = 2935, 2862, 1681, 1609, 1397, 1368, 1251, 1147, 891, 827 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.24 (s, 1 H), 5.72 (d, *J* = 3.2 Hz, 1 H), 5.52 (s, 1 H), 5.40 (d, *J* = 2.5 Hz, 1 H), 5.06 (d, *J* = 2.1 Hz, 1 H), 5.01 (dd, *J* = 4.9, 3.2 Hz, 1 H), 4.71 (dt, *J* = 4.7, 2.3 Hz, 1 H), 4.27–4.20 (m, 2 H), 4.13–4.01 (m, 2 H), 3.79 (s, 3 H), 3.07 (ddd, *J* = 16.3, 7.4, 4.8 Hz, 1 H), 2.97 (ddd, *J* = 16.3, 7.9, 4.8 Hz, 1 H), 2.65–2.60 (m, 5 H), 2.14–1.93 (m, 2 H), 1.18 (s, 9 H), 1.05 (s, 9 H), −0.34 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.8, 150.0, 148.9, 147.7, 144.2, 141.8, 130.6, 130.5, 120.0, 116.3, 115.8, 113.7, 108.6, 106.4, 100.3, 80.2, 80.1, 73.5, 66.1, 65.9, 61.0, 41.4, 26.6, 24.4, 24.2, 22.5, 21.7, 20.8, −0.3 ppm; HRMS (ESI-TOF) calcd for $C_{36}H_{51}O_9Si_2^+$ $[M+H]^+$ 683.3066, found 683.3055.

2,2-Di-*tert*-butyl-4-[(1*R*,3*S*,4*R*,5*S*)-1-(1,3-dioxolan-2-yl)-5-hydroxy-6-methylene-2,7-dioxabicyclo[2.2.1]hept-3-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (42a): 41a (50.0 mg, 73.3 µmol) was dissolved in a solution of TFA (0.1 M in THF:H_2O

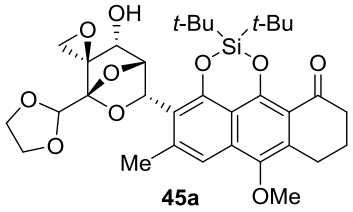


42a

5:1, 2.5 ml) at 23 °C. After stirring at this temperature for 3 h, the reaction was quenched with $NaHCO_3$ (sat. aq., 10 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel,

EtOAc:hexanes 1:4→1:2) to give the title compound (32.0 mg, 52 µmol, 72% yield) as a colorless oil. **42a**: R_f = 0.36 (silica gel, EtOAc:hexanes 1:2); $[\alpha]_D^{25}$ = +368.6 (*c* = 0.3, CH_2Cl_2); FT-IR (film): ν_{max} = 3474, 2935, 2862, 1679, 1608, 1556, 1472, 1372, 1066, 887 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.35 (s, 1 H), 5.69 (d, *J* = 3.3 Hz, 1 H), 5.53 (s, 1 H), 5.50 (d, *J* = 2.7 Hz, 1 H), 5.36–5.31 (m, 1 H), 5.22 (d, *J* = 2.3 Hz, 1 H), 4.69–4.60 (m, 1 H), 4.35–4.17 (m, 2 H), 4.14–3.98 (m, 2 H), 3.82 (s, 3 H), 3.02 (q, *J* = 6.1 Hz, 2 H), 2.66 (s, 3 H), 2.62 (dd, *J* = 7.1, 5.8 Hz, 2 H), 2.06 (p, *J* = 6.3 Hz, 2 H), 1.18 (s, 9 H), 1.09 (s, 9 H), 0.98 (d, *J* = 11.4 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.6, 150.3, 149.8, 148.1, 144.3, 138.9, 131.8, 131.0, 118.3, 117.8, 116.4, 113.9, 108.5, 107.4, 100.2, 79.8, 79.5, 75.5, 66.2, 66.0, 61.2, 41.3, 26.5, 26.4, 24.9, 24.3, 22.4, 21.4, 21.2 ppm; HRMS (ESI-TOF) calcd for $C_{33}H_{43}O_9Si^+$ $[M+H]^+$ 611.2671, found 611.2666.

2,2-Di-*tert*-butyl-4-[(1*R*,2*S*,3*R*,4*R*,5*S*)-1-(1,3-dioxolan-2-yl)-3-hydroxyspiro[6,7-dioxabicyclo-[2.2.1]heptane-2,2'-oxiran]-5-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxa-silin-11(8*H*)-one (45a): To a stirred solution of **42a** (22.3 mg, 0.037 mmol, 1.0 equiv) in acetone



45a

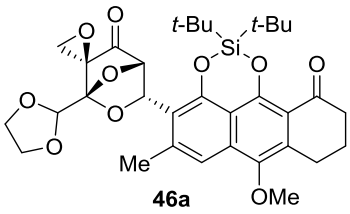
(1.1 ml) at 23 °C were sequentially added OsO_4 (0.08 M aq., 92 µl, 0.0073 mmol, 0.2 equiv) and NMO (0.48 M aq., 305 µl, 0.146 mmol, 4.0 equiv). The mixture was stirred at this temperature for 12 h before it was quenched with Na_2SO_3 (10% aq., 2 ml). The resulting mixture was stirred for another 30 min and was extracted with EtOAc (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was filtered through a short pad of silica gel to afford triol **43a** (20.0 mg, 0.0311mmol) as a colorless oil, which was used for the nest step without further purification.

To a stirred solution of the so obtained crude triol (20.0 mg, 0.0311 mmol, 1.0 equiv) in CH_2Cl_2 (2 ml) at 23 °C were sequentially added Et_3N (22 µl, 0.155 mmol, 5.0 equiv), 4-dimethyl-aminopyridine (1.9 mg, 0.016 mmol, 0.5 equiv) and TsCl (29.6 mg, 0.155 mmol, 5.0 equiv). The mixture was stirred at this temperature for 5 h before it was quenched with NH_4Cl (sat. aq., 2 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The so obtained residue was filtered through a short pad of silica gel to afford the tosylate (24.8 mg, 31.0 µmol) as a colorless foam, which was used for the nest step without further purification.

To a solution of the so obtained tosylate (24.8 mg, 31.0 µmol, 1.0 equiv) in MeOH (2 ml) at 23 °C was added K_2CO_3 (8.5 mg, 0.062 mmol, 2.0 equiv). The mixture was stirred at this temperature for 2

h and was then directly subjected to flash column chromatography (silica gel, EtOAc:hexanes 1:1) to give epoxyalcohol **45a** (18.0 mg, 0.0287 mmol, 78% for the three steps) as a colorless foam. **45a**: R_f = 0.52 (silica gel, hexanes:EtOAc 1:1); $[\alpha]_D^{25}$ = +117.3 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 3455, 2934, 2861, 1680, 1608, 1557, 1472, 1372, 1172, 1091, 970, 827, 661 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.38 (s, 1 H), 5.66 (d, *J* = 3.1 Hz, 1 H), 5.45 (dd, *J* = 5.1, 3.2 Hz, 1 H), 5.43 (s, 1 H), 4.35 (dd, *J* = 9.9, 5.0 Hz, 1 H), 4.25–4.18 (m, 1 H), 4.20–4.13 (m, 1 H), 4.06–3.97 (m, 2 H), 3.83 (s, 3 H), 3.37 (d, *J* = 5.4 Hz, 1 H), 3.08 (d, *J* = 5.3 Hz, 1 H), 3.03 (q, *J* = 6.3 Hz, 2 H), 2.71 (s, 3 H), 2.62 (dd, *J* = 7.2, 5.9 Hz, 2 H), 2.06 (quint, *J* = 6.4 Hz, 2 H), 1.30 (d, *J* = 10.1 Hz, 1 H), 1.18 (s, 9 H), 1.09 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.6, 150.3, 149.8, 144.4, 139.0, 132.0, 131.0, 117.7, 117.6, 116.5, 113.9, 108.0, 98.9, 79.6, 78.7, 76.5, 68.0, 66.3, 65.8, 61.2, 47.4, 41.3, 26.5, 26.4, 24.3, 24.2, 22.4, 21.4, 21.2 ppm; HRMS (ESI-TOF) calcd for $C_{33}H_{43}O_{10}Si^+$ $[M+H]^+$ 627.2620, found 627.2644.

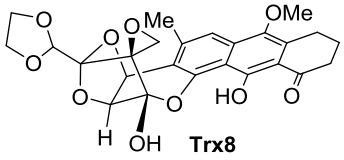
2,2-Di-*tert*-butyl-4-[(1*R*,2*S*,4*S*,5*S*)-1-(1,3-dioxolan-2-yl)-3-oxospiro[6,7-dioxabicyclo[2.2.1]-heptane-2,2'-oxiran]-5-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (46a): To a stirred solution of epoxy alcohol **45a** (18.0 mg, 0.0287 mmol, 1.0 equiv) in



46a

CH_2Cl_2 at 23 °C were sequentially added NMO (10.1 mg, 0.0861 mmol, 3.0 equiv) and TPAP (2.0 mg, 5.7 µmol, 0.2 equiv). The mixture was stirred at this temperature for 1 h and then subjected directly to flash column chromatography (silica gel, EtOAc:hexanes 1:2) to afford **46a** (16.8 mg, 0.0269 mmol, 94% yield) as a yellow foam. **46a**: R_f = 0.7 (silica gel, EtOAc:hexanes 1:2); $[\alpha]_D^{25}$ = +284.3 (*c* = 0.21, CH_2Cl_2); FT-IR (film): ν_{max} = 2934, 2860, 1787, 1682, 1609, 1398, 1372, 1040, 889 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.31 (d, *J* = 1.1 Hz, 1 H), 5.62 (d, *J* = 3.8 Hz, 1 H), 5.55 (s, 1 H), 5.50 (d, *J* = 3.8 Hz, 1 H), 4.32–4.24 (m, 1 H), 4.23–4.17 (m, 1 H), 4.11–4.07 (m, 1 H), 4.07–4.00 (m, 1 H), 3.82 (s, 3 H), 3.48 (d, *J* = 6.2 Hz, 1 H), 3.12 (d, *J* = 6.2 Hz, 1 H), 3.09–2.96 (m, 2 H), 2.66–2.61 (m, 2 H), 2.57 (s, 3 H), 2.07 (quint, *J* = 6.4 Hz, 2 H), 1.20 (s, 9 H), 1.08 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 202.3, 196.5, 150.5, 149.8, 144.3, 138.9, 132.2, 131.3, 117.6, 116.5, 116.2, 113.9, 107.5, 98.5, 78.3, 66.5, 65.9, 61.8, 61.2, 49.9, 41.3, 26.6, 26.3, 24.3, 23.9, 22.4, 21.5, 21.2 ppm; HRMS (ESI-TOF) calcd for $C_{33}H_{41}O_{10}Si^+$ $[M+H]^+$ 625.2464, found 625.2472.

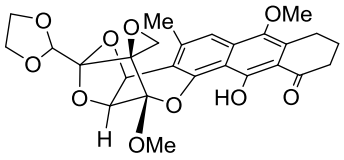
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-2-(1,3-Dioxolan-2-yl)-12,13a-dihydroxy-7-methoxy-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx8): To a solution of epoxide **46a** (16.8 mg, 0.0269 mmol, 1.0 equiv) in MeCN (1 ml) at 23 °C was added $Et_3N{\cdot}3HF$ (11.9 mg, 0.081 mmol, 3.0 equiv). The mixture was stirred at



Trx8

this temperature for 15 min before it was diluted with EtOAc (5 ml) and quenched with $NaHCO_3$ (sat. aq., 2 ml). The resulting mixture was extracted with EtOAc (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes1:1) to afford **Trx8** (11.6 mg, 0.0238 mmol, 89% yield) as a yellow foam. **Trx8**: R_f = 0.23 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +368.6 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2924, 1621, 1571, 1445, 1388, 1330, 1093, 978 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.91 (s, 1 H), 7.44 (s, 1 H), 5.40 (s, 1 H), 5.25 (d, *J* = 4.0 Hz, 1 H), 4.85 (d, *J* = 4.0 Hz, 1 H), 4.45 (s, 1 H), 4.13 (q, *J* = 6.9, 6.4 Hz, 1 H), 4.07–4.02 (m, 1 H), 4.02–3.98 (m, 1 H), 3.92–3.86 (m, 1 H), 3.78 (s, 3 H), 3.19 (d, *J* = 5.2 Hz, 1 H), 3.06 (d, *J* = 5.2 Hz, 1 H), 3.05–3.01 (m, 2 H), 2.73 (td, *J* = 6.0, 1.8 Hz, 2 H), 2.56 (s, 3 H), 2.15–2.03 (m, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.6, 163.0, 151.7, 142.6, 141.6, 135.4, 130.5, 116.0, 113.6, 113.4, 111.2, 103.8, 98.7, 98.6, 73.9, 70.1, 69.4, 66.3, 65.9, 61.0, 50.3, 38.9, 23.7, 22.2, 20.4 ppm; HRMS (ESI-TOF) calcd for $C_{25}H_{24}O_{10}Na^+$ $[M+Na]^+$ 507.1262, found 507.1260.

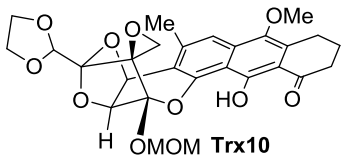
(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxolan-2-yl)-12-hydroxy-7,13a-dimethoxy-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx9): To a stirred mixture of **Trx8** (2.0 mg, 4.1 µmol, 1.0 equiv) and MeI (0.5 ml)



Trx9

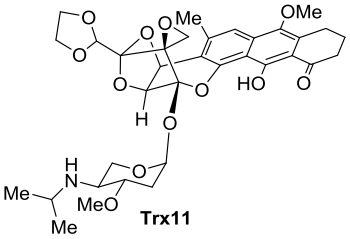
were sequentially added Ag_2O (4.8 mg, 21 µmol, 5.0 equiv) and $CaSO_4$ (2.8 mg, 21 µmol, 5.0 equiv) at 23 °C. The mixture was stirred at this temperature for 12 h before it was subjected to a flash column chromatography (silica gel, EtOAc:hexanes 1:1) to afford **Trx9** (1.3 mg, 2.61 µmol, 63% yield) as a yellow foam. **Trx9**: R_f = 0.4 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +159.7 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2924, 1621, 1571, 1445, 1388, 1235, 1180, 1093, 1073, 1017, 949 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.79 (s, 1 H), 7.46 (d, *J* = 1.2 Hz, 1 H), 5.44 (s, 1 H), 5.22 (d, *J* = 4.1 Hz, 1 H), 4.84 (d, *J* = 4.1 Hz, 1 H), 4.12 (q, *J* = 6.6 Hz, 1 H), 4.08–4.01 (m, 1 H), 4.03–3.96 (m, 1 H), 3.88 (q, *J* = 6.6 Hz, 1 H), 3.79 (s, 3 H), 3.76 (s, 3 H), 3.05 (td, *J* = 5.8, 3.1 Hz, 2 H), 2.97 (d, *J* = 5.6 Hz, 1 H), 2.88 (d, *J* = 5.6 Hz, 1 H), 2.73 (t, *J* = 6.5 Hz, 2 H), 2.57 (d, *J* = 1.0 Hz, 3 H), 2.10 (quint, *J* = 6.2 Hz, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.6, 163.1, 151.6, 142.6, 141.7, 135.4, 130.5, 115.8, 113.4, 111.2, 104.5, 102.3, 98.7, 72.0, 69.4, 69.1, 66.2, 65.9, 61.1, 53.0, 47.8, 39.0, 23.8, 22.3, 20.4 ppm; HRMS (ESI-TOF) calcd for $C_{26}H_{26}O_{10}Na^+$ $[M+Na]^+$ 521.1418, found 521.1416.

(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxolan-2-yl)-12-hydroxy-7-methoxy-13a-(methoxymethoxy)-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx10): To a stirred solution of **Trx8** (3.2 mg, 6.2 µmol, 1.0 equiv) in CH_2Cl_2 (1 ml) at 23 °C were sequentially added *N*,*N*-diisopropylethylamine (5.4 µl, 31 µmol, 5.0 equiv) and MOMCl (2.0 µl, 19 µmol, 3.0 equiv). The mixture was stirred at this temperature for 1 h before it was quenched with $NaHCO_3$ (sat. aq., 2 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:1) to afford **Trx10** (3.0 mg, 5.6 µmol, 90% yield) as a yellow foam. **Trx10**: R_f = 0.33 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +142.8 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2923, 1621, 1571, 1388, 1234, 1094, 1004, 984, 927, 913 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.75 (s, 1 H), 7.45 (d, *J* = 1.2 Hz, 1 H), 5.54 (d, *J* = 6.9 Hz, 1 H), 5.45 (s, 1 H), 5.26–5.08 (m, 2 H), 4.93 (d, *J* = 6.9 Hz, 1 H), 4.13 (q, *J* = 6.6 Hz, 1 H), 4.08–4.03 (m, 1 H), 4.03–3.94 (m, 1 H), 3.89 (q, *J* = 6.6 Hz, 1 H), 3.78 (s, 3 H), 3.57 (s, 3 H), 3.04 (td, *J* = 5.8, 2.5 Hz, 2 H), 2.98 (d, *J* = 5.7 Hz, 1 H), 2.86 (d, *J* = 5.7 Hz, 1 H), 2.73 (t, *J* = 6.4 Hz, 2 H), 2.57 (s, 3 H), 2.09 (quint, *J* = 6.4 Hz, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.6, 163.1, 151.6, 142.5, 141.7, 135.4, 130.5, 115.9, 113.6, 113.4, 111.2, 104.3, 101.8, 98.7, 92.8, 73.5, 69.5, 68.7, 66.2, 65.9, 61.1, 56.7, 47.8, 39.0, 23.7, 22.3, 20.4 ppm; HRMS (ESI-TOF) calcd for $C_{27}H_{28}O_{11}Na^+$ $[M+Na]^+$ 551.1524, found 551.1526.



Trx10

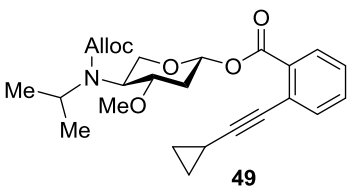
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-2-(1,3-Dioxolan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 2,4-dideoxy-4-(isopropylamino)-3-*O*-methylpentopyranoside (Trx11): To a stirred solution of **Trx8** (6.0 mg, 0.012 mmol, 1.0 equiv), carbohydrate donor **49** (54.6 mg, 0.124 mmol, 10 equiv) and 4 Å MS (250 mg) in CH_2Cl_2 (1.0 ml) at 0 °C was added $Ph_3PAuOTf$ (0.05 M in CH_2Cl_2, 2.48 µmol, 50 µL, 0.2 equiv) dropwise over 5 min. The reaction mixture was stirred at this temperature for 15 min, and then quenched with Et_3N (10 µL). The resulting mixture was filtered through Celite® and concentrated under reduced pressure. The so obtained residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:4) to give the corresponding mono-glycosylated product **50** (6.0 mg) as an orange foam.



Trx11

To a stirred solution of the above mono-glycosylated product **50** (6.0 mg, 8.3 μmol, 1.0 equiv) in CH_2Cl_2 (0.5 ml) was added $Pd(PPh_3)_2Cl_2$ (2.9 mg, 4.13 μmol, 0.5 equiv), followed by acetic acid (9.9 mg, 0.17 mmol, 20 equiv) and *n*-Bu_3SnH (24 mg, 22 μL, 0.086 mmol, 10 equiv) at 23 °C. After stirring at this temperature for 8 h, the reaction was quenched with NH_4Cl (sat. aq., 5 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), the combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, CH_2Cl_2:MeOH 10:1) to give the title compound (3.8 mg, 5.8 μmol, 47% over 2 steps) as an orange foam. **Trx11**: R_f = 0.57 (silica gel, CH_2Cl_2:MeOH 10:1); $[\alpha]_D^{25}$ = +256.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2958, 1621, 1571, 1445, 1388, 1234, 1108, 1095, 986, 731 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.71 (s, 1 H), 7.44 (s, 1 H), 5.77 (t, *J* = 2.9 Hz, 1 H), 5.44 (s, 1 H), 5.28 (d, *J* = 4.0 Hz, 1 H), 5.16 (d, *J* = 4.2 Hz, 1 H), 4.13 (dd, *J* = 12.6, 6.0 Hz, 1 H), 4.07–4.02 (m, 1 H), 4.02–3.98 (m, 1 H), 4.00 (dd, *J* = 12.1, 6.3 Hz, 1 H), 3.88 (dd, *J* = 13.1, 6.5 Hz, 2 H), 3.83 (br s, 1 H), 3.78 (s, 3 H), 3.70 (br s, 1 H), 3.43 (s, 3 H), 3.09–2.99 (m, 2 H), 2.95 (br s, 1 H), 2.92 (d, *J* = 5.8 Hz, 1 H), 2.80 (d, *J* = 5.8 Hz, 1 H), 2.80 (br s, 1 H), 2.75–2.70 (m, 2 H), 2.56 (s, 3 H), 2.47–2.39 (m, 1 H), 2.13–2.05 (m, 2 H), 1.70 (ddd, *J* = 13.2, 10.1, 3.5 Hz, 2 H), 1.13 (br s, 6 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.4, 163.0, 151.8, 142.4, 141.6, 135.2, 130.3, 115.7, 113.5, 113.3, 111.1, 104.3, 101.9, 98.4, 94.5, 72.6, 69.3, 68.3, 66.0, 65.7, 63.5, 60.9, 56.4, 56.2, 47.3, 47.1, 38.8, 34.0, 24.4, 23.6, 22.7, 22.1, 20.2 ppm; HRMS (ESI-TOF) calcd for $C_{34}H_{41}NO_{12}Na^+$ $[M+Na]^+$ 678.2521, found 678.2520.

4-{[(Allyloxy)carbonyl](isopropyl)amino}-1-*O*-[2-(cyclopropylethynyl)benzoyl]-2,4-dideoxy-3-*O*-methyl-*β*-L-*threo*-pentopyranose (49): To a stirred solution of *o*-alkynylbenzoic acid **48**[4]

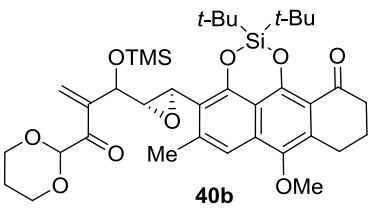


49

(380 mg, 2.04 mmol, 1.0 equiv) and 2,6-di-*tert*-butyl-4-methylpyridine (629 mg, 3.06 mmol, 1.5 equiv) in CH_2Cl_2 (16 ml) at 0 °C were sequentially added oxalyl chloride (388 mg, 262 μL, 3.06 mmol, 1.5 equiv) and *N*,*N*-dimethylformamide (7.5 mg, 7.9 μL, 0.103 mmol, 0.05 equiv). The reaction mixture was allowed to warm to 23 °C and stirred at this temperature for 2 h before all the volatiles were removed under reduced pressure. The *o*-alkynylbenzoyl chloride so obtained was dissolved in CH_2Cl_2 (15 ml) and to such yellowish solution at 0 °C were sequentially added a solution of Alloc-protected aminosugar **47**[5] (446 mg, 1.63 mmol, 0.8 equiv) in CH_2Cl_2 (1.0 ml), Et_3N (619 mg, 0.853 ml, 6.12 mmol, 3.0 equiv) and 4-dimethylaminopyridine (75 mg, 0.61 mmol, 0.3 equiv). The reaction mixture was stirred at the same temperature for 30 min and then

23 °C for 12 h before it was quenched with $NaHCO_3$ (sat. aq. 15 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 20 ml), and the combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:7) to give **49** (β-anomeric isomer, J = 11.0 Hz, 599 mg, 1.35 mmol, 83% yield) as a colorless oil. **49**: R_f = 0.48 (silica gel, EtOAc:hexanes 3:7); $[\alpha]_D^{25}$ = +27 (c = 0.4, $CHCl_3$); FT-IR (film): 2970, 2934, 2230, 1734, 1689, 1648, 1596, 1566, 1483, 1442, 1367, 1282, 1239 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.93 (d, J = 7.9 Hz, 1 H), 7.48 (d, J = 7.6 Hz, 1 H), 7.42 (t, J = 7.5 Hz, 1 H), 7.29 (t, J = 7.4 Hz, 1 H), 6.03–5.86 (m, 2 H), 5.40–5.16 (m, 2 H), 4.73–4.52 (m, 2 H), 4.38–4.10 (m, 2 H), 4.07–3.88 (m, 1 H), 3.82 (dd, J = 11.5, 5.1 Hz, 1 H), 3.35 (s, 3 H), 3.32 (br s, 1 H), 2.56 (ddd, J = 12.4, 4.8, 2.4 Hz, 1 H), 1.71 (q, J = 11.1 Hz, 1 H), 1.53–1.47 (m, 1 H), 1.22 (d, J = 6.7 Hz, 3 H), 1.19 (d, J = 6.8 Hz, 3 H), 0.93–0.88 (m, 4 H). ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 164.4, 155.2, 134.4, 133.2, 133.0, 132.1, 130.9, 130.7, 127.1, 125.2, 118.5, 117.3, 99.9, 93.6, 74.6, 73.3, 66.1, 65.8, 65.4, 64.6, 57.2, 56.1, 48.2, 36.2, 21.4, 21.1, 20.5, 9.0, 0.8 ppm (29 signals and broadened peaks were observed because of rotamers around Alloc group); HRMS (ESI-TOF) calcd for $C_{25}H_{31}NO_6Na^+$ $[M+Na]^+$ 464.2044, found 464.2032.

2,2-Di-*tert*-butyl-4-[(2*R*,3*S*)-3-{2-(1,3-dioxan-2-ylcarbonyl)-1-[(trimethylsilyl)oxy]prop-2-en-1-yl}oxiran-2-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (40b): To a stirred solution of aldehyde **35** (224 mg, 0.480 mmol, 1.0 equiv) in toluene (2.88 ml) at



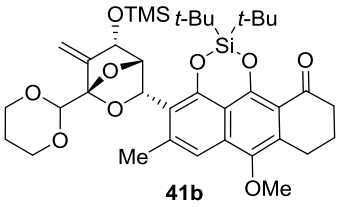
40b

23 °C were added H_2O_2 (30% wt in H_2O, 65 µl, 0.63 mmol, 1.3 equiv) and (*S*)-(−)-*α*,*α*-diphenyl-2-pyrrolidine methanol trimethylsilyl ether **36** (0.05 M in toluene, 1.92 ml, 0.096 mmol, 0.2 equiv). Four batches were separately processed at the same scale. After stirring at this temperature for 4 h, the four batches of reaction mixture were combined, diluted with EtOAc (10 ml) and washed with H_2O (2 × 10 ml), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude epoxide, which was used without further purification. To a solution of the so obtained epoxide **37** in THF (7 ml) at 23 °C was added DABCO (107 mg, 0.96mmol, 0.5 equiv), 4-nitrophenol (185 mg, 0.96 mmol, 0.5 equiv) and enone **38b** (371 mg, 2.88 mmol, 2.0 equiv). After stirring at this temperature for 5 h, the reaction mixture was diluted with EtOAc (30 ml). The resulting mixture was washed with brine (2 × 10 ml), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column

chromatography (silica gel, EtOAc:hexanes 1:4→1:2) to give the alcohol (699 mg, 1.12 mmol) as a pale yellow film.

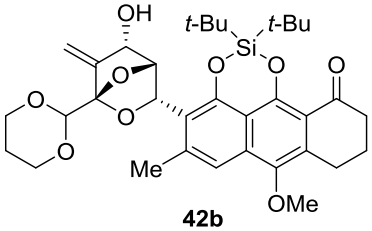
To a solution of the so obtained alcohol in CH_2Cl_2 (10 ml) at −78 °C were sequentially added a solution of imidazole (152 mg, 2.24 mmol, 2.0 equiv) in CH_2Cl_2 (10 ml) and TMSCl (210 µl, 1.68 mmol, 1.5 equiv). The resulting reaction mixture was stirred at this temperature for 5 min before it was quenched with $NaHCO_3$ (sat. aq., 5 ml). The resulting mixture was stirred at 23 °C for 15 min and then extracted with CH_2Cl_2 (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc: hexanes 1:6) to give the title compound (564 mg, 0.808 mmol, *dr ca*. 5:1, 72% yield) as a pale yellow foam. **40b** (plus **C4-*epi*-40b**): $R_f = 0.51$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{25} = -53.5$ ($c = 1.0$, CH_2Cl_2); FT-IR (film): $\nu_{max} = 2936$, 1682, 1559, 1445, 1371, 1236, 1147, 1084, 1060, 1015, 888 cm^{-1}; ^1H NMR (600 MHz, C_6D_6) $\delta = 7.54$ (s, 1 H, major), 7.51 (s, 1 H, minor), 6.95 (d, $J = 1.3$ Hz, 1 H, minor), 6.90 (d, $J = 1.7$ Hz, 1 H, major), 6.68 (s, 1 H, major), 6.67–6.66 (m, 1 H, minor), 5.53 (s, 1 H, minor), 5.31 (d, $J = 3.4$ Hz, 1 H, major), 5.02 (t, $J = 1.4$, 1 H, major), 5.02 (s, 1 H, minor), 4.48 (d, $J = 2.1$ Hz, 1 H, major), 4.08 (d, $J = 2.2$ Hz, 1 H, minor), 3.85 (t, $J = 2.3$ Hz, 1 H, minor), 3.74 (dd, $J = 3.5$, 2.3 Hz, 1 H, major), 3.71–3.62 (m, 4 H, major + minor), 3.49 (s, 6 H, major + minor), 3.26–3.08 (m, 4 H, major + minor), 2.75–2.63 (m, 4 H, major + minor), 2.57 (s, 3 H, major), 2.51 (s, 3 H, minor), 2.42–2.32 (m, 4 H, major + minor), 1.72–1.60 (m, 2 H, major + minor), 1.54 (p, $J = 6.3$ Hz, 4 H, major + minor), 1.28 (d, $J = 2.7$ Hz, 18 H, major + minor), 1.26 (s, 18 H, major + minor), 0.57–0.49 (m, 2 H, major + minor), 0.19 (s, 9 H, minor), 0.18 (s, 9 H, major) ppm; ^{13}C NMR (151 MHz, C_6D_6) $\delta = 194.8$ (major + minor), 192.1 (minor), 192.0 (major), 152.7 (minor), 152.3 (major), 150.4 (major + minor), 145.1 (major + minor), 144.6 (major), 143.3 (minor), 141.7 (major), 141.1 (minor), 132.3 (major), 132.2 (minor), 132.0 (major), 131.9 (minor), 131.4 (major), 131.1 (minor), 130.2 (minor), 119.83 (major), 119.78 (minor), 117.01 (major), 116.99 (minor), 115.43 (major), 115.41 (minor), 114.92 (major), 114.89 (minor), 102.8 (major + minor), 102.4 (major + minor), 101.5 (major + minor), 69.1 (major), 68.3 (minor), 66.9 (minor), 66.81 (major), 66.77 (minor), 66.7 (major), 66.4 (minor), 62.5 (major), 61.3 (minor), 60.5 (major), 53.1 (major), 51.4 (minor), 41.4 (major + minor), 26.62 (major), 26.59 (minor), 26.57 (major), 25.89 (major), 25.83 (minor), 24.4 (major + minor), 22.5 (major + minor), 21.7 (minor), 21.6 (major), 21.43 (major), 21.36 (minor), 21.24 (minor), 21.19 (major), 0.22 (minor), 0.21 (major) ppm; HRMS (ESI-TOF) calcd for $C_{37}H_{52}O_9Si_2Na^+$ $[M+Na]^+$ 719.3042, found 719.4052.

2,2-Di-*tert*-butyl-4-{(1*R*,3*S*,4*S*,5*S*)-1-(1,3-dioxan-2-yl)-6-methylene-5-[(trimethylsilyl)oxy]-2,7-dioxabicyclo[2.2.1]hept-3-yl}-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (41b): To a stirred solution of epoxy ketone **40b** (200 mg, 0.286 mmol, 1.0 equiv) in CH_2Cl_2 (8.6 ml) at −30 °C was added $BF_3{\cdot}OEt_2$ (0.1 M in CH_2Cl_2, 860 μL, 0.086 mmol, 0.3 equiv) dropwise. The reaction mixture was allowed to warm to 0 °C over 0.5 h, and was then quenched sequentially with Et_3N (40 μL) and $NaHCO_3$ (sat. aq., 20 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 10 ml), the combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:7) to give **41b** (98 mg, 0.140 mmol, 49% yield) as a yellow foam. R_f = 0.62 (silica gel, EtOAc:hexanes 1:2); $[\alpha]_D^{25}$ = +119.2 (*c* = 1.0, CH_2Cl_2); FT-IR (film): ν_{max} = 2935, 2861, 1681, 1609, 1557, 1472, 1366, 1251, 1109, 891, 827 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.23 (s, 1 H), 5.77 (d, *J* = 3.1 Hz, 1 H), 5.44 (d, *J* = 2.5 Hz, 1 H), 5.20 (s, 1 H), 5.09 (d, *J* = 2.1 Hz, 1 H), 5.00 (dd, *J* = 4.9, 3.2 Hz, 1 H), 4.73 (dt, 4.8, 2.3, 1 H), 4.34 (td, *J* = 11.4, 4.8 Hz, 2 H), 4.01–3.91 (m, 2 H), 3.79 (s, 3 H), 3.08 (ddd, *J* = 16.2, 7.3, 4.5 Hz, 1 H), 2.96 (ddd, *J* = 16.2, 8.2, 4.5 Hz, 1 H), 2.65 (s, 3 H), 2.62 (t, *J* = 6.5 Hz, 2 H), 2.37–2.25 (m, 1 H), 2.13–1.97 (m, 2 H), 1.47 (d, *J* = 13.6 Hz, 1 H), 1.17 (s, 9 H), 1.02 (s, 9 H), −0.33 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.9, 150.0, 148.9, 146.7, 144.2, 142.1, 130.6, 130.5, 119.8, 116.3, 115.8, 113.6, 107.7, 106.9, 98.7, 80.3, 80.1, 73.4, 67.7, 67.6, 61.0, 41.4, 26.6, 26.6, 25.9, 24.3, 24.2, 22.5, 21.7, 20.8, −0.3 ppm; HRMS (ESI-TOF) calcd for $C_{37}H_{52}O_9Si_2Na^+$ $[M+Na]^+$ 719.3042, found 719.3037.



41b

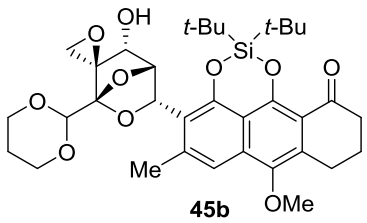
2,2-Di-*tert*-butyl-4-[(1*R*,3*S*,4*R*,5*S*)-1-(1,3-dioxan-2-yl)-5-hydroxy-6-methylene-2,7-dioxabicyclo[2.2.1]hept-3-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (42b): **41b** (98 mg, 0.140 mmol, 1.0 equiv) was dissolved in a solution of trifluoroacetic acid (0.1 M in THF:H_2O 5:1, 14 ml) at 23 °C. After stirring at this temperature for 5 h, the reaction was quenched with $NaHCO_3$ (sat. aq., 10 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 10 ml), the combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 1:10→1:4) to give the title compound (**42b**, 53.3 mg, 0.0854 mmol, 61% yield) as a yellow foam and recovered starting material **41b** (25.5 mg, 0.0364 mmol, 26% yield). **42b**: R_f = 0.55 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +114.2 (*c* = 1.0, CH_2Cl_2); FT-IR (film): ν_{max} = 3488,



42b

2934, 2860, 1680, 1608, 1555, 1372, 1101, 1017, 827, 661 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.35 (s, 1 H), 5.74 (d, *J* = 3.3 Hz, 1 H), 5.52 (d, *J* = 2.6 Hz, 1 H), 5.33–5.28 (m, 1 H), 5.25 (d, *J* = 2.2 Hz, 1 H), 5.19 (s, 1 H), 4.70–4.65 (*J* = 11.3, 4.3 Hz, 1 H), 4.34 (dt, *J* = 11.2, 4.8 Hz, 2 H), 3.97 (dt, *J* = 11.6, 8.5, 2.5 Hz, 2 H), 3.83 (s, 3 H), 3.08–2.98 (m, 2 H), 2.69 (s, 3 H), 2.63 (d, *J* = 6.6 Hz, 2 H), 2.37–2.25 (m, 1 H), 2.06 (dt, *J* = 12.7, 6.3 Hz, 2 H), 1.48 (d, *J* = 13.6 Hz, 1 H), 1.18 (s, 9 H), 1.07 (s, 9 H), 1.01 (d, *J* = 11.3 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.5, 150.2, 149.7, 147.0, 144.2, 138.8, 131.6, 130.9, 118.0, 117.7, 116.2, 113.8, 107.7, 107.4, 98.3, 79.6, 79.5, 75.2, 67.5, 61.0, 41.2, 26.3, 26.2, 25.7, 24.6, 24.1, 22.3, 21.3, 21.0 ppm; HRMS (ESI-TOF) calcd for $C_{34}H_{44}O_9SiNa^+$ $[M+Na]^+$ 647.2647, found 647.2651.

2,2-Di-*tert*-butyl-4-[(1*R*,2*S*,3*R*,4*R*,5*S*)-1-(1,3-dioxan-2-yl)-3-hydroxyspiro[6,7-dioxabicyclo-[2.2.1]heptane-2,2'-oxiran]-5-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]di-oxasilin-11(8*H*)-one (45b): To a stirred solution of the **42b** (53.3 mg, 0.0864 mmol, 1.0 equiv) in



45b

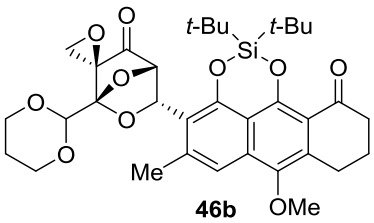
acetone (2.8 ml) at 23 °C was sequentially added OsO_4 (0.08 M aq., 216 μL, 0.0173 mmol, 0.2 equiv) and NMO (0.48 M aq., 720 μL, 0.346 mmol, 4.0 equiv). After stirring at this temperature for 12 h, the reaction was quenched with Na_2SO_3 (10% aq., 10 ml). The resulting mixture was stirred for another 30 min, then extracted with CH_2Cl_2 (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was filtered through a short pad of silica gel to afford triol **43b** (51.7 mg, 0.0786 mmol) as a colorless oil, which was used for the nest step without further purification.

To a stirred solution of the above triol (51.7 mg, 0.0786 mmol) in CH_2Cl_2 (2.4 ml) at 23 °C were sequentially added Et_3N (39.7 mg, 0.393 mmol, 5.0 equiv), 4-dimethylaminopyridine (4.8 mg, 0.0393 mmol, 0.5 equiv) and TsCl (75.1 mg, 0.393 mmol, 5.0 equiv). After stirring at this temperature for 12 h, the reaction was quenched with NH_4Cl (sat. aq., 5 ml) and the resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was filtered through a short pad of silica gel to afford the triol **44b** (59.3 mg, 0.0731 mmol) as a colorless oil, which was used for the nest step without further purification.

To a stirred solution of the above tosylate **44b** (59.3 mg, 0.0731 mmol) in MeOH (2.0 ml) at 0 °C was added K_2CO_3 (20.2 mg, 0.146 mmol, 2.0 equiv). The resulting reaction mixture was stirred at this

temperature for 1 h and was then directly subjected to flash column chromatography (silica gel, EtOAc:hexanes 1:1) to give the title compound (41.5 mg, 0.0648 mmol, 75% for the three steps) as a yellow foam. **45b**: R_f = 0.48 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +90.7 (*c* = 1.0, CH_2Cl_2); FT-IR (film): ν_{max} = 3479, 2935, 2861, 1678, 1608, 1555, 1471, 1371, 1104, 1055, 968, 827, 661 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.37 (s, 1 H), 5.76 (d, *J* = 3.1 Hz, 1 H), 5.40 (dd, *J* = 5.2, 3.1 Hz, 1 H), 5.06 (s, 1 H), 4.36–4.30 (m, 2 H), 4.22 (dd, *J* = 11.6, 5.0 Hz, 1 H), 3.95 (dt, *J* = 12.0, 2.5 Hz, 1 H), 3.85 (dt, *J* = 12.0, 2.5 Hz, 1 H), 3.84 (s, 3 H), 3.37 (d, *J* = 5.6 Hz, 1 H), 3.09 (d, *J* = 5.6 Hz, 1 H), 3.07–2.97 (m, 2 H), 2.75 (s, 3 H), 2.63 (t, *J* = 6.5 Hz, 2 H), 2.37–2.25 (m, 1 H), 2.06 (dt, *J* = 13.1, 6.5 Hz, 2 H), 1.42 (d, *J* = 13.6 Hz, 1 H), 1.24 (d, *J* = 11.8 Hz, 1 H), 1.18 (s, 9 H), 1.06 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.5, 150.1, 149.6, 144.2, 139.1, 131.8, 130.9, 117.6, 117.2, 116.3, 113.8, 106.8, 96.7, 79.6, 78.2, 76.4, 67.6, 67.4, 67.4, 61.1, 47.7, 41.2, 26.3, 26.3, 25.6, 24.1, 23.9, 22.3, 21.4, 20.9 ppm; HRMS (ESI-TOF) calcd for $C_{34}H_{44}O_{10}SiNa^+$ $[M+Na]^+$ 663.2596, found 663.2602.

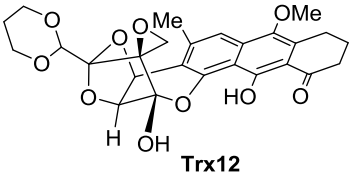
2,2-Di-*tert*-butyl-4-[(1*R*,2*S*,4*S*,5*S*)-1-(1,3-dioxan-2-yl)-3-oxospiro[6,7-dioxabicyclo[2.2.1]heptane-2,2'-oxiran]-5-yl]-7-methoxy-5-methyl-9,10-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-11(8*H*)-one (46b): To a stirred solution of the epoxy alcohol **45b** (20.0 mg, 31.3 µmol, 1.0 equiv) in



46b

CH_2Cl_2 at 0 °C were sequentially added NMO (12.7 mg, 93.9 µmol, 3.0 equiv) and TPAP (2.2 mg, 6.3 µmol, 0.2 equiv). The resulting reaction mixture was stirred at this temperature for 1 h, and then directly subjected to flash column chromatography (silica gel, EtOAc:hexanes 1:4) to give the title compound (**46b**, 18.2 mg, 0.0285 mmol, 91% yield) as a yellow foam. **46b**: R_f = 0.75 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +222.8 (*c* = 1.0, CH_2Cl_2); FT-IR (film): ν_{max} = 2936, 2861, 1788, 1682, 1609, 1372, 1103, 889 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.30 (s, 1 H), 5.72 (d, *J* = 3.8 Hz, 1 H), 5.42 (d, *J* = 3.8 Hz, 1 H), 5.19 (s, 1 H), 4.37 (dd, *J* = 11.3, 4.8 Hz, 1 H), 4.25 (dd, *J* = 11.3, 4.9 Hz, 1 H), 4.03–3.96 (m, 1 H), 3.92–3.86 (m, 1 H), 3.82 (s, 3 H), 3.48 (d, *J* = 6.5 Hz, 1 H), 3.15 (d, *J* = 6.5 Hz, 1 H), 3.08–2.96 (m, 2 H), 2.66–2.61 (m, 2 H), 2.59 (s, 3 H), 2.39–2.28 (m, 1 H), 2.09–2.03 (m, 2 H), 1.47 (d, *J* = 13.8 Hz, 1 H), 1.18 (s, 9 H), 1.06 (s, 9 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 202.3, 196.5, 150.4, 149.7, 144.2, 139.0, 132.0, 131.2, 117.4, 116.2, 115.8, 113.7, 106.2, 96.2, 82.3, 78.3, 67.5, 67.5, 61.8, 61.1, 50.3, 41.2, 26.4, 26.2, 25.5, 24.1, 23.5, 22.3, 21.4, 21.0 ppm; HRMS (ESI-TOF) calcd for $C_{34}H_{42}O_{10}SiNa^+$ $[M+Na]^+$ 661.2439, found 661.2440.

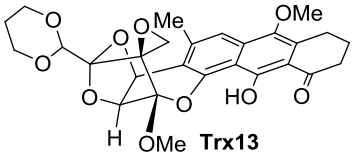
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-2-(1,3-Dioxan-2-yl)-12,13a-dihydroxy-7-methoxy-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx12): To a stirred solution of epoxy ketone **46b** (15.2 mg, 0.0238 mmol) in



Trx12

CH_3CN (0.6 ml) at 23 °C was added $Et_3N{\cdot}3HF$ (11.5 mg, 0.0714 mmol, 3.0 equiv). After stirring at this temperature for 15 min, the reaction was quenched with $NaHCO_3$ (5% aq., 5 ml) and diluted with EtOAc (10 ml). The resulting mixture was washed sequentially with H_2O (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 2:1) to give the title compound (10.3 mg, 0.0207 mmol, 87% yield) as an orange foam. **Trx12**: R_f = 0.24 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +414.0 (*c* = 0.15, CH_2Cl_2); FT-IR (film): ν_{max} = 3369, 2955, 2855, 1620, 1388, 1236, 1096, 977, 914, 729 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.93 (s, 1 H), 7.43 (s, 1 H), 5.30 (d, *J* = 4.0 Hz, 1 H), 5.06 (s, 1 H), 4.84 (d, *J* = 4.0 Hz, 1 H), 4.40 (s, 1 H), 4.29 (dd, *J* = 11.5, 4.8 Hz, 1 H), 4.15 (dd, *J* = 12.1, 4.1 Hz, 1 H), 3.90 (dt, *J* = 12.2, 2.4 Hz, 1 H), 3.79 (dt, *J* = 12.0, 2.1 Hz, 1 H), 3.77 (s, 3 H), 3.21 (d, *J* = 5.4 Hz, 1 H), 3.06 (d, *J* = 5.4 Hz, 1 H), 3.03 (dd, *J* = 5.6, 1.6 Hz, 2 H), 2.72 (dt, *J* = 6.2, 3.0 Hz, 2 H), 2.60 (s, 3 H), 2.27–2.16 (m, 1 H), 2.12–2.06 (m, 2 H), 1.39 (d, *J* = 13.7 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.4 162.9, 151.2, 142.4, 141.8, 135.3, 130.3, 115.8, 113.4, 113.2, 111.0, 102.4, 98.3, 96.4, 73.5, 70.0, 69.3, 67.5, 67.3, 60.9, 50.6, 38.8, 25.5, 23.6, 22.1, 20.7 ppm; HRMS (ESI-TOF) calcd for $C_{26}H_{26}O_{10}Na^+$ $[M+Na]^+$ 521.1418, found 521.1421.

(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxan-2-yl)-12-hydroxy-7,13a-dimethoxy-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx13): To a stirred mixture of **Trx12** (2.3 mg, 4.6 µmol, 1.0 equiv) and MeI (250 µL)

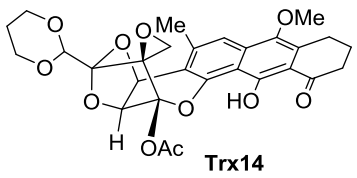


Trx13

were added Ag_2O (2.1 mg, 9.2 µmol, 2.0 equiv.) and $CaSO_4$ (3.8 mg, 28 µmol, 6.0 equiv) at 23 °C. The mixture was stirred at this temperature for 12 h. The resulting mixture was evaporated under reduced pressure and the so obtained residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:4) to give the title compound (1.6 mg, 3.1 µmol, 68% yield) as an orange foam. **Trx13**: R_f = 0.38 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +268.8 (*c* = 0.08, CH_2Cl_2); FT-IR (film): ν_{max} = 2920, 1620, 1570, 1445, 1389, 1236, 1180, 1094, 1074, 1014, 918 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.80 (s, 1 H), 7.43 (s, 1 H), 5.26 (d, *J* = 4.1 Hz, 1 H), 5.08 (s, 1 H), 4.84 (d, *J* = 4.1 Hz, 1 H), 4.29 (dd, *J* = 4.8, 11.4 Hz, 1 H), 4.12 (dd, *J* = 4.8, 11.4 Hz, 1 H), 3.89 (dt, *J* = 3.0, 12.6 Hz, 1 H),

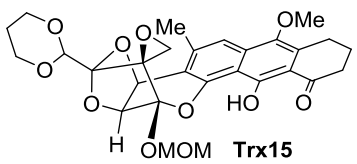
3.80–3.76 (m, 4H), 3.74 (s, 3H), 3.08–3.02 (m, 2H), 2.96 (d, J = 5. Hz, 1H), 2.87 (d, J = 5.8 Hz, 1H), 2.73 (t, J = 6.6 Hz, 2H), 2.61 (s, 3H), 2.26–2.17 (m, J = 1H), 2.11–2.07 (m, 2H), 1.40-1.35 (m, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.4, 163.01, 151.5, 142.4, 142.0, 135.2, 130.2, 115.6, 113.2, 113.2, 111.0, 103.1, 102.0, 96.3, 71.5, 69.2, 69.0, 67.5, 67.4, 60.9, 52.8, 38.8, 25.6, 23.6, 22.1, 20.7 ppm; HRMS (ESI-TOF) calcd for $C_{27}H_{28}O_{10}Na^+$ $[M+Na]^+$ 535.1575, found 521.1581.

(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl acetate (Trx14): To a stirred solution of **Trx12** (2.5 mg, 5.0 µmol, 1.0 equiv) in CH_2Cl_2 at 0 °C were sequentially added Et_3N (2.5 mg, 3.4 µL, 25 µmol, 5.0 equiv.), Ac_2O (1.5 mg, 1,4 µL, 0.015 mmol, 3.0 equiv) and 4-dimethylaminopyridine (0.61 mg, 5.0 µmol, 1.0 equiv.). The mixture was stirred at this temperature for 1 h before it was quenched with H_2O (5 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give the title compound (2.3 mg, 4.3 µmol, 85% yield) as an orange foam. **Trx14**: R_f = 0.24 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +205.5 (c = 0.055, CH_2Cl_2); FT-IR (film): ν_{max} = 2923, 2850, 1767, 1621, 1389, 1371, 1097, 1010, 876 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 14.65 (s, 1H), 7.44 (s, 1H), 5.62 (d, J = 4.1 Hz, 1H), 5.30 (d, J = 4.2 Hz, 1H), 5.08 (s, 1H), 4.30 (dd, J = 11.5, 4.9 Hz, 1H), 4.15 (dd, J = 11.4, 4.9 Hz, 1H), 3.90 (td, J = 12.2, 2.4 Hz, 1H), 3.79 (td, J = 12.3, 2.4 Hz, 1H), 3.76 (s, 3H), 3.06–3.01 (m, 2H), 3.03–3.01 (d, J = 5.9, 1 H, overlap), 3.00–2.97 (d, J = 5.9, 1H), 2.70 (d, J = 6.6 Hz, 2H), 2.60 (s, 3H), 2.26 (s, 3H), 2.25–2.17 (m, 1H), 2.12–2.03 (m, 2H), 1.39 (d, J = 13.7 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.3, 169.0, 163.0, 151.0, 142.3, 141.7, 135.3, 130.3, 116.0, 113.0, 112.7, 111.1, 102.6, 100.8, 96.3, 71.2, 69.5, 69.0, 67.5, 67.4, 60.9, 48.0, 38.8, 25.5, 23.6, 22.1, 21.8, 20.6 ppm; HRMS (ESI-TOF) calcd for $C_{28}H_{28}O_{11}Na^+$ $[M+Na]^+$ 563.1524, found 563.1525.



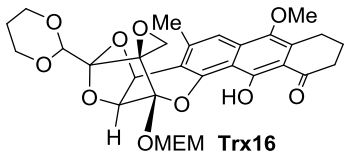
Trx14

(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxan-2-yl)-12-hydroxy-7-methoxy-13a-(methoxymethoxy)-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx15): To a stirred solution of **Trx12** (3.0 mg, 6.02 µmol) in CH_2Cl_2 at 23 °C were added *N*,*N*-diisopropylethylamine (3.9 mg, 5.3 µL, 0.030 mmol, 5.0 equiv.) and MOMCl (1.4 mg, 1.3 µL, 18 µmol, 3.0 equiv). The mixture was stirred at this temperature for 1.5 h before it



was quenched by H_2O (5 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give the title compound (1.6 mg, 2.9 µmol, 49% yield) as an orange foam. **Trx15**: R_f = 0.35 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +267.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2955, 2930, 1620, 1571, 1388, 1235, 1095, 1003, 983, 927, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.76 (s, 1 H), 7.43 (s, 1 H), 5.54 (d, *J* = 7.0 Hz, 1 H), 5.24 (d, *J* = 4.2 Hz, 1 H), 5.17 (d, *J* = 4.1 Hz, 1 H), 5.10 (s, 1 H), 4.91 (d, *J* = 7.0 Hz, 1 H), 4.31 (dd, *J* = 11.5, 4.9 Hz, 1 H), 4.13 (dd, *J* = 11.4, 4.9 Hz, 1 H), 3.92 (td, *J* = 12.2, 2.4 Hz, 1 H), 3.79 (dt, *J* = 12.0, 2.1 Hz, 1 H), 3.77 (s, 3 H), 3.56 (s, 3 H), 3.09–2.98 (m, 2 H), 2.97 (d, *J* = 5.8 Hz, 1 H), 2.85 (d, *J* = 5.8 Hz, 1 H), 2.74–2.68 (m, 2 H), 2.61 (s, 3 H), 2.26–2.14 (m, 1 H), 2.14–2.01 (m, 2 H), 1.38 (d, *J* = 13.7 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.4, 163.0, 151.5, 142.4, 142.0, 135.2, 130.3, 115.7, 113.3, 113.2, 111.0, 102.9, 101.5, 96.2, 92.6, 73.0, 69.3, 68.7, 67.5, 67.4, 60.9, 56.6, 48.0, 38.8, 25.6, 23.6, 22.1, 20.7 ppm; HRMS (ESI-TOF) calcd for $C_{28}H_{30}O_{11}Na^+$ $[M+Na]^+$ 565.1680, found 563.1686.

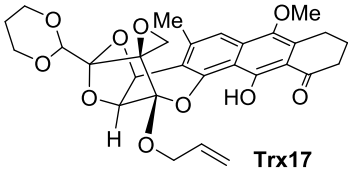
(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxan-2-yl)-12-hydroxy-7-methoxy-13a-[(2-methoxyethoxy)methoxy]-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx16): To a stirred solution of **Trx12** (2.7 mg, 5.4 mmol, 1.0 equiv)



in CH_2Cl_2 at 23 °C were added *N*,*N*-diisopropylethylamine (3.5 mg, 4.7 µL, 27 µmol, 5.0 equiv.) and MEMCl (3.4 mg, 3.1 µL, 27 µmol, 5.0 equiv.) The mixture was stirred at this temperature for 2 h before it was quenched by H_2O (5 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give the title compound (2.0 mg, 3.4 µmol, 65% yield) as an orange foam. **Trx16**: R_f = 0.25 (silica gel, EtOAc:hexanes 1:1); $[\alpha]_D^{25}$ = +170.0 (*c* = 0.05, CH_2Cl_2); FT-IR (film): ν_{max} = 2924, 1619, 1388, 1235, 1179, 1094, 1002, 914, 730 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.74 (s, 1 H), 7.42 (s, 1 H), 5.63 (d, *J* = 7.2 Hz, 1 H), 5.27 (d, *J* = 4.1 Hz, 1 H), 5.23 (d, *J* = 4.2 Hz, 1 H), 5.09 (s, 1 H), 5.03 (d, *J* = 7.2 Hz, 1 H), 4.31 (dd, *J* = 11.6, 4.9 Hz, 1 H), 4.16–4.08 (m, 2 H), 3.91 (td, *J* = 12.2, 2.4 Hz, 1 H), 3.83–3.73 (m, 2 H), 3.73 (s, 3 H), 3.56 (t, *J* = 4.6 Hz, 2 H), 3.36 (s, 3 H), 3.08–2.99 (m, 2 H), 2.97 (d, *J* = 5.8 Hz, 1 H), 2.84 (d, *J* = 5.8 Hz, 1 H), 2.75–2.67 (m, 2 H), 2.61 (s, 3 H),

2.27–2.16 (m, 1 H), 2.12–2.04 (m, 2 H), 1.38 (d, J = 13.6 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.4, 163.0, 151.5, 142.4, 142.0, 135.2, 130.2, 115.7, 113.3, 113.2, 111.0, 102.9, 101.4, 96.2, 91.4, 72.9, 71.5, 69.3, 68.7, 68.0, 67.5, 67.4, 60.9, 59.0, 48.0, 38.8, 25.6, 23.6, 22.1, 20.7 ppm; HRMS (ESI-TOF) calcd for $C_{30}H_{34}O_{12}Na^+$ $[M+Na]^+$ 609.1942, found 609.1942.

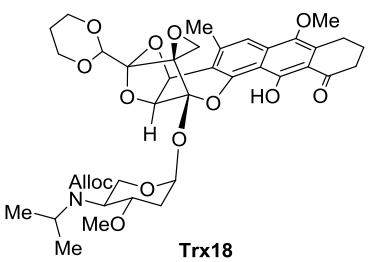
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-13a-(Allyloxy)-2-(1,3-dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-one (Trx17): To a stirring mixture of **Trx12** (2.8 mg, 5.6 μmol) and allyl bromide (0.1 ml)



Trx17

were sequentially added $CaSO_4$ (5.0 mg, 37 μmol, 6.6 equiv) and Ag_2O (5.0 mg, 22 μmol, 3.8 equiv) at 23 °C. The resulting mixture was stirred at this temperature for 5 h before it was subjected to a flash column chromatography (EtOAc: hexanes 1:1) to afford **Trx17** (2.0 mg, 3.7 μmol, 66% yield) as a yellow foam. **Trx17**: R_f = 0.34 (silica gel, EtOAc: hexanes 1:2); $[\alpha]_D^{25}$ = +79.5 (c = 0.258, $CHCl_3$); FT-IR (film): ν_{max} = 2957, 2928, 2871, 1728, 1621, 1572, 1462, 1285, 1125 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 14.78 (s, 1 H), 7.42 (d, J = 0.9 Hz, 1 H), 6.09 (ddt, J = 17.2, 10.3, 5.7 Hz, 1 H), 5.39 (dq, J = 17.2, 1.5 Hz, 2 H), 5.24 (d, J = 4.1 Hz, 1 H), 5.21 (dq, J = 10.3, 1.4 Hz, 1 H), 5.09 (s, 1 H), 4.83 (d, J = 4.1 Hz, 1 H), 4.53 (qdt, J = 12.6, 5.6, 1.4 Hz, 2 H), 4.29 (ddt, J = 11.5, 4.9, 1.6 Hz, 1 H), 4.12 (ddt, J = 11.6, 5.1, 1.6 Hz, 1 H), 3.90 (td, J = 12.0, 2.6 Hz, 1 H), 3.77 (s, 3 H), 3.09–2.97 (m, 2 H), 2.95 (d, J = 5.8 Hz, 1 H), 2.86 (d, J = 5.8 Hz, 1 H), 2.72 (dd, J = 7.4, 5.5 Hz, 2 H), 2.60 (d, J = 1.0 Hz, 3 H), 2.26–2.16 (m, 1 H), 2.09 (tdd, J = 8.5, 6.9, 4.1 Hz, 2 H), 1.37 (d, J = 13.6 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.6, 163.1, 151.5, 142.6, 142.1, 135.4, 134.7, 130.4, 117.4, 115.8, 113.5, 113.4, 111.2, 103.2, 102.1, 96.4, 72.8, 69.3, 67.6, 67.5, 66.8, 61.0, 48.4, 39.0, 25.7, 23.7, 22.3, 20.8 ppm. HRMS (ESI) calcd for $C_{29}H_{30}O_{10}Na^+$ $[M+Na]^+$ 561.1731, found 561.1731.

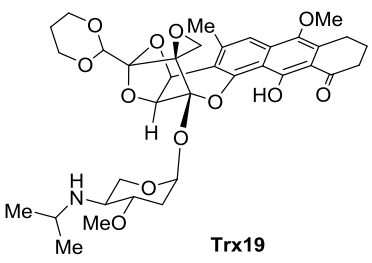
(1*S*,13a*S*)-2-(1,3-Dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 4-{[(allyloxy)carbonyl](isopropyl)amino}-2,4-dideoxy-3-*O*-methyl-*α*-L-*threo*-pentopyranoside (Trx18): To a stirred solution of **Trx12** (5.0 mg, 0.01 mmol, 1.0 equiv), carbohydrate donor **49** (44.1 mg, 0.100 mmol, 10 equiv) and 4 Å MS (250 mg) in CH_2Cl_2 (1.0 ml) at 0 °C was added $Ph_3PAuOTf$ (0.05 M in CH_2Cl_2, 2.0 μmol, 40 μL, 0.2 equiv) dropwise over 5 min. The reaction mixture was stirred at this temperature for 15 min, and then



Trx18

quenched with Et_3N (10 μL). The resulting mixture was filtered through Celite® and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:4) to give the title compound (6.1 mg, 8.3 mmol, 83% yield) as an orange foam. **Trx18**: R_f = 0.34 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +163.3 (*c* = 0.15, CH_2Cl_2); FT-IR (film): ν_{max} = 2962, 2930, 1693, 1620, 1444, 1389, 1370, 1094, 987, 925, 734 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.73 (s, 1 H), 7.42 (s, 1 H), 6.22–5.88 (m, 1 H), 5.85–5.74 (m, 1 H), 5.47–5.18 (m, 4 H), 5.19–5.01 (m, 1 H), 4.77–4.55 (m, 2 H), 4.56–4.37 (m, 2 H), 4.31 (dd, *J* = 11.7, 4.8 Hz, 1 H), 4.18–4.12 (m, 1 H), 3.97–3.83 (m, 1 H), 3.84–3.78 (m, 1 H), 3.77 (s, 3H), 3.62–3.47 (m, 1 H), 3.38 (s, 3 H), 3.13–2.99 (m, 2 H), 2.93 (d, *J* = 6.0 Hz, 1 H), 2.83 (d, *J* = 6.0 Hz, 1 H), 2.72 (dd, *J* = 7.3, 5.6 Hz, 2 H), 2.60 (s, 3 H), 2.58–2.49 (m, 1 H), 2.28–2.16 (m, 1 H), 2.09 (d, *J* = 6.7 Hz, 2 H), 1.39 (d, *J* = 13.6 Hz, 1 H), 1.32–1.27 (m, 2 H), 1.32–1.12 (m, 6 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.6, 163.2, 152.0, 142.5, 142.2, 135.4, 133.6, 131.6, 130.4, 115.8, 113.4, 113.3, 111.2, 103.2, 101.8, 96.5, 96.4, 94.6, 72.4, 69.6, 68.6, 67.64, 67.56, 65.9, 62.1, 61.0, 47.8, 39.0, 25.7, 23.7, 22.3, 21.2, 20.9, 20.4 ppm; HRMS (ESI-TOF) calcd for $C_{39}H_{47}NO_{14}Na^+$ $[M+Na]^+$ 776.2889, found 776.2885.

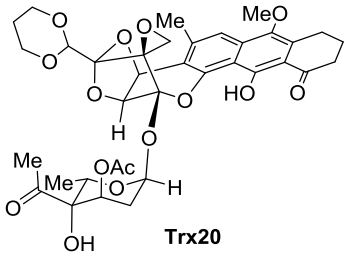
(1*S*,2*R*)-2-(1,3-dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 2,4-dideoxy-4-(isopropylamino)-3-*O*-methyl-*α*-L-*threo*-pentopyranoside (Trx19): To a stirred solution of **Trx18** (6.1 mg, 8.3 μmol) in CH_2Cl_2 (0.5 ml) was added $Pd(PPh_3)_2Cl_2$ (2.9 mg, 4.1 μmol, 0.5 equiv), followed by acetic acid (9.9 mg, 165 μmol, 20 equiv) and *n*-Bu_3SnH (24.0 mg, 82.5 μmol, 10 equiv) at 23 °C. After stirring at this temperature for 8 h, the reaction was quenched with NH_4Cl (sat. aq., 5 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml), the combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, CH_2Cl_2:MeOH 10:1) to give the title compound (4.8 mg, 7.2 μmol, 87% yield) as an orange foam. **Trx19**: R_f = 0.53 (silica gel, CH_2Cl_2:MeOH 10:1); $[\alpha]_D^{25}$ = +208.0 (*c* = 0.15, CH_2Cl_2); FT-IR (film): ν_{max} = 2960, 2855, 1620, 1389, 1108, 1095, 1003, 730 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.72 (s, 1 H), 7.41 (s, 1 H), 5.78 (br s, 1 H), 5.28 (br s, 1 H), 5.23 (d, *J* = 3.9 Hz, 1 H), 5.10 (s, 1 H), 4.27 (br s, 1 H), 4.11 (dd, *J* = 11.1, 5.5 Hz, 1 H), 3.93 (t, *J* = 11.1 Hz, 1 H), 3.93 (br s, 1 H), 3.82–3.74 (m, 1 H), 3.76 (s, 3 H), 3.45 (s, 3 H), 3.08–2.98 (m, 2 H), 2.90 (br s, 1 H), 2.90 (d, *J* = 6.0 Hz, 1 H), 2.78 (d, *J* = 6.0 Hz, 1 H), 2.72 (dd, *J* = 7.4, 5.6 Hz, 2 H), 2.60 (s, 3 H), 2.48 (br s, 1 H), 2.26–2.14



Trx19

(m, 1 H), 2.12–2.05 (m, 2 H), 1.71–1.66 (m, 1 H), 1.38 (d, J = 13.6 Hz, 1 H), 1.19 (br s, 6 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.4, 163.0, 142.4, 142.2, 135.2, 130.2, 115.6, 113.4, 113.2, 111.0, 103.0, 101.7, 96.2, 72.3, 69.3, 68.3, 67.5, 67.3, 60.9, 56.3, 56.2, 47.6, 38.8, 25.6, 23.6, 22.1, 20.7 ppm; HRMS (ESI-TOF) calcd for $C_{35}H_{43}NO_{12}Na^+$ $[M+Na]^+$ 692.2677, found 692.2677.

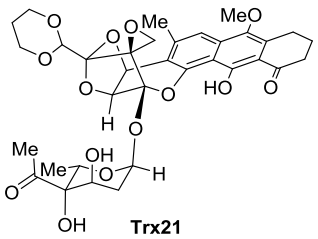
(1*S*,2*R*,13a*S*)-2-(1,3-dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 4-*C*-acetyl-3-*O*-acetyl-2,6-dideoxy-*α*-L-*lyxo*-hexopyranoside (Trx20): To a stirred solution of **Trx12**



Trx20

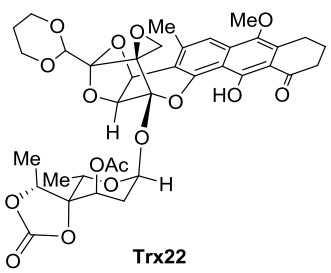
(5.0 mg, 10 μmol, 1.0 equiv), carbohydrate donor **51** (40.0 mg, 10 μmol, 10 equiv) and 4 Å MS (250 mg) in CH_2Cl_2 (2.0 ml) at 0 °C was added $Ph_3PAuOTf$ (0.05 M in CH_2Cl_2, 2.0 μmol, 40 μL, 0.2 equiv) dropwise over 5 min. The reaction mixture was stirred at this temperature for 15 min, and then quenched with Et_3N (10 μL). The resulting mixture was filtered through Celite® and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc 1:2) to give the title compound (6.4 mg, 9.0 μmol, 90% yield) as an orange foam. **Trx20**: R_f = 0.24 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +77.5 (c = 0.2, CH_2Cl_2); FT-IR (film): ν_{max} = 3465, 2937, 2852, 1737, 1620, 1388, 1236, 1095, 1012, 912, 733 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 14.65 (s, 1 H), 7.41 (s, 1 H), 5.85 (t, J = 3.1 Hz, 1 H), 5.29 (d, J = 4.1 Hz, 1 H), 5.24 (d, J = 4.1 Hz, 1 H), 5.05 (s, 1 H), 4.99 (q, J = 6.4 Hz, 1 H), 4.74 (t, J = 3.5 Hz, 1 H), 4.34 (dd, J = 11.5, 4.8 Hz, 1 H), 4.13 (dd, J = 11.2, 5.0 Hz, 1 H), 3.95 (td, J = 12.2, 2.3 Hz, 1 H), 3.88 (s, 1 H), 3.79 (td, J = 12.3, 2.3 Hz, 1 H), 3.76 (s, 3 H), 3.08–2.96 (m, 2 H), 2.91 (d, J = 6.0 Hz, 1 H), 2.77 (d, J = 6.0 Hz, 1 H), 2.71 (t, J = 6.4 Hz, 2 H), 2.61 (s, 3 H), 2.36 (s, 3 H), 2.35–2.30 (m, 2 H), 2.29–2.18 (m, 1 H), 2.23 (s, 3 H), 2.11–2.05 (m, 2 H), 1.40 (d, J = 13.5 Hz, 1 H), 1.06 (d, J = 6.4 Hz, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 208.8, 204.3, 170.3, 163.0, 151.8, 142.3, 141.9, 135.2, 130.3, 115.6, 113.1, 113.0, 111.0, 103.1, 101.4, 96.2, 92.2, 78.2, 72.4, 70.7, 69.4, 68.4, 67.4, 67.4, 64.4, 60.9, 47.4, 38.8, 28.8, 27.1, 25.6, 23.6, 22.1, 21.3, 20.6, 14.6 ppm; HRMS (ESI-TOF) calcd for $C_{36}H_{40}O_{15}Na^+$ $[M+Na]^+$ 735.2259, found 735.2257.

(1*S*,2*R*,13a*S*)-2-(1,3-dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 4-*C*-acetyl-2,6-dideoxy-*α*-L-*lyxo*-hexopyranoside (Trx21): To a stirred solution of **Trx20** (1.0 mg, 1.4 μmol, 1.0 equiv) in MeOH (0.15 ml) at 0 °C was added K_2CO_3 (1.4 mg, 9.8 μmol, 7.0 equiv). After stirring at this temperature for 30 min, the reaction mixture was diluted with EtOAc (10 ml) and quenched with NH_4Cl (2.0 mg). The mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, EtOA:hexane 2:1) to give the title compound (0.85 mg, 1.3 μmol, 93% yield) as an orange foam. **Trx21**: R_f = 0.24 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +132.9 (*c* = 0.85, CH_2Cl_2); FT-IR (film): ν_{max} = 3509, 2926, 2854, 1698, 1620, 1570, 1388, 1235, 1095, 996, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.68 (s, 1 H), 7.44 (s, 1 H), 5.88 (d, *J* = 2.7 Hz, 1 H), 5.33 (d, *J* = 4.1 Hz, 1 H), 5.28 (d, *J* = 4.1 Hz, 1 H), 5.11 (s, 1 H), 4.99 (q, *J* = 6.4 Hz, 1 H), 4.34 (dd, *J* = 11.5, 4.8 Hz, 1 H), 4.28 (d, *J* = 9.6 Hz, 1 H), 4.16–4.09 (m, 2 H), 3.96 (td, *J* = 12.2, 2.4 Hz, 1 H), 3.81 (td, *J* = 12.2, 2.3 Hz, 1 H), 3.77 (s, 3 H), 3.70 (dt, *J* = 9.8, 2.8 Hz, 1 H), 3.10–2.98 (m, 3 H), 2.92 (d, *J* = 5.8 Hz, 1 H), 2.73 (t, *J* = 6.4 Hz, 2 H), 2.62 (s, 3 H), 2.50 (s, 3 H), 2.43 (dt, *J* = 14.4, 3.4 Hz, 1 H), 2.31–2.17 (m, 1 H), 2.16–2.05 (m, 3 H), 1.41 (d, *J* = 13.6 Hz, 1 H), 1.08 (d, *J* = 6.4 Hz, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 210.5, 204.5, 162.9, 151.6, 142.39, 141.8, 135.2, 130.5, 115.9, 113.1, 112.9, 111.1, 103.2, 101.3, 96.1, 94.7, 79.6, 71.8, 70.2, 69.6, 68.4, 67.4, 63.7, 60.9, 48.1, 38.8, 31.5, 27.9, 25.6, 23.6, 22.1, 20.6, 14.7 ppm; HRMS (ESI-TOF) calcd for $C_{34}H_{38}O_{14}Na^+$ $[M+Na]^+$ 693.2154, found 693.2157.



Trx21

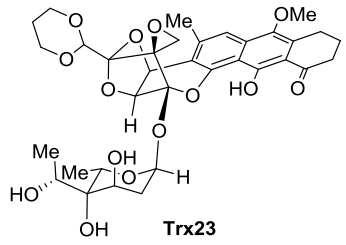
(4*R*,5*S*,6*R*,10*S*)-8-{[(1*S*,2*R*)-2-(1,3-Dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl]oxy}-4,6-dimethyl-2-oxo-1,3,7-trioxaspiro[4.5]dec-10-yl acetate (Trx22): To a stirred solution of **Trx12** (1.0 mg, 2.0 μmol, 1.0 equiv), carbohydrate donor **52** (10.0 mg, 10 μmol, 10 equiv) and 4 Å MS (50 mg) in CH_2Cl_2 (0.2 ml) at 0 °C was added $Ph_3PAuOTf$ (0.05 M in CH_2Cl_2, 0.4 μmol, 8 μL, 0.2 equiv) dropwise over 5 min. The reaction mixture was stirred at this temperature for 15 min, and then quenched with Et_3N (10 μL). The resulting mixture was filtered through Celite® and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, EtOAc) to give the title compound



Trx22

(1.3 mg, 1.8 µmol, 90% yield) as an orange foam. **Trx22**: R_f = 0.24 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +97.5 (*c* = 0.2, CH_2Cl_2); FT-IR (film): ν_{max} = 3629, 2951, 2854, 1813, 1748, 1619, 1388, 1235, 1095, 1048, 1014, 996, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.68 (s, 1 H), 7.43 (s, 1 H), 5.79 (dd, *J* = 3.9, 2.2 Hz, 1 H), 5.23 (d, *J* = 4.1 Hz, 1 H), 5.20 (d, *J* = 4.1 Hz, 1 H), 5.03–4.98 (m, 1 H), 5.01 (s, 1 H), 4.66–4.56 (m, 2 H), 4.33 (dd, *J* = 11.5, 4.7 Hz, 1 H), 4.12 (dd, *J* = 12.1, 4.1 Hz, 1 H), 3.93 (td, *J* = 12.2, 2.3 Hz, 1 H), 3.82–3.72 (m, 1 H), 3.76 (s, 3 H), 3.10–2.96 (m, 2 H), 2.90 (d, *J* = 6.0 Hz, 1 H), 2.76 (d, *J* = 6.0 Hz, 1 H), 2.72 (t, *J* = 6.4 Hz, 2 H), 2.60 (s, 3 H), 2.35 (ddd, *J* = 14.9, 3.9, 2.3 Hz, 1 H), 2.26 (t, *J* = 3.9 Hz, 1 H), 2.25–2.18 (m, 1 H), 2.23 (s, 3 H), 2.10–2.06 (m, 2 H), 1.60 (d, *J* = 6.8 Hz, 3 H), 1.40 (d, *J* = 12.3 Hz, 1 H), 1.34 (d, *J* = 6.4 Hz, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.4, 170.0, 162.9, 153.3, 151.6, 142.4, 141.8, 135.2, 130.4, 115.8, 113.1, 112.9, 111.1, 103.1, 101.4, 96.2, 91.0, 80.9, 80.6, 72.4, 70.6, 69.4, 68.3, 67.4, 67.4, 64.1, 60.9, 47.5, 38.8, 30.2, 25.5, 23.6, 22.1, 21.0, 20.6, 15.2, 14.9 ppm; HRMS (ESI-TOF) calcd for $C_{37}H_{40}O_{16}Na^+$ $[M+Na]^+$ 763.2209, found 763.2194.

(1*S*,2*R*,13a*S*)-2-(1,3-dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-13a-yl 2,6-dideoxy-4-*C*-[(1*R*)-1-hydroxyethyl]-*α*-L-*lyxo*-hexopyranoside (Trx23): To a stirred solution of **Trx22**

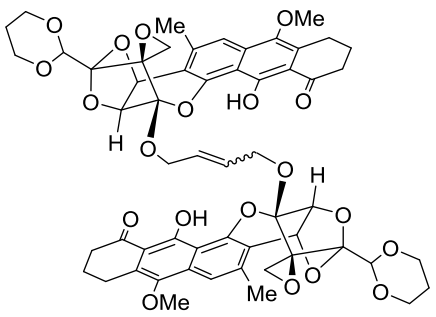


Trx23

(1.0 mg, 1.4 µmol, 1.0 equiv) in THF (0.15 ml) and ethylene glycol (15 µL) at 23 °C was added NaH (1.0 mg, 42 µmol, 30 equiv). After stirring at this temperature for 5 h, the reaction mixture was diluted with EtOAc (10 ml). The resulting mixture was washed sequentially with water (5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative HPLC (Atlantis Prep T3 OBD column, 5 µm, 19 × 150 mm, UV detection at 270 nm, gradient elution with 50→70% (1→2 min), then 70→100% (2→45 min) MeCN in H_2O, flow rate: 5 mL/min, 31.5→32.8 min) to give the title compound (0.8 mg, 1.19 µmol, 88% yield) as an orange foam. **Trx23:** R_f = 0.50 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +135.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 3488, 2938, 2857, 1621, 1389, 1096, 1049, 997 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 14.69 (s, 1 H), 7.44 (s, 1 H), 5.76 (d, *J* = 3.2 Hz, 1 H), 5.29 (d, *J* = 4.1 Hz, 1 H), 5.27 (d, *J* = 4.1 Hz, 1 H), 5.09 (s, 1 H), 5.08 (d, *J* = 6.6 Hz, 1 H), 4.31 (dd, *J* = 11.5, 4.9 Hz, 1 H), 4.20–4.16 (m, 1 H), 4.13–4.08 (m, 1 H), 4.01–3.94 (m, 2 H), 3.82–3.73 (m, 2 H), 3.77 (s, 3 H), 3.42 (d, *J* = 11.4 Hz, 1 H), 3.09–2.98 (m, 3 H), 2.87 (d, *J* = 5.8 Hz, 1 H), 2.76–2.69 (m, 2 H), 2.61 (s, 3 H), 2.31–2.17 (m, 2 H), 2.13–2.05 (m, 3 H), 1.83 (s, 1 H), 1.40 (d, *J* = 14.8 Hz, 1 H), 1.37 (d, *J* = 6.5 Hz, 3 H), 1.27 (d, *J* = 6.5 Hz, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 204.5, 162.9,

151.6, 142.4, 141.9, 135.2, 130.4, 115.9, 113.1, 113.0, 111.1, 103.1, 101.4, 96.0, 94.0, 71.6, 71.6, 71.0, 69.5, 68.6, 68.3, 67.5, 67.3, 65.1, 60.9, 48.1, 38.8, 32.4, 25.6, 23.6, 22.1, 20.6, 17.5, 13.4 ppm; HRMS (ESI-TOF) calcd for $C_{34}H_{40}O_{14}Na^+$ $[M+Na]^+$ 695.2310, found 695.2310.

(1*S*,2*S*,3a*S*,4*R*,13a*R*,1‴*S*,2‴*S*,3a‴*S*,4‴*R*,13a‴*R*)-13a,13a′-[(2*Z*)-but-2-ene-1,4-diylbis(oxy)]bis[2-(1,3-dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2′-oxiran]-11-one] (Trx24) and **(1*S*,2*S*,3a*S*,4*R*,13a*R*,1‴*S*,2‴*S*,3a‴*S*,4‴*R*,13a‴*R*)-13a,13a′-[(2*E*)-but-2-ene-1,4-diylbis(oxy)]bis[2-(1,3-dioxan-2-yl)-12-hydroxy-7-methoxy-5-methyl-3a,4,8,9,10,13a-hexahydro-11*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2′-oxiran]-11-one] (Trx25):** A suspension of **Trx17**

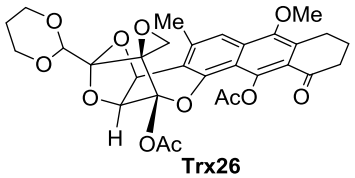


Trx24 (*Z*)
Trx25 (*E*)

(2.0 mg, 3.7 μmol) and Grubbs I catalyst (0.0053 M in CH_2Cl_2, 70 μL, 0.37 μmol, 0.1 equiv) was stirred at 23 °C for 14 h before the resulting mixture was directly subjected to preparative thin layer chromatography (silica gel, CH_2Cl_2: acetone 9:1) to afford (*Z*)-isomer **Trx24** (0.6 mg, 0.57 μmol, 31%, a yellow foam) as the major product and (*E*)-isomer **Trx25** (0.3 mg, 0.29 μmol, 16%, a yellow foam) as the minor product. **Trx24** (*Z*): $R_f = 0.70$ (silica gel, CH_2Cl_2: Et_2O 10:1); $[\alpha]_D^{25} = +209.9$ ($c = 0.0667$, $CHCl_3$); FT-IR (film): $\nu_{max} = 2926$, 1621, 1573, 1445, 1390, 1236, 1095 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) $\delta = 14.49$ (s, 2 H), 7.17 (d, $J = 1.2$ Hz, 2 H), 6.08–5.96 (m, 2 H), 5.16–5.10 (m, 4 H), 5.06 (s, 2 H), 4.82 (d, $J = 5.1$ Hz, 4 H), 4.28 (dd, $J = 11.7$, 4.8 Hz, 22 H), 4.08 (dd, $J = 11.6$, 4.8 Hz, 2 H), 3.88 (td, $J = 12.0$, 2.5 Hz, 2 H), 3.74 (td, $J = 12.1$, 2.5 Hz, 2 H), 3.63 (s, 6 H), 2.81 (d, $J = 5.9$ Hz, 2 H), 2.77 (td, $J = 5.8$, 2.5 Hz, 4 H), 2.67 (d, $J = 5.9$ Hz, 2 H), 2.51 (d, $J = 1.0$ Hz, 6 H), 2.50–2.45 (m, 2 H), 2.30 (dt, $J = 17.2$, 6.3 Hz, 2 H), 2.24–2.14 (m, 2 H), 1.91 (d, $J = 8.6$ Hz, 2 H), 1.35 (d, $J = 13.6$ Hz, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) $\delta = 204.3$, 163.1, 151.5, 142.4, 142.1, 135.3, 130.2, 130.0, 115.7, 113.6, 113.4, 111.0, 103.1, 102.2, 96.4, 72.9, 69.4, 69.3, 67.6, 67.5, 66.0, 61.0, 48.4, 38.9, 25.8, 23.7, 22.2, 20.8 ppm; HRMS (ESI) calcd for $C_{56}H_{56}O_{20}Na^+$ $[M+Na]^+$ 1071.3257, found 1071.3234. **Trx25** (*E*): $R_f = 0.72$ (silica gel, CH_2Cl_2: Et_2O 10:1); $[\alpha]_D^{25} = +144.9$ ($c = 0.055$, $CHCl_3$); FT-IR (film): $\nu_{max} = 2922$, 2851, 1621, 1571, 1447, 1389, 1235, 1095 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) $\delta = 14.72$ (s, 2 H), 7.39 (s, 2 H), 6.15–6.08 (m, 2 H), 5.23 (d, $J = 4.1$ Hz, 2 H), 5.09 (s, 2 H), 4.87 (d, $J = 4.1$ Hz, 2 H), 4.59 (dd, $J = 13.1$, 3.1 Hz, 2 H), 4.56–4.51 (m, 2 H), 4.29 (dd, $J = 11.5$, 4.8 Hz, 2 H), 4.11 (dd, $J = 11.7$, 4.9 Hz, 2 H), 3.90 (td, $J = 12.0$, 2.5 Hz, 2 H), 3.78 (td, $J = 12.4$, 2.3 Hz, 2 H), 3.75 (s, 6 H), 2.98 (t, $J = 6.2$ Hz, 4 H), 2.92 (d, $J = 5.8$ Hz, 2 H), 2.83 (d,

J = 5.8 Hz, 2 H), 2.71–2.60 (m, 4 H), 2.60 (d, J = 1.0 Hz, 6 H), 2.21 (ddd, J = 17.2, 12.4, 7.5 Hz, 2 H), 2.11–1.98 (m, 4 H), 1.36 (d, J = 13.7 Hz, 2 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 203.7, 162.8, 151.5, 141.9, 141.7, 134.8, 129.7, 129.6, 115.4, 113.7, 113.0, 110.4, 103.1, 102.1, 96.5, 72.1, 69.5, 68.9, 67.6, 67.5, 61.0, 60.9, 48.1, 38.6, 25.7, 23.37, 22.03, 20.87 ppm; HRMS (ESI) calcd for $C_{56}H_{56}O_{20}K^+$ $[M+K]^+$ 1087.2997, found 1087.2956.

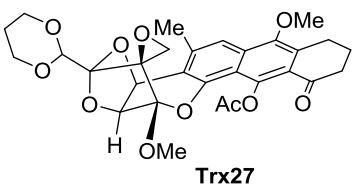
(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxan-2-yl)-7-methoxy-5-methyl-11-oxo-3a,4,8,9,10,11-hexahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxirane]-12,13a-diyl diacetate (Trx26): To a stirred solution of **Trx12** (9.3 mg, 19 µmol, 1.0 equiv) in CH_2Cl_2 (0.2 ml)



Trx26

were sequentially added 4-dimethylaminopyridine (1.4 mg, 9.3 µmol, 0.5 equiv), Et_3N (145 mg, 200 µL, 2.87 mmol, 151 equiv) and Ac_2O (106 mg, 0.10 ml, 1.06 mmol, 57 equiv) at 23 °C. The mixture was stirred at this temperature for 4 h before it was quenched with $NaHCO_3$ (sat. aq., 5 ml). The resulting mixture was stirred at this temperature for 30 min, and then extracted with CH_2Cl_2 (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc: hexanes 4:1) to give the titled compound (4.9 mg, 8.8 µmol, 67 % yield) as a pale yellow foam. **Trx26**: R_f = 0.49 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +264.6 (c = 0.3, CH_2Cl_2); FT-IR (film): ν_{max} = 2957, 1763, 1685, 1557, 1445, 1411, 1374, 1337, 1239, 1212, 1015 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6) δ = 7.62–7.48 (m, 1 H), 5.83–5.63 (m, 1 H), 5.18–5.07 (m, 1 H), 4.94–4.78 (m, 1 H), 3.72 (dd, J = 11.5, 4.7 Hz, 1 H), 3.59 – 3.45 (m, 1 H), 3.42–3.34 (m, 4 H), 3.28–3.18 (m, 1 H), 3.06 (td, J = 12.0, 2.5 Hz, 1 H), 2.97 (d, J = 5.9 Hz, 1 H), 2.70 (ddd, J = 16.3, 6.9, 4.4 Hz, 1 H), 2.44–2.35 (m, 4 H), 2.33 – 2.23 (m, 5 H), 1.76–1.72 (m, 3 H), 1.72–1.63 (m, 1 H), 1.50–1.36 (m, 2 H) 0.36 (d, J = 13.6, 1 H) ppm; ^{13}C NMR (151 MHz, C_6D_6) δ = 195.5, 170.5, 168.5, 149.7, 149.3, 145.4, 140.2, 133.3, 133.0, 122.8, 117.7, 116.3, 115.2, 103.8, 101.8, 97.0, 71.3, 69.3, 69.1, 66.9, 66.7, 60.6, 47.7, 40.9, 25.6, 24.0, 21.9, 21.3, 21.2, 20.0 ppm; HRMS (ESI) calcd for $C_{30}H_{30}O_{12}Na^+$ $[M+Na]^+$ 605.1629, found 605.1637.

