Supplementary Information

Regioselective synthesis of densely functionalized, enantiopure, sugar-pyrazole hybrids as potential scaffolds for drug discovery

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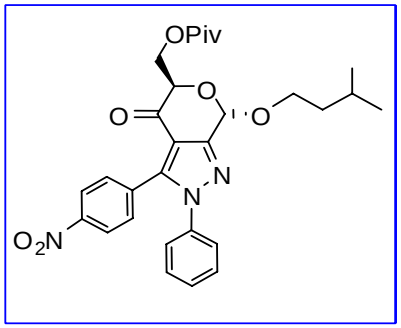
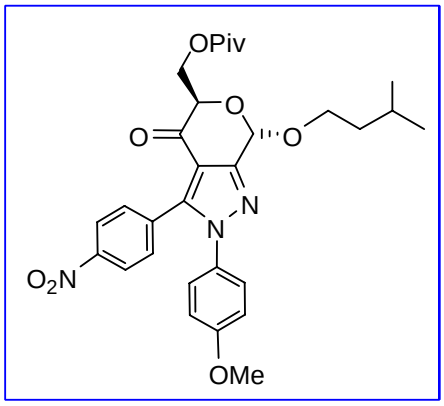
Experimental Section - Chemistry

General Remarks: Organic solvents were dried by standard methods. Analytical TLC was performed using 2.5 × 5 cm plates coated with a 0.25 mm thickness of silica gel (60 F-254), visualization was accomplished with $CeSO_4$ or 10% H_2SO_4/EtOH and subsequent charring over hot plate. Column chromatography was performed using silica gel (60-120), (100-200) and (230-400). All the products were characterized by ^1H, ^{13}C, DEPT pulse sequence, two-dimensional homonuclear COSY (Correlation Spectroscopy), Heteronuclear Single Quantum Correlation (HSQC), IR, MS (FAB), MS (ESI), HRMS (EI) and HRMS (DART). All NMR spectra were recorded with spectrometers at 300, 400 MHz (^1H) and 50, 75, MHz (^{13}C). Experiments were recorded in $CDCl_3$, $CDCl_3$+CCl_4 mixture at 25 °C. Chemical shifts are given on the δ scale. For ^{13}C NMR reference $CDCl_3$ appeared at 77.10 ppm or 77.40 ppm unless otherwise stated. Optical rotations were determined using a 1 dm cell in chloroform as solvent at 25 °C unless otherwise stated; concentrations mentioned are in g/100 mL.

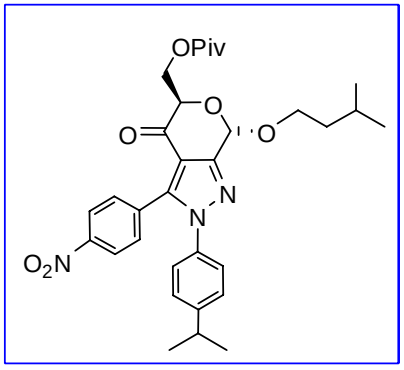


Compound 3: To a solution of hex-2-enopyranoside **1a** (269 mg, 0.6 mmol) in dry DCM (20 mL) was added Dess-Martin Periodinane (407 mg, 0.96 mmol) at -5 °C. Subsequently the reaction was allowed to warm to 5 °C and stirred for 3 h till all the starting material was converted into the oxidized product (TLC). The reaction was quenched by addition of excess of cold water. The organic layer was separated and the aqueous layer was extracted with DCM (4 × 4mL). The combined organic layers were dried over sodium sulphate and evaporated *in vacuo* at low temperature till all but 1-2 mL solvent remained. The crude product (**2a**) was now dissolved in 20 mL of 1,2-dichloroethane (DCE) and after addition of requisite amount of phenylhydrazine hydrochloride (347 mg, 2.4 mmol) the reaction was stirred at 90 °C for 4.5 h. On completion of the reaction (TLC) excess of water was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with DCM (5 x 4 mL). The combined organic layers were dried over sodium sulphate and evaporated *in vacuo* to obtain the crude product. The crude product was chromatographed (hexane/ethyl acetate, 9:1) to yield the pure compound **3** as a yellow solid. Yield - (158 mg, 49% over two steps); solid; mp 124-126 °C; R_f = 0.60 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1); $[\alpha]_D^{26}$ = +62.56 (*c* 0.100, $CHCl_3$); IR (KBR, cm^{-1}): 3444, 2928, 2366, 1732, 1688, 1216; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, 2H, *J* = 8.8 Hz), 7.52 (d, 2H, *J* = 6.6 Hz), 7.38-7.34 (m, 3H), 7.24-7.22 (m, 2H), 5.98 (s, 1H), 4.80 (dd, 1H, *J* = 2.4, *J* = 6.5), 4.67 (dd, 1H, *J* = 2.4, *J* = 12.0), 4.49 (dd, 1H, *J* = 6.6, *J* = 12.0), 4.03-3.97 (m, 1H), 3.83-3.77 (m, 1H), 1.79-1.72 (m, 1H), 1.64-1.58 (m, 2H), 1.19 (s, 9H), 0.94 (d, 6H, *J* = 6.6); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.8 (qC), 178.1 (qC), 154.0 (qC), 148.3 (qC), 140.6 (qC), 138.2 (qC), 133.6 (qC), 131.3 (CH), 129.5 (CH), 129.3 (CH), 125.6 (CH), 123.5 (CH), 113.8 (qC), 93.5 (CH), 73.1 (CH), 67.8 (CH_2), 62.7 (CH_2), 38.8 (qC), 38.3 (CH_2), 27.2 (CH_3), 25.1 (CH), 22.7 (CH_3), 22.5 (CH_3); HRMS (DART): Calcd for $C_{24}H_{22}N_3O_6$ $[M\text{-}C_5H_{11}O]^+$ 448.1508; found 448.1478.

Compound **4-15** were prepared using a similar procedure as reported for compound **3**.

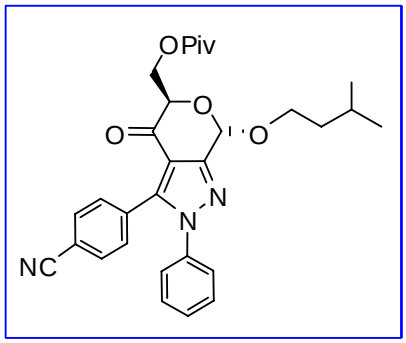


Compound **4.** Yield - (170 mg, 50% over two steps); solid; mp 90-92 °C; R_f = 0.6 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1); $[\alpha]_D^{25}$ = +11.08 (*c* 0.200, $CHCl_3$); IR (KBr, cm^{-1}): 2927, 2368, 1730, 1691; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.19 (d, 2H, *J* = 8.8 Hz), 7.52 (d, 2H, *J* = 8.7 Hz), 7.15 (d, 2H, *J* = 8.9 Hz), 6.86 (d, 2H, *J* = 9.0 Hz), 5.98 (s, 1H), 4.79 (dd, 1H, *J* = 2.3 Hz, *J* = 6.4 Hz), 4.67 (dd, 1H, *J* = 2.4 Hz, *J* = 12.0 Hz), 4.49 (dd, 1H, *J* = 6.6 Hz, *J* = 11.8 Hz), 4.04-3.96 (m, 1H), 3.81-3.76 (m, 1H), 1.78-1.69 (m, 1H), 1.67-1.57 (m, 2H), 1.22 (s, 9H), 0.94 (d, 6H, *J* = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.8 (qC), 178.1 (qC), 160.1 (qC), 153.8 (qC), 148.3 (qC), 140.5 (qC), 133.7 (qC), 131.3 (CH), 130.1 (qC), 126.9 (CH), 123.5 (CH), 114.7 (CH), 113.5 (qC), 93.5 (CH), 73.0 (CH), 67.8 (CH_2), 62.8 (CH_2), 55.6 (CH_3), 38.8 (qC), 38.3 (CH_2), 27.2 (3 × CH_3), 25.1 (CH), 22.7 (CH_3), 22.5 (CH_3); HRMS (DART): Calcd for $C_{25}H_{24}N_3O_7$ $[M\text{-}C_5H_{11}O]^+$ 478.1614; found 478.1603.

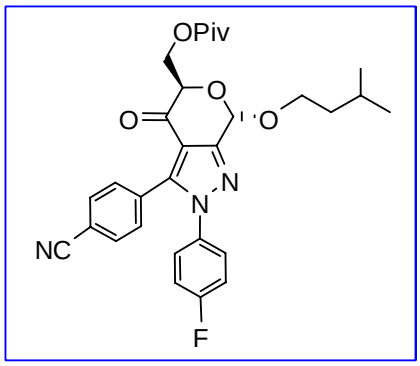


Compound 5. Yield - (135 mg, 39% over two steps); glassy solid; R_f = 0.38 (hexane/ethyl acetate, 4:1); eluent for column chromatography (hexane/ethyl acetate, 24:1); $[\alpha]_D^{29}$ = +19.67 (*c* 0.21, $CHCl_3$); IR (KBr, cm^{-1}): 3021, 2348, 1785, 1597; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.19 (d, 2H, *J* = 8.8 Hz), 7.53 (d, 2H, *J* = 8.8 Hz), 7.23-7.12 (m, 4H), 5.98 (s, 1H), 4.80 (dd, 1H, *J* = 2.4, *J* = 6.5), 4.67 (dd, 1H, *J* = 2.5, *J* =12.0), 4.49 (dd, 1H, *J* = 6.6, *J* = 11.9), 4.04-3.96 (m, 1H), 3.84-3.76 (m, 1H), 2.96-2.87 (m, 1H), 1.78-1.69 (m, 1H), 1.67-1.60 (m, 2H), 1.24-1.20 (m, 15H),

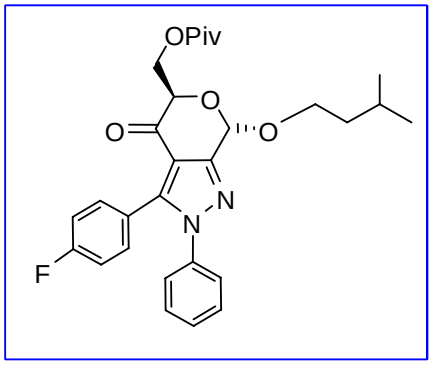
0.94 (d, 6H, J = 6.5); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.6 (qC), 178.2 (qC), 153.8 (qC), 150.5 (qC), 148.3 (qC), 140.5 (qC), 135.9 (qC), 133.7 (qC), 131.3 (CH), 127.5 (CH), 125.4 (CH), 123.5 (CH), 113.7 (qC), 93.5 (CH), 73.0 (CH), 67.8 (CH_2), 62.8 (CH_2) 38.8 (qC), 38.3 (CH_2), 33.3 (CH), 27.2 (CH_3), 25.1 (CH), 23.8 (CH_3), 22.7 (CH_3), 22.5 (CH_3); HRMS (DART): Calcd for $C_{27}H_{28}N_3O_6$ $[M\text{-}C_5H_{11}O]^+$ 490.1978; found 490.1960.



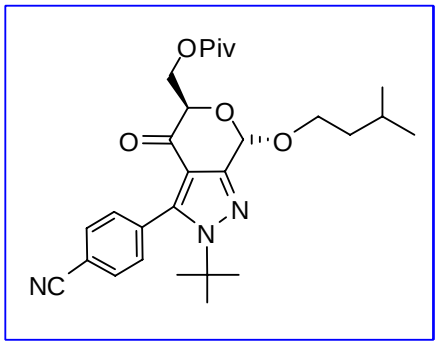
Compound 6. Yield - (130mg, 42% over two steps); solid; mp 133-135 °C; R_f = 0.52 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 22:3); $[\alpha]_D^{19}$ = +92.21 (*c* 0.72, $CHCl_3$); IR (KBr, cm^{-1}): 3422, 3022, 2360, 1652, 1522; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.62 (d, 2H, J = 8.52 Hz), 7.45 (d, 2H, J = 8.52 Hz), 7.38-7.33 (m, 3H), 7.23-7.20 (m, 2H), 5.98 (s, 1H), 4.79 (dd, 1H, J = 2.4, J = 6.5), 4.67 (dd, 1H, J = 2.5, J = 12.0), 4.49 (dd, 1H, J = 6.6, J = 12.0), 4.04-3.96 (m, 1H), 3.83-3.75 (m, 1H), 1.77-1.67 (m, 1H), 1.65-1.57 (m, 2H), 1.19 (s, 9H), 0.93 (d, 6H, J = 6.5); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.8 (qC), 178.1 (qC), 153.9 (qC), 141.0 (qC), 138.2 (qC), 132.0 (CH), 131.7 (qC), 130.9 (CH), 129.5(CH), 129.3 (CH), 125.6 (CH), 118.1 (qC), 113.6 (qC), 93.5 (CH), 73.0 (CH), 67.8 (CH_2), 62.7 (CH_2), 38.8 (qC), 38.3 (CH_2), 27.2 (3 x CH_3), 25.1 (CH), 22.7 (CH_3), 22.5 (CH_3); HRMS (DART): Calcd for $C_{25}H_{22}N_3O_4$ $[M\text{-}C_5H_{11}O]^+$ 428.1610; found 428.1598.



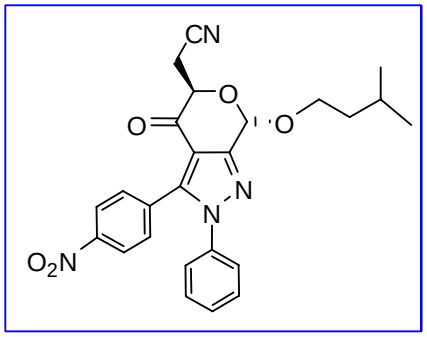
Compound 7. Yield – (90mg, 28% over two steps); solid; 80-82 °C; R_f = 0.52 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1); $[\alpha]_D^{19}$ = +107.03 (*c* 0.55, $CHCl_3$); IR (KBr, cm^{-1}): 3426, 3020, 2357, 1693, 1647; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.64 (d, 2H, *J* = 8.3 Hz), 7.44 (d, 2H, *J* = 8.3 Hz), 7.24-7.20 (m, 2H), 7.09-7.04 (m, 2H), 5.96 (s, 1H), 4.78 (dd, 1H, *J* = 2.2 Hz, *J* = 6.3 Hz), 4.66 (dd, 1H, *J* = 2.4 Hz , *J* = 12.0 Hz), 4.48 (dd, 1H, *J* = 6.5 Hz, *J* = 12.0 Hz), 4.03-3.96 (m, 1H), 3.83-3.76 (m, 1H), 1.78-1.67 (m, 1H), 1.65-1.59 (m, 2H), 1.19 (s, 9H), 0.94 (d, 6H, *J* = 6.5); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.7 (qC) 178.1 (qC), 164.2 (qC), 160.8 (qC) 154.0 (qC), 141.0 (qC), 134.37 (qC), 134.33 (qC), 132.1 (CH), 131.5 (qC), 130.9 (CH),127.5 (CH), 127.4 (CH), 118.0 (qC), 116.8 (CH), 116.4 (CH), 113.8 (qC), 113.7 (qC), 93.4 (CH), 73.0 (CH), 67.8 (CH_2), 62.7 (CH_2), 38.8 (qC), 38.3 (CH_2), 27.2 (CH_3), 25.1 (CH), 22.7 (CH_3), 22.5 (CH_3); HRMS (DART): Calcd for $C_{25}H_{21}FN_3O_4$ $[M\text{-}C_5H_{11}O]^+$ 446.1516; found 446.1505.



Compound 8. Yield - (134 mg, 44% over two steps); solid; 119-121 °C; R_f = 0.47 (hexane/ethyl acetate, 17:3); eluent for column chromatography (hexane/ethyl acetate, 23:2); $[\alpha]_D^{30}$ = +116.24 (*c* 0.1, $CHCl_3$); IR (KBr, cm^{-1}): 3021, 2360, 1725, 1511; ^1H NMR ($CDCl_3$, 300 MHz): δ7.36 - 7.30 (m, 5H), 7.24 - 7.22 (m, 2H), 7.02 (t, 2H, *J* = 8.6 Hz), 5.97 (s, 1H), 4.79 (dd, 1H, *J* = 2.3 Hz, *J* = 6.5 Hz), 4.68 (dd, 1H, *J* = 2.4 Hz, *J* = 11.9 Hz), 4.49 (dd, 1H, *J* = 6.6 Hz, *J* = 11.9 Hz), 4.04-3.96 (m, 1H), 3.83-3.75 (m, 1H), 1.80-1.69 (m, 1H), 1.67-1.55 (m, 2H), 1.20, (s, 9H), 0.93 (d, 6H, *J* = 6.2); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.7 (qC), 178.2 (qC), 165.1 (qC), 161.8 (qC), 153.7 (qC), 142.4 (qC), 138.6 (qC), 132.4 (CH), 132.3 (CH), 129.3 (CH), 128.8 (CH), 125.6 (CH), 123.3 (qC), 123.2 (qC) 115.8 (CH), 115.5 (CH), 113.1 (qC), 93.6 (CH), 73.1 (CH), 67.7 (CH_2), 62.9 (CH_2), 38.8 (qC), 38.3 (CH), 27.2 (CH_3), 25.1 (CH), 22.7, (CH_3), 22.5 (CH_3); HRMS (DART): Calcd for $C_{24}H_{22}F_1N_2O_4$ $[M\text{-}C_5H_{11}O]^+$ 421.1563; found 421.1548.

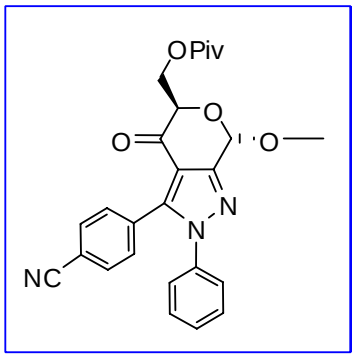


Compound 9. Yield - (93mg, 31% over two steps); glassy solid; Oil; R_f = 0.62 (hexane/ethyl acetate, 4:1); eluent for column chromatography (hexane/ethyl acetate, 22:3); $[\alpha]_D^{26}$ = +10.29 (*c* 0.38, $CHCl_3$); IR (KBr, cm^{-1}): 3457, 3019, 2372, 1721, 1604; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.74 (d, 2H, *J* = 8.3 Hz), 7.43 (d, 2H, *J* = 8.0 Hz), 5.88 (s, 1H), 4.65 (dd, 1H, *J* = 2.2 Hz , *J* = 6.6 Hz), 4.54 (dd, 1H, *J* = 2.3, *J* = 12.0), 4.37 (dd, 1H, *J* = 6.8, *J* = 11.9), 3.99-3.92 (m, 1H), 3.84-3.74 (m, 1H), 1.76-1.69 (m, 1H), 1.64-1.59 (m, 2H), 1.47 (s, 9H), 1.17 (s, 9H), 0.94 (d, 6H, *J* = 6.5), ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.7 (qC), 178.1 (qC), 150.8 (qC), 140.7 (qC), 136.0 (qC), 132.0 (CH), 130.6 (CH), 118.1 (qC), 113.6 (qC), 93.6 (CH), 72.7 (CH), 67.6 (CH_2), 63.8 (qC), 62.7 (CH_2), 38.8 (qC), 38.3 (CH_2), 31.2 (CH_3), 27.2 (CH_3), 25.2 (CH), 22.8 (CH_3), 22.5 (CH_3); HRMS (DART): Calcd for $C_{23}H_{26}N_3O_4$ $[M\text{-}C_5H_{11}O]^+$ 408.1923; found 408.1908.

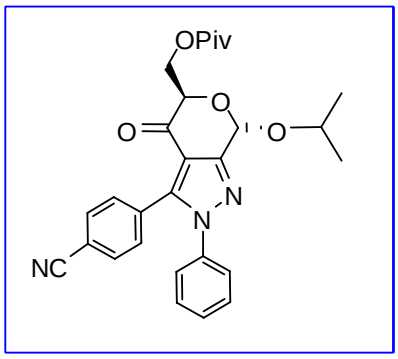


Compound 10. Yield - (127 mg, 46% over two steps); glassy solid; R_f = 0.40 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 93:7); $[\alpha]_D^{27}$ = +10.45 (*c* 0.56, $CHCl_3$); IR (KBr, cm^{-1}): 3441, 3021, 2375, 1696, 1601; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.19 (d, 2H, *J* = 8.8 Hz), 7.52 (d, 2H, *J* = 8.8 Hz), 7.41-7.36 (m, 3H), 7.25-7.22 (m, 2H), 6.02 (s, 1H), 4.85 (dd, 1H, *J* = 3.7 Hz, *J* = 7.8 Hz), 4.12-4.04 (m, 1H), 3.90-3.82 (m, 1H), 3.10 (dd, 1H, *J* = 3.8 Hz, *J* = 17.0 Hz), 2.86 (dd, 1H, *J* = 7.9, *J* = 17.0), 1.82-1.70 (m, 1H), 1.68-1.58 (m, 1H)1.25 (s, 9H), 0.97-0.95 (m, 6H); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.1 (qC), 153.7 (qC), 148.4 (qC), 141.0 (qC), 138.0 (qC), 133.2 (qC), 131.4 (CH), 129.6 (CH), 129.5 (CH), 125.6 (CH), 123.6 (CH), 116.9 (qC), 113.2 (qC), 94.0 (CH), 70.2 (CH), 68.3 (CH_2), 38.3 (CH_2), 25.0 (CH),

22.7 (CH_3), 22.4 (CH_3), 19.0 (CH_2); HRMS (DART): Calcd for $C_{20}H_{13}N_4O_4$ $[M\text{-}C_5H_{11}O]^+$ 373.0936; found 373.0956.

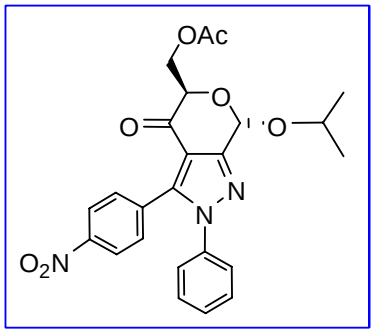


Compound 11. Yield - (106 mg, 38% over two steps); glassy solid; R_f = 0.54 (hexane/ethyl acetate, 3:2); eluent for column chromatography (hexane/ethyl acetate, 21:4); $[\alpha]_D = [\alpha]_D^{28}$ = +27.34 (*c* 0.18, $CHCl_3$); IR (KBr, cm^{-1}): 3376, 2363, 1640; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.62 (d, 2H, *J* = 8.2 Hz), 7.45 (d, 2H, *J* = 8.2 Hz), 7.39-7.37 (m, 3H), 7.24-7.21 (m, 2H), 5.89 (s, 1H), 4.78 (dd, 1H, *J* = 2.3, *J* = 6.4 Hz), 4.69 (dd, 1H, *J* = 2.4 Hz, *J* = 12.0 Hz), 4.49 (dd, 1H, *J* = 6.6 Hz, *J* = 11.9 Hz), 3.67 (s, 3H), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.5 (qC), 178.1 (qC), 153.7 (qC), 141.0 (qC), 138.2 (qC), 132.1 (CH), 131.7 (qC), 130.9 (CH), 129.5 (CH), 129.3 (CH), 125.6 (CH), 118.0 (qC), 113.7 (qC), 113.6 (qC), 94.5 (CH), 73.0 (CH), 62.6 (CH_2), 56.3 (CH_3), 38.8 (qC), 27.5 (CH_3); HRMS (DART): Calcd for $C_{25}H_{22}N_3O_4$ $[M\text{-}CH_3O]^+$ 428.1610; found 428.1595.

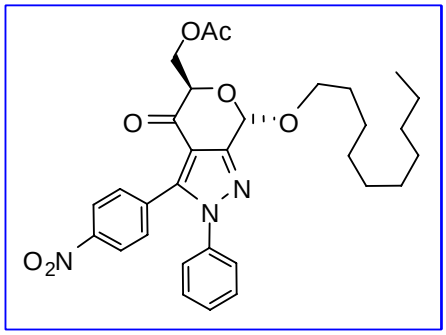


Compound 12. Yield – (118mg, 40% over two steps); solid; mp 91-93 °C; R_f = 0.56 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1); $[\alpha]_D^{30}$ = +45.99 (*c* 0.48, $CHCl_3$); IR (KBr, cm^{-1}): 3441, 2364, 1728, 1691, 1567; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.62 (d, 2H, *J* = 8.3 Hz), 7.44 (d, 2H, *J* = 8.3 Hz), 7.38-7.35 (m, 3H), 7.24-7.20 (m, 2H), 6.10 (s, 1H), 4.85 (dd, 1H, *J* = 2.3 Hz, *J* = 6.6 Hz), 4.69 (dd, 1H, *J* = 2.4 Hz , *J* = 12.0 Hz), 4.45

(dd, 1H, J = 6.8 Hz, J = 11.9 Hz), 4.26 (pent, 1H, J = 6.2 Hz), 1.36 (d, 6H, J = 6.2 Hz), 1.19 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.9 (qC), 178.2 (qC), 154.1 (qC), 141.0 (qC), 138.2 (qC), 132.0 (CH), 131.8 (qC), 130.9 (CH), 129.5 (CH), 129.2 (CH), 125.7 (CH), 117.0 (qC), 113.6 (qC), 91.8 (CH), 73.0 (CH), 71.1 (CH), 62.9 (CH_2), 38.8 (qC), 27.5 (3 × CH_3), 23.3 (CH), 21.7 (2 × CH_3); HRMS (DART): Calcd for $C_{25}H_{22}N_3O_4$ $[M\text{-}C_3H_7O]^+$ 428.1610; found 428.1609.

