Supporting Information

Synthesis of Novel Pyrrolidine 3,4-Diol Derivatives as Inhibitors of α-L-Fucosidases.

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General Methods: Optical rotations were measured in a 1.0 cm or 1.0 dm tube with a Perkin–Elmer 241MC spectropolarimeter. ^{1}H and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$, [d_6]DMSO, CD_3OD and D_2O. All the assignments were confirmed by two-dimensional NMR experiments. The FAB mass spectra were obtained using glycerol or 3-nitrobenzyl alcohol as the matrix. TLC was performed on silica gel HF_{254} (Merck), with detection by UV light charring with H_2SO_4 or with Pancaldi reagent [$(NH_4)_6MoO_4$, $Ce(SO_4)_2$, H_2SO_4, H_2O]. Silica gel 60 (Merck, 230 mesh) was used for preparative chromatography.

For experimental procedures, spectroscopic data and NMR spectra for compounds **26-37**, **18a**, **18b** see: A. J. Moreno Vargas, A. T. Carmona, F. Mora, P. Vogel, I. Robina *Chem. Commun.* **2005**, 4949 (Supporting Information).

5-deoxy-2,3-*O*-isopropylidene-L-lyxofuranose (41): To a stirred solution of L-fucose (4 g, 24.36 mmol) in DMF (55 mL) at 0 ºC was added 2,2-dimethoxypropane (13.8 mL) and PTSA (90 mg, 0.53 mmol). The reaction was stirred for 3 h at r.t. and then treated with Na_2CO_3. The mixture was filtered and the solution evaporated under reduced presure. The residue was then dissolved in water and washed with petroleum ether. $NaIO_4$ (6 g, 28 mmol) was added to the aqueous phase and the mixture was stirred for 1 h at r.t.. NaOH (1N) was then added until basic pH and the reaction was stirred at r.t. for 1 h. The reaction mixture was then neutralized with HCl (1N) and extracted with ethyl acetate. The organic phase was dried (Na_2SO_4), filtered and concentrated. The resulting residue was purified by column chromatography (petroleum ether:ethyl acetate, 3:1) to give pure **41** (2.76 g, 65%). P.f. = 48-50 ºC; $[\alpha]_D^{20}$ -28.0 (*c* 1 in CH_2Cl_2); IR (ν cm^{-1}) 3442 (OH), 2985, 2930, 1382, 1210, 1055; CIMS 157 [$(M-H_2O + H)^+$, 89%]. Anal. calcd. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C,54.90; H, 7.83. Data for α-anomer: ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) δ 1.31-1.33 (6H, m, 4-Me, $C(CH_3)_2$), 1.47 (3H, s,

C(C*H*$_3$)$_2$), 2.51 (1H, brs, O*H*), 4.31 (1H, qd, $J_{4,Me}$ = 6.3, $J_{4,3}$ = 3.0, 4-H), 4.59-4.64 (2H, m, 2-H, 3-H), 5.34 (1H, s, 1-H). ^{13}C NMR (75.4 MHz, CD_3Cl, δ ppm) δ 13.6 (4-Me), 25.2 (C(*C*H$_3$)$_2$), 26.3 (C(*C*H$_3$)$_2$), 76.3 (C-4), 81.2, 86.2 (C-2, C-3), 101.2 (C-1), 112.5 (*C*(CH$_3$)$_2$); Data for β-anomer: ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) δ 1.32 (3H, m, Me-4), 1.38 (3H, s, C(C*H*$_3$)$_2$), 1.54 (3H, s, C(C*H*$_3$)$_2$), 3.65 (1H, qd, $J_{4,Me}$ = 6.3, $J_{4,3}$ = 3.0, 4-H), 3.84 (1H, d, $J_{OH,1}$ = 12.3, O*H*), 4.49 (1H, dd, $J_{2,3}$ = 6.0, $J_{2,1}$ = 3.3, 2-H), 4.54 (1H, dd, 3-H), 4.95 (1H, dd, 1-H). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 13.4 (4-Me), 25.1 (C(*C*H$_3$)$_2$), 26.0 (C(*C*H$_3$)$_2$), 71.9 (C-4), 79.4, 81.2 (C-2, C-3), 96.7 (C-1), 113.1 (*C*(CH$_3$)$_2$).

(*Z*) and (*E*)- Ethyl 2,3,7-trideoxy-4,5-*O*-isopropylidene-L-*lyxo*-hept-2-enoate (42 and 43): To a solution of **41** (2.66 g, 15.27 mmol) in dry toluene (31 mL), ethoxycarbonyltriphenylmethylenephosphorane (10 g, 28.7 mmol) was added, and the mixture was heated under reflux for 4 h. Then, the solvent was evaporated and the resulting residue was purified by column chromatography (ether:petroleum ether 1:2→1:1) to afford **42** (433 mg, 12%) and **43** (2.17 g, 58%), both as oils. Data for **42**: $[\alpha]_D^{20}$ +100.7 (*c* 1.1 in CH_2Cl_2); IR (ν cm^{-1}) 3542 (OH), 2983, 2936, 1725 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) δ 1.17 (3H, d, $J_{Me,6}$ = 6.3, 6-Me), 1.28 (3H, t, $^2J_{H,H}$ = 7.2, CH_2CH_3), 1.39, 1.52 (3H each, 2s, C(C*H*$_3$)$_2$), 3.62 (1H, m, 6-H), 4.15 (2H, q, CH_2CH_3), 4.29 (1H, dd, $J_{5,4}$ = 7.5, $J_{5,6}$ = 3.0, 5-H), 5.60 (1H, td, $J_{4,3}$ = 7.5, $J_{4,2}$ = 1.5, 4-H), 5.92 (1H, dd, $J_{2,3}$ = 11.7, 2-H), 6.44 (1H, dd, 3-H). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 14.3 (CH_2CH_3), 20.6 (6-Me), 24.5, 26.4 (C(*C*H$_3$)$_2$), 60.6 (CH_2CH_3), 65.7 (C-6), 74.9 (C-4), 82.2 (C-5), 108.8 (*C*(CH$_3$)$_2$), 120.1 (C-2), 147.6 (C-3), 166.0 (C=O); CIMS 229 [(M-Me)$^+$, 15%], 245 [(M + H)$^+$, 2%]; CIHRMS *m/z* found 245.1376, calcd. for $C_{12}H_{21}O_5$ (M+H)$^+$: 245.1389. Data for **43**: $[\alpha]_D^{20}$ -1.6 (*c* 1.3 in CH_2Cl_2); IR (ν cm^{-1})

3454 (OH), 2984, 2937, 1722 (C=O), 1372, 1303, 1263; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) δ 1.16 (3H, d, $J_{Me,6}$ = 6.3, 6-Me), 1.29 (3H, t, CH_2CH_3), 1.40, 1.54 (3H each, 2s, $C(CH_3)_2$), 3.73 (1H, q, $J_{6,5}$ = 6.3, 6-H), 4.03 (1H, t, $J_{5,4}$ = 6.6, 5-H), 4.20 (2H, q, $^{2}J_{H,H}$ = 7.2, CH_2CH_3), 4.69 (1H, td, $J_{4,3}$ = 6.6, $J_{4,2}$ = 1.2, 4-H), 6.07 (1H, dd, $J_{2,3}$ = 15.6, 2-H), 6.88 (1H, dd, 3-H). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 14.3 (CH_2CH_3), 19.3 (6-Me), 25.4, 27.8 ($C(CH_3)_2$), 60.8 (CH_2CH_3), 66.0 (C-6), 76.4 (C-4), 82.7 (C-5), 109.6 ($C(CH_3)_2$), 123.9 (C-2), 142.6 (C-3), 165.9 (C=O); CIMS 245 [$(M + H)^+$, 9%]; CIHRMS *m/z* found 245.1390, calcd. for $C_{12}H_{21}O_5$ $(M+H)^+$: 245.1389

Ethyl 2,3,6,7-tetradeoxy-3,6-imino-4,5-*O*-isopropylidene-D-*altro*-heptanoate and ethyl 2,3,6,7-tetradeoxy-3,6-imino-4,5-*O*-isopropylidene-D-*allo*-heptanoate ((2*R* and 2*S*,3*S*,4*R*,5*R*)-2-ethoxycarbonylmethyl-3,4-*O*-isopropylidene-5-methyl-pyrrolidine-3,4-diol) (25a and 25b): A solution of **43** (2.1 g, 8.60 mmol) in dry CH_2Cl_2 was added dropwise to a stirred solution of methanesulphonyl chloride (2.4 mL, 31.1 mmol) in dry pyridine (9 mL) cooled to 0 ºC. The mixture was left at r.t. overnight. Then, the mixture was cooled to 0 ºC, water was added and the reaction was stirred for 15 min at r.t.. The solvent was evaporated, the crude diluted with dichloromethane, washed with H_2O and brine. The organic phase was dried, filtered and concentrated. The residue was then dissolved in EtOH, cooled to 0 ºC, and saturated with NH_3. After 5 days at r.t., the solvent was evaporated and the residue was treated with NH_4OH (25%) and extracted with CH_2Cl_2. The organic phase was washed with satd. aq. sol. of $NaHCO_3$ and H_2O until neutral pH. The organic phase was dried (Na_2SO_4), filtered and concentrated. The resulting residue was purified by column chromatography (ethyl acetate (1% Et_3N) to afford **25a** (1.09 g) and **25b** (0.22 g) (63%, 2 steps). Data for **25a**: $[\alpha]_D^{20}$ -40.5 (*c* 1.2 in CH_2Cl_2); IR (ν cm^{-1}) 2980, 2934, 1734 (C=O), 1373, 1263, 1209, 1066, 1045, 872; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) δ 1.05 (3H, d, $J_{Me,6}$ = 7.2, 6-Me), 1.26 (3H, t, $^{2}J_{H,H}$ =

7.2, CH_2CH_3), 1.29, 1.44 (3H each, 2s, $C(CH_3)_2$), 2.15 (1H, s, N*H*), 2.56 (1H, dd, $^2J_{2a,2b}$ = 16.2, $J_{2a,3}$ = 6.6, 2a-H), 2.65 (1H, dd, $J_{2b,3}$ = 7.5, 2b-H), 3.31 (1H, q, 6-H), 3.44 (1H, m, 3-H), 4.15 (2H, q, CH_2CH_3), 4.39 (1H, d, $J_{5,4}$ = 5.7, 5-H), 4.66 (1H, dd, $J_{4,3}$ = 4.7, 4-H). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 14.3 (CH_2CH_3), 17.4 (6-Me), 24.2, 26.1 ($C(CH_3)_2$), 33.8 (C-2), 56.5 (C-3), 58.7 (C-6), 60.6 (CH_2CH_3), 82.7 (C-4), 87.3 (C-5), 111.1 ($C(CH_3)_2$), 172.1 (C=O); CIMS 245 [$(M + H)^+$, 14%], 244 [$(M)^+$, 100%]; CIHRMS *m/z* found 244.1553, calcd. for $C_{12}H_{22}NO_4$ $(M+H)^+$: 244.1549. Anal.calcd. for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 58.91; H, 8.28; N, 5.68. Data for **25b**: $[\alpha]_D^{20}$ -17.6 (*c* 1.31 in CH_2Cl_2); IR (ν cm^{-1}) 3349 (NH), 2981, 2930, 1733 (C=O), 1372; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) δ 1.21 (3H, d, $J_{Me,6}$ = 6.6, 6-Me), 1.24 (3H, t, $^2J_{H,H}$ =7.2, CH_2CH_3), 1.29, 1.49 (3H each, 2s, $C(CH_3)_2$), 2.28 (1H, br s, N*H*), 2.46 (1H, dd, $^2J_{2a,2b}$ = 16.2, $J_{2a,3}$ = 9.0, 2a-H), 2.72 (1H, dd, $J_{2b,3}$ = 4.2, 2b-H), 3.20 (1H, m, 6-H), 3.45 (1H, m, 3-H), 4.09-4.20 (3H, m, 5-H, CH_2CH_3), 4.26 (1H, dd, $J_{4,5}$ = 7.2, $J_{4,3}$ = 5.1, 4-H). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 14.3 (CH_2CH_3), 19.5 (6-Me), 25.5, 27.5 ($C(CH_3)_2$), 38.6 (C-2), 59.7 (C-6), 60.7, 60.8 (C-3, CH_2CH_3), 84.7 (C-4), 87.3 (C-5), 117.2 ($C(CH_3)_2$), 172.1 (C=O); CIMS 245 [$(M + H)^+$, 6%], 244 [$(M)^+$, 54%]; CIHRMS *m/z* found 244.1544, calcd. for $C_{12}H_{22}NO_4$ $(M+H)^+$: 244.1549.

Ethyl *N*-Benzyloxycarbonyl-2,3,6,7-tetradeoxy-3,6-imino-4,5-*O*-isopropylidene-D-*altro*-heptanoate ((2*R*,3*S*,4*R*,5*R*)-*N*-Benzyloxycarbonyl-2-ethoxycarbonylmethyl-3,4-*O*-isopropylidene-5-methyl-pyrrolidine-3,4-diol) (47): To a solution of **25a** (0.866 g, 3.56 mmol) in 1:1 EtOH:H_2O (48 mL), $NaHCO_3$ (0.51 g, 6.05 mmol) and CbzCl (0.562 mL, 3.92 mmol) were added. After stirring for 2 h at r.t., the mixture was poured into satd. aq. sol. of $NaHCO_3$ and extracted with AcOEt. The organic phases were dried (Na_2SO_4), filtered and concentrated. The resulting residue was purified by

column chromatography (ether:petroleum ether 1:2) to give pure **47** (1.21 g, 90%). $[\alpha]_D^{20}$ -76.6 (*c* 1.1 in CH_2Cl_2); IR (ν cm^{-1}) 2983, 1732 (C=O), 1703 (C=O); ^{1}H NMR (500 MHz, DMSO-*d*$_6$, 353 K, δ ppm) δ 1.12 (3H, d, $J_{6,Me}$ = 6.9, 6-Me), 1.18 (3H, t, $^2J_{H,H}$ = 7.0, CH_2CH_3), 1.26, 1.38 (3H each, 2s, $C(CH_3)_2$), 2.49 (1H, dd, $^2J_{2a,2b}$ = 16.5, $J_{2a,3}$ = 9.0, 2a-H), 3.14 (1H, m, 2b-H), 4.00 (1H, q, 6-H), 4.07 (2H, m, CH_2CH_3), 4.14 (1H, m, 3-H), 4.43 (1H, d, $J_{5,4}$ = 6.0, 5-H), 4.83 (1H, t, $J_{4,3}$ = 6.0, 4-H), 5.06 (1H, d, $^2J_{H;H}$ = 12.5, CH_2 of Cbz), 5.11 (1H, d, CH_2 of Cbz), 7.31-7.38 (5H, m, H-arom.). ^{13}C NMR (125.7 MHz, DMSO-*d*$_6$, 353 K, δ ppm) δ 13.5 (CH_2CH_3), 16.2 (6-Me), 24.4, 25.2 ($C(CH_3)_2$), 39.5 (C-2), 56.0 (C-3), 57.9, 59.1 (C-6, CH_2CH_3), 65.7 (CH_2 of Cbz), 78.4 (C-4), 82.9 (C-5), 110.4 ($C(CH_3)_2$), 127.2, 127.4, 127.9, 136.4, (C-Ar), 154.0 (C=O of Cbz), 170.2 (COOEt); CIMS 378 [$(M + H)^+$, 7%], 377 [$(M)^+$, 4%]; CIHRMS *m/z* found 378.1930, calcd. for $C_{20}H_{28}NO_6$ $(M+H)^+$: 378.1916.

***(2R,3S,4R,5R)*-*N*-Benzyloxycarbonyl-(2-(2-aminophenylcarbamoylmethyl)-3,4-*O*-isopropylidene- 5-methylpyrrolidine-3,4-diol (48):** A solution of **47** (1.18 g, 3.12 mmol) in 2:1 EtOH: NaOH (90 mL) was heated to 50 ºC for 1.5 h. The mixture was neutralized with IRA-120H^+, filtered and concentrated. The crude acid was then dissolved in DMF and *o*-phenylenediamine (0.371 g, 3.43 mmol), DIPEA (1.07 mL, 6.24 mmol) and pyBOP (1.79 g, 3.43 mmol) were added. The mixture was stirred at r.t. for 4 h. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 and washed with satd. aq. sol. of citric acid and brine. The organic phase was dried (Na_2SO_4), filtered and concentrated. The resulting residue was purified by column chromatography (CH_2Cl_2:MeOH, 40:1) to give pure **48** (1.22 g, 89%, 2 steps). $[\alpha]_D^{20}$ -49 (*c* 0.95 in CH_2Cl_2); IR (ν cm^{-1}) 3446 (NH), 3364 (NH), 3030, 2984, 2932, 1697 (C=O); ^{1}H NMR (500 MHz, DMSO-*d*$_6$, 353 K, δ ppm) δ 1.13 (3H, d, $J_{Me,5}$ = 7.0, 5-Me), 1.28, 1.44 (3H each, 2s, $C(CH_3)_2$), 2.63 (1H, dd, $^2J_{1'a,1'b}$ = 15.5, $J_{1'a,2}$ = 9.0, 1'a-H), 3.31 (1H,

br d, 1'b-H), 4.02 (1H, q, 5-H), 4.23 (1H, m, 2-H), 4.42 (1H, d, $J_{4,3}$= 6.0, 4-H), 4.67 (2H, brs, N*H*$_2$), 4.84 (1H, t, $J_{3,2}$ = 6.0, 3-H), 5.09 (1H, d, $^2J_{H,H}$ = 12.5, C*H*$_2$ of Cbz), 5.12 (1H, d, C*H*$_2$ of Cbz), 6.52 (1H, td, *J* = 7.5, *J* = 1.5, H-arom.), 6.71 (1H, dd, *J* = 8.0, *J* = 1.5, H-arom), 6.90 (1H, td, *J* = 8.0, *J* = 1.5, H-arom.), 7.09 (1H, d, *J* = 7.5, H-arom), 7.29-7.39 (5H, m, H-arom. of Cbz), 8.79 (1H, brs, CON*H*). ^{13}C NMR (125.7 MHz, DMSO-d_6, 353 K, δ ppm) δ 16.1 (Me-5), 24.5, 25.6 (C(*C*H$_3$)$_2$), 34.9 (C-1'), 56.3 (C-2), 58.3 (C-5), 65.6 (CH$_2$ of Cbz), 79.0 (C-3), 82.8 (C-4), 110.3 (*C*(CH$_3$)$_2$), 115.2, 115.7, 123.1, 125.6, 127.2, 127.4, 127.9, 136.5, 142.3 (C-Ar), 154.1 (C=O of Cbz), 169.1 (*C*ONH); CIMS 440 [(M + H)$^+$, 8%], 439 [(M)$^+$, 18%], 91 (100); CIHRMS *m/z* found 439.2110, calcd. for $C_{24}H_{29}N_3O_5$ (M)$^+$: 439.2107. Anal. calcd. for $C_{24}H_{29}N_3O_5$: C, 65.59; H, 6.65; N, 9.56. Found: C, 65.58; H, 6.72; N, 9.13.

(2*R*,3*S*,4*R*,5*R*)-*N*-Benzyloxycarbonyl-(2-(1*H*-Benzoimidazol-2-ylmethyl)-3,4-*O*-isopropylidene-5-methylpyrrolidine-3,4-diol (49): A solution of **48** (41 mg, 0.09 mmol) in glacial AcOH (1.5 mL) was stirred at 65 ºC for 4 h. Then, the solvent was evaporated and the resulting residue was purified by column chromatography (ether:petroleum ether, 10:1) to give pure **49** (39 mg, 100%). $[\alpha]_D^{20}$ -48.6 (*c* 1.1 in CH_2Cl_2); IR (ν cm^{-1}) 2895, 2933, 1701 (C=O); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm) δ 1.18 (3H, d, $J_{Me,5}$ = 6.9, 5-Me), 1.23, 1.43 (3H each, 2s, C(C*H*$_3$)$_2$), 3.15 (1H, m, 1'a-H), 3.90 (1H, dd, $^2J_{1'b,1'a}$ = 15.9, $J_{1'b,2}$ = 3.6, 1'b-H), 4.08 (1H, q, 5-H), 4.44 (1H, d, $J_{4,3}$ = 6.0, 4-H), 4.53 (1H, m, 2-H), 4.88 (1H, t, $J_{3,2}$ = 6.0, 3-H), 5.09 (2H, s, C*H*$_2$ of Cbz), 7.09-7.14 (2H, m, H-arom.), 7.27-7.37 (5H, m, H-arom.), 7.46 (2H, brs, H-arom.), 11.81 (1H, s, N*H*). ^{13}C NMR (75.4 MHz, DMSO-d_6, δ ppm) δ 16.1 (5-Me), 24.5, 25.7 (C(*C*H$_3$)$_2$), 27.4 (C-1'), 57.6 (C-2), 58.8 (C-5), 65.7 (CH$_2$ of Cbz), 78.8 (C-3), 82.8 (C-4), 110.4 (*C*(CH$_3$)$_2$), 119.2, 127.2, 127.4, 127.9, 136.5, 152.5 (C-Ar), 154.6 (C=O of

Cbz); CIMS 422 [$(M + H)^+$, 100%], 421 [$(M)^+$, 51%]; CIHRMS *m/z* found 422.2061, calcd. for $C_{24}H_{28}N_3O_4$ $(M+H)^+$: 422.2079.

(2*R*,3*S*,4*R*,5*R*)-2-(1*H*-Benzoimidazol-2-ylmethyl)-5-methylpyrrolidine-3,4-diol hydrochloride (19b): A solution of **49** (50 mg, 0.119 mmol) in MeOH (6 mL) was hydrogenated with Pd-C (10%) as catalyst. After 30 min, the catalyst was filtered off and the solution concentrated. The residue was purified by column chromatography (CH_2Cl_2:MeOH, 14:1) and the pure product thus obtained (27.3 mg, 0.095 mmol, 80%) was treated with 4M HCl (1 mL) and stirred for 12 h at r.t. After evaporation of the solvent, the resulting residue was purified by column chromatography (CH_2Cl_2:MeOH, 4:1) to give pure **19b** (19.7 mg, 73%). $[\alpha]_D^{25}$ + 20.5 (*c* 1.3 in MeOH); IR (ν cm^{-1}) 3252-2927 (OH, NH), 1445, 1272, 1129, 743; ^{1}H NMR (300 MHz, CD_3OD, δ ppm) δ 1.48 (3H, d, $J_{Me,5}$ = 6.6, 5-Me), 3.39 (1H, dd, $^2J_{1'a,1'b}$ = 15.9, $J_{1'a,2}$ = 7.8, 1'a-H), 3.54 (1H, dd, $J_{1'b,2}$ = 7.2, 1'b-H), 3.61 (1H, m, 5-H), 3.98 (1H, dd, $J_{4,5}$ = 9.0, 4-H), 4.18 (1H, t, $J_{3,2}$ = $J_{3,4}$= 3.6, 3-H), 4.28 (1H, m, 2-H), 7.25 (2H, dd, H-arom.), 7.55 (2H, dd, *J* = 3.3, *J* = 6.0, H-arom.). ^{13}C NMR (75.4 MHz, CD_3OD, δ ppm) δ 15.8 (5-Me), 27.3 (C-1'), 58.2 (C-5), 59.8 (C-2), 72.1 (C-3), 78.3 (C-4), 115.6, 123.8, 139.3, 151.5 (C-Ar); CIMS 248 [$(M+H)^+$, 45%]; CIHRMS *m/z* found 248.1396, calcd. for $C_{13}H_{18}N_3O_2$ $(M + H)^+$: 248.1399.

Data for compound **50**: ^{1}H NMR (300 MHz, CD_3OD, δ ppm) δ 1.31 (3H, d, *J* = 6.3), 2.85 (1H, m), 2.92 (1H, dd, *J* = 17.5, *J* = 6.5), 3.43 (1H, dd, *J* = 17.5, *J* = 8.7), 3.77 (1H, dd, *J* = 6.3, *J* = 5.8,), 3.85 (1H, dt, *J* = 8.7, *J* = 6.3), 4.28 (1H, t, *J* = 6.3), 5.05 (1H, d, *J* = 12.6), 5.26 (1H, d, *J* = 12.6), 7.19-7.27 (2H, m), 7.46-7.51 (1H, m), 7.54-7.60 (1H, m). ^{13}C NMR (75.4 MHz, CD_3OD, δ ppm) δ 17.7, 23.2, 58.5, 59.6, 61.4, 71.7, 78.3, 110.4, 118.9, 123.2, 123.4, 134.6, 143.0, 152.3; CIMS 259 [$(M)^+$, 30%], 260 [$(M+H)^+$, 100%]; CIHRMS *m/z* found 259.1319, calcd. for $C_{13}H_{18}N_3O_2$ $(M)^+$: 259.1321.

Ethyl *N*-Benzyloxycarbonyl-2,3,6-trideoxy-3,6-imino-4,5:7,8-di-*O*-isopropylidene-D-*glycero*-L-*altro* and L-*allo*-octonates (58): To a solution of ethyl 2,3,6-trideoxy-3,6-imino-4,5:7,8-di-*O*-isopropylidene-D-glicero-L-*altro*- and L-*allo*-octonates[1] (4.07 g, 12.37 mmol) in EtOH:H_2O (1/1, 80 mL), $NaHCO_3$ (1.76 g, 21.05 mmol) and CbzCl (1.92 mL, 13.63 mmol) were added. After stirring 12 h at r.t., sat. aq. soln. of $NaHCO_3$ was added and the mixture was extracted with ethyl acetate. The organic phase was dried over Na_2SO_4 and concentrated. The residue was used in the next step without further purification.

Ethyl *N*-Benzyloxycarbonyl-2,3,6-trideoxy-3,6-imino-4,5-*O*-isopropylidene-D-*glycero*- L-*altro* and L-*allo* -octonates (59 and 60): To a solution of **58** (540 mg, 1.166 mmol) in MeCN (5.3 mL), $Zn(NO_3)_2{\cdot}6H_2O$ (1.04 g, 3.50 mmol) was added. After heating at 50 ºC for 8 h, the solvent was evaporated. The residue was diluted with CH_2Cl_2 and washed with water and brine. The organic phases were dried, filtered and concentrated. Column chromatography (petroleum ether:AcOEt, 1:1 $\rightarrow$ 1:3) afforded **60** (10.7 mg, 9%) and **59** (160.1 mg, 66%) as syrups. Data for **60**: $[\alpha]_D^{22}$ +39.2 (*c* 1.0 in CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6, 363 K, δ ppm) δ 1.18 (3H, t, $J_{H,H}$ = 7.0, OCH_2CH_3), 1.25, 1.32 (3H each, 2s, $C(CH_3)_2$), 2.67 (1H, dd, $^2J_{2a,2b}$ = 15.0, $J_{2a,3}$ = 5.0, 2a-H), 2.82 (1H, dd, $J_{2b,3}$ = 10.0, 2b-H), 3.28 (1H, dd, $^2J_{8a,8b}$ = 11.0, $J_{8a,7}$ = 6.5, 8a-H), 3.42 (1H, dd, $J_{8b,7}$ = 5.0, 8b-H), 3.68 (1H, m, H-7), 4.07 (2H, m, OCH_2CH_3), 4.15 (1H, brs, O*H*-8), 4.19 (1H, d, $J_{6,7}$ = 3.5, 6-H), 4.23 (1H, ddd, $J_{3,4}$ = 1.7, 3-H), 4.48 (1H, dd, $J_{4,5}$ = 5.7, 4-H), 4.72 (1H, d, 5-H), 4.83 (1H, brs, O*H*-7), 5.14 (2H, s, CH_2Ph), 7.30-7.37 (5H, m, Ph). ^{13}C NMR (125.7 MHz, DMSO-d_6, 363 K, δ ppm) δ 13.5 (OCH_2CH_3), 24.7, 26.7 ($C(CH_3)_2$), 37.3 (C-2), 59.4 (OCH_2CH_3), 62.7 (C-8), 62.8 (C-3), 65.8 (C-6), 66.1 (CH_2Ph), 71.5 (C-7), 82.2 (C-5), 84.0 (C-4), 110.0 ($C(CH_3)_2$), 126.7, 127.3, 127.9, (C

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arom.), 136.5 (Cq arom.), 154.9 (C=O of Cbz), 170.1 (*C*OOEt). CIHRMS *m/z* found 424.1960, cald. for $C_{21}H_{29}NO_8$+H: 424.1971. Data for **59**: $[\alpha]_D^{22}$ +66.7 (*c* 1.6 in CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6, 363 K, δ ppm) δ 1.18 (3H, t, $J_{H,H}$ = 7.0, OCH_2CH_3), 1.27, 1.36 (3H each, 2s, $C(CH_3)_2$), 2.46 (1H, dd, $^2J_{2a,2b}$ = 17.0, $J_{2a,3}$ = 8.5, 2a-H), 3.22 (1H, brs, 2b-H), 3.29 (1H, dt, $^2J_{8a,8b}$ = 11.0, $J_{8a,7}$ = $J_{8a,OH}$ = 5.7, 8a-H), 3.38 (1H, dt, $J_{8b,7}$ = $J_{8b,OH}$= 4.5, 8b-H), 3.82 (1H, brs, 6-H), 4.04-4.10 (3H, m, 7-H, OCH_2CH_3), 4.22-4.25 (2H, m, 3-H, O*H*-8), 4.73 (1H, dd, $J_{4,3}$ = 6.0, 4-H), 4.77 (1H, t, $J_{5,4}$ = $J_{5,6}$ = 6.5, 5-H), 5.02, 5.10 (1H each, 2d, $J_{H,H'}$ = 12.7, CH_2Ph), 7.32-7.37 (5H, m, Ph). ^{13}C NMR (125.7 MHz, DMSO-d_6, 363 K, δ ppm) δ 13.5 (OCH_2CH_3), 24.4, 25.3 ($C(CH_3)_2$), 33.6 (C-2), 58.0 (C-3), 59.0 (OCH_2CH_3), 62.3 (C-8), 64.8 (C-7), 65.6 (CH_2Ph), 70.2 (C-6), 79.3 (C-4), 79.7 (C-5), 109.8 ($C(CH_3)_2$), 127.1, 127.3, 127.8 (C arom.), 136.4 (Cq. arom.), 154.0 (C=O of Cbz), 170.3 (*C*OOEt). CIHRMS *m/z* found 424.1955, cald. for $C_{21}H_{29}NO_8$+H: 424.1971.