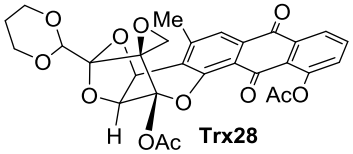
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-2-(1,3-Dioxan-2-yl)-7,13a-dimethoxy-5-methyl-11-oxo-3a,8,9,10,11,13a-hexahydro-4*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-12-yl acetate (Trx27): To a stirred solution of **Trx13** (4.7 mg, 9.2 µmol, 1.0 equiv) in CH_2Cl_2 (0.1 ml) were sequentially added 4-dimethylaminopyridine (0.56 mg, 0.46 µmol, 0.5 equiv), Et_3N (290 mg, 0.4 ml, 2.87 mmol,



Trx27

320 equiv) and Ac_2O (52.5 mg, 50 µl, 529 µmol, 58 equiv) at 23°C. The mixture was stirred at this temperature overnight before it was quenched with $NaHCO_3$ (sat. aq., 5 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc: hexanes 4:1) to give the titled compound (4.9 mg, 8.8 µmol, 96 % yield) as a pale yellow foam. **Trx27**: R_f = 0.49 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +264.6 (c = 0.3, CH_2Cl_2); FT-IR (film): ν_{max} = 2957, 1763, 1685, 1557, 1445, 1411, 1374, 1337, 1239, 1212, 1015 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.61–7.51 (m, 1 H), 5.38–5.25 (m, 1 H), 5.10–4.98 (m, 2 H), 4.33–4.26 (m, 1 H), 4.18–4.08 (m, 1 H), 3.93–3.87 (m, 1 H), 3.87–3.83 (m, 3 H), 3.81–3.74 (m, 1 H), 3.70–3.54 (m, 2 H), 3.21 (dt, J = 16.9, 6.3 Hz, 1 H), 3.03–2.89 (m, 2 H), 2.89–2.80 (m, 1 H), 2.70–2.64 (m, 2 H), 2.63–2.59 (m, 3 H), 2.47–2.38 (m, 3 H), 2.28–2.19 (m, 1 H), 2.18–2.12 (m, 1 H), 2.11–1.96 (m, 1 H), 1.37 (d, J = 13.6 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$, rotamers) δ = 196.8, 171.0, 170.8, 150.1, 150.0, 149.7, 149.6, 144.9, 144.7, 140.3, 140.2, 133.3, 133.1, 133.0, 122.2, 122.1, 117.3, 117.2, 116.1, 116.0, 114.6, 114.1, 103.6, 103.2, 103.1, 102.9, 96.2, 69.7, 69.4, 68.9, 68.6, 68.5, 68.2, 67.7, 67.6, 67.53, 67.51, 61.4, 52.6, 52.4, 48.2, 47.7, 41.0, 25.7, 24.13, 24.12, 22.2, 22.1, 21.4, 21.0, 20.8 ppm; HRMS (ESI-TOF) calcd for $C_{29}H_{30}O_{11}Na^+$ $[M+Na]^+$ 577.1680, found 577.1697.

(1*S*,2*S*,3a*S*,4*R*,13a*S*)-2-(1,3-Dioxan-2-yl)-5-methyl-7,12-dioxo-3a,4,7,12-tetrahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxirane]-11,13a-diyl diacetate (Trx28):

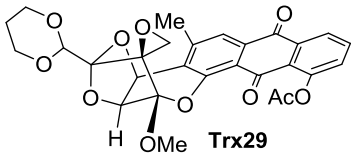


Trx28

To a solution of **Trx26** (5.4 mg, 9.3 µmol, 1.0 equiv) in EtOAc (0.2 ml) was added PhSeCl (2.1 mg, 11.1 µmol, 1.2 equiv) at 23 °C. The mixture was stirred at this temperature for 24 h before it was diluted with EtOAc (5 ml) and quenched with H_2O (5 ml). The resulting mixture was extracted with EtOAc (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give the crude phenylseleno ketone which was dissolved in CH_2Cl_2 (1 ml). To the stirred solution at 0 °C was added H_2O_2 (30 wt% in H_2O, 128µL, 128 µmol, 13.8 equiv) and the resulting mixture was stirred at this temperature for 0.5 h. The mixture was quenched with Na_2SO_3 (sat. aq., 2 ml) and extracted with CH_2Cl_2 (3 × 5 ml) with no precautions to exclude air. At this stage, ^1H NMR spectroscopic analysis ($CDCl_3$, 600 MHz) revealed a mixture of methoxy acetate phenol **Trx26c** and quinone **Trx28**, with the former being converted to the latter upon exposure to air through acetate migration (**Trx26d**) and air oxidation (~2 h). Removal of the

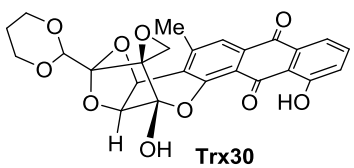
solvent and purification of the residue by preparative thin layer chromatography (silica gel, EtOAc:hexanes 2:1) afforded **Trx28** (2.54 mg, 4.49 μmol, 48% for the two steps) as a yellow foam. R_f = 0.43 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +72.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 1771, 1677, 1594, 1458, 1333, 1270, 1194, 1096, 1040, 1001 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 8.15 (dt, *J* = 7.9, 1.2 Hz, 1 H), 7.77 (s, 1 H), 7.74–7.66 (m, 1 H), 7.38 (dt, *J* = 8.0, 1.1 Hz, 1 H), 5.57 (d, *J* = 4.3 Hz, 1 H), 5.32–5.19 (m, 1 H), 5.07 (s, 1 H), 4.37–4.24 (m, 1 H), 4.20–4.14 (m, 1 H), 3.95–3.86 (m, 1 H), 3.80 (td, *J* = 12.1, 2.6 Hz, 1 H), 3.09 (d, *J* = 5.9 Hz, 1 H), 3.05 (d, *J* = 5.9 Hz, 1 H), 2.60 (s, 3 H), 2.43 (d, *J* = 1.1 Hz, 3 H), 2.32–2.18 (m, 4 H), 1.40 (d, *J* = 13.7 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.7, 180.0, 169.8, 168.6, 150.9, 149.7, 146.5, 135.0, 134.3, 134.0, 130.2, 126.8, 125.3, 123.7, 122.2, 120.7, 103.5, 101.3, 96.2, 71.9, 69.0, 68.9, 67.7, 67.5, 48.2, 25.7, 21.8, 21.4, 20.2 ppm; HRMS (ESI-TOF) calcd for $C_{29}H_{24}NaO_{12}^+$ $[M+Na]^+$ 587.1160, found 587.1166.

(1*S*,2*S*,3a*S*,4*R*,13a*R*)-2-(1,3-Dioxan-2-yl)-13a-methoxy-5-methyl-7,12-dioxo-3a,7,12,13a-tetrahydro-4*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-yl acetate (Trx29): **Trx28** was synthesized from **Trx27** (2.0 mg, 3.6 μmol) following the same procedure as that used for the preparation of **Trx28**. Yield: 1.12 mg, 2.02 μmol, 56% for the two steps; yellow foam; R_f = 0.60 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +145.7 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2921, 1772, 1676, 1593, 1445, 1335, 1271, 1192, 1097, 996 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 8.17 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.76 (s, 1 H), 7.72 (t, *J* = 7.9 Hz, 1 H), 7.40 (dd, *J* = 8.0, 1.3 Hz, 1 H), 5.21 (d, *J* = 4.0 Hz, 1 H), 5.07 (s, 1 H), 4.85 (d, *J* = 4.0 Hz, 1 H), 4.29 (dd, *J* = 11.7, 4.8 Hz, 1 H), 4.14 (dd, *J* = 11.5, 4.9 Hz, 1 H), 3.91 (td, *J* = 12.3, 2.6 Hz, 1 H), 3.82–3.77 (m, 1 H), 3.76 (s, 3 H), 2.99 (d, *J* = 5.7 Hz, 1 H), 2.92 (d, *J* = 5.7 Hz, 1 H), 2.60 (s, 3 H), 2.42 (s, 3 H), 2.27–2.16 (m, 1 H), 1.38 (d, *J* = 13.7 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.7, 180.6, 169.9, 151.5, 149.7, 146.8, 134.9, 134.4, 134.1, 130.1, 126.8, 125.3, 124.3, 121.9, 120.8, 103.8, 102.4, 96.2, 72.0, 69.1, 68.7, 67.7, 67.5, 52.9, 48.3, 25.7, 21.4, 20.3 ppm; HRMS (ESI-TOF) calcd for $C_{28}H_{24}NaO_{11}^+$ $[M+Na]^+$ 559.1211, found 559.1222.



Trx29

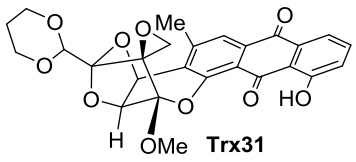
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-2-(1,3-Dioxan-2-yl)-11,13a-dihydroxy-5-methyl-3a,13a-dihydro-4*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxirane]-7,12-dione (Trx30): To a solution of **Trx28** (2.1 mg, 3.7 μmol, 1.0 equiv) in THF (0.4 ml) at 0 °C was added LiOH (1.0 N in H_2O, 0.2 ml, 200 μmol, 54 equiv). The mixture was stirred at this temperature for 1 h before it was quenched



Trx30

with $NaHCO_3$ (sat. aq., 1 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 2 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, EtOAc:hexanes 2:1) to give the titled compound (1.4 mg, 2.9 µmol, 78 % yield) as a pale yellow oil. **Trx30**: R_f = 0.38 (silica gel, EtOAc:hexanes 2:1); $[\alpha]_D^{25}$ = +177.5 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2851, 1719, 1672, 1634, 1591, 1559, 1454, 1356, 1318, 1268, 982 cm^{-1}; ^1H NMR (600 MHz, , $CDCl_3$) δ = 12.86 (s, 1 H), 7.84 (s, 1 H), 7.77 (dd, *J* = 7.5, 1.3 Hz, 1 H), 7.62 (dd, *J* = 8.4, 7.5 Hz, 1 H), 7.29 (dd, *J* = 8.3, 1.2 Hz, 1 H), 5.27 (d, *J* = 3.9 Hz, 1 H), 5.06 (s, 1 H), 4.89 (d, *J* = 3.9 Hz, 1 H), 4.50 (s, 1 H), 4.32–4.27 (m, 1 H), 4.22–4.12 (m, 1 H), 3.90 (td, *J* = 12.1, 2.6 Hz, 1 H), 3.80 (td, *J* = 11.8, 2.5 Hz, 1 H), 3.28 (d, *J* = 5.3 Hz, 1 H), 3.07 (d, *J* = 5.3 Hz, 1 H), 2.63 (s, 3 H), 2.26–2.18 (m, 1 H), 1.44–1.36 (m, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 187.9, 182.4, 162.6, 152.7, 148.2, 136.1, 135.8, 132.7, 125.2, 124.3, 123.0, 119.2, 118.8, 117.1, 103.2, 99.0, 96.4, 73.8, 69.4, 69.3, 67.7, 67.5, 50.7, 25.7, 20.5 ppm; HRMS (ESI-TOF) calcd for $C_{25}H_{20}NaO_{10}^+$ $[M+Na]^+$ 503.0949, found 503.0964.

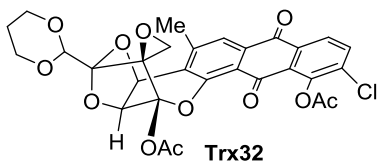
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-2-(1,3-Dioxan-2-yl)-11-hydroxy-13a-methoxy-5-methyl-3a,13a-dihydro-4*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxirane]-7,12-dione (Trx31): To a solution of **Trx29** (1.0 mg, 1.8 µmol, 1.0 equiv) in THF (0.2 ml) at 0 °C was added LiOH (1.0 N in H_2O, 0.1 ml, 100 µmol, 56 equiv). The mixture was stirred at this temperature for 1 h before it was quenched with $NaHCO_3$ (sat. aq., 1 ml). The resulting mixture was extracted with CH_2Cl_2 (3 × 2 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc:hexanes 2:1) to give the titled compound (0.74 mg, 1.5 µmol, 83 % yield) as a pale yellow oil. **Trx31**: R_f = 0.65 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +156.0 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2851, 1714, 1671, 1635, 1592, 1456, 1320, 1269, 1193, 1068, 954 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 7.84 (s, 1 H), 7.77 (dd, *J* = 7.5, 1.2 Hz, 1 H), 7.63 (t, *J* = 7.9 Hz, 1 H), 7.30 (dd, *J* = 8.3, 1.2 Hz, 1 H), 5.24 (d, *J* = 4.0 Hz, 1 H), 5.09 (s, 1 H), 4.89 (d, *J* = 4.0 Hz, 1 H), 4.29 (dd, *J* = 11.7, 5.0 Hz, 1 H), 4.14 (dd, *J* = 11.6, 4.9 Hz, 1 H), 3.90 (td, *J* = 12.1, 2.6 Hz, 1 H), 3.81–3.77 (m, 1 H); 3.80 (s, 3 H), 3.02 (d, *J* = 5.7 Hz, 1 H), 2.87 (d, *J* = 5.7 Hz, 1 H), 2.63 (s, 3 H), 2.27–2.17 (m, 1 H), 1.39 (d, *J* = 13.7 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 187.8, 182.5, 162.6, 152.5, 148.1, 136.1, 135.7, 132.7, 125.1, 124.3, 122.8, 119.1, 118.8, 117.1, 103.9, 102.6, 96.2, 71.8, 69.1, 68.6, 67.7, 67.5, 53.2, 48.2, 25.7,



Trx31

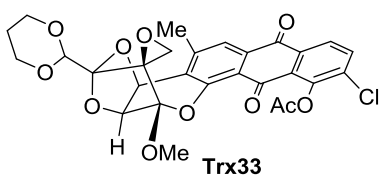
20.5 ppm; HRMS (ESI-TOF) calcd for $C_{26}H_{22}NaO_{10}^+$ $[M+Na]^+$ 517.1105, found 517.1118.

(1*S*,2*S*,3a*S*,4*R*,13a*S*)-10-Chloro-2-(1,3-dioxan-2-yl)-5-methyl-7,12-dioxo-3a,4,7,12-tetrahydro-13a*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxirane]-11,13a-diyl diacetate (Trx32): To a solution of **Trx26** (3.8 mg, 6.5 μmol, 1.0 equiv) in EtOAc (0.2 ml) was added PhSeCl (12.4 mg, 65 μmol, 10.0 equiv) at 23 °C. The mixture was stirred at this temperature for 72 h before it was diluted with EtOAc (5 ml) and quenched with H_2O (5 ml). The resulting mixture was extracted with EtOAc (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, EtOAc:hexanes 4:1) to afford **Trx32** (1.8 mg, 3.0 μmol, 46% yield) as a yellow foam. R_f = 0.44 (silica gel, EtOAc: hexanes 2:1); $[\alpha]_D^{25}$ = +67.7 (*c* = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 1781, 1678, 1597, 1580, 1463, 1368, 1333, 1272, 1187, 1096 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 8.4 Hz, 1 H), 7.81–7.75 (m, 2 H), 5.57 (d, *J* = 4.0 Hz, 1 H), 5.25 (d, *J* = 4.0 Hz, 1 H), 5.08 (s, 1 H), 4.29 (dd, *J* = 11.6, 4.8 Hz, 1 H), 4.16 (dd, *J* = 11.6, 4.9 Hz, 1 H), 3.90 (td, *J* = 12.1, 2.5 Hz, 1 H), 3.80 (td, *J* = 12.0, 2.5 Hz, 1 H), 3.08 (d, *J* = 6.1 Hz, 1 H), 3.05 (d, *J* = 5.8 Hz, 1 H), 2.60 (s, 3 H), 2.48 (s, 3 H), 2.26 (s, 3 H), 2.26–2.19 (m, 1 H), 1.40 (d, *J* = 13.7 Hz, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 181.9, 179.1, 168.7, 168.6, 151.0, 146.8, 146.2, 136.2, 134.8, 134.4, 132.5, 128.1, 125.7, 123.9, 122.3, 120.5, 103.4, 101.3, 96.2, 71.8, 69.0, 68.8, 67.7, 67.5, 48.2, 25.6, 21.8, 21.0, 20.2 ppm; HRMS (ESI-TOF) calcd for $C_{29}H_{23}ClNaO_{12}^+$ $[M+Na]^+$ 621.0770, found 621.0781.



Trx32

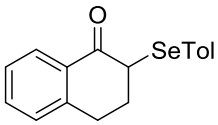
(1*S*,2*S*,3a*S*,4*R*,13a*R*)-10-Chloro-2-(1,3-dioxan-2-yl)-13a-methoxy-5-methyl-7,12-dioxo-3a,7,12,13a-tetrahydro-4*H*-spiro[2,4-epoxyfuro[3,2-*b*]naphtho[2,3-*h*]chromene-1,2'-oxiran]-11-yl acetate (Trx33): To a solution of **Trx27** (4.4 mg, 7.9 μmol, 1.0 equiv) in EtOAc (0.3 ml) was added PhSeCl (15.2 mg, 79 μmol, 10.0 equiv) at 23 °C. The mixture was stirred at this temperature for 72 h before it was diluted with EtOAc (5 ml) and quenched with H_2O (5 ml). The resulting mixture was extracted with EtOAc (3 × 5 ml). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (silica gel, EtOAc:hexanes 4:1) to afford **Trx33** (1.9 mg, 3.3 μmol, 42% yield) as a yellow foam. R_f = 0.67 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +164.0



Trx33

(c = 0.1, CH_2Cl_2); FT-IR (film): ν_{max} = 2852, 1781, 1677, 1595, 1580, 1456, 1336, 1273, 1187, 995 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ = 8.11 (d, J = 8.4 Hz, 1 H), 7.79 (d, J = 8.4 Hz, 1 H), 7.75 (s, 1 H), 5.21 (d, J = 4.0 Hz, 1 H), 5.07 (s, 1 H), 4.86 (br s, 1 H), 4.29 (dd, J = 11.5, 4.9 Hz, 1 H), 4.14 (dd, J = 11.5, 4.9 Hz, 1 H), 3.89 (td, J = 12.0, 2.5 Hz, 1 H), 3.79 (td, J = 12.1, 2.6 Hz, 1 H), 3.76 (s, 3 H), 2.99 (d, J = 5.7 Hz, 1 H), 2.91 (d, J = 5.7 Hz, 1 H), 2.61 (s, 3 H), 2.47 (s, 3 H), 2.22 (qt, J = 12.7, 5.0 Hz, 1 H), 1.41–1.36 (m, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.0, 179.7, 168.6, 151.6, 147.1, 146.1, 136.2, 134.7, 134.5, 132.5, 128.1, 125.7, 124.4, 122.0, 120.6, 103.9, 102.5, 96.2, 71.7, 69.0, 68.6, 67.7, 67.5, 52.9, 48.2, 25.7, 21.0, 20.3 ppm; HRMS (ESI-TOF) calcd for $C_{28}H_{23}ClNaO_{11}^+$ $[M+Na]^+$ 593.0821, found 593.0827.

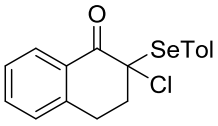
2-(*p*-Tolylselanyl)-3,4-dihydronaphthalen-1(2*H*)-one (III): To a stirred solution of α-tetralone (77.0 mg, 529 µmol, 1.0 equiv) in EtOAc (2 ml) at 23 °C was added tolylselenyl chloride[6] (109 mg, 529 µmol, 1.0 equiv). The mixture was stirred at this temperature for 2 h before it was directly subjected to preparative thin layer chromatography (silica gel, Et_2O:CH_2Cl_2:hexanes 1:3:9) to afford the title compound as a colorless oil (70.2 mg, 222 µmol, 42% yield) and recovered starting material (23.5 mg, 31% yield).



III

III: R_f = 0.35 (silica gel, Et_2O:CH_2Cl_2:hexanes 1:3:9); FT-IR (film): ν_{max} = 3065, 3021, 2923, 1672, 1598, 1488, 1454, 1431, 1350, 1298; ^1H NMR (600 MHz, $CDCl_3$) δ = 8.06 (dd, J = 7.8, 1.4 Hz, 1 H), 7.52–7.46 (m, 3 H), 7.32 (t, J = 7.6 Hz, 1 H), 7.23 (d, J = 7.6 Hz, 1 H), 7.11 (d, J = 7.8 Hz, 2 H), 4.26–4.13 (m, 1 H), 3.24 (ddd, J = 16.3, 10.9, 4.6 Hz, 1 H), 2.87 (dt, J = 17.0, 4.5 Hz, 1 H), 2.50 (ddt, J = 14.2, 11.0, 4.4 Hz, 1 H), 2.40–2.29 (m, 4 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 193.7, 143.0, 138.7, 135.9, 133.6, 131.4, 130.2, 128.8, 128.3, 127.0, 123.9, 48.9, 29.4, 27.1, 21.4 ppm; HRMS (ESI-TOF) calcd for $[M+H]^+$ $C_{17}H_{17}OSe^+$ 317.0439, found 317.0428.

2-Chloro-2-(*p*-tolylselanyl)-3,4-dihydronaphthalen-1(2*H*)-one (VIIIa): To a stirred solution of CSA (7.0 mg, 0.031 mmol, 1.0 equiv) and compound **III** (9.7, 0.031 mmol, 1.0 equiv) in EtOAc (0.3 ml) at 23 °C was added PhSeCl (11.8 mg, 0.062 mmol, 2.0 equiv). The reaction mixture was stirred at this temperature for 2 h before it was directly subjected to preparative thin layer chromatography (Et_2O:CH_2Cl_2:hexanes 1:3:9) to afford the title compound as a colorless oil (2.2 mg, 6.3 µmol, 20% yield) and recovered starting material (5.7 mg, 0.018 mmol, 59% yield). This product proved rather labile to prolonged reaction times and subsequent manipulation. The reaction was therefore stopped



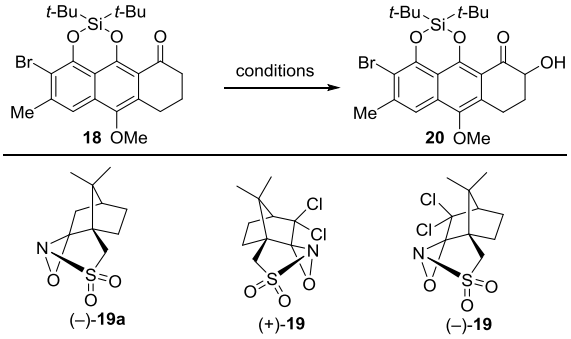
VIIIa

before completion and caution was taken during isolation to minimize decomposition. **III**: $R_f = 0.44$ (silica gel, Et_2O:CH_2Cl_2:hexanes 1:3:9); FT-IR (film): $\nu_{max} = 3398$, 2920, 2851, 1686, 1599, 1488, 1455, 1388, 1290, 1234, 1218, 1015; ^1H NMR (600 MHz, $CDCl_3$) $\delta = 8.12$ (dd, $J = 7.8$, 1.4 Hz, 1 H), 7.51 (dd, $J = 8.1$, 1.9 Hz, 3 H), 7.37 (dd, $J = 8.5$, 6.3 Hz, 1 H), 7.24 (d, $J = 7.4$ Hz, 1 H), 7.17 (d, $J = 7.8$ Hz, 2 H), 3.21 (ddd, $J = 17.2$, 10.0, 5.1 Hz, 1 H), 3.02 (dt, $J = 17.2$, 4.9 Hz, 1 H), 2.75–2.64 (m, 2 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) $\delta = 186.9$, 142.1, 140.5, 138.0, 134.0, 132.5, 130.1, 129.4, 128.6, 127.4, 122.1, 75.4, 40.4, 28.4, 21.6 ppm; HRMS (ESI-TOF) calcd for $[M+Na]^+$ $C_{17}H_{15}ClOSeNa^+$ 372.9869, found 372.9896.

HPLC Traces of Compounds

1. **HPLC traces for determining the enantiomeric ratio of the *α*-hydroxylation with oxaziridine reagents:** The HPLC analysis was carried out on Chiralcel OD-H, 25 °C; flow rate: 1 mL/min; hexanes/isopropanol: 99.5/0.5; detector 254 nm.

Table S1. Optimization of *α*-Hydroxylation of Bromide 18 with Oxaziridine Reagents[a]



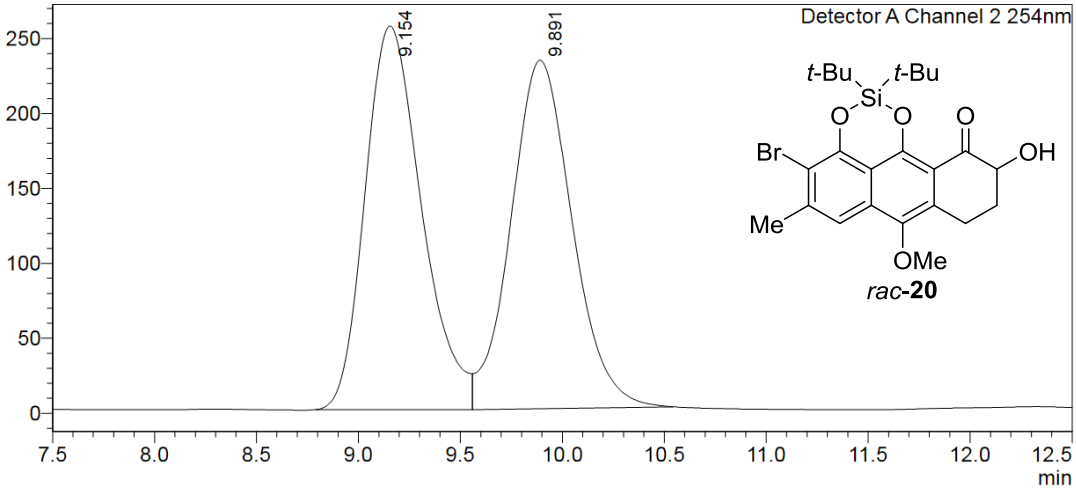
entry	oxaziridine	base	ϑ (°C)	t (h)	rsm (%)[b]	yield (%)[c]	*er* (*R*):(*S*)[d]
1	(–)-**19a**	NHMDS	–78→0	2	41	33	1.9:1
2	(+)-**19**	NHMDS	–78	1	—	54	21:1
3	(+)-**19**	LHMDS	–78	1	—	55	21:1
4	(+)-**19**	LDA	–78	0.5	9	66	14:1
5[e]	(+)-**19**	LDA	–78	0.5	30	37	3.2:1
6	(–)-**19**	LTMP	–78	0.5	7	77	1:27

[a]Reactions were carried out on 0.10 mmol scale, with 1.5 equiv base and 1.5 equiv oxaziridine in THF; [b]recovered starting material; [c]isolated yield; [d]absolute configuration of **20** was determined by Mosher ester analysis; [e]HMPA as additive.

***rac*-20**

<Chromatogram>

mV



<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.154	4949136	255920	0.000	50.433
2	9.891	4864107	232578	0.000	49.567
Total		9813243	488497		100.000

Entry 1: (−)-19a; NHMDS

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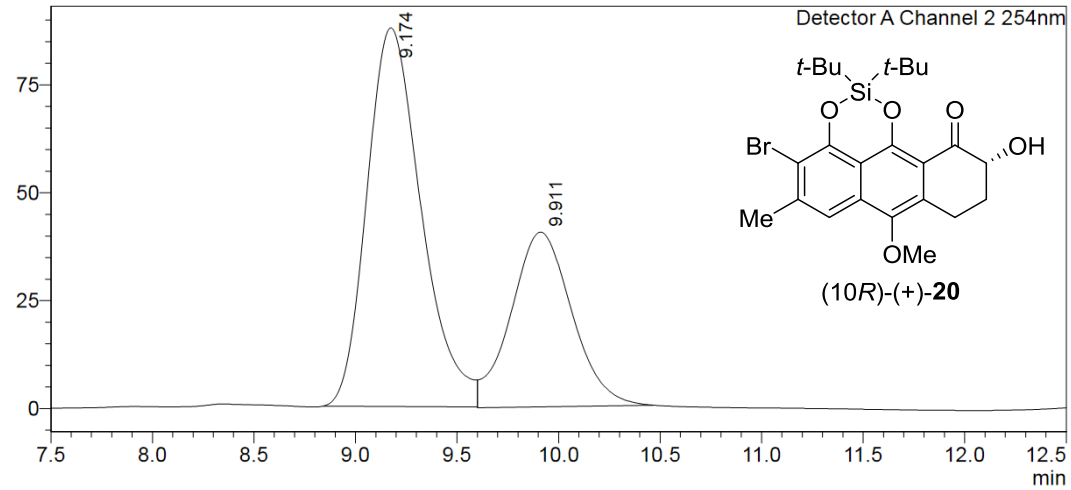
mV



<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.174	1632178	87716	65.877	65.877
2	9.911	845429	40468	34.123	34.123
Total		2477608	128184		100.000

Entry 2: (+)-19; NHMDS

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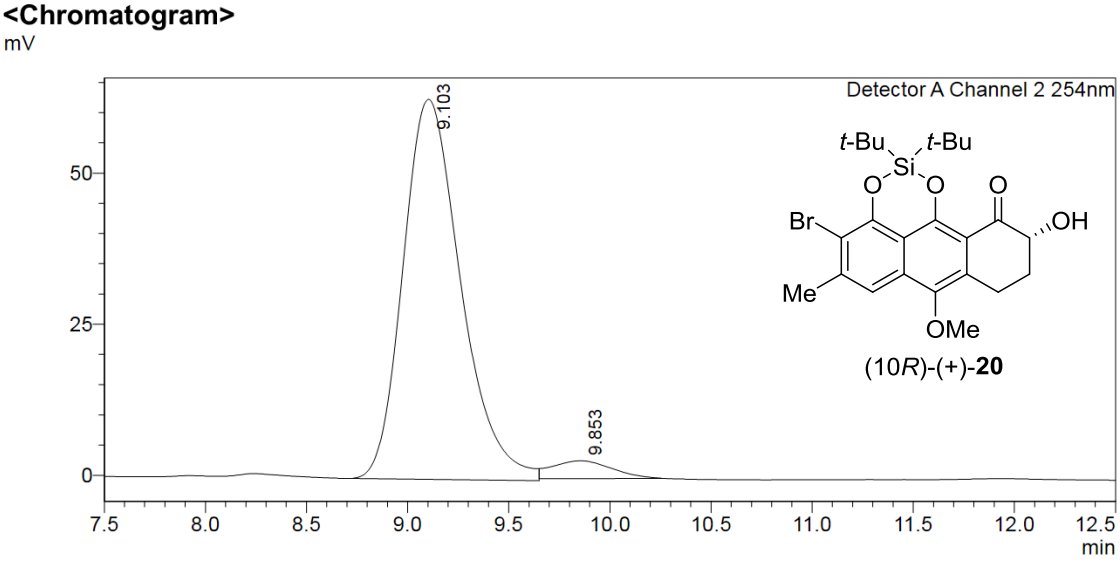

<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.103	1249575	62857	95.359	95.359
2	9.853	60810	2948	4.641	4.641
Total		1310385	65805		100.000

Entry 3: (+)-19; LHMDS

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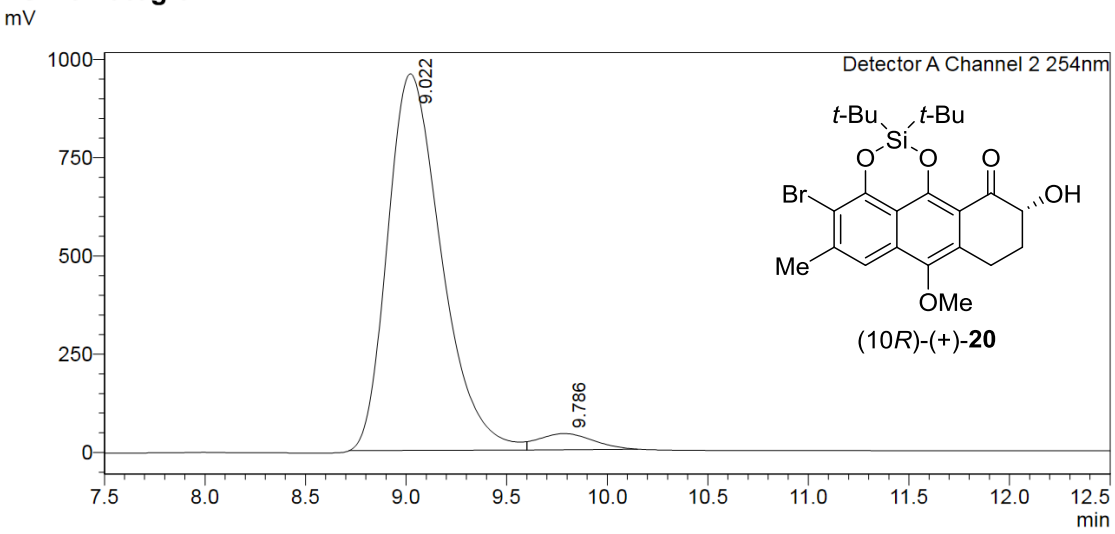

<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.
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2	9.786	773454	41271	4.148
Total		18648024	999758	

Entry 4: (+)-19; LDA

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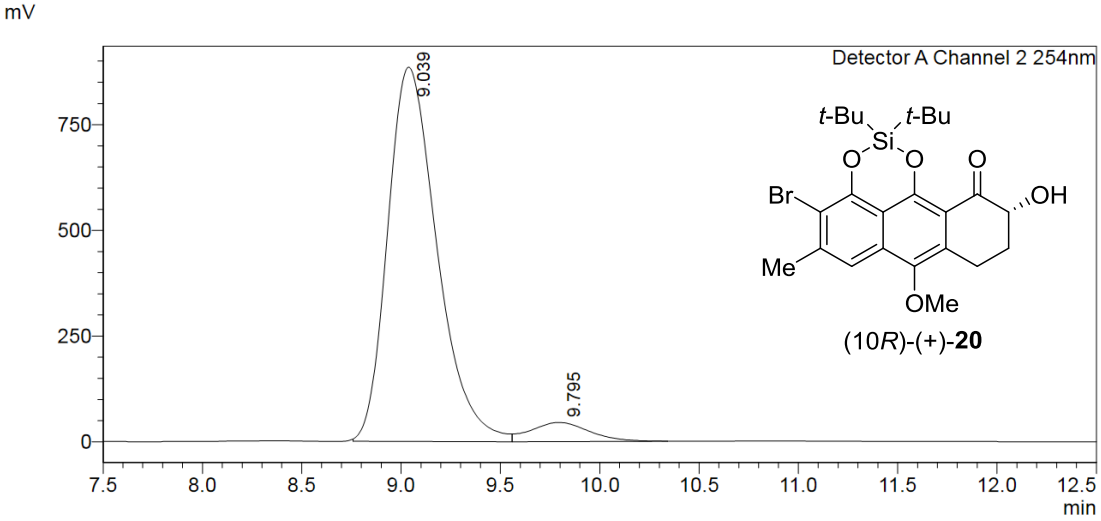


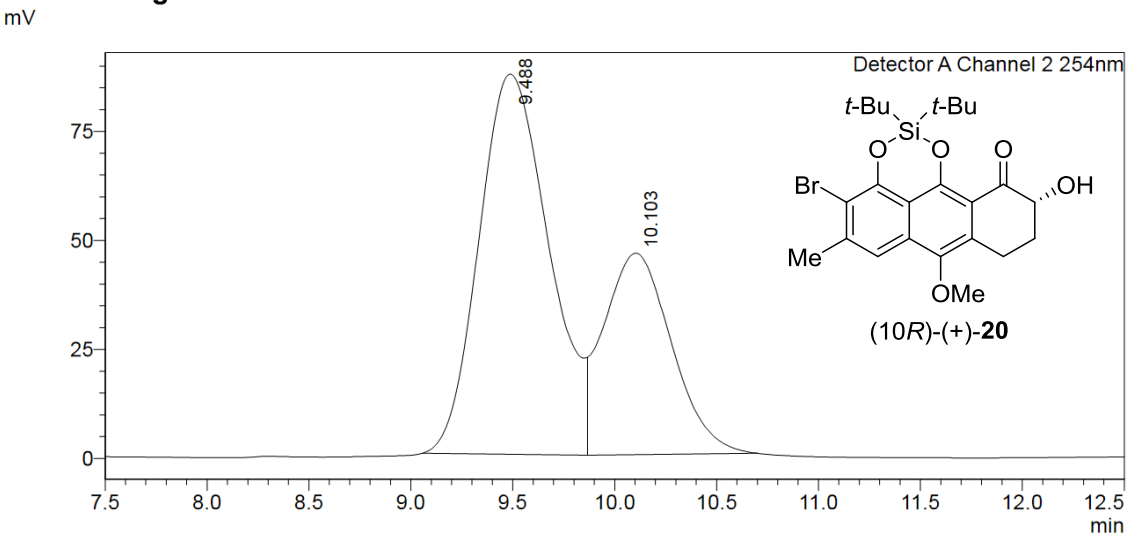
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.039	15299107	884583	94.293	94.293
2	9.795	925884	45114	5.707	5.707
Total		16224991	929697		100.000

Entry 5: (+)-19; LDA + HMPA

<Chromatogram>



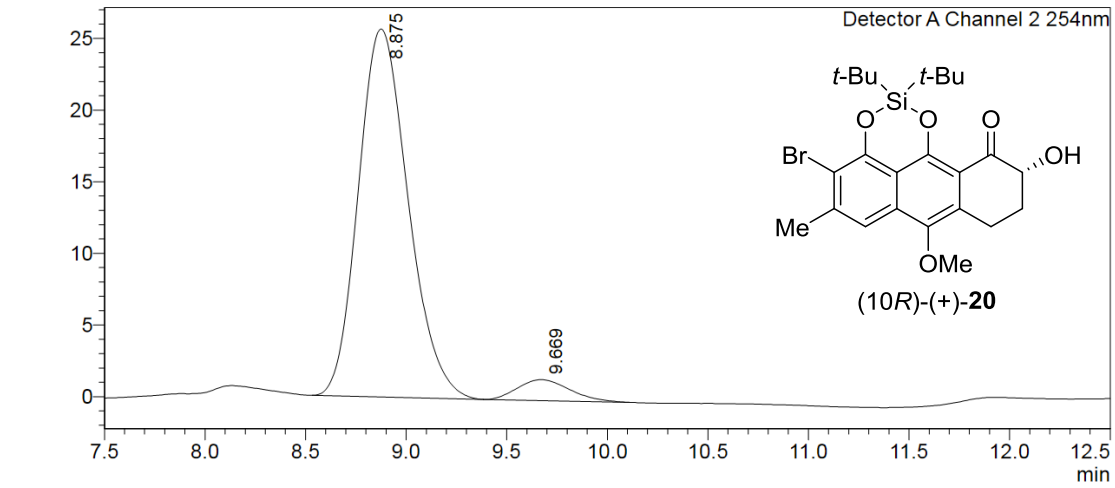
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.488	2090683	87174	66.220	66.220
2	10.103	1066482	46201	33.780	33.780
Total		3157164	133375		100.000

Entry 6: (+)-19; LTMP

<Chromatogram>



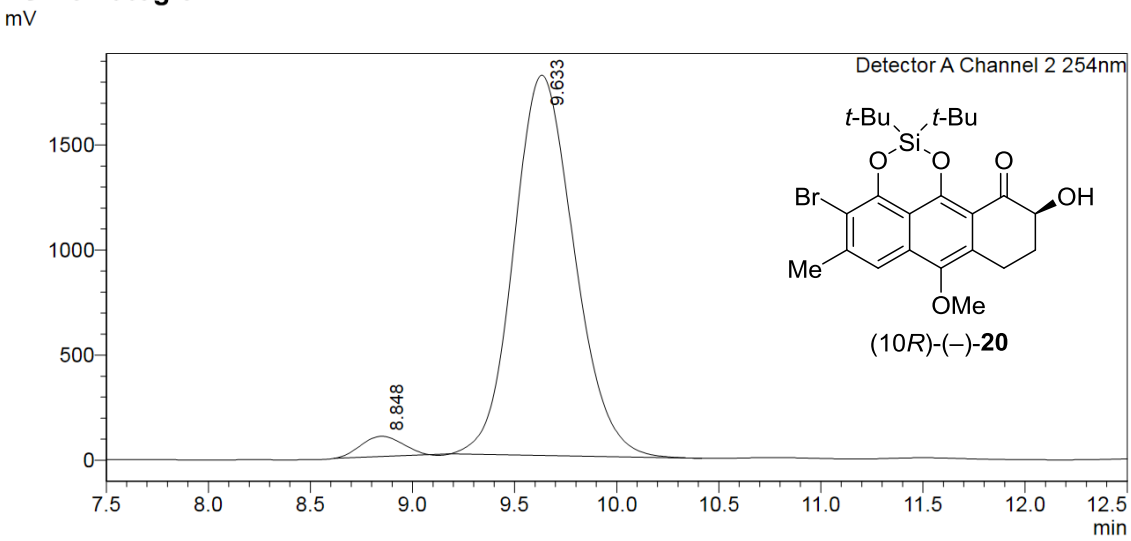
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.875	442817	25697	94.328
2	9.669	26628	1462	5.672
Total		469445	27159	

Entry 7: (−)-19; LTMP

<Chromatogram>



<Peak Table>

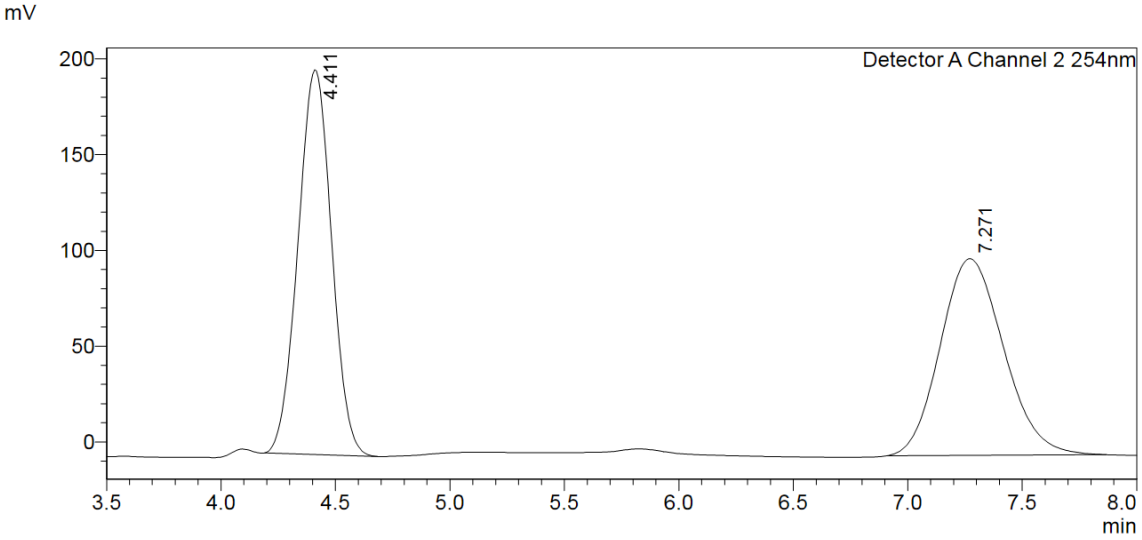
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.848	1353766	96478	3.500
2	9.633	37320318	1811113	96.500
Total		38674085	1907591	

2. **HPLC trances of compound 13 (from the 2nd improved route):** The HPLC analysis was carried out on Chiralcel OD-H, 25 °C; flow rate: 1 mL/min; hexanes/isopropanol: 95/5; detector: 254 nm.

***rac*-13:**

<Chromatogram>



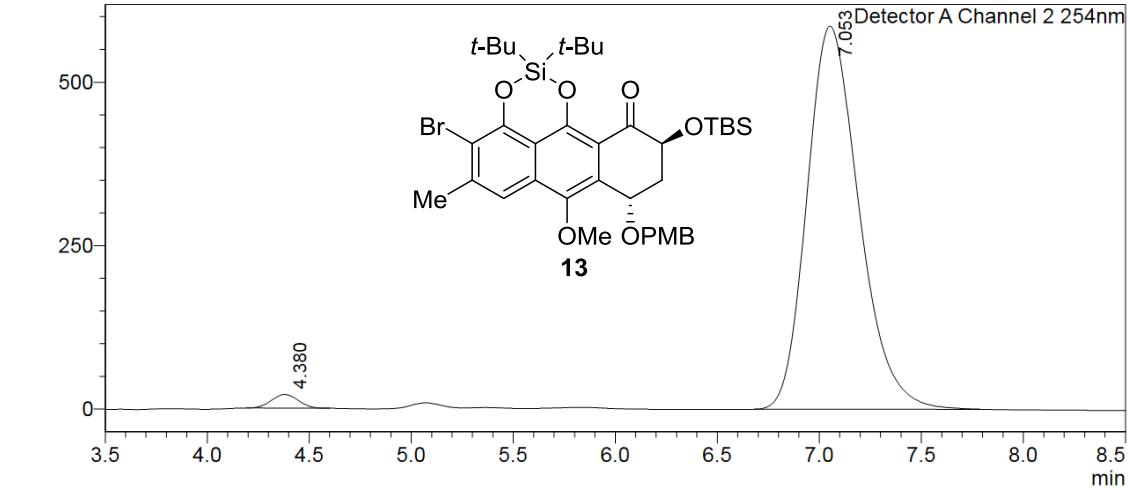
<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	4.411	2048940	200885	50.863	50.863
2	7.271	1979375	102664	49.137	49.137
Total		4028315	303550		100.000

13:

<Chromatogram>



<Peak Table>

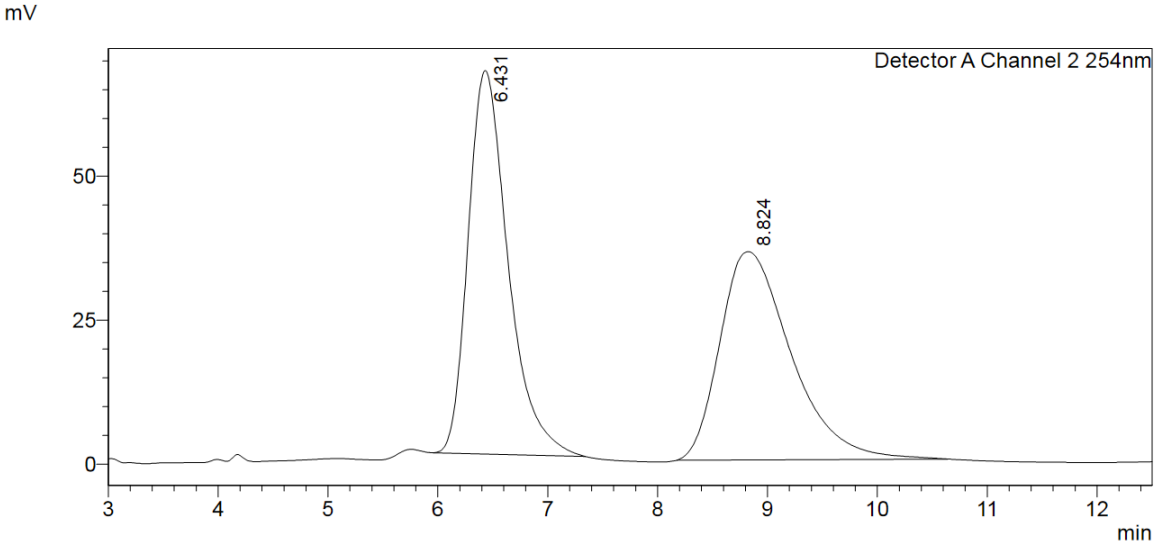
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	4.380	192911	20948	1.822	1.822
2	7.053	10394918	586101	98.178	98.178
Total		10587829	607049		100.000

3. **HPLC traces for determining the enantiomeric ratio of compound 42b:** The HPLC analysis was carried out on Chiralcel OD-H, 25 °C; flow rate: 1 mL/min; hexanes/isopropanol: 95/5; detector: 254 nm.

***rac*-42b:**

<Chromatogram>



<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	6.431	1684886	66589	50.864	50.864
2	8.824	1627660	36174	49.136	49.136
Total		3312546	102763		100.000

42b:

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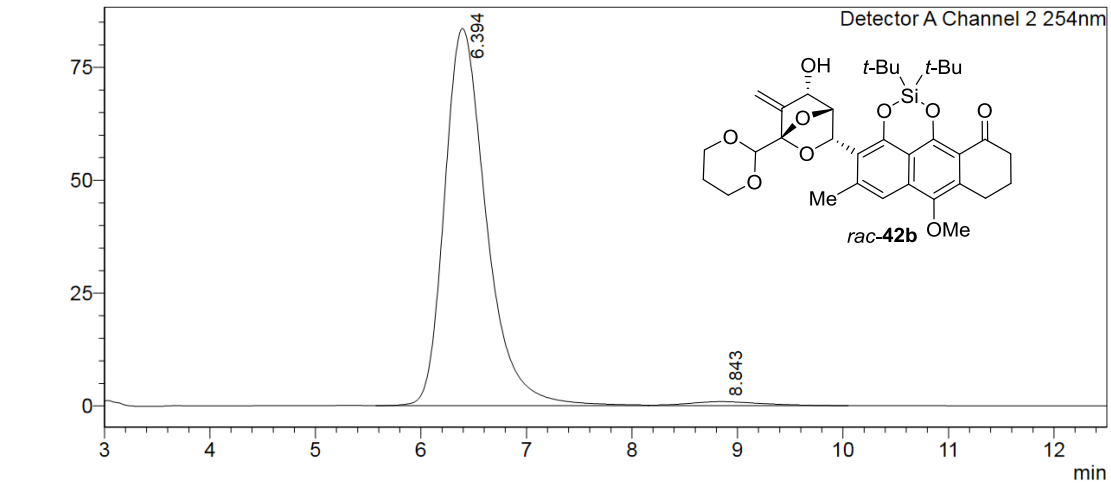


<Peak Table>

Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	6.394	2310577	83594	98.081	98.081
2	8.843	45201	907	1.919	1.919
Total		2355779	84502		100.000

Biological Evaluations

***In vitro* cytotoxicity assay description:**

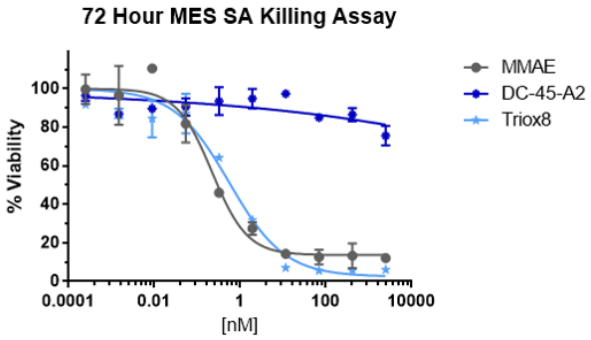
Cells were cultured in a T75 flask to ~50–80% confluency and harvested with trypsin into a single cell suspension. Five hundred (500) cells per well were seeded in tissue culture plates in 50 μL/well culture media and incubated at 37 °C for 18–24 hours. Compounds were diluted as 400x final desired concentrations in DMSO. Serial dilutions in DMSO were then diluted in culture media for a final DMSO concentration of 0.25% and 50 μl/well of the final dilution was added to the cells (Vf = 100 μl). Upon plating and treatment, cells were returned to the incubator for an additional 72 hours. CellTiter-Glo reagent was prepared per manufacturer's instructions and added at 100 μL/well to the cultures. CellTiter-Glo allows for relative enumeration of metabolically active cells by quantifying intracellular ATP concentrations. After 5 minutes of incubation with CellTiter-Glo at ambient room temperature, 125 μl/well of the Cell Titer Glo/cell lysate solution was transferred into black assay plates, which were then read in a luminometer within 30 minutes. Luminescence readings obtained from cultures that did not receive any treatment (cell culture media only) were set as 100% control and all other luminescence values were normalized to these controls (e.g. Normalized RLU, relative luminescence unit).

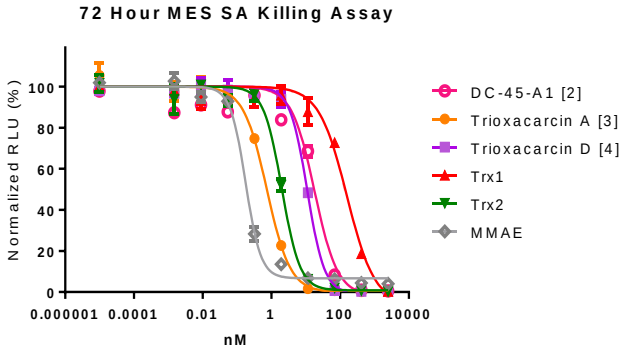
Cell lines:

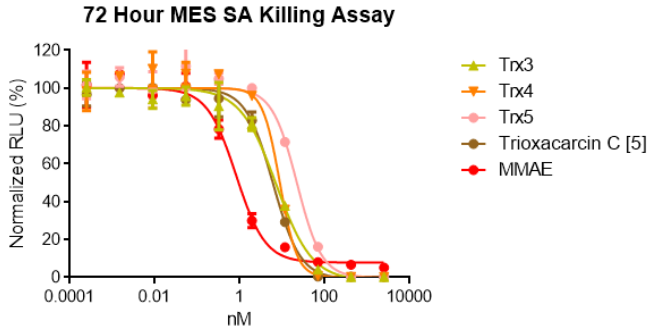
MES SA and MES SA/Dx cells are uterine sarcoma. MES SA Dx cell line was generated from MES SA to achieve upregulation of MDR1. MES-SA/Dx cells exhibit marked cross-resistance to a number of chemotherapeutic agents (including daunorubicin, dactinomycin, vincristine, taxol, colchicine) and moderate cross-resistance to mitomycin C and melphalan.

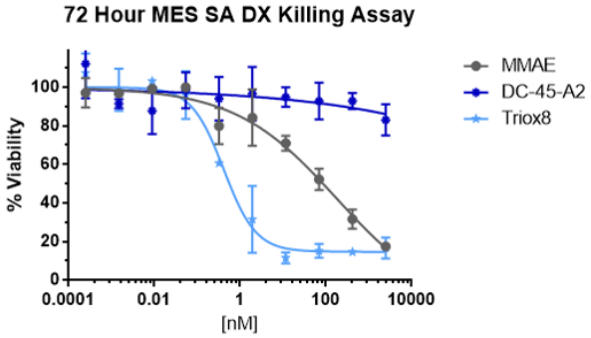
293T cells are human embryonic kidney cell line.

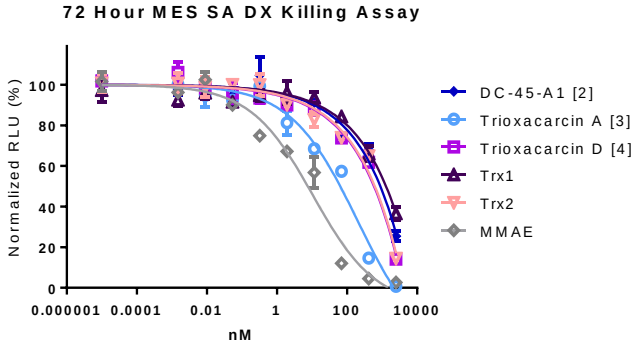
In Vitro Cytotoxicity Assay Graphs

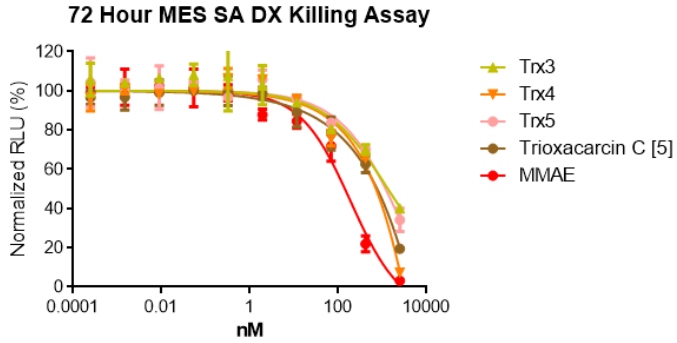


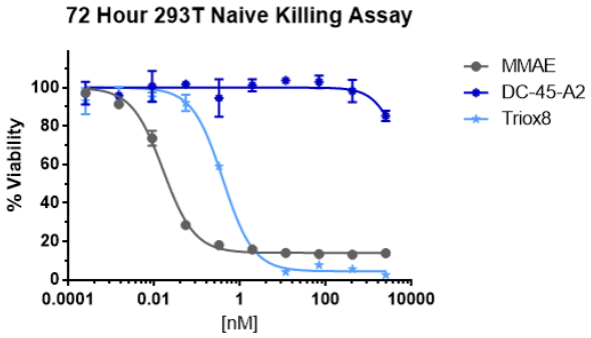


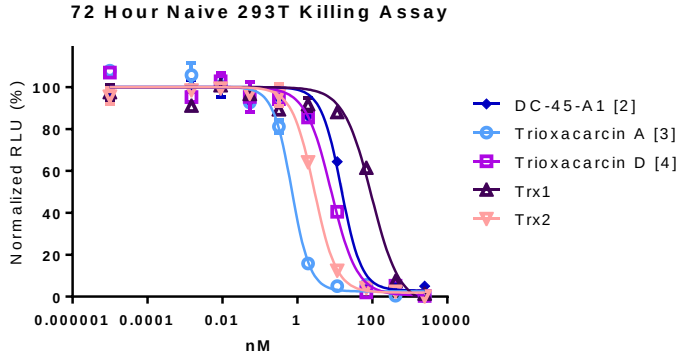


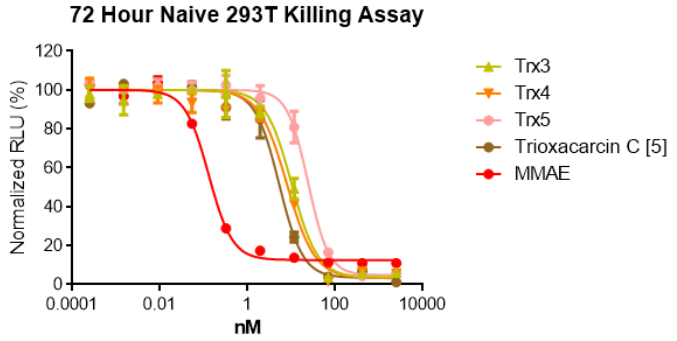


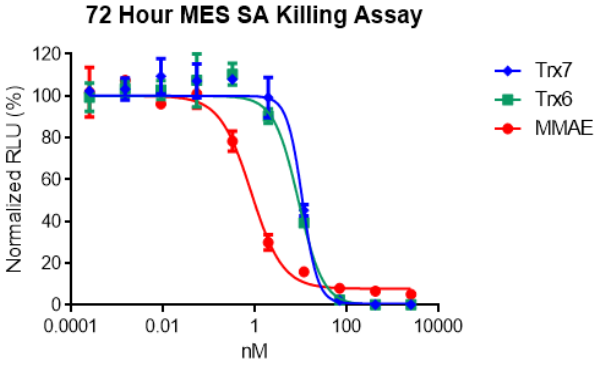


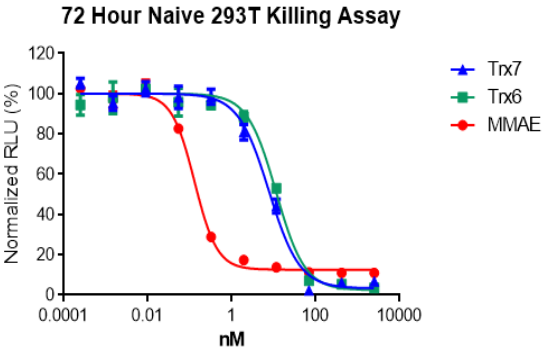


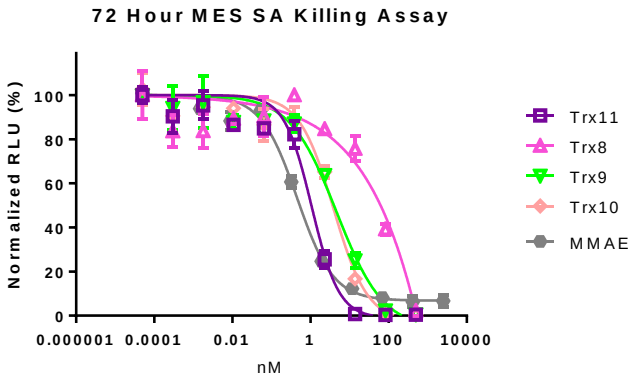


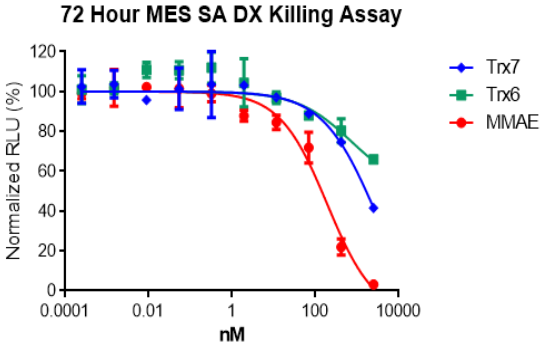


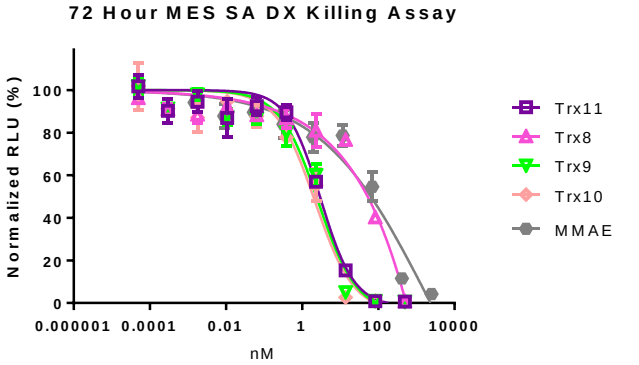


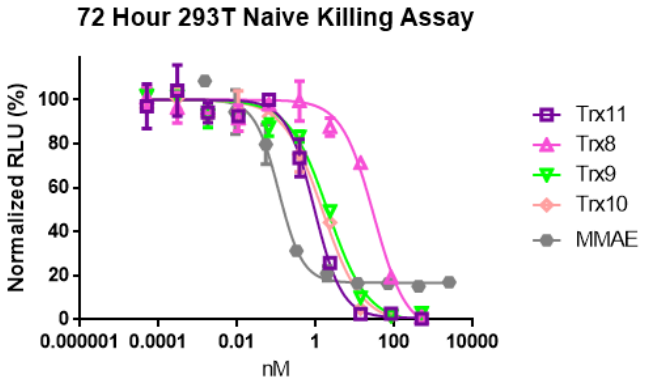

72 Hour MES SA Killing Assay
Normalized RLU (%)
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
nM
Trx7
Trx6
MMAE

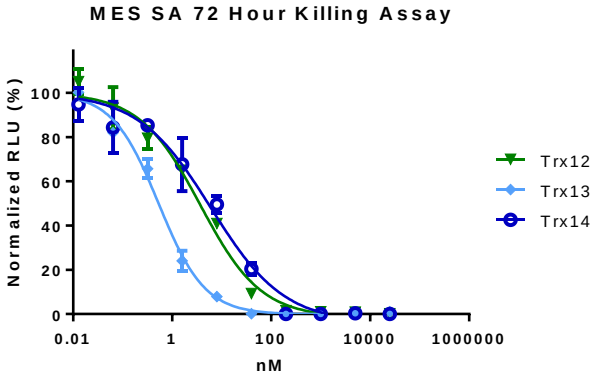

72 Hour Naive 293T Killing Assay
Normalized RLU (%)
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
nM
Trx7
Trx6
MMAE

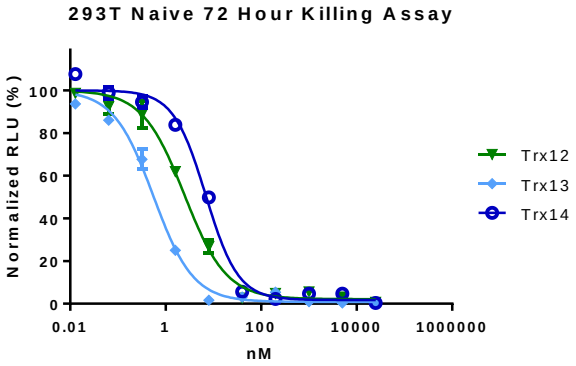

72 Hour MES SA Killing Assay
Normalized RLU (%)
100
80
60
40
20
0
0.000001
0.0001
0.01
1
100
10000
nM
Trx11
Trx8
Trx9
Trx10
MMAE

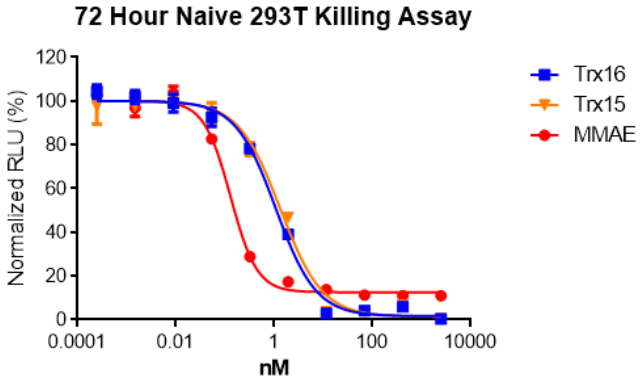

72 Hour MES SA DX Killing Assay
Normalized RLU (%)
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
nM
Trx7
Trx6
MMAE


72 Hour MES SA DX Killing Assay
Normalized RLU (%)
100
80
60
40
20
0
0.000001
0.0001
0.01
1
100
10000
nM
Trx11
Trx8
Trx9
Trx10
MMAE


72 Hour 293T Naive Killing Assay
Normalized RLU (%)
100
80
60
40
20
0
0.000001
0.0001
0.01
1
100
10000
nM
Trx11
Trx8
Trx9
Trx10
MMAE


MES SA 72 Hour Killing Assay
Normalized RLU (%)
100
80
60
40
20
0
0.01
1
100
10000
1000000
nM
Trx12
Trx13
Trx14


293T Naive 72 Hour Killing Assay
Normalized RLU (%)
100
80
60
40
20
0
0.01
1
100
10000
1000000
nM
Trx12
Trx13
Trx14


72 Hour Naive 293T Killing Assay
Normalized RLU (%)
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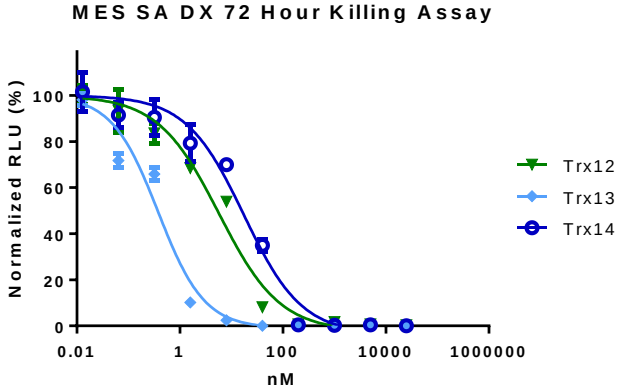
100
80
60
40
20
0
0.0001
0.01
1
100
10000
nM
Trx16
Trx15
MMAE


MES SA DX 72 Hour Killing Assay
Normalized RLU (%)
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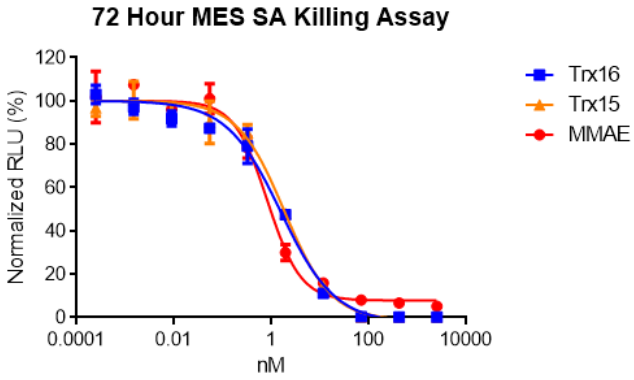
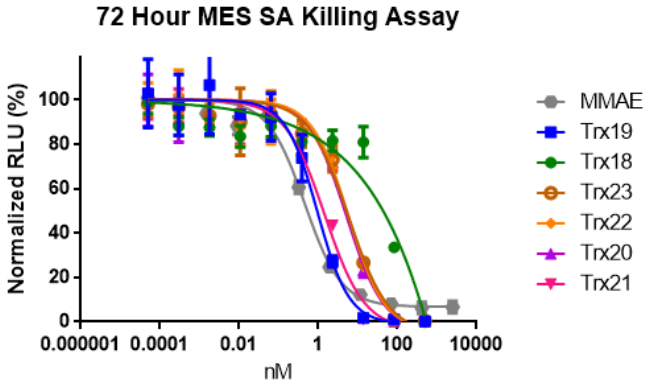
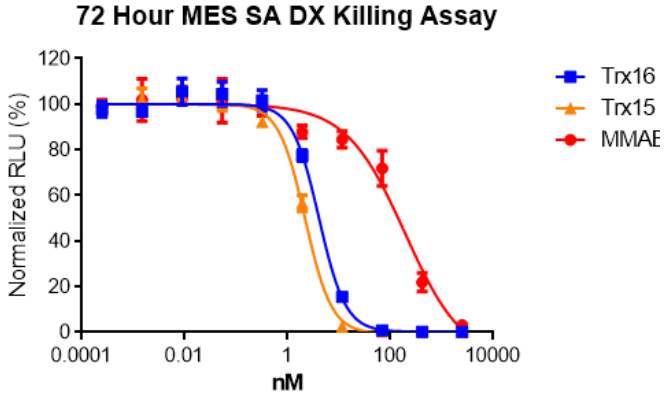
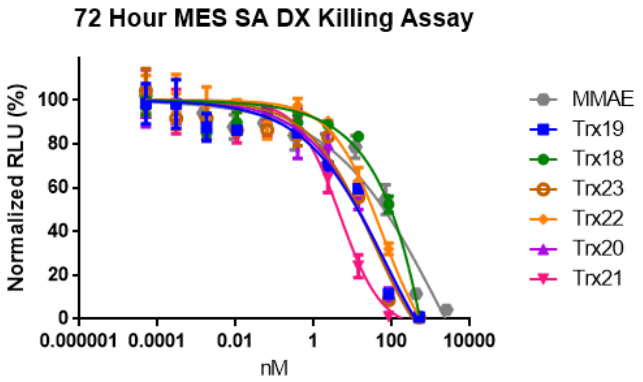
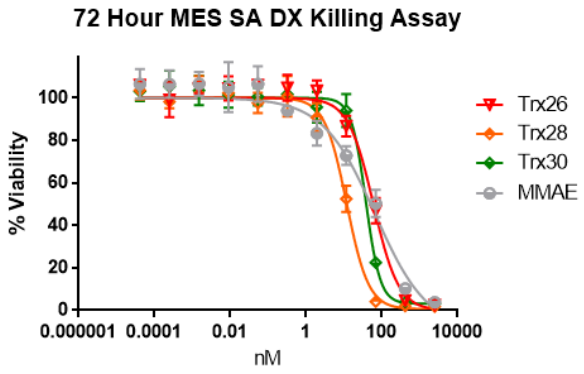
80
60
40
20
0
0.01
1
100
10000
1000000
nM
Trx12
Trx13
Trx14

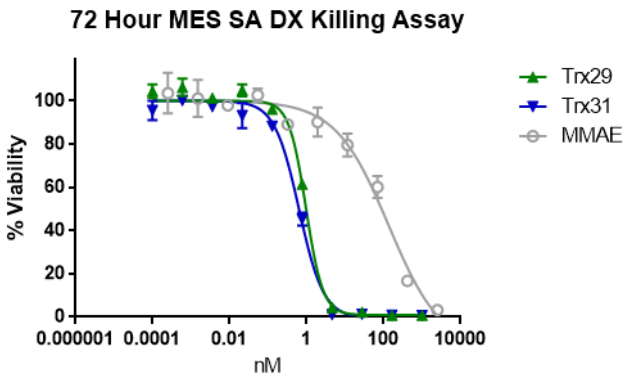

72 Hour MES SA Killing Assay
Normalized RLU (%)
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
nM
Trx16
Trx15
MMAE

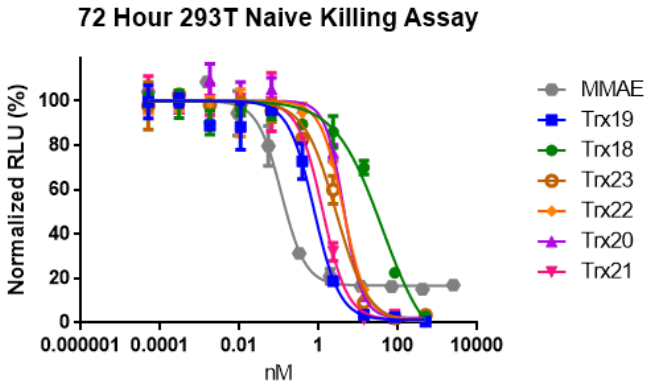

72 Hour MES SA Killing Assay
Normalized RLU (%)
100
80
60
40
20
0
0.000001
0.0001
0.01
1
100
10000
nM
MMAE
Trx19
Trx18
Trx23
Trx22
Trx20
Trx21

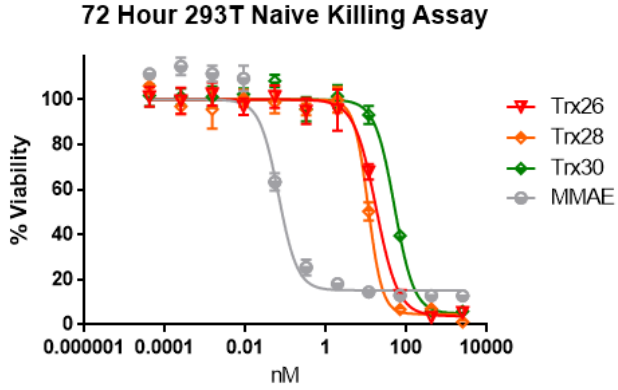

72 Hour MES SA DX Killing Assay
Normalized RLU (%)
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
nM
Trx16
Trx15
MMAE

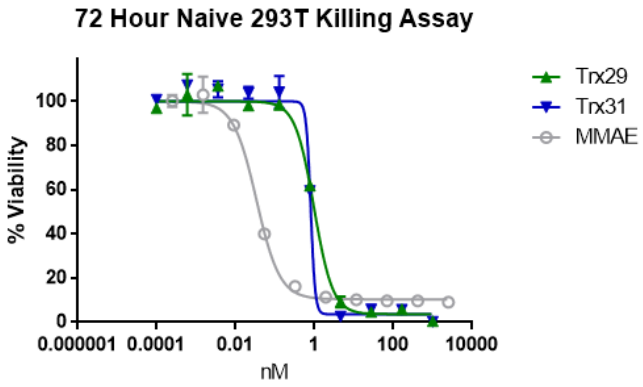

72 Hour MES SA DX Killing Assay
Normalized RLU (%)
nM
MMAE
Trx19
Trx18
Trx23
Trx22
Trx20
Trx21

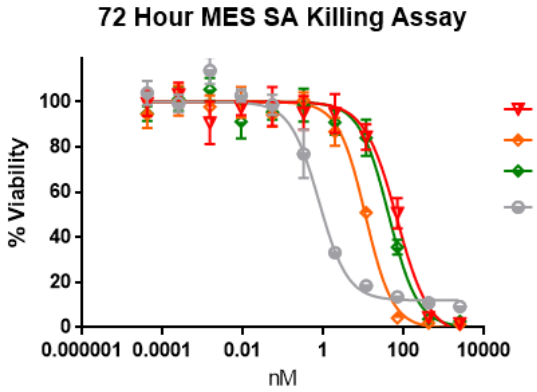

72 Hour MES SA DX Killing Assay
% Viability
nM
Trx26
Trx28
Trx30
MMAE

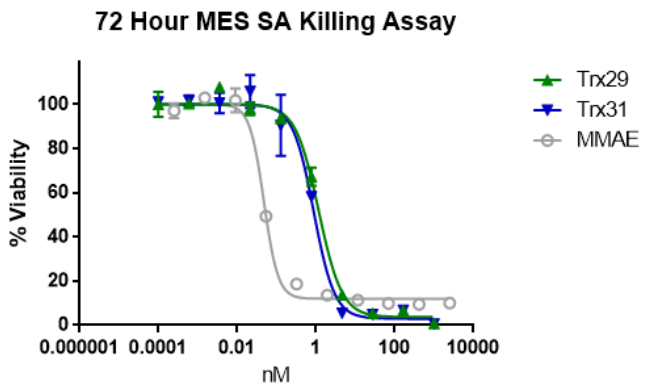

72 Hour MES SA DX Killing Assay
% Viability
nM
Trx29
Trx31
MMAE

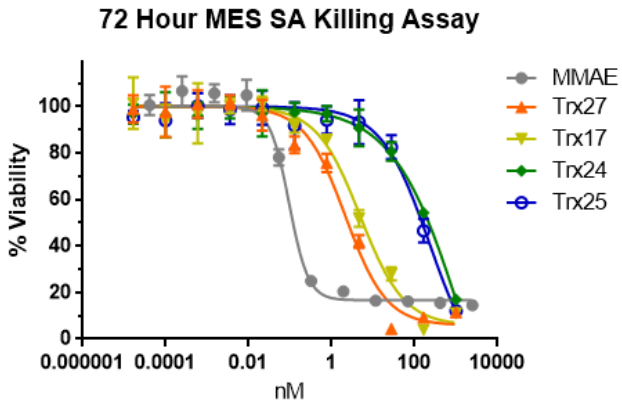

72 Hour 293T Naive Killing Assay
Normalized RLU (%)
nM
MMAE
Trx19
Trx18
Trx23
Trx22
Trx20
Trx21

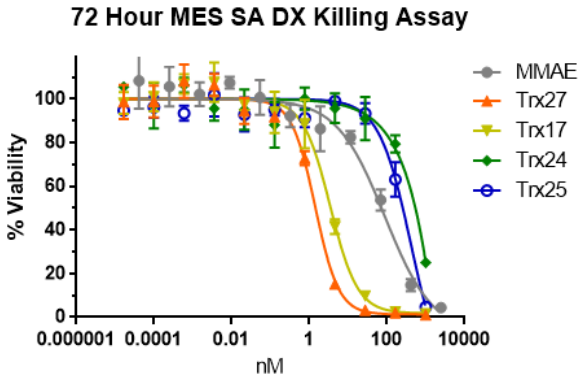

72 Hour 293T Naive Killing Assay
% Viability
nM
Trx26
Trx28
Trx30
MMAE

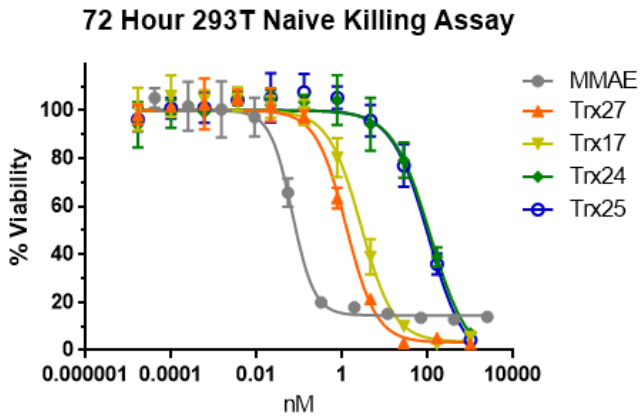

72 Hour Naive 293T Killing Assay
% Viability
nM
Trx29
Trx31
MMAE

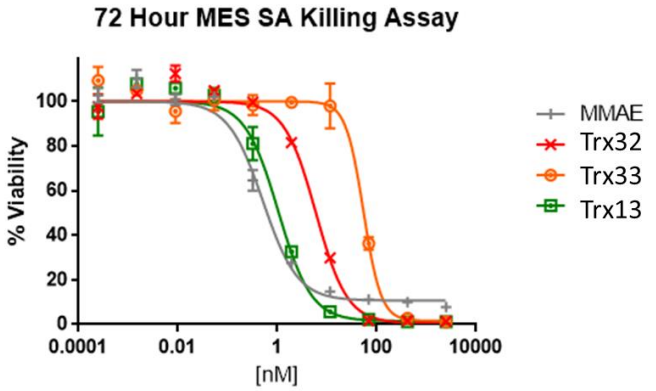

72 Hour MES SA Killing Assay
% Viability
nM
Trx26
Trx28
Trx30
MMAE

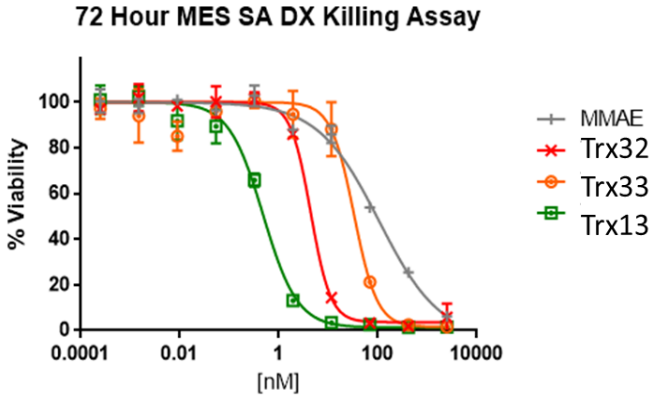

72 Hour MES SA Killing Assay
% Viability
nM
Trx29
Trx31
MMAE

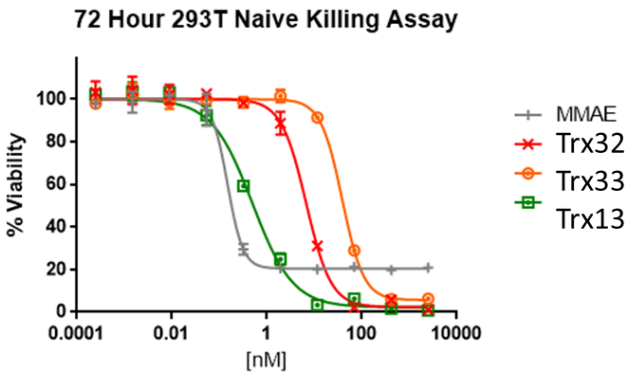

72 Hour MES SA Killing Assay
% Viability
100
80
60
40
20
0
0.000001
0.0001
0.01
1
100
10000
nM
MMAE
Trx27
Trx17
Trx24
Trx25


72 Hour MES SA DX Killing Assay
% Viability
100
80
60
40
20
0
0.000001
0.0001
0.01
1
100
10000
nM
MMAE
Trx27
Trx17
Trx24
Trx25


72 Hour 293T Naive Killing Assay
% Viability
100
80
60
40
20
0
0.000001
0.0001
0.01
1
100
10000
nM
MMAE
Trx27
Trx17
Trx24
Trx25


72 Hour MES SA Killing Assay
% Viability
100
80
60
40
20
0
0.0001
0.01
1
100
10000
[nM]
MMAE
Trx32
Trx33
Trx13


72 Hour MES SA DX Killing Assay
% Viability
100
80
60
40
20
0
0.0001
0.01
1
100
10000
[nM]
MMAE
Trx32
Trx33
Trx13

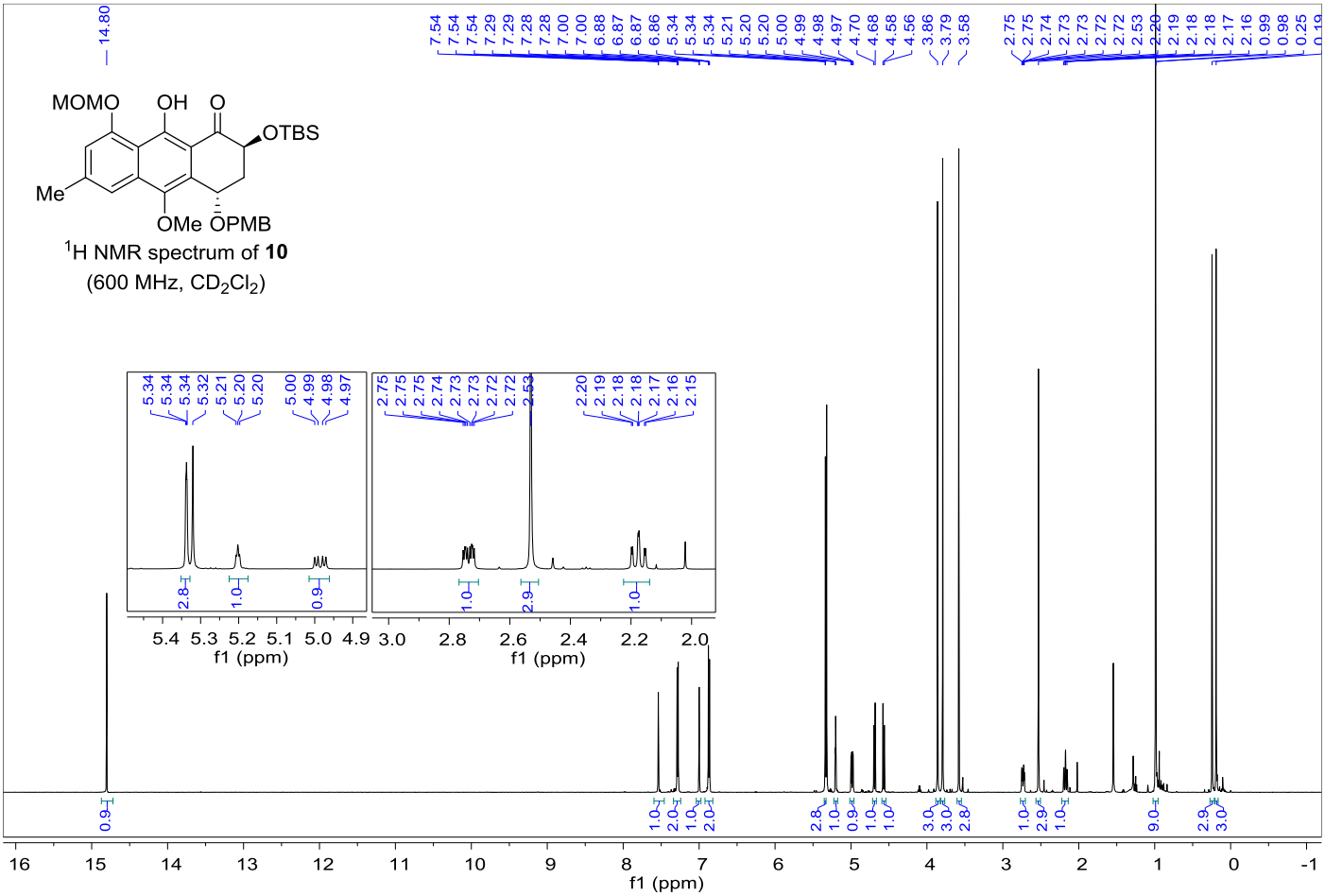

72 Hour 293T Naive Killing Assay
% Viability
100
80
60
40
20
0
0.0001
0.01
1
100
10000
[nM]
MMAE
Trx32
Trx33
Trx13

Note Regarding the Multiplicity Edited HSQC Spectra

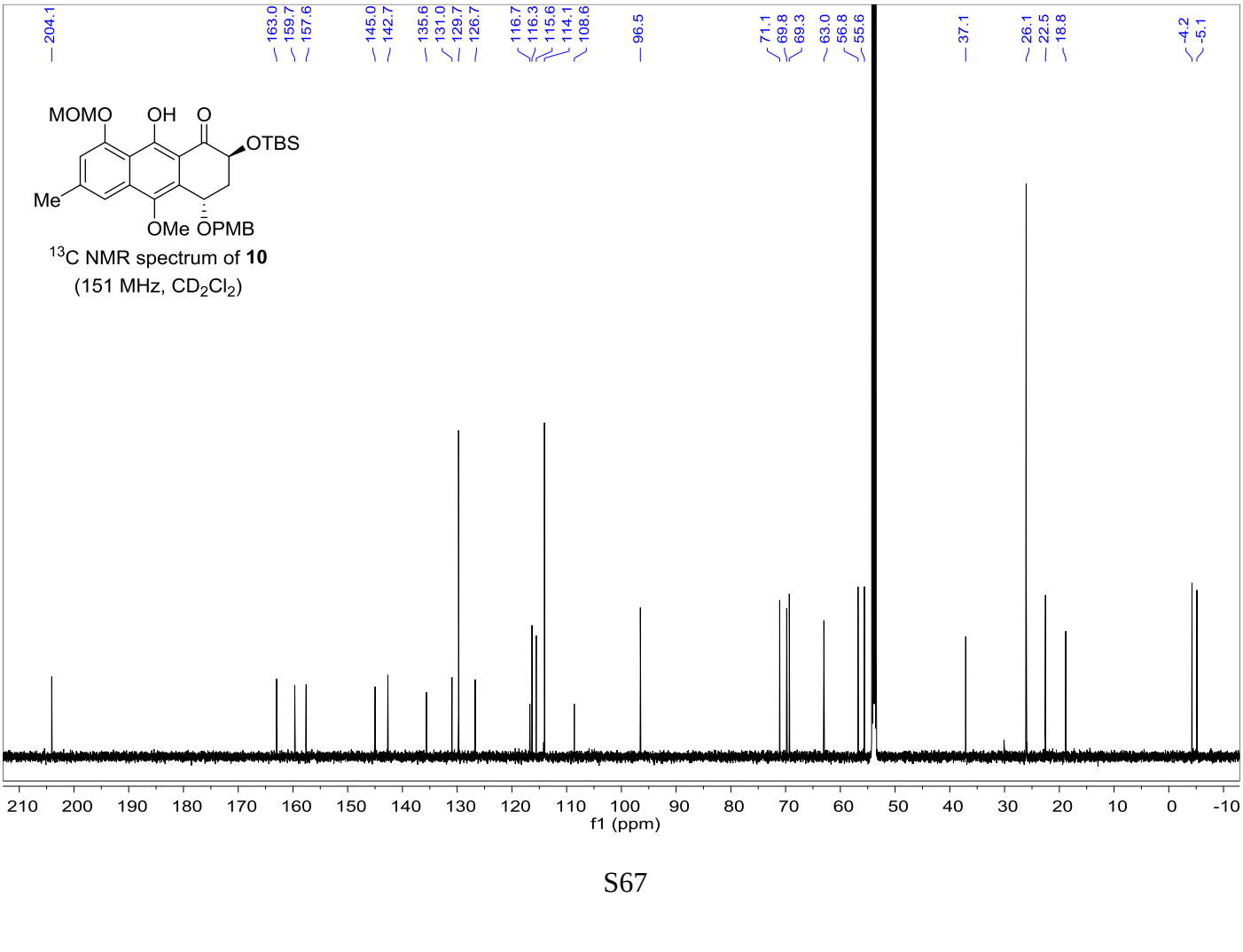
After obtaining the multiplicity edited HSQC spectra (see pages S122–S125, S134, S136) it was realized that the d21 and d24 parameters used for the acquisition of the spectra were incorrectly set for the given $^{1}J_{CH}$ value [cnst2 = 145 Hz] by the software (the values are defined as follows: d21 = 0.5/cnst2; d24 = 0.125/cnst2; and as a result d21:d24 = 4:1). The wrong calculation of d21 and d24 seems to be an inherent issue of the software used to acquire the spectra. Several examples in the literature can be found with the same wrong settings, albeit not being further discussed there (for a small selection of examples see ref. 7). The value of the spectra with regard to the structural elucidation was not affected by the slightly incorrect values for d21 and d24. However, the slightly improper values for d21 and d24 caused the cross peaks for epoxy methylene subunits to show the wrong phase in our experiments. Similar phase anomalies on oxirane containing molecules can be found in the literature,[8] presumably due to the wrong values for d21 and d24 (unfortunately these acquisition parameters were not pointed out within these publications). For compound **Trx12** (see pages S124 and S125) we were able to manually overwrite these improper values (page S124) and obtain the included multiplicity edited HSQC spectrum with the correct set of parameters (page S125). In this case all cross peaks exhibited the correct phase [as opposed to the comparison experiment with the same value for cnst2 = 160 Hz but with the automatically set (wrong) values for d21 and d24; cf. pages S124 and S125].

