Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Design, Synthesis and Glycosidase Inhibition Studies of Novel Triazole Fused Iminocyclitol-δ-lactams

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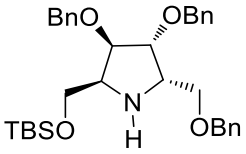
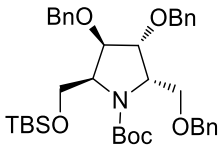


A solution of compound **11** (5.0 g, 7.1 mmol) in dry THF (50 mL) was cooled to –78 °C. A solution of sodium napthalenide {prepared separately by the addition of sodium (1.56 g, 67.6 mmol) to naphthalene (9.2 g, 71.2 mmol) in dry THF} was added slowly and the reaction mixture was stirred at –78 °C for 20 minutes. The reaction mixture was brought to room temperature and quenched with aqueous sodium carbonate solution (50 mL). It was then extracted with ethyl acetate (50 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get **17** (3.3 g, 85%) as a pale yellow viscous oil. R_f: 0.4 (hexane/ethyl acetate, 2:1); Specific rotation: $[\alpha]_D^{34}$–3.6 (*c* 1.3, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3348, 3062, 3031, 2928, 2858, 1600, 1460, 1363, 1251, 1093, 840, 777, 739, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.25 (m, 15H), 4.52–4.43 (m, 6H), 3.99 (brm, 2H), 3.78–3.65 (m, 4H), 3.57–3.45 (m, 2H), 2.06–2.02 (br m, 1H exchangeable with D_2O), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3 (2 x s), 138.2 (s), 128.2 (d), 127.5 (d), 127.4 (d), 127.3 (d), 82.5 (d), 82.2 (d), 73.1 (t), 72.1 (t), 72.0 (t), 69.8 (t), 61.9 (t), 60.2 (d), 57.9 (d), 25.8 (q), 18.1 (s), –5.4 (q); HRMS (ESI): *m/z* calcd for $C_{33}H_{46}NO_4Si$ $[M+H]^+$ 548.3191 found 548.3207.

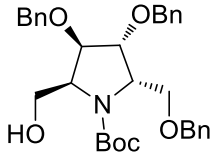
(2*S*,3*R*,4*R*,5*S*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(*tert*-butyldimethyl silanyloxymethyl)-1-*N*-(*tert*-butoxycarbonyl)-pyrrolidine 19.



To a solution of pyrrolidine **17** (2.65 g, 4.83 mmol) in dry ethyl acetate (25 mL), potassium carbonate (2.0 g, 14.47 mmol) and Boc_2O (1.35 mL, 5.87 mmol) were added and the reaction mixture was stirred at 35 °C for 16 h. The reaction mixture was then

diluted with ethyl acetate (50 mL) and washed with water (2 x 50 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get **19** (2.89 g, 92%) as a colourless oil. The data provided is for a mixture of rotamers in the ratio of 56:44. R_f: 0.8 (hexane/ethyl acetate, 5:1); Specific rotation: $[\alpha]_D^{30}$–19.1 (*c* 1.22, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3061, 3030, 2928, 2859, 1695, 1461, 1389, 1325, 1252, 1113, 1058, 839, 775, 737, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.56–7.46 (m, 15H), 4.98–4.55 (m, 8H), 4.29 (dd, *J* = 9.9, 3.0 Hz, 1H), 4.23–4.09 (m, 2H), 4.05–3.77 (m, 3H), 1.68 (s, 5H), 1.63 (s, 4H), 1.05 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.8 (s), 153.7 (s), 139.0 (s), 138.8 (s), 138.7 (s), 138.6 (s), 128.2 (d), 128.17 (d), 128.11 (d), 127.5 (d), 127.45 (d), 127.40 (d), 127.3 (d), 127.28 (d), 127.20 (d), 80.9 (d), 80.48 (d), 80.41 (d), 79.4 (s), 73.3 (t), 73.2 (t), 72.9 (t), 72.8 (t), 72.6 (t), 67.6 (t), 66.1 (t), 59.0 (t), 57.6 (t), 57.5 (d), 57.2 (d), 56.5 (d), 56.4 (d), 28.5 (q), 28.4 (q), 25.8 (q), 18.0 (s), –5.5 (q), –5.6 (q); HRMS (ESI): *m/z* calcd for $C_{38}H_{53}NNaO_6Si$ $[M+Na]^+$ 670.3534 found 670.3532.

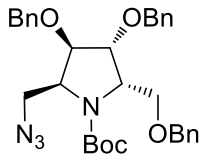
(2*S*,3*R*,4*R*,5*S*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(hydroxymethyl)-1-*N*-(*tert*-butoxycarbonyl)-pyrrolidine 9.



To a solution of compound **19** (2.6 g, 4.01 mmol) in dry methanol (25 mL), camphorsulfonic acid (260 mg, 10% w/w) was added and the reaction mixture was stirred at 31 °C for 16 h. Solvent was then concentrated under reduced pressure and the residue was dissolved in ethyl acetate (50 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 25 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get **9** (1.85 g, 86%) as a colourless oil. The data provided is for a mixture of rotamers in the ratio of 63:36. R_f: 0.4 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{30}$–19.3 (*c* 1.28, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3548, 3474, 3416, 3029, 2969, 2925, 2871, 1688, 1455, 1389, 1109, 1032, 738, 697, 610 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ

7.31–7.26 (m, 15H), 4.81–4.59 (m, 4H), 4.53–4.47 (m, 3H), 4.31–4.15 (m, 1H), 4.06–3.89 (m, 3H), 3.81–3.67 (m, 2H), 3.61–3.55 (m, 1H), 3.40 (br s, 0.6H, exchangeable with D_2O), 2.54 (br s, 0.3H, exchangeable with D_2O), 1.46 (s, 4H), 1.41 (s, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.0 (s), 153.7 (s), 138.6 (s), 138.2 (s), 138.0 (s), 137.9 (s), 137.7 (s), 128.4 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.7 (d), 127.6 (d), 127.4 (d), 127.37 (d), 127.33 (d), 127.1 (d), 81.6 (d), 81.5 (d), 81.4 (d), 80.8 (d), 80.3 (s), 80.1 (s), 73.4 (t), 73.39 (t), 73.32 (t), 73.1 (t), 72.9 (t), 66.5 (t), 65.2 (t), 62.3 (t), 61.8 (t), 58.6 (d), 57.4 (d), 56.3 (d), 55.9 (d), 28.3 (q); HRMS (ESI): *m/z* calcd for $C_{32}H_{39}NNaO_6$ $[M+Na]^+$ 556.2670 found 556.2672.

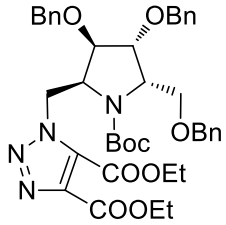
(2*S*,3*R*,4*R*,5*S*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(azidomethyl)-1-*N*-(*tert*-butoxycarbonyl)-pyrrolidine 7.



Compound **9** (1.0 g, 1.87 mmol) was dissolved in dry THF (10 mL), and the solution was cooled to 0 °C. Triphenylphosphine (0.74 g, 2.82 mmol) and trimethylsilyl azide (0.38 mL, 2.86 mmol) were added followed by dropwise addition of diethyl azodicarboxylate (0.74 mL, 4.68 mmol), after which the reaction mixture was warmed to 21 °C. When TLC indicated the completion of the reaction (24 h), the reaction was stopped and solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (10:1) as an eluent to get **7** (754 mg, 72%) as a pale yellow oil. The data provided is for a mixture of rotamers in the ratio of 63:36. R_f: 0.8 (hexane/ethyl acetate, 9:1); Specific rotation: $[\alpha]_D^{30}$–17.0 (*c* 0.60, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3061, 3030, 2973, 2928, 2870, 2102, 1695, 1448, 1386, 1257, 1151, 1110, 1024, 742, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.31–7.24 (m, 15H), 4.75–4.58 (m, 4H), 4.54–4.30 (m, 4H), 4.04–3.89 (m, 3H), 3.75–3.66 (m, 1H), 3.57 (d, *J* = 9.6 Hz, 1H), 3.38 (d, *J* = 12.0 Hz, 0.4H), 3.26 (d, *J* = 11.4 Hz, 0.6H), 1.46 (s, 3H), 1.41 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.7 (s), 153.4 (s), 138.7 (s), 138.3 (s), 138.2 (s), 138.1 (s), 138.0 (s), 128.3 (d), 128.2 (d), 128.1 (d), 127.6 (d), 127.5 (d), 127.4 (d), 127.3 (d), 127.2 (d), 81.3 (d), 80.7 (d), 80.4 (d), 80.3 (s), 80.2 (s), 80.0 (d), 73.35 (t), 73.32 (t), 73.2 (t), 73.19 (t), 73.11 (t), 66.6 (t), 65.3 (t), 56.3 (d), 56.1

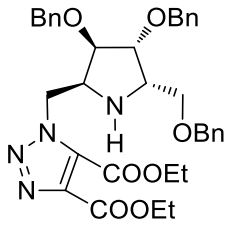
(d), 55.9 (d), 49.7 (t), 48.1 (t), 28.3 (q); HRMS (ESI): *m/z* calcd for $C_{32}H_{38}N_4NaO_5$ $[M+Na]^+$ 581.2734 found 581.2720.

Diethyl-1-(((2*S*,3*R*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)-1-(*tert*-butoxy carbonyl)pyrrolidin-2-yl) methyl)1*H*-1',2',3'-triazole-4',5'-dicarboxylate 21.



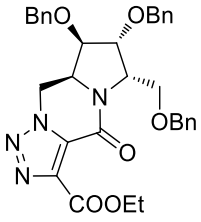
Compound **7** (1.1 g, 1.97 mmol) was dissolved in dry toluene (12 mL) and diethyl acetylene dicarboxylate (1.6 mL, 9.97 mmol) was added. The reaction mixture was heated at 110 °C for 4 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (4:1) as an eluent to get **21** (1.2 g, 83%) as a pale yellow oil. The data provided is for a mixture of rotamers in the ratio of 60:40. R_f: 0.5 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{30}$+13.9 (*c* 0.48, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3029, 2976, 2931, 2874, 1729, 1698, 1552, 1457, 1372, 1271, 1213, 1161, 1100, 1064, 1020, 771, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.29–7.20 (m, 15H), 5.10 (dd, *J* = 14.4, 3.9 Hz, 0.6H), 4.91 (dd, *J* = 13.8, 4.8 Hz, 0.4H), 4.75 (dd, *J* = 14.1, 4.5 Hz, 1H), 4.69–4.12 (m, 12H), 4.00–3.95 (m, 0.4H), 3.88–3.84 (m, 0.4H), 3.76–3.66 (m, 2H), 3.53–3.46 (m, 1H), 3.27 (t, *J* = 8.7 Hz, 0.6H), 1.42–1.28 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.2 (s), 158.7 (s), 153.9 (s), 153.3 (s), 139.6 (s), 139.4 (s), 138.5 (s), 138.2 (s), 137.7 (s), 137.4 (s), 131.5 (s), 131.1 (s), 128.38 (d), 128.31 (d), 128.2 (d), 128.1 (d), 127.8 (d), 127.7 (d), 127.59 (d), 127.54 (d), 127.4 (d), 127.3 (d), 127.1 (d), 80.7 (s), 80.3 (s), 80.2 (d), 79.9 (d), 79.8 (d), 79.5 (d), 73.2 (t), 73.1 (t), 73.0 (t), 72.9 (t), 72.8 (t), 66.2 (t), 64.4 (t), 62.4 (t), 62.2 (t), 61.58 (t), 61.51 (t), 56.1 (d), 55.4 (d), 55.0 (d), 49.2 (t), 47.7 (t), 28.3 (q), 28.1 (q), 14.1 (q), 13.7 (q); HRMS (ESI): *m/z* calcd for $C_{40}H_{48}N_4NaO_9$ $[M+Na]^+$ 751.3314 found 751.3312.

Diethyl-1-(((2*S*,3*R*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)pyrrolidin-2-yl) methyl)-1*H*-1',2',3'-triazole-4',5'-dicarboxylate 5.



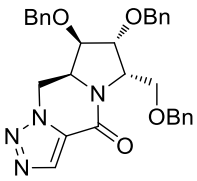
To a solution of compound **21** (1.2 g, 1.64 mmol) in dry dichloromethane (15 mL), trifluoroacetic acid (1.26 mL, 16.45 mmol) was added at 0 °C and the reaction mixture was stirred at 26 °C for 4 h. Solvent was then concentrated under reduced pressure and the residue was dissolved in ethyl acetate (25 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 20 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get **5** (815 mg, 79%) as a light brown oil. R_f: 0.4 (hexane/ethyl acetate, 3:1); Specific rotation: $[\alpha]_D^{30}$+5.9 (*c* 0.9, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3334, 3030, 2982, 2922, 2866, 1730, 1551, 1457, 1369, 1308, 1268, 1208, 1095, 1021, 740, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.24 (m, 15H), 4.67–4.65 (m, 2H), 4.59–4.26 (m, 10H), 4.06–4.00 (m, 2H), 3.85–3.83 (m, 1H), 3.55–3.46 (m, 3H), 1.84 (br s, 1H, exchangeable with D_2O), 1.38 (dt, *J* = 7.2, 3.0 Hz, 3H), 1.29 (dt, *J* = 7.2, 3.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.2 (s), 158.8 (s), 139.6 (s), 138.1 (s), 137.9 (s), 137.6 (s), 131.5 (s), 128.5 (d), 128.46 (d), 128.40 (d), 127.9 (d), 127.8 (d), 127.77 (d), 127.73 (d), 127.6 (d), 82.37 (d), 82.35 (d), 73.3 (t), 72.4 (t), 72.2 (t), 68.7 (t), 62.6 (t), 61.6 (t), 58.7 (d), 58.5 (d), 50.8 (t), 14.2 (q), 13.8 (q); HRMS (ESI): *m/z* calcd for $C_{35}H_{41}N_4O_7$ $[M+H]^+$ 629.2970 found 629.2967.

(6*S*,7*R*,8*R*,8a*S*)-Ethyl-7,8-bis(benzyloxy)-6-((benzyloxy)methyl)-4-oxo-4,6,7,8,8a,9-hexahydropyrrolo[1,2*a*] [1',2',3']triazolo[1',5'-*d*]pyrazine-3-carboxylate 23.



Compound **5** (400 mg, 0.636 mmol) was dissolved in dry toluene (4 mL) and camphorsulfonic acid monohydrate (32 mg, 0.127 mmol) was added. The reaction mixture was heated at 110 °C for 9 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get **23** (311 mg, 84%) as a light brown oil. R_f: 0.6 (hexane/ethyl acetate, 1:1); Specific rotation: $[\alpha]_D^{28}$–60.9 (*c* 0.34, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3060, 3029, 2927, 2867, 1734, 1676, 1448, 1411, 1361, 1206, 1096, 1021, 743, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.36–7.21 (m, 15H),4.68 (d, *J* = 11.7 Hz, 2H), 4.61–4.58 (m, 2H), 4.51–4.34 (m, 9H), 4.25–4.21 (m, 1H), 4.04 (dd, *J* = 9.3, 1.8 Hz, 1H), 3.87 (dd, *J* = 9.3, 5.4 Hz, 1H), 1.42 (t,*J* = 7.2 Hz, 3H);^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6 (s), 152.8 (s), 139.1 (s), 137.8 (s), 137.1 (s), 136.9 (s), 129.9 (s), 128.6 (d), 128.5 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.8 (d), 127.7 (d), 127.6 (d), 127.5 (d), 81.1 (d), 80.1 (d), 73.5 (t), 73.3 (t), 72.9 (t), 66.2 (t), 61.8 (t), 57.1 (d), 56.9 (d), 46.7 (t), 14.1 (q); HRMS (ESI): *m/z* calcd for $C_{33}H_{34}N_4NaO_6$ $[M+Na]^+$ 605.2370 found 605.2366.

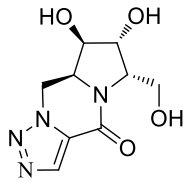
(6*S*,7*R*,8*R*,8a*S*)-7,8-Bis(benzyloxy)-6-((benzyloxy)methyl)-7,8,8a,9-tetrahydro pyrrolo[1,2-*a*][1',2',3']triazolo[1',5'*d*]pyrazin-4(6*H*)-one 29.



Compound **23** (500 mg, 0.86 mmol) was dissolved in dry methanol (5 mL) and potassium carbonate (356 mg, 2.57 mmol) was added. The reaction mixture was stirred at 25 °C for 6 h, after which the solvent was evaporated under reduced pressure. To the resulting milky white residue, a mixture of ethyl acetate and water (20 mL, 1:1) was added. Conc. HCl was then added to the mixture until a clear solution was obtained. The organic layer was then separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue contains **27** was dissolved in glacial acetic acid (5 mL) and heated at 120 °C for 24 h. The reaction mixture was then quenched with aqueous sodium bicarbonate solution (20 mL) and extracted with ethyl acetate (2 x 10 mL). The organic layer was then dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue

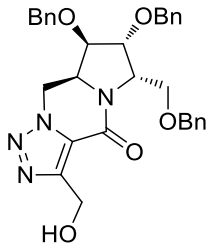
was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get **29** (250 mg, 57% over two steps) as a pale yellow oil. R_f: 0.6 (hexane/ethyl acetate, 1:1); Specific rotation: $[\alpha]_D^{28}$–29.8 (*c* 1.75, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3060, 3029, 2926, 2865, 1664, 1551, 1450, 1413, 1360, 1204, 1095, 1025, 739, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.39–7.24 (m, 15H), 4.67 (d, *J* = 11.7 Hz, 2H), 4.61–4.45 (m, 7H), 4.42–4.29 (m, 2H), 4.24 (dd, *J* = 6.6, 5.1 Hz, 1H), 4.02 (dd, *J* = 9.3, 2.4 Hz, 1H), 3.85 (dd, *J* = 9.3, 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.7 (s), 137.8 (s), 137.2 (s), 137.0 (s), 134.1 (d), 129.6 (s), 128.6 (d), 128.5 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.86 (d), 127.80 (d), 127.7 (d), 127.6 (d), 81.5 (d), 80.4 (d), 73.6 (t), 73.3 (t), 72.9 (t), 66.3 (t), 57.5 (d), 56.7 (d), 46.1 (t); HRMS (ESI): *m/z* calcd for $C_{30}H_{30}N_4NaO_4$ $[M+Na]^+$ 533.2159 found 533.2152.

(6*S*,7*R*,8*R*,8a*S*)-7,8-Dihydroxy-6-(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazin-4(6*H*)-one 1.



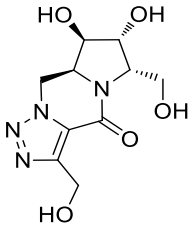
Compound **29** (250 mg, 0.49 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (250 mg, 100% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 22 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (10:1) as an eluent to get **1** as colourless oil (102 mg, 87%). R_f: 0.3 (acetonitrile/NH_4OH, 9:1); Specific rotation: $[\alpha]_D^{29}$–46.1 (*c* 0.41, CH_3OH); IR (KBr): $\bar{\upsilon}$ =3338, 3198, 1661, 1403, 1205, 1112, 1075, 756, 570 cm^{-1}; ^1H NMR (400 MHz, D_2O): δ 8.20 (s, 1H), 4.99 (dd, *J* = 13.2, 5.2 Hz, 1H), 4.72–4.66 (m, 1H), 4.53 (d, *J* = 13.2 Hz, 1H), 4.49–4.45 (m, 2H), 4.32 (q, *J* = 4.8 Hz, 1H), 4.07 (dd, *J* = 12.0, 4.4 Hz, 1H), 4.03 (dd, *J* = 12.0, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, D_2O): δ 156.7 (s), 133.7 (d), 129.8 (s), 75.3 (d), 73.5 (d), 60.9 (d), 58.9 (d), 58.2 (t), 45.0 (t); HRMS (ESI): *m/z* calcd for $C_9H_{12}N_4NaO_4$ $[M+Na]^+$ 263.0751 found 263.0751.

(6*S*,7*R*,8*R*,8a*S*)-7,8-Bis(benzyloxy)-6-((benzyloxy)methyl)-3-(hydroxymethyl)-7,8, 8a,9-tetrahydropyrrolo[1,2*a*][1,2,3]triazolo[1,5-*d*]pyrazin-4(6*H*)-one 25.



Compound **23** (430 mg, 0.74 mmol) was dissolved in dry THF (5 mL) and lithium borohydride (16 mg, 0.74 mmol) was added. The reaction mixture was stirred at 21 °C for 2 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (1:1) as an eluent to get **25** (281 mg, 70%) as a pale yellow oil. R_f: 0.4 (hexane/ethyl acetate, 1:1); Specific rotation: $[\alpha]_D^{29}$–26.4 (*c* 0.47, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3471, 2922, 2857, 1647, 1453, 1365, 1267, 1200, 1108, 1029, 751, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.37–7.22 (m, 15H), 4.92 (d, *J* = 6.3 Hz, 2H), 4.67 (d, *J* = 11.7 Hz, 2H), 4.62–4.58 (m, 2H, 1H exchangeable with D_2O), 4.53–4.41 (m, 6H), 4.39–4.33 (m, 2H), 4.24 (t, *J* = 6.0 Hz, 1H), 4.04 (dd, *J* = 9.6, 2.4 Hz, 1H), 3.85 (dd, *J* = 9.3, 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.2 (s), 150.2 (s), 137.7 (s), 137.1 (s), 136.9 (s), 128.69 (d), 128.64 (d), 128.4 (d), 128.3 (d), 128.2 (d), 127.9 (d), 127.8 (d), 127.7 (d), 127.6 (d), 126.3 (s), 81.4 (d), 80.2 (d), 73.7 (t), 73.4 (t), 72.9 (t), 66.1 (t), 57.8 (d), 57.2 (t), 57.1 (d), 46.1 (t); HRMS (ESI): *m/z* calcd for $C_{31}H_{32}KN_4O_5$ $[M+K]^+$ 579.2004 found 579.2011.

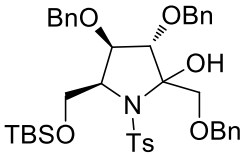
(6*S*,7*R*,8*R*,8a*S*)-7,8-Dihydroxy-3,6-bis(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo [1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazin-4(6*H*)-one 2.



Compound **25** (340 mg, 0.63 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (340 mg, 100% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 24 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure

and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (6:1) as an eluent to get **2** as colourless oil (120 mg, 70%). R_f: 0.3 (acetonitrile/NH_4OH, 4:1); Specific rotation: $[\alpha]_D^{28}$–14.9 (*c* 0.78, CH_3OH); IR (KBr): $\bar{\upsilon}$ = 3343, 2942, 1646, 1588, 1448, 1373, 1332, 1199, 1112, 1074, 1026, 751, 623 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 5.70 (d, *J* = 4.5 Hz, 1H exchangeable with D_2O), 5.54 (d, *J* = 4.2 Hz, 1H exchangeable with D_2O), 5.22 (t, *J* = 4.2 Hz, 1H exchangeable with D_2O), 4.86–4.82 (m, 2H, 1H exchangeable with D_2O), 4.71 (dd, *J* = 12.6, 6.0 Hz, 1H), 4.62 (dd, *J* = 12.6, 5.4 Hz, 1H), 4.47–4.30 (m, 2H), 4.17–4.10 (m, 2H), 3.99–3.95 (m, 2H), 3.77–3.70 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 155.8 (s), 147.6 (s), 125.7 (s), 74.9 (d), 73.4 (d), 61.9 (d), 59.2 (d), 58.0 (t), 53.8 (t), 44.9 (t); HRMS (ESI): *m/z* calcd for $C_{10}H_{14}N_4NaO_5$ $[M+Na]^+$ 293.0856 found 293.0859.

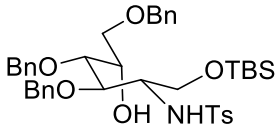
Compound 15:



To a solution of compound **14** (4.2 g, 5.83 mmol) in dry dichloromethane (45 mL), Dess-Martin periodinane (4.95 g, 11.67 mmol) was added at 0 °C and the reaction mixture was stirred at room temperature for 5 h. Then the reaction mixture was diluted with dichloromethane (50 mL), washed with aqueous sodium thiosulfate solution (50 mL x 2) followed by water (50 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get **15** (3.57 g, 85%) as a colourless oil in a diastereomeric ratio of 3:1. Data for the mixture of diastereomers: R_f: 0.8 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{31}$–18.59 (*c* 0.57, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3476, 3034, 2937, 2867, 1602, 1457, 1346, 1253, 1147, 1101, 837, 742, 697, 670, 564 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (mixture of diastereomers) δ 7.84 (d, *J* = 6.6 Hz, 2H), 7.77 (d, J = 6.6 Hz, 0.5H), 7.68 (d, J = 7.8 Hz, 0.2H), 7.32–7.20 (m, 23H), 7.14 (m, 0.5H), 7.10–7.09 (m, 3H), 4.83–4.76 (m, 0.6H), 4.70–4.51 (m, 8H), 4.42–4.30 (m, 2H), 4.26–4.17 (m, 2H), 4.09–3.95 (m, 3H, 1H exchangeable with D_2O), 3.89–3.67 (m, 5H), 3.56–3.53 (m, 1H), 3.42–3.36 (m, 0.15H), 3.31–3.26 (m, 0.12H), 2.39 (s, 3H), 2.31

(s, 0.7H), 0.89 (s, 9H), 0.80 (s, 2H), 0.79 (s, 1H), 0.25 (s, 6H), (–0.05)–(–0.077) (m, 2H), (–0.086)–(–0.11) (m, 0.75H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereomers) δ 143.0 (s), 138.3 (s), 138.0 (s), 137.7 (s), 137.5 (s), 137.4 (s), 129.6 (d), 129.2 (d), 129.0 (d), 128.5 (d), 128.4 (d), 128.29 (d), 128.26 (d), 128.24 (d), 128.21 (d), 128.15 (d), 128.07 (d), 127.9 (d), 127.8 (d), 127.7 (d), 127.6 (d), 127.5 (d), 127.4 (d), 127.3 (d), 127.2 (d), 127.1 (d), 92.6 (s), 88.9 (s), 83.8 (d), 80.2 (d), 78.2 (d), 75.1 (t), 73.7 (t), 73.3 (t), 72.8 (t), 72.7 (t), 62.3 (t), 59.8 (d), 59.3 (d), 25.9 (q), 25.8 (q), 25.7 (q), 21.4 (q), 18.3 (s), –5.5 (q); HRMS (ESI): *m/z* calcd for $C_{40}H_{51}NNaO_7SSi$ $[M+Na]^+$ 740.3048 found 740.3041.

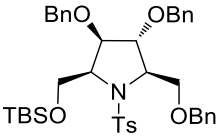
1-*O*-(*tert*-Butyldimethylsilyl)-3,4,6-tri-*O*-benzyl-2-deoxy-2-(*p*-toluenesulfonamido)-L-iditol 16:



To a solution of compound **15** (3.4 g, 4.73 mmol) in dry MeOH (35 mL), $CeCl_3.7H_2O$ (2.12 g, 5.68 mmol) was added at –78 °C and stirred for 1 h. Sodium borohydride (720 mg, 18.97 mmol) was added in portions and the reaction mixture was stirred at –78 °C for 4 h. It was brought to room temperature and the solvent was concentrated under reduced pressure. The resulting residue was dissolved in ethyl acetate (20 mL) and washed with water (20 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get **16** (1.89 g, 56%) as an off-white solid, alongwith compound **14** (1.02 g, 30%) as an off white solid. Data for compound **16**: M.P: 72–75 °C; R_f: 0.5 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{29}$+4.58 (*c* 1.92, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3546, 3475, 3416, 3150, 3030, 2931, 2861, 1620, 1462, 1330, 1156, 1100, 1052, 837, 772, 745, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.5 Hz, 2H), 7.38–7.24 (m, 17H), 5.02 (d, *J* = 7.2 Hz, 1H, exchangeable with D_2O), 4.87 (d, *J* = 11.1 Hz, 1H), 4.79 (d, *J* = 11.1 Hz, 1H), 4.60 (d, *J* = 11.1 Hz, 1H), 4.52 (m, 2H), 4.47 (d, *J* = 11.1 Hz, 1H), 4.24 (d, *J* = 8.7 Hz, 1H), 3.82 (br m, 1H), 3.58 (d, *J* = 9.0 Hz, 1H), 3.51–3.43 (m, 4H), 3.23 (dd, *J* = 9.3 Hz, 4.2 Hz, 1H), 2.41 (s, 3H), 2.33 (br s, 1H, exchangeable with D_2O), 0.87 (s, 9H), 0.00 (s, 3H), –0.013 (s, 3H); ^{13}C NMR (75 MHz,

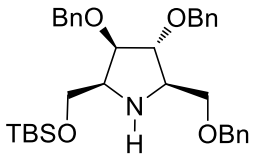
$CDCl_3$) δ 143.3 (s), 138.3 (s), 138.2 (s), 137.98 (s), 137.96 (s), 129.6 (d), 128.38 (d), 128.30 (d), 128.2 (d), 127.84 (d), 127.80 (d), 127.7 (d), 127.6 (d), 126.9 (d), 79.0 (d), 76.9 (d), 75.5 (t), 75.0 (t), 73.3 (t), 71.8 (t), 69.3 (d), 61.9 (t), 54.9 (d), 25.7 (q), 21.4 (q), 18.0 (s), –5.5 (q), –5.6 (q); HRMS (ESI): *m/z* calcd for $C_{40}H_{53}NNaO_7SSi$ $[M+Na]^+$ 742.3204 found 742.3222.

(2*S*,3*R*,4*R*,5*R*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(*tert*-butyldimethyl silanyloxymethyl)-1-*N*-(*p*-tolylsulfonyl)pyrrolidine 12.



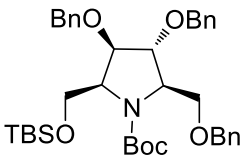
Compound **16** (3.0 g, 4.16 mmol) was dissolved in dry THF (30 mL), and the solution was cooled to 0 °C. Triphenylphosphine (2.73 g, 10.4 mmol) was added followed by dropwise addition of diethyl azodicarboxylate (1.65 mL, 10.4 mmol), after which the reaction mixture was warmed to room temperature. When TLC indicated the completion of the reaction (3 h), the reaction was stopped and solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (10:1) as an eluent to get **12** (2.45 g, 84%) as a pale yellow oil. R_f: 0.8 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{29}$– 14.9 (*c* 0.53, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3031, 2932, 2859, 1620, 1458, 1349, 1253, 1161, 1089, 838, 776, 740, 698, 666 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.21–7.11 (m, 15H), 6.88 (d, *J* = 3.6 Hz, 2H), 4.48–4.32 (m, 4H), 4.09–4.05 (m, 3H), 3.92–3.83 (m, 2H), 3.75–3.67 (m, 4H), 3.55–3.51 (m, 1H), 2.24 (s, 3H), 0.82 (s, 9H), 0.0 (s, 3H), –0.017 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5 (s), 138.3 (s), 137.8 (s), 137.6 (s), 133.7 (s), 129.4 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.9 (d), 127.67 (d), 127.61 (d), 127.5 (d), 127.4 (d), 127.3 (d), 81.7 (d), 80.8 (d), 73.2 (t), 72.8 (t), 71.2 (t), 70.7 (t), 64.6 (d), 63.7 (d), 61.4 (t), 25.9 (q), 21.4 (q), 18.2 (s), –5.3 (q), –5.4 (q); HRMS (ESI): *m/z* calcd for $C_{40}H_{51}NNaO_6SSi$ $[M+Na]^+$ 724.3099 found 724.3073.

(2*S*,3*R*,4*R*,5*R*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(*tert*-butyldimethylsilanyl oxymethyl)pyrrolidine 18:



A solution of compound **12** (2.45 g, 3.49 mmol) in dry THF (25 mL) was cooled to –78 °C. A solution of sodium napthalenide {prepared separately by the addition of sodium (765 mg, 33.26 mmol) to naphthalene (4.5 g, 35.12 mmol) in dry THF} was added slowly and the reaction mixture was stirred at –78 °C for 20 minutes. The reaction mixture was brought to room temperature, quenched with aqueous sodium carbonate solution (25 mL) and extracted with ethyl acetate (25 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get **18** (1.55 g, 81%) as a pale yellow viscous oil. R_f: 0.4 (hexane/ethyl acetate, 2:1); Specific rotation: $[\alpha]_D^{29}$+6.9 (*c* 3.8, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3436, 3030, 2929, 2859, 1640, 1457, 1363, 1253, 1097, 839, 776, 739, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.19 (m, 15H), 4.51–4.41 (m, 6H), 3.89–3.88 (m, 1H), 3.82–3.74 (m, 2H), 3.68 (dd, *J* = 9.6 Hz, 6.0 Hz, 1H),3.54 (dd, *J* = 9.0 Hz, 5.7 Hz, 1H), 3.46 (dd, *J* = 9.0 Hz, 6.0 Hz, 1H), 3.34–3.23 (m, 2H), 2.08 (br s, 1H exchangeable with D_2O), 0.84 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4 (s), 138.28 (s), 138.21 (s), 128.3 (d), 128.28 (d), 128.25 (d), 127.6 (d), 127.5 (d), 127.4 (d), 85.0 (d), 82.9 (d), 73.1 (t), 71.8 (t), 71.59 (t), 71.56 (t), 63.2 (d), 62.8 (d), 61.9 (t), 25.9 (q), 18.2 (s), –5.3 (q), –5.4 (q); HRMS (ESI): *m/z* calcd for $C_{33}H_{46}NO_4Si$ $[M+H]^+$ 548.3191 found 548.3192.

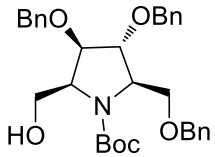
(2*S*,3*R*,4*R*,5*R*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(*tert*-butyldimethylsilanyl oxymethyl)-1-*N*-(*tert*-butoxycarbonyl)-pyrrolidine 20.



To a solution of pyrrolidine **18** (4.2 g, 7.66 mmol) in dry ethyl acetate (50 mL), sodium carbonate (2.5 g, 23.59 mmol) and Boc_2O (2.0 mL, 8.70 mmol) were added and

the reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was then diluted with ethyl acetate (20 mL) and washed with water (2 x 20 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get **20** (4.1 g, 83%) as a colourless oil. The data provided is for a mixture of rotamers: R_f: 0.8 (hexane/ ethyl acetate, 5:1); Specific rotation: $[\alpha]_D^{23}$–9.7 (*c* 0.3, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3029, 2931, 2865, 1696, 1605, 1461, 1379, 1252, 1172, 1097, 842, 742, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.27–7.21 (m, 15H), 4.63–4.47 (m, 6H), 4.18–4.06 (m, 3H), 3.85–3.60 (m, 5H), 1.41 (*br* s, 9H), 0.84 (s, 9H), 0.00 (s, 3H), –0.014 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.8 (s), 138.4 (s), 138.3 (s), 138.2 (s), 128.2 (d), 127.7 (d), 127.5 (d), 127.49 (d), 127.42 (d), 83.7 (d), 82.8 (d), 82.2 (d), 79.8 (s), 73.0 (t), 72.7 (t), 71.8 (t), 70.3 (t), 69.5 (t), 61.7 (d), 60.9 (t), 59.9 (d), 28.3 (q), 25.9 (q), 18.2 (s), –5.3 (q), –5.4 (q); HRMS (ESI): *m/z* calcd for $C_{38}H_{53}KNO_6Si$ $[M+K]^+$ 686.3274 found 686.3238.

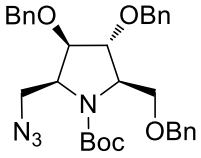
(2*S*,3*R*,4*R*,5*R*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(hydroxymethyl)-1-*N*-(*tert*-butoxycarbonyl)-pyrrolidine 10.



To a solution of compound **20** (4.0 g, 6.17 mmol) in dry methanol (40 mL), camphorsulfonic acid monohydrate (400 mg, 10% w/w) was added and the reaction mixture was stirred at 25 °C for 16 h. Solvent was then concentrated under reduced pressure and the residue was dissolved in ethyl acetate (40 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 20 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get **10** (2.7 g, 82%) as a colourless oil. The data provided is for a mixture of rotamers in a ratio of 2:1. R_f: 0.4 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{23}$–10.6 (*c* 0.7, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3438, 3061, 3030, 2970, 2927, 2869, 1691, 1605, 1454, 1395, 1315, 1256, 1171, 1100, 1033, 914, 854, 743, 700, 606 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.30–7.23 (m, 15H), 4.66–4.41 (m, 6H), 4.31–

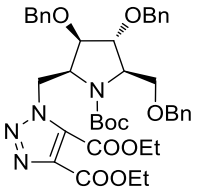
3.89 (m, 4H), 3.85–3.68 (m, 4H), 3.55–3.52 (m, 1H), 3.33 (br s, 0.3H exchangeable with D_2O, for –OH signal of one rotamer), 1.44 (s, 3H), 1.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.7 (s), 154.2 (s), 137.9 (s), 137.6 (s), 137.3 (s), 129.8 (d), 128.8 (d), 128.4 (d), 128.35 (d), 128.32 (d), 128.2 (d), 128.18 (d), 128.11 (d), 128.0 (d), 127.8 (d), 127.79 (d), 127.77 (d), 127.73 (d), 127.5 (d), 127.3 (d), 126.8 (d), 126.7 (d), 82.9 (d), 82.2 (d), 81.2 (d), 80.6 (s), 80.2 (s), 73.1 (t), 72.5 (t), 72.2 (t), 72.0 (t), 68.4 (t), 67.7 (t), 62.4 (t), 61.8 (d), 61.2 (d), 60.6 (d), 59.5 (d), 28.2 (q); HRMS (ESI): *m/z* calcd for $C_{32}H_{39}NNaO_6$ $[M+Na]^+$ 556.2670 found 556.2673.

(2*S*,3*R*,4*R*,5*R*)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(azidomethyl)-1-*N*-(*tert*-butoxycarbonyl)-pyrrolidine 8.