(2*S*,3*R*,4*S*,5*S*)-*N*-Benzyloxycarbonyl-2-ethoxycarbonylmethyl-5-formyl-3,4-*O*-isopropylidene-pyrrolidine-3,4-diol (61): A solution of $NaIO_4$ (356 mg, 1.65 mmol) in water (6 mL) was added dropwise to a solution of **59** (348 mg, 0.823 mmol) in THF (5 mL) cooled to 0ºC. After stirring 3 h at r.t., THF was evaporated and the residue dissolved in CH_2Cl_2 (20 mL) and washed successively with water, sat. aq. soln. of $NaHCO_3$ and brine. The organic phase was dried, filtered and concentrated to give crude aldehyde **61** (300 mg, 93%) which was used for the next step without further purification. ^{1}H NMR (300 MHz, DMSO-d_6, 363 K, δ ppm) δ 1.18 (3H, t, $J_{H,H}$ = 7.0, OCH_2CH_3), 1.29, 1.41 (3H each, 2s, $C(CH_3)_2$), 2.60 (1H, dd, $^2J_{1'a,1'b}$ = 16.5, $J_{1'a,2}$ = 9.3, 1'a-H), 3.18 (1H, m, 1'b-H), 4.06 (2H, m, OCH_2CH_3), 4.28 (1H, m, 2-H), 4.46 (1H, brs, 5-H), 4.70 (1H, t, $J_{3,2}$ = $J_{3,4}$ = 6.3, 3-H), 4.79 (1H, t, $J_{4,5}$ = 6.3, 4-H), 5.08 (2H, s, CH_2Ph), 7.31-7.37 (5H, m, Ph), 9.55 (1H, d, $J_{CHO,5}$= 1.5, C*H*O). ^{13}C NMR (75.4 MHz,

DMSO-d_6, 363 K, δ ppm) δ 13.4 (OCH_2CH_3), 24.4, 25.3 ($C(CH_3)_2$), 33.3 (C-1'), 57.7 (C-2), 59.1 (OCH_2CH_3), 66.2 (CH_2Ph), 70.8 (C-5), 77.1 (C-4), 78.8 (C-3), 111.2 ($C(CH_3)_2$), 127.1, 127.4, 127.8, (C arom.), 135.8 (Cq arom.), 154.1 (C=O of Cbz), 169.8 (*C*OOEt), 197.7 (*C*HO). CIHRMS *m/z* found 392.1711, cald. for $C_{20}H_{25}NO_7$+H: 392.1709.

(2*S*,3*R*,4*S*,5*S*)-*N*-Benzyloxycarbonyl-2-ethoxycarbonylmethyl-5-carboxy-3,4-*O*-isopropylidene-pyrrolidine-3,4-diol (62): To a stirred solution of aldehyde **61** (300 mg, 0.767 mmol) and 2-methyl-2-butene (0.85 mL) in *t*-butanol (9.4 mL), a solution of $NaClO_2$ (0.77 g, 18.53 mmol) and NaH_2PO_4 (1.33 mg, 18.53 mmol) in water (7.5 mL) was added. The reaction mixture was stirred overnight at r.t. Then, the solvent was evaporated, the resulting residue was dissolved in CH_2Cl_2, washed with water, the organic phase dried (Na_2SO_4) and the solvent evaporated to give **62** (272 mg, 87 %), which was used in the next step without further purification.

(2*S*,3*S*,4*R*,5*S*)-*N*-Benzyloxycarbonyl-2-(2-aminophenylcarbamoyl)-5-ethoxycarbonylmethyl-3,4-*O*-isopropylidene-pyrrolidine-3,4-diol (63): To a solution of **62** (250 mg, 0.614 mmol) and *o*-phenylenediamine (72.8 mg, 0.676 mmol) in DMF, PyBOP (350 mg, 1.35 mmol) and DIPEA (208 μL, 1.35 mmol) were added, and the mixture was stirred at r.t. for 12 h. Then, the solvent was evaporated, the resulting residue was dissolved in CH_2Cl_2 and washed with HCl 1N, sat. aq. soln. of $NaHCO_3$ and brine. The resulting crude was purified by column chromatography (petroleum ether:AcOEt, 4:1→1:1) to give **63** (268 mg, 88%). $[\alpha]_D^{22}$ +44.8 (*c* 1.3 in CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6, 363 K, δ ppm) δ 1.20 (3H, t, $J_{H,H}$ = 7.5, OCH_2CH_3), 1.33, 1.46 (3H each, 2s, $C(CH_3)_2$), 2.57 (1H, dd, $J_{1'a,1'b}$ = 16.5, $J_{1'a,5}$ = 9.5, 1'a-H), 3.23 (1H, m, 1'b-H), 4.09 (2H, m, OCH_2CH_3), 4.44 (1H, m, 5-H), 4.68 (1H, s, 2-H), 4.83-4.87 (2H, m, 4-H, 3-H), 5.05, 5.13 (1H each, 2d, $J_{H,H'}$ = 14.0, CH_2Ph), 6.53 (1H, t, *J* = 7.0,

Ar), 6.75 (1H, d, *J* = 6.9, Ar), 6.93 (1H, t, *J* = 6.8, Ar), 7.11 (1H, d, *J* = 7.0, Ar), 7.27-7.35 (5H, m, Ph), 9.43 (1H, brs, N*H*). ^{13}C NMR (125.7 MHz, DMSO-d_6, 363 K, δ ppm) δ 13.5 (OCH_2CH_3), 24.4, 25.3 ($C(CH_3)_2$), 34.0 (C-1'), 58.4 (C-5), 59.1 (OCH_2CH_3), 66.0 (CH_2Ph), 66.3 (C-2), 78.9, 81.1 (C-4, C-3), 110.9 ($C(CH_3)_2$), 115.5, 115.8, 122.2, 125.1, 125.8, 126.9, 127.3, 127.8, 135.9, 141.6 (C arom.), 154.8 (C=O of Cbz), 168.2 (*C*ONH), 170.0 (*C*OOEt). CIHRMS *m/z* found 497.2157, cald. for $C_{26}H_{31}N_3O_7$: 497.2162.

(2*S*,3*S*,4*R*,5*S*)-*N*-Benzyloxycarbonyl-2-(1*H*-benzoimidazol-2-yl)-5-ethoxycarbonylmethyl-3,4-*O*-isopropylidene-pyrrolidine-3,4-diol (64): Compound **63** (250 mg, 0.503 mmol) was disolved in glacial AcOH (8.5 mL) and the mixture was stirred for 5 h at 50 ºC. Then, the solvent was evaporated and the resulting residue was purified by column chromatography (petroleum ether:AcOEt 1:1) to give pure **64** (231 mg, 96 %). $[\alpha]_D^{22}$ +98.4 (*c* 1.3 in CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6, 363 K, δ ppm) δ 1.21 (3H, t, $J_{H,H}$ = 7.0, OCH_2CH_3), 1.30, 1.48 (3H each, 2s, $C(CH_3)_2$), 2.66 (1H, dd, $J_{1'a,1'b}$ = 17.0, $J_{1'a,5}$ = 9.0, 1'a-H), 3.35 (1H, brd, 1'b-H), 4.11 (2H, m, OCH_2CH_3), 4.68 (1H, m, 5-H), 4.81 (1H, d, $J_{3,4}$ = 5.8, 3-H), 4.97 (1H, t, $J_{4,5}$ = 5.8, 4-H), 4.91, 4.99 (1H each, 2d, $J_{H,H'}$ = 12.5, CH_2Ph), 5.21 (1H, s, 2-H), 7.06-7.55 (9H, m, Ar), 12.29 (1H, brs, N*H*). ^{13}C NMR (125.7 MHz, DMSO-d_6, 363 K, δ ppm) δ 13.5 (OCH_2CH_3), 24.4, 25.3 ($C(CH_3)_2$), 33.7 (C-1'), 58.1 (C-5), 59.1 (OCH_2CH_3), 61.2 (C-2), 65.7 (CH_2Ph), 79.0 (C-4), 82.0 (C-3), 110.9 ($C(CH_3)_2$), 118.3-135.9 (Ar), 152.2 (C=N), 154.4 (C=O of Cbz), 170.1 (*C*OOEt). CIHRMS *m/z* found 480.2125, cald. for $C_{26}H_{29}N_3O_6$+H: 480.2135.

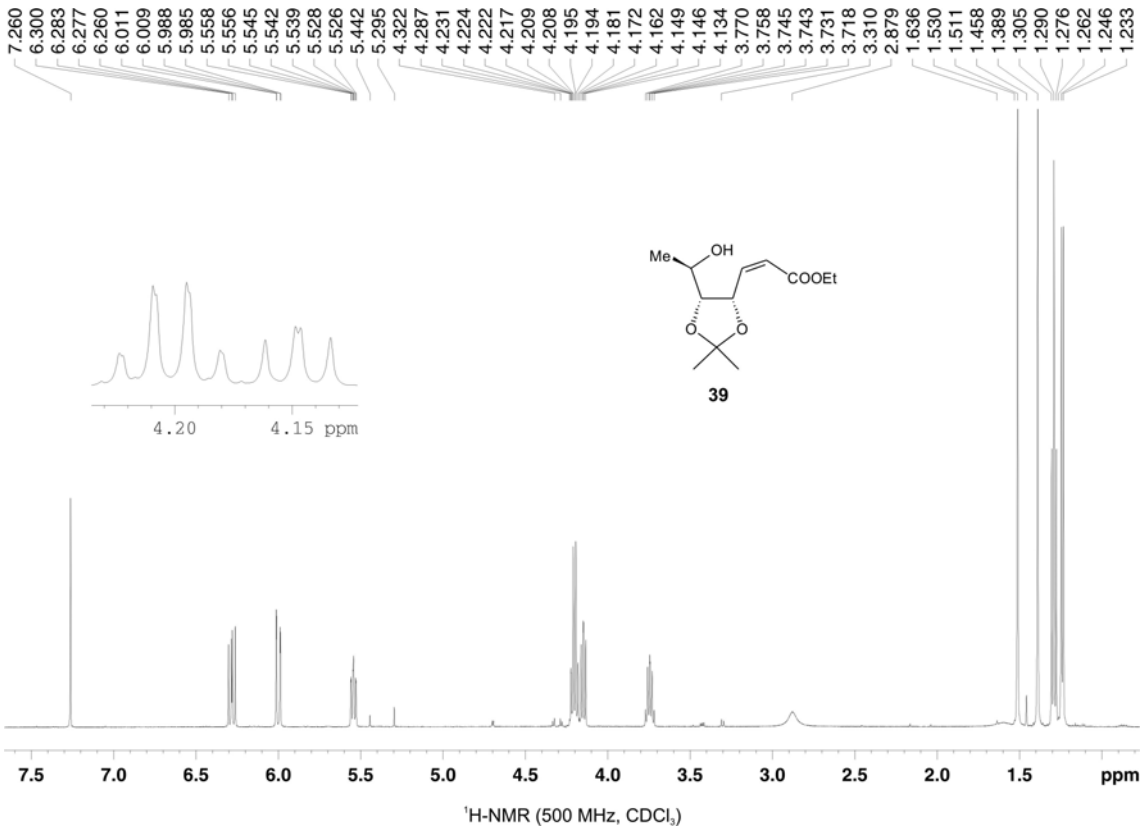
(2*S*,3*S*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-2-(1*H*-benzoimidazol-2-yl)-5-ethoxycarbonylmethyl-3,4-*O*-isopropylidene-pyrrolidine-3,4-diol (65): To a solution of compound **64** (310 mg, 0.647 mmol) in THF (2 mL) and a few drops of MeOH, Pd/C

(38.7 mg) and $(Boc)_2O$ (155 mg, 0.711 mmol) were added. The mixture was hydrogenated overnight. After filtration through celite, the filtrate was purified by column chromatography (petroleum ether:AcOEt 2:1) to give **65** (230.2 mg, 80%). $[\alpha]_D^{22}$ +73.2 (*c* 0.9 in CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6, 363 K, δ ppm) δ 1.11 (9H, s, C(*CH*$_3$)), 1.23 (3H, t, $J_{H,H}$ = 7.1, OCH_2CH_3), 1.29, 1.49 (3H each, 2s, $C(CH_3)_2$), 2.60 (1H, dd, $J_{1'a,1'b}$ = 16.5, $J_{1'a,5}$ = 4.5, 1'a-H), 3.29 (1H, dd, $J_{1'b,5}$ = 10.0, H-1'b), 4.12 (2H, q, OCH_2CH_3), 4.62 (1H, ddd, $J_{5,4}$ = 6.2, 5-H), 4.74 (1H, d, $J_{3,4}$ = 6.2, 3-H), 4.95 (1H, t, 4-H), 5.05 (1H, s, 2-H), 7.15-7.51 (9H, m, Ar), 12.25 (1H, brs, N*H*). ^{13}C NMR (125.7 MHz, DMSO-d_6, 363 K, δ ppm) δ 13.6 (OCH_2CH_3), 24.4, 25.3 ($C(CH_3)_2$), 27.3 ($C(CH_3)_3$), 33.9 (C-1'), 57.8 (C-5), 59.1 (OCH_2CH_3), 61.4 (C-2), 78.8 (C-4), 79.2 ($C(CH_3)_3$), 82.1 (C-3), 111.0 ($C(CH_3)_2$), 111.1-121.2 (Ar), 153.1 (C=N), 154.0 (C=O of Cbz), 170.3 (*C*OOEt). CIHRMS *m/z* found 446.2294, cald. for $C_{23}H_{31}N_3O_6$ + H: 446.2291.

(2*S*,3*S*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-2-(1*H*-benzoimidazol-2-yl)-5-(2-hydroxyethyl)-3,4-*O*-isopropylidene-pyrrolidine-3,4-diol (66): To a cooled solution of **65** (100 mg, 0.215 mmol) in dry THF (10 mL), $LiAlH_4$ (74 mg) was added. After 1 h at 0 ºC, the reaction was quenched with H_2O (500 µL) and 1M NaOH (200 µL). The reaction mixture was dried over Na_2SO_4 and purified by column chromatography (petroleum ether:AcOEt 1:4) to give **66** (87 mg, 96%). $[\alpha]_D^{22}$ +61.0 (*c* 1.5 in CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-d_6, 363 K, δ ppm) δ 1.12 (9H, s, $C(CH_3)_3$), 1.31, 1.50 (3H each, 2s, $C(CH_3)_2$), 1.94 (1H, m, 1'a-H), 2.50 (1H, m, 1'b-H), 3.55-3.64 (2H, m, 2'a-H, 2'b-H), 4.26 (1H, m, 5-H), 4.73 (1H, d, $J_{3,4}$ = 6.0, 3-H), 4.86 (1H, dd, $J_{4,5}$ = 5.5, 4-H), 5.00 (1H, s, 2-H), 7.14 (2H, m, Ar), 7.50 (2H, brs, Ar), 12.25 (1H, brs, N*H*). ^{13}C NMR (125.7 MHz, DMSO-d_6, 363 K, δ ppm) δ 24.5, 25.9 ($C(CH_3)_2$), 27.3 ($C(CH_3)_3$), 31.4 (C-1'), 58.2 (C-2'), 58.9 (C-5), 62.2 (C-2), 78.6 ($C(CH_3)_3$), 79.5 (C-4), 80.1 (C-3),

110.6 ($C(CH_3)_2$), 111.1-121.0 (Ar), 153.5, 154.0 (C=N, C=O of Boc). CIMS 404 [$(M+H)^+$, 98%]; CIHRMS *m/z* found 404.2201, cald. for $C_{21}H_{30}N_3O_5$ + H: 404.2185.

(2*S*,3*S*,4*R*,5*S*)-2-(1*H*-benzoimidazol-2-yl)-5-(2-hydroxyethyl)-pyrrolidine-3,4-diol (18c): Compound **66** (49.3 mg, 0.122 mmol) was treated with 4N HCl (4 mL) and stirred for 2 h at r.t. After evaporation of the solvent, the residue was treated with sat. aq. soln. of NH_4OH for 1 h. Then, elimination of the solvent and purification through chromatography column (DCM/MeOH/NH_4OH 10:1:0.1 → 2:1:0.1) afforded **18c** (30 mg, 92%). $[\alpha]_D^{22}$ -23.0 (*c* 1.0 in MeOH). ^{1}H NMR (300 MHz, CD_3OD, δ ppm) δ 2.01 (2H, m, 1'a-H, 1'b-H), 3.75 (2H, m, 2'a-H, 2'b-H), 4.06 (1H, td, $J_{5,1'a} = J_{5,1'b} = 6.9$, $J_{5,4}$ = 3.0, 5-H), 4.29 (1H, t, $J_{4,3}$ = 3.0, 4-H), 4.67-4.75 (2H, m, 2-H, 3-H). ^{13}C NMR (125.7 MHz, CD_3OD, δ ppm) δ 31.6 (C-1'), 59.4 (C-2), 59.9 (C-2'), 62.2 (C-5), 73.2 (C-4), 78.8 (C-3), 116.8, 120.7, 125.9, 140.1 (C arom.), 150.3 (C=N). CIHRMS *m/z* found 264.1353, cald. for $C_{13}H_{17}N_3O_3$+H: 264.1348.



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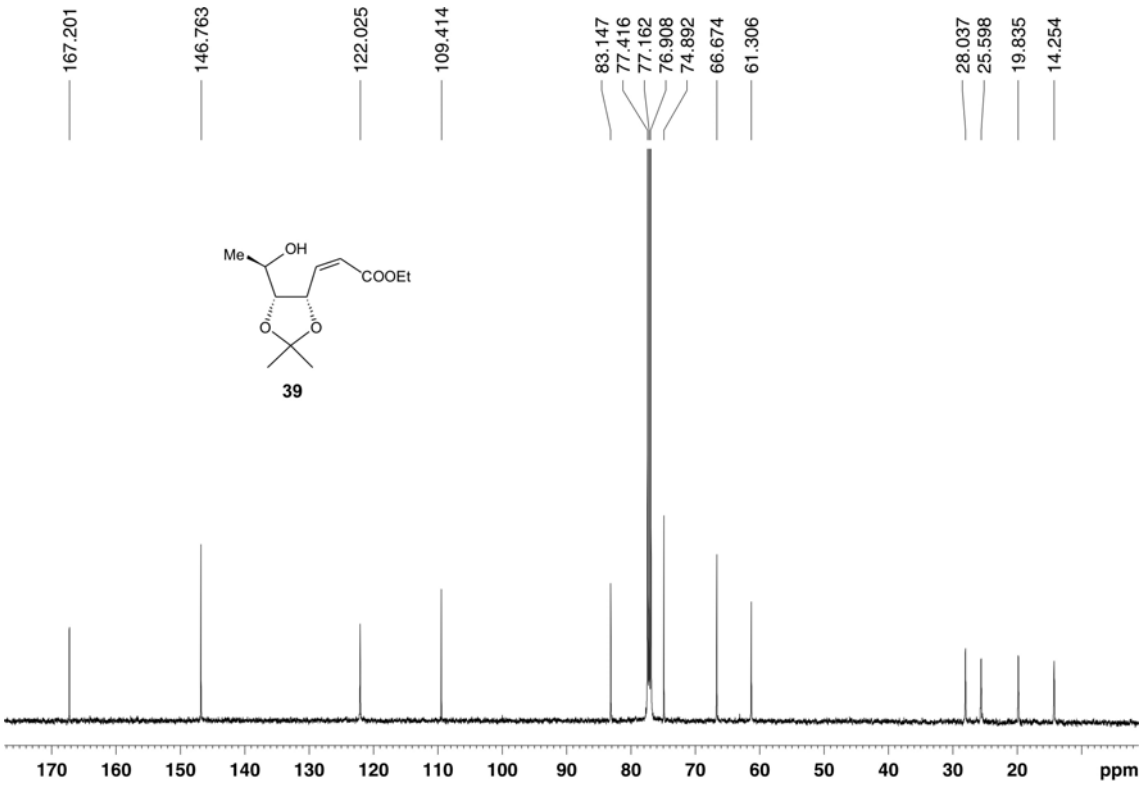
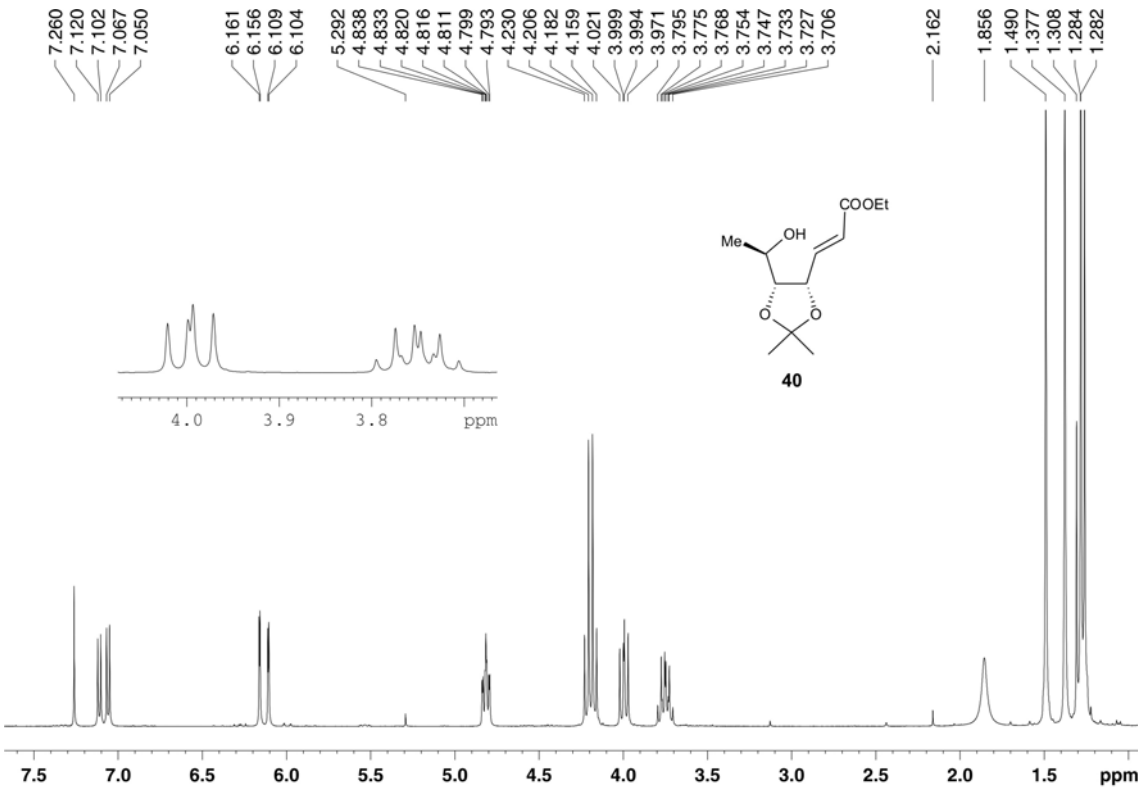
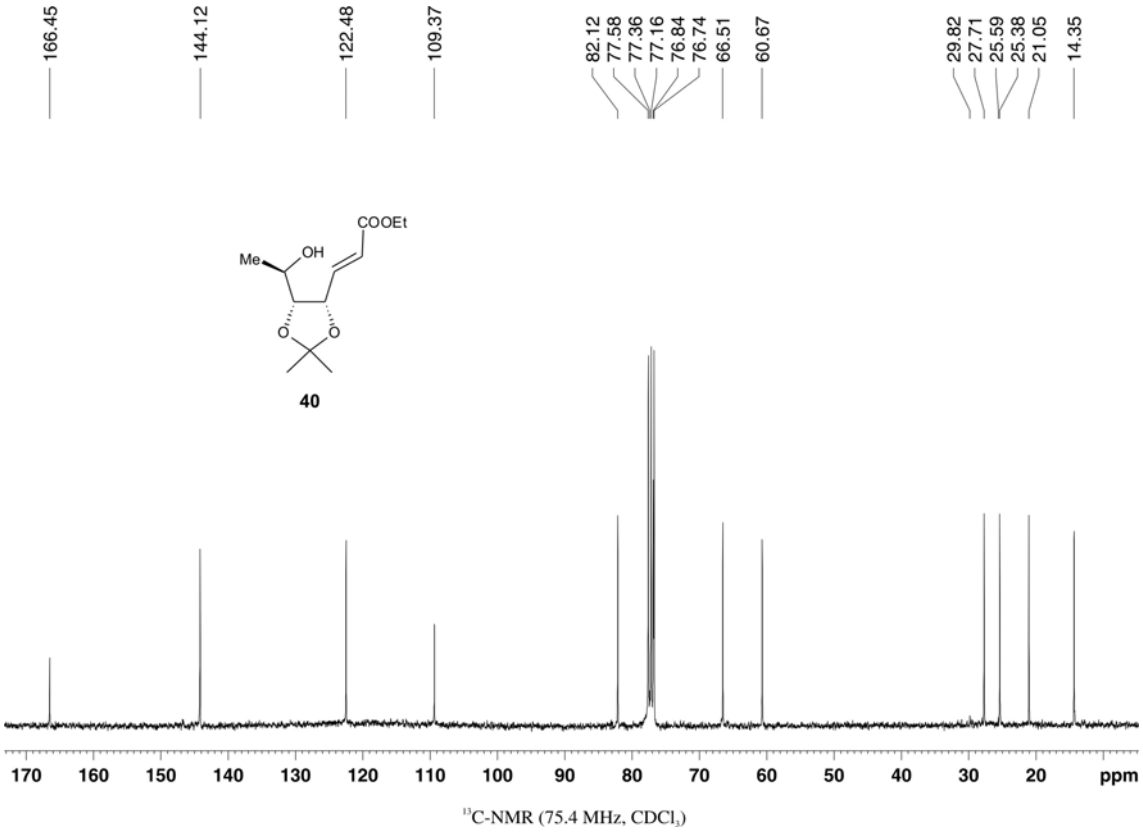


^{13}C-NMR (125 MHz, $CDCl_3$)



^{1}H-NMR (300 MHz, $CDCl_3$)



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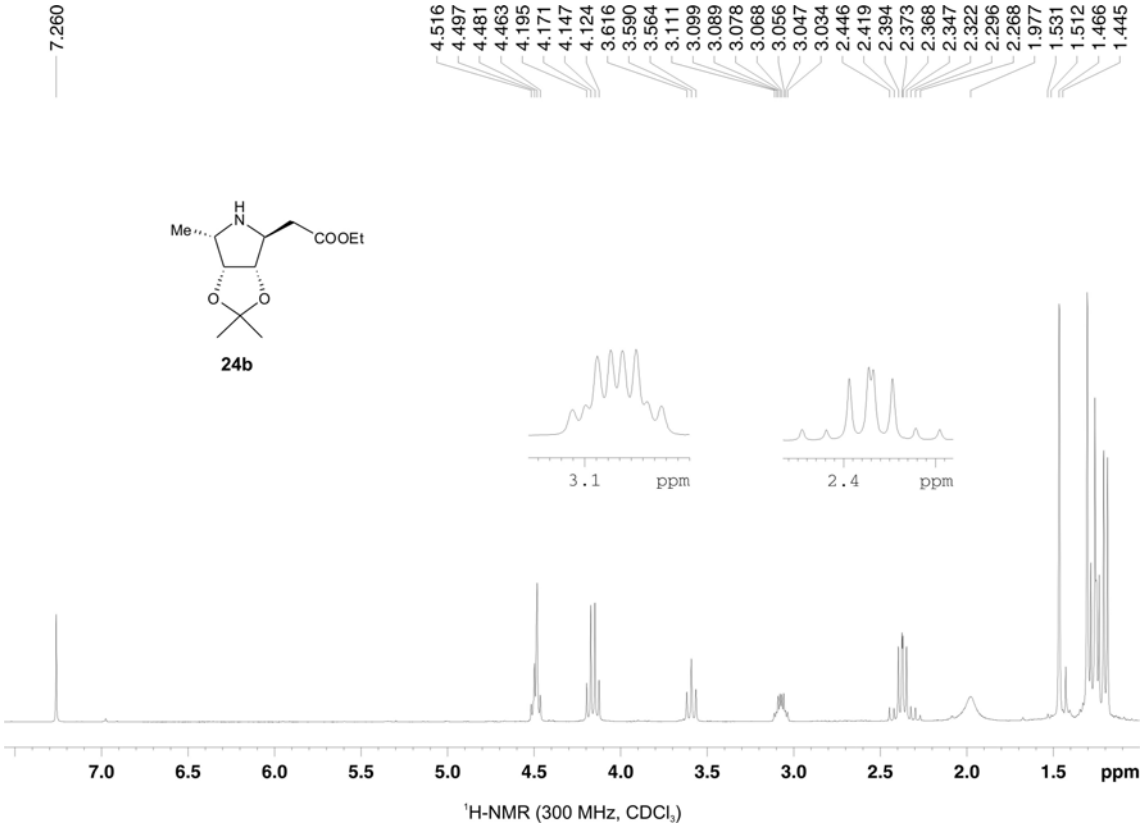

