Supporting Information

Synthesis and Identification of New Sacubitril Derivatives as Lead Compounds for Antibacterial, Antifungal and Antitubercular (TB) Activities against Dormant Tuberculosis

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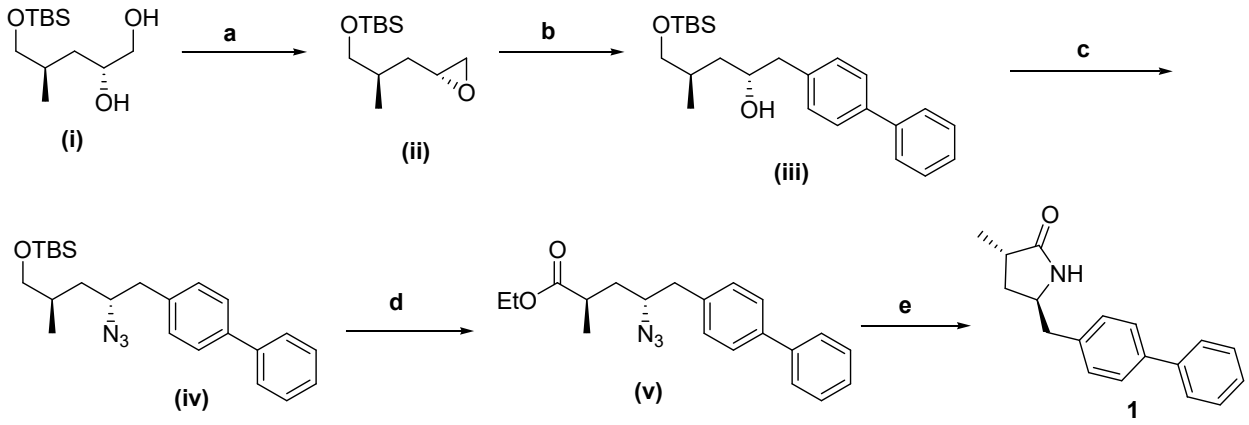
1. Synthesis of the compound 1



Reagents and conditions: (a) $C_4F_9SO_2F$, DBU, DCM, 0 °C: (b) (1,1'-biphenyl)-4-ylmegnesium bromide, CuBr.Me_2S, 0°C; (c) (i) MsCl, Et_3N, DMAP, DCM, 0°C, 3h; (ii) NaN_3, DMF, 60°C, 6h; (d) (i) Jones oxidation, 0°C; (ii) $SOCl_2$, EtOH, RT; (e) Pd/C, H_2, MeOH.

2. Procedure for the synthesis of (2R,4S)-5-([1,1'-biphenyl]-4-yl)-4-(amino)-2-methylpentanoic acid. HCl (2).

The a stirred solution of (3R,5S)-5-[(Biphenyl-4-yl)methyl]-3-methylpyrrolidin-2-one1 (1.0 mmol), Acetic acid (1.5 mmol) and HCl(1.5 mmol) and heated for 15h at 90 °C. The reaction mixture (RM) was allowed to room temperature (RT), Add ethyl acetate and stir for 2-3 hr at 10-15°C. Filter the compound and wash with EtOAc. To get compound 2 as off-white solid (85% yield). M.P.194.3-197.8 °C;^{1}H NMR (300 MHz, DMSO-d6) δ: 12.32 (S, 1H), 8.22 (s, 2H), 7.66 (t, 4H), 7.46 (t, 2H), 7.37 (d, J = 7.5 Hz, 3H), 3.41 (m, 1H), 3.05 (m, 1H), 2.85 (m, 1H), 2.66 (m, 1H), 1.85 (m, 1H), 1.28 (m, 1H), 1.06 (d, J = 6.9, 3H) ; ^{13}C NMR (75 MHz, DMSO) δ: 176.5, 139.7, 138.5,135.6,130.0, 128.9, 127.3, 126.7, 126.5, 50.3, 38.0, 35.7, 34.9, 17.5; IR (neat): υ_{max} 3427, 2931, 1617, 1580, 1404, 1159, 759 cm^{-1}; MS: *m/z* 284.1 (M+H$^+$).

Procedure for the synthesis of (2R,4S)-5-([1,1'-biphenyl]-4-yl)-4-((tert-butoxycarbonyl)amino)-2-methylpentanoic acid (3).

To a stirred solution of compound 2 (1 mmol) in DCM (150 ml) at RT. Add DIPEA (2.1 mmol) and stir the RM for15 minutes, Boc anhydride (1.2 mmol) was added then the RM was stirred for 6h at RT. Add water and extracted with DCM (2 x 100 ml). The combined organic layer was washed with brine solution, dried over Na_2SO_4 and the solvent were evaporated under reduced pressure. To afford compound 3 as off-white solid (89% yield). M.P. 145.2-149.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.05 (s, 1H), 7.55 (m, 4H), 7.42 (t, 3H), 7.32 (m, 1H), 7.25 (m, 2H), 3.69 (m, 1H), 2.76 (m, 2H), 2.61 (m, 1H), 1.89 (m, 2H), 1.20 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 181.3,157.4,140.9, 139.4, 139.3, 137.8, 136.7, 129.9, 128.8, 127.1, 127.0, 79.8, 49.9, 42.3, 38.4, 36.6, 28.4, 17.7; IR (neat): υ_{max} 3024, 2930, 2533, 1700, 1647, 1602, 1414, 1214, 764 cm^{-1}; MS: *m/z* 382.1 (M-H$^+$).

Procedure for the synthesis of (2R,4S)-5-([1,1'-biphenyl]-4-yl)-4-(amino)-2-methylpentanoic acid ethyl ester hydrochloride (4).

To the solution of compound 3 (1 mmol) in Ethanol (50 mL). Heat to at 80 °C, then add $SOCl_2$ (1.5 mmol) to RM. Stir the reaction mass for 18 hrs at reflux. Then distill out the solvent under reduced pressure. Cool to RT and add n-Hexane. Stir for 45 mins. Filter the solid and to get compound 4 as white solid (94% yield). M.P:156.4-160.2 °C;^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.62 (s, 2H), 7.54 (t, 4H), 7.41(t, 2H), 7.30 (m, 3H), 4.06 (q, 2H), 3.67 (s, 1H), 3.38 (m, 1H), 2.96 (m, 2H), 2.03 (m, 1H), 1.84 (m, 1H), 1.16 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 175.3, 140.7, 140.1, 134.7, 129.9, 128.8, 127.6, 127.4, 127.1, 60.9, 52.3, 39.5, 36.2, 36.1, 17.9, 14.2; IR (neat): υ_{max} 2609, 1729, 1606, 1575, 1487, 1409, 1346, 1214, 1160, 761 cm^{-1}; MS: *m/z* 311.9 (M +H$^+$).

3. Synthesis and Spectral data for 5a-v.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-bormo-5-fluorobenzoylamino)-2-methylpentanoic acid ethyl ester amide (5a).

Under N_2 atmosphere to a stirred solution of compound (4) 40 mg (0.13 mmol, 1.0 eq) in dry dichloromethane (4 mL) at room temperature added the Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium (HATU) (59 mg, 0.15 mmol, 1.2 eq) and DIPEA (44 µ, 0.26 mmol, 2.0 eq) simultaneously, after five minutes added the 2-bromo-5-fluoro benzoic acid (31 mg, 0.14 mmol, 1.1 eq) to the mixture. Later, the reaction mixture was stirred for 12 hours. After the completion of reaction, the crude product was diluted with an excess of DCM (10 mL), washed with saturated bicarbonate (3 mL) solution and brine solution. The organic layer dried with sodium sulfate and distilled out completely under a vacuum. The crude product was purified using column chromatography with ethyl acetate: Hexane mixture to get compound, 5a (58 mg, 88%).

Off white solid, 88% yield; M.P: 205-207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (m, 5H), 7.43 (t, 2H), 7.33 (m, 3H), 7.07 (dd ,1H), 6.97 (m, 1H), 5.85 (d, J = 8.8 Hz, 1H), 4.49-4.44 (m, 1H), 4.15 (q, 2H), 2.99 (d, J = 6.4 Hz, 2H), 2.73-2.68 (m, 1H), 2.08-2.01 (m, 1H), 1.70-1.56 (m, 1H), 1.26-1.21 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.4, 169.7, 161.2, 140.9, 139.7, 136.6, 135.0, 134.9,130.0, 128.9, 127.3, 127.1, 118.6, 118.3, 116.9, 116.5, 60.8, 49.6, 40.6, 37.6, 36.6, 17.9, 14.3; IR (cm^{-1}): 3313.71, 1736.08, 1643.12, 1440.72, 1486.646, 1378.33, 1304.225, 664.50; MS: *m/z* 511.2 (*M*+H), Calcd. for $C_{27}H_{27}BrFNO_3$: C, 63.29; H, 5.31; N, 2.73. Found: C, 64.03; H, 5.68; N, 2.54.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-(2-chlorophenyl)acetylamino)-2-methylpentanoic acid ethyl ester amide (5b).

Similar method of synthesis of compound 5a, was employed for the synthesis of compounds 5(b-v) and the spectral data as follows.

Off white solid, 92% yield; M.P: 184-189 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (t, 2H), 7.45 (q, 4H), 7.38 (m, 2H), 7.26-7.20 (m, 3H), 7.09 (d, *J* = 8.0 Hz, 2H), 5.30 (t, 1H), 4.24 (q,1H), 4.13 (q, 2H), 3.65(q, 2H), 2.83-2.75 (m, 2H), 2.53-2.48 (m,1H), 1.93-1.86 (m,1H), 1.47-1.39 (m,1H), 1.23 (t, 3H), 1.14 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 169.1, 140.9, 139.3, 136.5, 134.4, 133.1, 131.7, 129.8, 129.8,128.9, 128.8, 127.4, 127.2, 127.1, 127.0, 60.6, 48.7, 41.7, 403, 37.7, 36.6, 17.8, 14.3; IR (cm^{-1}): 3306.83, 3057.67, 1725.23, 1644.70, 1485.59, 741.33; MS: *m/z*4 64.1 (M+H^+), Calcd. for $C_{28}H_{30}ClNO_3$: C, 72.48; H, 6.52; N, 3.02. Found: C, 72.89; H, 6.10; N, 2.64.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2,6-dimethoxybenzoylamino)-2-methylpentanoicacid ethyl ester amide (5c).

Off white solid, 82% yield; M.P: 217-223 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (d, *J* = 7.2 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.42 (t, 2H), 7.35 (q, 3H), 7.22 (d, *J* = 8.8 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 2H), 5.56 (d, *J* = 8.8 Hz, 1H), 4.43 (q,1H), 4.14 (q, 2H), 3.80 (s, 6H), 3.00 (d, *J* = 5.6 Hz, 2H), 2.80-2.75 (m, 1H), 2.04-1.97 (m, 1H), 1.59-1.50 (m, 1H), 1.25-1.20 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.5, 165.4, 157.3, 141.0, 139.2, 137.0, 130.5, 130.4,128.8, 127.1, 127.0, 126.9, 116.4, 103.9, 60.4, 55.8, 49.0, 40.4, 37.6, 36.4, 18.0, 14.2; IR (cm^{-1}): 3311.87, 1727.58, 1518.93, 1592.04, 1642.09, 1252.46, MS: *m/z* 475.2 (M+H^+), Calcd. for $C_{29}H_{33}NO_5$:C, 73.24; H, 6.99; N, 2.95. Found: C, 72.54; H, 6.64; N, 2.49.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-hydroxybenzoylamino)-2-methylpentanoicacid ethyl ester amide (5d).

Off white solid, 91% yield; M.P: 232-236 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.46 (s, 1H), 7.59-7.53 (m, 4H), 7.43 (t, 2H), 7.40(t, 2H), 7.33 (m, 3H), 6.98 (t, 1H), 6.84-6.80 (m,1H), 6.57 (d, *J* = 8.0 Hz, 1H), 4.49 (s, 1H), 4.15- 4.04 (m, 2H), 3.06 (q, 1H), 2.92 (q, 1H), 2.66-2.61 (m, 1H), 2.04- 1.97 (m,1H), 1.77- 1.70 (m, 1H), 1.22- 1.17 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.9, 169.6, 161.7, 140.7, 139.6, 136.4, 134.2, 129.9, 128.8, 127.3, 127.0, 125.4, 118.7, 118.6, 114.3, 60.9, 48.4, 40.5, 36.4, 36.3, 17.2, 14.1; IR (cm^{-1}): 3397.68, 1702.11, 1637.54, 1588.76, 1488.93, 1303.96 ; MS: *m/z* 432.0 (*M*+H^+), Calcd. for $C_{27}H_{29}NO_4$: C, 75.15; H, 6.77; N, 3.25. Found: C, 76.13; H, 7.15; N, 3.06.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(3-(trifluoromethyl)benzoylamino)-2-methylpentanoic acid ethyl ester amide (5e).

Off white solid, 94% yield; M.P:201-205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.58- 7.53 (m, 5H), 7.43 (t, 2H), 7.34 (q, 3H), 6.42 (d, *J* =8.0 Hz, 1H), 4.45 (s,1H), 4.15- 4.07 (m, 2H), 3.08 (q, 1H), 2.96 (q, 1H), 2.6 (m, 1H), 2.05- 1.98 (m, 1H), 1.77- 1.74 (m, 1H), 1.25- 1.19 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.9, 165.5, 14.0, 139.6, 138.3, 136.7, 130.0, 128.9, 127.8, 127.6, 127.3, 127.1, 125.8, 125.8, 125.7, 125.4, 60.6, 49.0, 40.2, 36.6, 36.5, 17.6, 14.3; IR (cm^{-1}): 3248.91, 1725.57, 1631.15, 1436.13, 1486.73, 1071.48; MS: *m/z* 484.1 (*M*+H^+), Calcd. for $C_{28}H_{28}F_3NO_3$: C, 69.55; H, 5.84; N, 2.90. Found: C, 68.59; H, 5.41; N, 3.40.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(4-(trifluoromethyl)benzoylamino)-2-methylpentanoic acid ethyl ester amide (5f).

Off white solid, 89% yield; M.P: 187-191°C; ^{1}H NMR 400 MHz, $CDCl_3$) δ: 7.83 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.58- 7.53 (m, 4H), 7.43 (t, 2H), 7.33 (t, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.39 (d, *J* = 8.0 Hz, 1H), 4.46 (s, 1H), 4.12- 4.07 (m, 2H), 3.07 (q, 1H), 2.96 (q, 1H), 2.67 (t, 1H), 2.01 (q, 1H), 1.78 (t, 1H), 1.24 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.9, 165.6, 140.8, 139.7, 138.0, 136.7, 130.0, 128.9, 127.4, 127.3, 127.3, 127.3, 127.1, 125.8, 125.7, 125.7, 125.6, 60.9, 49.2, 40.3, 36., 36.5, 17.3, 14.2; IR (cm^{-1}): 3336.61, 1724.61, 1635.30, 1577.6, 1528.12, 1321.60; MS: *m/z* 484.1 (*M*+H^+), Calcd. for $C_{28}H_{28}F_3NO_3$: C, 69.55; H, 5.84; N, 2.90. Found: C, 69.86; H, 6.05; N, 2.75.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-fluorobenzoylamino)-2-methylpentanoicacid ethyl ester amide (5g).

Off white solid, 88% yield; M.P:179-185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07- 8.02 (m, 1H), 7.58 (d, *J* = 1.2 Hz, 2H), 7.55 (d, J = 12.0 Hz, 2H), 7.42 (t, 3H), 7.32 (t, 3H), 7.25 (d, J = 5.2 Hz, 1H), 7.10 (q, 1H), 6.56 (q, 1H), 4.51 (d, *J* = 2.8 Hz, 1H), 4.12- 4.06 (m, 2H), 3.02-2.92 (m, 2H), 2.65- 2.60 (m, 1H), 1.16- 1.58 (m, 1H), 1.47 (t, 1H), 1.20 (d, *J* = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.2, 162.9, 159.4, 140.9, 139.5, 136.7, 133.3, 133.2, 130.0, 128.8, 127.2, 127.0, 124.9, 121.3, 121.2, 116.2, 115.9, 60.4, 49.3, 40.6, 37.7, 36.7, 17.8, 14.2, 8.2; IR (cm^{-1}): 3346.15, 1722.81, 1642.24, 1613.66, 1447.75, 1147.03; MS: *m/z* 434.6 (*M*+H^+), Calcd. for $C_{27}H_{28}FNO_3$: C, 74.80; H, 6.51; N, 3.23. Found: C, 73.99; H, 6.28; N, 2.98.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(3,4-dichlorobenzoylamino)-2-methylpentanoicacid ethyl ester amide (5h).

Off white solid, 93% yield; M.P: 214-218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (d, *J* = 2.0 Hz, 1H), 7.58- 7.51 (m, 6H), 7.49- 7.41 (m, 3H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 1.6 Hz, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 4.42 (q, 1H), 4.15- 4.07 (m, 2H), 3.05 (dd, 1H), 2.94 (dd,

1H), 2.69- 2.62 (m, 1H), 2.03- 1.96 (m, 1H), 1.79- 1.72 (m, 1H), 1.25- 1.18 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.8, 164.7, 140.7, 139.6, 136.6, 135.8, 134.5, 133.0, 130.6, 129.9, 129.2, 128.8, 127.3, 127.0, 126.0, 60.9, 49.3, 40.3, 36.6, 36.5, 17.3, 14.2; IR (cm^{-1}): 3278.01, 1721.18, 1633.32, 1586.14, 1488.68, 760.89; MS: *m/z* 484.2 (*M*+H^+), Calcd. for $C_{27}H_{27}Cl_2NO_3$: C, 66.95; H, 5.62; N, 2.89. Found: C, 67.51; H, 5.98; N, 3.16.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-(2,4-dichlorophenyl)acetylamino)-2-methylpentanoicacid ethyl ester amide(5i).

Off white solid, 86% yield; M.P: 198-203 °C; ^{1}H NMR 400 MHz, $CDCl_3$) δ: 7.58 (t, 2H), 7.44 (t, 4H), 7.38 - 7.32 (m, 2H), 7.20- 7.15 (m, 2H), 7.11 (d, *J* = 2.0 Hz, 2H), 5.35 (d, *J* = 8.8 Hz, 1H), 4.26- 4.20 (m, 1H), 4.13 (q, 2H), 3.59 (q, 2H), 2.85- 2.75 (m, 2H), 2.55- 2.50 (m, 1H), 1.94- 1.88 (m, 1H), 1.52- 1.45 (m, 1H), 1.24 (t, 3H), 1.15 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.4, 160.5, 140.8, 139.5, 136.5, 135.0, 134.0, 132.4, 131.7, 129.8, 129.5, 128.9, 127.6, 127.3, 127.1, 127.0, 60.6, 48.8, 41.0, 40.3, 37.6, 36.6, 17.8, 14.3; IR (cm^{-1}): 3326.62, 1723.91, 1642.66, 1642.68, 1587.85, 1533.42, 759.91; MS: *m/z* 498.1 (*M*+H^+), Calcd. for $C_{28}H_{29}Cl_2NO_3$: C, 67.47; H, 5.86; N, 2.81. Found: C, 68.43; H, 6.25; N, 2.62.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-(2,4,5-trifluorophenyl)acetylamino)-2-methylpentanoic acid ethyl ester amide (5j).

Off white solid, 79% yield; M.P: 238-242 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, *J* = 7.6 Hz, 2H), 7.49- 7.42 (m, 4H), 7.34 (t, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.10 (q, 1H), 6.93- 6.87 (m, 1H), 5.46 (d, *J* = 8.4 Hz, 1H) 4.22 (d, *J* = 3.6 Hz, 1H), 4.14 (q, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.83 (q, 2H), 2.52 (d, *J* = 4.8 Hz, 1H), 1.92 (q, 1H), 1.56- 1.50 (m, 1H), 1.24 (t, 3H) 1.16 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.4, 168.4, 157.0, 154.5, 150.6, 148.1, 148.0, 140.7, 139.5, 136.5, 129.8, 127.3, 127.1, 127.0, 119.3, 119.1, 118.5, 105.8, 105.6, 105.5, 105.3, 60.7, 48.9, 40.3, 37.4, 36.5, 36.1, 29.6, 17.6, 14.2.;^{19}F NMR (400 MHz, $CDCl_3$)

δ: -118.8 (s, 1F), -134.5 (t, 1F), -142.0 (t, 1F); IR (cm^{-1}): 3294.27, 1646.52, 1730.84, 1542.48, 1486.07, 1465.23, 1517.83, 1173.96; MS: *m/z* 484.2 (*M*+H^+), Calcd. for $C_{28}H_{28}F_3NO_3$: C, 69.55; H, 5.84; N, 2.90. Found: C, 69.88; H, 6.18; N, 2.68.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-(3,4,5-trimethoxyphenyl)acetylamino)-2-methylpentanoic acid ethyl ester amide (5k).

Off white solid, 90% yield; M.P: 264-267 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.57 (d, *J* = 7.5 Hz, 2H), 7.50 (d 2H), 7.42 (t, 2H), 7.35 (dd, 3H), 7.23 (t, 1H), 6.53 (d, *J* =8.4 Hz, 2H), 5.58 (d, *J* = 8.4 Hz, 2H), 4.43 (m, 2H), 3.80 (t, 9H), 3.01 (d, *J*= 5.6 Hz, 2H), 2.80- 2.75 (m, 1H), 2.04- 1.97 (m, 1H), 1.57- 1.50 (m, 1H), 1.25- 1.20 (m, 6H): ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.2, 170.3, 153.6, 140.6, 139.3, 137.2, 136.5, 130.5, 129.9, 128.8, 127.3, 127.0, 126.9, 106.3, 60.9, 60.6, 56.1, 48.6, 44.4, 40.1, 37.5, 36.6, 17.8, 14.2; IR (cm^{-1}): 3312, 1740, 1680, 1625, 1440, 1533, 752; MS: *m/z* 520.2 (*M*+H^+), Calcd. for $C_{31}H_{37}NO_6$: C, 71.65; H, 7.18; N, 2.70. Found: C, 70.94; H, 6.85; N, 3.08.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-(4-fluorophenyl)acetylamino)-2-methylpentanoic acid ethyl ester amide (5l).

Off white solid, 86% yield; M.P: 196-199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, *J* = 7.6 Hz, 2H), 7.45 (t, 4H), 7.35 (t, 1H), 7.09 (t, 4H), 6.98 (t, 2H), 5.22 (d, *J* = 8.4 Hz, 1H), 4.22 (d, *J* = 4.8 Hz, 1H), 4.13 (q, 2H), 3.45 (s, 2H), 2.83 (dd, 1H), 2.75 (dd, 1H), 2.50 (q, 1H), 1.93-1.86 (m, 1H), 1.50- 1.42 (m, 1H), 1.24 (t, 3H), 1.14 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.3, 170.1, 160.4, 140.7, 139.4, 136.5, 131.0, 130.9, 130.7, 130.7, 129.8, 127.3, 127.1, 127.0, 115.9, 115.6, 60.6, 48.6, 43.1, 40.2, 37.6, 36.6, 17.7, 14.2; IR (cm^{-1}): 3296.02, 1741.70, 1724.97, 1637.68, 1534.18, 1172.03, 698.34; MS: *m/z* 448.3 (*M*+H^+), Calcdfor $C_{28}H_{30}FNO_3$: C, 75.14; H, 6.76; N, 3.13. Found: C, 74.62; H, 6.40; N, 3.45.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(isonicotinoylamino)-2-methylpentanoicacid ethyl ester amide (5m).

Pale yellow solid, 79% yield; M.P: 223-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.72 (d, *J* = 5.2 Hz, 2H), 7.57 (q, 6H), 7.43 (t, 2H), 7.35 (t, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.51 (d, *J* = 8.0 Hz, 1H), 4.44 (s, 1H), 4.14- 4.07 (m, 2H), 3.06 (dd, 1H), 2.95 (q, 1H), 2.65 (d, *J* = 4.4 Hz, 1H), 2.04 1.97 (m, 1H), 1.81- 1.74 (m, 1H), 1.25- 1.19 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.9, 164.9, 150.7, 141.7, 140.7, 139.7, 136.5, 130.0, 128.9, 128.3, 127.3, 127.0, 120.8, 60.9, 49.3, 40.2, 36.5, 36.4, 17.3, 14.2; IR (cm^{-1}): 3271.06, 1730.83, 1637.43, 1597.78, 1545.06, 1227.93, 842.63; MS: *m/z* 417.2 (*M*+H^+), Calcd. for $C_{26}H_{28}N_2O_3$: C, 74.97; H, 6.78; N, 6.73. Found: C, 75.72; H, 6.99; N, 6.28.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(4-nitrobenzoylamino)-2-methylpentanoicacid ethyl ester (5n).

Yellow solid, 87% yield; M.P:228-233 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.26 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.57 (q, 4H), 7.43 (t, 2H), 7.33 (t, 1H), 7.27 (t, 2H), 6.58 (d, *J* = 7.8 Hz, 1H), 4.45 (s, 1H), 4.15- 4.07 (m, 2H), 3.07 (dd, 1H), 2.96 (dd, 1H), 2.70- 2.65 (m, 1H), 2.05- 1.98 (m, 1H), 1.82- 1.75 (m, 1H), 1.29- 1.20 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.9, 164.9, 149.5, 140.7, 140.3, 139.6, 136.6, 129.9, 128.8, 128.1, 127.3, 127.2, 127.0, 123.0, 60.9, 49.4, 40.2, 36.5, 36.5, 17.3, 14.2; IR (cm^{-1}): 3348.55, 1722.96, 1646.17, 1601.95, 1533.12, 1350.19, 1192.6, 757.38; MS: *m/z* 458.9 (*M*-H^+), Calcd. for $C_{27}H_{28}N_2O_5$: C, 70.42; H, 6.13; N, 6.08. Found: C, 69.84; H, 5.79; N, 6.59.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(tetradecanoylamino)-2-methylpentanoicacid ethyl ester (5o).

Off white solid, 96% yield; M.P: 176-179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, *J* = 7.6 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.43 (t, 2H), 7.33 (t, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.30 (d, *J* = 8.8 Hz, 1H), 4.25 (d, J = 4.0 Hz, 1H), 4.13 (q, 2H), 2.85 (d, *J* = 6.3 Hz, 2H), 2.54 (d, *J* = 8.8 Hz, 1H), 2.09 (q, 2H), 1.97- 1.90 (m, 1H), 1.54 (t, 2H), 1.25 (q, 24H), 1.17 (d, J = 7.2 Hz, 3H), 0.87 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.5, 172.7, 140.9, 139.4, 136.9, 130.0, 128.8, 127.2, 127.1, 127.0, 60.6, 48.3, 40.5, 37.5,37.1, 36.6, 32.0, 29.8, 29.7, 29.6, 29.5,29.4, 29.3, 25.8, 22.8, 17.7, 14.3, 14.2; IR (cm^{-1}): 3305.52, 1725.99, 1636.65, 1533.99, 1488.02, 1439.08, 1375.20, 1311.43, 1161.01, 759.94, 609.20; MS: *m/z* 522.3 (*M*+H^+), Calcd. for $C_{34}H_{51}NO_3$: C, 78.26; H, 9.85; N, 2.68. Found: C, 77.21; H, 9.24; N, 3.12.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(1-(tert-butoxycarbonyl)piperidine-4-carboxoylamino)-2-methylpentanoic acid ethyl ester (5p).

Off white solid, 92% yield; M.P: 204-208 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (s, 1H), 7.96 (d, *J*=8.4 Hz, 2H), 7.55 (t, 2H), 7.44 (t, 2H), 7.34 (t, 1H), 7.31-7.26 (m, 1H), 5.72 (d, *J*= 5.6 Hz, 1H), 4.23 (s, 1H), 4.13 (q, 4H), 3.05 (dd, 2H), 2.92 (dd, 2H), 2.69- 2.64 (m, 1H), 2.34 (s, 3H), 2.11- 2.04 (m, 3H), 1.73- 1.66 (m, 6H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.5, 173.8, 154.7, 140.8, 139.5, 136.8, 130.0, 128.8, 127.3, 127.1, 127.0, 79.7, 60.7, 48.3, 43.5, 40.5, 37.3, 36.6, 28.7, 28.6, 28.5, 17.6, 14.3; IR (cm^{-1}): 2973.48, 1729.10, 1690.56, 1534.42, 1486.57, 1161.35, 760.68; MS: *m/z* 523.2 (*M*+H^+), Calcd. for $C_{31}H_{42}N_2O_5$: C, 71.24; H, 8.10; N, 5.36. Found: C, 72.09; H, 8.47; N, 5.16.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(cyclopropanecarboxoylamino)-2-methylpentanoic acid ethyl ester (5q).

Off white solid, 88% yield; M.P:187-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (t, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.43 (t, 2H), 7.33 (t, 1H), 7.25 (d, *J* = 6.8 Hz, 2H), 5.54 (d, *J* = 8.4 1H), 4.26 (q, 1H), 4.14 (q, 2H), 2.92- 2.80 (m, 2H), 2.61- 2.56 (m, 1H), 1.97- 1.90 (m, 1H),

1.59- 1.52 (m, 1H), 1.27- 1.22 (m, 4H), 1.16 (d, *J* = 7.2 Hz, 3H), 0.95- 0.90 (m, 2H) 0.71 (q, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.5, 173.0, 140.9, 139.3, 136.9, 130.0, 128.8, 127.2, 127.1, 127.0, 60.6, 48.6, 40.5, 37.3, 36.5, 17.6, 14.8, 14.2, 7.0, 6.9; IR (cm^{-1}): 3313.72, 1637.24, 1529.19, 1486.21, 1441.99, 133.93, 1120.39, 762.28; MS: *m/z* 380.1 (*M*+H^+), Calcd. for $C_{24}H_{29}NO_3$: C, 75.96; H, 7.70; N, 3.69. Found: C, 76.59; H, 7.43; N, 3.47.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(cyclopentanecarboxoylamino)-2-methylpentanoic acid ethyl ester(5r).

Off white solid, 91% yield; M.P:197-200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, *J* = 7.2 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.43 (t, 2H), 7.33 (m, 1H), 5.33 (d, *J* = 8.8 Hz, 2H), 4.26-4.20 (m, 1H), 4.14 (q, 2H), 2.85 (d, *J* = 6.4 Hz, 2H), 2.56 (q, 1H), 2.40 (q, 1H), 1.96- 1.89 (m, 1H), 1.78- 1.64 (m, 5H), 1.59- 1.52 (m, 4H), 1.24 (t, 3H), 1.17 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.5, 175.7, 140.9, 139.4, 137.0, 130.0, 128.8, 127.2, 127.1, 127.0, 60.6, 48.3, 46.1, 40.5, 37.5, 36.6, 30.5, 30.3, 26.0, 25.9, 17.6, 14.3; IR (cm^{-1}): 3281.80, 3082.60, 1729.31, 1638.38, 1554.88, 1487.39, 1447.09, 1368.69, 1170.49, 694.79; MS: *m/z* 408.2 (*M*+H^+), Calcd. for $C_{26}H_{33}NO_3$: C, 76.62; H, 8.16; N, 3.44. Found: C, 76.15; H, 8.49; N, 3.06.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-chloro-5-nitrobenzoylamino)-2-methylpentanoic acid ethyl ester (5s).

Pale yellow solid, 83% yield; M.P:235-239 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (d, *J* = 2.4 Hz, 1H), 8.18 (dd, 1H), 7.59- 7.54 (m, 5H), 7.43 (t, 2H), 7.35-7.26 (m, 3H), 6.07 (d, *J* = 8.8 Hz, 1H), 4.49 (d, *J* = 3.2 Hz, 1H), 4.17 (q, 2H), 3.01 (t, 2H), 2.69 (q, 1H), 2.06 (t, 1H), 1.73 (t, 1H), 1.27- 1.23 (m, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ: 176.3, 164.1, 146.3, 140.7, 139.7, 137.7, 137.0, 136.4, 131.3, 129.9, 128.8, 127.3, 127.0, 125.4, 124.5, 60.8, 49.8, 40.5, 37.5, 36.5, 17.8, 14.2; IR (cm^{-1}): 3300.79, 1727.50, 1644.88, 1609.53, 1526.299, 1486.75,

1464.77, 1345.87, 1281.49, 763.48; MS: *m/z* 494.9 (*M*+H^+), Calcd. for $C_{27}H_{27}ClN_2O_5$: C, 65.52; H, 5.50; N, 5.66. Found: C, 66.20; H, 5.96; N, 5.14.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-methyl-4-nitrobenzoylamino)-2-methylpentanoic acid ethyl ester (5t).

Pale yellow solid, 92% yield; M.P: 217-221 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (t, 2H), 7.56 (t, 4H), 7.44 (t, 2H), 7.35(d, *J* = 7.2 Hz, 1H), 7.29 (t, 3H), 5.70 (d, *J* = 8.7 Hz, 1H), 4.51 (m, 1H), 4.14 (q, 2H), 3.04 (q, 1H), 2.90 (q, 1H), 2.66 (s, 1H), 2.35 (s, 3H), 2.06 (d, *J* = 9.6 Hz, 1H), 1.71 (m, 1H), 1.26- 1.23 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.3, 167.7, 148.1, 142.6, 140.7, 139.7, 138.2, 136.6, 129.8, 128.9, 127.3, 127.2, 127.0, 125.5, 120.9, 60.8, 49.0, 40.8, 37.9, 36.7, 19.4, 17.8, 14.2 ; IR (cm^{-1}): 3288.67, 1725.63, 1638.37, 1605.7, 1521.52, 1485.97, 1379.27, 1178.38, 761.97, 609.76; MS: *m/z* 475.3 (*M*+H^+), Calcd. for $C_{28}H_{30}N_2O_5$: C, 70.87; H, 6.37; N, 5.90. Found: C, 71.67; H, 6.81; N, 5.38.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(4-(cyanomethyl)benzoylamino)-2-methylpentanoic acid ethyl ester (5u).

Off white solid, 95% yield; M.P: 184-188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, *J* = 8.0 Hz, 2H), 7.55 (q, 4H), 7.45- 7.37 (m, 4H), 7.33 (t, 1H), 7.27 (t, 2H), 6.31 (d, *J* = 8.4 Hz, 1H), 4.45 (s, 1H), 4.14- 4.05 (m, 2H), 3.79 (s, 2H), 3.05 (dd, 1H), 2.94 (q, 1H), 2.66 (q, 1H), 2.05- 1.98 (m, 1H), 1.78- 1.71 (m, 1H), 1.21 (q, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.8, 166.0, 140.8, 139.6, 136.8, 134.6, 133.3, 130.0, 128.8, 128.2, 127.8, 127.3, 127.2, 127.0, 117.3, 60.8, 49.1, 40.3, 36.7, 36.6, 23.6, 17.4, 14.2; IR (cm^{-1}): 3340.227, 2252.17, 1722.04, 1632.87, 1527.09, 1463.57, 1333.48, 752.12, 620.04; MS: *m/z* 454.2 (*M*+H^+), Calcd. for $C_{29}H_{30}N_2O_3$: C, 76.63; H, 6.65; N, 6.16. Found: C, 75.95; H, 6.34; N, 6.84.

(2R,4S)-5-([1,1'-Biphenyl]-4-yl)-4-(2-amino-4-chlorobenzoylamino)-2-methylpentanoic acid ethyl ester (5v).

Off white solid, 87% yield; M.P:195-198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (q, 4H), 7.43 (t, 2H), 7.33 (t, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 1H), 6.64 (d, 1H), 6.57 (dd, 1H), 559 (s, 1H), 5.60 (s, 2H), 4.42 (t, 1H), 4.13- 4.07 (m, 2H), 2.95 (t, 2H), 2.62 (q, 1H), 2.04- 1.97 (m, 1H), 1.71- 1.64 (m, 1H), 1.25- 1.18 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.6, 168.1, 149.8, 140.8, 139.5, 137.9, 136.8, 130.0, 128.8, 128.3, 127.2, 127.2, 127.0, 116.6, 116.5, 114.5, 60.7, 48.5, 40.5, 37.1, 36.5, 17.5, 14.2; IR (cm^{-1}): 3473.43, 3365.16, 1712.24, 1629.80, 1611.19, 1512.37, 1370.01, 1257.09, 1214.50, 870.61, 698.53; MS: *m/z* 465.1 (*M*+H^+), Calcd. for $C_{27}H_{29}ClN_2O_3$: C, 69.74; H, 6.29; N, 6.02. Found: C, 69.53; H, 6.10; N, 6.38.