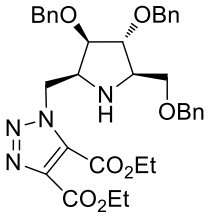
Compound **10** (460 mg, 0.86 mmol) was dissolved in dry THF (5 mL), and the solution was cooled to 0 °C. Triphenylphosphine (452 mg, 1.72 mmol) and trimethylsilyl azide (0.28 mL, 2.15 mmol) were added followed by dropwise addition of diethyl azodicarboxylate (0.4 mL, 2.58 mmol), after which the reaction mixture was warmed to 24 °C. When TLC indicated the completion of the reaction (24 h), the reaction was stopped and solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (10:1) as an eluent to get **8** (274 mg, 57%) as a colourless oil. The data provided is for a mixture of rotamers: R_f: 0.8 (hexane/ethyl acetate, 9:1); Specific rotation: $[\alpha]_D^{23}$–9.4 (*c* 0.82, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ = 3062, 3031, 2973, 2926, 2866, 2099, 1696, 1453, 1386, 1289, 1171, 1098, 1030, 911, 856, 741, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.29–7.23 (m, 15H), 4.59–4.47 (m, 6H), 4.26–4.23 (m, 2H), 4.10–4.06 (m, 1H), 4.00 (m, 0.4H), 3.85 (m, 0.6H), 3.66–3.55 (m, 3H), 3.35 (dd, *J* = 11.7, 6.6 Hz, 1H), 1.44 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.7 (s), 138.1 (s), 137.9 (s), 137.3 (s), 128.4 (d), 128.36 (d), 128.31 (d), 127.9 (d), 127.8 (d), 127.77 (d), 127.72 (d), 127.6 (d), 82.3 (d), 81.8 (d), 80.8 (d), 80.4 (s), 73.0 (t), 72.5 (t), 72.0 (t), 68.8 (t), 61.8 (d), 58.1 (d), 49.6 (t), 28.3 (q); HRMS (ESI): *m/z* calcd for $C_{32}H_{38}N_4NaO_5$ $[M+Na]^+$ 581.2734 found 581.2734.

Diethyl-1-(((2*S*,3*R*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)-1-(*tert*-butoxy carbonyl)pyrrolidin-2-yl)methyl)-1*H*-1',2',3'-triazole-4',5'-dicarboxylate 22.



Compound **8** (0.52 g, 0.93 mmol) was dissolved in dry toluene (6 mL) and diethylacetylene dicarboxylate (0.75 mL, 4.67 mmol) was added. The reaction mixture was heated at 110 °C for 4 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (4:1) as an eluent to get **22** (515 mg, 76%) as a pale yellow oil. The data provided is for a mixture of rotamers: R_f: 0.5 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{23}$–52.9 (*c* 0.61, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3063, 3030, 2979, 2930, 2873, 1730, 1696, 1555, 1471, 1454, 1391, 1272, 1208, 1171, 1100, 1015, 854, 739, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.25 (m, 15H), 4.86–4.39 (m, 14H), 4.19–4.18 (m, 1H), 4.00 (br m, 0.5H, due to one rotamer), 3.83 (br m, 1H), 3.70–3.63 (m, 1.5H), 1.42–1.22 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.4 (s), 158.6 (s), 154.3 (s), 153.8 (s), 140.2 (s), 139.9 (s), 138.1 (s), 137.9 (s), 137.1 (s), 130.1 (s), 129.7 (s), 128.4 (d), 128.3 (d), 128.2 (d), 127.9 (d), 127.7 (d), 127.6 (d), 127.4 (d), 82.7 (d), 81.8 (d), 81.5 (d), 80.5 (s), 73.2 (t), 72.4 (t), 72.2 (t), 69.2 (t), 68.7 (t), 62.5 (t), 61.8 (d), 61.6 (t), 61.3 (d), 57.4 (d), 57.1 (d), 50.3 (t), 49.7 (t), 28.1 (q), 27.8 (q), 14.1 (q), 13.7 (q); HRMS (ESI): *m/z* calcd for $C_{40}H_{48}KN_4O_9$ $[M+K]^+$ 767.3053 found 767.3049.

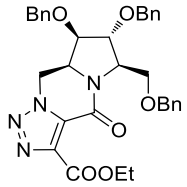
Diethyl-1-(((2*S*,3*R*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)pyrrolidin-2-yl) methyl)-1*H*-1',2',3'-triazole-4',5'-dicarboxylate 6.



To a solution of compound **22** (650 mg, 0.89 mmol) in dry dichloromethane (7 mL), trifluoroacetic acid (0.7 mL, 9.14 mmol) was added at 0 °C and the reaction mixture was stirred at 26 °C for 4 h. Solvent was then concentrated under reduced

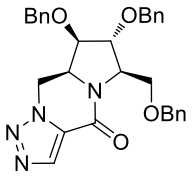
pressure and the residue was dissolved in ethyl acetate (25 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 20 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was passed through column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get **6** as pale yellow oil (430 mg, 77%) and proceeded without any further purification.

(6*S*,7*R*,8*R*,8a*R*)-Ethyl-7,8-bis(benzyloxy)-6-((benzyloxy)methyl)-4-oxo-4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*] [1',2',3']triazolo[1',5'-*d*]pyrazine-3-carboxylate 24.



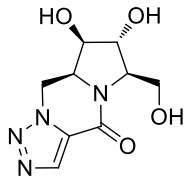
Compound **6** (320 mg, 0.509 mmol) was dissolved in dry toluene (4 mL) and camphorsulfonic acid monohydrate (26 mg, 0.104 mmol) was added. The reaction mixture was heated at 110 °C for 9 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get **24** (240 mg, 81%) as a light brown oil. R_f: 0.6 (hexane/ethyl acetate, 1:1); Specific rotation: $[\alpha]_D^{23}$ –127.3 (*c* 0.15, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3060, 3030, 2924, 2859, 1735, 1679, 1564, 1446, 1410, 1364, 1213, 1179, 1080, 1023, 744, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.26 (m, 13H),7.15–7.12 (m, 2H), 4.72 (dd, *J* = 13.2, 4.0 Hz, 1H), 4.67–4.62 (m, 2H), 4.60–4.54 (m, 1H), 4.51–4.39 (m, 7H), 4.35 (s, 1H) 4.24 (d, *J* = 11.6 Hz, 1H), 4.13 (dd, *J* = 9.2, 4.8 Hz, 1H), 4.05 (d, *J* = 4.0 Hz, 1H), 3.45 (dd, *J* = 10.4, 8.8 Hz, 1H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7 (s), 153.6 (s), 139.4 (s), 137.9 (s), 136.9 (s), 136.2 (s), 129.9 (s), 128.7 (d), 128.5 (d), 128.46 (d), 128.40 (d), 128.1 (d), 127.9 (d), 127.88 (d), 127.81 (d), 127.7 (d), 79.9 (d), 78.9 (d), 73.2 (t), 71.5 (t), 71.1 (t), 66.9 (t), 61.9 (t), 61.5 (d), 59.4 (d), 46.4 (t), 14.1 (q); HRMS (ESI): *m/z* calcd for $C_{33}H_{34}N_4NaO_6$ $[M+Na]^+$ 605.2371 found 605.2348.

(6*S*,7*R*,8*R*,8a*R*)-7,8-Bis(benzyloxy)-6-((benzyloxy)methyl)-7,8,8a,9-tetrahydropyrrolo [1,2-*a*][1',2',3']triazolo[1',5'-*d*]pyrazin-4(6*H*)-one 30.



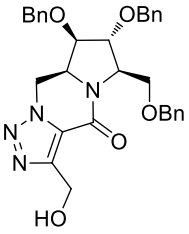
Compound **24** (220 mg, 0.378 mmol) was dissolved in dry methanol (3 mL) and potassium carbonate (157 mg, 1.13 mmol) was added. The reaction mixture was stirred at 26 °C for 6 h, after which the solvent was evaporated under reduced pressure. To the resulting milky white residue, a mixture of ethyl acetate and water (20 mL, 1:1) was added. Conc. HCl was then added to the mixture until a clear solution was obtained. The organic layer was then separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue contains **28** was dissolved in glacial acetic acid (3 mL) and heated at 120 °C for 24 h. The reaction mixture was then quenched with aqueous sodium bicarbonate solution (20 mL) and extracted with ethyl acetate (2 x 10 mL). The organic layer was then dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get **30** (156 mg, 80% over two steps) as a pale yellow oil. R_f: 0.6 (hexane/ethyl acetate, 1:1); Specific rotation: $[\alpha]_D^{23}$–60.4 (*c* 0.22, $CHCl_3$); IR (KBr): $\bar{\upsilon}$ =3062, 3030, 2925, 2868, 1667, 1553, 1495, 1453, 1416, 1363, 1256, 1204, 1110, 1091, 1027, 983, 742, 698, 606 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.34–7.25 (m, 13H), 7.14–7.04 (m, 2H), 4.73–4.67 (m, 2H), 4.64–4.63 (m, 1H), 4.59–4.33 (m, 7H), 4.23 (d, *J* = 12.0 Hz, 1H), 4.10–4.03 (m, 2H), 3.45–3.39 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5 (s), 137.8 (s), 136.9 (s), 136.3 (s), 134.2 (d), 129.9 (s), 128.6 (d), 128.5 (d), 128.3 (d), 128.0 (d), 127.9 (d), 127.8 (d), 127.7 (d), 79.8 (d), 79.0 (d), 73.1 (t), 71.4 (t), 71.0 (t), 67.0 (t), 61.1 (d), 59.7 (d), 45.7 (t); HRMS (ESI): *m/z* calcd for $C_{30}H_{31}N_4O_4$ $[M+H]^+$ 511.2340 found 511.2338.

(6*S*,7*R*,8*R*,8a*R*)-7,8-Dihydroxy-6-(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazin-4 (6*H*)-one 3.



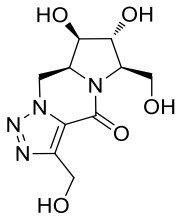
Compound **30** (140 mg, 0.27 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (140 mg, 100% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 26 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (10:1) as an eluent to get **3** as colourless oil (53 mg, 80%). R_f: 0.3 (acetonitrile/NH_4OH, 9:1); Specific rotation: $[\alpha]_D^{23}$–67.2 (*c* 0.19, CH_3OH); IR (KBr): $\bar{\upsilon}$ =3390, 2927, 2849, 1655, 1558, 1425, 1370, 1200, 1109, 1079, 1052, 1031, 758, 611 cm^{-1}; ^1H NMR (400 MHz, D_2O): δ 8.21 (s, 1H), 5.04 (dd, *J* = 11.2, 2.4 Hz, 1H), 4.66–4.55 (m, 2H), 4.42 (m, 1H), 4.34 (d, *J* = 3.2 Hz, 1H), 4.13–4.10 (m, 1H), 3.98–3.91 (m, 2H); ^{13}C NMR (100 MHz, D_2O): δ 157.3 (s), 133.7 (d), 129.9 (s), 77.2 (d), 74.1 (d), 66.0 (d), 60.6 (d), 58.9 (t), 45.6 (t); HRMS (ESI): *m/z* calcd for $C_9H_{12}N_4NaO_4$ $[M+Na]^+$ 263.0751 found 263.0750.

(6*S*,7*R*,8*R*,8a*R*)-7,8-Bis(benzyloxy)-6-((benzyloxy)methyl)-3-(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazin-4(6*H*)-one 26.



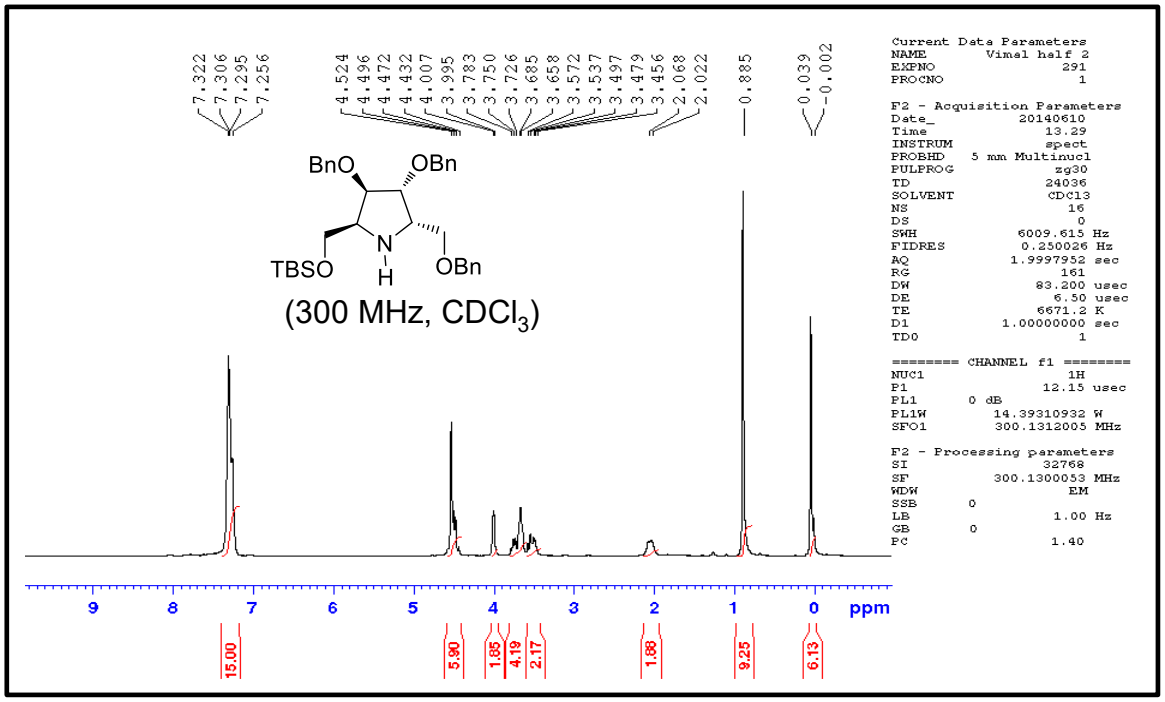
Compound **24** (120 mg, 0.21 mmol) was dissolved in dry THF (2 mL) and lithium borohydride (4.5 mg, 0.21 mmol) was added. The reaction mixture was stirred at 26 °C for 2 h, after which the solvent was evaporated under reduced pressure and the residue was passed through column chromatography over silica gel using a mixture of hexane and ethyl acetate (1:1) as an eluent to get **26** (82 mg, 74%) as a pale yellow oil and the product was proceeded without further purification.

(6*S*,7*R*,8*R*,8a*R*)-7,8-Dihydroxy-3,6-bis(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo [1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazin-4(6*H*)-one 4.

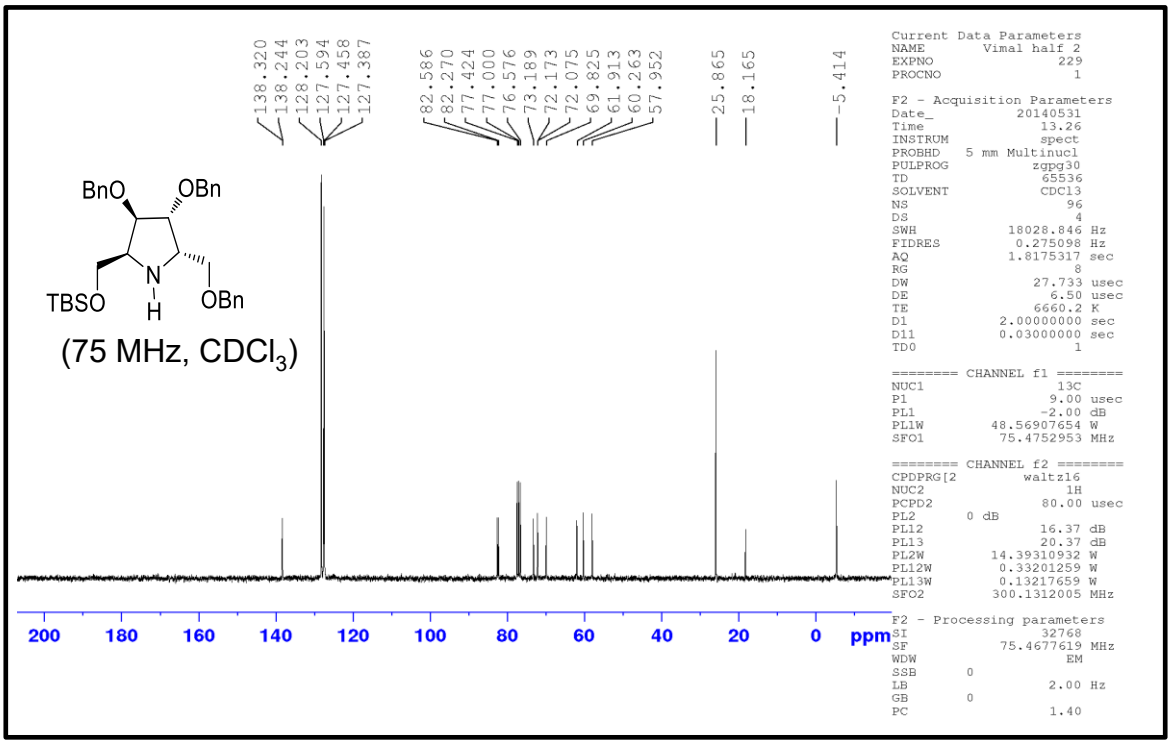


Compound **26** (82 mg, 0.152 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (80 mg, 100% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 29 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (6:1) as an eluent to get **4** as colourless oil (35 mg, 85%). R_f: 0.3 (acetonitrile/NH_4OH, 4:1); Specific rotation: $[\alpha]_D^{23}$–21.1 (*c* 0.09, CH_3OH); IR (KBr): $\bar{\upsilon}$ =3433, 2951, 2843, 1649, 1560, 1453, 1427, 1402, 1111, 1018, 613 cm^{-1}; ^1H NMR (400 MHz, D_2O): δ 5.03 (dd, *J* = 10.8, 2.0 Hz, 1H), 4.92 (d, *J* = 13.6 Hz, 1H), 4.88 (d, *J* = 13.2 Hz, 1H), 4.64–4.59 (m, 2H), 4.44 (m, 1H), 4.36 (d, *J* = 2.8 Hz, 1H), 4.15–4.13 (m, 1H), 3.98–3.96 (m, 2H); ^{13}C NMR (100 MHz, D_2O): δ 157.4 (s), 147.0 (s), 126.3 (s), 77.3 (d), 74.1 (d), 65.9 (d), 60.6 (d), 59.0 (t), 54.0 (t), 45.6 (t); HRMS (ESI): *m/z* calcd for $C_{10}H_{14}N_4NaO_5$ $[M+Na]^+$ 293.0856 found 293.0854.

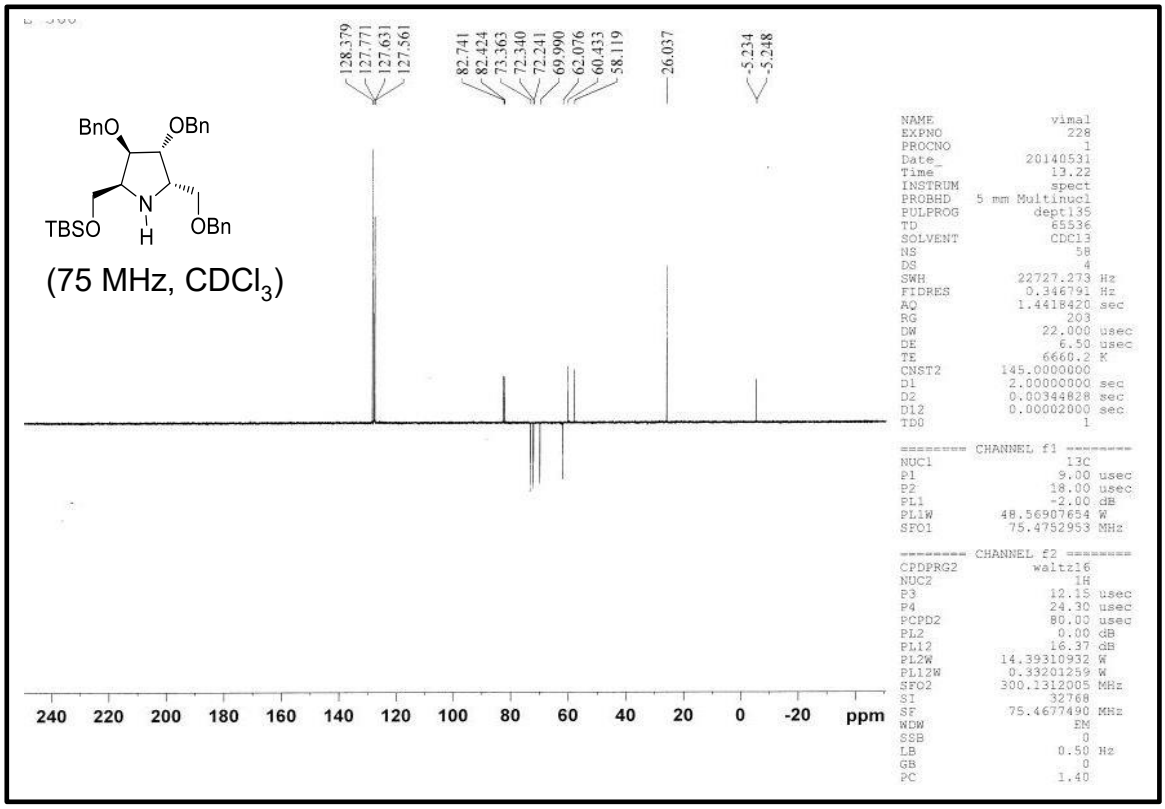
^{1}H–NMR spectrum of compound **17**



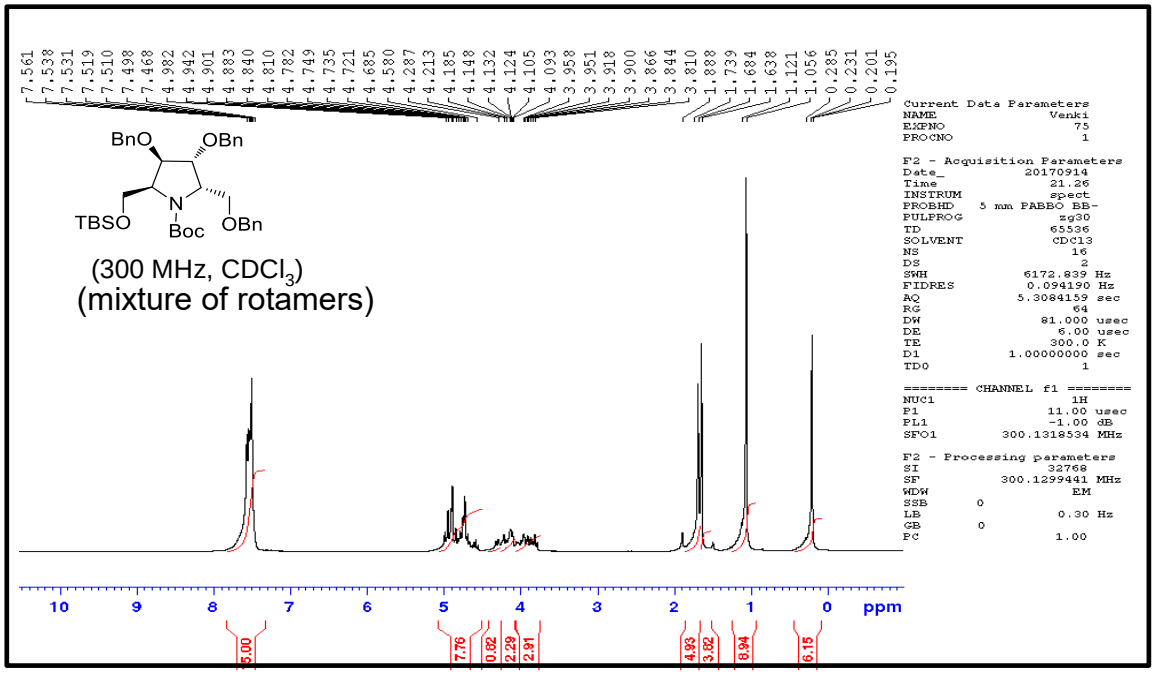
^{13}C–NMR spectrum of compound **17**



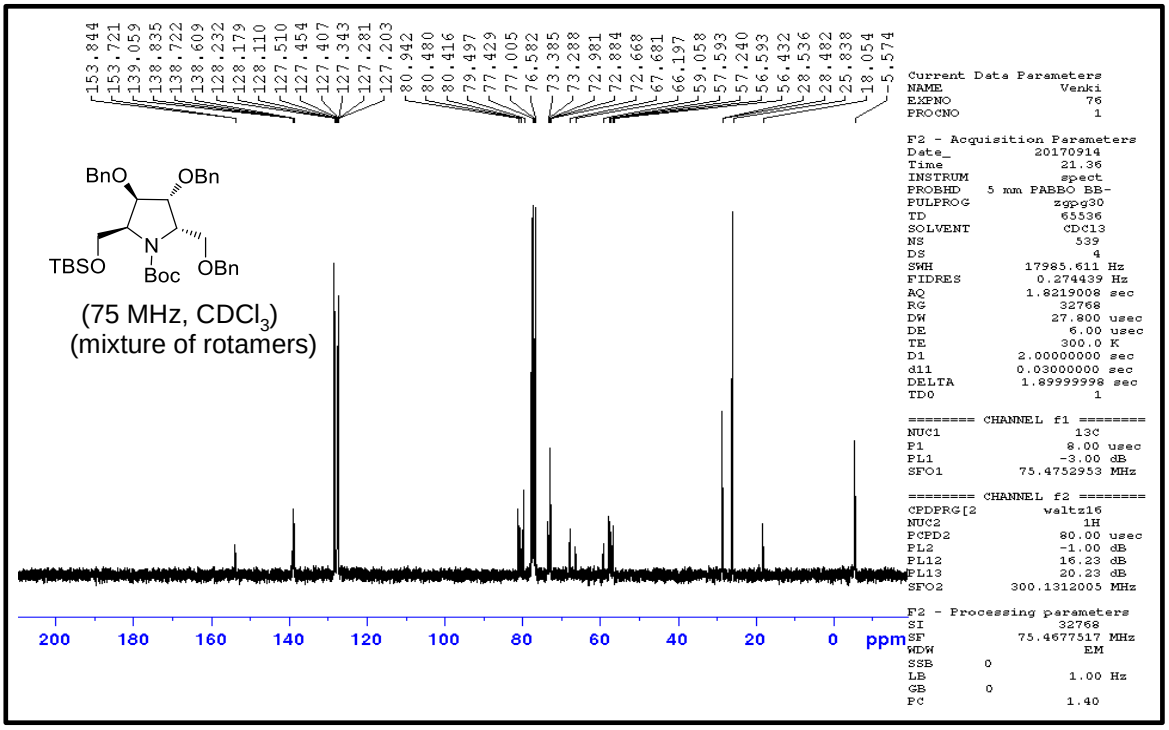
DEPT-135 spectrum of compound **17**



^{1}H–NMR spectrum of compound **19**

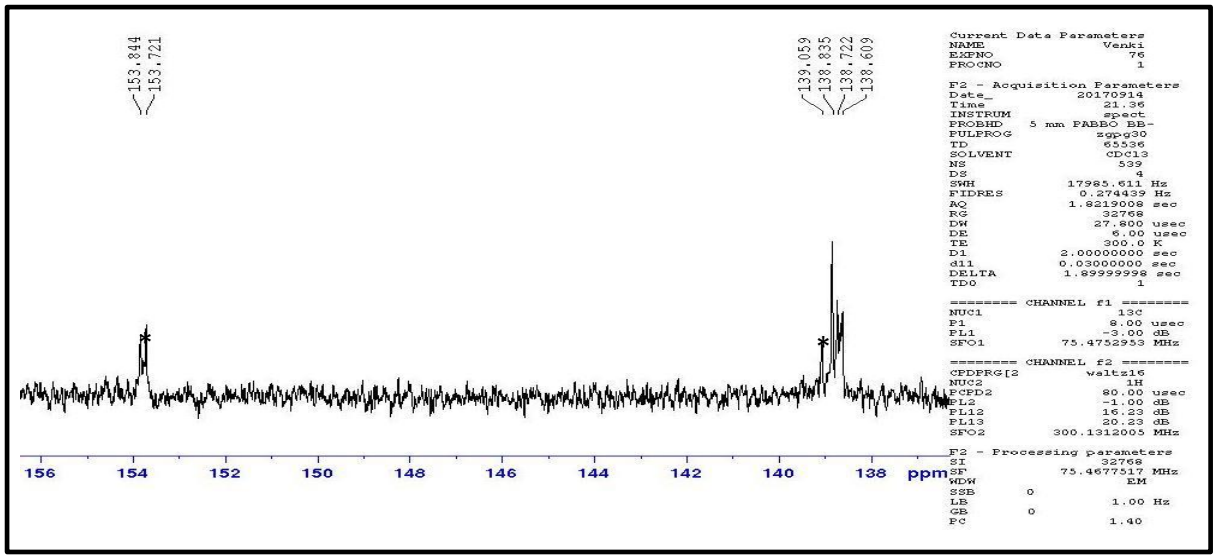


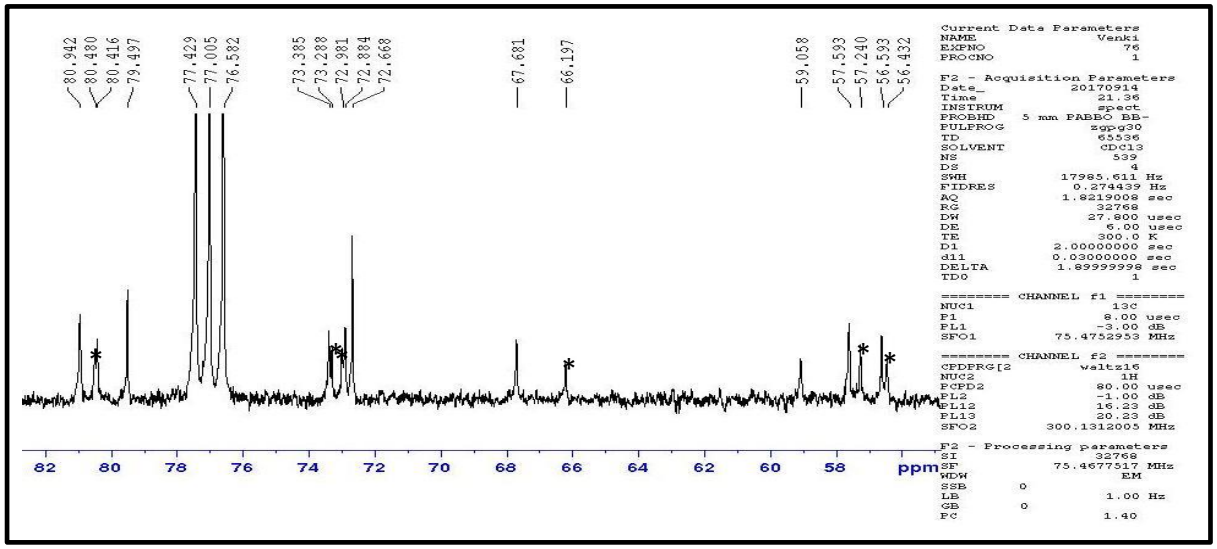
^{13}C–NMR spectrum of compound **19**

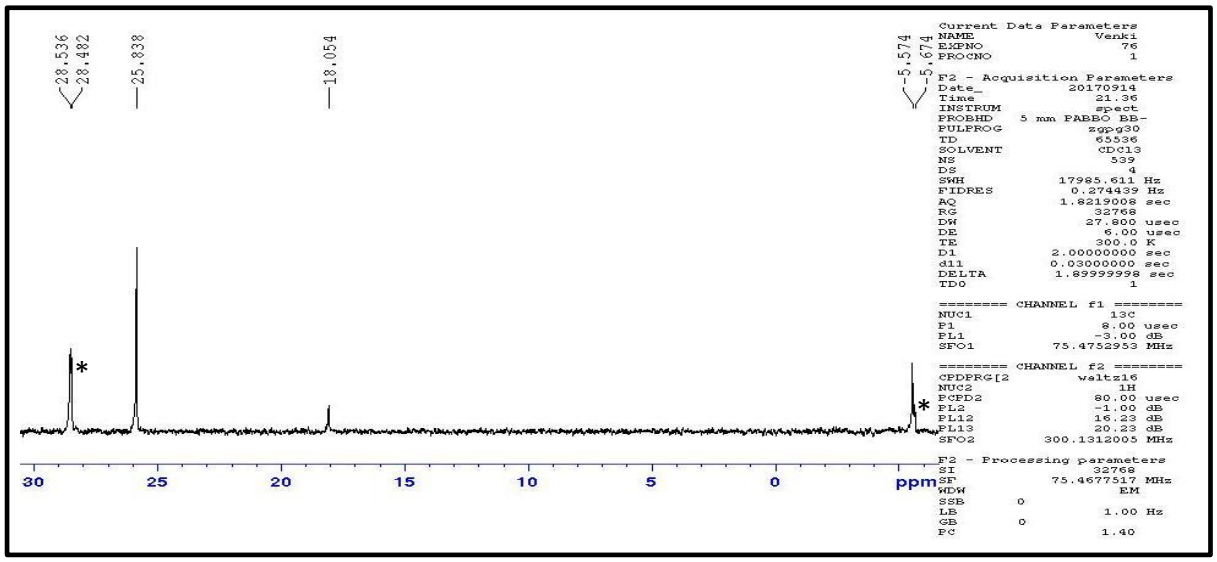


^{13}C-NMR spectrum of compound **19** (expanded)

