

Structure-activity relationship studies of pyrimidine-4-carboxamides as inhibitors of *N*-acylphosphatidylethanolamine phospholipase D (NAPE-PLD)

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¹H and ¹³C NMR spectra for compounds 1-107

HPLC-traces for 1 (LEI-401) and 2

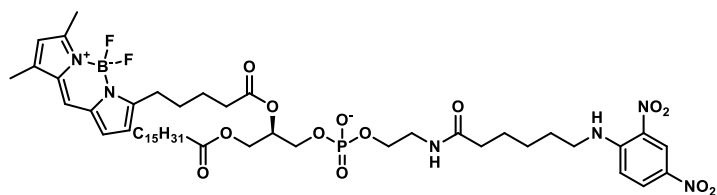


Figure S1. Structure of fluorescence-quenched substrate PED6.

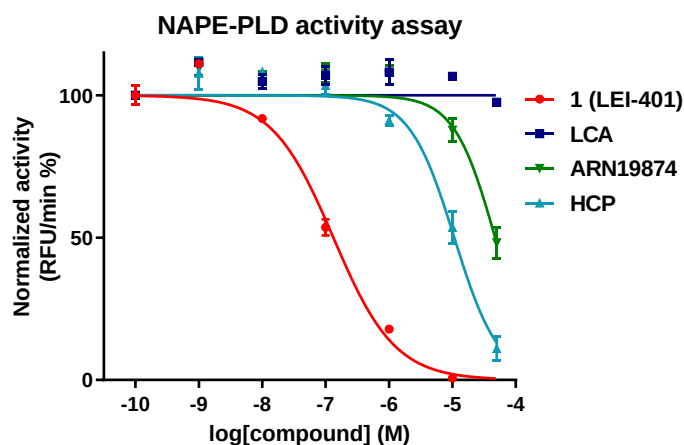


Figure S2. NAPE-PLD PED6 activity assay dose-response curves for **1 (LEI-401)** and reference inhibitors lithocholic acid (LCA), ARN19874 and hexachlorophene (HCP). Data represent mean values $\pm$ SEM ($N = 2$, $n = 2$).

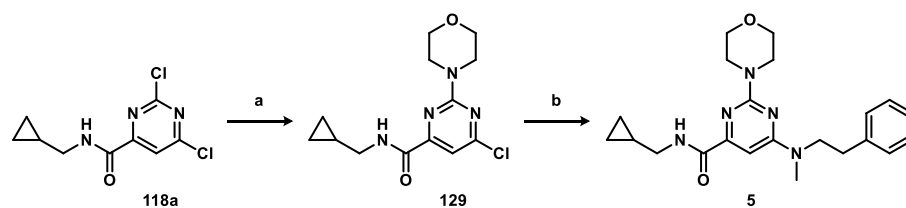
Table S1. NAPE-PLD inhibitory activities of **1 (LEI-401)** and reference inhibitors.

ID	PED6 assay					Reported IC_{50} (μM)
	$pIC_{50} \pm SEM$	IC_{50} (μM)	K_i (μM)	cLogP ^a	LipE ^b	
1 (LEI-401)	7.14 ± 0.04	0.072	0.027	3.46	3.68	-
Lithocholic acid	< 4.3	-	-	6.60	-	68 ¹
Hexachlorophene	4.94 ± 0.07	11	4.27	7.03	-2.09	1.6 ²
ARN19874	4.27 ± 0.07	54	20.1	2.13	2.08	34 ³

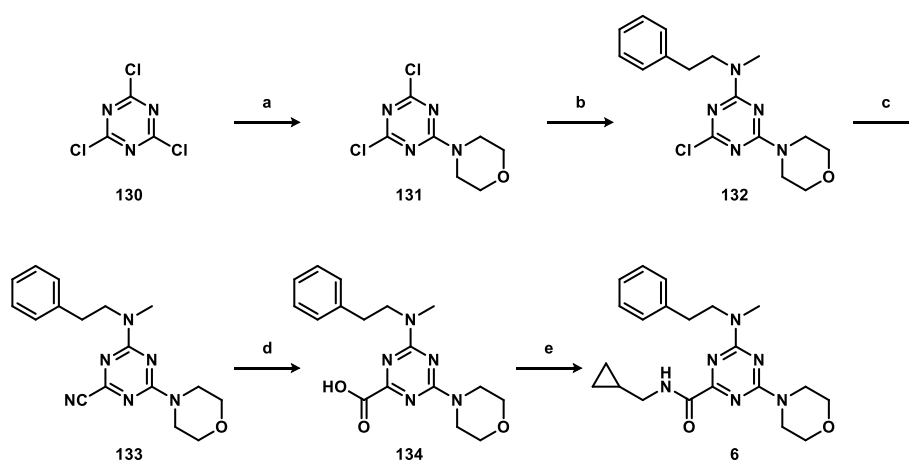
^a cLogP was calculated using Chemdraw 15; ^b Lipophilic efficiency (LipE) = $pIC_{50} - cLogP$.

References

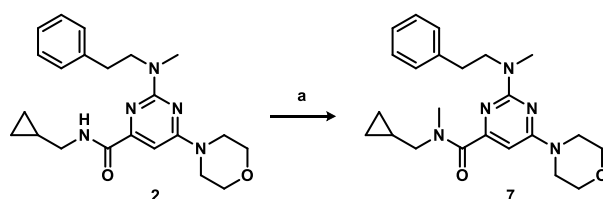
- (1) Margheritis, E.; Castellani, B.; Magotti, P.; Peruzzi, S.; Romeo, E.; Natali, F.; Mostarda, S.; Gioiello, A.; Piomelli, D.; Garau, G. Bile acid recognition by NAPE-PLD. *ACS Chem. Biol.* **2016**, 11, 2908-2914.
- (2) Aggarwal, G.; Zarrow, J. E.; Mashhadi, Z.; Flynn, C. R.; Vinson, P.; Weaver, C. D.; Davies, S. S. Symmetrically substituted dichlorophenes inhibit *N*-acyl-phosphatidylethanolamine phospholipase D. *J. Biol. Chem.* **2020**, 295, 7289-7300.
- (3) Castellani, B.; Diamanti, E.; Pizzirani, D.; Tardia, P.; Maccesi, M.; Realini, N.; Magotti, P.; Garau, G.; Bakkum, T.; Rivara, S.; Mor, M.; Piomelli, D. Synthesis and characterization of the first inhibitor of *N*-acylphosphatidylethanolamine phospholipase D (NAPE-PLD). *ChemComm* **2017**, 53, 12814-12817.



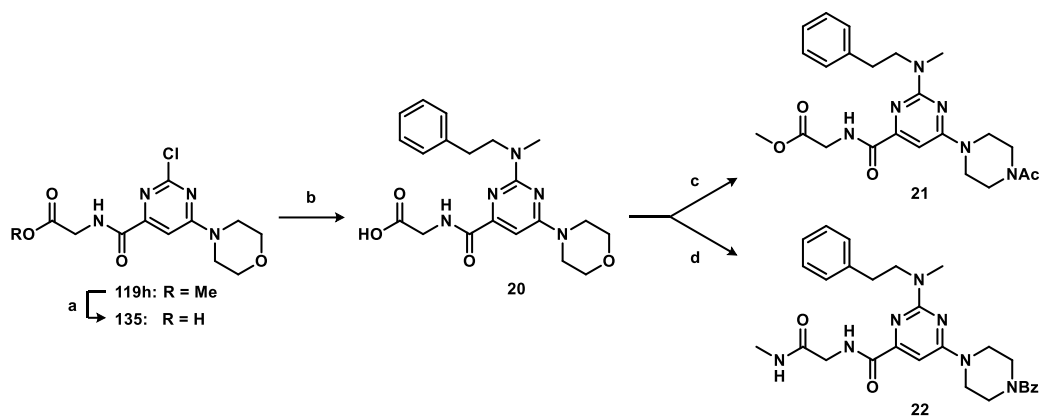
Scheme S1. Synthesis of pyrimidine regioisomer **5**. Reagents and conditions: a) morpholine, DiPEA, MeOH, 0 °C, 5% (+ 89% regioisomer **29**); b) *N*-methylphenethylamine, DiPEA, MeOH, 70 °C, 71%.



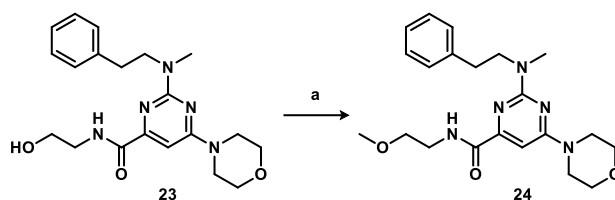
Scheme S2: Synthesis of triazine **6**. Reagents and conditions: a) morpholine, DiPEA, DCM, rt, 72%; b) *N*-methylphenethylamine, K_2CO_3 , acetone, rt, 68%; c) KCN, DABCO, DMF, rt, 53%; d) NaOH, H_2O , THF, 60 °C, 85%; e) cyclopropylmethanamine, PyBOP, DiPEA, DMF, rt, 67%.



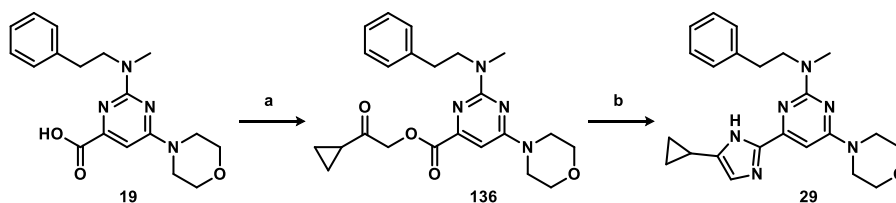
Scheme S3. Synthesis of R_1 cyclopropylmethanamine analogue **7**. Reagents and conditions: a) NaH, MeI, DMF, 0 °C to rt, 48%.



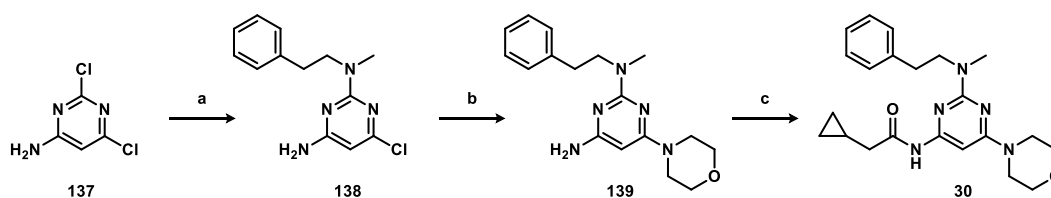
Scheme S4. Synthesis of R₁ cyclopropylmethylamine analogues **20-22**. Reagents and conditions: a) NaOH, THF, MeOH, H₂O, rt, 99%; b) *N*-methylphenethylamine, DiPEA, *n*-BuOH, 120 °C, 20%; c) EDC·HCl, HOBT, MeOH, DCM, rt, 62%; d) MeNH₂·HCl, PyBOP, DiPEA, DMF, 48%.



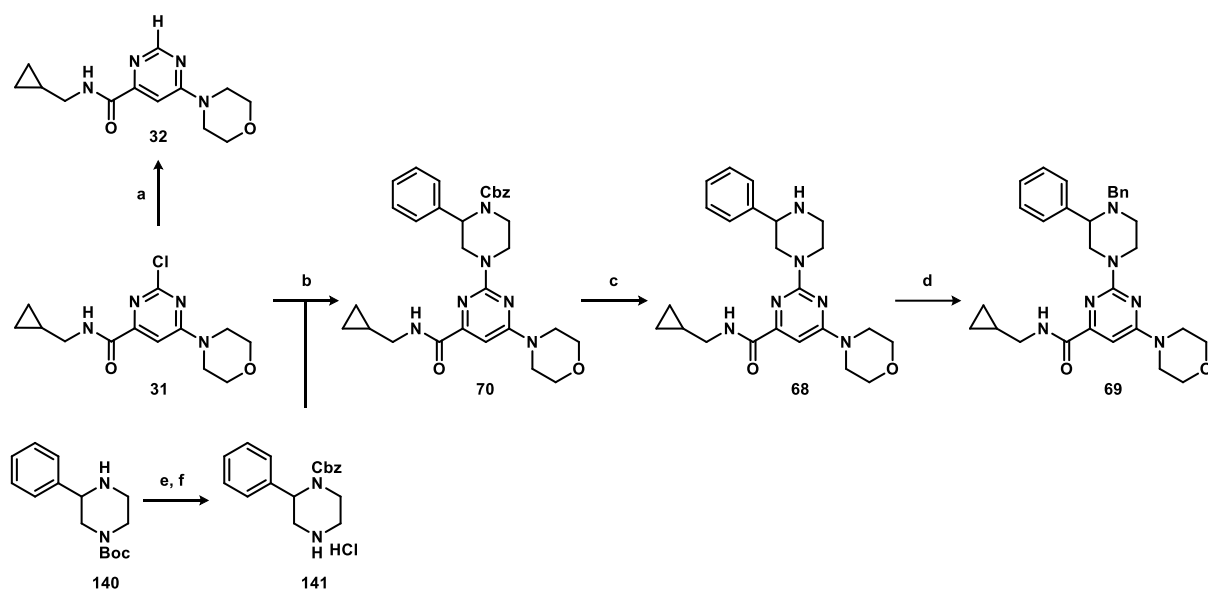
Scheme S5. Synthesis of R₁ cyclopropylmethylamine analogue **24**. Reagents and conditions: a) NaOtBu, MeI, DMF, 0 °C to rt, 28%.



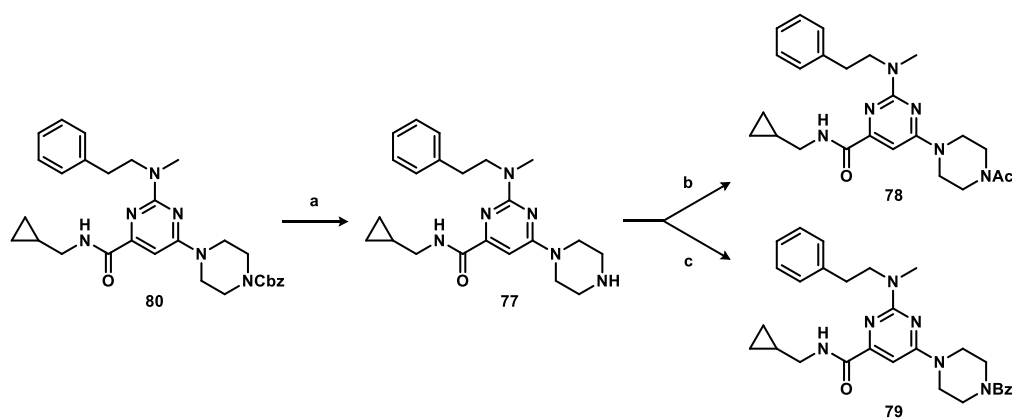
Scheme S6. Synthesis of R₁ cyclopropylmethylamine analogue **29**. Reagents and conditions: a) 2-bromocyclopropylethanone, Cs₂CO₃, DMF, rt, 53%; b) NH₄OAc, xylene, 140 °C, 6%.



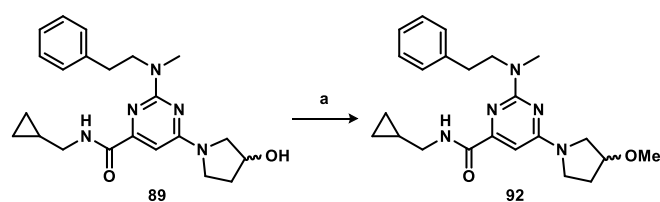
Scheme S7. Synthesis of **30**. Reagents and conditions: a) *N*-methylphenethylamine, DiPEA, 2-PrOH, reflux, 64%; b) morpholine, DiPEA, *n*-BuOH, μ W, 180 °C, 89%; c) *i.* 2-cyclopropylacetic acid, oxalyl chloride, DCM-d₂, rt; *ii.* **139**, DCM, rt, 34%.



Scheme S8. Synthesis of R_2 analog **32** and 3-phenylpiperazine analogues **68-70**. Reagents and conditions: a) Pd/C, H_2 , MeOH, rt, 95%; b) **141**, DiPEA, *n*-BuOH, 120 °C, 99%; c) Pd/C, H_2 , MeOH, rt, 90%; d) BnBr, DiPEA, CH_3CN , rt, 74%; e) CbzCl, $NaHCO_3$, THF, H_2O , 0 °C to rt, 90%; f) 4 M HCl, 1,4-dioxane, rt, quant.



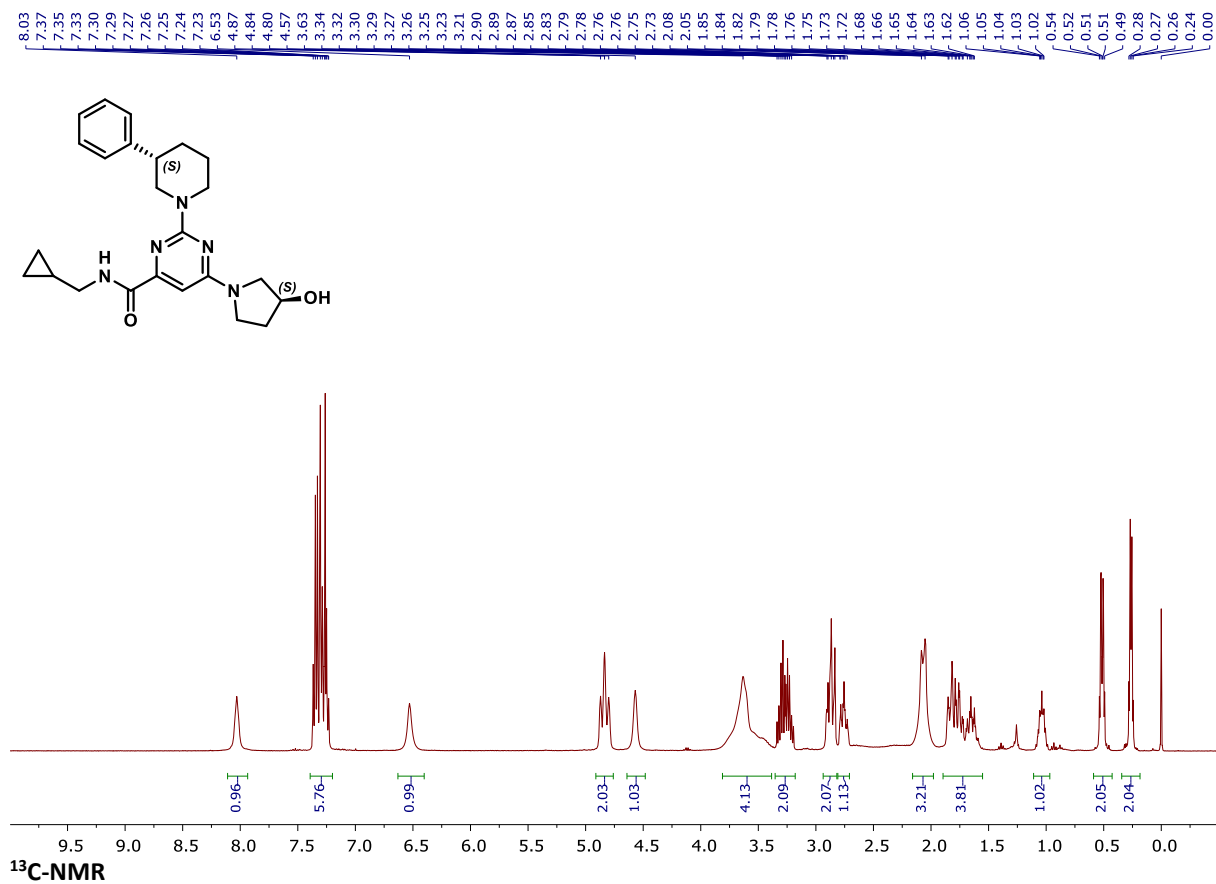
Scheme S9. Synthesis of R_3 morpholine analogues **77-79**. Reagents and conditions: a) Pd/C, H_2 , MeOH, AcOH, rt, 63%; b) Ac_2O , DiPEA, DCM, rt, 78%; c) $BzCl$, Et_3N , DCM, rt, 74%.



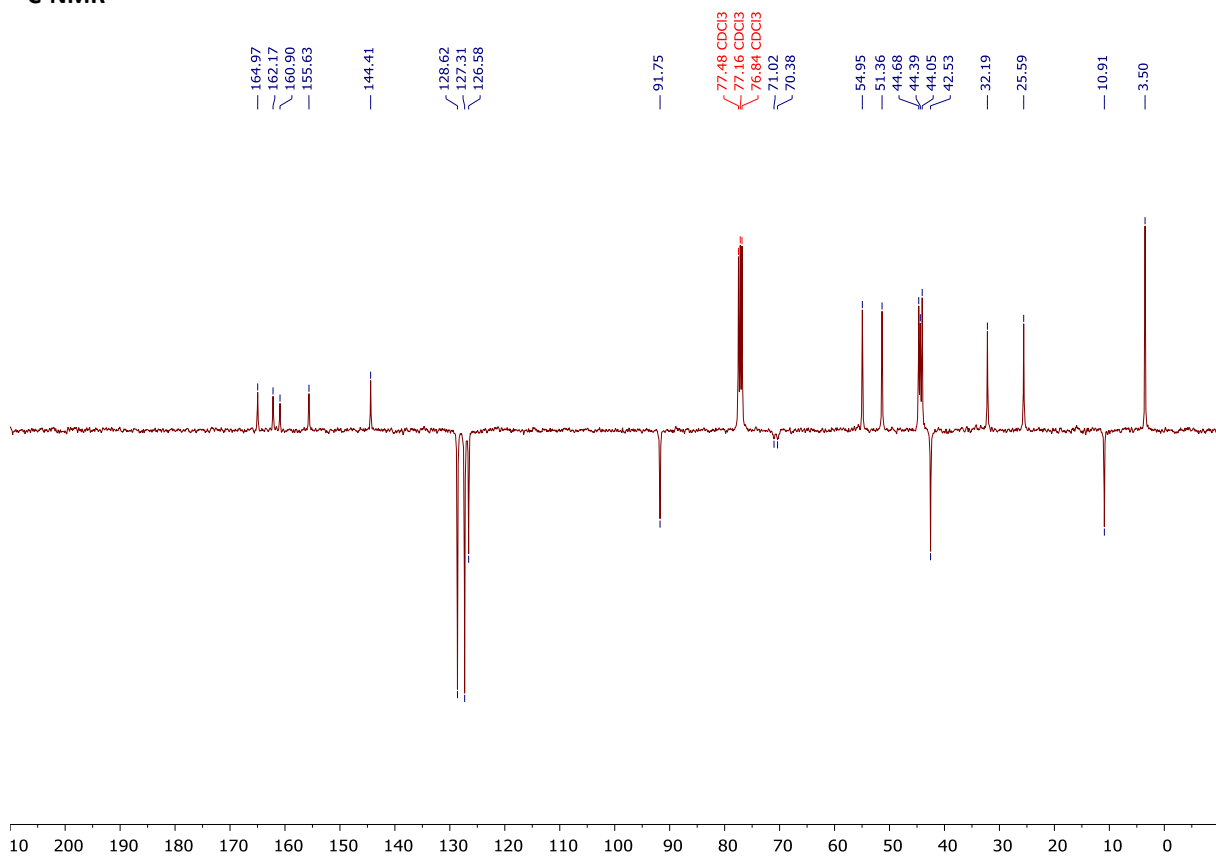
Scheme S10. Synthesis of R_3 morpholine analogue **92**. Reagents and conditions: a) NaH, MeI, DMF, 0 °C to rt, 44%.

