

## Supplementary Information

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

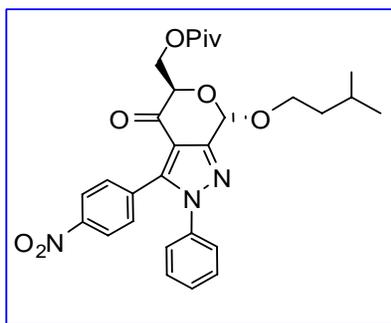
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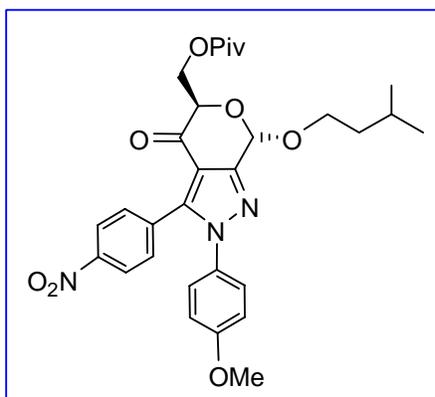
## Experimental Section - Chemistry

**General Remarks:** Organic solvents were dried by standard methods. Analytical TLC was performed using  $2.5 \times 5$  cm plates coated with a 0.25 mm thickness of silica gel (60 F-254), visualization was accomplished with  $\text{CeSO}_4$  or 10%  $\text{H}_2\text{SO}_4/\text{EtOH}$  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  $^1\text{H}$ ,  $^{13}\text{C}$ , 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 ( $^1\text{H}$ ) and 50, 75, MHz ( $^{13}\text{C}$ ). Experiments were recorded in  $\text{CDCl}_3$ ,  $\text{CDCl}_3+\text{CCl}_4$  mixture at 25 °C. Chemical shifts are given on the  $\delta$  scale. For  $^{13}\text{C}$  NMR reference  $\text{CDCl}_3$  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.

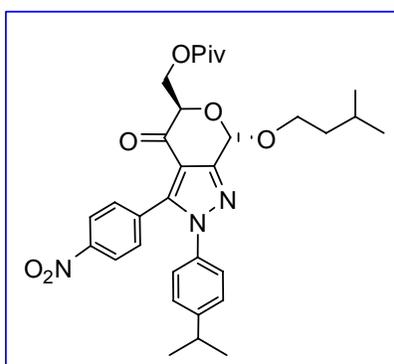


**Compound 3:** To a solution of hex-2-enopyranoside **1a** (269 mg, 0.6 mmol) in dry DCM (20 mL) was added Dess-Martin Periodinane (407 mg, 0.96 mmol) at  $-5\text{ }^{\circ}\text{C}$ . Subsequently the reaction was allowed to warm to  $5\text{ }^{\circ}\text{C}$  and stirred for 3 h till all the starting 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 ( $4 \times 4\text{ mL}$ ). 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  $90\text{ }^{\circ}\text{C}$  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 ( $5 \times 4\text{ mL}$ ). 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  $124\text{--}126\text{ }^{\circ}\text{C}$ ;  $R_f = 0.60$  (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1);  $[\alpha]_D^{26} = +62.56$  ( $c\ 0.100$ ,  $\text{CHCl}_3$ ); IR (KBR,  $\text{cm}^{-1}$ ): 3444, 2928, 2366, 1732, 1688, 1216;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  8.17 (d, 2H,  $J = 8.8\text{ Hz}$ ), 7.52 (d, 2H,  $J = 6.6\text{ Hz}$ ), 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,  $J = 6.6$ );  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 62.7 ( $\text{CH}_2$ ), 38.8 (qC), 38.3 ( $\text{CH}_2$ ), 27.2 ( $\text{CH}_3$ ), 25.1 (CH), 22.7 ( $\text{CH}_3$ ), 22.5 ( $\text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{24}\text{H}_{22}\text{N}_3\text{O}_6$   $[\text{M}-\text{C}_5\text{H}_{11}\text{O}]^+$  448.1508; found 448.1478.

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

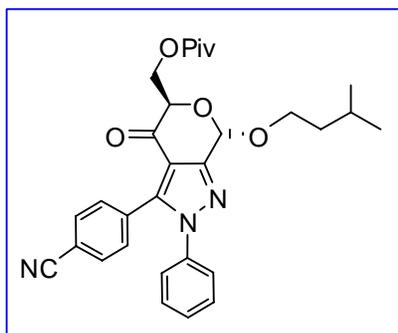


**Compound 4.** Yield - (170 mg, 50% over two steps); solid; mp 90-92 °C;  $R_f = 0.6$  (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1);  $[\alpha]_D^{25} = +11.08$  ( $c$  0.200,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 2927, 2368, 1730, 1691;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 62.8 ( $\text{CH}_2$ ), 55.6 ( $\text{CH}_3$ ), 38.8 (qC), 38.3 ( $\text{CH}_2$ ), 27.2 ( $3 \times \text{CH}_3$ ), 25.1 (CH), 22.7 ( $\text{CH}_3$ ), 22.5 ( $\text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{25}\text{H}_{24}\text{N}_3\text{O}_7$  [ $\text{M}-\text{C}_5\text{H}_{11}\text{O}$ ] $^+$  478.1614; found 478.1603.

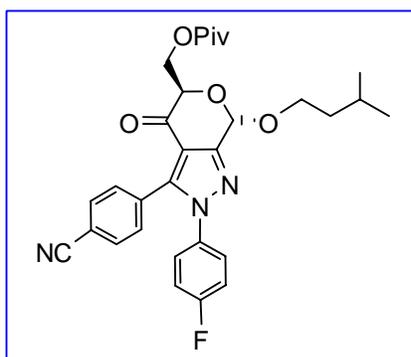


**Compound 5.** Yield - (135 mg, 39% over two steps); glassy solid;  $R_f = 0.38$  (hexane/ethyl acetate, 4:1); eluent for column chromatography (hexane/ethyl acetate, 24:1);  $[\alpha]_D^{29} = +19.67$  ( $c$  0.21,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 3021, 2348, 1785, 1597;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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),

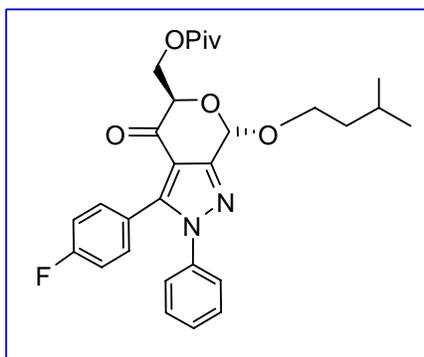
0.94 (d, 6H,  $J = 6.5$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  188.6 (qC), 178.2 (qC), 153.8 (qC), 150.5 (qC), 148.3 (qC), 140.5 (qC), 135.9 (qC), 133.7 (qC), 131.3 (CH), 127.5 (CH), 125.4 (CH), 123.5 (CH), 113.7 (qC), 93.5 (CH), 73.0 (CH), 67.8 ( $\text{CH}_2$ ), 62.8 ( $\text{CH}_2$ ) 38.8 (qC), 38.3 ( $\text{CH}_2$ ), 33.3 (CH), 27.2 ( $\text{CH}_3$ ), 25.1 (CH), 23.8 ( $\text{CH}_3$ ), 22.7 ( $\text{CH}_3$ ), 22.5 ( $\text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{27}\text{H}_{28}\text{N}_3\text{O}_6$   $[\text{M}-\text{C}_5\text{H}_{11}\text{O}]^+$  490.1978; found 490.1960.



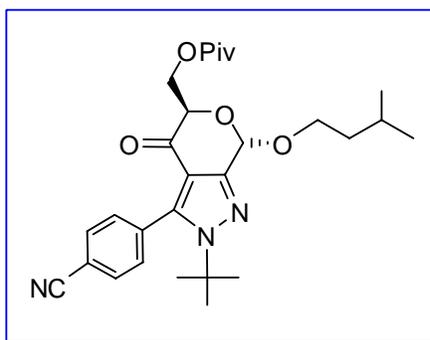
**Compound 6.** Yield - (130mg, 42% over two steps); solid; mp 133-135 °C;  $R_f = 0.52$  (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 22:3);  $[\alpha]_D^{19} = +92.21$  ( $c$  0.72,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 3422, 3022, 2360, 1652, 1522;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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,  $J = 6.5$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 62.7 ( $\text{CH}_2$ ), 38.8 (qC), 38.3 ( $\text{CH}_2$ ), 27.2 (3 x  $\text{CH}_3$ ), 25.1 (CH), 22.7 ( $\text{CH}_3$ ), 22.5 ( $\text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{25}\text{H}_{22}\text{N}_3\text{O}_4$   $[\text{M}-\text{C}_5\text{H}_{11}\text{O}]^+$  428.1610; found 428.1598.



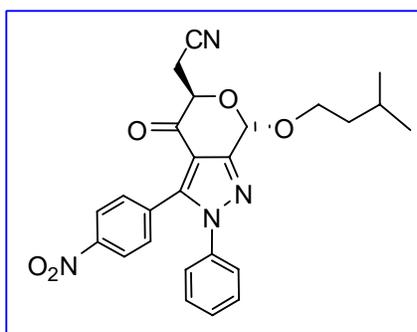
**Compound 7.** Yield – (90mg, 28% over two steps); solid; 80-82 °C;  $R_f = 0.52$  (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1);  $[\alpha]_D^{19} = +107.03$  ( $c$  0.55,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 3426, 3020, 2357, 1693, 1647;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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,  $J = 6.5$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 62.7 ( $\text{CH}_2$ ), 38.8 (qC), 38.3 ( $\text{CH}_2$ ), 27.2 ( $\text{CH}_3$ ), 25.1 (CH), 22.7 ( $\text{CH}_3$ ), 22.5 ( $\text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{25}\text{H}_{21}\text{FN}_3\text{O}_4$   $[\text{M}-\text{C}_5\text{H}_{11}\text{O}]^+$  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,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 3021, 2360, 1725, 1511;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.36 - 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,  $J = 6.2$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 62.9 ( $\text{CH}_2$ ), 38.8 (qC), 38.3 (CH), 27.2 ( $\text{CH}_3$ ), 25.1 (CH), 22.7, ( $\text{CH}_3$ ), 22.5 ( $\text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{24}\text{H}_{22}\text{F}_1\text{N}_2\text{O}_4$   $[\text{M}-\text{C}_5\text{H}_{11}\text{O}]^+$  421.1563; found 421.1548.

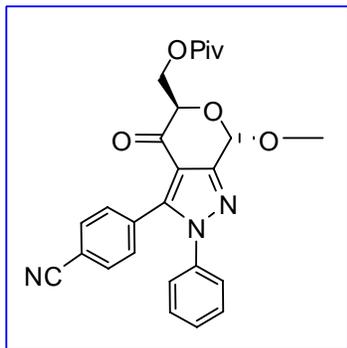


**Compound 9.** Yield - (93mg, 31% over two steps); glassy solid; Oil;  $R_f = 0.62$  (hexane/ethyl acetate, 4:1); eluent for column chromatography (hexane/ethyl acetate, 22:3);  $[\alpha]_D^{26} = +10.29$  ( $c$  0.38,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 3457, 3019, 2372, 1721, 1604;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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,  $J = 6.5$ ),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 63.8 (qC), 62.7 ( $\text{CH}_2$ ), 38.8 (qC), 38.3 ( $\text{CH}_2$ ), 31.2 ( $\text{CH}_3$ ), 27.2 ( $\text{CH}_3$ ), 25.2 (CH), 22.8 ( $\text{CH}_3$ ), 22.5 ( $\text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{23}\text{H}_{26}\text{N}_3\text{O}_4$  [ $\text{M}-\text{C}_5\text{H}_{11}\text{O}$ ] $^+$  408.1923; found 408.1908.

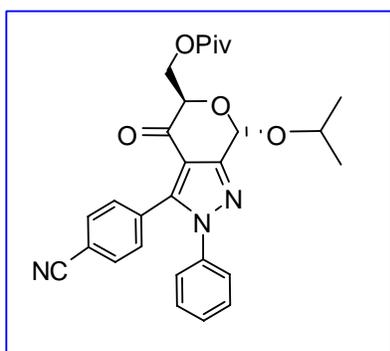


**Compound 10.** Yield - (127 mg, 46% over two steps); glassy solid;  $R_f = 0.40$  (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 93:7);  $[\alpha]_D^{27} = +10.45$  ( $c$  0.56,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 3441, 3021, 2375, 1696, 1601;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 38.3 ( $\text{CH}_2$ ), 25.0 (CH),

22.7 (CH<sub>3</sub>), 22.4 (CH<sub>3</sub>), 19.0 (CH<sub>2</sub>); HRMS (DART): Calcd for C<sub>20</sub>H<sub>13</sub>N<sub>4</sub>O<sub>4</sub> [M-C<sub>5</sub>H<sub>11</sub>O]<sup>+</sup> 373.0936; found 373.0956.

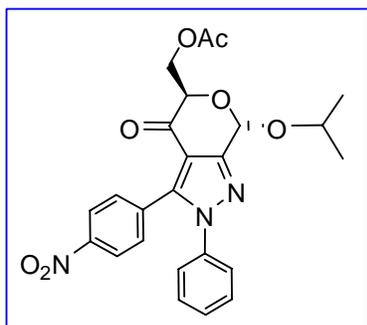


**Compound 11.** Yield - (106 mg, 38% over two steps); glassy solid;  $R_f = 0.54$  (hexane/ethyl acetate, 3:2); eluent for column chromatography (hexane/ethyl acetate, 21:4);  $[\alpha]_D^{28} = +27.34$  ( $c$  0.18, CHCl<sub>3</sub>); IR (KBr, cm<sup>-1</sup>): 3376, 2363, 1640; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  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); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75MHz):  $\delta$  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<sub>2</sub>), 56.3 (CH<sub>3</sub>), 38.8 (qC), 27.5 (CH<sub>3</sub>); HRMS (DART): Calcd for C<sub>25</sub>H<sub>22</sub>N<sub>3</sub>O<sub>4</sub> [M-CH<sub>3</sub>O]<sup>+</sup> 428.1610; found 428.1595.

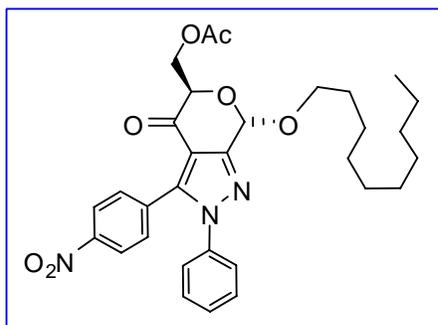


**Compound 12.** Yield - (118mg, 40% over two steps); solid; mp 91-93 °C;  $R_f = 0.56$  (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 9:1);  $[\alpha]_D^{30} = +45.99$  ( $c$  0.48, CHCl<sub>3</sub>); IR (KBr, cm<sup>-1</sup>): 3441, 2364, 1728, 1691, 1567; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  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);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 38.8 (qC), 27.5 ( $3 \times \text{CH}_3$ ), 23.3 (CH), 21.7 ( $2 \times \text{CH}_3$ ); HRMS (DART): Calcd for  $\text{C}_{25}\text{H}_{22}\text{N}_3\text{O}_4$   $[\text{M}-\text{C}_3\text{H}_7\text{O}]^+$  428.1610; found 428.1609.

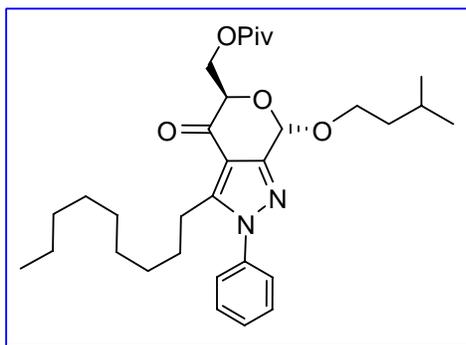


**Compound 13.** Yield - (115mg, 41% over two steps); solid; mp 199-201 °C;  $R_f = 0.43$  (hexane/ethyl acetate, 7:3); eluent for column chromatography (hexane/ethyl acetate, 87:13);  $[\alpha]_D^{27} = +49.15$  ( $c$  0.84,  $\text{CHCl}_3$ ); IR (KBr,  $\text{cm}^{-1}$ ): 3020, 2360, 1732, 1664;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 23.2 ( $\text{CH}_3$ ), 22.0 ( $\text{CH}_3$ ), 20.8 ( $\text{CH}_3$ ); HRMS (DART): Calc for  $\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}_6$   $[\text{M}-\text{C}_3\text{H}_7\text{O}]^+$  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,  $\text{CHCl}_3$ ); IR (neat,  $\text{cm}^{-1}$ ): 3021, 2359, 1690, 1522;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 62.4 ( $\text{CH}_2$ ), 31.9 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 29.6 ( $\text{CH}_2$ ), 29.4 ( $\text{CH}_2$ ), 29.3 ( $\text{CH}_2$ ), 26.3 ( $\text{CH}_2$ ), 22.7 ( $\text{CH}_2$ ), 20.9 ( $\text{CH}_3$ ), 14.1 ( $\text{CH}_3$ ). HRMS (EI) : Calc for  $\text{C}_{29}\text{H}_{33}\text{N}_3\text{O}_5$   $[\text{M} - \text{C}_2\text{H}_4\text{O}_2]^+$  503.2056; found 503.2040.

**Compound 15.**

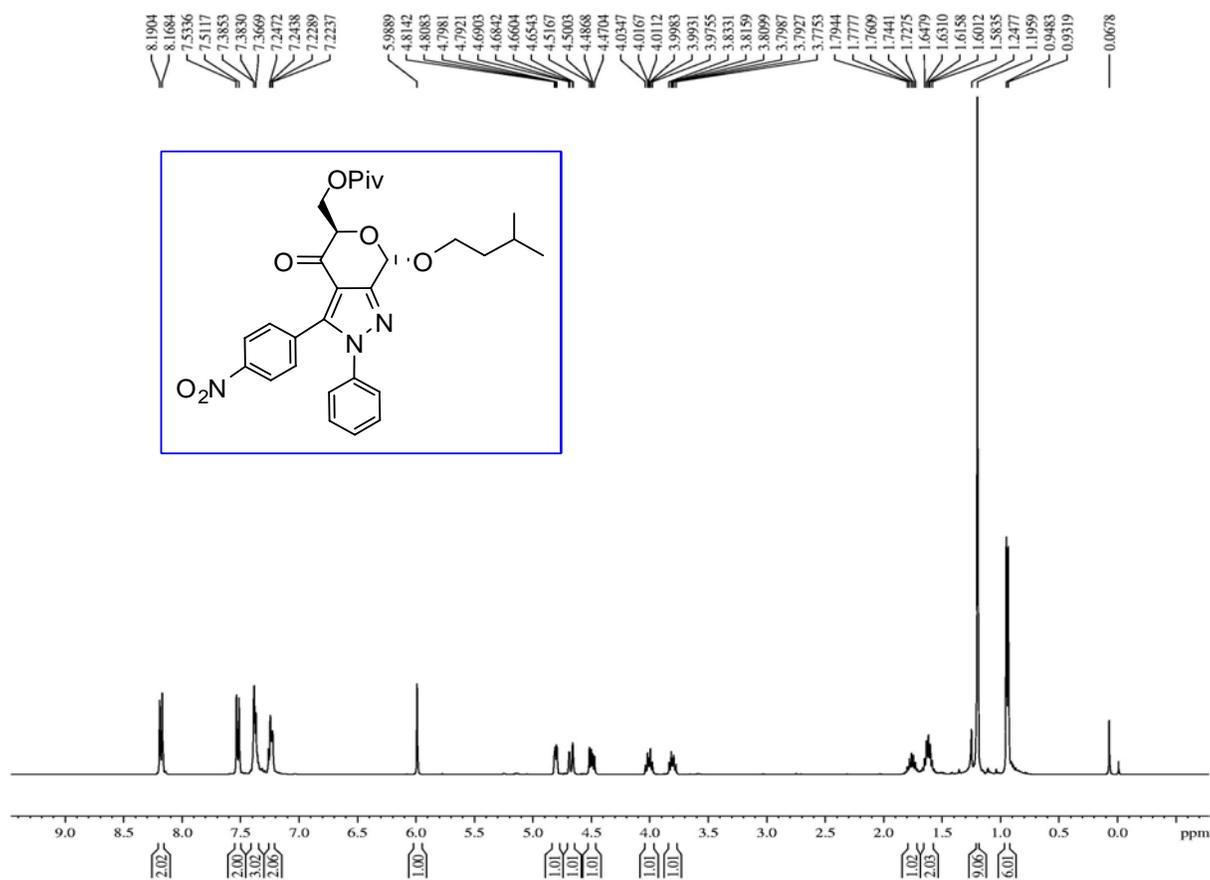
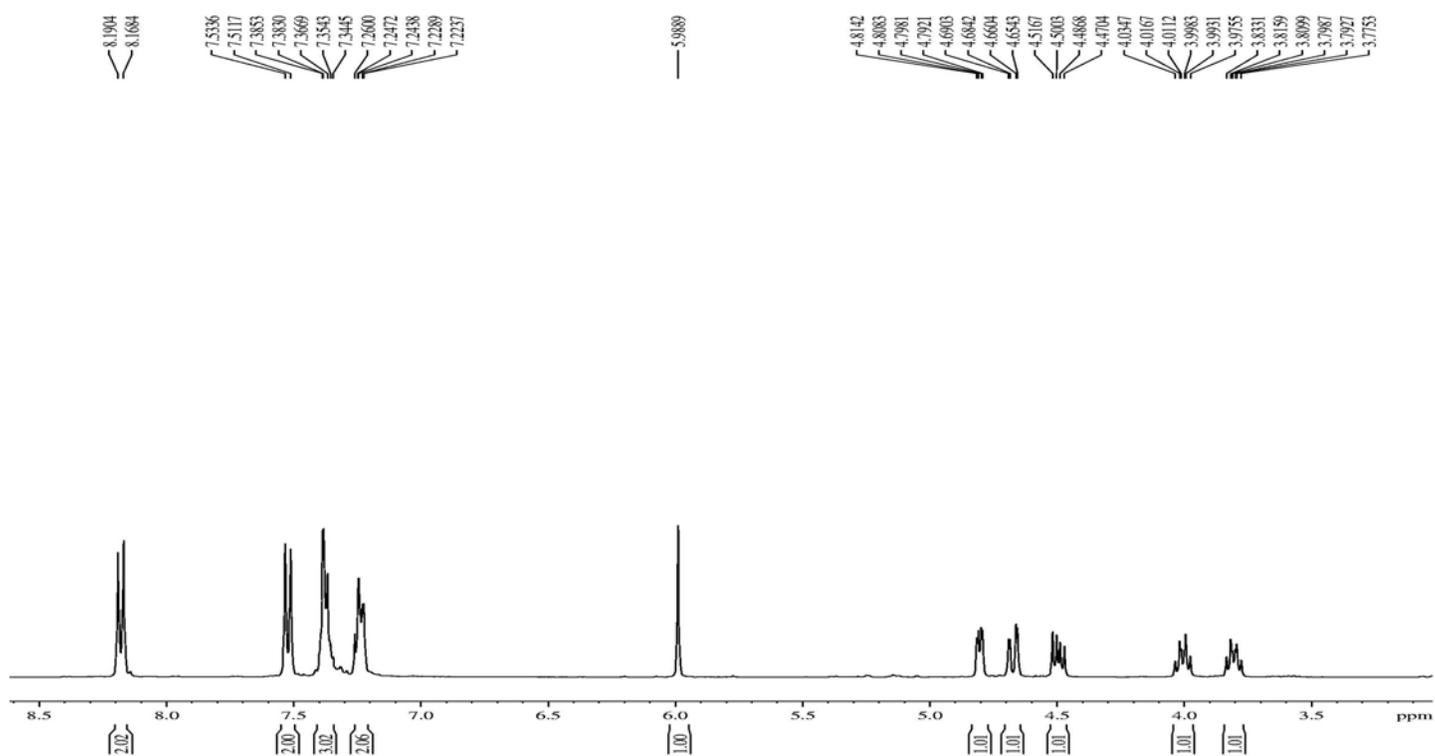


Yield - (98mg, 30% over two steps); Oil;  $R_f = 0.60$  (hexane/ethyl acetate, 4:1); eluent for column chromatography (hexane/ethyl acetate, 97:3);  $[\alpha]_D^{26} = +32.60$  ( $c$  0.14,  $\text{CHCl}_3$ ); IR (neat,  $\text{cm}^{-1}$ ): 3499, 1726, 1700, 1599;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  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);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75MHz):  $\delta$  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 ( $\text{CH}_2$ ), 62.9 ( $\text{CH}_2$ ), 38.8 (qC), 38.3 ( $\text{CH}_2$ ), 31.9 ( $\text{CH}_2$ ), 29.39 ( $\text{CH}_2$ ), 29.34 ( $\text{CH}_2$ ), 29.2 ( $\text{CH}_2$ ), 29.0 ( $\text{CH}_2$ ), 28.5 ( $\text{CH}_2$ ), 27.2 ( $\text{CH}_3$ ), 25.5 (CH), 22.79 ( $\text{CH}_3$ ), 22.71 (CH), 22.5 ( $\text{CH}_3$ ), 14.3 ( $\text{CH}_3$ ); HRMS (ESI): Calcd for  $\text{C}_{32}\text{H}_{48}\text{N}_2\text{NaO}_5$   $[\text{M} + \text{Na}]^+$  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**.



