Supporting Information

Targeted Covalent Inhibition of Telomerase

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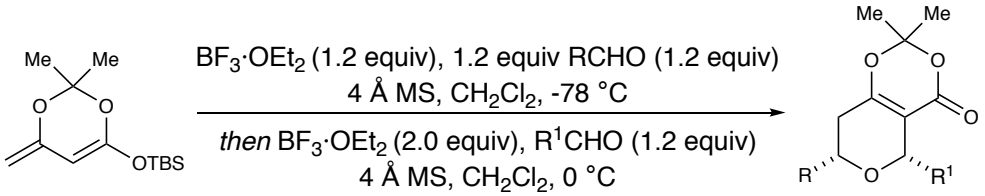
Table of Contents

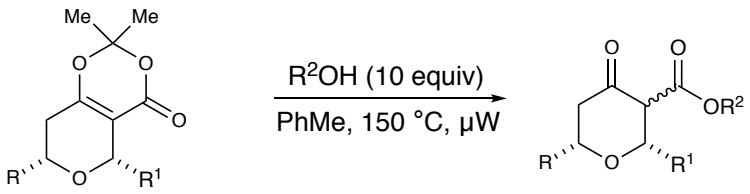
General Information for Chemistry

All reactions were carried out under an argon or nitrogen atmosphere in flame-dried glassware with magnetic stirring. Solvents used in reactions were purified by passage through a bed of activated alumina. Unless stated otherwise, reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Purification of reaction products was carried out by flash chromatography on Biotage Isolera 4 systems with Ultra-grade silica cartridges. Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light. Infrared spectra were recorded on a Bruker Tensor 37 FT-IR spectrometer. ^{1}H NMR spectra were recorded on an AVANCE III 500 MHz spectrometer with direct cryoprobe (500 MHz) and Bruker Avance III 600 MHz (151 MHz) system. Spectra are reported in ppm using solvent as an internal standard ($CHCl_3$ at 7.26 ppm). Peak multiplicities are reported as (s = singlet, d = doublet, t = triplet, q = quartet, quint= quintet, m = multiplet, br= broad; coupling constant(s) in Hz; integration.) Proton-decoupled ^{13}C NMR spectra were recorded on an AVANCE III 500 MHz with direct cryoprobe (125 MHz) spectrometer or Bruker Avance III 600 MHz (151 MHz) system. These are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). Low-resolution mass spectra were obtained on WATERS Acquity-H UPLC-MS with a single quad detector (ESI) Varian1200 Quadrupole Mass Spectrometer. High-resolution mass spectra were obtained using an Agilent 6120A LC-time of flight mass spectrometer. Gas chromatography experiments were run on Agilent 7890A/5975C GC/MS System.

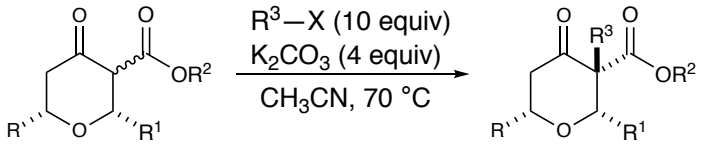
General Procedure for Synthesis of Racemic Analogues



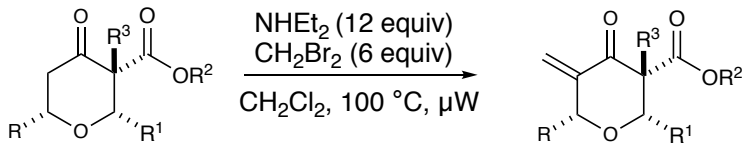
tert-butyl((2,2-dimethyl-4-methylene-4*H*-1,3-dioxin-6-yl)oxy)dimethylsilane (1.0 equiv) and the desired aldehyde (1.2 equiv) were added to a 20 mL oven dried scintillation vial equipped with a magnetic stir bar. 4 Å MS (200 wt% relative to *tert*-butyl((2,2-dimethyl-4-methylene-4*H*-1,3-dioxin-6-yl)oxy)dimethylsilane) was added, and the vial was sealed and placed under inert atmosphere, followed by addition of CH_2Cl_2 (0.2 M). The reaction vial was cooled to -78 °C. BF_3•OEt_2 (1.2 equiv) was added dropwise over a period of 15 minutes. The reaction was monitored by UPLC-MS until complete consumption of *tert*-butyl((2,2-dimethyl-4-methylene-4*H*-1,3-dioxin-6-yl)oxy)dimethylsilane was observed (typically 2–4 hours). When consumption was complete, the reaction was warmed to 0 °C. Subsequently, the second aldehyde (1.2 equiv) was added by syringe, followed by BF_3•OEt_2 (2.0 equiv). The reaction was stirred at 0 °C, and the reaction progress was monitored by UPLC-MS until complete consumption of the β-hydroxydioxinone was observed. Upon complete consumption, 0.1 M potassium phosphate buffer (pH 7.0) was added by syringe and the reaction was warmed to room temperature. The reaction mixture was diluted with CH_2Cl_2 and the suspension was then filtered through a Biotage Isolute phase separator and then concentrated. Typically, reactions were of sufficient purity for the subsequent reaction.



To a microwave vial equipped with a stir bar was added bicyclic dioxinone pyran (1.0 equiv), which was dissolved in toluene (0.2 M). The corresponding alcohol (10 equiv) was added, the microwave vial was capped, and the reaction was heated in a Biotage microwave reactor at 150 °C for 90 min. After the vial was cooled to room temperature, the solution was concentrated, and the crude product was of sufficient purity for the subsequent reaction.

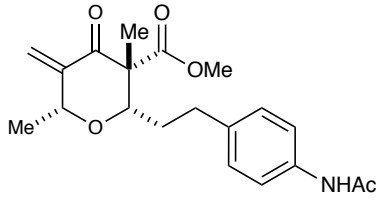


In a microwave vial equipped with a magnetic stir bar was added β-keto ester (1.0 equiv), which was dissolved in acetonitrile (0.2 M). To the solution was added potassium carbonate (4 equiv) and alkyl halide (10 equiv). The reaction mixture was heated to 70 °C, and conversion of the starting material was monitored by UPLC-MS (typically 2-4 hours) before cooling to room temperature. The reaction mixture was diluted with CH_2Cl_2, filtered through a Biotage Isolute phase separator and concentrated to afford the crude product, which was of sufficient purity for the subsequent reaction. When benzyl bromide was used, the concentrated vial was dried under high vacuum at 40 °C overnight to remove residual benzyl bromide.



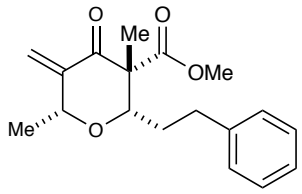
To a microwave vial equipped with a magnetic stir bar was added the alkylated β-keto ester (1.0 equiv), which was dissolved in CH_2Cl_2 (0.5 M). To the solution was added CH_2Br_2 (6 equiv) and Et_2NH (12 equiv). The container was sealed and the reaction heated in a Biotage microwave reactor at 100 °C for 1 hour. After the vial was cooled to room temperature, the reaction solution was concentrated. Diethyl ether was added to the crude reaction mixture to precipitate out the ammonium salts. The mixture was filtered, and the filtrate was concentrated. The crude product was purified by flash chromatography to yield the desired product.

Characterization of Racemic Telomerase Inhibitors



(±) methyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

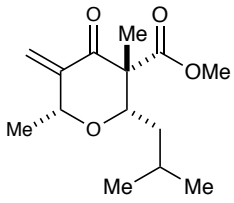
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.30 (m, 2H), 7.13 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.14 (d, *J* = 2.2 Hz, 1H), 5.38 (d, *J* = 2.2 Hz, 1H), 4.50 – 4.41 (m, 1H), 4.09 – 4.02 (m, 1H), 3.62 (s, 3H), 2.63 (dt, *J* = 14.8, 8.4 Hz, 2H), 2.15 (s, 3H), 1.92 – 1.78 (m, 2H), 1.46 (d, *J* = 6.3 Hz, 3H), 1.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 171.2, 168.2, 142.5, 137.9, 129.0, 124.4, 122.7, 119.9, 117.4, 77.9, 74.7, 60.9, 52.4, 32.2, 29.7, 24.8, 20.2, 14.6. LCMS (ESI): Mass calculated for $C_{20}H_{26}NO_5$ $[M+H]^+$: 360.1733, Found 360.1745



(±) methyl (2*S*,3*R*,6*R*)-3,6-dimethyl-5-methylene-4-oxo-2-phenethyltetrahydro-2*H*-pyran-3-carboxylate

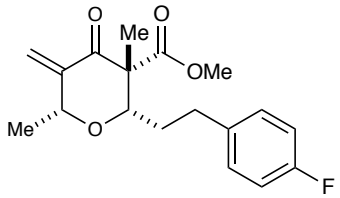
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.30 – 7.13 (m, 5H), 6.14 (d, *J* = 2.1 Hz, 1H), 5.37 (d, *J* = 2.1 Hz, 1H), 3.73 – 3.61 (m, 2H), 3.61 (s, 3H), 2.94 – 2.79 (m, 2H), 2.73 – 2.54 (m, 2H), 1.54 (s, 3H), 1.44 (d, *J* = 2.1 Hz 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.4, 171.1, 144.3,

141.4, 128.5, 128.4, 128.4, 126.0, 122.6, 77.9, 74.7, 60.9, 52.3, 32.2, 32.2, 20.2, 14.5. LCMS (ESI): Mass calculated for $C_{18}H_{23}O_4$ $[M+H]^+$: 303.1518, Found 303.1522



(±) methyl (2*S*,3*R*,6*R*)-2-isobutyl-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

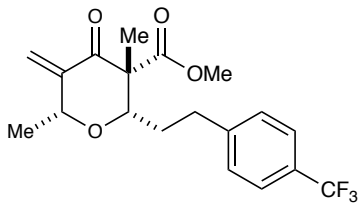
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.15 (d, *J* = 2.3, 0.8 Hz, 1H), 5.37 (d, *J* = 2.2, 0.8 Hz, 1H), 4.52 – 4.44 (m, 1H), 4.19 – 4.13 (m, 1H), 3.70 (s, 3H), 1.89 – 1.50 (m, 3H), 1.43 (d, *J* = 6.3 Hz, 3H), 1.30 (s, 3H), 0.98 – 0.82 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 171.3, 144.4, 122.5, 77.2, 74.6, 61.1, 52.3, 39.6, 25.0, 23.4, 21.7, 20.3, 14.4. LCMS (ESI): Mass calculated for $C_{14}H_{23}O_4$ $[M+H]^+$: 255.1518, Found 255.1522



(±) methyl (2*S*,3*R*,6*R*)-2-(4-fluorophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

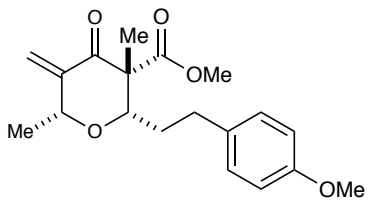
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.34 – 7.20 (m, 3H), 6.93 (d, *J* = 3.8 Hz, 1H), 6.15 (d, *J* = 2.2 Hz, 1H), 5.38 (d, *J* = 2.2 Hz, 1H), 4.48 – 4.39 (m, 1H), 4.04 – 3.94 (m, 1H), 3.63 (s, 3H), 2.87 (dq, *J* = 13.0, 7.3, 5.4 Hz, 2H), 1.94 – 1.83 (m, 2H), 1.46 (d, *J* = 6.2 Hz, 3H), 1.32

(s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.1, 162.9 (d, J = 248 Hz), 144.1, 130.0 (d, J = 3.2 Hz), 124.8, 124.6 (d, J = 8.2 Hz) 122.8, 115.2 (d, J = 21.5 Hz), 77.7, 74.7, 67.1, 52.4, 32.0, 31.9, 20.2, 14.5. LCMS (ESI): Mass calculated for $C_{18}H_{22}FO_4$ $[M+H]^+$: 321.1424, Found 321.1430



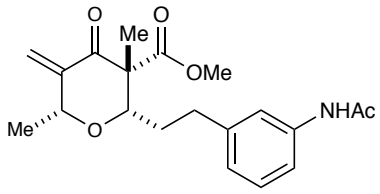
(±) methyl (2*S*,3*R*,6*R*)-3,6-dimethyl-5-methylene-4-oxo-2-(4-(trifluoromethyl)phenethyl)tetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 (dd, *J* = 13.9, 5.6 Hz, 2H), 7.33 – 7.20 (m, 2H), 6.15 (d, *J* = 2.2 Hz, 1H), 5.38 (d, *J* = 2.2 Hz, 1H), 4.91 – 4.65 (m, 1H), 4.55 – 4.39 (m, 1H), 3.62 (s, 3H), 2.99 – 2.66 (m, 2H), 2.11 – 1.79 (m, 2H), 1.45 (d, *J* = 6.2 Hz, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 171.1, 145.5, 144.0, 128.8 (q, J = 32.6 Hz), 127.7, 125.4 (q, J = 3.7 Hz), 123.2 (q, J = 3.7 Hz), 100.3, 77.8, 74.8, 60.8, 52.5, 32.1, 29.4, 20.2, 14.5. LCMS (ESI): Mass calculated for $C_{19}H_{22}F_3O_4$ $[M+H]^+$: 371.1392, Found 371.1401



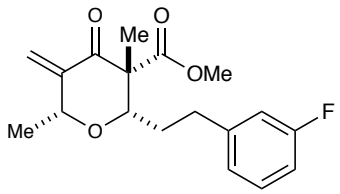
(±) methyl (2*S*,3*R*,6*R*)-2-(4-methoxyphenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.26 – 7.19 (m, 2H), 6.97 – 6.94 (m, 2H), 6.30 (d, *J* = 2.2 Hz, 1H), 5.53 (d, *J* = 2.2 Hz, 1H), 4.64 – 4.55 (m, 1H), 4.19 – 4.10 (m, 1H), 3.92 (s, 3H), 3.78 (s, 3H), 2.74 – 2.68 (m, 2H), 2.07 – 2.01 (m, 2H), 1.62 (d, *J* = 6.3 Hz, 3H), 1.47 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.4, 171.2, 157.8, 144.3, 133.7, 129.3, 129.3, 122.6, 113.8, 77.9, 74.7, 55.3, 52.7, 34.3, 30.0, 20.2, 14.6. LCMS (ESI): Mass calculated for $C_{19}H_{25}O_5$ $[M+H]^+$: 333.1624, Found 333.1609



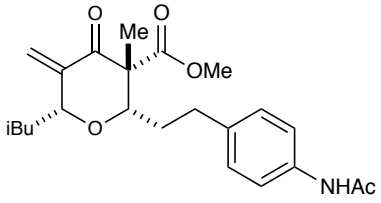
(±) methyl (2*S*,3*R*,6*R*)-2-(3-acetamidophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 2.9 Hz, 2H), 7.19 – 7.15 (m, 1H), 7.11 (d, *J* = 2.4 Hz, 1H), 6.14 (d, *J* = 2.1 Hz, 1H), 5.37 (d, *J* = 2.2 Hz, 1H), 4.43 – 4.38 (m 1H), 4.02 (m, 1H), 3.62 (s, 3H), 2.61 – 2.55 (m, 2H), 2.14 (s, 3H), 1.92 – 1.77 (m, 2H), 1.45 (d, *J* = 6.3 Hz, 3H), 1.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.4, 171.1, 168.2, 144.2, 137.4, 135.9, 135.2, 129.7, 128.9, 122.7, 120.0, 77.8, 74.7, 60.9, 52.4, 32.1, 31.5, 24.6, 20.3, 14.5. LCMS (ESI): Mass calculated for $C_{20}H_{26}NO_5$ $[M+H]^+$: 360.1733, Found 360.1745



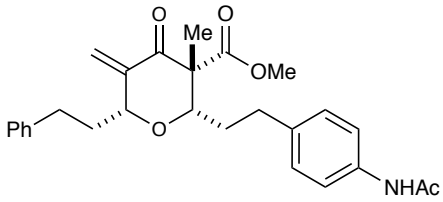
(±) methyl (2*S*,3*R*,6*R*)-2-(3-fluorophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.17 – 7.03 (m, 2H), 6.95 – 6.86 (m, 2H), 6.15 (d, *J* = 2.3 Hz, 1H), 5.38 (d, *J* = 2.3 Hz, 1H), 4.32 (t, *J* = 5.7 Hz, 1H), 4.02 – 3.92 (m, 1H), 3.63 (s, 3H), 2.81 – 2.63 (m, 2H), 2.05 – 1.91 (m, 2H), 1.46 (d, *J* = 6.3 Hz, 3H), 1.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 171.1, 160.4, 144.2, 137.0, 129.7 (d, J = 3.2 Hz), 122.7, 115.2 (d, J = 21.5 Hz), 103.6, 100.5, 77.8, 74.7, 60.9, 52.8, 35.8, 32.3, 20.2, 14.5. LCMS (ESI): Mass calculated for $C_{18}H_{22}FO_4$ $[M+H]^+$: 321.1424, Found 321.1432



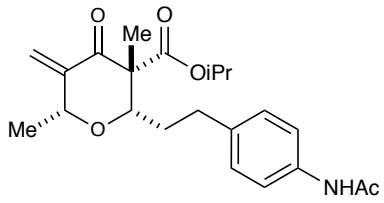
(±) methyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-6-isobutyl-3-methyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.24 (d, *J* = 3.4 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 2H), 6.14 (d, *J* = 2.1 Hz, 1H), 5.37 (d, *J* = 2.1 Hz, 1H), 3.77 – 3.71 (m, 1H), 3.56 – 3.51 (m, 1H), 3.49 (s, 3H), 2.26 – 2.06 (m, 2H), 1.97 (s, 3H), 1.79 – 1.65 (m, 2H), 1.55 – 1.44 (m, 2H), 1.17 (s, 3H), 1.07 – 0.99 (m, 1H), 0.82 – 0.69 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.6, 171.4, 168.3, 144.2, 137.3, 136.0, 128.9, 120.0, 79.3, 75.3, 62.4, 52.2, 45.4, 32.3, 31.7, 24.5, 24.4, 23.3, 22.0, 14.3. LCMS (ESI): Mass calculated for $C_{23}H_{32}NO_5$ $[M+H]^+$: 402.2202, Found 402.2210



(±) methyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3-methyl-5-methylene-4-oxo-6-phenethyltetrahydro-2*H*-pyran-3-carboxylate

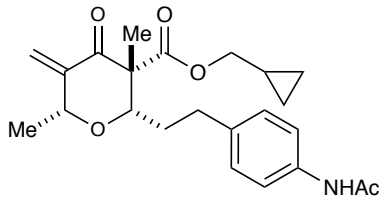
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.54 – 7.48 (m, 2H), 7.37 – 7.28 (m, 2H), 7.26 – 7.19 (m, 3H), 7.14 – 7.09 (m, 2H), 6.14 (d, *J* = 2.1 Hz, 1H), 5.37 (d, *J* = 2.1 Hz, 1H), 3.75 – 3.67 (m, 1H), 3.67 (s, 3H), 3.22 – 3.18 (m, 1H), 2.98 – 2.90 (m, 1H), 2.83 – 2.73 (m, 1H), 2.73 – 2.62 (m, 1H), 2.61 – 2.57 (m, 2H), 2.50 – 2.27 (m, 2H), 2.16 (s, 3H), 2.09 – 1.90 (m, 2H), 1.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.3, 171.3, 168.9, 162.6, 141.2, 136.7, 128.7, 128.5, 128.4, 126.0, 120.0, 79.2, 75.9, 62.3, 52.1, 46.8, 43.6, 37.8, 36.5, 31.4, 24.2, 14.2, 8.7. LCMS (ESI): Mass calculated for $C_{27}H_{32}NO_5$ $[M+H]^+$: 449.2202, Found 449.2198



(±) isopropyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

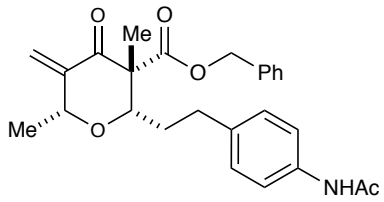
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.35 (m, 2H), 7.08 – 7.00 (m, 2H), 6.12 (d, *J* = 2.1 Hz, 1H), 5.36 (d, *J* = 2.0 Hz, 1H), 4.99 (d, *J* = 6.4 Hz, 1H), 4.43 – 4.33 (m, 1H), 4.04 – 3.98 (m, 1H), 2.89 – 2.55 (m, 2H), 2.15 (s, 3H), 2.06 – 1.84 (m, 2H), 1.46 (d, *J* = 6.2 Hz, 3H), 1.28 (s, 3H), 1.26 – 1.09 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6, 170.1, 168.1, 144.4,

137.4, 135.9, 129.0, 122.4, 120.0, 77.6, 77.2, 74.7, 68.8, 60.7, 31.5, 29.7, 24.7, 21.4, 20.2, 14.5. LCMS (ESI): Mass calculated for $C_{22}H_{30}NO_5$ $[M+H]^+$: 388.2046, Found 388.2044



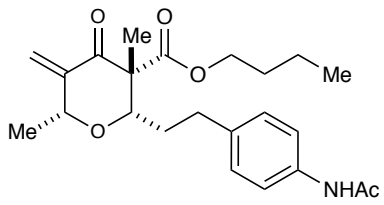
(±) cyclopropylmethyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.24 (m, 2H), 7.10 – 6.99 (m, 2H), 6.14 (d, *J* = 2.1 Hz, 1H), 5.37 (d, *J* = 2.1 Hz, 1H), 4.45 – 4.28 (m, 1H), 4.13 – 4.04 (m, 1H), 4.02 – 3.79 (m, 2H), 2.94 – 2.80 (m, 2H), 2.63 – 2.55 (m, 2H), 2.14 (s, 3H), 1.46 (d, *J* = 6.2 Hz, 3H), 1.31 (s, 3H), 1.06 – 0.95 (m, 1H), 0.56 – 0.43 (m, 2H), 0.29 – 0.15 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 170.8, 168.2, 144.3, 137.4, 129.0, 126.6, 122.6, 120.0, 77.9, 74.7, 69.9, 60.9, 32.1, 31.6, 24.7, 20.2, 14.6, 9.7, 3.3, 3.2. LCMS (ESI): Mass calculated for $C_{23}H_{30}NO_5$ $[M+H]^+$: 400.2046, Found 400.2040



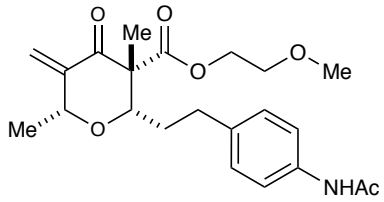
(±) benzyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 4H), 7.10 – 7.05 (m, 1H), 7.04 – 7.01 (m, 1H), 6.98 – 6.90 (m, 3H), 6.14 (d, *J* = 2.1 Hz, 1H), 5.37 (d, *J* = 2.1 Hz, 1H), 5.20 – 5.03 (m, 2H), 4.42 – 4.33 (m, 1H), 4.03 – 3.94 (m, 1H), 2.87 – 2.46 (m, 2H), 2.15 (s, 3H), 1.89 – 1.66 (m, 2H), 1.45 (d, *J* = 6.3 Hz, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 170.5, 168.1, 144.3, 137.3, 135.8, 135.6, 128.9, 128.5, 128.3, 128.2, 122.6, 119.9, 77.9, 74.7, 66.9, 60.9, 32.1, 31.6, 24.6, 20.2, 14.6. LCMS (ESI): Mass calculated for $C_{26}H_{30}NO_5$ $[M+H]^+$: 436.2046, Found 436.2061



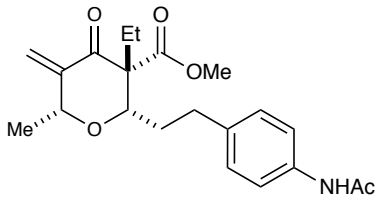
(±) butyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.33 (m, 2H), 7.14 – 7.05 (m, 2H), 6.18 – 6.11 (m, 1H), 5.40 – 5.32 (m, 1H), 4.15 – 3.99 (m, 2H), 2.85 – 2.65 (m, 2H), 2.14 (s, 3H), 1.79 – 1.62 (m, 2H), 1.46 (d, *J* = 6.2 Hz, 3H), 1.38 – 1.20 (m, 4H), 1.27 (d, *J* = 32.3 Hz, 3H), 0.94 – 0.82 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 170.7, 168.1, 144.4, 137.4, 135.9, 129.0, 122.4, 119.9, 77.9, 74.7, 65.2, 60.9, 32.2, 31.6, 30.4, 24.6, 20.3, 19.0, 14.5, 13.7. LCMS (ESI): Mass calculated for $C_{23}H_{32}NO_5$ $[M+H]^+$: 402.2202, Found 402.2185



(±) 2-methoxyethyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

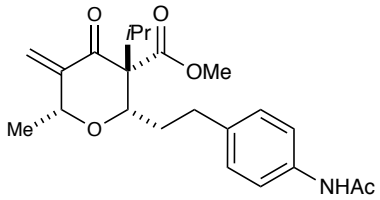
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 3.9 Hz, 2H), 7.17 – 7.05 (m, 2H), 6.14 (d, *J* = 2.1 Hz, 1H), 5.37 (d, *J* = 2.1 Hz, 1H), 4.50 – 4.40 (m, 1H), 4.33 – 4.14 (m, 2H), 4.12-4.08 (m, 1H), 3.58 – 3.44 (m, 2H), 3.29 (s, 3H), 2.90 – 2.80 (m, 1H), 2.73 – 2.55 (m, 2H), 2.14 (s, 3H), 1.89-1.79 (m, 2H), 1.46 (d, *J* = 6.3 Hz, 3H), 1.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.3, 170.6, 168.1, 144.2, 137.5, 135.8, 129.0, 122.6, 120.0, 78.0, 77.2, 74.7, 70.2, 64.0, 60.9, 58.9, 32.1, 31.7, 24.7, 20.2, 14.5. LCMS (ESI): Mass calculated for $C_{22}H_{30}NO_6$ $[M+H]^+$: 404.1995, Found 404.2001



(±) methyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3-ethyl-6-methyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42-7.33 (m, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.17 (d, *J* = 2.2 Hz, 1H), 5.41 (d, *J* = 2.2 Hz, 1H), 4.53 – 4.45 (m, 1H), 4.15 – 4.01 (m, 1H), 3.65 (s, 3H), 2.66 (dt, *J* = 14.8, 8.4 Hz, 2H), 2.18 (s, 3H), 1.99 – 1.84 (m, 2H), 1.49 (d, *J* = 6.3 Hz, 3H), 0.99-0.91 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 171.5,

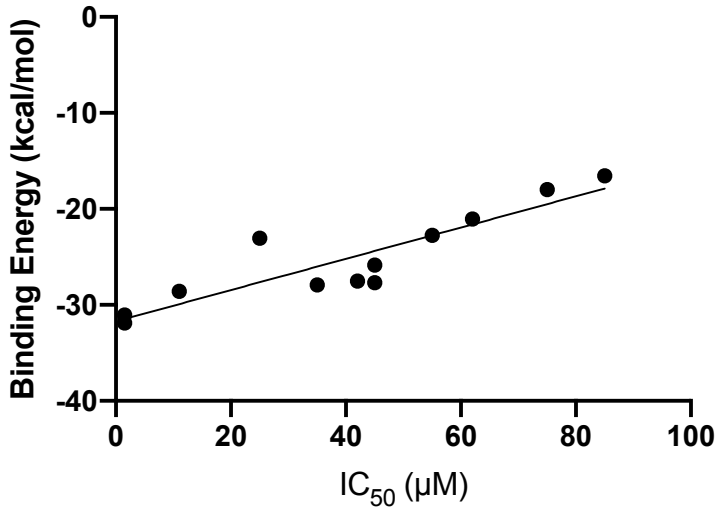
168.5, 142.9, 138.4, 129.5, 124.7, 123.1, 120.3, 117.7, 78.3, 75.0, 61.3, 52.7, 32.6, 30.1, 25.1, 20.6, 14.9, 14.8. LCMS (ESI): Mass calculated for $C_{21}H_{28}NO_5$ $[M+H]^+$: 374.1967, Found 374.1962



(±) methyl (2*S*,3*R*,6*R*)-2-(4-acetamidophenethyl)-3-isopropyl-6-methyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36-7.29 (m, 2H), 7.12 (d, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.13 (d, *J* = 2.2 Hz, 1H), 5.37 (d, *J* = 2.2 Hz, 1H), 4.47 – 4.40 (m, 1H), 4.09 – 43.99 (m, 1H), 3.61 (s, 3H), 2.61 (dt, *J* = 14.8, 8.4 Hz, 2H), 2.14 (s, 3H), 1.92 – 1.80 (m, 2H), 1.45 (d, *J* = 6.3 Hz, 3H), 0.93-0.86 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 171.3, 168.3, 142.7, 138.1, 129.1, 124.5, 122.9, 120.1, 117.6, 78.1, 74.9, 61.1, 52.6, 32.3, 29.9, 24.9, 20.4, 14.8, 14.7. LCMS (ESI): Mass calculated for $C_{22}H_{30}NO_5$ $[M+H]^+$: 388.2123, Found 388.2110

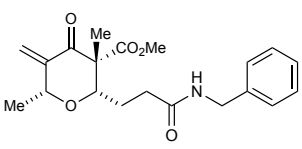
Correlation Analysis Between Binding Energy and IC_{50} Values for 1st Gen Library



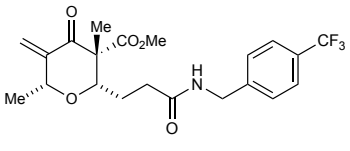
	Binding Energy (kcal/mol)
R square	0.8069

The binding energies and IC_{50} of all compounds in Table 1 and Table 2 that demonstrated the ability to inhibit telomerase activity by TRAP assay <100 μM were analyzed to see if a correlation existed between binding energies and IC_{50}. Linear regression analysis demonstrated that a positive correlation was observed, with an $R^2 = 0.8069$