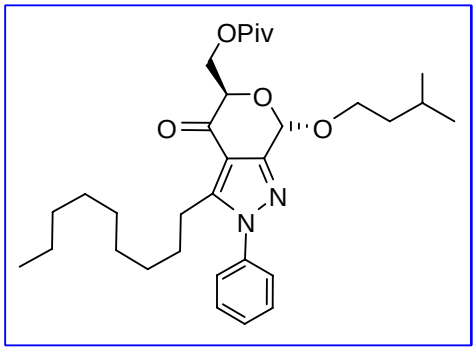


Compound 13. Yield - (115mg, 41% over two steps); solid; mp 199-201 °C; R_f = 0.43 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 87:13); $[\alpha]_D^{27}$ = +49.15 (*c* 0.84, $CHCl_3$); IR (KBr, cm^{-1}): 3020, 2360, 1732, 1664; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.18 (d, 2H, J = 8.8 Hz), 7.53 (d, 2H, J = 8.8 Hz), 7.39-7.37 (m, 3H), 7.24-7.21 (m, 2H), 6.13 (s, 1H), 4.86 (dd, 1H, J = 2.7 Hz, J = 5.3 Hz), 4.63 (dd, 1H, J = 2.8 Hz , J = 12.0 Hz), 4.55 (dd, 1H, J = 5.5 Hz, J = 11.9 Hz), 4.26 (pent, 1H, J = 6.2 Hz), 2.06 (s, 3H), 0.94 (d, 6H, J = 6.2 Hz); ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.8 (qC), 170.7 (qC), 154.1 (qC), 148.3 (qC), 140.7 (qC), 138.1 (qC), 133.5 (qC), 131.4 (CH), 129.5 (CH), 129.3 (CH), 125.7 (CH), 123.5 (CH), 113.9 (qC), 92.3 (CH), 72.6 (CH), 71.7 (CH), 62.4 (CH_2), 23.2 (CH_3), 22.0 (CH_3), 20.8 (CH_3); HRMS (DART): Calc for $C_{21}H_{16}N_3O_6$ $[M\text{-}C_3H_7O]^+$ 406.1039; found 406.1030.



Compound 14. Yield - (153, 45% in 2 steps); glassy solid; R_f = 0.53 (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 22 :3); $[\alpha]_D^{24}$ = +29.25 (*c* 0.22, $CHCl_3$); IR (neat, cm^{-1}): 3021, 2359, 1690, 1522; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.19 (dd, 2H, *J* = 1.8 Hz, *J* = 7.0 Hz,) 7.54 (dd, 2H, *J* = 1.9 Hz, *J* = 7.0 Hz), 7.40-7.36 (m, 3H), 7.25-7.22 (m, 2H), 6.02 (s, 1H, H-2), 4.81 (dd, 1H, *J* = 5.2 Hz, *J* = 2.9 Hz), 4.64 (dd, 1H, *J* = 12.0 Hz, *J* = 2.9 Hz), 4.57 (dd, 1H, *J* = 11.9 Hz, *J* = 5.3 Hz), 3.99-3.91 (m, 1H), 3.84-3.76 (m, 1H), 2.08 (s, 3H), 1.75-1.68 (m, 2H), 1.25 (s, 14H), 0.87-0.82 (m, 3H). ^{13}C NMR ($CDCl_3$, 75MHz): δ 188.7 (qC), 170.7 (qC), 153.9 (qC), 148.4 (qC), 140.7 (qC), 138.2 (qC), 133.5 (qC), 131.4 (CH), 129.6 (CH), 129.4 (CH), 125.6 (CH), 123.5 (CH), 113.9 (qC), 93.8 (CH), 72.7 (CH), 69.7 (CH_2), 62.4 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 26.3 (CH_2), 22.7 (CH_2), 20.9 (CH_3), 14.1 (CH_3). HRMS (EI) : Calc for $C_{29}H_{33}N_3O_5$ $[M- C_2H_4O_2]^{+\cdot}$ 503.2056; found 503.2040.

Compound 15.

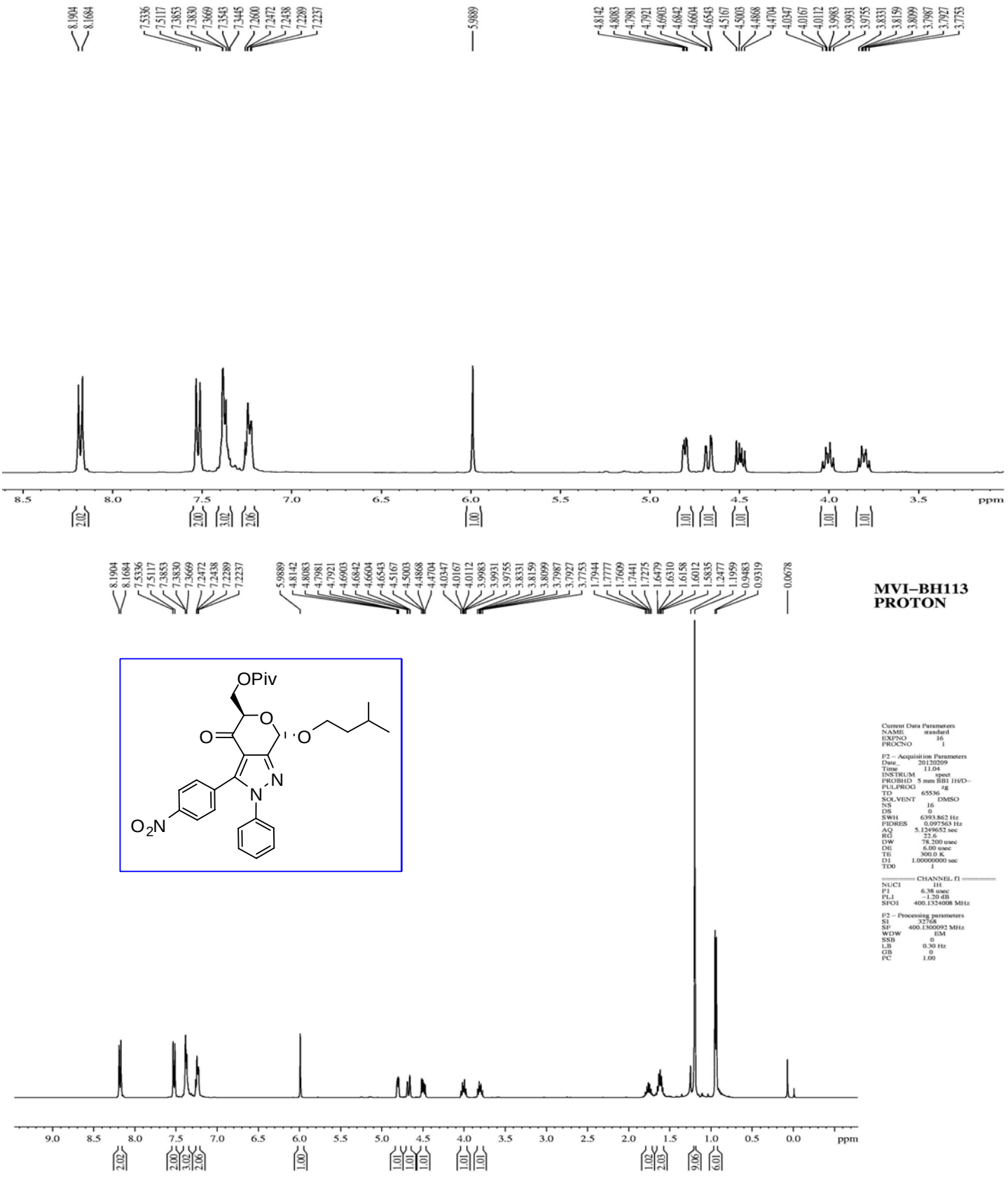


Yield - (98mg, 30% over two steps); Oil; R_f = 0.60 (hexane/ethyl acetate, 4:1); eluent for column chromatography (hexane/ethyl acetate, 97:3); $[\alpha]_D^{26}$ = +32.60 (*c* 0.14, $CHCl_3$); IR (neat, cm^{-1}): 3499, 1726, 1700, 1599; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.52 - 7.49 (m, 3H), 7.41(d, 2H, *J* = 7.9 Hz), 5.89 (s, 1H), 4.75 - 4.67 (m, 3H), 4.54 (dd, 1H, *J* = 6.3 Hz,*J* = 11.8 Hz), 4.00 - 3.92 (m, 1H), 3.79 - 3.71 (m, 1H), 2.96 - 2.83 (m, 2H), 1.76 - 1.67 (m, 1H), 1.62 - 1.55 (m, 4H), 1.20 (s, 21 H), 0.92 (d, 6H), 0.86 (t, 3H);^{13}C NMR ($CDCl_3$, 75MHz): δ 189.5 (qC), 178.2 (qC) 153.3 (qC), 146.9 (qC), 138.4 (qC), 129.46 (CH), 129.41 (CH),125.9 (CH), 112.9 (qC), 93.8 (CH), 73.0 (CH), 67.6 (CH_2), 62.9 (CH_2), 38.8 (qC), 38.3 (CH_2), 31.9 (CH_2), 29.39 (CH_2), 29.34 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.5 (CH_2), 27.2 (CH_3), 25.5 (CH), 22.79 (CH_3), 22.71 (CH), 22.5 (CH_3), 14.3 (CH_3); HRMS (ESI): Calcd for $C_{32}H_{48}N_2NaO_5$ $[M+ Na]^+$ 563.3460; found 563.3490.

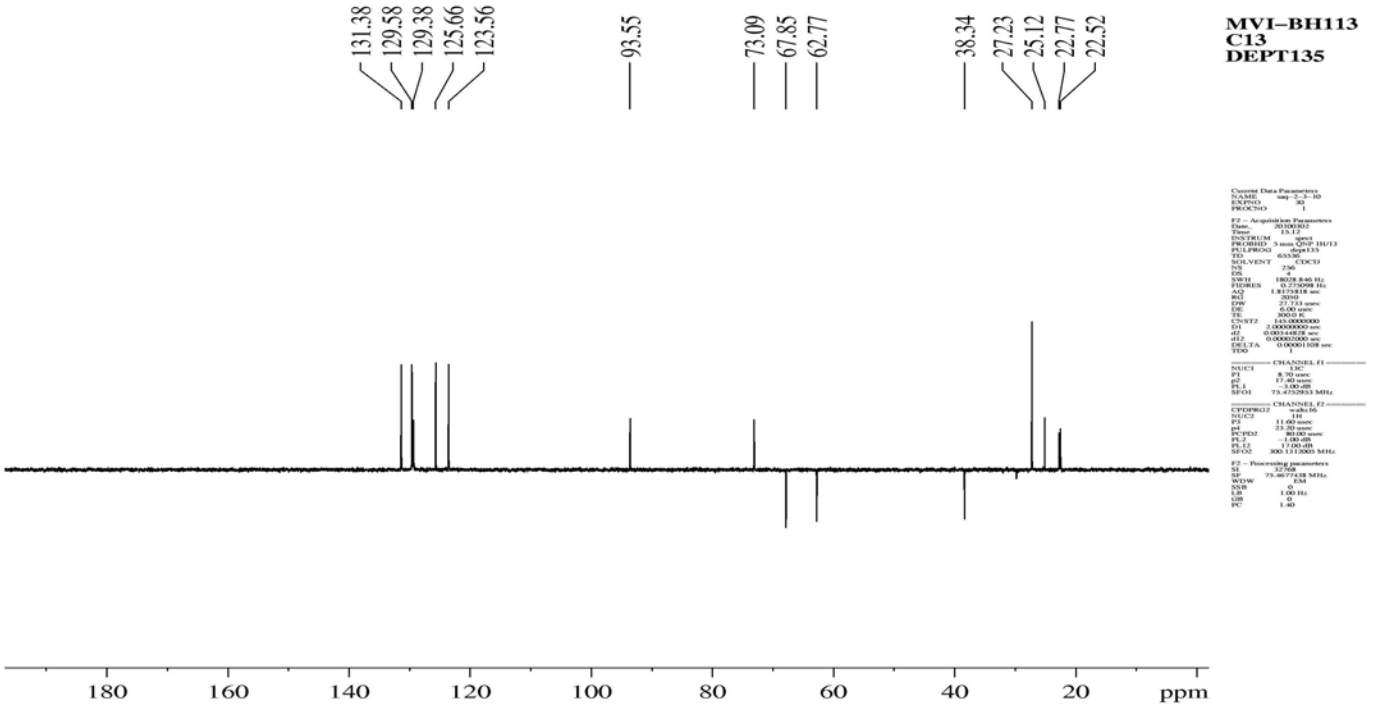
Procedure for sequential one pot synthesis of compound 4

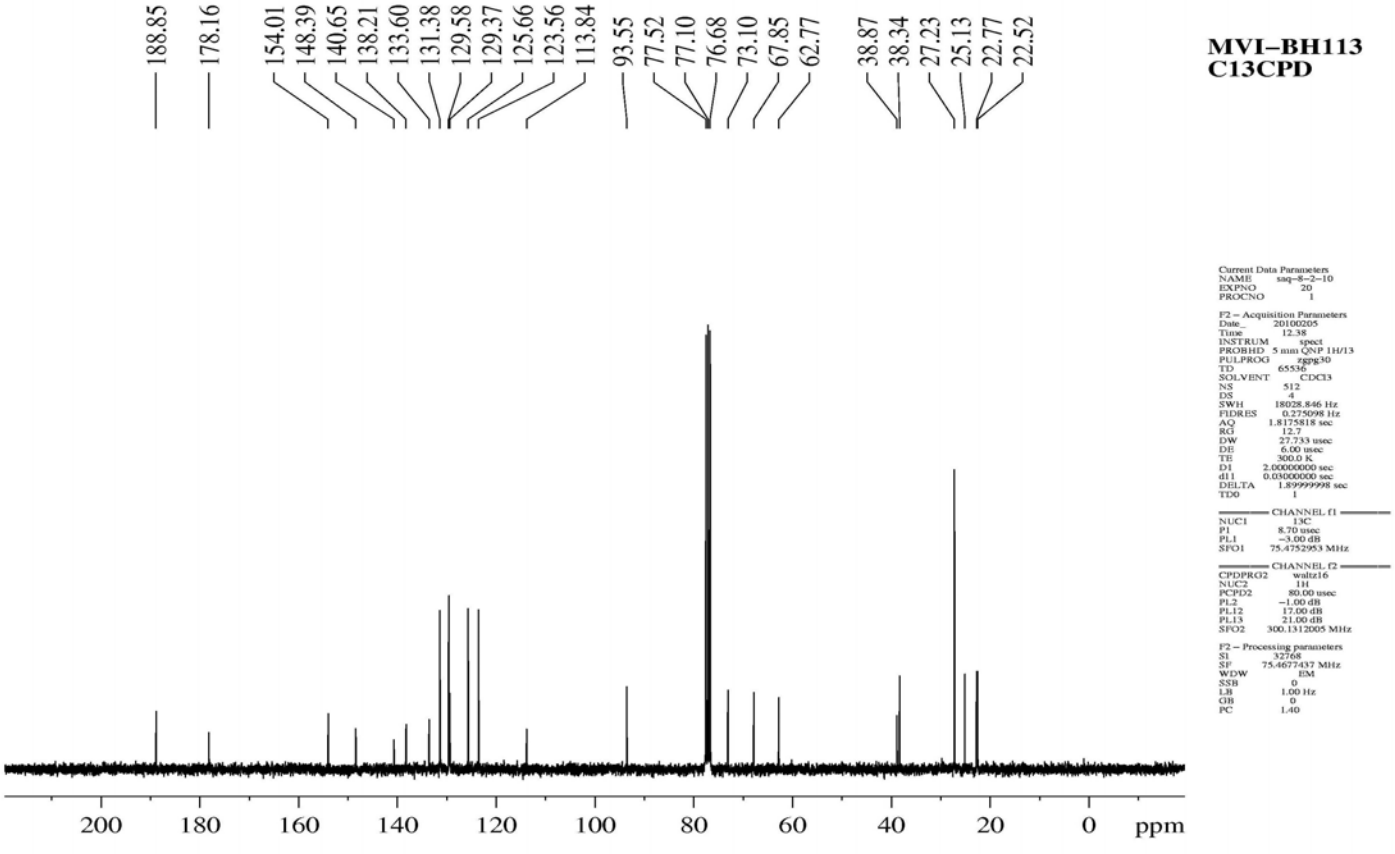
To a solution of hex-2-enopyranoside **1a** (269 mg, 0.6 mmol) in dry DCE (20 mL) was added Dess-Martin Periodinane (407 mg, 0.96 mmol) at -5 °C. Subsequently the reaction was allowed to warm to 5 °C and stirred for 3 h till all the starting material was converted into the oxidized product (TLC). To the reaction mixture was now added 4-methoxy phenylhydrazine hydrochloride (417 mg, 2.4 mmol) and the reaction was stirred at 90 °C for 2 h. On completion of the reaction (TLC) excess of water was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with DCM (5 x 4 mL). The combined organic layers were dried over sodium sulphate and evaporated *in vacuo* to obtain the crude product. The crude product was chromatographed (hexane/ethyl acetate, 9:1) to yield the pure compound **4** as a yellow solid (177 mg, 52% over two steps).

Sugar pyrazole hybrid molecules **10**, **11** and **13** were prepared in a sequential one pot fashion using a similar procedure as reported for compound **4**.

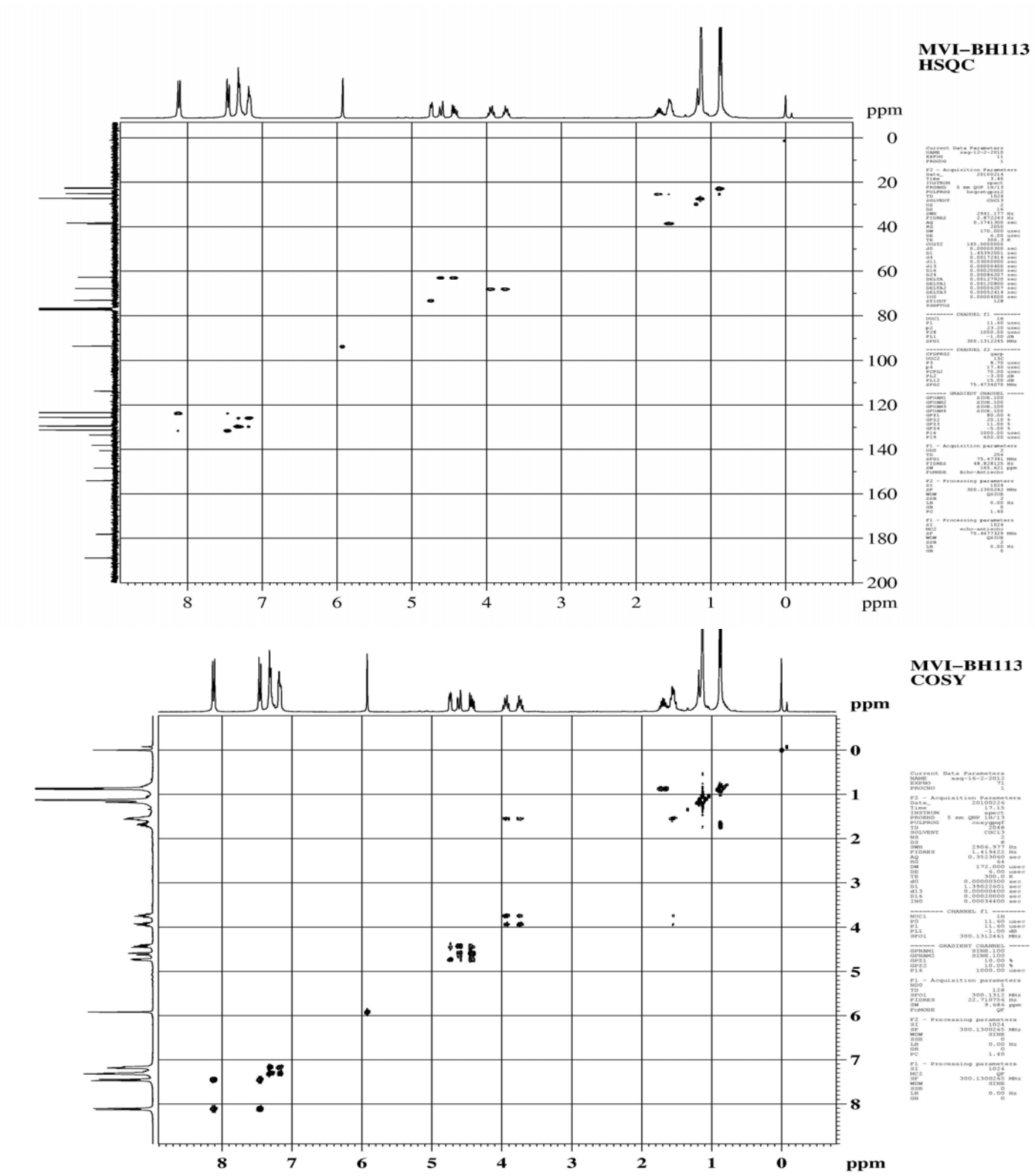


^{1}H NMR spectrum of compound **3** and its expansion

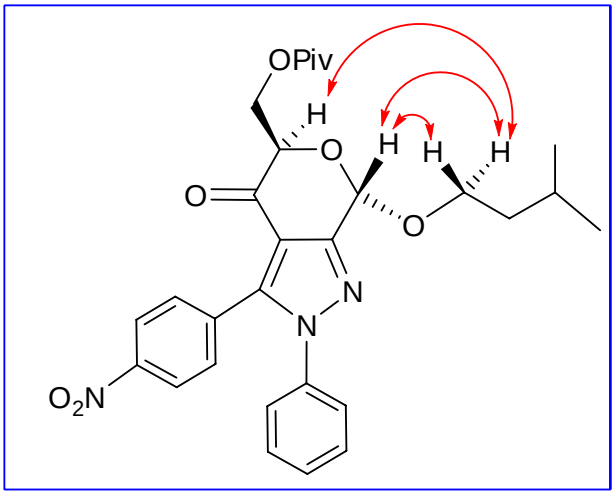




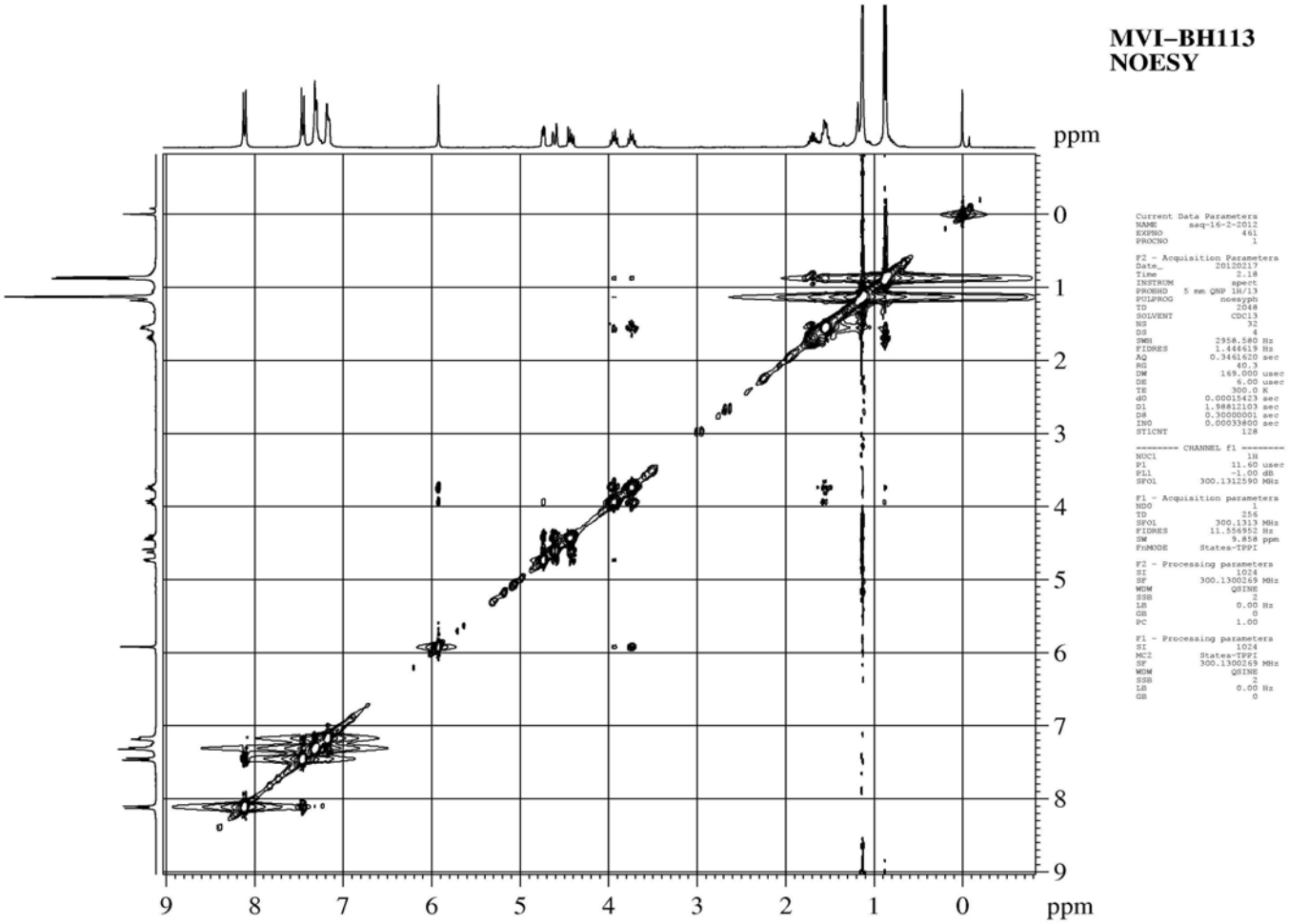
^{13}C and Dept 135 NMR spectra of compound **3**