In-vitro antimycobacterial activity:

Briefly, the inoculum was prepared from fresh LJ medium re-suspended in 7H9-S medium (7H9 broth, 0.1% casitone, 0.5% glycerol, supplemented oleic acid, albumin, dextrose, and catalase [OADC]), adjusted to a OD_{590} 1.0, and diluted 1:20; 100 µl was used as inoculum. Each drug stock solution was thawed and diluted in 7H9-S at four-fold the final highest concentration tested. Serial two-fold dilutions of each drug were prepared directly in a sterile 96-well microtiter plate using 100 µl 7H9-S. A growth control containing no antibiotic and a sterile control were also prepared on each plate. Sterile water was added to all perimetre wells to avoid evaporation during the incubation. The plate was covered, sealed in plastic bags and incubated at 37 °C in normal atmosphere. After 7 days incubation, 30 µl of alamar blue solution was added to each well, and the plate was re-incubated overnight. A change in colour from blue (oxidised state) to pink (reduced) indicated the growth of bacteria, and the MIC was defined as the lowest concentration of drug that prevented this change in colour.

X-ray Crystallography.

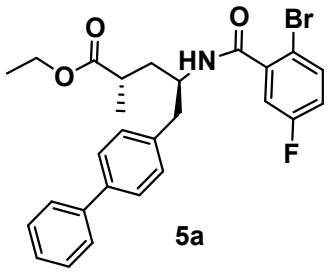
X-ray data for the compound 5n was collected at room temperatureon a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-100 detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1].The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, andU_{iso}(H) = 1.5U_{eq}(C) for methyl H or 1.2U_{eq}(C) for other H atoms].

1. Bruker (2016). APEX3, SAINT and SADABS. Bruker AXS, Inc., Madison, Wisconsin, USA.
2. Sheldrick G. M. (2015) ActaCrystallogrC71:3-8.

Table S1. Crystal data and structure refinement parameters for compound, 5n.

Parameters	5n
Empirical Formula	$C_{27}H_{28}N_2O_5$
Crystal system	Monoclinic
Space group	$P2_1$
Crystal size (mm)	0.32× 0.28 × 0.19
a (Å)	9.2869(2)
b (Å)	5.3667(1)
c (Å)	23.7254(4)
α (°)	90
β (°)	93.0970(8)
γ (°)	90
Volume ($Å^3$)	2134.7(5)
Z	2
Formula mass	460.51
ρ_{calc} (gcm^{-3})	1.295
λ *Å*	0.71073 *(MoKα)*
μ(mm^{-1})	0.090
θ range (˚)	2.196 to 30.633
Total data collected	32089
Unique data	7239
Observed data (I > 2σ(I))	4714
R indexes [I > 2 σ(I)]	R_1 = 0.0541, wR_2 = 0.1242
Goodness of fit	1.027

^{1}H NMR Spectrum of compound 5a



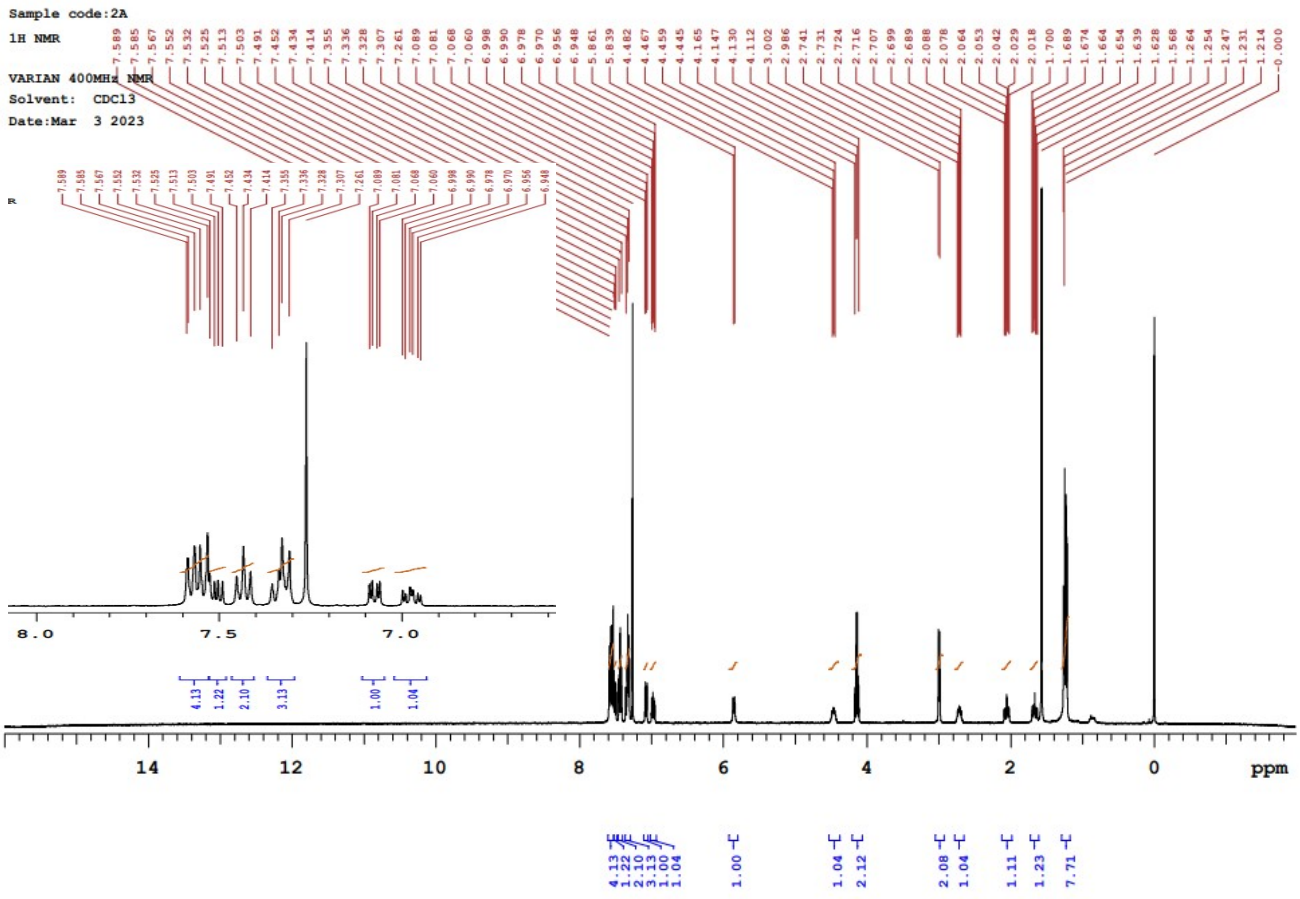


Figure S1: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5a.

^{13}C NMR Spectrum of compound 5a

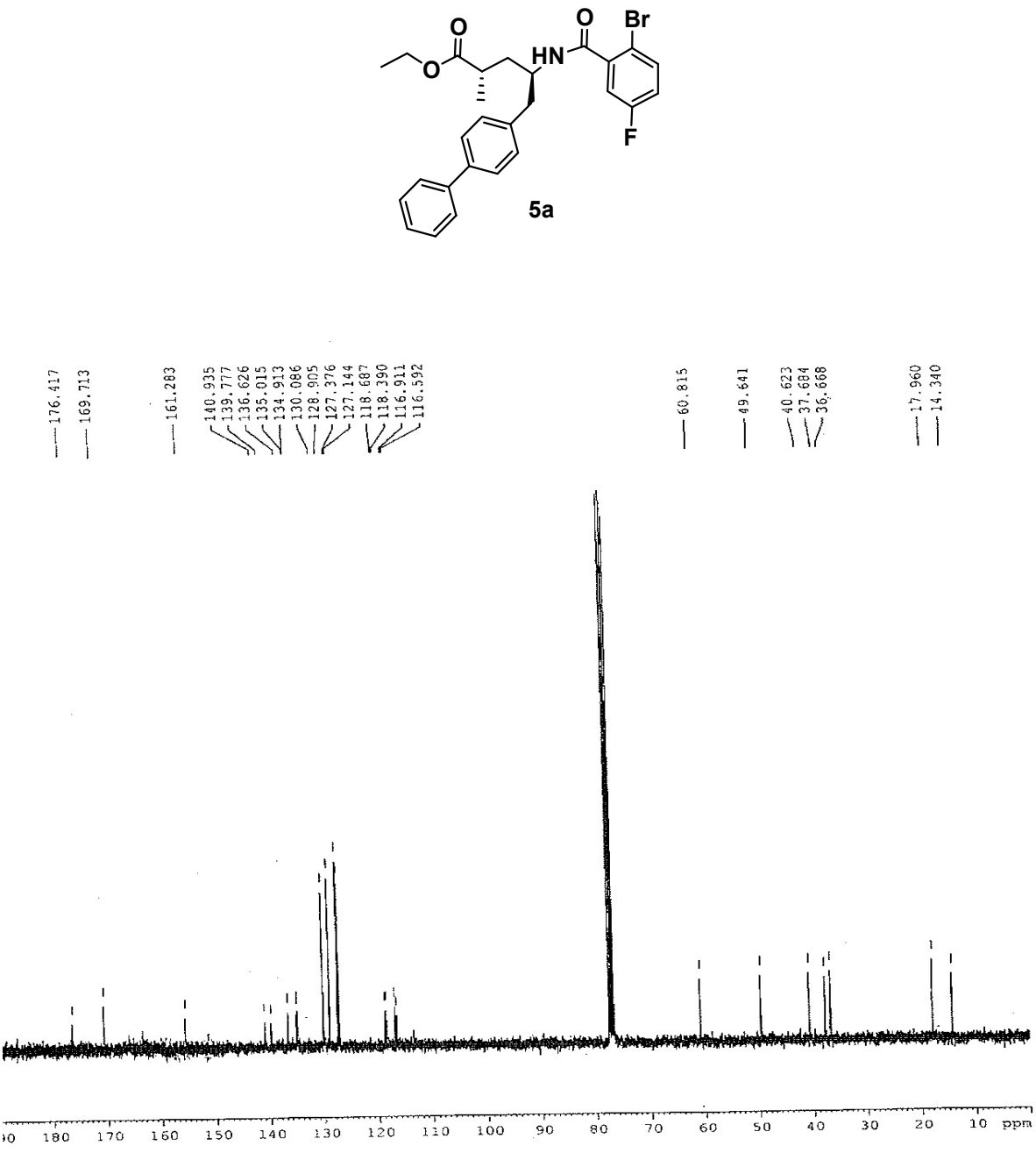
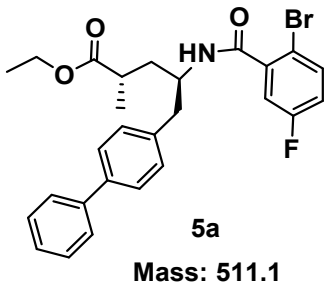


Figure S2: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of compound, 5a.

Mass spectrum of compound 5a



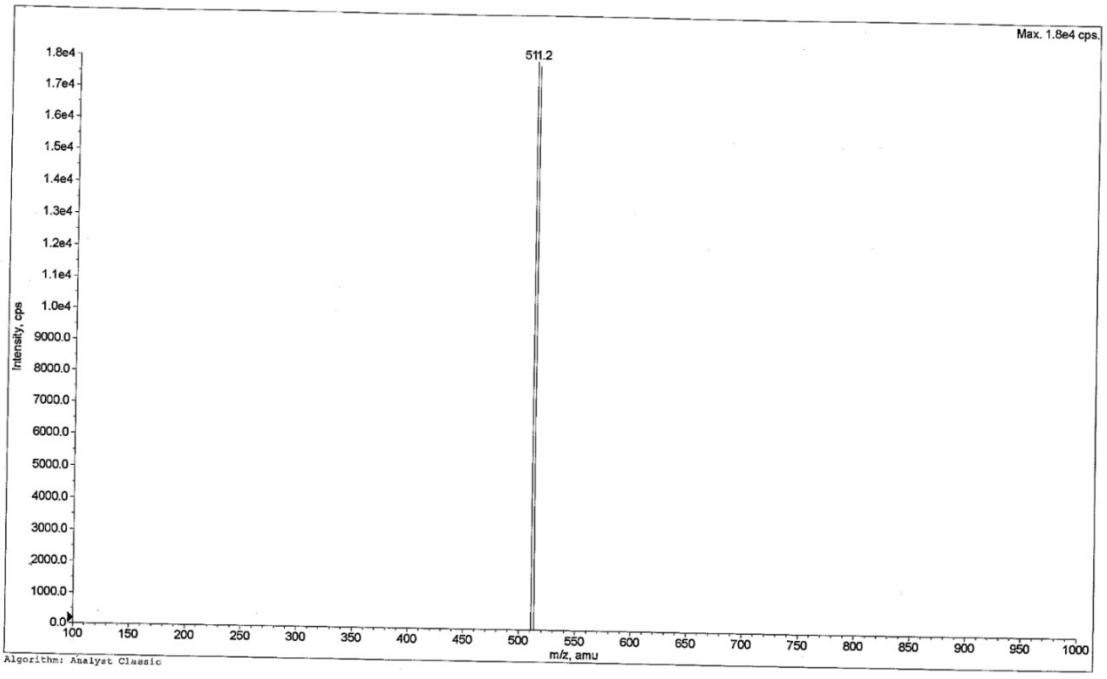
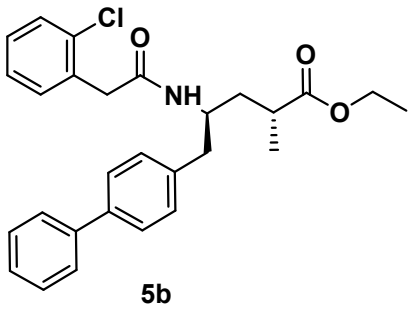


Figure S3: ESI Mass (M+H) spectrum of compound, 5a.

^{1}H NMR Spectrum of compound 5b



5b

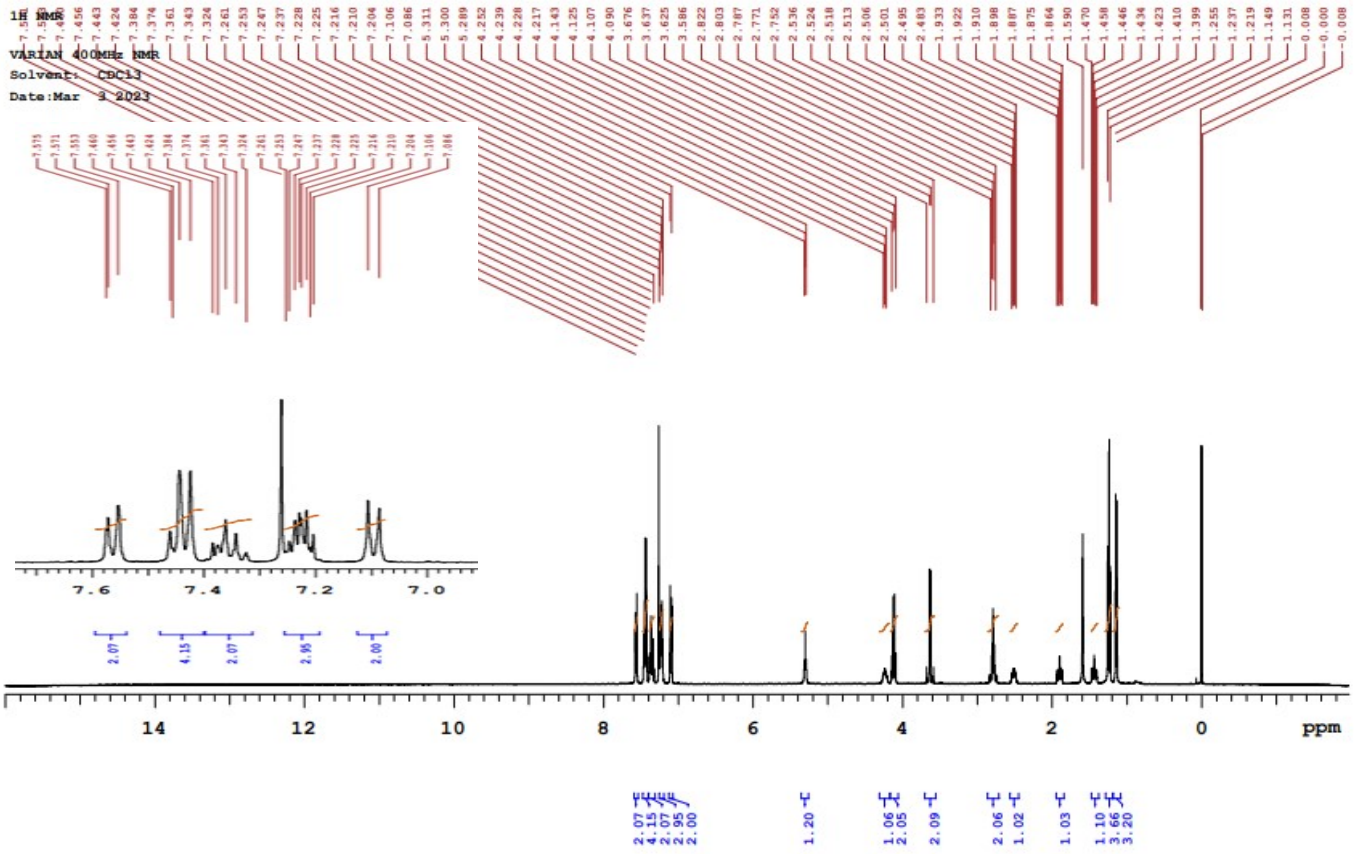
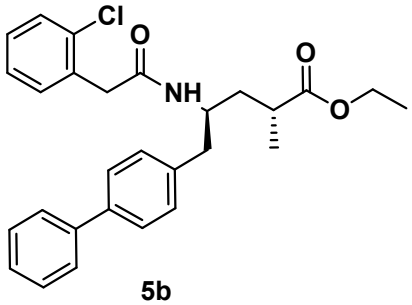


Figure S4: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5b.

^{13}C NMR Spectrum of compound 5b



5b

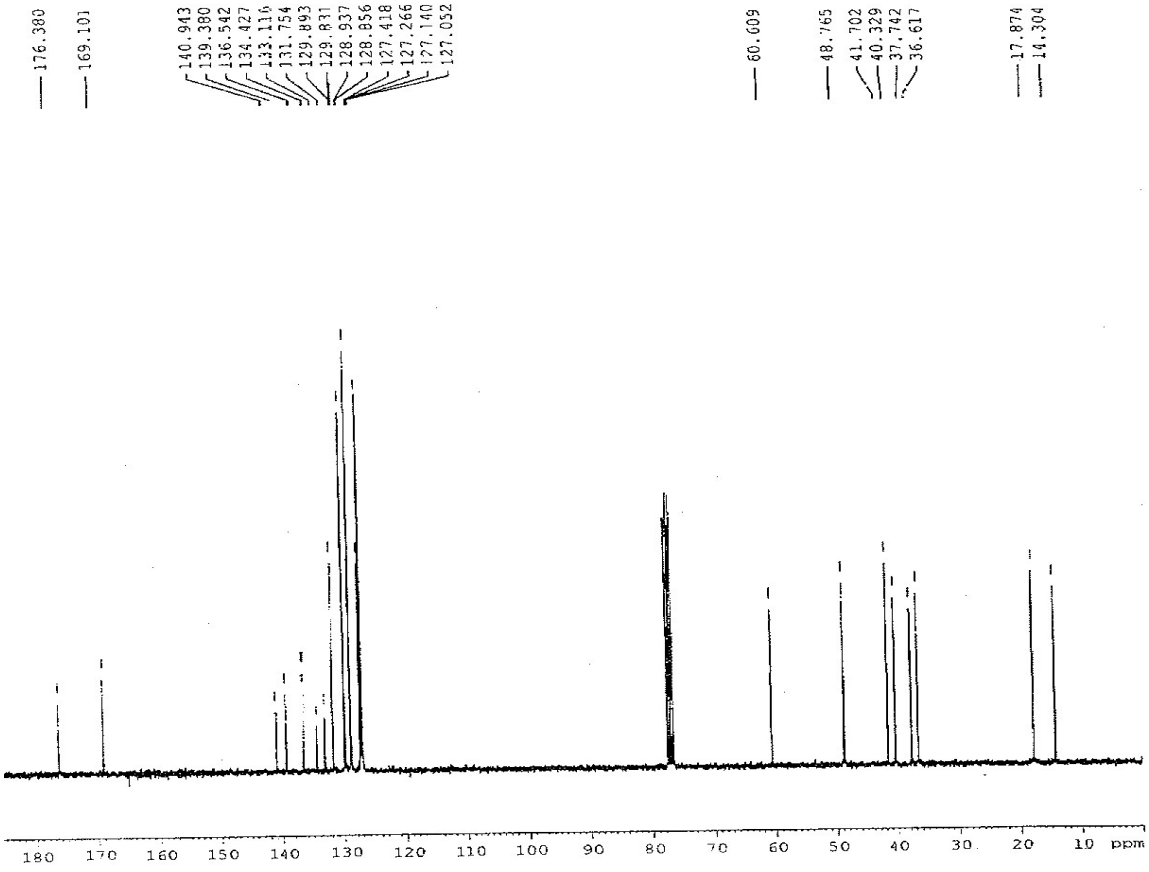
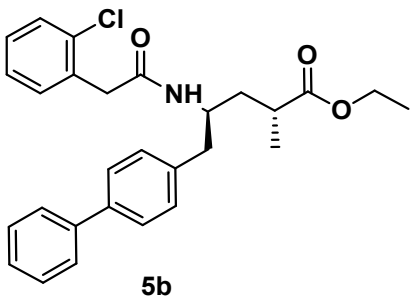


Figure S5: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5b.

Mass spectrum of compound 5b



5b

Mass: 463.1

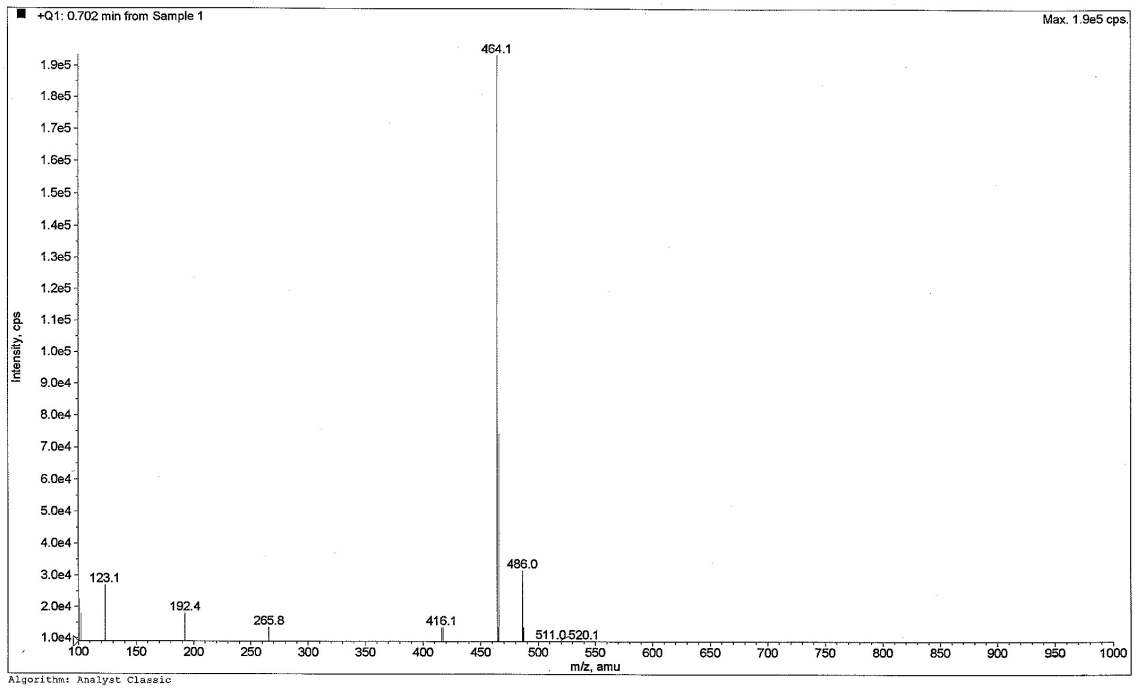
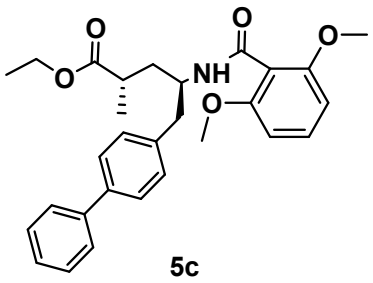


Figure S6: ESI Mass (M+H$^+$) spectrum of compound, 5b.

^{1}H NMR Spectrum of compound 5c



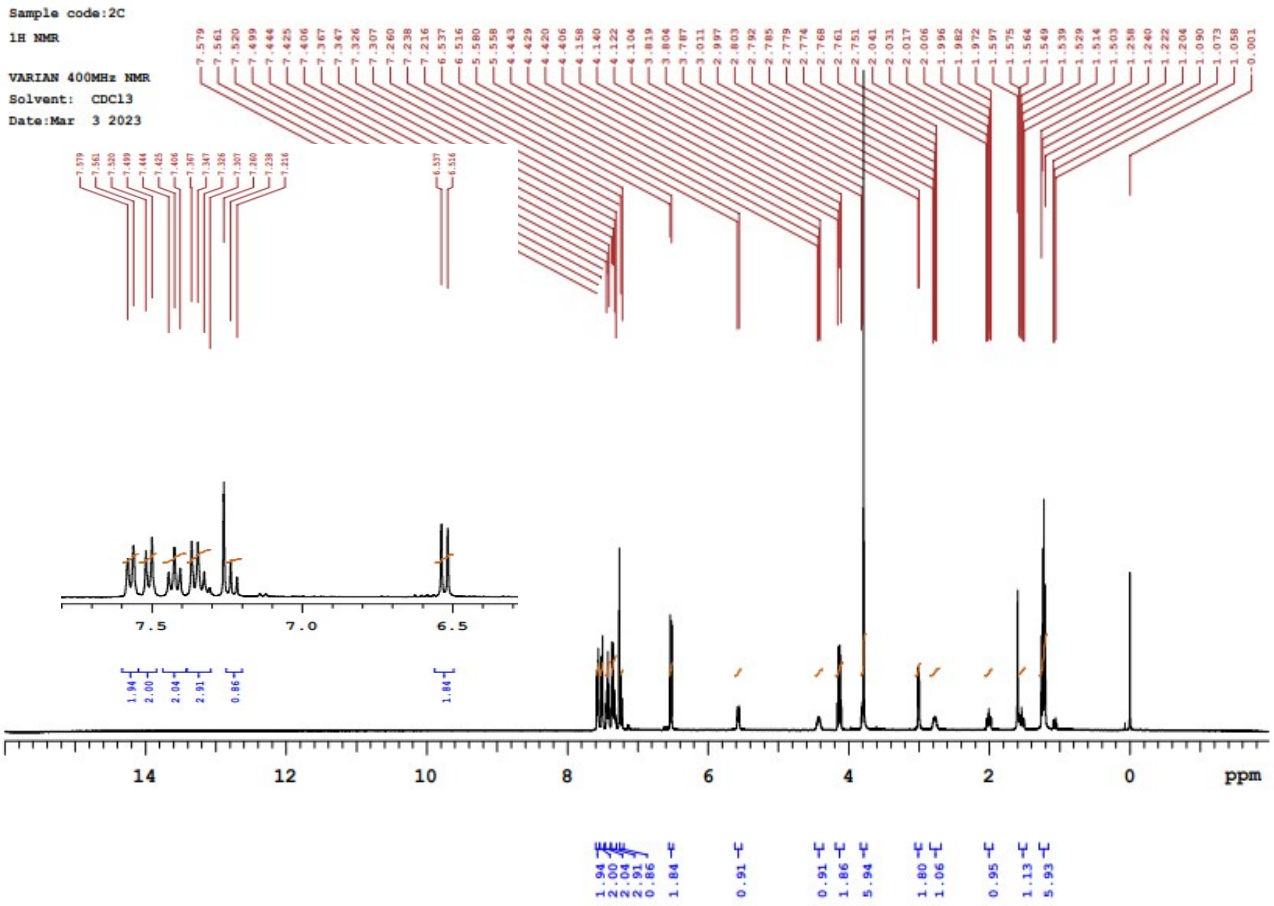
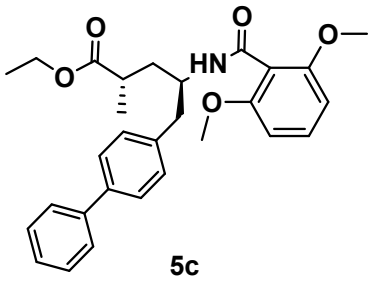


Figure S7: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5c.

^{13}C NMR Spectrum of compound 5c



5c

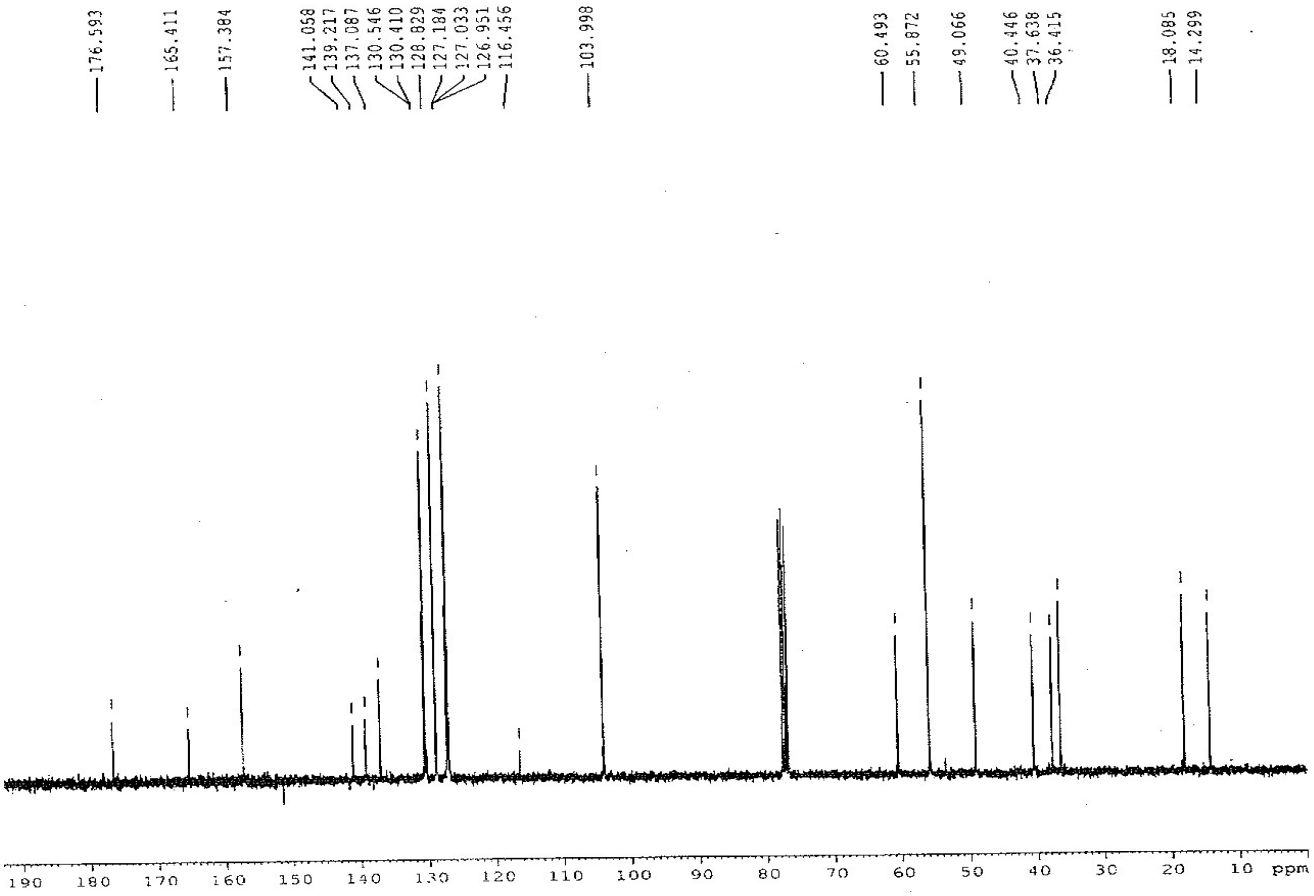
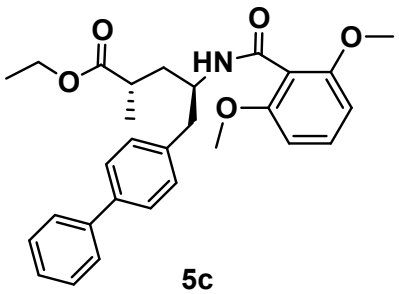


Figure S8: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5c.

Mass spectrum of compound 5c



5c

Mass: 475.2

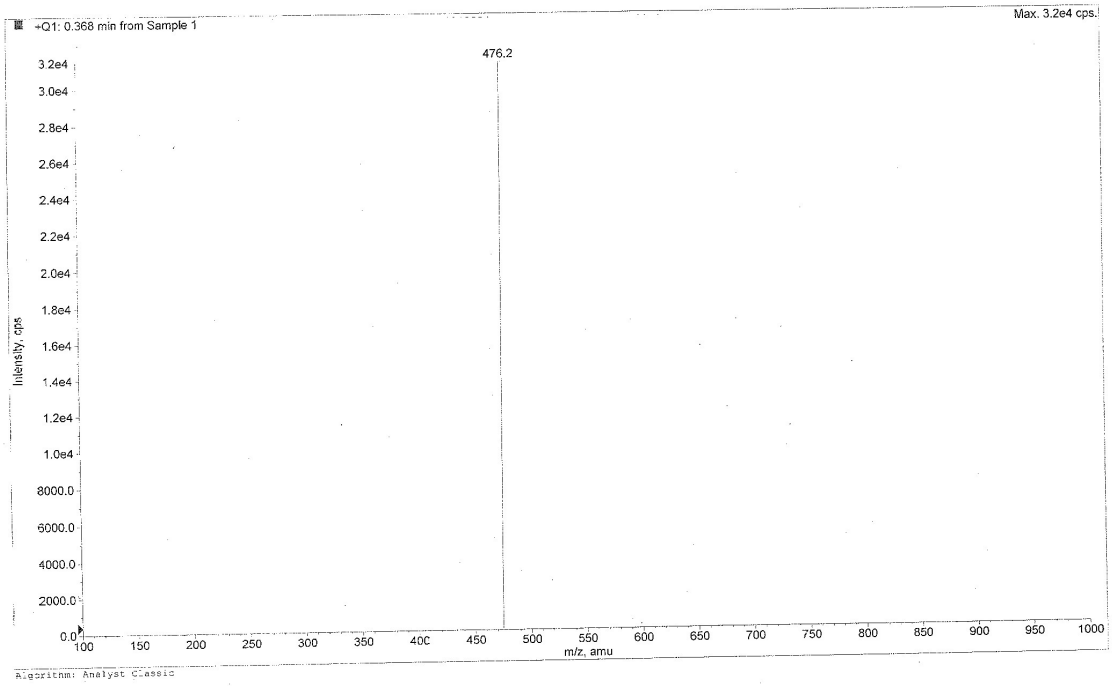


Figure S9: ESI Mass (M+H$^+$) spectrum of compound, 5c.