**MVI-BH113  
 PROTON**

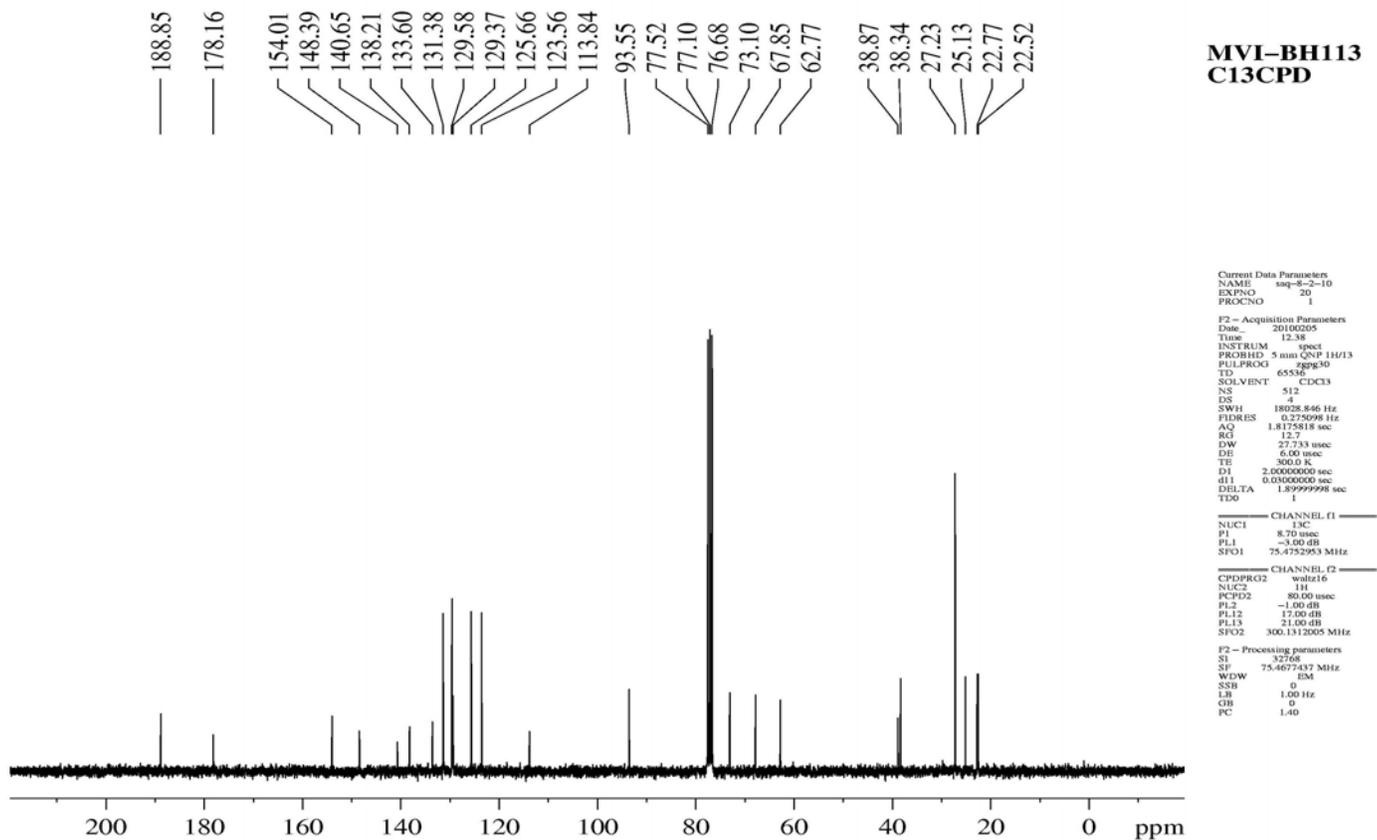
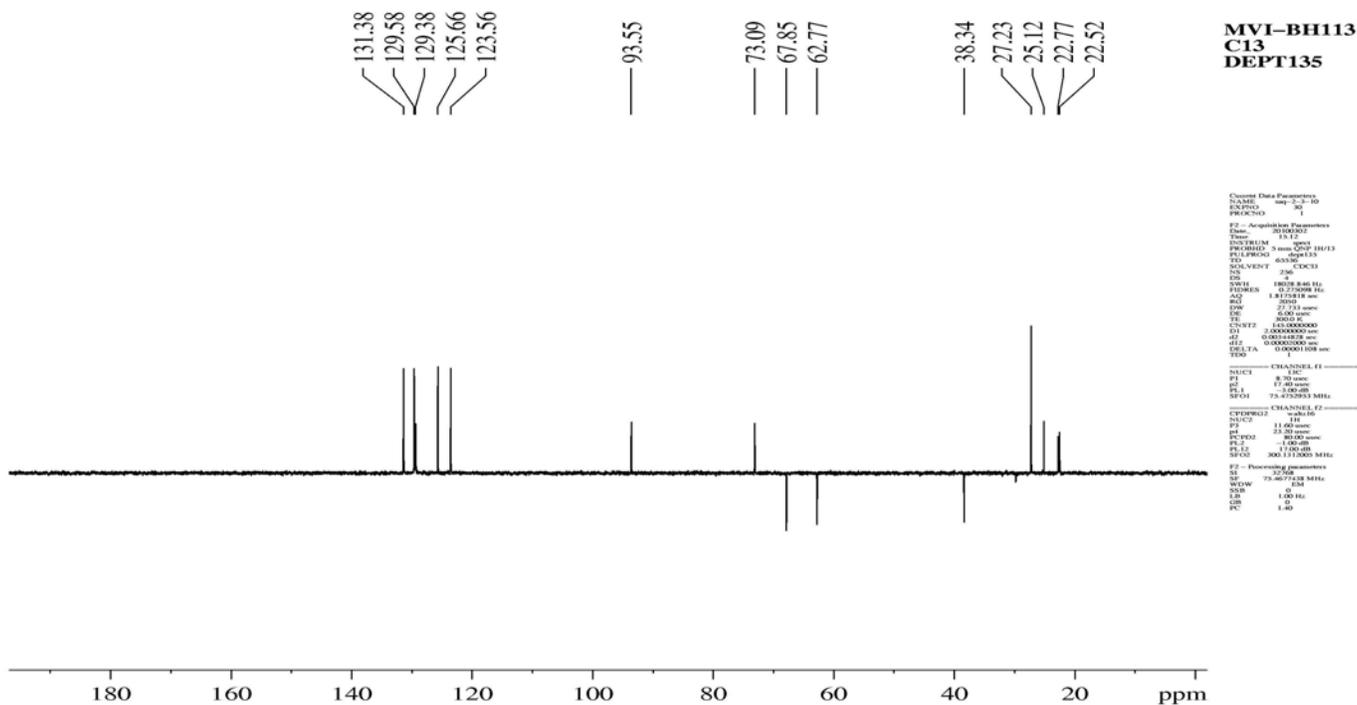
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 PROCNO 1

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 PULPROG zgpg30  
 TD 65536  
 FIDRES 0.097563 Hz  
 AN 5.1249652 sec  
 RG 22.0  
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 D1 1.00000000 sec  
 TD0 1

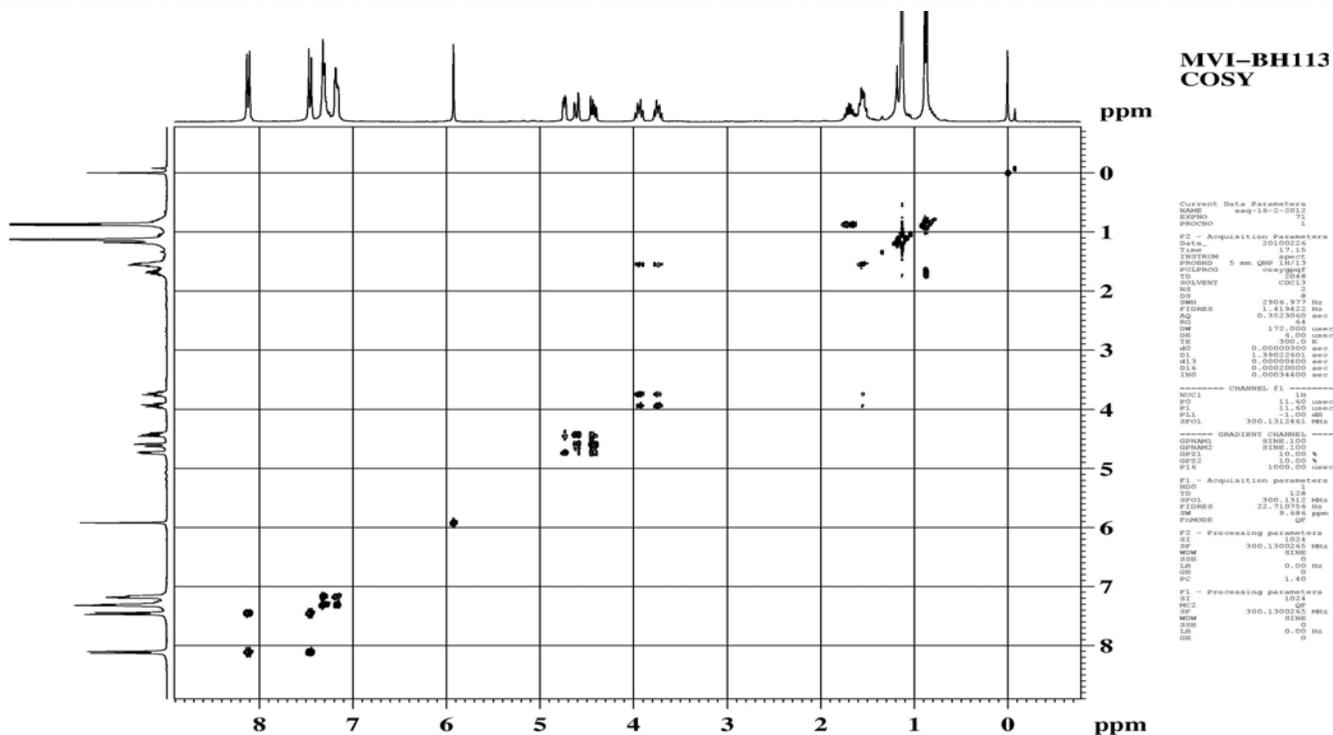
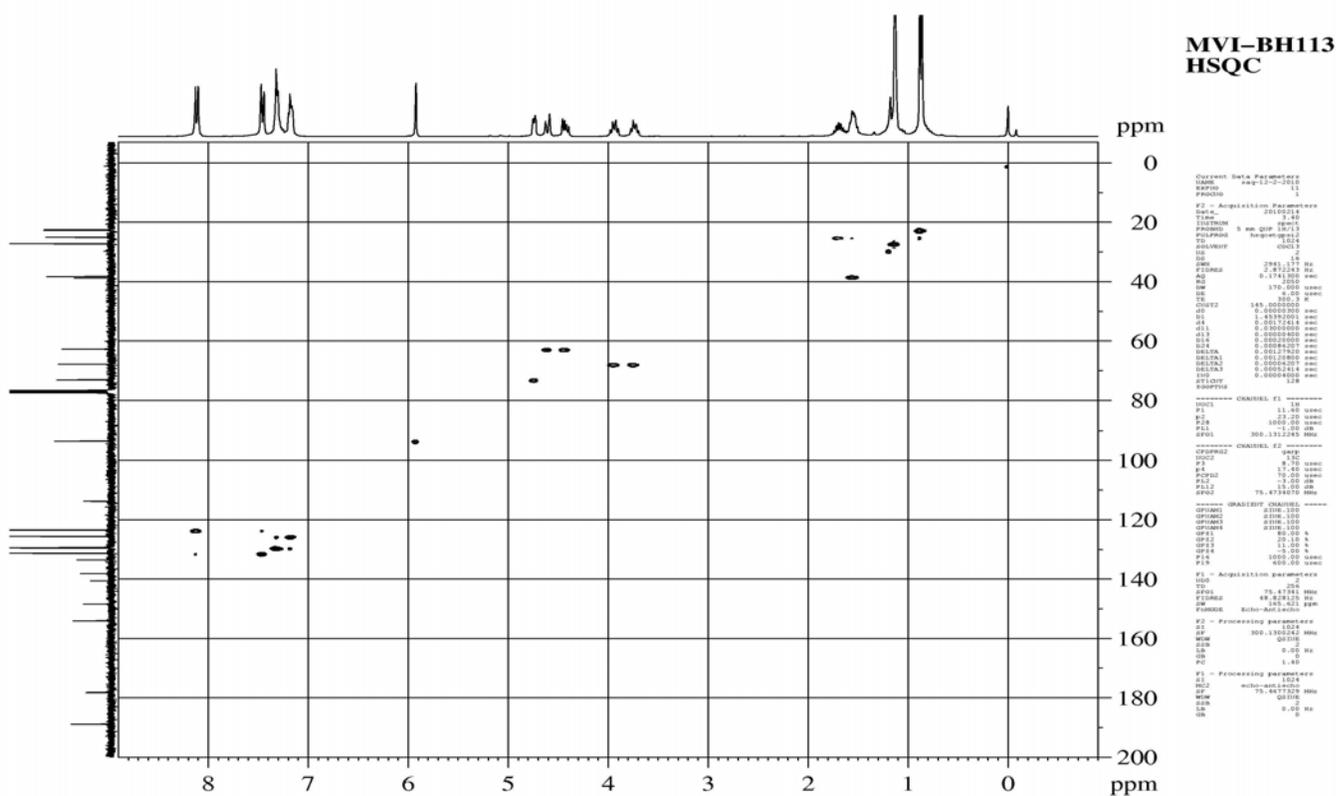
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 GB 0  
 PC 1.00

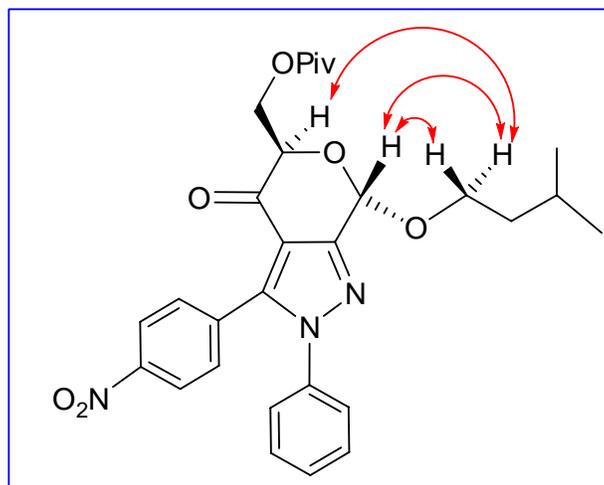
<sup>1</sup>H NMR spectrum of compound 3 and its expansion



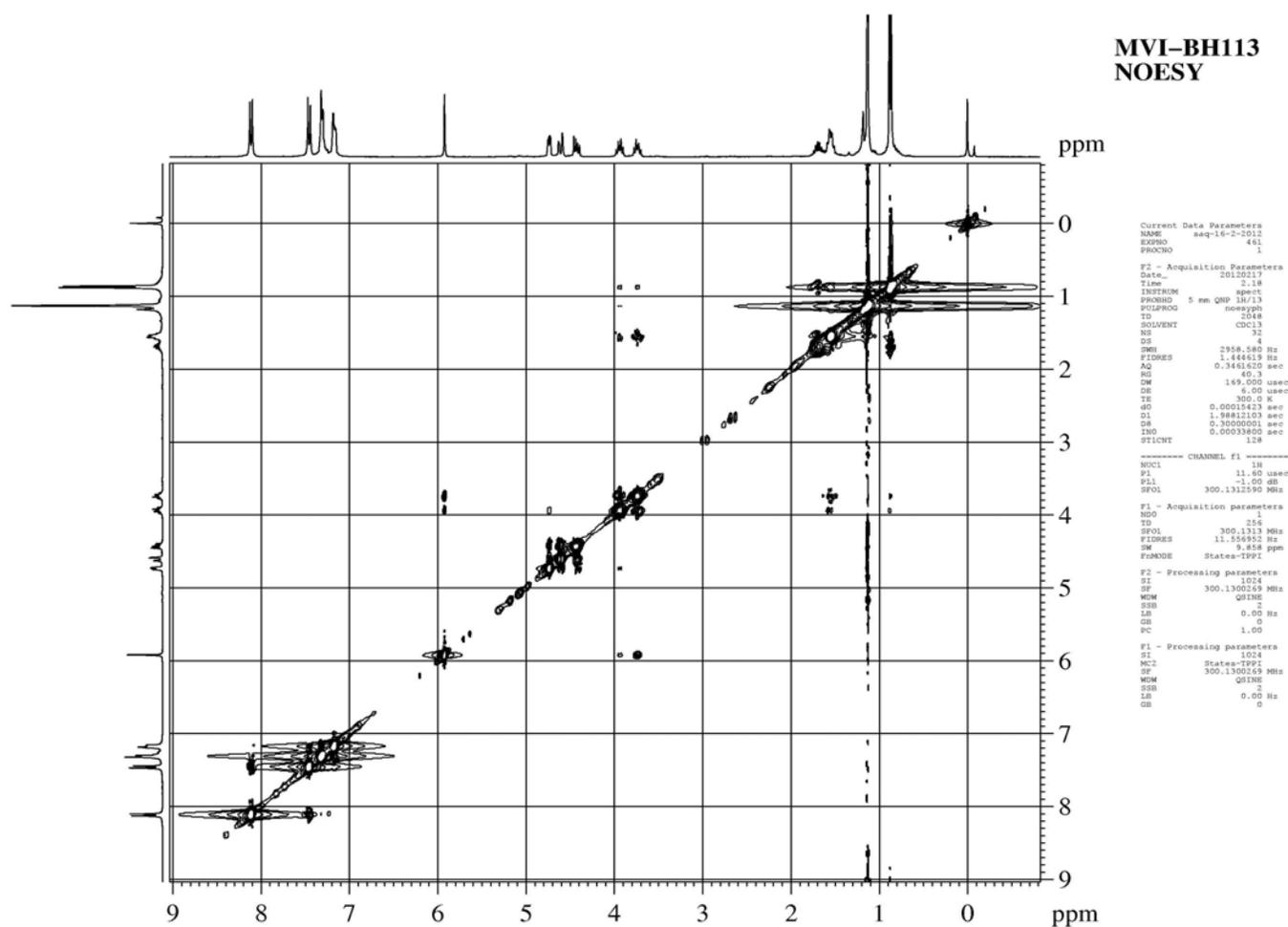
<sup>13</sup>C and Dept 135 NMR spectra of compound 3