NMR Spectra

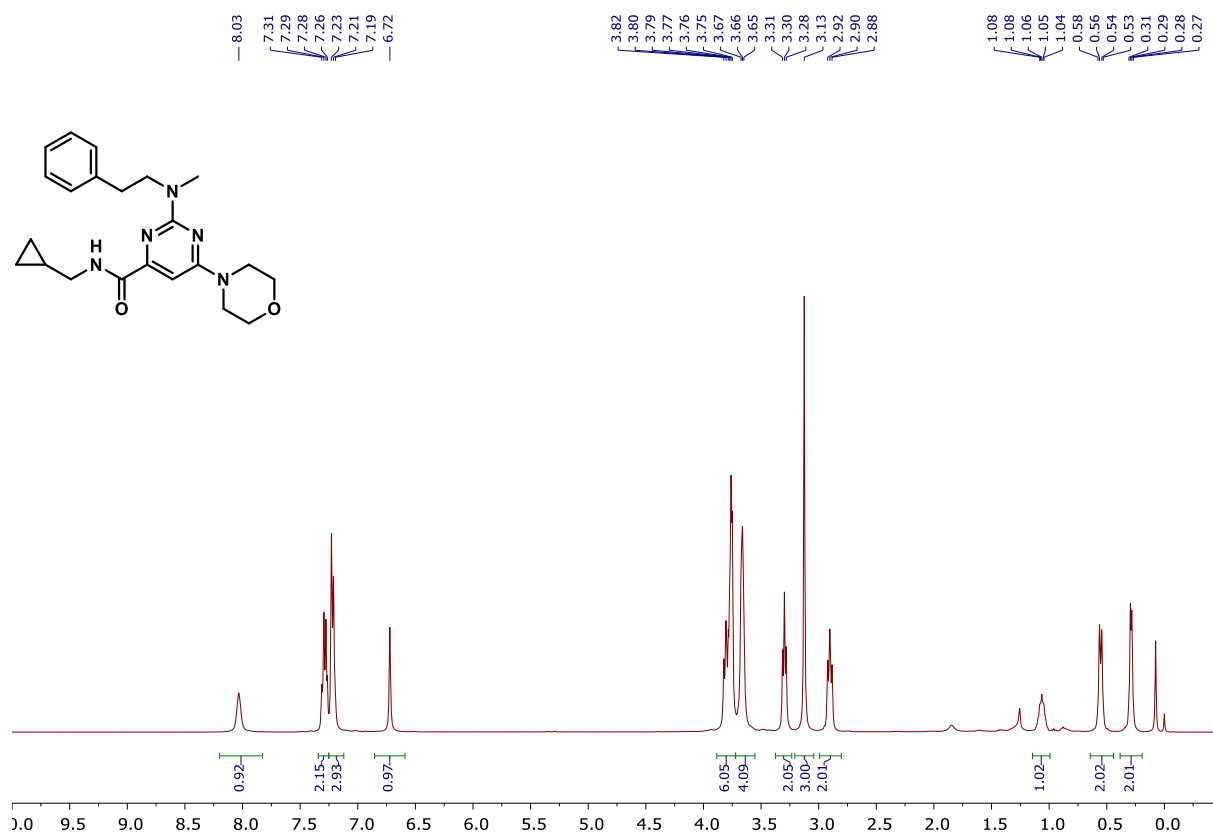
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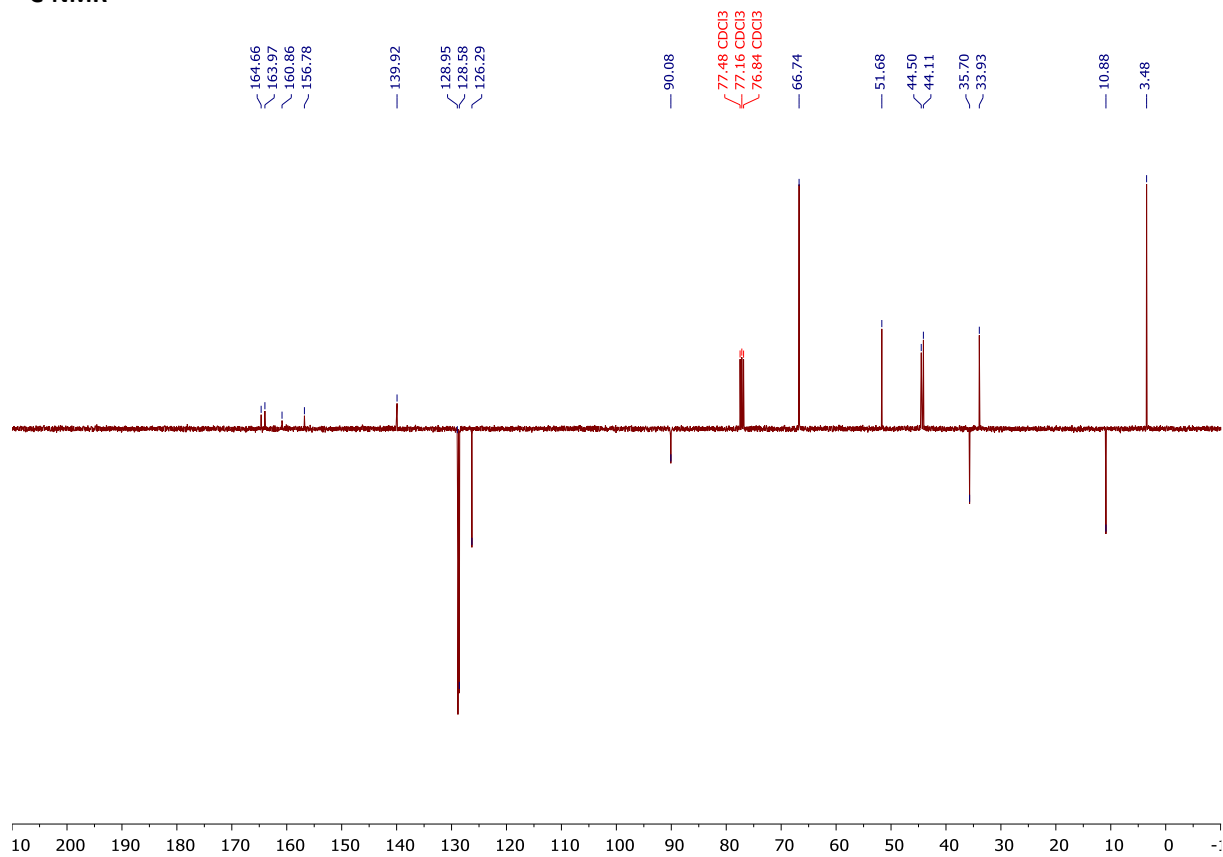
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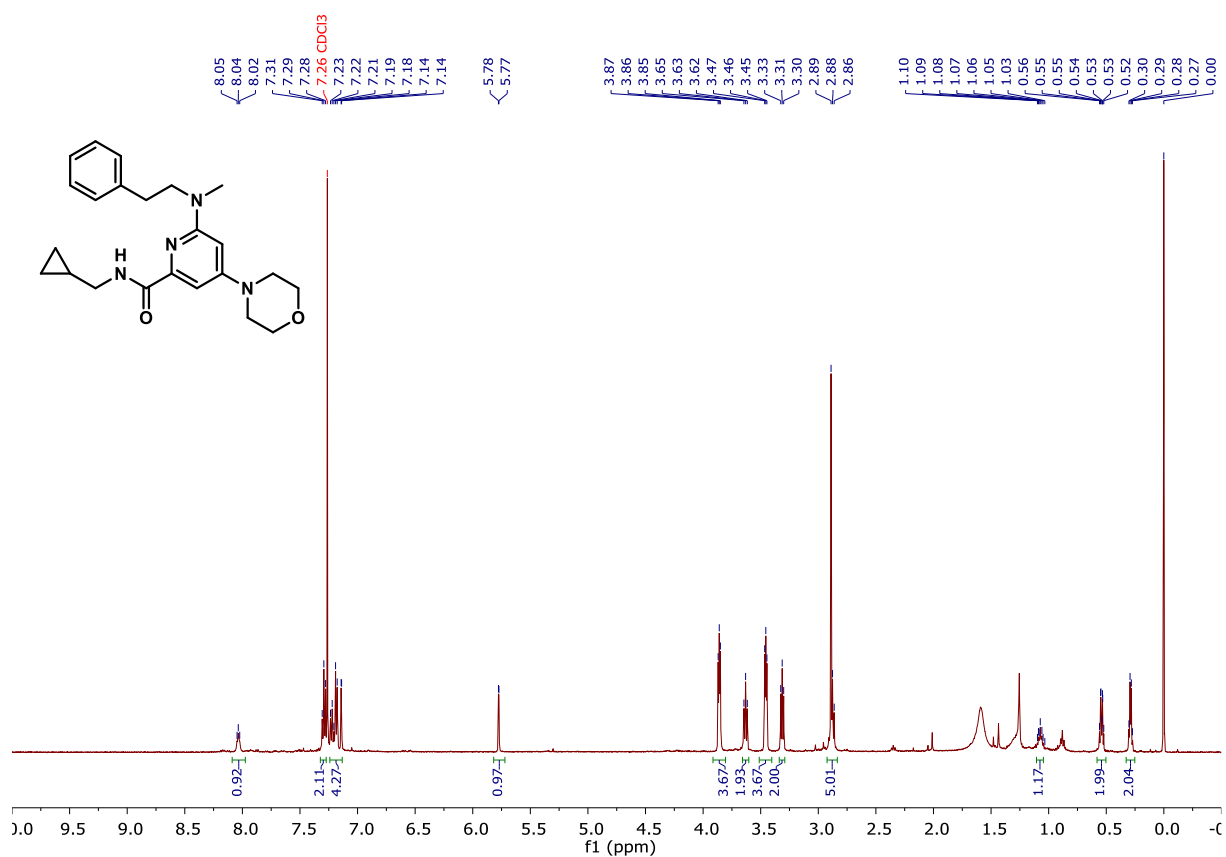
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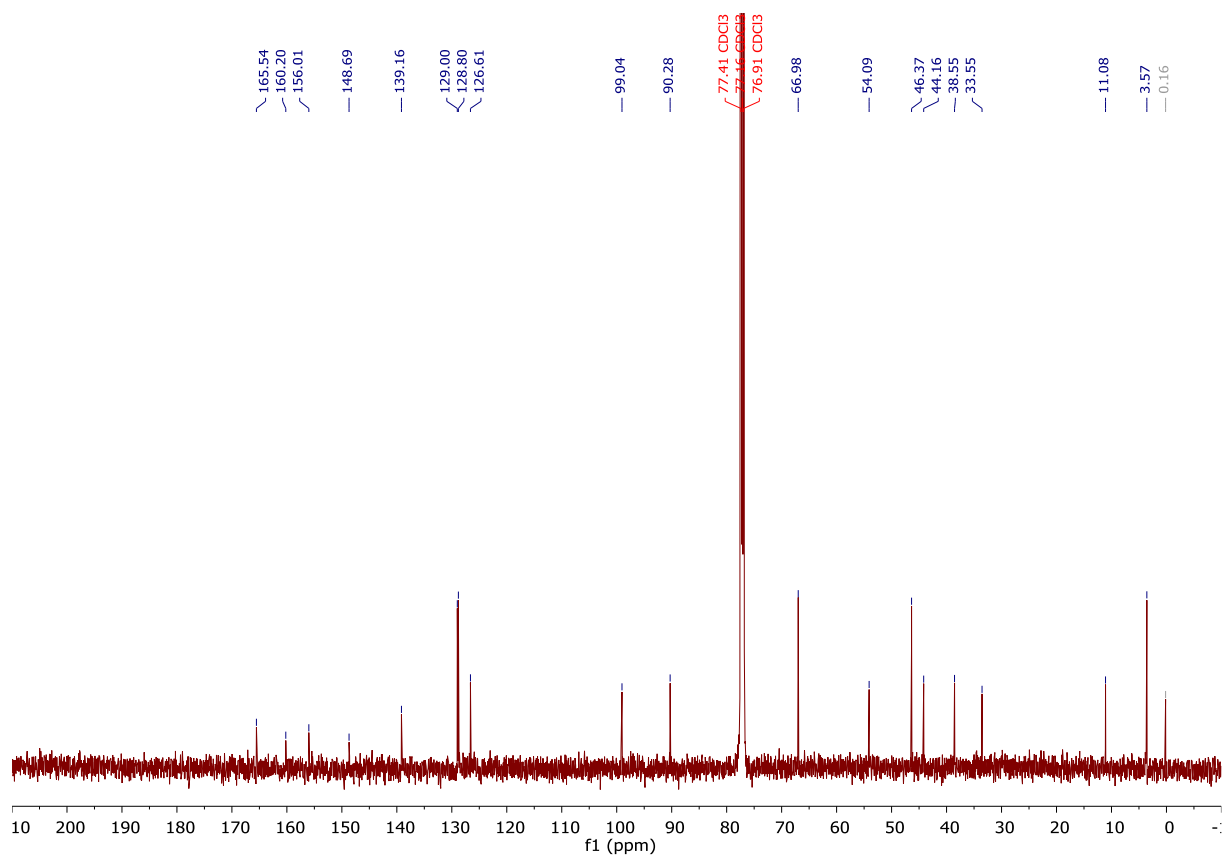
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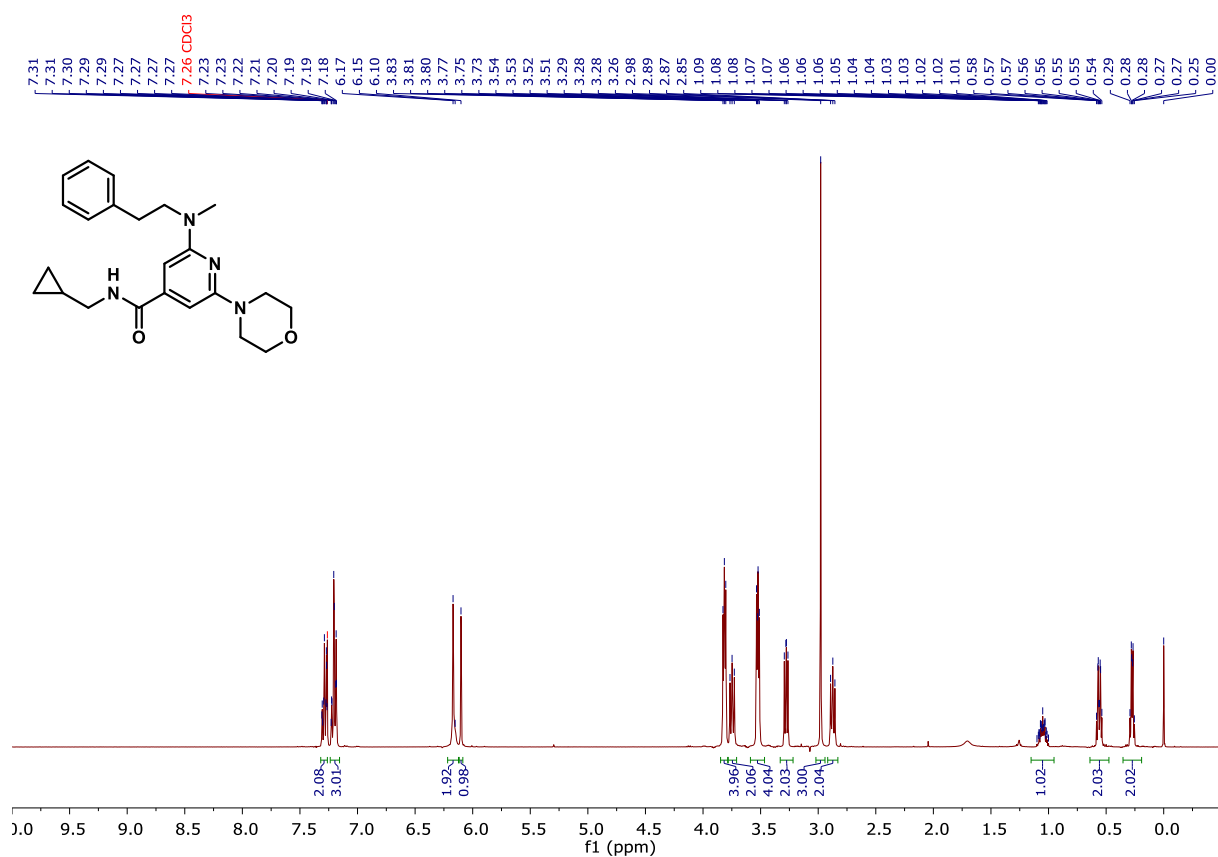
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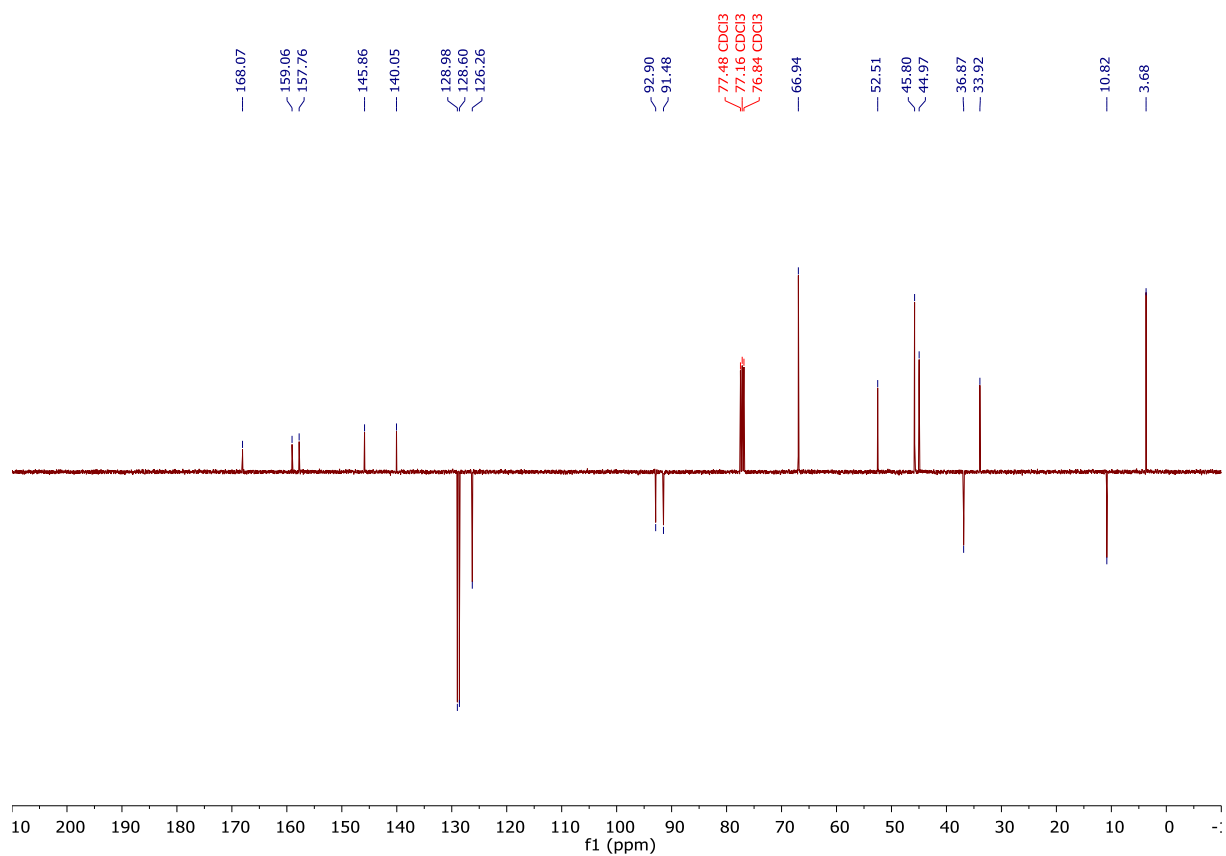
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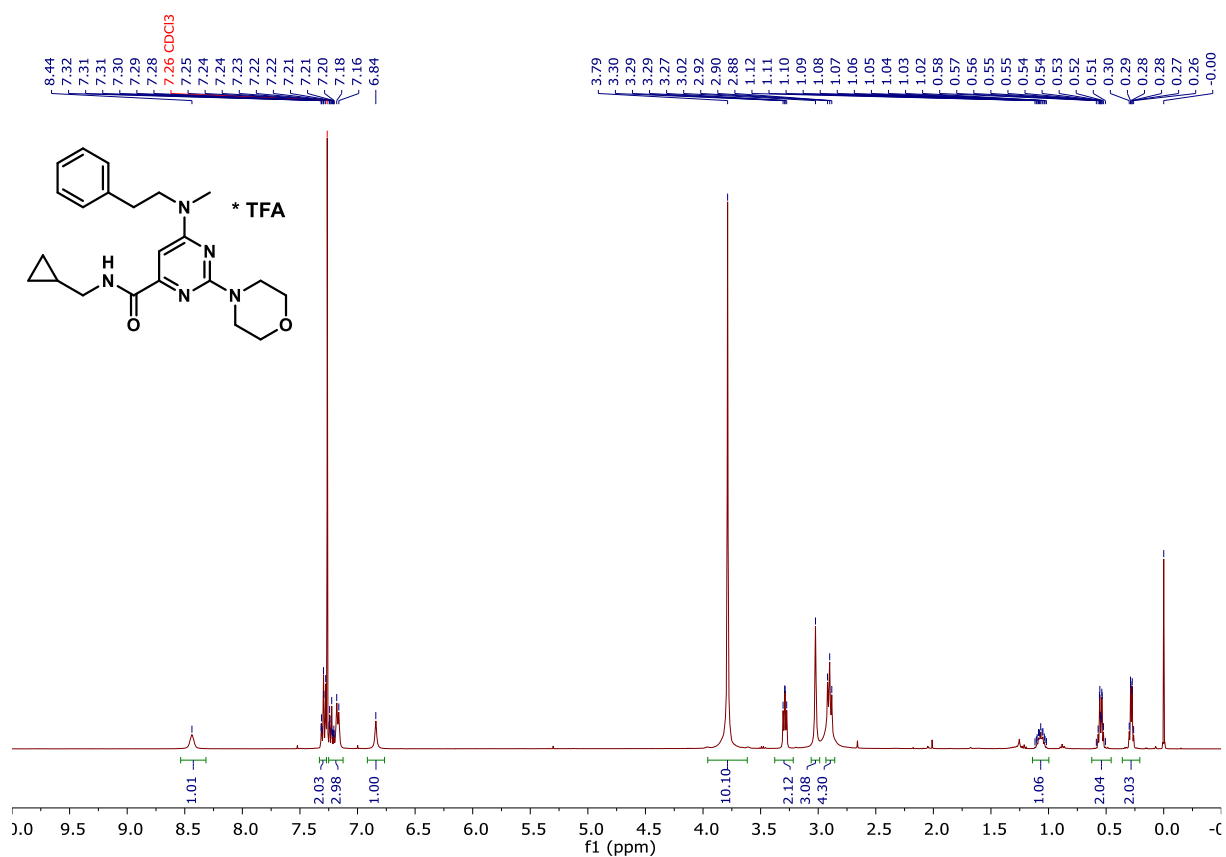
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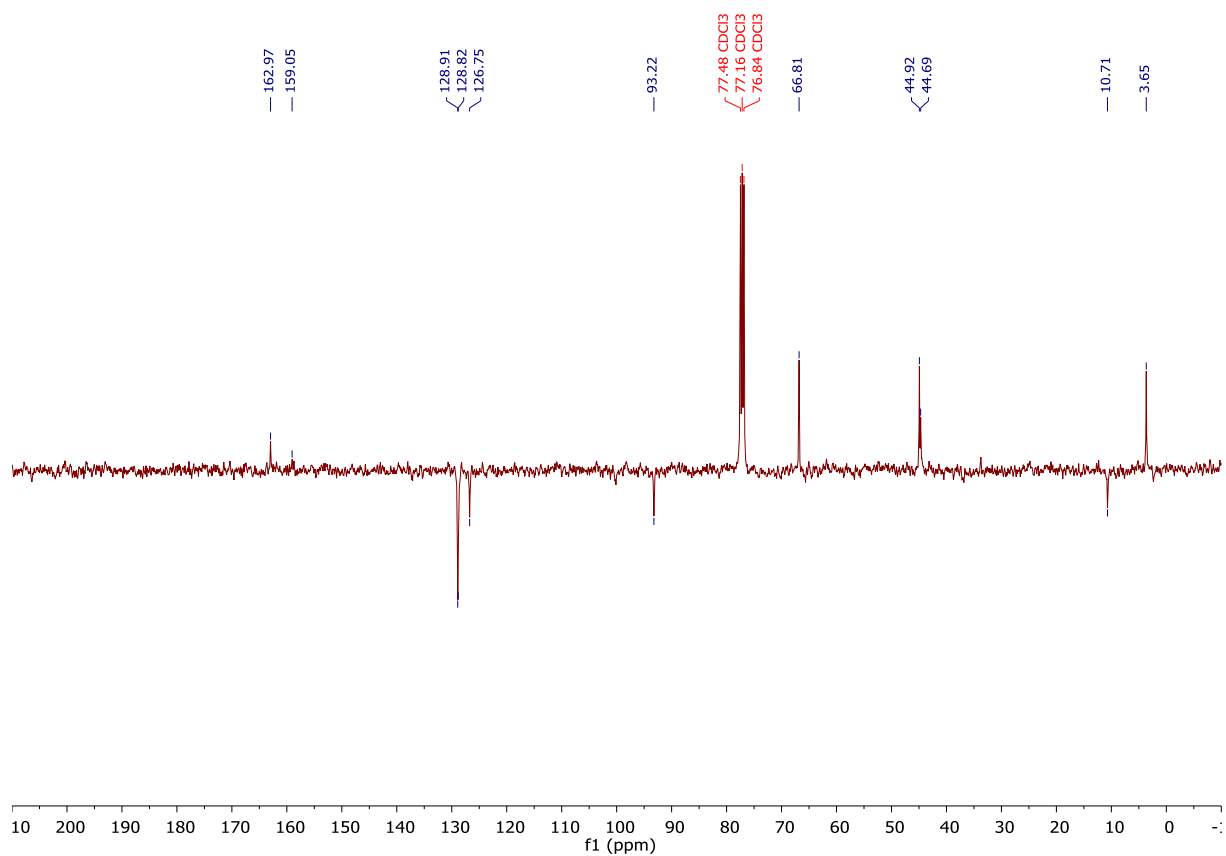
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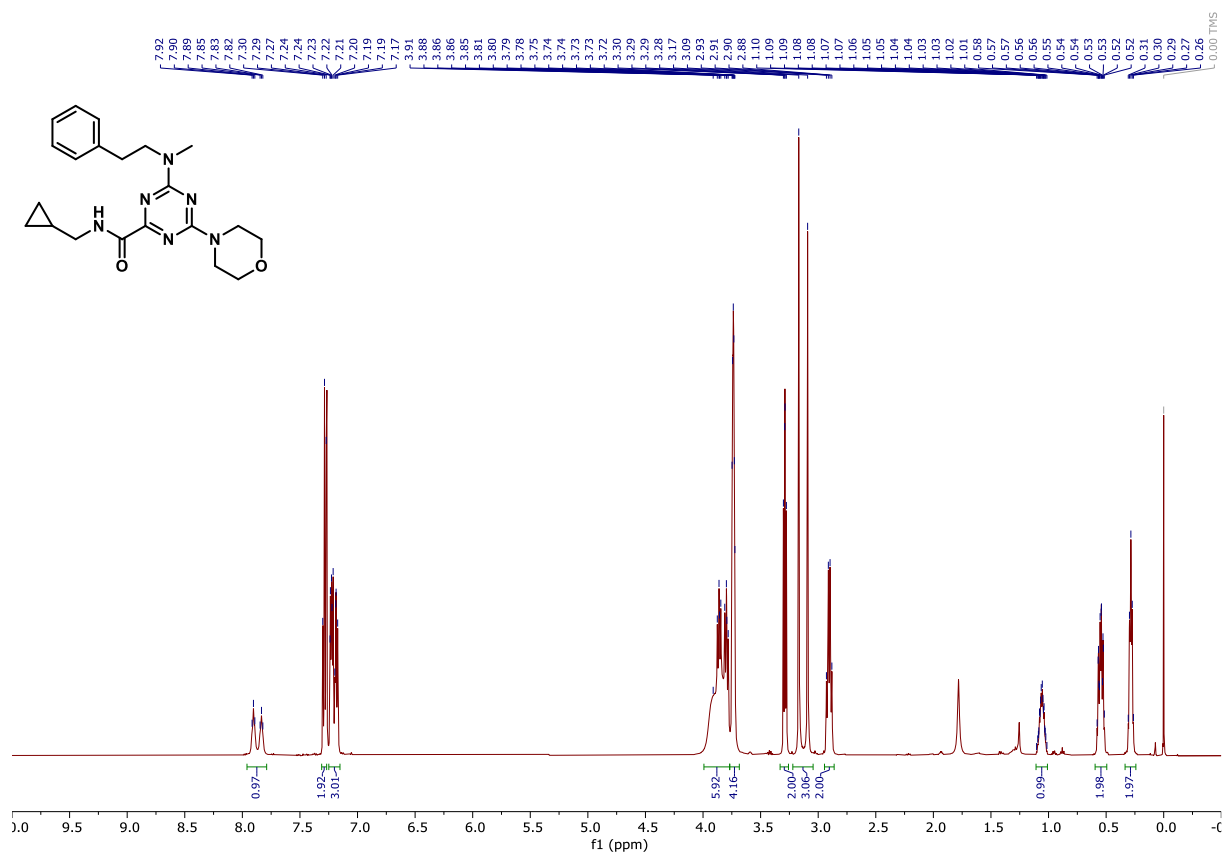
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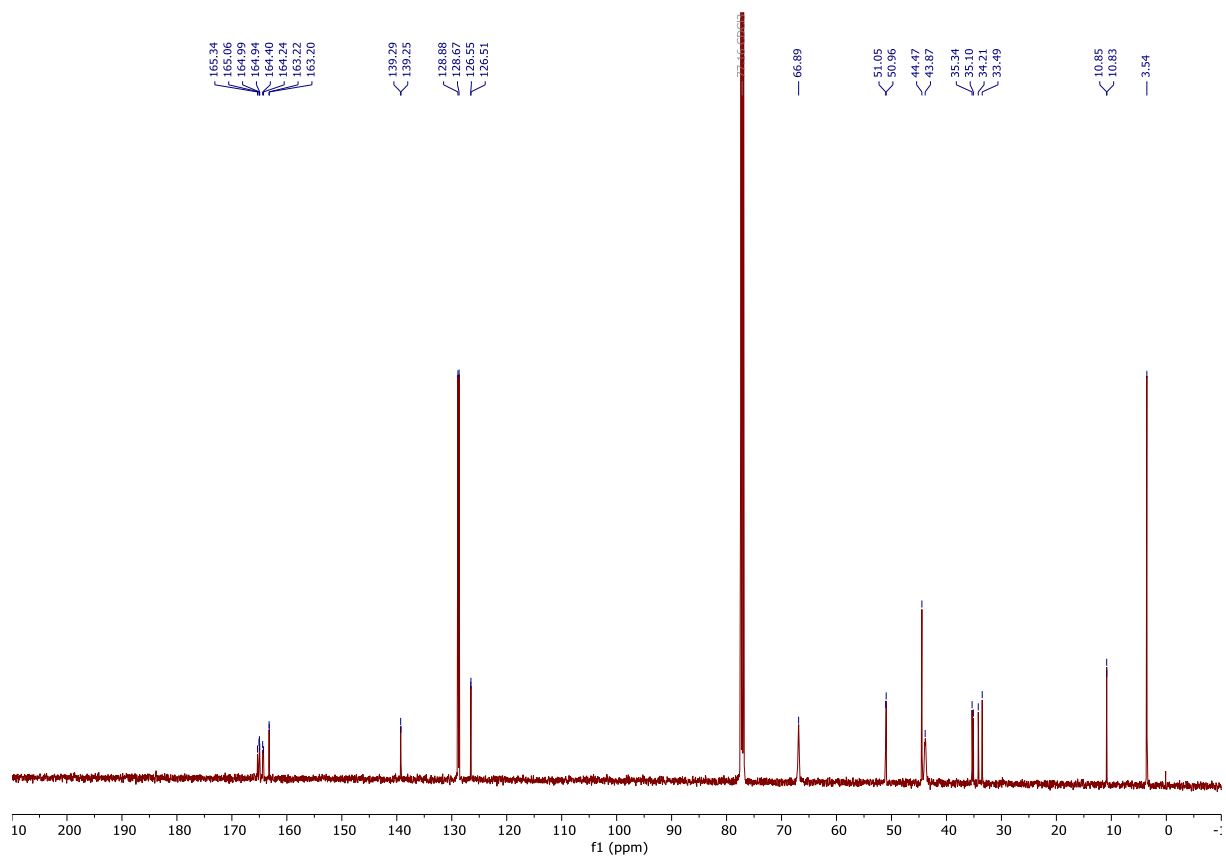
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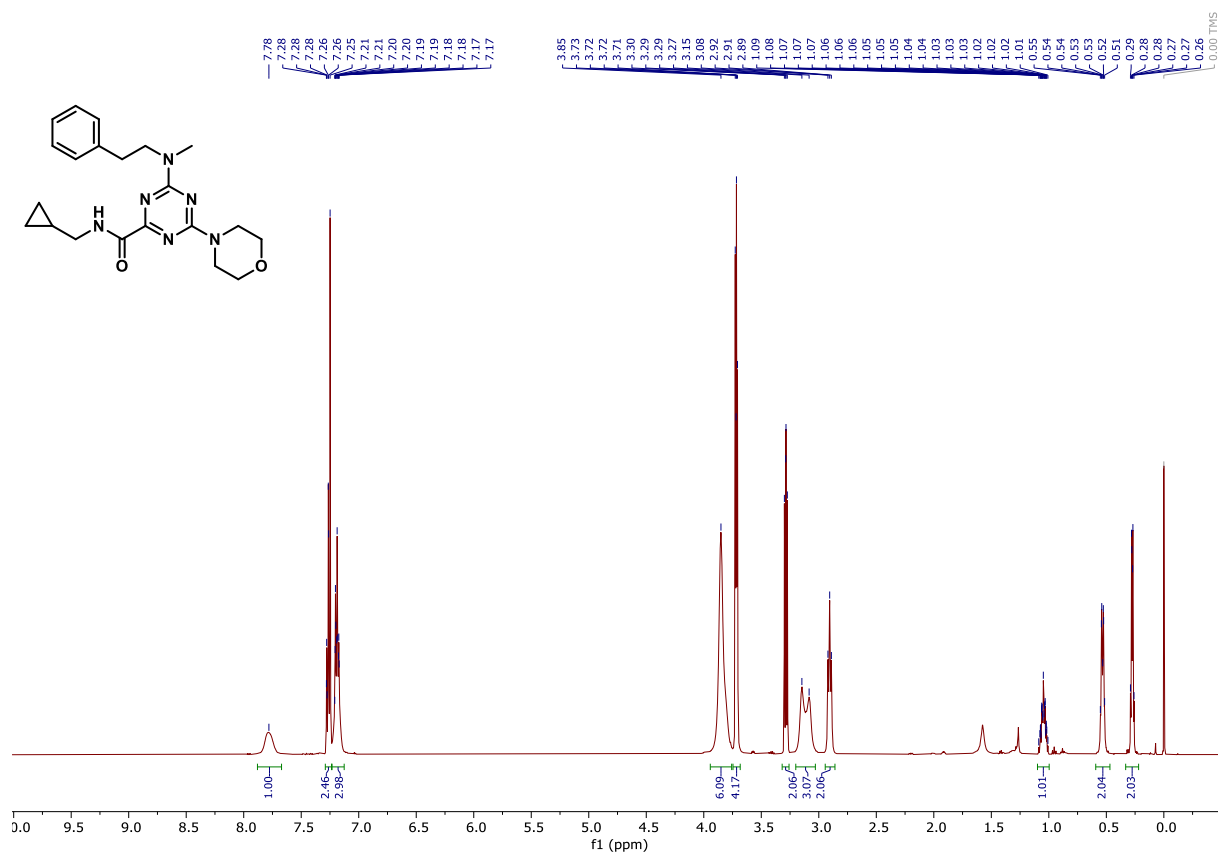
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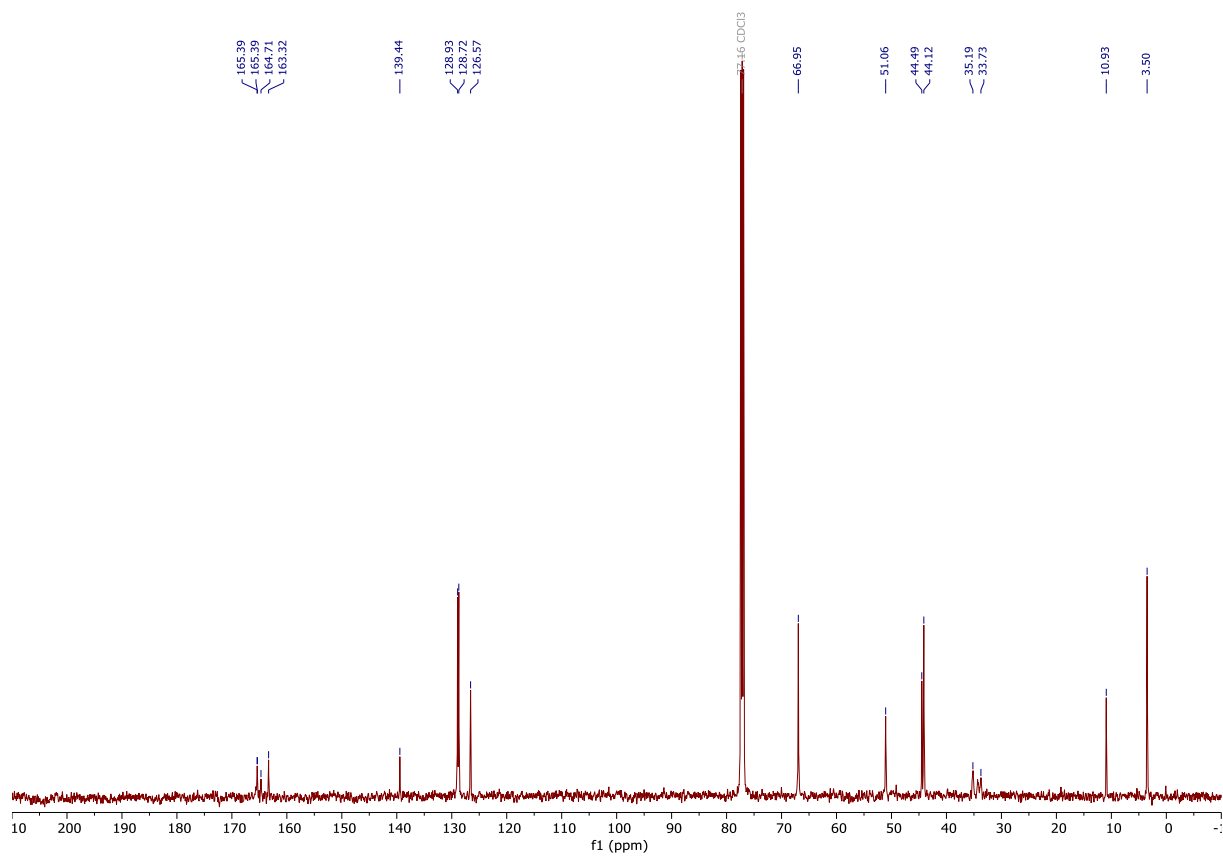
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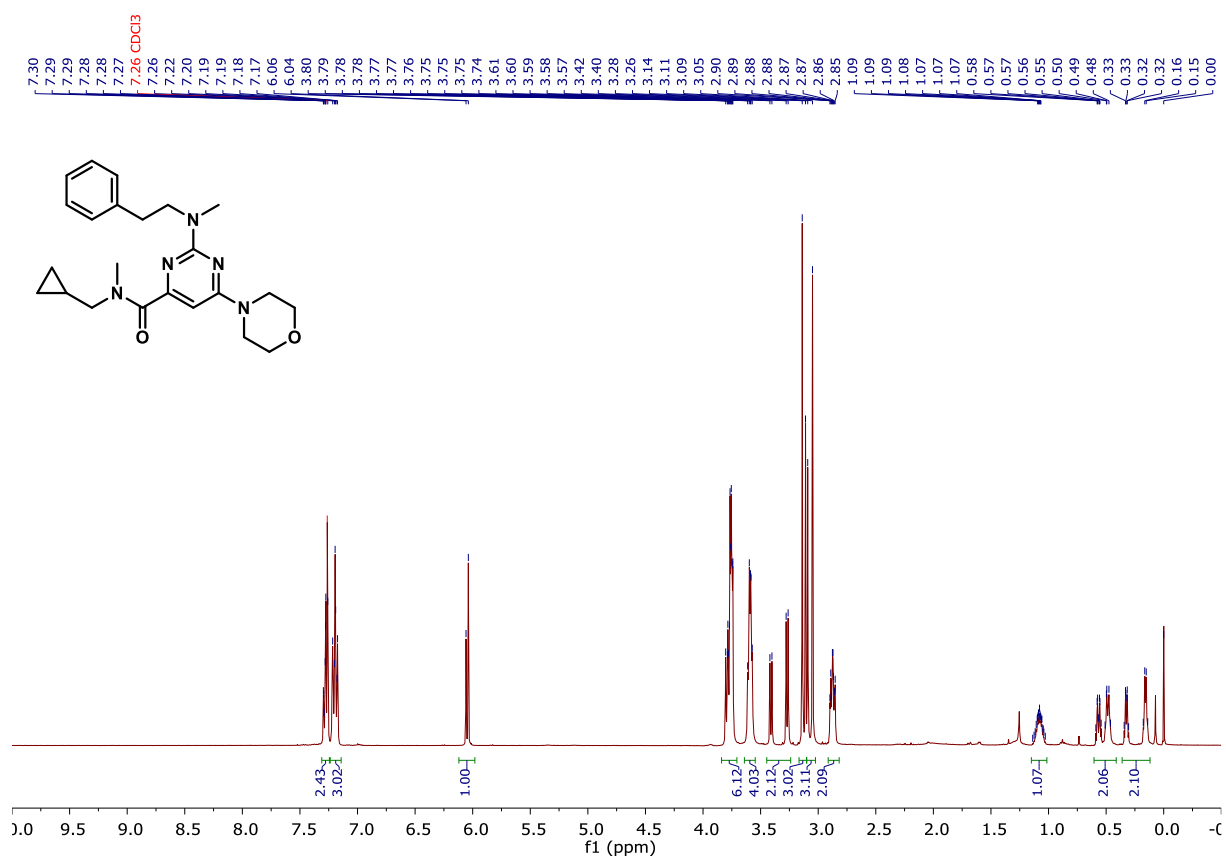
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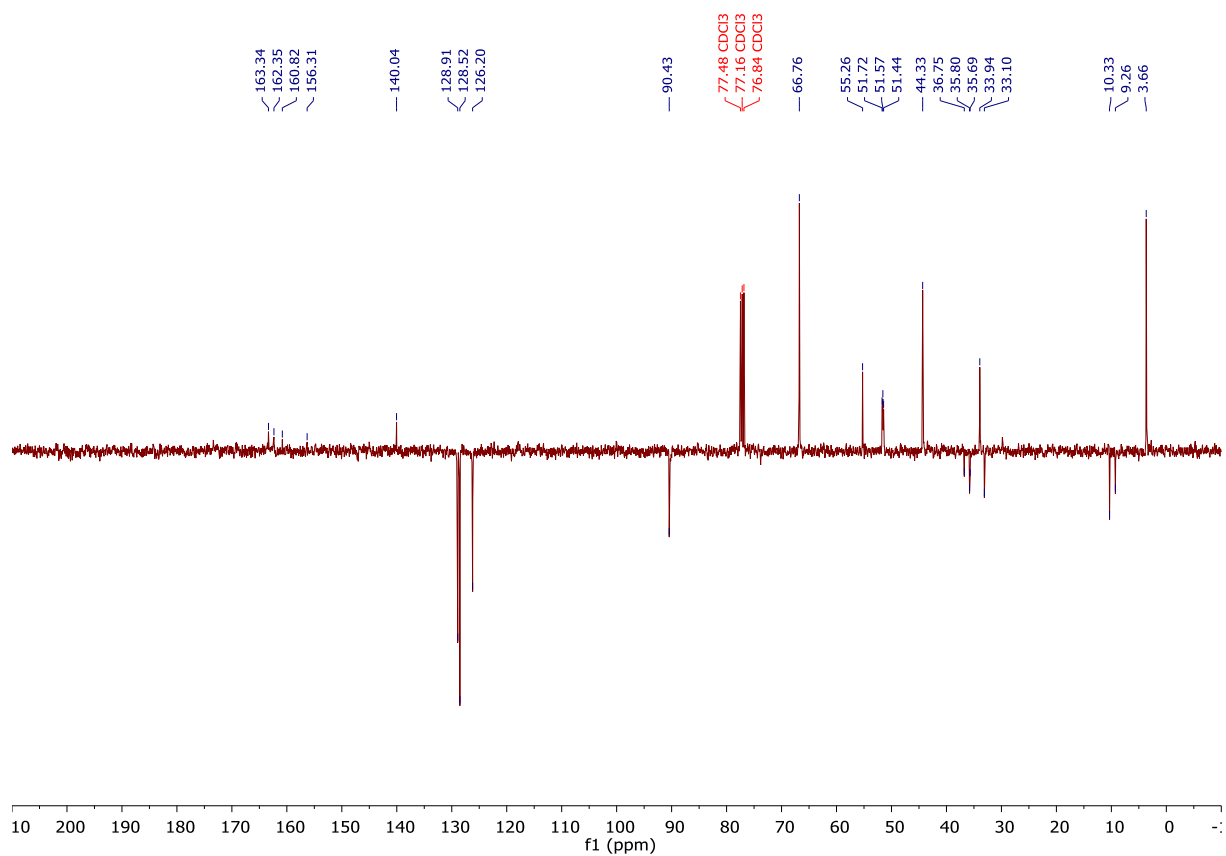
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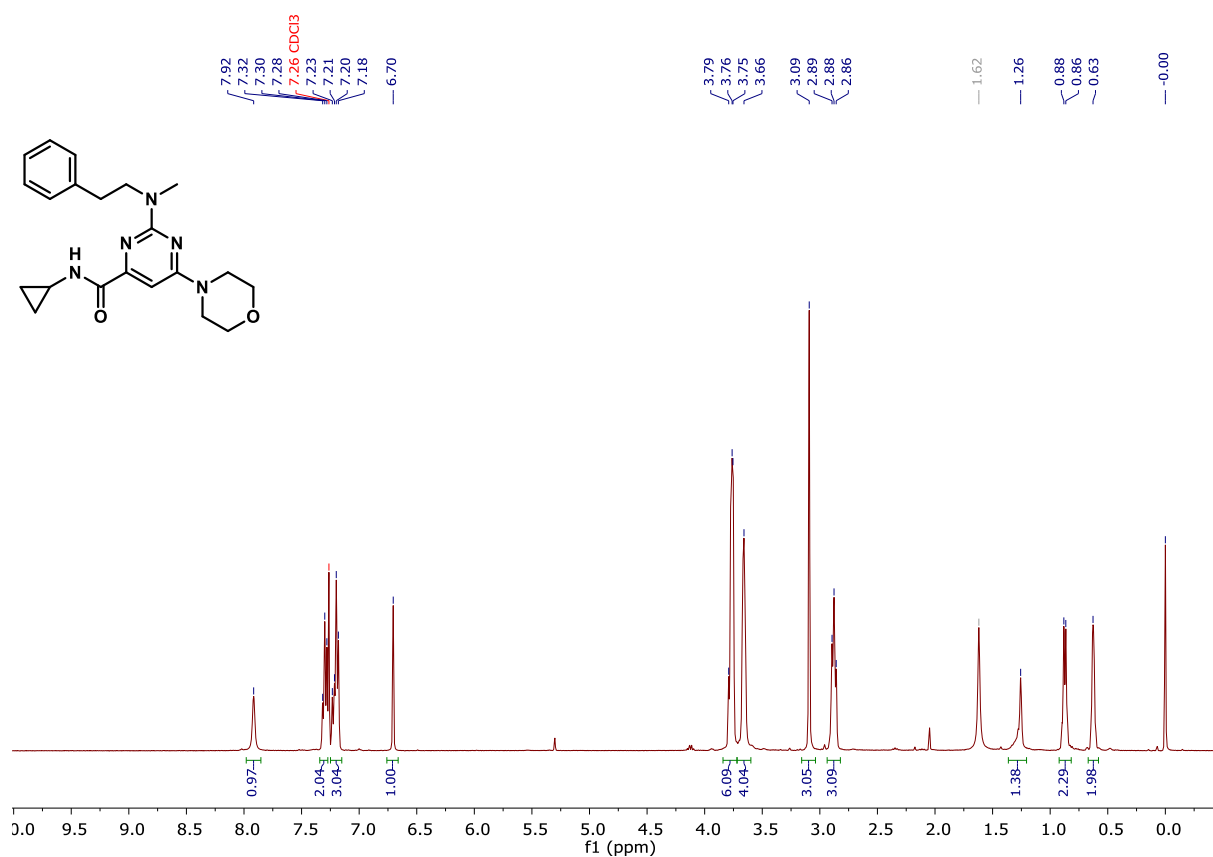
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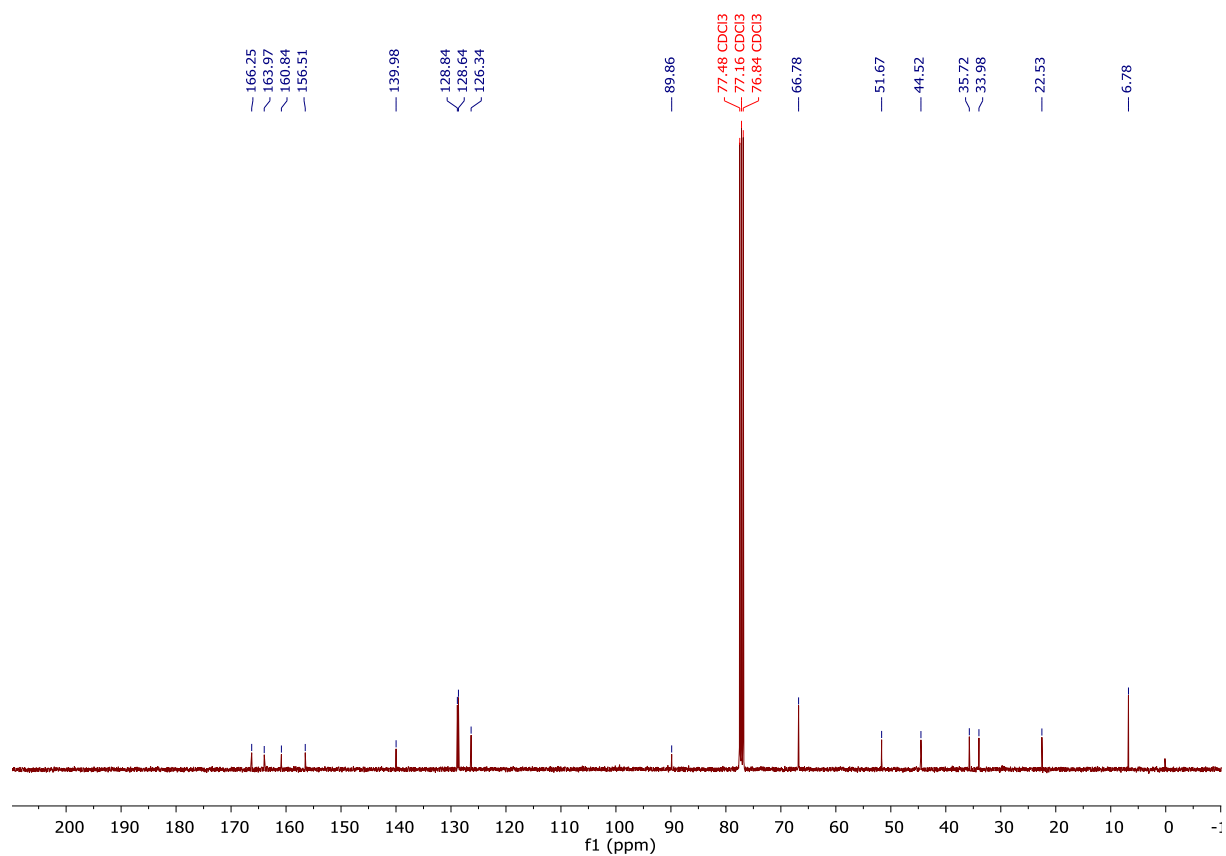
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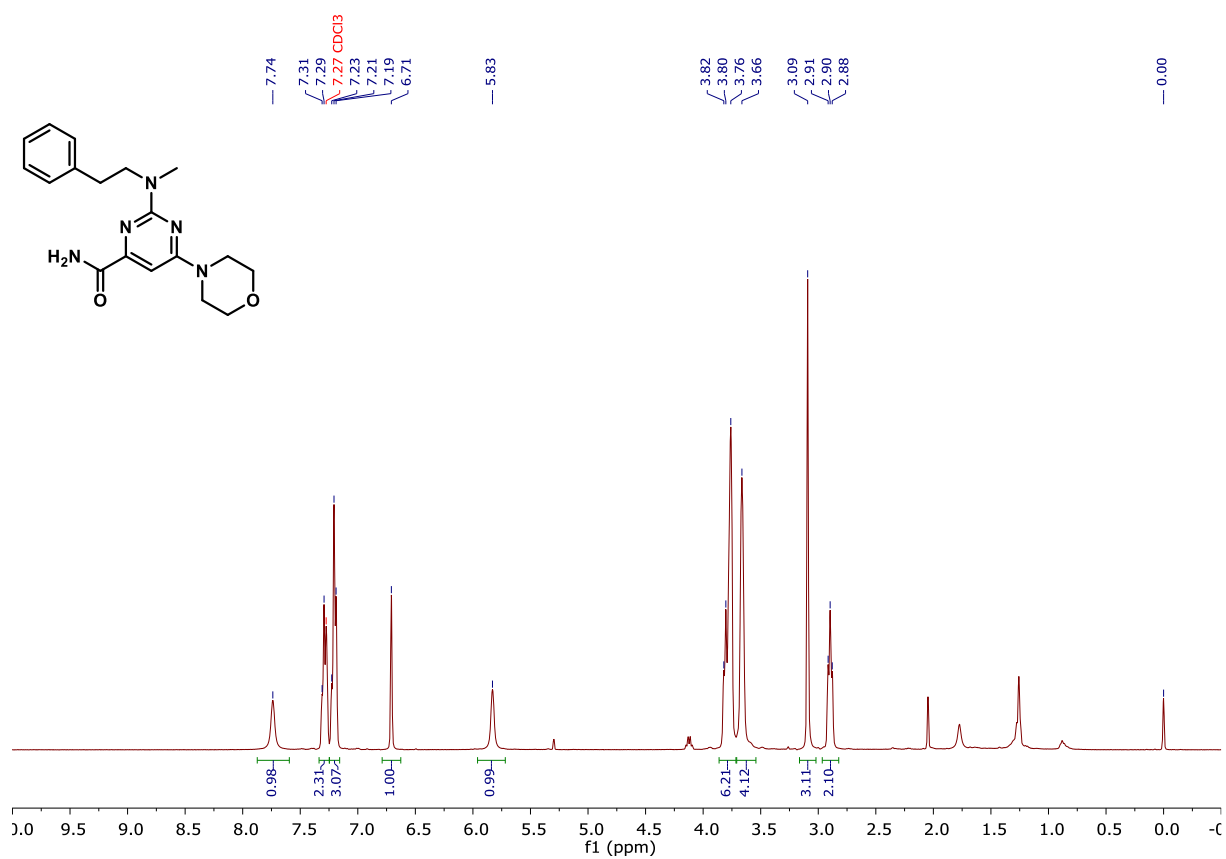
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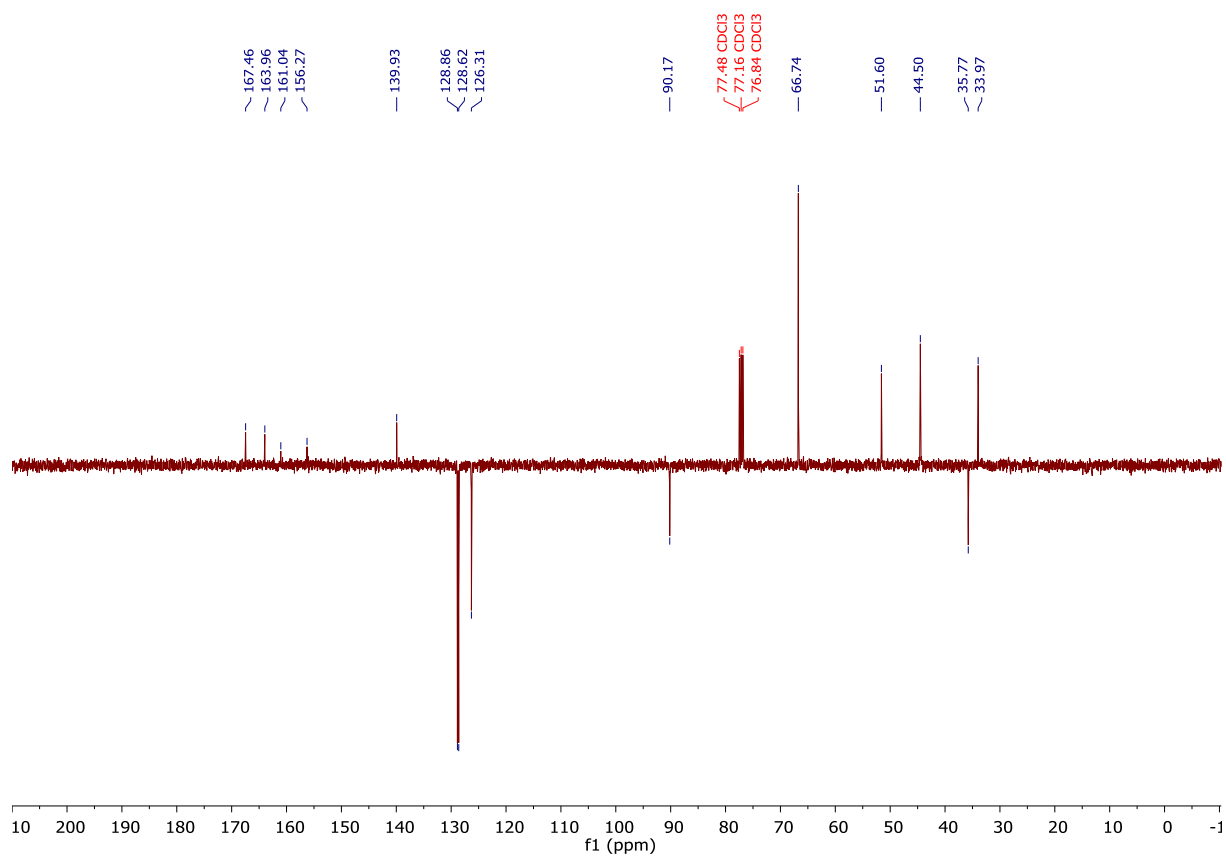
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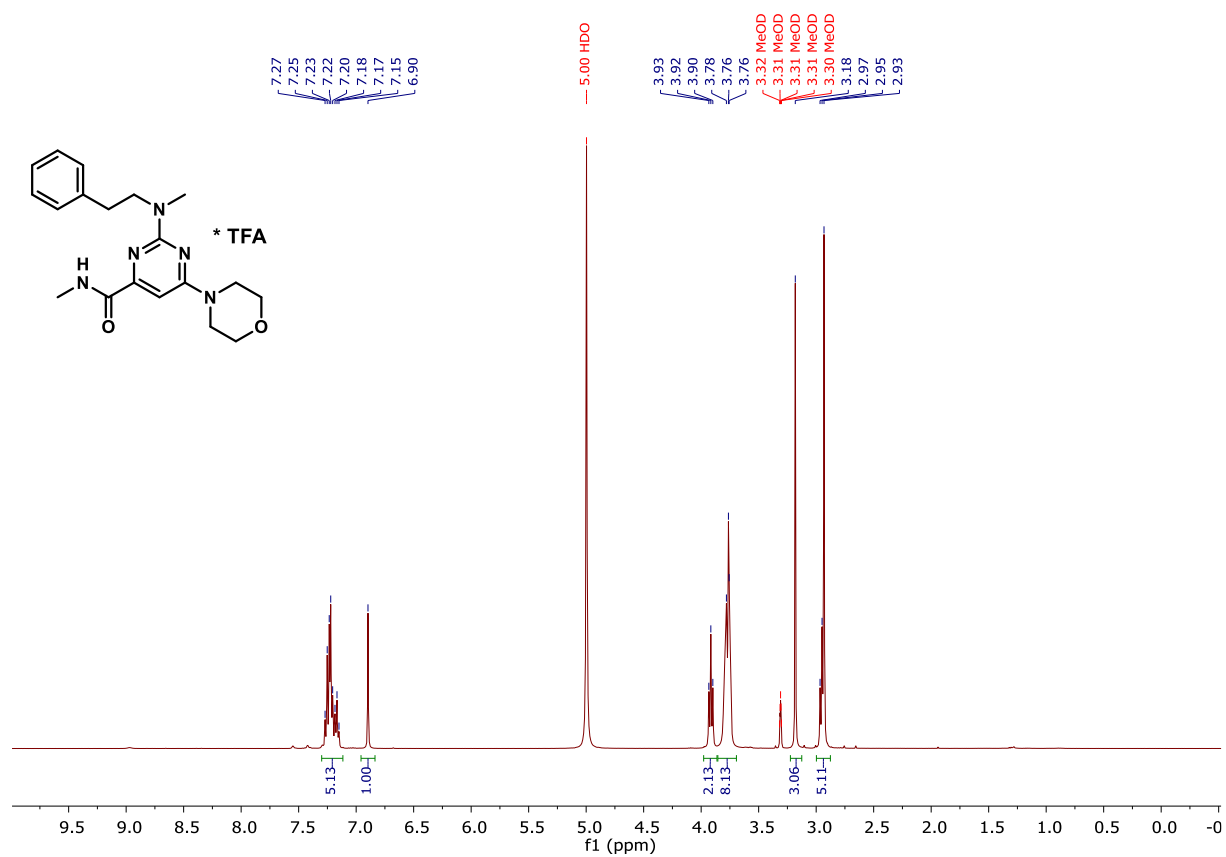
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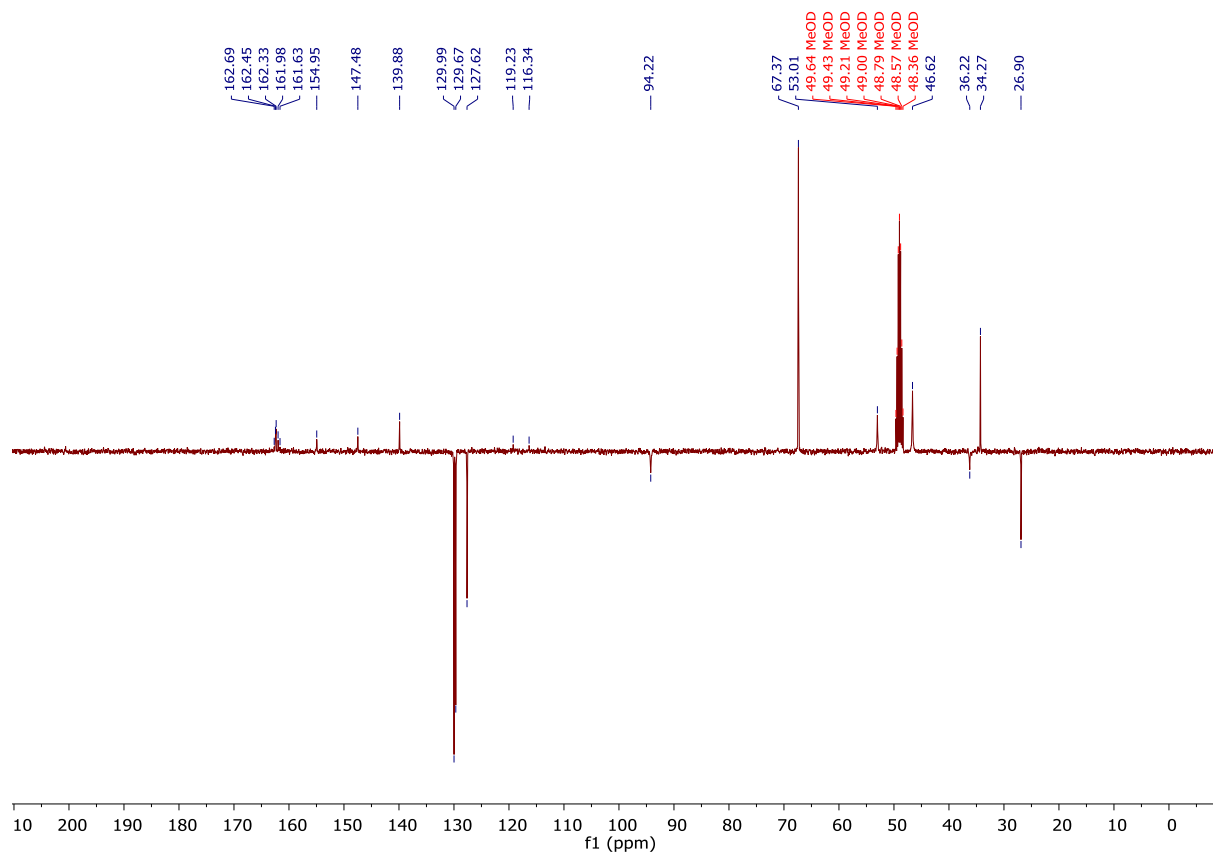
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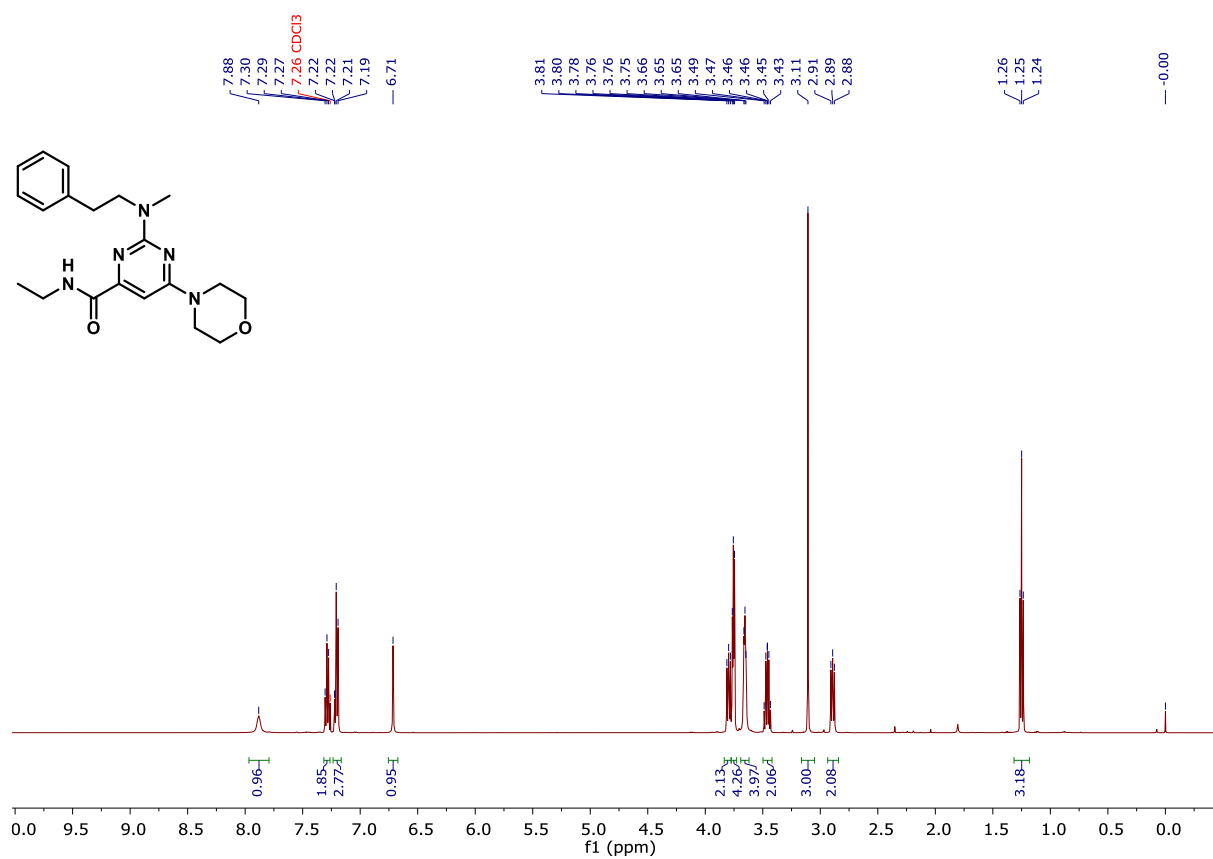
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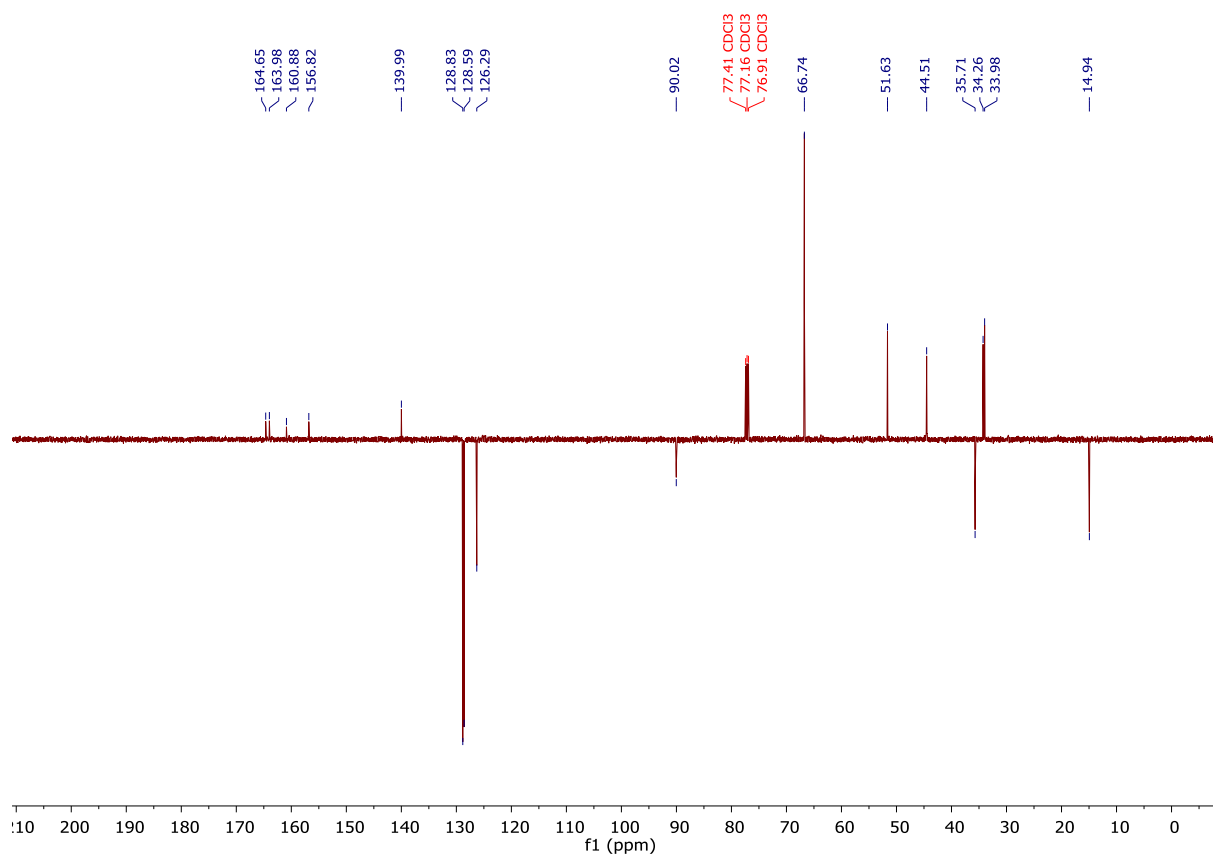
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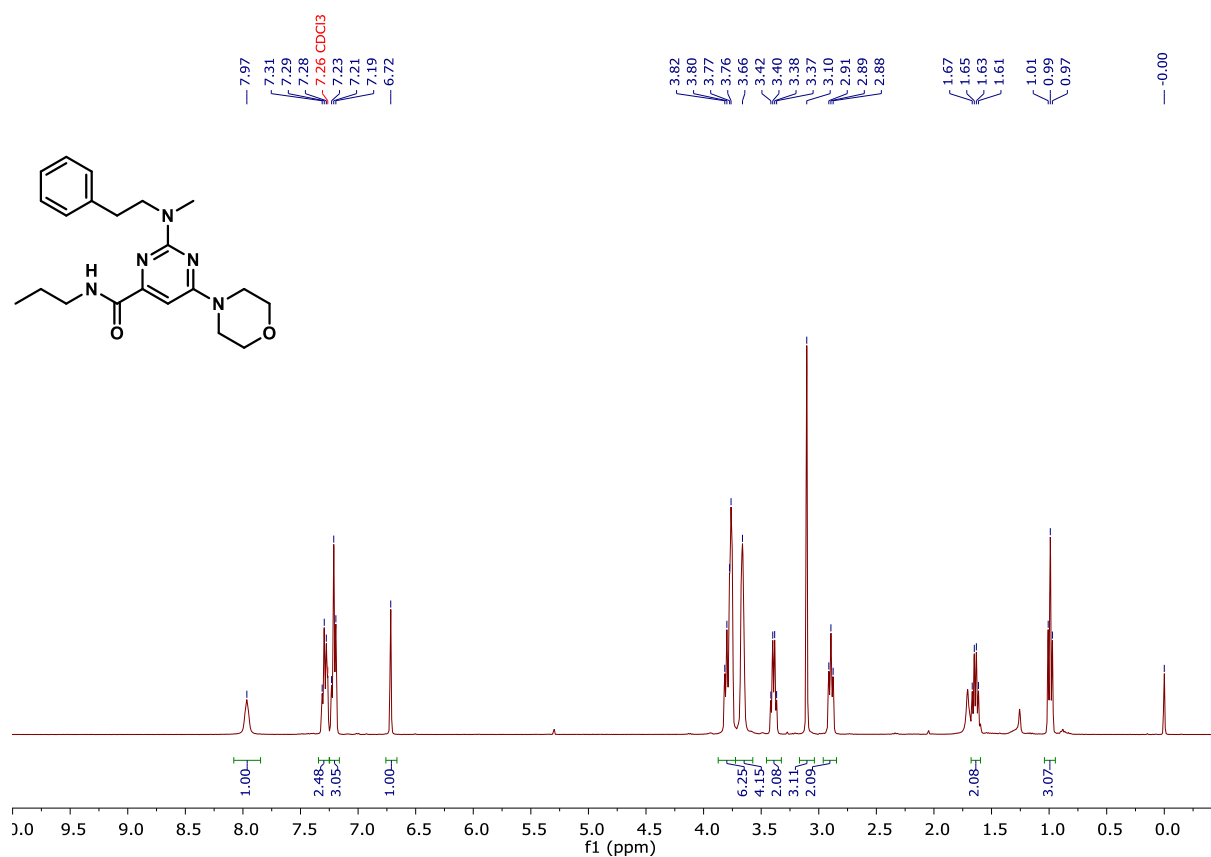
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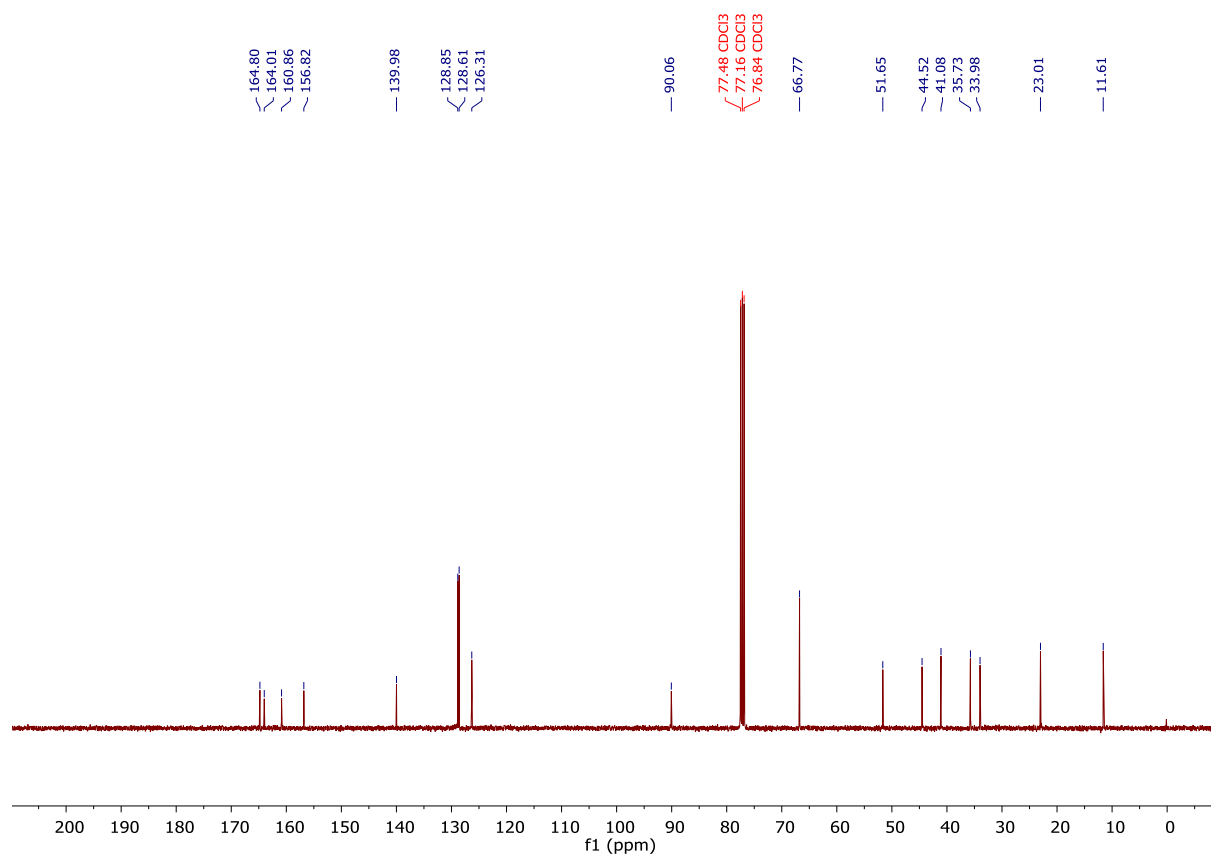
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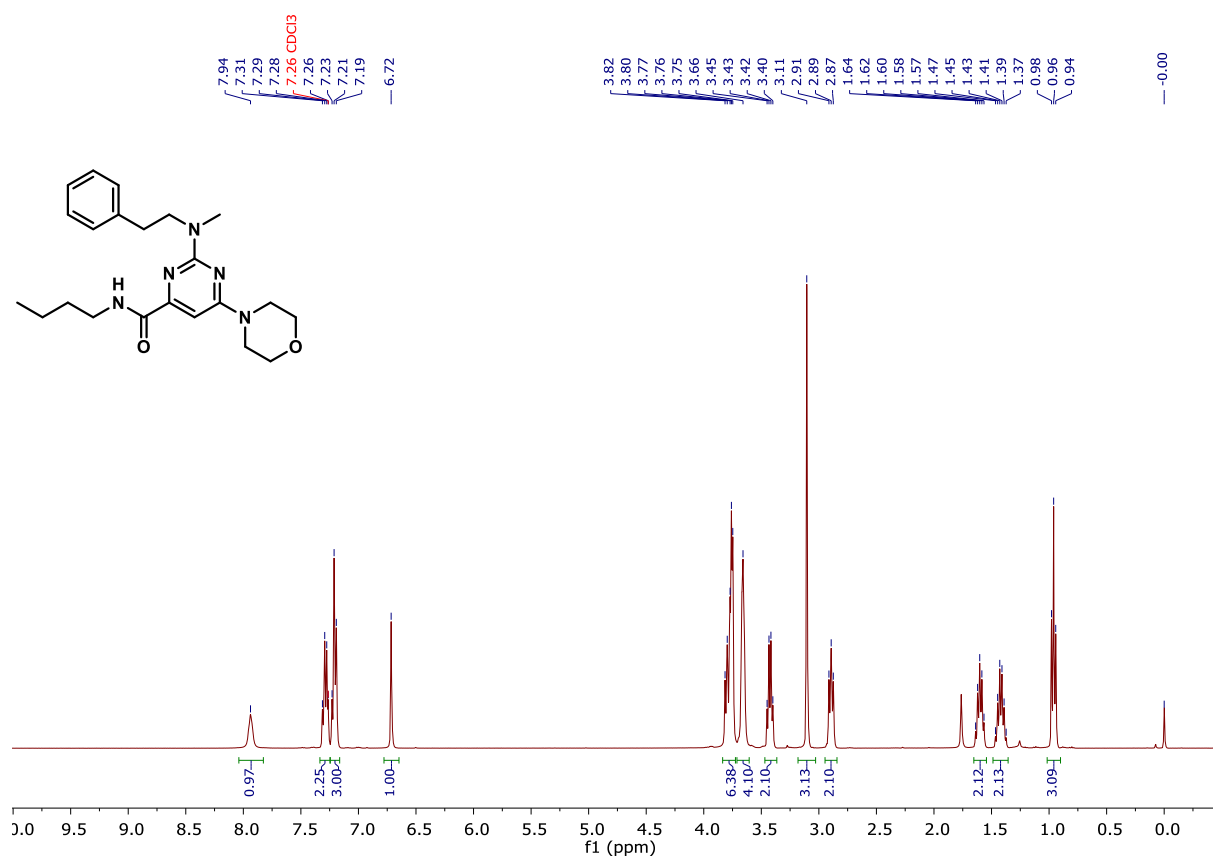
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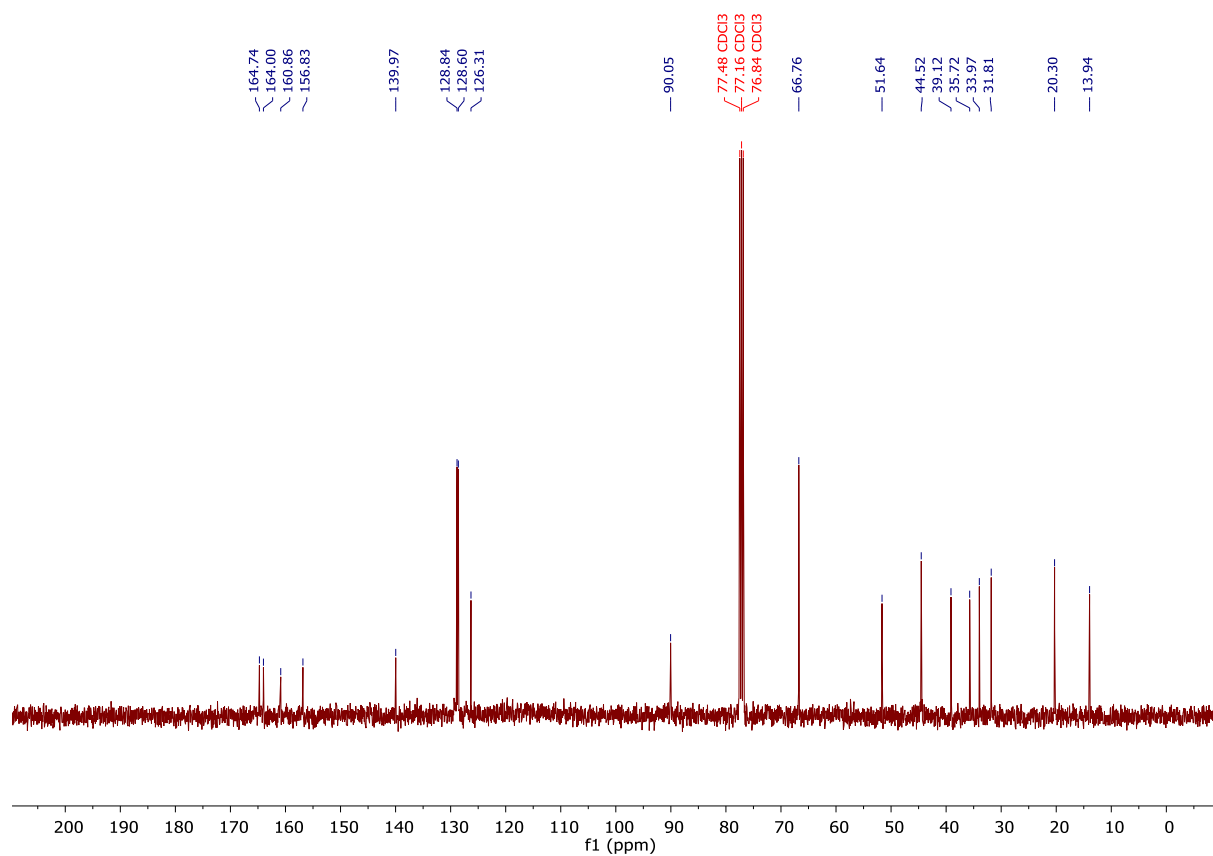
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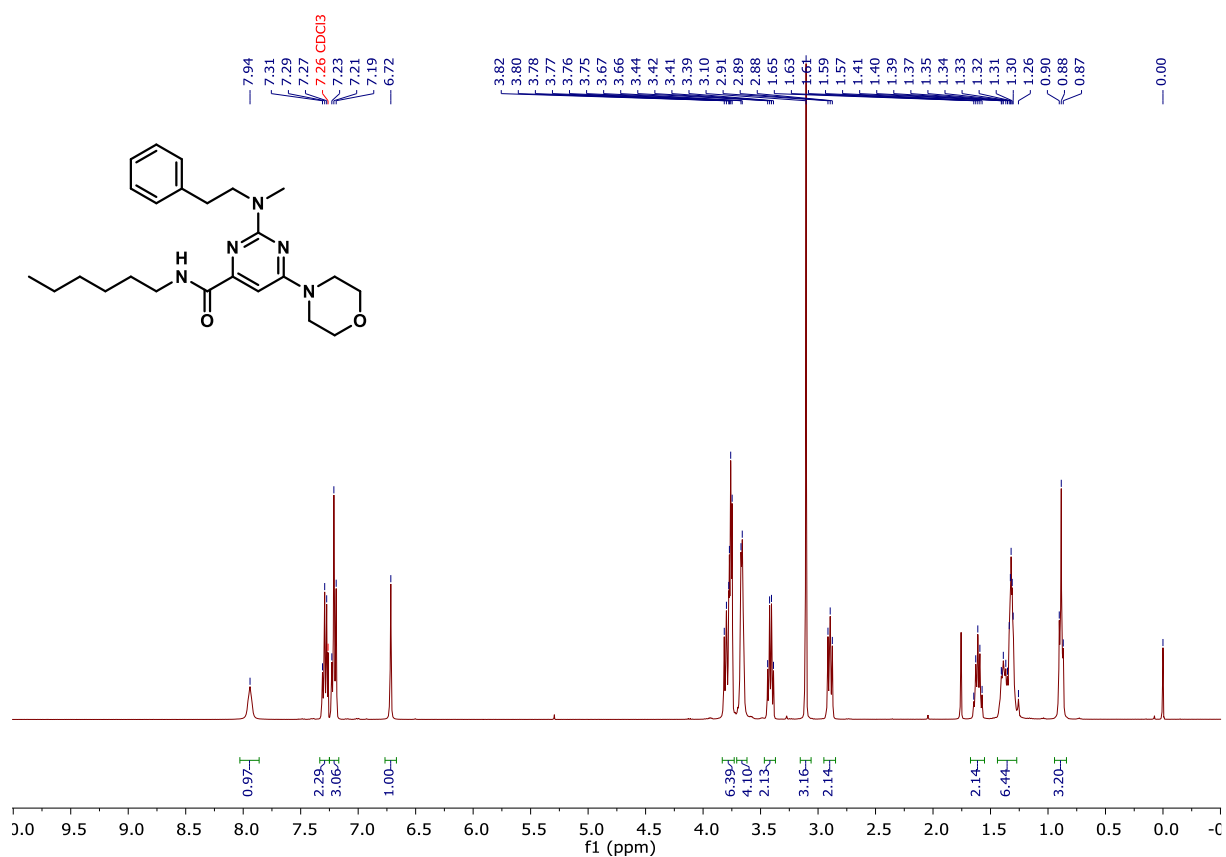
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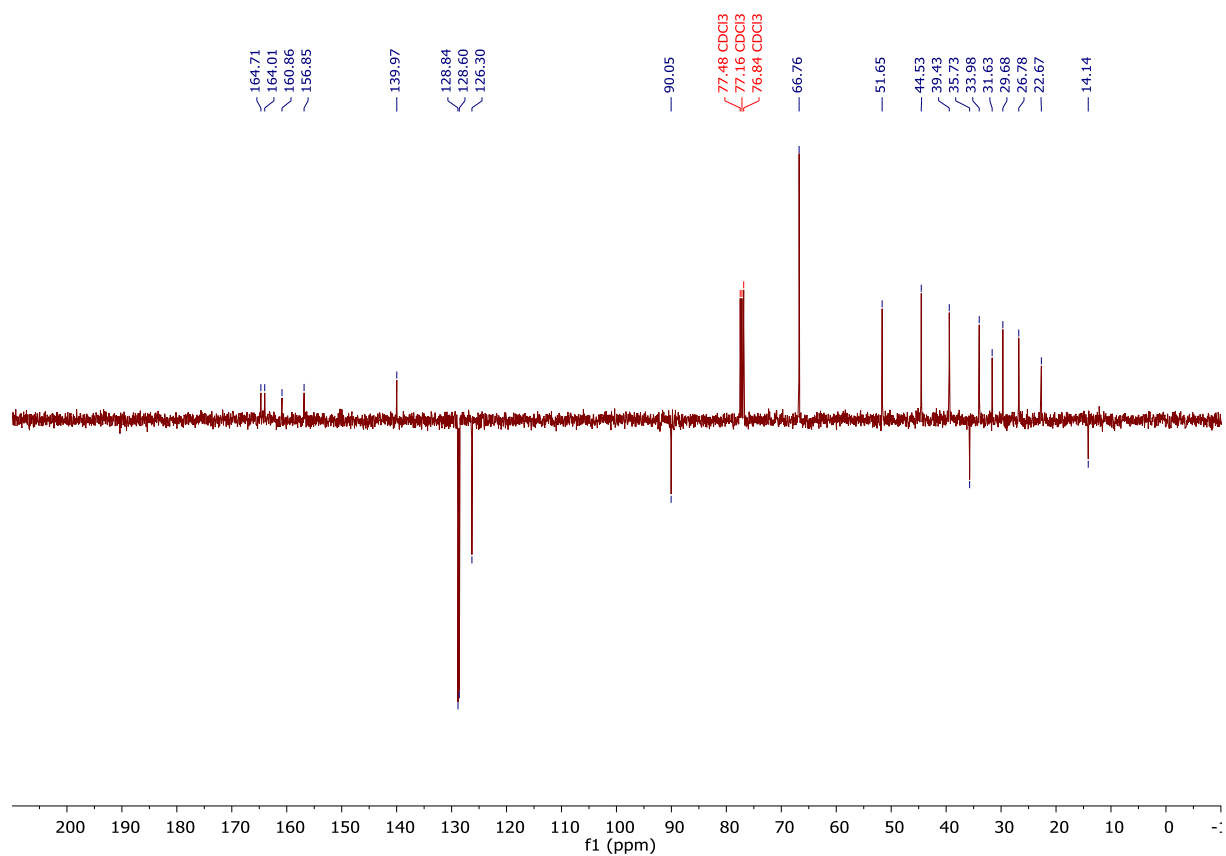
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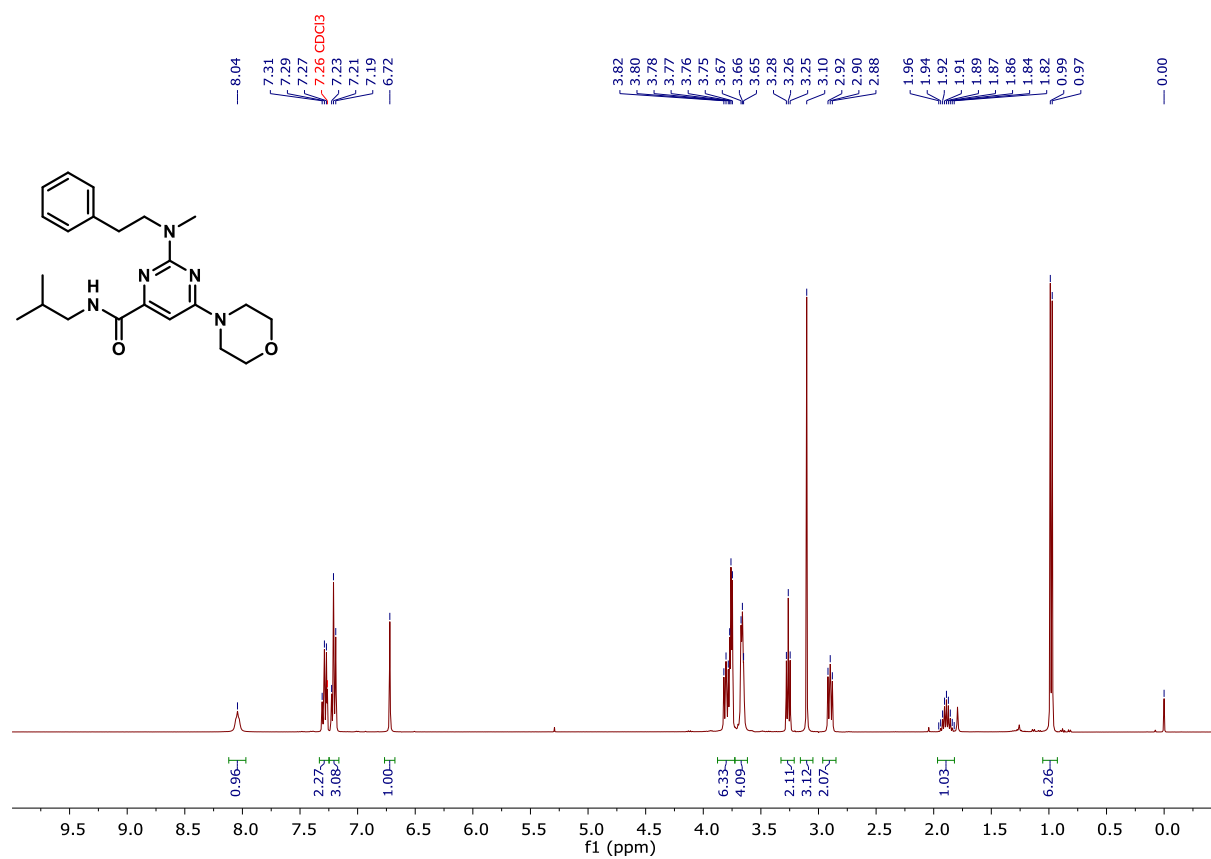
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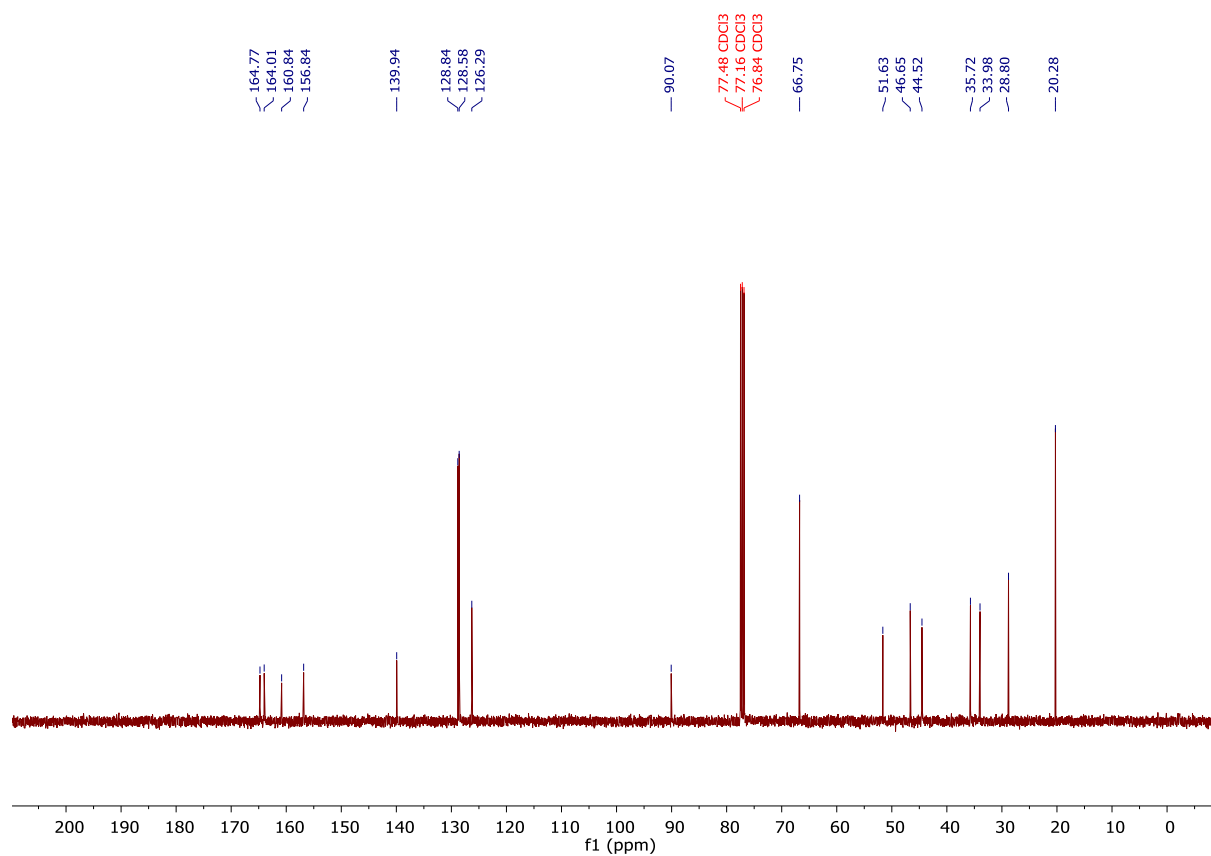
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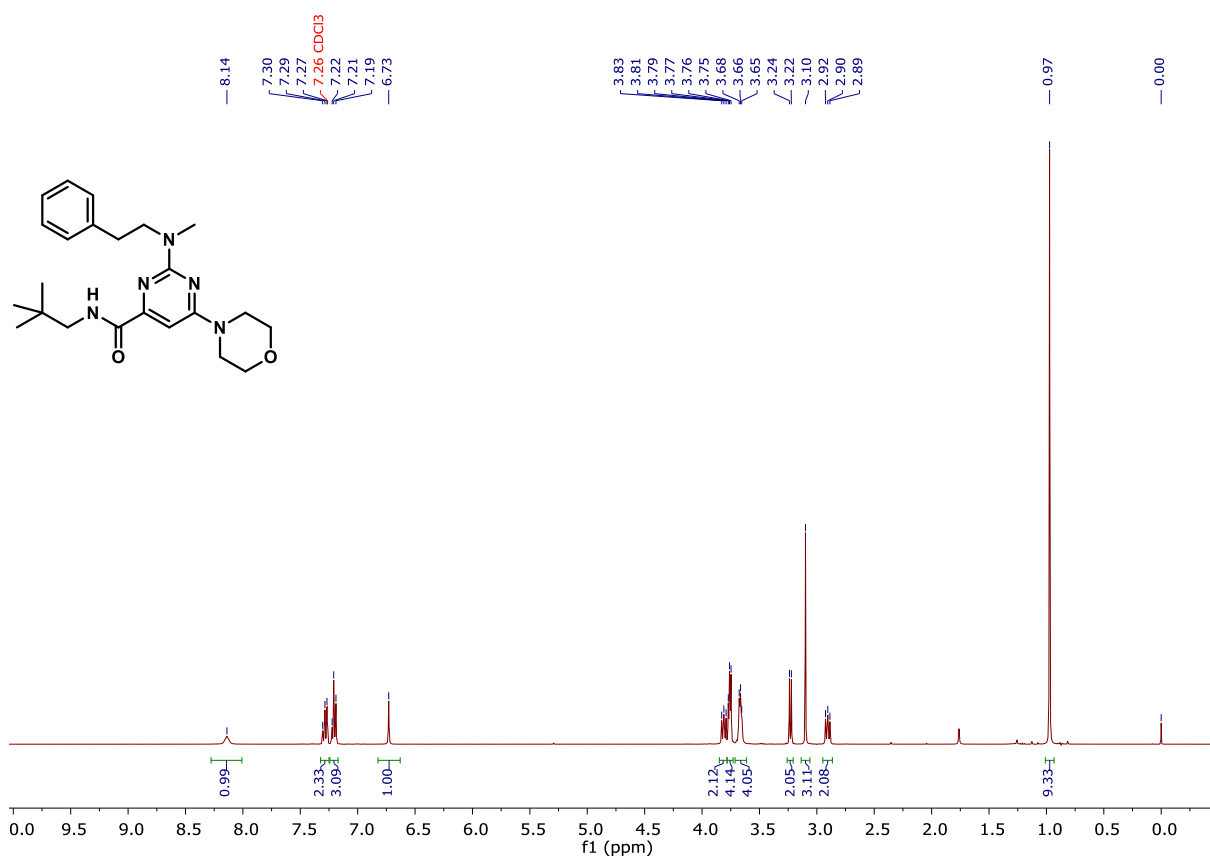
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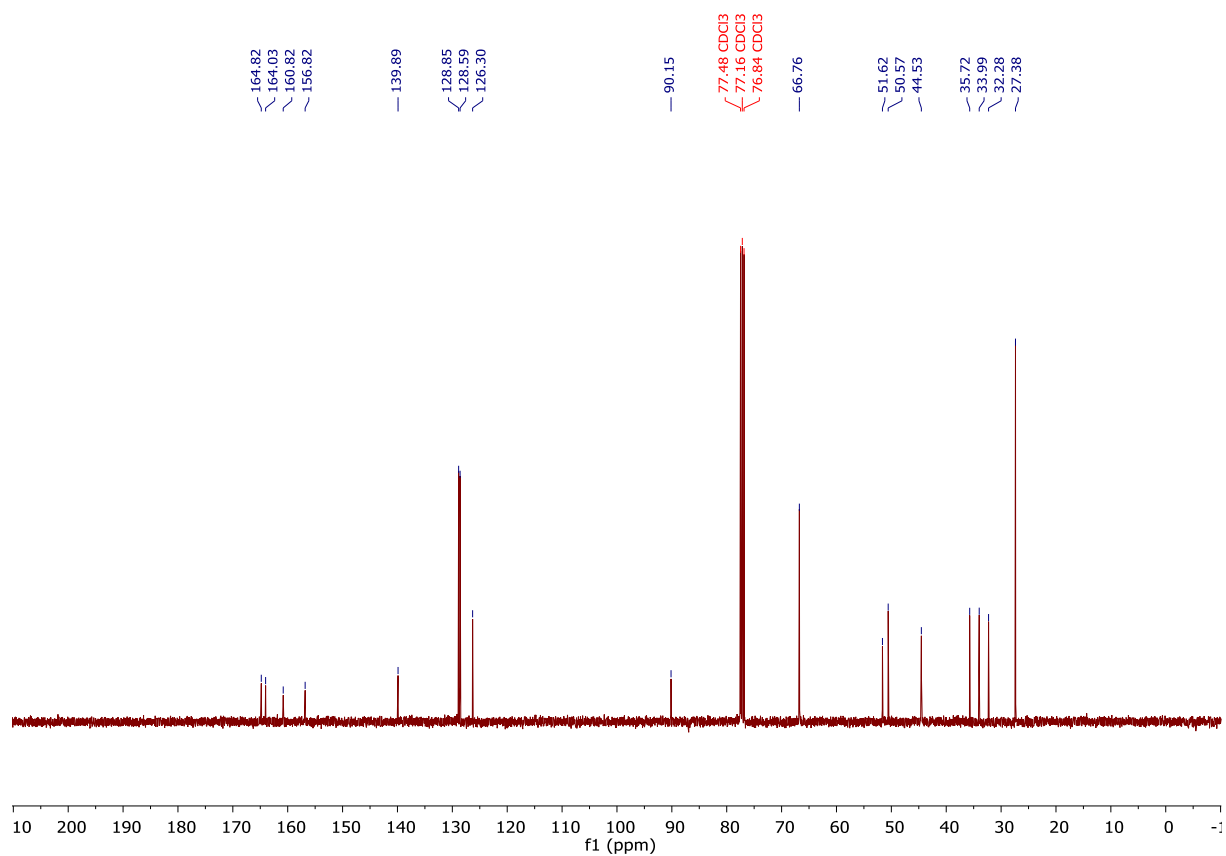
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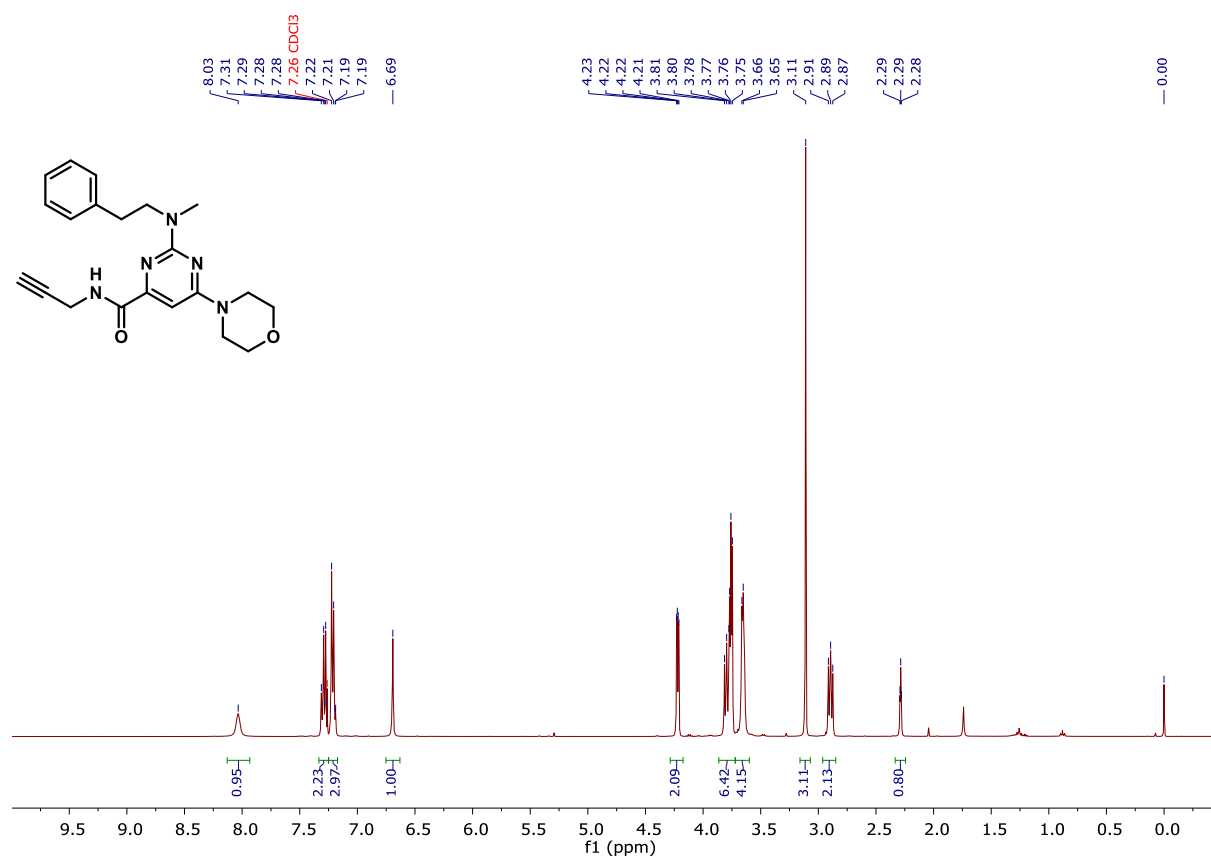
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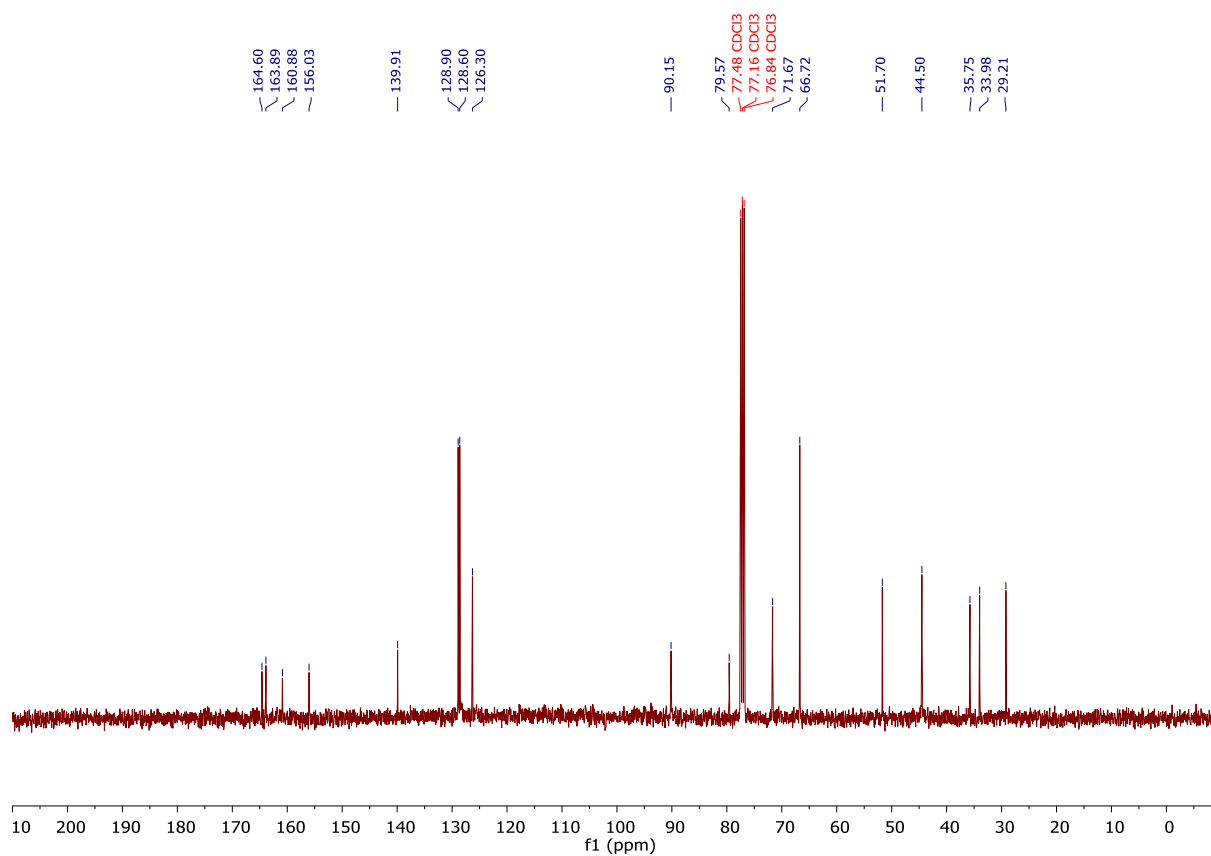
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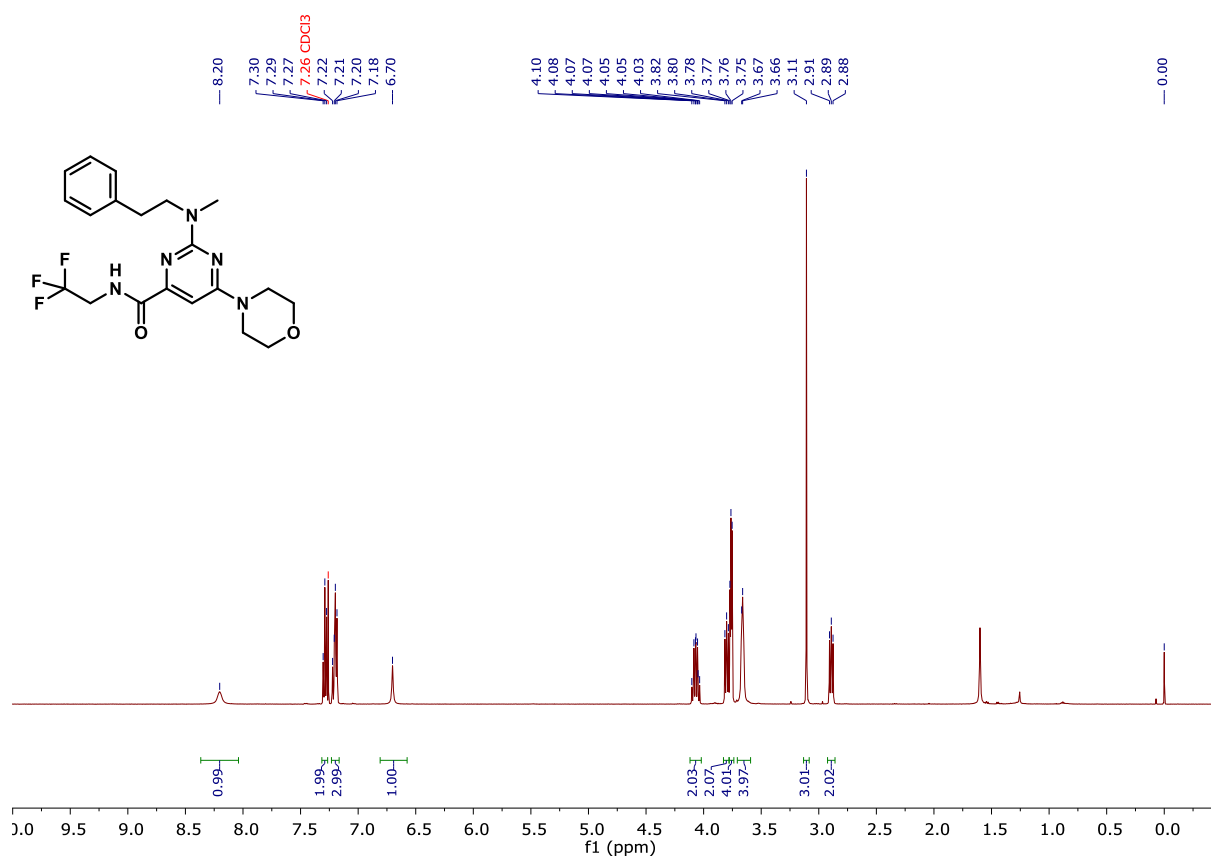
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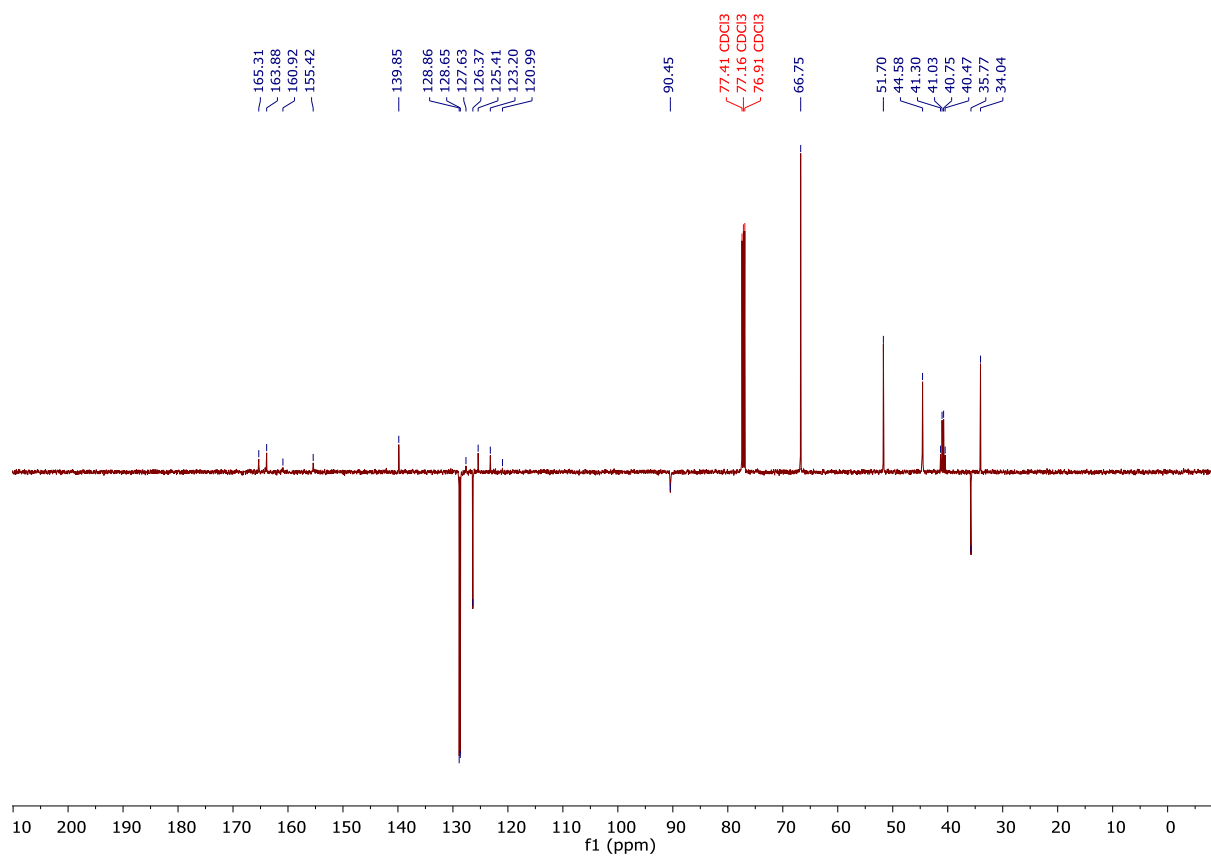
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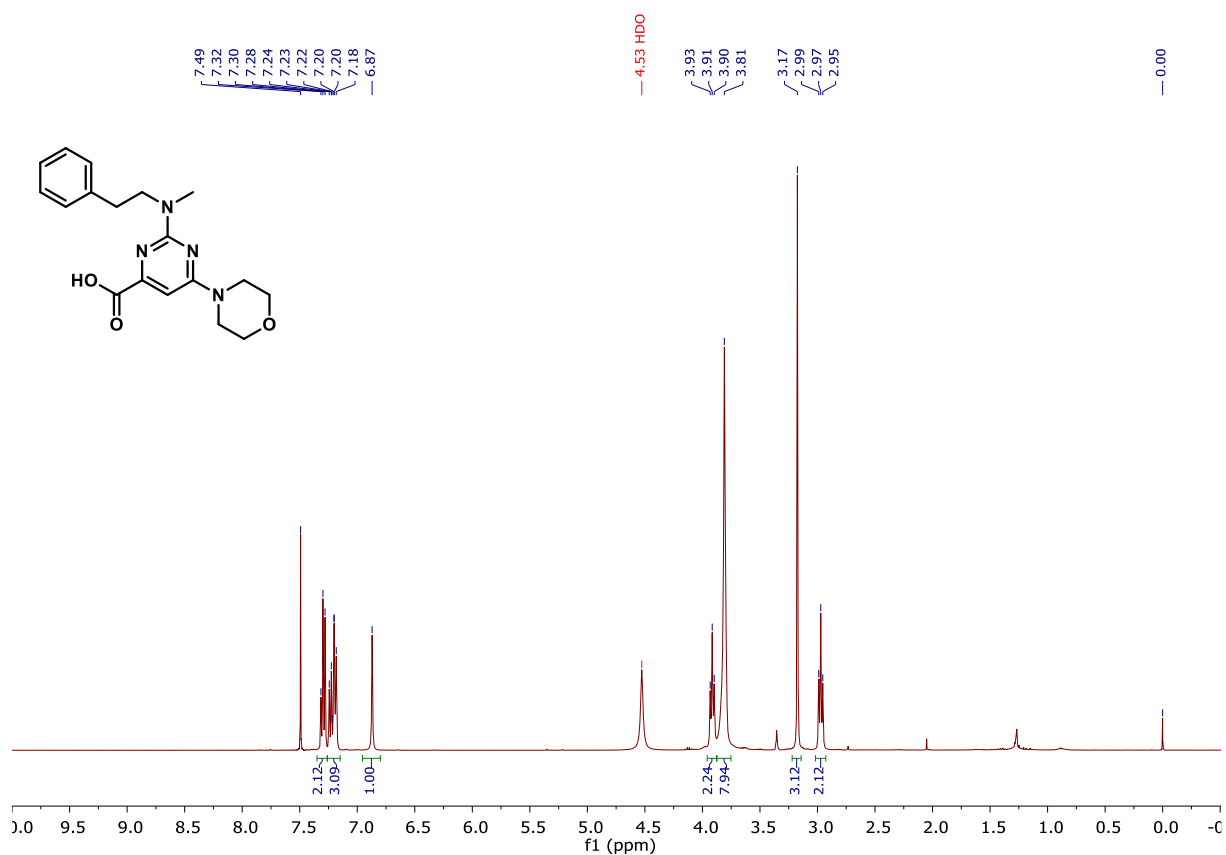
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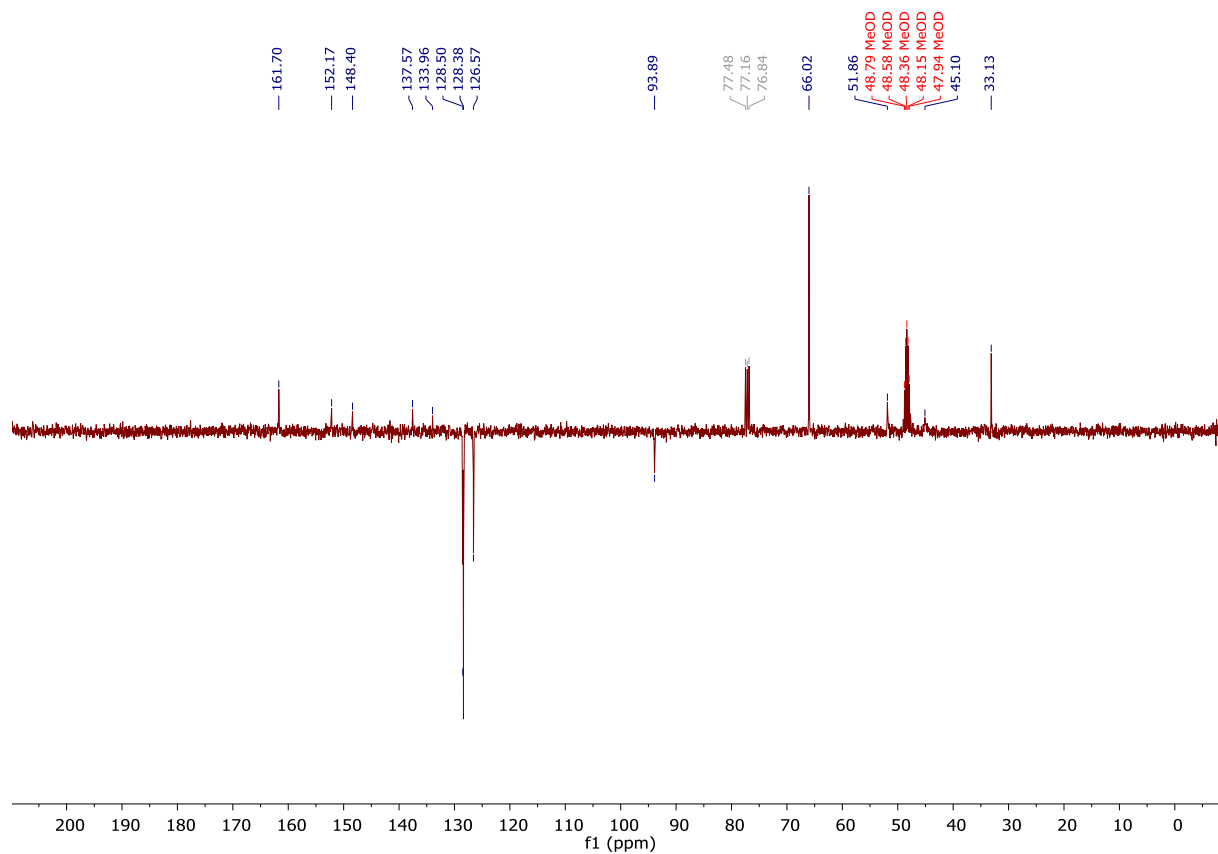
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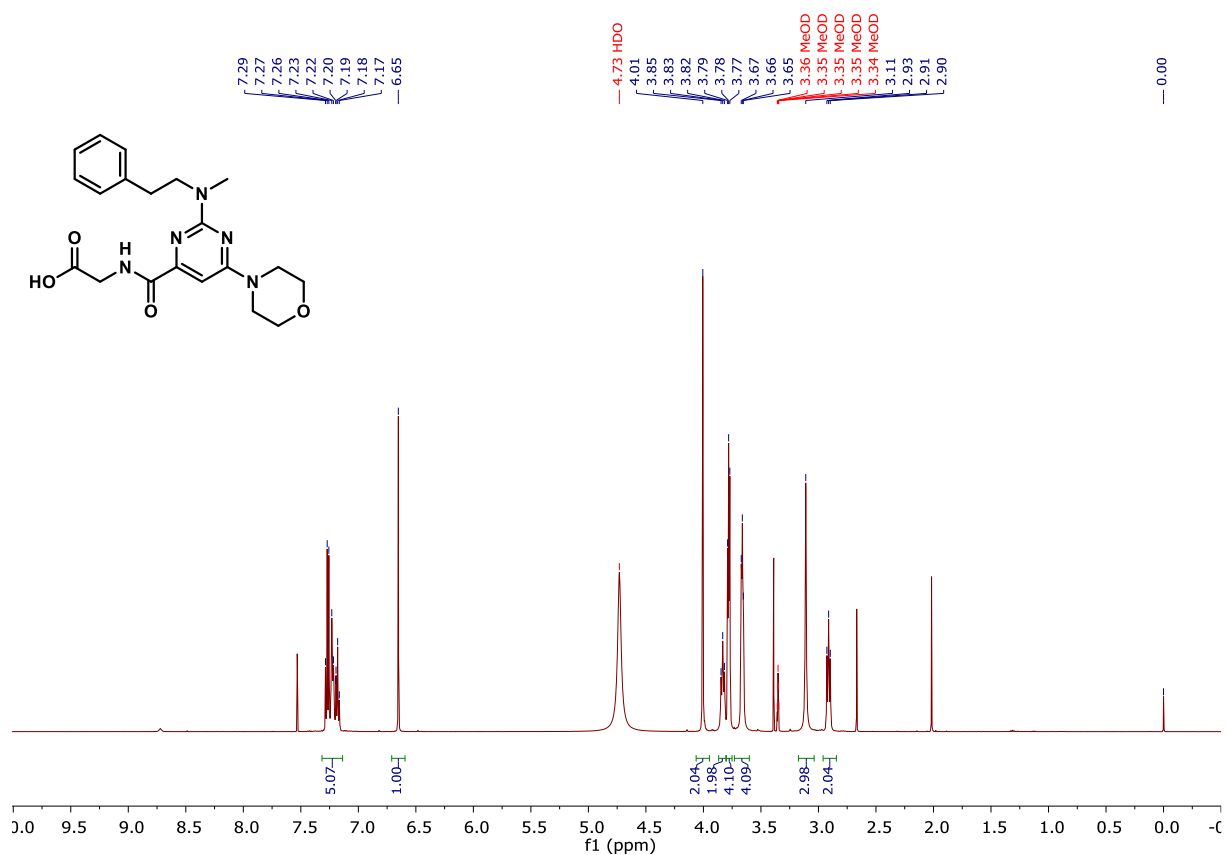
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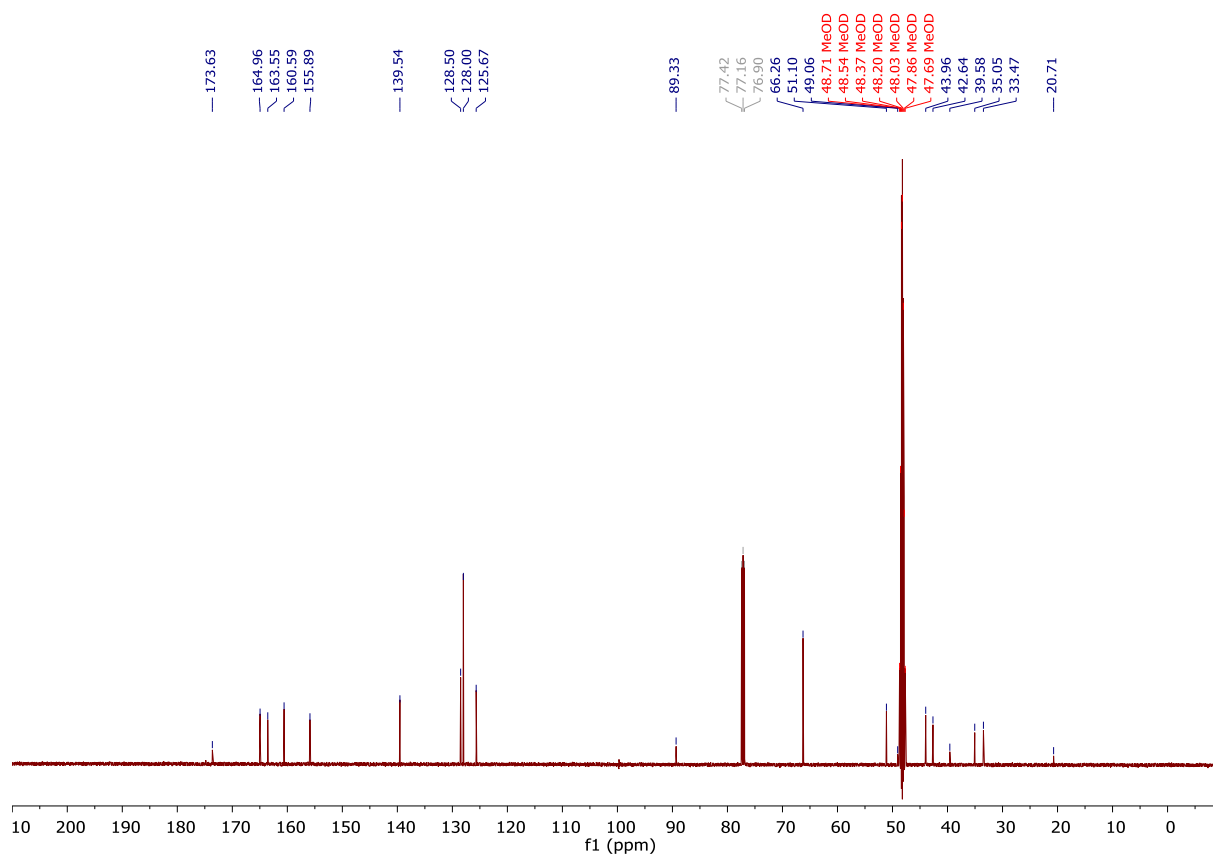
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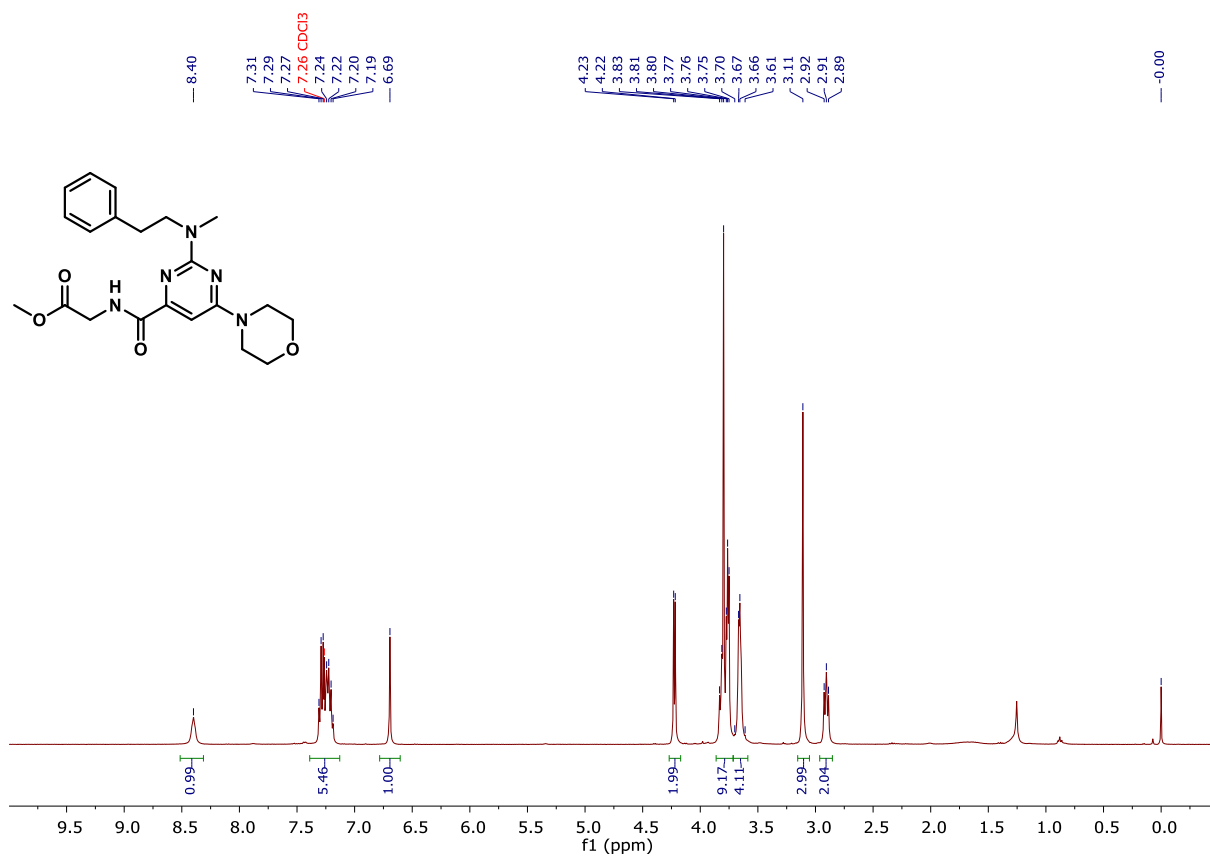
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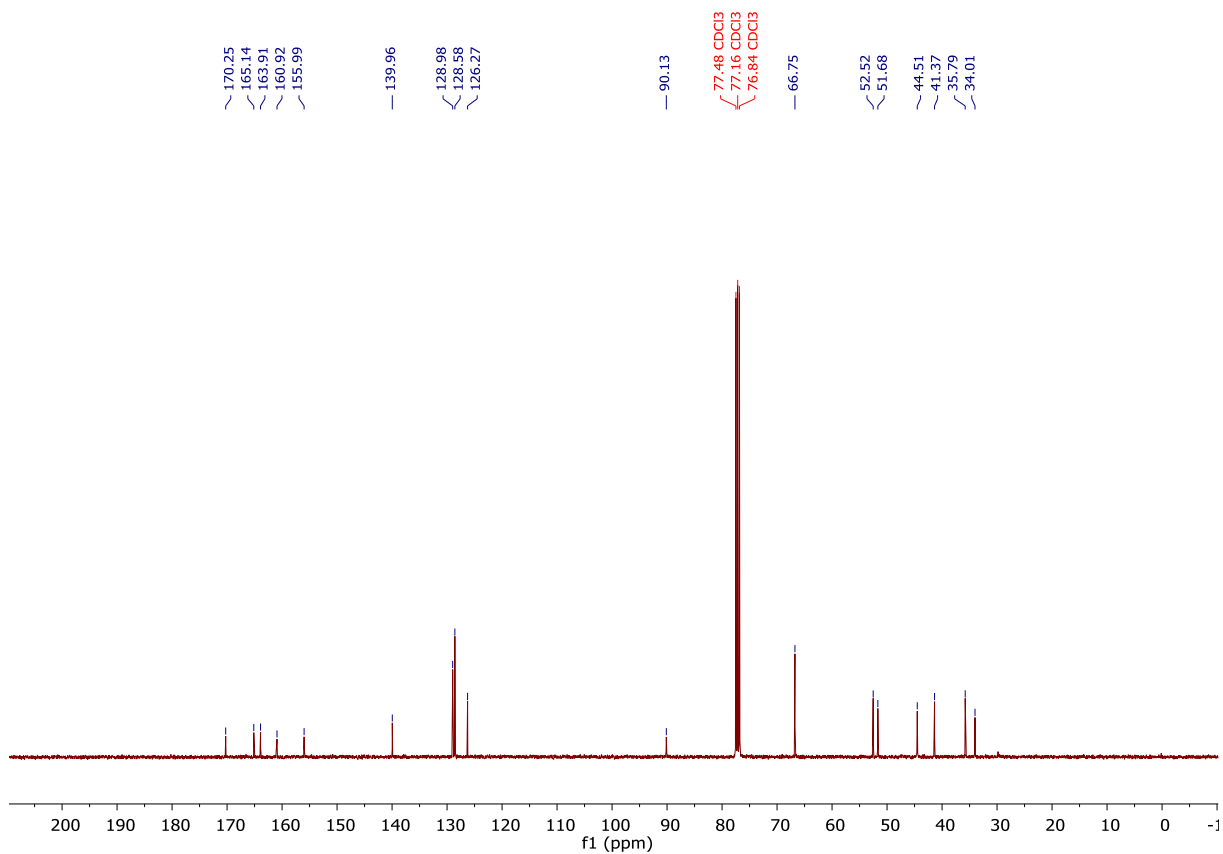
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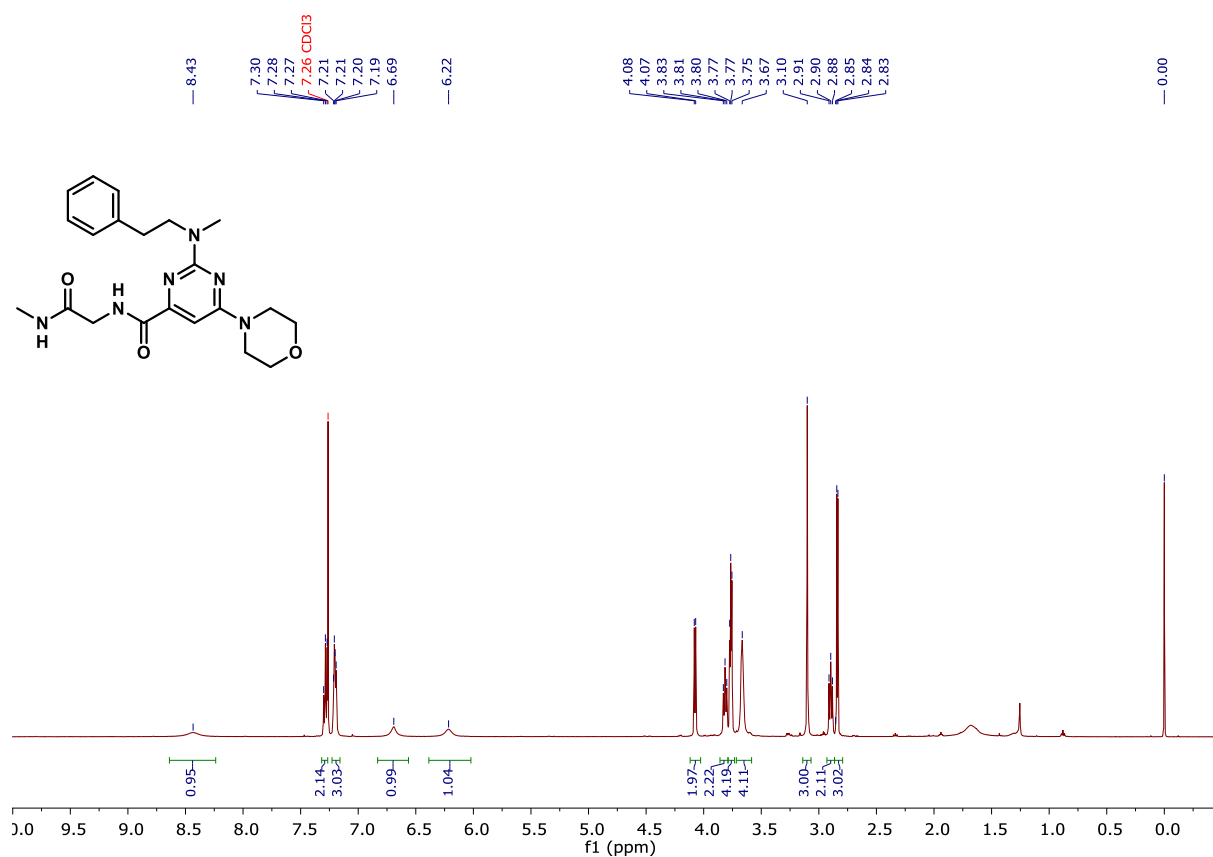
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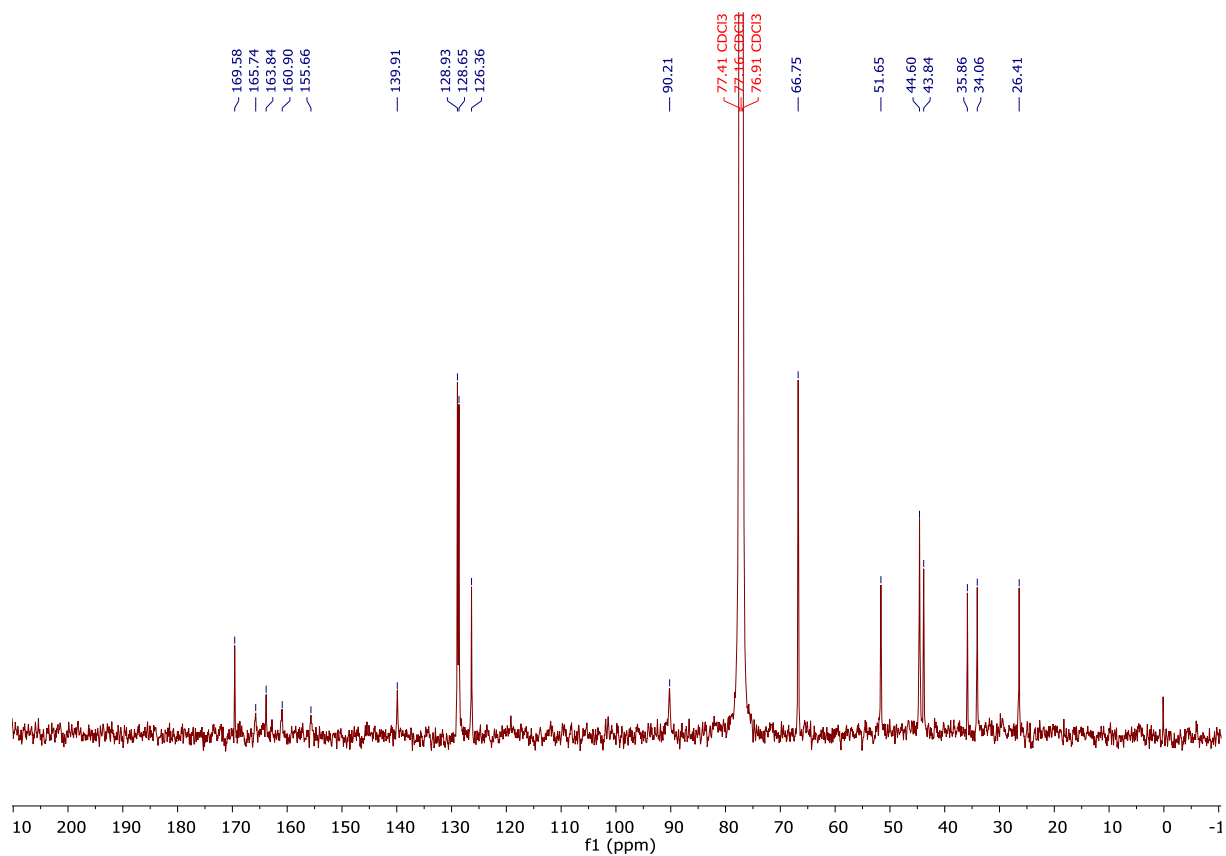
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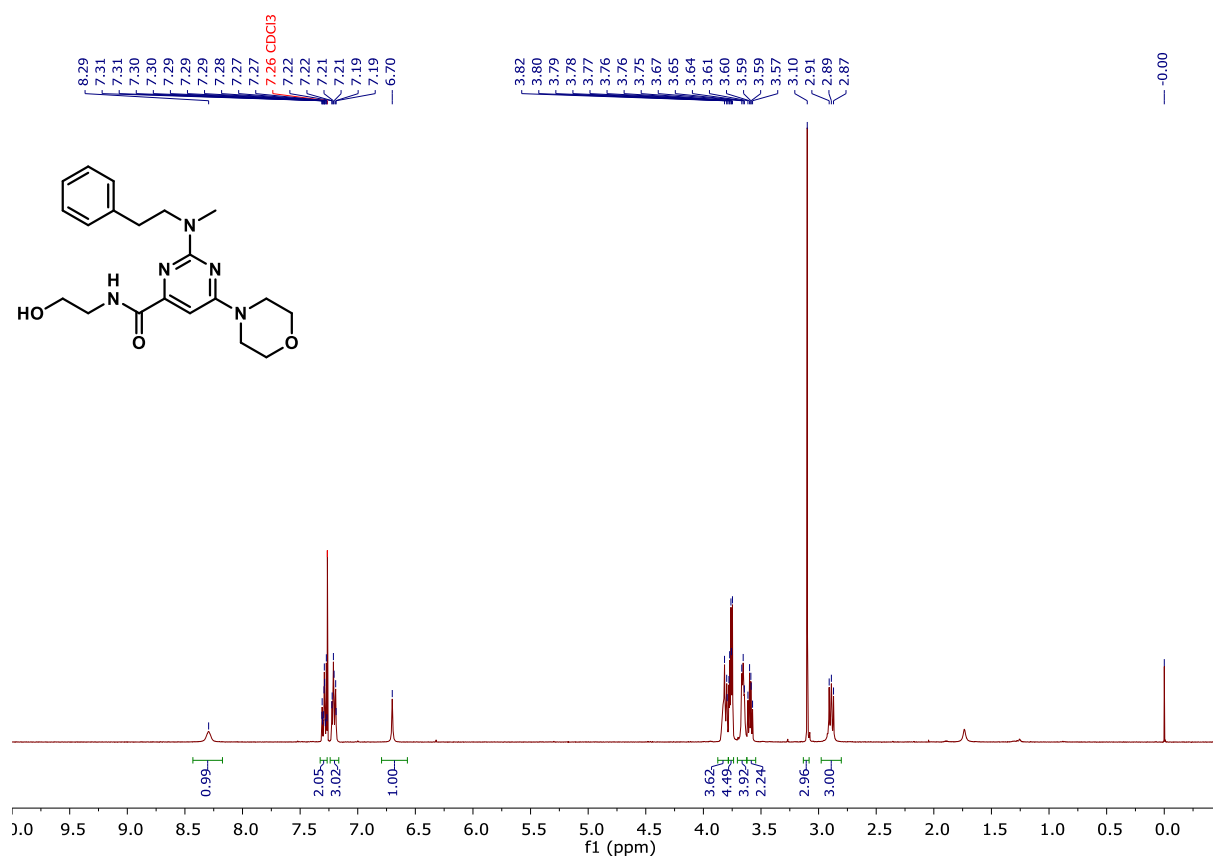
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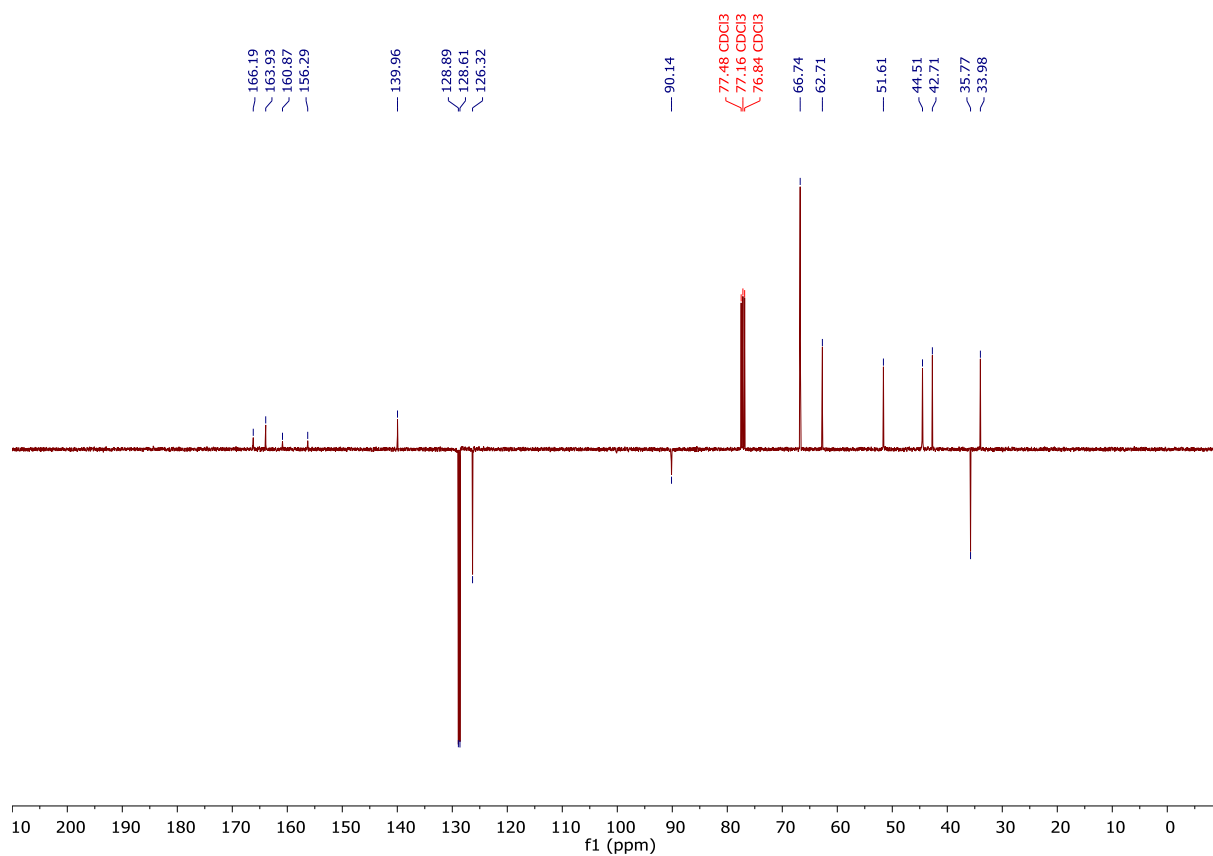
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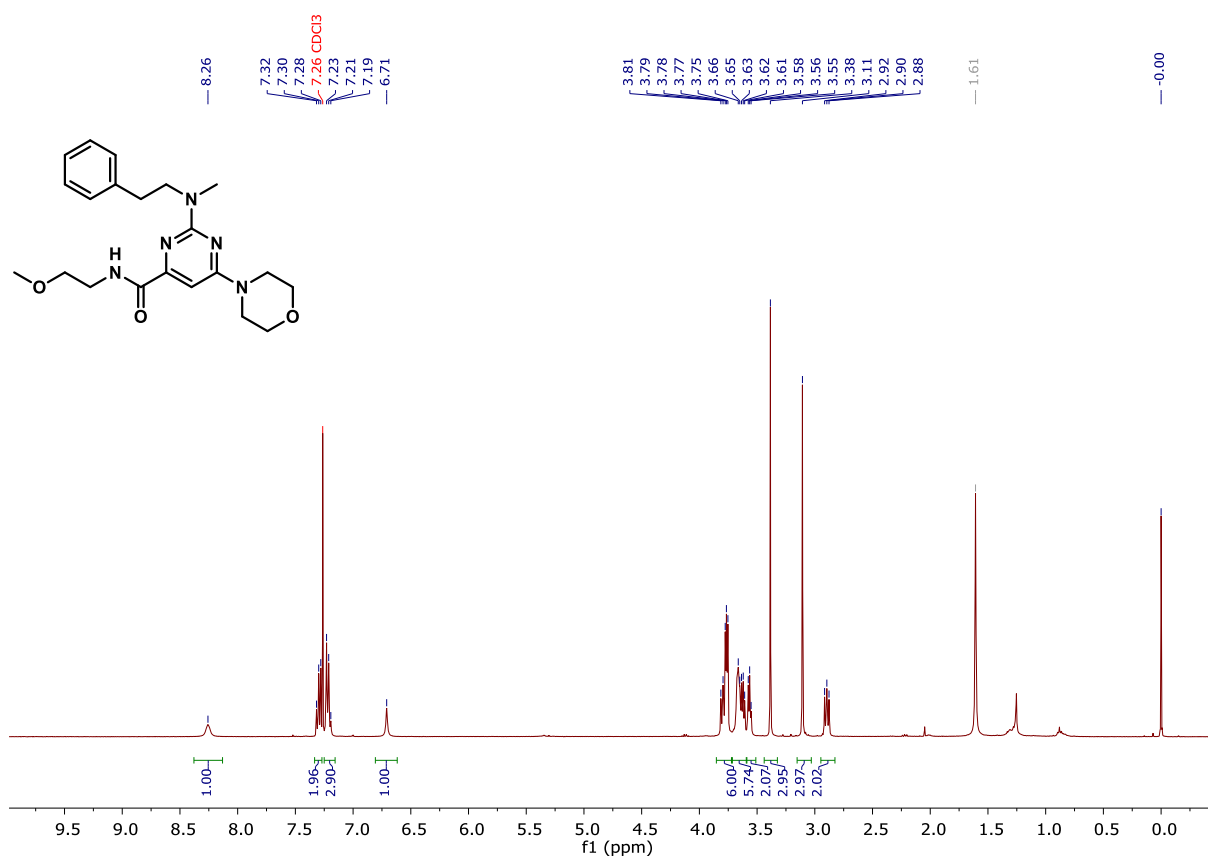
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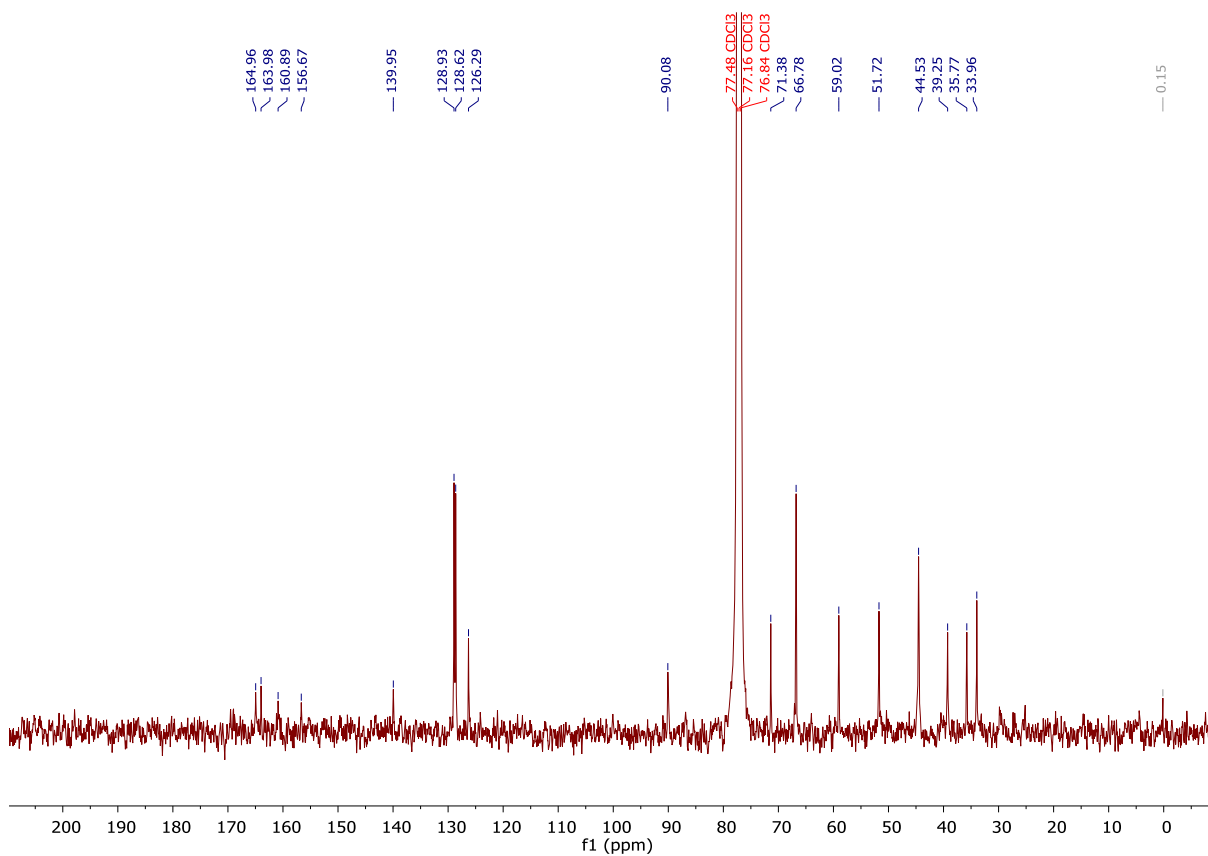
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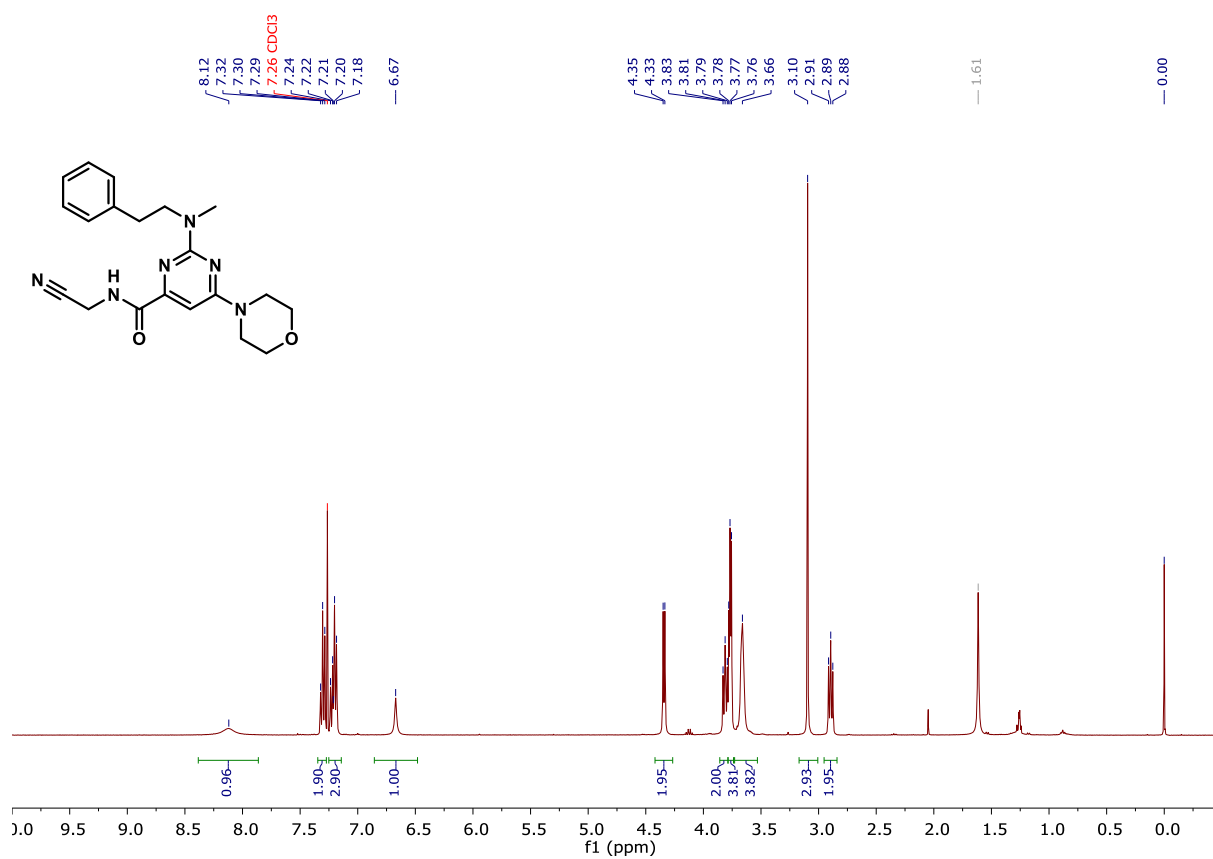
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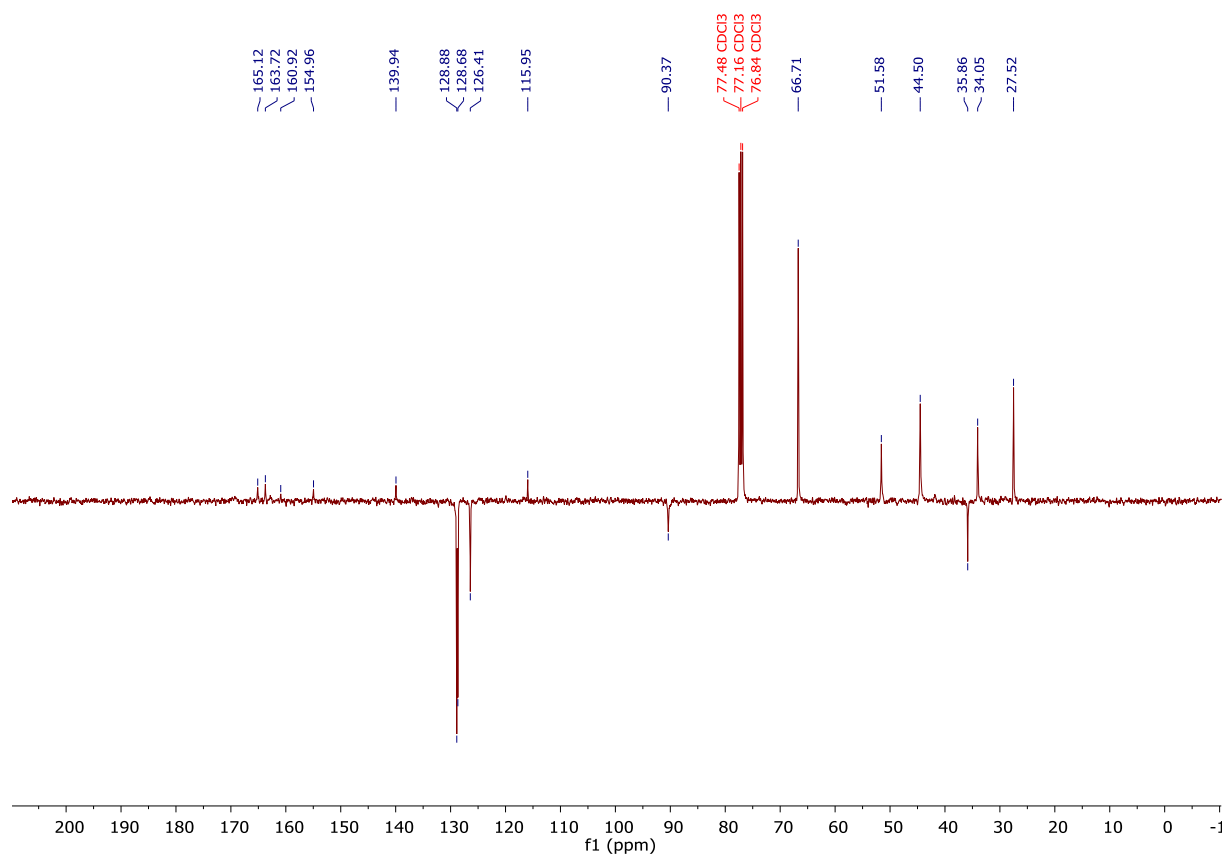
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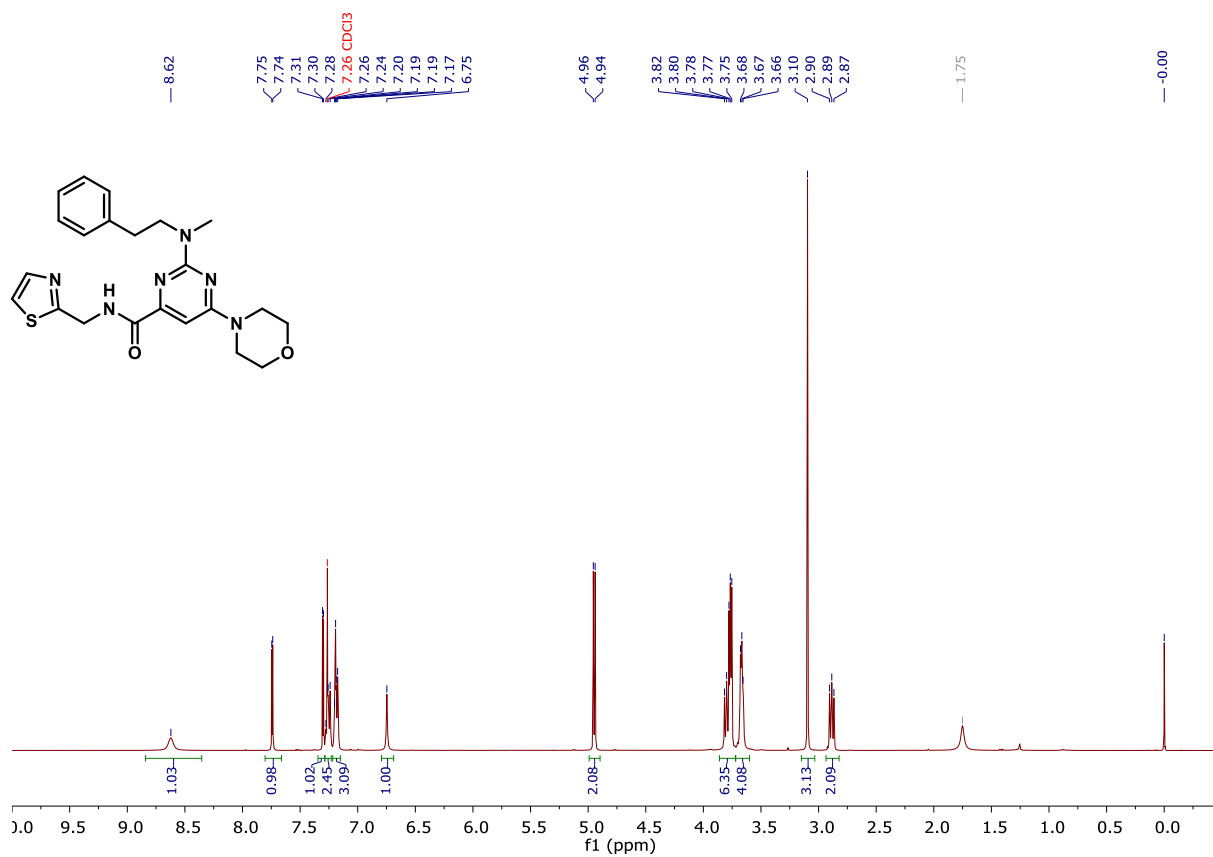
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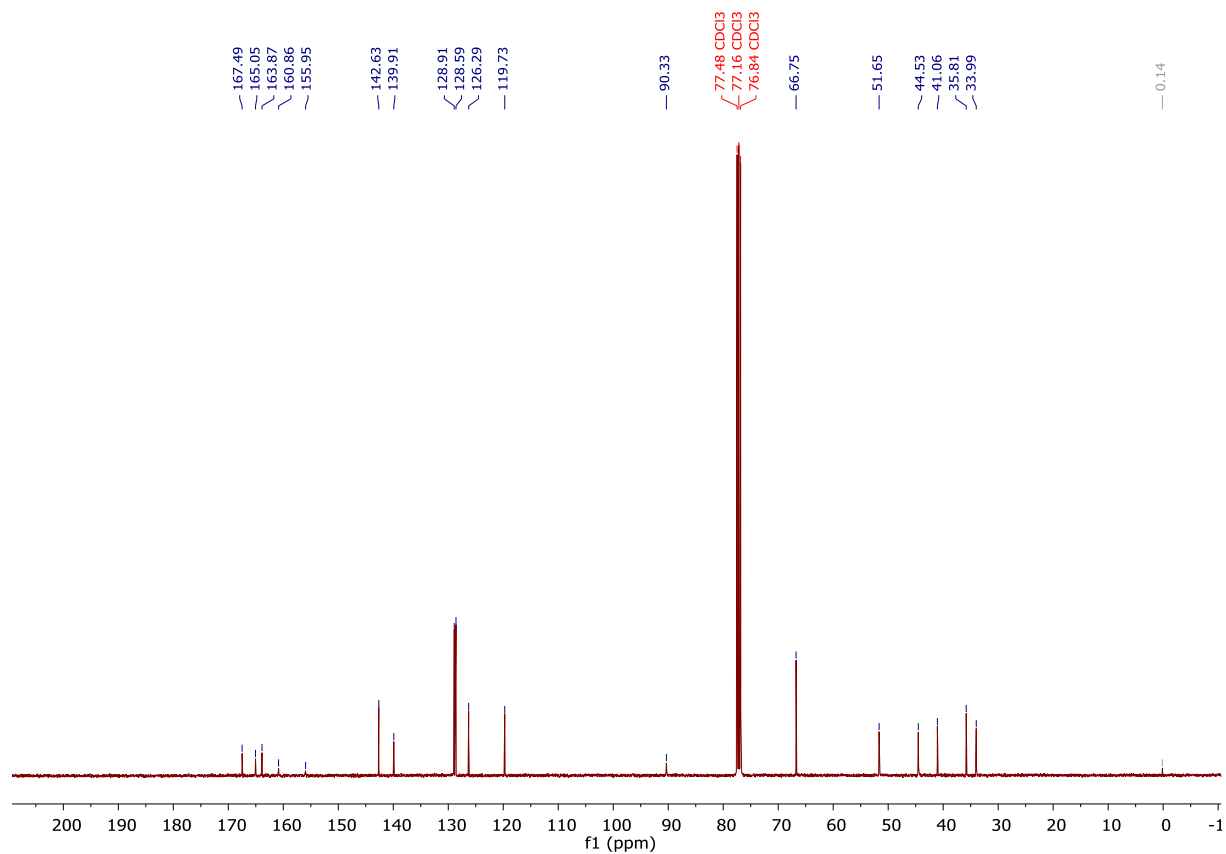
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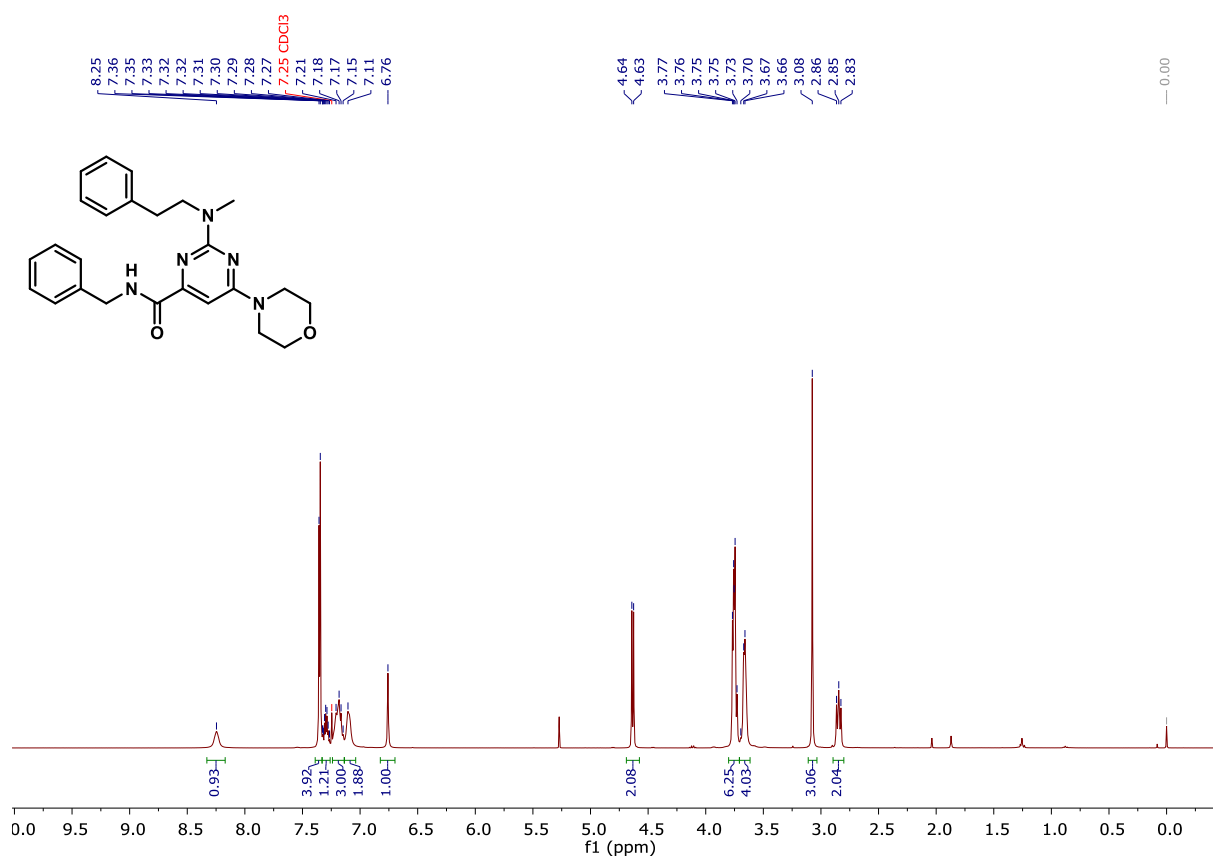
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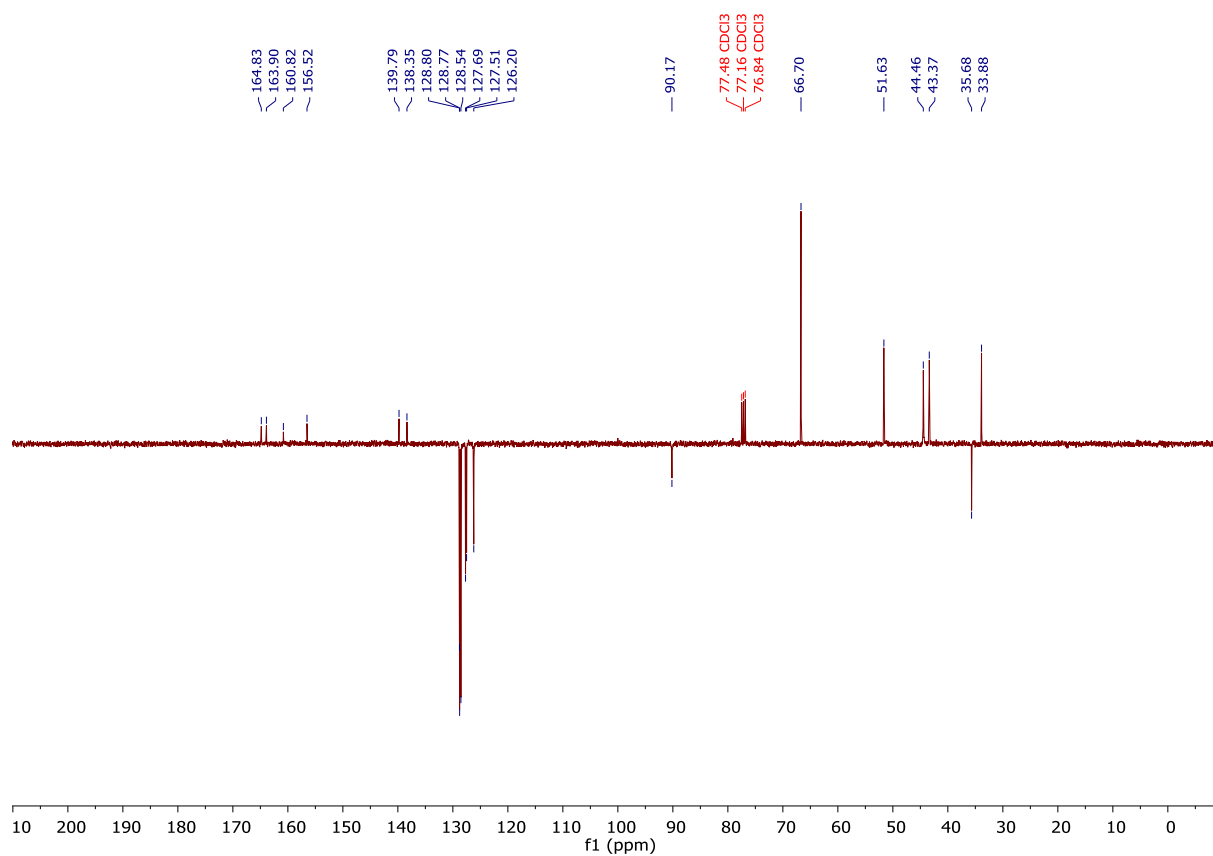
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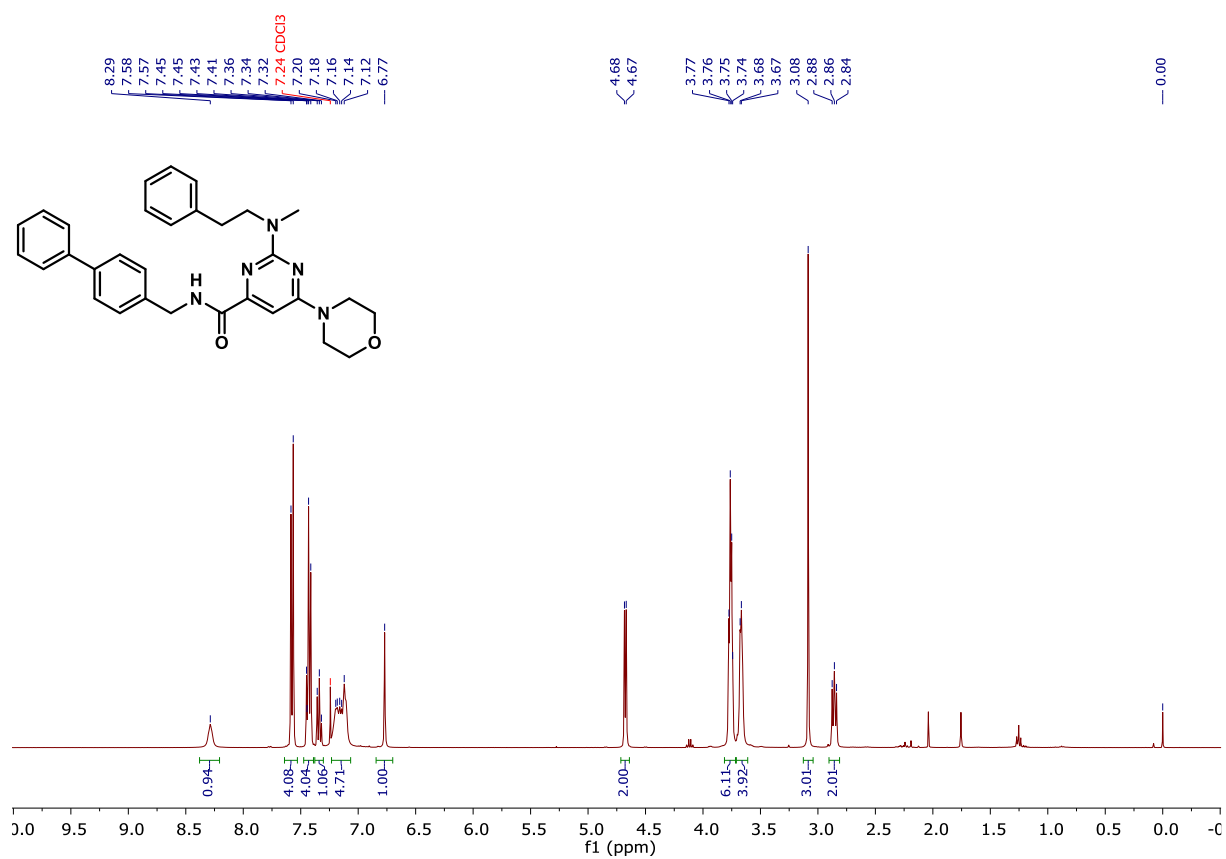
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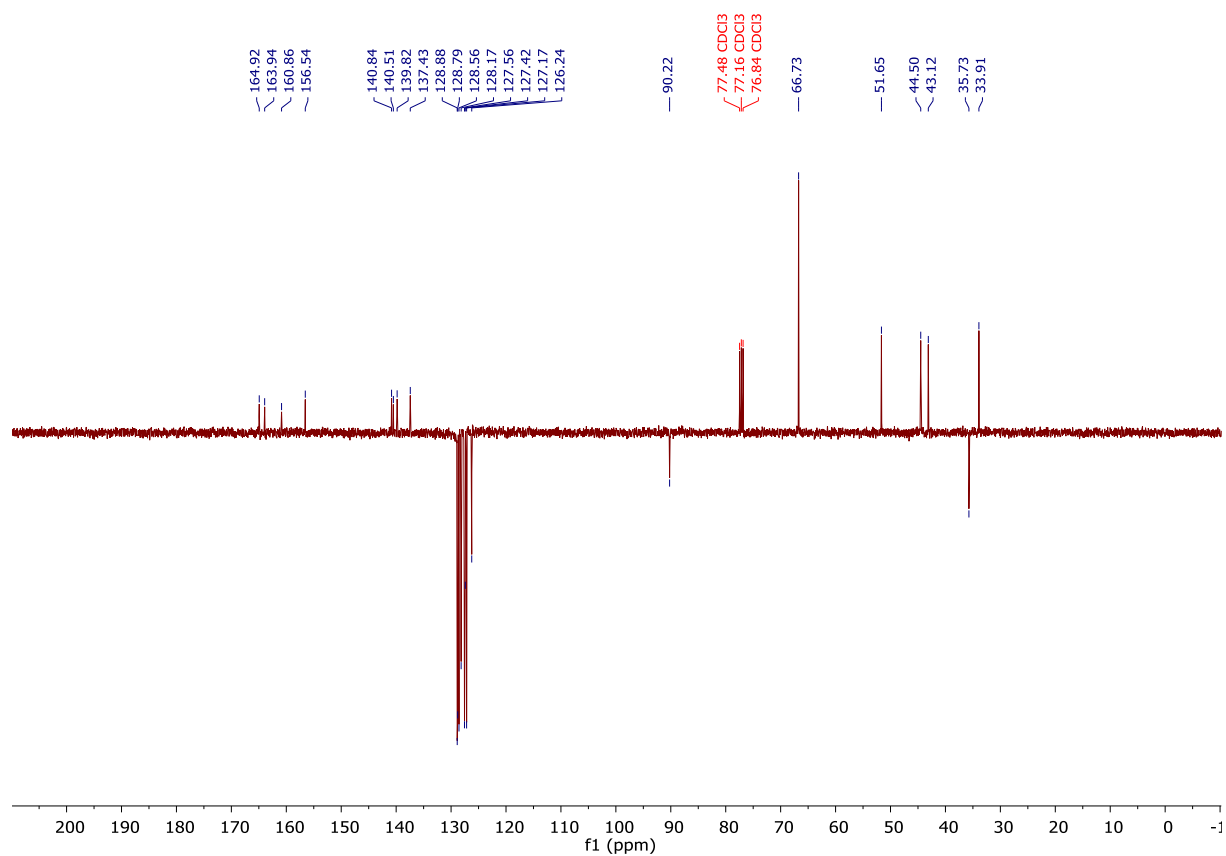
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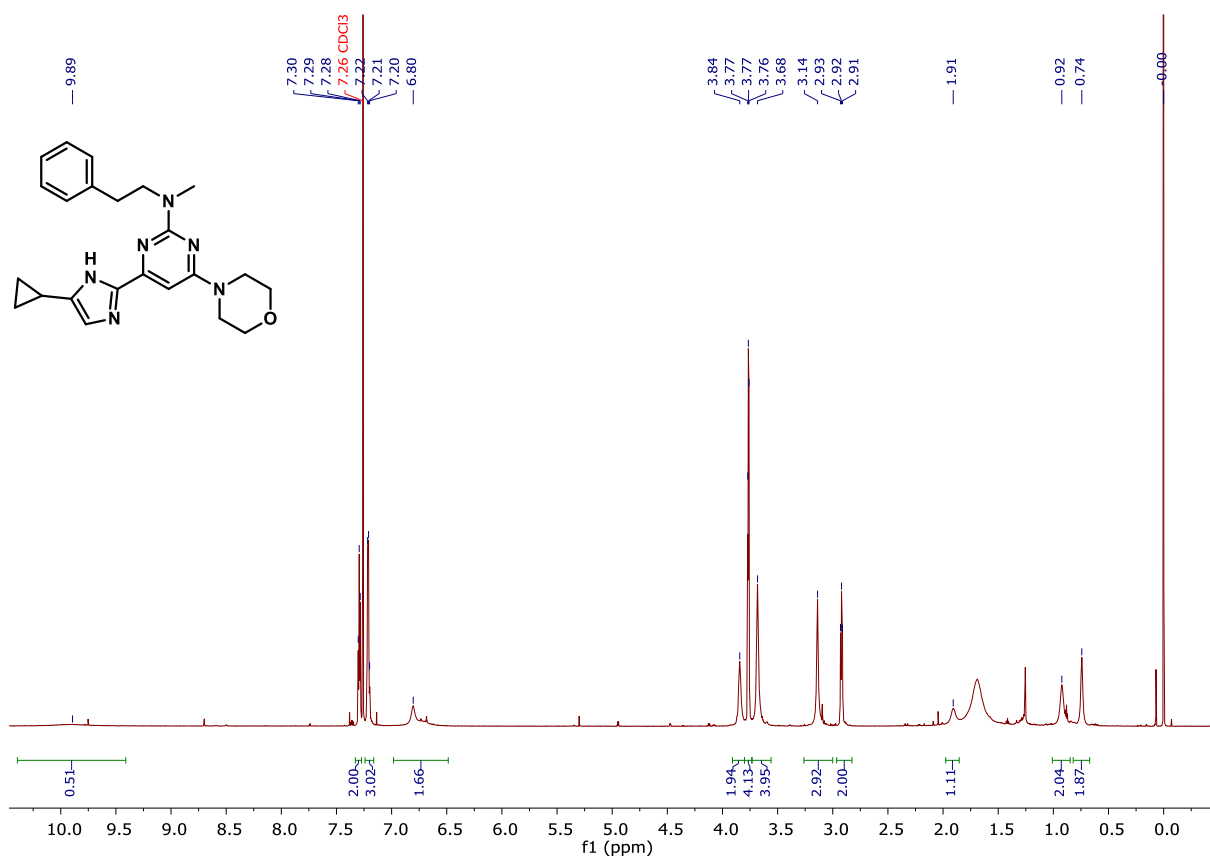
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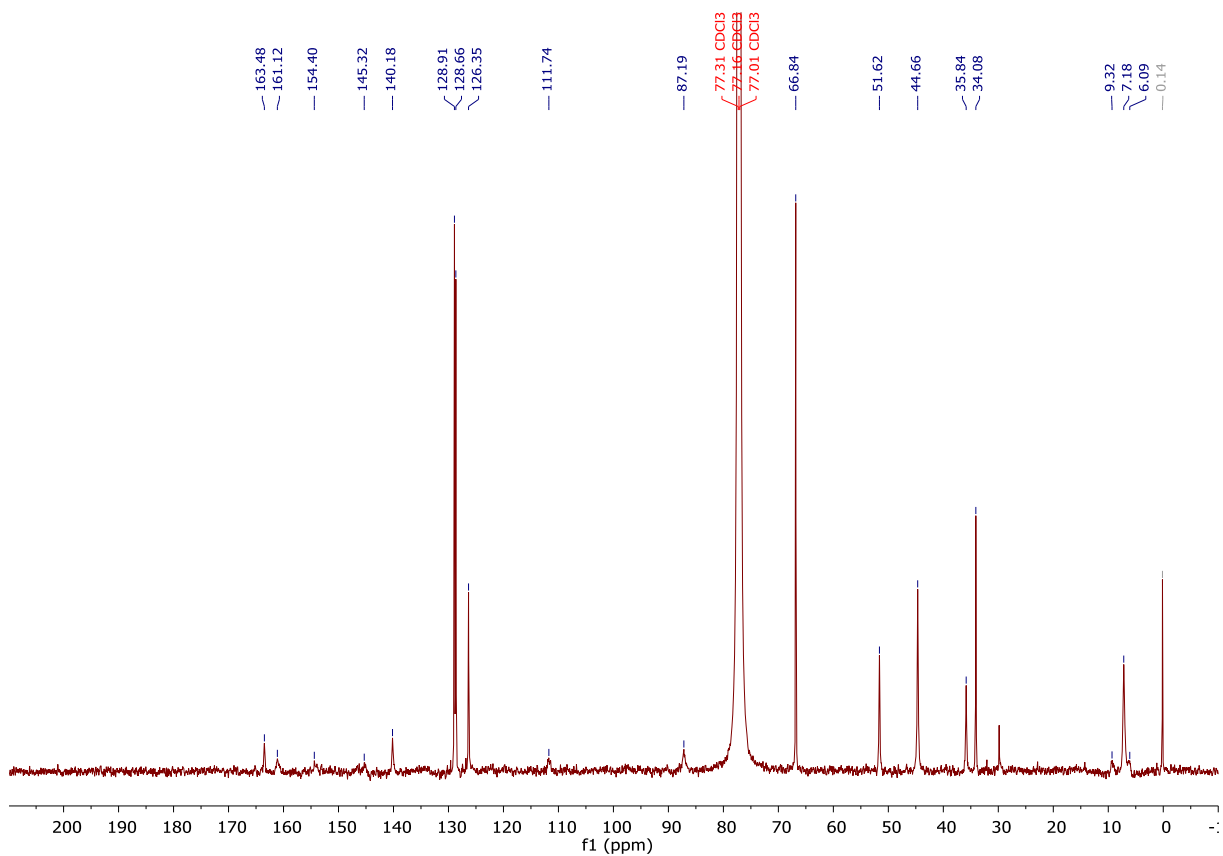
¹³C-NMR