Lastly, it should be noted that even with the correctly adjusted parameters (i.e., cnst2, d21, and d24) the phase of certain cross peaks might show the wrong phase if their $^{1}J_{CH}$ values differ significantly from the set cnst2 parameter (unpublished results).

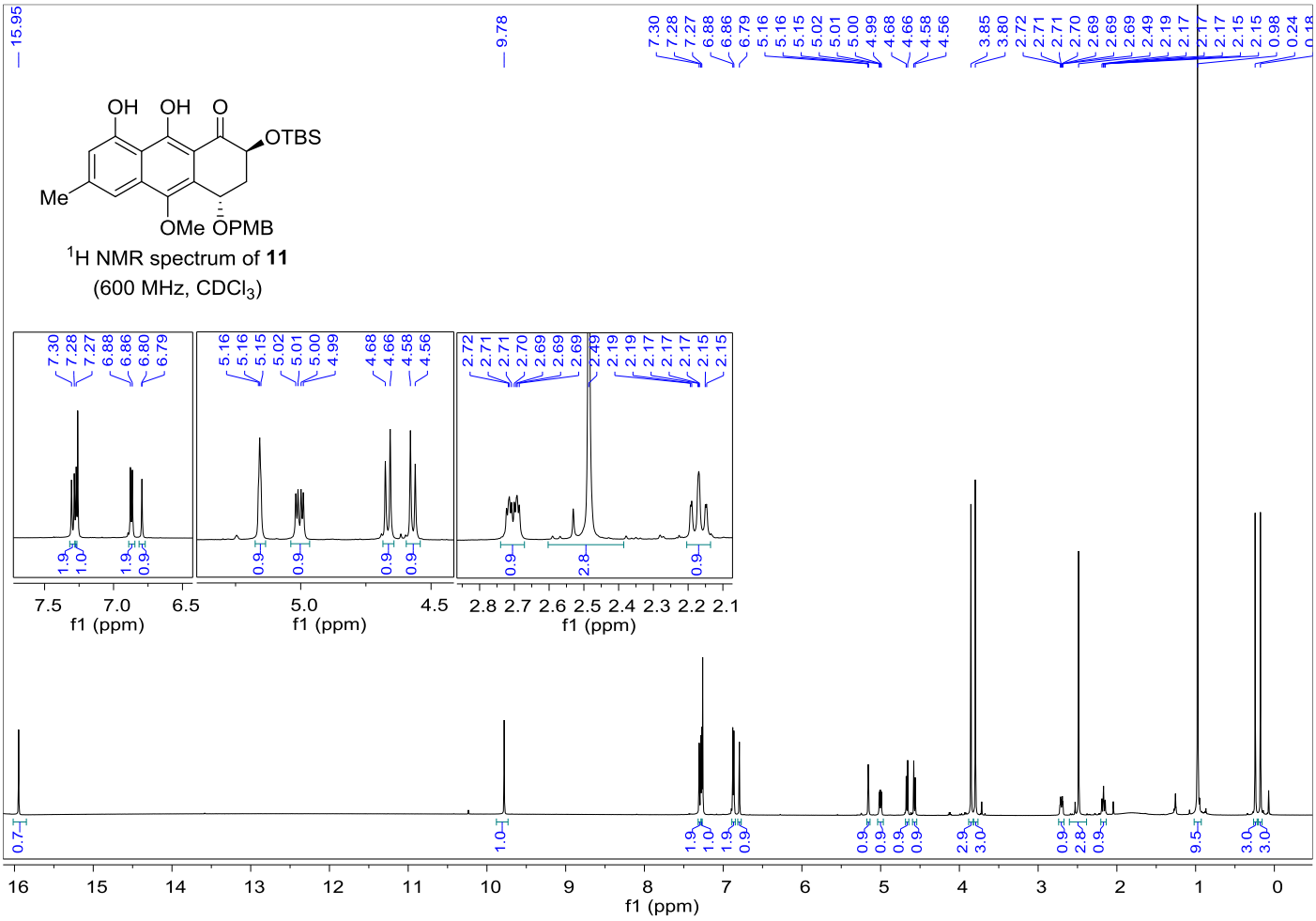
^{1}H, ^{13}C and 2D NMR Spectra of Compounds



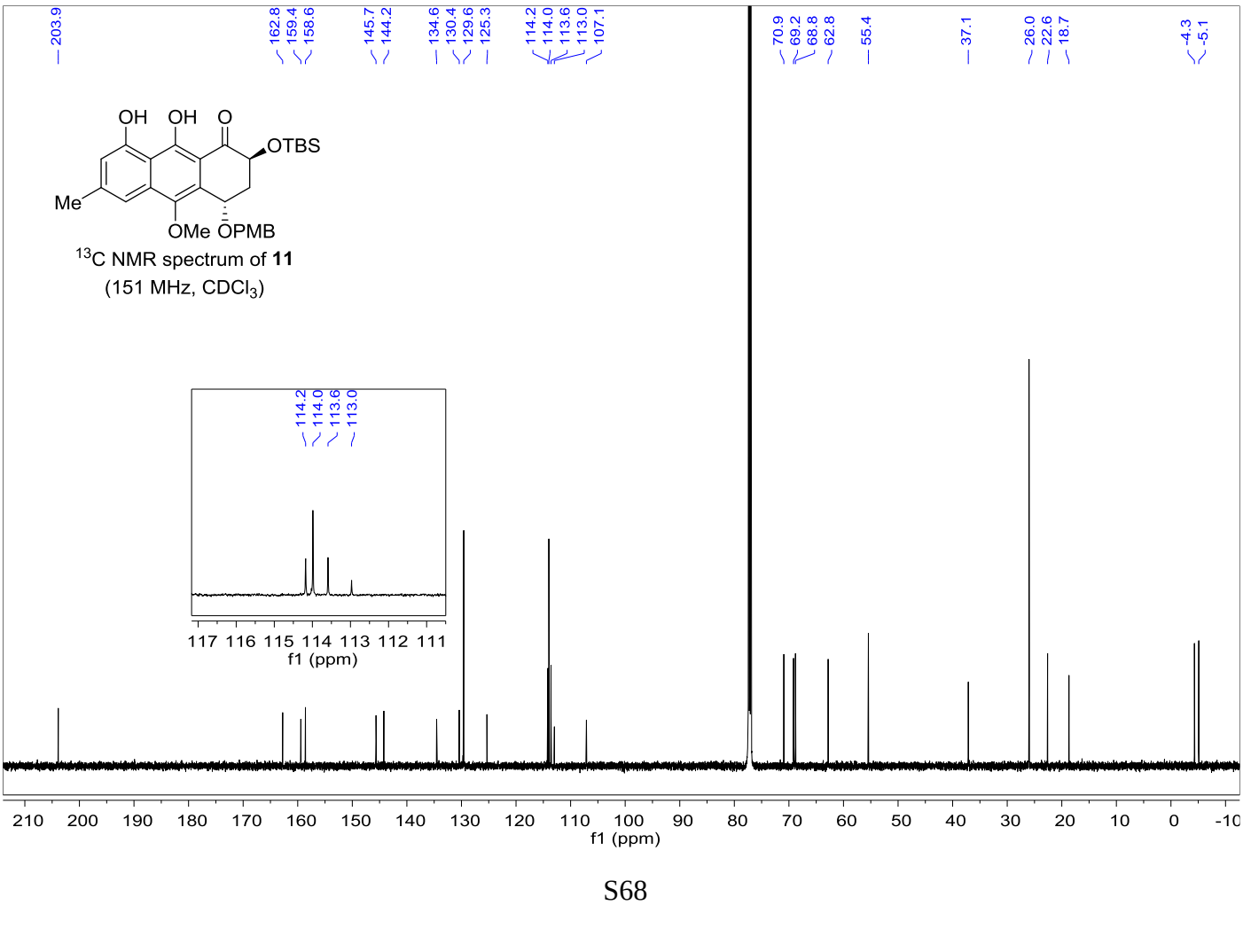
^{1}H NMR spectrum of **10**
(600 MHz, CD_2Cl_2)



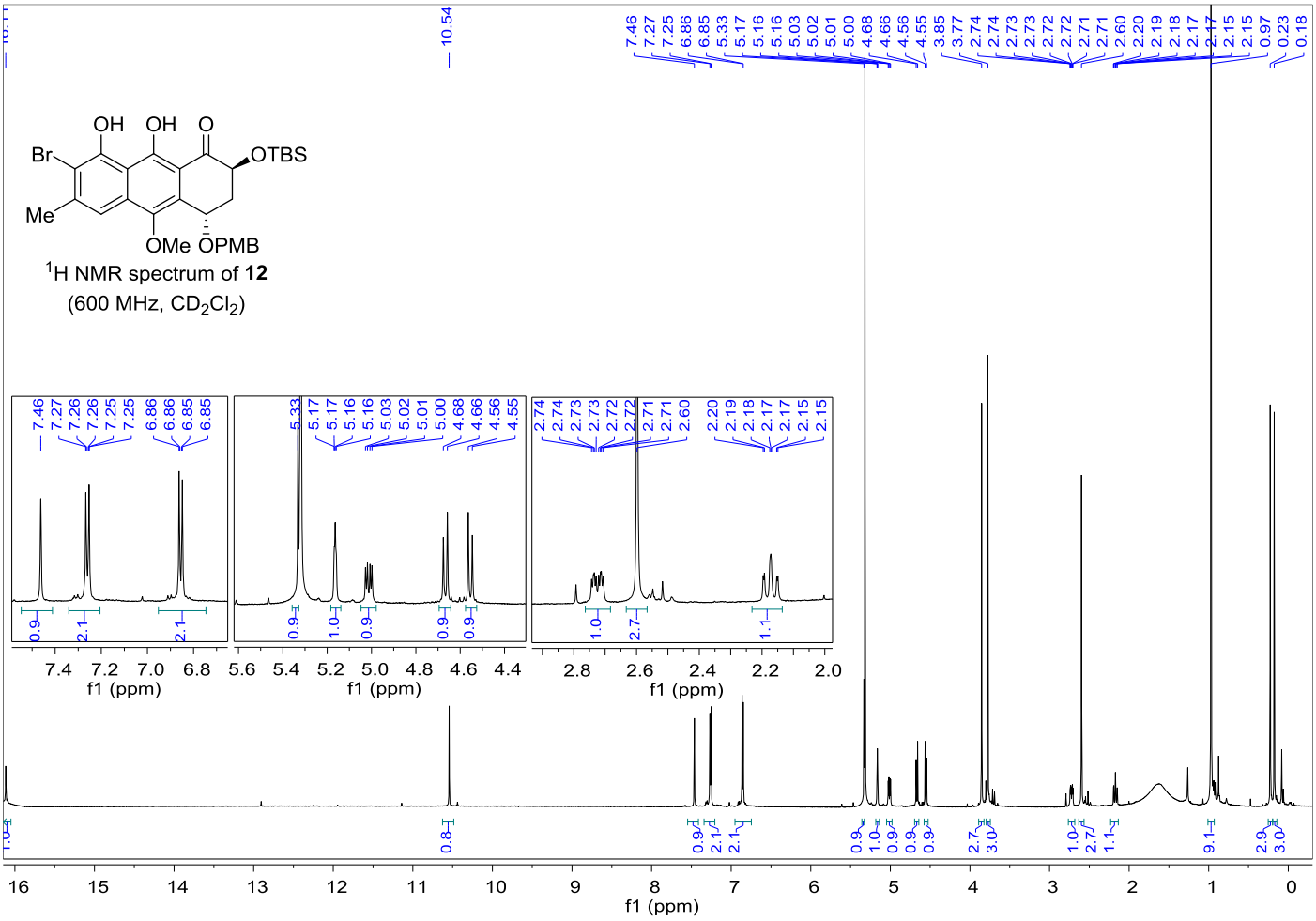
^{13}C NMR spectrum of **10**
(151 MHz, CD_2Cl_2)



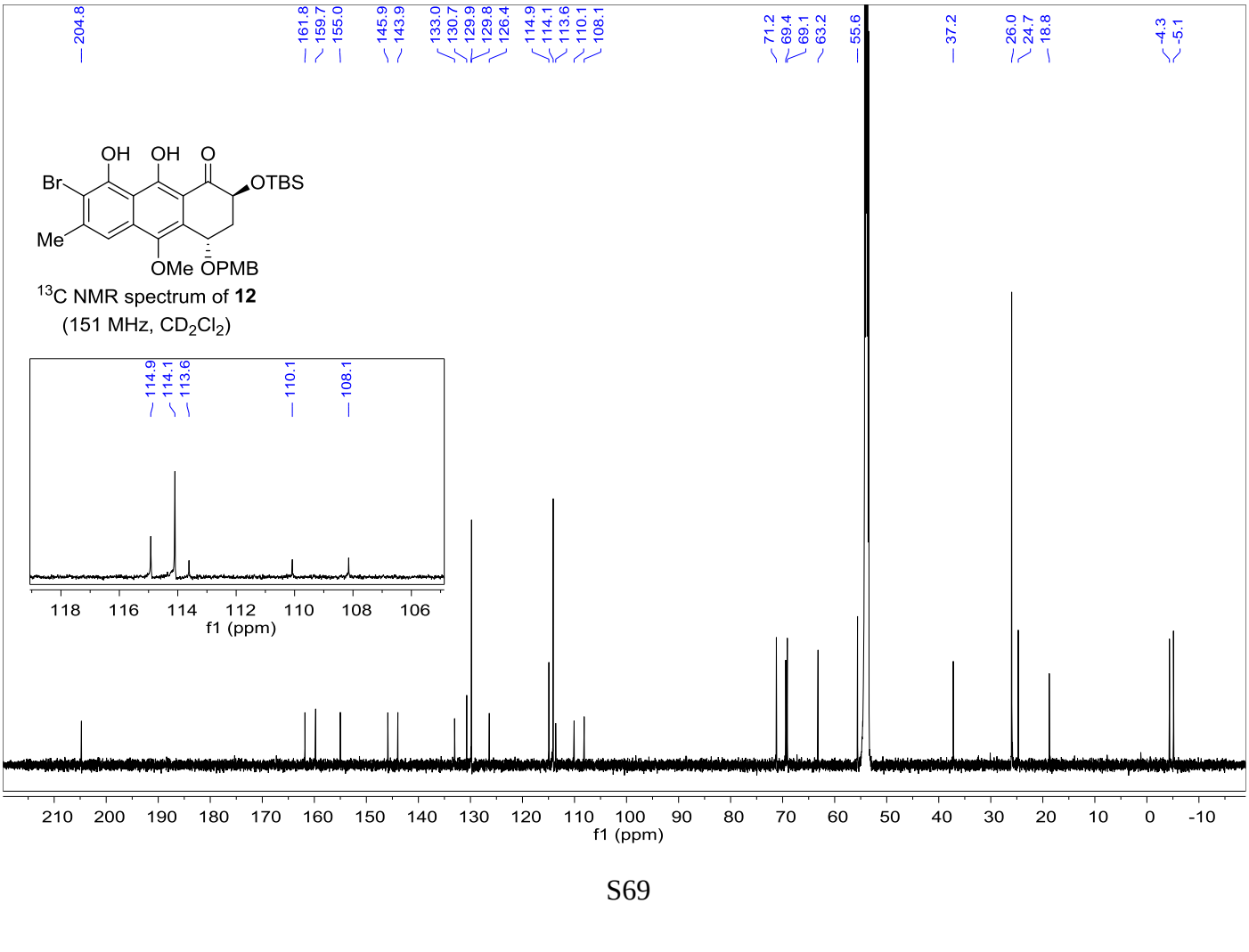
^{1}H NMR spectrum of **11**
(600 MHz, $CDCl_3$)



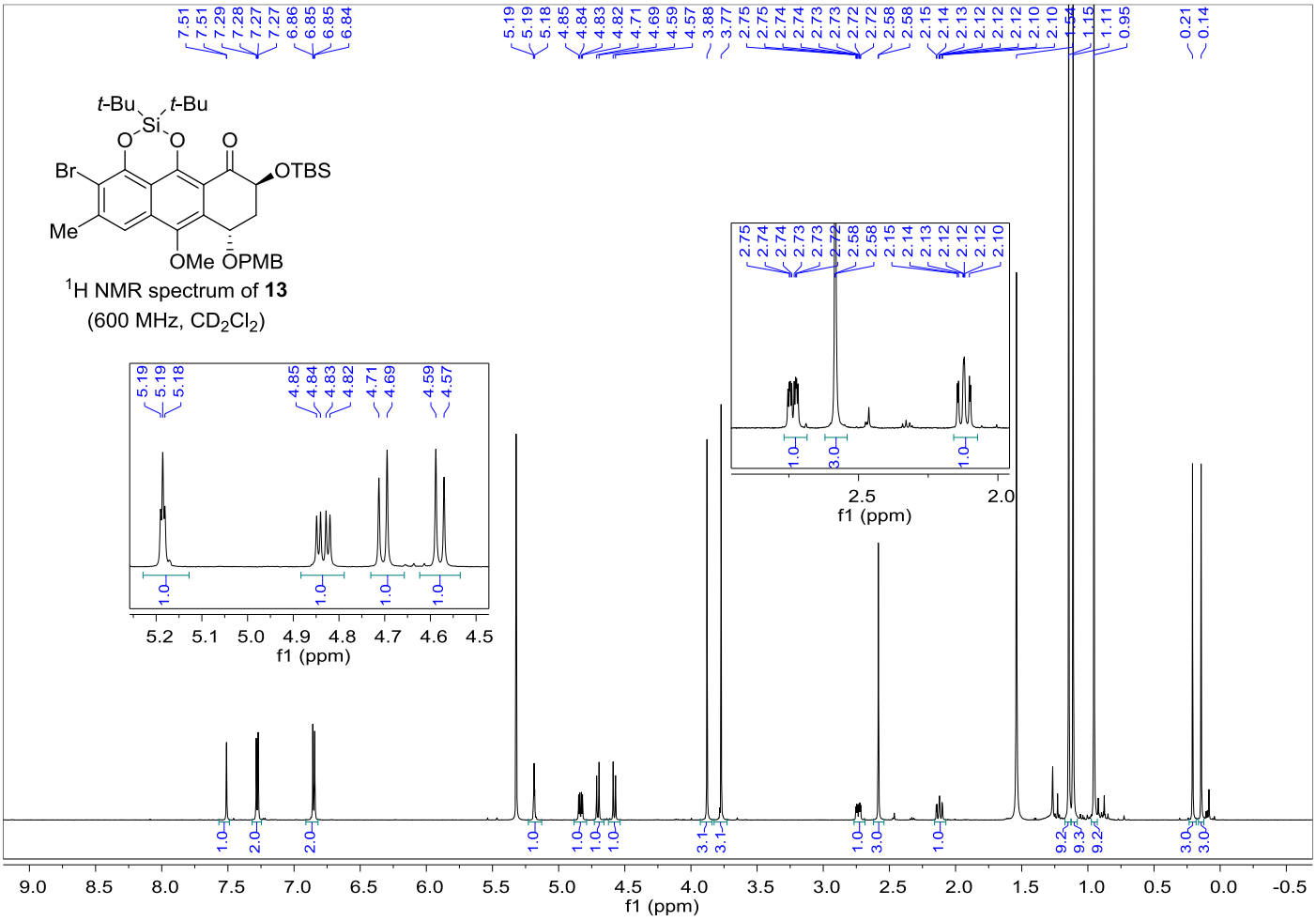
^{13}C NMR spectrum of **11**
(151 MHz, $CDCl_3$)

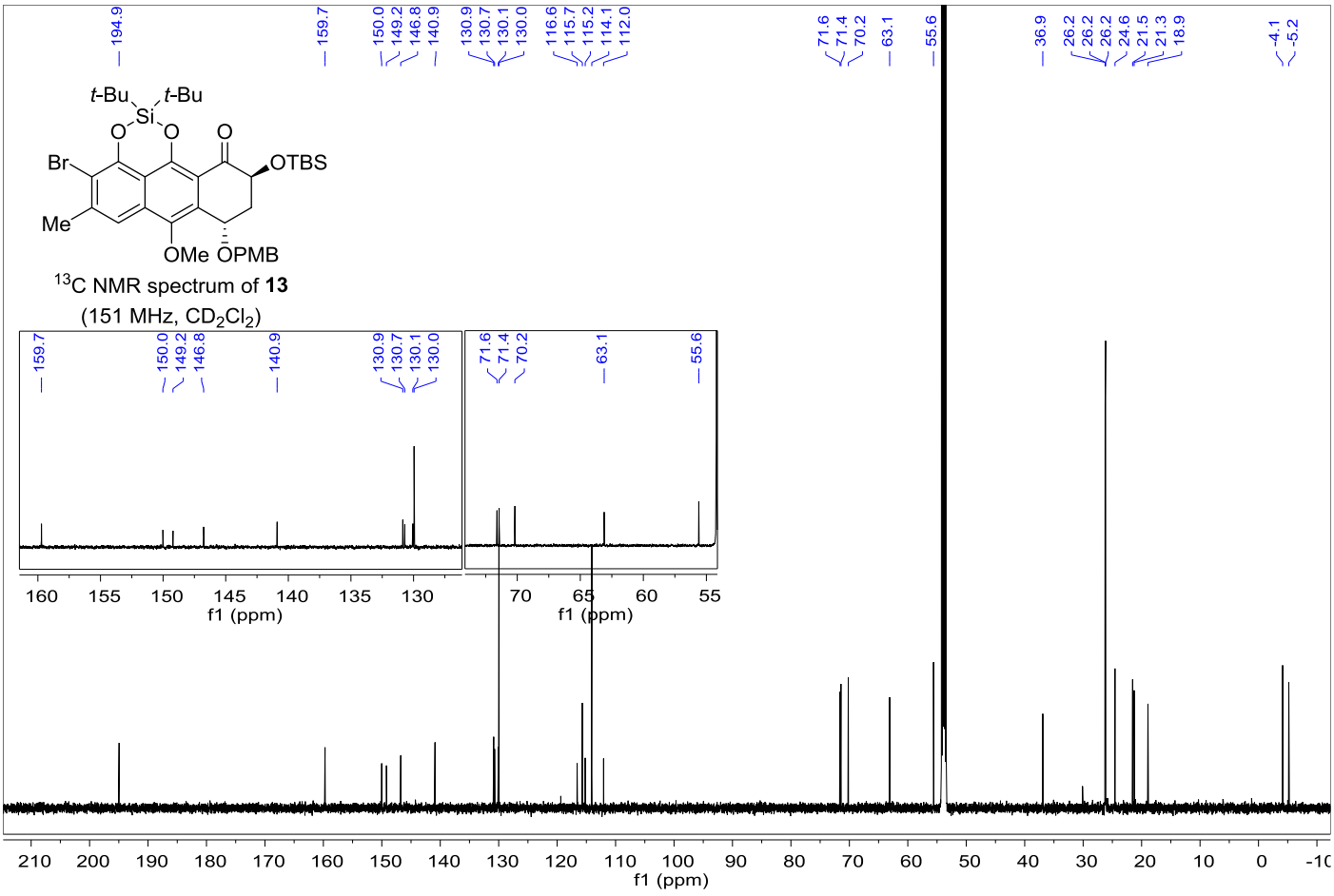


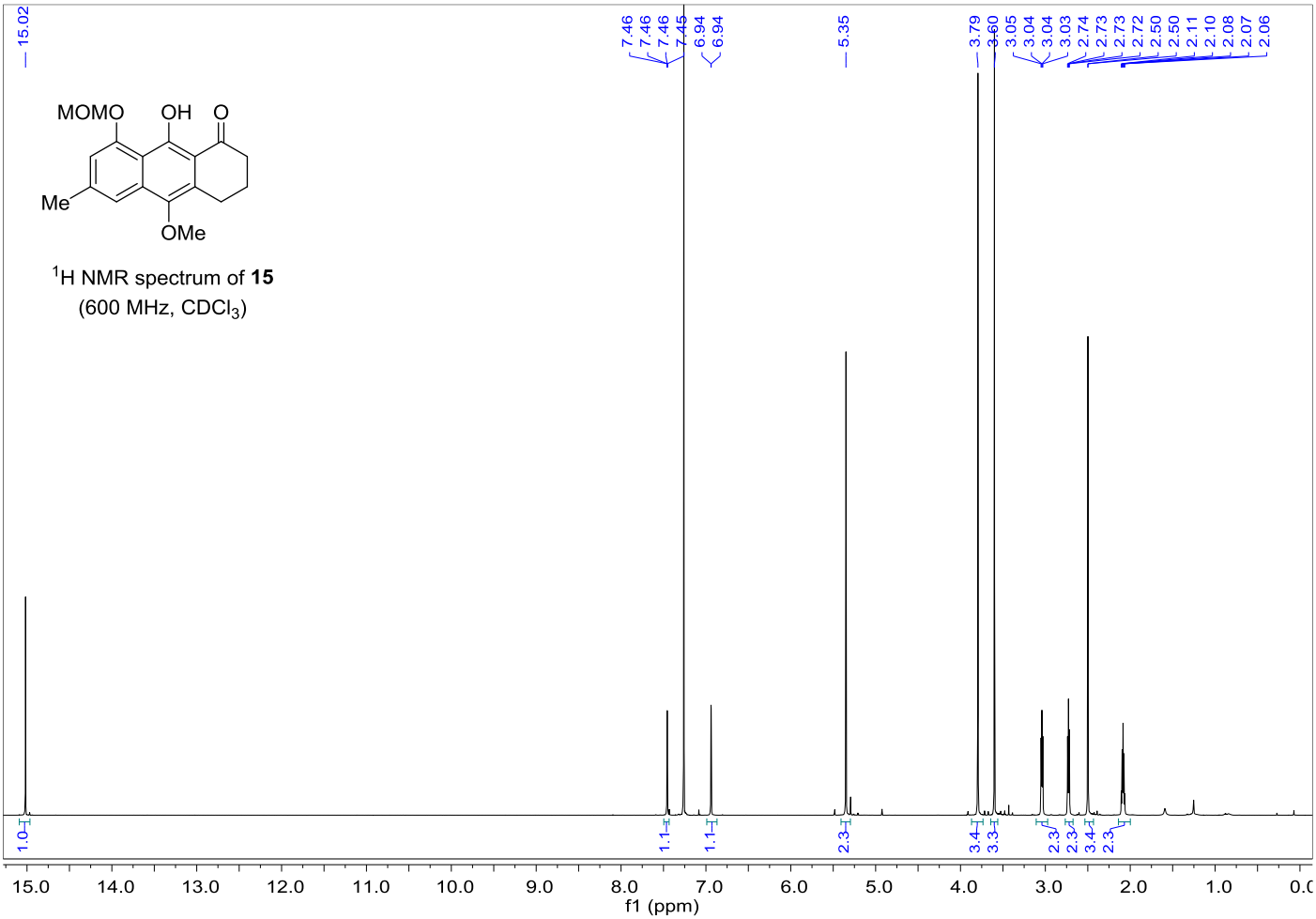
^{1}H NMR spectrum of **12**
(600 MHz, CD_2Cl_2)



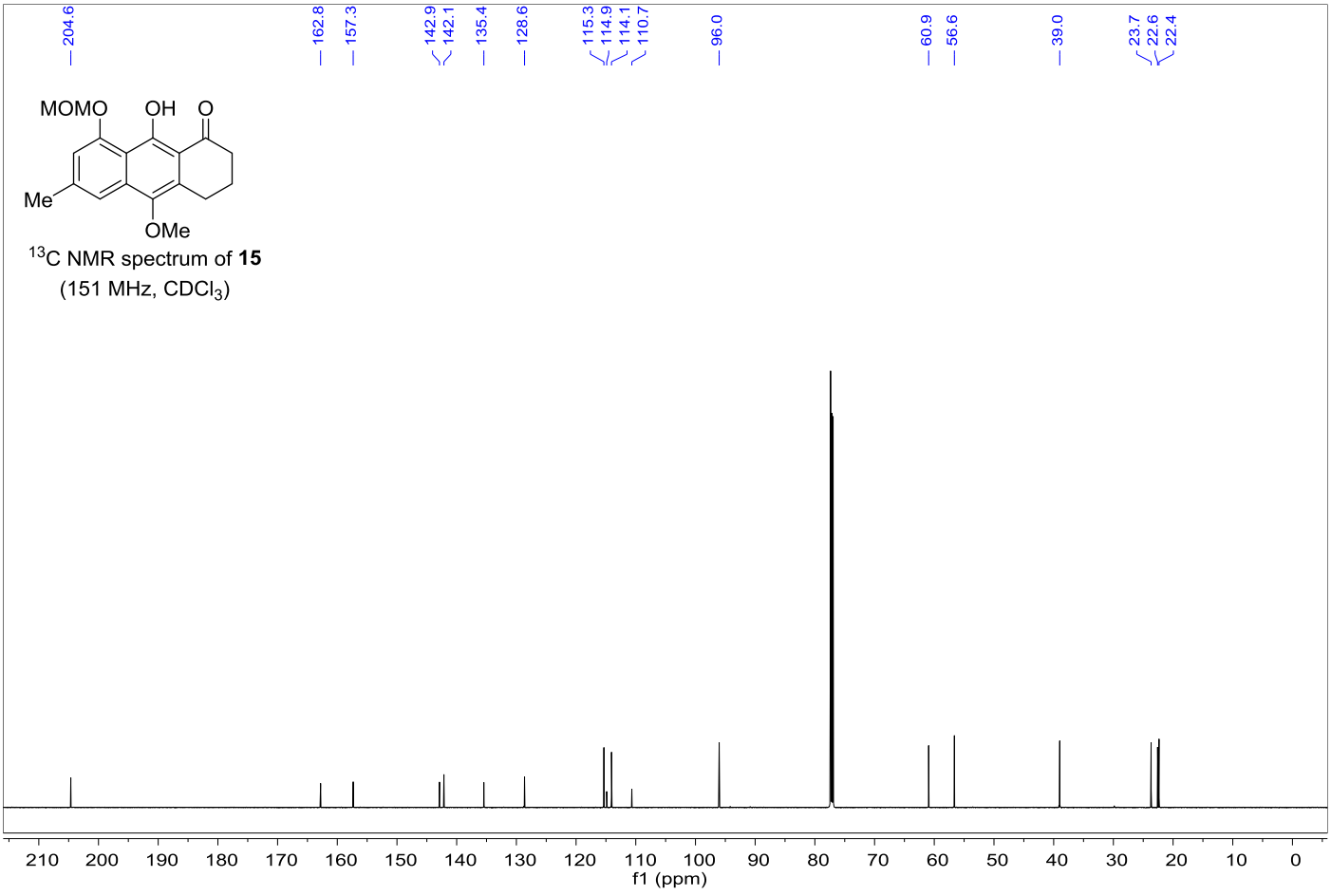
^{13}C NMR spectrum of **12**
(151 MHz, CD_2Cl_2)


t-Bu
t-Bu
Si
O
O
O
Br
OTBS
Me
OMe
OPMB
1H NMR spectrum of 13
(600 MHz, CD2Cl2)
f1 (ppm)

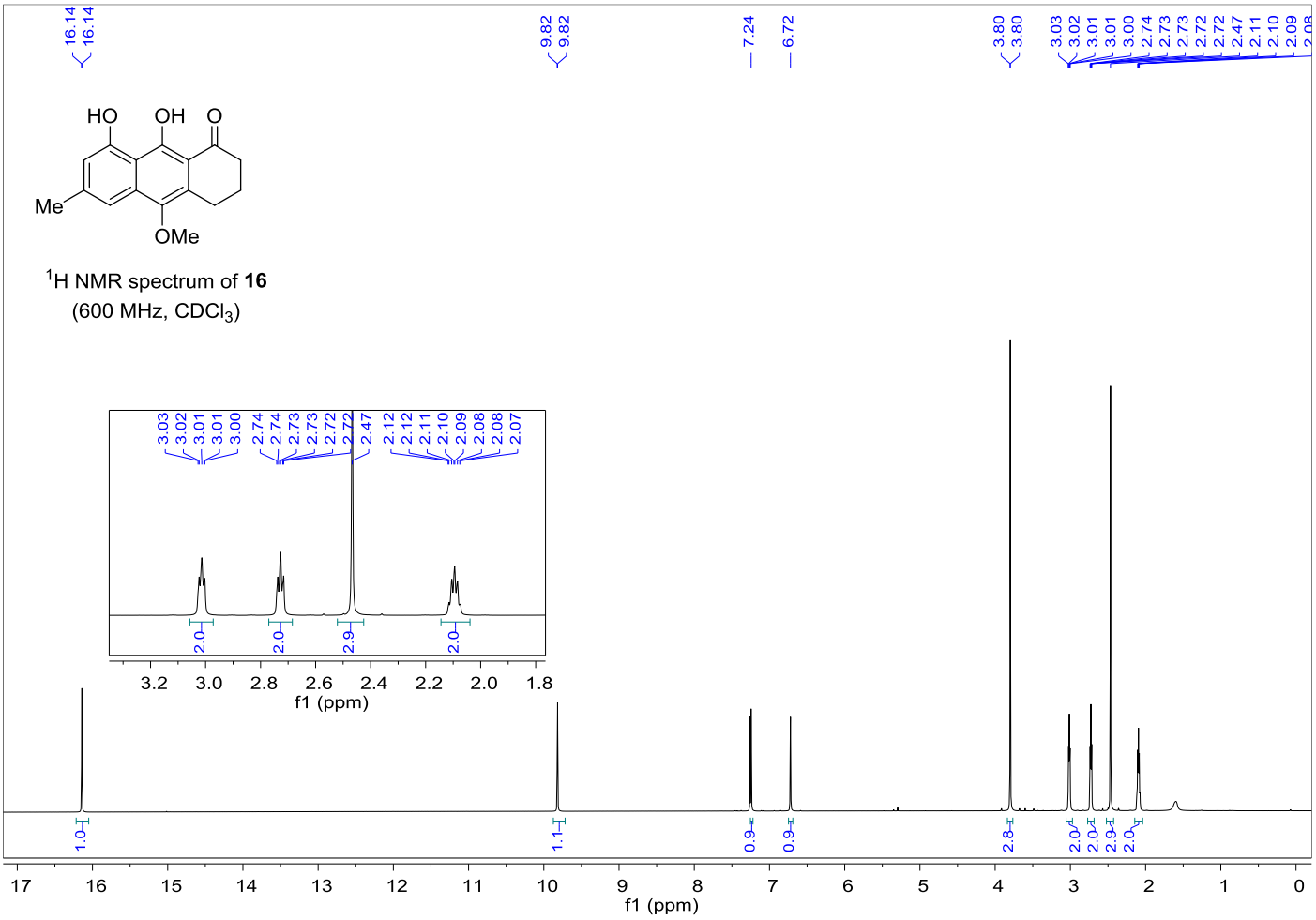

t-Bu
t-Bu
Si
O
O
O
Br
OTBS
Me
OMe
OPMB
13C NMR spectrum of 13
(151 MHz, CD2Cl2)
f1 (ppm)



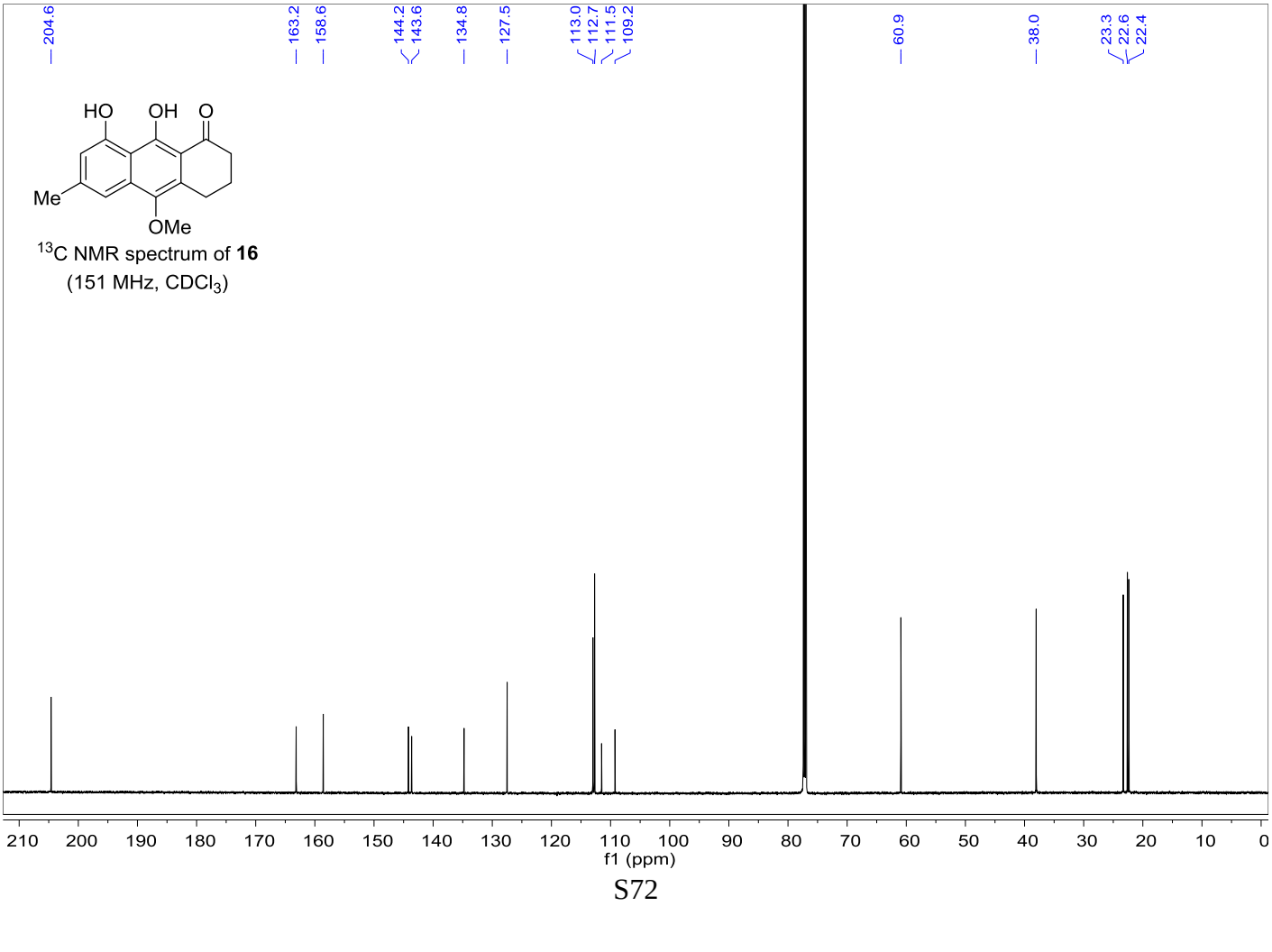
^{1}H NMR spectrum of **15**
(600 MHz, $CDCl_3$)



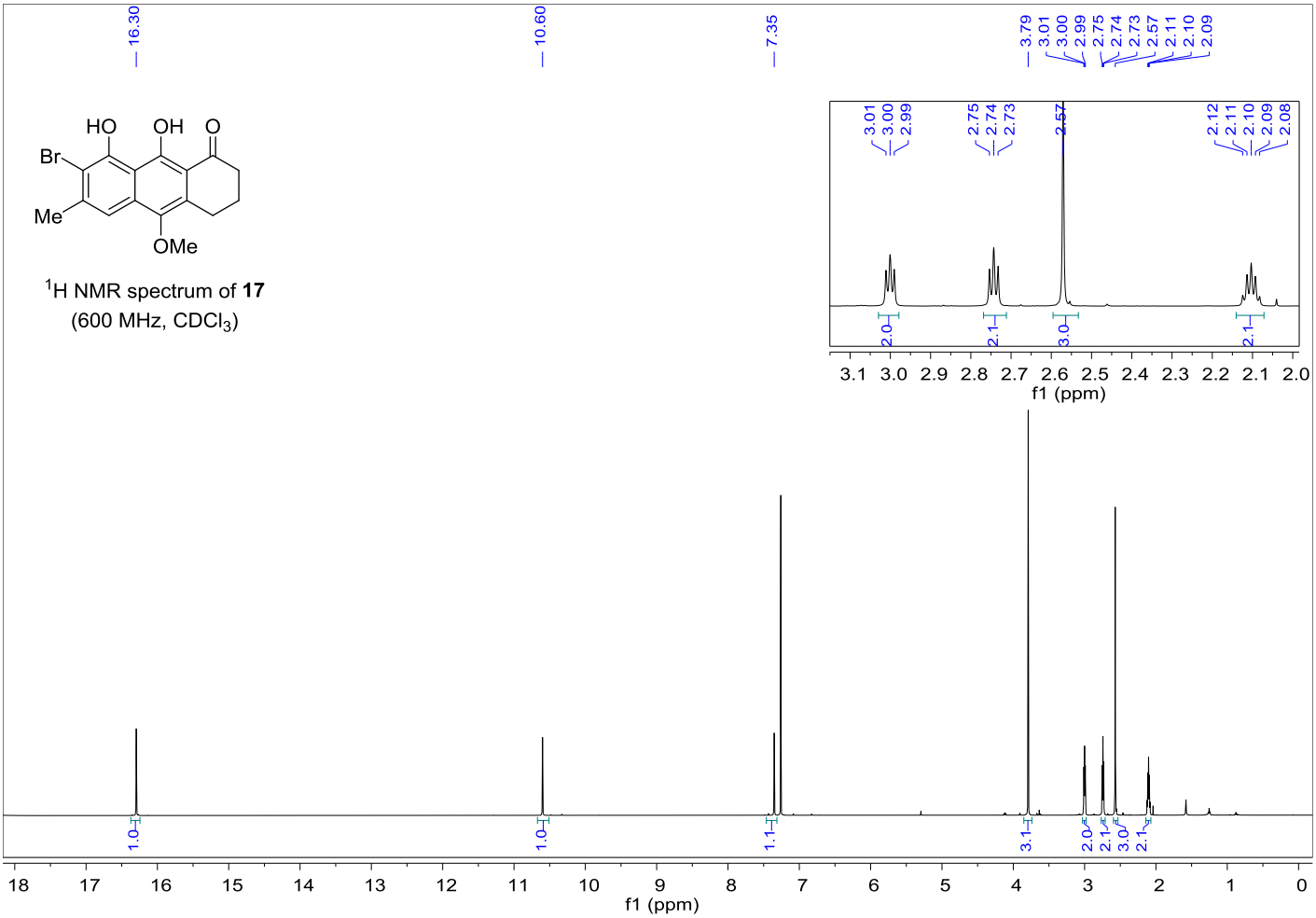
^{13}C NMR spectrum of **15**
(151 MHz, $CDCl_3$)



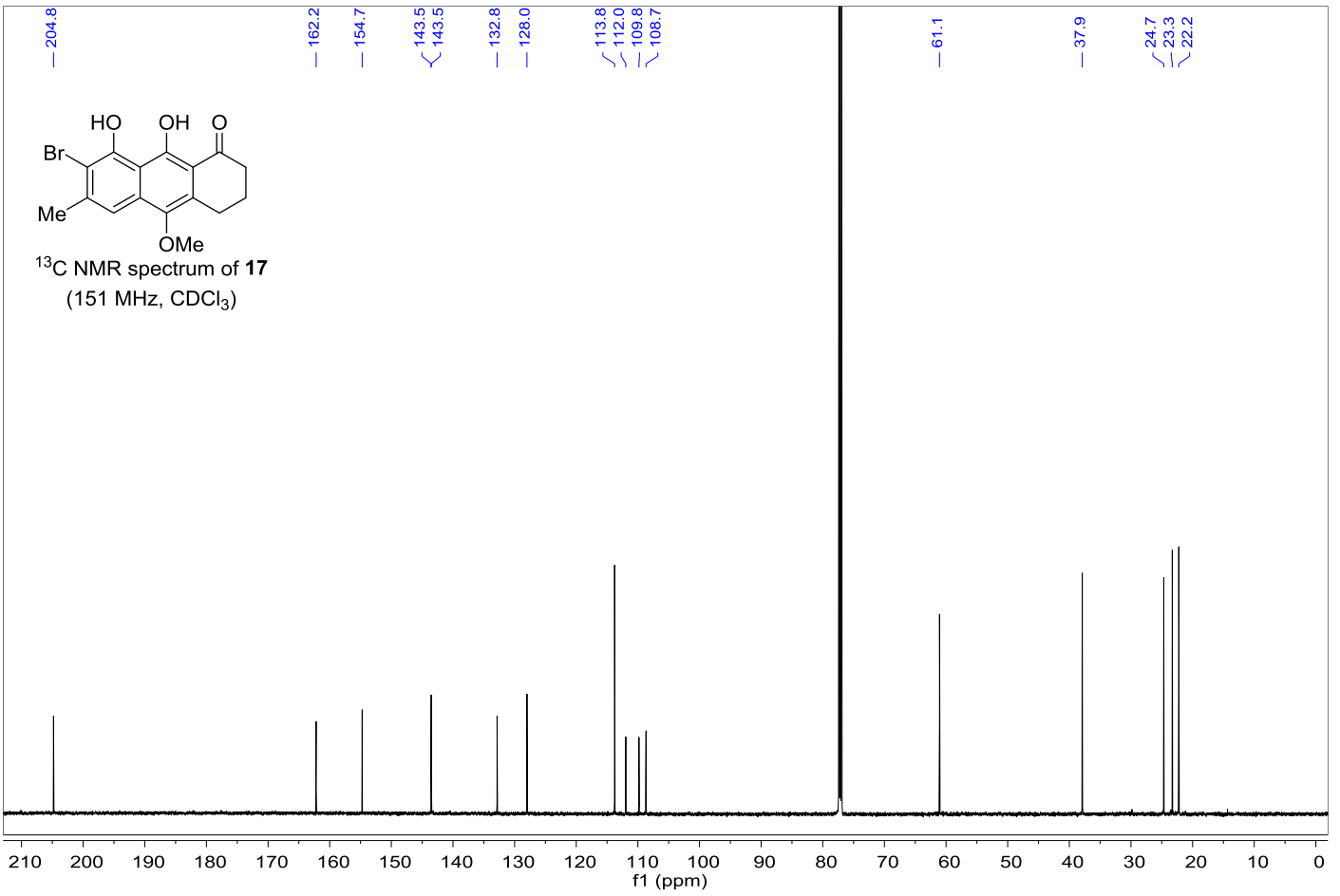
^{1}H NMR spectrum of **16**
(600 MHz, $CDCl_3$)



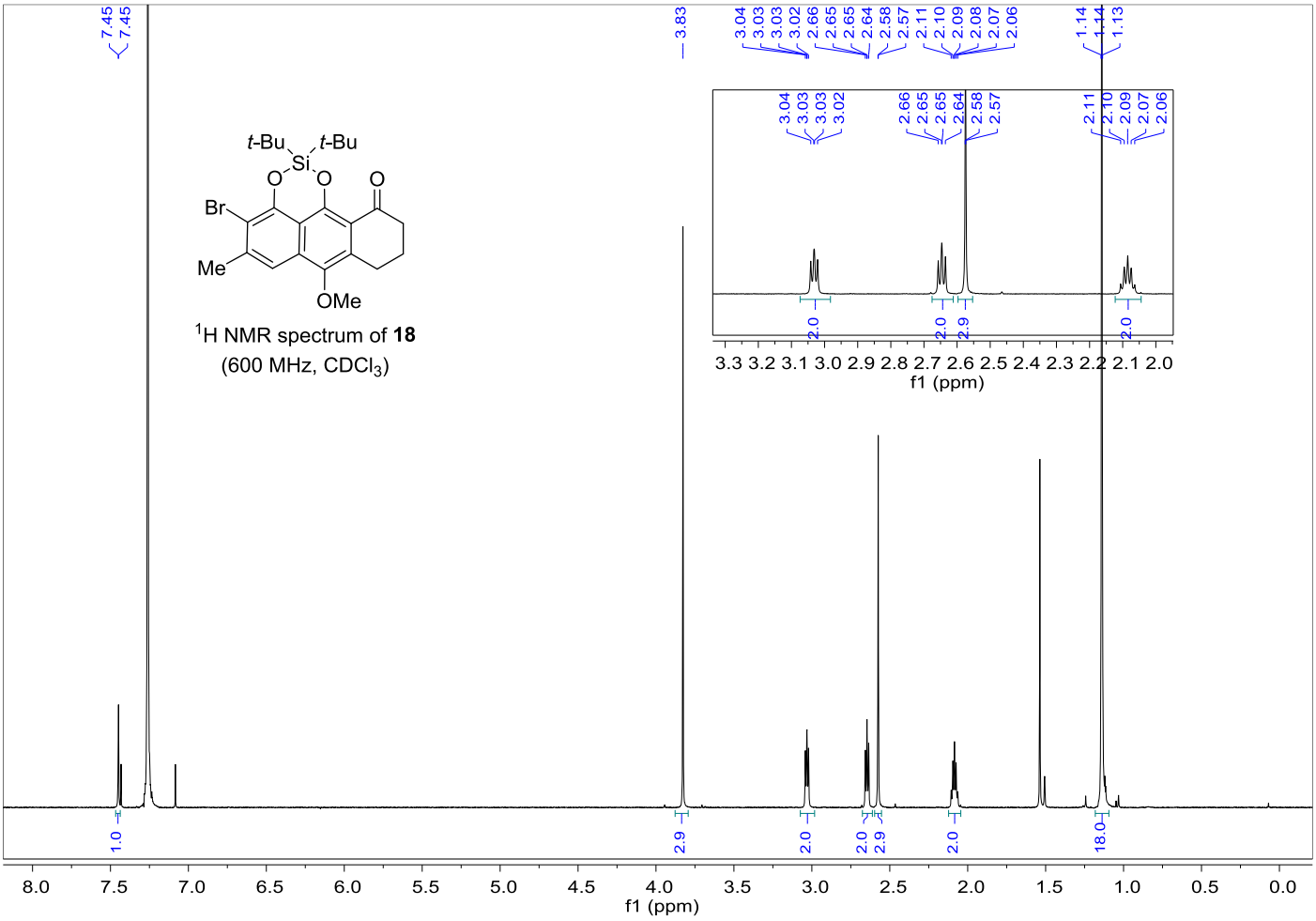
^{13}C NMR spectrum of **16**
(151 MHz, $CDCl_3$)

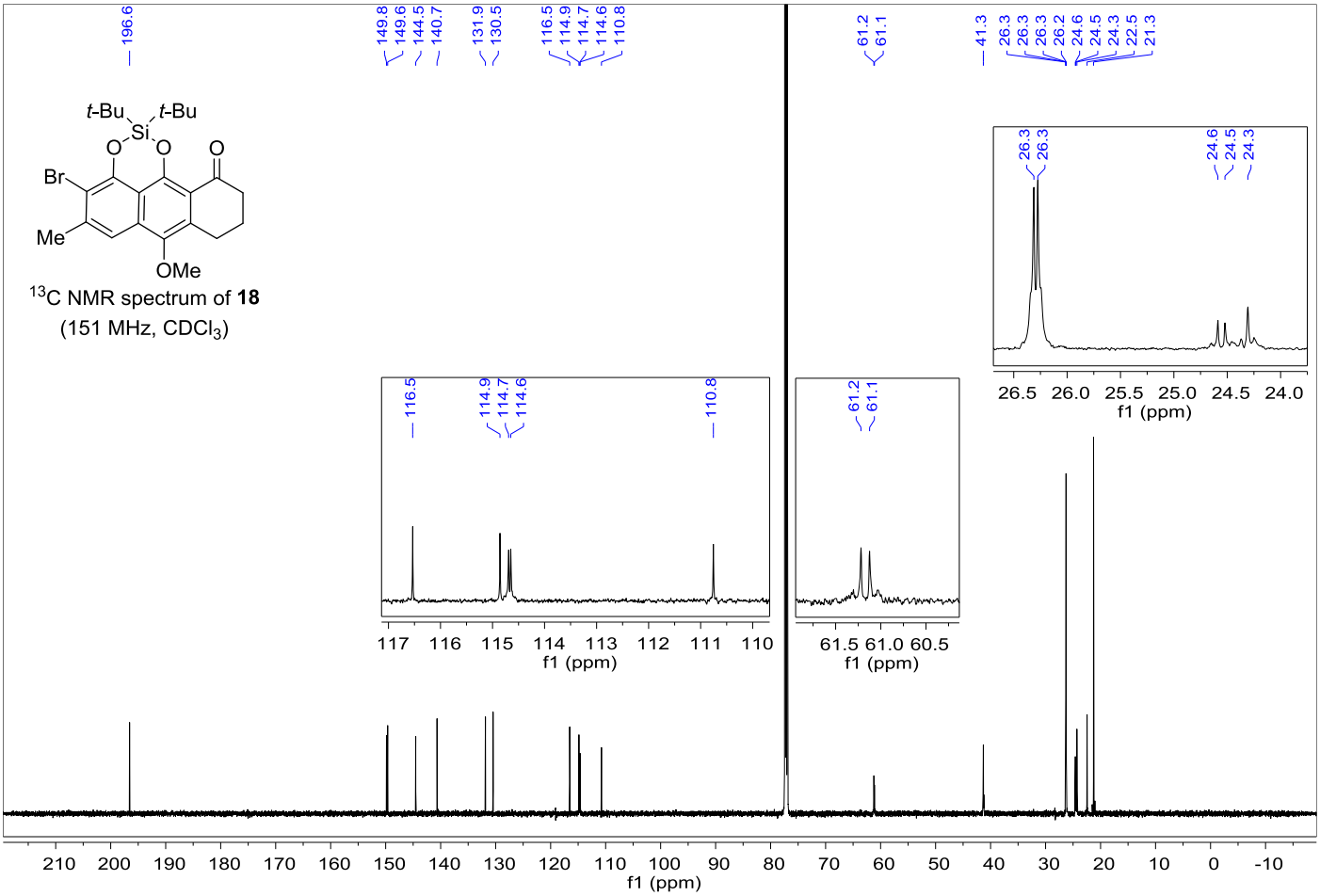


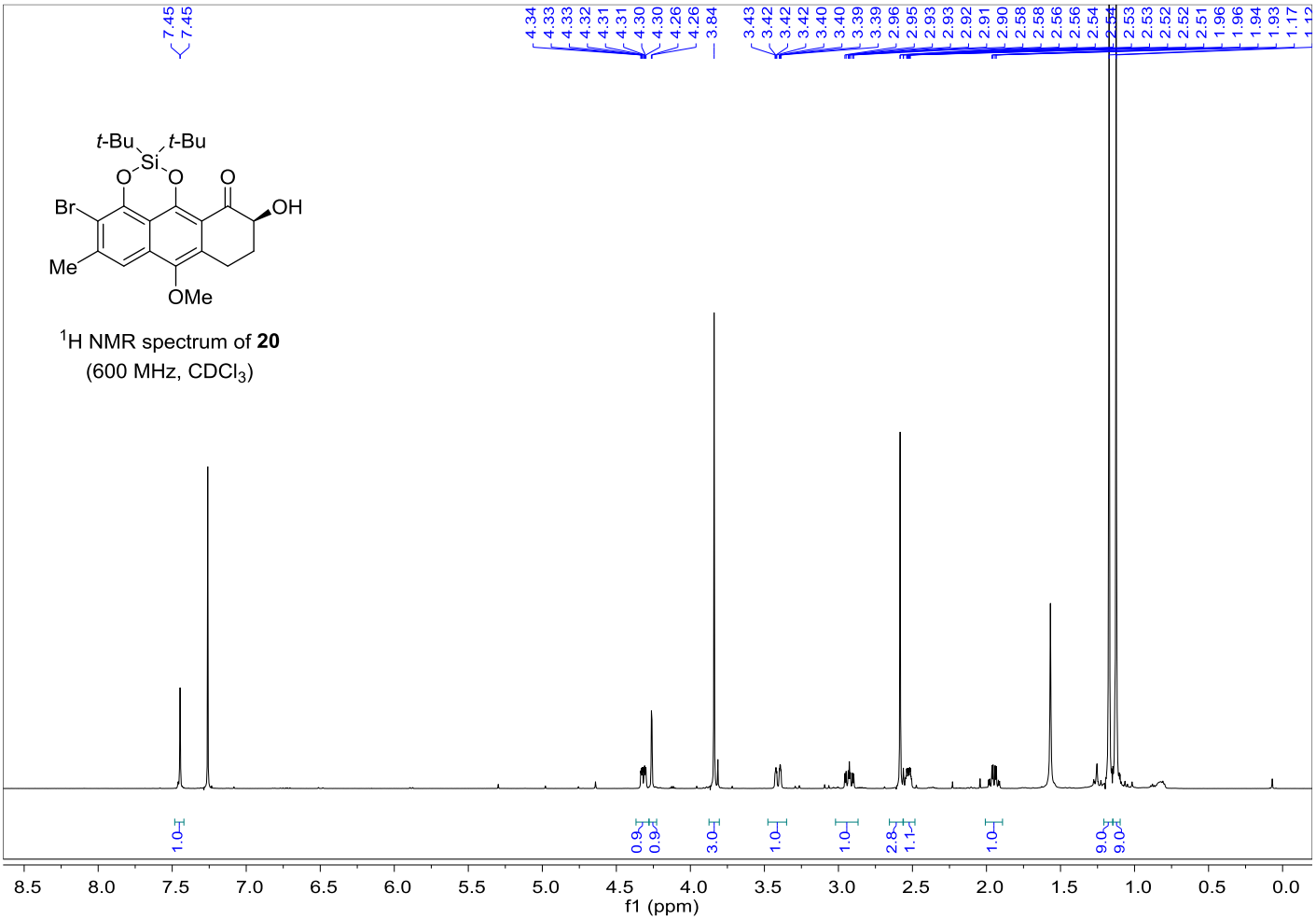
^{1}H NMR spectrum of **17**
(600 MHz, $CDCl_3$)



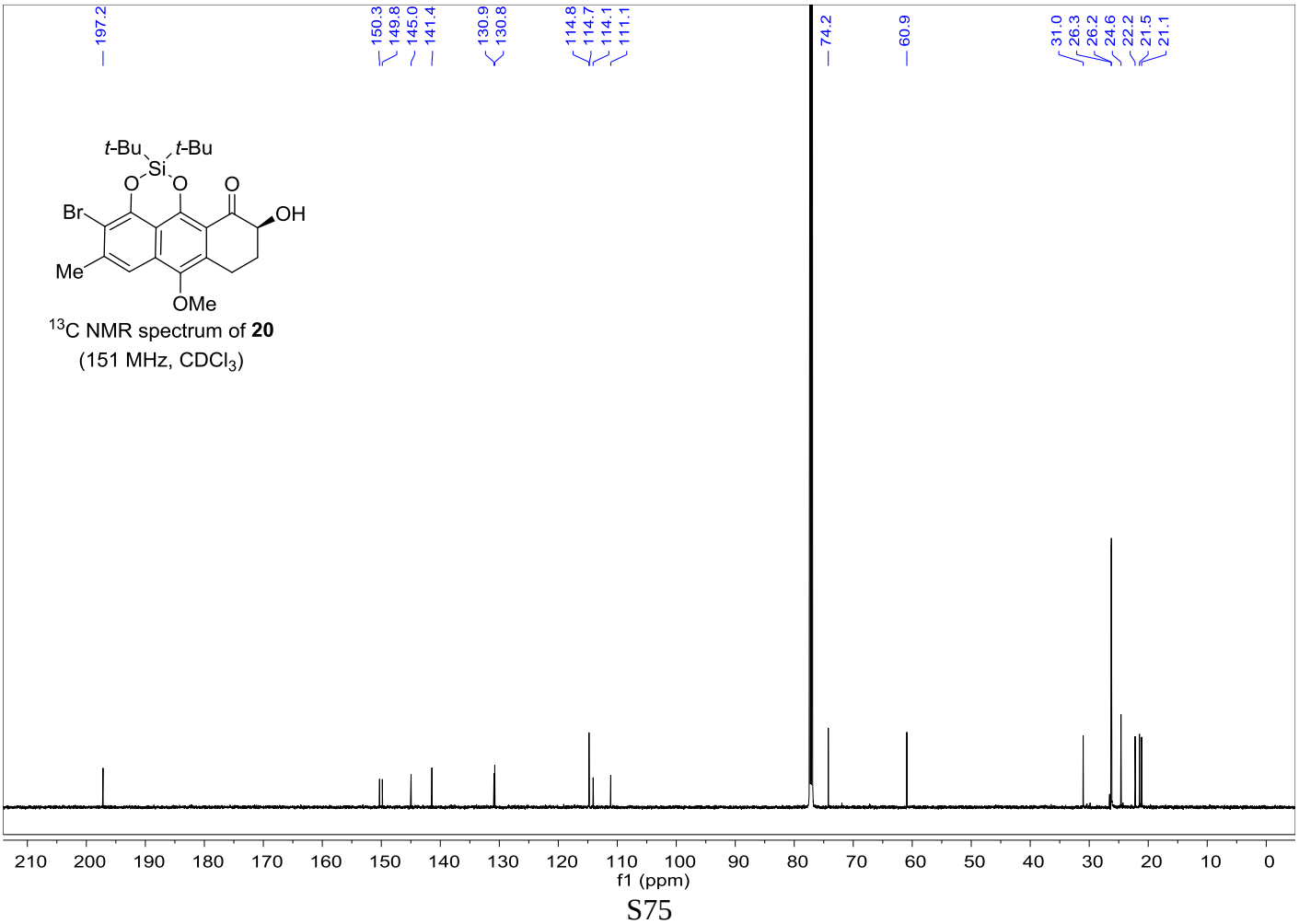
^{13}C NMR spectrum of **17**
(151 MHz, $CDCl_3$)


t-Bu
t-Bu
Si
O
O
O
Br
Me
OMe
1H NMR spectrum of 18
(600 MHz, CDCl3)
f1 (ppm)

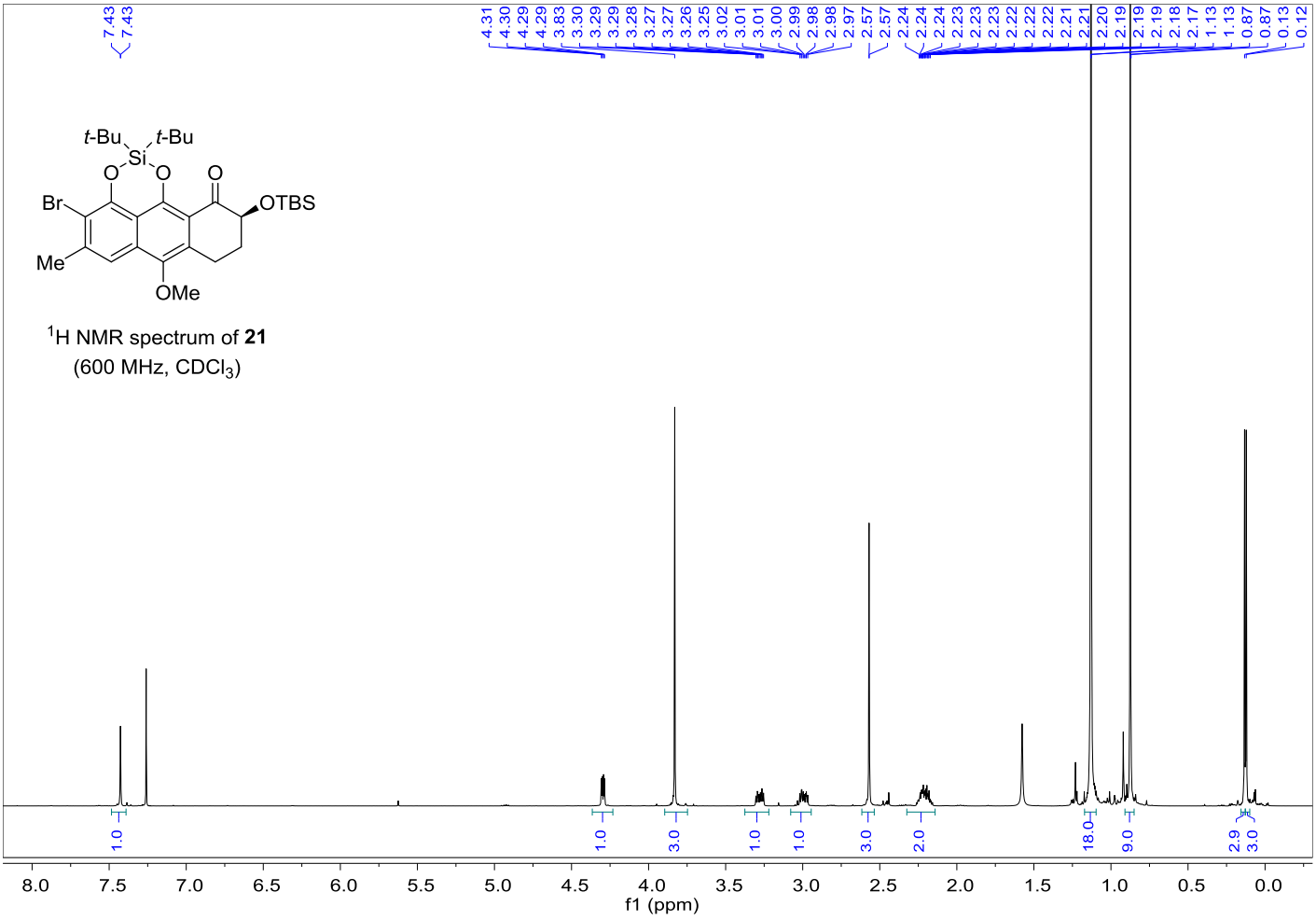

t-Bu
t-Bu
Si
O
O
O
Br
Me
OMe
13C NMR spectrum of 18
(151 MHz, CDCl3)
f1 (ppm)



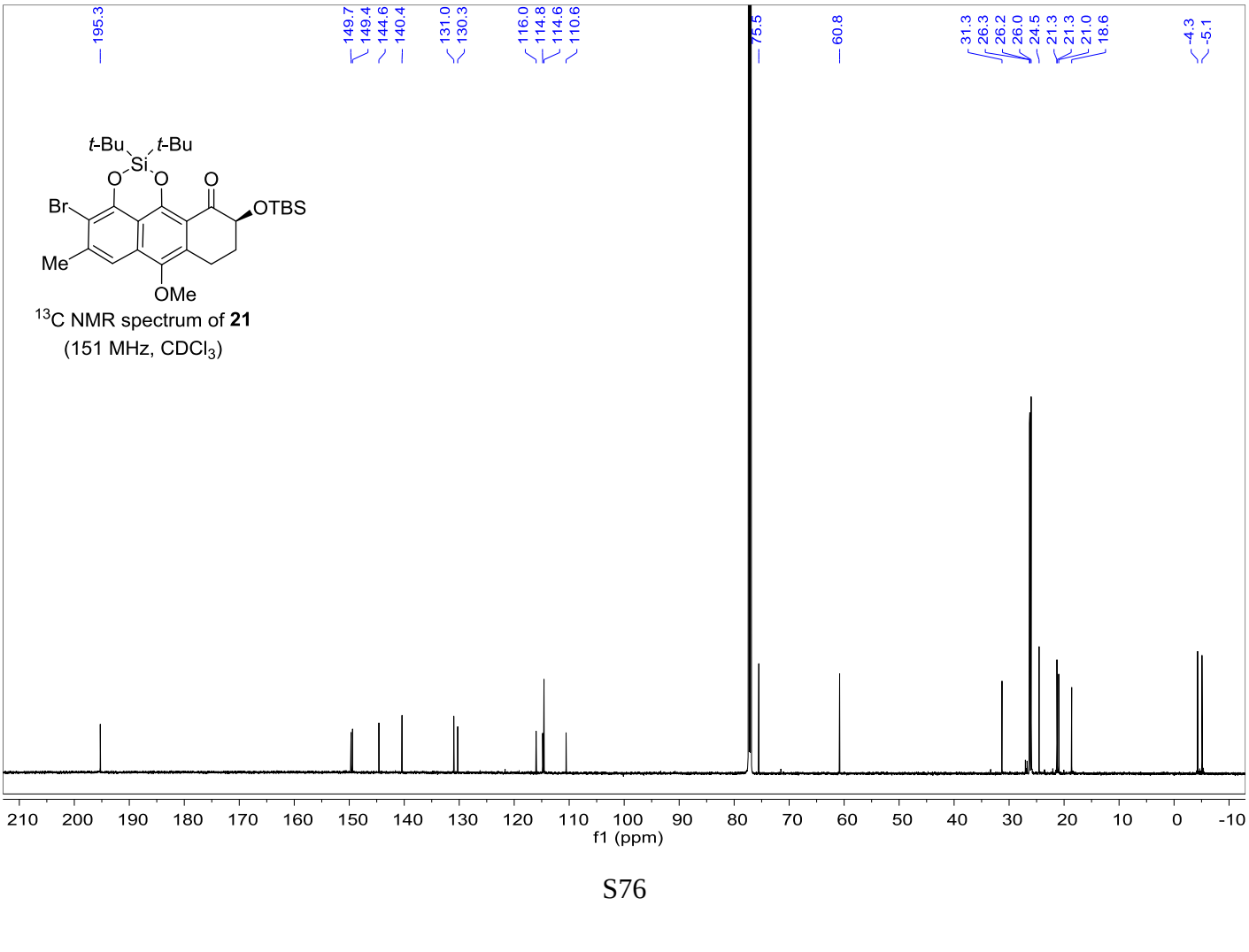
^{1}H NMR spectrum of **20**
(600 MHz, $CDCl_3$)



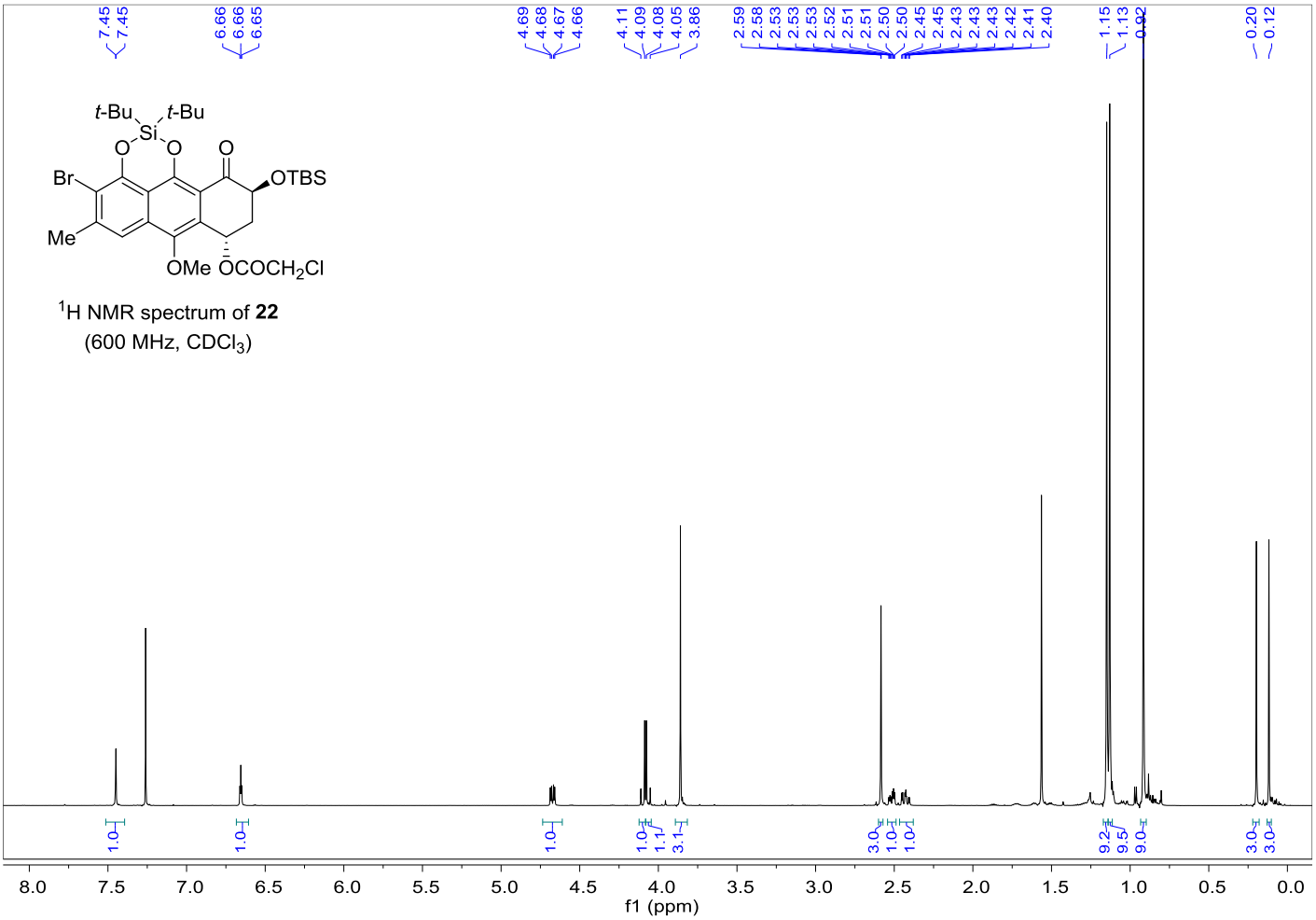
^{13}C NMR spectrum of **20**
(151 MHz, $CDCl_3$)



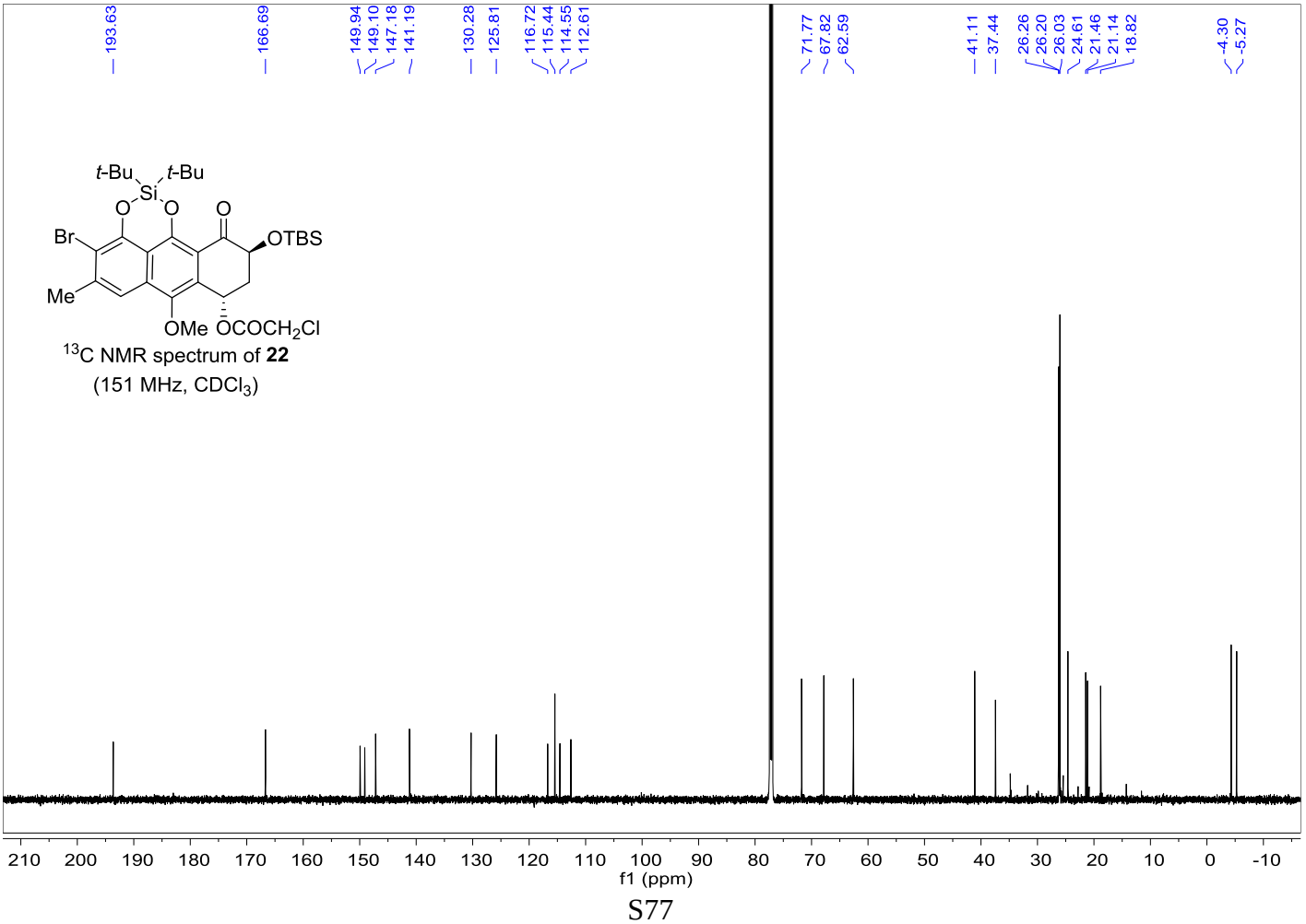
^{1}H NMR spectrum of **21**
(600 MHz, $CDCl_3$)



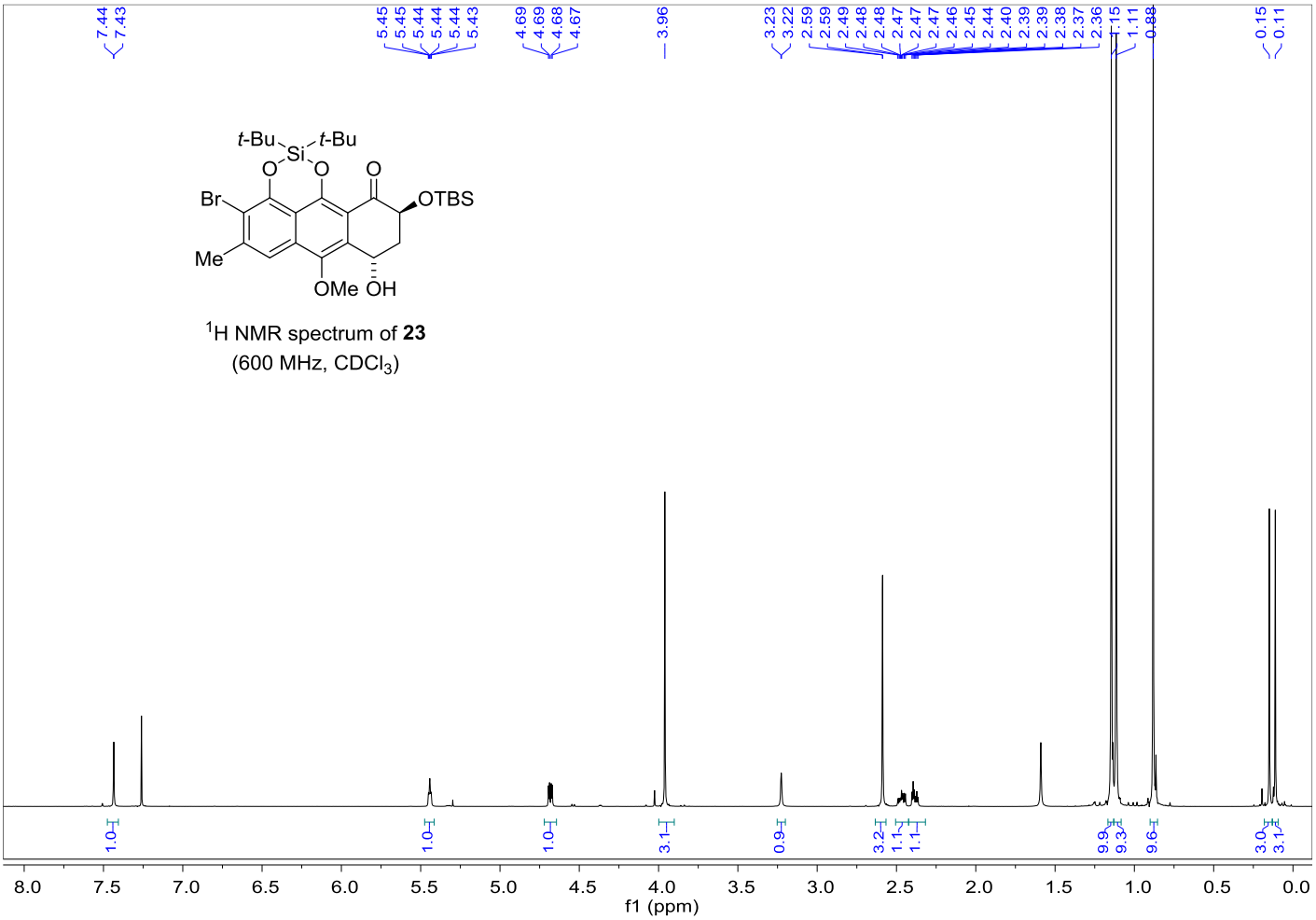
^{13}C NMR spectrum of **21**
(151 MHz, $CDCl_3$)



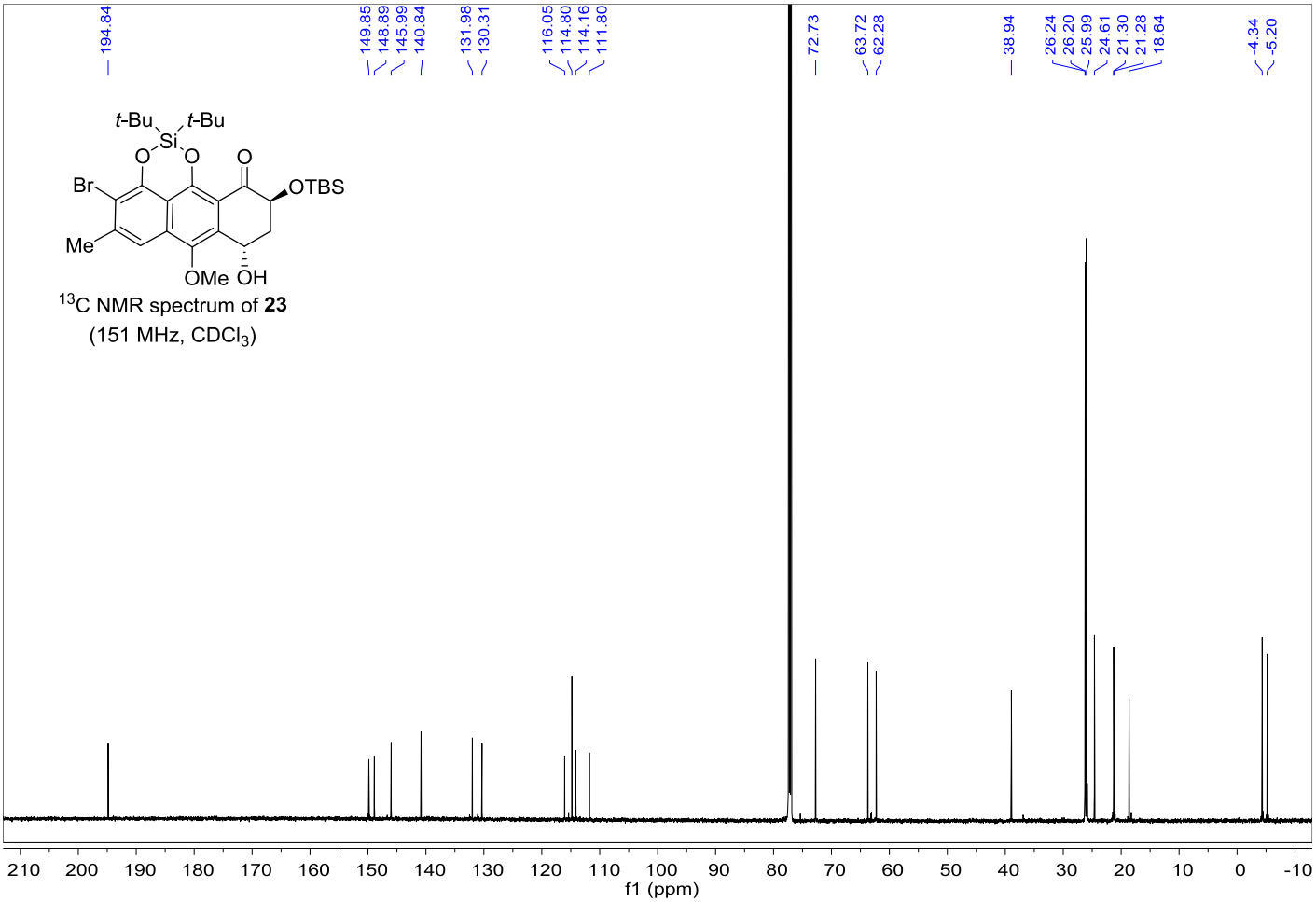
^{1}H NMR spectrum of **22**
(600 MHz, $CDCl_3$)