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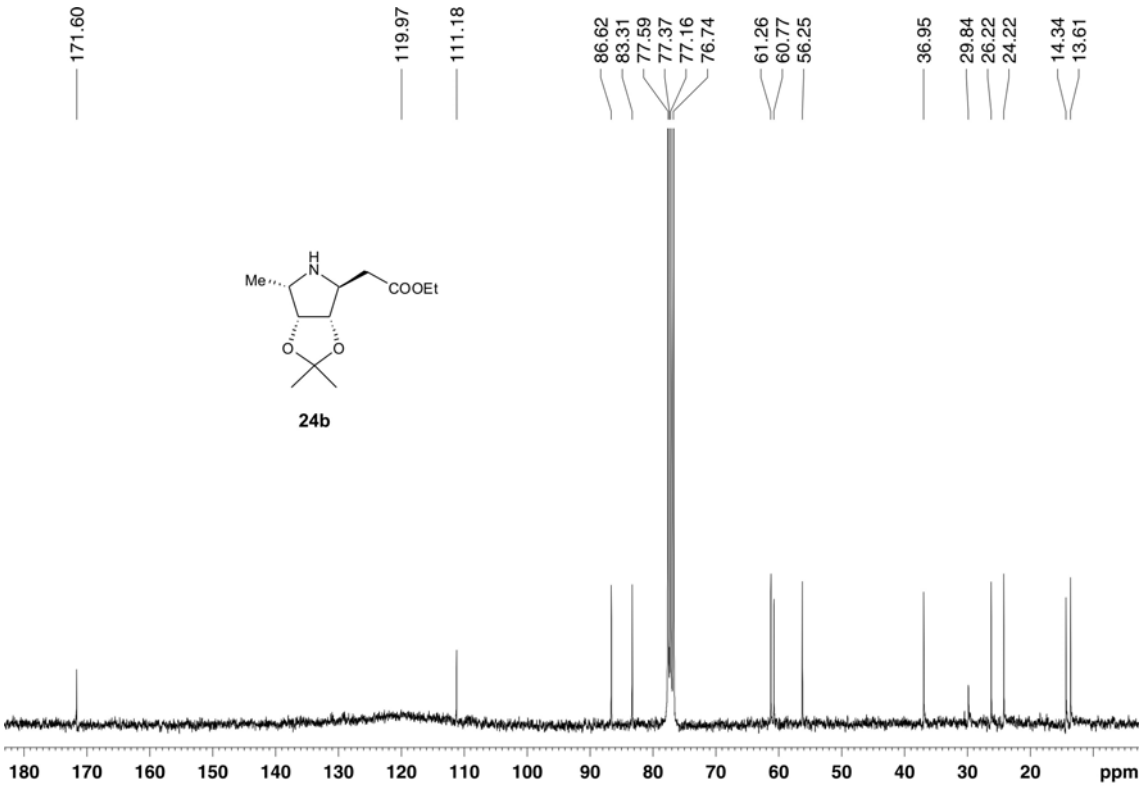

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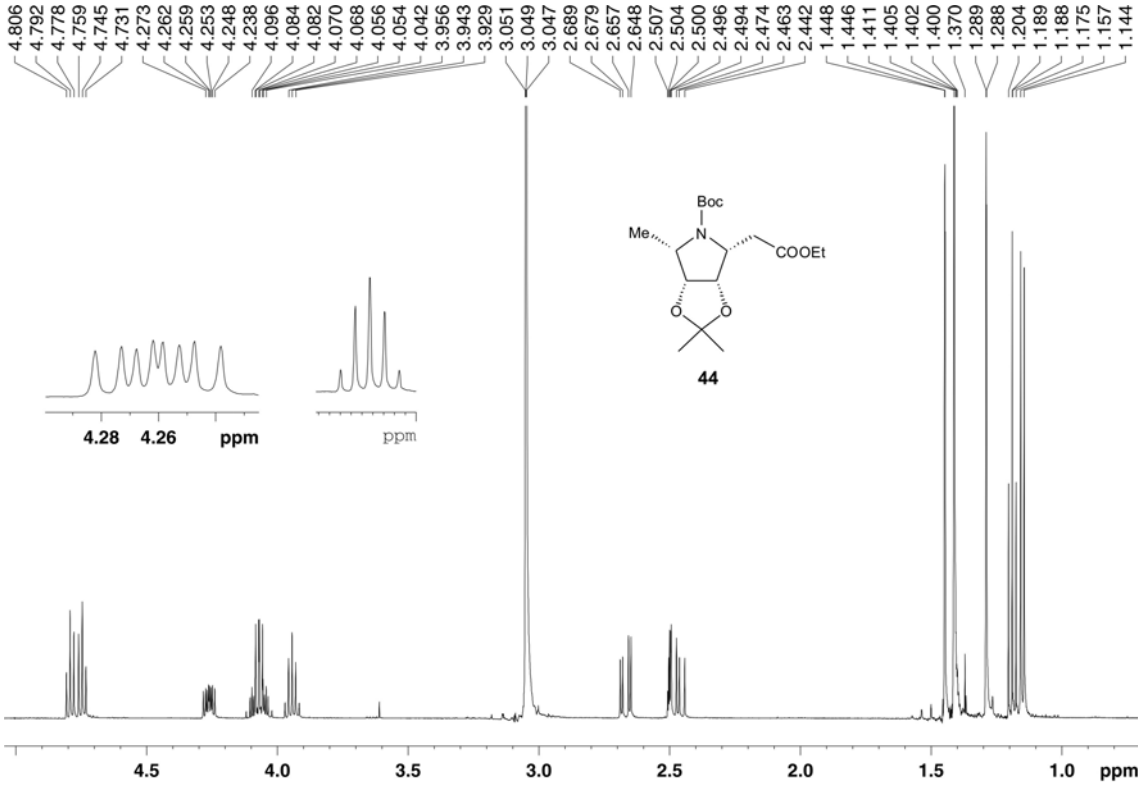

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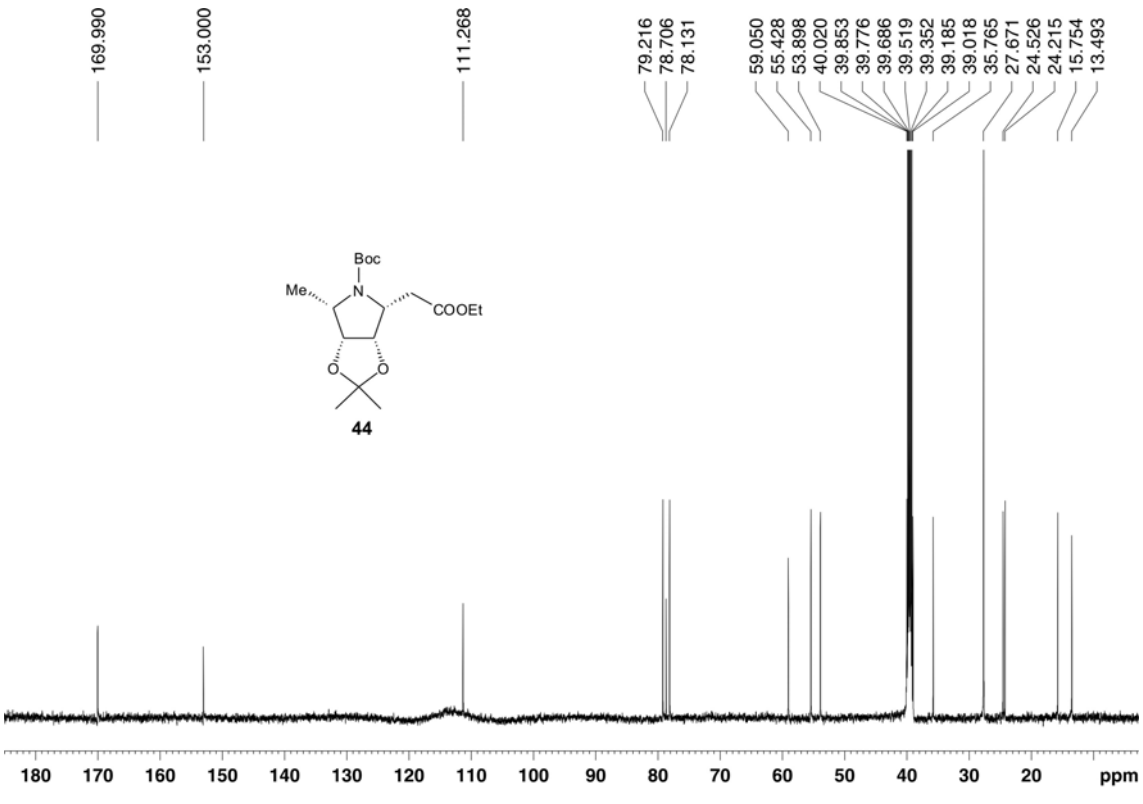

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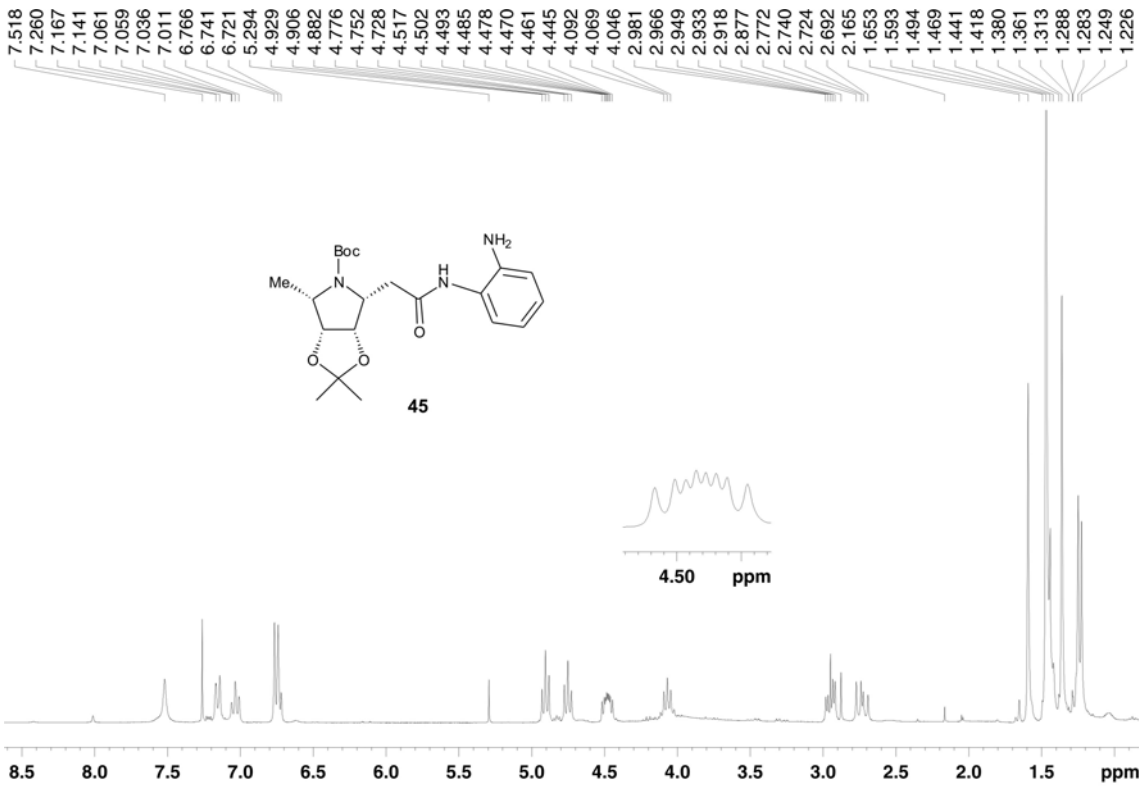

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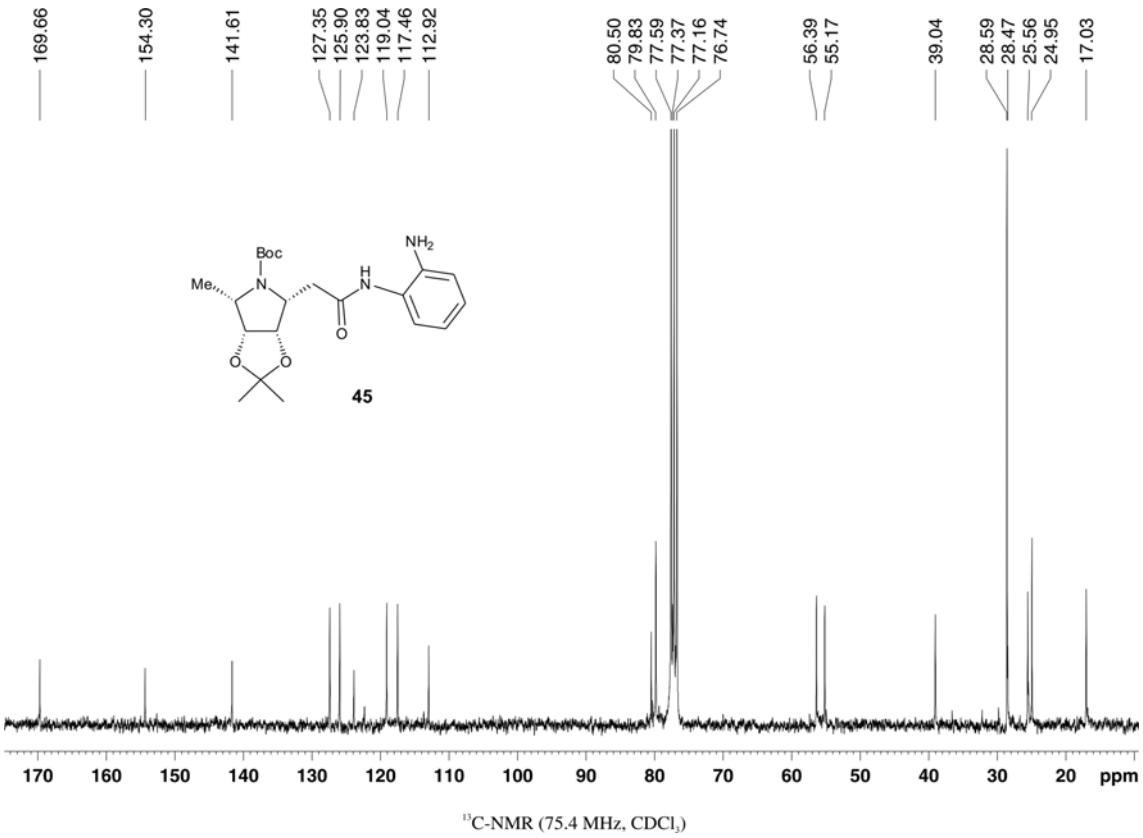

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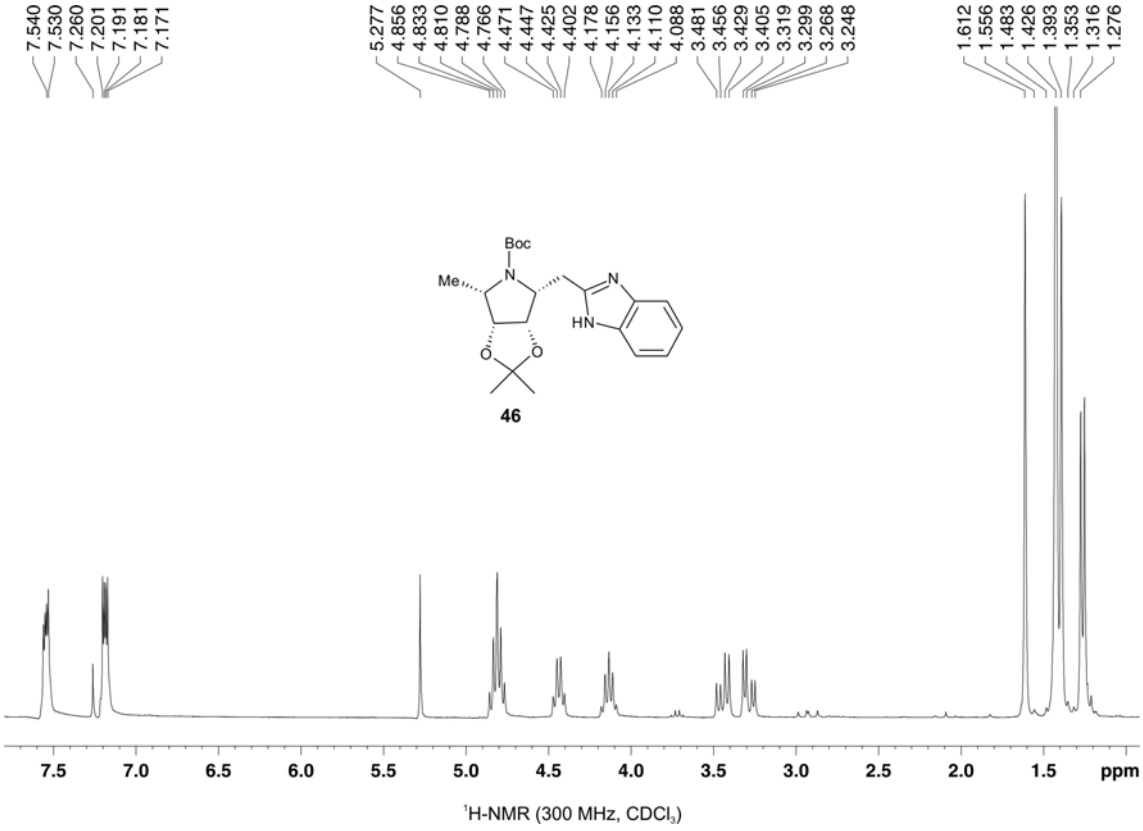
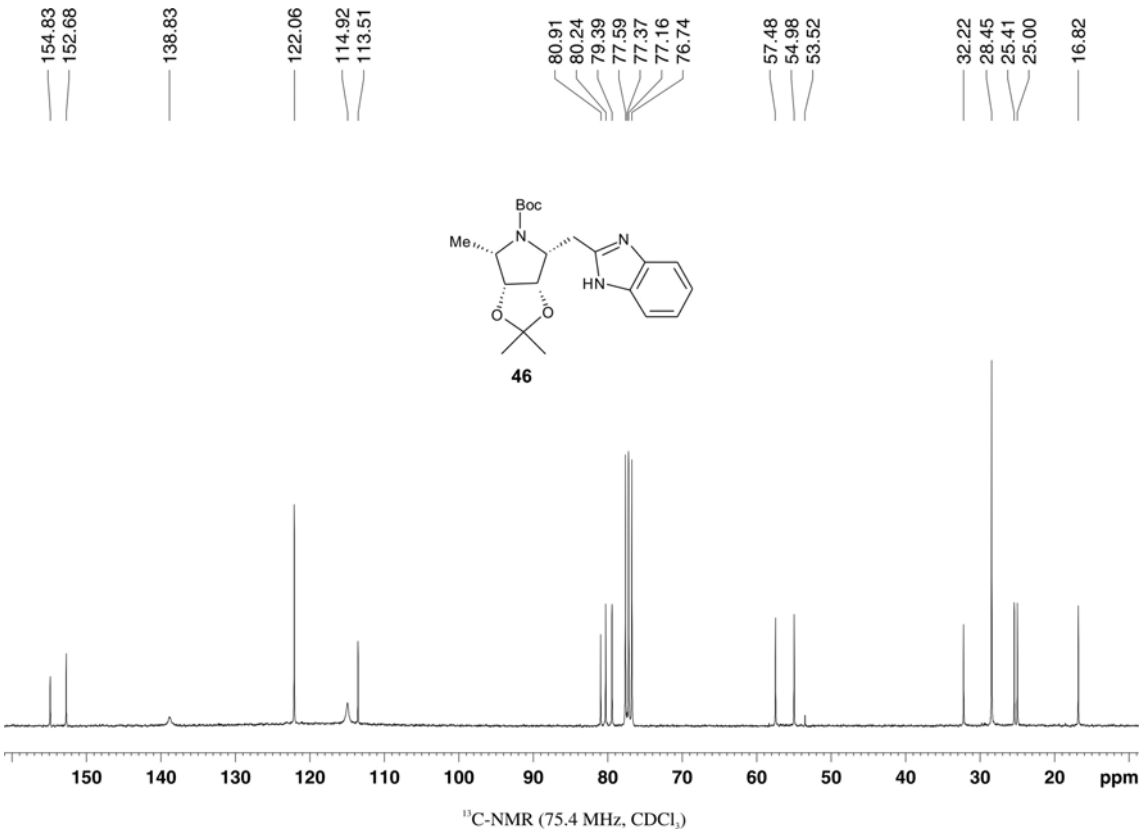


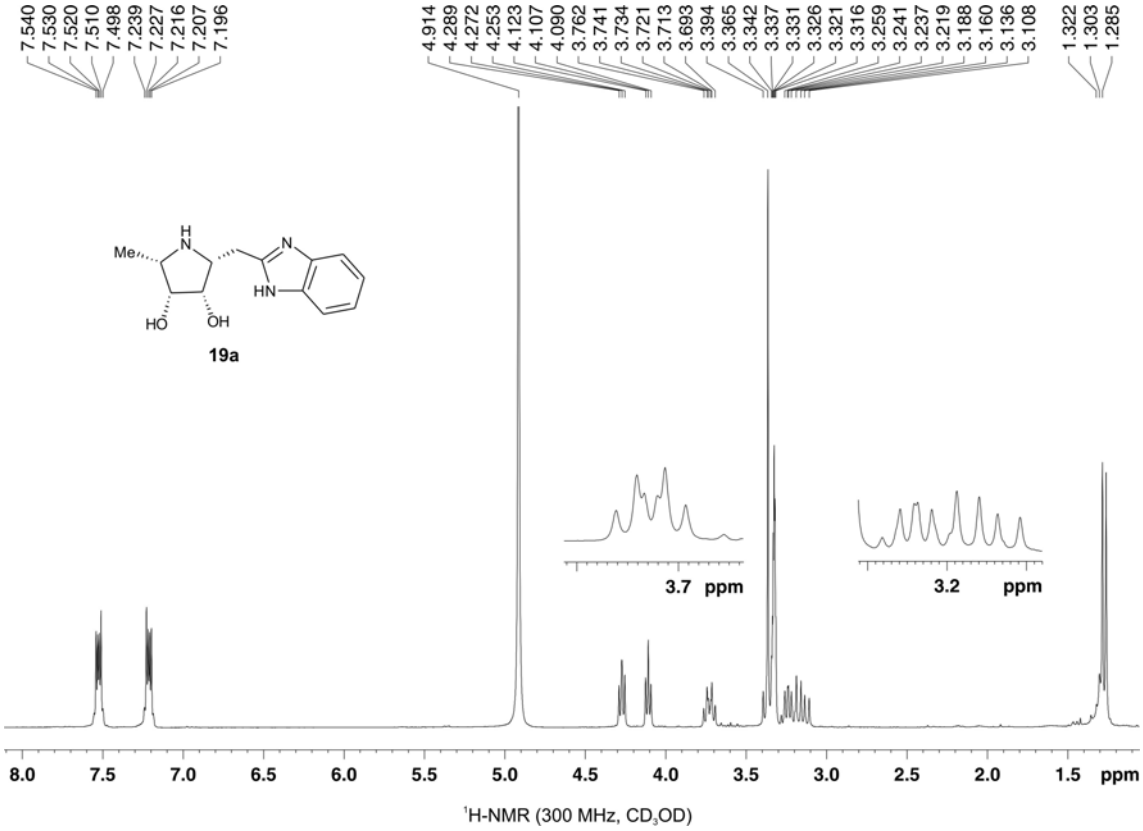
46

^{1}H-NMR (300 MHz, $CDCl_3$)

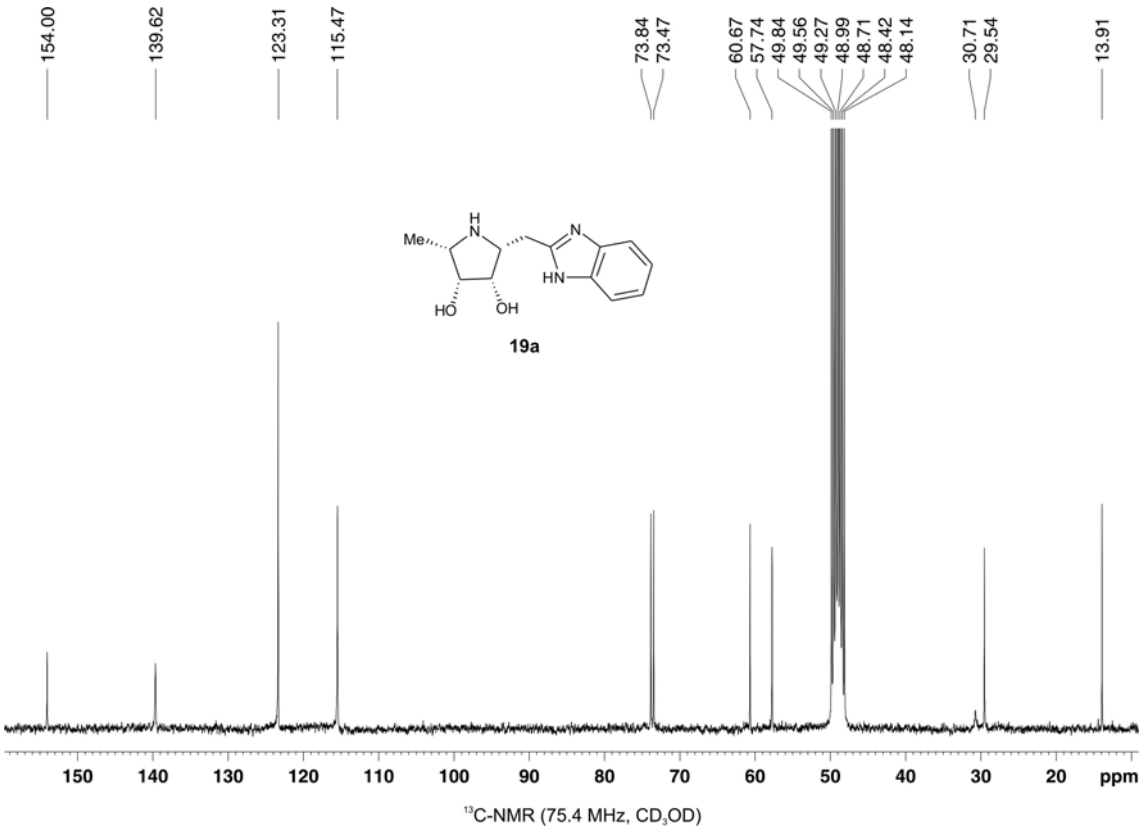


46

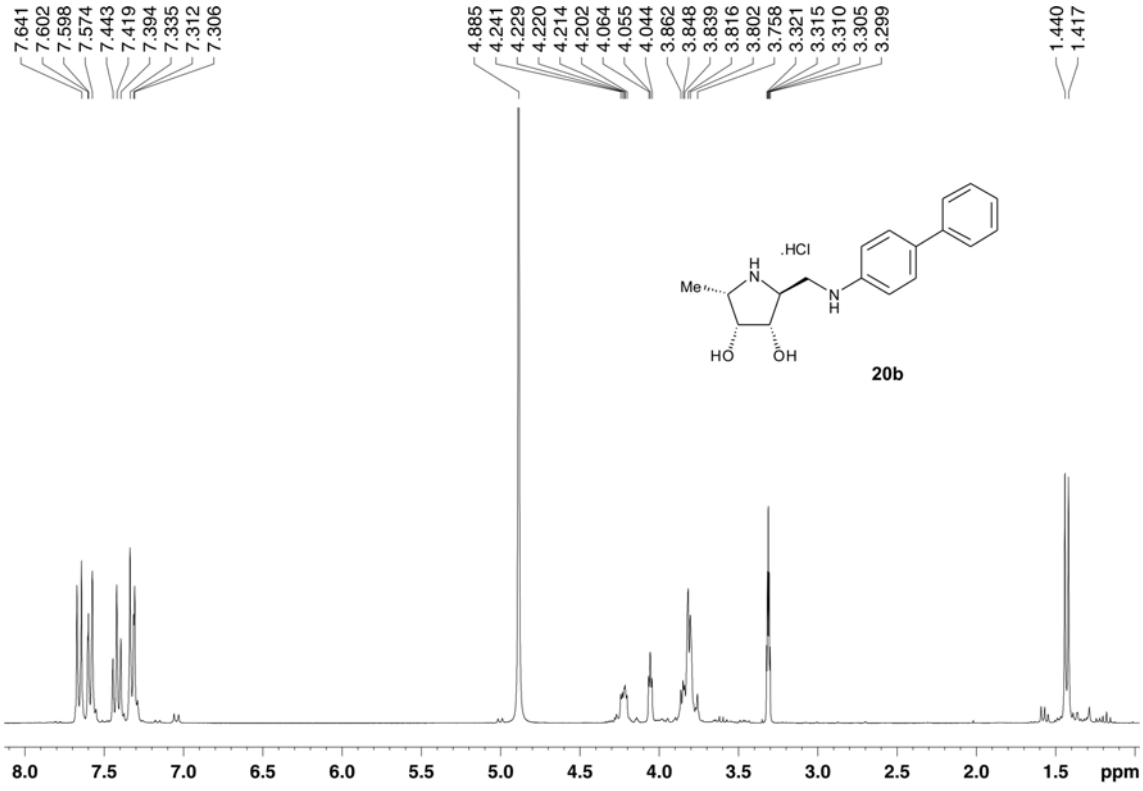
^{13}C-NMR (75.4 MHz, $CDCl_3$)