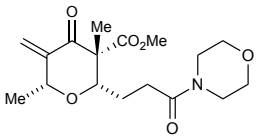
2nd Generation Library Subset



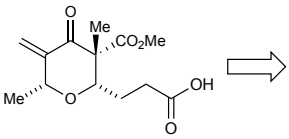
IC_{50} = 7.5 μM

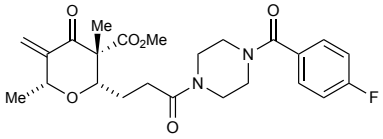


IC_{50} = 1.1 μM

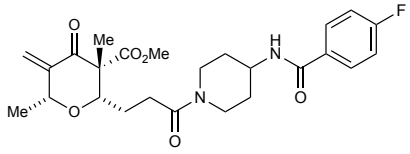


IC_{50} = 20 μM

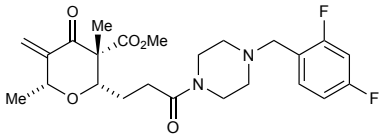




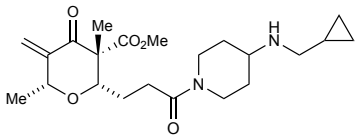
IC_{50} = 900 nM



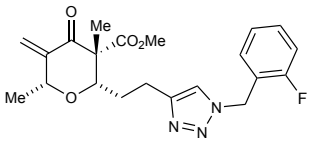
IC_{50} = 650 nM



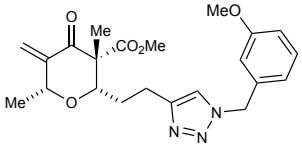
IC_{50} = 500 nM



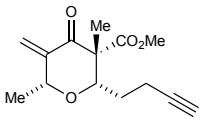
IC_{50} = 2.2 μM

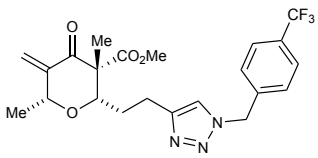


IC_{50} = 300 nM

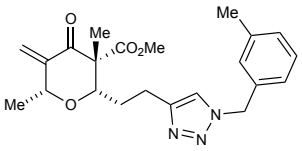


IC_{50} = 475 nM

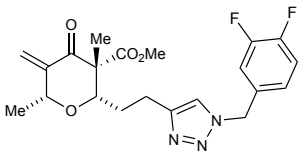




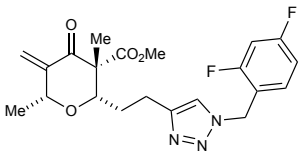
IC_{50} = 220 nM



IC_{50} = 650 nM

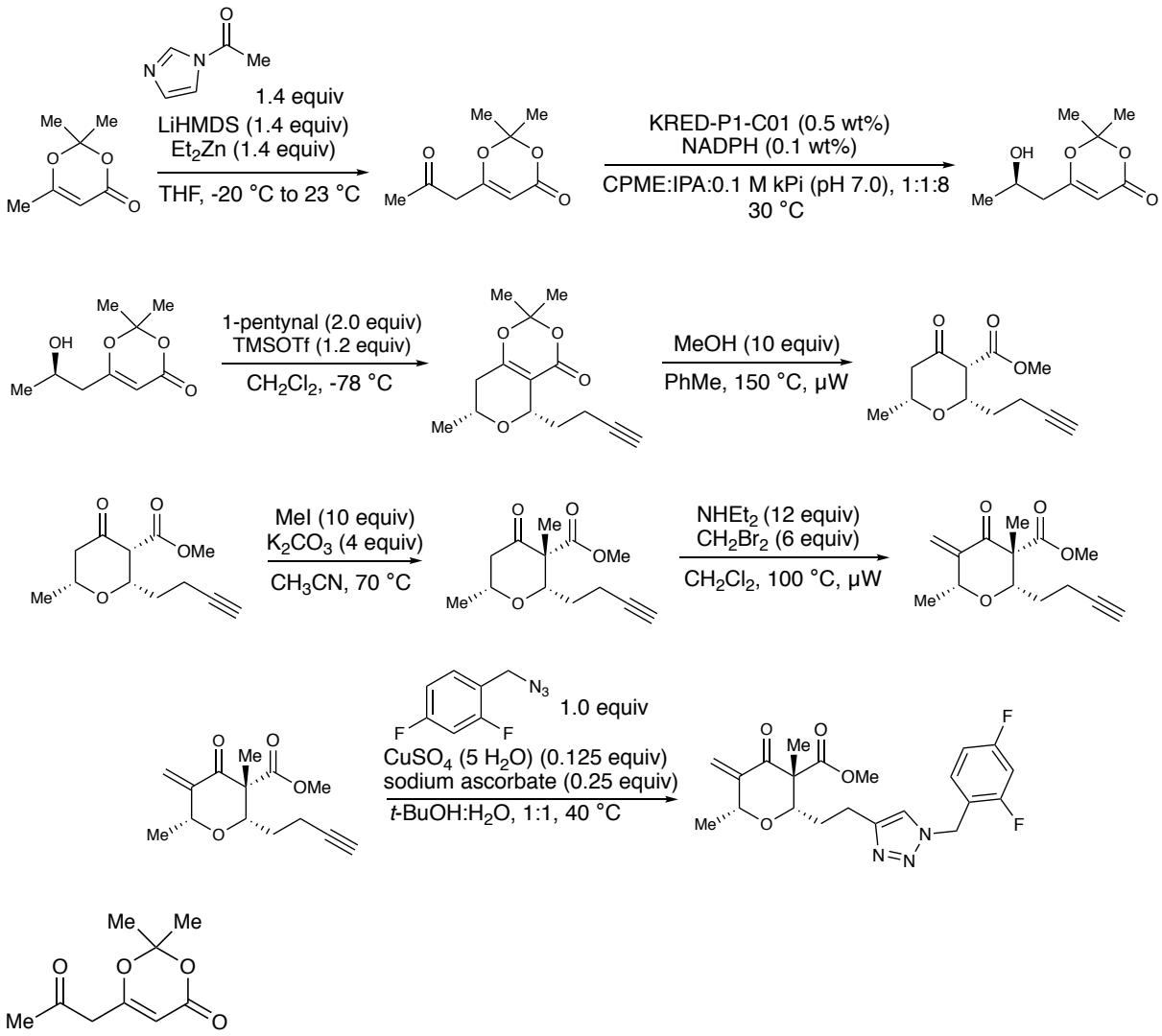


IC_{50} = 165 nM



IC_{50} = 90 nM

Synthesis of NU-1

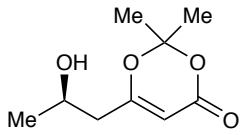


2,2-Dimethyl-6-(2-oxo-2-methylethyl)-4H-1,3-dioxin-4-one (S1)

Prepared according to literature precedent.[2] Dioxinone (1.0 equiv) in THF (2.0 M) was added dropwise to LiHMDS in THF (1.4 equiv, 1.0 M) and THF (1.0 M) at -20 °C, and after 45 min, diethylzinc in hexanes (1.4 equiv, 1.0 M) was added over 2 h. After a further 30 min, the reaction mixture was allowed to warm up to -10 °C and *N*-acetylimidazole (1.4 equiv) was added portionwise over 15 min. After 3.5 h, H_2O:THF (1:9; 75 mL) was added dropwise, followed by 6.0 M HCl (100 mL) and EtOAc (250 mL). The pH was adjusted to pH 1-2 using 1.0 M HCl (265 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (250 mL), and the combined organic extracts were washed with brine (250 mL), dried

($MgSO_4$), rotary evaporated, and chromatographed (hexanes:EtOAc 3:2) to give S1 as pale yellow crystals.

Analytical Data: ^{1}H NMR spectroscopy (500 MHz, $CDCl_3$) δ 5.35 (s, 1H), 3.37 (s, 2H), 2.25, (s, 3H), 1.72 (s, 6H); ^{13}C NMR spectroscopy (125 MHz, $CDCl_3$) δ 200.9, 164.4, 160.7, 107.2, 96.6, 47.9, 30.2, 25.0. All physical data for this product correspond with literature values.[3]

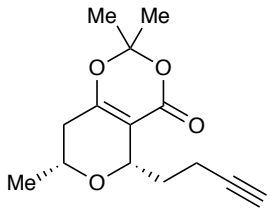


(*R*)-6-(2-hydroxypropyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (S2)

Prepared according to literature precedent.[4] 160 mL of 0.1 M phosphate buffer (pH 7.0) was added to a 500 mL 3 neck round bottom flask equipped with an overhead stirrer, a nitrogen inlet, and a septum. 100 mg of KRED-P01-C01 was then added followed by 50 mg of NADPH. In a separate 100 mL round bottom flask, 20.0 g of S1, 20 mL isopropanol (IPA), and 20 mL cyclopentylmethyl ether (CPME) were added. Upon the β-ketodioxinone substrate completely dissolving (required slight heating and stirring), this solution was added to the solution containing KRED-P01-C01. The reaction was stirred for 72 hours at 30 °C. Upon reaction completion, solid NaCl was added to the reaction mixture. The solution was then filtered, extracted with ethyl acetate (5 x 150 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to obtain >99% pure β-hydroxydioxinone S2

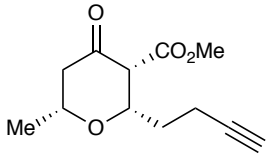
Analytical Data: ^{1}H NMR spectroscopy (500 MHz, $CDCl_3$) δ 5.33 (s, 1H), 4.16-4.08 (m, 1H), 2.38 (1H, d, J = 2.8), 2.37 (s, 1H), 1.70 (s, 6H), 1.27 (3H, d, J = 6.2). ^{13}C NMR spectroscopy (125 MHz, $CDCl_3$) δ 169.3, 161.3, 106.6, 94.9, 65.1, 43.2, 25.2, 24.9, 23.5.

All physical data for this product corresponds with literature values.[3]



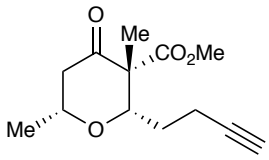
(5S,7R)-5-(but-3-yn-1-yl)-2,2,7-trimethyl-7,8-dihydro-4H,5H-pyrano[4,3-d][1,3]dioxin-4-one (S3)

A flask was charged with 4 Å MS (2:1 by wt), pent-4-ynal (4.0 equiv) and S2 (1.0 equiv). Dichloromethane (0.25 M) was added and the reaction was cooled to –78 °C. Then, TMS-OTf (2.0 equiv) was added dropwise and stirred for 5 h. The reaction was quenched at –78 °C with a 1:1 mixture of NEt_3/MeOH and allowed to warm to room temperature. The suspension was then filtered through a Biotage Isolute phase separator and then concentrated. The crude product was of sufficient purity and immediately used in the next reaction.



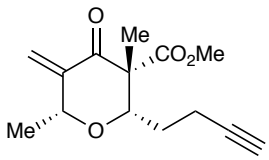
methyl (2S,3R,6R)-2-(but-3-yn-1-yl)-6-methyl-4-oxotetrahydro-2H-pyran-3-carboxylate (S4)

In a microwave vial S3 (1.0 equiv) was dissolved in toluene (0.2 M). Dry methanol (10 equiv) was added, the reaction vial was capped, and the reaction heated in a Biotage microwave reactor at 150 °C for 40 m. After the vial was cooled to room temperature, the solution was concentrated. The crude product was of sufficient purity and was immediately used in the next reaction.



methyl (2*S*,3*R*,6*R*)-2-(but-3-yn-1-yl)-3,6-dimethyl-4-oxotetrahydro-2*H*-pyran-3-carboxylate (S5)

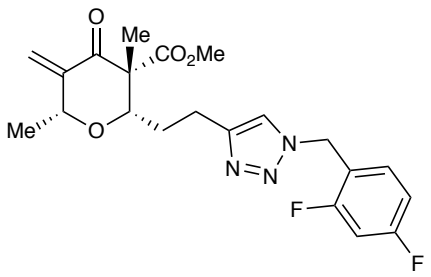
S4 (1.0 equiv) was dissolved in acetonitrile (0.2 M) in a vial with stir bar. To the solution was added potassium carbonate (4 equiv) and methyl iodide (10 equiv). The reaction mixture was heated to 70 °C for 2 hours before cooling to room temperature and quenching with saturated aqueous NH_4Cl. The mixture was diluted with CH_2Cl_2, filtered through a Biotage Isolute phase separator, and concentrated. The crude product was of sufficient purity and immediately used in the next reaction.



methyl (2*S*,3*R*,6*R*)-2-(but-3-yn-1-yl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2*H*-pyran-3-carboxylate (S6)

Prepared according to literature precedent.[5] To a solution of S5 (1.0 equiv) in CH_2Cl_2 (0.2 M) in a microwave vial, CH_2Br_2 (6.0 equiv) and Et_2NH (12.0 equiv) were added. The container was sealed, and the reaction heated in a Biotage microwave reactor at 100 °C for 1 hour. After the vial was cooled to room temperature, the reaction solution was concentrated. Diethyl ether was added to the crude reaction mixture to precipitate out the ammonium salts.

The mixture was filtered, and the filtrate was concentrated. The crude product was of sufficient purity and immediately used in the next reaction.



methyl (2S,3R,6R)-2-(2-(1-(2,4-difluorobenzyl)-1H-1,2,3-triazol-4-yl)ethyl)-3,6-dimethyl-5-methylene-4-oxotetrahydro-2H-pyran-3-carboxylate (NU-1)

1-(Azidomethyl)-2,4-difluorobenzene (1.0 equiv) and S6 (1.0 equiv) were dissolved in t-BuOH (0.2 M) room temperature. To this, a solution of copper (II) sulfate pentahydrate (0.12 equiv) and sodium (R)-2-((S)-1,2-dihydroxyethyl)-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate (0.25 equiv) in water (0.2 M) was added. The reaction mixture was stirred at 40 °C for 5 h. After completion, the reaction mixture was extracted with EtOAc (3 x). The organic layer was dried over sodium sulfate, and the excess solvent was removed under reduced pressure. The crude product was purified by column chromatography to yield NU-1.

^{1}H NMR (500 MHz, Chloroform-d) δ 7.36 – 7.24 (m, 2H), 7.22 – 7.10 (m, 2H), 6.15 (d, *J* = 2.1 Hz, 1H), 5.50 (s, 2H), 5.38 (d, *J* = 2.1 Hz, 1H), 4.45 – 4.24 (m, 1H), 4.05 (dd, *J* = 10.2, 2.0 Hz, 1H), 3.61 (s, 3H), 2.73 – 2.56 (m, 2H), 2.10 – 1.78 (m, 2H), 1.48 – 1.39 (m, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 171.1, 163.5, 160.4, 144.2, 137.0, 136.8, 129.8 (d, J = 3.5 Hz), 125.8, 115.2 (d, J = 21.5 Hz), 103.6, 100.5, 77.8, 77.3, 77.0, 76.8, 74.7, 60.9, 52.8, 35.8, 32.3, 20.2, 14.5. LCMS (ESI): Mass calculated for $C_{21}H_{24}F_2N_3O_4$ [M+H]+ 420.1657, Found 420.1650

Supplemental Figures

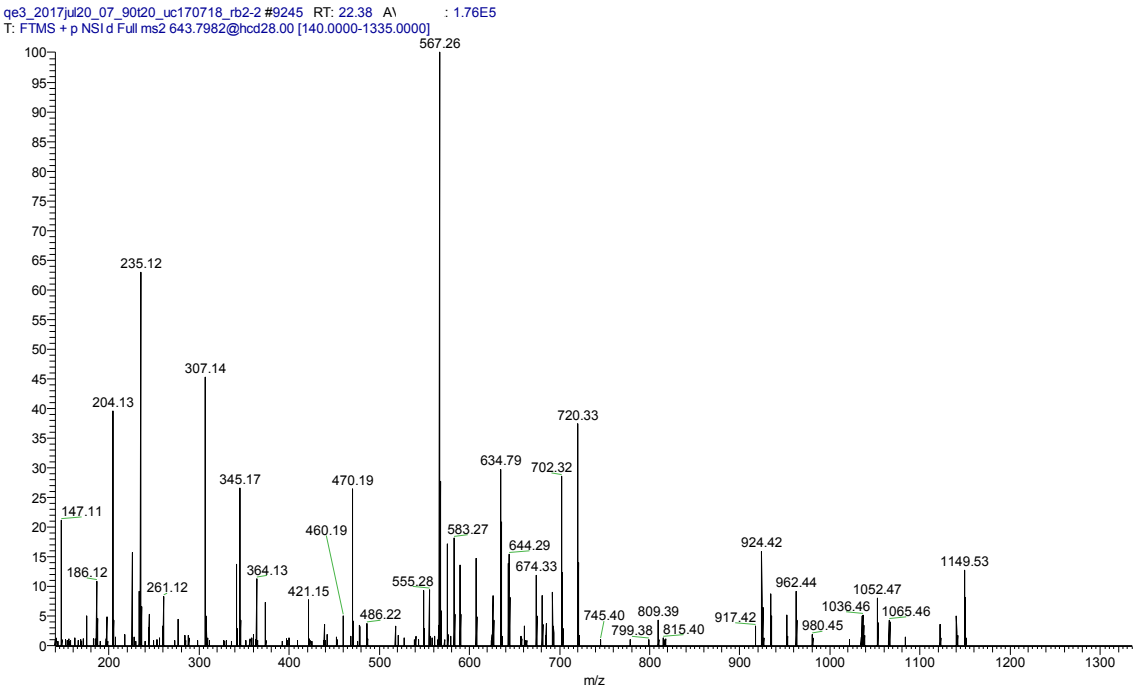


Fig S1: HPQDEIPYCGK Peptide of DMSO control treated tcTERT.

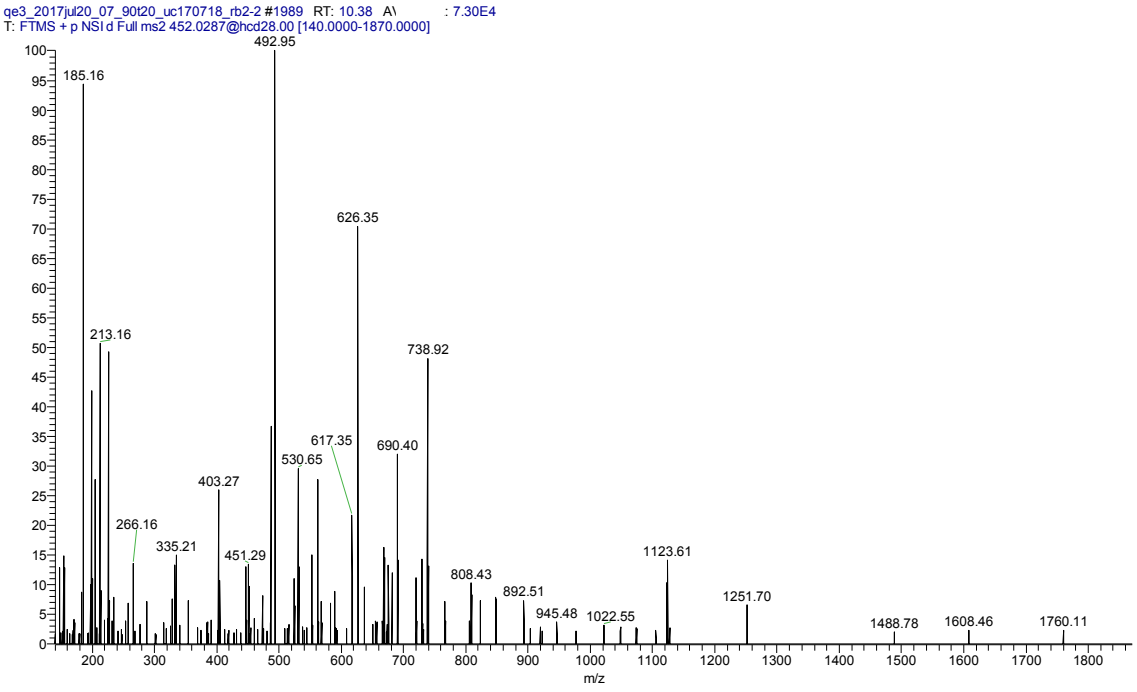


Fig S2: HPQDEIPYCGK Peptide of chrolactomycin (1) treated tcTERT.

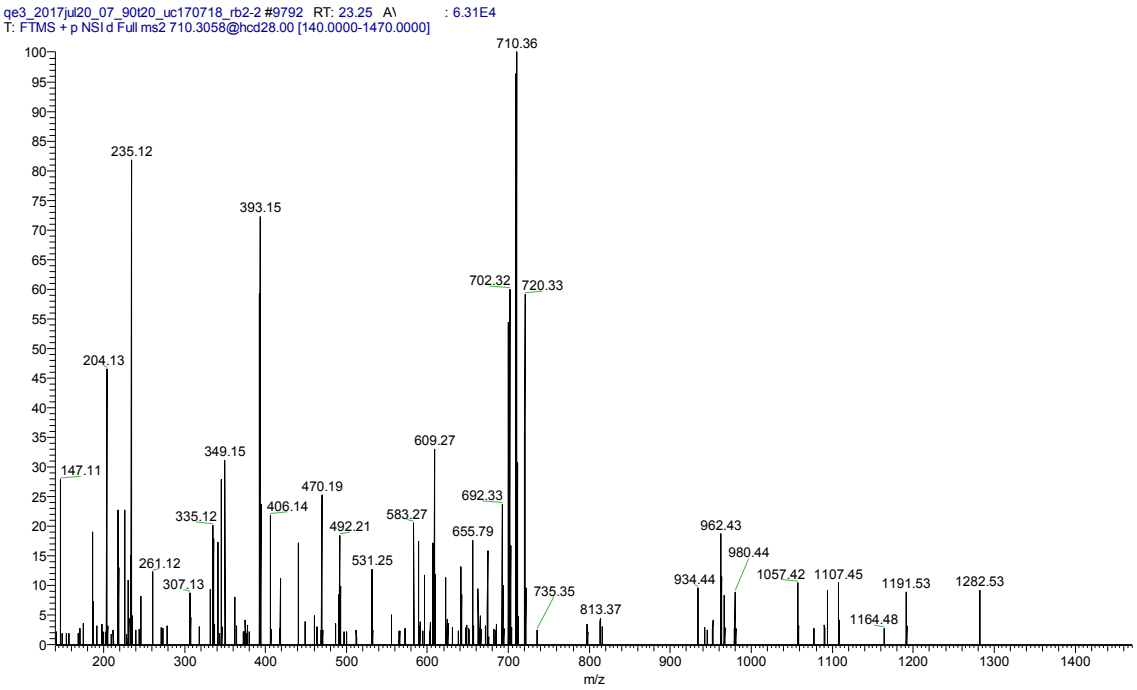
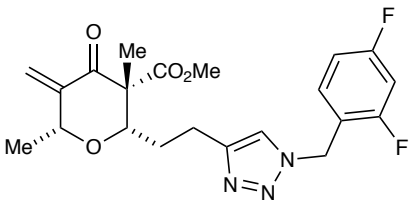


Fig S3: HPQDEIPYCGK Peptide of NU-1 treated tcTERT.



NU-1

Experimental *in vitro* drug like properties

Human Plasma Stability ($t_{1/2}$): 41 min
Mouse Liver Microsomes ($t_{1/2}$): 31 min
N-acetyl cysteine kinetics ($t_{1/2}$): 42 min
logD: 2.8
CYP1A2 inhibition: 13% (@ 10 μM)
PAMPA (pH 5.0, 6.2, 7.4, Log(Pe)): -3.6, -3.8, -3.7

Fig S4: Experimental *in vitro* drug like properties of NU-1

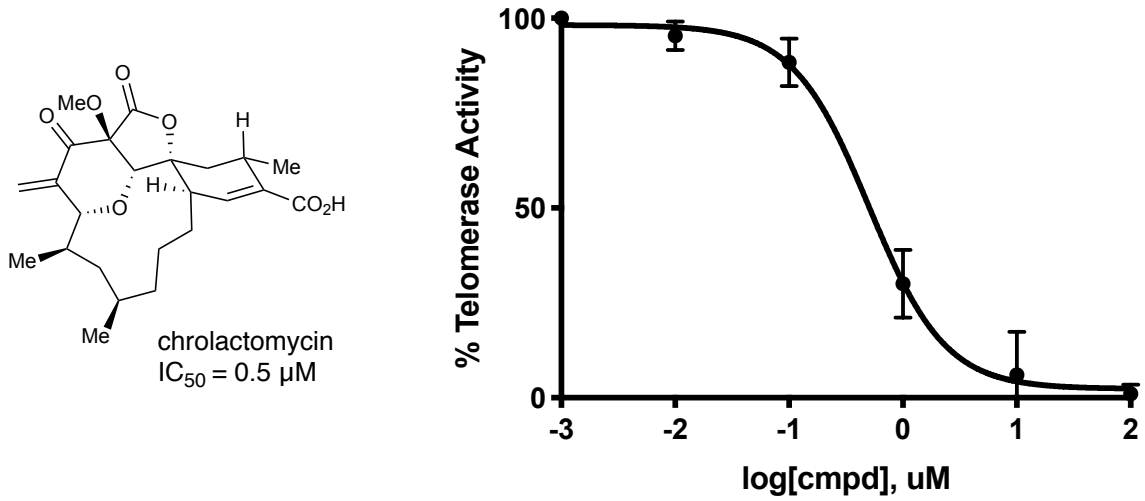


Fig S5: IC_{50} curve of chrolactomycin measured in MCF-7 cell lysates. IC_{50} = 0.5 µM

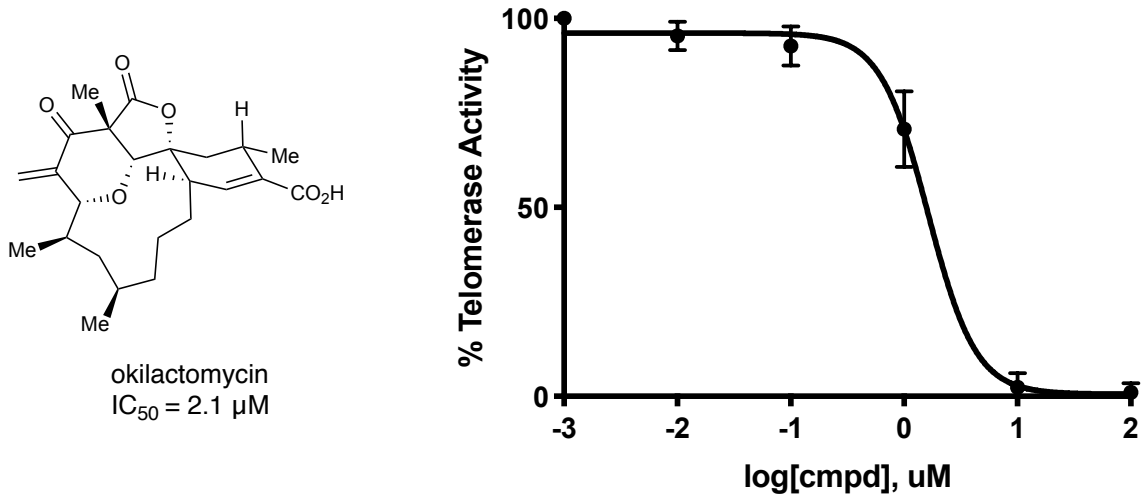
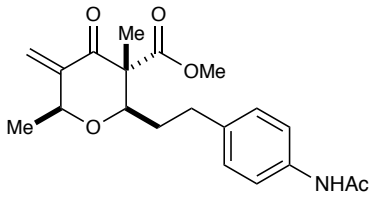


Fig S6: IC_{50} curve of okilactomycin measured in MCF-7 cell lysates. IC_{50} = 2.1 µM



racemic
IC_{50} = 1.5 µM

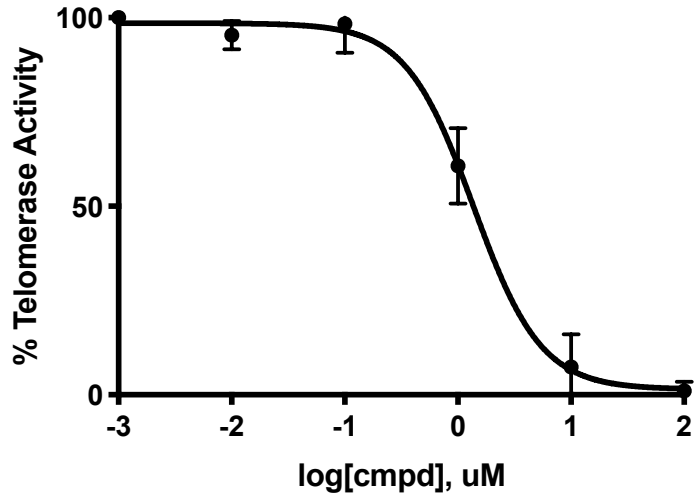
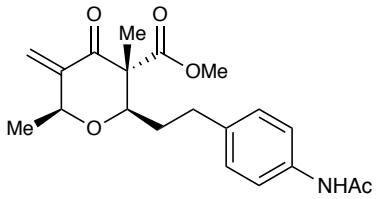


Fig S7: IC_{50} curve of racemic 4a measured in MCF-7 cell lysates. IC_{50} = 1.5 µM



IC_{50} = 4.5 µM

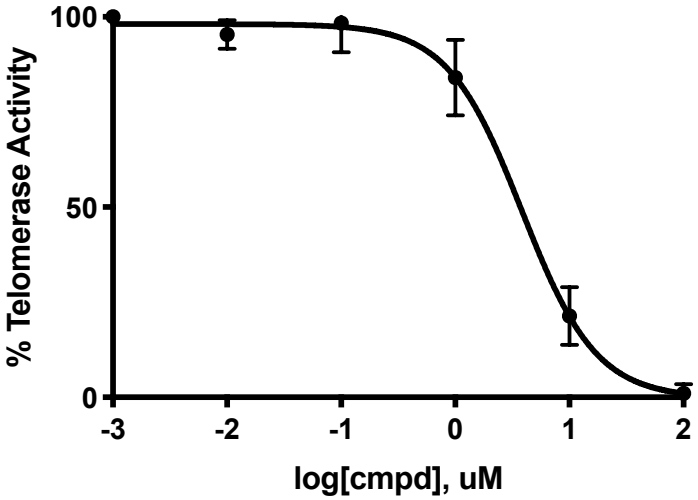


Fig S8: IC_{50} curve of enantiopure 4a measured in MCF-7 cell lysates. IC_{50} = 4.5 µM

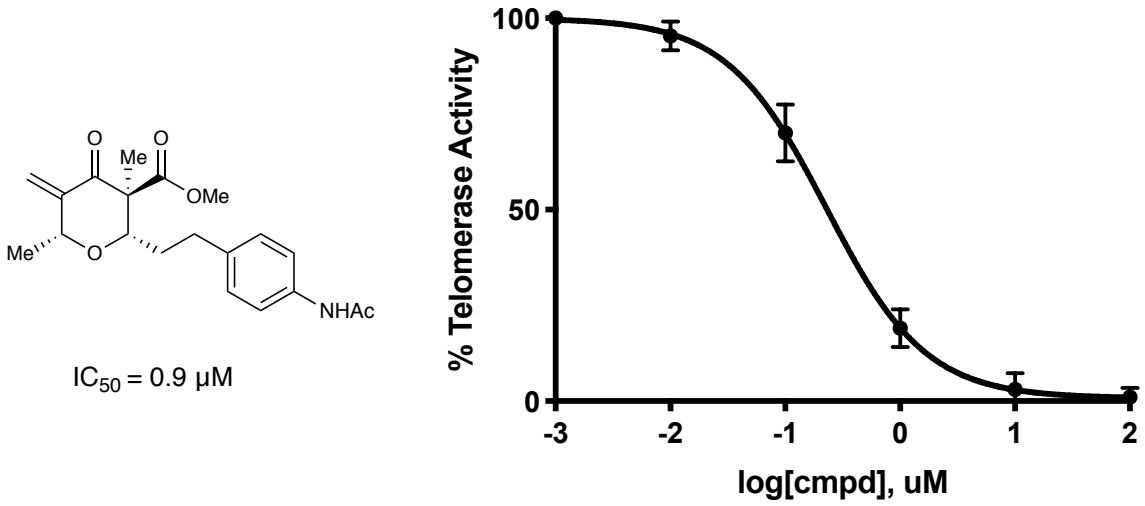
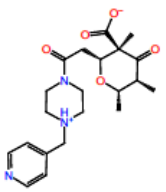