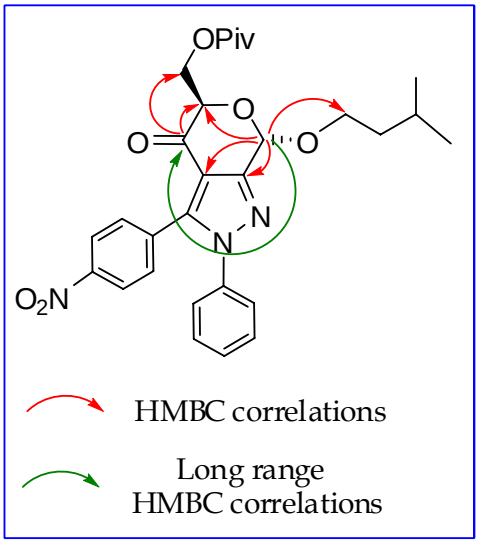
^{1}H-^{1}H COSY and ^{1}H-^{13}C HMBC spectra of compound **3**

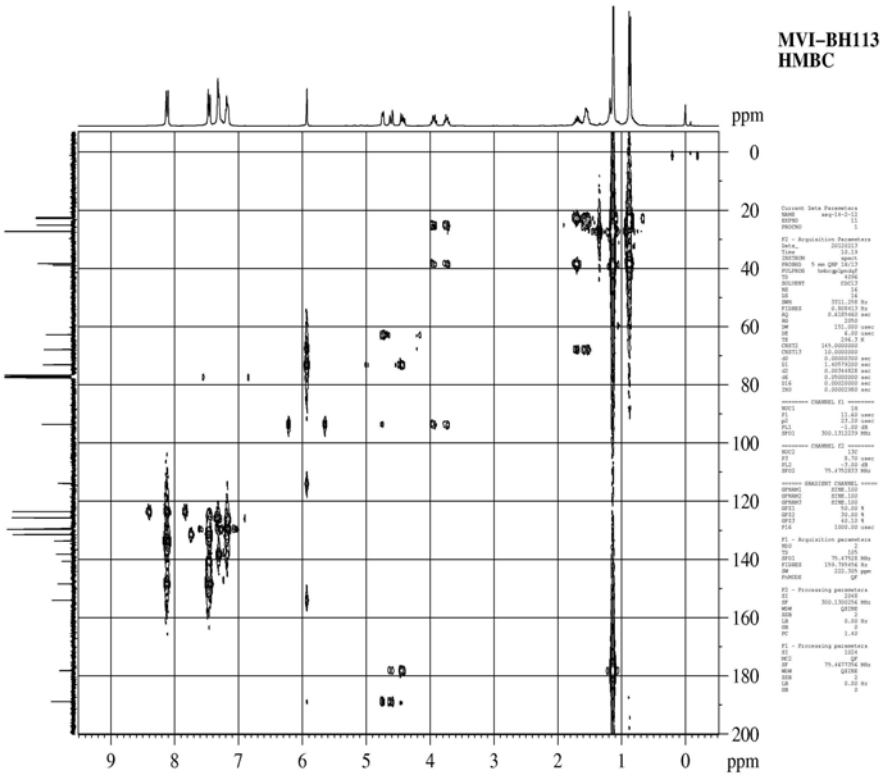


Key NOESY correlations in compound **3**

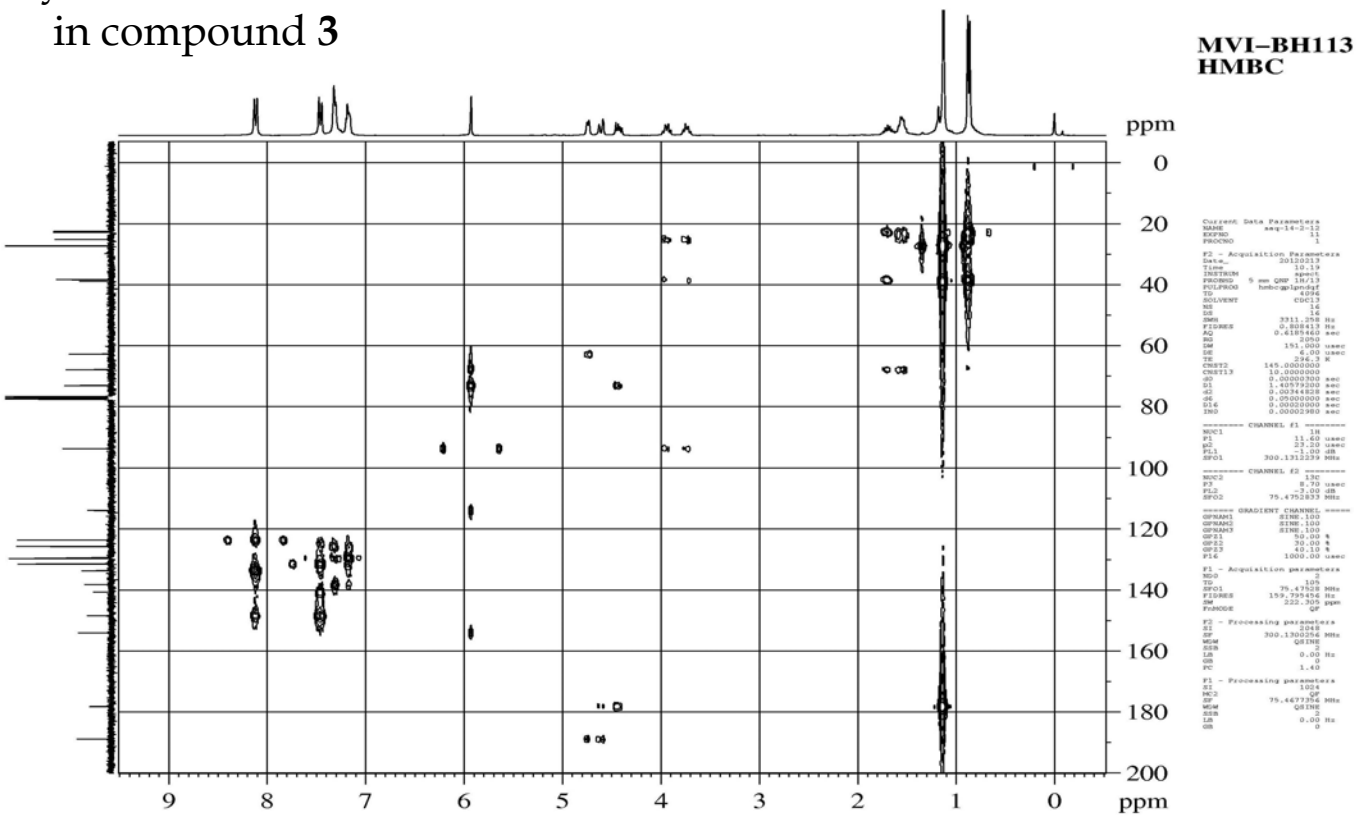


NOESY spectrum of compound **3**

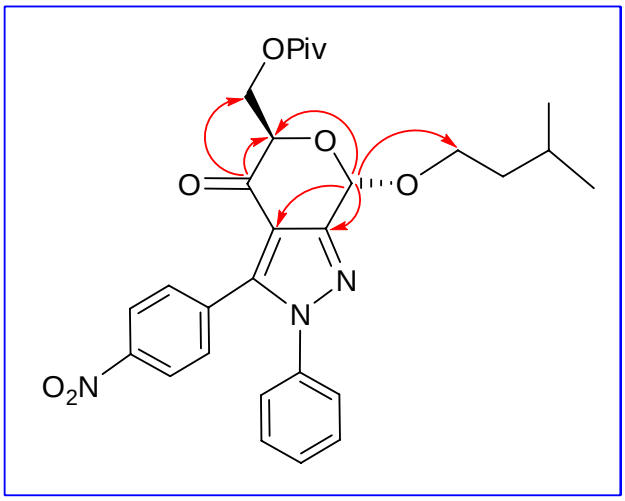




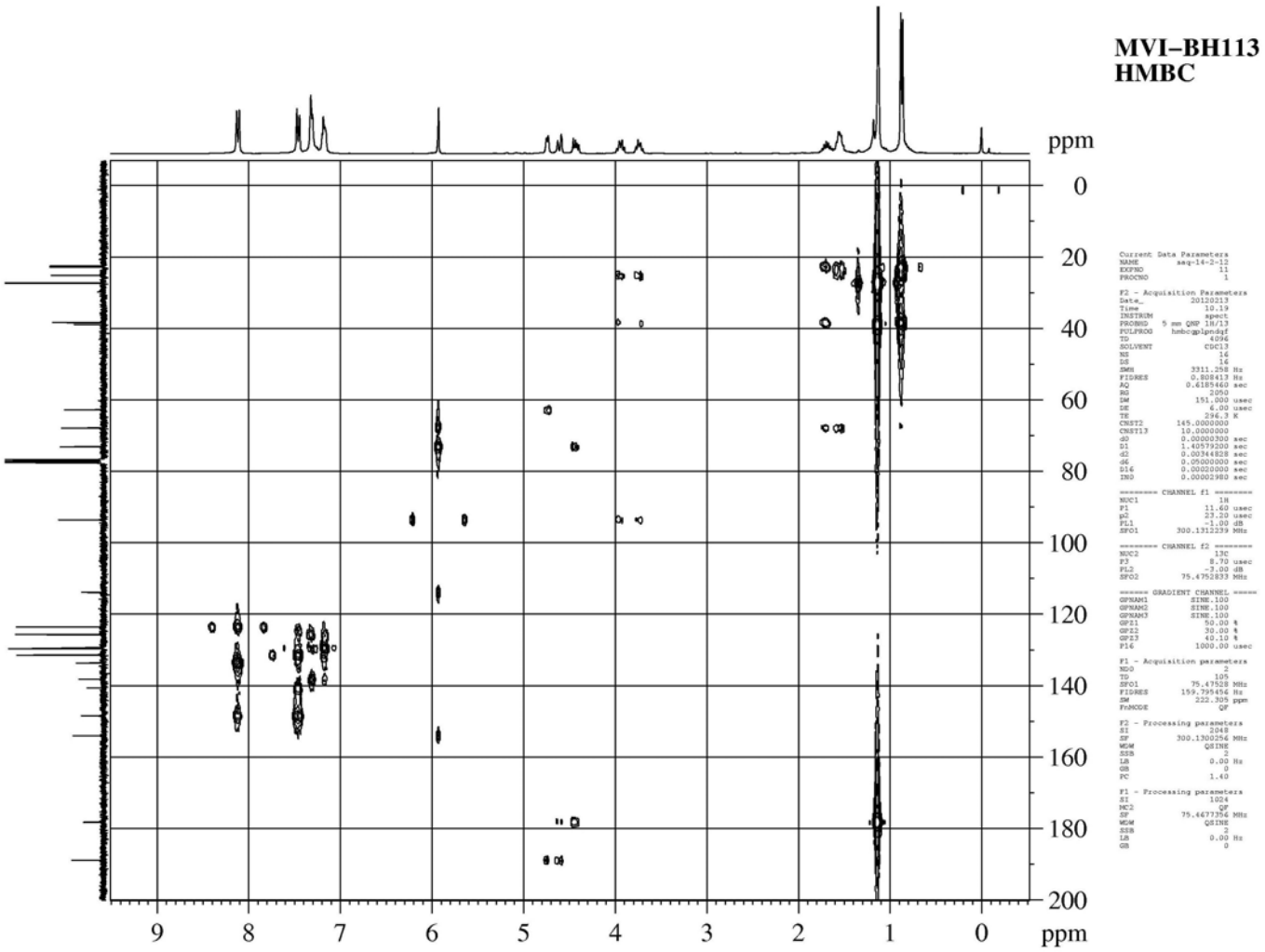
Key HMBC correlations in compound **3**



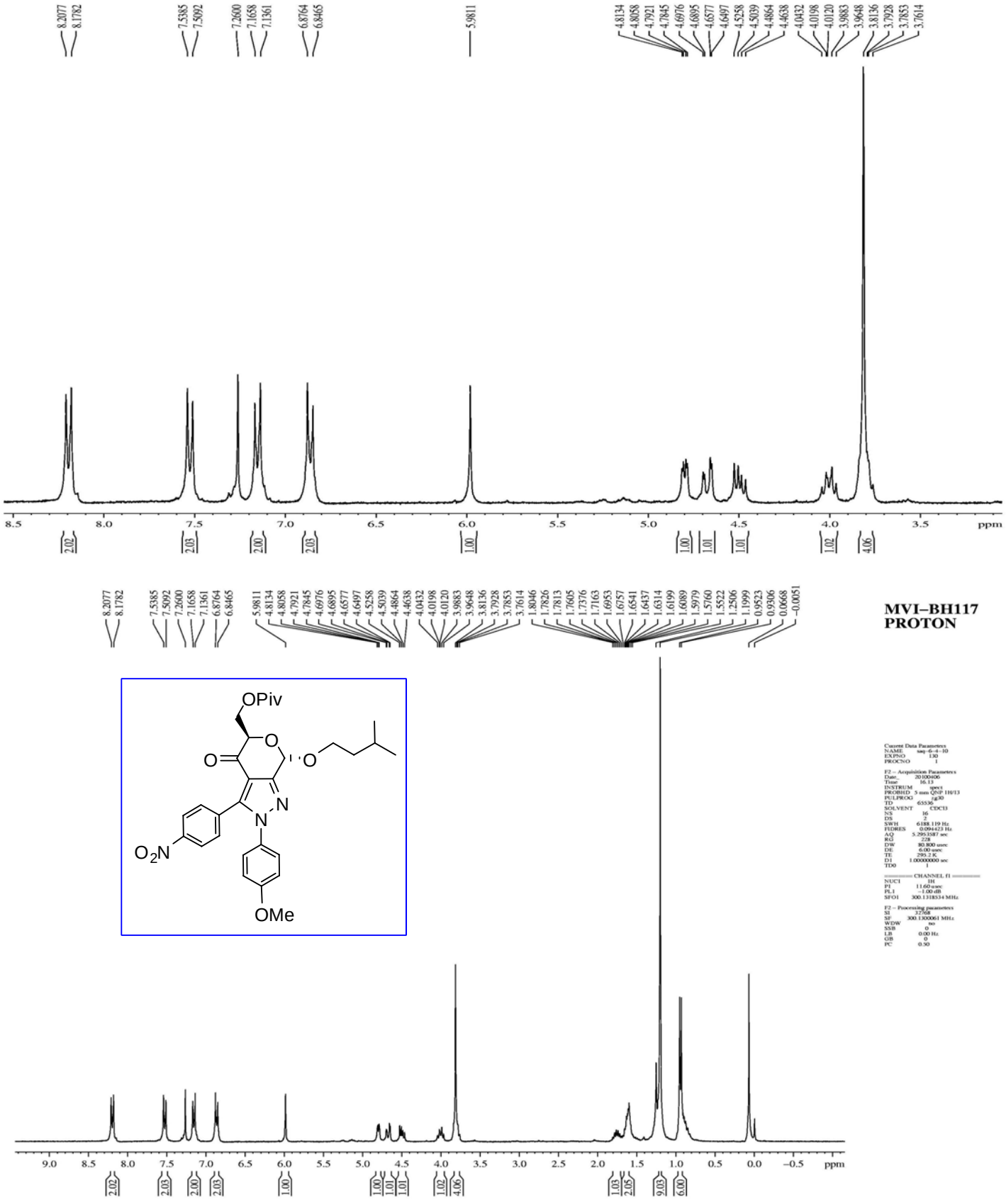
^{1}H-^{13}C HMBC spectra of compound **3**