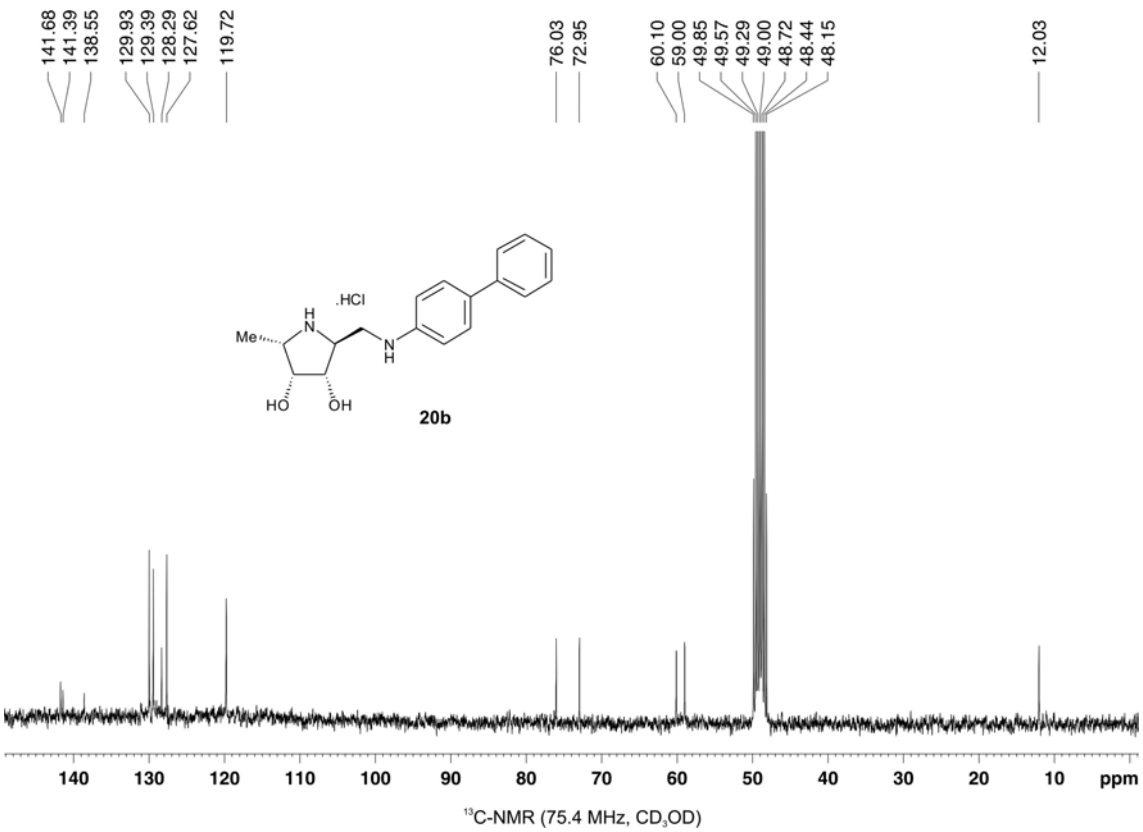
^{1}H-NMR (300 MHz, CD_3OD)



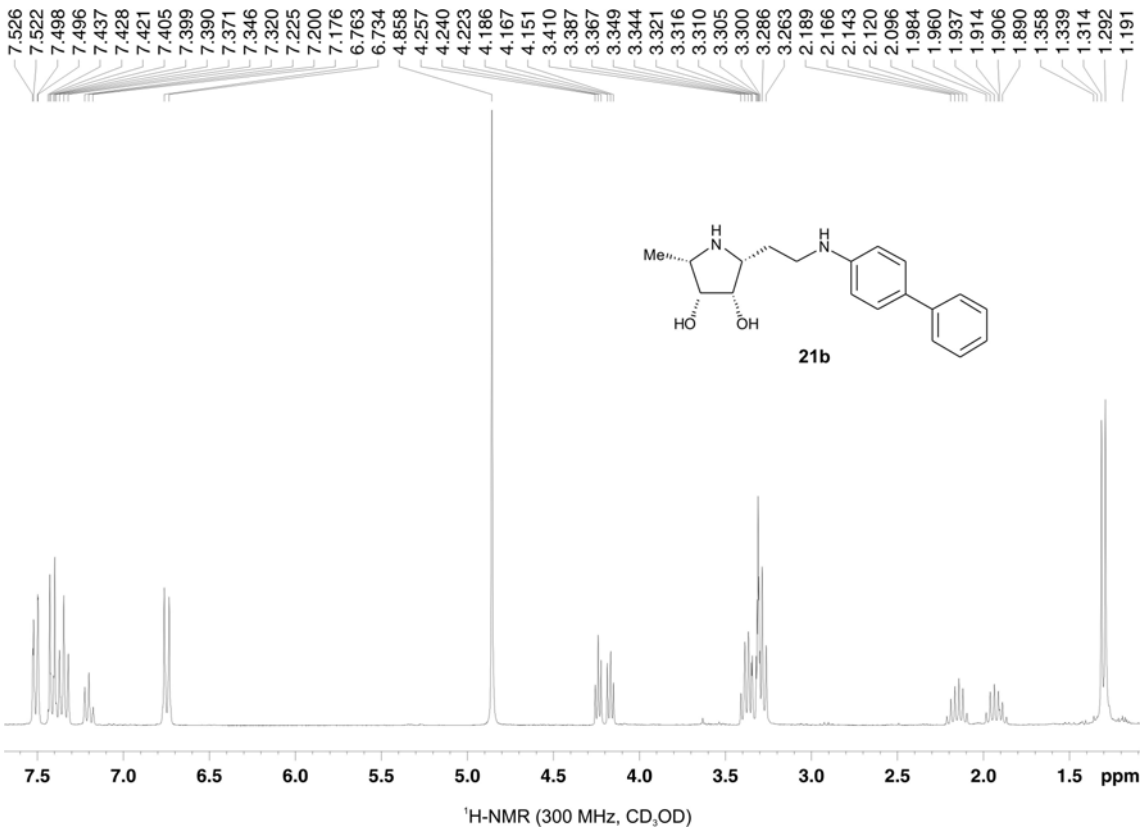
^{13}C-NMR (75.4 MHz, CD_3OD)



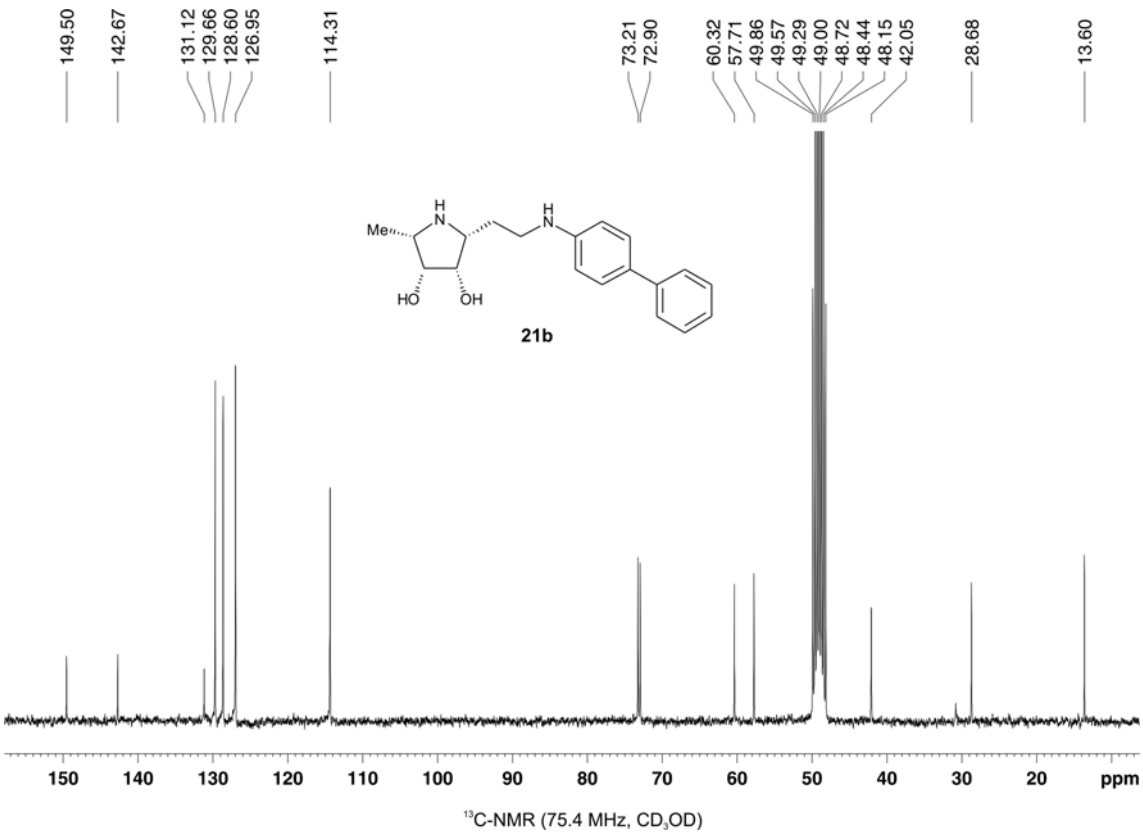
^{1}H-NMR (300 MHz, CD_3OD)



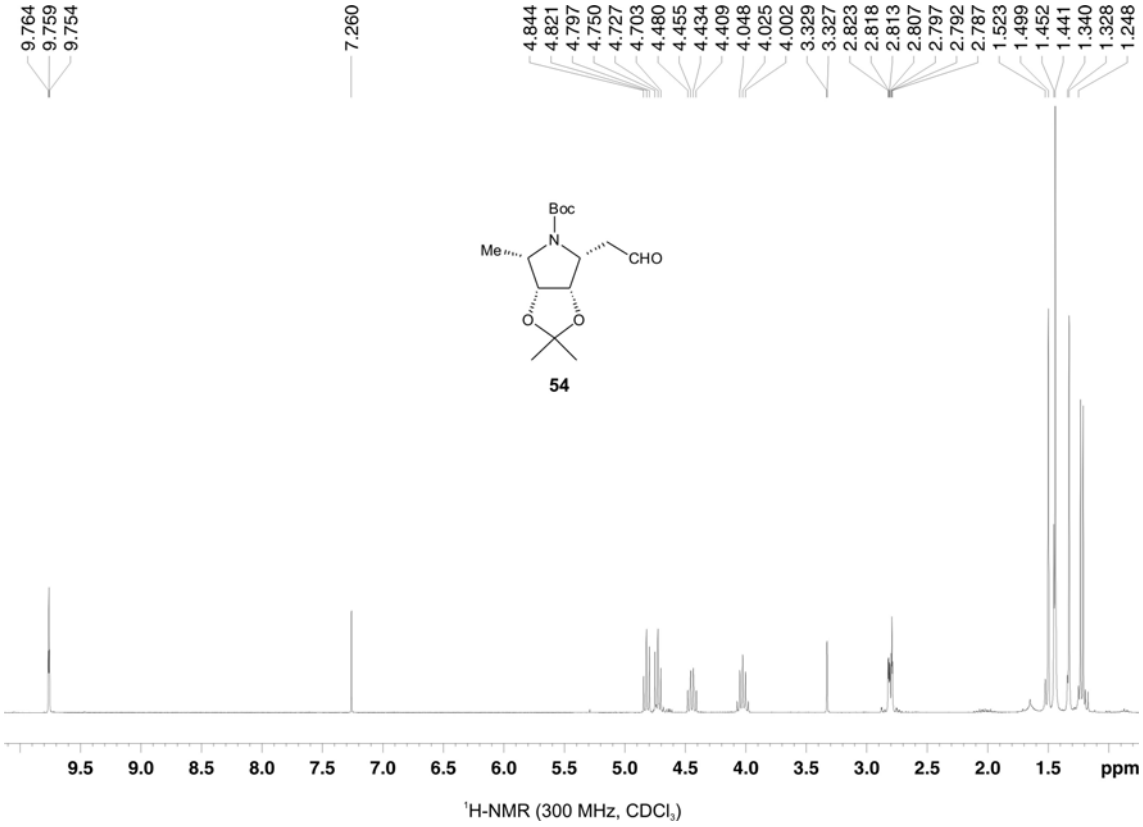
^{13}C-NMR (75.4 MHz, CD_3OD)



^{1}H-NMR (300 MHz, CD_3OD)

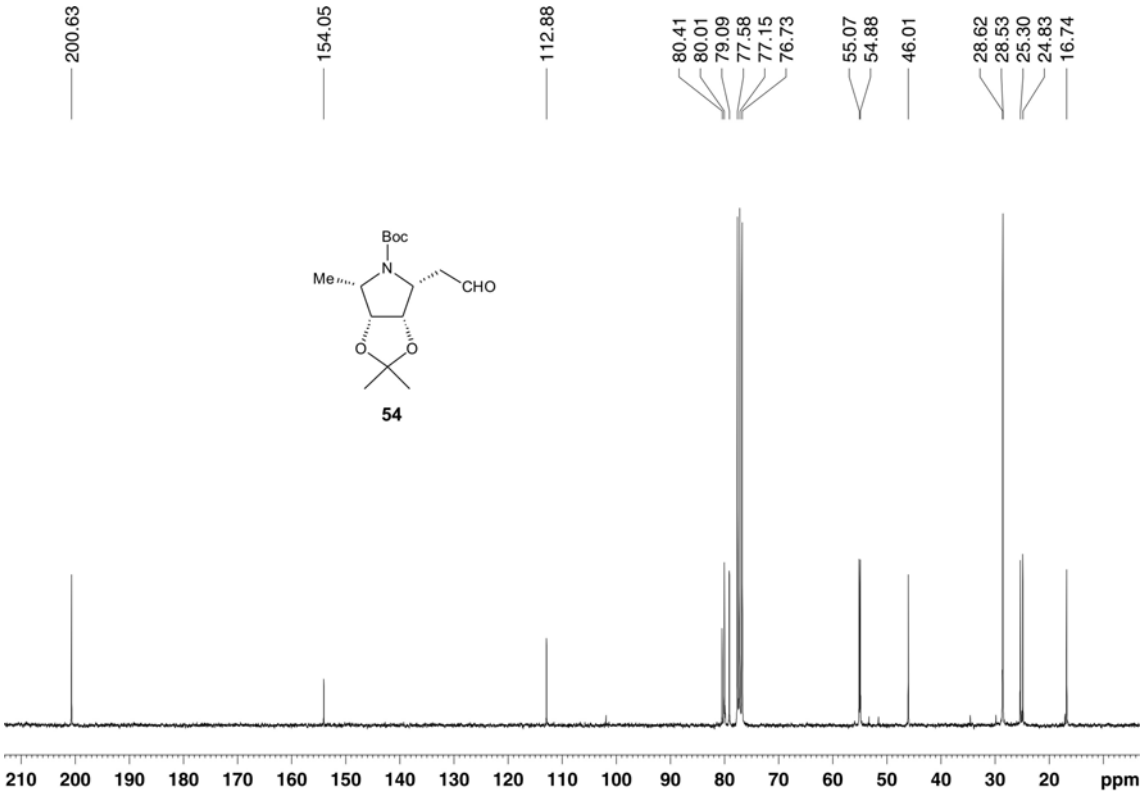


^{13}C-NMR (75.4 MHz, CD_3OD)



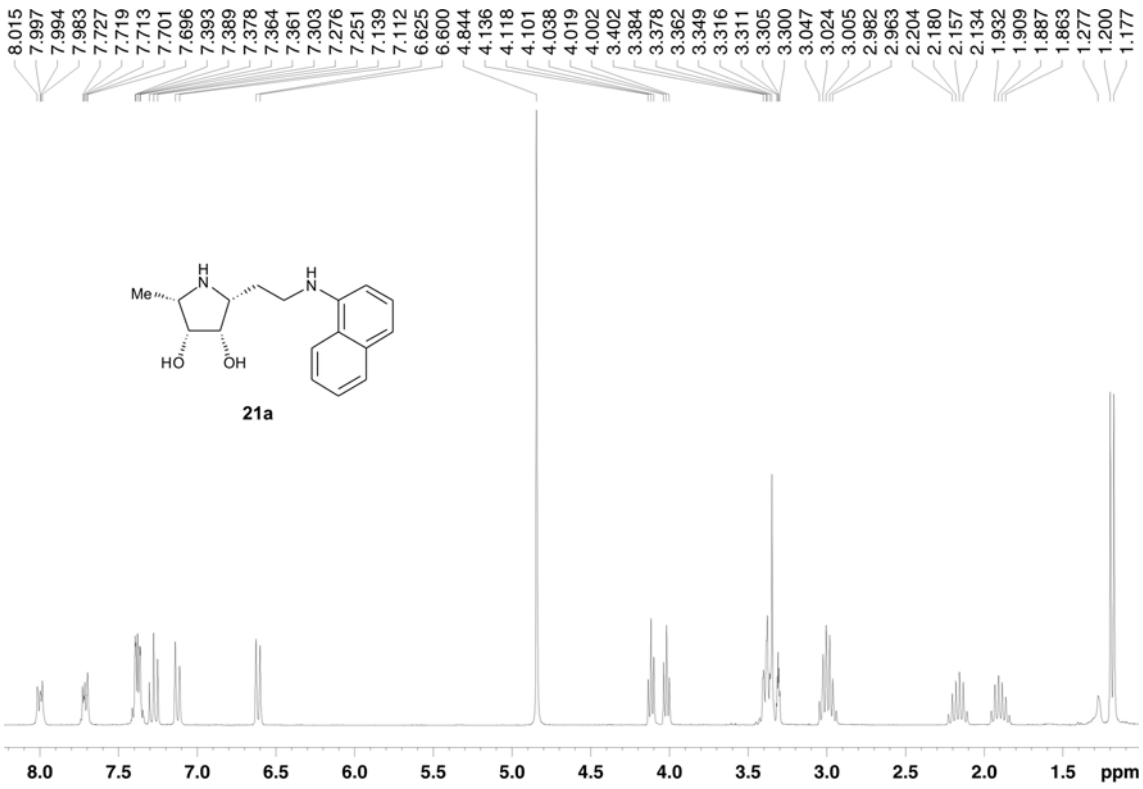
54

^{1}H-NMR (300 MHz, $CDCl_3$)

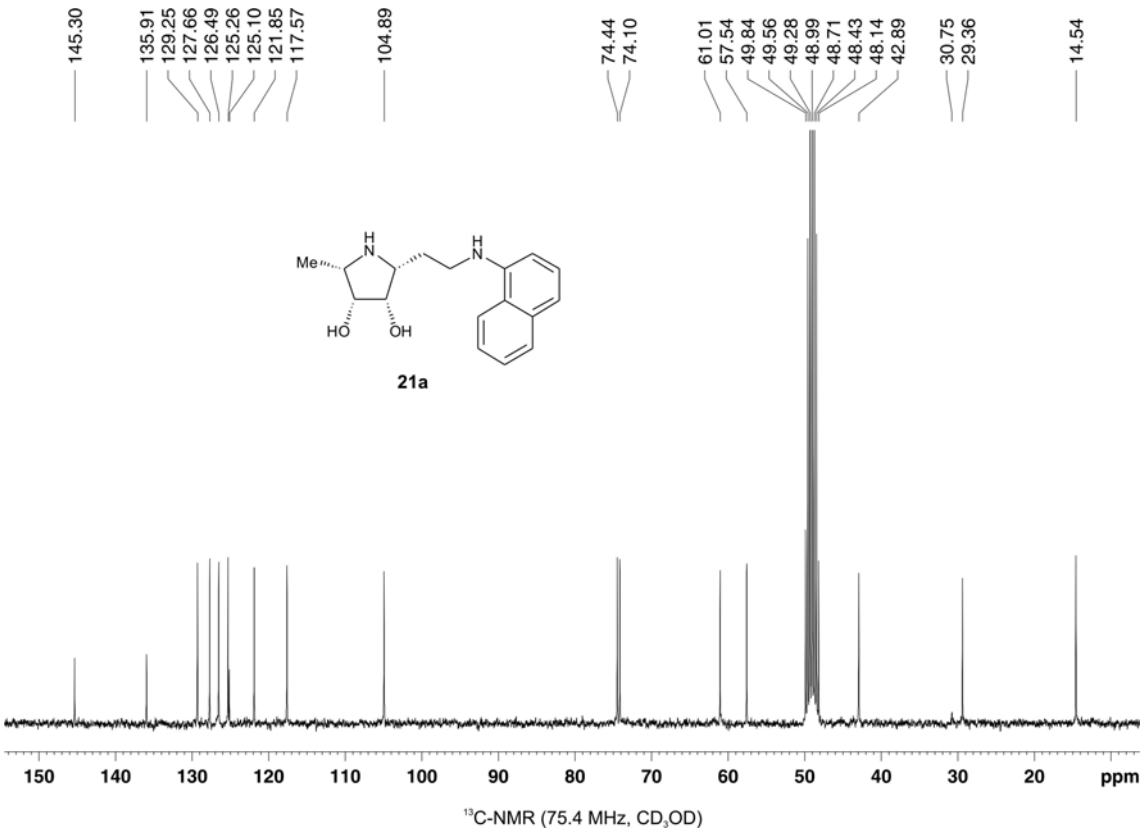


54

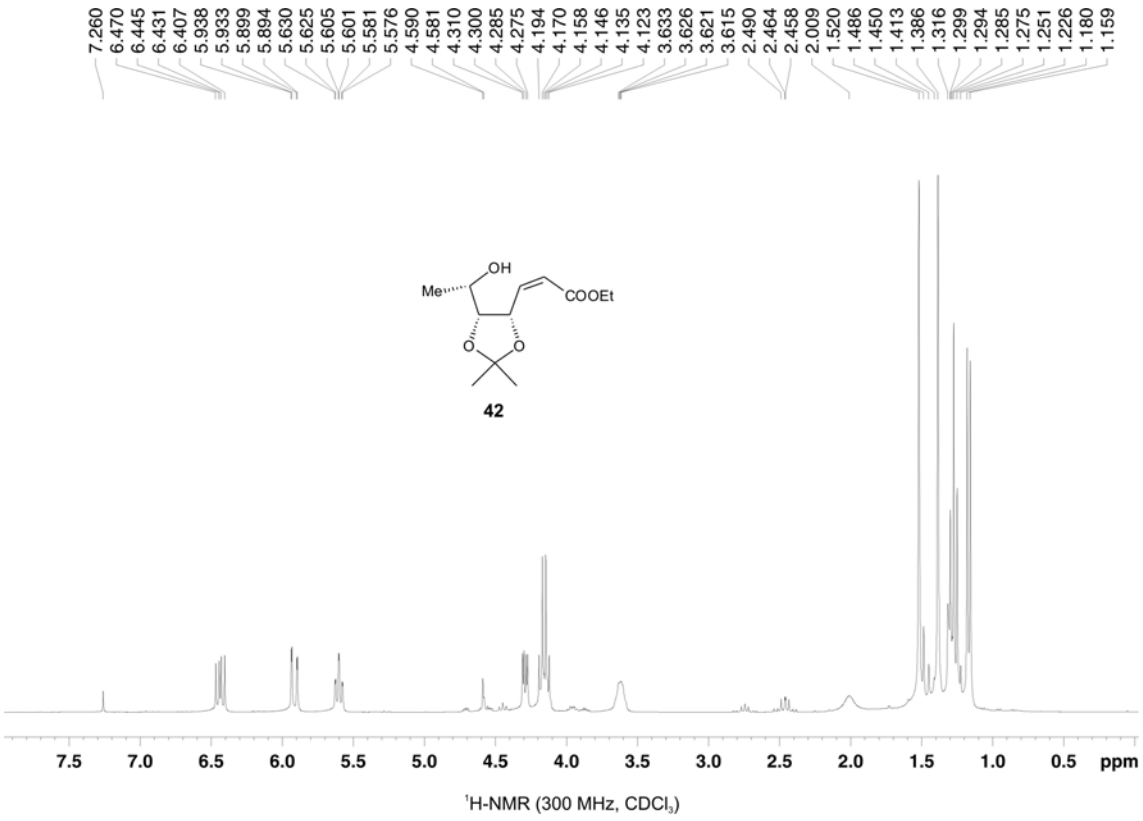
^{13}C-NMR (75.4 MHz, $CDCl_3$)



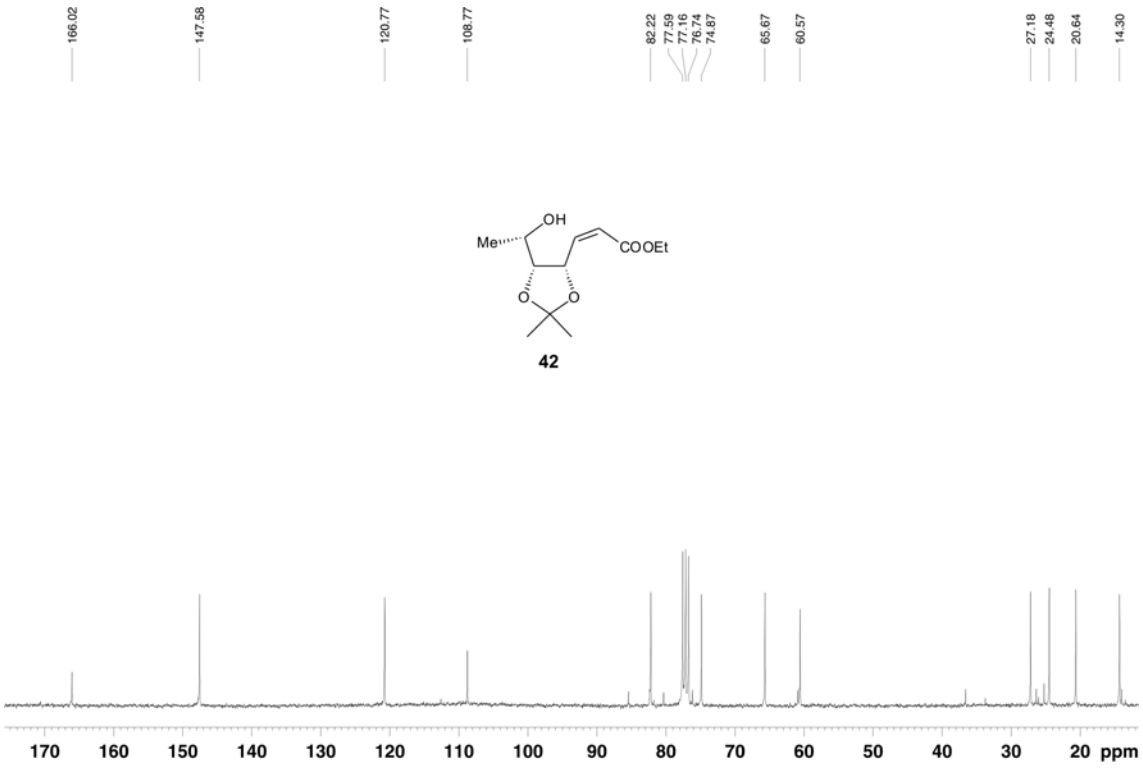
^{1}H-NMR (300 MHz, CD_3OD)