Fig S9: IC_{50} curve of enantiopure 4a measured in MCF-7 cell lysates. IC_{50} = 0.9 µM

Full List of 2nd Generation Compounds Computationally Modeled



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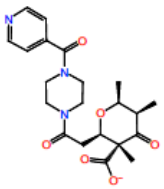

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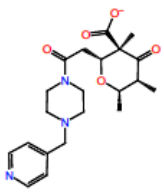

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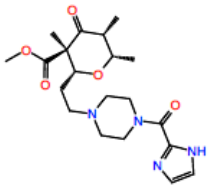

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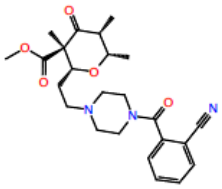

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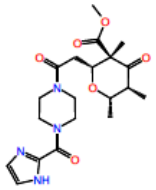

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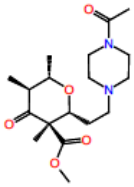

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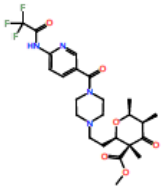

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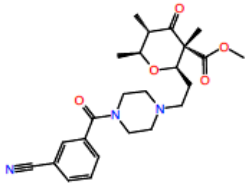

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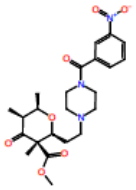

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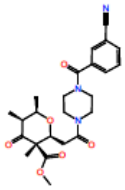

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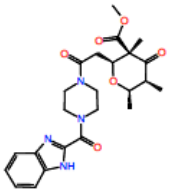

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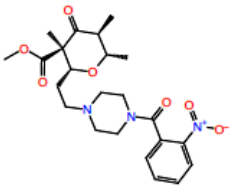

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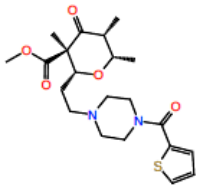

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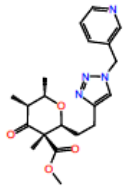

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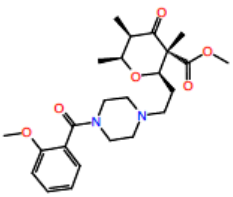

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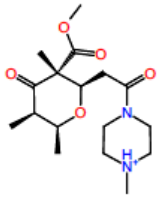

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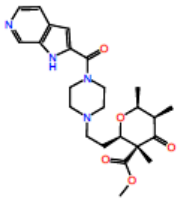

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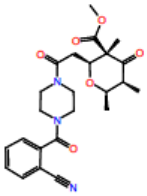

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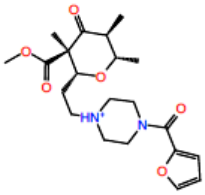

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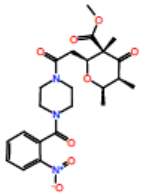

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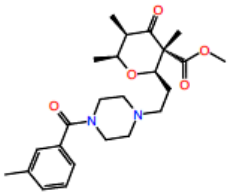

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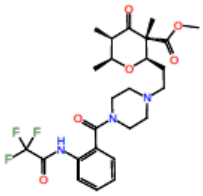

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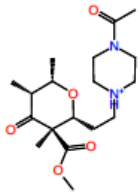

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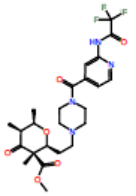

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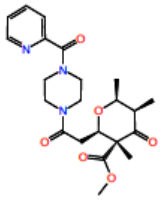

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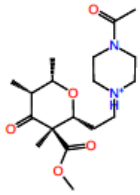

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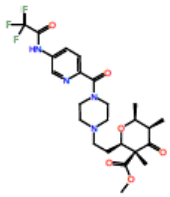

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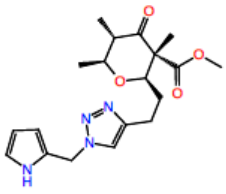

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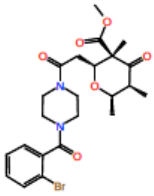

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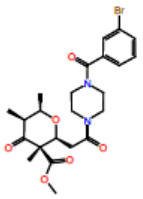

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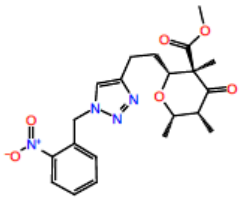

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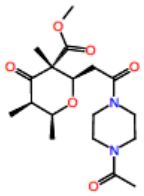

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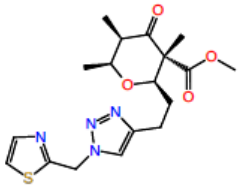

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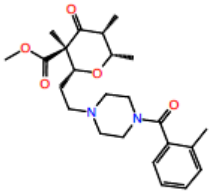

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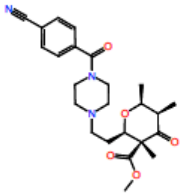

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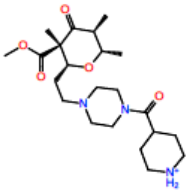

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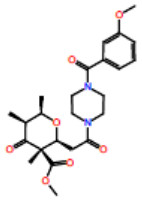

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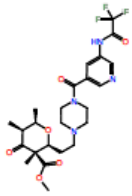

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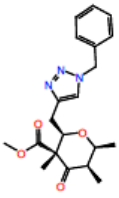
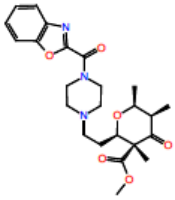
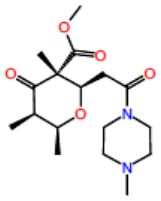


title: molecule_47

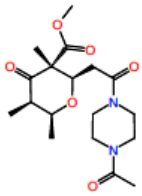


title: molecule_163

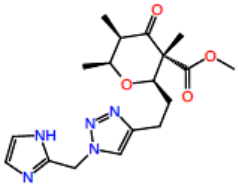
title: molecule_73



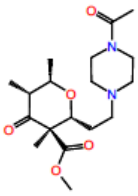
title: molecule_79



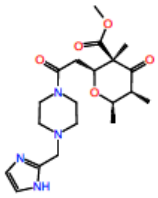
title: molecule_107



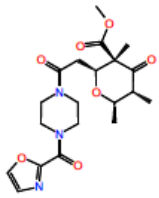
title: molecule_42



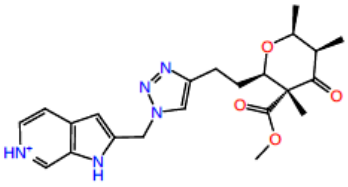
title: molecule_49



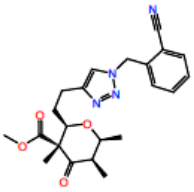
title: molecule_190



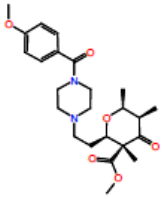
title: molecule_233



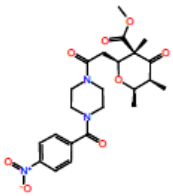
title: molecule_31



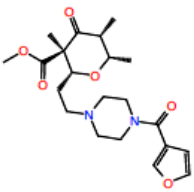
title: molecule_17



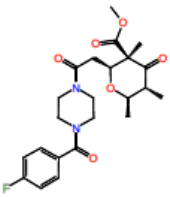
title: molecule_54



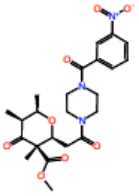
title: molecule_101



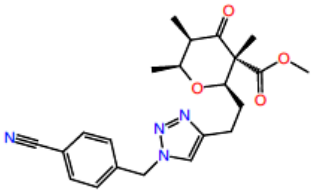
title: molecule_173



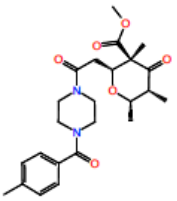
title: molecule_89



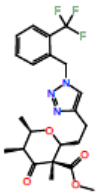
title: molecule_100



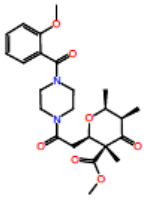
title: molecule_19



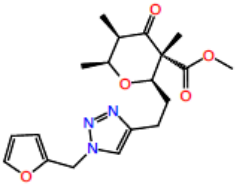
title: molecule_115



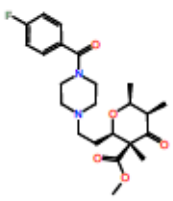
title: molecule_23



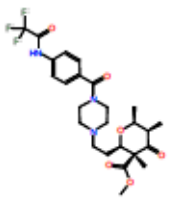
title: molecule_110



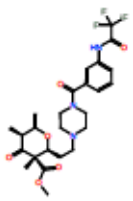
title: molecule_38



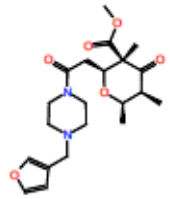
title: molecule_60



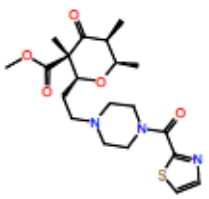
title: Set_2_18



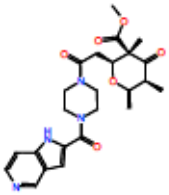
title: Set_2_17



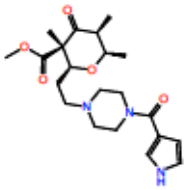
title: molecule_192



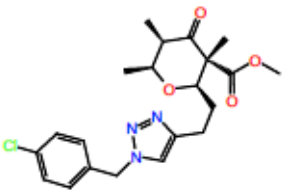
title: molecule_175



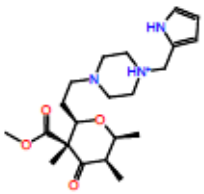
title: molecule_223



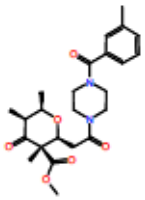
title: molecule_172



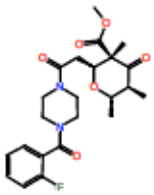
title: molecule_13



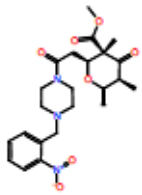
title: molecule_206



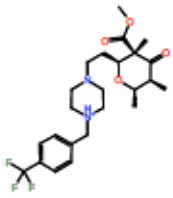
title: molecule_114



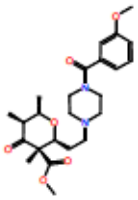
title: molecule_116



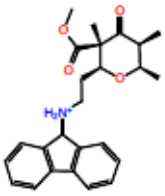
title: molecule_128



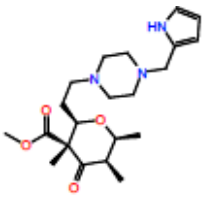
title: molecule_160



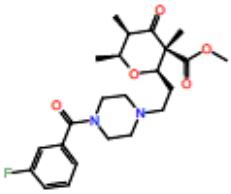
title: molecule_53



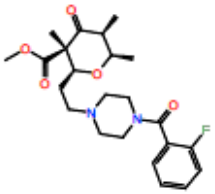
title: Set_2_23



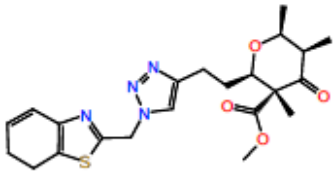
title: molecule_206



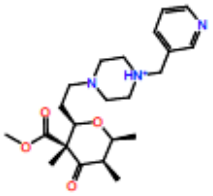
title: molecule_59



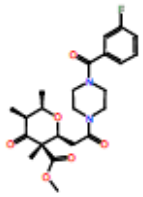
title: molecule_58



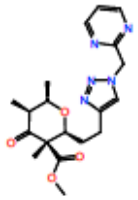
title: molecule_27



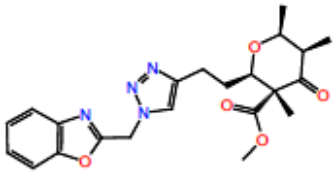
title: molecule_216



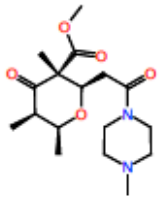
title: molecule_88



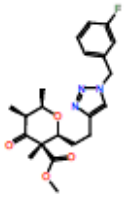
title: molecule_46



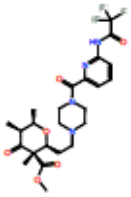
title: molecule_26



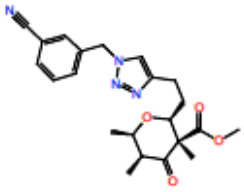
title: molecule_108



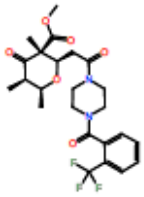
title: molecule_9



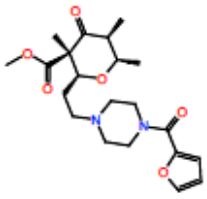
title: Set_2_26



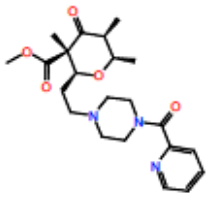
title: molecule_18



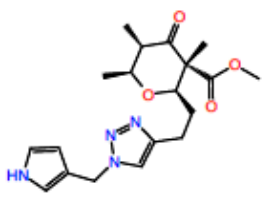
title: molecule_102



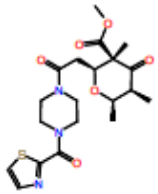
title: molecule_169



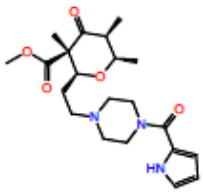
title: molecule_177



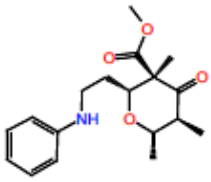
title: molecule_35



title: molecule_232



title: molecule_168



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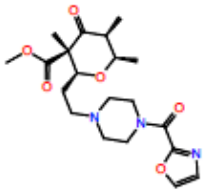
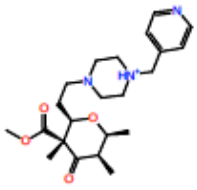
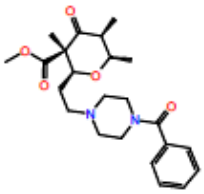


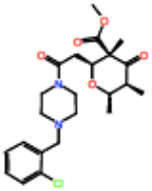
title: molecule_176



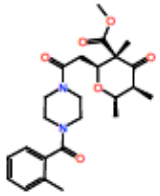
title: molecule_217



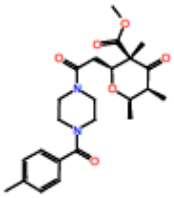
title: molecule_51



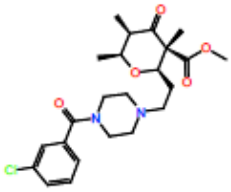
title: molecule_119



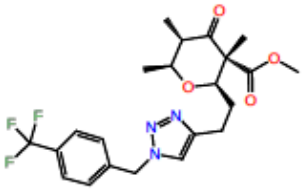
title: molecule_113



title: molecule_86



title: molecule_62



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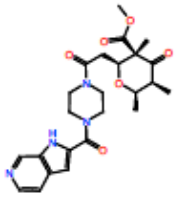
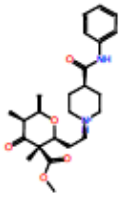
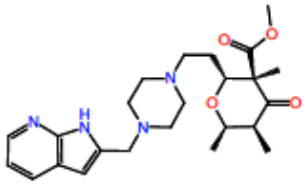


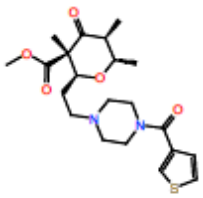
title: molecule_222



title: Set_2_1



title: molecule_202



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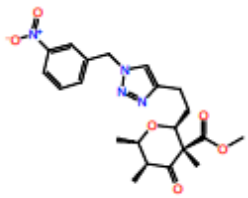
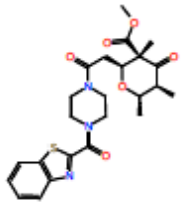
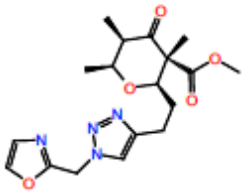


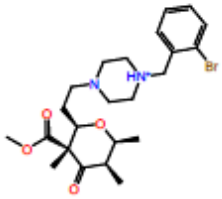
title: molecule_21



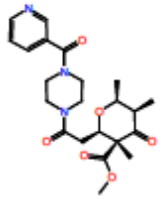
title: molecule_219



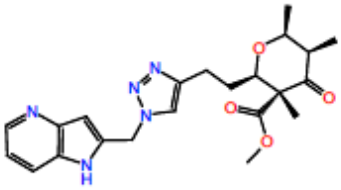
title: molecule_40



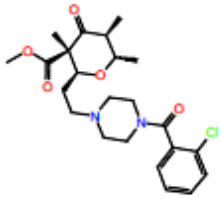
title: molecule_149



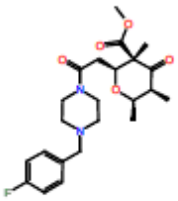
title: molecule_235



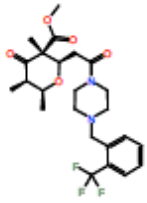
title: molecule_33



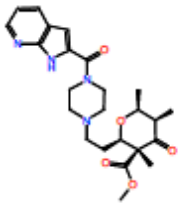
title: molecule_61



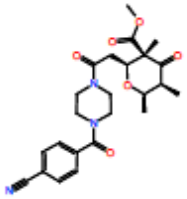
title: molecule_118



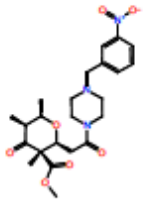
title: molecule_131



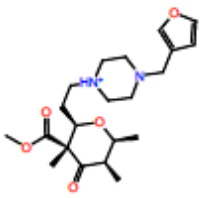
title: molecule_164



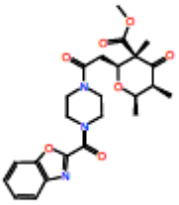
title: molecule_98



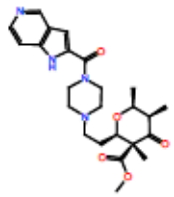
title: molecule_129



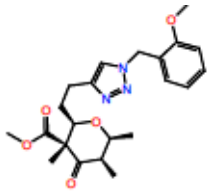
title: molecule_211



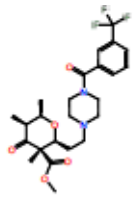
title: molecule_220



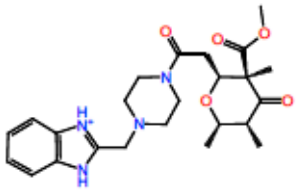
title: molecule_166



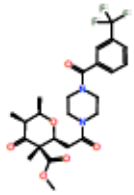
title: molecule_2



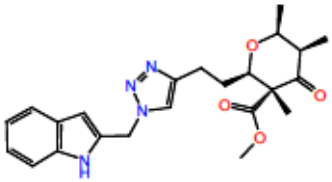
title: molecule_74



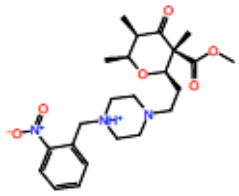
title: molecule_180



title: molecule_103



title: molecule_29



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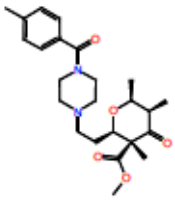
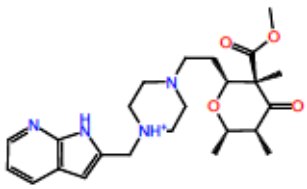
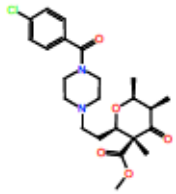


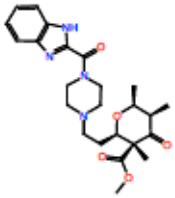
title: molecule_57



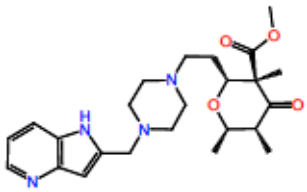
title: molecule_202



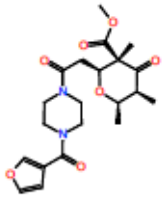
title: molecule_63



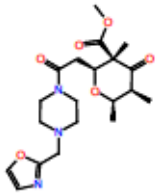
title: molecule_161



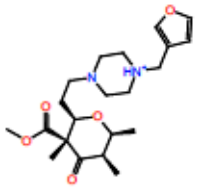
title: molecule_205



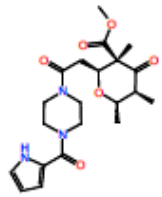
title: molecule_230



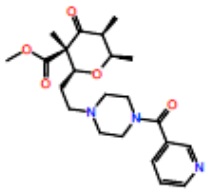
title: molecule_195



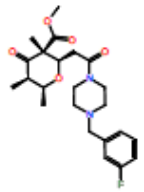
title: molecule_211



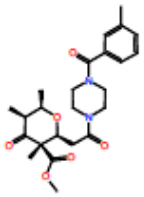
title: molecule_225



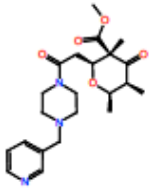
title: molecule_178



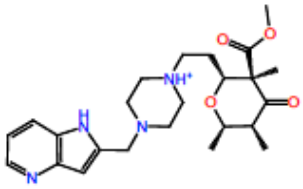
title: molecule_117



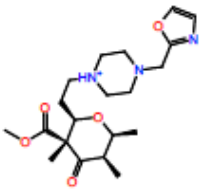
title: molecule_85



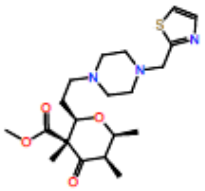
title: molecule_197



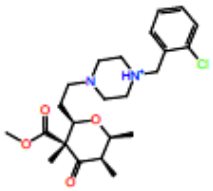
title: molecule_205



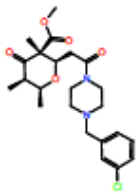
title: molecule_214



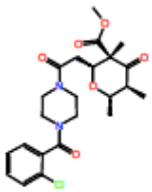
title: molecule_213



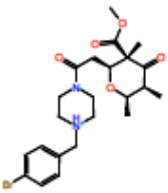
title: molecule_146



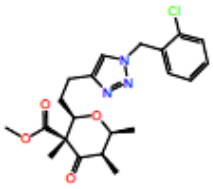
title: molecule_120



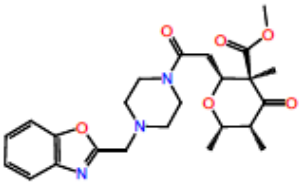
title: molecule_90



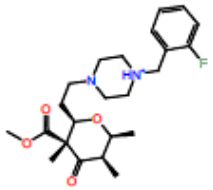
title: molecule_124



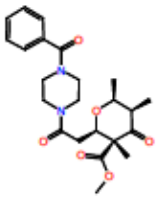
title: molecule_11



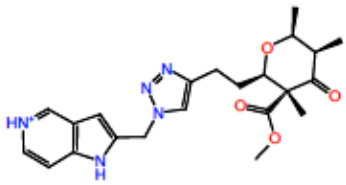
title: molecule_182



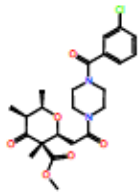
title: molecule_143



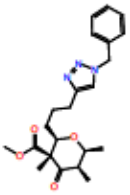
title: molecule_80



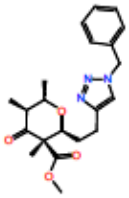
title: molecule_32



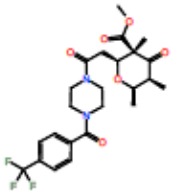
title: molecule_91



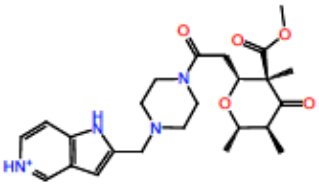
title: molecule_48



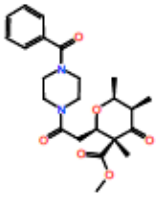
title: molecule_1



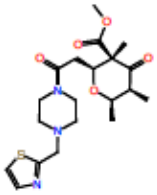
title: molecule_104



title: molecule_185



title: molecule_109



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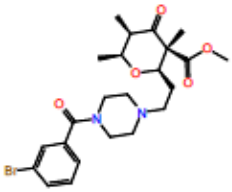
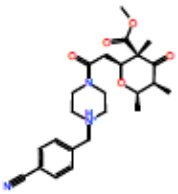
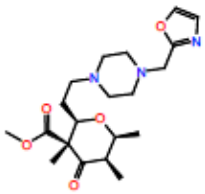