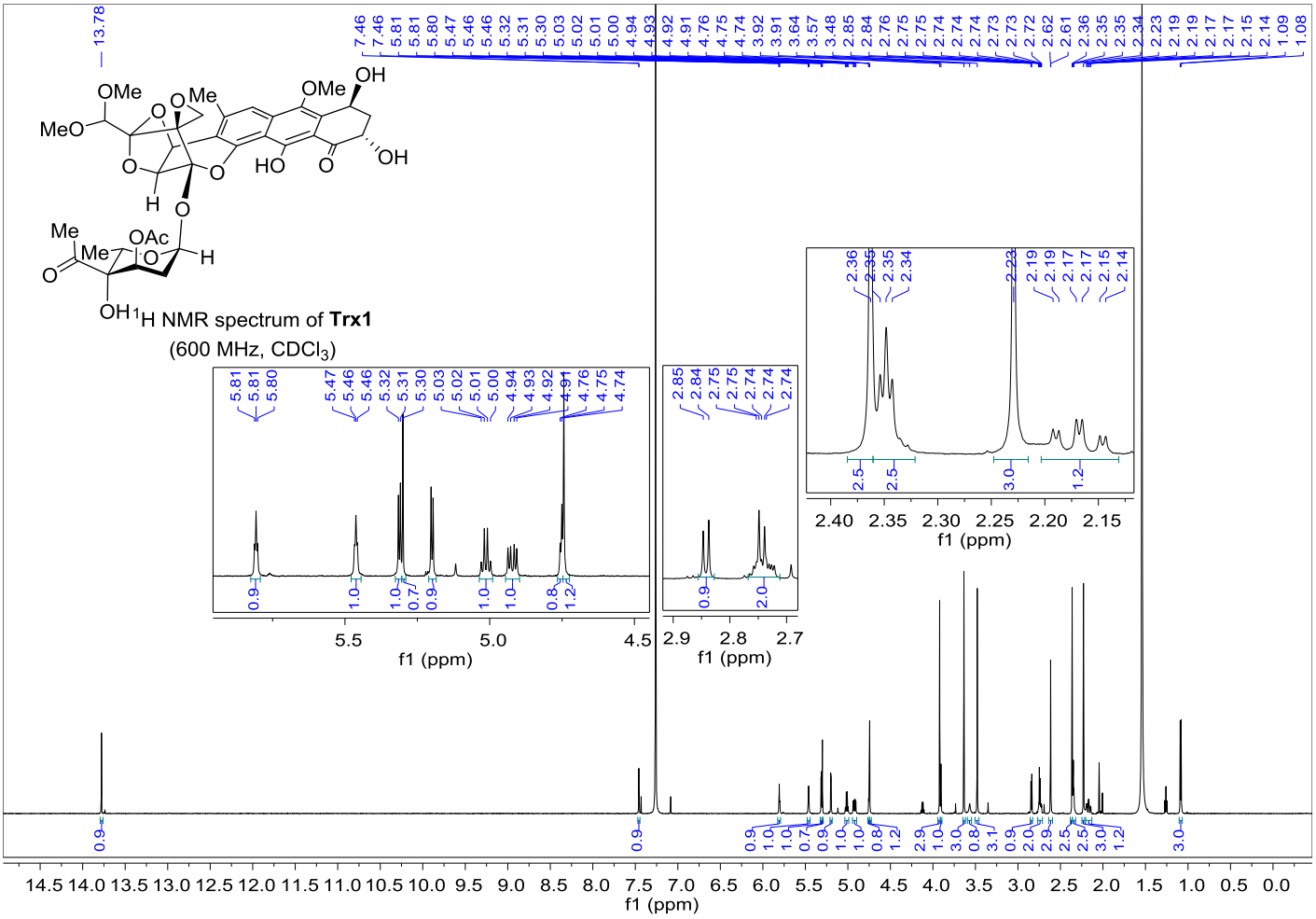
^{13}C NMR spectrum of **22**
(151 MHz, $CDCl_3$)

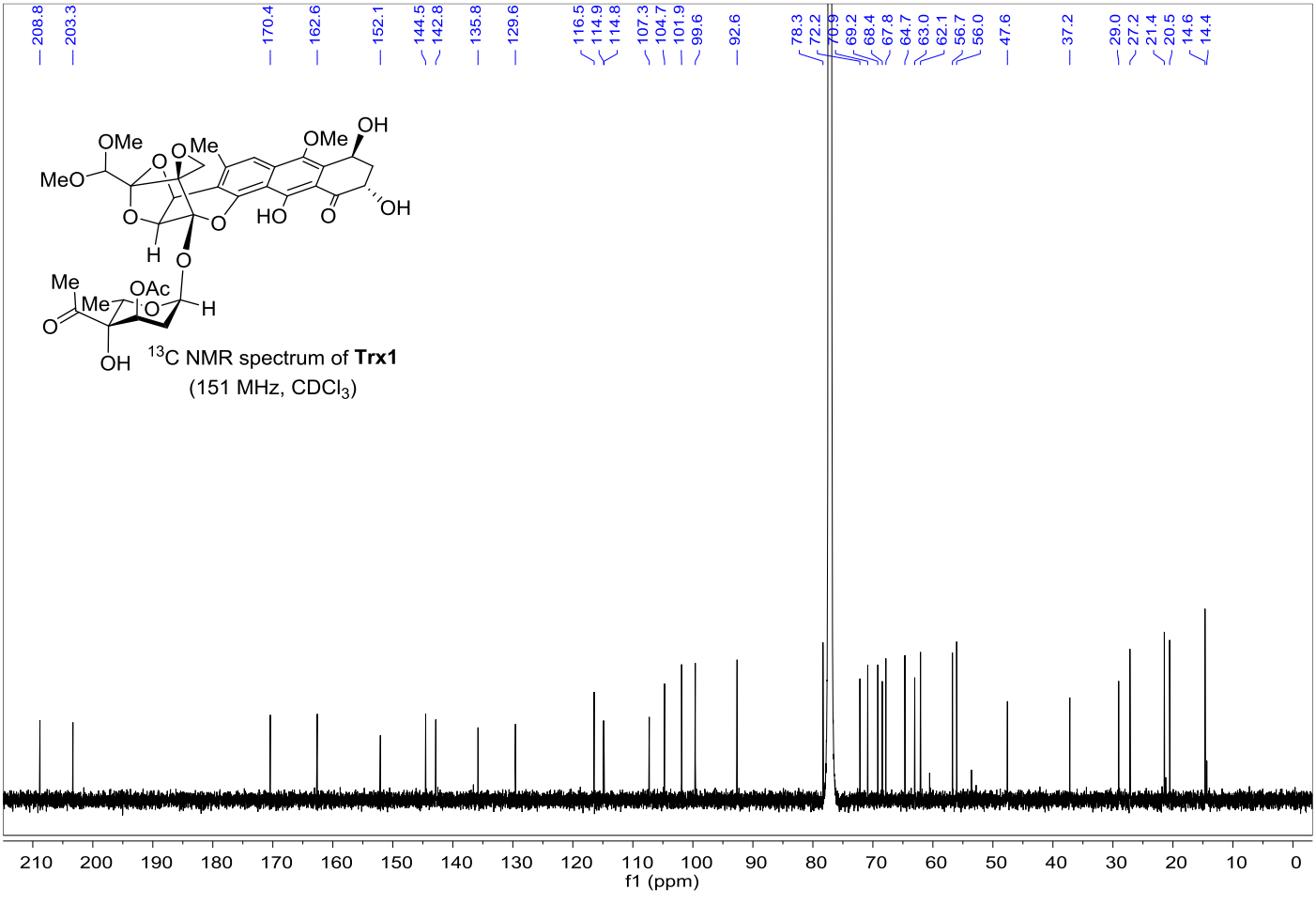


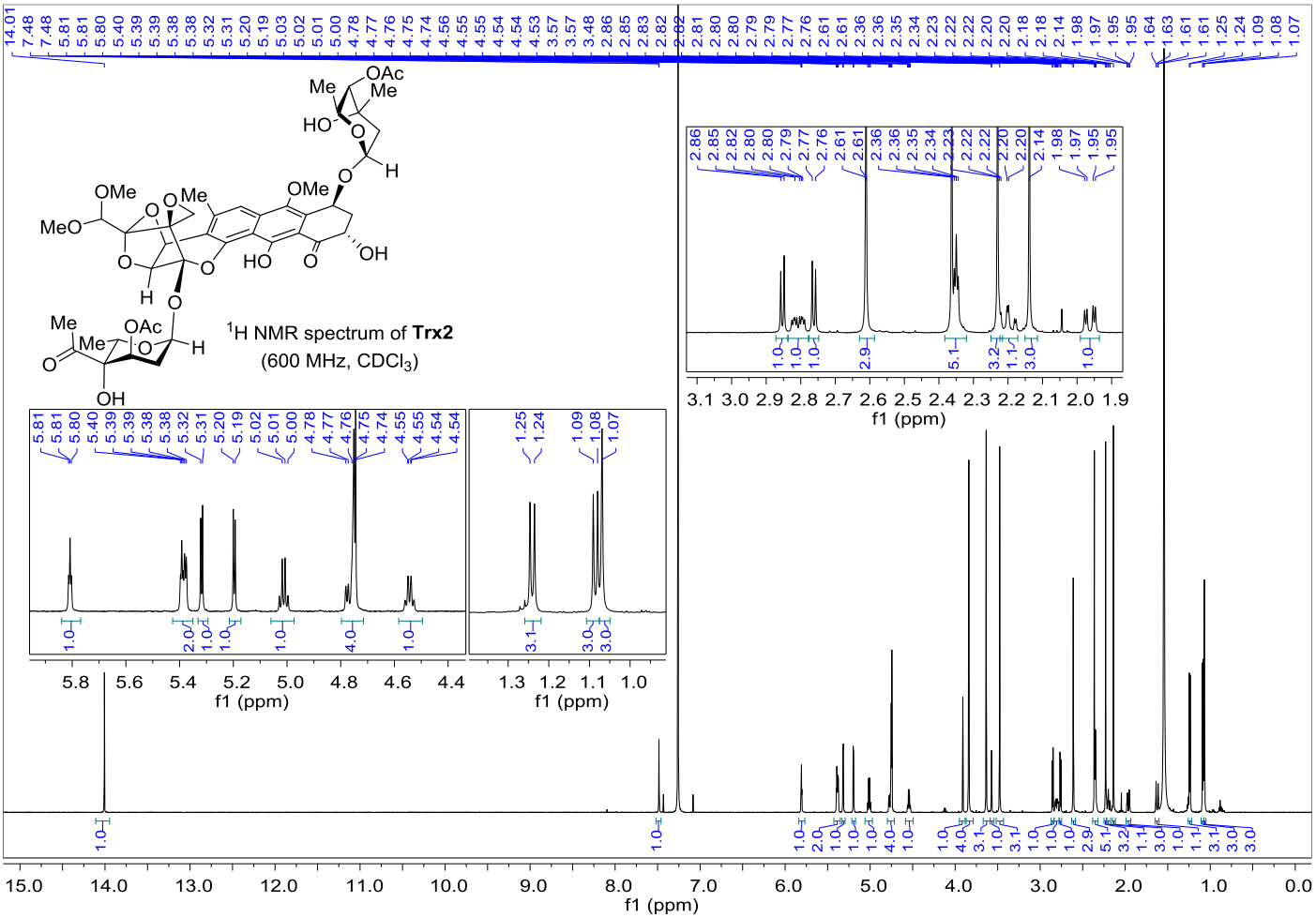
^{1}H NMR spectrum of **23**
(600 MHz, $CDCl_3$)

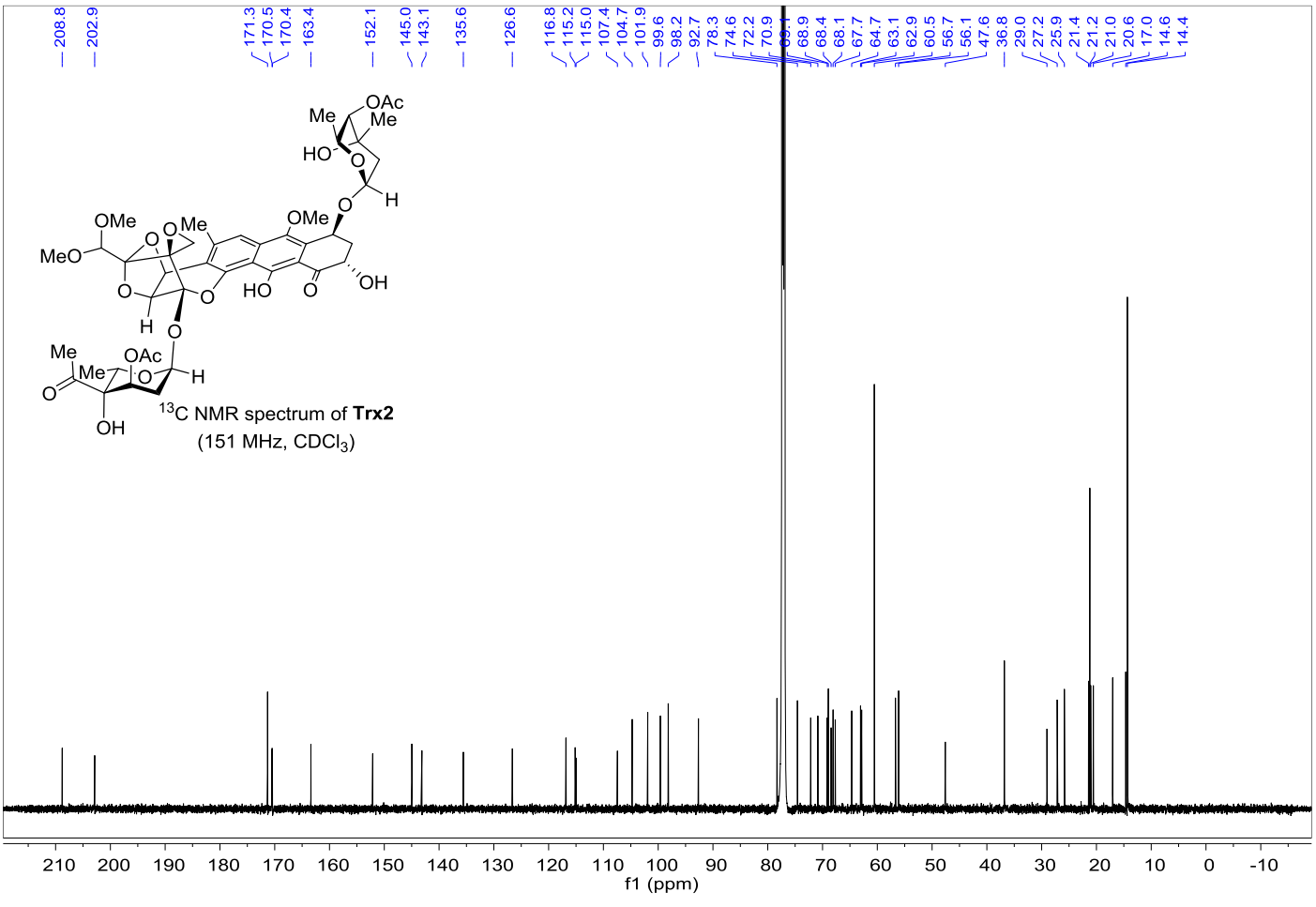


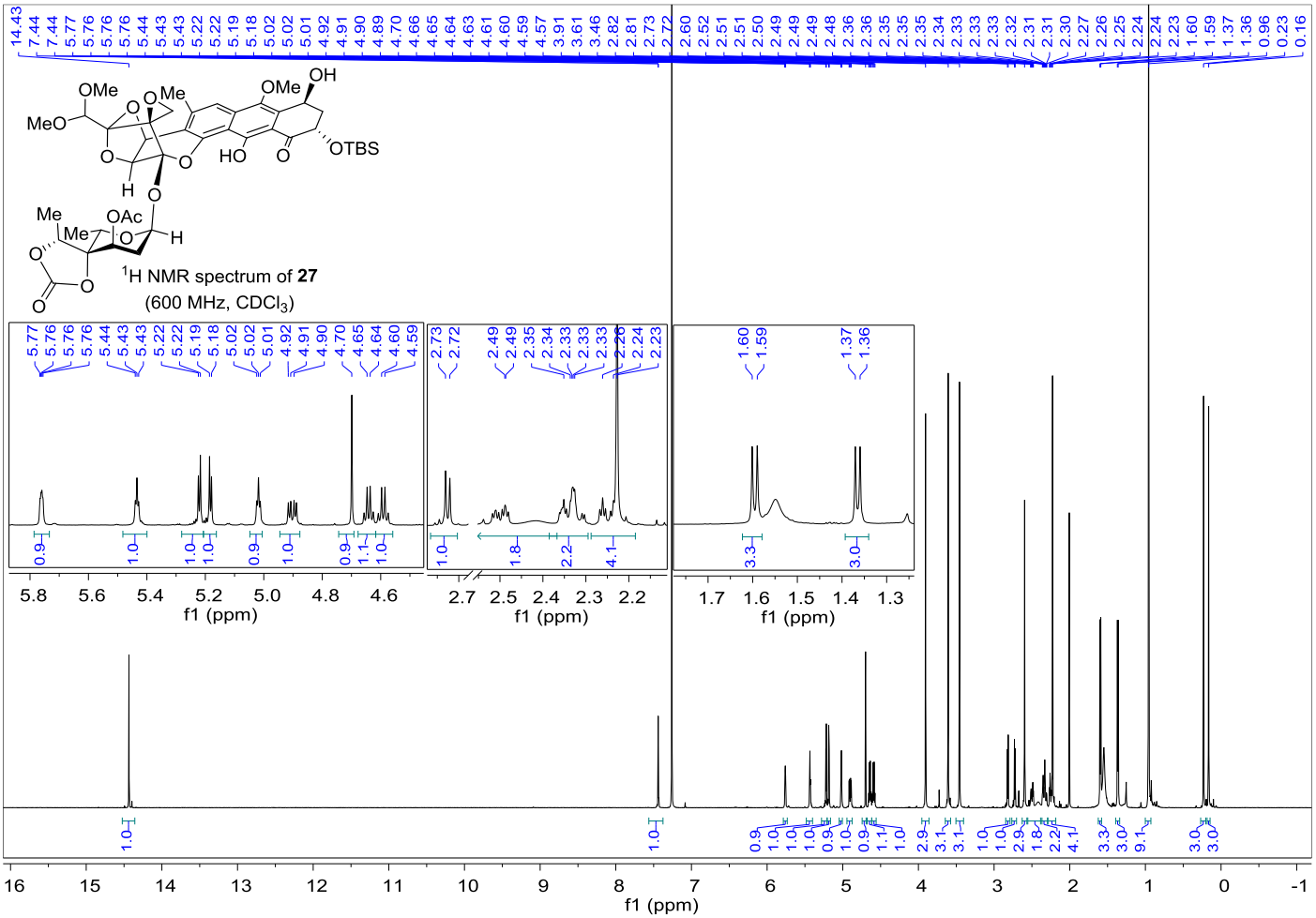
^{13}C NMR spectrum of **23**
(151 MHz, $CDCl_3$)


^{1}H NMR spectrum of **Trx1**
(600 MHz, $CDCl_3$)
f1 (ppm)

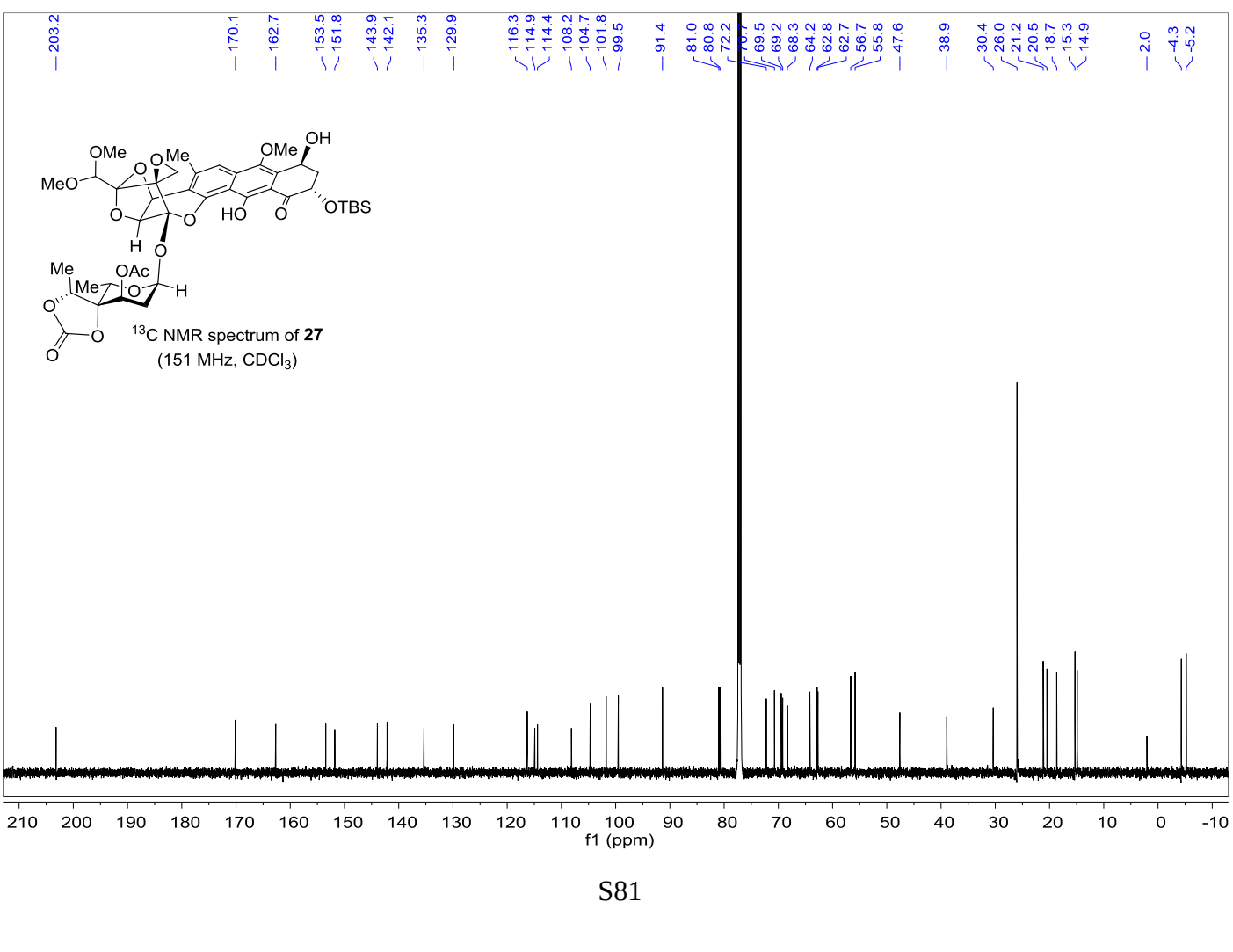

^{13}C NMR spectrum of **Trx1**
(151 MHz, $CDCl_3$)
f1 (ppm)


^{1}H NMR spectrum of **Trx2**
(600 MHz, $CDCl_3$)
f1 (ppm)

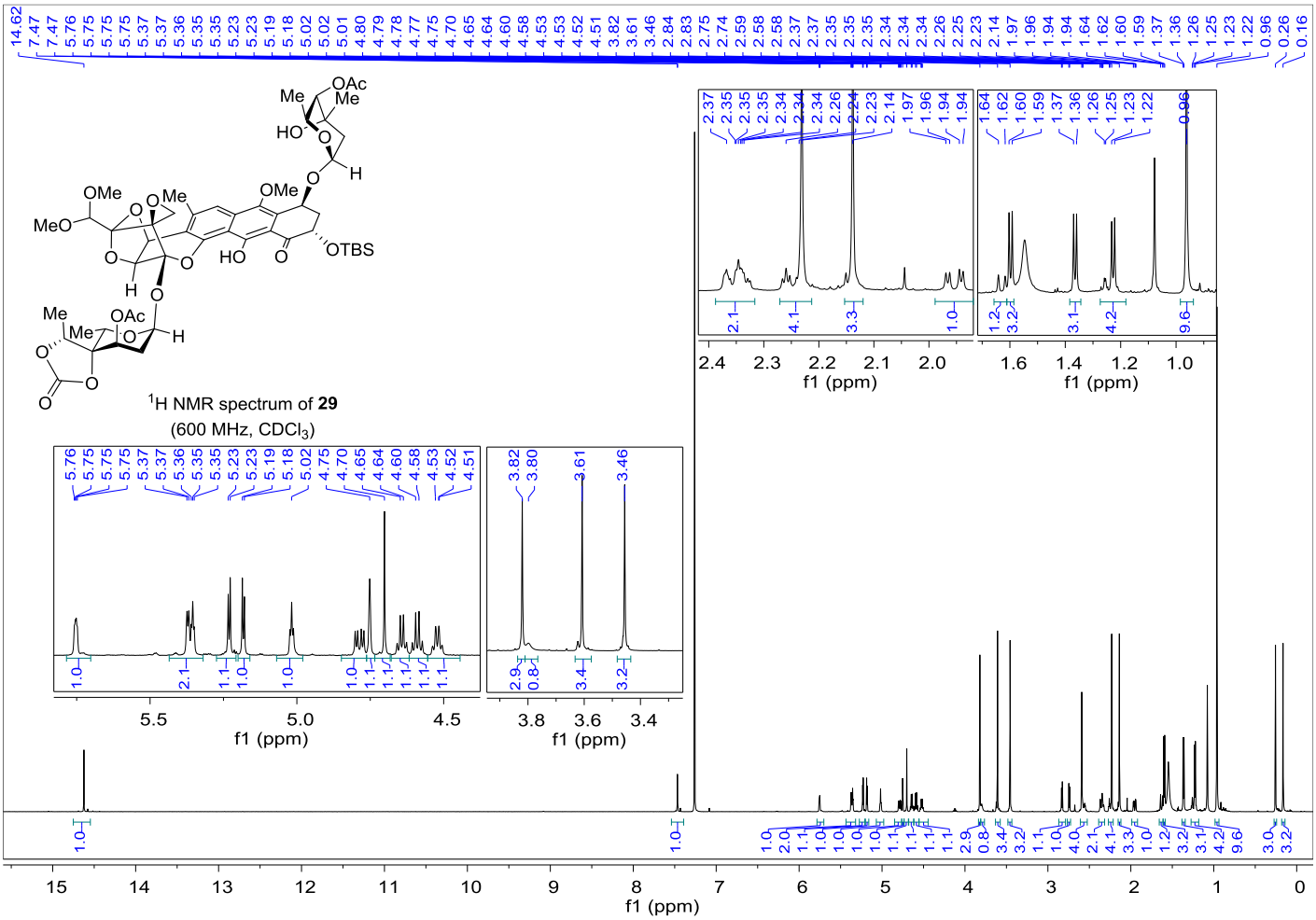

^{13}C NMR spectrum of **Trx2**
(151 MHz, $CDCl_3$)
f1 (ppm)



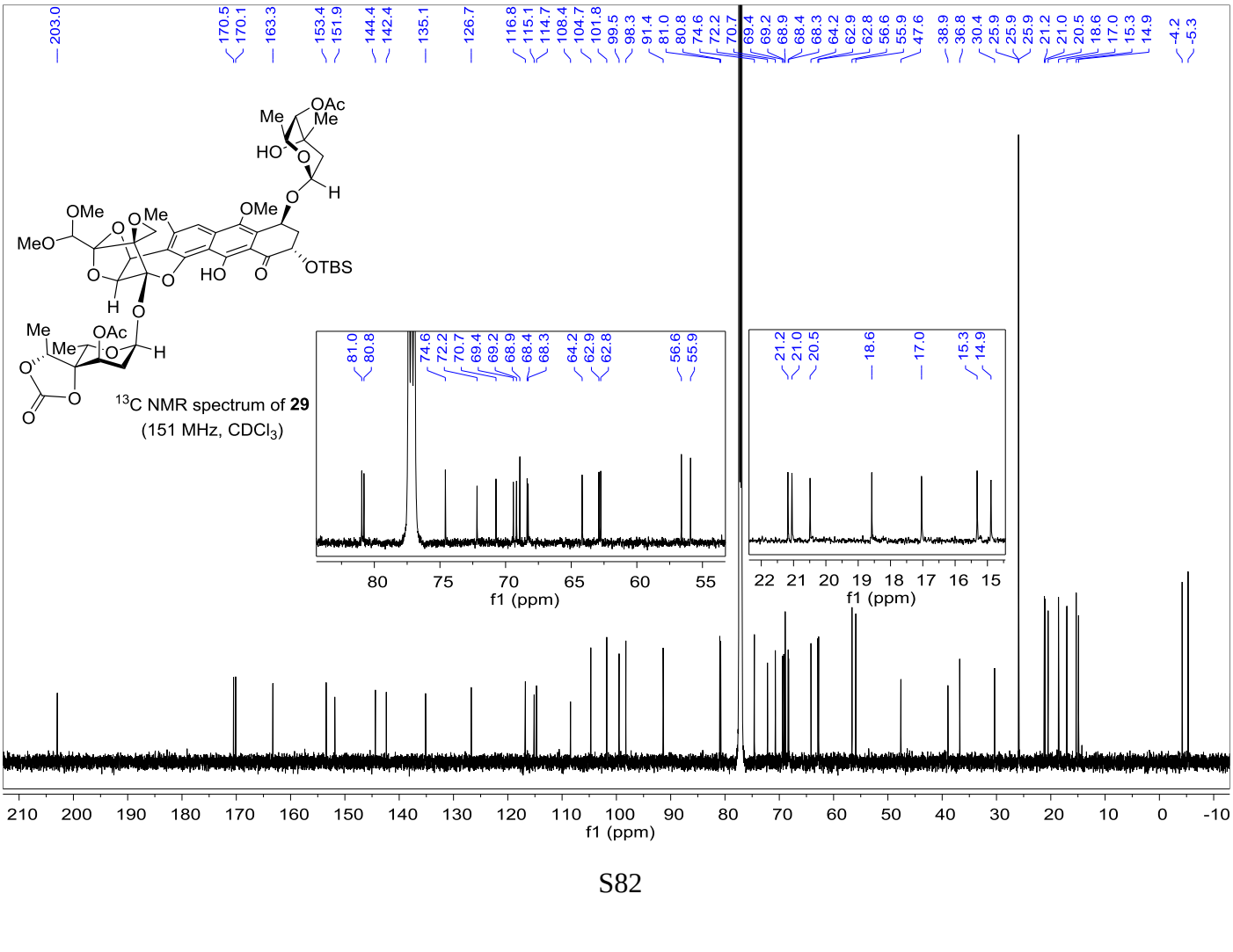
^{1}H NMR spectrum of **27**
(600 MHz, $CDCl_3$)



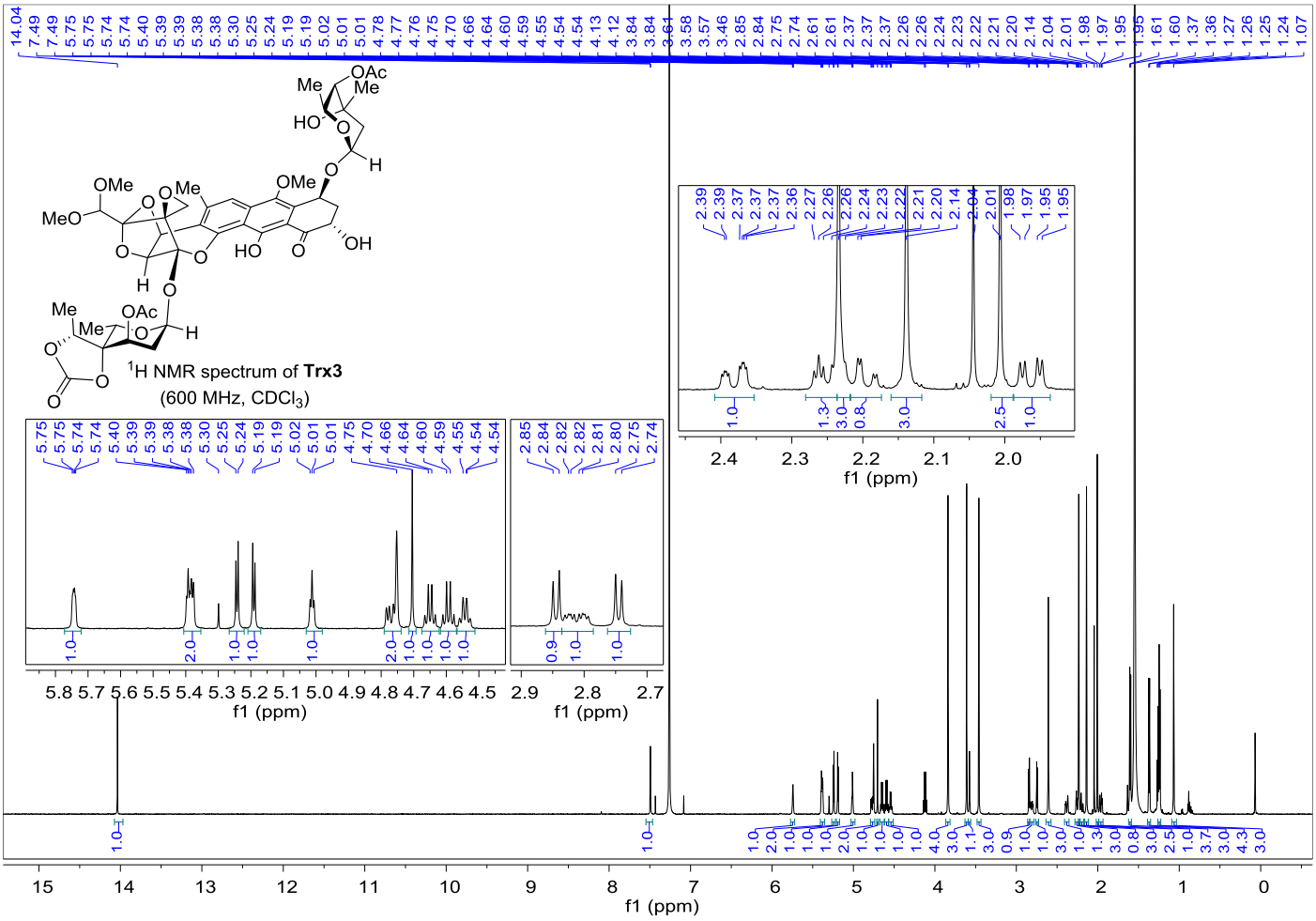
^{13}C NMR spectrum of **27**
(151 MHz, $CDCl_3$)

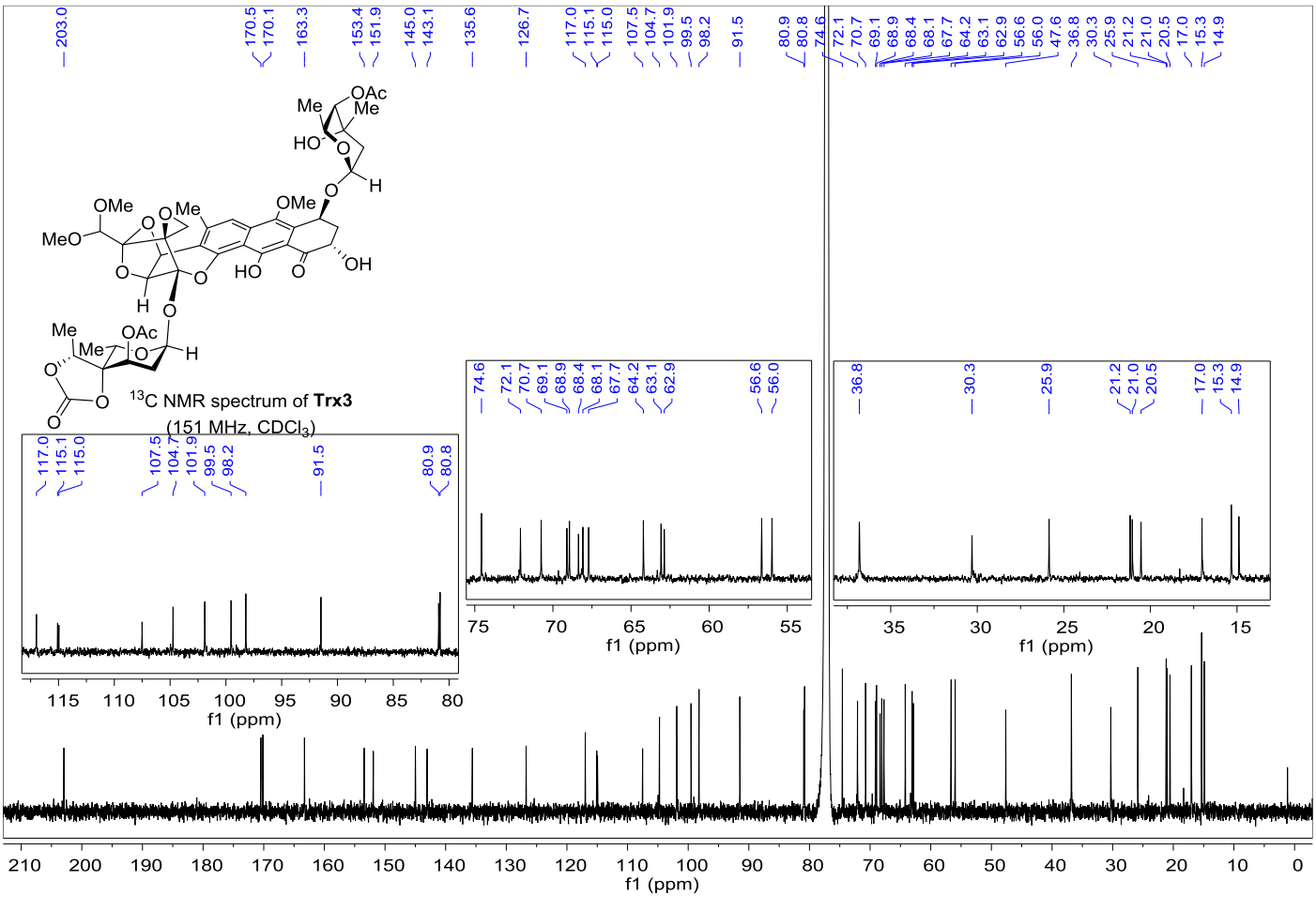


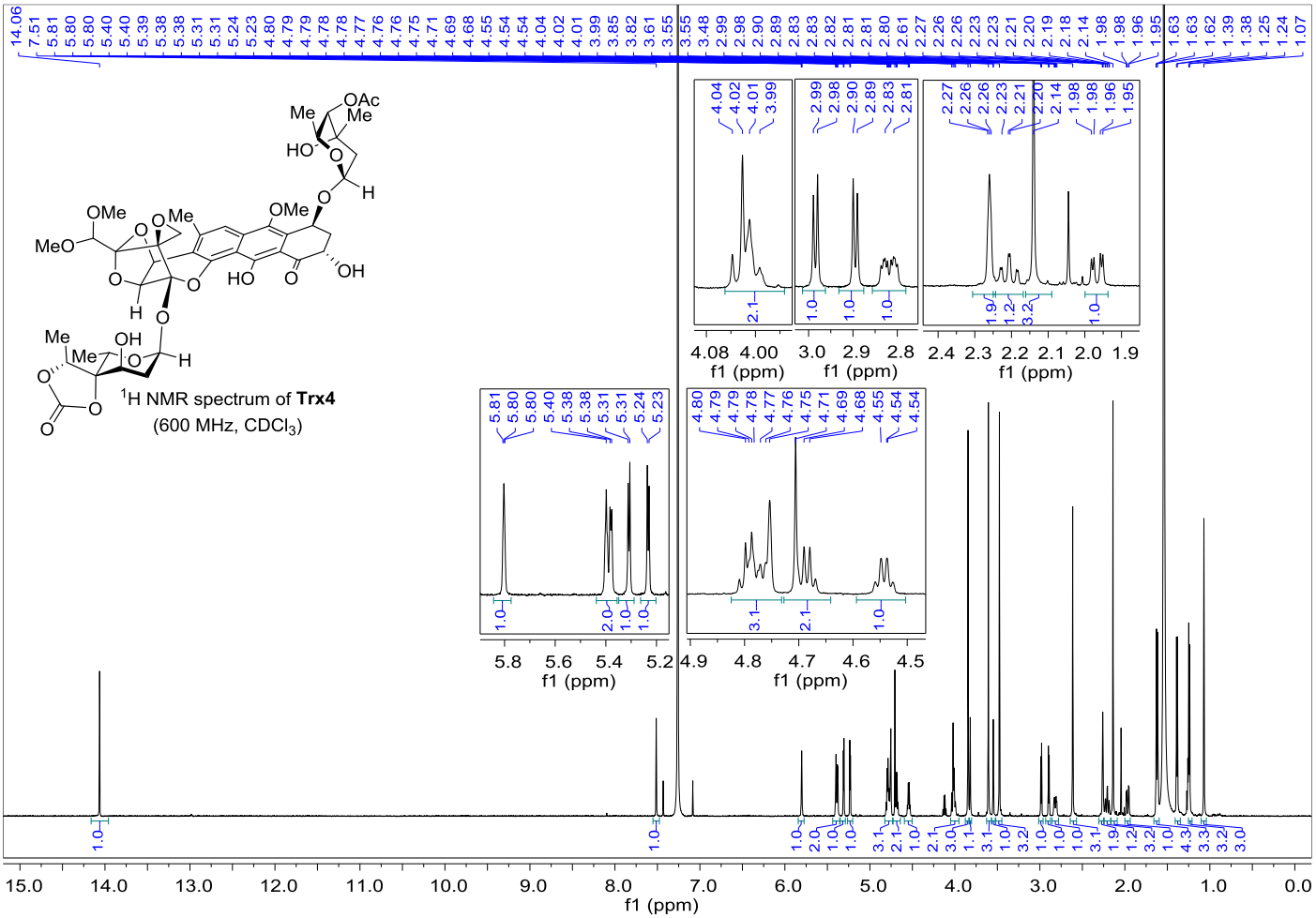
^{1}H NMR spectrum of **29**
(600 MHz, $CDCl_3$)

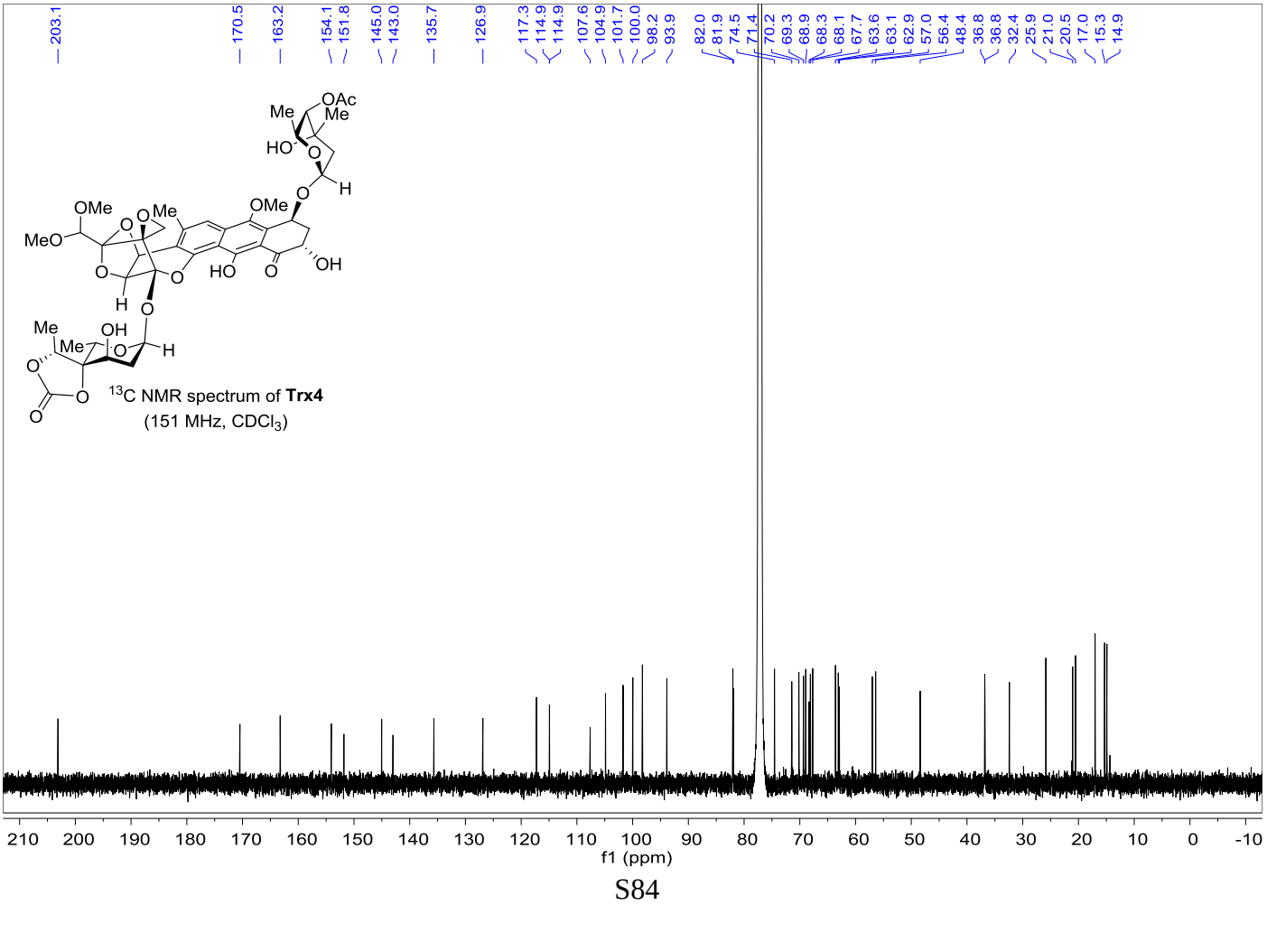


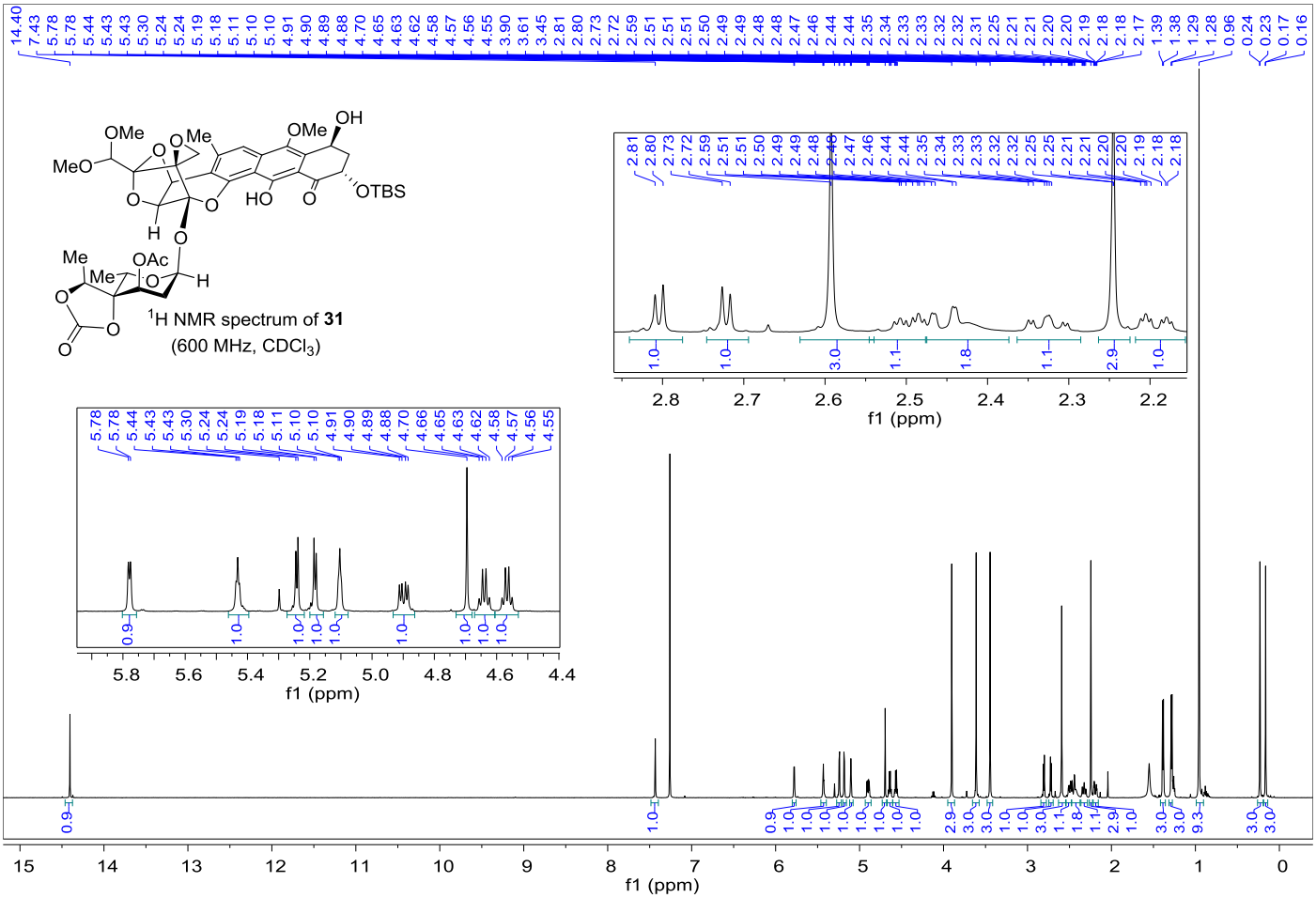
^{13}C NMR spectrum of **29**
(151 MHz, $CDCl_3$)

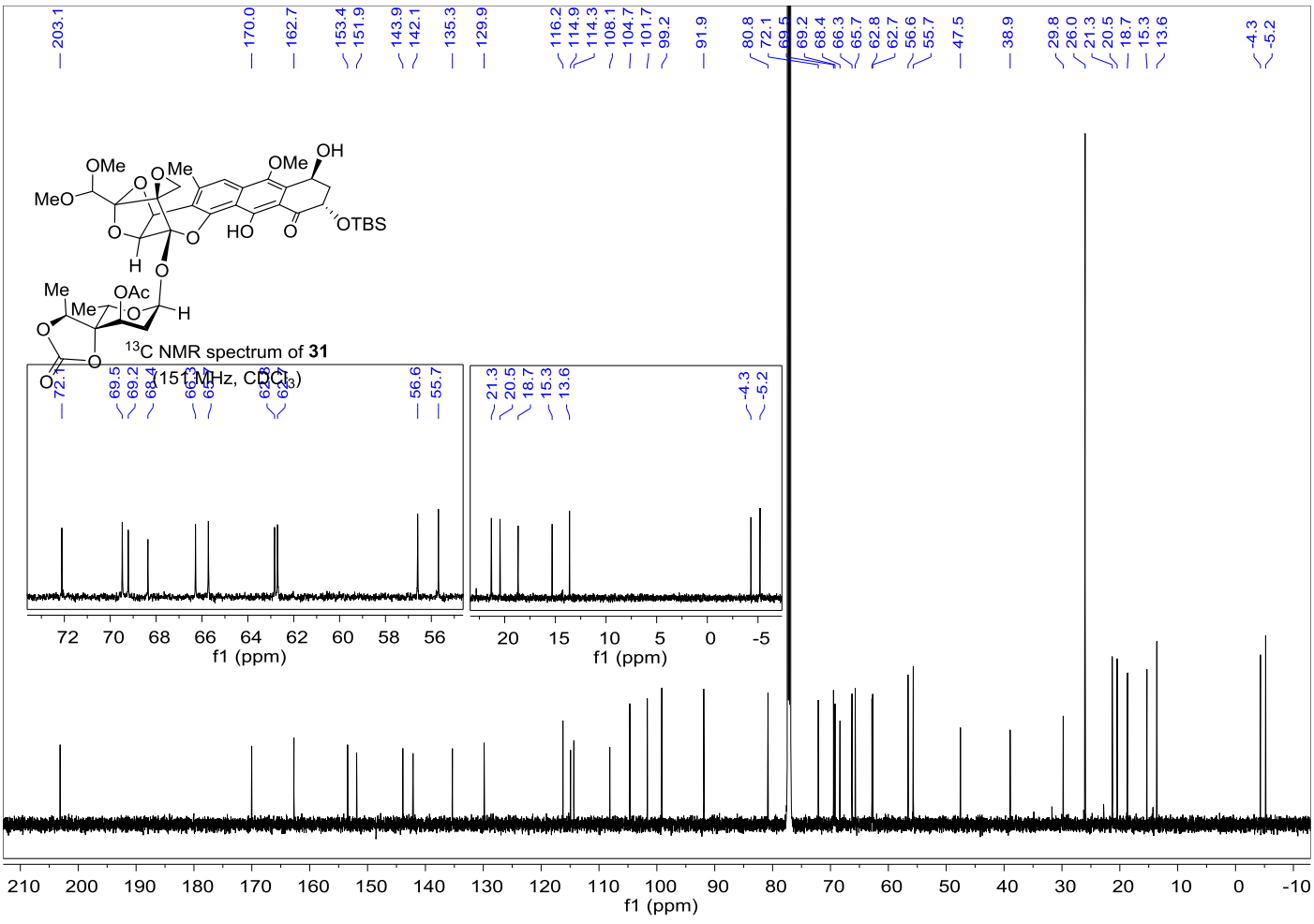

^{1}H NMR spectrum of **Trx3**
(600 MHz, $CDCl_3$)
f1 (ppm)

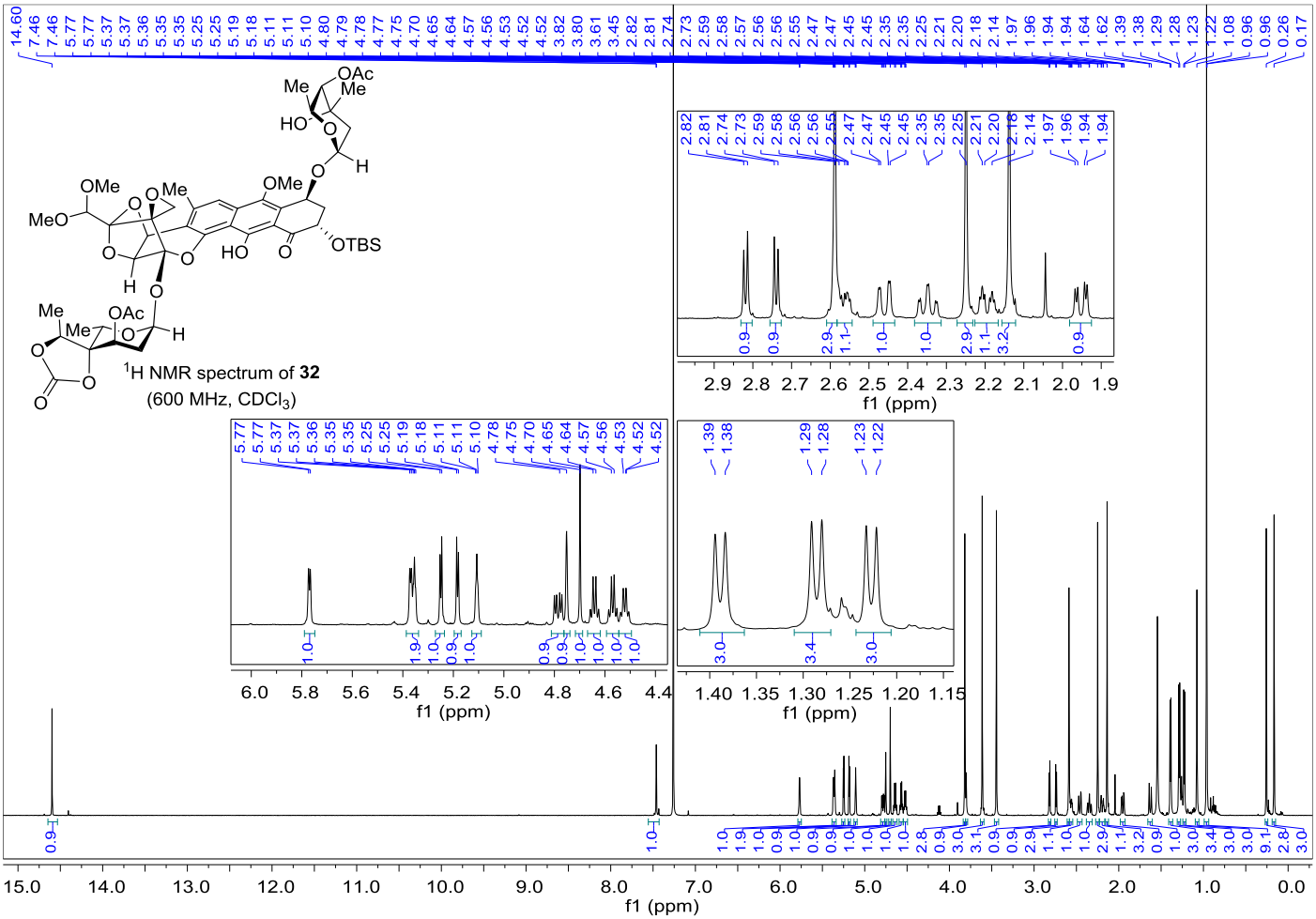

^{13}C NMR spectrum of **Trx3**
(151 MHz, $CDCl_3$)
f1 (ppm)

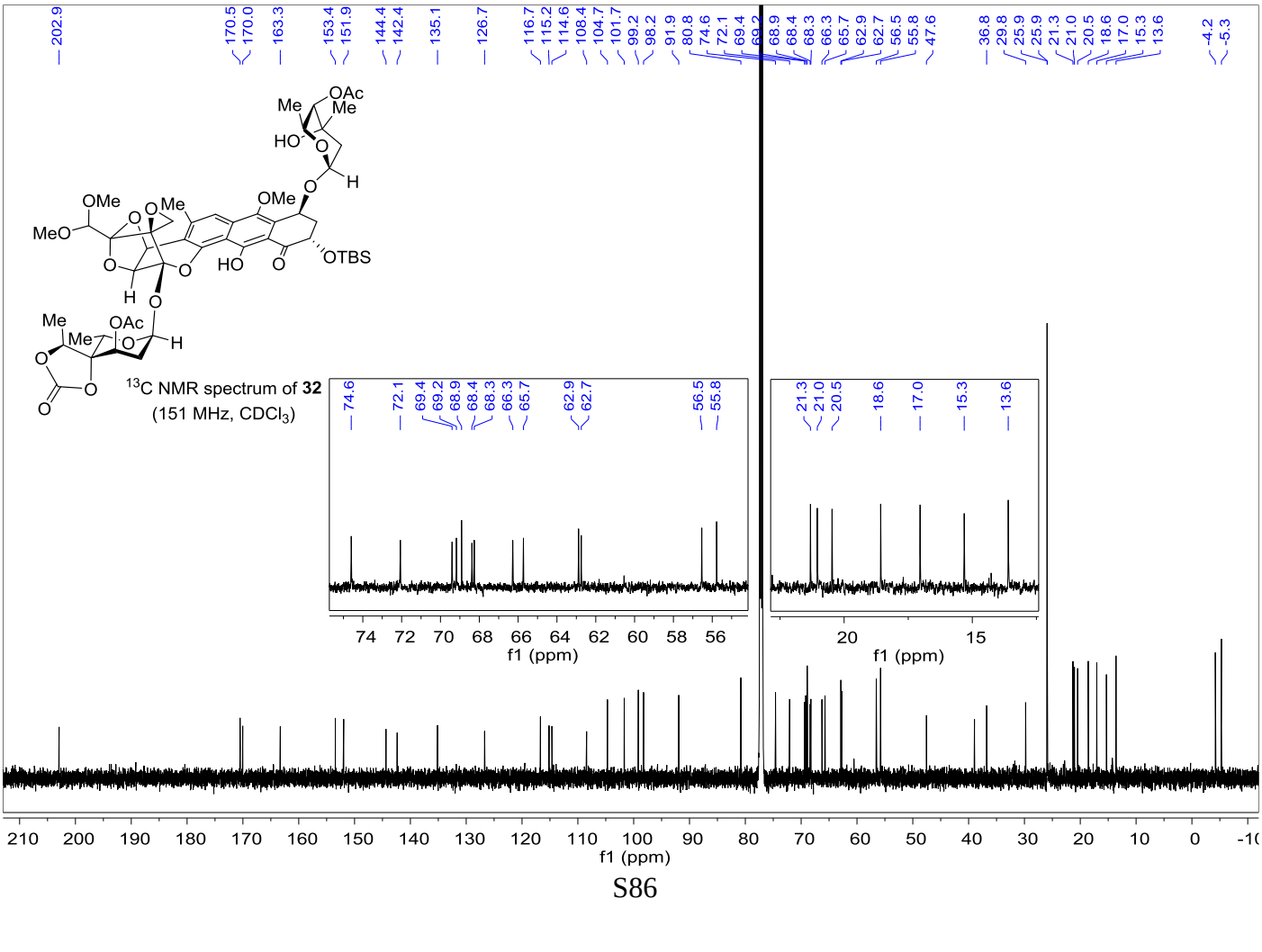

OAc
Me
Me
HO
O
H
OMe
OMe
OMe
MeO
O
O
O
HO
O
OH
H
O
Me
OH
Me
O
H
O
O
^{1}H NMR spectrum of **Trx4**
(600 MHz, CDCl$_3$)
f1 (ppm)

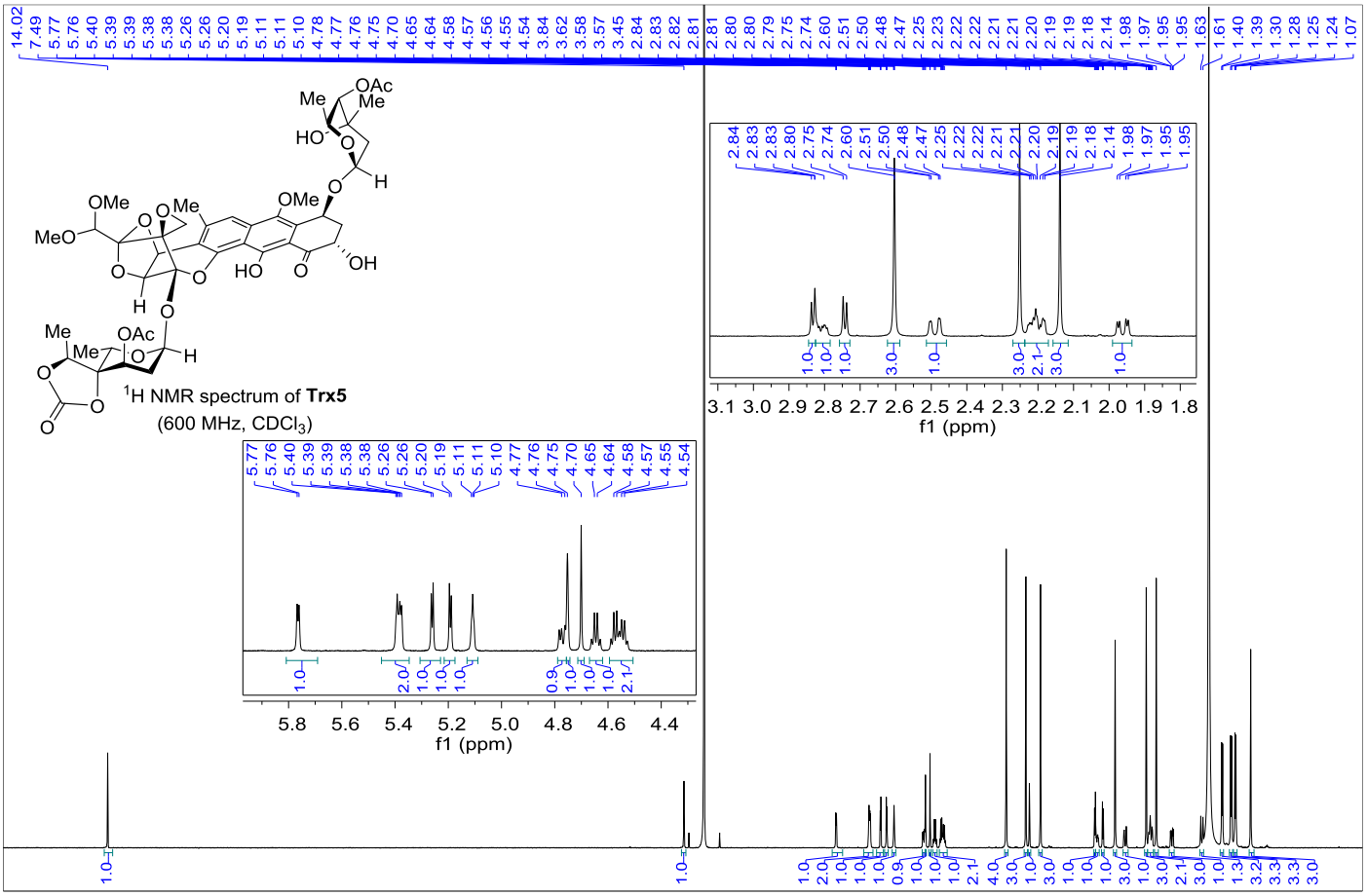

OAc
Me
Me
HO
O
H
OMe
OMe
OMe
MeO
O
O
O
HO
O
OH
H
O
Me
OH
Me
O
H
O
O
^{13}C NMR spectrum of **Trx4**
(151 MHz, CDCl$_3$)
f1 (ppm)

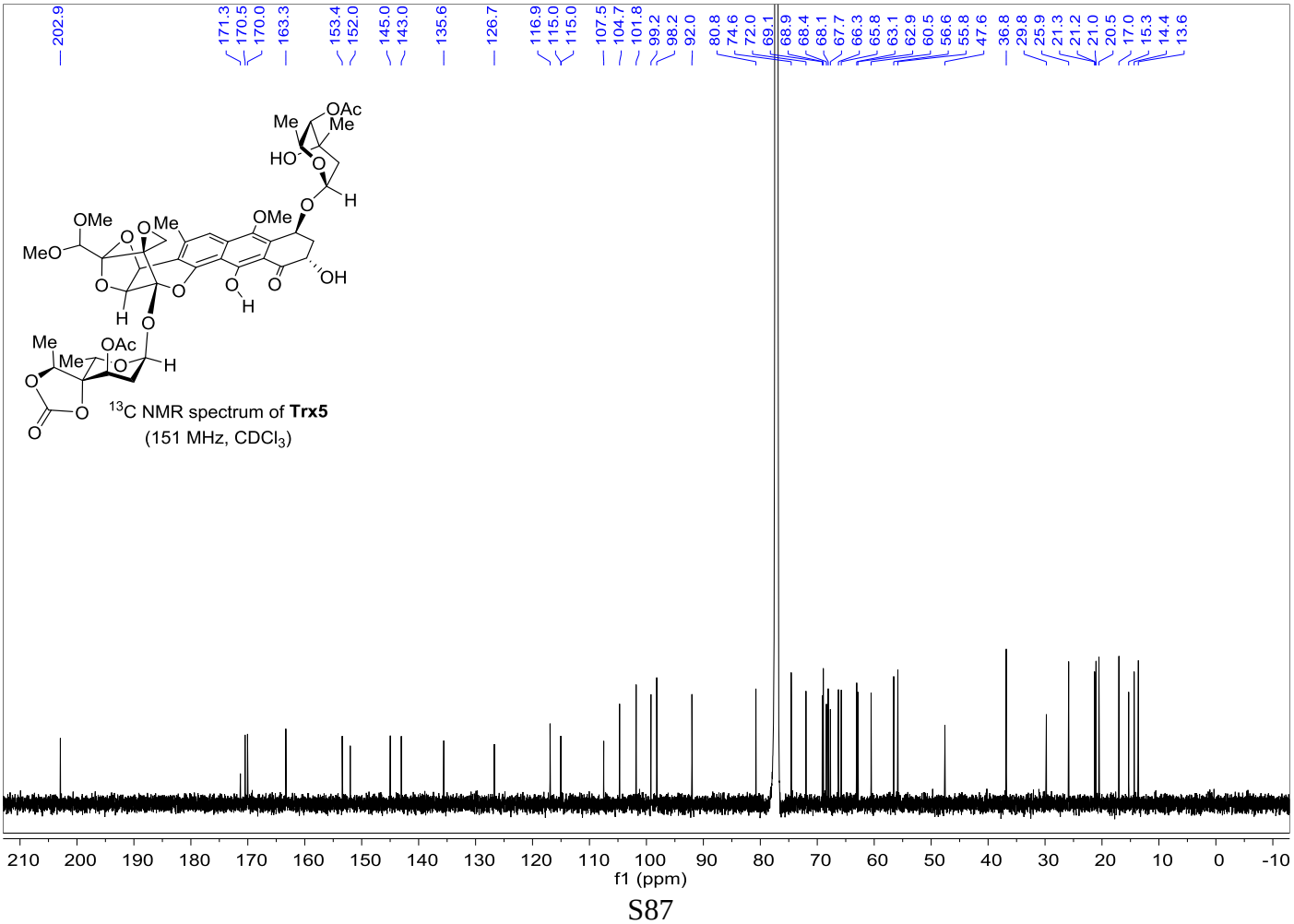

OMe
MeO
OMe
OH
HO
OTBS
Me
OAc
H
^{1}H NMR spectrum of **31**
(600 MHz, $CDCl_3$)
f1 (ppm)

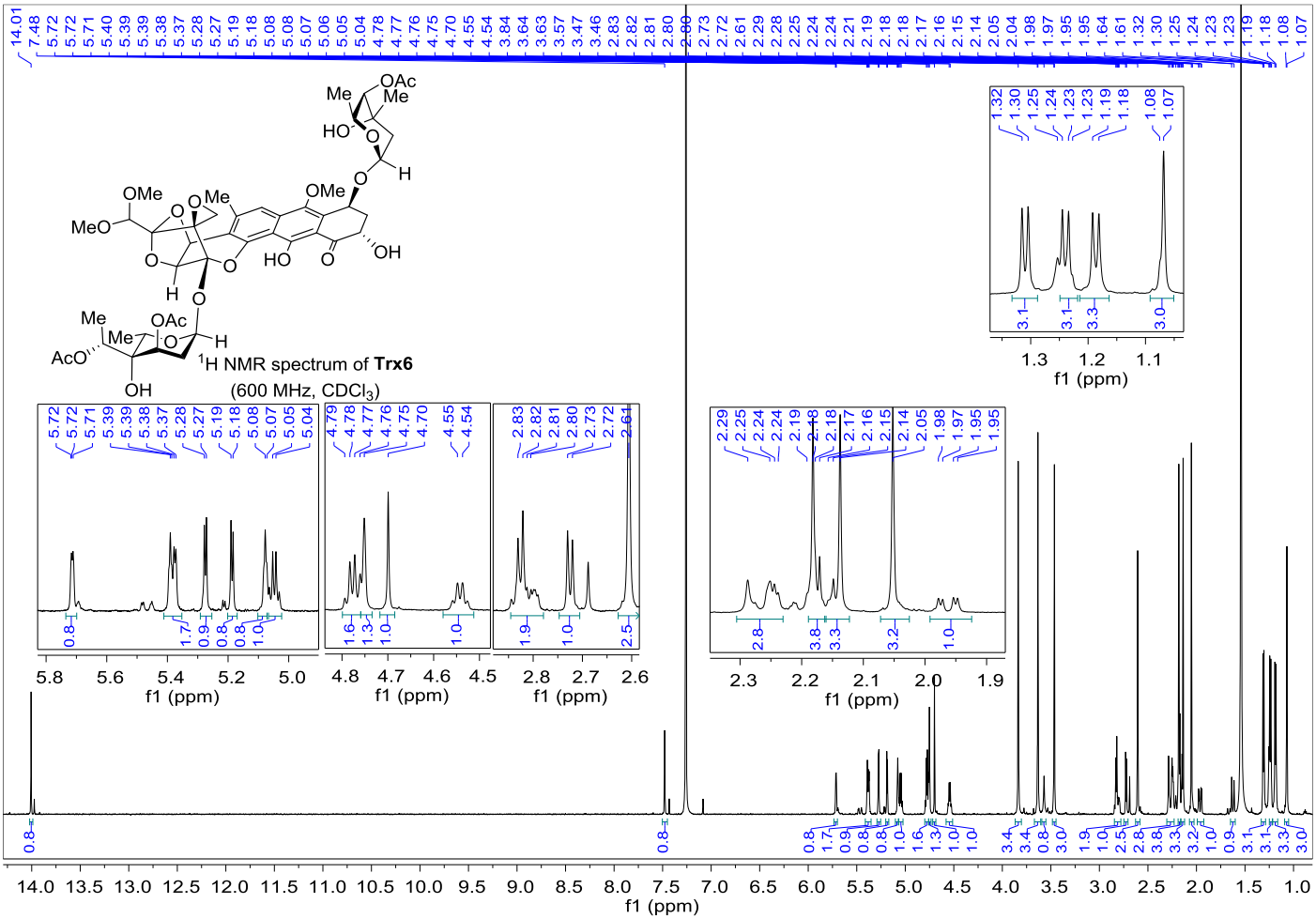

OMe
MeO
OMe
OH
HO
OTBS
Me
OAc
H
^{13}C NMR spectrum of **31**
(151 MHz, $CDCl_3$)
f1 (ppm)

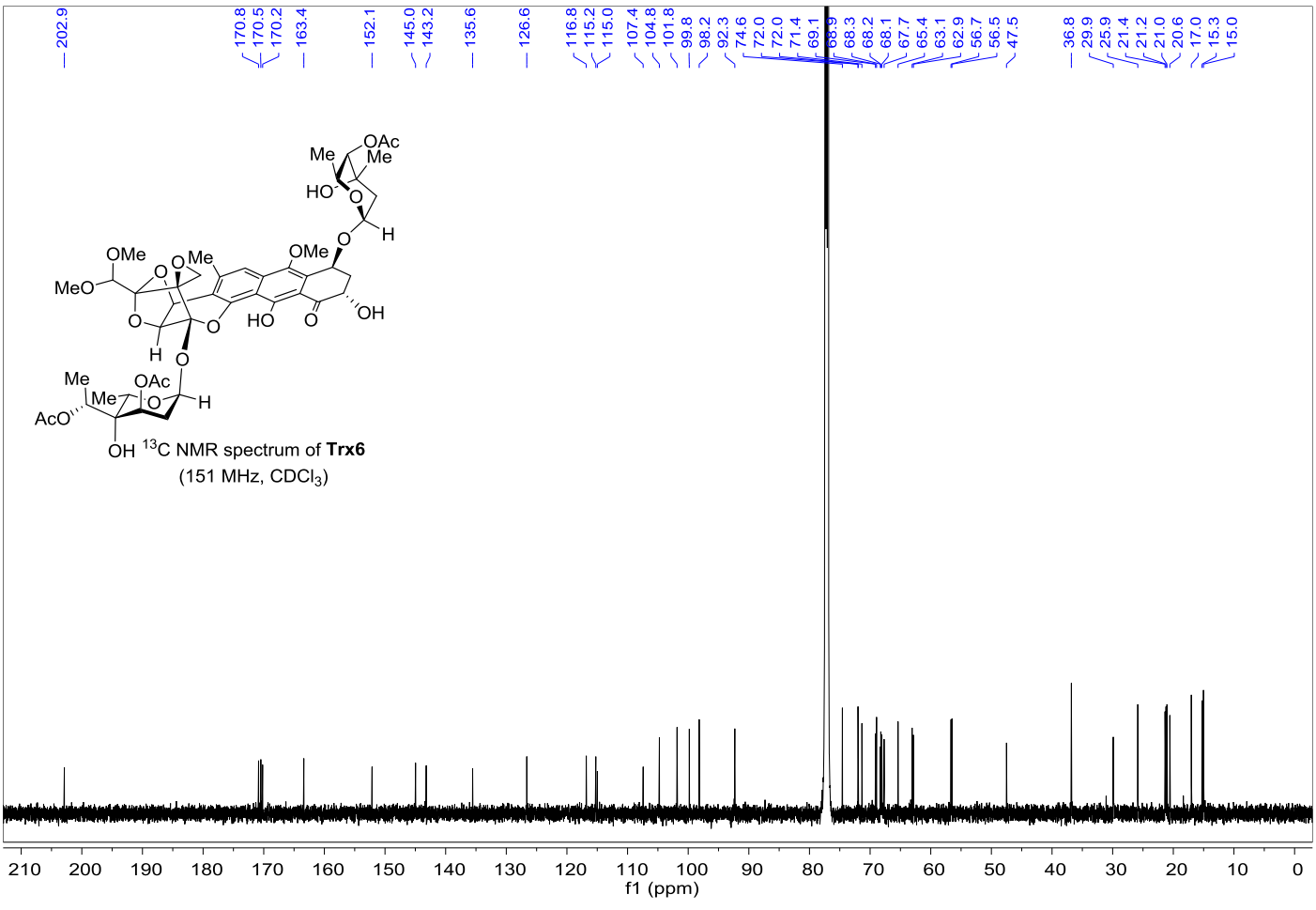

OAc
Me
Me
HO
O
H
OMe
MeO
OMe
OMe
HO
O
OTBS
Me
OAc
Me
H
O
O
O
O
^{1}H NMR spectrum of **32**
(600 MHz, $CDCl_3$)
f1 (ppm)

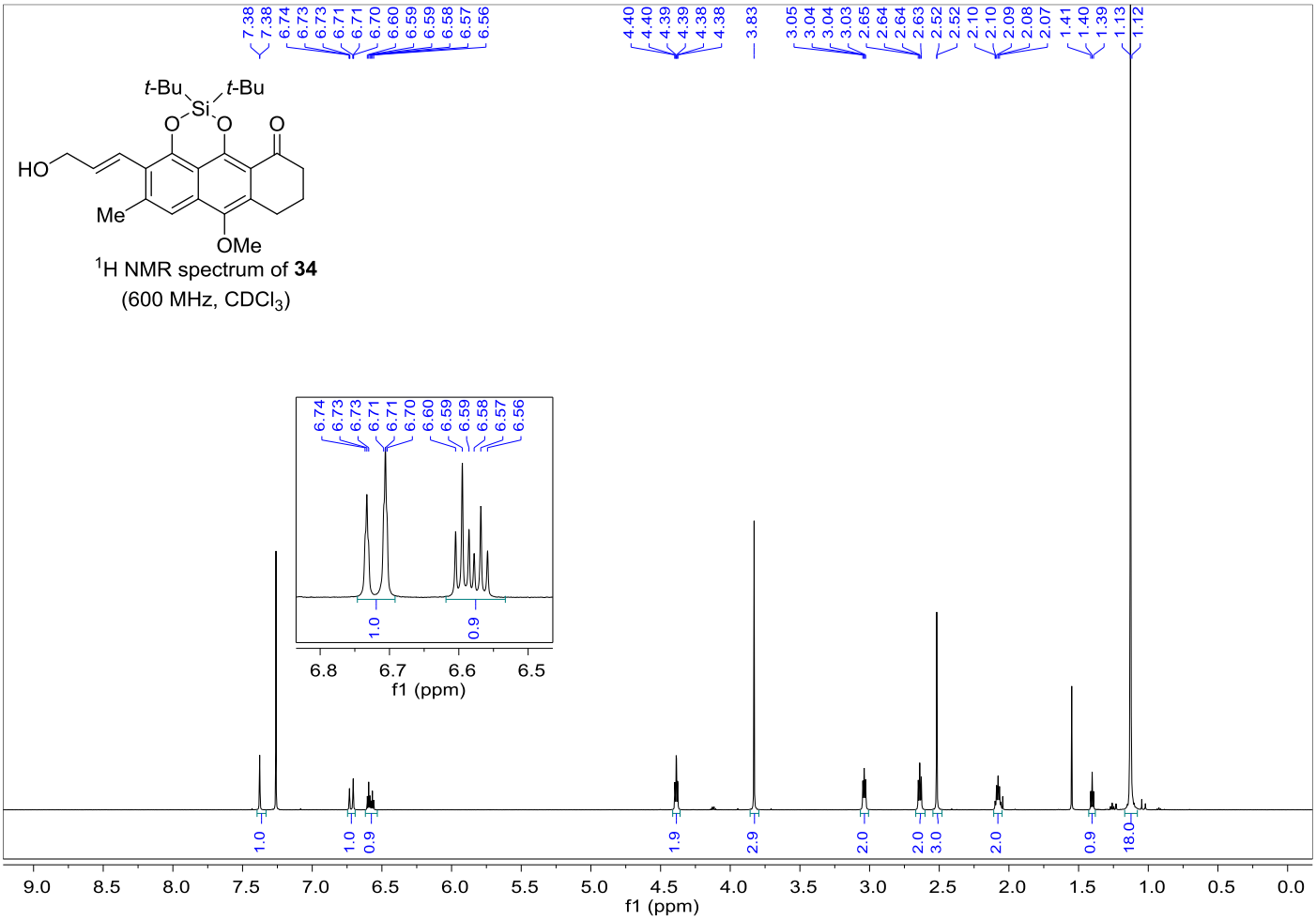

OAc
Me
Me
HO
O
H
OMe
MeO
OMe
OMe
HO
O
OTBS
Me
OAc
Me
H
O
O
O
O
^{13}C NMR spectrum of **32**
(151 MHz, $CDCl_3$)
f1 (ppm)


^{1}H NMR spectrum of **Trx5**
(600 MHz, $CDCl_3$)
f1 (ppm)

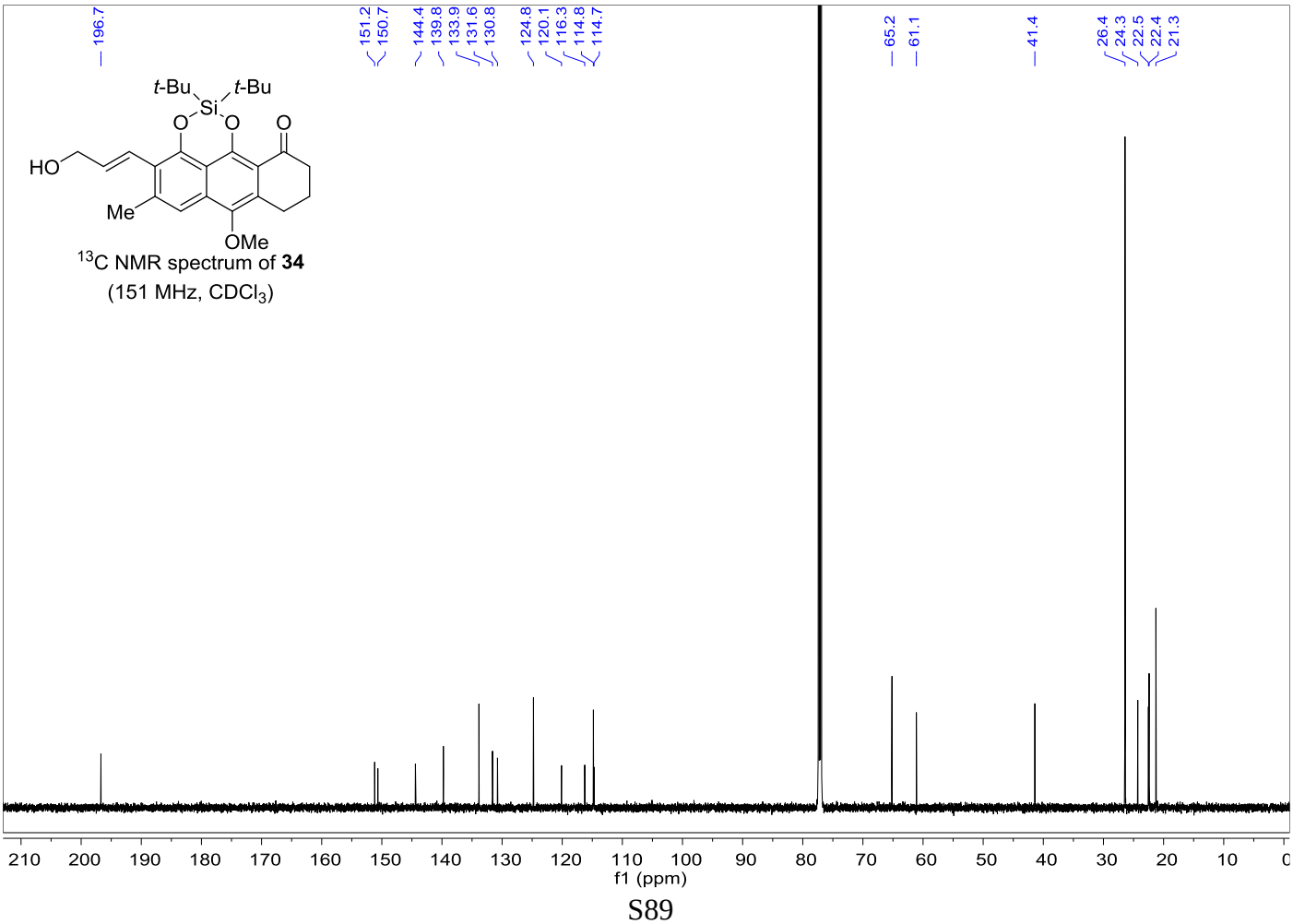

^{13}C NMR spectrum of **Trx5**
(151 MHz, $CDCl_3$)
f1 (ppm)


^{1}H NMR spectrum of **Trx6**
(600 MHz, $CDCl_3$)
f1 (ppm)

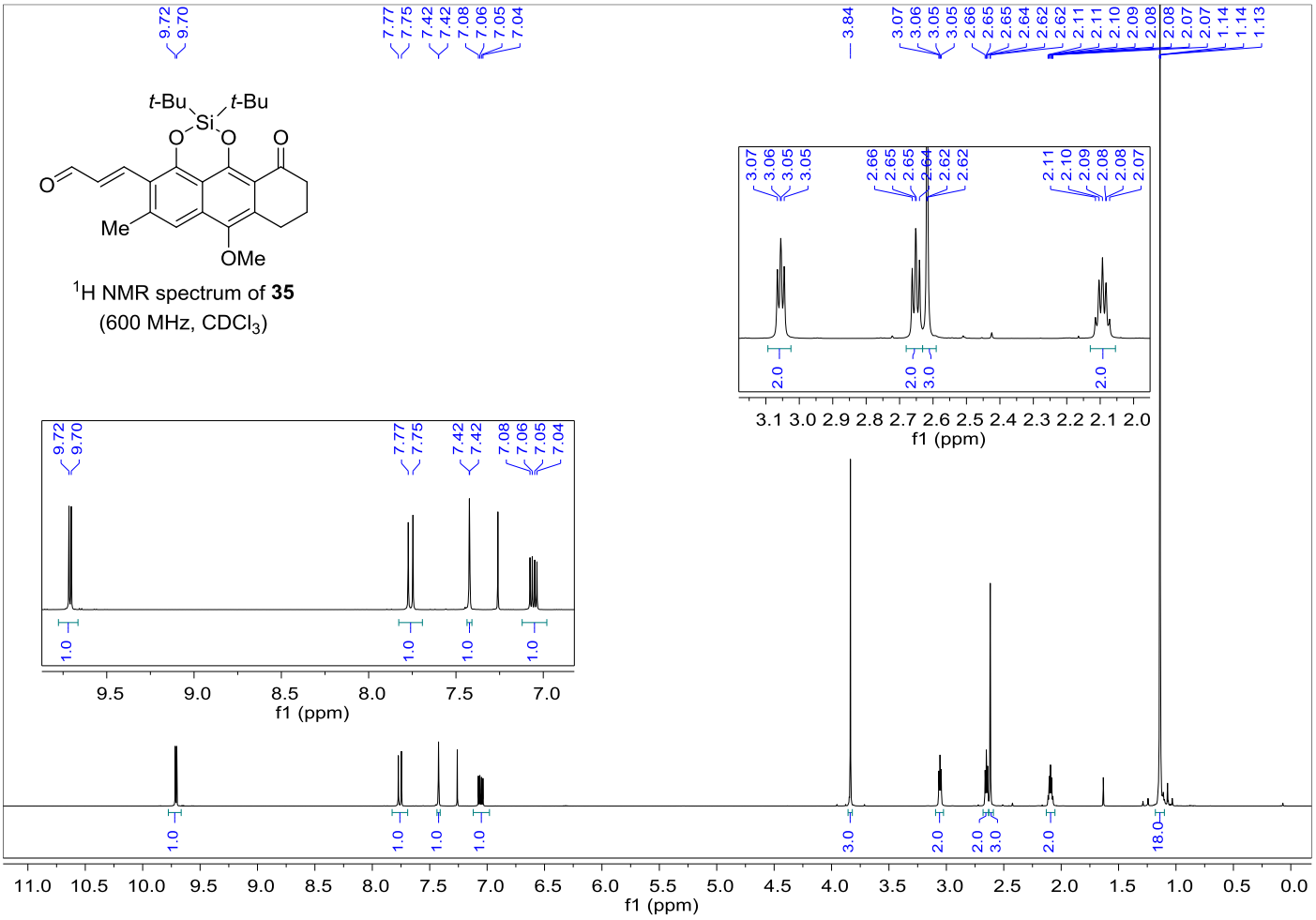

^{13}C NMR spectrum of **Trx6**
(151 MHz, $CDCl_3$)
f1 (ppm)