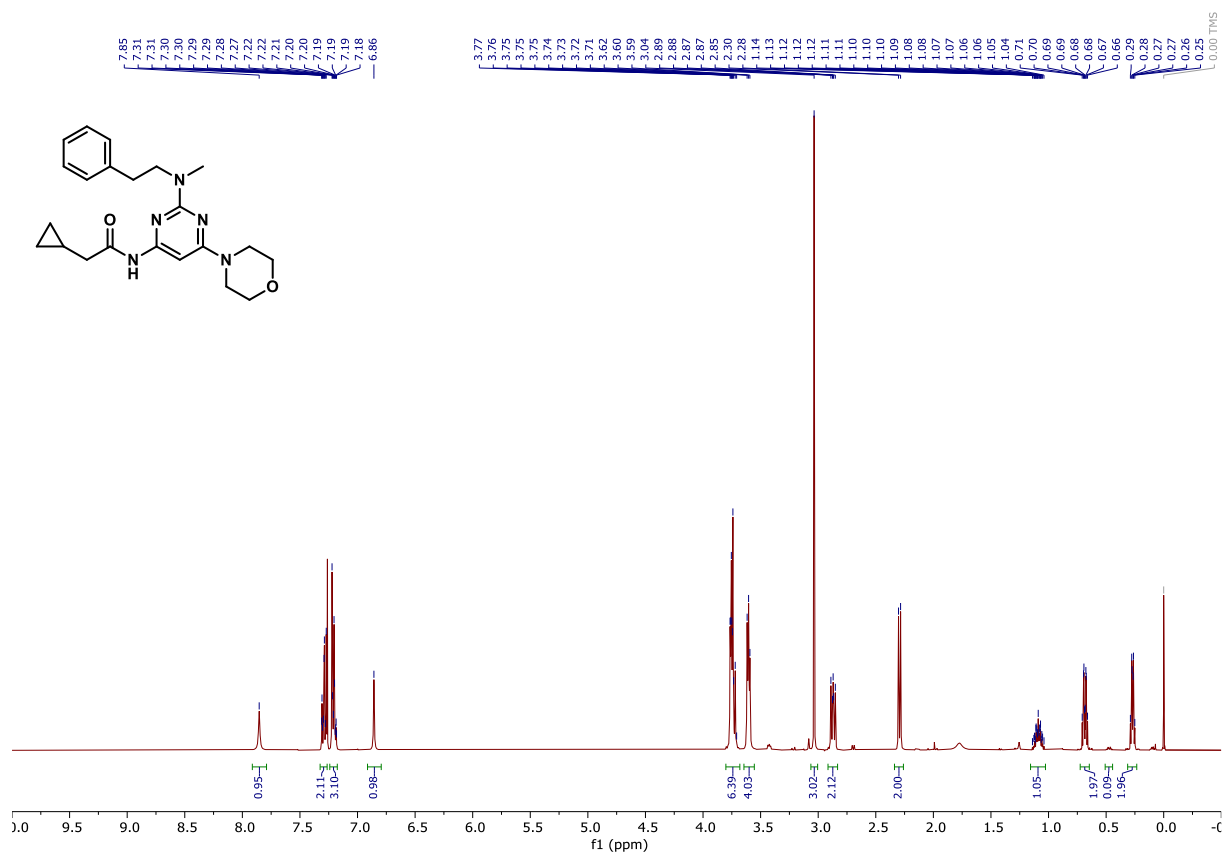
¹H-NMR: 29



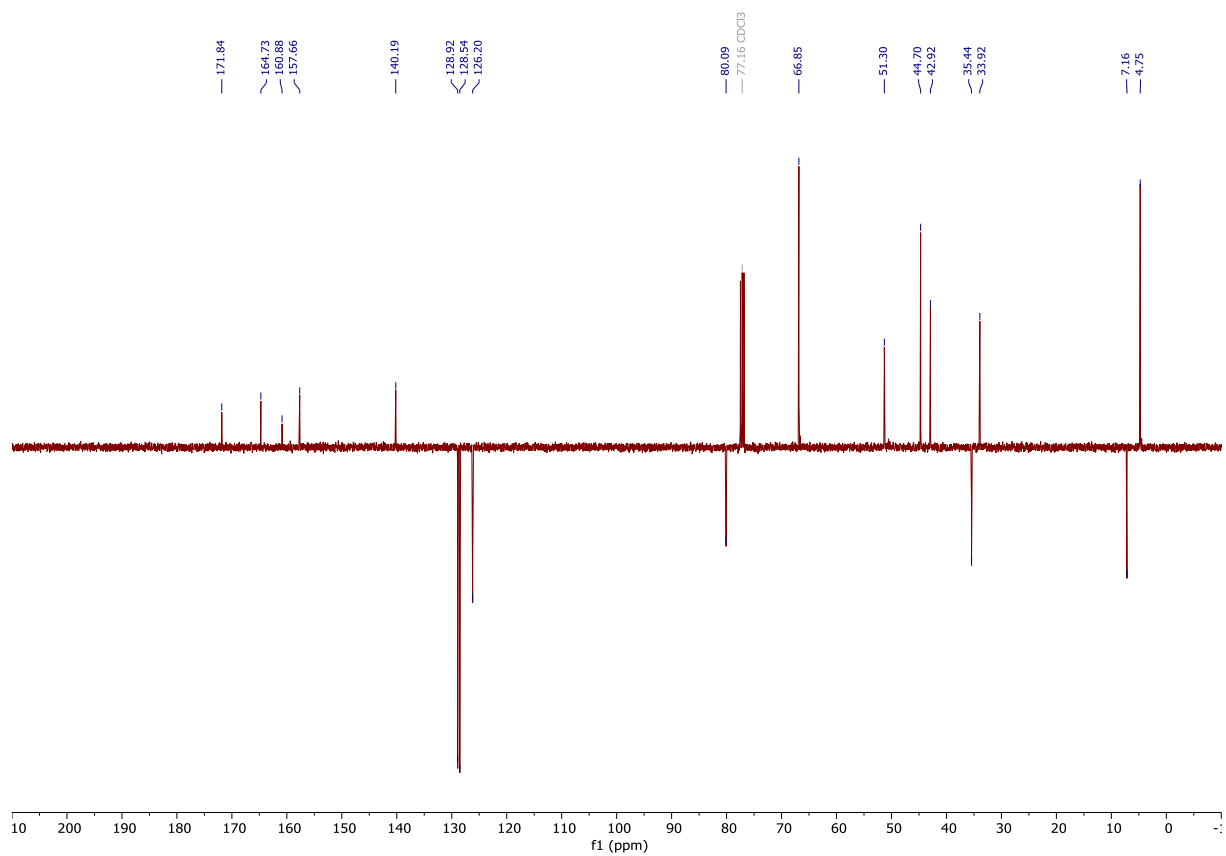
¹³C-NMR



¹H-NMR: 30



¹³C-NMR



Chemical structure: C1CC1CCNC(=O)c2cc(Cl)nnc2N3CCOCC3

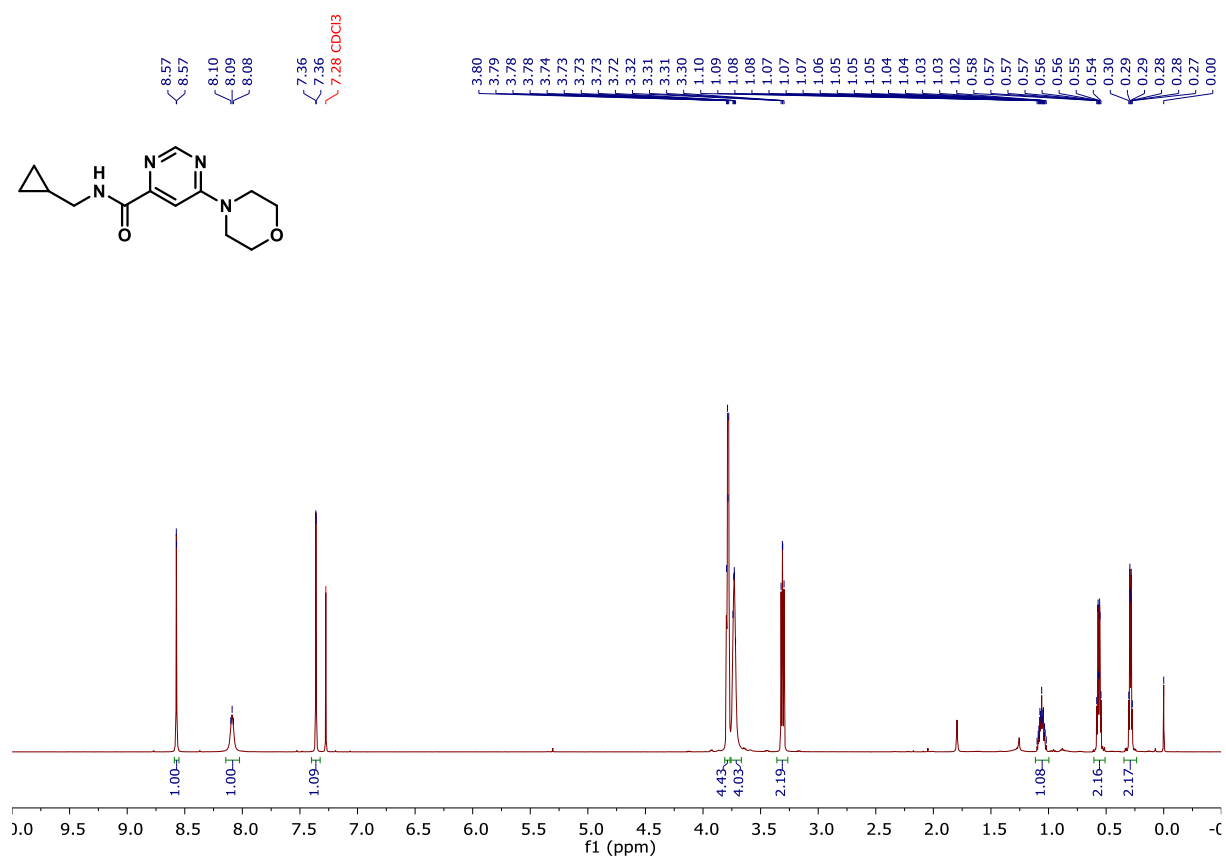
¹H NMR spectrum (ppm):

- 7.95, 7.94, 7.92 (aromatic, integration 1.04)
- 7.28 (aromatic, integration 1.00)
- 3.79, 3.78, 3.77, 3.74, 3.31, 3.29, 3.27 (multiplet, integration 8.23)
- 3.49, 3.48, 3.47, 3.46, 3.45, 3.44, 3.43, 3.42, 3.41, 3.40, 3.39, 3.38, 3.37, 3.36, 3.35, 3.34, 3.33, 3.32, 3.31, 3.30, 3.29, 3.28, 3.27, 3.26, 3.25, 3.24, 3.23, 3.22, 3.21, 3.20, 3.19, 3.18, 3.17, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00, 2.99, 2.98, 2.97, 2.96, 2.95, 2.94, 2.93, 2.92, 2.91, 2.90, 2.89, 2.88, 2.87, 2.86, 2.85, 2.84, 2.83, 2.82, 2.81, 2.80, 2.79, 2.78, 2.77, 2.76, 2.75, 2.74, 2.73, 2.72, 2.71, 2.70, 2.69, 2.68, 2.67, 2.66, 2.65, 2.64, 2.63, 2.62, 2.61, 2.60, 2.59, 2.58, 2.57, 2.56, 2.55, 2.54, 2.53, 2.52, 2.51, 2.50, 2.49, 2.48, 2.47, 2.46, 2.45, 2.44, 2.43, 2.42, 2.41, 2.40, 2.39, 2.38, 2.37, 2.36, 2.35, 2.34, 2.33, 2.32, 2.31, 2.30, 2.29, 2.28, 2.27, 2.26, 2.25, 2.24, 2.23, 2.22, 2.21, 2.20, 2.19, 2.18, 2.17, 2.16, 2.15, 2.14, 2.13, 2.12, 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96, 1.95, 1.94, 1.93, 1.92, 1.91, 1.90, 1.89, 1.88, 1.87, 1.86, 1.85, 1.84, 1.83, 1.82, 1.81, 1.80, 1.79, 1.78, 1.77, 1.76, 1.75, 1.74, 1.73, 1.72, 1.71, 1.70, 1.69, 1.68, 1.67, 1.66, 1.65, 1.64, 1.63, 1.62, 1.61, 1.60, 1.59, 1.58, 1.57, 1.56, 1.55, 1.54, 1.53, 1.52, 1.51, 1.50, 1.49, 1.48, 1.47, 1.46, 1.45, 1.44, 1.43, 1.42, 1.41, 1.40, 1.39, 1.38, 1.37, 1.36, 1.35, 1.34, 1.33, 1.32, 1.31, 1.30, 1.29, 1.28, 1.27, 1.26, 1.25, 1.24, 1.23, 1.22, 1.21, 1.20, 1.19, 1.18, 1.17, 1.16, 1.15, 1.14, 1.13, 1.12, 1.11, 1.10, 1.09, 1.08, 1.07, 1.06, 1.05, 1.04, 1.03, 1.02, 1.01, 1.00, 0.99, 0.98, 0.97, 0.96, 0.95, 0.94, 0.93, 0.92, 0.91, 0.90, 0.89, 0.88, 0.87, 0.86, 0.85, 0.84, 0.83, 0.82, 0.81, 0.80, 0.79, 0.78, 0.77, 0.76, 0.75, 0.74, 0.73, 0.72, 0.71, 0.70, 0.69, 0.68, 0.67, 0.66, 0.65, 0.64, 0.63, 0.62, 0.61, 0.60, 0.59, 0.58, 0.57, 0.56, 0.55, 0.54, 0.53, 0.52, 0.51, 0.50, 0.49, 0.48, 0.47, 0.46, 0.45, 0.44, 0.43, 0.42, 0.41, 0.40, 0.39, 0.38, 0.37, 0.36, 0.35, 0.34, 0.33, 0.32, 0.31, 0.30, 0.29, 0.28, 0.27, 0.26, 0.25, 0.24, 0.23, 0.22, 0.21, 0.20, 0.19, 0.18, 0.17, 0.16, 0.15, 0.14, 0.13, 0.12, 0.11, 0.10, 0.09, 0.08, 0.07, 0.06, 0.05, 0.04, 0.03, 0.02, 0.01, 0.00

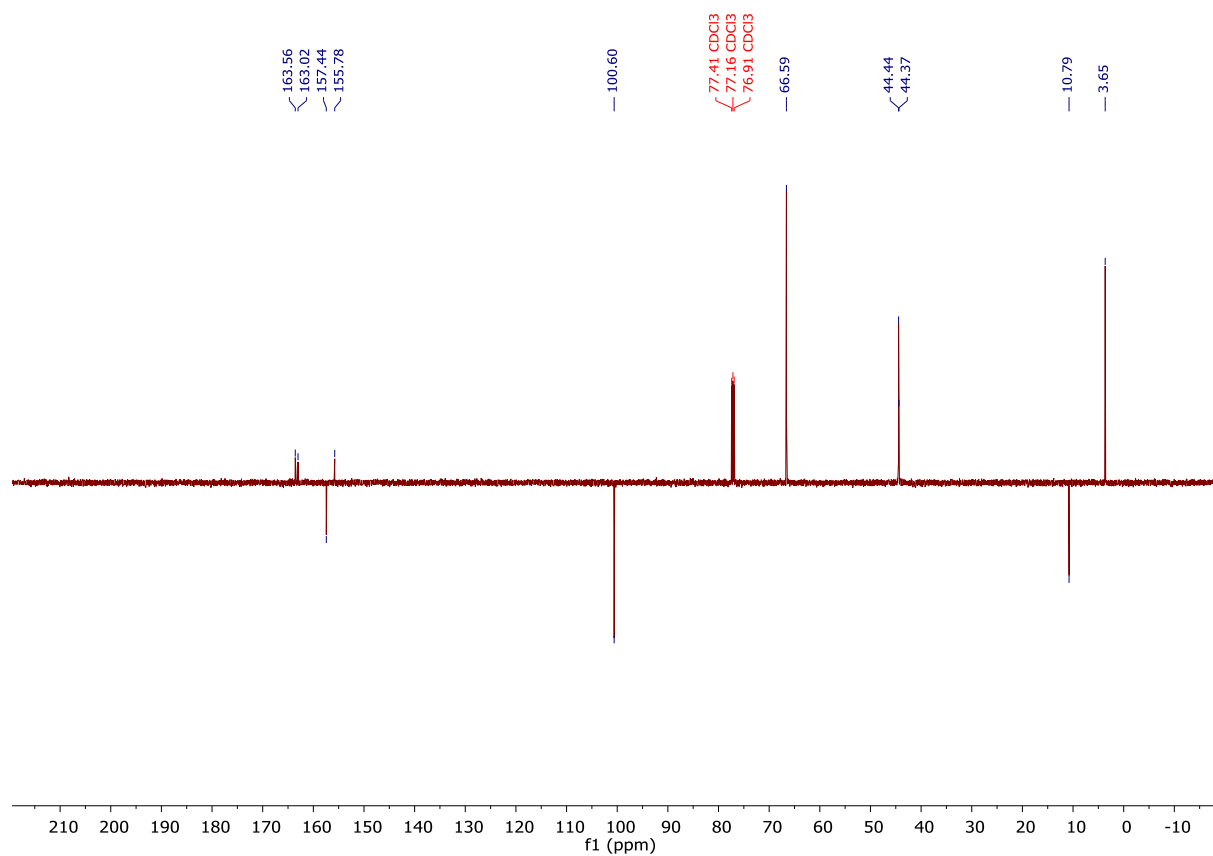
¹³C NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift f1 (ppm) from 10 to 210. The spectrum shows several peaks, with the following chemical shifts (ppm) labeled above the baseline:

- 163.83
- 162.21
- 159.84
- 157.90
- 99.36
- 77.48 CDCl₃
- 77.16 CDCl₃
- 76.84 CDCl₃
- 66.35
- 44.45
- 10.65
- 3.64