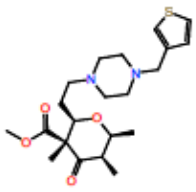
title: molecule_65



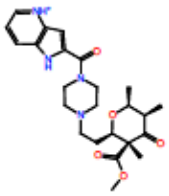
title: molecule_127



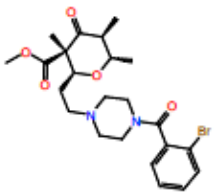
title: molecule_214



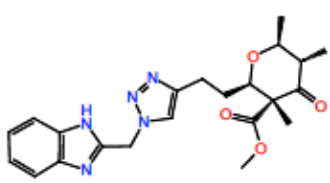
title: molecule_212



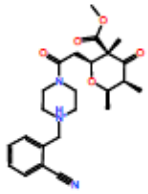
title: molecule_167



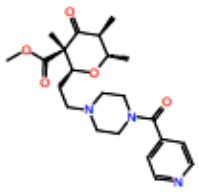
title: molecule_64



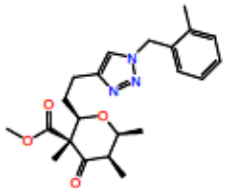
title: molecule_28



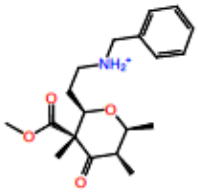
title: molecule_125



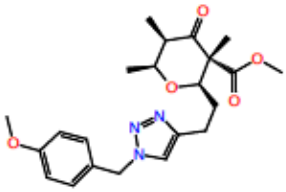
title: molecule_179



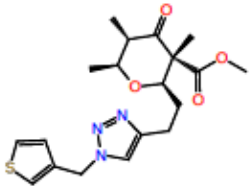
title: molecule_5



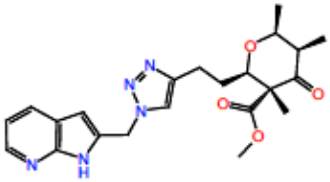
title: Set_2_21



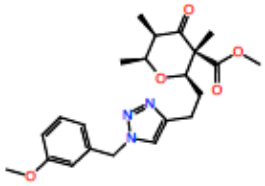
title: molecule_4



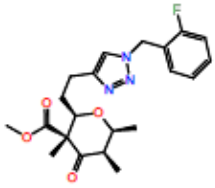
title: molecule_37



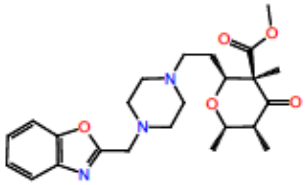
title: molecule_30



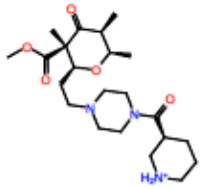
title: molecule_3



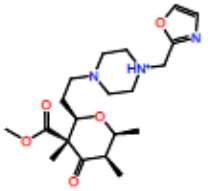
title: molecule_8



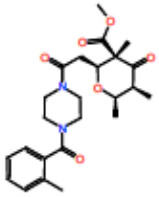
title: molecule_201



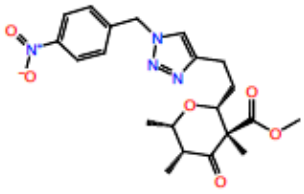
title: Set_2_15



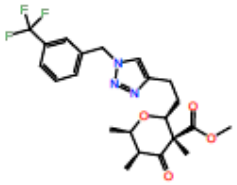
title: molecule_214



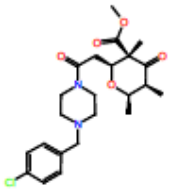
title: molecule_84



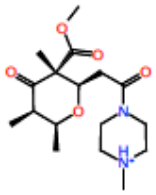
title: molecule_22



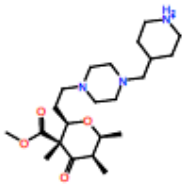
title: molecule_24



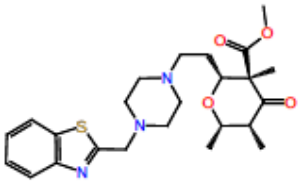
title: molecule_121



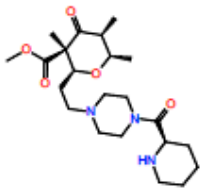
title: molecule_108



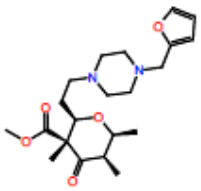
title: Set_2_9



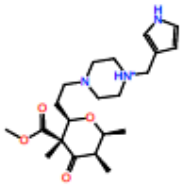
title: molecule_200



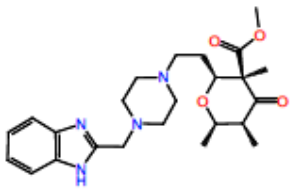
title: Set_2_16



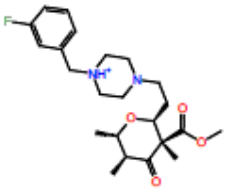
title: molecule_207



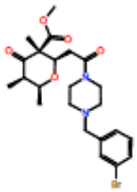
title: molecule_210



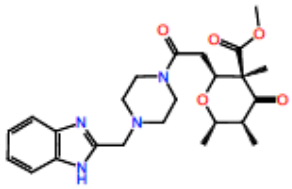
title: molecule_199



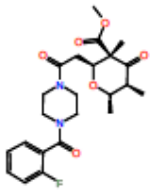
title: molecule_144



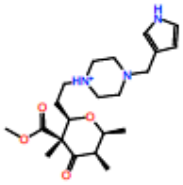
title: molecule_123



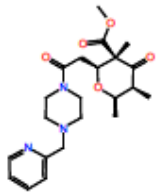
title: molecule_180



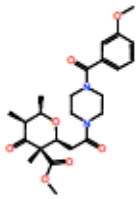
title: molecule_87



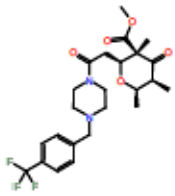
title: molecule_210



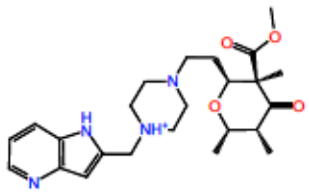
title: molecule_196



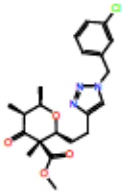
title: molecule_82



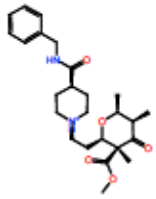
title: molecule_133



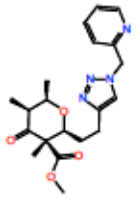
title: molecule_205



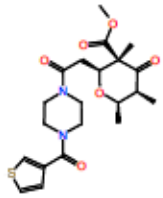
title: molecule_12



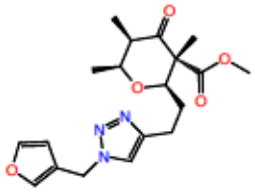
title: Set_2_2



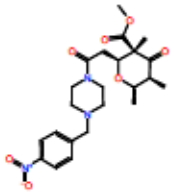
title: molecule_43



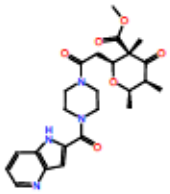
title: molecule_231



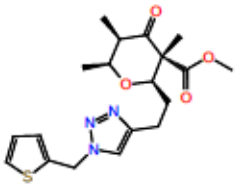
title: molecule_39



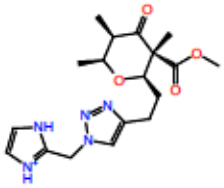
title: molecule_130



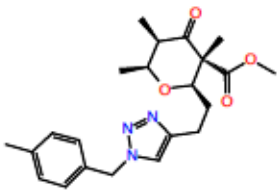
title: molecule_224



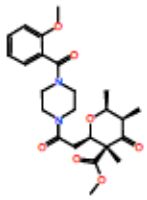
title: molecule_36



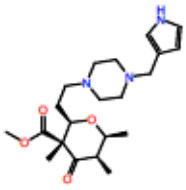
title: molecule_42



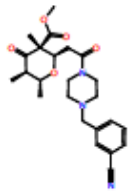
title: molecule_7



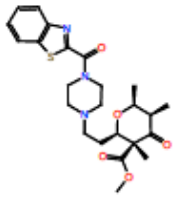
title: molecule_81



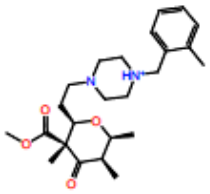
title: molecule_210



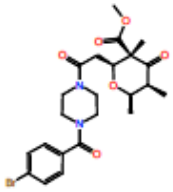
title: molecule_126



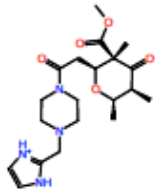
title: molecule_162



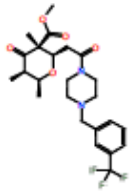
title: molecule_140



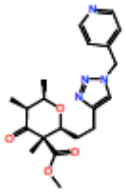
title: molecule_95



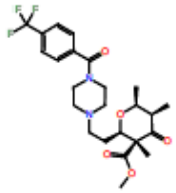
title: molecule_190



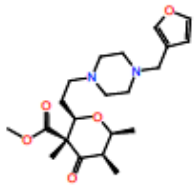
title: molecule_132



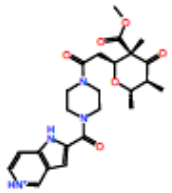
title: molecule_45



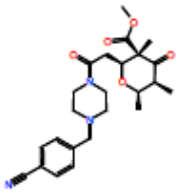
title: molecule_75



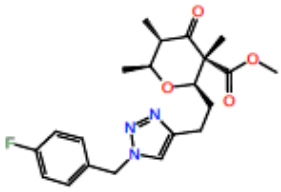
title: molecule_211



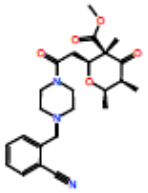
title: molecule_223



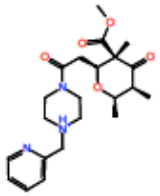
title: molecule_127



title: molecule_10



title: molecule_125



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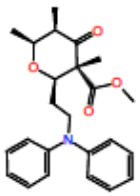
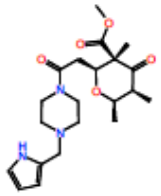
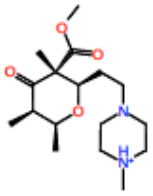