^{1}H NMR Spectrum of compound 5d

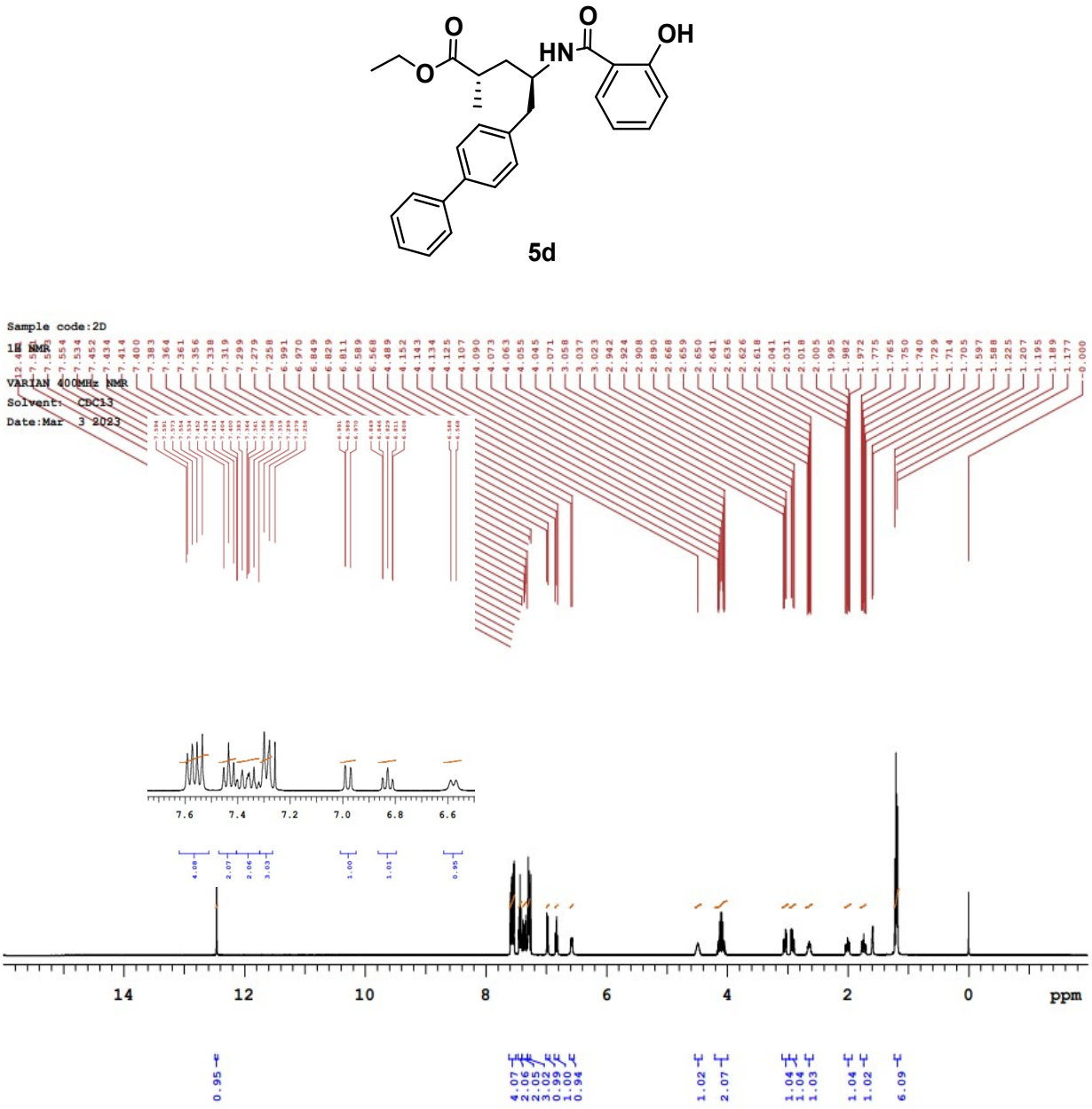
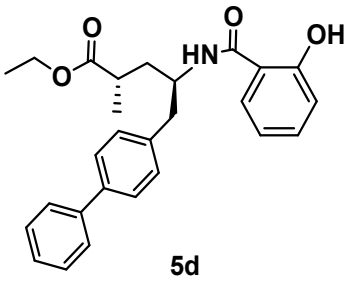


Figure S10: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5d.

^{13}C NMR Spectrum of compound 5d



5d

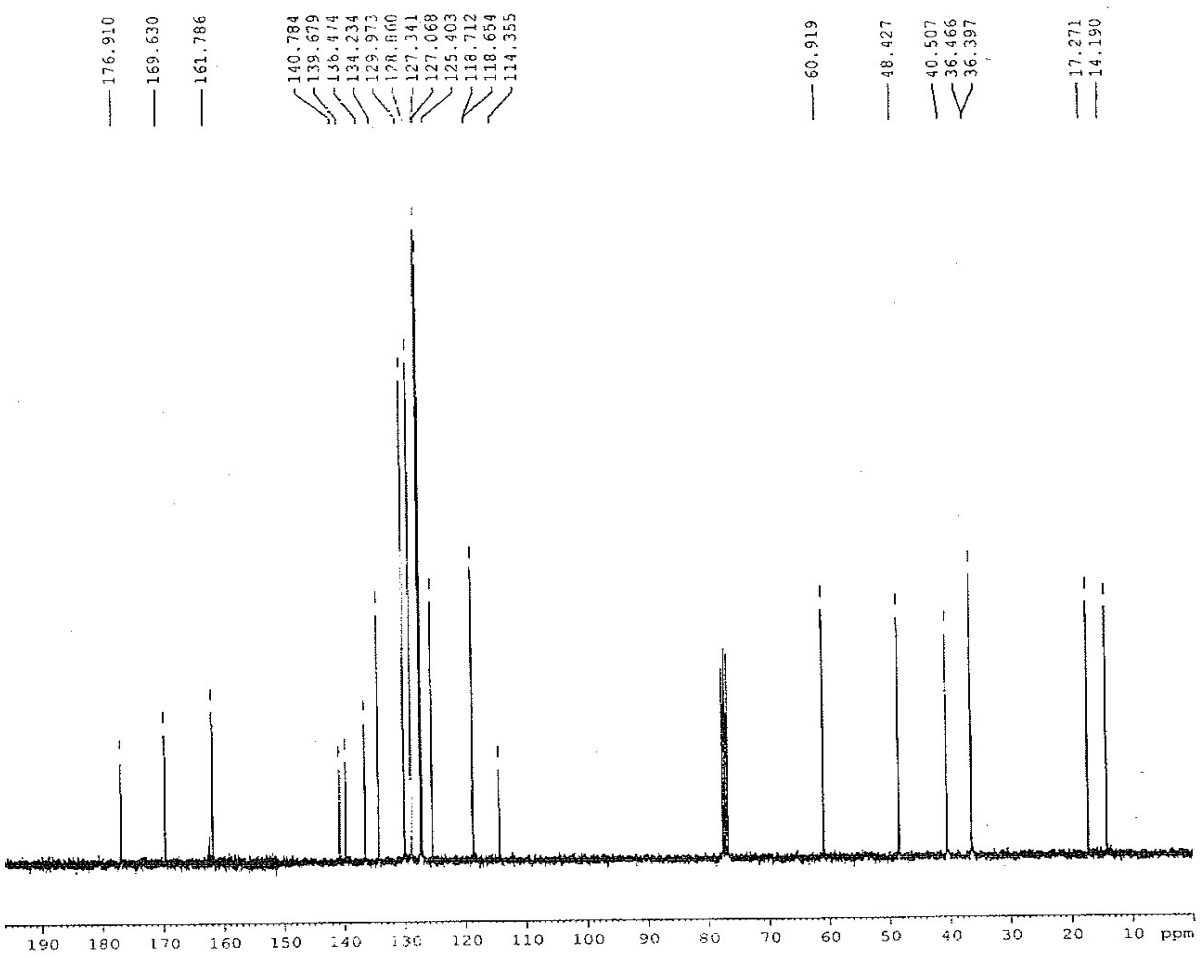
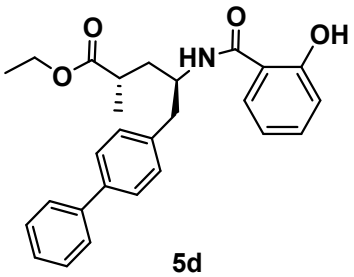


Figure S11: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5d.

Mass spectrum of compound 5d



5d

Mass: 431.2

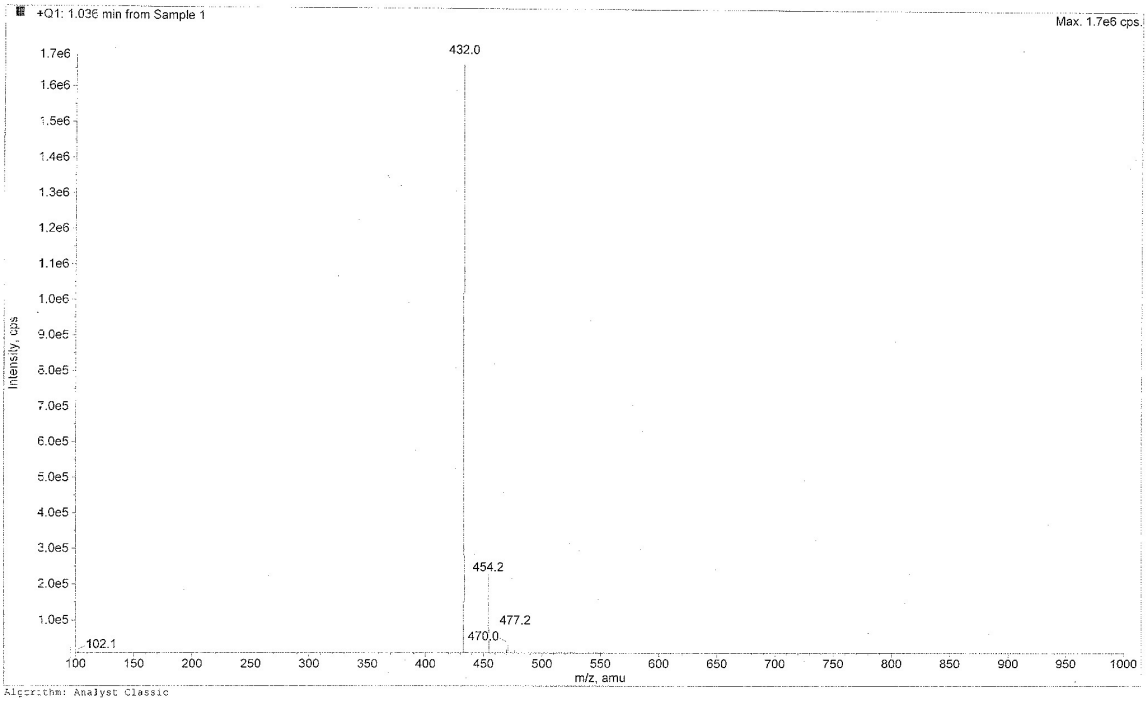
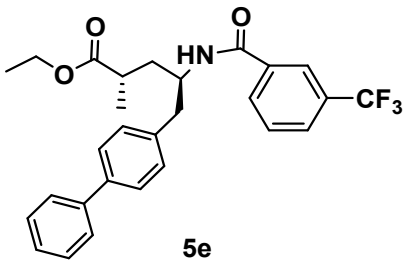


Figure S12: ESI Mass (M+H^+) spectrum of compound, 5d.

^{1}H NMR Spectrum of compound 5e



5e

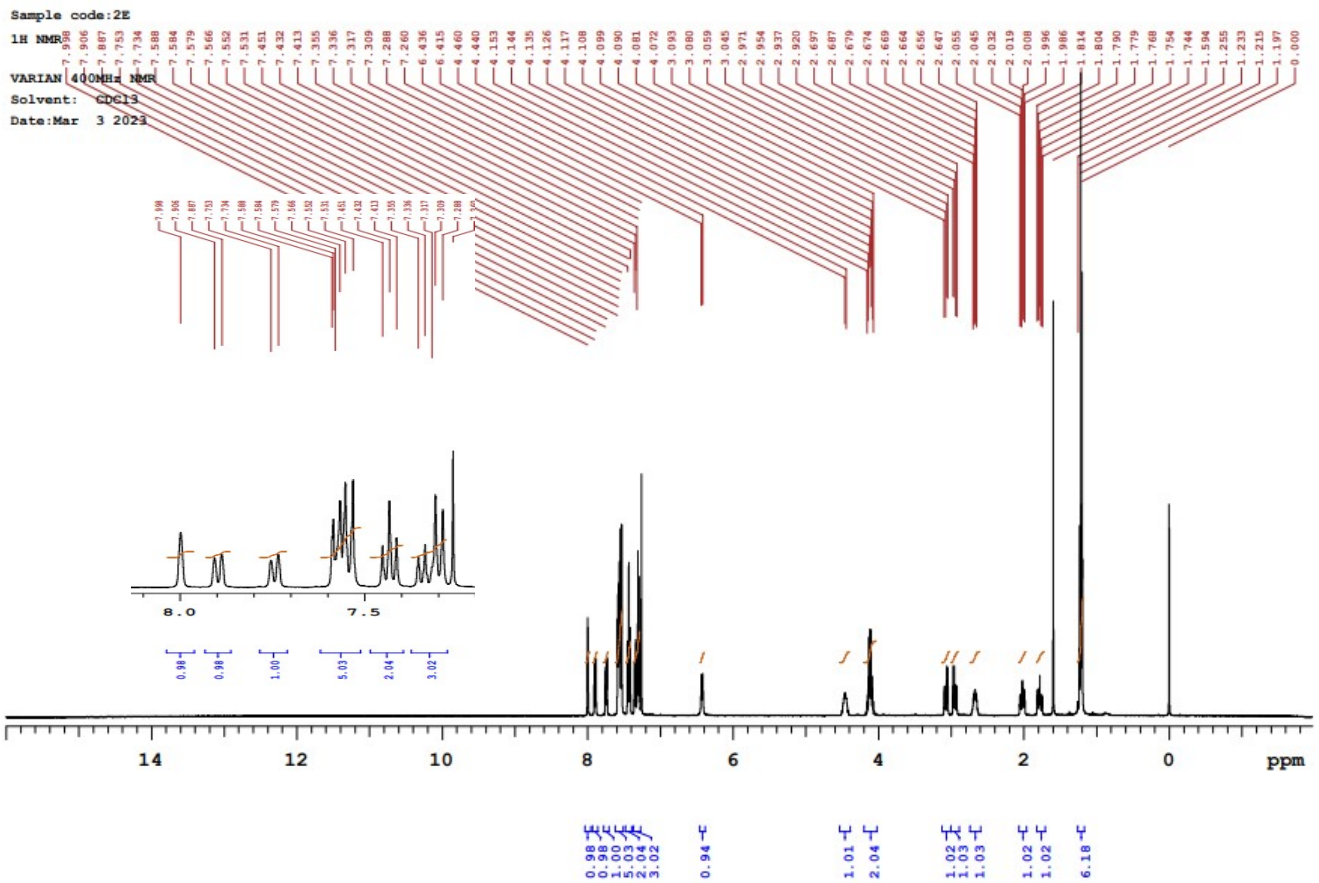
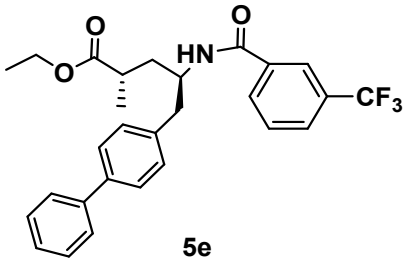


Figure S13: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5e.

^{13}C NMR Spectrum of compound 5e



5e

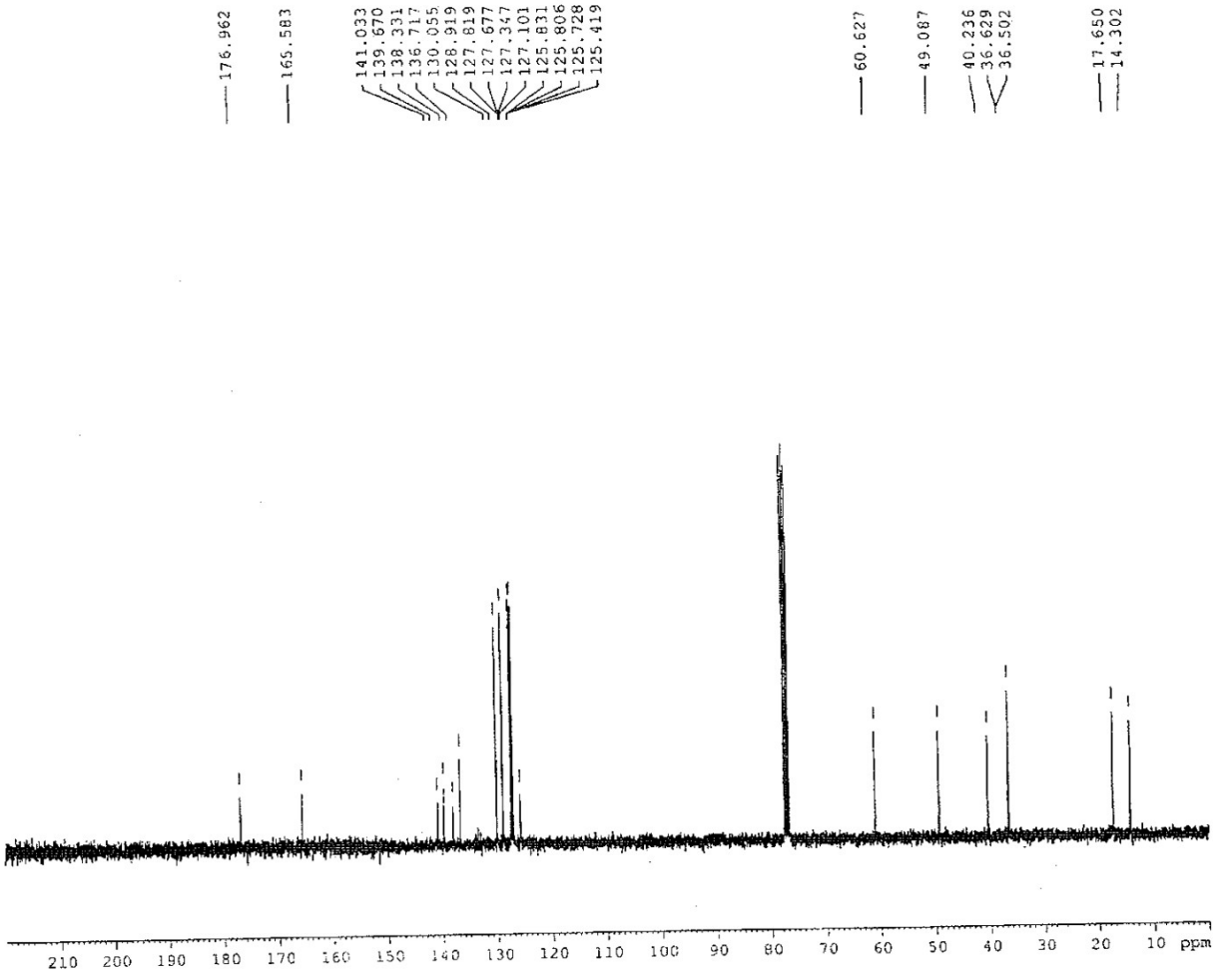
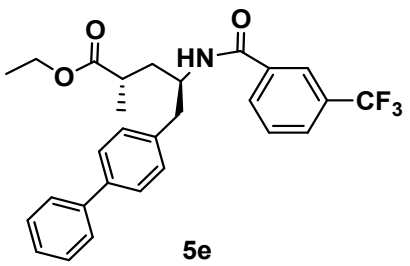


Figure S14: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5e.

Mass spectrum of compound 5e



5e

Mass: 483.2

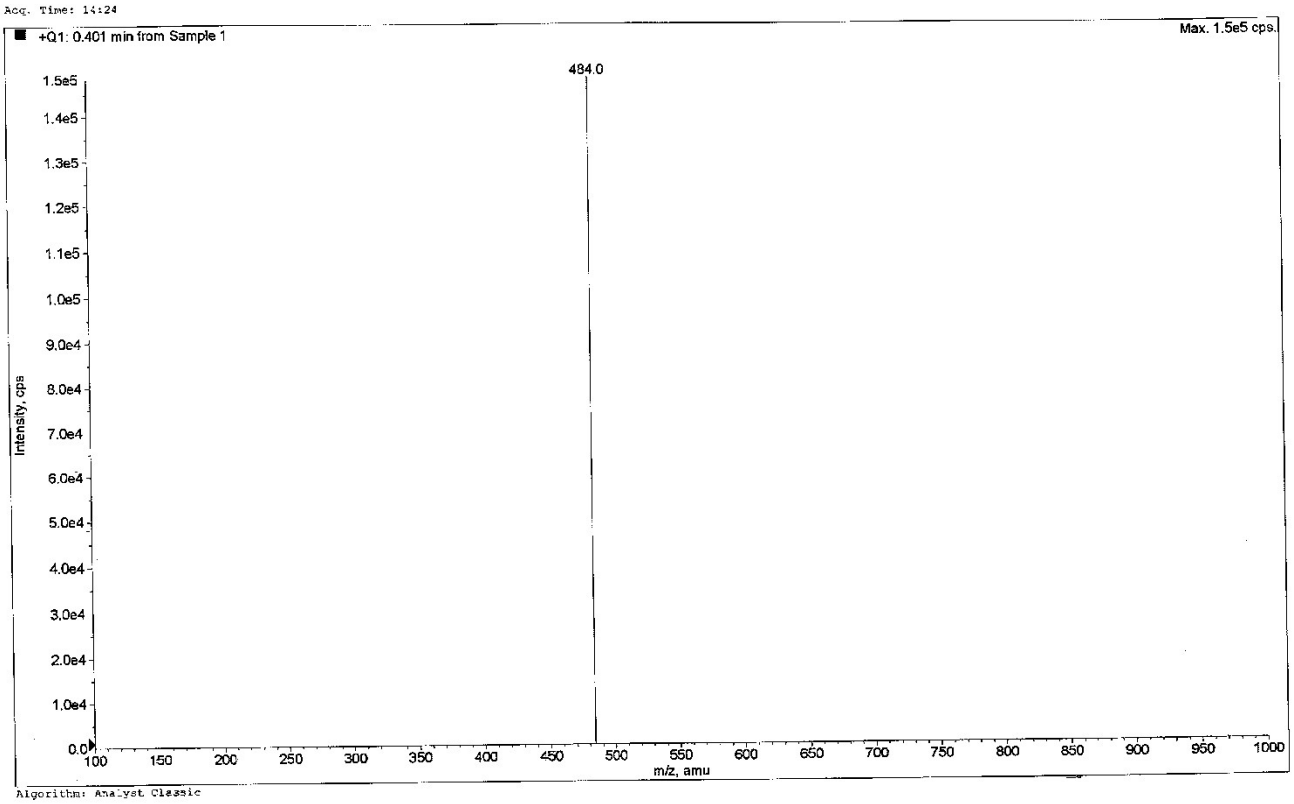
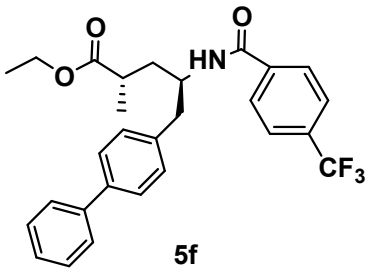


Figure S15: ESI Mass (M+H$^+$) spectrum of compound, 5e.

^{1}H NMR Spectrum of compound 5f



5f

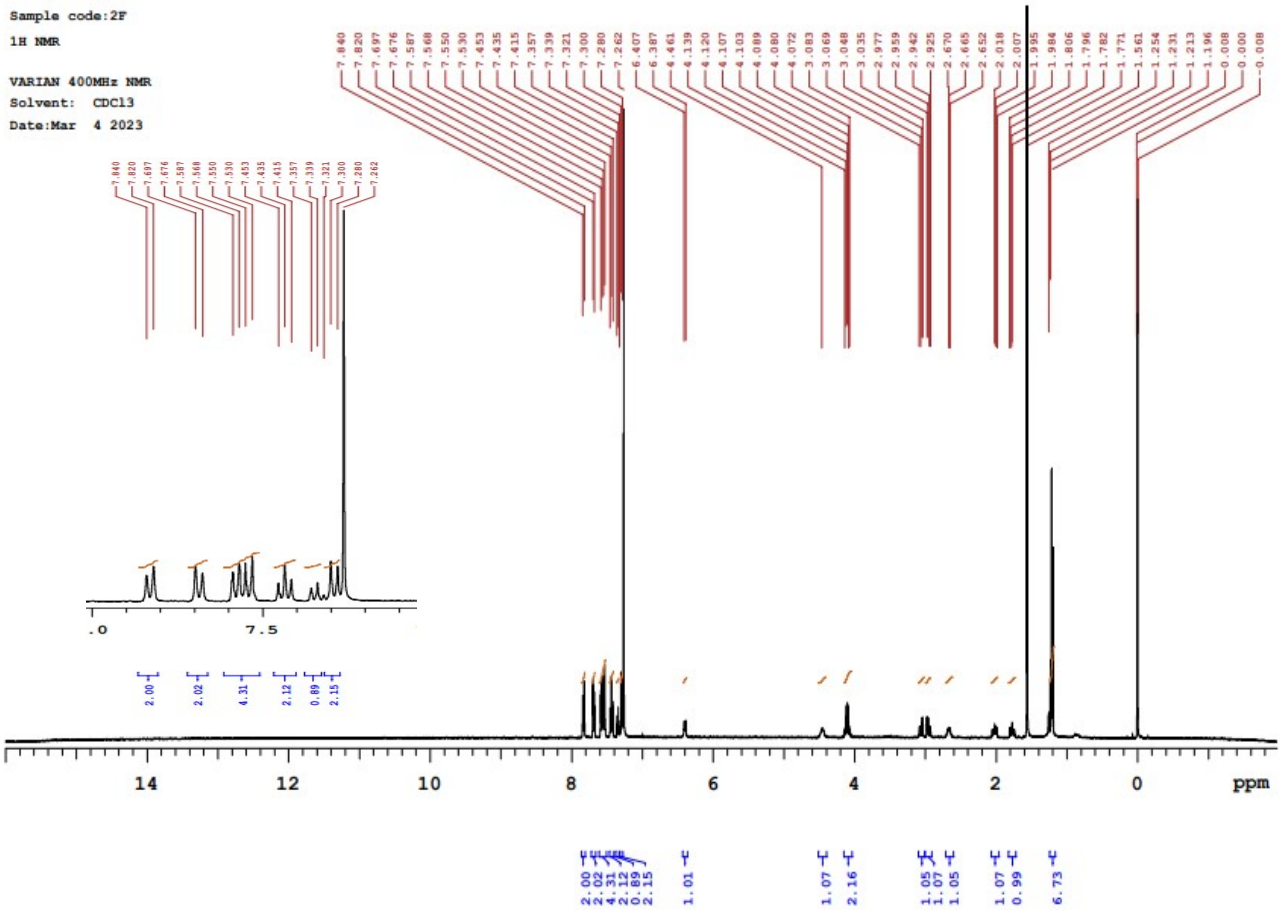
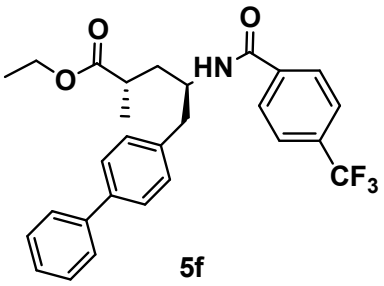


Figure S16: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5f.

^{13}C NMR Spectrum of compound 5f



5f

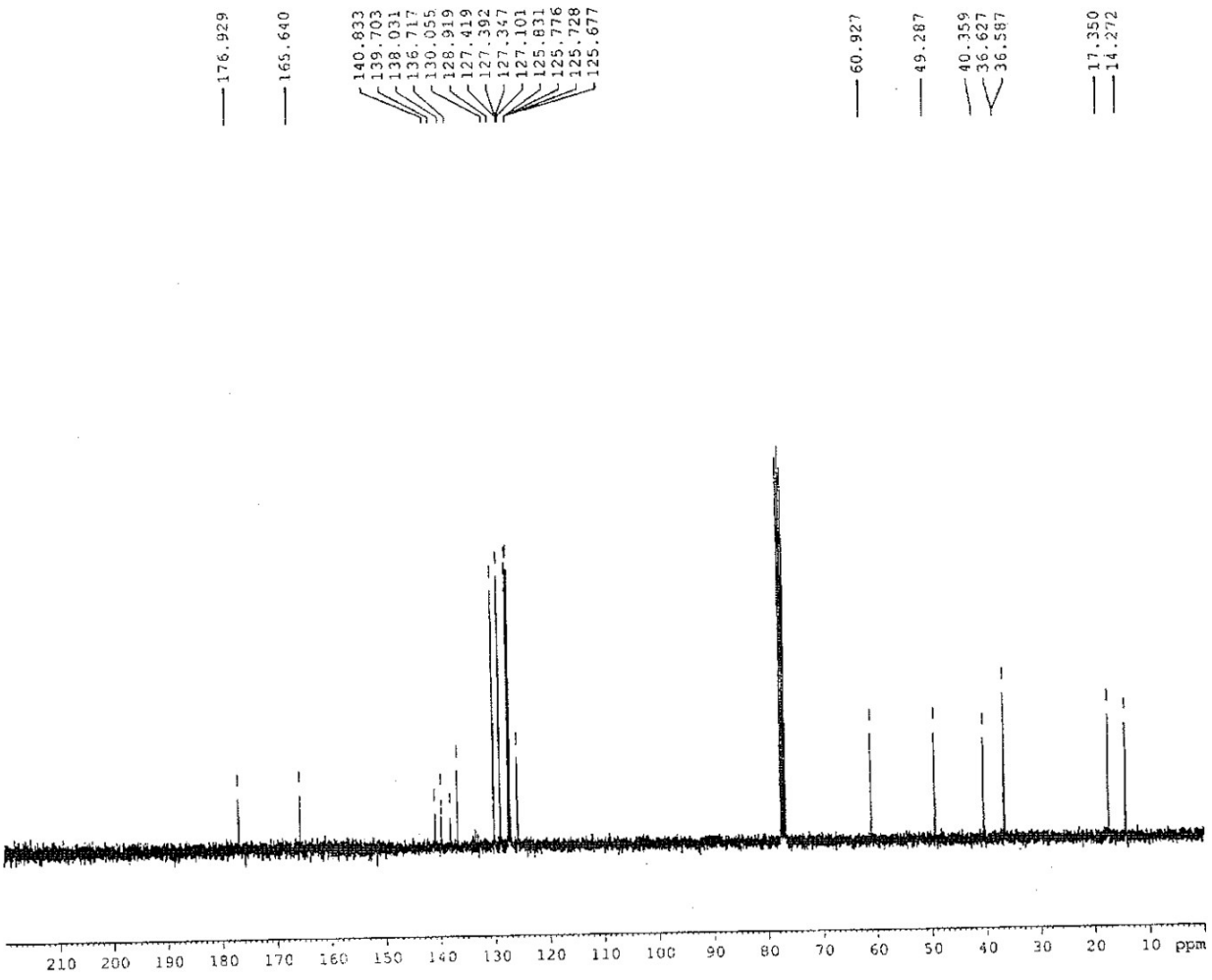
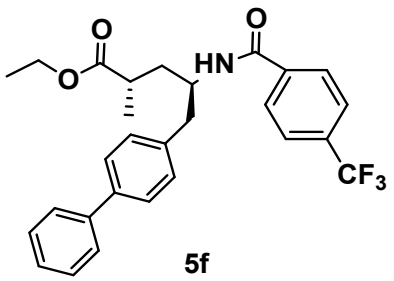


Figure S17: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5f.

Mass spectrum of compound 5f



5f

Mass: 483.2

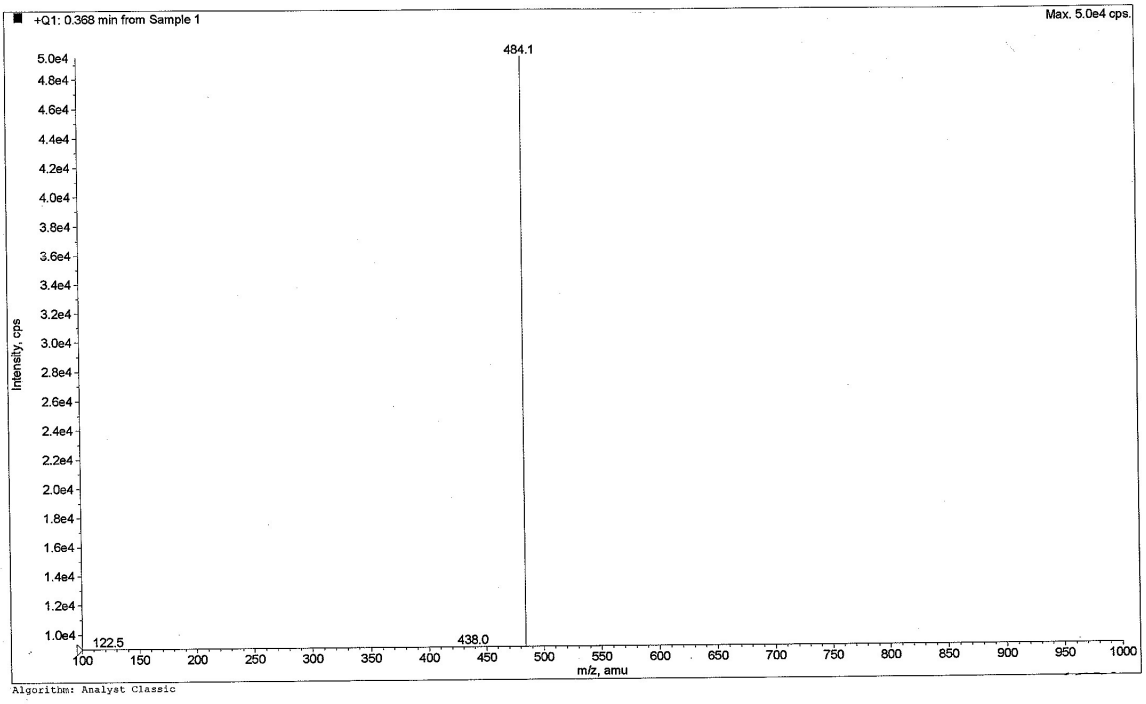
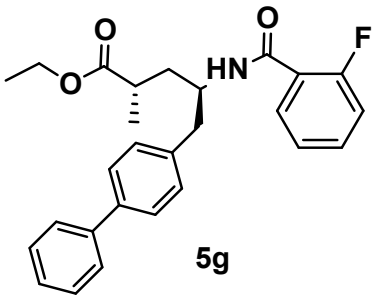


Figure S18: ESI Mass (M+H^+) spectrum of compound, 5f.

^{1}H NMR Spectrum of compound 5g



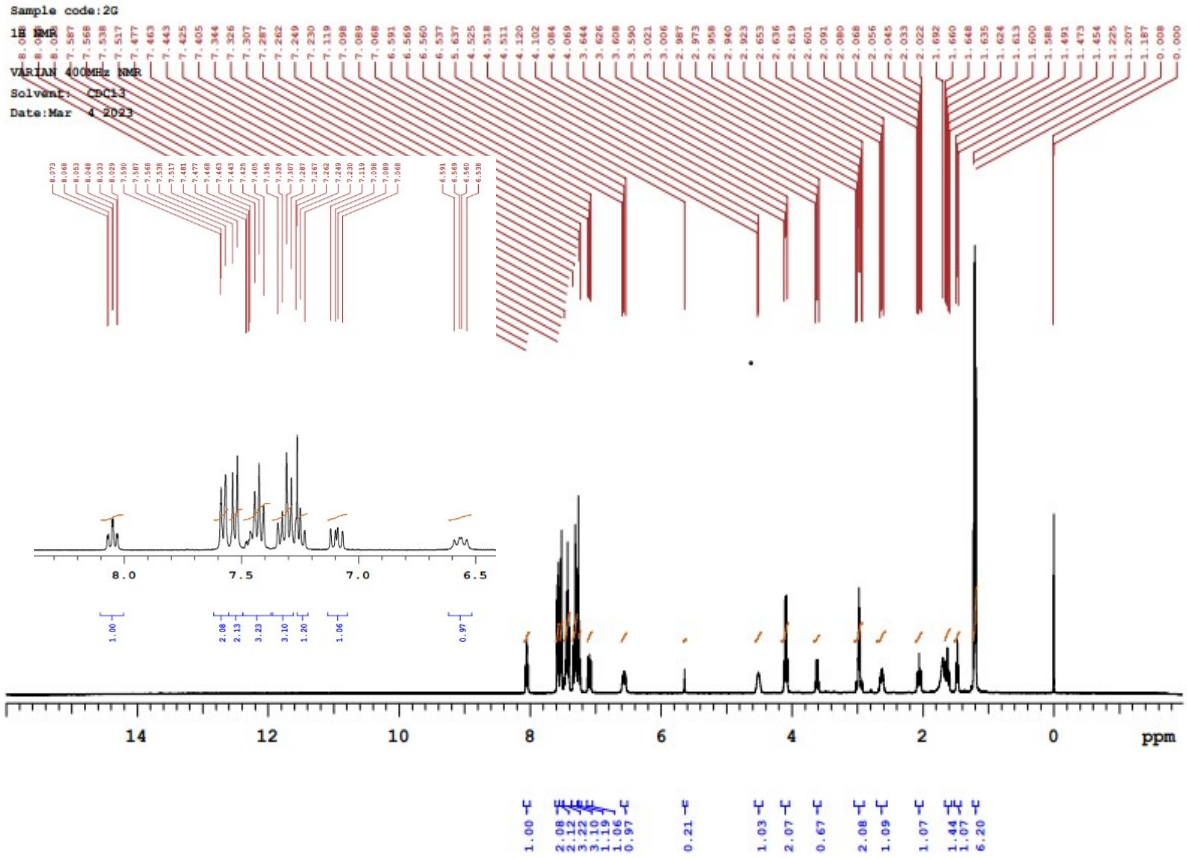
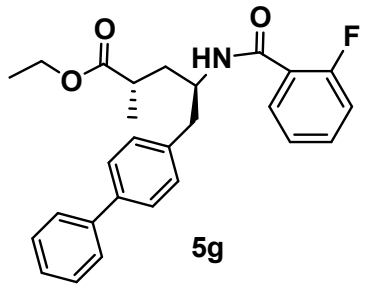


Figure S19: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5g.