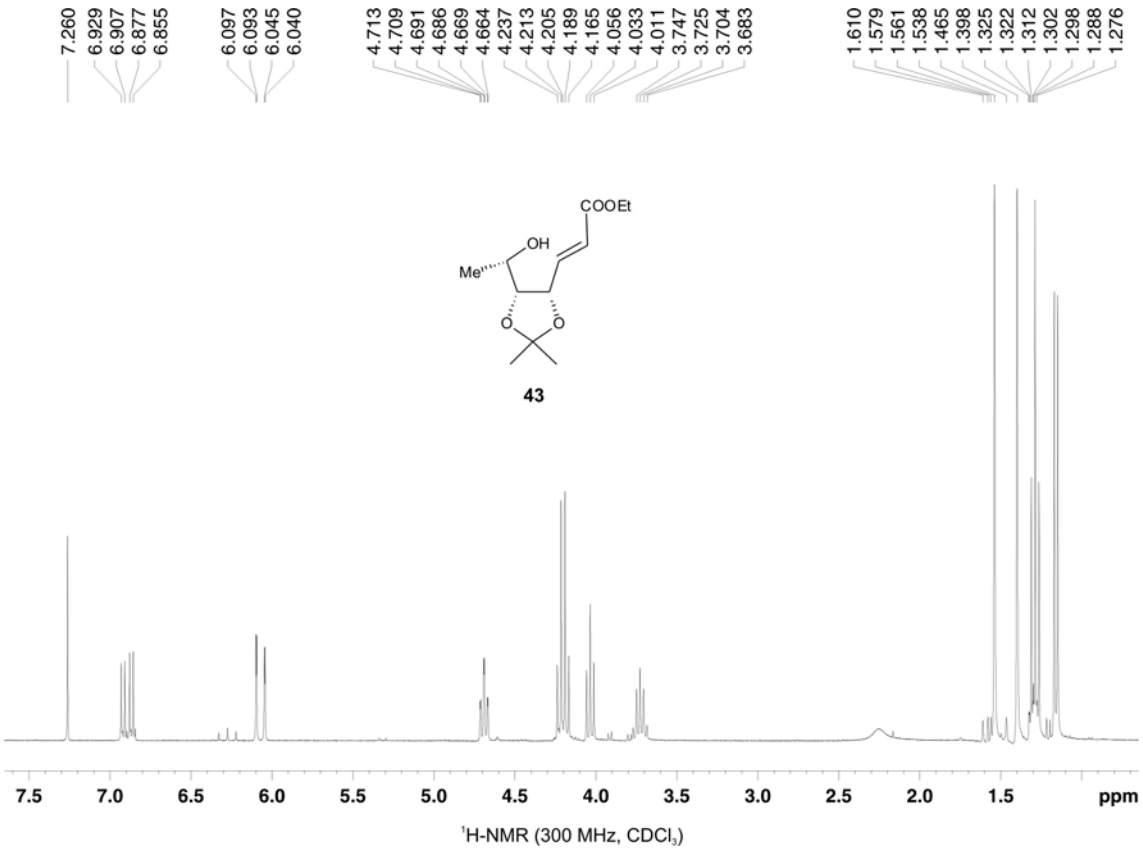
^{13}C-NMR (75.4 MHz, CD_3OD)



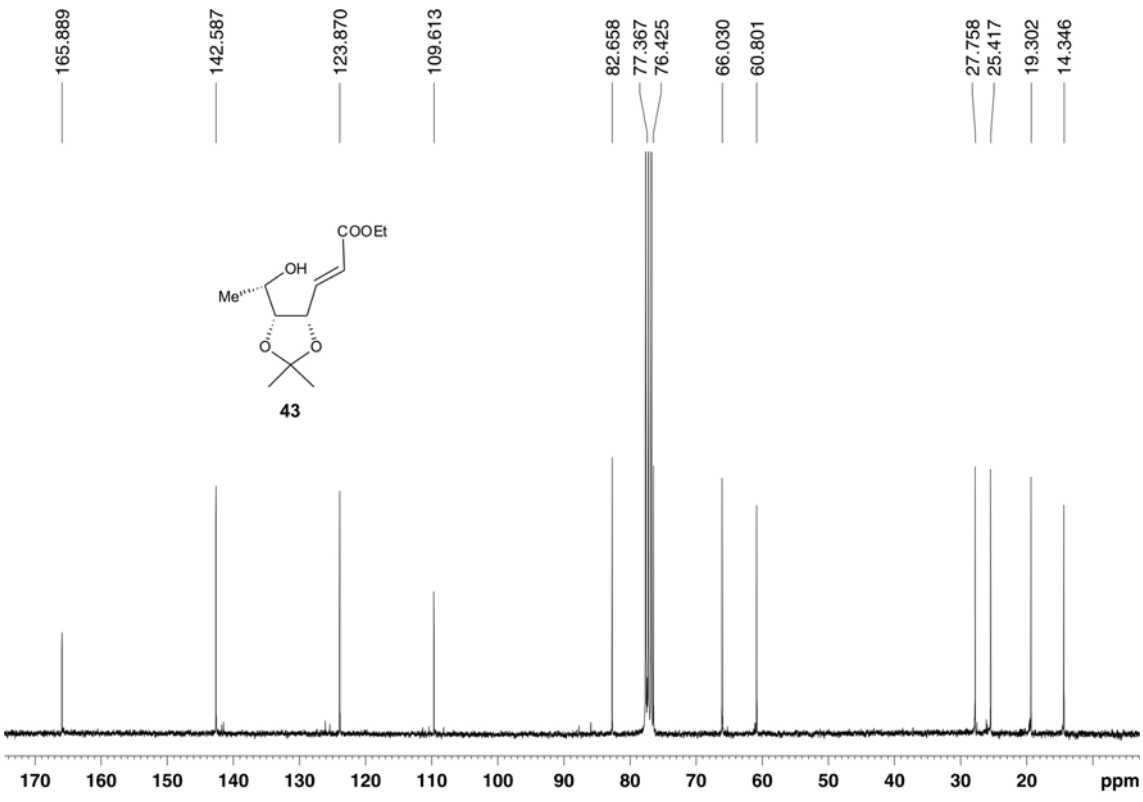
^{1}H-NMR (300 MHz, $CDCl_3$)



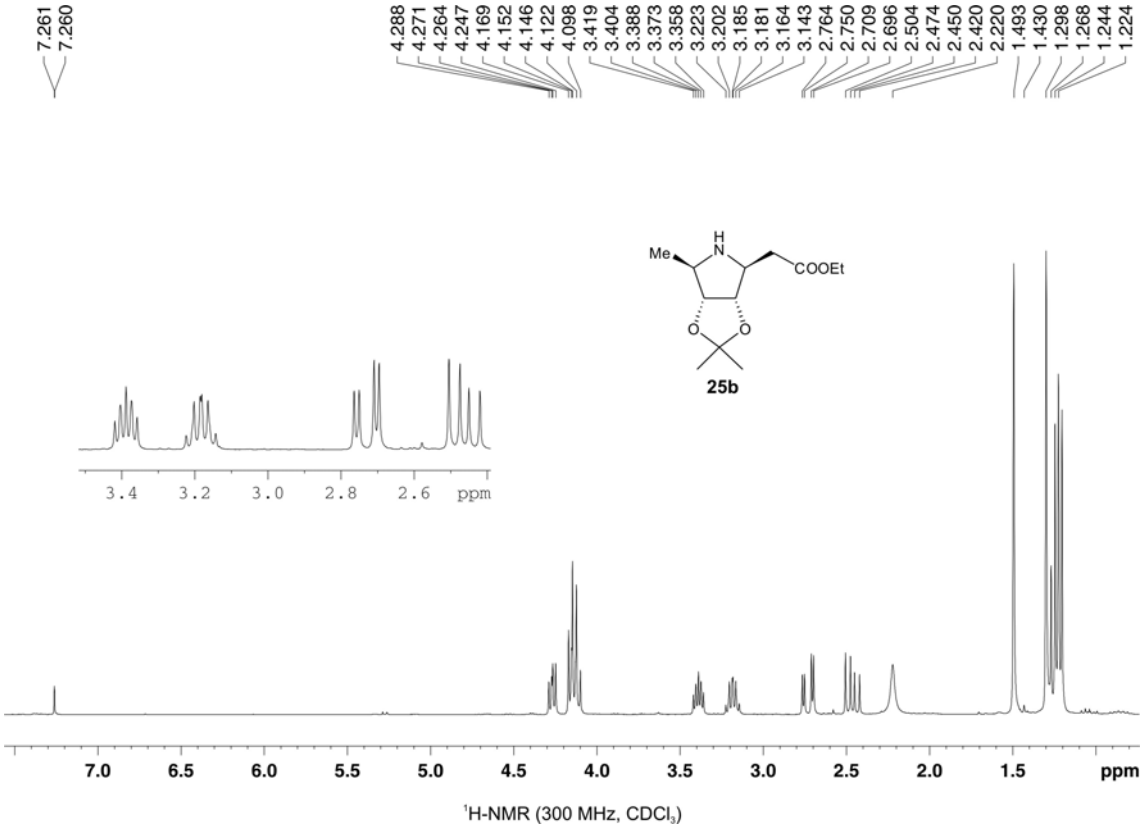
^{13}C-NMR (75.4 MHz, $CDCl_3$)



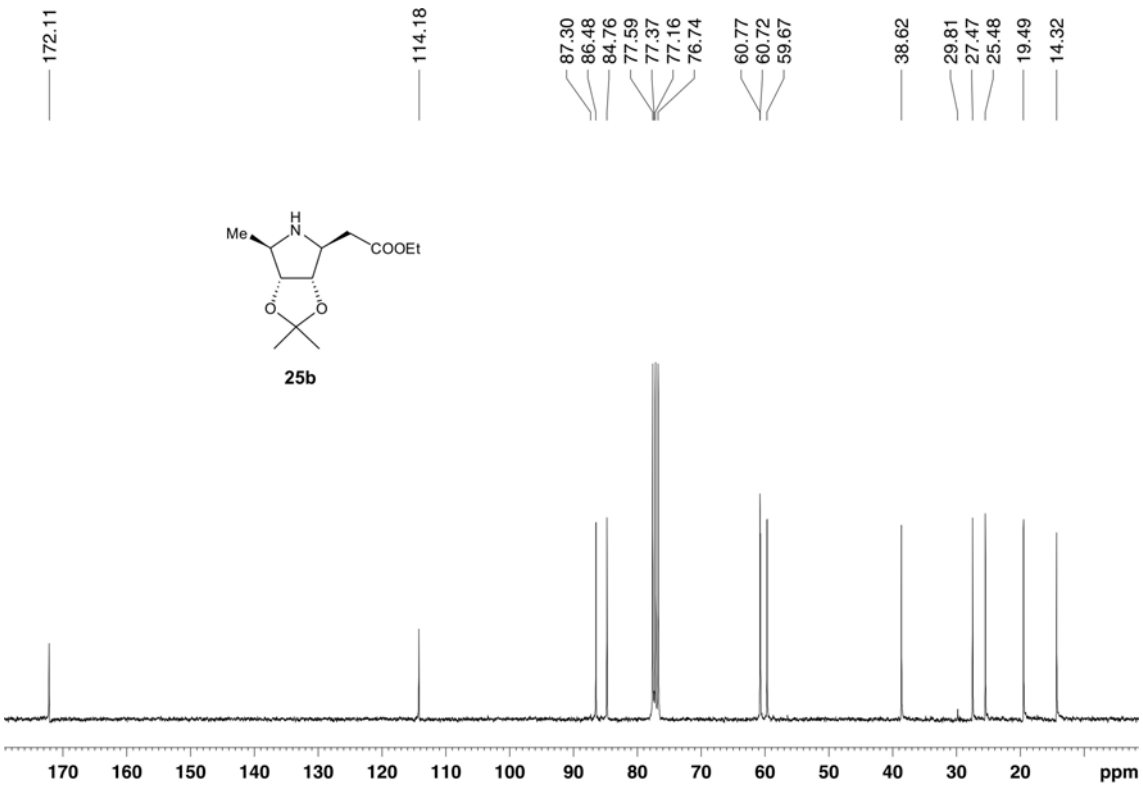
^{1}H-NMR (300 MHz, $CDCl_3$)



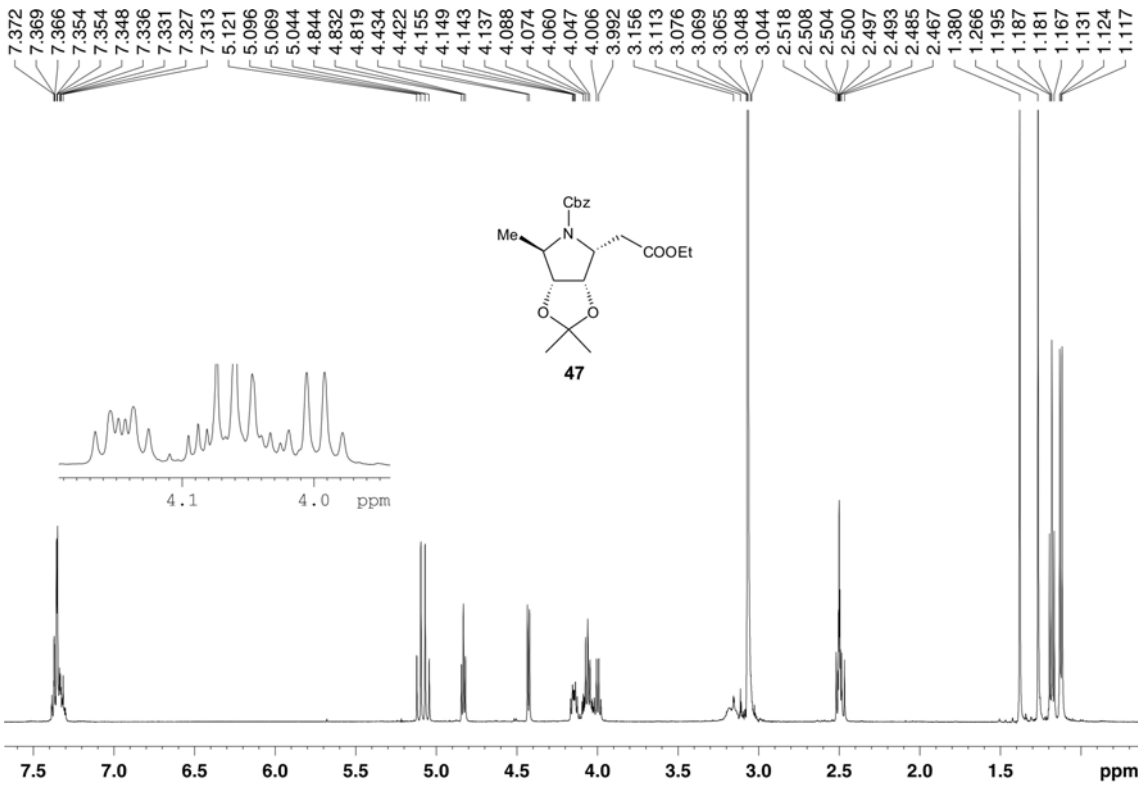
^{13}C-NMR (75.4 MHz, $CDCl_3$)



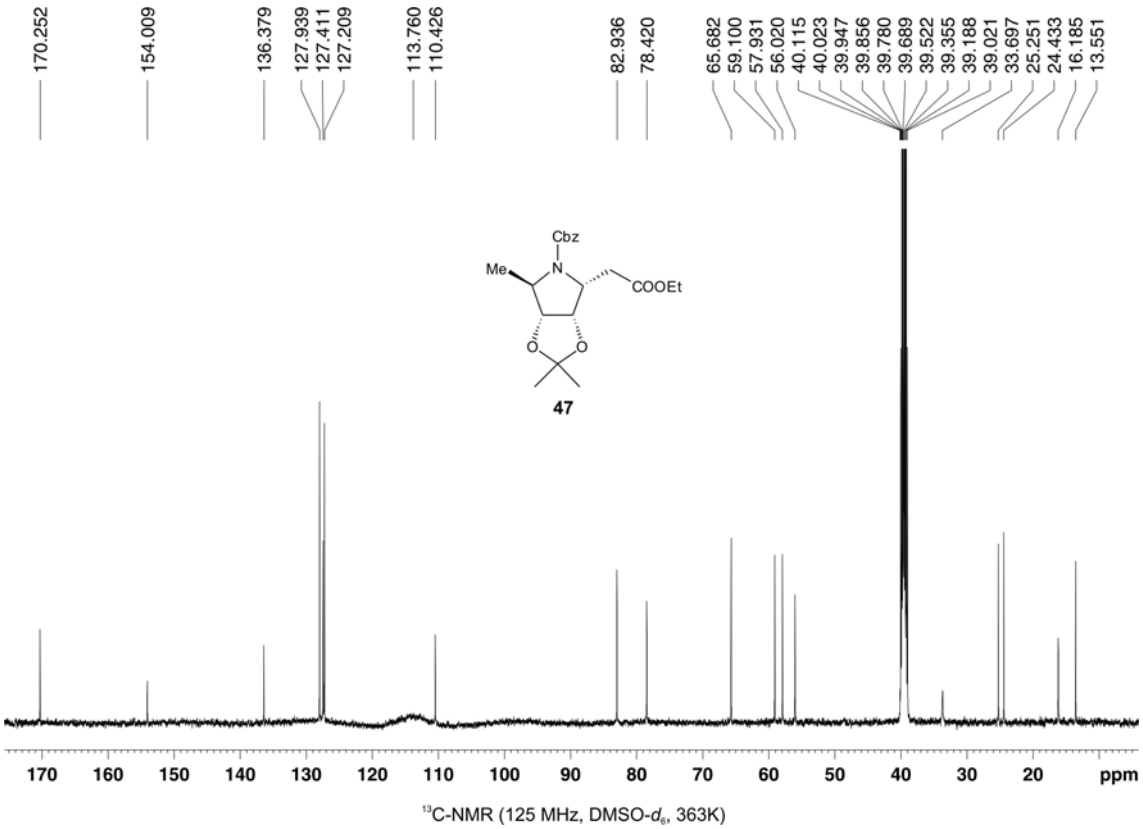
^{1}H-NMR (300 MHz, $CDCl_3$)



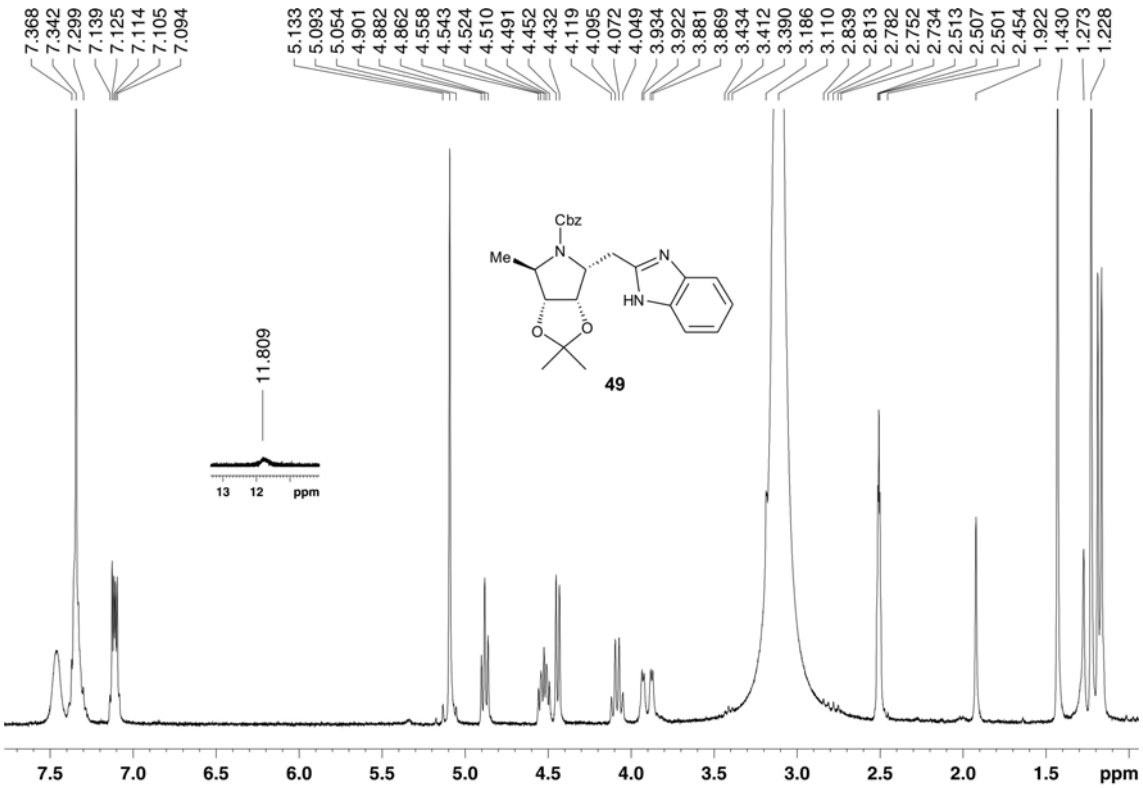
^{13}C-NMR (75.4 MHz, $CDCl_3$)



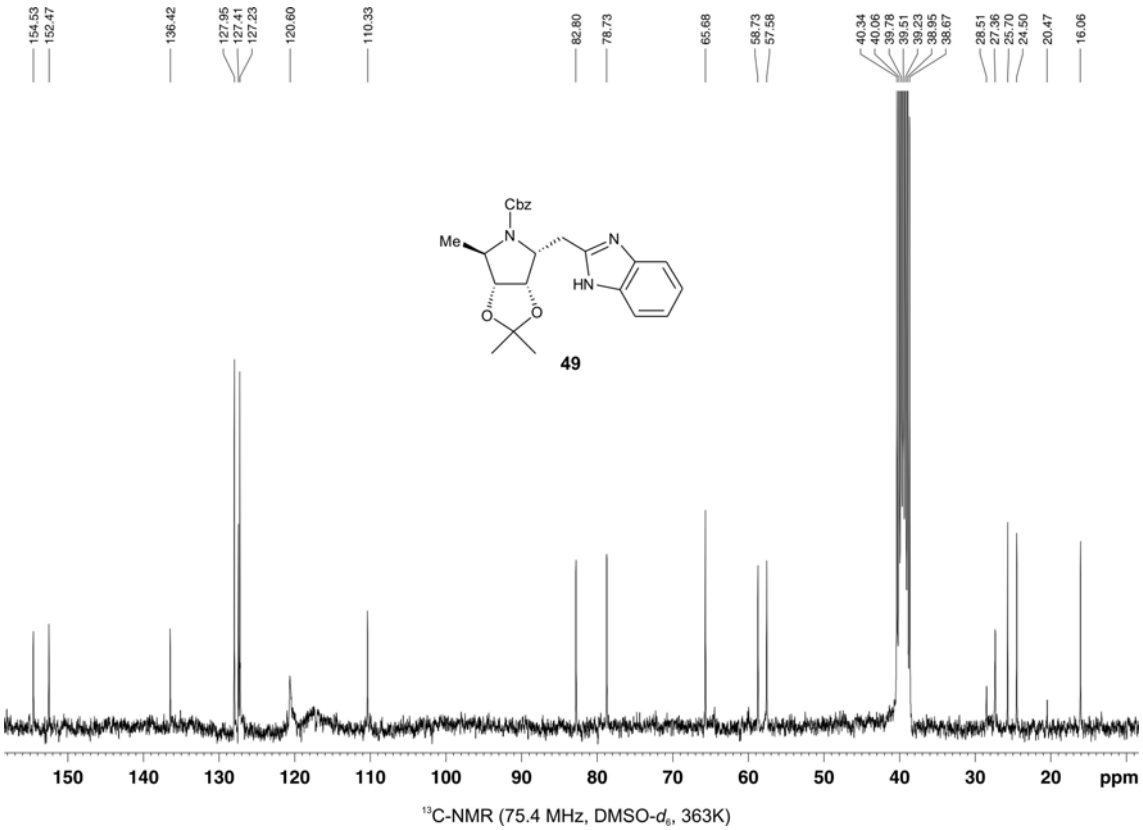
^{1}H-NMR (500 MHz, DMSO-d_6, 363K)



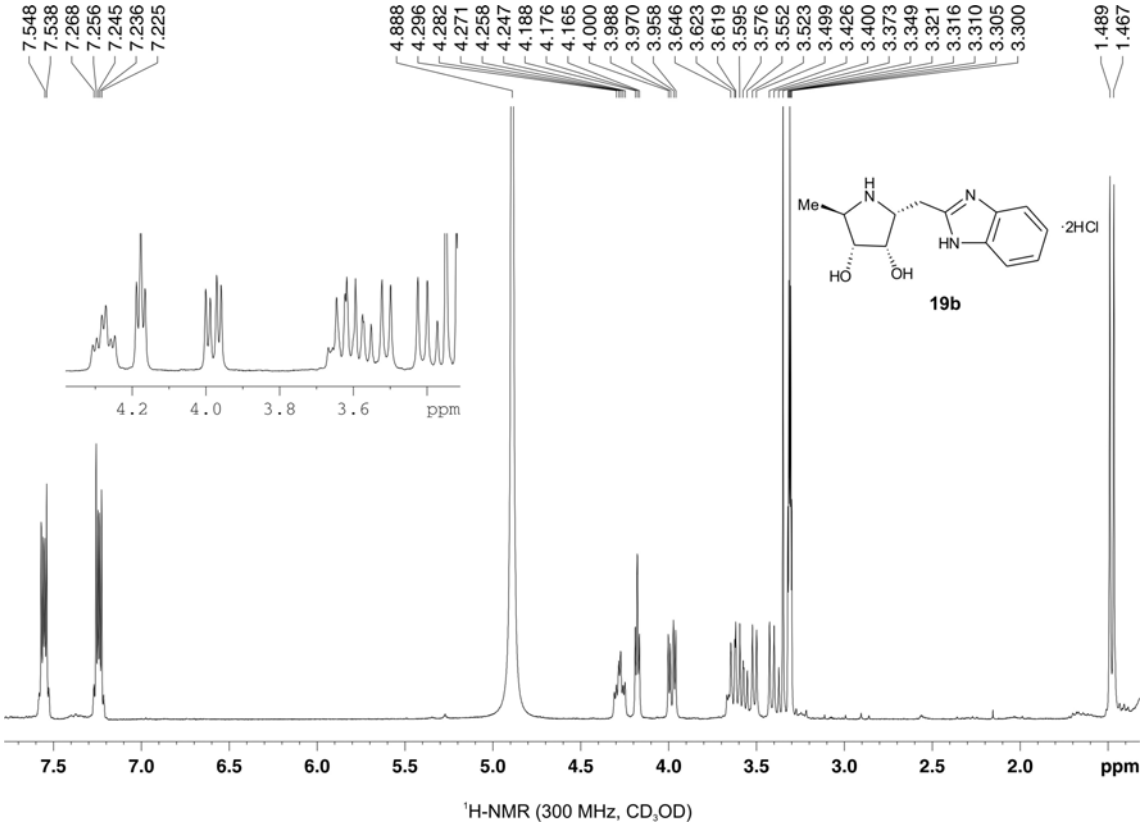
^{13}C-NMR (125 MHz, DMSO-d_6, 363K)



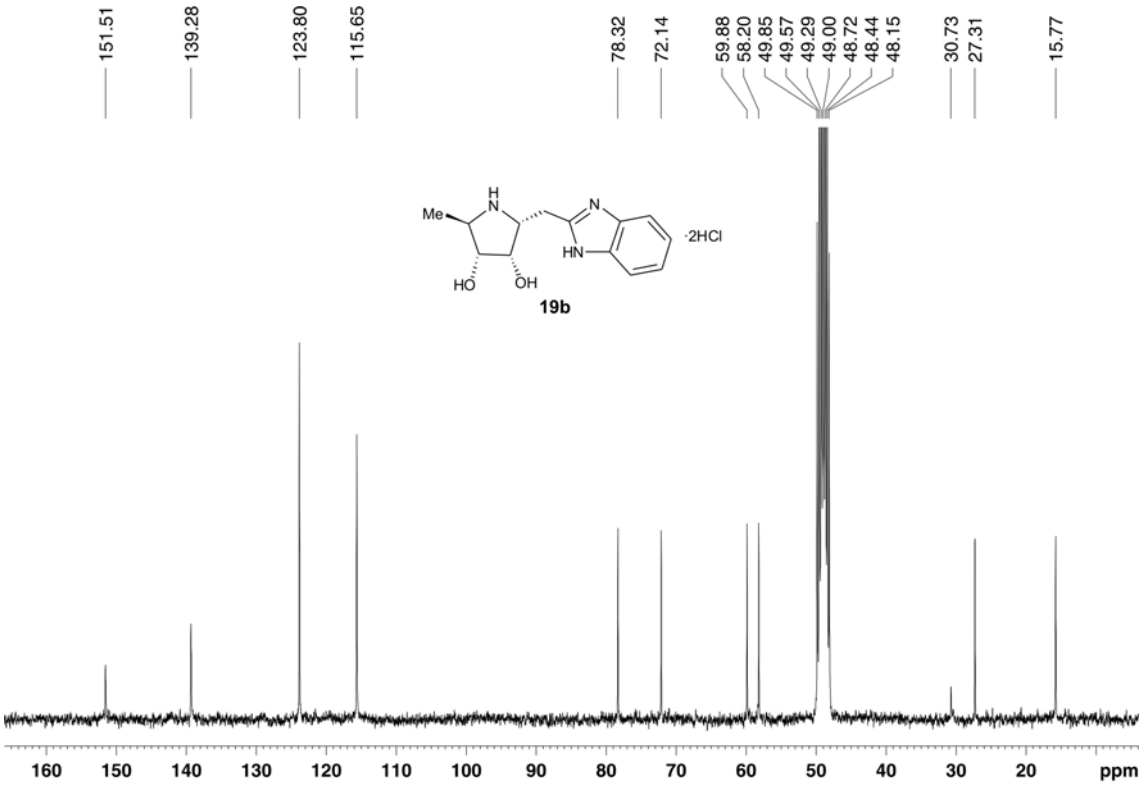
^{1}H-NMR (300 MHz, DMSO-d_6, 363K)