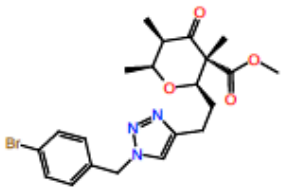
title: Set_2_22



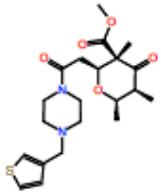
title: molecule_187



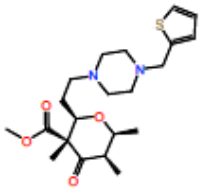
title: molecule_50



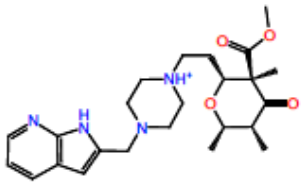
title: molecule_16



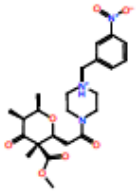
title: molecule_193



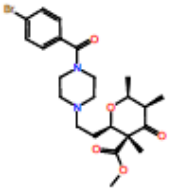
title: molecule_208



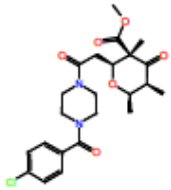
title: molecule_202



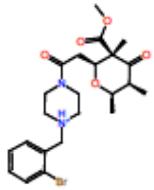
title: molecule_129



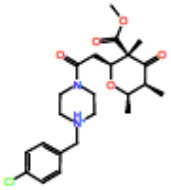
title: molecule_66



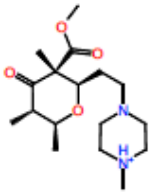
title: molecule_92



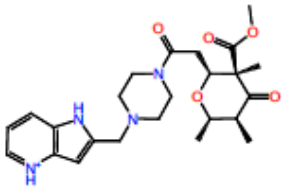
title: molecule_122



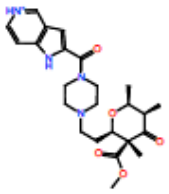
title: molecule_121



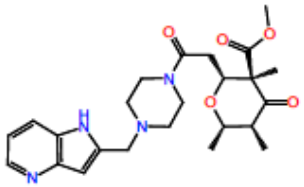
title: molecule_135



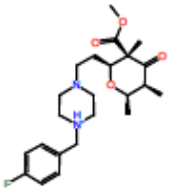
title: molecule_186



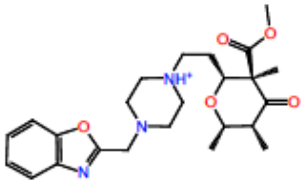
title: molecule_166



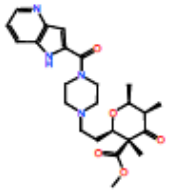
title: molecule_186



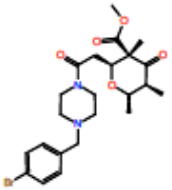
title: molecule_145



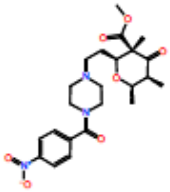
title: molecule_201



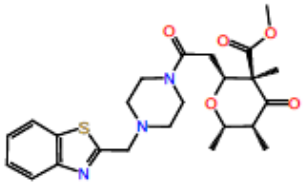
title: molecule_167



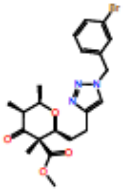
title: molecule_124



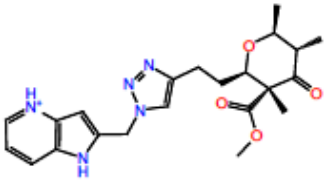
title: molecule_72



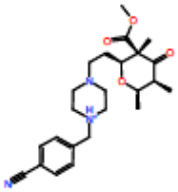
title: molecule_181



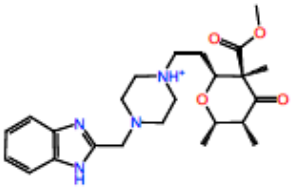
title: molecule_15



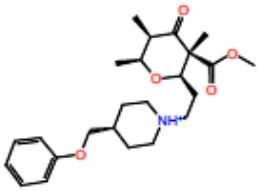
title: molecule_33



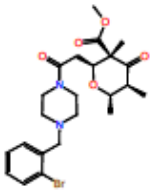
title: molecule_154



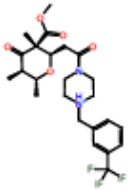
title: molecule_199



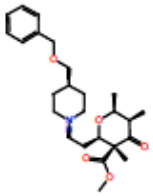
title: Set_2_13



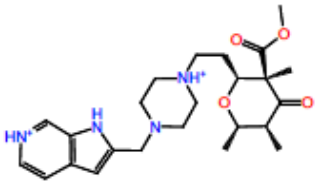
title: molecule_122



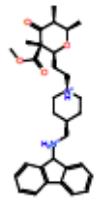
title: molecule_132



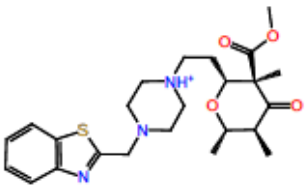
title: Set_2_14



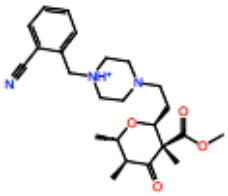
title: molecule_203



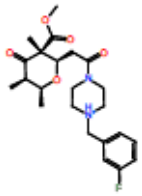
title: Set_2_19



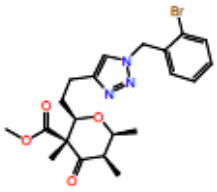
title: molecule_200



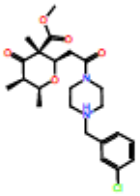
title: molecule_152



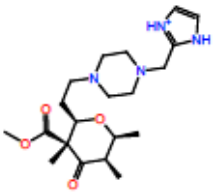
title: molecule_117



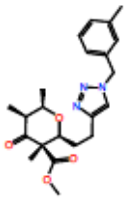
title: molecule_14



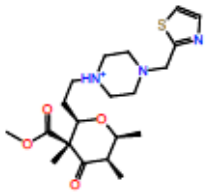
title: molecule_120



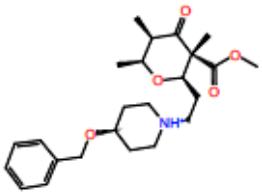
title: molecule_209



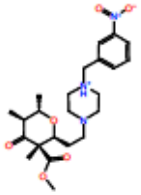
title: molecule_6



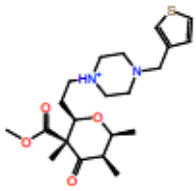
title: molecule_213



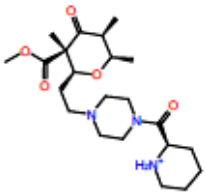
title: Set_2_12



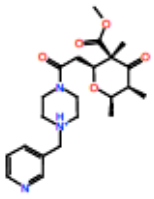
title: molecule_156



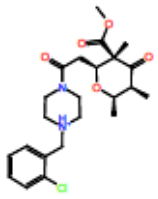
title: molecule_212



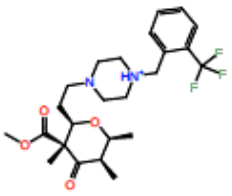
title: Set_2_16



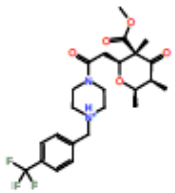
title: molecule_197



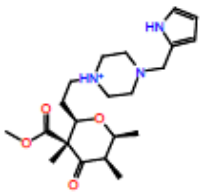
title: molecule_119



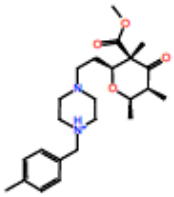
title: molecule_158



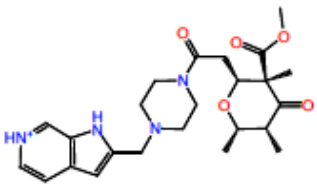
title: molecule_133



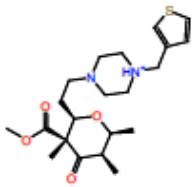
title: molecule_206



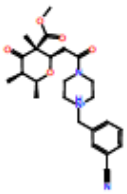
title: molecule_142



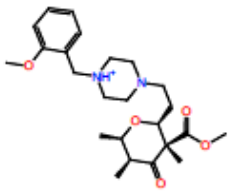
title: molecule_184



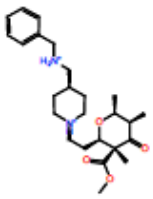
title: molecule_212



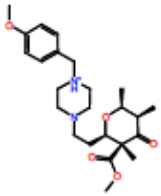
title: molecule_126



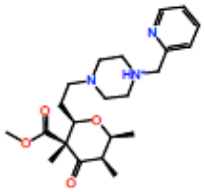
title: molecule_137



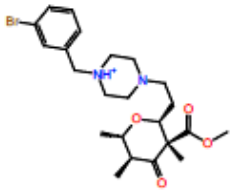
title: Set_2_4



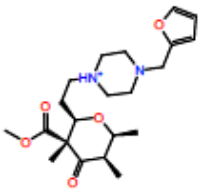
title: molecule_139



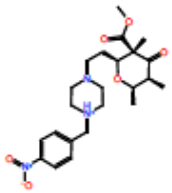
title: molecule_215



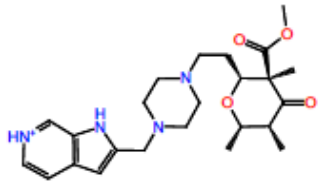
title: molecule_150



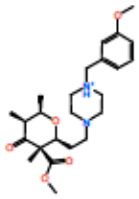
title: molecule_207



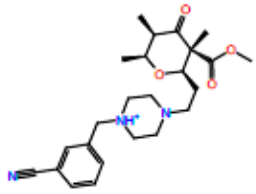
title: molecule_157



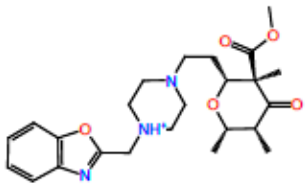
title: molecule_203



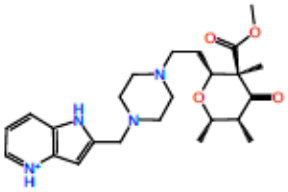
title: molecule_138



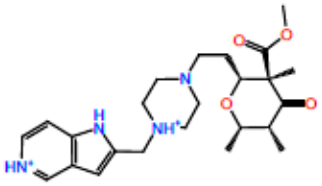
title: molecule_153



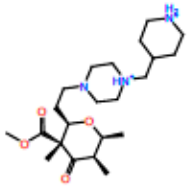
title: molecule_201



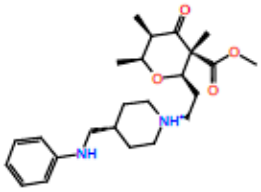
title: molecule_205



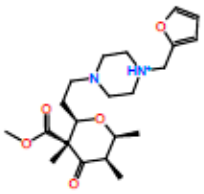
title: molecule_204



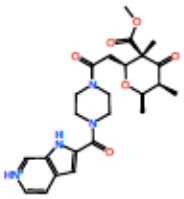
title: Set_2_9



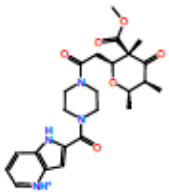
title: Set_2_3



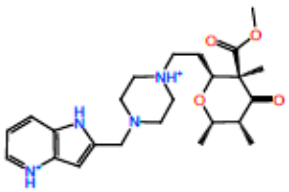
title: molecule_207



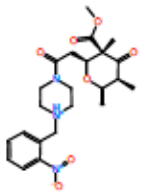
title: molecule_222



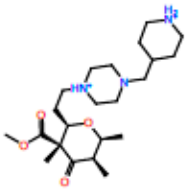
title: molecule_224



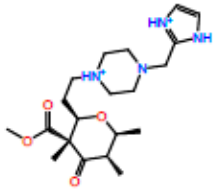
title: molecule_205



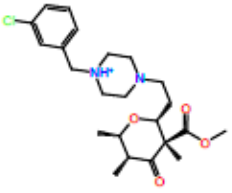
title: molecule_128



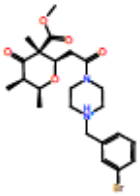
title: Set_2_9



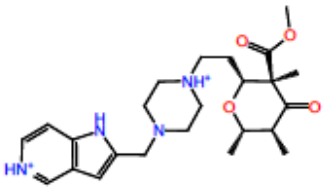
title: molecule_209



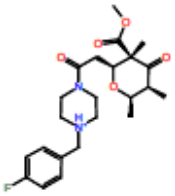
title: molecule_147



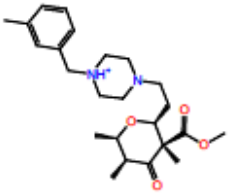
title: molecule_123



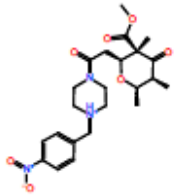
title: molecule_204



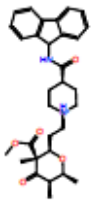
title: molecule_118



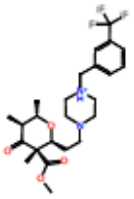
title: molecule_141



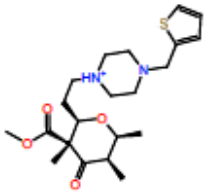
title: molecule_130



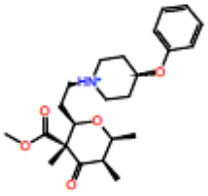
title: Set_2_6



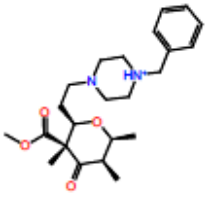
title: molecule_159



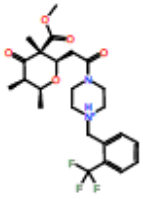
title: molecule_208



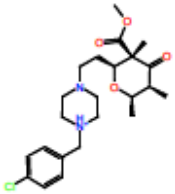
title: Set_2_11



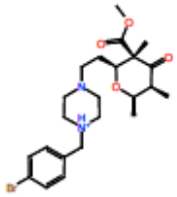
title: molecule_136



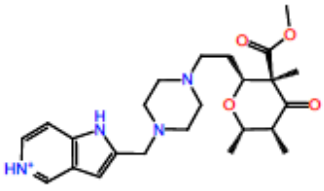
title: molecule_131



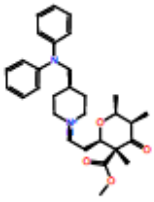
title: molecule_148



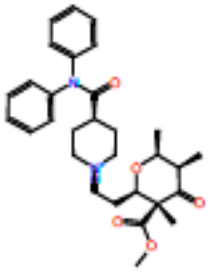
title: molecule_151



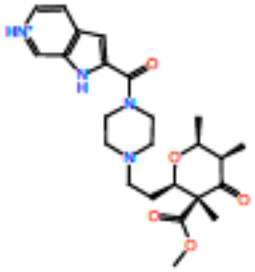
title: molecule_204



title: Set_2_7

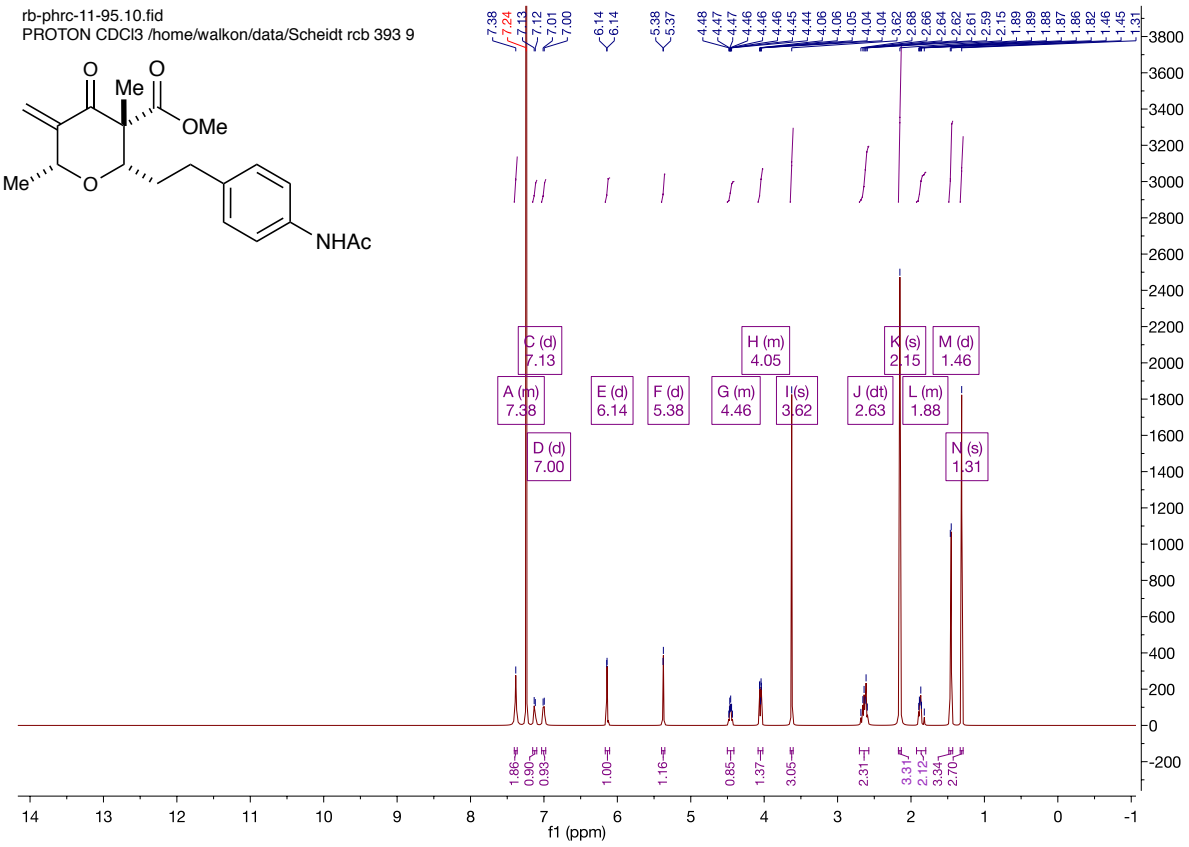


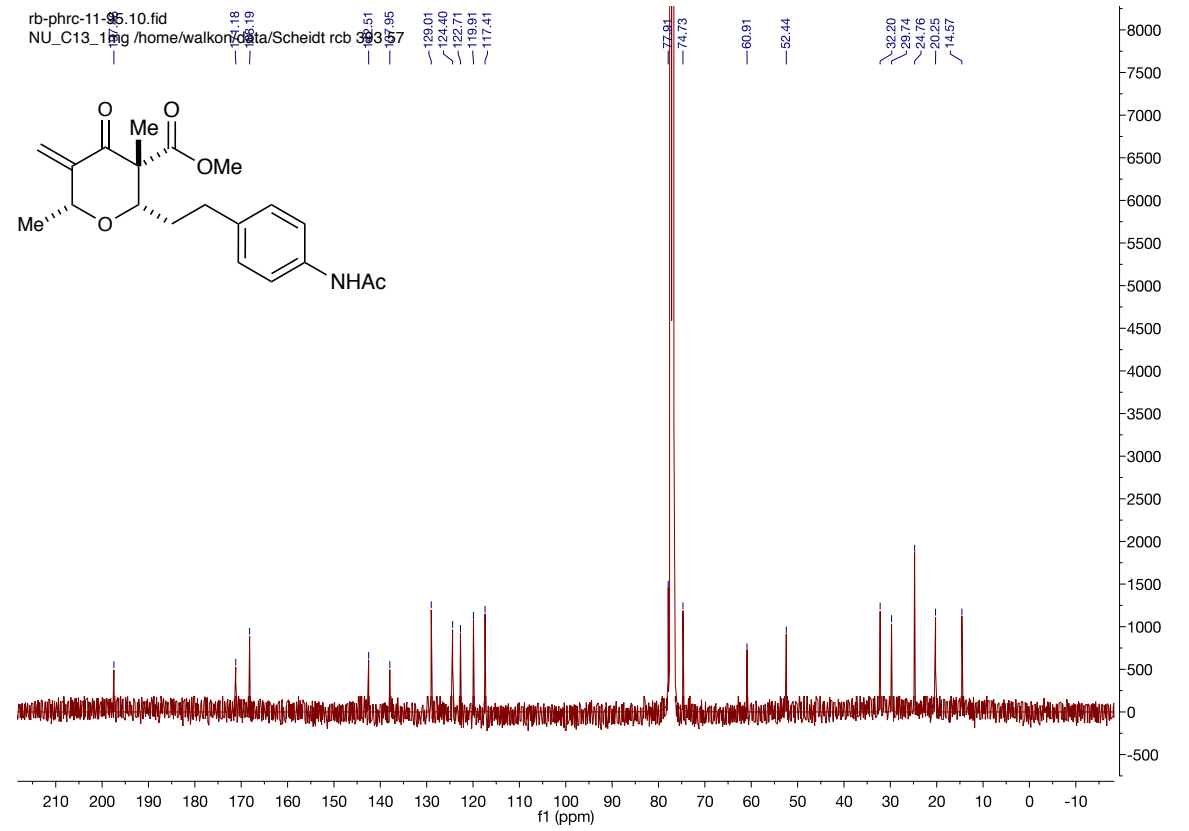
title: Set_2_5

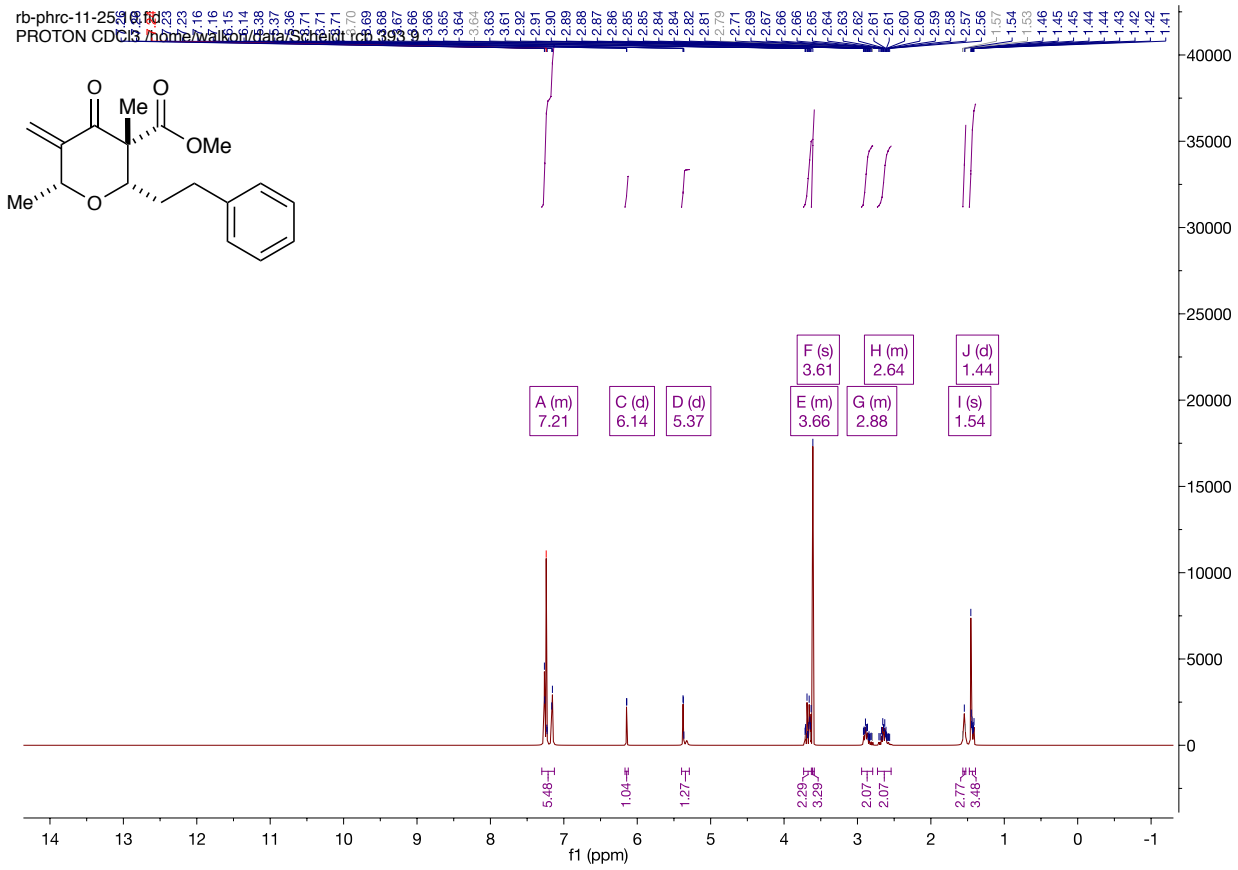


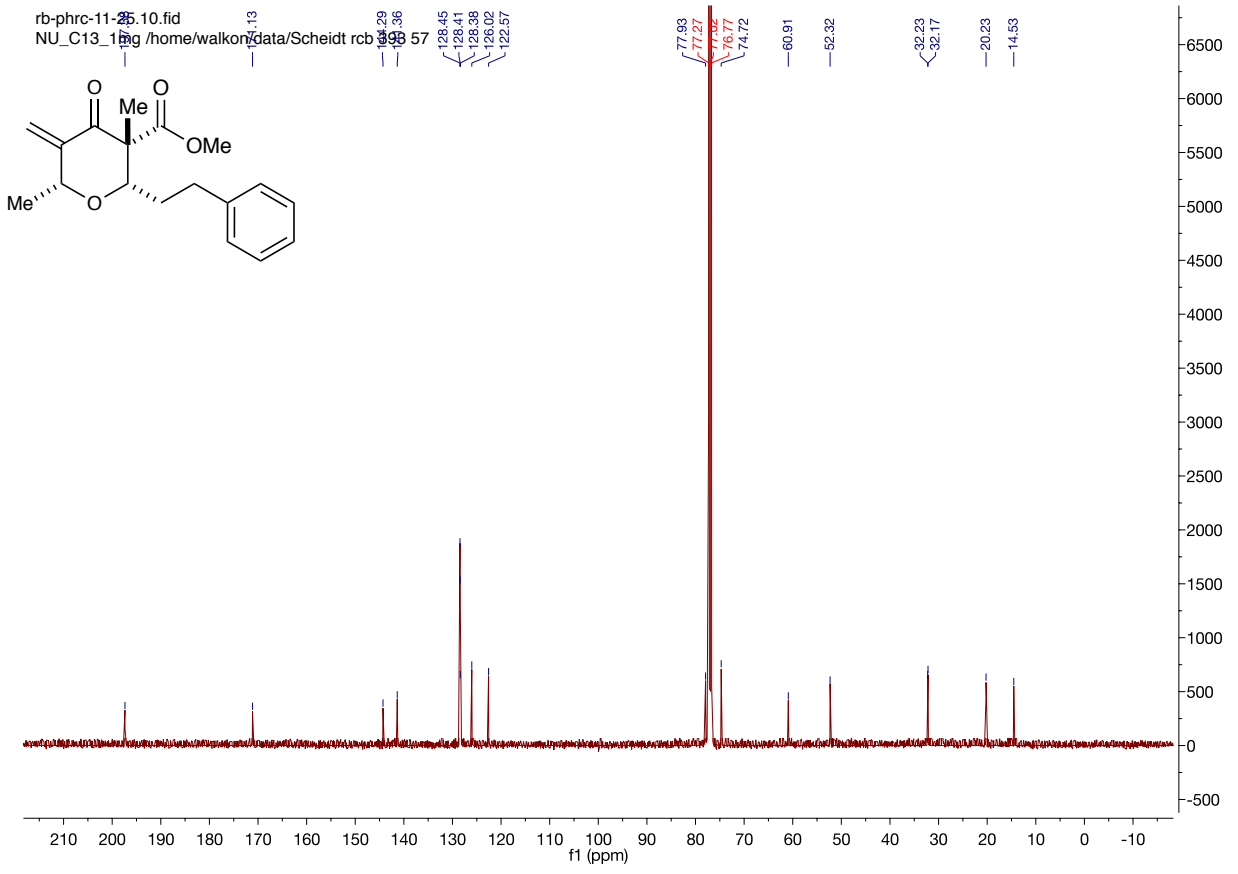
title: molecule_165

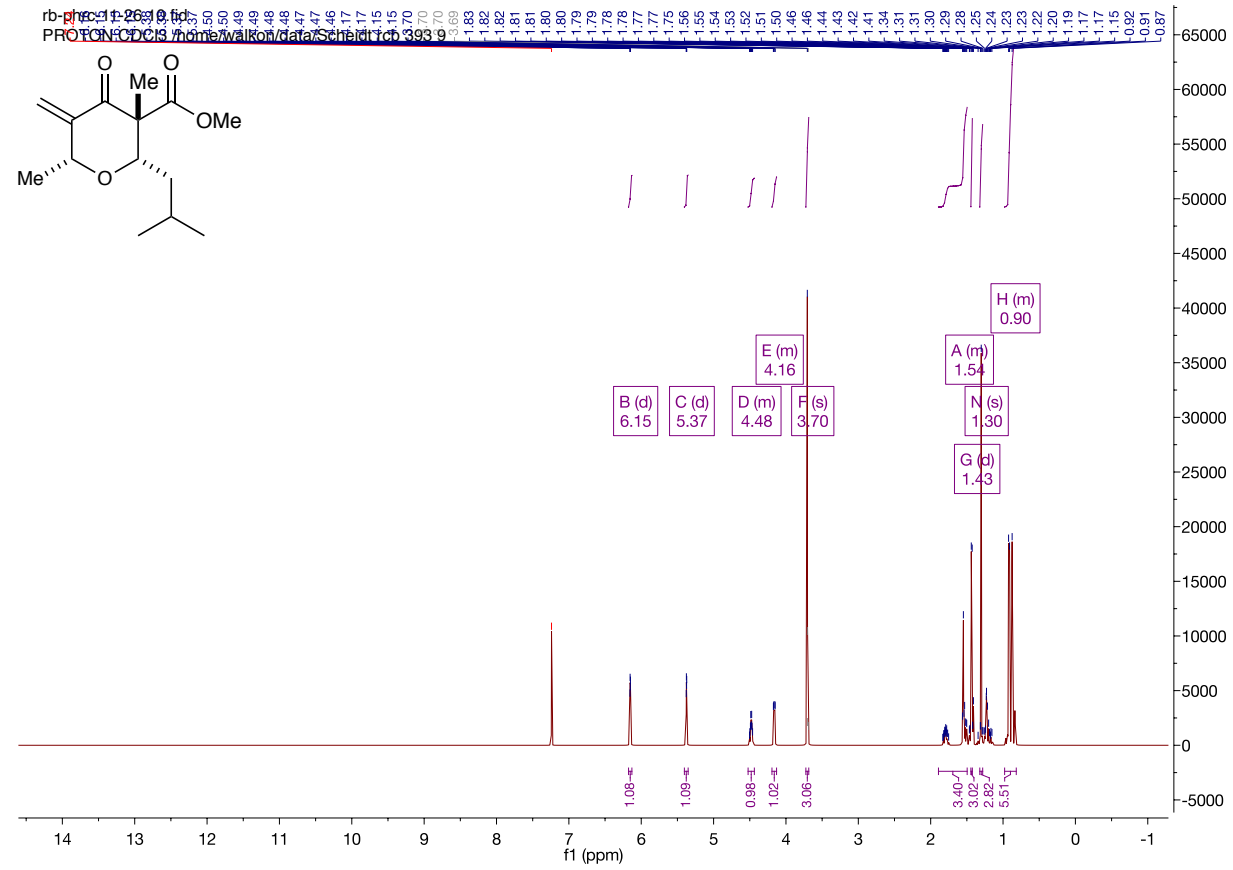
NMR Spectra for Telomerase Inhibitors

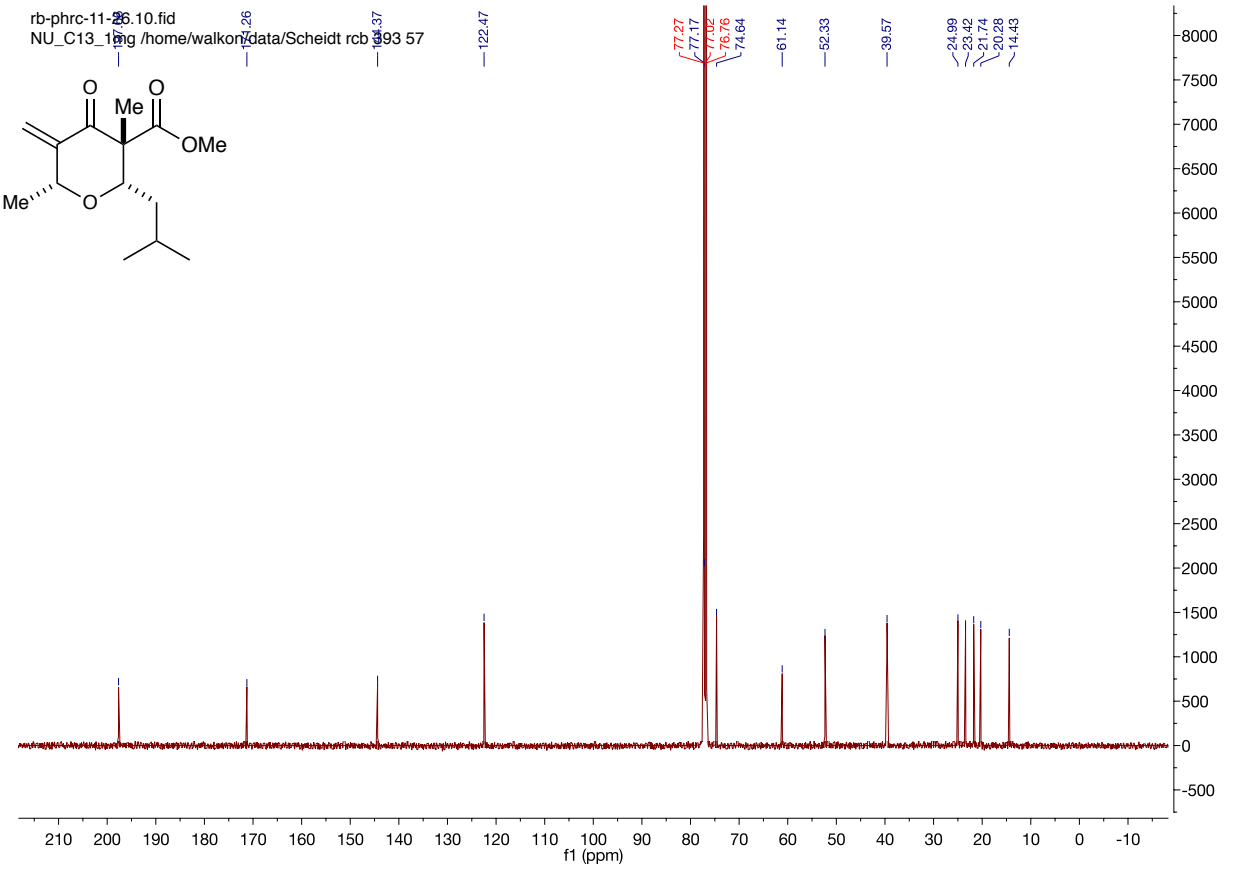


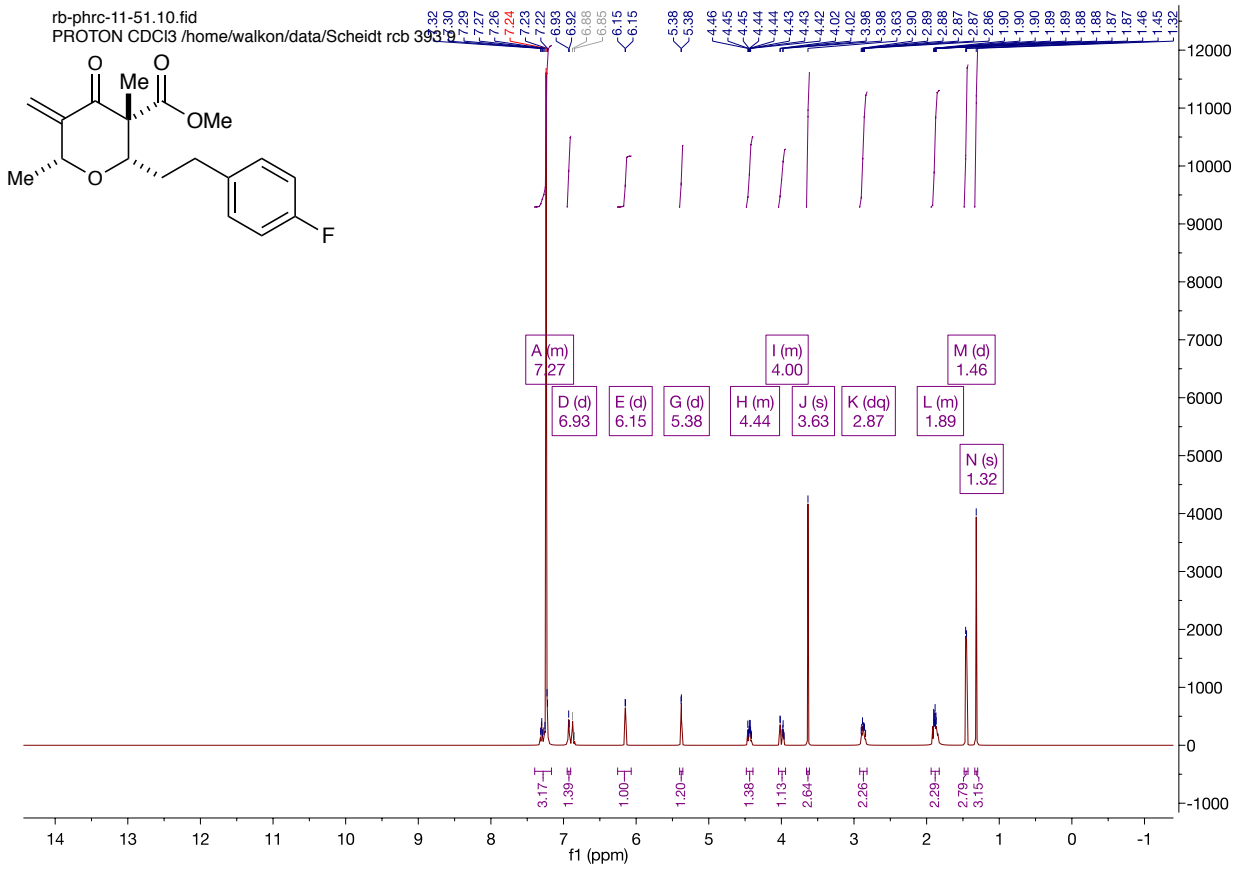


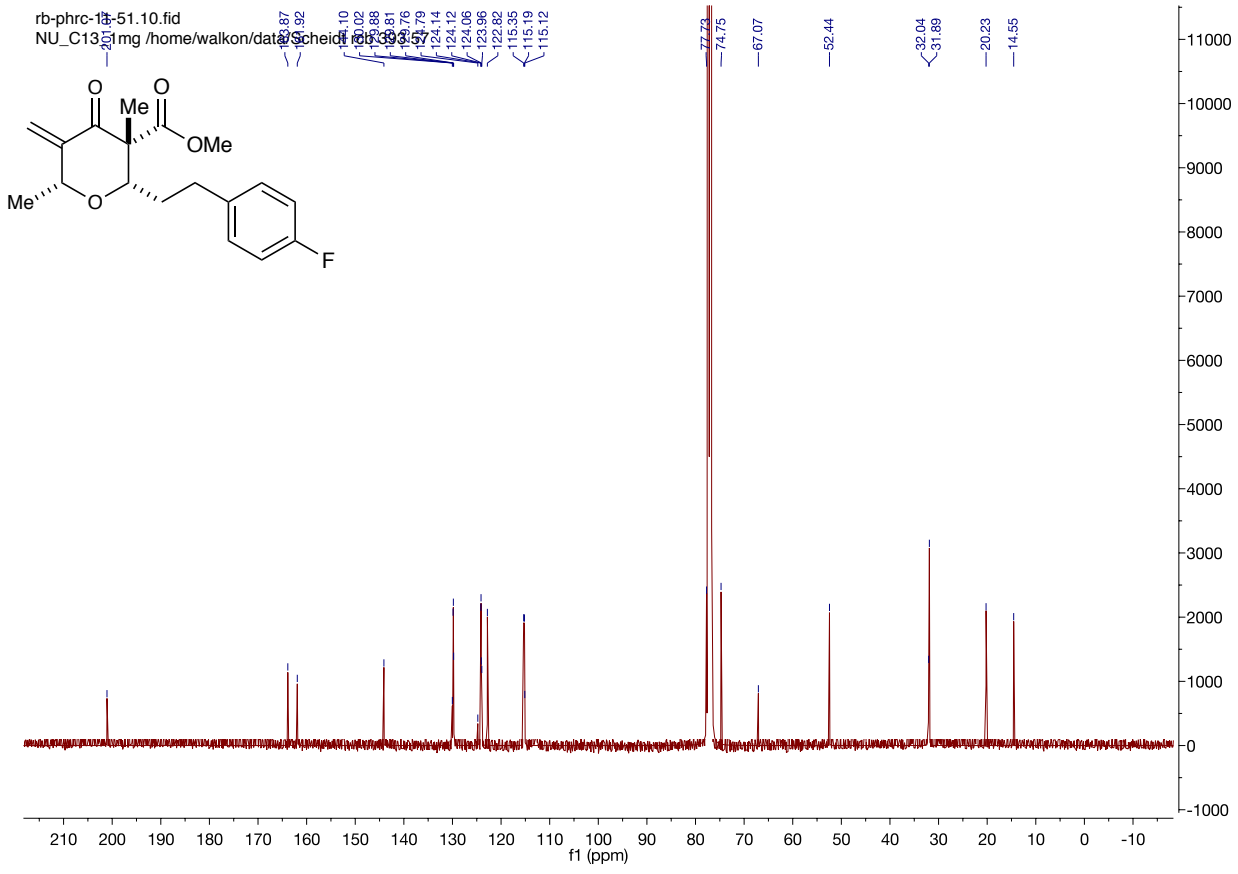

O
O
Me
OMe
Me
O
A (m) 7.21
C (d) 6.14
D (d) 5.37
E (m) 3.66
F (s) 3.61
G (m) 2.88
H (m) 2.64
I (s) 1.54
J (d) 1.44
5.48
1.04
1.27
2.29
3.29
2.07
2.07
2.77
3.48
f1 (ppm)

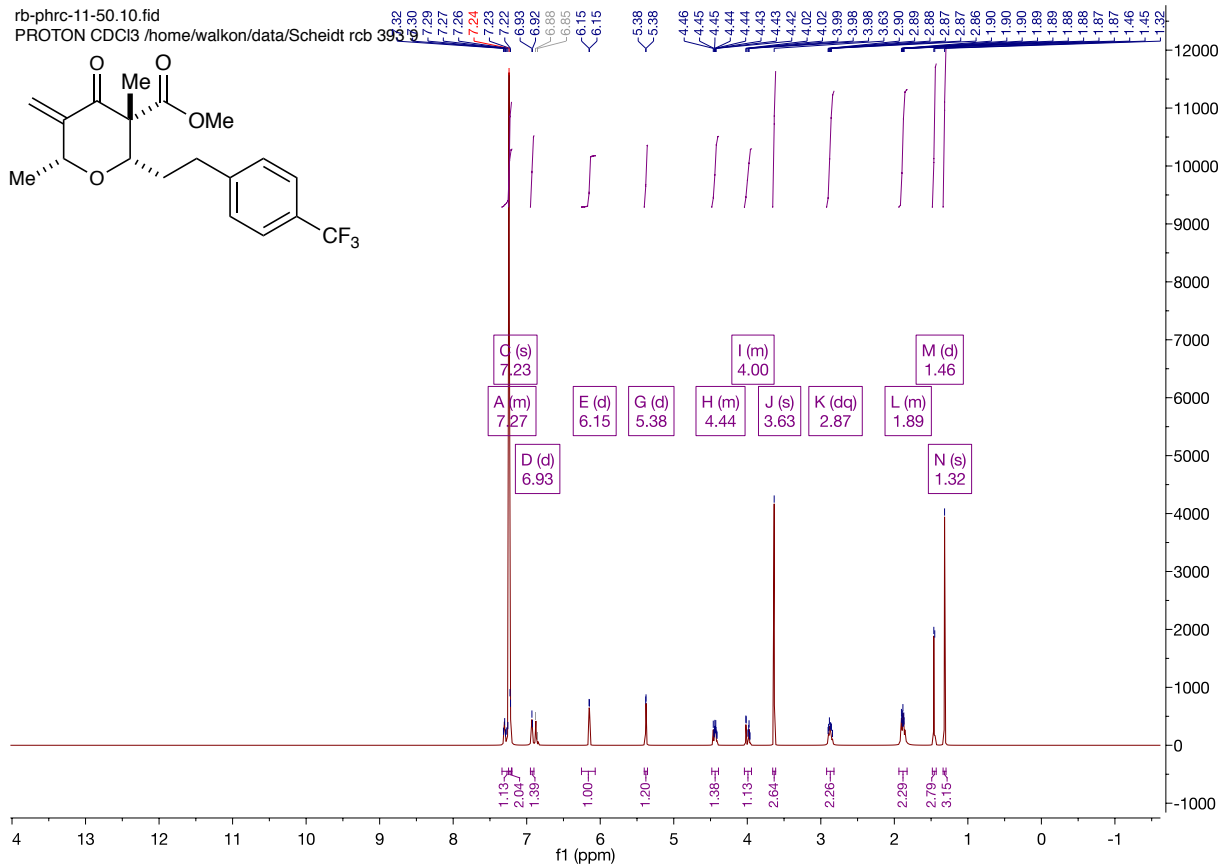

O
O
Me
OMe
Me
O
77.93
77.27
76.77
74.72
60.91
52.32
32.23
32.17
20.23
14.53
f1 (ppm)

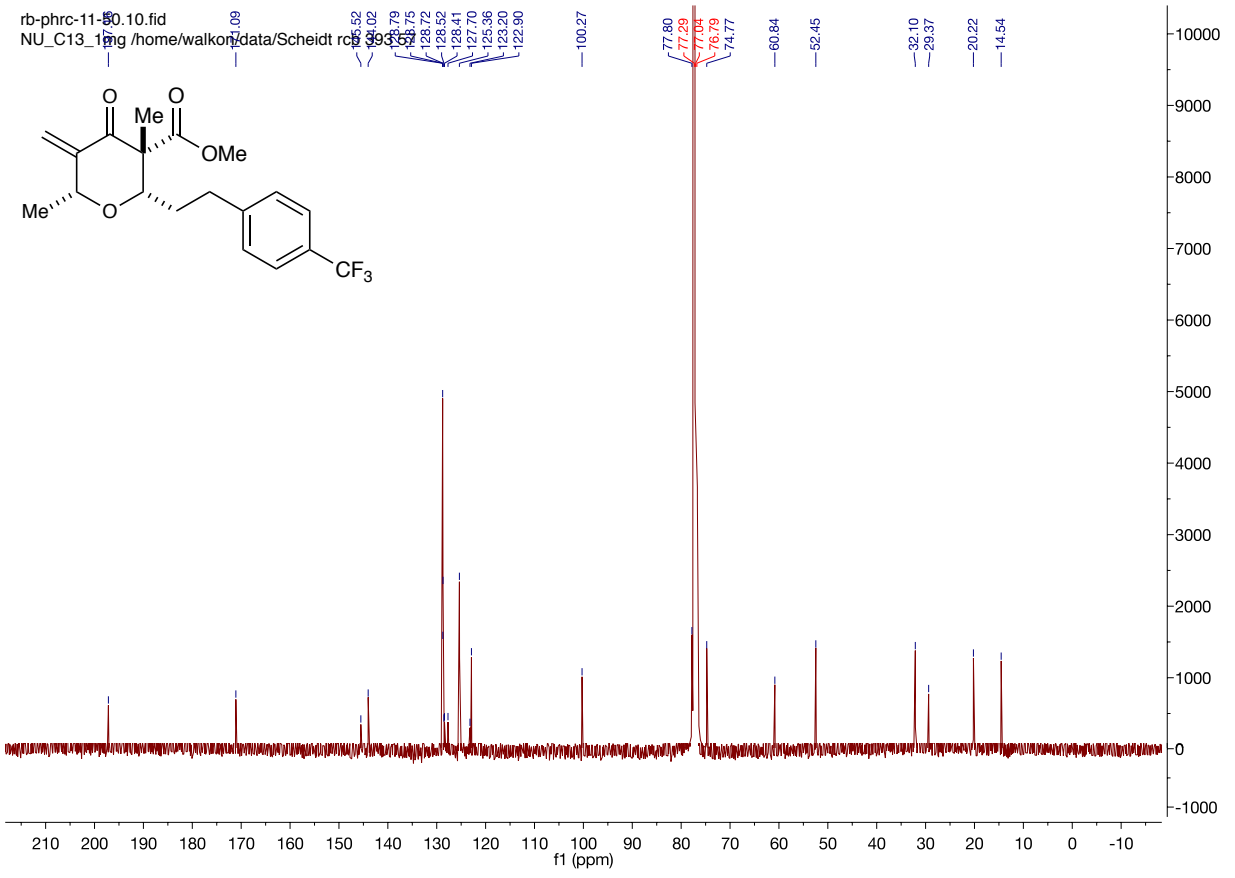

rb-phrc-11-26.10.fid
PROTON-CDCl3 /home/walkon/data/Scheidt rcb 393 9
O
Me
O
OMe
Me
O
H (m)
0.90
E (m)
4.16
A (m)
1.54
B (d)
6.15
C (d)
5.37
D (m)
4.48
F (s)
3.70
N (s)
1.30
G (d)
1.43
1.08
1.09
0.98
1.02
3.06
3.40
3.02
2.82
5.51
f1 (ppm)

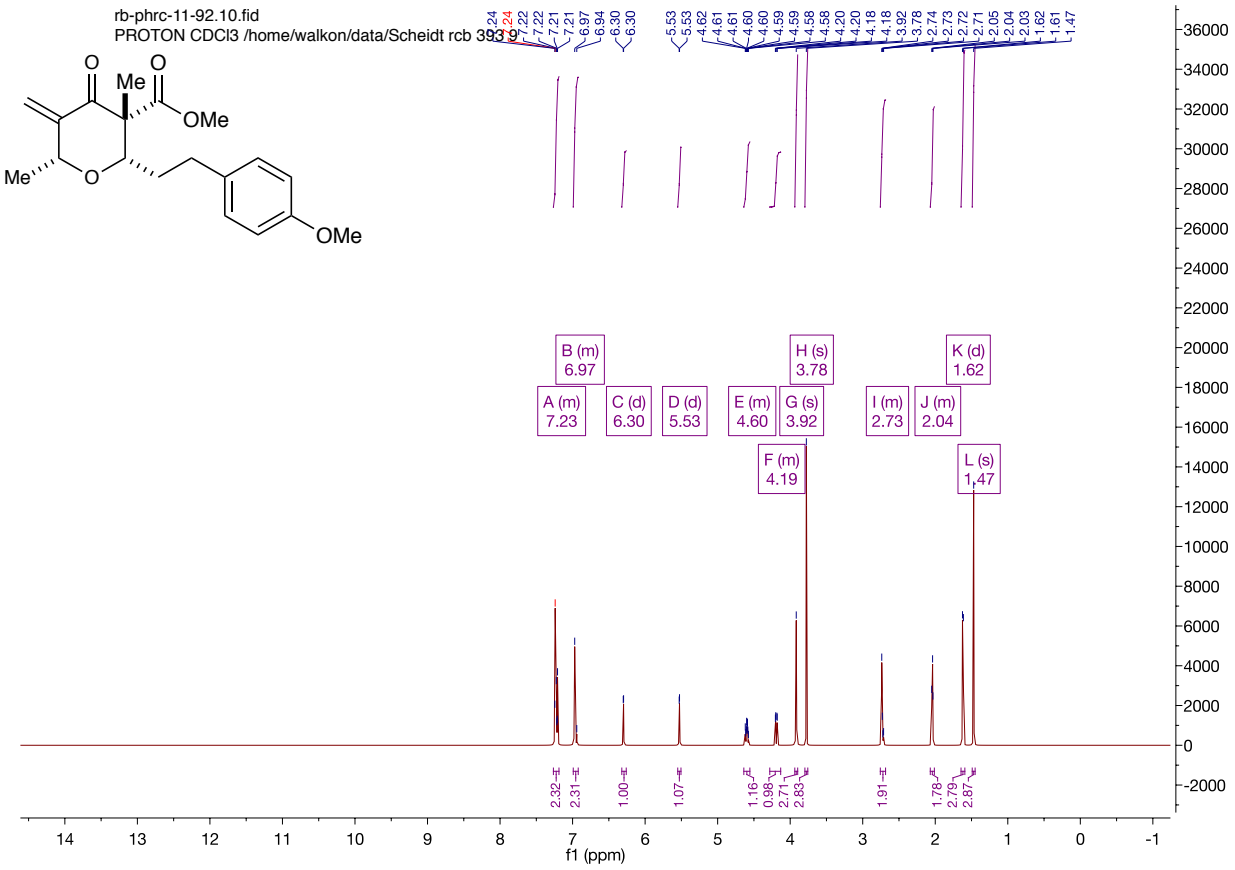

rb-phrc-11-26.10.fid
NU_C13_1
/home/walkon/data/Scheidt rcb 393 57
O
Me
O
OMe
Me
O
77.27
77.17
76.76
74.64
61.14
52.33
39.57
24.99
23.42
21.74
20.28
14.43
f1 (ppm)

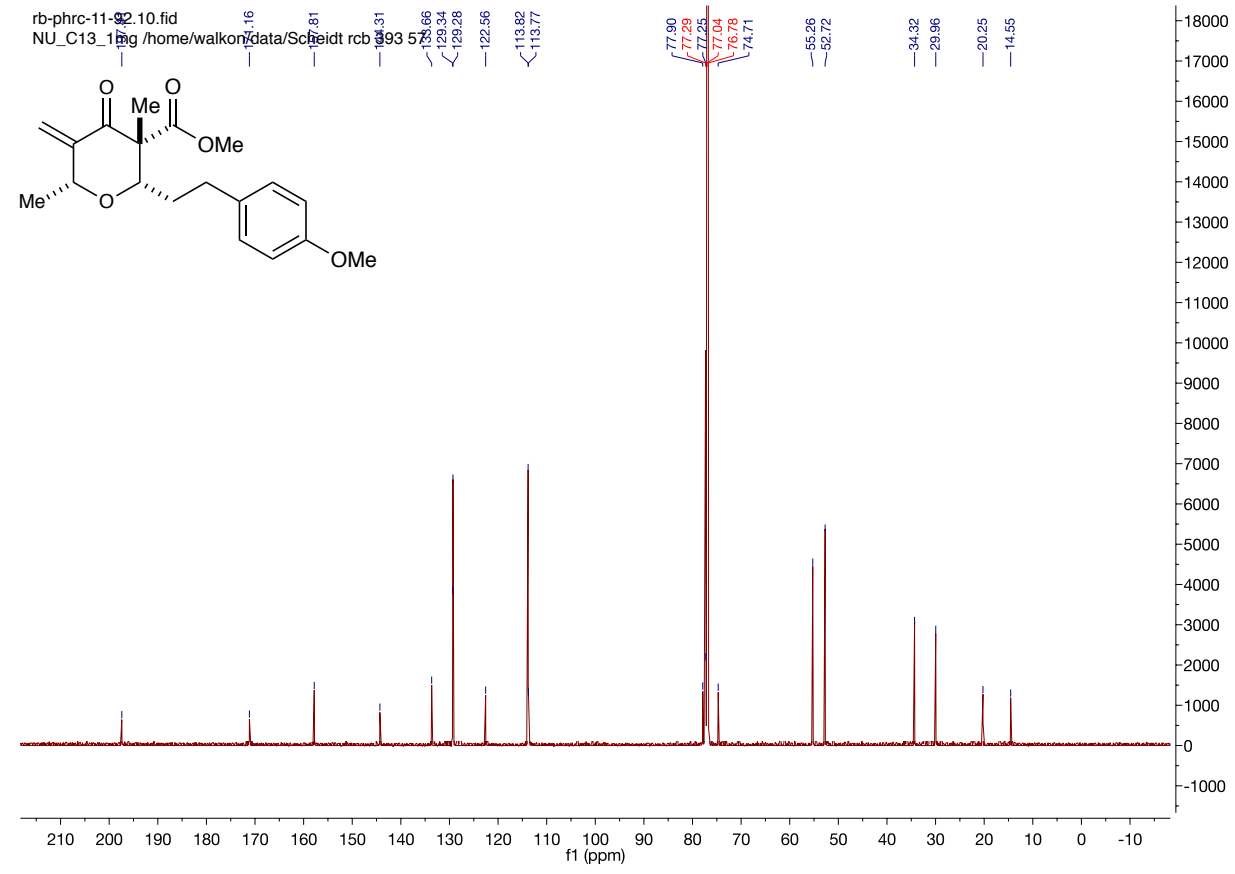

rb-phrc-11-51.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393.9
A (m) 7.27
D (d) 6.93
E (d) 6.15
G (d) 5.38
H (m) 4.44
I (m) 4.00
J (s) 3.63
K (dq) 2.87
L (m) 1.89
M (d) 1.46
N (s) 1.32
f1 (ppm)