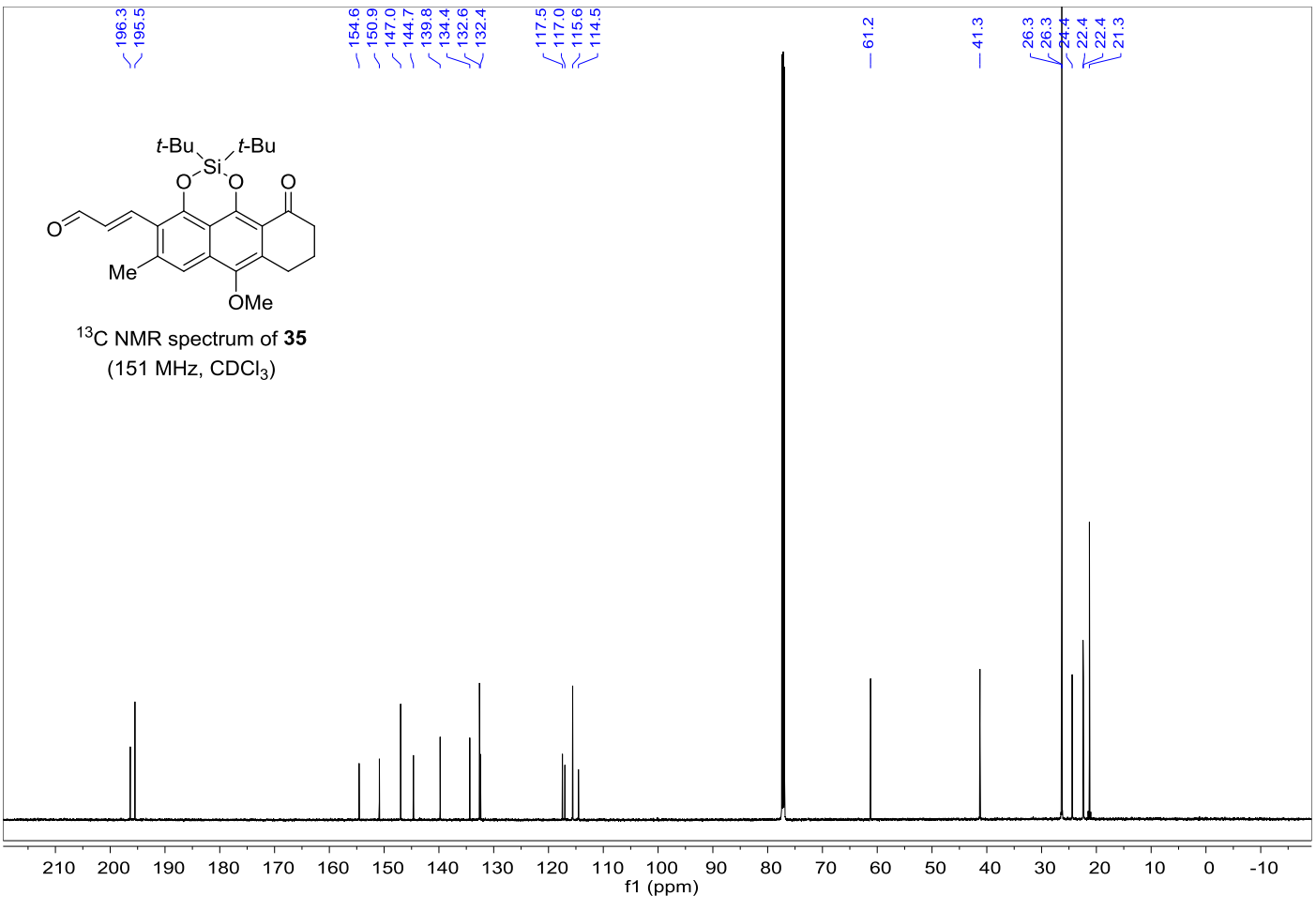
^{1}H NMR spectrum of **34**
(600 MHz, $CDCl_3$)



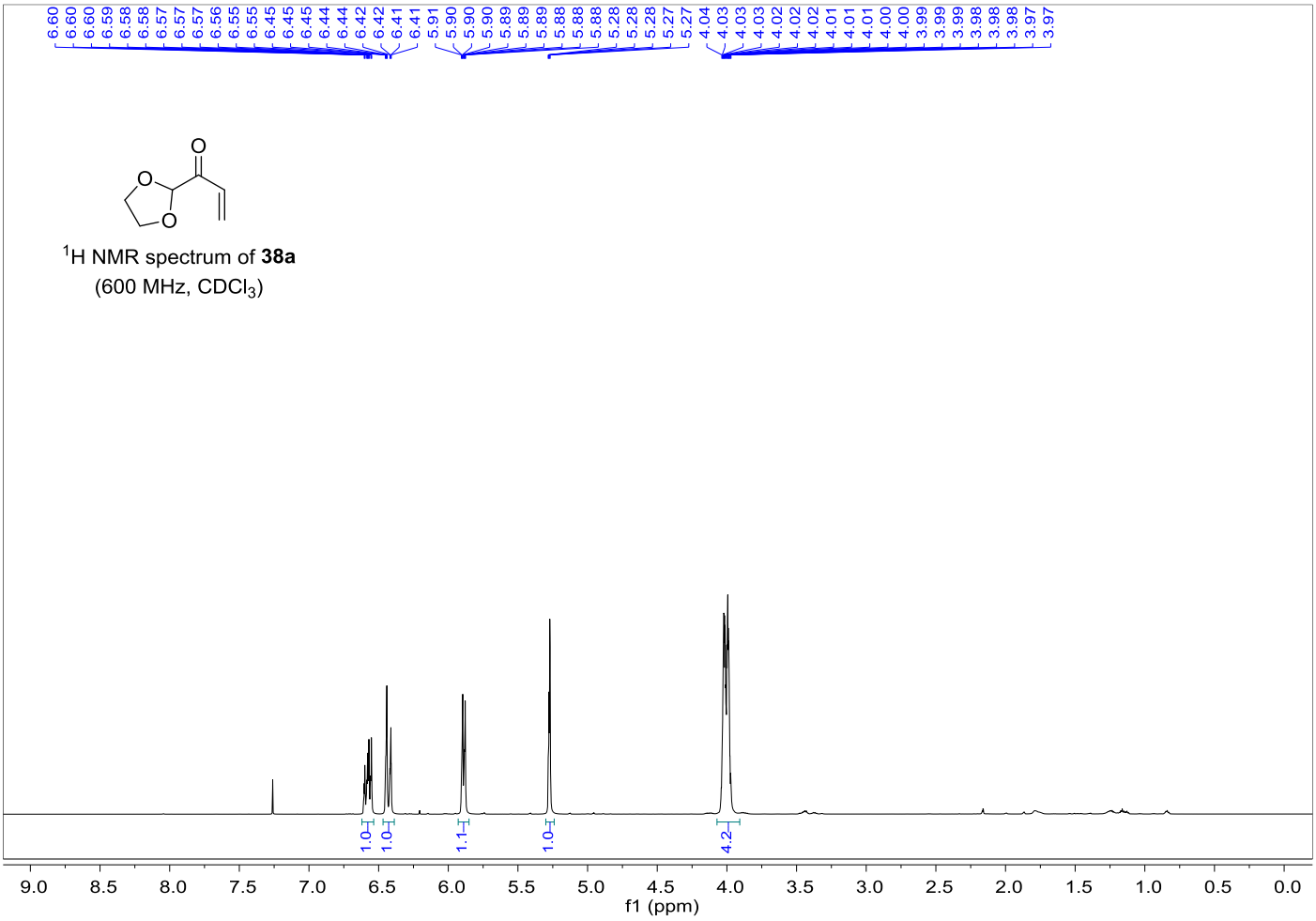
^{13}C NMR spectrum of **34**
(151 MHz, $CDCl_3$)



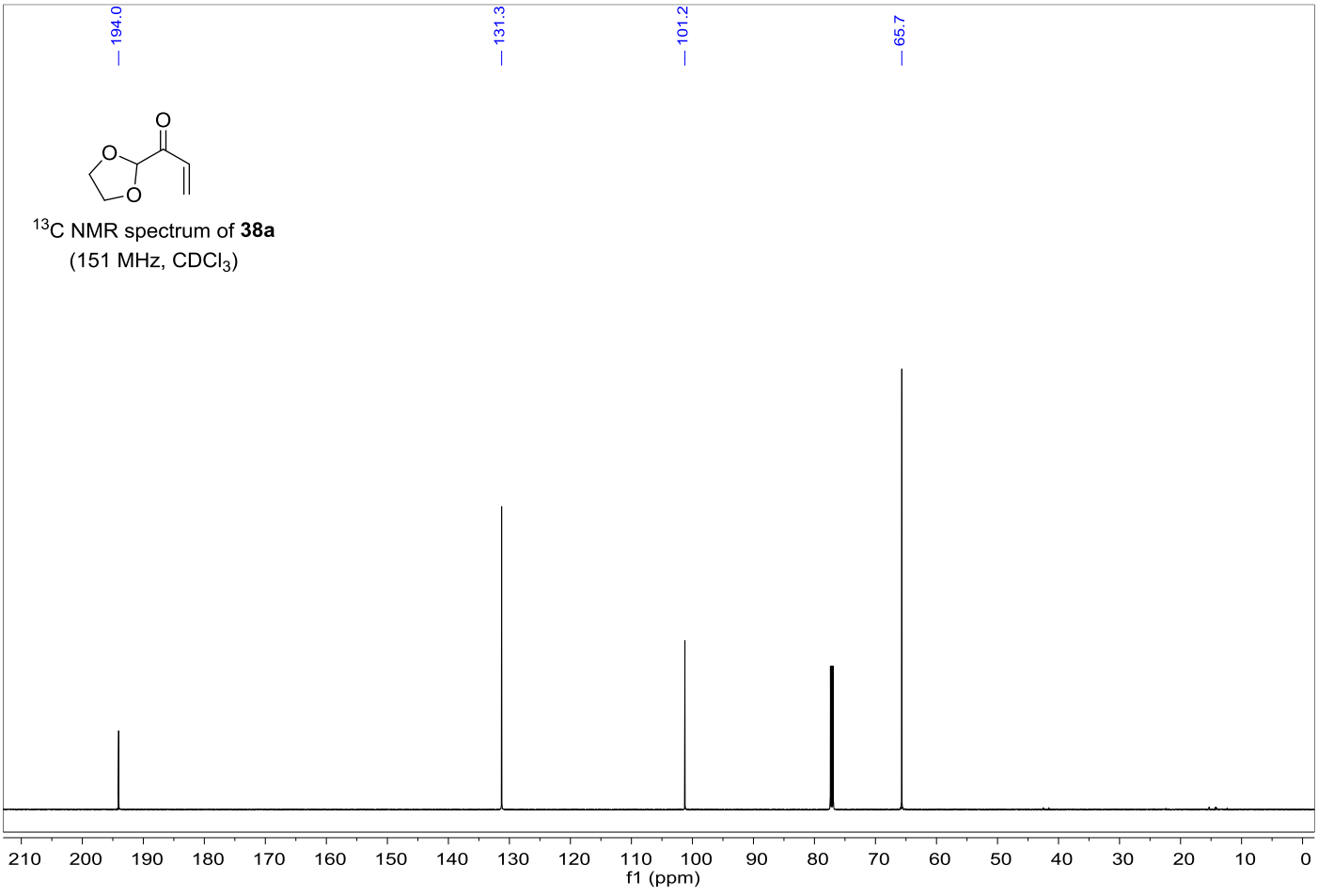
^{1}H NMR spectrum of **35**
(600 MHz, $CDCl_3$)



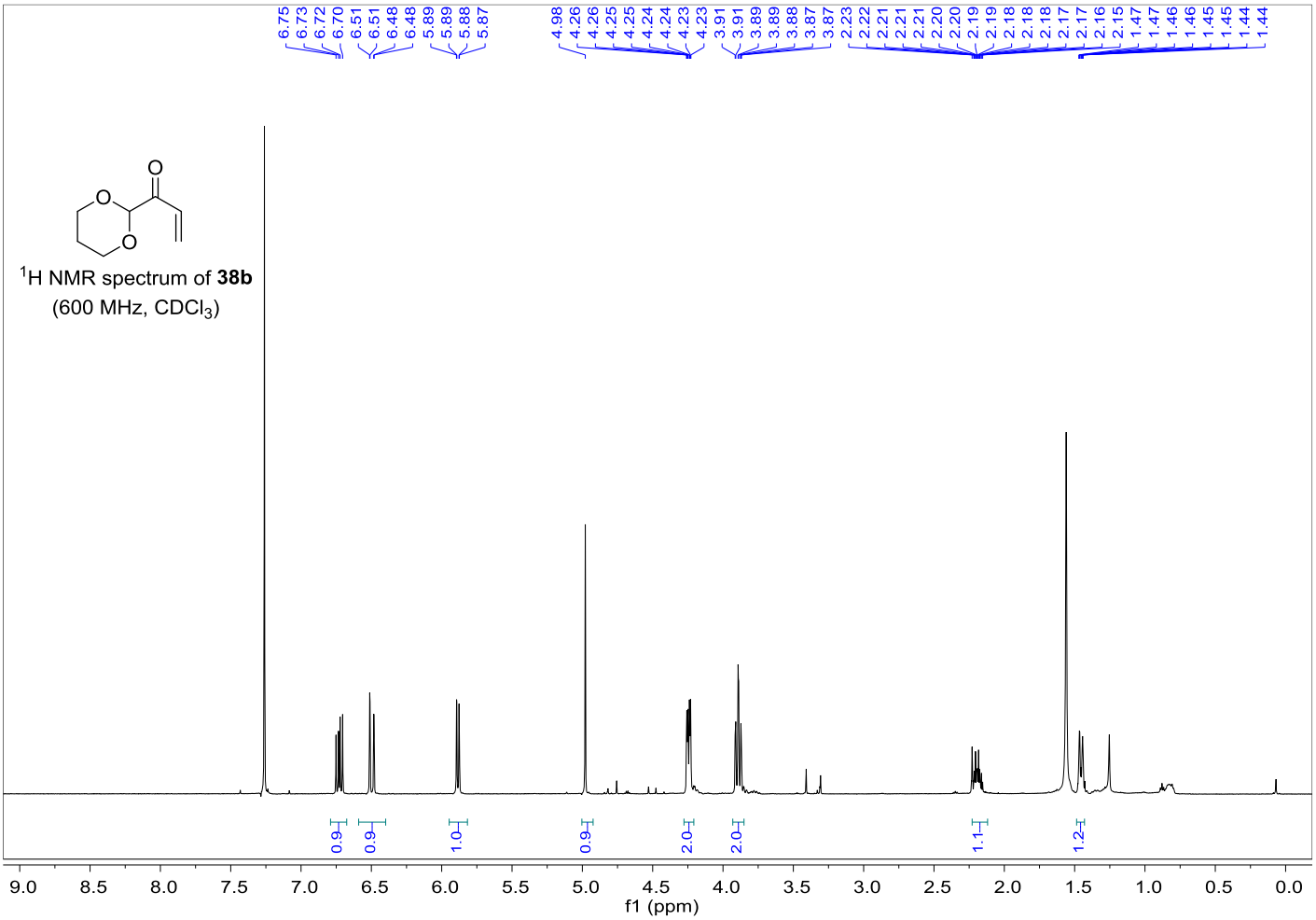
^{13}C NMR spectrum of **35**
(151 MHz, $CDCl_3$)



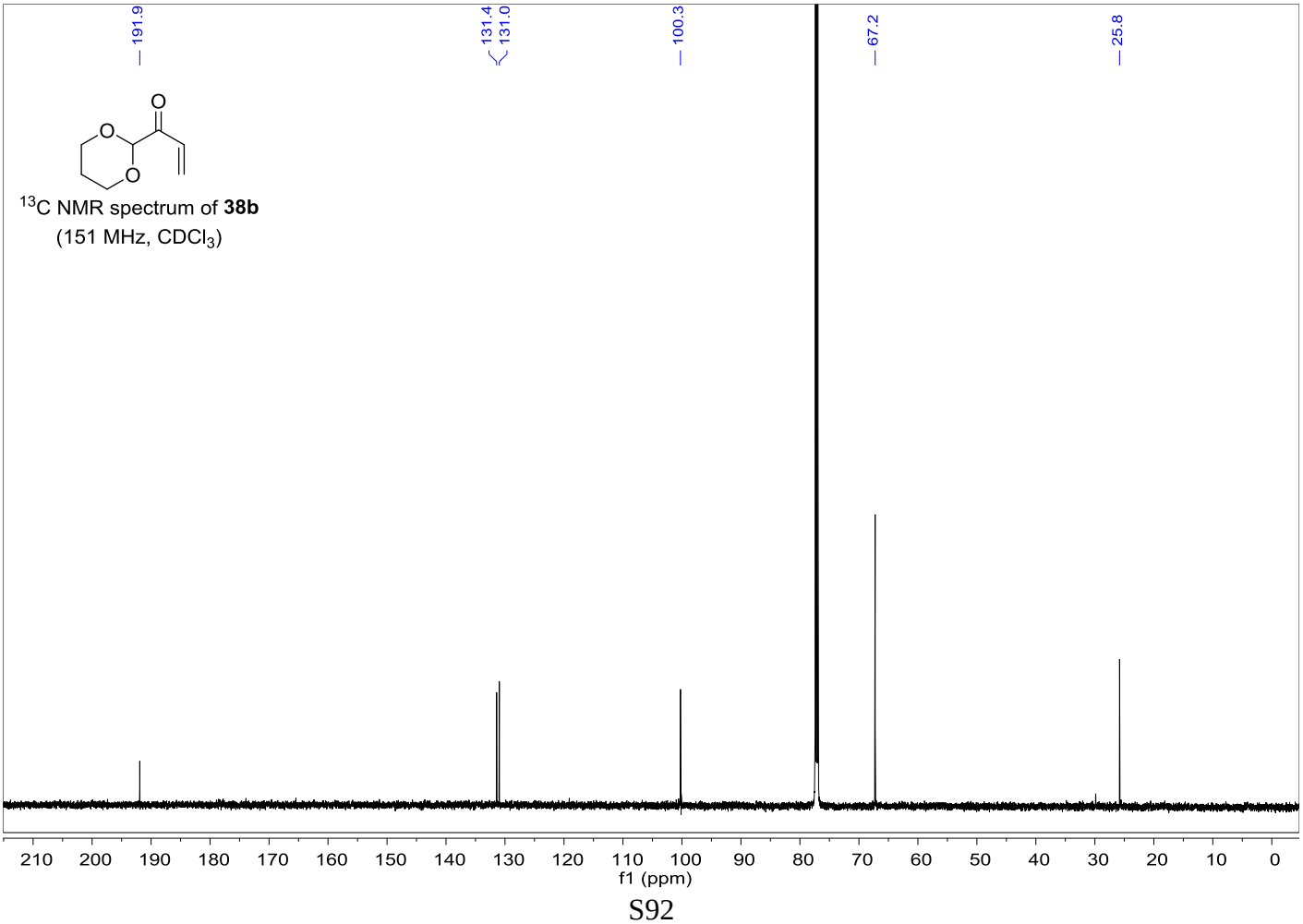
^{1}H NMR spectrum of **38a**
(600 MHz, $CDCl_3$)



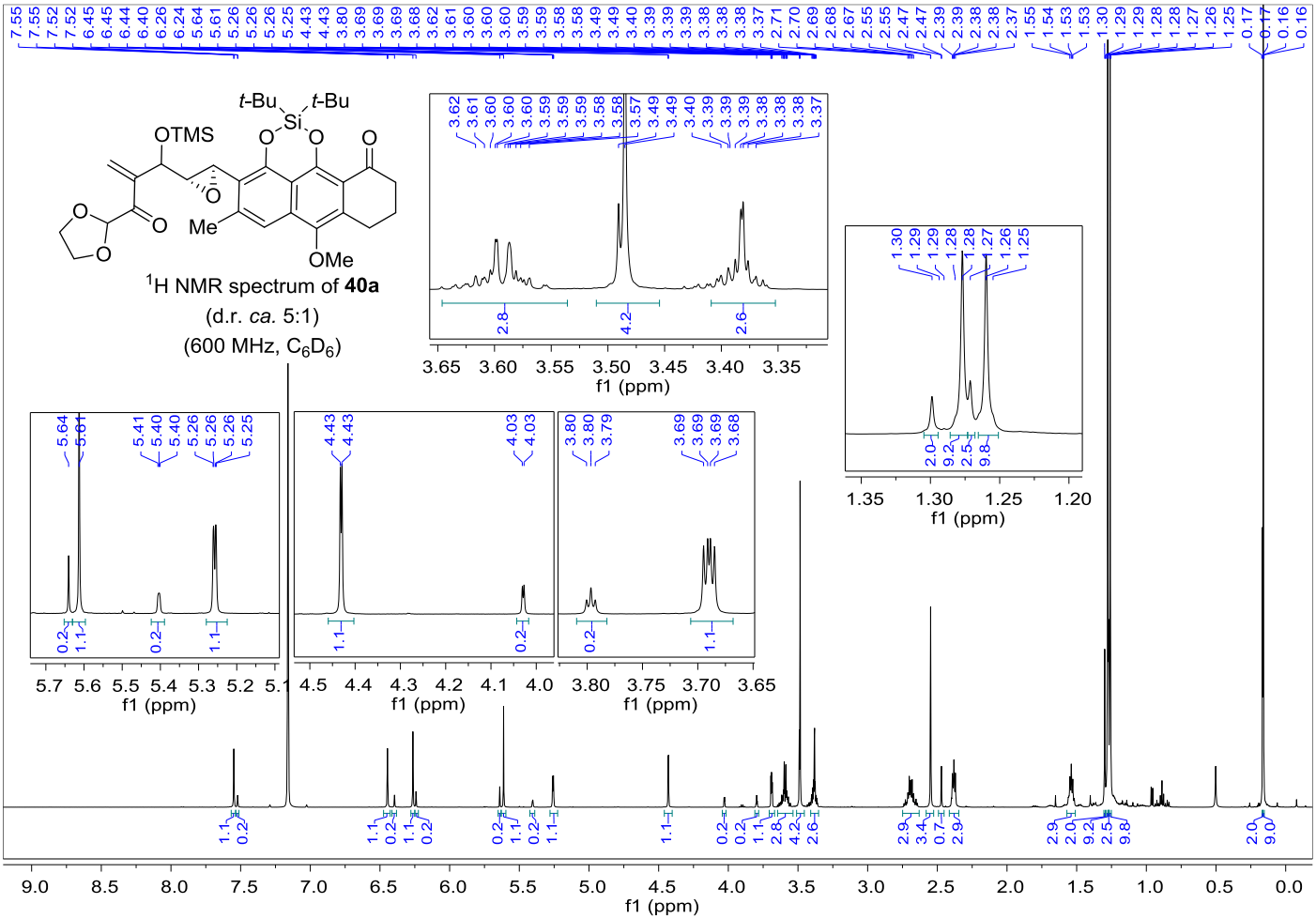
^{13}C NMR spectrum of **38a**
(151 MHz, $CDCl_3$)

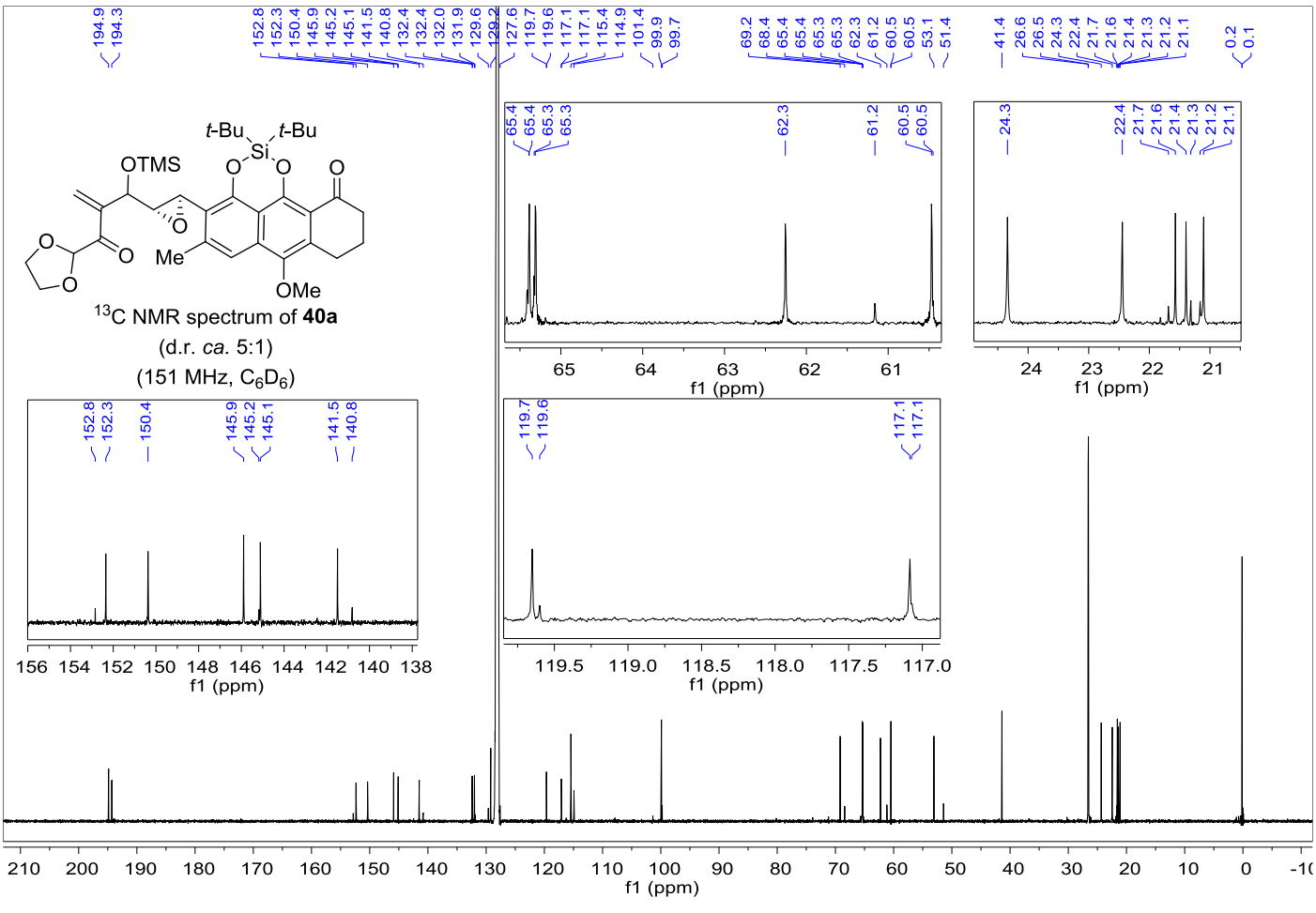


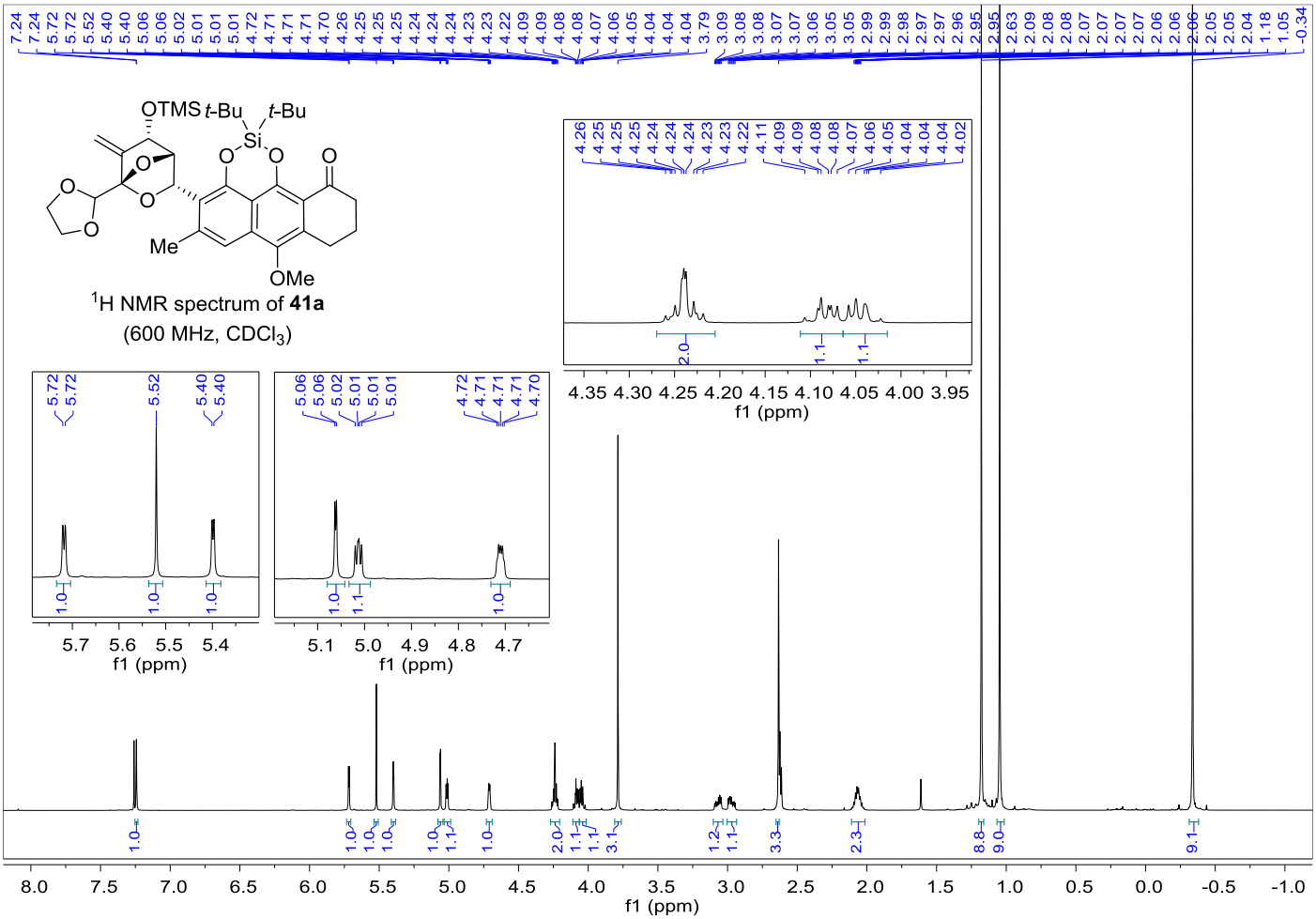
^{1}H NMR spectrum of **38b**
(600 MHz, $CDCl_3$)



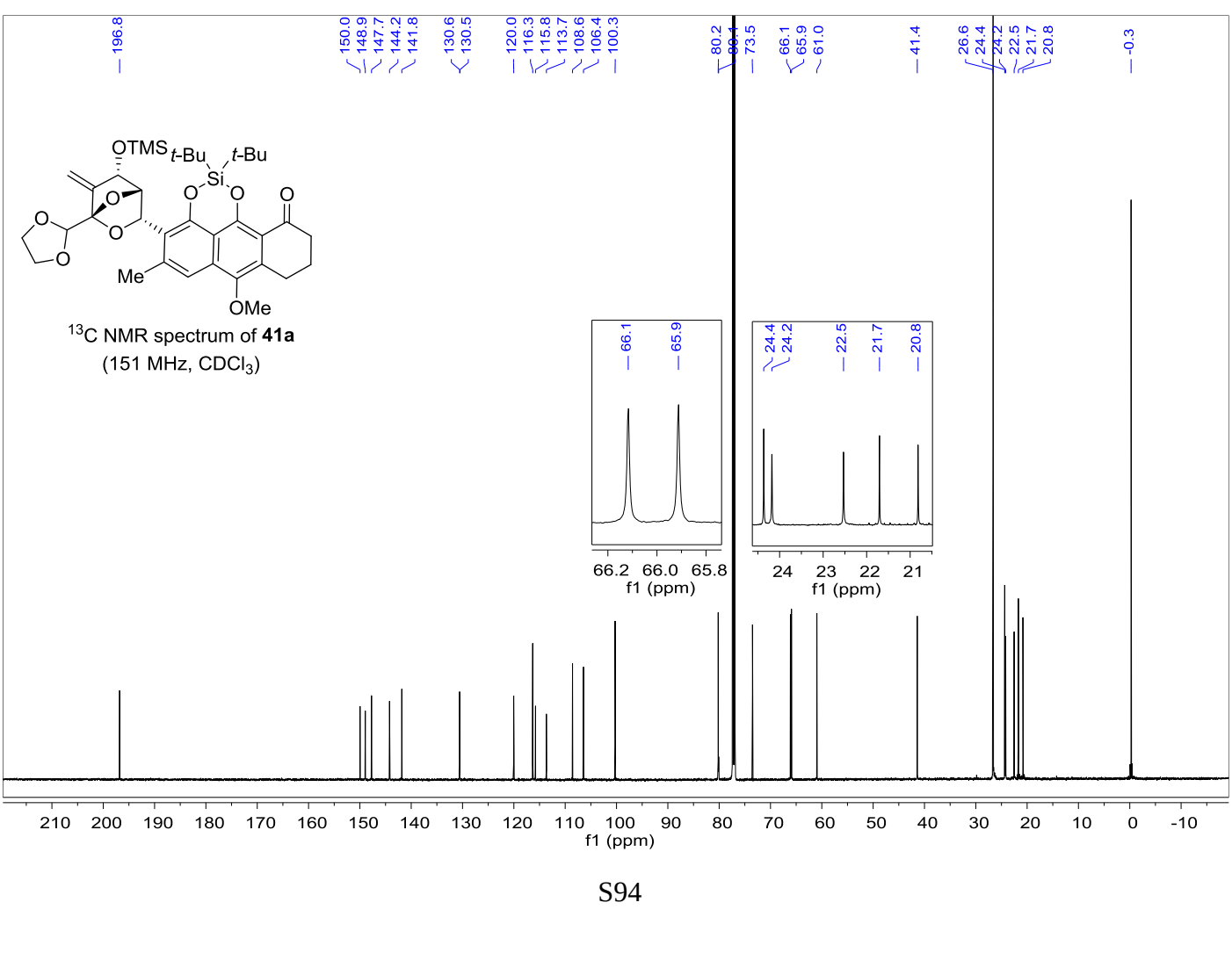
^{13}C NMR spectrum of **38b**
(151 MHz, $CDCl_3$)


t-Bu
t-Bu
Si
OTMS
O
Me
OMe
^{1}H NMR spectrum of **40a**
(d.r. *ca.* 5:1)
(600 MHz, C_6D_6)
f1 (ppm)

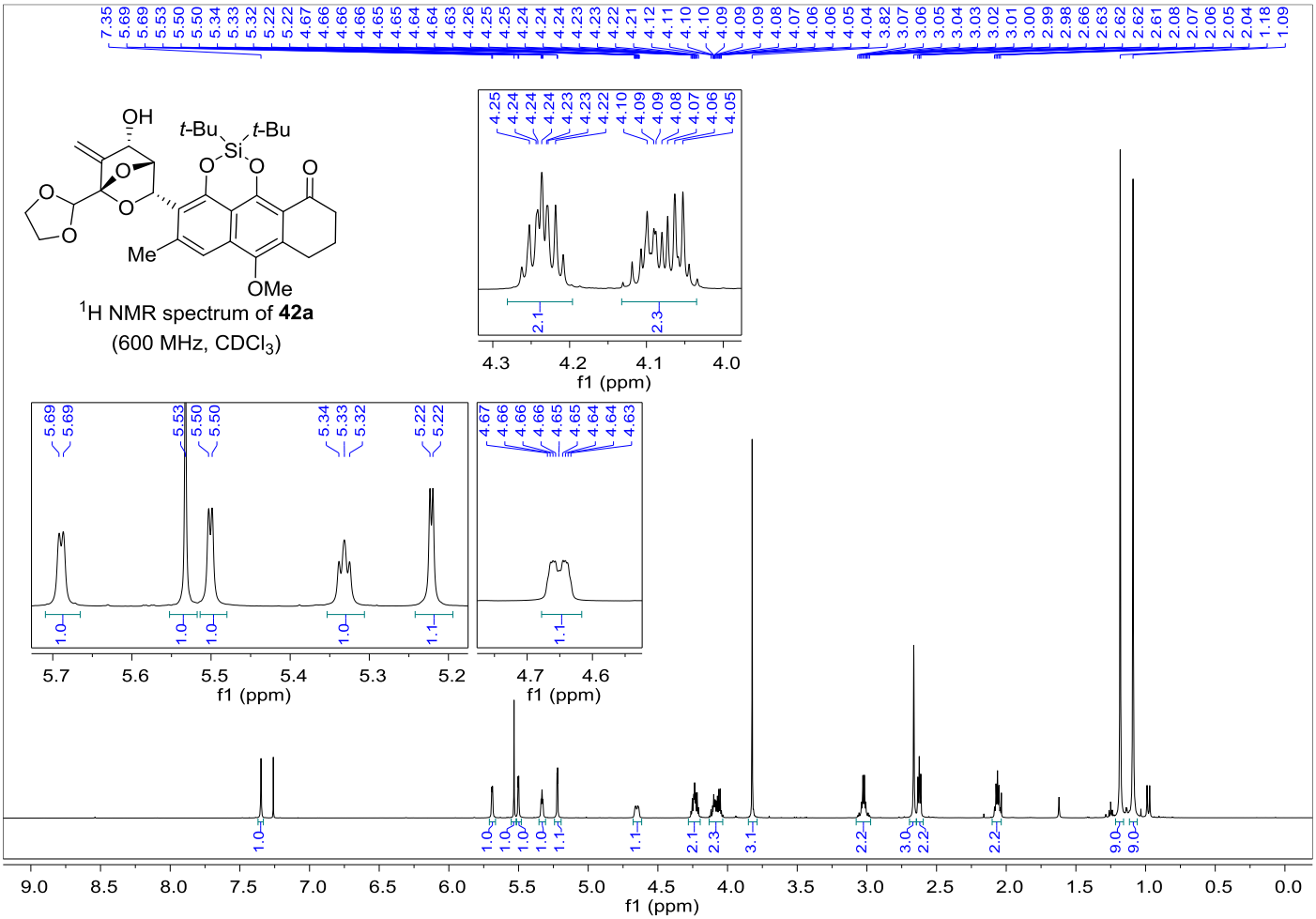

t-Bu
t-Bu
Si
OTMS
O
Me
OMe
^{13}C NMR spectrum of **40a**
(d.r. *ca.* 5:1)
(151 MHz, C_6D_6)
f1 (ppm)



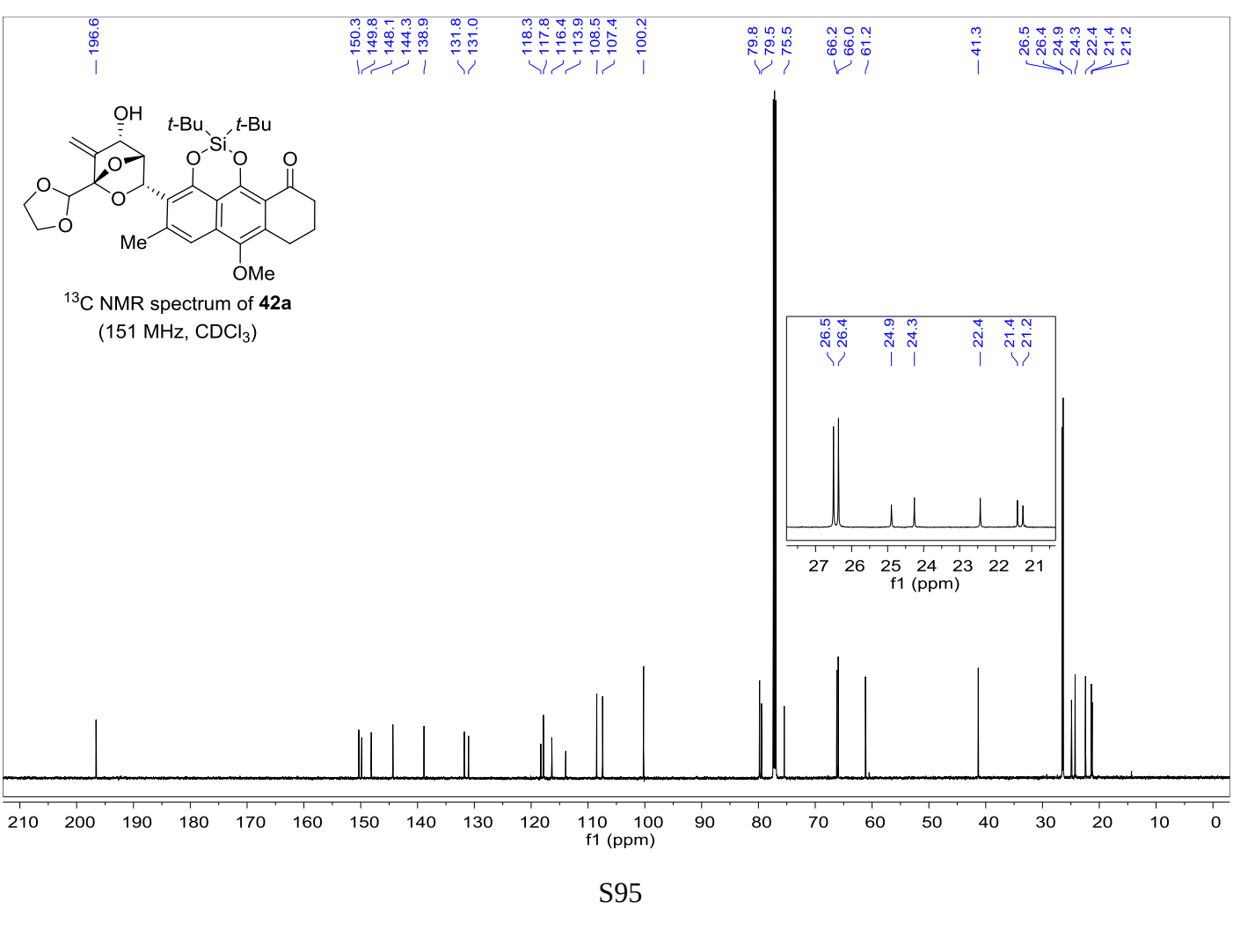
^{1}H NMR spectrum of **41a**
(600 MHz, $CDCl_3$)



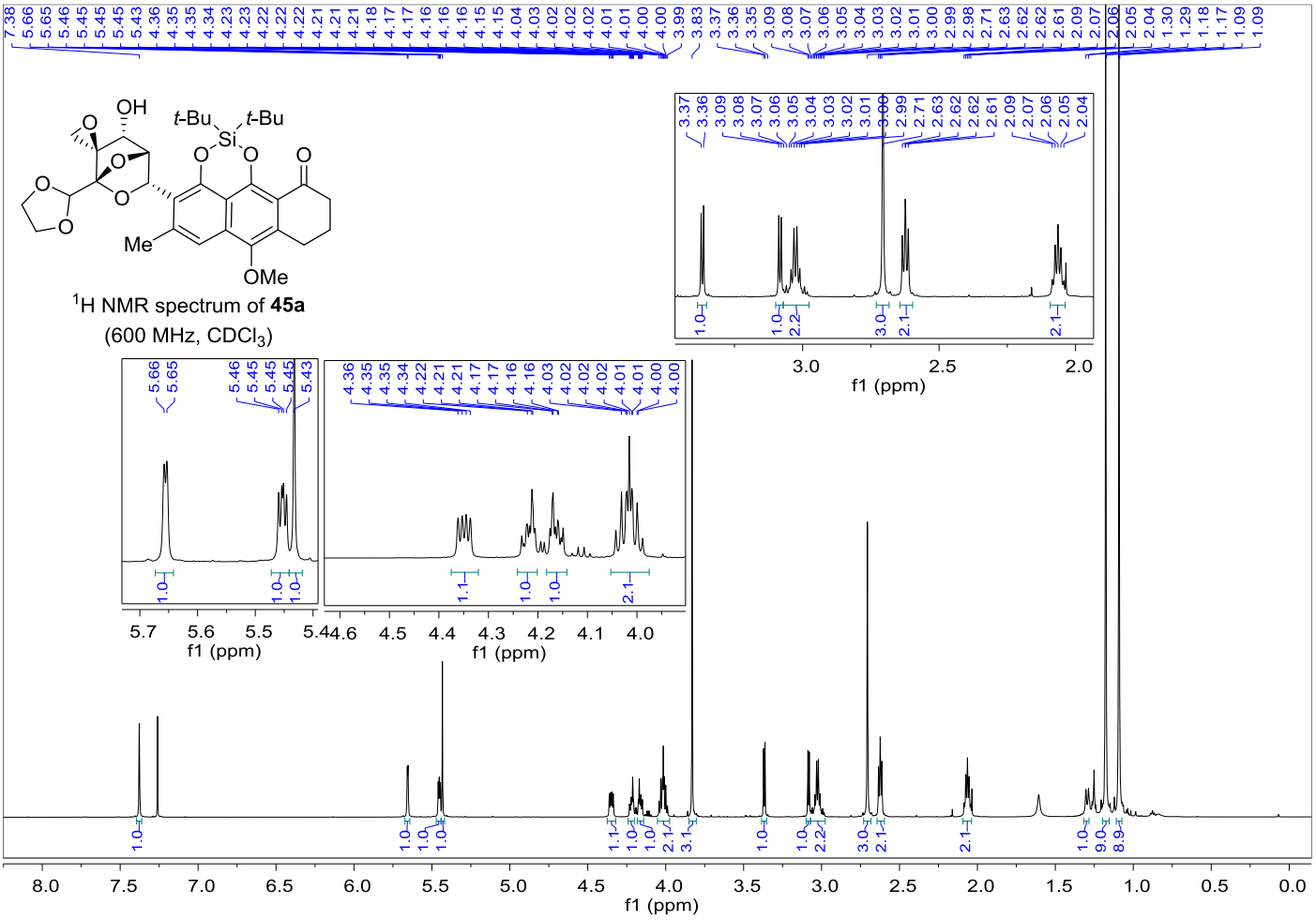
^{13}C NMR spectrum of **41a**
(151 MHz, $CDCl_3$)



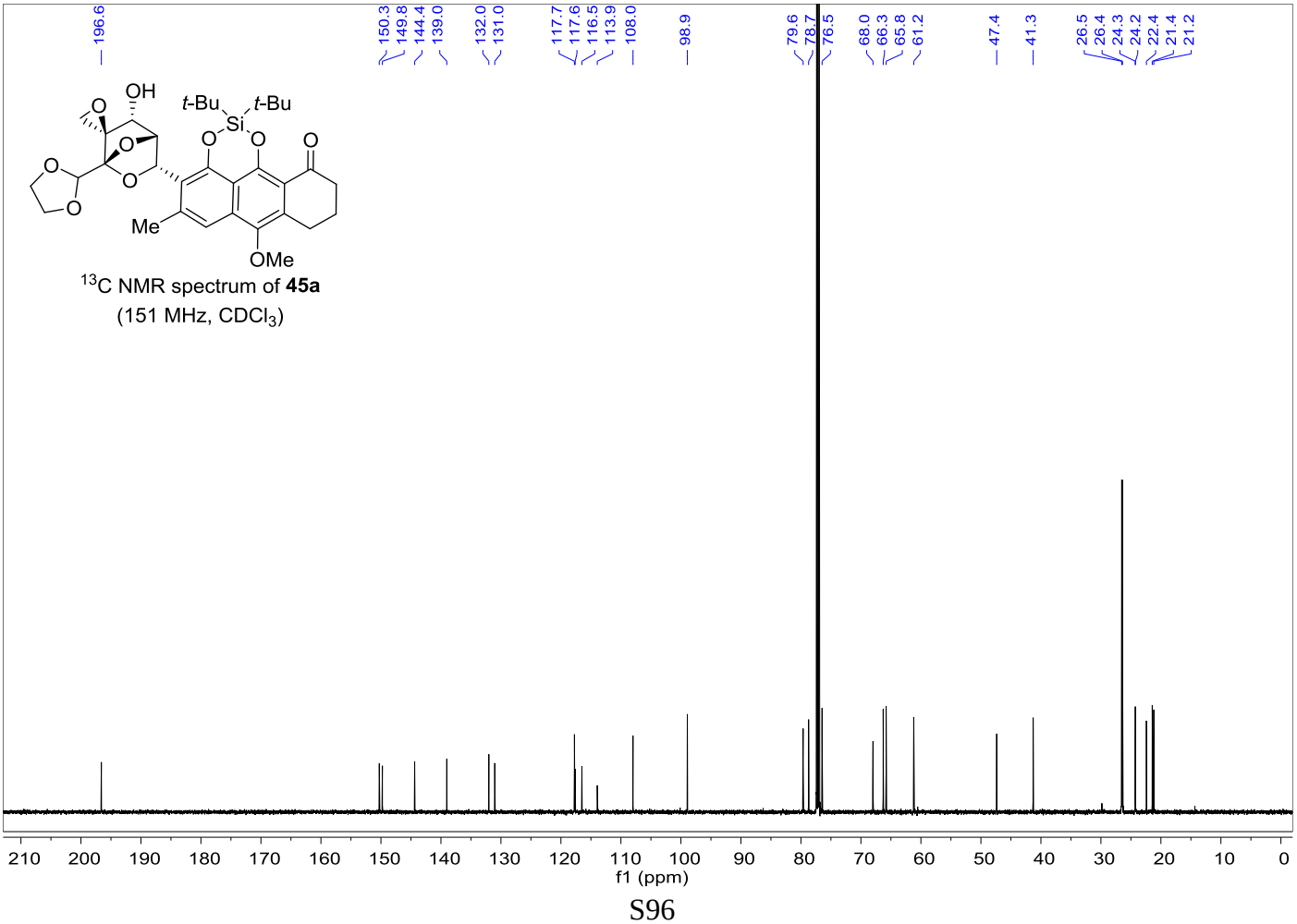
^{1}H NMR spectrum of **42a**
(600 MHz, $CDCl_3$)



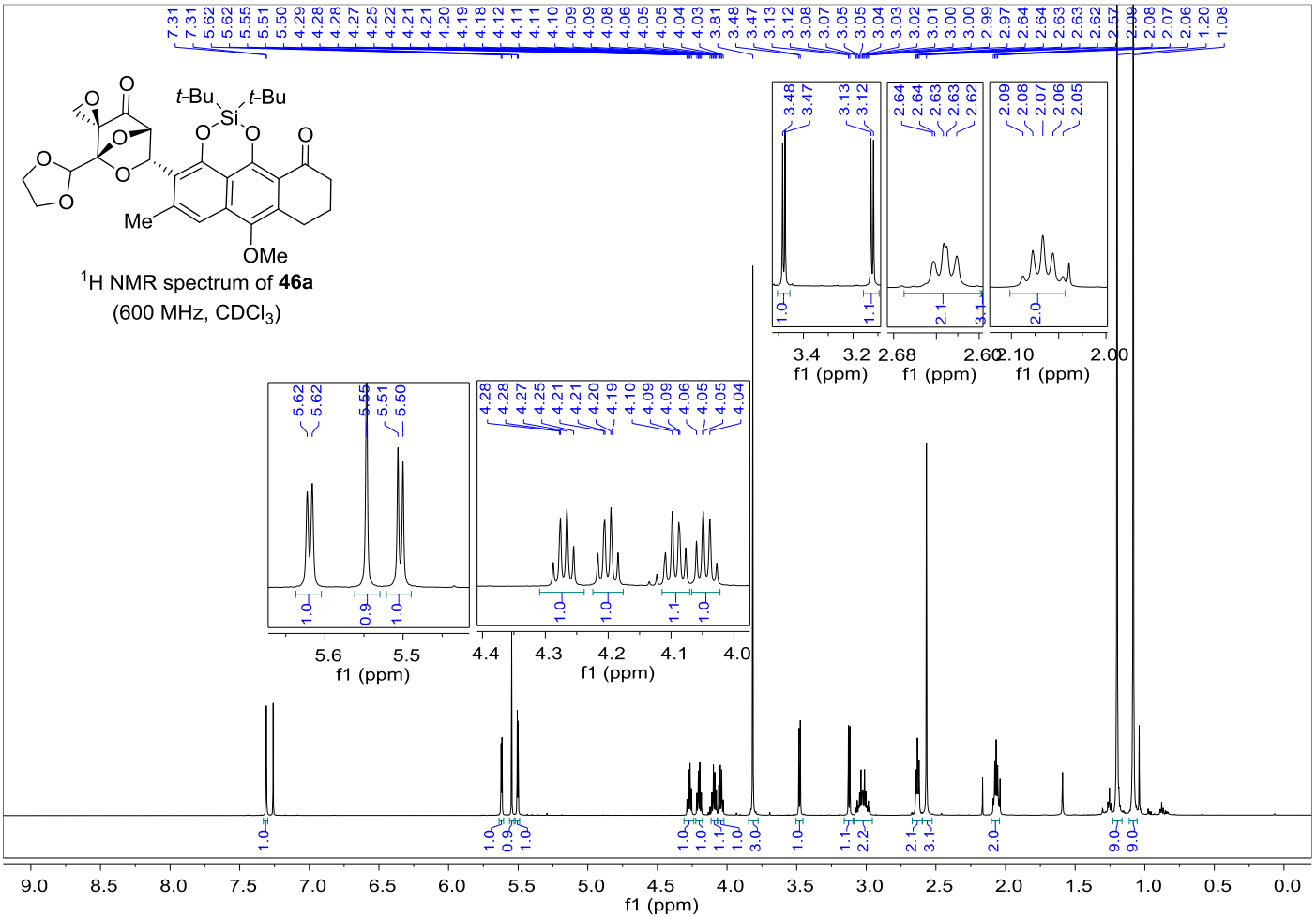
^{13}C NMR spectrum of **42a**
(151 MHz, $CDCl_3$)



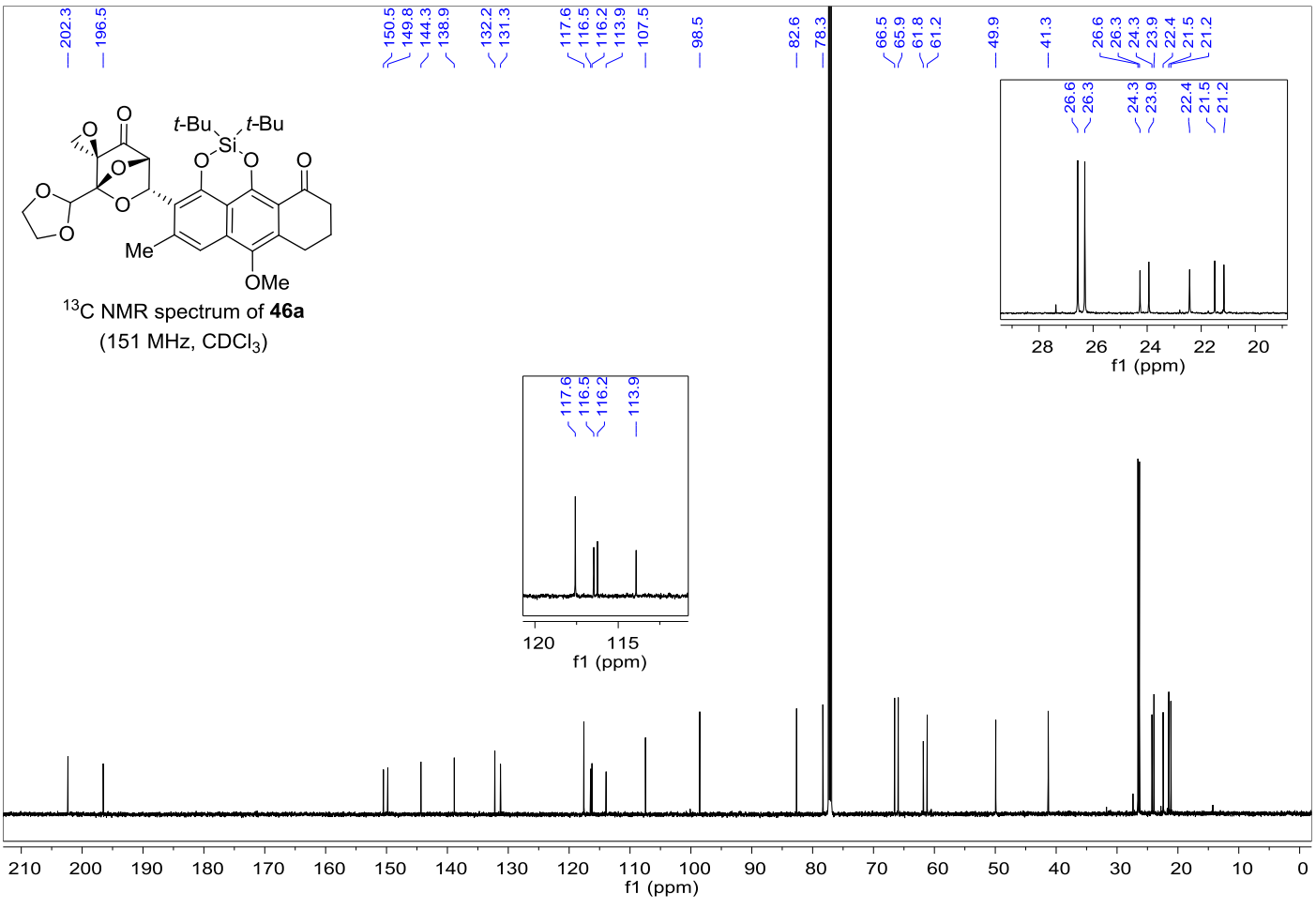
^{1}H NMR spectrum of **45a**
(600 MHz, $CDCl_3$)



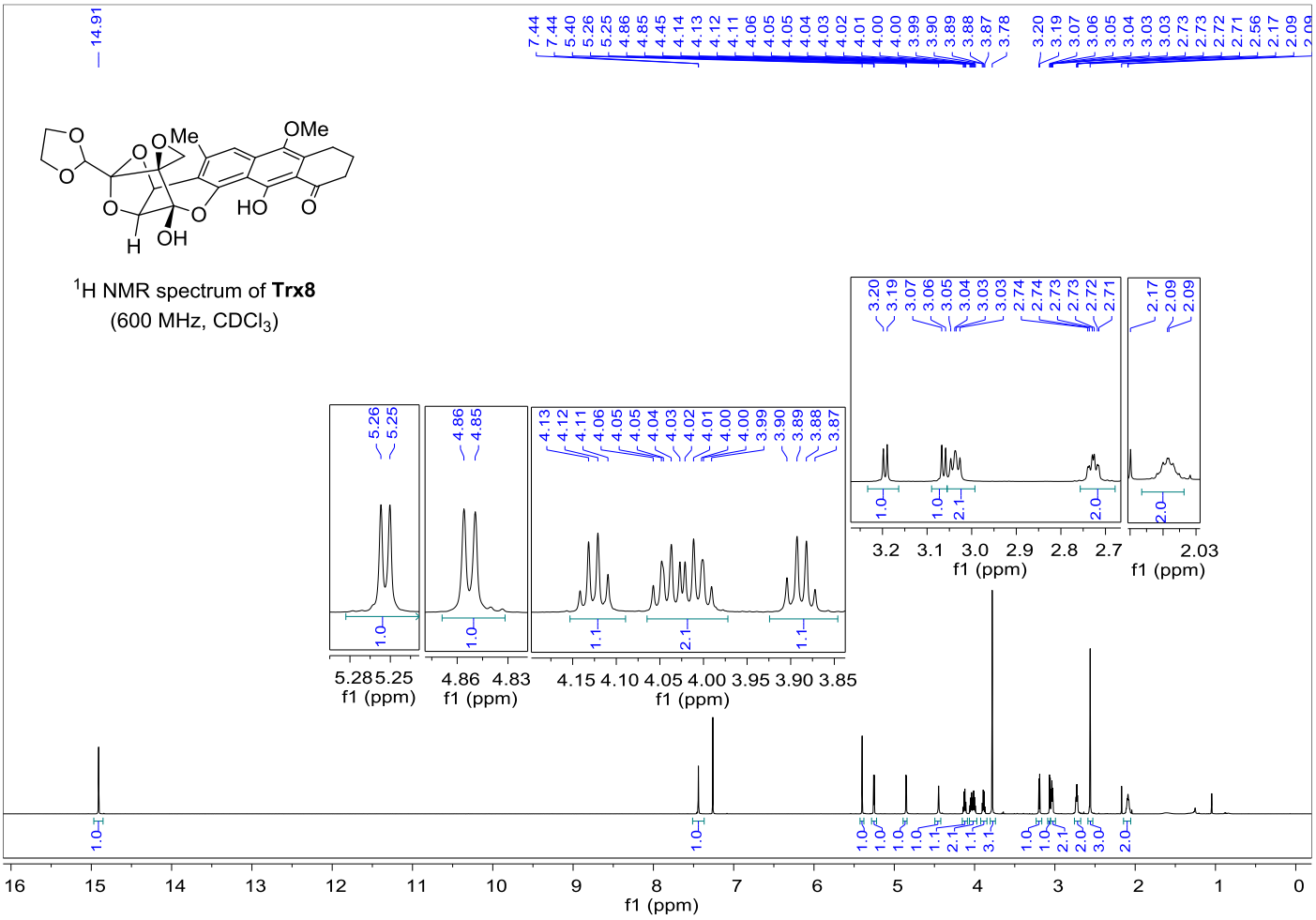
^{13}C NMR spectrum of **45a**
(151 MHz, $CDCl_3$)

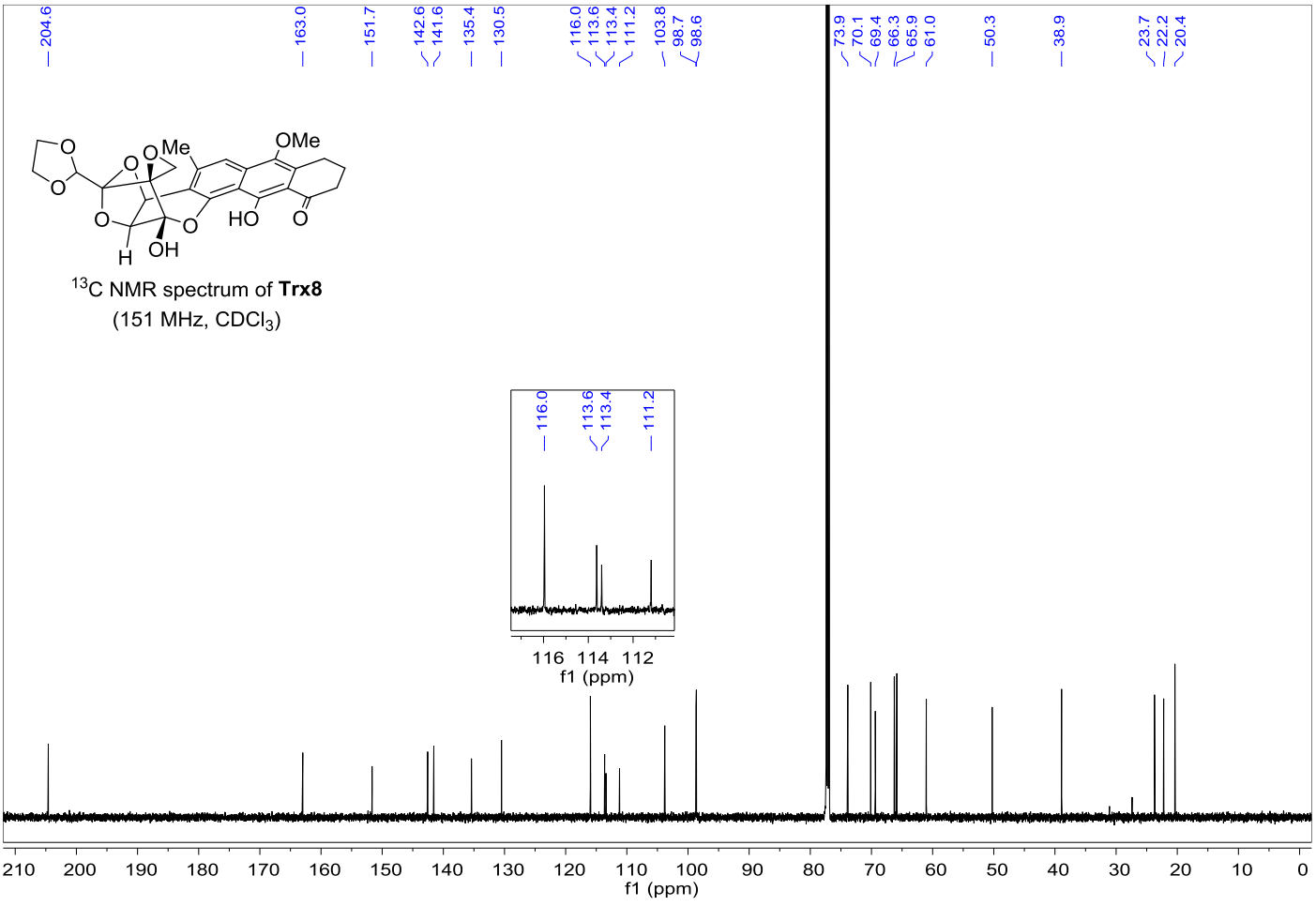


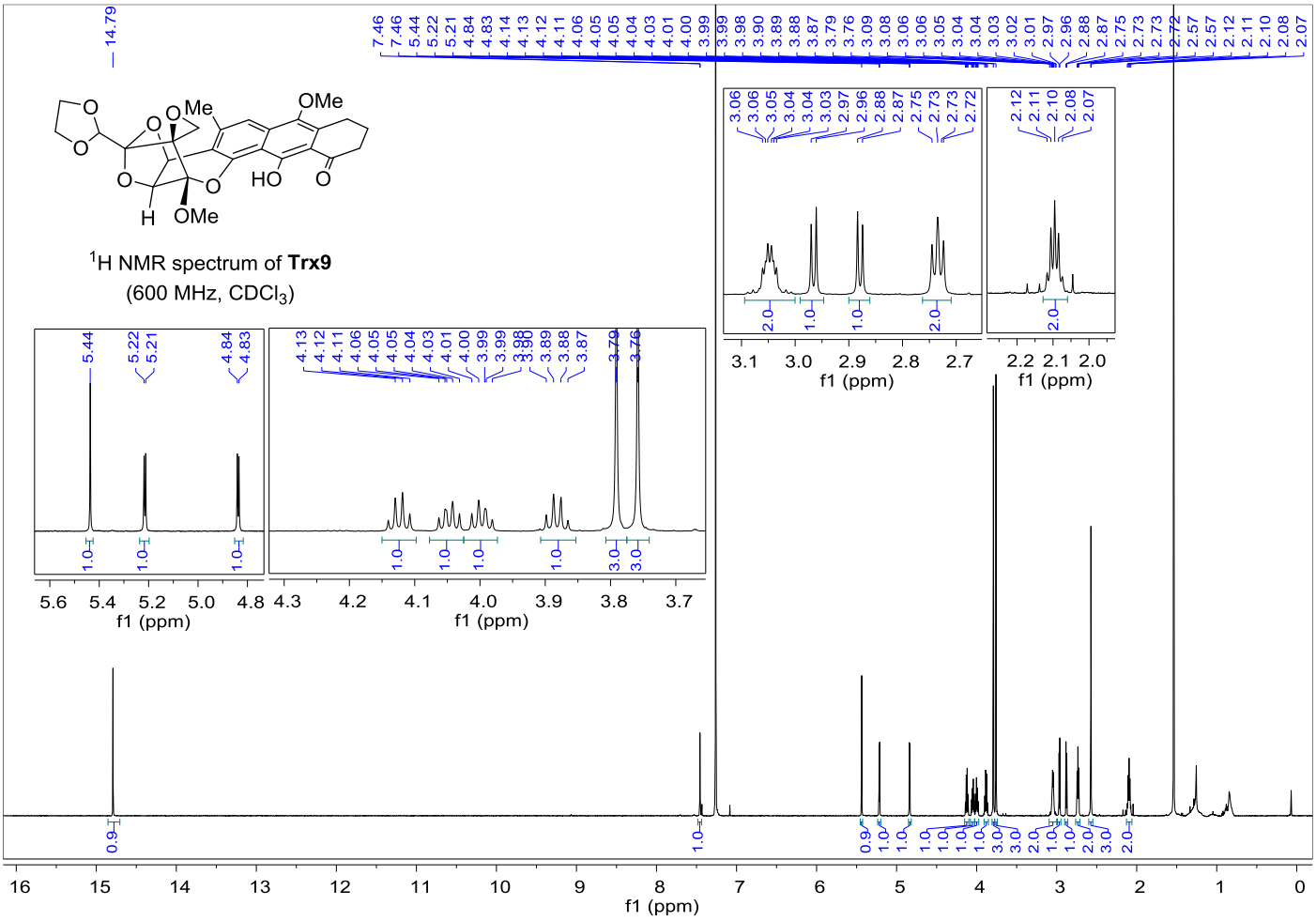
^{1}H NMR spectrum of **46a**
(600 MHz, $CDCl_3$)



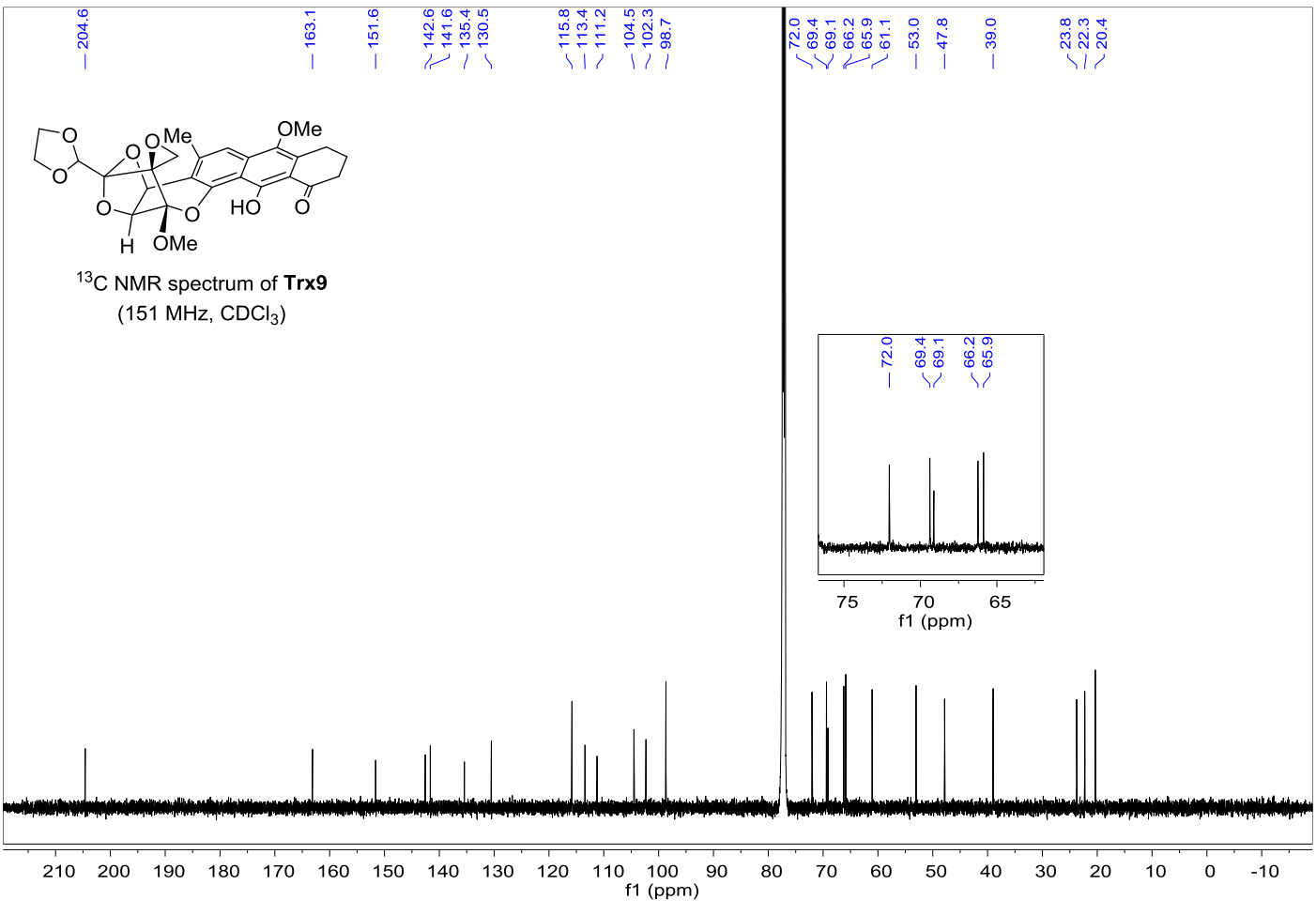
^{13}C NMR spectrum of **46a**
(151 MHz, $CDCl_3$)


14.91
7.44 7.44 5.40 5.26 5.25 4.86 4.85 4.45 4.14 4.13 4.12 4.11 4.06 4.05 4.05 4.04 4.03 4.02 4.01 4.00 4.00 3.99 3.90 3.89 3.88 3.87 3.78
3.20 3.19 3.07 3.06 3.05 3.04 3.03 3.03 2.74 2.74 2.73 2.73 2.72 2.71 2.17 2.09 2.09
5.26 5.25 4.86 4.85 4.13 4.12 4.11 4.06 4.05 4.05 4.04 4.03 4.02 4.01 4.00 4.00 3.99 3.90 3.89 3.88 3.87
Me
OMe
HO
O
OH
H
1H NMR spectrum of Trx8
(600 MHz, CDCl3)
f1 (ppm)

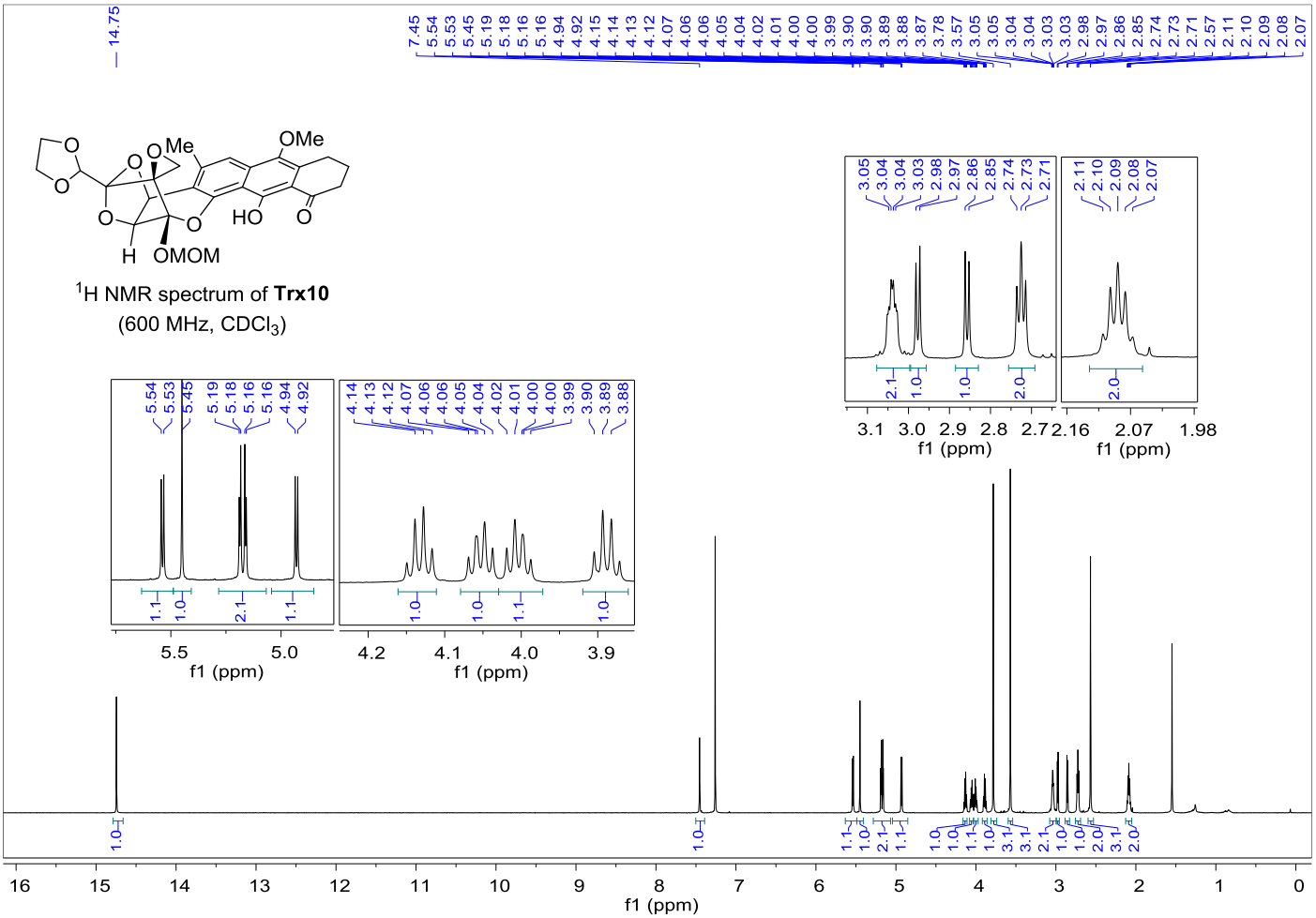

204.6 163.0 151.7 142.6 141.6 135.4 130.5 116.0 113.6 113.4 111.2 103.8 98.7 98.6 73.9 70.1 69.4 66.3 65.9 61.0 50.3 38.9 23.7 22.2 20.4
Me
OMe
HO
O
OH
H
13C NMR spectrum of Trx8
(151 MHz, CDCl3)
f1 (ppm)

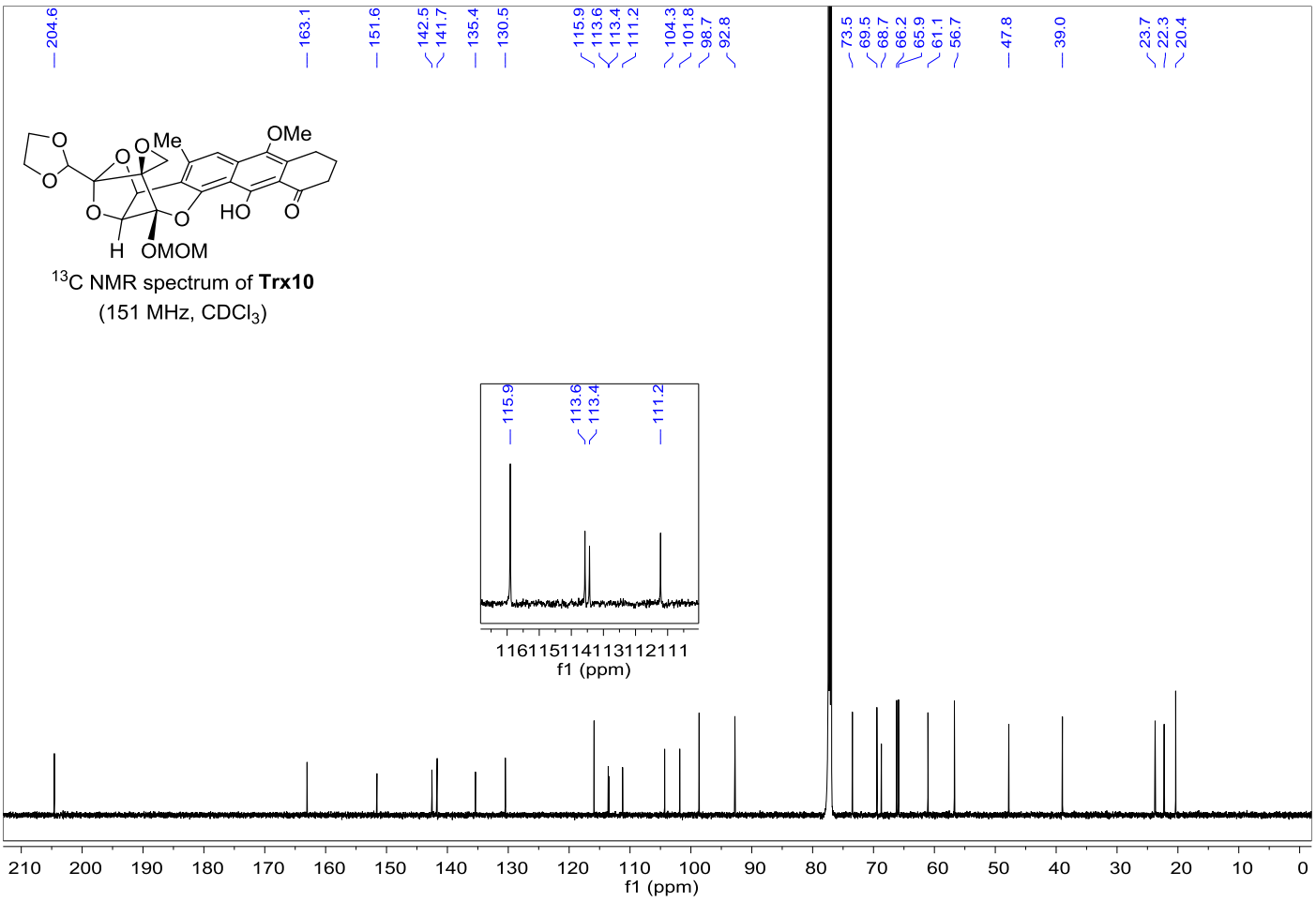


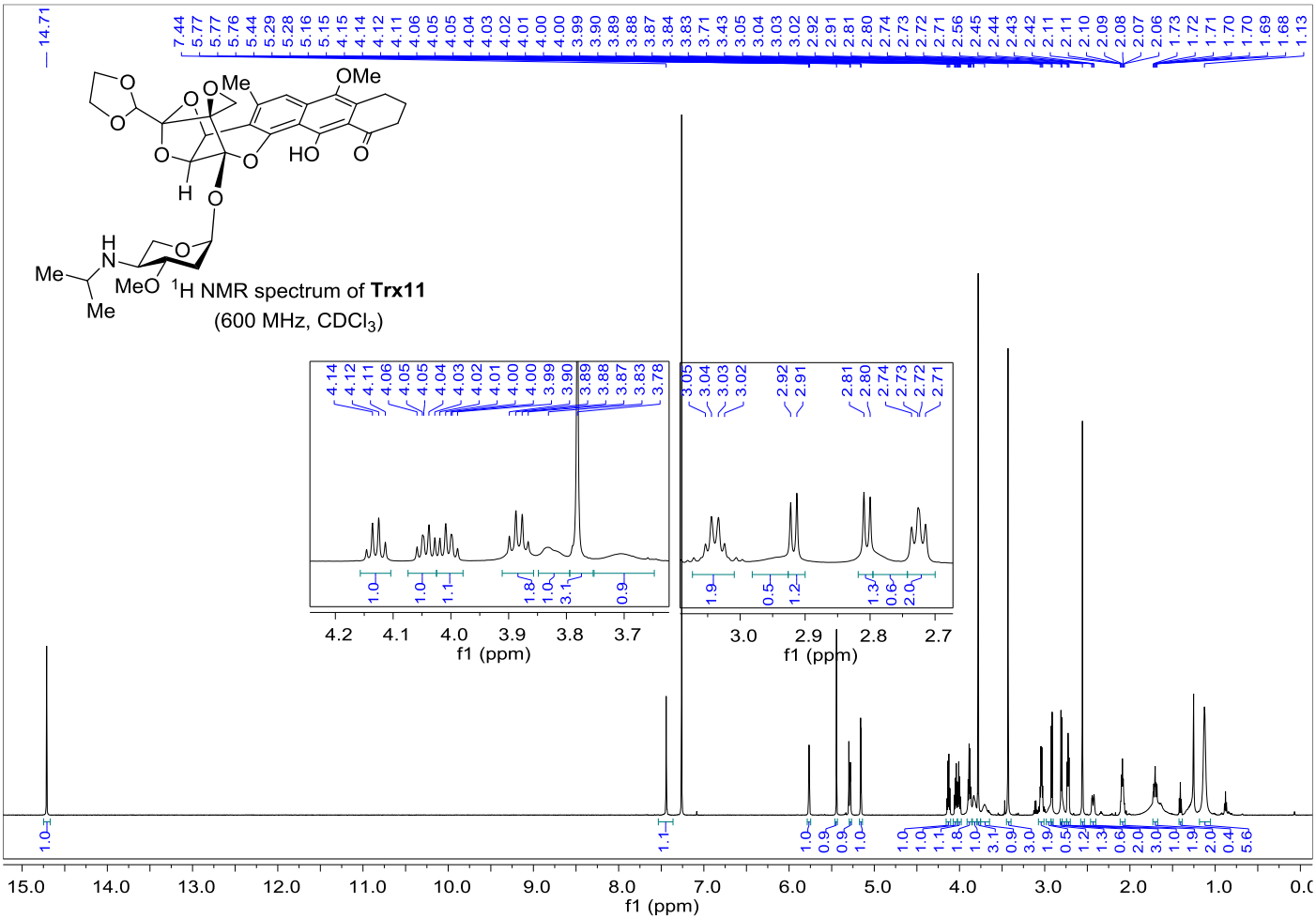
^{1}H NMR spectrum of **Trx9**
(600 MHz, $CDCl_3$)