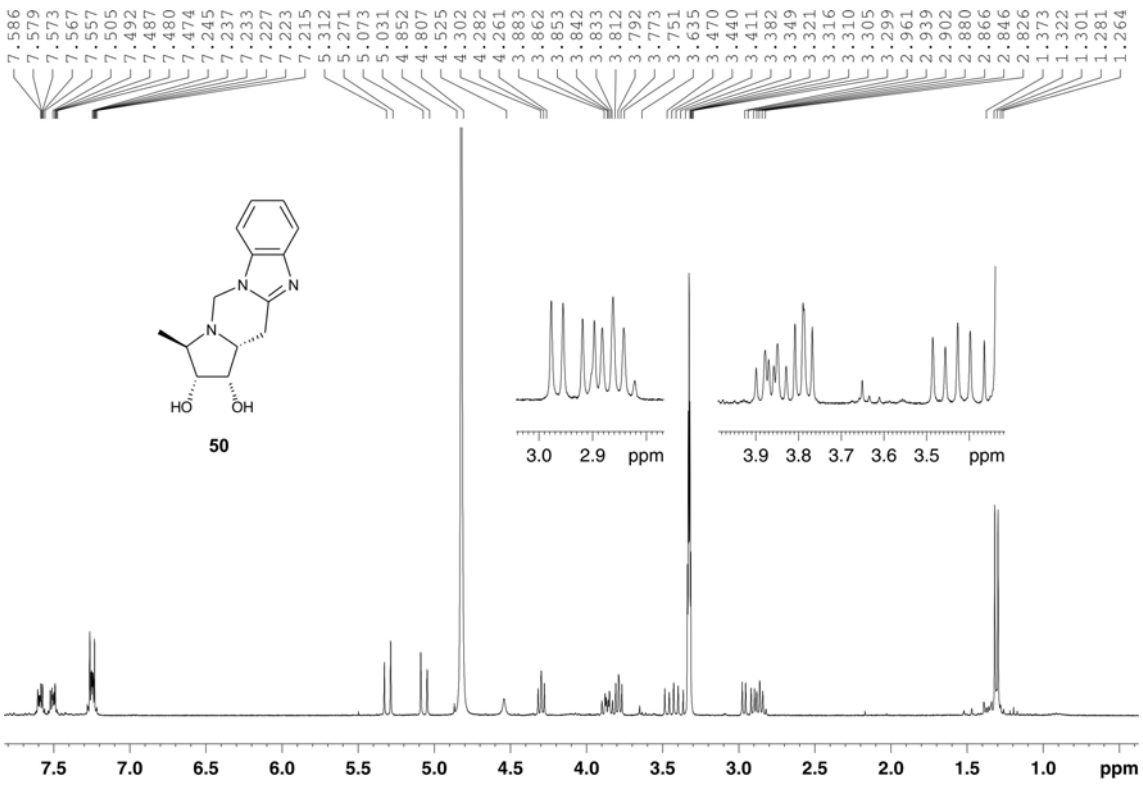
^{13}C-NMR (75.4 MHz, DMSO-d_6, 363K)



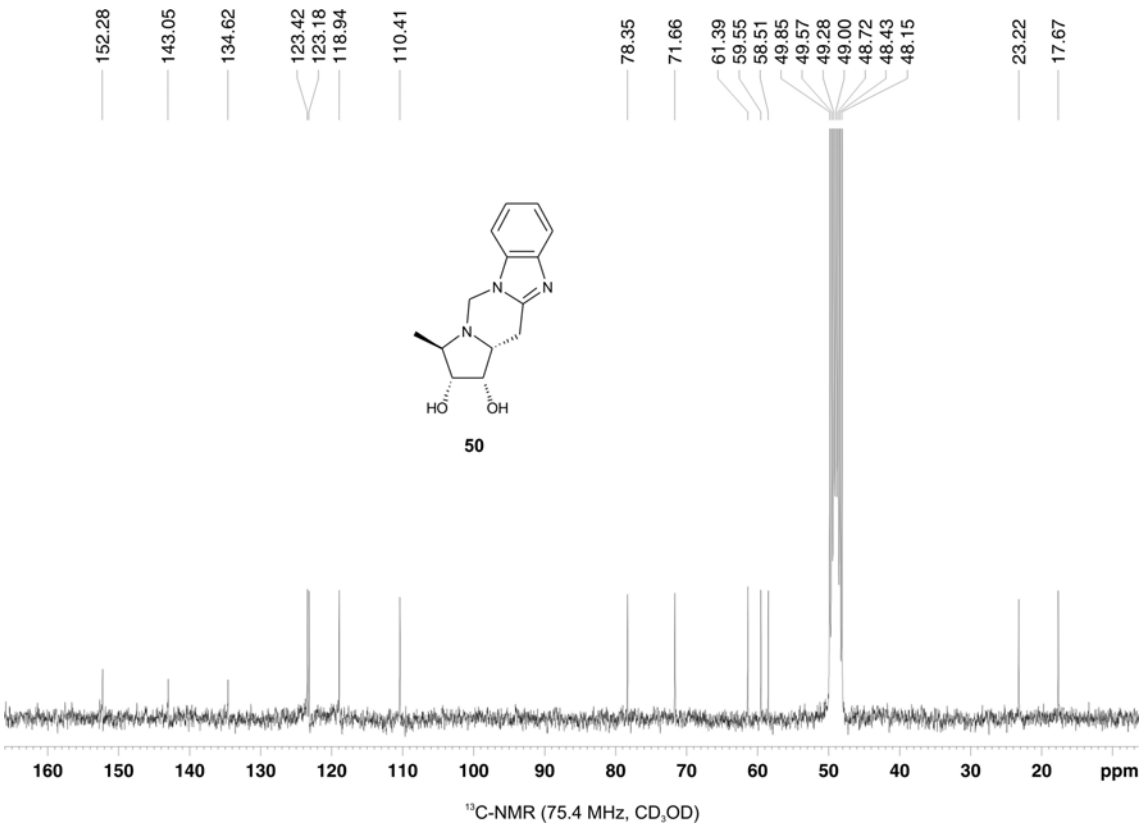
^{1}H-NMR (300 MHz, CD_3OD)



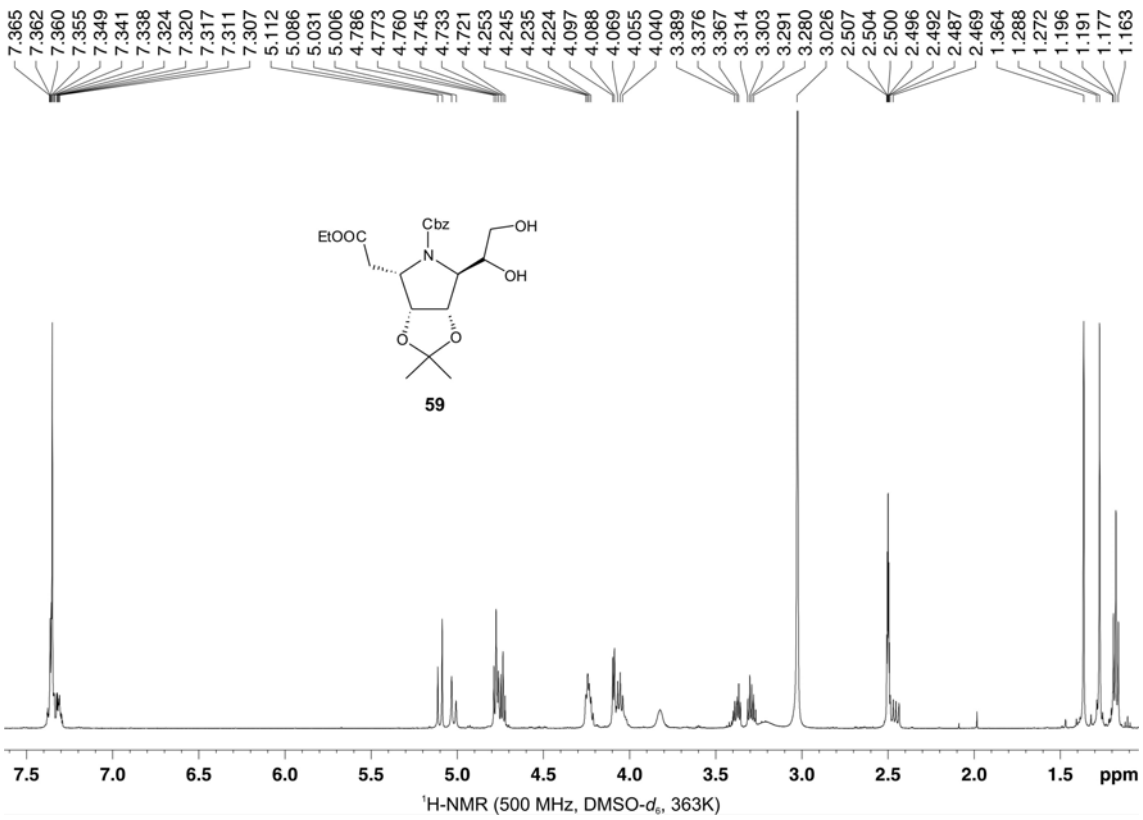
^{13}C-NMR (75.4 MHz, CD_3OD)



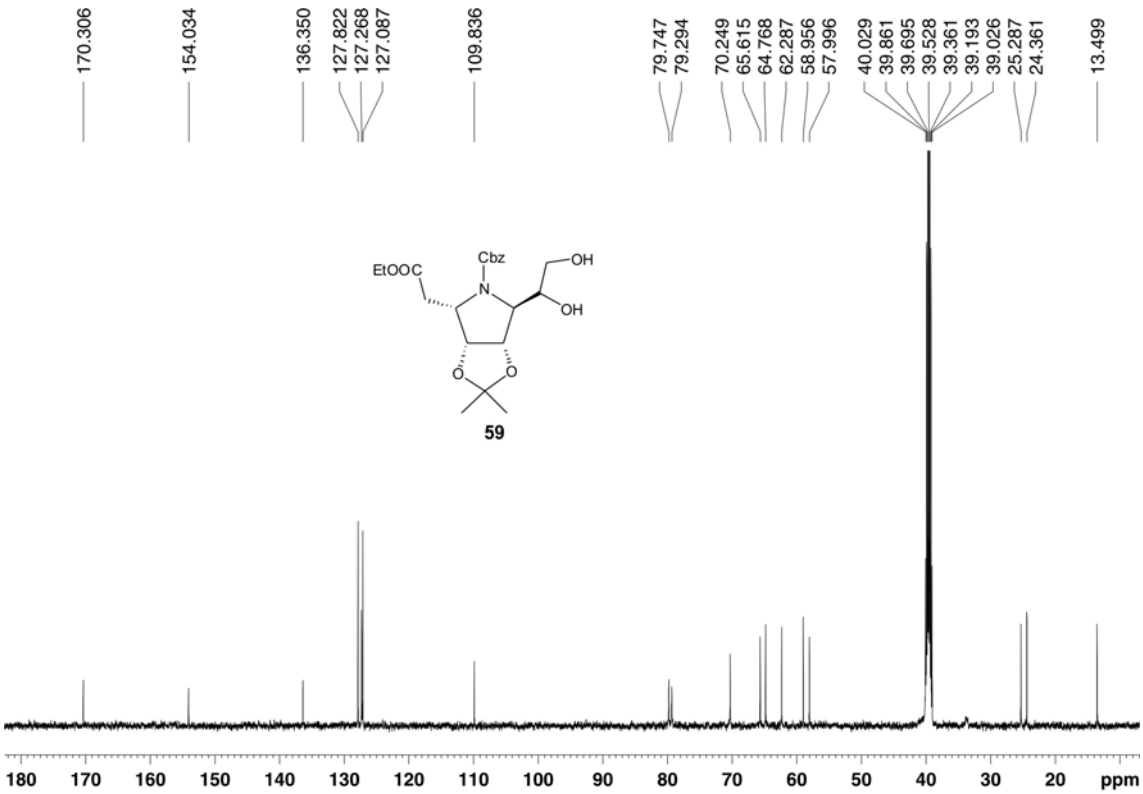
^{1}H-NMR (300 MHz, CD_3OD)



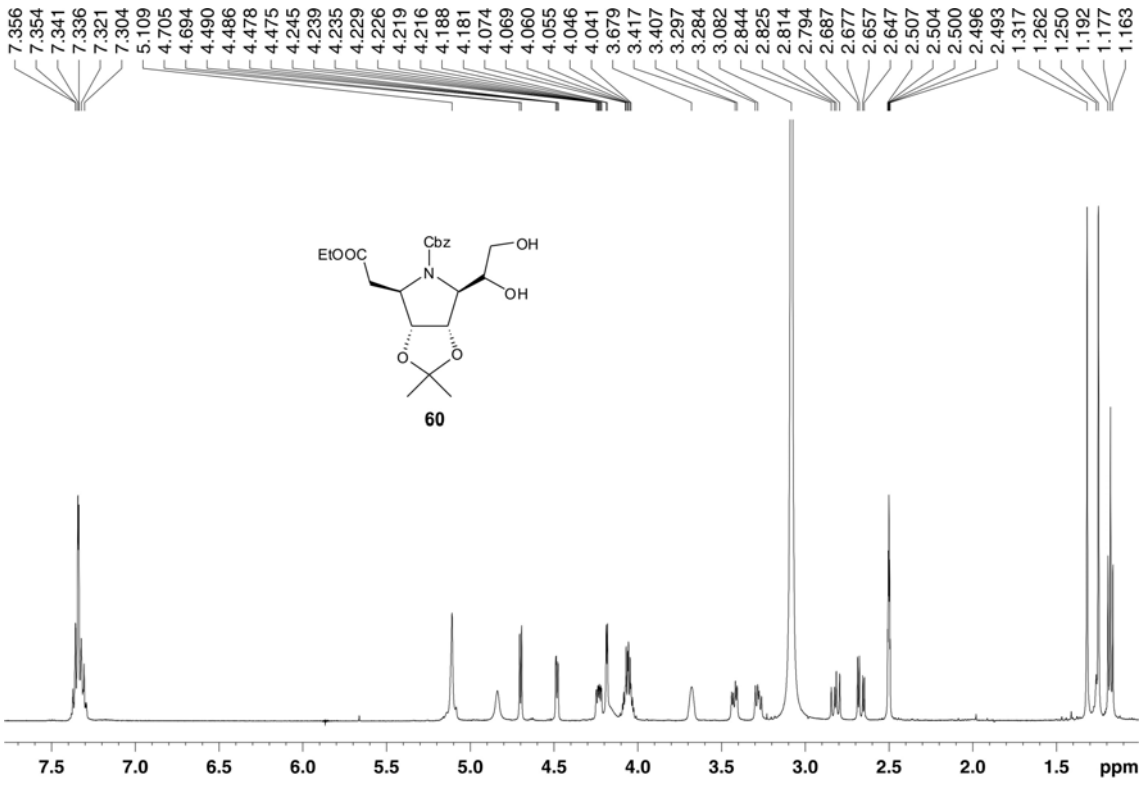
^{13}C-NMR (75.4 MHz, CD_3OD)



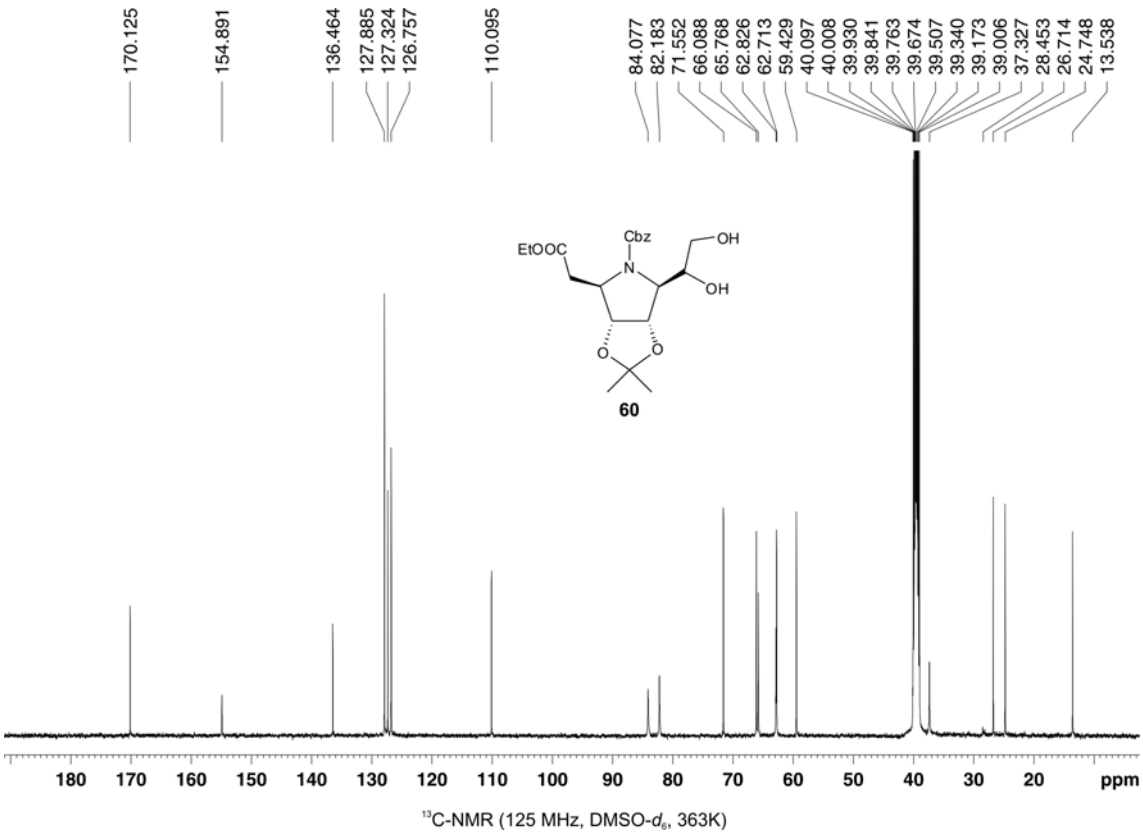
^{1}H-NMR (500 MHz, DMSO-d_6, 363K)



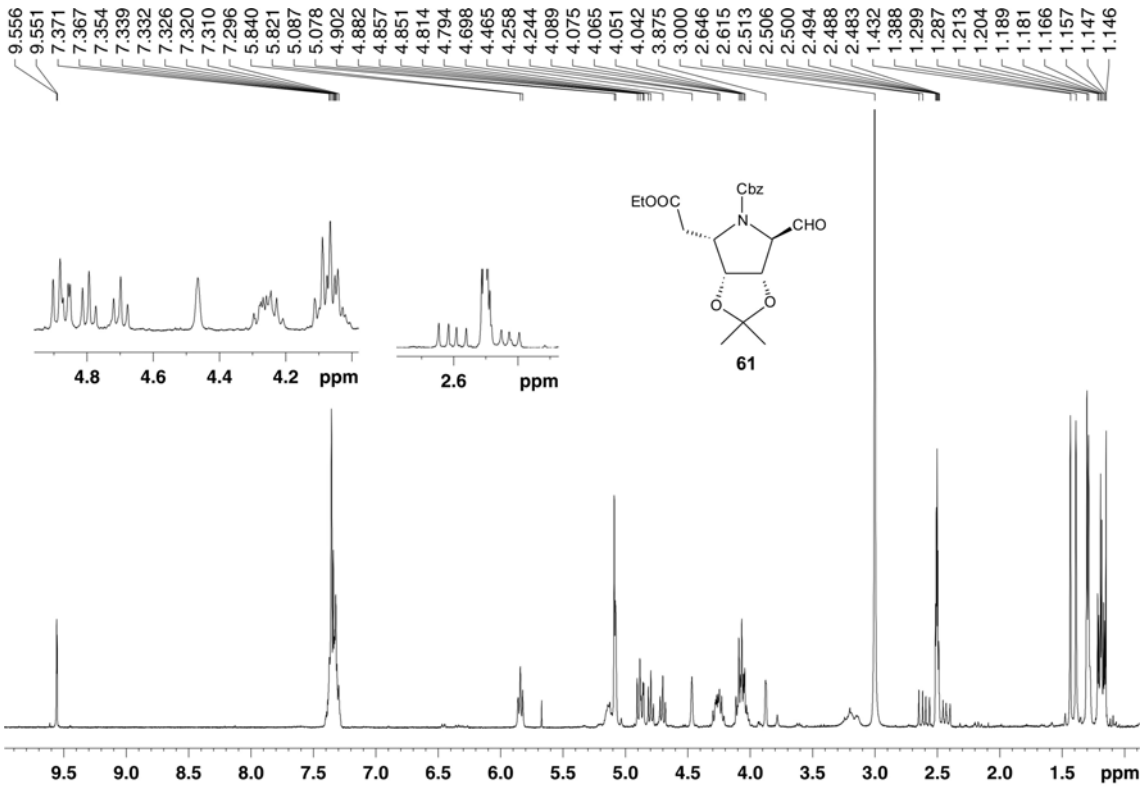
^{13}C-NMR (125 MHz, DMSO-d_6, 363K)



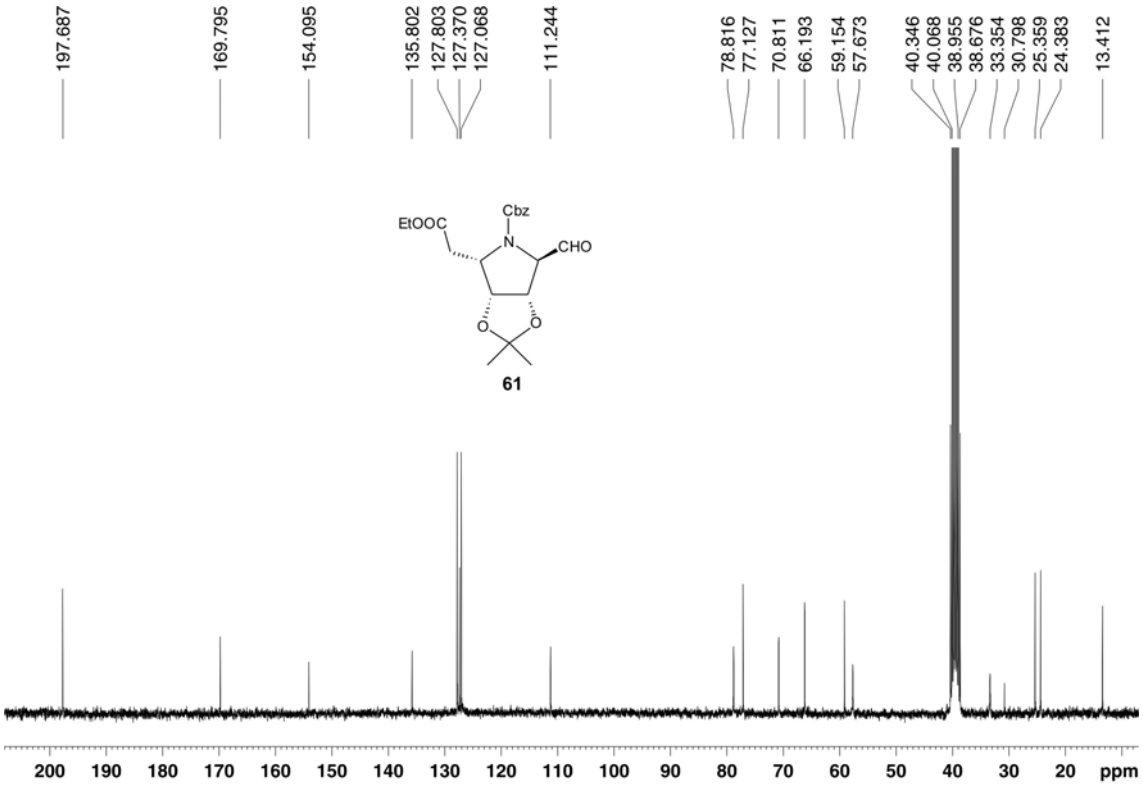
^{1}H-NMR (500 MHz, DMSO-d_6, 363K)



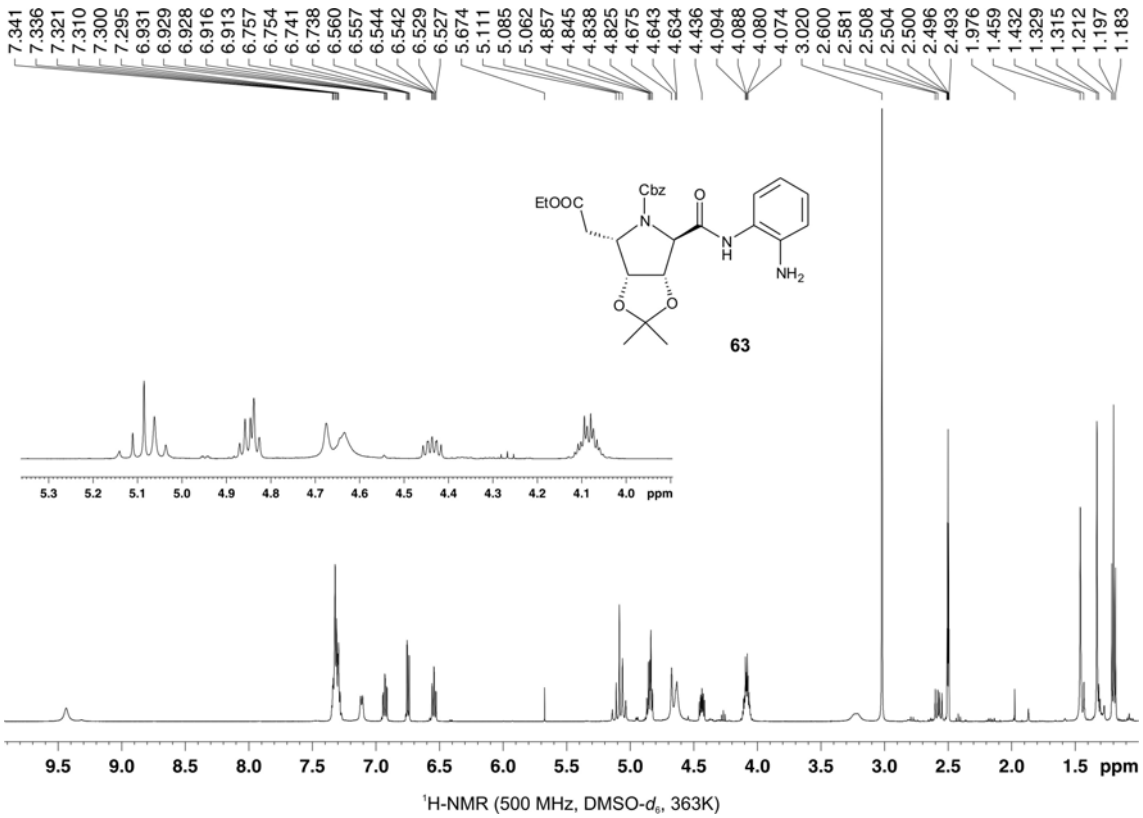
^{13}C-NMR (125 MHz, DMSO-d_6, 363K)