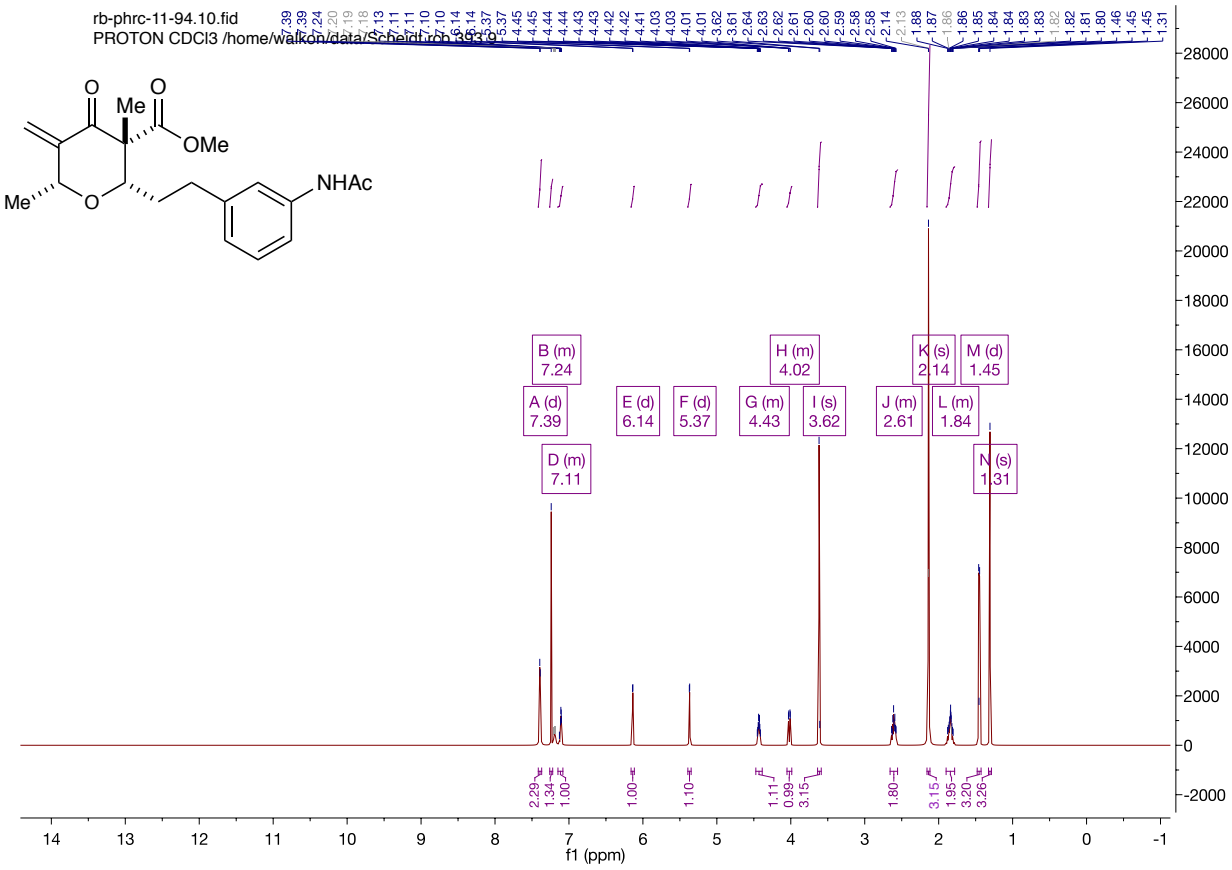

rb-phrc-11-51.10.fid
NU_C13_1mg /home/walkon/data/Scheidt rcb 393.57
f1 (ppm)

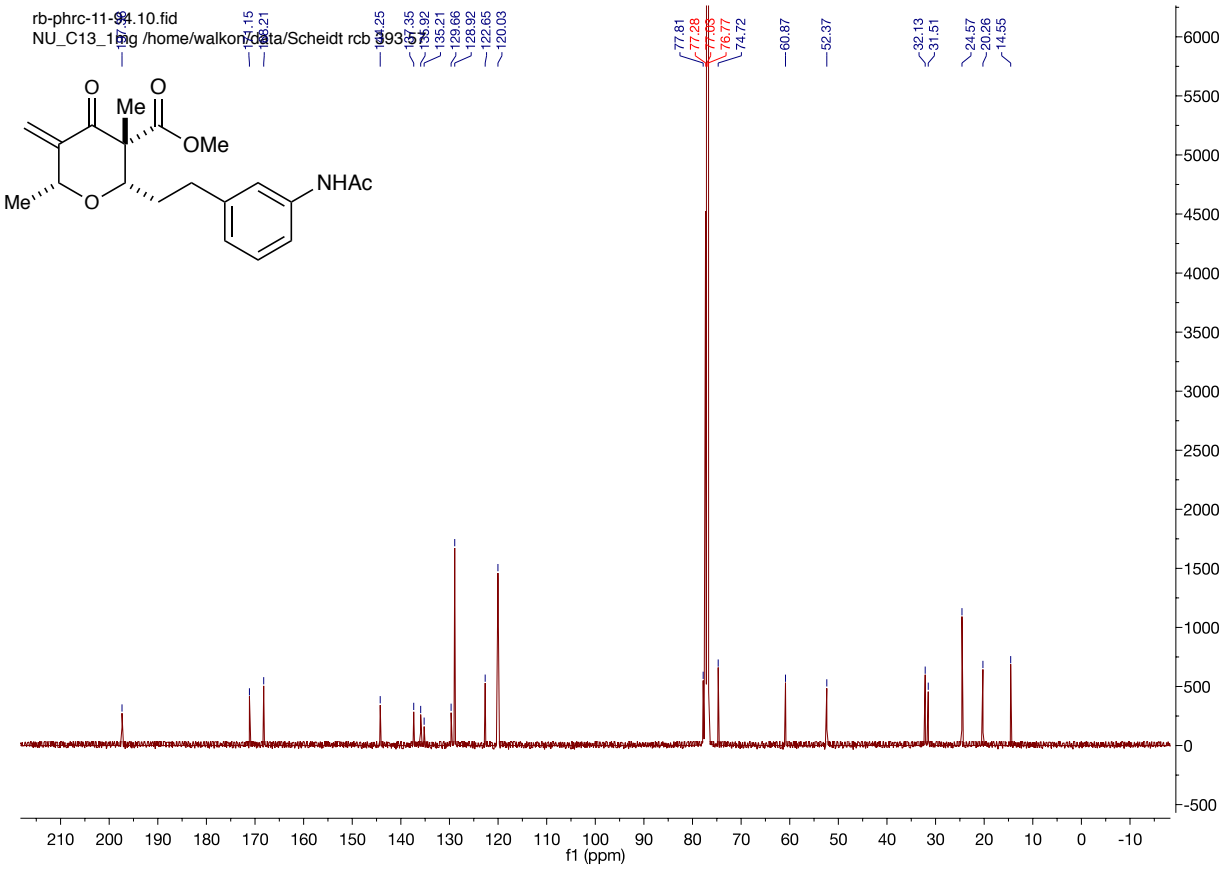

rb-phrc-11-50.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 39319
O
Me
O
OMe
Me
O
CF3
C (s) 7.23
I (m) 4.00
M (d) 1.46
A (m) 7.27
E (d) 6.15
G (d) 5.38
H (m) 4.44
J (s) 3.63
K (dq) 2.87
L (m) 1.89
D (d) 6.93
N (s) 1.32
f1 (ppm)

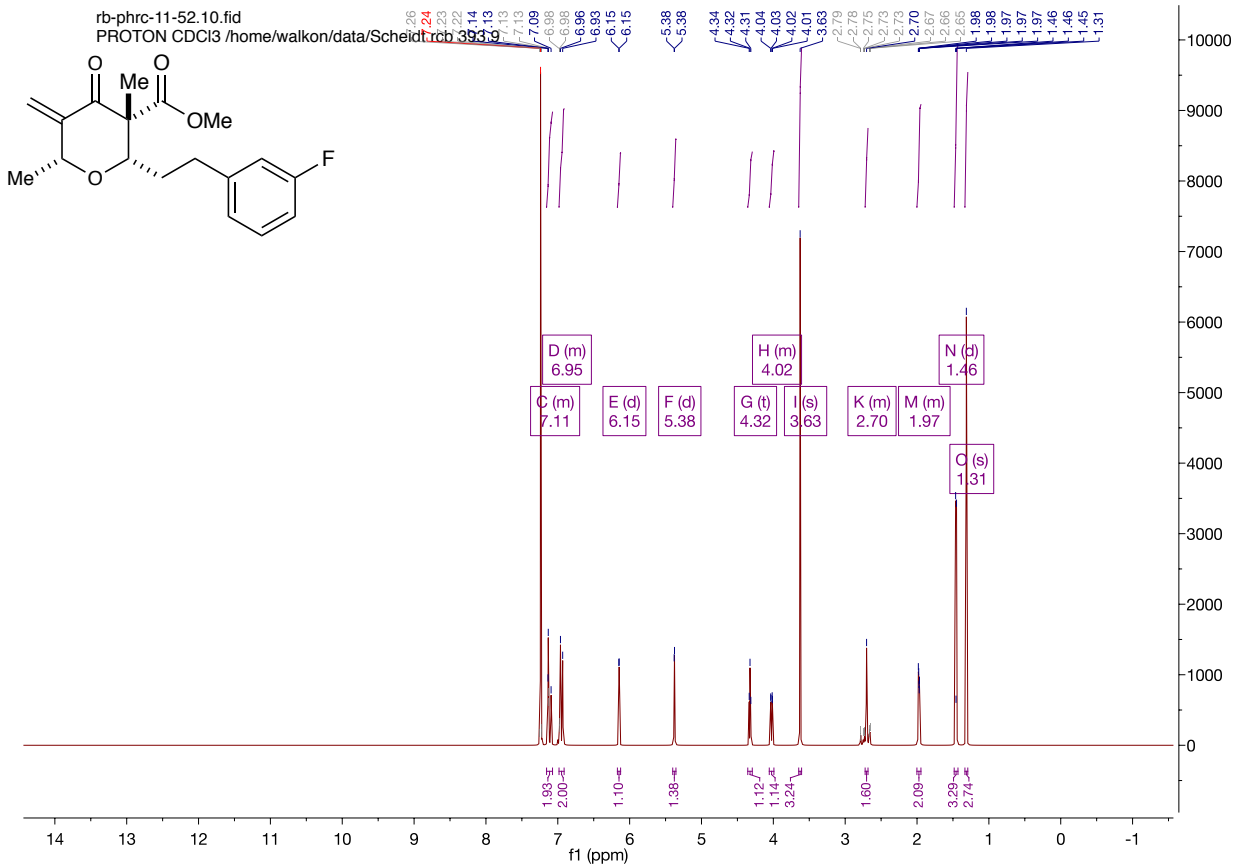

rb-phrc-11-50.10.fid
NU_C13_1prg /home/walkon/data/Scheidt rcb 39319
O
Me
O
OMe
Me
O
CF3
f1 (ppm)

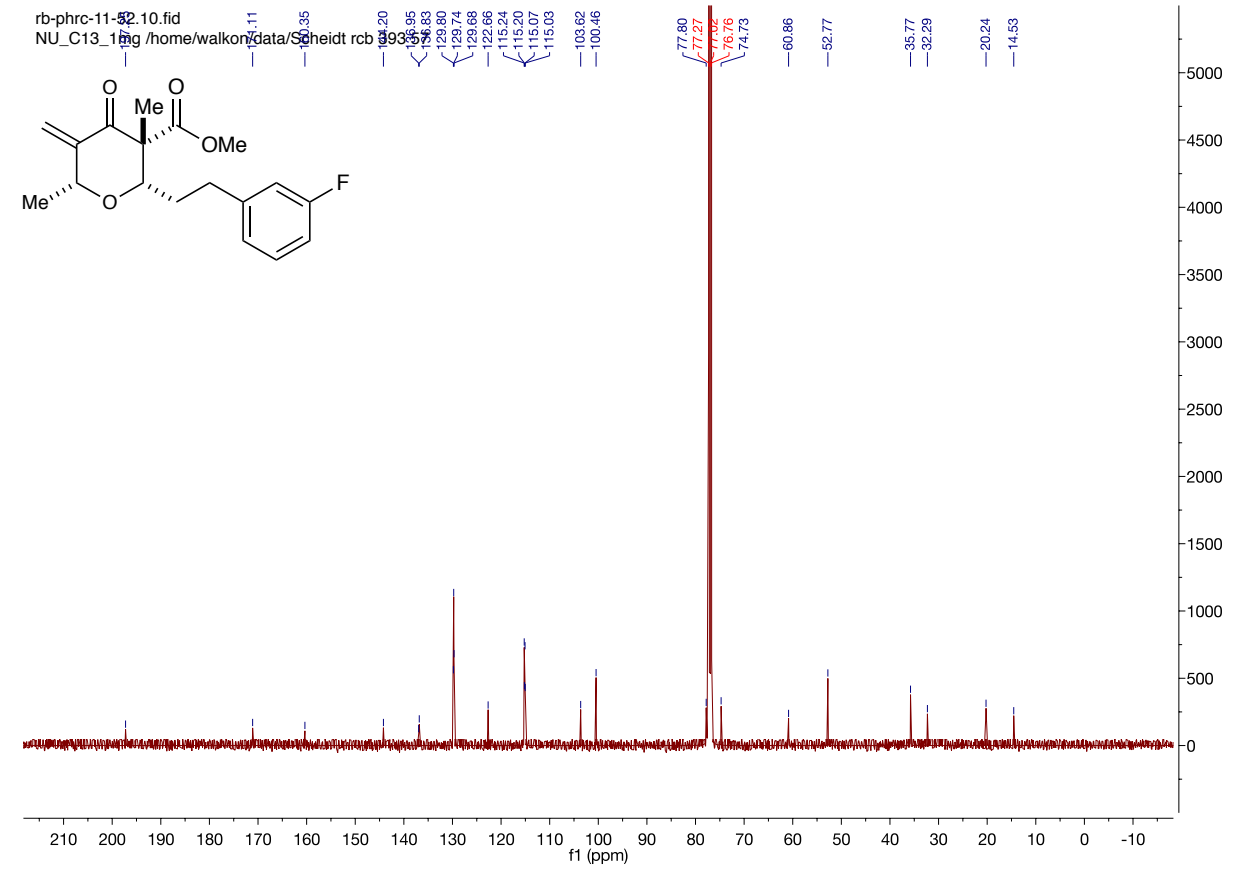

rb-phrc-11-92.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393 9
B (m) 6.97
H (s) 3.78
K (d) 1.62
A (m) 7.23
C (d) 6.30
D (d) 5.53
E (m) 4.60
G (s) 3.92
I (m) 2.73
J (m) 2.04
F (m) 4.19
L (s) 1,47
f1 (ppm)

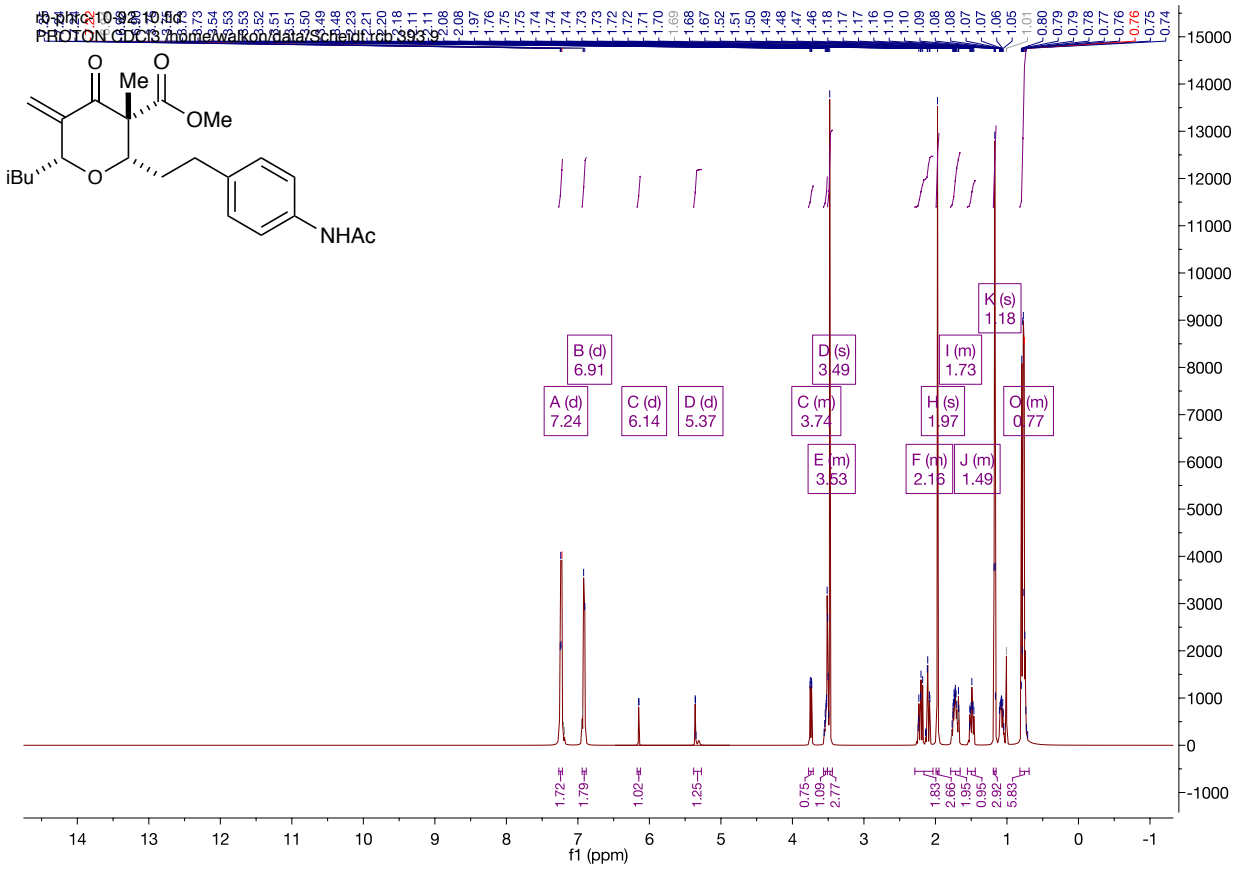

rb-phrc-11-92.10.fid
NU_C13_1mg /home/walkon/data/Scheidt rcb 393 57
f1 (ppm)

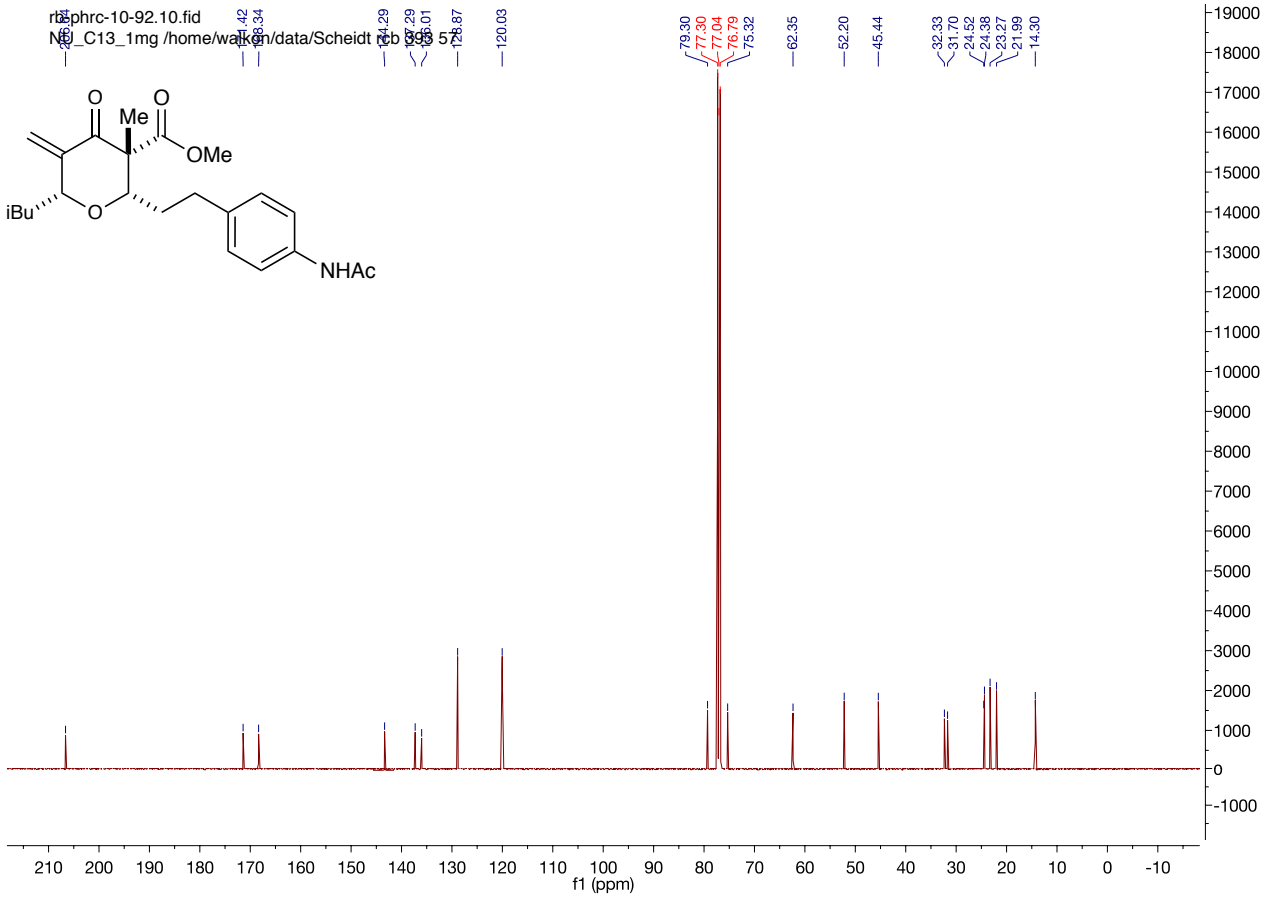

rb-phrc-11-94.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393.9
O
O
Me
OMe
Me
O
NHAc
B (m) 7.24
A (d) 7.39
E (d) 6.14
F (d) 5.37
D (m) 7.11
G (m) 4.43
H (m) 4.02
I (s) 3.62
J (m) 2.61
K (s) 2.14
L (m) 1.84
M (d) 1.45
N (s) 1.31
f1 (ppm)

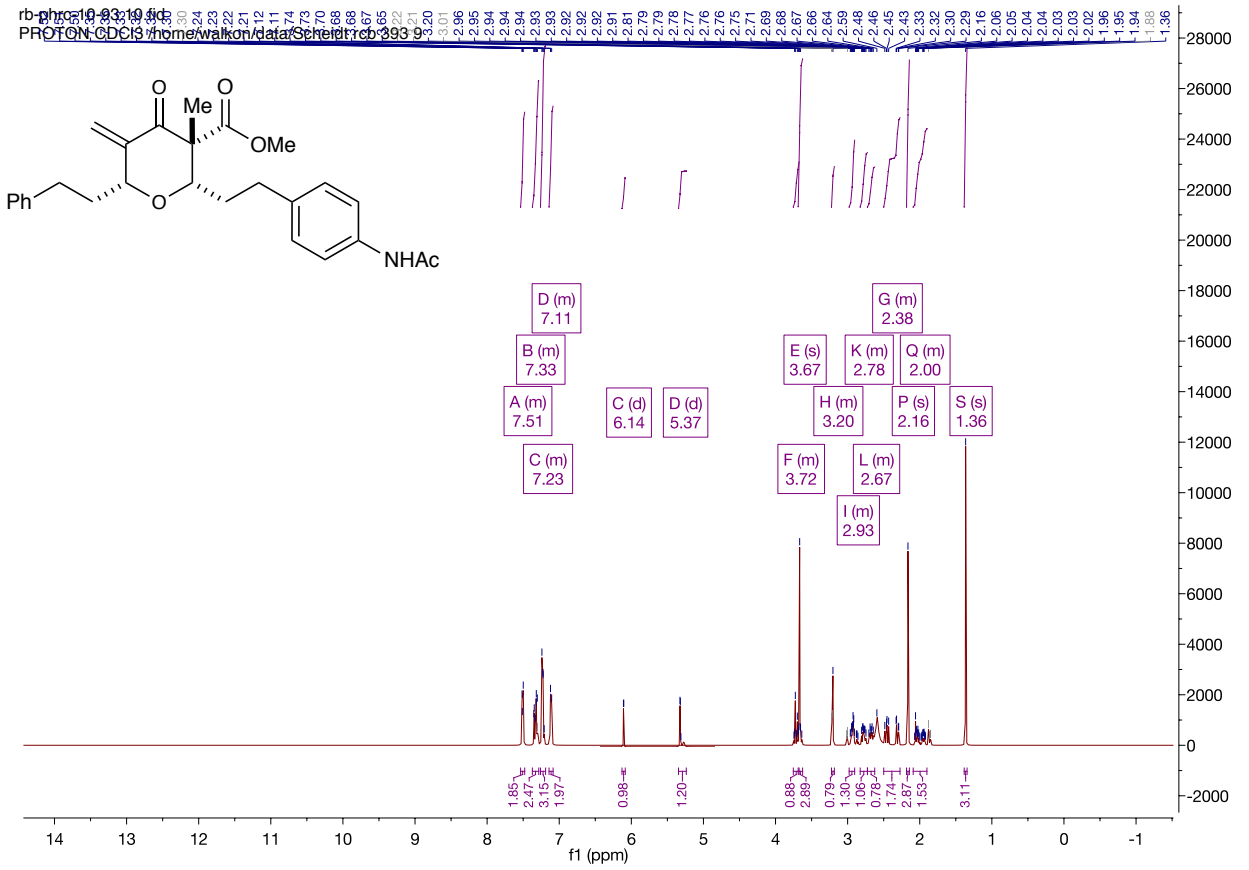

rb-phrc-11-94.10.fid
NU_C13_1mg /home/walkon/data/Scheidt rcb 393.9
O
O
Me
OMe
Me
O
NHAc
77.81
77.28
77.03
76.77
74.72
60.87
52.37
32.13
31.51
24.57
20.26
14.55
f1 (ppm)

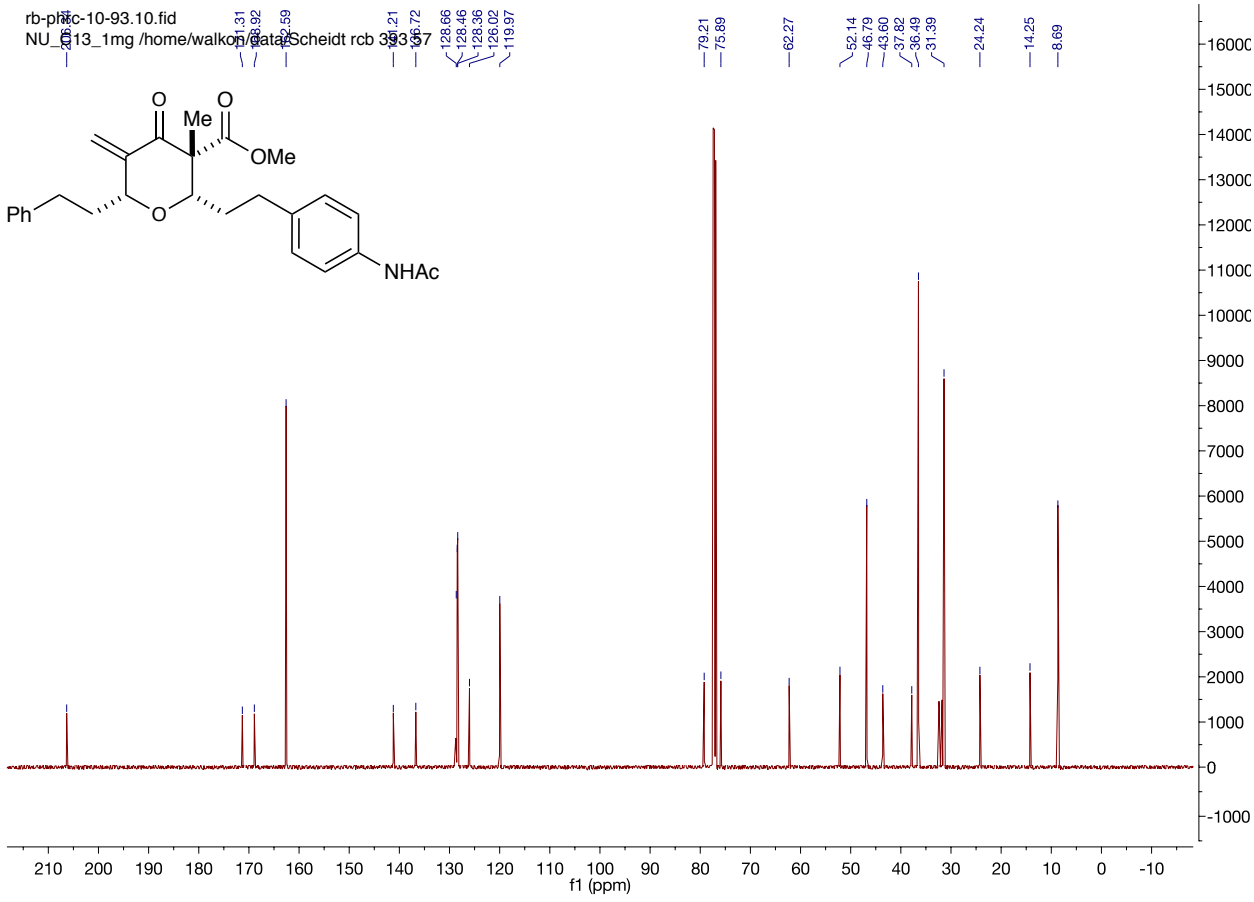

rb-phrc-11-52.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393.9
D (m) 6.95
C (m) 7.11
E (d) 6.15
F (d) 5.38
H (m) 4.02
G (t) 4.32
I (s) 3.63
K (m) 2.70
M (m) 1.97
N (d) 1.46
O (s) 1.31
f1 (ppm)

