Furan-based Thiamine Antagonists for Pyruvate Dehydrogenase: SAR Investigation, Biochemical Evaluation and Computational Analysis

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Comparison of human and porcine PDH E1

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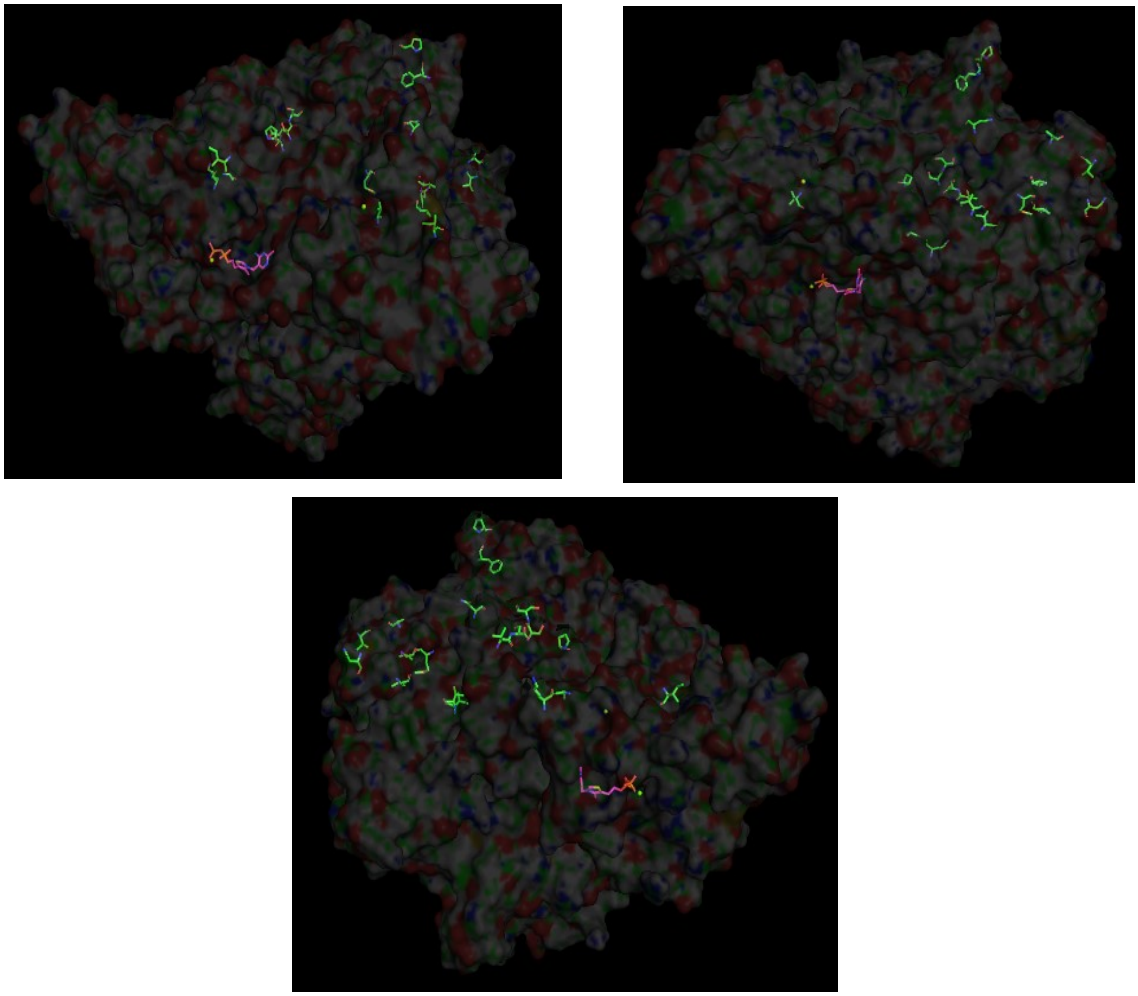


Figure S1. **Similarity between human and porcine PDH E1. (Top)** NCBI Protein Blast Alignment of PDH E1 α (**left**) and b (**right**) subunits with query being human and subject being porcine. **(Bottom)** The amino acid residues that are different between human PDH E1 and porcine PDH E1 are highlighted (green carbons) and shown to be distal to the active site (where TPP is accommodated – purple carbons). Three views at different angles are shown; Mg^{2+} shown as yellow-green sphere.

Computational docking (Methods and Results)

Docking of TPP and compounds were executed using CCDC GOLD docking program with PDB: 6CFO and 6U3J for human PDH E1 and human OGDH E1 respectively. The TPP or equivalent ligand were selected as the binding site. Our molecules were generated using Mercury. GA runs were set at 20 and was user defined with population size of 200 and 200000 number of operations. No early termination was permitted. Similarity and scaffold constraint to the original ligand were implemented on our compounds to mimic their binding positions. CHEMPLP and GoldScore were the docking scoring and rescoring respectively.[1] Interactions between docked compounds and protein models are shown using CCDC GOLD.

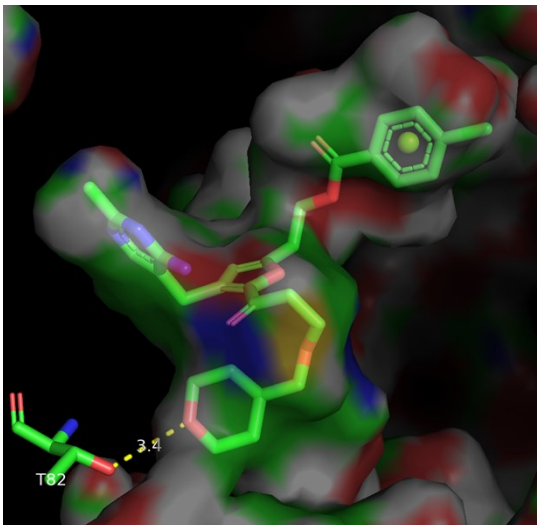


Figure S2. Molecular docking of **24i** in human PDH E1 (PDB: 6CFO) where the bulky C2-substituent is projected into the C2-pocket and the terminal oxygen atom forms hydrogen bond with a threonine; Mg^{2+} shown as a yellow-green sphere.

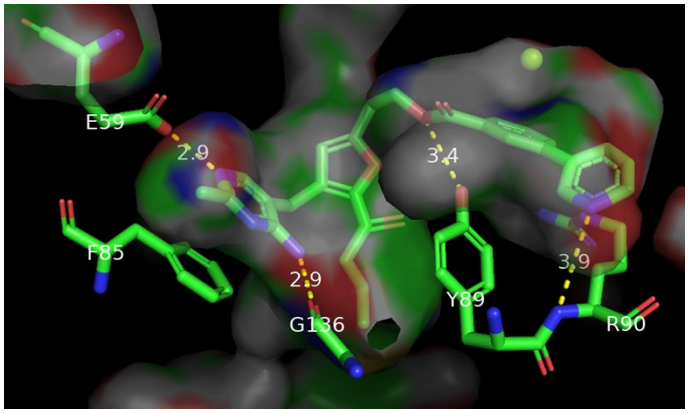


Figure S3. Individual interactions (summarised in Figure 2b) between **25** and human PDH E1 TPP pocket from molecular docking with GOLD; Mg^{2+} shown as yellow-green sphere.

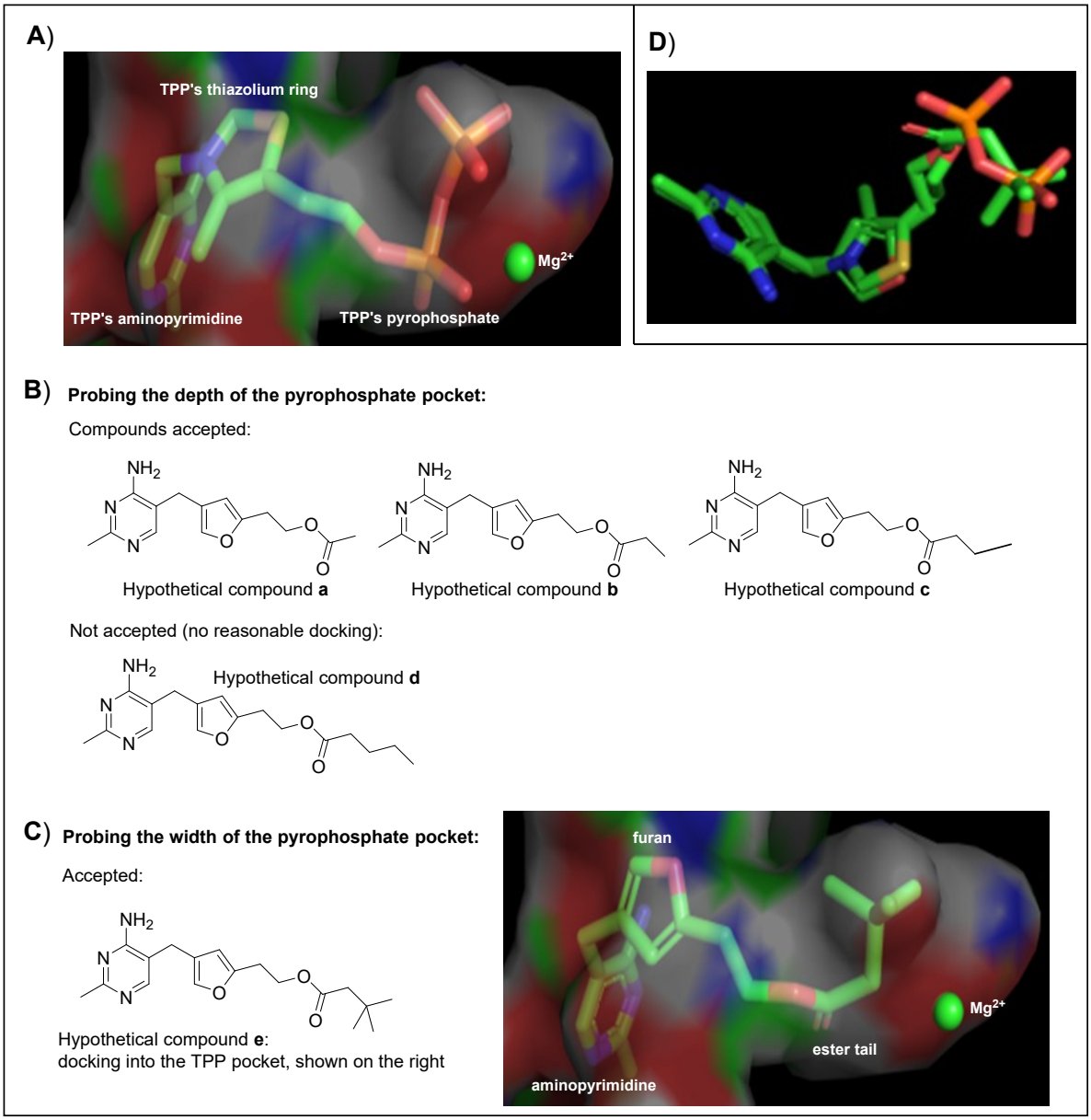


Figure S4. Investigation of the size of the OGDH E1 pyrophosphate pocket. (**A**) Binding mode of TPP in human OGDH E1 (PDB: 6U3J). (**B**) Hypothetical compounds with increasing lengths of the ester aliphatic tail (**a-d**) were docked into the active site: **c** was the longest one that could still be accepted. (**C**) Hypothetical compound **e** (a bulkier version of **c**) could be accepted by the pocket, and **e** was docked in the TPP pocket. The *tert*-butyl group of the ester tail was shown to almost come into contact with the 'ceiling' of the pyrophosphate pocket, and this provides the explanation why hypothetical compound **d** was too long to be accommodated in the pyrophosphate pocket. (**D**) Hypothetical compound **e** was overlaid onto TPP showing that the *tert*-butyl group of **e** is similar in size and position to the terminal phosphoryl group of TPP.

Inhibition of Cell Growth (Methods and Results)

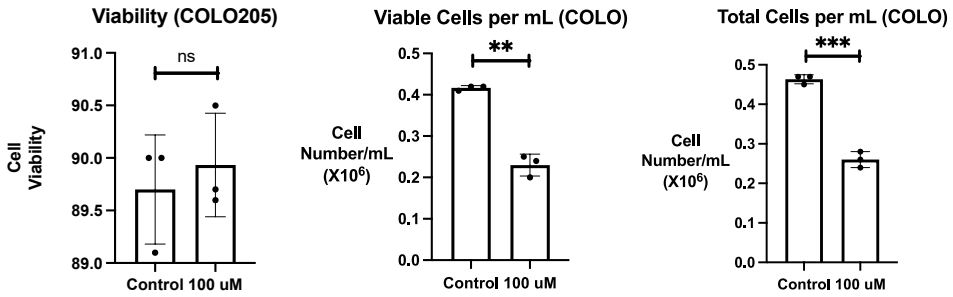
Protocol for viability/cell count assay

Cells were seeded at $2.5x10^5$ cells (except COLO205 at $5x10^5$ cells) per well in Nunc™ Cell-Culture 6 well plates, and the volume adjusted to a final volume of 2 mL using the appropriate cell culture medium. Cells were then pulsed with either **33** (100 mM stock solution in DMSO) to a final concentration of 100 µM or DMSO alone. Cells were incubated for 48 hours at 37 °C and 5% CO_2. The medium was then placed into a centrifuge tube, the flasks and cells were washed with PBS (phosphate buffered saline; water, NaCl, KCl, Na_2HPO_4, KH_2PO_4; Fisher Scientific, Loughborough, UK). Each well was treated with Gibco 0.25% Trypsin- 1 mM EDTA (0.5 mL) per well and returned to the incubator for 3 minutes to facilitate dissociation from vessel. The trypsin was quenched by addition of cell media (1.5 mL) and the contents of each well were transferred to the centrifuge tube, centrifuged (1000 g, 4 °C, 3 min) and resuspended in media (5 mL). The viability and cell concentration were then assessed using a Vi-CELL™ XR Cell Viability Analyzer.

		Viability % (Mean ± SD)[a]	Viable Cells (Mean $x10^6$ cell/ml ± SD)[a]	Total Cells (Mean $x10^6$ cell/ml ± SD)[a]
COLO-205	Treated	89.9 ± 0.5	0.230 ± 0.026	0.260 ± 0.020
	Control	89.7 ± 0.5	0.417 ± 0.006	0.463 ± 0.012
HEK	Treated	78.3 ± 12.6	0.038 ± 0.010	0.048 ± 0.004
	Control	96.5 ± 2.1	0.127 ± 0.021	0.133 ± 0.015
MDA-MB-231	Treated	95.2 ± 6.5	0.039 ± 0.010	0.042 ± 0.012
	Control	94.8 ± 2.7	0.104 ± 0.014	0.113 ± 0.012
PANC-1	Treated	91.9 ± 2.2	0.091 ± 0.016	0.100 ± 0.018
	Control	94.9 ± 1.6	0.098 ± 0.278	0.101 ± 0.025

[a] Data are the means of measurements in three technical replicates.

Colo-205:



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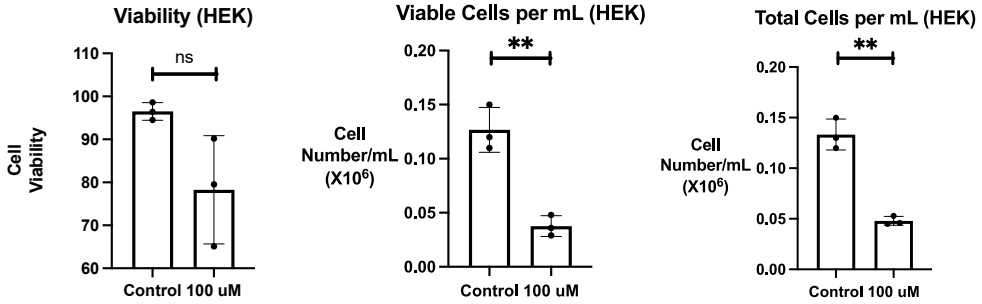

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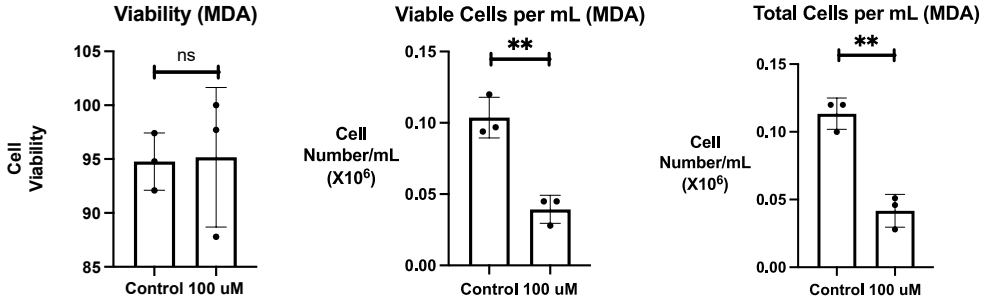

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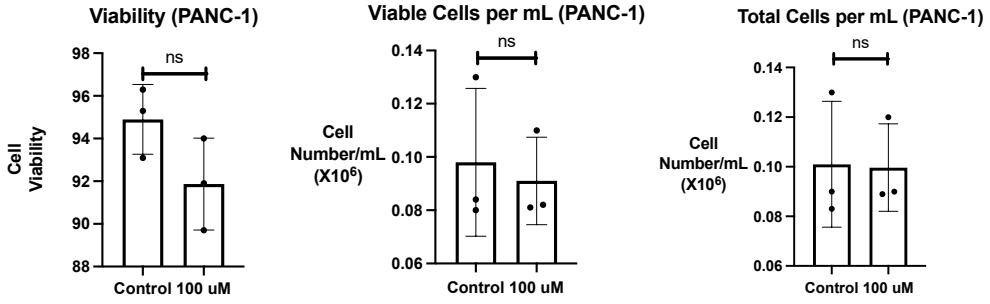


Figure S5. **Effects of amide 33 on four fast-growing human cell lines: Colo-205, HEK, MDA-MB-231 and PANC-1.** See above for the experimental method. Left: cell viability percentage of each sample. Middle: number of viable cells per mL. Right: total cells per mL. Measurements in three technical replicates. Statistical analysis was performed using an unpaired t-test with Welch correction (**** P≤0.0001, *** P≤0.001, ** P≤0.01, * P≤0.05).

Enzyme assays (Methods and Results)

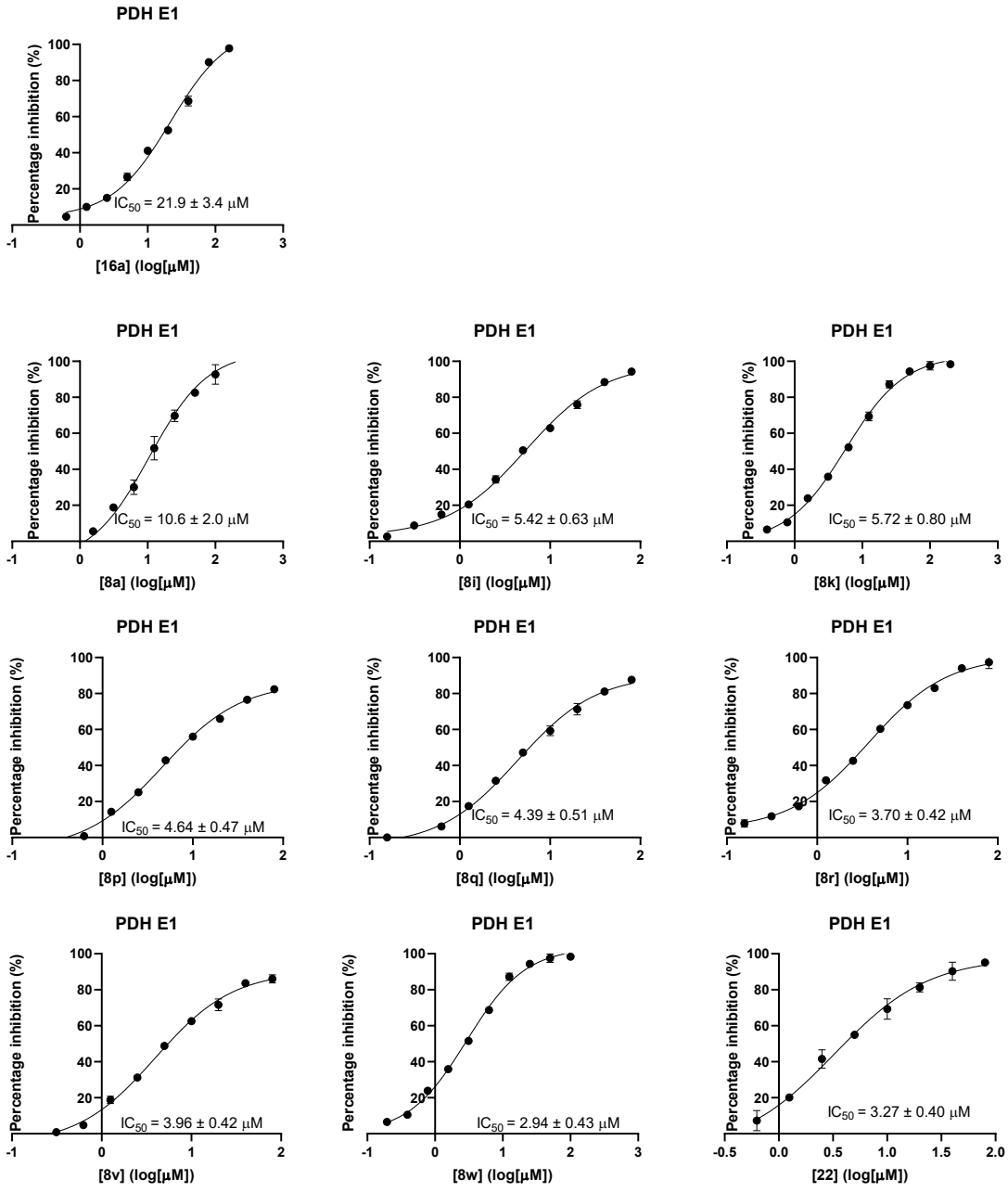
PDH E1 inhibitory activity assay. Porcine PDH E1 was purchased from Sigma. Its activity was determined by monitoring 2,6-dichlorophenolindophenol (DCPIP) reduction at 600 nm using a microplate reader (CLARIOstar) and conducted as described[2] with some modifications. The percentage inhibition of compounds against porcine PDH E1 was assayed at the specified final concentration. The reaction buffer (50 mM KH_2PO_4 and 1 mM $MgCl_2$, pH 7) contained TPP at the specified concentration, 0.25 mM DCPIP, and 2 mg/ml porcine PDH E1. The reaction mixture was preincubated at 37 °C for 30 min, then the reaction was initiated by adding pyruvate to a final concentration of 50 mM. To determine the half-maximal inhibitory concentration (IC_{50}), TPP concentration was lowered to 10 μM, and inhibitor concentration was varied (0.4-200 μM). Specific activity was calculated using the molar extinction coefficient of DCPIP, 21 mM^{-1} cm^{-1}.[3] The enzyme IC_{50} values were calculated from non-linear regression curve fitting using GraphPad Prism. K_M(TPP) was found to be 0.05 μM, consistent with the reported value.[4]

***S. cerevisiae* PDC inhibitory activity assay.** *S. cerevisiae* PDC was purchased from Sigma. Its activity was determined by monitoring DCPIP reduction at 600 nm using a microplate reader (CLARIOstar) and conducted as described above with some modifications. The percentage inhibition of compounds was assayed at a final concentration of 200 μM. The reaction buffer (50 mM KH_2PO_4 and 1 mM $MgCl_2$, pH 7) contained 200 μM TPP, 0.27 mM DCPIP, and 0.15 mg/ml *S. cerevisiae* PDC. The reaction mixture was preincubated at 37 °C for 60 min, then reaction was initiated by adding pyruvate to a final concentration of 70 mM. To determine the half-maximal inhibitory concentration (IC_{50}) TPP concentration was set at 200 μM, and inhibitor concentration was varied (8-4000 μM). Specific activity was calculated using the molar extinction coefficient of DCPIP, 21 mM^{-1} cm^{-1}.[4] The enzyme IC_{50} values were calculated as described for the PDH E1 assay.

***E. coli* OGDH E1 inhibitory activity assay.** *E. coli* OGDH E1 was from our previous work[5] and had been donated by R. Frank. Its activity was determined by monitoring DCPIP reduction at 600 nm using a microplate reader (CLARIOstar) and conducted as described[5] with some modifications. The percentage inhibition of compounds against *E. coli* OGDH E1 was assayed at a final concentration of 50 μM. The reaction buffer (50 mM KH_2PO_4 and 2 mM $MgCl_2$, pH 7) contained 50 μM TPP, 0.5 mM DCPIP, and 6.7 mg/ml *E. coli* OGDH E1. The reaction mixture was preincubated at 37 °C for 60 min, then reaction was initiated by adding α-ketoglutarate to a final concentration of 10 mM. To determine the IC_{50}, TPP concentration was lowered to 40 μM, and inhibitor concentration was varied (2-1000 μM). Specific activity was calculated using the molar extinction coefficient of DCPIP, 21 mM^{-1} cm^{-1}.[4] The enzyme IC_{50} values were calculated as described for the PDH E1 assay.

***A. viridans* PO inhibitory activity assay.** *A. viridans* PO and horseradish peroxidase were purchased from Sigma. *A. viridans* PO activity was determined by monitoring appearance of quinoneimine dye at 550 nm using a microplate reader (CLARIOstar) and conducted as described[6] with some modifications. The percentage inhibition of compounds against *A. viridans* PO was assayed at a final concentration of 50 μM. The reaction buffer (50 mM KH_2PO_4 and 10 mM $MgCl_2$, pH 5.9) contained 50 μM TPP, 10 μM flavin adenine dinucleotide (FAD), 0.15% 4-aminoantipyrine, 0.3% N-ethyl-N-(2-hydroxy-3-sulfopropyl)-m-toluidine (EHSPT), 50 μg/mL horseradish peroxidase and 0.35 U/mL *A. viridans* PO. The reaction mixture was preincubated at 37 °C for 30 min, then reaction was initiated by adding pyruvate to a final concentration of 50 mM. To determine the IC_{50}, inhibitor concentration was varied (2-1000 μM) with TPP concentration at 40 μM. 1 unit of PO activity is defined as 1 μmol of hydrogen peroxide produced per minute. The enzyme IC_{50} values were calculated as described for the PDH E1 assay.

***Z. mobilis* PDC inhibitory activity assay.** *Z. mobilis* PDC was expressed and purified following a reported method.[7] *Z. mobilis* PDC activity was determined by monitoring reduced nicotinamide adenine dinucleotide (NADH) consumption at 340 nm using a microplate reader (CLARIOstar) and conducted as described[7] with some modifications. The percentage inhibition of compounds was assayed at a final concentration of 50 µM. The reaction buffer (50 mM MES-KOH and 5 mM $MgCl_2$, pH 6.5) contained 50 µM TPP, 150 µM NADH, 10 U/ml alcohol dehydrogenase (ADH) and 0.5 µM of active sites of *Z. mobilis* PDC. To determine the IC_{50}, inhibitor concentration was varied (0.4-200 µM) with TPP concentration at 40 µM. The reaction mixture was preincubated at 37 °C for 60 min, then reaction was initiated by adding pyruvate to a final concentration of 10 mM. The enzyme IC_{50} values were calculated as described for the PDH E1 assay.



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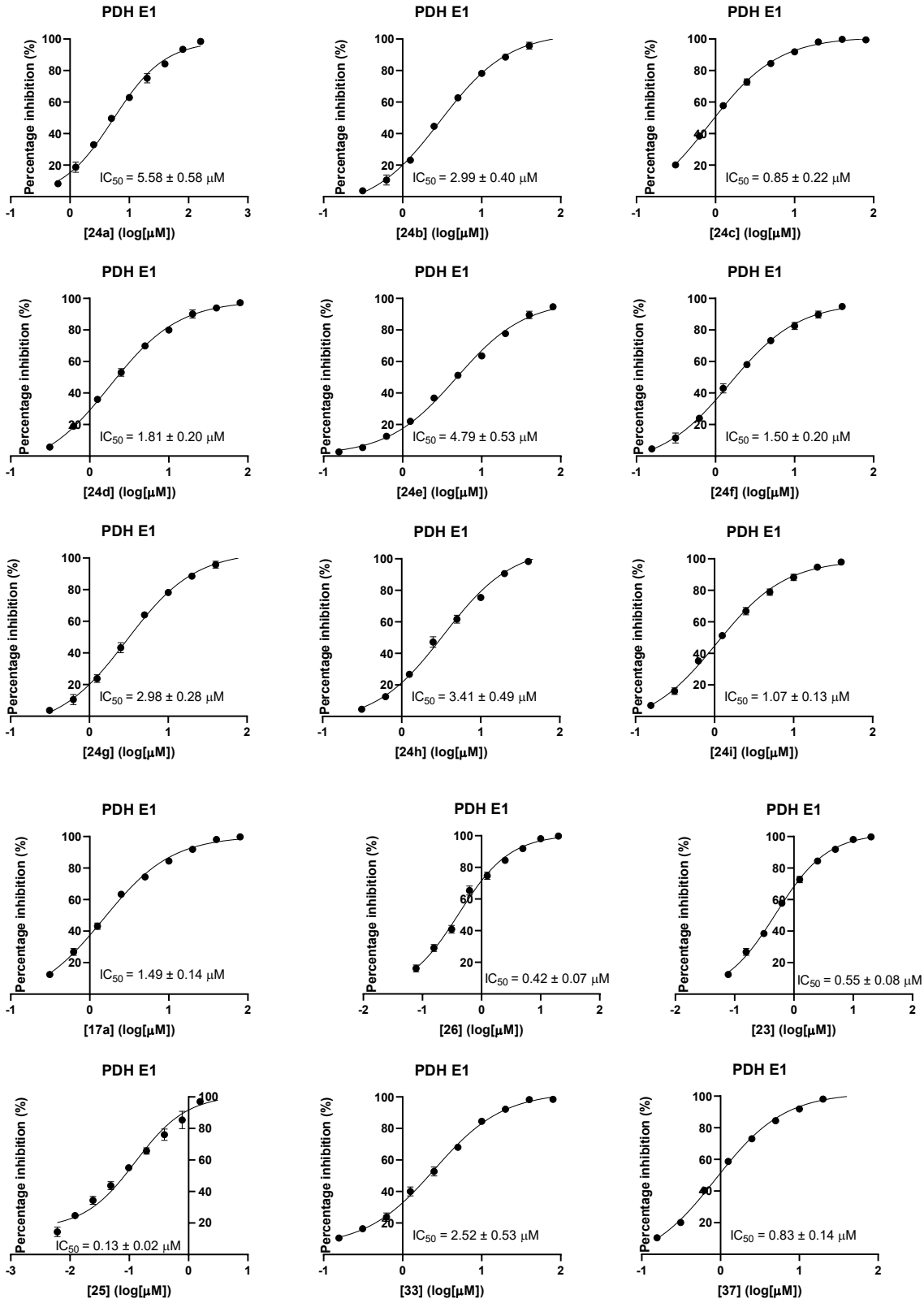

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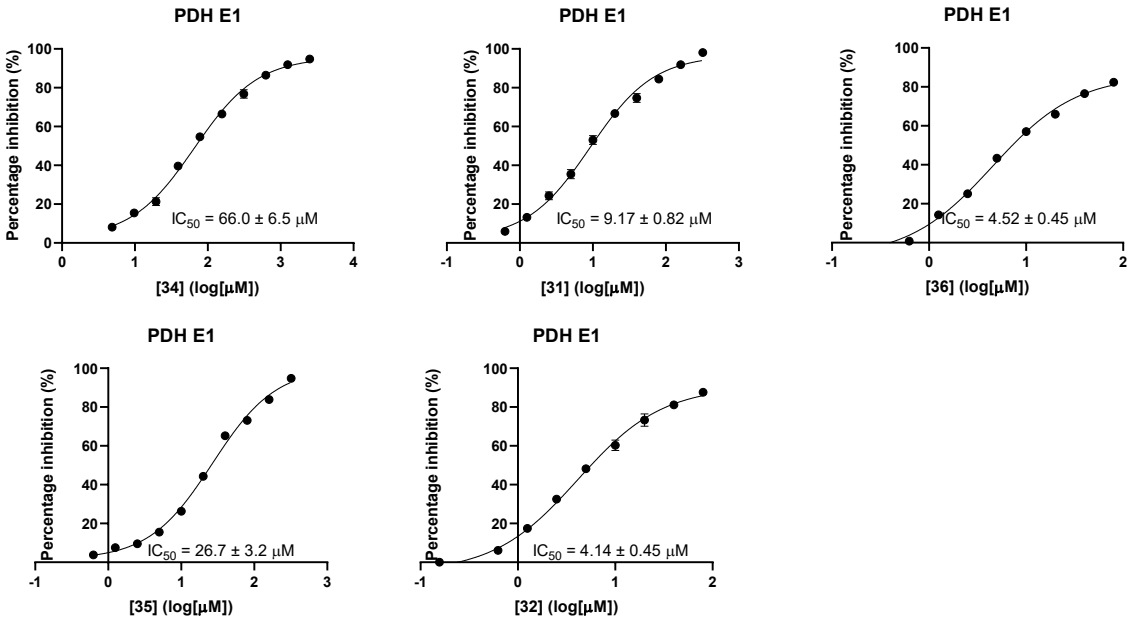


Figure S6. IC_{50} values for compounds on PDH E1. Measurements were made in three technical replicates under assay conditions as described above. Where the error bars are not visible, they are smaller than the symbols. Best-fit nonlinear regression curves are shown.

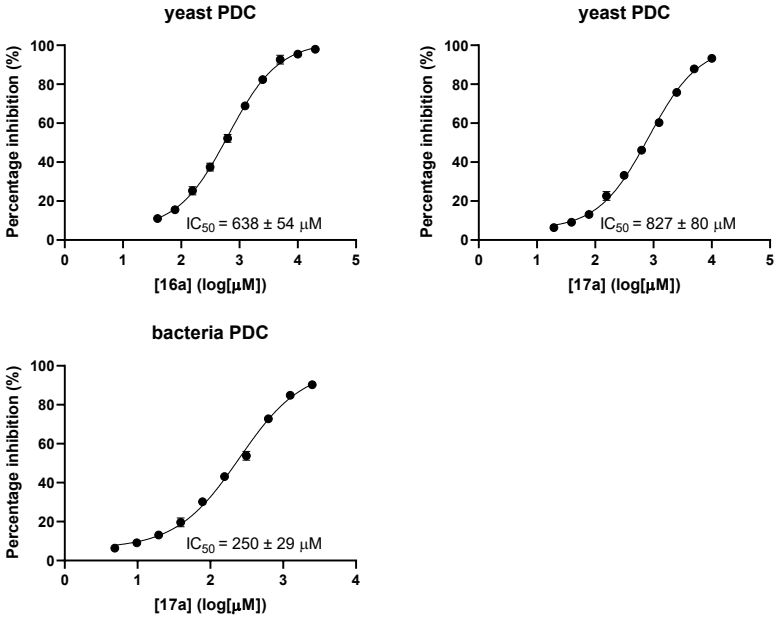


Figure S7. IC_{50} values for compounds on yeast and *Z. mobilis* PDC. Measurements were made in three technical replicates under assay conditions as described previously. Where the error bars are not visible, they are smaller than the symbols. Best-fit nonlinear regression curves are shown.

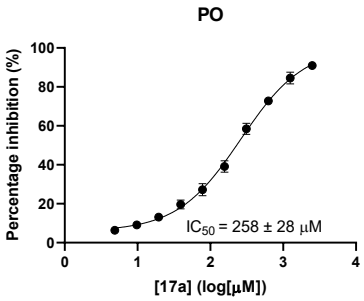


Figure S8. IC_{50} values for compounds on PO. Measurements were made in three technical replicates under assay conditions as described previously. Where the error bars are not visible, they are smaller than the symbols. Best-fit nonlinear regression curves are shown.

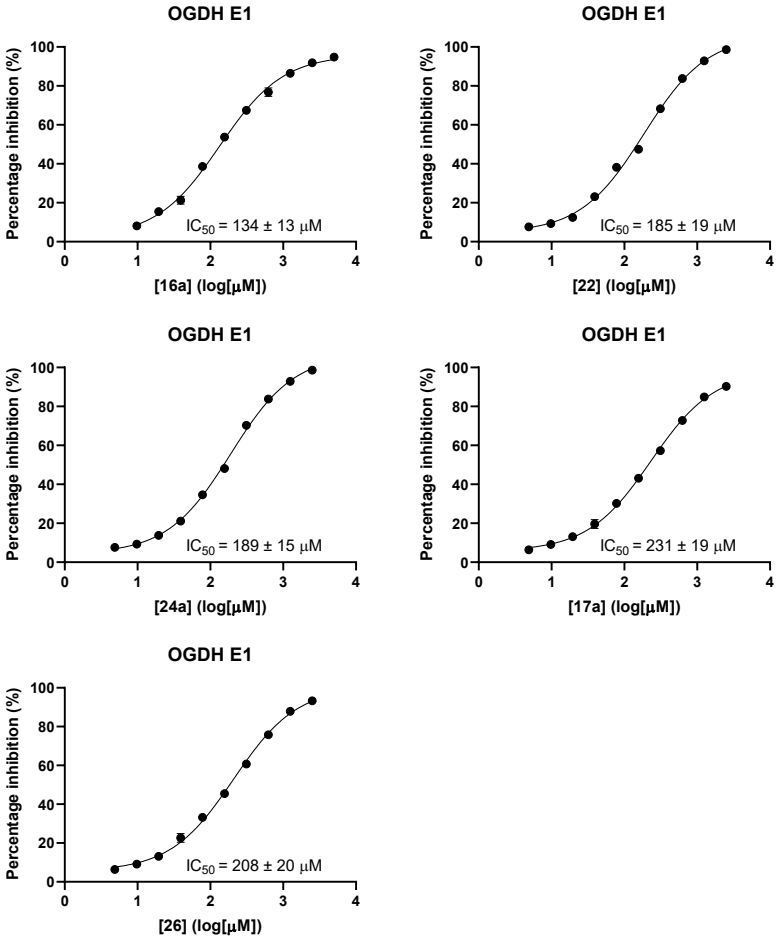


Figure S9. IC_{50} values for compounds on OGDH E1. Measurements were made in three technical replicates under assay conditions as described previously. Where the error bars are not visible, they are smaller than the symbols. Best-fit nonlinear regression curves are shown.

General synthesis methods

Oxygen- and moisture-sensitive reactions were carried out in flame-dried glassware under a nitrogen atmosphere. Unless otherwise stated, all chemicals and reagents were purchased from commercial suppliers and used without further purification. Reaction progress was monitored by analytical thin-layer chromatography (TLC). TLC was conducted using Merck glass plates with silica Kieselgel 60 F254 of thickness 0.25 mm and visualised under 254 nm UV lamp or potassium permanganate staining solution (with light heating). Flash column chromatography was carried out in the indicated solvent system using prepacked silica gel cartridges for use on the Biotage Purification System. All solvents were removed under reduced pressure using a Büchi rotary evaporator with dry ice traps.

All yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. Compounds subjected to biological assays were characterised by, at minimum, ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy and HRMS. ^{1}H NMR spectra were recorded at 400 MHz or 700 MHz in $CDCl_3$, CD_3OD or CD_3SOCD_3 solution on a Bruker 400 MHz or 700 MHz spectrometer and chemical shifts were recorded in parts per million (ppm). ^{13}C NMR spectra were recorded on either a Bruker 400 MHz or 700 MHz spectrometer. ^{19}F NMR spectra were recorded on either a Bruker 400 MHz or 700 MHz spectrometer. Resonances are described using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), sext (sextet), m (multiplet), br (broad), dd (doublet of doublets), etc. Coupling constants (*J*) are given in Hz and are rounded to the nearest 0.1 Hz. All NMR data were collected at 25 °C. Mass spectra used electrospray ionisation (ESI). Melting points of compounds were measured using a Reichert machine and are uncorrected. The synthesis and characterisation data for **6**[8], **7**[8], the tosylate of **7**[8], **8a-g**[9], **8h**[10], **8p**[10], **16a**[7] and **28**[7] have been described.

Experimental procedures – Synthesis

General procedure for preparation of 8h-x:

To a stirred solution of the carboxylic acid (0.39 mmol, 1.3 equiv.) and DCC (3 equiv.) in dry DMF (0.2 M) under nitrogen at 0 °C was added DMAP (1.3 equiv.) and **7**[8] (0.3 mmol, 1 equiv.). The resultant mixture was stirred at r.t. for 2 days, diluted with DCM, filtered through cotton wool (to remove DCC/DCU), treated with aqueous phosphate buffer (pH 7), and extracted with DCM. The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield ester **8h-x** as a solid.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 4-sulfamoylbenzoate **8i**

Prepared from 4-sulfamoylbenzoic acid. White solid (34 mg, 27%). m.p. 233-235 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.06 (d, 2H, *J* = 8.7 Hz), 8.05 (s, 1H), 7.97 (d, 2H, *J* = 8.7 Hz), 7.91 (s, 1H), 5.48 (s, 1H), 4.60 (t, 2H, *J* = 6.3 Hz), 3.21 (t, 2H, *J* = 6.3 Hz), 2.43 (s, 1H). ^{13}C NMR (100 MHz, CD_3OD) δ 167.5, 165.1, 162.1, 154.8, 147.8, 144.5, 132.9, 129.7, 126.0, 122.7, 108.5, 63.8, 47.2, 24.8, 23.6. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{17}H_{19}N_7O_4S$: 418.1297; found: 418.1295.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 3-(trifluoromethyl)benzoate **8j**

Prepared from 3-trifluoromethylbenzoic acid. White solid (62 mg, 51%). m.p. 188-190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.17 (s, 1H), 8.15 (d, 1H, *J* = 7.7 Hz), 7.83 (d, 1H, *J* = 7.7 Hz), 7.58 (t, 1H, *J* = 7.7 Hz), 7.43 (s, 1H), 5.67 (br, NH_2), 5.35 (s, 2H), 4.63 (t, 2H, *J* = 6.7 Hz), 3.22 (t, 2H, *J* = 6.7 Hz), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 165.1, 161.9, 156.0, 145.1, 132.7, 131.0 (q, *J* = 33 Hz), 130.8, 129.6 (q, *J* = 4 Hz), 129.1, 126.5 (q, *J* = 3 Hz), 123.5 (q, *J* = 274 Hz), 121.5, 107.9, 63.8, 48.8, 25.7, 25.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.8. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{18}H_{17}F_3N_6O_2$: 407.1443; found: 407.1455.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 3-amino-5-(trifluoromethyl)benzoate **8k**

Prepared 3-amino-5-(trifluoromethyl)benzoic acid. White solid (69 mg, 54%). m.p. 222-223 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.57 (s, 1H), 7.42 (s, 1H), 7.36 (s, 1H), 7.05 (s, 1H), 5.63 (br, NH_2), 5.35 (s, 2H), 4.59 (t, 2H, *J* = 6.6 Hz), 4.16 (br, NH_2), 3.19 (t, 2H, *J* = 6.6 Hz), 2.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 165.3, 161.8, 156.0, 147.2, 145.2, 131.9, 131.7 (q, *J* = 32 Hz), 123.5 (q, *J* = 273 Hz), 121.6, 118.4, 115.8 (q, *J* = 4Hz), 115.3 (q, *J* = 3 Hz), 108.2, 63.6, 48.9, 25.7, 25.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7. IR (neat) ν_{max} 1563, 1597, 1631, 1714, 3144, 3334 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{18}H_{18}F_3N_7O_2$: 422.1552; found: 422.1539.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 2-(2-amino-1,3-thiazol-4-yl)acetate **8l**

Prepared from 2-amino-4-thiazoleacetic acid. White solid (28 mg, 25%). m.p. 169-170 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.05 (s, 1H), 7.77 (s, 1H), 6.30 (s, 1H), 5.47 (s, 2H), 4.35 (t, 2H, *J* = 6.4 Hz), 3.51 (s, 2H), 3.04 (t, 2H, *J* = 6.4 Hz), 2.42 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 170.5, 169.9, 167.6, 162.1, 154.9, 144.5, 143.5, 122.6, 108.5, 104.0, 63.2, 47.3, 36.1, 24.7, 23.6. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{15}H_{18}N_8O_2S$: 375.1351; found: 375.1363.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl pyridine-3-carboxylate **8m**

Prepared from nicotinic acid. White solid (60 mg, 59%). m.p. 177-178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.77 (d, 1H, *J* = 3.5 Hz), 8.22 (d, 1H, *J* = 7.9 Hz), 8.17 (s, 1H), 7.43 (s, 2H), 7.38 (dd, 1H, *J* = 3.5 and 7.9 Hz), 5.72 (br, NH_2), 5.34 (s, 2H), 4.62 (t, 2H, *J* = 6.7 Hz), 3.20 (t, 2H, *J* = 6.7 Hz), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 165.1, 161.9, 156.0, 153.5, 150.8, 145.0 137.1, 125.9, 123.4, 121.5, 108.0, 63.8, 48.8, 25.6, 25.5. IR (neat) ν_{max} 1566, 1592, 1655, 1716, 3124, 3435 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{16}H_{17}N_7O_2$: 340.1522; found: 340.1511.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl pyridine-4-carboxylate **8n**

Prepared from isonicotinic acid. White solid (60 mg, 59%). m.p. 186-188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, 2H, *J* = 5.7 Hz), 8.17 (s, 1H), 7.76 (d, 2H, *J* = 5.7 Hz), 7.42 (s, 1H), 5.68 (br, NH_2), 5.35 (s, 2H), 4.63 (t, 2H, *J* = 6.7 Hz), 3.20 (t, 2H, *J* = 6.7 Hz), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 164.9, 161.9, 156.0, 150.6, 145.0 137.1, 122.7, 121.5, 108.0, 64.2, 48.8, 25.6, 25.4. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{16}H_{17}N_7O_2$: 340.1522; found: 340.1535.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 2-fluoropyridine-4-carboxylate **8o**

Prepared from 2-fluoro-4-pyridinecarboxylic acid. White solid (67 mg, 63%). m.p. 194-196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.37 (d, 1H, *J* = 5.0 Hz), 7.70 (d, 1H, *J* = 5.0 Hz), 7.56 (s, 1H), 7.45 (s, 1H), 5.81 (br, NH_2), 5.44 (s, 2H), 4.66 (t, 2H, *J* = 6.7 Hz), 3.22 (t, 2H, *J* = 6.7 Hz), 2.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 164.1 (d, *J* = 240 Hz), 163.4 (d, *J* = 4 Hz), 162.1, 155.1, 148.4 (d, *J* = 14 Hz), 144.3, 143.1 (d, *J* = 8 Hz), 122.7, 120.6 (d, *J* = 5 Hz), 109.1 (d, *J* = 39 Hz), 108.4, 64.6, 48.5, 24.6, 23.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -69.1. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{16}H_{16}FN_7O_2$: 358.1428; found: 358.1438.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl furan-3-carboxylate **8q**

Prepared from 3-furoic acid. White solid (38 mg, 38%). m.p. 171-172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.96 (dd, 1H, *J* = 0.7 and 1.5 Hz), 7.45 (s, 1H), 7.42 (dd, 1H, *J* = 1.5 and 1.9 Hz), 6.68 (dd, 1H, *J* = 0.7 and 1.9 Hz), 5.77 (br, NH_2), 5.37 (s, 2H), 4.51 (t, 2H, *J* = 6.7 Hz), 3.15 (t, 2H, *J* = 6.7 Hz), 2.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 162.8, 162.0, 155.4, 147.8, 145.3, 143.0, 121.6, 119.1, 109.3, 108.2, 63.0, 48.6, 25.6, 25.5. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{15}H_{16}N_6O_3$: 329.1362; found: 329.1354.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 6-fluorobenzofuran-3-carboxylate **8r**

Prepared from 6-fluorobenzofuran-3-carboxylic acid. White solid (65 mg, 55%). m.p. 243-245 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.17 (s, 1H), 7.88 (dd, 2H, *J* = 5.5 and 8.6 Hz), 7.42 (s, 1H), 7.26 (dd, 1H, *J* = 2.3 and 8.6 Hz), 7.09 (m, 1H), 5.60 (br, NH_2), 5.32 (s, 2H), 4.63 (t, 2H, *J* = 6.4 Hz), 3.22 (t, 2H, *J* = 6.7 Hz), 2.51 (s, 3H). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 169.2, 162.8, 161.9, 161.2 (d, *J* = 244 Hz), 156.0, 155.4 (d, *J* = 13 Hz), 151.5 (d, *J* = 4 Hz), 145.3, 122.4 (d, *J* = 10 Hz), 121.5, 120.7 (d, *J* = 2 Hz), 114.3, 112.7 (d, *J* = 24 Hz), 107.9, 99.5 (d, *J* = 26 Hz), 63.1, 48.9, 25.7, 25.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.4. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{19}H_{17}FN_6O_3$: 397.1424; found: 397.1444.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl naphthalene-2-carboxylate **8s**

Prepared from 2-naphthoic acid. White solid (70 mg, 60%). m.p. 220-222 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.17 (s, 1H), 7.98 (m, 1H), 7.95 (m, 1H), 7.88 (m, 2H), 7.61 (m, 1H), 7.57 (m, 1H), 7.46 (s, 1H), 5.63 (br, NH_2), 5.34 (s, 2H), 4.66 (t, 2H, *J* = 6.6 Hz), 3.26 (t, 2H, *J* = 6.6 Hz), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 166.6, 161.9, 155.9, 145.4, 135.6, 132.4, 131.1, 129.3, 128.4, 128.2, 127.8, 127.1, 126.7, 125.0, 121.6, 108.1, 63.6, 48.9, 25.7, 25.6. IR (neat) ν_{max} 1562, 1592, 1655, 1712, 3142, 3329, 3412 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{21}H_{20}N_6O_2$: 389.1726; found: 389.1733.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl quinoline-3-carboxylate **8t**

Prepared from 3-quinolinecarboxylic acid. White solid (76 mg, 65%). m.p. 213-214 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 9.29 (m, 1H), 8.95 (m, 1H), 8.21 (m, 1H), 8.12 (m, 1H), 8.04 (s, 1H), 7.91-7.97 (m, 2H), 7.74 (m, 1H), 6.87 (br, NH_2), 5.42 (s, 2H), 4.60 (t, 2H, *J* = 6.7 Hz), 3.17 (t, 2H, *J* = 6.7 Hz), 2.28 (s, 3H). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 167.3, 165.1, 161.8, 156.3, 149.8, 149.7, 143.7, 139.0, 132.7, 130.1, 129.3, 128.1, 126.9, 123.3, 123.1, 108.9, 64.6, 47.2, 25.6, 25.4. IR (neat) ν_{max} 1563, 1594, 1656, 1717, 3142, 3329, 3412 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{20}H_{19}N_7O_2$: 390.1678; found: 390.1692.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl quinoline-6-carboxylate **8u**

Prepared from 6-quinolinecarboxylic acid. White solid (64 mg, 55%). m.p. 237-238 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (m, 1H), 8.55 (s, 1H), 8.27 (m, 1H), 8.24 (m, 1H), 8.18 (s, 1H), 8.15 (m, 1H), 7.50 (m, 1H), 7.46 (s, 1H), 5.60 (br, NH_2), 5.35 (s, 2H), 4.68 (t, 2H, *J* = 6.6 Hz), 3.26 (t, 2H, *J* = 6.6 Hz), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 165.9, 161.9, 156.0, 152.6, 150.1, 145.3, 137.4, 131.1, 129.9, 128.8, 127.9, 127.4, 121.9, 121.5, 108.0, 63.8, 48.9, 25.7, 25.6. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{20}H_{19}N_7O_2$: 390.1678; found: 390.1659.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl [1,1'-biphenyl]-3-carboxylate **8v**

Prepared from biphenyl-3-carboxylic acid. White solid (46 mg, 37%). m.p. 180-181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (m, 1H), 8.17(s, 1H), 7.95 (m, 1H), 7.81 (m, 1H), 7.60-7.64 (m, 2H), 7.46-7.54 (m, 3H), 7.38-7.45 (m, 2H), 5.62 (br, NH_2), 5.33 (s, 2H), 4.63 (t, 2H, *J* = 6.7 Hz), 3.23 (t, 2H, *J* = 6.7 Hz), 2.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 166.3, 162.0, 155.9, 145.4, 141.6, 140.7, 131.7, 130.5, 128.9, 128.8, 128.3, 128.2, 127.8, 127.1, 121.6, 108.1, 63.6, 48.8, 25.7, 25.6. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{23}H_{22}N_6O_2$: 415.1882; found: 415.1895.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 3-(pyridin-3-yl)benzoate **8w**

Prepared from 3-(pyridin-3-yl)-benzoic acid. White solid (62 mg, 50%). m.p. 222-223 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 8.92 (d, 1H, *J* = 1.5 Hz), 8.63 (dd, 1H, *J* = 1.5 and 4.7 Hz), 8.20 (s, 1H), 8.12 (d, 1H, *J* = 7.9 Hz), 8.03 (d, 1H, *J* = 7.8 Hz), 8.01 (s, 1H), 7.94 (d, 1H, *J* = 7.8 Hz), 7.93 (s, 1H), 7.66 (t, 1H, *J* = 7.8 Hz), 7.51 (dd, 1H, *J* = 4.7 and 7.9 Hz), 6.90 (br, NH_2), 5.41 (s, 2H), 4.53 (t, 2H, *J* = 6.6 Hz), 3.13 (t, 2H, *J* = 6.6 Hz), 2.30 (s, 3H). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 167.0, 165.8, 161.9, 156.3, 149.0, 148.2, 143.8, 138.1, 135.0, 134.8, 132.2, 131.1, 130.2, 129.1, 127.8, 124.4, 123.4, 108.9, 64.3, 47.0, 25.7, 25.4. IR (neat) ν_{max} 1563, 1600, 1657, 1716, 3066, 3110, 3329, 3426 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{22}H_{21}N_7O_2$: 416.1834; found: 416.1850.

2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl 4-(pyridin-3-yl)benzoate **8x**

Prepared from 4-(pyridin-3-yl)-benzoic acid. White solid (37 mg, 30%). m.p. 232-233 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.89 (s, 1H), 8.60 (d, 1H, *J* = 4.5 Hz), 8.19 (d, 1H, *J* = 7.5 Hz), 8.07 (s, 1H), 8.05 (d, 2H, *J* = 7.6 Hz), 7.91 (s, 1H), 7.79 (d, 2H, *J* = 7.6 Hz), 7.58 (d, 1H, *J* = 4.5 and 7.5 Hz), 5.50 (s, 2H), 4.61 (t, 2H, *J* = 7.1 Hz), 3.22 (t, 2H, *J* = 7.1 Hz), 2.36 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 167.6, 165.9, 162.1, 155.1, 148.2, 147.1, 144.6, 141.8, 136.0, 135.4, 129.9, 129.6, 126.9, 124.1, 122.8, 108.5, 63.4, 47.2, 24.8, 23.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{22}H_{21}N_7O_2$: 416.1834; found: 416.1831.