^{13}C NMR Spectrum of compound 5g



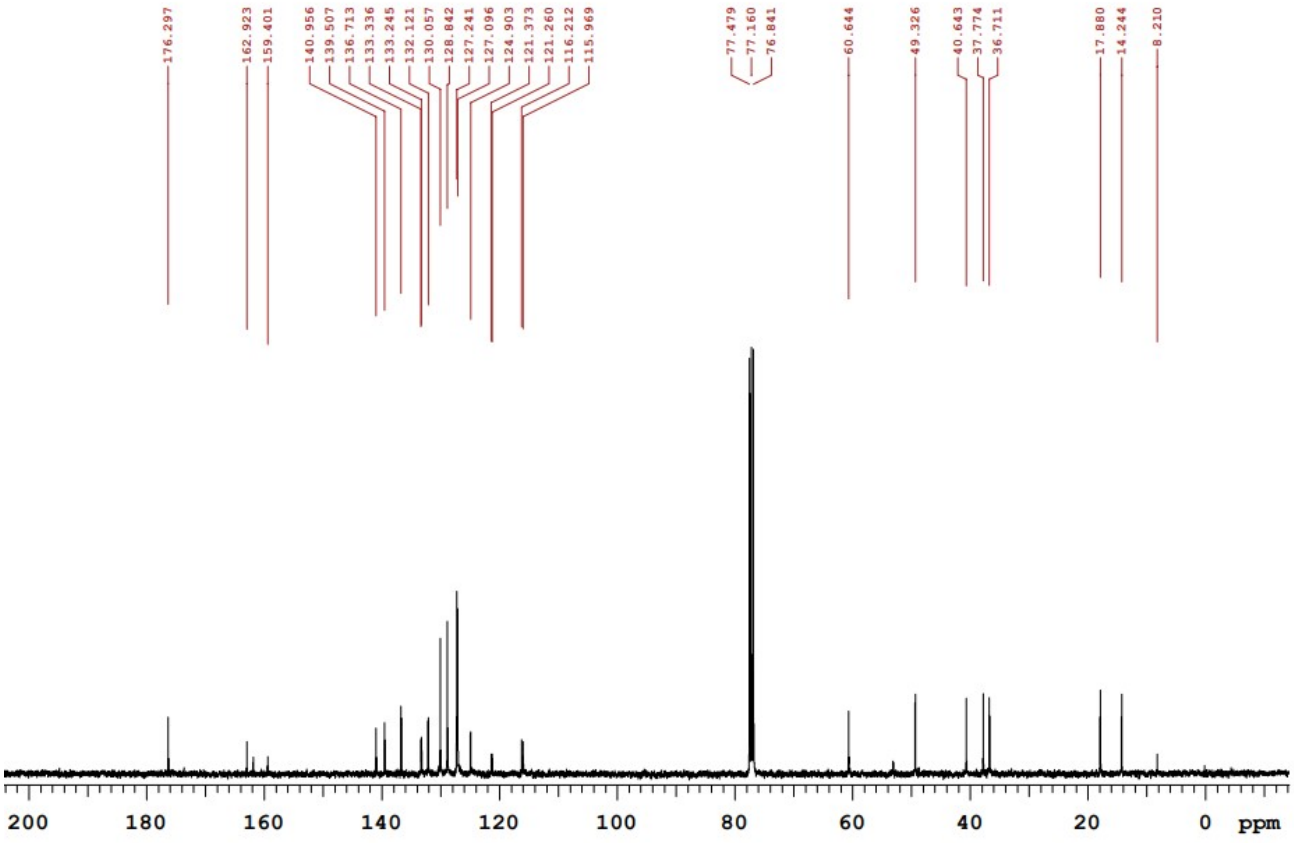
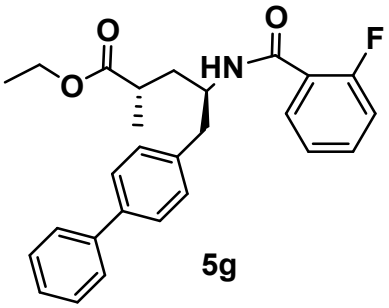


Figure S20: ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound, 5g.

Mass spectrum of compound 5g



5g

Mass: 433.2

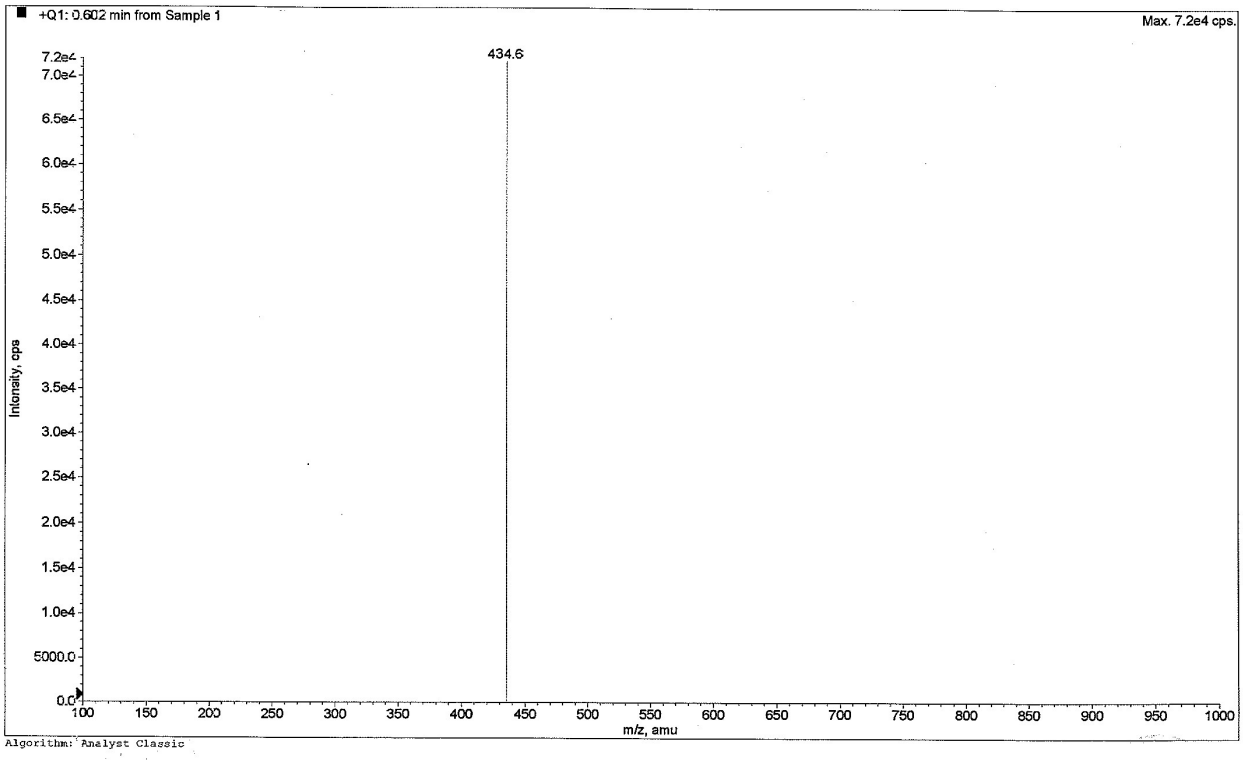


Figure S21: ESI Mass (M+H$^+$) spectrum of compound, 5g.

^{1}H NMR Spectrum of compound 5h

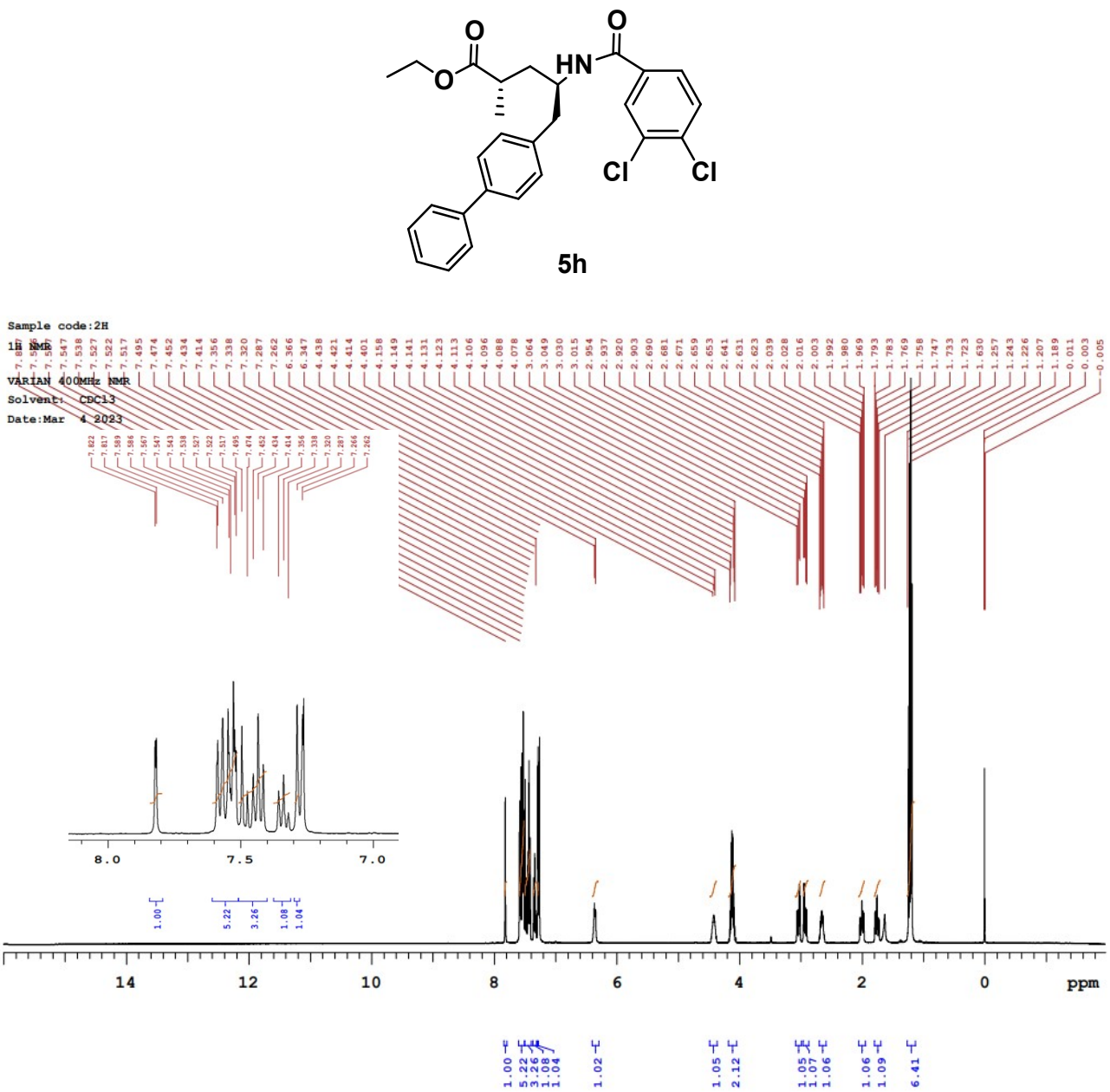
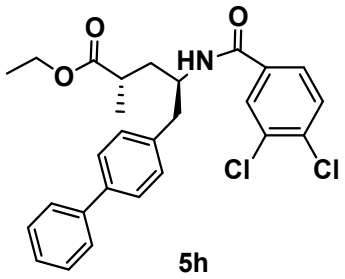


Figure S22: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5h.

^{13}C NMR Spectrum of compound 5h



5h

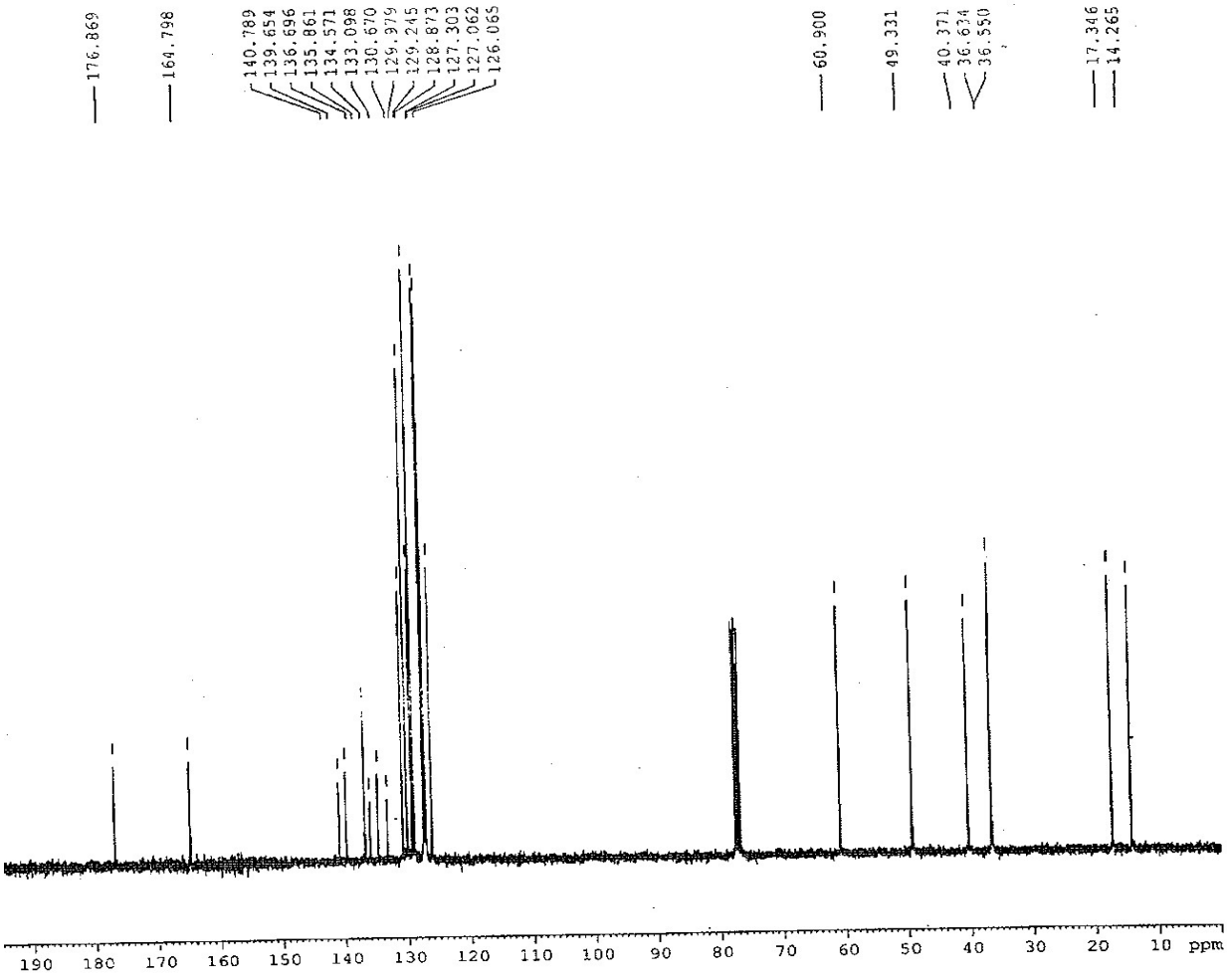
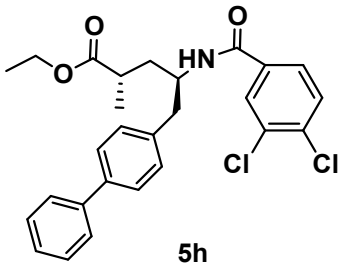


Figure S23: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5h.

Mass spectrum of compound 5h



5h

Mass: 483.1

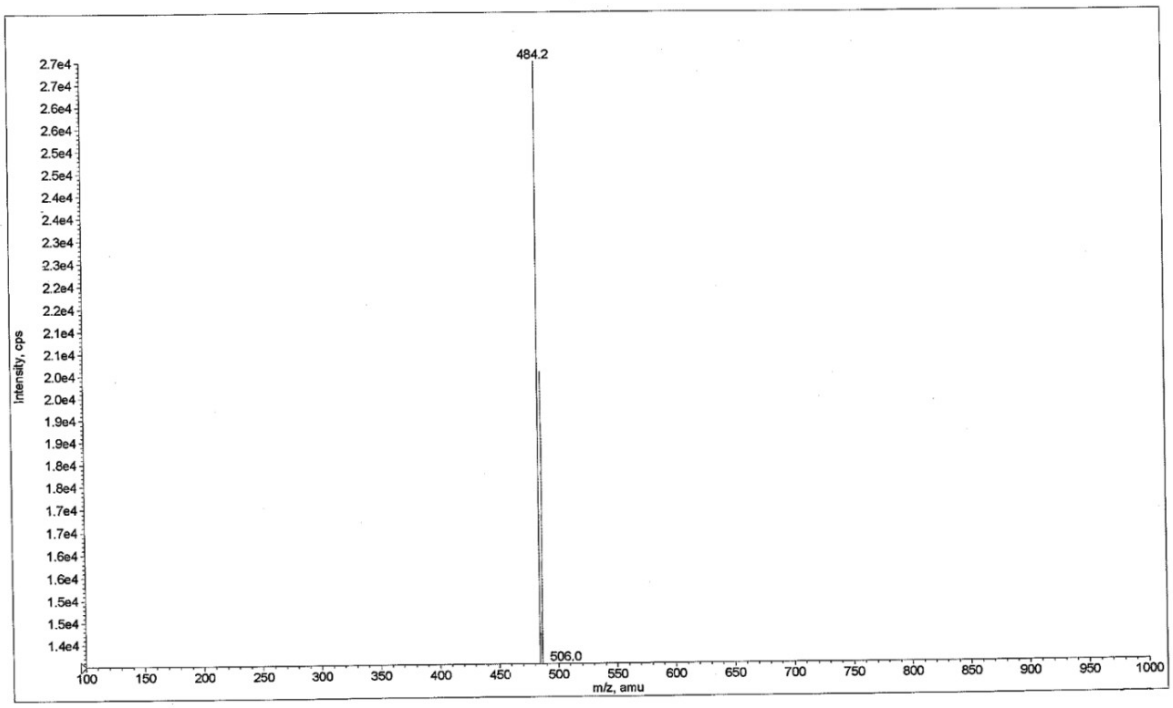
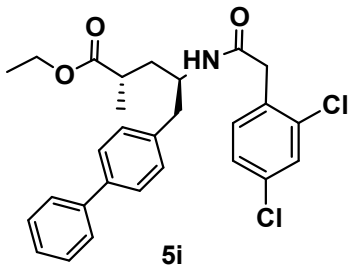


Figure S24: ESI Mass (M+H^+) spectrum of compound, 5h.

^{1}H NMR Spectrum of compound 5i



5i

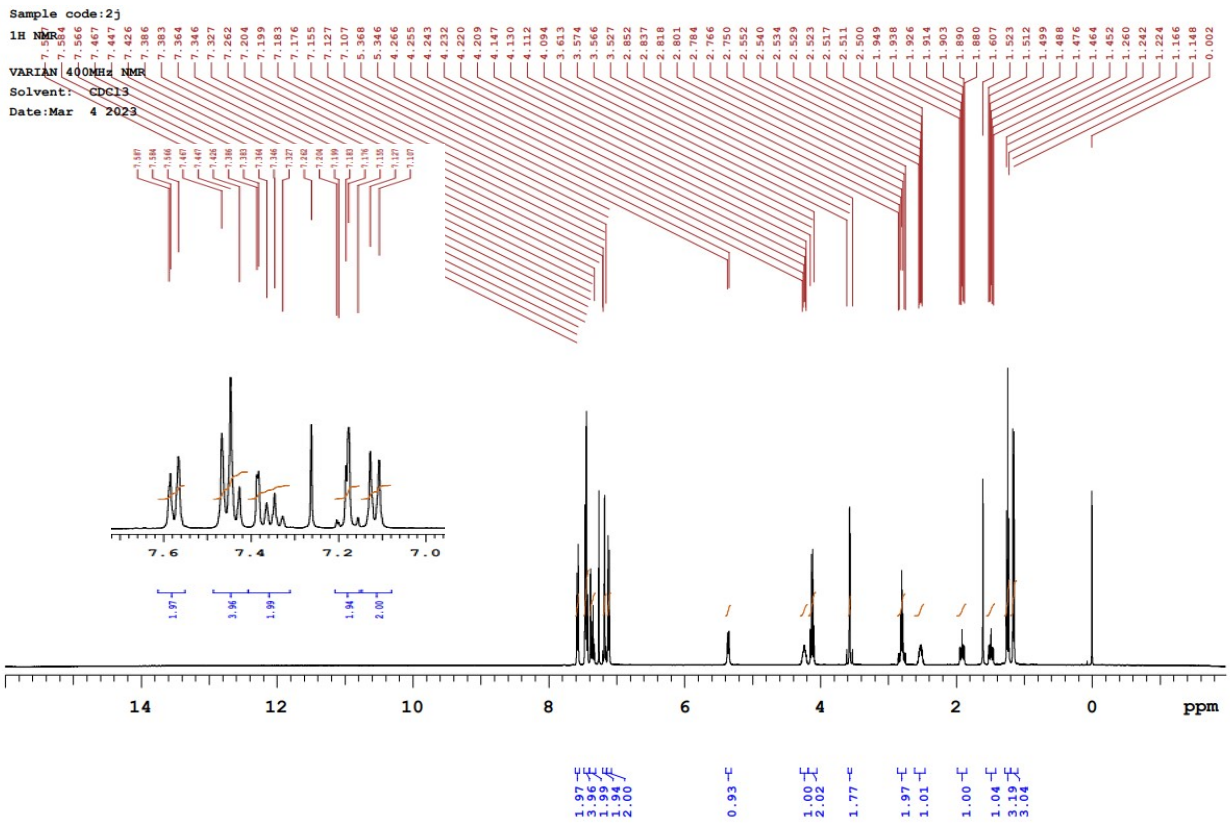
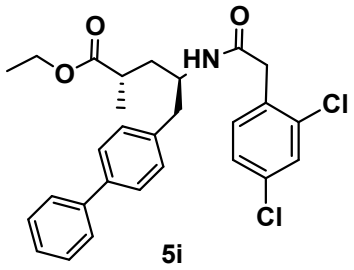


Figure S25: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5i.

^{13}C NMR Spectrum of compound 5i



5i

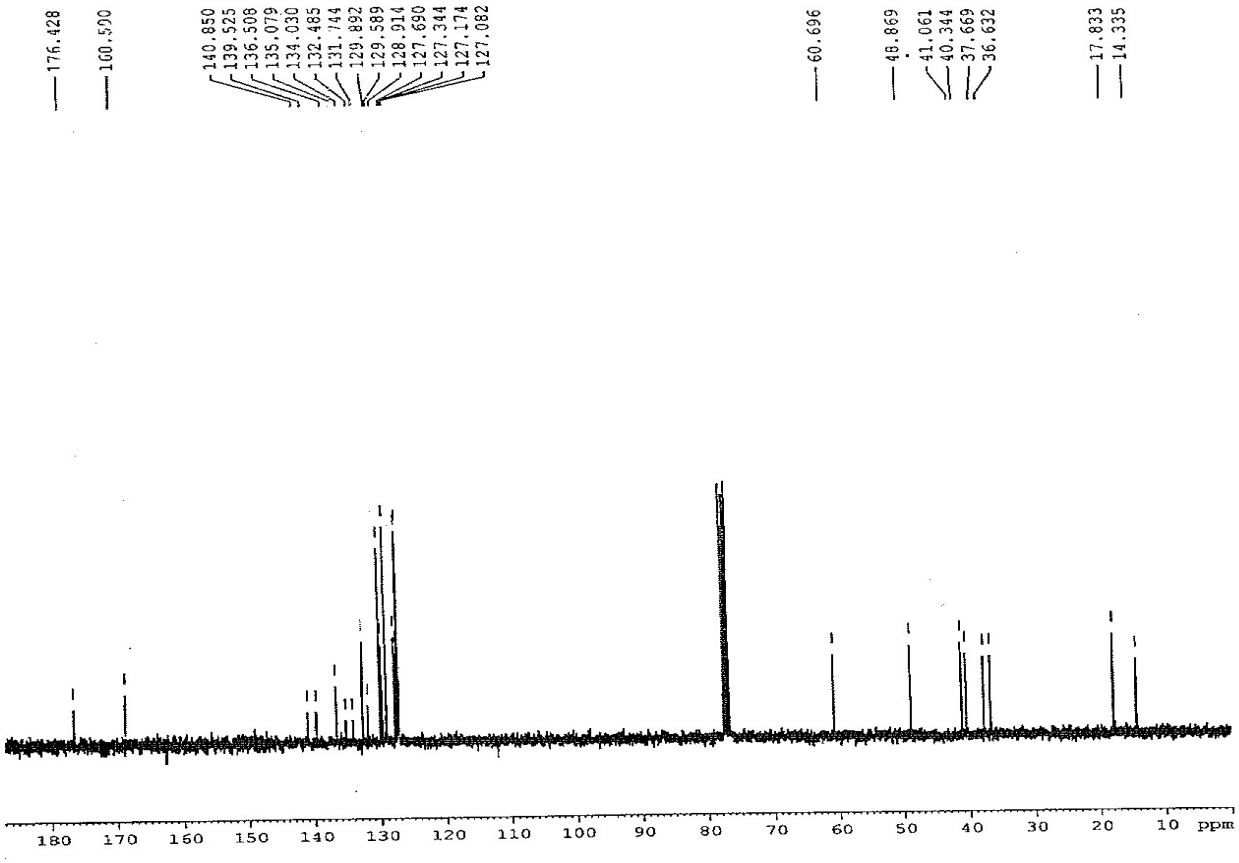
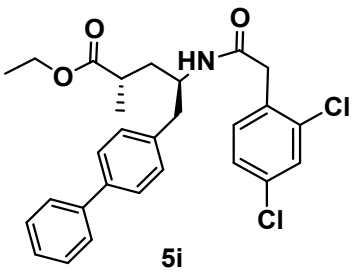


Figure S26: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5i.

Mass spectrum of compound 5i



5i

Mass: 497.1

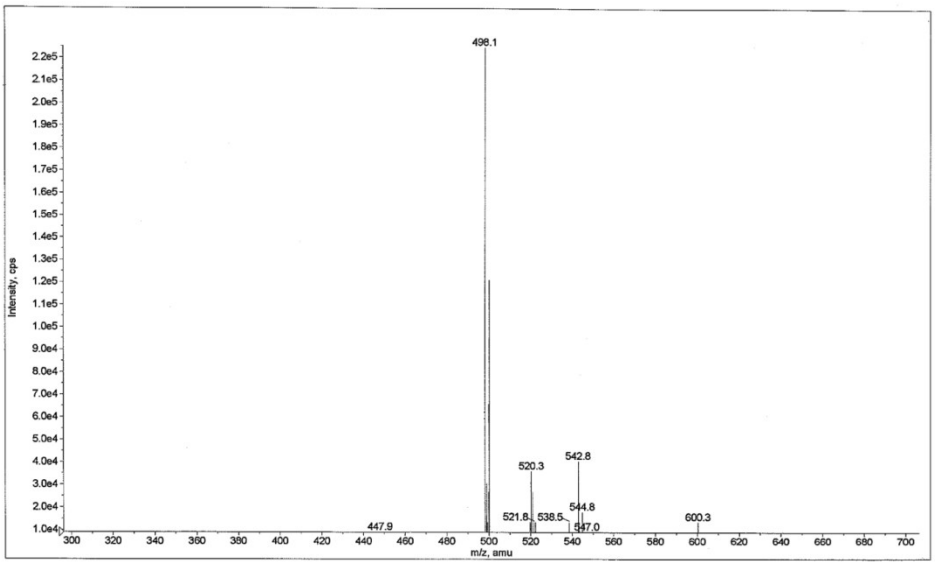
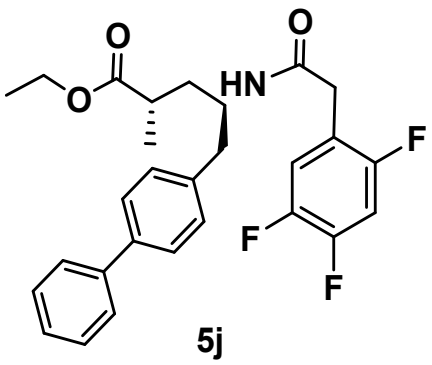


Figure S27: ESI Mass (M+H^+) spectrum of compound, 5i.

^{1}H NMR Spectrum of compound 5j



5j

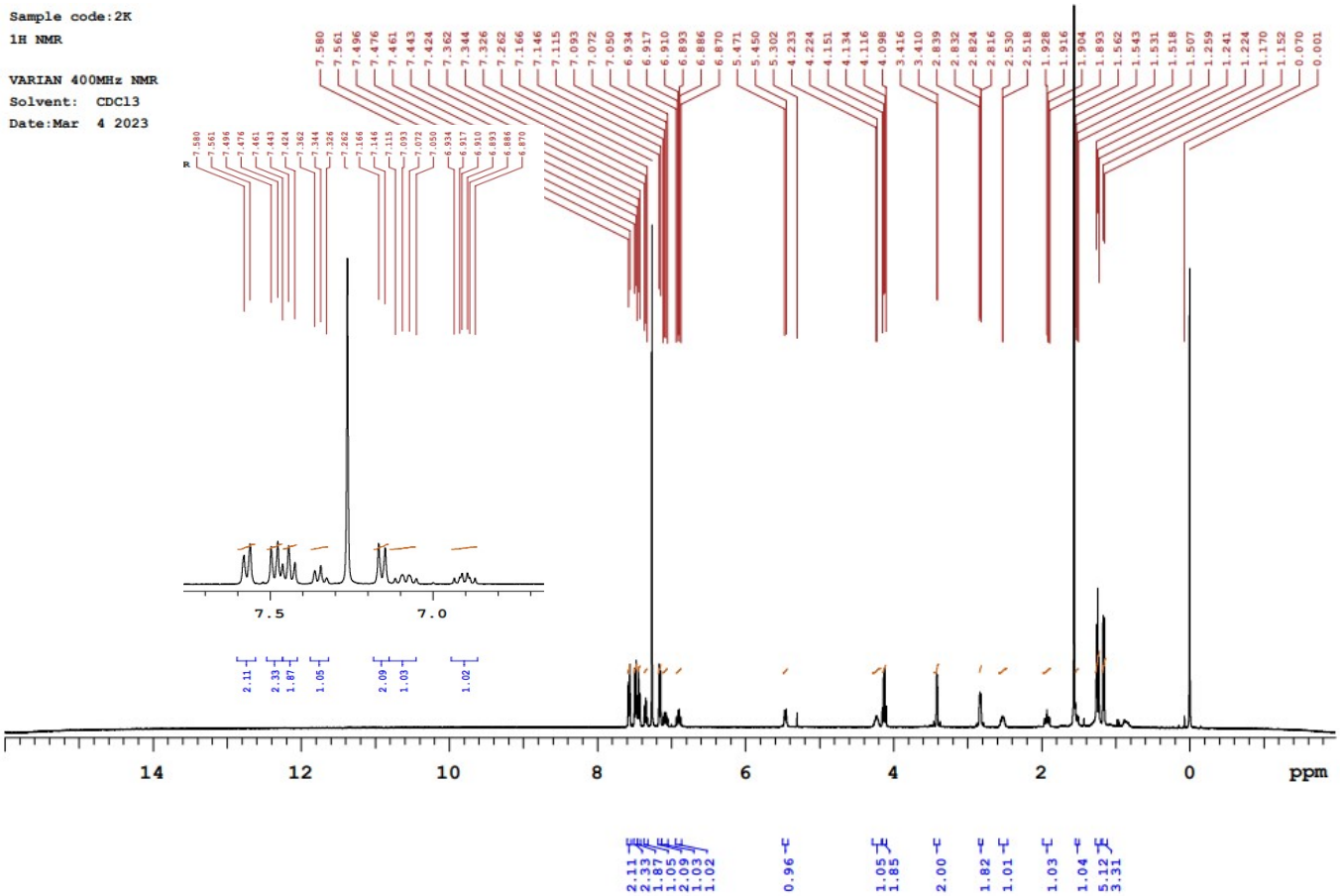


Figure S28: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5j.

^{13}C NMR Spectrum of compound 5j

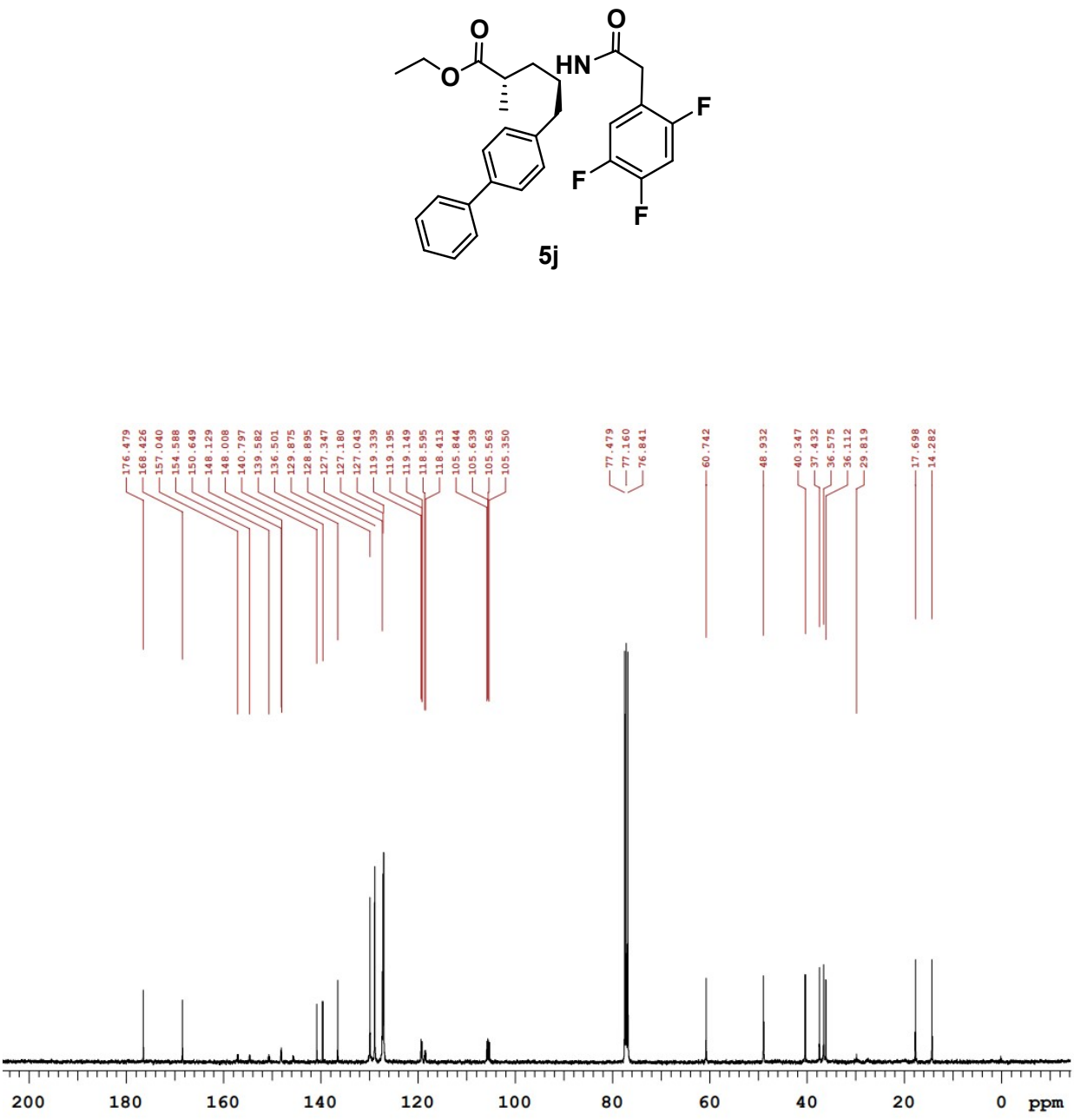
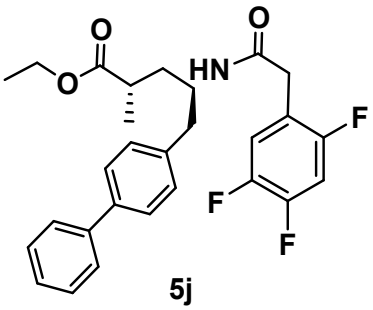


Figure S29: ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound, 5j.