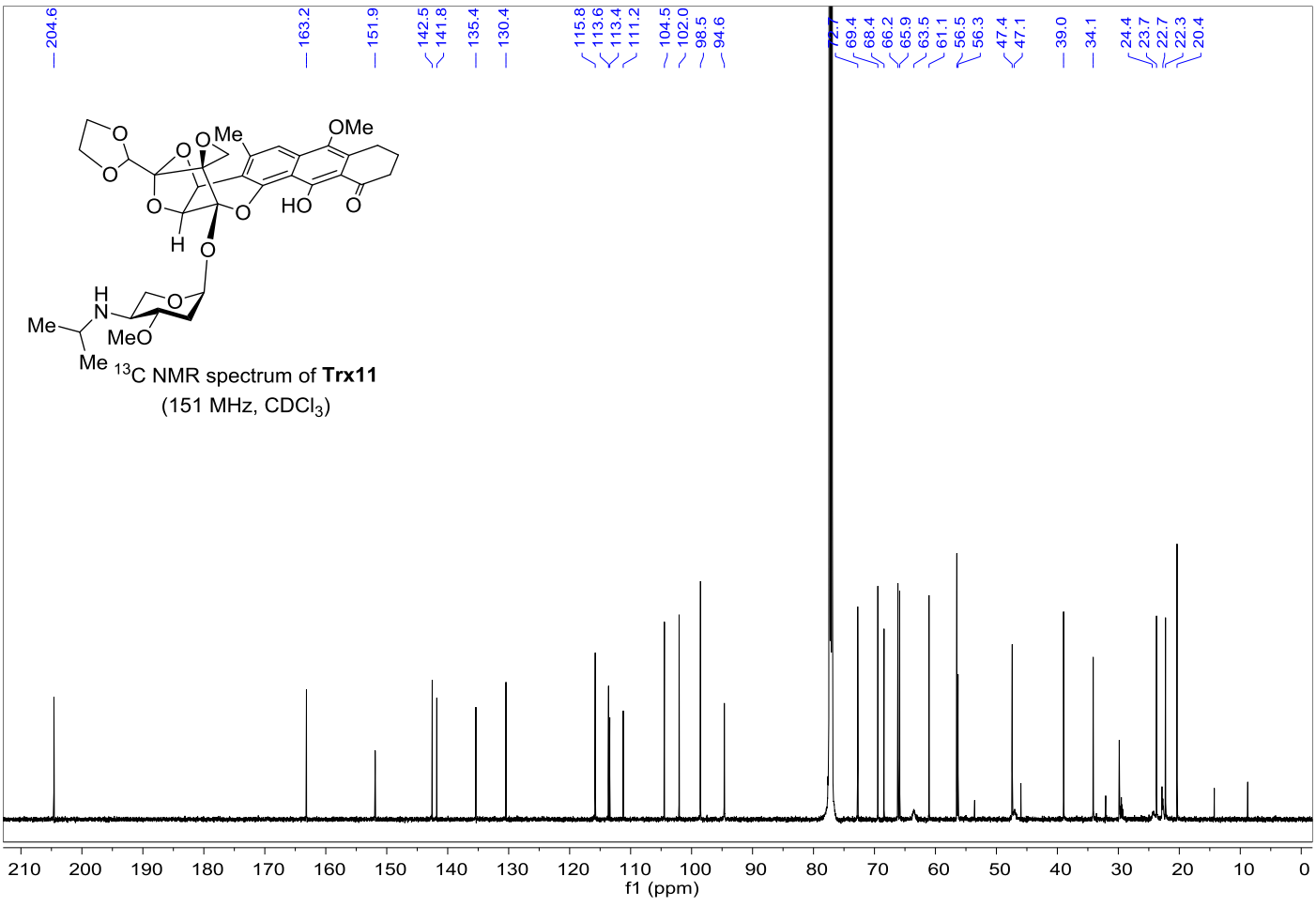


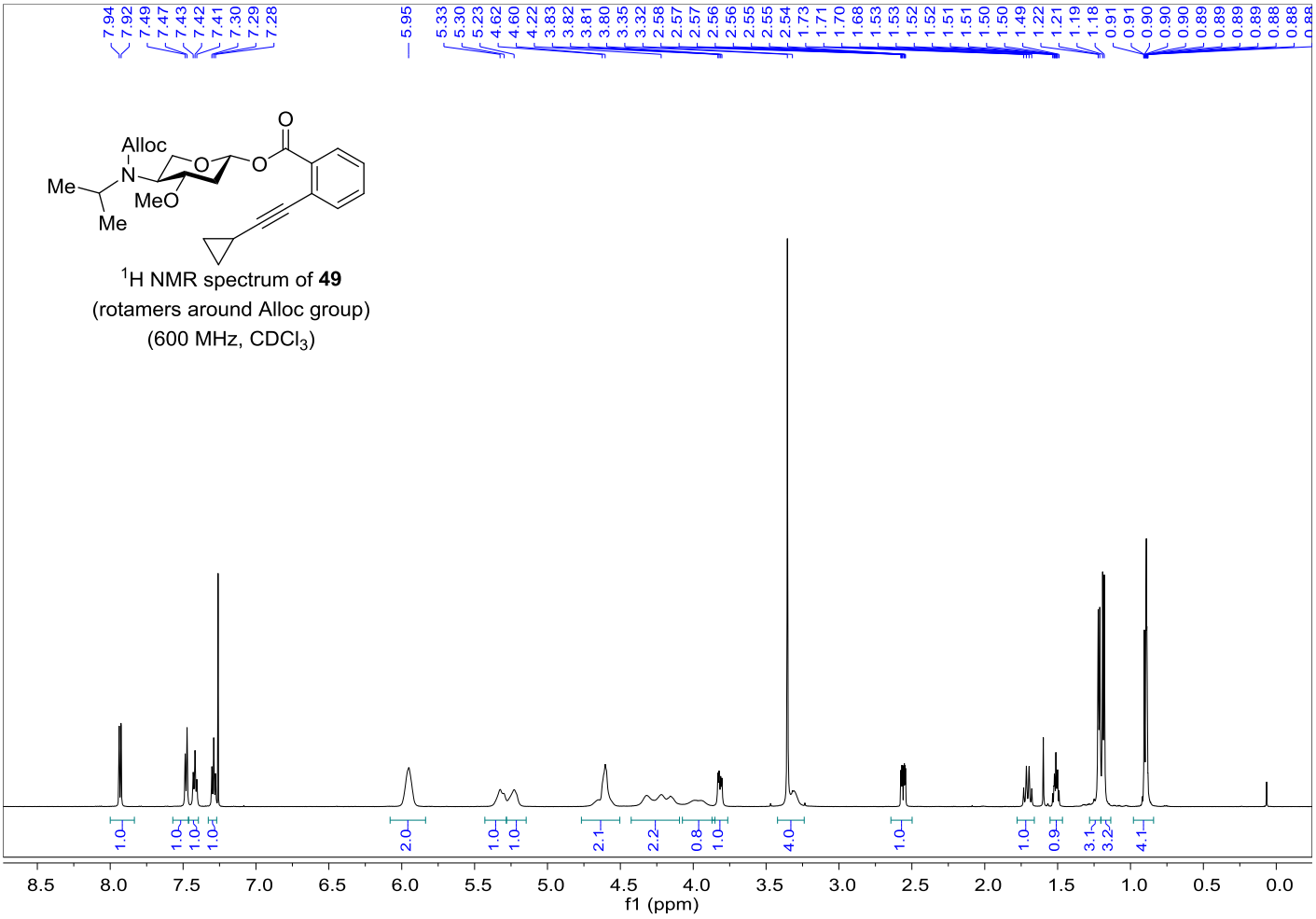
^{13}C NMR spectrum of **Trx9**
(151 MHz, $CDCl_3$)


14.75
7.45 5.54 5.53 5.45 5.19 5.18 5.16 5.16 4.94 4.92 4.15 4.14 4.13 4.12 4.07 4.06 4.06 4.05 4.04 4.02 4.01 4.00 4.00 3.99 3.90 3.90 3.89 3.88 3.87 3.78 3.57 3.05 3.05 3.04 3.04 3.03 3.03 2.98 2.97 2.86 2.85 2.74 2.73 2.71 2.57 2.11 2.10 2.09 2.08 2.07
Me
OMe
HO
O
H OMOM
1H NMR spectrum of Trx10
(600 MHz, CDCl3)
f1 (ppm)

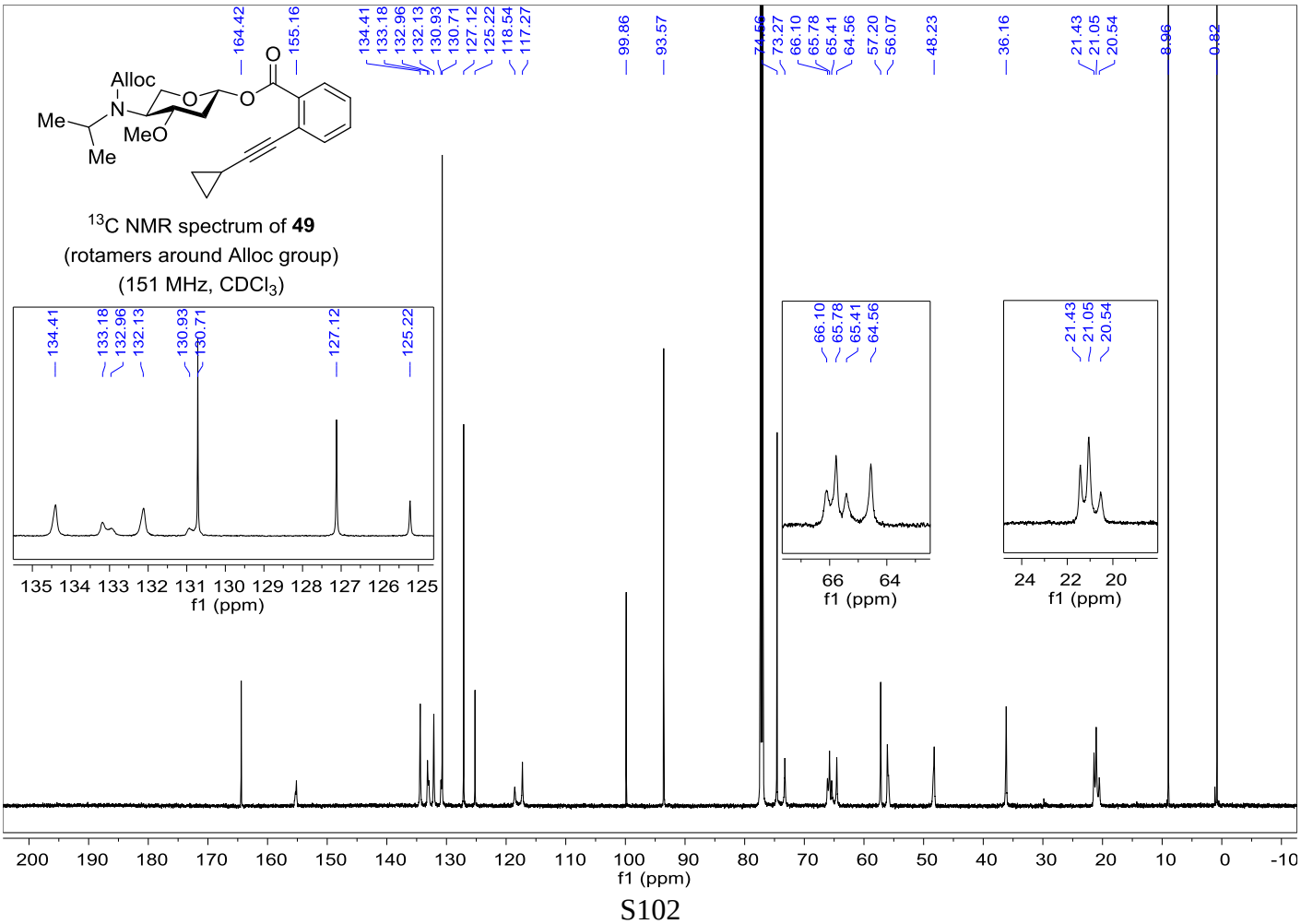

204.6 163.1 151.6 142.5 141.7 135.4 130.5 115.9 113.6 113.4 111.2 104.3 101.8 98.7 92.8 73.5 69.5 68.7 66.2 65.9 61.1 56.7 47.8 39.0 23.7 22.3 20.4
Me
OMe
HO
O
H OMOM
13C NMR spectrum of Trx10
(151 MHz, CDCl3)
f1 (ppm)


^{1}H NMR spectrum of **Trx11**
(600 MHz, $CDCl_3$)
f1 (ppm)

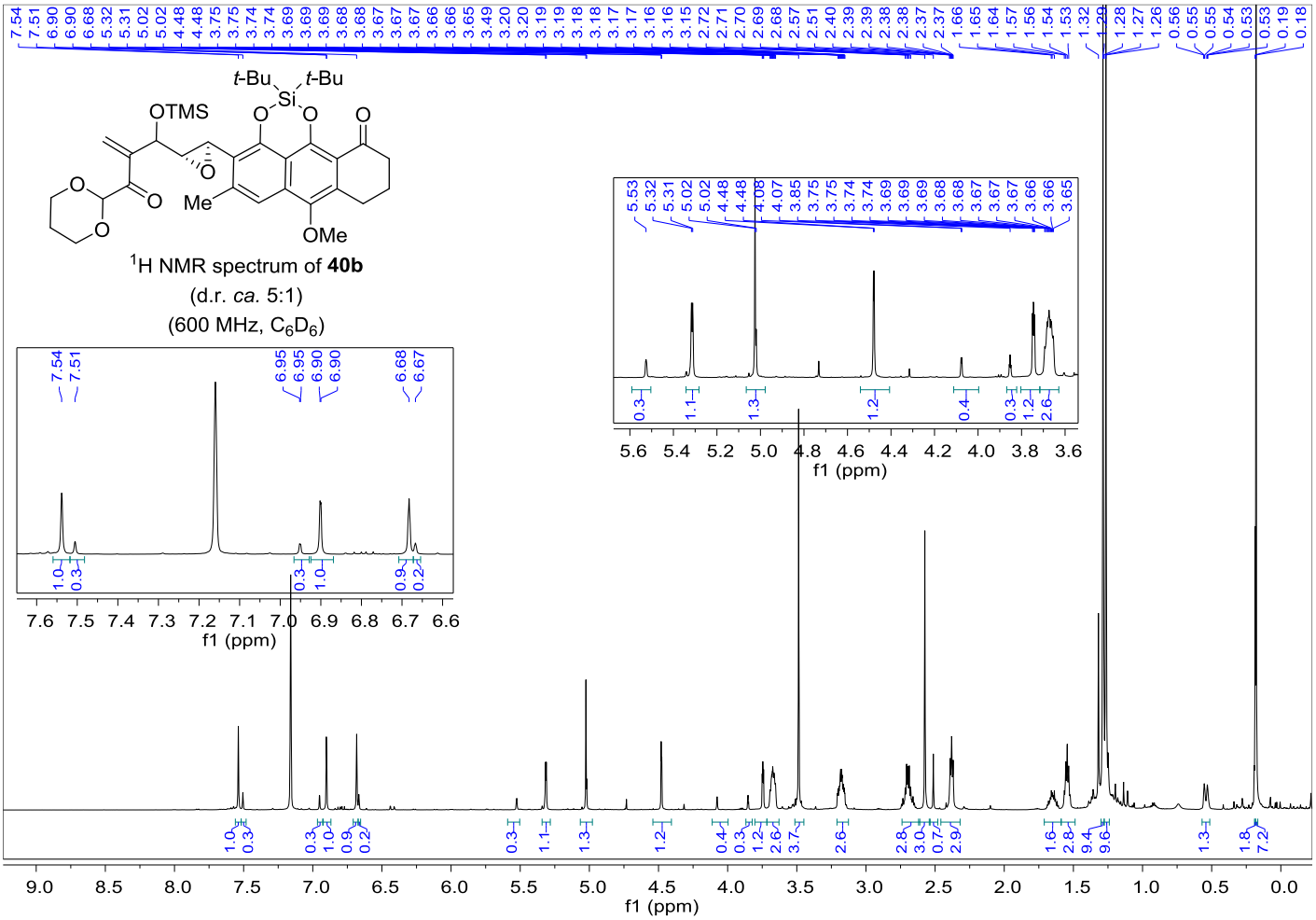

^{13}C NMR spectrum of **Trx11**
(151 MHz, $CDCl_3$)
f1 (ppm)



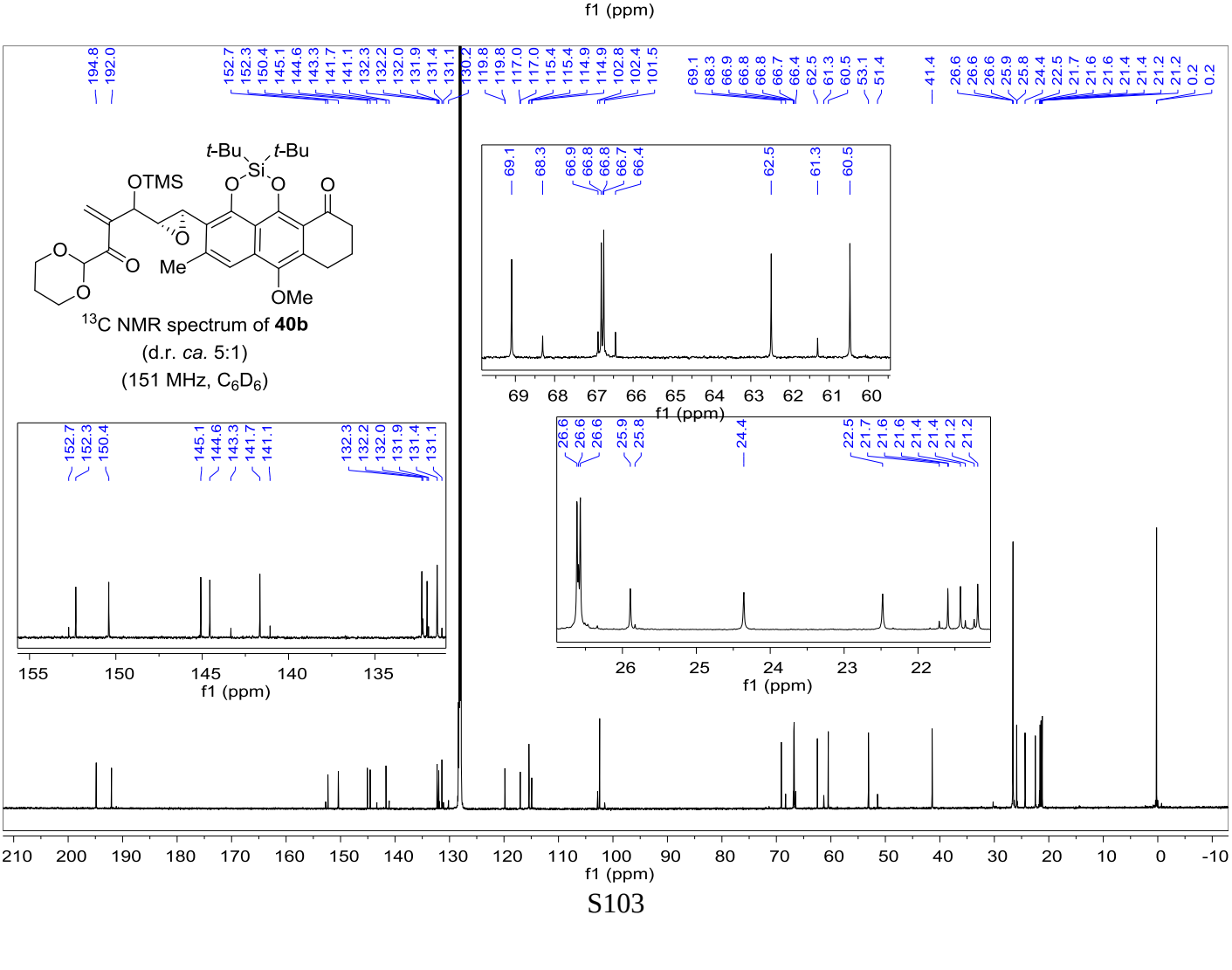
^{1}H NMR spectrum of **49**
(rotamers around Alloc group)
(600 MHz, $CDCl_3$)



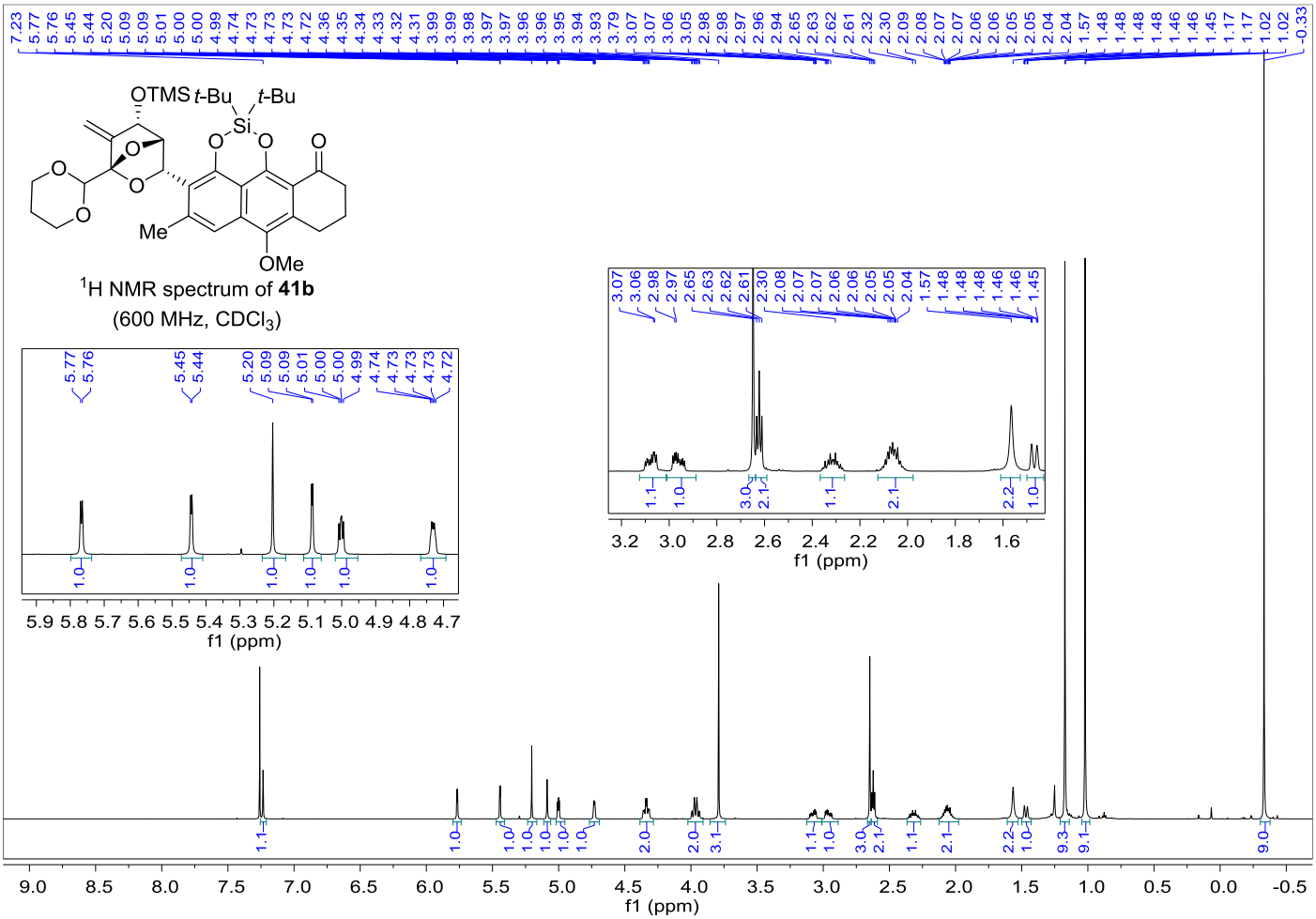
^{13}C NMR spectrum of **49**
(rotamers around Alloc group)
(151 MHz, $CDCl_3$)



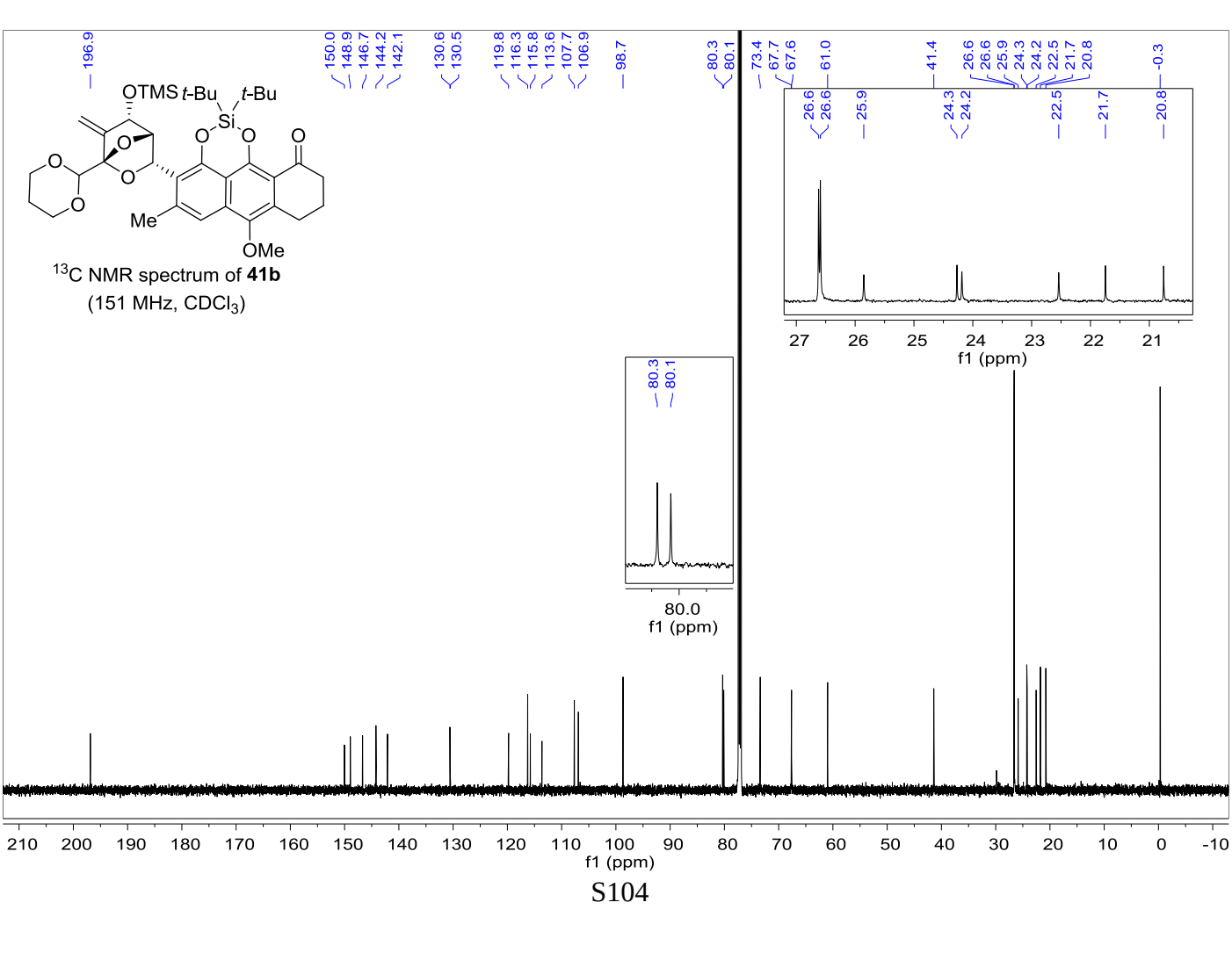
^{1}H NMR spectrum of **40b**
(d.r. *ca.* 5:1)
(600 MHz, C_6D_6)



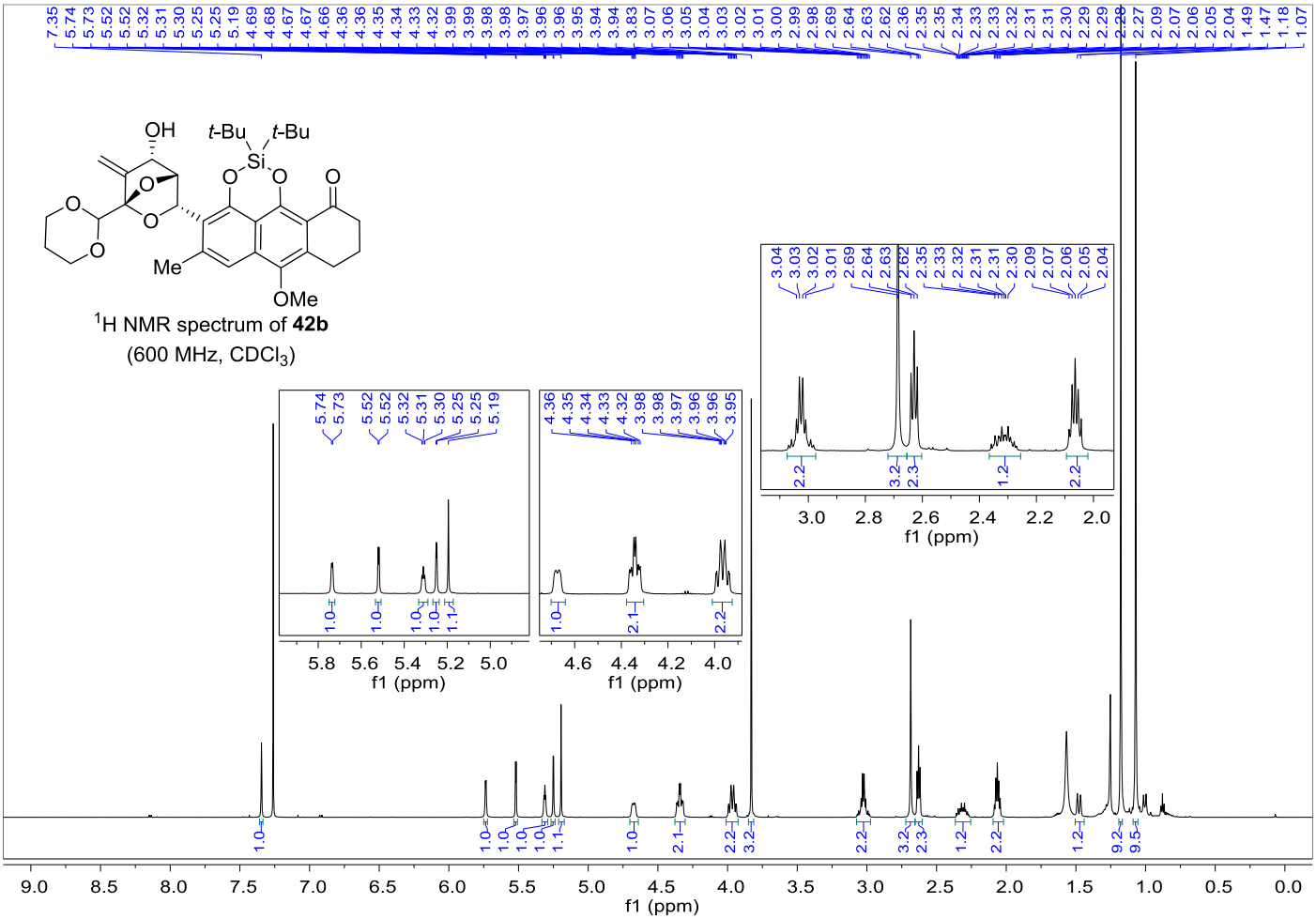
^{13}C NMR spectrum of **40b**
(d.r. *ca.* 5:1)
(151 MHz, C_6D_6)



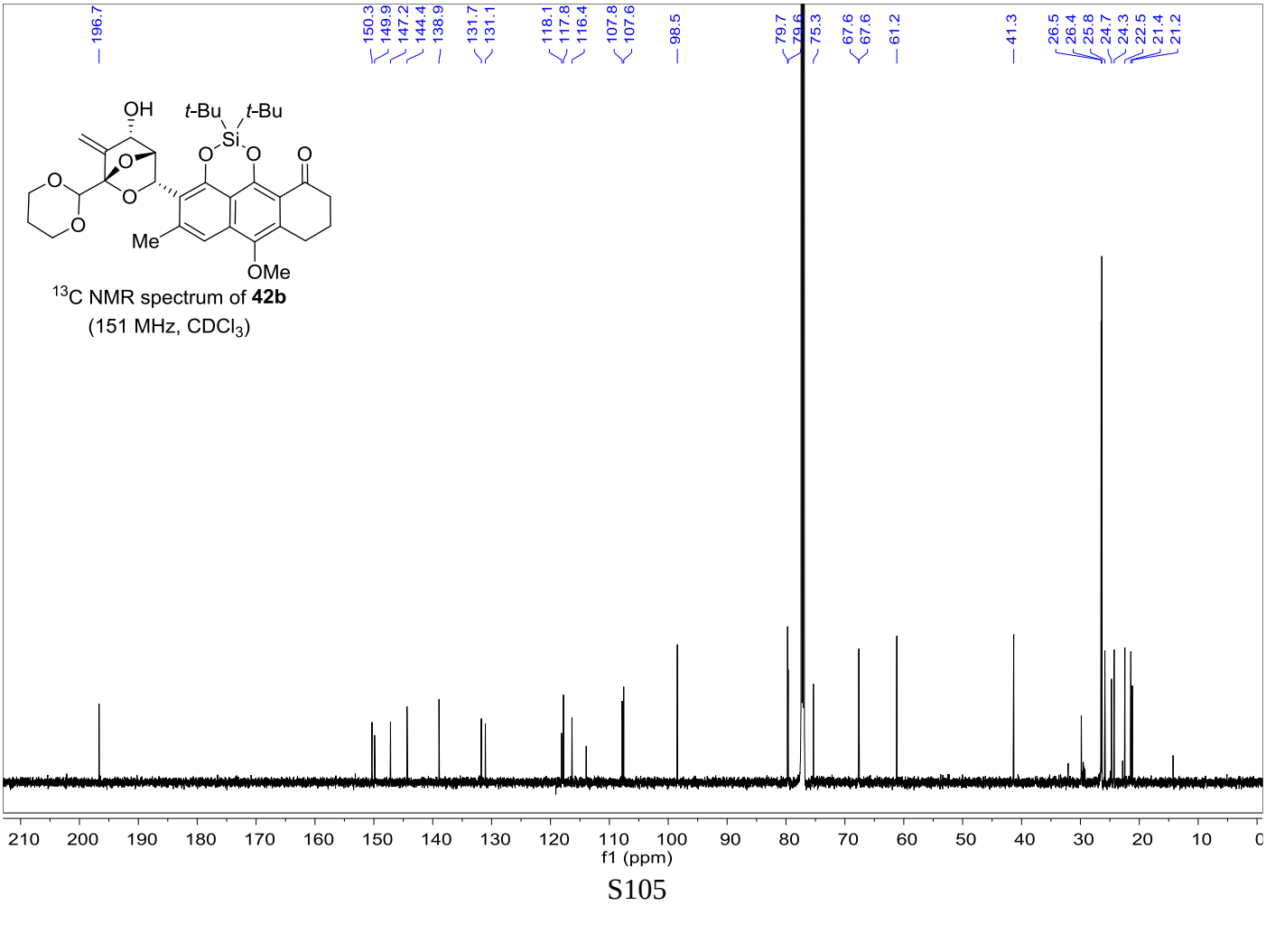
^{1}H NMR spectrum of **41b**
(600 MHz, $CDCl_3$)



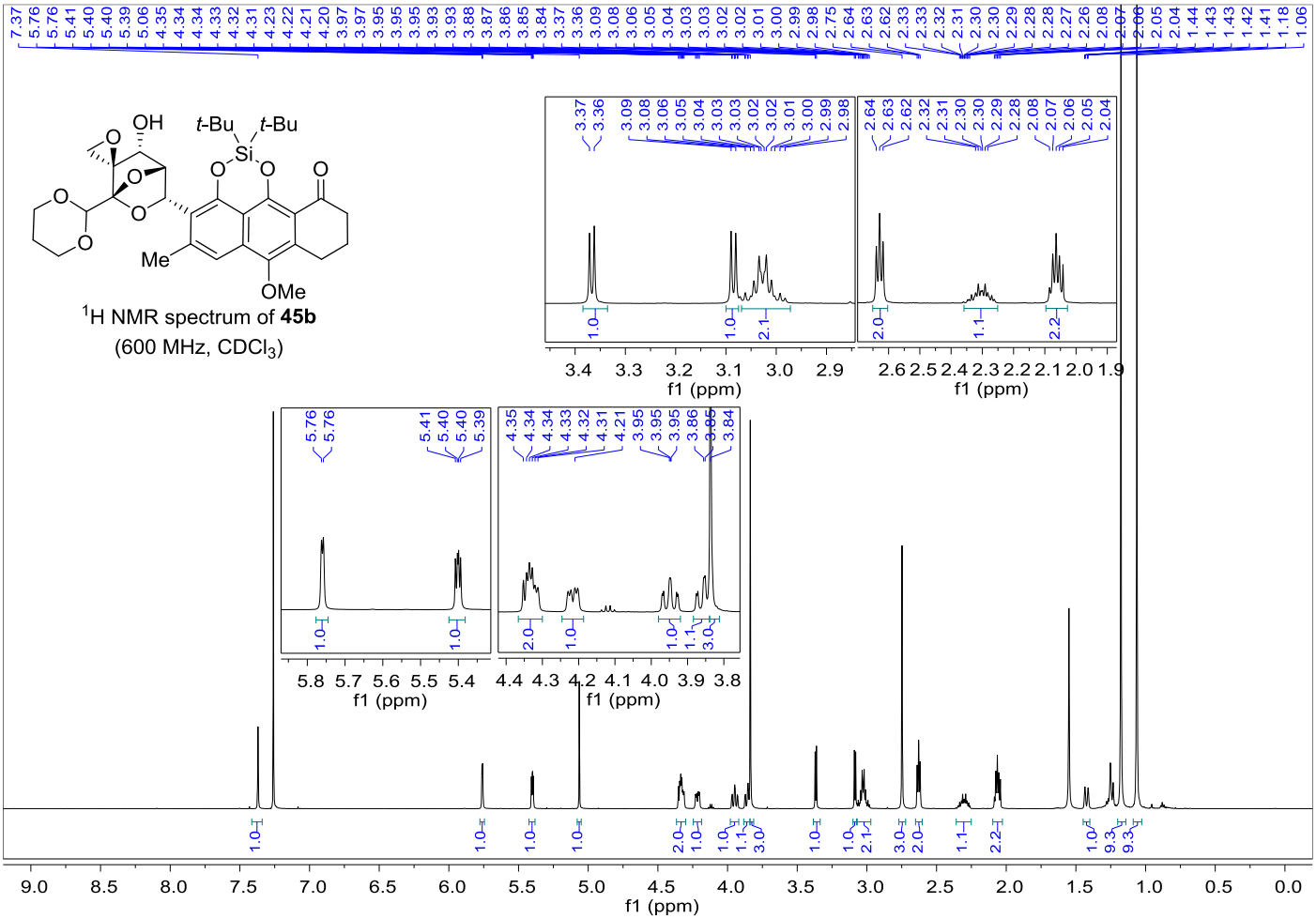
^{13}C NMR spectrum of **41b**
(151 MHz, $CDCl_3$)



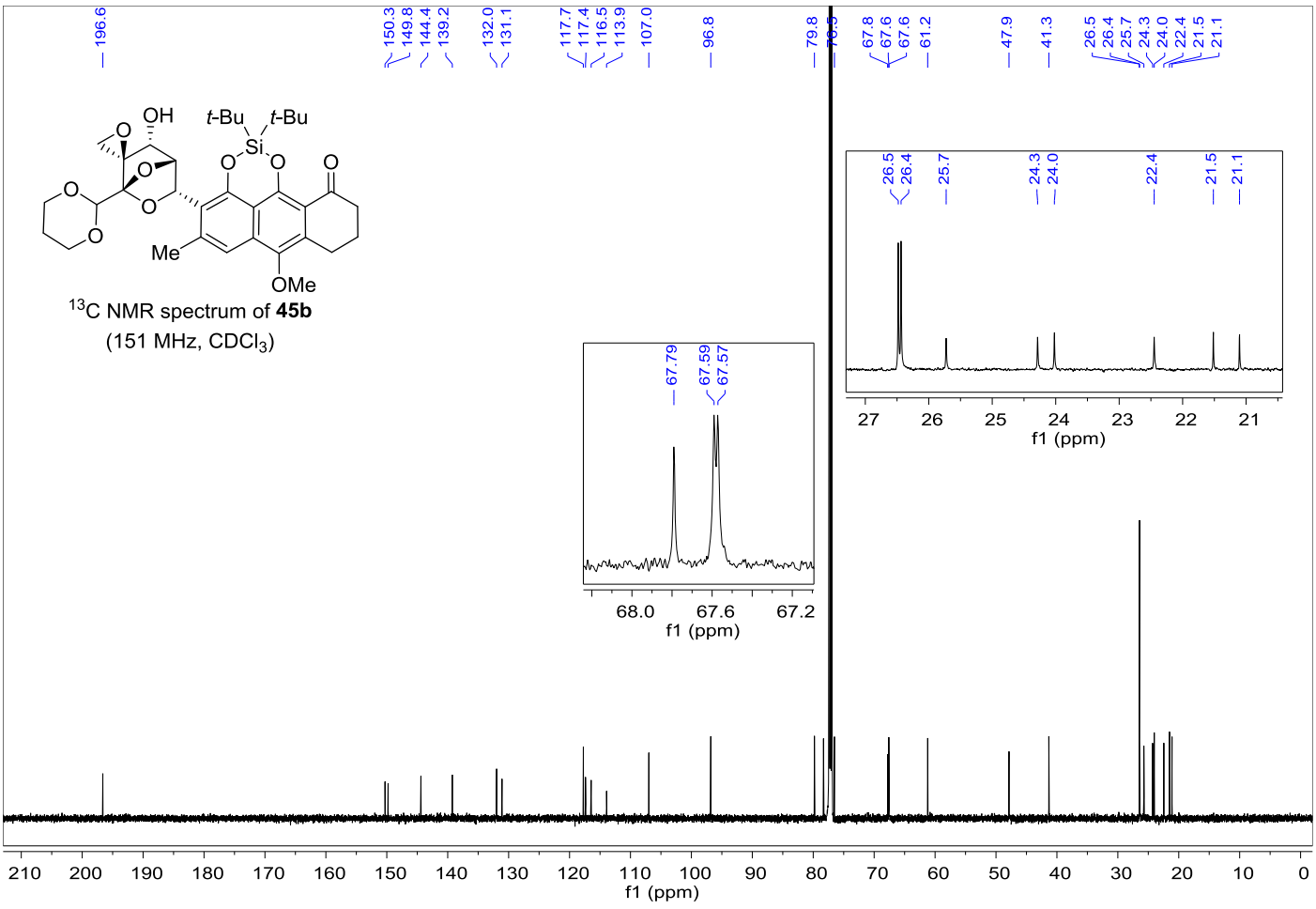
^{1}H NMR spectrum of **42b**
(600 MHz, $CDCl_3$)



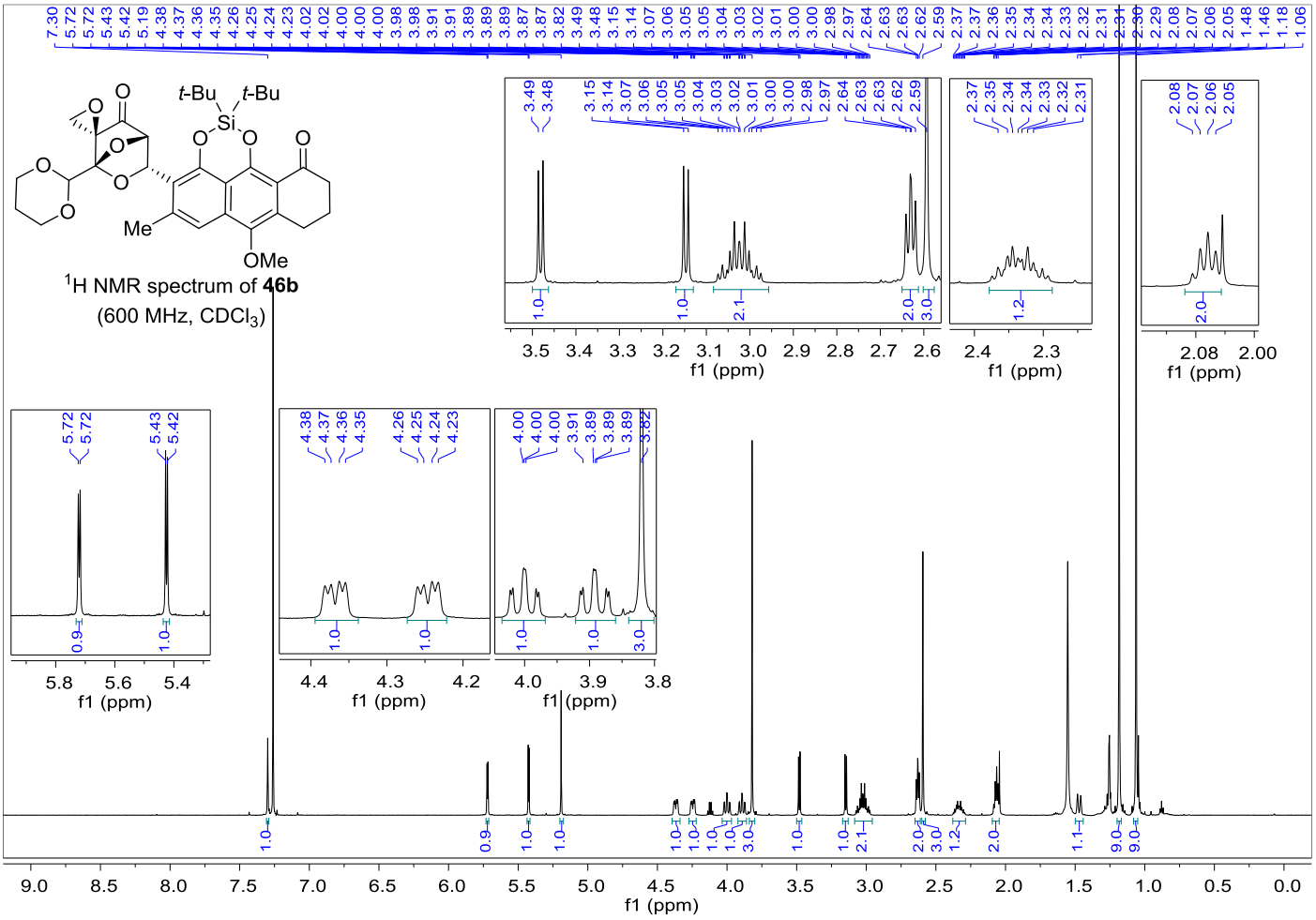
^{13}C NMR spectrum of **42b**
(151 MHz, $CDCl_3$)



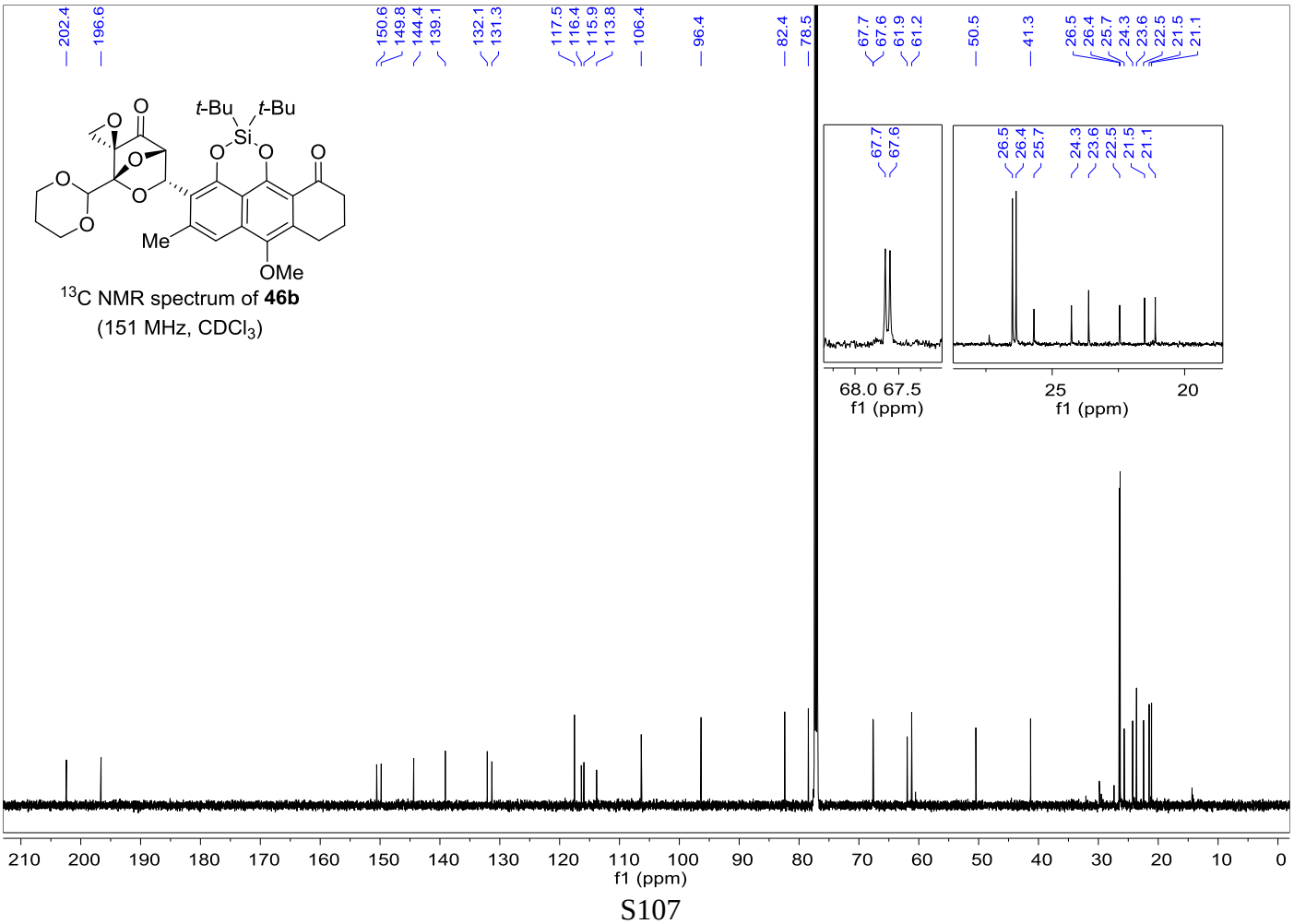
^{1}H NMR spectrum of **45b**
(600 MHz, $CDCl_3$)



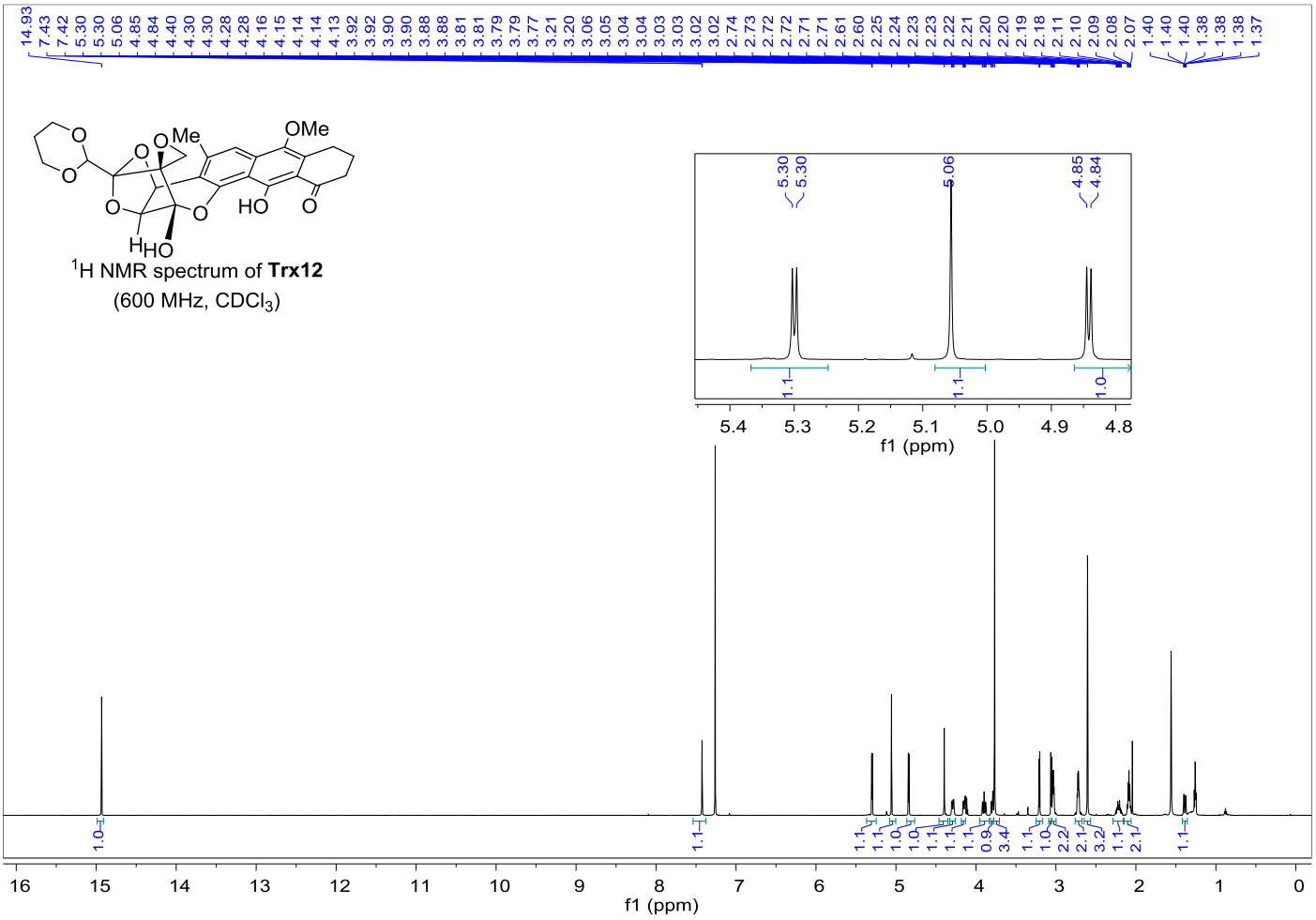
^{13}C NMR spectrum of **45b**
(151 MHz, $CDCl_3$)



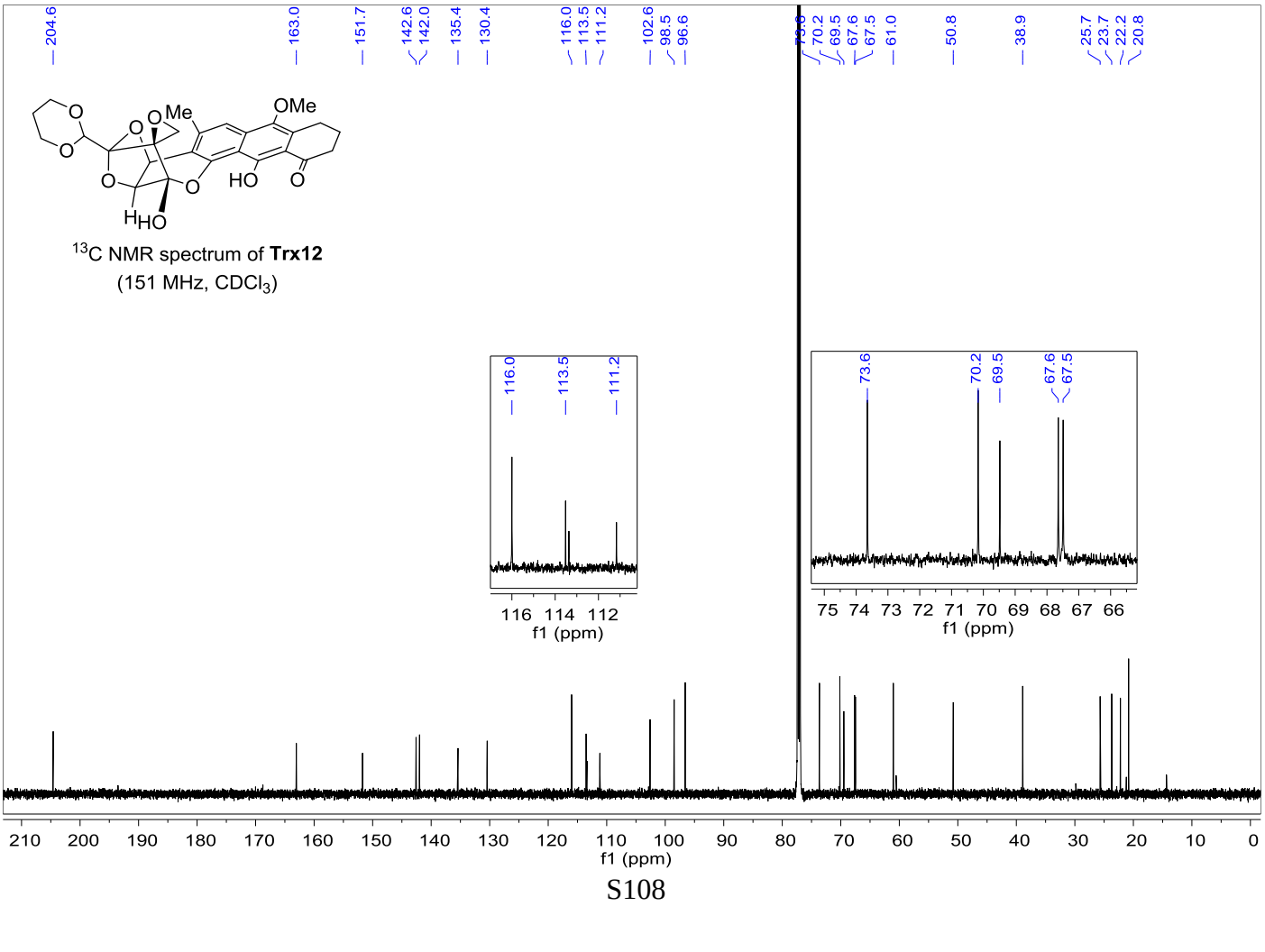
^{1}H NMR spectrum of **46b**
(600 MHz, $CDCl_3$)



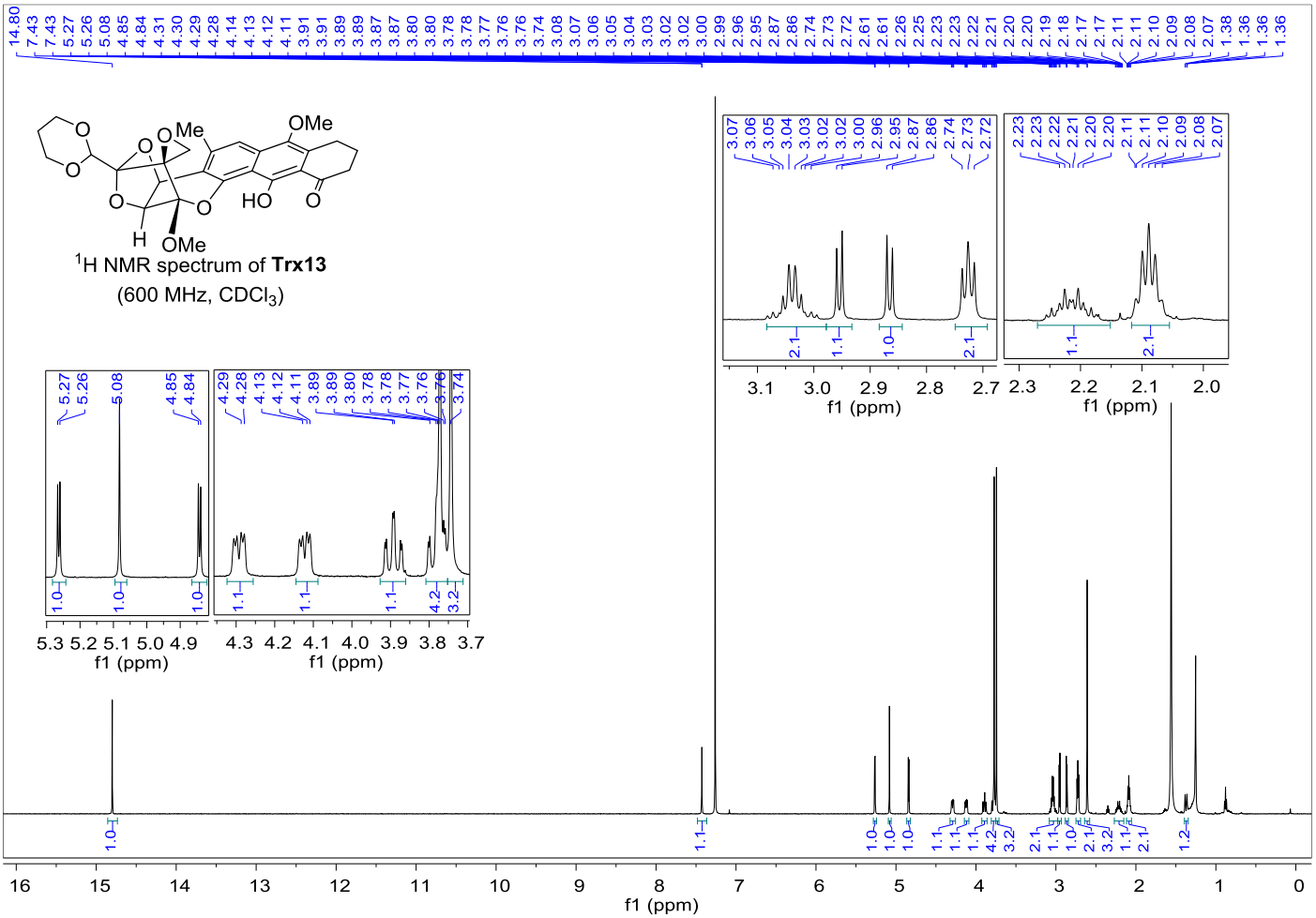
^{13}C NMR spectrum of **46b**
(151 MHz, $CDCl_3$)



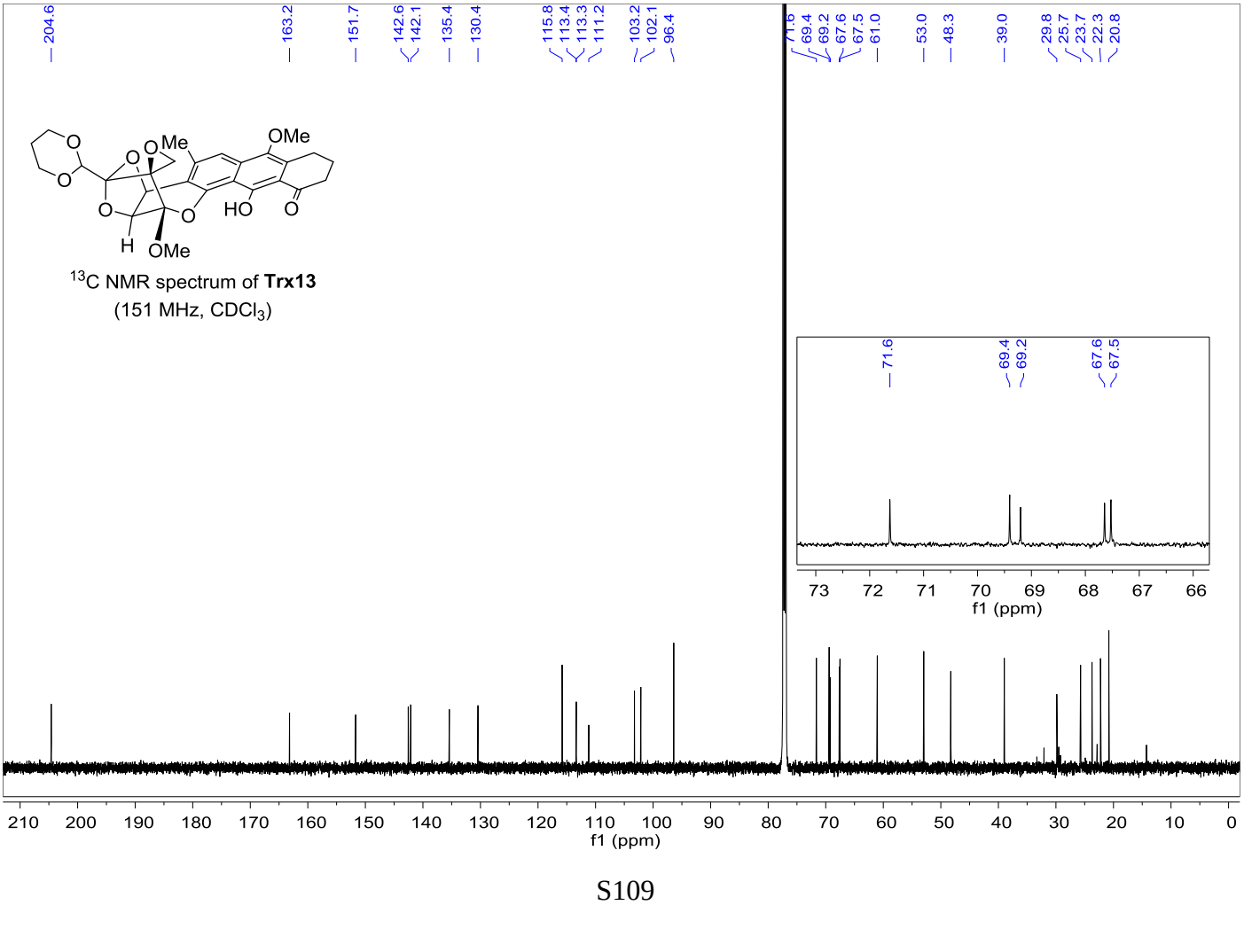
^{1}H NMR spectrum of **Trx12**
(600 MHz, $CDCl_3$)



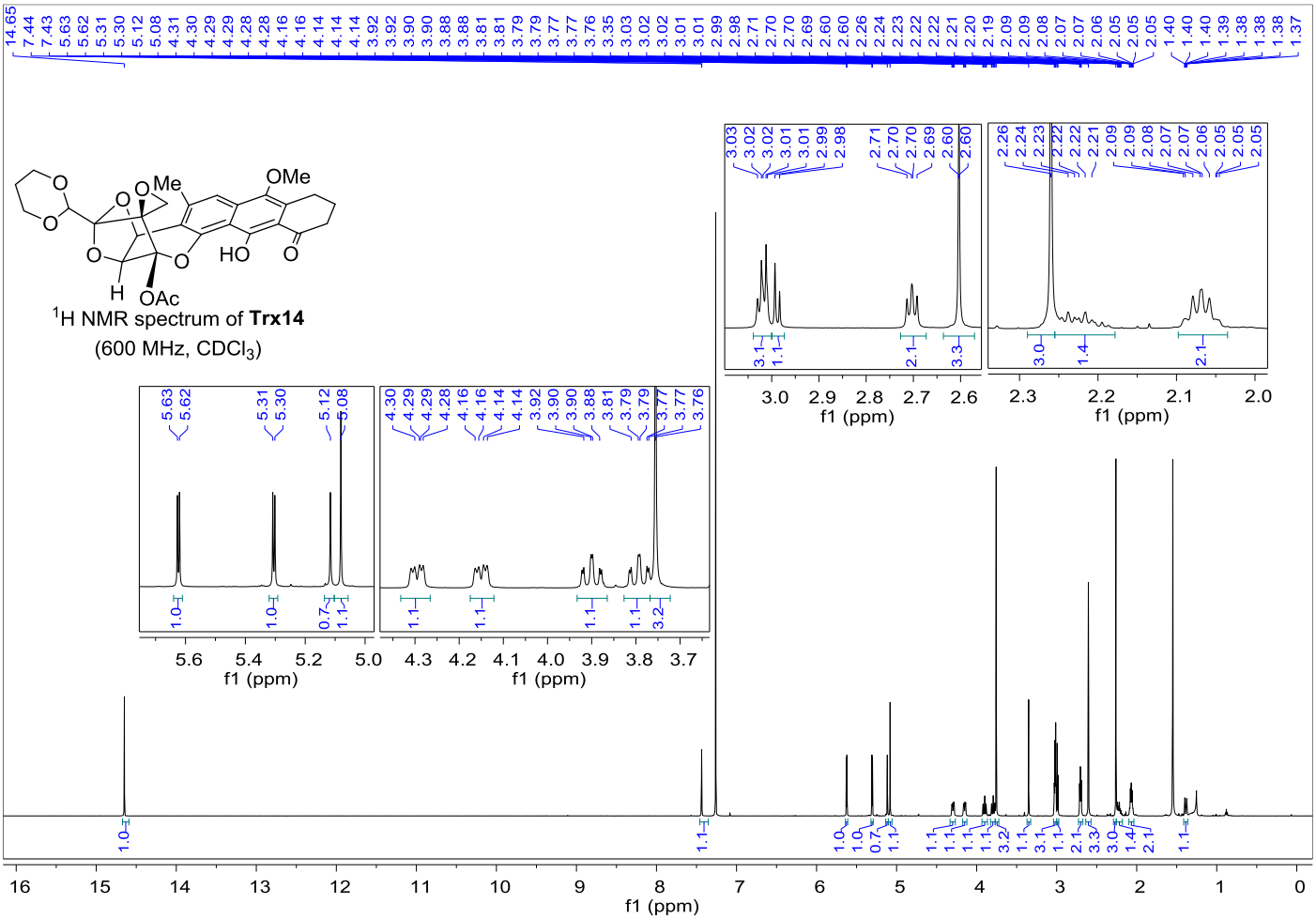
^{13}C NMR spectrum of **Trx12**
(151 MHz, $CDCl_3$)



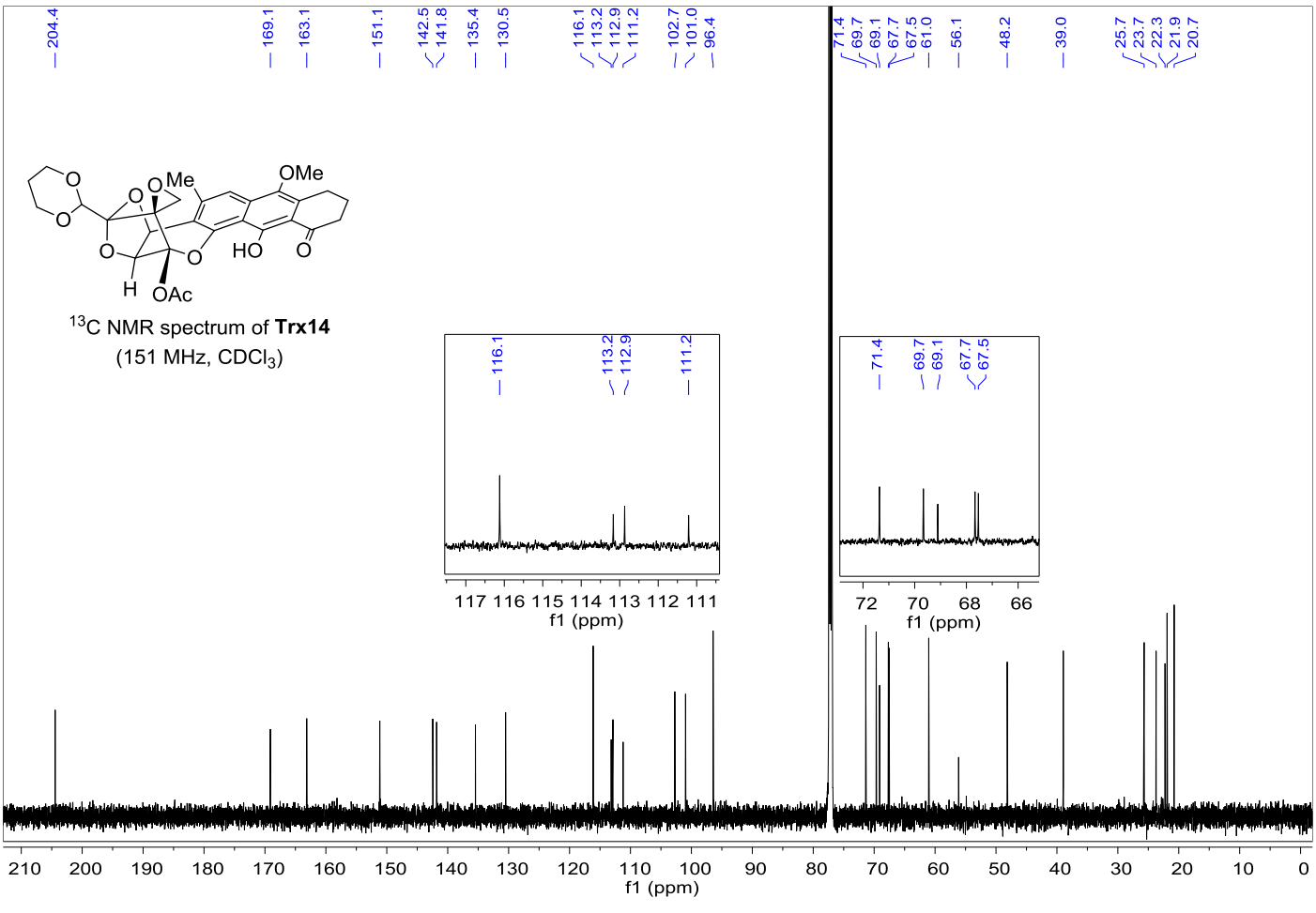
^{1}H NMR spectrum of **Trx13**
(600 MHz, $CDCl_3$)



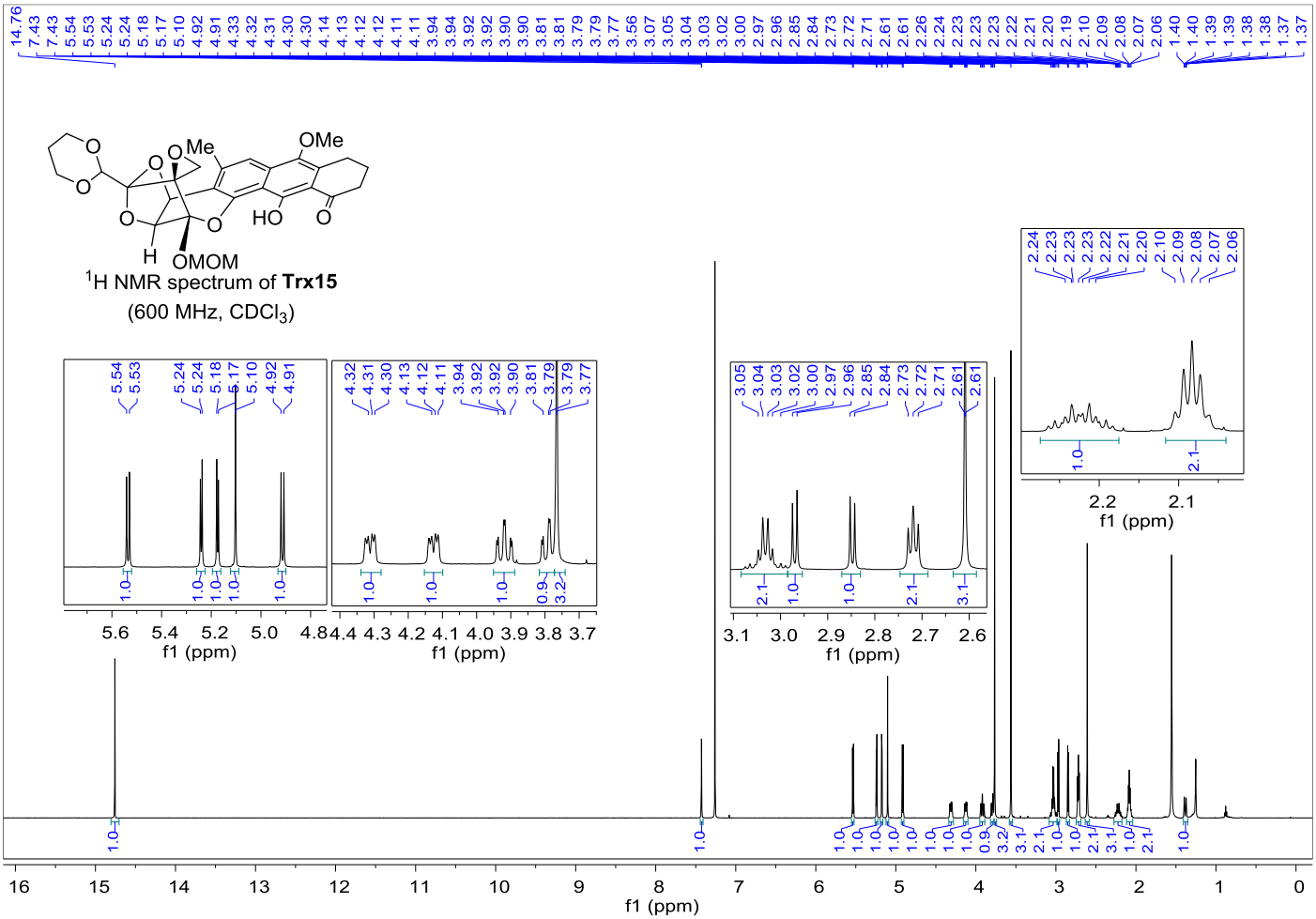
^{13}C NMR spectrum of **Trx13**
(151 MHz, $CDCl_3$)



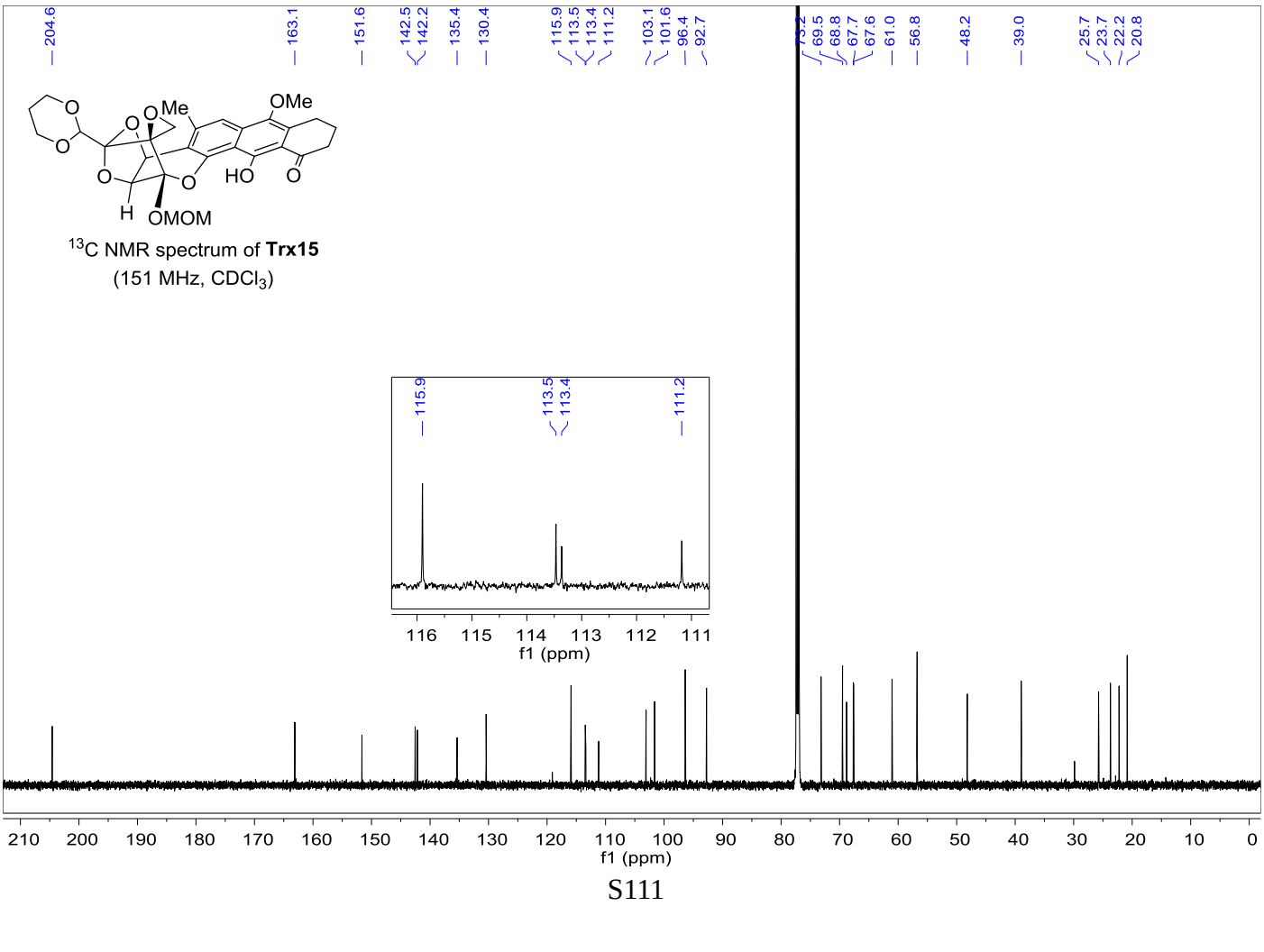
^{1}H NMR spectrum of **Trx14**
(600 MHz, $CDCl_3$)



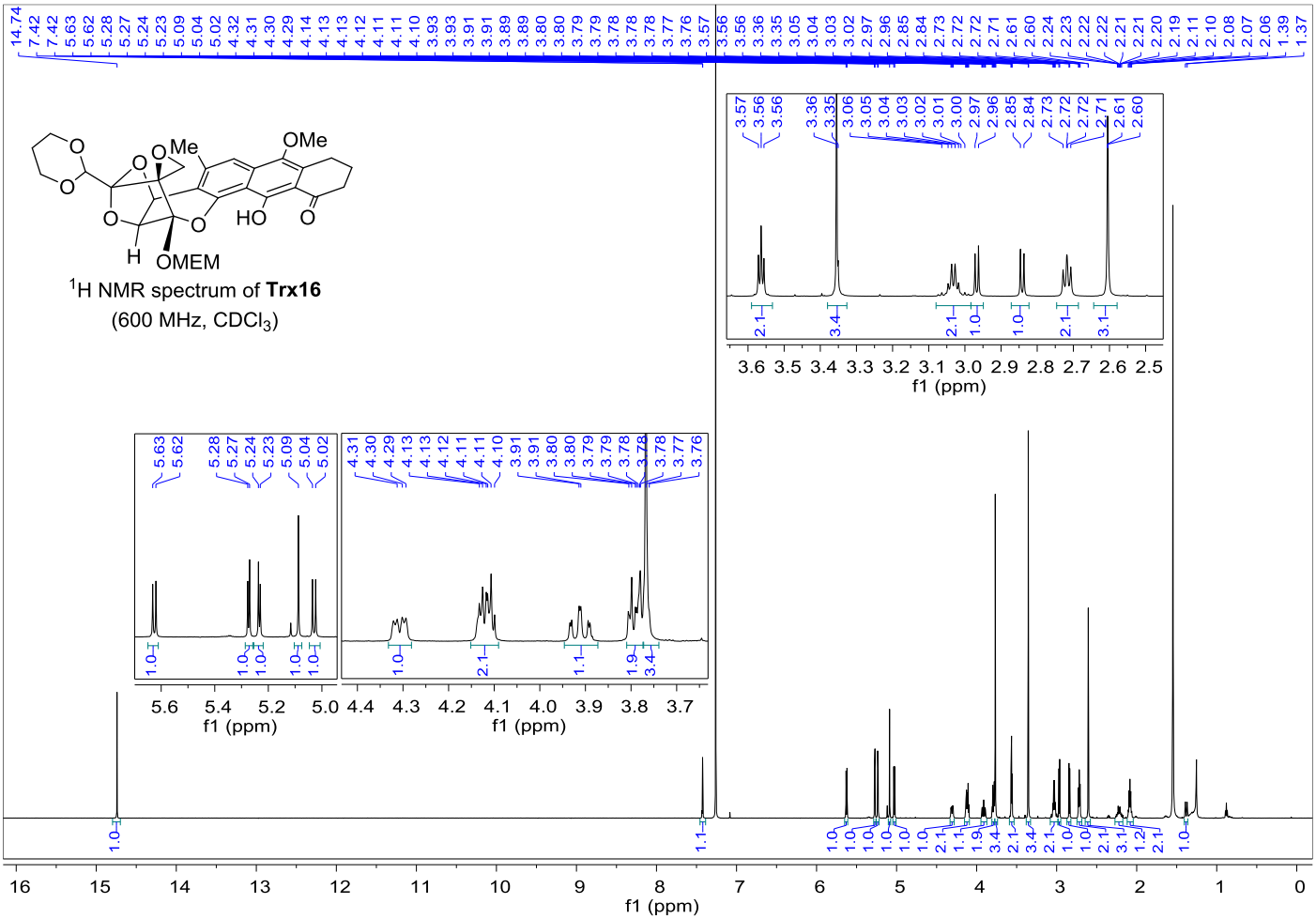
^{13}C NMR spectrum of **Trx14**
(151 MHz, $CDCl_3$)



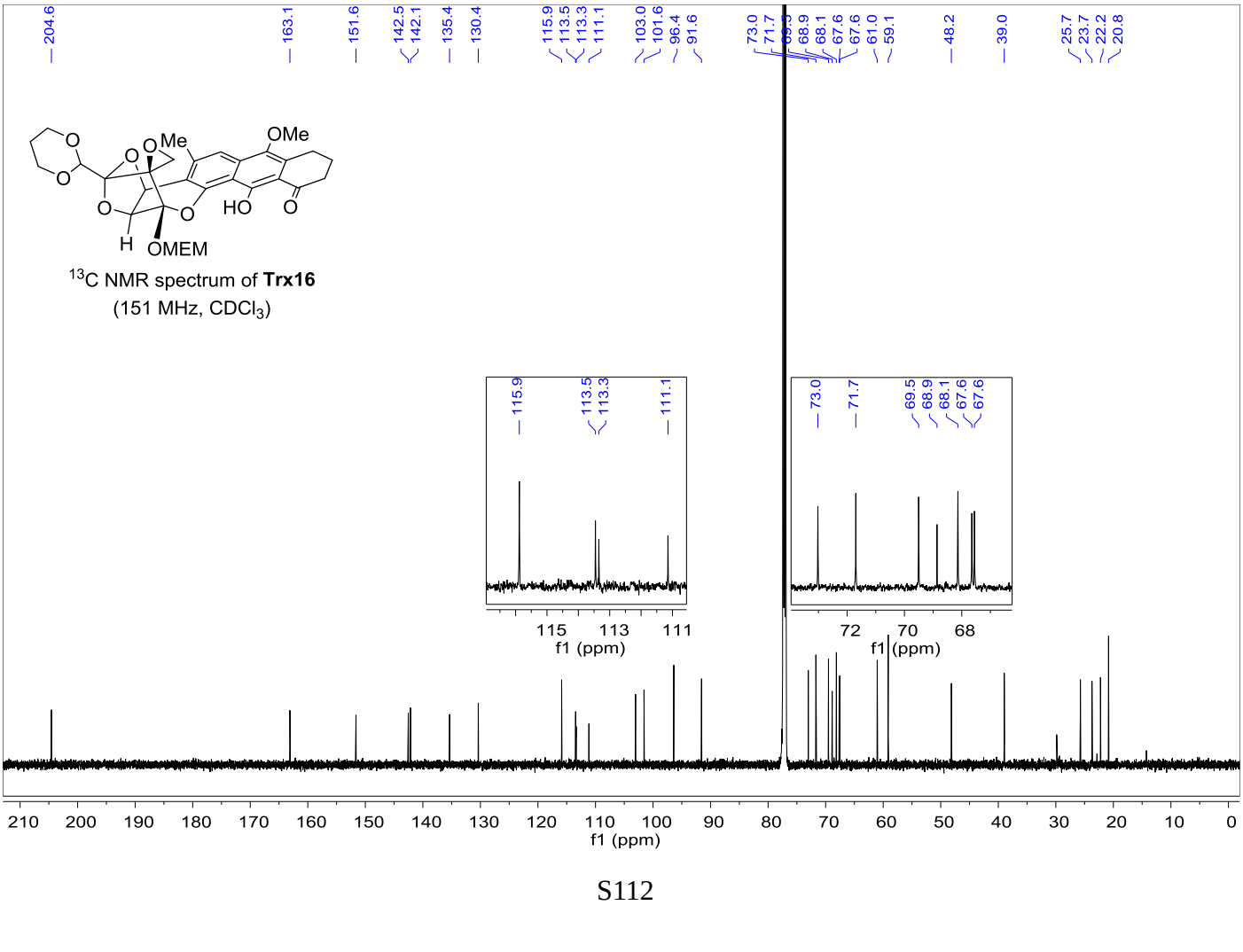
^{1}H NMR spectrum of **Trx15**
(600 MHz, $CDCl_3$)