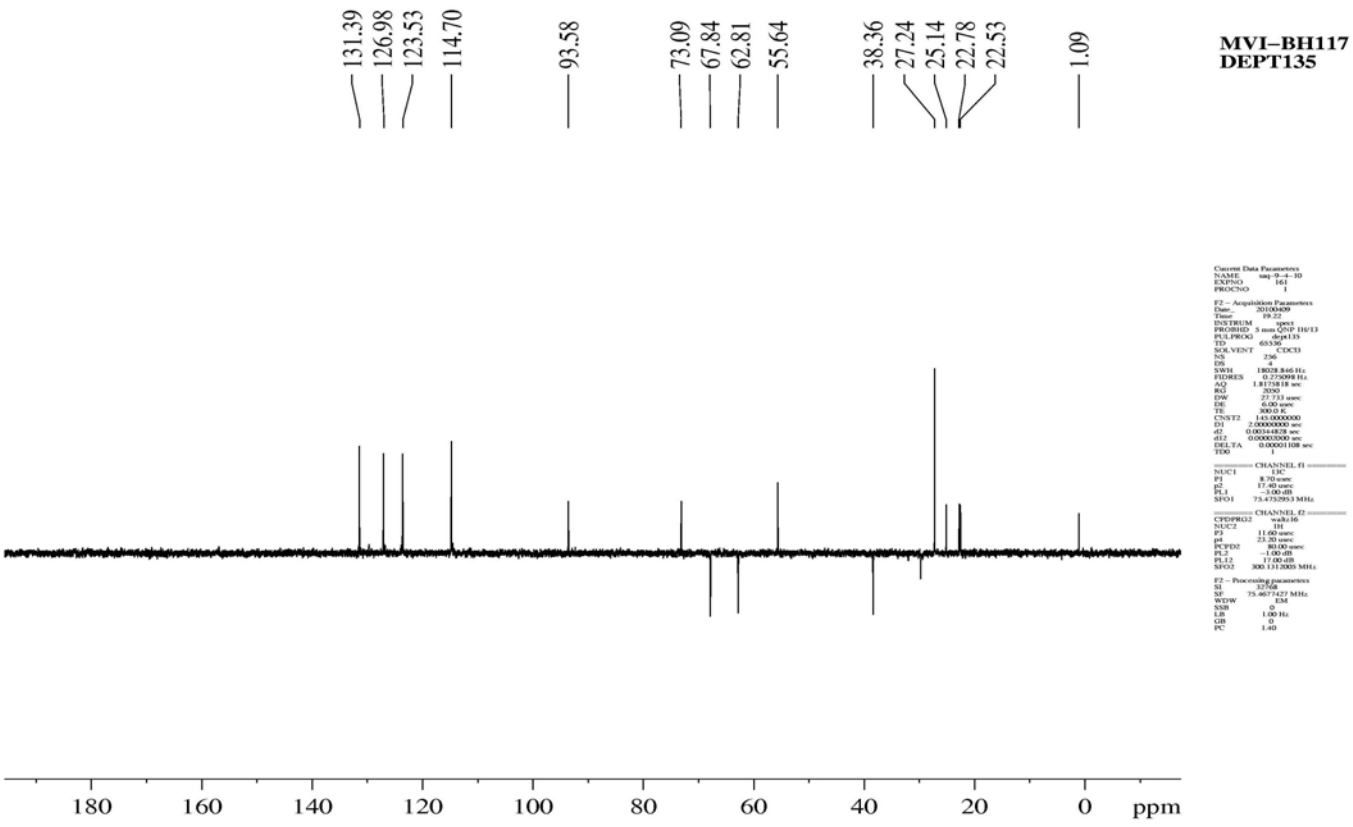
Key HMBC correlations in compound **3**

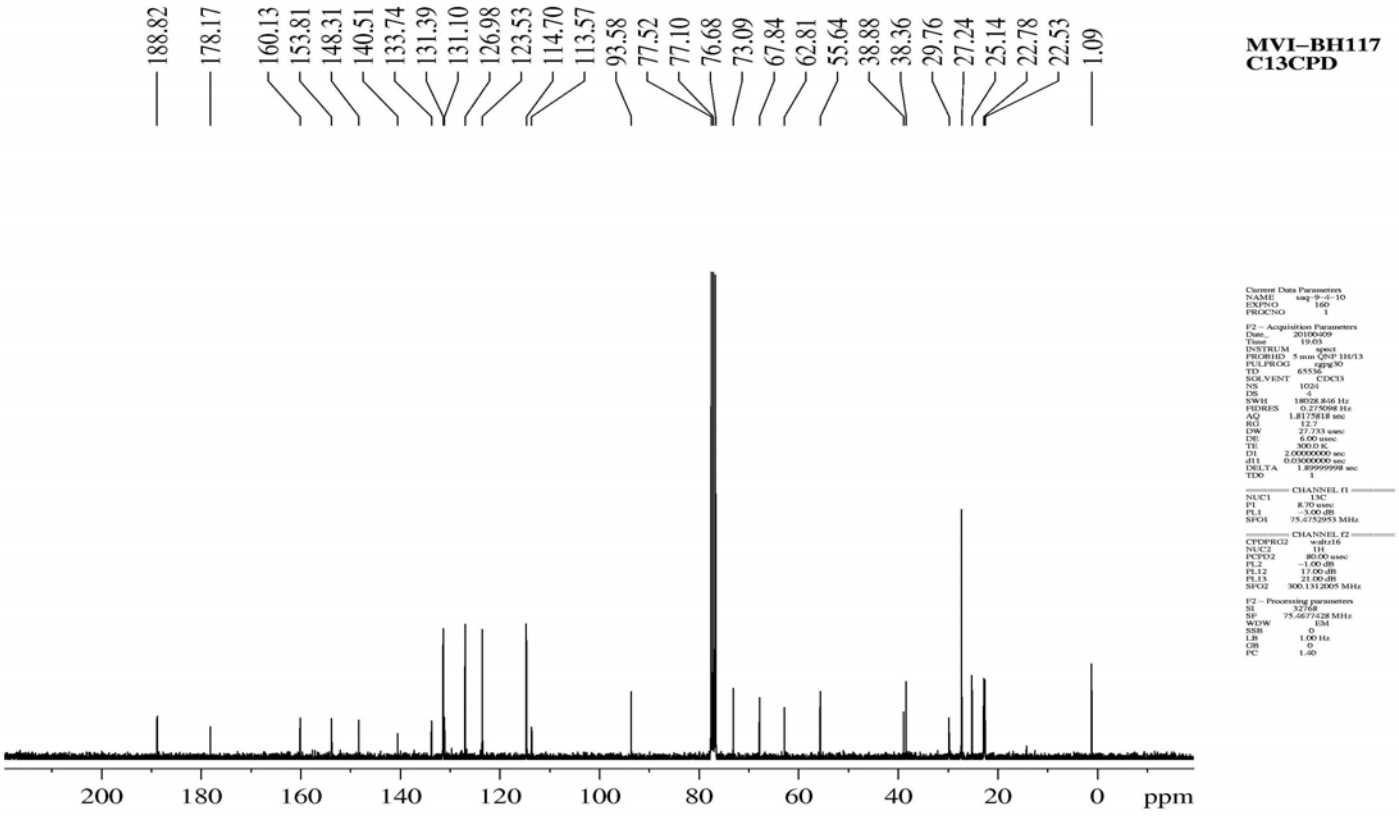


^{1}H-^{13}C HMBC spectra of compound **3**

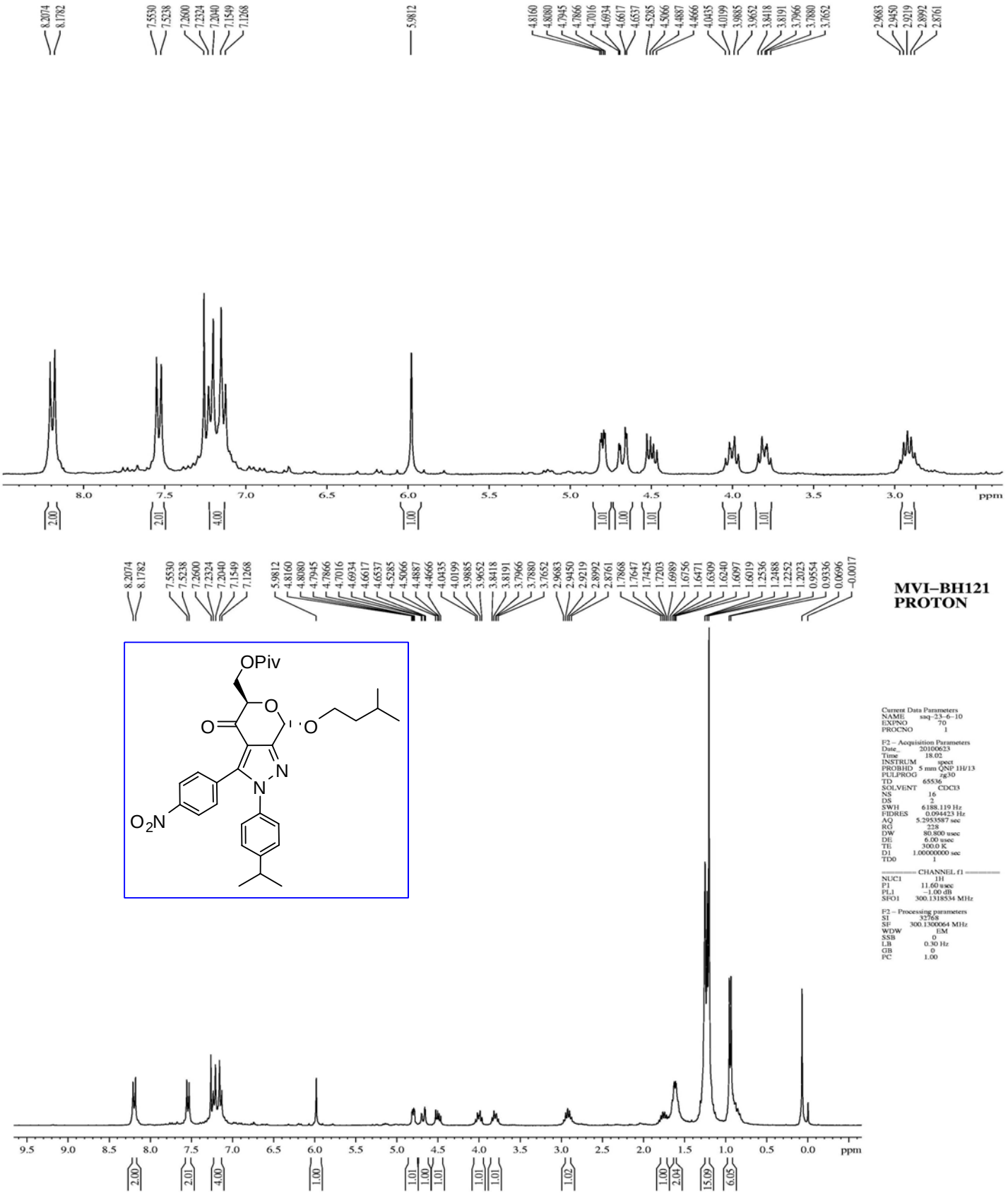


^{1}H NMR spectrum of compound **4** and its expansion

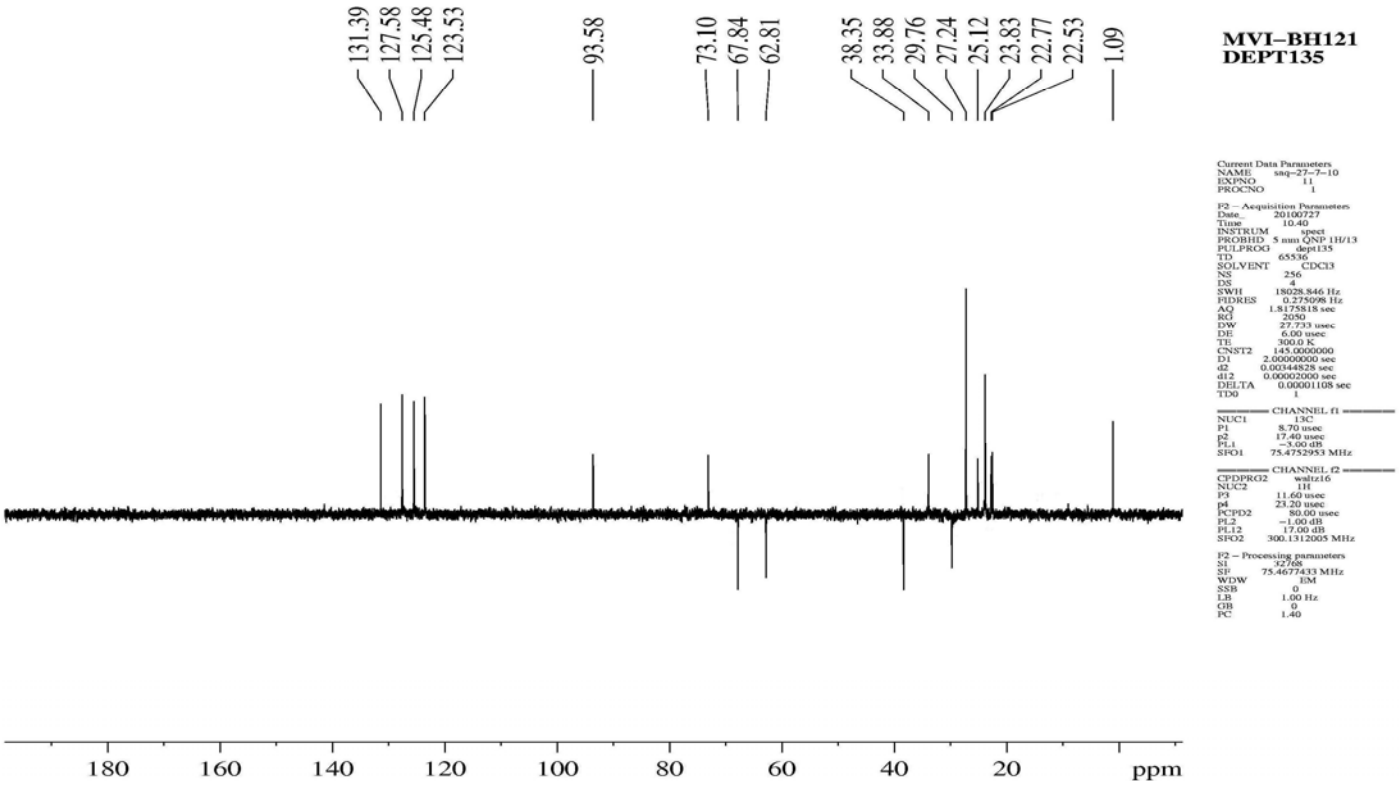


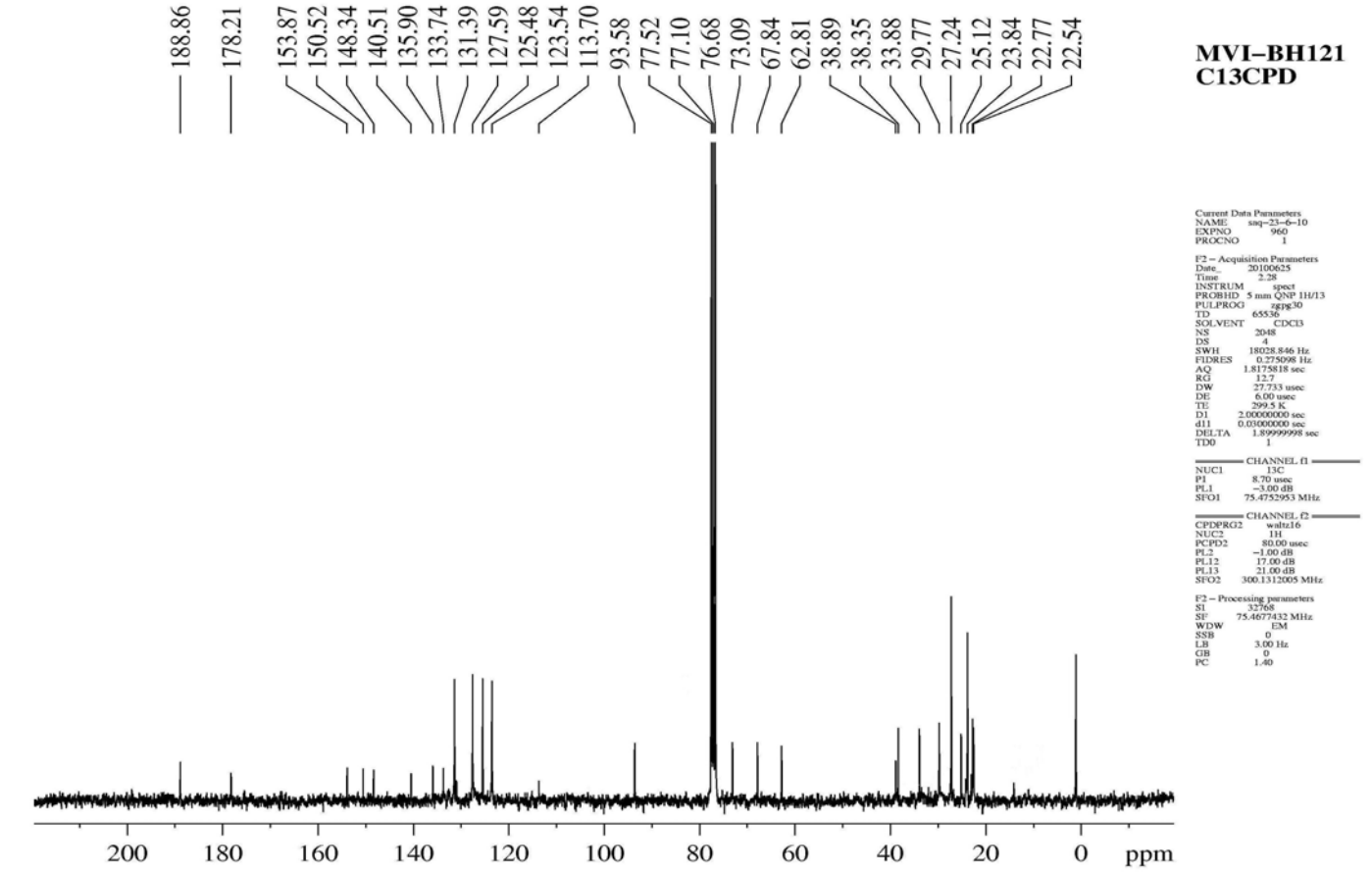


^{13}C and Dept 135 NMR spectra of compound **4**

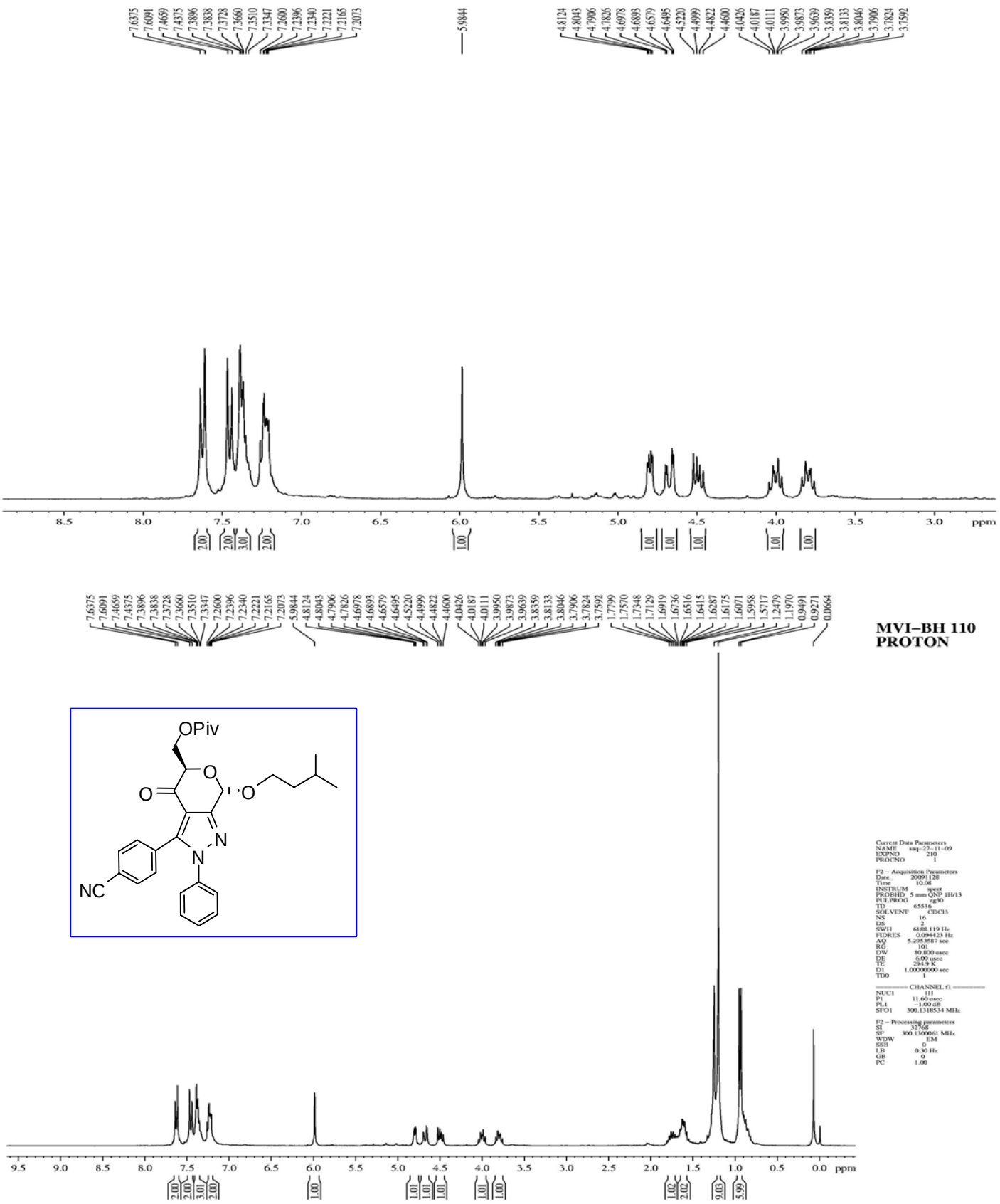


^{1}H NMR spectrum of compound **5** and its expansion

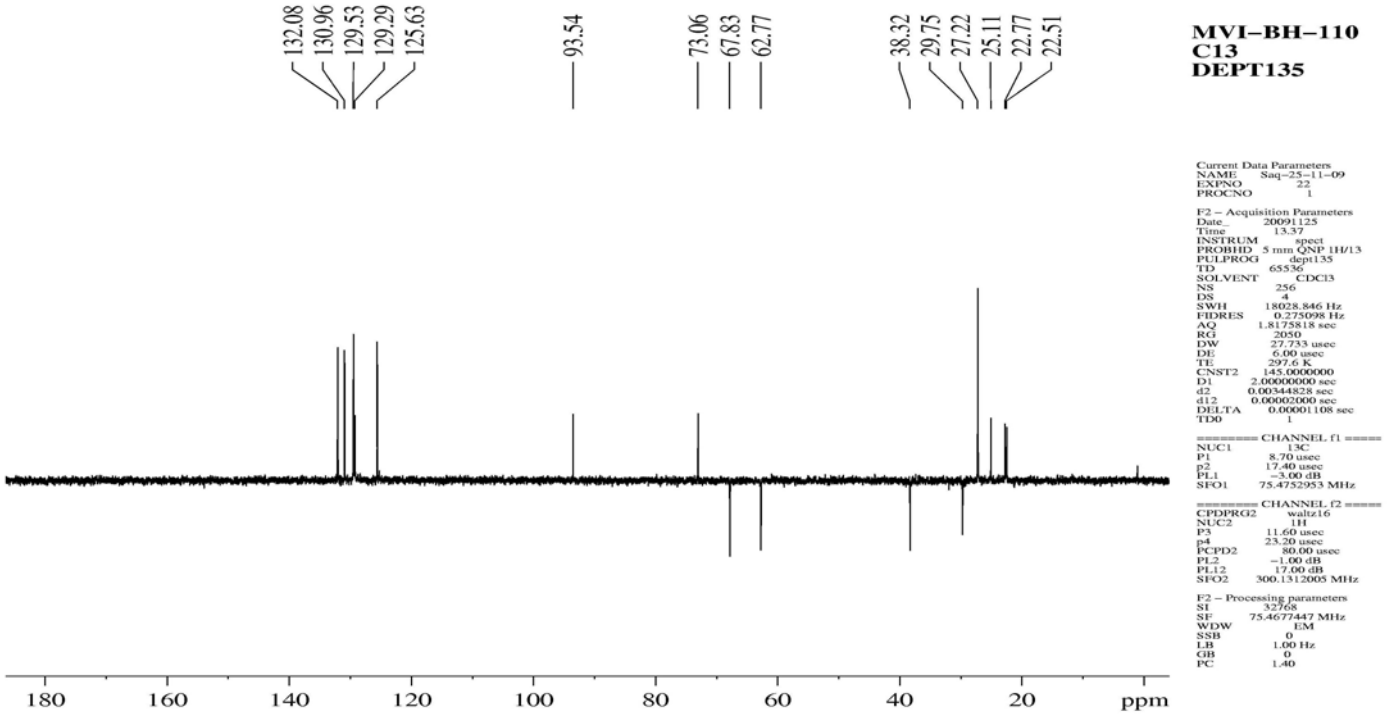


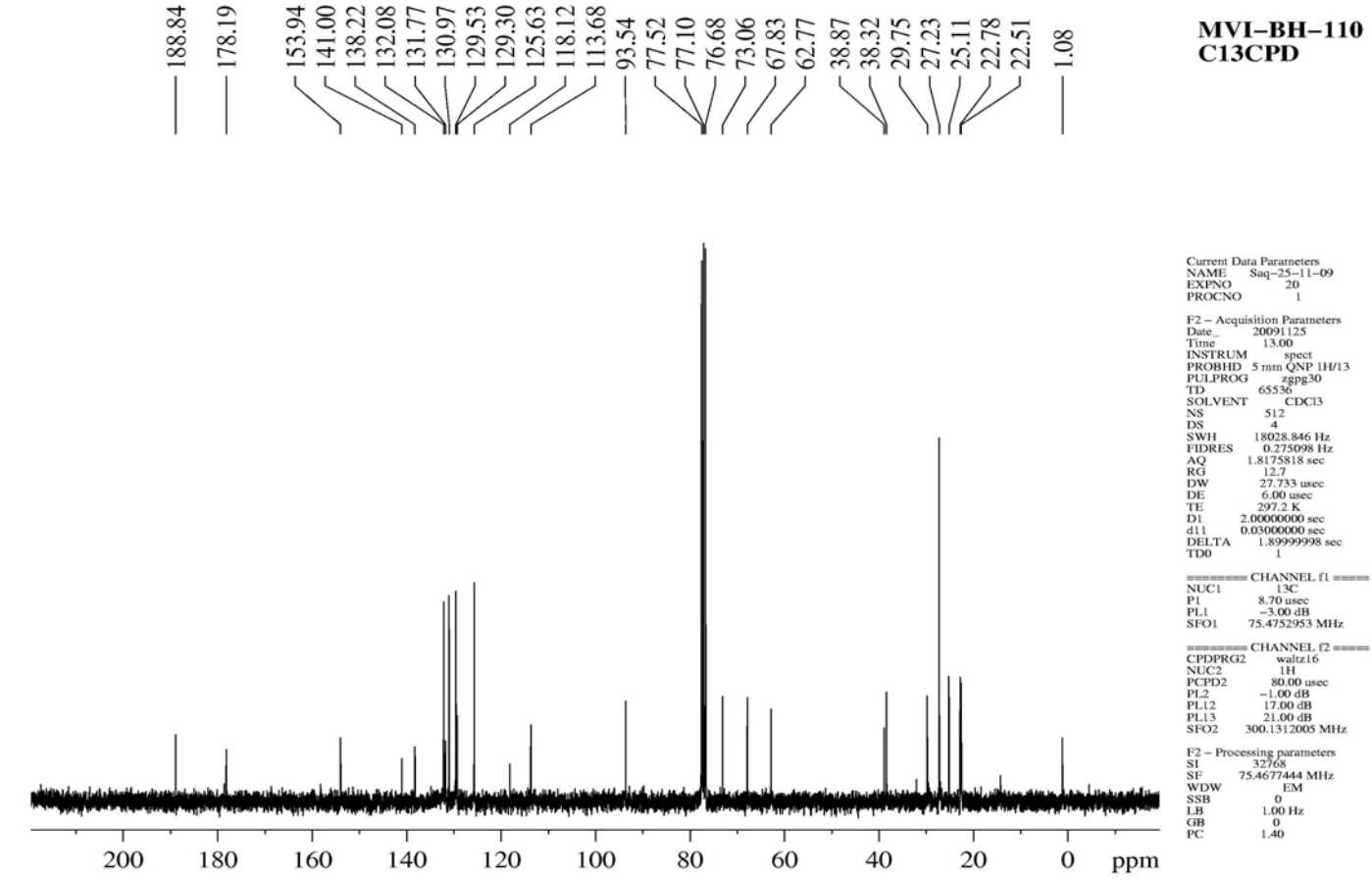