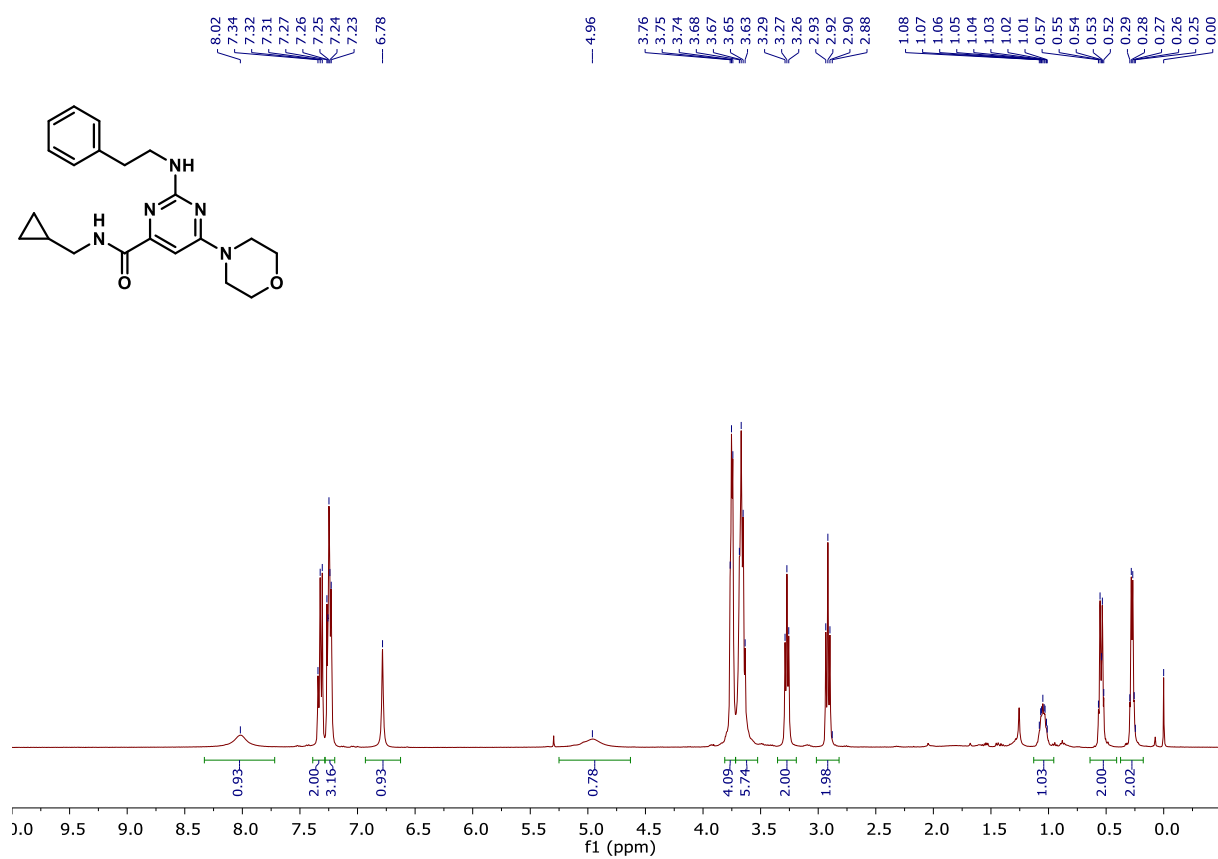
¹H-NMR: 32



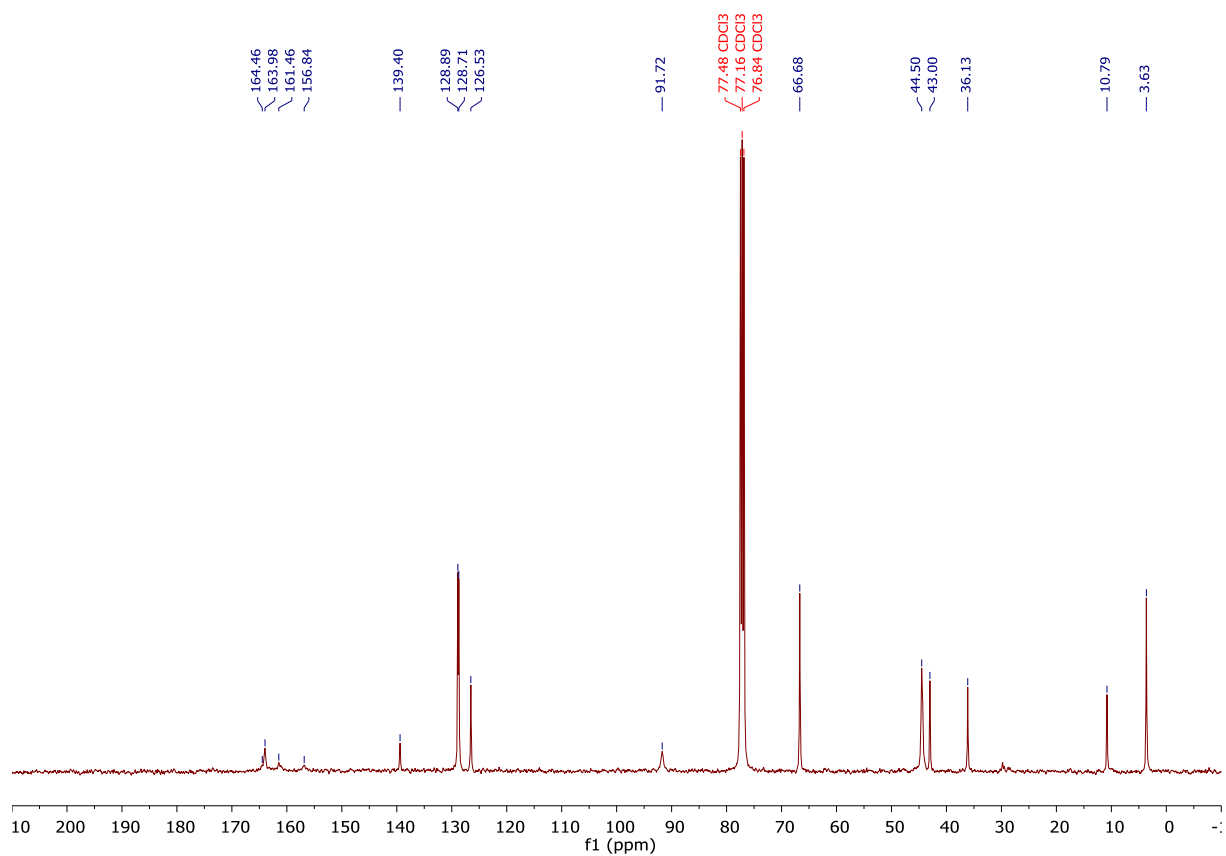
¹³C-NMR



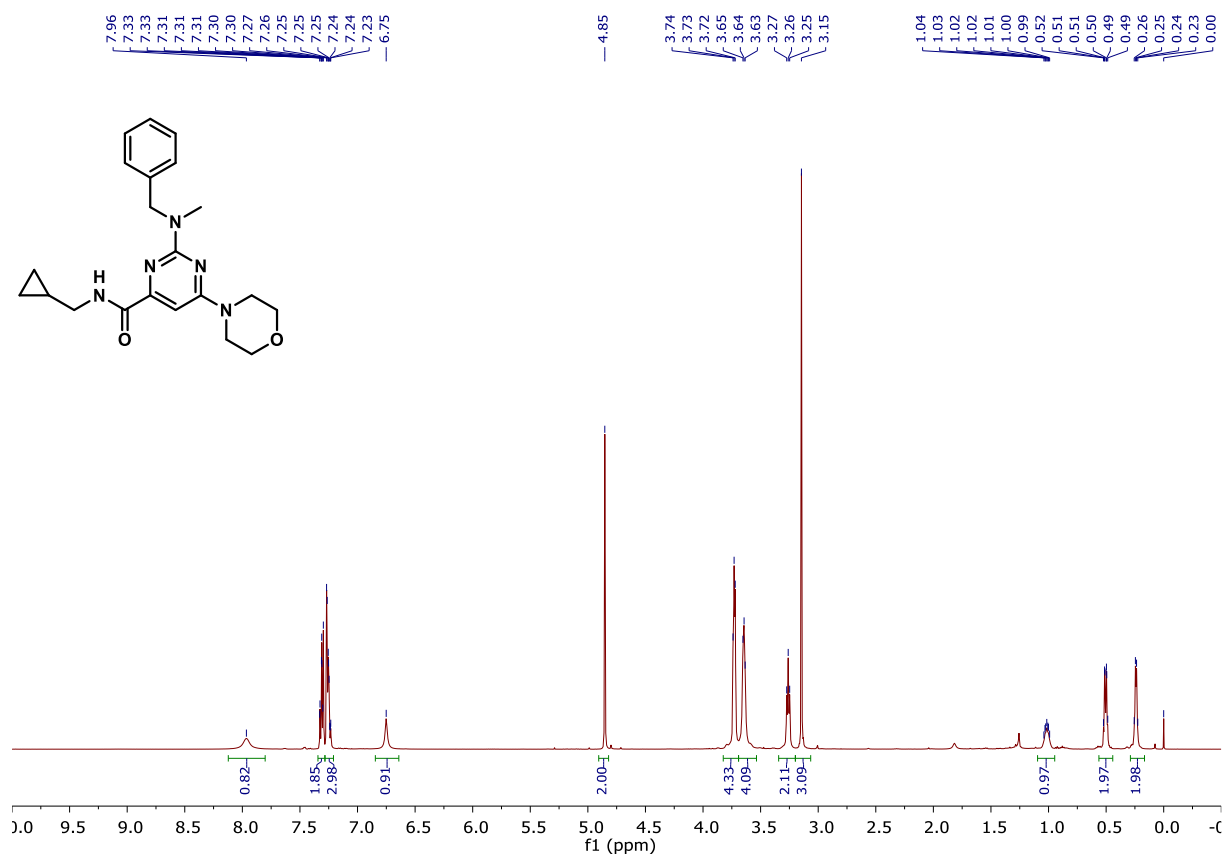
¹H-NMR: 33



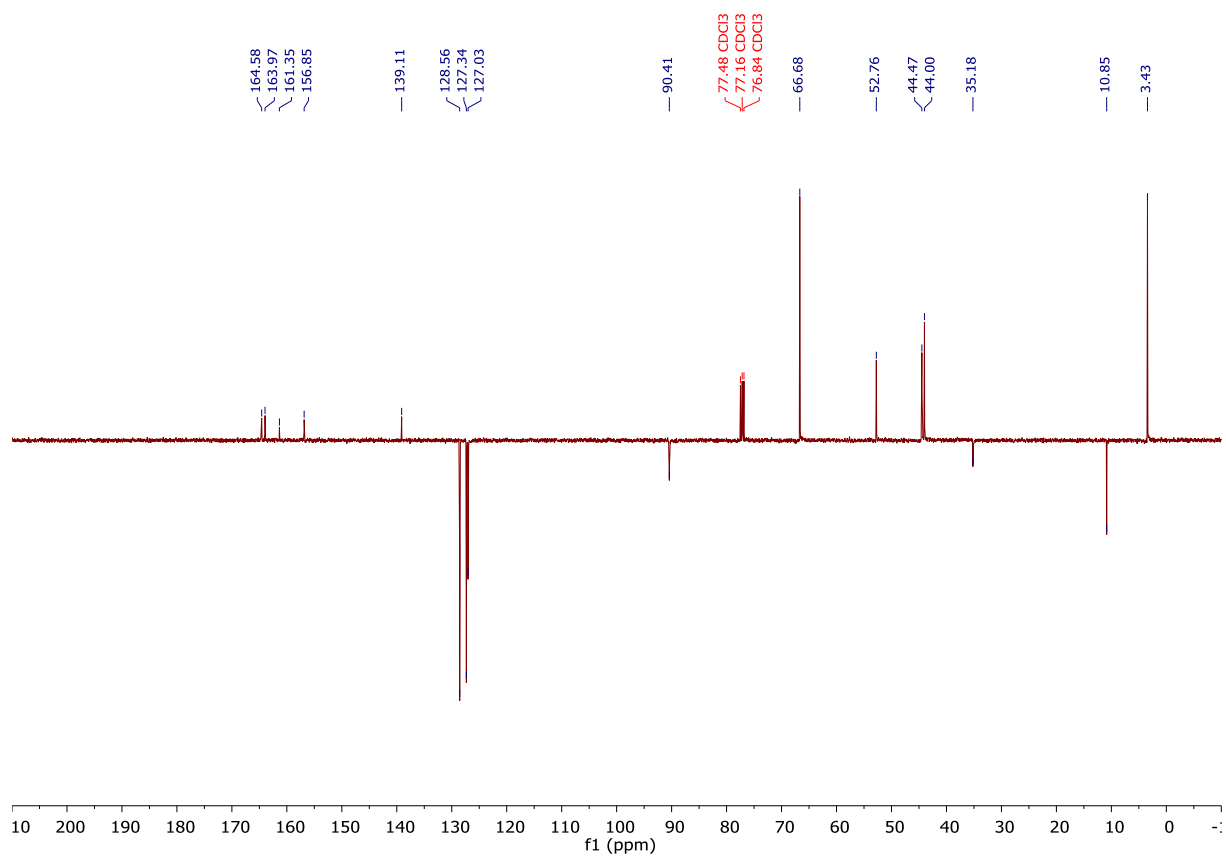
¹³C-NMR



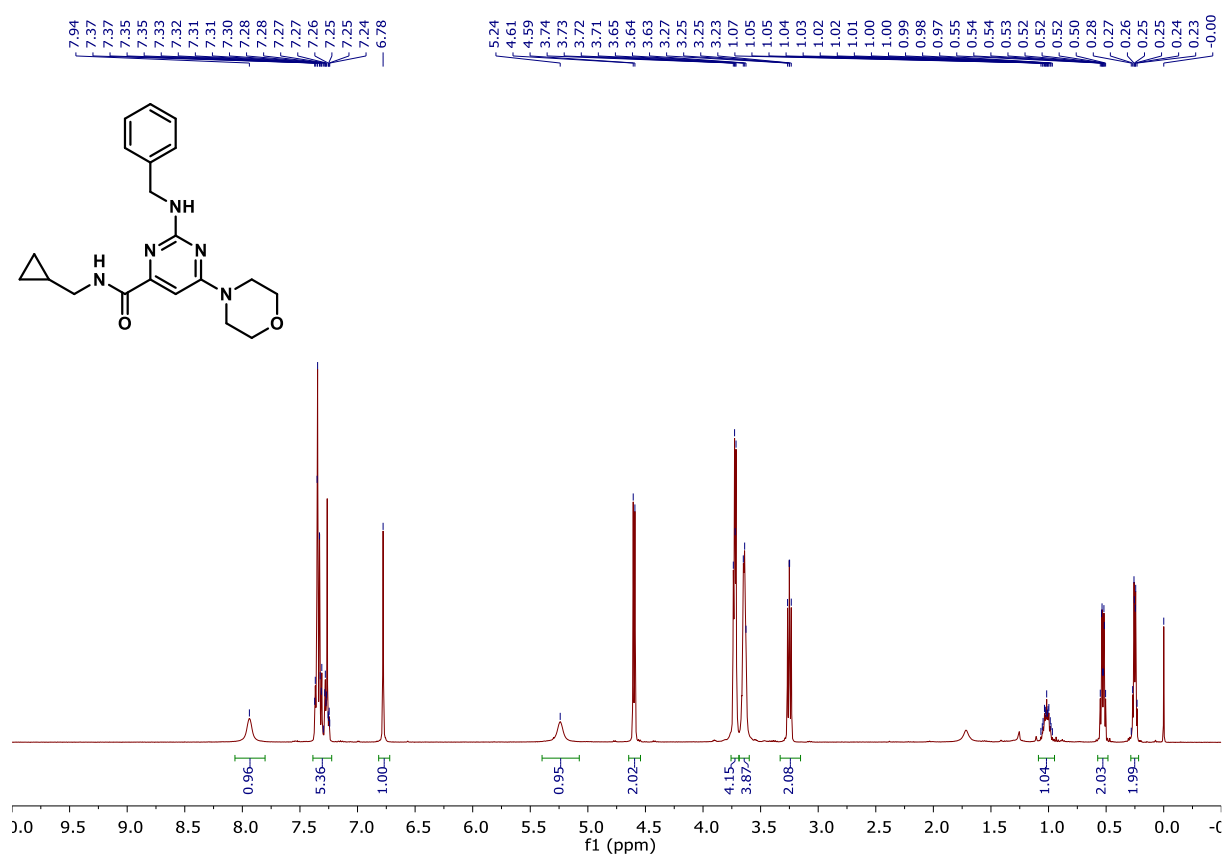
¹H-NMR: 34



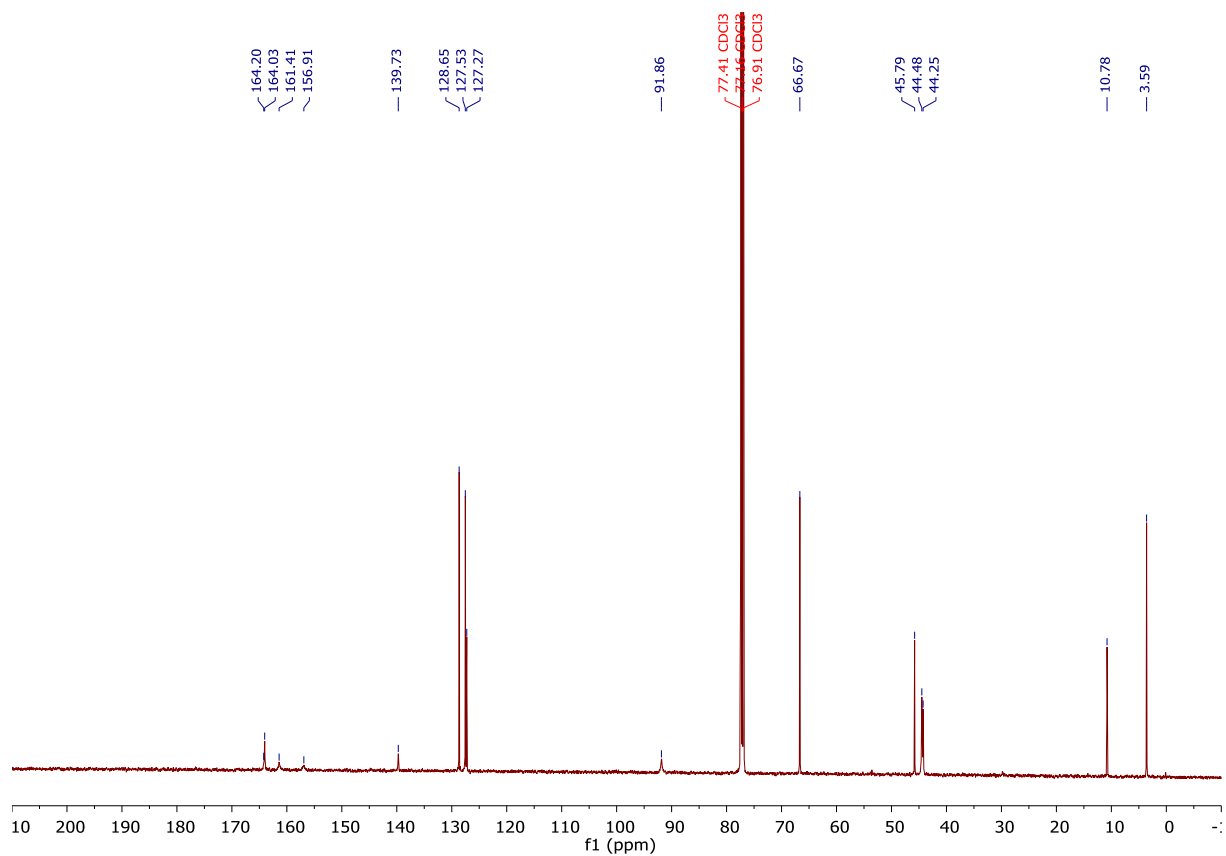
¹³C-NMR



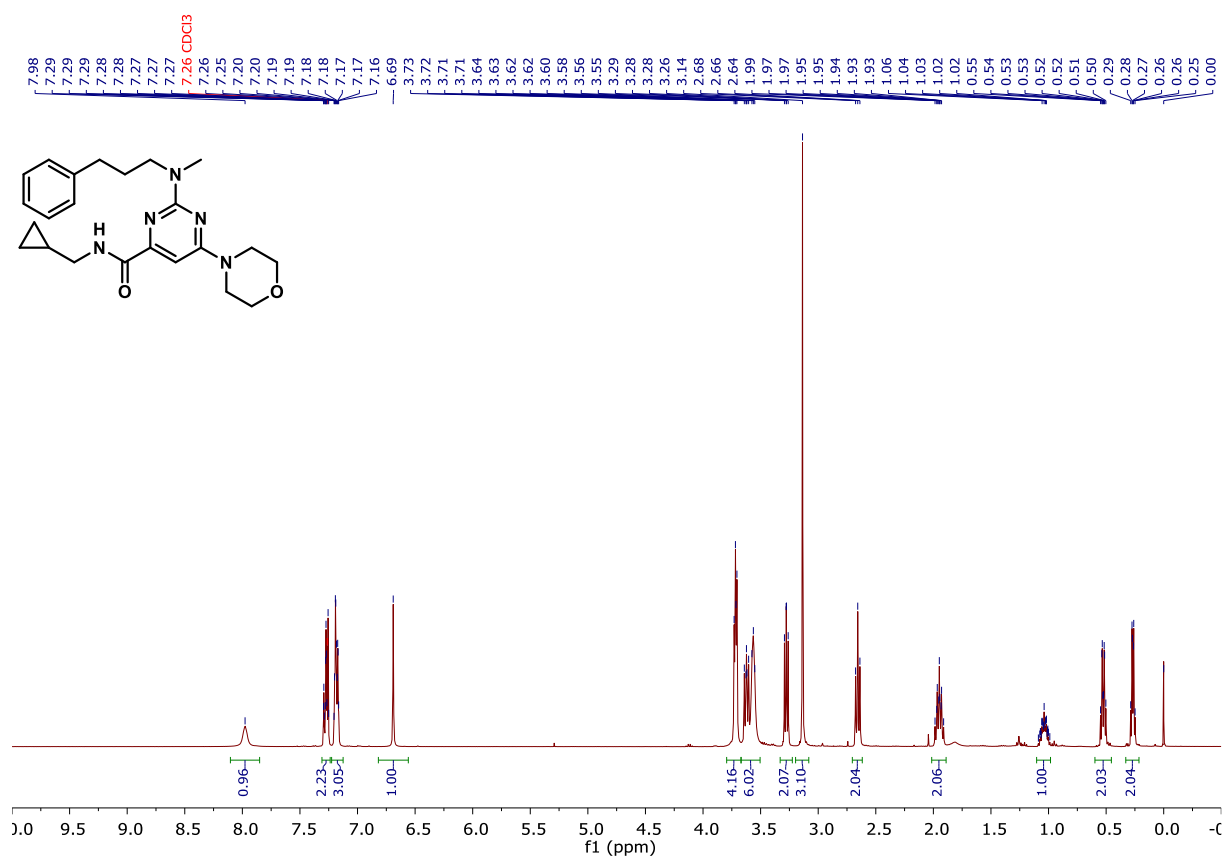
¹H-NMR: 35



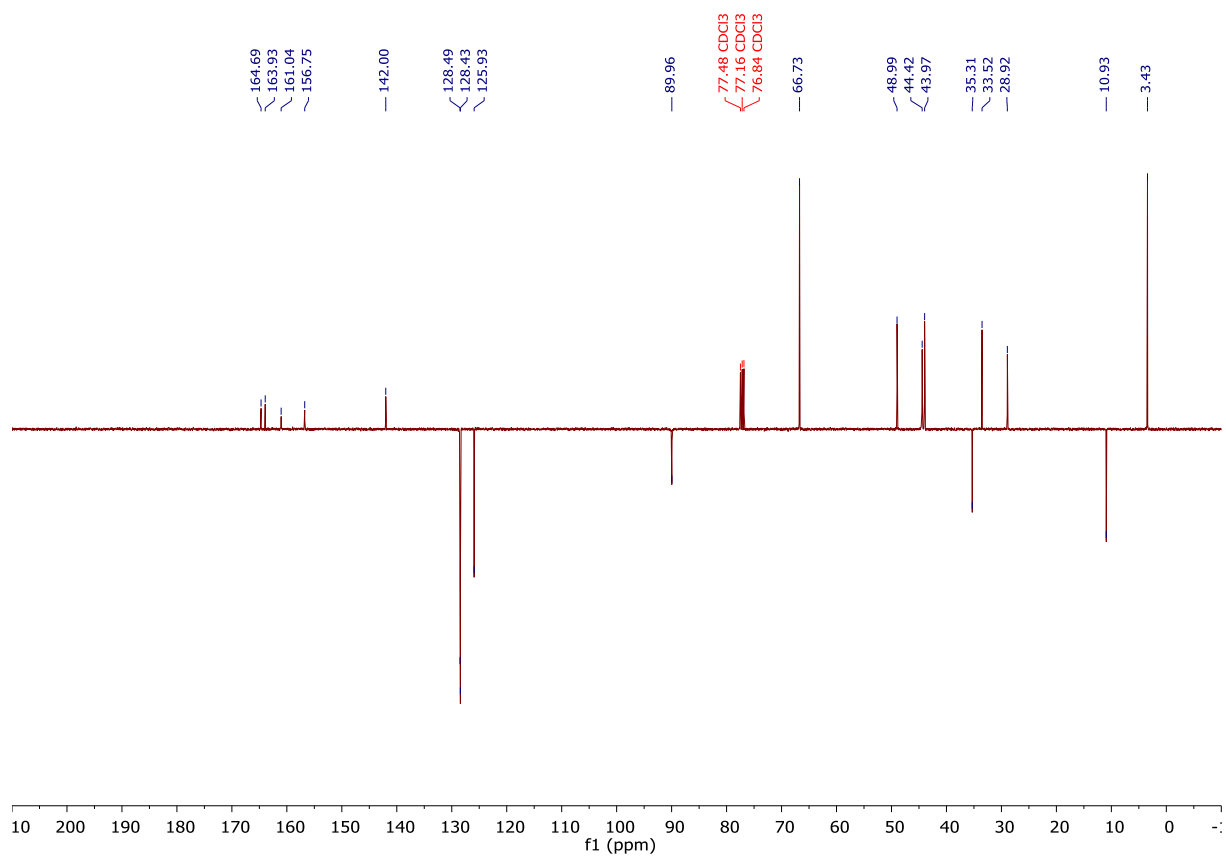
¹³C-NMR



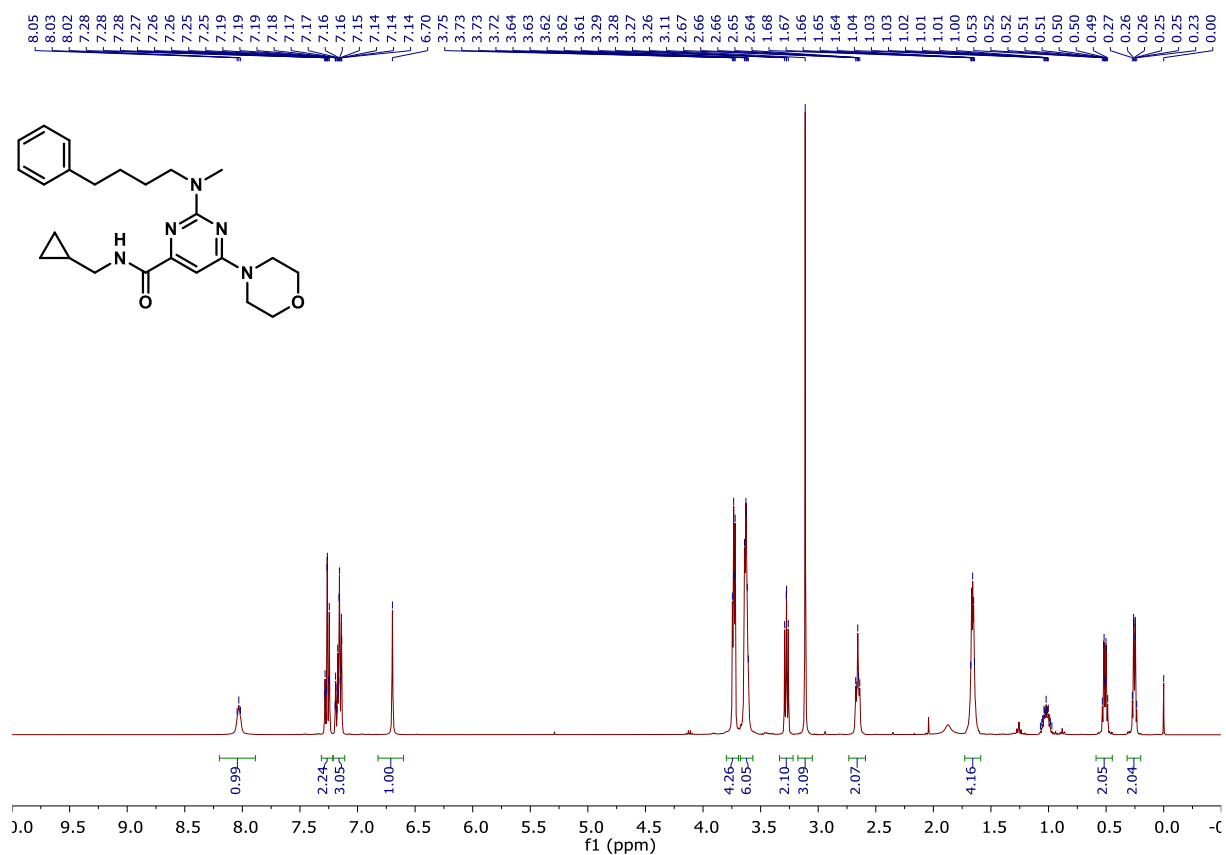
¹H-NMR: 36



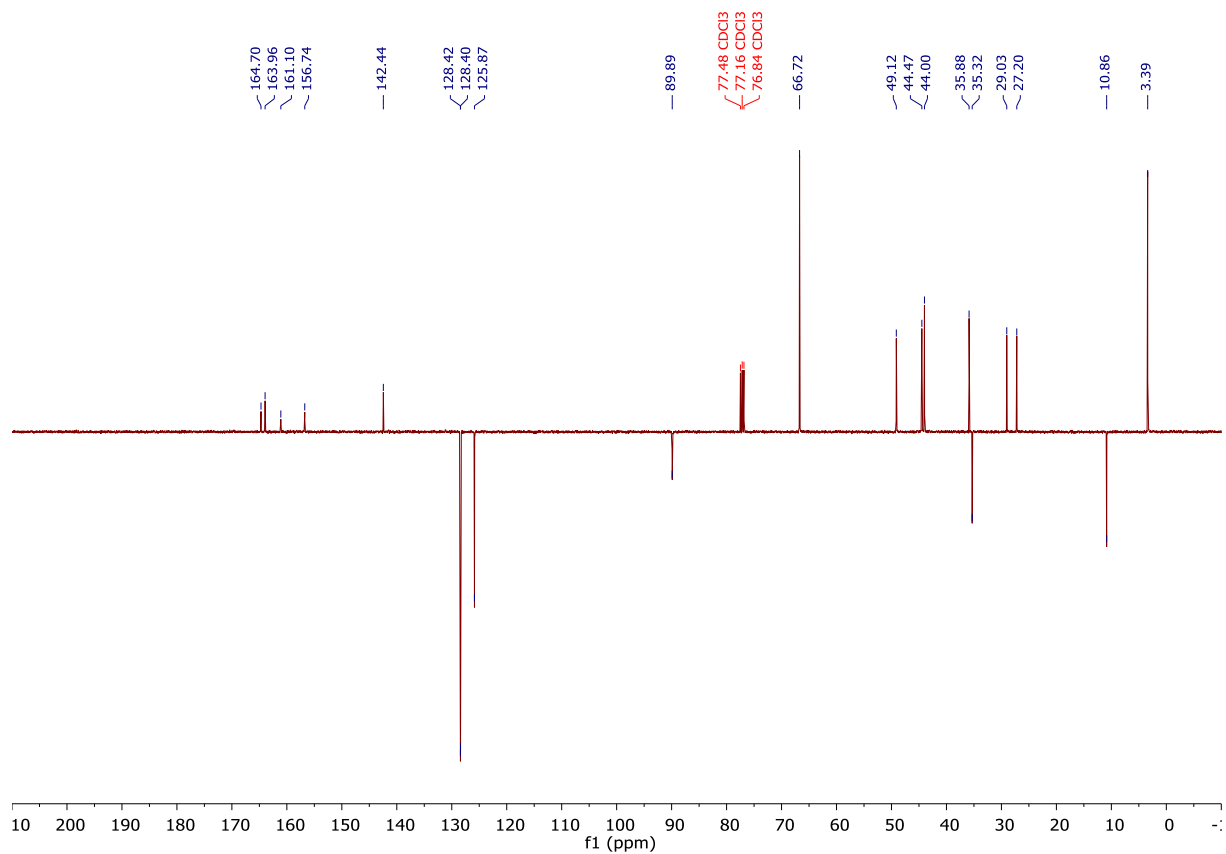
¹³C-NMR



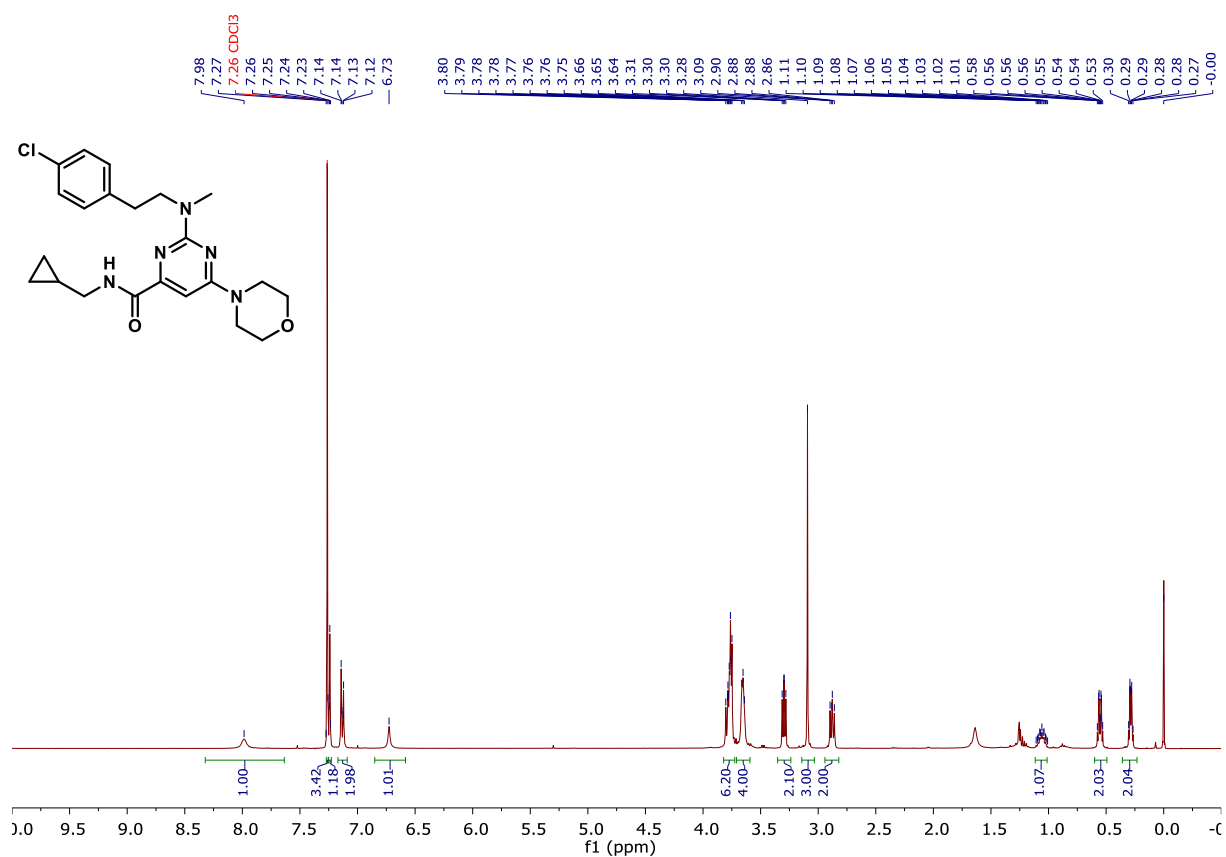
¹H-NMR: 37



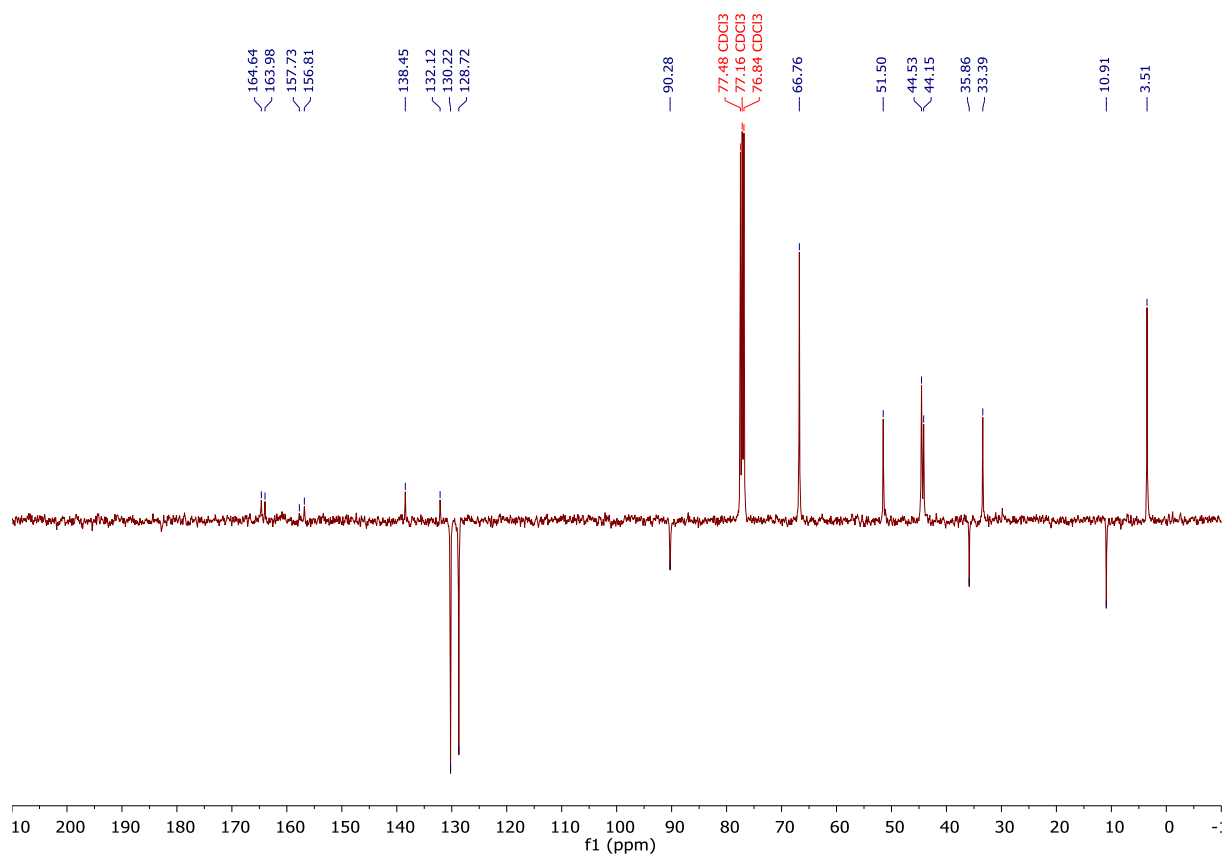
¹³C-NMR



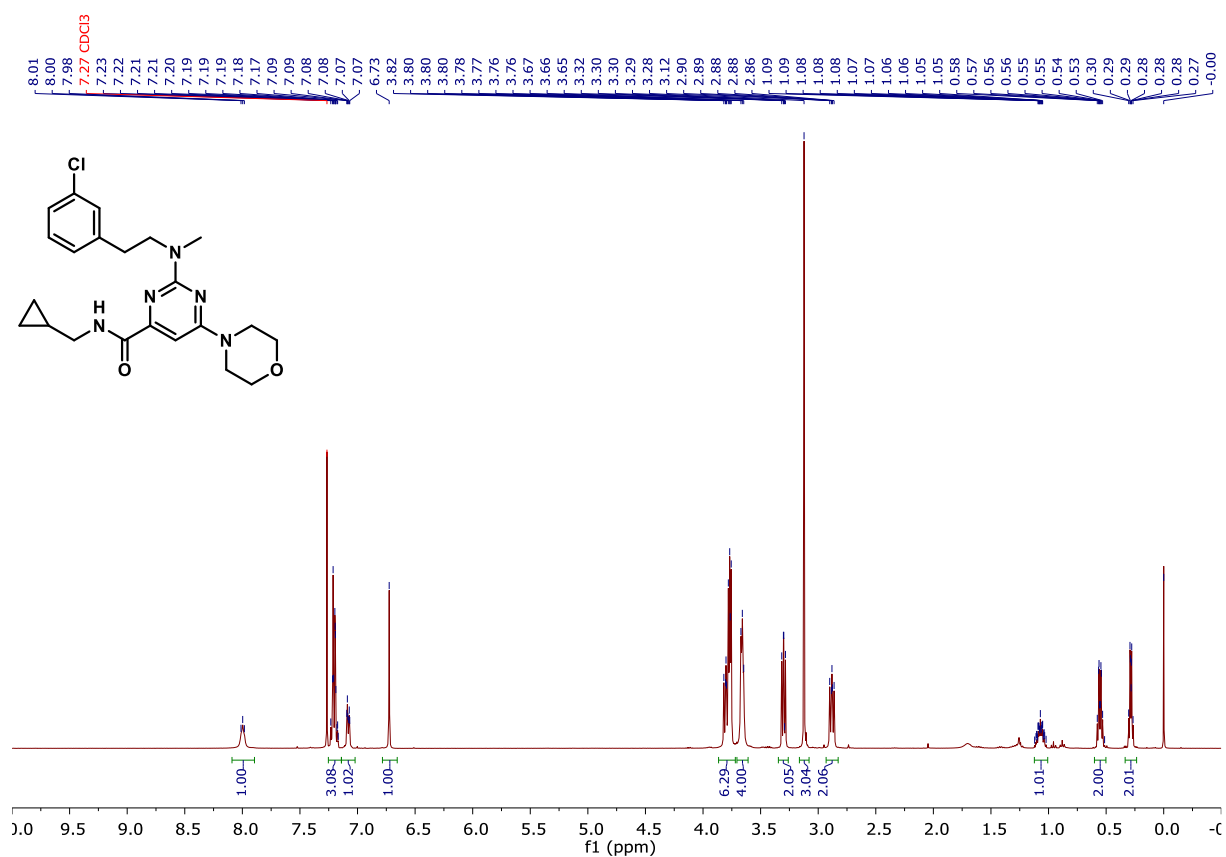
¹H-NMR: 38



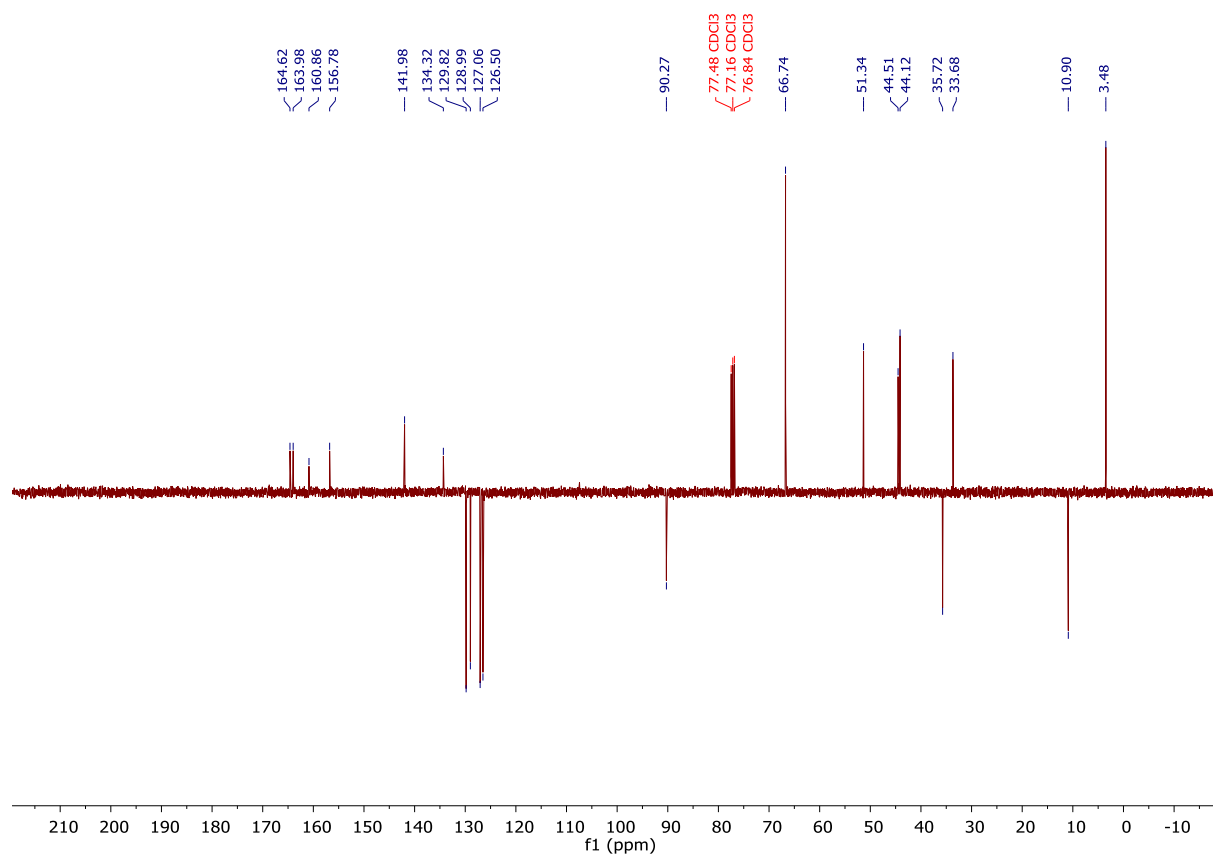
¹³C-NMR



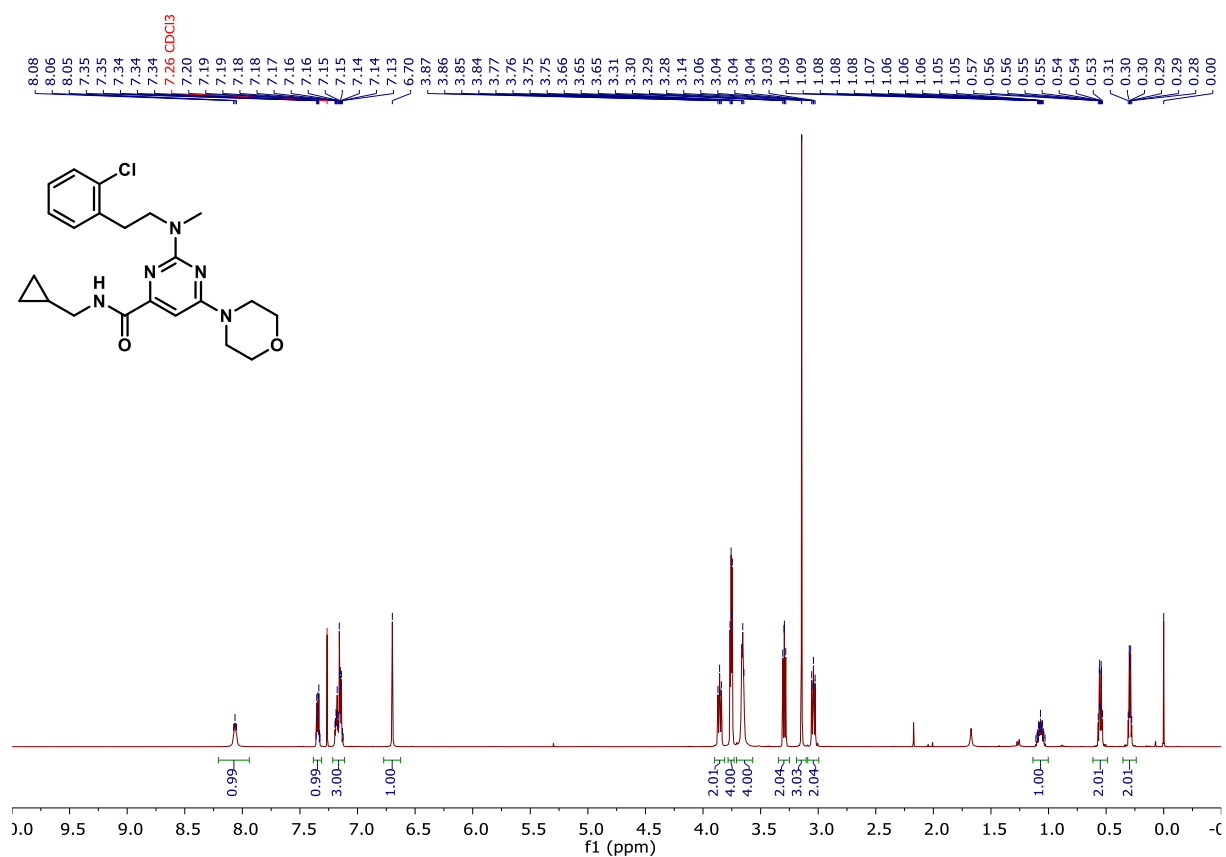
¹H-NMR: 39



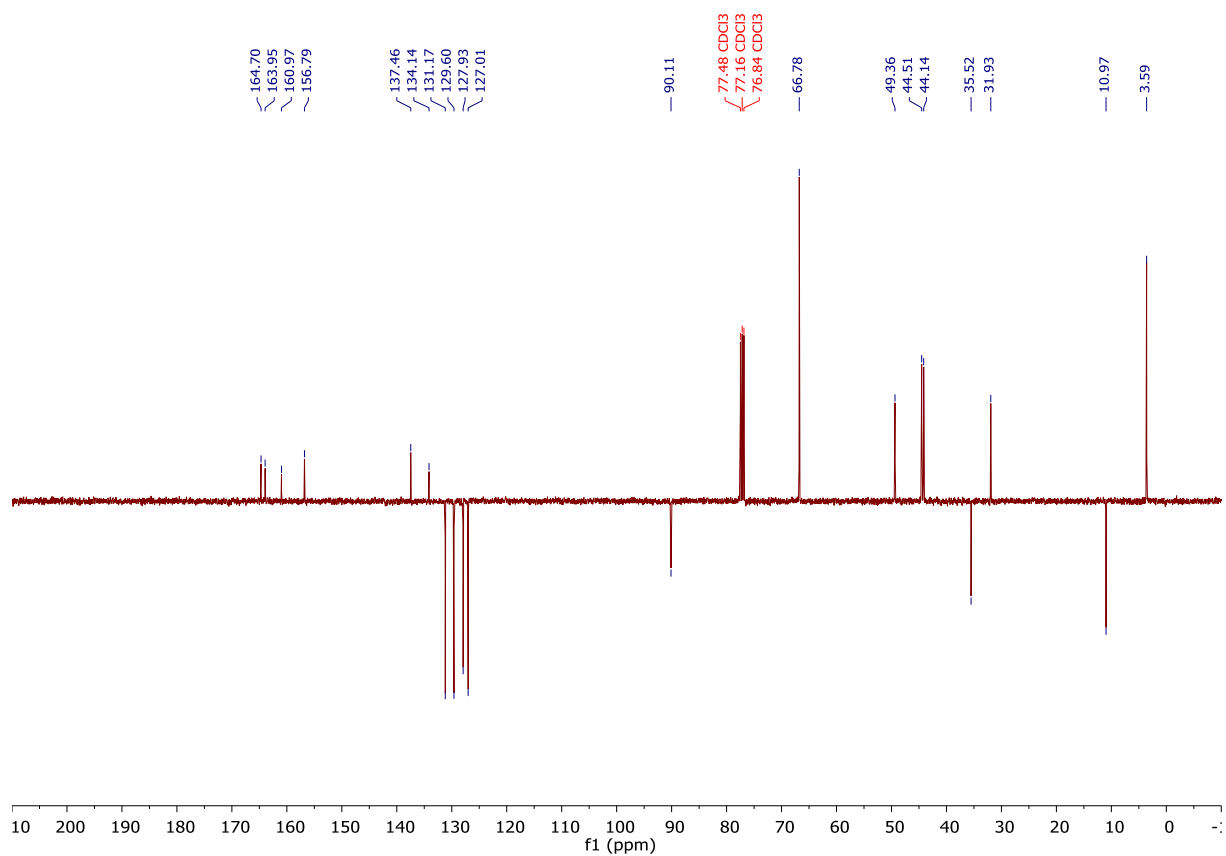
¹³C-NMR



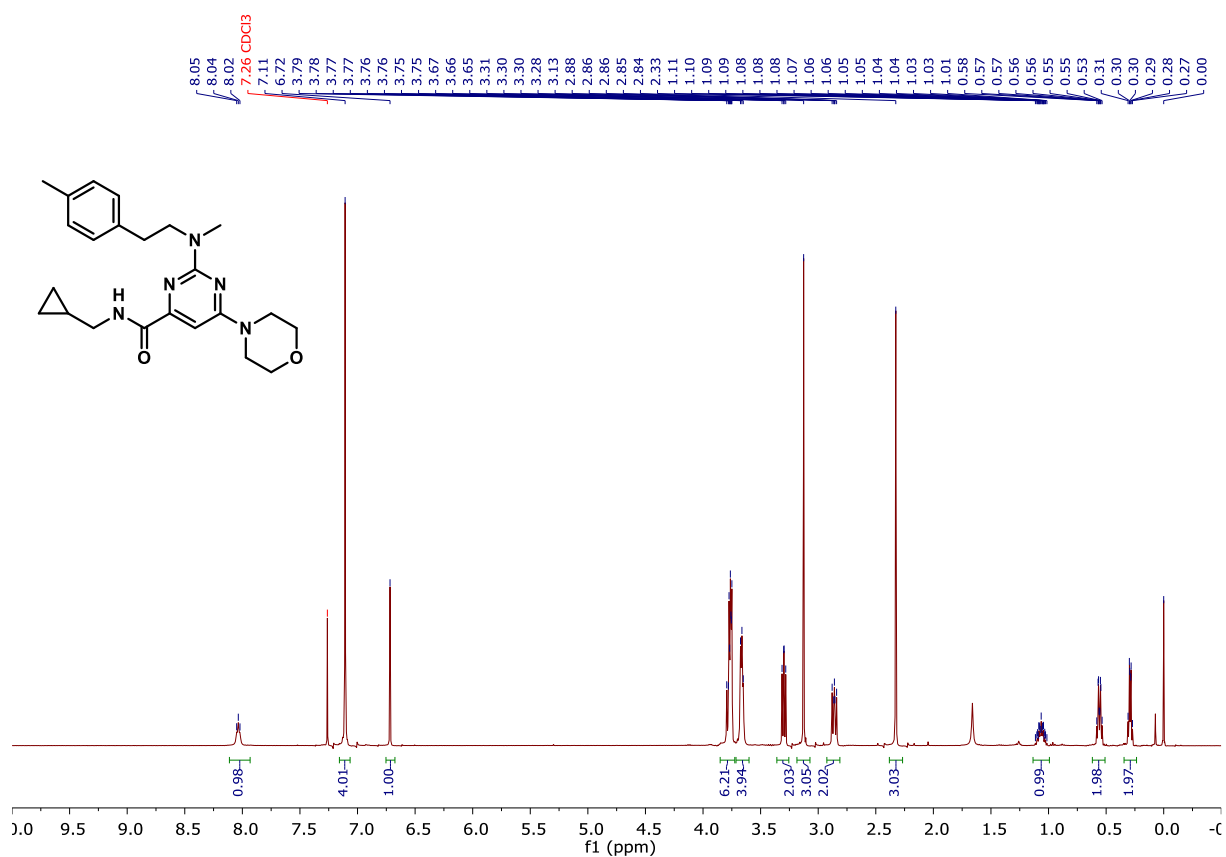
¹H-NMR: 40



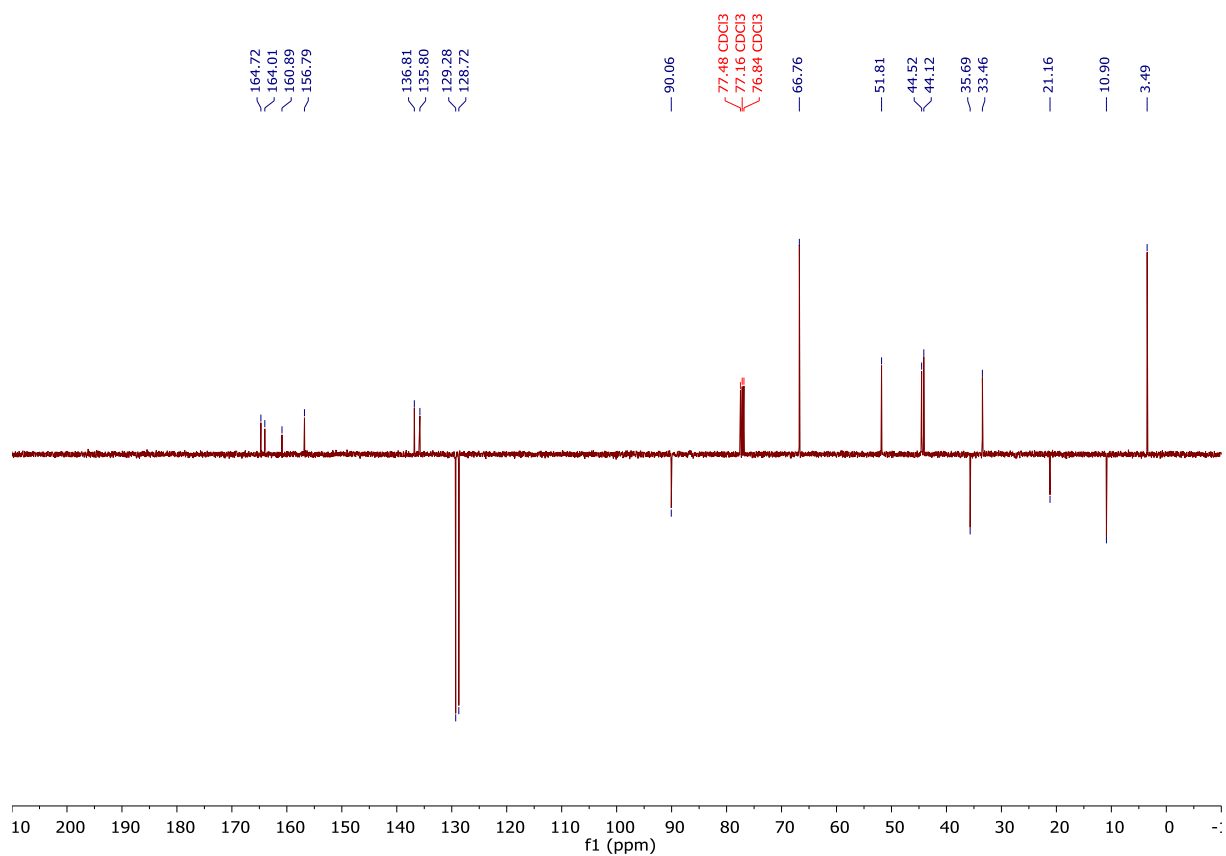
¹³C-NMR



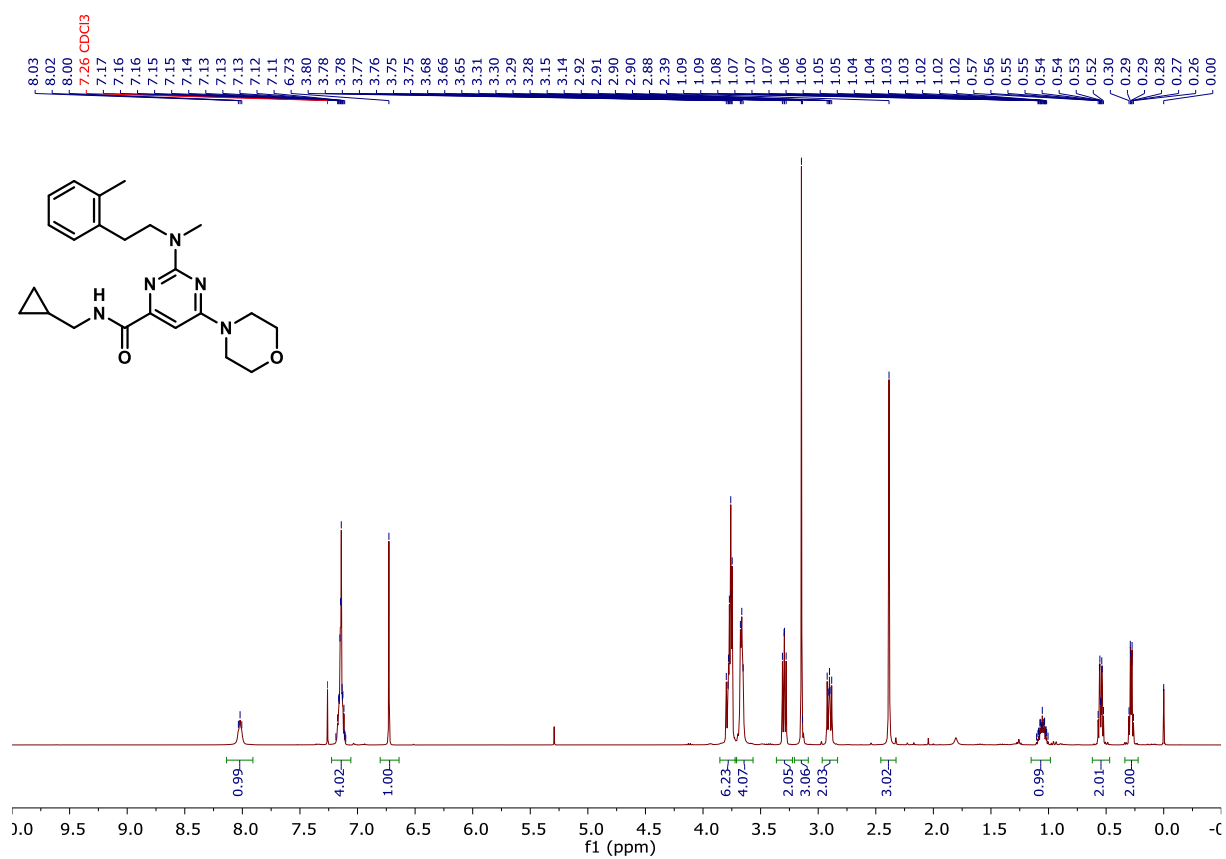
¹H-NMR: 41



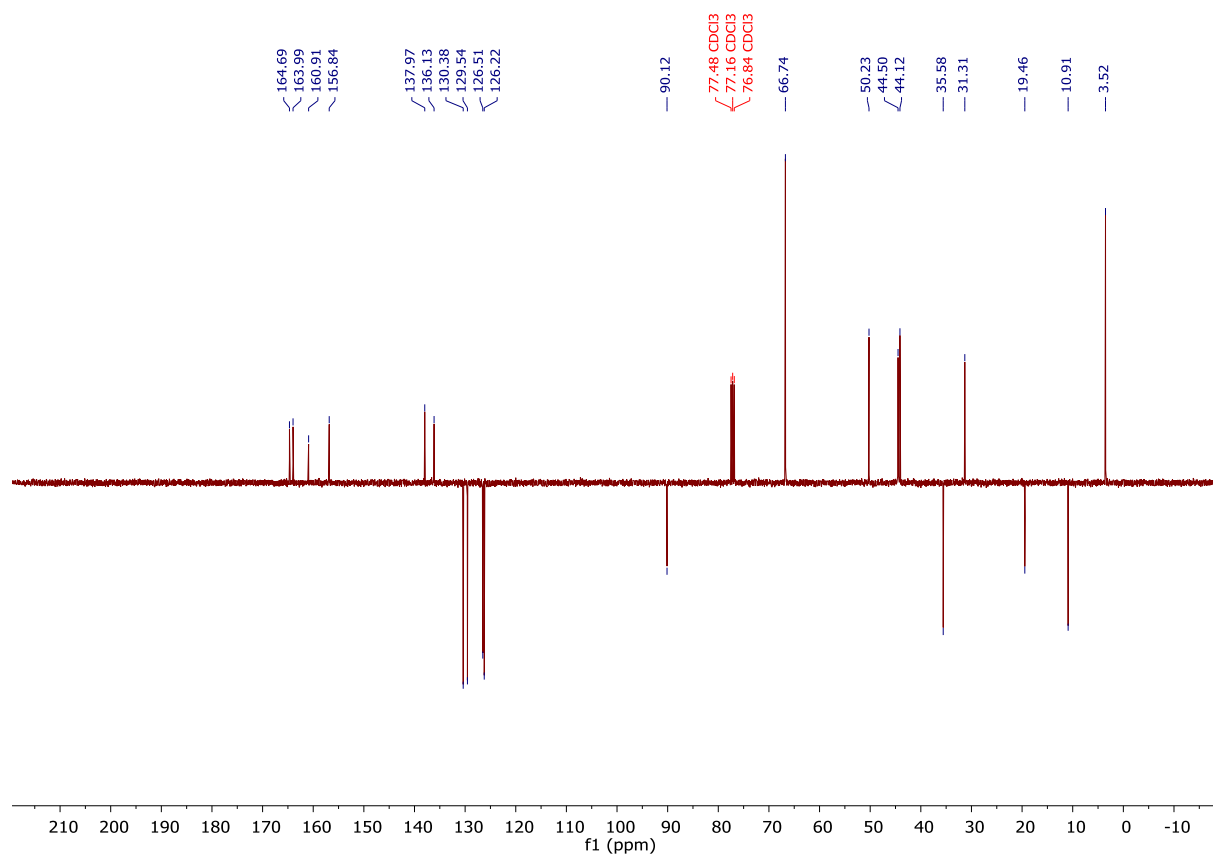
¹³C-NMR



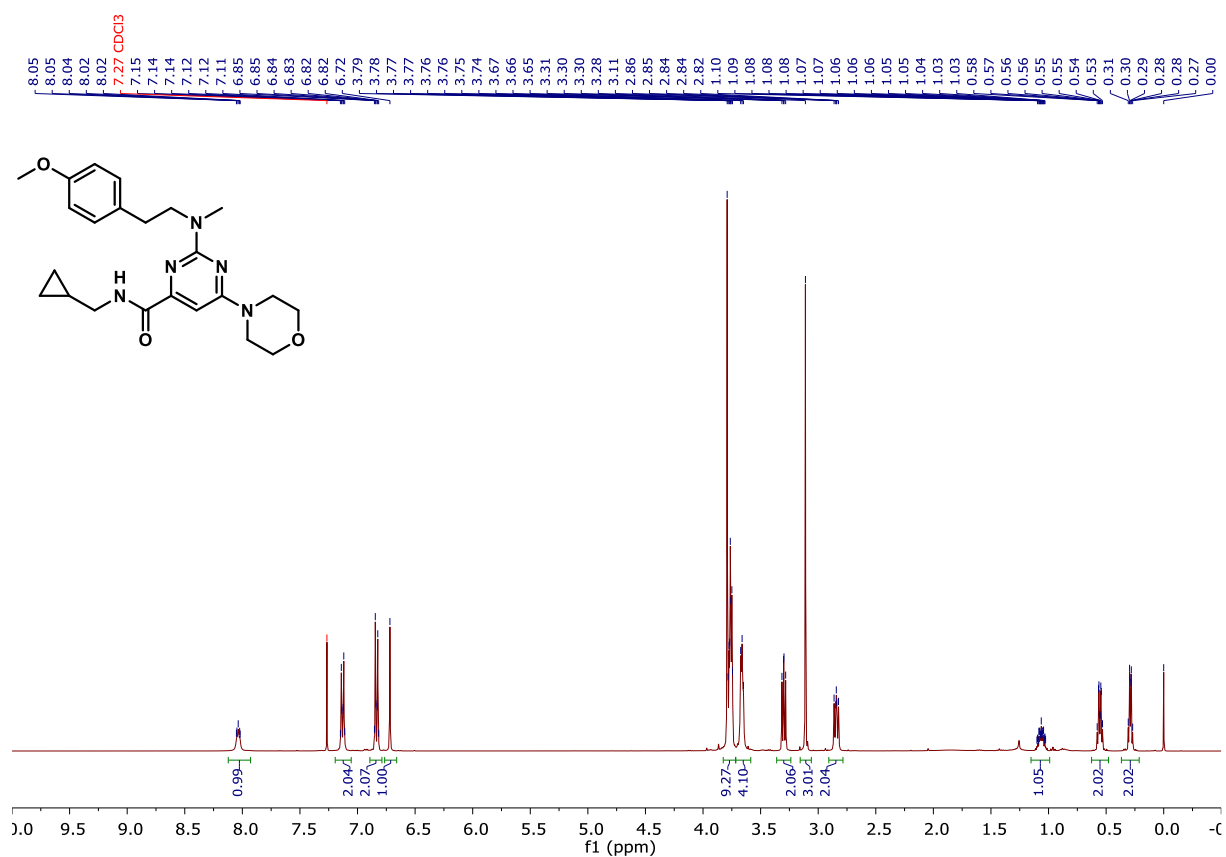
¹H-NMR: 42



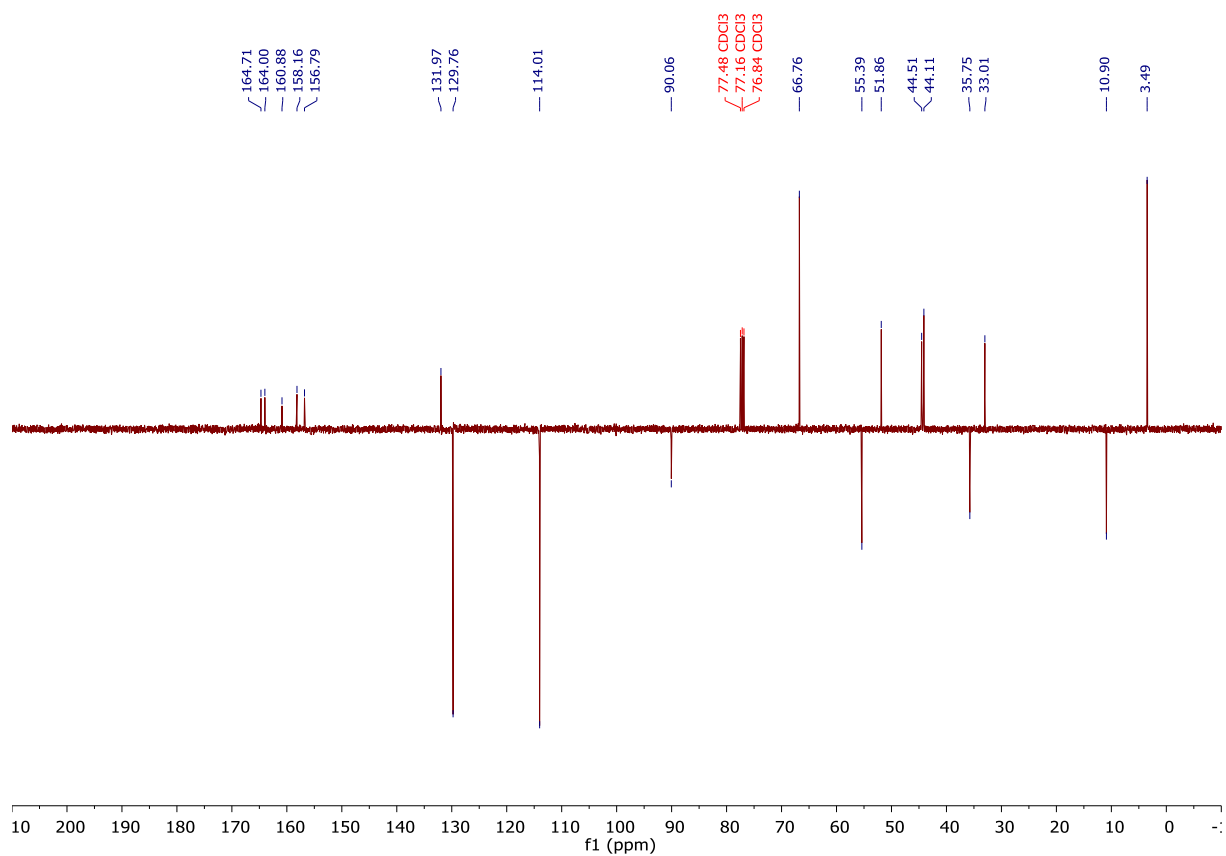
¹³C-NMR



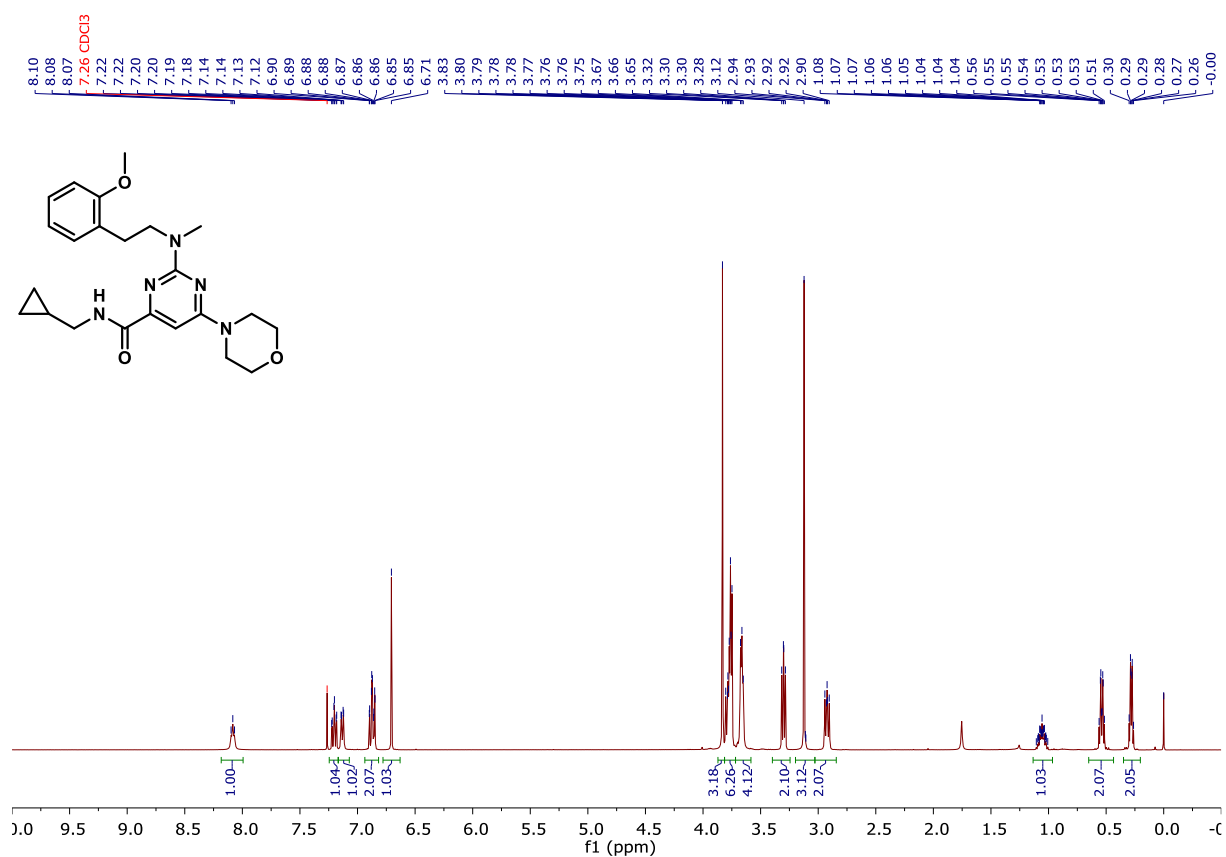
¹H-NMR: 43



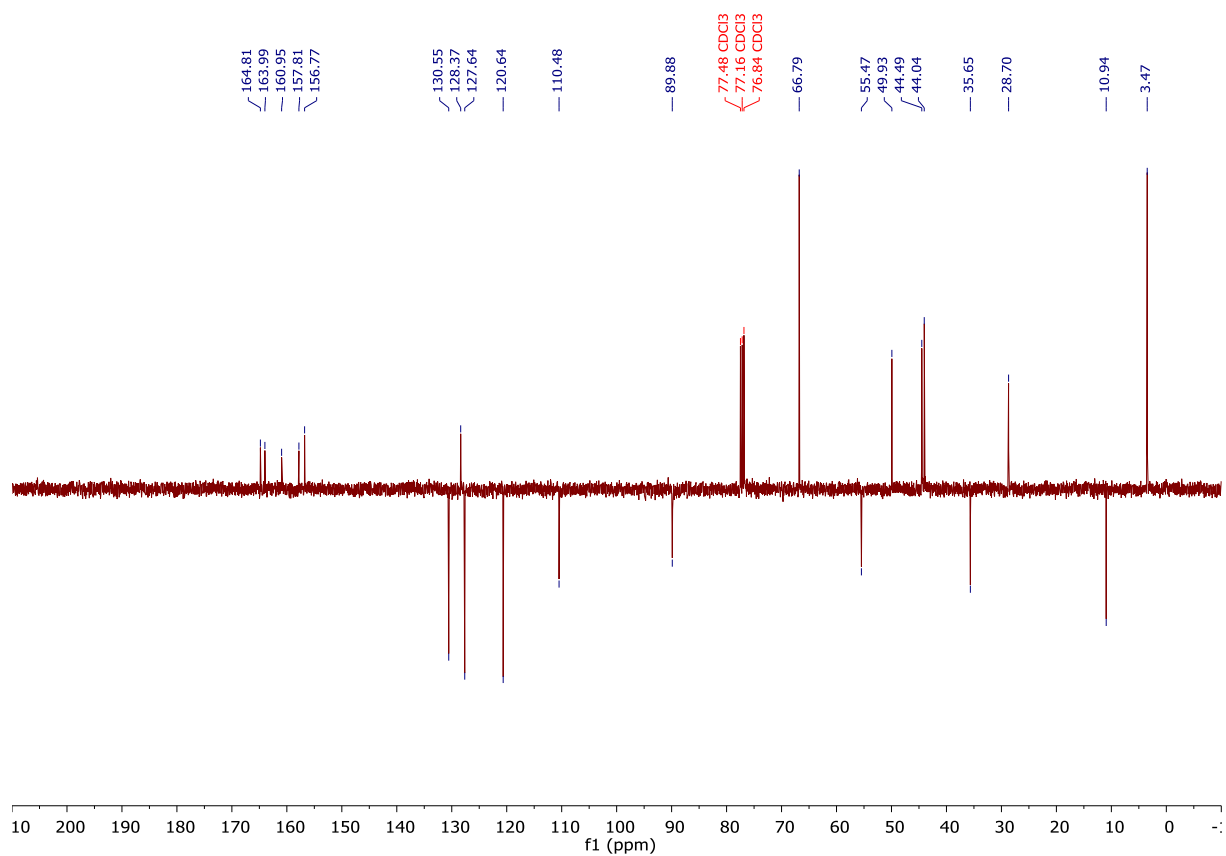
¹³C-NMR



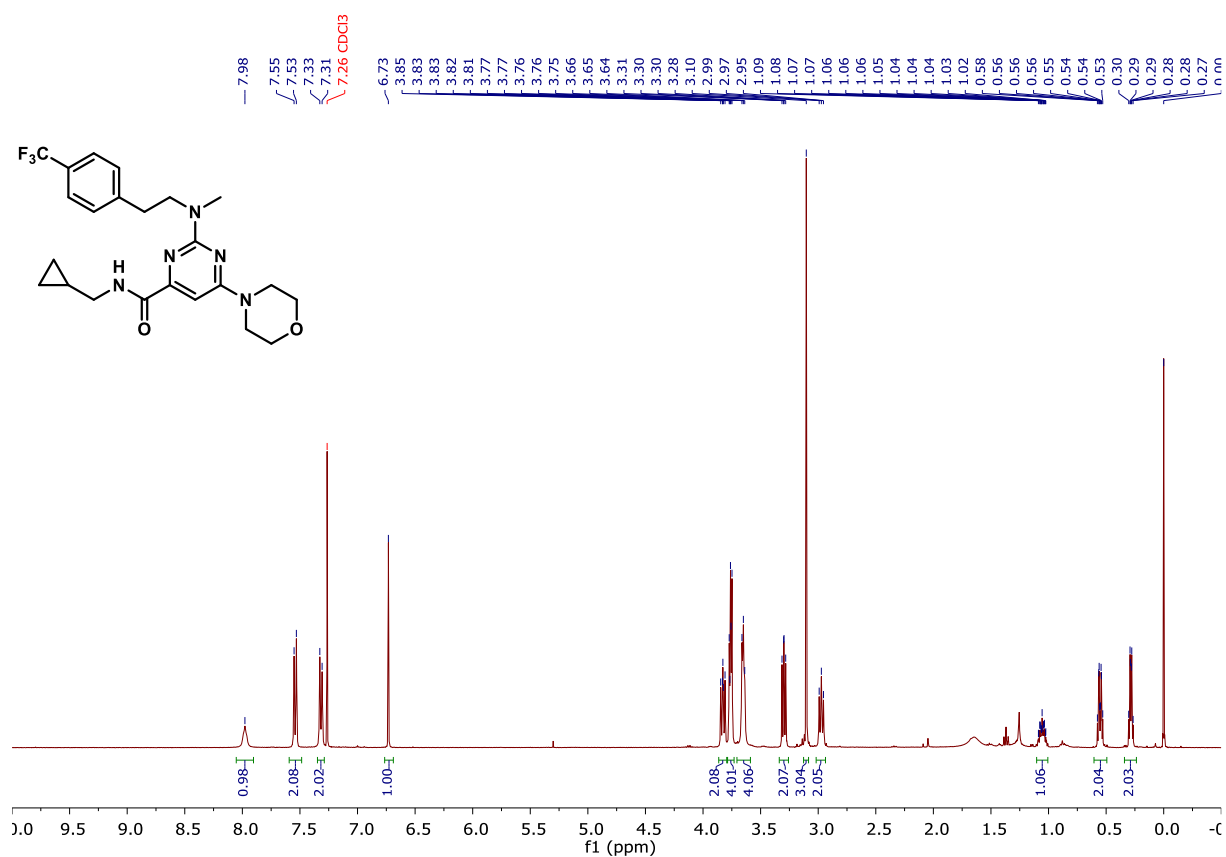
¹H-NMR: 44



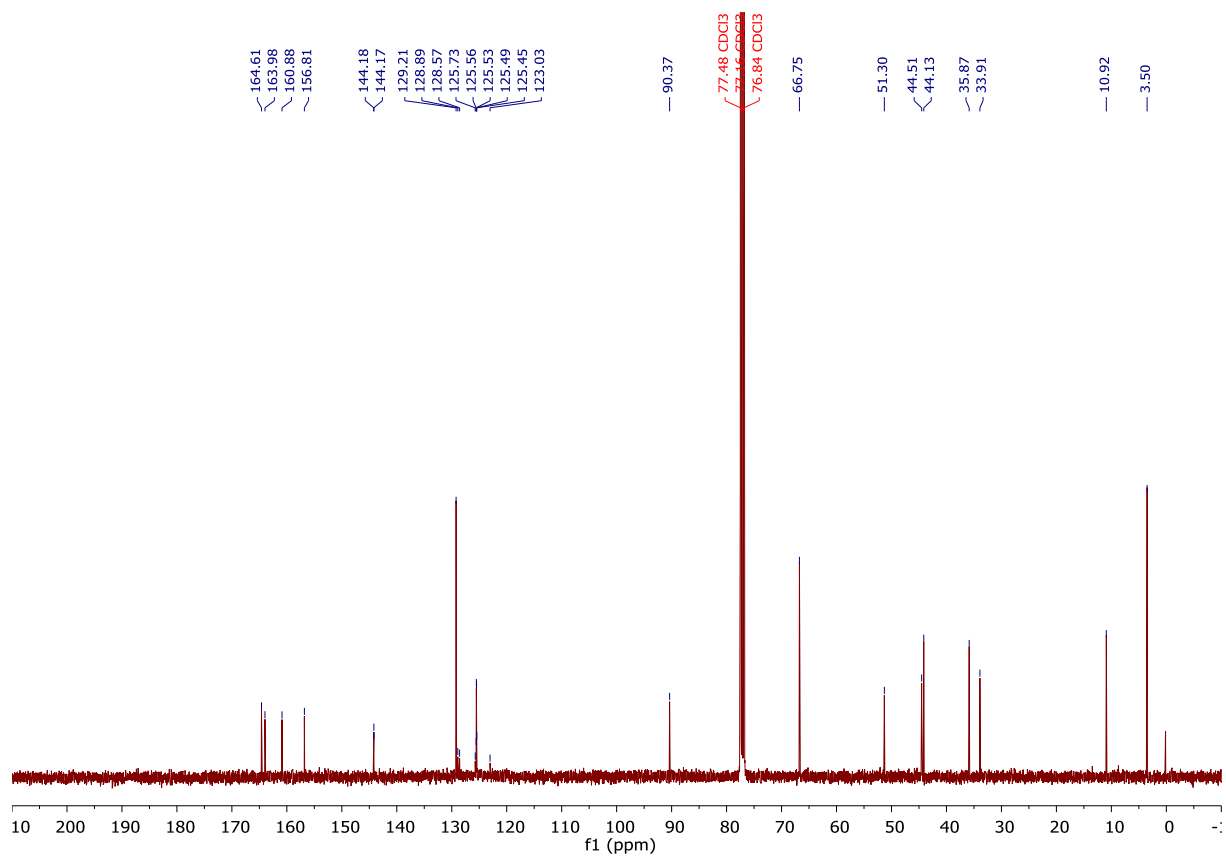
¹³C-NMR



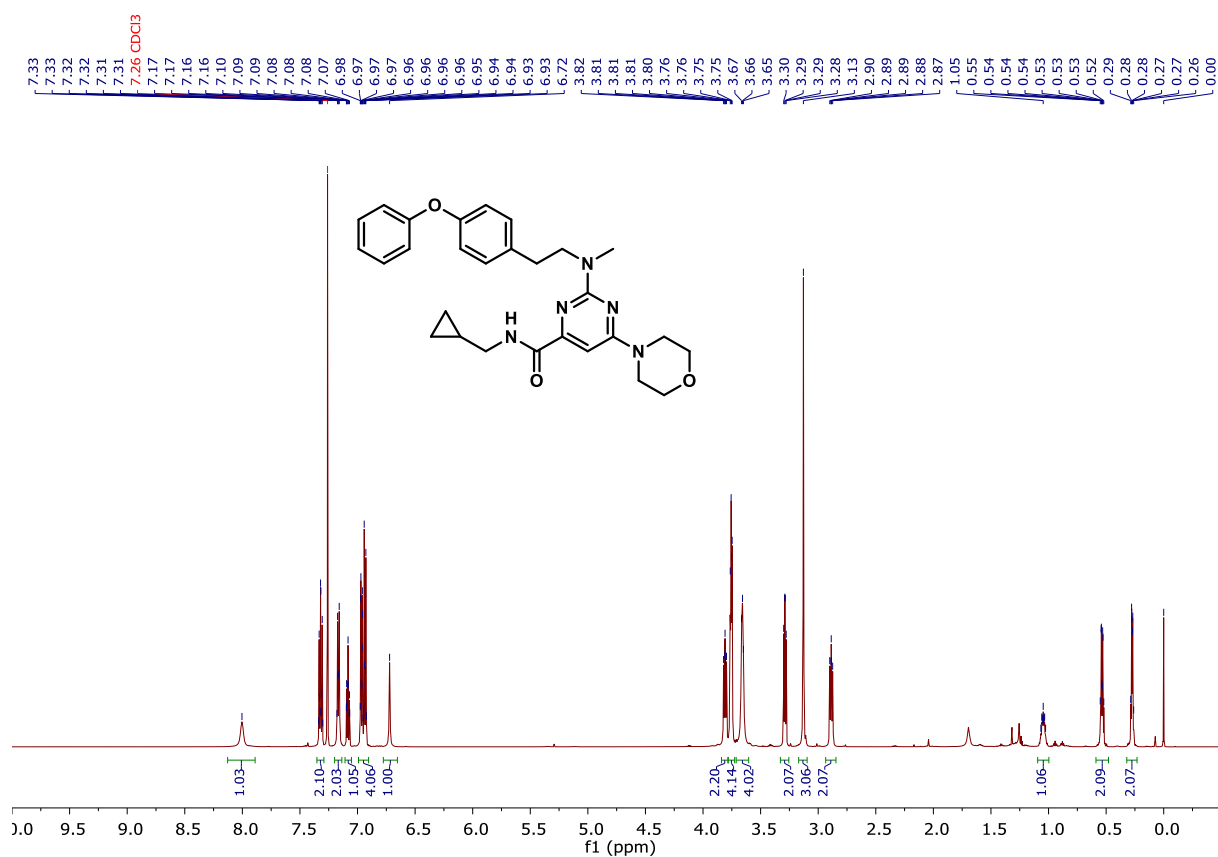
¹H-NMR: 45



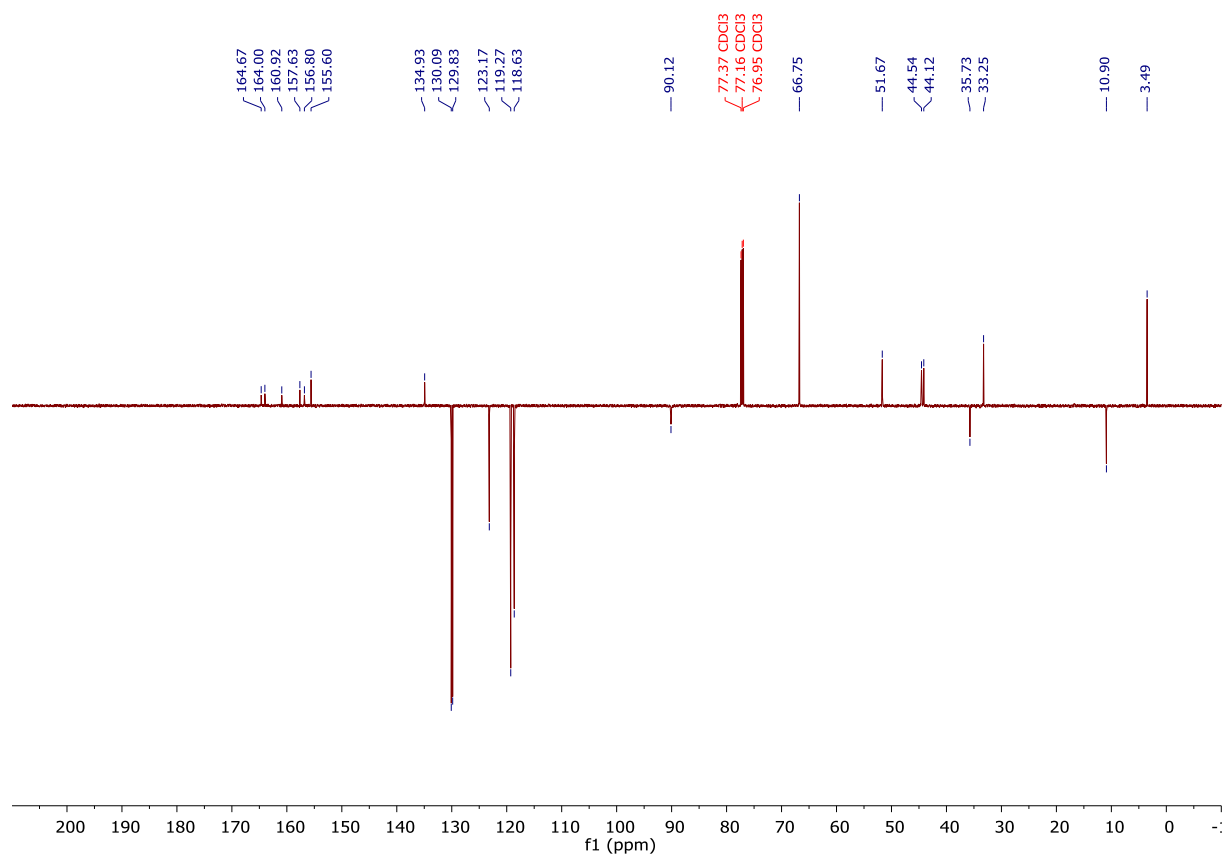
¹³C-NMR



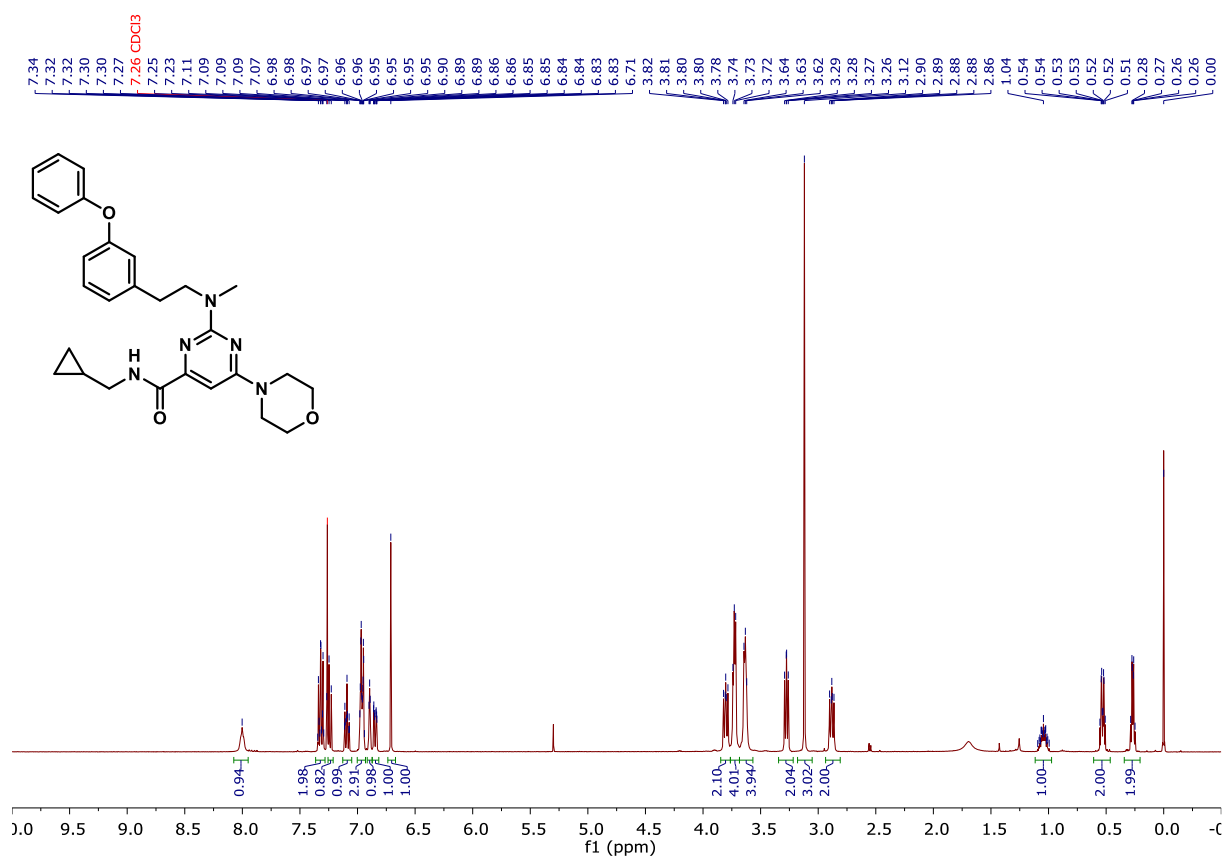
¹H-NMR: 46



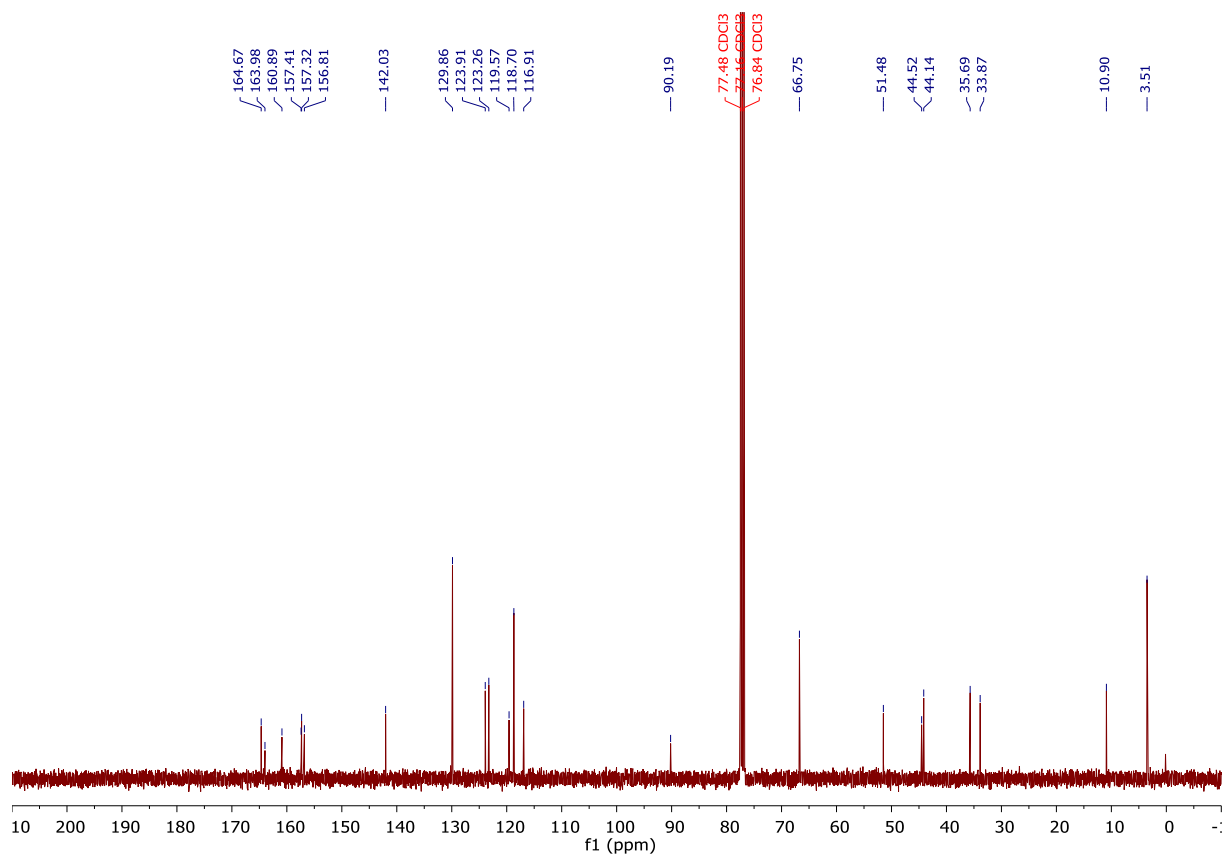
¹³C-NMR



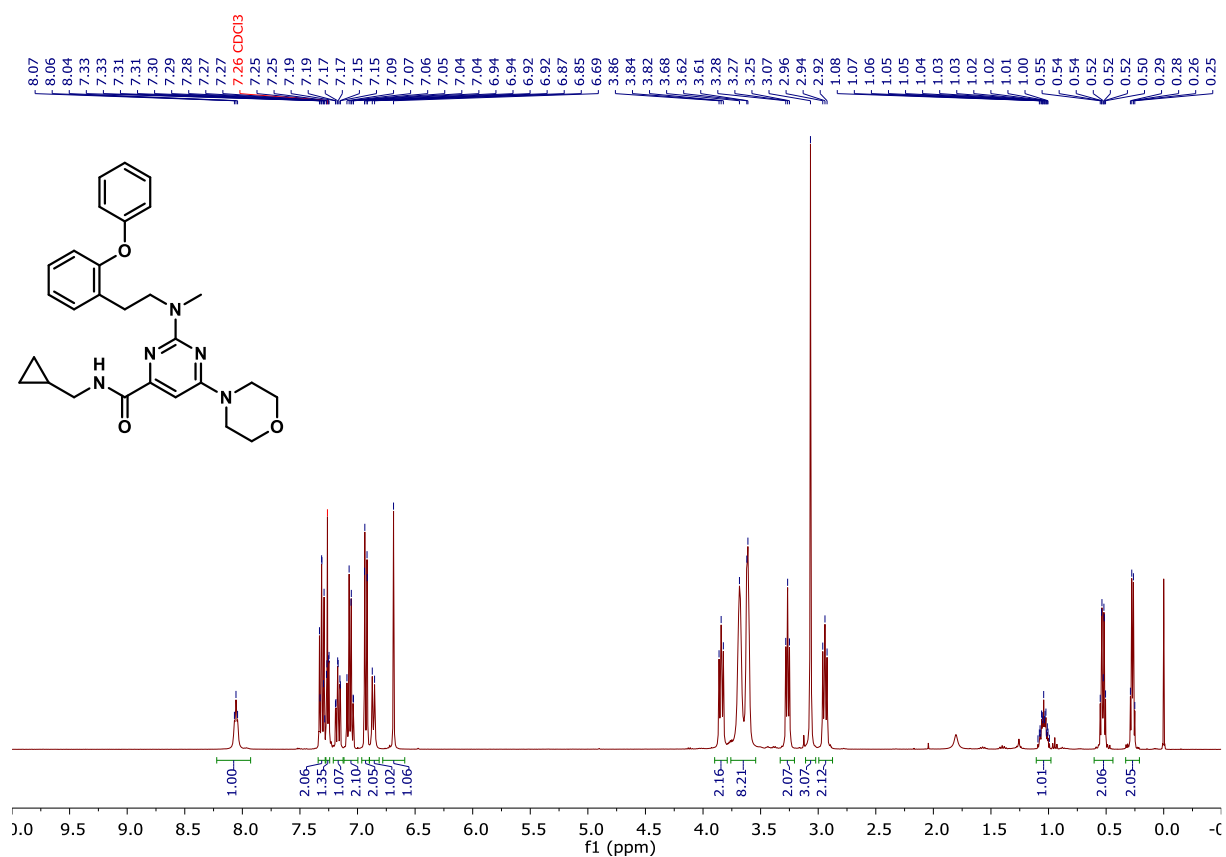
¹H-NMR: 47



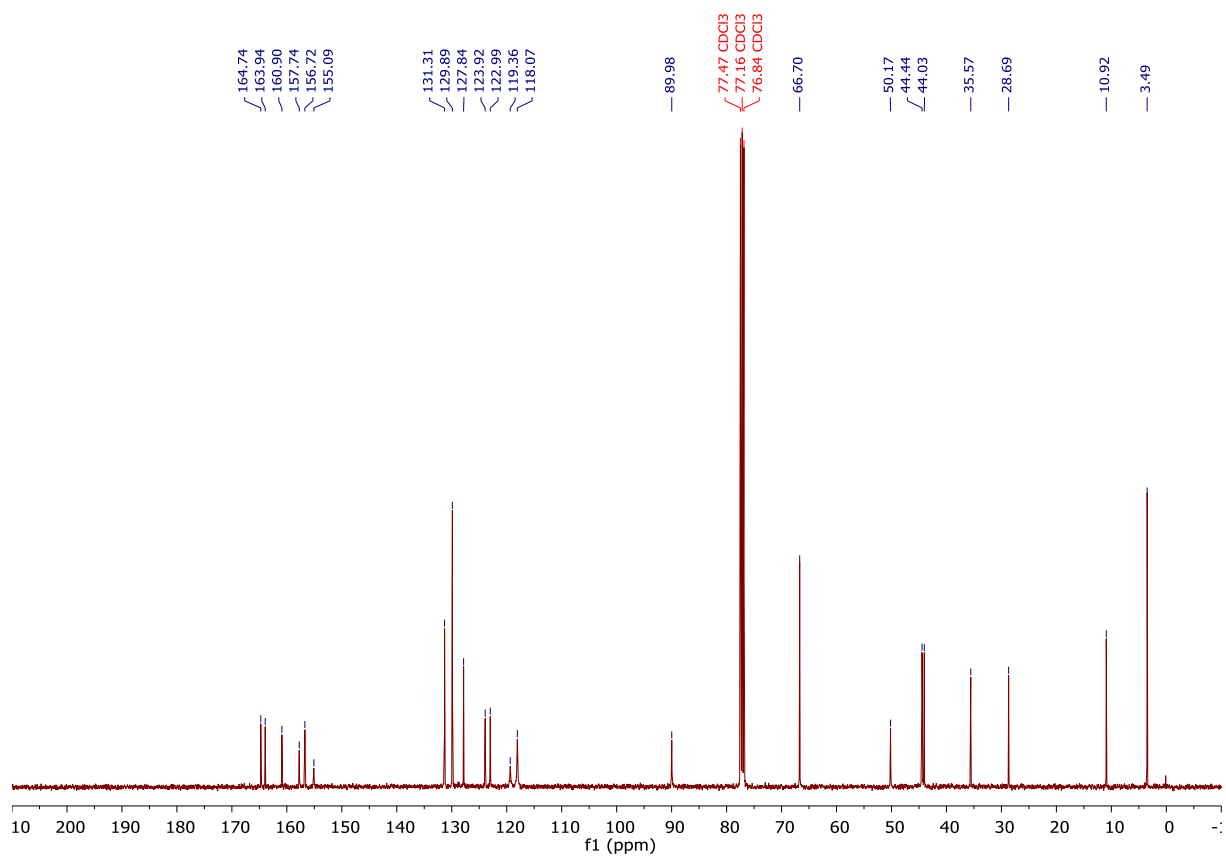
¹³C-NMR



¹H-NMR: 48

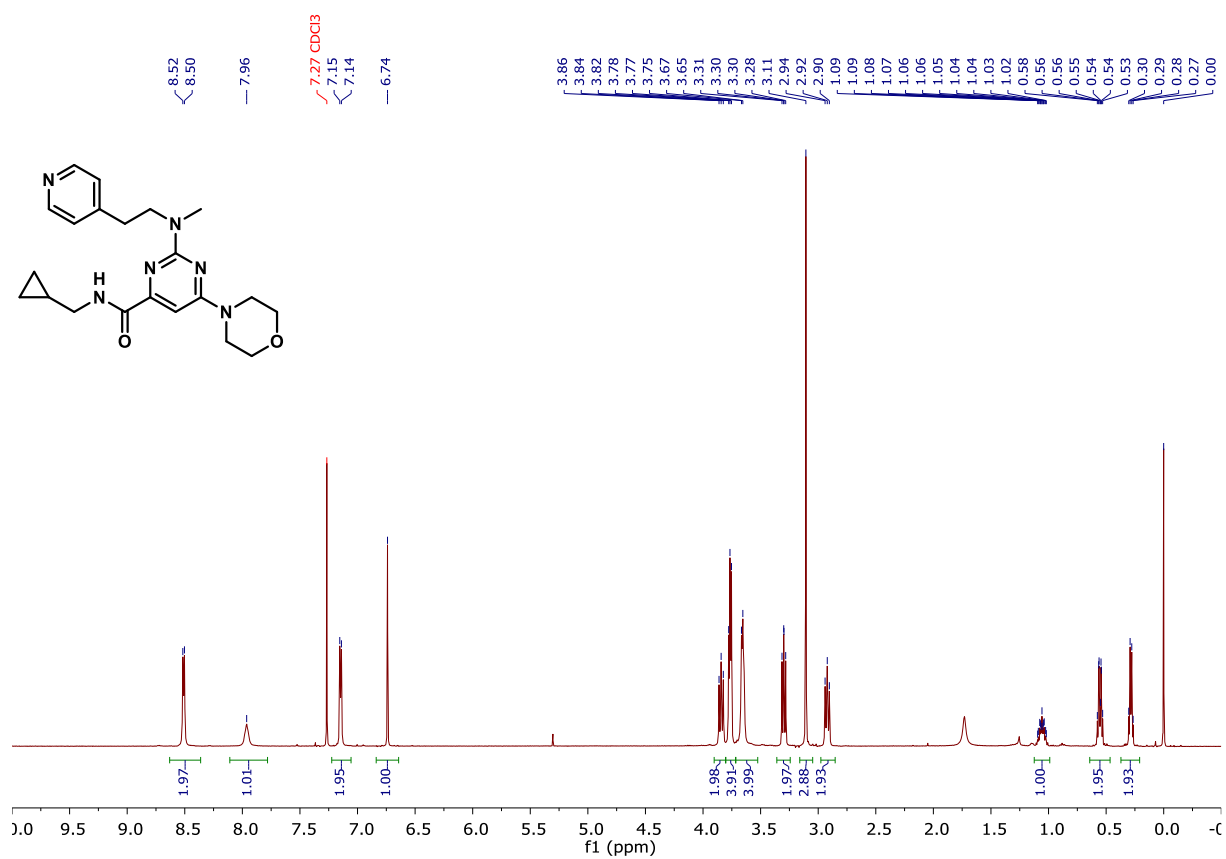


¹³C-NMR

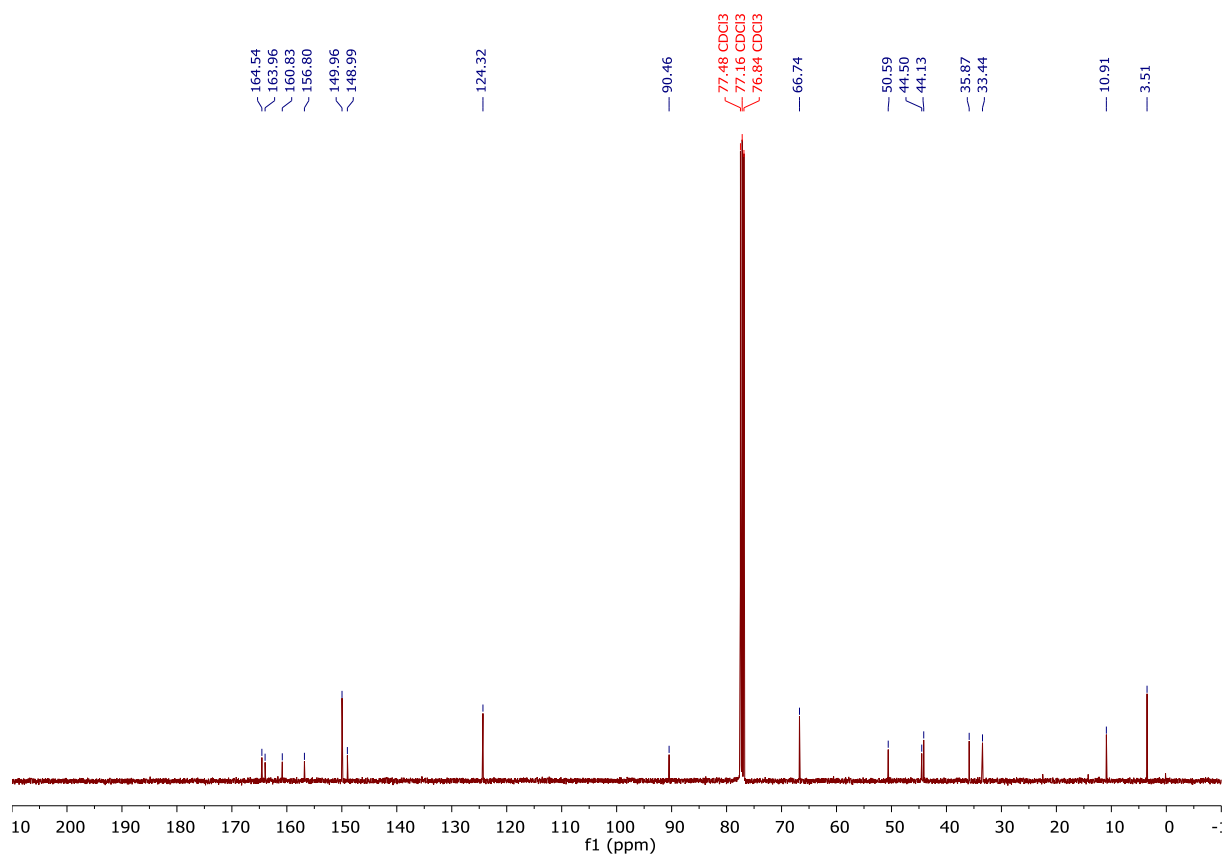


13C NMR spectrum (CDCl₃) of compound 10. The x-axis is labeled 'f1 (ppm)' and ranges from 10 to 210. The spectrum shows several peaks in the aromatic region (126-164 ppm) and aliphatic region (3.47-10.90 ppm). Solvent peaks for CDCl₃ are visible at 77.16, 77.48, and 76.84 ppm. A peak at 66.72 ppm is also present. The peaks are labeled with their chemical shifts: 164.69, 163.87, 160.70, 156.65, 142.44, 141.63, 137.33, 130.26, 129.83, 129.28, 128.15, 127.56, 126.94, 126.29, 89.99, 77.48 CDCl₃, 77.16 CDCl₃, 76.84 CDCl₃, 66.72, 51.00, 44.44, 44.04, 35.31, 30.93, 10.90, and 3.47.