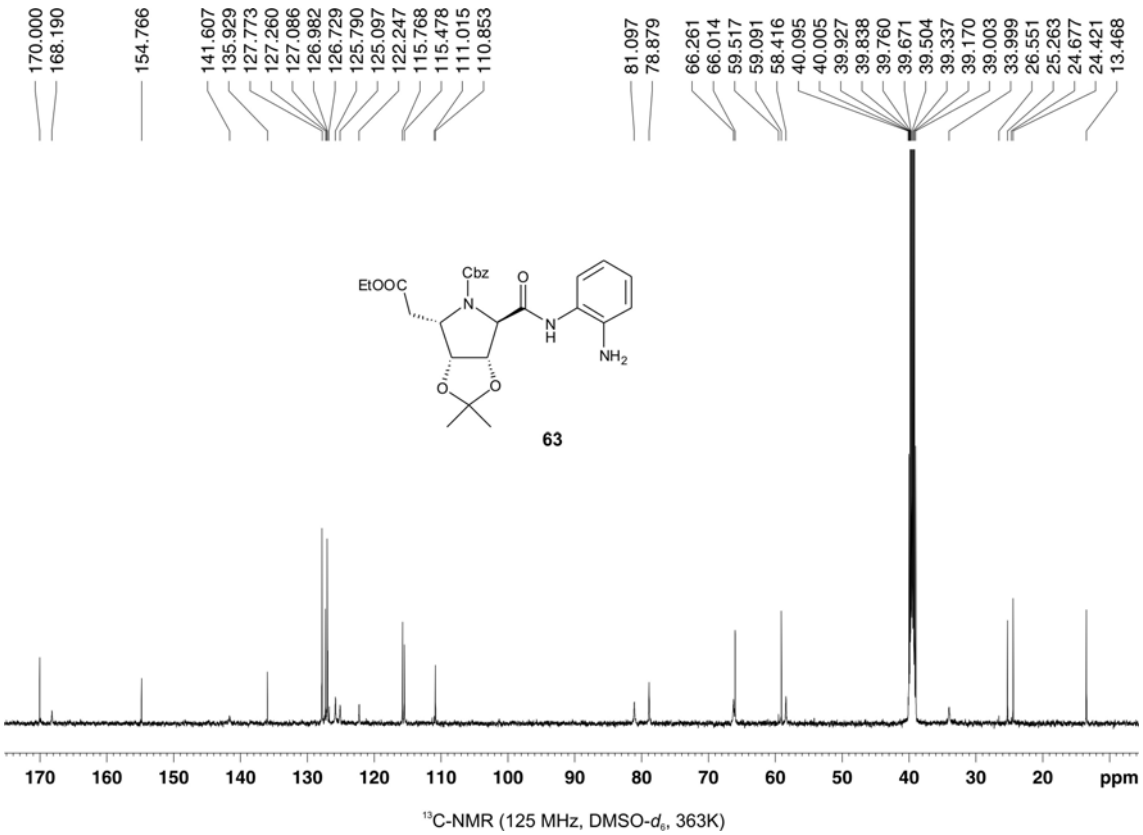
^{1}H-NMR (300 MHz, DMSO-d_6, 363K)



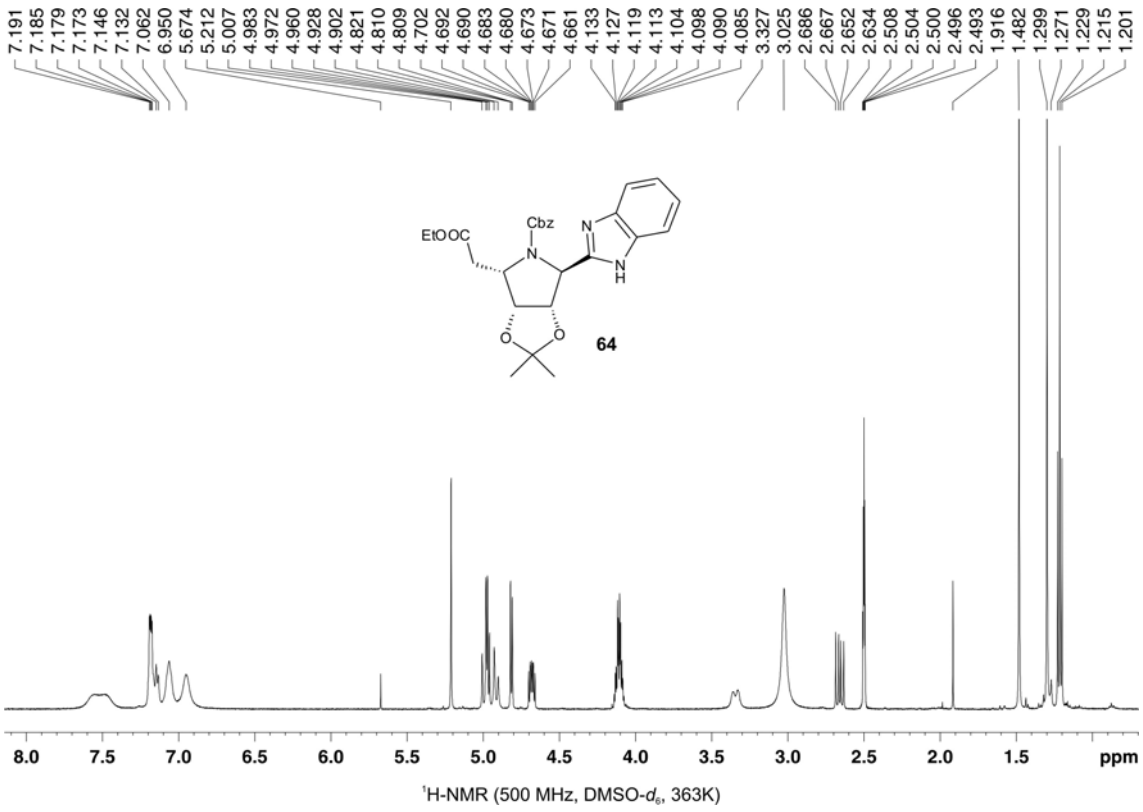
^{13}C-NMR (75.4 MHz, DMSO-d_6, 363K)



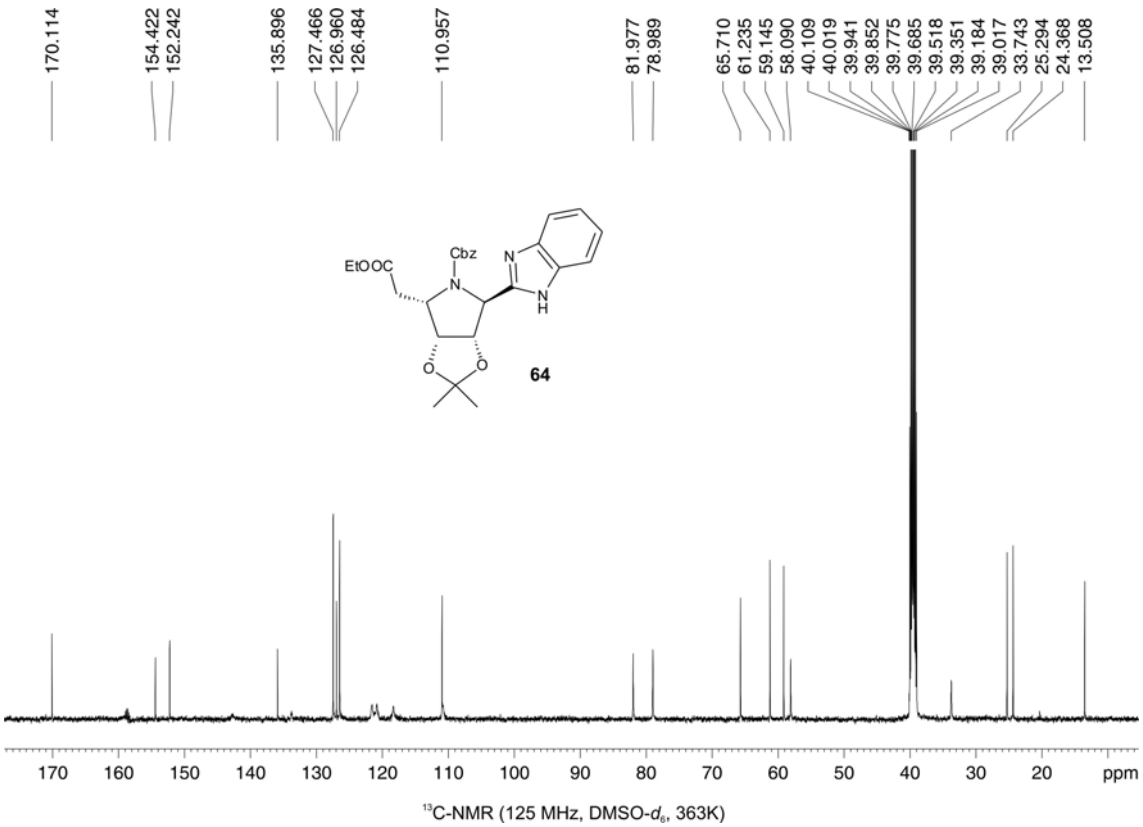
^{1}H-NMR (500 MHz, DMSO-d_6, 363K)



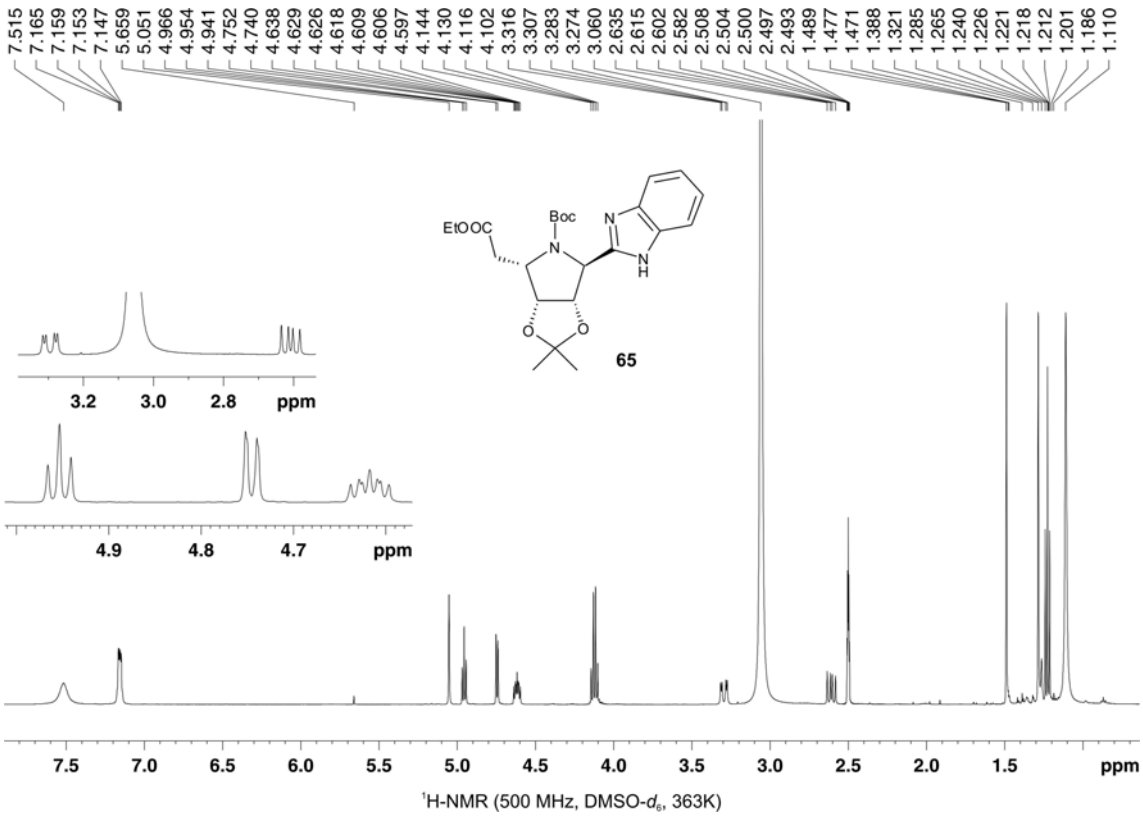
^{13}C-NMR (125 MHz, DMSO-d_6, 363K)



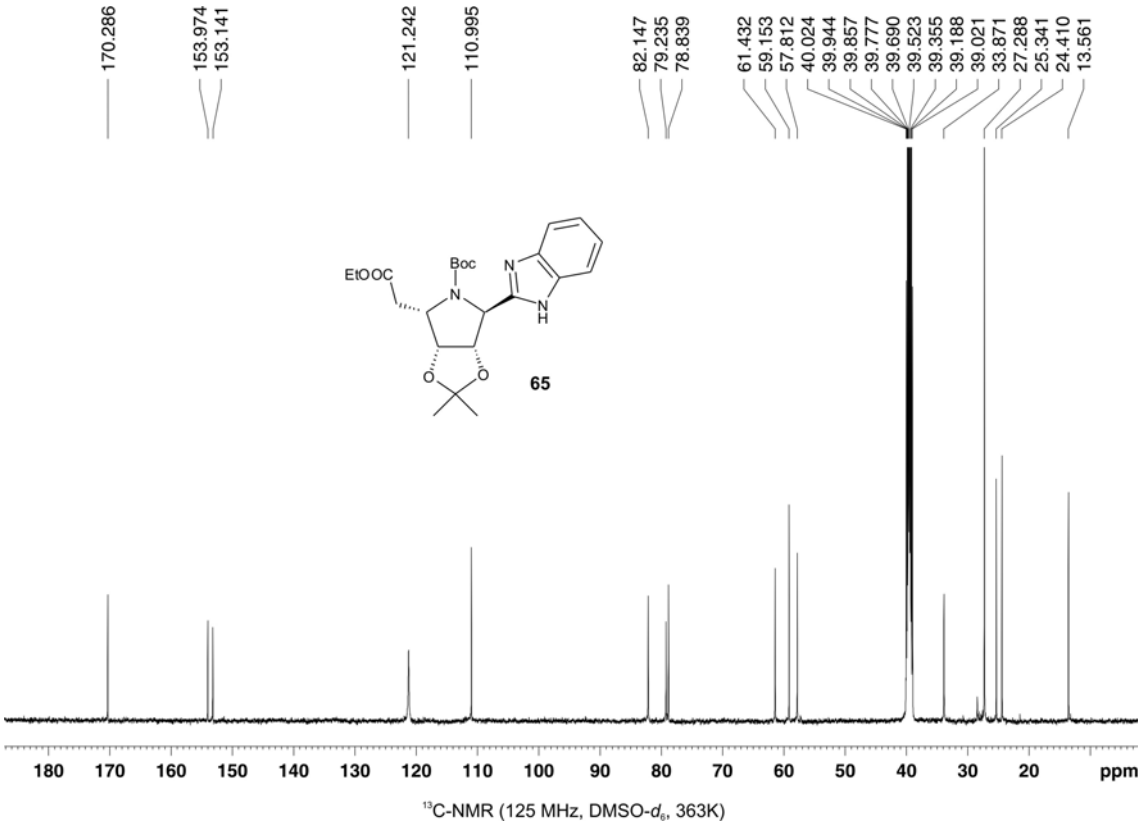
^{1}H-NMR (500 MHz, DMSO-d_6, 363K)



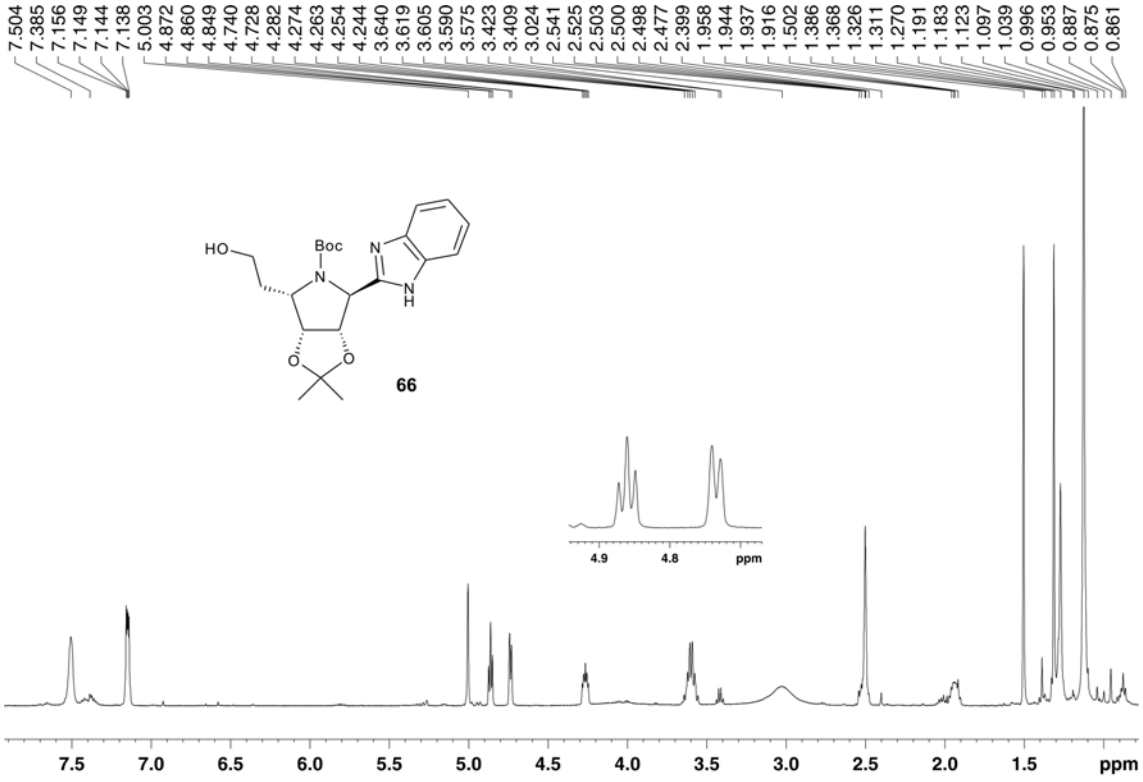
^{13}C-NMR (125 MHz, DMSO-d_6, 363K)



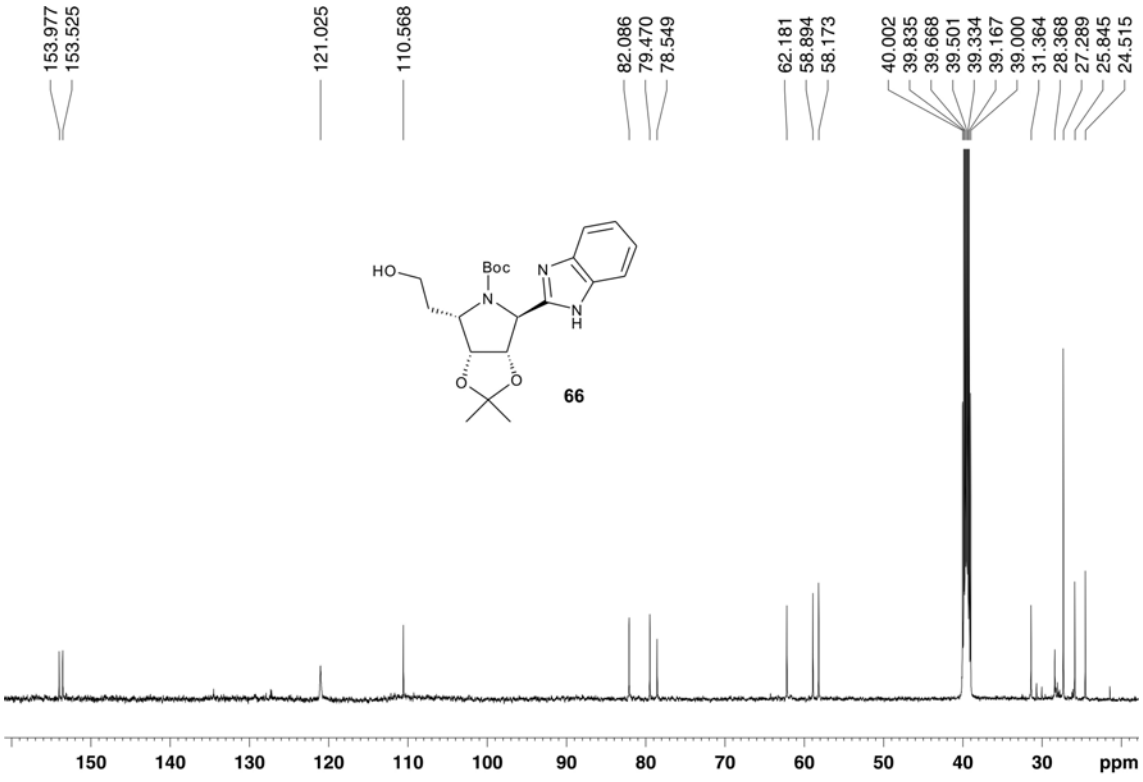
^{1}H-NMR (500 MHz, DMSO-d_6, 363K)



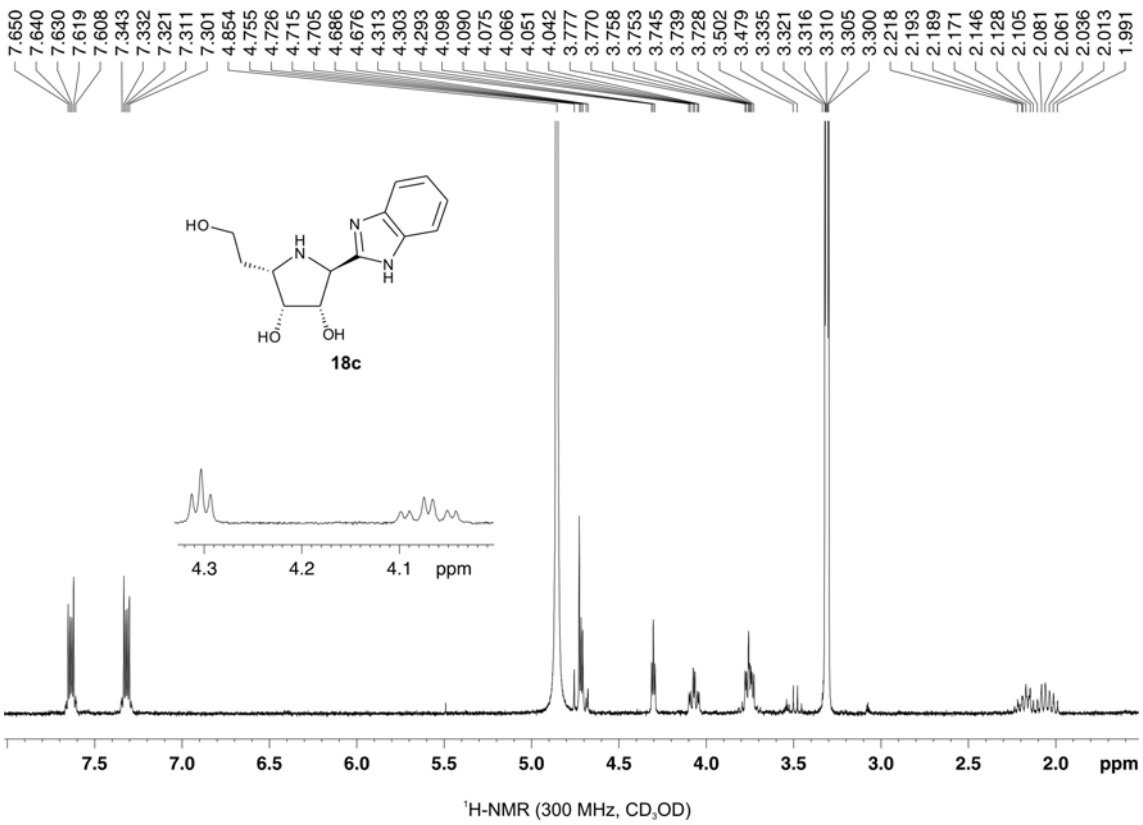
^{13}C-NMR (125 MHz, DMSO-d_6, 363K)



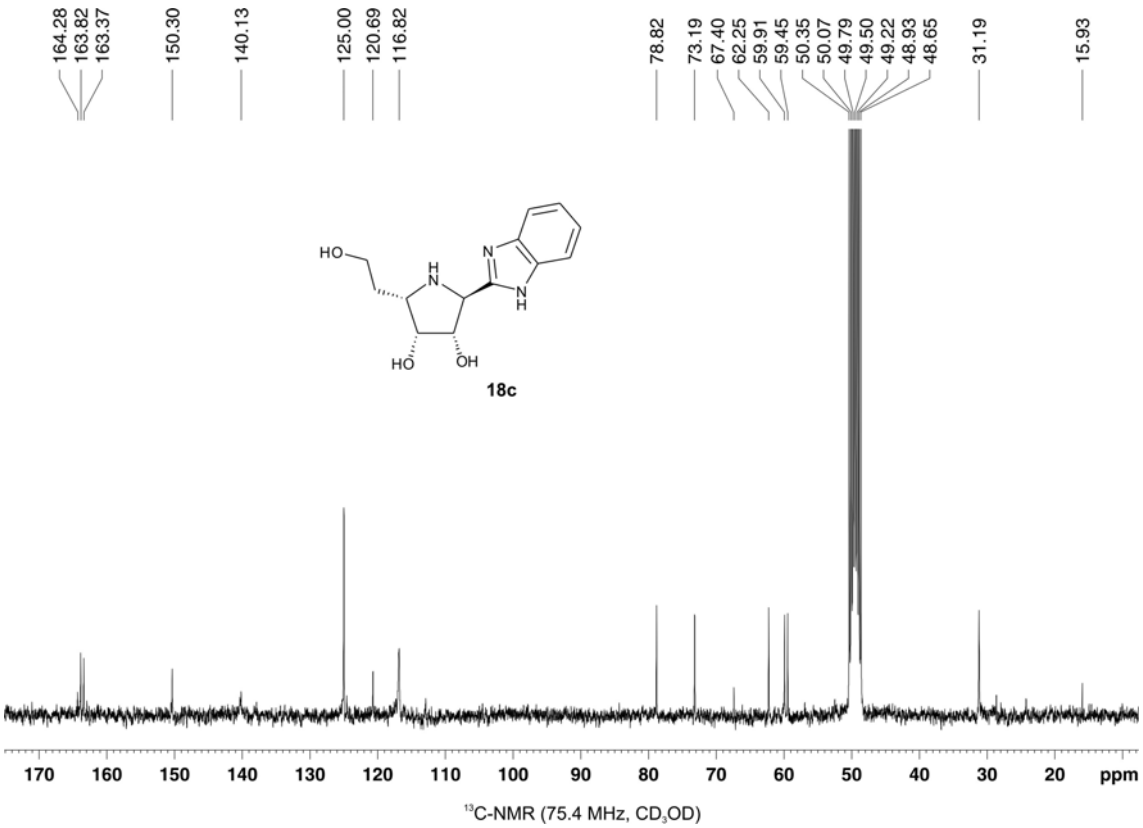
^{1}H-NMR (500 MHz, DMSO-d_6, 363K)



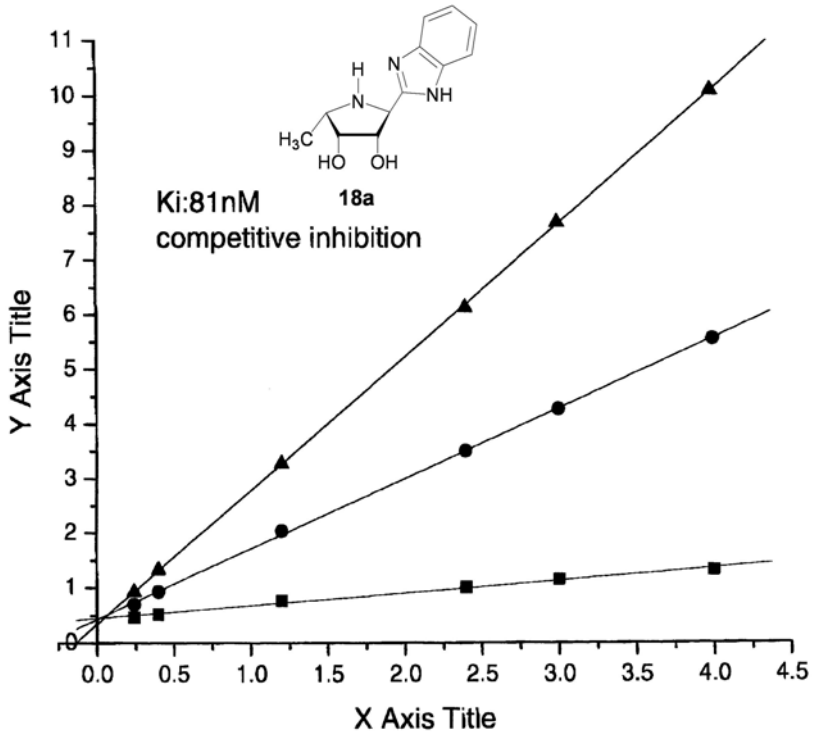
^{13}C-NMR (125 MHz, DMSO-d_6, 363K)