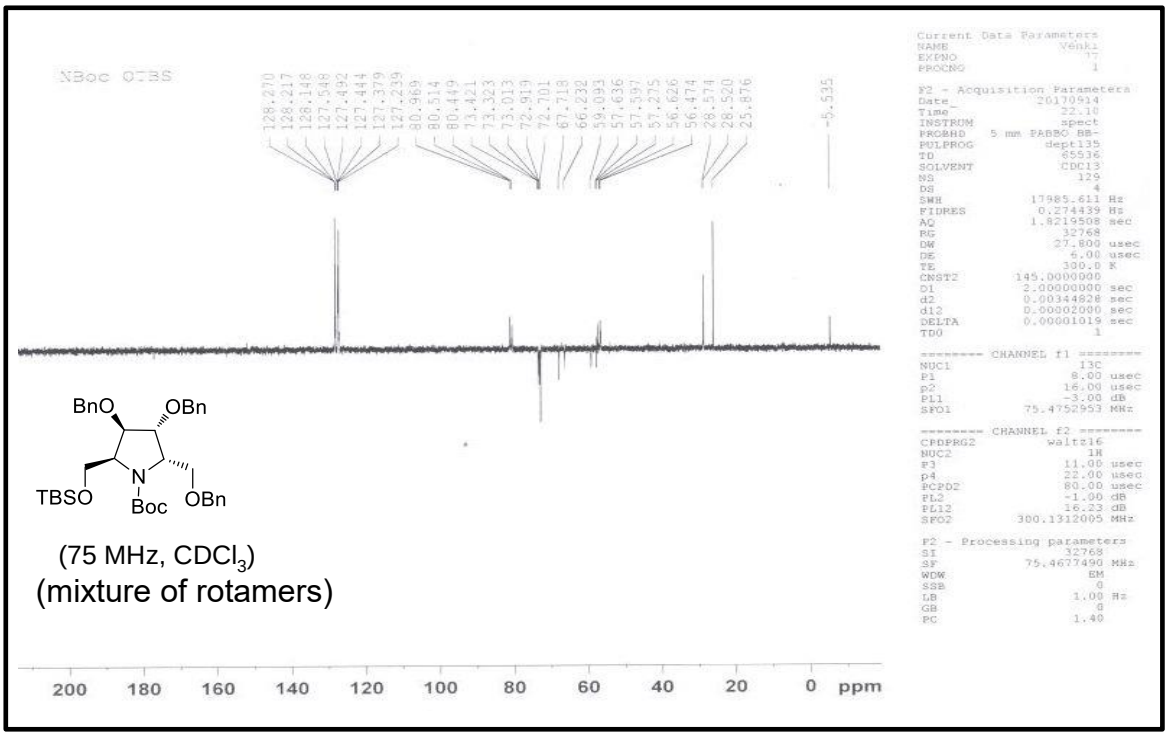
*indicates signals due to rotamers



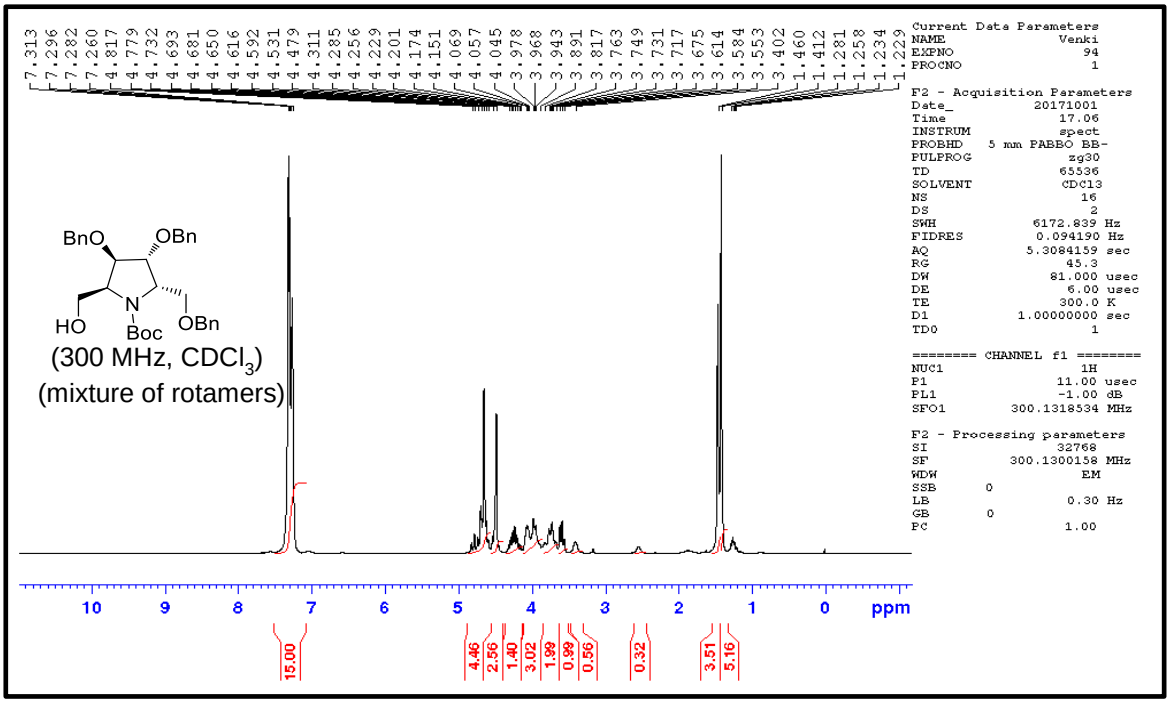




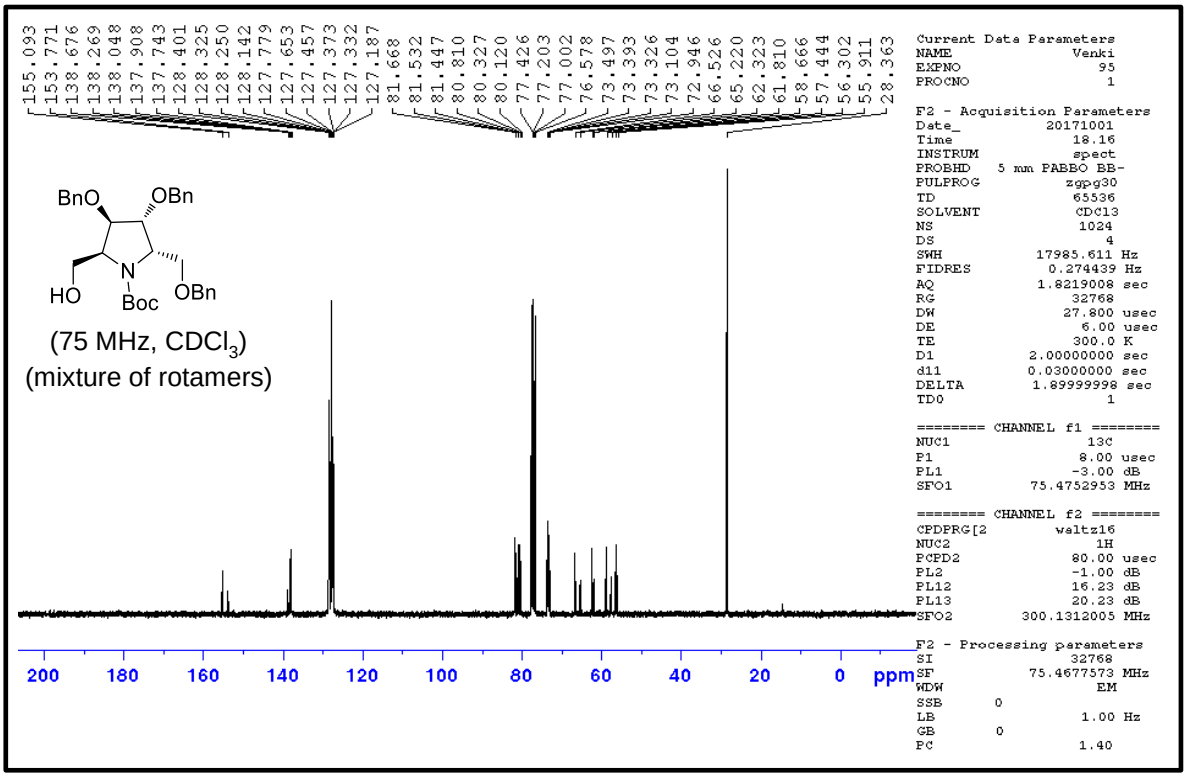
DEPT-135 spectrum of compound **19**



^{1}H–NMR spectrum of compound **9**

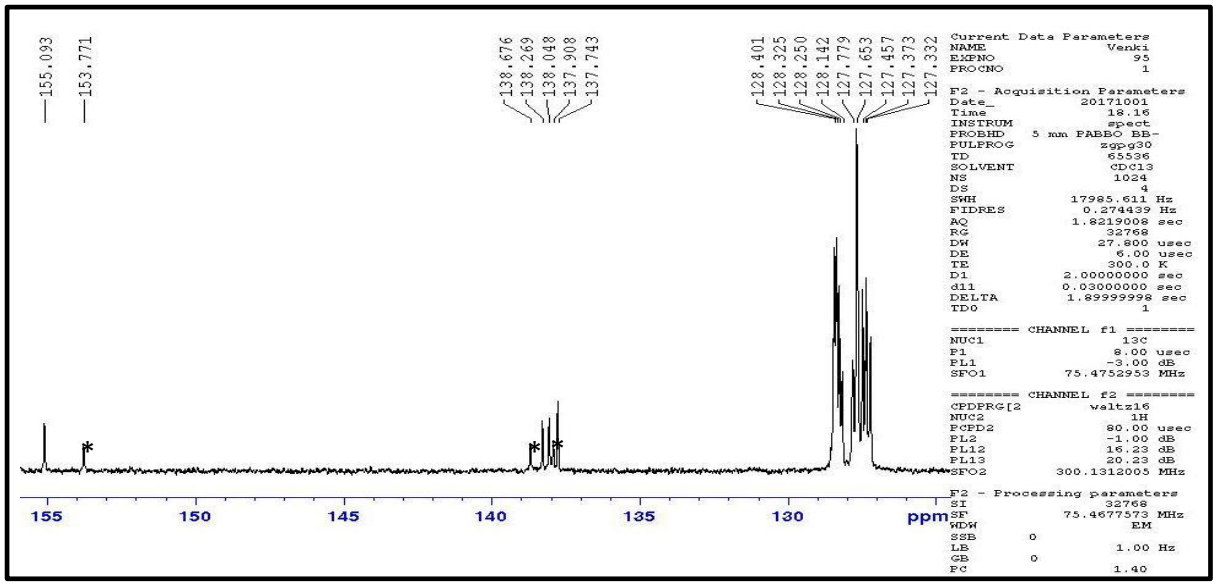


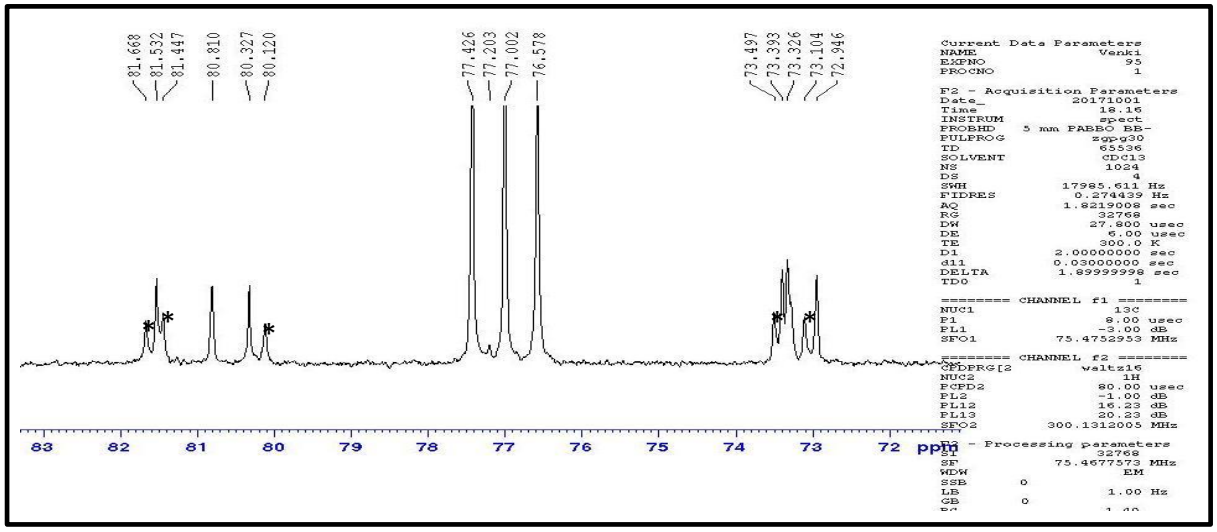
^{13}C–NMR spectrum of compound **9**

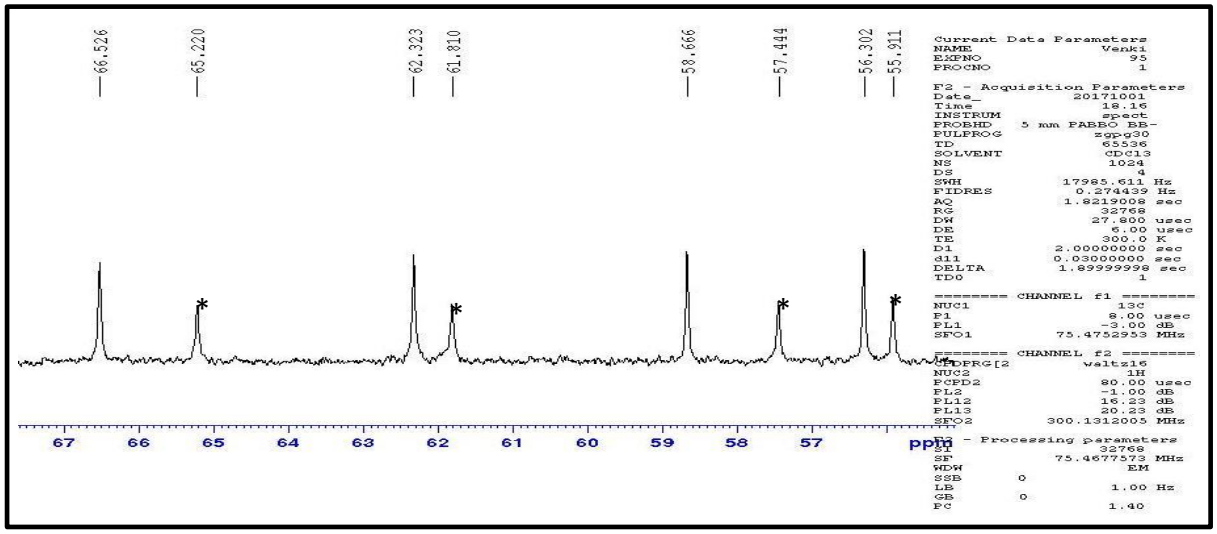


^{13}C-NMR spectrum of compound **9** (expanded)

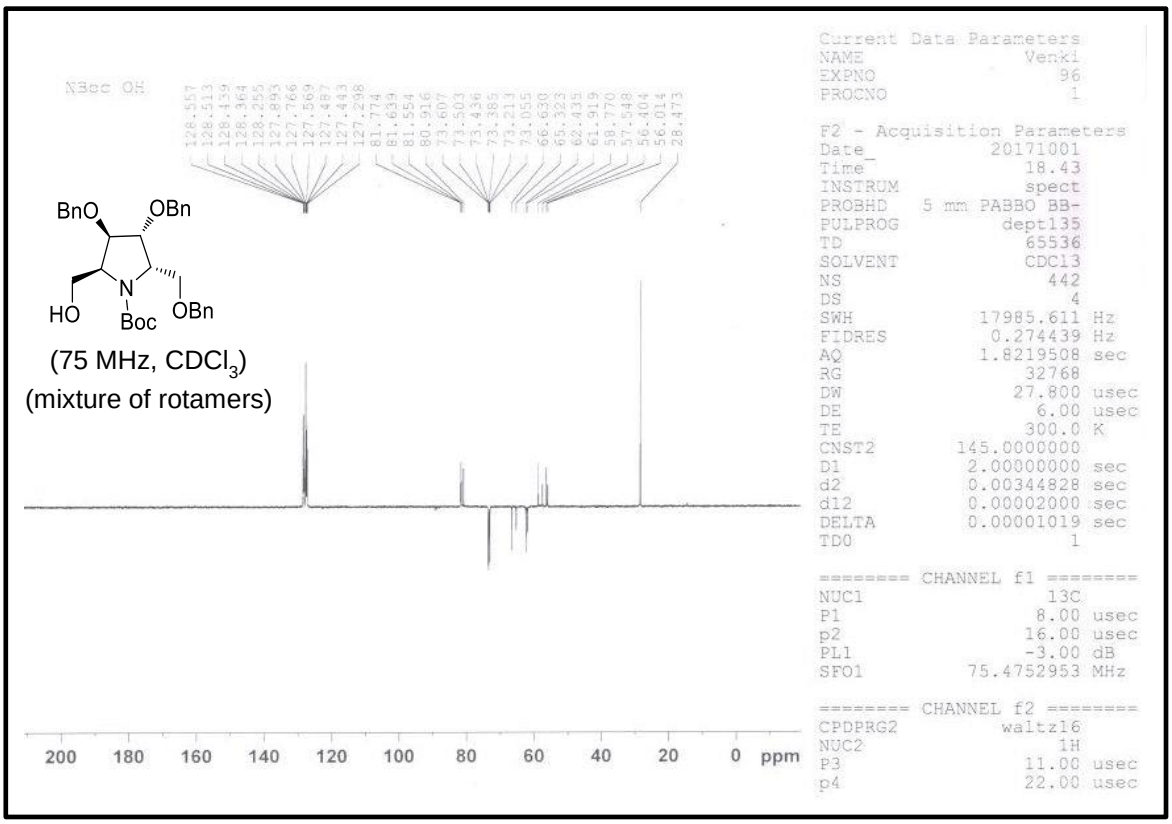
*indicates signals due to rotamers



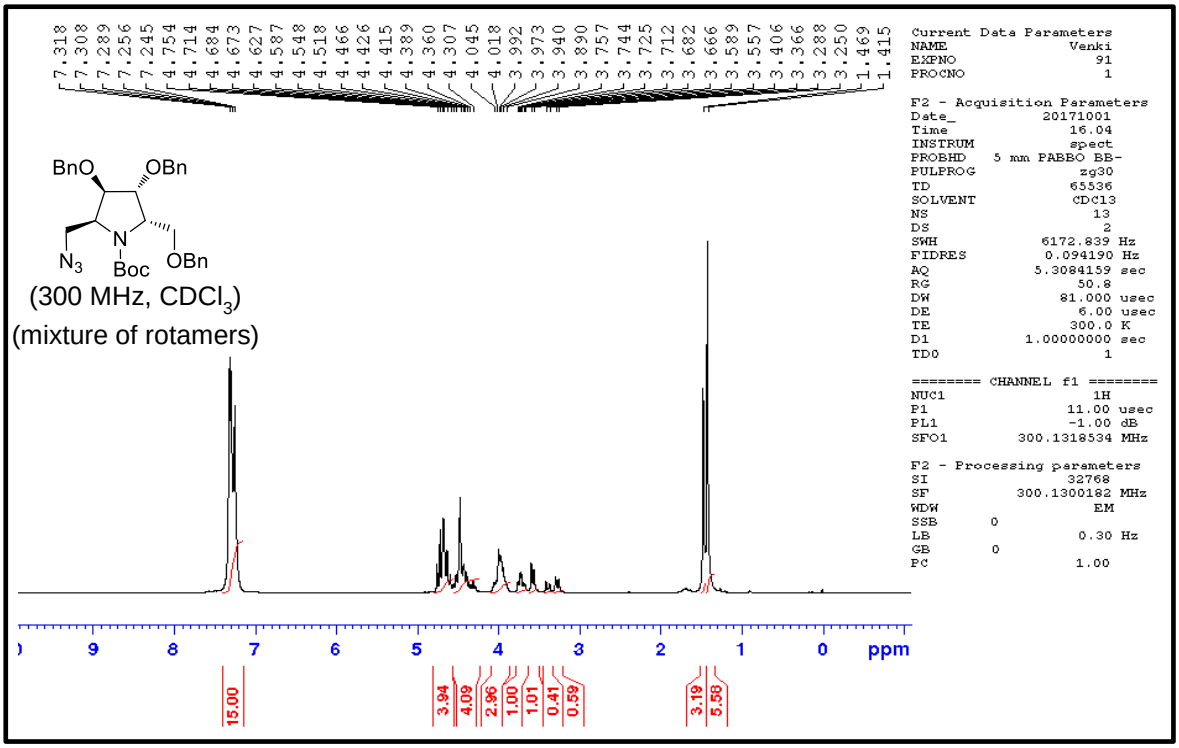




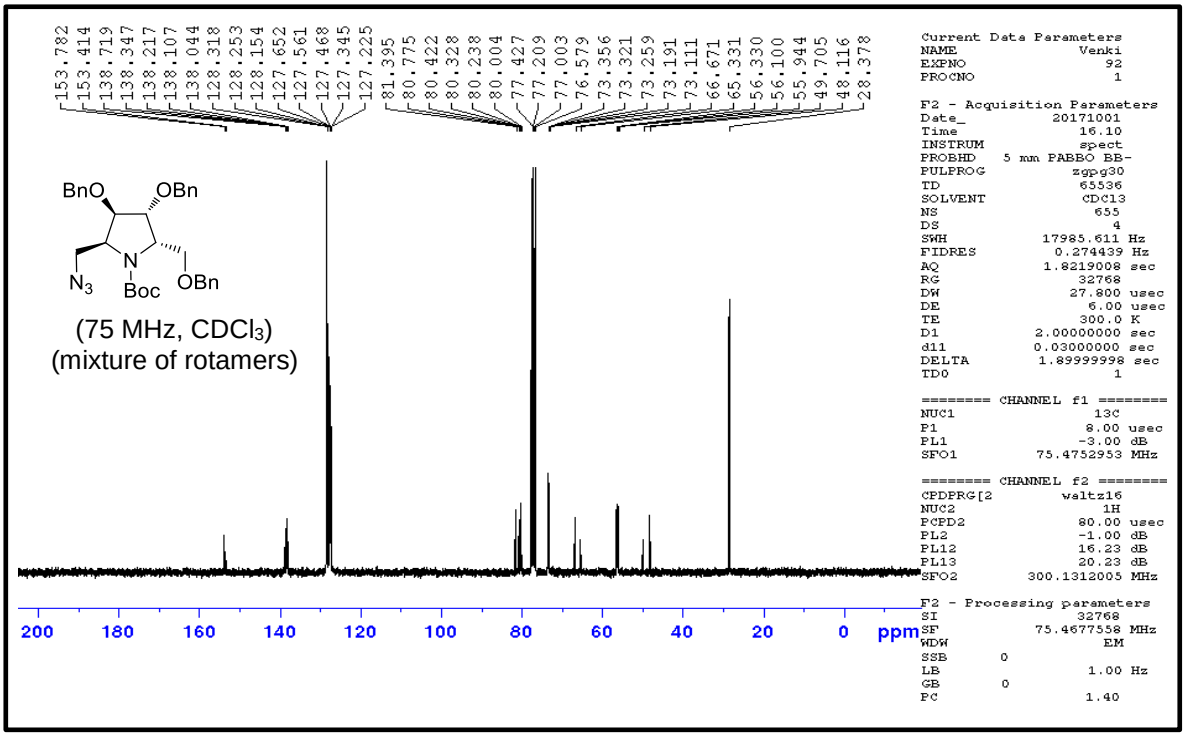
DEPT-135 spectrum of compound **9**



^{1}H–NMR spectrum of compound **7**

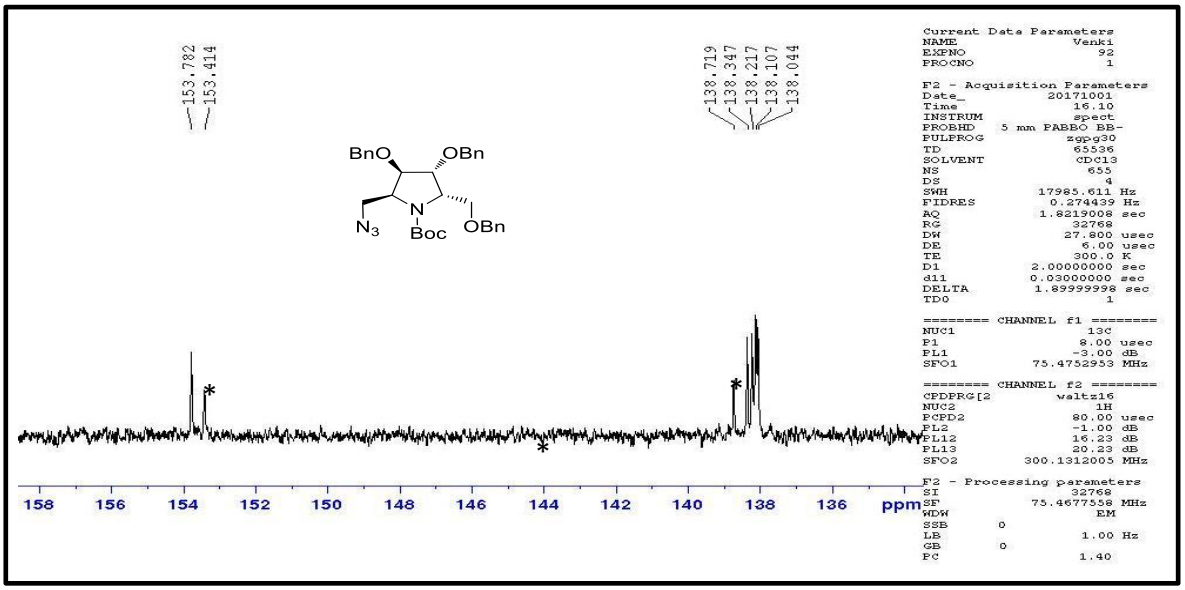


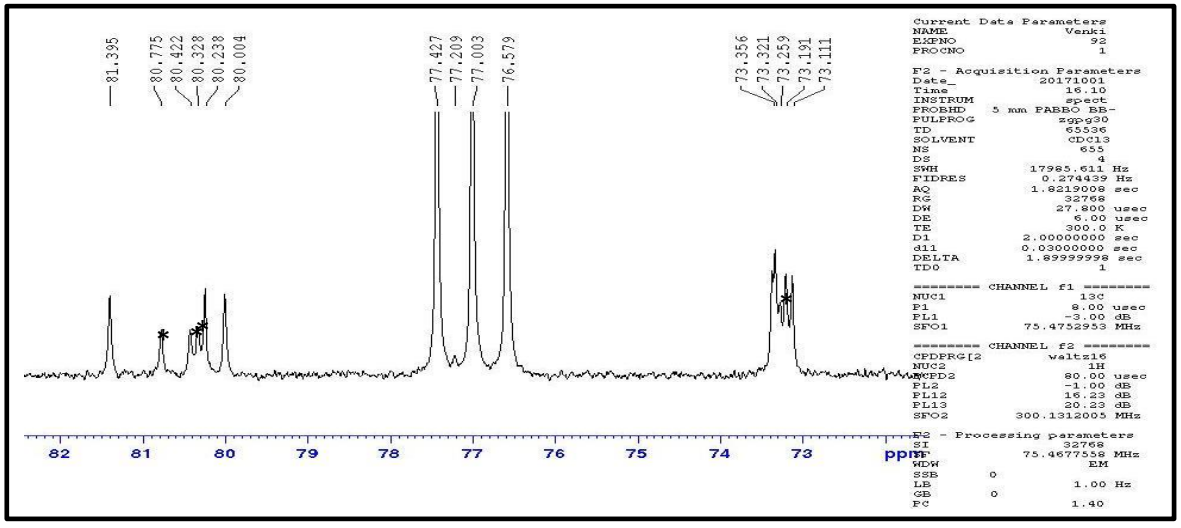
^{13}C–NMR spectrum of compound **7**

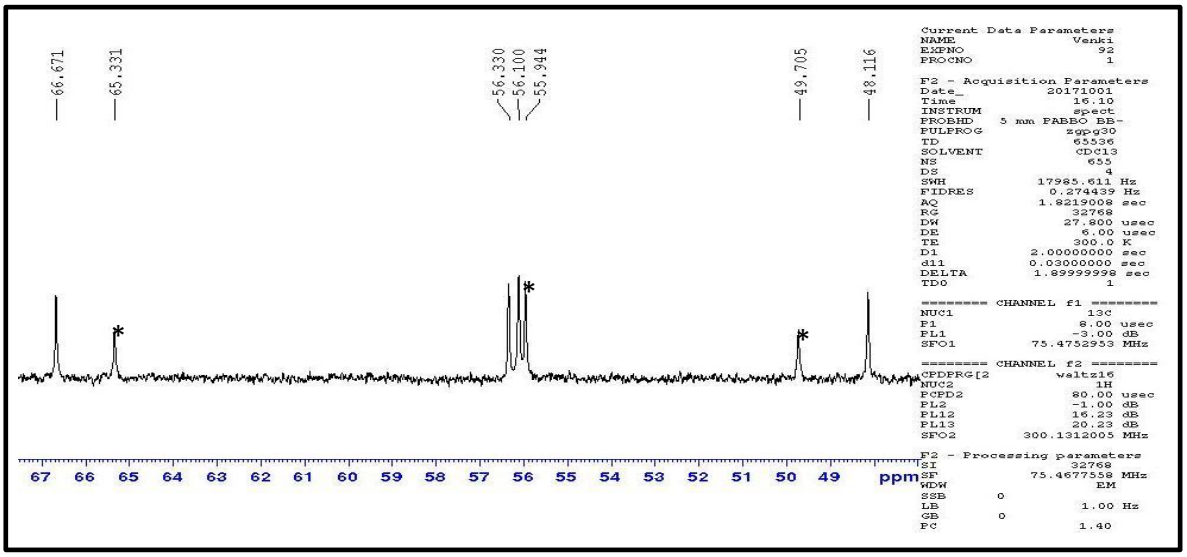


^{13}C-NMR spectrum of compound **7** (expanded)

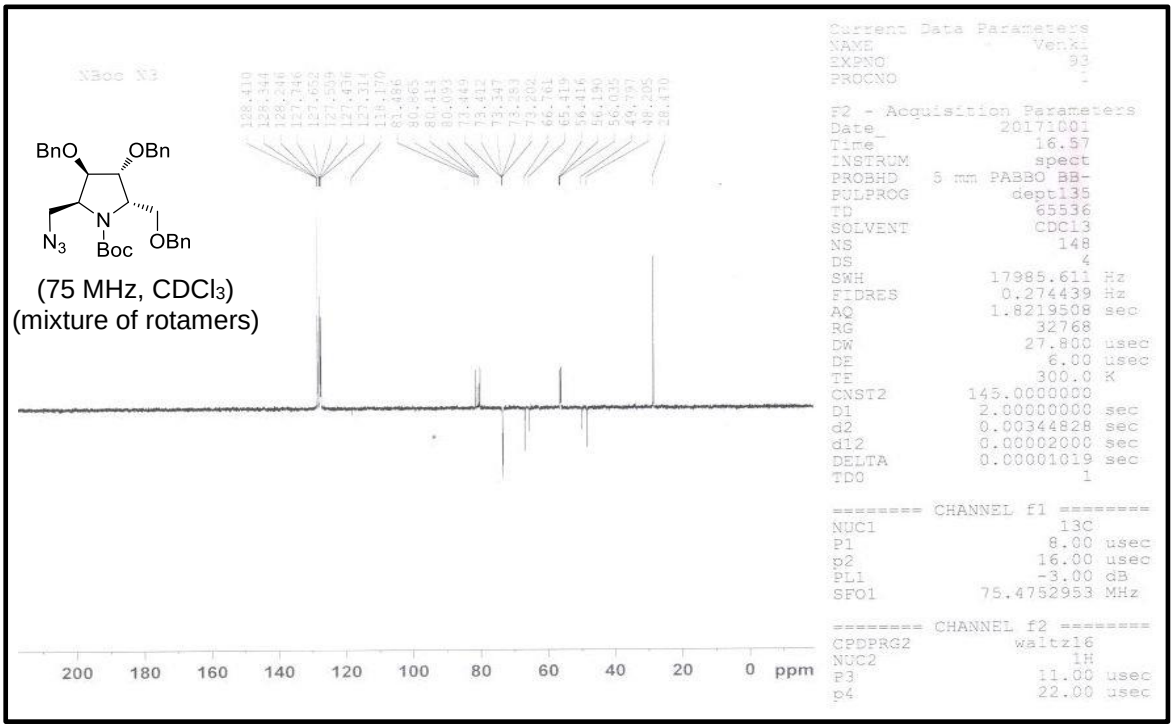
*indicates signals due to rotamers



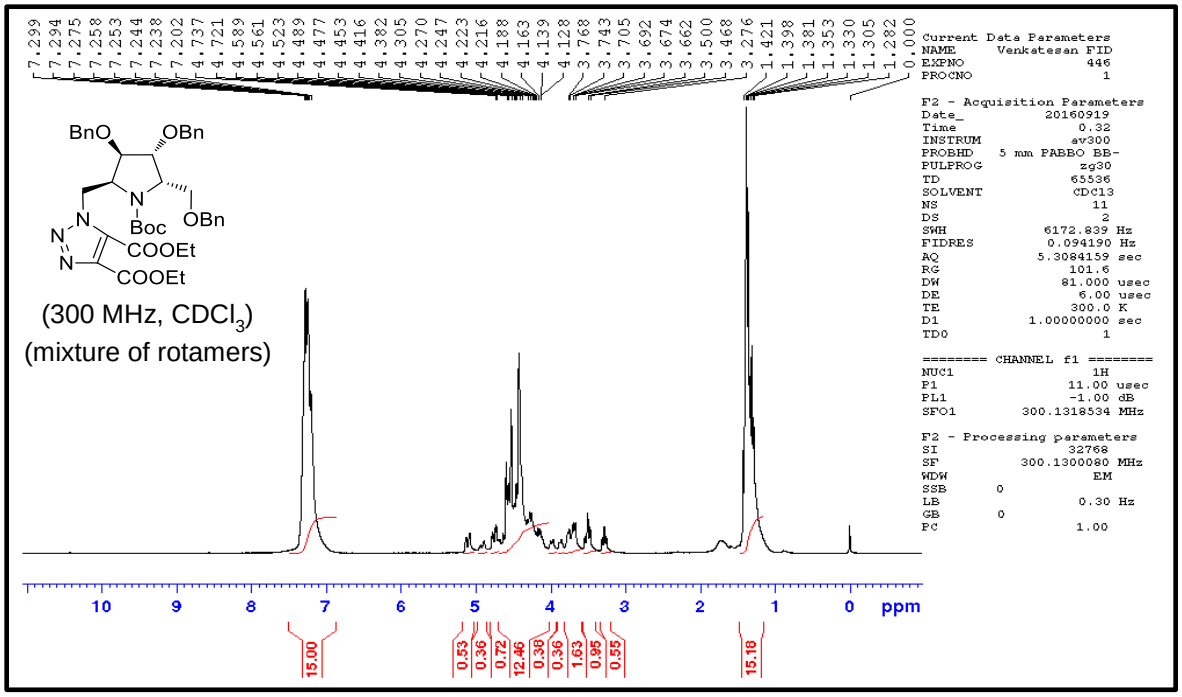




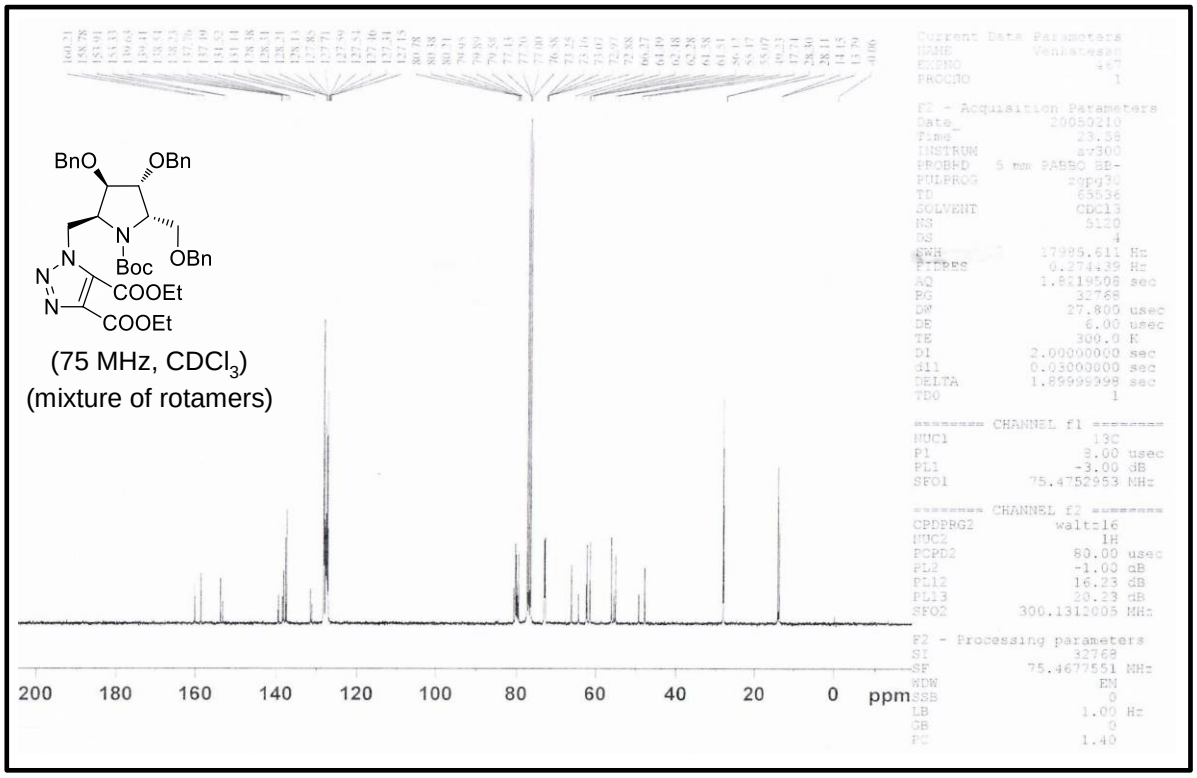
DEPT-135 spectrum of compound **7**



^{1}H–NMR spectrum of compound **21**

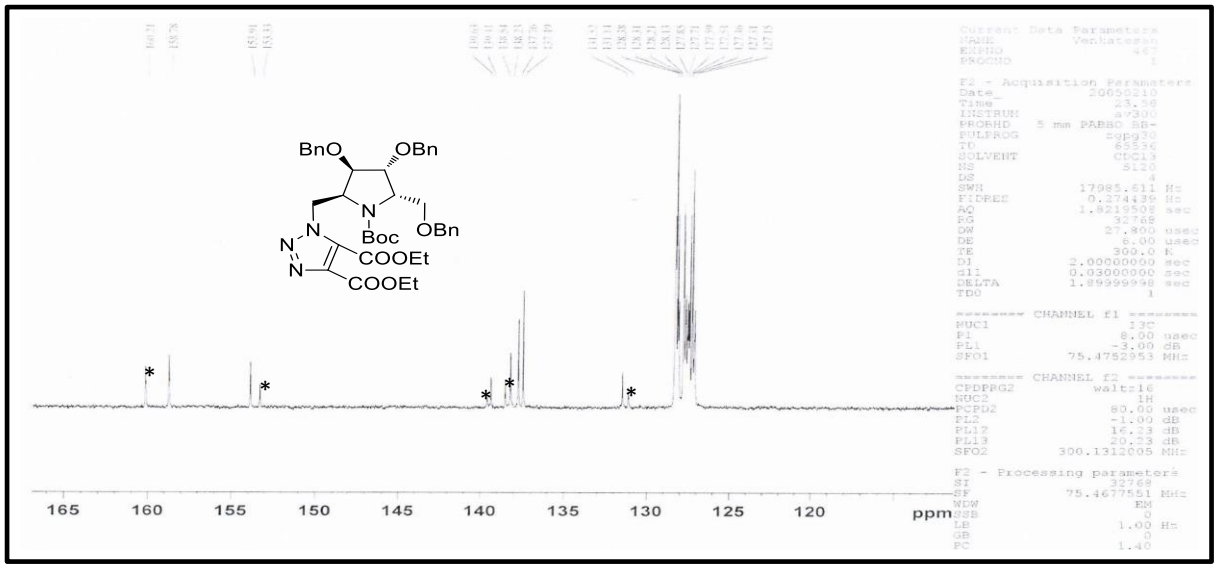


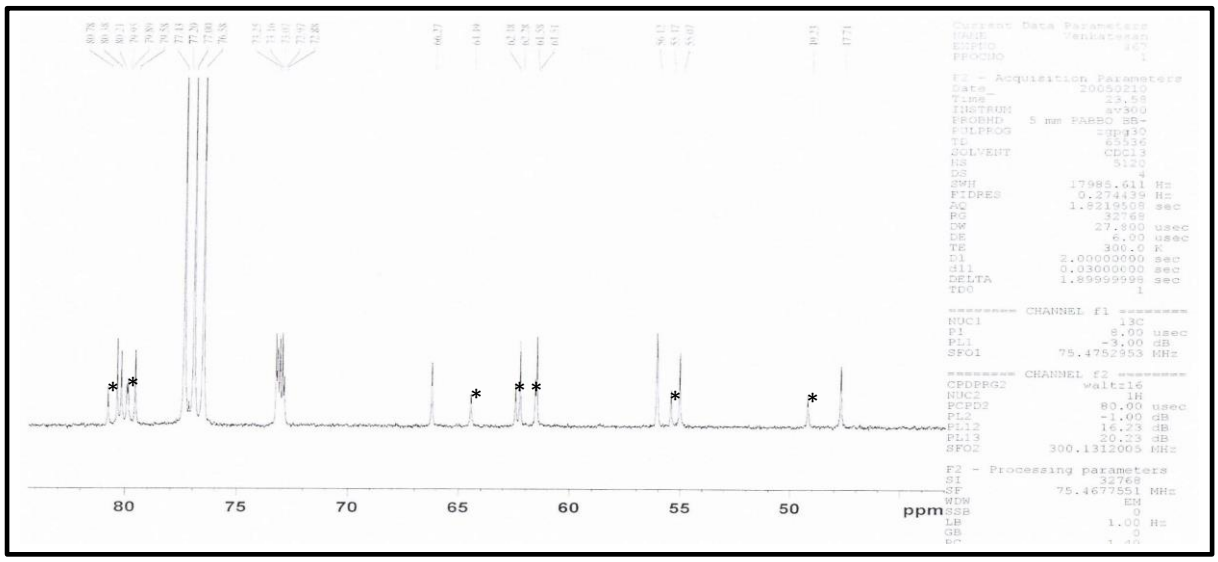
^{13}C–NMR spectrum of compound **21**

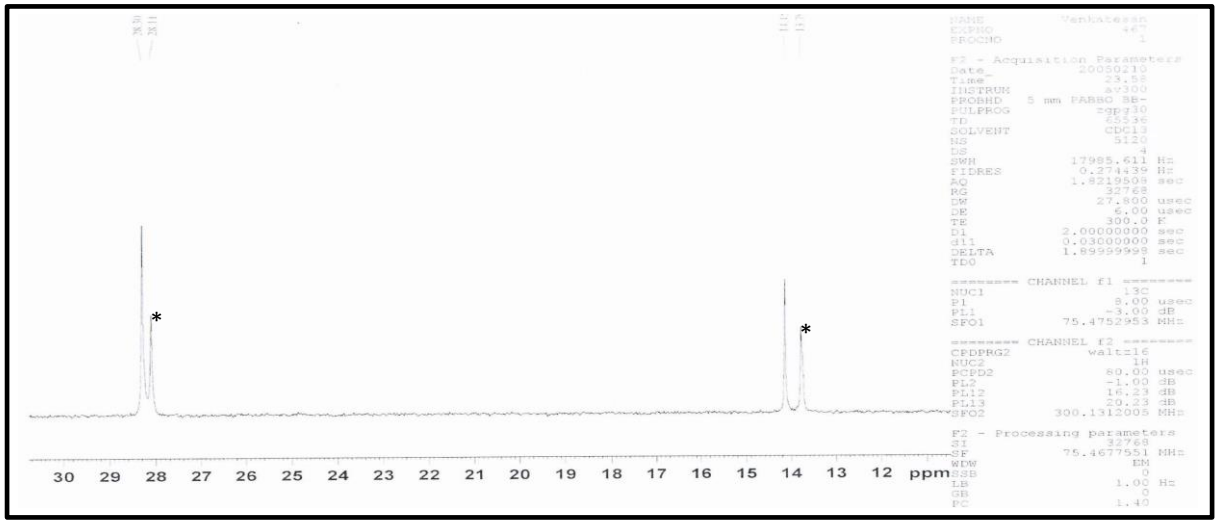


^{13}C-NMR spectrum of compound **21** (expanded)