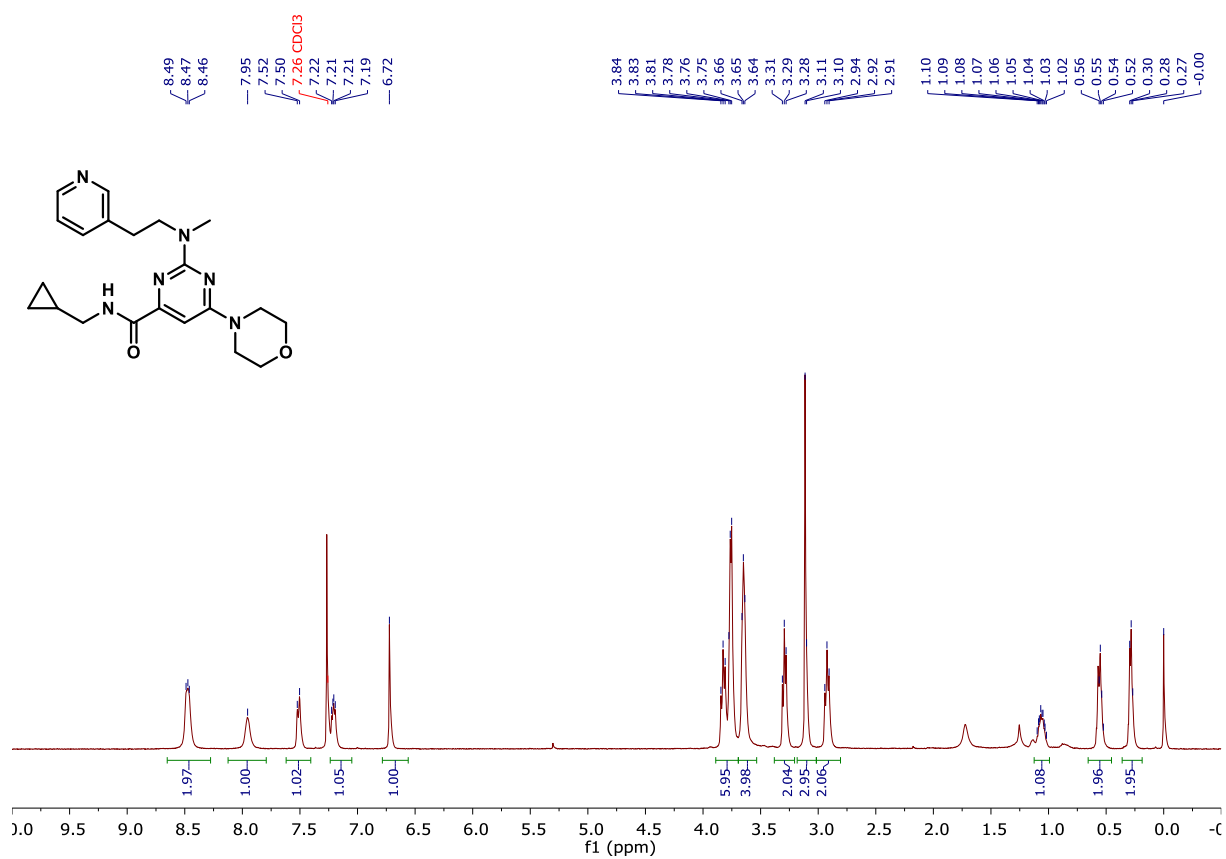
¹H-NMR: 50



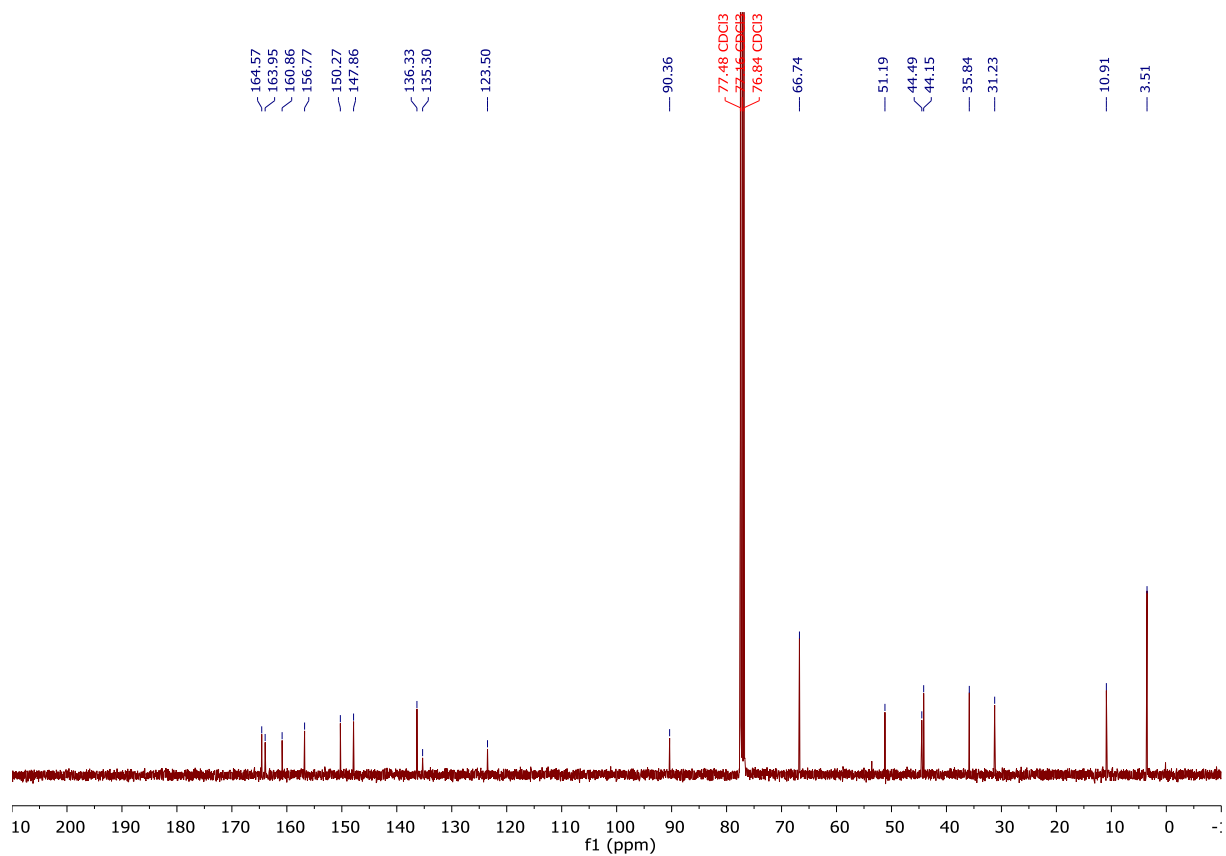
¹³C-NMR



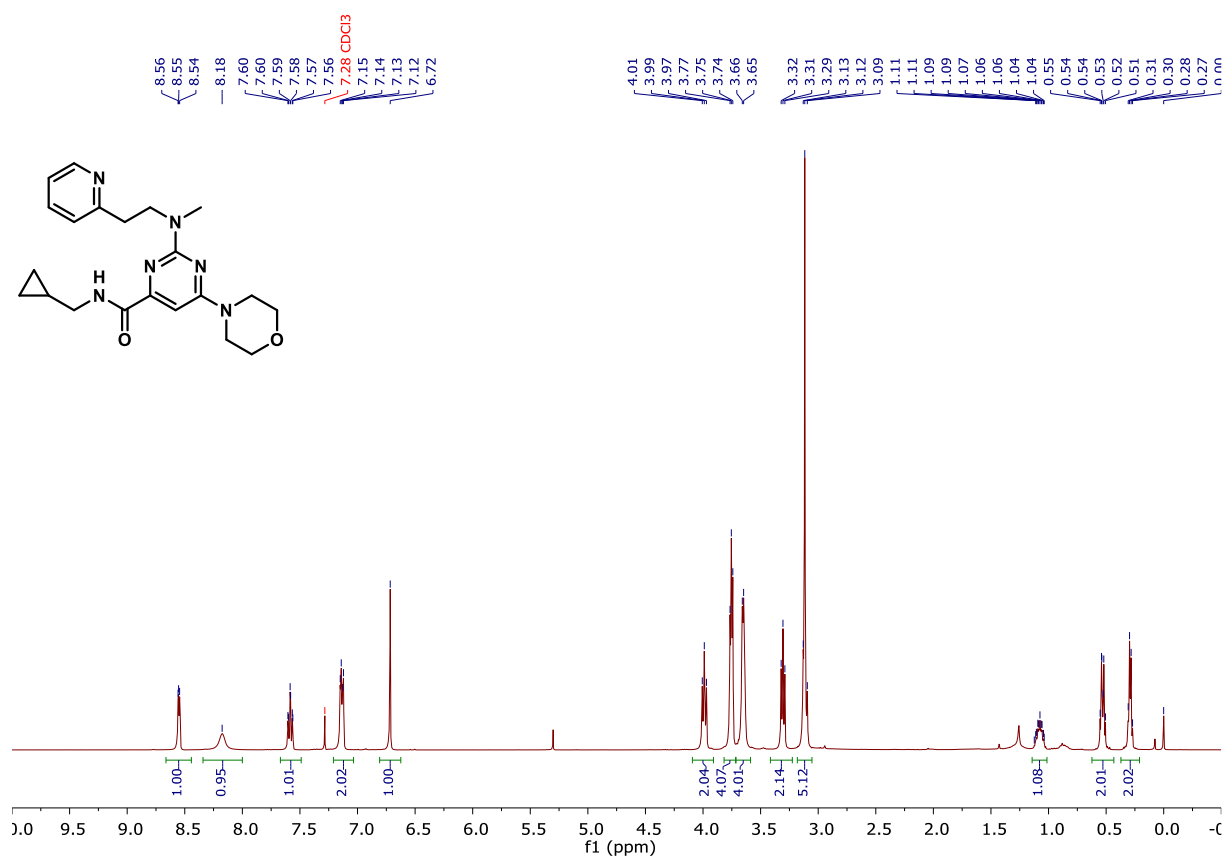
¹H-NMR: 51



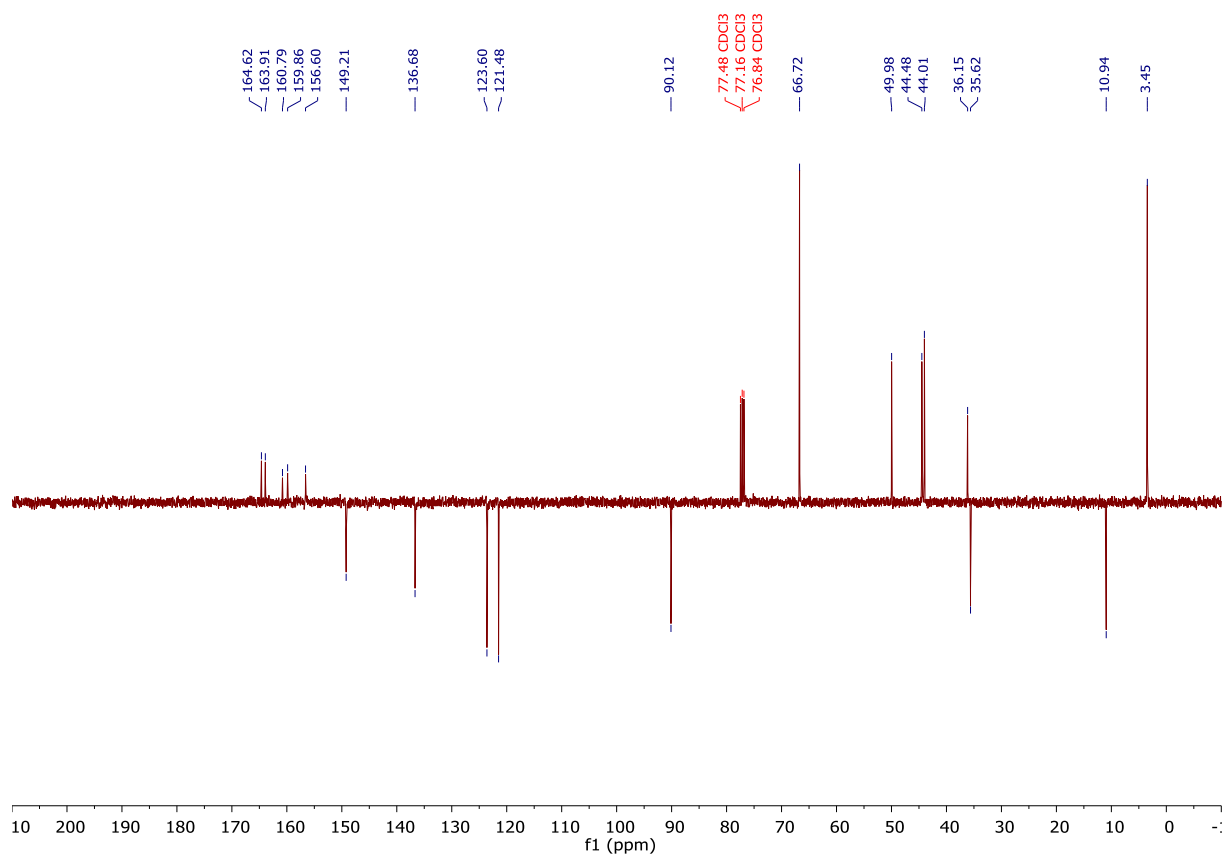
¹³C-NMR



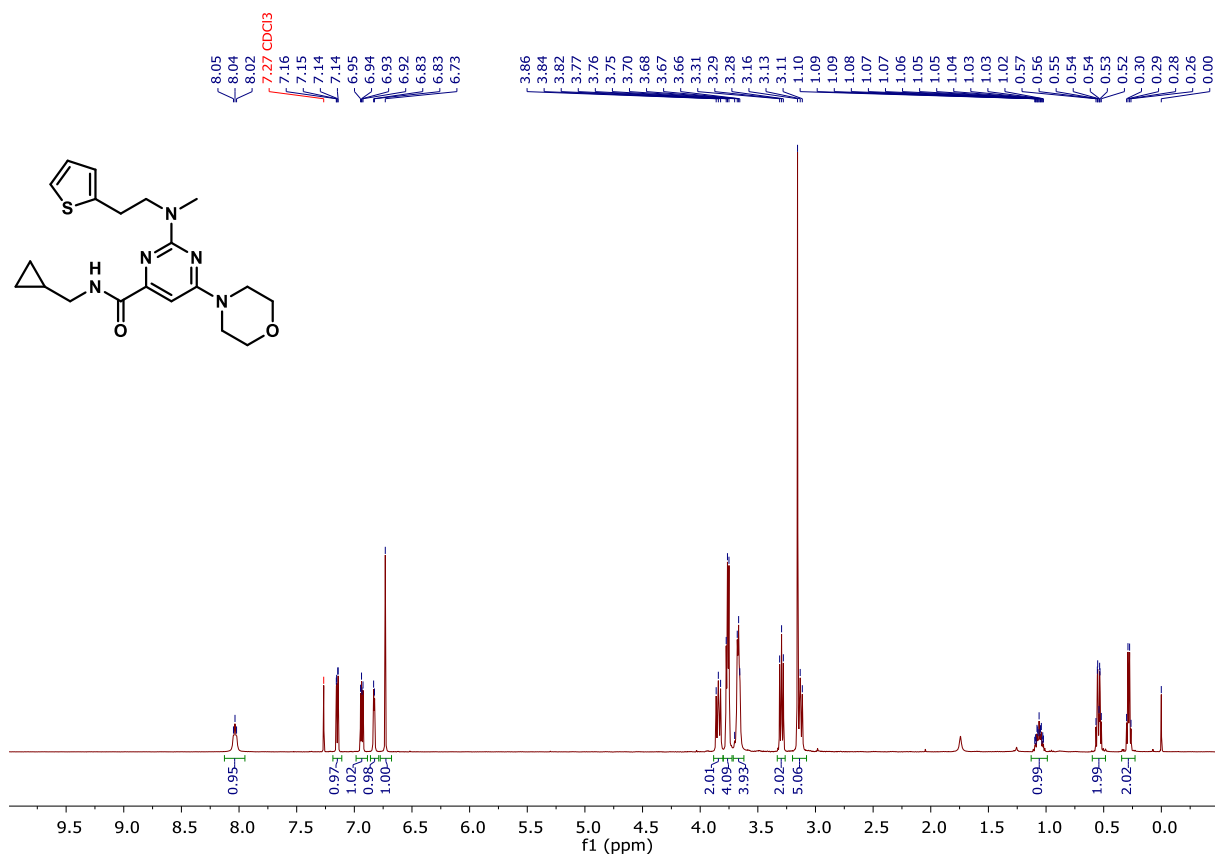
¹H-NMR: 52



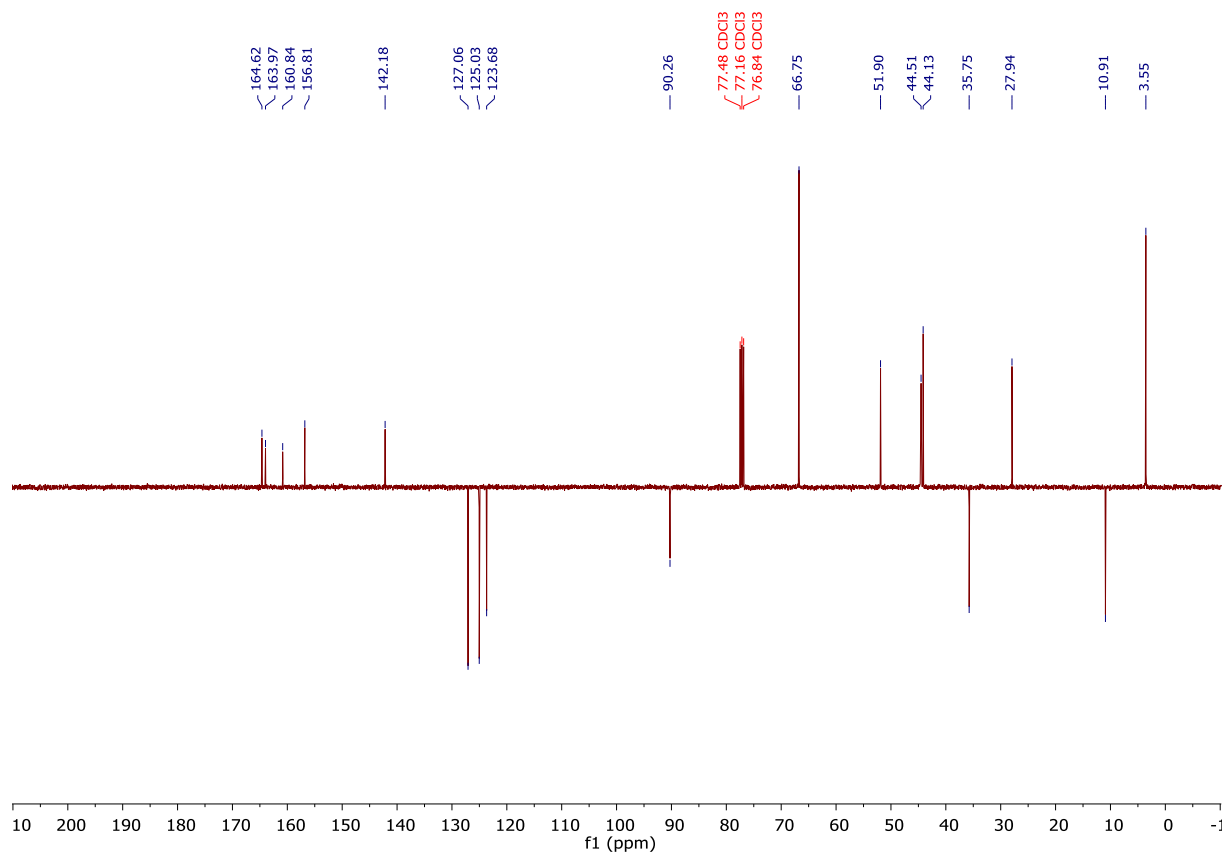
¹³C-NMR



¹H-NMR: 53



¹³C-NMR

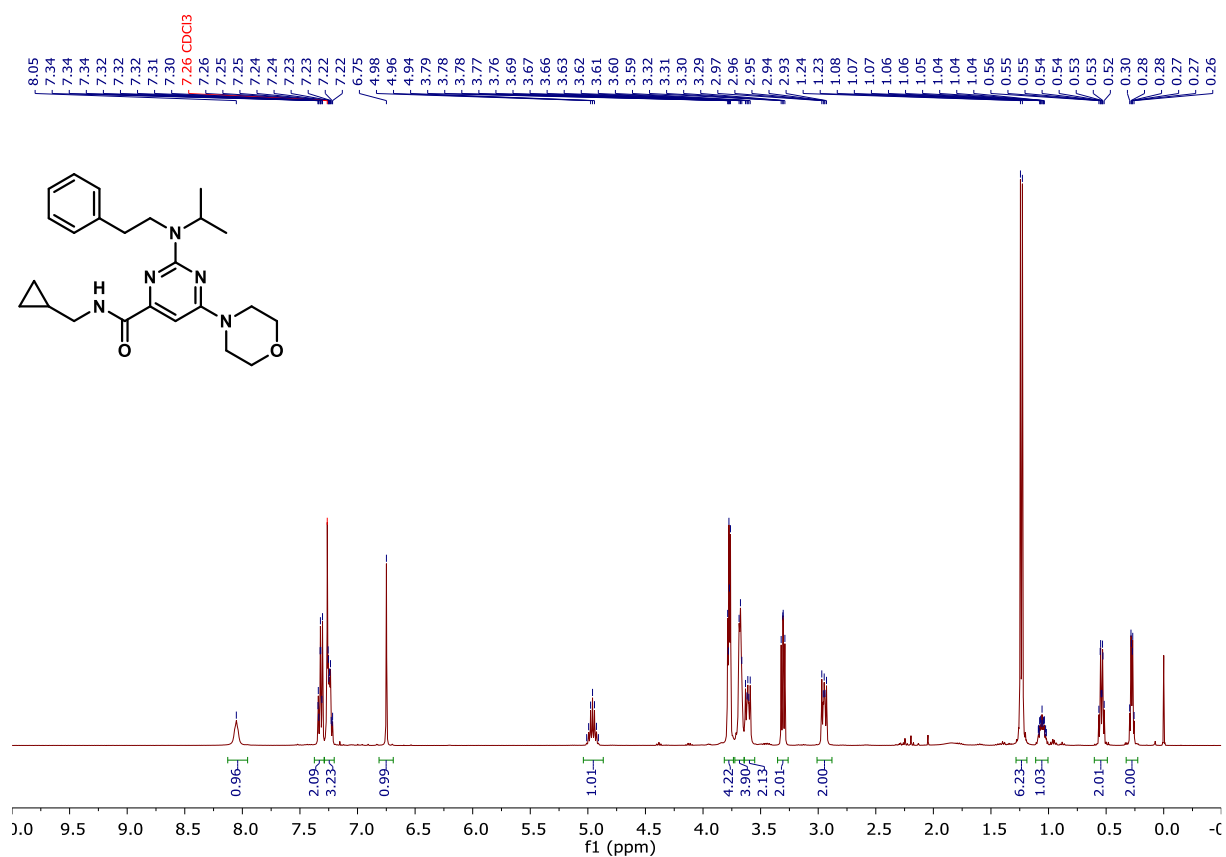


CCN(CCc1ccccc1)c2nc3c(ncn3CO)C(=O)NCC4CC4

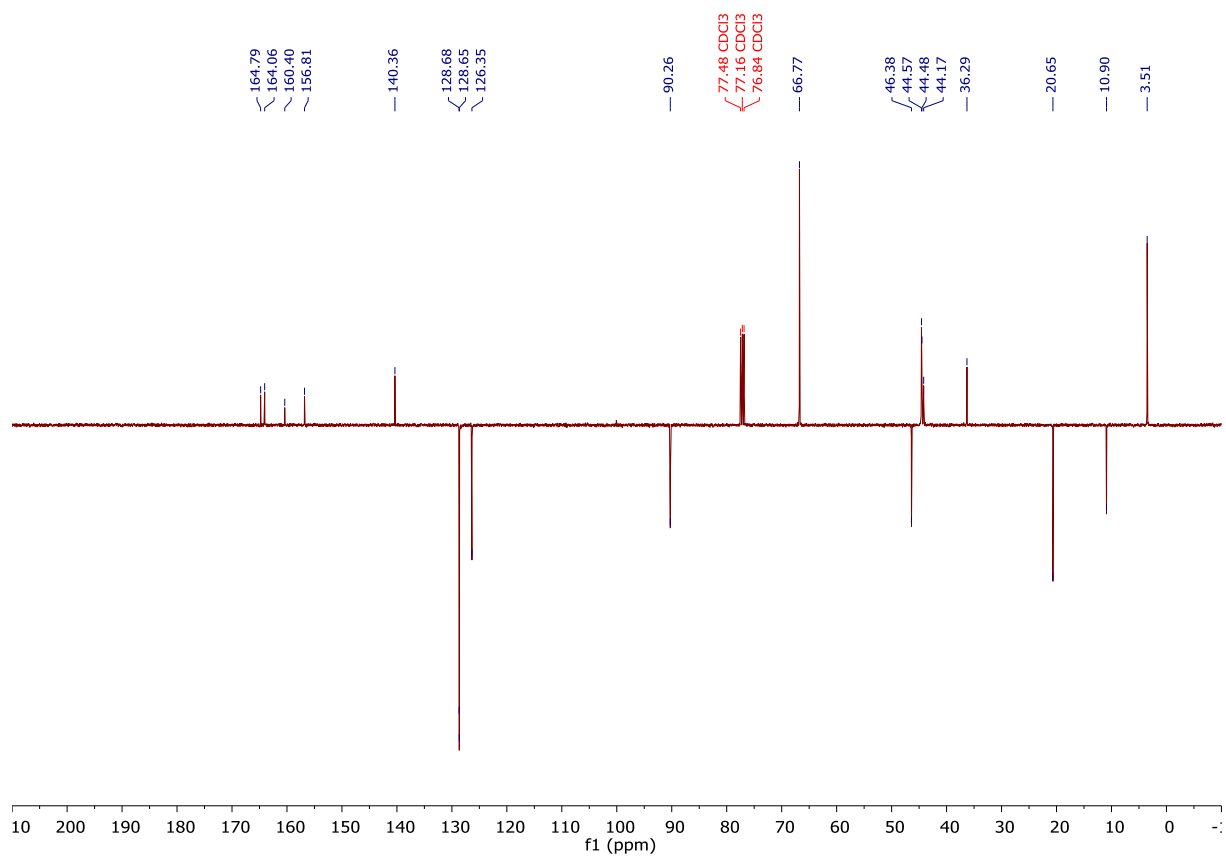
¹H NMR spectrum (CDCl₃) of 1-((2-((2-ethoxyphenyl)amino)ethyl)phenyl)pyrrolidine-4-carboxamide. The spectrum shows peaks from 0.00 to 8.05 ppm. Integration values are provided for several peaks: 0.97, 2.08, 2.92, 1.00, 6.01, 4.03, 2.04, 2.00, 2.02, 2.89, 1.03, 1.97, 1.99, and 0.29. The solvent peak for CDCl₃ is at 7.26 ppm.

¹³C NMR spectrum (CDCl₃) of compound 10. The x-axis is labeled 'f1 (ppm)' and ranges from 10 to 210. The spectrum shows several peaks with chemical shifts labeled above them: 164.74, 164.12, 160.29, 156.86, 140.06, 128.83, 126.62, 126.32, 90.06, 77.48 CDCl₃, 77.16 CDCl₃, 76.84 CDCl₃, 66.78, 49.83, 44.53, 44.09, 43.04, 34.76, 13.24, 10.90, and 3.44. The solvent triplet is centered at 77 ppm.

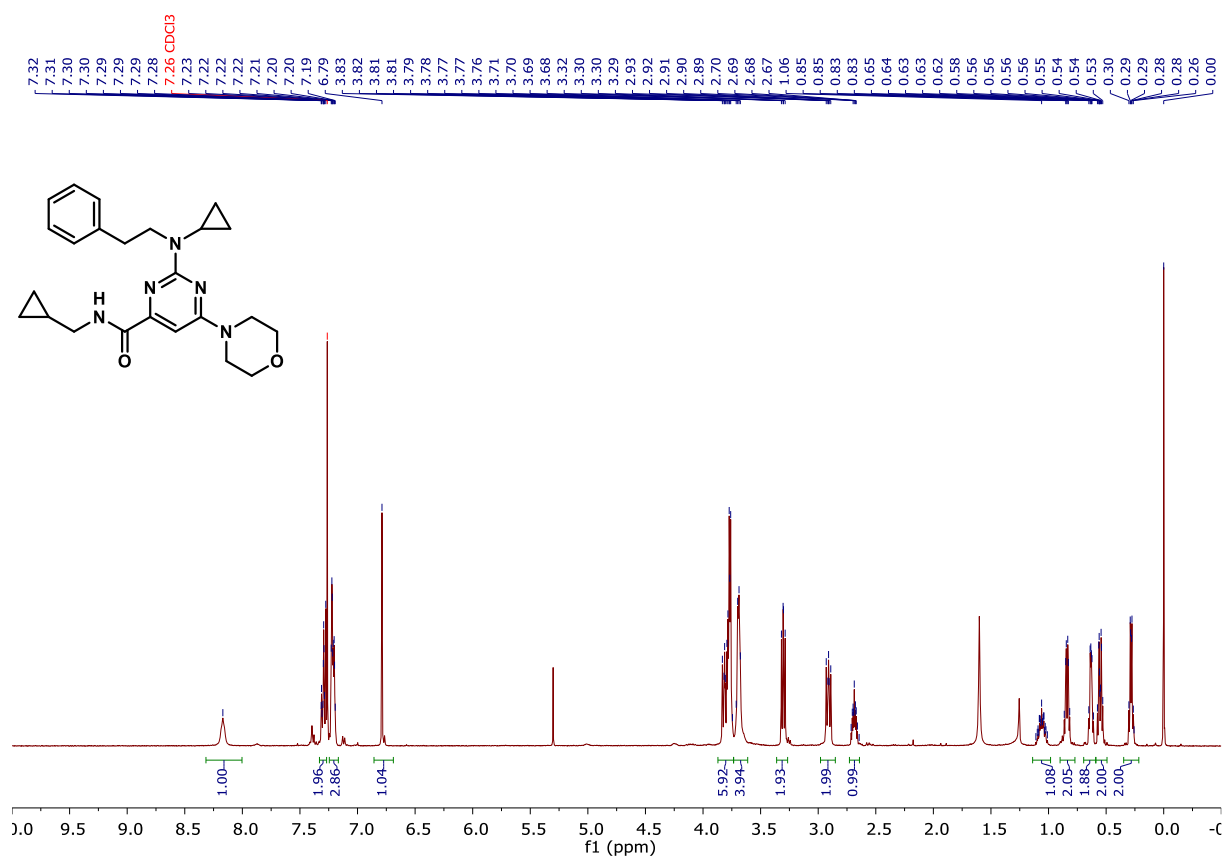
¹H-NMR: 55



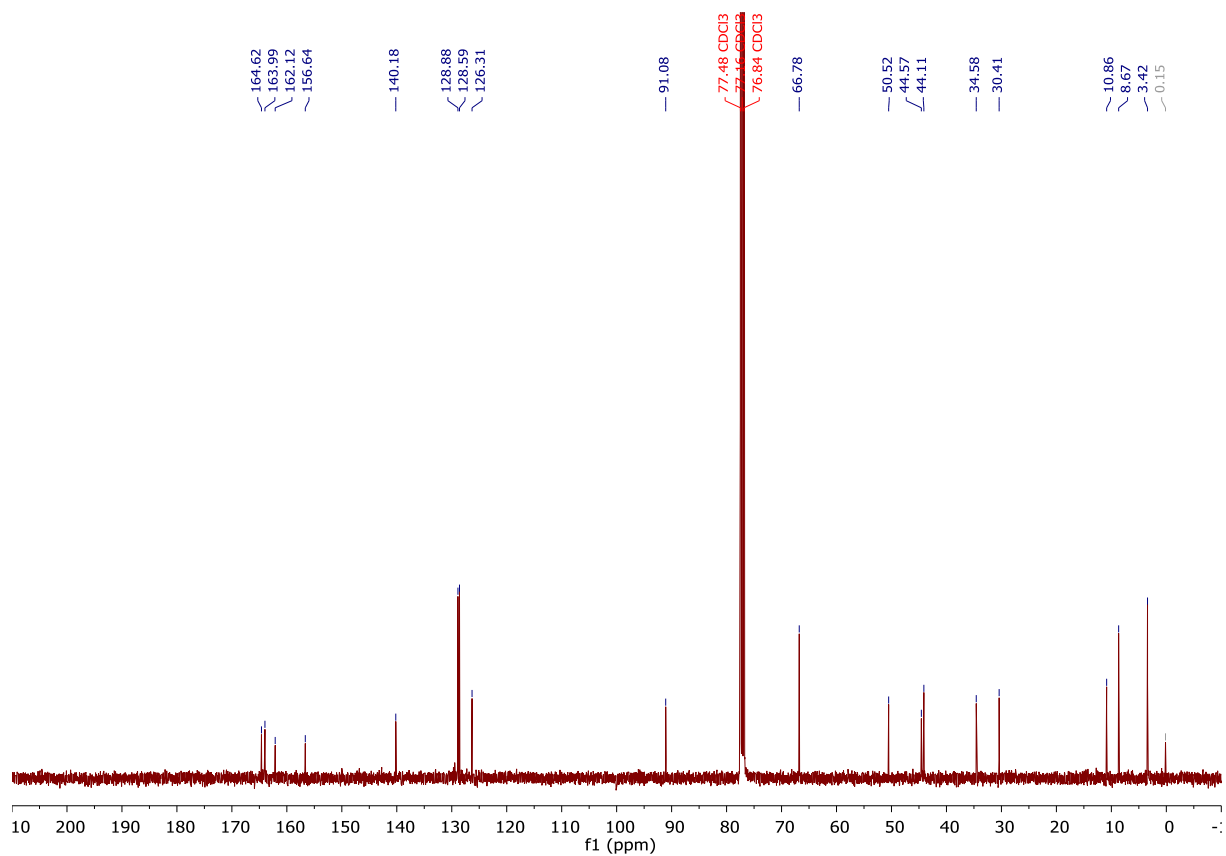
¹³C-NMR



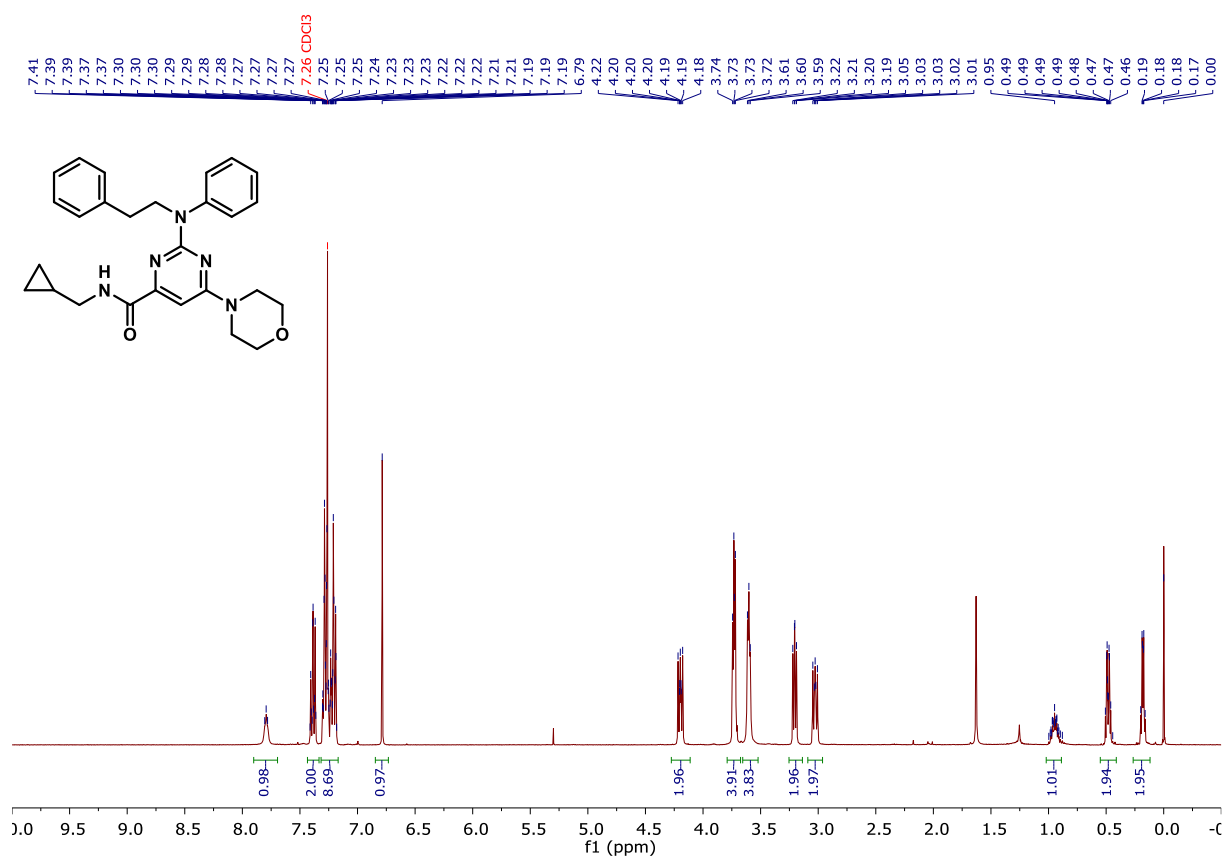
¹H-NMR: 56



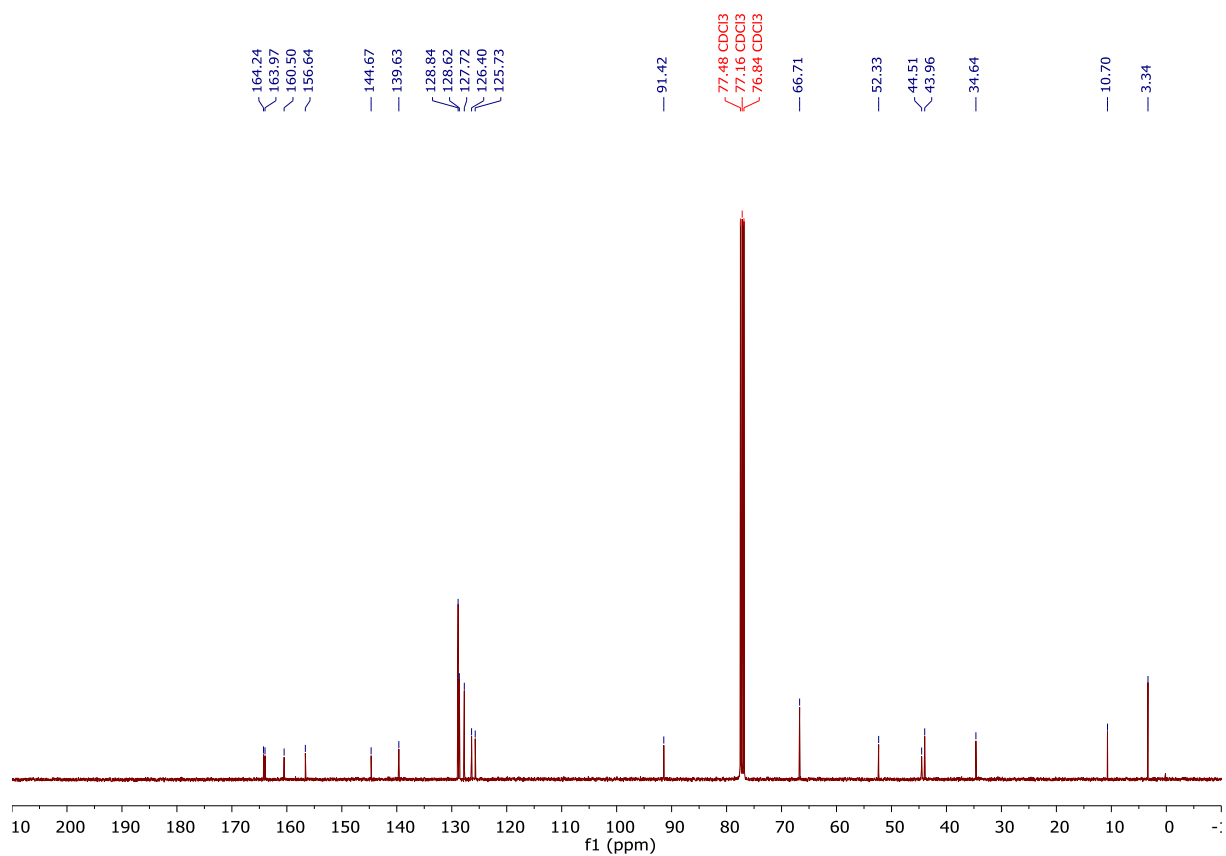
¹³C-NMR



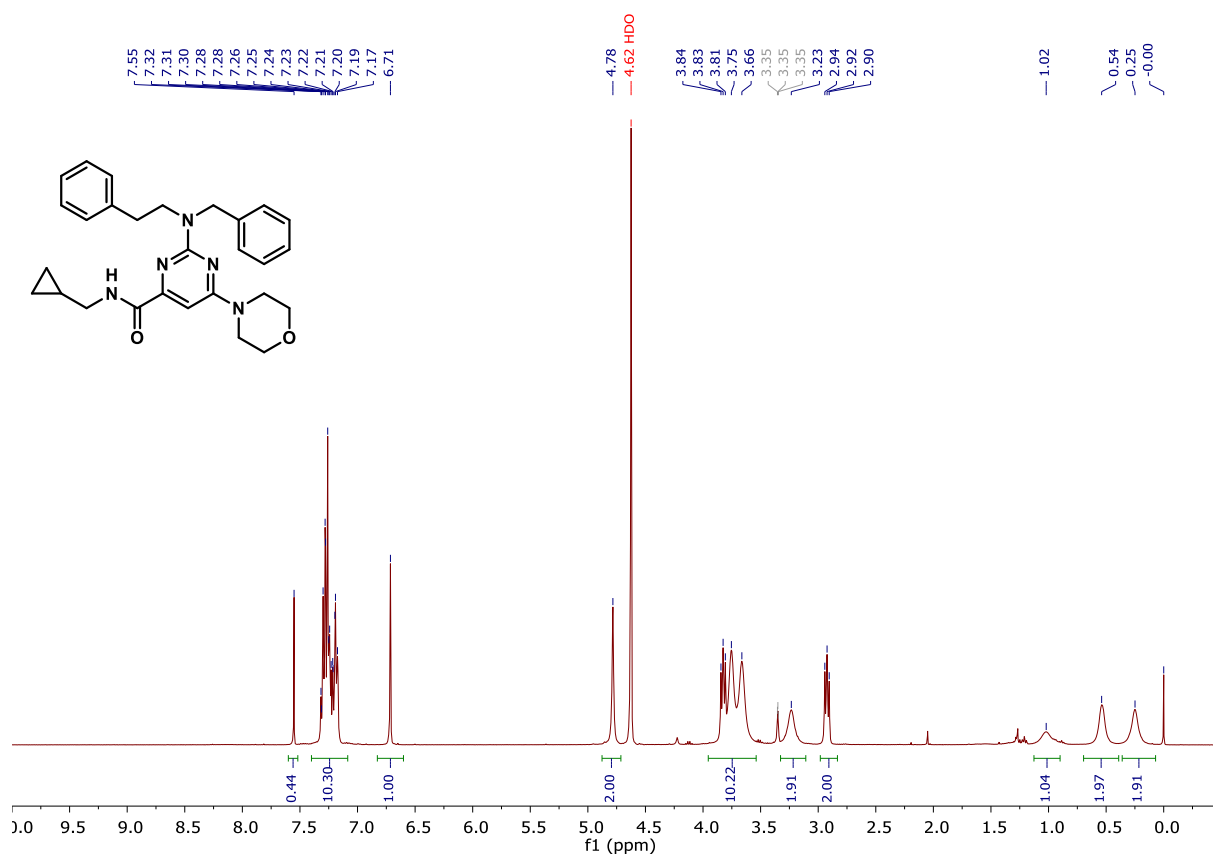
¹H-NMR: 57



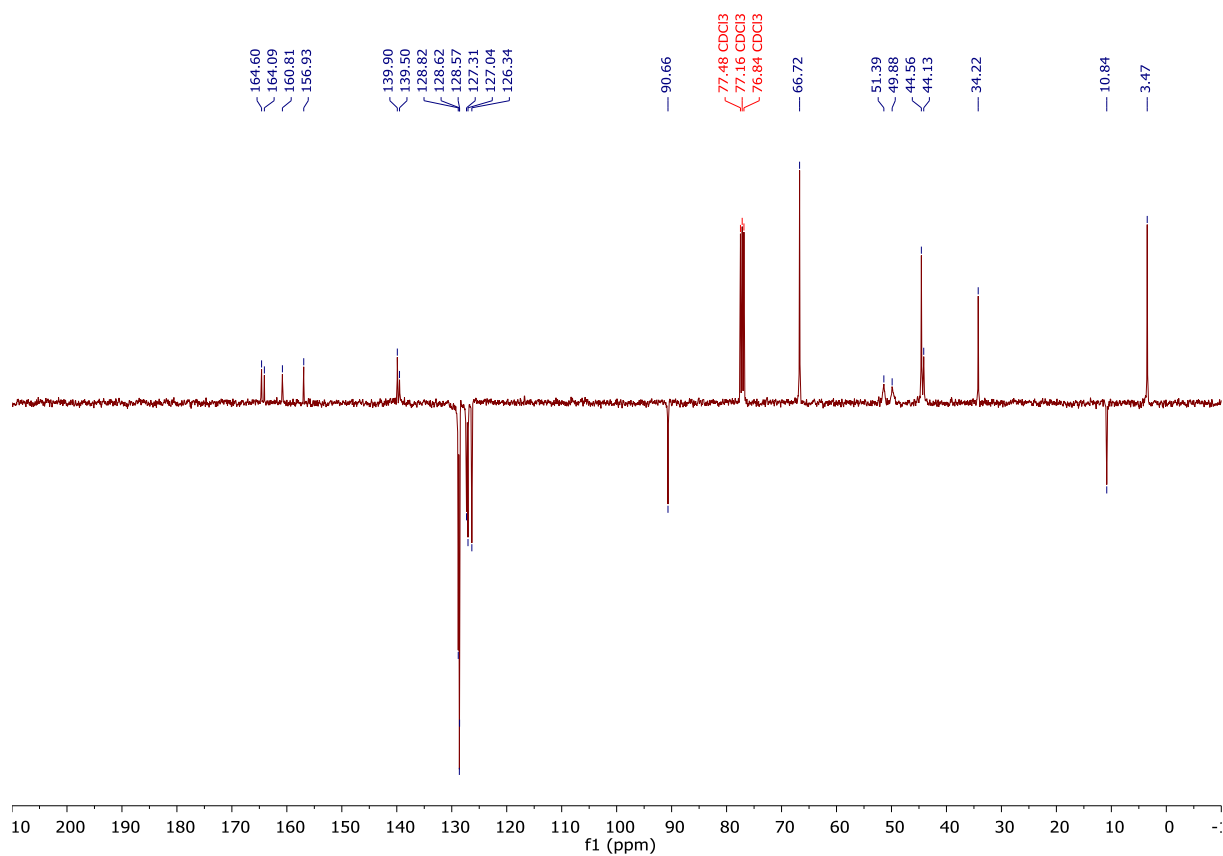
¹³C-NMR



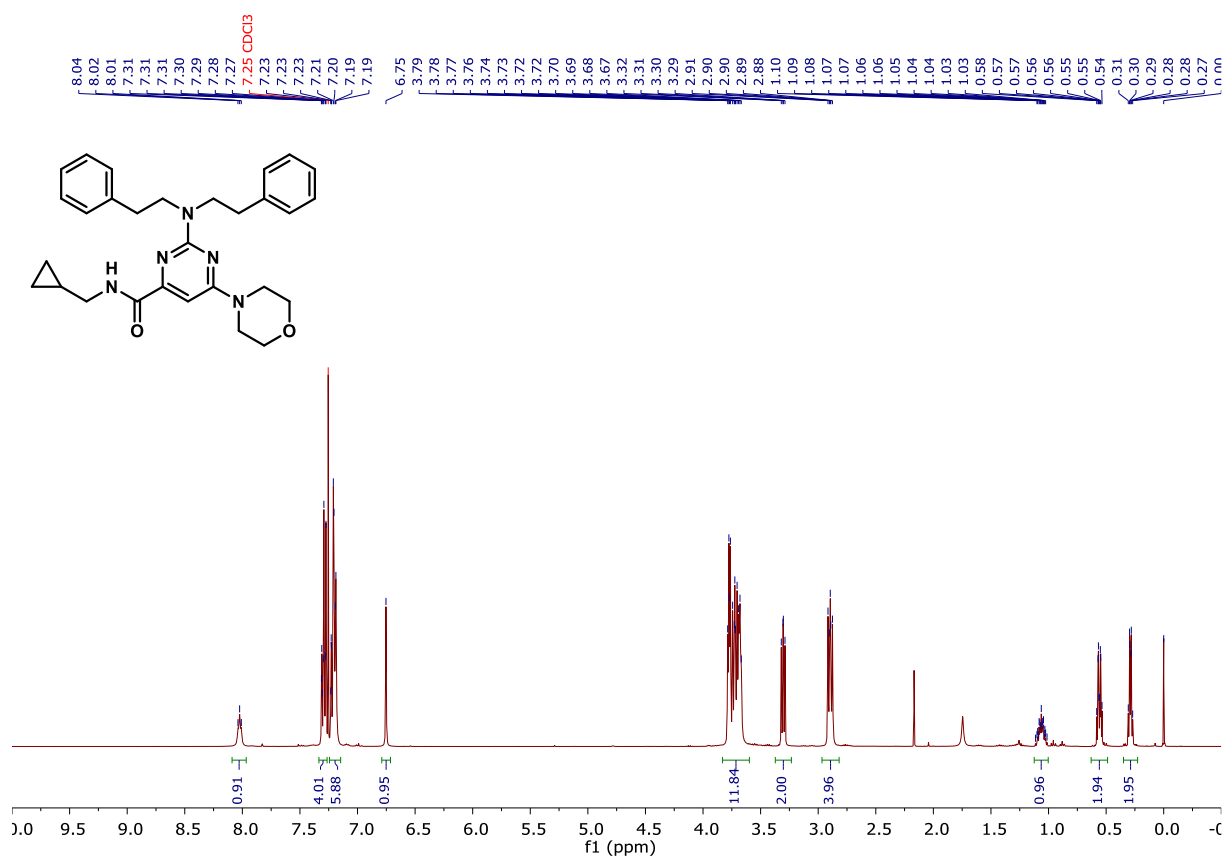
¹H-NMR: 58 (MeOD + CDCl₃)



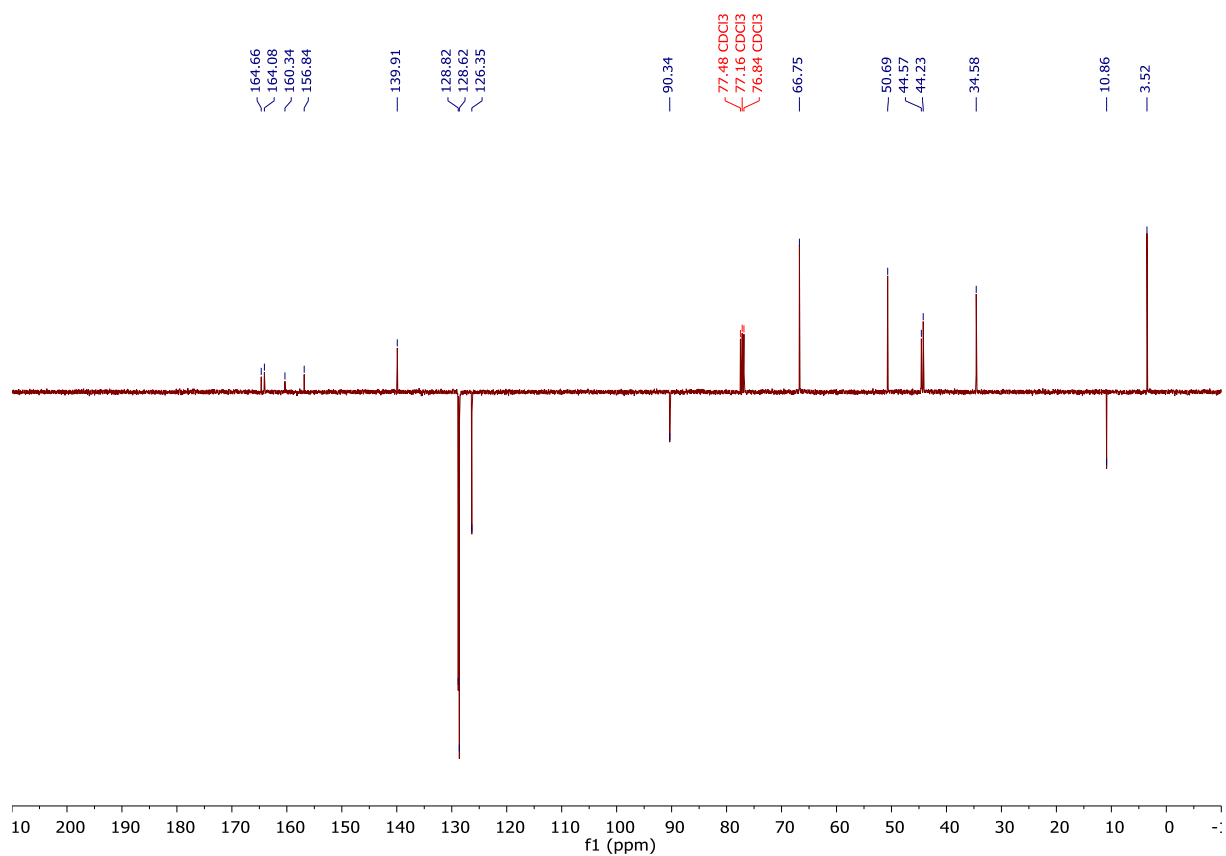
¹³C-NMR (CDCl₃)



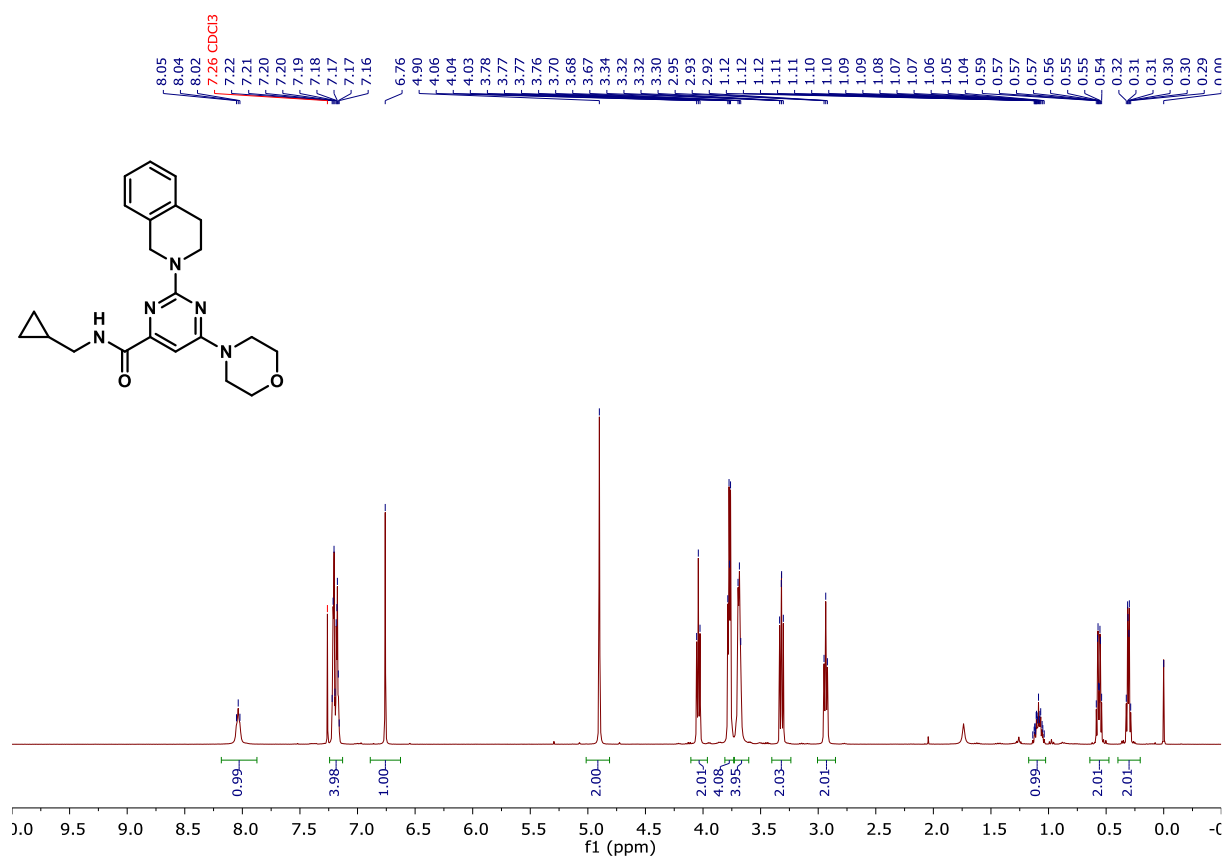
¹H-NMR: 59



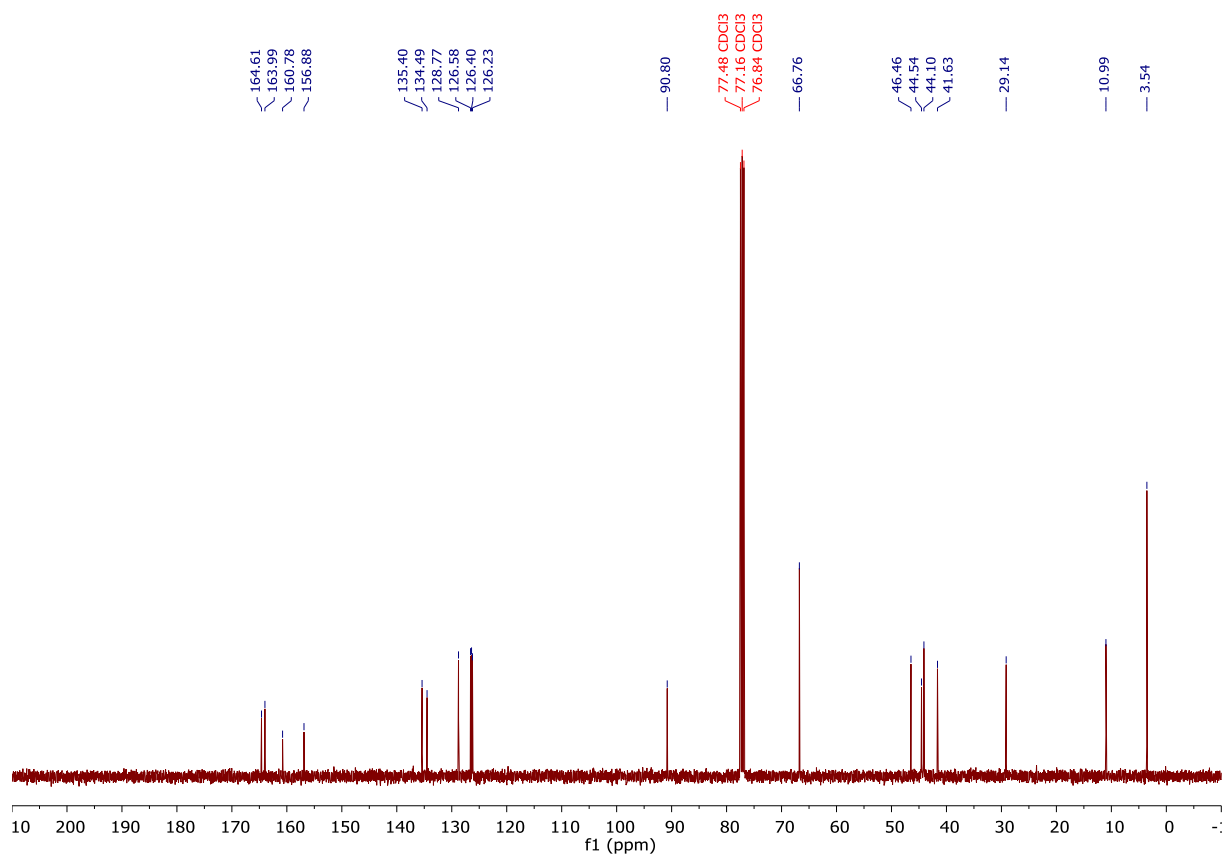
¹³C-NMR



¹H-NMR: 60



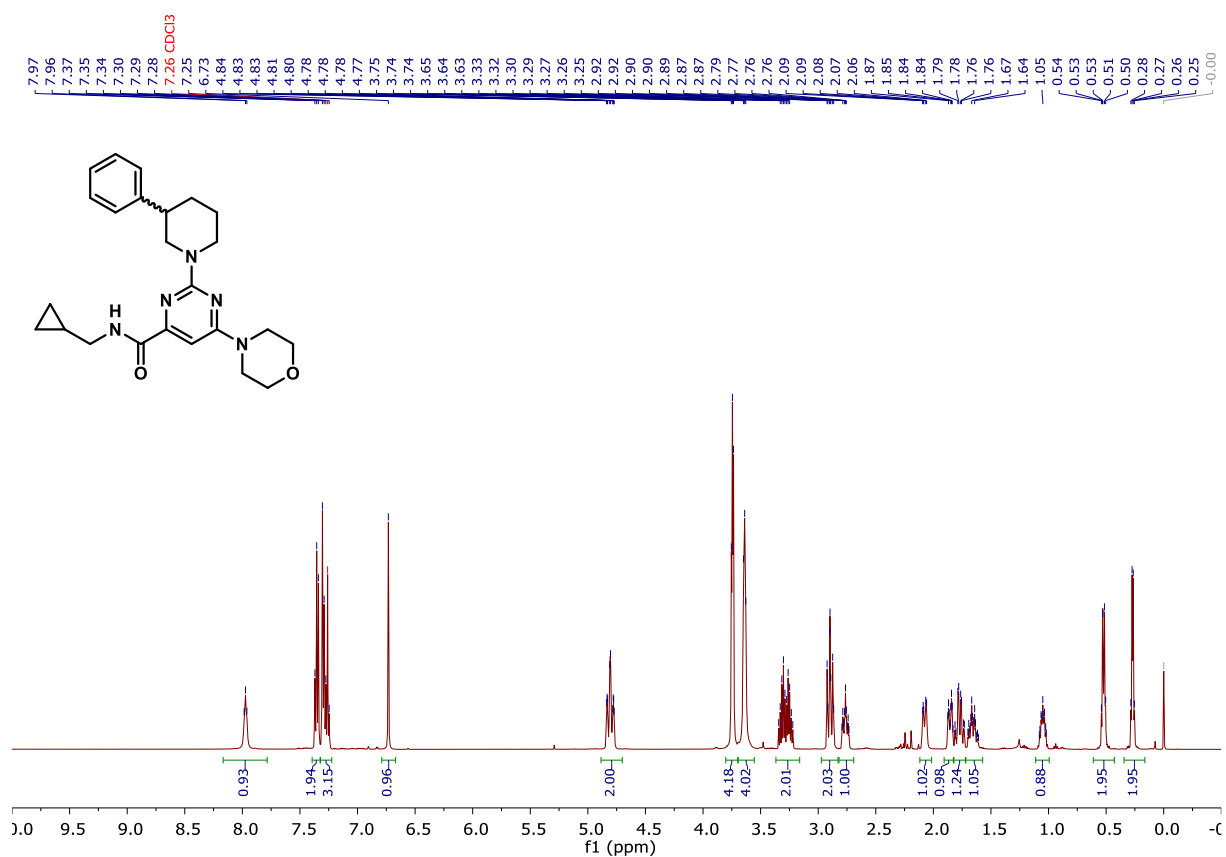
¹³C-NMR



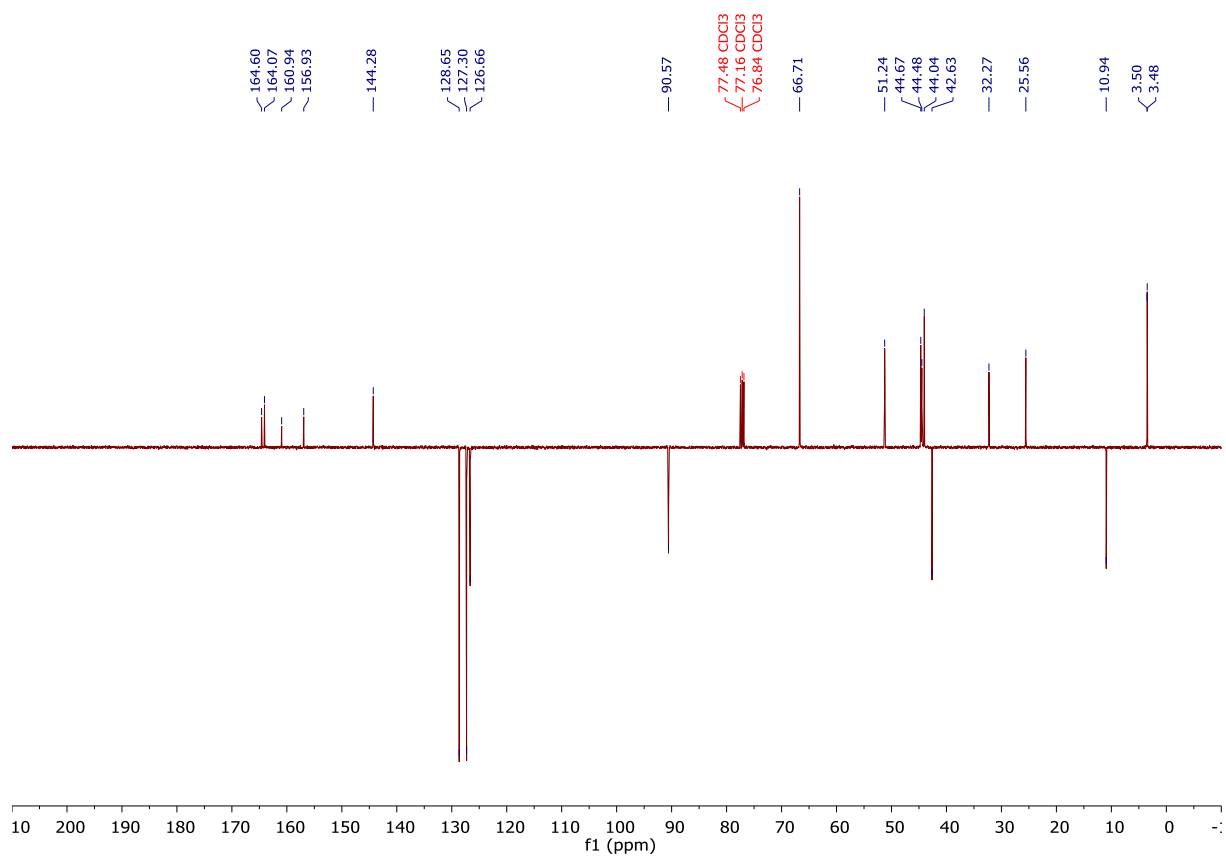
[illegible]

¹³C NMR spectrum (CDCl₃) of compound 10. The x-axis is labeled 'f1 (ppm)' and ranges from 0 to 210. The spectrum shows several peaks, with the following chemical shifts labeled: 164.65, 163.89, 159.58, 156.77, 142.22, 128.70, 127.29, 126.84, 90.15, 77.48 CDCl₃, 77.16 CDCl₃, 76.84 CDCl₃, 66.73, 53.27, 46.49, 44.42, 44.19, 44.02, 33.28, 10.90, and 3.49. The CDCl₃ solvent triplet is centered at 77 ppm.

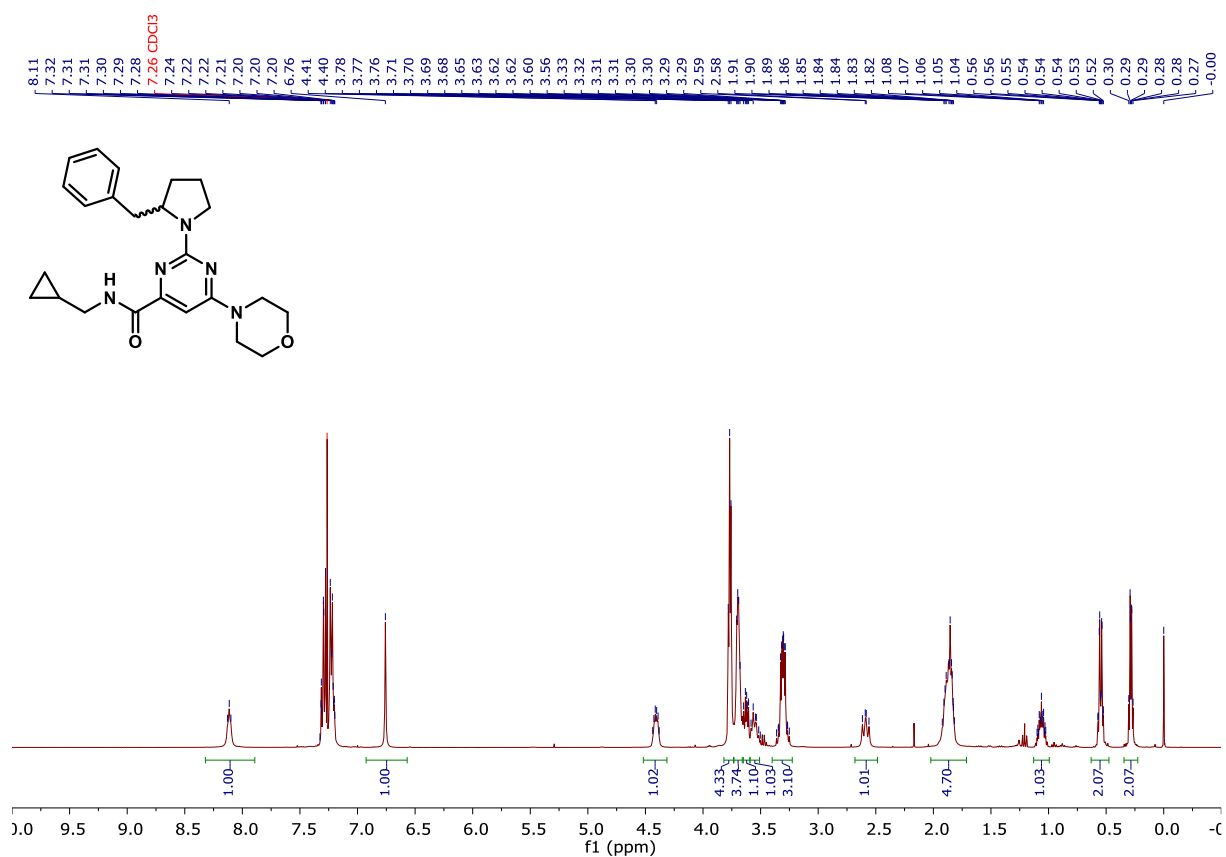
¹H-NMR: 62



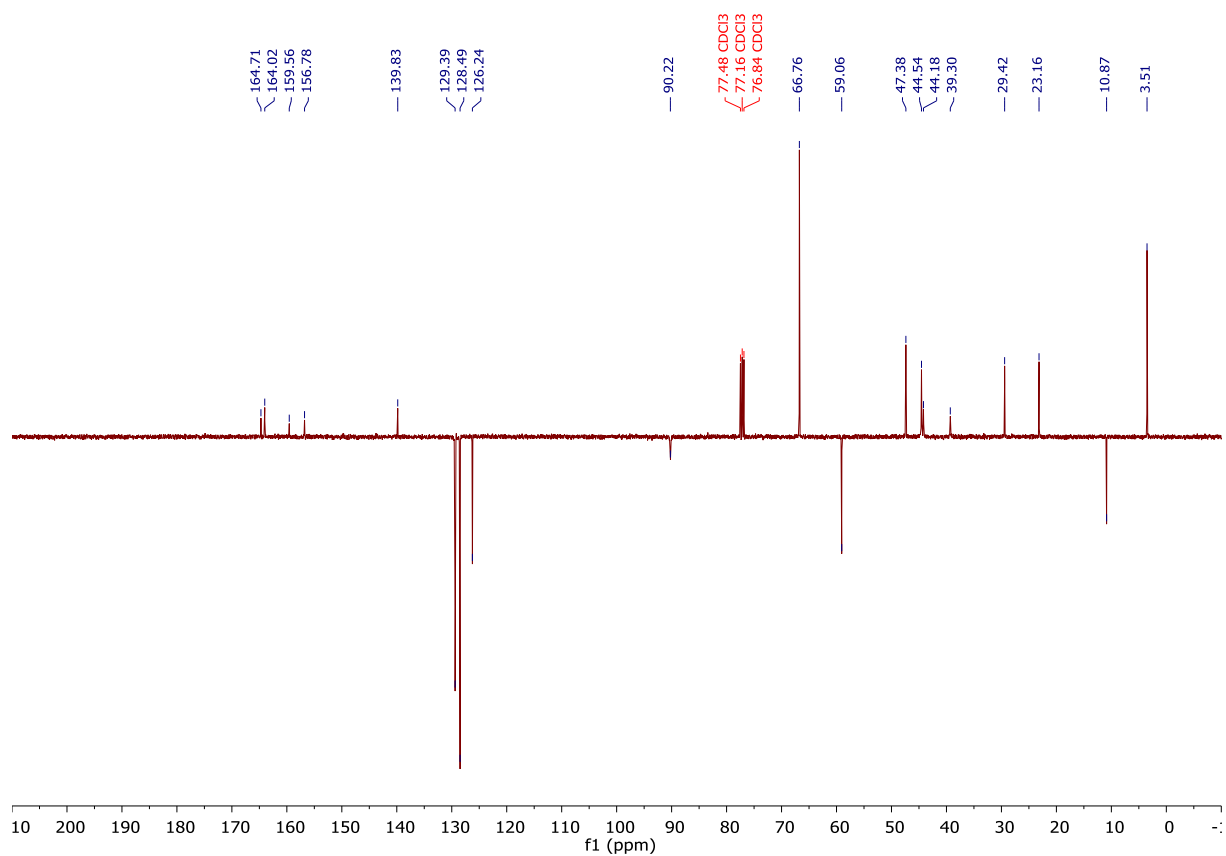
¹³C-NMR



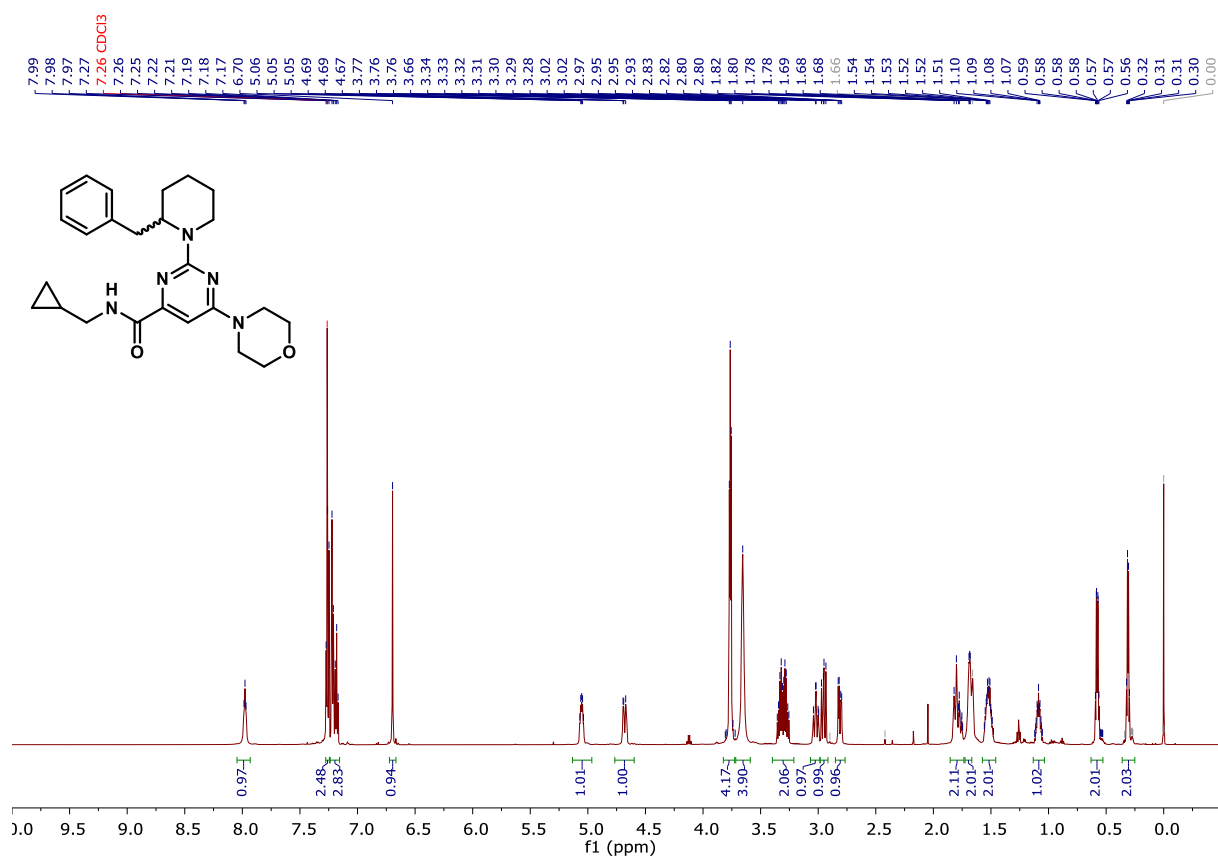
¹H-NMR: 63



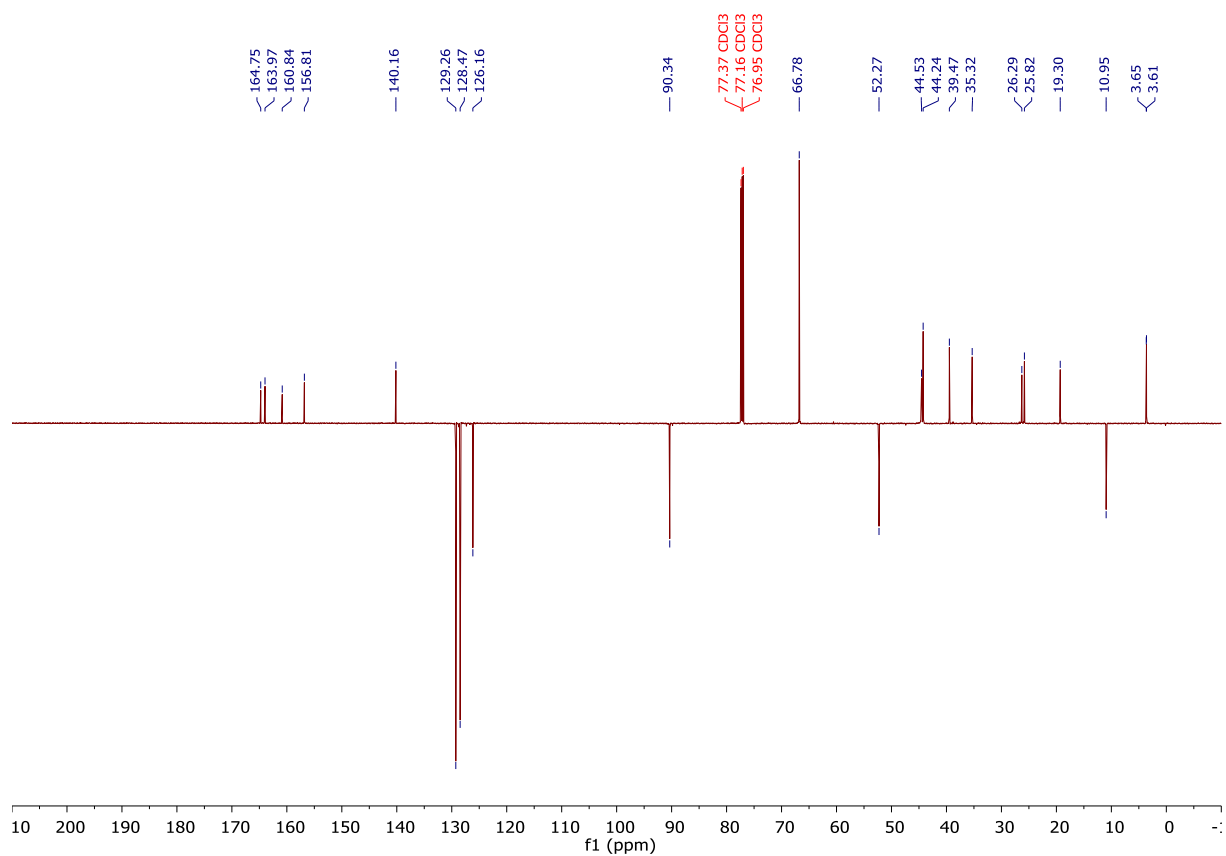
¹³C-NMR



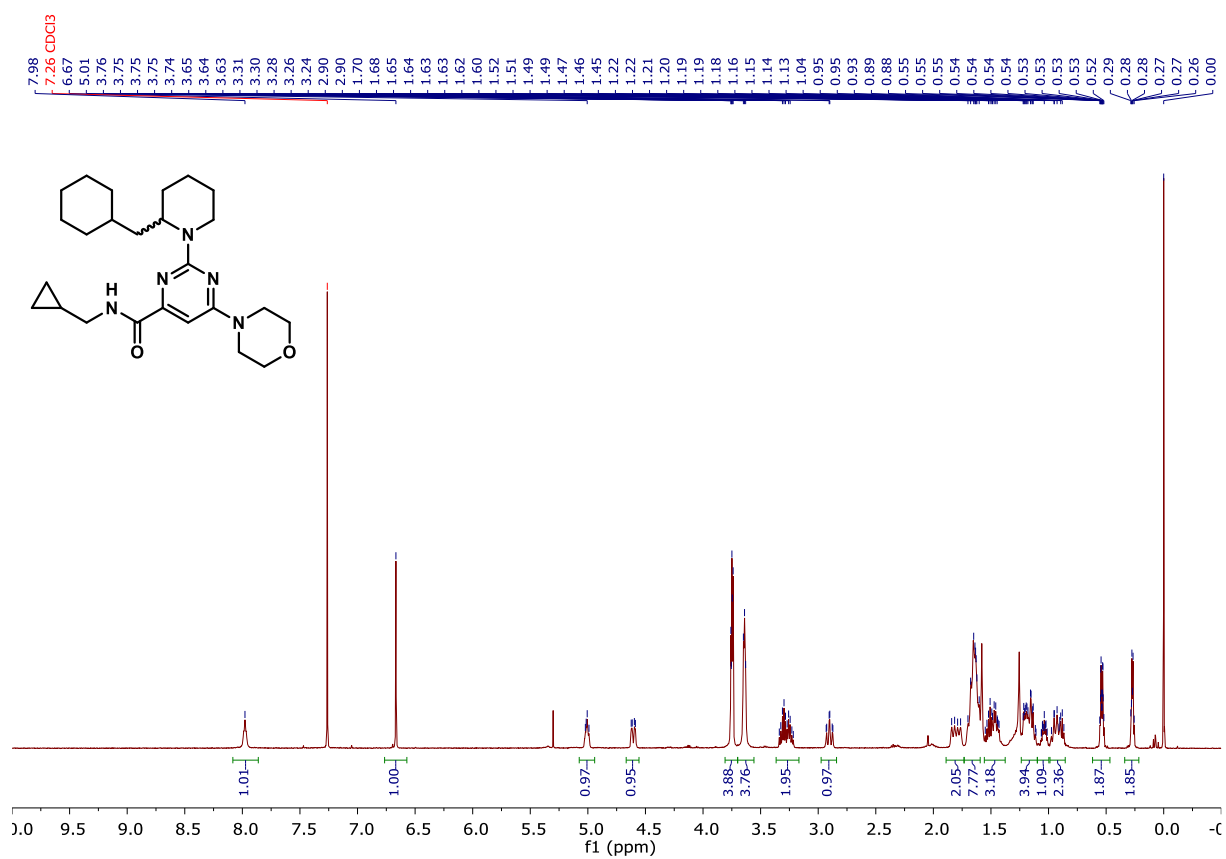
¹H-NMR: 64



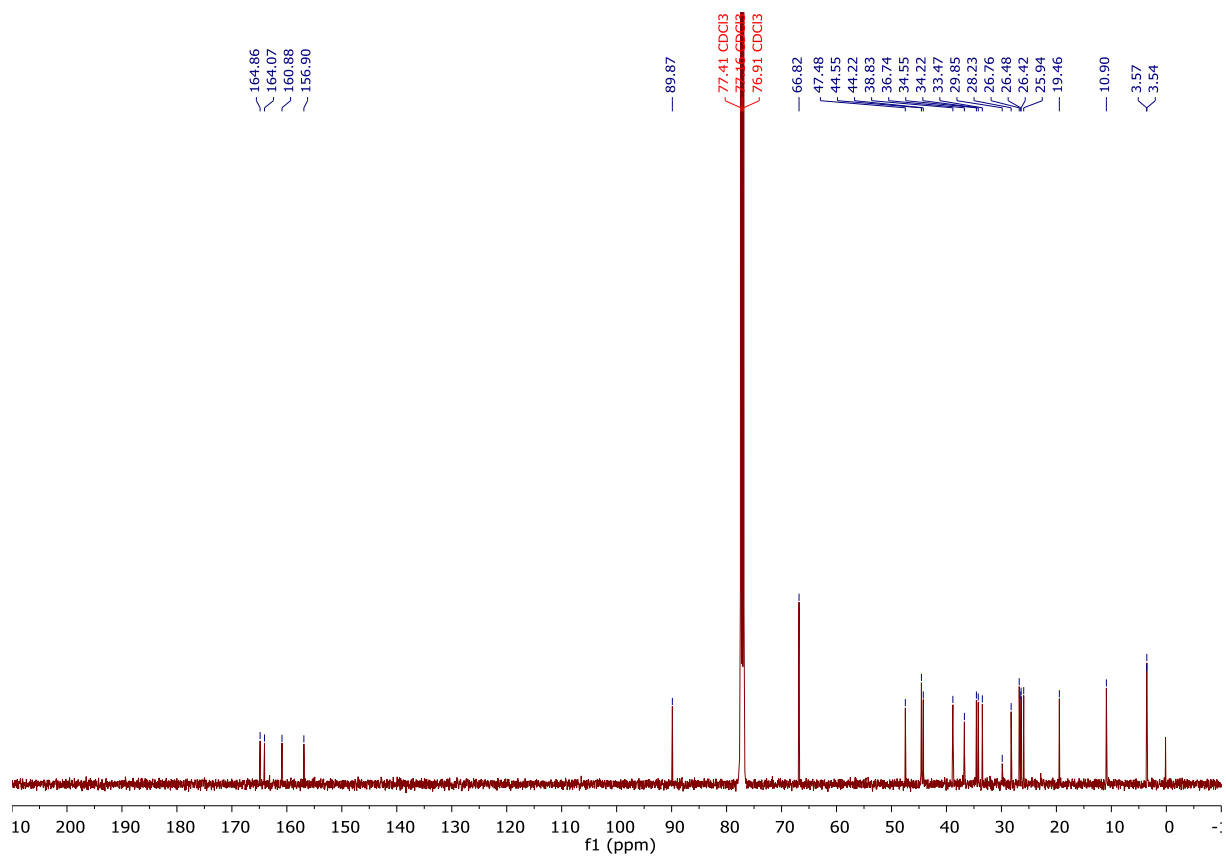
¹³C-NMR



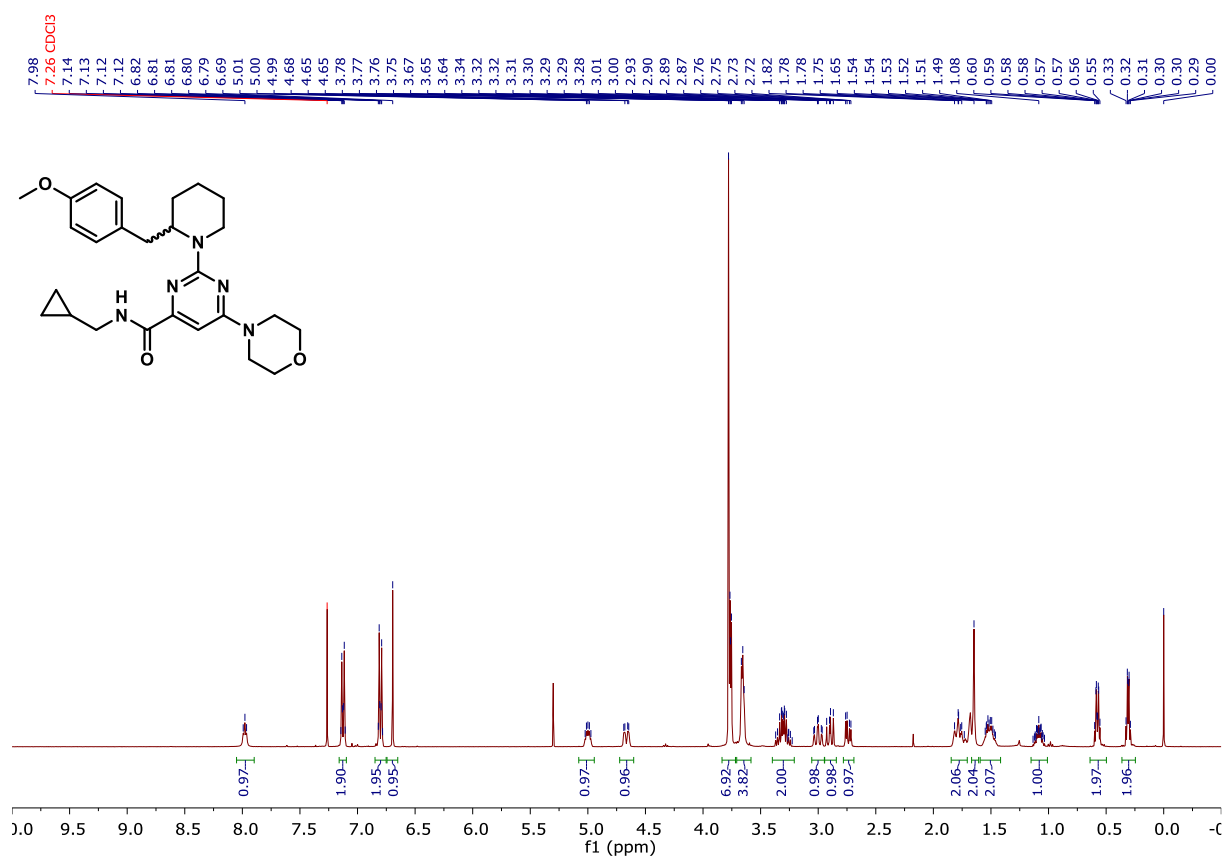
¹H-NMR: 65



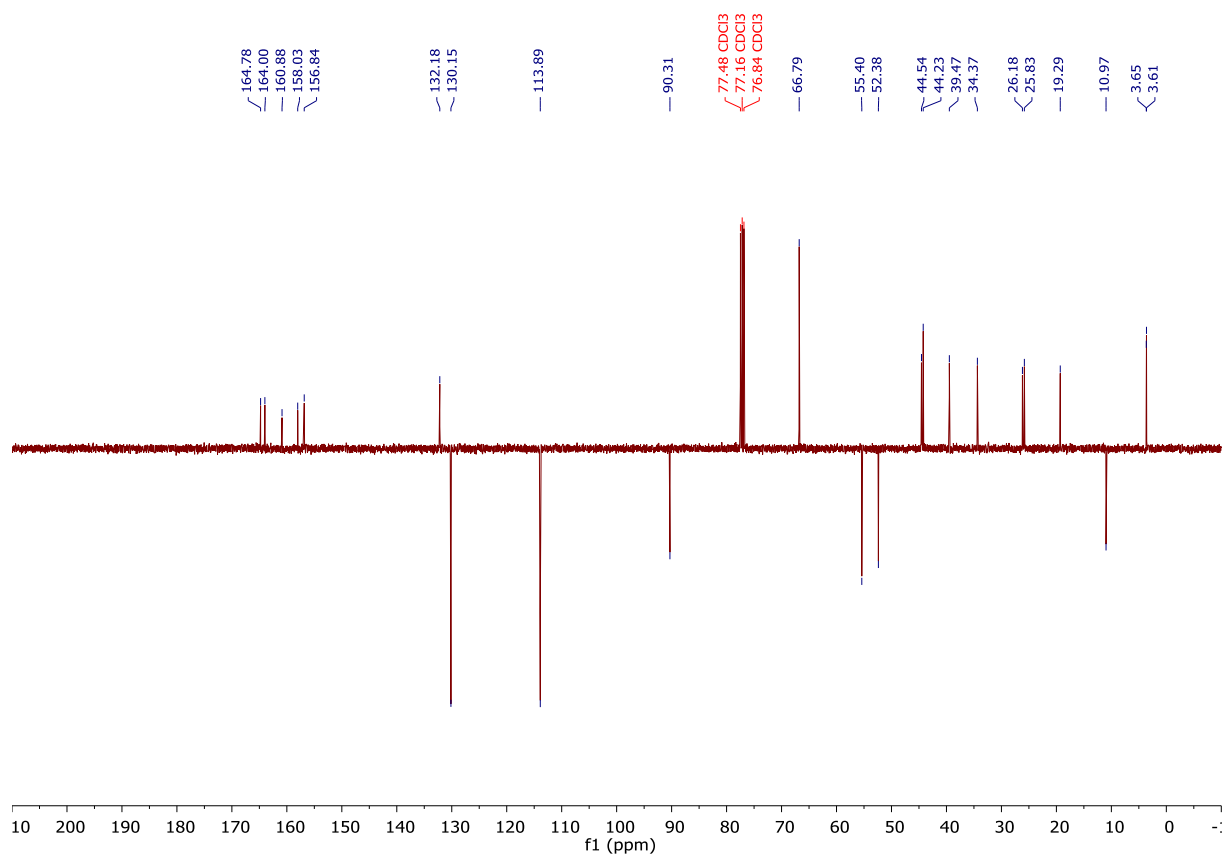
¹³C-NMR



¹H-NMR: 66



¹³C-NMR

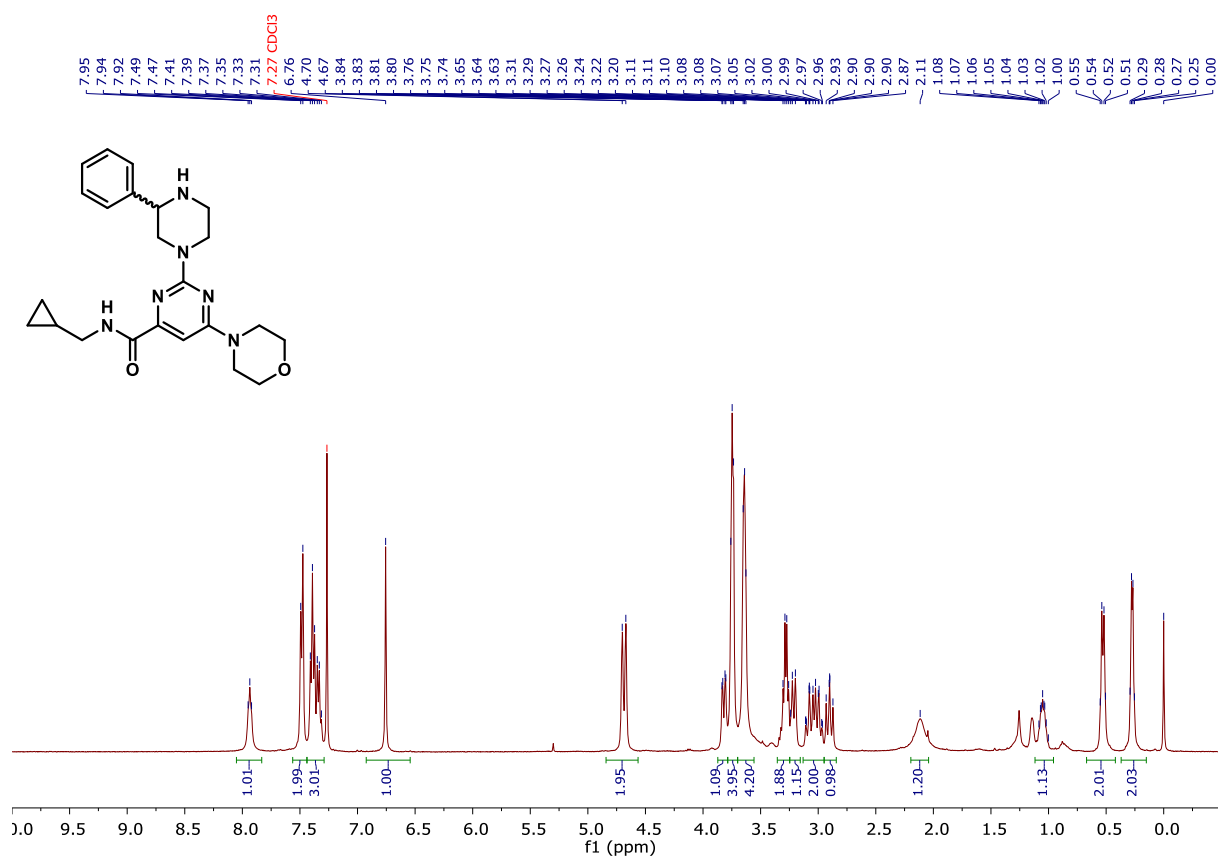


Chemical structure of compound 10: C1CC1CC(=O)c2nc(N3CCOCC3)cnc2N4CCOC(C5=CC=CC=C5)C4

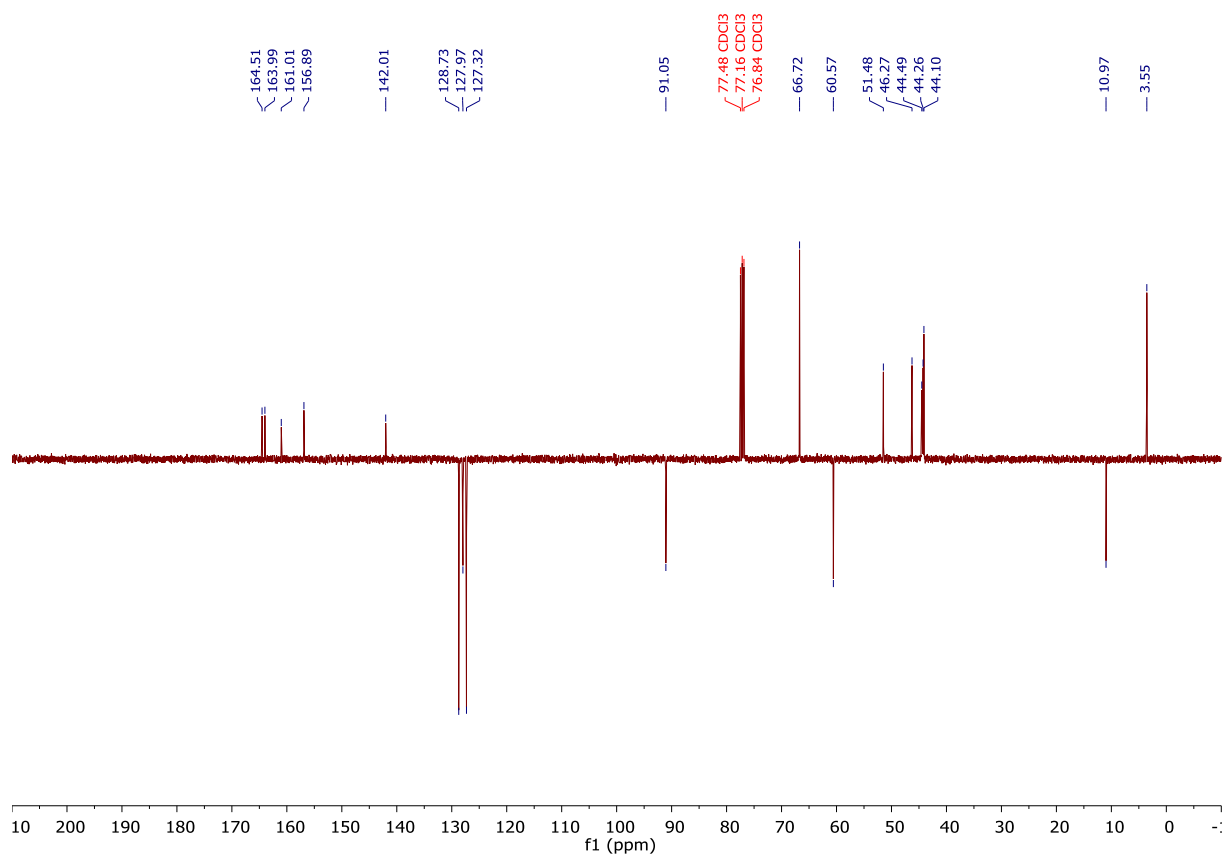
¹H NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift in ppm, ranging from 0.00 to 7.92. The spectrum shows several peaks, with integration values indicated below the baseline.