^{19}F NMR Spectrum of compound 5j



5j

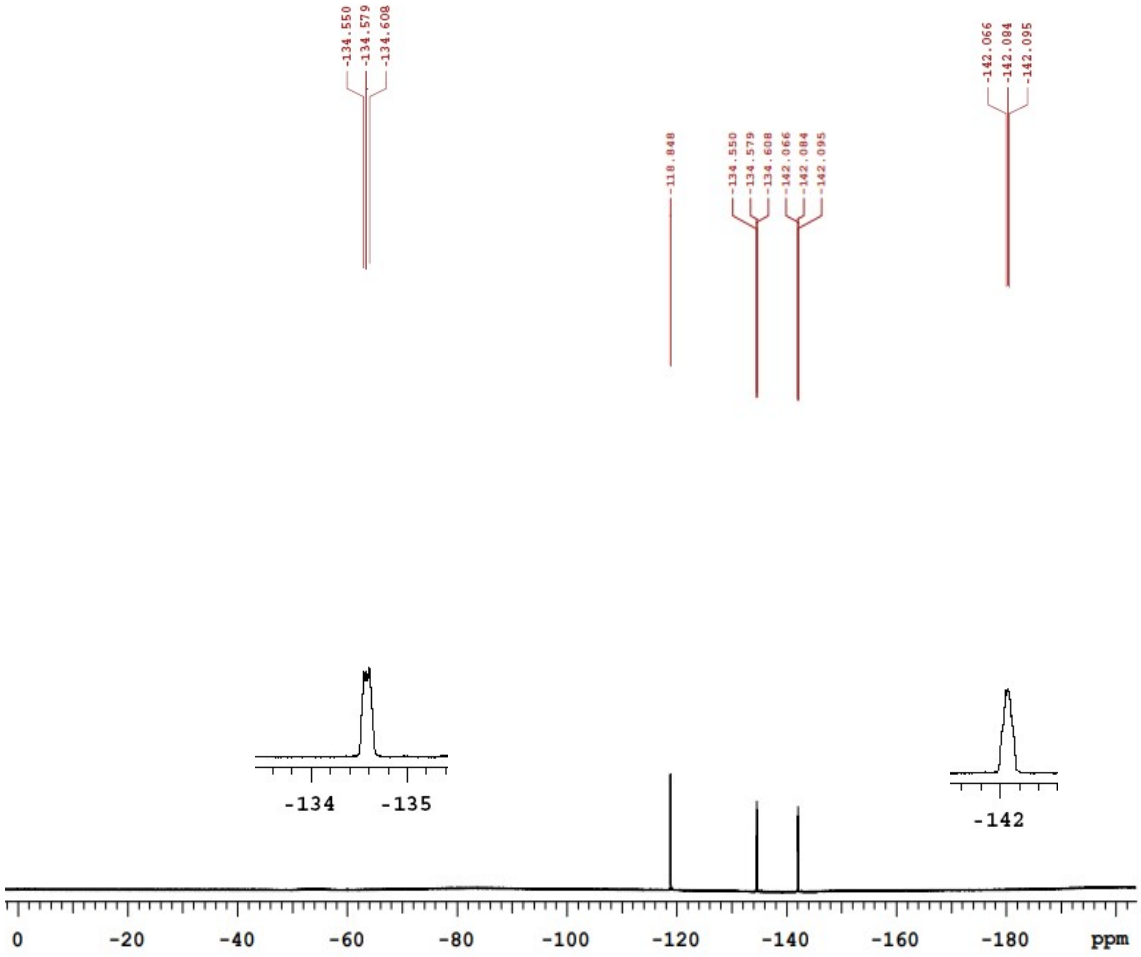
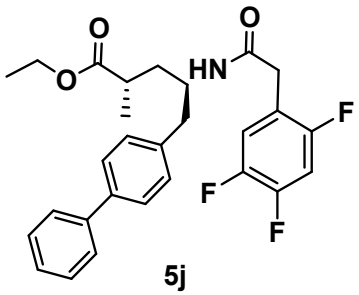


Figure S30: ^{19}F-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5j.

Mass spectrum of compound 5j



5j

Mass: 483.2

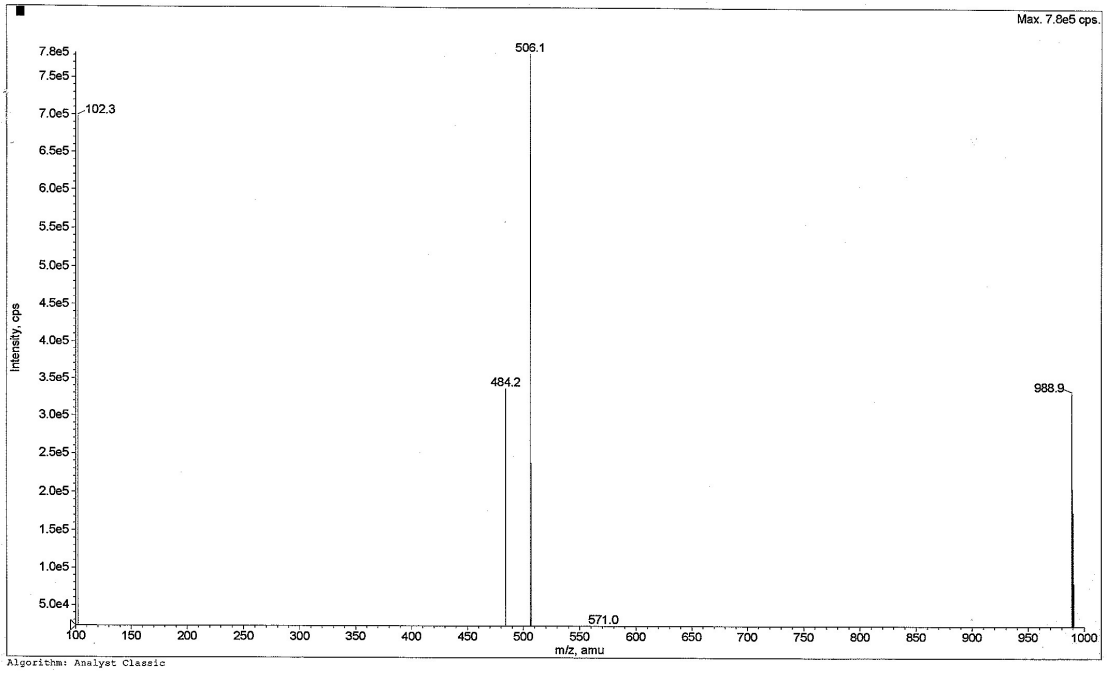
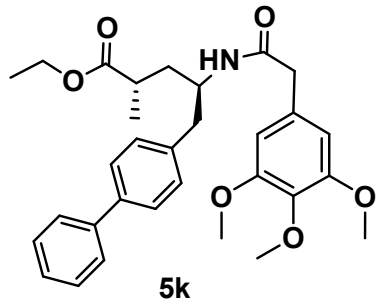


Figure S31: ESI Mass (M+H$^+$) spectrum of compound, 5j.

^{1}H NMR Spectrum of compound 5k



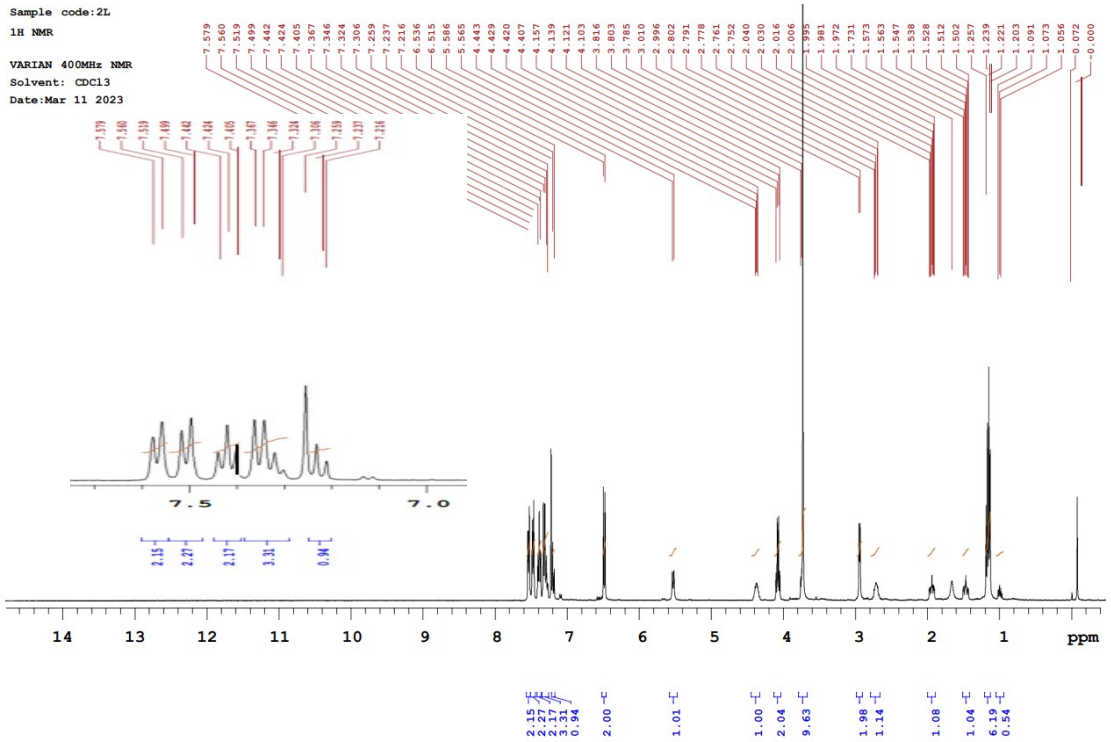
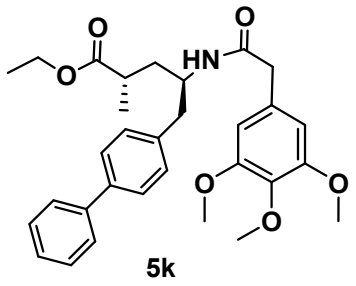


Figure S32: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound, 5k.

^{13}C NMR Spectrum of compound 5k



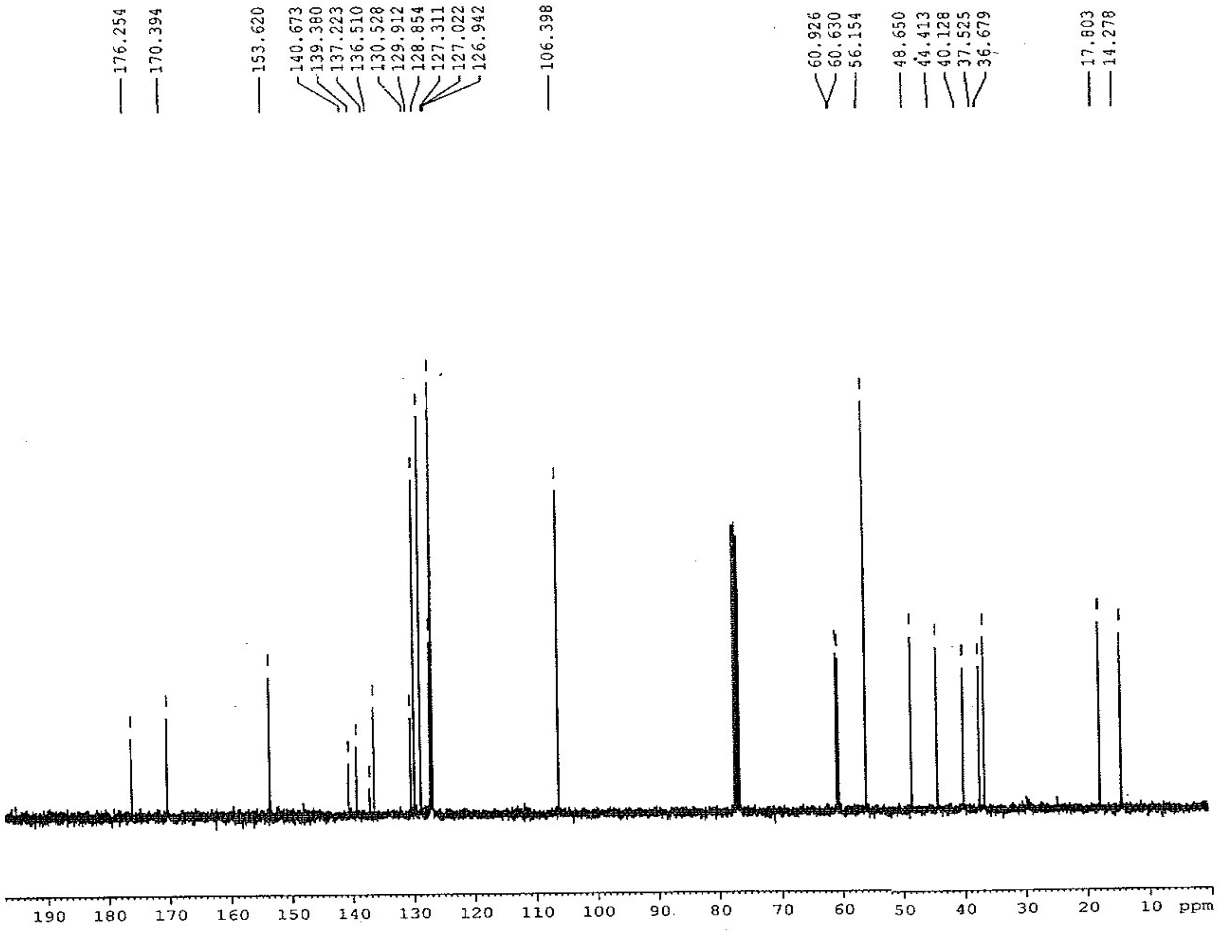
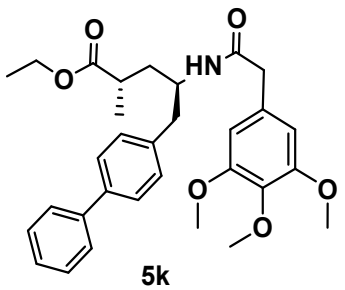


Figure S33: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5k.

Mass spectrum of compound 5k



Mass: 519.2

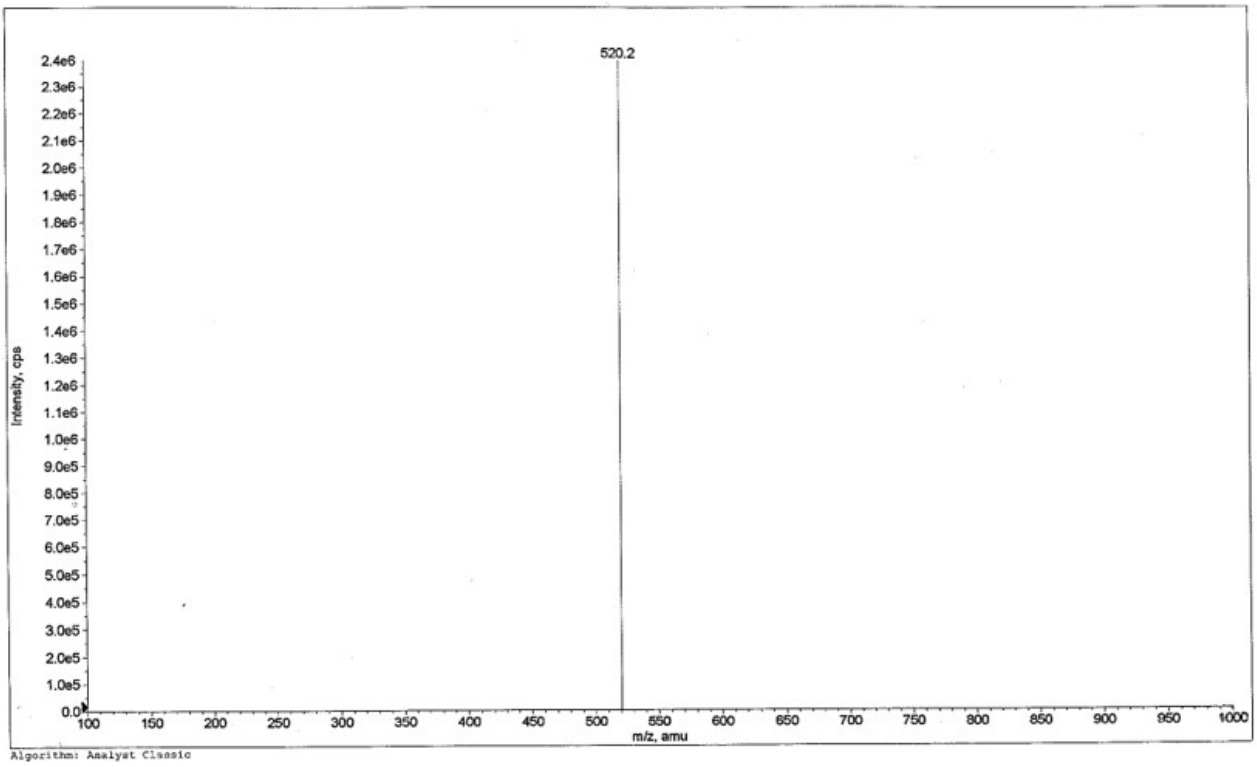
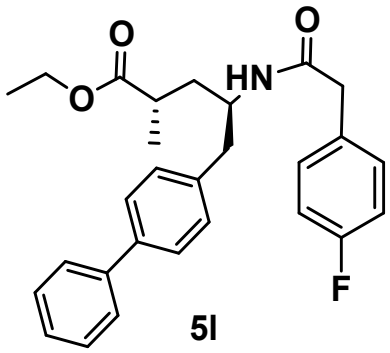


Figure S34: ESI Mass (M+H$^+$) spectrum of compound, 5k.

^{1}H NMR Spectrum of compound 5l



5l

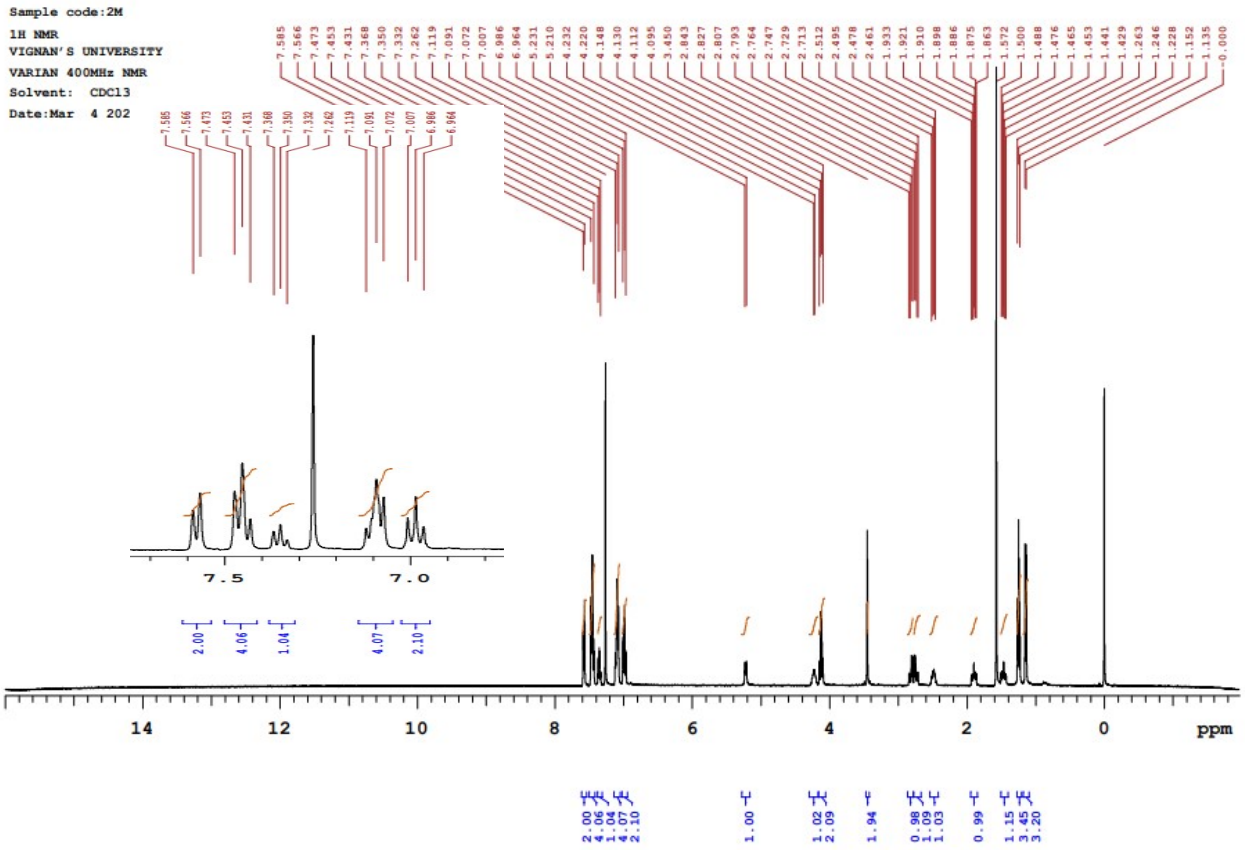


Figure S35: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5l.

^{13}C NMR Spectrum of compound 5l

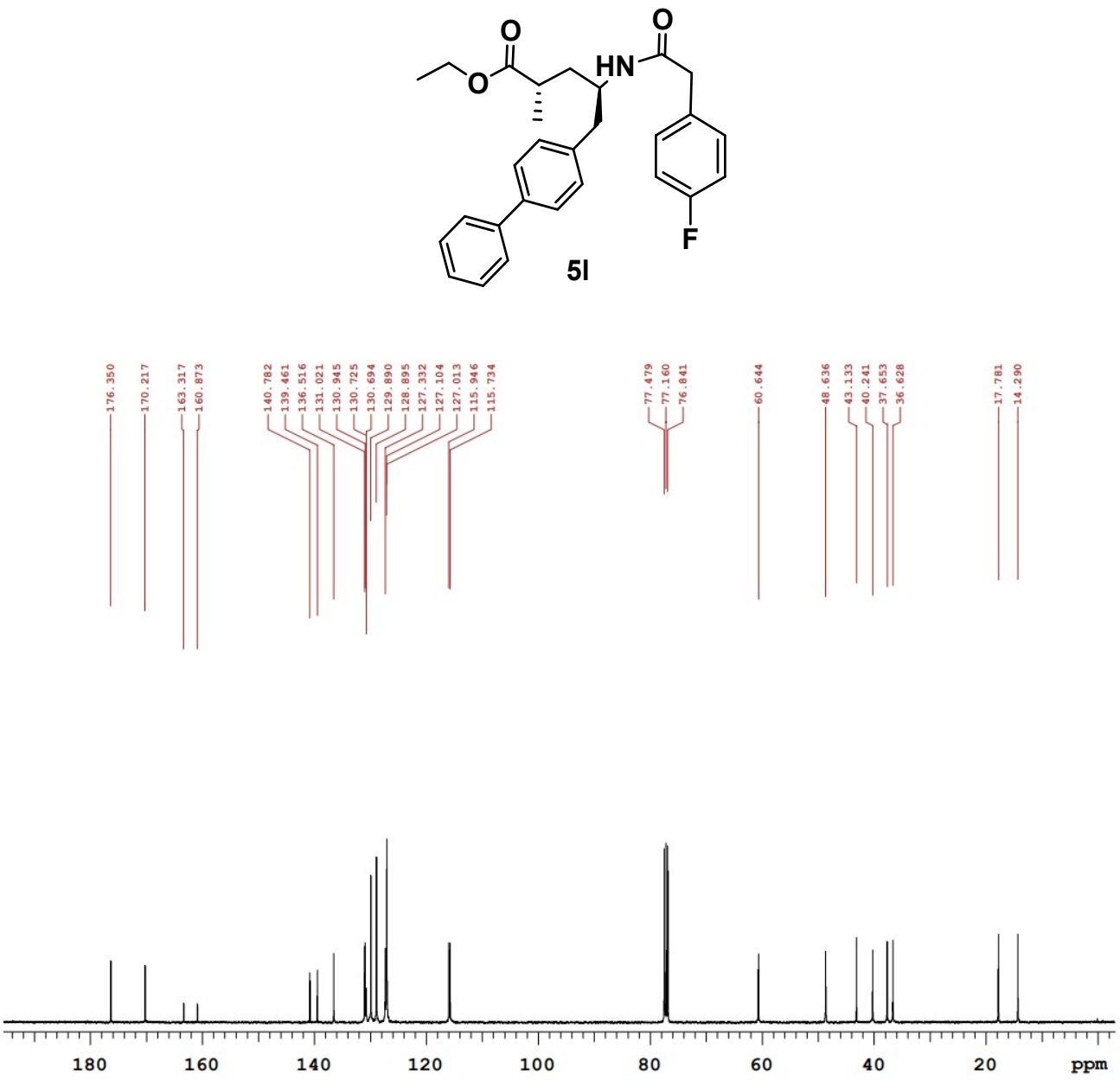
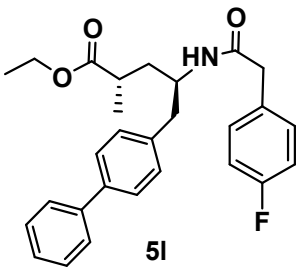


Figure S36: ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound, 5l.

Mass spectrum of compound 5l



5l

Mass: 447.2

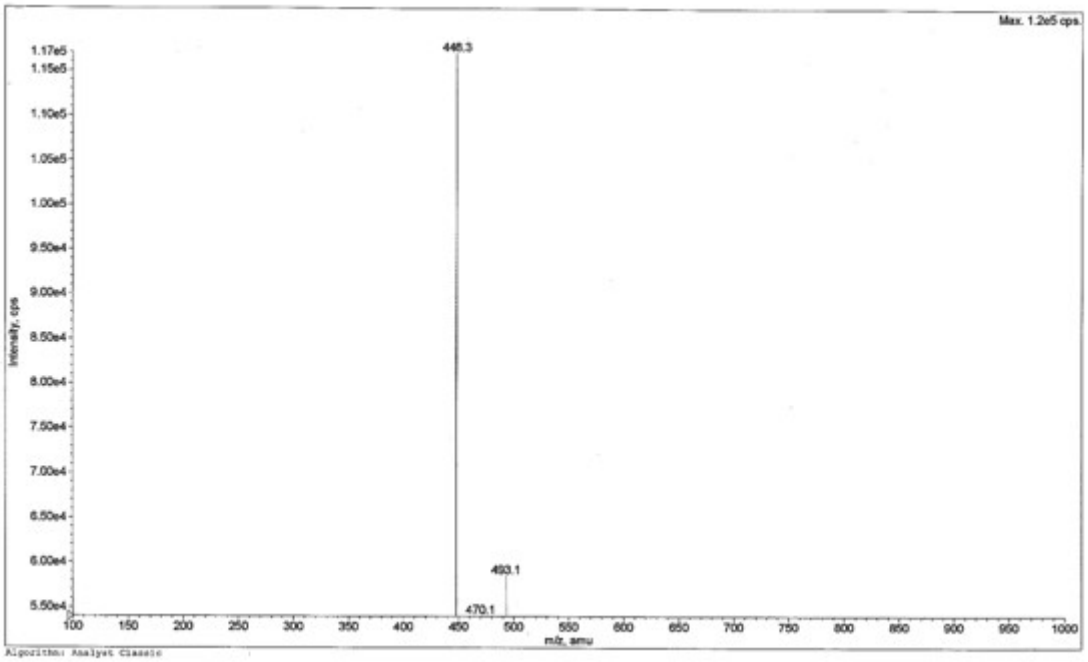
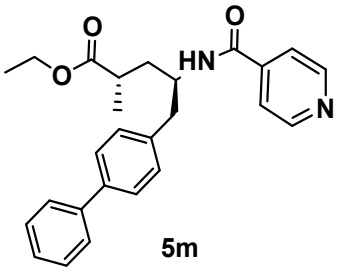


Figure S37: ESI Mass (M+H^+) spectrum of compound, 5l.

^{1}H NMR Spectrum of compound 5m



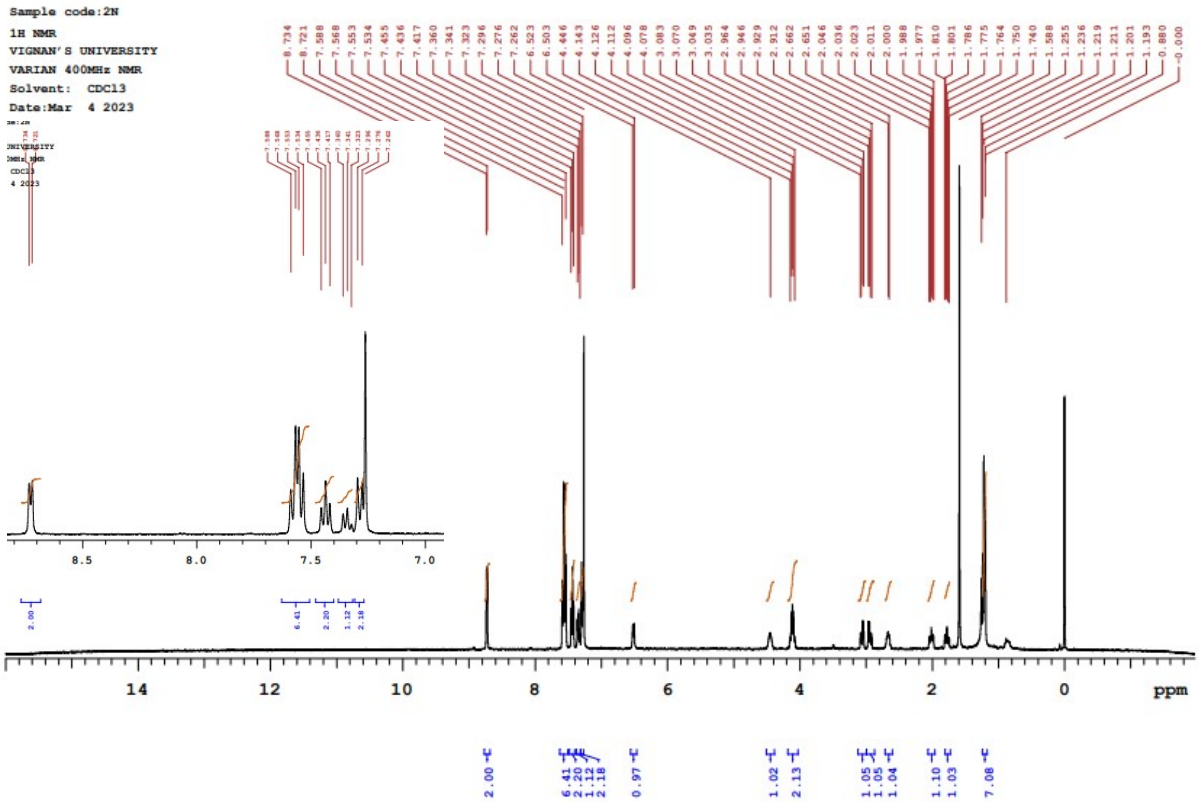


Figure S38: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5m.

^{13}C NMR Spectrum of compound 5m

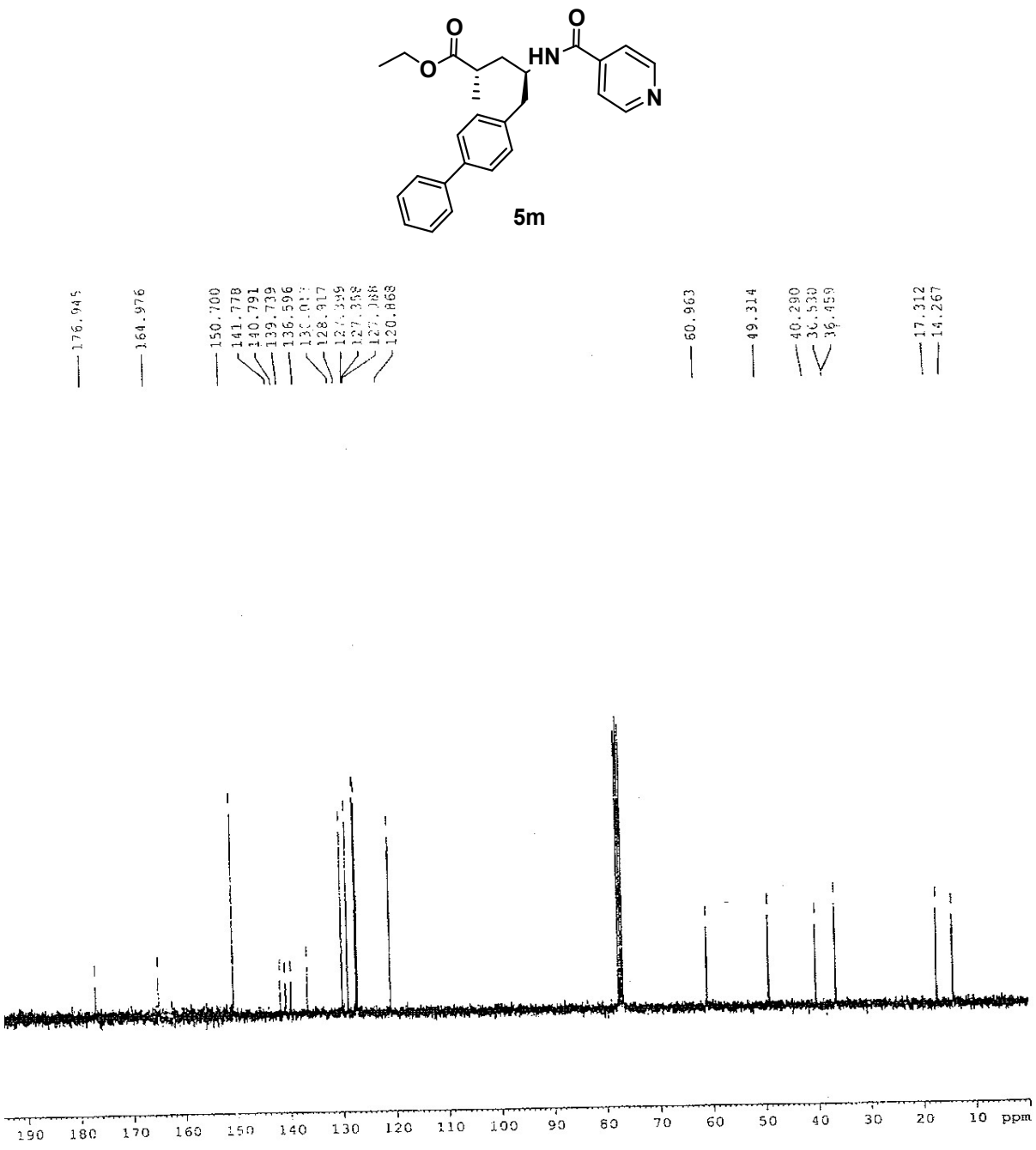
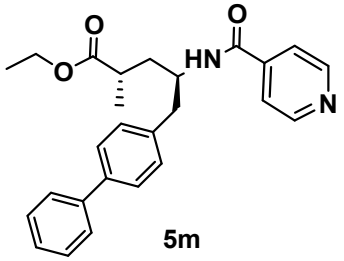


Figure S39: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5m.

Mass spectrum of compound 5m



5m

Mass: 416.2

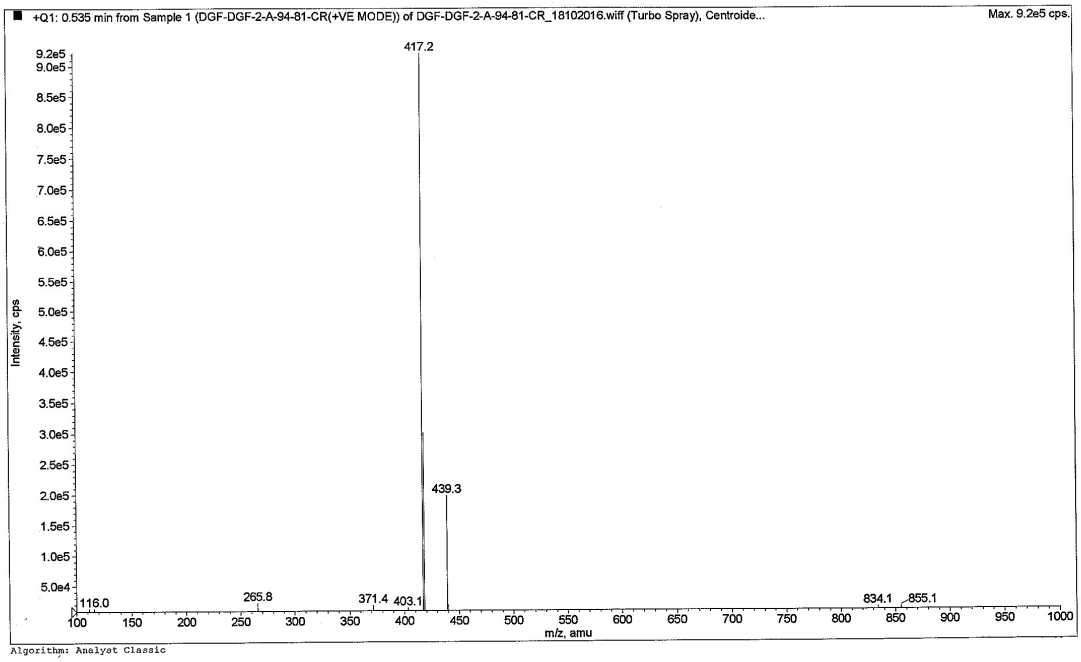
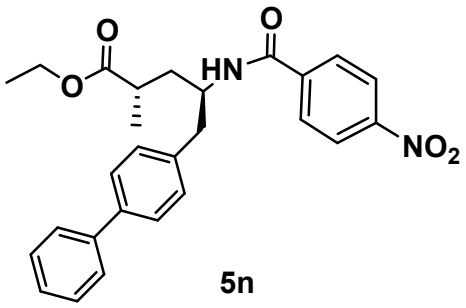


Figure S40: ESI Mass (M+H$^+$) spectrum of compound, 5m.