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

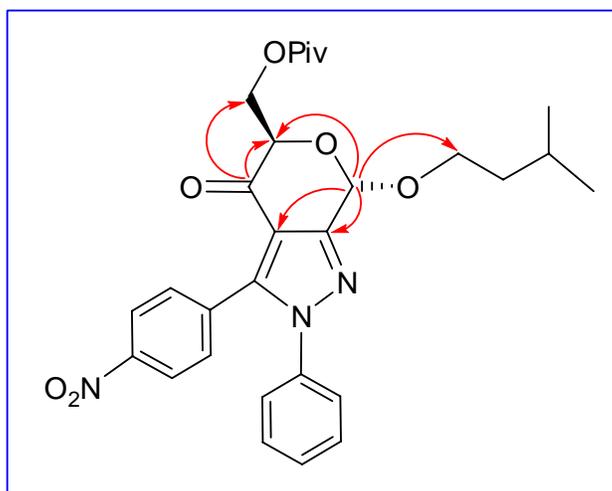


Key NOESY correlations in compound 3

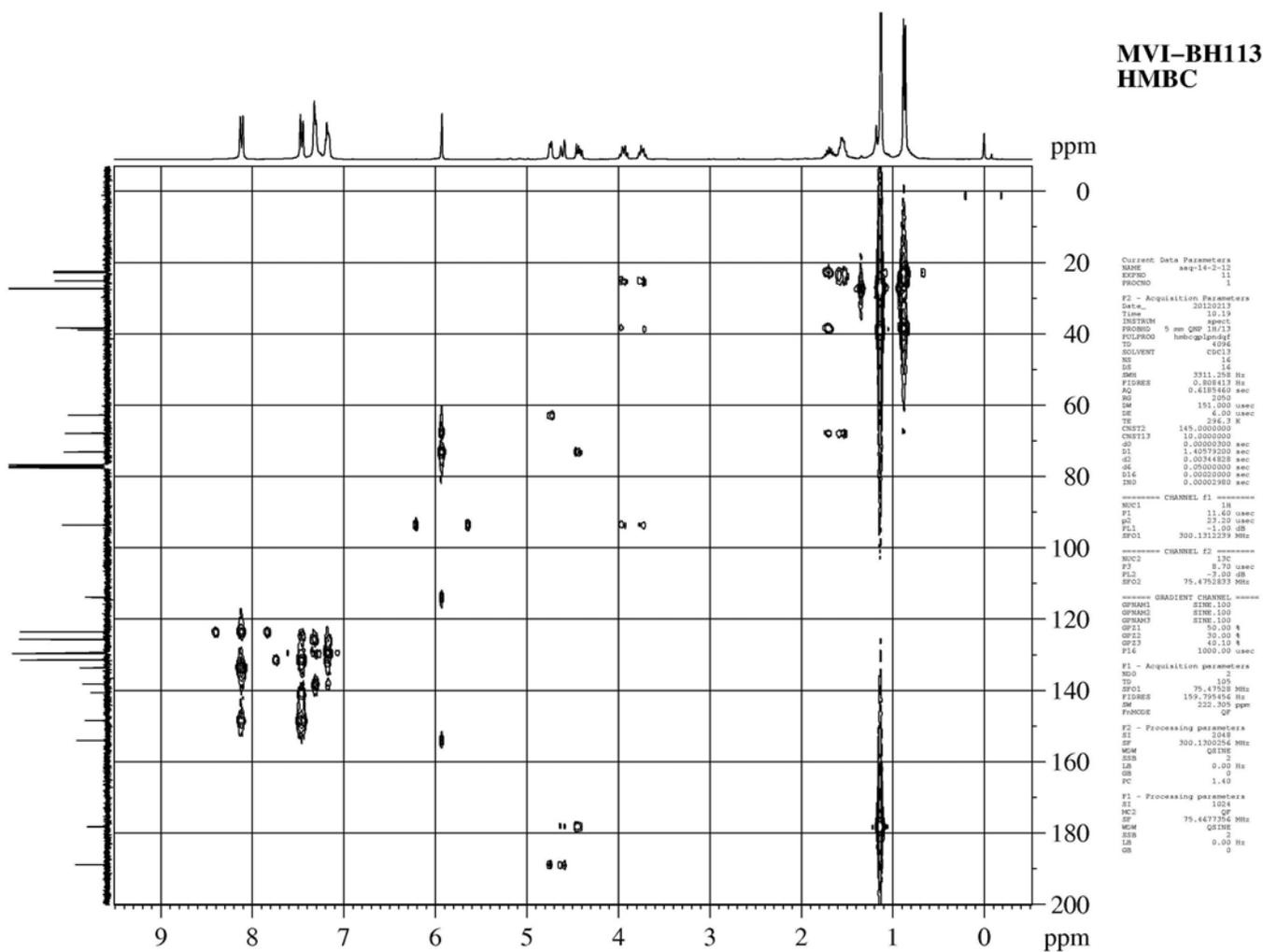


NOESY spectrum of compound 3



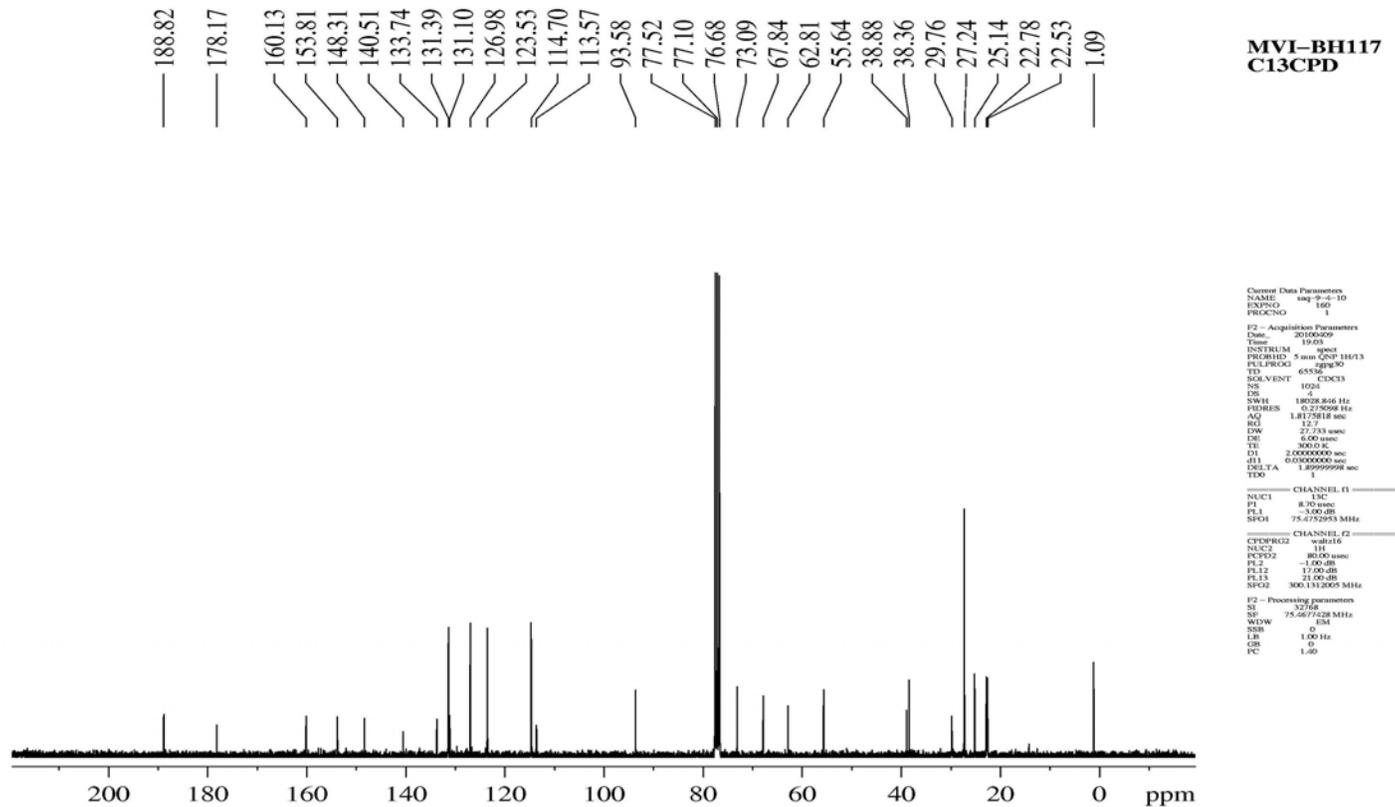
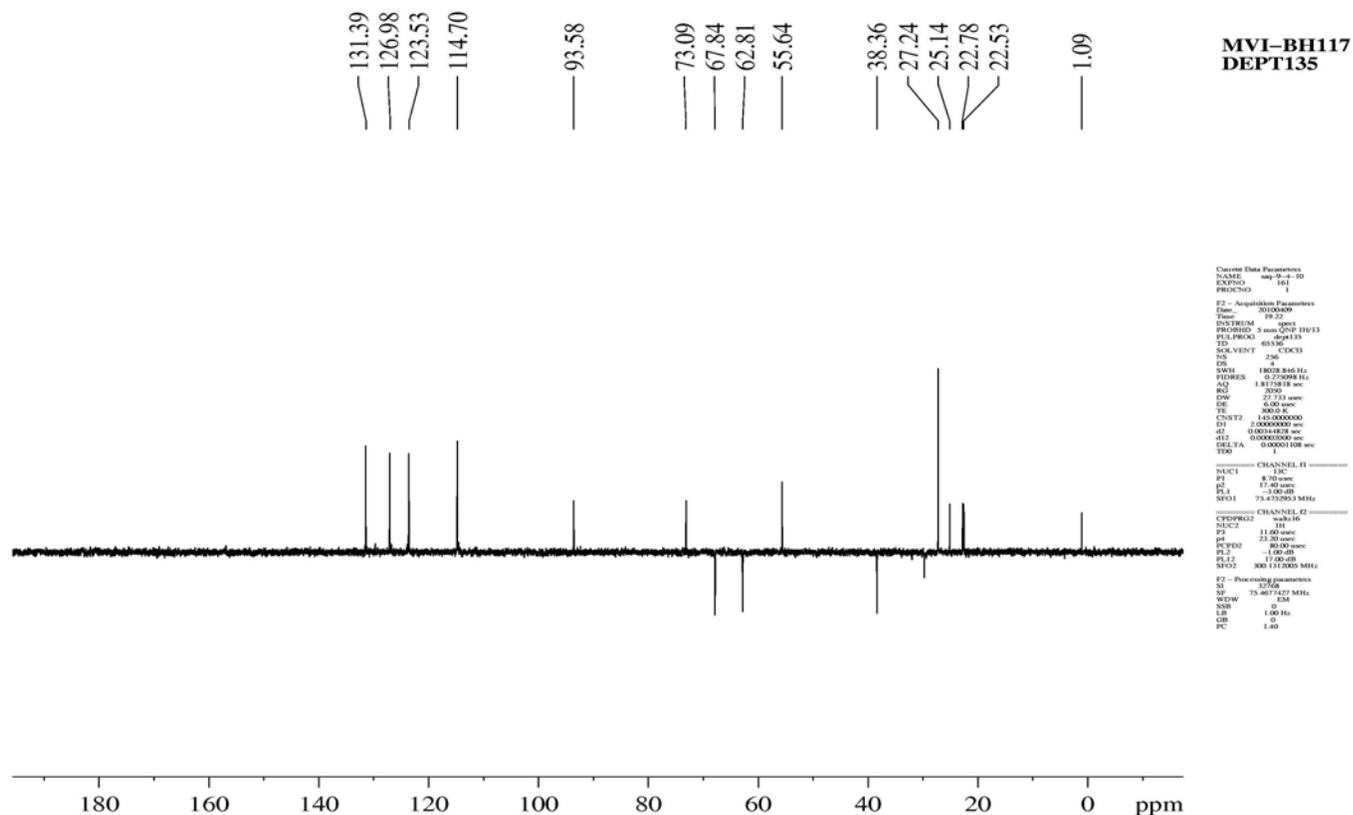


### Key HMBC correlations in compound 3



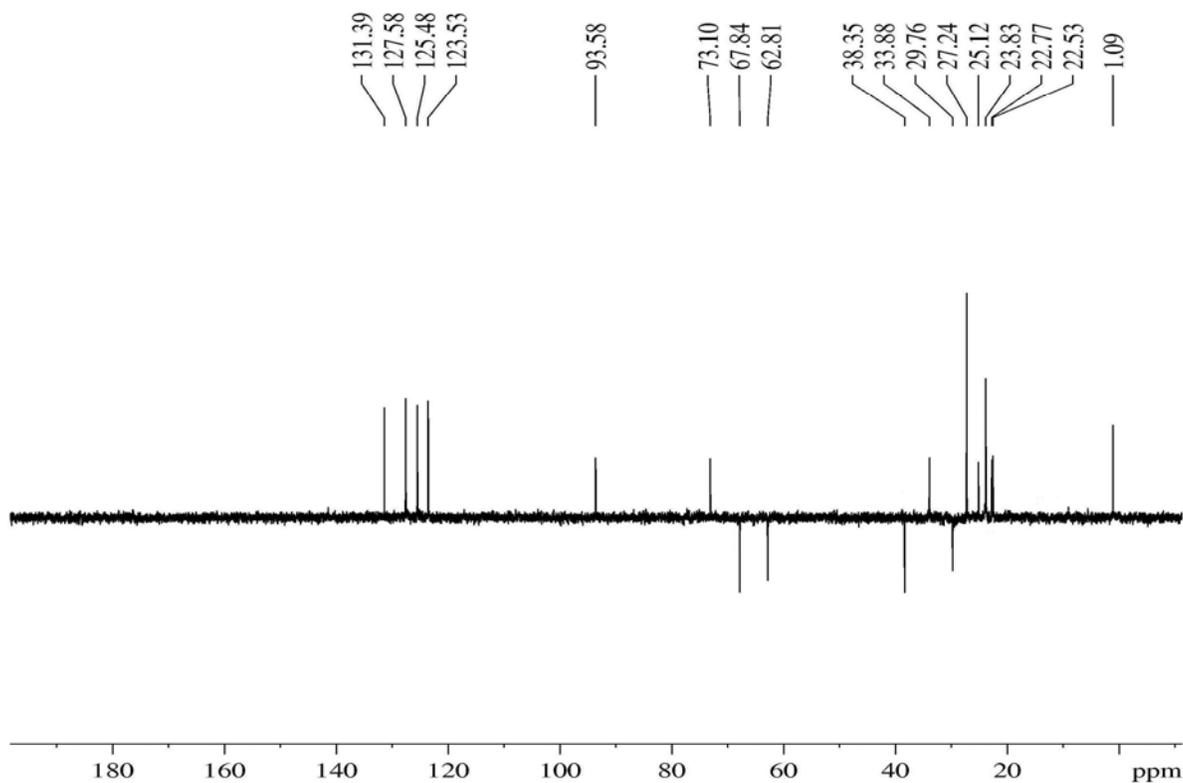
<sup>1</sup>H-<sup>13</sup>C HMBC spectra of compound 3





<sup>13</sup>C and Dept 135 NMR spectra of compound 4

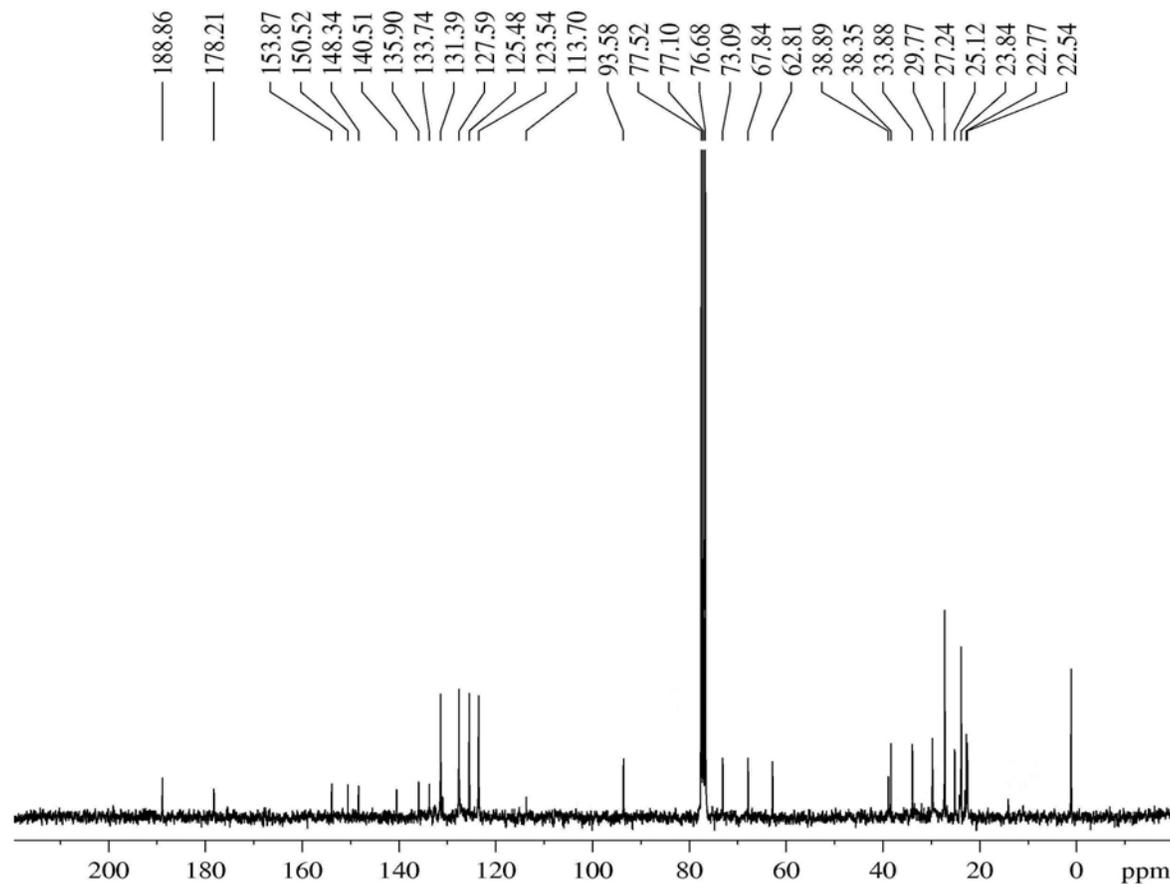




**MVI-BH121**  
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 RG 127  
 DW 27.733 usec  
 DE 6.00 usec  
 TE 299.5 K  
 CNST12 145.0000000  
 D1 2.0000000 sec  
 d2 0.00144628 sec  
 d12 0.00002000 sec  
 DELTA 0.00001108 sec  
 TDO 1

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 PL1 17.40 dB  
 PL2 -3.00 dB  
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 PL2 23.20 dB  
 PL3 80.00 usec  
 PL4 -1.00 dB  
 PL5 17.00 dB  
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 SSB 0  
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 GB 0  
 PC 1.40



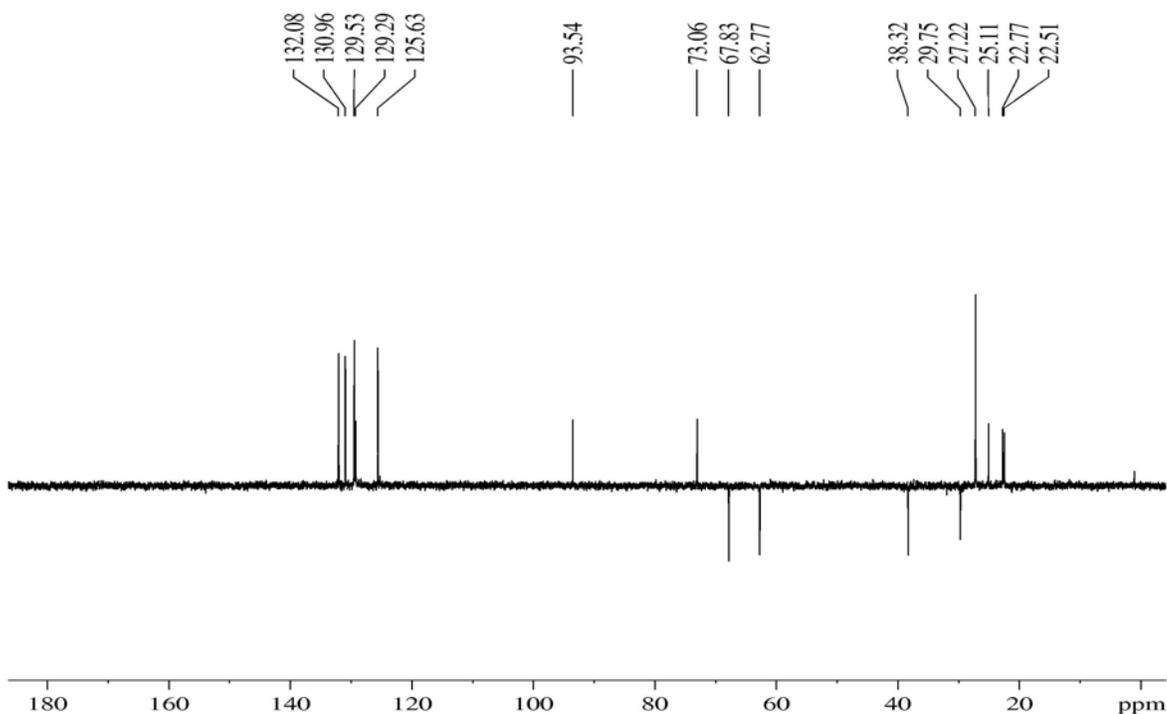
**MVI-BH121**  
**C13CPD**

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 FIDRES 0.275098 Hz  
 AQ 1.8175818 sec  
 RG 127  
 DW 27.733 usec  
 DE 6.00 usec  
 TE 299.5 K  
 D1 2.0000000 sec  
 d11 0.00000000 sec  
 DELTA 1.89999998 sec  
 TDO 1

CHANNEL f1  
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 PL1 -3.00 dB  
 SF01 75.4752953 MHz  
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 NUC2 1H  
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 PL3 17.00 dB  
 PL13 21.00 dB  
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 F2 - Processing parameters  
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 SF 75.4677432 MHz  
 WDW EM  
 SSB 0  
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 PC 1.40

<sup>13</sup>C and DEPT 135 NMR spectra of compound 5





**MVI-BH-110  
 C13  
 DEPT135**

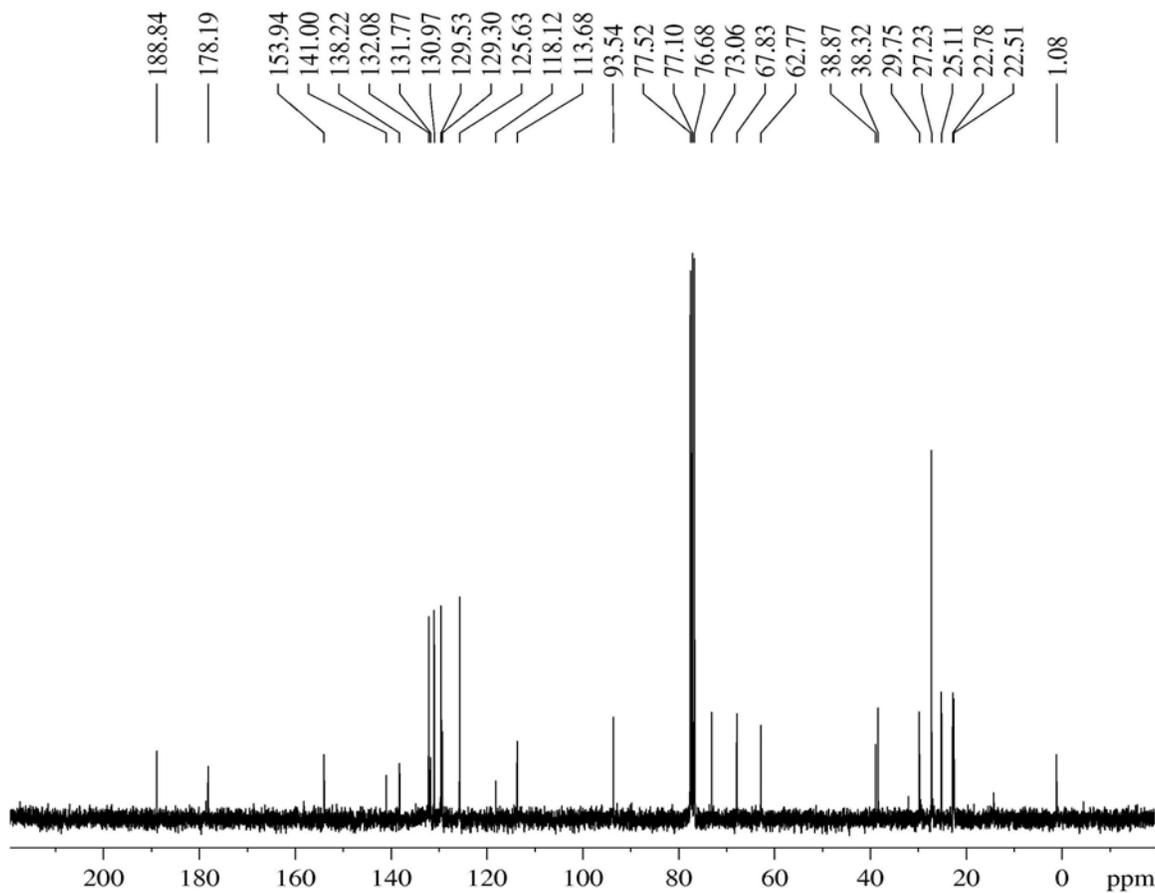
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 NS 256  
 DS 4  
 SWH 18028.846 Hz  
 FIDRES 0.275098 Hz  
 AQ 1.8175818 sec  
 RG 2050  
 DW 27.753 usec  
 DE 6.00 usec  
 TE 297.6 K  
 CNST2 145.000000  
 D1 2.00000000 sec  
 d2 0.00544828 sec  
 d12 0.00020000 sec  
 DELTA 0.00001108 sec  
 TD0

===== CHANNEL f1 =====  
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 P2 17.40 usec  
 PL1 -3.00 dB  
 SFO1 75.4752953 MHz

===== CHANNEL f2 =====  
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 NUC2 1H  
 P3 11.60 usec  
 P4 23.20 usec  
 PCPD2 80.00 usec  
 PL2 -1.00 dB  
 PL12 17.00 dB  
 SFO2 300.1312005 MHz

F2 - Processing parameters  
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**MVI-BH-110  
 C13CPD**

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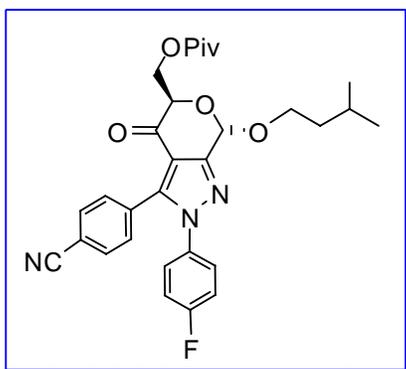
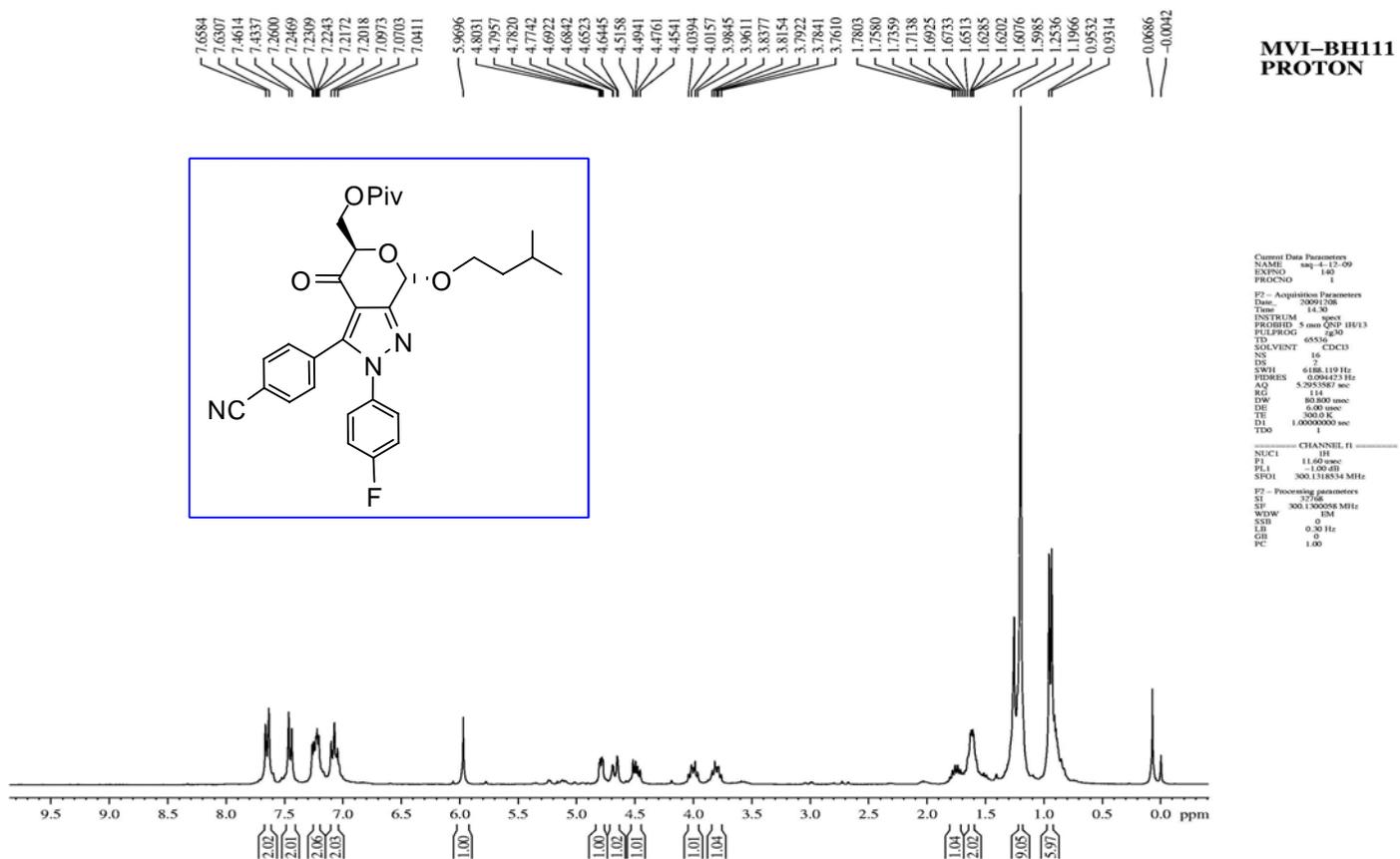
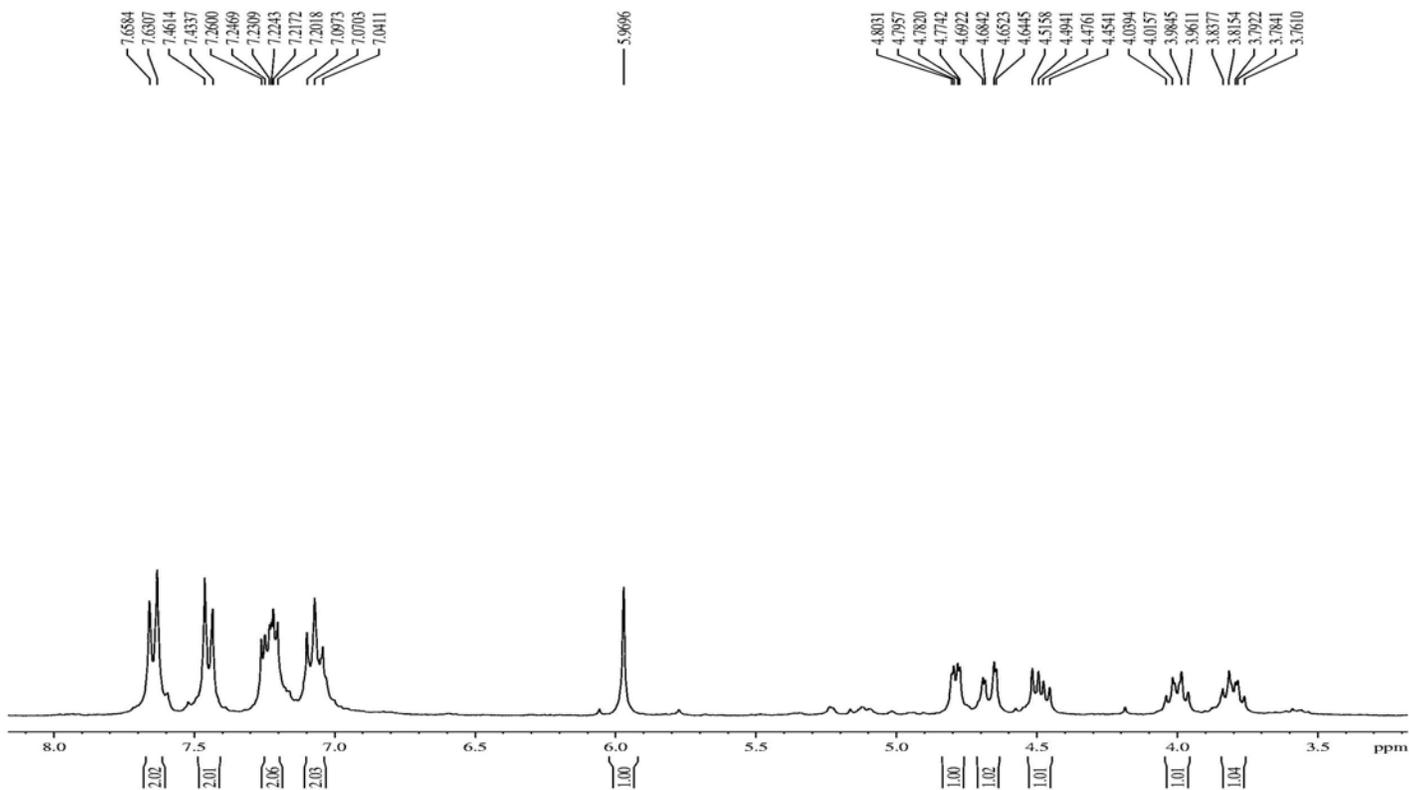
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 FIDRES 0.275098 Hz  
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 RG 12.7  
 DW 27.753 usec  
 DE 6.00 usec  
 TE 297.2 K  
 D1 2.00000000 sec  
 d11 0.03000000 sec  
 DELTA 1.89999998 sec  
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===== CHANNEL f1 =====  
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 SFO1 75.4752953 MHz