Integration values (from left to right): 0.97, 5.09, 1.00, 1.03, 2.03, 1.01, 1.28, 3.94, 2.05, 1.02, 1.01, 1.00, 2.03, 2.02.

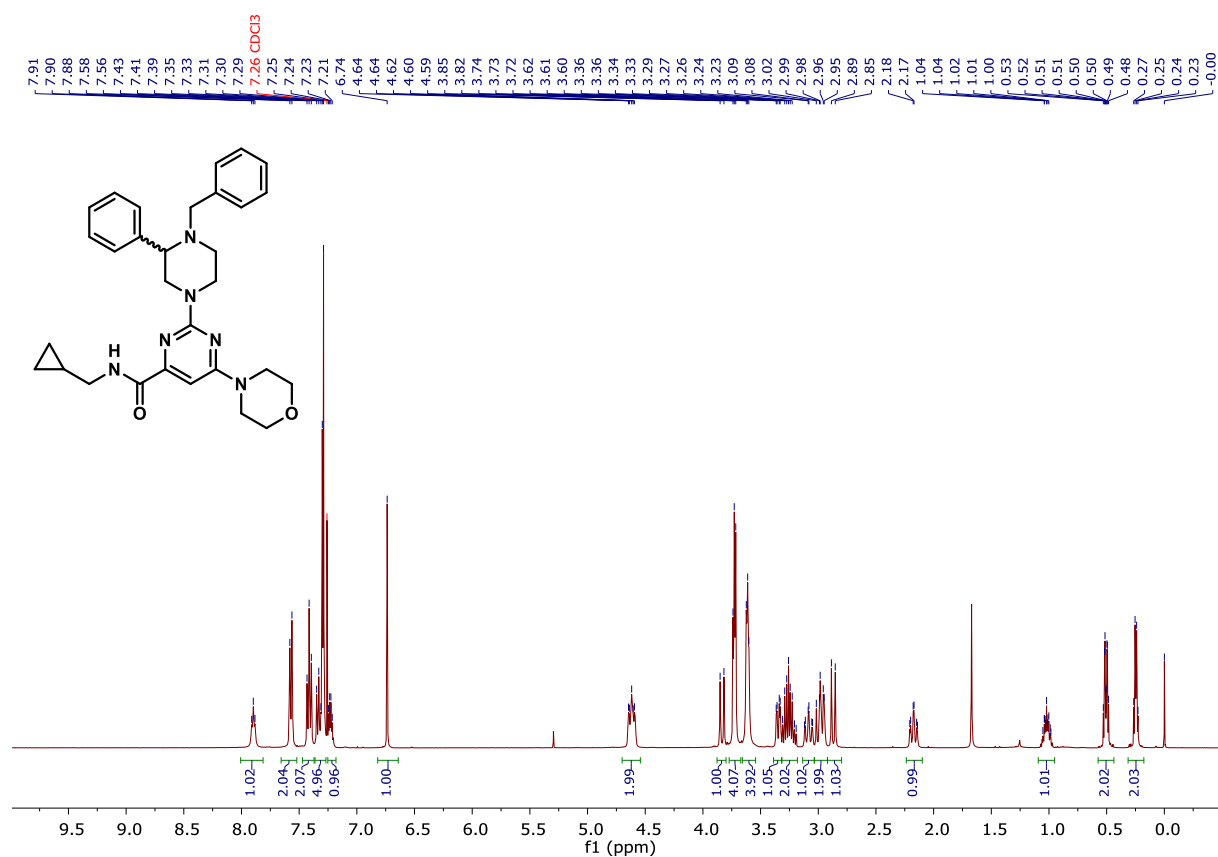
¹H-NMR: 68



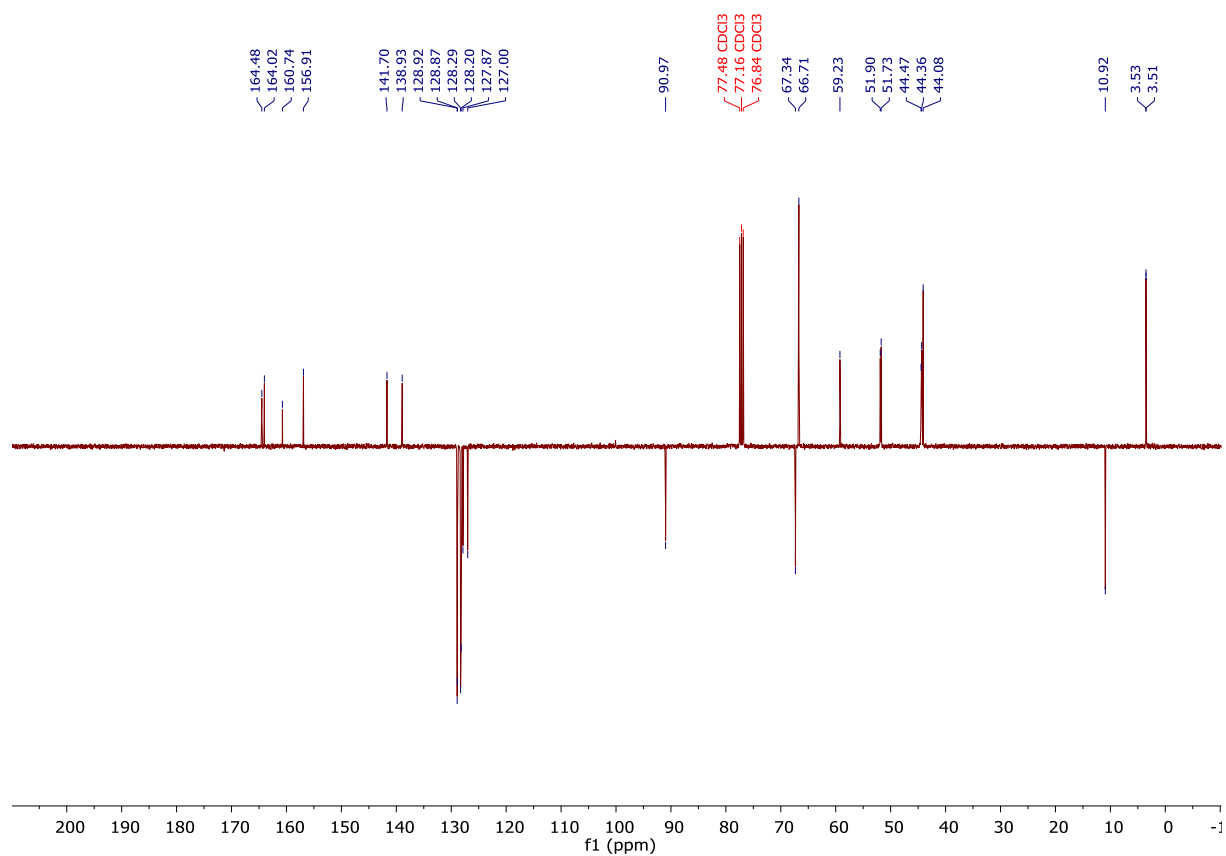
¹³C-NMR



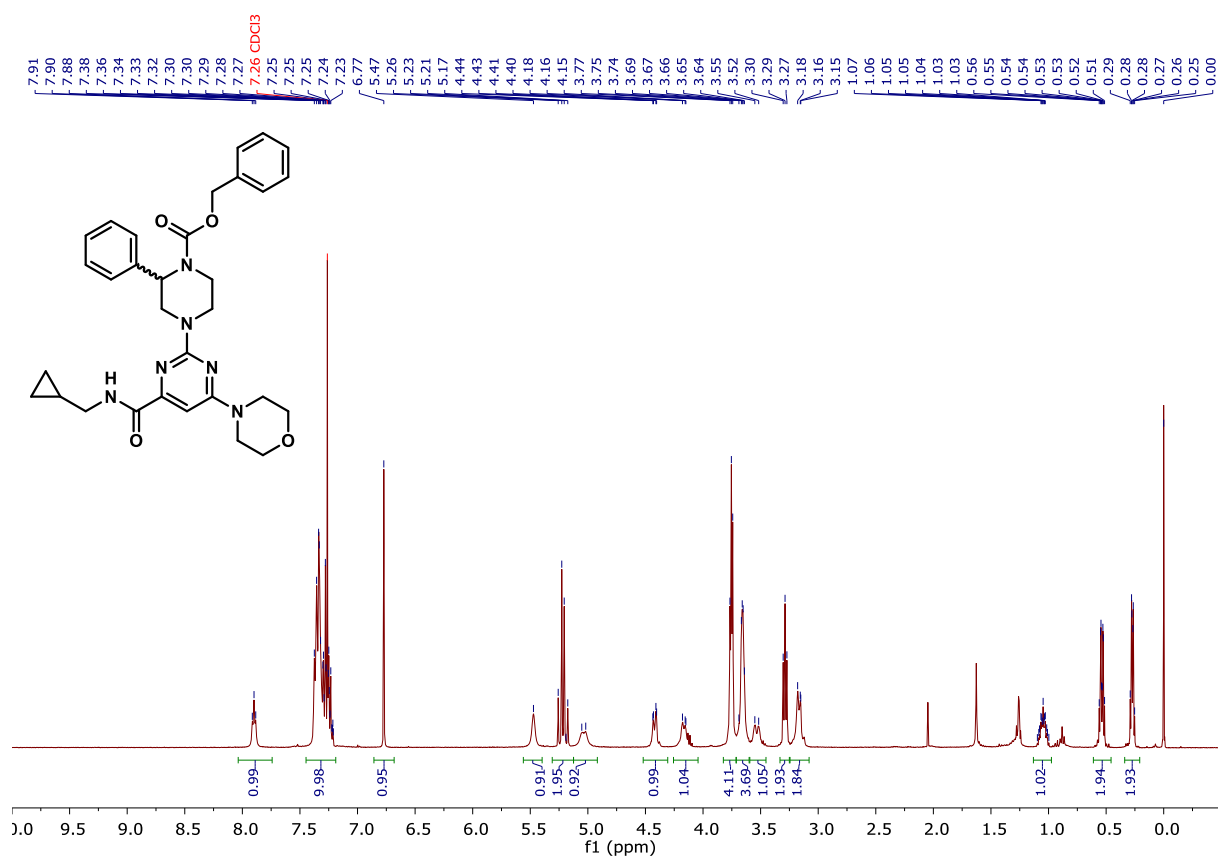
¹H-NMR: 69



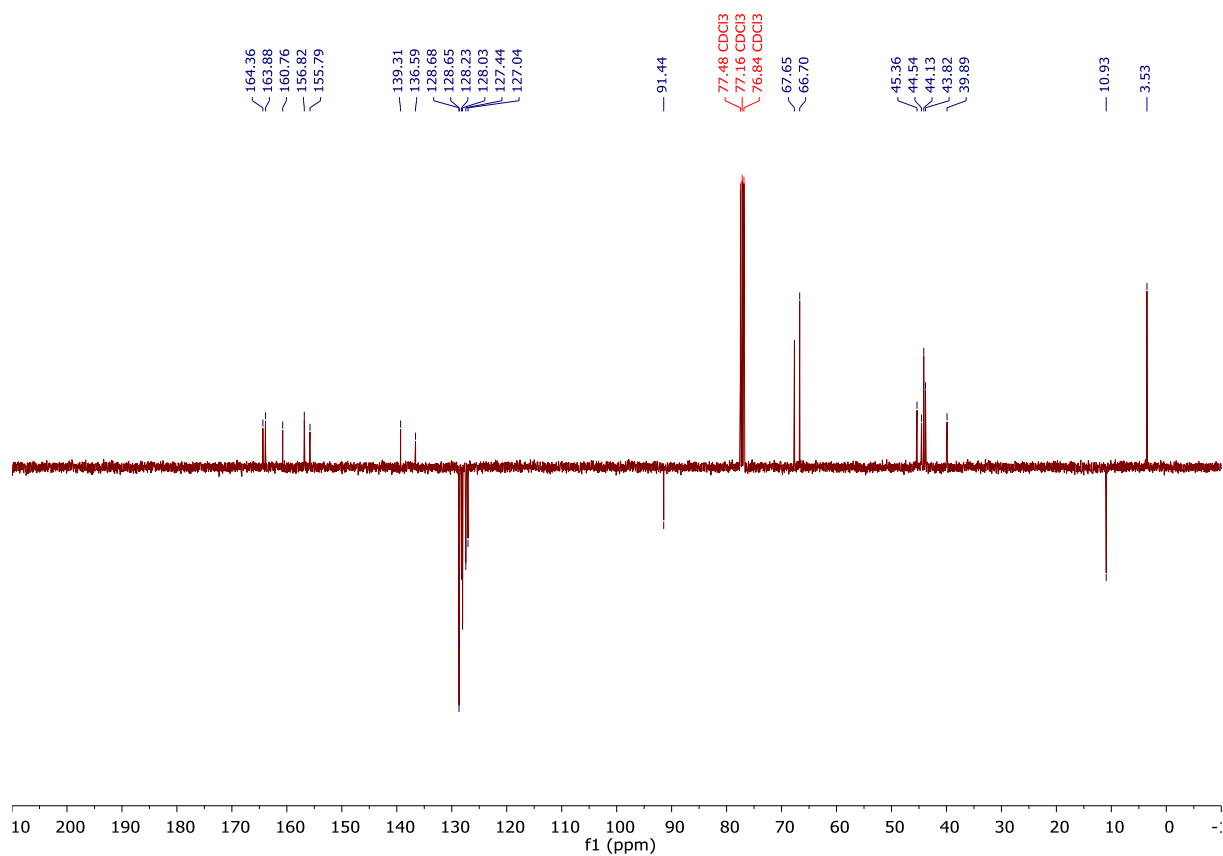
¹³C-NMR



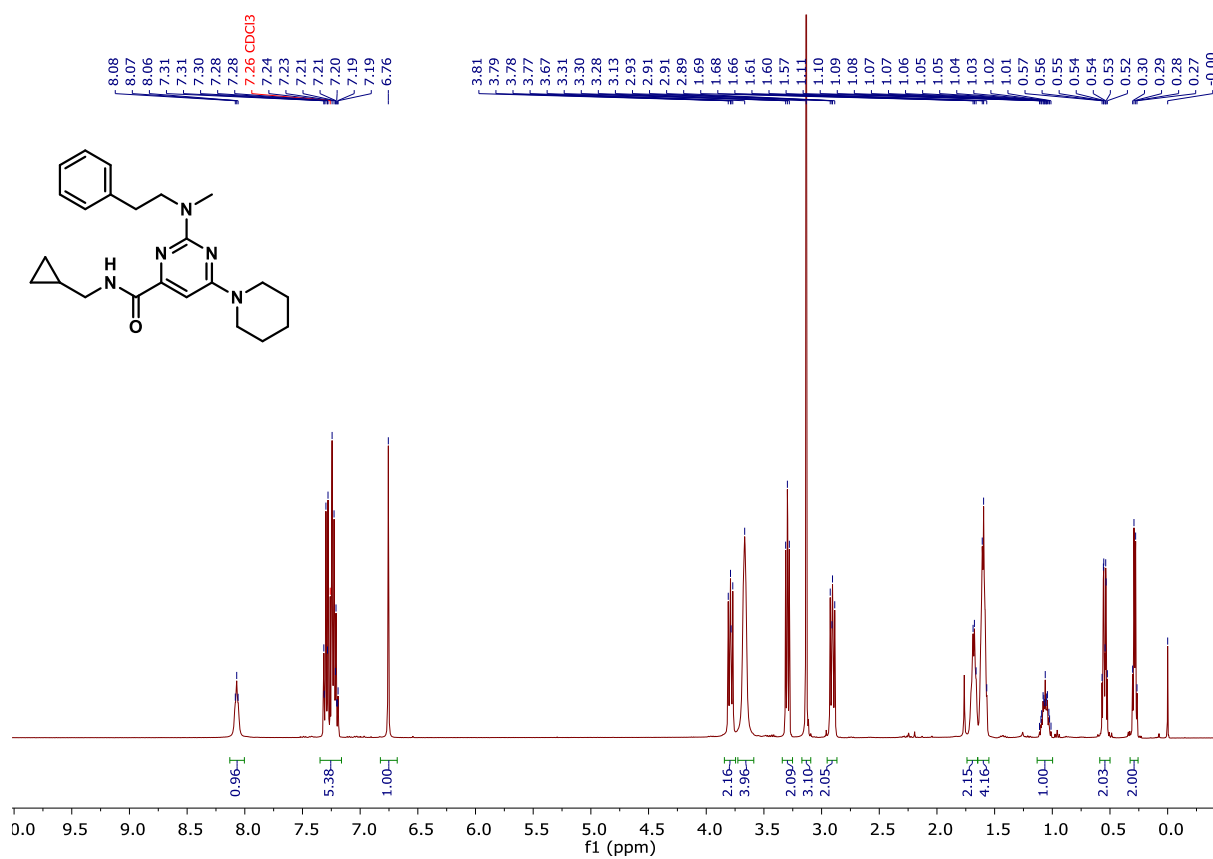
¹H-NMR: 70



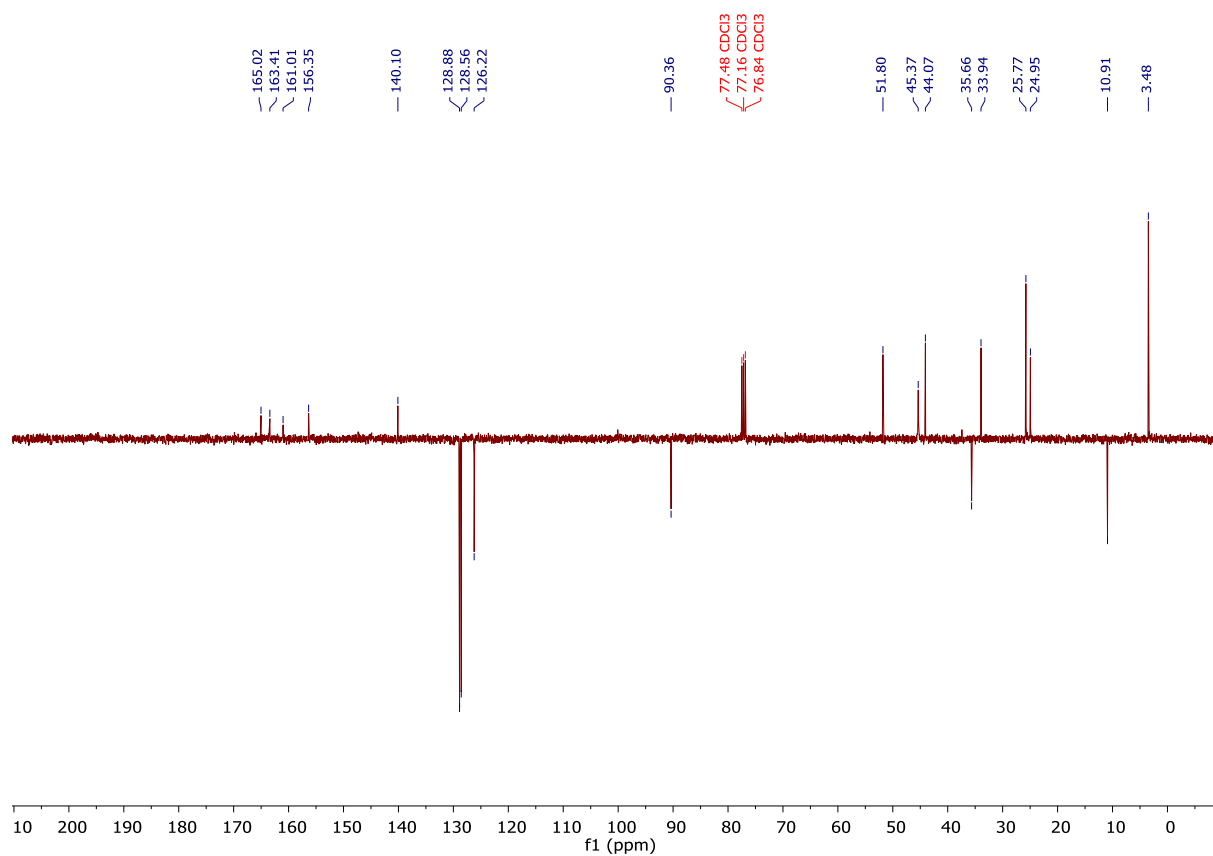
¹³C-NMR



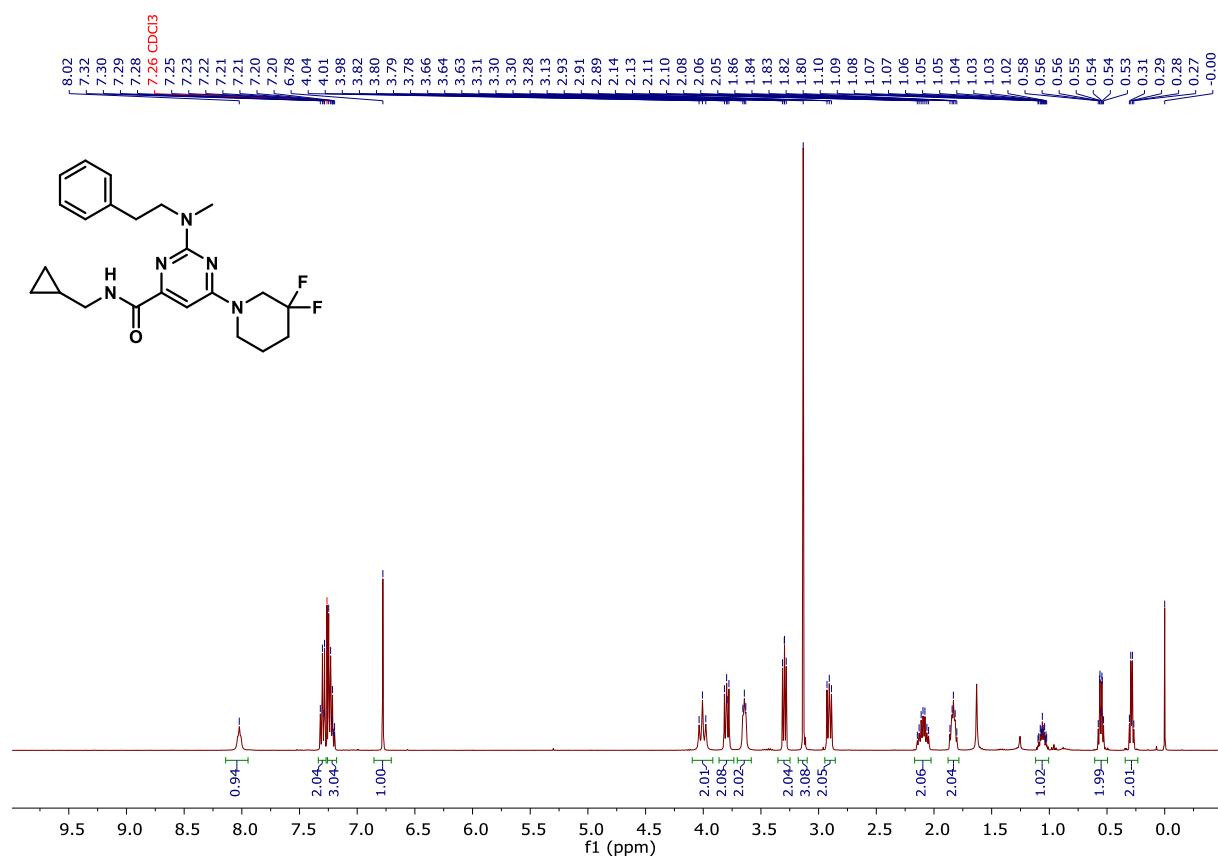
¹H-NMR: 71



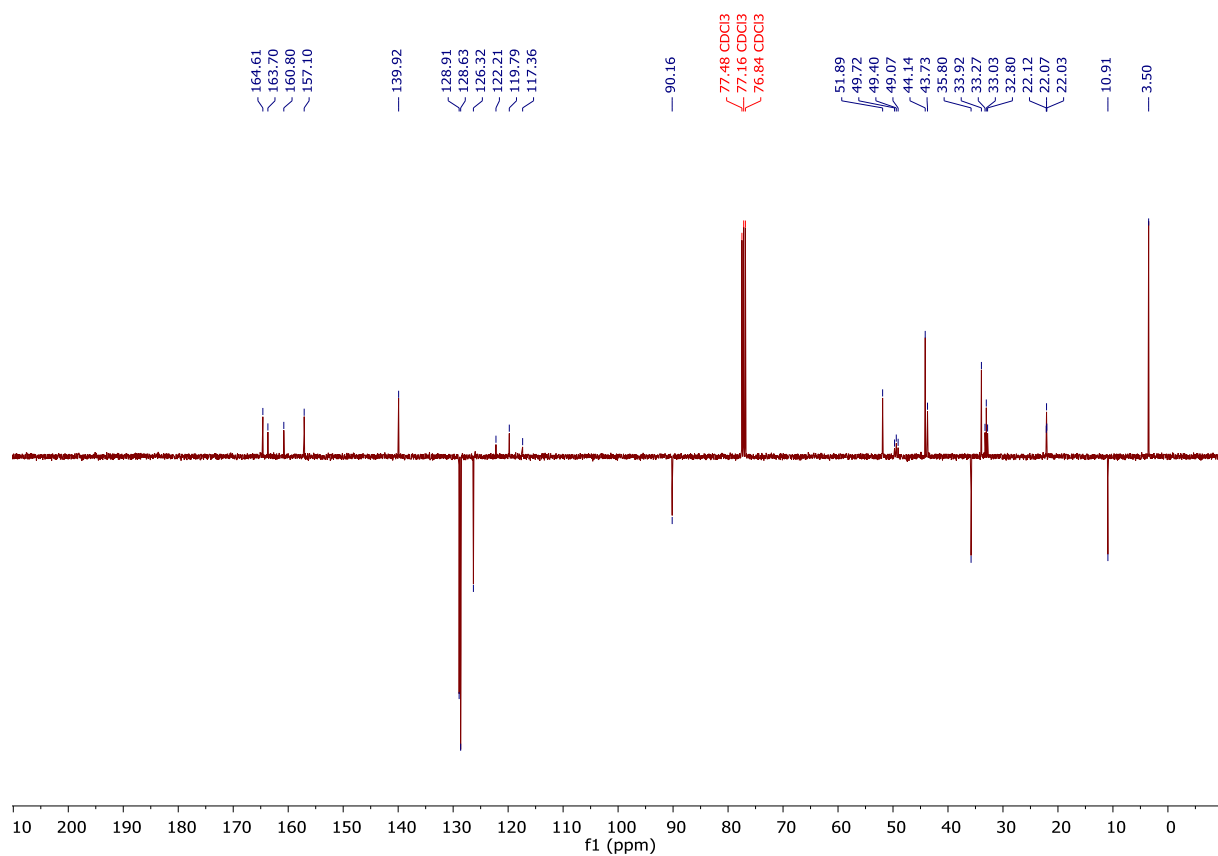
¹³C-NMR



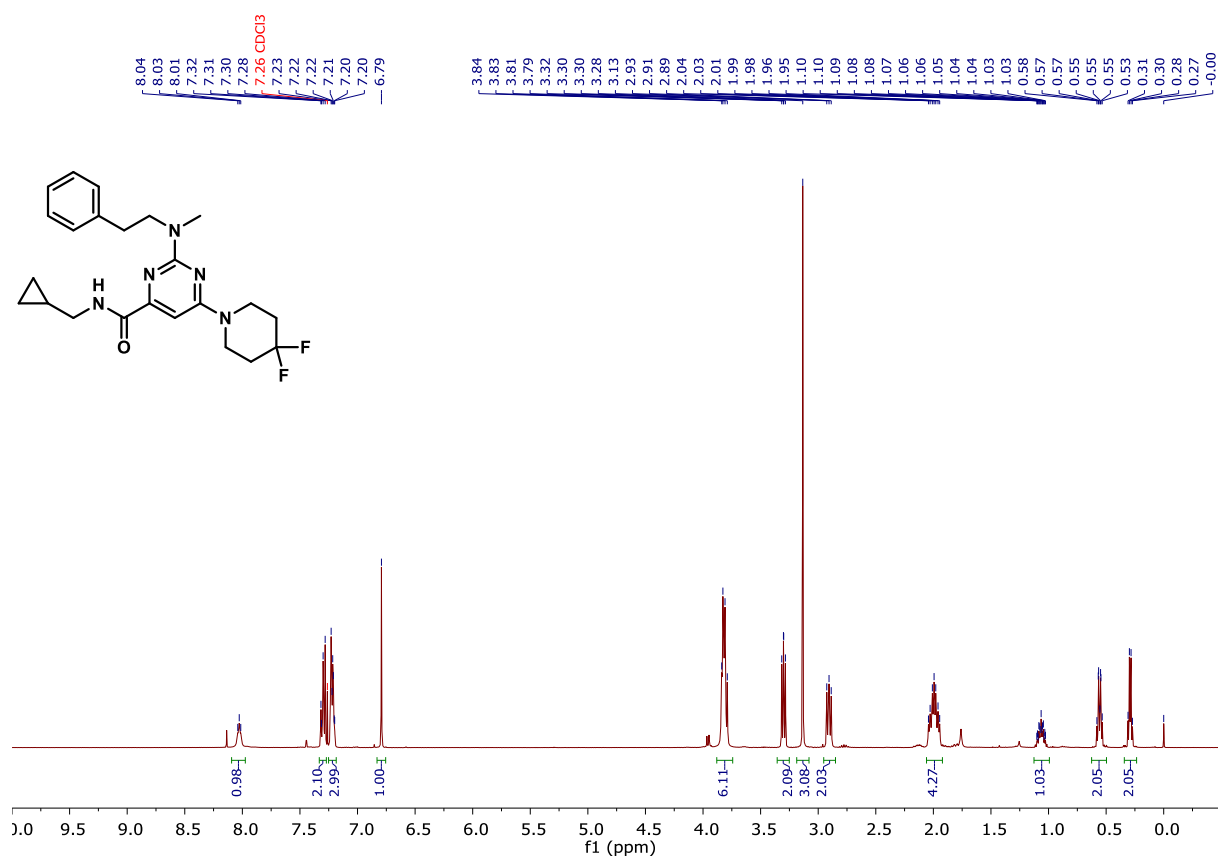
¹H-NMR: 72



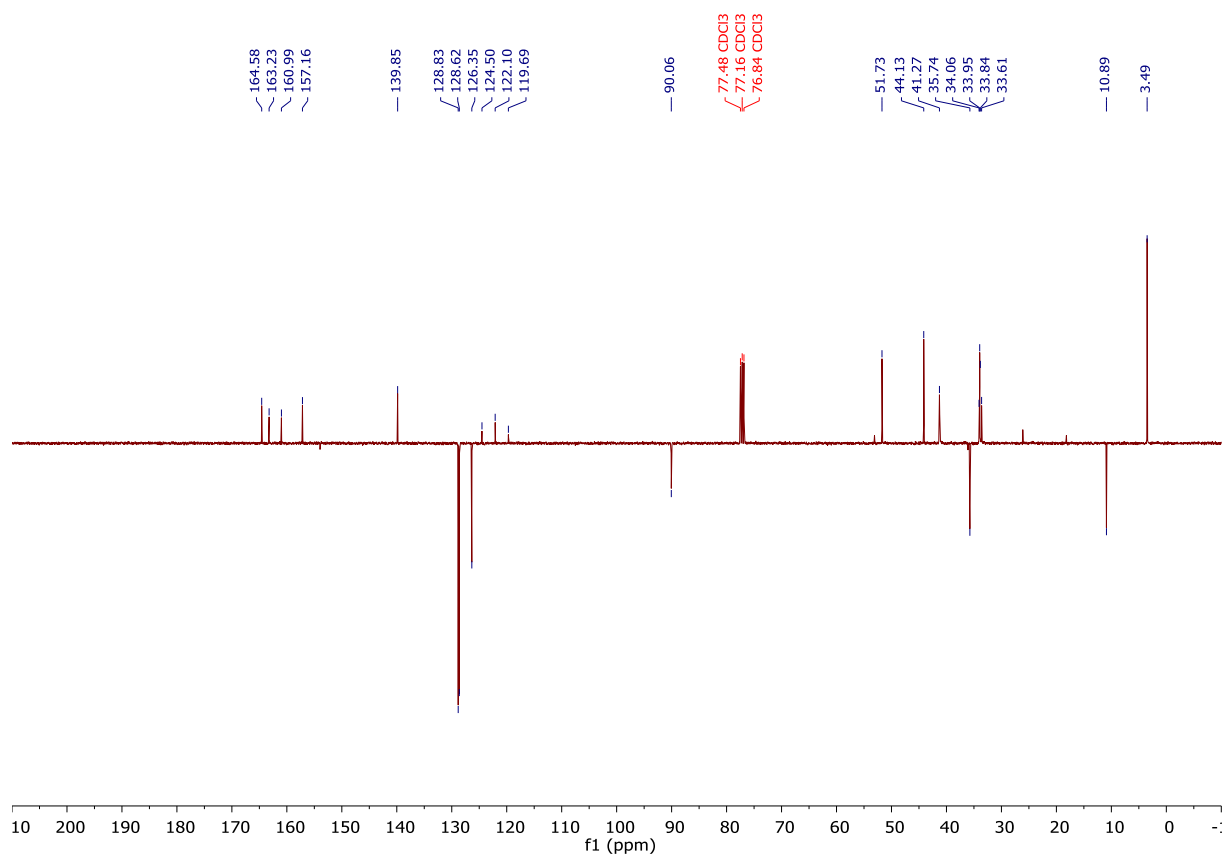
¹³C-NMR



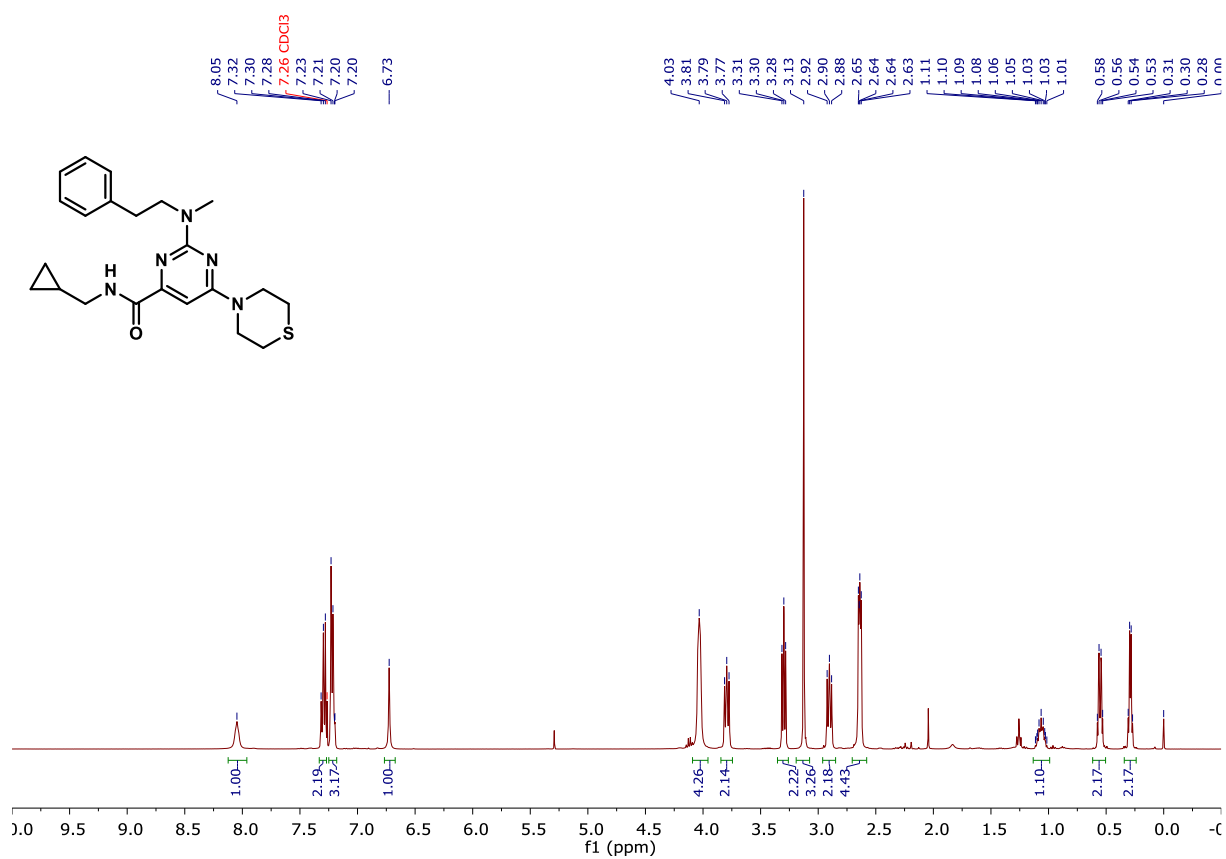
¹H-NMR: 73



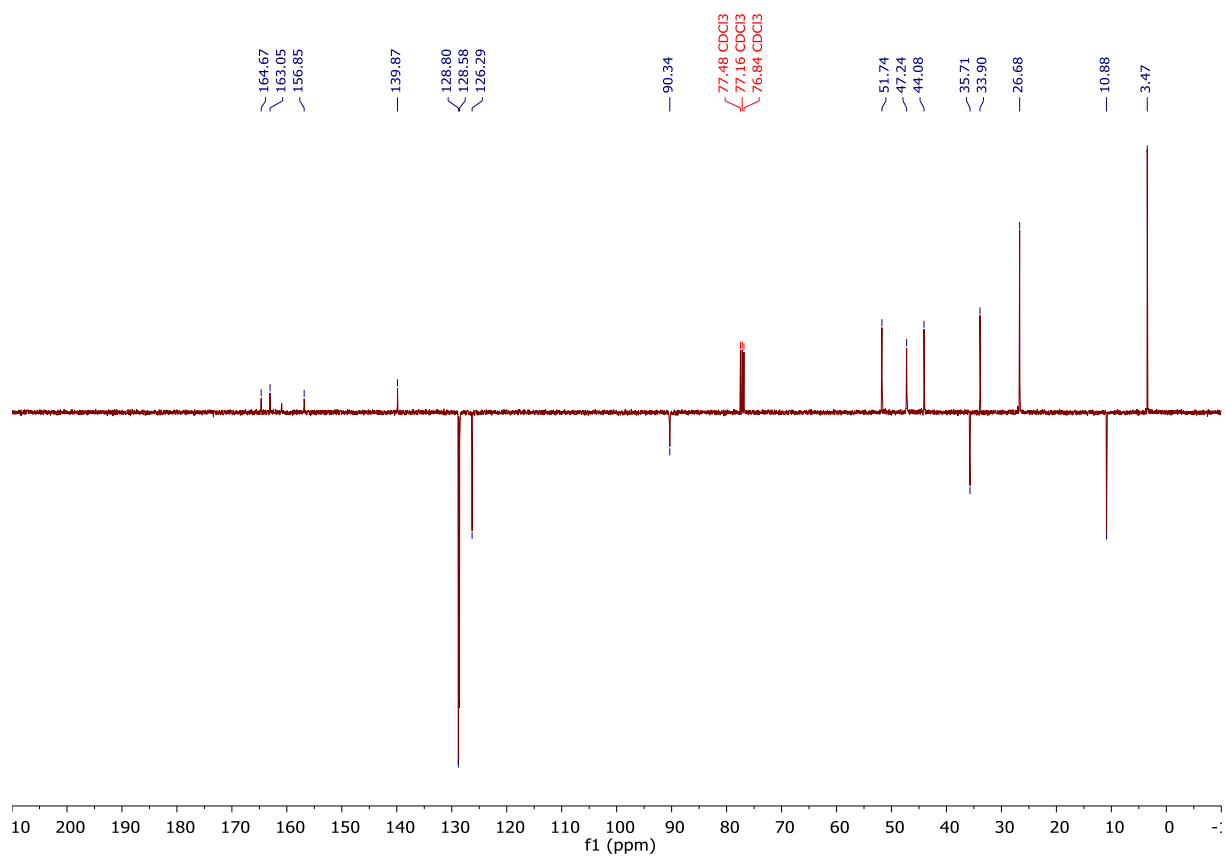
¹³C-NMR



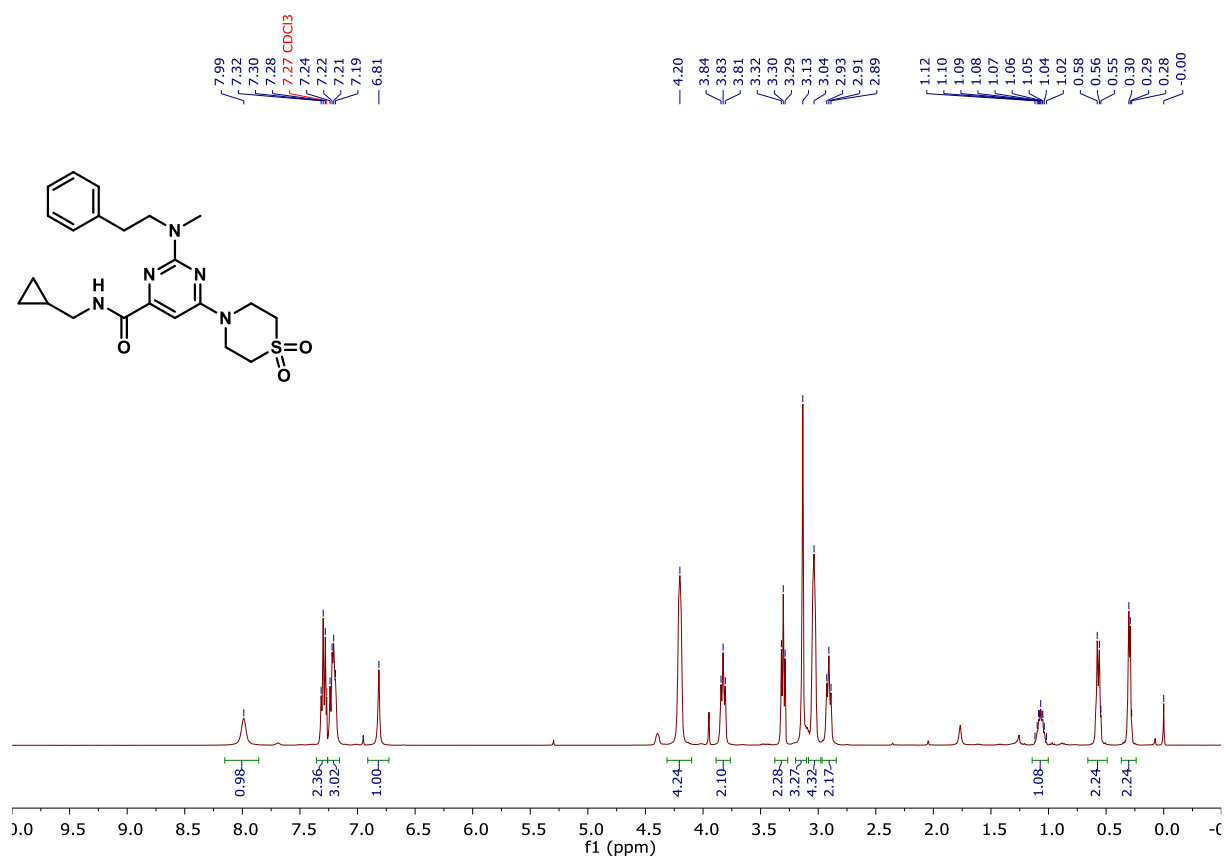
¹H-NMR: 74



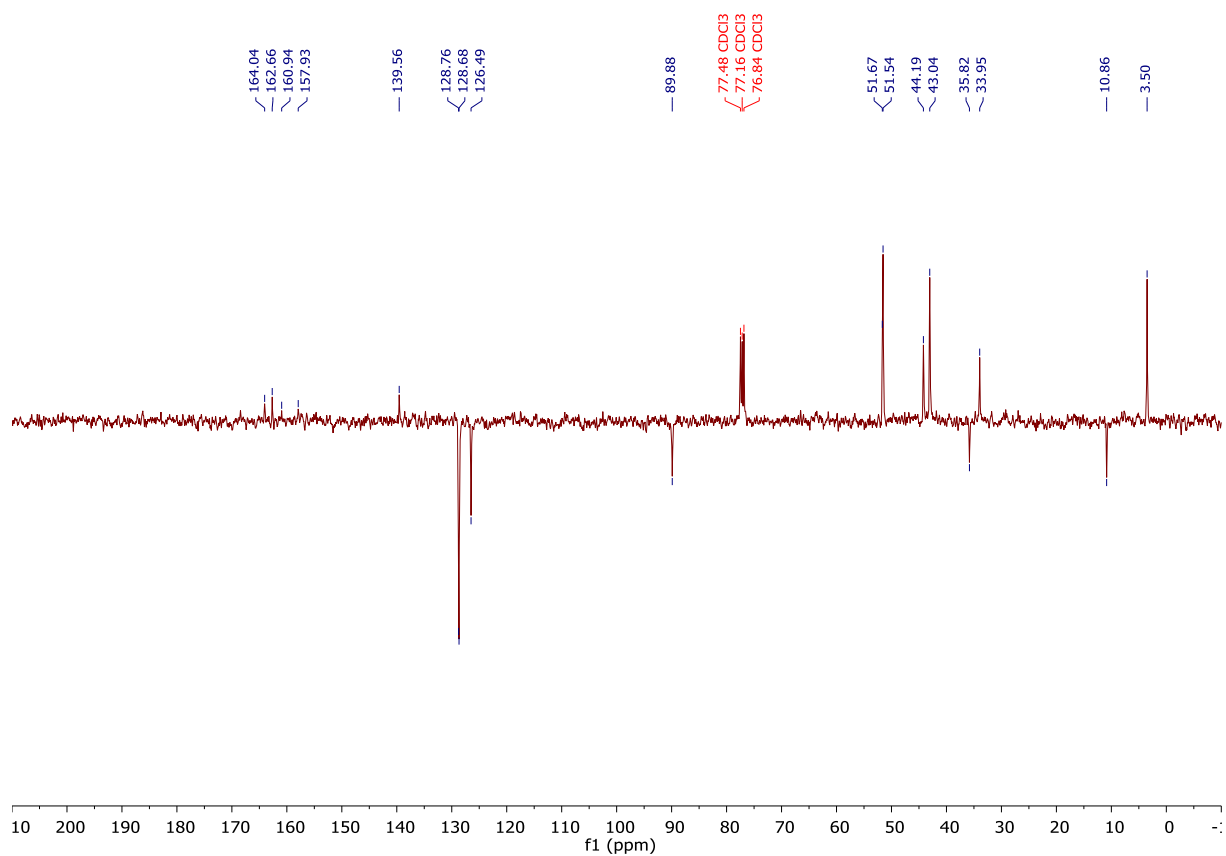
¹³C-NMR



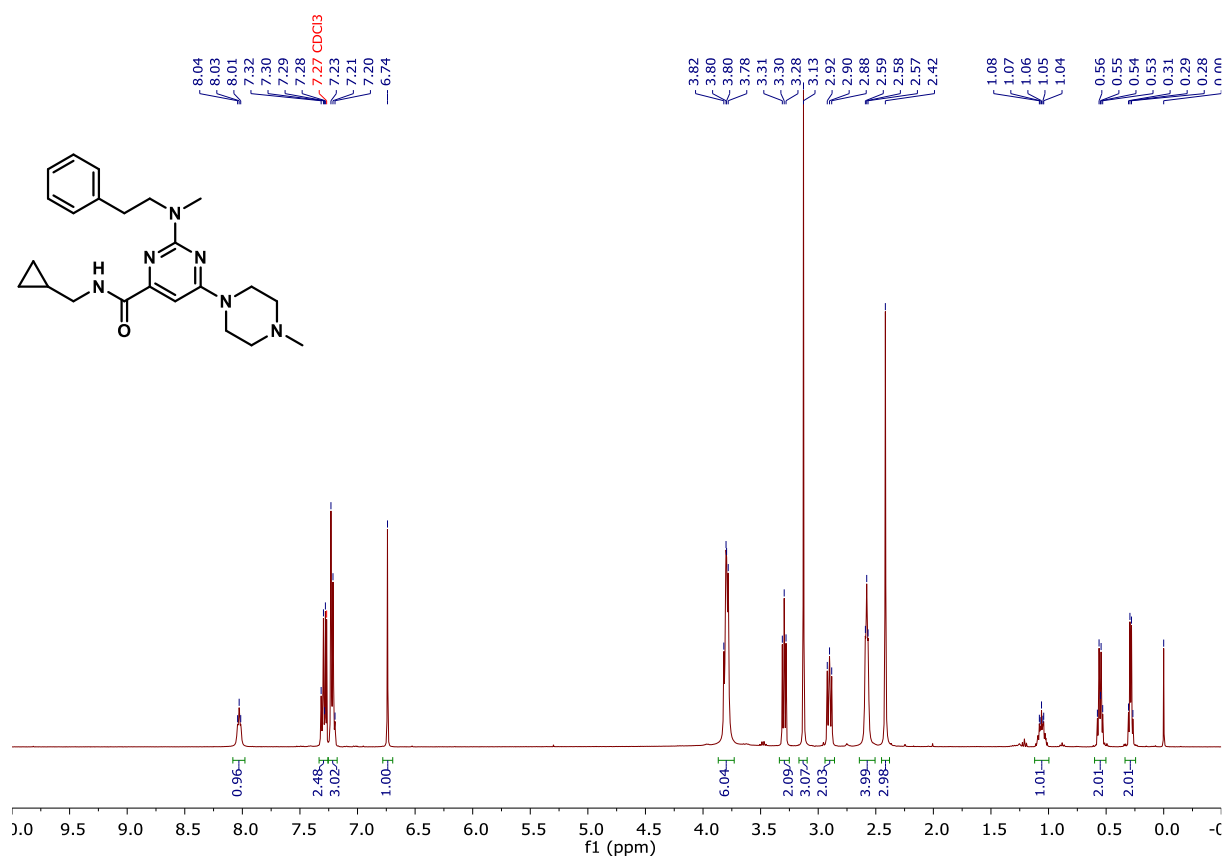
¹H-NMR: 75



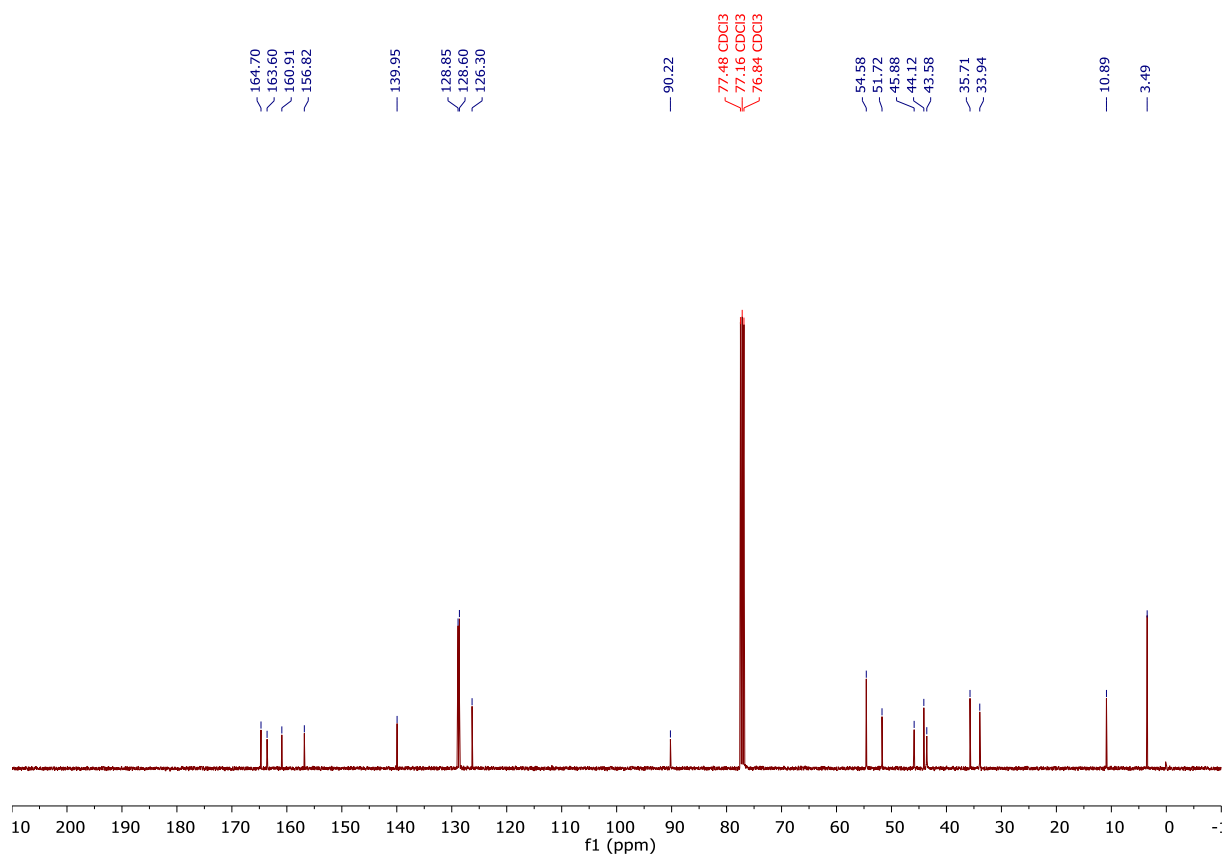
¹³C-NMR



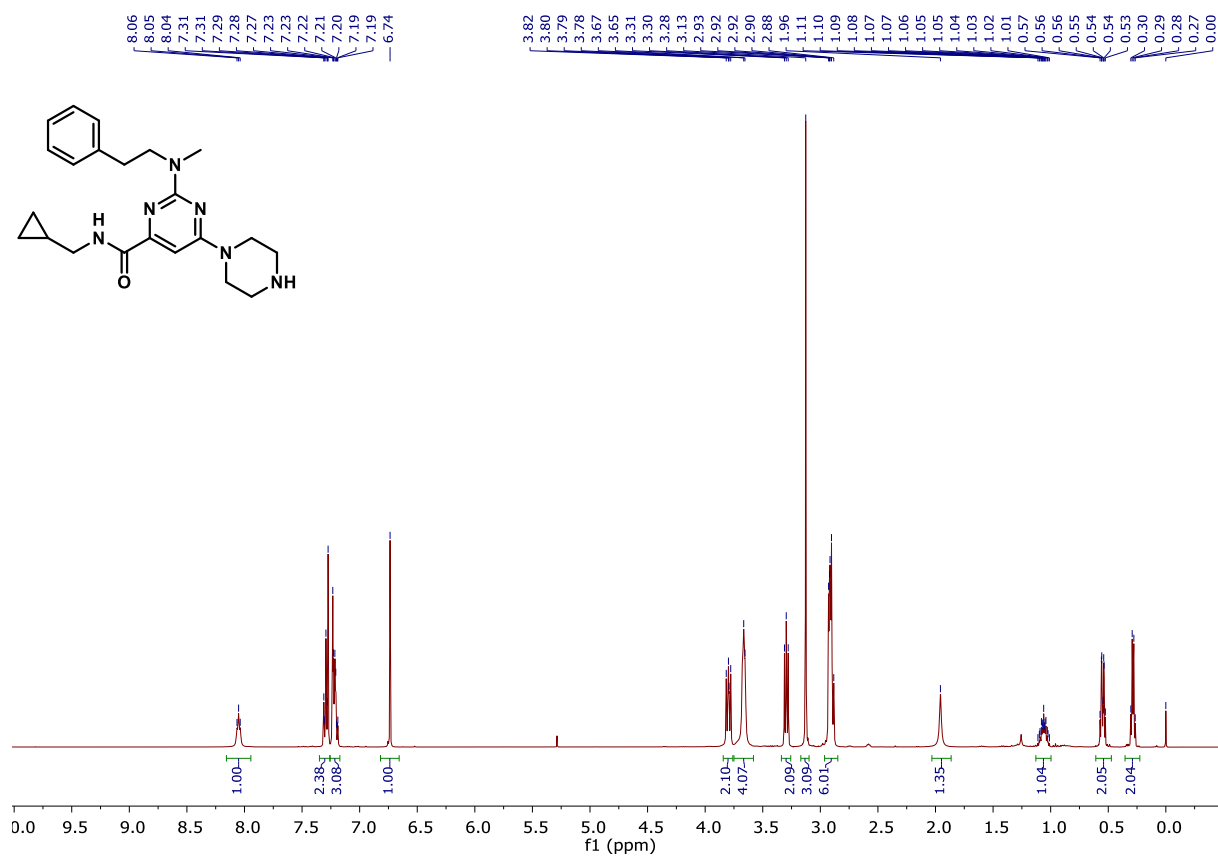
¹H-NMR: 76



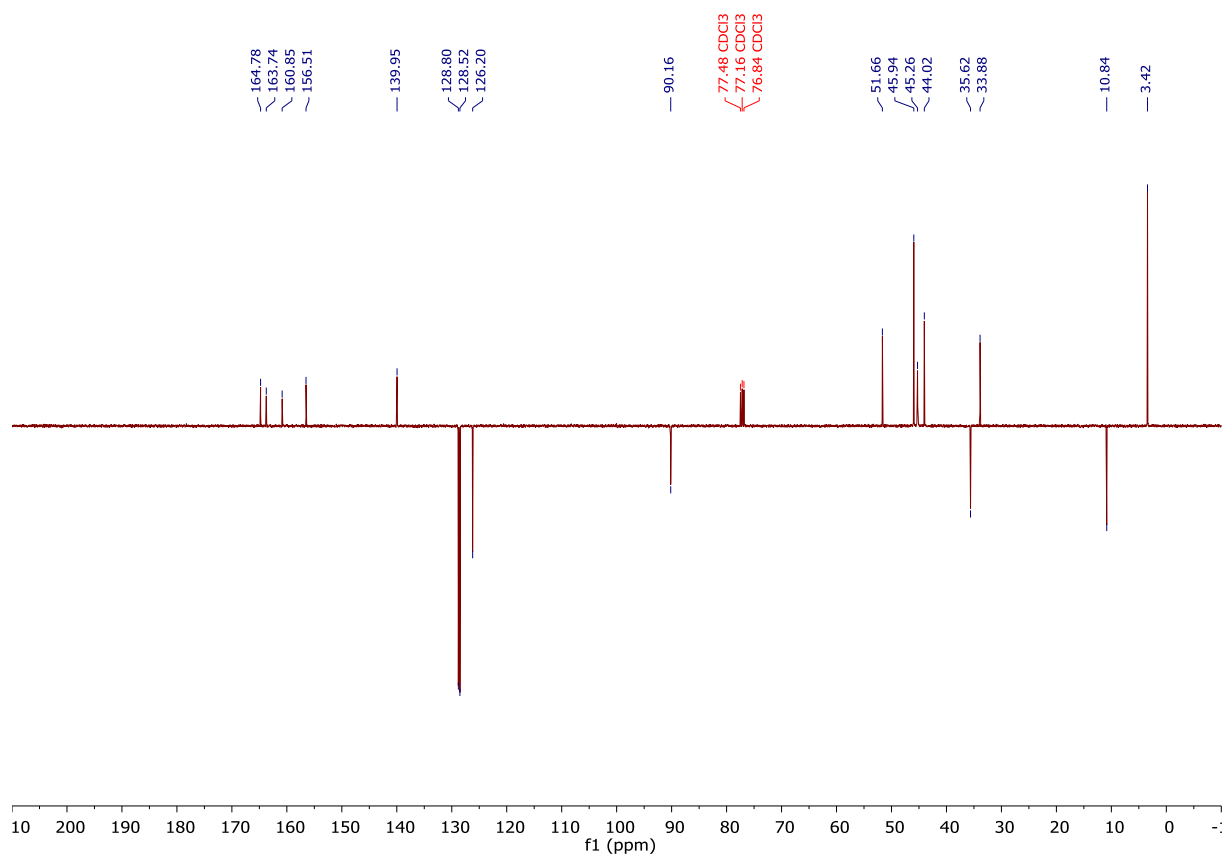
¹³C-NMR



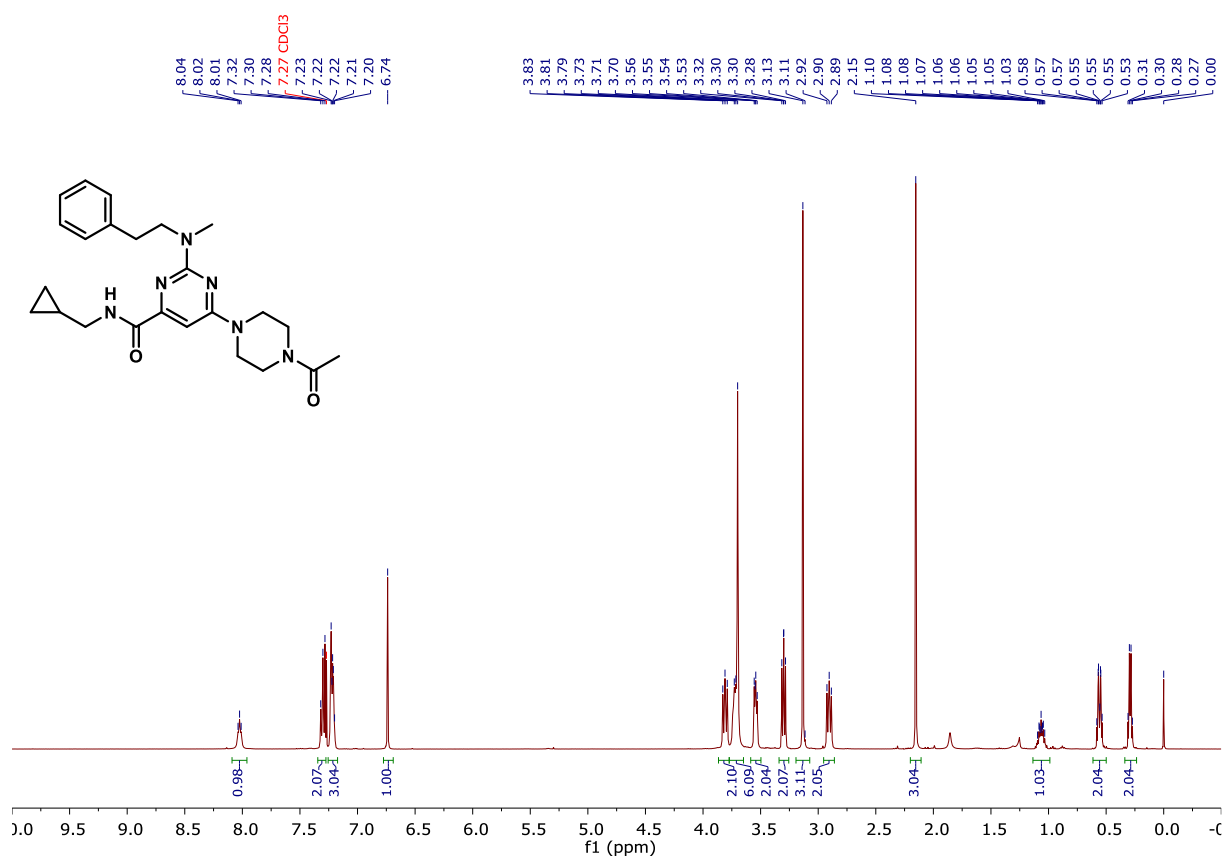
¹H-NMR: 77



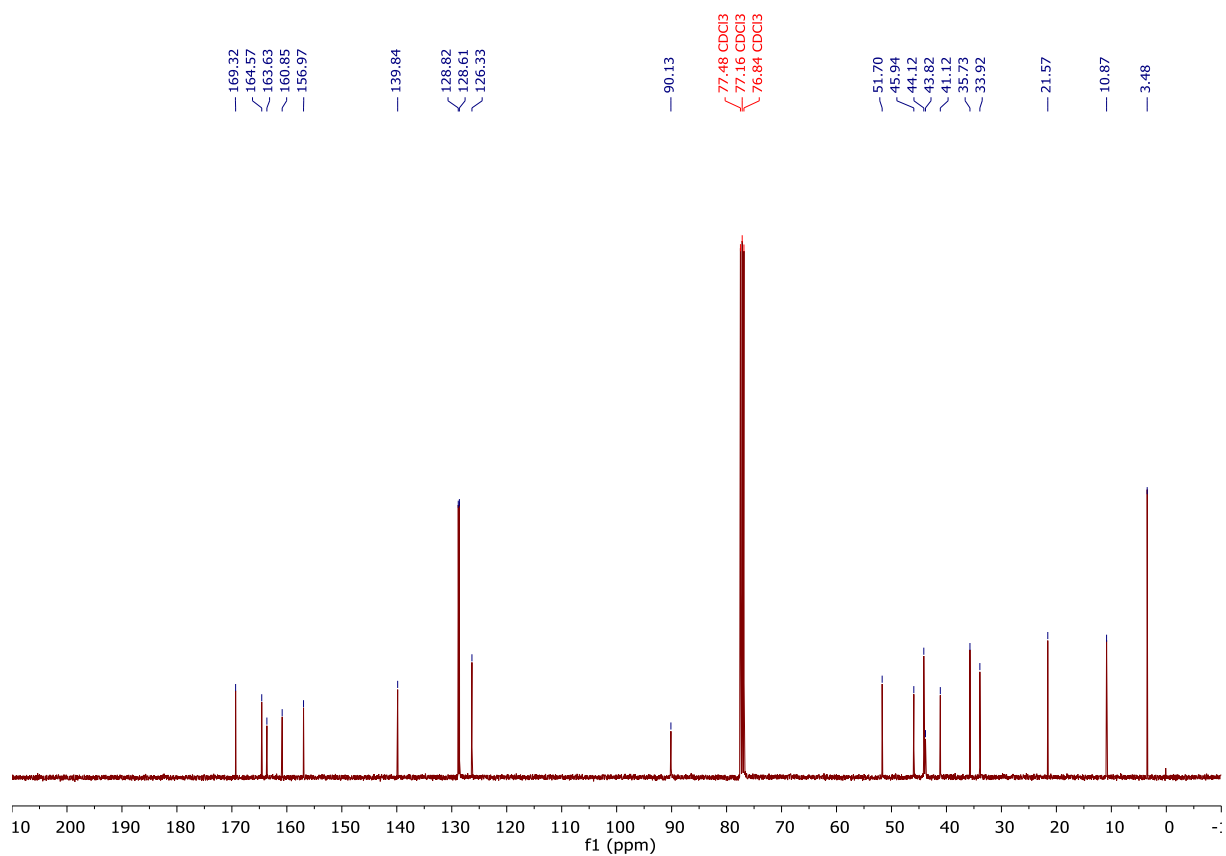
¹³C-NMR



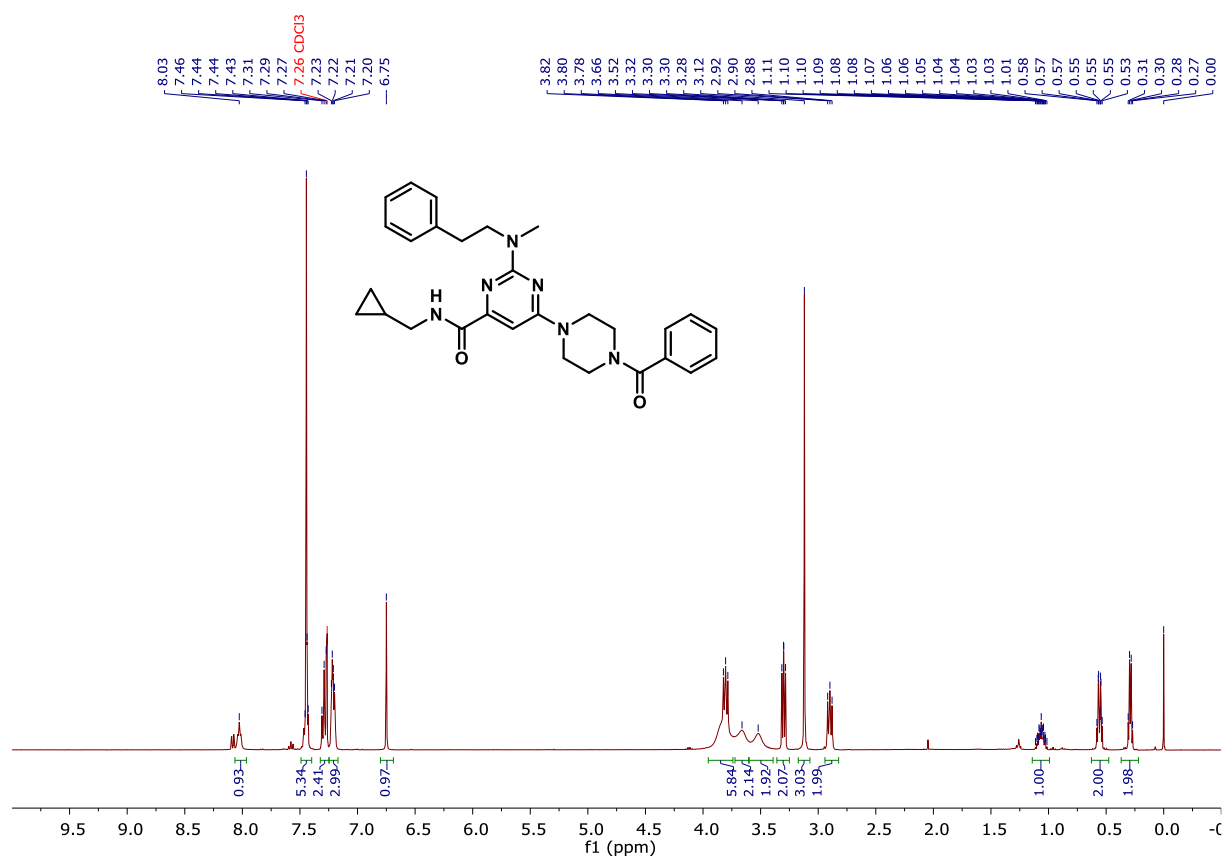
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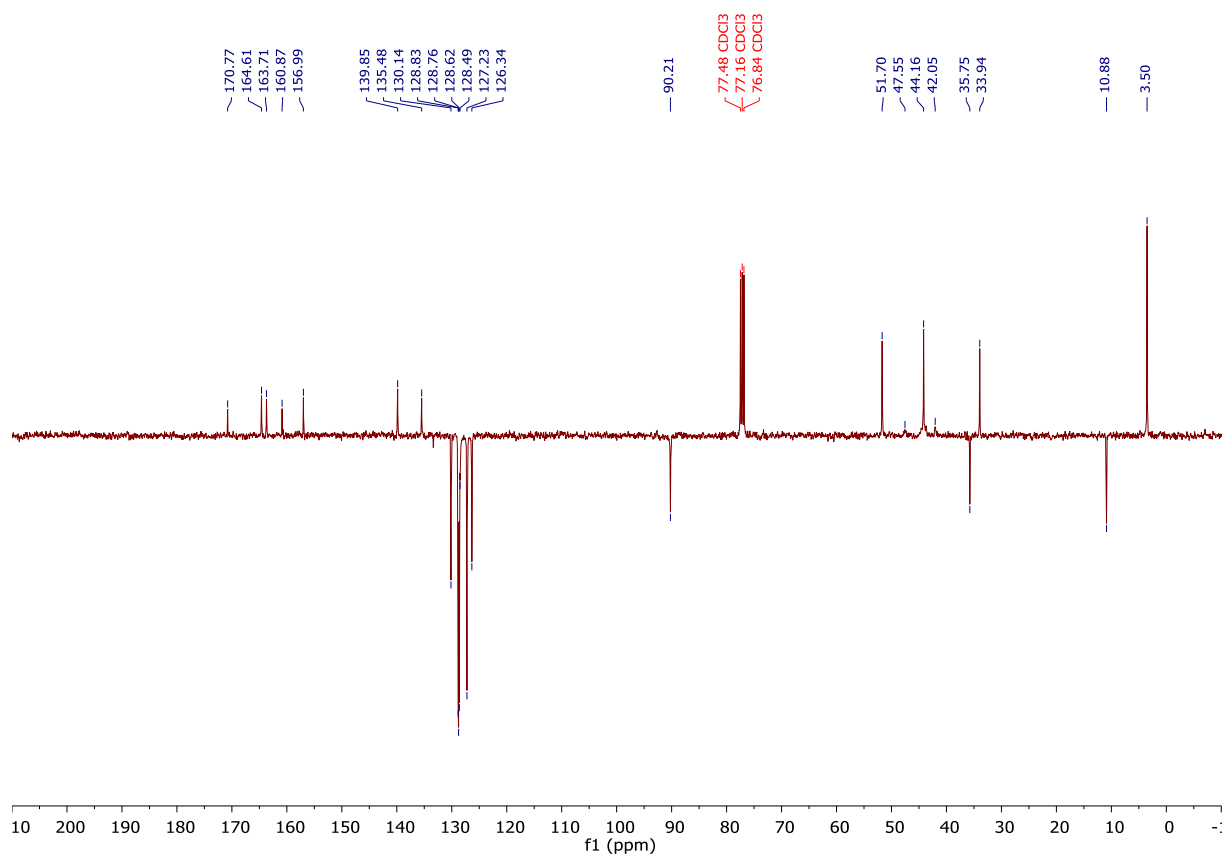
¹³C-NMR