^{13}C and DEPT 135 NMR spectra of compound **5**

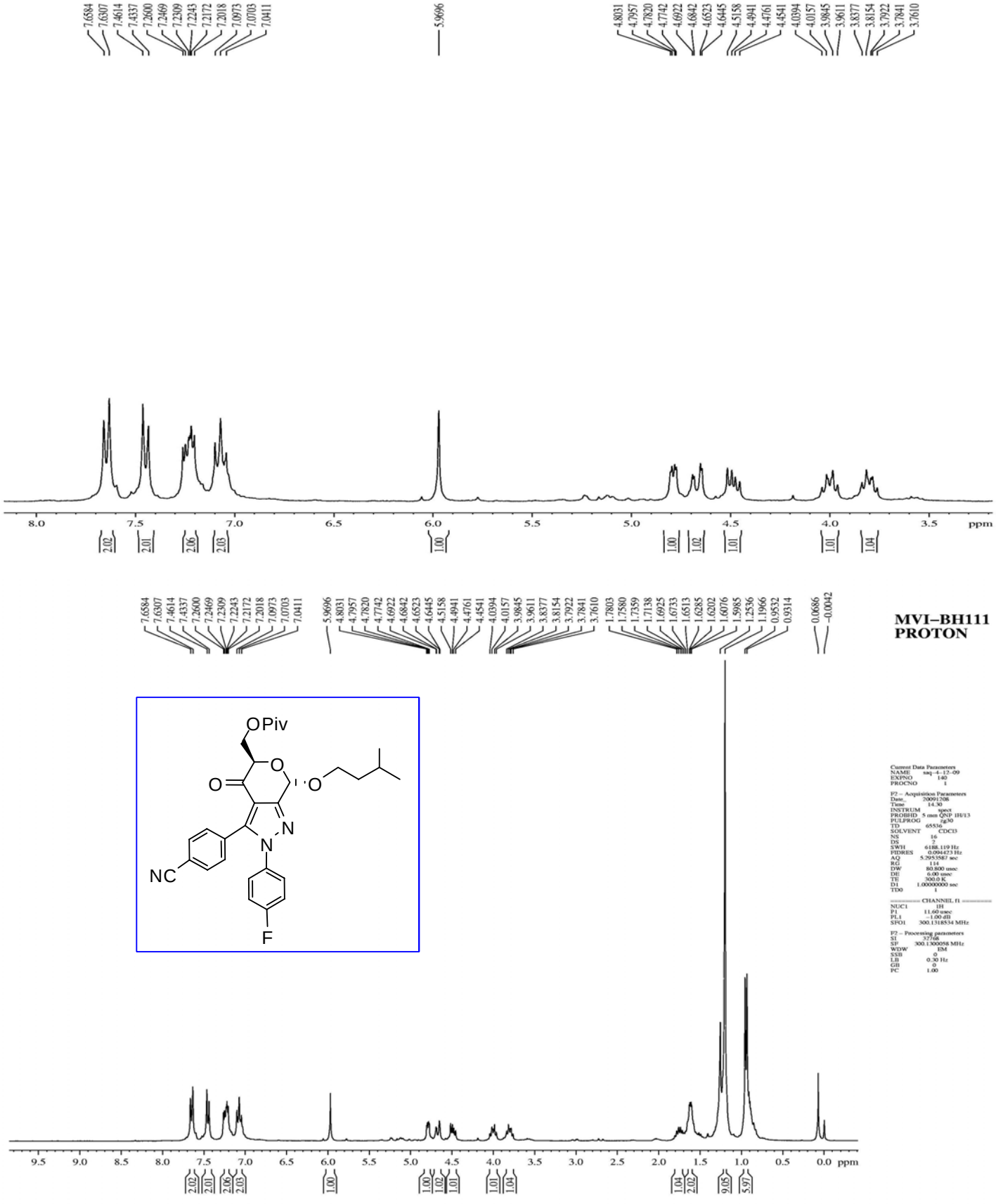


^{1}H NMR spectrum of compound **6** and its expansion

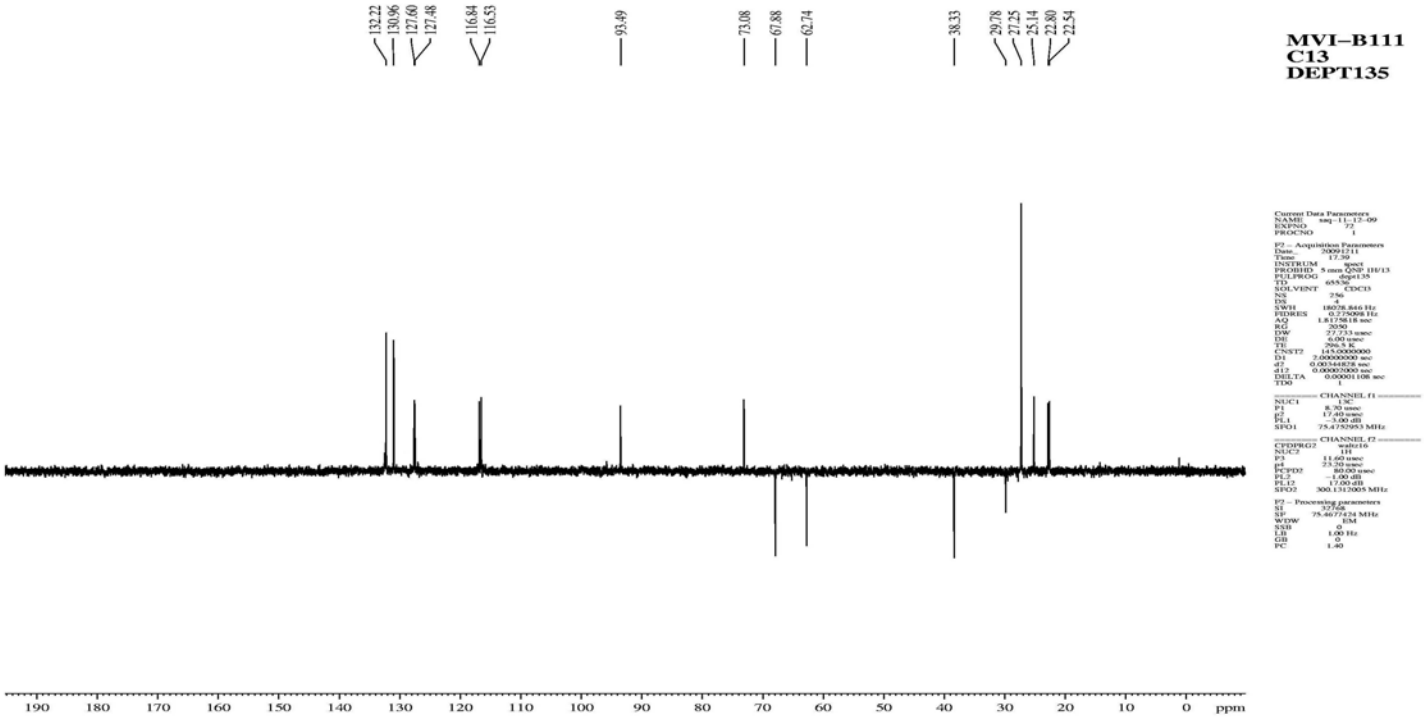


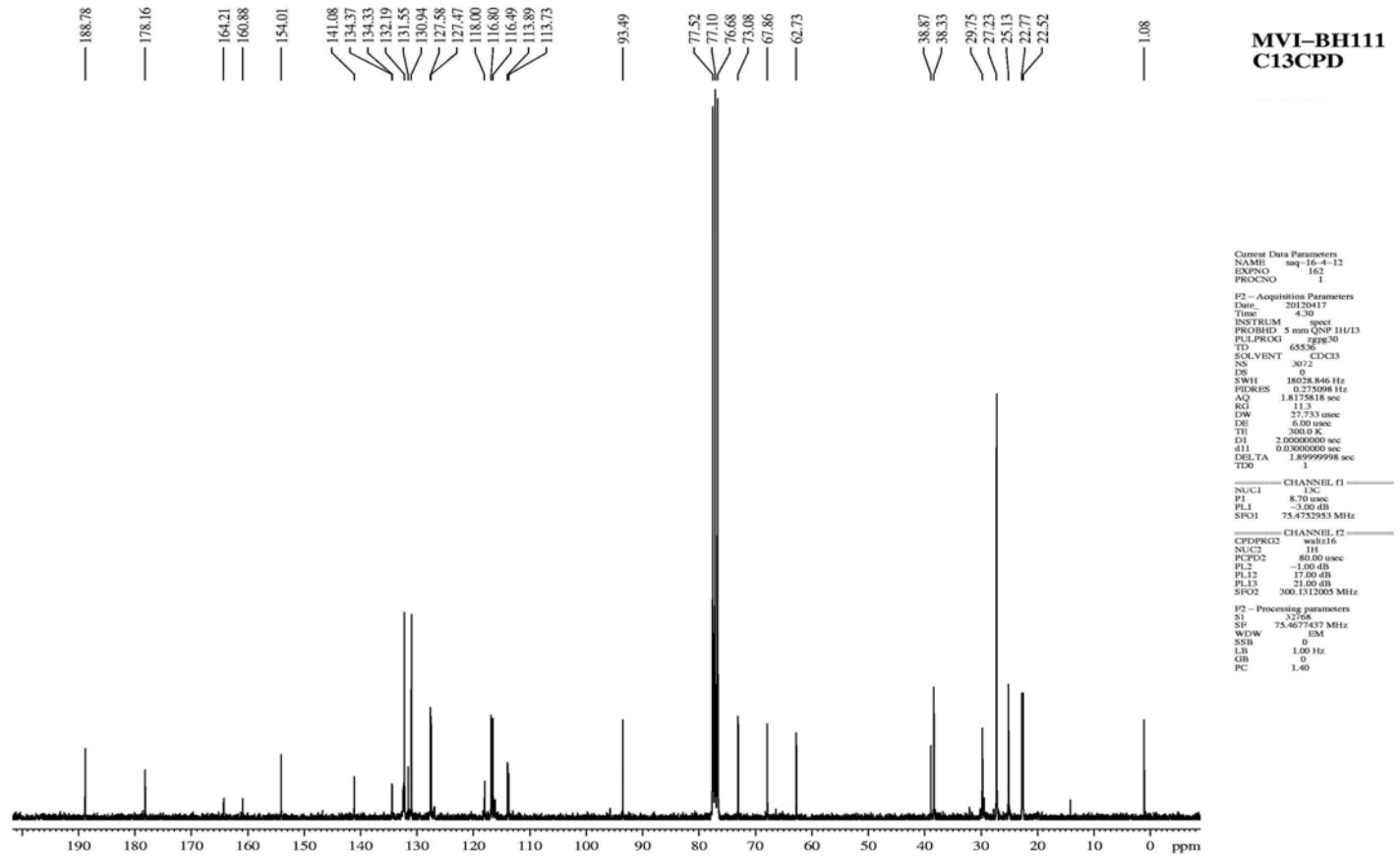


^{13}C and DEPT 135 NMR spectra of compound **6**

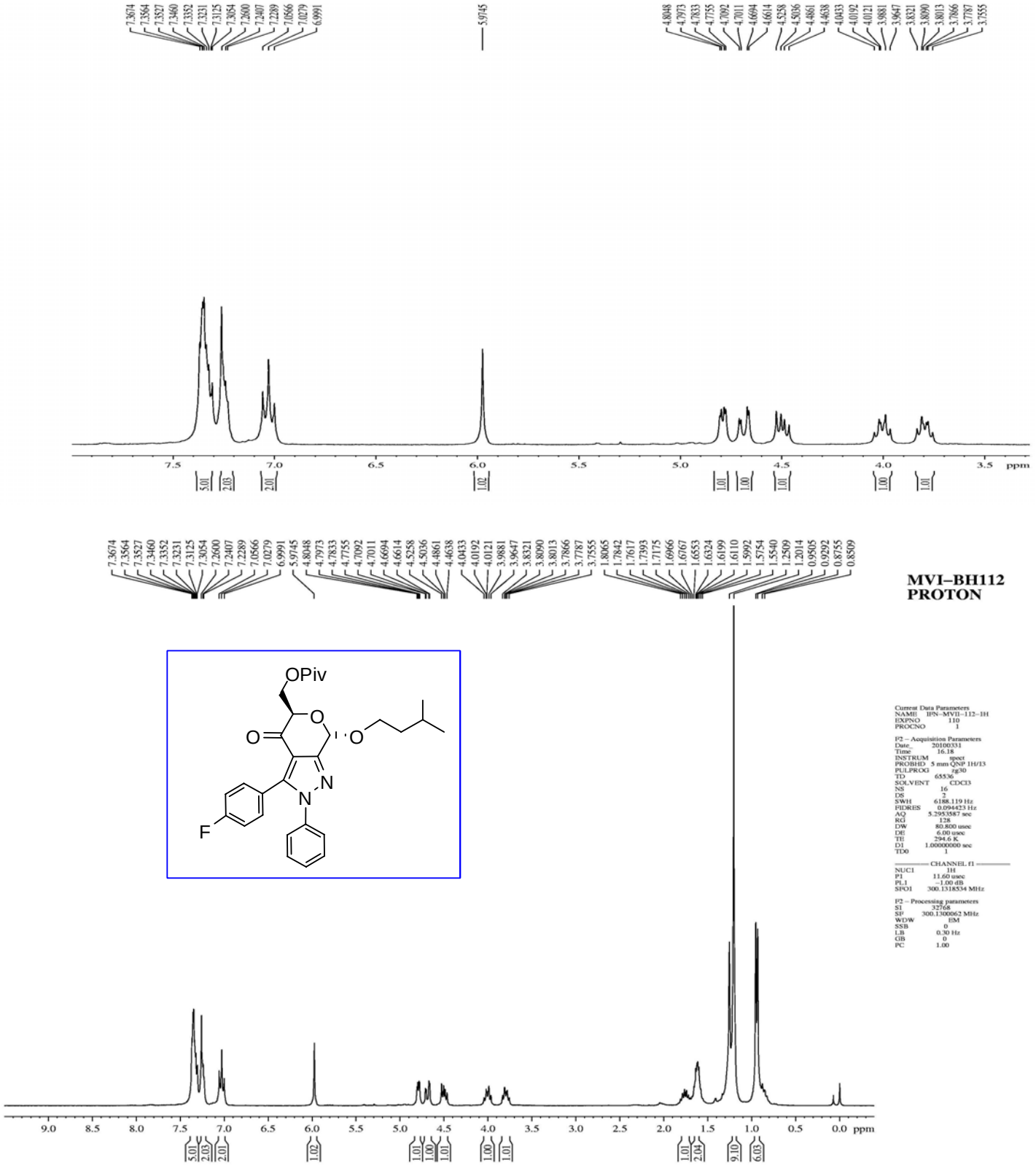


^{1}H NMR spectrum of compound **7** and its expansion

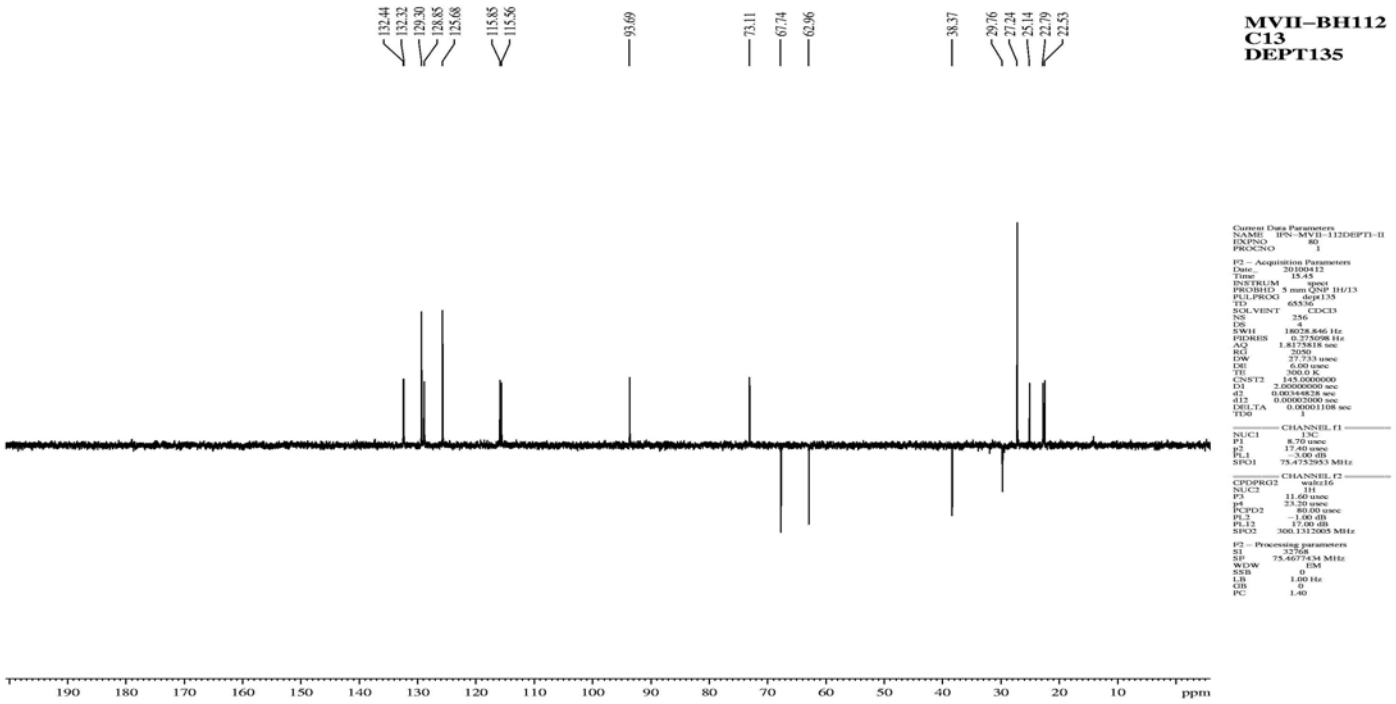


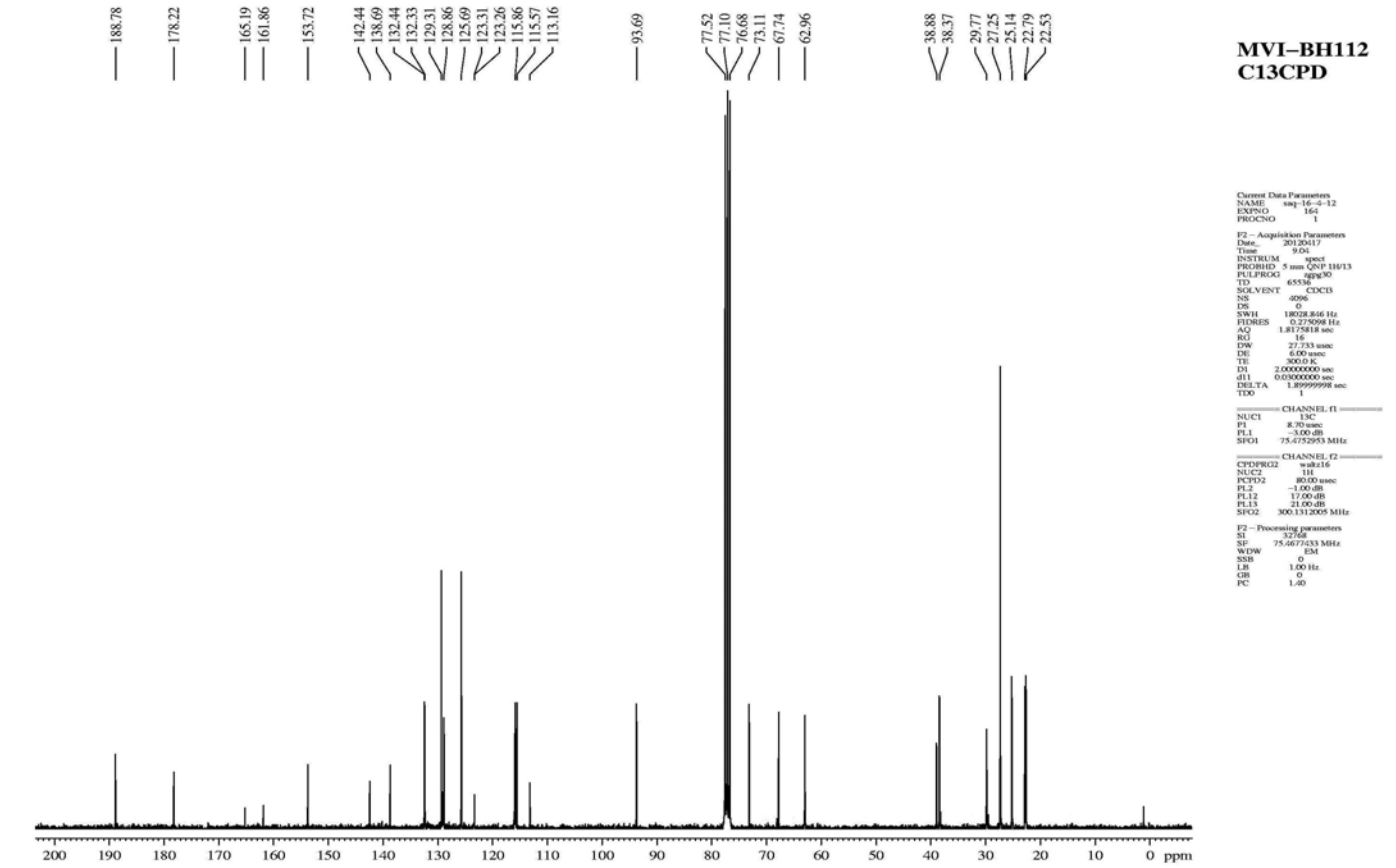


^{13}C and DEPT 135 NMR spectra of compound **7**

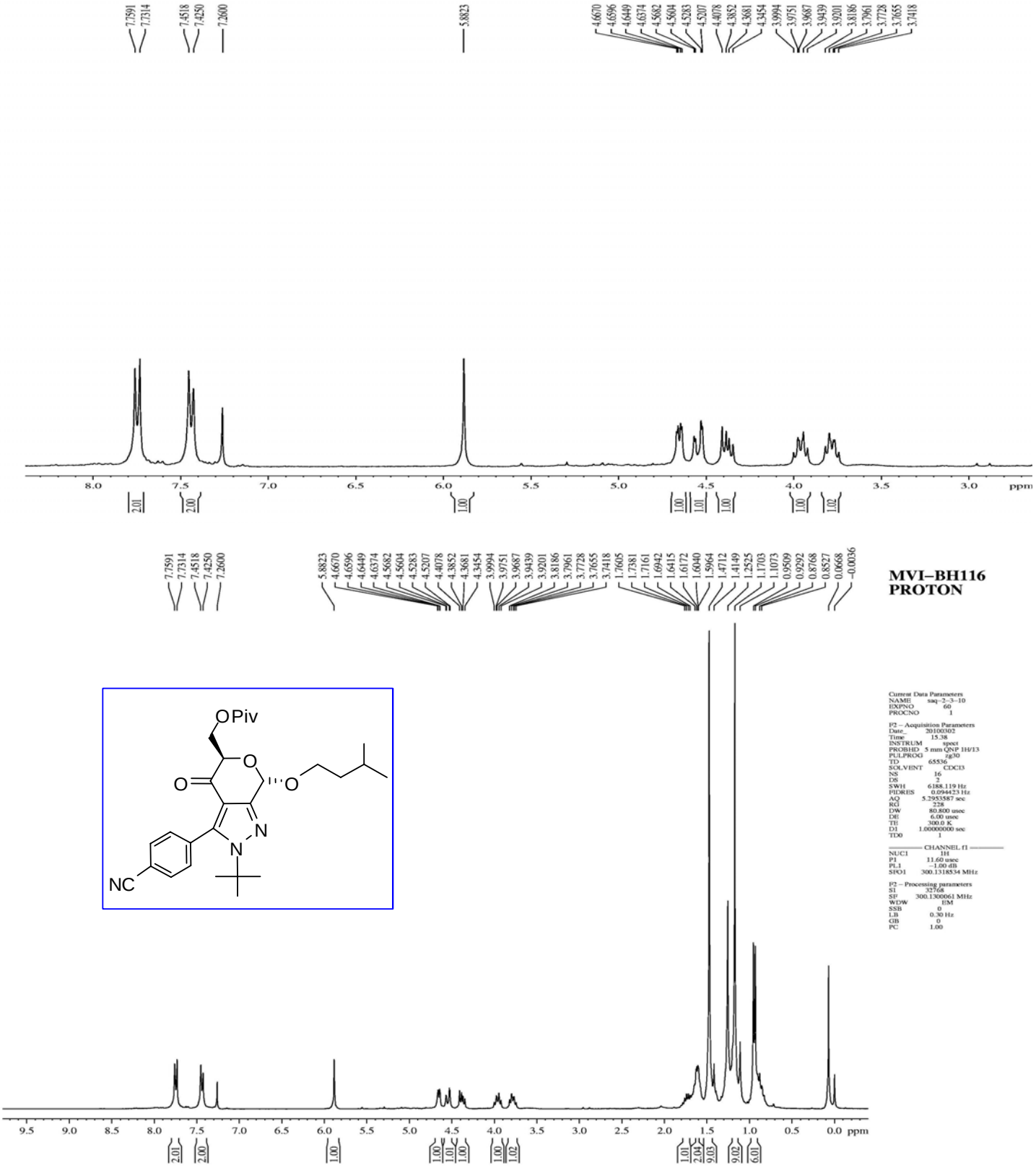


^{1}H NMR spectrum of compound **8** and its expansion