(But-3-yn-1-yloxy)t-butyldimethylsilane **9**

To a stirred solution of 3-butyn-1-ol (20 mL, 265 mmol) in dry DCM (530 mL, 0.5 M) under nitrogen was added imidazole (54 g ,794 mmol) and TBDMS-Cl (60 g, 398 mmol). The resultant mixture was stirred at r.t. overnight, concentrated under reduced pressure, diluted with Et_2O (500 mL), washed with aqueous phosphate buffer (pH 7) (3 x 300 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5-10% Et_2O in hexane) to yield **19** as a colourless oil (40 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (t, 2H, *J* = 7.2 Hz), 2.39 (dt, 2H, *J* = 2.4 and 7.2Hz), 1.94 (t, 1H, *J* = 2.4 Hz), 0.89 (s, 9H), 0.06 (s, 6H). Analytical data are consistent with those previously reported.[7]

1,2-Bis(t-butyldimethylsilyloxy)propan-2-one **10**

To a stirred solution of dihydroxyacetone (30 g, 333 mmol) in dry DMF (330 mL, 1 M) under nitrogen was added imidazole (68 g, 1 mol) and TBDMS-Cl (125 g, 833 mmol). The resultant mixture was stirred at r.t. for 3 days, diluted with water and extracted with hexane extensively. The combined organic phases were washed with aqueous phosphate buffer (pH 7), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% EtOAc in hexane) to yield **20** as a colourless oil (82.7 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39 (s, 4H), 0.90 (s, 18H), 0.07 (s, 12H). Analytical data are consistent with those previously reported.[7]

1,6-Bis-(t-butyldimethylsilyloxy)-2-(t-butyldimethylsilyloxymethyl)hex-3-yn-2-ol **11**

To a stirred solution of **9** (31 g, 168 mmol) in dry THF (84 mL, 2 M) under nitrogen at -78 °C was added *n*-BuLi (1.6 M in hexane, 102 mL, 163 mmol) dropwise. The resultant mixture was stirred at -78 °C for 1.5 h, then treated with **10** (2 M in dry THF, 84 mL, 163 mmol) slowly at -78 °C, and stirred at -78 °C for 2 h and then at r.t. for 3 h. The reaction mixture was quenched with sat. aq. NH_4Cl (50 mL) at 0 °C, concentrated under reduced pressure (to remove THF), and extracted with Et_2O (500 mL). The organic phase was washed with sat. aq. $NaHCO_3$ (2 x 200 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% EtOAc in hexane) to yield **11** as a colourless oil (64 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (t, 2H, *J* = 7.6 Hz), 3.67 (d, 2H, *J* = 9.5 Hz), 3.57 (d, 2H, *J* = 9.5 Hz), 2.90 (br, OH), 2.40 (t, 2H, *J* = 7.6 Hz), 0.92 (s, 18H), 0.91 (s, 9H), 0.10 (s, 12H), 0.08 (s, 6H). Analytical data are consistent with those previously reported.[7]

2-(Hydroxymethyl)hex-3-yne-1,2,6-triol **12**

To a stirred solution of **11** (1 g, 2 mmol) in dry THF (2 mL, 1 M) under nitrogen at 0 °C was added TBAF (1 M in THF, 6.6 mL, 6.6 mmol) dropwise. The resultant mixture was stirred at r.t. for 3 h, and treated with $CaCO_3$ (1.3 g, 200 mg / 1 mmol of TBAF), Dowex 50WX8-400 (4 g, 600 mg / 1 mmol of TBAF) and MeOH (5 mL). The reaction mixture was stirred at r.t. for 3 h, filtered through Celite, and concentrated under reduced pressure to yield **12** as a white solid (314 mg, 98%), which was used in the next step without further purification. ^{1}H NMR (400 MHz, CD_3OD) δ 3.65 (t, 2H, *J* = 6.8 Hz), 3.60 (d, 2H, *J* = 10.8 Hz), 3.55 (d, 2H, *J* = 10.8 Hz), 2.45 (t, 2H, *J* = 6.8 Hz). Analytical data are consistent with those previously reported.[7]

2-[4-(Hydroxymethyl)furan-2-yl]ethan-1-ol **13**

To a stirred suspension of **12** (8.7 g, 54.4 mmol) in warm MeCN (272 mL, 0.2 M) was added $HgCl_2$ (2.2 g, 8.16 mmol). The resultant mixture was stirred at r.t. for 2 h, quenched with TEA (5 mL), concentrated under reduced pressure (to remove MeCN), diluted with EtOAc (300 mL), washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (40% acetone in hexane) to yield **13** as a viscous pale-yellow oil (6.8 g, 88%). ^{1}H NMR (400 MHz, CD_3OD) δ 7.31 (s, 1H), 6.13 (s, 1H), 4.40 (s, 2H), 3.76 (t, 2H, *J* = 6.8 Hz), 2.79 (t, 2H, *J* = 6.8 Hz). Analytical data are consistent with those previously reported.[7]

5-(2-Hydroxyethyl)furan-3-carbaldehyde **14**

To a stirred suspension of **13** (7.2 g, 50.7 mmol) in chloroform (250 mL, 0.2 M) was added activated manganese oxide (66 g, 760 mmol). The resultant mixture was stirred vigorously at r.t. for 2 days, filtered through Celite, and concentrated under reduced pressure. The residue was purified by silica flash chromatography (30% acetone in hexane) to yield **14** as a thin pale-yellow oil (3.55 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.96 (s, 1H), 6.50 (s, 1H), 3.90 (t, 2H, *J* = 5.2 Hz), 2.91 (t, 2H, *J* = 5.2 Hz). Analytical data are consistent with those previously reported.[7]

(2Z)-2-{[5-(2-Hydroxyethyl)furan-3-yl]methyl}-3-(phenylamino)prop-2-enenitrile **15**

To a stirred solution of **14** (4.1 g, 29.3 mmol) and β-anilinopropionitrile (5.5 g, 38.1 mmol) in dry DMSO (98 mL, 0.3 M) under nitrogen at 40 °C was added NaOMe (2.5 M in dry MeOH, 17.6 mL, 44 mmol) dropwise. The resultant mixture was stirred at 45 °C overnight, quenched with ice water (150 mL) at 0 °C and extracted with EtOAc (3 x 500 mL). The combined organic phases were concentrated under reduced pressure, diluted with EtOAc (500 mL), washed with aqueous phosphate buffer (pH 7) (200 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (40% EtOAc in hexane) to yield **15** as a brown solid (4.3 g, 55%). The product was coeluted with a smaller amount of its *E*-isomer; both were subjected to the next step without further separation. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 2H), 7.26 (s, 1H), 7.18 (d, 1H, *J* = 12.8 Hz), 7.02 (t, 1H, *J* = 7.2 Hz), 6.87 (t, 2H, *J* = 7.4 Hz), 6.70 (br, NH), 6.10 (s, 1H), 3.89 (t, 2H, *J* = 6.1 Hz), 3.30 (s, 2H), 2.89 (t, 2H, *J* = 6.1 Hz). Analytical data are consistent with those previously reported.[7]

General procedure for preparation of 16a-d

To a stirred solution of **15** (0.5 mmol, 1 equiv.) and the amidine or guanidine (2 equiv.) in dry EtOH (0.2 M) under nitrogen was added NaOEt (3 M in dry EtOH, 0.7 mL, 2 mmol) dropwise. The reaction mixture was stirred at 85 °C for 3-4 days and then concentrated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield alcohols **16b-d**.

2-{4-[(4-Amino-2-ethylpyrimidin-5-yl)methyl]furan-2-yl}ethan-1-ol **16b**

Prepared from propionamidine hydrochloride. White solid (31 mg, 25%). m.p. 111-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.26 (s, 1H), 6.03 (s, 1H), 3.77 (t, 2H, *J* = 6.8 Hz), 3.55 (s, 2H), 2.80 (t, 2H, *J* = 6.8 Hz), 2.68 (q, 2H, *J* = 7.6 Hz), 1.28 (t, 3H, *J* = 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 162.6, 154.1, 152.1, 138.4, 121.6, 113.6, 107.2, 59.8, 31.2, 31.0, 22.9, 11.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{13}H_{17}N_3O_2$: 248.1398; found: 248.1401.

2-(4-{[4-Amino-2-(trifluoromethyl)pyrimidin-5-yl]methyl}furan-2-yl)ethan-1-ol **16c**

Prepared from trifluoroacetamidine. White solid (24 mg, 17%). m.p. 122-123 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.03 (s, 1H), 7.29 (s, 1H), 6.05 (s, 1H), 3.78 (t, 2H, *J* = 6.7 Hz), 3.62 (s, 2H), 2.81 (t, 2H, *J* = 6.7 Hz). ^{13}C NMR (100 MHz, CD_3OD) δ 162.8, 154.3, 154.0 (q, *J* = 35 Hz), 153.1, 138.6, 120.9, 119.6 (q, *J* = 274 Hz), 118.2, 107.1, 59.7, 31.1, 23.1. ^{19}F NMR (376 MHz, CD_3OD) δ -73.43. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{12}H_{12}F_3N_3O_2$: 288.0959; found: 288.0960.

2-{4-[(2,4-Diaminopyrimidin-5-yl)methyl]furan-2-yl}ethan-1-ol **16d**

Prepared from guanidine hydrochloride. White solid (58 mg, 50%). m.p. 218-221 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 7.45 (s, 1H), 7.27 (s, 1H), 6.04 (s, 1H), 3.78 (t, 2H, *J* = 6.3 Hz), 3.47 (s, 2H), 2.81 (t, 2H, *J* = 6.3 Hz). ^{13}C NMR (100 MHz, CD_3OD) δ 164.1, 157.5, 154.2, 144.7, 138.6, 121.6, 107.8, 107.1, 59.9, 31.2, 22.3. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{11}H_{14}N_4O_2$: 235.1194; found: 235.1185.

General procedure for preparation of 17a-d

To a stirred solution of 4-sulfamoylbenzoic acid (0.26 mmol, 1.3 equiv.) and DCC (3 equiv.) in dry DMF (0.2 M) under nitrogen at 0 °C was added DMAP (1.3 equiv.) and alcohol **16a-d** (0.2 mmol, 1 equiv.). The resultant mixture was stirred at r.t. for 2 days, diluted with DCM, filtered through cotton wool (to remove DCC/DCU), treated with aqueous phosphate buffer (pH 7), and extracted with DCM. The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield ester **17a-d**.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl 4-sulfamoylbenzoate **17a**

Prepared from **16a**. White solid (29 mg, 35%). m.p. 202-203 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.09 (d, 2H, *J* = 7.6 Hz), 7.99 (d, 2H, *J* = 7.6 Hz), 7.84 (s, 1H), 7.30 (s, 1H), 6.10 (s, 1H), 4.57 (t, 2H, *J* = 6.5 Hz), 3.54 (s, 2H), 3.10 (t, 2H, *J* = 6.6 Hz), 2.41 (s, 1H). ^{13}C NMR (100 MHz, CD_3OD) δ 165.2, 165.1, 161.8, 153.1, 152.9, 147.8, 139.0, 133.1, 129.7, 125.9, 122.0, 113.3, 107.7, 63.2, 27.3, 23.3, 22.8. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{19}H_{20}N_4O_5S$: 417.1232; found: 417.1235.

2-{4-[(4-Amino-2-ethylpyrimidin-5-yl)methyl]furan-2-yl}ethyl 4-sulfamoylbenzoate **17b**

Prepared from **16b**. Brown solid (13 mg, 15%). m.p. 197-198 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 8.08 (d, 2H, *J* = 8.3 Hz), 7.96 (d, 2H, *J* = 8.3 Hz), 7.82 (s, 1H), 7.56 (br, NH_2), 7.42 (s, 1H), 6.55 (br, NH_2), 6.14 (s, 1H), 4.50 (t, 2H, *J* = 6.5 Hz), 3.43 (s, 2H), 3.04 (t, 2H, *J* = 6.5 Hz), 2.55 (q, 2H, *J* = 7.6 Hz), 1.16 (t, 3H, *J* = 7.6 Hz). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 169.2, 165.1, 162.0, 154.5, 152.5, 148.5, 139.2, 132.8, 130.3, 126.5, 123.0, 113.1, 108.8, 63.5, 31.8, 27.7, 23.1, 13.0. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{20}H_{22}N_4O_5S$: 431.1389; found: 431.1393.

2-(4-{[4-Amino-2-(trifluoromethyl)pyrimidin-5-yl]methyl}furan-2-yl)ethyl 4-sulfamoylbenzoate **17c**

Prepared from **16c**. White solid (19 mg, 20%). m.p. 185-188 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.13 (d, 2H, *J* = 8.1 Hz), 8.03 (d, 2H, *J* = 8.1 Hz), 8.02 (s, 1H), 7.33 (s, 1H), 6.14 (s, 1H), 4.58 (t, 2H, *J* = 6.4 Hz), 3.62 (s, 2H), 3.12 (t, 2H, *J* = 6.4 Hz). ^{13}C NMR (100 MHz, CD_3OD) δ 165.1, 162.4, 154.4, 154.0 (q, *J* = 35 Hz), 152.7, 147.8, 138.7, 133.2, 129.7, 125.9, 121.2, 119.5 (q, *J* = 264 Hz), 117.9, 107.9, 63.1, 27.3, 23.0. ^{19}F NMR (376 MHz, CD_3OD) δ -73.4. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{19}H_{17}F_3N_4O_5S$: 471.0949; found: 471.0951.

2-{4-[(2,4-Diaminopyrimidin-5-yl)methyl]furan-2-yl}ethyl 4-sulfamoylbenzoate **17d**

Prepared from **16d**. Yellow solid (22 mg, 26%). m.p. 255-256 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.08 (d, 2H, *J* = 8.5 Hz), 8.00 (d, 2H, *J* = 8.5 Hz), 7.55 (s, 1H), 7.28 (s, 1H), 6.08 (s, 1H), 4.56 (t, 2H, *J* = 6.3 Hz), 3.45 (s, 2H), 3.08 (t, 2H, *J* = 6.3 Hz). ^{13}C NMR (100 MHz, CD_3OD) δ 165.0, 162.9, 161.5, 153.7, 152.7, 147.7 138.6, 133.1, 129.6, 125.9, 123.1, 107.8, 106.3, 63.0, 27.3, 22.6. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{18}H_{19}N_5O_5S$: 418.1184; found: 418.1185.

5-[(5-{2-[(t-Butyldimethylsilyl)oxy]ethyl}furan-3-yl)methyl]-2-methylpyrimidin-4-amine **18**

To a stirred solution of **16a** (70 mg, 0.3 mmol) in dry DMF (1.2 mL, 0.25 M) under nitrogen was added imidazole (27 mg, 0.39 mmol) and TBDMS-Cl (55 mg, 0.36 mmol). The resultant mixture was stirred at r.t. for 3 days, diluted with EtOAc (60 mL), washed with aqueous phosphate buffer (pH 7) (2 x 20 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5% MeOH in DCM) to yield **18** as a yellow solid (71 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.14 (s, 1H), 5.92 (s, 1H), 4.92 (br, NH_2), 3.83 (t, 2H, *J* = 6.5 Hz), 3.54 (s, 2H), 2.80 (t, 2H, *J* = 6.5 Hz), 2.53 (s, 3H), 0.87 (s, 9H), 0.01 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 161.6, 155.0, 154.9, 137.9, 121.6, 112.3, 107.4, 61.4, 31.9, 25.8, 25.3, 24.5, 18.2, -5.4. ESI-MS *m/z*: 348.21 [M+H$^+$].

N-{5-[(5-{2-[(t-Butyldimethylsilyl)oxy]ethyl}furan-3-yl)methyl]-2-methylpyrimidin-4-yl}acetamide **19**

To a stirred solution of **18** (71 mg, 0.21 mmol) and dry diisopropylethylamine (0.073 mL, 0.42 mmol) in dry 1,2-dichloroethane (2.5 mL, 0.1 M) under nitrogen at 0 °C was added acetyl chloride (0.018 mL, 0.256 mmol) dropwise. The resultant mixture was stirred at 45 °C overnight, quenched with cold aqueous phosphate buffer (pH 7) (30 mL) at 0 °C and extracted with DCM (70 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5% MeOH in DCM) to yield **19** as a yellow oil (45 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.65 (br, NH), 7.13 (s, 1H), 5.85 (s, 1H), 3.82 (t, 2H, *J* = 6.8 Hz), 3.66 (s, 2H), 2.79 (t, 2H, *J* = 6.8 Hz), 2.64 (s, 3H), 2.45 (s, 3H), 0.85 (s, 9H), 0.003 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 166.2, 158.3, 155.7, 155.0, 138.1, 122.5, 121.3, 107.3, 61.4, 31.9, 25.8, 25.5, 25.0, 24.7, 18.2, -5.4. ESI-MS *m/z*: 390.22 [M+H$^+$].

N-(5-{[5-(2-Hydroxyethyl)furan-3-yl]methyl}-2-methylpyrimidin-4-yl)acetamide **20**

To a stirred solution of **19** (45 mg, 0.12 mmol) in dry THF (1.2 mL, 0.1 M) under nitrogen at 0 °C was added TBAF (1 M in THF, 0.13 mL, 0.13 mmol) dropwise. The reaction mixture was stirred at 35 °C for 4 days and then concentrated under reduced pressure. The residue was purified by silica flash chromatography (5% MeOH in DCM) to yield **20** as a white solid (25 mg, 75%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.42 (s, 1H), 7.22 (s, 1H), 5.94 (s, 1H), 3.75 (t, 2H, *J* = 6.7 Hz), 3.74 (s, 2H), 2.79 (t, 2H, *J* = 6.7 Hz), 2.61 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 170.9, 165.6, 158.2, 156.4, 154.2, 138.5, 123.3, 121.9, 107.0, 59.7, 31.2, 23.8, 23.5, 22.3. ESI-MS *m/z*: 276.13 [M+H$^+$].

2-{4-[(4-Acetamido-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl 4-chlorobenzoate **21**

To a stirred solution of 4-chlorobenzoic acid (20 mg, 0.123 mmol) and DCC (60 mg, 0.285 mmol) in dry DMF (1.2 mL, 0.1 M) under nitrogen at 0 °C was added DMAP (15 mg, 0.123 mmol) and **20** (25 mg, 0.09 mmol). The resultant mixture was stirred at r.t. for 2 days, diluted with DCM, filtered through cotton wool (to remove DCC/DCU), treated with aqueous phosphate buffer (pH 7) (40 mL), and extracted with DCM (3 x 50 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5% MeOH in DCM) to yield **21** as a white solid (15 mg, 38%). m.p. 164-165 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.93 (d, 2H, *J* = 8.2 Hz), 7.68 (br, NH), 7.42 (d, 2H, *J* = 8.2 Hz), 7.17 (s, 1H), 5.93 (s, 1H), 4.53 (t, 2H, *J* = 6.3 Hz), 3.68 (s, 2H), 3.06 (t, 2H, *J* = 6.3 Hz), 2.65 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 167.5, 165.4, 158.2, 155.7, 153.5, 139.5, 138.9, 131.0, 128.8, 128.4, 121.5, 116.0, 107.6, 62.7, 27.9, 25.4, 25.0, 24.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{21}H_{20}ClN_3O_4$: 414.1220; found: 414.1225.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl 4-chlorobenzoate **22**

To a stirred solution of 4-chlorobenzoic acid (203 mg, 1.3 mmol) and DCC (618 mg, 3 mmol) in dry DMF (10 mL, 0.1 M) under nitrogen at 0 °C was added DMAP (158 mg, 1.3 mmol) and **16a** (233 mg, 1 mmol). The resultant mixture was stirred at r.t. for 2 days, diluted with DCM, filtered through cotton wool (to remove DCC/DCU), treated with aqueous phosphate buffer (pH 7), and extracted with DCM. The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue

was purified by silica flash chromatography (5% MeOH in DCM) to yield **22** as a white solid (237 mg, 64%). m.p. 166-167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.93 (d, 2H, *J* = 7.9 Hz), 7.42 (d, 2H, *J* = 7.9 Hz), 7.18 (s, 1H), 5.98 (s, 1H), 4.91 (br, NH_2), 4.53 (d, 2H, *J* = 6.6 Hz), 3.54 (s, 2H), 3.06 (t, 2H, *J* = 6.6 Hz), 2.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.5, 161.6, 155.0, 153.4, 139.5, 138.6, 130.9, 128.7, 128.5, 121.8, 112.0, 107.8, 62.7, 27.9, 25.3, 24.5. IR (neat) *v* 1555, 1595, 1654, 1716, 3137, 3332 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{19}H_{18}ClN_3O_3$: 372.1115; found: 372.1111.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl 3-(pyridin-3-yl)benzoate **23**

To a stirred solution of 3-(pyridin-3-yl)benzoic acid (78 mg, 0.39 mmol) and DCC (185 mg, 0.9 mmol) in dry DMF (3 mL, 0.1 M) under nitrogen at 0 °C was added DMAP (48 mg, 0.39 mmol) and **16a** (111 mg, 0.3 mmol). The resultant mixture was stirred at r.t. for 2 days, diluted with DCM, filtered through cotton wool (to remove DCC/DCU), treated with aqueous phosphate buffer (pH 7) (20 mL), and extracted with DCM (4 x 40 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5% MeOH in DCM) to yield **23** as a white solid (81 mg, 65%). m.p. 188-190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.65 (s, 1H), 8.23 (s, 1H), 8.05 (s, 1H), 8.03 (s, 1H), 7.92 (d, 1H, *J* = 7.7 Hz), 7.79 (d, 1H, *J* = 7.7 Hz), 7.57 (t, 1H, *J* = 7.7 Hz), 7.42 (m, 1H), 7.18 (s, 1H), 6.01 (s, 1H), 5.03 (br, NH_2), 4.58 (t, 2H, *J* = 6.6 Hz), 3.55 (s, 2H), 3.09 (t, 2H, *J* = 6.6 Hz), 2.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.9, 161.6, 154.6, 153.3, 148.9, 148.1, 138.7, 138.1, 135.7, 134.4, 131.5, 131.0, 129.3, 129.1, 128.2, 123.7, 121.7, 112.1, 107.8, 62.7, 27.9, 25.2, 24.4. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{24}H_{22}N_4O_3$: 415.1770; found: 415.1769.

General procedure for preparation of 24a-h:

To a stirred solution of **22** (0.2 mmol, 1 equiv.) and aluminium chloride (5 equiv.) in dry DCM (0.1 M) under nitrogen at 0 °C was added the acyl chloride (8 equiv.) dropwise. The resultant mixture was stirred at 0 °C for 30 min and then at r.t. for 4-5 h, quenched with cold aqueous phosphate buffer (pH 7) (30 mL) at 0 °C, extracted with DCM (100 mL), washed with aqueous phosphate buffer (pH 7) (30 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5-10% MeOH in DCM) to yield ester **24a-h** as a solid.

2-{5-Acetyl-4-[(4-amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl 4-chlorobenzoate **24a**

Prepared from acetyl chloride. White solid (37 mg, 45%). m.p. 170-172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.90 (d, 2H, *J* = 8.5 Hz), 7.42 (d, 2H, *J* = 8.5 Hz), 6.21 (s, 1H), 5.75 (br, NH_2), 4.58 (t, 2H, *J* = 6.5 Hz), 3.90 (s, 2H), 3.12 (t, 2H, *J* = 6.5 Hz), 2.50 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2, 166.2, 165.3, 161.6, 156.1, 154.6, 147.3, 139.8, 132.3, 130.9, 128.9, 128.1, 112.4, 111.6, 62.0, 28.1, 26.9, 25.3, 24.8. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{21}H_{20}ClN_3O_4$: 414.1220; found: 414.1222.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-propanoylfuran-2-yl}ethyl 4-chlorobenzoate **24b**

Prepared from propionyl chloride. White solid (51 mg, 60%). m.p. 174-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.88 (d, 2H, *J* = 8.8 Hz), 7.40 (d, 2H, *J* = 8.8 Hz), 6.18 (s, 1H), 5.84 (br, NH_2), 4.56 (t, 2H, *J* = 6.4 Hz), 3.88 (s, 2H), 3.09 (t, 2H, *J* = 6.4 Hz), 2.87 (q, 2H, *J* = 7.3 Hz), 2.47 (s, 3H), 1.17 (t, 3H, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.5, 166.0, 165.3, 161.7, 155.7, 154.4, 147.0, 139.7, 132.0, 130.9, 128.8, 128.1, 112.2, 111.8, 62.0, 32.3, 28.0, 25.1, 24.7, 7.6. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{22}H_{22}ClN_3O_4$: 428.1377; found: 428.1385.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-butanoylfuran-2-yl}ethyl 4-chlorobenzoate **24c**

Prepared from butyryl chloride. White solid (33 mg, 37%). m.p. 178-180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.90 (d, 2H, *J* = 8.2 Hz), 7.42 (d, 2H, *J* = 8.2 Hz), 6.20 (s, 1H), 5.79 (br, NH_2), 4.58 (t, 2H, *J* = 6.4 Hz), 3.90 (s, 2H), 3.11 (t, 2H, *J* = 6.4 Hz), 2.83 (t, 2H, *J* = 7.2 Hz), 2.47 (s, 3H), 1.73 (m, 2H), 0.98 (t, 3H, *J* = 7.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 166.3, 165.3, 161.6, 155.7, 154.9, 147.2, 139.8, 132.1, 130.9, 128.8, 128.2, 112.3, 111.7, 62.0, 41.0, 28.1, 25.4, 24.8, 17.3, 13.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{23}H_{24}ClN_3O_4$: 442.1533; found: 442.1538.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-pentanoylfuran-2-yl}ethyl 4-chlorobenzoate **24d**

Prepared from valeroyl chloride. White solid (36 mg, 40%). m.p. 183-184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.90 (d, 2H, *J* = 8.5 Hz), 7.42 (d, 2H, *J* = 8.5 Hz), 6.20 (s, 1H), 5.79 (br, NH_2), 4.58 (t, 2H, *J* = 6.3 Hz), 3.91 (s, 2H), 3.11 (t, 2H, *J* = 6.3 Hz), 2.85 (t, 2H, *J* = 7.3 Hz), 2.48 (s, 3H), 1.68 (m, 2H), 1.37 (m, 2H), 0.94 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 165.9, 165.3, 161.7, 155.8, 154.1, 147.2, 139.7, 132.0, 130.9, 128.8, 128.1, 112.3, 111.9, 62.0, 38.8, 28.1, 25.9, 25.1, 24.8, 22.3, 13.8. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{24}H_{26}ClN_3O_4$: 456.1690; found: 456.1692.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-hexanoylfuran-2-yl}ethyl 4-chlorobenzoate **24e**

Prepared from hexanoyl chloride. White solid (24 mg, 25%). m.p. 184-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.91 (d, 2H, *J* = 8.4 Hz), 7.42 (d, 2H, *J* = 8.4 Hz), 6.21 (s, 1H), 5.80 (br, NH_2), 4.58 (t, 2H, *J* = 6.5 Hz), 3.91 (s, 2H), 3.12 (t, 2H, *J* = 6.5 Hz), 2.84 (t, 2H, *J* = 7.6 Hz), 2.49 (s, 3H), 1.69 (m, 2H), 1.34 (m, 4H), 0.92 (t, 3H, *J* = 6.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 166.1, 165.3, 161.6, 155.8, 154.3, 147.2, 139.8, 132.0, 130.9, 128.8, 128.0, 112.3, 111.8, 62.0, 39.1, 31.4, 28.2, 25.3, 24.8, 23.4, 22.4, 14.0. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{25}H_{28}ClN_3O_4$: 470.1846; found: 470.18468.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-cyclopropanecarbonylfuran-2-yl}ethyl 4-chlorobenzoate **24f**

Prepared from cyclopropanecarbonyl chloride. White solid (31 mg, 35%). m.p. 166-168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.90 (d, 2H, *J* = 8.4 Hz), 7.42 (d, 2H, *J* = 8.4 Hz), 6.23 (s, 1H), 5.77 (br, NH_2), 4.60 (t, 2H, *J* = 6.4 Hz), 3.89 (s, 2H), 3.14 (t, 2H, *J* = 6.4 Hz), 2.72 (m, 1H), 2.47 (s, 3H), 1.25 (m, 2H), 1.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 166.4, 165.4, 161.6, 156.0, 155.0, 147.6, 139.7, 131.5, 130.9, 128.8, 128.2, 112.3, 111.8, 62.1, 28.2, 25.5, 24.8, 17.6, 12.0. IR (neat) ν_{max} 1525, 1595, 1639, 1666, 1716, 3126, 3332 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{23}H_{22}ClN_3O_4$: 440.1377; found: 440.1389.

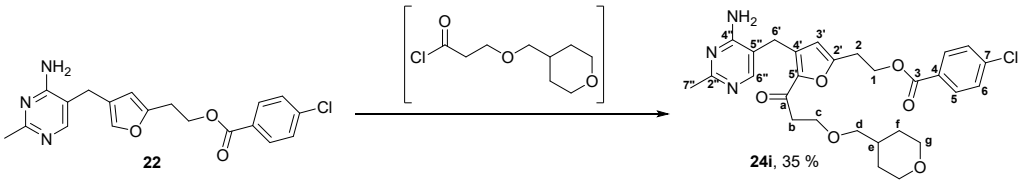
2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-(2-cyclopentylacetyl)furan-2-yl}ethyl 4-chlorobenzoate **24g**

Prepared from cyclopentylacetyl chloride. White solid (58 mg, 60%). m.p. 180-181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.91 (d, 2H, *J* = 8.3 Hz), 7.43 (d, 2H, *J* = 8.3 Hz), 6.21 (s, 1H), 5.69 (br, NH_2), 4.58 (t, 2H, *J* = 6.3 Hz), 3.91 (s, 2H), 3.12 (t, 2H, *J* = 6.3 Hz), 2.87 (d, 2H, *J* = 7.2 Hz), 2.48 (s, 3H), 2.34 (m, 1H), 1.83 (m, 2H), 1.64 (m, 2H), 1.57 (m, 2H), 1.16 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 166.4, 165.3, 161.5, 155.7, 155.1, 147.3, 139.8, 132.2, 130.9, 128.8, 128.1, 112.3, 111.7, 62.2, 45.2, 35.8, 32.6, 28.1, 25.5, 24.9, 24.8. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{26}H_{28}ClN_3O_4$: 482.1846; found: 482.1850.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-(3-cyclopentylpropanoyl)furan-2-yl}ethyl 4-chlorobenzoate **24h**

Prepared from 3-cyclopentylpropanoyl chloride. White solid (30 mg, 30%). m.p. 185-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.91 (d, 2H, *J* = 7.6 Hz), 7.43 (d, 2H, *J* = 7.6 Hz), 6.20 (s, 1H), 5.71 (br, NH_2), 4.59 (t, 2H, *J* = 6.3 Hz), 3.90 (s, 2H), 3.12 (t, 2H, *J* = 6.3 Hz), 2.86 (t, 2H, *J* = 7.7 Hz), 2.48 (s, 3H), 1.76-1.81 (m, 3H), 1.70 (m, 2H), 1.64 (m, 2H), 1.54 (m, 2H), 1.13 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 166.4, 165.3, 161.5, 155.8, 155.0, 147.2, 139.8, 132.2, 130.9, 128.8, 128.2, 112.3, 111.7, 62.0, 39.7, 38.4, 32.6, 30.0, 28.1, 25.4, 25.1, 24.8. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{27}H_{30}ClN_3O_4$: 496.2003; found: 496.2013.

The following scheme was used to prepare **24i**:



t-Butyl 3-[(oxan-4-yl)methoxy]propanoate (commercially available)

To a stirred solution of tetrahydropyran-4-methanol (0.12 mL, 1 mmol) in *t*-BuOH (5 mL, 0.2 M) under nitrogen was added caesium carbonate (0.65 g, 2 mmol) and tert-butyl acrylate (2.9 mL, 20 mmol). The resultant mixture was stirred at 60 °C for 2 days, quenched with aqueous phosphate buffer (pH 7) (20 mL) and extracted with Et_2O (3 x 50 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (40% Et_2O in hexane) to yield *t*-butyl 3-[(oxan-4-yl)methoxy]propanoate as a pale-yellow oil (207 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (m, 2H, H-4'$_{equ}$), 3.67 (t, 2H, *J* = 6.6 Hz, H-3), 3.39 (m, 2H, H-4'$_{ax}$), 3.29 (d, 2H, *J* = 6.6 Hz, H-1'), 2.48 (t, 2H, *J* = 6.4 Hz, H-2), 1.84 (m, 1H, H-2'), 1.64 (m, 2H, H-3'$_{equ}$), 1.46 (s, 9H, H-2"), 1.32 (m, 2H, H-3'$_{ax}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (C-1), 80.5 (C-1"), 76.1 (C-1'), 67.7 (C-4'), 66.7 (C-3), 36.4 (C-2), 35.4 (C-2'), 29.9 (C-3'), 28.1 (C2"). ESI-MS *m/z*: 245.18 [M+H$^+$].

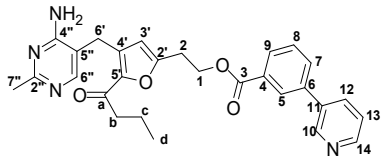
3-[(Oxan-4-yl)methoxy]propanoic acid (commercially available)

To a stirred solution of *t*-butyl 3-[(oxan-4-yl)methoxy]propanoate (866 mg, 3.55 mmol) in dry DCM (15 mL, 0.3 M) under nitrogen was added TFA (5 mL, 70 mmol) slowly. The resultant mixture was stirred at r.t. overnight. The reaction mixture was diluted with MeOH (20 mL) and then concentrated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield 3-[(oxan-4-yl)methoxy]propanoic acid as a white solid (493 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (m, 2H, H-4'$_{equ}$), 3.72 (t, 2H, *J* = 6.2 Hz, H-3), 3.41 (m, 2H, H-4'$_{ax}$), 3.33 (d, 2H, *J* = 6.6 Hz, H-1'), 2.64 (t, 2H, *J* = 6.2 Hz, H-2), 1.86 (m, 1H, H-2'), 1.65 (m, 2H, H-3'$_{equ}$), 1.33 (m, 2H, H-3'$_{ax}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5 (C-1), 76.3 (C-1'), 67.6 (C-4'), 66.0 (C-3), 35.2 (C-2), 34.8 (C-2'), 29.8 (C-3'). ESI-MS *m/z*: 189.11 [M+H$^+$].

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-{3-[(oxan-4-yl)methoxy]propanoyl}furan-2-yl}ethyl 4-chlorobenzoate **24i**

To a stirred solution of 3-[(oxan-4-yl)methoxy]propanoic acid (212 mg, 1.13 mmol) in dry 1,2-dichloroethane (2.2 mL, 0.5 M) under nitrogen at 0 °C was added thionyl chloride (0.09 mL, 1.24 mmol) dropwise. The resultant mixture was stirred at 60 °C for 2.5 h, concentrated under reduced pressure and then redissolved in dry 1,2-dichloroethane (1 mL). To a stirred solution of **22** (60 mg, 0.16 mmol) and aluminium chloride (96 mg, 0.72 mmol) in dry 1,2-dichloroethane (1 mL) under nitrogen at 0 °C was added the above solution dropwise. The resultant mixture was stirred at 0 °C for 15 minutes and then at r.t. overnight. The reaction mixture was quenched with cold aqueous phosphate buffer (pH 7) (15 mL) at 0 °C and extracted with DCM (x 50 mL). The combined organic phases were washed with aqueous phosphate buffer (pH 7) (3 x 30 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield **24i** as a white solid (29 mg, 35%). m.p. 244-245 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H, H-6"), 7.90 (d, 2H, *J* = 8.4 Hz, H-5), 7.42 (d, 2H, *J* = 8.4 Hz, H-6), 6.21 (s, 1H, H-3'), 5.69 (br, NH_2), 4.57 (t, 2H, *J* = 6.5 Hz, H-1), 3.96 (m, 2H, H-g$_{equ}$), 3.90 (s, 2H, H-6'), 3.81 (t, 2H, *J* = 6.3 Hz, H-c), 3.38 (m, 2H, H-g$_{ax}$), 3.31 (d, 2H, *J* = 6.4 Hz, H-d), 3.12 (m, 4H, H-b and H-2), 2.47 (s, 3H, H-7"), 1.81 (m, 1H, H-e), 1.60 (m, 2H, H-f$_{equ}$), 1.30 (m, 2H, H-f$_{ax}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3 (C-a), 166.4 (C-2"), 165.3 (C-3), 161.5 (C-4"), 156.1 (C-2'), 155.1 (C-6"), 147.2 (C-5'), 139.7 (C-4), 132.7 (C-4'), 130.9 (C-5), 128.8 (C-6), 128.1 (C-7), 112.4 (C-3'), 111.6 (C-5"), 76.2 (C-d), 67.6 (C-g), 65.6 (C-c), 62.0 (C-1), 39.3 (C-b), 35.3 (C-e), 29.8 (C-f), 28.2 (C-2), 25.4 (C-7"), 24.7 (C-6'). HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{28}H_{32}ClN_3O_6$: 542.2058; found: 542.2068.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-butanoylfuran-2-yl}ethyl 3-(pyridin-3-yl)benzoate **25**



To a stirred solution of **23** (30 mg, 0.072 mmol) and aluminium chloride (53 mg, 0.396 mmol) in dry 1,2-dichloroethane (0.8 mL, 0.1 M) under nitrogen at 0 °C was added butyryl chloride (0.06 mL, 0.58 mmol) dropwise. The resultant mixture was stirred at 0 °C for 15 minutes and then at r.t. overnight. The reaction mixture was quenched with cold aqueous phosphate buffer (pH 7) (15 mL) at 0 °C and extracted with DCM (50 mL). The organic phase was washed with aqueous phosphate buffer (pH 7) (50 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield **25** as a white solid (15 mg, 45%). m.p. 198-200 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (m, 1H, H-10), 8.67 (m, 1H, H-14), 8.24 (s, 1H, H-5), 8.11 (s, 1H, H-6”), 8.02 (d, 1H, *J* = 7.7 Hz, H-12), 7.92 (d, 1H, *J* = 7.8 Hz, H-7), 7.81 (d, 1H, *J* = 7.8 Hz, H-9), 7.58 (t, 1H, *J* = 7.8 Hz, H-8), 7.44 (m, 1H, H-13), 6.23 (s, 1H, H-3’), 5.85 (br, NH_2), 4.63 (t, 2H, *J* = 6.4 Hz, H-1), 3.91 (s, 2H, H-6’), 3.15 (t, 2H, *J* = 6.4 Hz, H-2), 2.82 (t, 2H, *J* = 7.3 Hz, H-b), 2.48 (s, 3H, H-7”), 1.70 (m, 2H, H-c), 0.95 (t, 3H, *J* = 7.4 Hz, H-d). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0 (C-a), 166.1 (C-2”), 165.9 (C-3), 161.6 (C-4”), 155.9 (C-2’), 154.3 (C-6”), 148.9 (C-14), 148.2 (C-10), 147.2 (C-5’), 138.3 (C-6), 135.5 (C-11), 134.3 (C-7), 132.0 (C-4’), 131.8 (C-9), 130.7 (C-4), 129.3 (C-8), 129.1 (C-12), 128.3 (C-5), 123.8 (C-13), 112.3 (C-3’), 111.9 (C-5”), 62.2 (C-1), 41.0 (C-b), 28.1 (C-2), 25.2 (C-7”), 24.7 (C-6’), 17.3 (C-c), 13.8 (C-d). HRMS (ESI) *m*/*z*: [M+H$^+$] calculated for $C_{28}H_{28}N_4O_4$: 485.2189; found: 485.2183.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl acetate

To a stirred solution of **16a** (117 mg, 0.5 mmol) in dry pyridine (1.25 mL, 0.4 M) under nitrogen was added acetic anhydride (0.052 mL, 0.55 mmol) dropwise. The resultant mixture was stirred at 40 °C for 3 h, diluted with *n*-BuOH (150 mL), washed with sat. aq. $CuSO_4$ (3 x 25 mL) and water (50 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5% MeOH in DCM) to yield acetate as a brown solid (83 mg, 60%). m.p. 120-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.15 (s, 1H), 5.93 (s, 1H), 4.98 (br, NH_2), 4.28 (t, 2H, *J* = 6.8 Hz), 3.54 (s, 2H), 2.92 (t, 2H, *J* = 6.8 Hz), 2.51 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 166.3, 161.6, 155.2, 153.4, 138.4, 121.8, 111.9, 107.6, 62.0, 27.9, 25.4, 24.5, 20.9. HRMS (ESI) *m*/*z*: [M+H$^+$] calculated for $C_{14}H_{17}N_3O_3$: 276.1348; found: 276.1366.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-butanoylfuran-2-yl}ethyl acetate **27**

To a stirred solution of *2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl acetate* (83 mg, 0.3 mmol) and aluminium chloride (200 mg, 1.5 mmol) in dry 1,2-dichloroethane (3 mL, 0.1 M) under nitrogen at 0 °C was added butyryl chloride (0.25 mL, 2.4 mmol) dropwise. The resultant mixture was stirred at 0 °C for 15 min and then at r.t. for 3 h. The reaction mixture was quenched with cold aqueous phosphate buffer (pH 7) (35 mL) at 0 °C and then extracted with DCM (3 x 50 mL). The combined organic phases were washed with aqueous phosphate buffer (pH 7) (2 x 20 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield **27** as a white solid (51 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 6.15 (s, 1H), 5.84 (br, NH_2), 4.32 (t, 2H, *J* = 6.4 Hz), 3.90 (s, 2H), 2.97 (t, 2H, *J* = 6.4 Hz), 2.87 (t, 2H, *J* = 7.0 Hz), 2.47 (s, 3H), 2.04 (s, 3H), 1.75 (m, 2H), 1.01 (t, 3H, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 170.7, 166.3, 161.7, 155.9, 154.9, 147.1, 132.1, 112.2, 111.7, 61.3, 41.1, 28.1, 25.5, 24.8, 20.9, 17.4, 13.9. ESI-MS *m*/*z*: 346.17 [M+H$^+$]. Analytical data are consistent with those previously reported.[7]

1-{3-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-(2-hydroxyethyl)furan-2-yl}butan-1-one

To a stirred solution of **27** (40 mg, 0.116 mmol) in dry MeOH (0.6 mL, 0.2 M) under nitrogen was added potassium carbonate (32 mg, 0.23 mmol). The resultant mixture was stirred at r.t. for 1 h, concentrated under reduced pressure, diluted with *n*-BuOH (50 mL), washed with aqueous phosphate buffer (pH 7) (15 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield alcohol as a white solid (24 mg, 69%). m.p. 144-147 °C ^{1}H NMR (400 MHz, CD_3OD) δ 7.99 (s, 1H), 6.33 (s, 1H), 3.94 (s, 2H), 3.84 (t, 2H, *J* = 6.5 Hz), 2.90 (m, 4H), 2.38 (s, 3H), 1.74 (m, 2H), 1.01 (t, 3H, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, CD_3OD) δ 193.3, 165.2, 162.1, 158.1, 153.4, 147.0, 132.4, 112.5, 111.7, 59.2, 40.4, 31.3, 23.9, 23.3, 17.2, 12.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{16}H_{21}N_3O_3$: 304.1661; found: 304.1675.

2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-butanoylfuran-2-yl}ethyl 4-sulfamoylbenzoate **26**

To a stirred solution of 4-sulfamoylbenzoic acid (21 mg, 0.1 mmol) and DCC (50 mg, 0.24 mmol) in dry DMF (1 mL, 0.08 M) under nitrogen at 0 °C was added DMAP (13 mg, 0.1 mmol) and *1-{3-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-(2-hydroxyethyl)furan-2-yl}butan-1-one* (24 mg, 0.08 mmol). The resultant mixture was stirred at r.t. for 2 days, diluted with DCM, filtered through cotton wool (to remove DCC/DCU), treated with aqueous phosphate buffer (pH 7) (20 mL), and extracted with DCM (3 x 50 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield **26** as a white solid (17 mg, 44%). m.p. 199-200 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 8.06 (d, 2H, *J* = 8.4 Hz), 7.96 (d, 2H, *J* = 8.4 Hz), 7.84 (s, 1H), 7.58 (br, NH_2), 6.65 (br, NH_2), 6.41 (s, 1H), 4.57 (t, 2H, *J* = 5.9 Hz), 3.83 (s, 2H), 3.16 (t, 2H, *J* = 5.9 Hz), 2.72 (t, 2H, *J* = 7.2 Hz), 2.29 (s, 3H), 1.56 (m, 2H), 0.84 (t, 3H, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 191.7, 165.3, 165.0, 162.1, 156.3, 154.4, 148.6, 147.3, 132.7, 132.6, 130.3, 126.6, 112.8, 111.9, 62.9, 40.6, 27.9, 25.4, 24.2, 17.3, 13.9. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{23}H_{26}N_4O_6S$: 487.1651; found: 487.1655.

5-{[5-(2-Azidoethyl)furan-3-yl]methyl}-2-methylpyrimidin-4-amine **29**

To a stirred suspension of **28**[7] (142 mg, 0.37 mmol) in dry DMF (0.8 mL, 0.5 M) under nitrogen at 0 °C was added sodium azide (48 mg, 0.74 mmol). The resultant mixture was stirred at r.t. for 2 days, quenched with aqueous phosphate buffer (pH 7) (10 mL) and extracted with *n*-BuOH (40 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5% MeOH in DCM) to yield **29** as a white semi-solid (75 mg, 80%). ^{1}H NMR (400 MHz, CD_3OD) δ 7.84 (s, 1H), 7.30 (s, 1H), 6.09 (s, 1H), 3.55 (s, 2H), 3.52 (t, 2H, *J* = 6.8 Hz), 2.88 (t, 2H, *J* = 6.8 Hz), 2.40 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 165.0, 162.2, 153.2, 152.9, 138.8, 122.0, 113.3, 107.9, 49.3, 27.5, 23.3, 22.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{12}H_{14}N_6O$: 259.1307; found: 259.1322.

5-{[5-(2-Aminoethyl)furan-3-yl]methyl}-2-methylpyrimidin-4-amine **30**

A stirred solution of **29** (70 mg, 0.27 mmol) in MeOH (3 mL, 0.1 M) at r.t. was treated with 10% Pd/C (7 mg) under nitrogen. The flask was evacuated and flushed with hydrogen gas (three times). The resultant mixture was stirred vigorously at r.t. under an atmosphere of hydrogen (1 atm, H_2 balloon) for 4 h. The reaction mixture was filtered through Celite and concentrated under reduced pressure to yield **30** as a white solid (60 mg, 95% yield), which was used in the next step without further purification. m.p. 131-133 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 7.84 (s, 1H), 7.27 (s, 1H), 6.03 (s, 1H), 3.55 (s, 2H), 2.90 (t, 2H, *J* = 6.9 Hz), 2.76 (t, 2H, *J* = 6.9 Hz), 2.40 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 165.0, 162.1, 154.3, 153.0, 138.7, 121.8, 113.3, 107.1, 39.6, 30.6, 23.3, 22.8. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{12}H_{16}N_4O$: 233.1402; found: 233.1425.

General procedure for preparation of 31-35

To a stirred solution of the carboxylic acid (0.39 mmol, 1.3 equiv.) and DCC (3 equiv.) in dry DMF (0.2 M) under nitrogen at 0 °C was added DMAP (1.3 equiv.) and corresponding amine (0.3 mmol, 1 equiv.). The resultant mixture was stirred at r.t. for 2 days, diluted with DCM, filtered through cotton wool (to remove DCC/DCU), treated with aqueous phosphate buffer (pH 7), and extracted with DCM. The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (5-15% MeOH in DCM) to yield amide **31-35** as a solid.

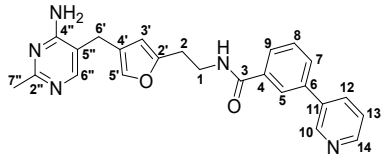
N-(2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl)-4-chlorobenzamide **31**

Prepared from 4-chlorobenzoic acid and **30**. White solid (47 mg, 42%). m.p. 171-172 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 8.65 (t, NH, *J* = 5.3 Hz), 7.81 (d, 2H, *J* = 8.5 Hz), 7.79 (s, 1H), 7.53 (d, 2H, *J* = 8.5 Hz), 7.38 (s, 1H), 6.56 (br, NH_2), 6.05 (s, 1H), 3.47 (dd, 2H, *J* = 5.3 and 7.3 Hz), 3.43 (s, 2H), 2.81 (t, 2H, *J* = 7.3 Hz), 2.29 (s, 3H). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 165.7, 165.0, 162.0, 154.4, 153.9, 139.0, 136.3, 133.7, 129.5, 128.8, 122.8, 112.9, 108.1, 38.5, 28.1, 25.5, 23.1. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{19}H_{19}ClN_4O_2$: 371.1274; found: 371.1285.

N-(2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl)-4-sulfamoylbenzamide **32**

Prepared from 4-sulfamoylbenzoic acid and **30**. White solid (19 mg, 15%). m.p. 198-200 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 8.77 (t, NH, *J* = 5.0 Hz), 7.94 (d, 2H, *J* = 8.0 Hz), 7.89 (d, 2H, *J* = 8.0 Hz), 7.81 (s, 1H), 7.48 (br, NH_2), 7.39 (s, 1H), 6.56 (br, NH_2), 6.06 (s, 1H), 3.49 (dd, 2H, *J* = 5.0 and 6.9 Hz), 3.43 (s, 2H), 2.83 (t, 2H, *J* = 6.9 Hz), 2.28 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 165.7, 165.1, 162.0, 154.4, 153.8, 146.6, 139.0, 137.8, 128.2, 126.1, 122.9, 112.9, 108.1, 38.5, 28.1, 25.5, 23.1. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{19}H_{21}N_5O_4S$: 416.1392; found: 416.1383.

N-(2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl)-3-(pyridin-3-yl)benzamide **33**



Prepared from 3-(pyridin-3-yl)benzoic acid and **30**. White solid (55 mg, 45%). m.p. 200-202 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.86 (s, 1H, H-10), 8.56 (d, 1H, *J* = 4.5 Hz, H-14), 8.13 (d, 1H, *J* = 7.9 Hz, H-12), 8.08 (s, 1H, H-5), 7.81-7.87 (m, 3H, H-6", H-7 and H-9), 7.59 (t, 1H, *J* = 7.7 Hz, H-8), 7.55 (dd, 1H, *J* = 4.5 and 7.9 Hz, H-13), 7.28 (s, 1H, H-5'), 6.06 (s, 1H, H-3'), 3.65 (t, 2H, *J* = 7.0 Hz, H-1), 3.53 (s, 1H, H-6'), 2.94 (t, 2H, *J* = 7.0 Hz, H-2), 2.38 (s, 3H, H-7"). ^{13}C NMR (100 MHz, CD_3OD) δ 168.4 (C-2"), 164.9 (C-3), 162.1 (C-4"), 154.1 (C-2'), 152.8 (C-6"), 147.8 (C-14), 147.0 (C-10), 138.7 (C-5'), 137.5 (C-6), 136.4 (C-11), 135.3 (C-12), 135.1 (C-4), 129.7 (C-7), 129.1 (C-8), 126.7 (C-9), 125.6 (C-5), 124.1 (C-13), 121.8 (C-4'), 113.3 (C-5"), 107.3 (C-3'), 38.4 (C-1), 27.6 (C-2), 23.3 (C-7"), 22.8 (C-6'). IR (neat) *v* 1541, 1591, 1633, 2927, 3165, 3313 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{24}H_{23}N_5O_2$: 414.1930; found: 414.1943.

N-(2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl)-4-chlorobenzamide **34**

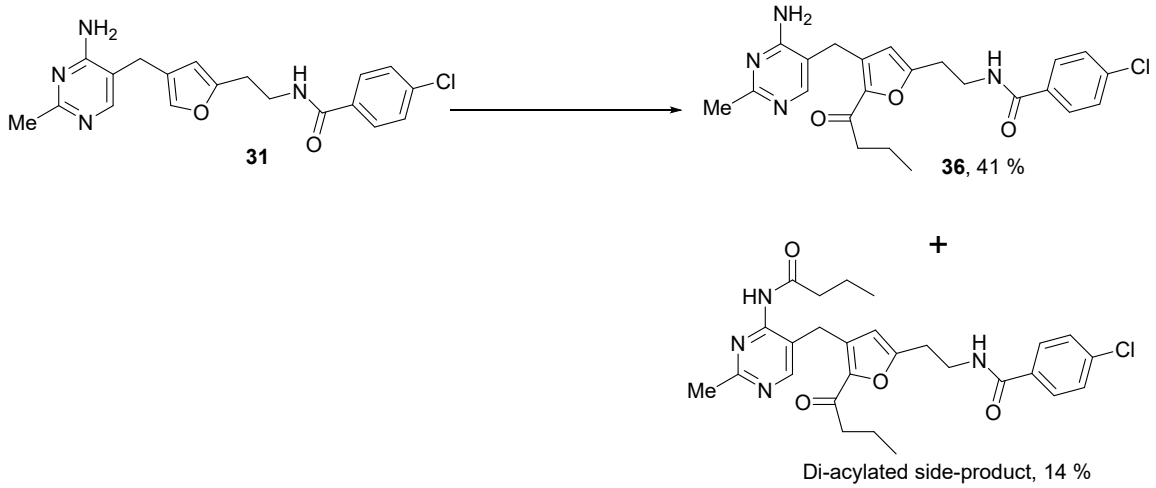
Prepared from 4-chlorobenzoic acid and *5-{[4-(2-Aminoethyl)-1H-1,2,3-triazol-1-yl]methyl}-2-methylpyrimidin-4-amine*[11]. White solid (45 mg, 40%). m.p. 228-230 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 8.64 (t, NH, *J* = 5.0 Hz), 7.95 (s, 1H), 7.91 (s, 1H), 7.81 (d, 2H, *J* = 7.5 Hz), 7.53 (d, 2H, *J* = 7.5 Hz), 6.89 (br, NH_2), 5.39 (s, 2H), 3.49 (dd, 2H, *J* = 5.0 and 7.2 Hz), 2.88 (t, 2H, *J* = 7.2 Hz), 2.31 (s, 3H). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 167.3, 165.7, 161.9, 156.4, 144.9, 136.4, 133.7, 129.5, 128.8, 122.9, 108.9, 47.2, 39.6, 25.7, 25.6. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{17}H_{18}ClN_7O$: 372.1340; found: 372.1347.

N-(2-{1-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-1H-1,2,3-triazol-4-yl}ethyl)-4-sulfamoylbenzamide **35**

Prepared from 4-sulfamoylbenzoic acid and *5-{[4-(2-Aminoethyl)-1H-1,2,3-triazol-1-yl]methyl}-2-methylpyrimidin-4-amine*[11]. White solid (37 mg, 30%). m.p. 239-240 °C. ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 8.76 (t, NH, *J* = 5.2 Hz), 7.85-7.95 (m, 6H), 7.49 (br, NH_2), 6.88 (br, NH_2), 5.39 (s, 2H), 3.49 (masked by the solvent peak), 2.89 (t, 2H, *J* = 7.1 Hz), 2.31 (s, 3H). ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 167.3, 165.8, 161.8, 156.3, 146.6, 144.9, 137.8, 128.2, 126.1, 123.0, 108.8, 47.1, 39.6, 25.6, 25.5. IR (neat) *v* 1539, 1597, 1641, 3027, 3317, 3447 cm^{-1}. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{17}H_{20}N_8O_3S$: 417.1457; found: 417.1462.

The following scheme was used to prepare **36** and a **di-acylated side-product**:

N-(2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-butanoylfuran-2-yl}ethyl)-4-chlorobenzamide **36**



To a stirred solution of **31** (37 mg, 0.1 mmol) and aluminium chloride (67 mg, 0.5 mmol) in dry 1,2-dichloroethane (1 mL, 0.1 M) under nitrogen at 0 °C was added butyryl chloride (0.083 mL, 0.8 mmol) dropwise. The resultant mixture was stirred at 0 °C for 15 minutes and then at r.t. overnight. The reaction mixture was quenched with cold aqueous phosphate buffer (pH 7) (15 mL) at 0 °C and extracted with DCM (50 mL). The organic phase was washed with aqueous phosphate buffer (pH 7) (50 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (12% *MeOH* in DCM) to yield amides **36** and a di-acylated side-product.

For **36**: white solid (18 mg, 41%). m.p. 180-182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.66 (d, 2H, *J* = 8.3 Hz), 7.41 (d, 2H, *J* = 8.3 Hz), 6.40 (br, NH), 6.23 (s, 1H), 5.93 (br, NH_2), 3.92 (s, 2H), 3.75 (m, 2H), 3.00 (t, 2H, *J* = 6.6 Hz), 2.84 (t, 2H, *J* = 7.3 Hz), 2.49 (s, 3H), 1.73 (m, 2H), 0.99 (t, 3H, *J* = 7.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 166.6, 165.2, 161.8, 157.1, 153.6, 147.2, 138.0, 132.5, 132.0, 128.9, 128.2, 112.1, 111.8, 41.0, 38.1, 28.5, 24.7, 24.7, 17.3, 13.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{23}H_{25}ClN_4O_3$: 441.1693; found: 441.1699.

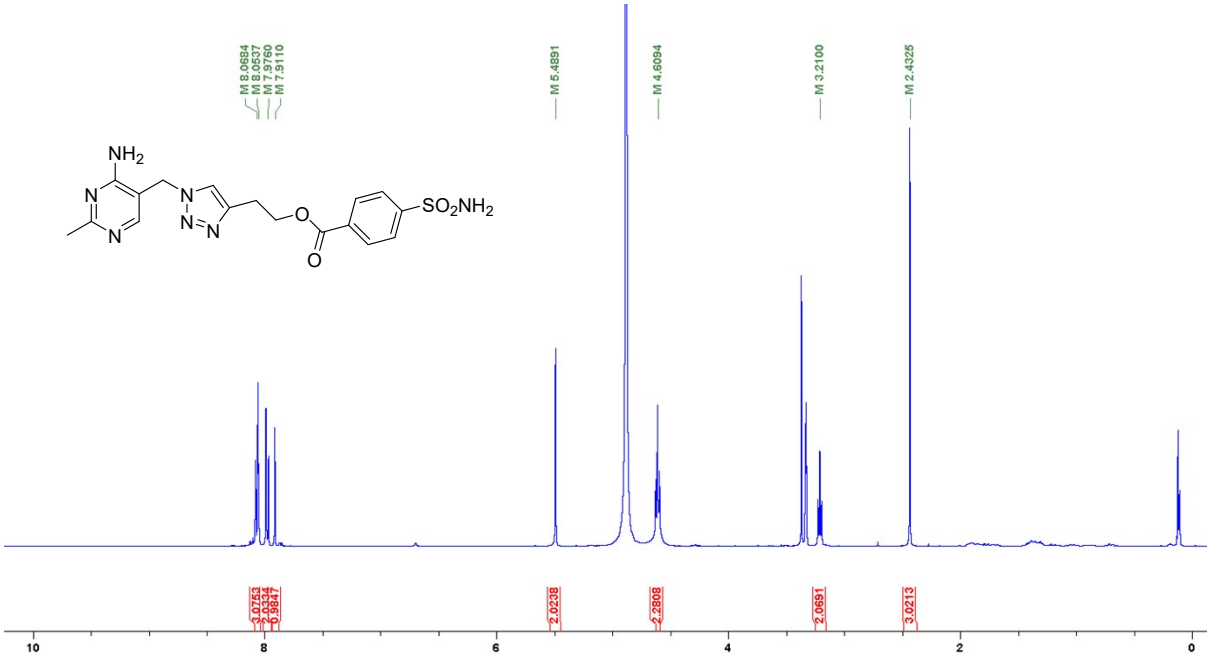
For di-acylated side-product: yellow oil (7 mg, 14% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (br, NH), 8.43 (s, 1H), 7.67 (d, 2H, *J* = 8.4 Hz), 7.40 (d, 2H, *J* = 8.4 Hz), 6.52 (br, NH), 6.21 (s, 1H), 4.03 (s, 2H), 3.74 (m, 2H), 3.00 (t, 2H, *J* = 6.6 Hz), 2.83 (t, 2H, *J* = 7.3 Hz), 2.65 (s, 3H), 2.59 (t, 2H, *J* = 7.5 Hz), 1.73 (m, 4H), 0.99 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 172.8, 166.6, 166.5, 157.5, 157.4, 156.4, 147.1, 137.9, 132.4, 131.7, 128.9, 128.3, 117.3, 111.8, 40.8, 39.6, 38.2, 28.5, 25.6, 24.7, 18.5, 17.2, 13.8, 13.8. ESI-MS *m/z*: 511.21 [M+H$^+$]. This compound was subjected to PDH E1 enzyme assay evaluation and found to be inactive.