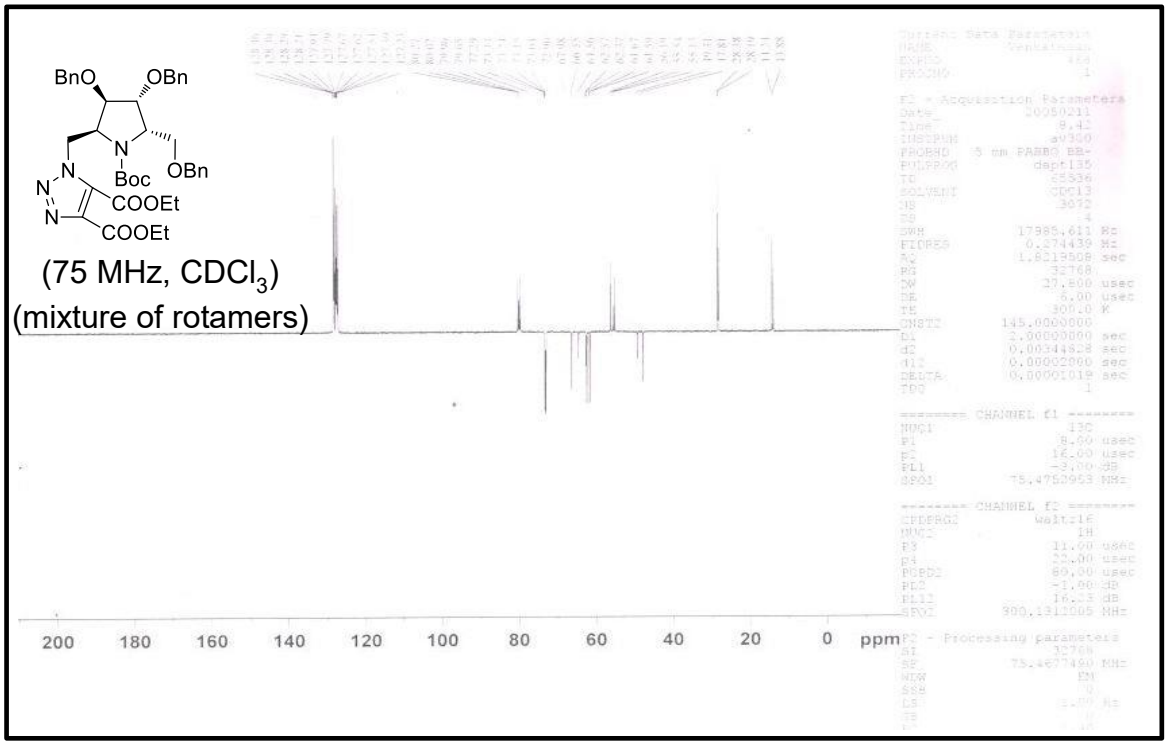
*indicates signals due to rotamers



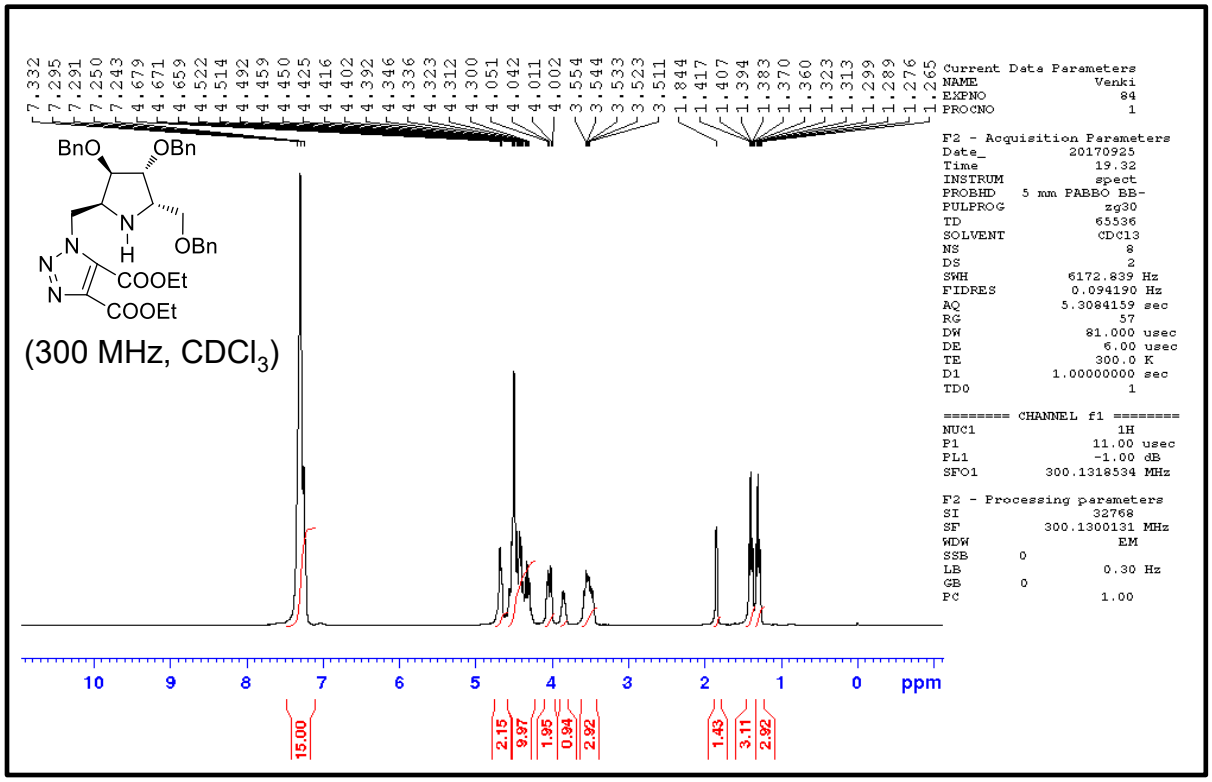




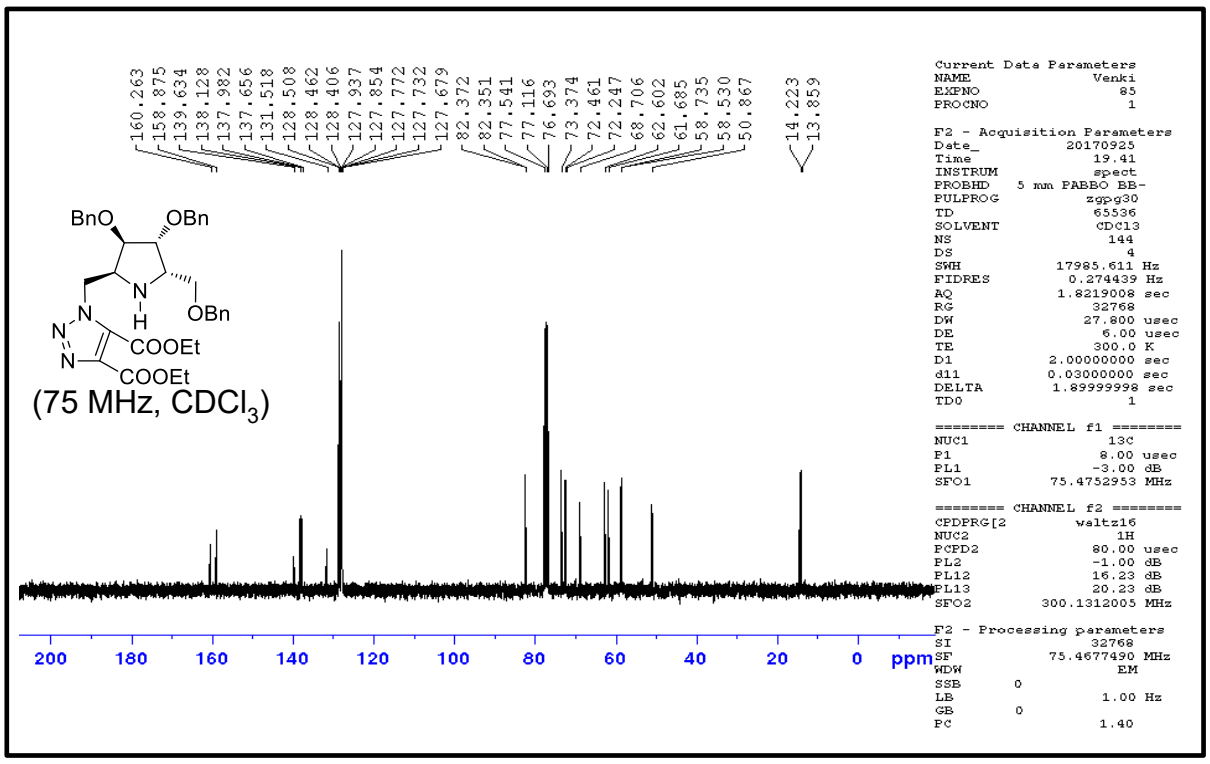
DEPT-135 spectrum of compound **21**



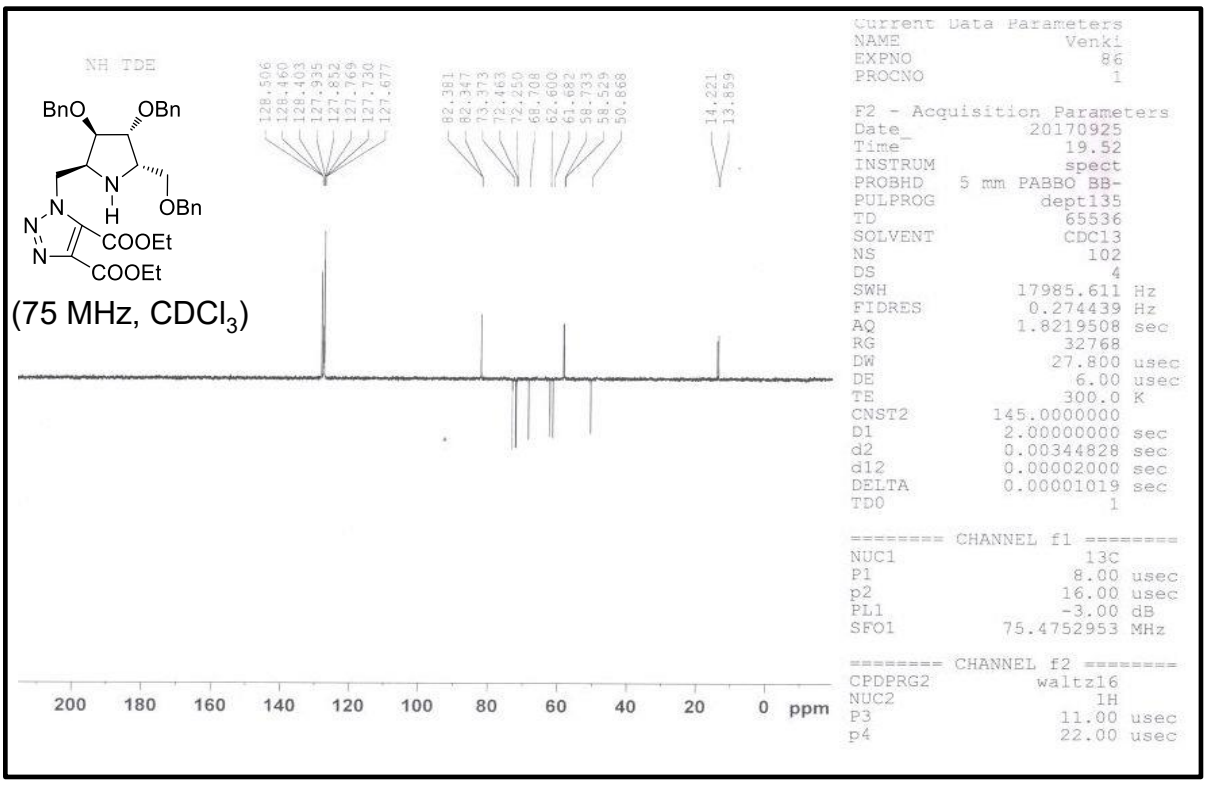
^{1}H–NMR spectrum of compound **5**



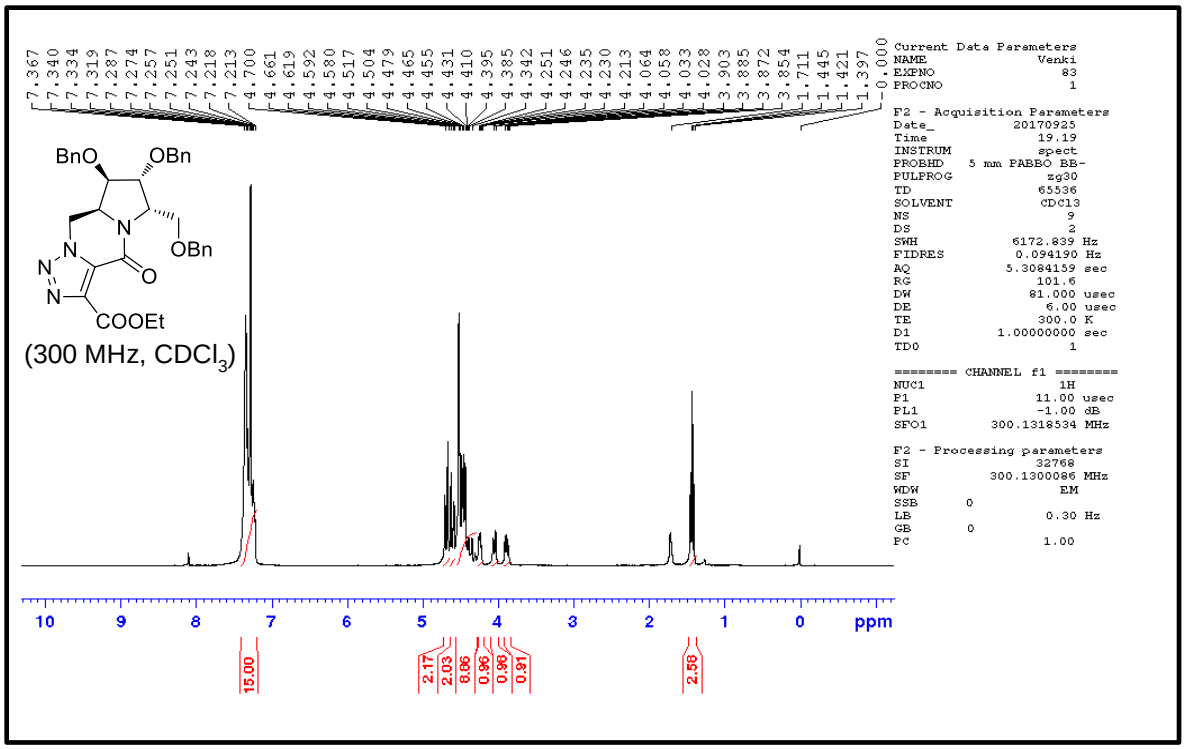
^{13}C–NMR spectrum of compound **5**



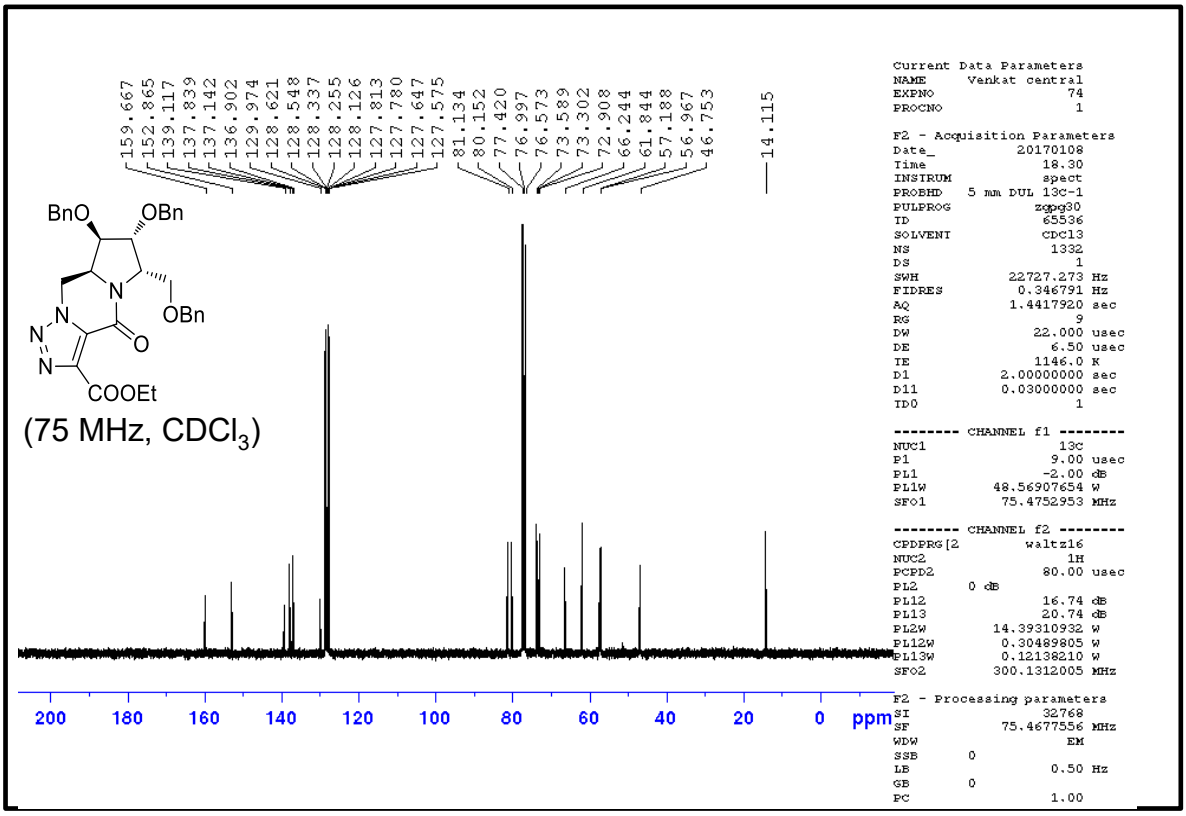
DEPT-135 spectrum of compound **5**



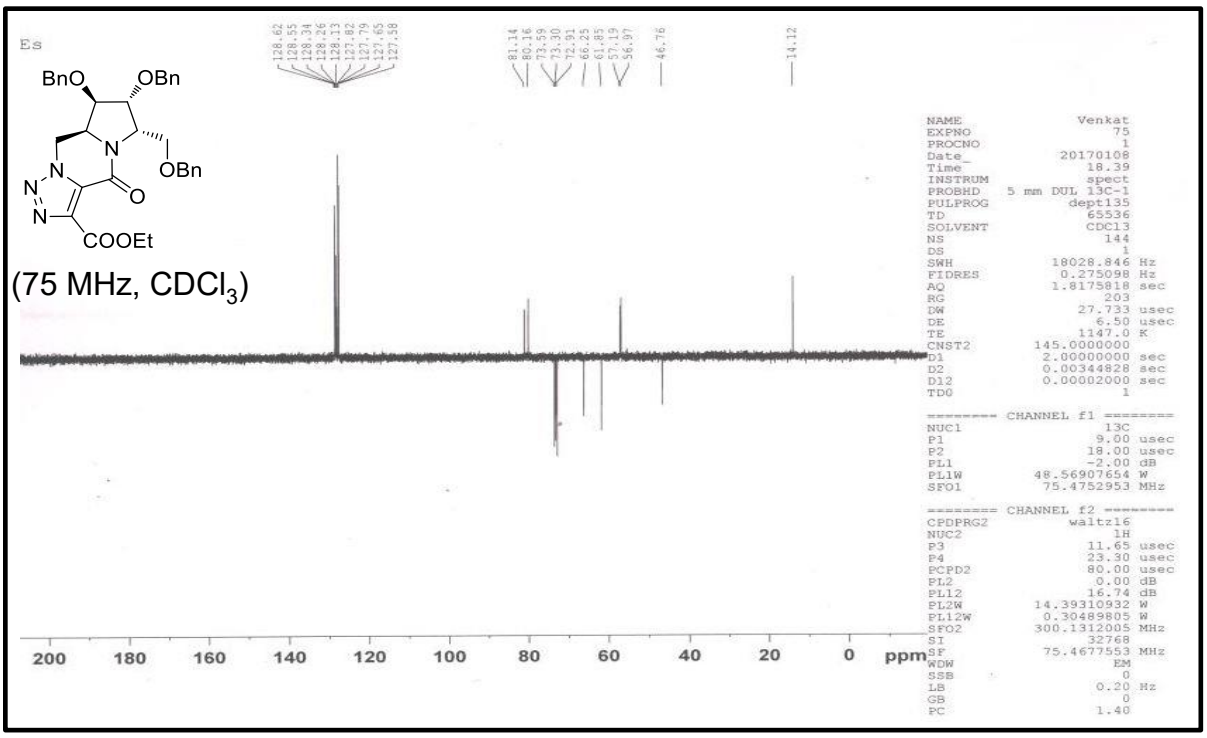
^{1}H–NMR spectrum of compound **23**



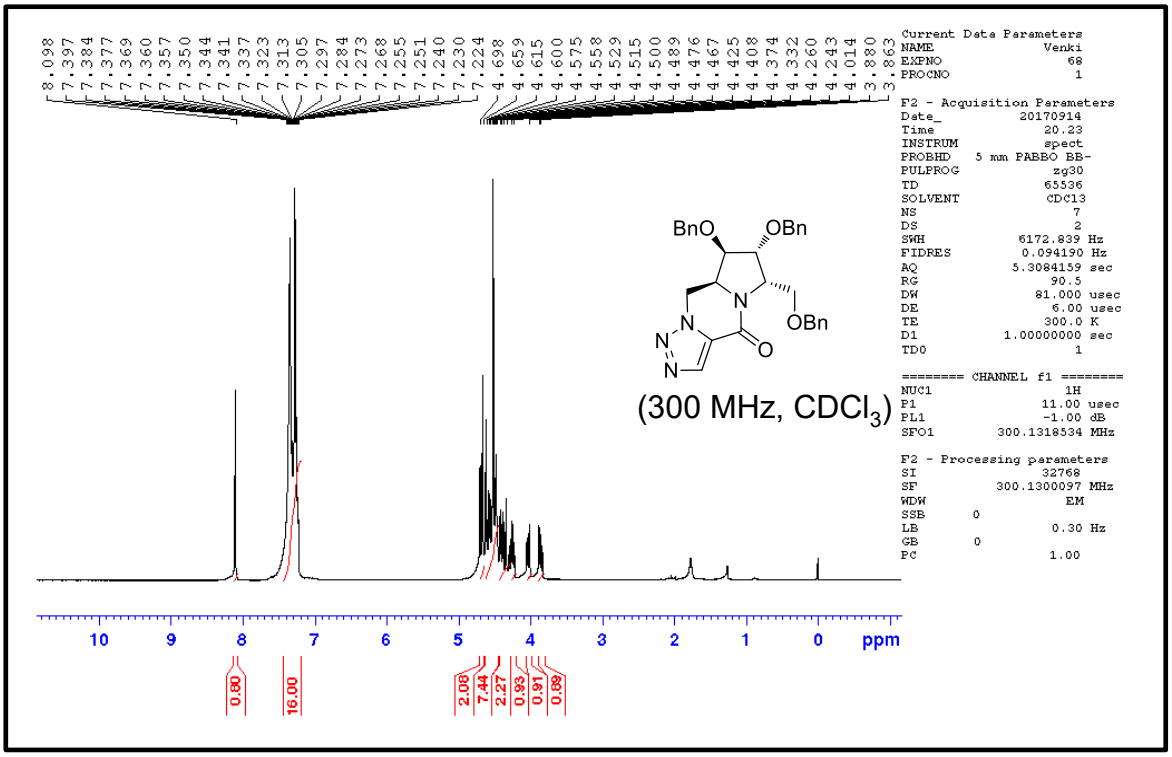
^{13}C–NMR spectrum of compound **23**



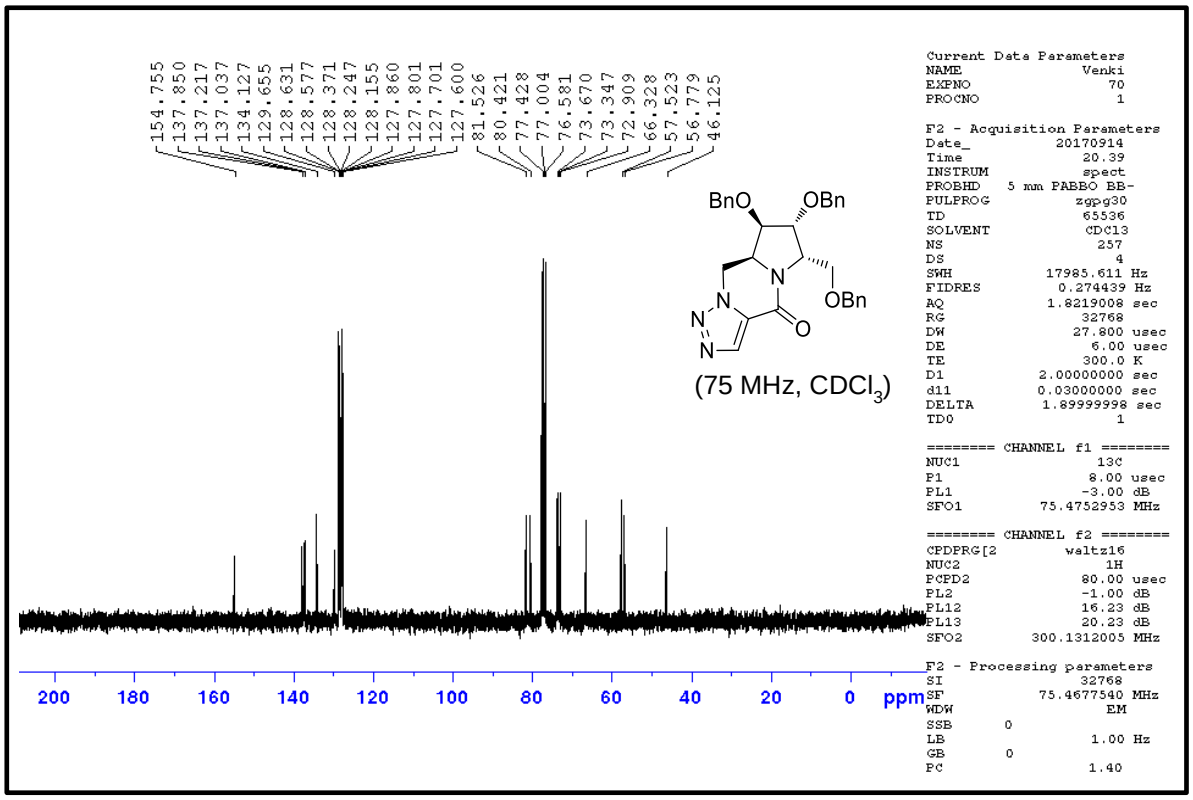
DEPT-135 spectrum of compound **23**



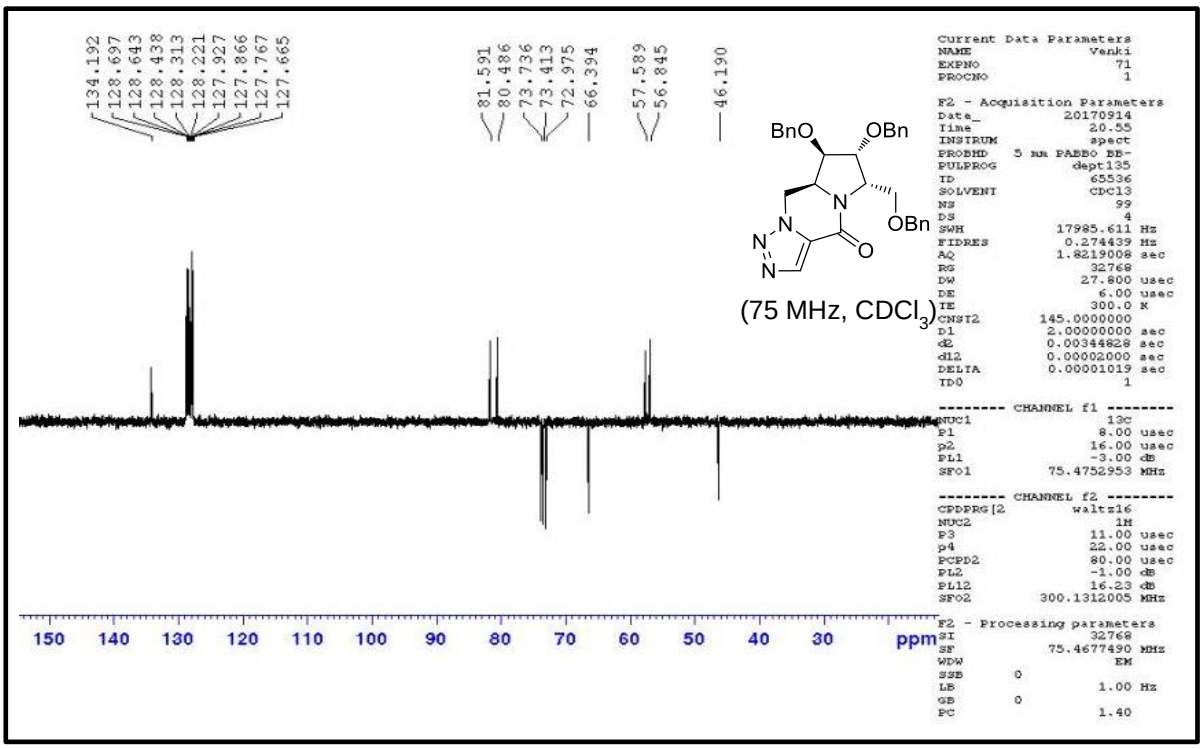
^{1}H–NMR spectrum of compound **29**



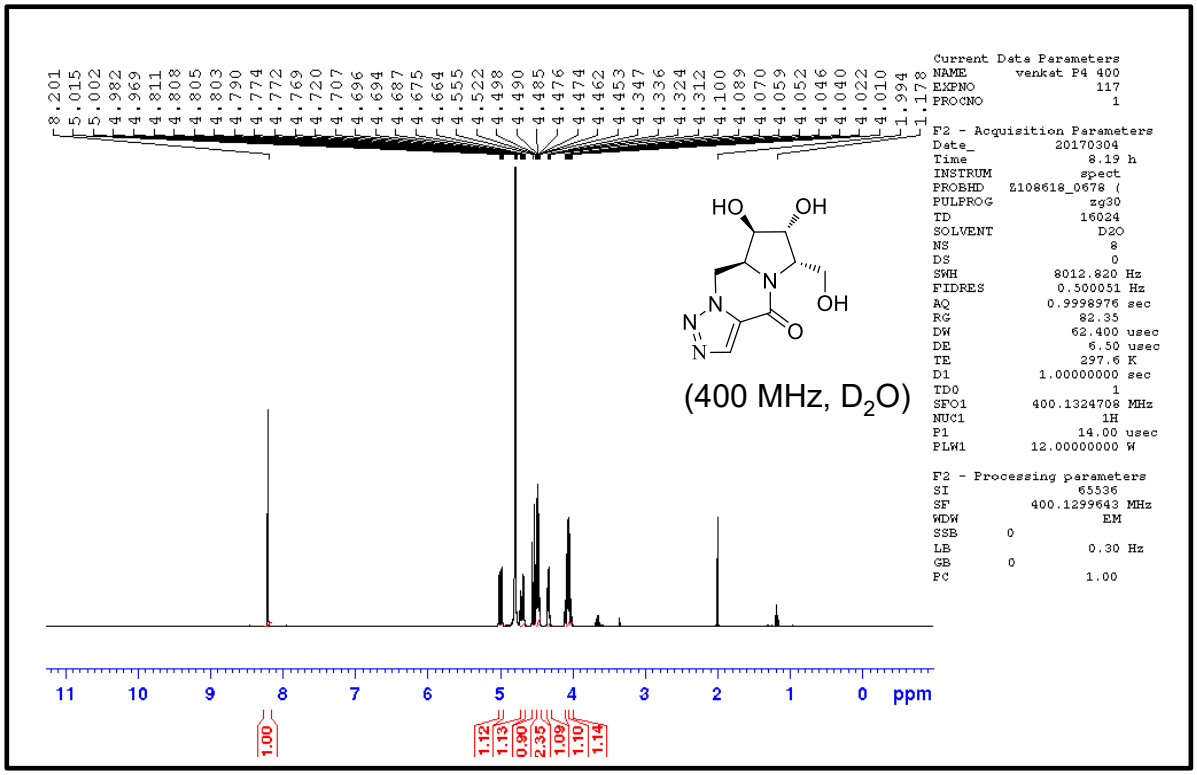
^{13}C–NMR spectrum of compound **29**



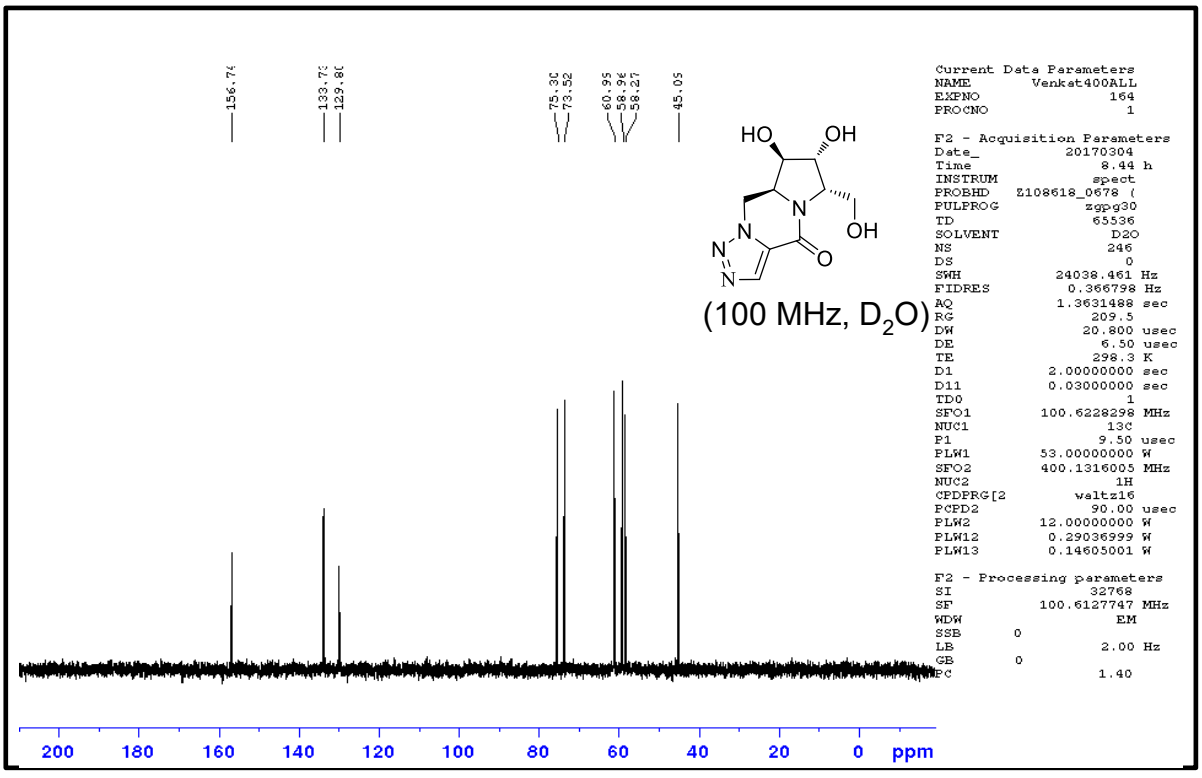
DEPT-135 spectrum of compound **29**



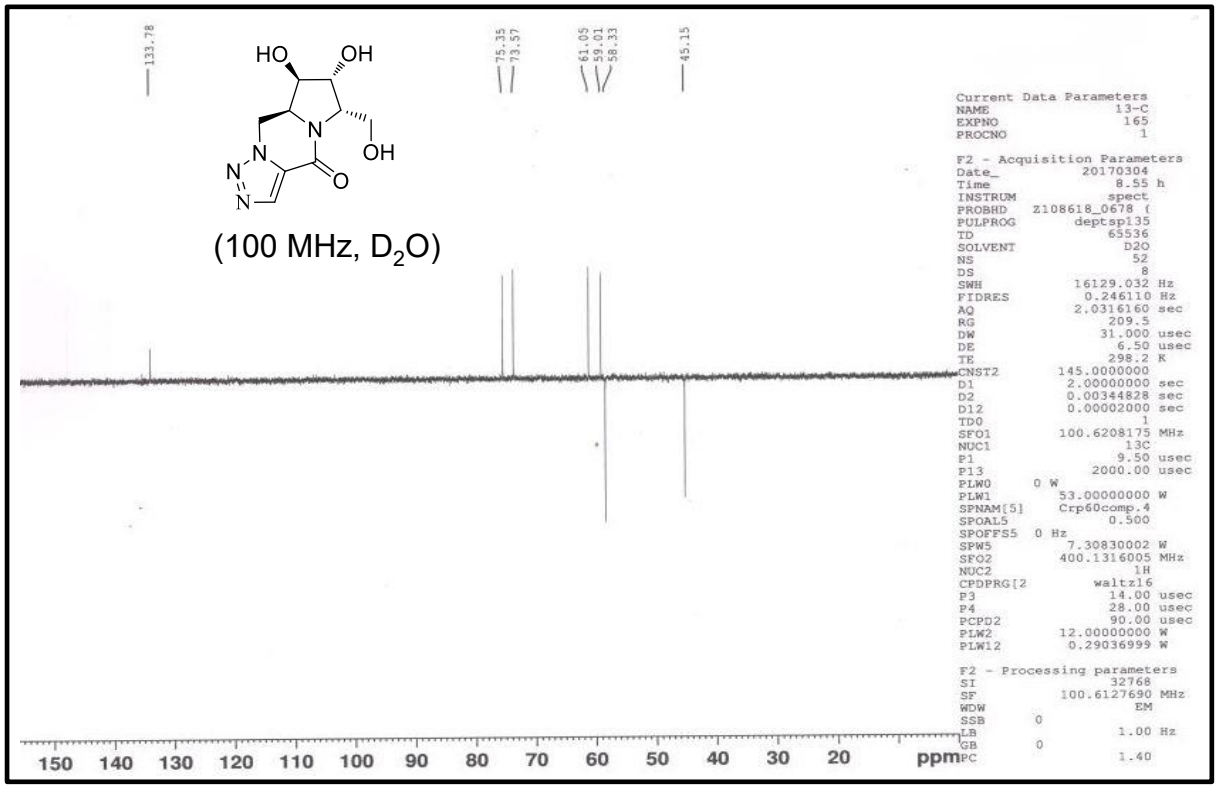