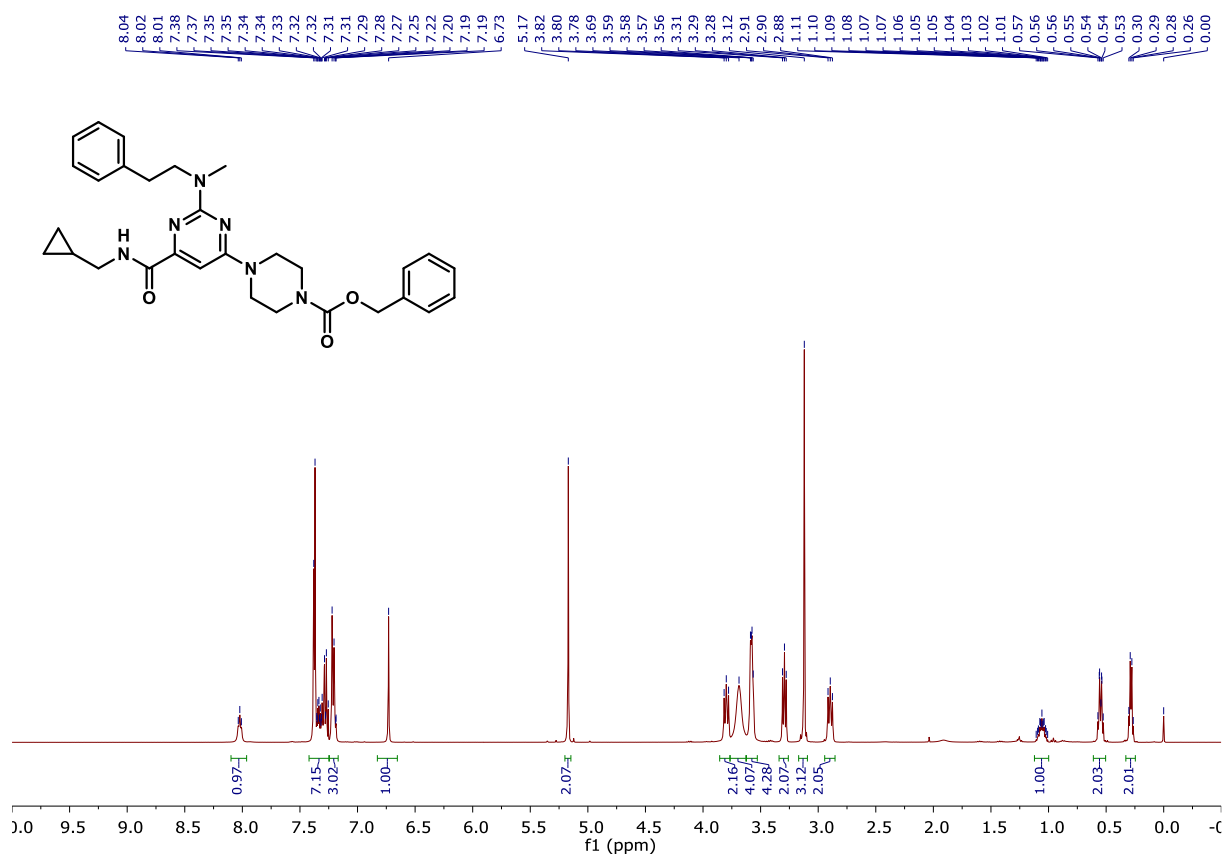
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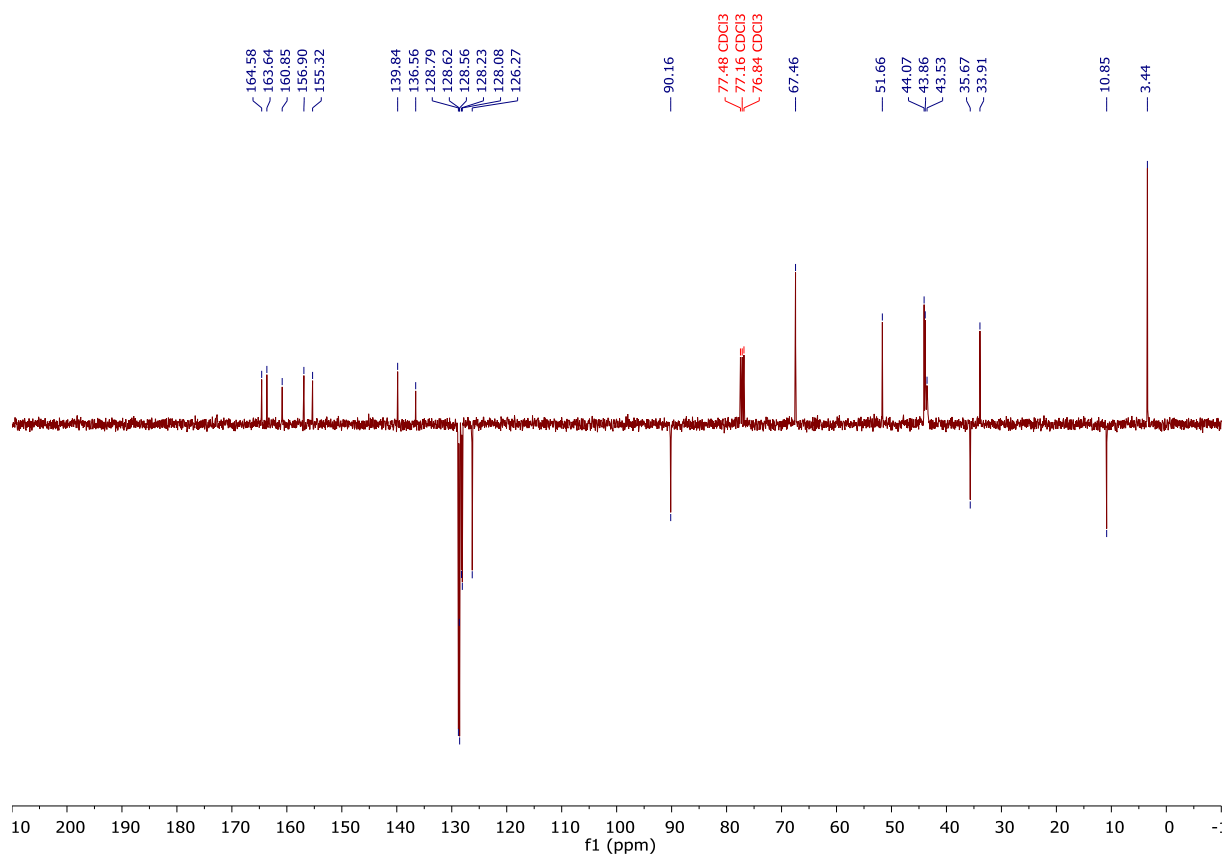
¹³C-NMR