N-(2-{4-[(4-Amino-2-methylpyrimidin-5-yl)methyl]-5-butanoylfuran-2-yl}ethyl)-3-(pyridin-3-yl)benzamide **37**

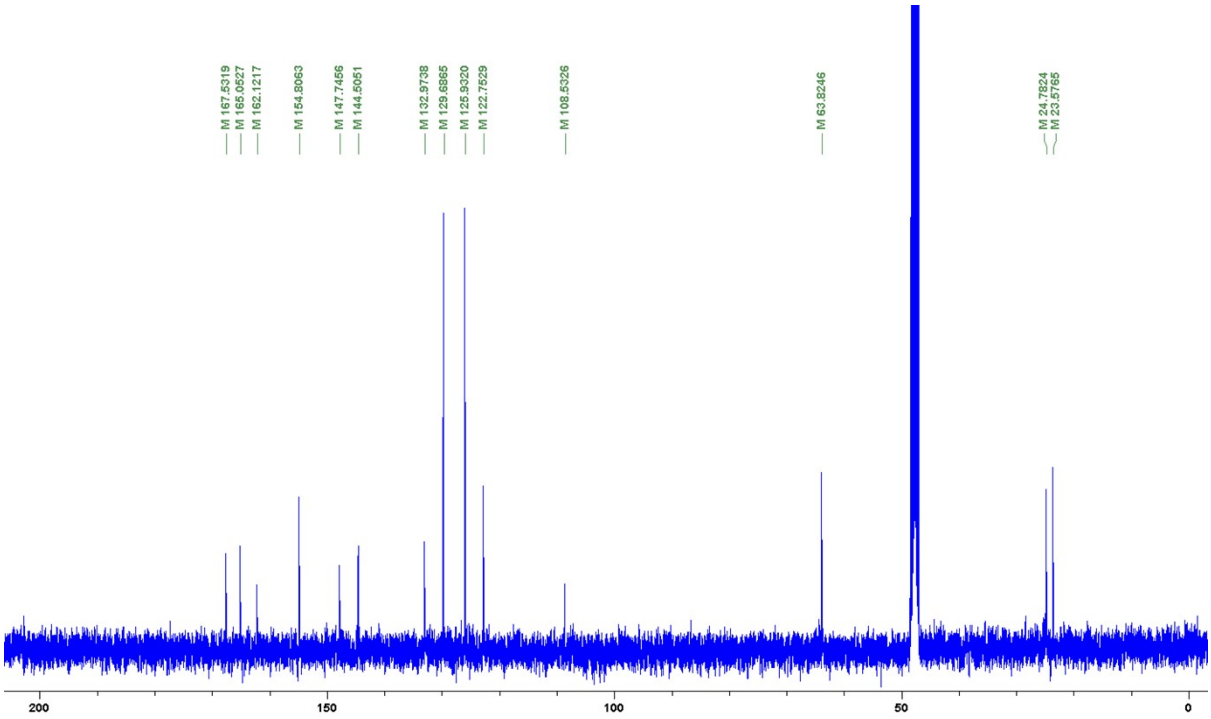
To a stirred solution of **33** (41 mg, 0.1 mmol) and aluminium chloride (74 mg, 0.55 mmol) in dry 1,2-dichloroethane (1.5 mL, 0.1 M) under nitrogen at 0 °C was added butyryl chloride (0.083 mL, 0.8 mmol) dropwise. The resultant mixture was stirred at 0 °C for 15 minutes and then at r.t. overnight. The reaction mixture was quenched with cold aqueous phosphate buffer (pH 7) (15 mL) at 0 °C and extracted with EtOAc (50 mL). The organic phase was washed with aqueous phosphate buffer (pH 7) (50 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica flash chromatography (10% MeOH in DCM) to yield **37** as a white solid (7 mg, 15%). m.p. 213-216 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.88 (s, 1H), 8.59 (m, 1H), 8.16 (d, 1H, *J* = 7.6 Hz), 8.09 (s, 1H), 7.96 (s, 1H), 7.88 (d, 1H, *J* = 7.8 Hz), 7.83 (d, 1H, *J* = 7.8 Hz), 7.61 (t, 1H, *J* = 7.8 Hz), 7.58 (m, 1H), 6.35 (s, 1H), 3.93 (s, 2H), 3.72 (t, 2H, *J* = 6.6 Hz), 3.05 (t, 2H, *J* = 6.6 Hz), 2.79 (t, 2H, *J* = 7.3 Hz), 2.36 (s, 3H), 1.64 (m, 2H), 0.89 (t, 3H, *J* = 7.5 Hz). ^{13}C NMR (100 MHz, CD_3OD) δ 193.8, 167.7, 165.0, 162.2, 156.9, 153.5, 147.6, 147.5, 147.1, 137.8, 136.5, 135.7, 135.5, 132.3, 129.8, 129.7, 126.9, 125.8, 124.6, 113.0, 112.7, 40.5, 38.8, 27.9, 23.5, 23.3, 17.5, 12.7. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{28}H_{29}N_5O_3$: 484.2348; found: 484.2345.

NMR spectra

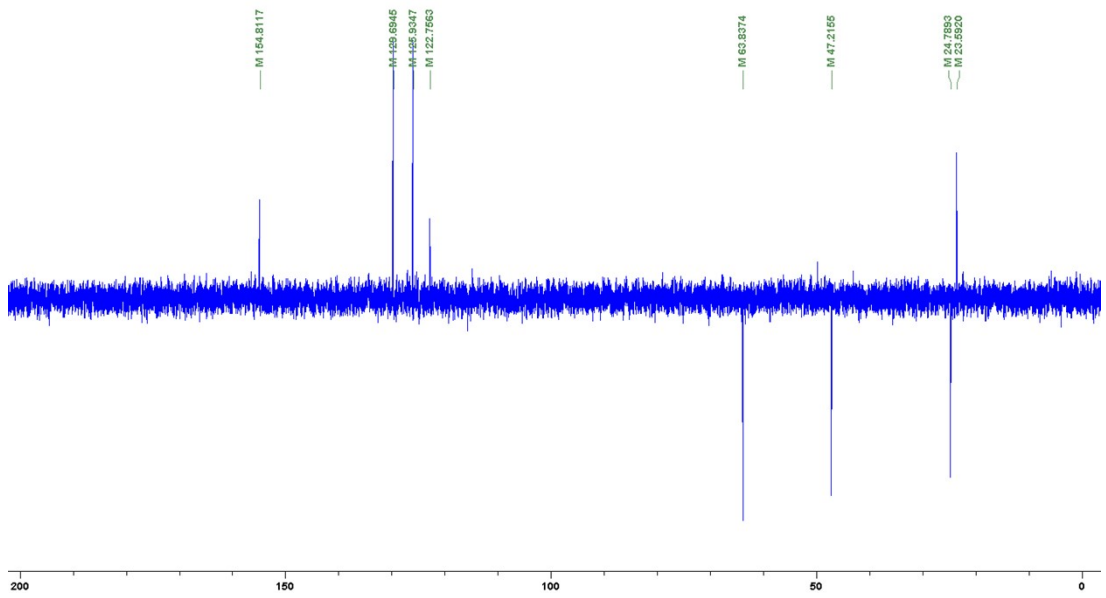
^{1}H NMR of **8i** in CD_3OD:



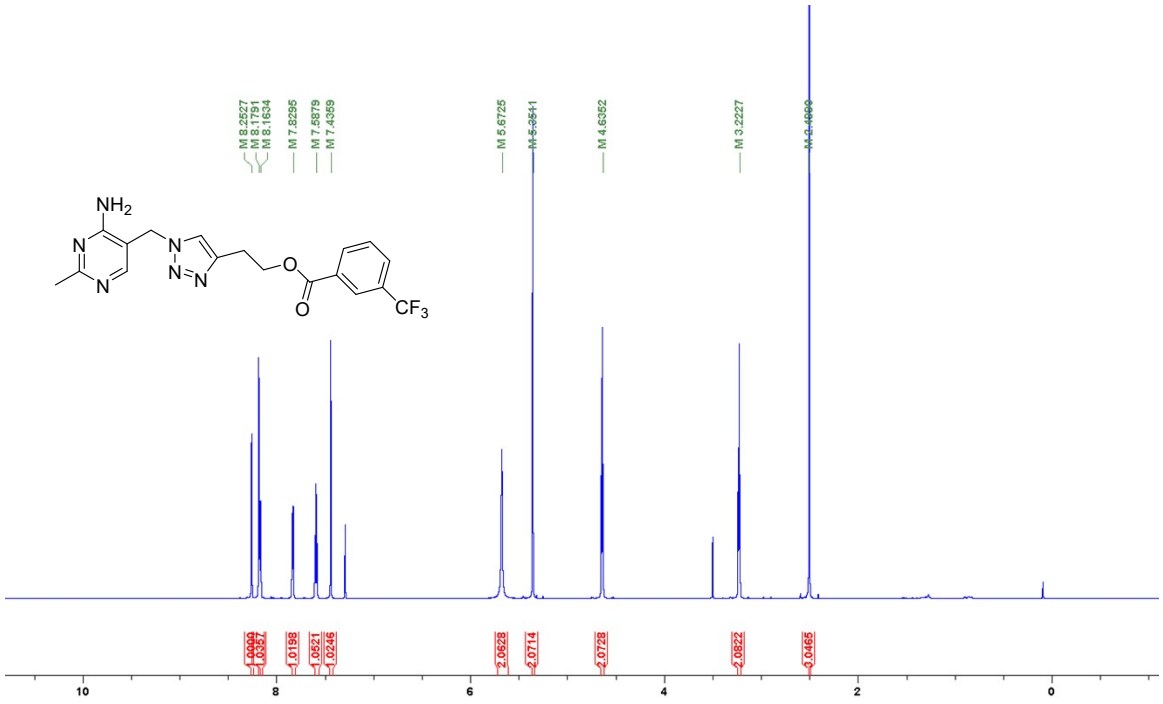
^{13}C NMR of **8i** in CD_3OD: (the peak at 47.2 is shielded by the solvent peak)



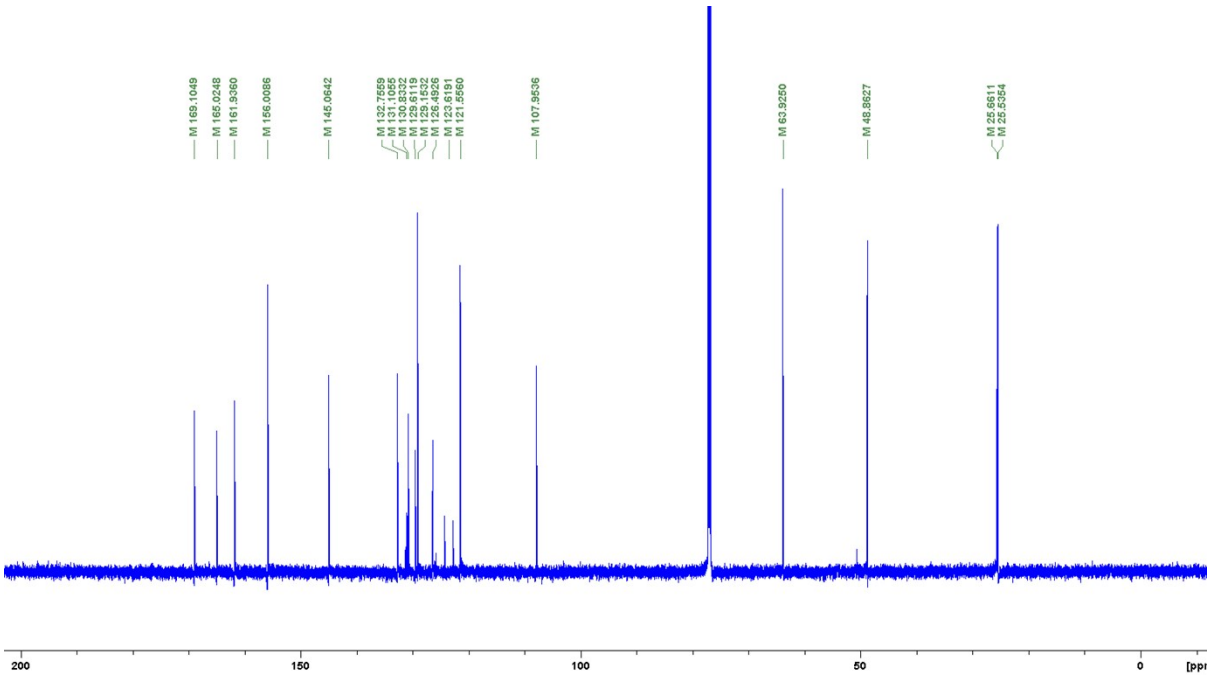
^{13}C DEPT-135 NMR of **8i** in CD_3OD: (the peak at 47.2 shielded by the solvent peak is unmasked in the DEPT-135 spectrum)



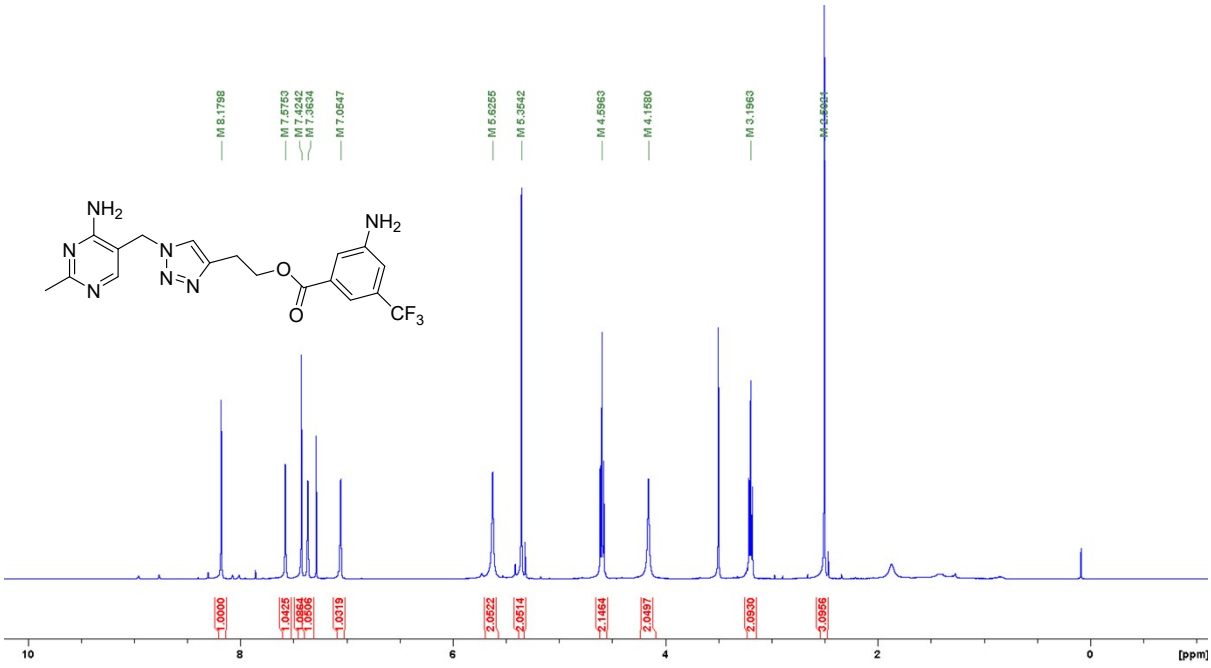
^{1}H NMR of **8j** in $CDCl_3$:



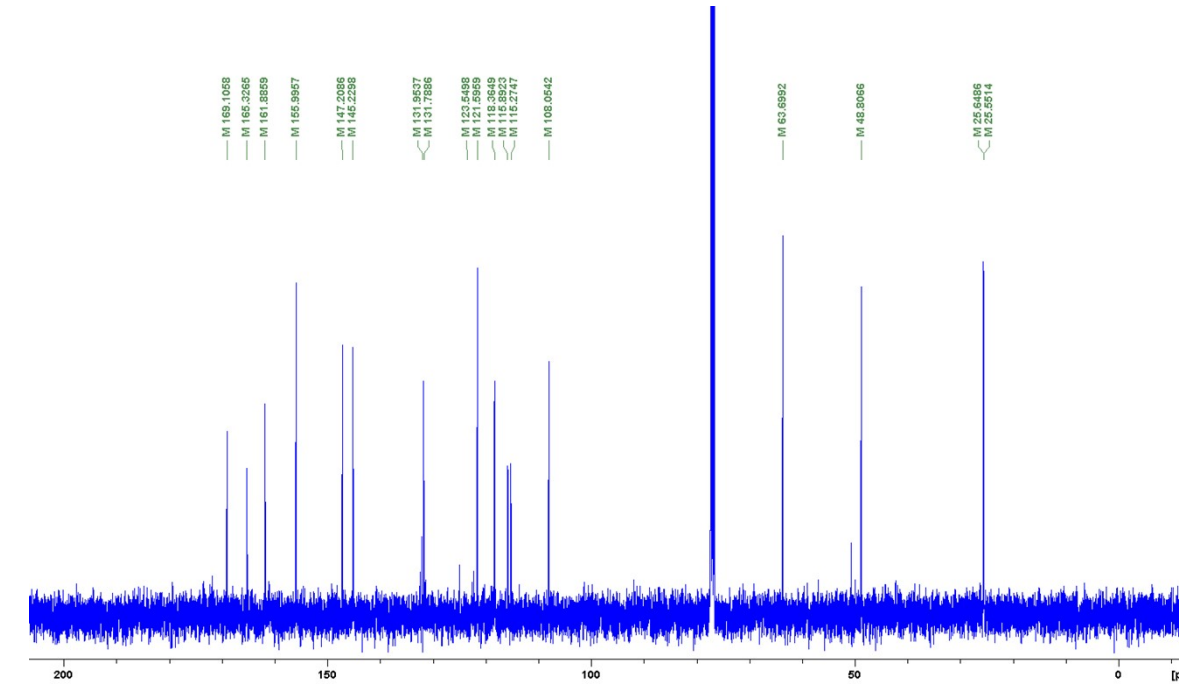
^{13}C NMR of **8j** in $CDCl_3$:



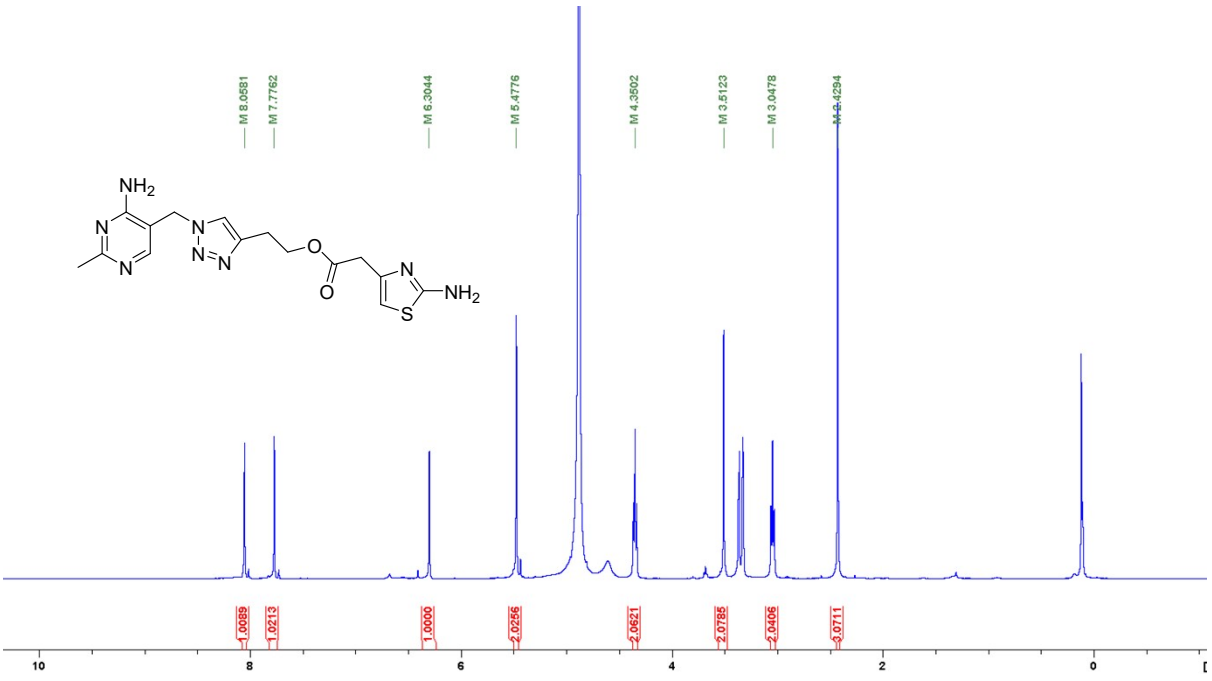
^{1}H NMR of **8k** in $CDCl_3$:



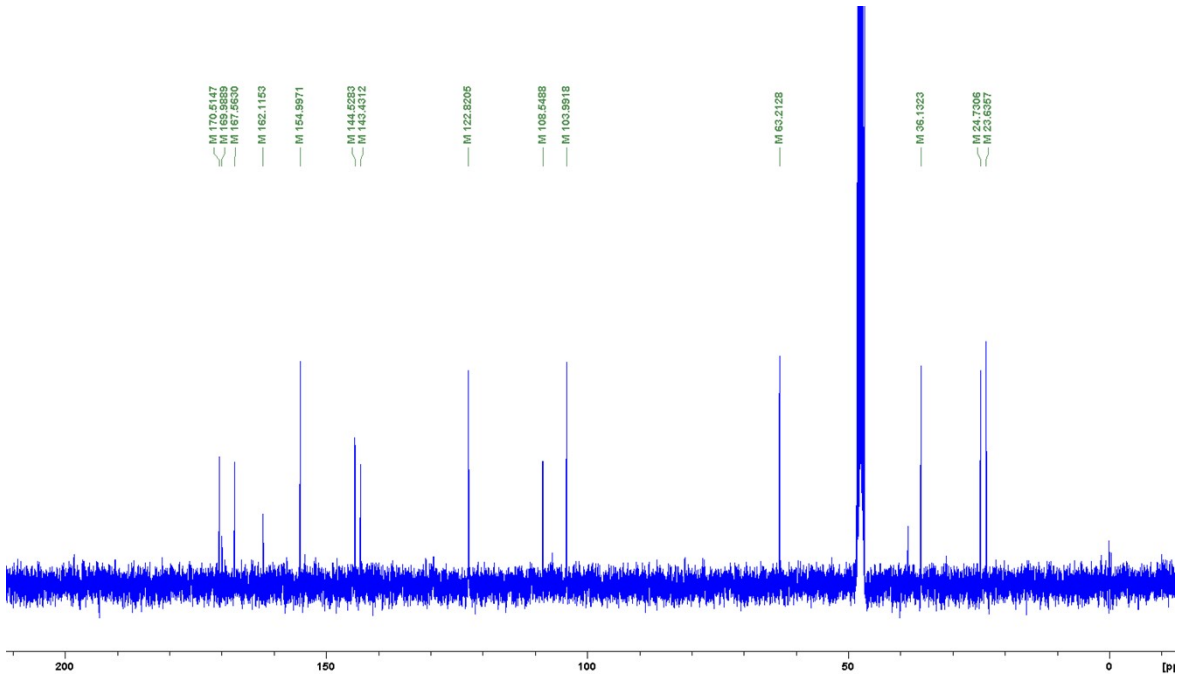
^{13}C NMR of **8k** in $CDCl_3$:



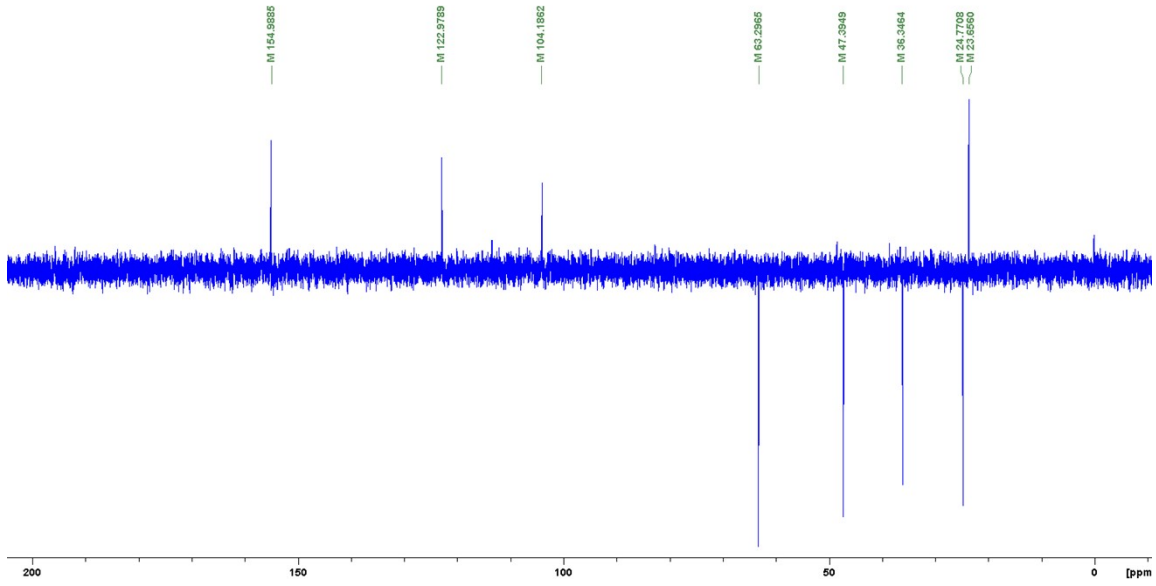
^{1}H NMR of **8l** in CD_3OD:



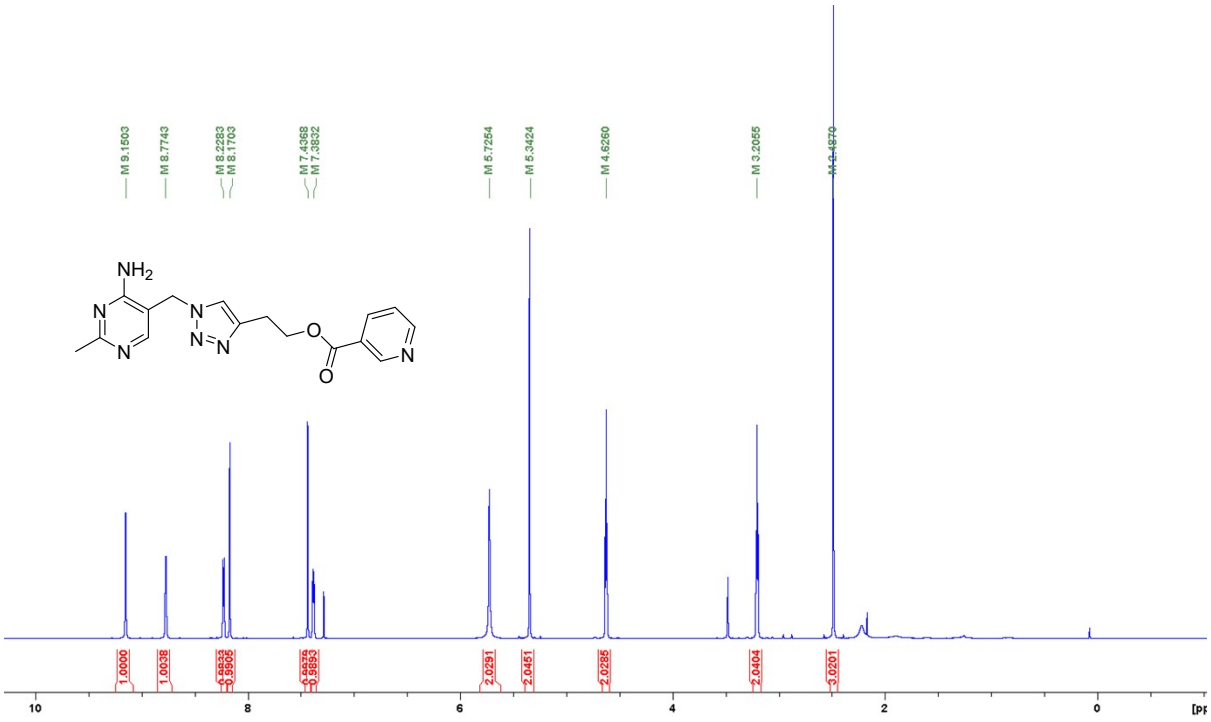
^{13}C NMR of **8l** in CD_3OD: (the peak at 47.4 is shielded by the solvent peak)



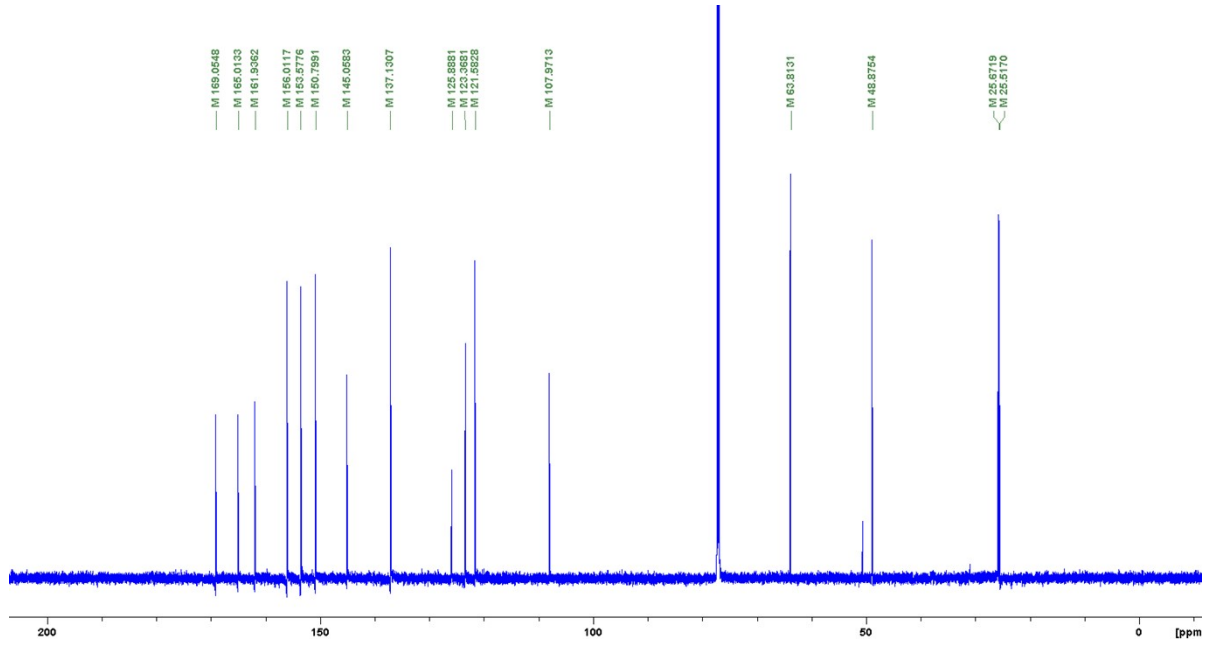
^{13}C DEPT-135 NMR of **8l** in CD_3OD: (the peak at 47.2 shielded by the solvent peak is unmasked in the DEPT-135 spectrum)



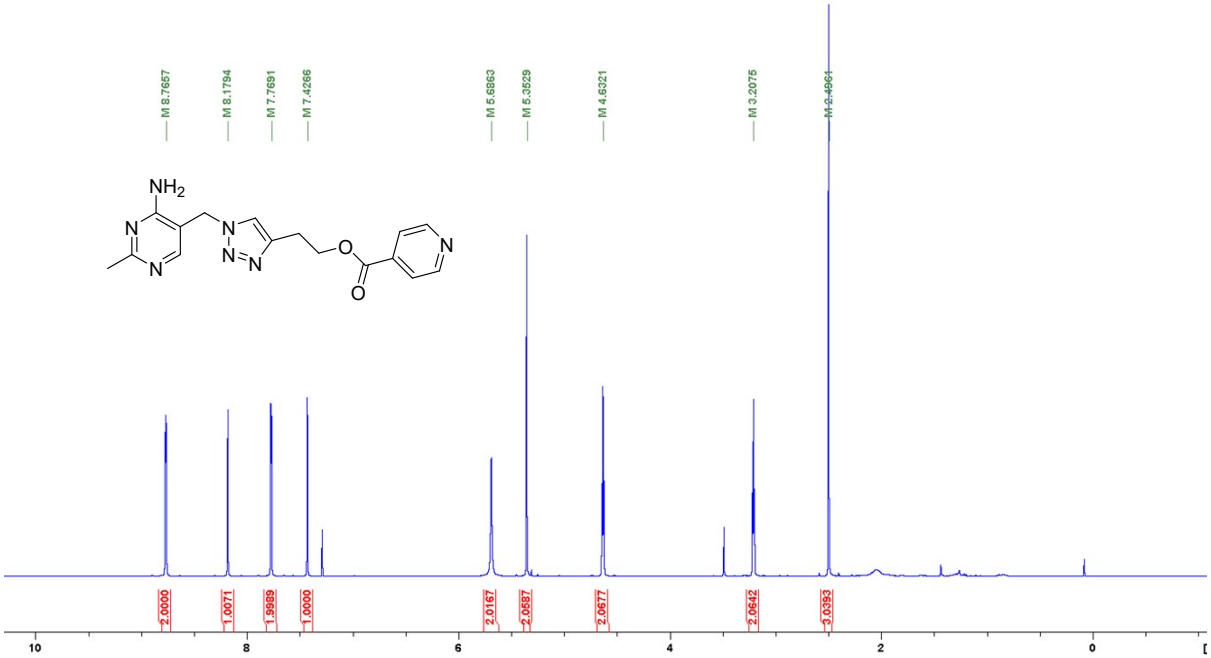
^{1}H NMR of **8m** in $CDCl_3$:



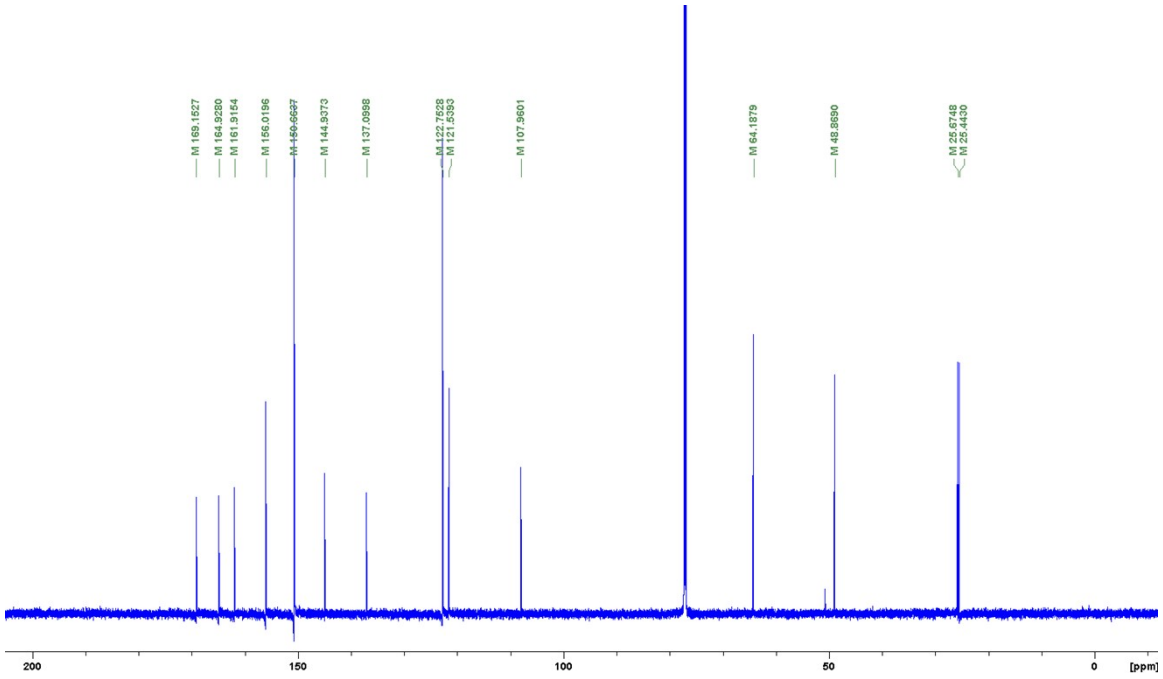
^{13}H NMR of **8m** in $CDCl_3$:



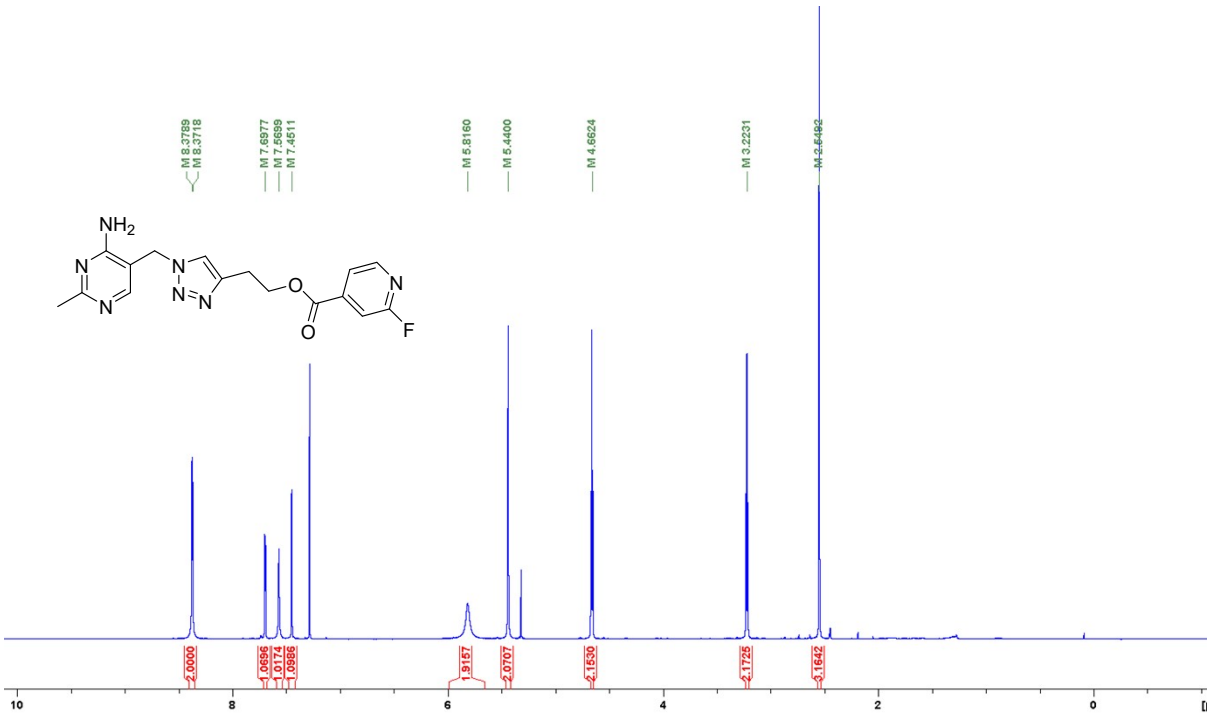
^{1}H NMR of **8n** in $CDCl_3$:



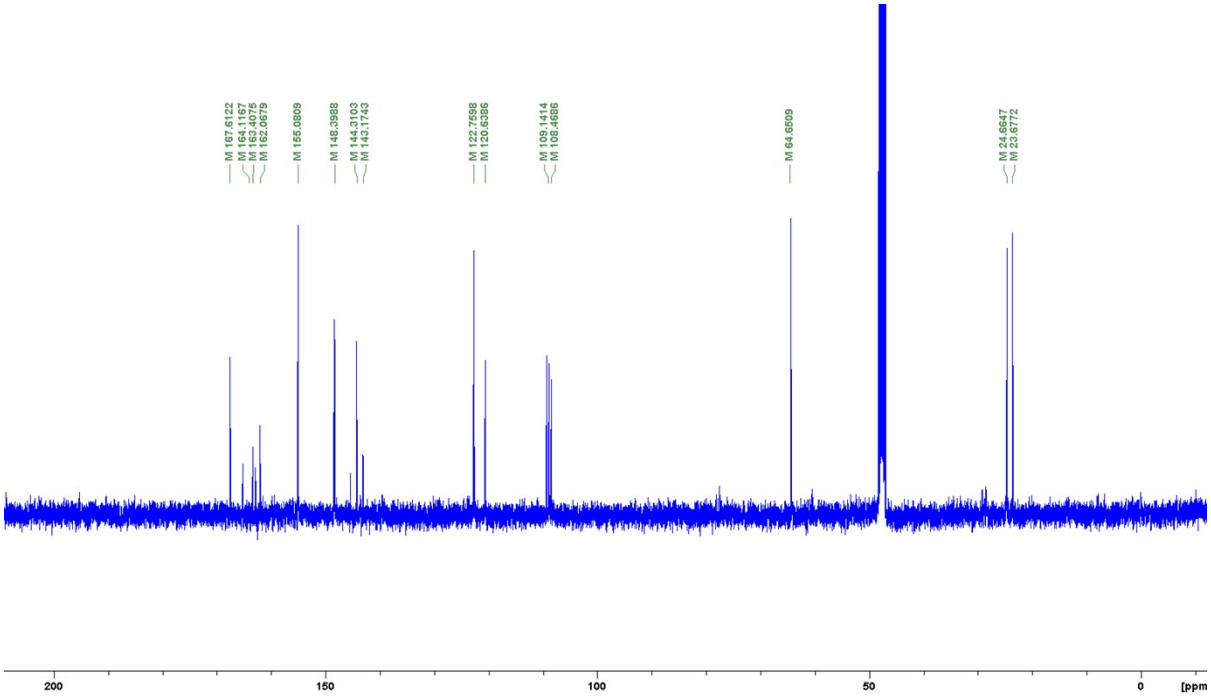
^{13}C NMR of **8n** in $CDCl_3$:



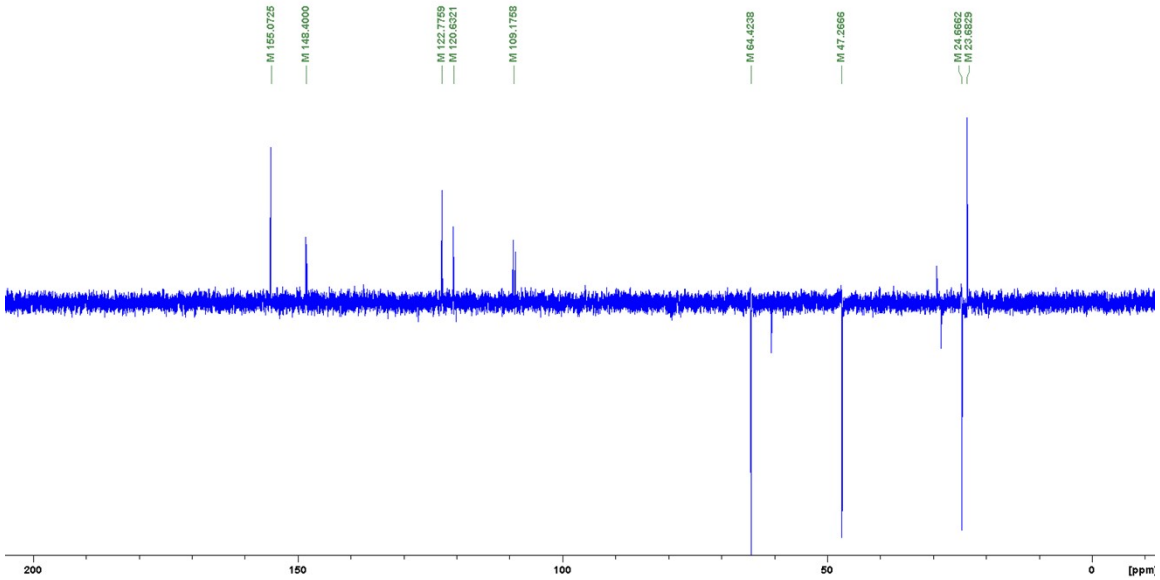
^{1}H NMR of **8o** in $CDCl_3$:



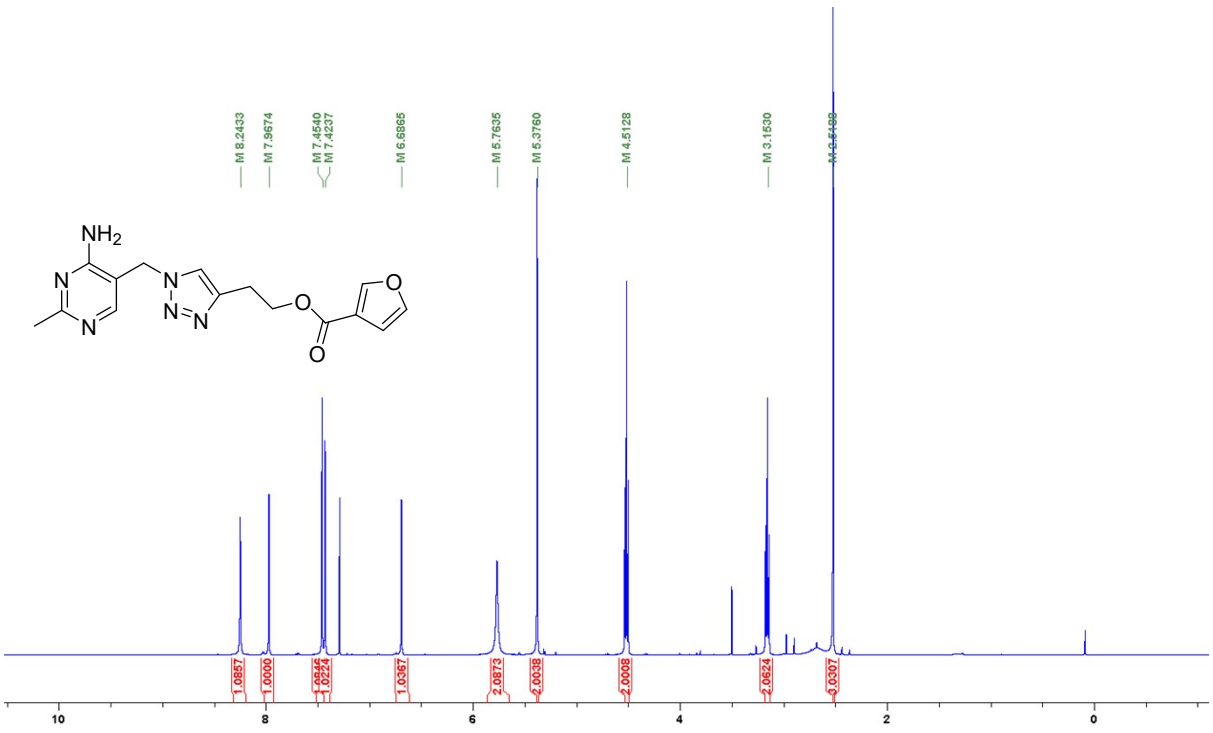
^{13}C NMR of **8o** in $CDCl_3$: (the peak at 47.2 is shielded by the solvent peak)



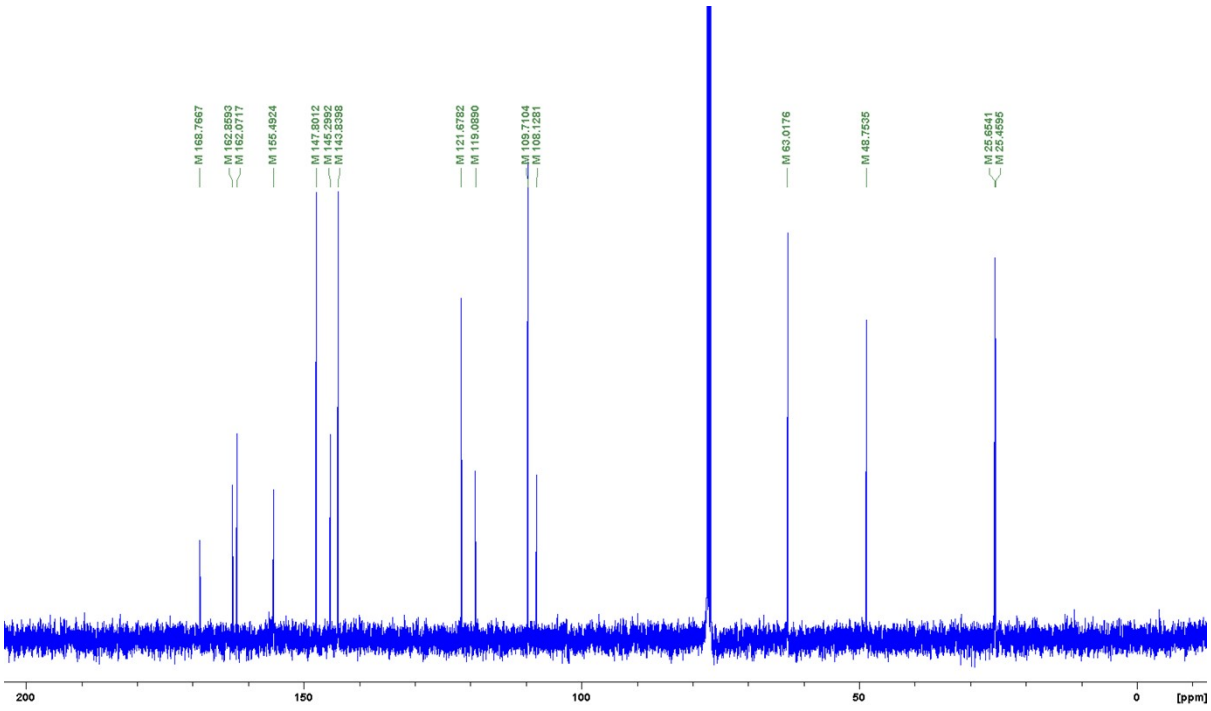
^{13}C DEPT-135 NMR of **8o** in CD_3OD: (the peak at 47.2 shielded by the solvent peak is unmasked in the DEPT-135 spectrum)



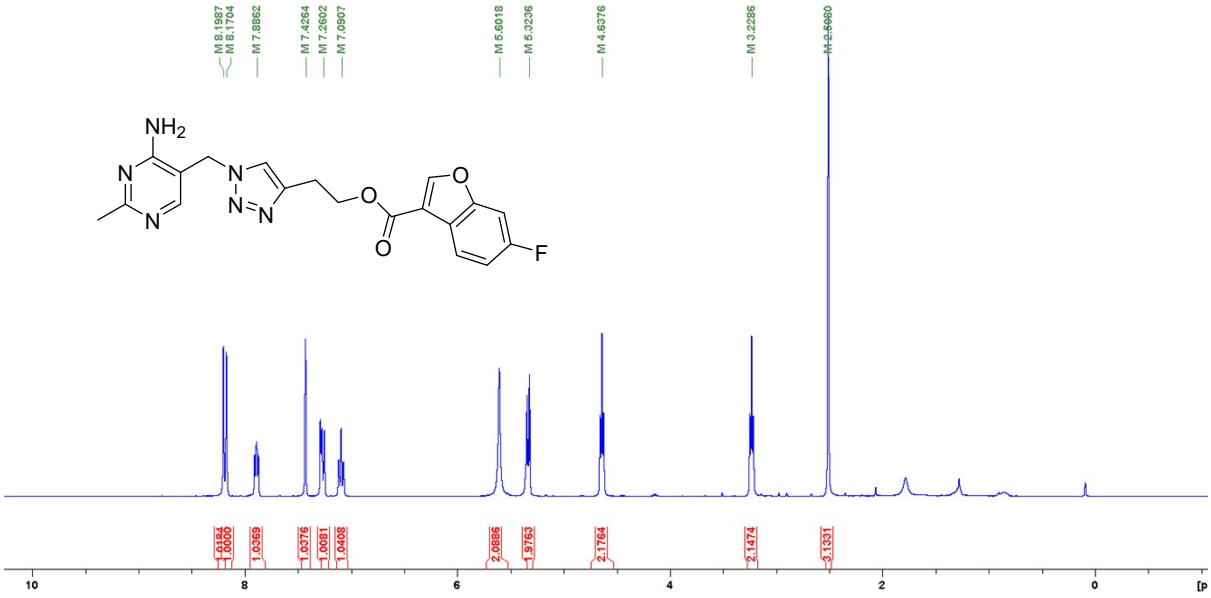
^{1}H NMR of **8q** in $CDCl_3$:



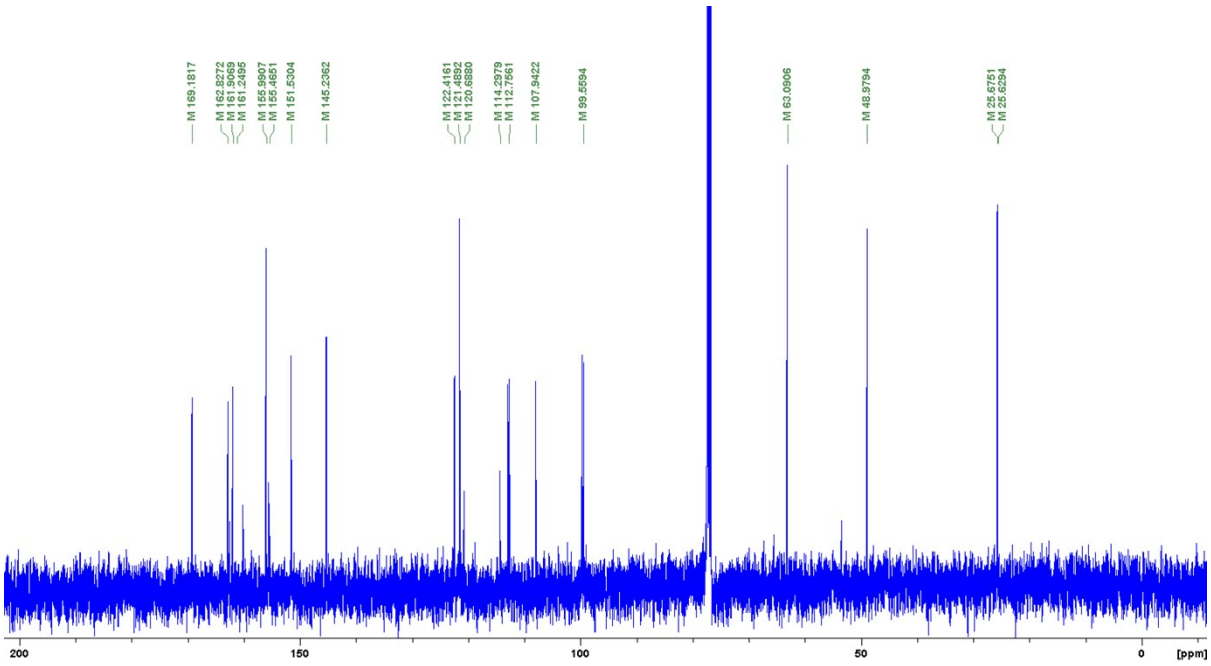
^{13}C NMR of **8q** in $CDCl_3$:



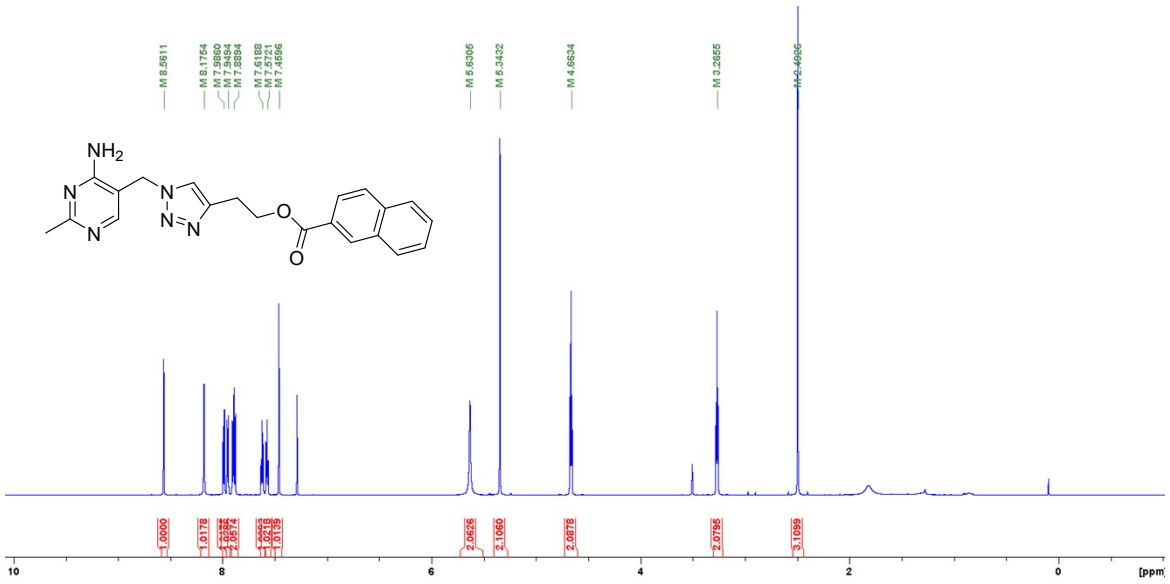
^{1}H NMR of **8r** in $CDCl_3$:



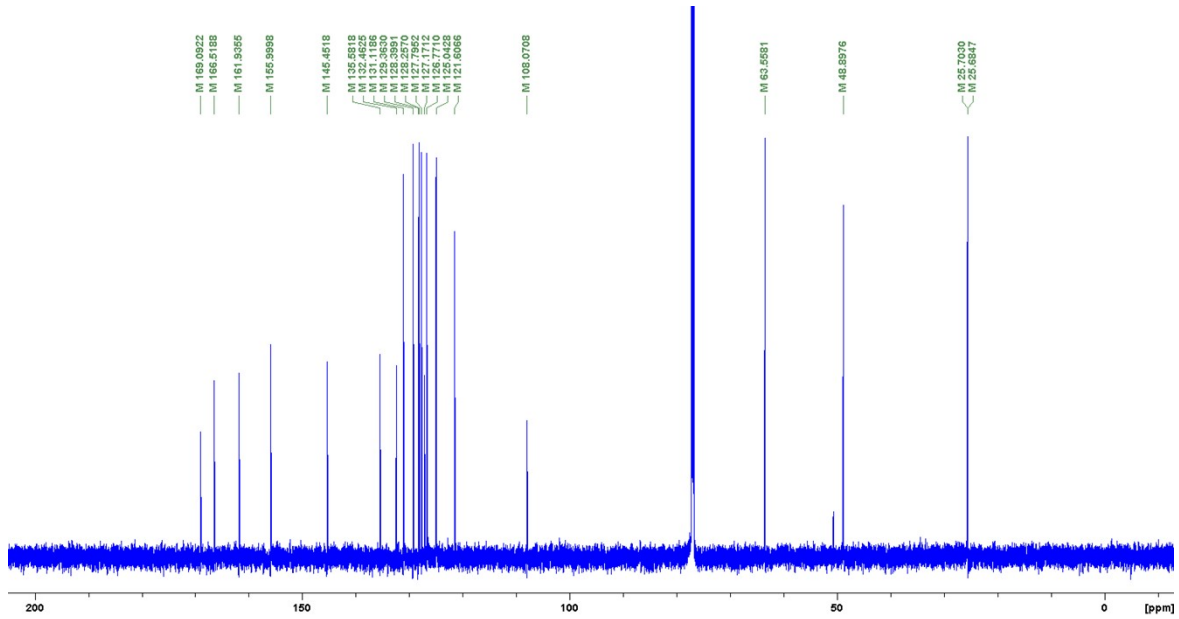
^{13}C NMR of **8r** in $CDCl_3$:



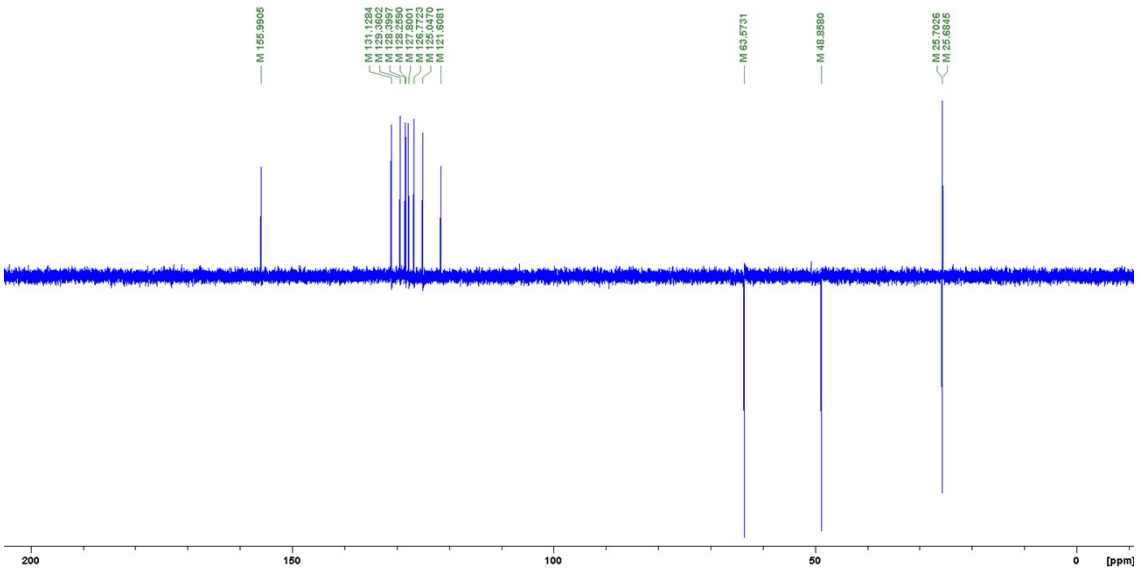
^{1}H NMR of **8s** in $CDCl_3$:



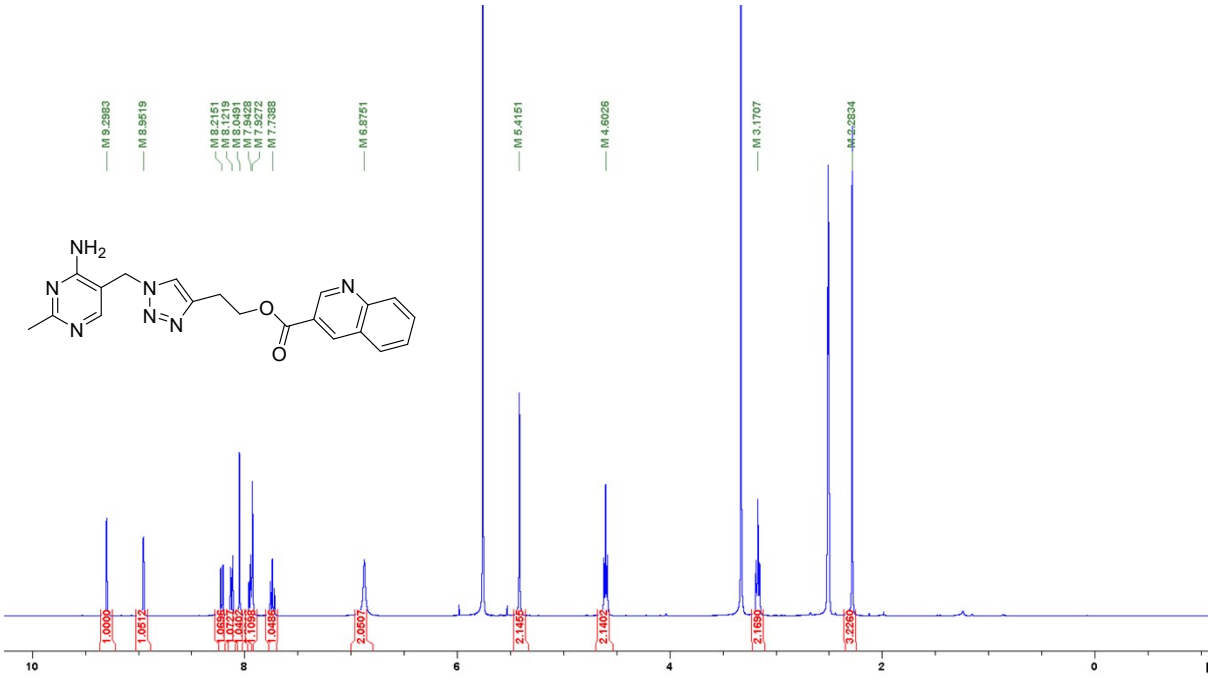
^{13}C NMR of **8s** in $CDCl_3$:



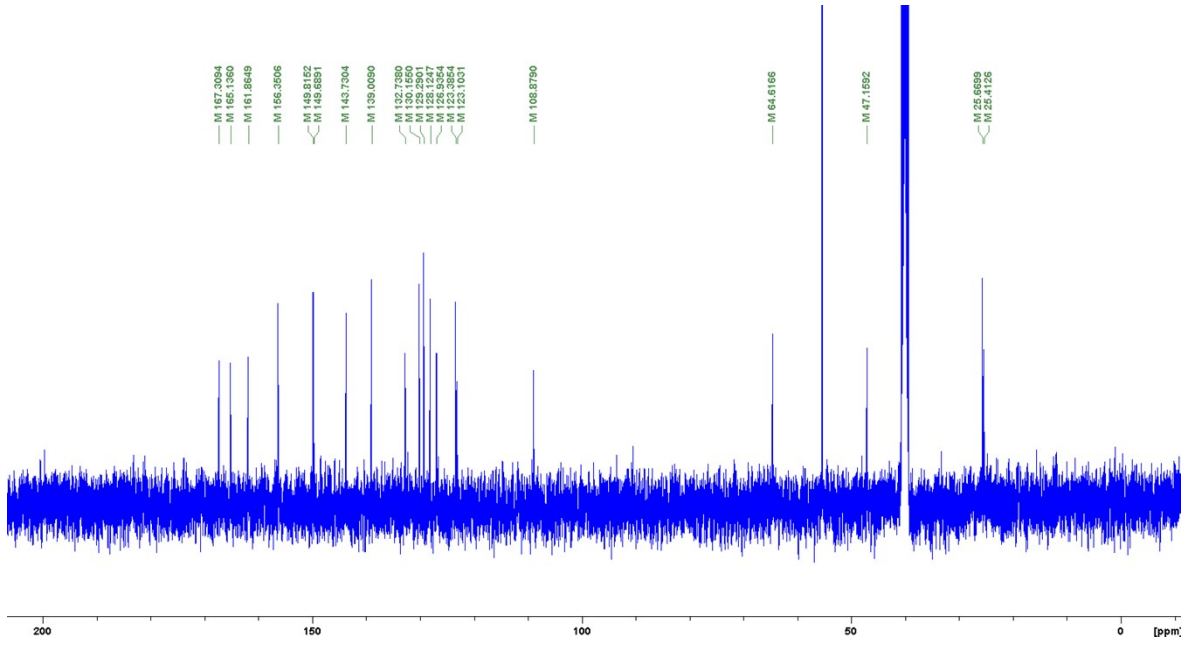
^{13}C DEPT-135 NMR of **8s** in $CDCl_3$:



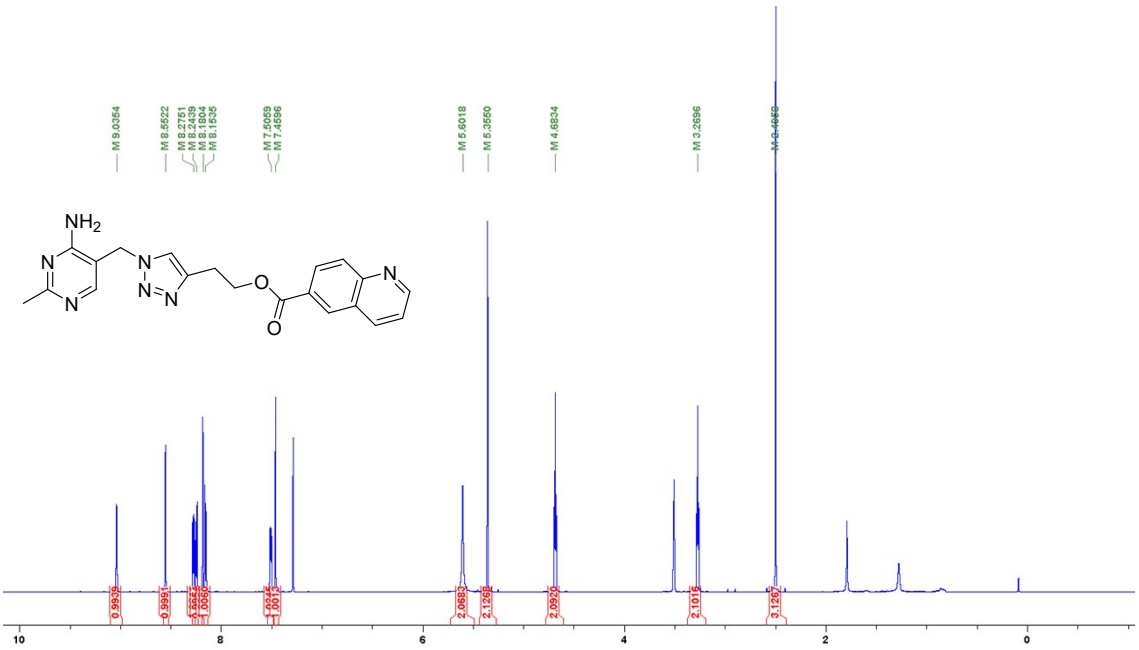
^{1}H NMR of **8t** in CD_3SOCD_3:



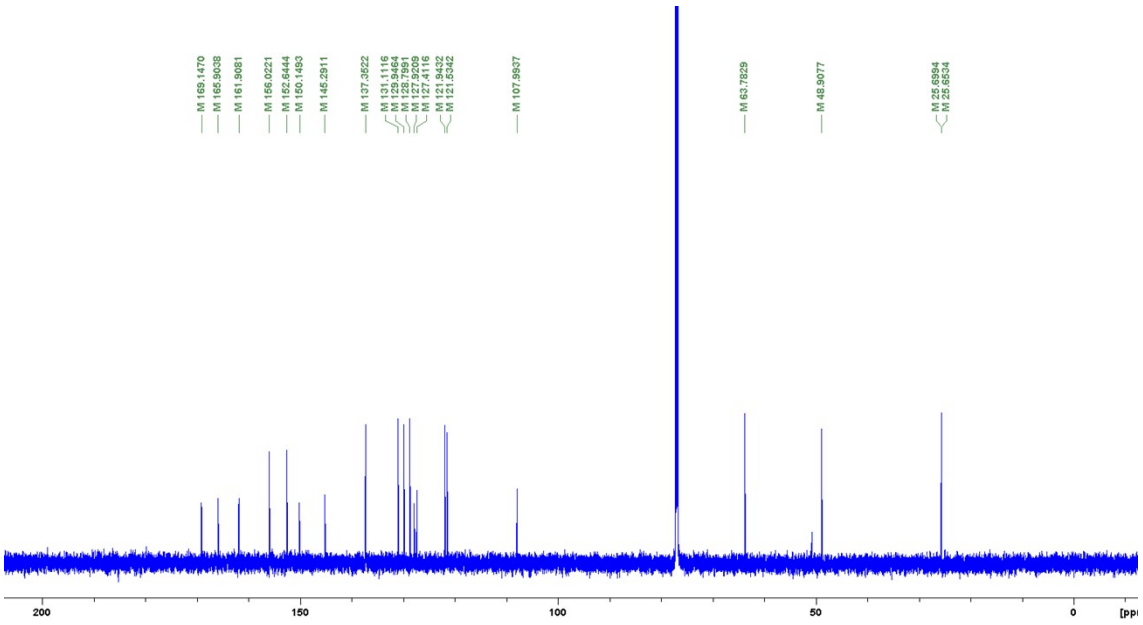
^{13}C NMR of **8t** in CD_3SOCD_3:



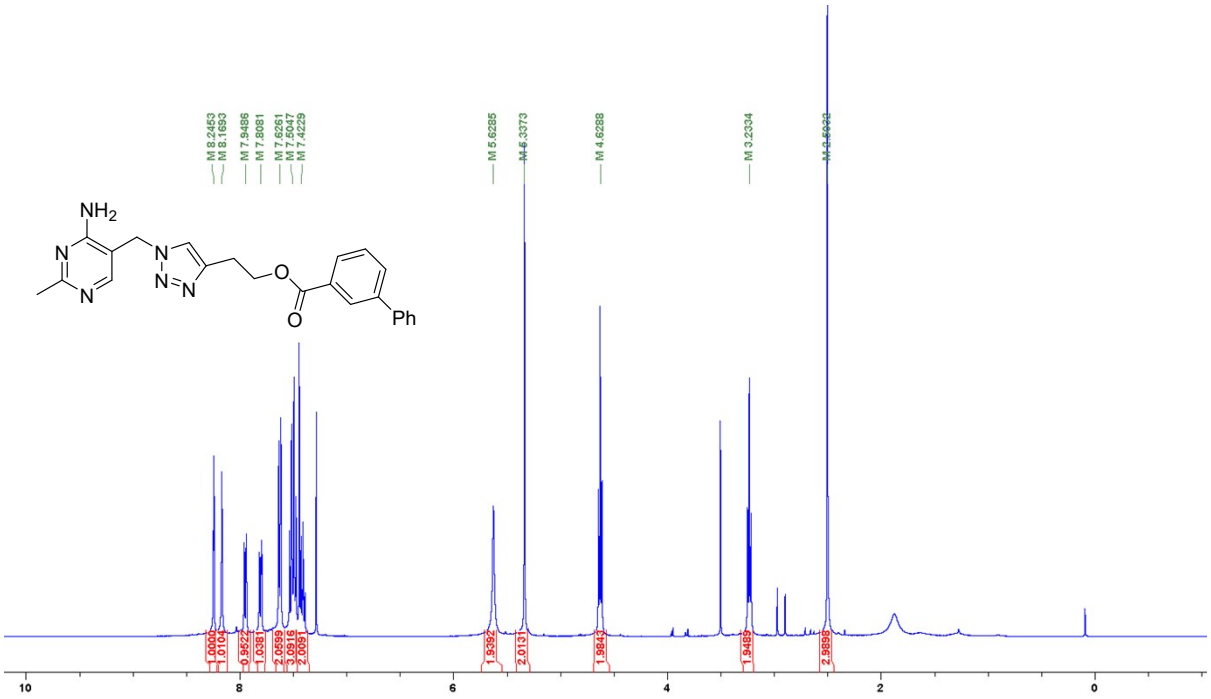
^{1}H NMR of **8u** in $CDCl_3$:



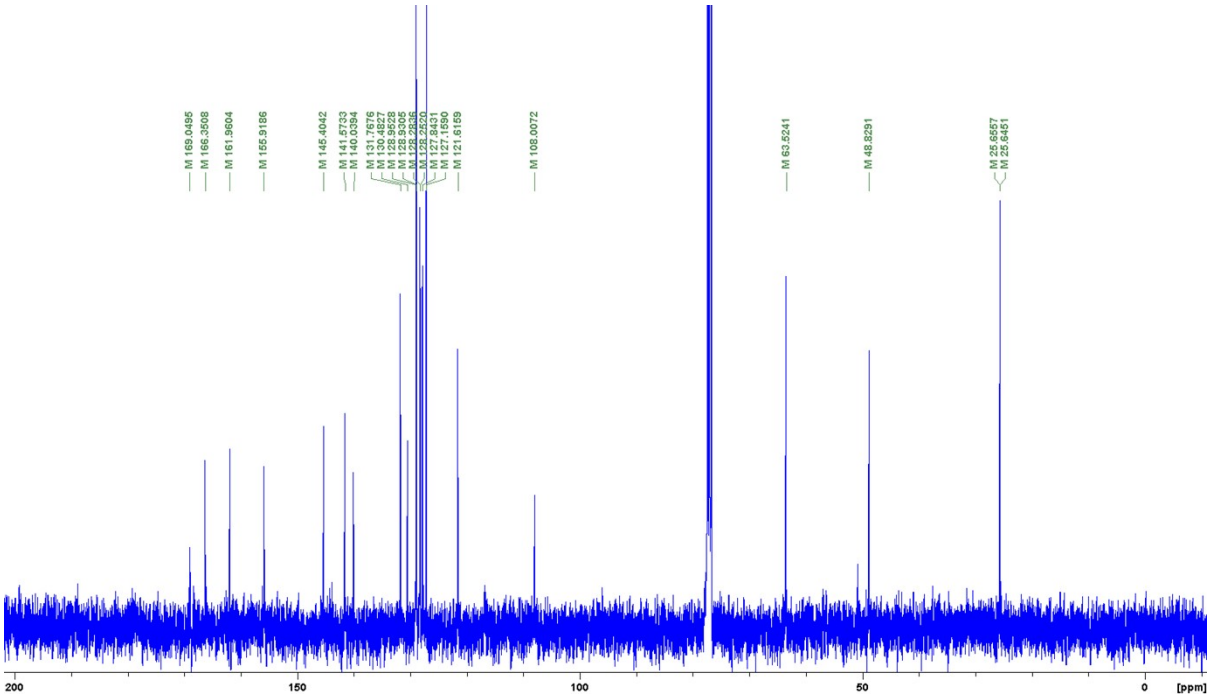
^{13}C NMR of **8u** in $CDCl_3$:



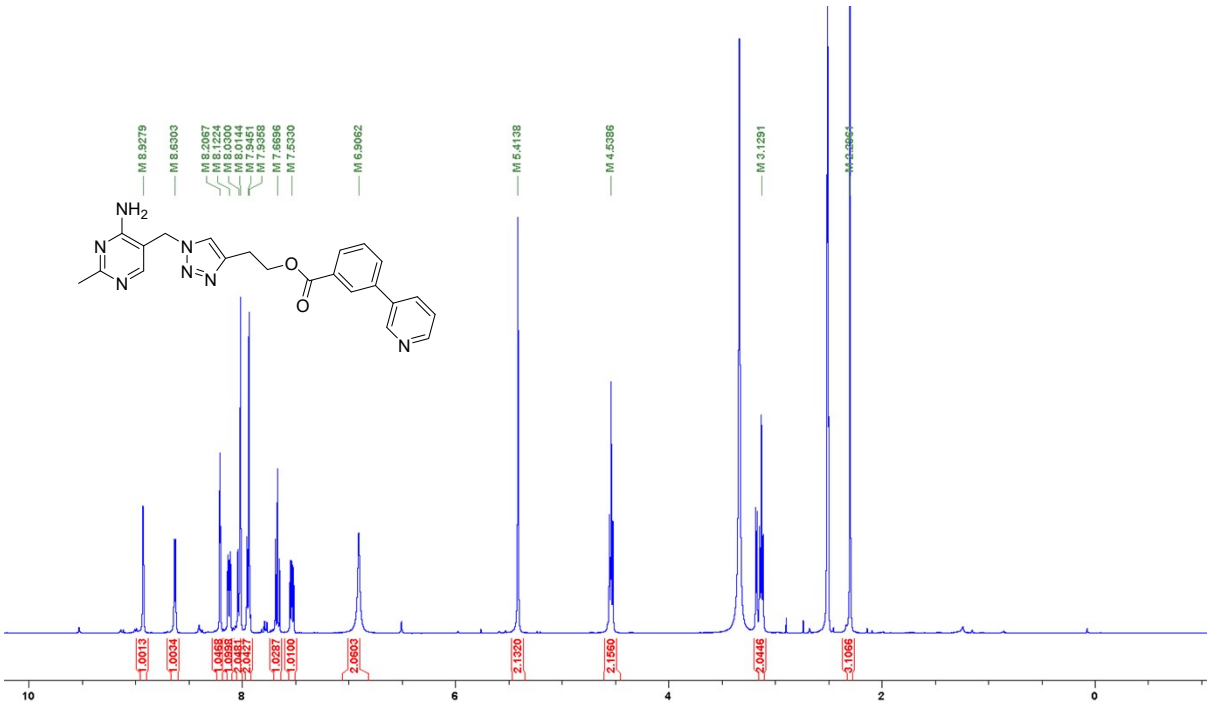
^{1}H NMR of **8v** in $CDCl_3$:



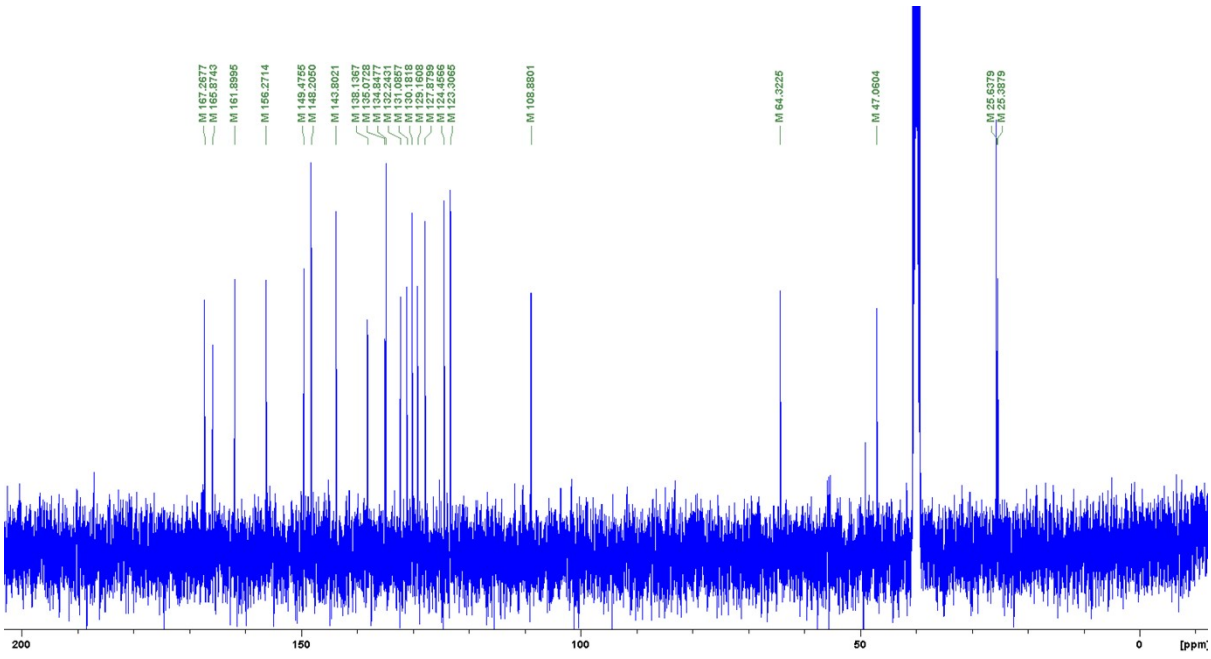
^{13}C NMR of **8v** in $CDCl_3$:



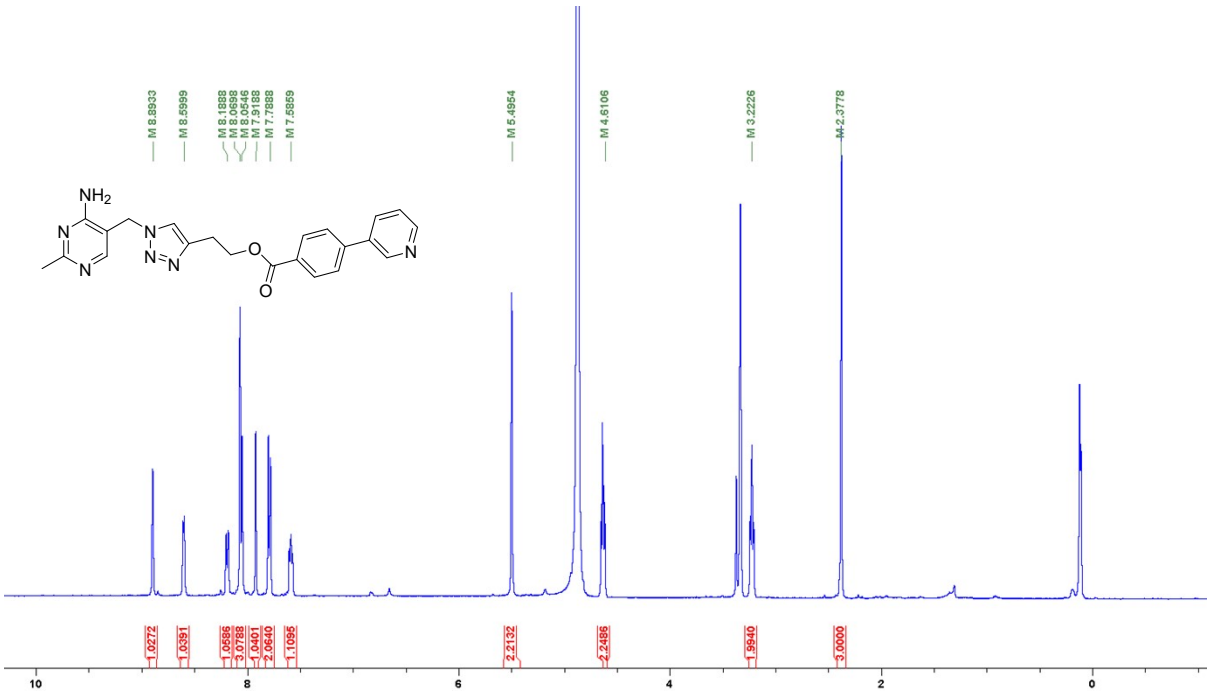
^{1}H NMR of **8w** in CD_3SOCD_3:



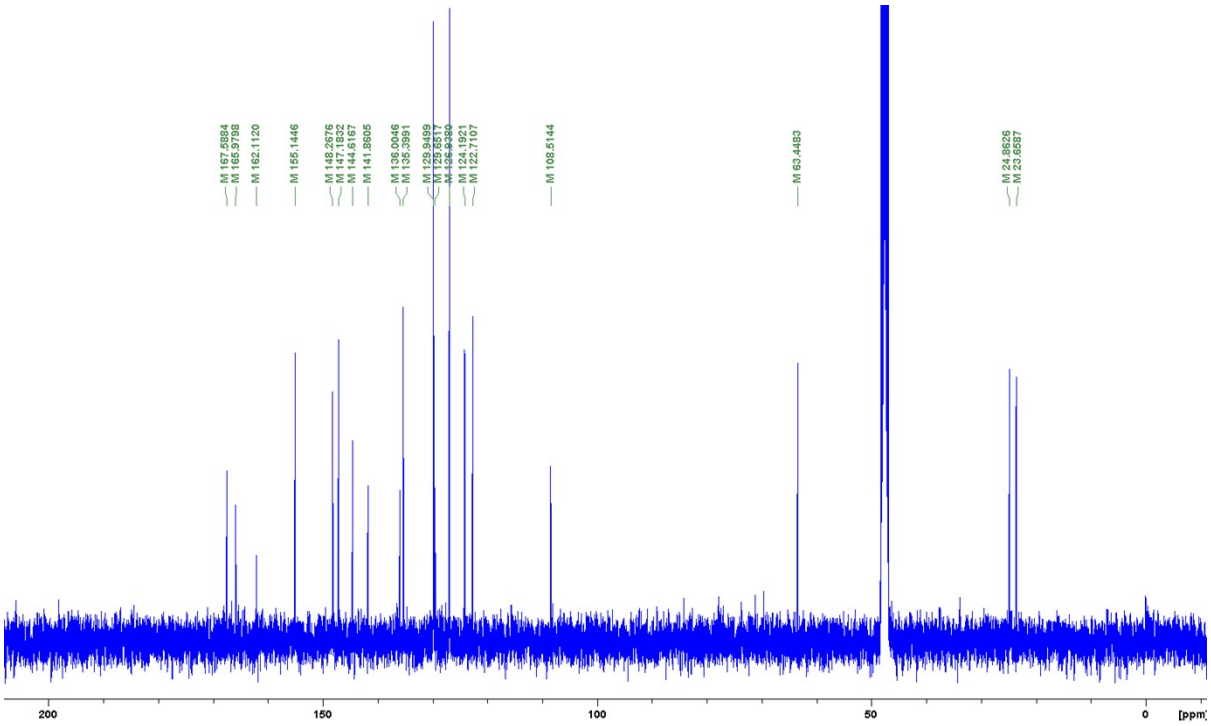
^{13}C NMR of **8w** in CD_3SOCD_3:



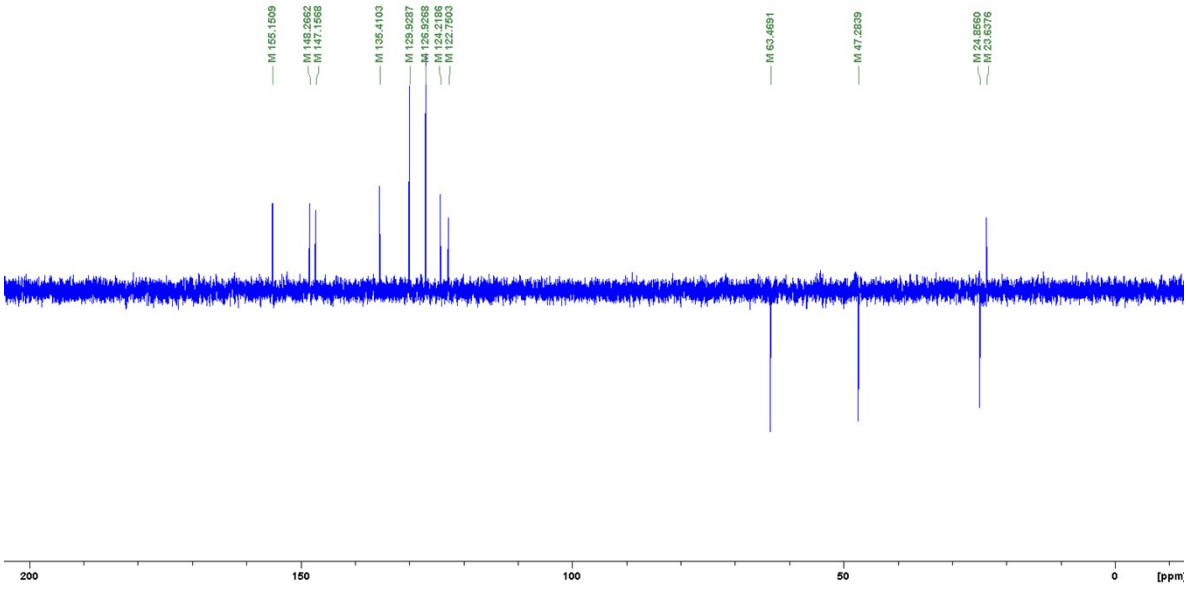
^{1}H NMR of **8x** in CD_3OD:



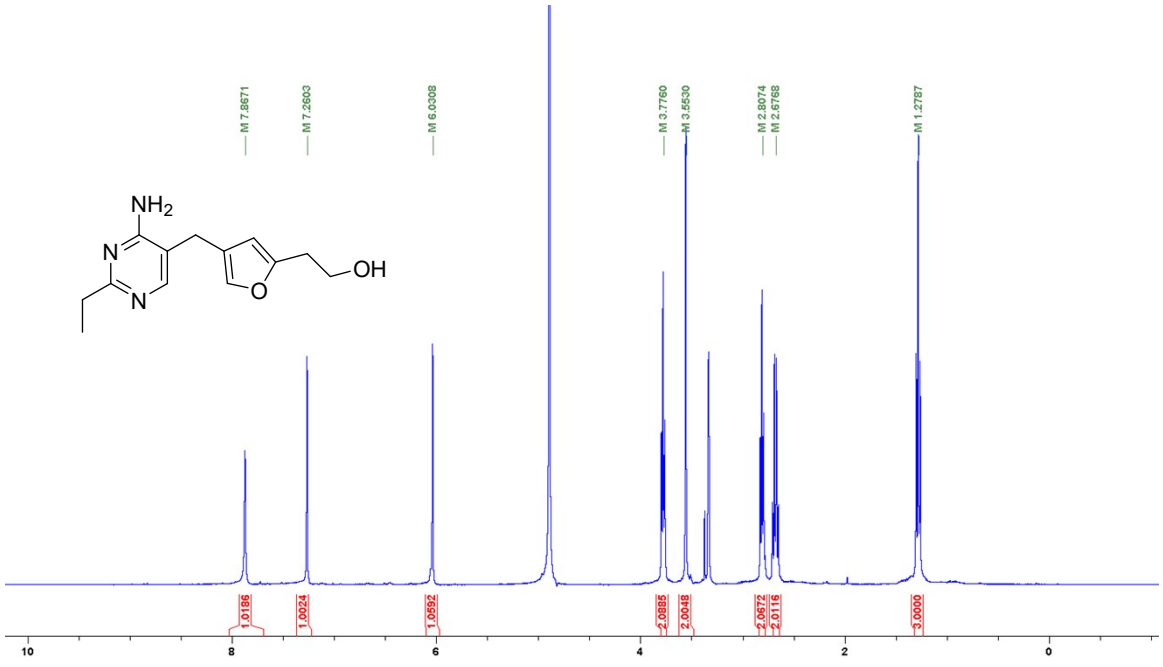
^{13}C NMR of **8x** in CD_3OD: (the peak at 47.2 is shielded by the solvent peak)



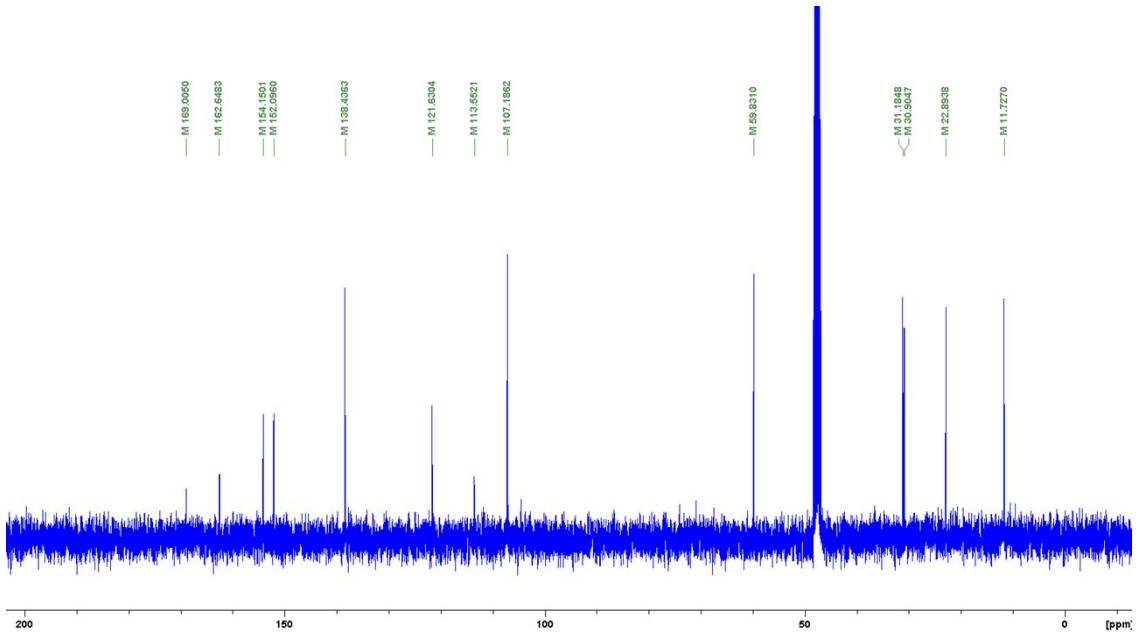
^{13}C DEPT-135 NMR of **8x** in CD_3OD: (the peak at 47.2 shielded by the solvent peak is unmasked in the DEPT-135 spectrum)



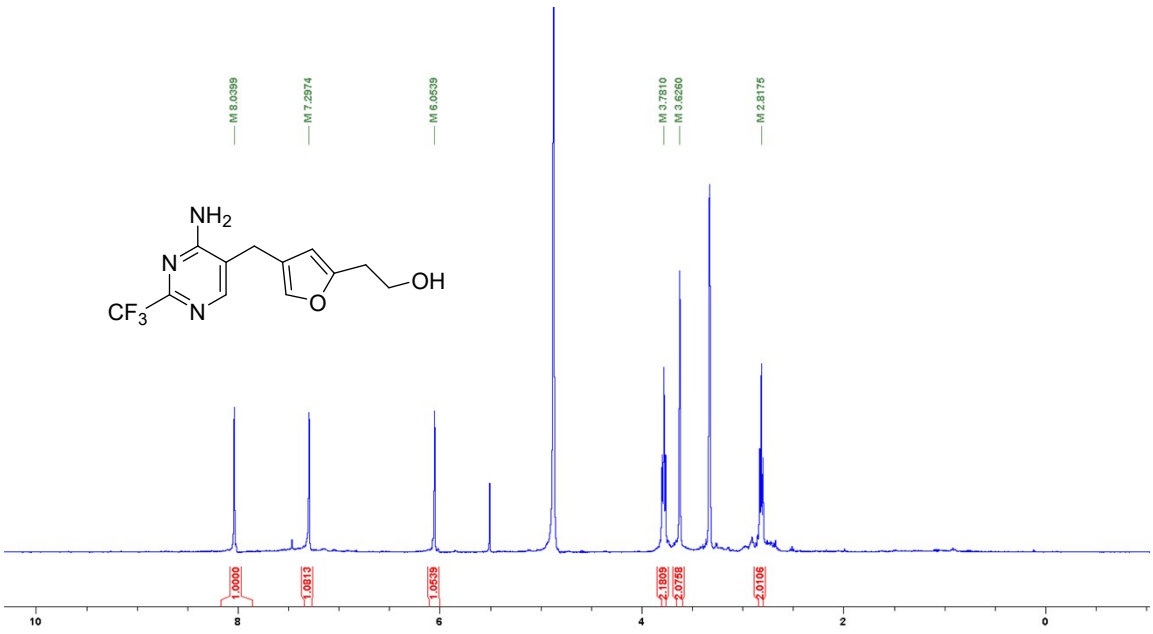
^{1}H NMR of **16b** in $CDCl_3$:



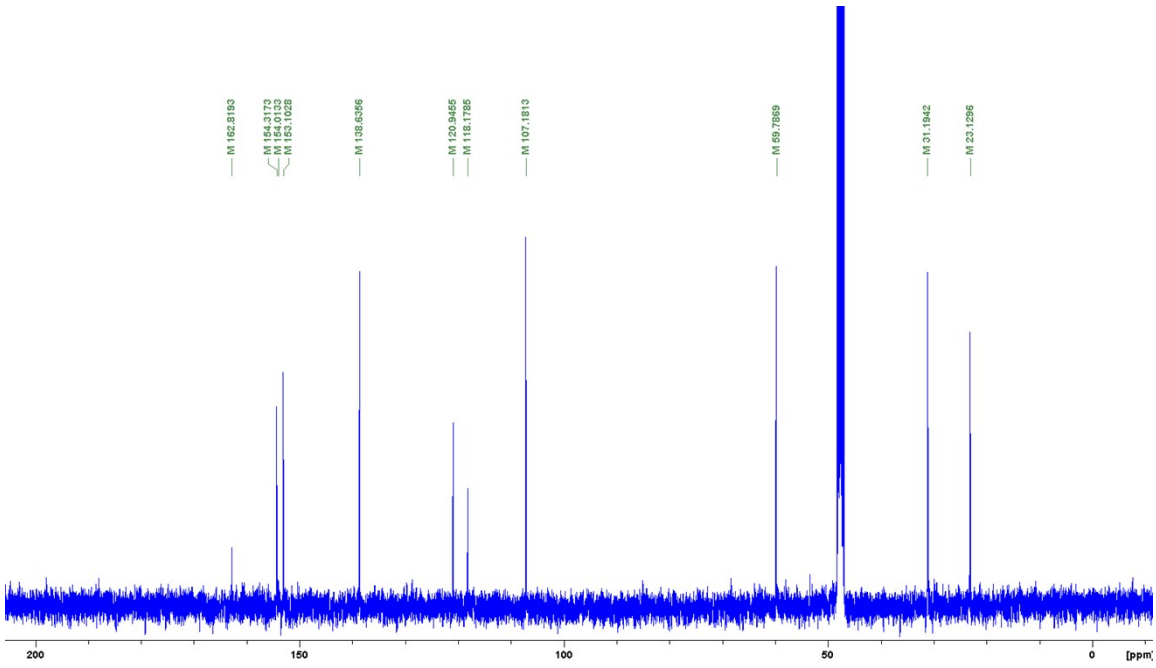
^{13}C NMR of **16b** in $CDCl_3$:



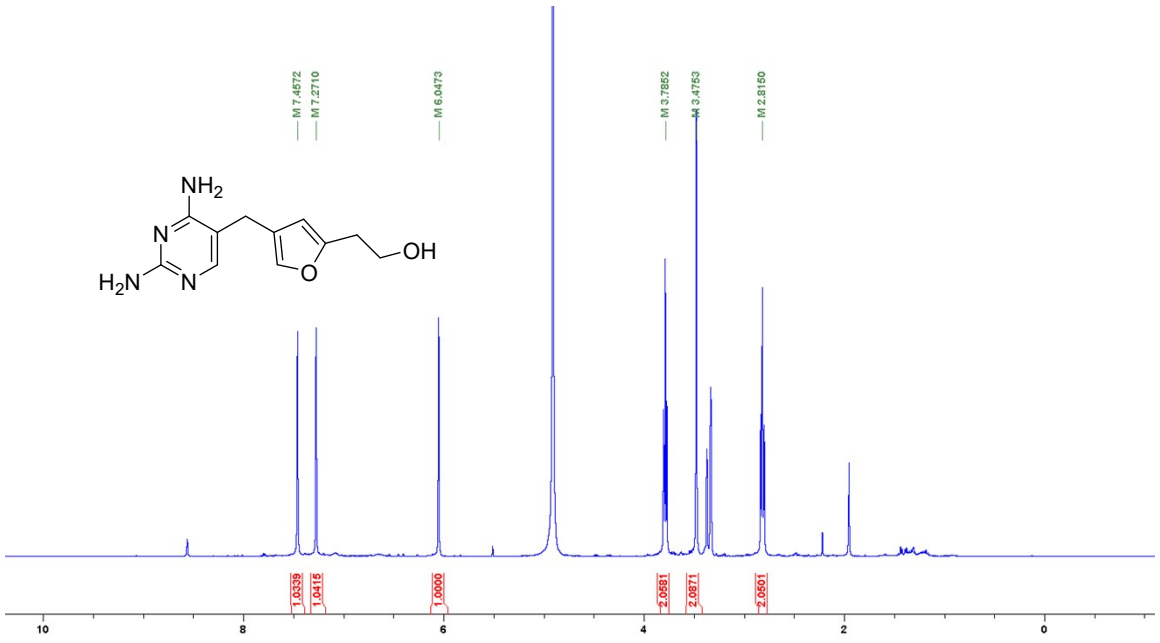
^{1}H NMR of **16c** in CD_3OD:



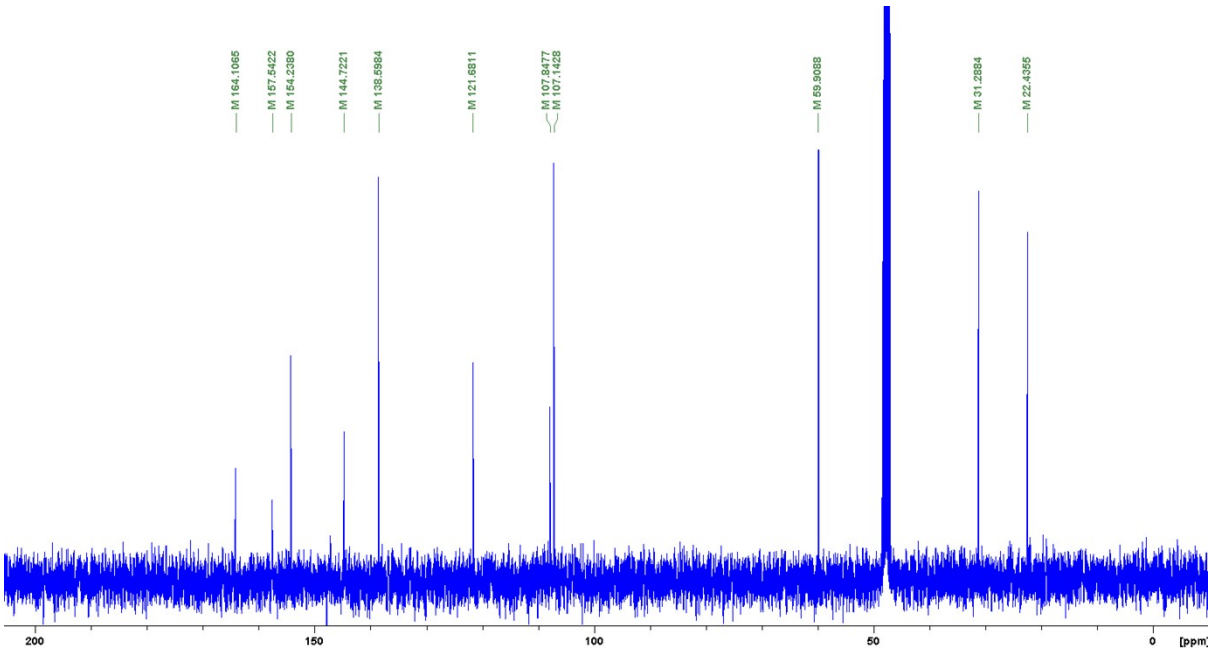
^{13}C NMR of **16c** in CD_3OD:



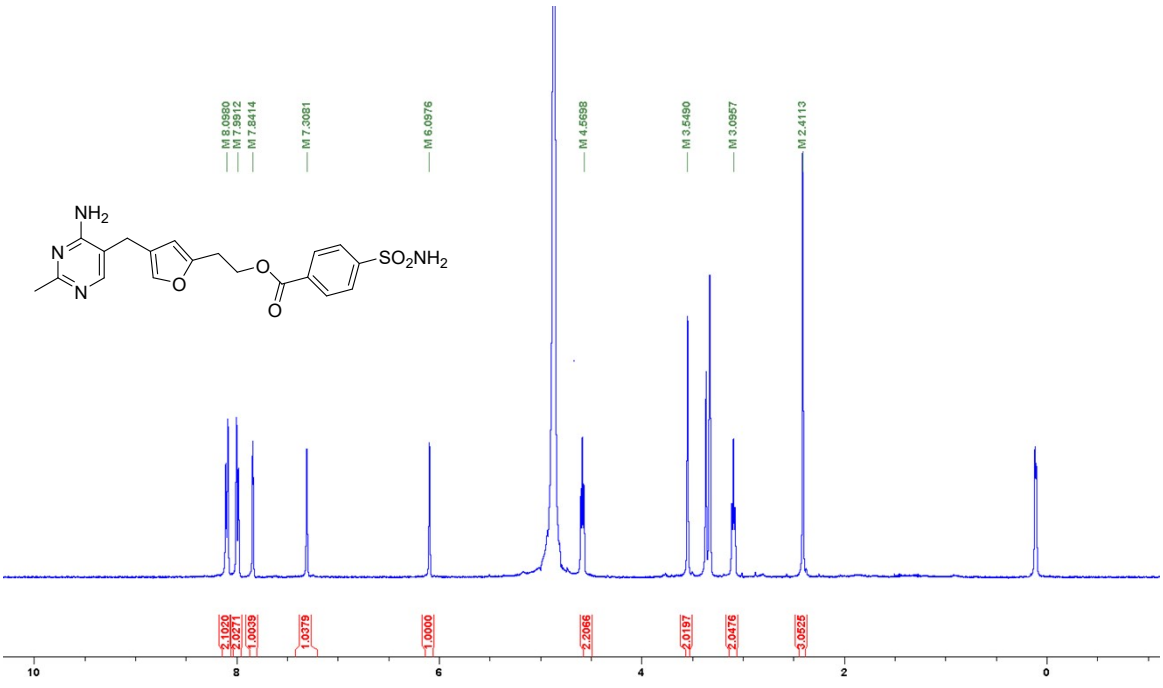
^{1}H NMR of **16d** in CD_3OD:



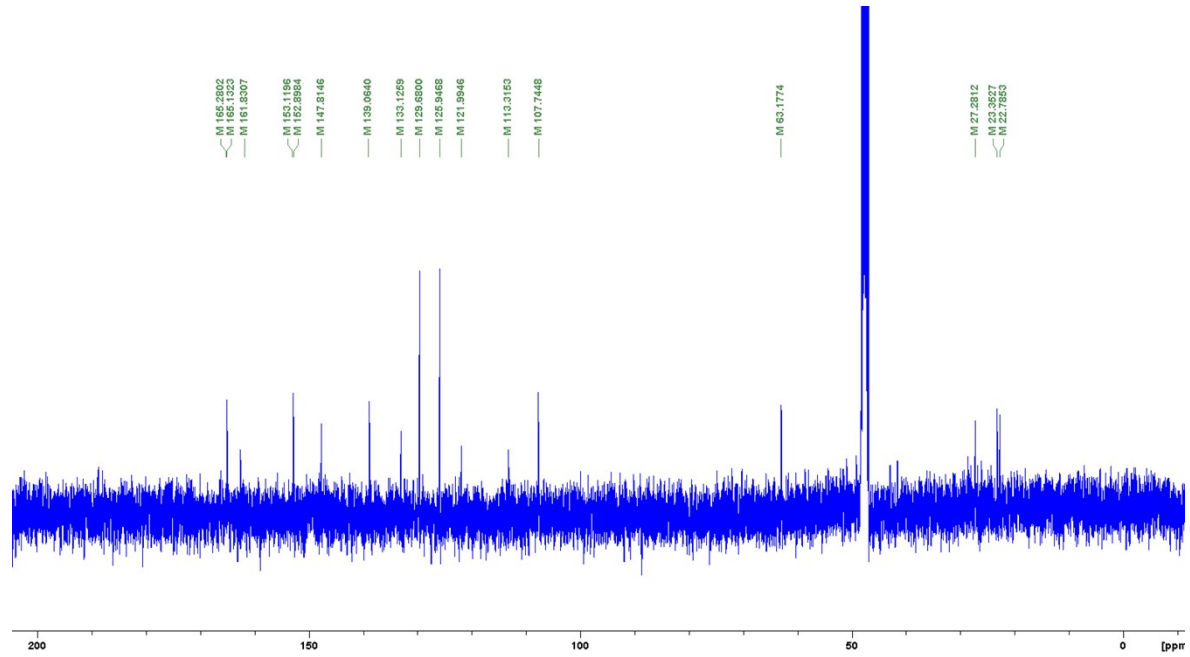
^{13}C NMR of **16d** in CD_3OD:



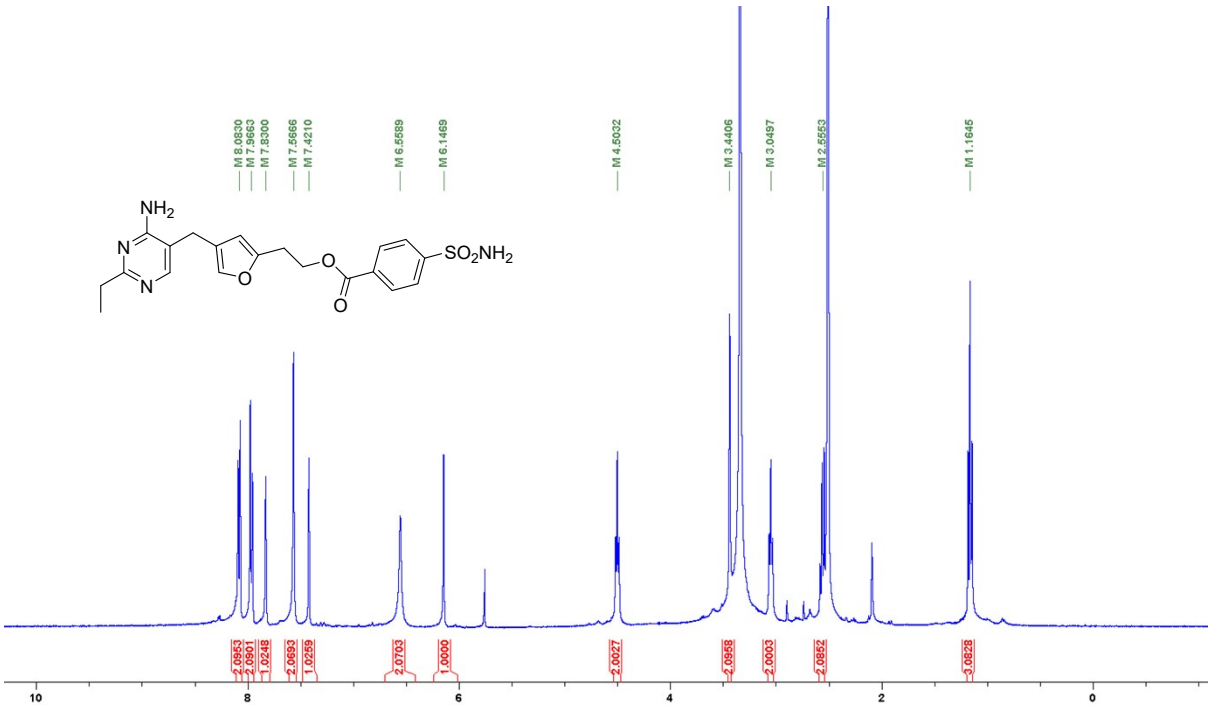
^{1}H NMR of **17a** in CD_3OD:



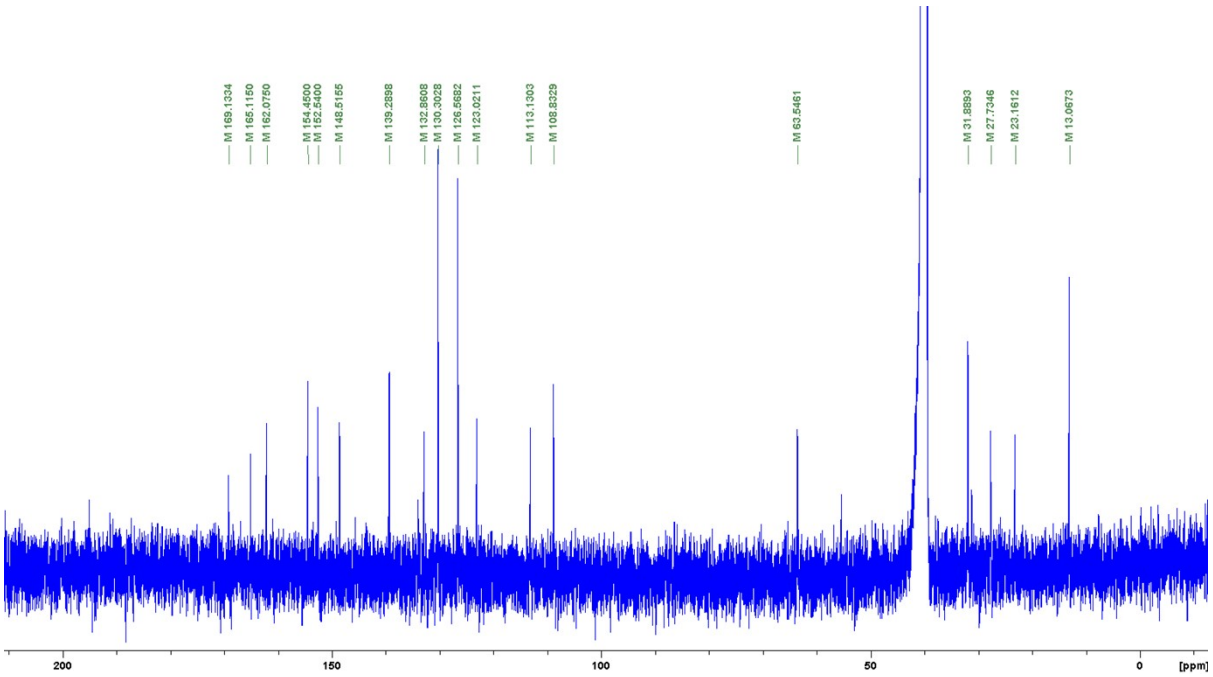
^{13}C NMR of **17a** in CD_3OD:



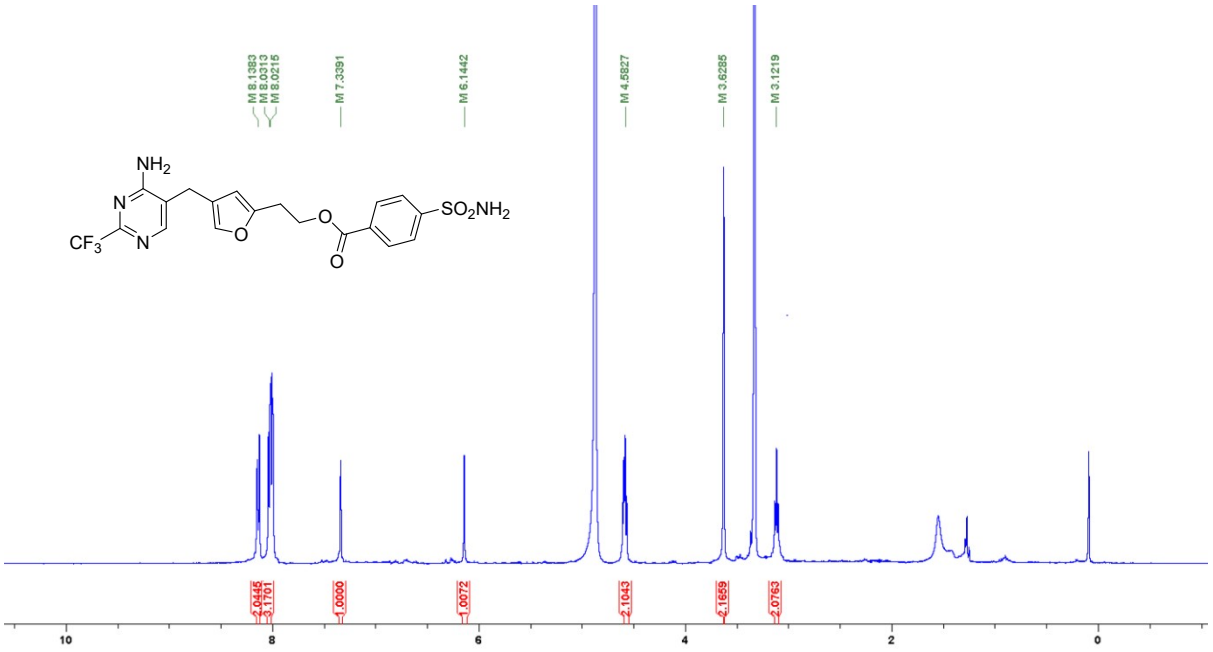
^{1}H NMR of **17b** in CD_3SOCD_3:



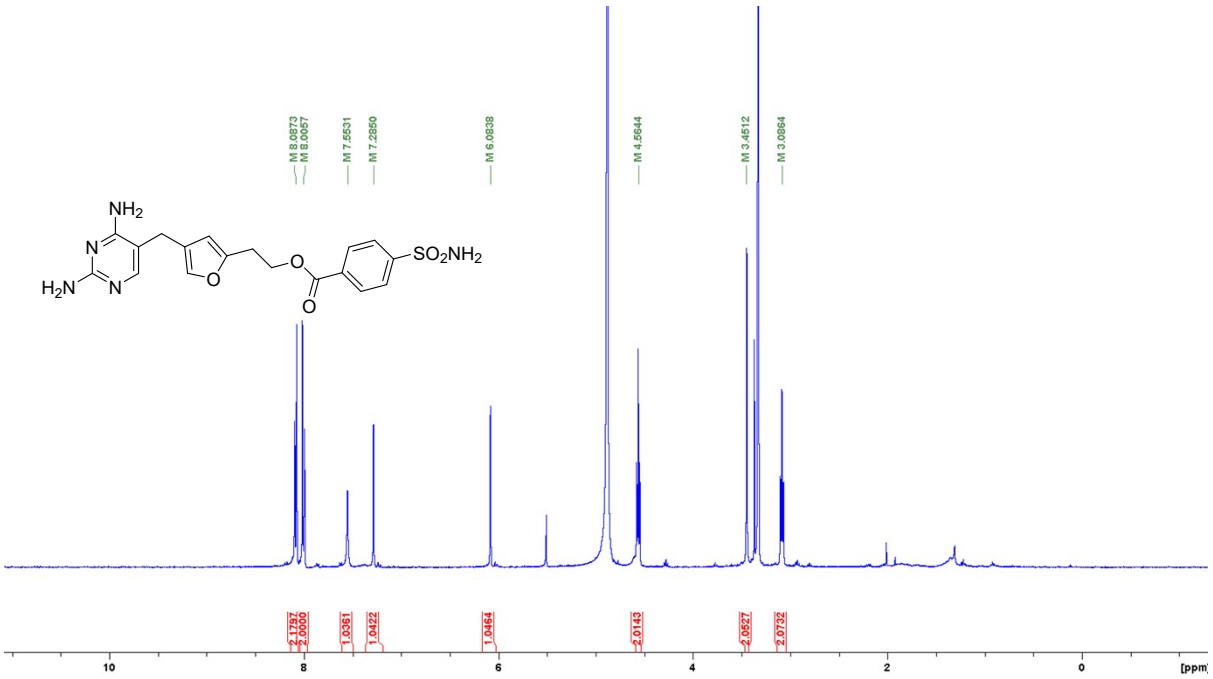
^{13}C NMR of **17b** in CD_3SOCD_3:



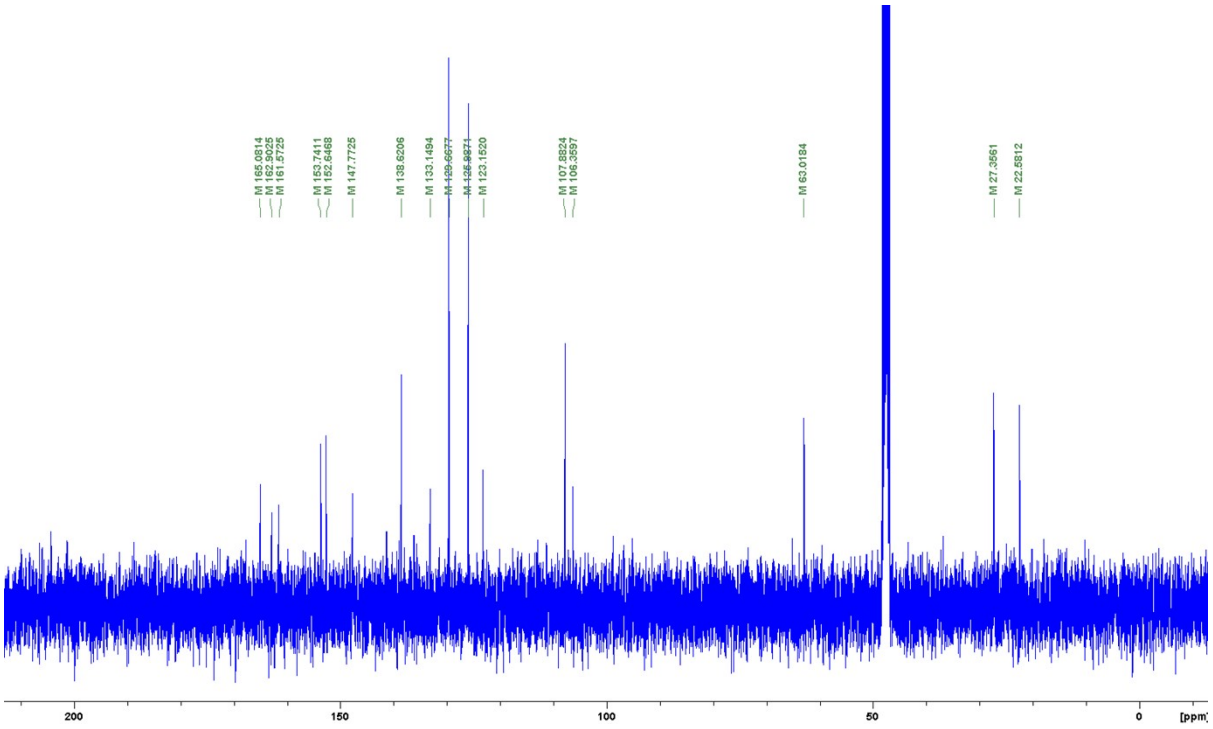
^{1}H NMR of **17c** in CD_3OD:



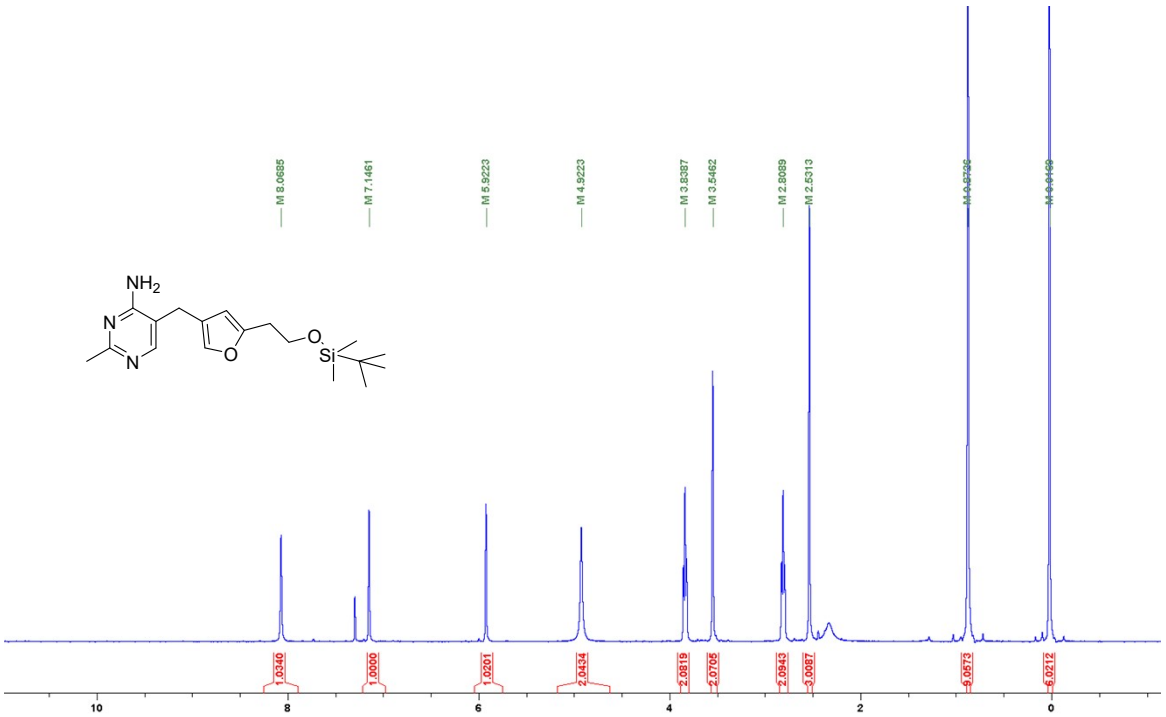
^{1}H NMR of **17d** in CD_3OD:



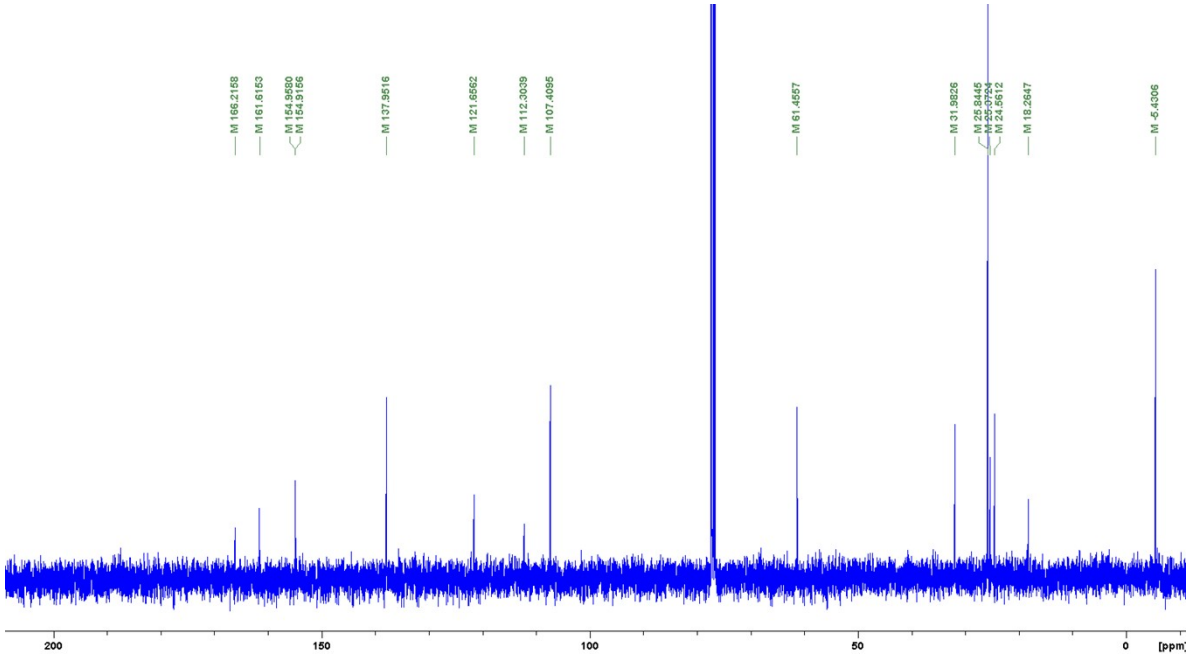
^{13}C NMR of **17d** in CD_3OD:



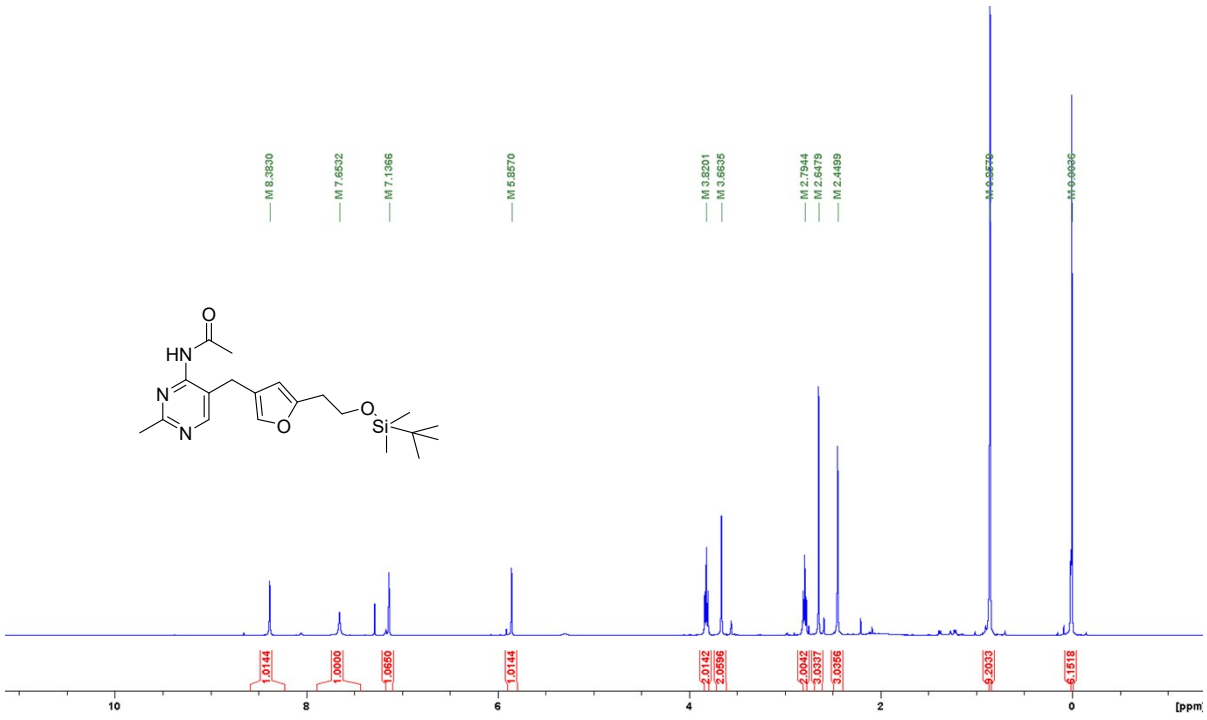
^{1}H NMR of **18** in $CDCl_3$:



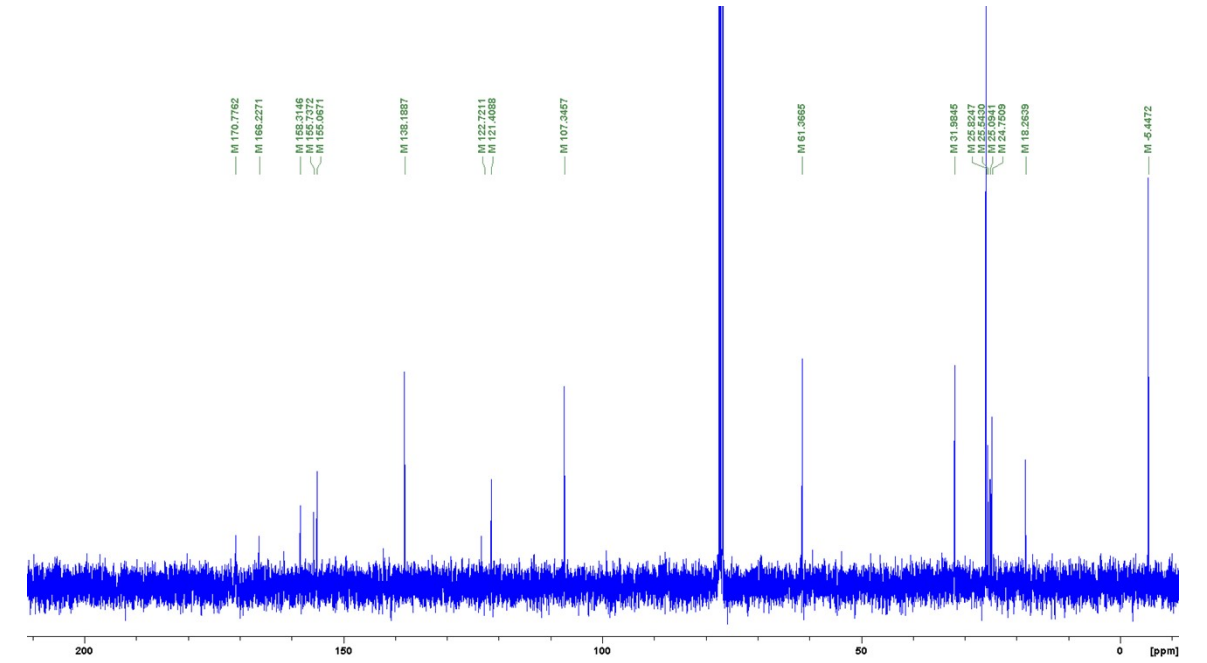
^{13}C NMR of **18** in $CDCl_3$:



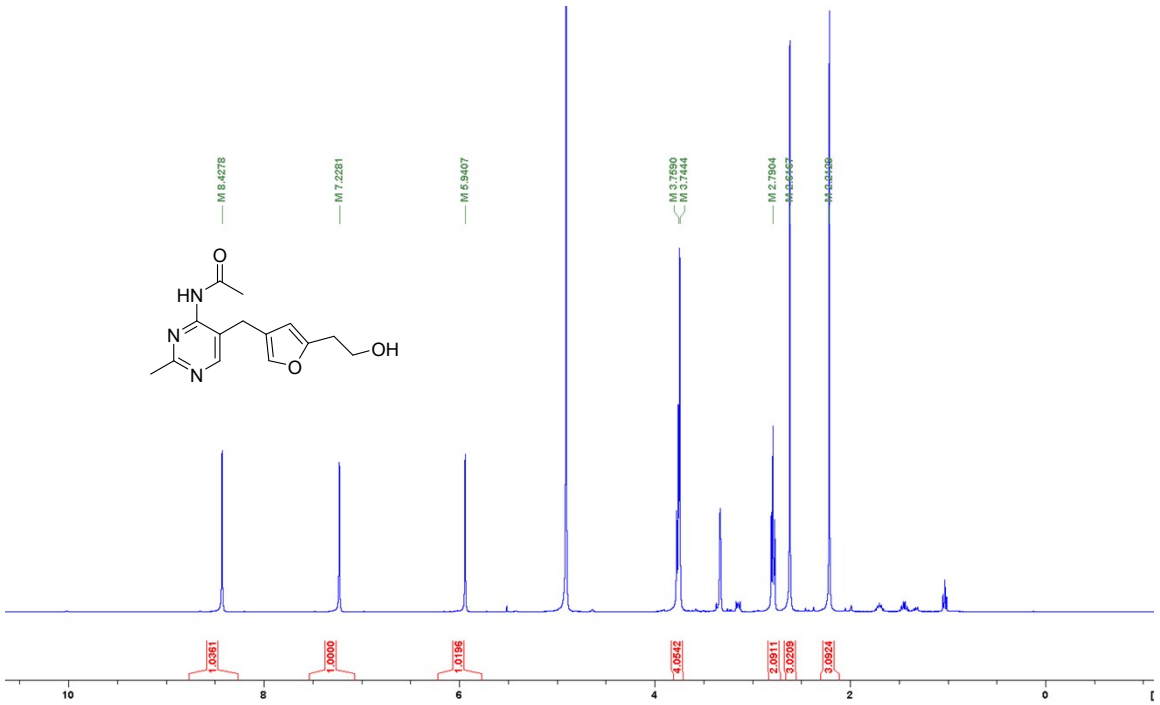
^{1}H NMR of **19** in $CDCl_3$:



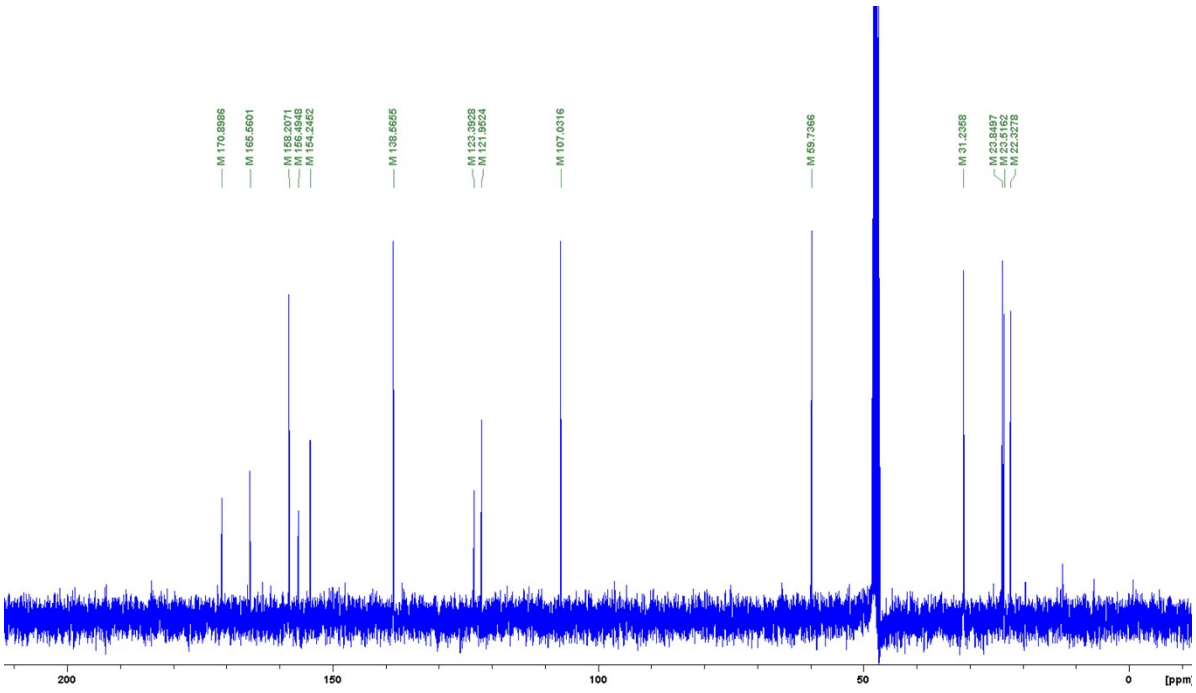
^{13}C NMR of **19** in $CDCl_3$:



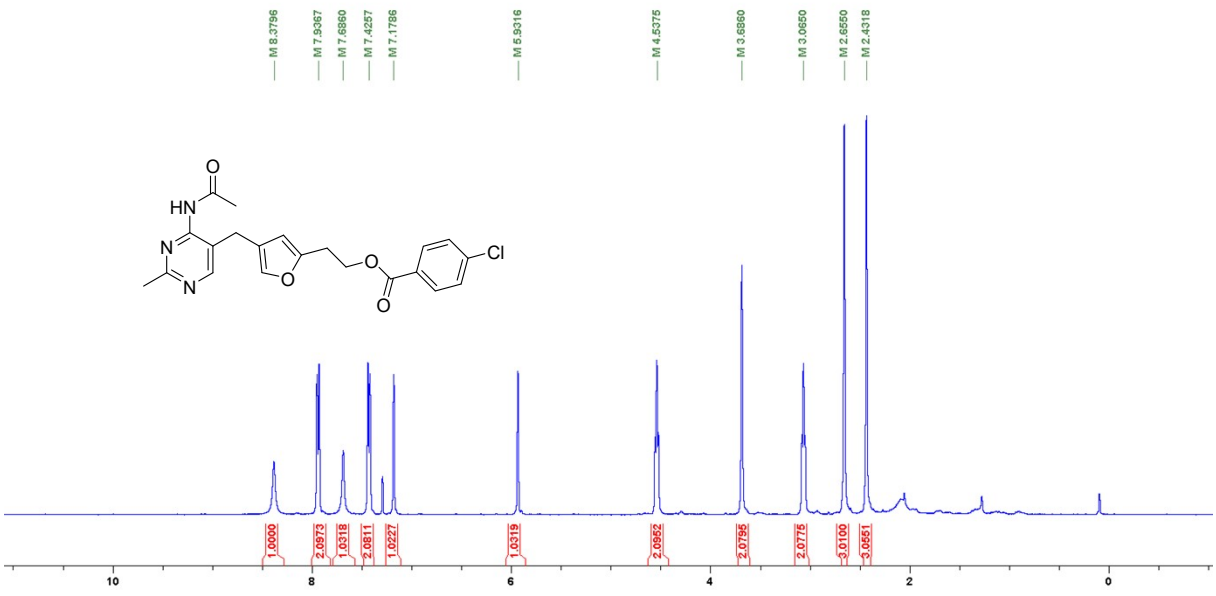
^{1}H NMR of **20** in CD_3OD:



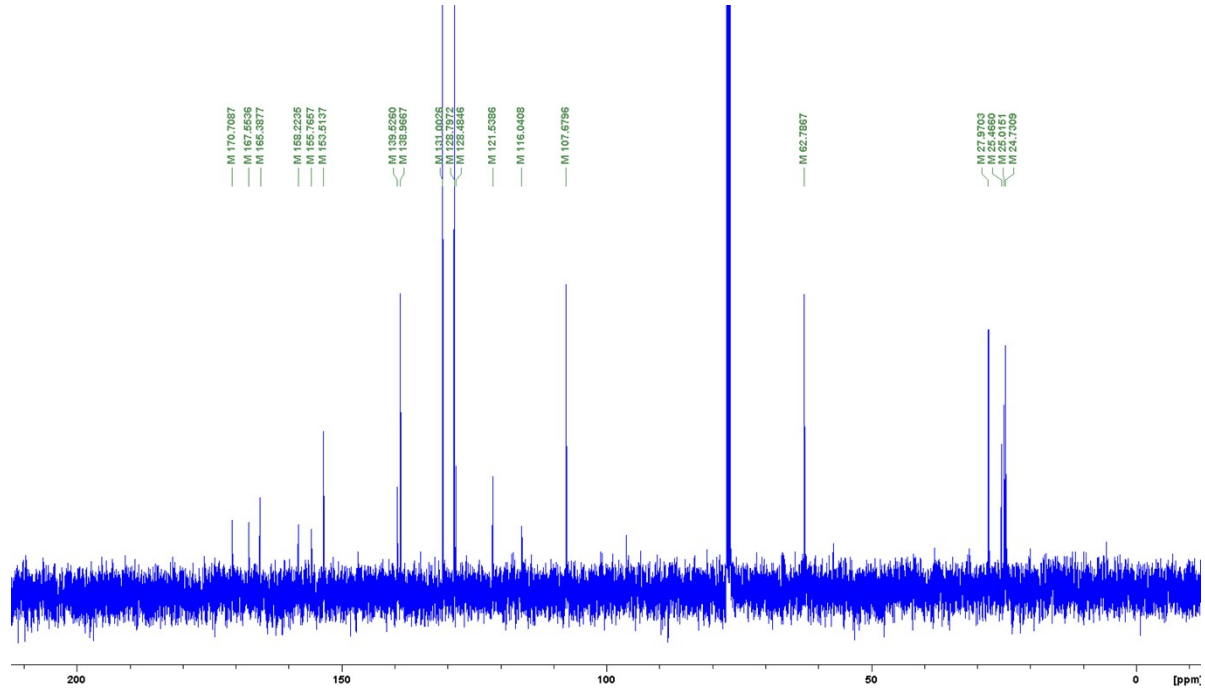
^{13}C NMR of **20** in CD_3OD:



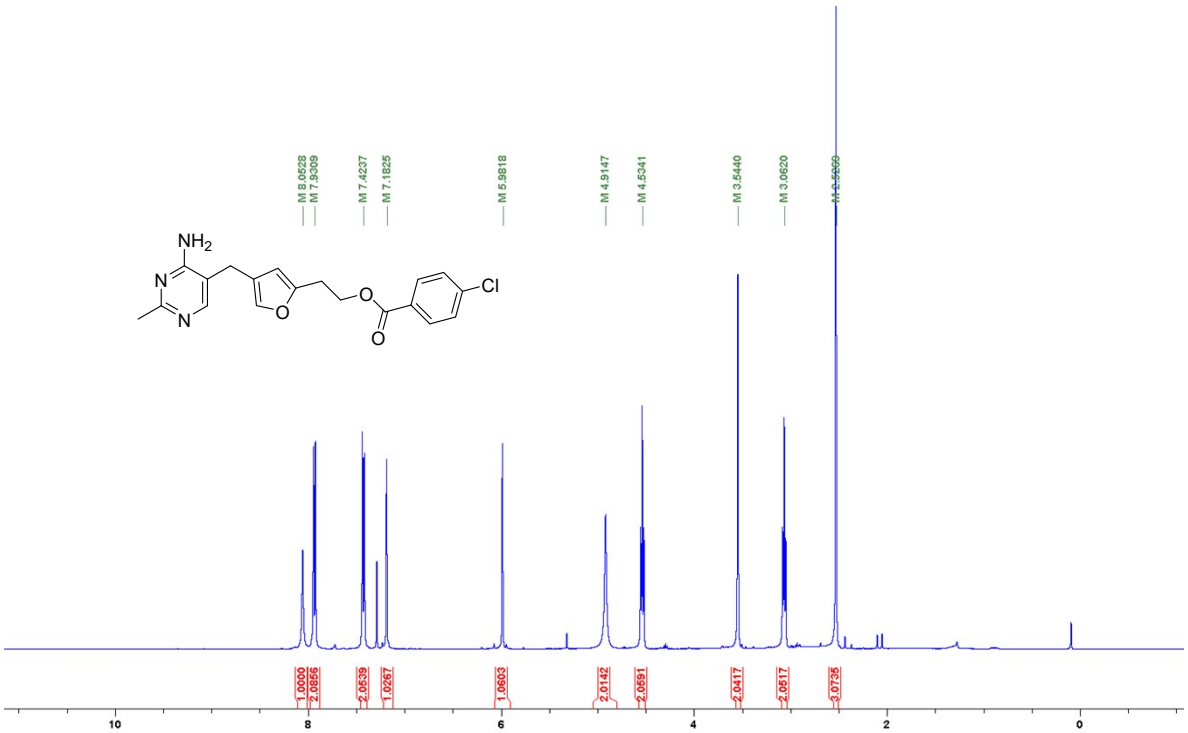
^{1}H NMR of **21** in $CDCl_3$:



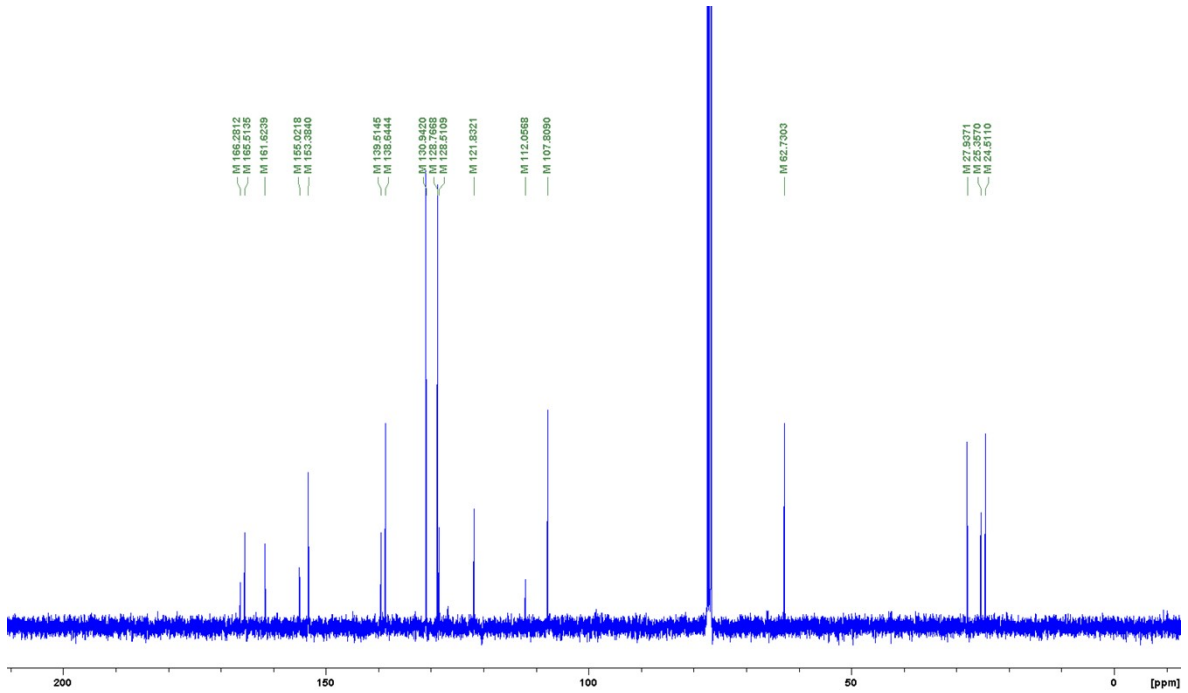
^{13}C NMR of **21** in $CDCl_3$:



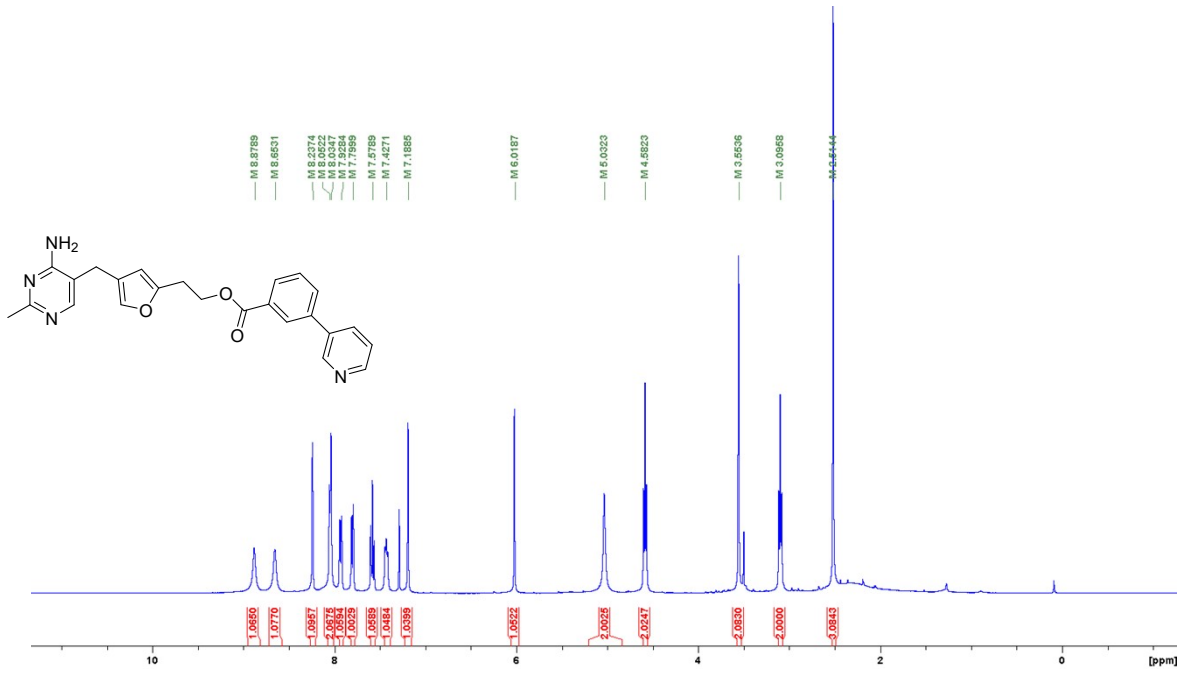
^{1}H NMR of **22** in $CDCl_3$:



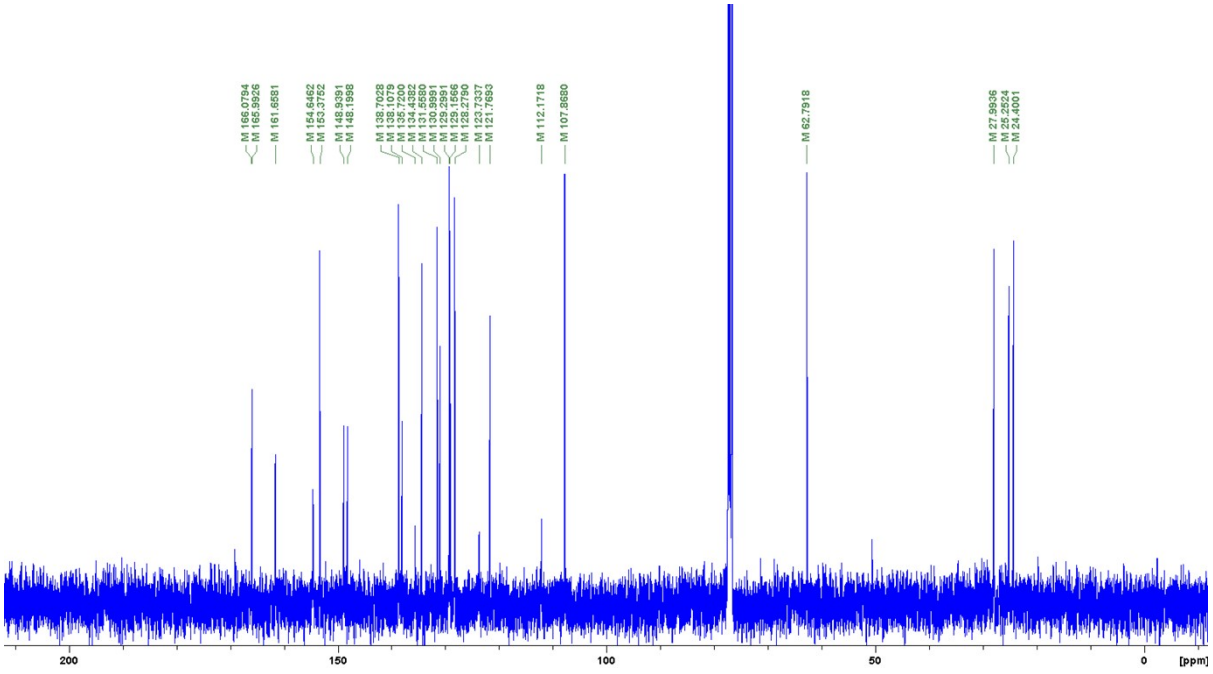
^{13}C NMR of **22** in $CDCl_3$:



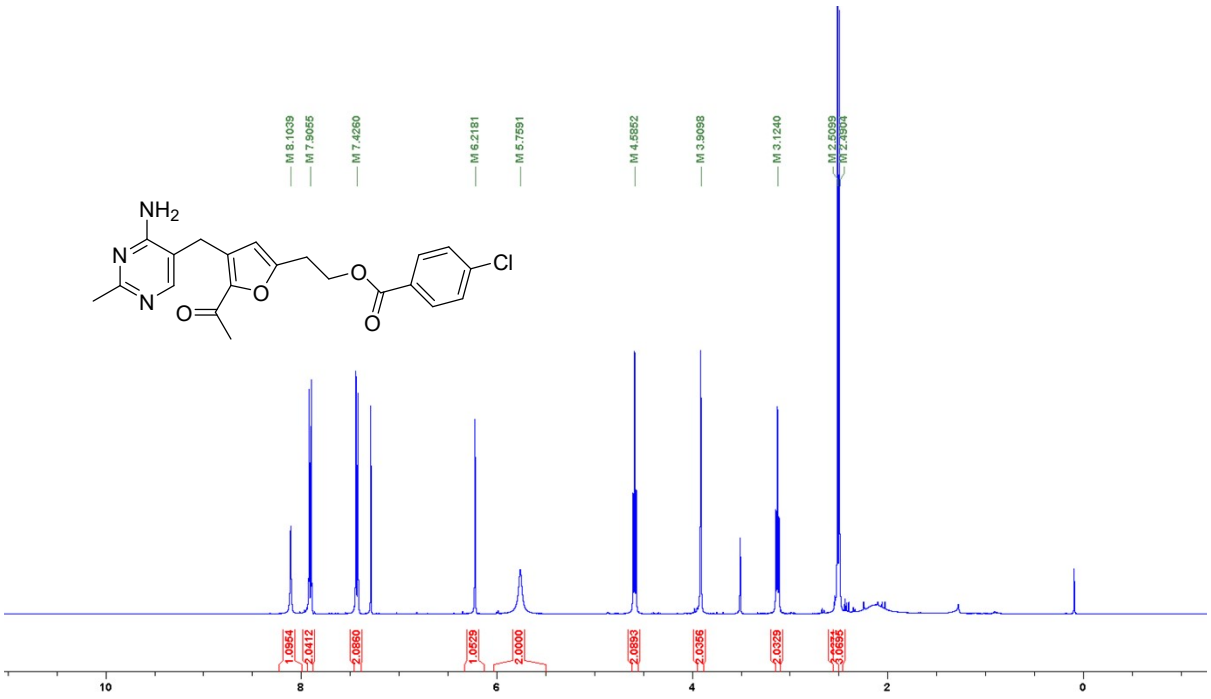
^{1}H NMR of **23** in $CDCl_3$:



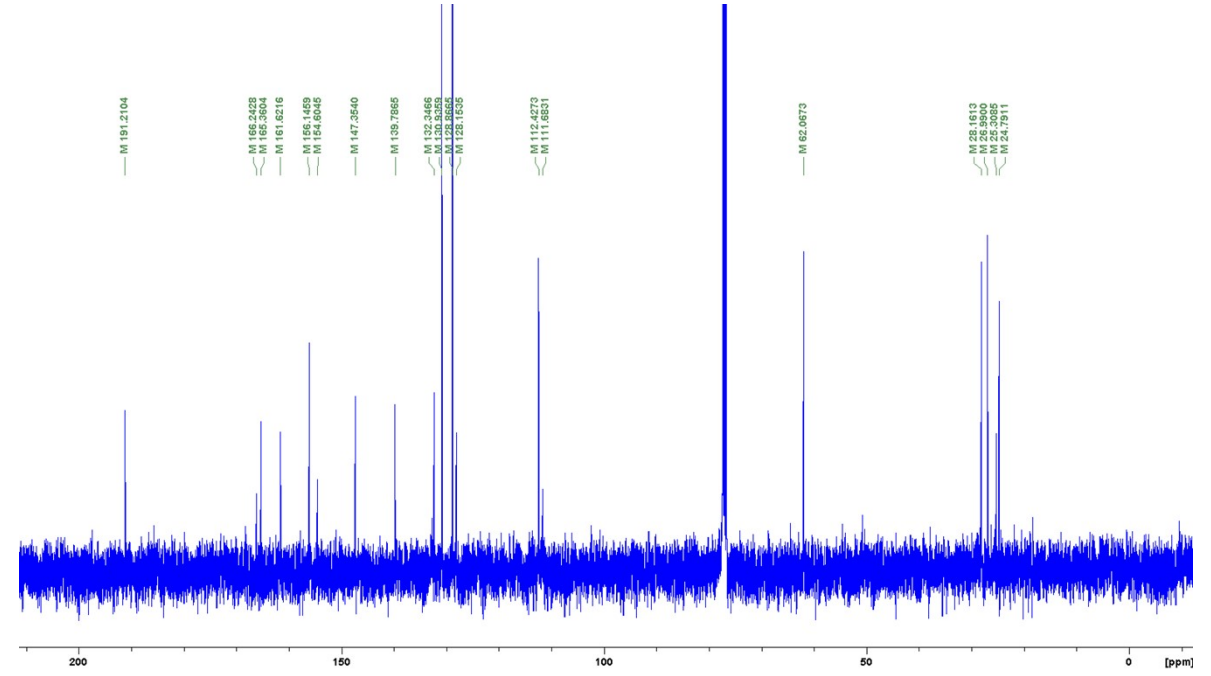
^{13}C NMR of **23** in $CDCl_3$:



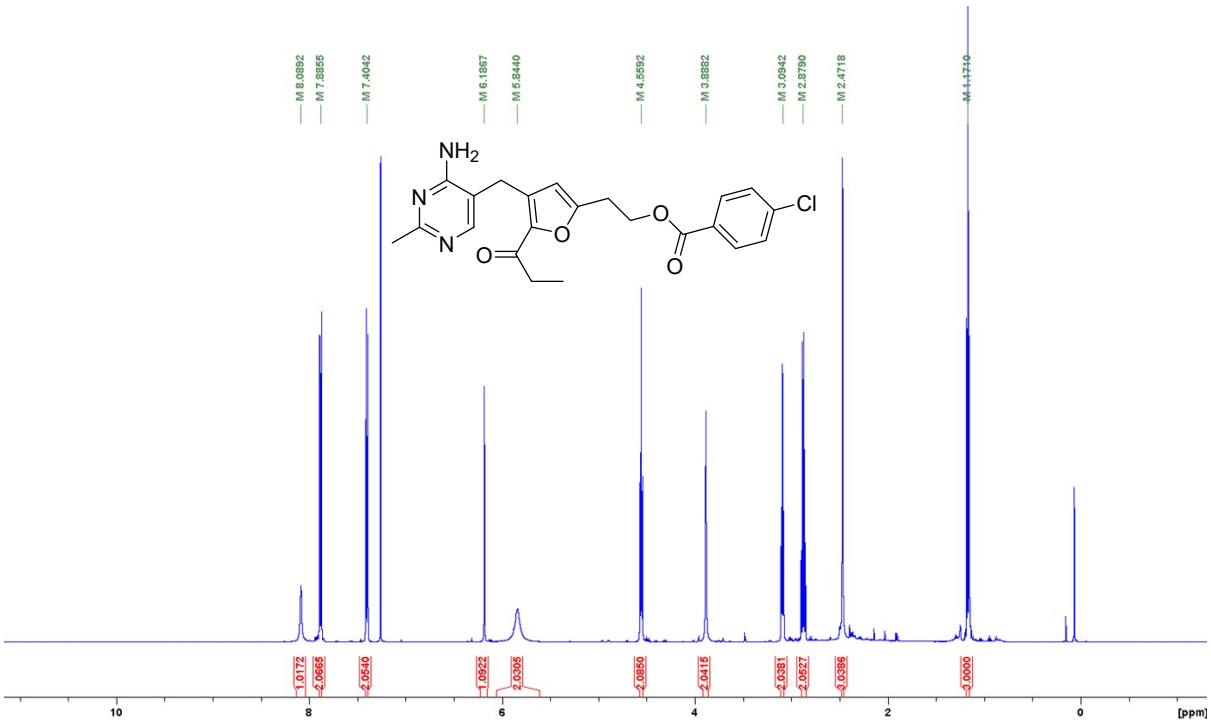
^{1}H NMR of **24a** in $CDCl_3$:



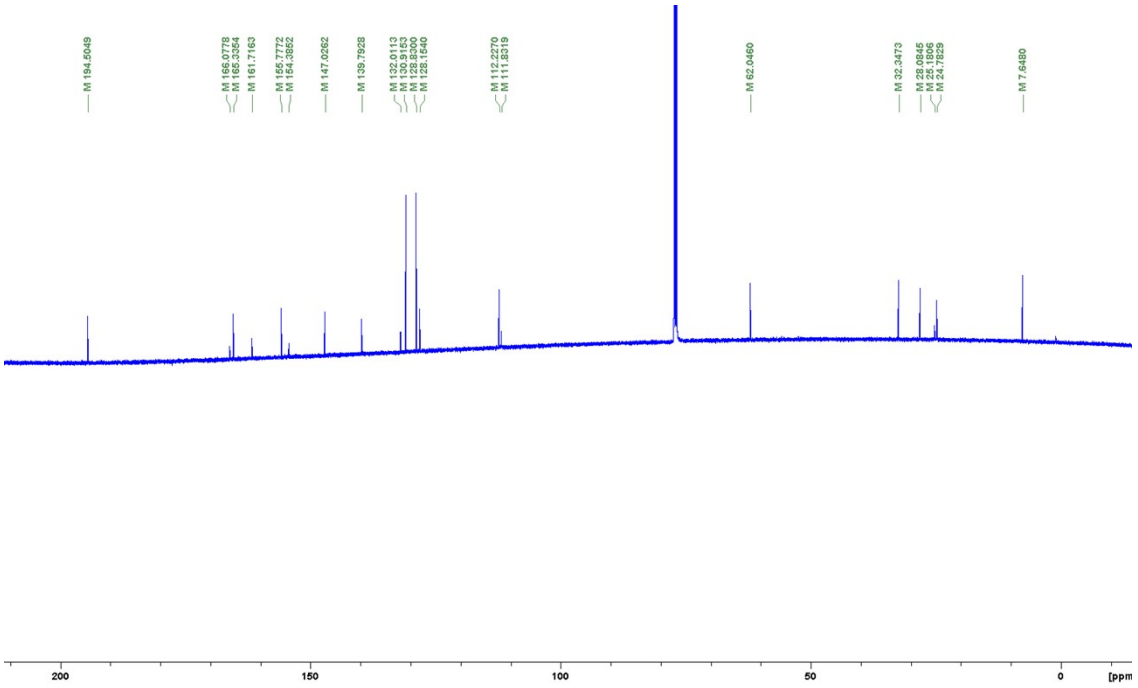
^{13}C NMR of **24a** in $CDCl_3$:



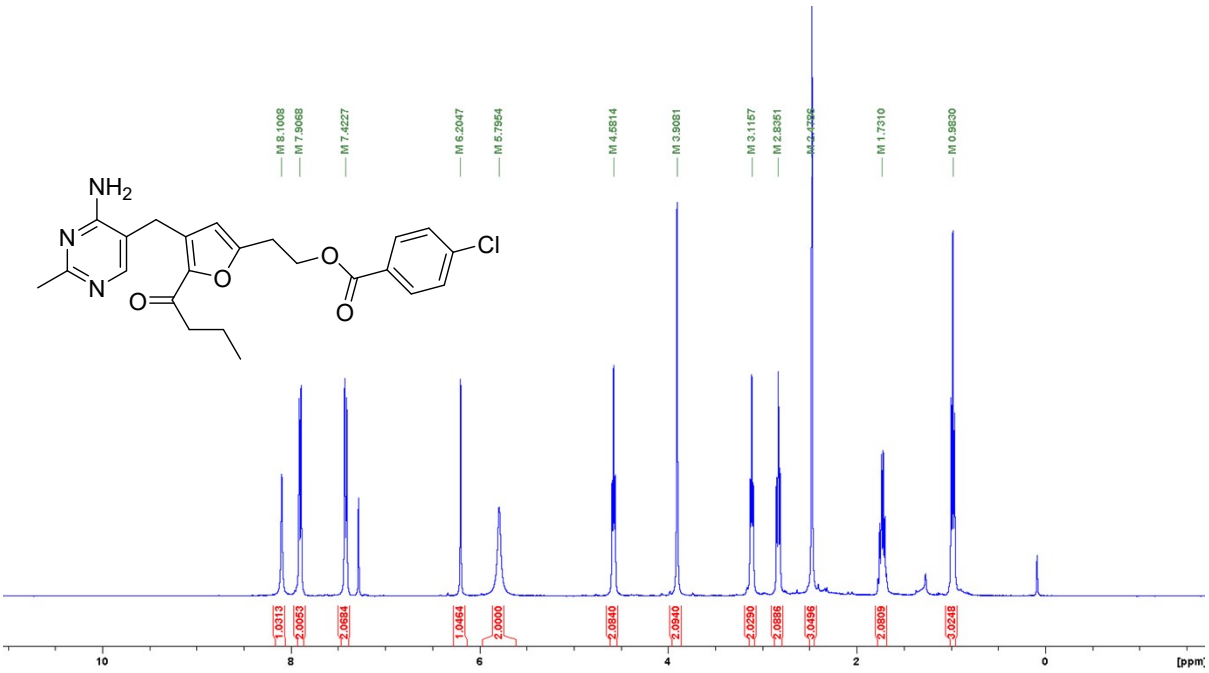
^{1}H NMR of **24b** in $CDCl_3$:



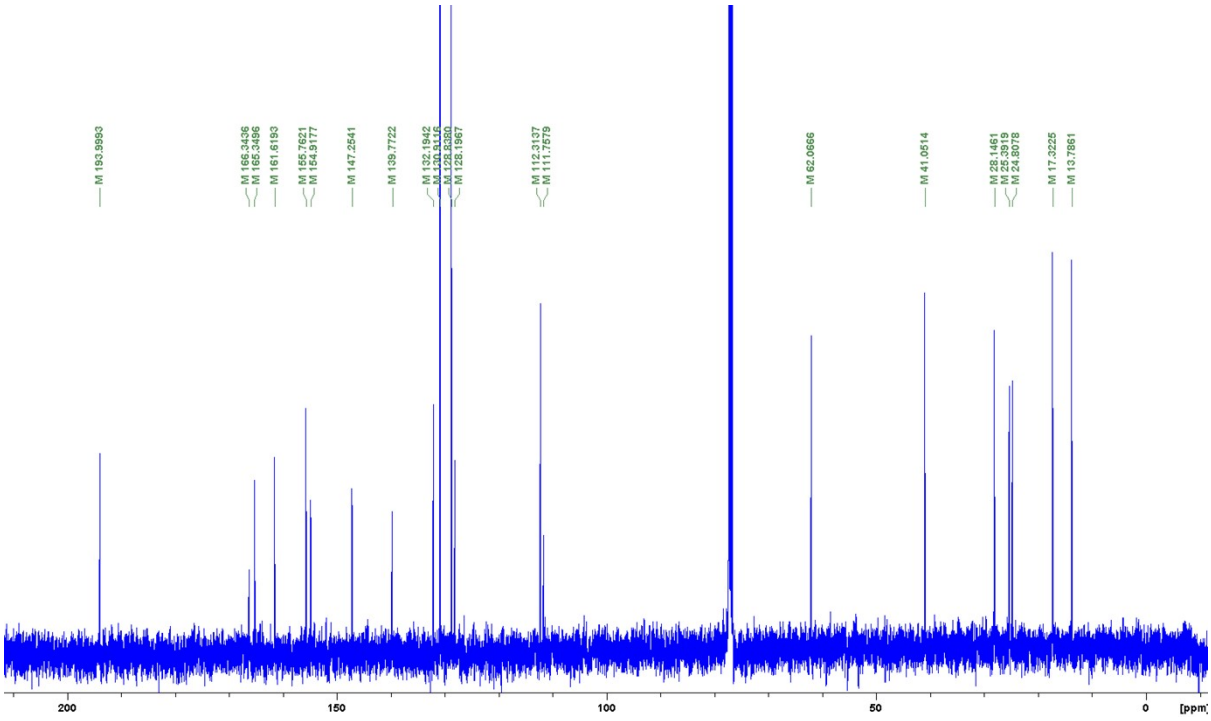
^{13}C NMR of **24b** in $CDCl_3$:



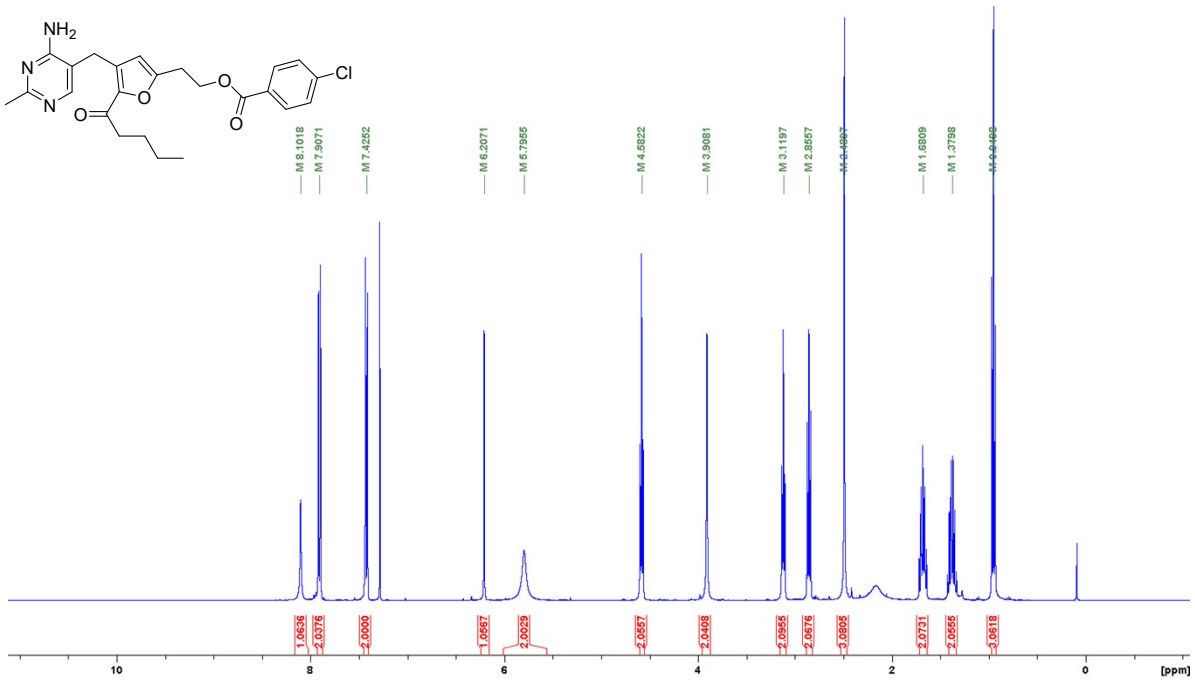
^{1}H NMR of **24c** in $CDCl_3$:



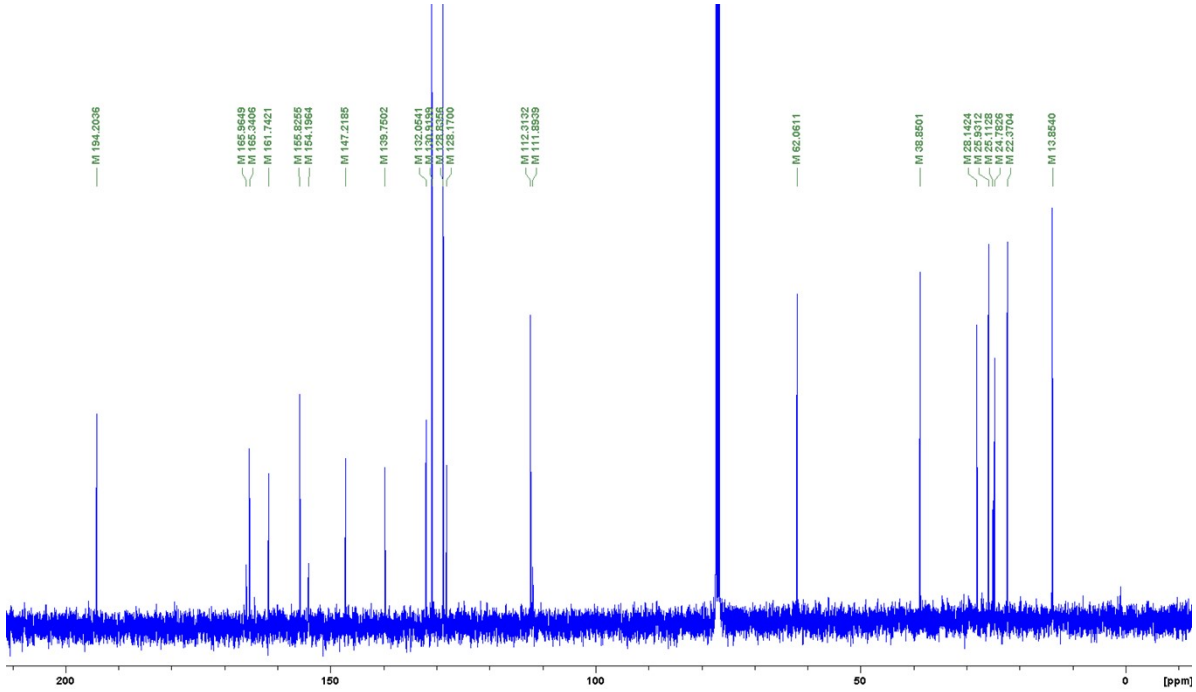
^{13}C NMR of **24c** in $CDCl_3$:



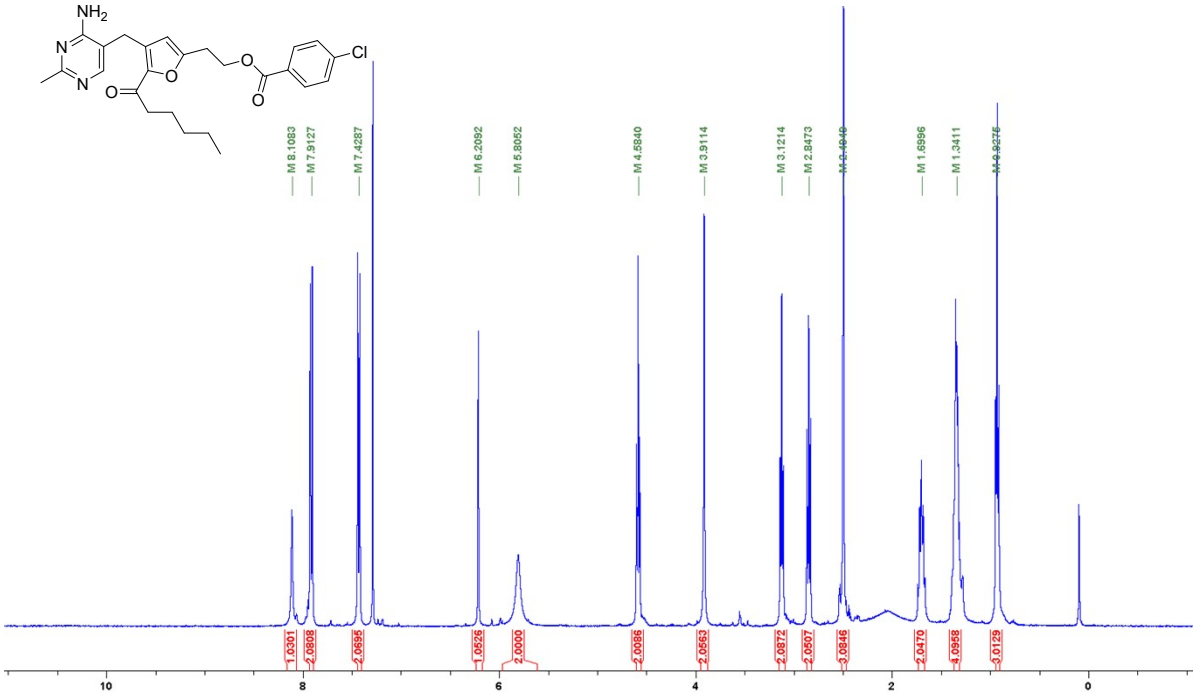
^{1}H NMR of **24d** in $CDCl_3$:



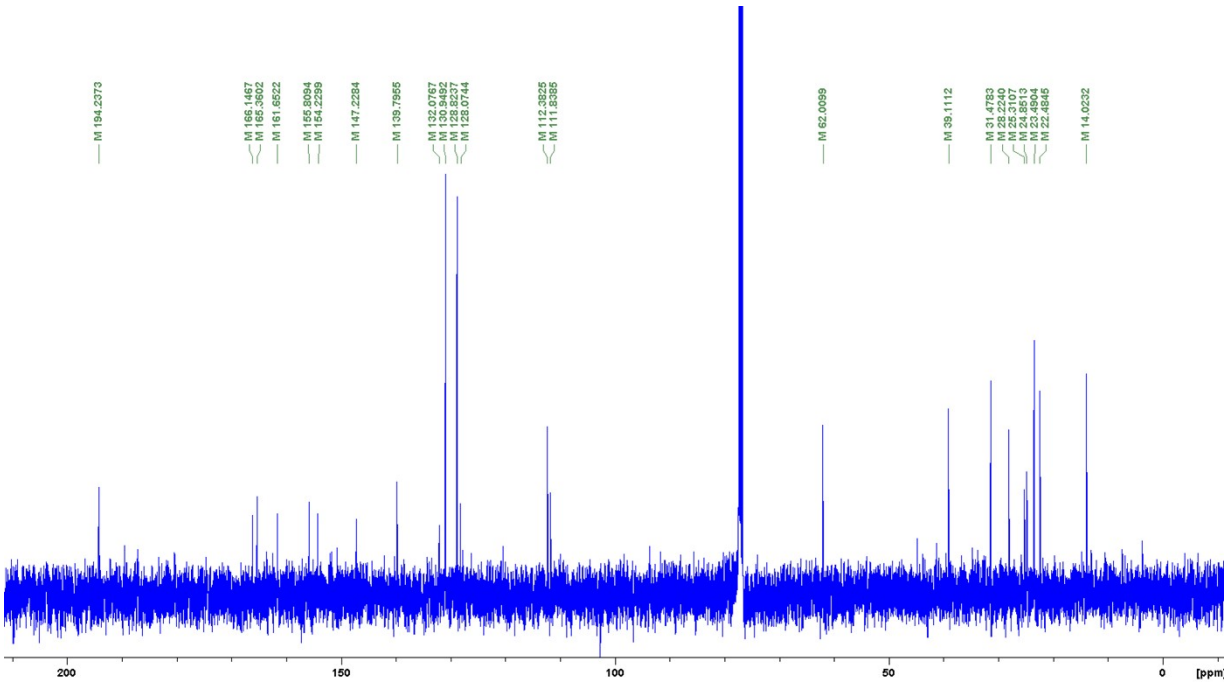
^{13}C NMR of **24d** in $CDCl_3$:



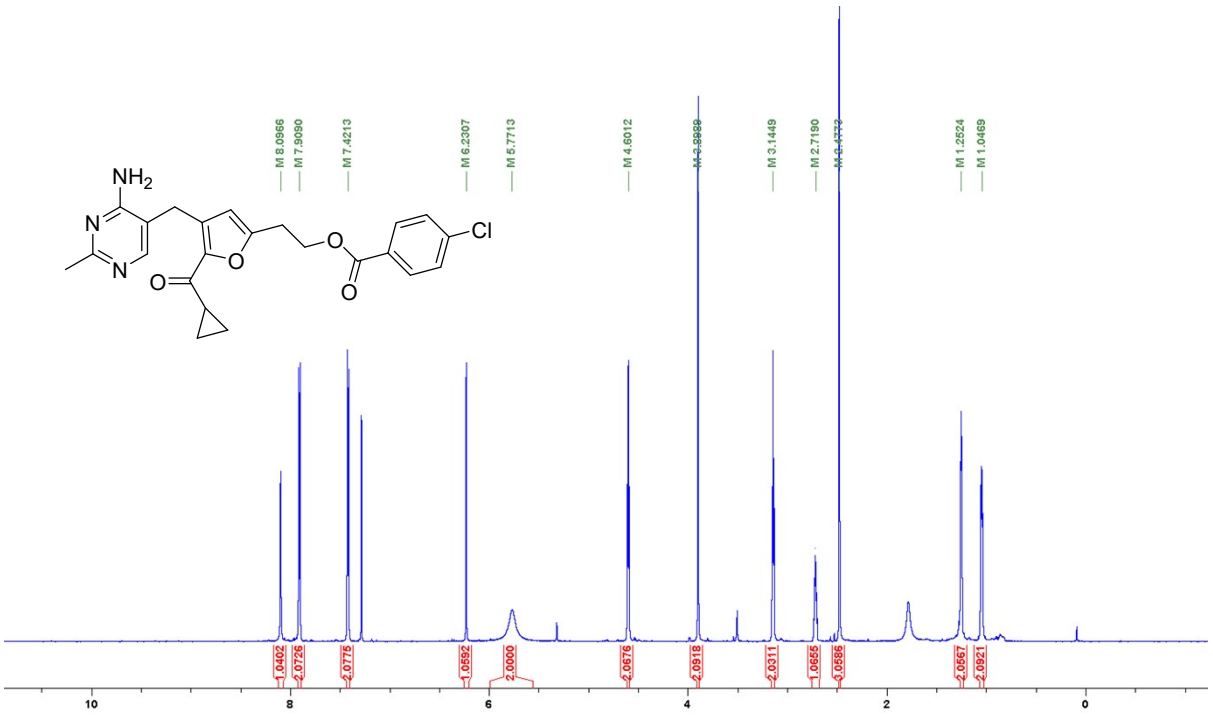
^{1}H NMR of **24e** in $CDCl_3$:



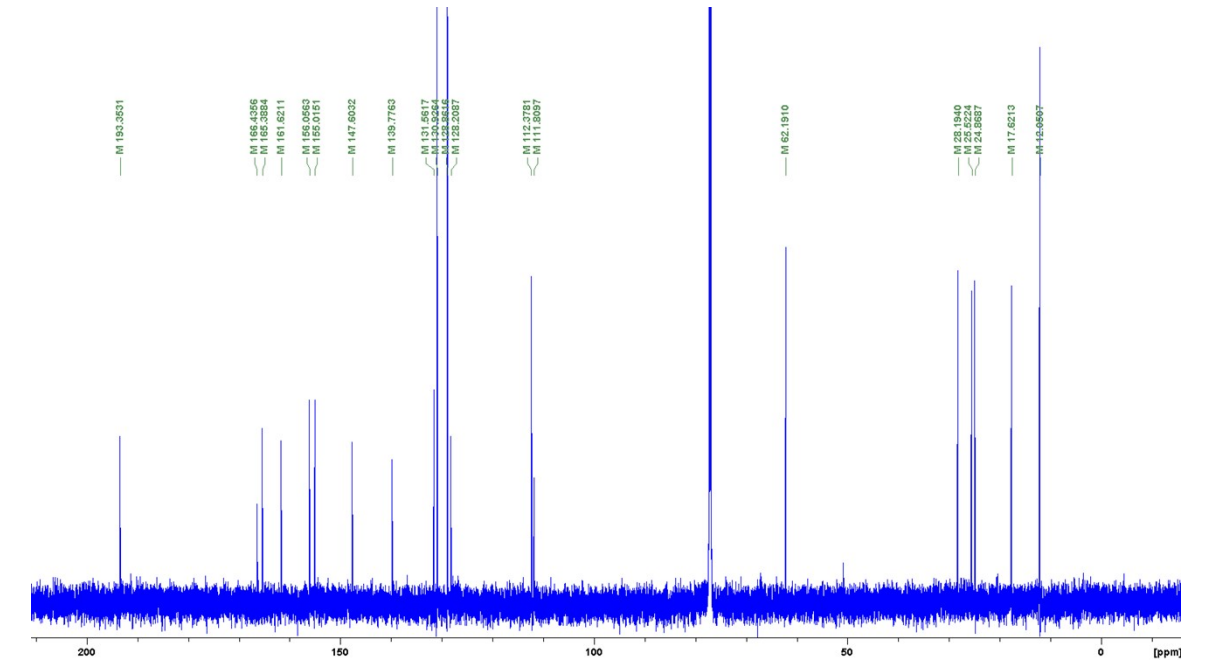
^{13}C NMR of **24e** in $CDCl_3$:



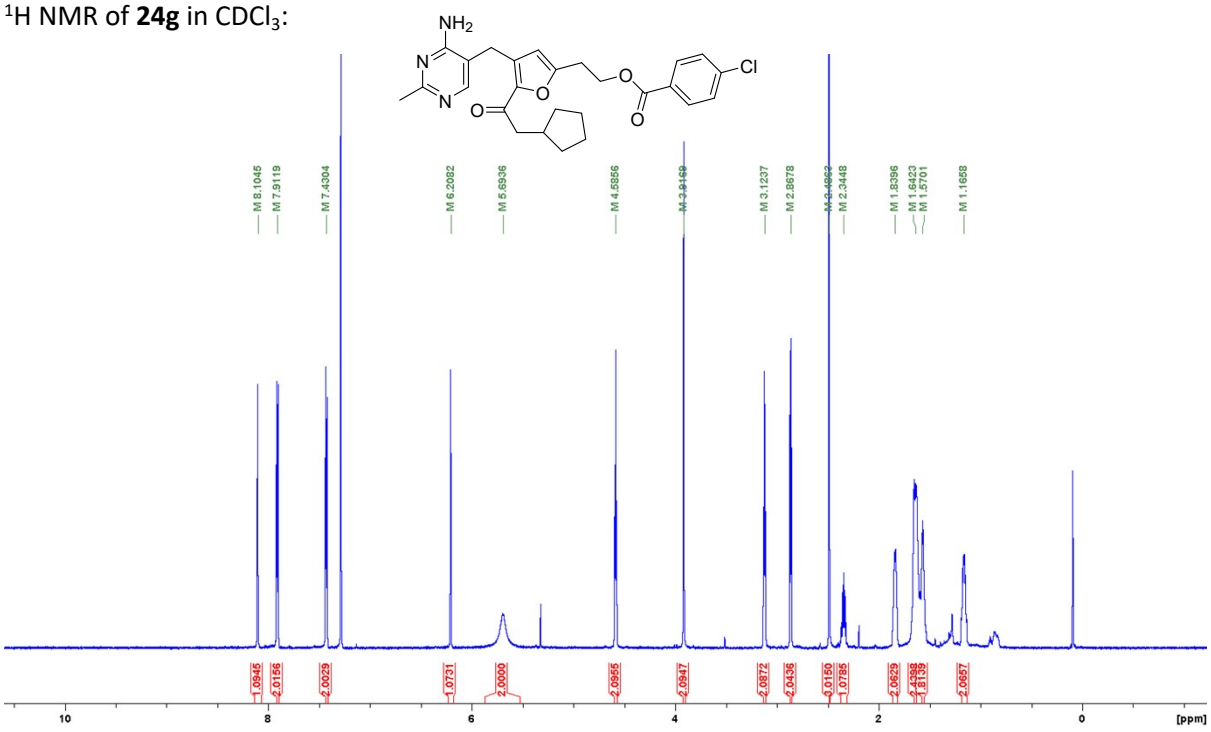
^{1}H NMR of **24f** in $CDCl_3$:



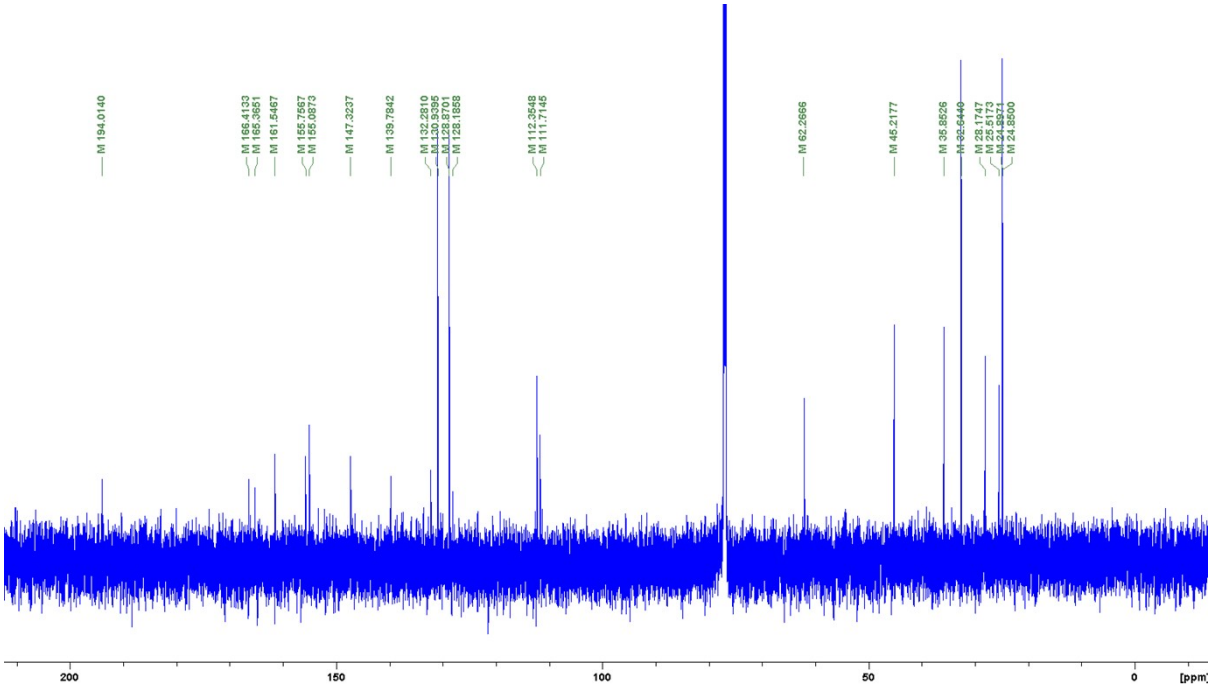
^{13}C NMR of **24f** in $CDCl_3$:



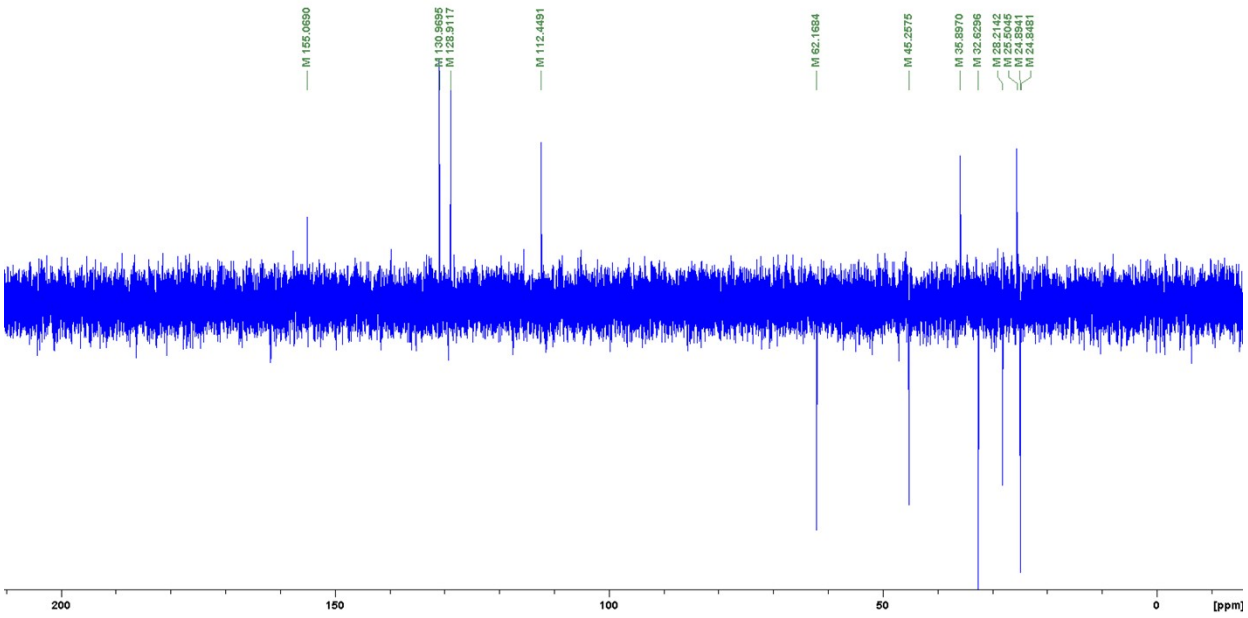
^{1}H NMR of **24g** in $CDCl_3$:



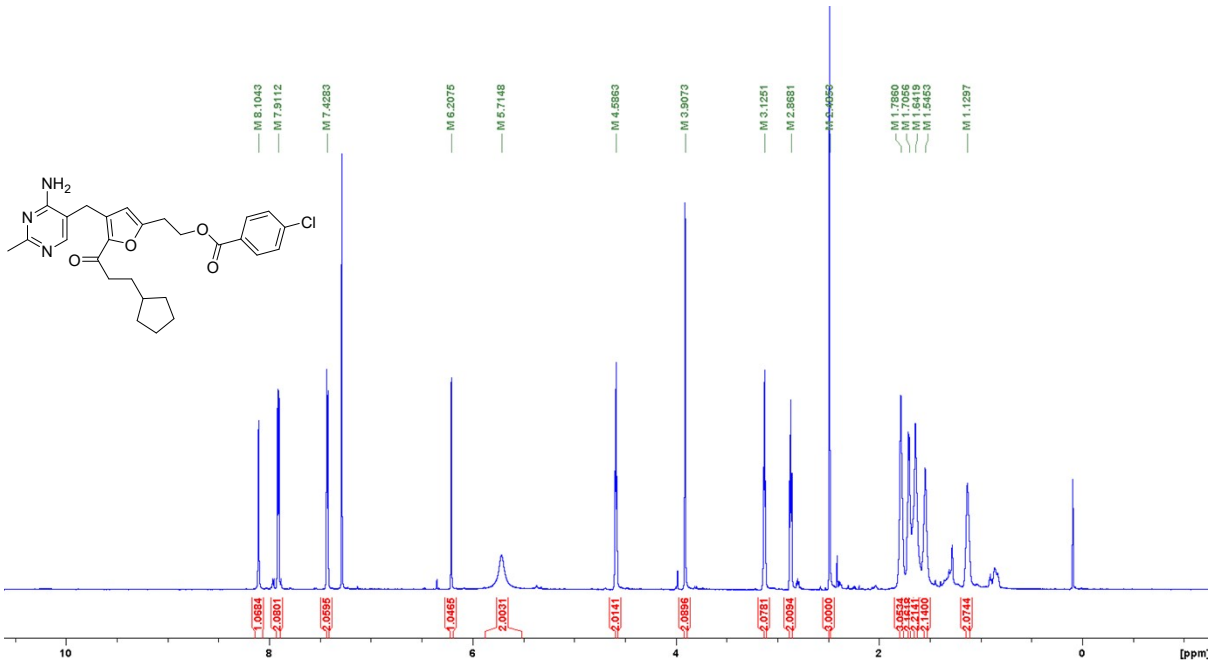
^{13}C NMR of **24g** in $CDCl_3$:



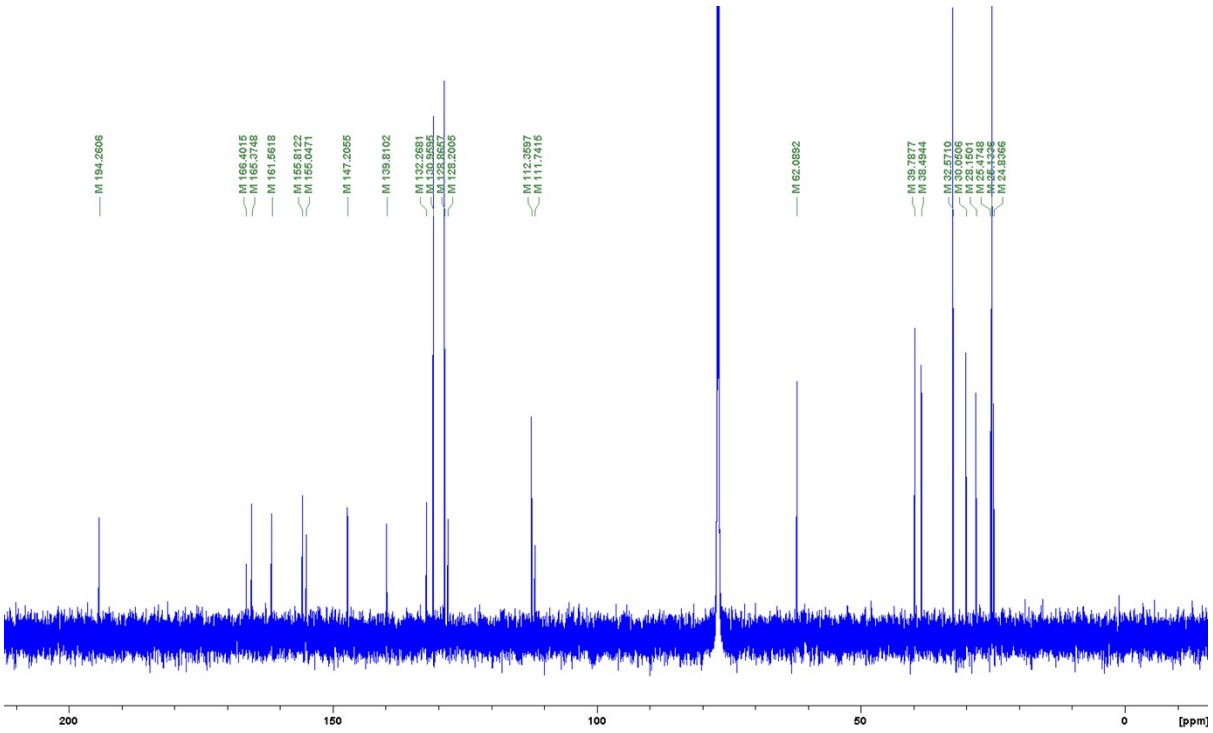
^{13}C DEPT-135 NMR of **24g** in $CDCl_3$:



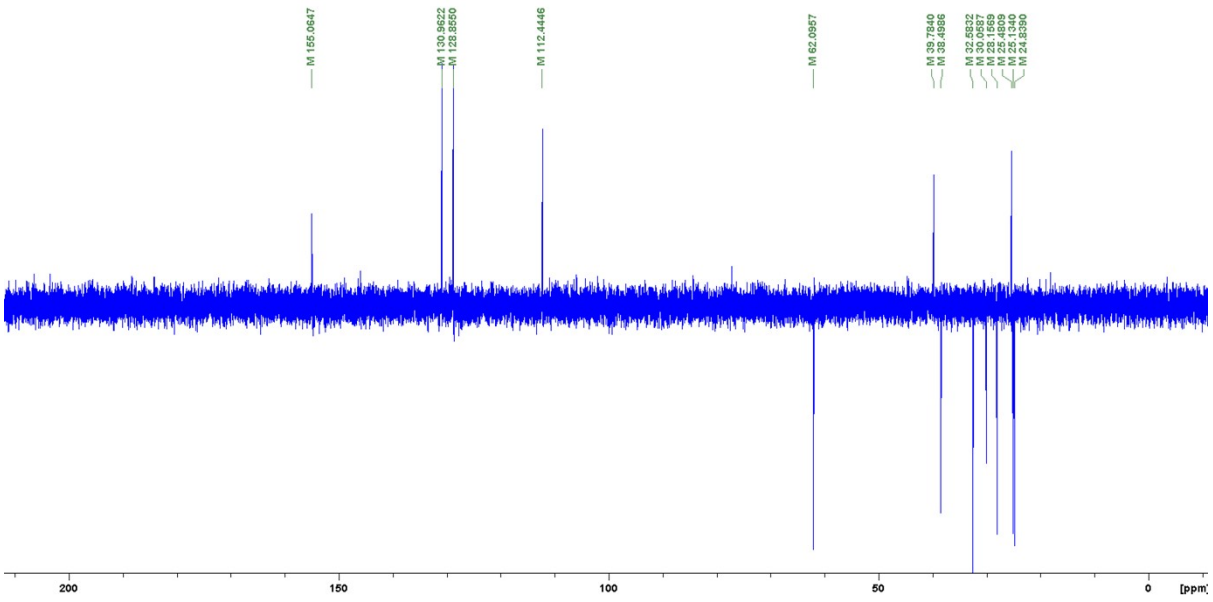
^{1}H NMR of **24h** in $CDCl_3$:



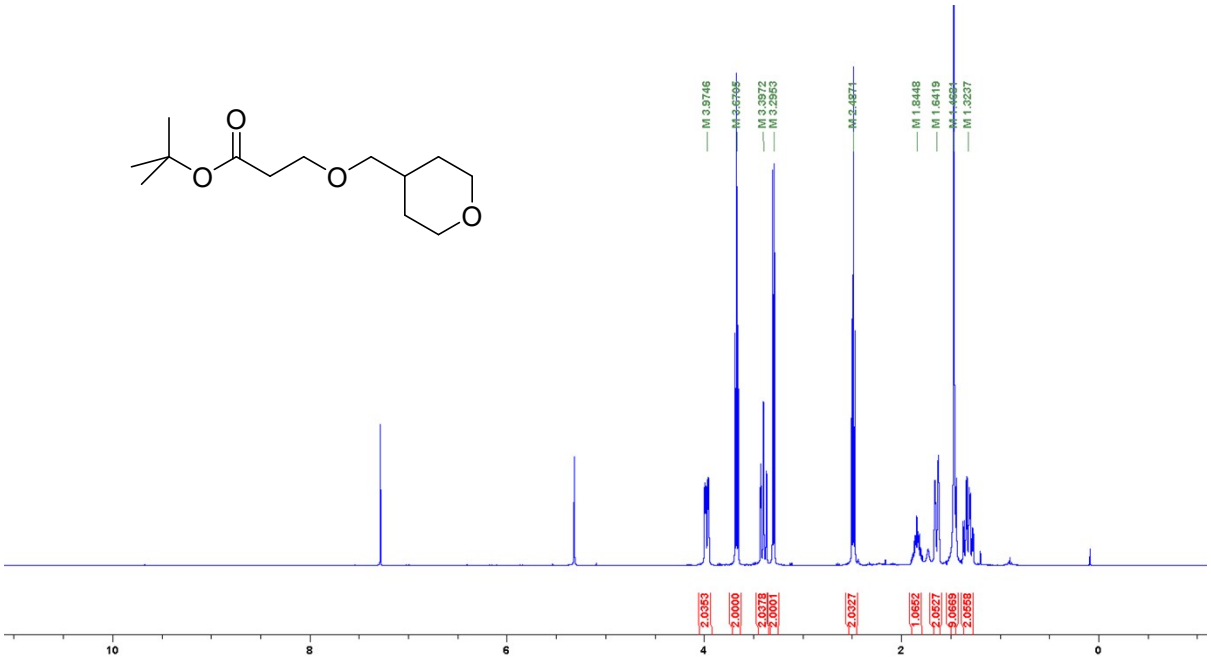
^{13}C NMR of **24h** in $CDCl_3$:



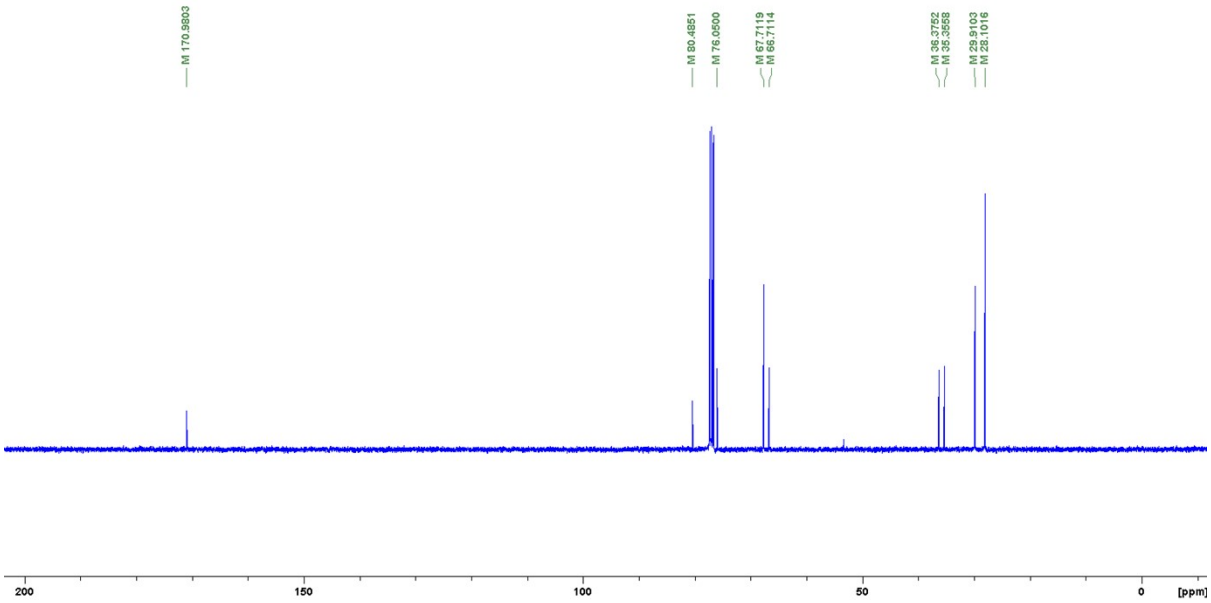
^{13}C DEPT-135 NMR of **24h** in $CDCl_3$:



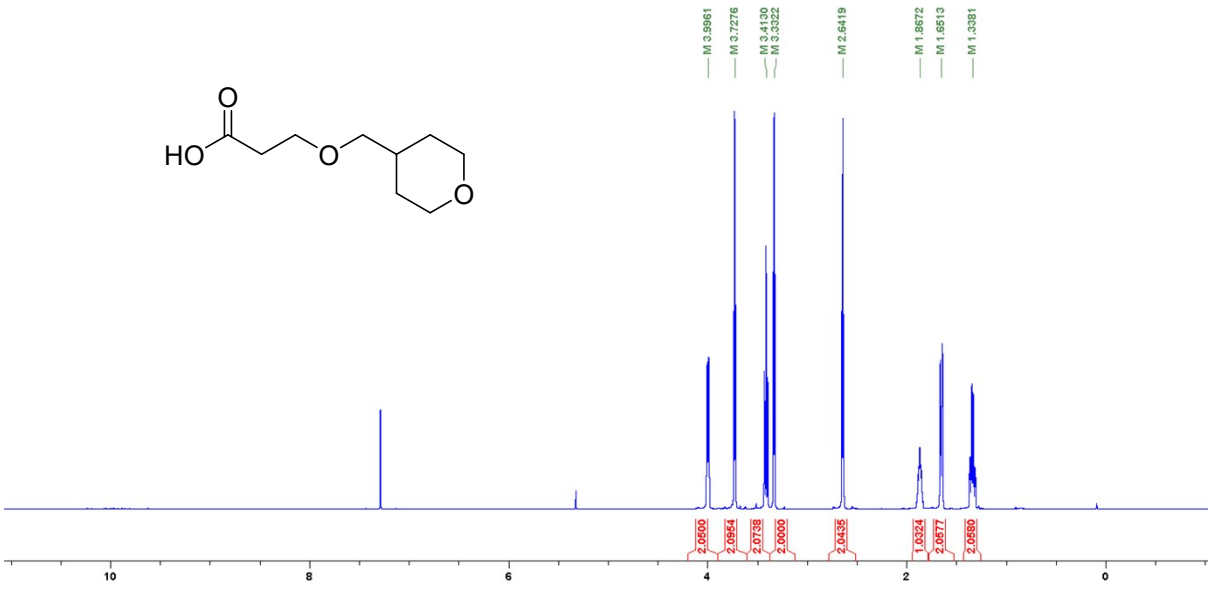
^{1}H NMR of *t*-butyl 3-[(oxan-4-yl)methoxy]propanoate in $CDCl_3$:



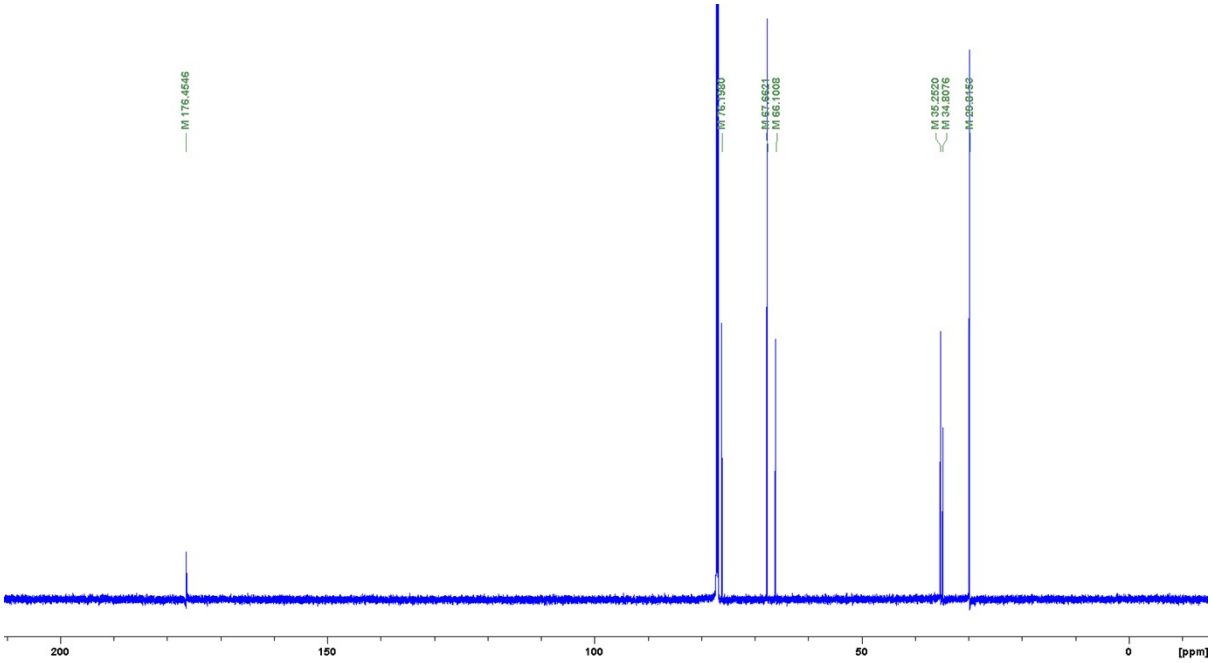
^{13}C NMR of *t*-butyl 3-[(oxan-4-yl)methoxy]propanoate in $CDCl_3$:



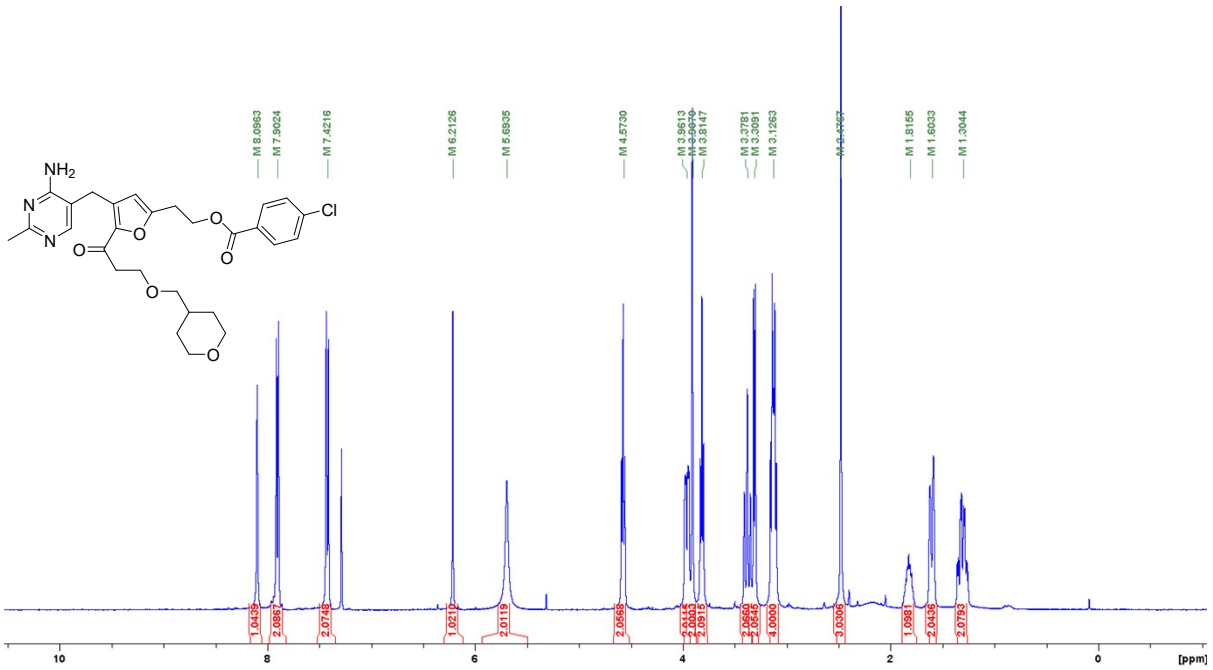
^{1}H NMR of 3-[(oxan-4-yl)methoxy]propanoic acid in $CDCl_3$:



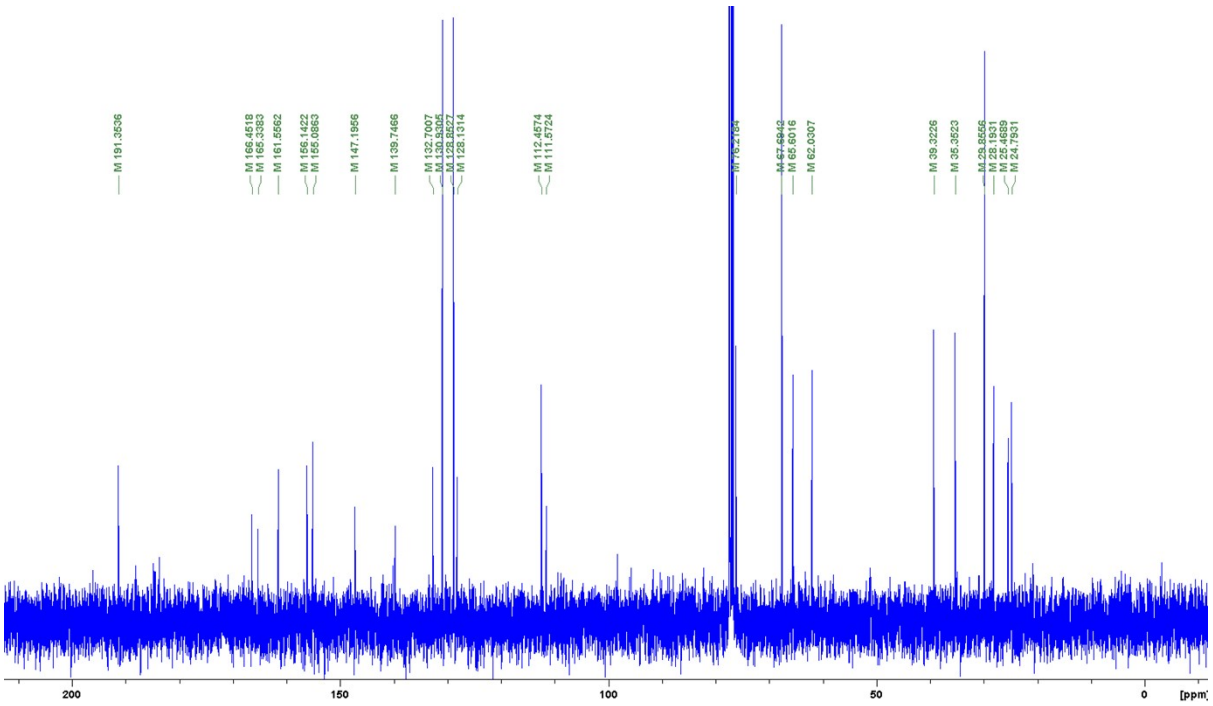
^{13}C NMR of 3-[(oxan-4-yl)methoxy]propanoic acid in $CDCl_3$:



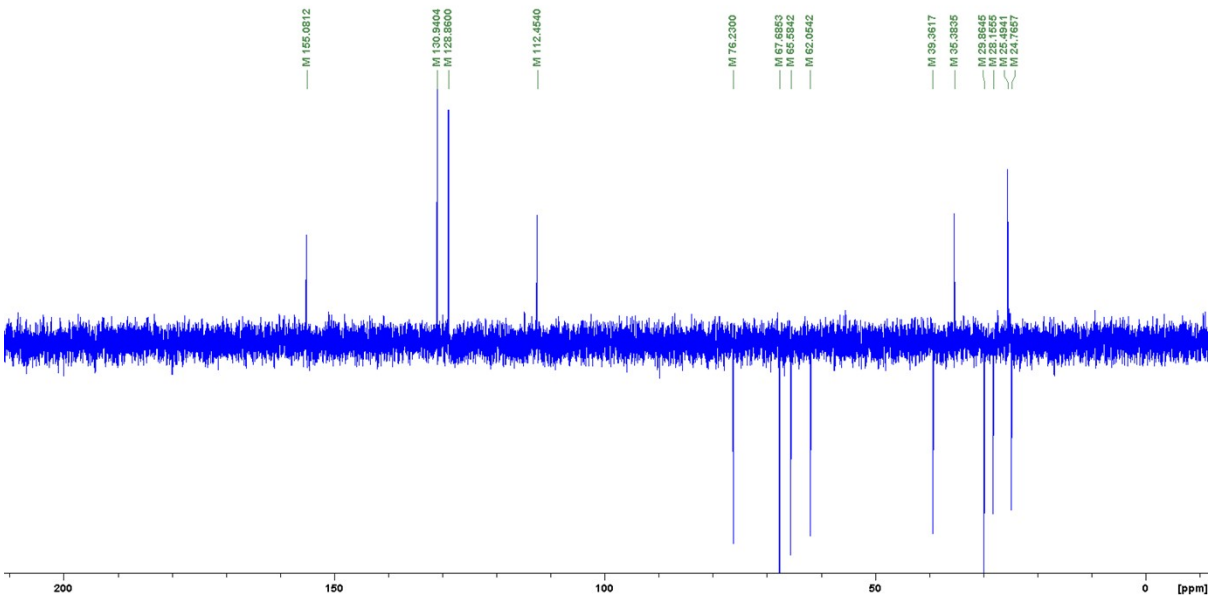
^{1}H NMR of **24i** in $CDCl_3$:



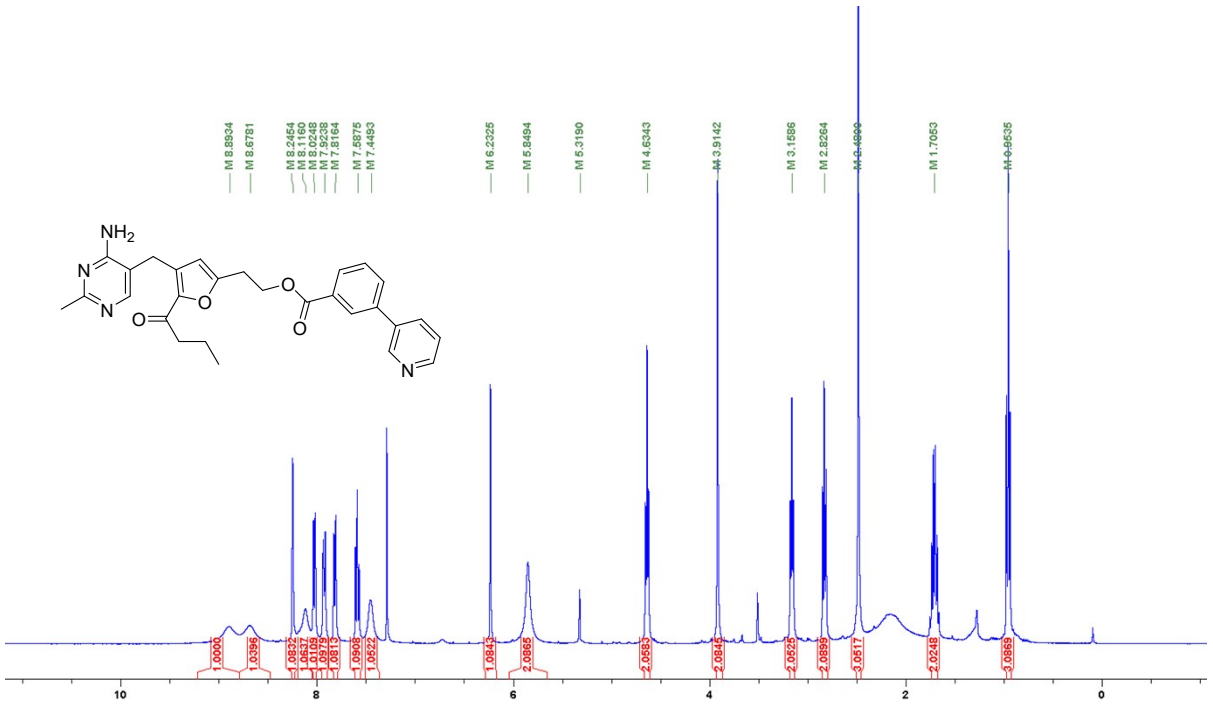
^{13}C NMR of **24i** in $CDCl_3$:



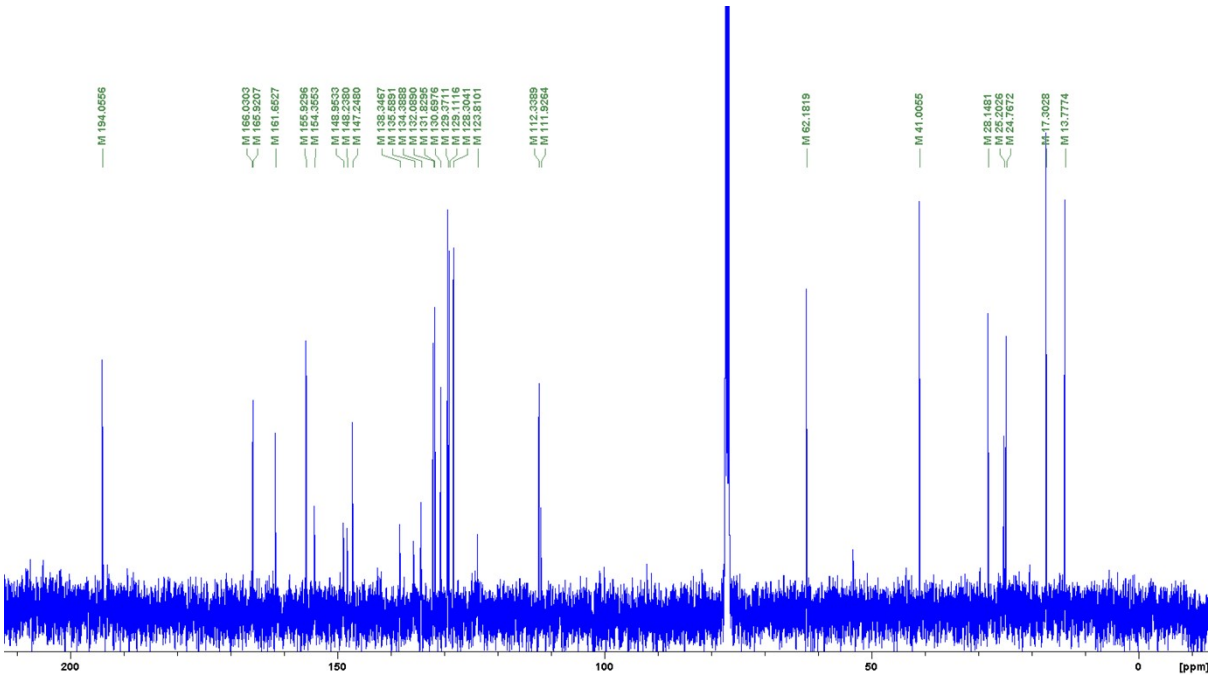
^{13}C DEPT-135 NMR of **24i** in $CDCl_3$:



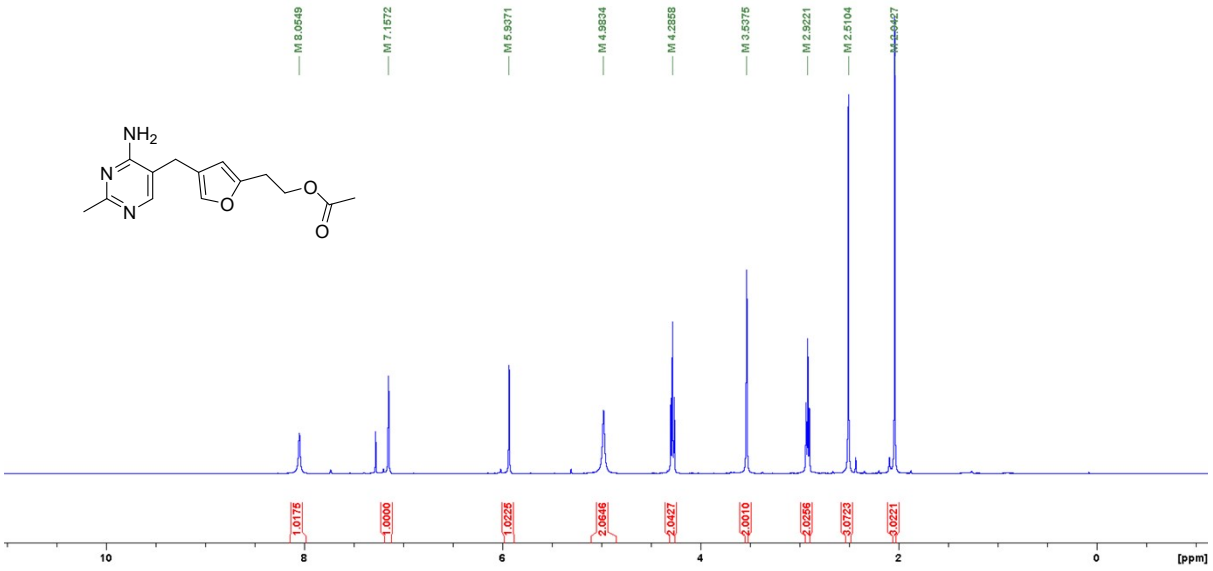
^{1}H NMR of **25** in $CDCl_3$:



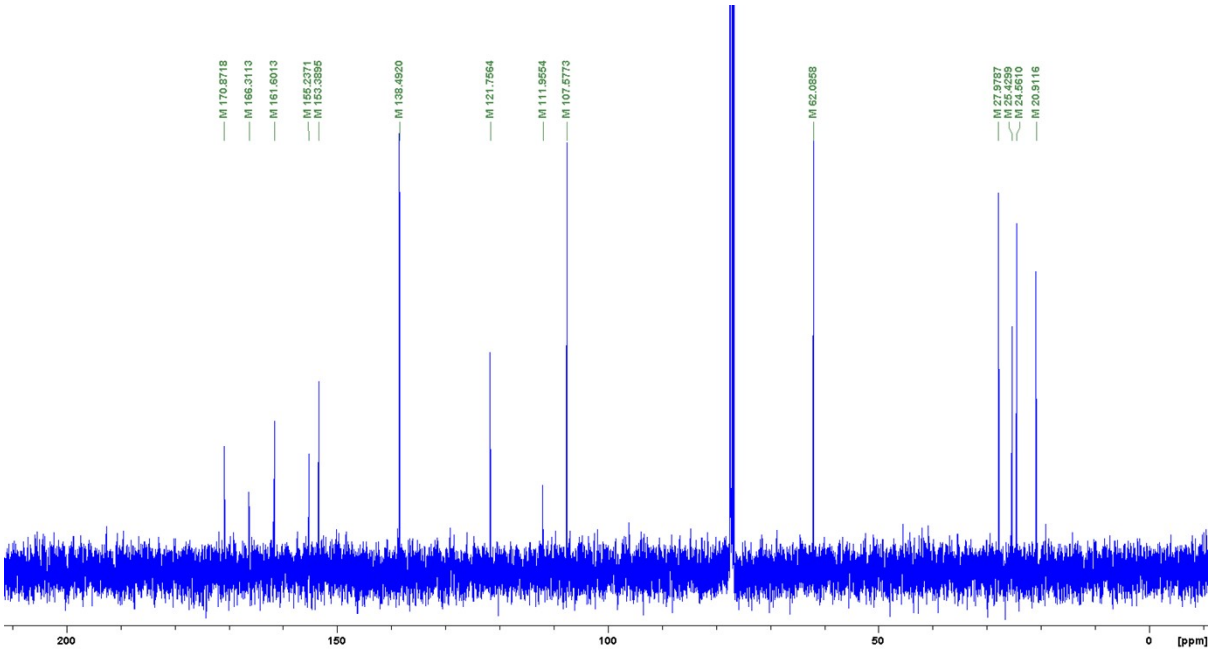
^{13}C NMR of **25** in $CDCl_3$:



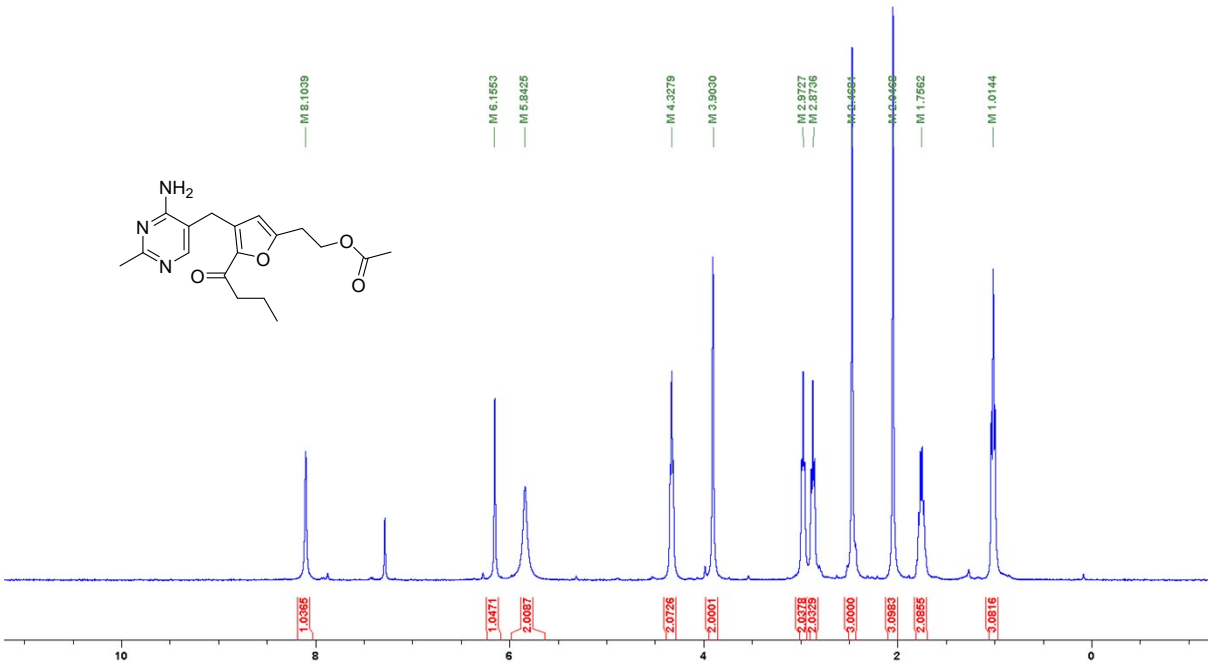
^{1}H NMR of 2-{4-[(4-amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl acetate in $CDCl_3$:



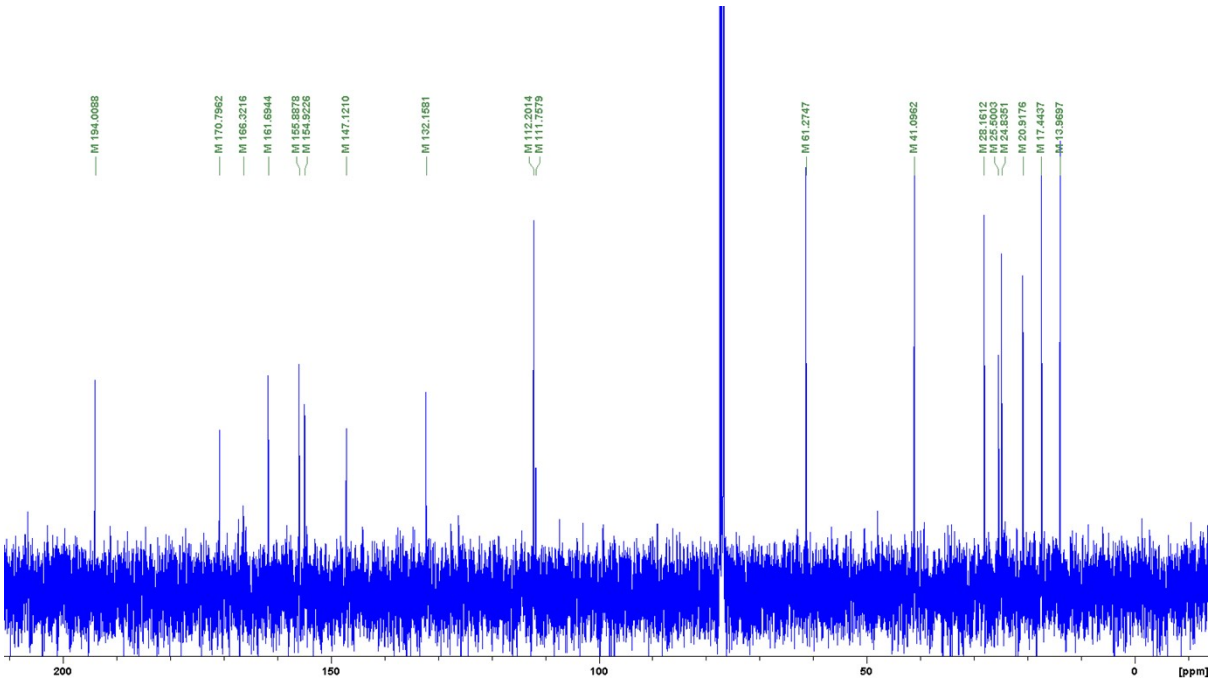
^{13}C NMR of 2-{4-[(4-amino-2-methylpyrimidin-5-yl)methyl]furan-2-yl}ethyl acetate in $CDCl_3$:



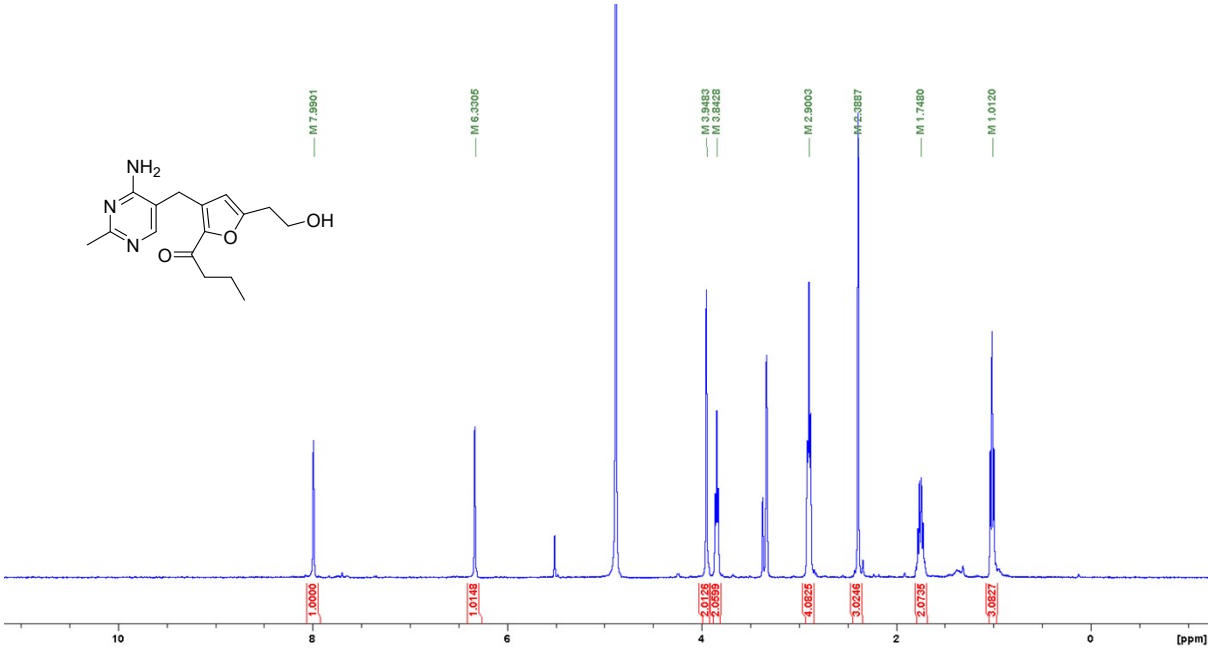
^{1}H NMR of **27** in $CDCl_3$:



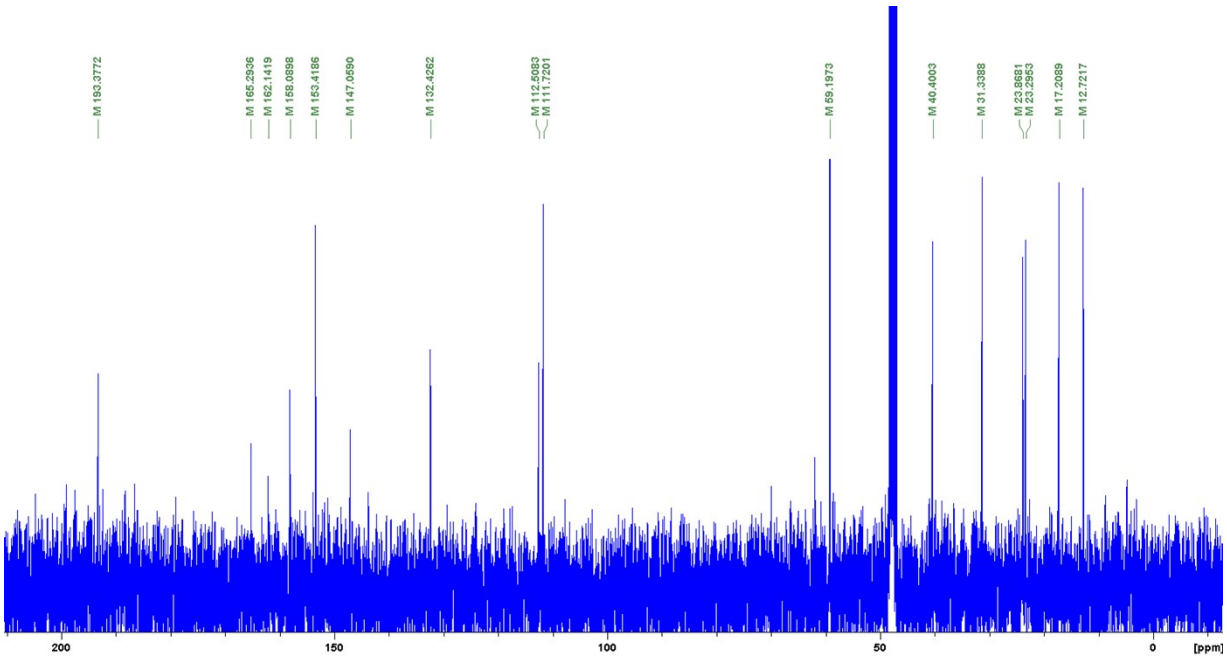
^{13}C NMR of **27** in $CDCl_3$:



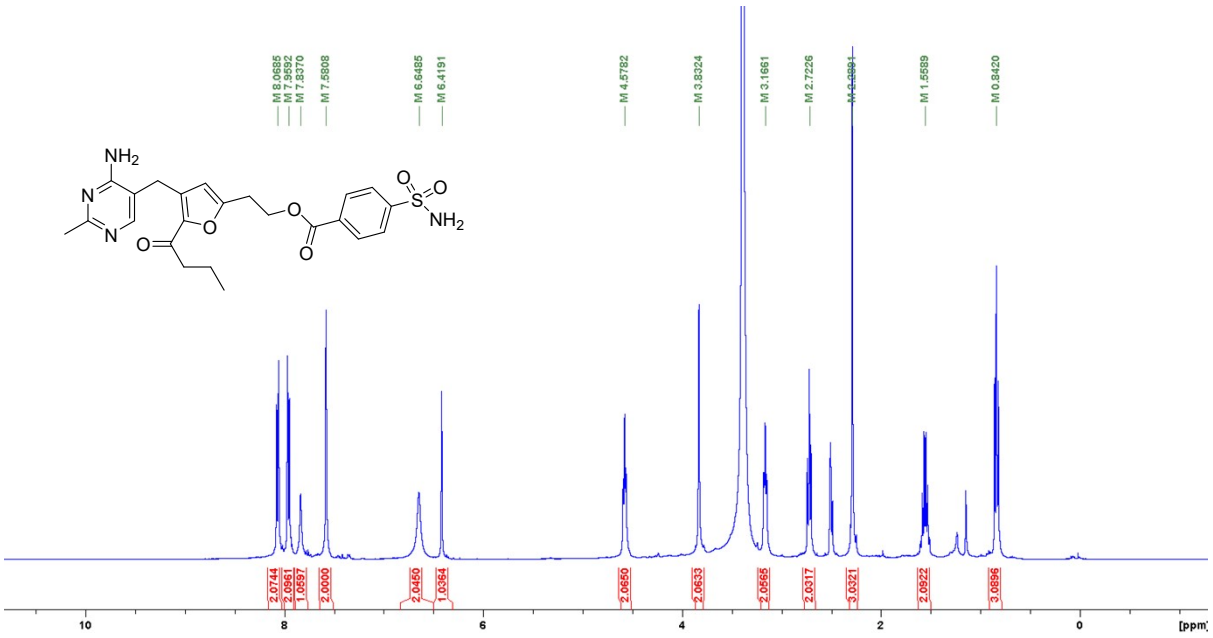
^{1}H NMR of 1-{3-[(4-amino-2-methylpyrimidin-5-yl)methyl]-5-(2-hydroxyethyl)furan-2-yl}butan-1-one in CD_3OD:



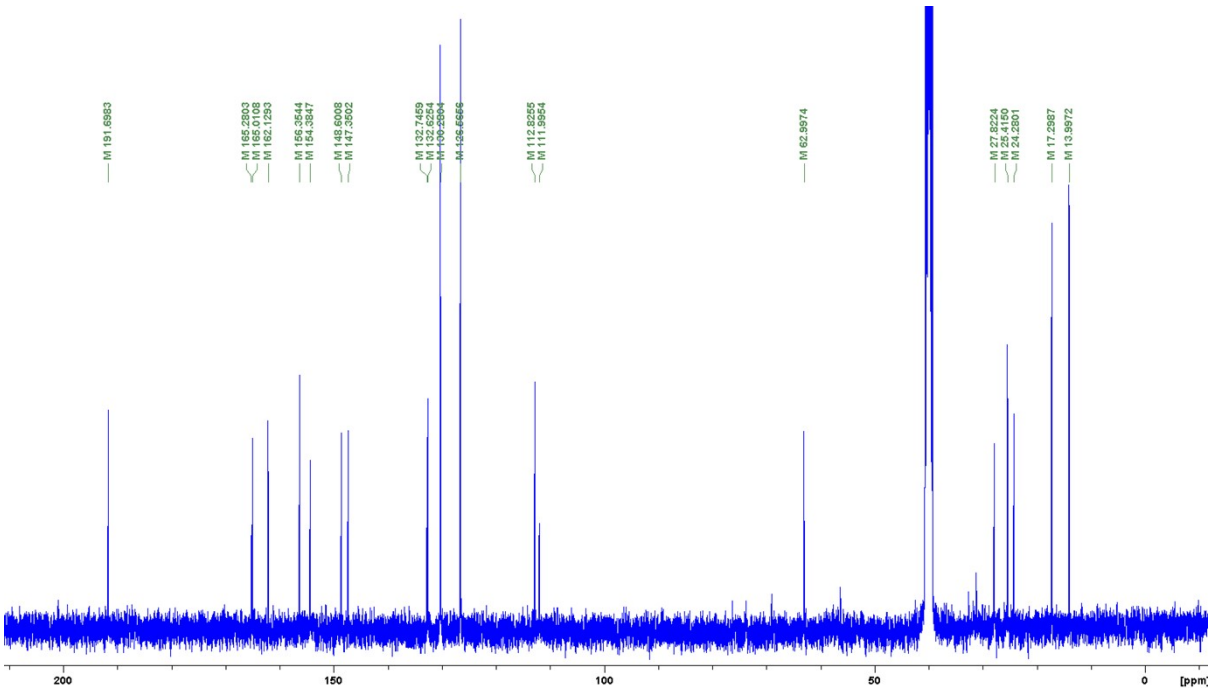
^{13}C NMR of 1-{3-[(4-amino-2-methylpyrimidin-5-yl)methyl]-5-(2-hydroxyethyl)furan-2-yl}butan-1-one in CD_3OD:



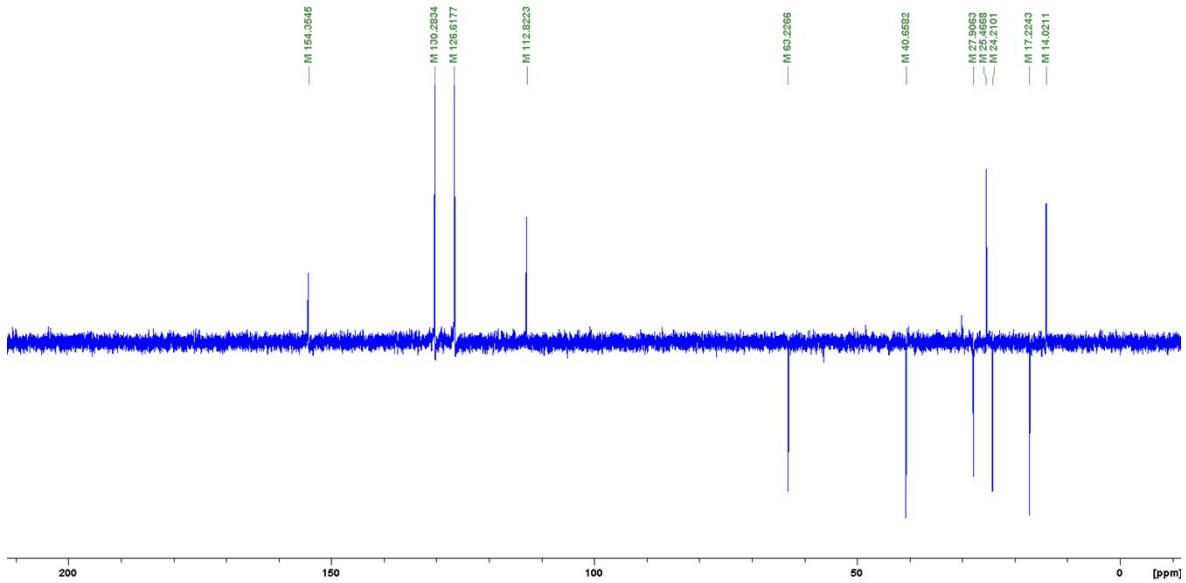
^{1}H NMR of **26** in CD_3SOCD_3:



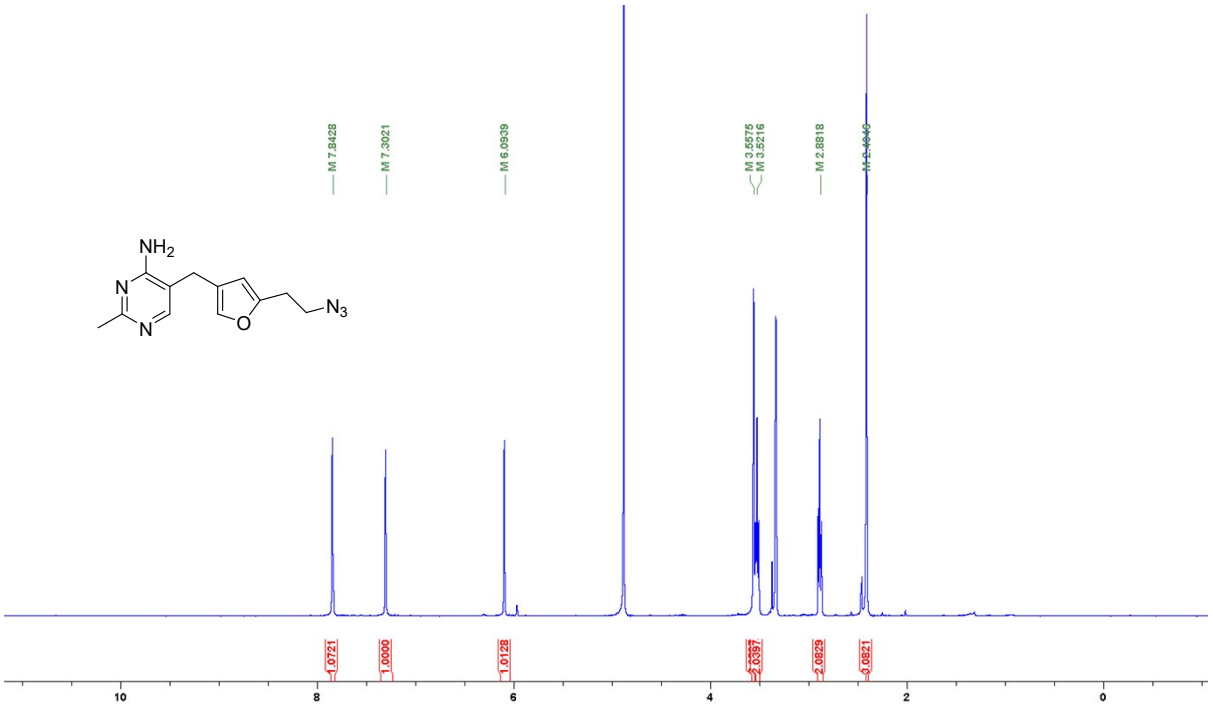
^{13}C NMR of **26** in CD_3SOCD_3: (the peak at 40.6 is shielded by the solvent peak)



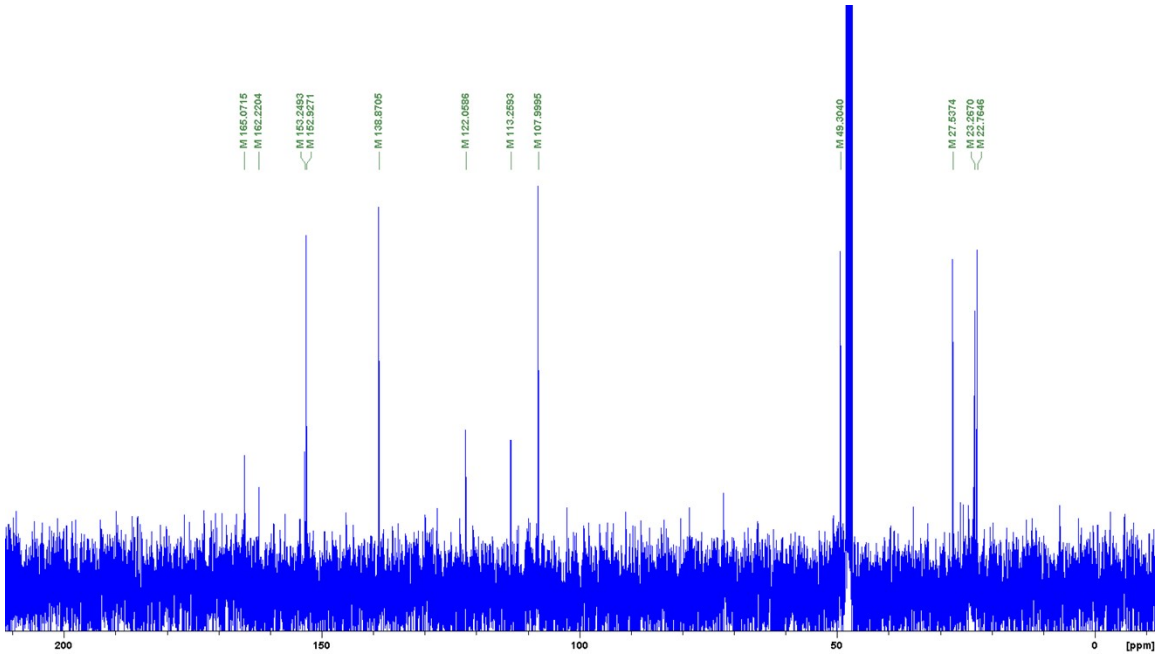
^{13}C DEPT-135 NMR of **26** in CD_3SOCD_3: (the peak at 40.6 shielded by the solvent peak is unmasked in the DEPT-135 spectrum)



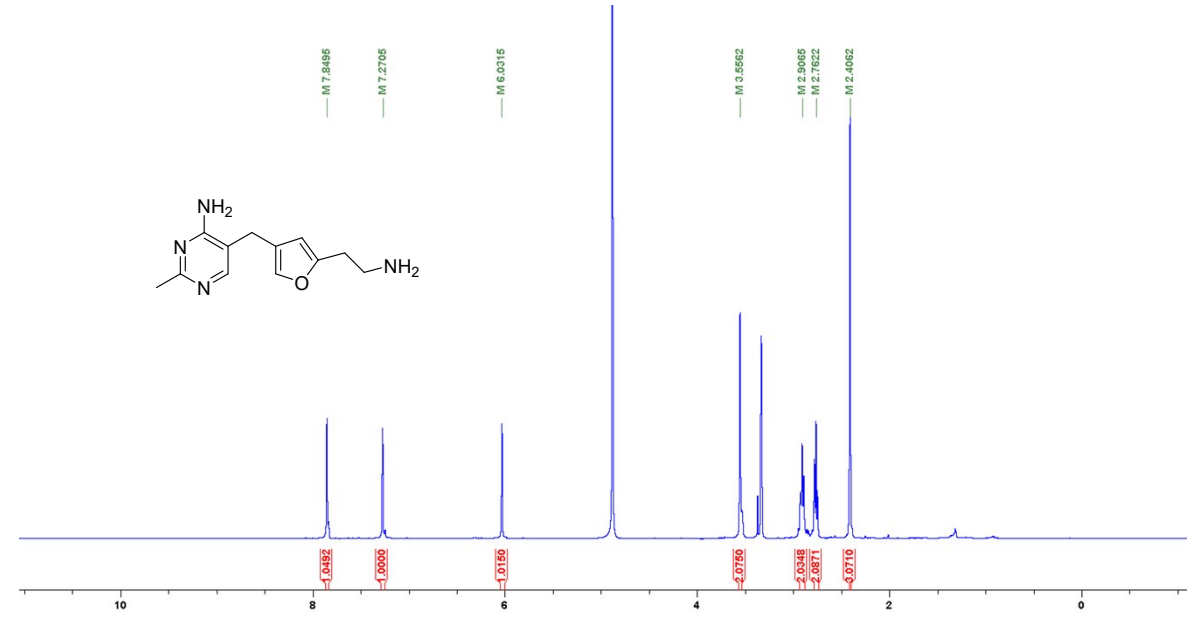
^{1}H NMR of **29** in CD_3OD:



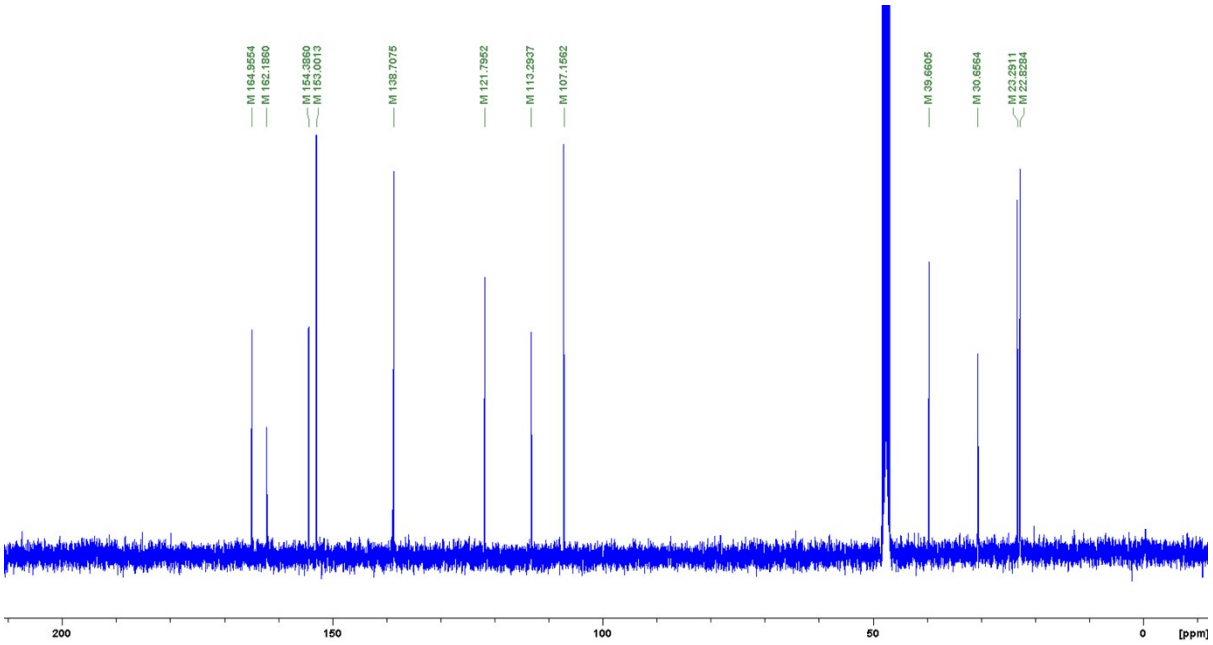
^{13}C NMR of **29** in CD_3OD:



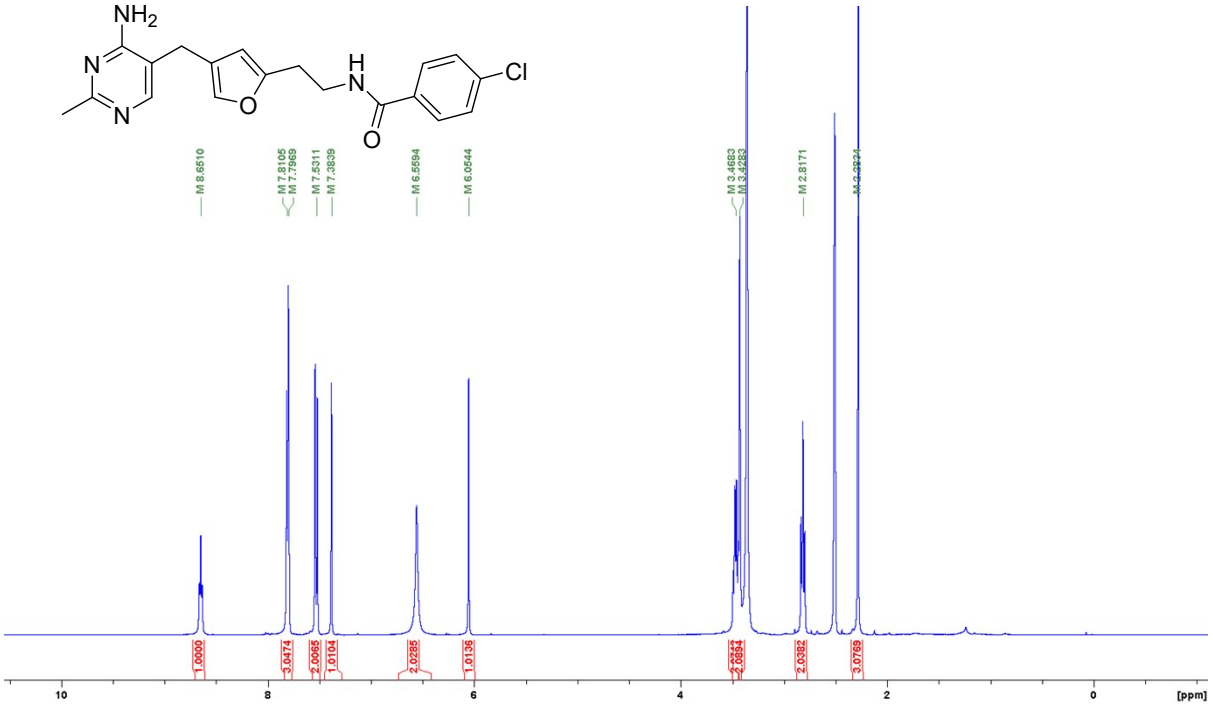
^{1}H NMR of **30** in CD_3OD:



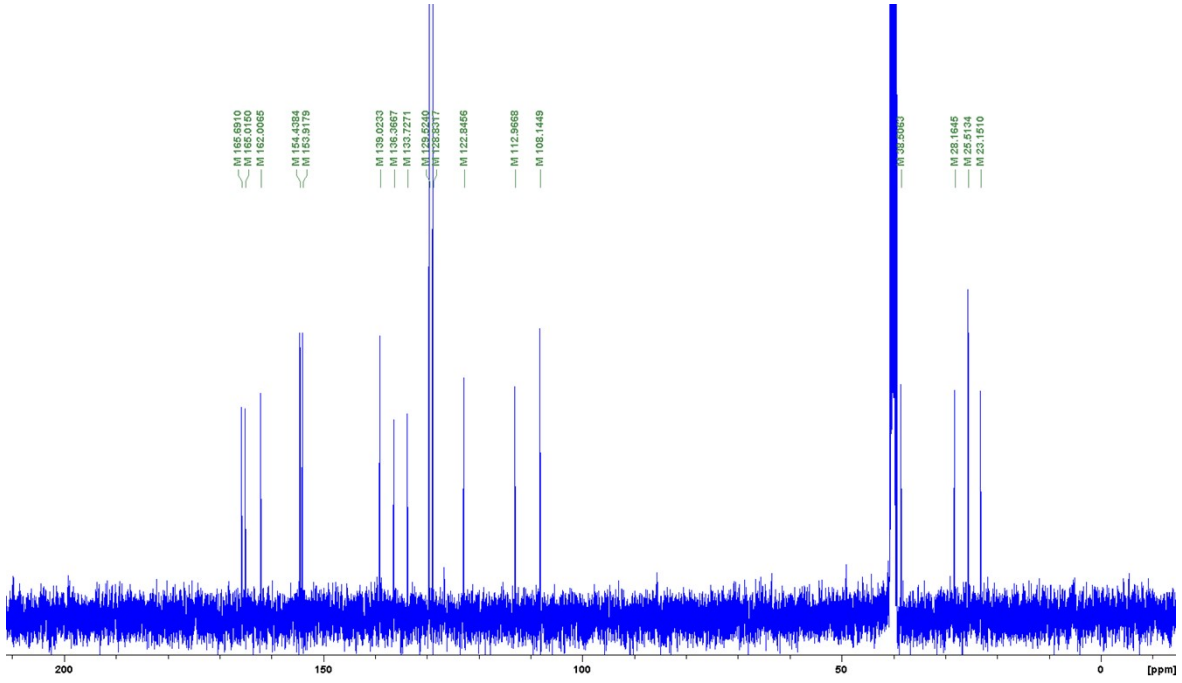
^{13}C NMR of **30** in CD_3OD:



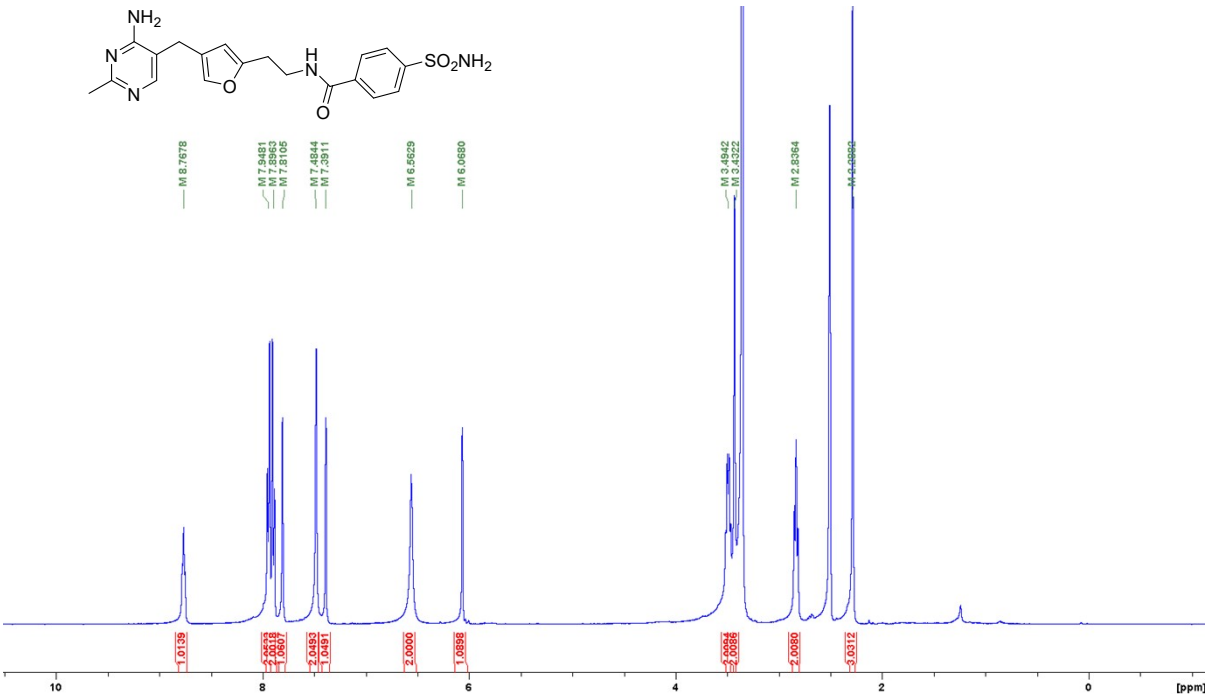
^{1}H NMR of **31** in CD_3SOCD_3:



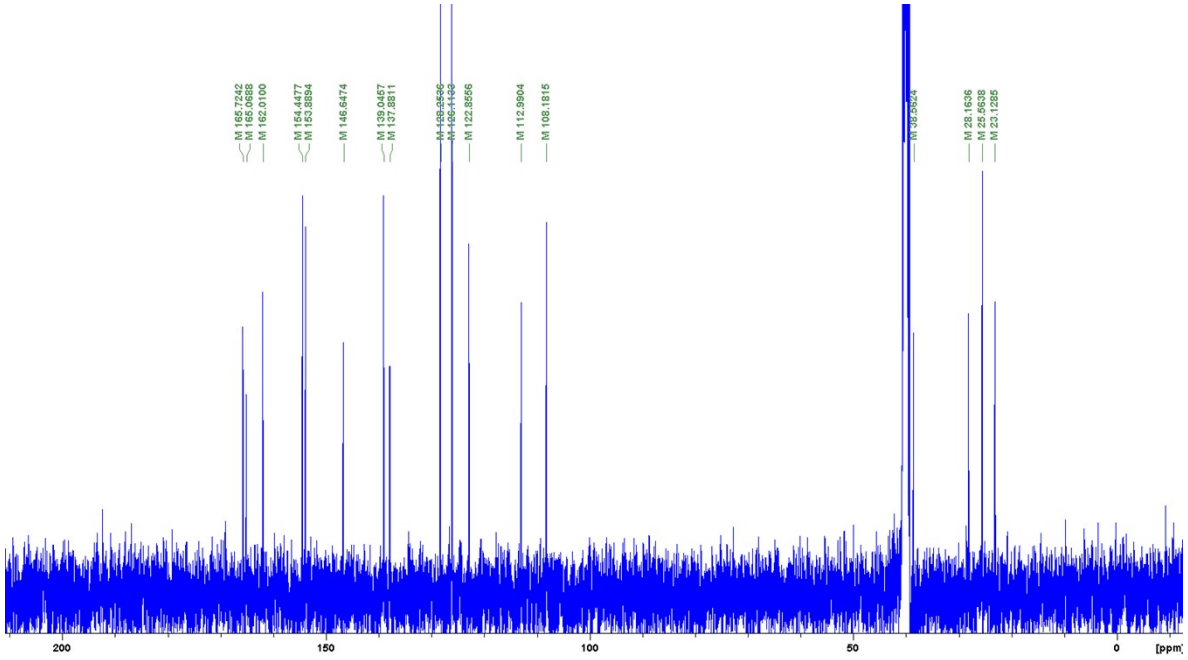
^{13}C NMR of **31** in CD_3SOCD_3:



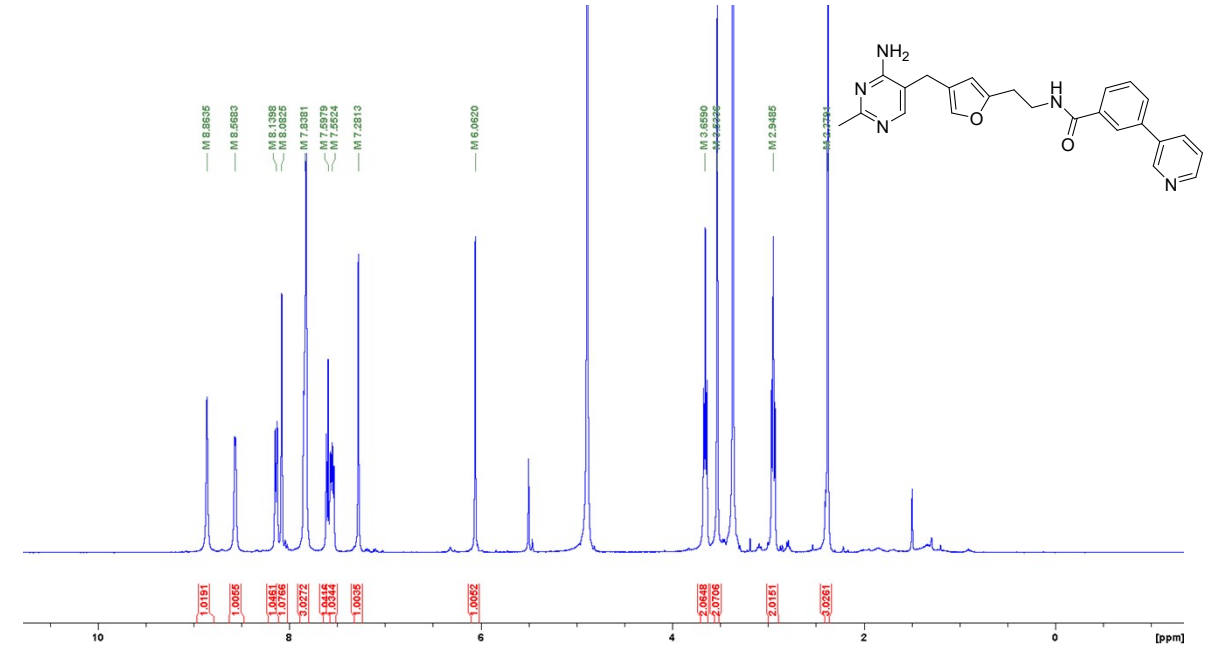
^{1}H NMR of **32** in CD_3SOCD_3:



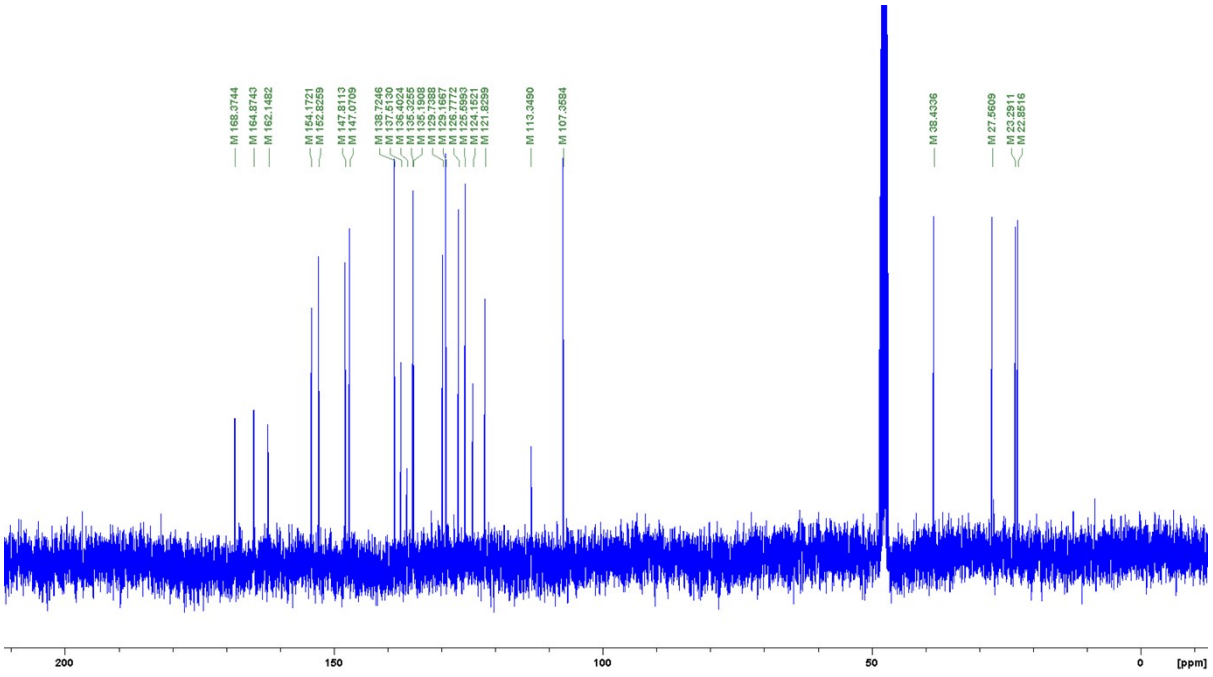
^{13}C NMR of **32** in CD_3SOCD_3:



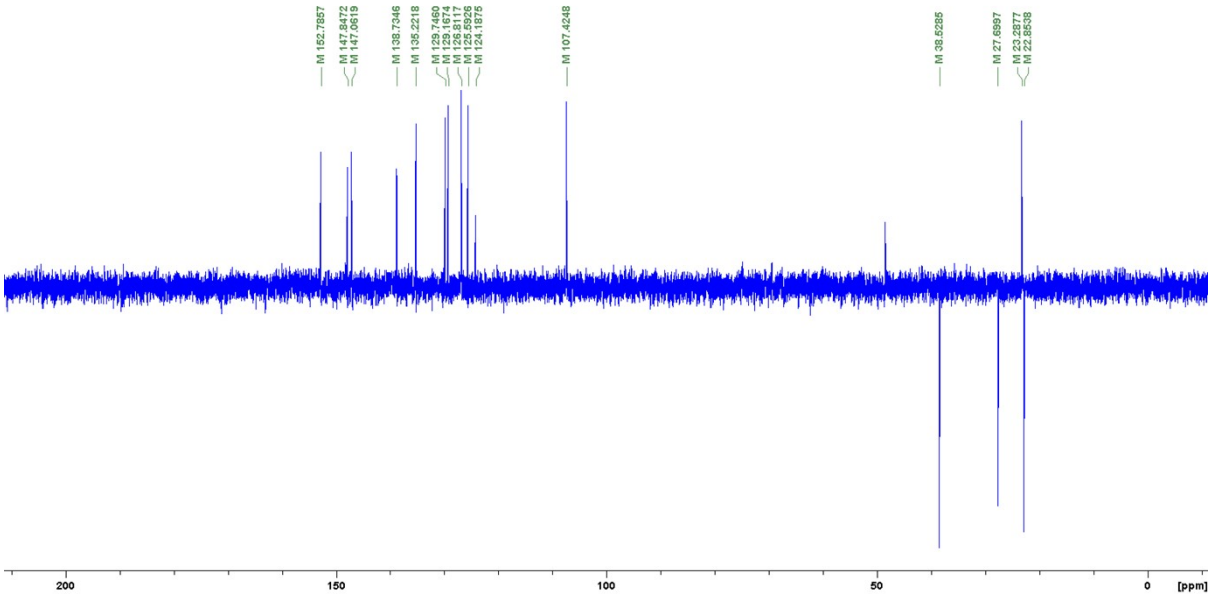
^{1}H NMR of **33** in CD_3OD:



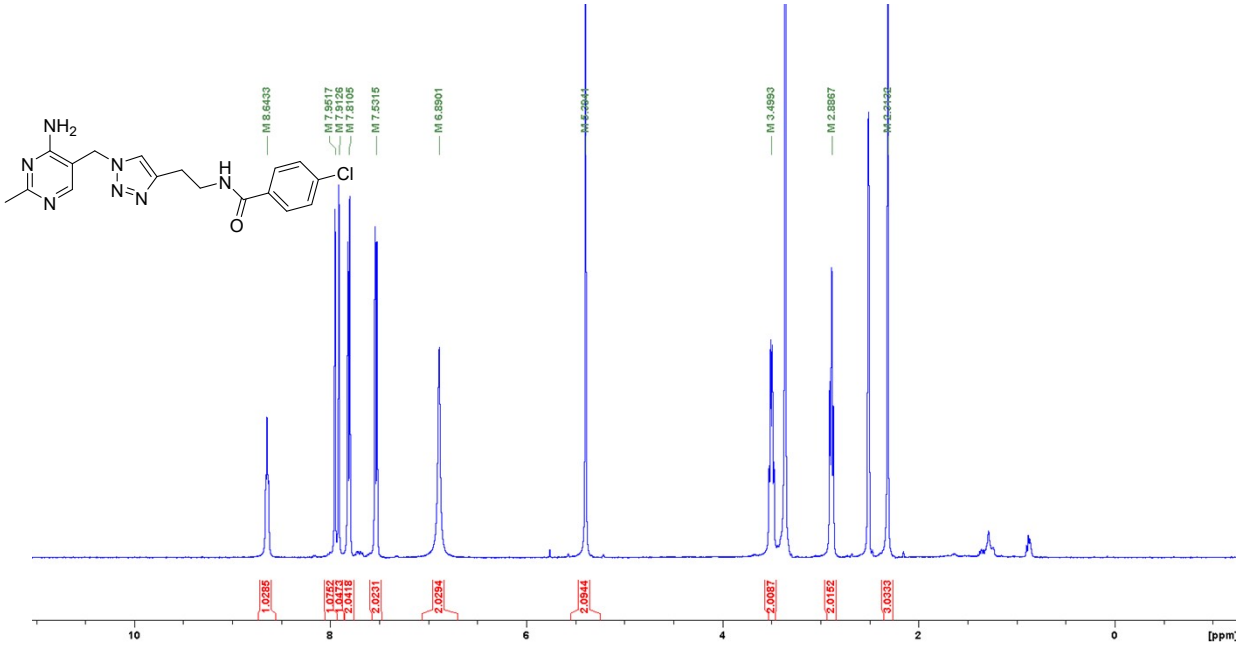
^{13}C NMR of **33** in CD_3OD:



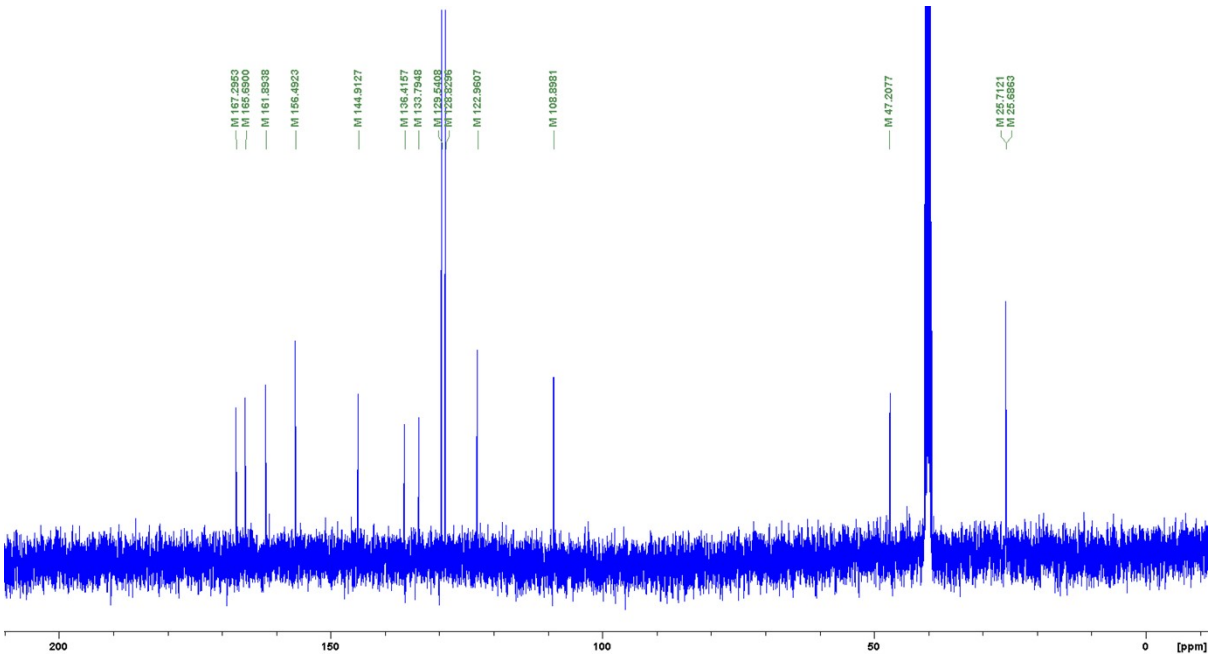
^{13}C DEPT-135 NMR of **33** in CD_3OD:



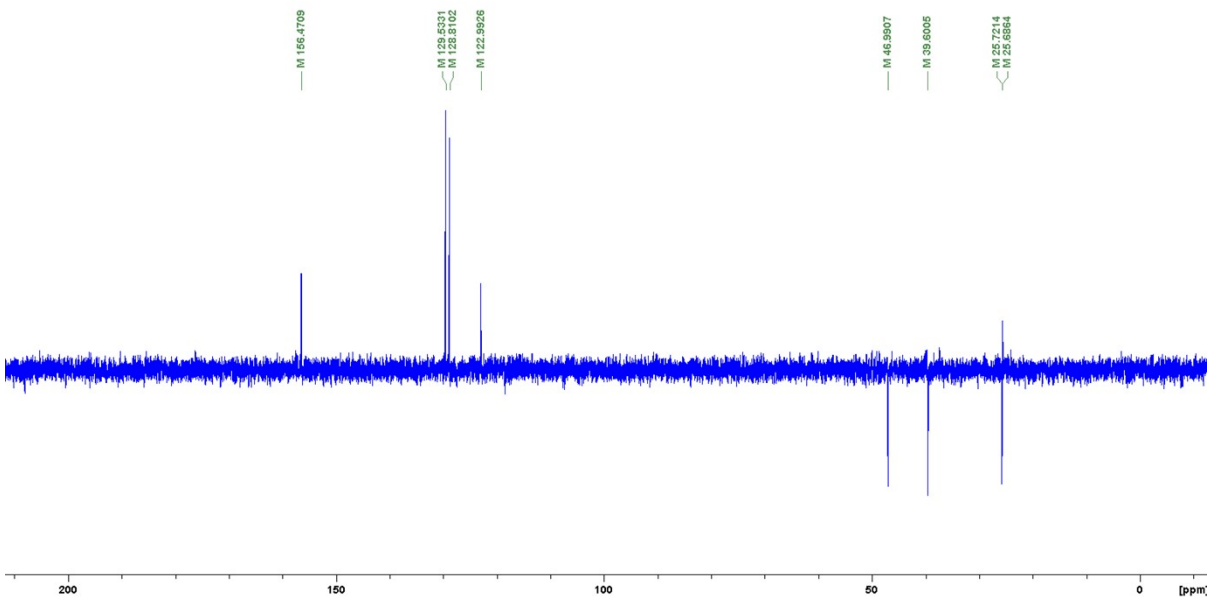
^{1}H NMR of **34** in CD_3SOCD_3:



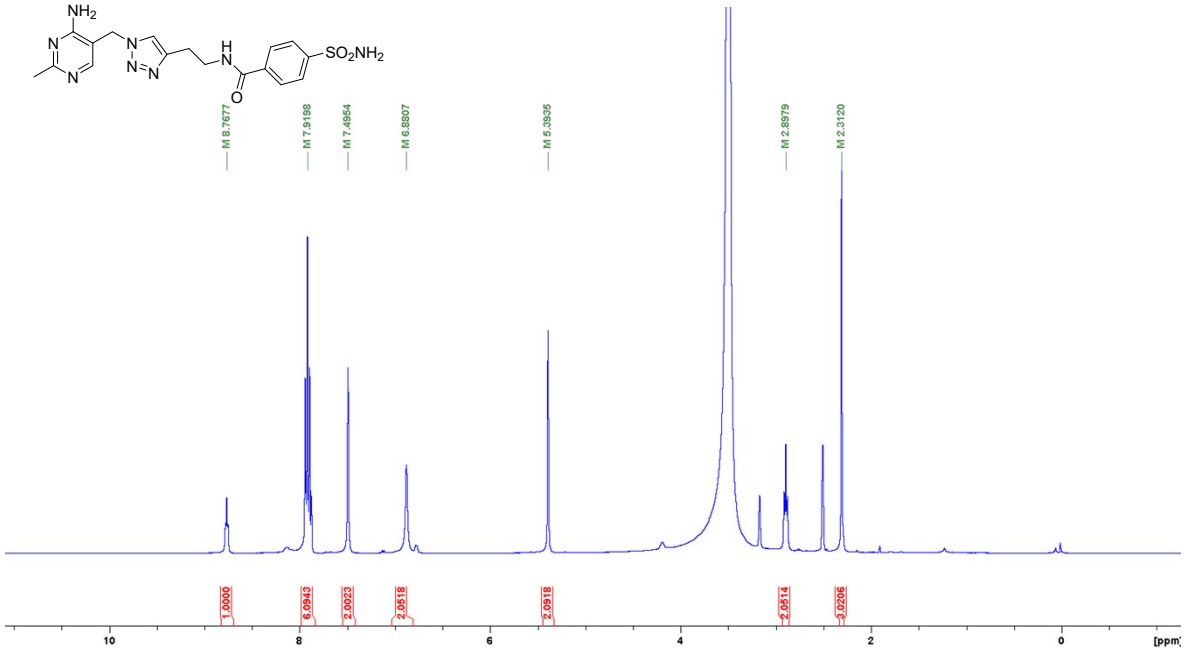
^{13}C NMR of **34** in CD_3SOCD_3: (the peak at 39.6 is shielded by the solvent peak)



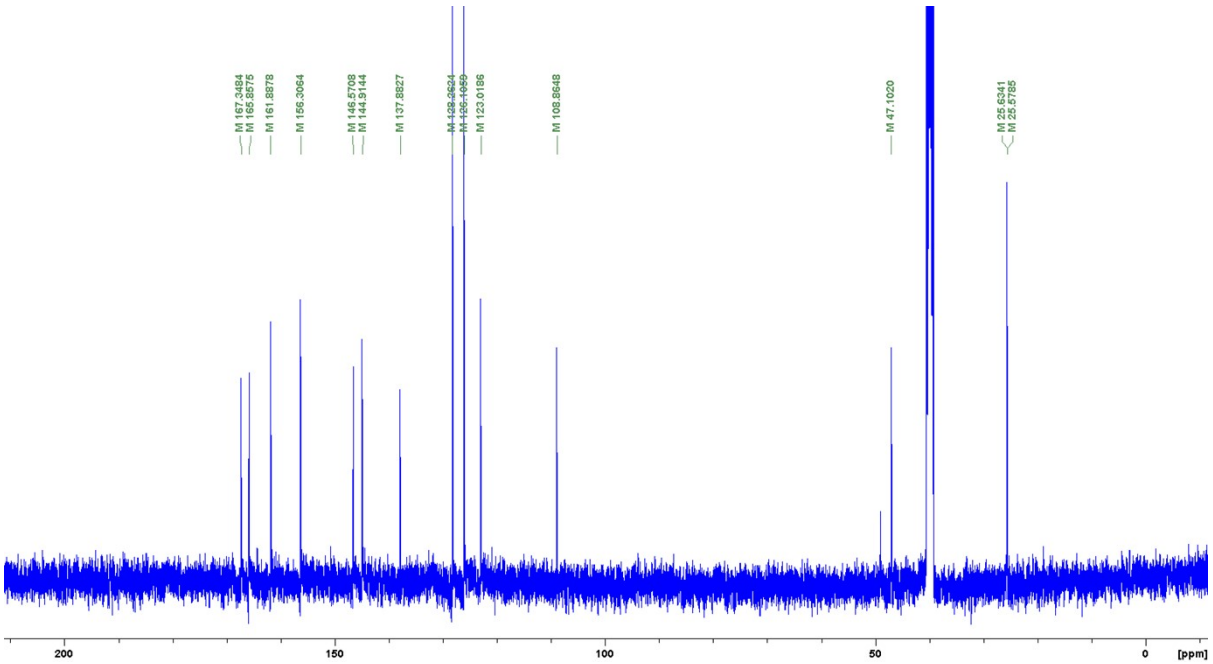
^{13}C DEPT-135 NMR of **34** in CD_3SOCD_3: (the peak at 39.6 shielded by the solvent peak is unmasked in the DEPT-135 spectrum)



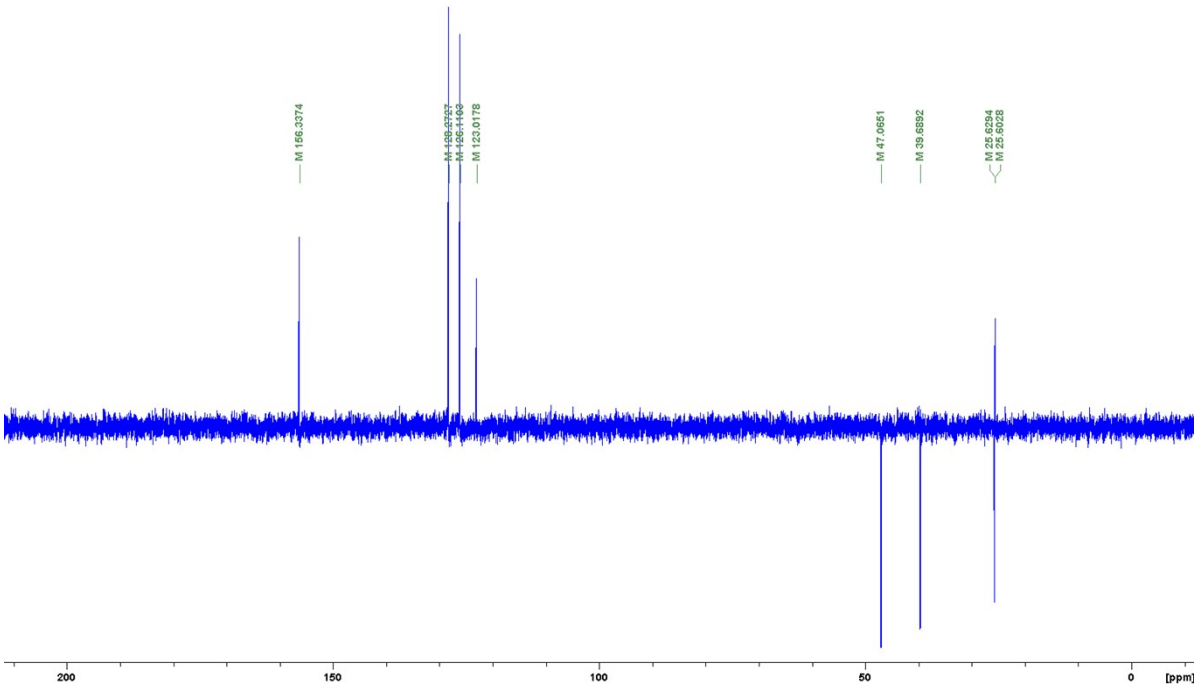
^{1}H NMR of **35** in CD_3SOCD_3: (the peak at 3.49 is shielded by the solvent peak)



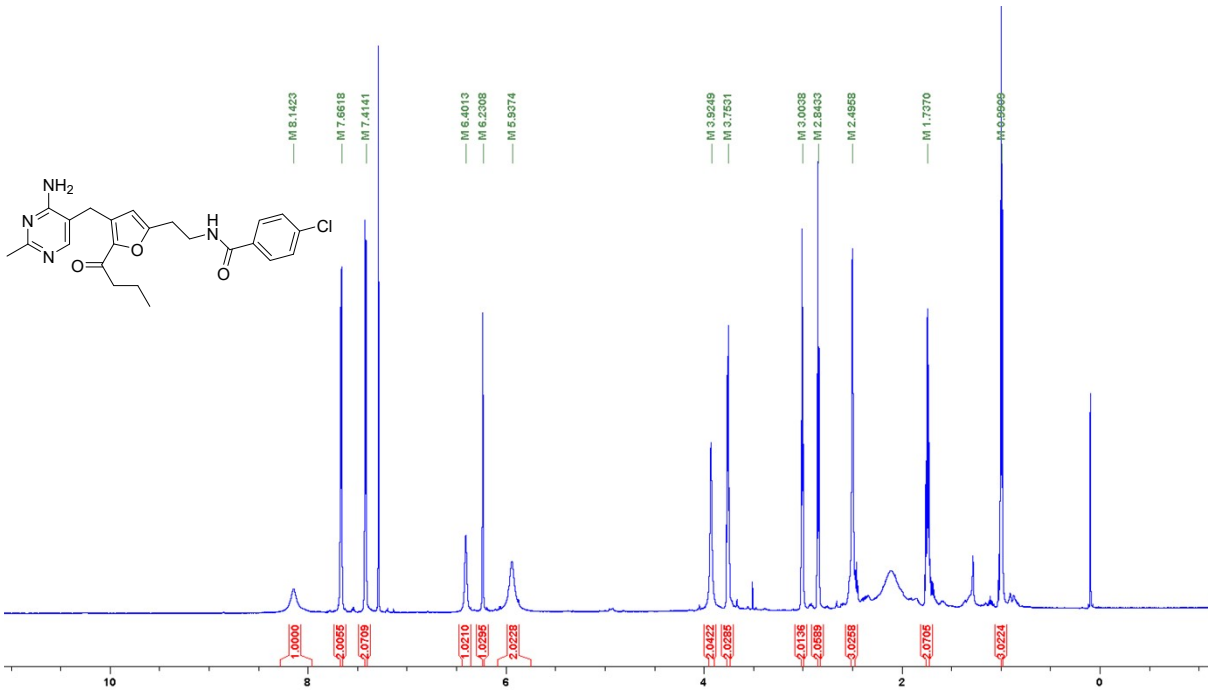
^{13}C NMR of **35** in CD_3SOCD_3: (the peak at 39.6 is shielded by the solvent peak)



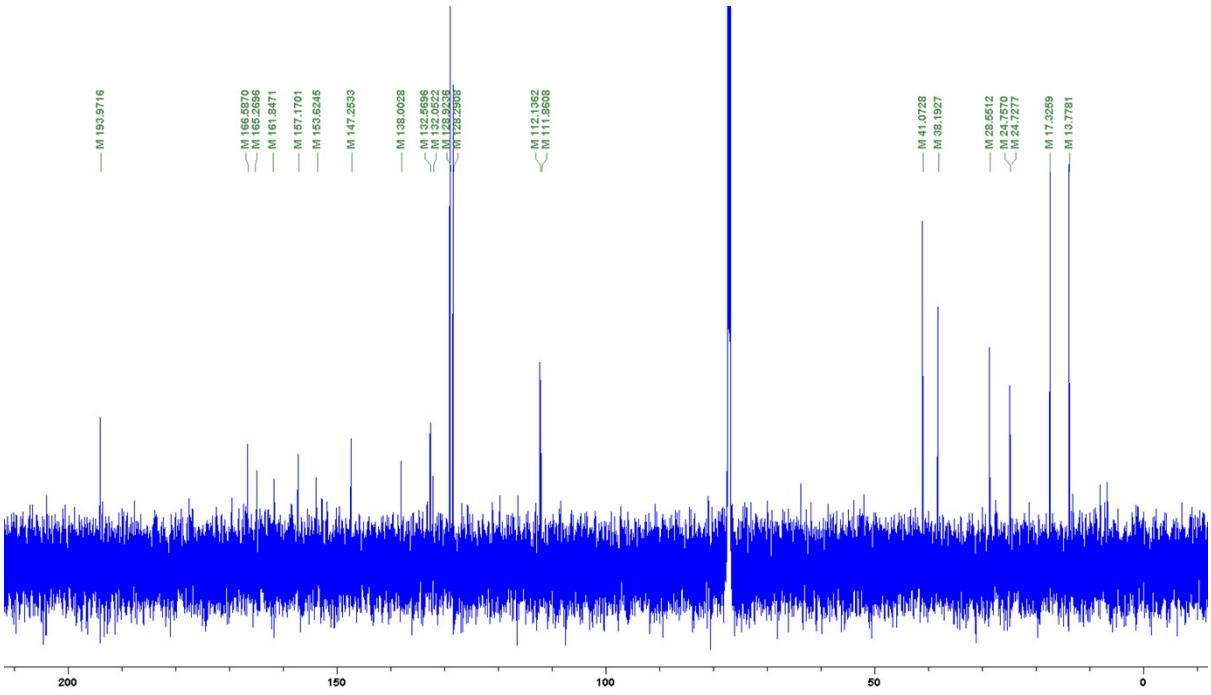
^{13}C DEPT-135 NMR of **35** in CD_3SOCD_3: (the peak at 39.6 shielded by the solvent peak is unmasked in the DEPT-135 spectrum)



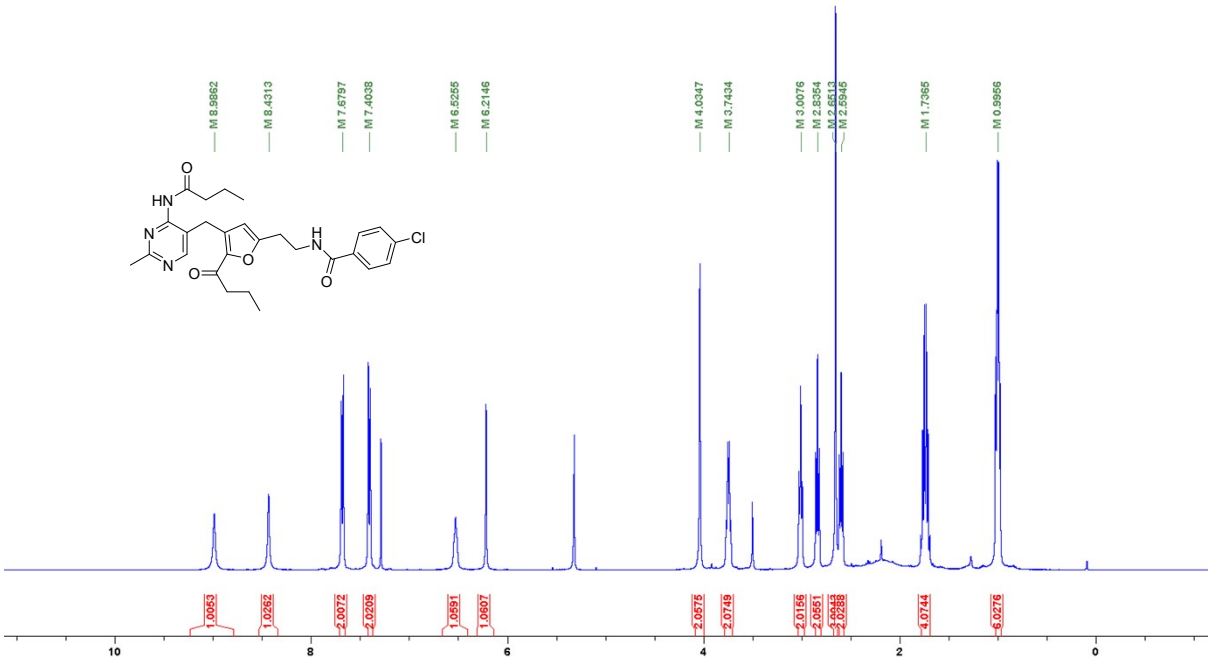
^{1}H NMR of **36** in $CDCl_3$:



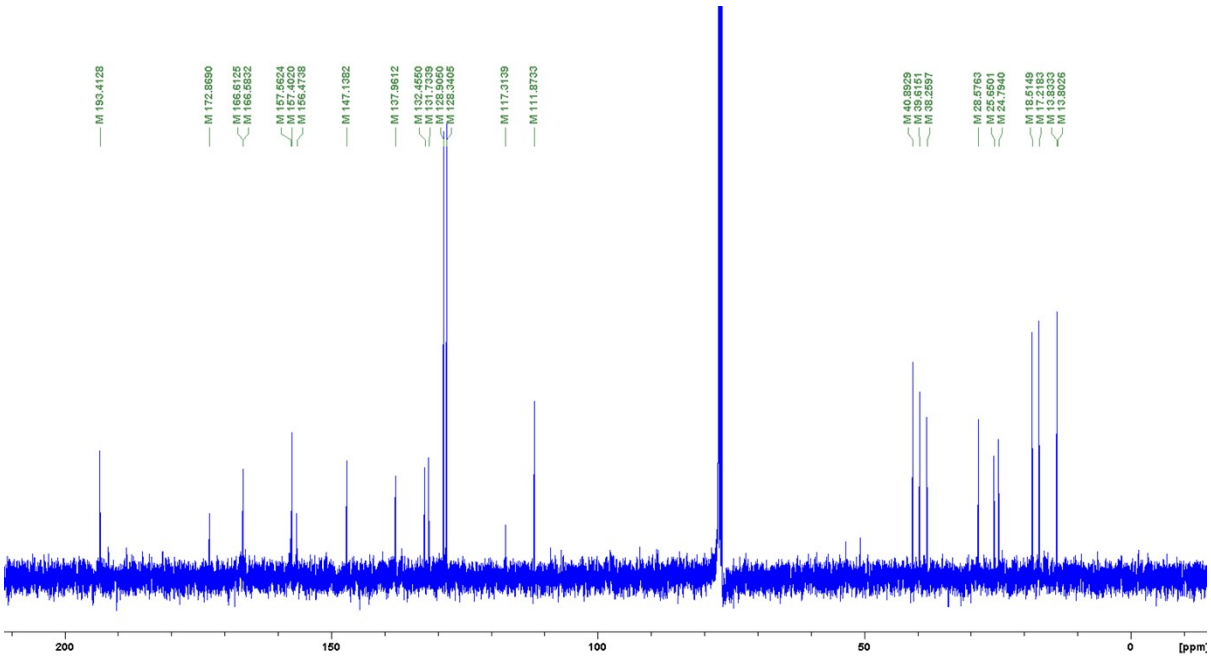
^{13}C NMR of **36** in $CDCl_3$:



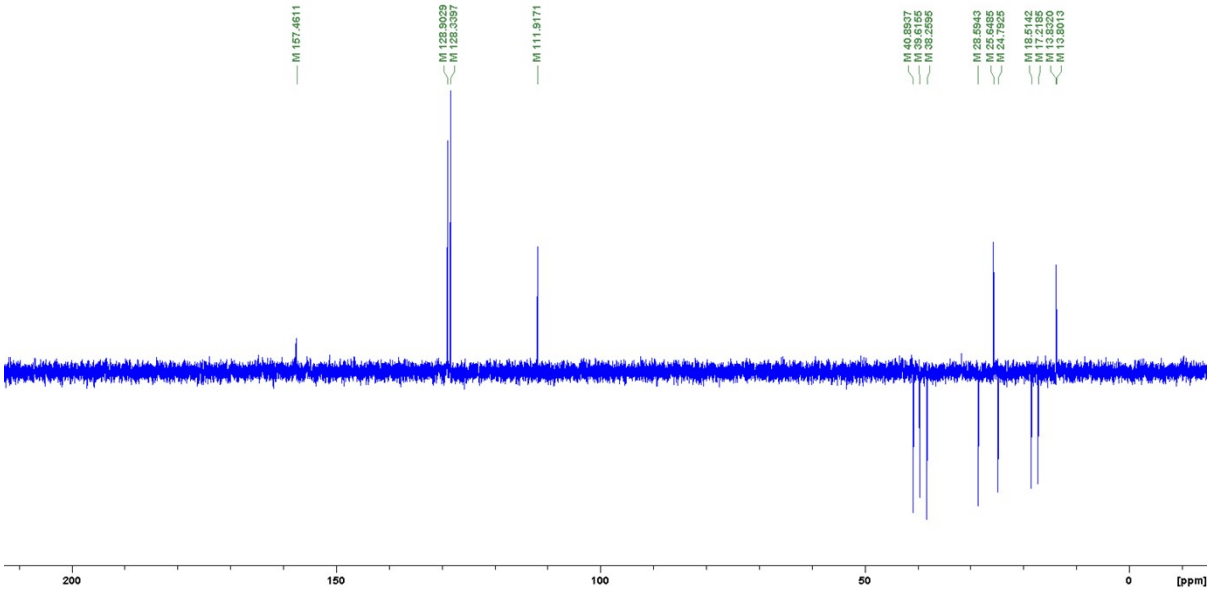
^{1}H NMR of di-acylated side-product in $CDCl_3$:



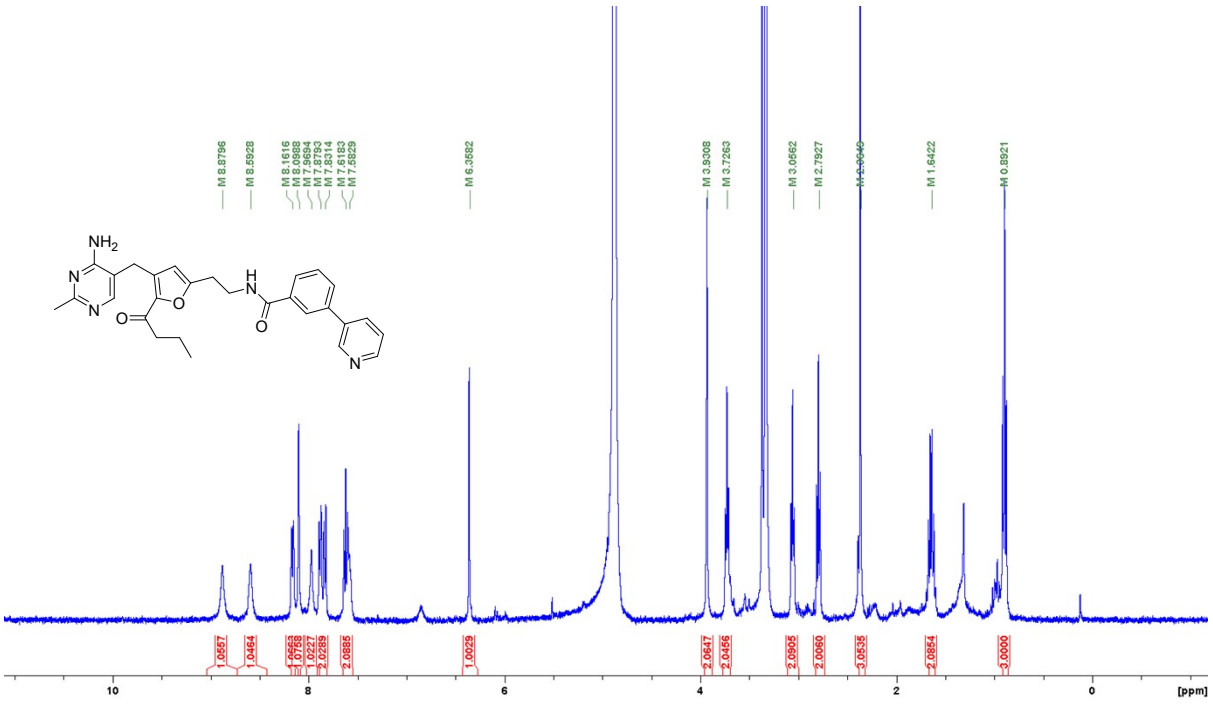
^{13}C NMR of di-acylated side-product in $CDCl_3$:



^{13}C DEPT-135 NMR of di-acylated side-product in $CDCl_3$:



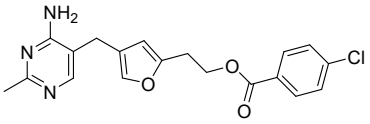
^{1}H NMR of **37** in CD_3OD:



HRMS spectra

Compound **22**:

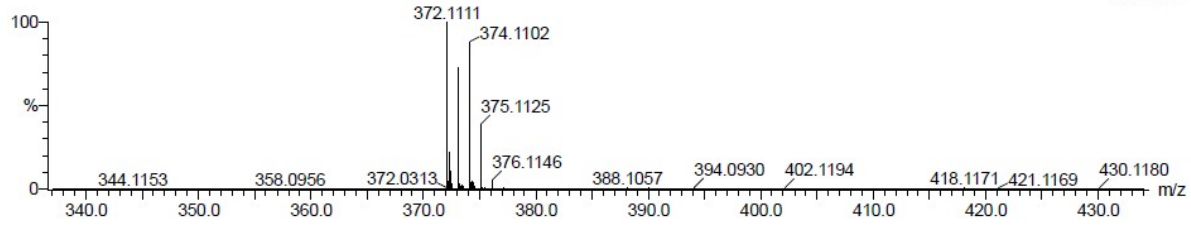
Elemental Composition Report



Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
27 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-19 H: 0-19 N: 0-3 O: 0-3 Cl: 0-1

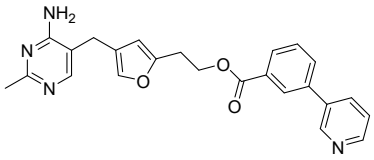
1238 (2.671) Cm (1205:1339) 1: TOF MS ES+ 2.49e+008



Minimum:				-1.5				
Maximum:		5.0	100.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
372.1111	372.1115	-0.4	-1.1	11.5	1975.5	n/a	n/a	C19 H19 N3 O3 Cl

Compound **23**:

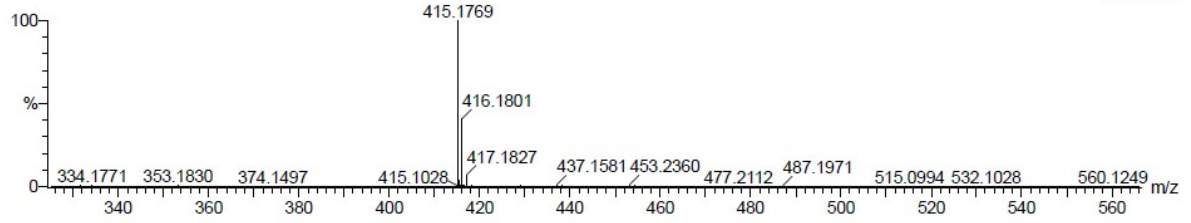
Elemental Composition Report



Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

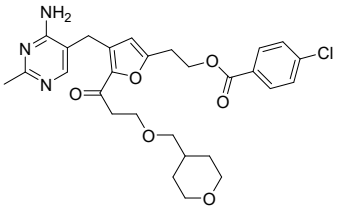
Monoisotopic Mass, Even Electron Ions
15 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-24 H: 0-23 N: 0-4 O: 0-3

885 (1.920) Cm (854:993) 1: TOF MS ES+ 9.90e+007



Minimum:				-1.5				
Maximum:		5.0	100.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
415.1769	415.1770	-0.1	-0.2	15.5	1646.9	n/a	n/a	C24 H23 N4 O3

Compound **24i**:

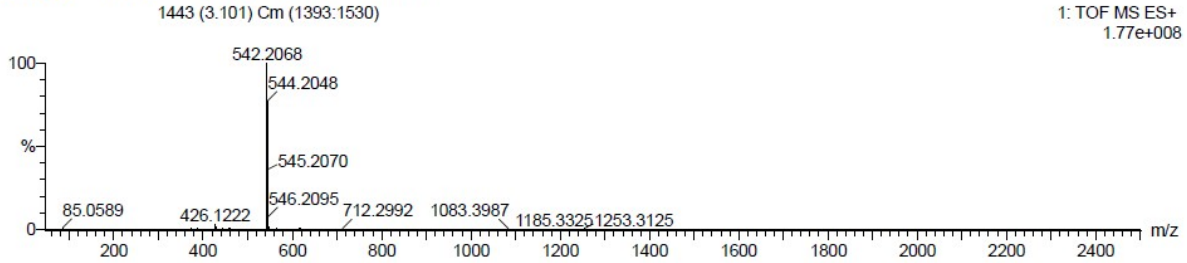


Elemental Composition Report

Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

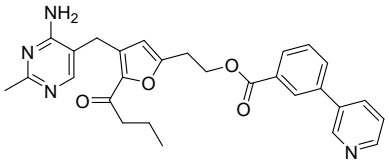
Monoisotopic Mass, Odd and Even Electron Ions
50 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-28 H: 0-33 N: 0-3 O: 0-6 Cl: 0-1

1443 (3.101) Cm (1393:1530)



Minimum:				-1.5				
Maximum:		5.0	100.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
542.2068	542.2058	1.0	1.8	13.5	1417.9	n/a	n/a	C28 H33 N3 O6 Cl

Compound **25**:

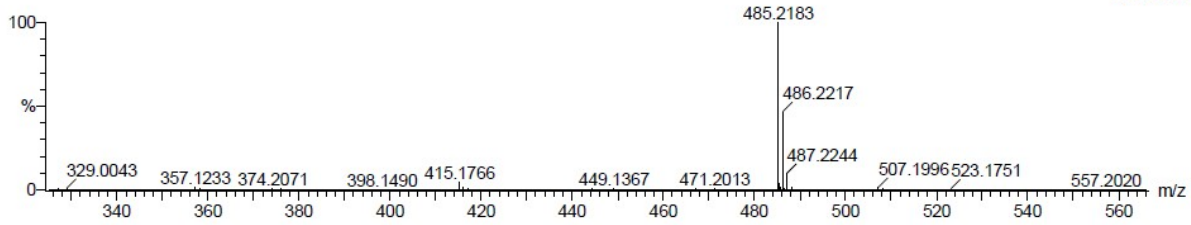


Elemental Composition Report

Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
20 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-28 H: 0-29 N: 0-4 O: 0-4

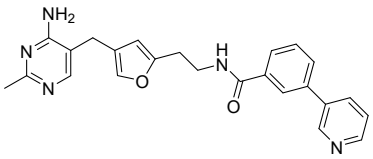
1167 (2.516) Cm (1133:1309)



Minimum:				-1.5				
Maximum:		5.0	100.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
485.2183	485.2189	-0.6	-1.2	16.5	1538.2	n/a	n/a	C28 H29 N4 O4

Compound **33**:

Elemental Composition Report

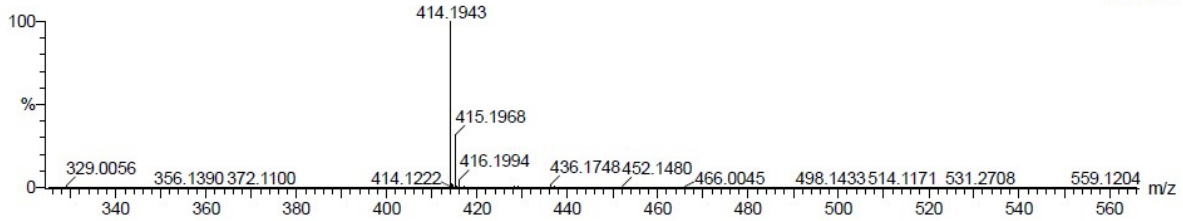


Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
13 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-24 H: 0-24 N: 0-5 O: 0-2

519 (1.144) Cm (482:602)

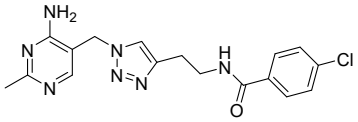
1: TOF MS ES+
7.05e+007



Minimum:				-1.5				
Maximum:		5.0	100.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
414.1943	414.1930	1.3	3.1	15.5	1468.9	n/a	n/a	C24 H24 N5 O2

Compound **34**:

Elemental Composition Report

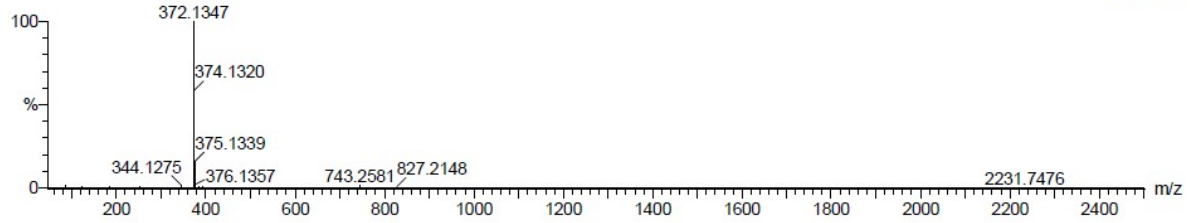


Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
28 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-17 H: 0-19 N: 0-7 O: 0-1 Cl: 0-1

724 (1.574) Cm (690:827)

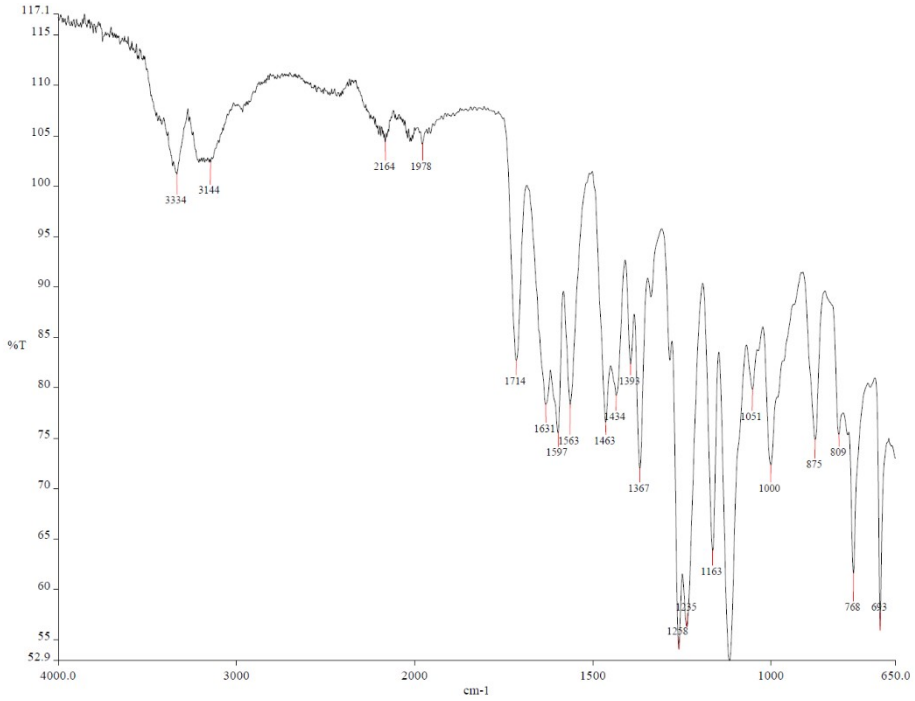
1: TOF MS ES+
1.22e+008



Minimum:				-1.5				
Maximum:		5.0	100.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
372.1347	372.1340	0.7	1.9	11.5	1873.1	n/a	n/a	C17 H19 N7 O Cl

IR Spectra

8k



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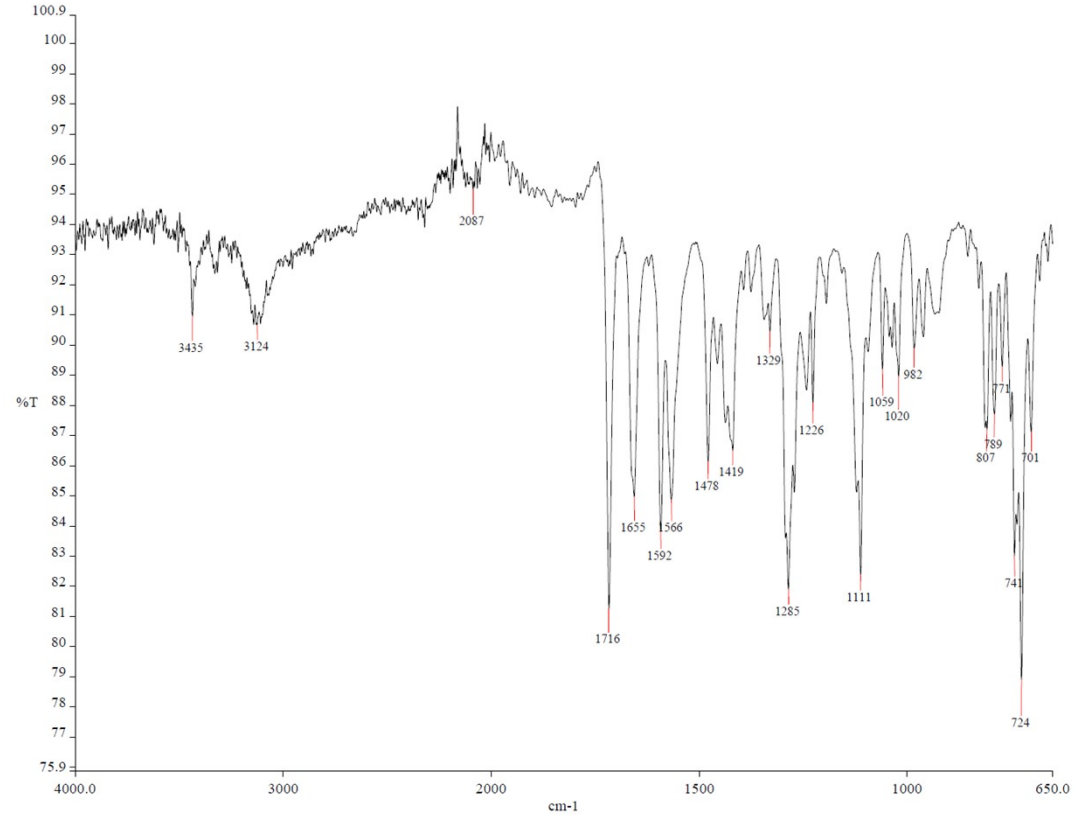

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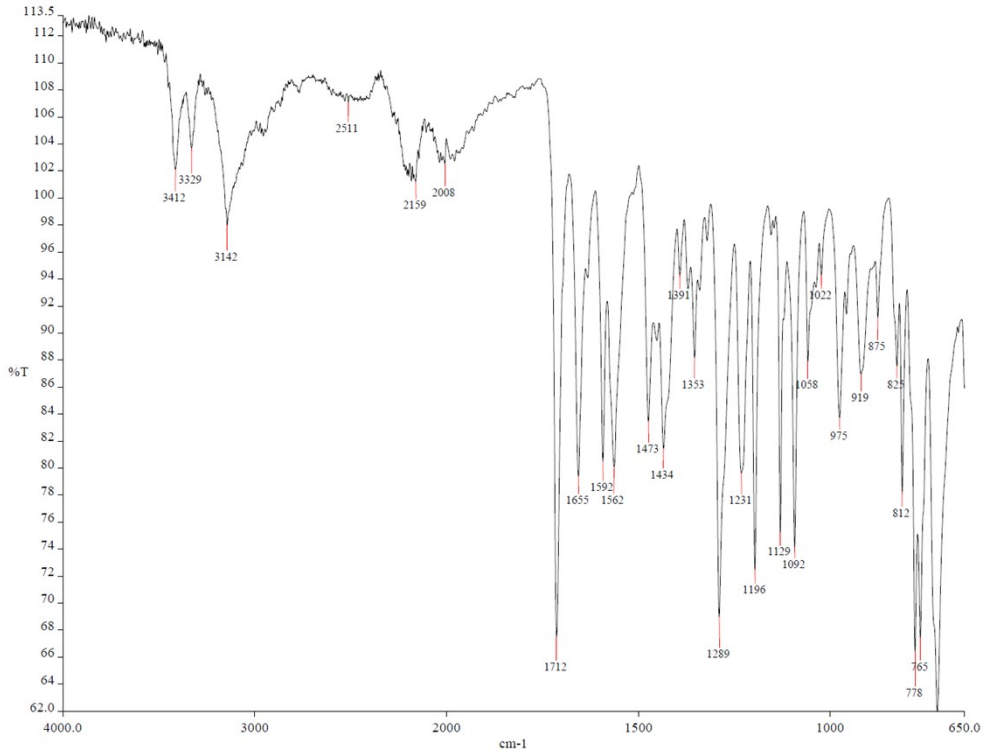
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812
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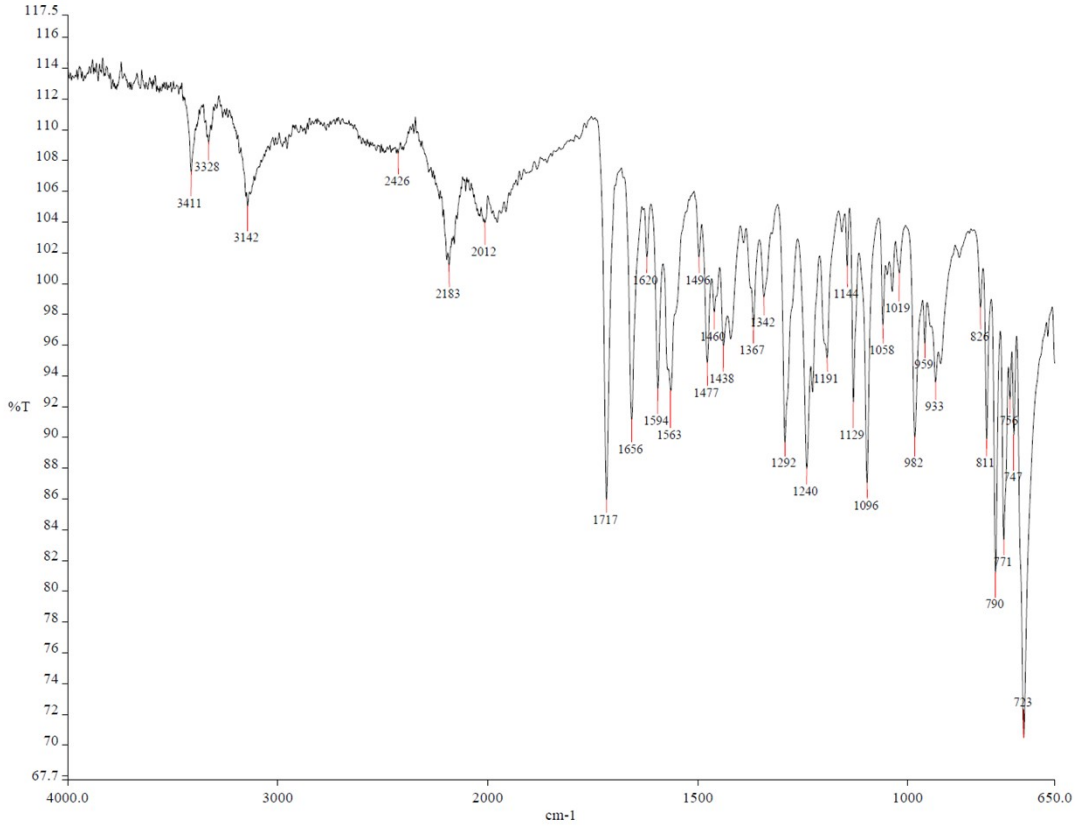
765

8t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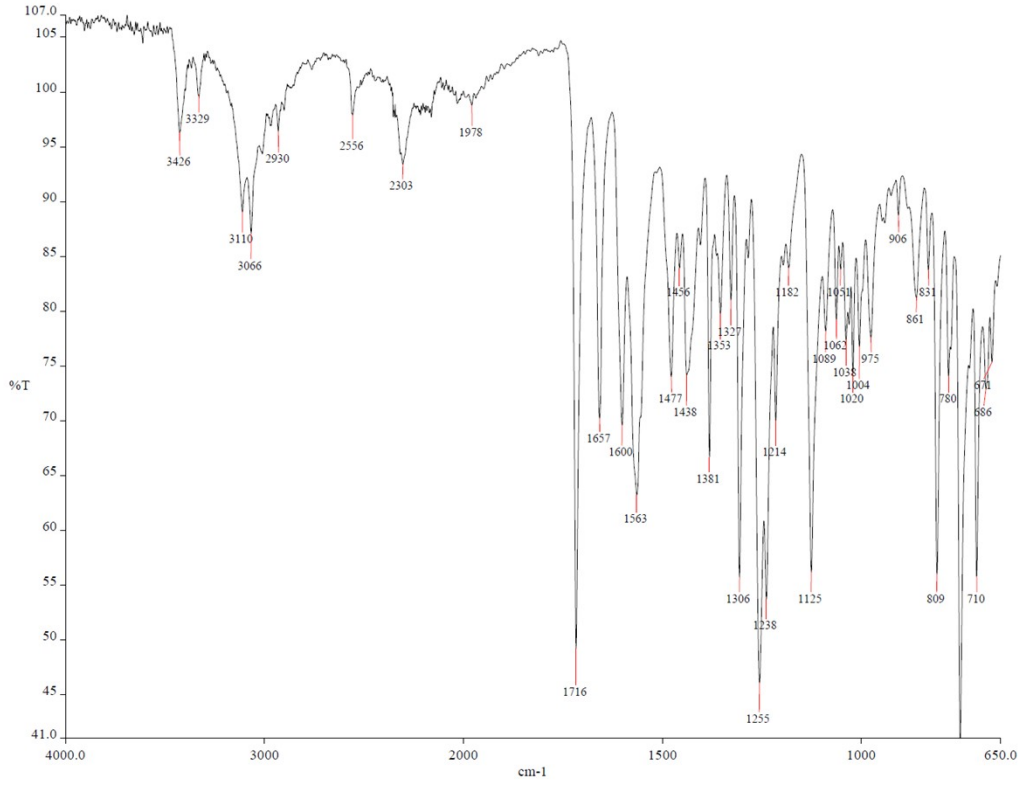
8w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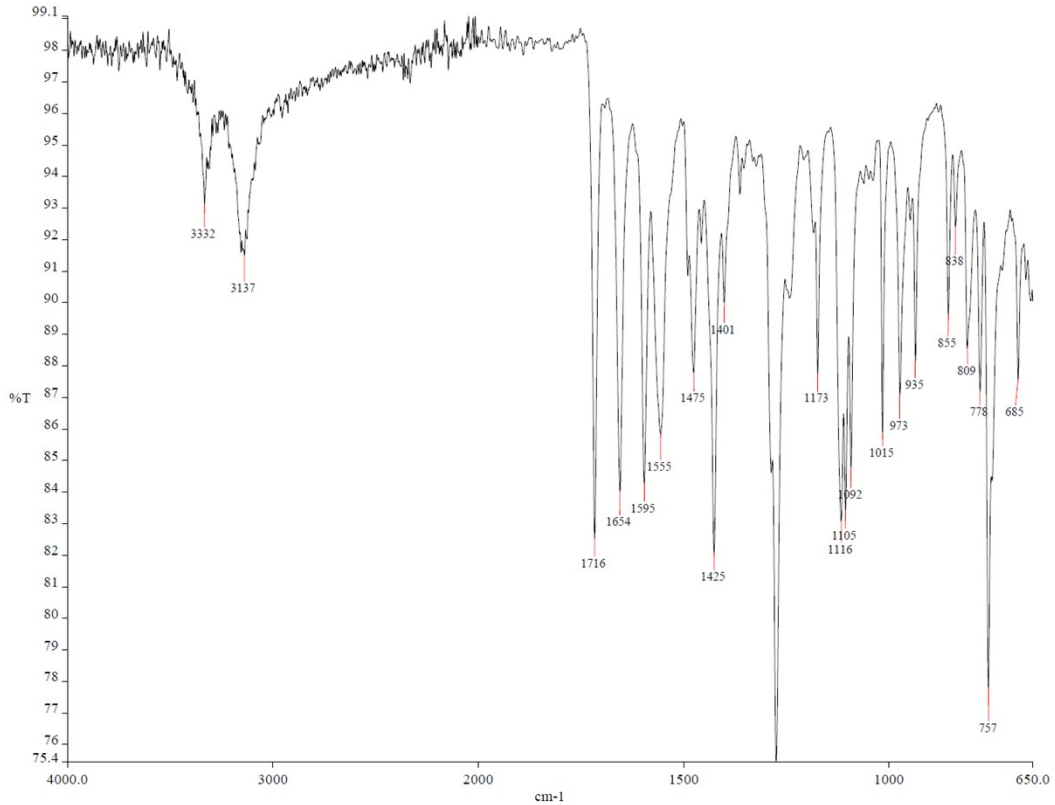
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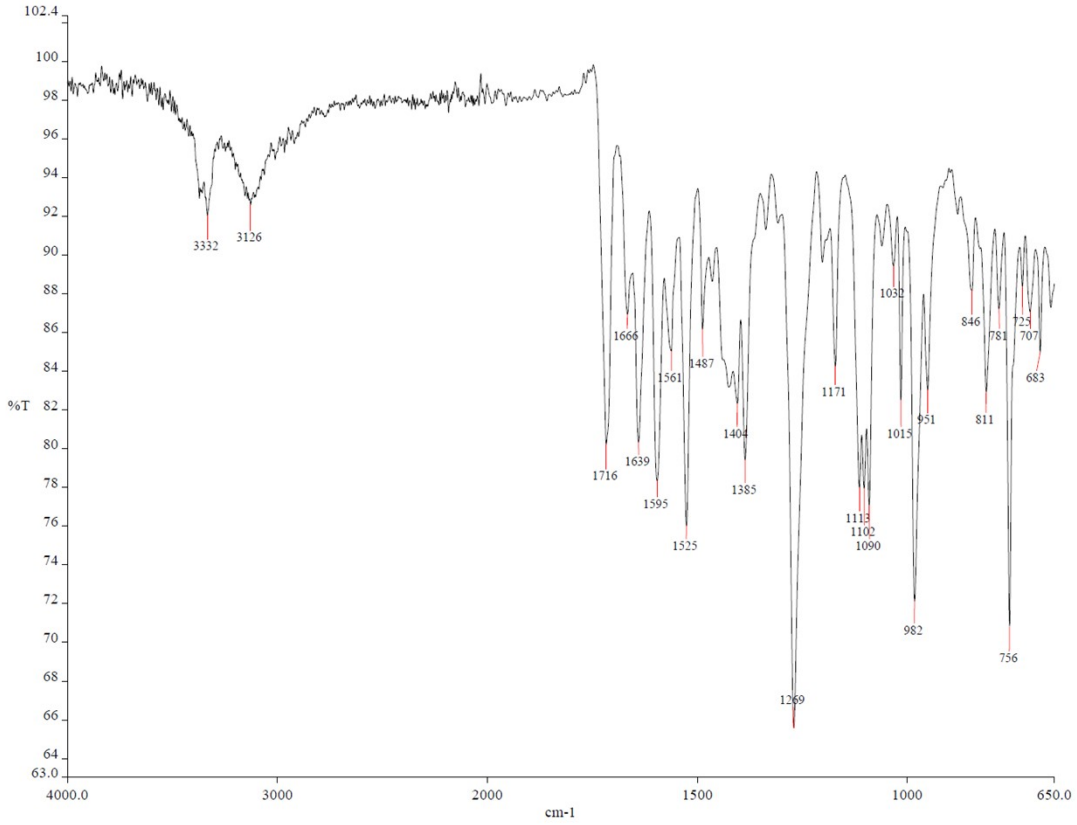
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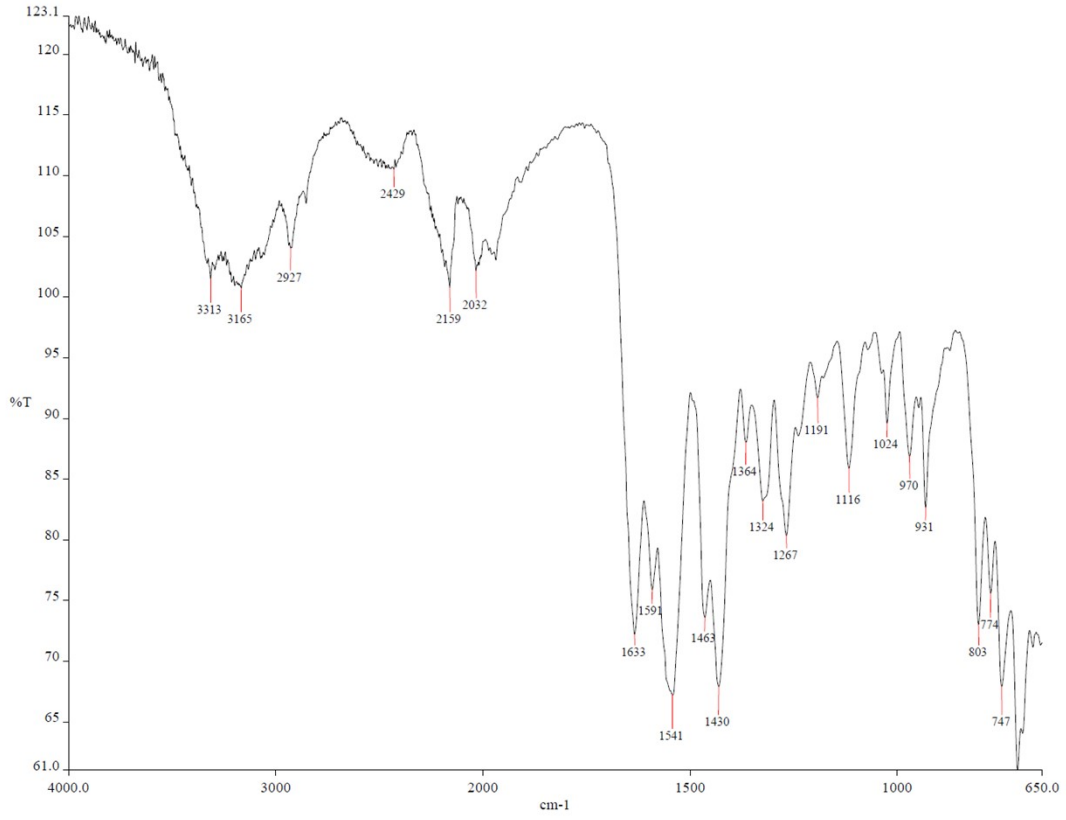
33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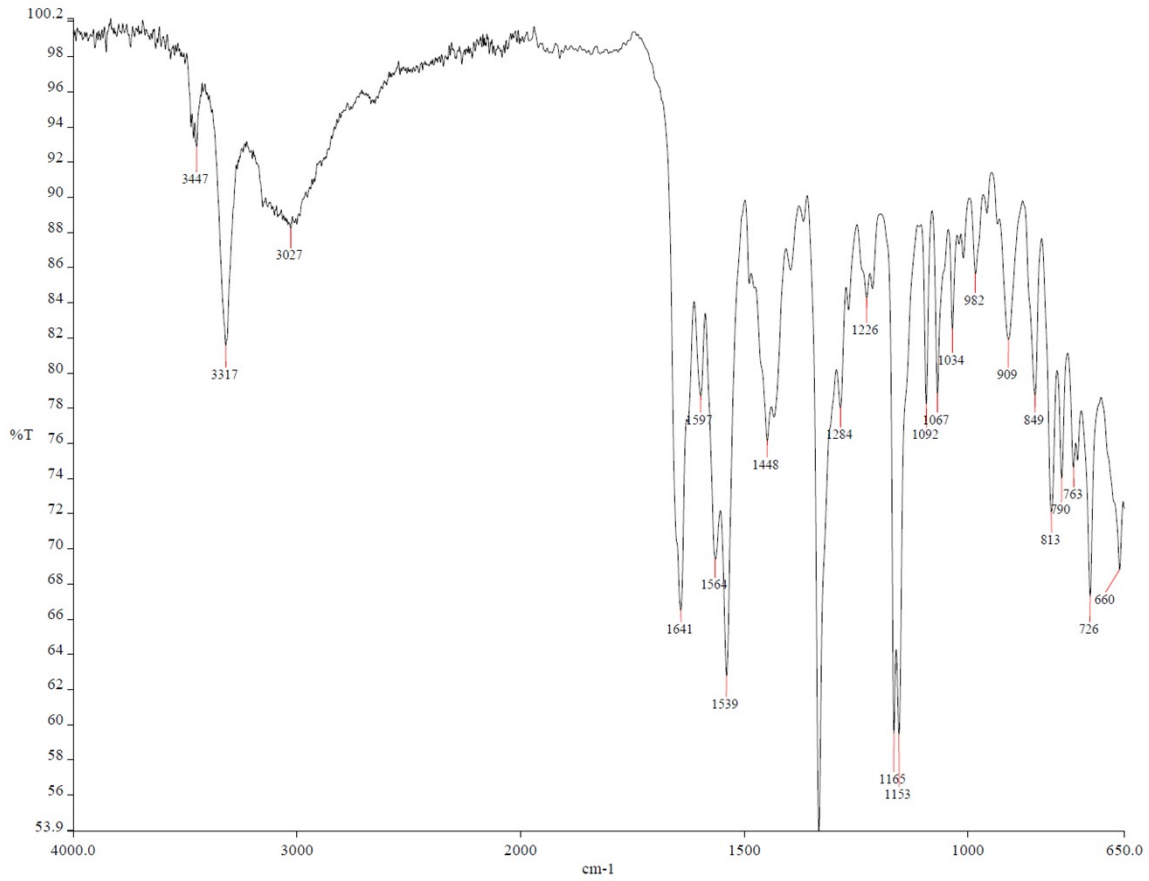
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660

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