^{1}H–NMR spectrum of compound **1**



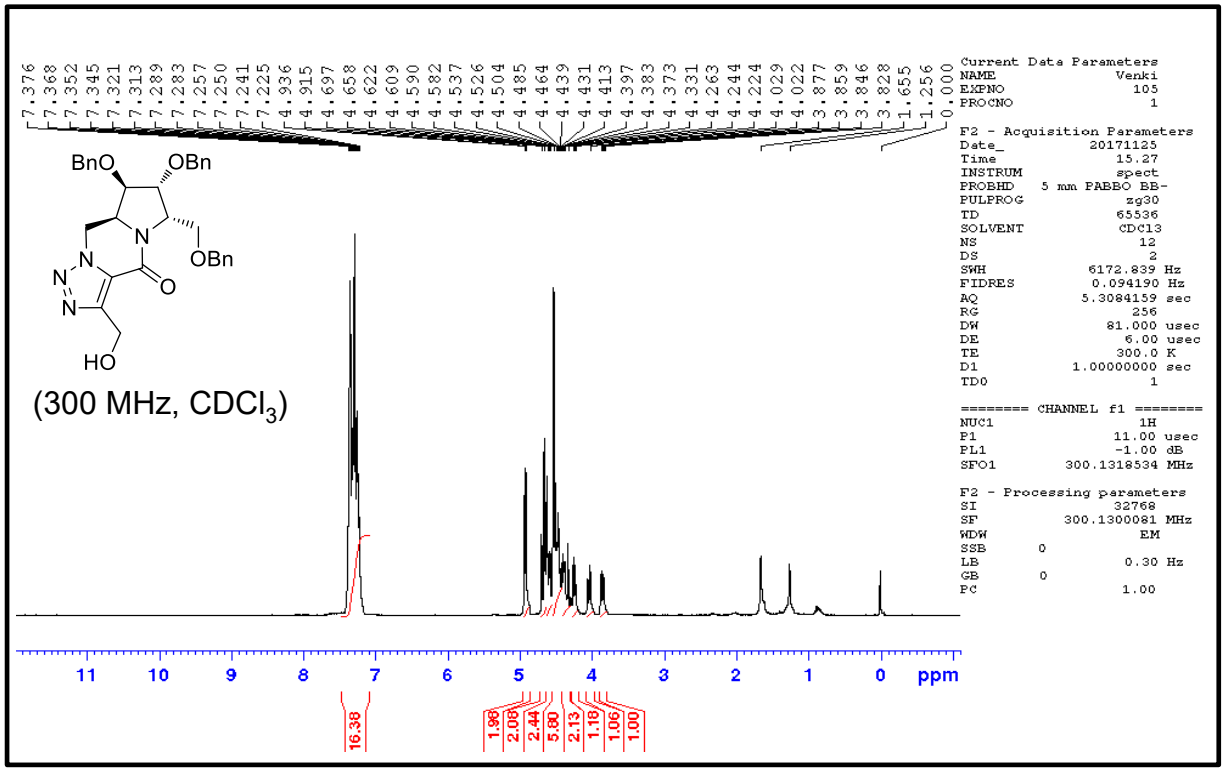
^{13}C–NMR spectrum of compound **1**



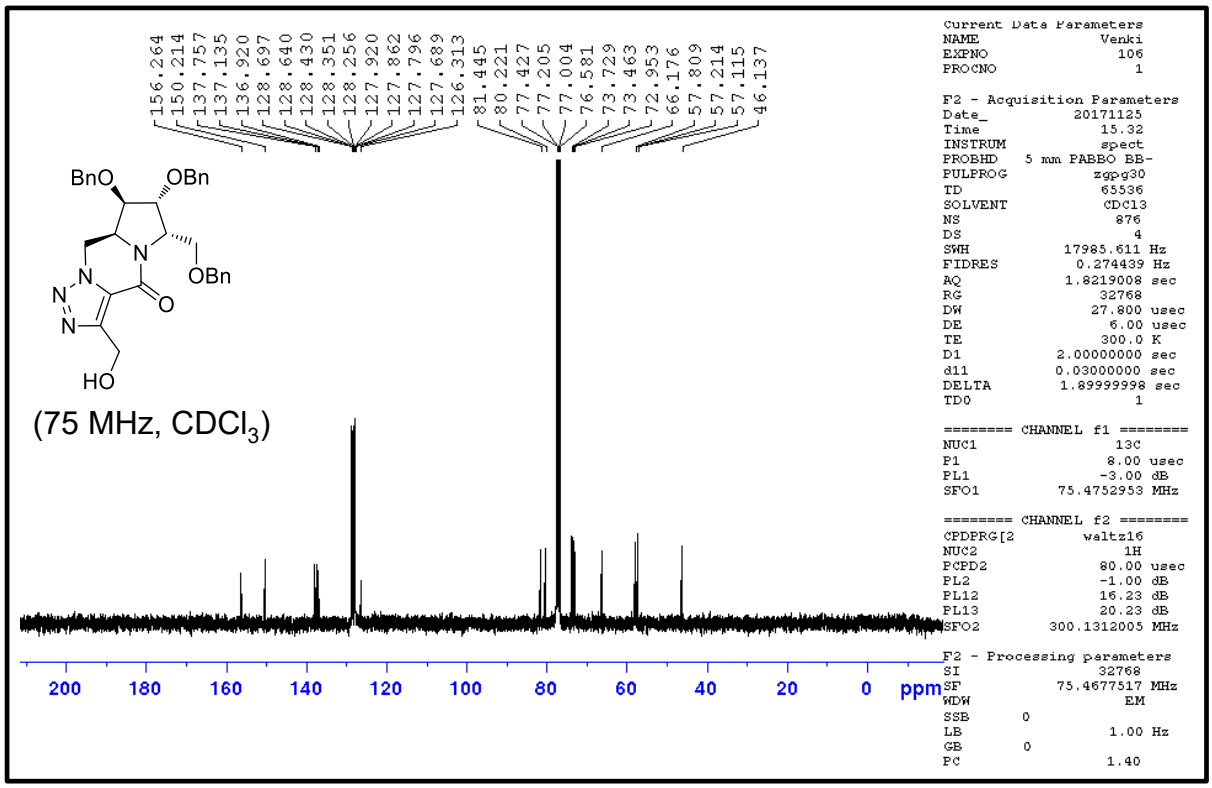
DEPT-135 spectrum of compound **1**



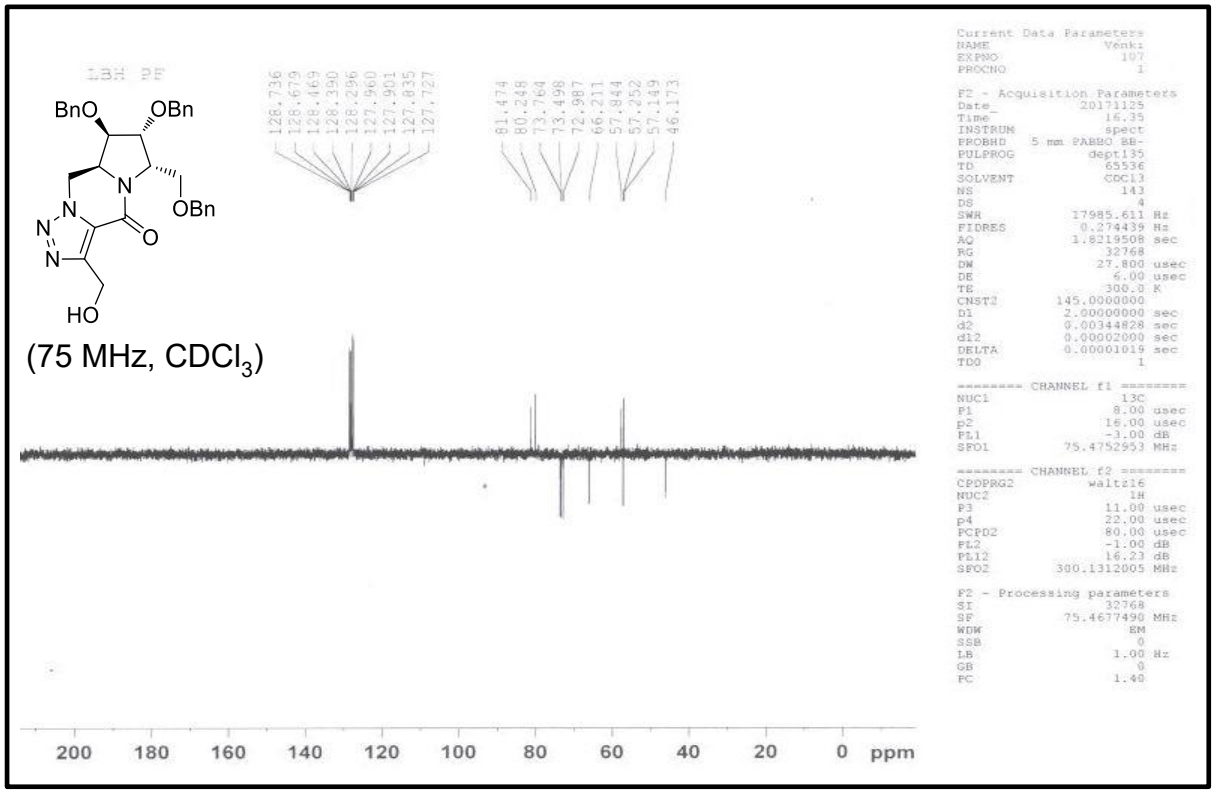
^{1}H–NMR spectrum of compound **25**



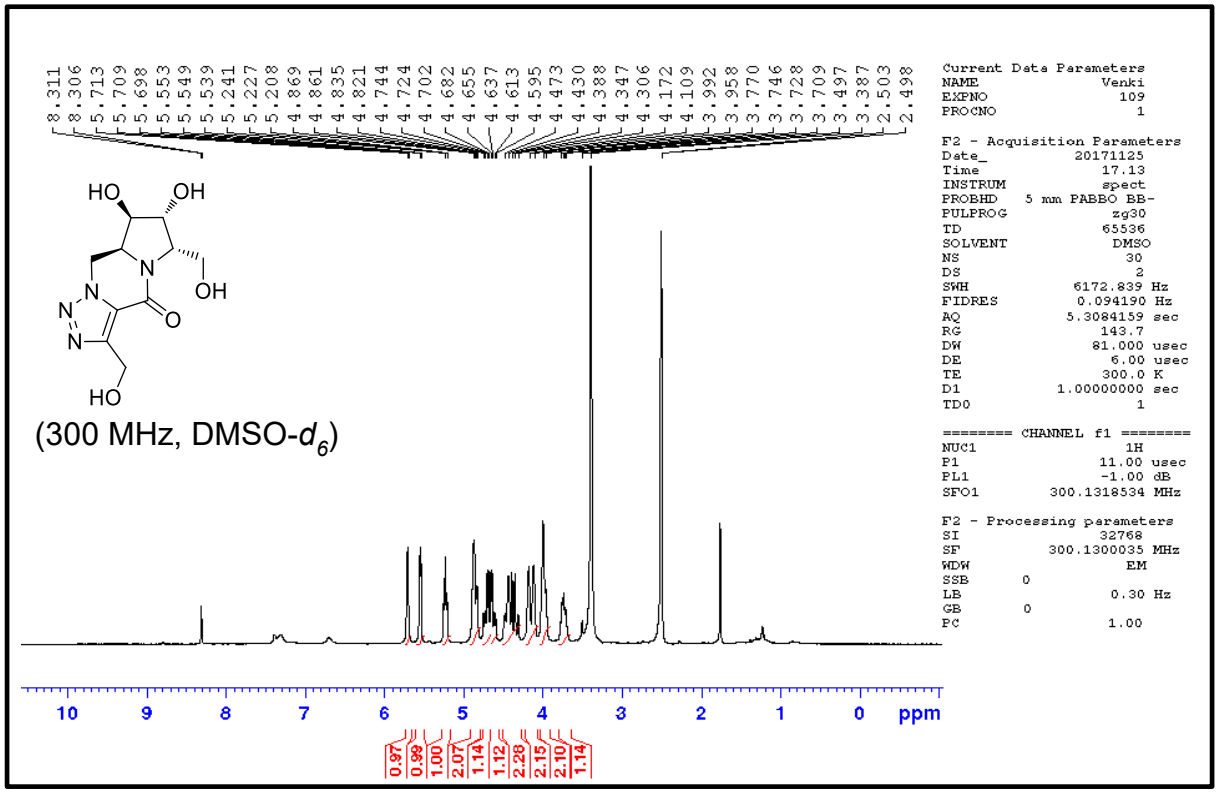
^{13}C–NMR spectrum of compound **25**



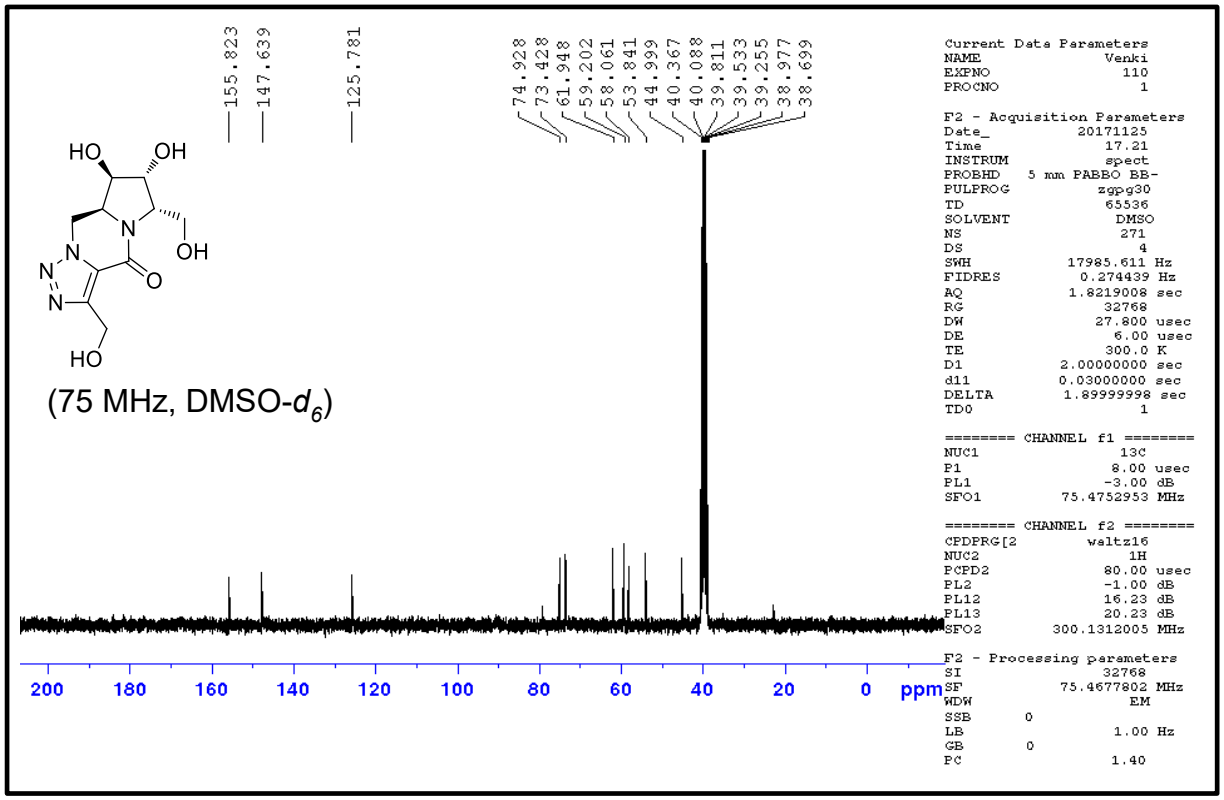
DEPT-135 spectrum of compound **25**



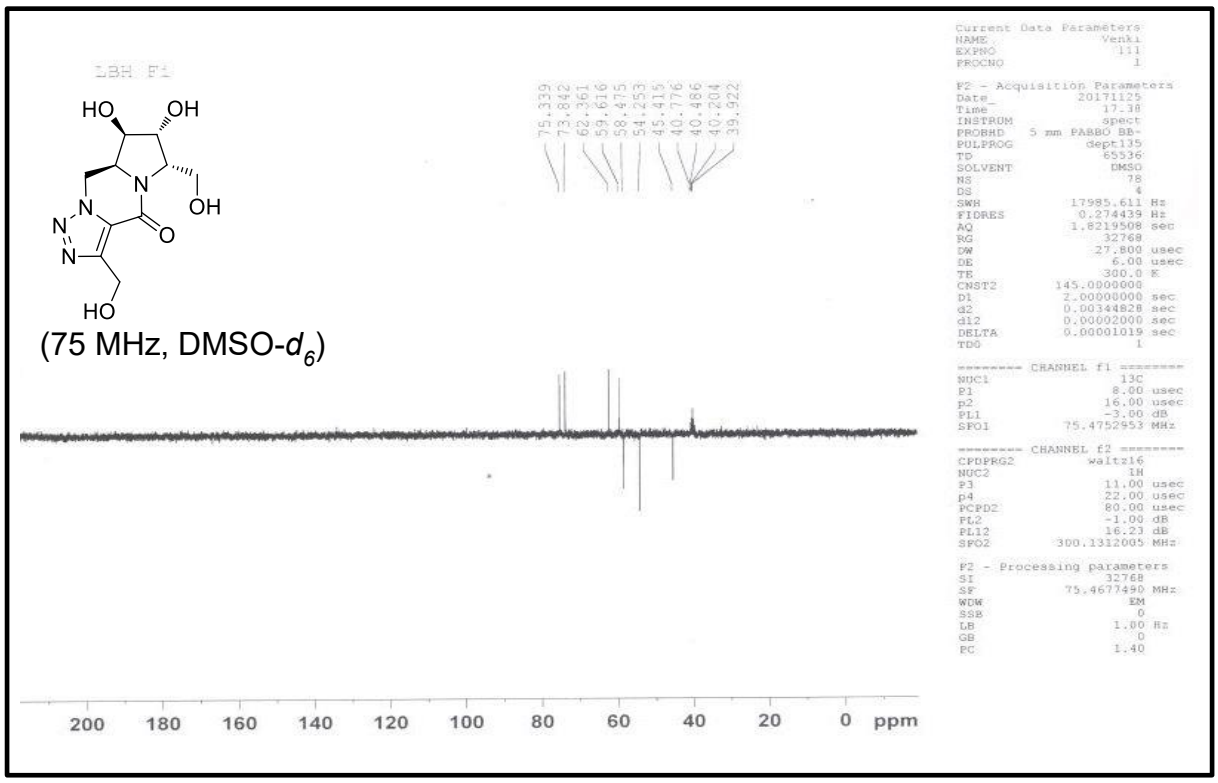
^{1}H–NMR spectrum of compound **2**



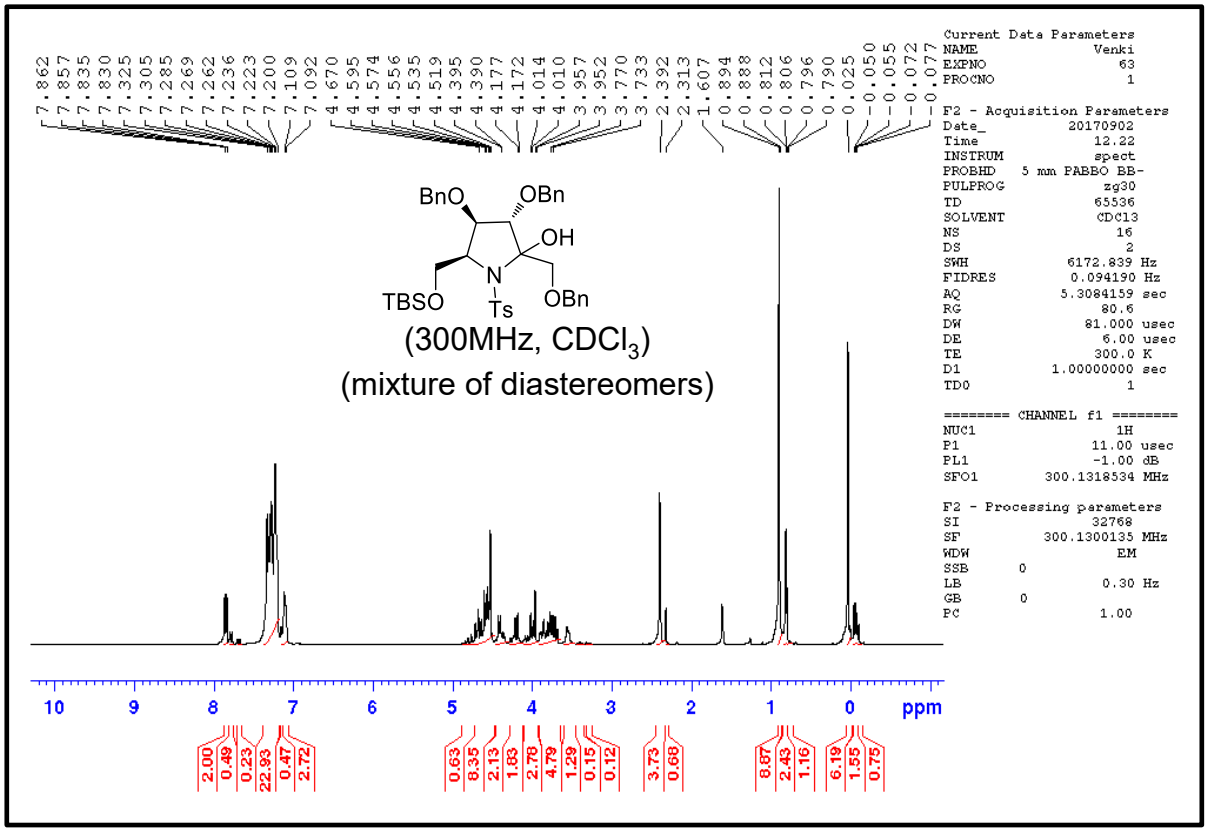
^{13}C–NMR spectrum of compound **2**



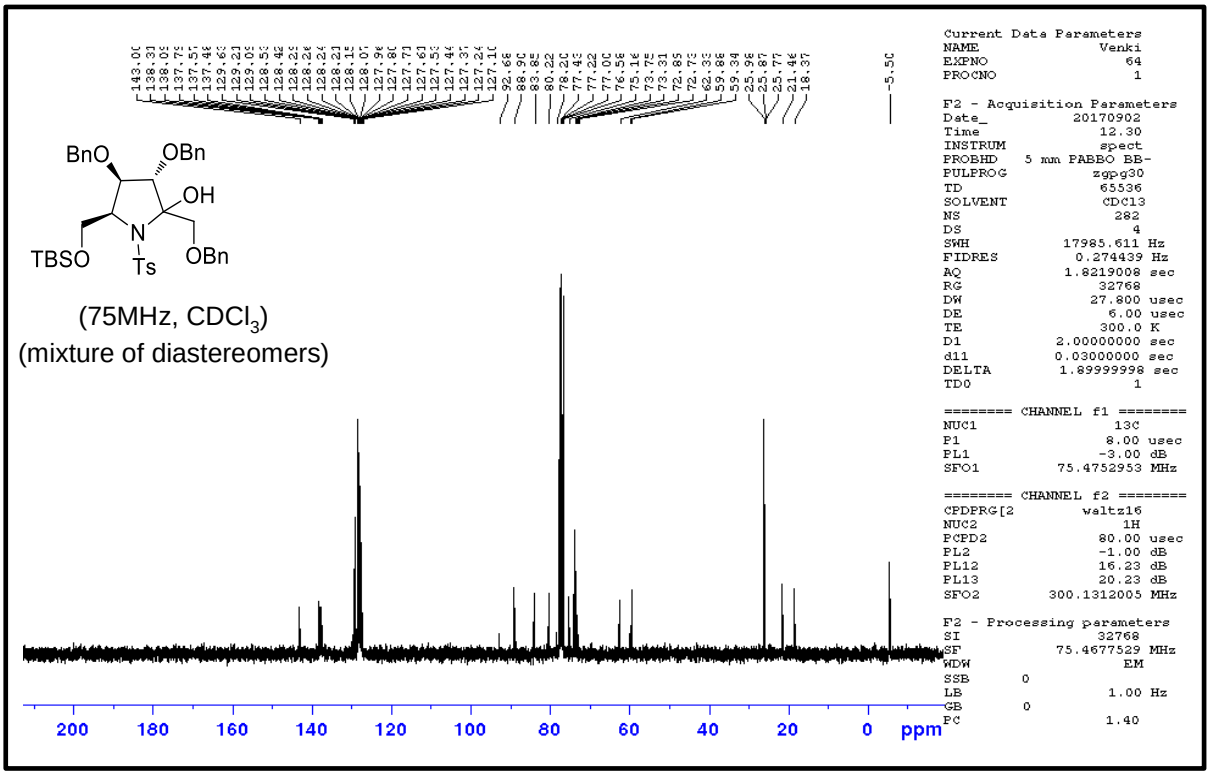
DEPT-135 spectrum of compound **2**



^{1}H–NMR spectrum of compound **15**

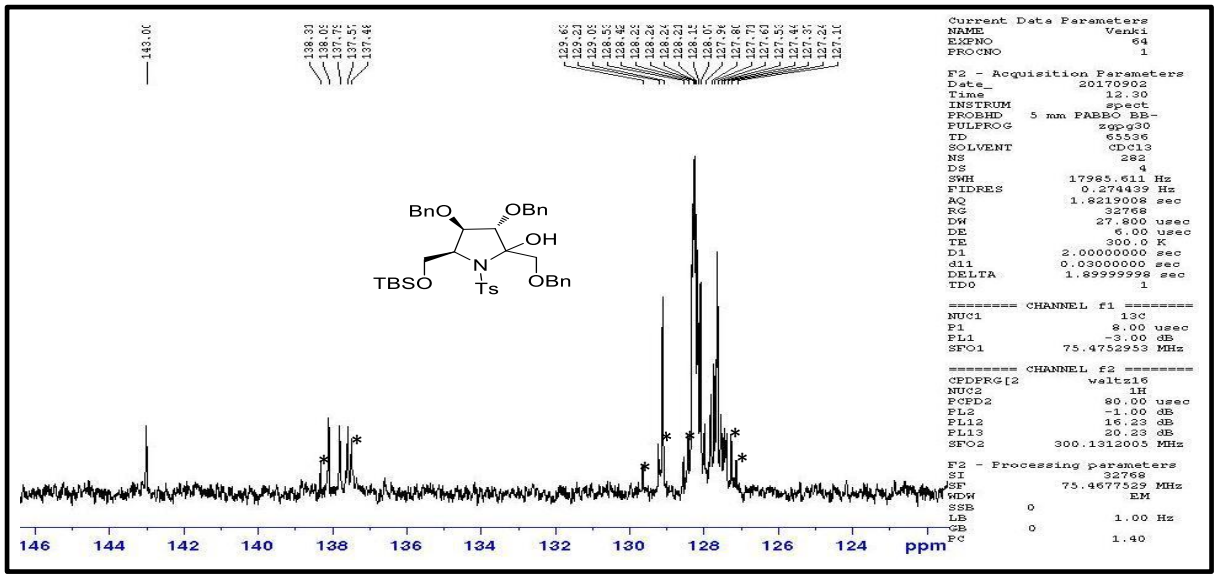


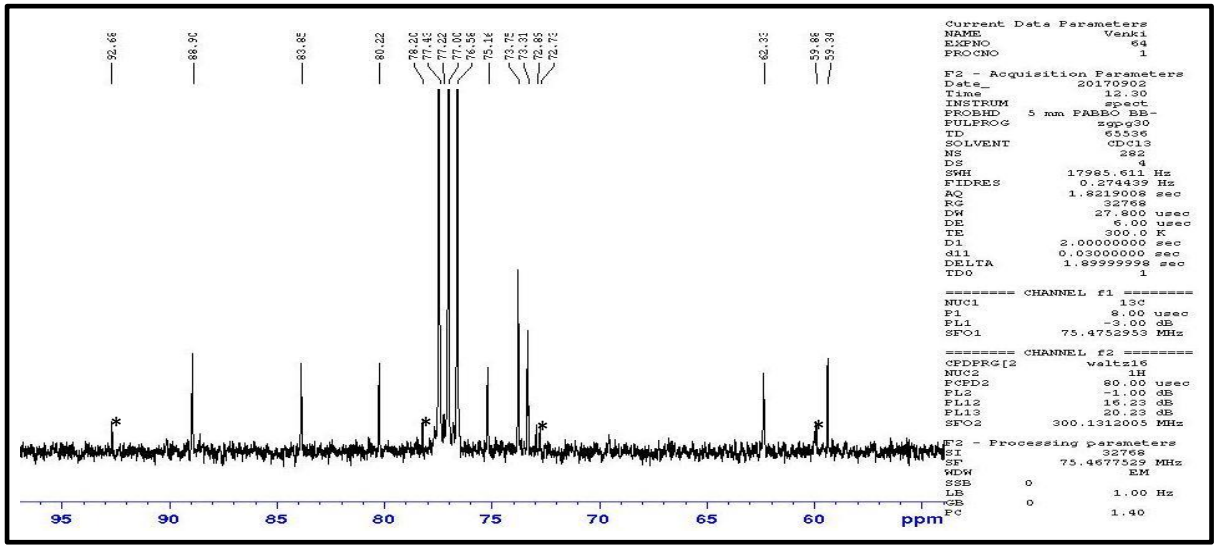
^{13}C–NMR spectrum of compound **15**

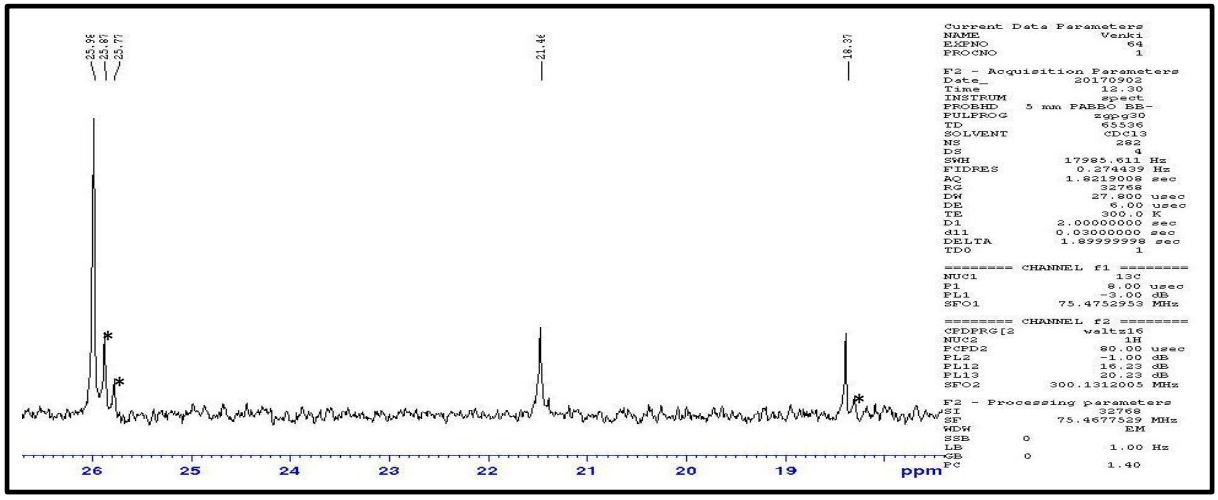


^{13}C-NMR spectrum of compound **15** (expanded)