===== CHANNEL f2 =====  
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 PL2 -1.00 dB  
 PL12 17.00 dB  
 PL13 21.00 dB  
 SFO2 300.1312005 MHz

F2 - Processing parameters  
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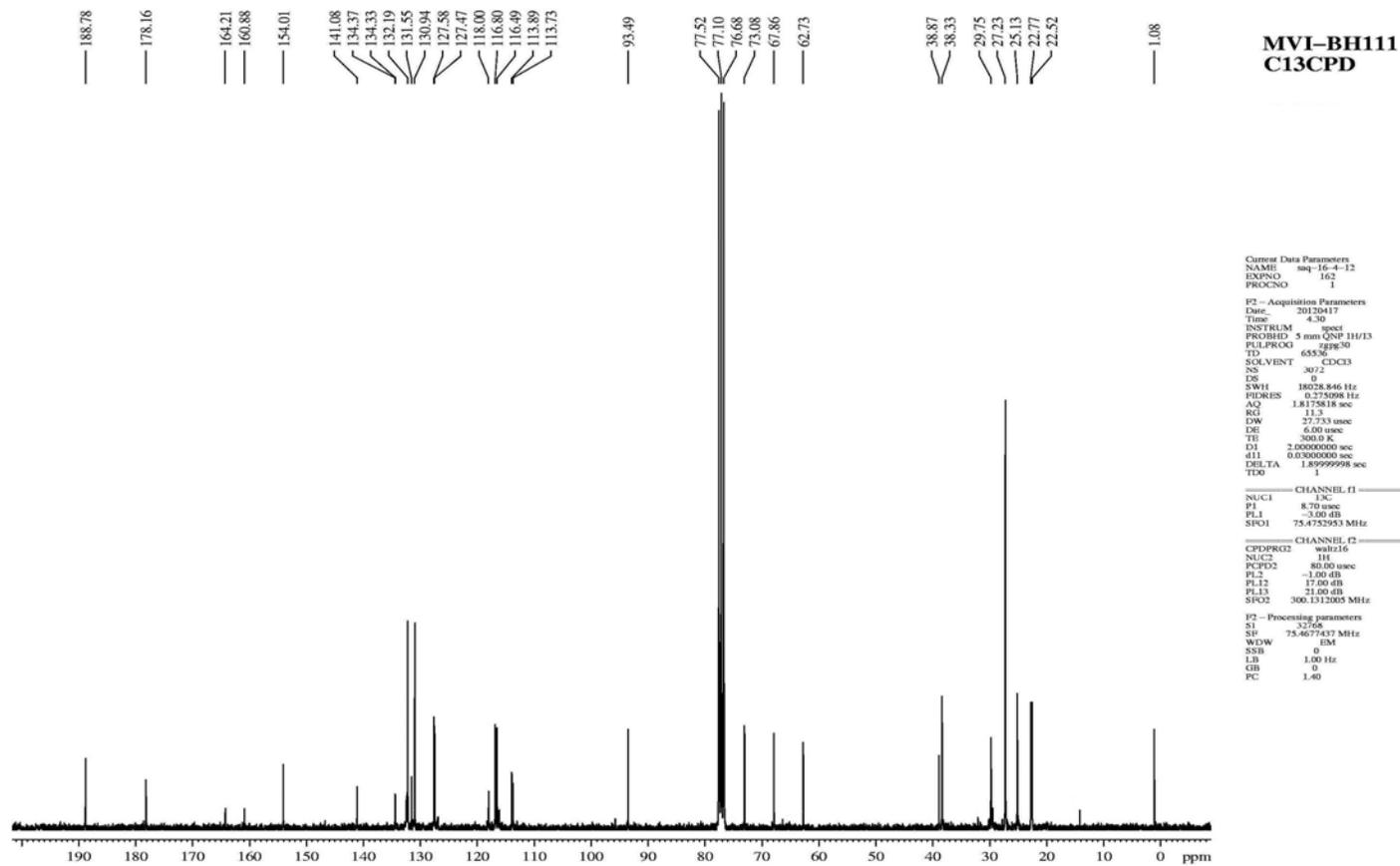
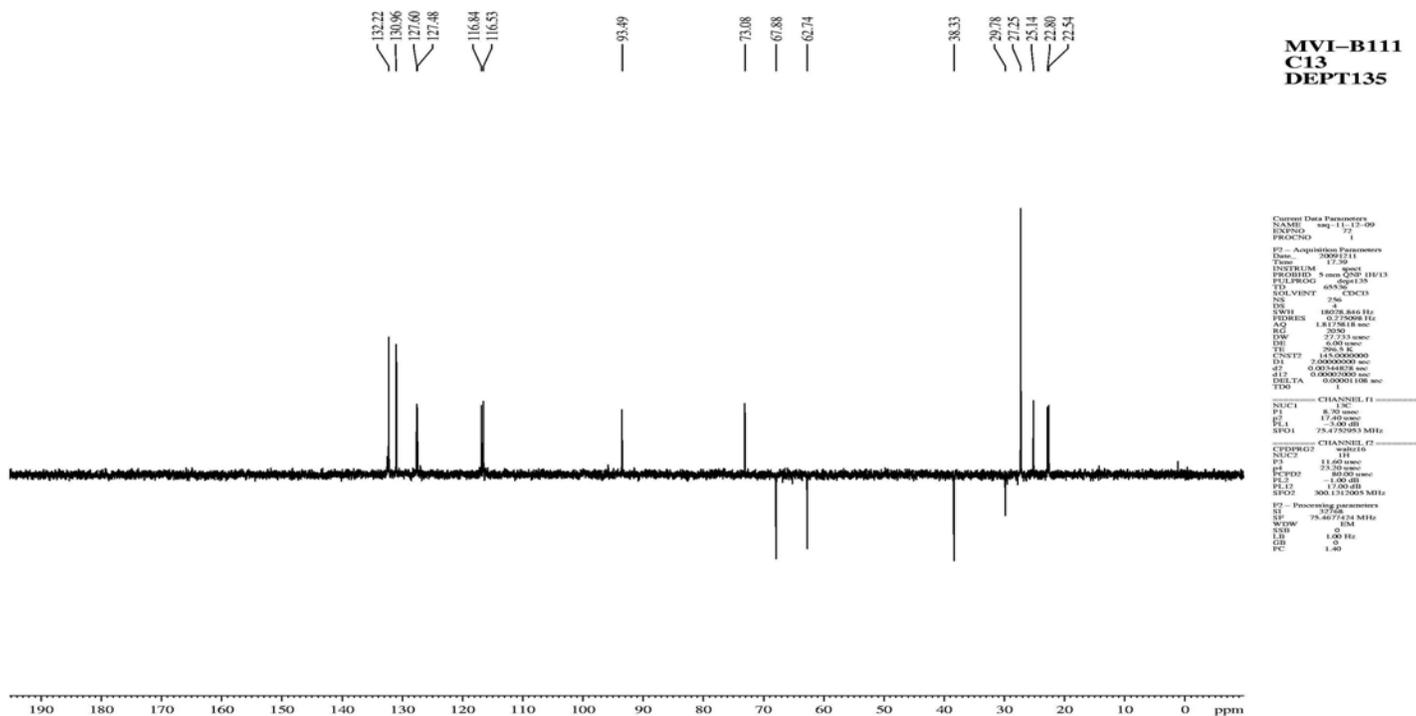
<sup>13</sup>C and DEPT 135 NMR spectra of compound 6



**MVI-BH111  
 PROTON**

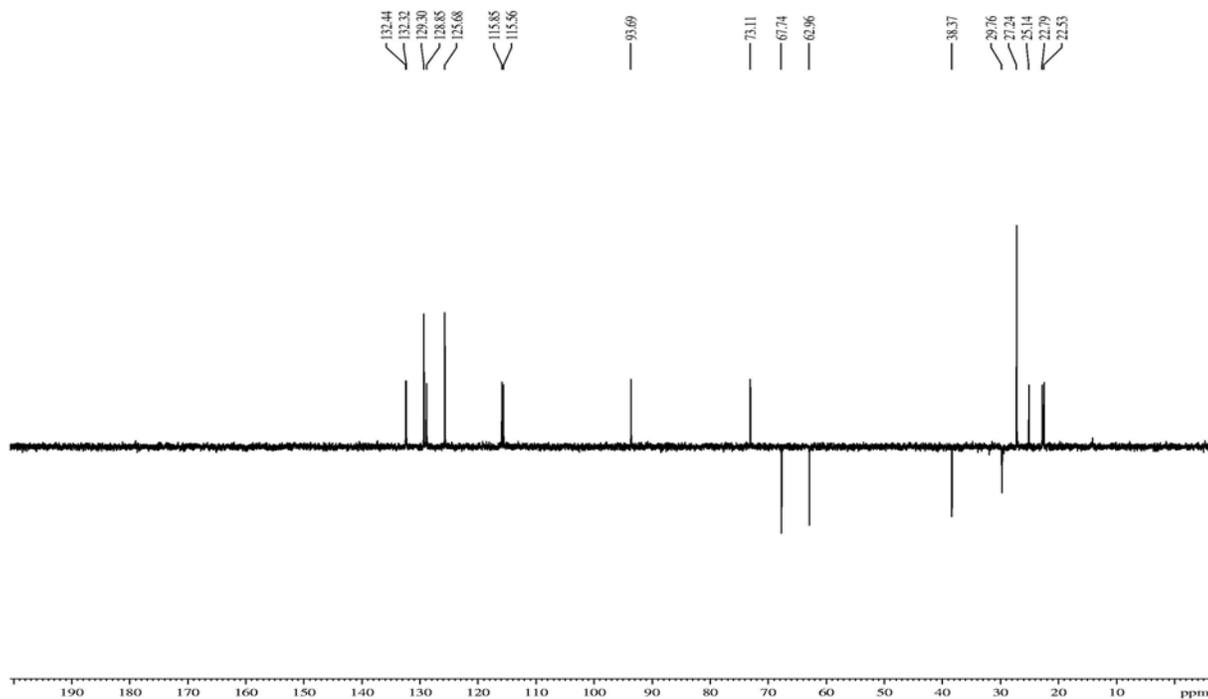
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 PULPROG: zg30  
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 NS: 16  
 DS: 4  
 SWH: 6188.119 Hz  
 FIDRES: 0.096473 Hz  
 AQ: 5.293587 sec  
 RG: 134  
 DW: 80.800 nsec  
 DE: 0.00 nsec  
 TE: 300.2 K  
 DQ: 1  
 TDO: 1.0000000 sec  
 CHANSEL: f1  
 NUCL1: 1H  
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 PL1: -1.00 dB  
 SFO1: 300.1318354 MHz  
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 SF: 300.1300508 MHz  
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 PC: 1.00

<sup>1</sup>H NMR spectrum of compound 7 and its expansion



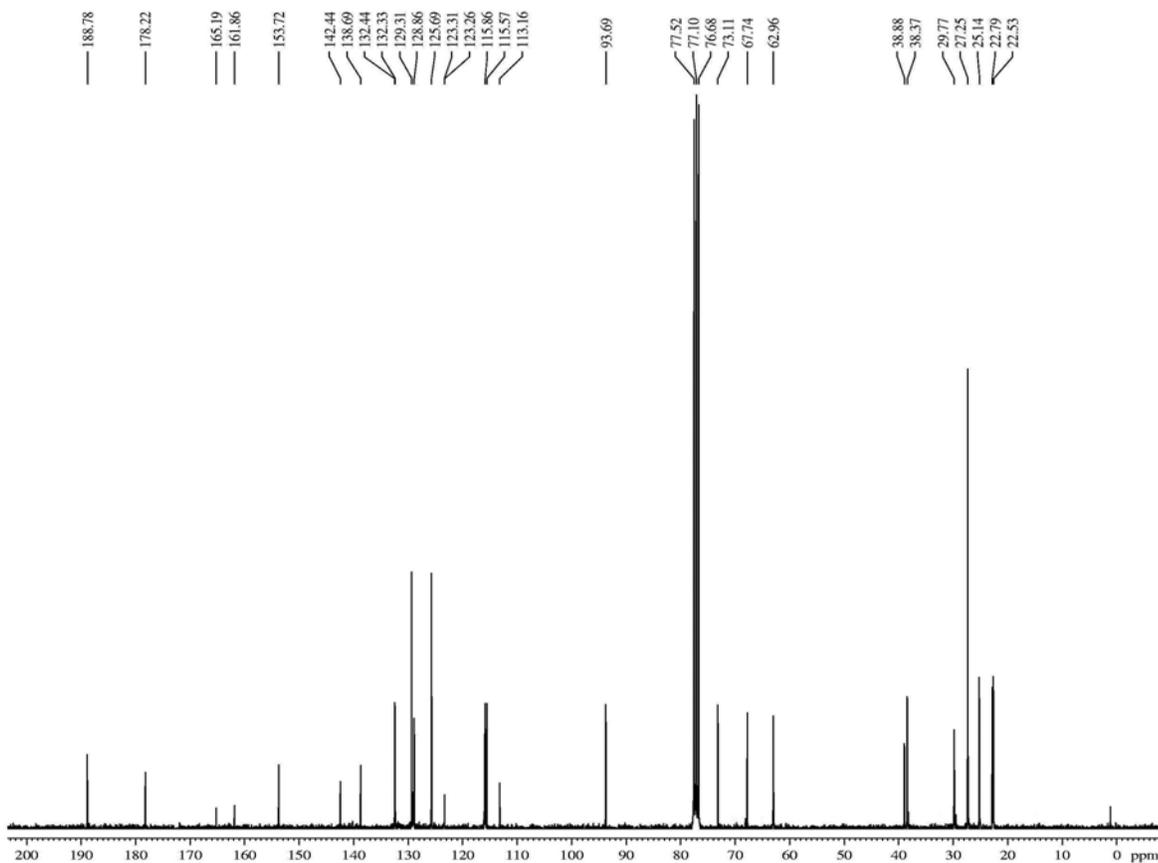
<sup>13</sup>C and DEPT 135 NMR spectra of compound 7





**MVII-BH112  
 C13  
 DEPT135**

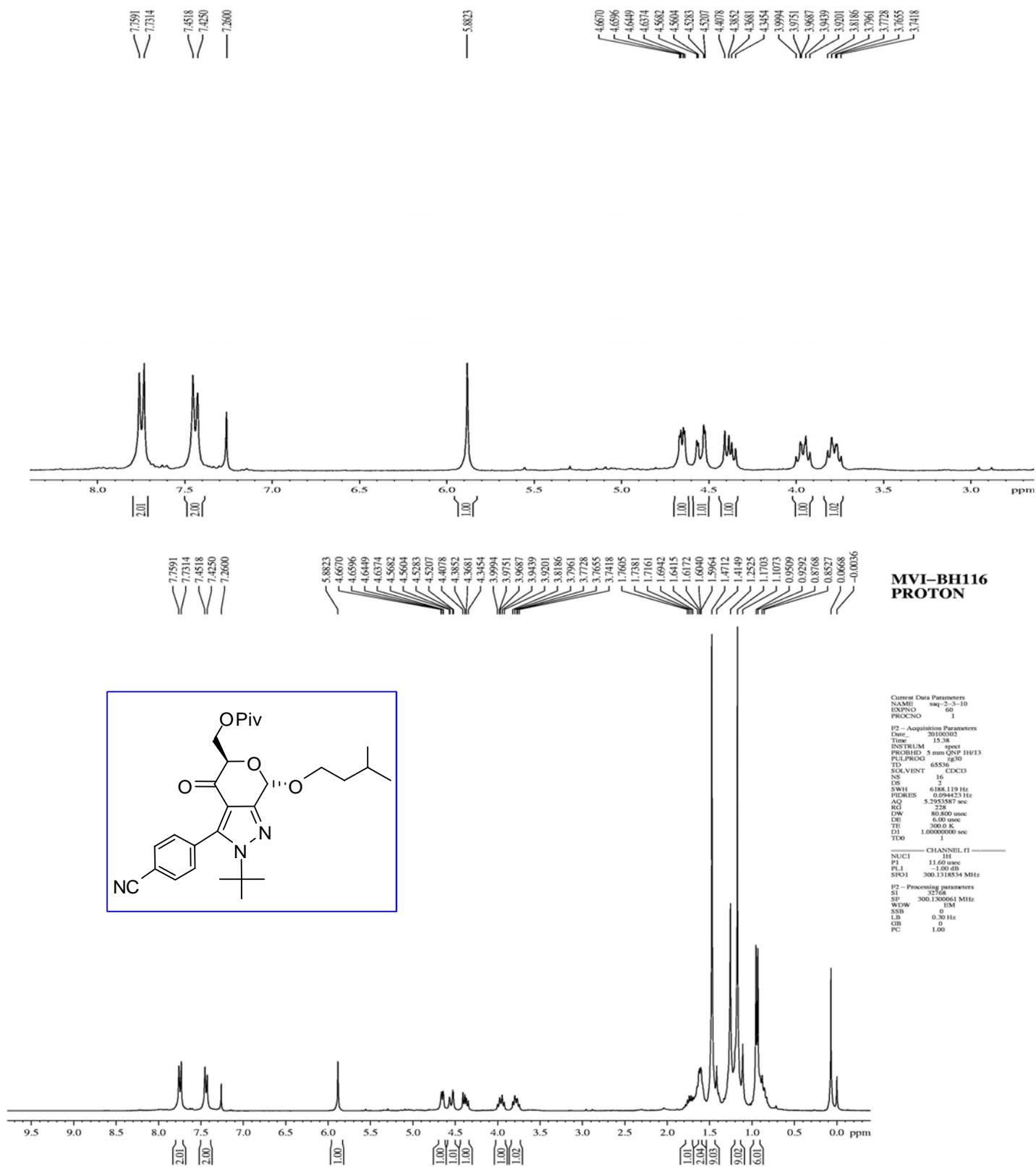
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 SOLVENT: CDCl3  
 NS: 354  
 DS: 4  
 SWH: 18028.856 Hz  
 FIDRES: 0.273098 Hz  
 AQ: 1.8175818 sec  
 RG: 18  
 DW: 27.733 usec  
 DE: 6.00 usec  
 TE: 300.2 K  
 CPDPRG2: zgpg30  
 D1: 2.0000000 sec  
 d11: 0.0000000 sec  
 d12: 0.0000000 sec  
 DELTA: 0.0000108 sec  
 TDO: 1  
 CHANNEL f1  
 NUC1: 13C  
 P1: 8.70 usec  
 PL1: -1.00 dB  
 SFO1: 75.4752953 MHz  
 CHANNEL f2  
 CPDPRG2: waltz16  
 NUC2: 1H  
 P2: 11.60 usec  
 PL2: 28.20 usec  
 PL12: -1.00 dB  
 PL13: 17.00 dB  
 SFO2: 300.1312005 MHz  
 F2 - Processing parameters  
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 SF: 75.467333 MHz  
 WDW: EM  
 SSB: 0  
 LB: 1.00 Hz  
 GB: 0  
 PC: 1.40



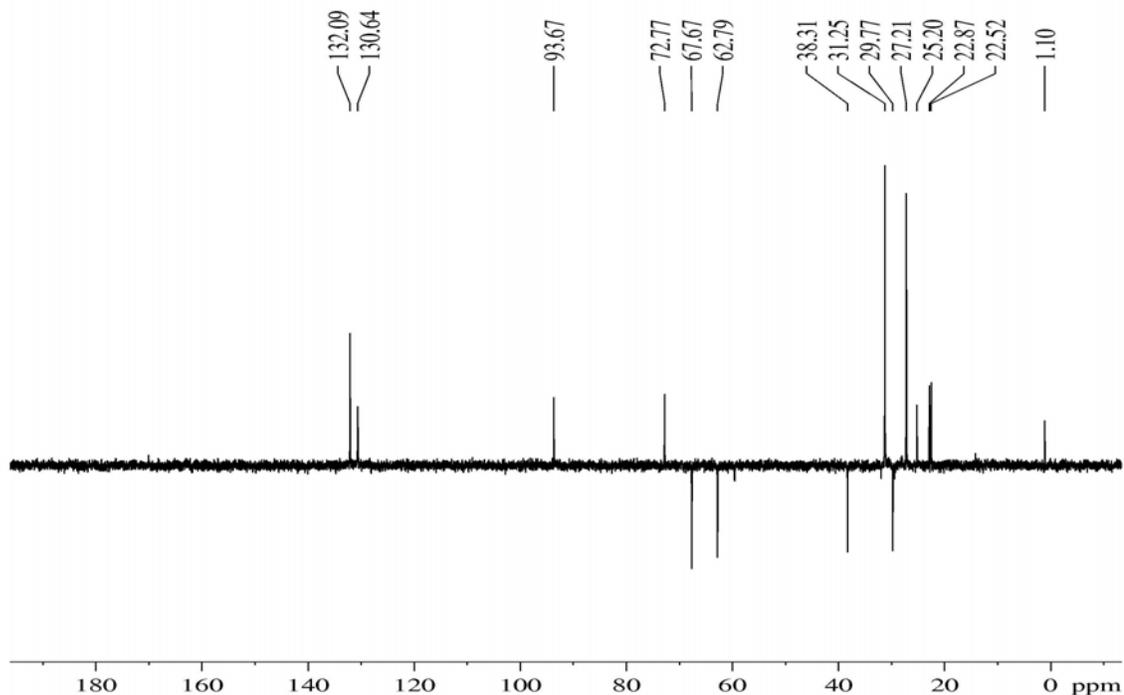
**MVI-BH112  
 C13CPD**

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 F2 - Acquisition Parameters  
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 Time: 9.05  
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 PULPROG: zgpg30  
 SOLVENT: CDCl3  
 NS: 696  
 DS: 4  
 SWH: 18028.856 Hz  
 FIDRES: 0.273098 Hz  
 AQ: 1.8175818 sec  
 RG: 18  
 DW: 27.733 usec  
 DE: 6.00 usec  
 TE: 300.2 K  
 CPDPRG2: zgpg30  
 D1: 2.0000000 sec  
 d11: 0.0000000 sec  
 DELTA: 1.8999998 sec  
 TDO: 1  
 CHANNEL f1  
 NUC1: 13C  
 P1: 8.70 usec  
 PL1: -1.00 dB  
 SFO1: 75.4752953 MHz  
 CHANNEL f2  
 CPDPRG2: waltz16  
 NUC2: 1H  
 P2: 11.60 usec  
 PL2: -1.00 dB  
 PL12: 17.00 dB  
 PL13: 21.00 dB  
 SFO2: 300.1312005 MHz  
 F2 - Processing parameters  
 SI: 32768  
 SF: 75.467333 MHz  
 WDW: EM  
 SSB: 0  
 LB: 1.00 Hz  
 GB: 0  
 PC: 1.40