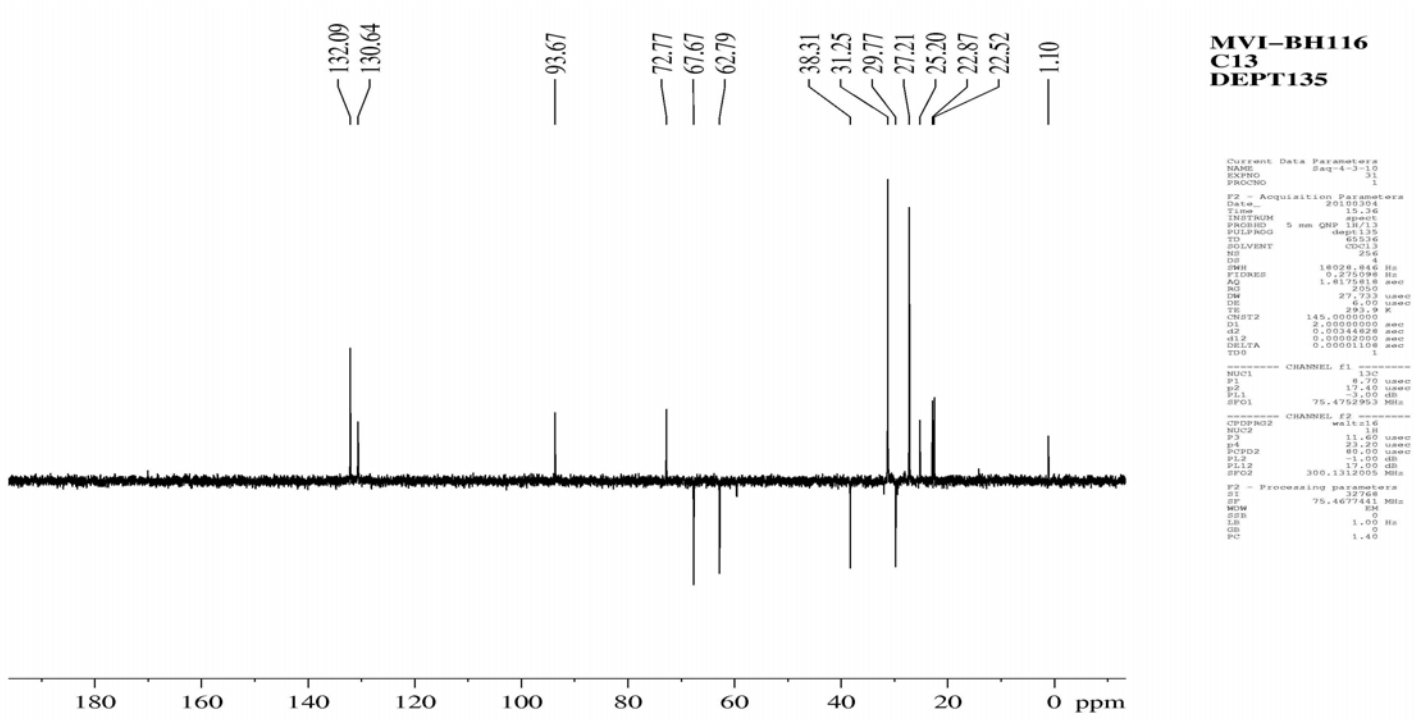


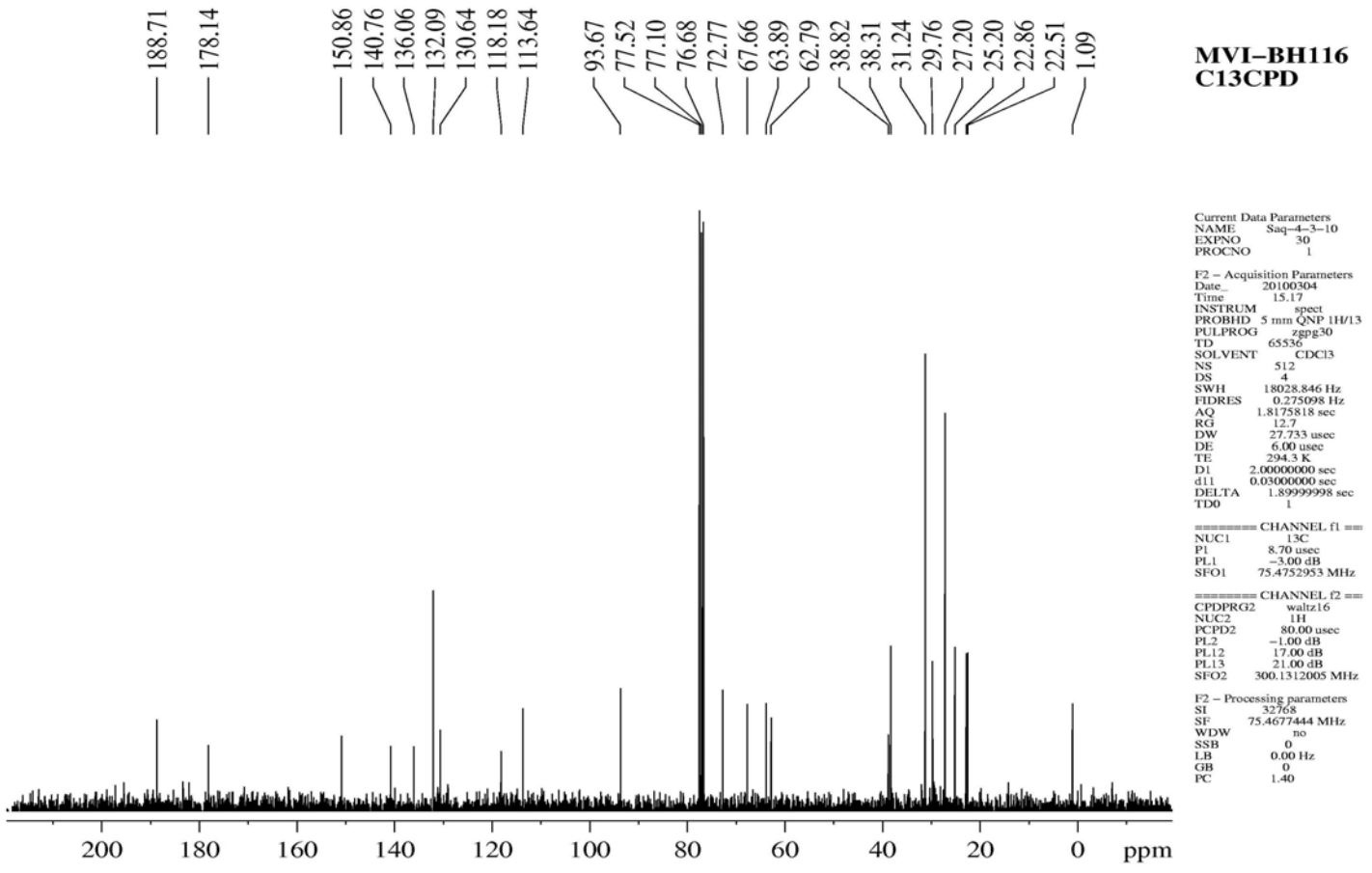


^{13}C and DEPT 135 NMR spectra of compound **8**

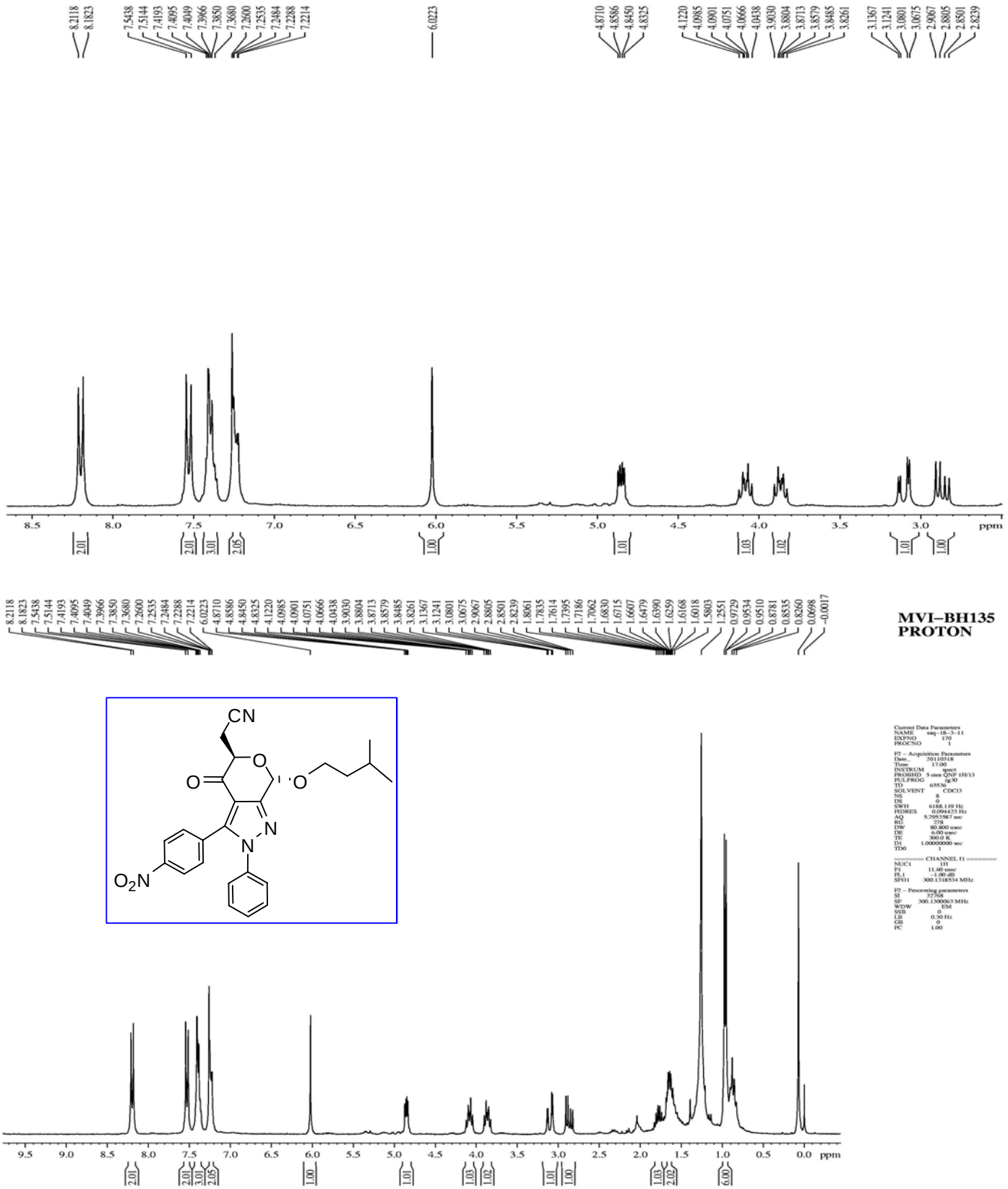


^{1}H NMR spectrum of compound **9** and its expansion

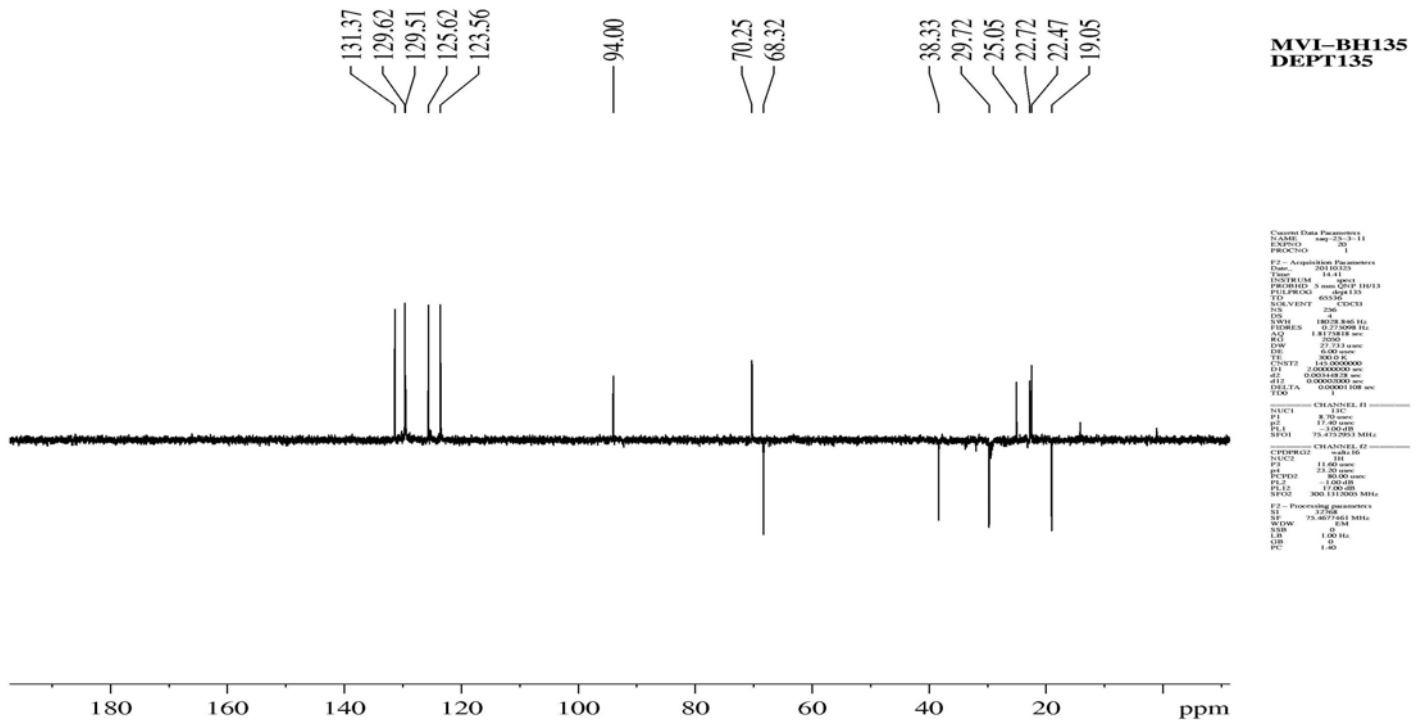


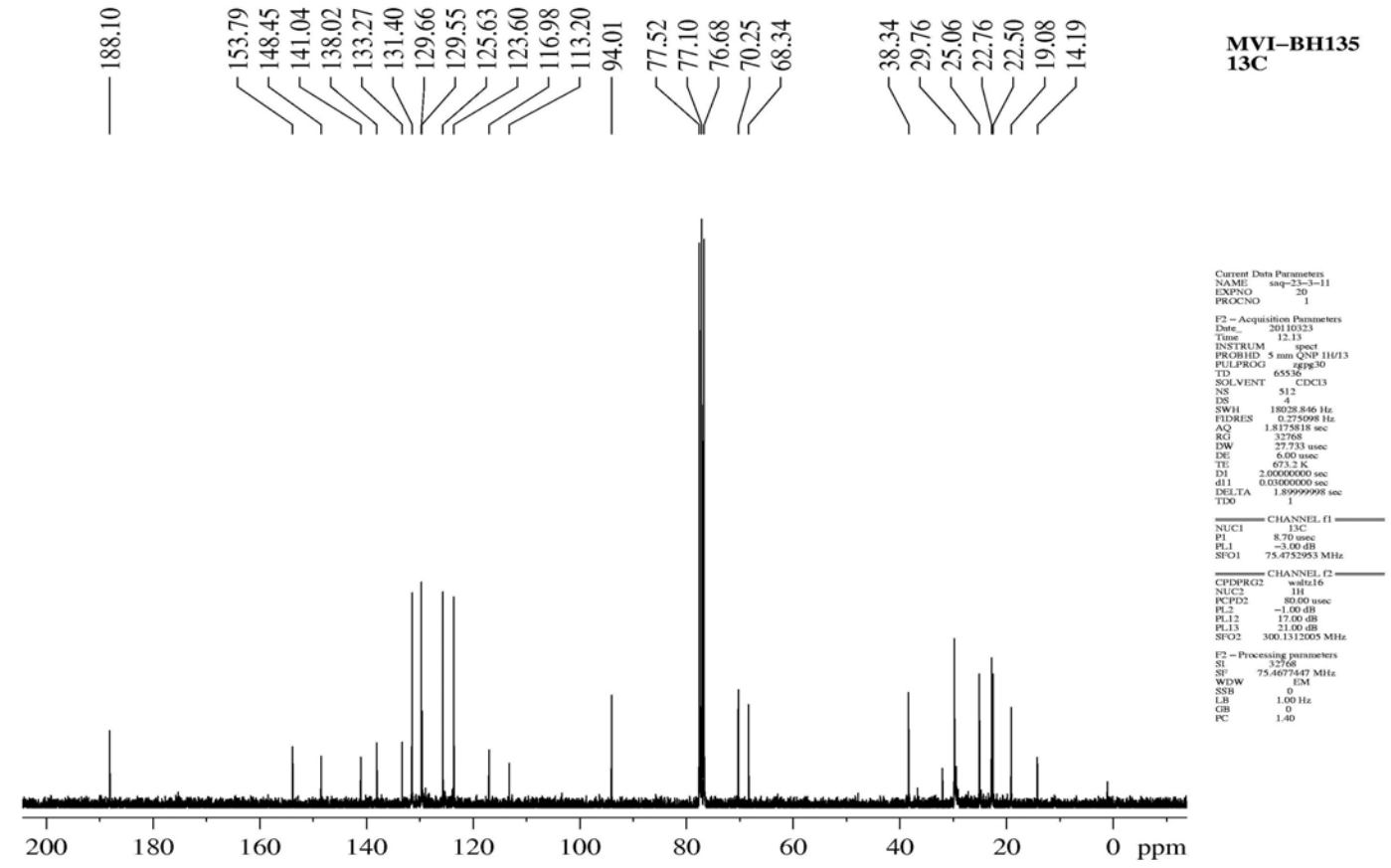


^{13}C and DEPT 135 NMR spectra of compound **9**

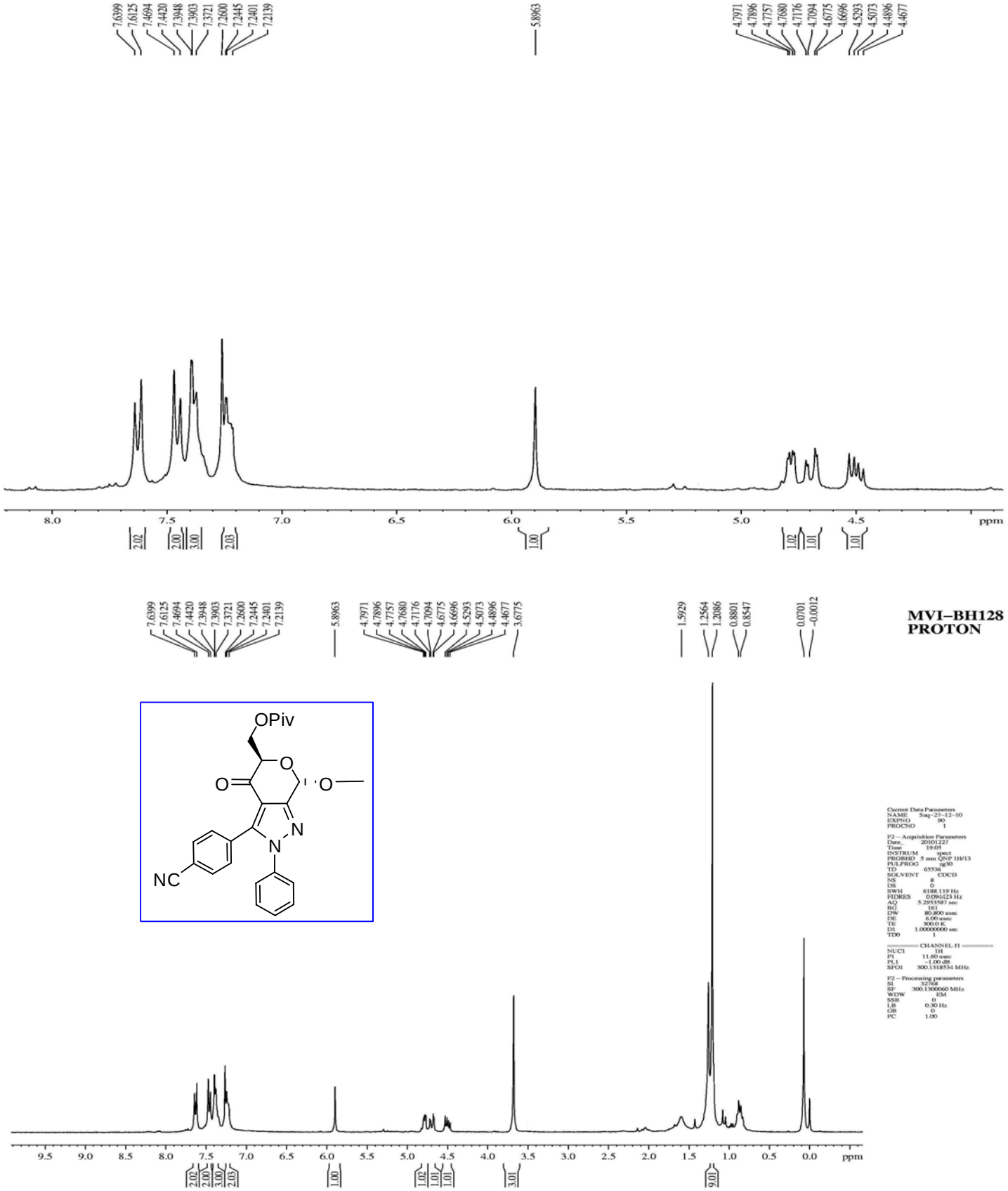


^{1}H NMR spectrum of compound **10** and its expansion

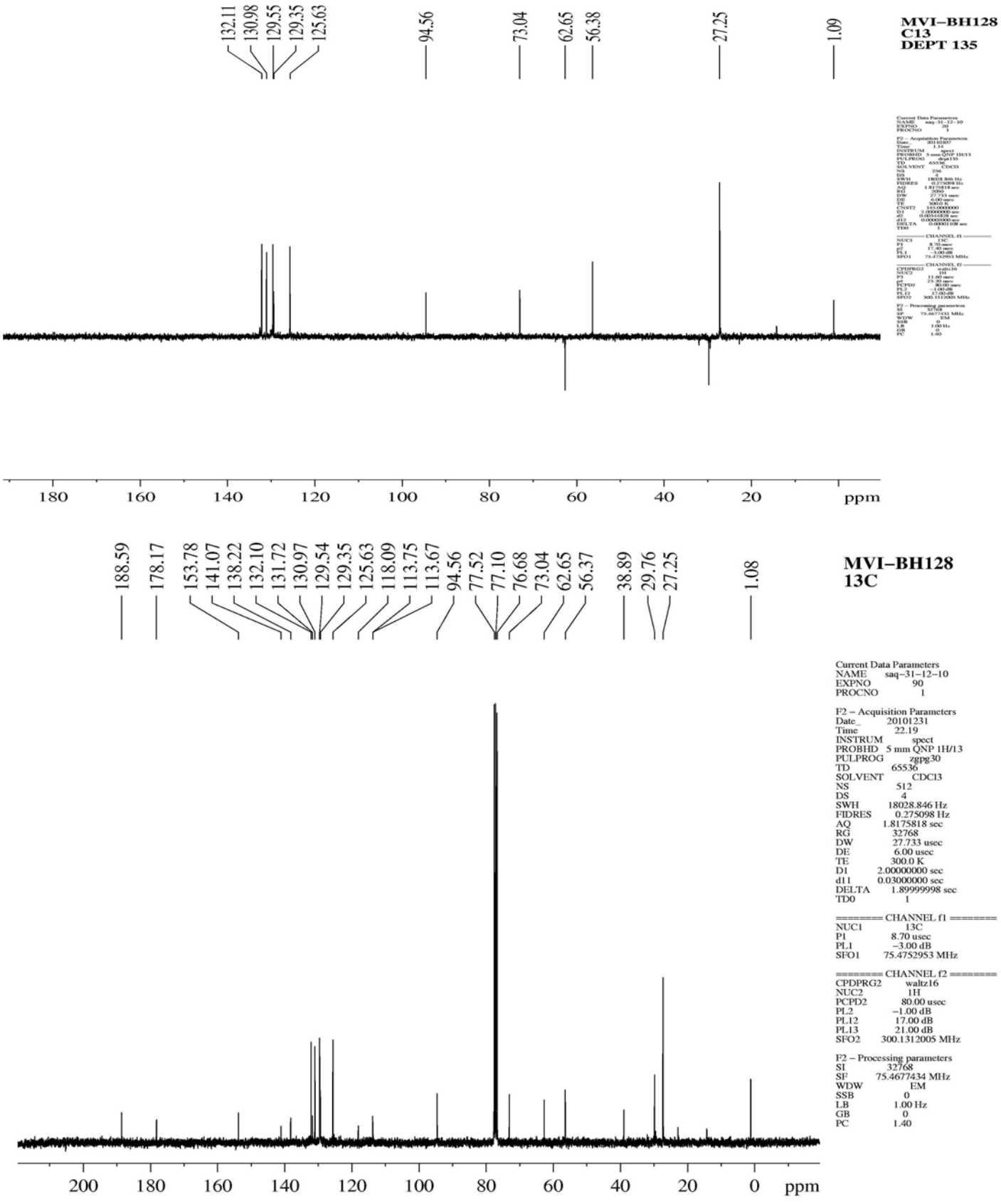




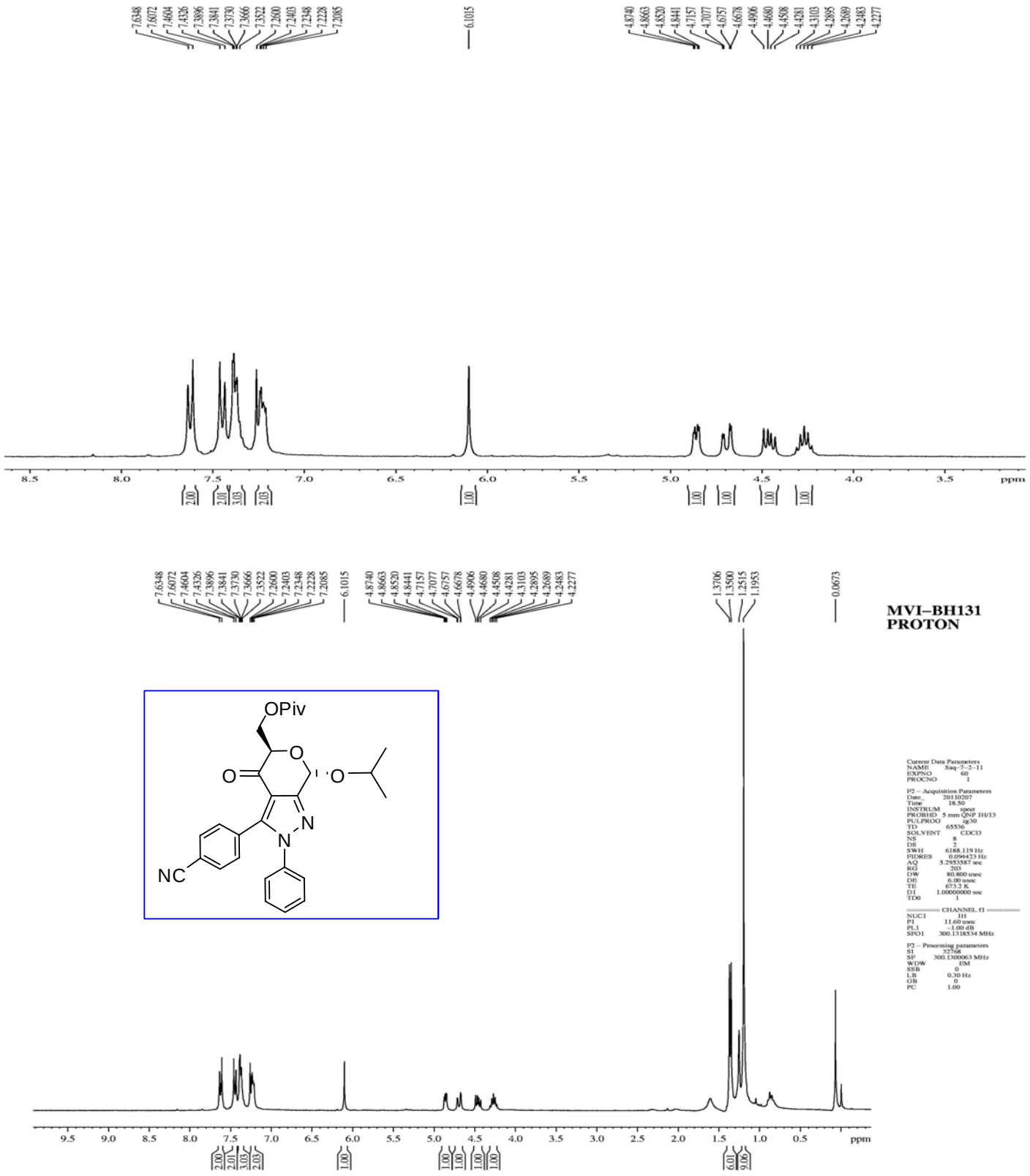
^{13}C and DEPT 135 NMR spectra of compound **10**