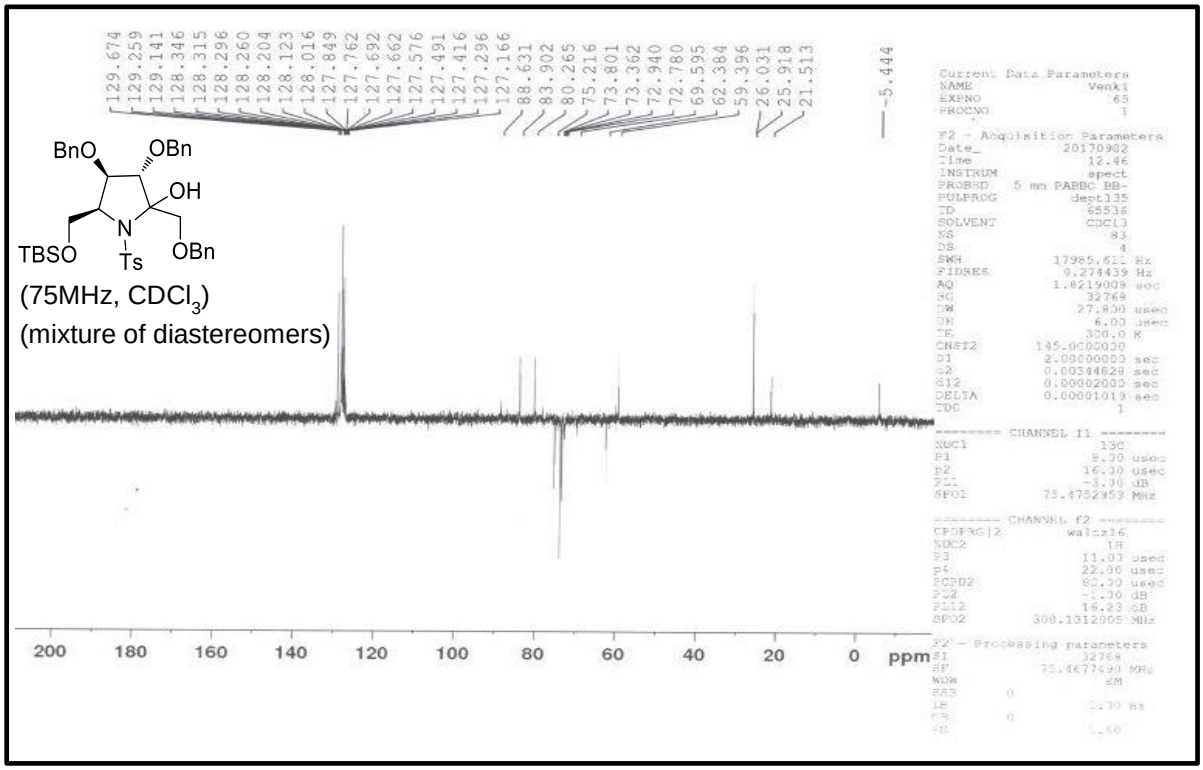
*indicates signals due to diastereomers



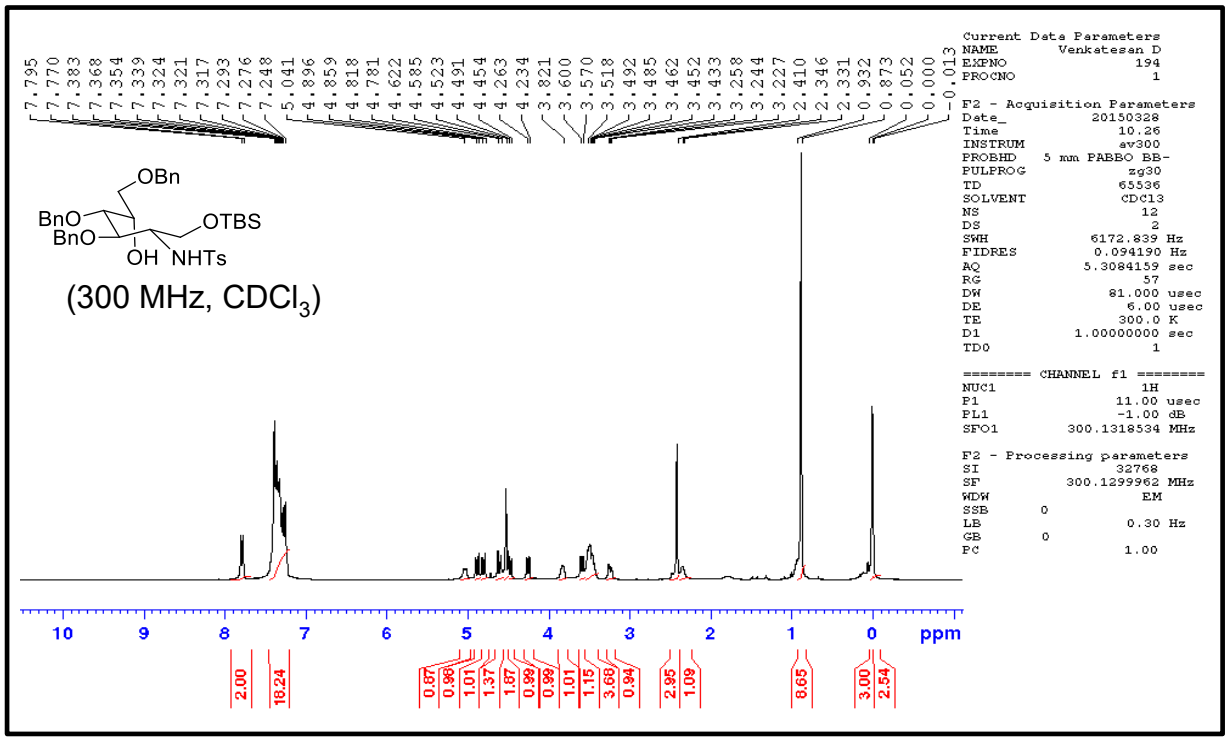




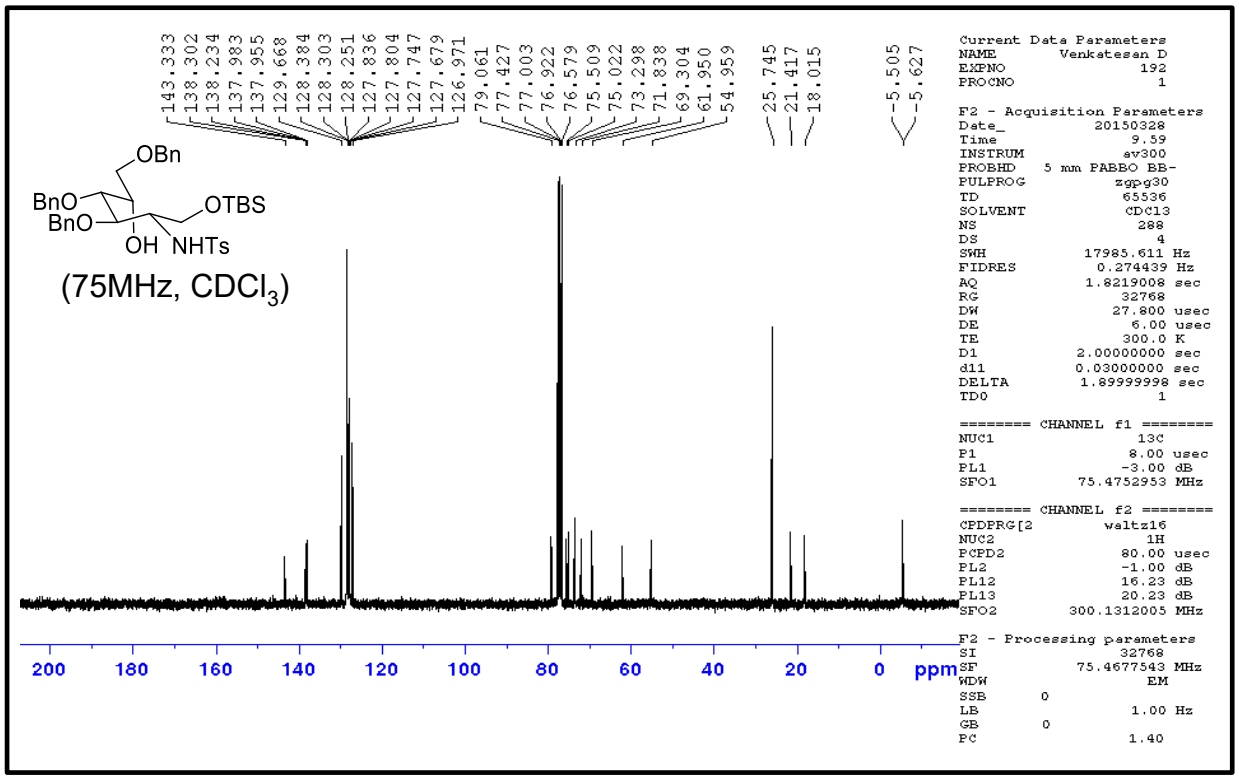
DEPT-135 spectrum of compound **15**



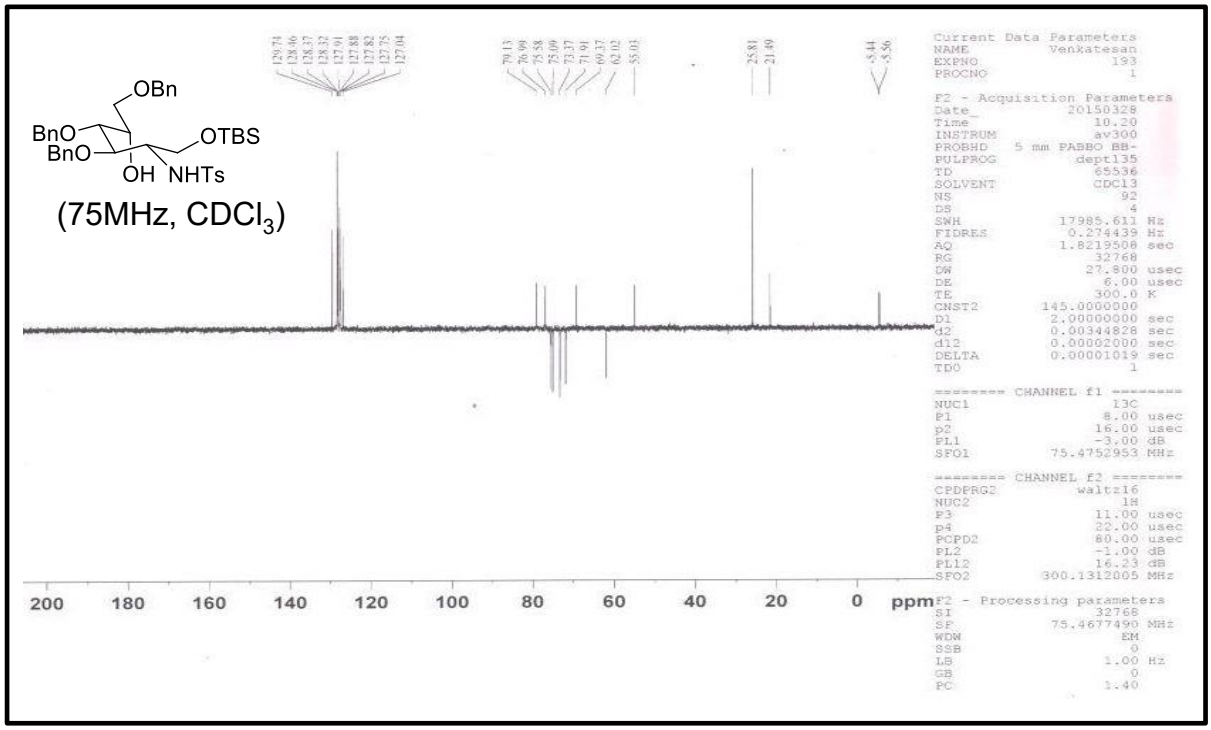
^{1}H–NMR spectrum of compound **16**



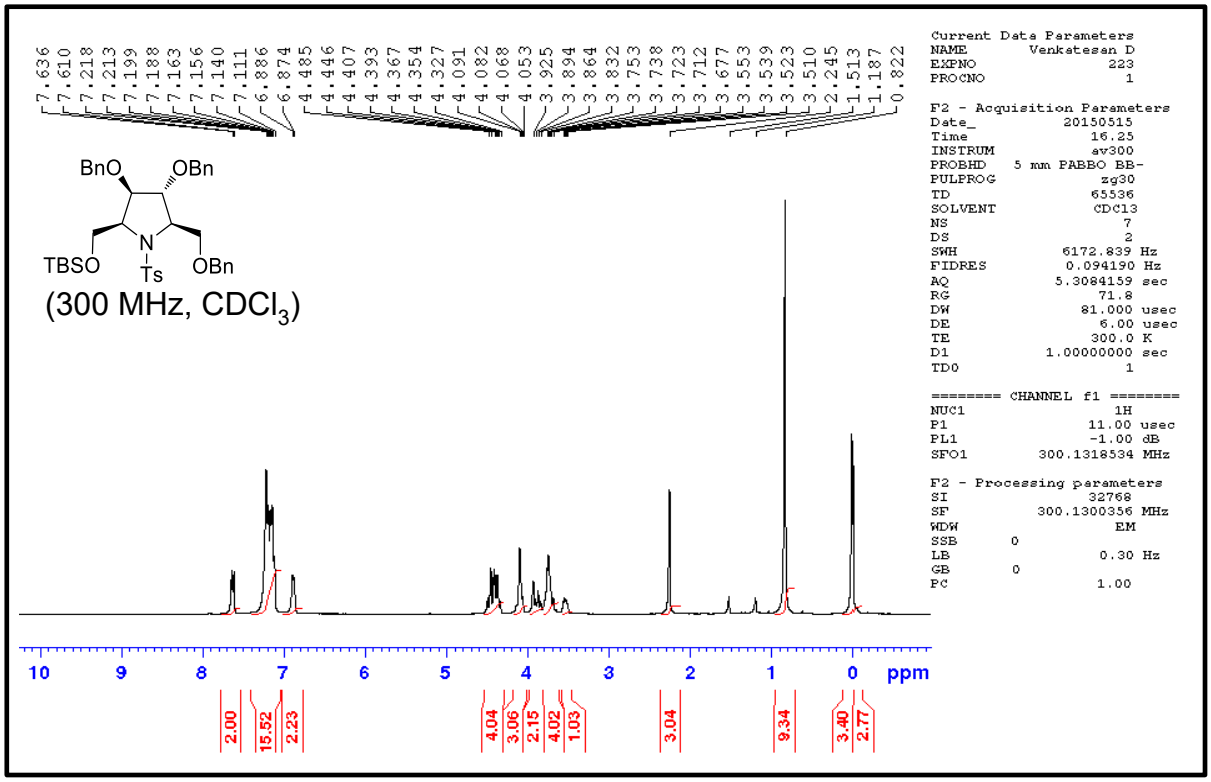
^{13}C–NMR spectrum of compound **16**



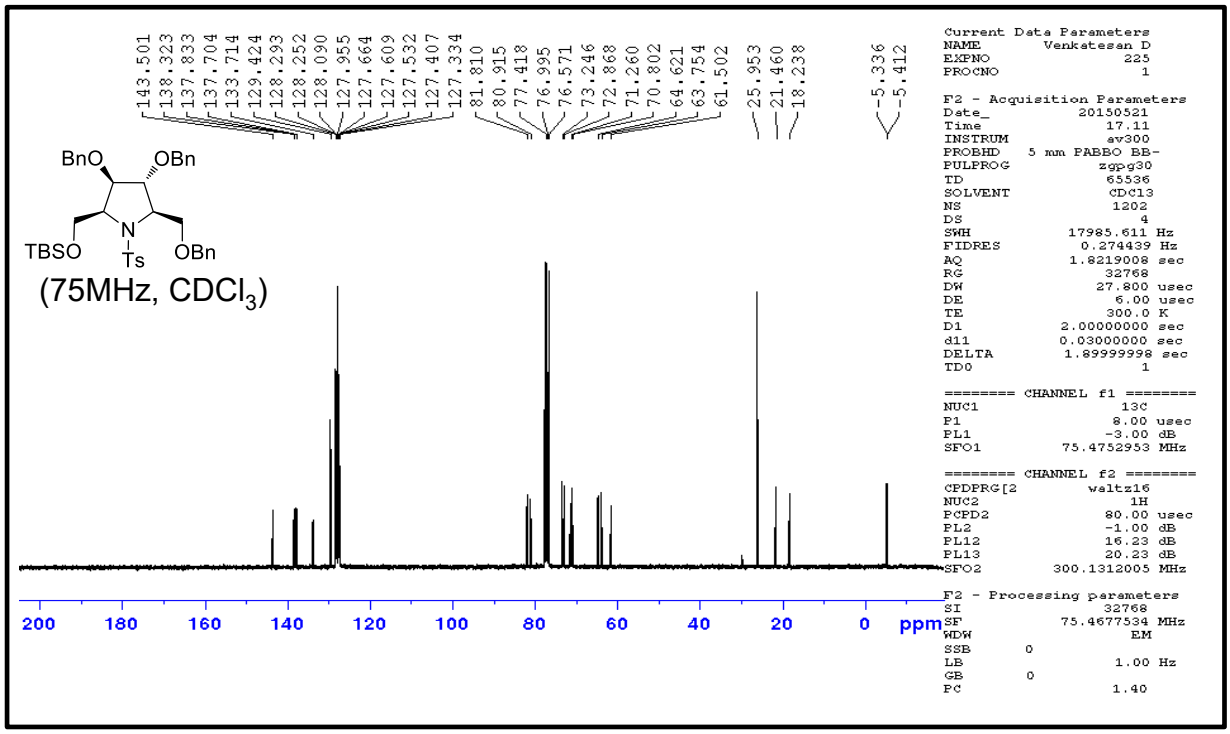
DEPT-135 spectrum of compound **16**



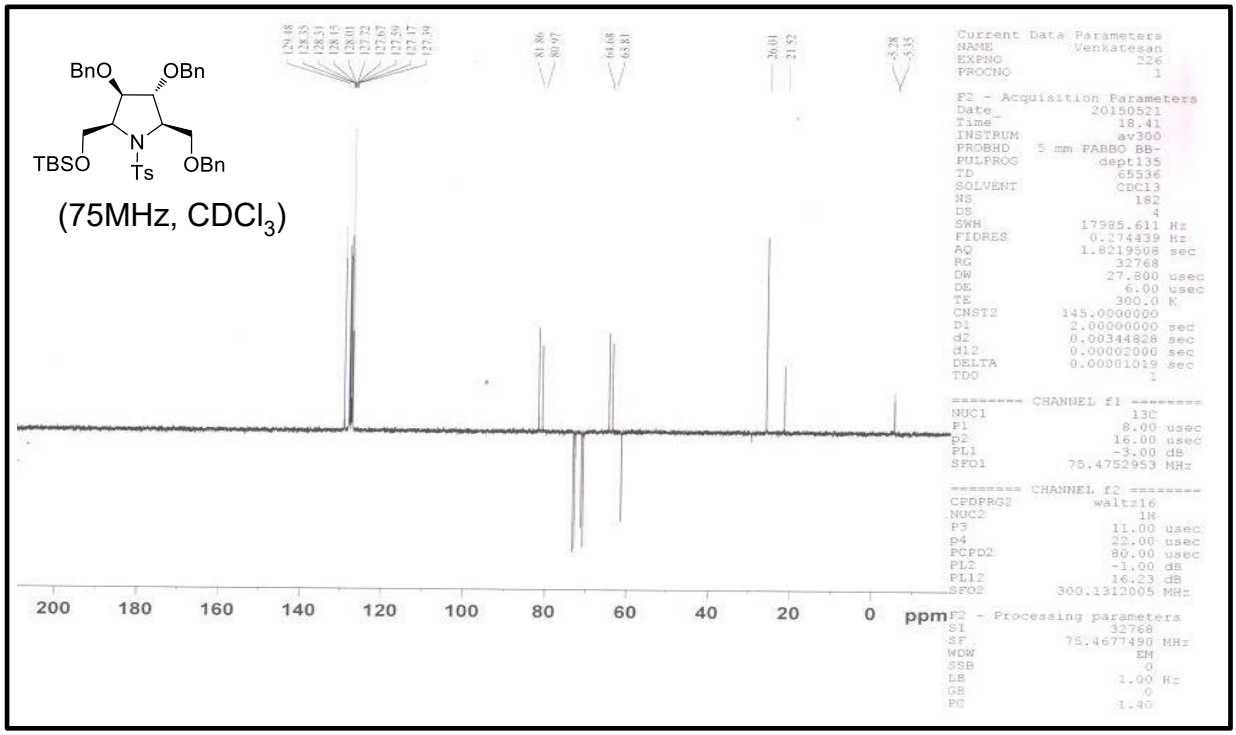
^{1}H–NMR spectrum of compound **12**



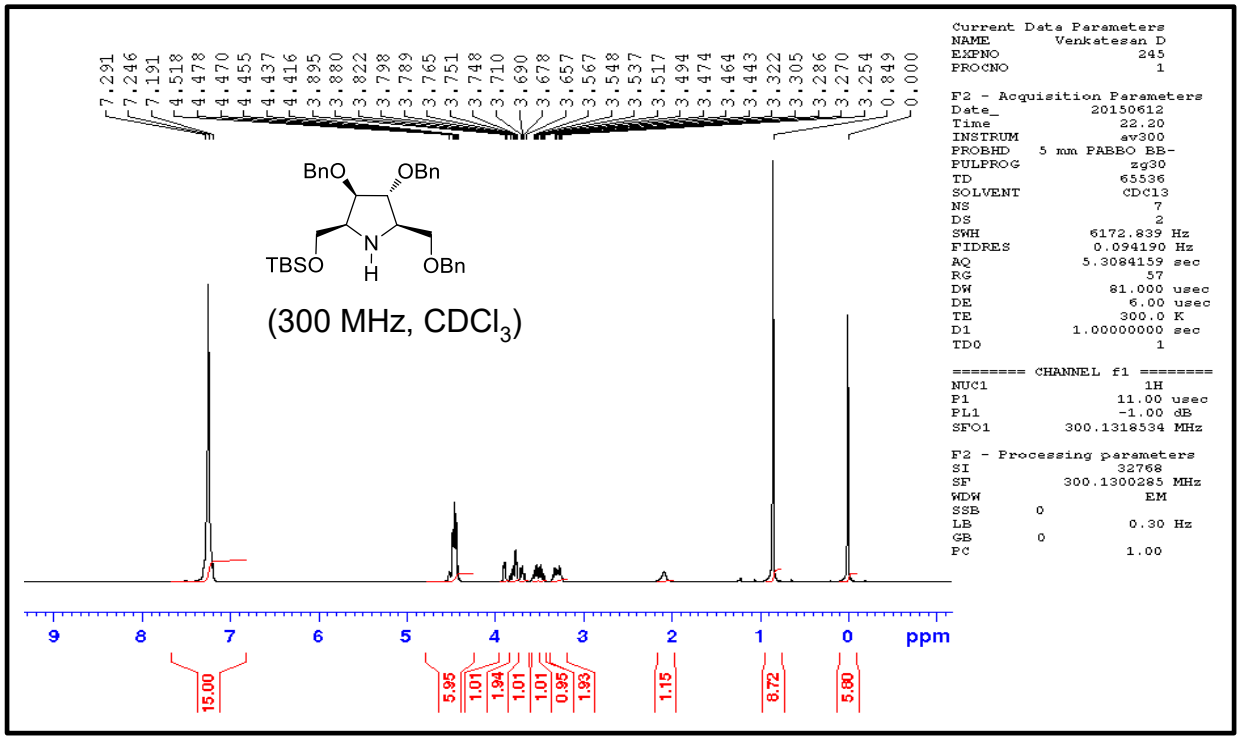
^{13}C–NMR spectrum of compound **12**



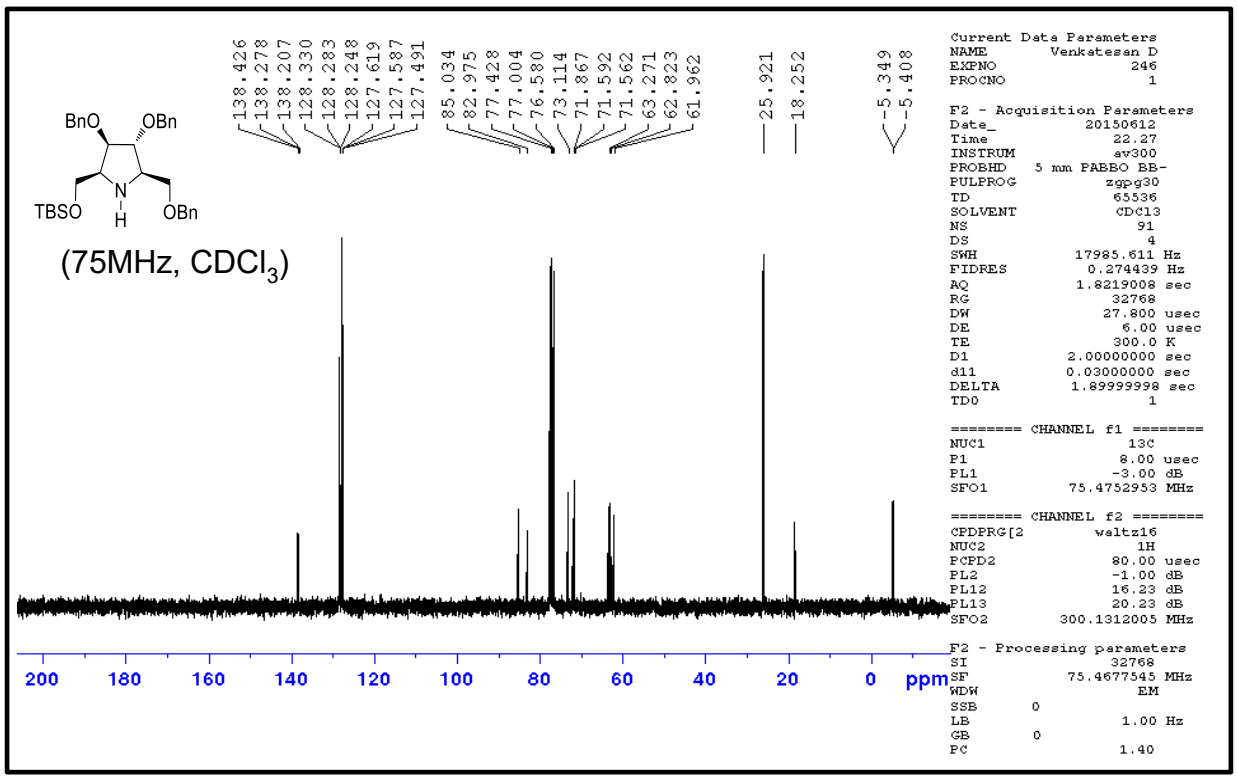
DEPT-135 spectrum of compound **12**



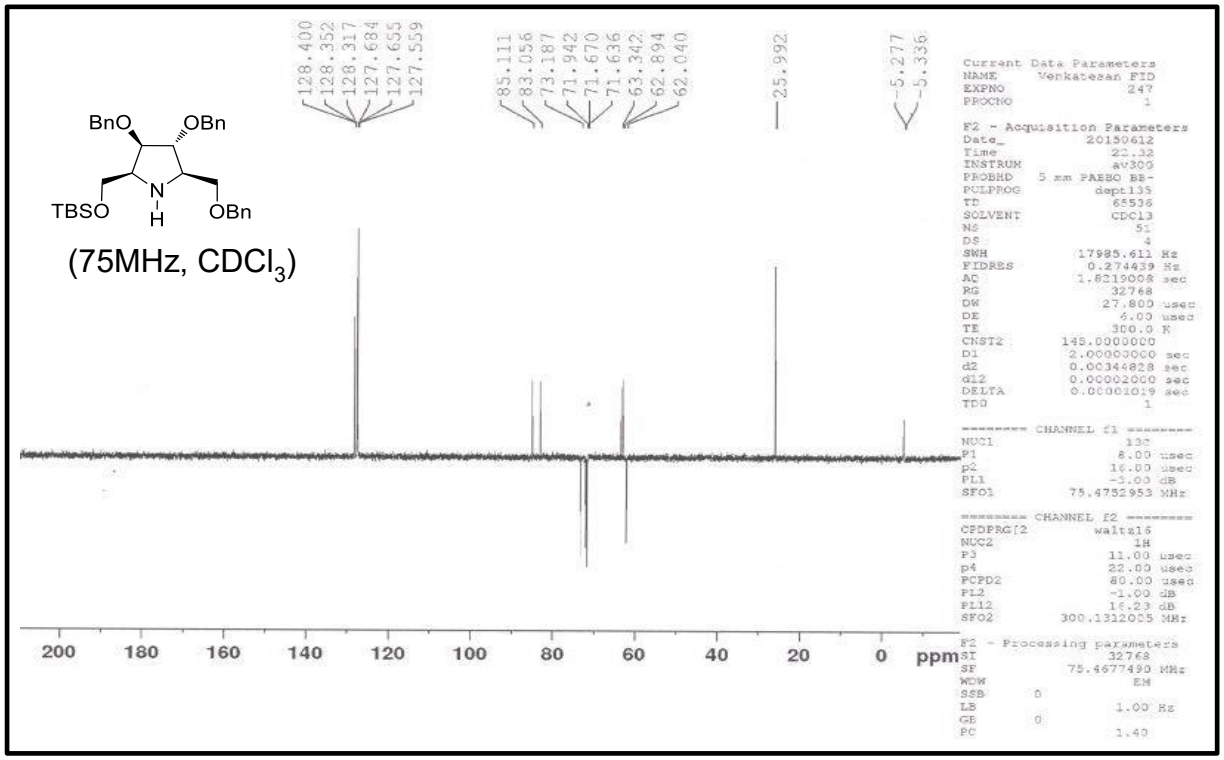
^{1}H–NMR spectrum of compound **18**



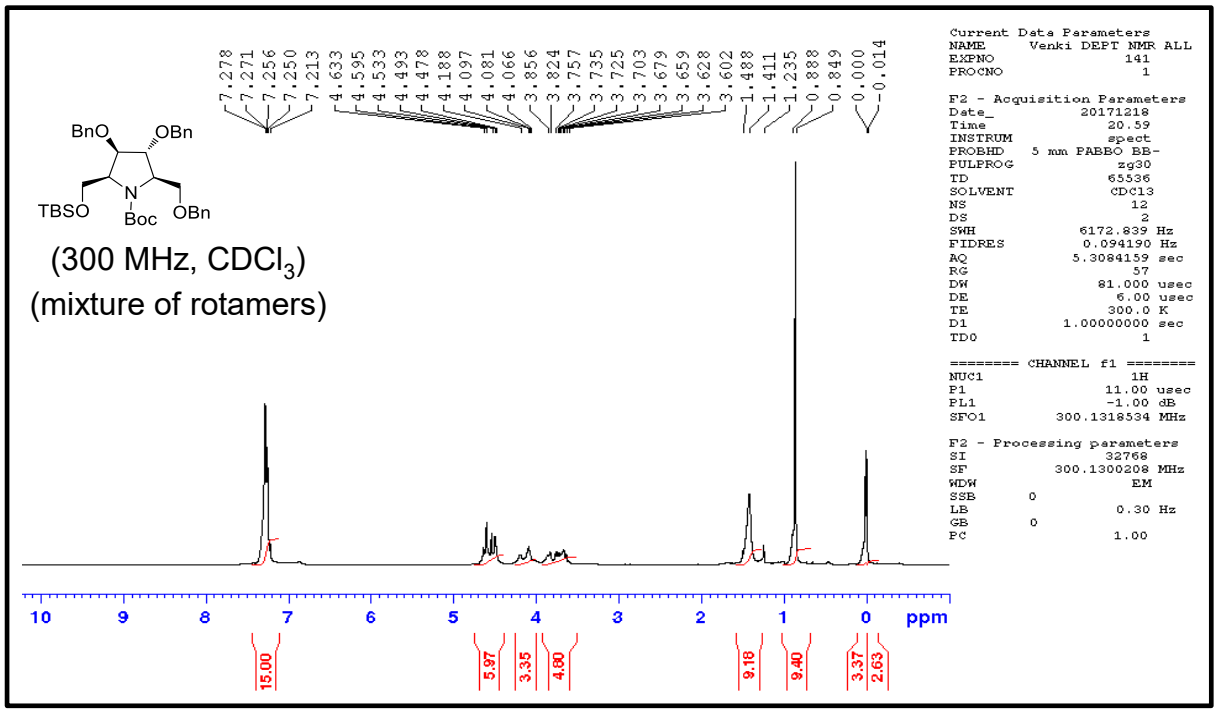
^{13}C–NMR spectrum of compound **18**



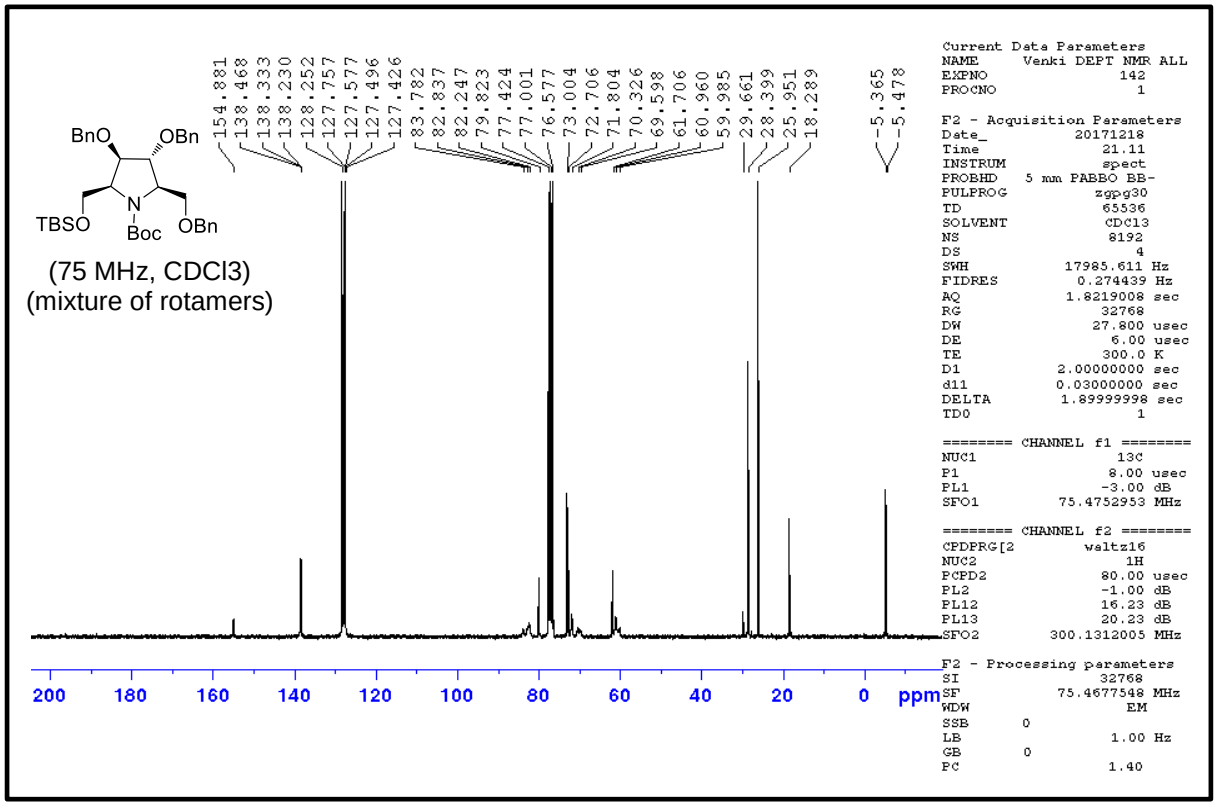
DEPT-135 spectrum of compound **18**



^{1}H–NMR spectrum of compound **20**

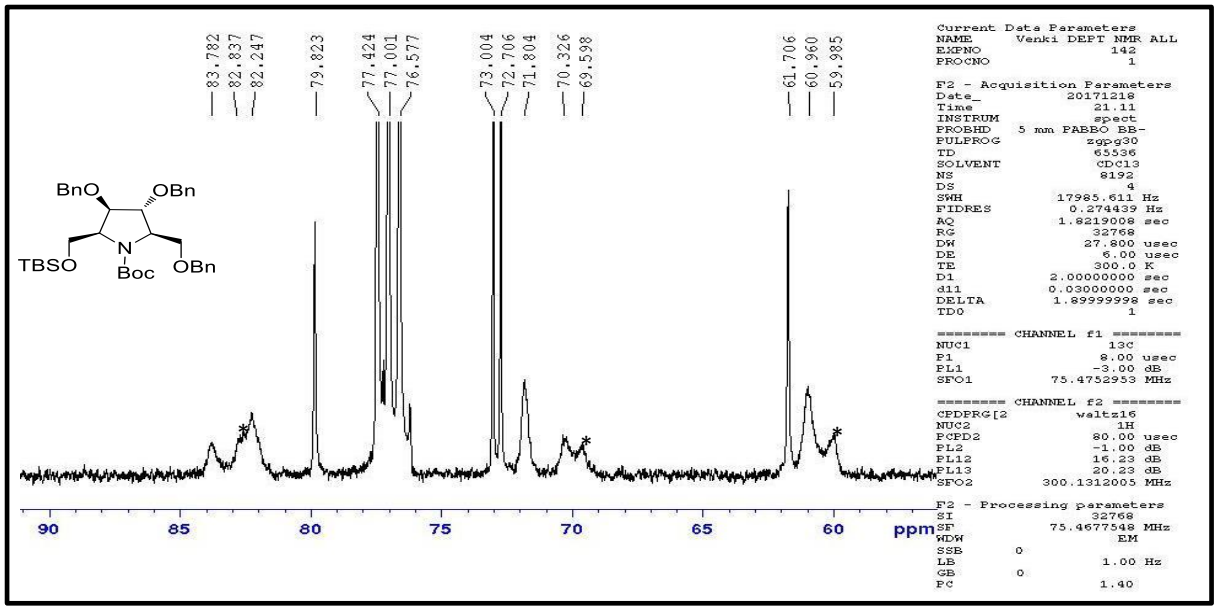


^{13}C–NMR spectrum of compound **20**

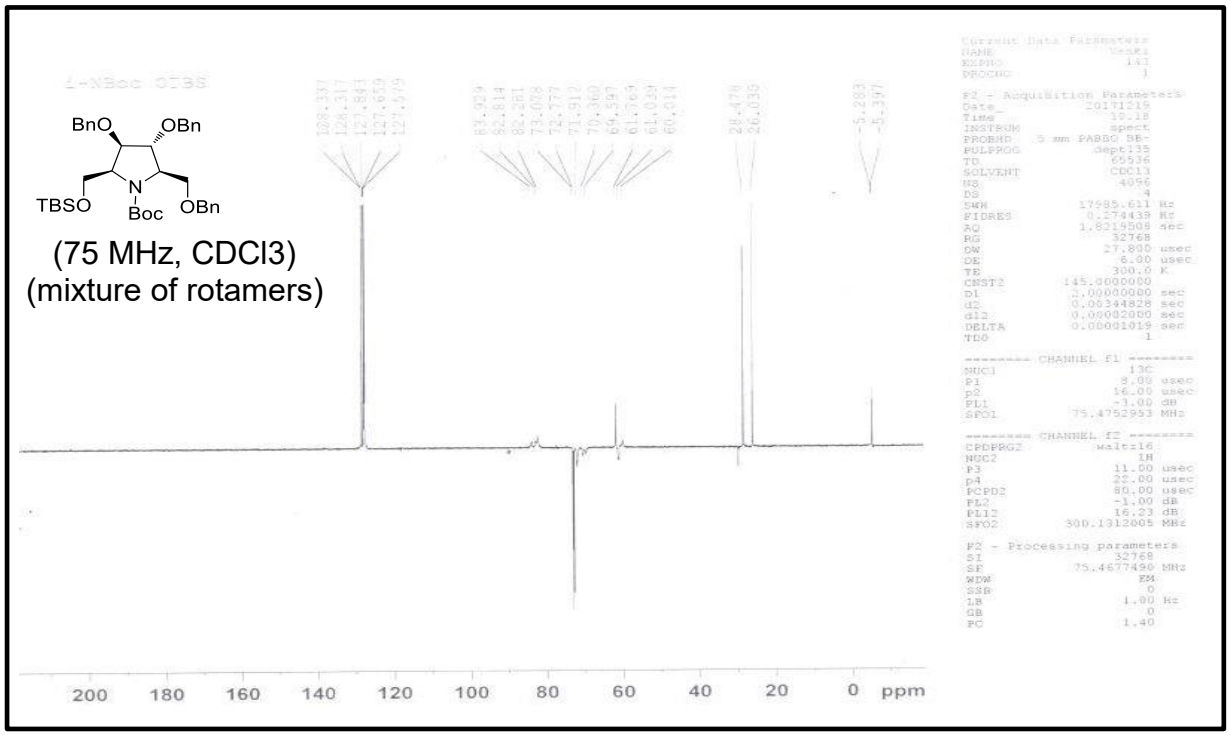


^{13}C-NMR spectrum of compound **20** (expanded)