<sup>13</sup>C and DEPT 135 NMR spectra of compound 8



<sup>1</sup>H NMR spectrum of compound 9 and its expansion



**MVI-BH116  
 C13  
 DEPT135**

```

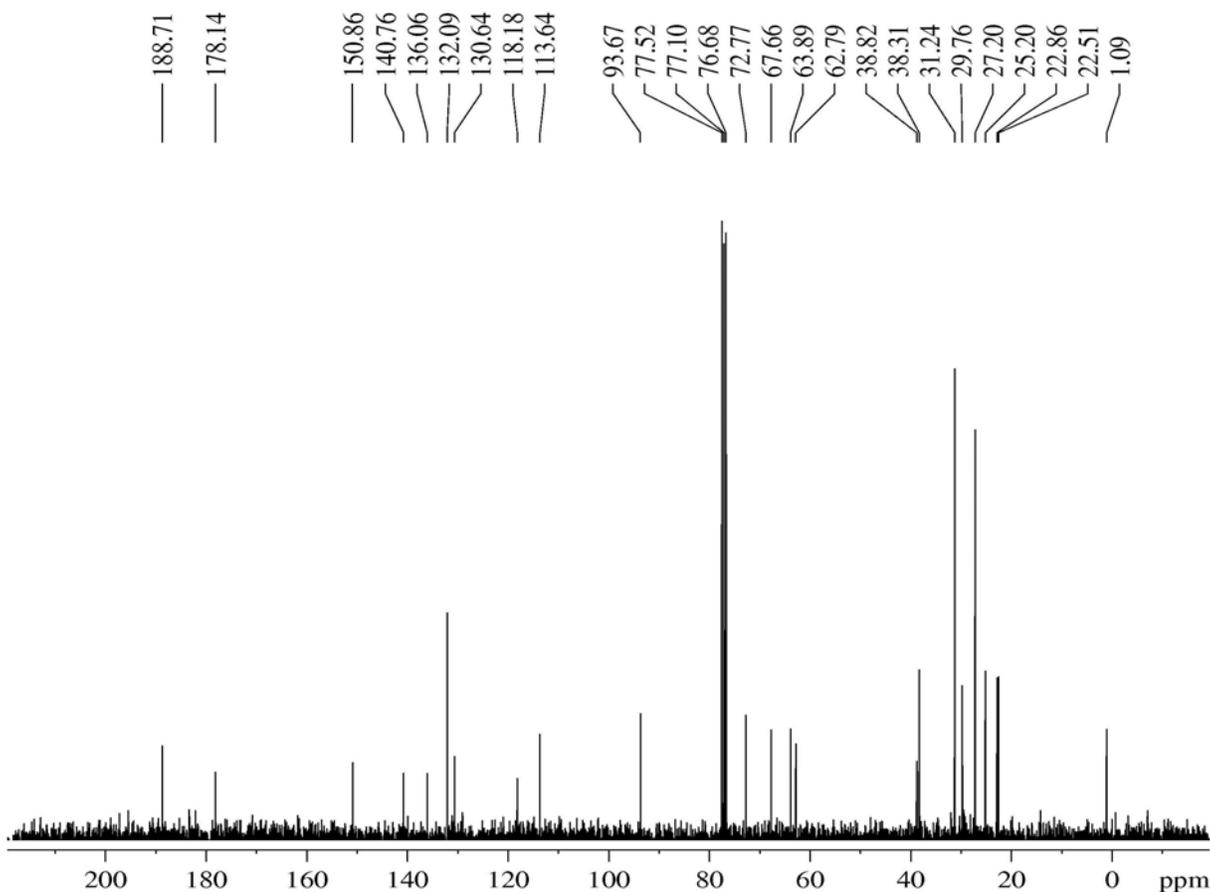
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NAME      Saq-4-3-10
EXPNO    1
PROCNO   1

F2 - Acquisition Parameters
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PULPROG  zgpg30
TD        65536
SOLVENT  CDCl3
NS        4
DS        4
SWH      18028.846 Hz
FIDRES   0.275098 Hz
AQ        1.8175818 sec
RG        12.7
DW        27.733 usec
DE        6.00 usec
TE        294.3 K
D1        2.0000000 sec
d11       0.03000000 sec
DELTA    0.0000100 sec
TDO       1

===== CHANNEL f1 =====
NUC1      13C
P1        8.70 usec
PL1       -3.00 dB
SFO1      75.4752953 MHz

===== CHANNEL f2 =====
CPDPRG2  waltz16
NUC2      1H
P2        23.20 usec
PL2       -1.00 dB
SFO2      300.1312005 MHz

F2 - Processing parameters
SI        32768
SF        75.4677444 MHz
WDW       no
SSB       0
LB        0.00 Hz
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PC        1.40
    
```