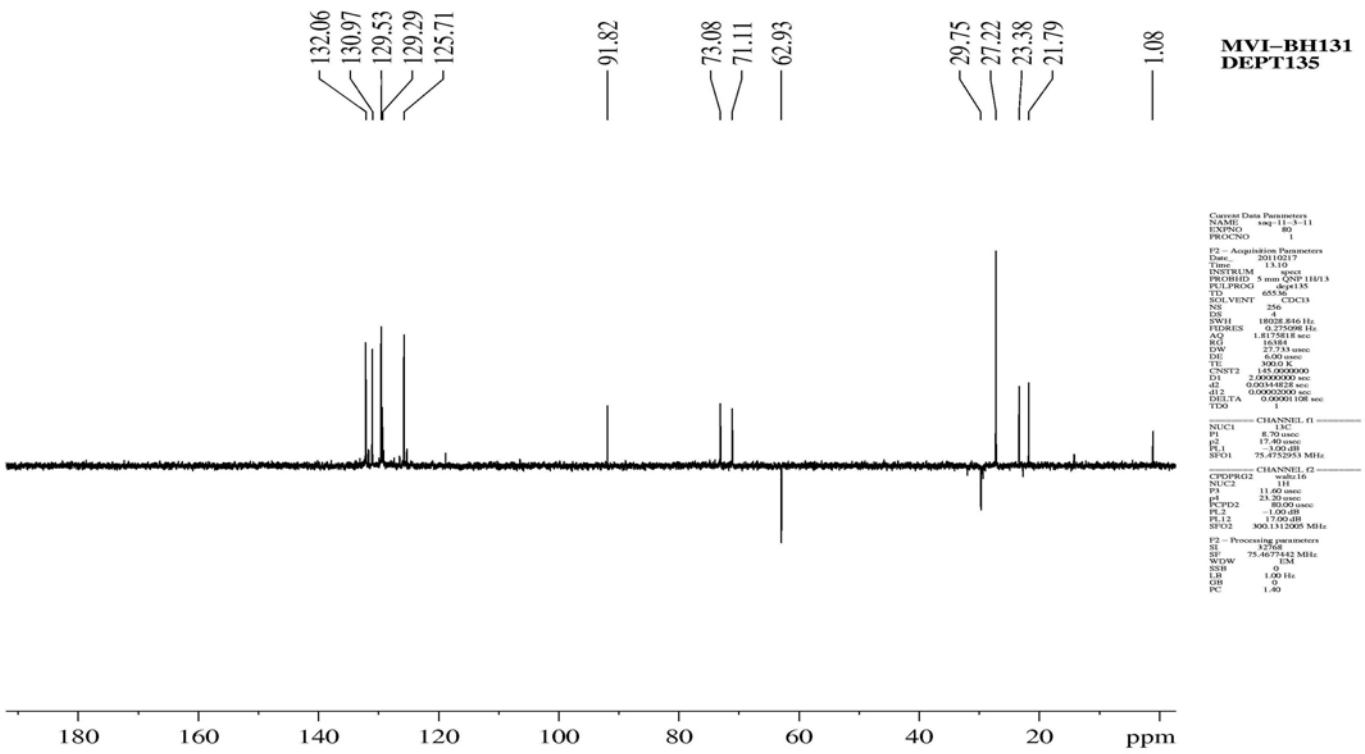
^{1}H NMR spectrum of compound **11** and its expansion

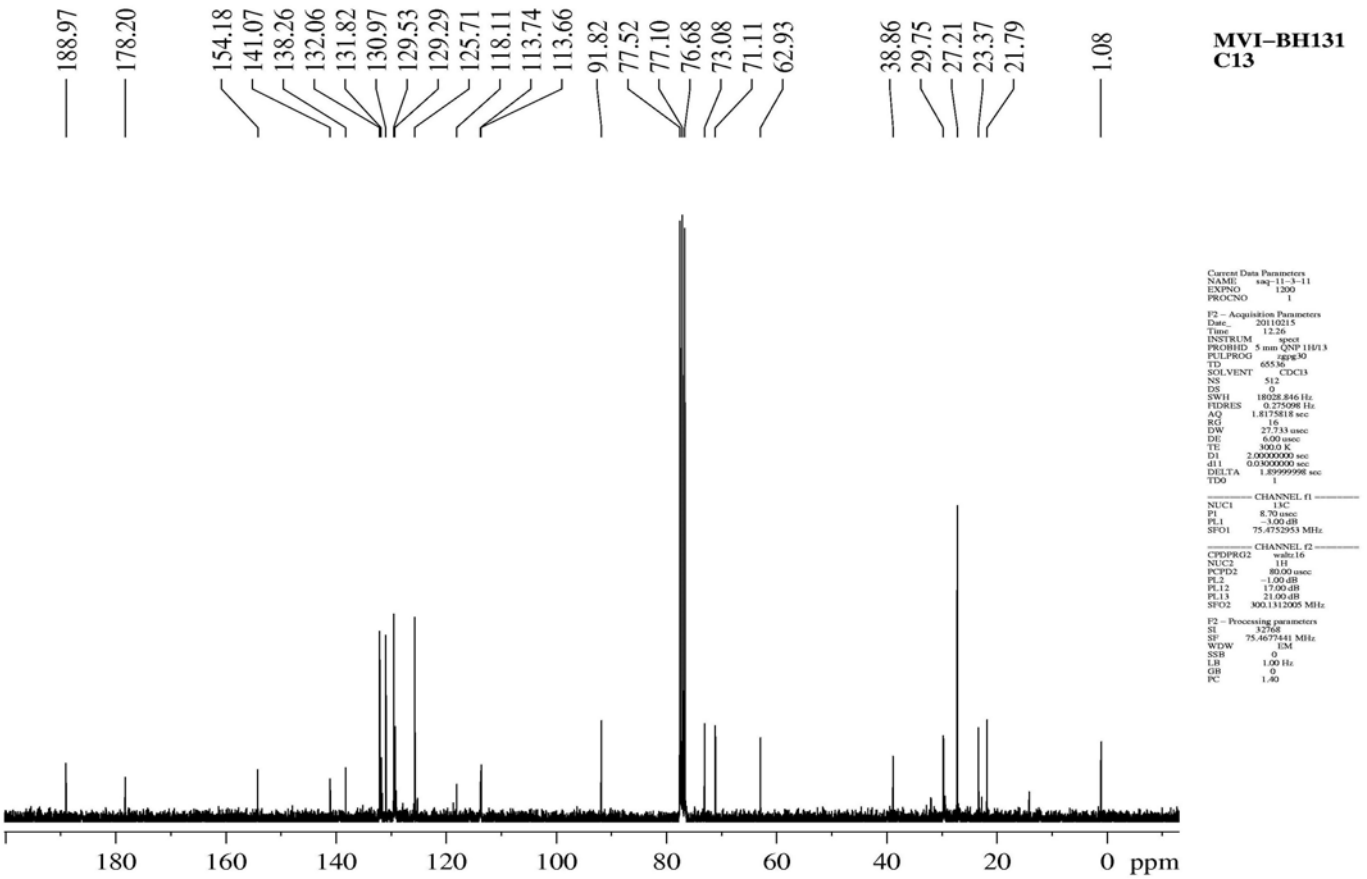


^{13}C and DEPT 135 NMR spectra of compound **11**

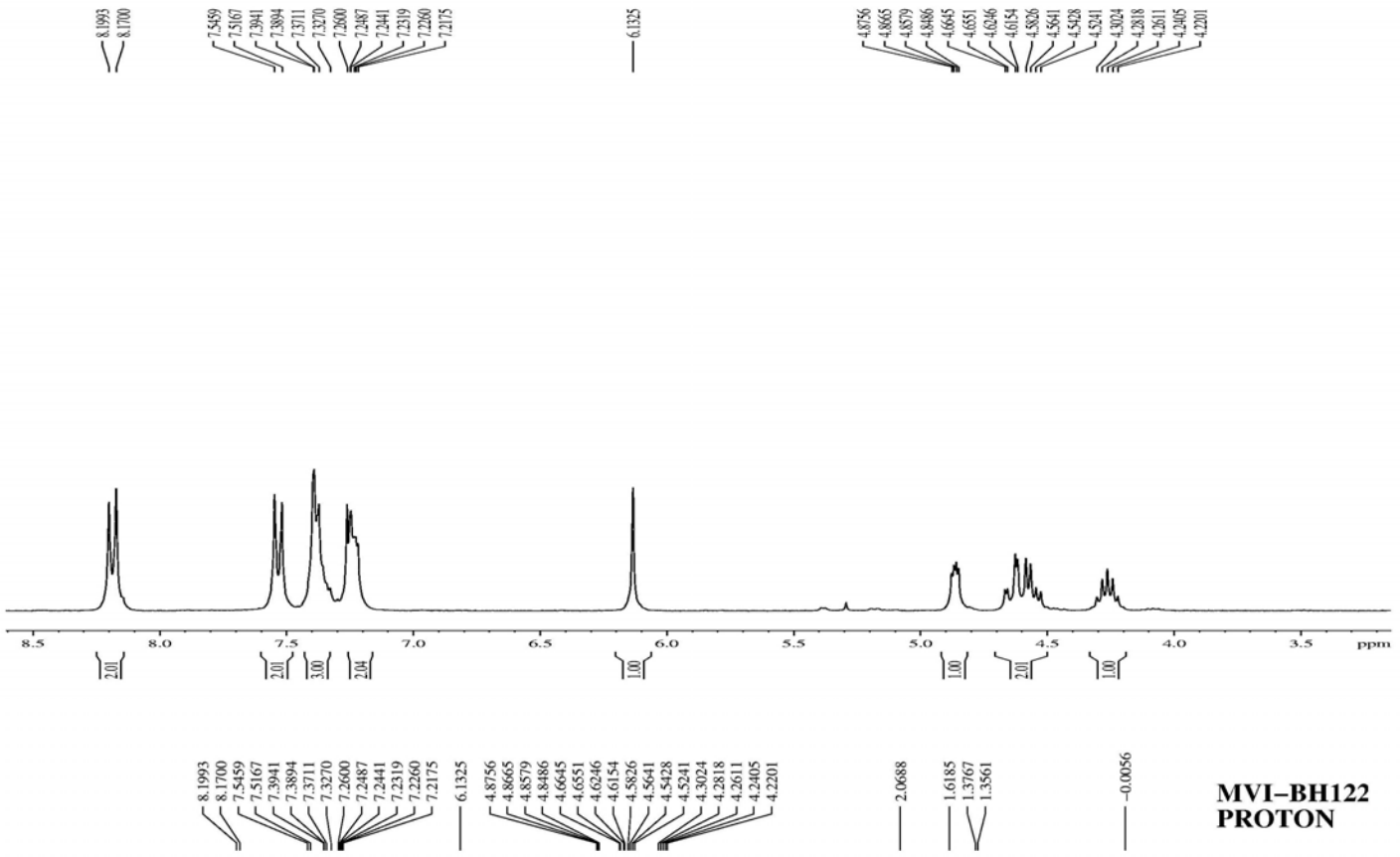


^{1}H NMR spectrum of compound **12** and its expansion

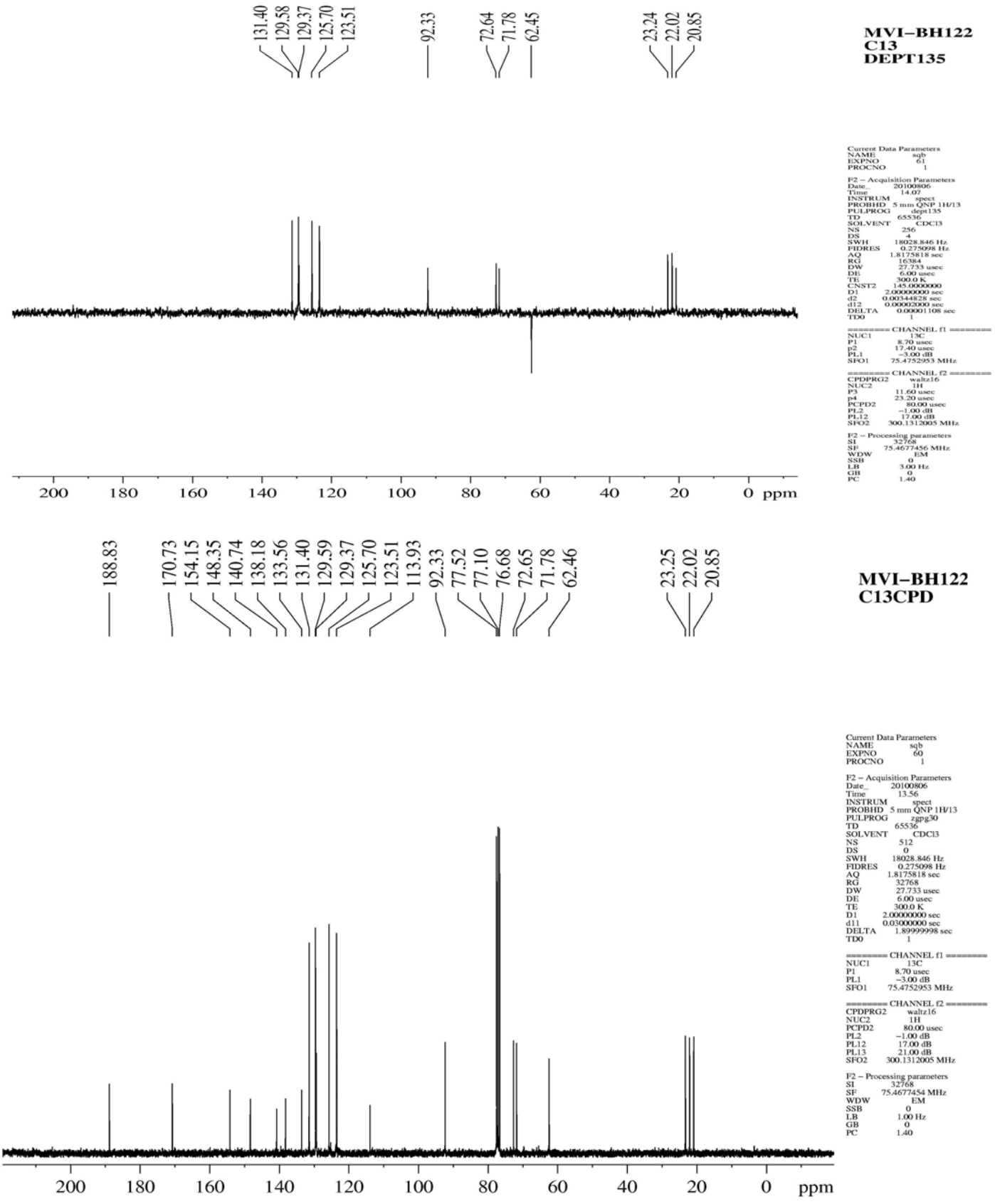




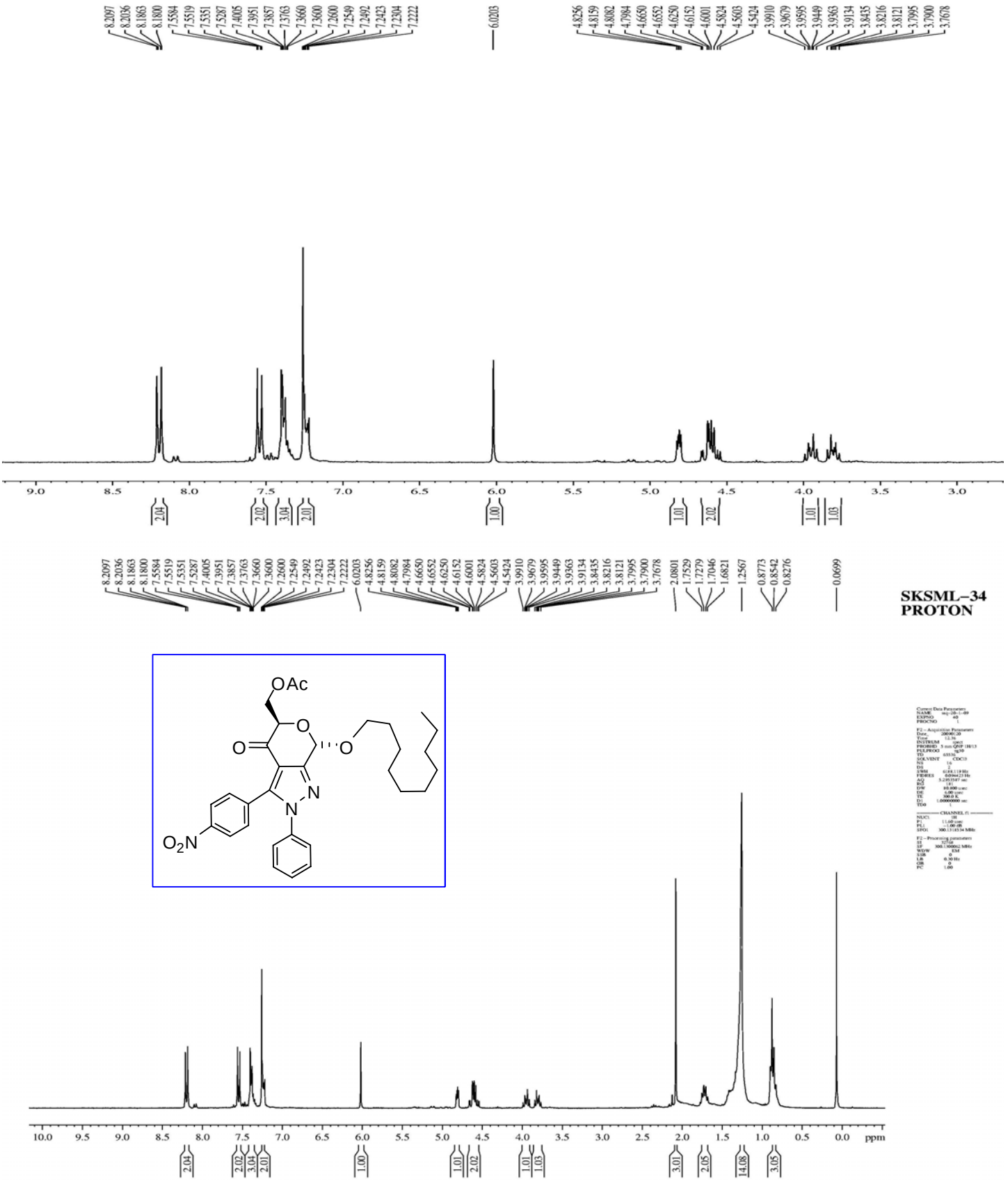
^{13}C and DEPT 135 NMR spectra of compound **12**



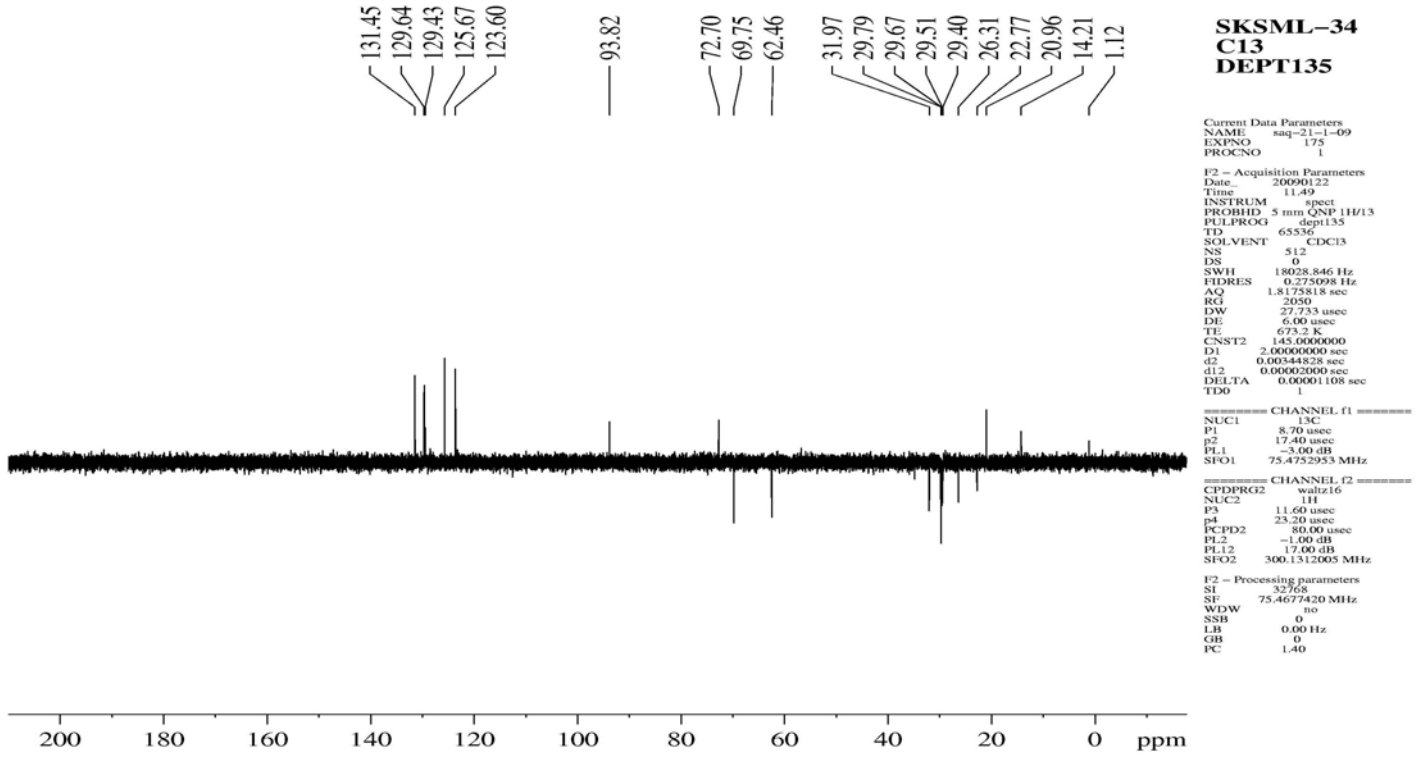
^{1}H NMR spectrum of compound **13** and its expansion