^{1}H NMR Spectrum of compound 5n



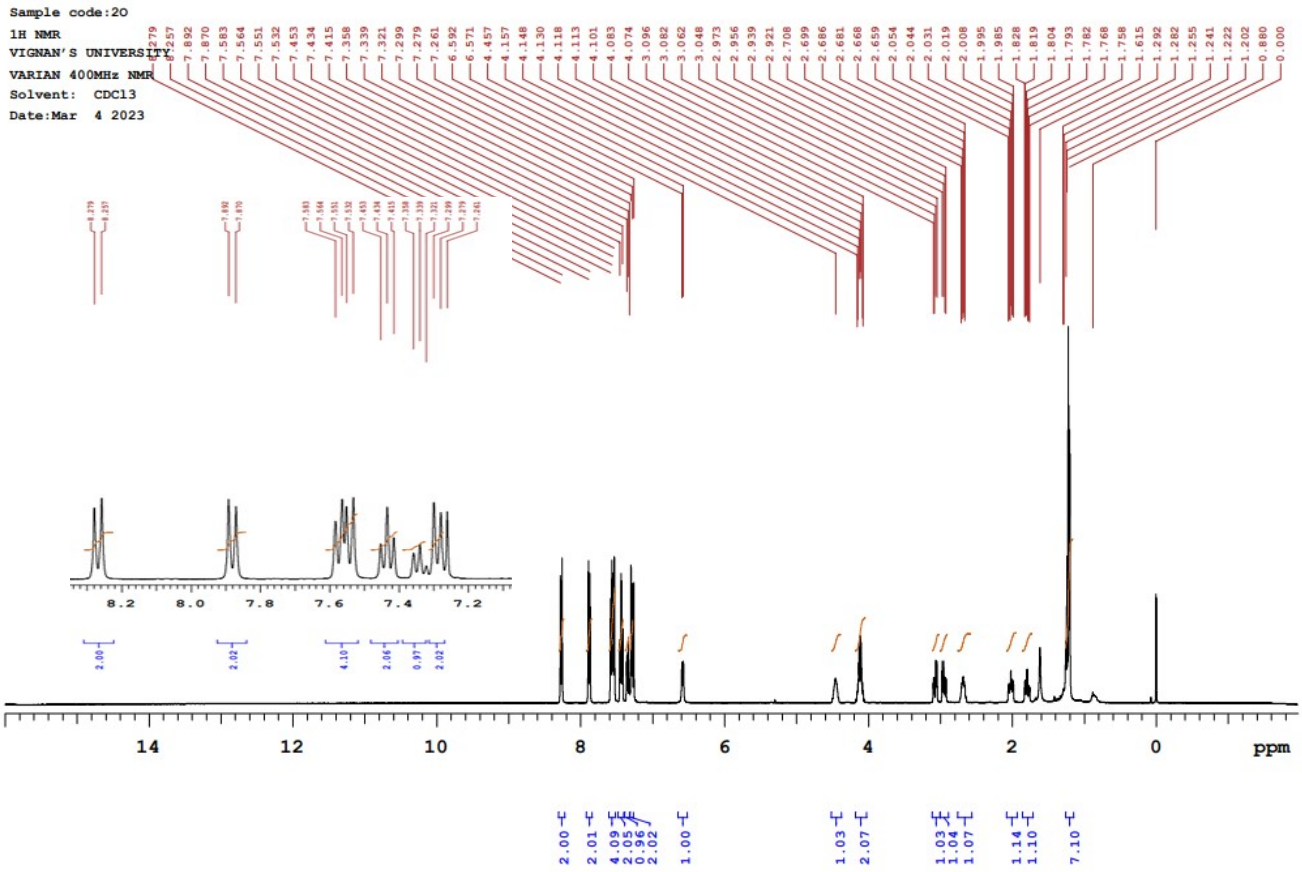


Figure S41: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5n.

^{13}C NMR Spectrum of compound 5n

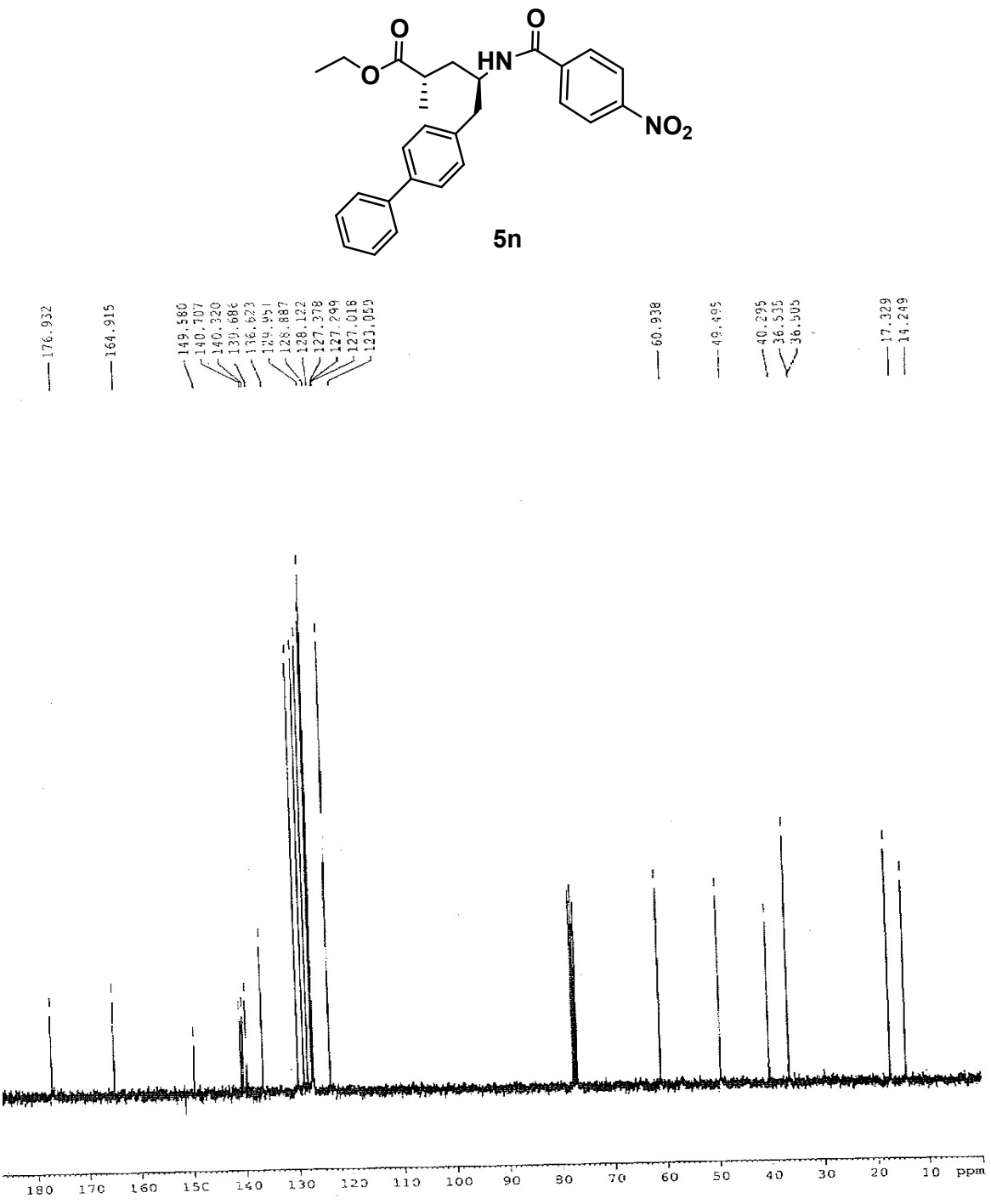
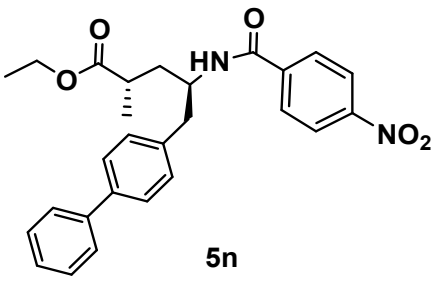


Figure S42: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5n.

Mass spectrum of compound 5n



5n

Mass: 460.5

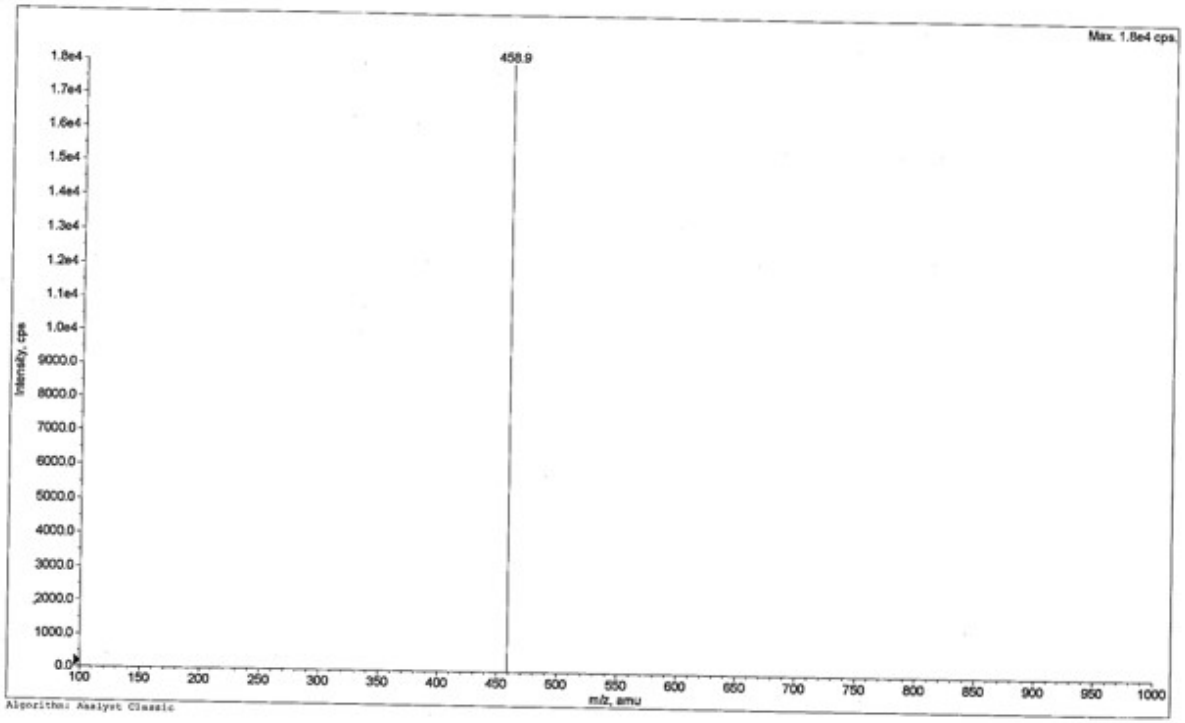
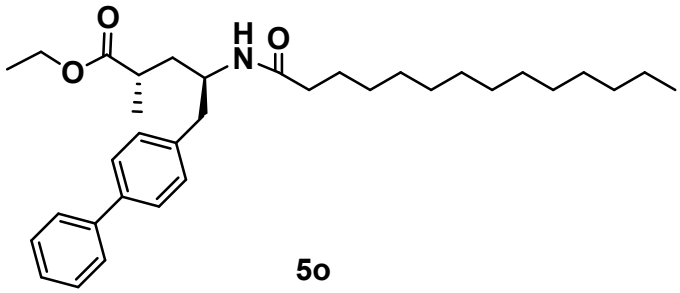


Figure S43: ESI Mass (M-H^+) spectrum of compound, 5n.

^{1}H NMR Spectrum of compound 5o



5o

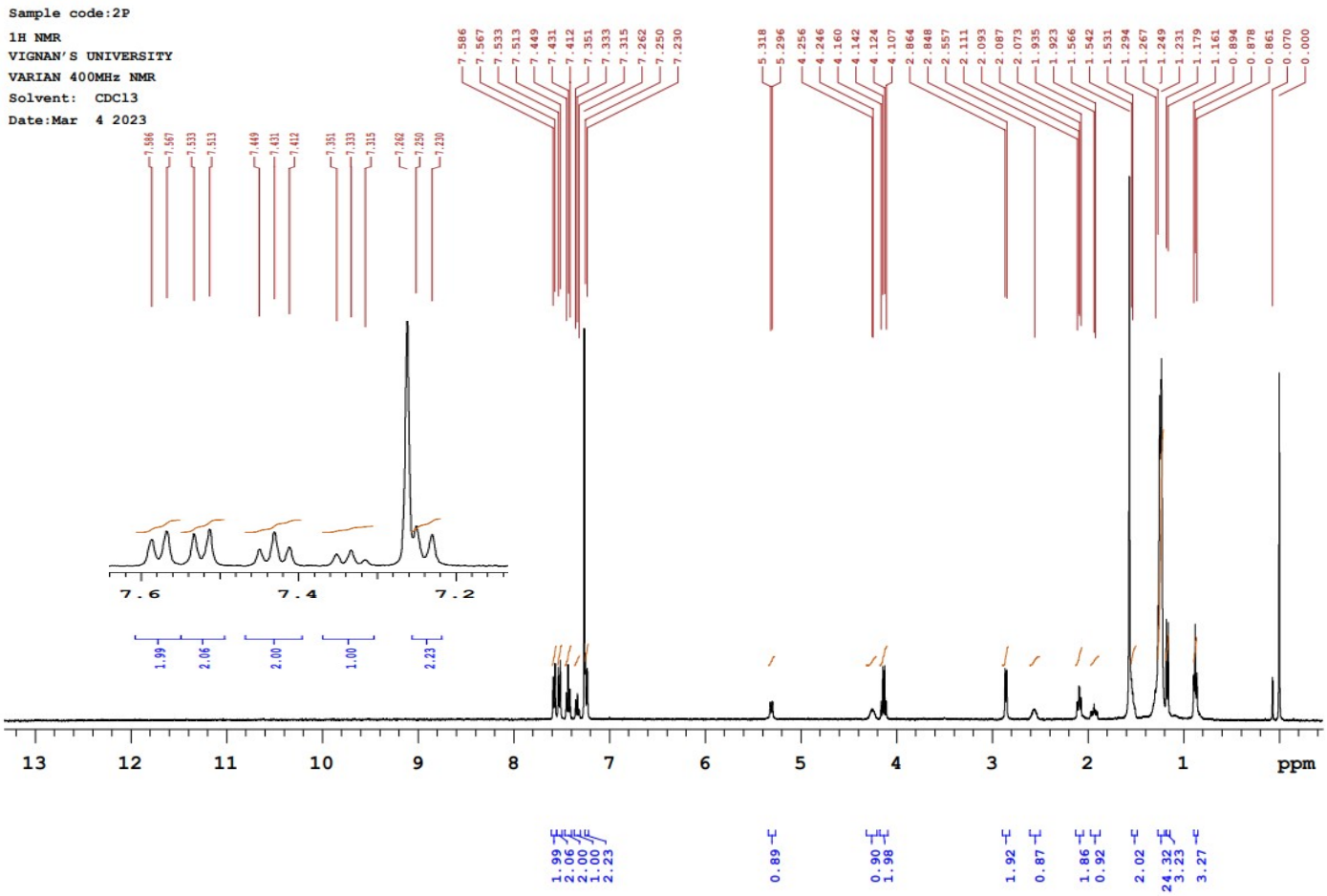


Figure S44: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5o.

^{13}C NMR Spectrum of compound 5o

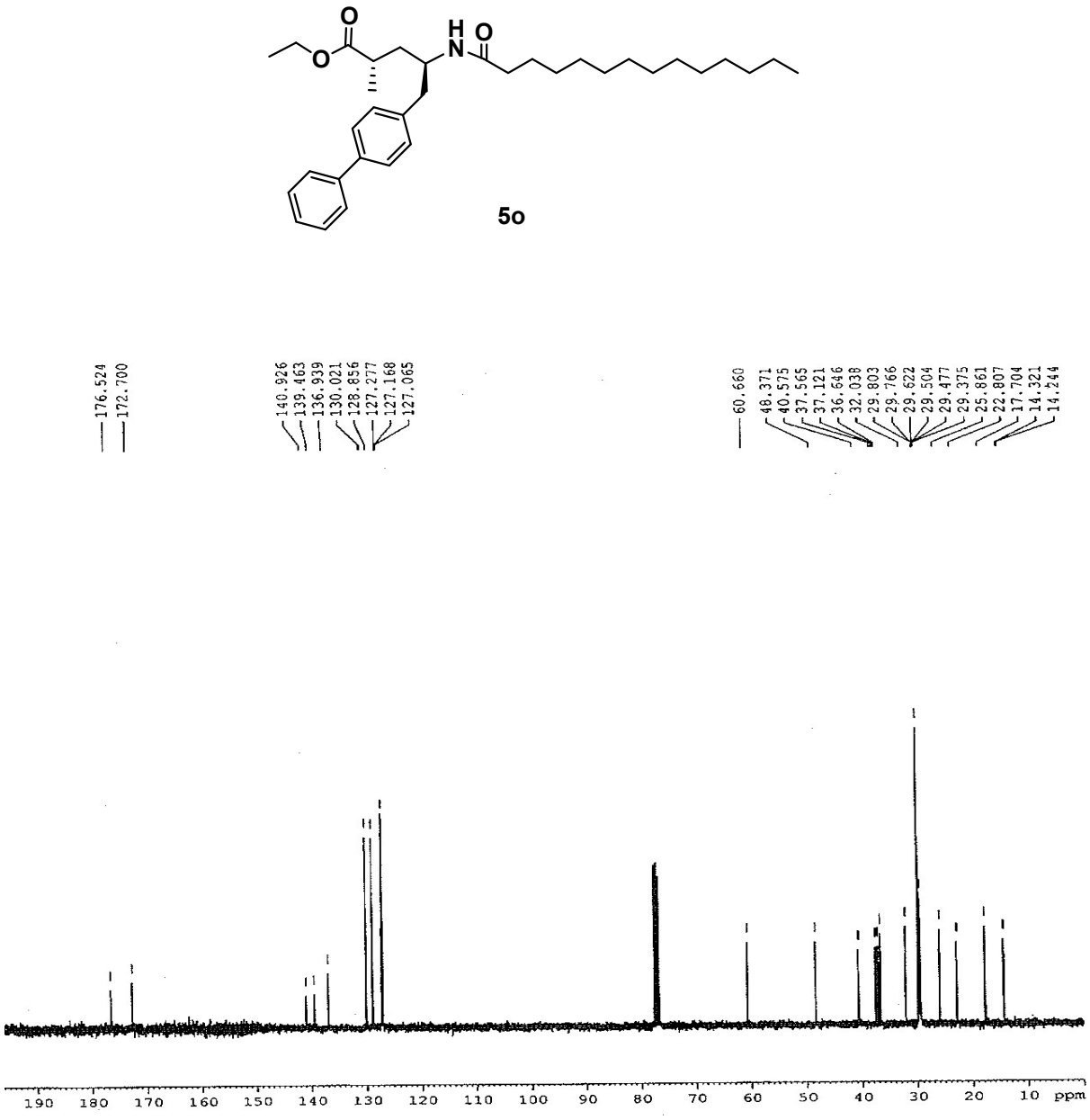
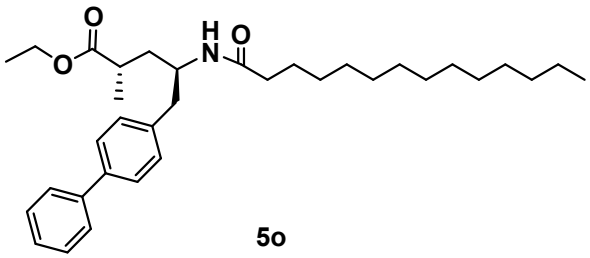


Figure S45: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5o.

Mass spectrum of compound 5o



5o

Mass: 521.3

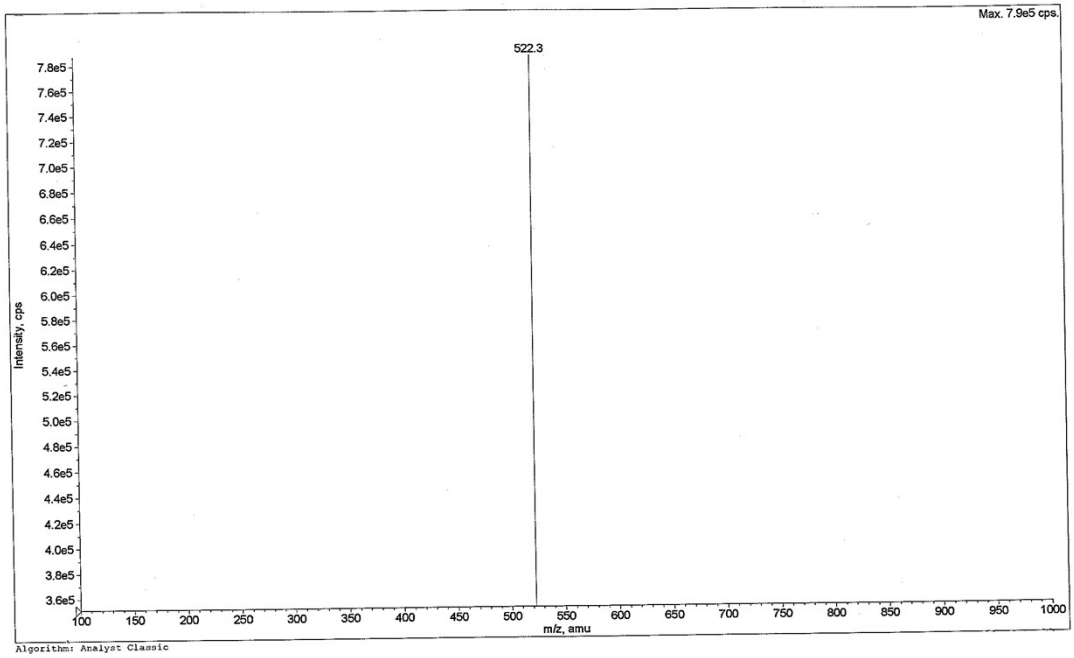


Figure S46: ESI Mass (M+H^+) spectrum of compound, 5o.

[1]HNMR Spectrum of compound 5p

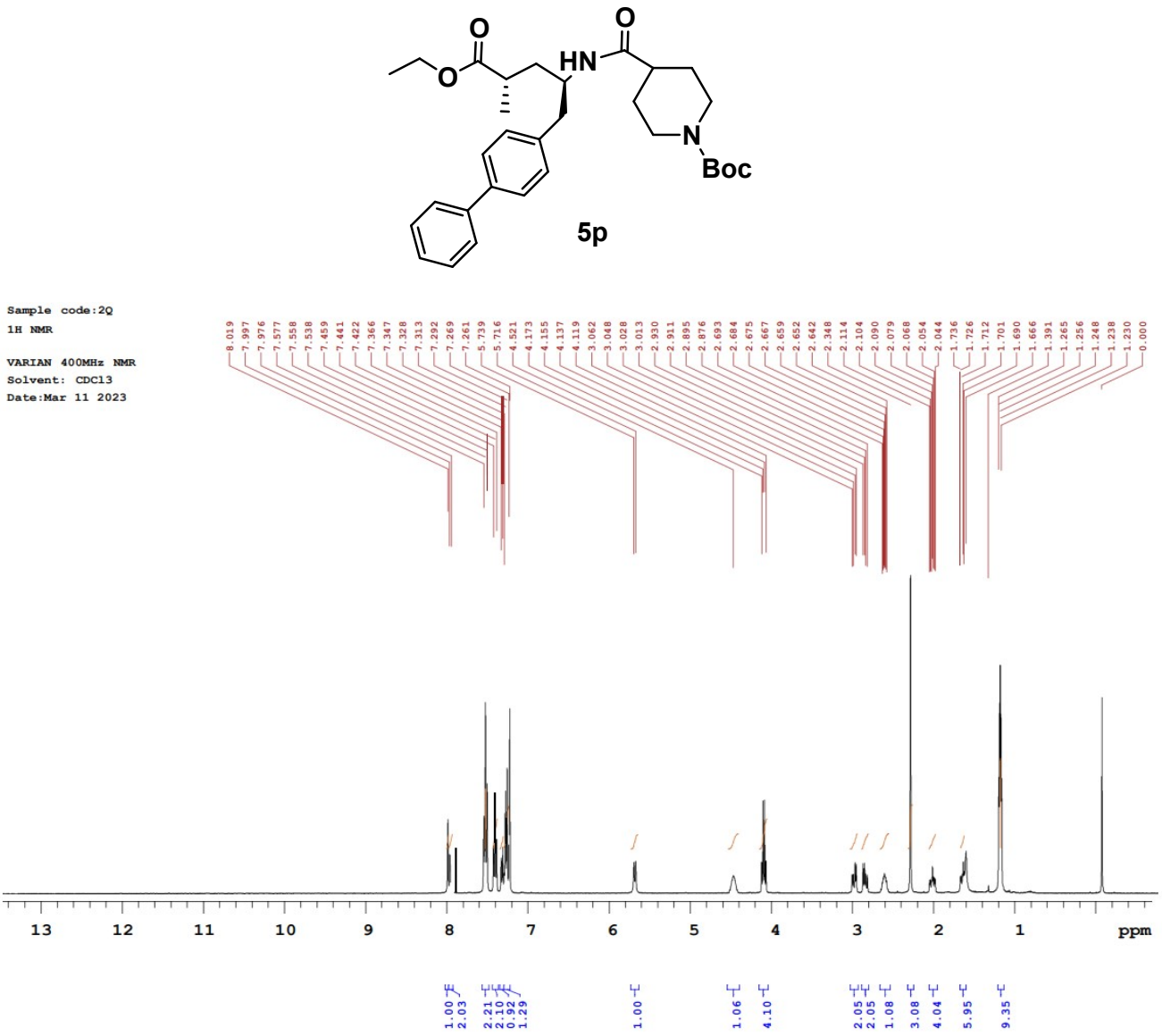
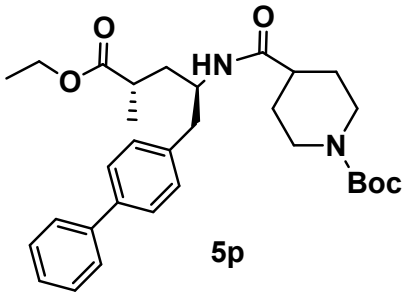


Figure S47: [1]H-NMR (300 MHz, $CDCl_3$) spectrum of compound, 5p.

^{13}C NMR Spectrum of compound 5p



5p

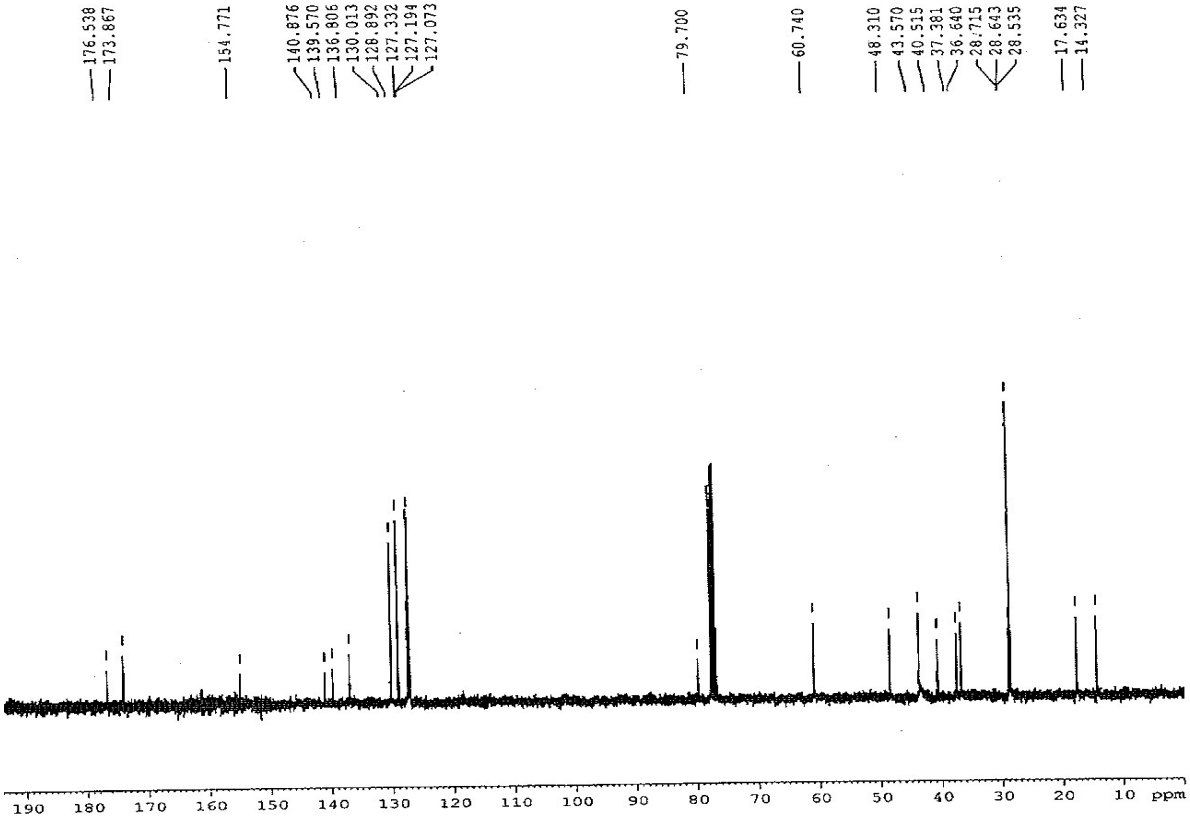
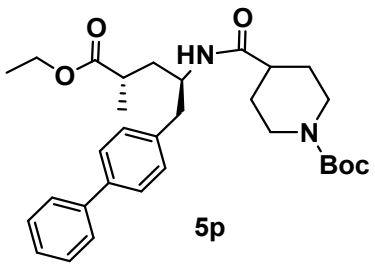


Figure S48: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5p.

Mass spectrum of compound 5p



5p

Mass: 522.3

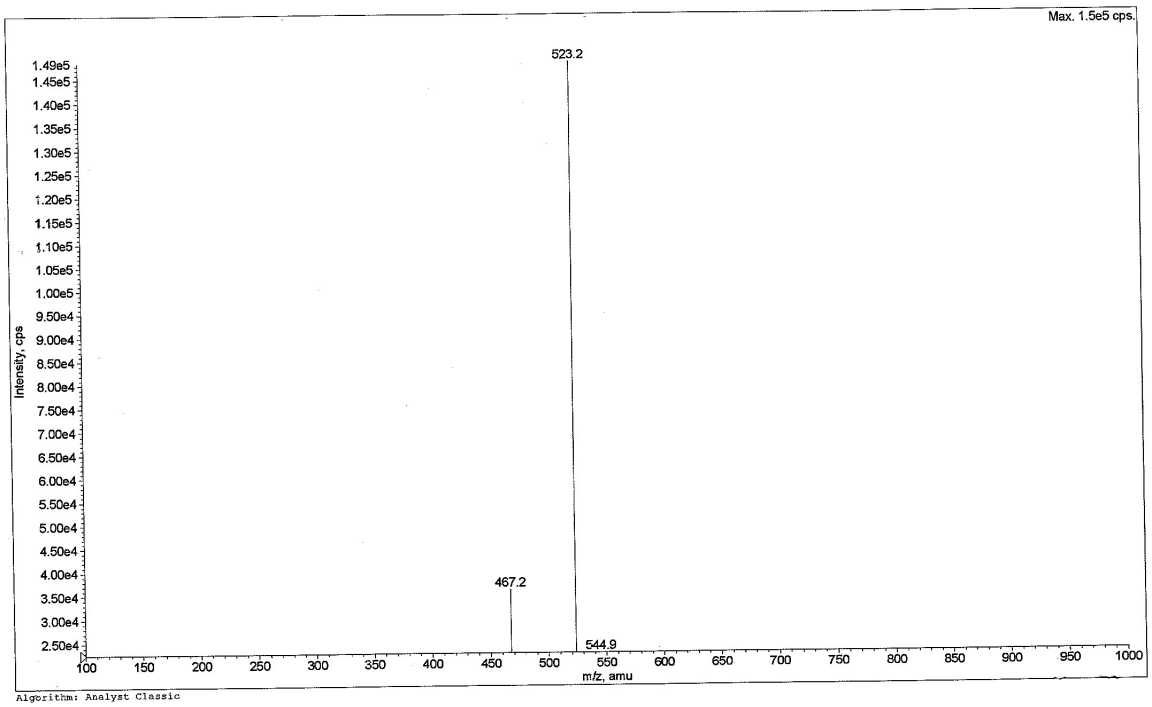
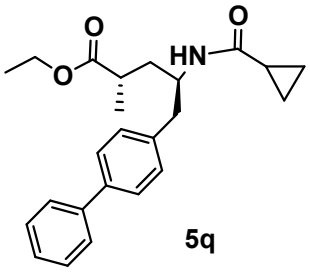


Figure S49: ESI Mass (M+H$^+$) spectrum of compound, 5p.

^{1}H NMR Spectrum of compound 5q



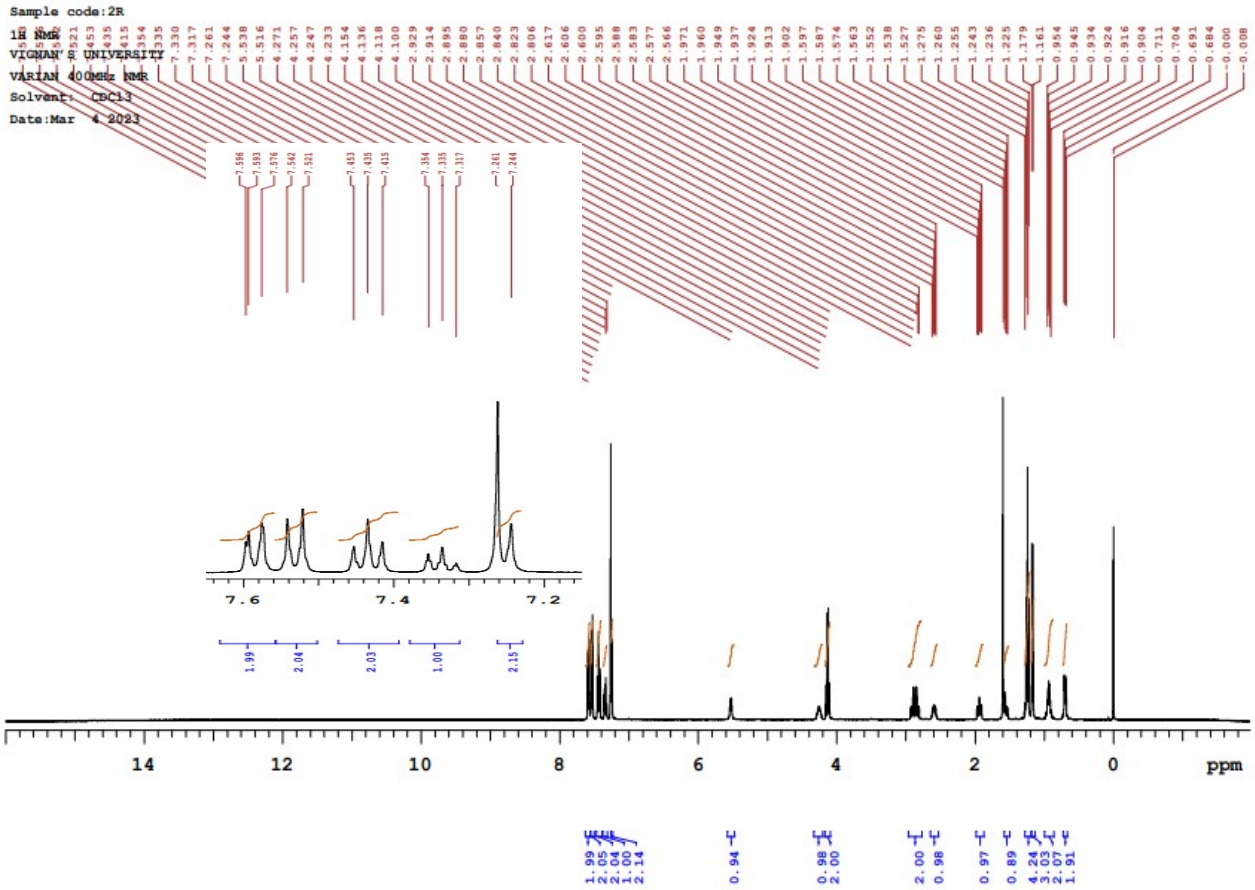
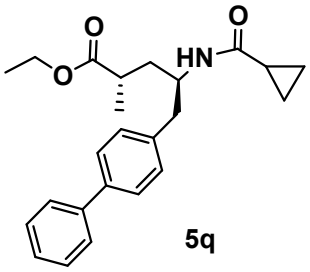


Figure S50: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5q.