**MVI-BH116  
 C13CPD**

```

Current Data Parameters
NAME      Saq-4-3-10
EXPNO    30
PROCNO   1

F2 - Acquisition Parameters
Date_    20100304
Time     15.17
INSTRUM  spect
PROBHD   5 mm QNP 1H/13
PULPROG  zgpg30
TD        65536
SOLVENT  CDCl3
NS        512
DS        4
SWH      18028.846 Hz
FIDRES   0.275098 Hz
AQ        1.8175818 sec
RG        12.7
DW        27.733 usec
DE        6.00 usec
TE        294.3 K
D1        2.0000000 sec
d11       0.03000000 sec
DELTA    1.89999998 sec
TDO       1

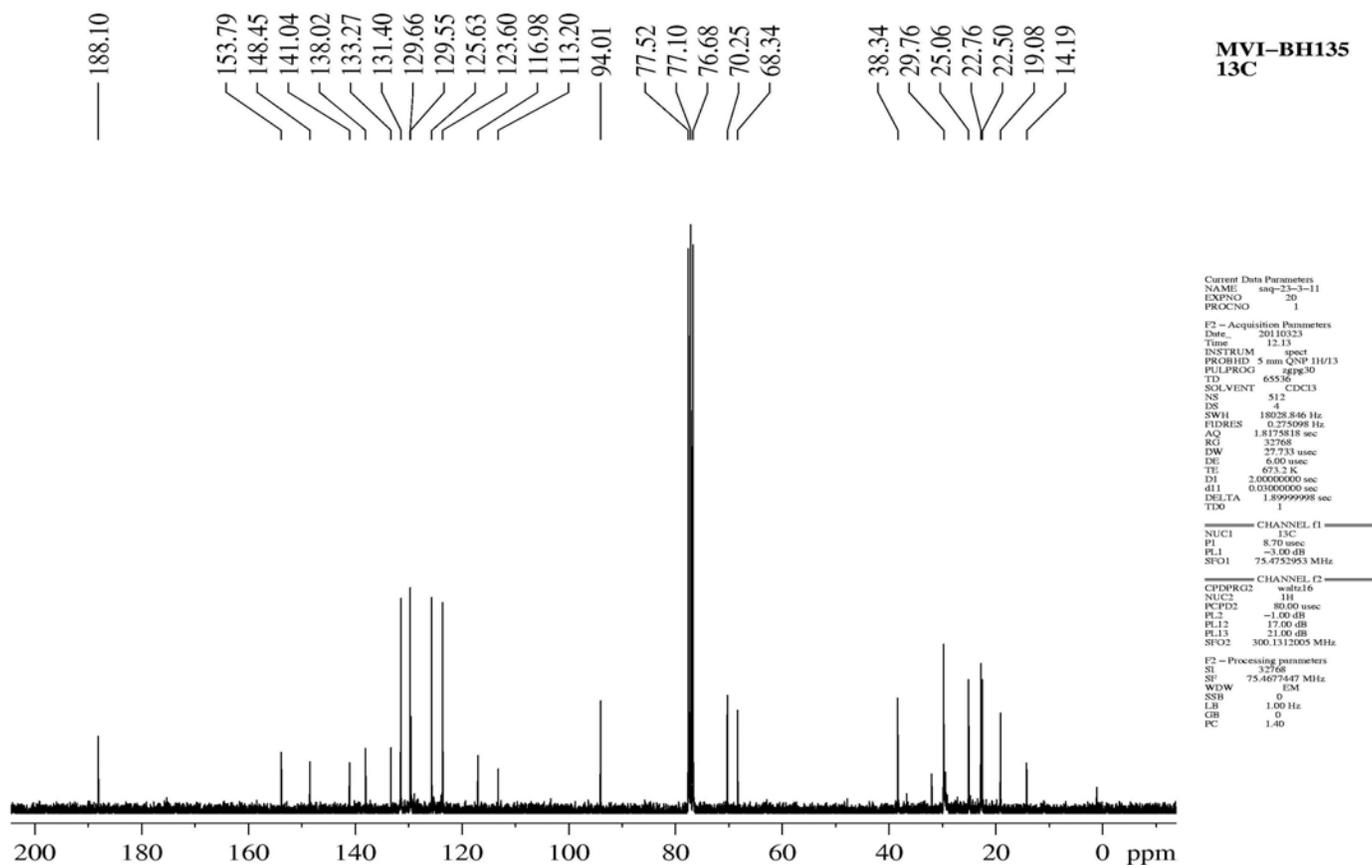
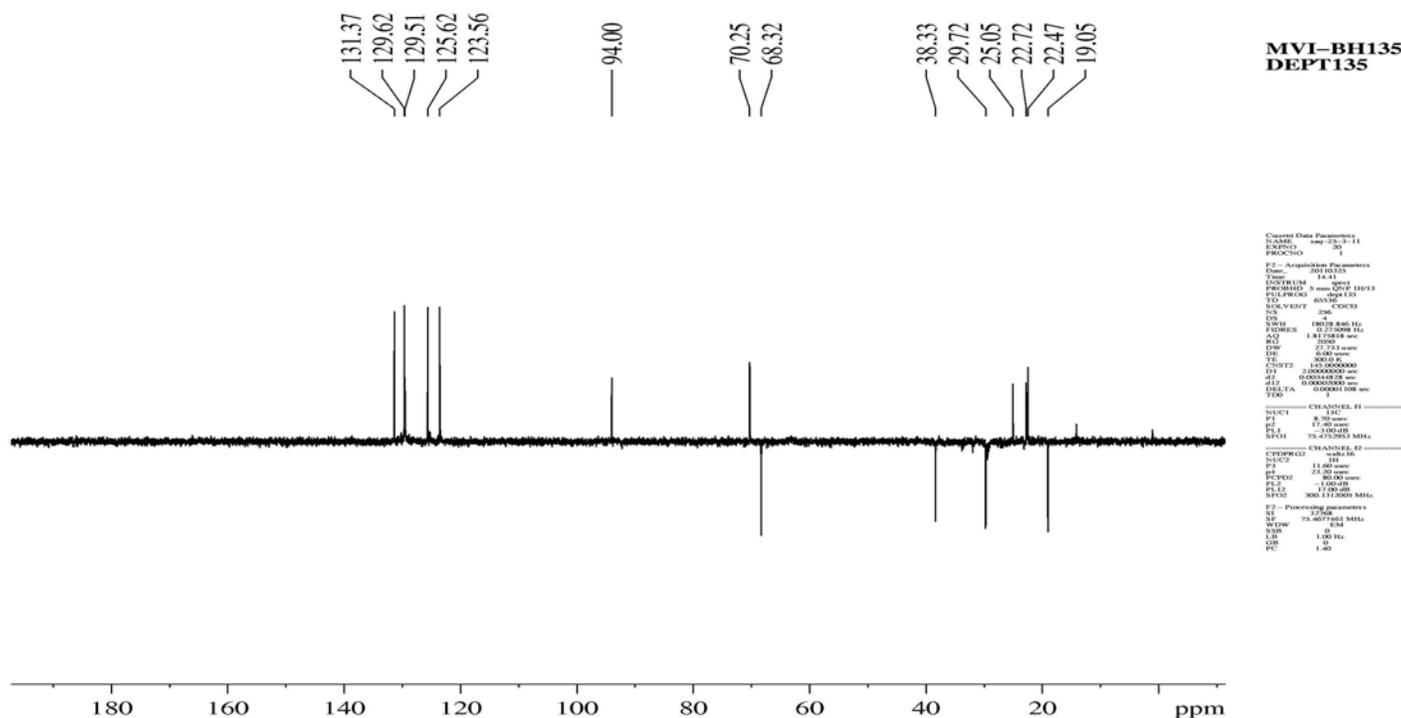
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P1        8.70 usec
PL1       -3.00 dB
SFO1      75.4752953 MHz

===== CHANNEL f2 =====
CPDPRG2  waltz16
NUC2      1H
P2        80.00 usec
PL2       -1.00 dB
SFO2      300.1312005 MHz

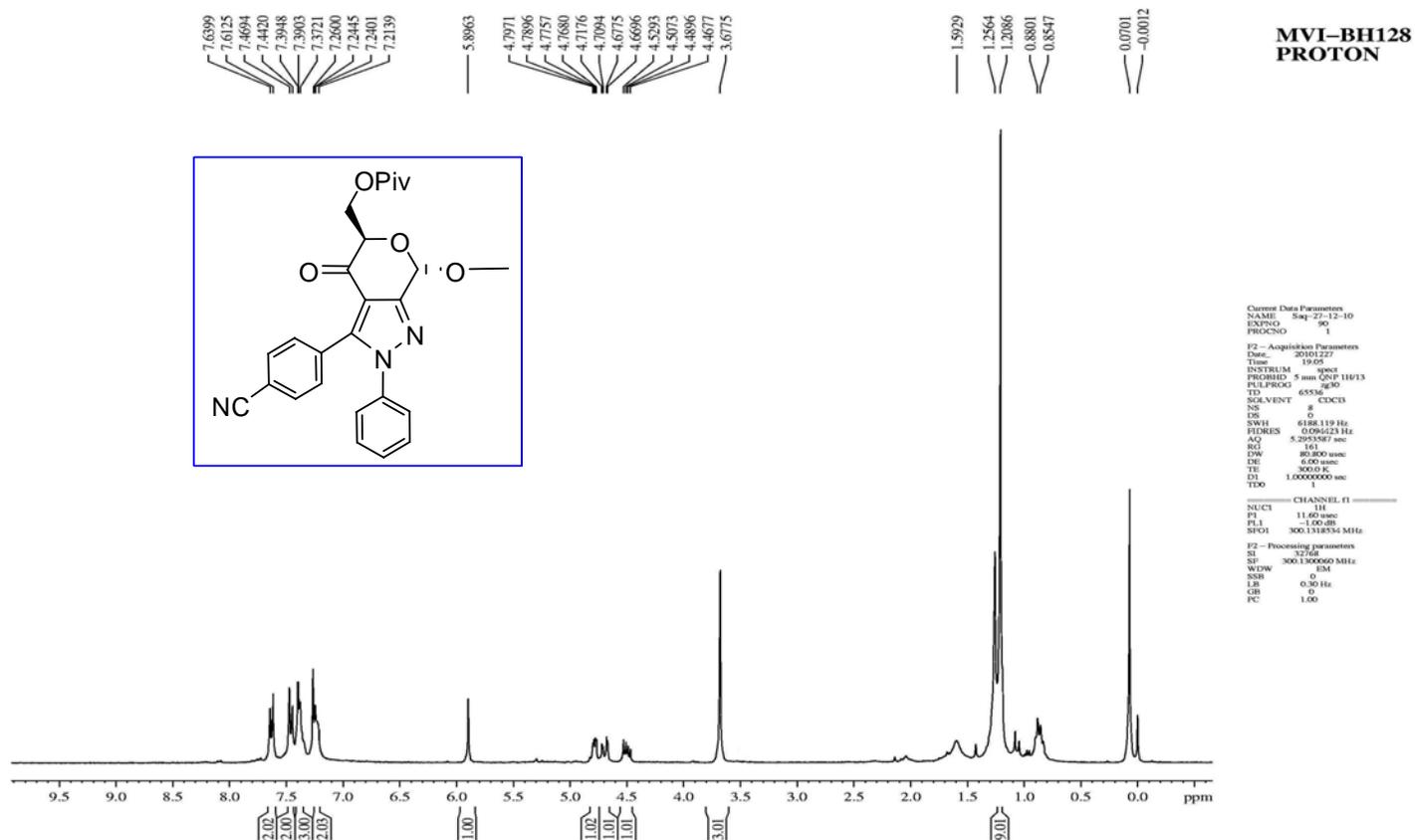
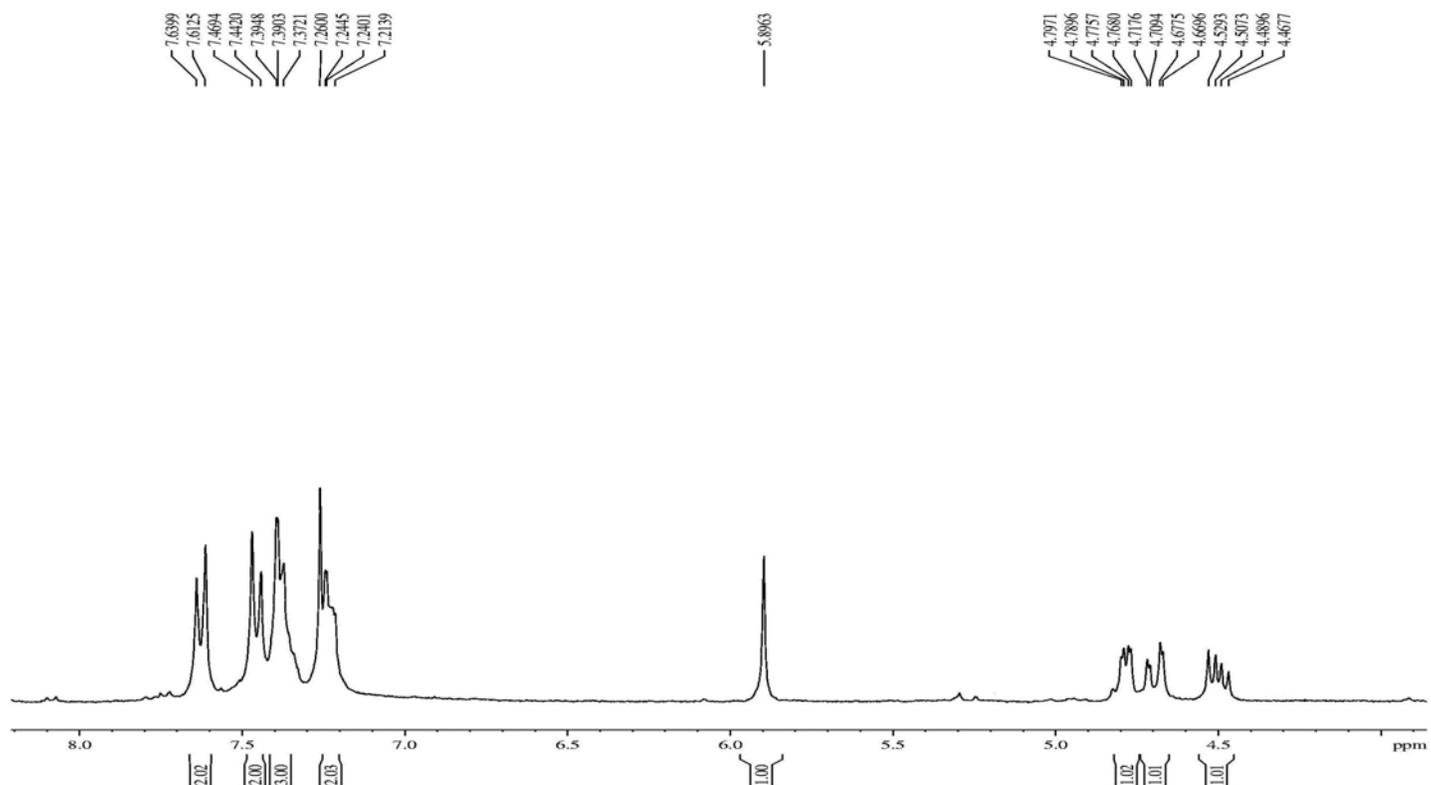
F2 - Processing parameters
SI        32768
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WDW       no
SSB       0
LB        0.00 Hz
GB        0
PC        1.40
    
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<sup>13</sup>C and DEPT 135 NMR spectra of compound 9

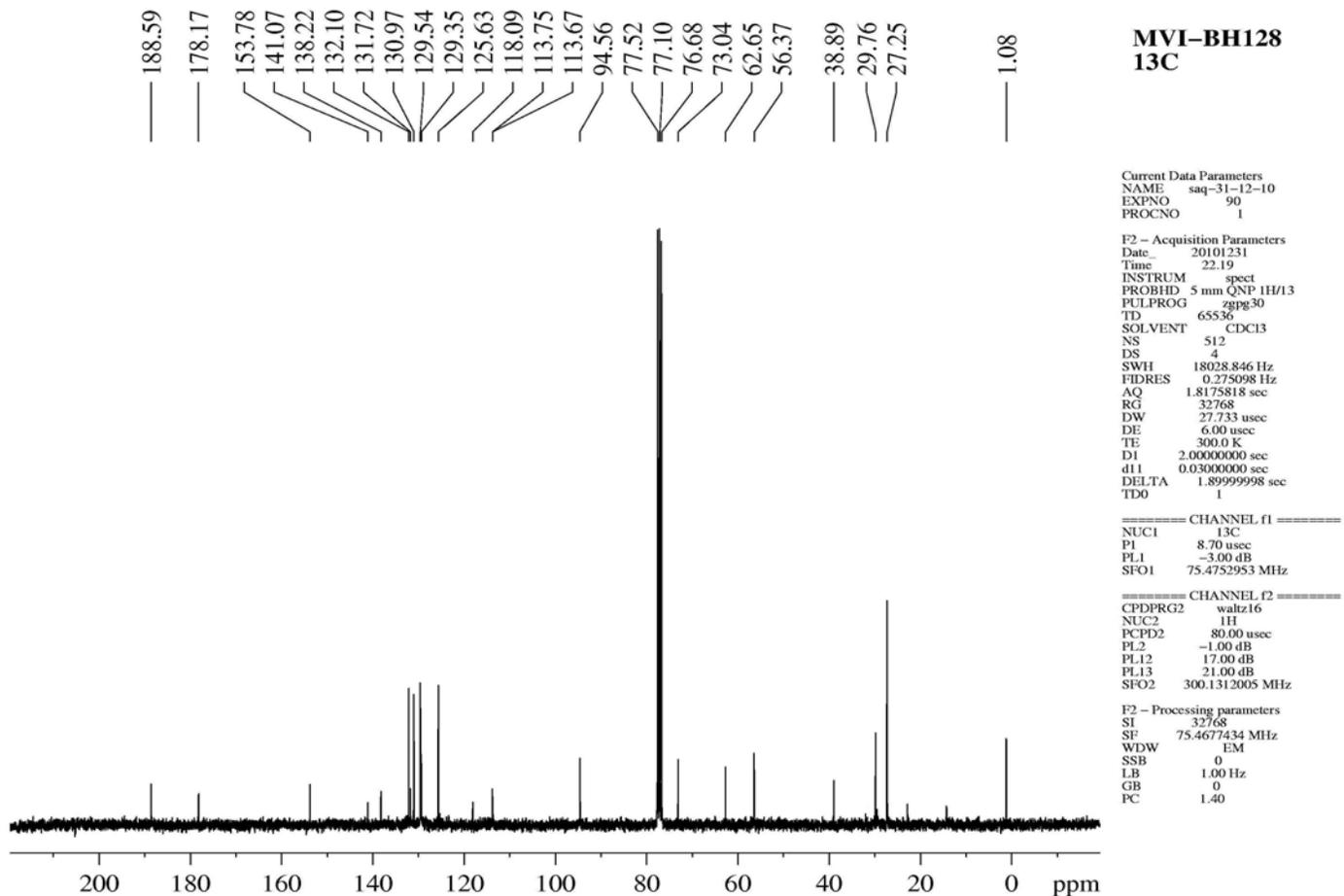
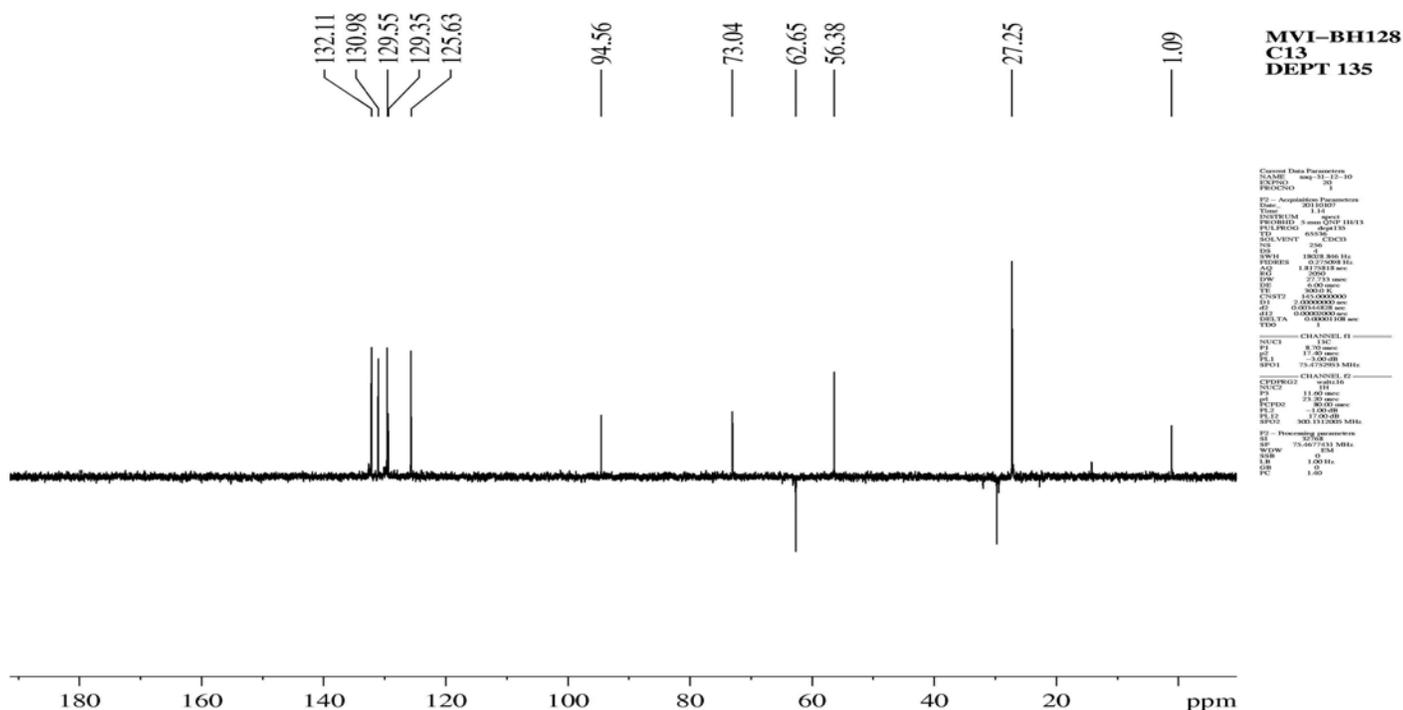




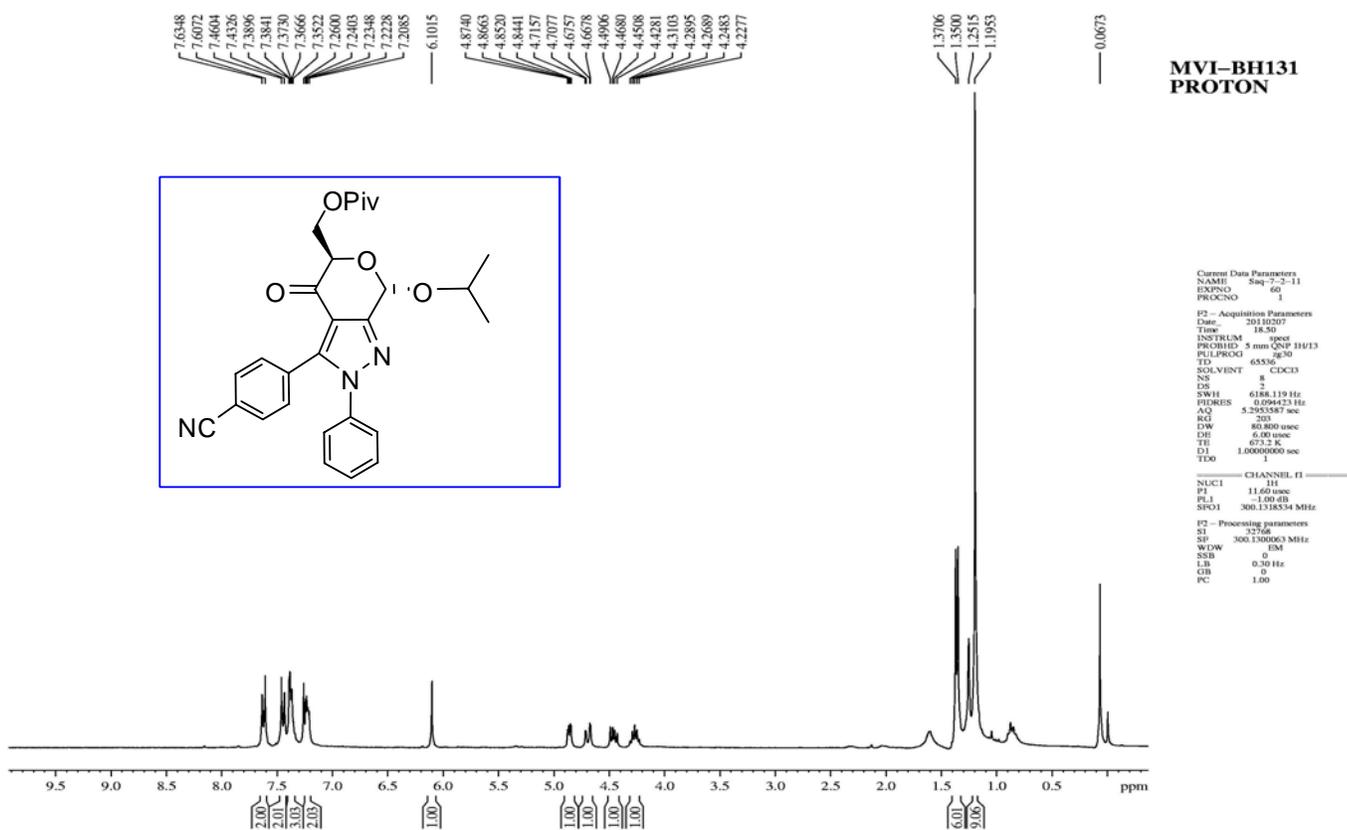
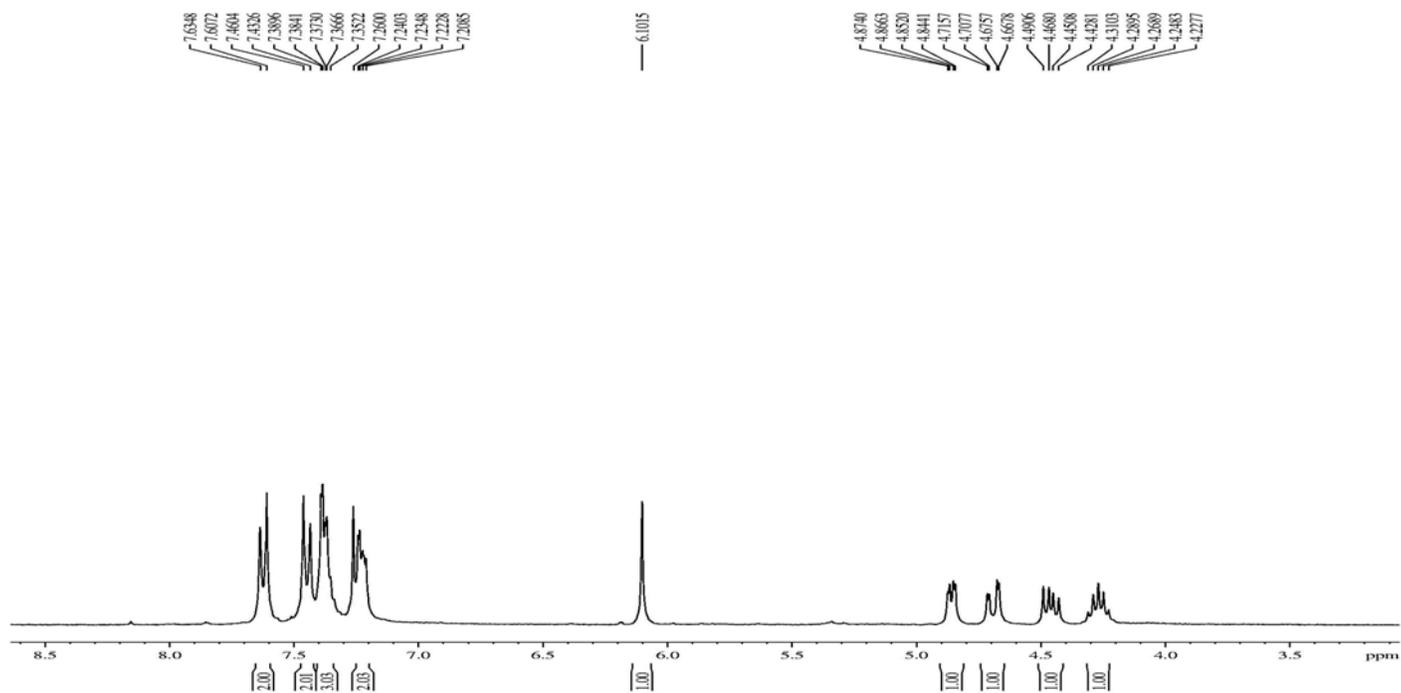
$^{13}\text{C}$  and DEPT 135 NMR spectra of compound 10



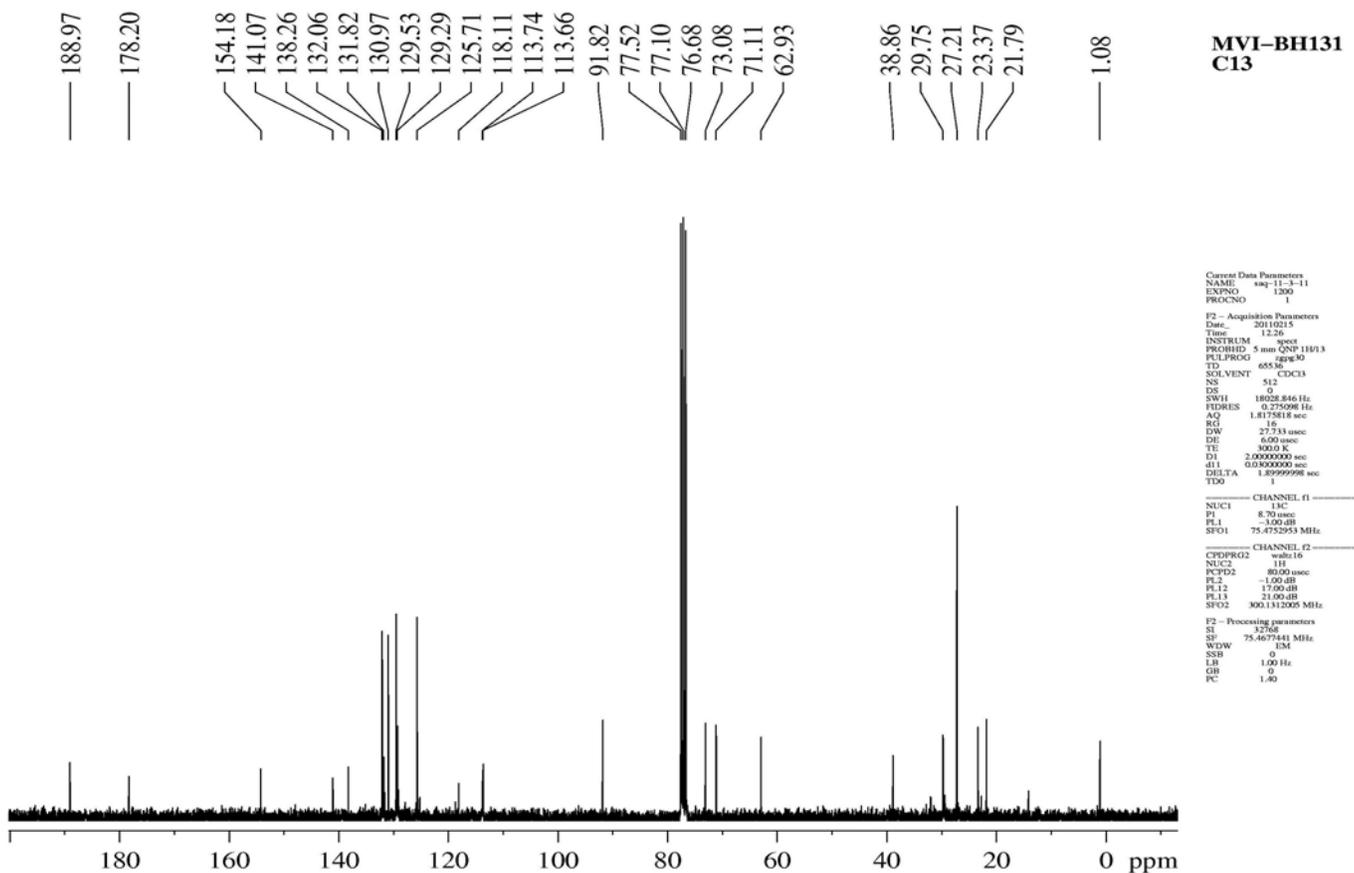
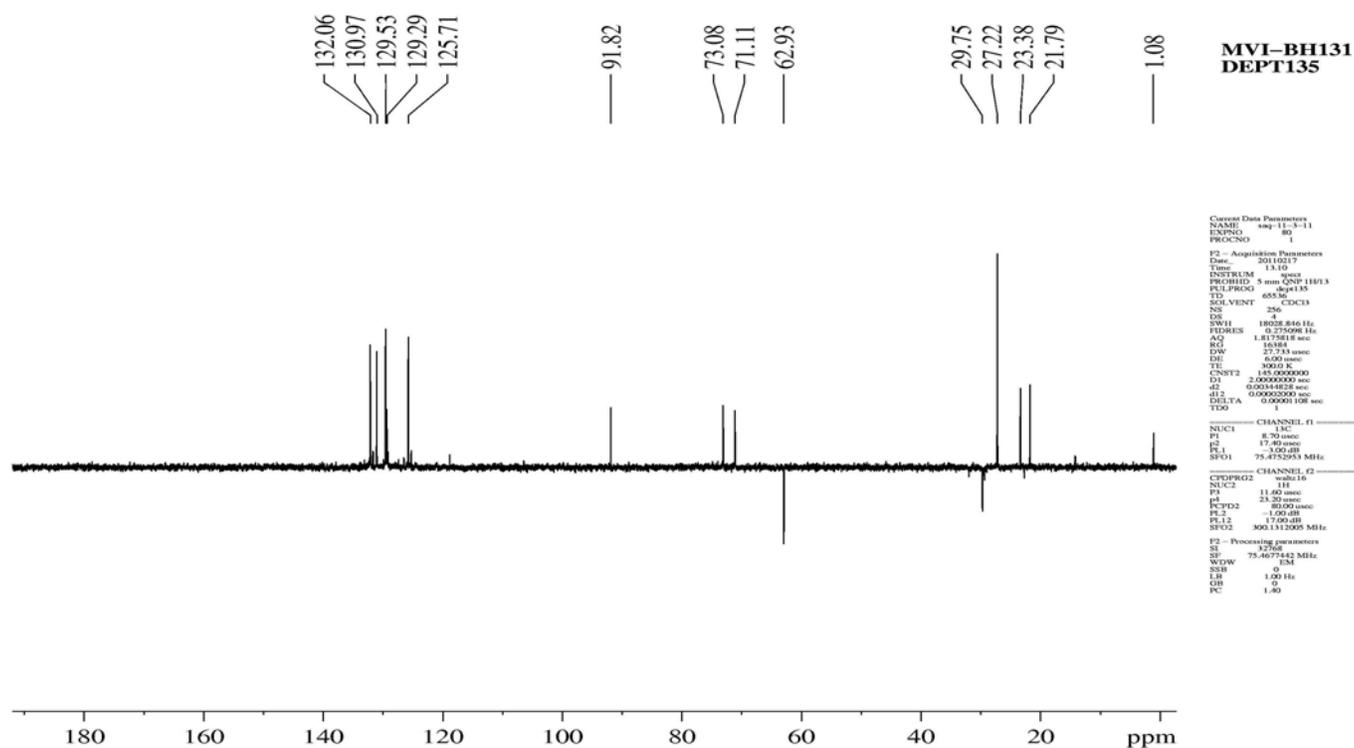
<sup>1</sup>H NMR spectrum of compound **11** and its expansion



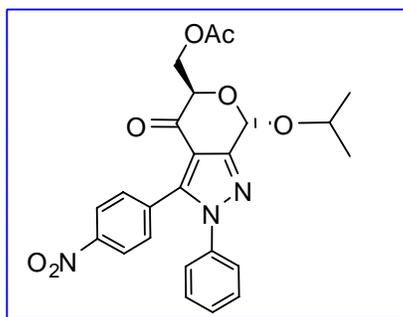
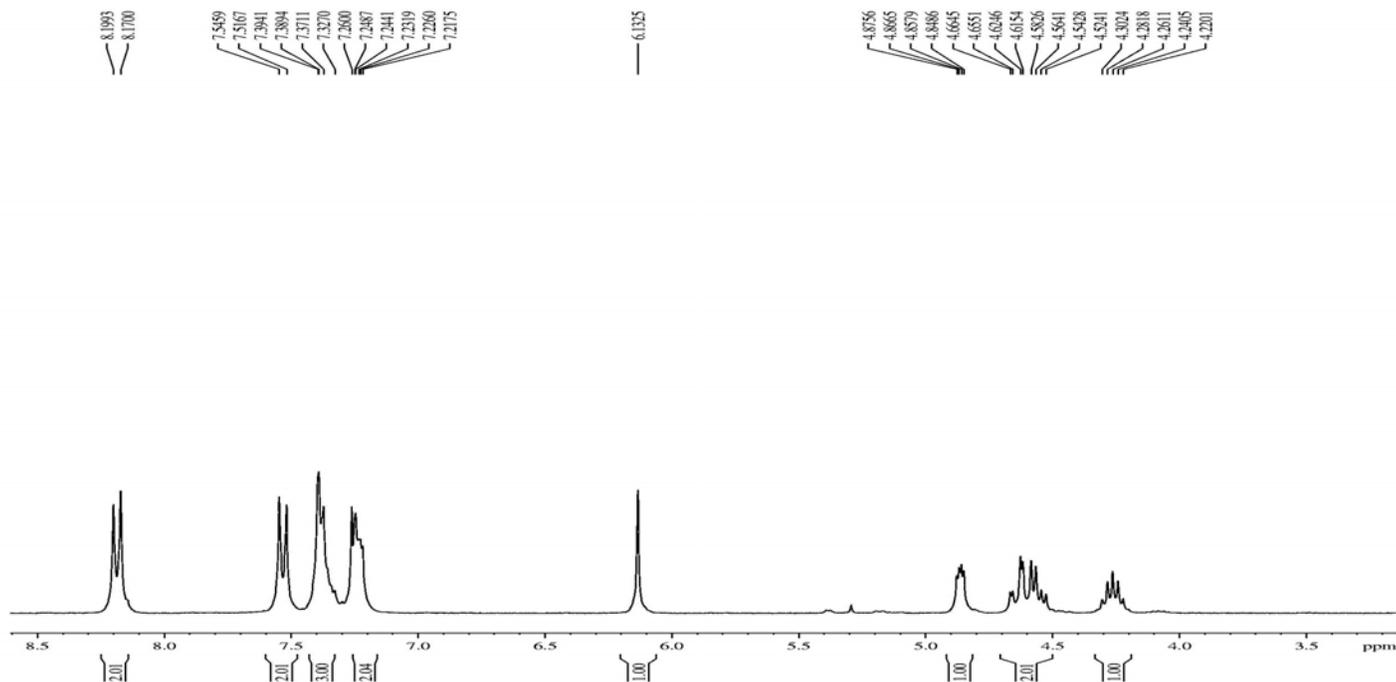
$^{13}\text{C}$  and DEPT 135 NMR spectra of compound **11**



<sup>1</sup>H NMR spectrum of compound **12** and its expansion



<sup>13</sup>C and DEPT 135 NMR spectra of compound **12**



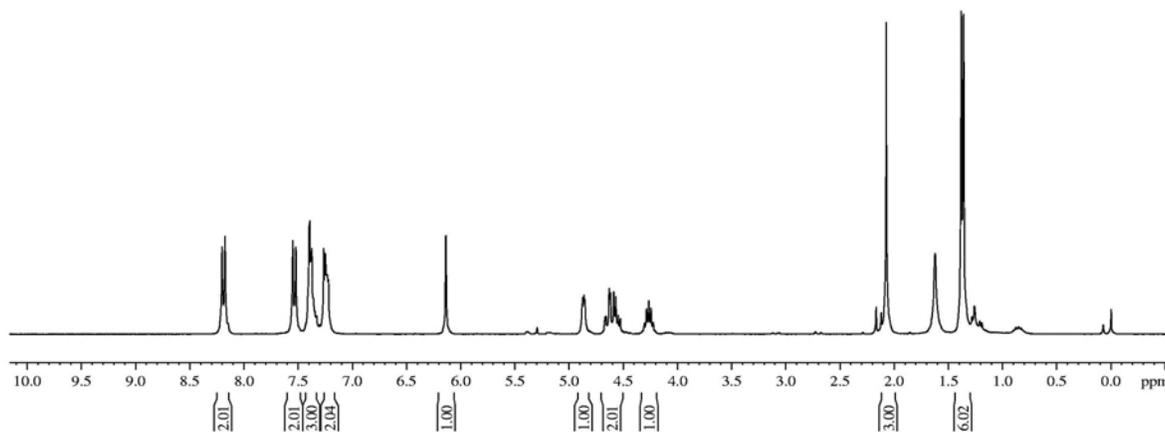
**MVI-BH12  
 PROTON**

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 PROCNO 1

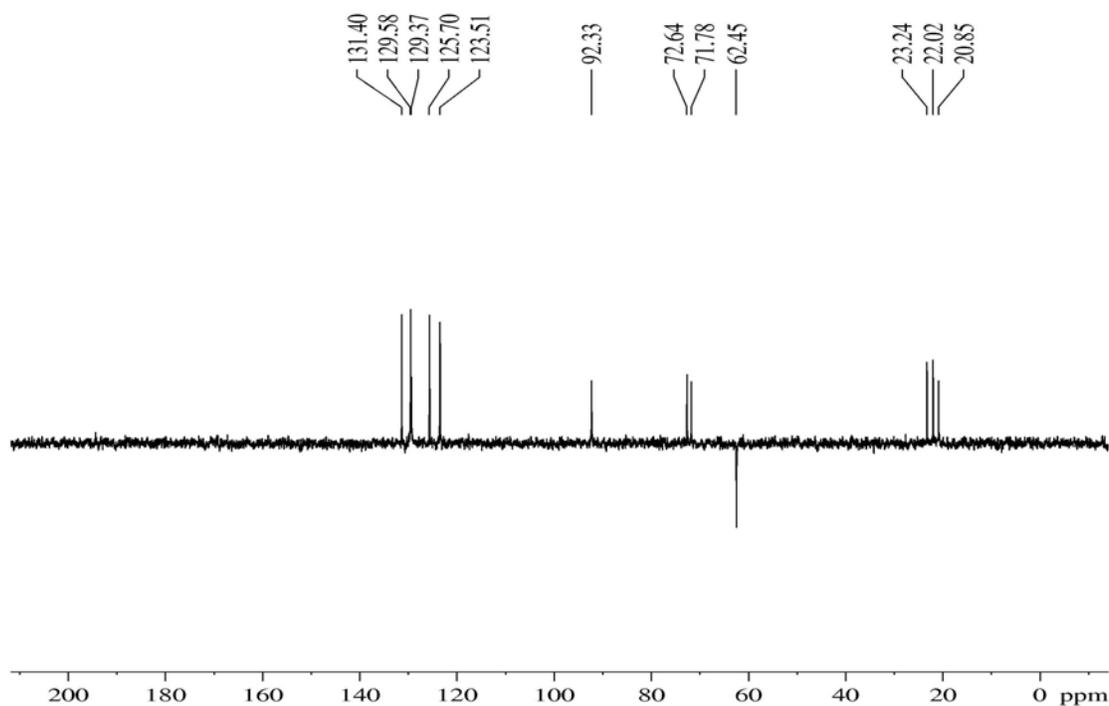
F2 - Acquisition Parameters  
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 Time 12.40  
 INSTRUM spect  
 PROBHD 5 mm QNP 1H/13  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 8  
 DS 0  
 SWH 6188.119 Hz  
 FIDRES 0.094423 Hz  
 AQ 5.295557 sec  
 RG 144  
 DW 80.800 usec  
 DE 6.00 usec  
 TE 300.0 K  
 D1 1.0000000 sec  
 TDO

CHANEL f1  
 NUC1 1H  
 P1 11.60 usec  
 PL1 -1.00 dB  
 SFO1 300.1318534 MHz

F2 - Processing parameters  
 SI 32768  
 SF 300.1300061 MHz  
 EM  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00



<sup>1</sup>H NMR spectrum of compound **13** and its expansion

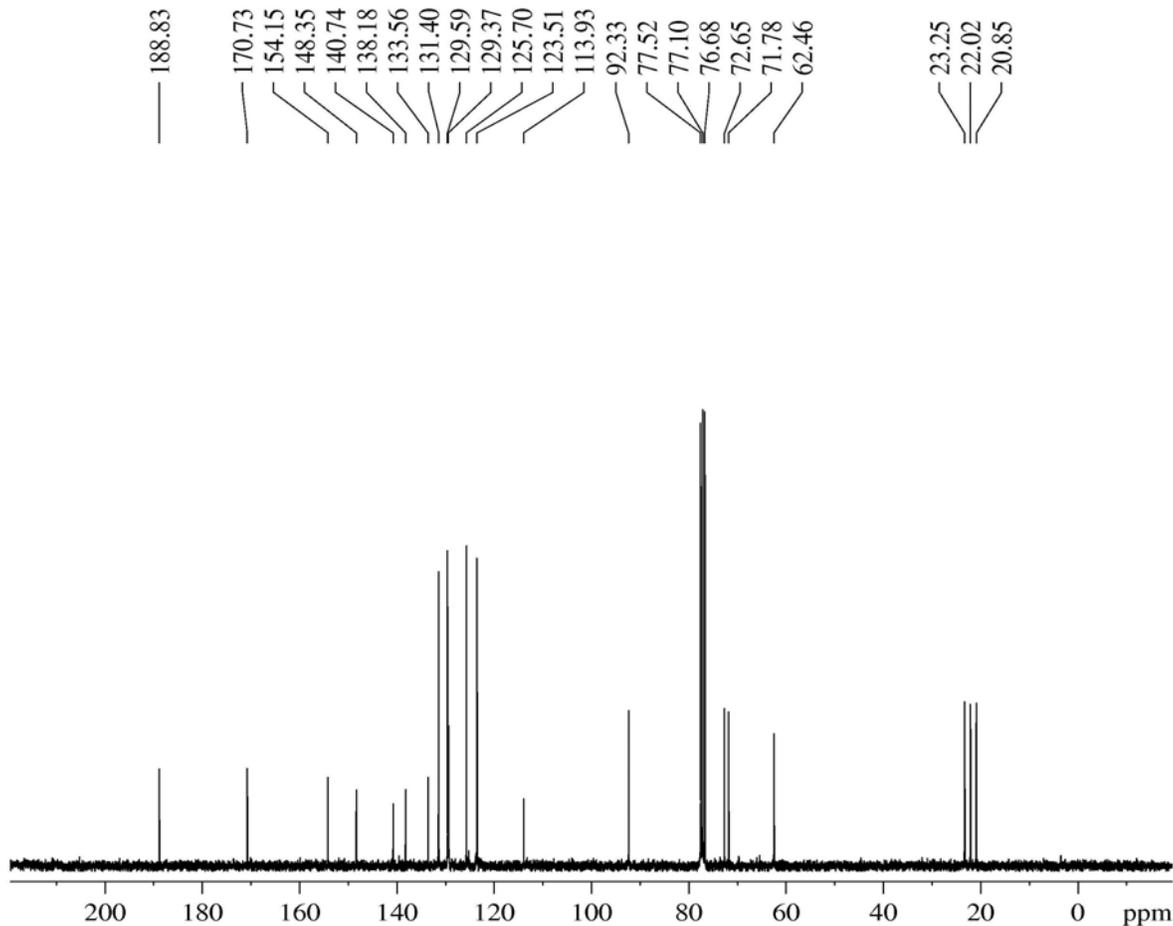


**MVI-BH122  
C13  
DEPT135**

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 PROCNO 1  
 F2 - Acquisition Parameters  
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 Time 14.47  
 INSTRUM spect  
 PROBHID 5 mm QNP 1H/13  
 PULPROG dept135  
 TD 65536  
 SOLVENT CDCl3  
 NS 256  
 DS 4  
 SWH 18028.846 Hz  
 FIDRES 0.275098 Hz  
 AQ 1.8175818 sec  
 RG 16384  
 DW 27.733 usec  
 DE 6.00 usec  
 TE 300.0 K  
 CNST2 145.0000000  
 D1 2.00000000 sec  
 d12 0.00000000 sec  
 DELTA 0.00001108 sec  
 TDO 1

===== CHANNEL f1 =====  
 NUC1 13C  
 P1 8.70 usec  
 PL1 -3.00 dB  
 SFO1 75.4752953 MHz  
 ===== CHANNEL f2 =====  
 CPDPRG2 waltz16  
 NUC2 1H  
 P3 11.60 usec  
 PL3 23.20 dB  
 PCPD2 80.00 usec  
 PL2 -1.00 dB  
 PL12 17.00 dB  
 SFO2 300.1312005 MHz

F2 - Processing parameters  
 SI 32768  
 SF 75.4677456 MHz  
 WDW EM  
 SSB 0  
 LB 3.00 Hz  
 GB 0  
 PC 1.40

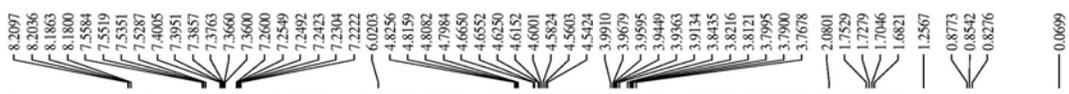
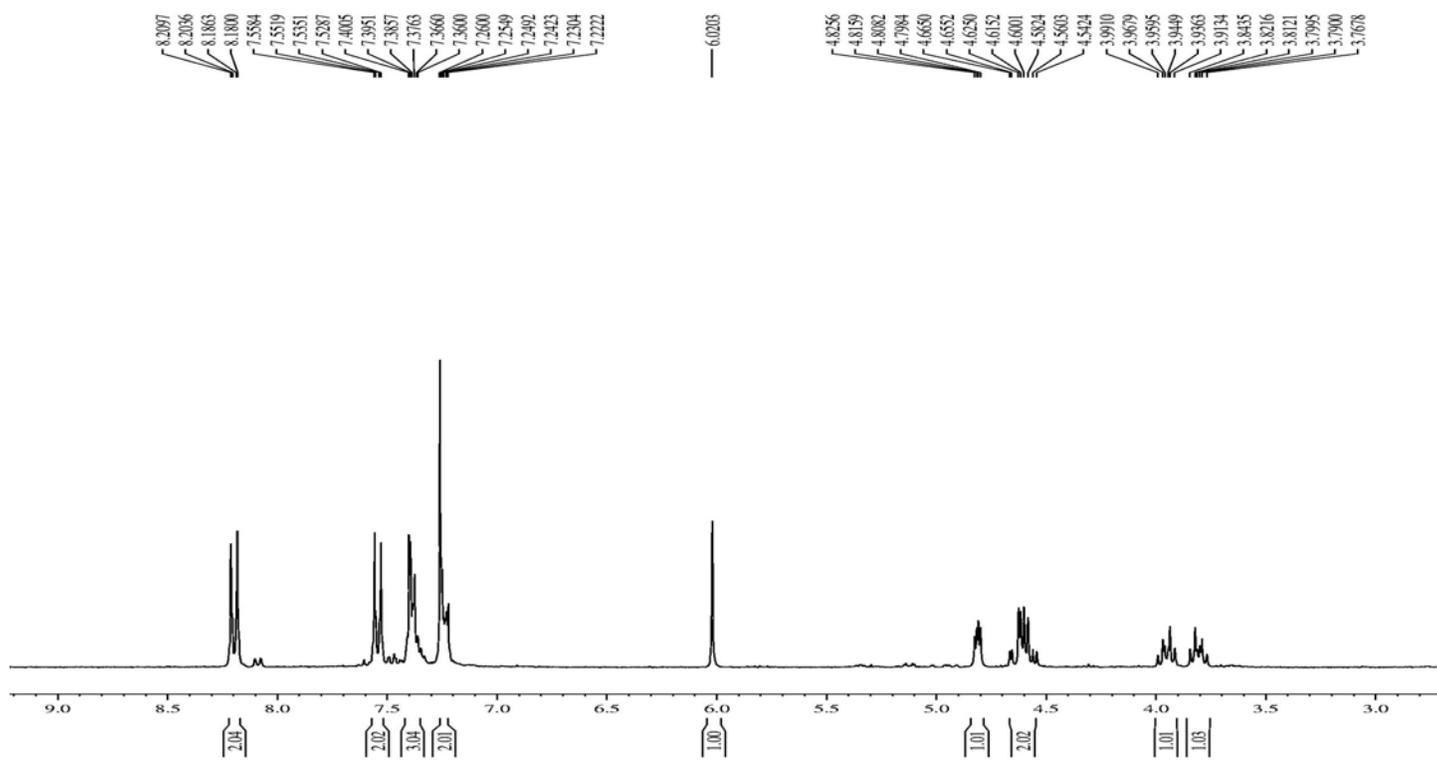


**MVI-BH122  
C13CPD**

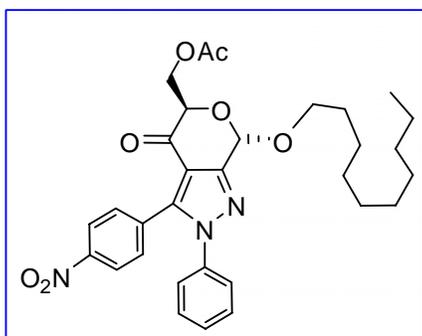
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 PROCNO 1  
 F2 - Acquisition Parameters  
 Date\_ 20100806  
 Time 13.56  
 INSTRUM spect  