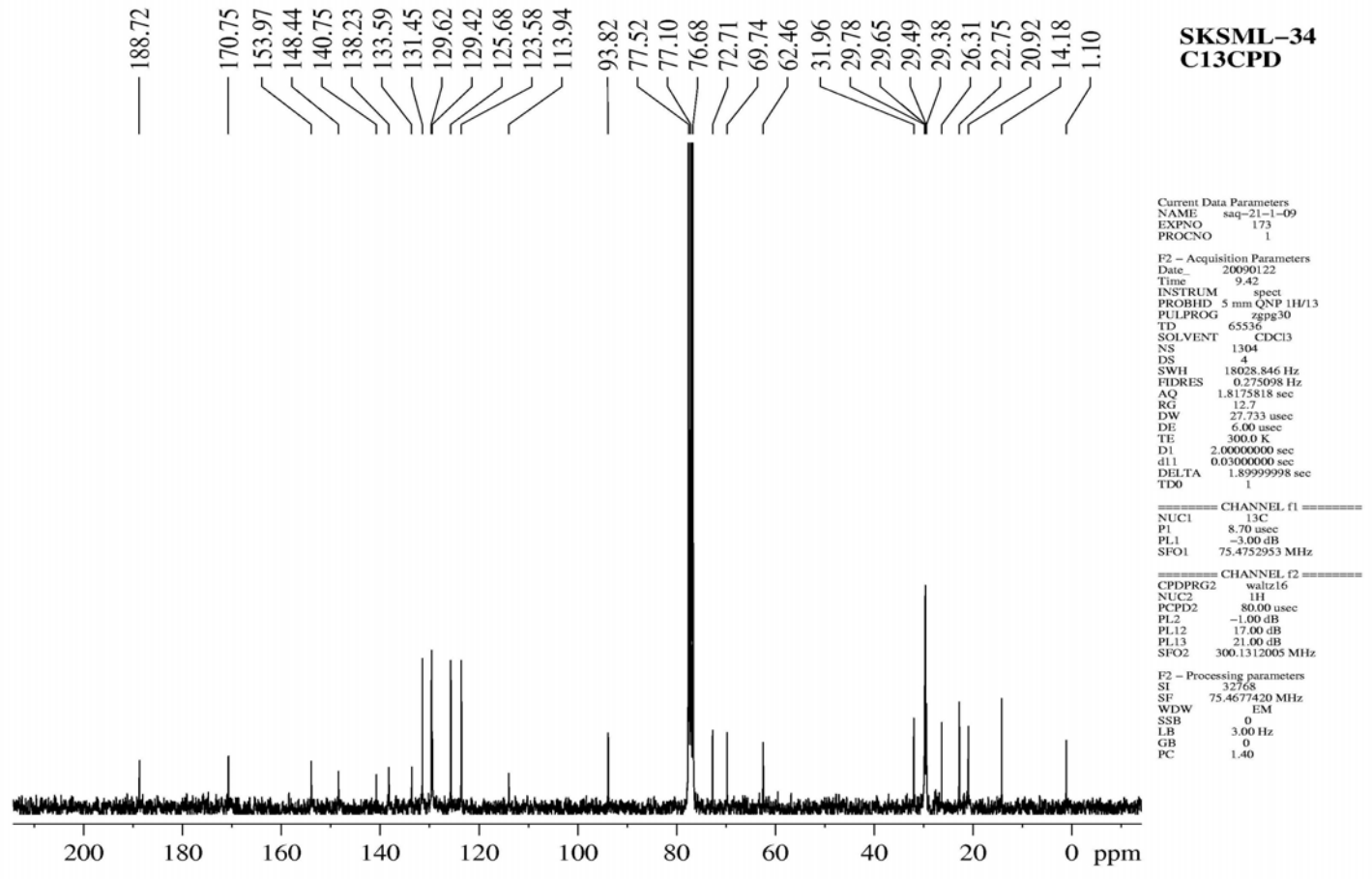


^{13}C and DEPT 135 NMR spectra of compound **13**

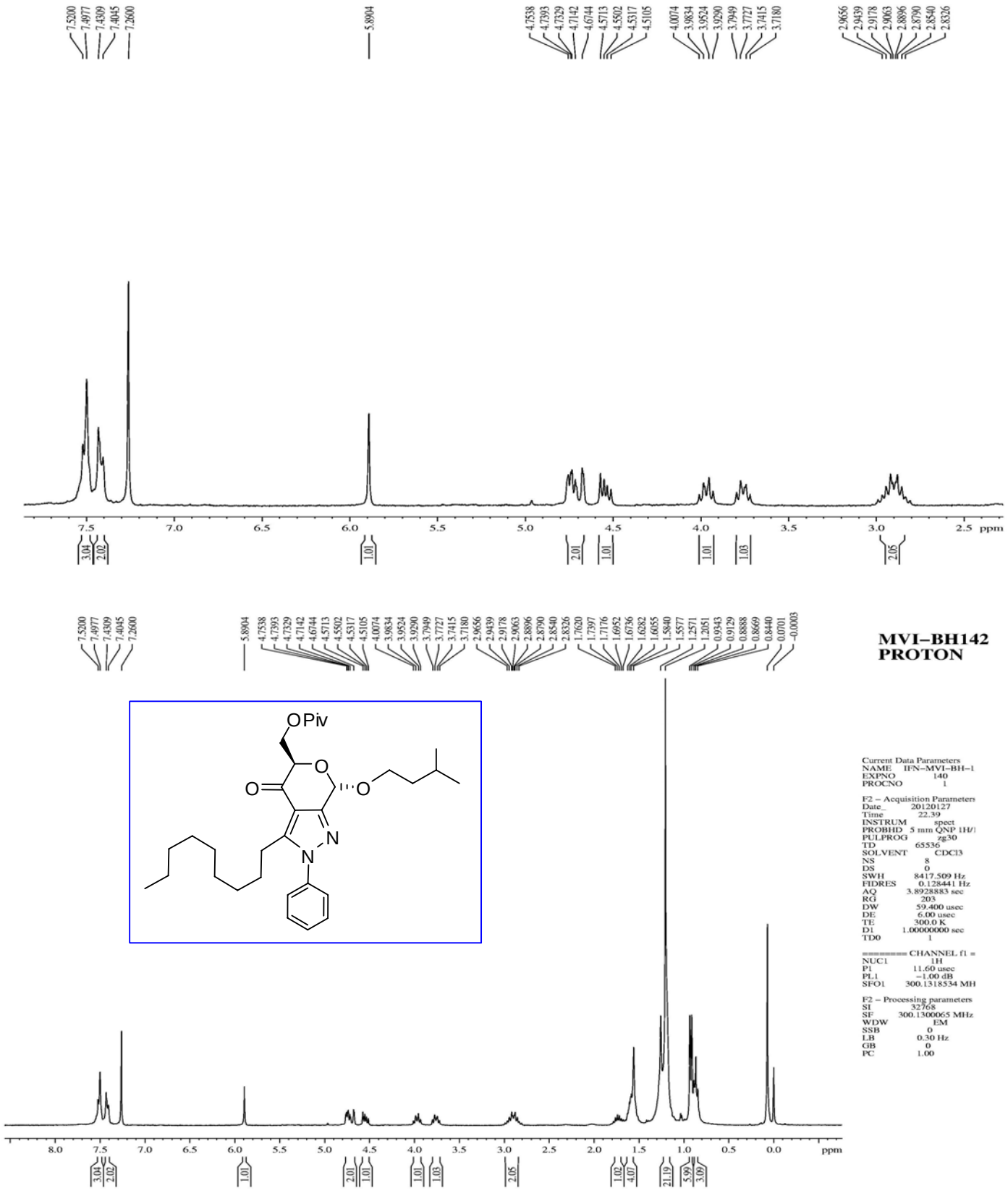


^{1}H NMR spectrum of compound **14** and its expansion

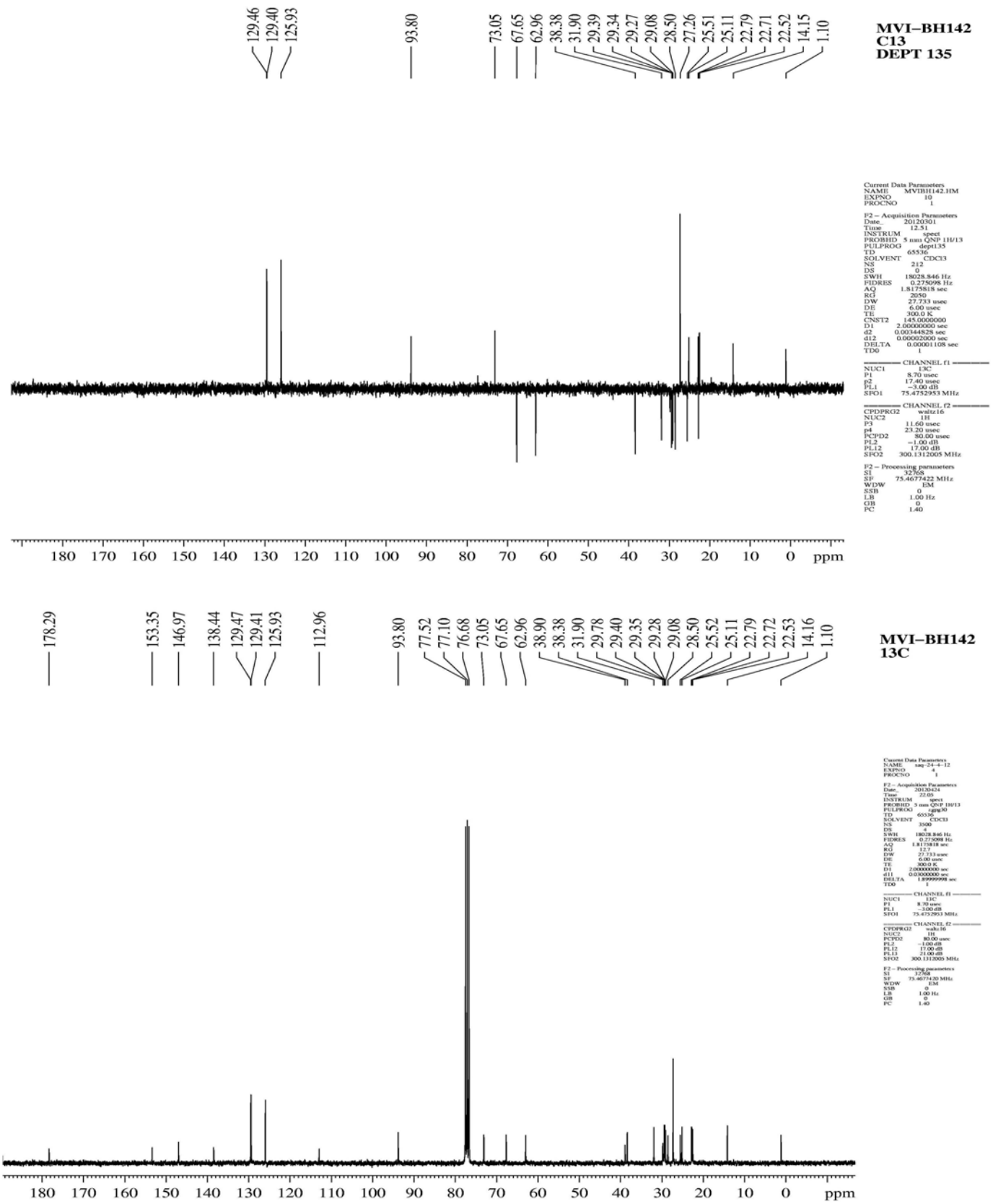




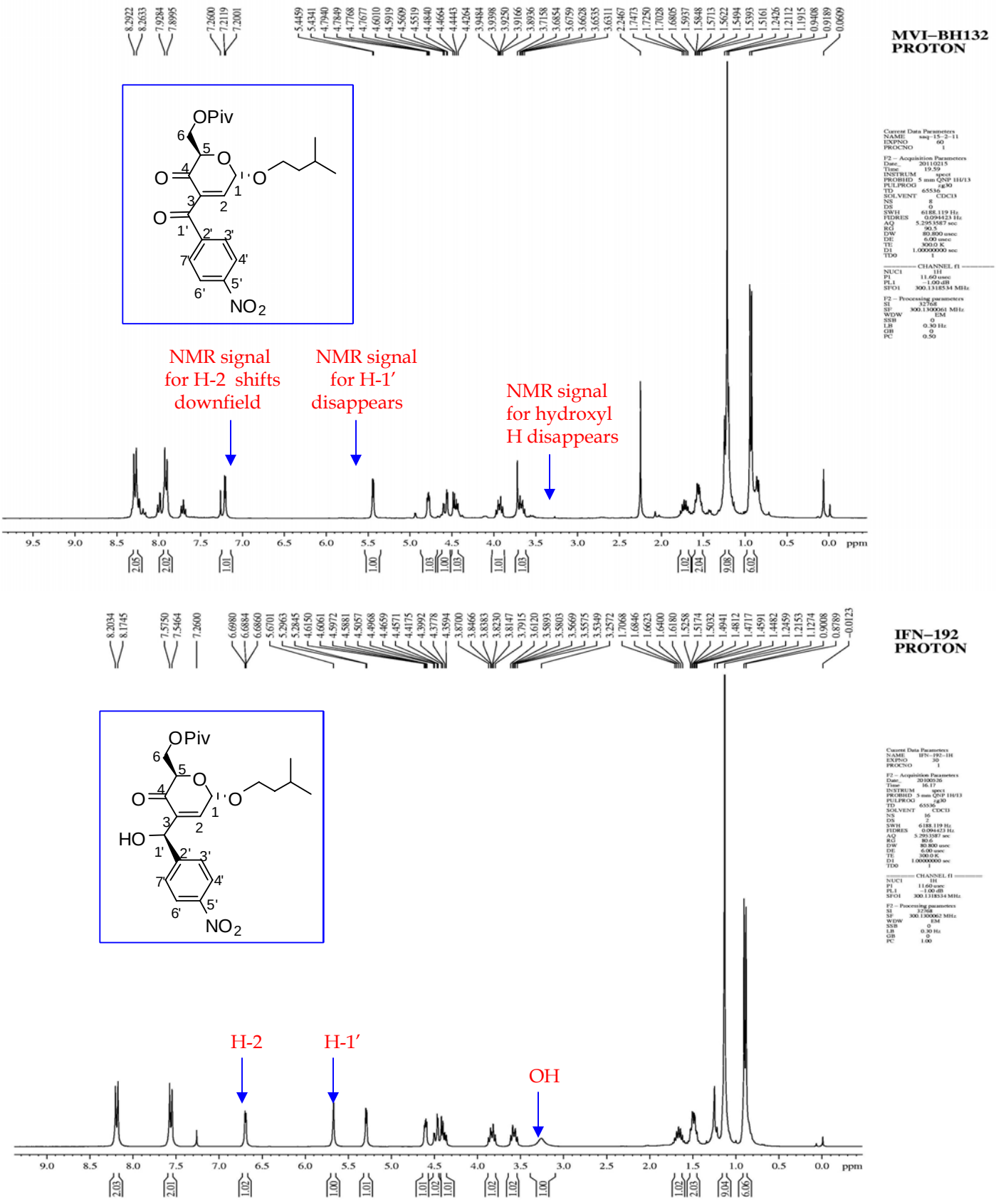
^{13}C and DEPT 135 NMR spectra of compound **14**



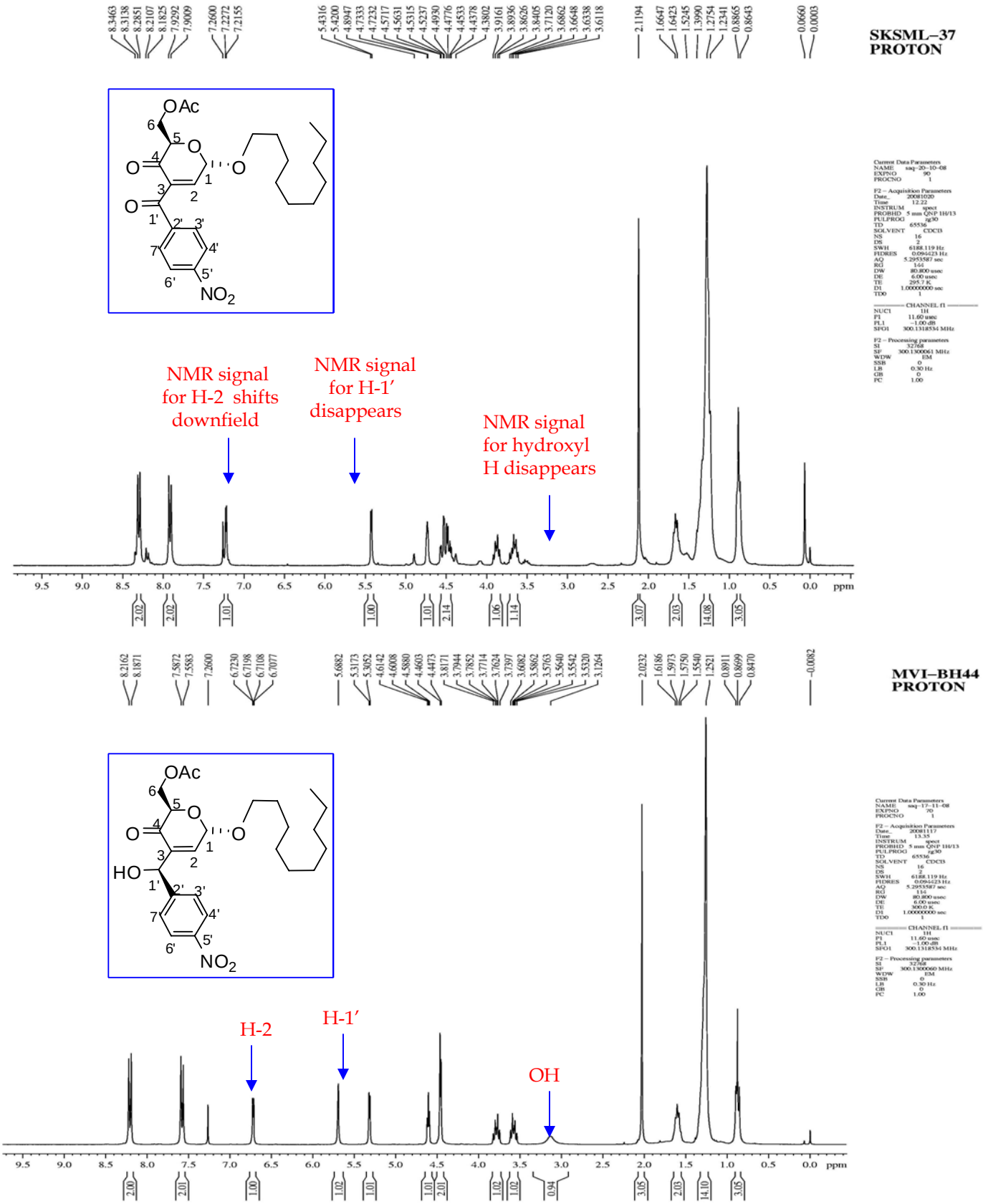
^{1}H NMR spectrum of compound **15** and its expansion



^{13}C and DEPT 135 NMR spectra of compound **15**



^{1}H NMR spectra of MBH adduct **1a** and crude product mixture of its oxidized derivative **2a** (above)



^{1}H NMR spectra of MBH adduct **1h** and crude product mixture of its oxidized derivative **2h** (above)

Single crystal X-ray crystallographic study of compound **13**

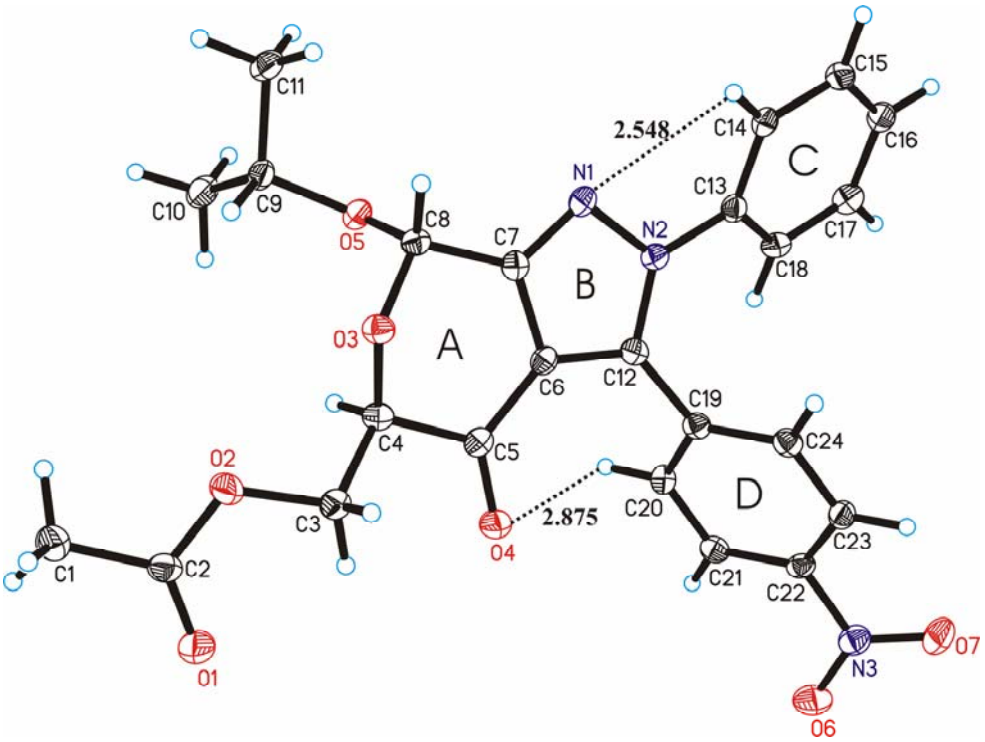


Fig. 1S. ORTEP diagram showing the molecular structure of compound **13** ($C_{24}H_{23}N_3O_7$) at 30% probability

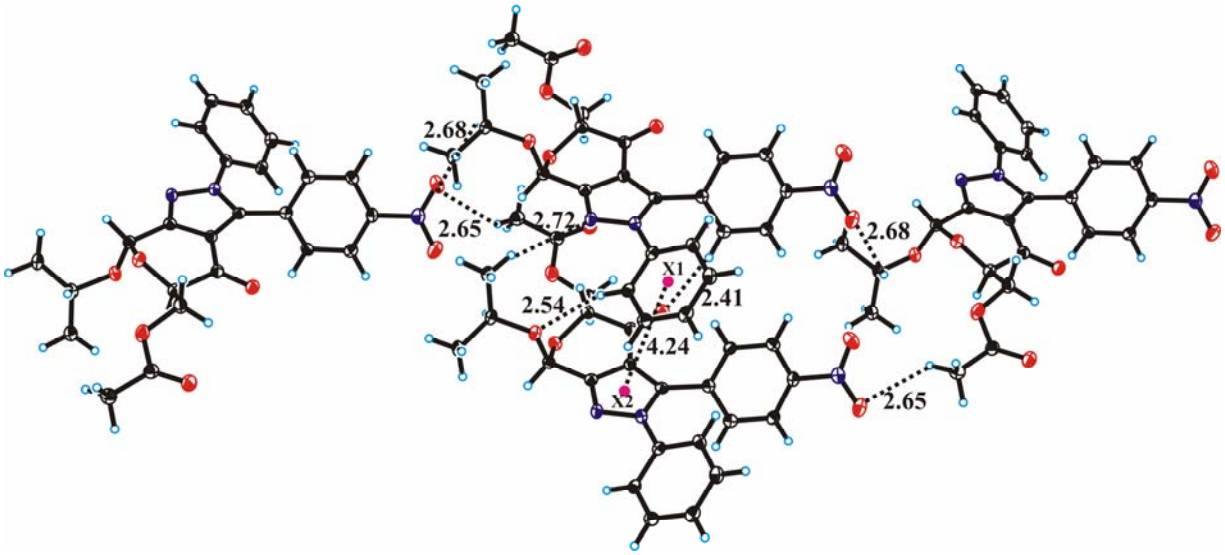


Fig. 2S The partial crystal-packing diagram of compound **13** showing intermolecular C-H...O and C-H...N and π…π interactions.

The conformation of compound **13** was studied by single crystal X-ray diffraction analysis. The compound **13** crystallizes in $P2_12_12_1$ space group with one molecule in asymmetric unit. The *ORTEP* diagram (Figure1S) shows the molecular structure of **13** with atomic numbering scheme. The molecule consists of Four rings (A, B, C, D) to which two isopropoxy and acetoxymethyl substituents are attached at the C8 and C4 positions respectively, one carbonyl group substituted at C5 and one nitro functional group is attached at C22 position in the molecule. Rings B, C, D are almost planar. There are two short intramolecular C–H···O (C20-O4 =3.111Å, H20...O4 = 2.875Å, <C20-H20-O4 = 95.38°) and C–H···N interactions (C14-N1 = 2.824 Å, H14...N1 = 2.548Å, <C14-H14-N1 = 96.88°) in the crystal structure. The geometric parameters suggest the repulsive nature of these interactions[21] which could be the possible reason of the mutual orientation of aromatic rings C and D adopted in the conformation of the molecule (the torsion angle of C20-C19-C12-C6 is 59.79° and of C14-C13-N2-N1 is 31.88° while the dihedral angle between the least-squares mean planes of ring C and ring D is 57.17(6)°). Ring A has a half chair conformation with atom O3 is puckered out of the plane; deviations of atom O3 is 0.602(3) Å from the mean plane through atoms C4, C5, C6, C7 and C8. Further, the X-ray analysis also shows the presence of edge-to-face intermolecular π…π interaction (centroid separation X1…X2 = 4.24Å, symmetry code: 1+x, y, z). In addition the crystal packing (Fig. 2S) reveals the presence of intermolecular C-H...O and C-H...N interactions which provides stabilization to the molecular structure. Few important intermolecular interactions are shown in figure 2S and their hydrogen bonding parameters are summarized in table 1.

Table S1. Hydrogen bond Geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C9-H9···O7^{i}	1.00	2.68	3.32	120
C14–H14···O5^{ii}	0.95	2.54	3.45	161
C24-H24···O4^{ii}	0.95	2.41	3.33	164
C1^{ii} -H1C ^{ii} ···O7^{i}	0.98	2.65	3.43	136
C10^{ii}–H10A^{ii}···N1	0.98	2.72	3.63	155
C9^{iii}-H9^{iii}···O7	1.00	2.68	3.32	122
C1^{iii}-H1C^{iii}···O7^{ii}	0.95	2.41	3.33	164

Symmetry codes: (i) 1/2-x, 2-y, -1/2+z (ii) 1+ x, y, z (iii) 1/2-x, 2-y, 1/2+z

The crystal data of compound **13**: $C_{24}H_{23}N_3O_7$, M = 465.45, Orthorhombic, $P\ 2_1\ 2_1\ 2_1$, a = 5.9798(9)Å, b = 14.147(2)Å, c = 25.909(4)Å, V = 2191.8(6)Å^3, Z= 4, D_c = 1.411 g cm^{-3}, μ (Mo-Kα) = 0.11 mm^{-1}, F(000) = 976, rectangular block, Dark brown, size = 0.22 x 0.16 x 0.12 mm ,11937 reflections measured (R_{int} = 0.0473), 4075 unique, wR_2 = 0.1010 for all data, conventional $R1$ = 0.0464 for 3287 Fo > 4σ(Fo) and 0.0624 for all 4075 data, S = 1.004 for all data and 310 parameters. Unit cell determinations and intensity data collection were performed on Bruker SMART APEX CCD area-detector instruments. Structure solutions by direct methods and refinements by full-matrix least-squares methods on F^2. Programs: SMART (Bruker, 2001), SMART 32 (Bruker), SAINT (Bruker, 2001), SHELXTL-NT [Bruker AXS Inc.: Madison, Wisconsin, USA 1997]. CCDC (deposit No: CCDC 894734) contains the supplementary crystallographic data. These data can be obtained free of charge from www.ccdc.cam.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, U. K; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk.

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Determination of anti-cancer efficacy using human cancer cell lines

The human cancer cell lines- KB (oral squamous cell carcinoma), C33A (cervical carcinoma), MCF7 (breast adenocarcinoma), A549 (lung carcinoma) and mouse embryo fibroblast (NIH3T3) were obtained from American Type Culture Collection (ATCC, USA) and grown in recommended media in a 5% CO_2 humidified atmosphere at 37 ^{0}C. The colorimetric sulforhodamine B assay[19] was used for the determination of cytotoxicity. In brief, 10^4 cells were added to each well of 96-well culture plates and incubated overnight to allow for cell attachment. Stock solutions of test compounds and standard drug (doxorubicin) were prepared in DMSO and their serial dilutions were tested against the selected cell types. Untreated cells served as control. After 48 h of exposure, cells were fixed with ice-cold TCA (50%, w/v), stained with SRB (0.4%, w/v; made in 1% acetic acid), washed and air dried. Bound dye was dissolved in Tris base (10 mM) and plates were read at 540 nm absorbance on a plate reader (Polarstar Galaxy, BMG, Germany). The cytotoxic effects of compounds were calculated as % inhibition in cell growth as per the formula: [100-(Absorbance of compound treated cells/ Absorbance of untreated cells)] x 100. The half maximal inhibitory concentrations (IC_{50}) were calculated using Graph Prism software. A compound showing IC_{50} value of <20 μM was considered as 'active'.

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