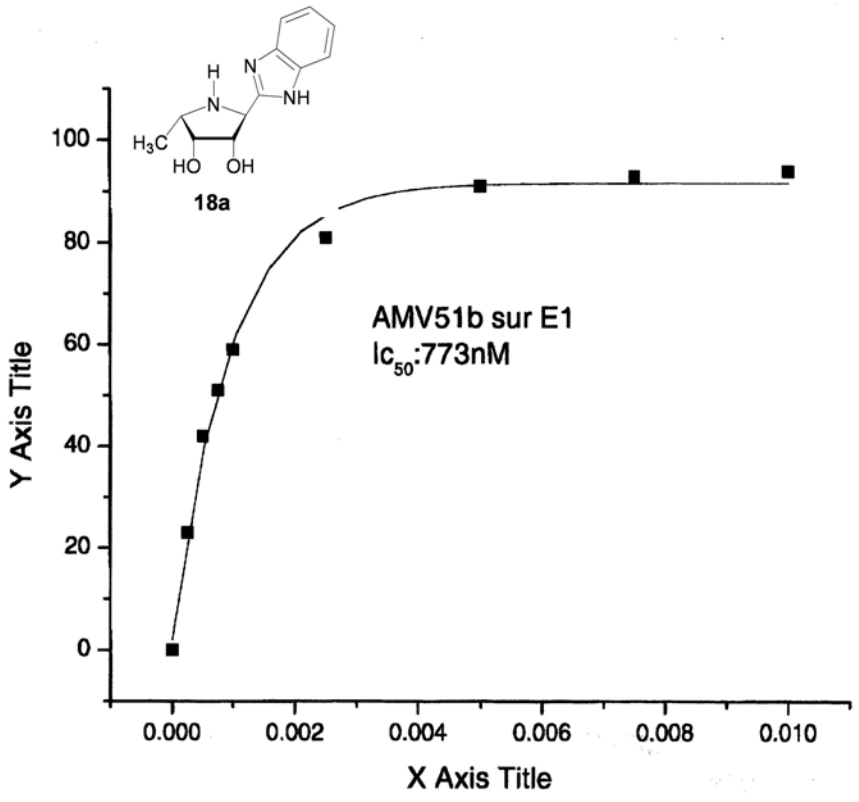


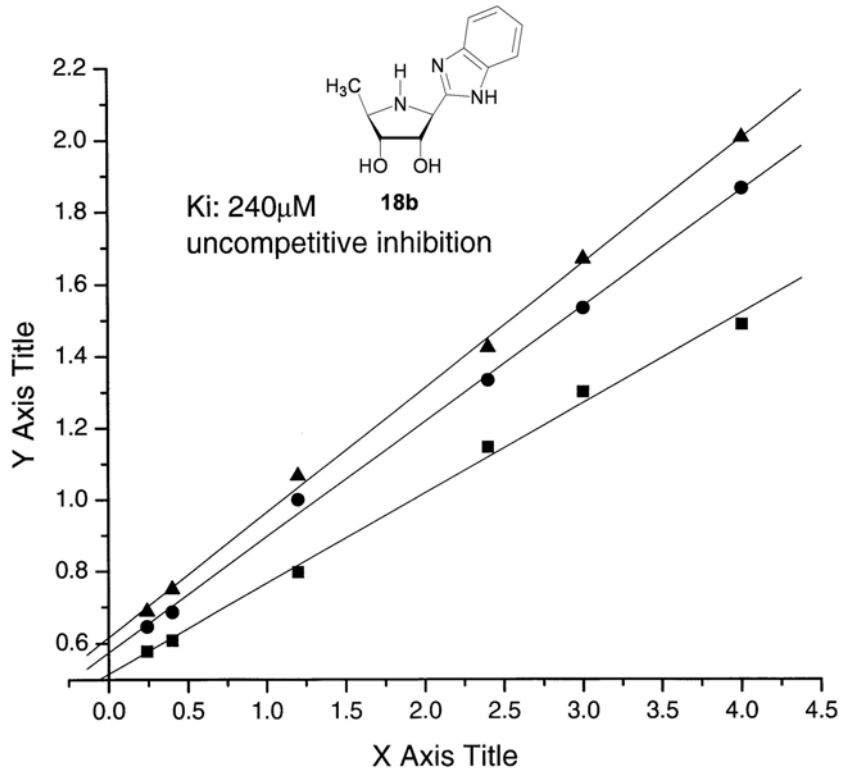
^{1}H-NMR (300 MHz, CD_3OD)

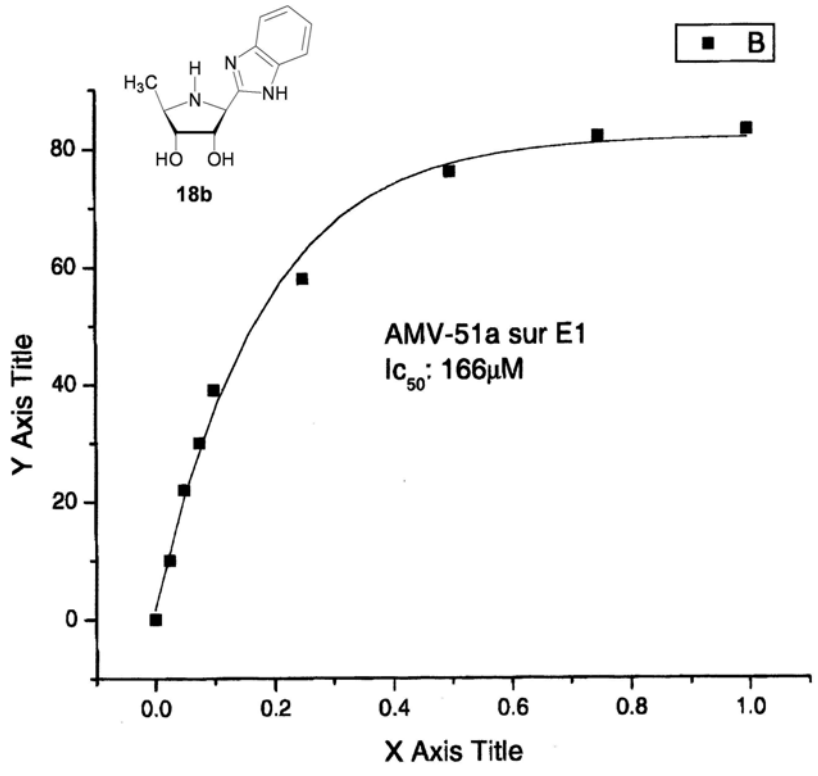


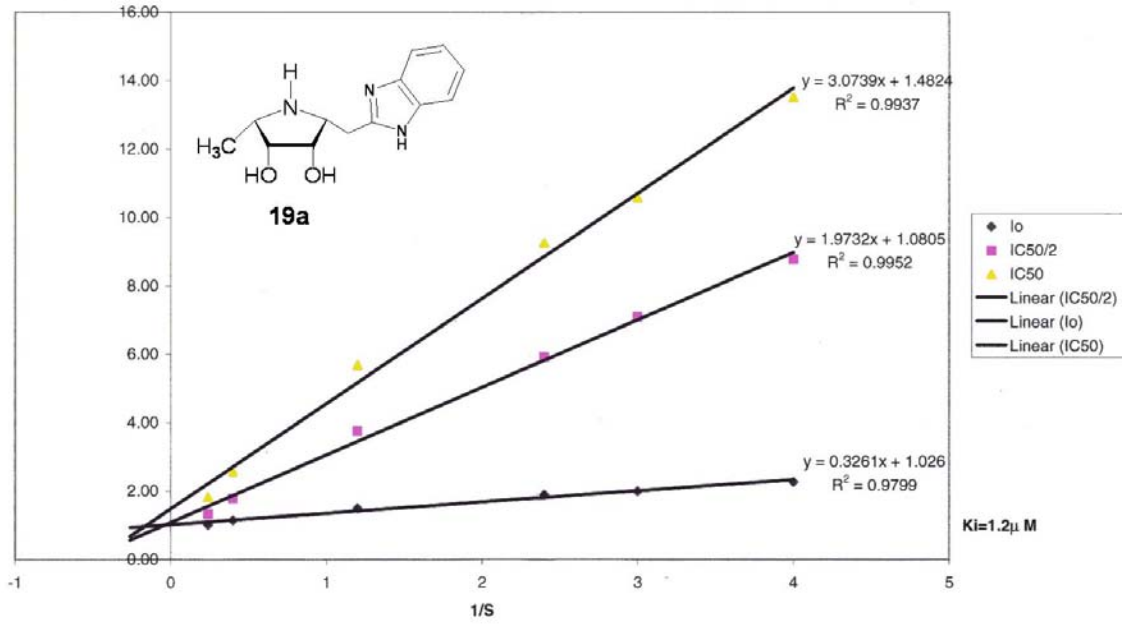
^{13}C-NMR (75.4 MHz, CD_3OD)

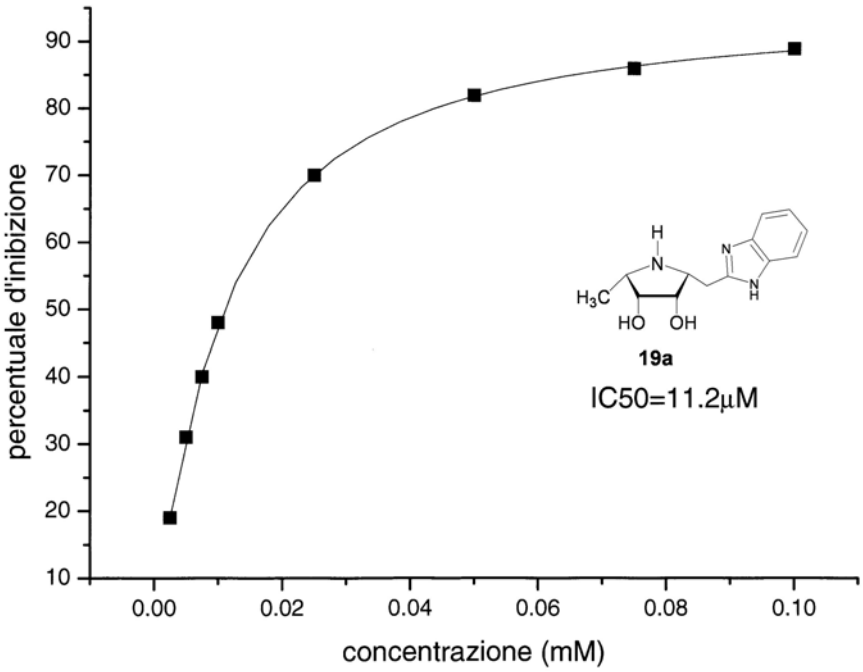

Ki:81nM
competitive inhibition
18a
Y Axis Title
X Axis Title
0
1
2
3
4
5
6
7
8
9
10
11
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5

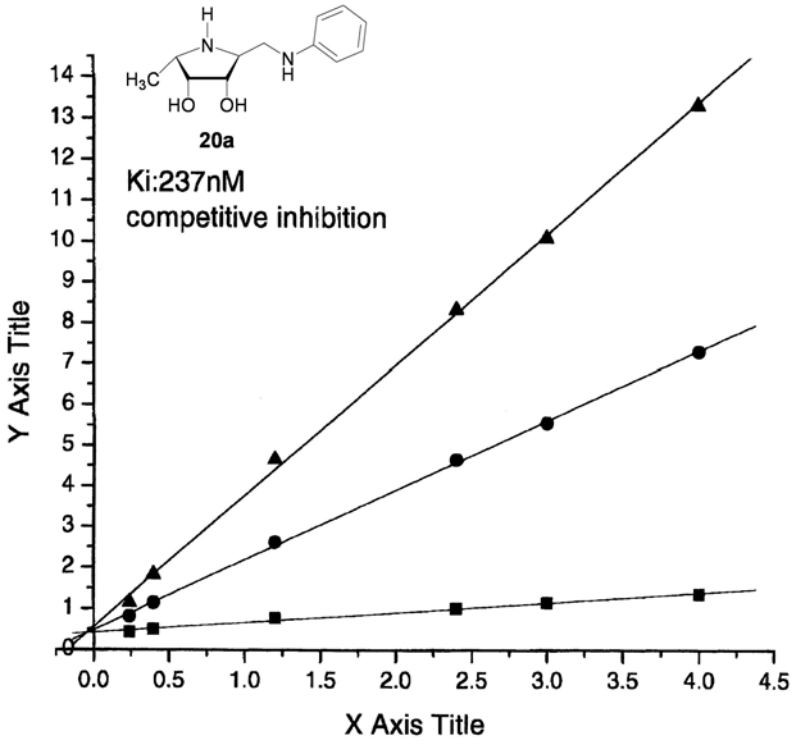

18a
AMV51b sur E1
Ic50:773nM
Y Axis Title
X Axis Title
0
20
40
60
80
100
0.000
0.002
0.004
0.006
0.008
0.010

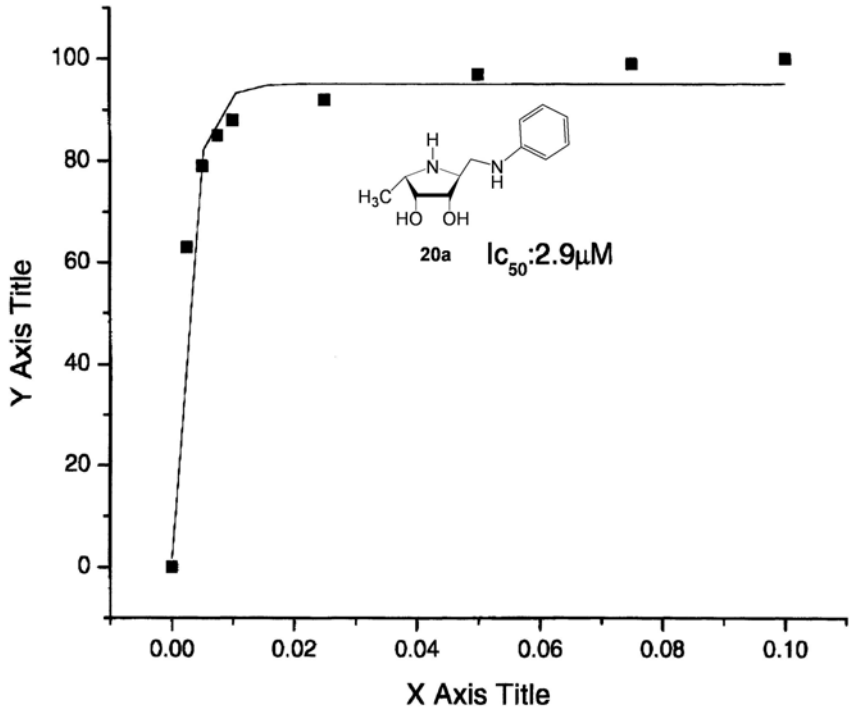

Ki: 240µM
uncompetitive inhibition
18b
Y Axis Title
X Axis Title

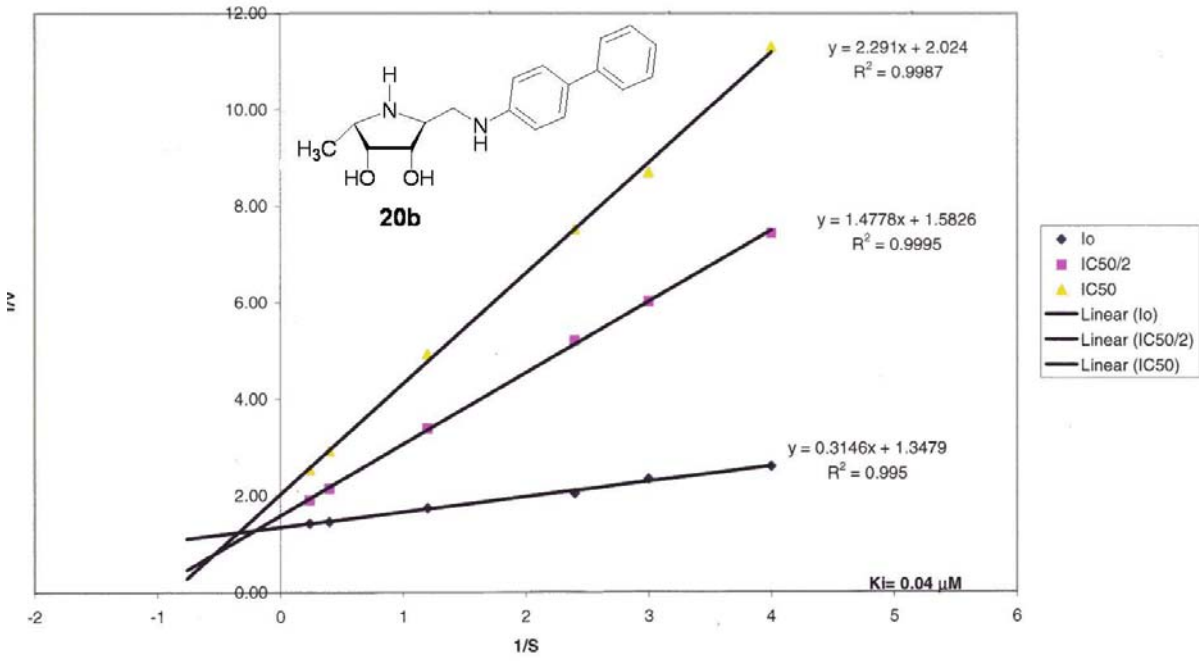

B
18b
AMV-51a sur E1
Ic50: 166µM
Y Axis Title
X Axis Title

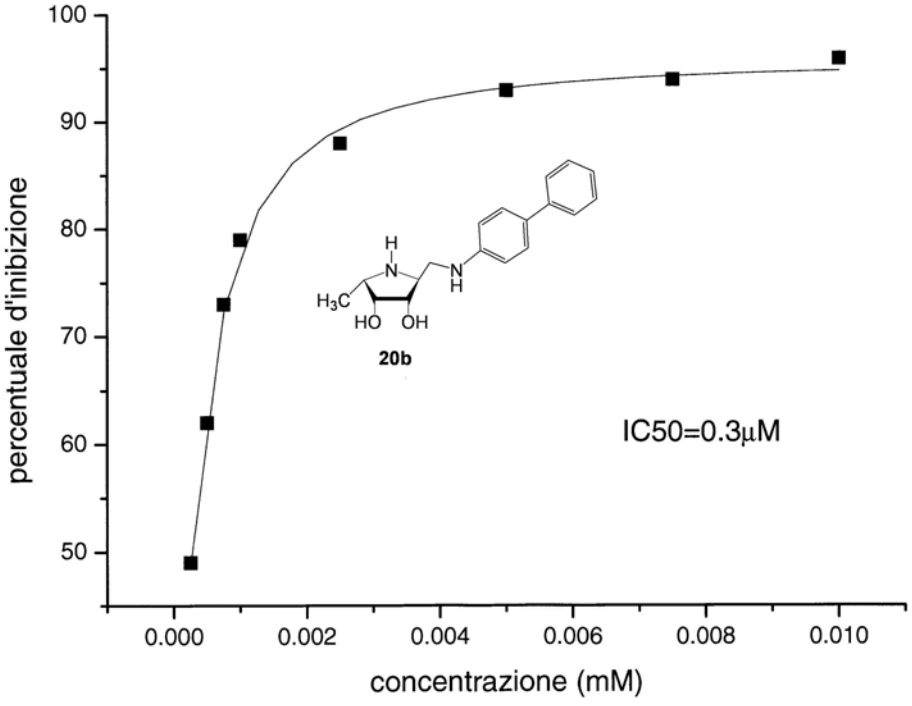

16.00
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
-1
0
1
2
3
4
5
1/S
y = 3.0739x + 1.4824
R² = 0.9937
y = 1.9732x + 1.0805
R² = 0.9952
y = 0.3261x + 1.026
R² = 0.9799
Io
IC50/2
IC50
Linear (IC50/2)
Linear (Io)
Linear (IC50)
Ki=1.2μ M
19a

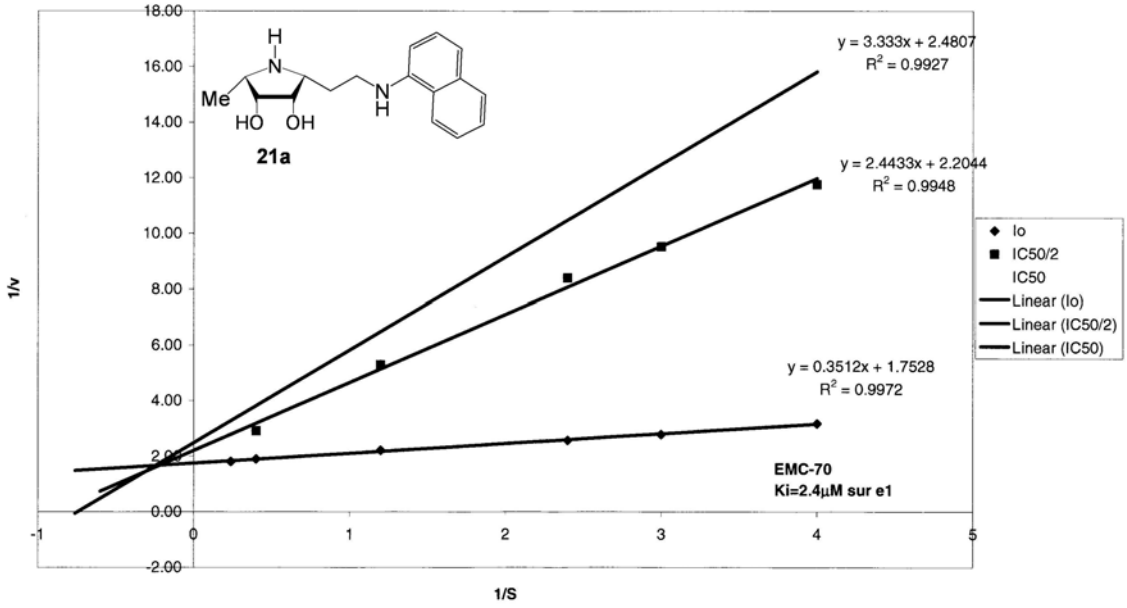

percentuale d'inibizione
concentrazione (mM)
90
80
70
60
50
40
30
20
10
0.00
0.02
0.04
0.06
0.08
0.10
19a
IC50=11.2μM

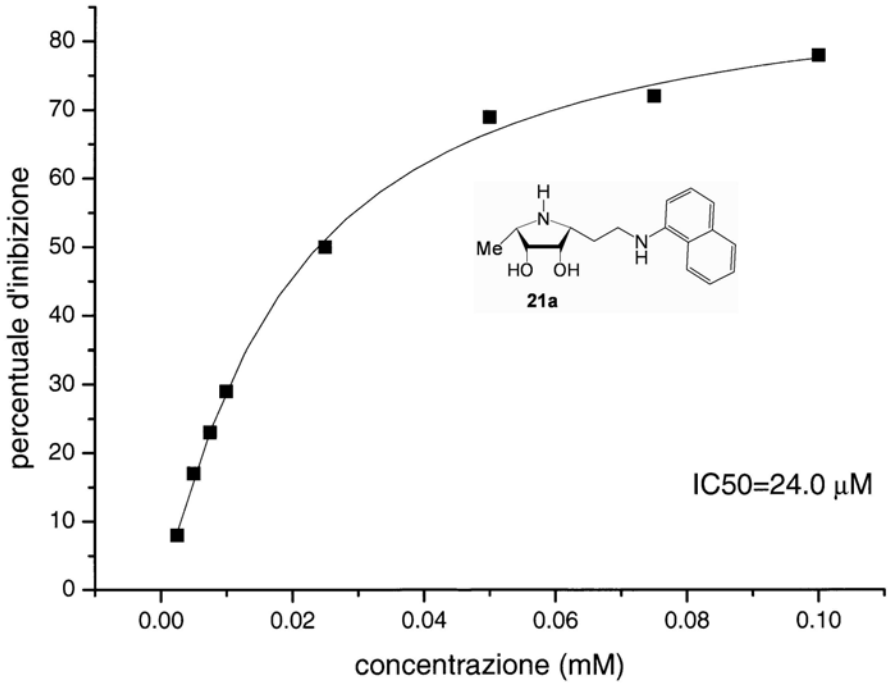

20a
Ki:237nM
competitive inhibition
Y Axis Title
X Axis Title

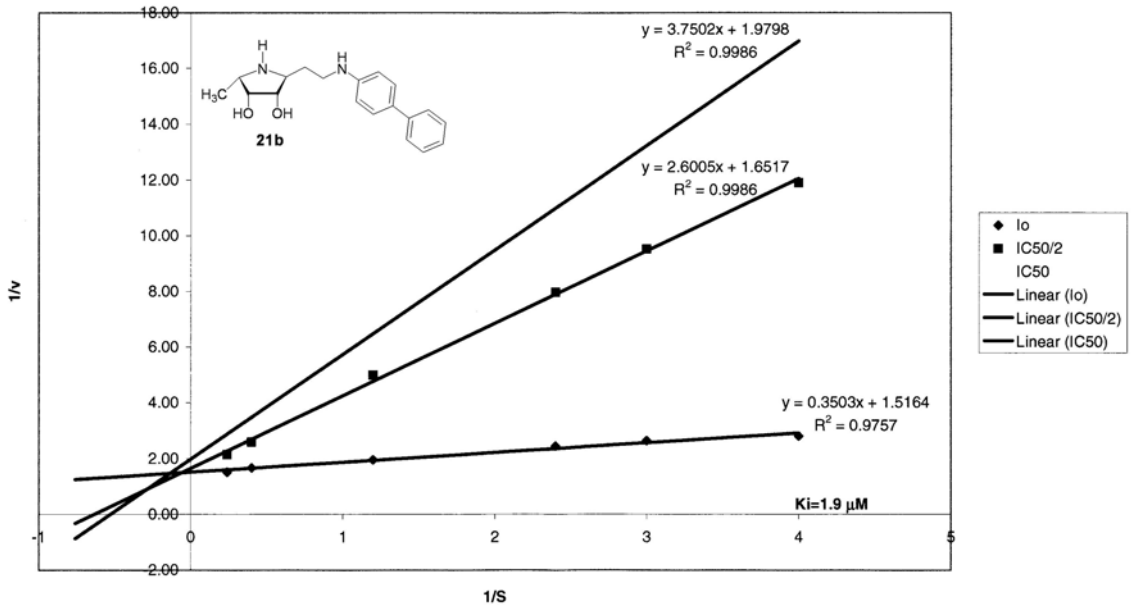

20a
Ic50:2.9μM
Y Axis Title
X Axis Title

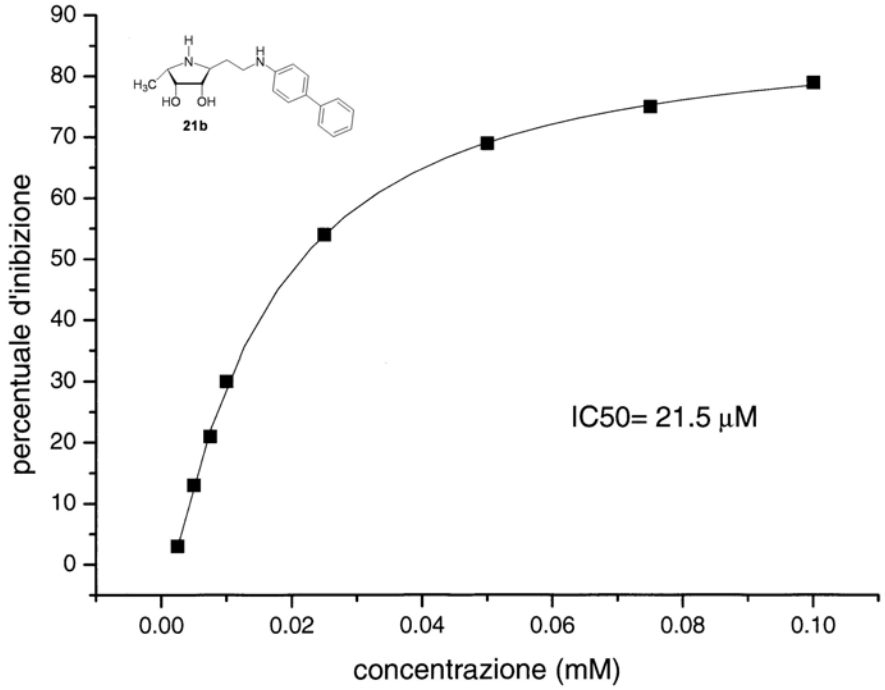

y = 2.291x + 2.024
R² = 0.9987
y = 1.4778x + 1.5826
R² = 0.9995
y = 0.3146x + 1.3479
R² = 0.995
Ki= 0.04 µM
20b
Io
IC50/2
IC50
Linear (Io)
Linear (IC50/2)
Linear (IC50)
1/V
1/S


percentuale d'inibizione
concentrazione (mM)
IC50=0.3µM
20b


y = 3.333x + 2.4807
R² = 0.9927
y = 2.4433x + 2.2044
R² = 0.9948
y = 0.3512x + 1.7528
R² = 0.9972
Io
IC50/2
IC50
Linear (Io)
Linear (IC50/2)
Linear (IC50)
EMC-70
Ki=2.4µM sur e1
1/v
1/S
21a


percentuale d'inibizione
concentrazione (mM)
IC50=24.0 µM
21a


y = 3.7502x + 1.9798
R² = 0.9986
y = 2.6005x + 1.6517
R² = 0.9986
y = 0.3503x + 1.5164
R² = 0.9757
Ki=1.9 µM
21b
1/v
1/S
Io
IC50/2
IC50
Linear (Io)
Linear (IC50/2)
Linear (IC50)


21b
percentuale d'inibizione
concentrazione (mM)
IC50= 21.5 µM