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 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 512  
 DS 0  
 SWH 18028.846 Hz  
 FIDRES 0.275098 Hz  
 AQ 1.8175818 sec  
 RG 32768  
 DW 27.733 usec  
 DE 6.00 usec  
 TE 300.0 K  
 D1 2.00000000 sec  
 d11 0.03000000 sec  
 DELTA 1.89999998 sec  
 TDO 1

===== CHANNEL f1 =====  
 NUC1 13C  
 P1 8.70 usec  
 PL1 -3.00 dB  
 SFO1 75.4752953 MHz  
 ===== CHANNEL f2 =====  
 CPDPRG2 waltz16  
 NUC2 1H  
 PCPD2 80.00 usec  
 PL2 -1.00 dB  
 PL12 17.00 dB  
 PL13 21.00 dB  
 SFO2 300.1312005 MHz

F2 - Processing parameters  
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 SF 75.4677454 MHz  
 WDW EM  
 SSB 0  
 LB 3.00 Hz  
 GB 0  
 PC 1.40



SKSML-34  
 PROTON

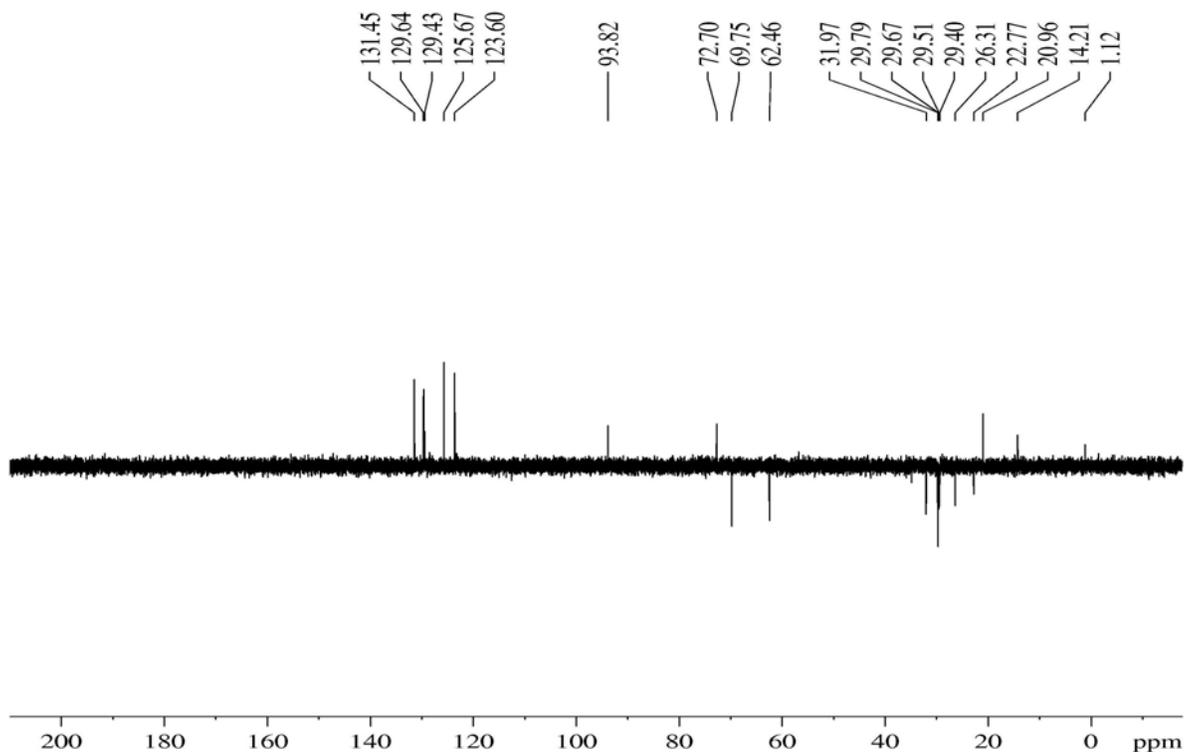


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 NAME: 89-26-1-09  
 PROCNO: 49  
 F2 - Acquisition Parameters  
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 TIME: 09:26:30  
 INSTRUM: spect  
 F1PRGRM: zgpg30 (zgpg30) 1813  
 F2PRGRM: zgpg30  
 ID: 6313670  
 SOLVENT: CDCl3  
 NS: 2  
 DS: 2  
 SWH: 4121.814 Hz  
 FIDRES: 0.004421 Hz  
 AQ: 3.215151 sec  
 RG: 655  
 DW: 19.000 nsec  
 DE: 6.000 nsec  
 TE: 300.2 K  
 SI: 1000000.00 sec  
 EQ: 4

----- CHANNEL F1 -----  
 NUC1: 13C  
 P1: 11.000 nsec  
 PL1: -1.00 dB  
 SFO1: 100.1253194 MHz

F2 - Processing parameters  
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 SF: 300.135000 MHz  
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 GB: 0 Hz  
 PC: 1.00

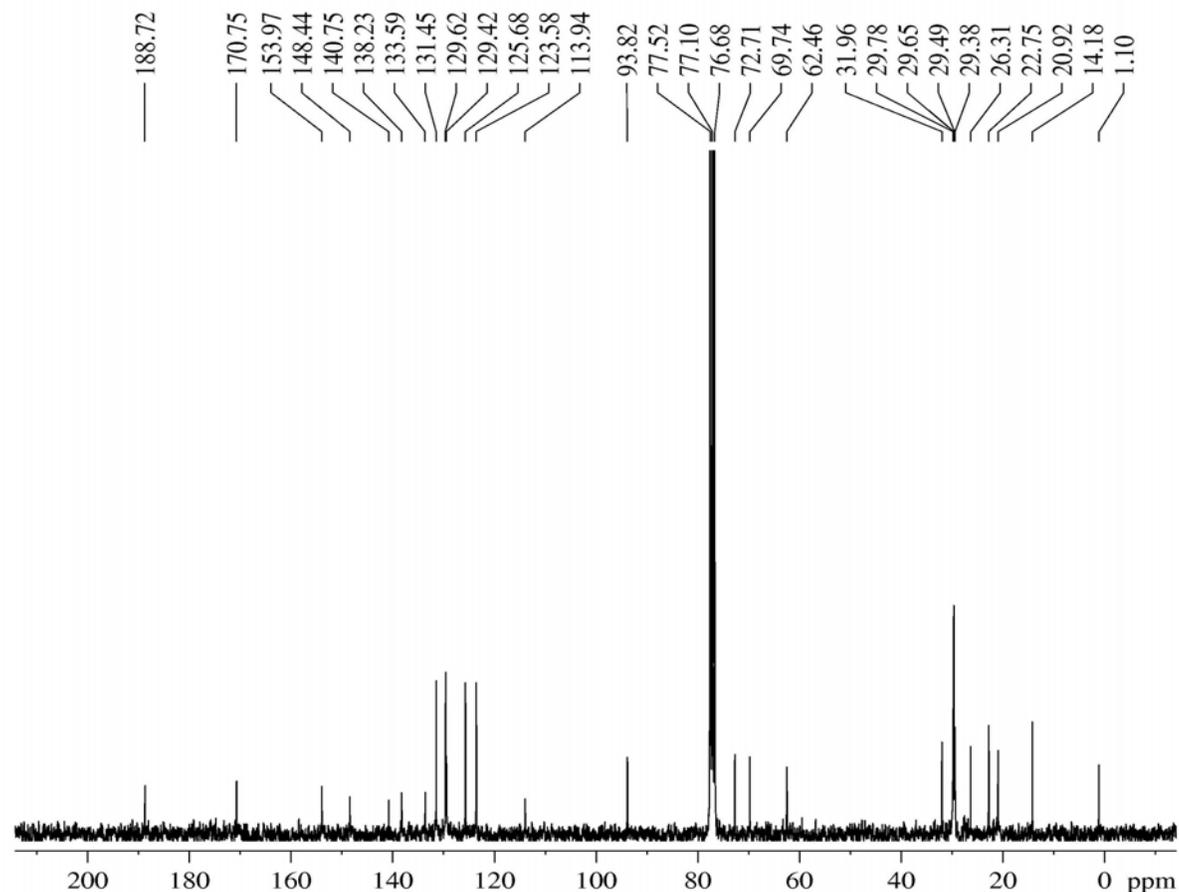
<sup>1</sup>H NMR spectrum of compound 14 and its expansion



**SKSML-34  
 C13  
 DEPT135**

Current Data Parameters  
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 PROCNO 1  
 F2 - Acquisition Parameters  
 Date\_ 20090122  
 Time 11.49  
 INSTRUM spect  
 PROBHD 5 mm QNP 1H/13  
 PULPROG dept135  
 TD 65536  
 SOLVENT CDCl3  
 NS 512  
 DS 0  
 SWH 18028.846 Hz  
 FIDRES 0.275098 Hz  
 AQ 1.8175818 sec  
 RG 2050  
 DW 27.733 usec  
 DE 6.00 usec  
 TE 673.2 K  
 CNST2 145.0000000  
 D1 2.000000000 sec  
 d2 0.00344828 sec  
 d12 0.00002000 sec  
 DELTA 0.00001108 sec  
 TD0 1

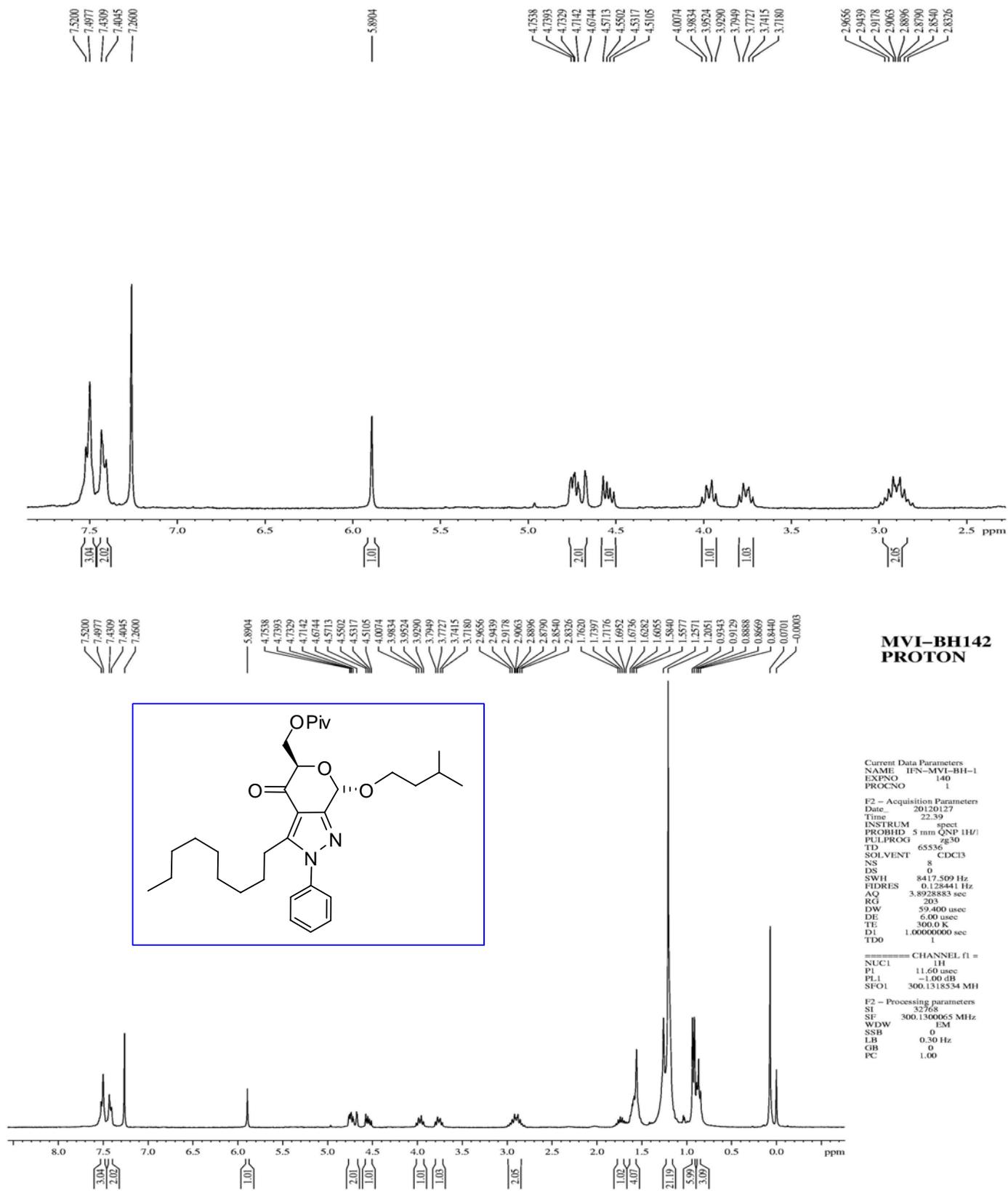
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 NUC1 13C  
 P1 8.70 usec  
 p2 17.40 usec  
 PL1 -3.00 dB  
 SFO1 75.4752953 MHz  
 ===== CHANNEL f2 =====  
 CPDPRG2 waltz16  
 NUC2 1H  
 P3 11.60 usec  
 p4 23.20 usec  
 PCPD2 80.00 usec  
 PL2 -1.00 dB  
 PL12 17.00 dB  
 SFO2 300.1312005 MHz  
 F2 - Processing parameters  
 SI 32768  
 SF 75.4677420 MHz  
 WDW no  
 SSB 0  
 LB 0.00 Hz  
 GB 0  
 PC 1.40



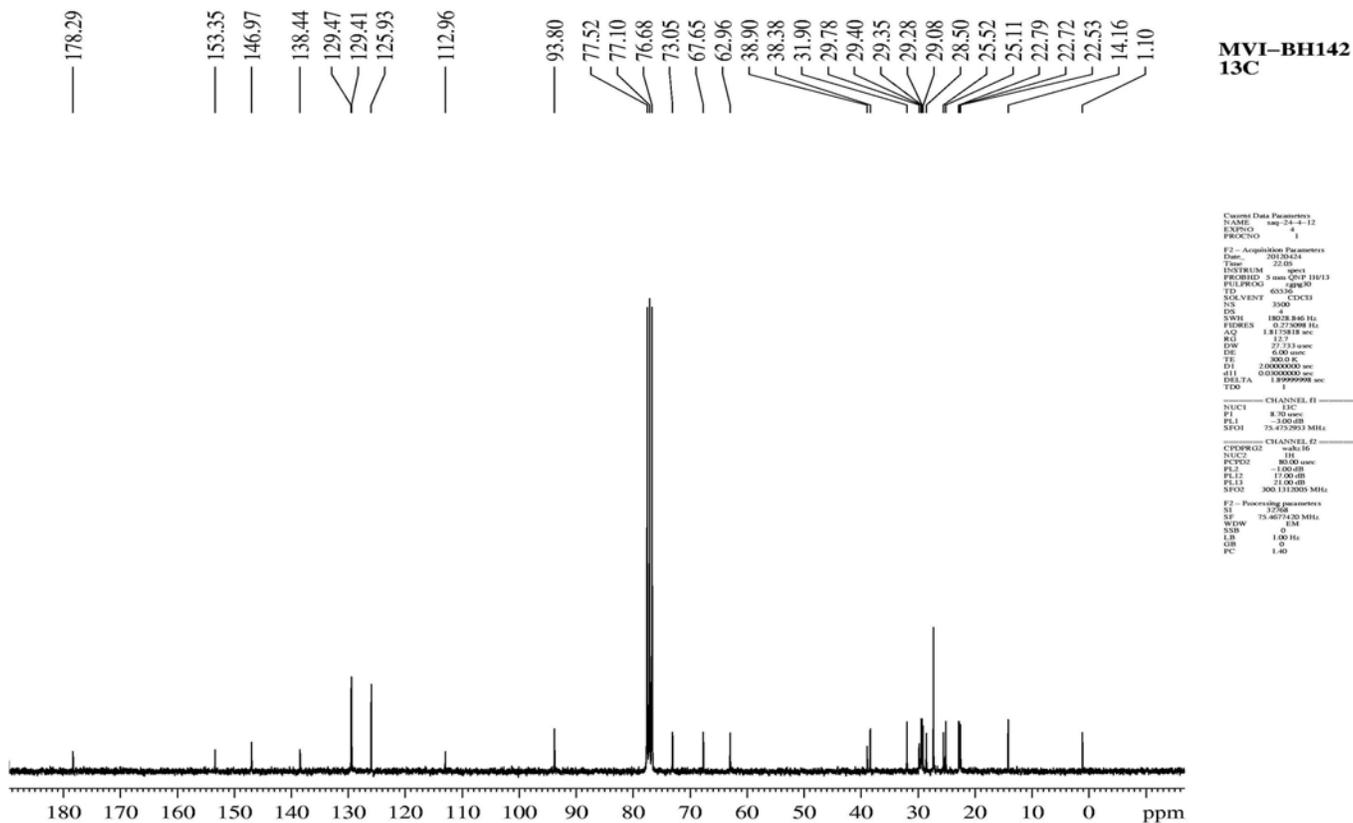
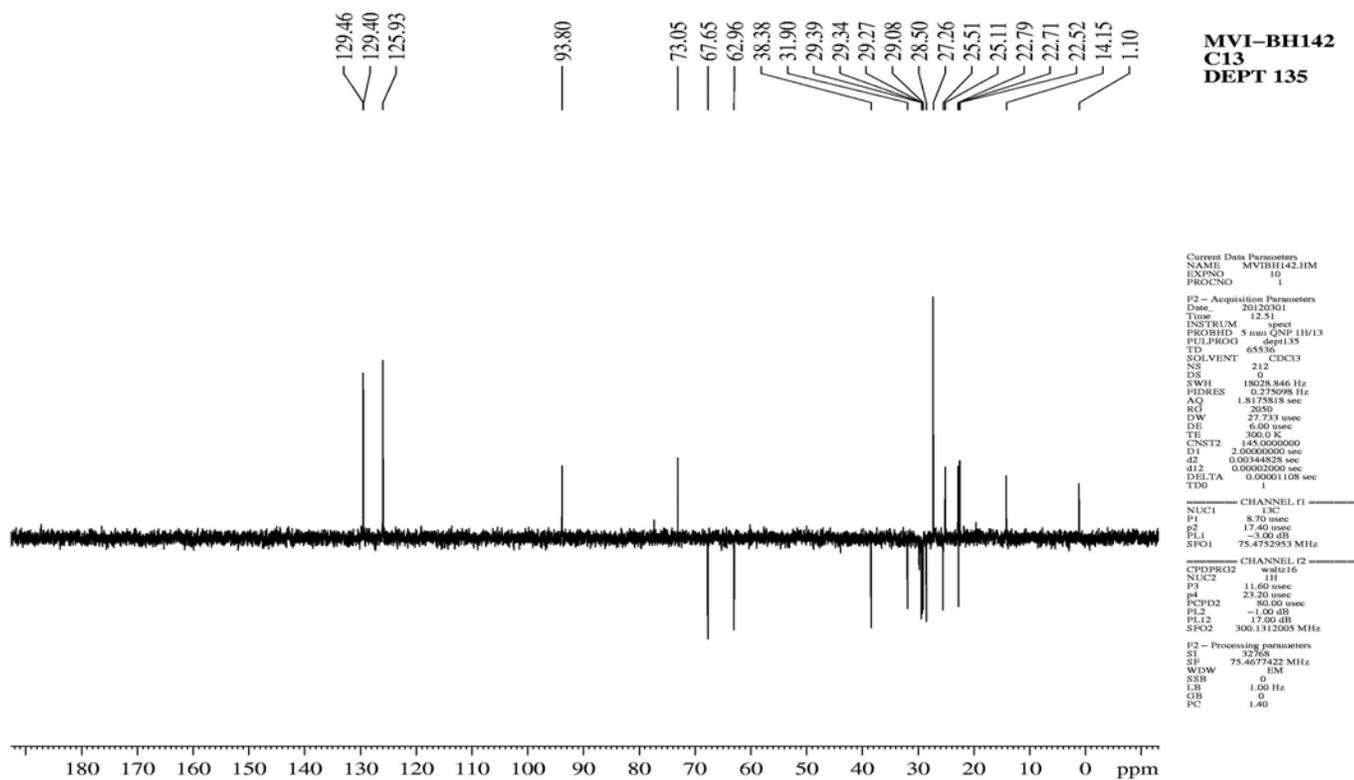
**SKSML-34  
 C13CPD**

Current Data Parameters  
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 EXPNO 173  
 PROCNO 1  
 F2 - Acquisition Parameters  
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 Time 9.42  
 INSTRUM spect  
 PROBHD 5 mm QNP 1H/13  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 1304  
 DS 4  
 SWH 18028.846 Hz  
 FIDRES 0.275098 Hz  
 AQ 1.8175818 sec  
 RG 12.7  
 DW 27.733 usec  
 DE 6.00 usec  
 TE 300.0 K  
 D1 2.000000000 sec  
 d11 0.03000000 sec  
 DELTA 1.89999998 sec  
 TD0 1

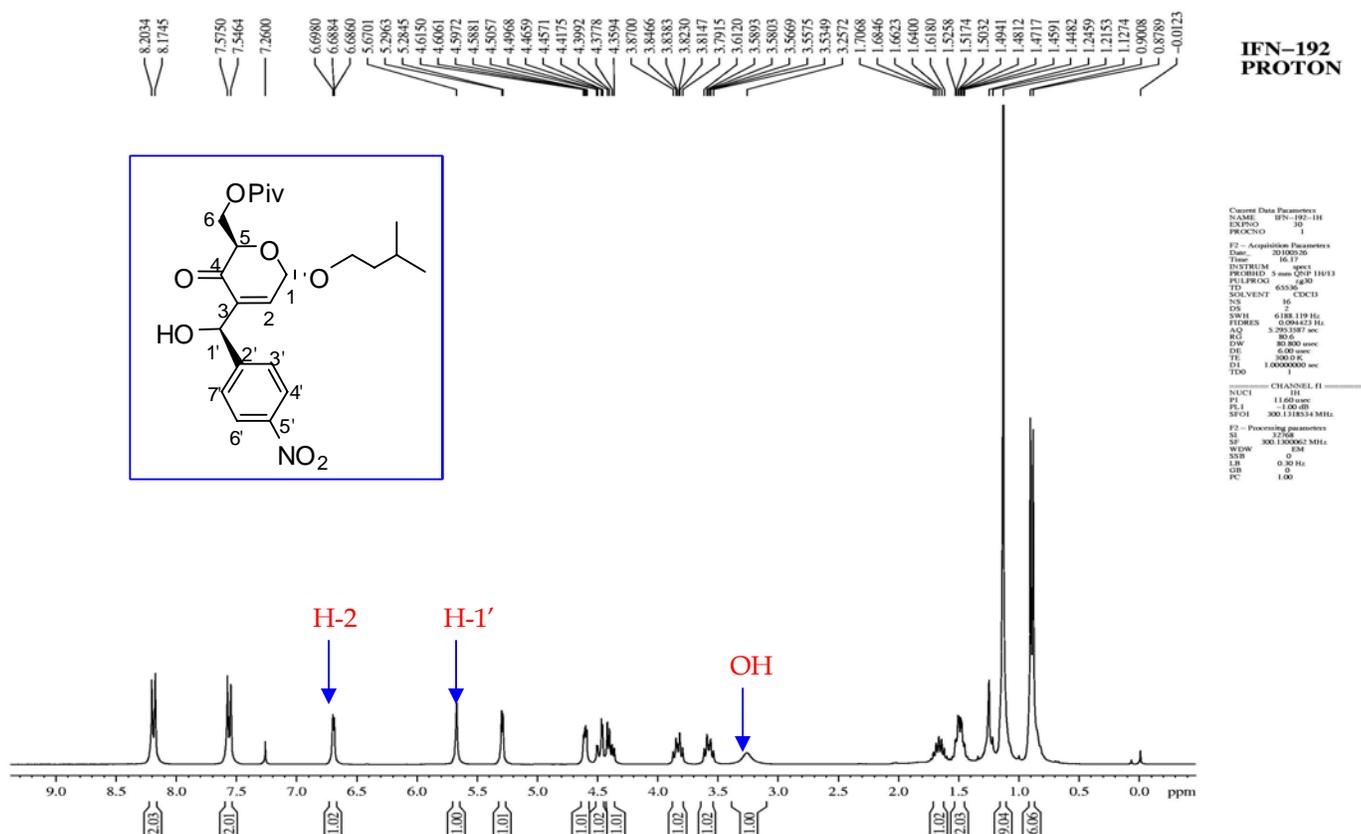
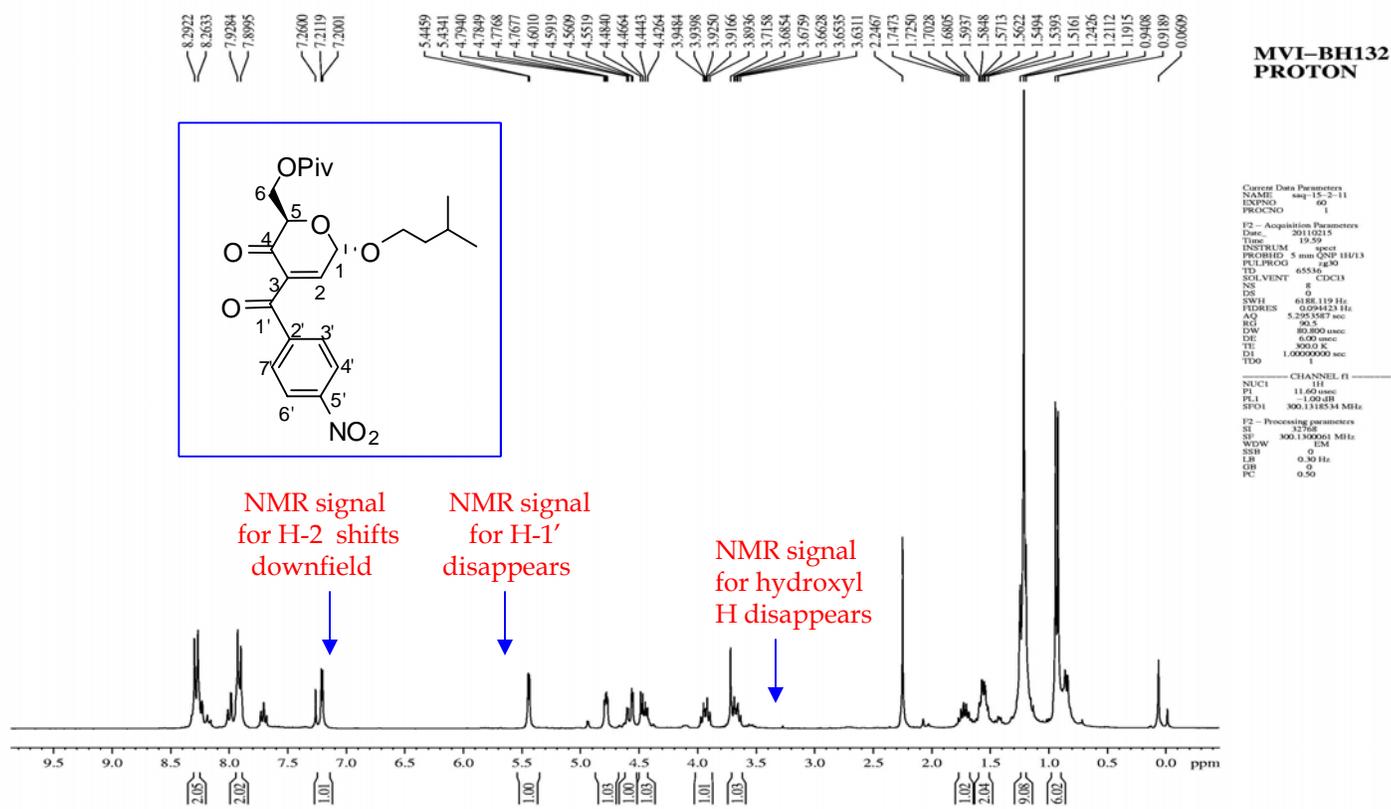
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 P1 8.70 usec  
 PL1 -3.00 dB  
 SFO1 75.4752953 MHz  
 ===== CHANNEL f2 =====  
 CPDPRG2 waltz16  
 NUC2 1H  
 PCPD2 80.00 usec  
 PL2 -1.00 dB  
 PL13 21.00 dB  
 SFO2 300.1312005 MHz  
 F2 - Processing parameters  
 SI 32768  
 SF 75.4677420 MHz  
 WDW EM  
 SSB 0  
 LB 3.00 Hz  
 GB 0  
 PC 1.40



<sup>1</sup>H NMR spectrum of compound **15** and its expansion

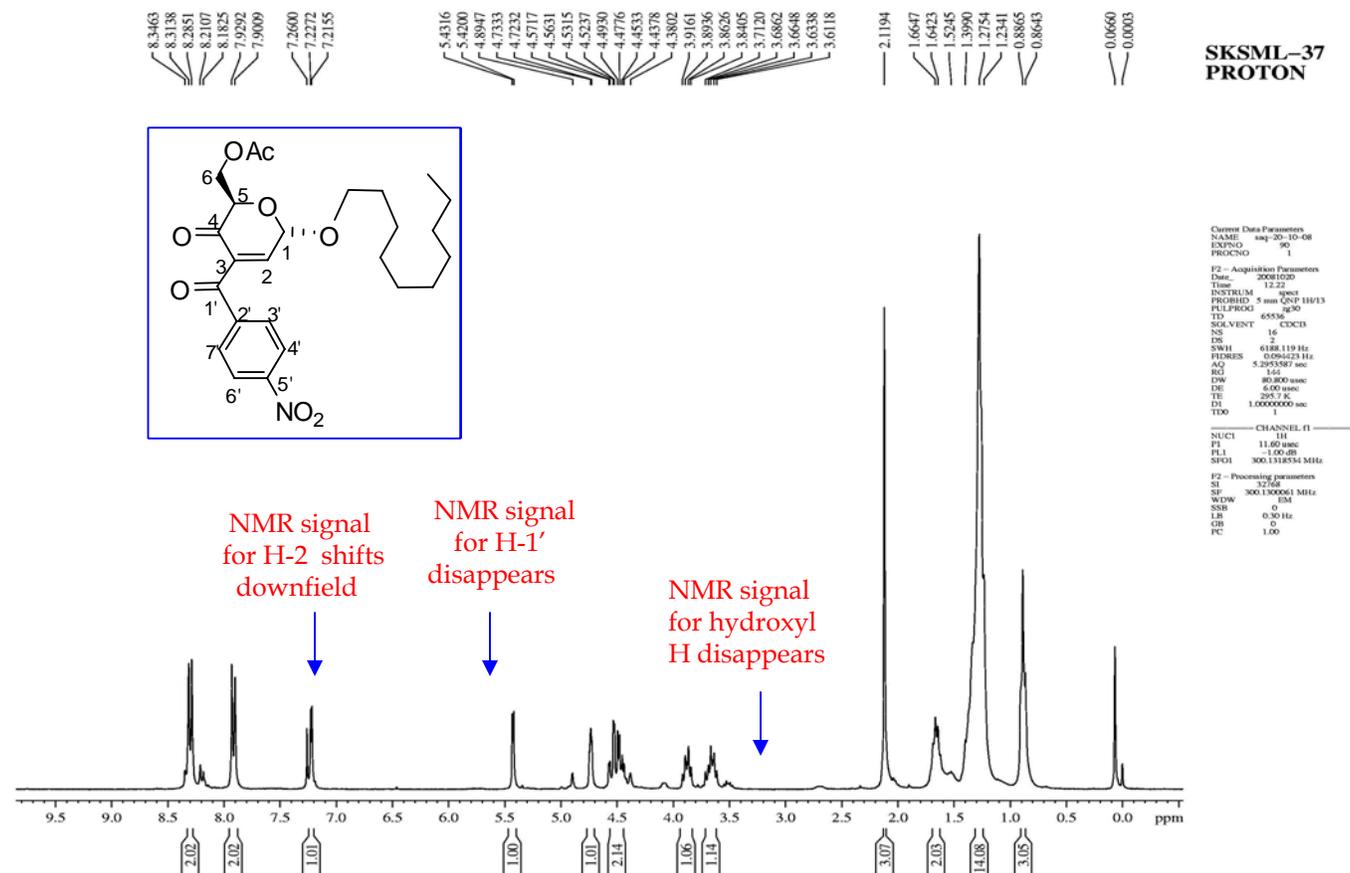


<sup>13</sup>C and DEPT 135 NMR spectra of compound 15



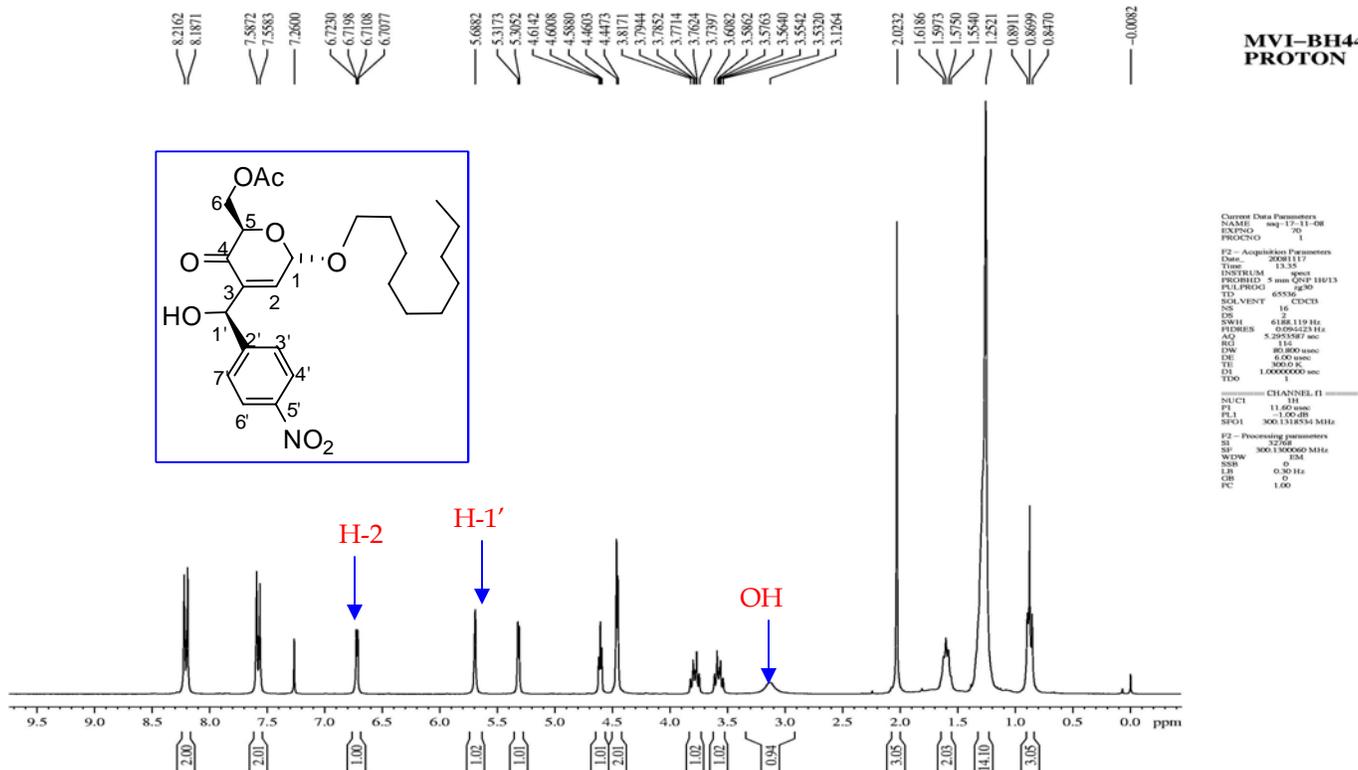