^{13}C NMR Spectrum of compound 5q



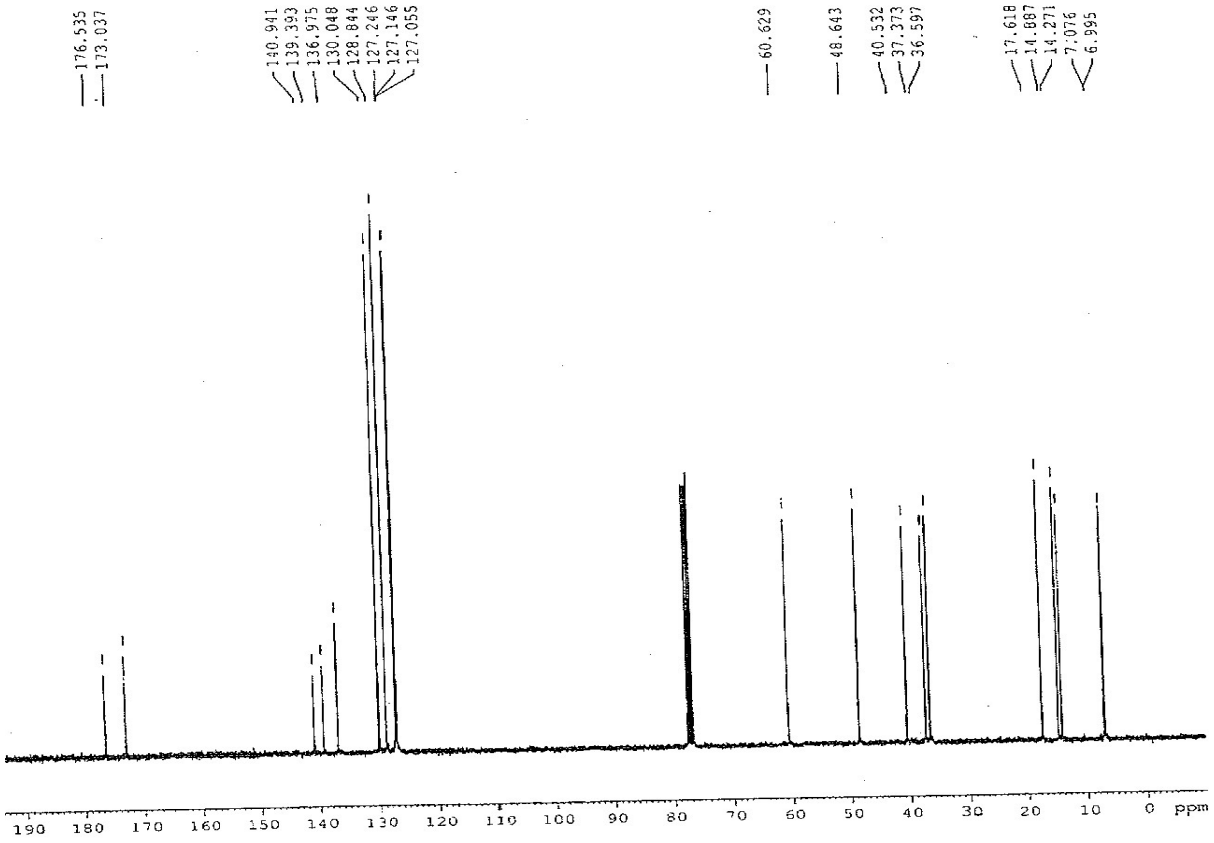
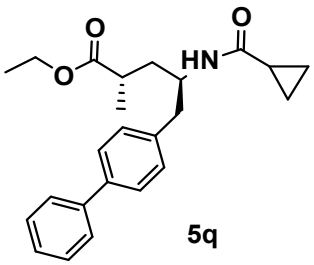


Figure S51: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5q.

Mass spectrum of compound 5q



5q

Mass: 379.2

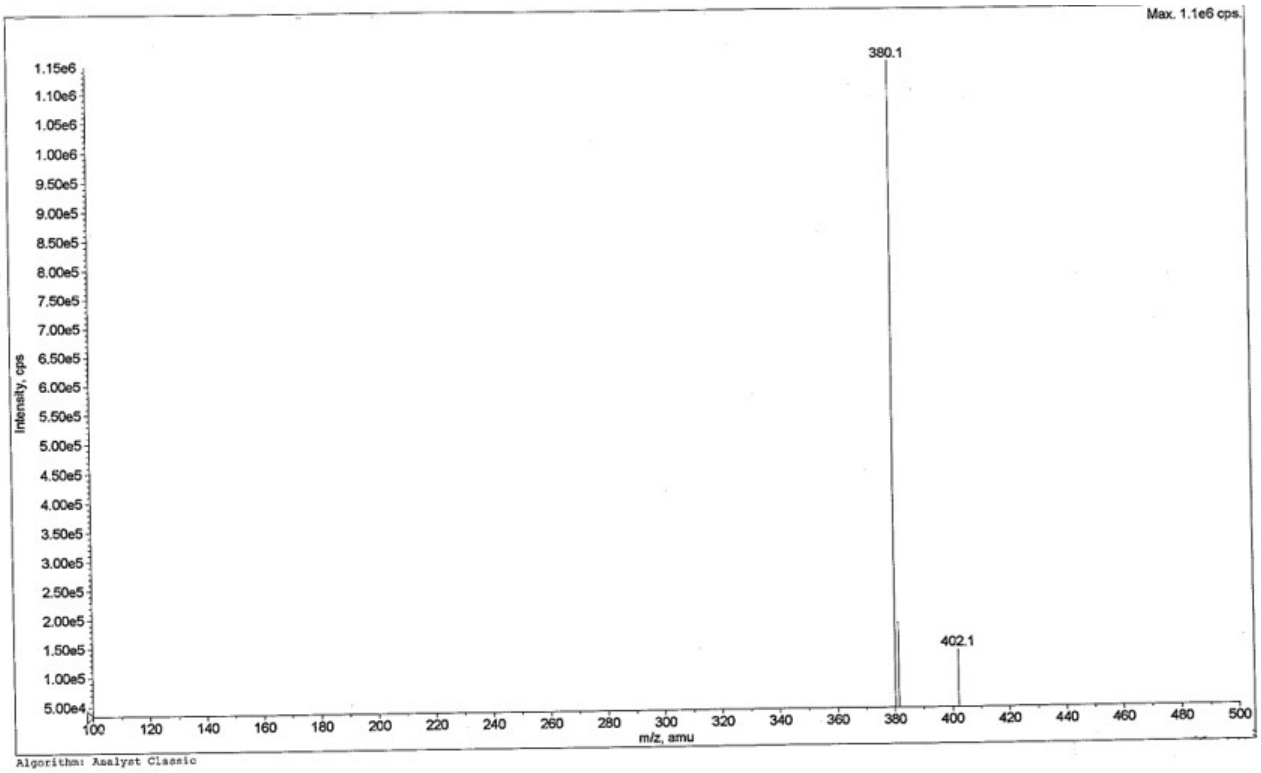


Figure S52: ESI Mass (M+H^+) spectrum of compound, 5q.

^{1}H NMR Spectrum of compound 5r

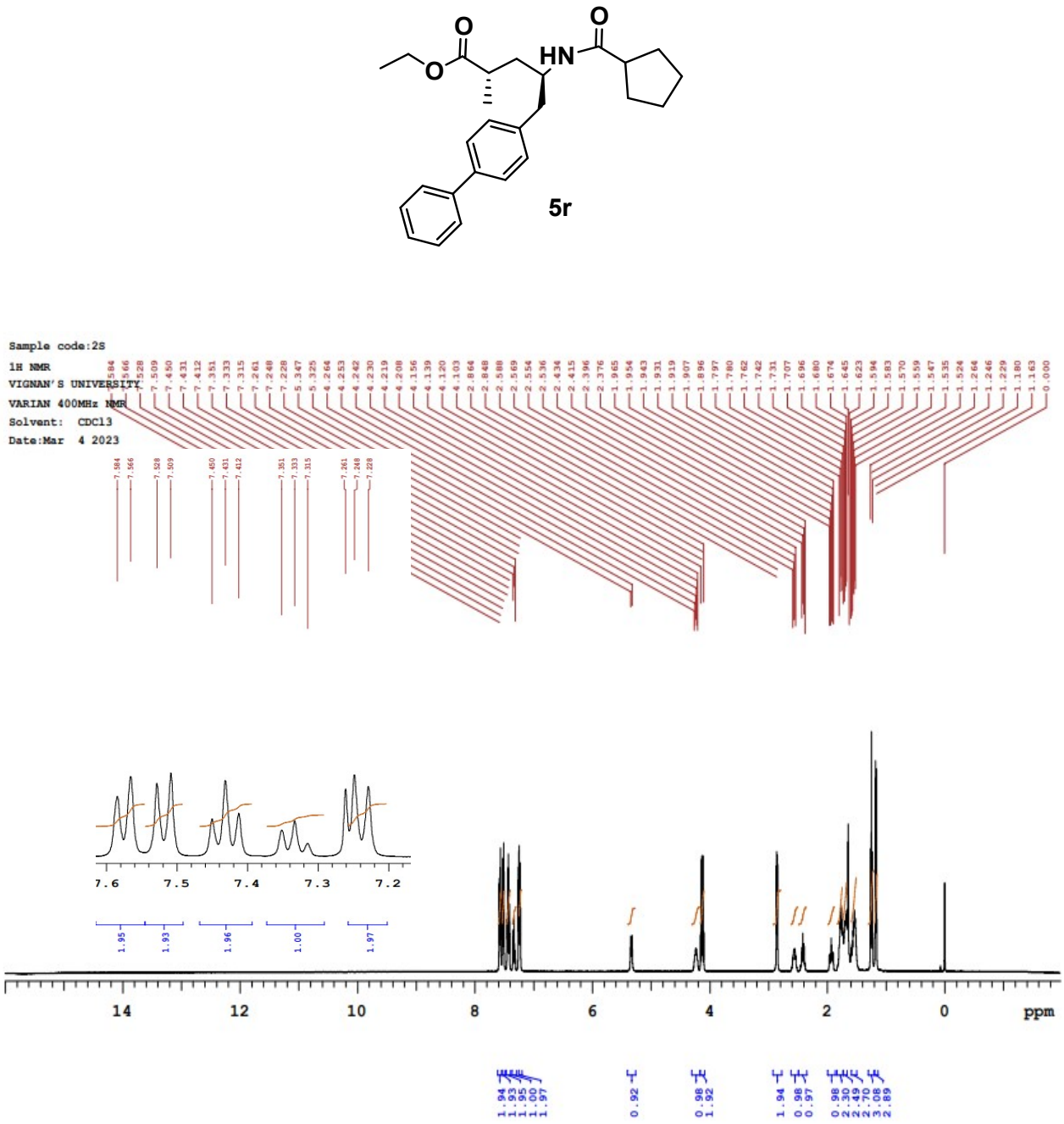


Figure S53: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5r.

^{13}C NMR Spectrum of compound 5r

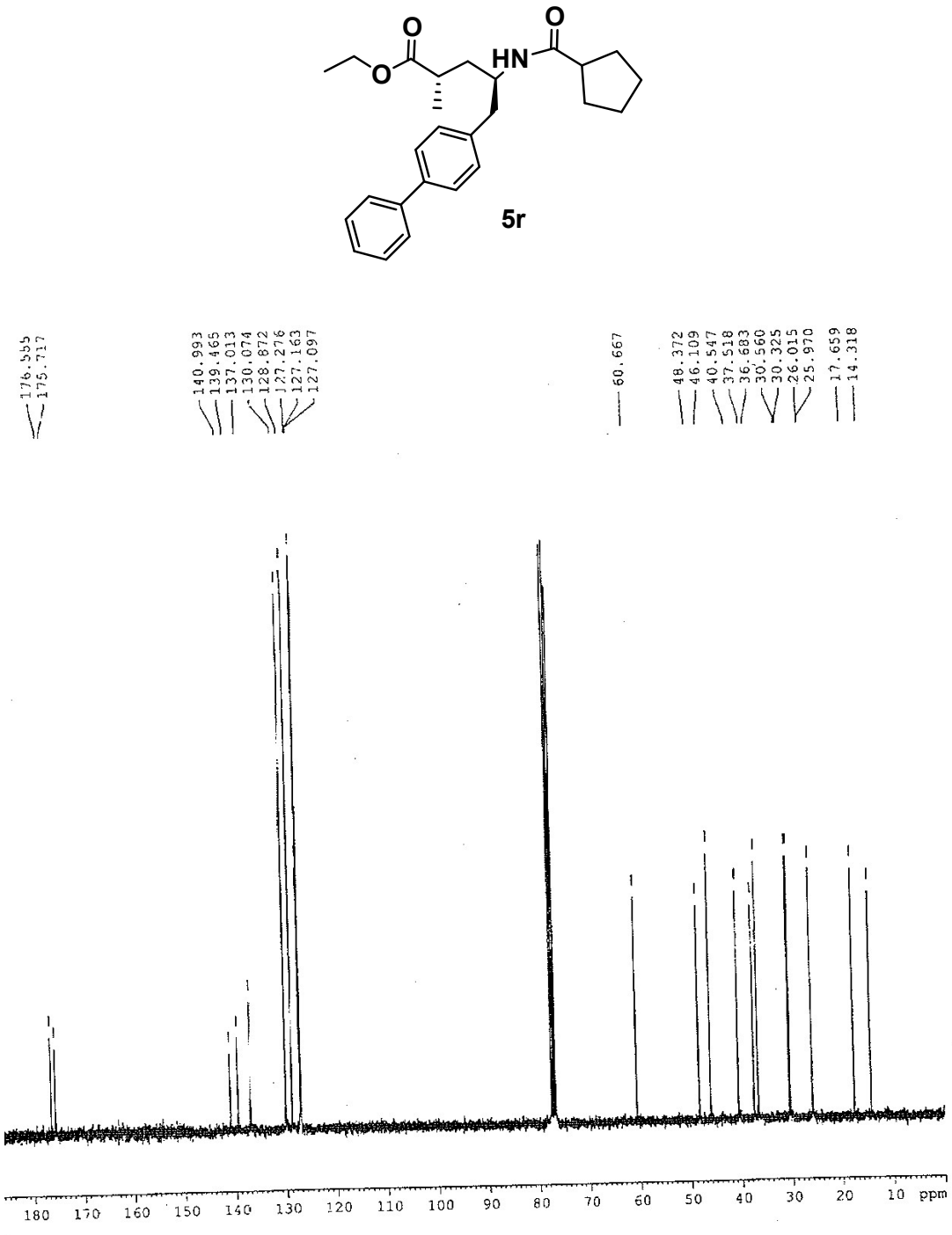
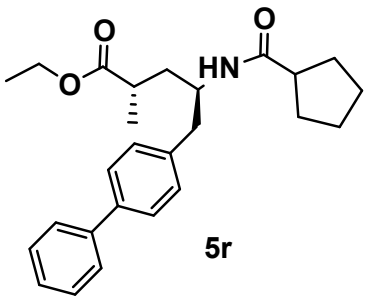


Figure S54: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5r.

Mass spectrum of compound 5r



Mass: 407.2

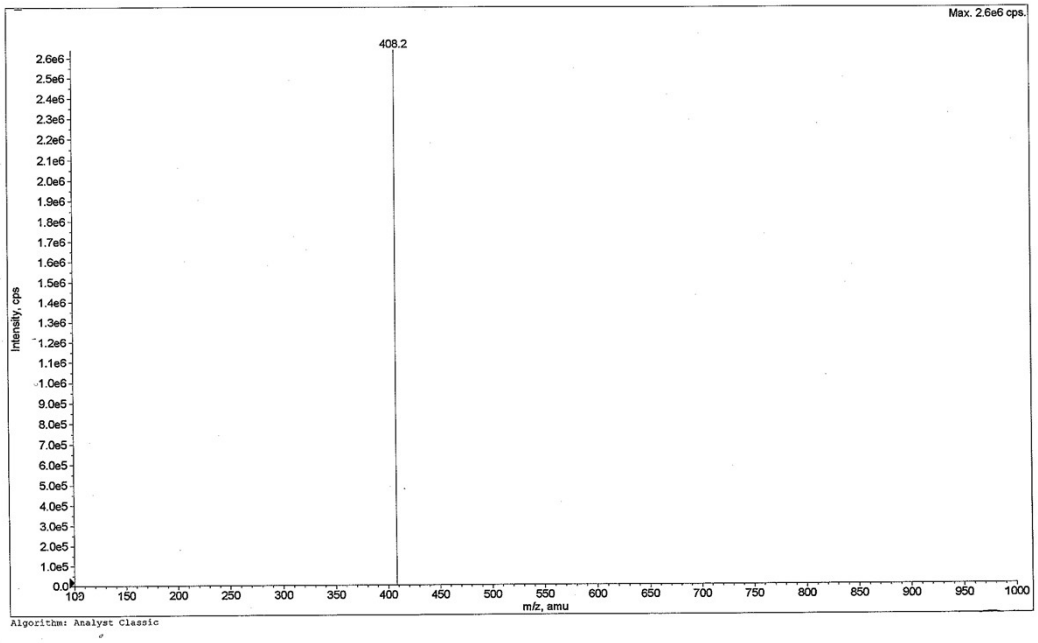
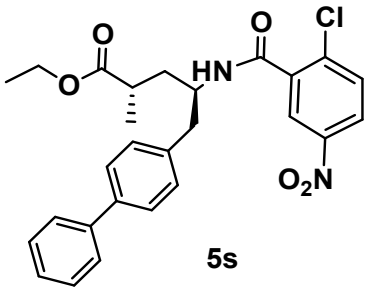


Figure S55: ESI Mass (M+H^+) spectrum of compound, 5r.

^{1}H NMR Spectrum of compound 5s



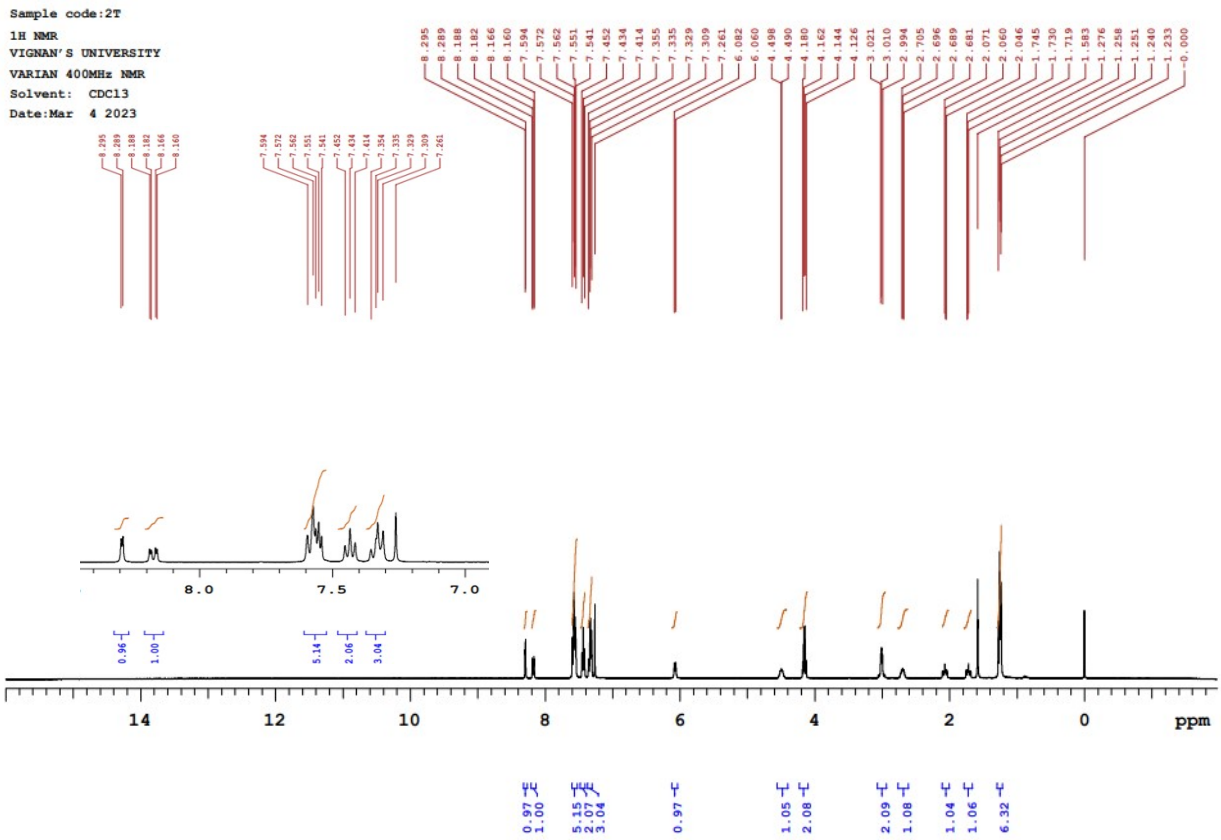


Figure S56: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5s.

^{13}C NMR Spectrum of compound 5s

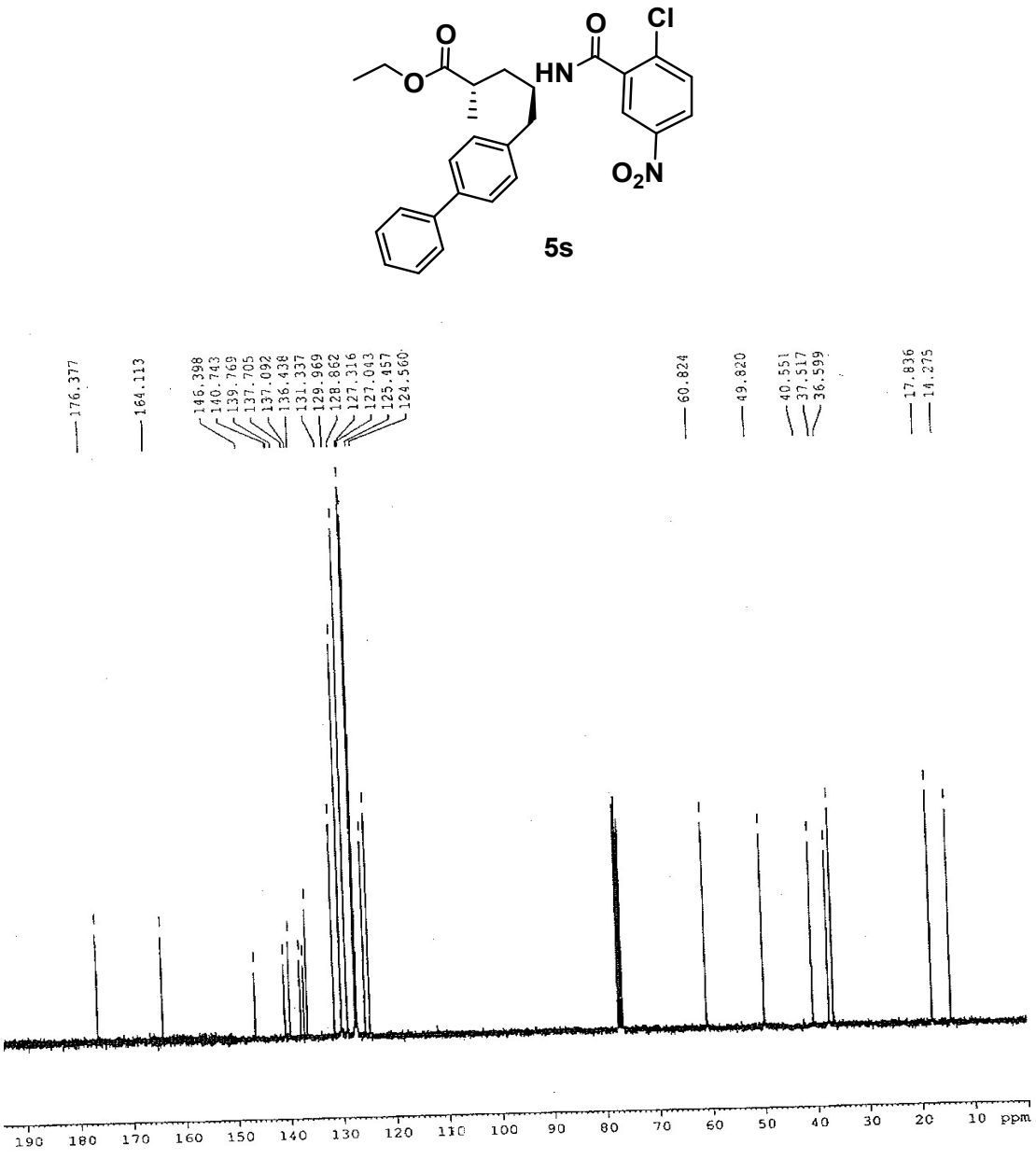
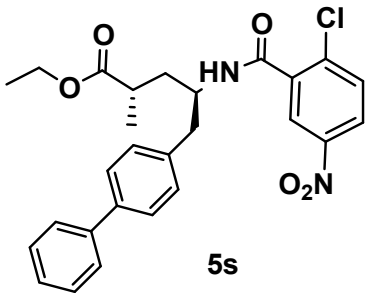


Figure S57: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5s.

Mass spectrum of compound 5s



5s

Mass: 494.1

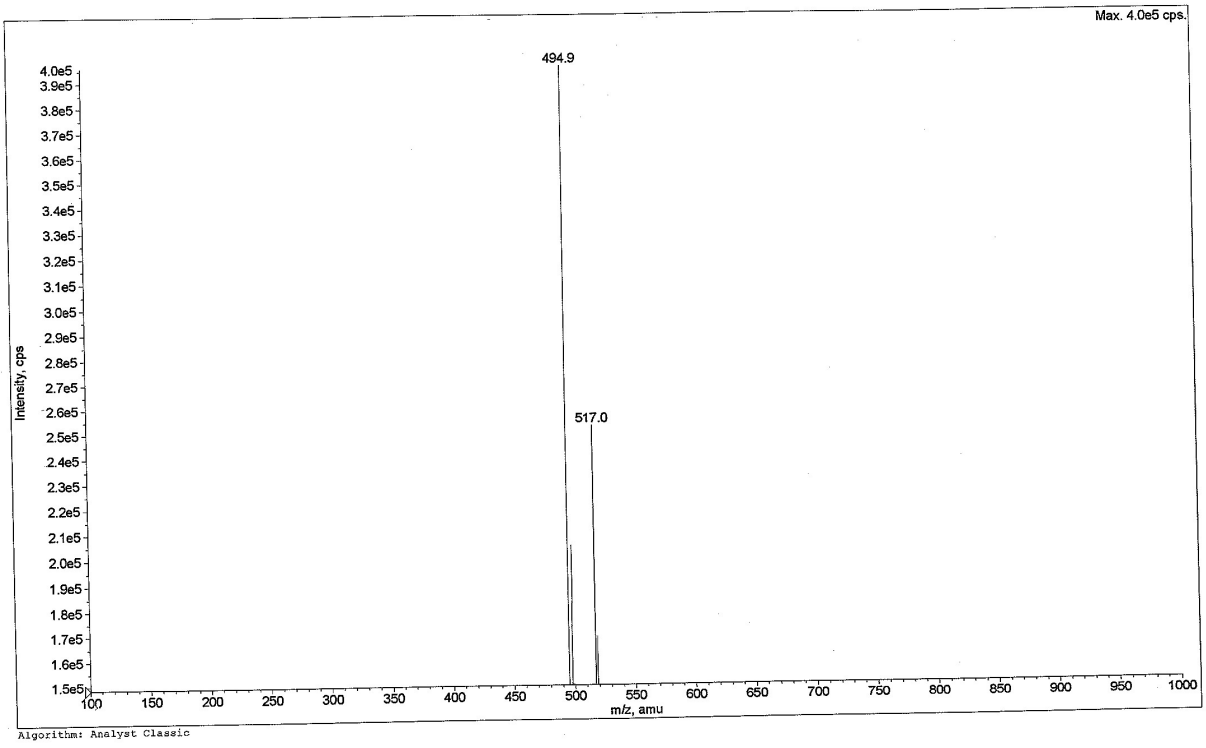
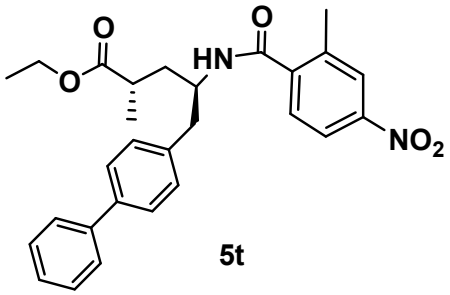


Figure S58: ESI Mass (M+H^+) spectrum of compound, 5s.

^{1}H NMR Spectrum of compound 5t



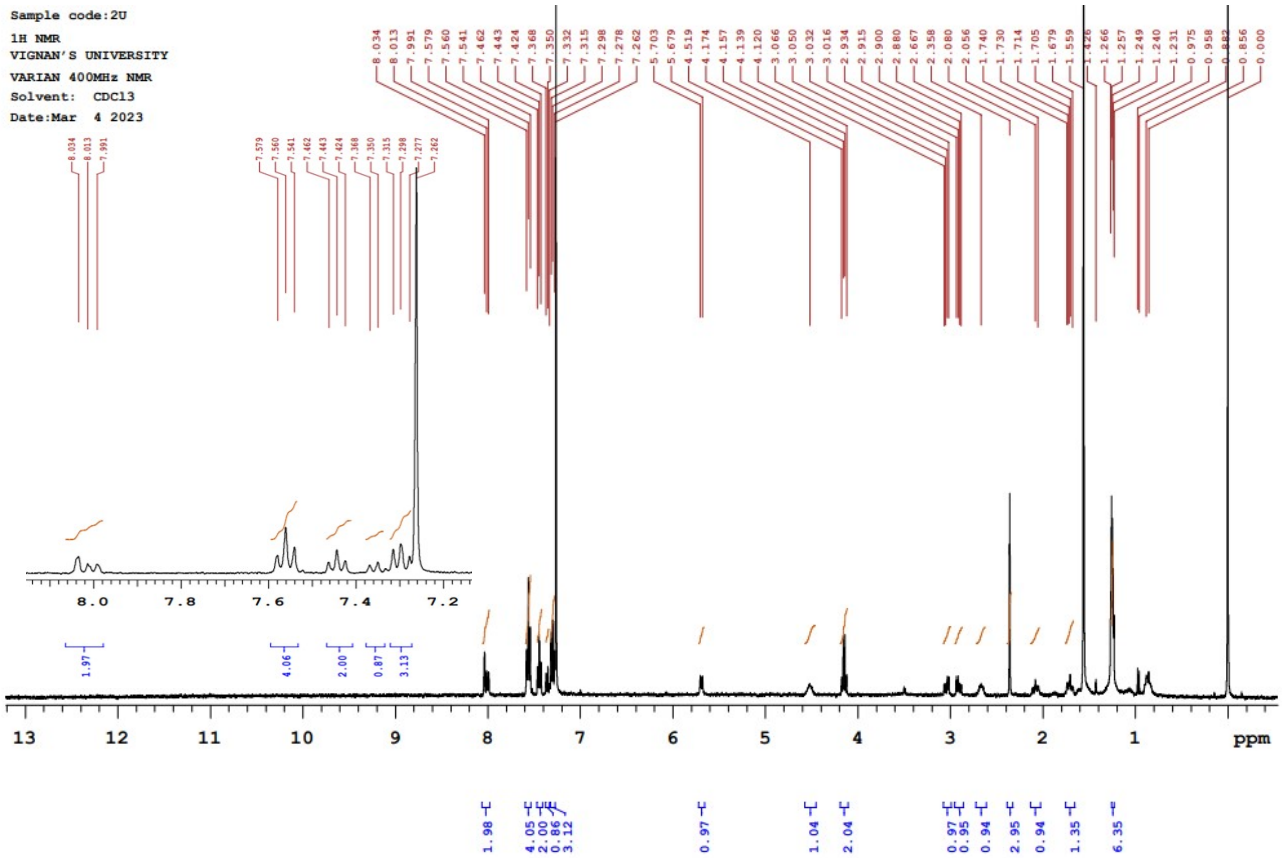
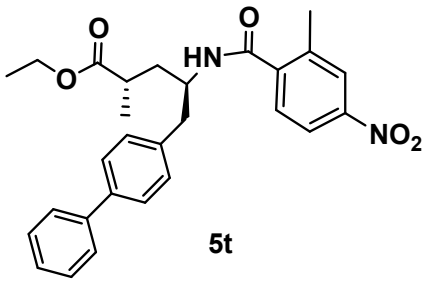


Figure S59: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5t.

^{13}C NMR Spectrum of compound 5t



5t

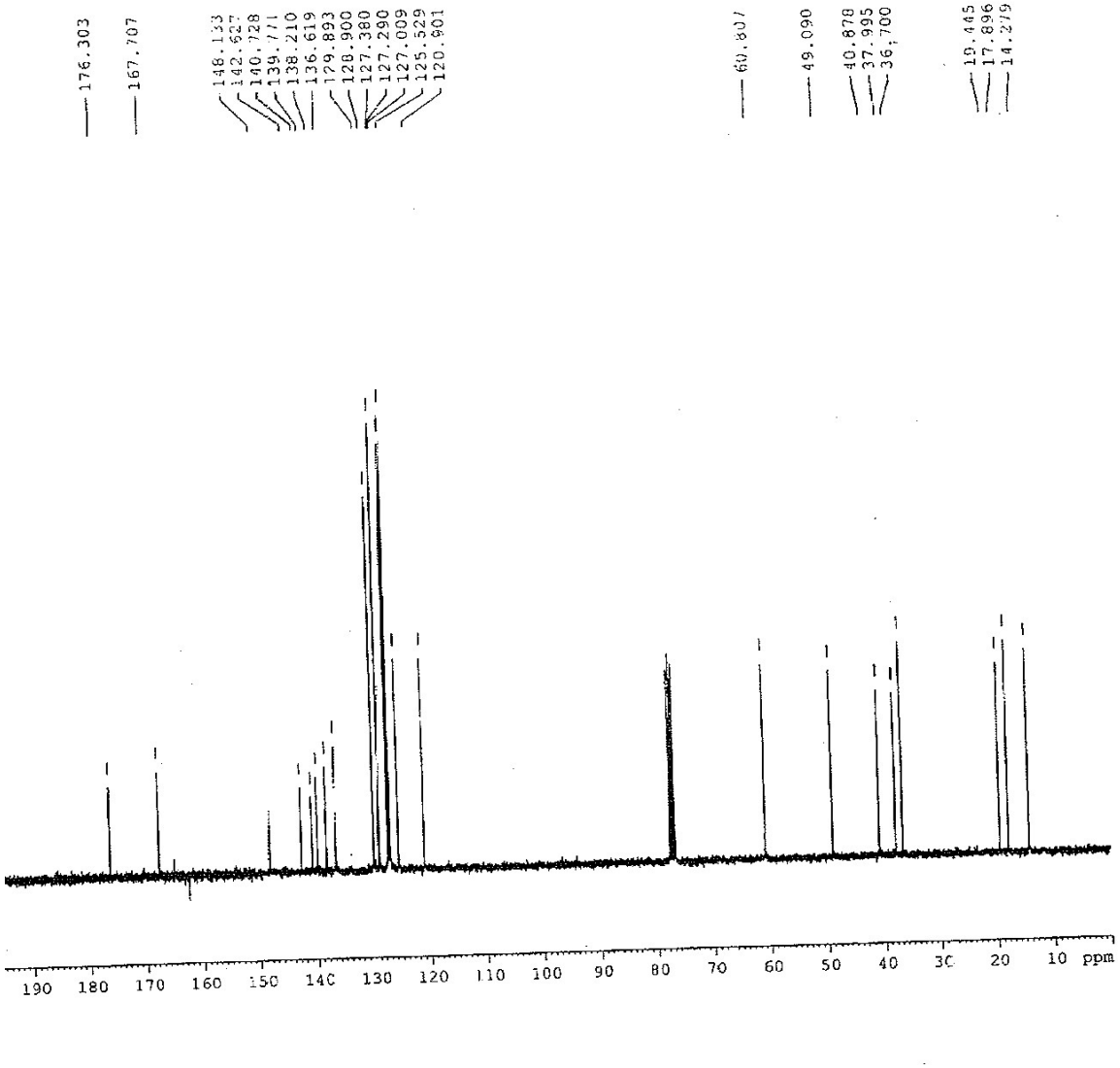
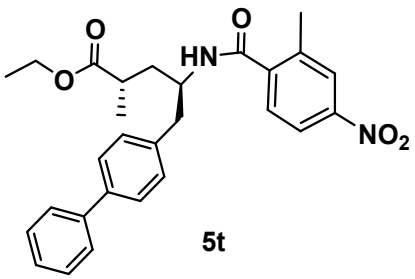


Figure S60: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5t.