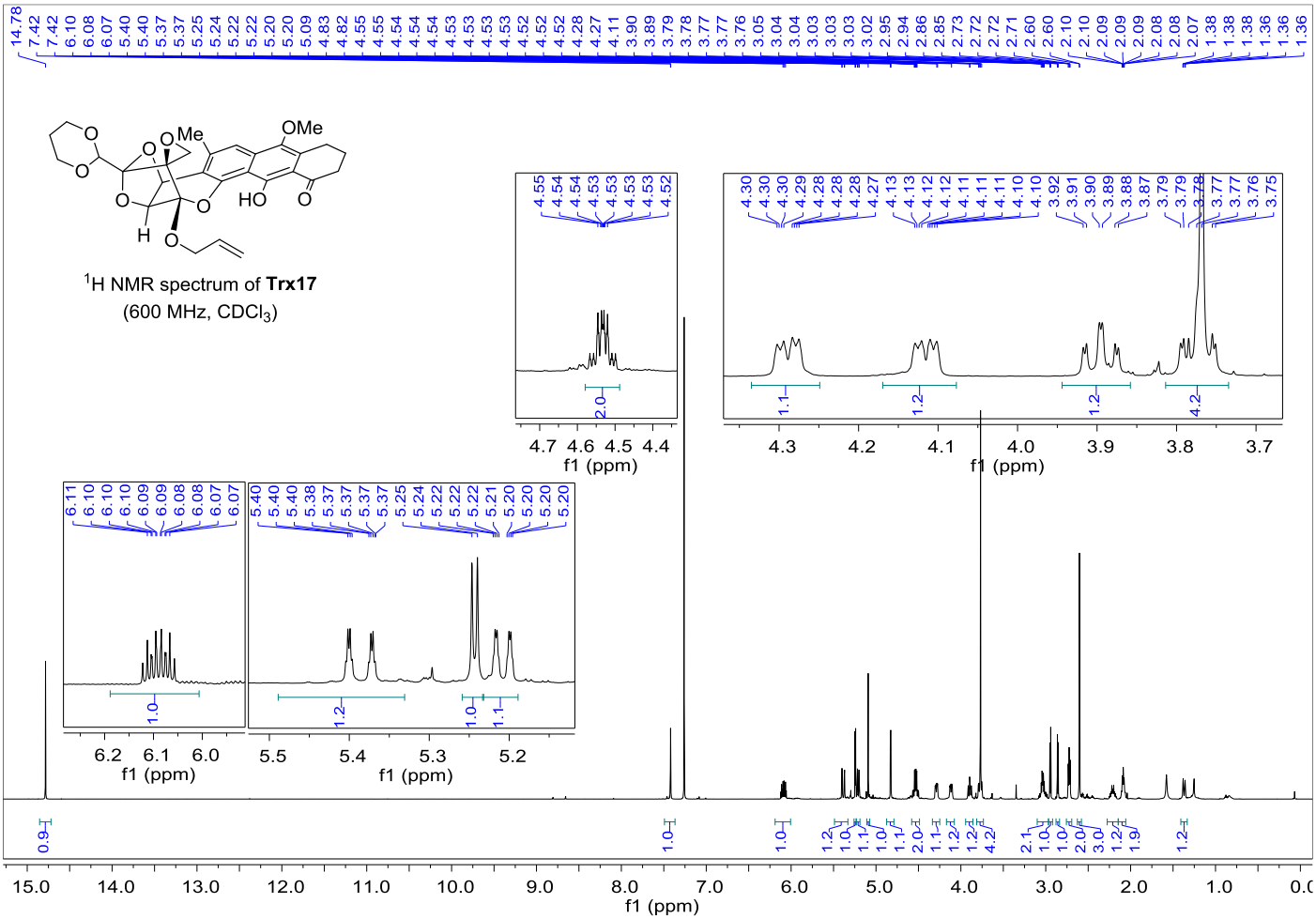
^{13}C NMR spectrum of **Trx15**
(151 MHz, $CDCl_3$)



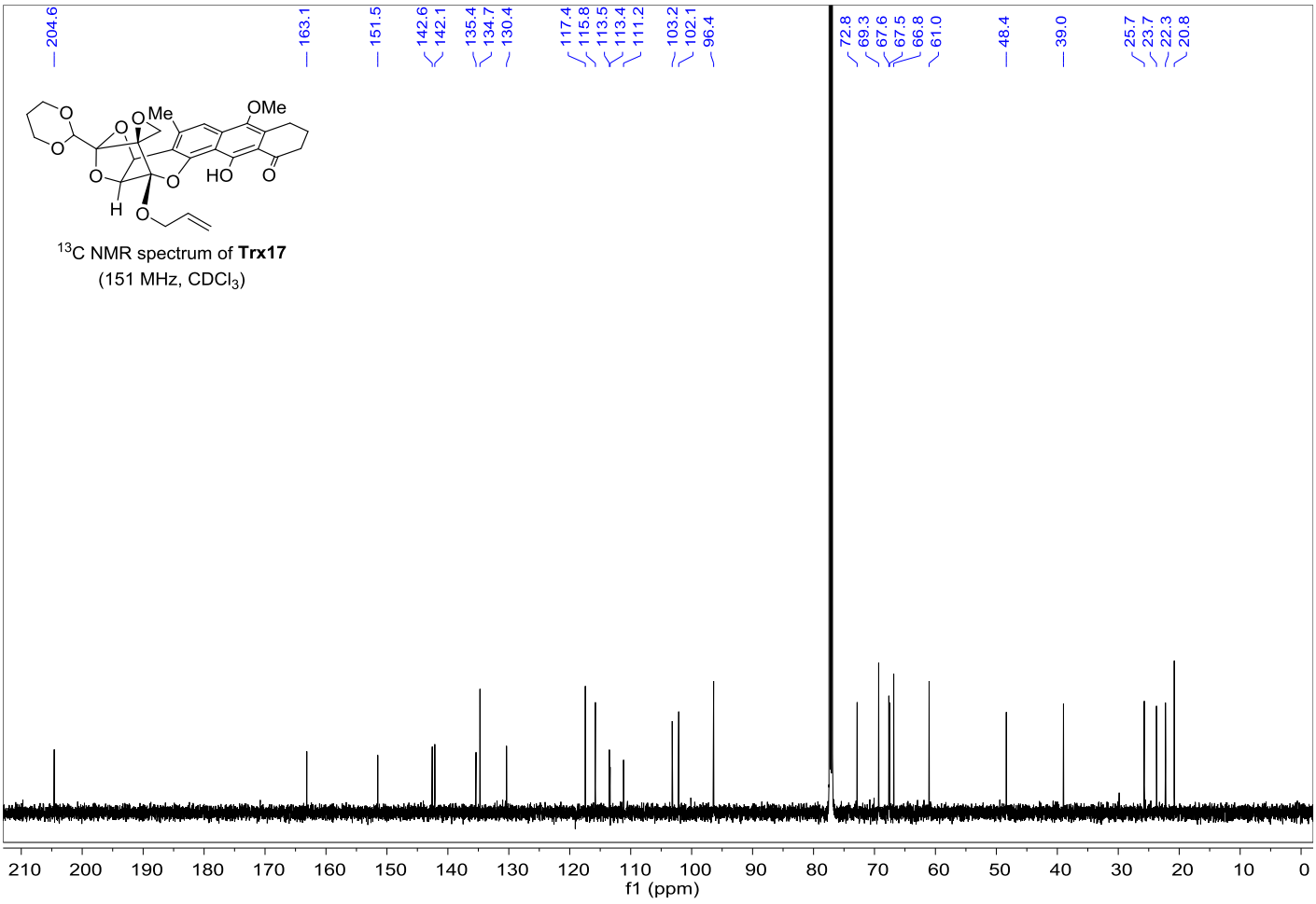
^{1}H NMR spectrum of **Trx16**
(600 MHz, $CDCl_3$)



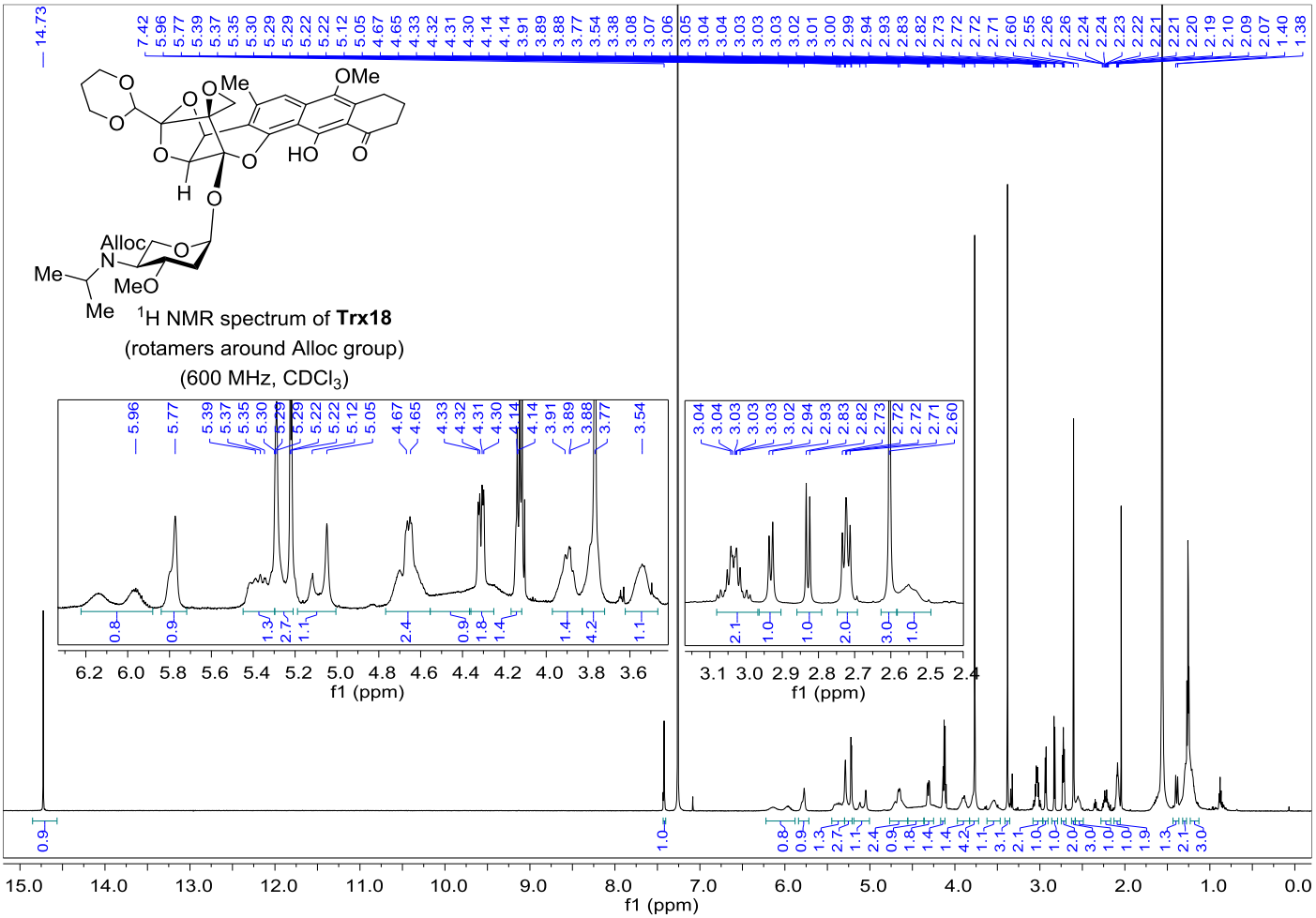
^{13}C NMR spectrum of **Trx16**
(151 MHz, $CDCl_3$)



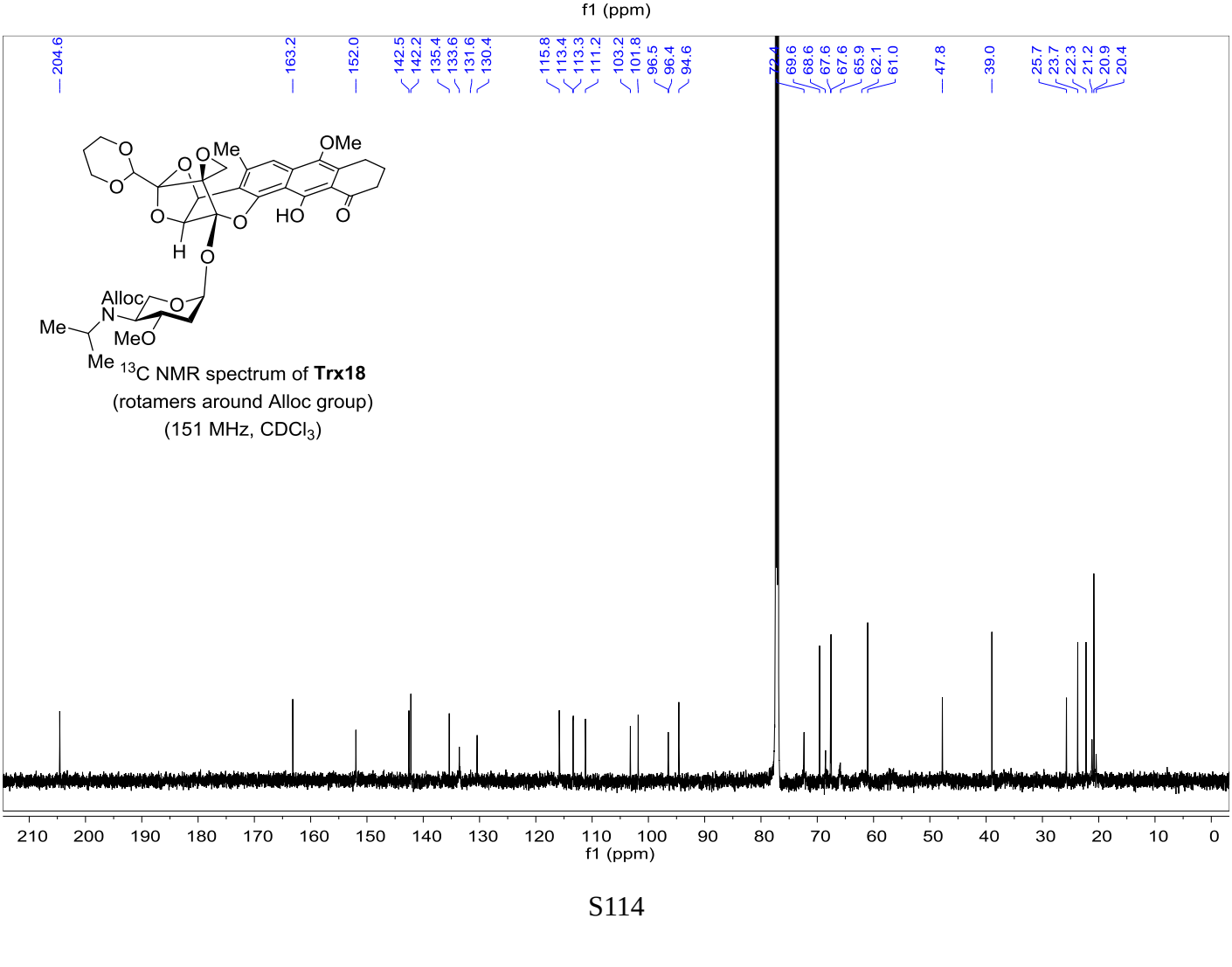
^{1}H NMR spectrum of **Trx17**
(600 MHz, $CDCl_3$)



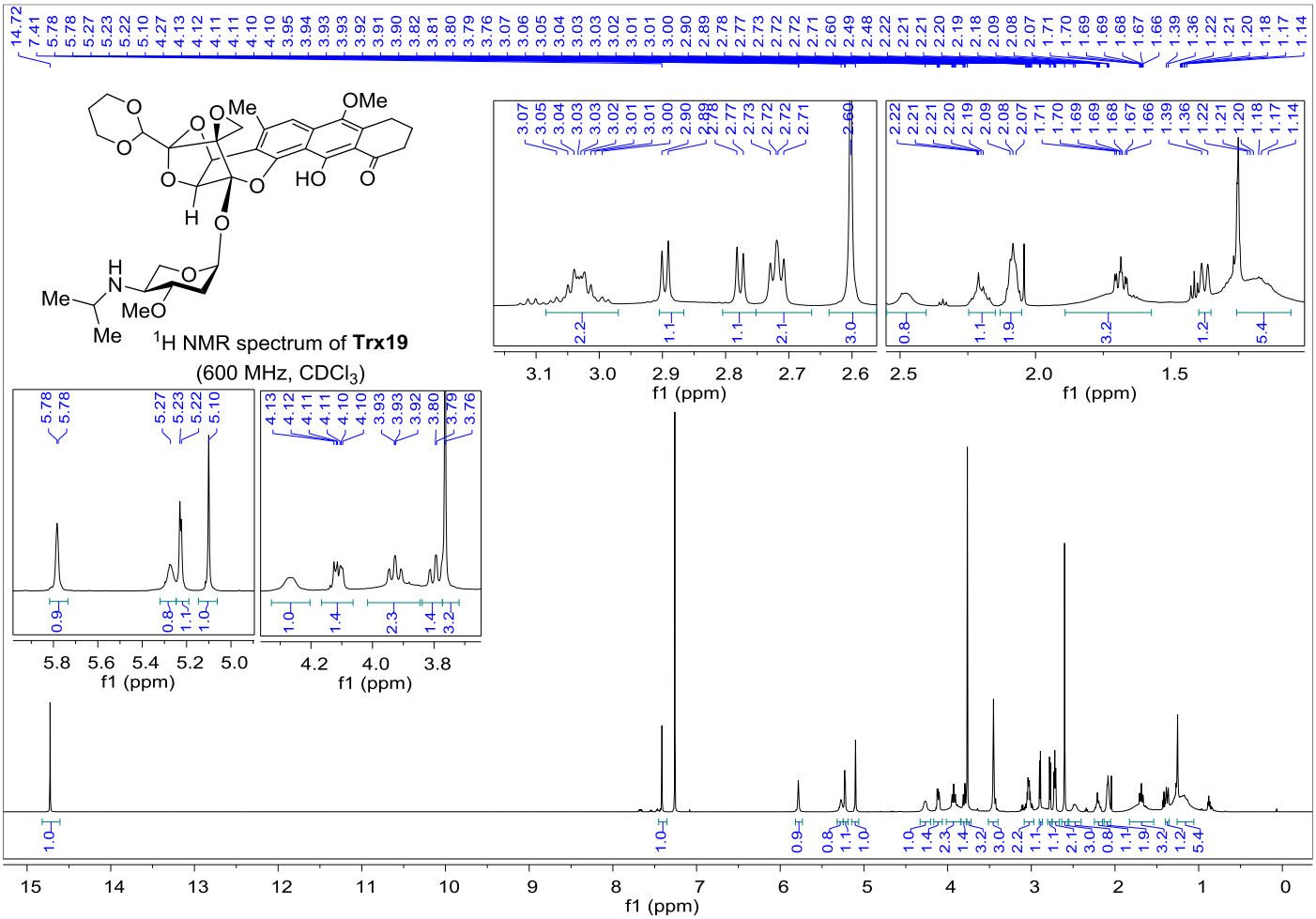
^{13}C NMR spectrum of **Trx17**
(151 MHz, $CDCl_3$)



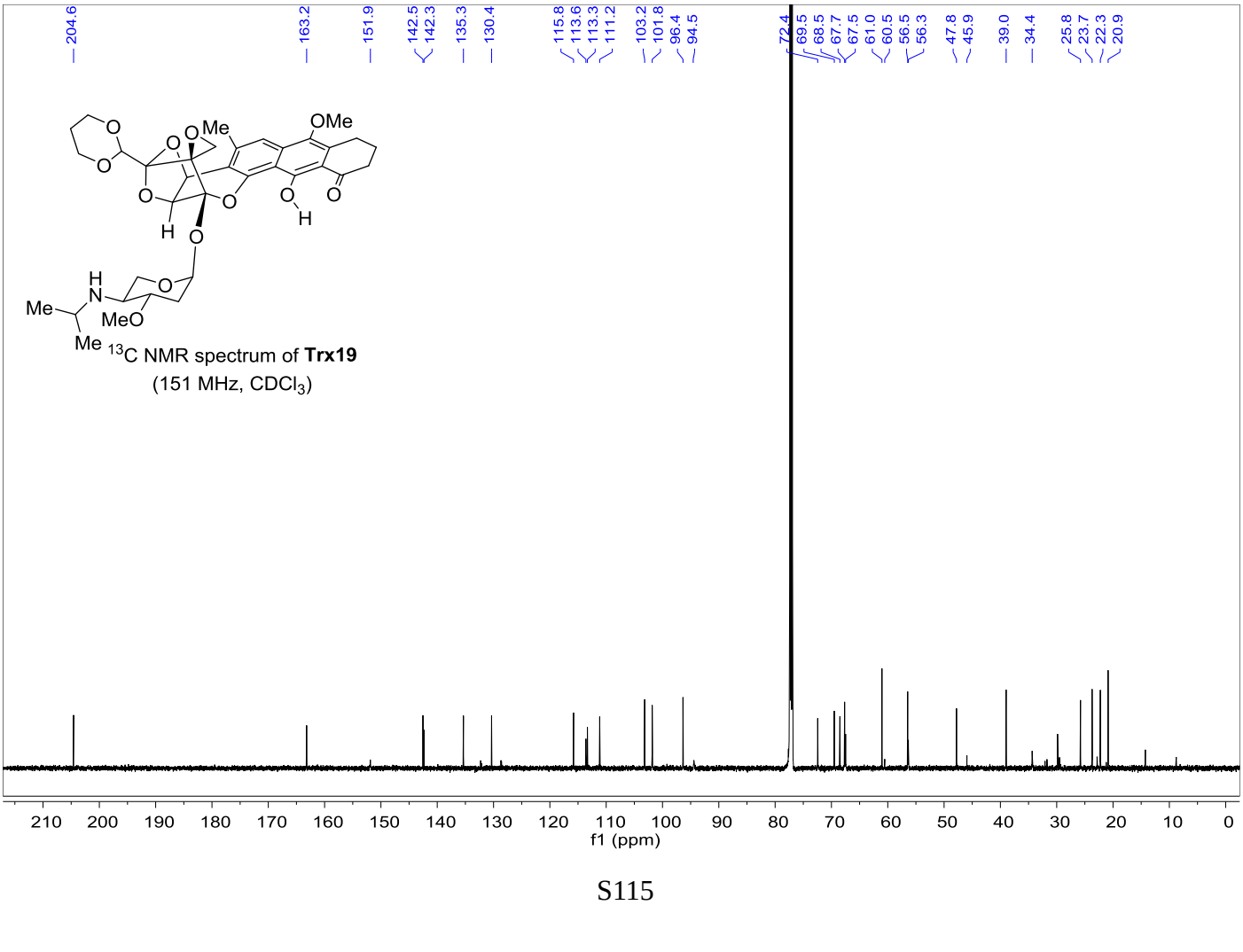
^{1}H NMR spectrum of **Trx18**
(rotamers around Alloc group)
(600 MHz, $CDCl_3$)



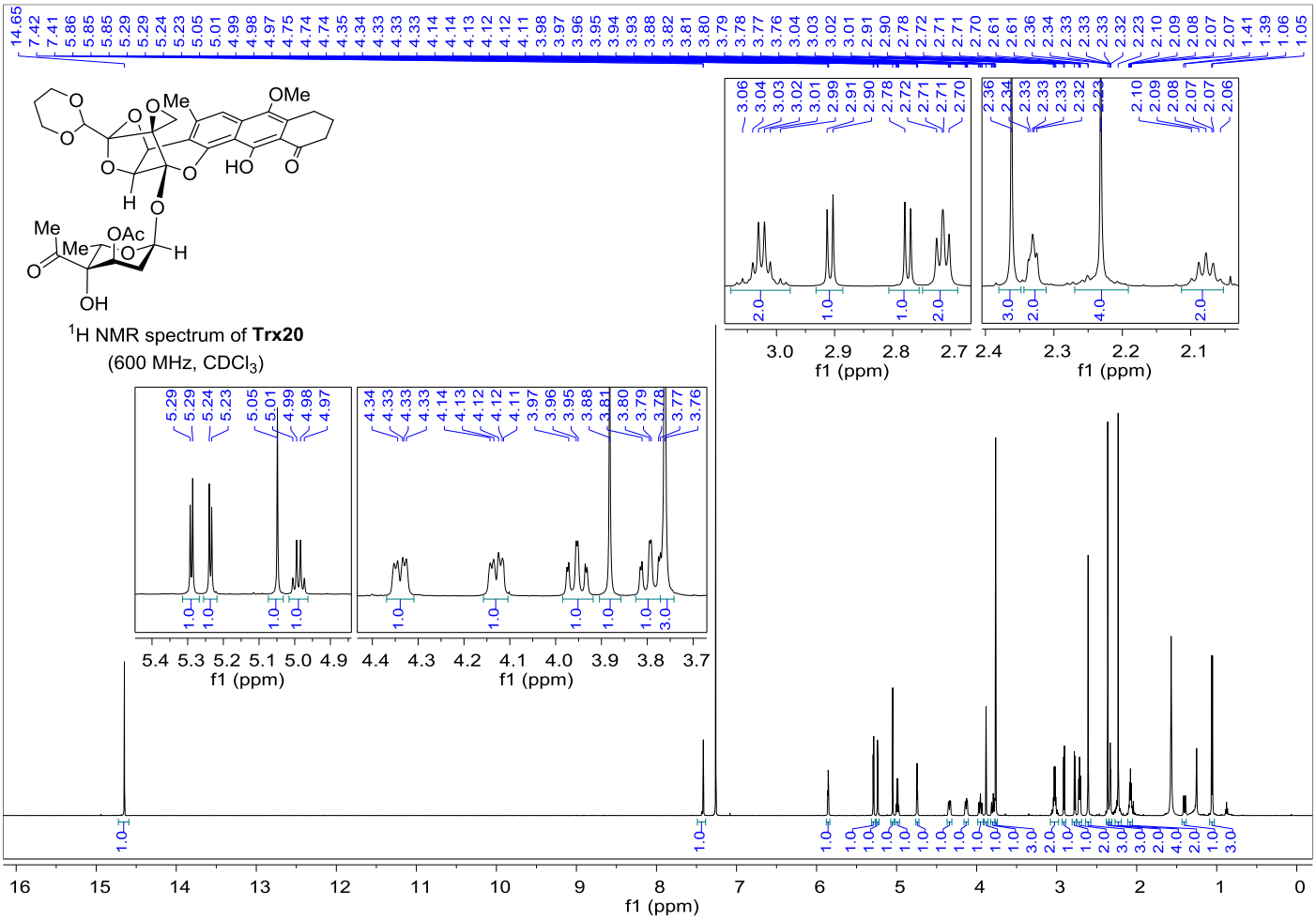
^{13}C NMR spectrum of **Trx18**
(rotamers around Alloc group)
(151 MHz, $CDCl_3$)



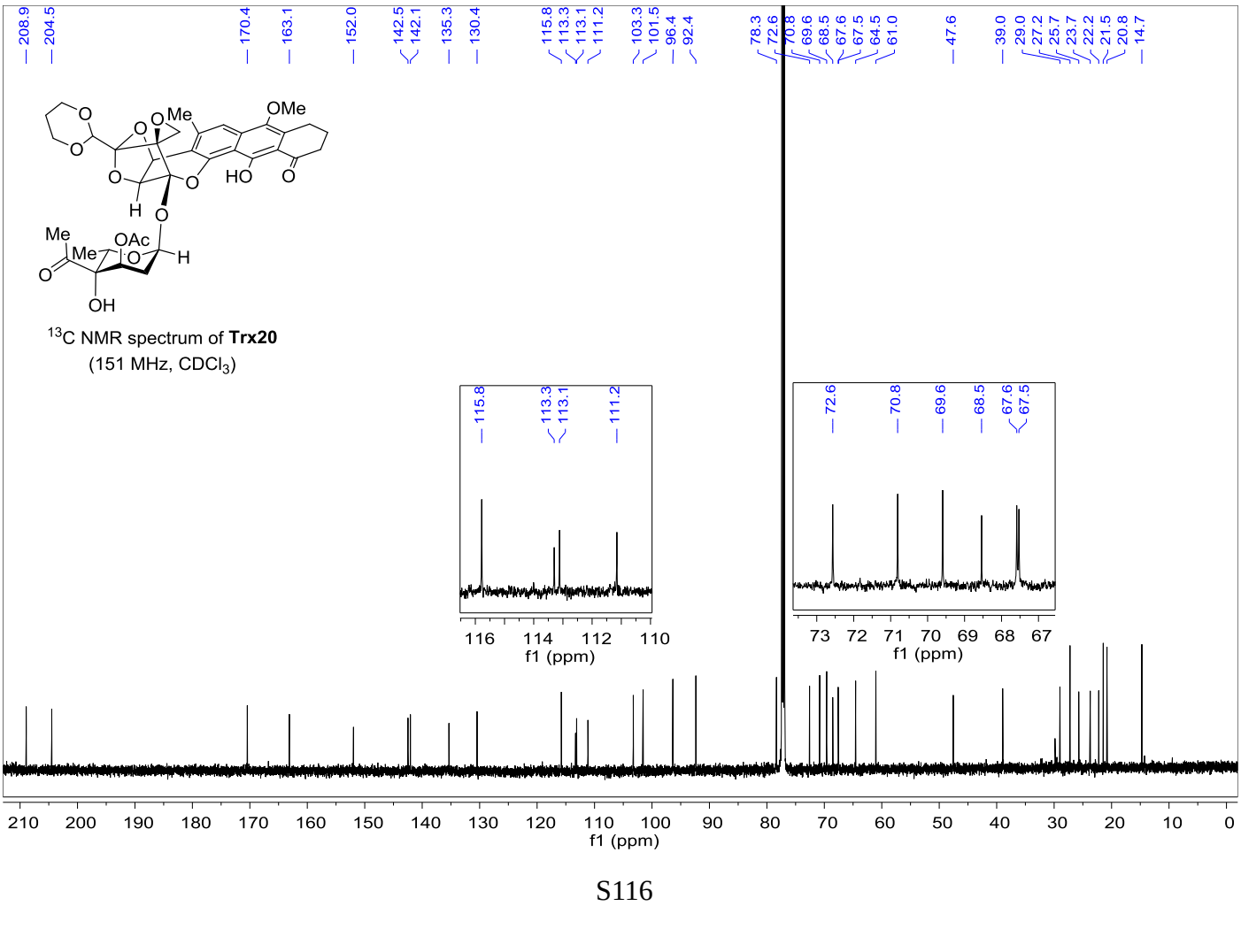
^{1}H NMR spectrum of **Trx19**
(600 MHz, $CDCl_3$)



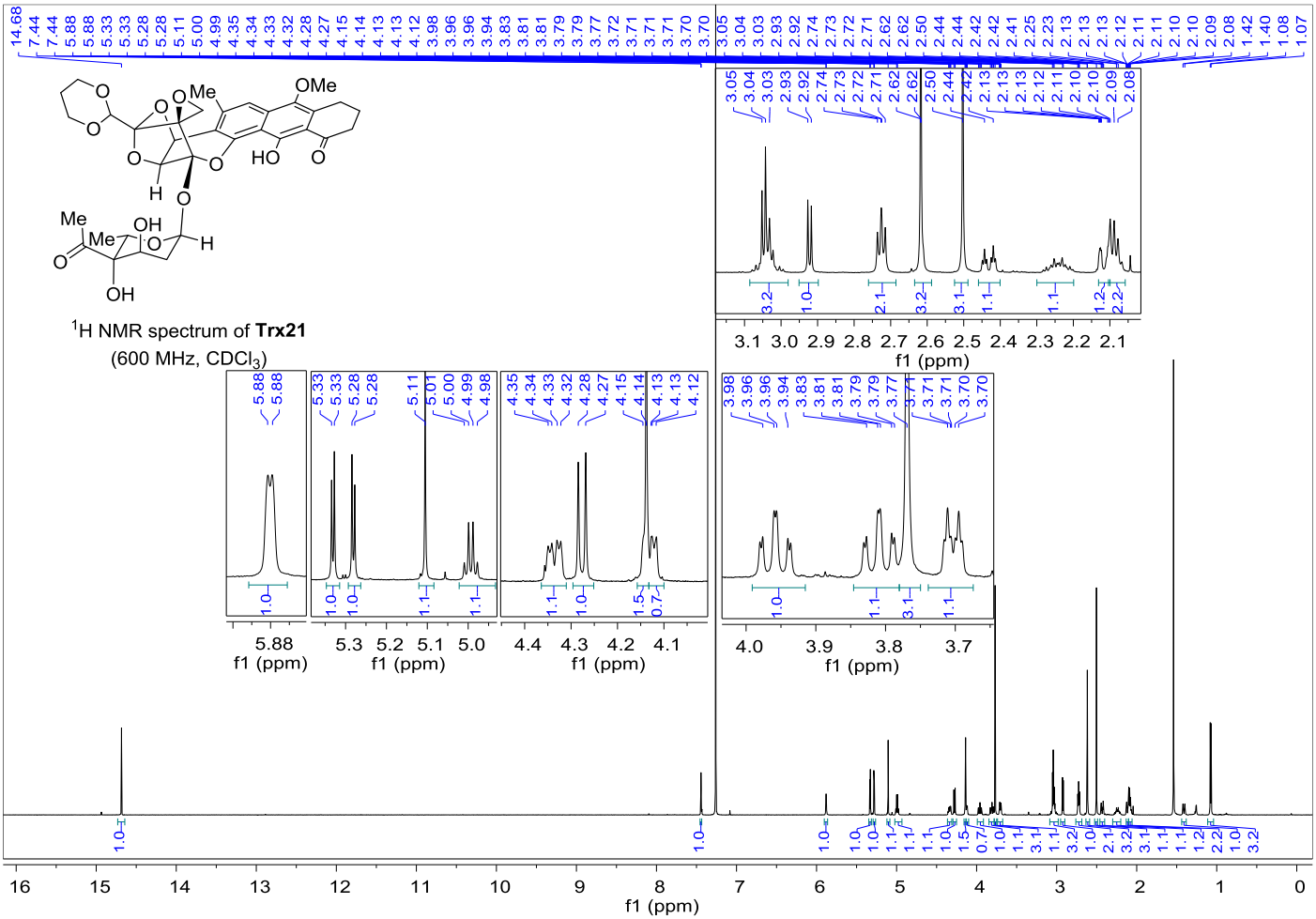
^{13}C NMR spectrum of **Trx19**
(151 MHz, $CDCl_3$)

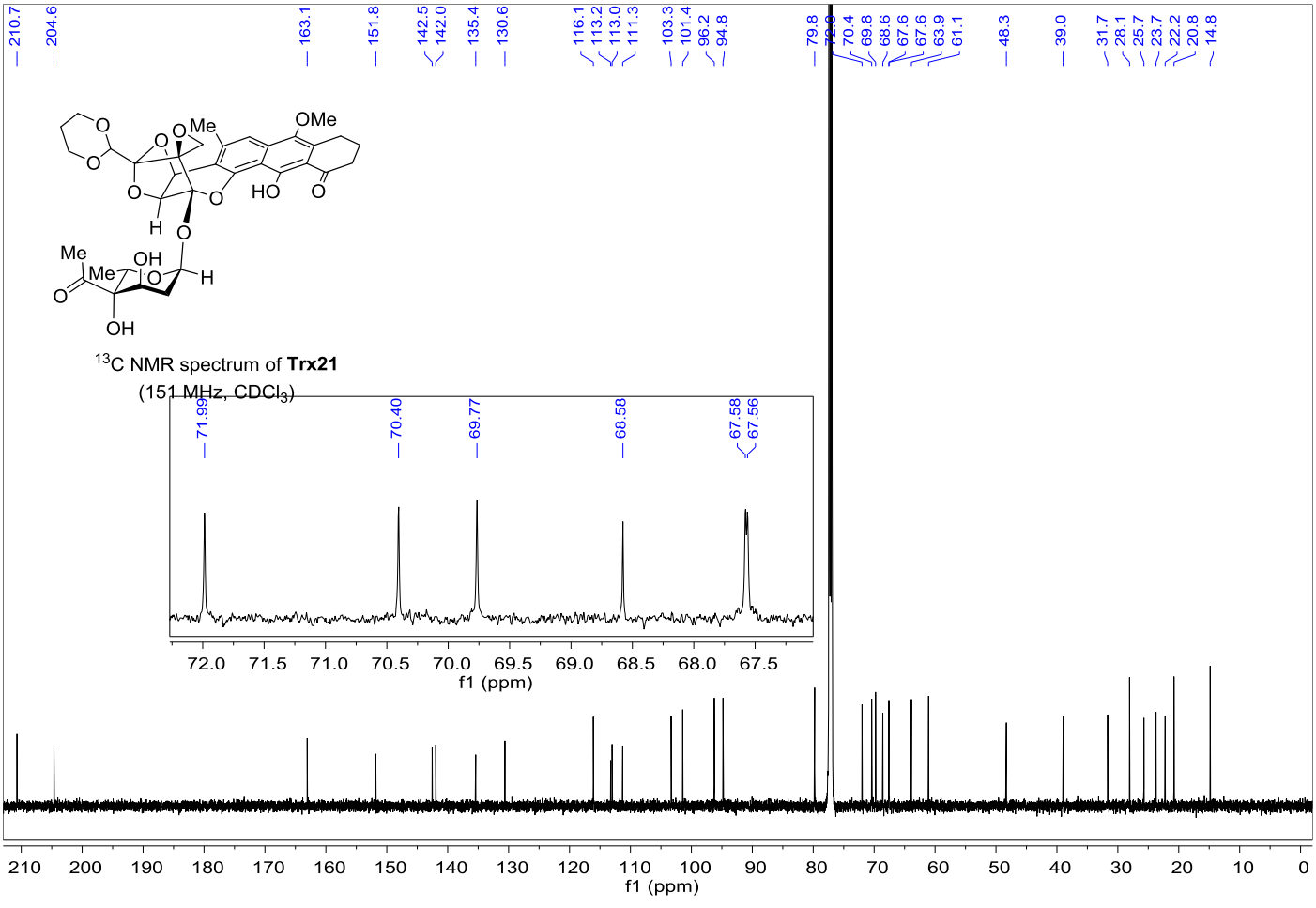


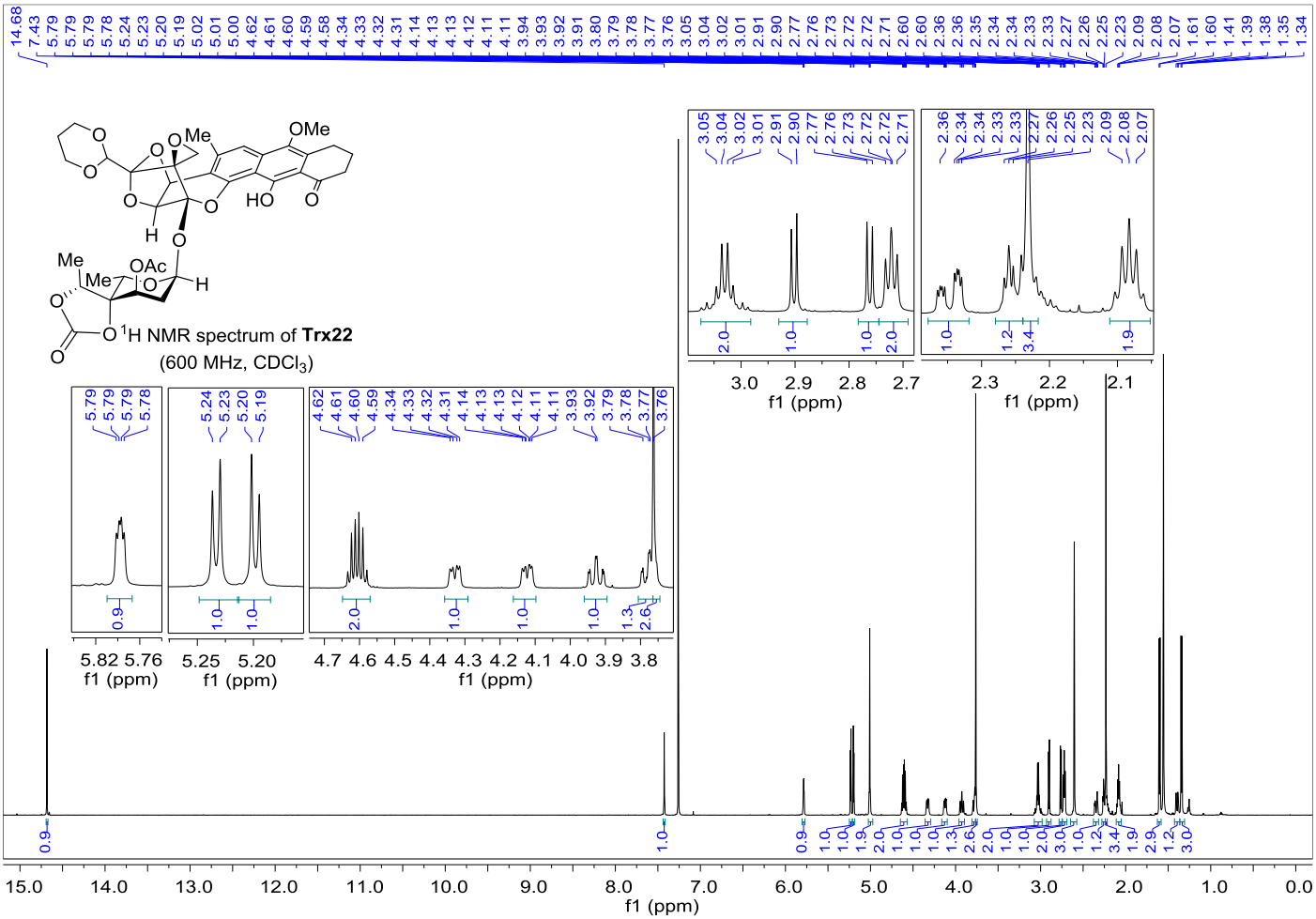
^{1}H NMR spectrum of **Trx20**
(600 MHz, $CDCl_3$)

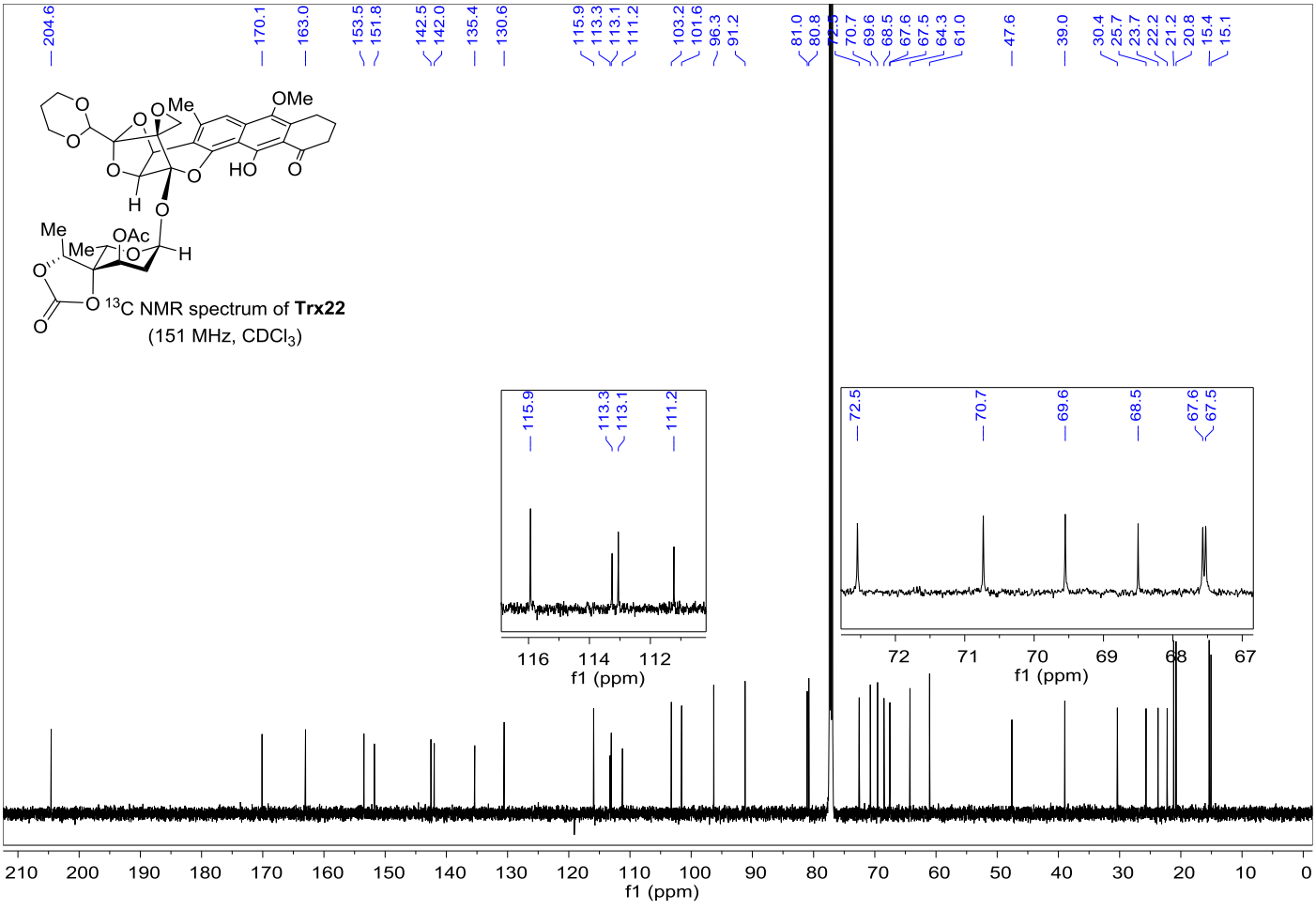


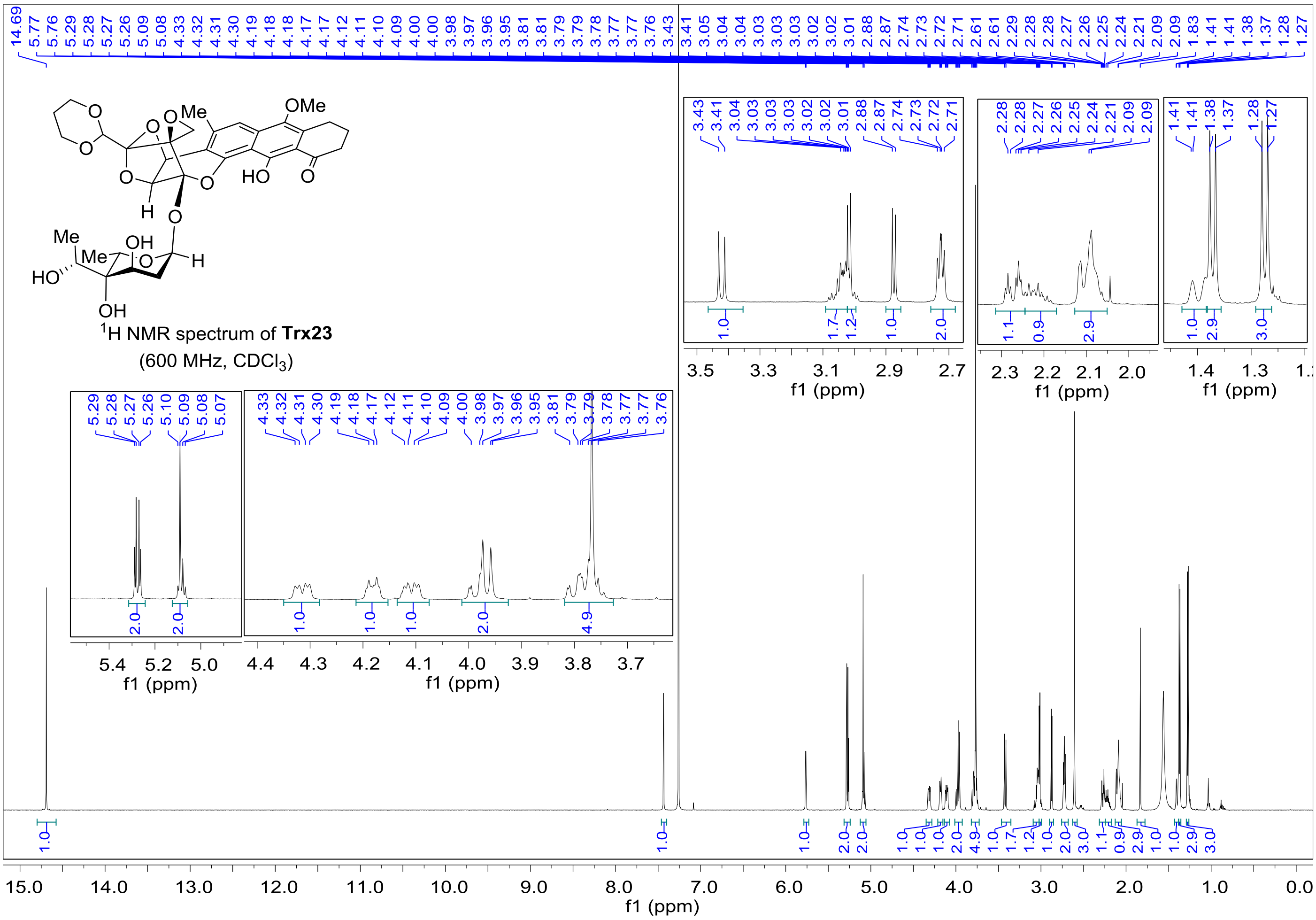
^{13}C NMR spectrum of **Trx20**
(151 MHz, $CDCl_3$)


^{1}H NMR spectrum of **Trx21**
(600 MHz, $CDCl_3$)
f1 (ppm)

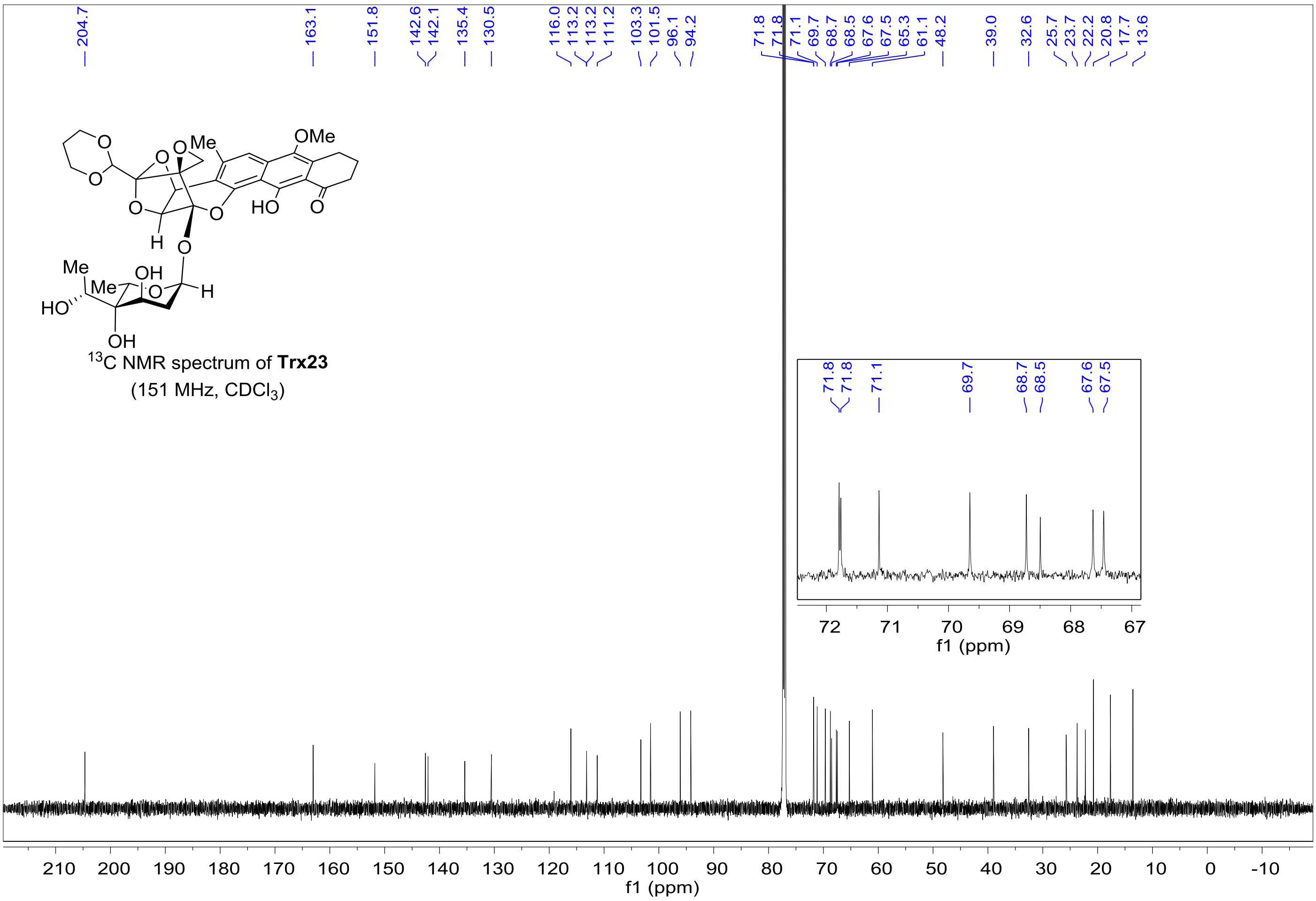

^{13}C NMR spectrum of **Trx21**
(151 MHz, $CDCl_3$)
f1 (ppm)


^{1}H NMR spectrum of **Trx22**
(600 MHz, $CDCl_3$)
f1 (ppm)

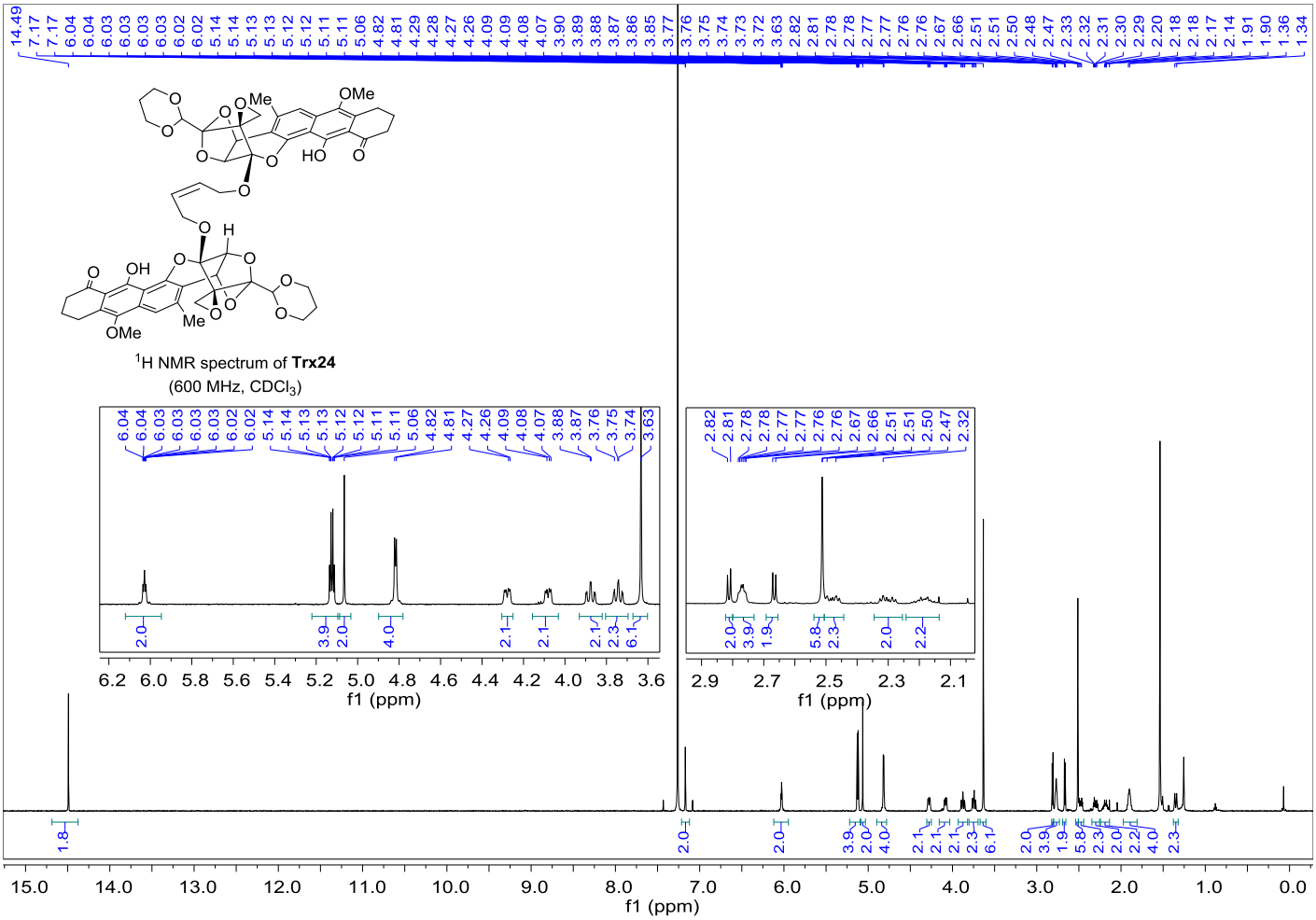

^{13}C NMR spectrum of **Trx22**
(151 MHz, $CDCl_3$)
f1 (ppm)



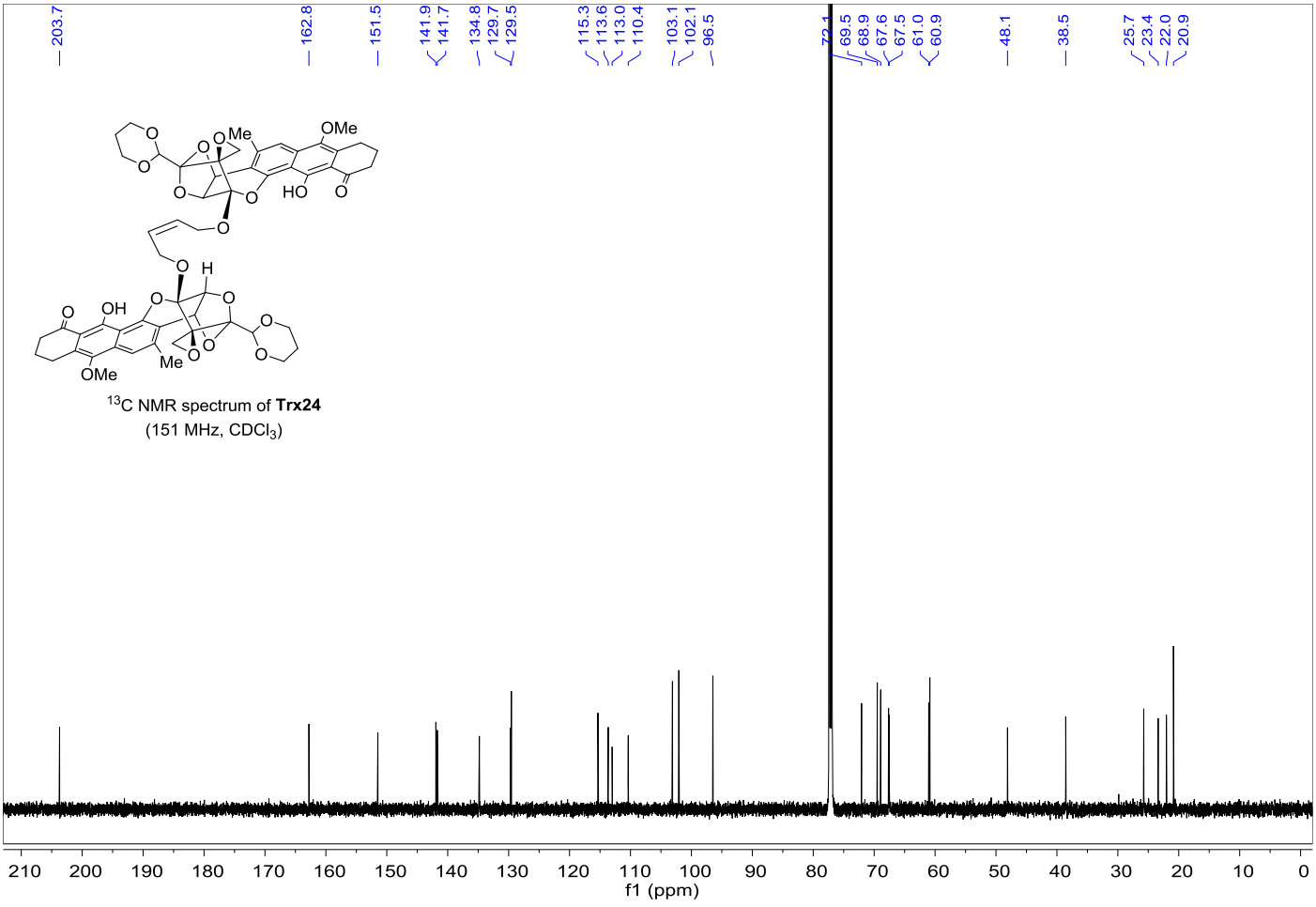
[1]H NMR spectrum of **Trx23**
(600 MHz, CDCl$_3$)



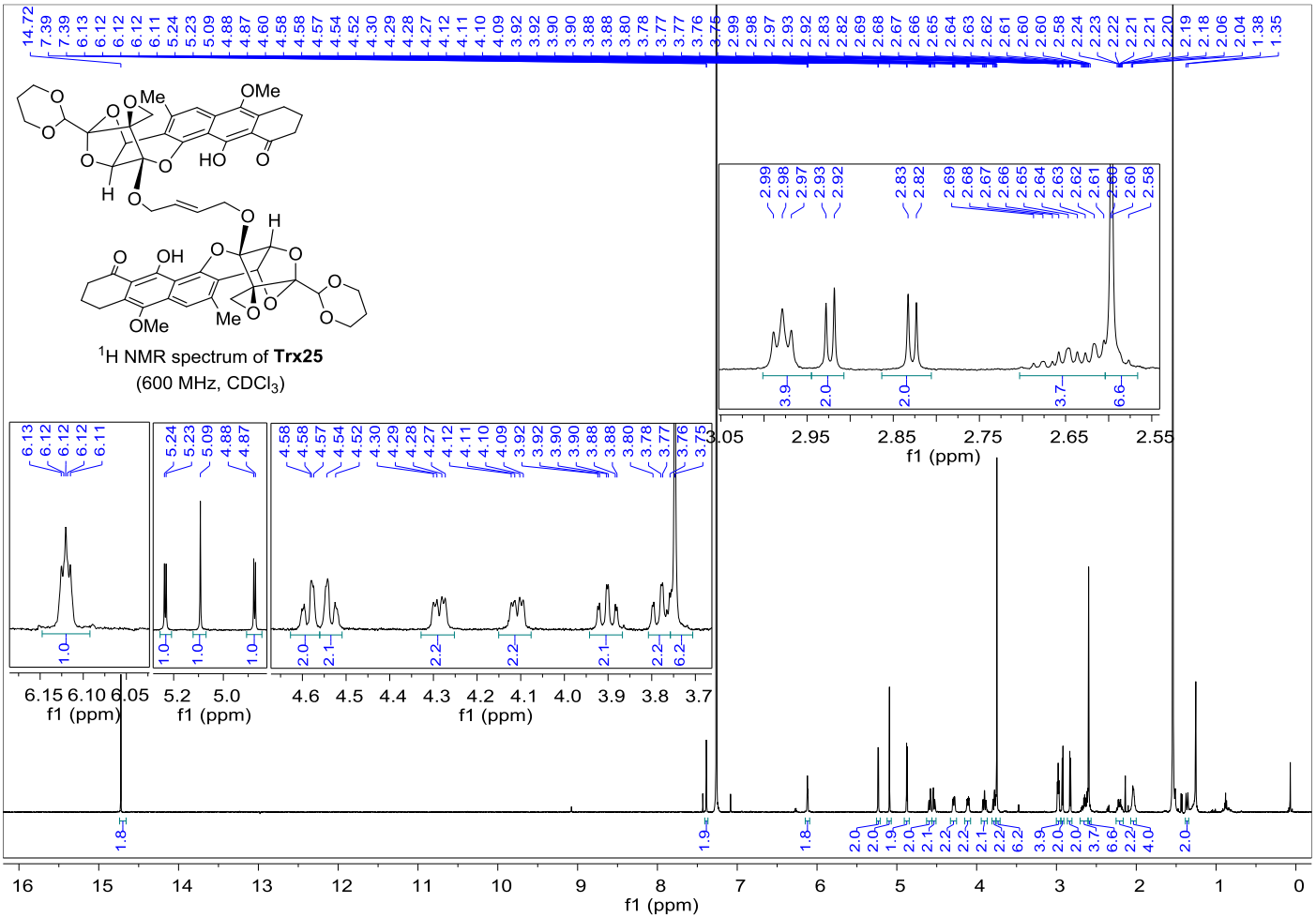
[13]C NMR spectrum of **Trx23**
(151 MHz, CDCl$_3$)



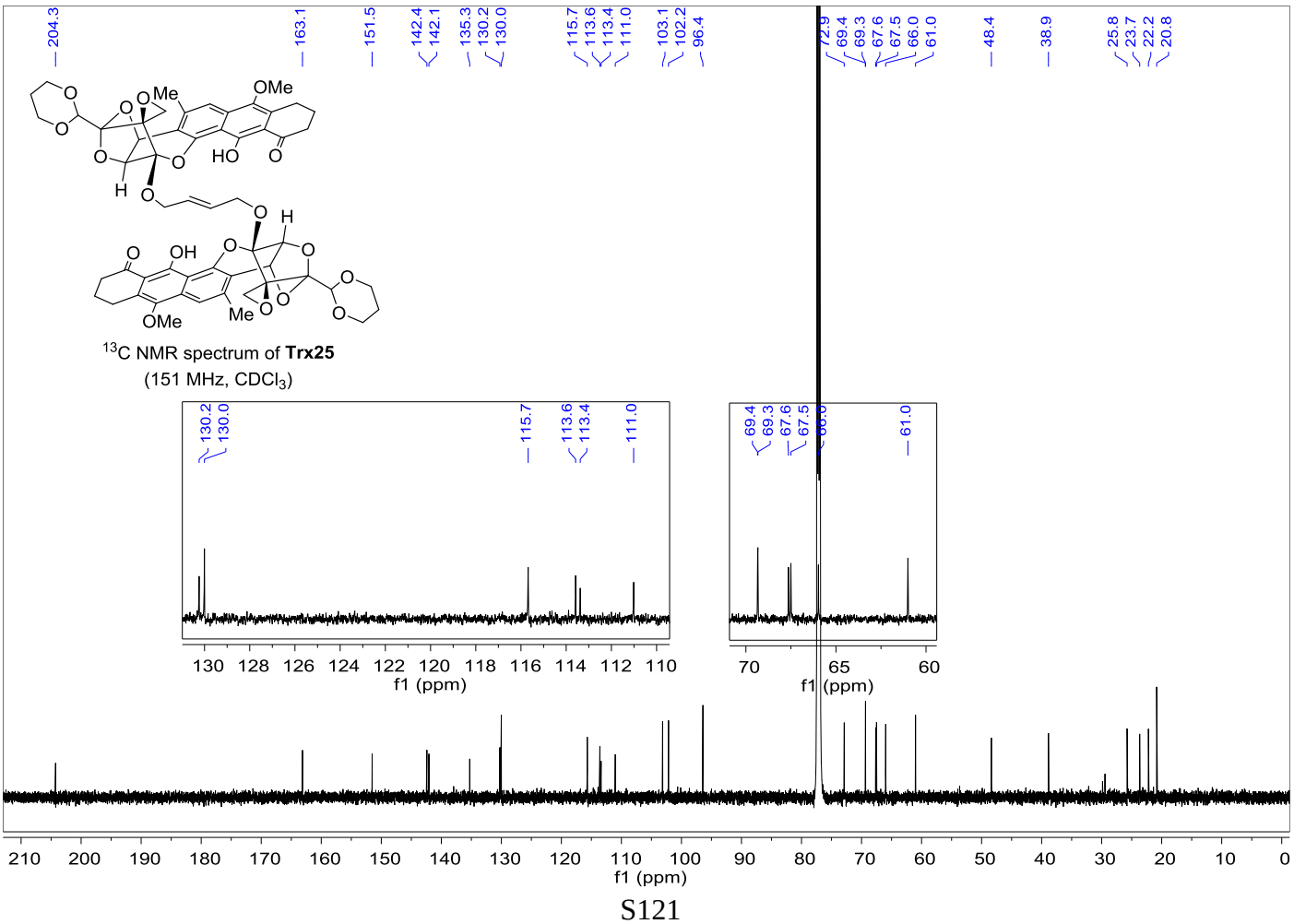
^{1}H NMR spectrum of **Trx24**
(600 MHz, $CDCl_3$)



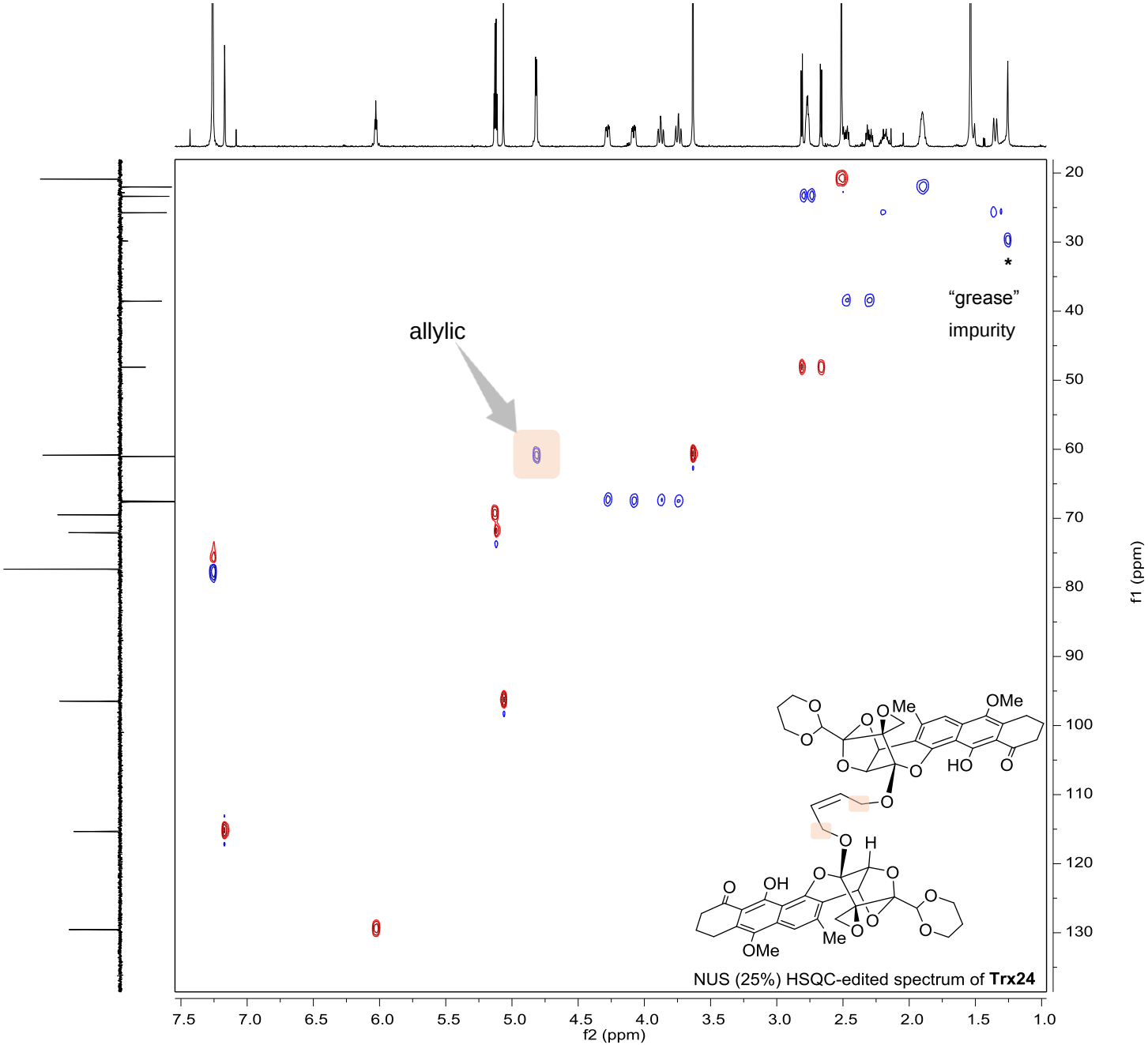
^{13}C NMR spectrum of **Trx24**
(151 MHz, $CDCl_3$)



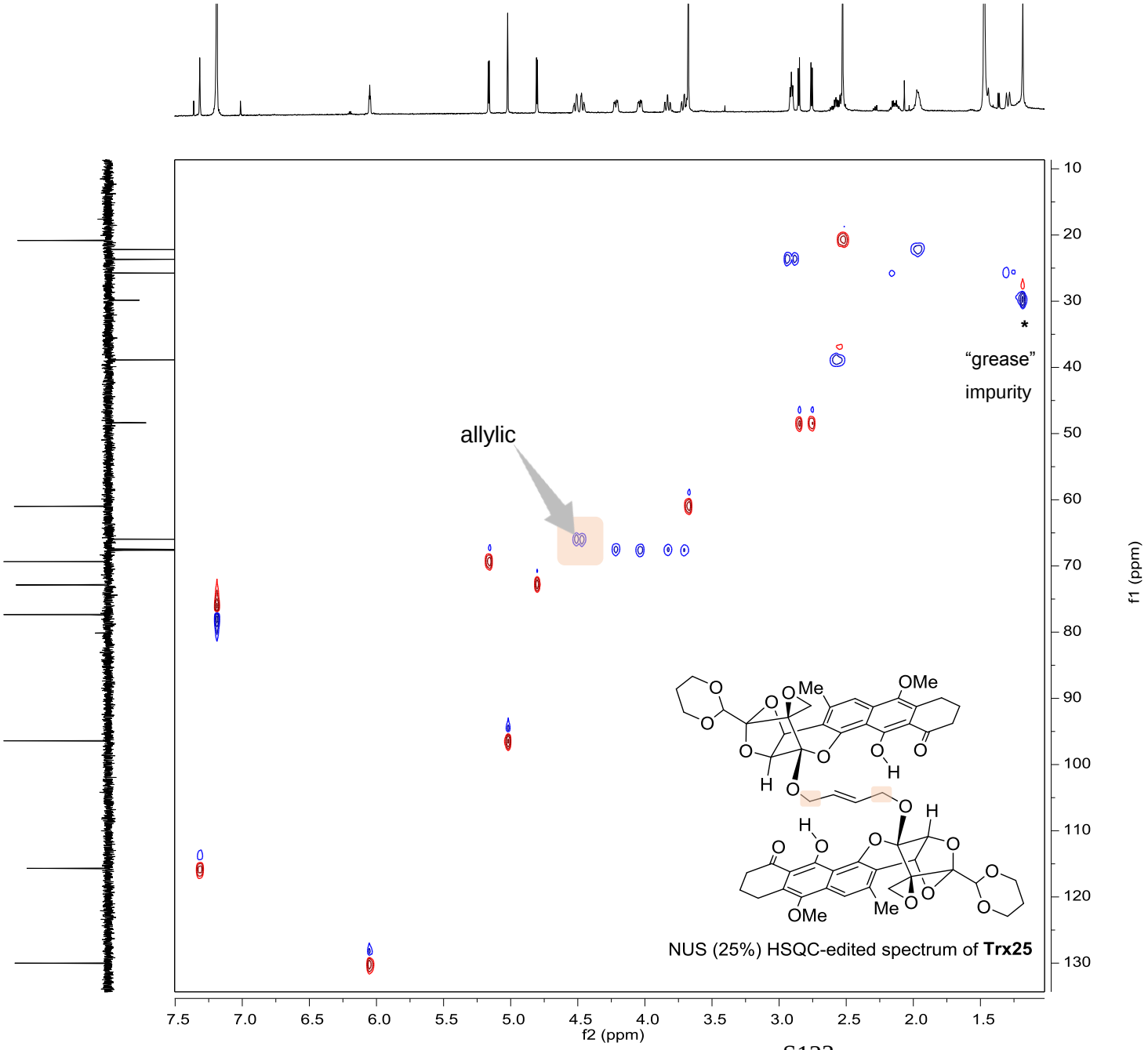
^{1}H NMR spectrum of **Trx25**
(600 MHz, $CDCl_3$)



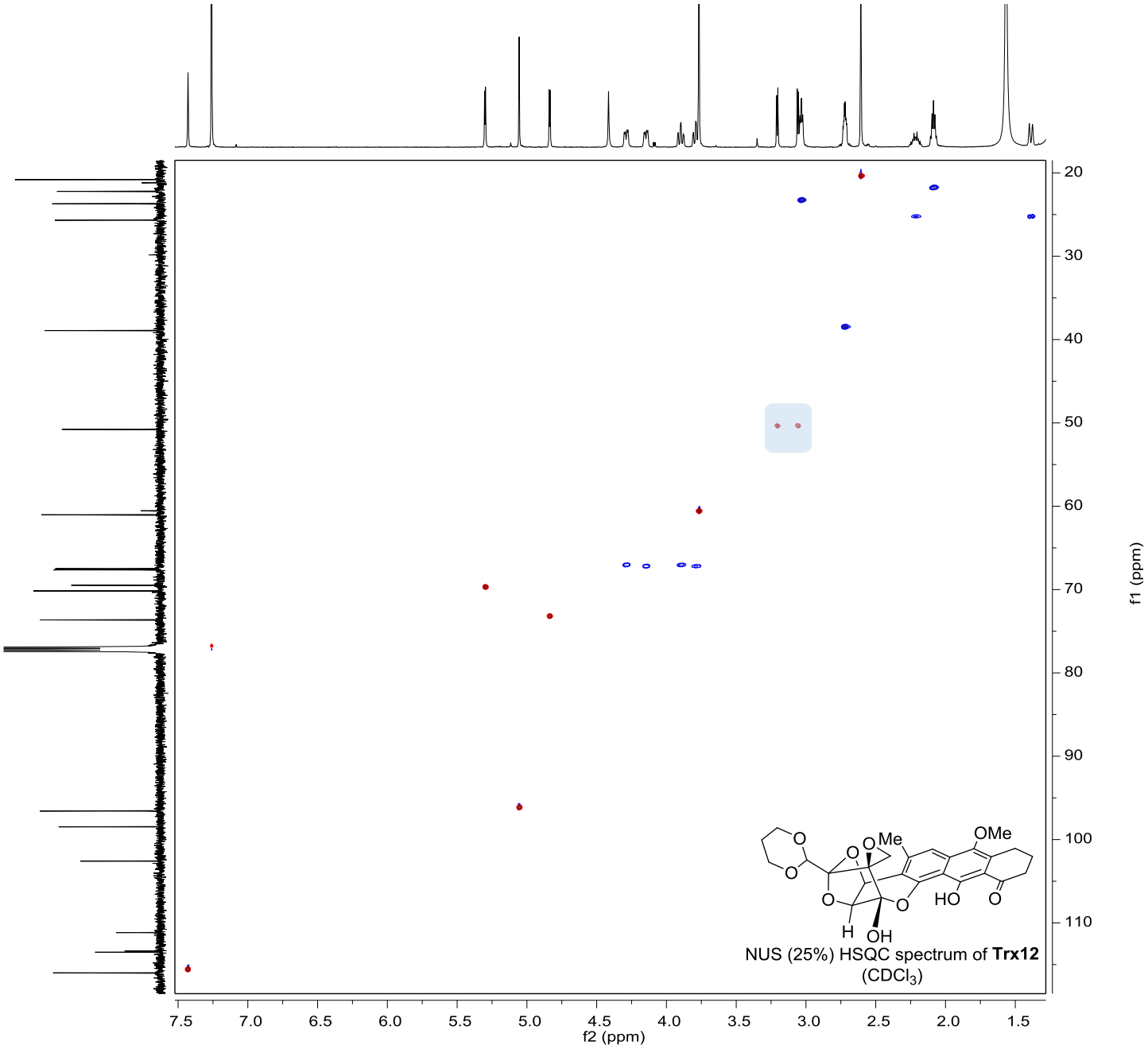
^{13}C NMR spectrum of **Trx25**
(151 MHz, $CDCl_3$)



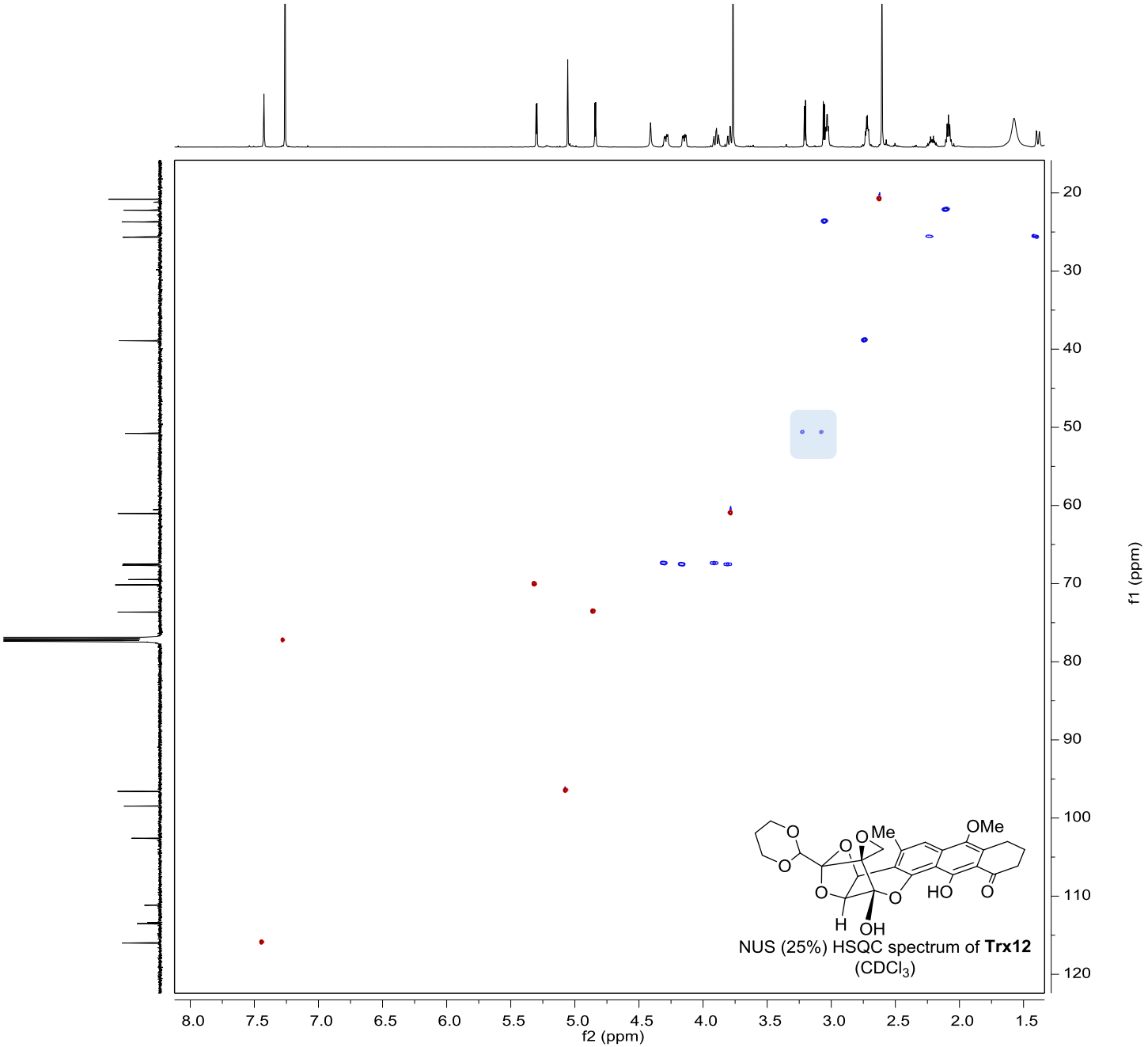
Parameter	Value
Temperature	300.0
Pulse Sequence	hsqcedetgpsisp2.3
Number of Scans	32
Receiver Gain	186.1
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	0.0852
Spectrometer Frequency	(600.18, 150.93)
Spectral Width	(12019.2, 33112.6)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)
cnst2	**145**
d21	**0.00360000**
d24	**0.00089000**
NUS amount	25%



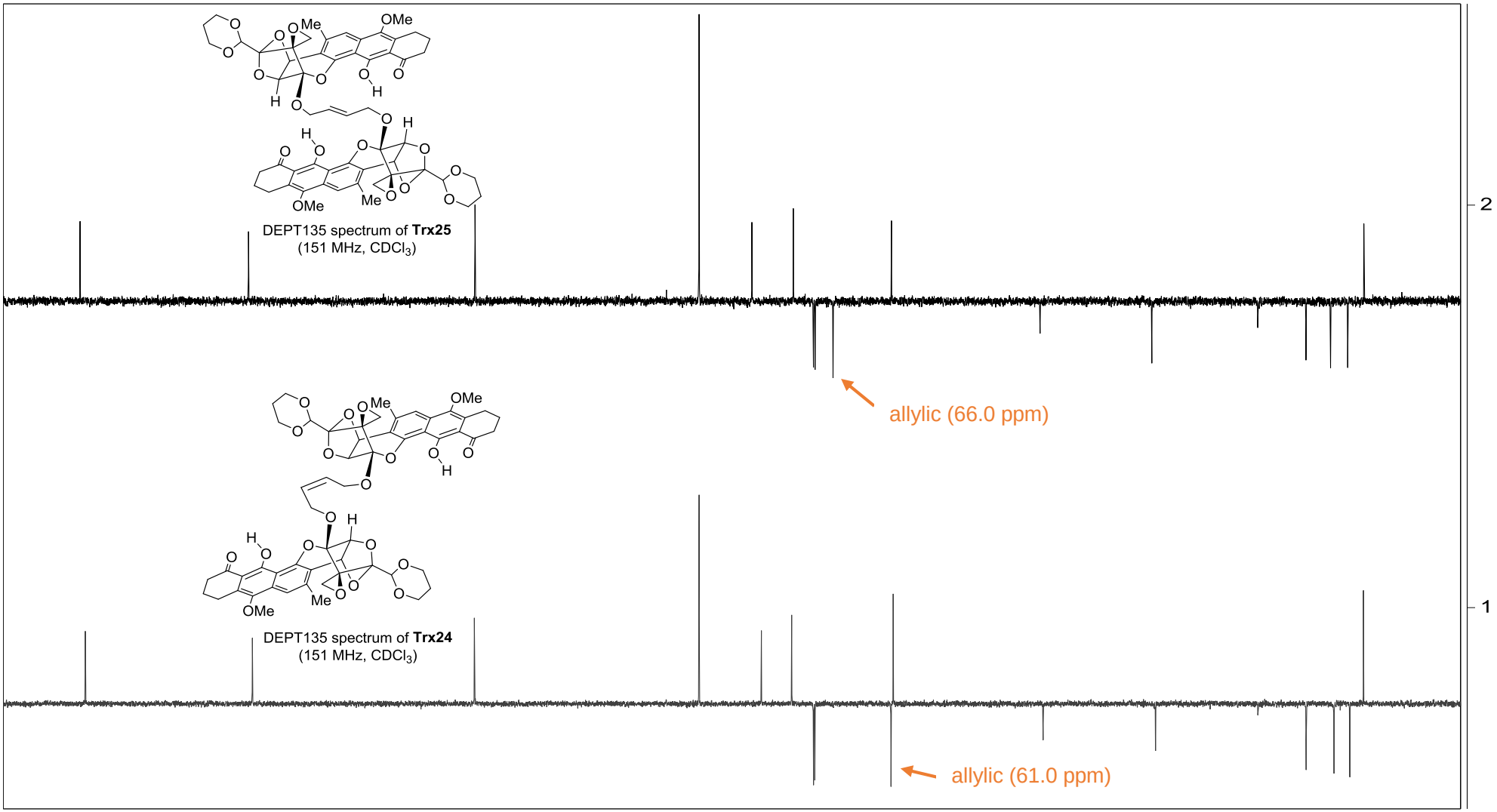
Parameter	Value
Origin	Bruker BioSpin GmbH
Temperature	300.0
Pulse Sequence	hsqcedetgpsisp2.3
Number of Scans	32
Receiver Gain	186.1
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	0.0852
Spectrometer Frequency	(600.18, 150.93)
Spectral Width	(12019.2, 33112.6)
Acquired Size	(1024, 64)
Spectral Size	(1024, 1024)
cnst2	**145**
d21	**0.00360000**
d24	**0.00089000**
NUS amount	25%