<sup>1</sup>H NMR spectra of MBH adduct **1a** and crude product mixture of its oxidized derivative **2a** (above)

**SKSML-37  
 PROTON**



Current Data Parameters  
 NAME: saq-20-10-08  
 EXPNO: 20  
 PROCNO: 1  
 F2 - Acquisition Parameters  
 Date\_: 20081020  
 Time: 12.22  
 INSTRUM: spect  
 PROBHD: 5 mm QNP 1H/13  
 PULPROG: zgpg30  
 TD: 65536  
 SOLVENT: CDCl3  
 NS: 16  
 DS: 2  
 SWH: 6188.119 Hz  
 FREQS: 0.096213 Hz  
 AQ: 3.295357 sec  
 RG: 154  
 DW: 80.800 usec  
 DE: 6.00 usec  
 TE: 295.3 K  
 D1: 1.0000000 sec  
 TDO: 1  
 CHANNEL f1  
 NUC1: 1H  
 P1: 11.60 usec  
 PL1: -1.00 dB  
 SFO1: 300.1318534 MHz  
 F2 - Processing parameters  
 SI: 32768  
 SF: 300.1300061 MHz  
 WDW: EM  
 SSB: 0  
 LB: 0.30 Hz  
 GB: 0  
 PC: 1.00

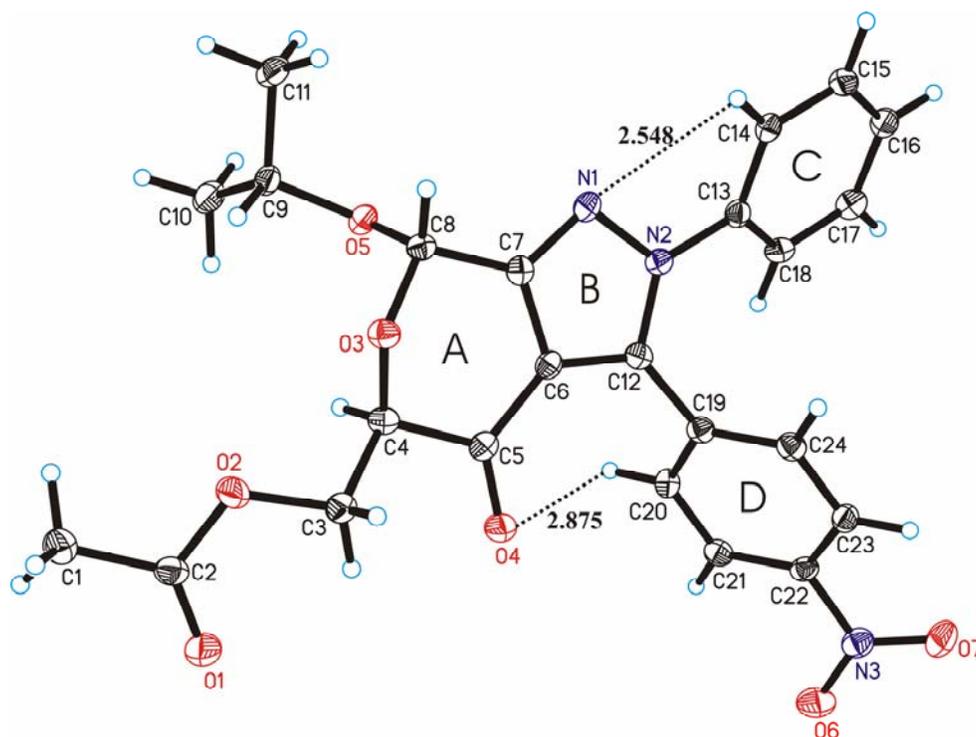
**MVI-BH44  
 PROTON**



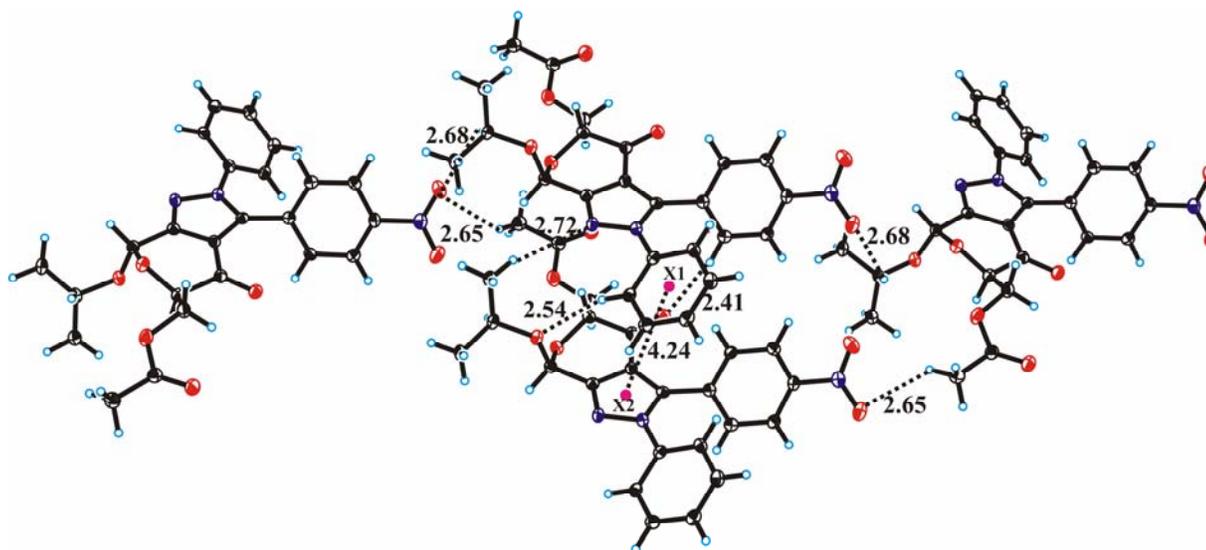
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 F2 - Acquisition Parameters  
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 Time: 13.35  
 INSTRUM: spect  
 PROBHD: 5 mm QNP 1H/13  
 PULPROG: zgpg30  
 TD: 65536  
 SOLVENT: CDCl3  
 NS: 16  
 DS: 2  
 SWH: 6188.119 Hz  
 FREQS: 0.096213 Hz  
 AQ: 3.295357 sec  
 RG: 154  
 DW: 80.800 usec  
 DE: 6.00 usec  
 TE: 295.3 K  
 D1: 1.0000000 sec  
 TDO: 1  
 CHANNEL f1  
 NUC1: 1H  
 P1: 11.60 usec  
 PL1: -1.00 dB  
 SFO1: 300.1318534 MHz  
 F2 - Processing parameters  
 SI: 32768  
 SF: 300.1300060 MHz  
 WDW: EM  
 SSB: 0  
 LB: 0.30 Hz  
 GB: 0  
 PC: 1.00

<sup>1</sup>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  $\pi$ ... $\pi$  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 (Figure 1S) 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 = 3.111 Å, H20...O4 = 2.875 Å,  $\angle$ C20-H20-O4 = 95.38°) and C-H...N interactions (C14-N1 = 2.824 Å, H14...N1 = 2.548 Å,  $\angle$ C14-H14-N1 = 96.88°) in the crystal structure. The geometric parameters suggest the repulsive nature of these interactions<sup>21</sup> 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  $\pi$ ... $\pi$  interaction (centroid separation X1...X2 = 4.24 Å, 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 <sup>i</sup>	1.00	2.68	3.32	120
C14-H14...O5 <sup>ii</sup>	0.95	2.54	3.45	161
C24-H24...O4 <sup>ii</sup>	0.95	2.41	3.33	164
C1 <sup>ii</sup> -H1C <sup>ii</sup> ...O7 <sup>i</sup>	0.98	2.65	3.43	136
C10 <sup>ii</sup> -H10A <sup>ii</sup> ...N1	0.98	2.72	3.63	155
C9 <sup>iii</sup> -H9 <sup>iii</sup> ...O7	1.00	2.68	3.32	122
C1 <sup>iii</sup> -H1C <sup>iii</sup> ...O7 <sup>ii</sup>	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<sub>24</sub>H<sub>23</sub>N<sub>3</sub>O<sub>7</sub>,  $M = 465.45$ , 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<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.411$  g cm<sup>-3</sup>,  $\mu$  (Mo-K $\alpha$ ) = 0.11 mm<sup>-1</sup>,  $F(000) = 976$ , 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  $F_o > 4\sigma(F_o)$  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.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.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](mailto:deposit@ccdc.cam.ac.uk)].

<sup>21</sup> G. R. Desiraju and T. Steiner, in *The Weak Hydrogen Bond in Structural Chemistry and Biology*, Oxford University Press, New York, 1999.

## 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<sub>2</sub> humidified atmosphere at 37 °C. The colorimetric sulforhodamine B assay<sup>19</sup> was used for the determination of cytotoxicity. In brief, 10<sup>4</sup> 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:  $[100 - (\text{Absorbance of compound treated cells} / \text{Absorbance of untreated cells})] \times 100$ . The half maximal inhibitory concentrations (IC<sub>50</sub>) were calculated using Graph Prism software. A compound showing IC<sub>50</sub> value of <20 μM was considered as 'active'.

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