Mass spectrum of compound 5t



5t

Mass: 474.2

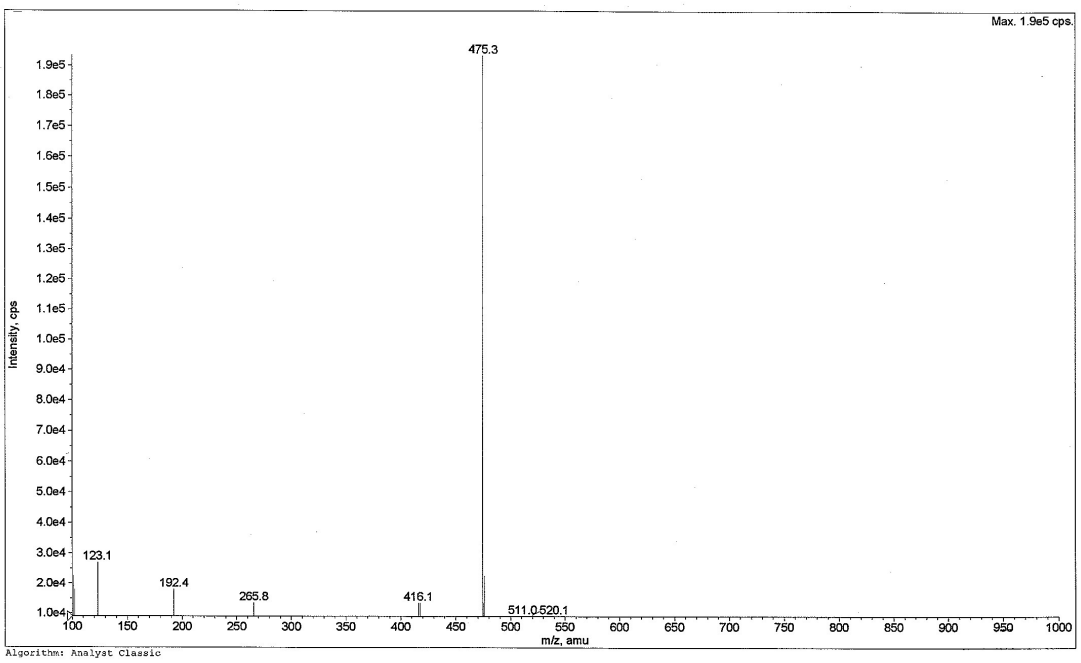


Figure S61: ESI Mass (M+H$^+$) spectrum of compound, 5t.

^{1}H NMR Spectrum of compound 5u

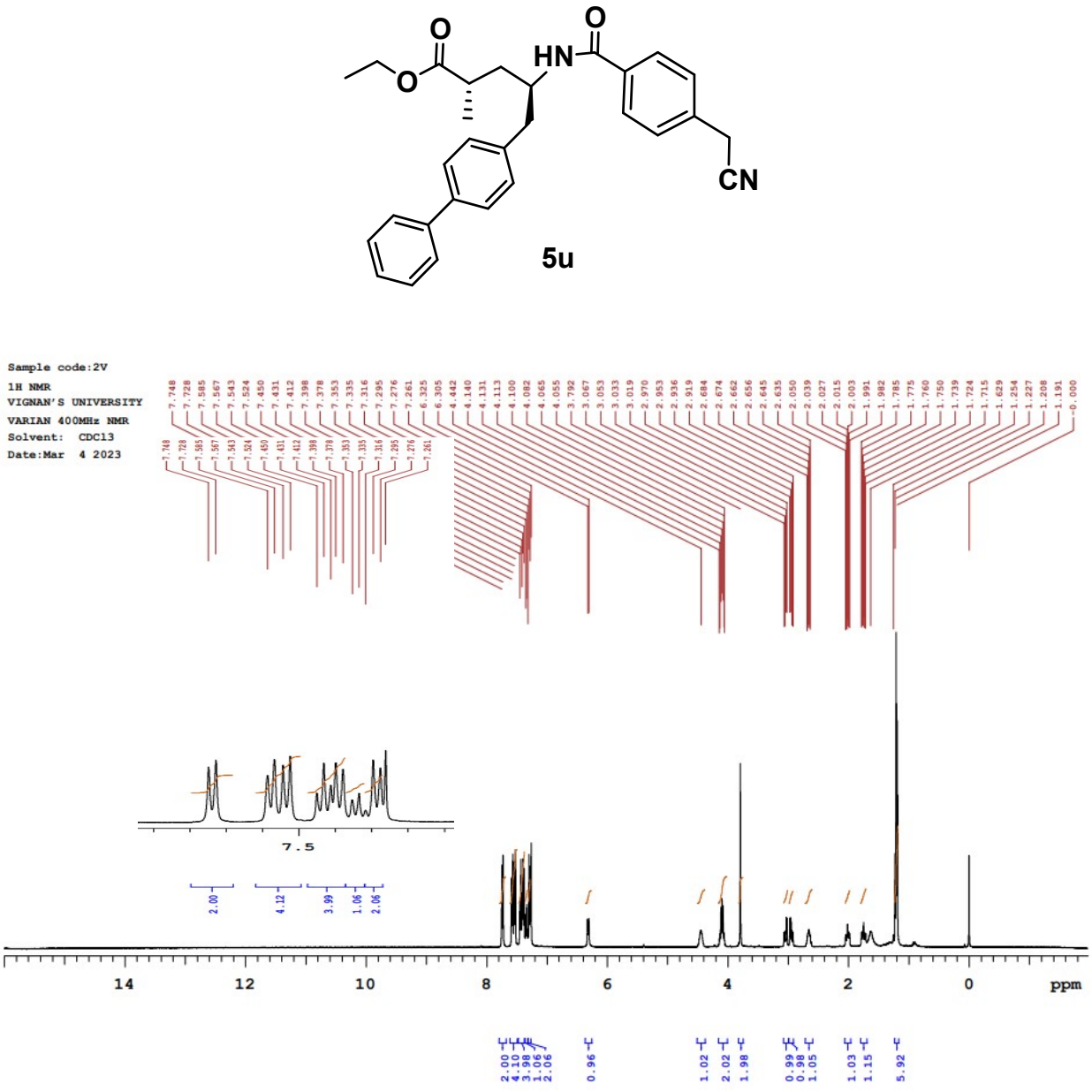
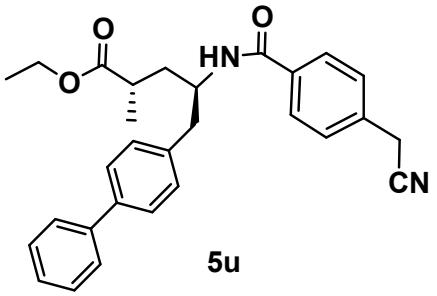


Figure S62: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5u.

^{13}C NMR Spectrum of compound 5u



5u

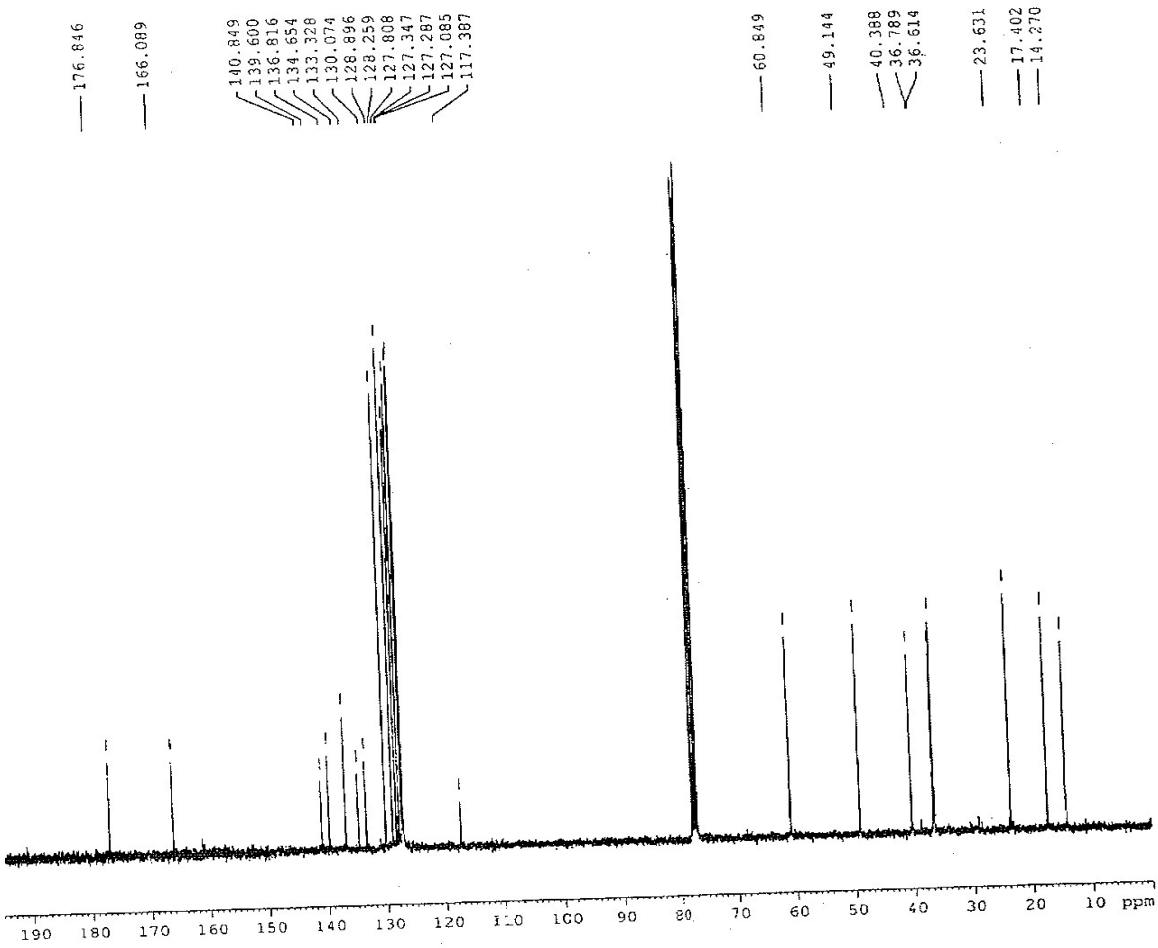
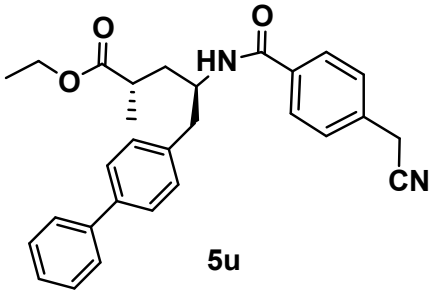


Figure S63: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5u.

Mass spectrum of compound 5u



5u

Mass: 454.2

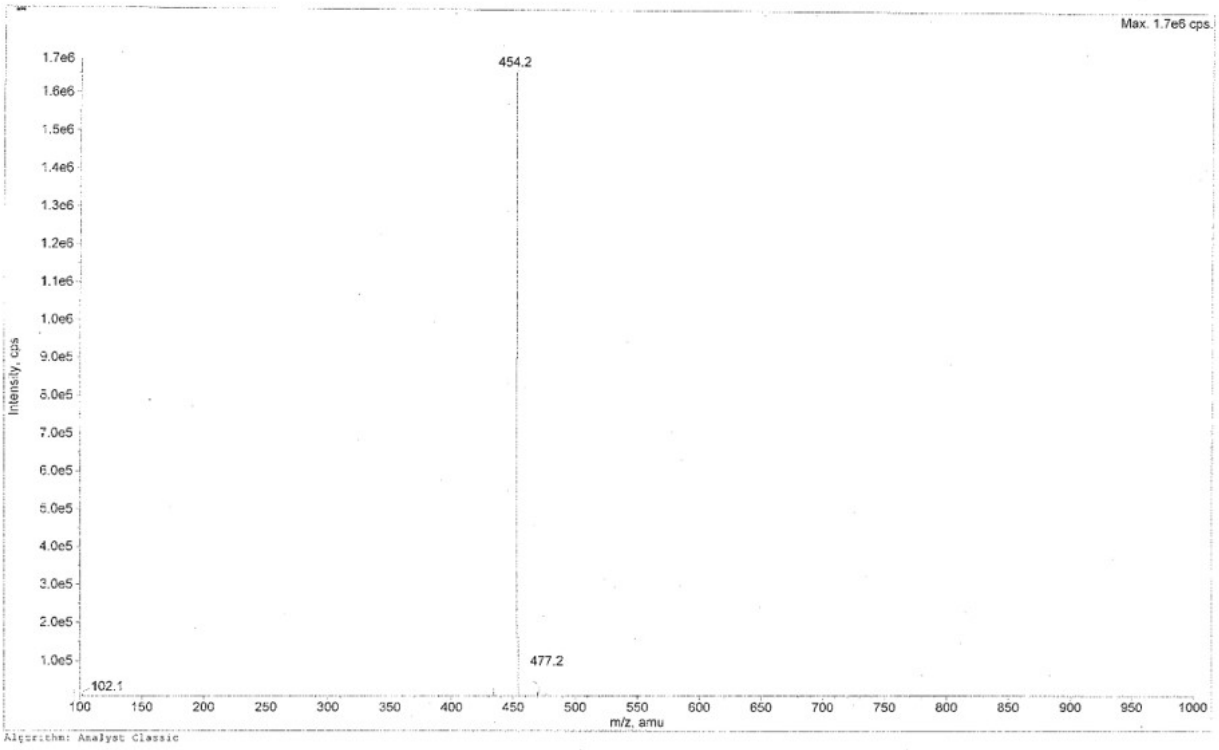
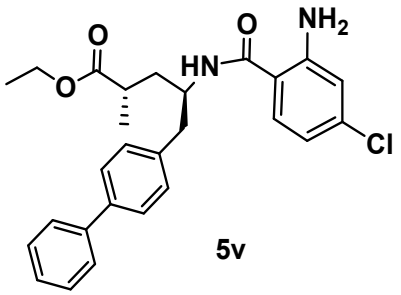


Figure S64: ES-I Mass (*M*+H) spectrum of compound, 5u.

^{1}H NMR Spectrum of compound 5v



5v

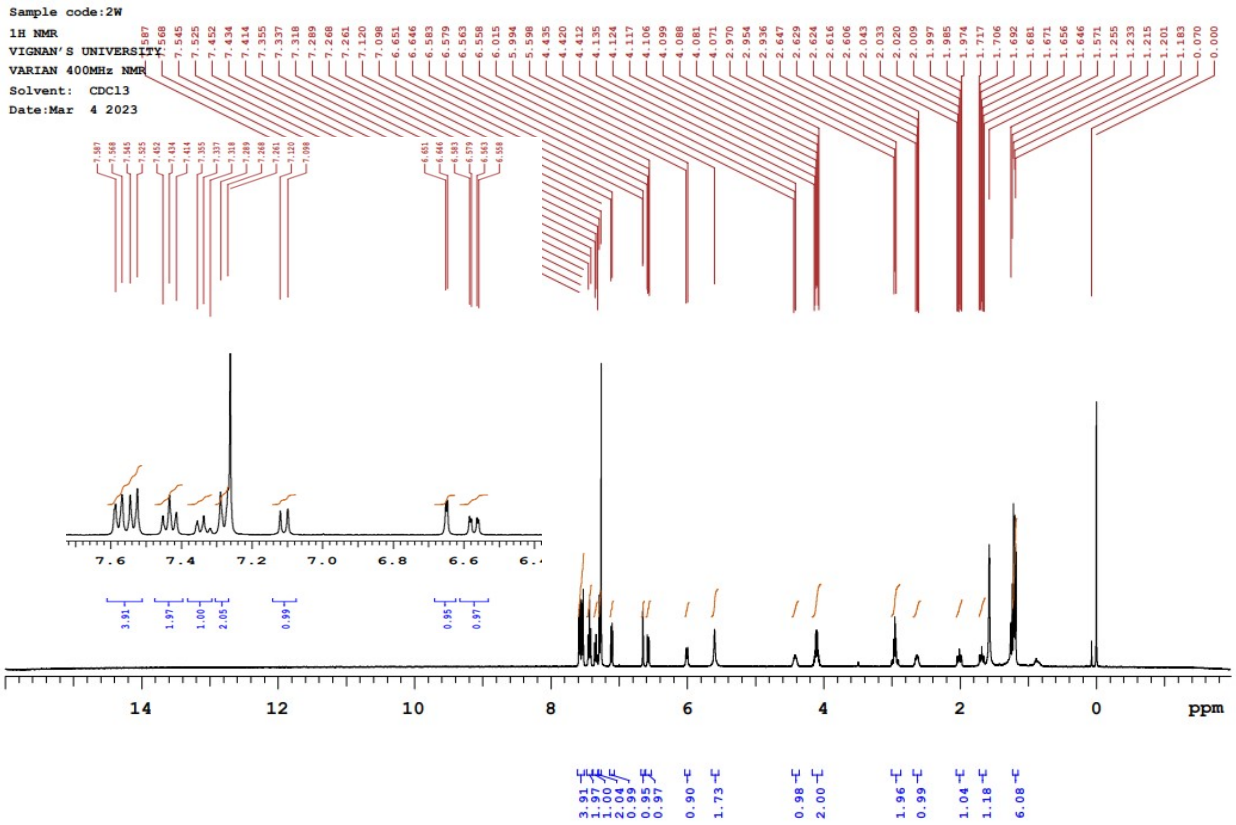


Figure S65: ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound, 5v.

^{13}C NMR Spectrum of compound 5v

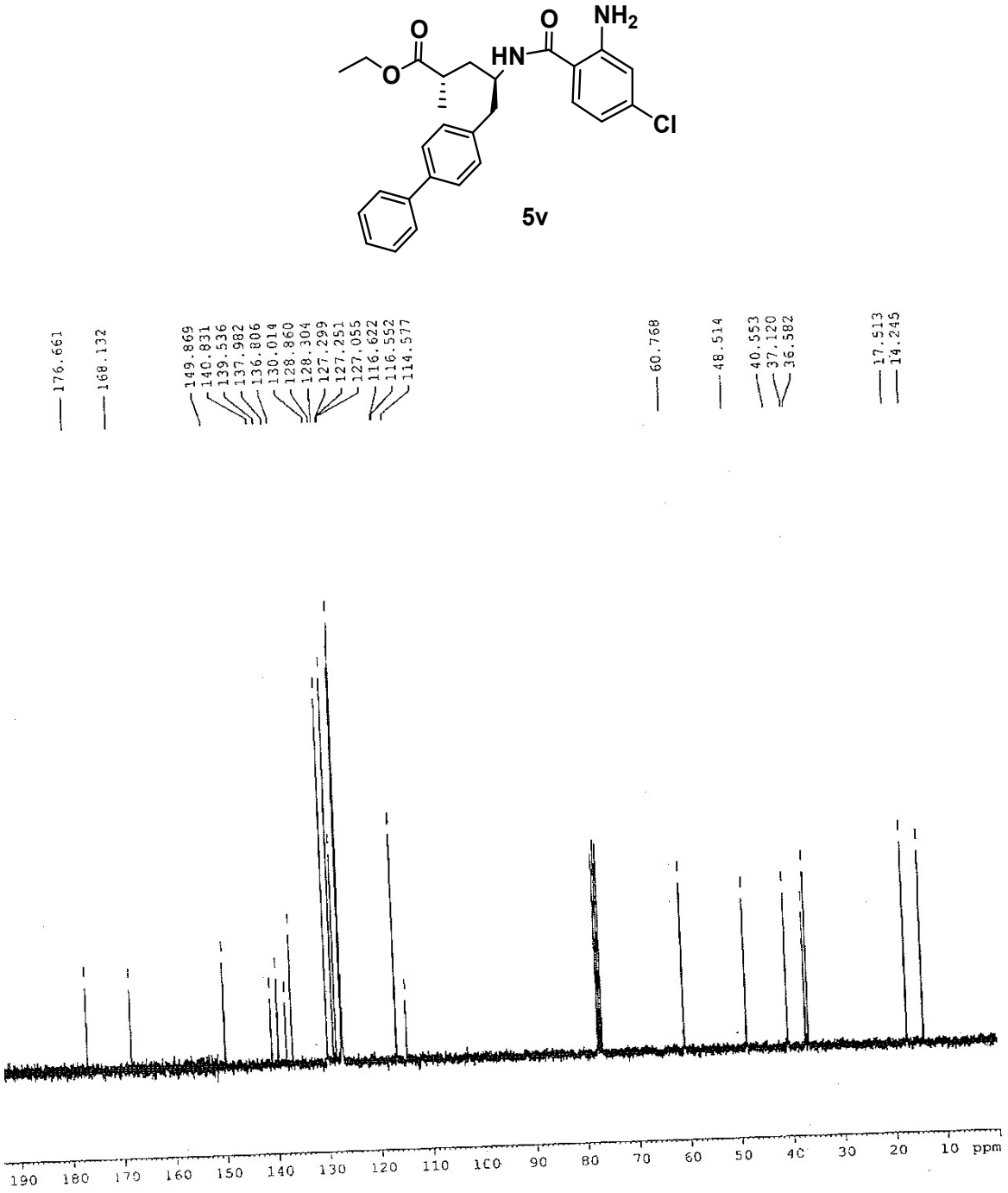
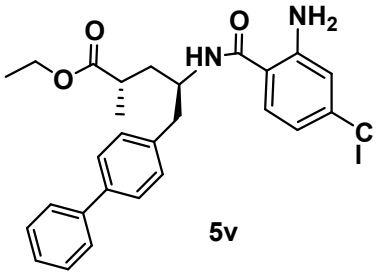


Figure S66: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound, 5v.

Mass spectrum of compound 5v



5v

Mass: 464.1

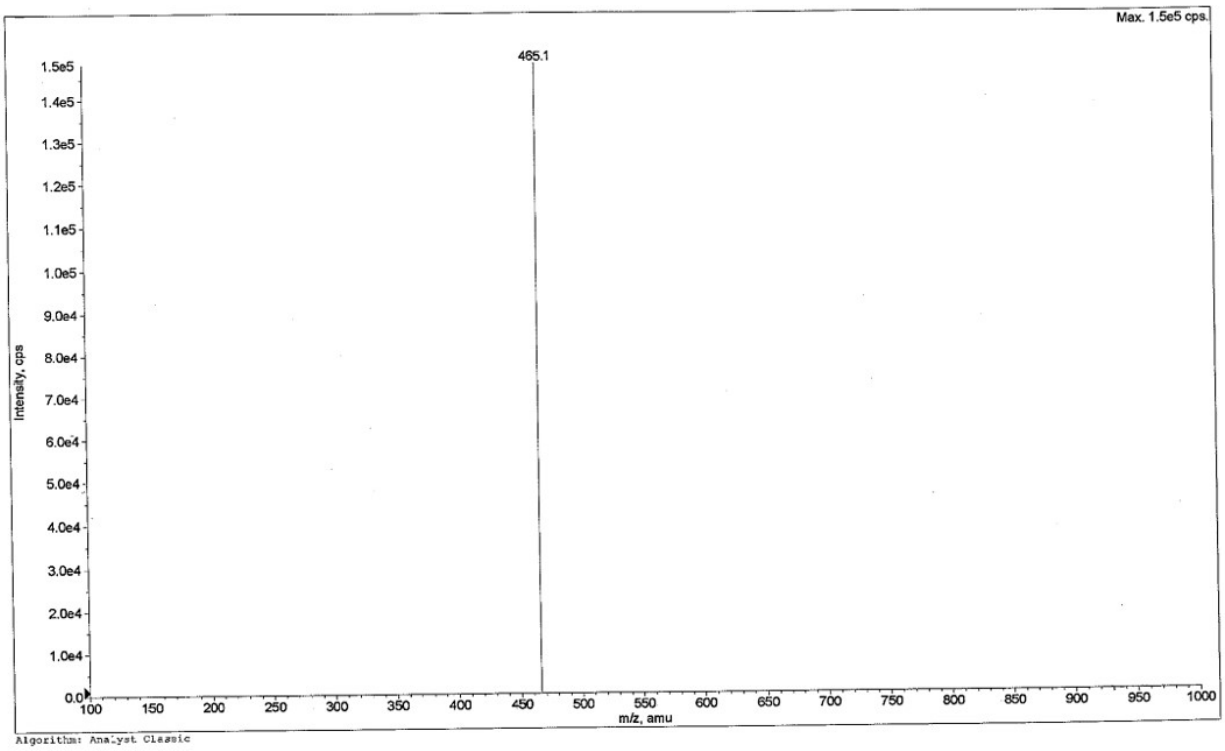


Figure S67: ESI Mass (M+H$^+$) spectrum of compound, 5v.

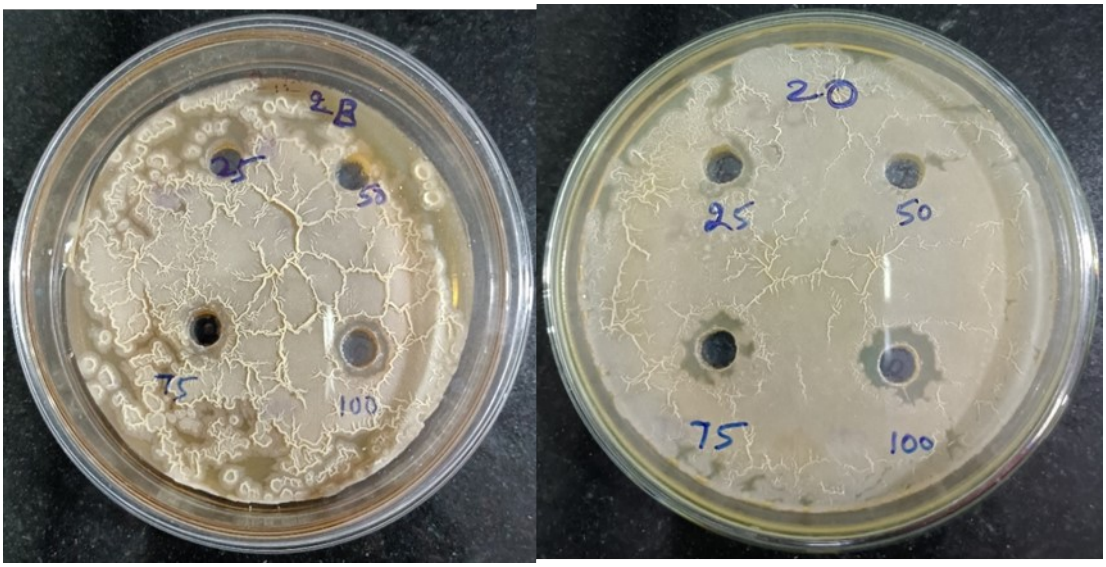
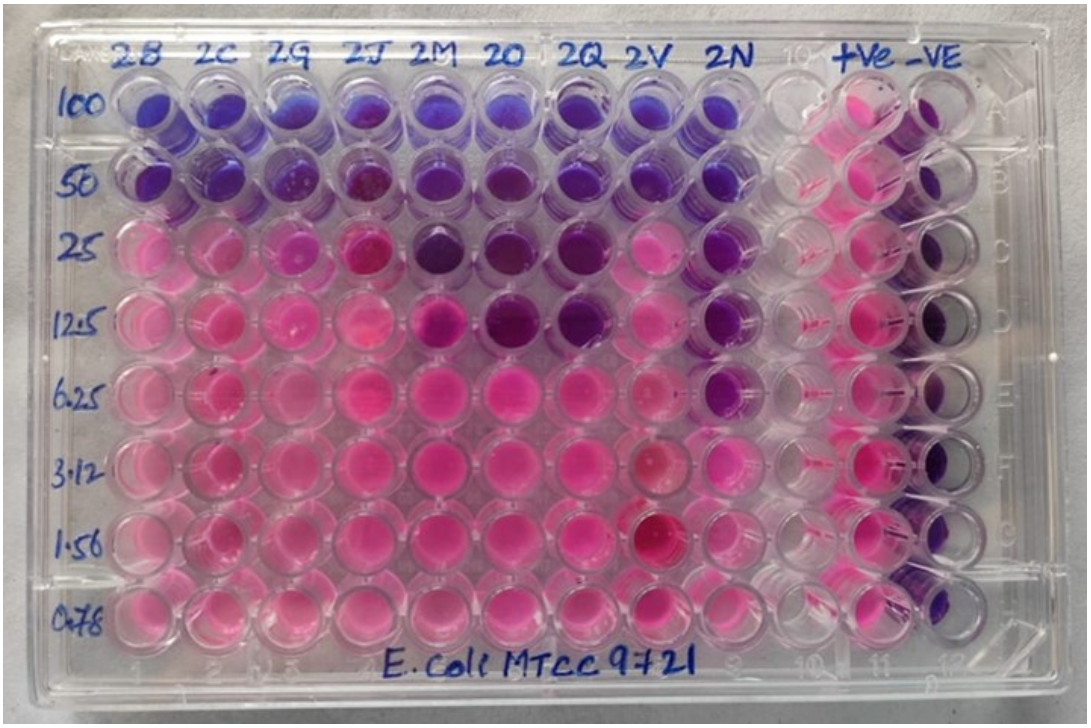


Figure S68. Determination of antifungal activities values for the compounds 5b, and 5n and codes for 2B, and 2O, respectively using Candida albicans *Fungi*.



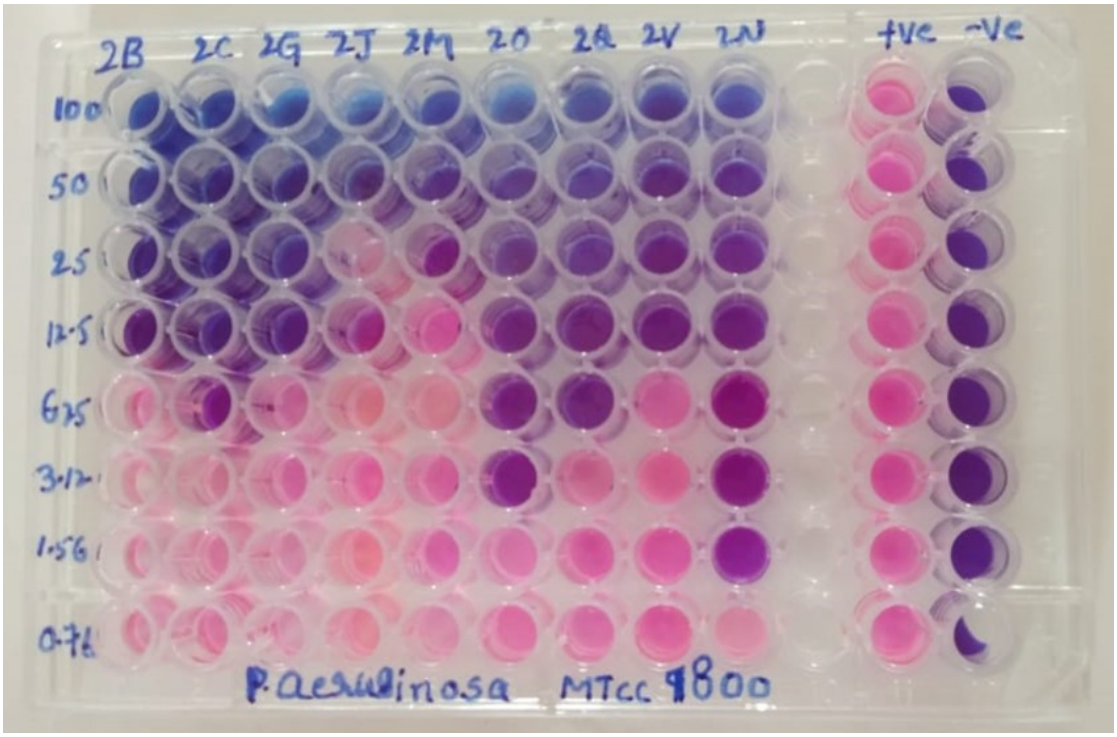


Figure S69. Determination of antibacterial activities MIC values for the compounds 5b, 5c, 5g, 5i, 5l, 5m, 5n, 5p and 5u and codes for 2B, 2C, 2G, 2J, 2M, 2O, 2Q, 2V and 2N, respectively using *E. coli* and *P. aeruginosa* bacteria.

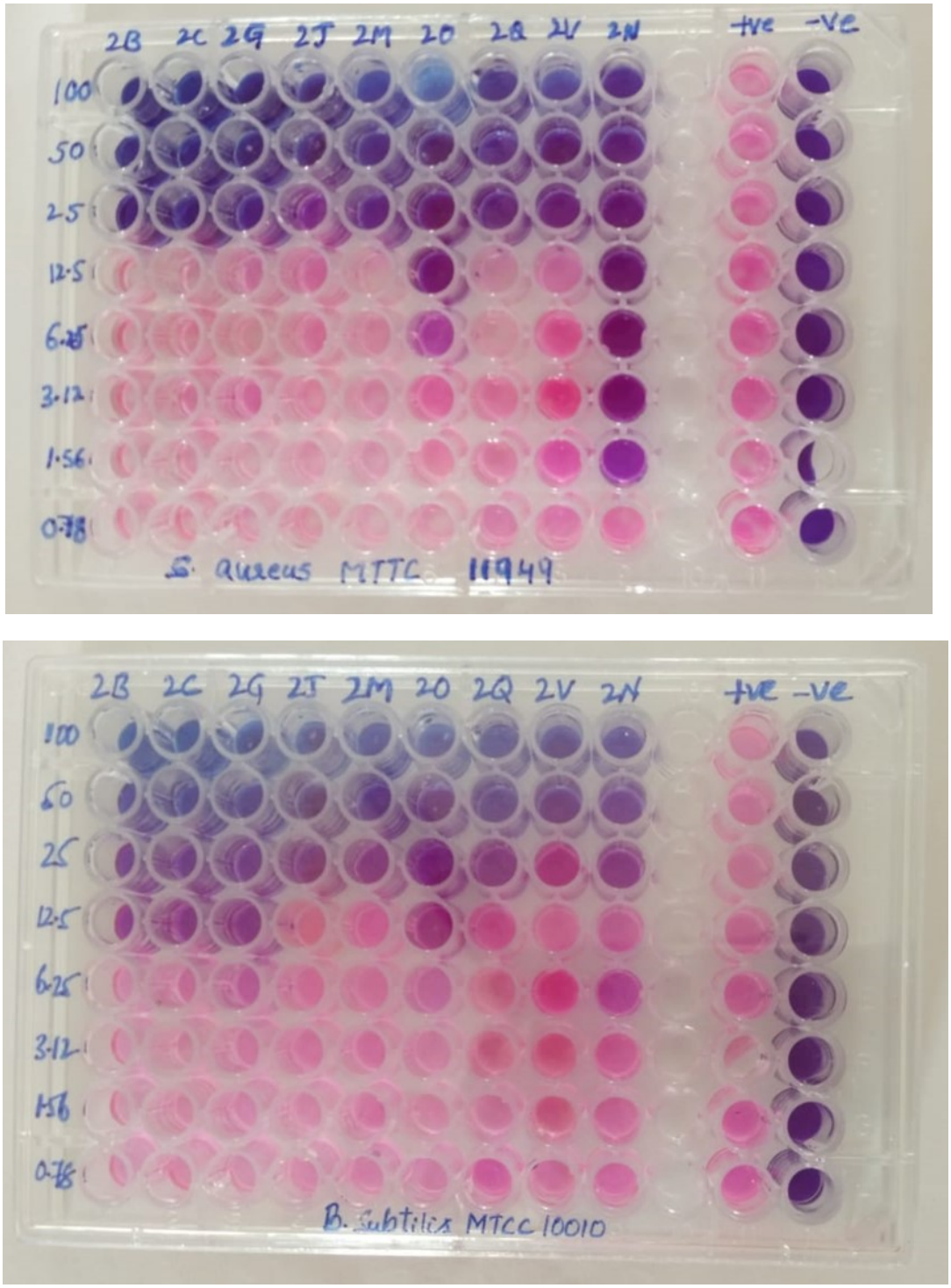


Figure S70. Determination of antibacterial activities MIC values for the compounds 5b, 5c, 5g, 5i, 5l, 5m, 5n, 5p and 5u and codes for 2B, 2C, 2G, 2J, 2M, 2O, 2Q, 2V and 2N, respectively using *S. aureus* and *B. subtilis* bacteria.