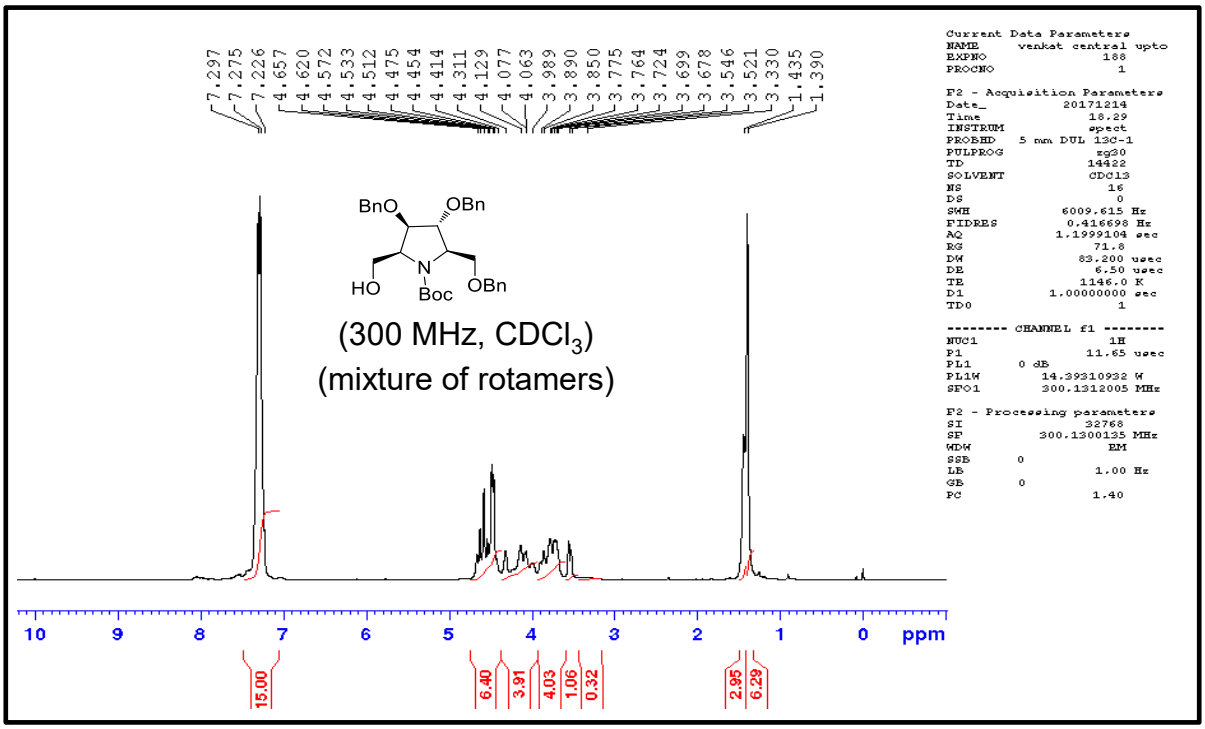
*indicates signals due to rotamers



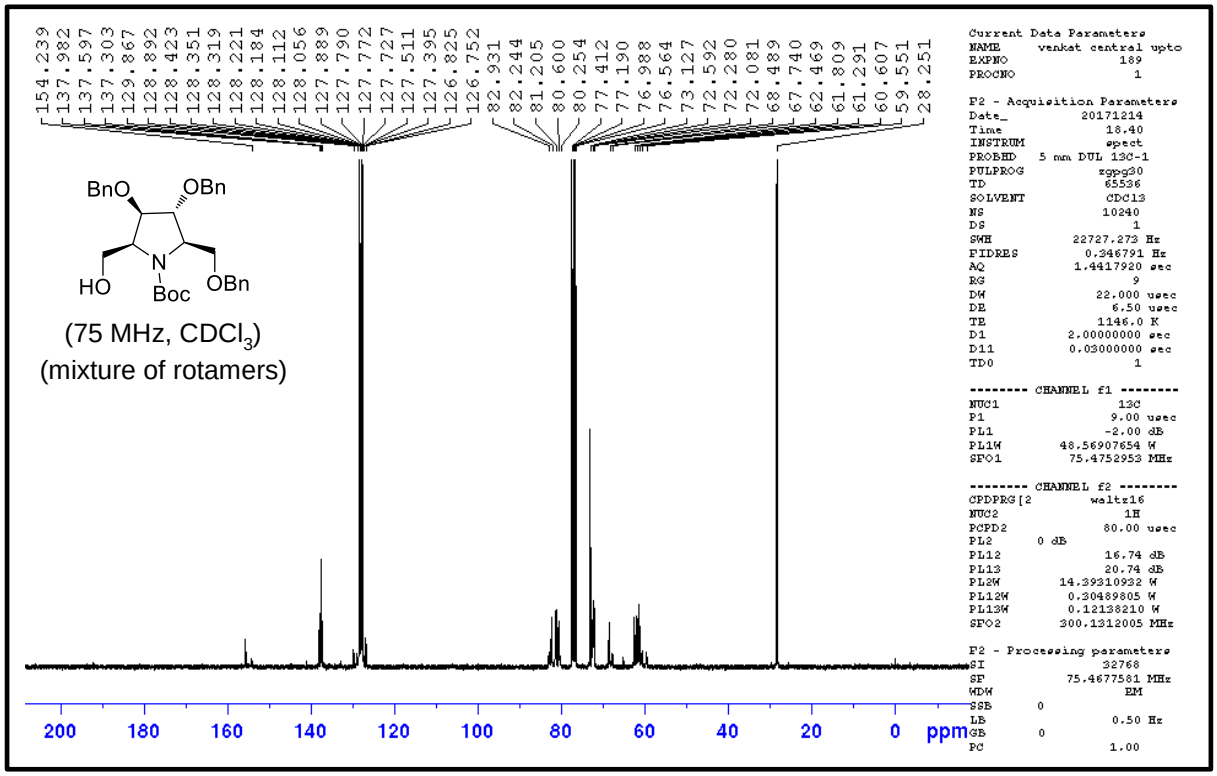
DEPT-135 spectrum of compound **20**



^{1}H–NMR spectrum of compound **10**

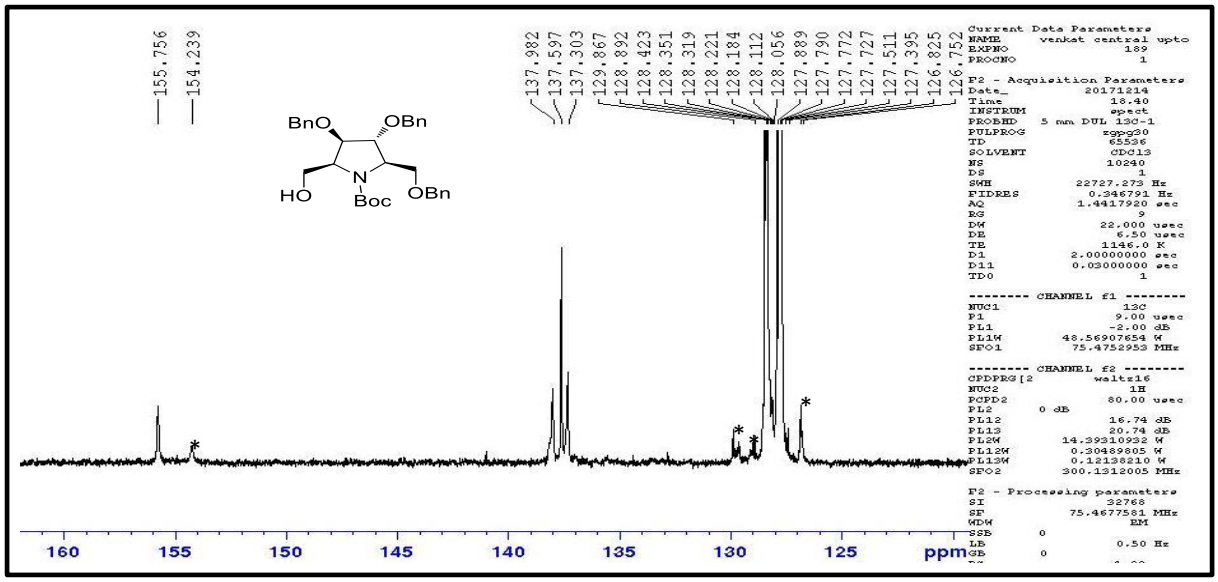


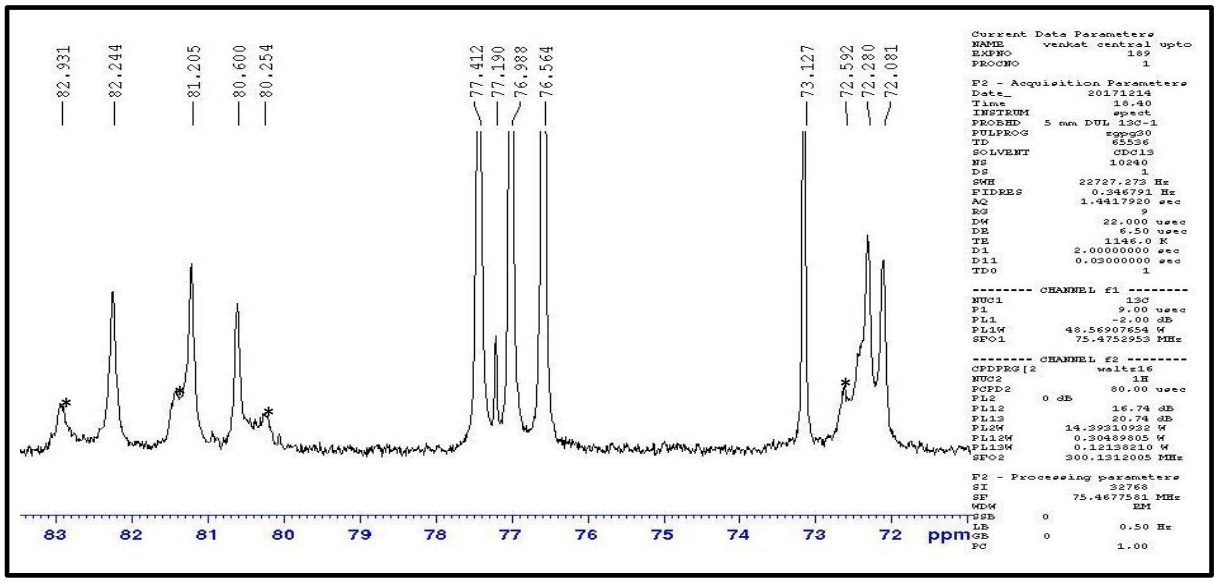
^{13}C–NMR spectrum of compound **10**

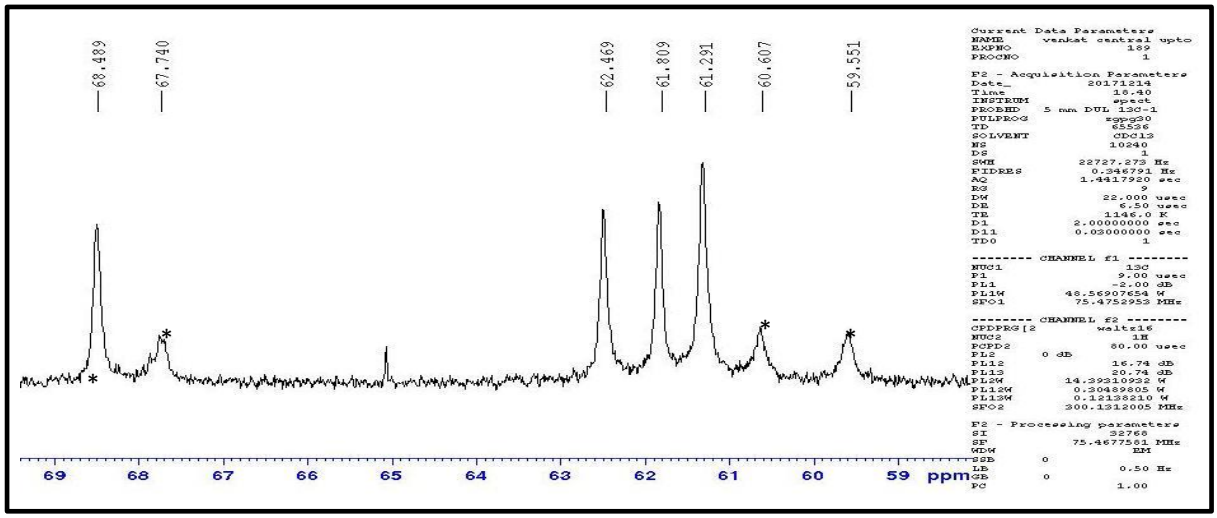


^{13}C-NMR spectrum of compound **10** (expanded)

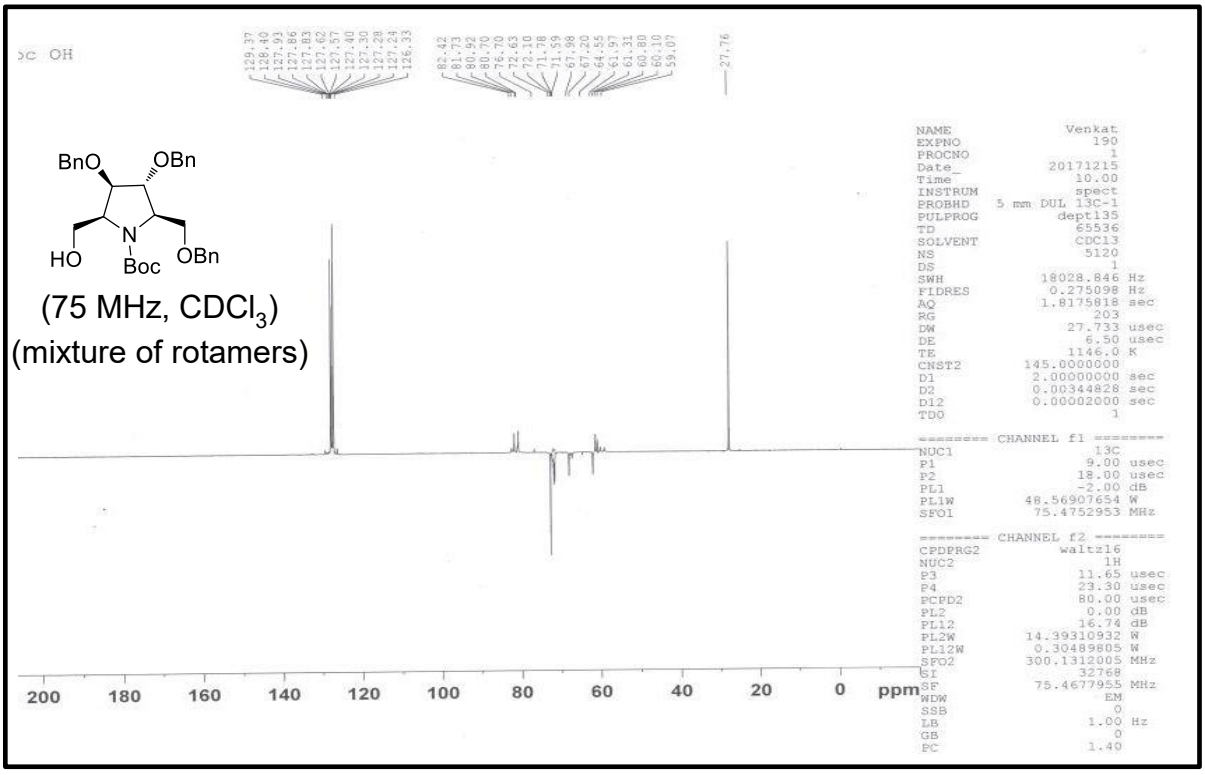
*indicates signals due to rotamers



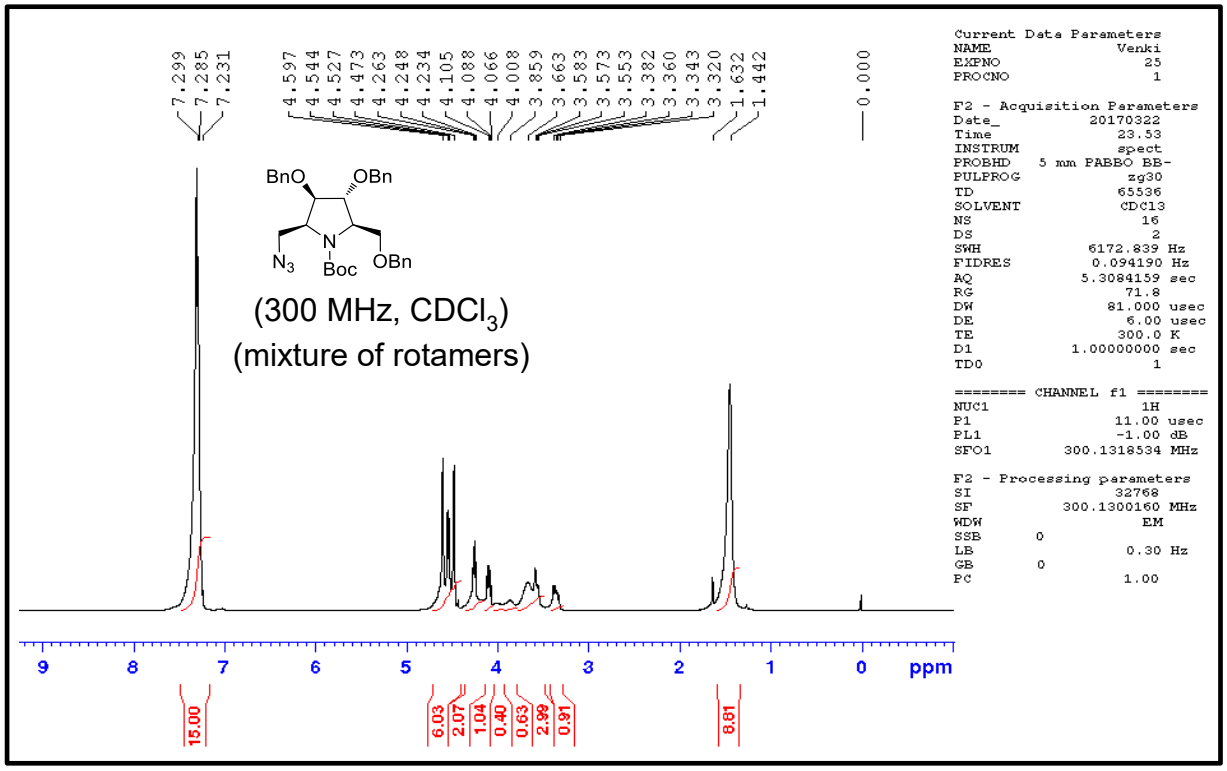




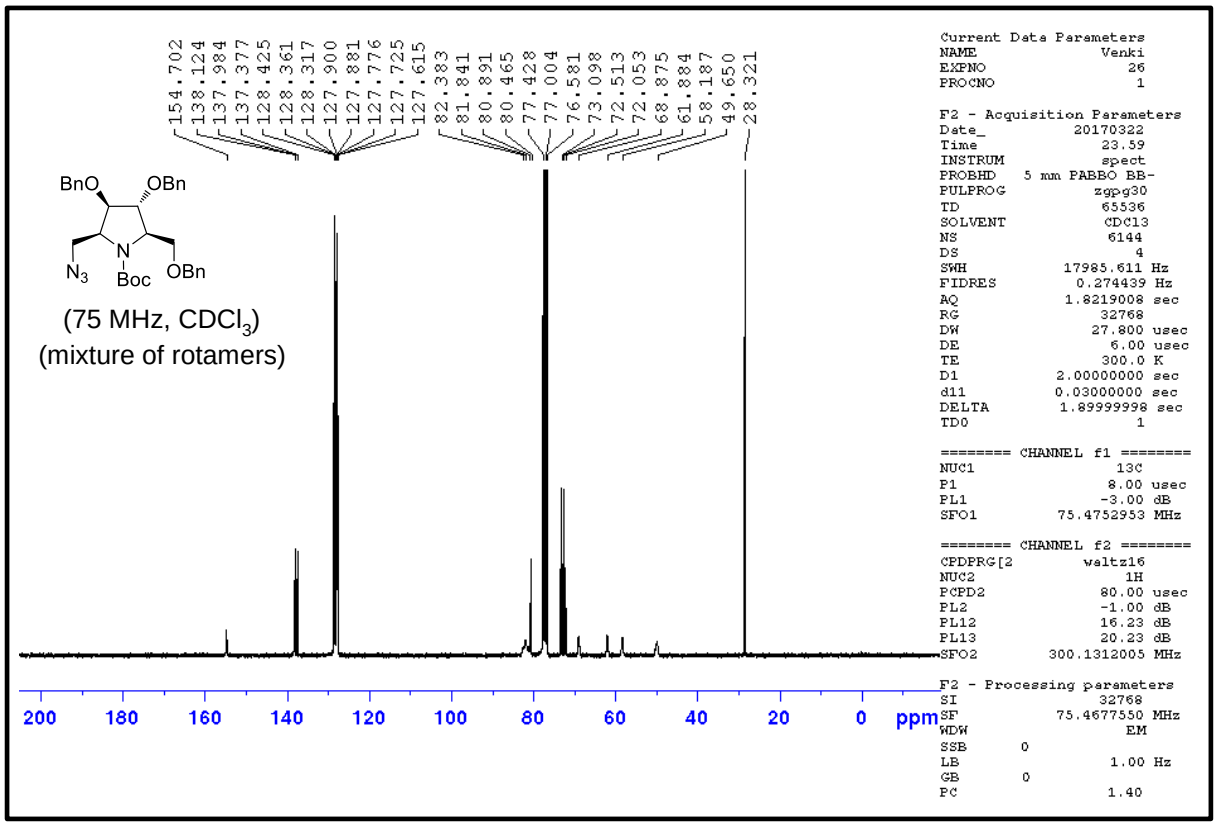
DEPT-135 spectrum of compound **10**



^{1}H–NMR spectrum of compound **8**

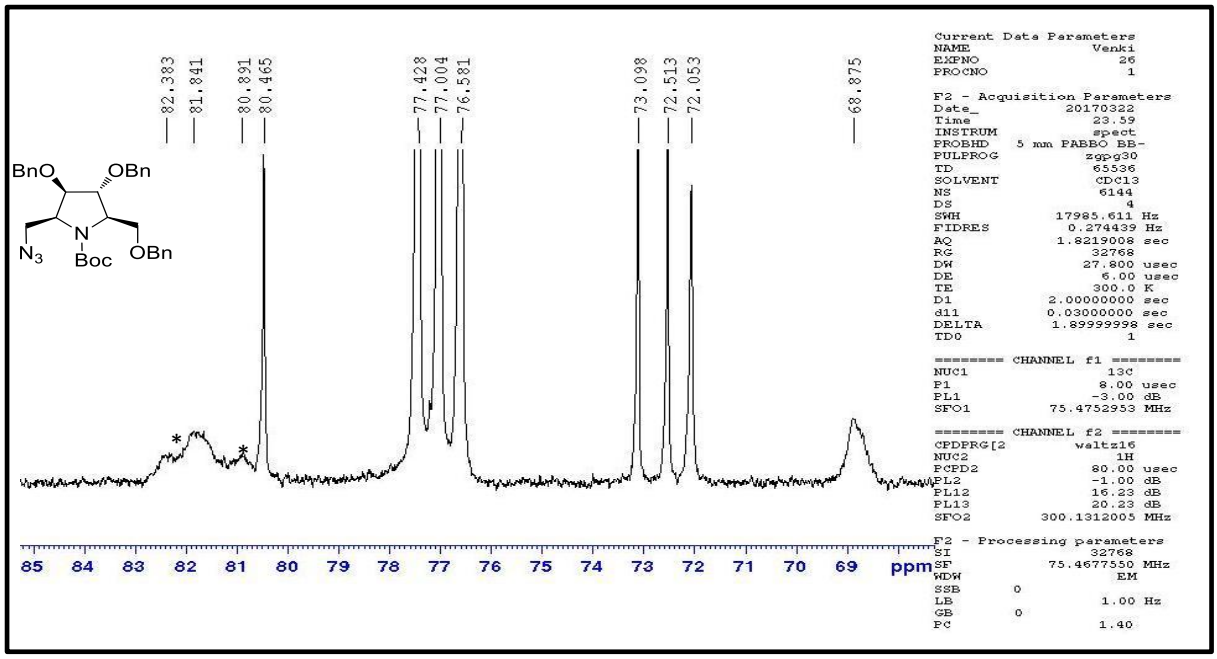


^{13}C–NMR spectrum of compound **8**

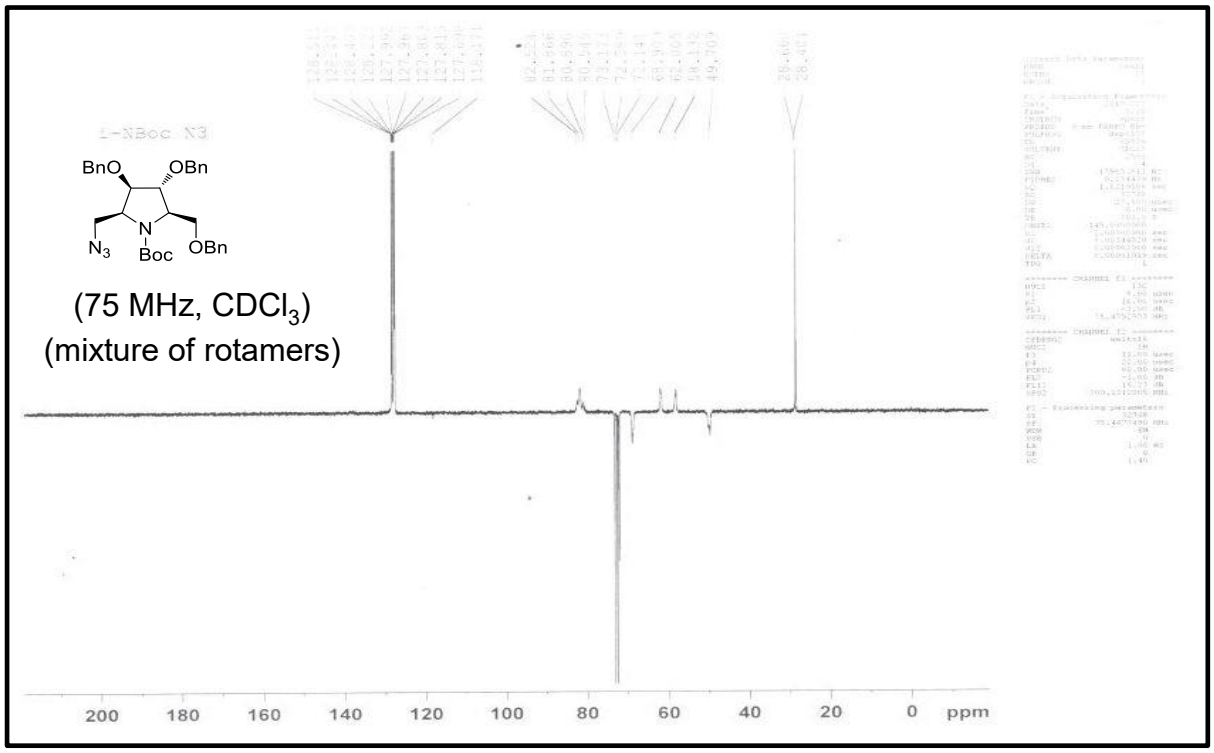


^{13}C-NMR spectrum of compound **8** (expanded)

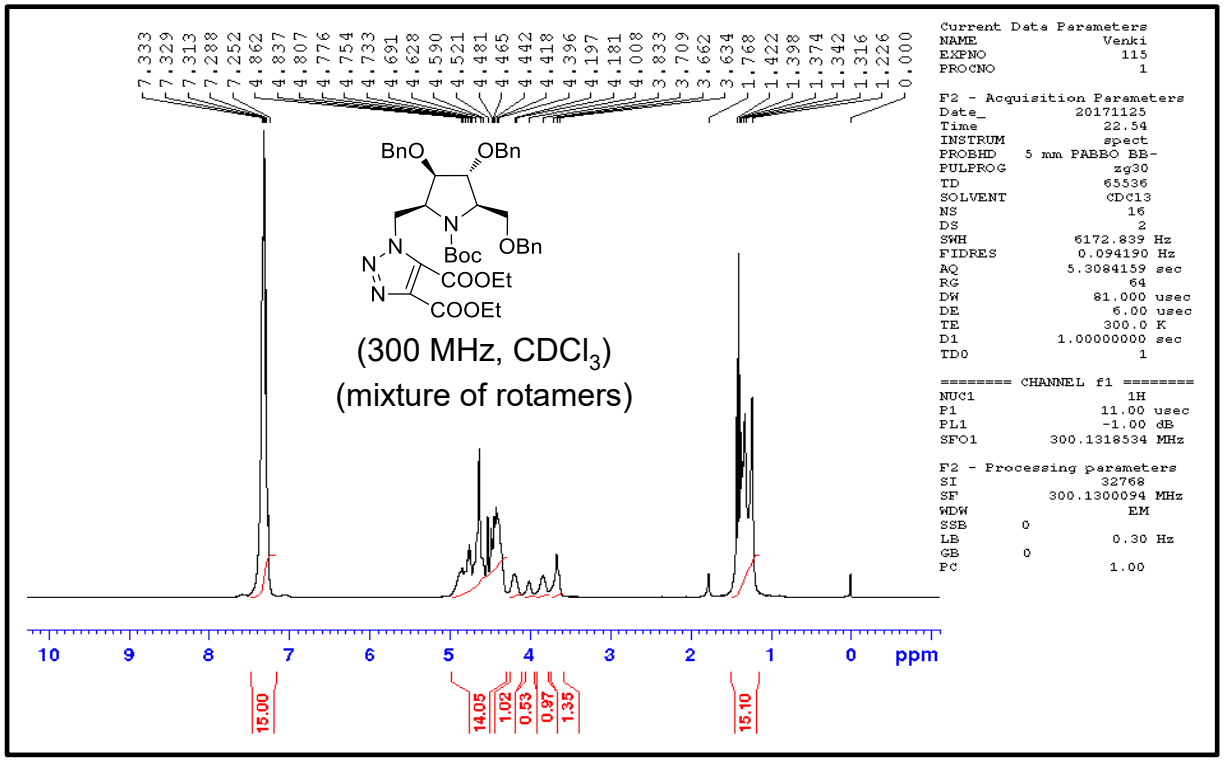
*indicates signals due to rotamers



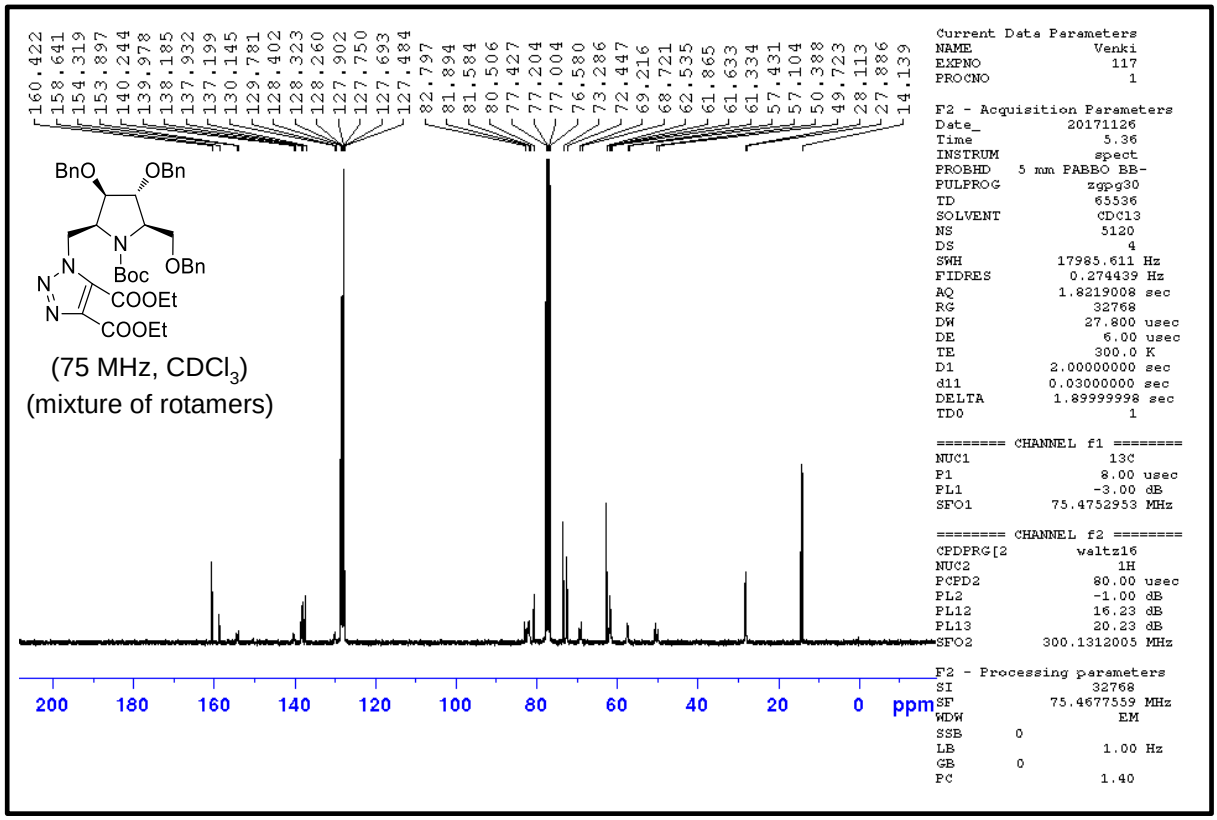
DEPT-135 spectrum of compound **8**



^{1}H–NMR spectrum of compound **22**

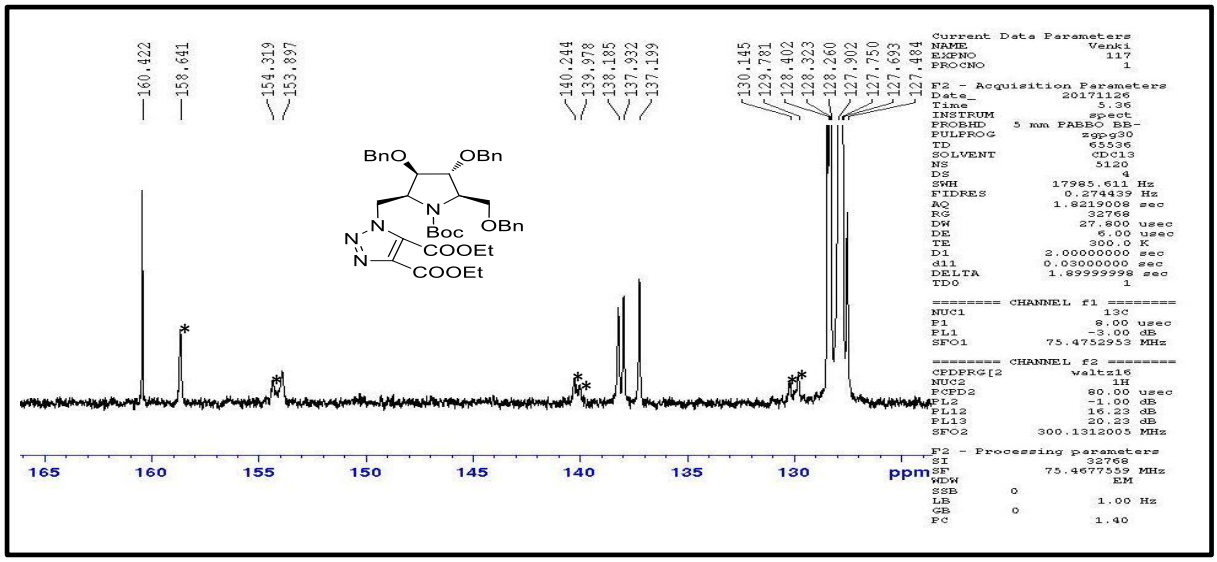


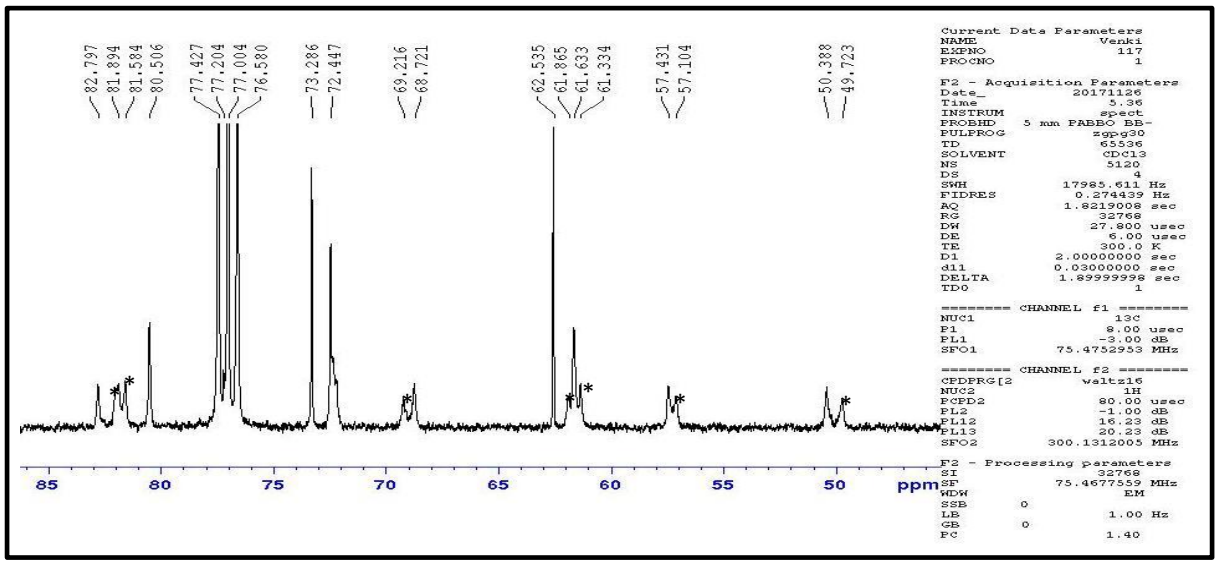
^{13}C–NMR spectrum of compound **22**

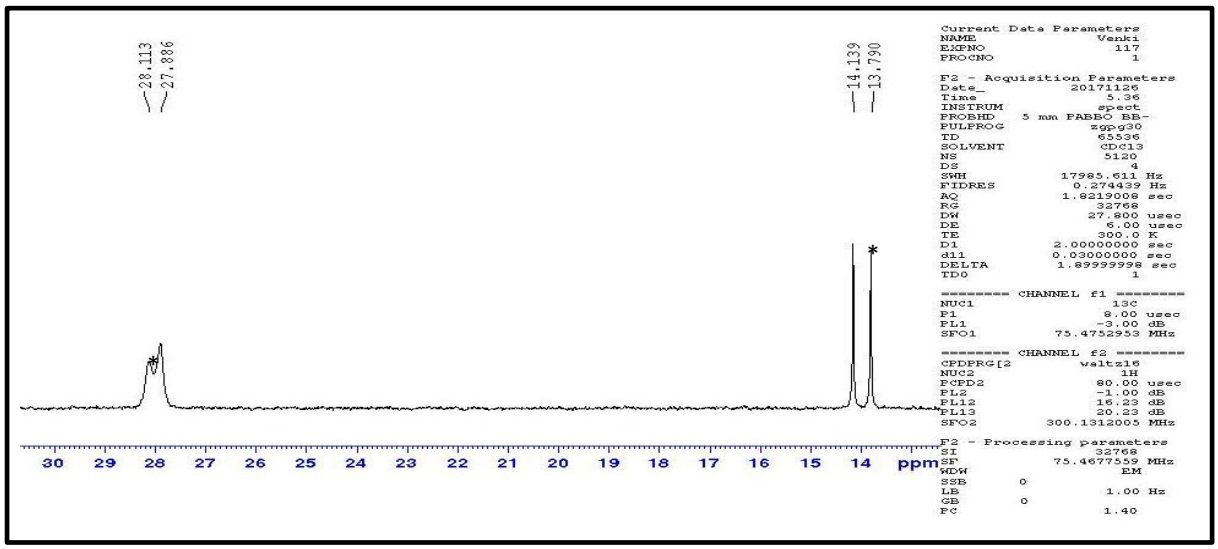


^{13}C-NMR spectrum of compound **22** (expanded)