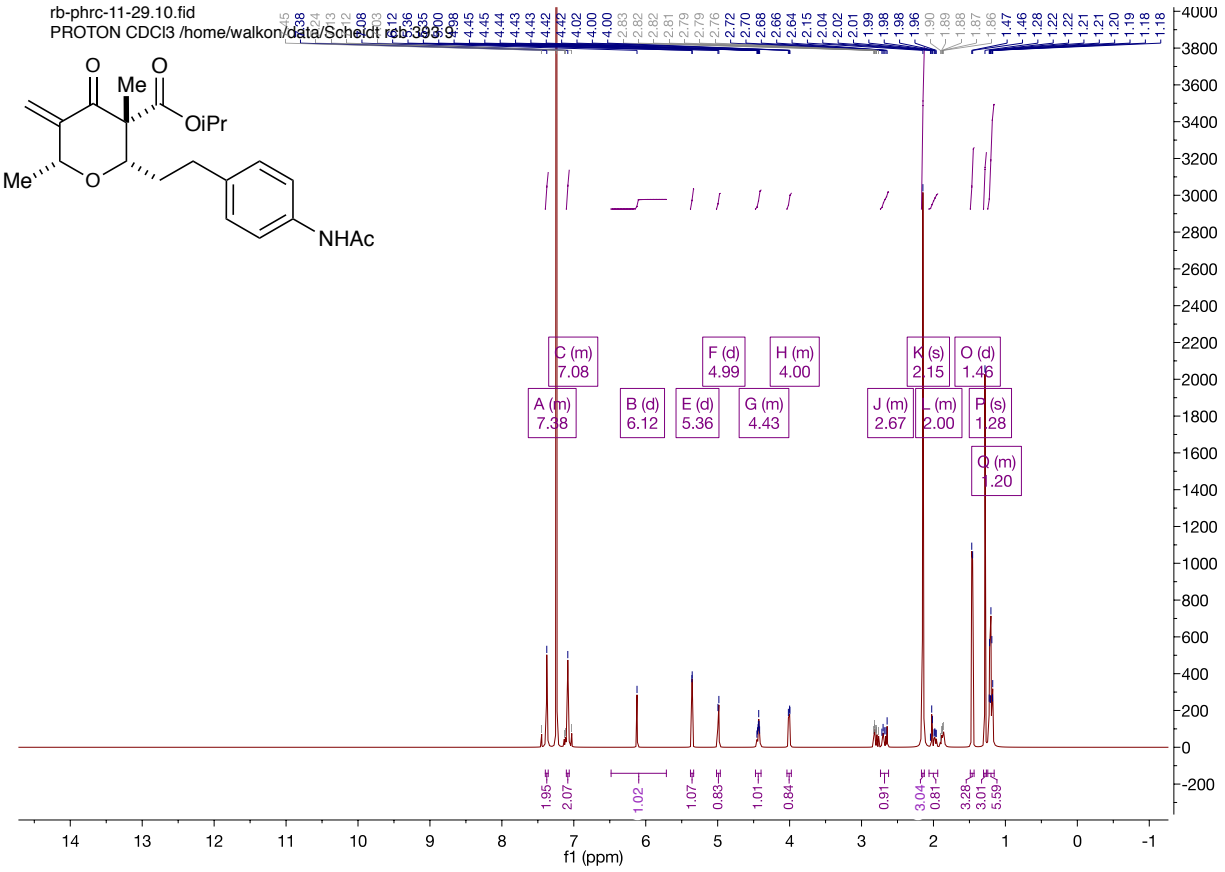

rb-phrc-11-52.10.fid
NU_C13_1mg /home/walkon/data/Scheidt rcb 393.5
f1 (ppm)

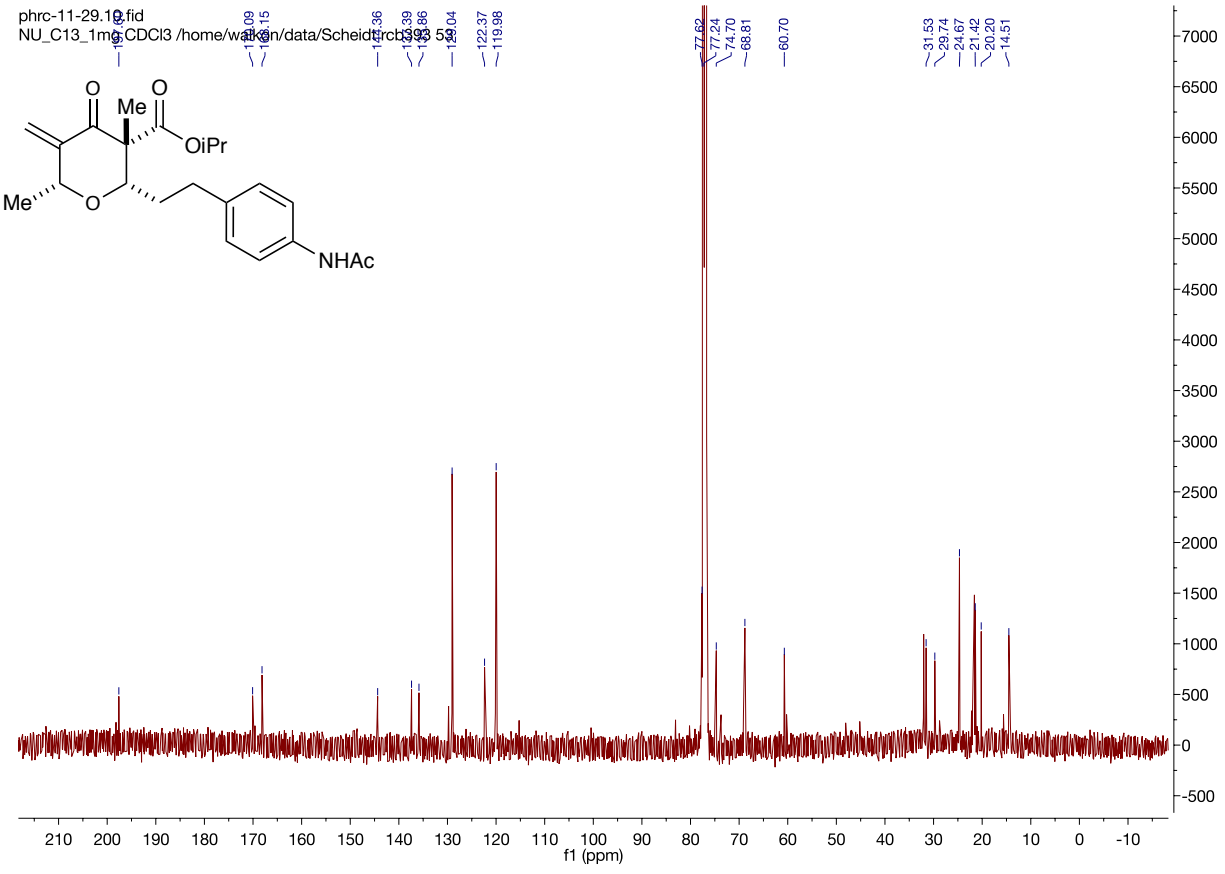

rb-phrc-10-92.10.fid
PROTON GDCI3 /home/walkon/data/Scheidt rcb 393.9
O
Me
O
OMe
iBu
O
NHAc
A (d) 7.24
B (d) 6.91
C (d) 6.14
D (d) 5.37
C (m) 3.74
D (s) 3.49
E (m) 3.53
F (m) 2.15
H (s) 1.97
I (m) 1.73
J (m) 1.49
K (s) 1.18
O (m) 0.77
f1 (ppm)

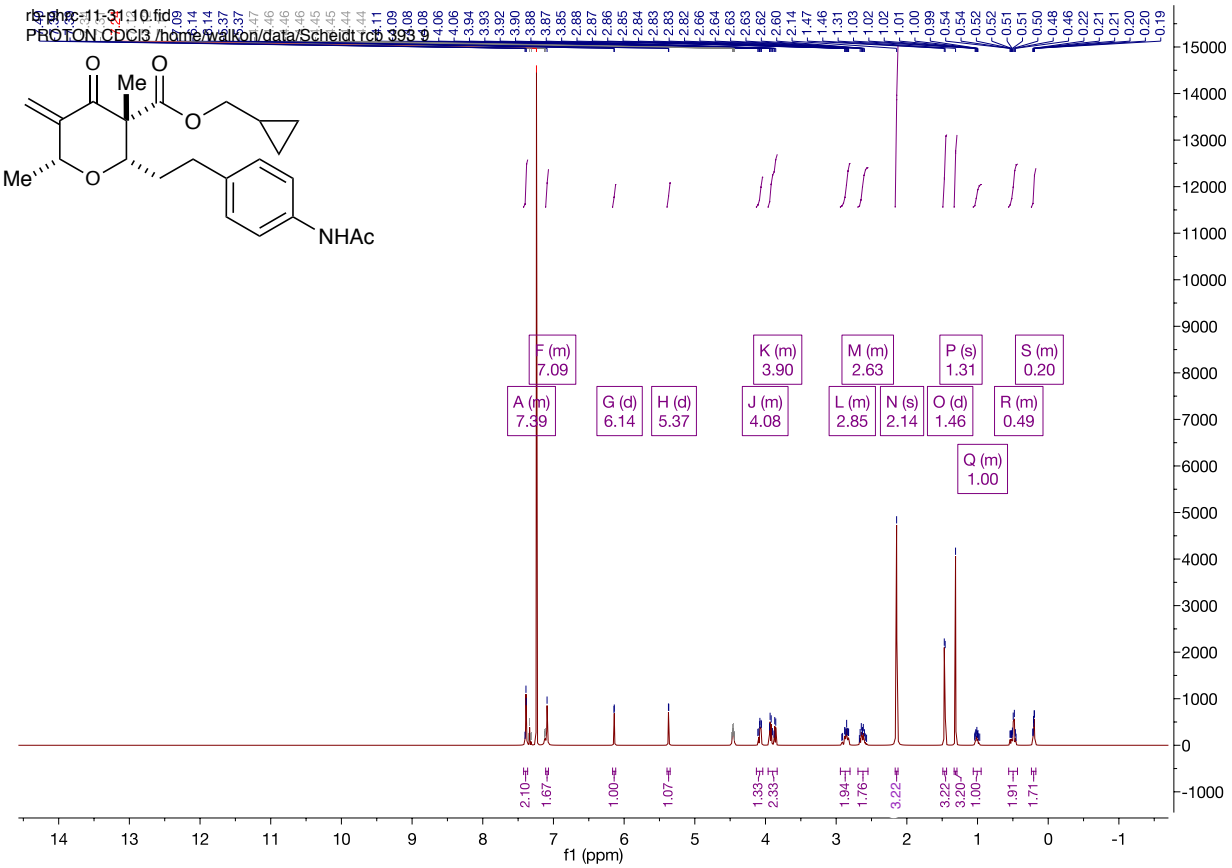

rb-phrc-10-92.10.fid
NEU_C13_1mg /home/walkon/data/Scheidt rcb 393 57
O
Me
O
OMe
iBu
O
NHAc
f1 (ppm)

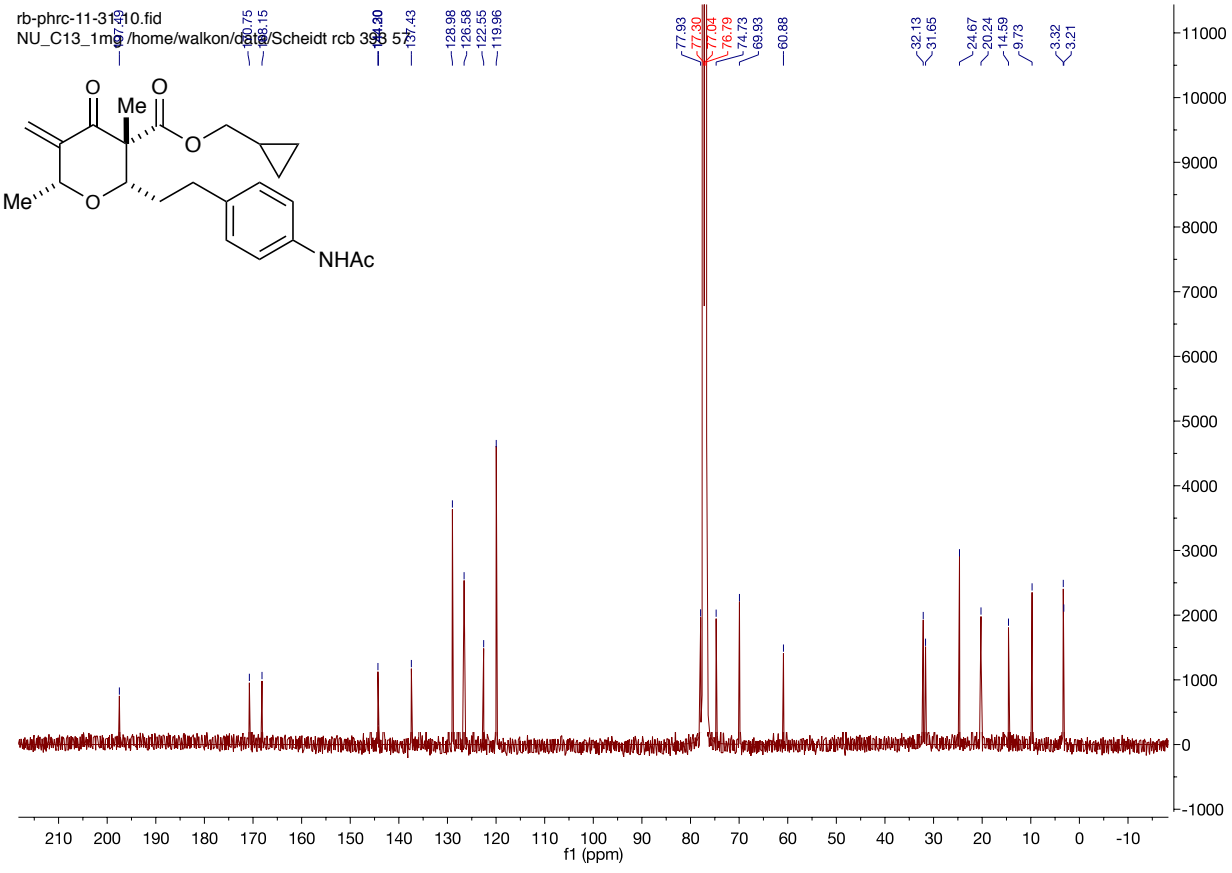

rb-phxc-10-93.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393 9
O
Me
O
OMe
Ph
O
NHAc
D (m) 7.11
B (m) 7.33
A (m) 7.51
C (m) 7.23
C (d) 6.14
D (d) 5.37
G (m) 2.38
E (s) 3.67
K (m) 2.78
Q (m) 2.00
H (m) 3.20
P (s) 2.16
S (s) 1.36
F (m) 3.72
L (m) 2.67
I (m) 2.93
f1 (ppm)

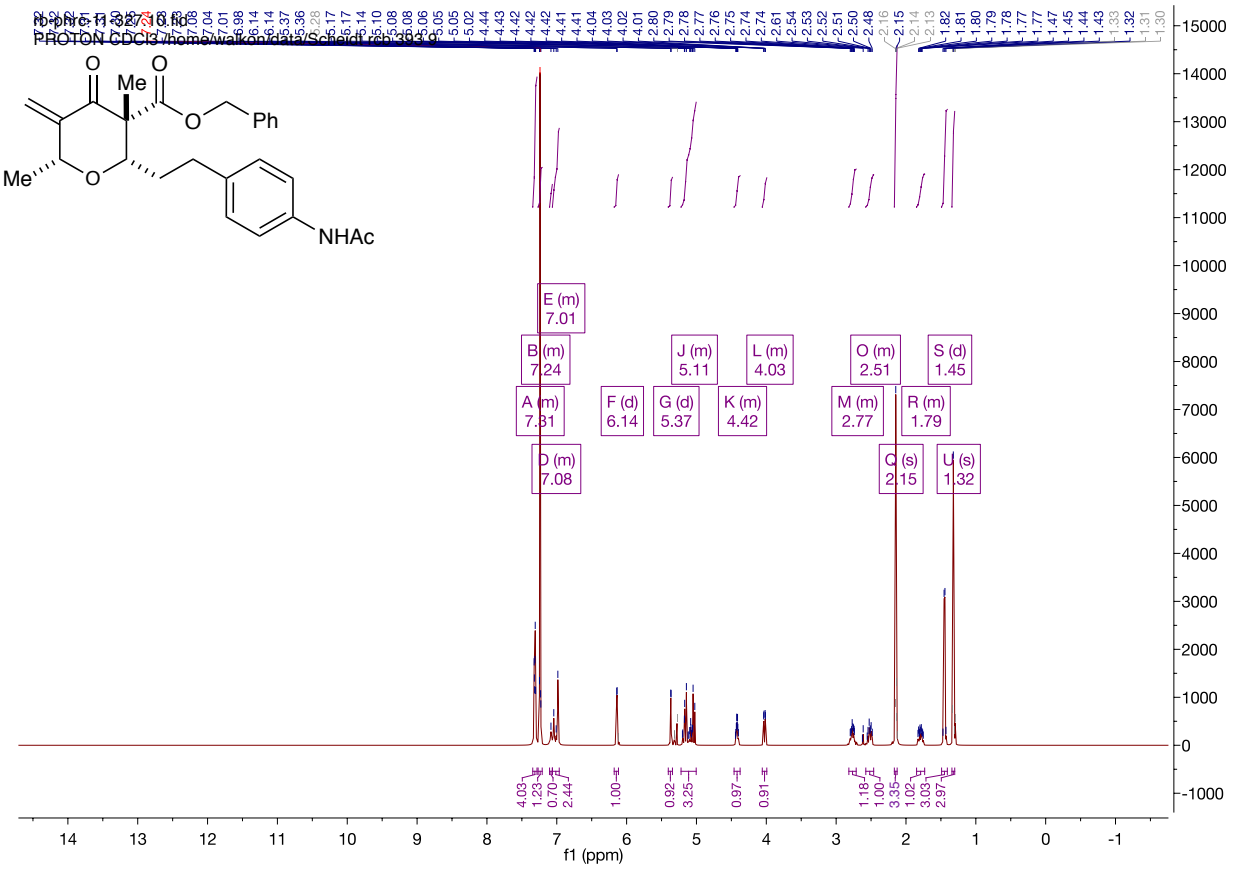

rb-phxc-10-93.10.fid
NU_213_1mg /home/walkon/data/Scheidt rcb 393 57
O
Me
O
OMe
Ph
O
NHAc
79.21
75.89
62.27
52.14
46.79
43.60
37.82
36.49
31.39
24.24
14.25
8.89
f1 (ppm)

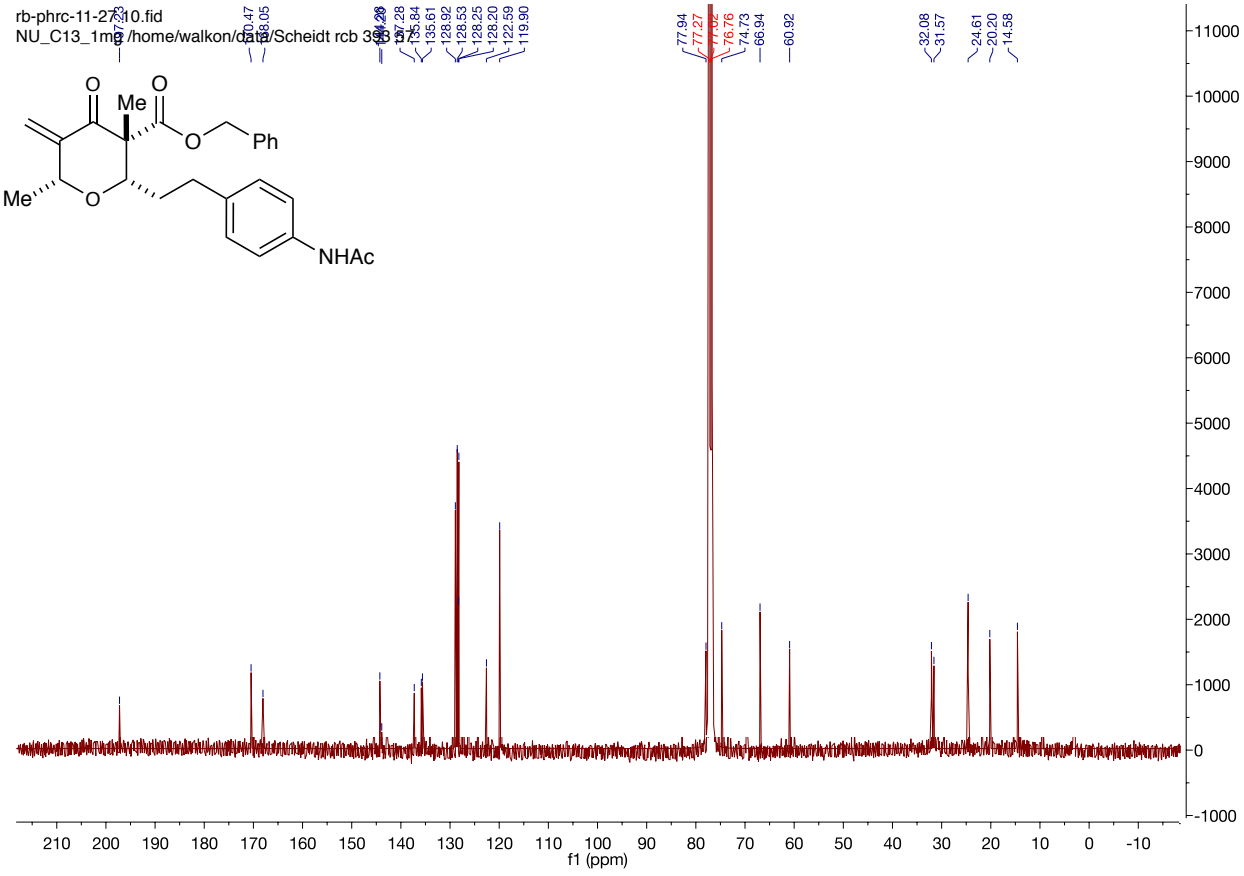

rb-phrc-11-29.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393 5
Me
O
O
OiPr
Me
O
NHAc
C (m) 7.08
A (m) 7.38
B (d) 6.12
E (d) 5.36
F (d) 4.99
G (m) 4.43
H (m) 4.00
J (m) 2.67
K (s) 2.15
L (m) 2.00
O (d) 1.46
P (s) 1.28
Q (m) 1.20
f1 (ppm)

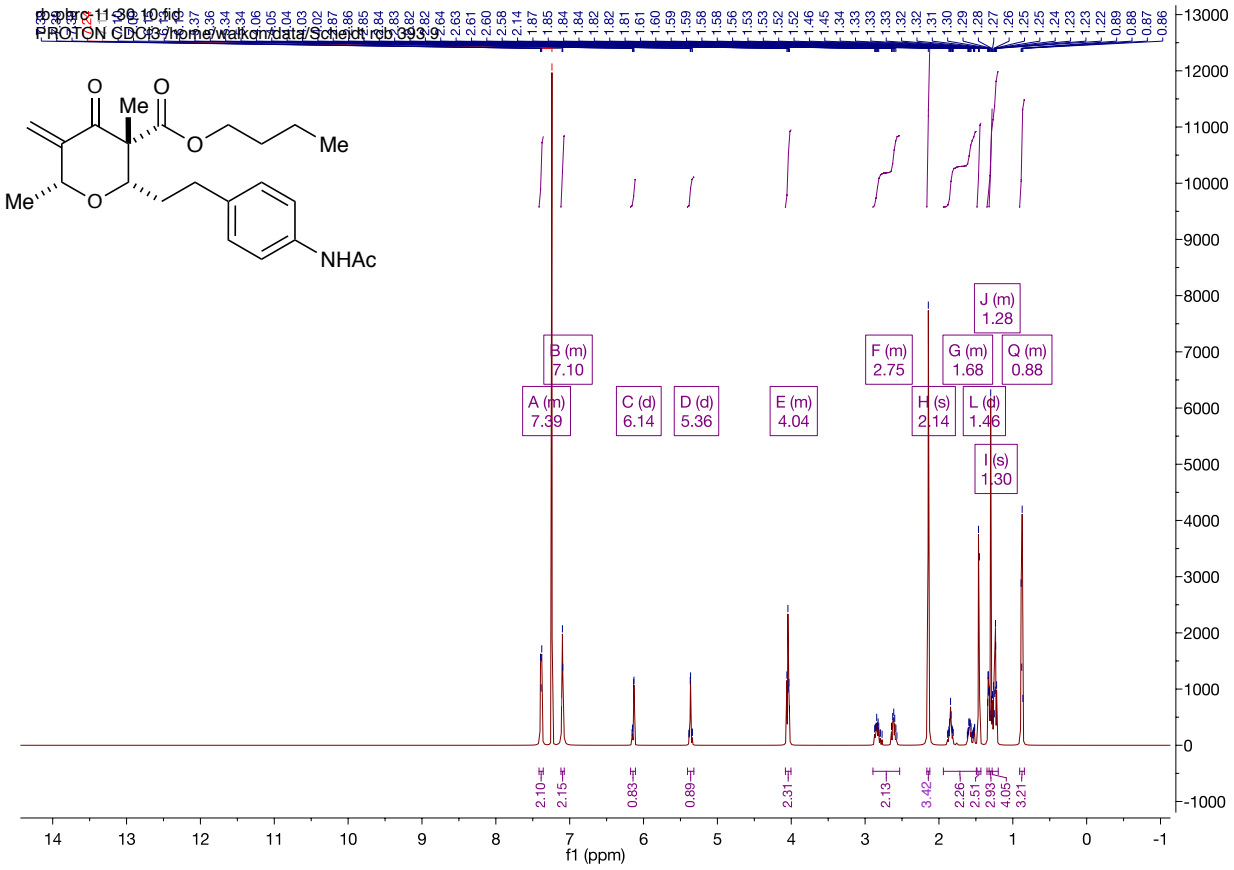

phrc-11-29.10.fid
NU_C13_1mg CDCl3 /home/walkon/data/Scheidt rcb 393 5
Me
O
O
OiPr
Me
O
NHAc
77.62
77.24
74.70
68.81
60.70
31.53
29.74
24.67
21.42
20.20
14.51
f1 (ppm)

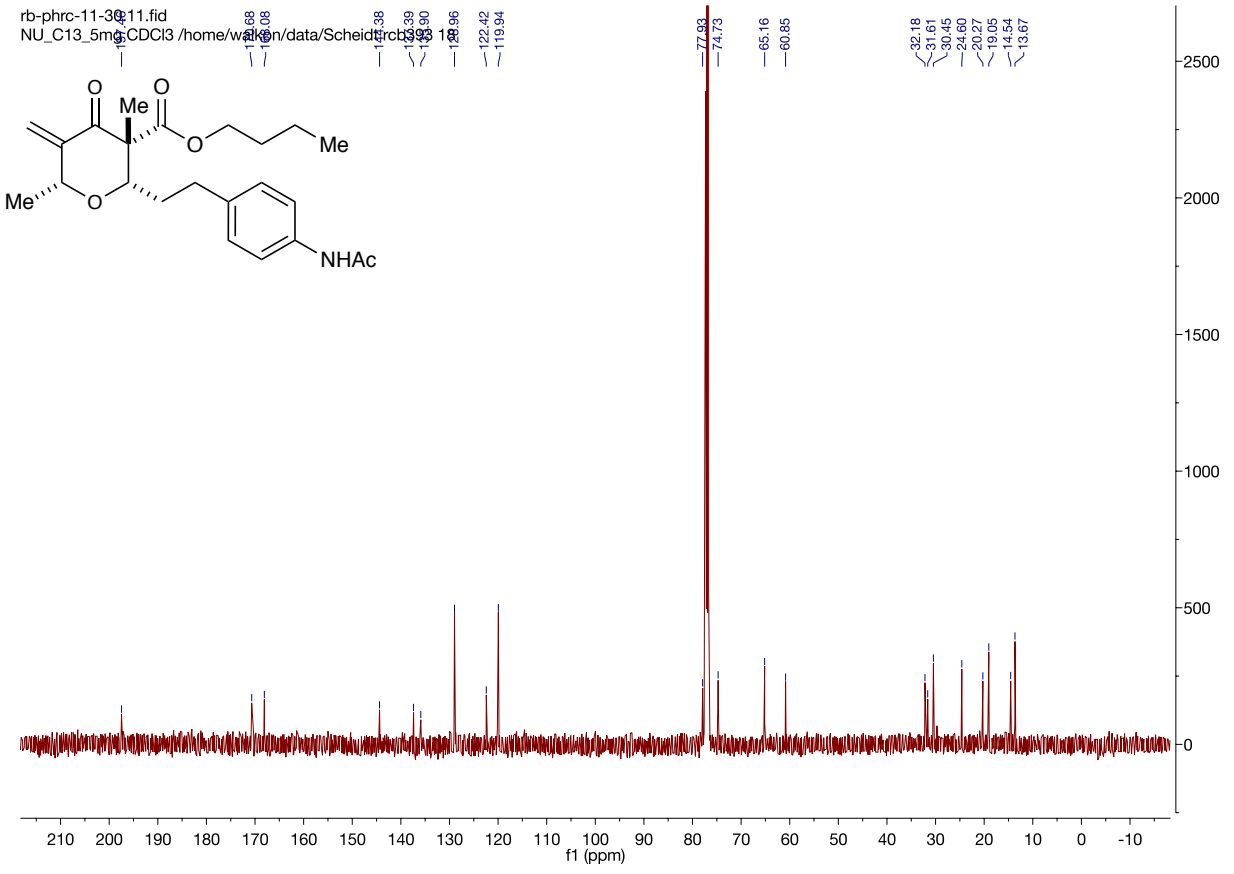

rb-phrc-11-3110.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393 9
Me
O
O
Me
O
O
NHAc
F (m) 7.09
A (m) 7.39
G (d) 6.14
H (d) 5.37
K (m) 3.90
J (m) 4.08
M (m) 2.63
L (m) 2.85
N (s) 2.14
P (s) 1.31
O (d) 1.46
S (m) 0.20
R (m) 0.49
Q (m) 1.00
f1 (ppm)