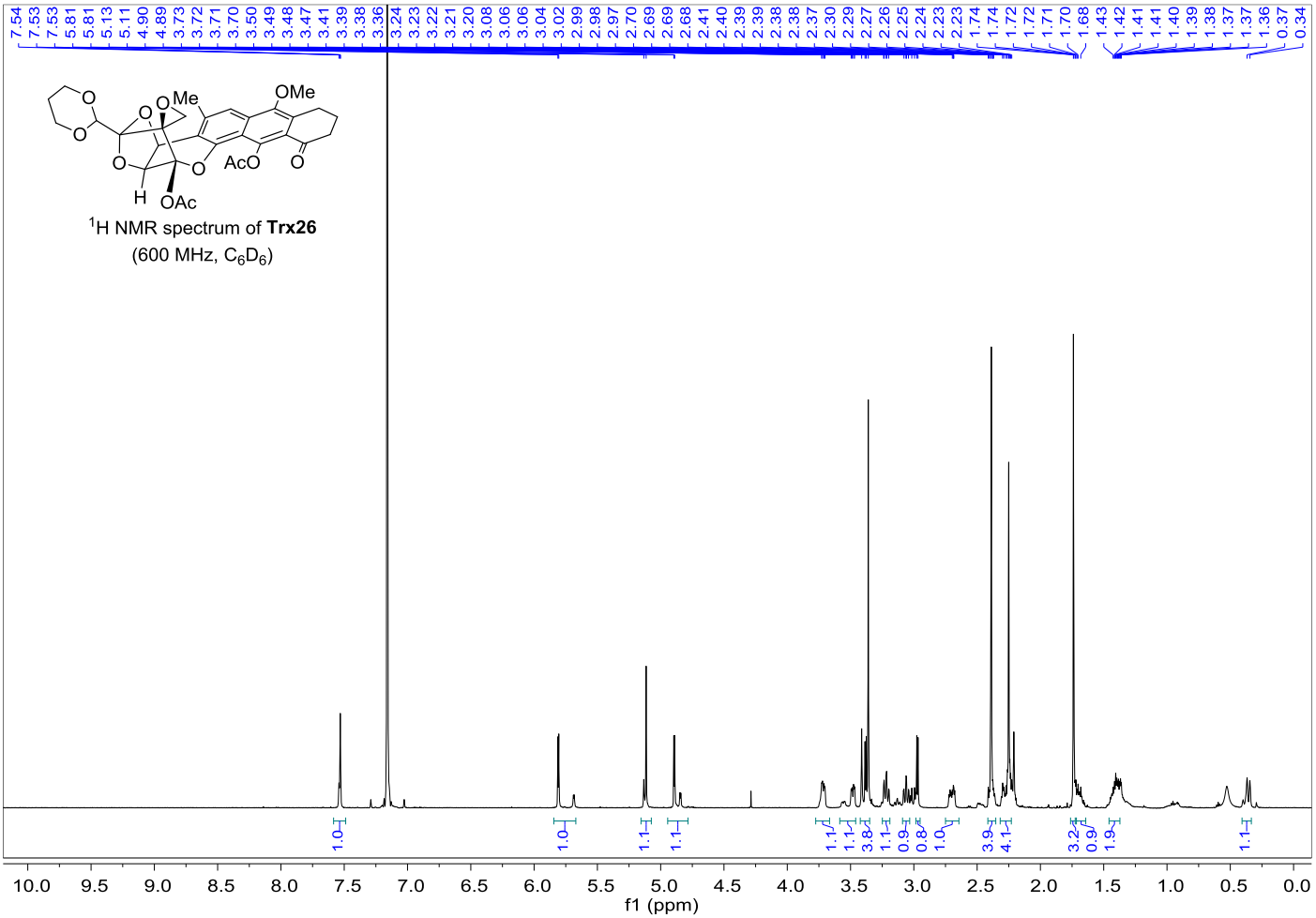


Parameter	Value
Origin	Bruker BioSpin GmbH
Temperature	300.0
Pulse Sequence	hsqcedetgpsisp2.3
Number of Scans	8
Receiver Gain	186.1
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	0.1420
Spectrometer Frequency	(600.18, 150.93)
Spectral Width	(7211.5, 24875.6)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)
cnst2	**160**
d21	**0.00360000**
d24	**0.00089000**
NUS amount	25%

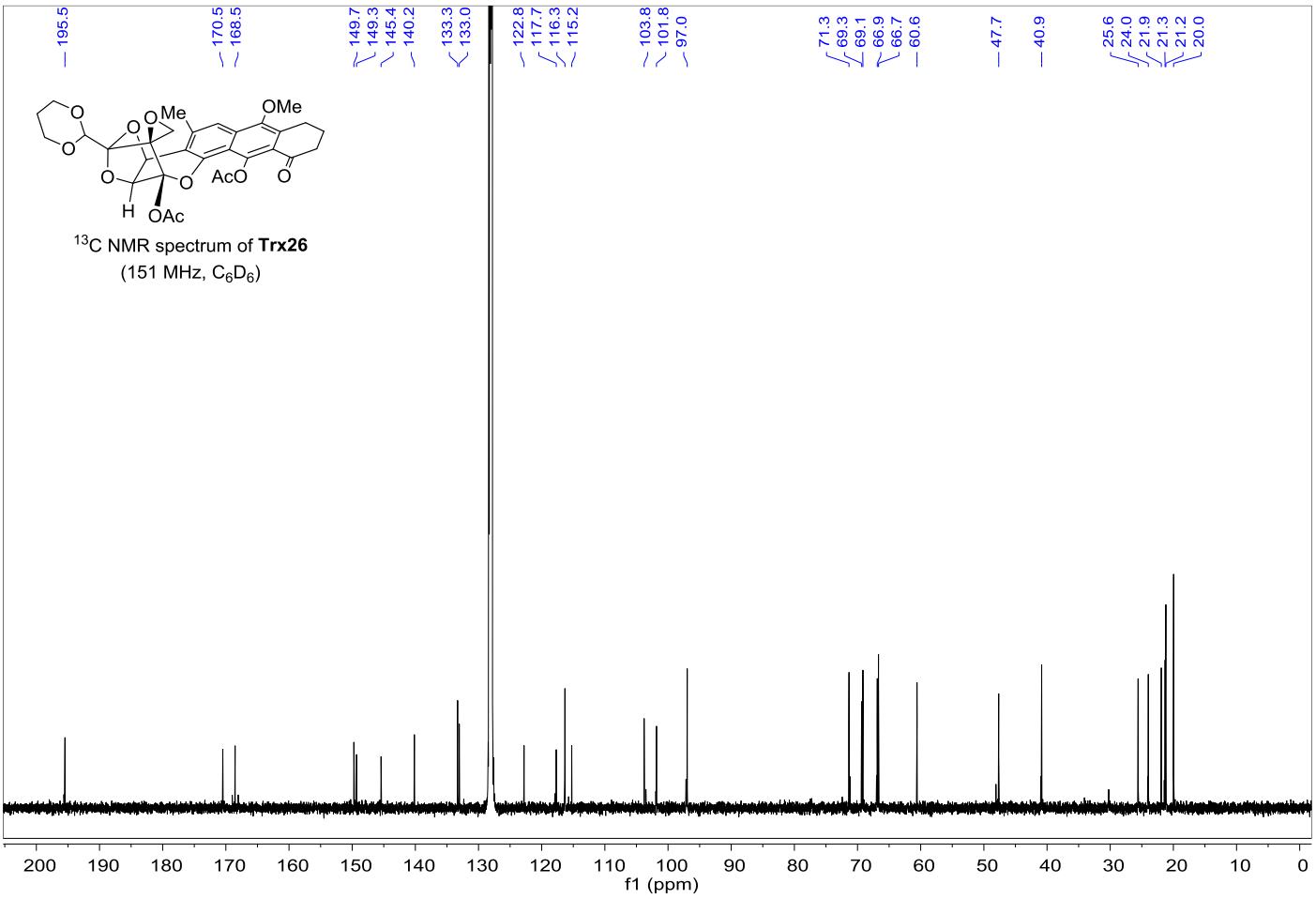


Parameter	Value
Origin	Bruker BioSpin GmbH
Temperature	300.0
Pulse Sequence	hsqcedetgpsisp2.3
Number of Scans	8
Receiver Gain	186.1
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	0.1420
Spectrometer Frequency	(600.18, 150.93)
Spectral Width	(7211.5, 24875.6)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)
cnst2	**160**
d21	**0.003125000**
d24	**0.000781250**
NUS amount	25%

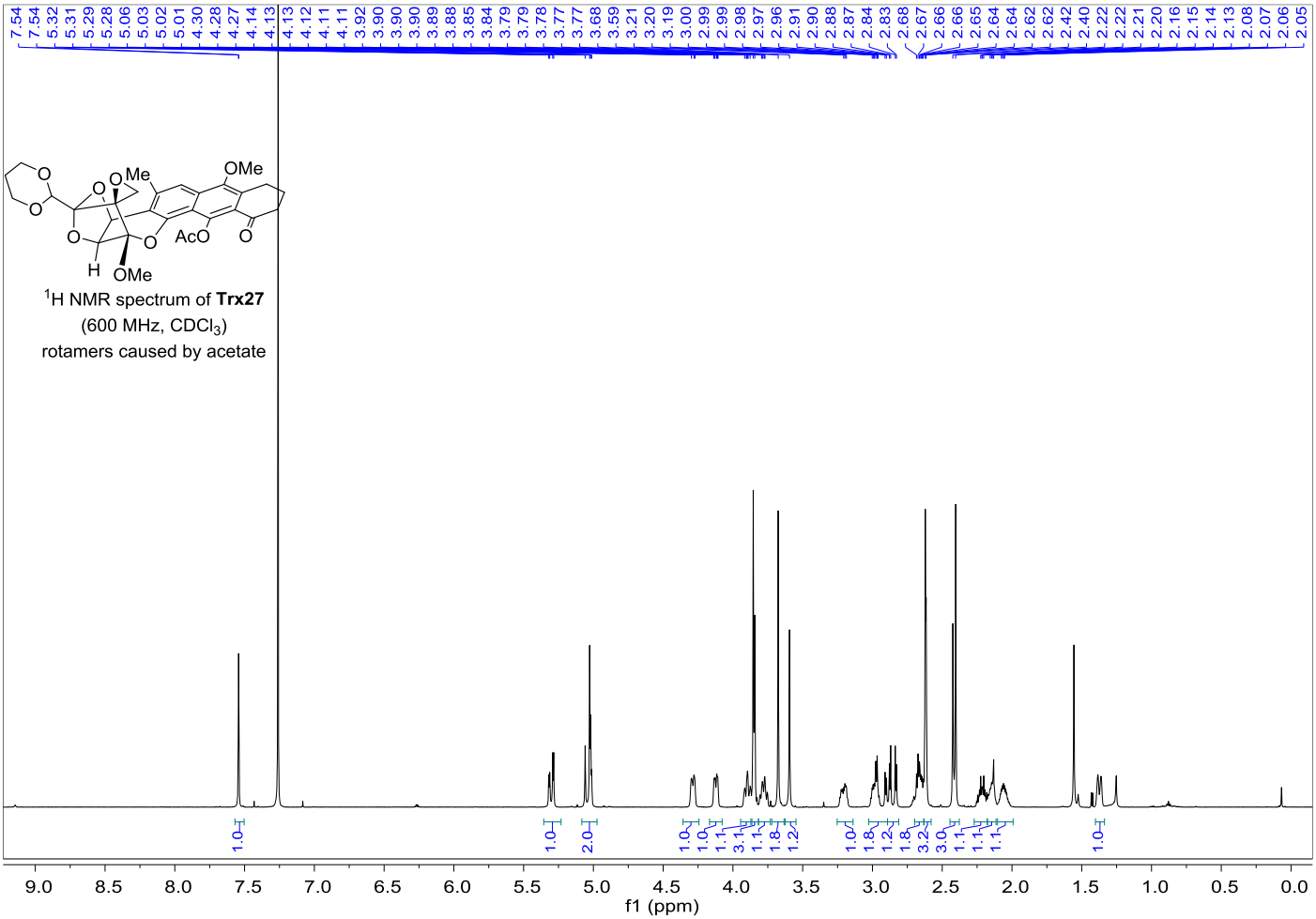

DEPT135 spectrum of **Trx25**
(151 MHz, $CDCl_3$)
allylic (66.0 ppm)
DEPT135 spectrum of **Trx24**
(151 MHz, $CDCl_3$)
allylic (61.0 ppm)
2
1
135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)



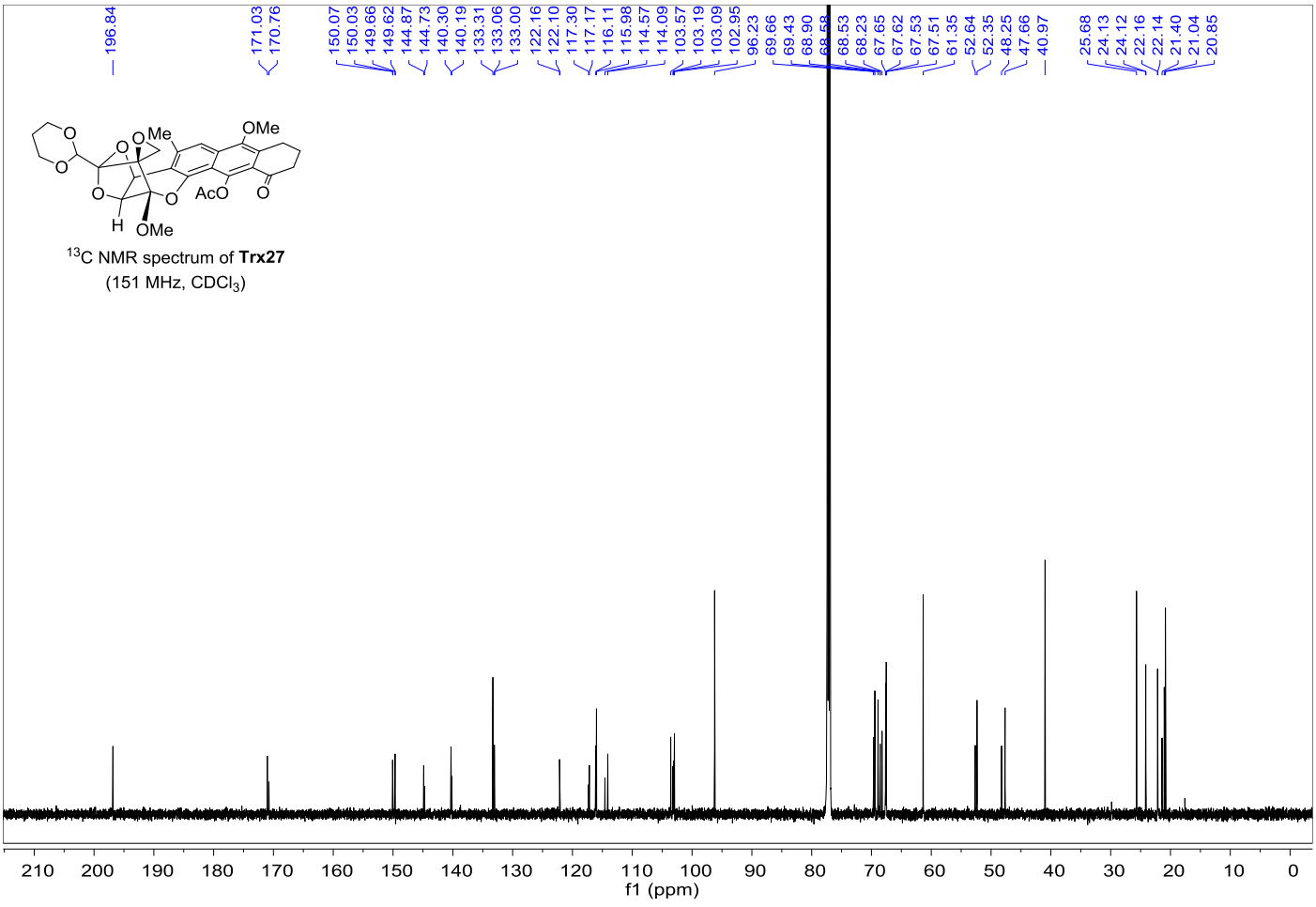
^{1}H NMR spectrum of **Trx26**
(600 MHz, C_6D_6)



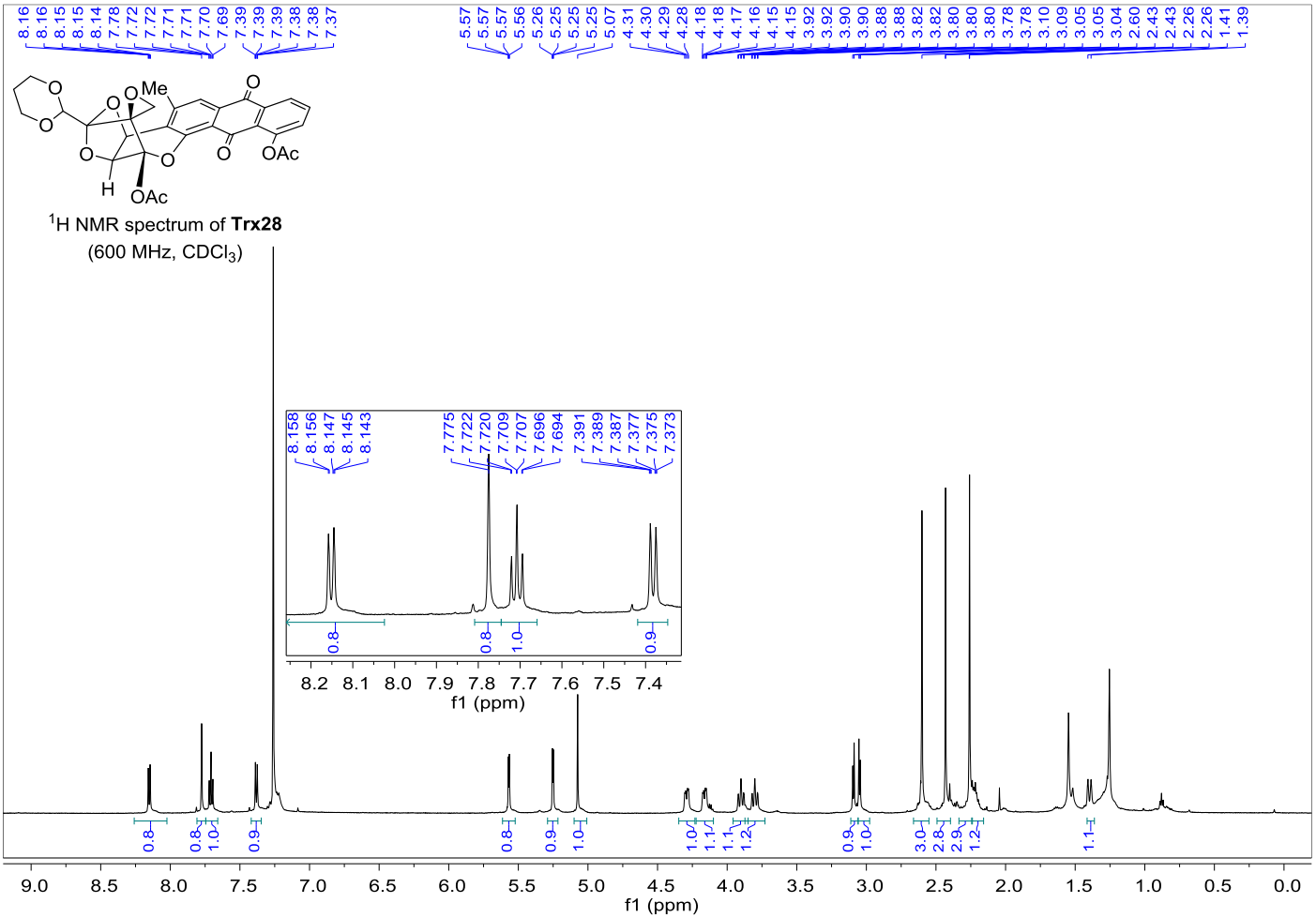
^{13}C NMR spectrum of **Trx26**
(151 MHz, C_6D_6)

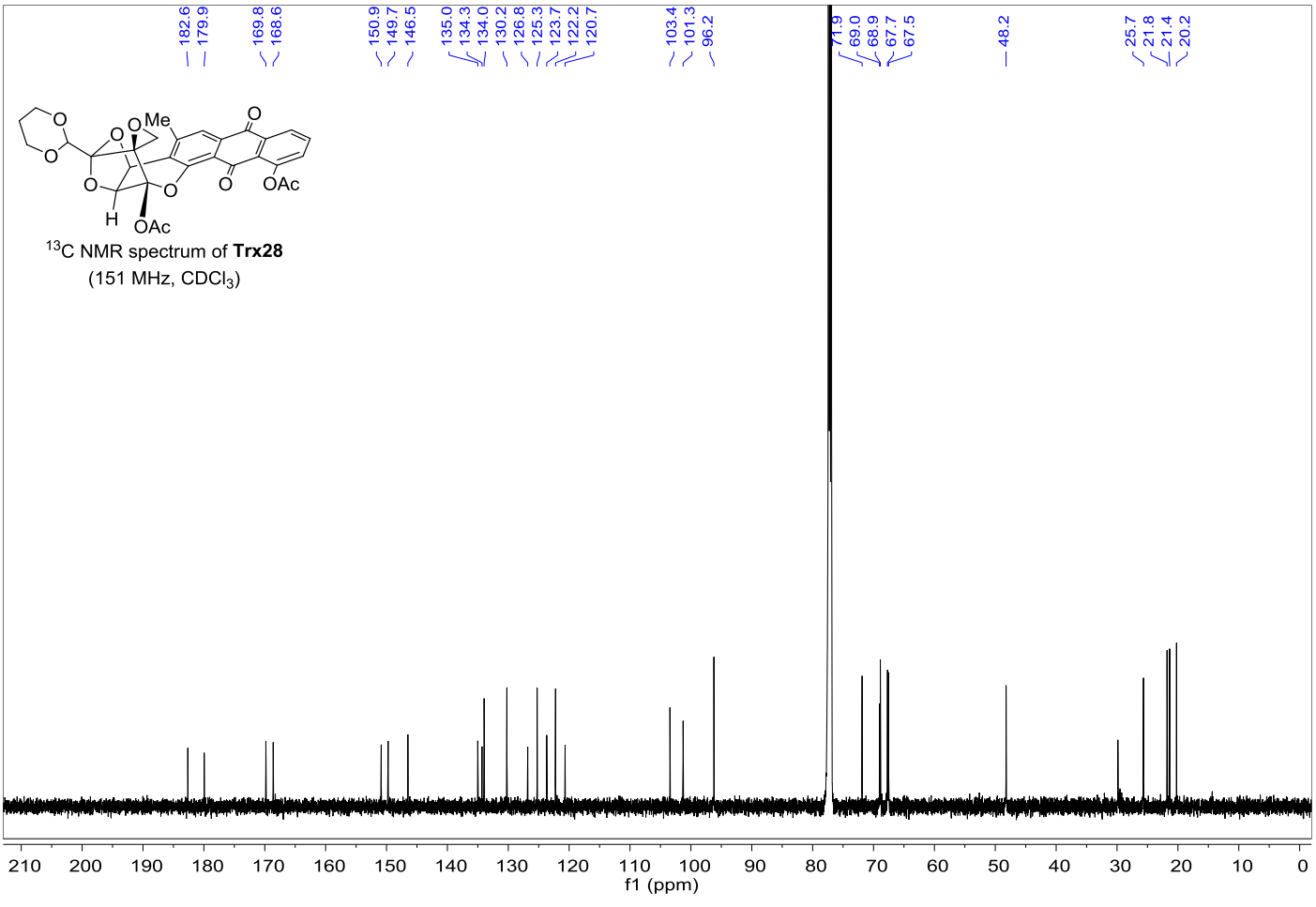


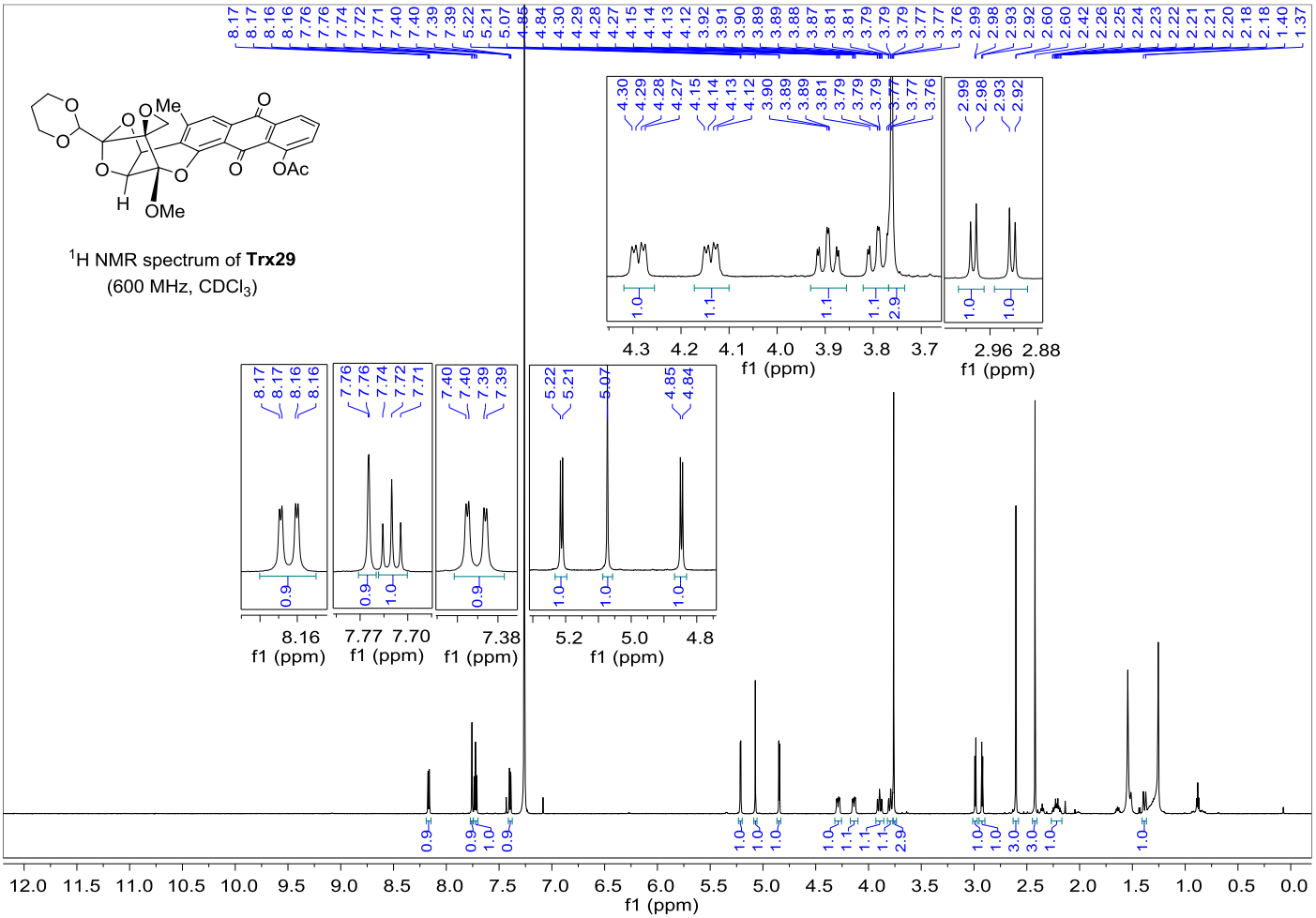
^{1}H NMR spectrum of **Trx27**
(600 MHz, $CDCl_3$)
rotamers caused by acetate



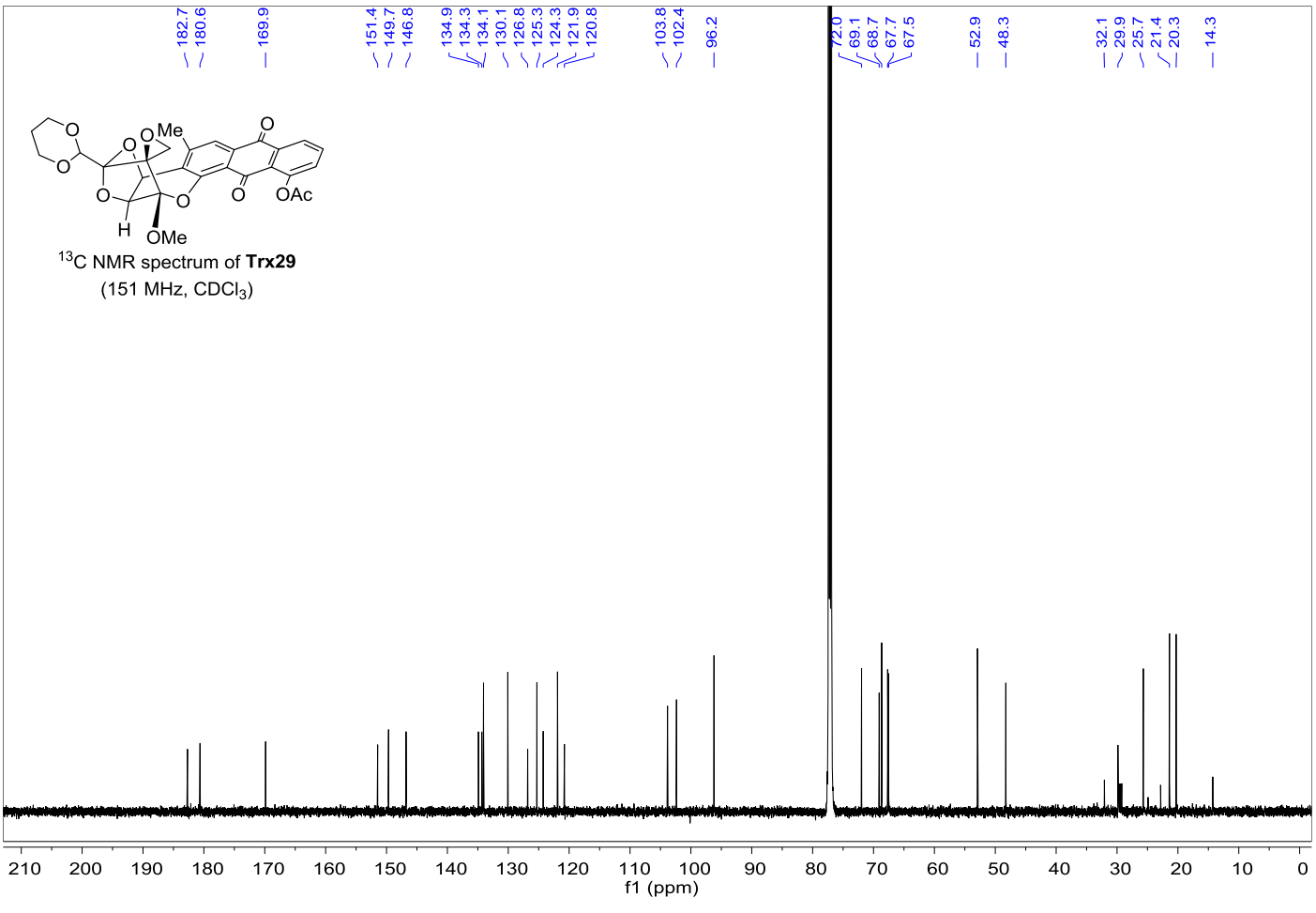
^{13}C NMR spectrum of **Trx27**
(151 MHz, $CDCl_3$)


Me
OAc
OAc
H
^{1}H NMR spectrum of **Trx28**
(600 MHz, $CDCl_3$)
f1 (ppm)

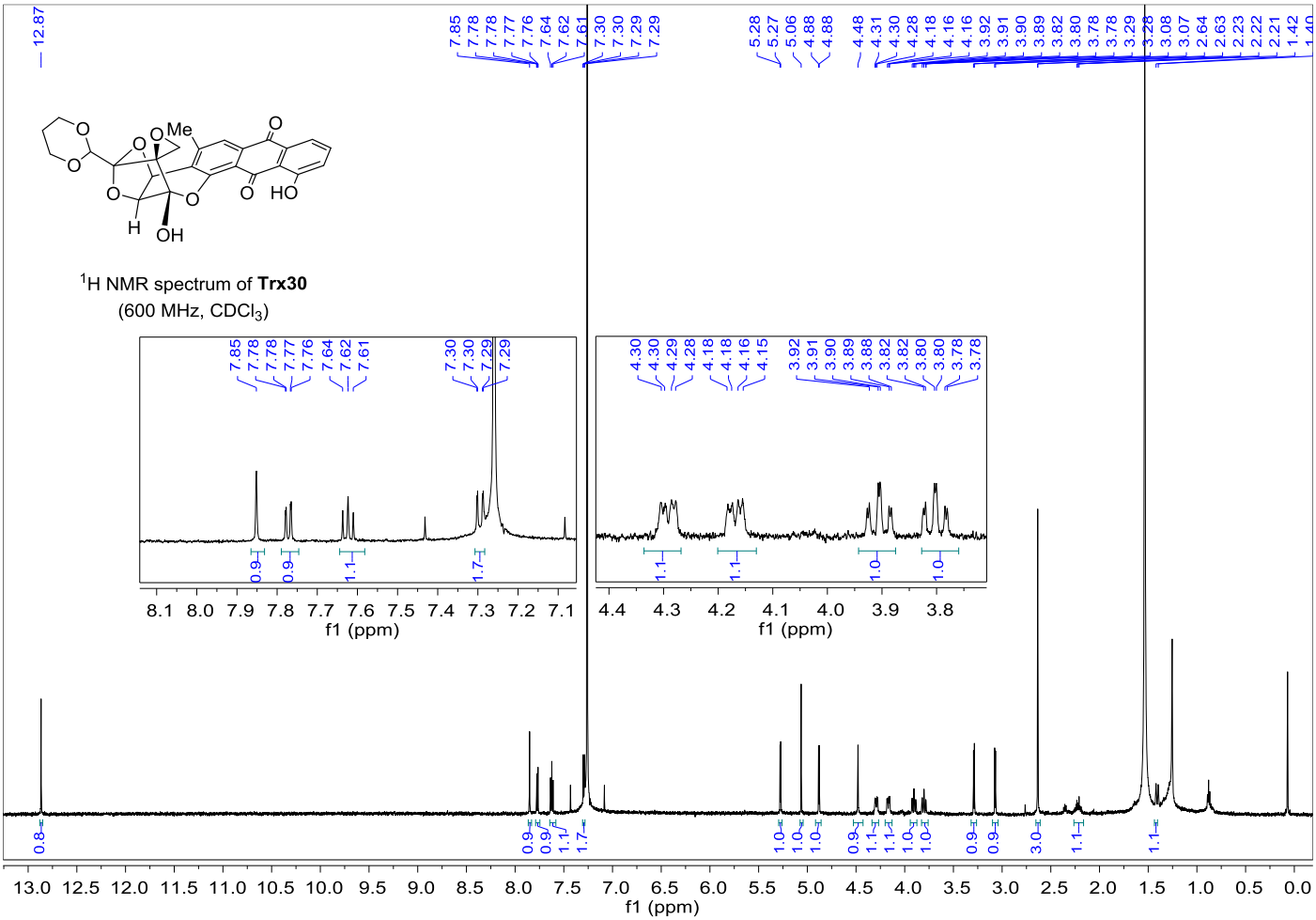

Me
OAc
OAc
H
^{13}C NMR spectrum of **Trx28**
(151 MHz, $CDCl_3$)
f1 (ppm)



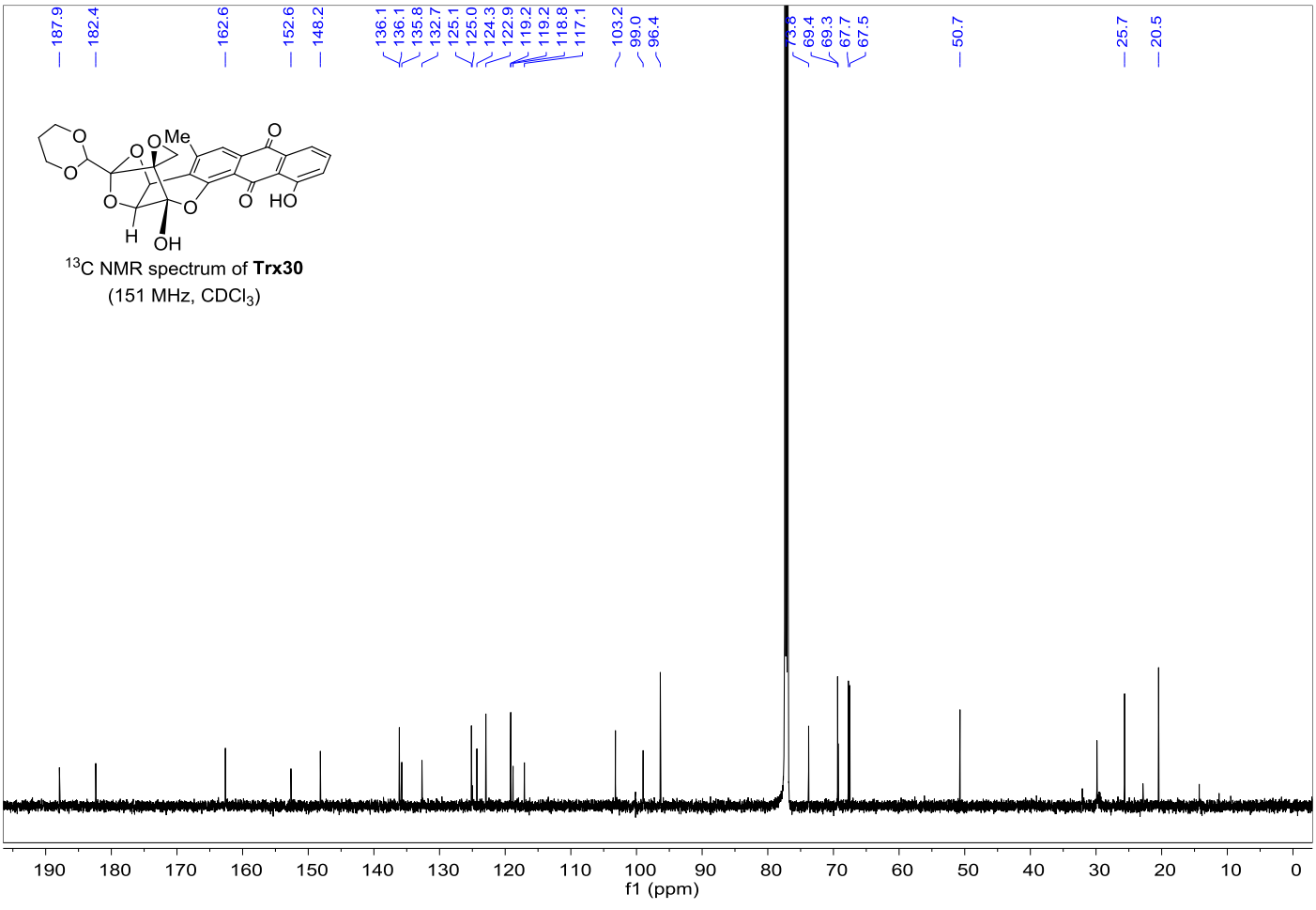
^{1}H NMR spectrum of **Trx29**
(600 MHz, $CDCl_3$)



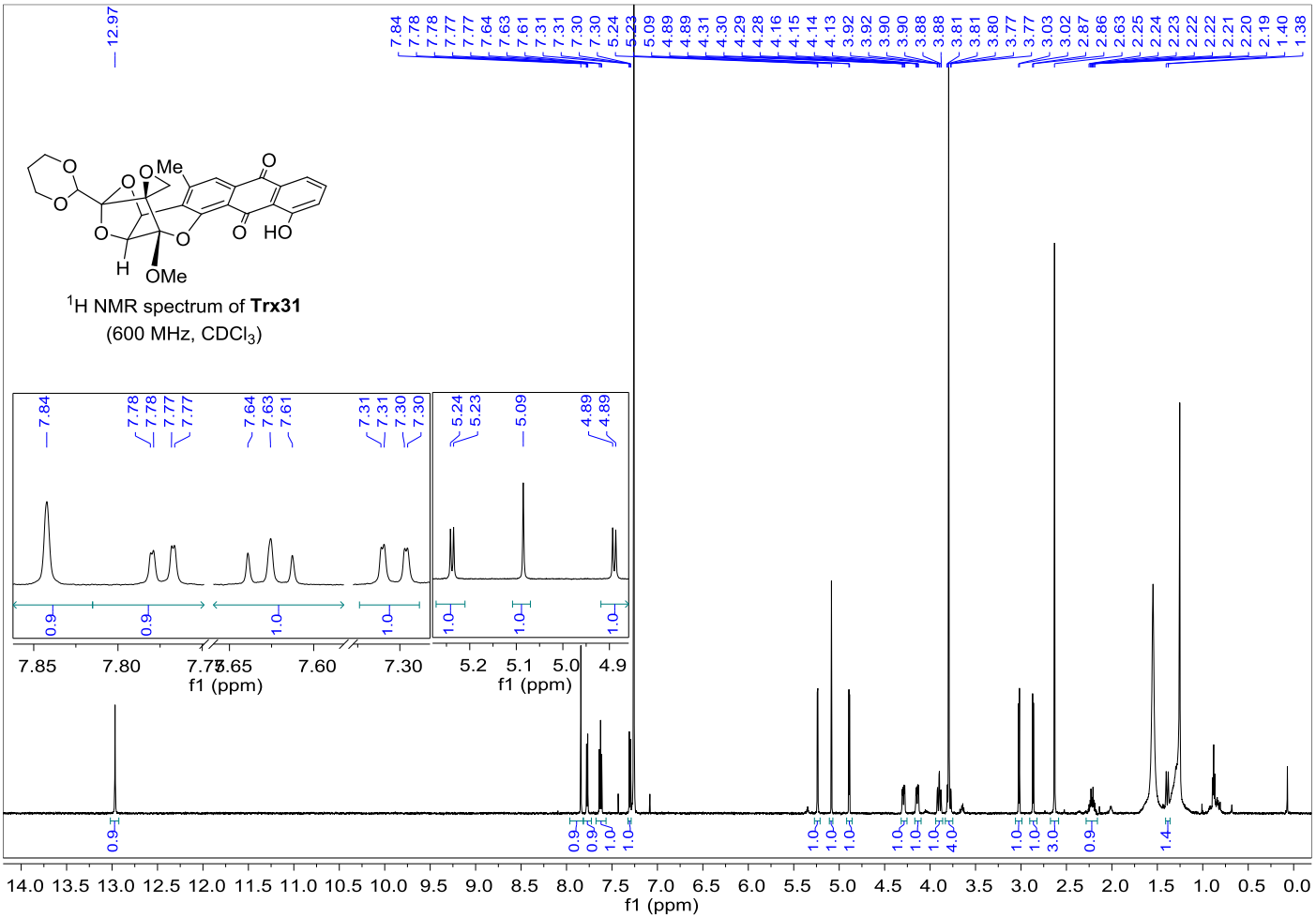
^{13}C NMR spectrum of **Trx29**
(151 MHz, $CDCl_3$)

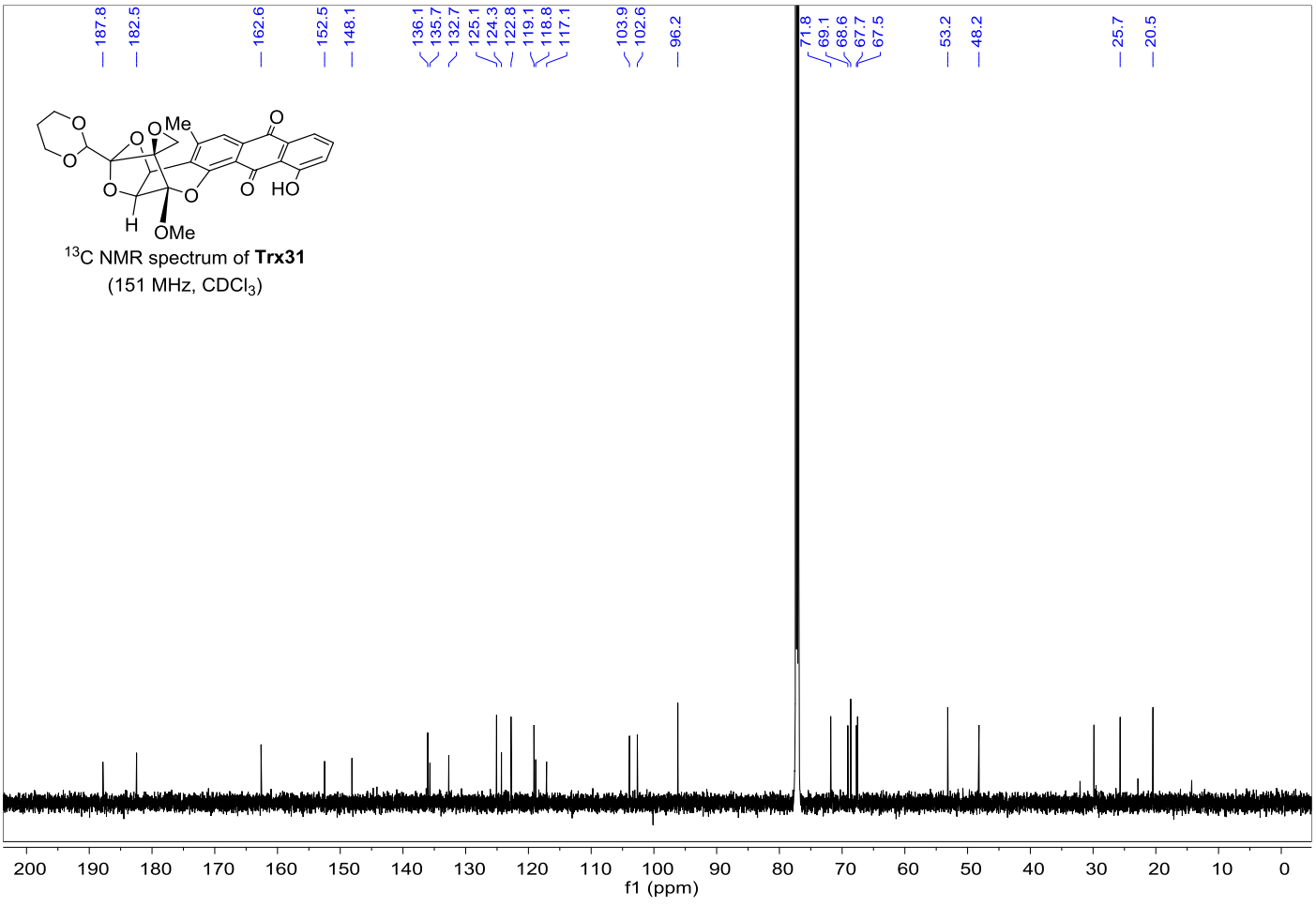


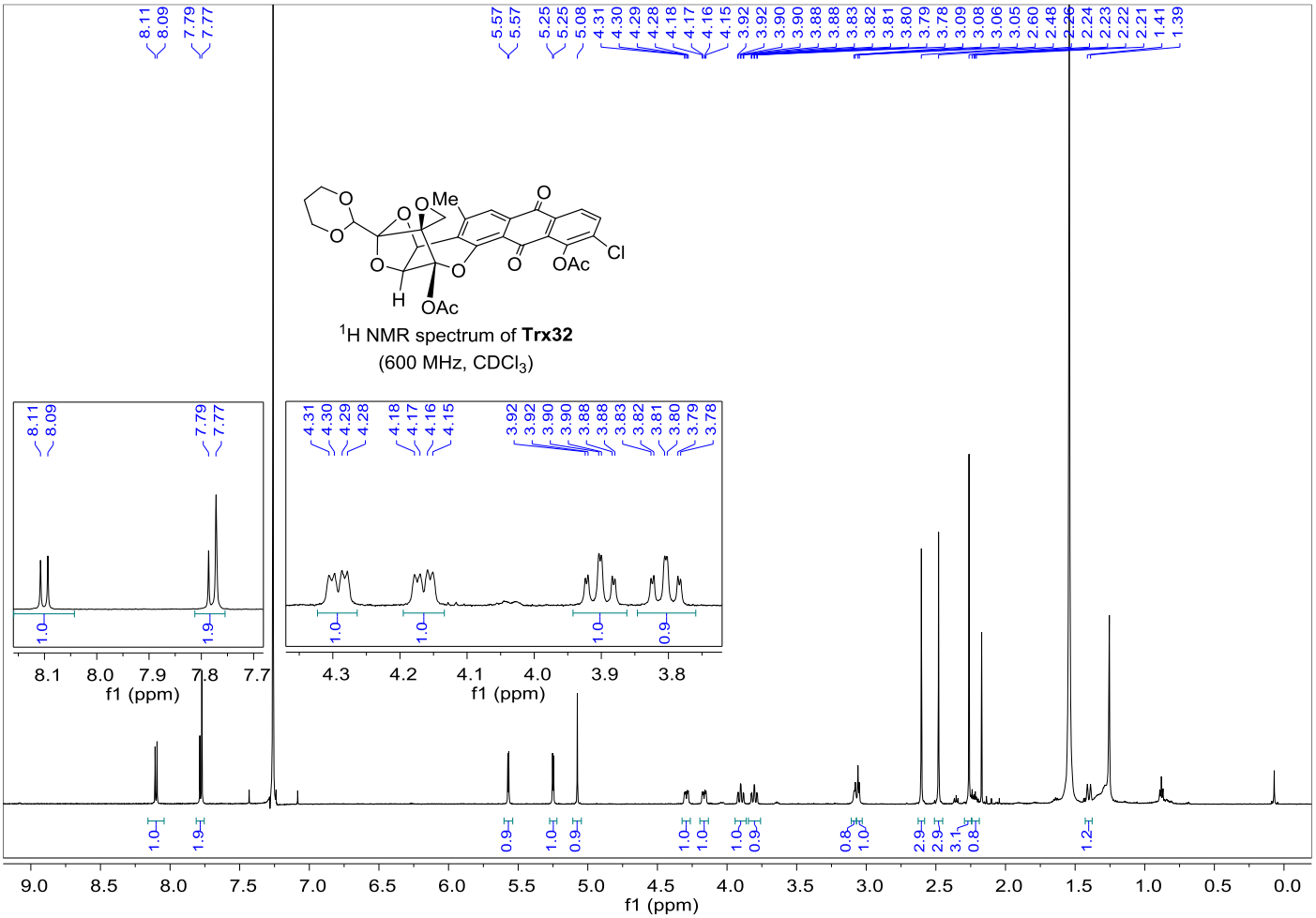
^{1}H NMR spectrum of **Trx30**
(600 MHz, $CDCl_3$)



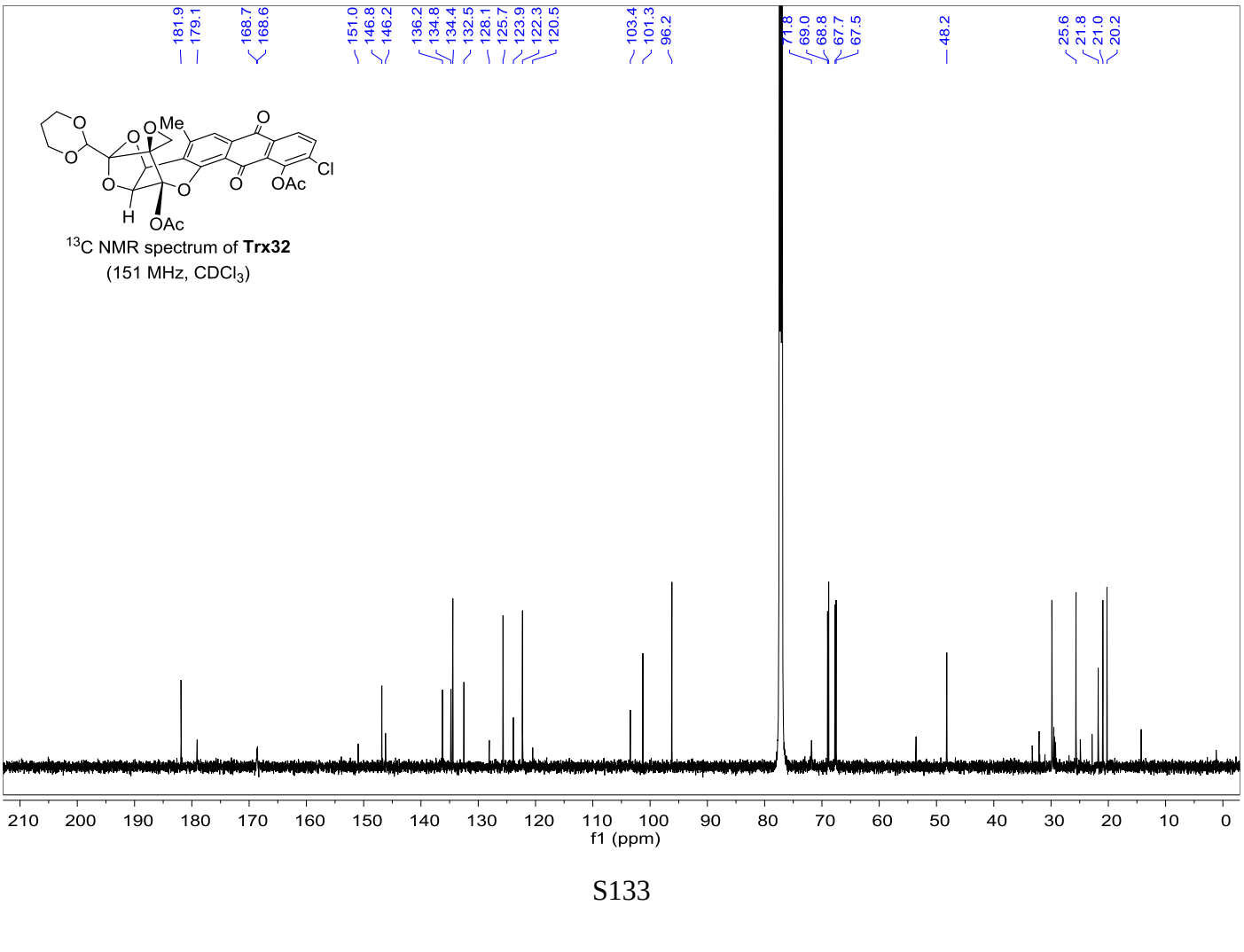
^{13}C NMR spectrum of **Trx30**
(151 MHz, $CDCl_3$)


12.97
7.84 7.78 7.78 7.77 7.77 7.64 7.63 7.61 7.31 7.31 7.30 7.30 5.24 5.23 5.09 4.89 4.89 4.31 4.30 4.29 4.28 4.16 4.15 4.14 4.13 3.92 3.92 3.90 3.90 3.88 3.88 3.81 3.81 3.80 3.77 3.77 3.03 3.02 2.87 2.86 2.63 2.25 2.24 2.23 2.22 2.22 2.21 2.20 2.19 1.40 1.38
O Me O O O O O HO H OMe
1H NMR spectrum of Trx31
(600 MHz, CDCl3)
f1 (ppm)
f1 (ppm)
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

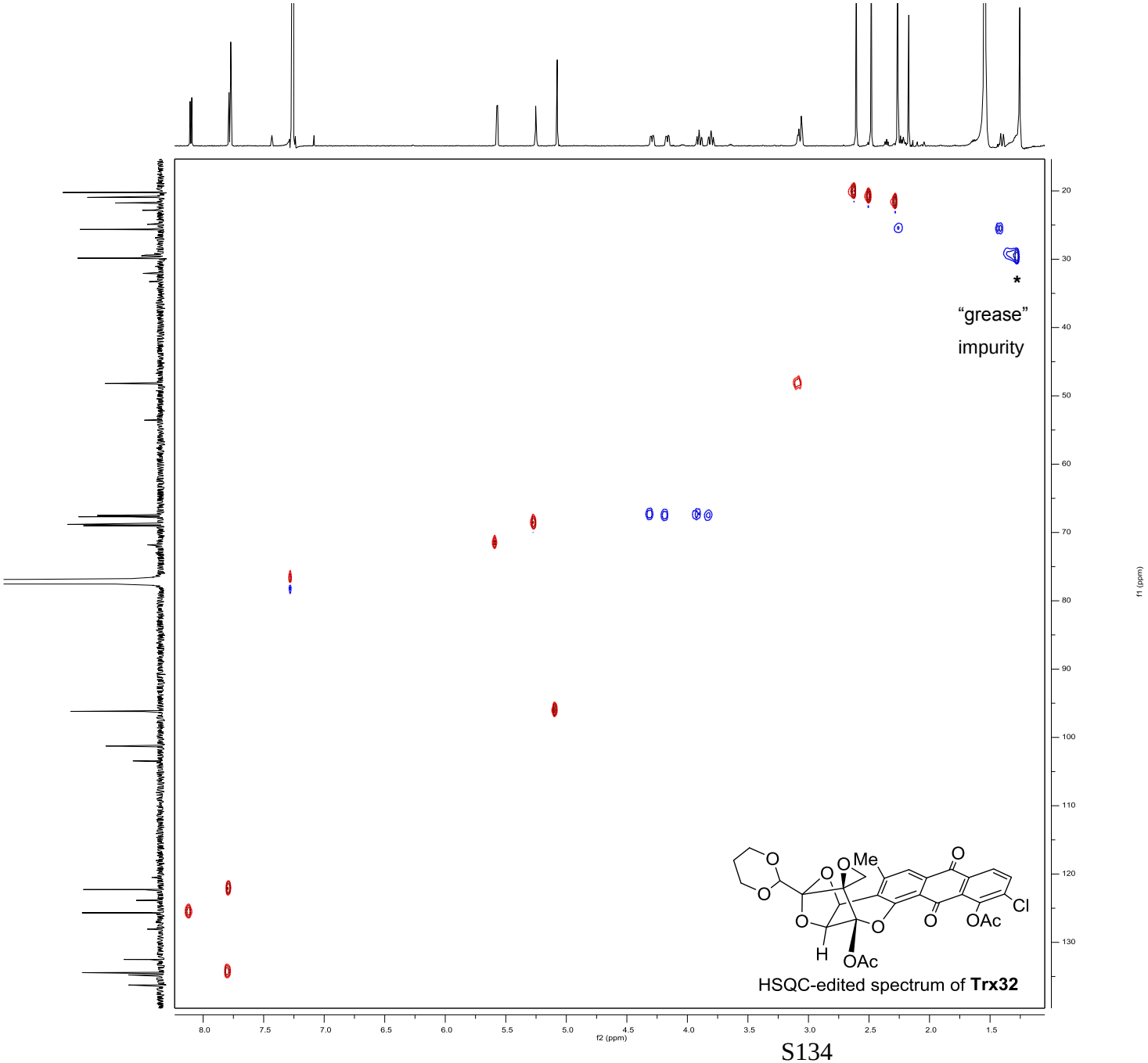

187.8 182.5 162.6 152.5 148.1 136.1 135.7 132.7 125.1 124.3 122.8 119.1 118.8 117.1 103.9 102.6 96.2 71.8 69.1 68.6 67.7 67.5 53.2 48.2 25.7 20.5
O Me O O O O O HO H OMe
13C NMR spectrum of Trx31
(151 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



^{1}H NMR spectrum of **Trx32**
(600 MHz, $CDCl_3$)

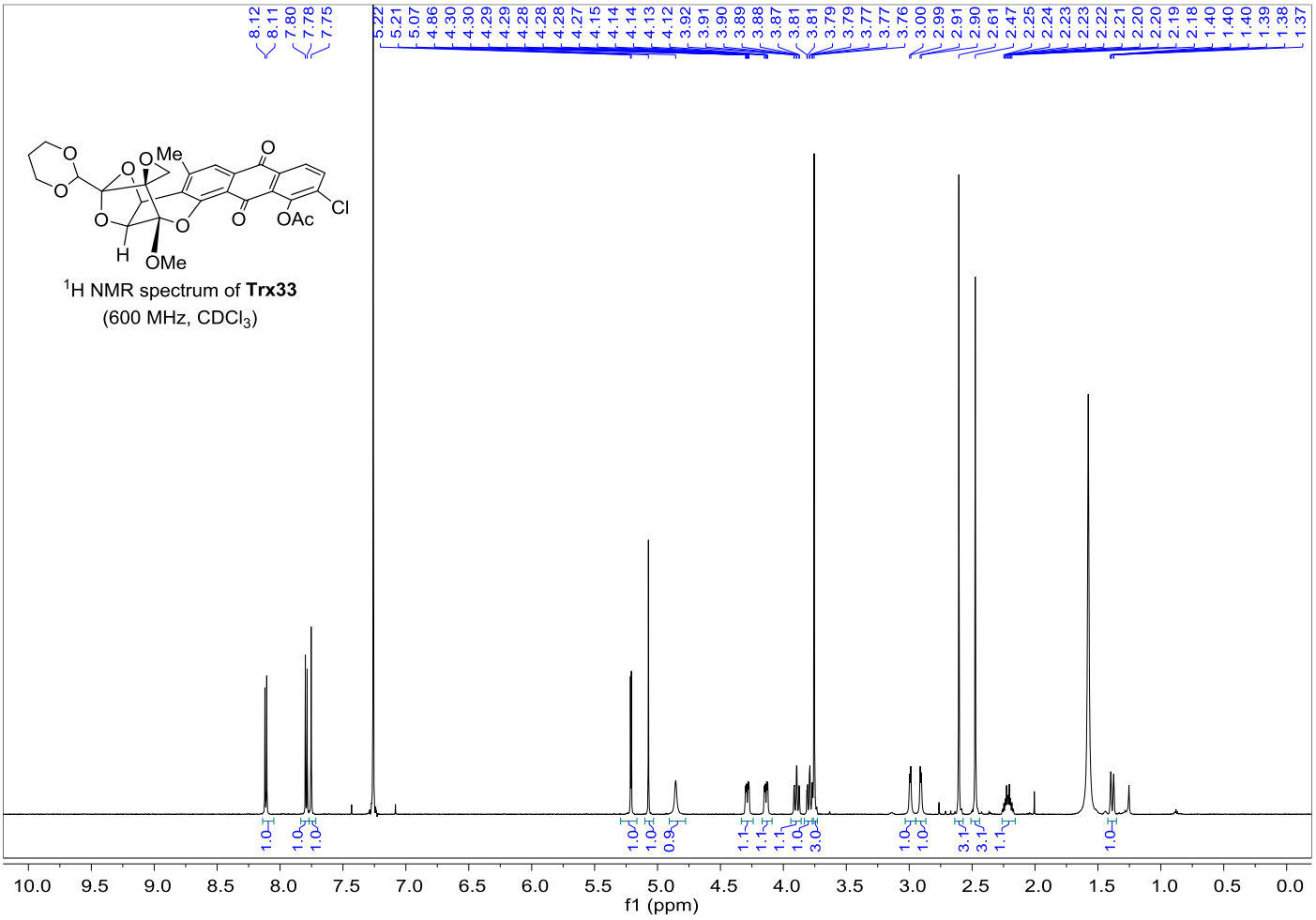


^{13}C NMR spectrum of **Trx32**
(151 MHz, $CDCl_3$)

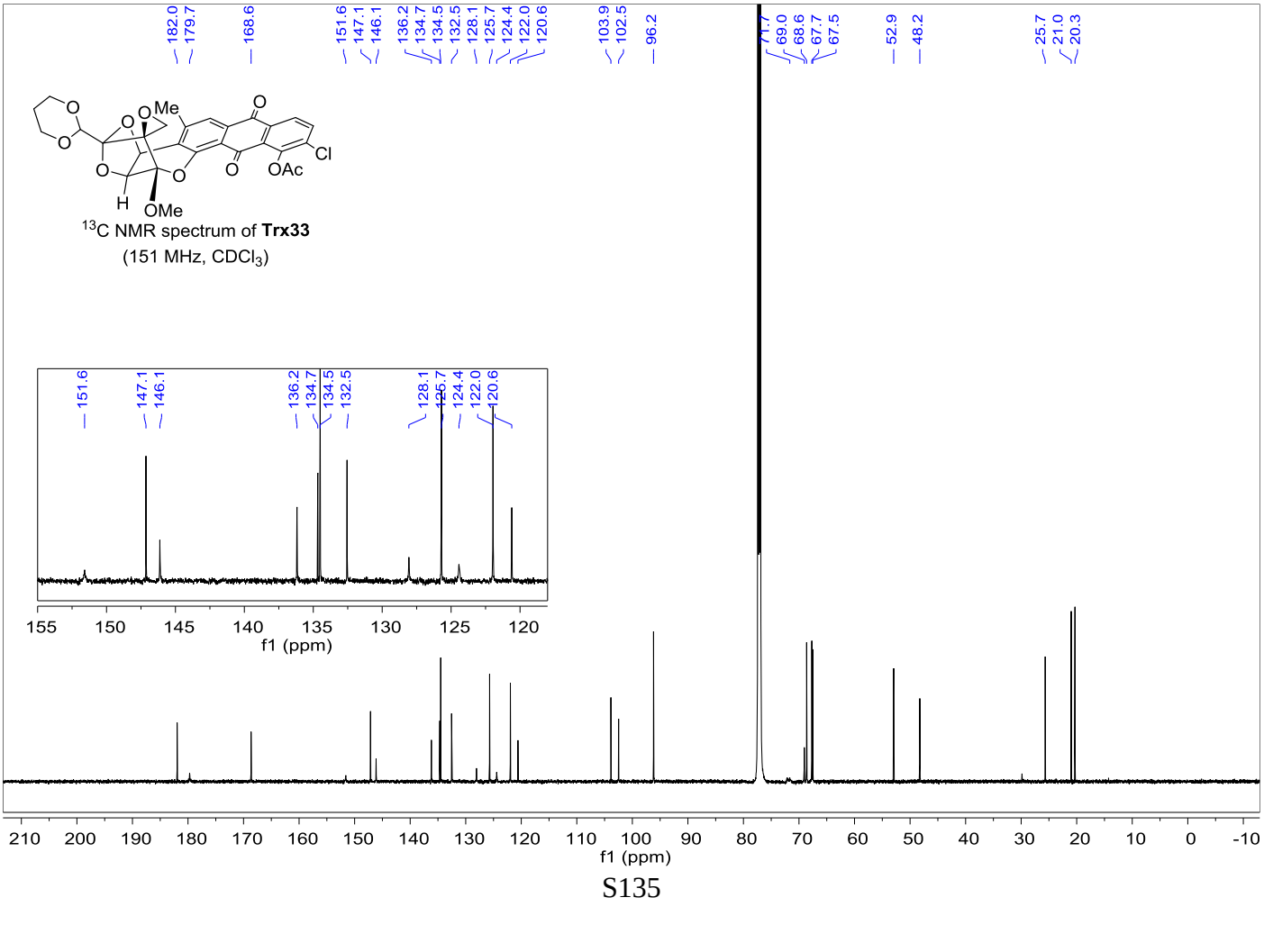


HSQC-edited spectrum of **Trx32**

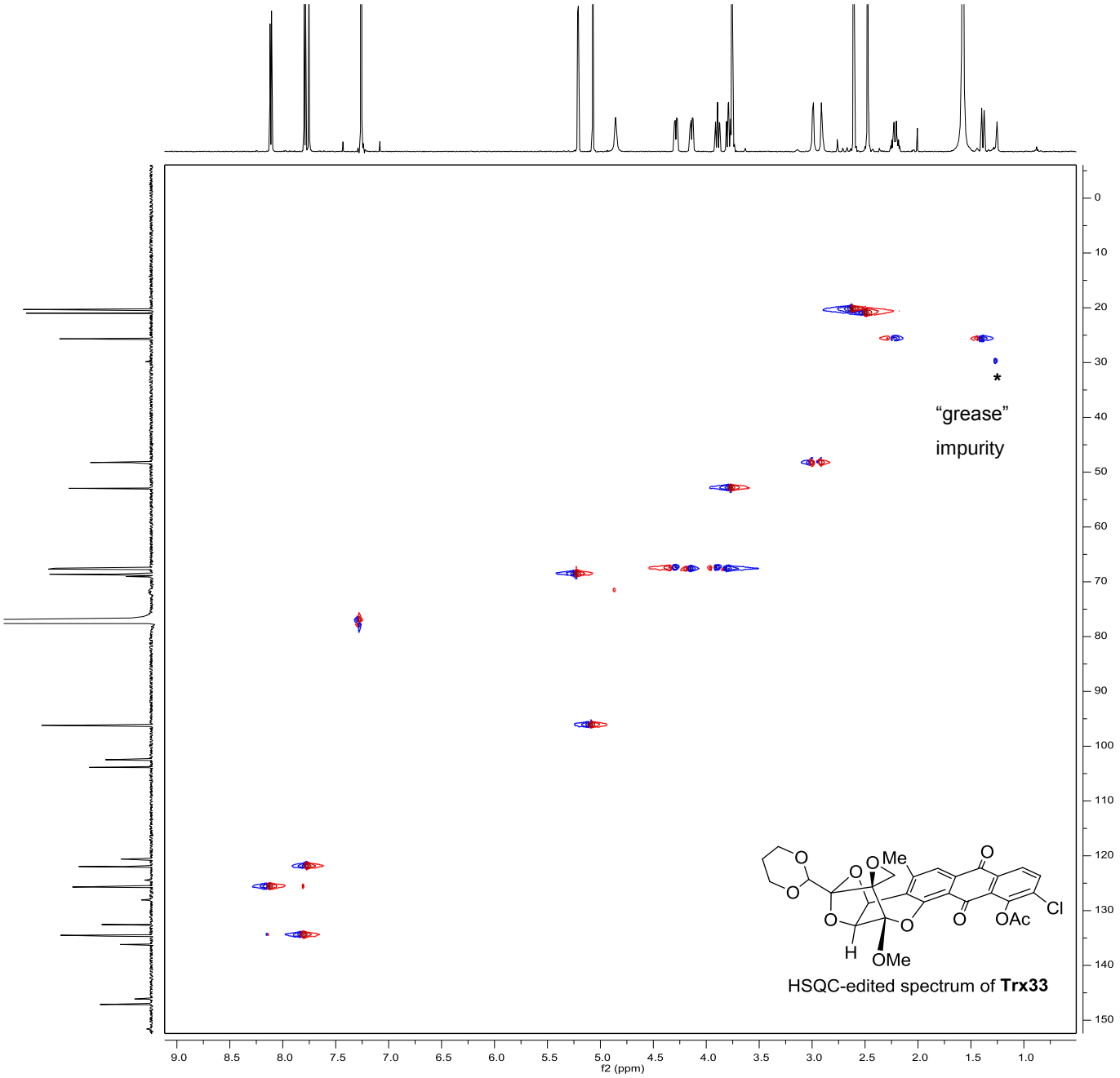
Parameter	Value
Origin	Bruker BioSpin GmbH
Temperature	300.0
Pulse Sequence	hsqcedetgpsisp2.3
Number of Scans	16
Receiver Gain	186.1
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	0.1420
Spectrometer Frequency	(600.18, 150.93)
Spectral Width	(7211.5, 24875.6)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)
cnst2	**145**
d21	**0.00360000**
d24	**0.00089000**



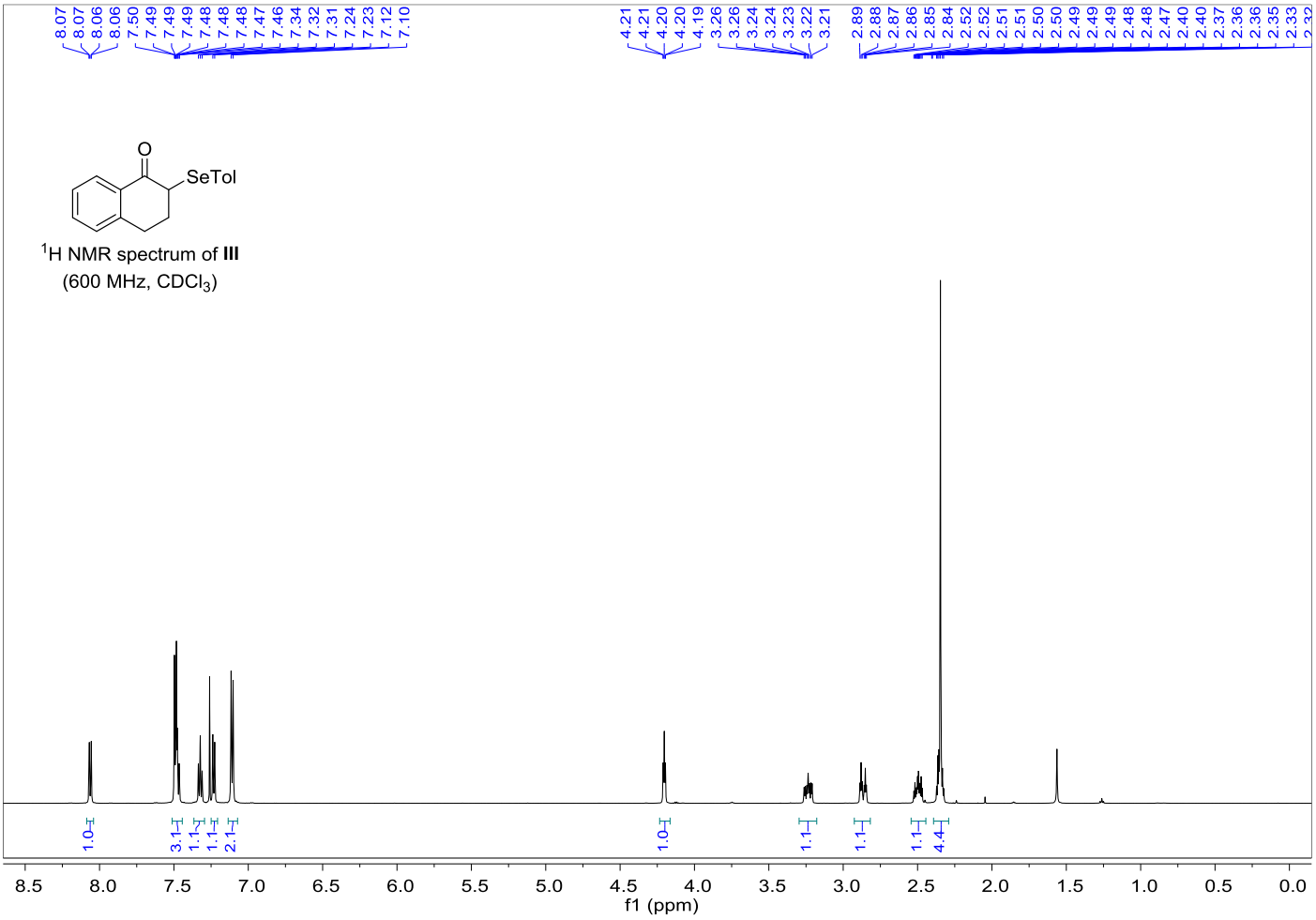
^{1}H NMR spectrum of **Trx33**
(600 MHz, $CDCl_3$)



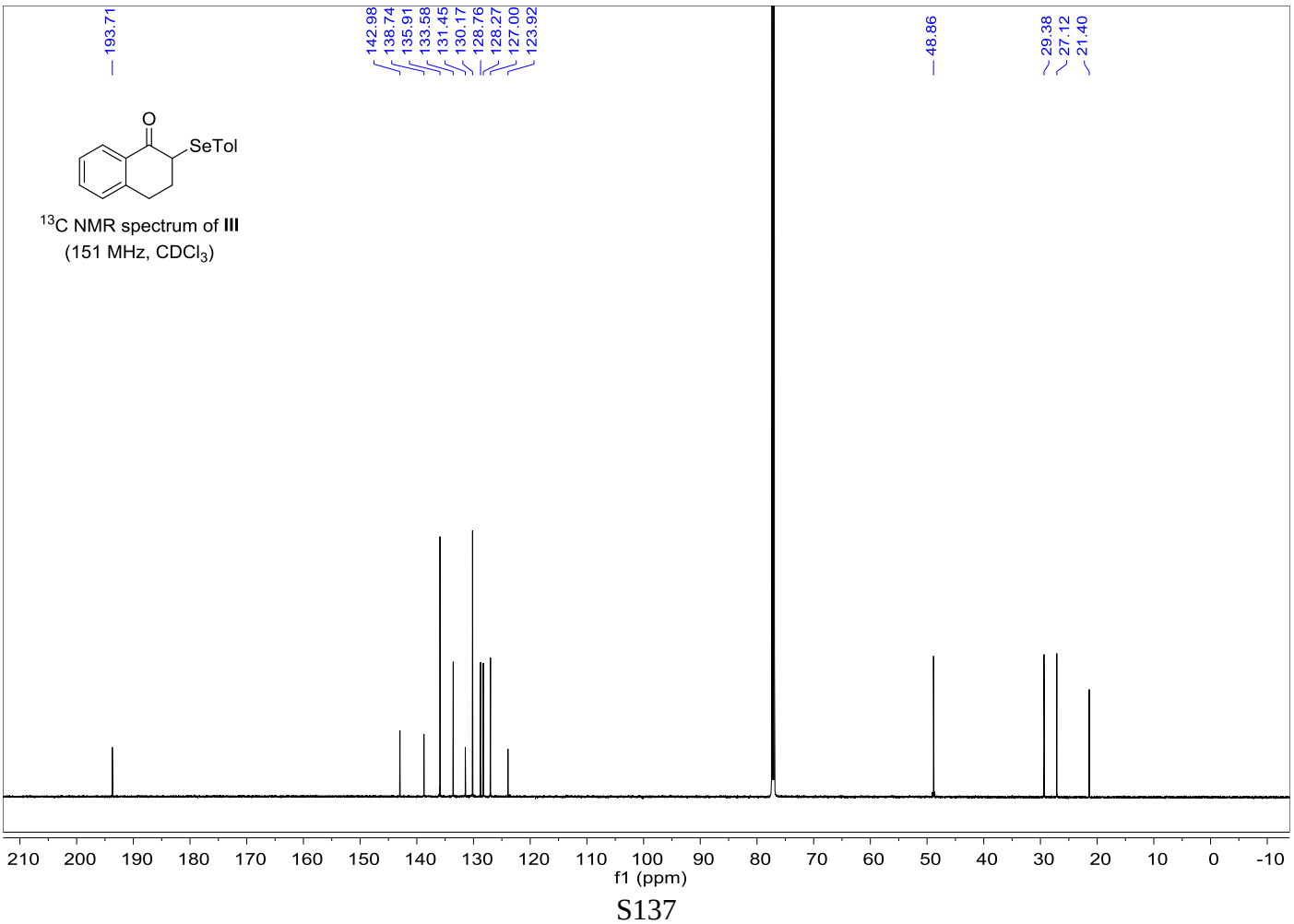
^{13}C NMR spectrum of **Trx33**
(151 MHz, $CDCl_3$)



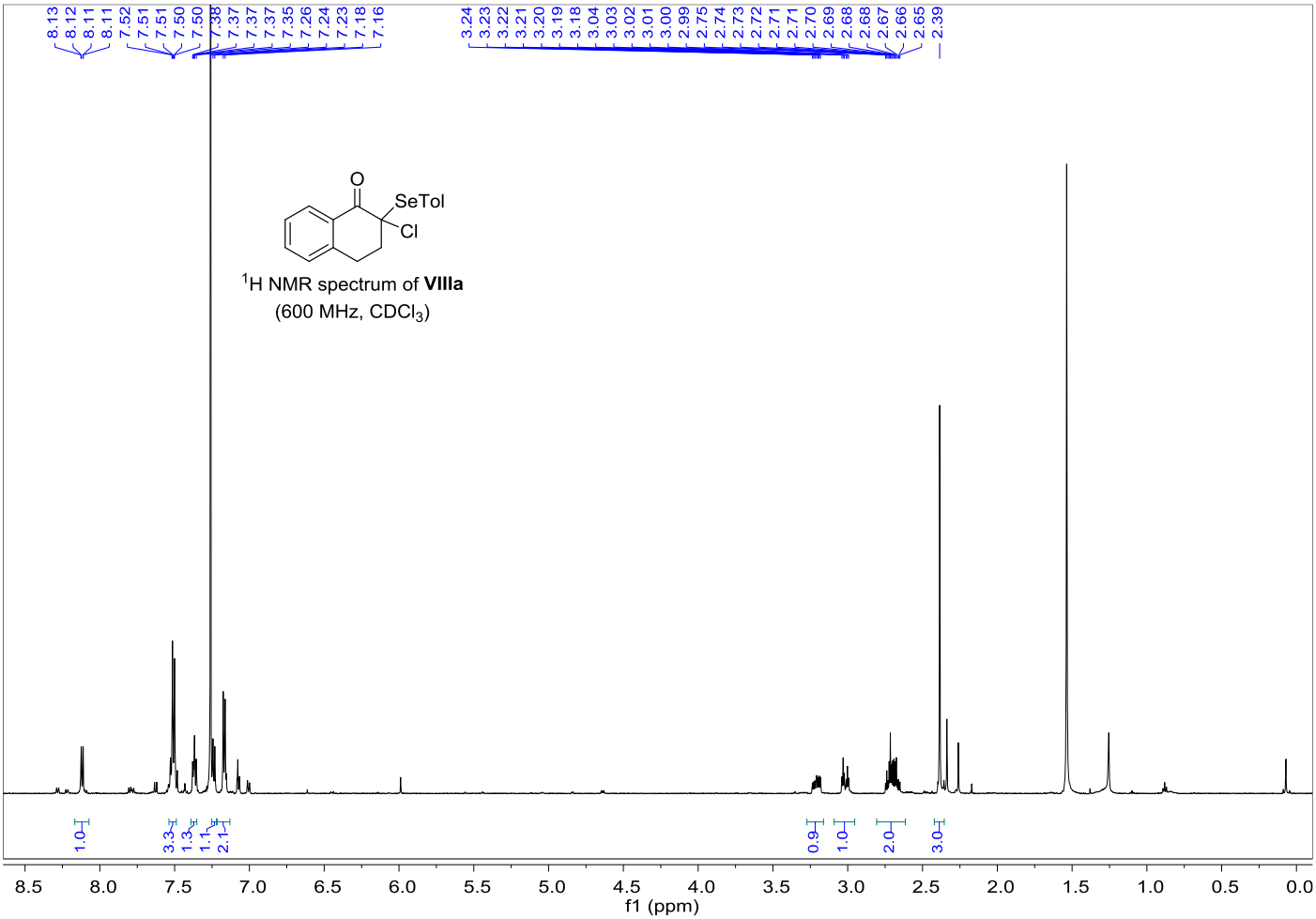
Parameter	Value
Origin	Bruker BioSpin GmbH
Temperature	300.0
Pulse Sequence	hsqcedetgpsisp2.3
Number of Scans	16
Receiver Gain	186.1
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	0.1420
Spectrometer Frequency	(600.18, 150.92)
Spectral Width	(7211.5, 24875.6)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)
cnst2	**145**
d21	**0.00360000**
d24	**0.00089000**



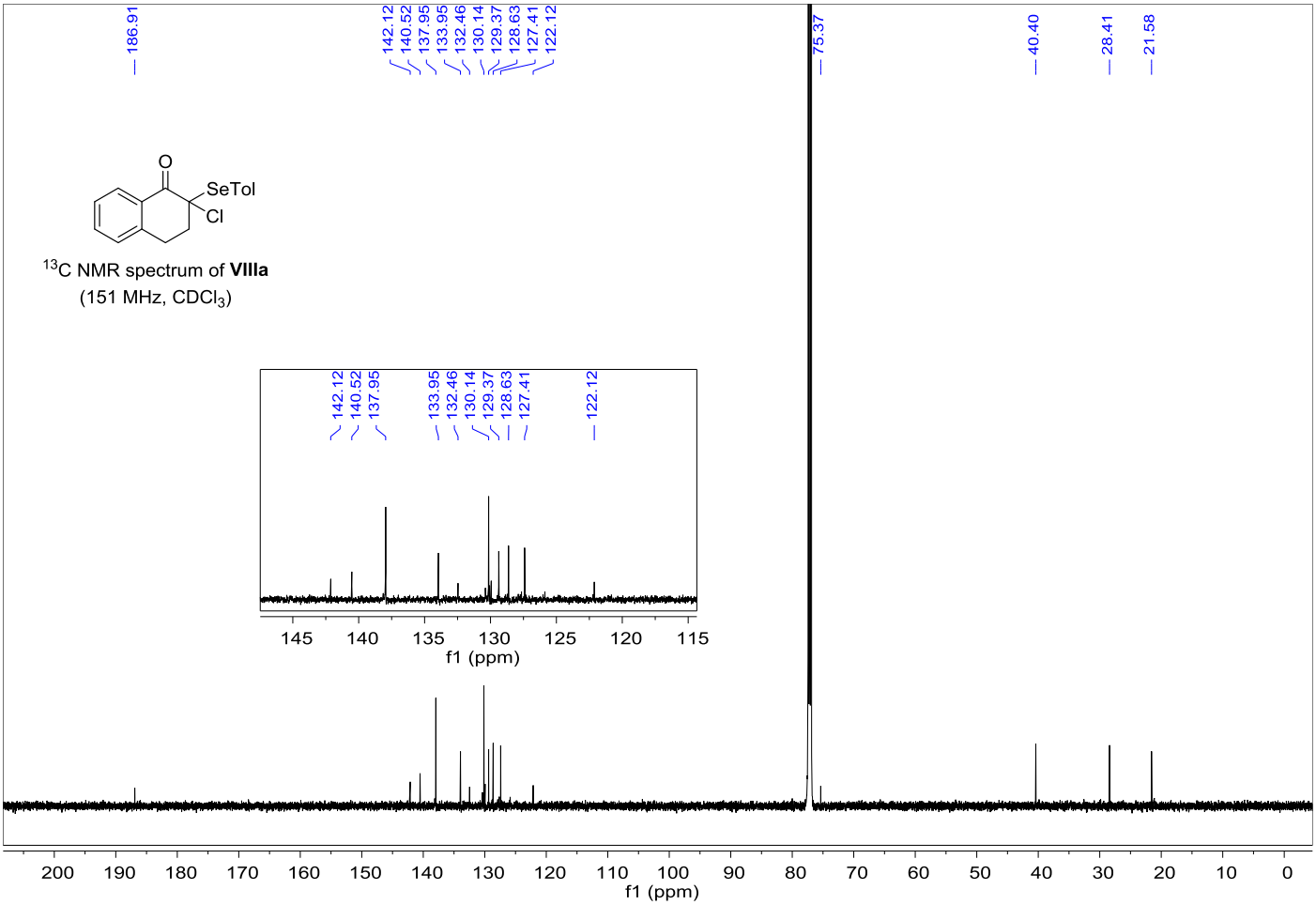
^{1}H NMR spectrum of **III**
(600 MHz, $CDCl_3$)



^{13}C NMR spectrum of **III**
(151 MHz, $CDCl_3$)



^{1}H NMR spectrum of **VIIIa**
(600 MHz, $CDCl_3$)



^{13}C NMR spectrum of **VIIIa**
(151 MHz, $CDCl_3$)

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