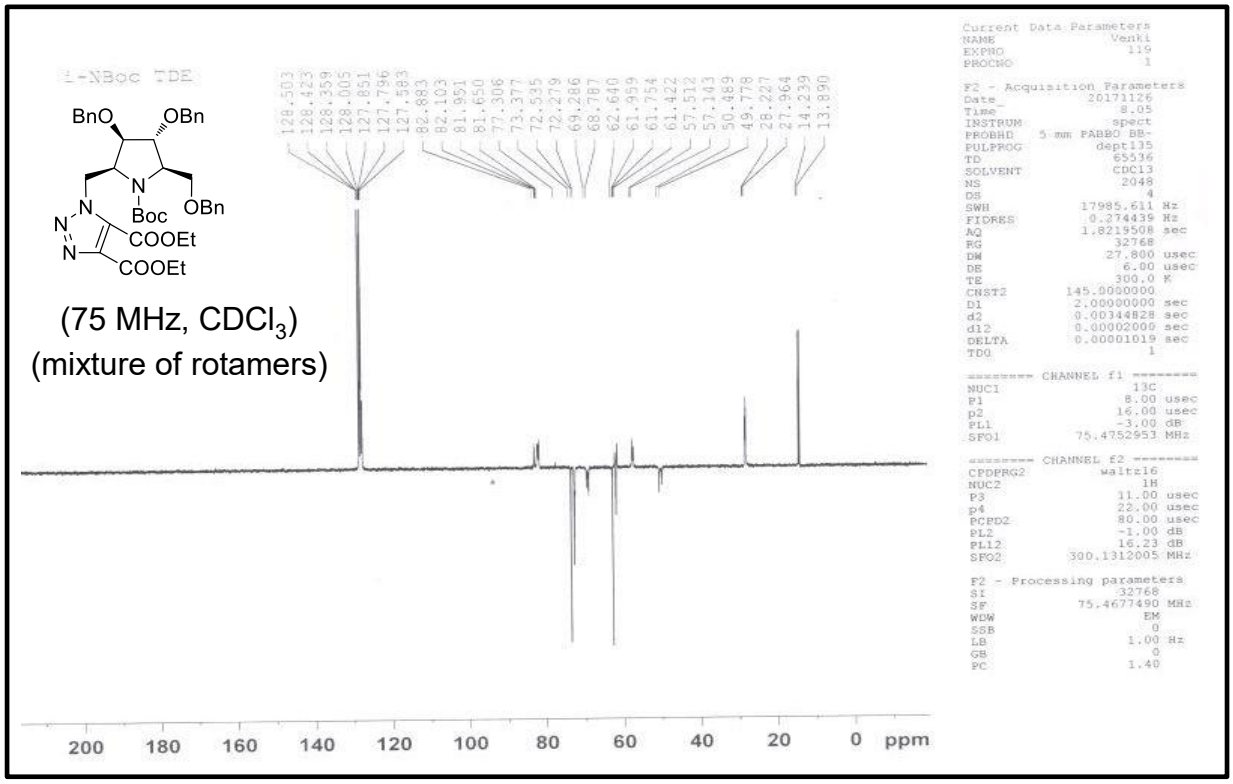
*indicates signals due to rotamers



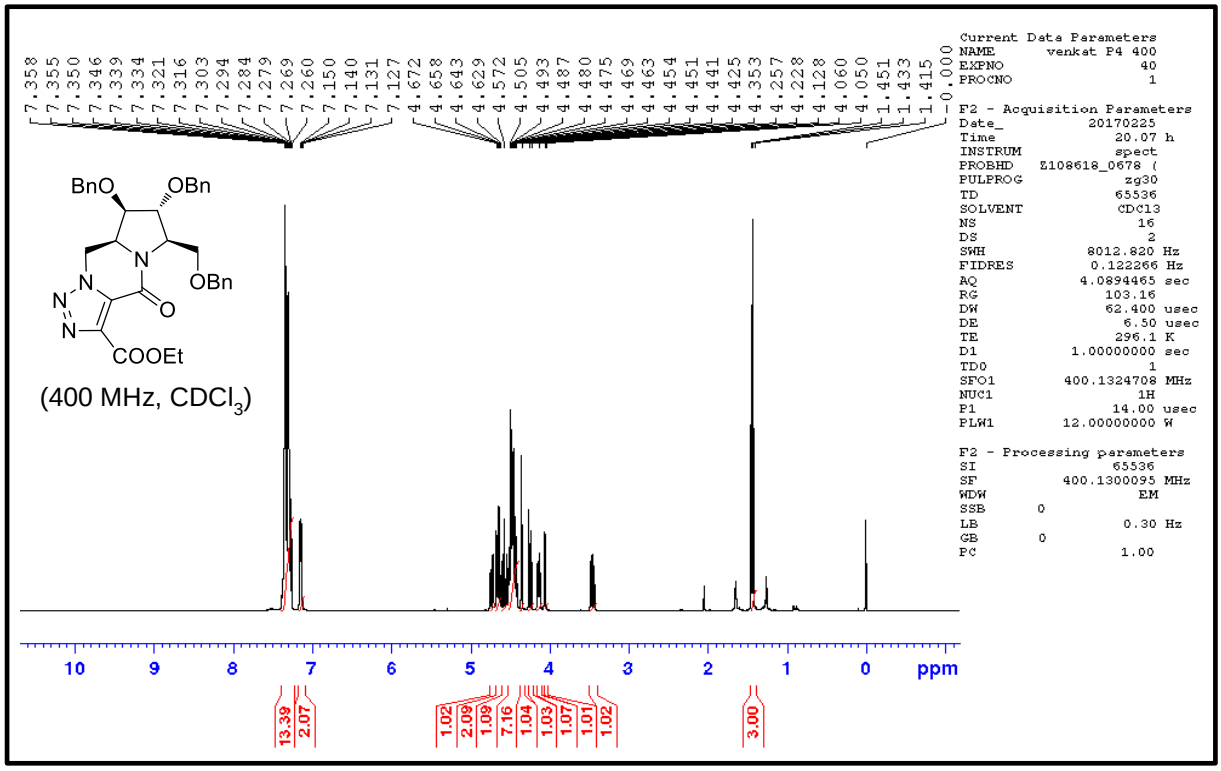




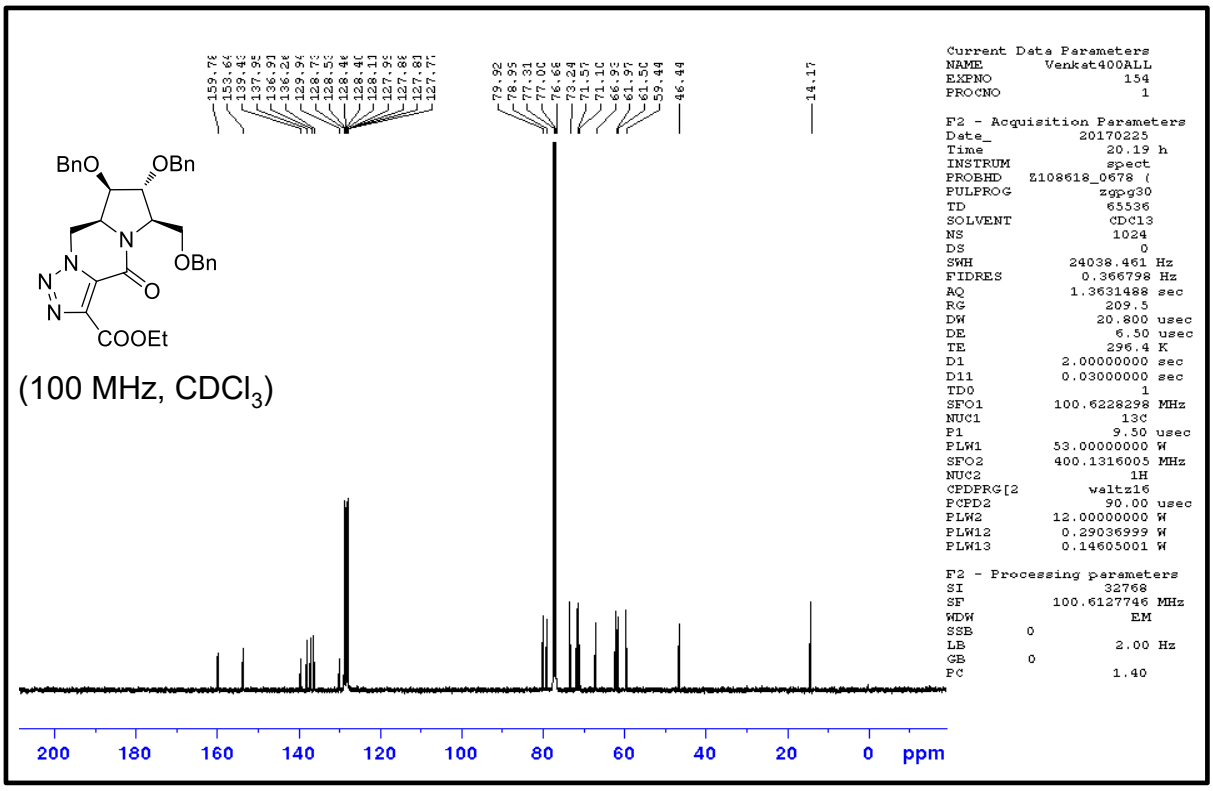
DEPT-135 spectrum of compound **22**



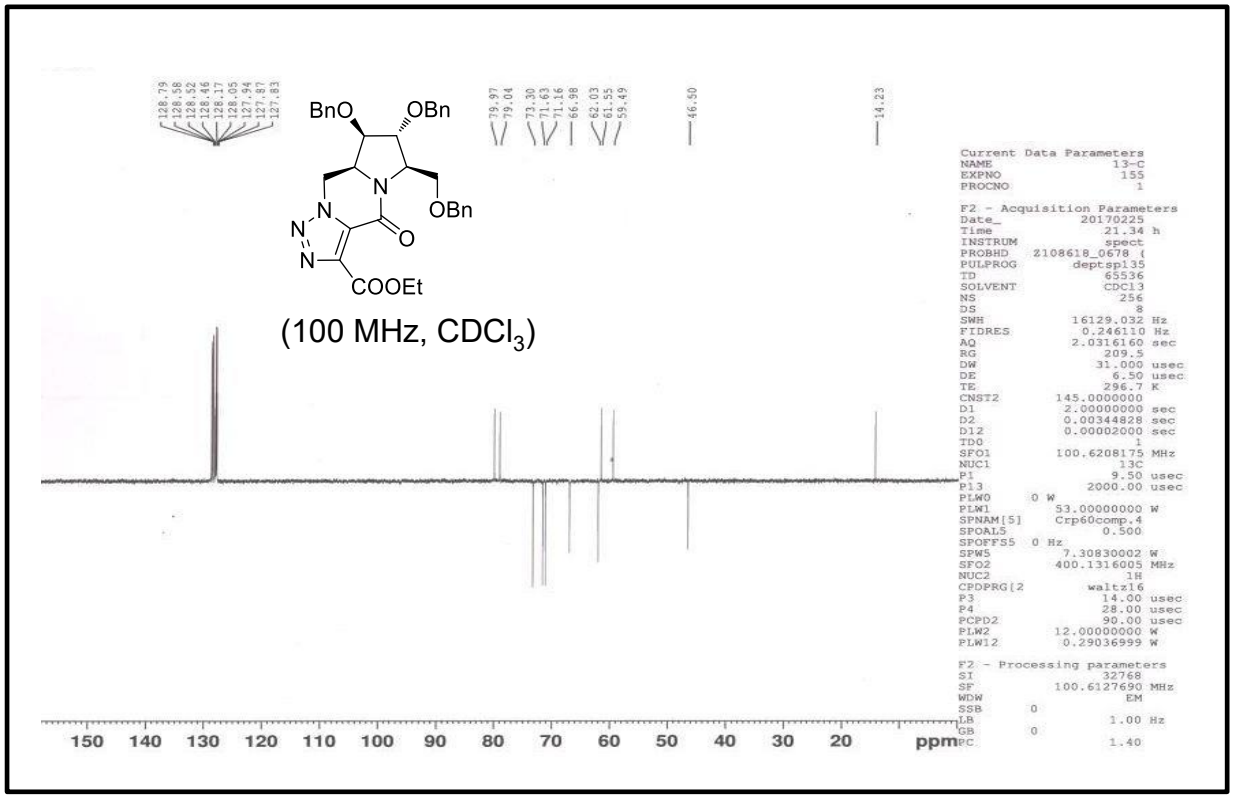
^{1}H–NMR spectrum of compound **24**



^{13}C–NMR spectrum of compound **24**



DEPT-135 spectrum of compound **24**



Current Data Parameters
NAME 13-C
EXPNO 155
PROCNO 1

F2 - Acquisition Parameters
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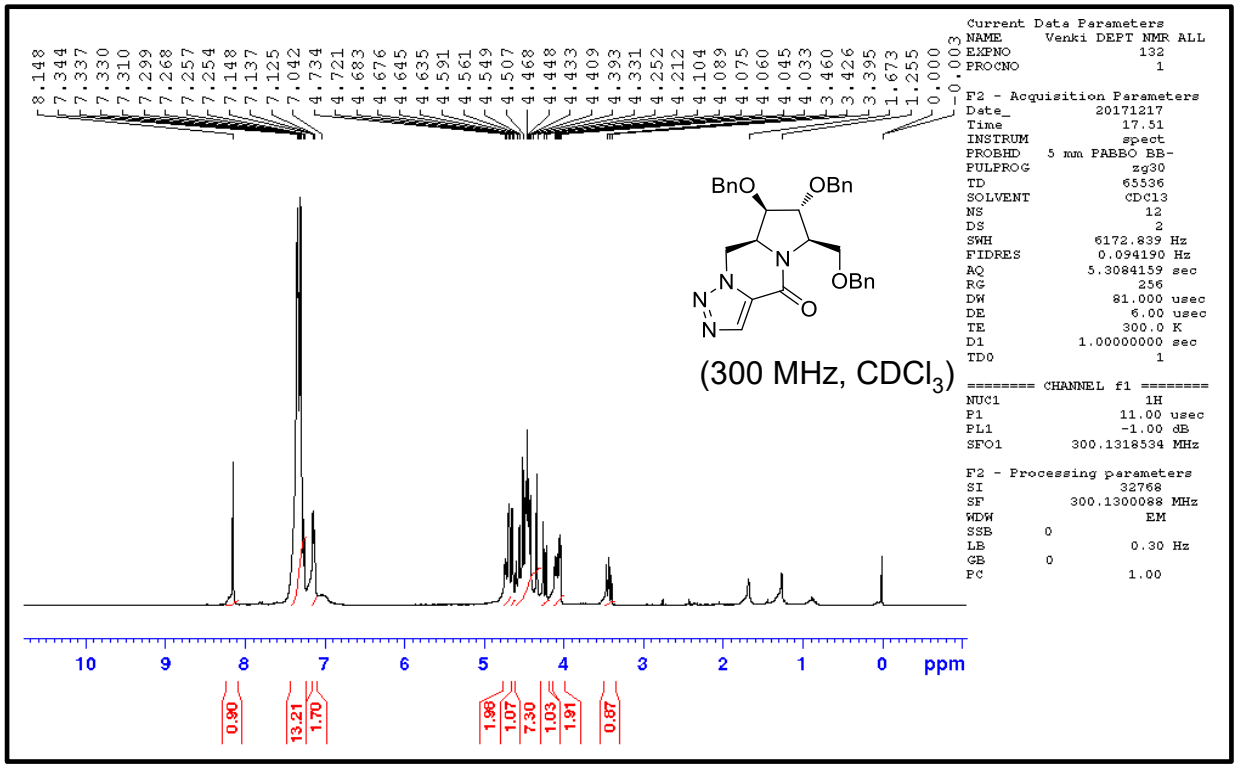
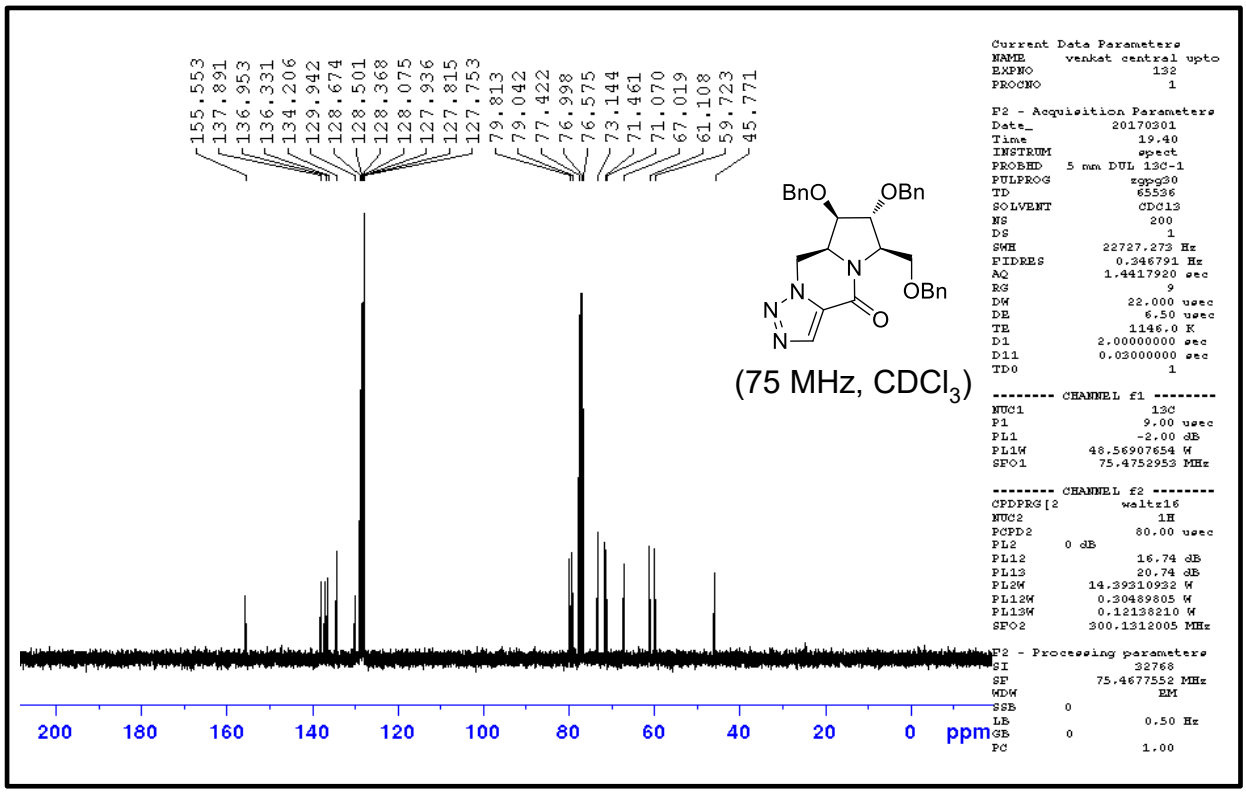
Time 21.34 h
INSTRUM spect
PROBHD Z108618_0678 (
PULPROG deptsp135
TD 65536
SOLVENT CDCl3
NS 256
DS 8
SWH 16129.032 Hz
FIDRES 0.246110 Hz
AQ 2.0316160 sec
RG 209.5
DW 31.000 usec
DE 6.50 usec
TE 296.7 K
CNST2 145.0000000
D1 2.00000000 sec
D2 0.00344828 sec
D12 0.00002000 sec
TD0 1
SFO1 100.6208175 MHz
NUC1 13C
P1 9.50 usec
P13 2000.00 usec
PLW0 0 W
PLW1 53.00000000 W
SPNAM[5] Crp60comp.4
SPOAL5 0.500
SPOFFS5 0 Hz
SPW5 7.30830002 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG[2 waltz16
P3 14.00 usec
P4 28.00 usec
PCPD2 90.00 usec
PLW2 12.00000000 W
PLW12 0.29036999 W

F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

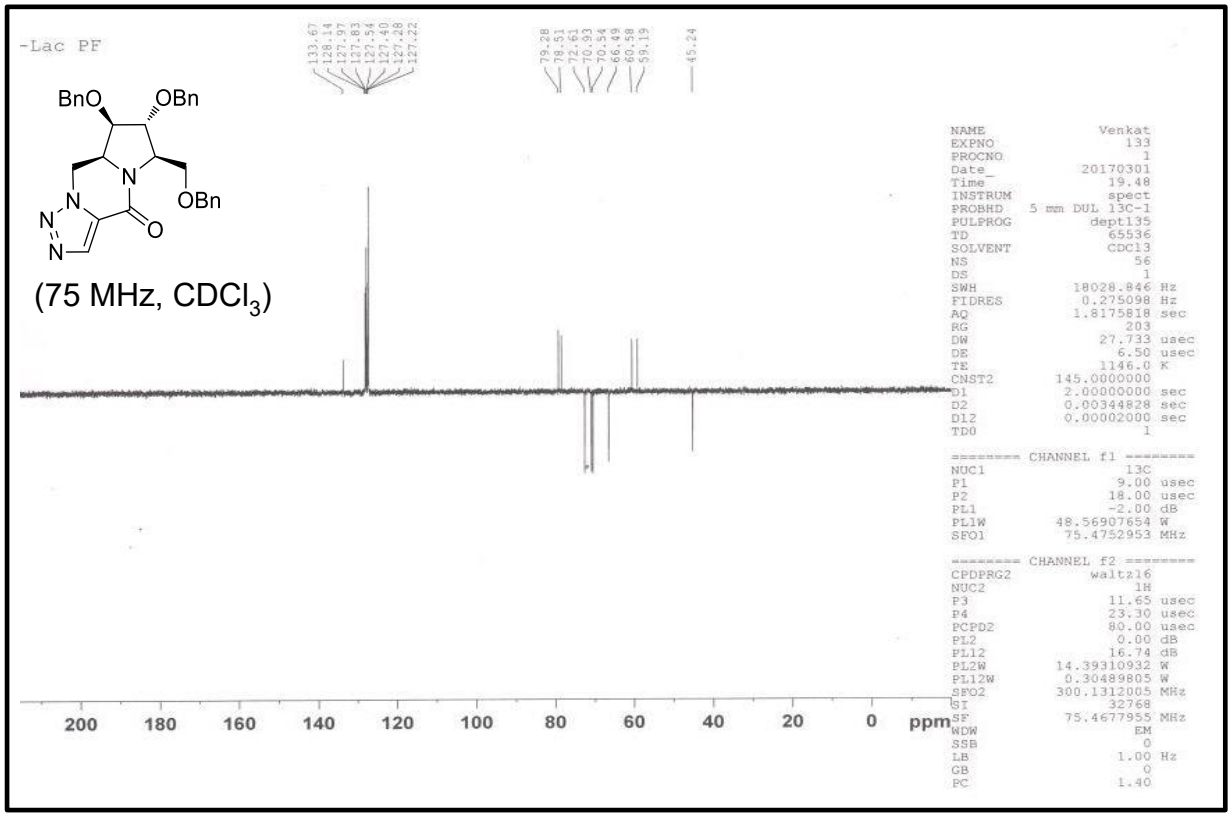
^{1}H–NMR spectrum of compound **30**



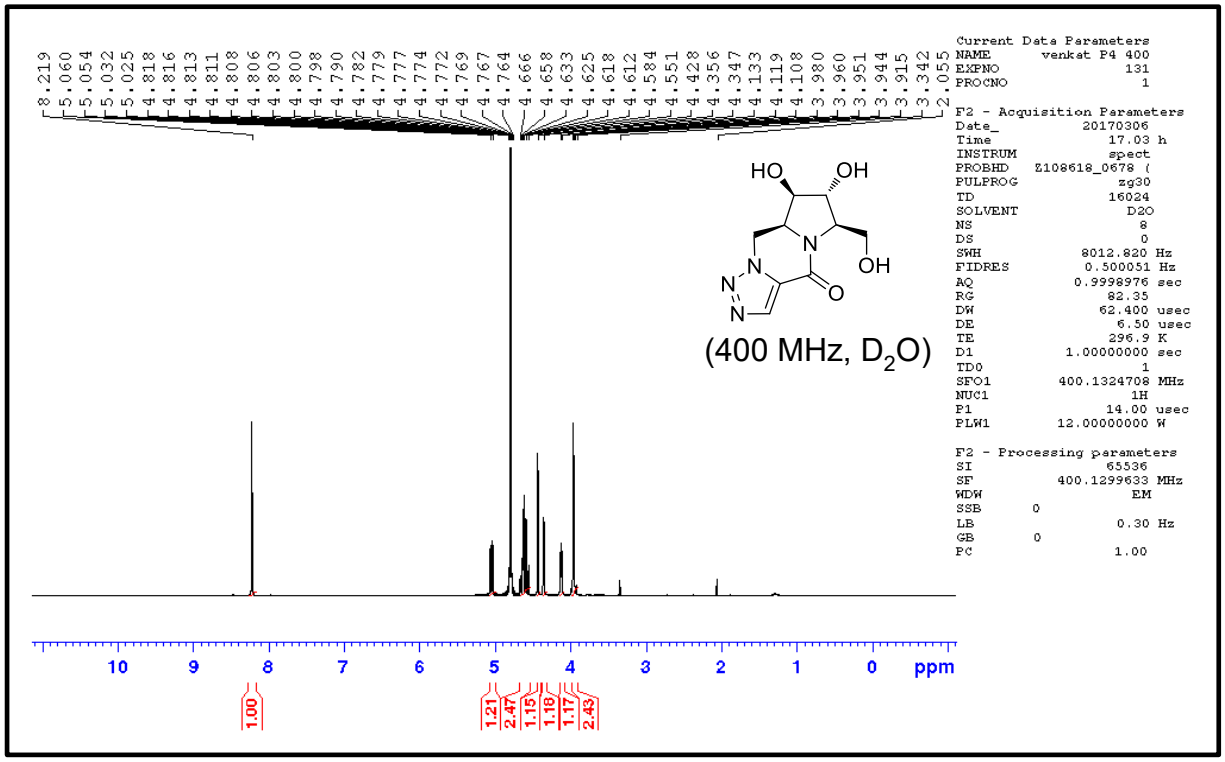
^{13}C–NMR spectrum of compound **30**



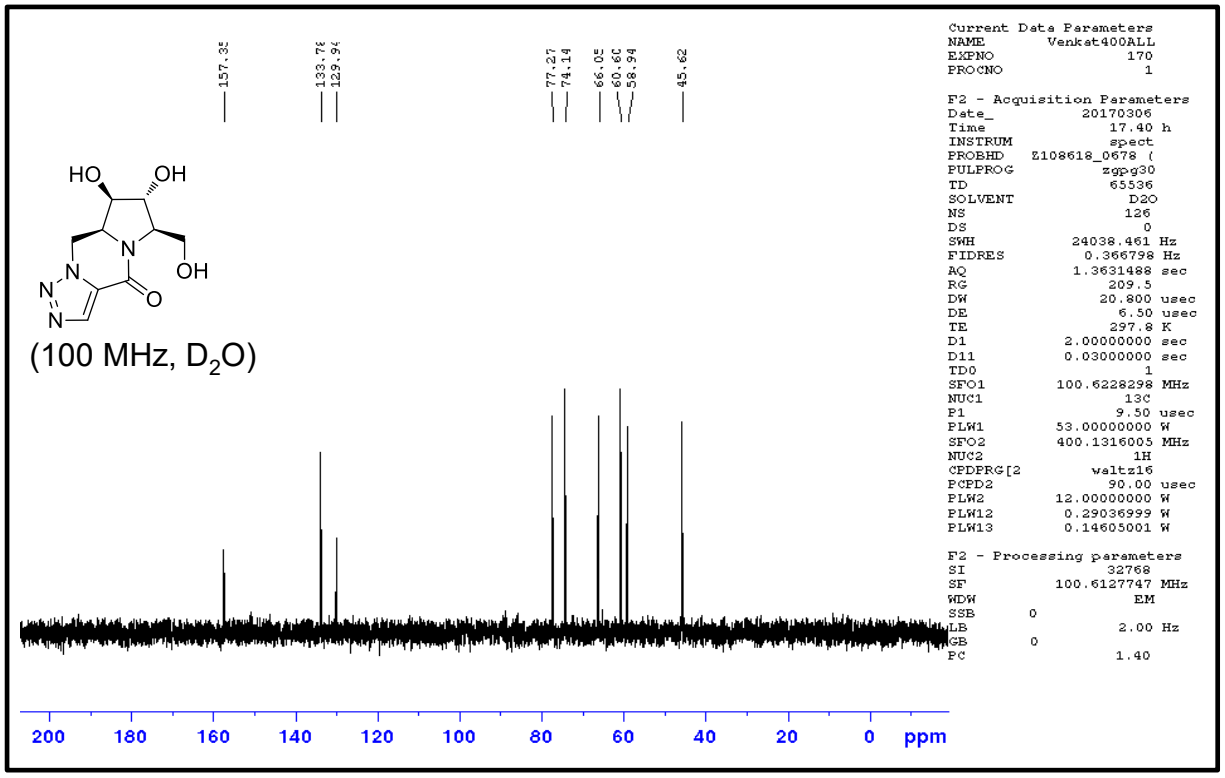
DEPT-135 spectrum of compound **30**



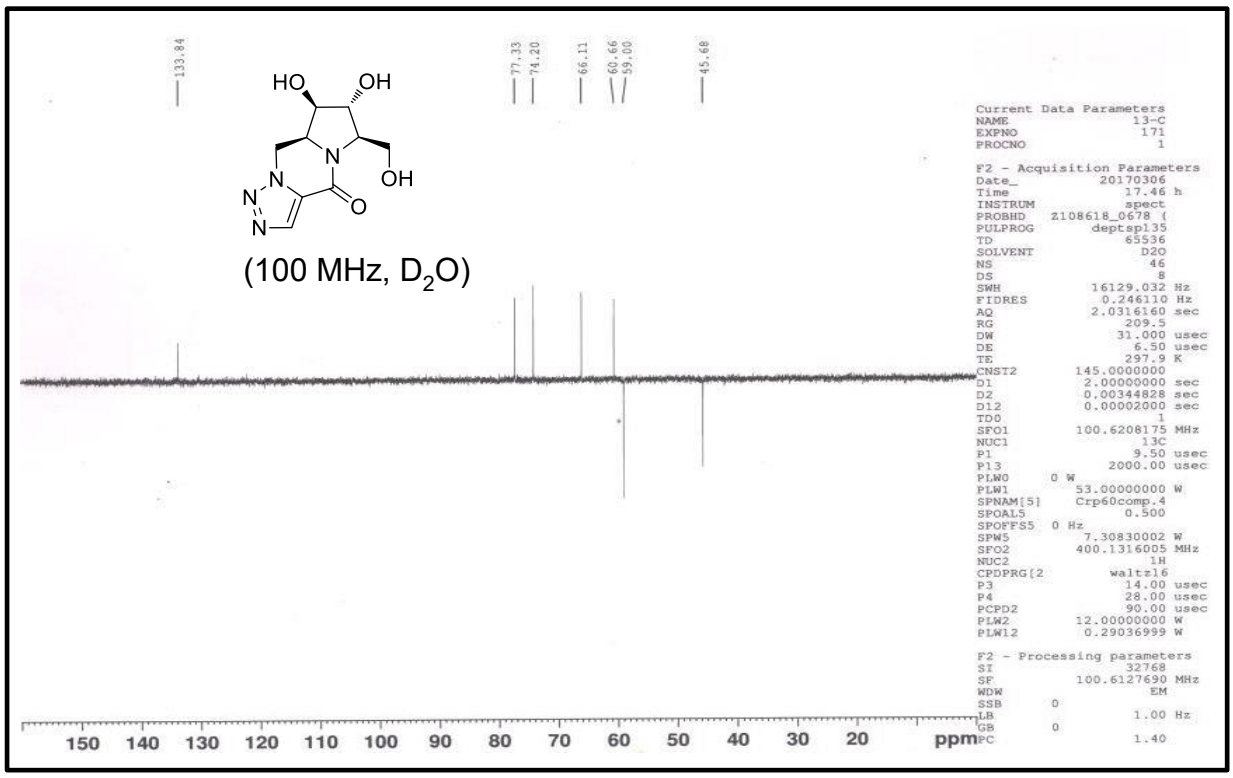
^{1}H–NMR spectrum of compound **3**



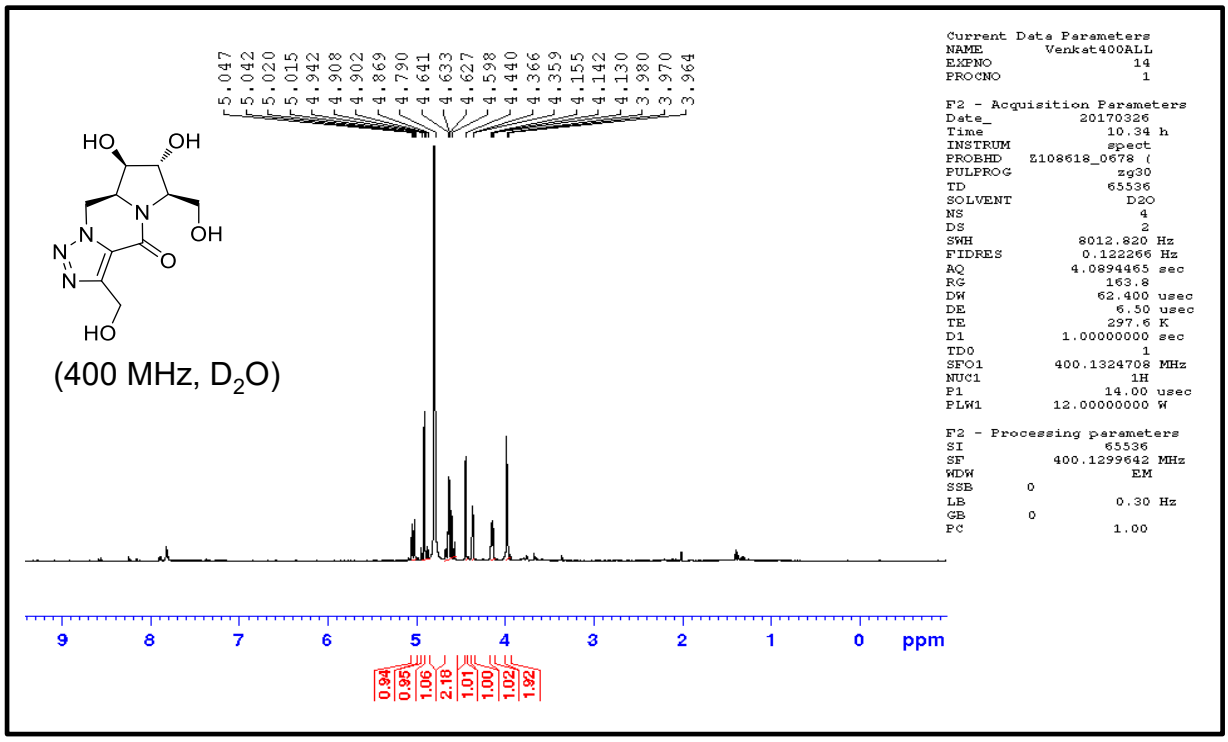
^{13}C–NMR spectrum of compound **3**



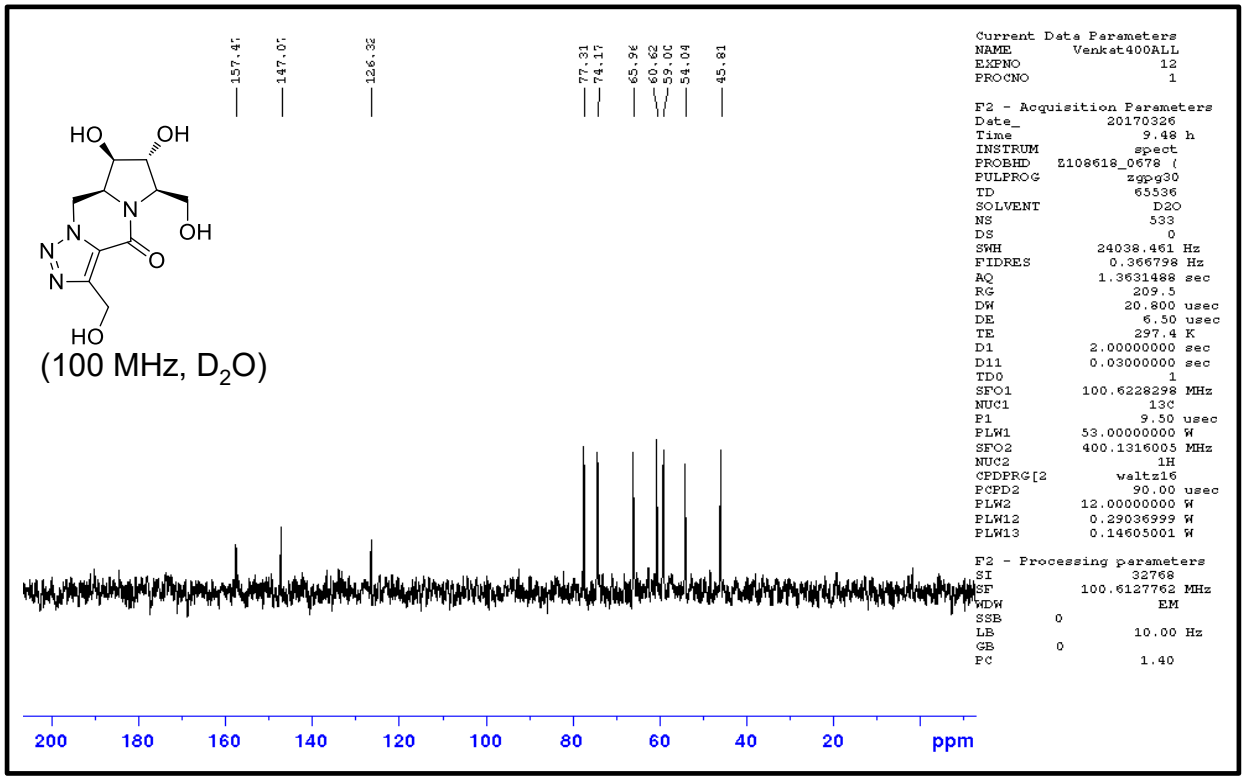
DEPT-135 spectrum of compound **3**



^{1}H–NMR spectrum of compound **4**



^{13}C–NMR spectrum of compound **4**



DEPT-135 spectrum of compound **4**