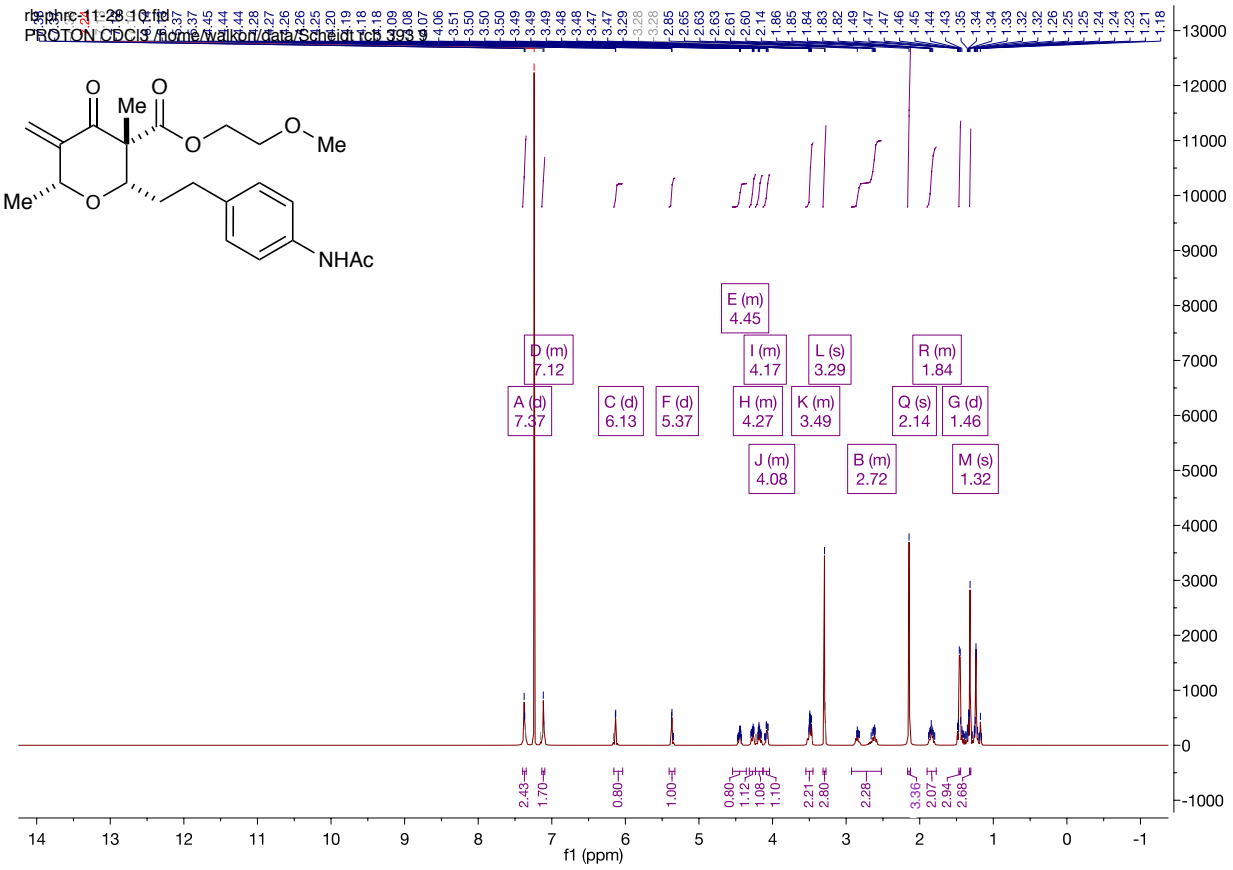

rb-phrc-11-3110.fid
NU_C13_1mg /home/walkon/data/Scheidt rcb 393 57
Me
O
O
Me
O
O
NHAc
f1 (ppm)

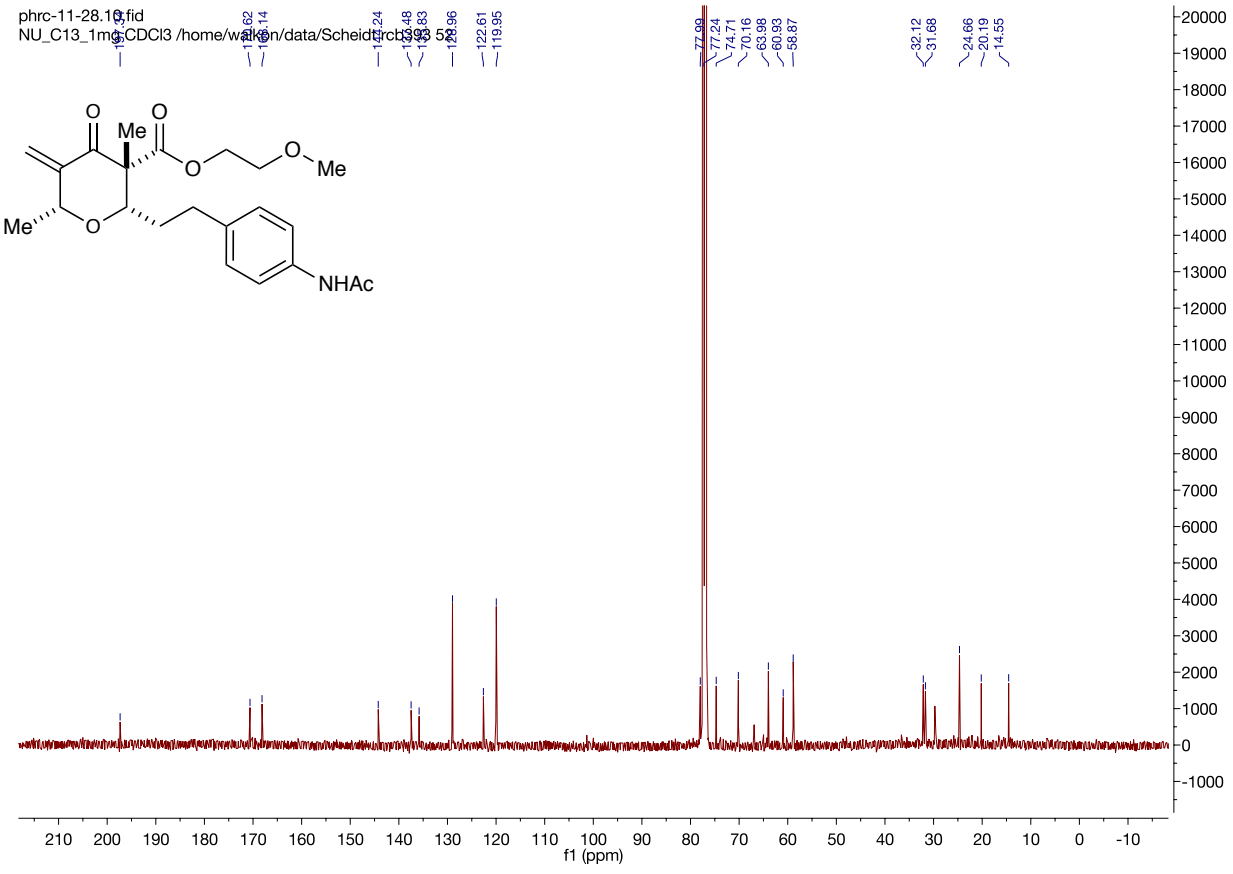

rb-phrc-11-27-10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393 5
Me
O
O
Ph
Me
O
NHAc
E (m) 7.01
B (m) 7.24
A (m) 7.31
D (m) 7.08
F (d) 6.14
J (m) 5.11
G (d) 5.37
L (m) 4.03
K (m) 4.42
O (m) 2.51
M (m) 2.77
S (d) 1.45
R (m) 1.79
Q (s) 2.15
U (s) 1.32
f1 (ppm)

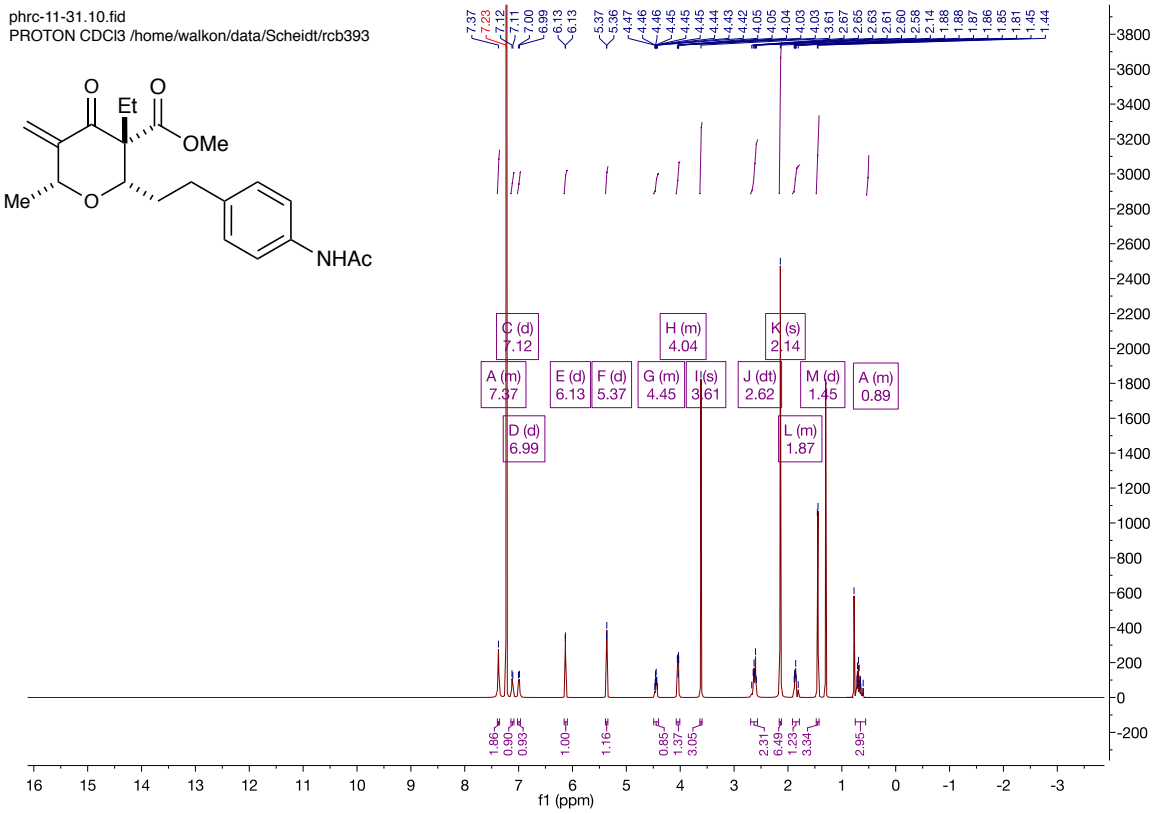

rb-phrc-11-27-10.fid
NU_C13_1mg /home/walkon/data/Scheidt rcb 393 5
Me
O
O
Ph
Me
O
NHAc
f1 (ppm)

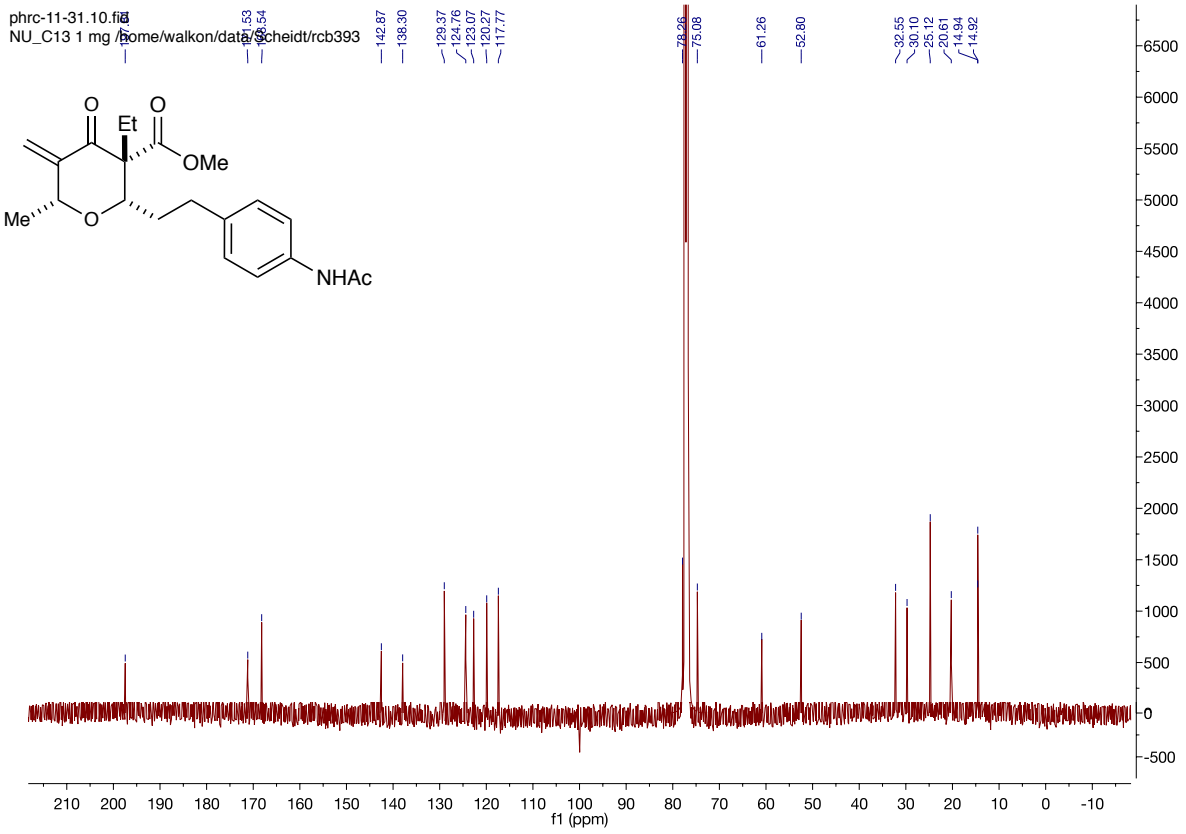

rb-phrc-11-30.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt/rcb393.9
Me
O
O
Me
O
Me
O
NHAc
A (m) 7.39
B (m) 7.10
C (d) 6.14
D (d) 5.36
E (m) 4.04
F (m) 2.75
G (m) 1.68
H (s) 2.14
I (s) 1.30
J (m) 1.28
L (d) 1.46
Q (m) 0.88
f1 (ppm)

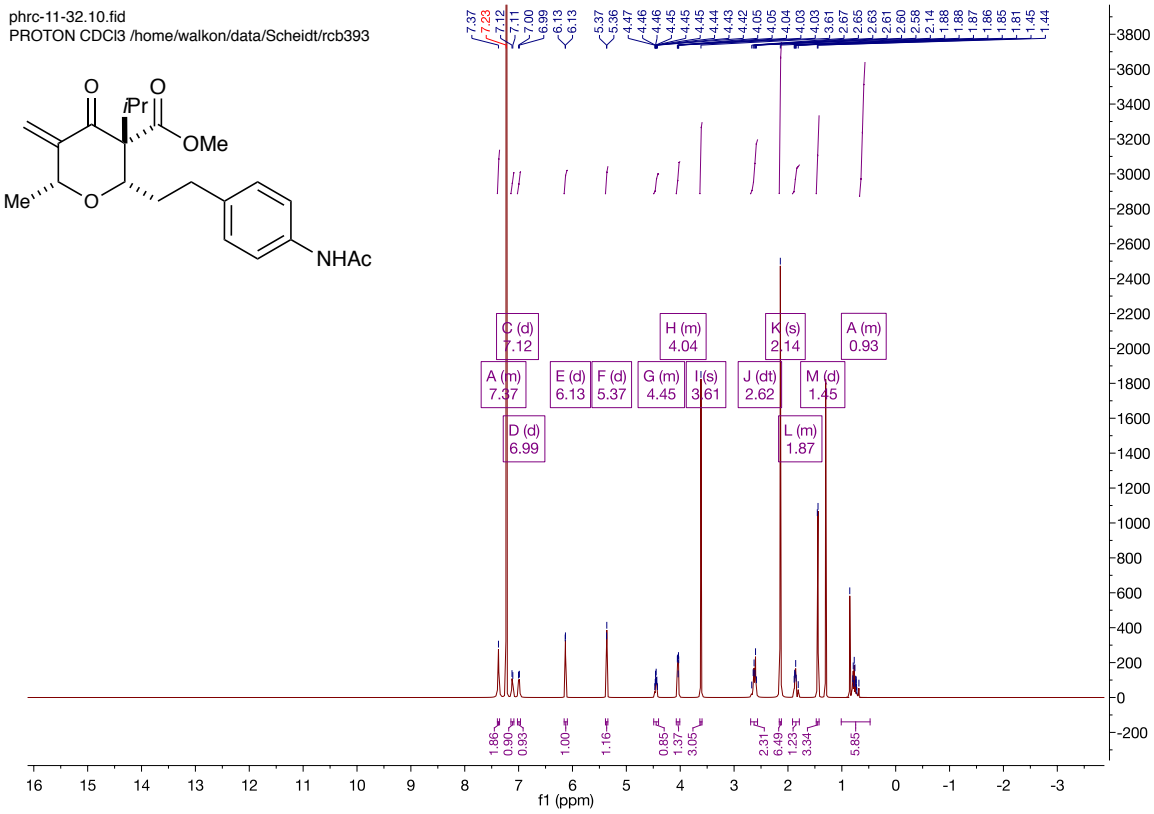

rb-phrc-11-30.11.fid
NU_C13_5mg CDCl3 /home/walkon/data/Scheidt/rcb393.10
Me
O
O
Me
O
Me
O
NHAc
77.93
74.73
65.16
60.85
32.18
31.61
30.45
24.60
20.27
19.05
14.54
13.67
f1 (ppm)

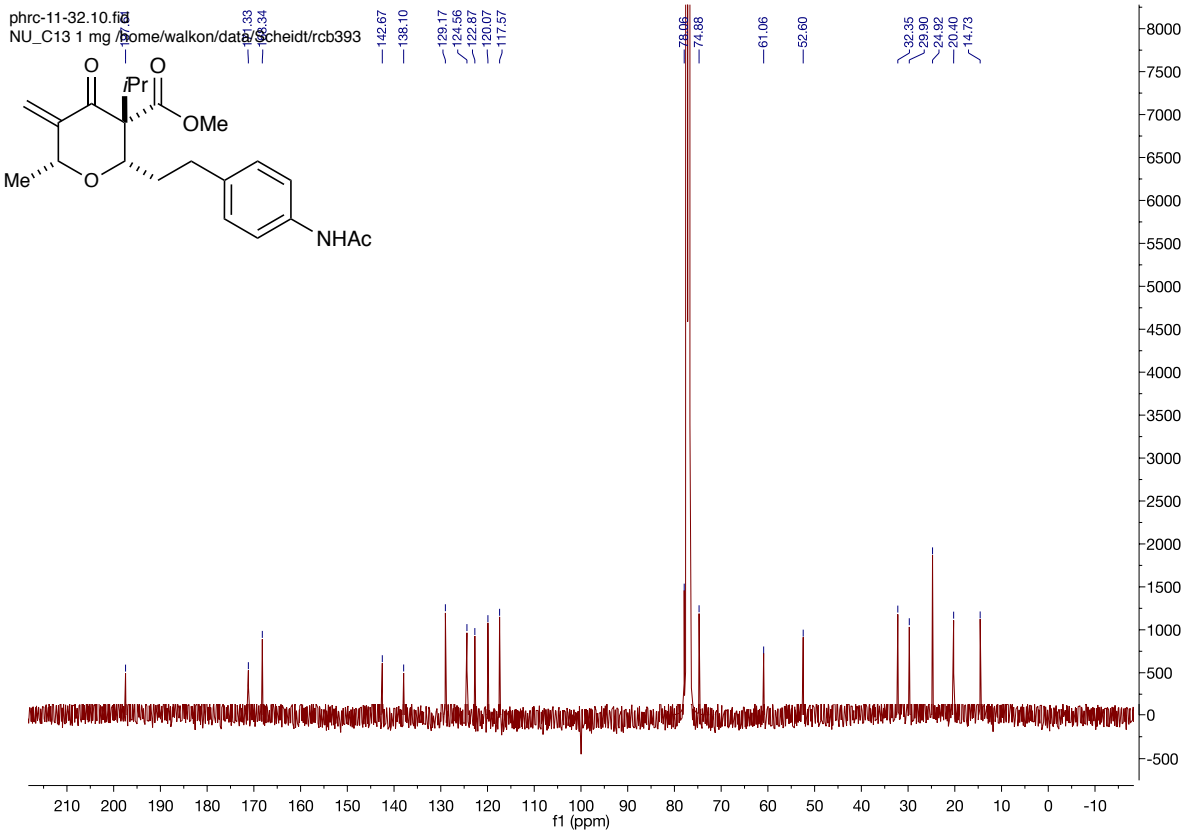

rbphrc-11-28.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rcb 393 9
O
O
Me
O
O
Me
Me
O
NHAc
E (m)
4.45
D (m)
7.12
I (m)
4.17
L (s)
3.29
R (m)
1.84
A (d)
7.37
C (d)
6.13
F (d)
5.37
H (m)
4.27
K (m)
3.49
Q (s)
2.14
G (d)
1.46
J (m)
4.08
B (m)
2.72
M (s)
1.32
2.43
1.70
0.80
1.00
0.80
1.12
1.08
1.10
2.21
2.80
2.28
3.36
2.07
2.94
2.68
f1 (ppm)

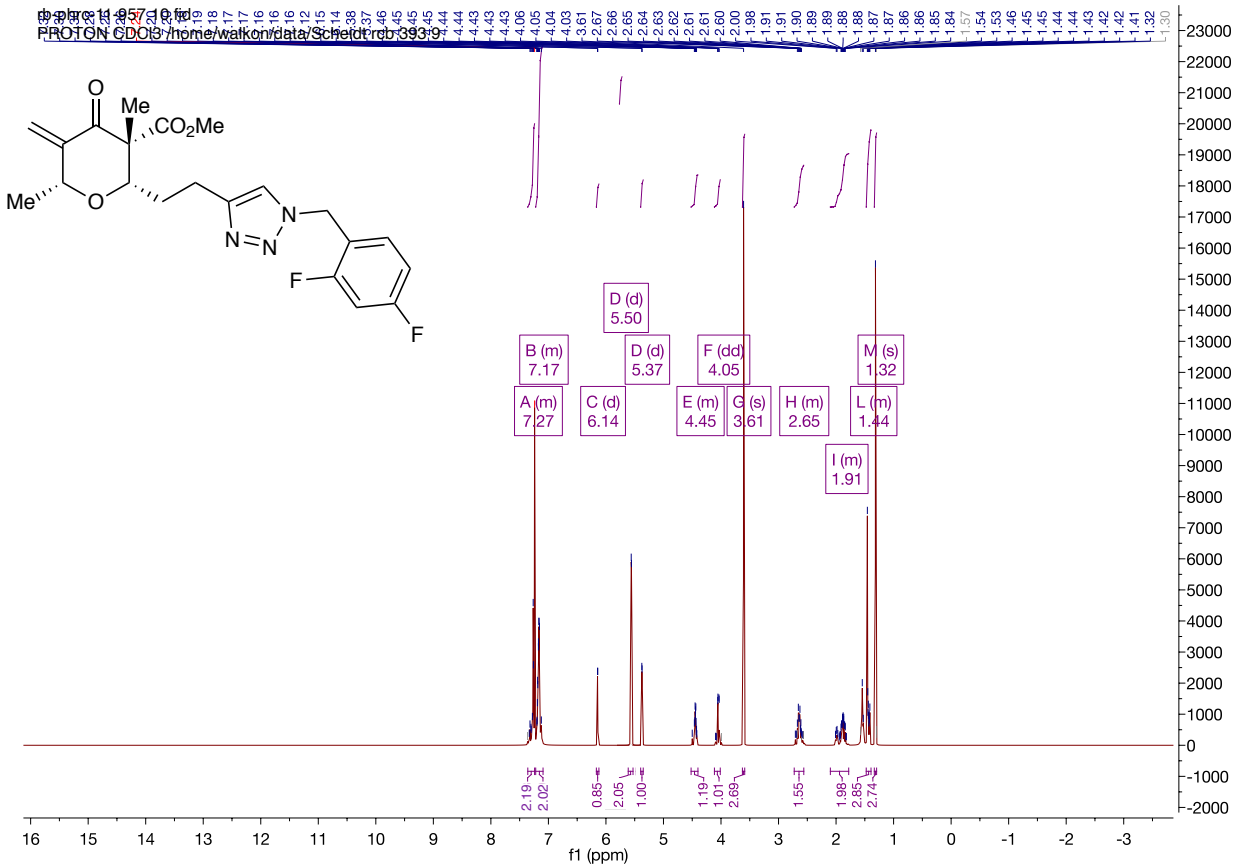

phrc-11-28.10.fid
NU_C13_1mg CDCl3 /home/walkon/data/Scheidt rcb 393 52
O
O
Me
O
O
Me
Me
O
NHAc
77.99
77.24
74.71
70.16
63.98
60.93
58.87
32.12
31.68
24.66
20.19
14.55
f1 (ppm)

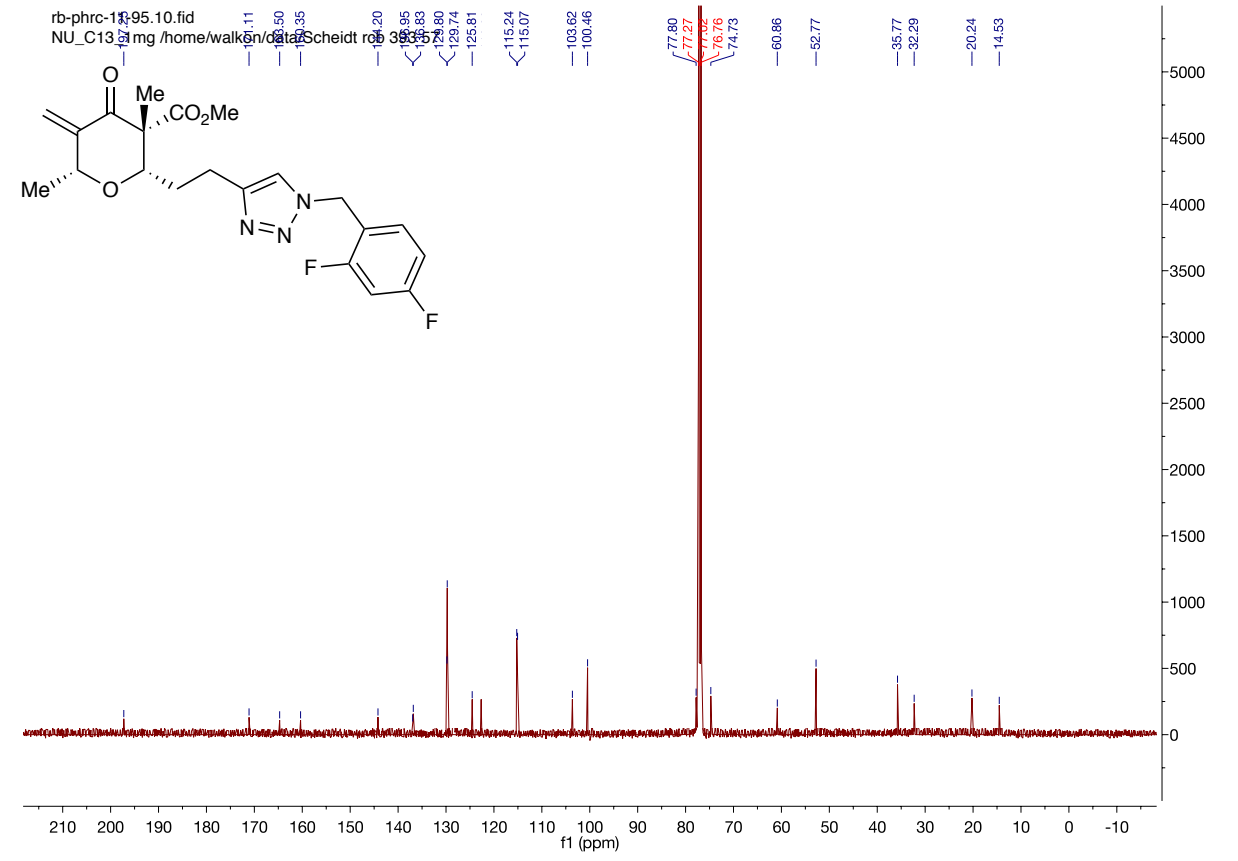

phrc-11-31.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt/rcb393
Et
OMe
Me
NHAc
C (d) 7.12
H (m) 4.04
K (s) 2.14
A (m) 7.37
E (d) 6.13
F (d) 5.37
G (m) 4.45
I (s) 3.61
J (dt) 2.62
M (d) 1.45
A (m) 0.89
D (d) 6.99
L (m) 1.87
f1 (ppm)


phrc-11-31.10.fid
NU_C13 1 mg /home/walkon/data/Scheidt/rcb393
Et
OMe
Me
NHAc
f1 (ppm)


phrc-11-32.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt/rcb393
iPr
OMe
Me
NHAc
C (d) 7.12
H (m) 4.04
K (s) 2.14
A (m) 0.93
A (m) 7.37
E (d) 6.13
F (d) 5.37
G (m) 4.45
I (s) 3.61
J (dt) 2.62
M (d) 1.45
D (d) 6.99
L (m) 1.87
f1 (ppm)


phrc-11-32.10.fid
NU_C13 1 mg /home/walkon/data/Scheidt/rcb393
iPr
OMe
Me
NHAc
142.67
138.10
129.17
124.56
122.87
120.07
117.57
78.06
74.88
61.06
52.60
32.35
29.90
24.92
20.40
14.73
f1 (ppm)


rb-phrc-11-95.10.fid
PROTON CDCl3 /home/walkon/data/Scheidt rob 393 9
O
Me
CO2Me
Me
O
N
N
N
F
F
D (d)
5.50
B (m)
7.17
D (d)
5.37
F (dd)
4.05
M (s)
1.32
A (m)
7.27
C (d)
6.14
E (m)
4.45
G (s)
3.61
H (m)
2.65
L (m)
1.44
I (m)
1.91
2.19
2.02
0.85
2.05
1.00
1.19
1.01
2.69
1.55
1.98
2.85
2.74
f1 (ppm)


rb-phrc-11-95.10.fid
NU_C13_1 mg /home/walkon/data/Scheidt rob 393 9
O
Me
CO2Me
Me
O
N
N
N
F
F
77.80
77.27
76.76
74.73
60.86
52.77
35.77
32.29
20.24
14.53
f1 (ppm)

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