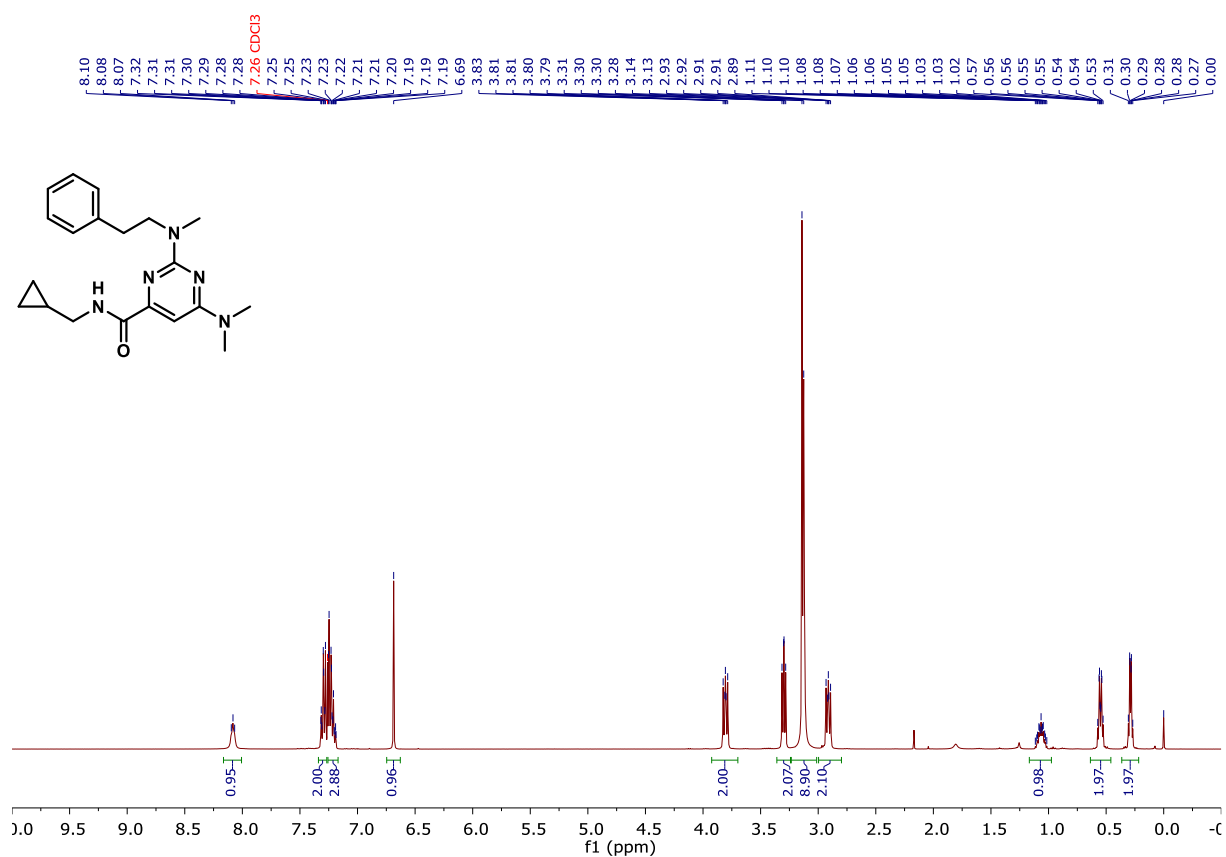
¹H-NMR: 80



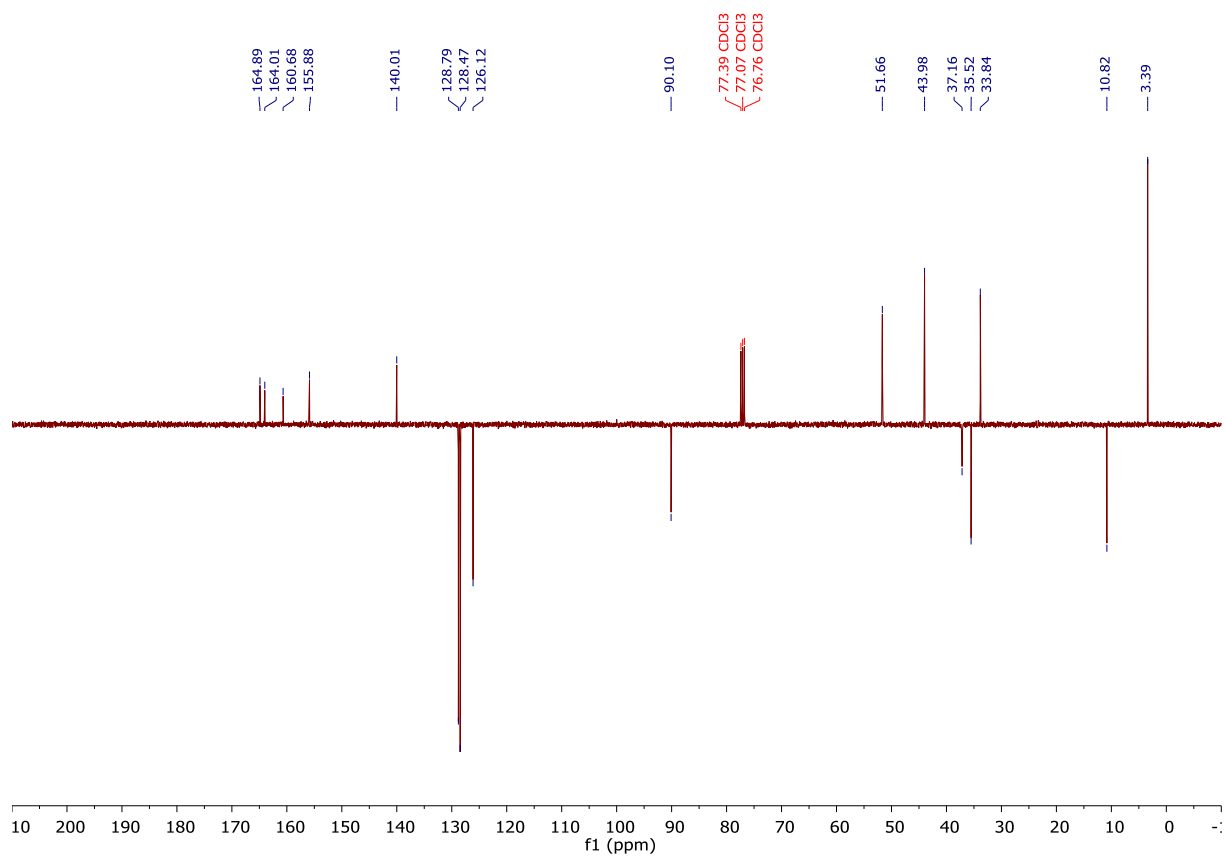
¹³C-NMR



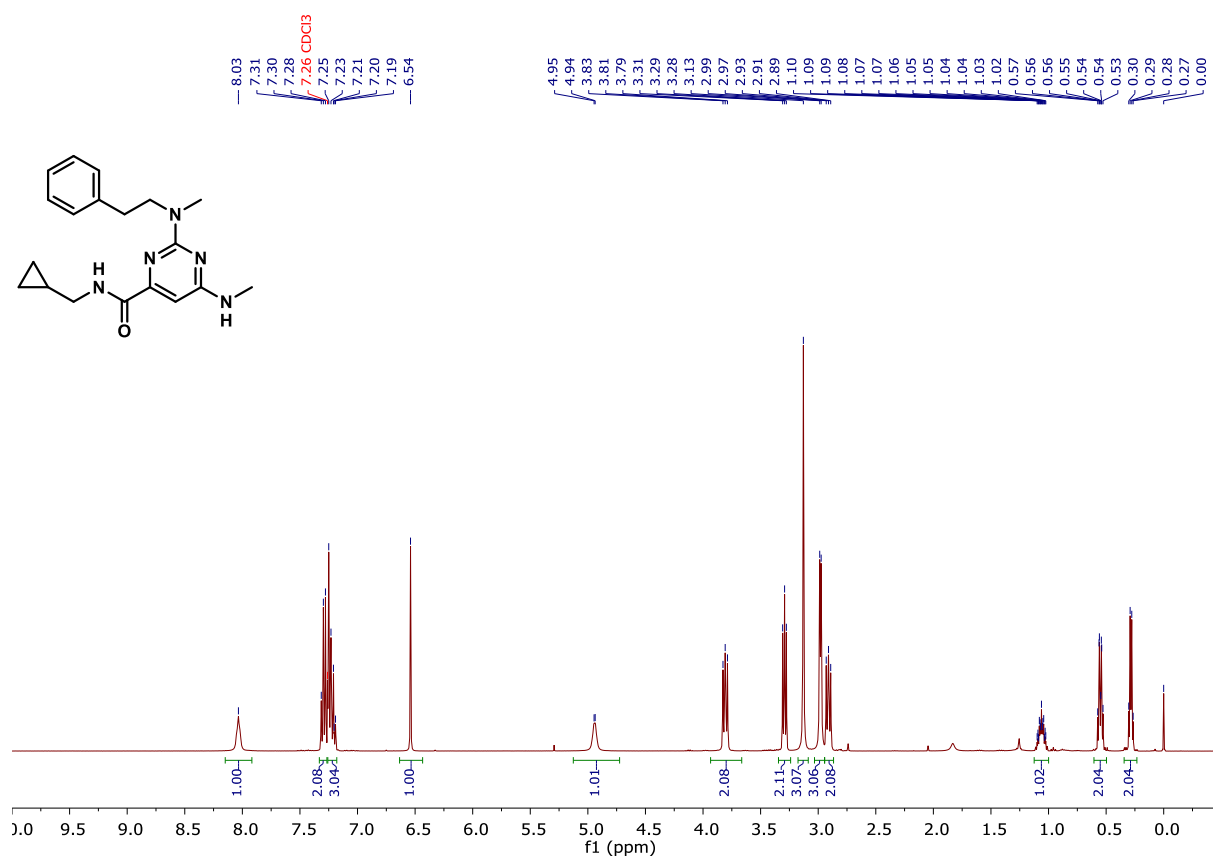
¹H-NMR: 81



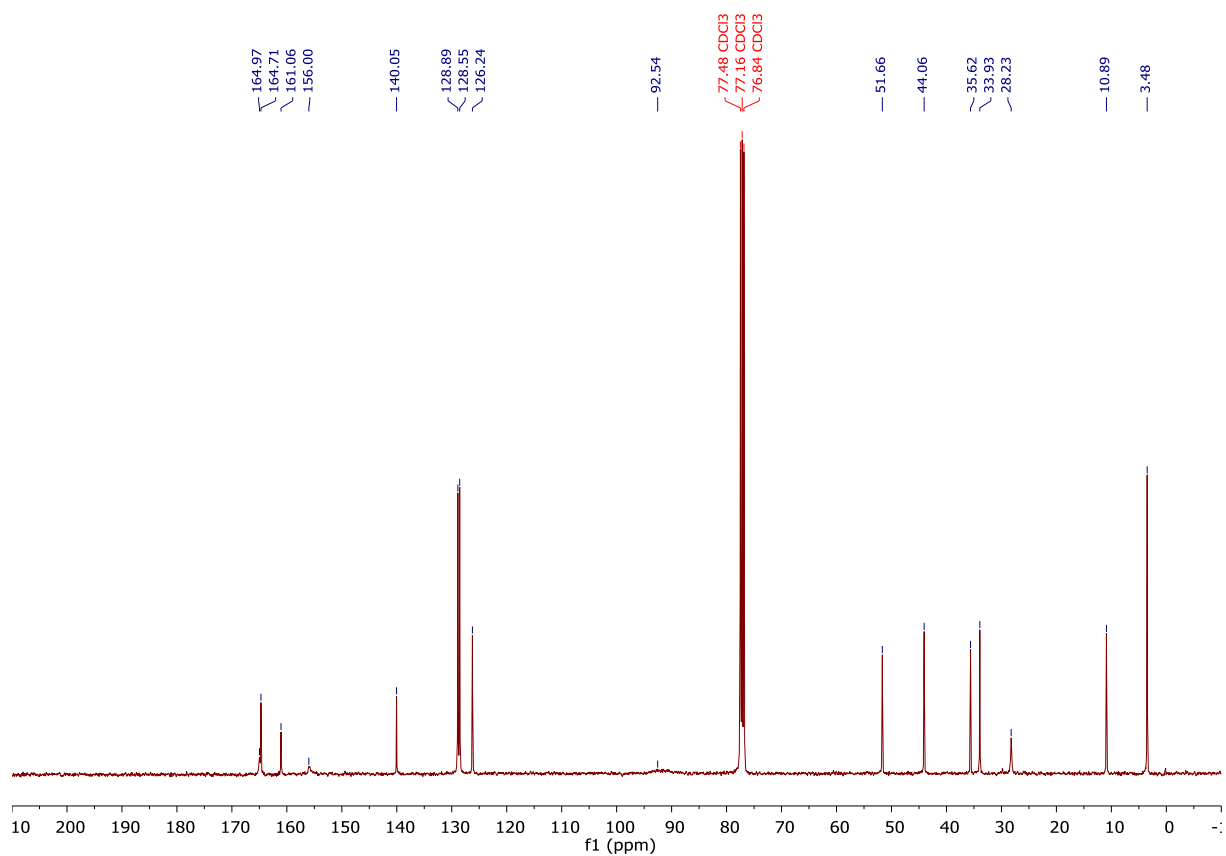
¹³C-NMR



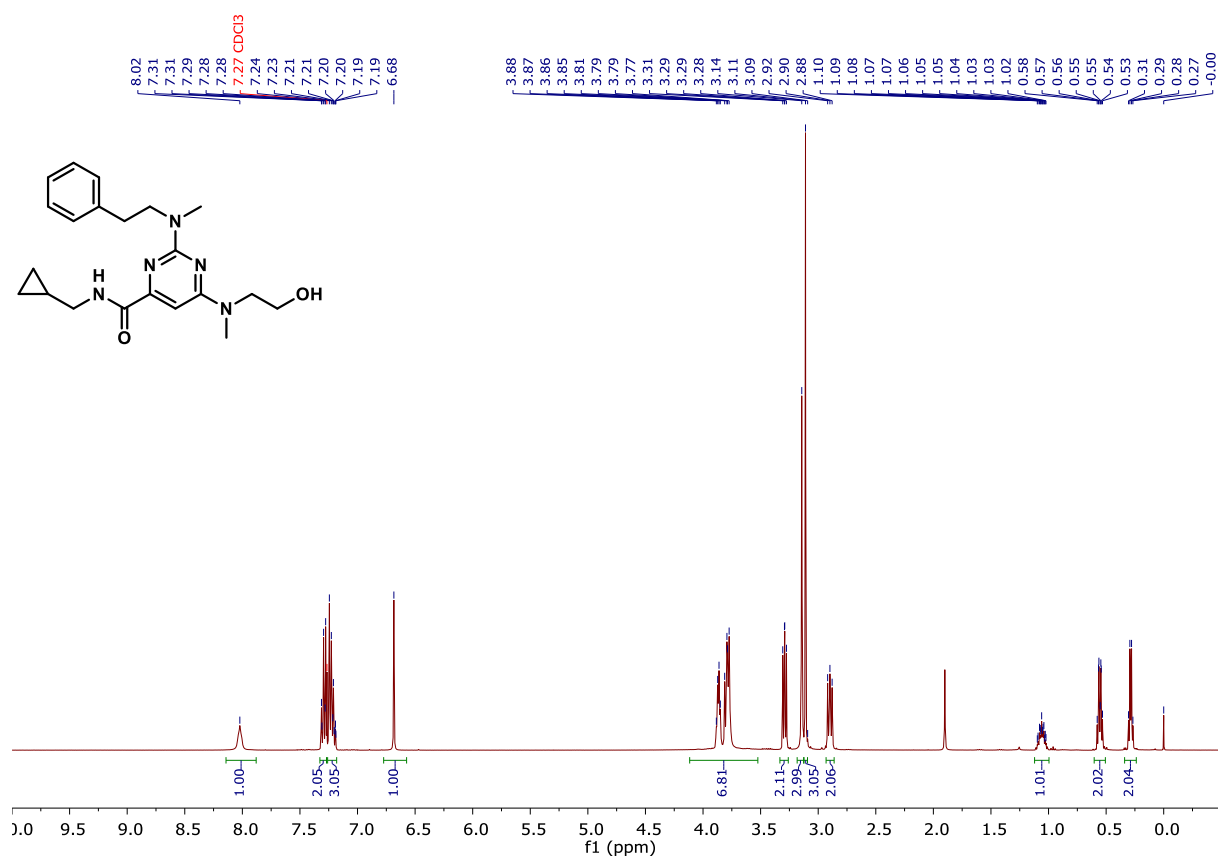
¹H-NMR: 82



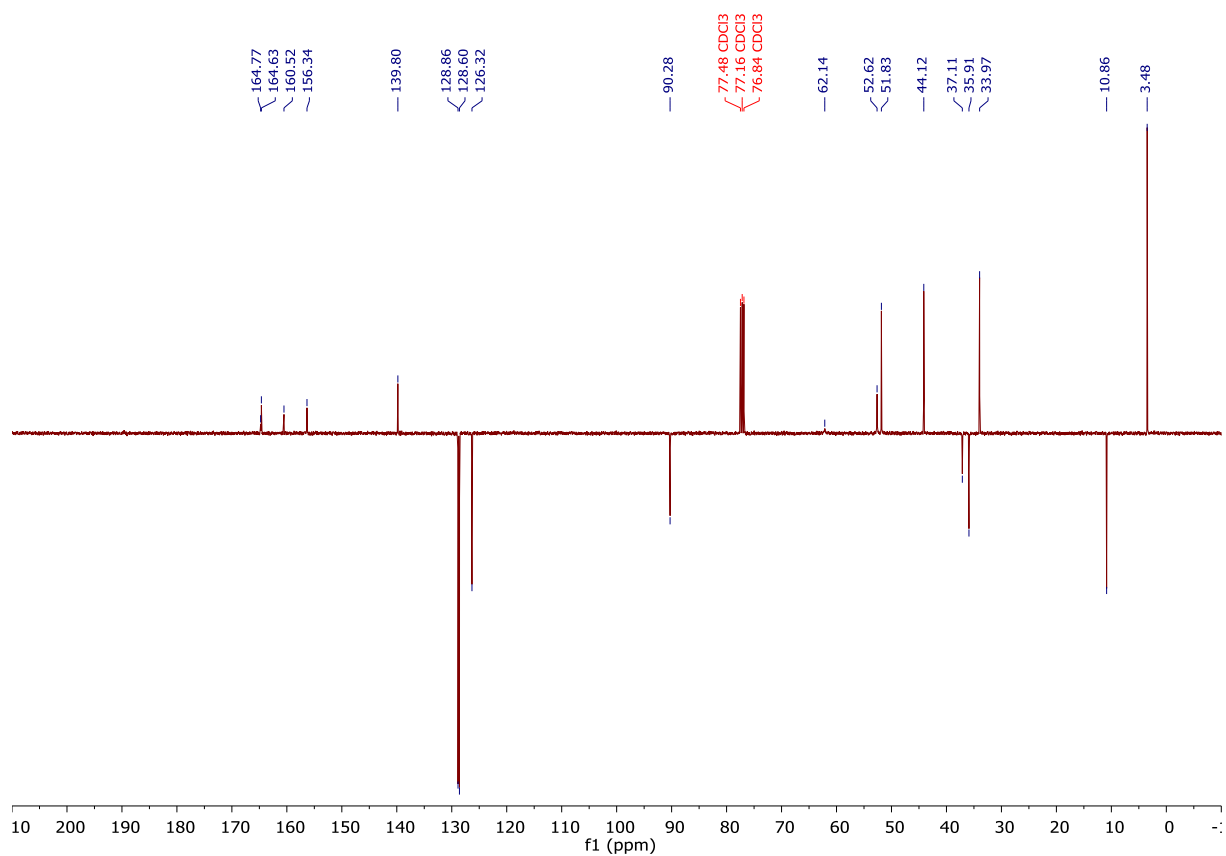
¹³C-NMR



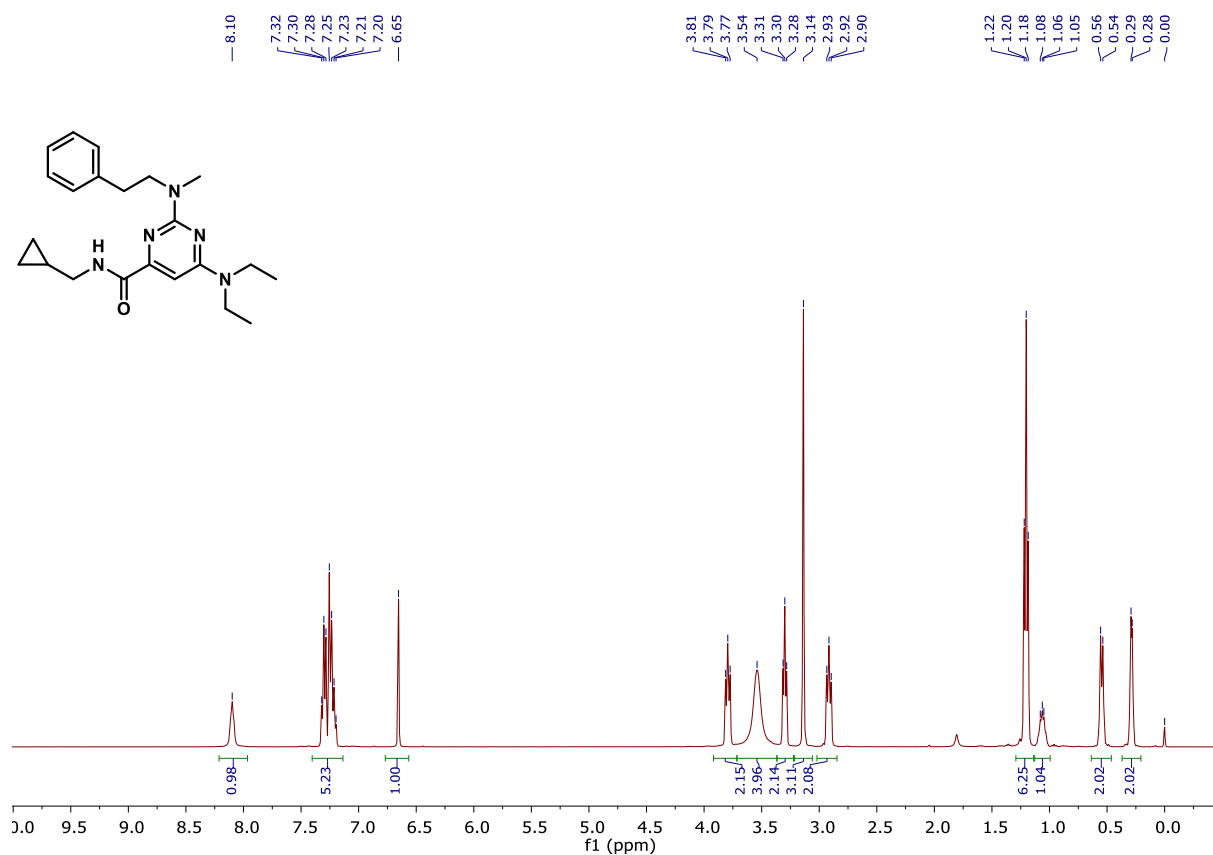
¹H-NMR: 83



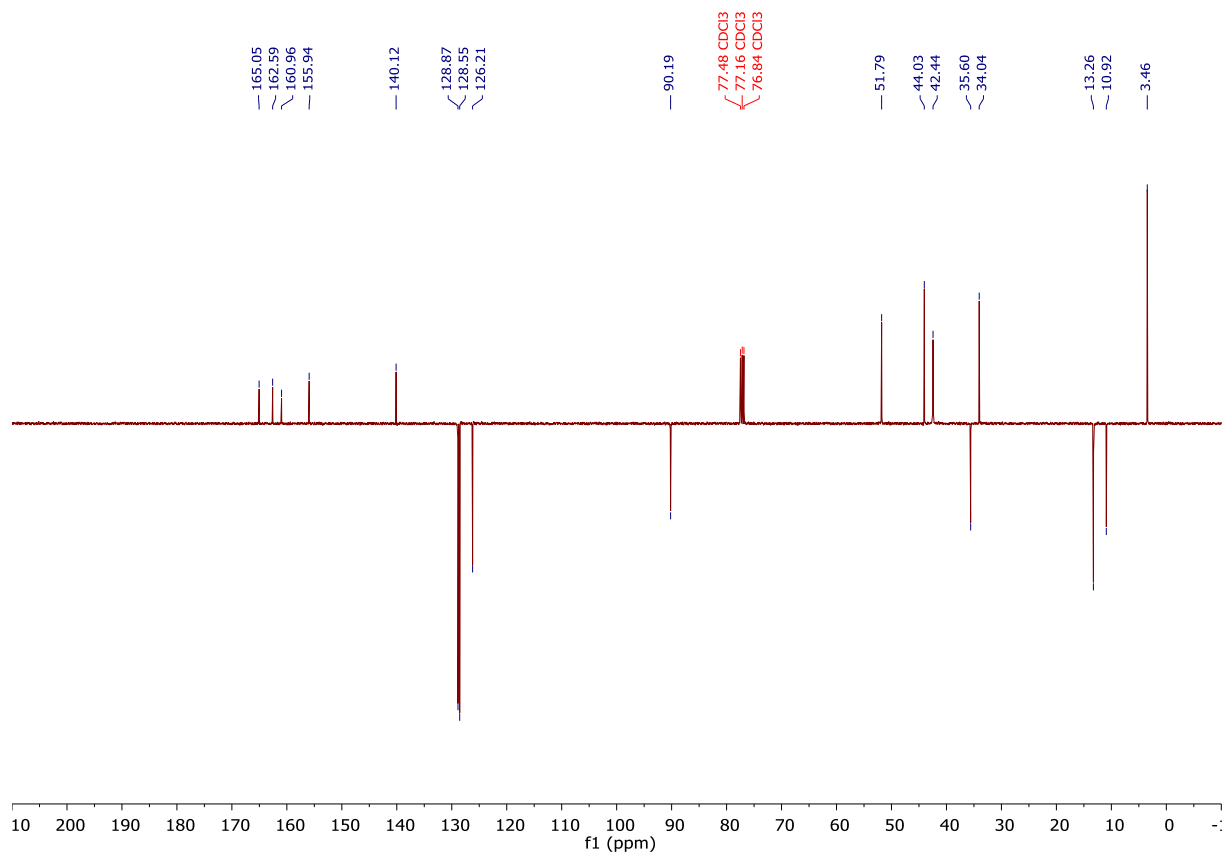
¹³C-NMR



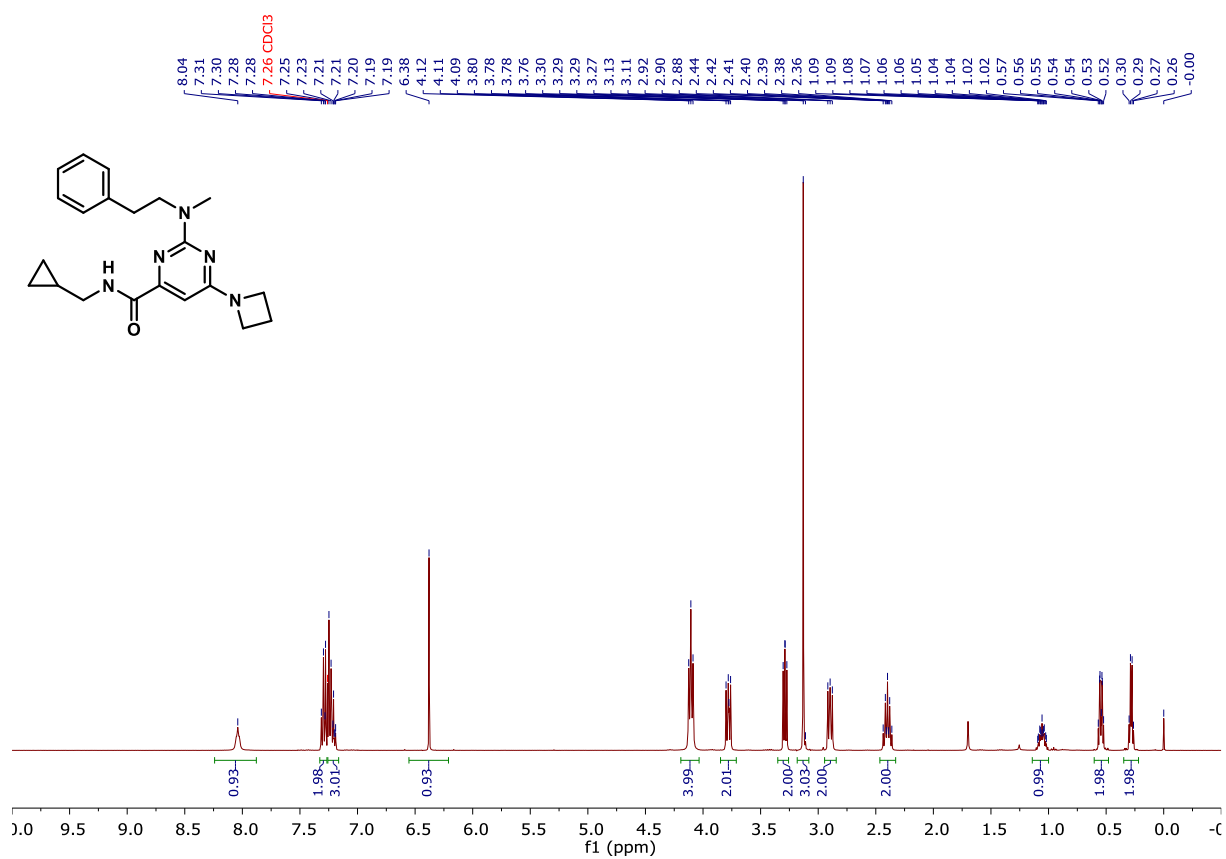
¹H-NMR: 84



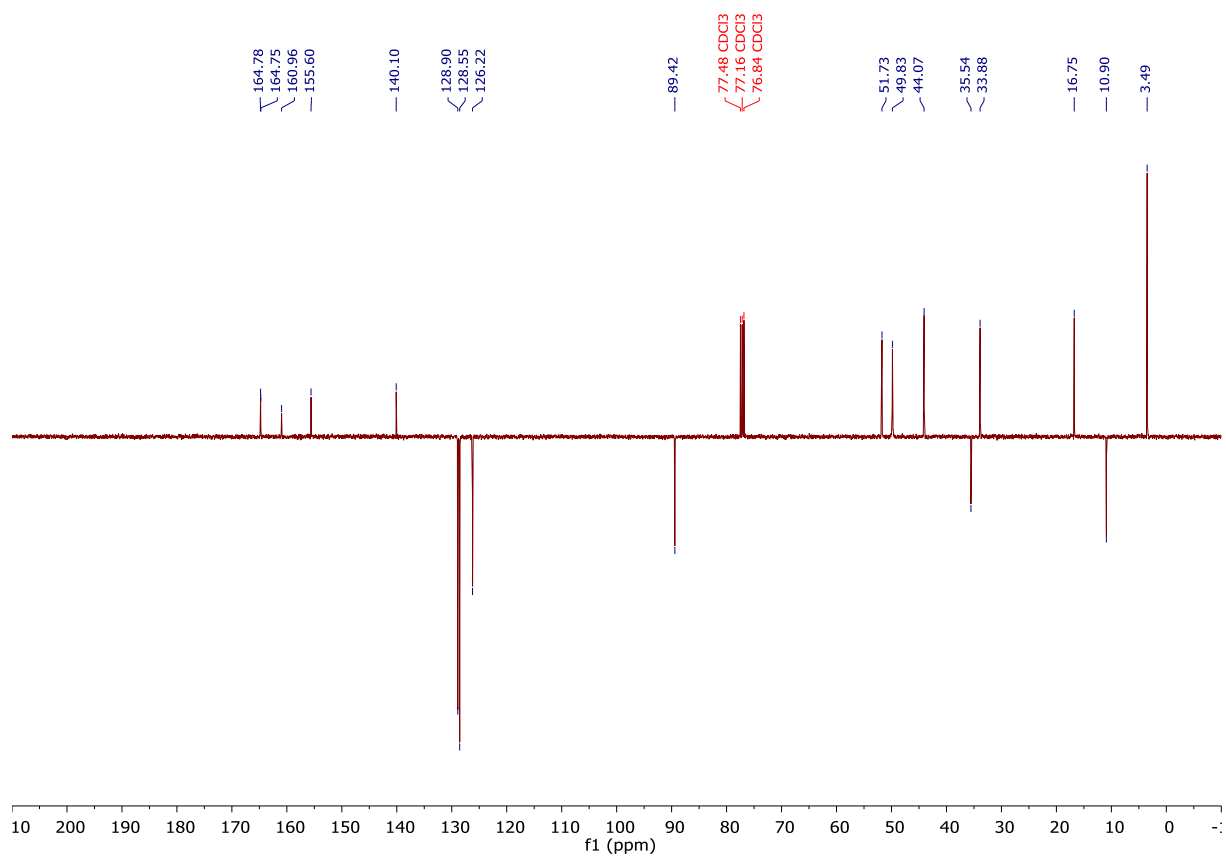
¹³C-NMR



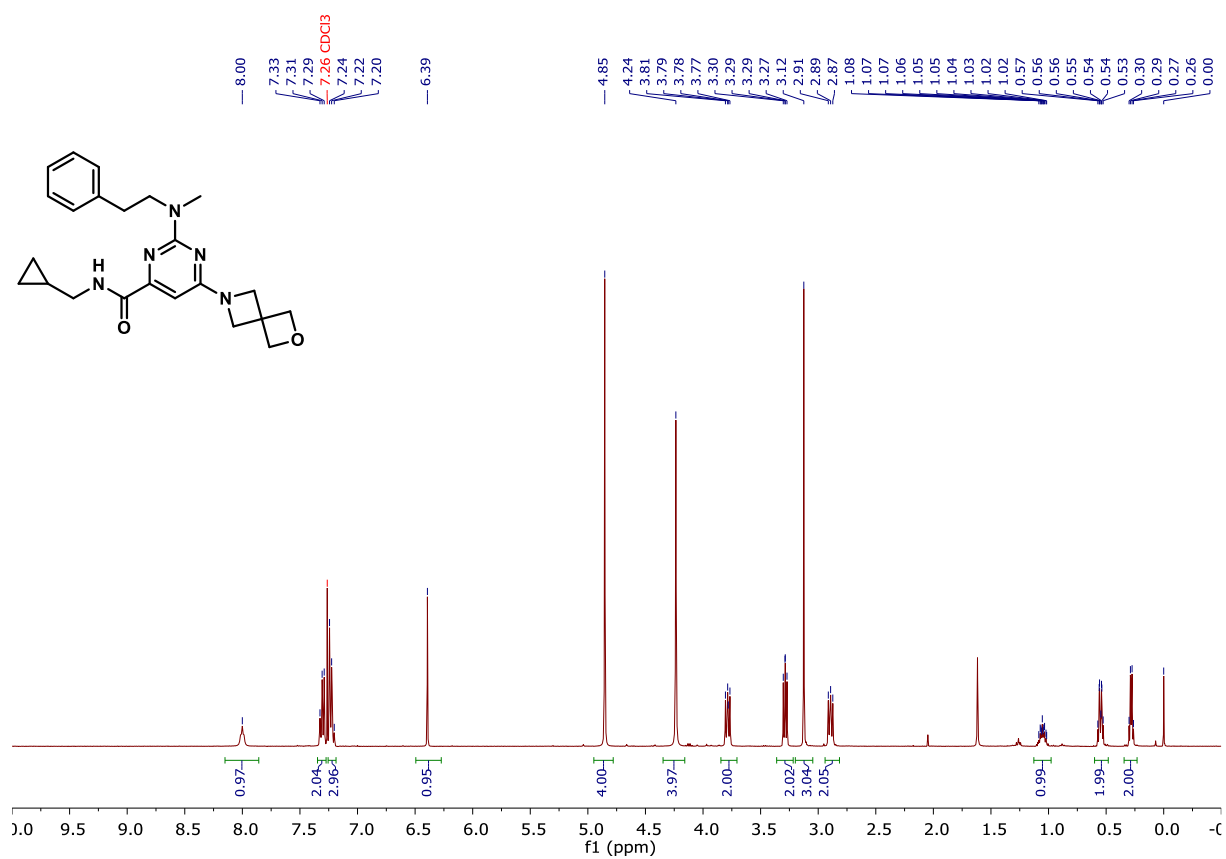
¹H-NMR: 85



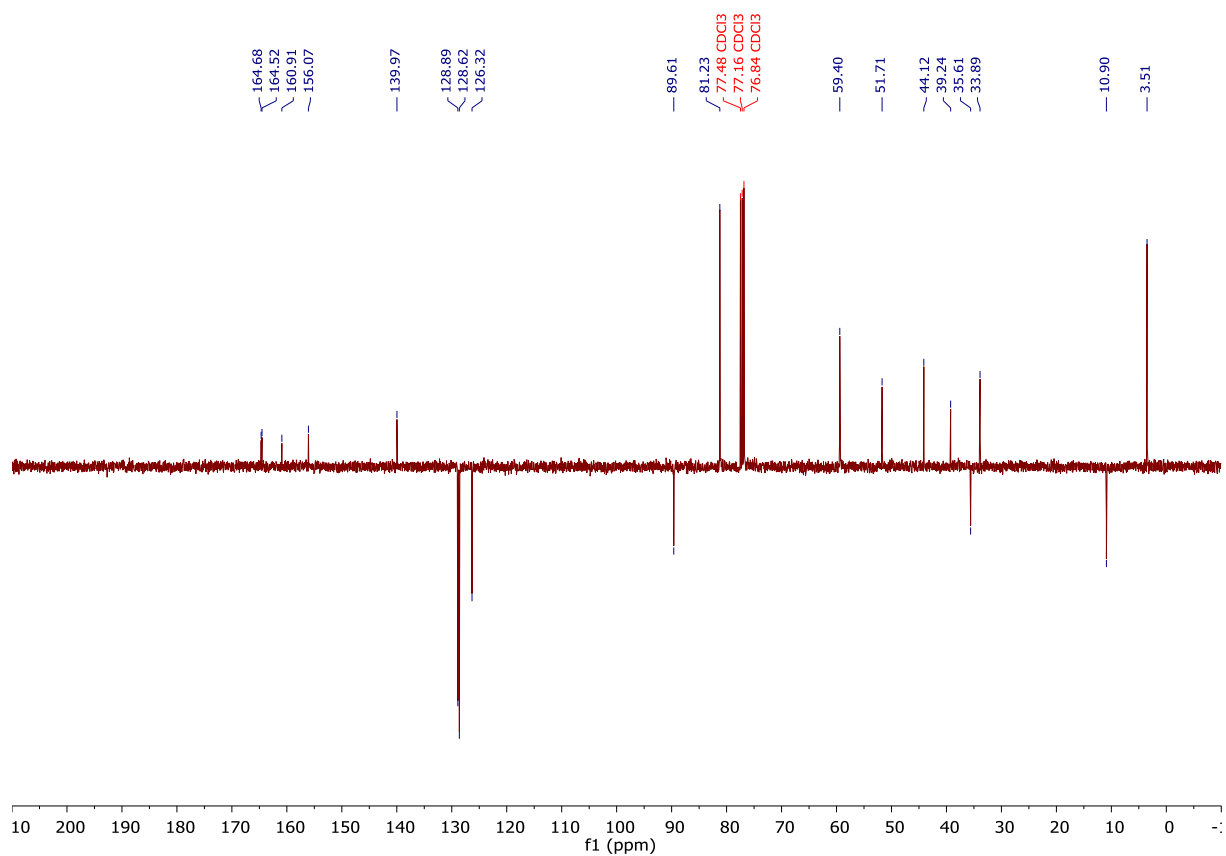
¹³C-NMR



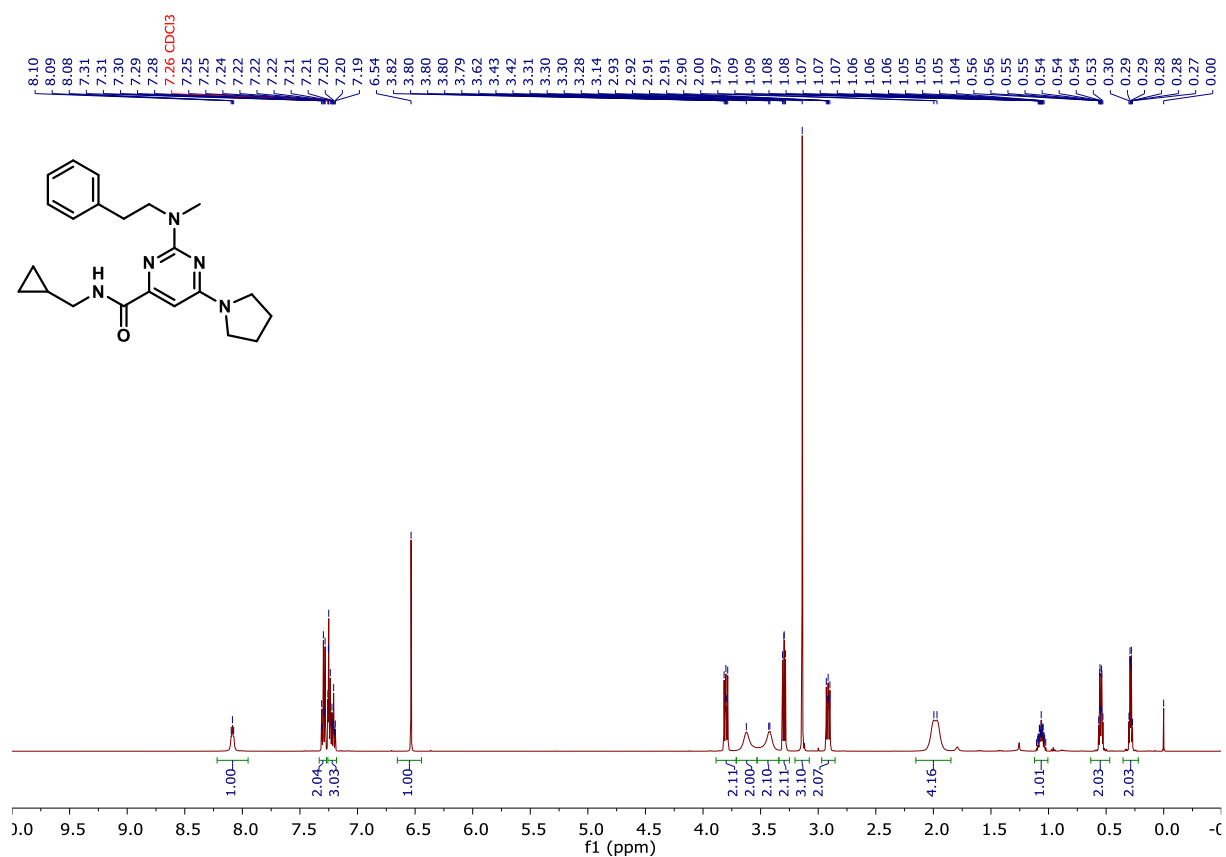
¹H-NMR: 86



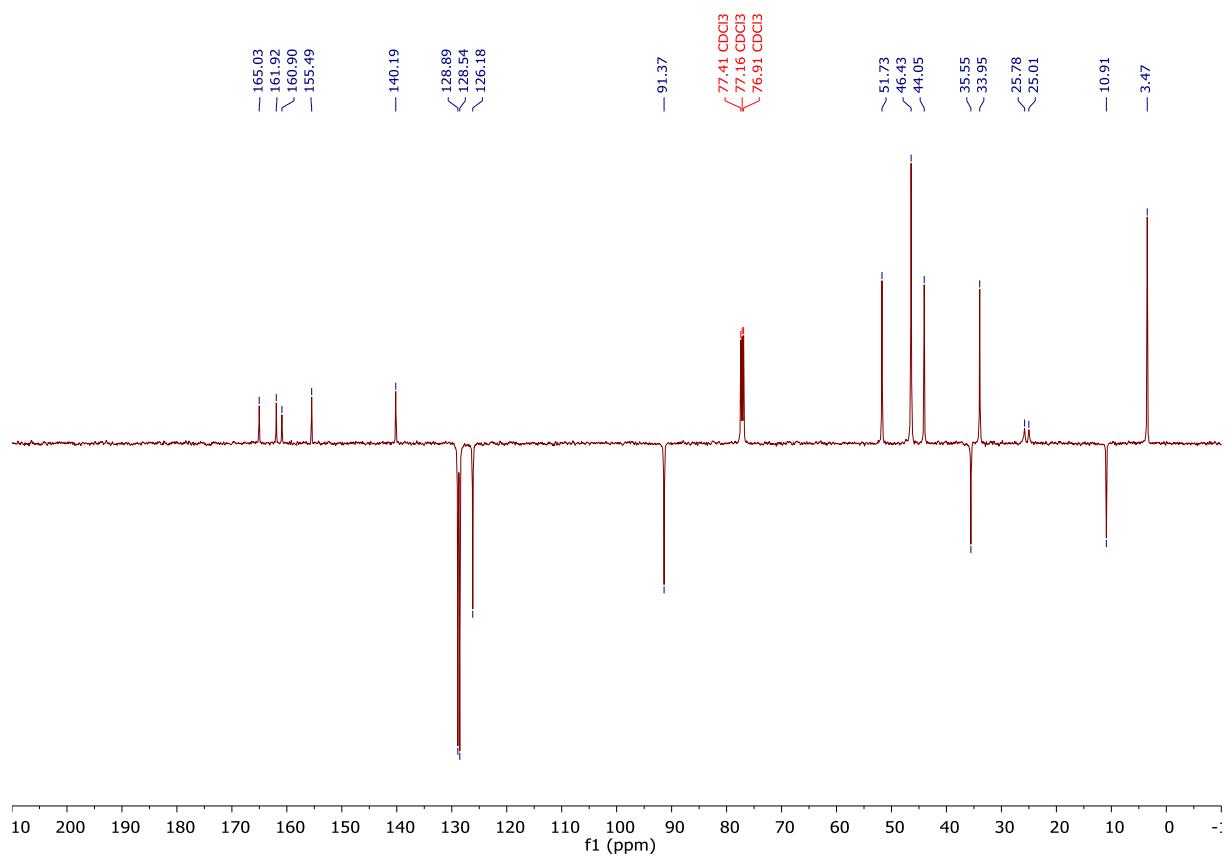
¹³C-NMR



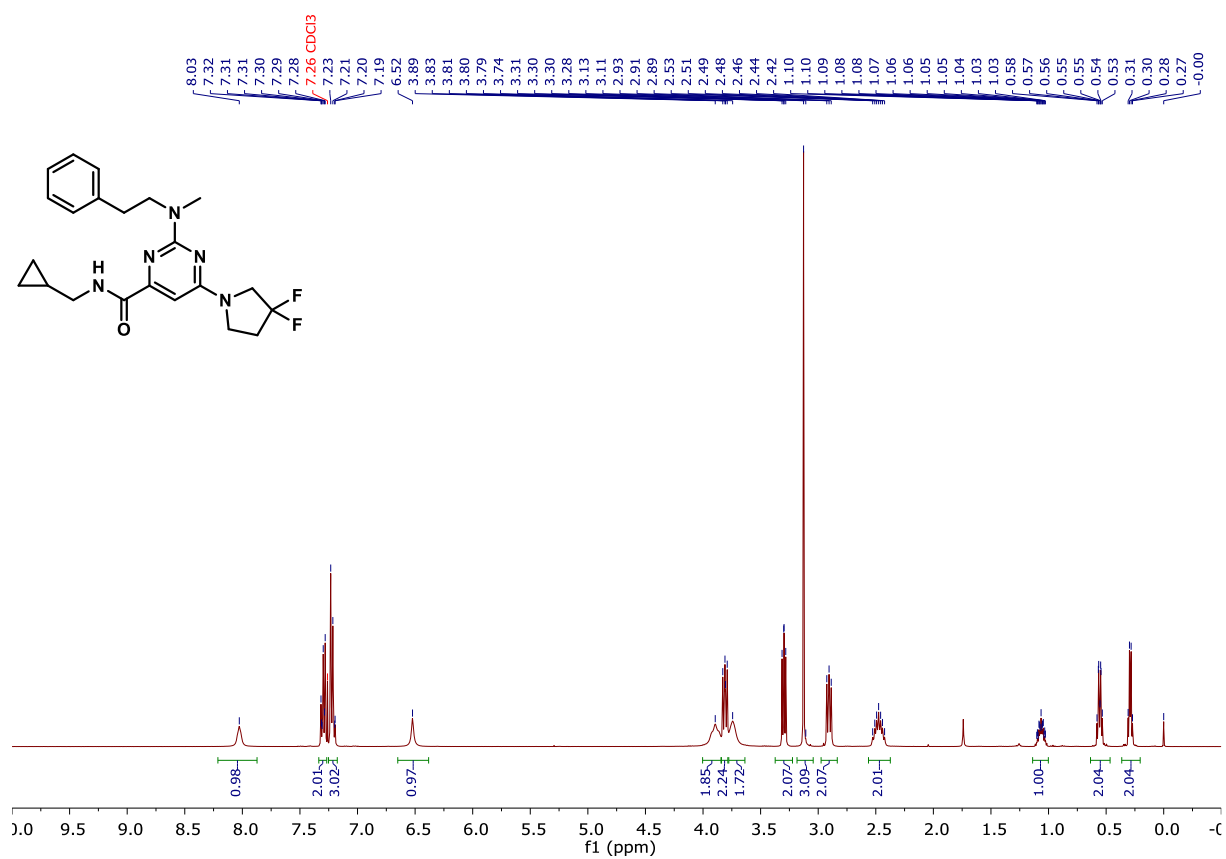
¹H-NMR: 87



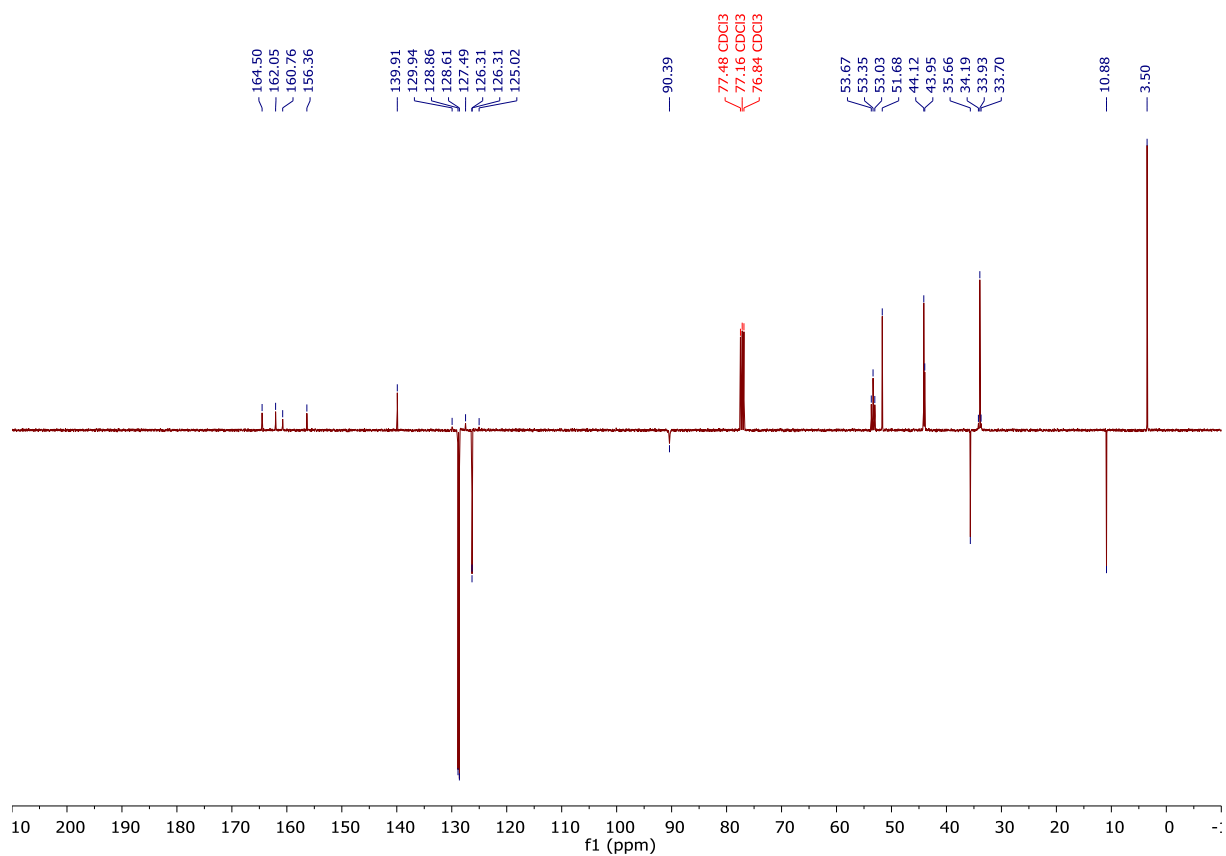
¹³C-NMR



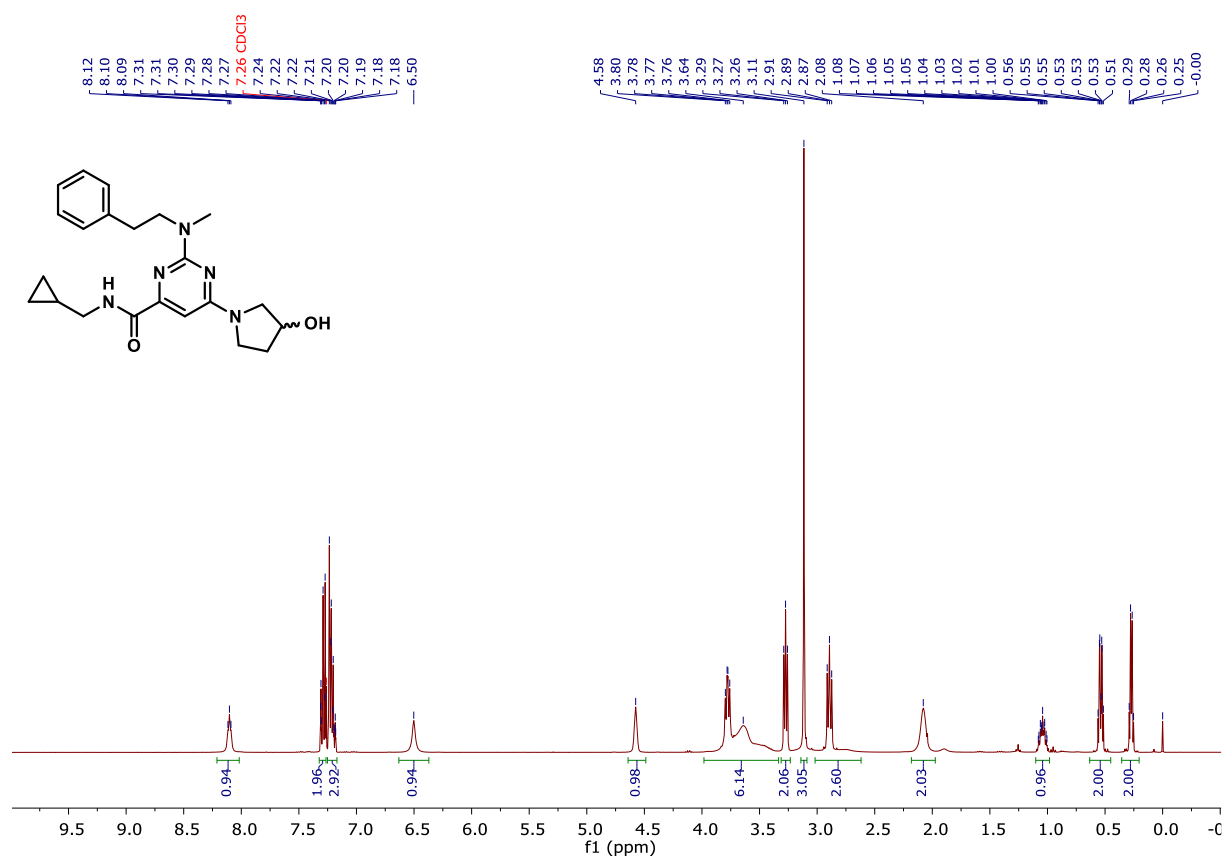
¹H-NMR: 88



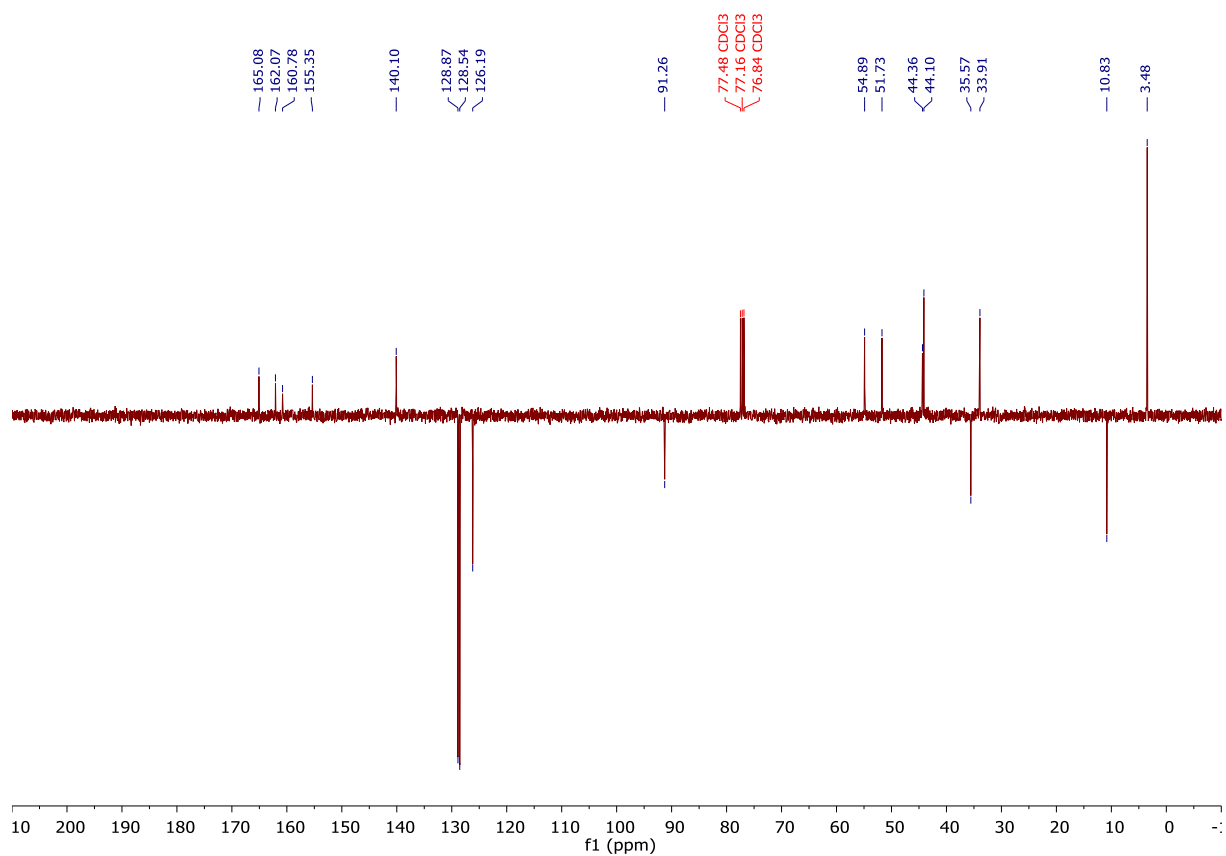
¹³C-NMR



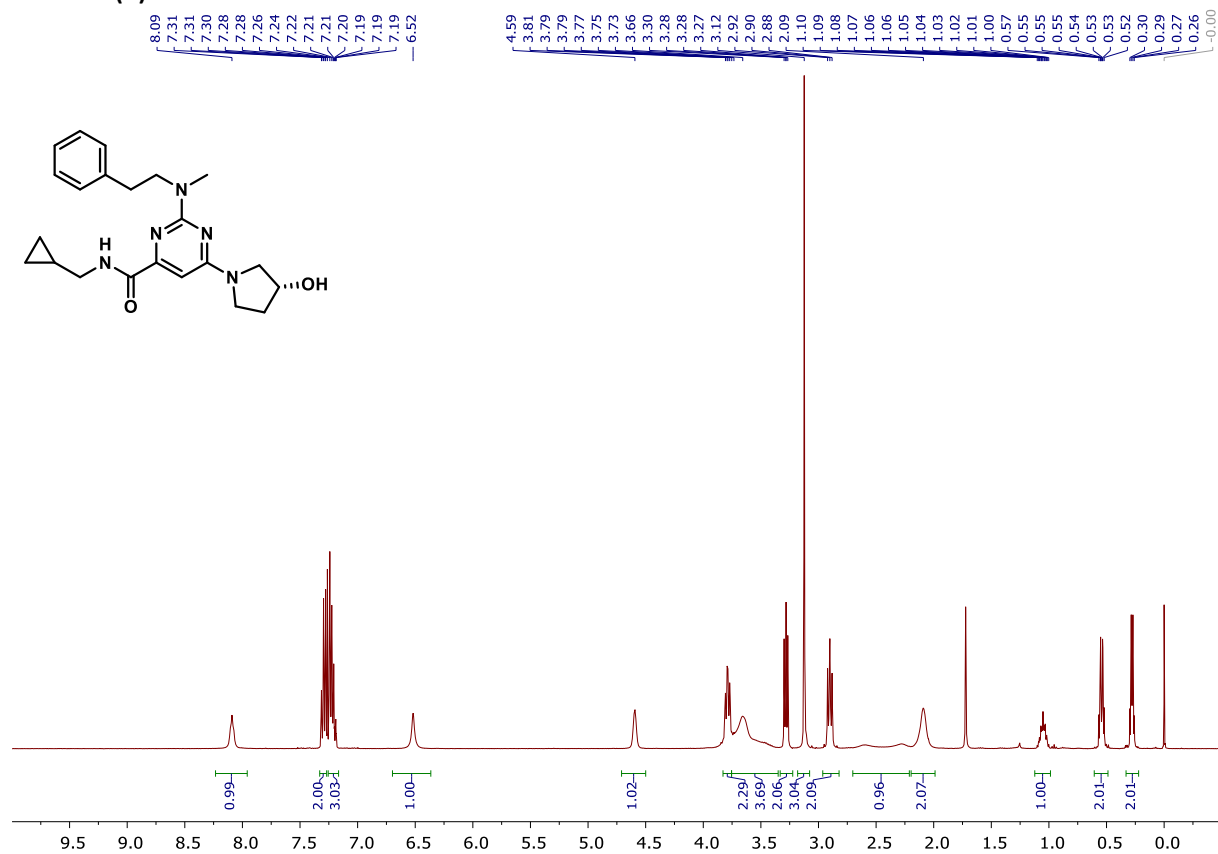
¹H-NMR: 89



¹³C-NMR



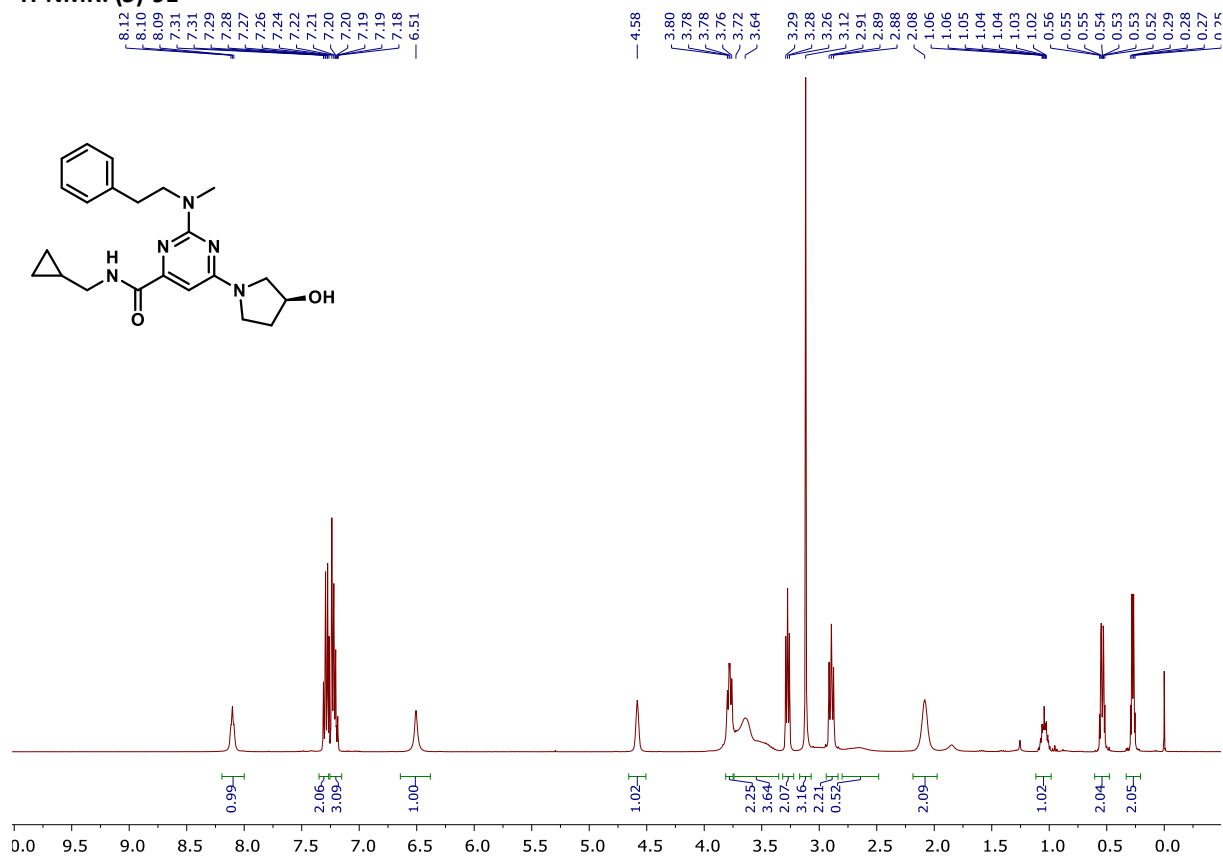
¹H-NMR: (R)-90



¹³C-NMR



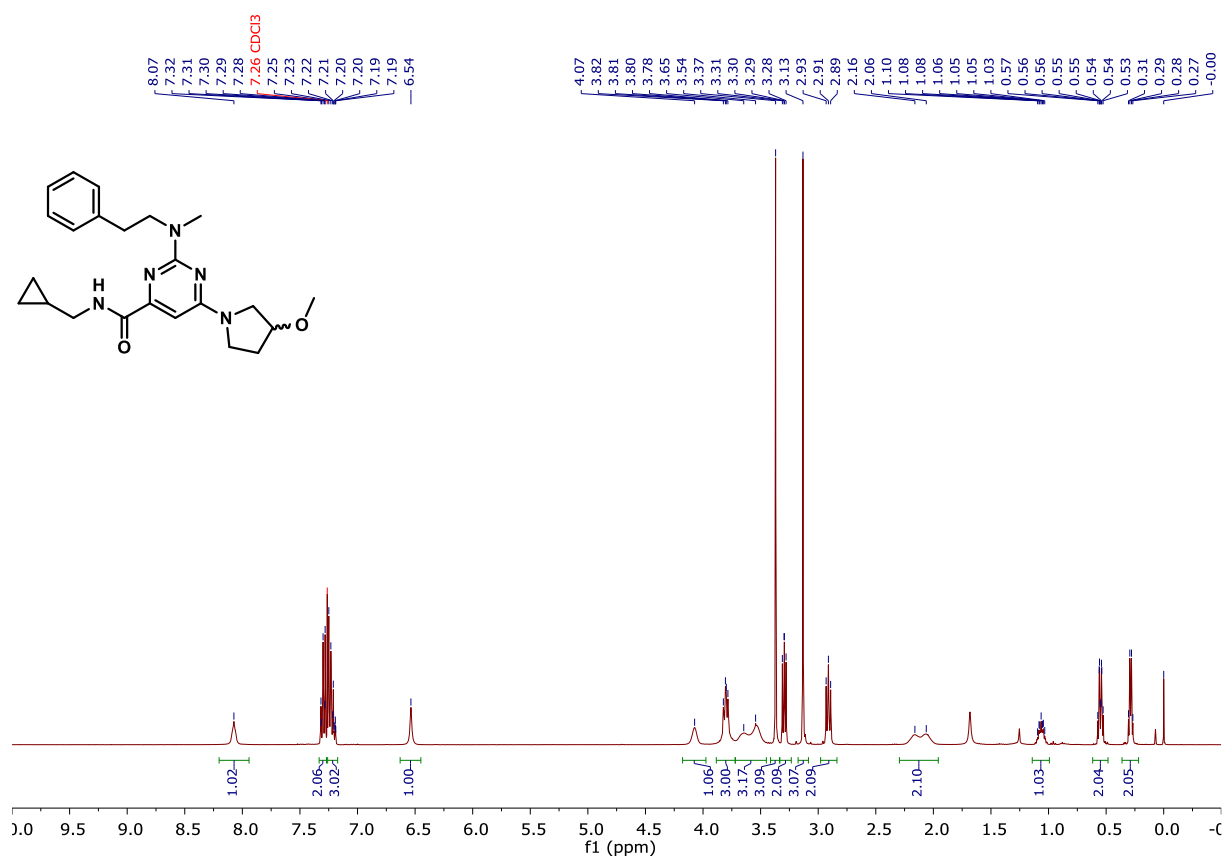
¹H-NMR: (S)-91



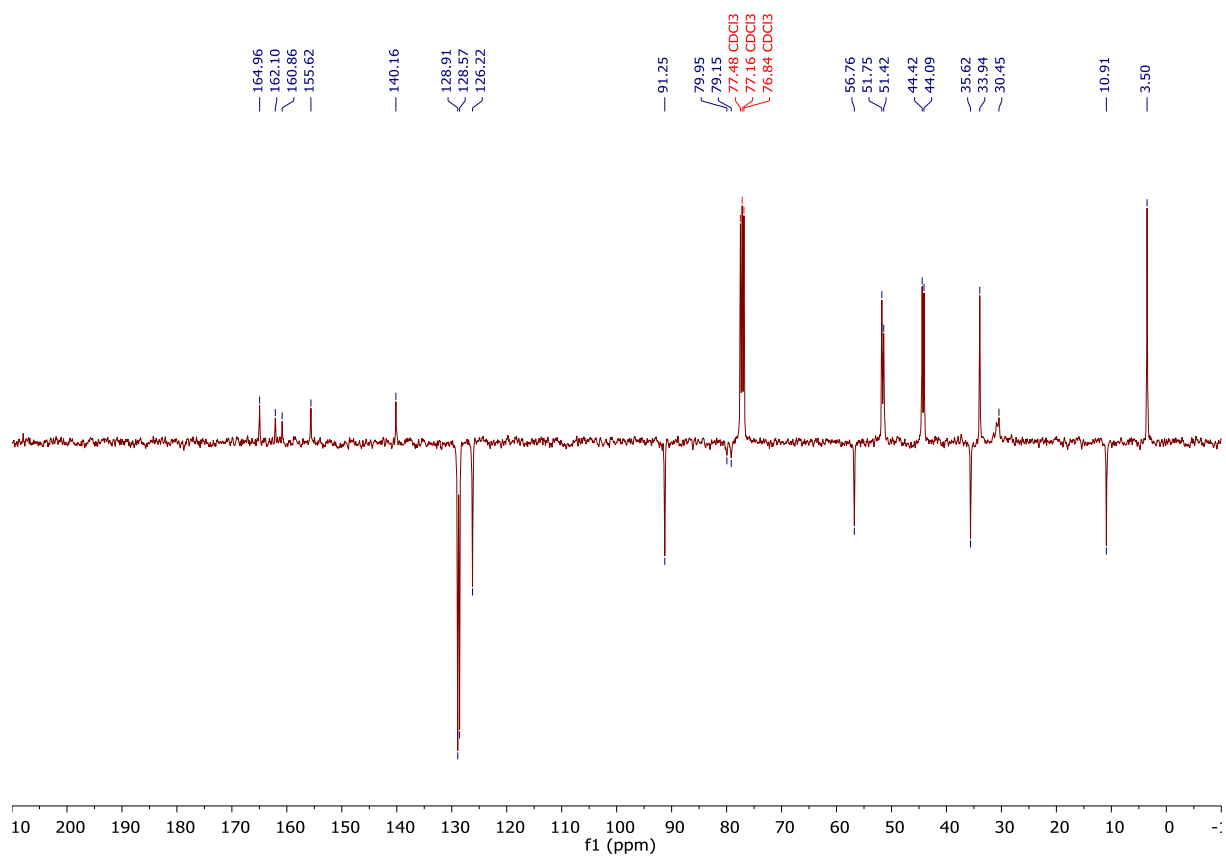
¹³C-NMR



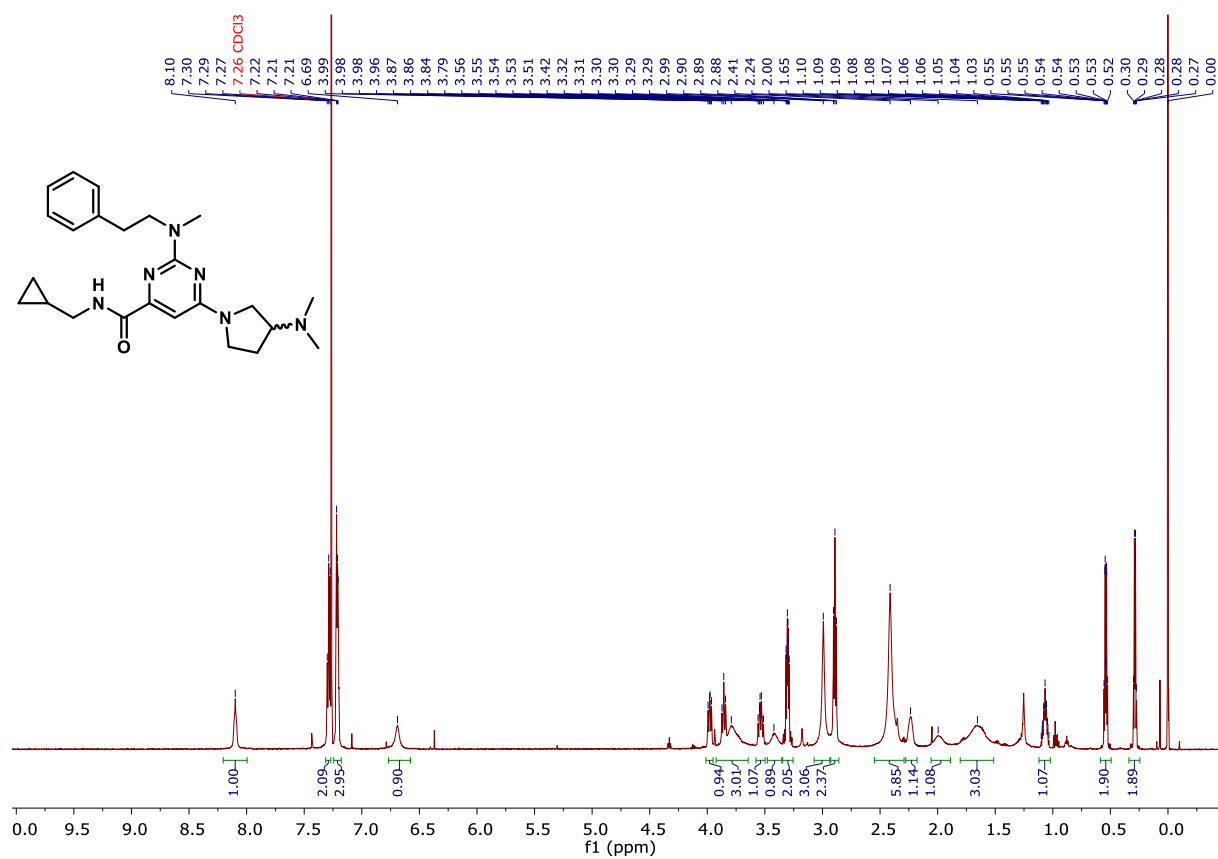
¹H-NMR: 92



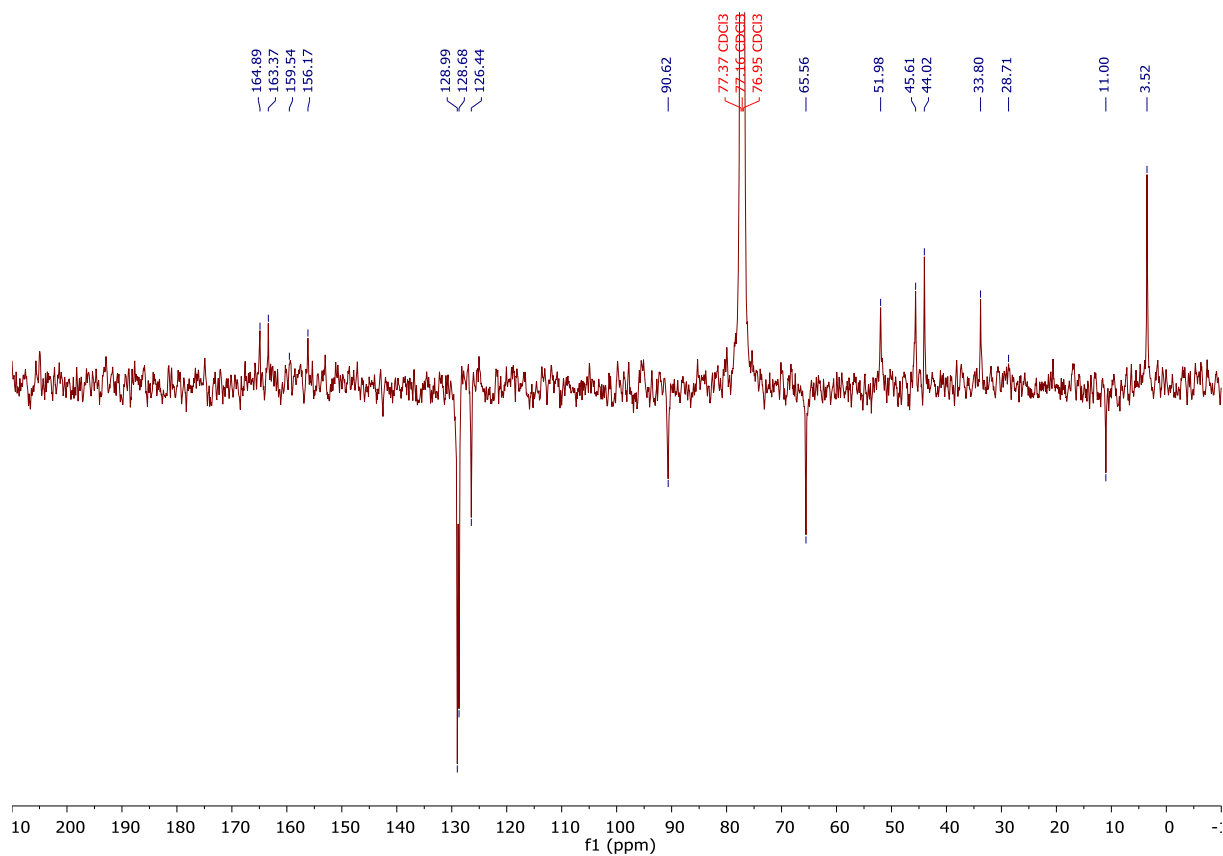
¹³C-NMR



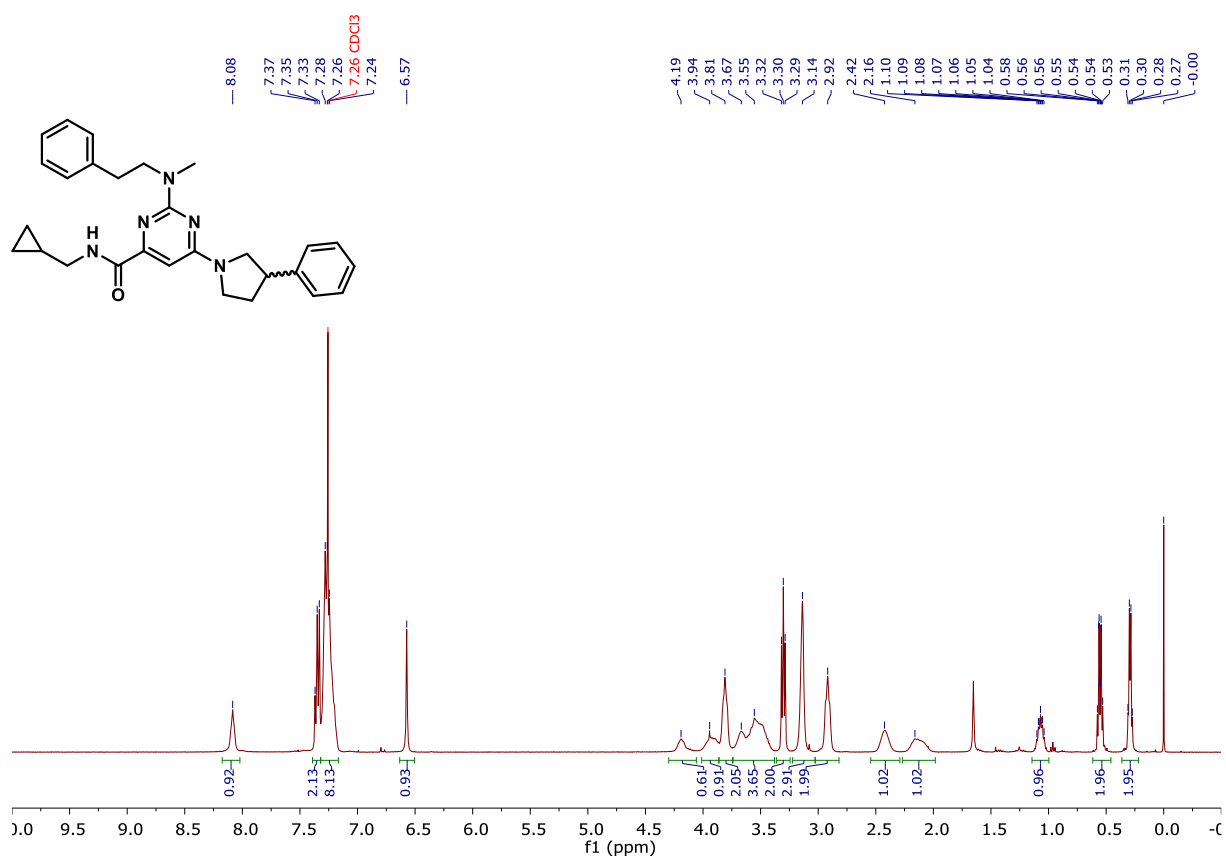
¹H-NMR: 93



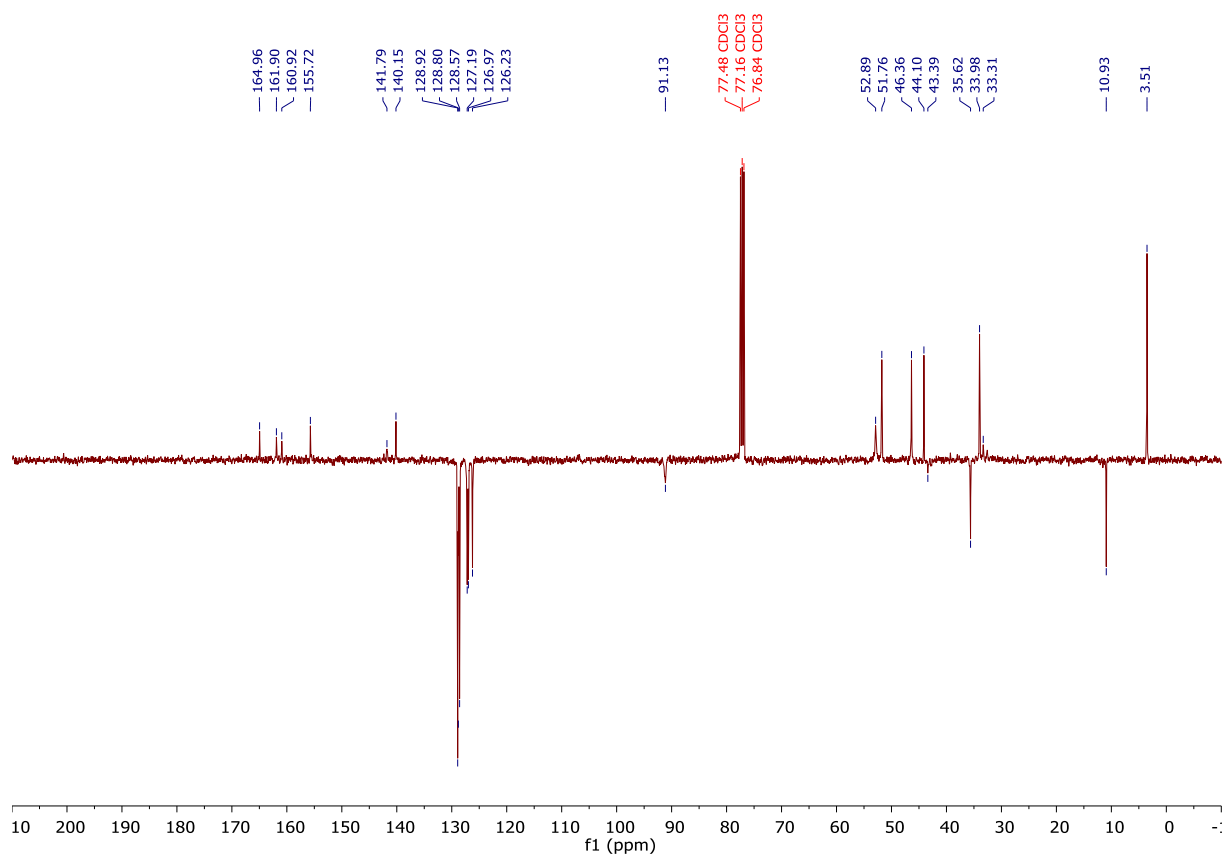
¹³C-NMR



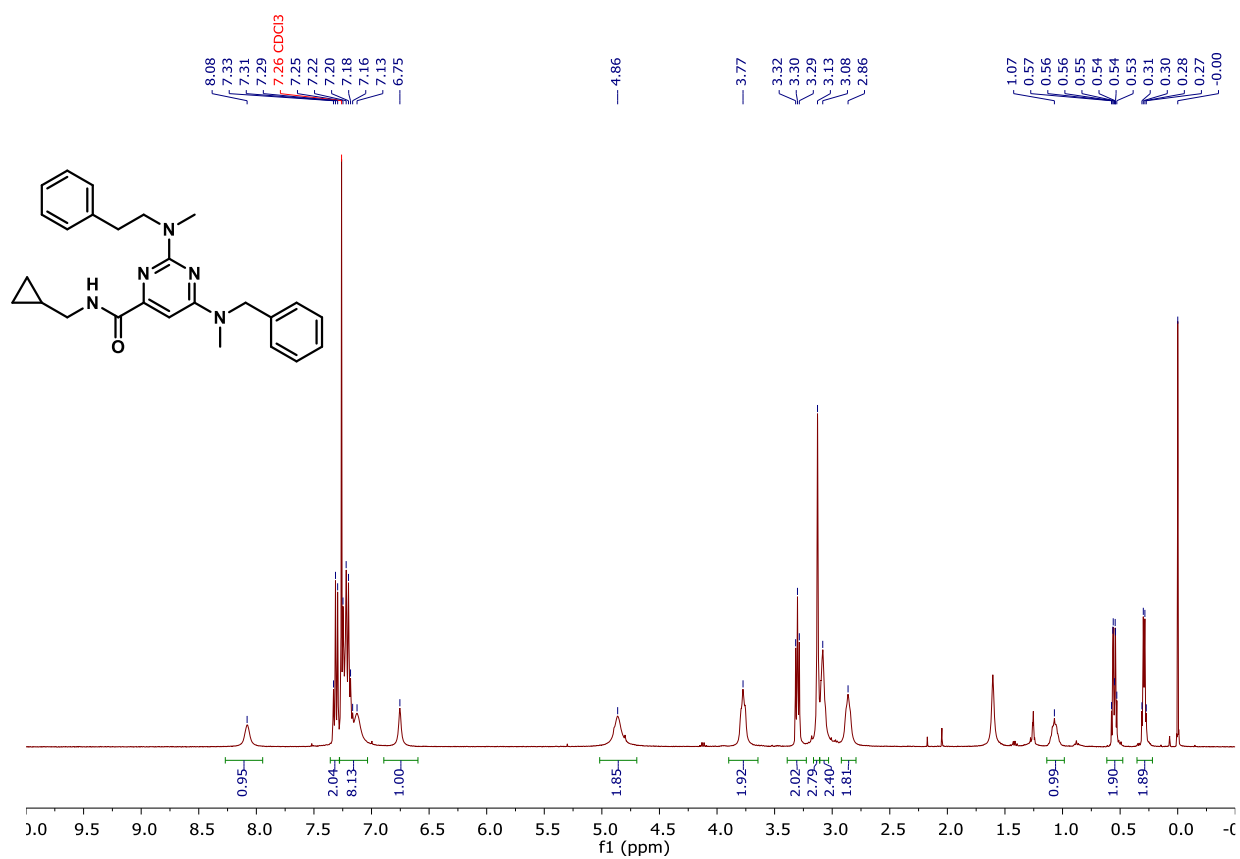
¹H-NMR: 94



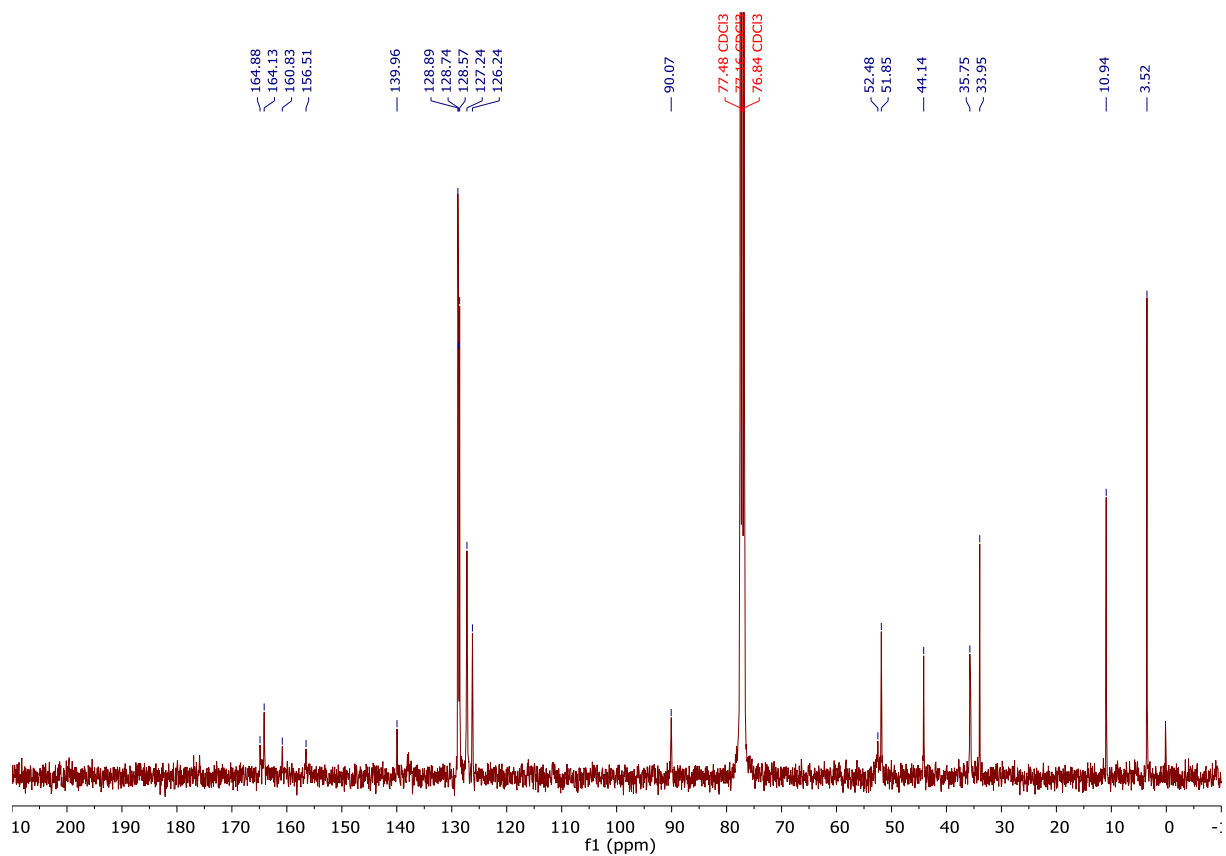
¹³C-NMR



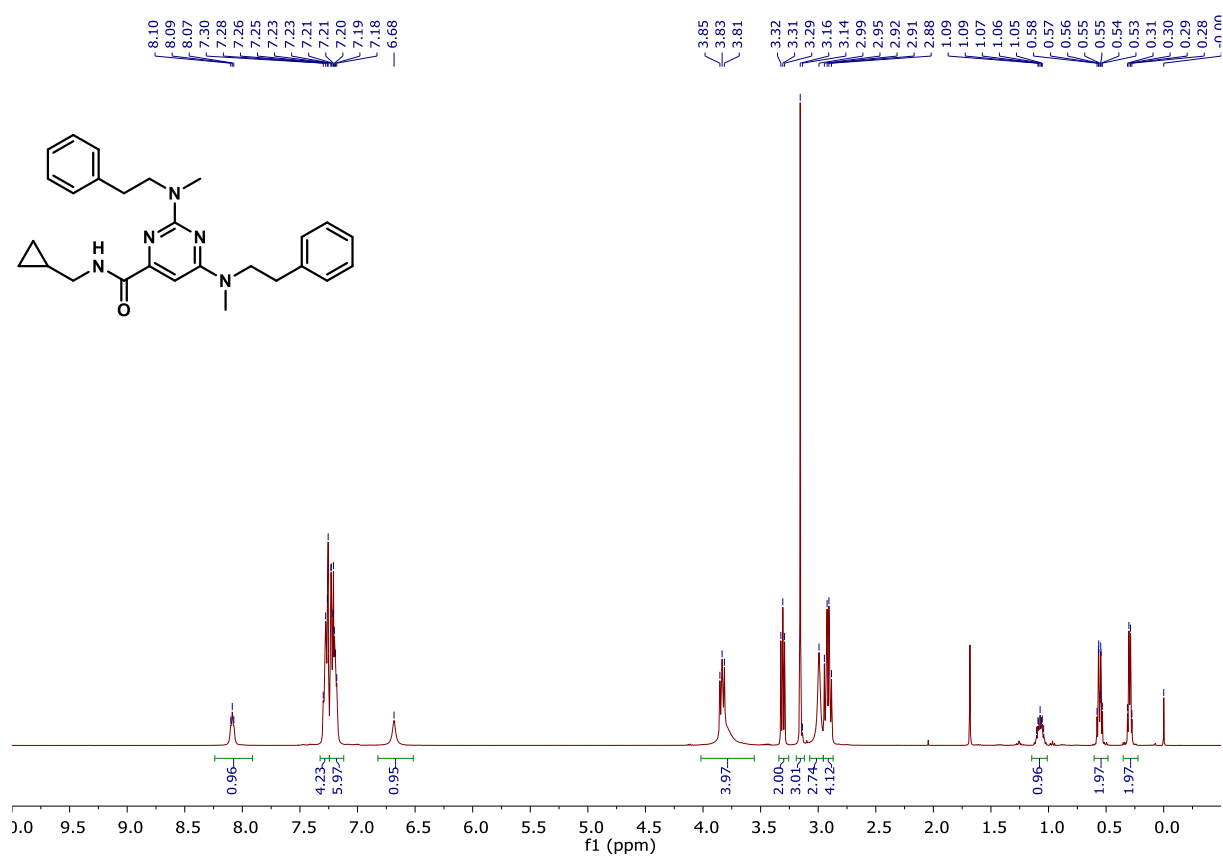
¹H-NMR: 95



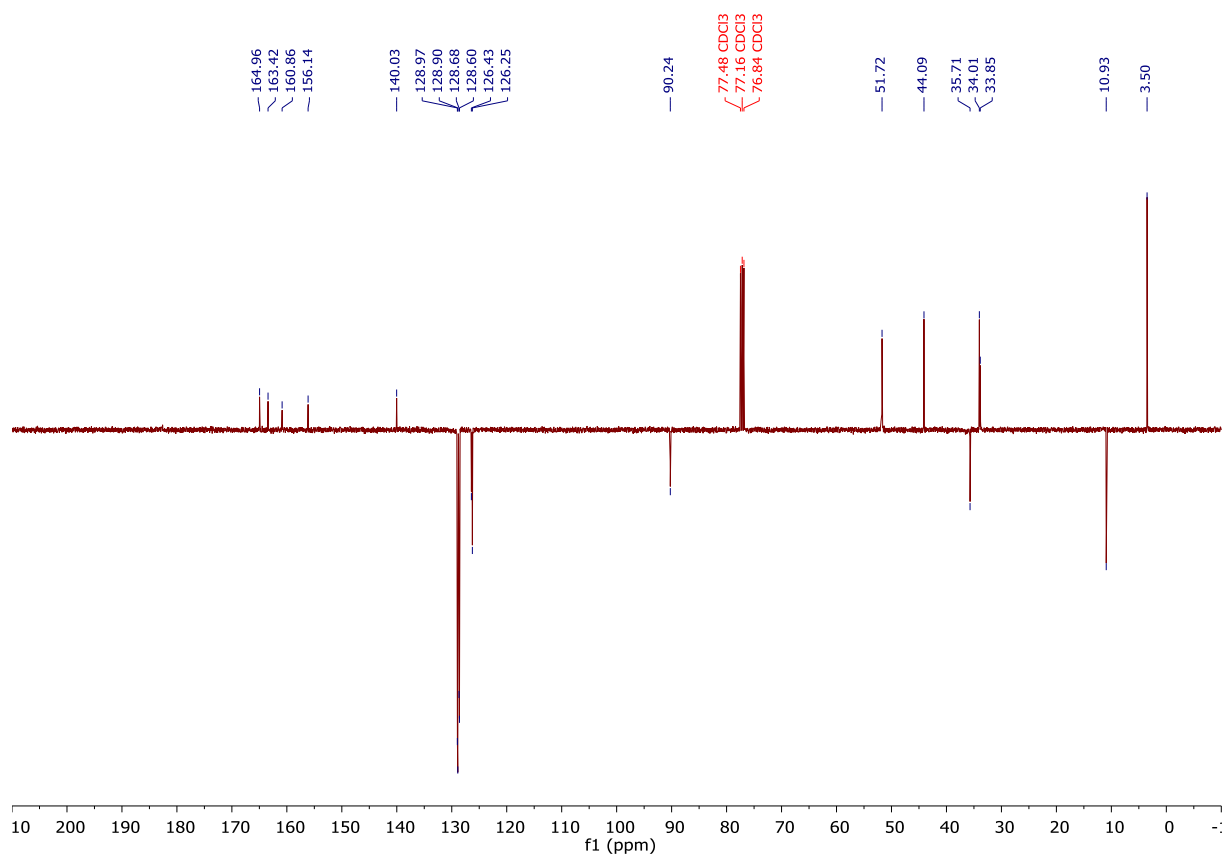
¹³C-NMR



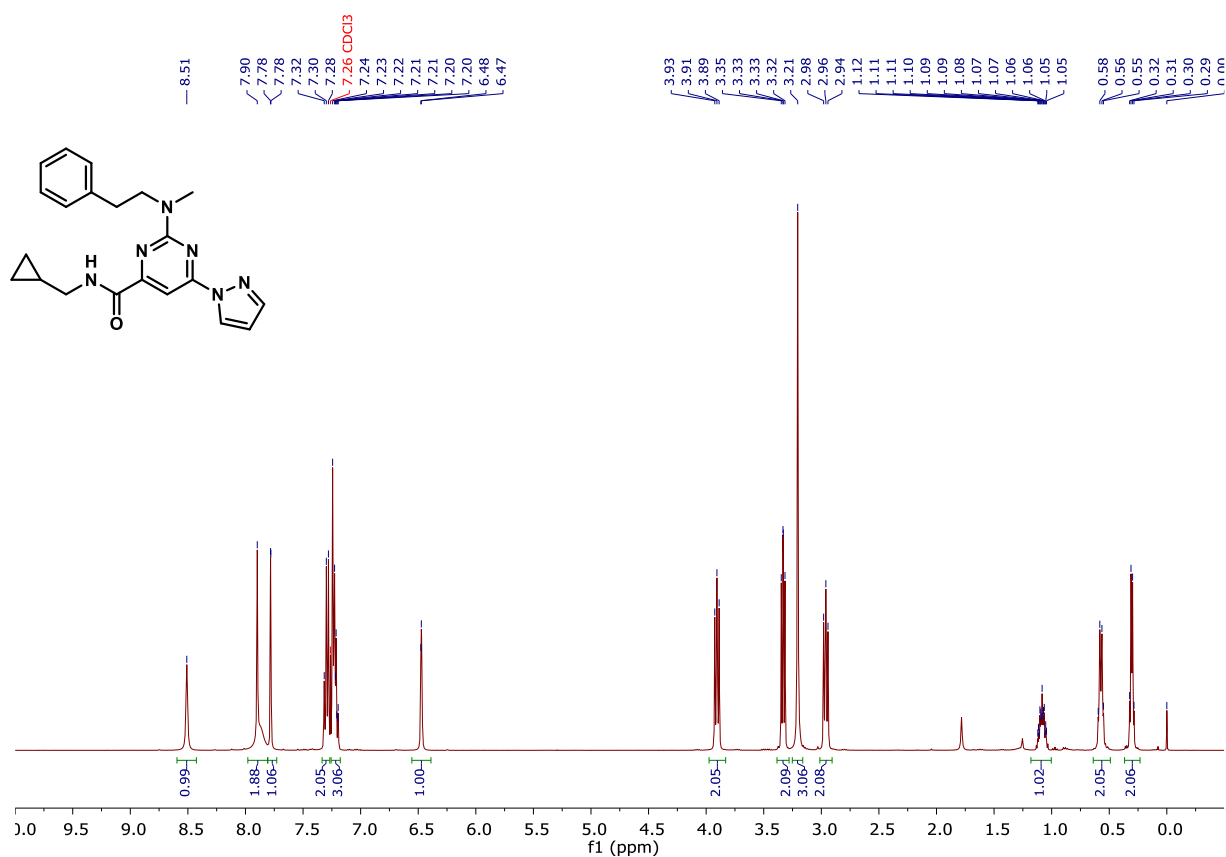
¹H-NMR: 96



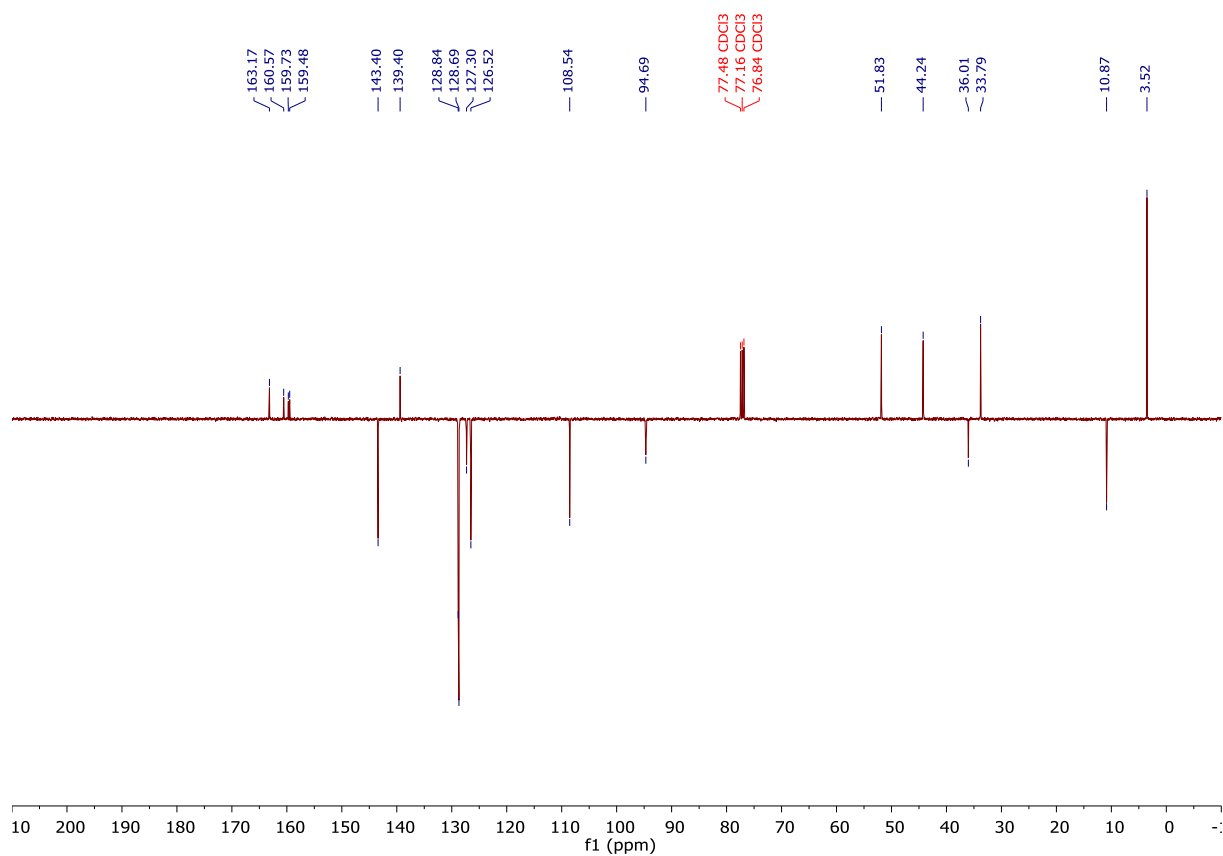
¹³C-NMR



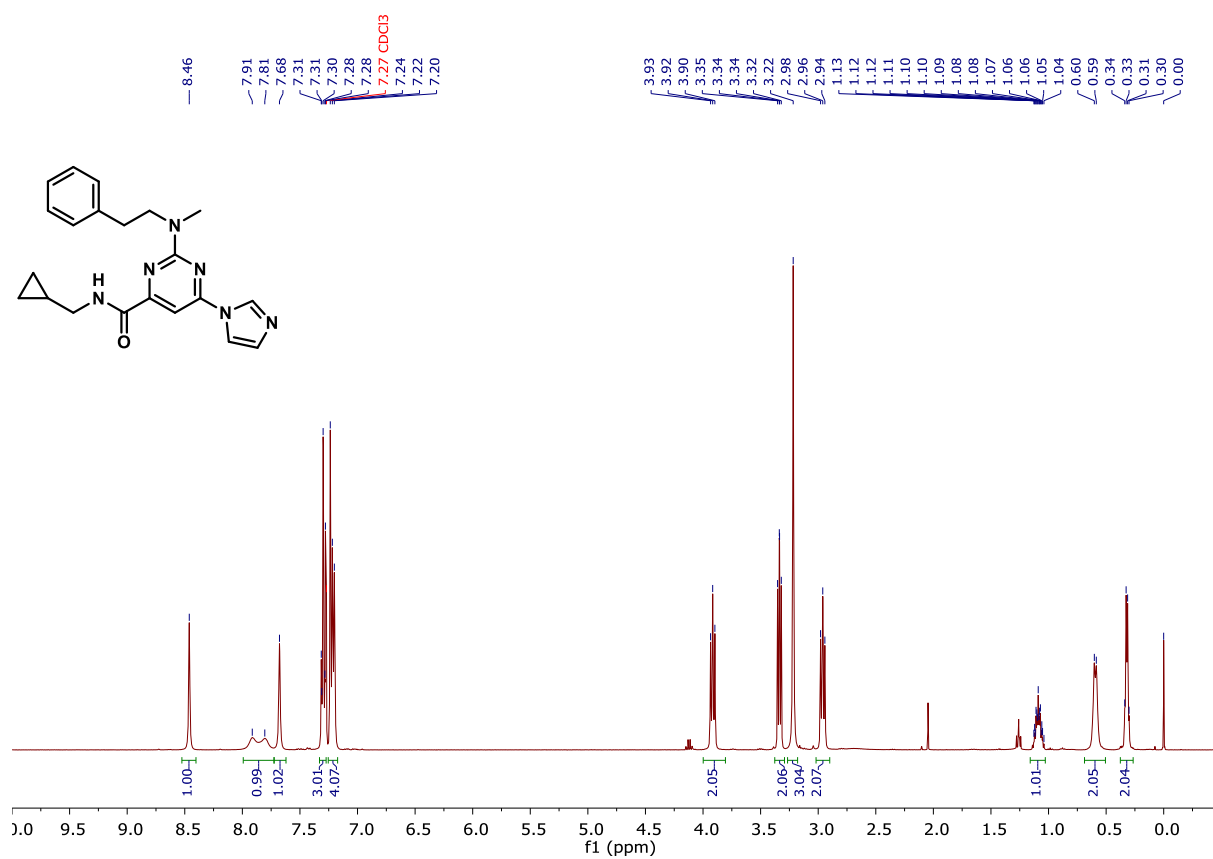
¹H-NMR: 97



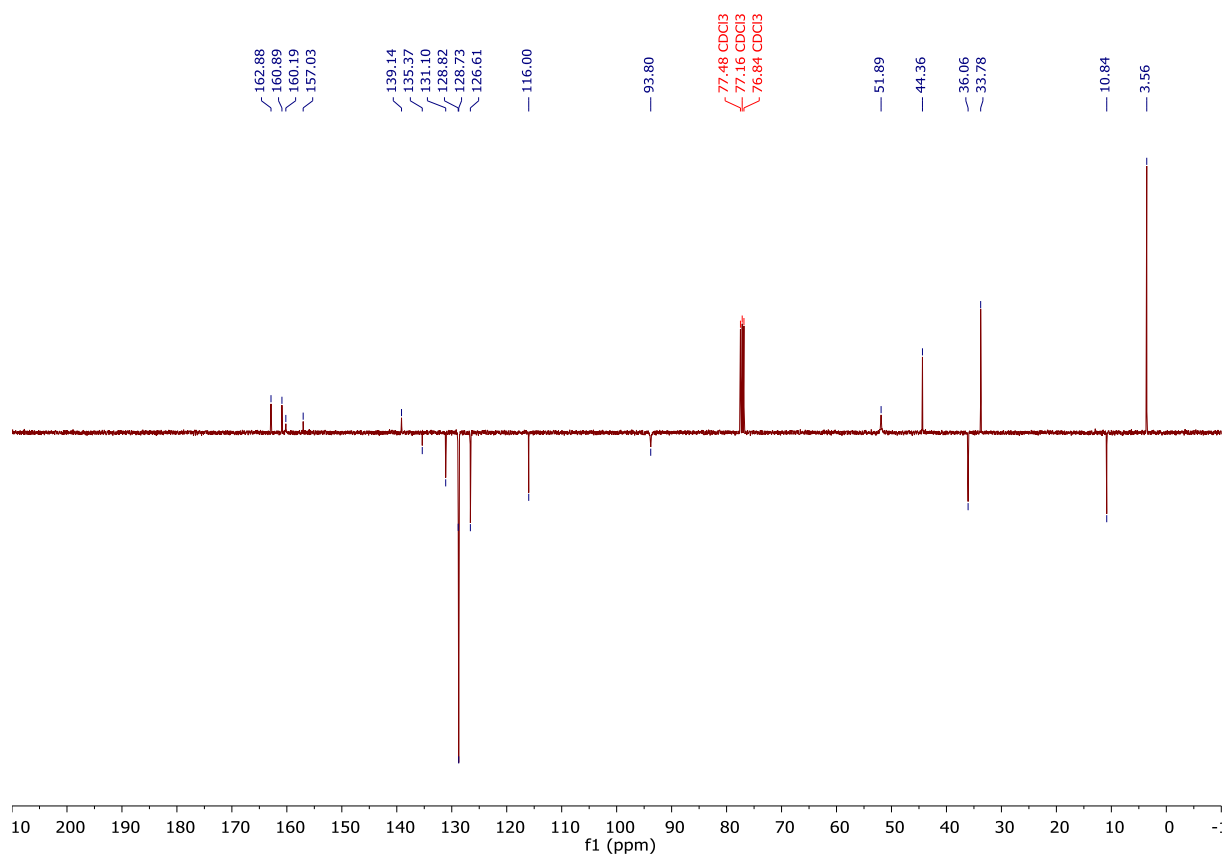
¹³C-NMR



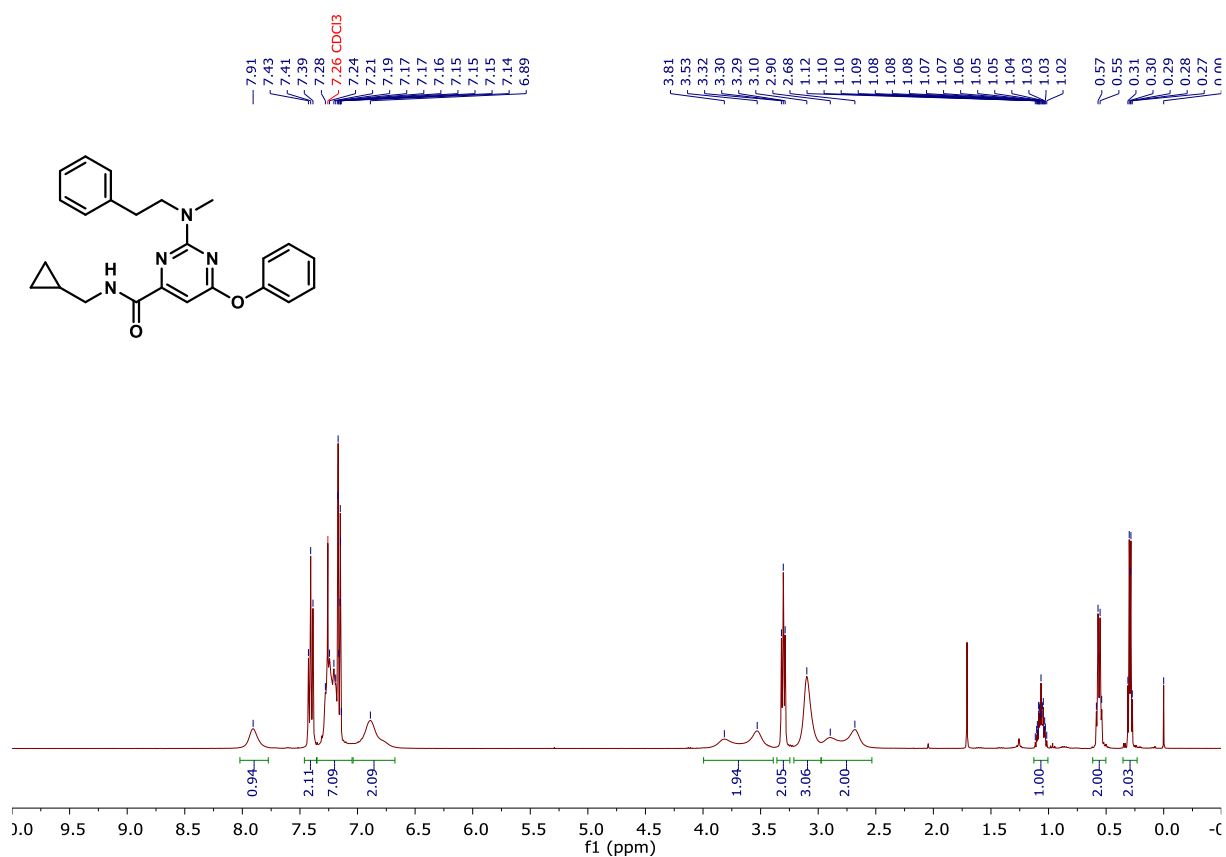
¹H-NMR: 98



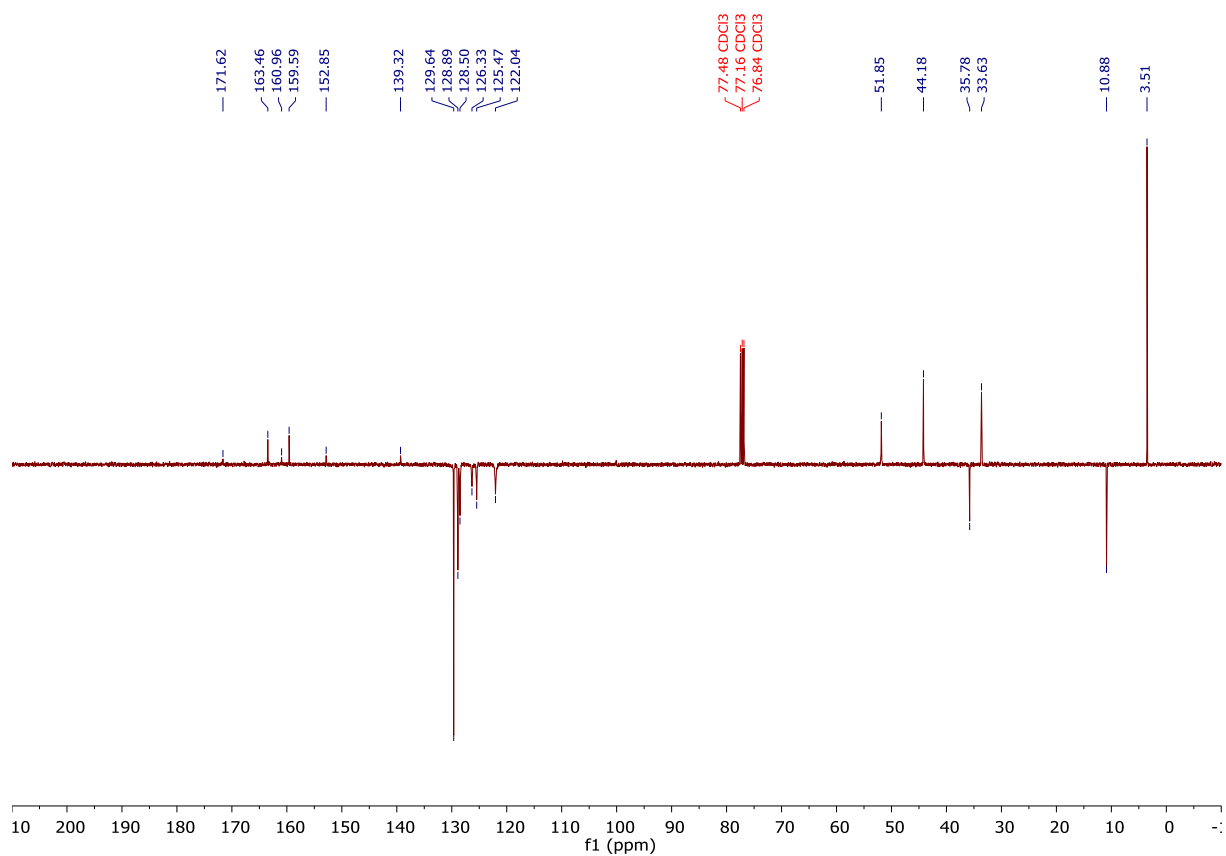
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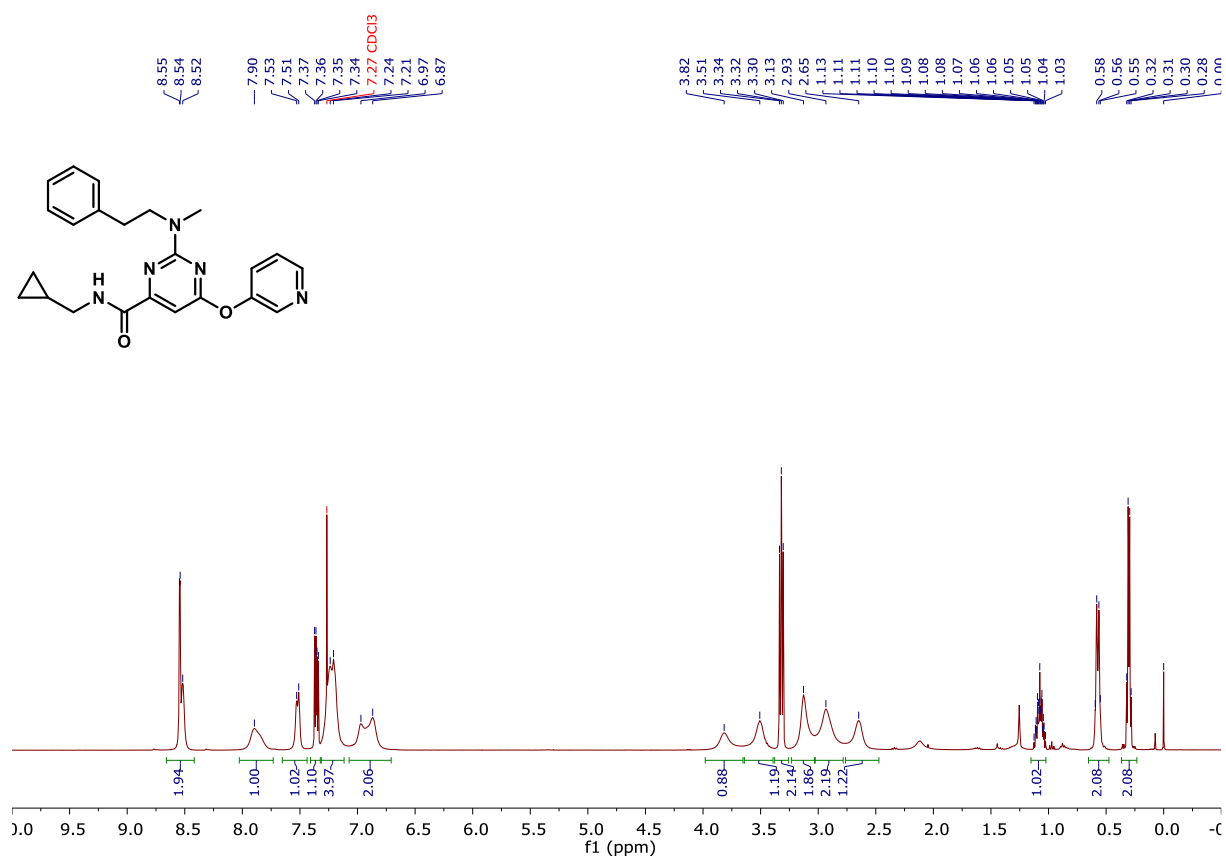
¹H-NMR: 99



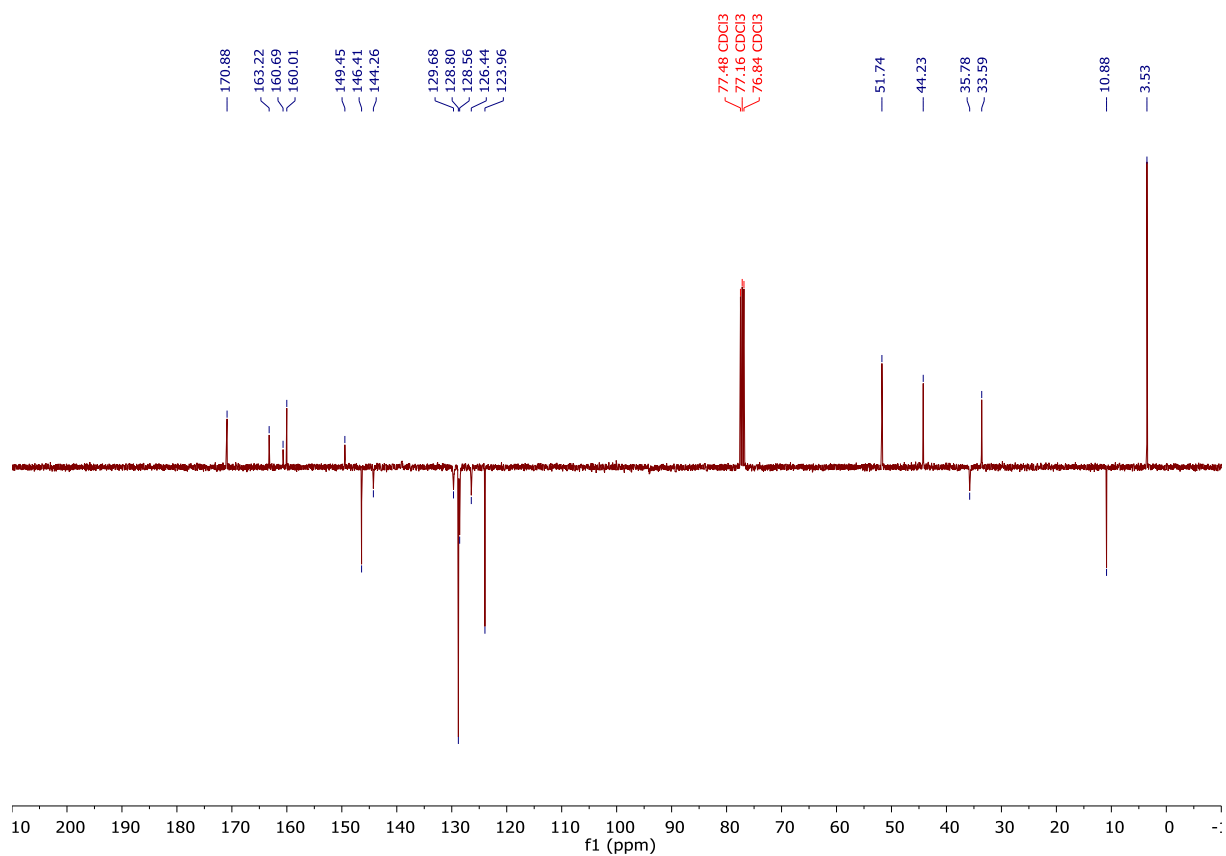
¹³C-NMR



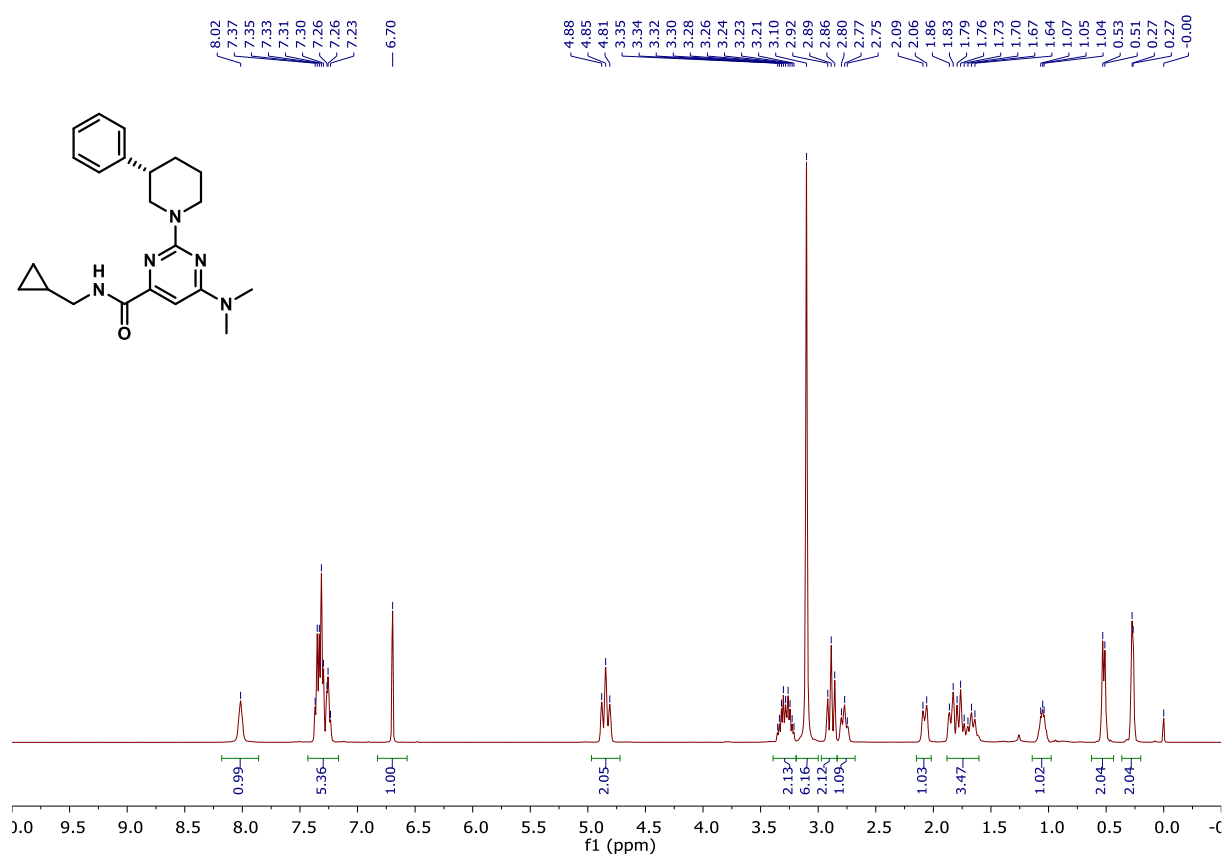
¹H-NMR: 100



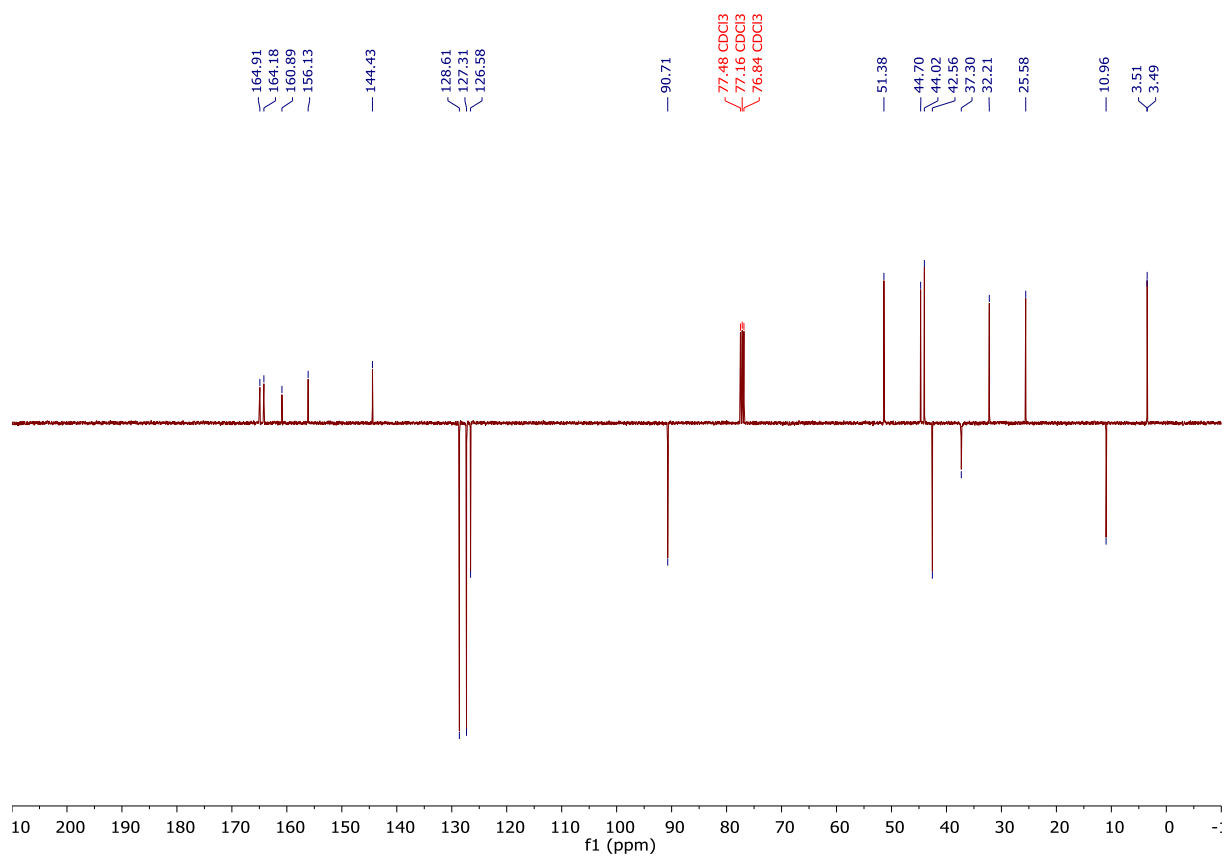
¹³C-NMR



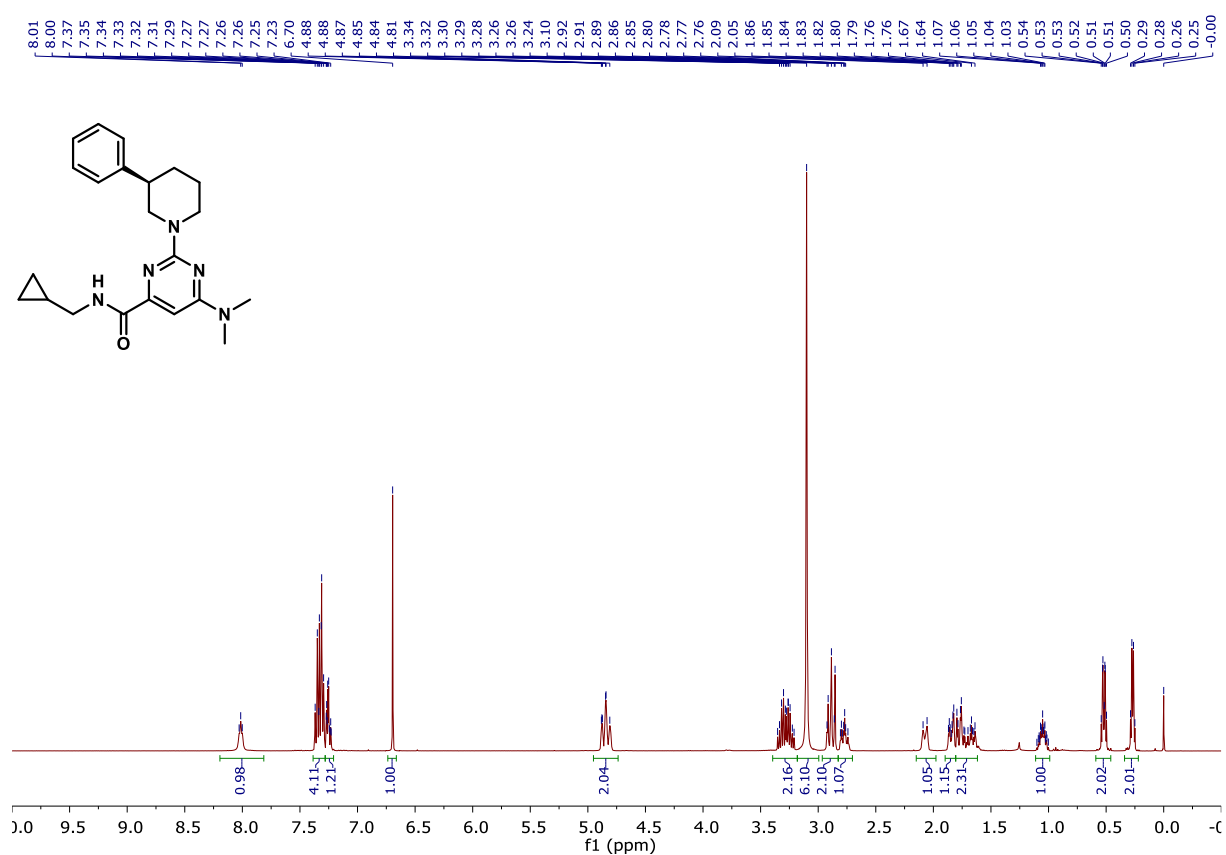
¹H-NMR: (S)-101



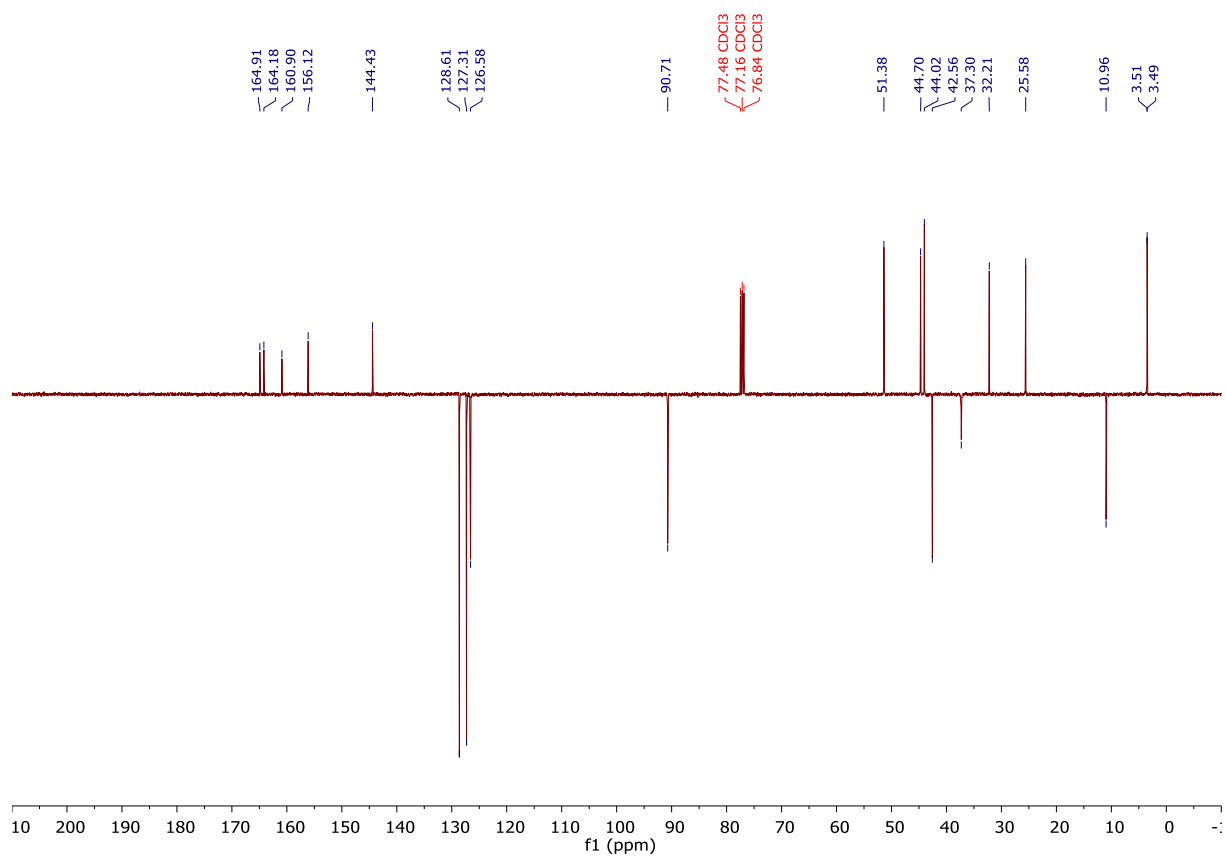
¹³C-NMR



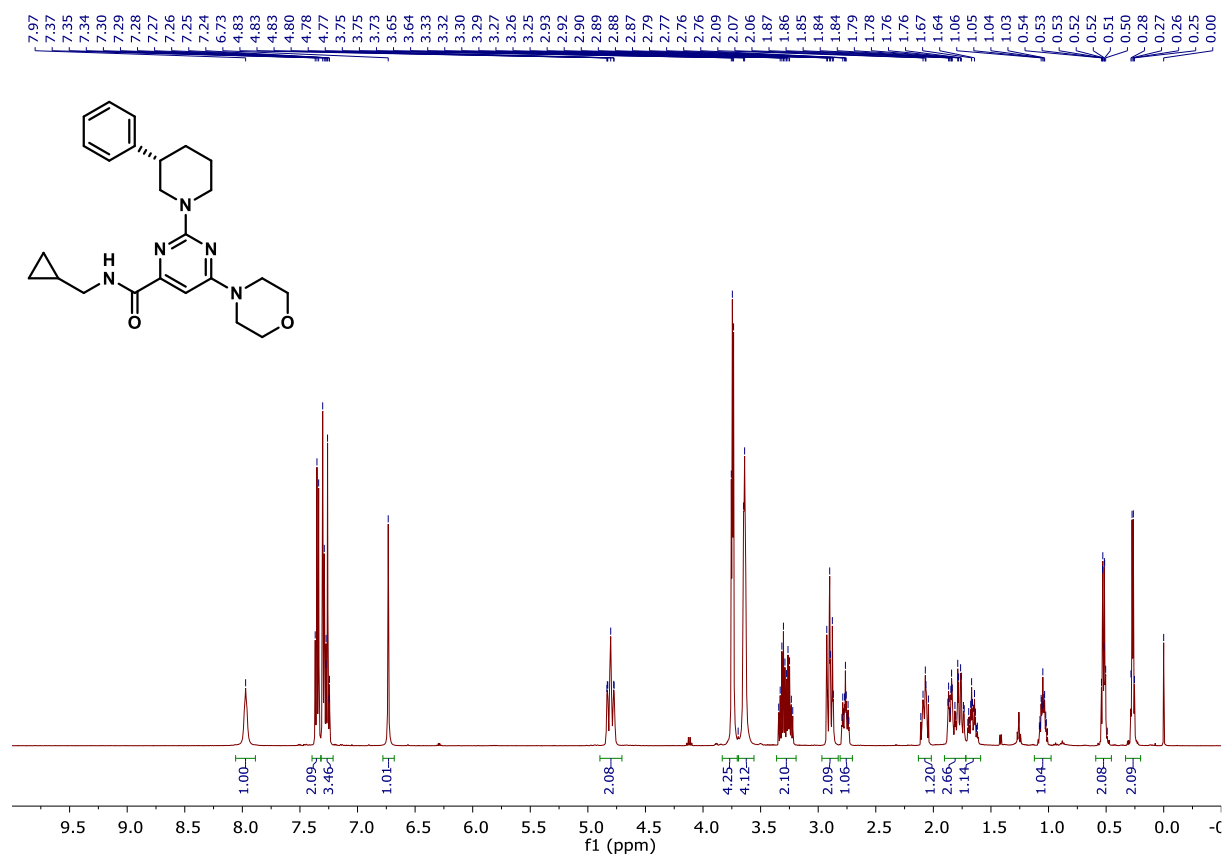
¹H-NMR: (R)-102



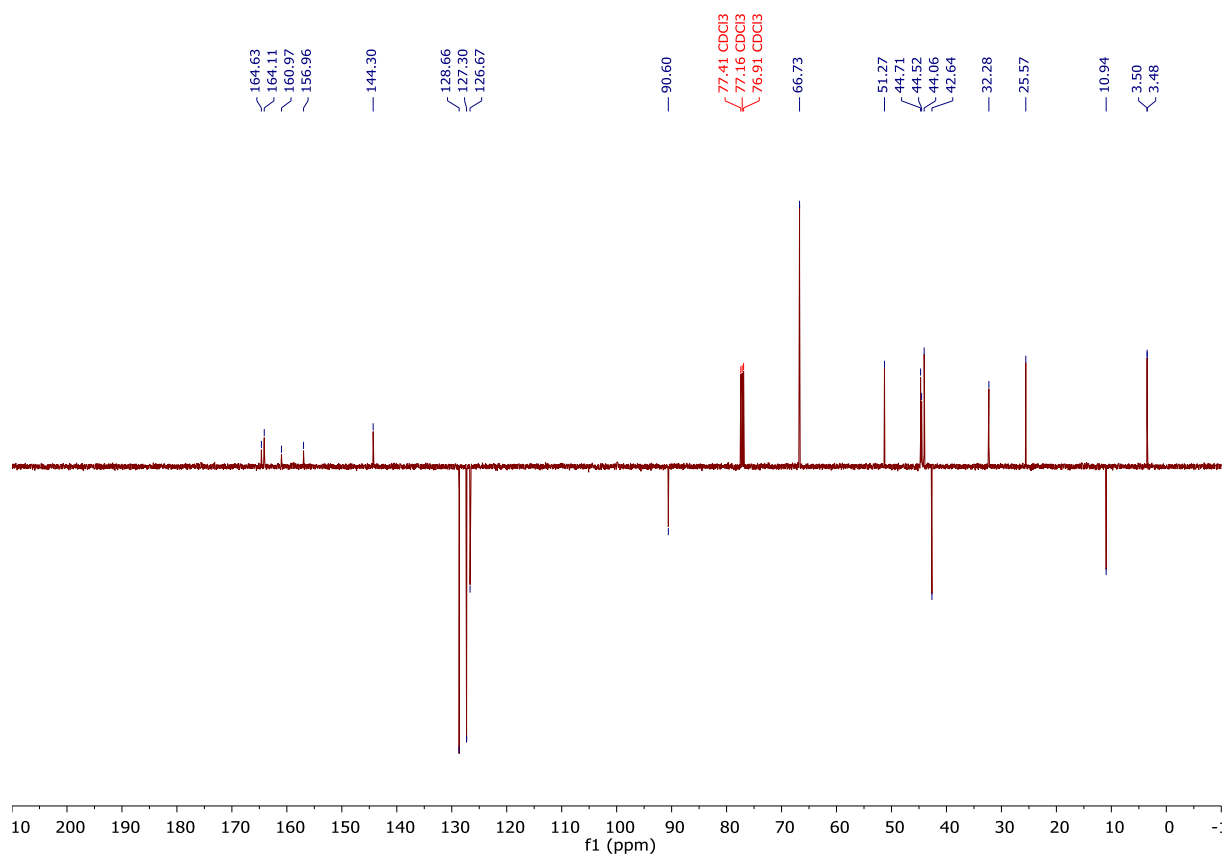
¹³C-NMR



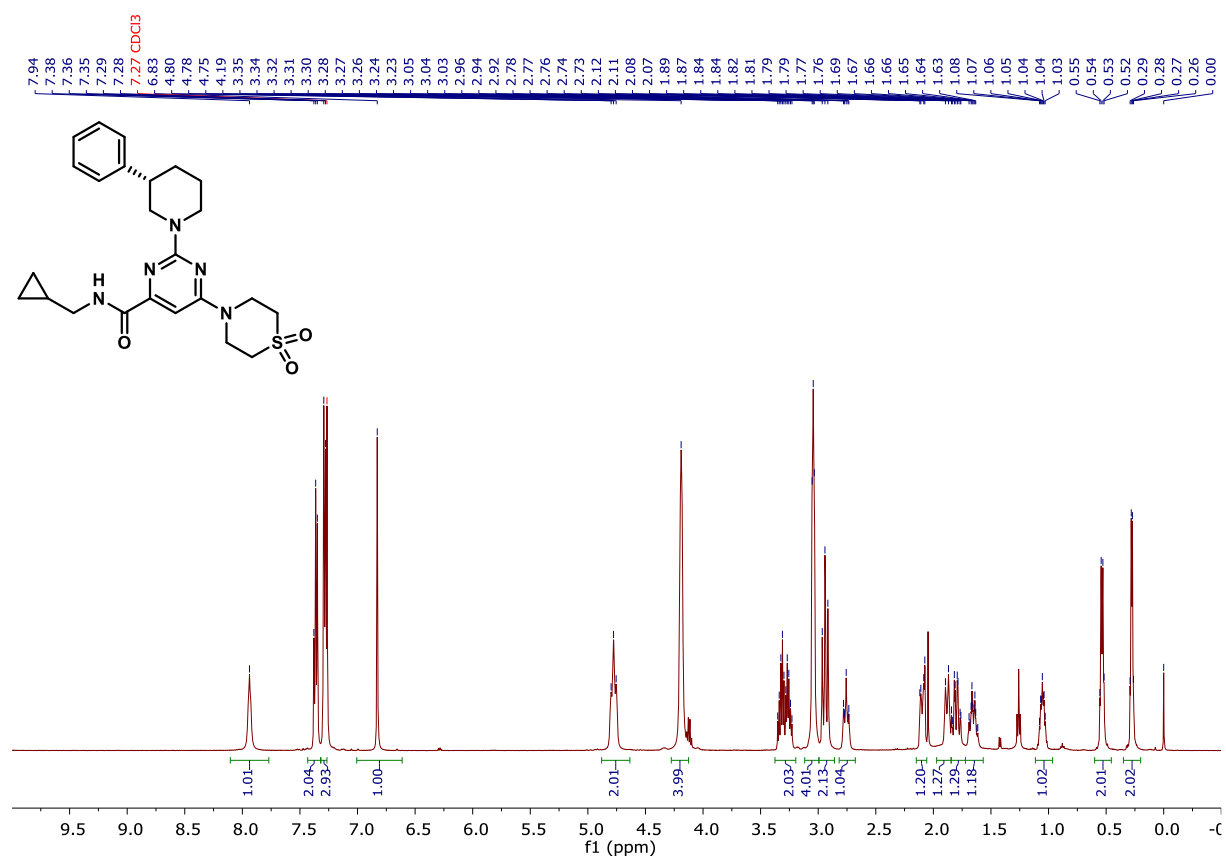
¹H-NMR: (S)-103



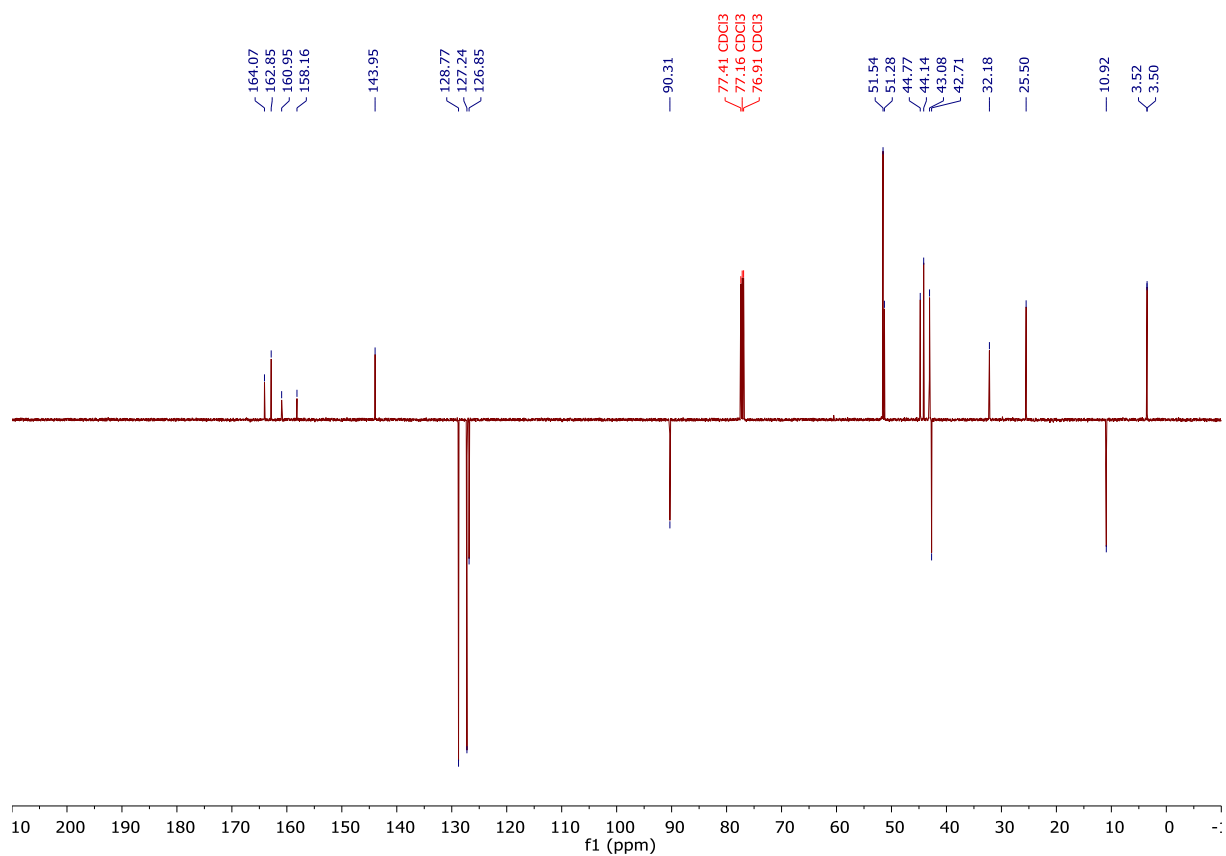
¹³C-NMR



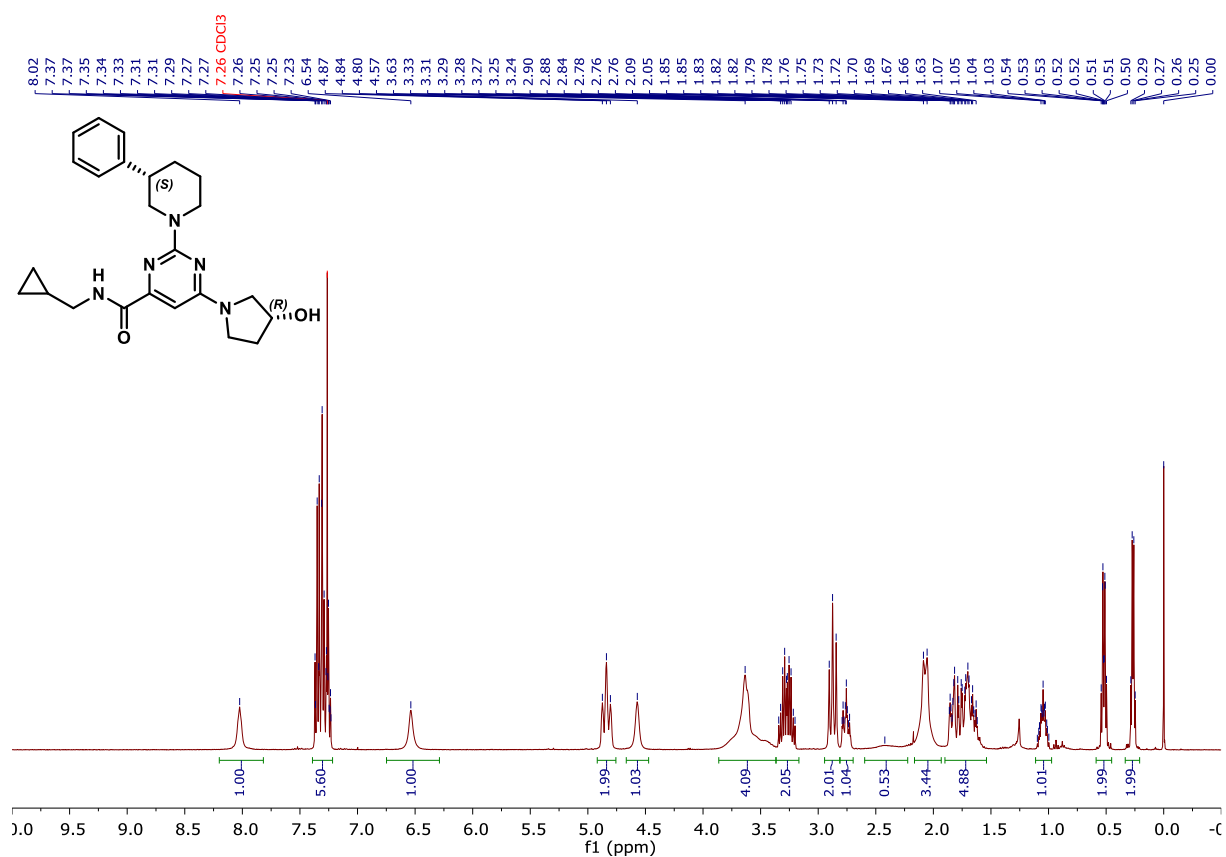
¹H-NMR: (S)-104



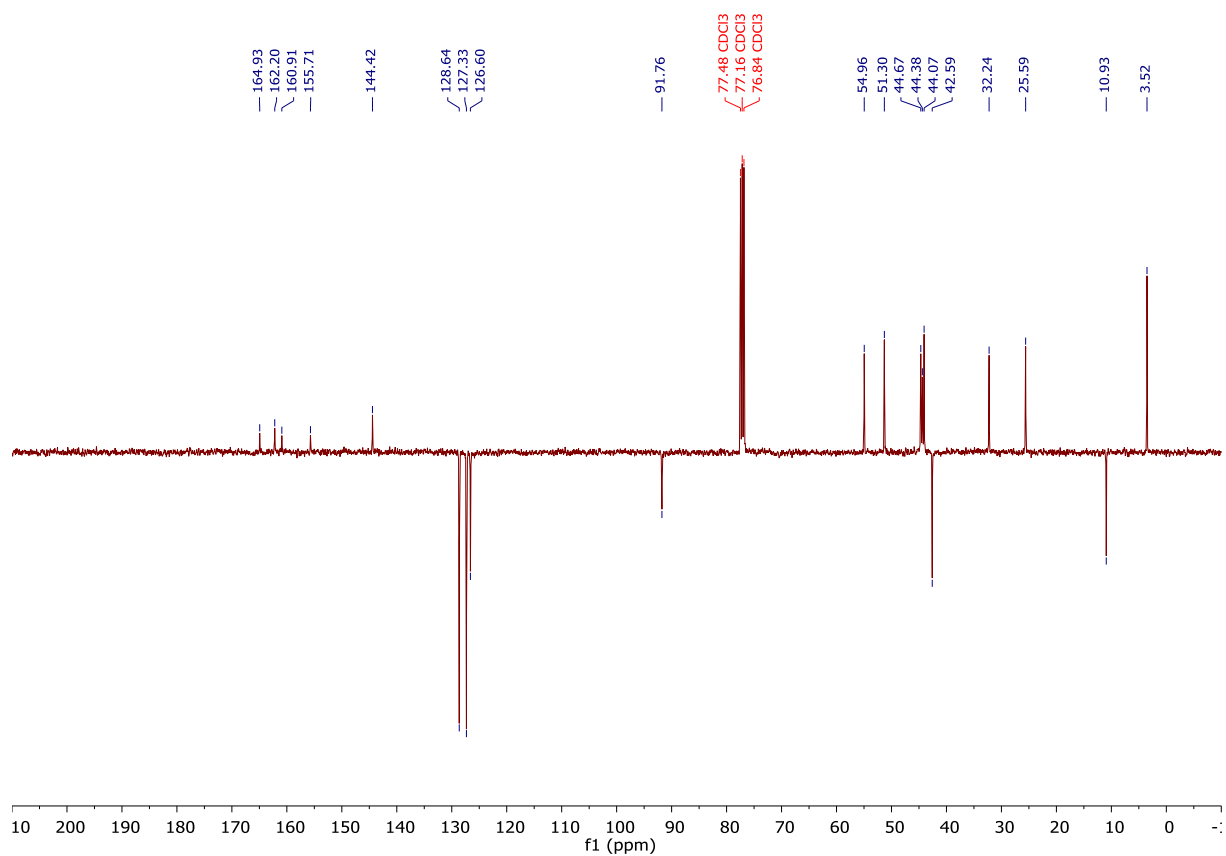
¹³C-NMR

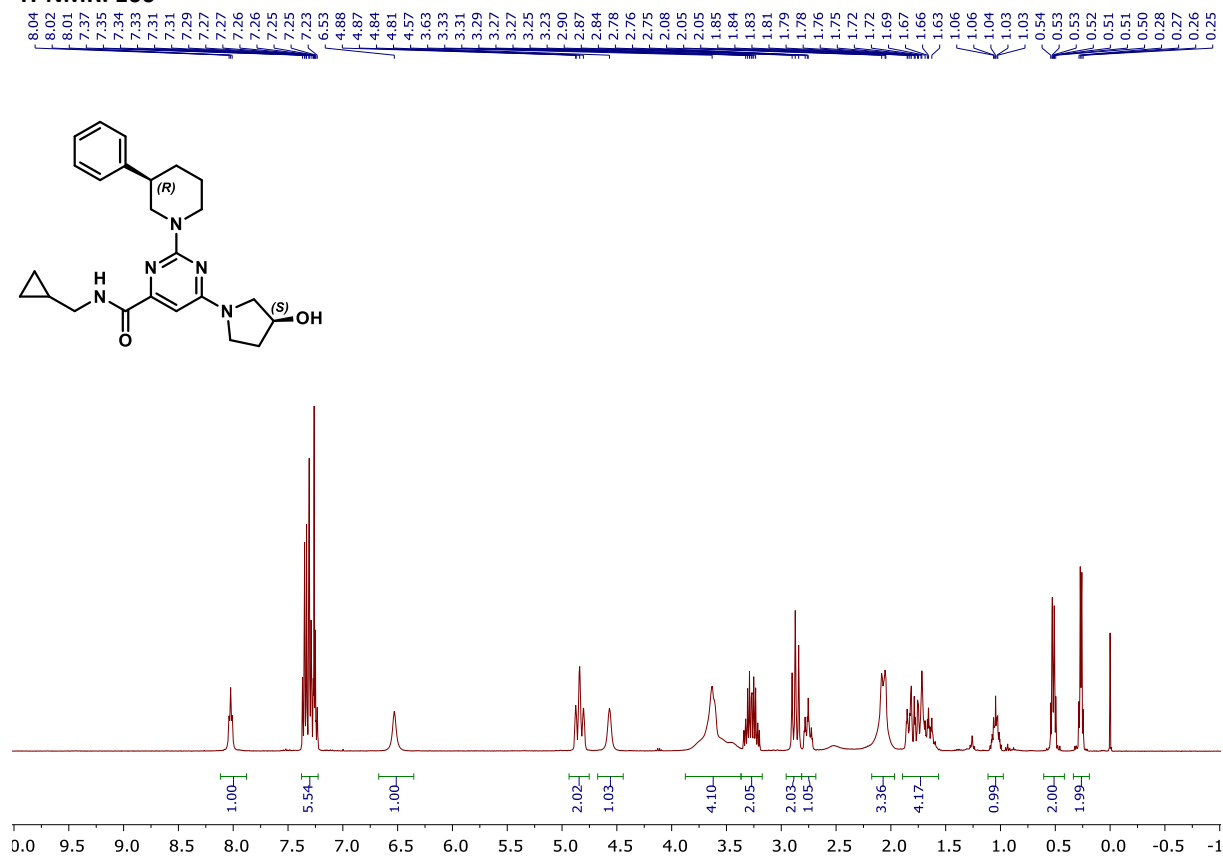
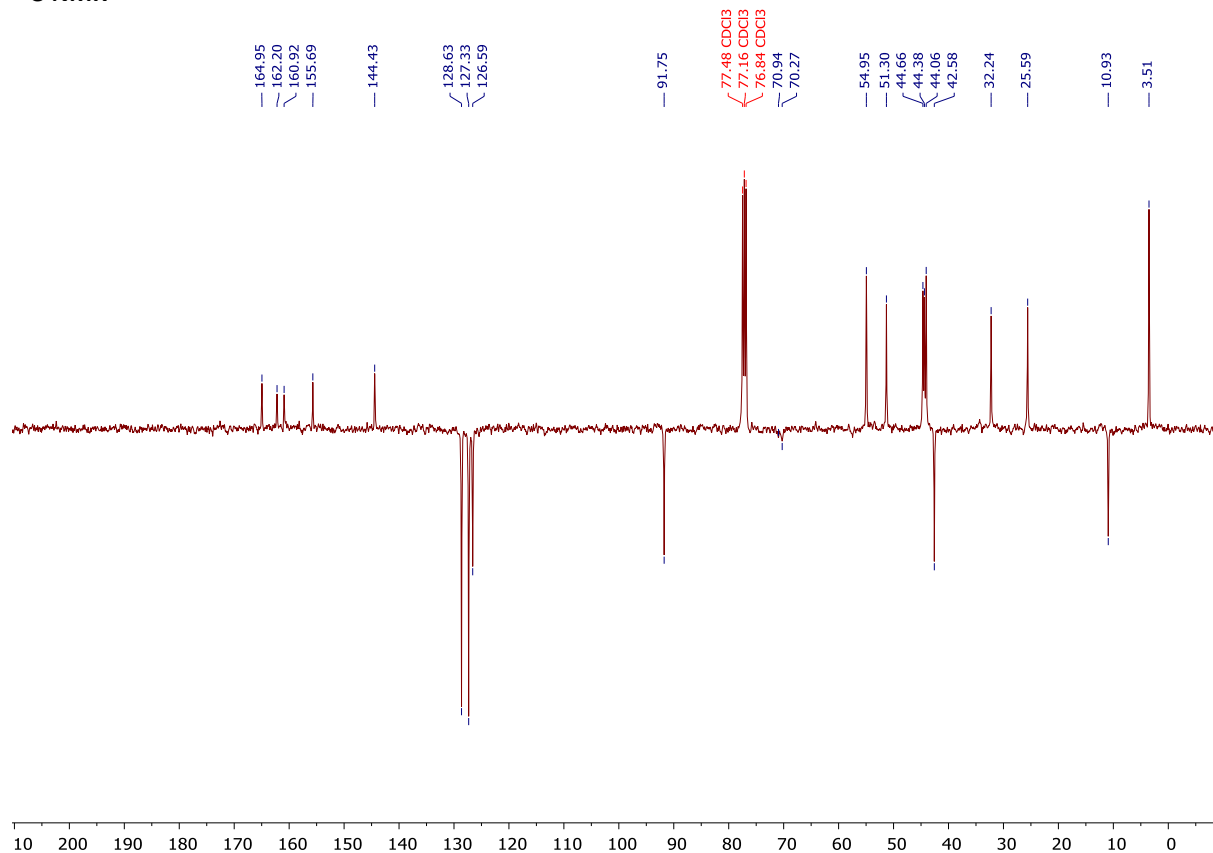


¹H-NMR: 105

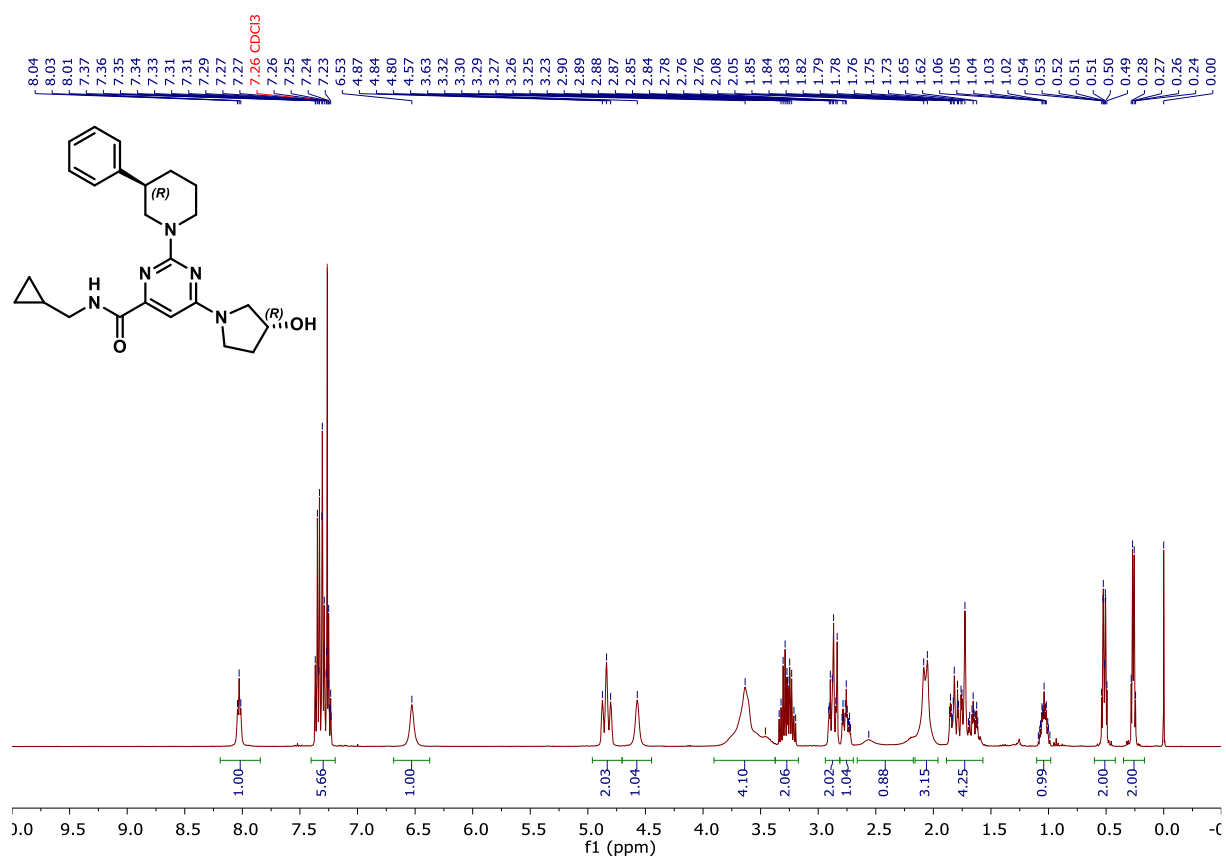


¹³C-NMR

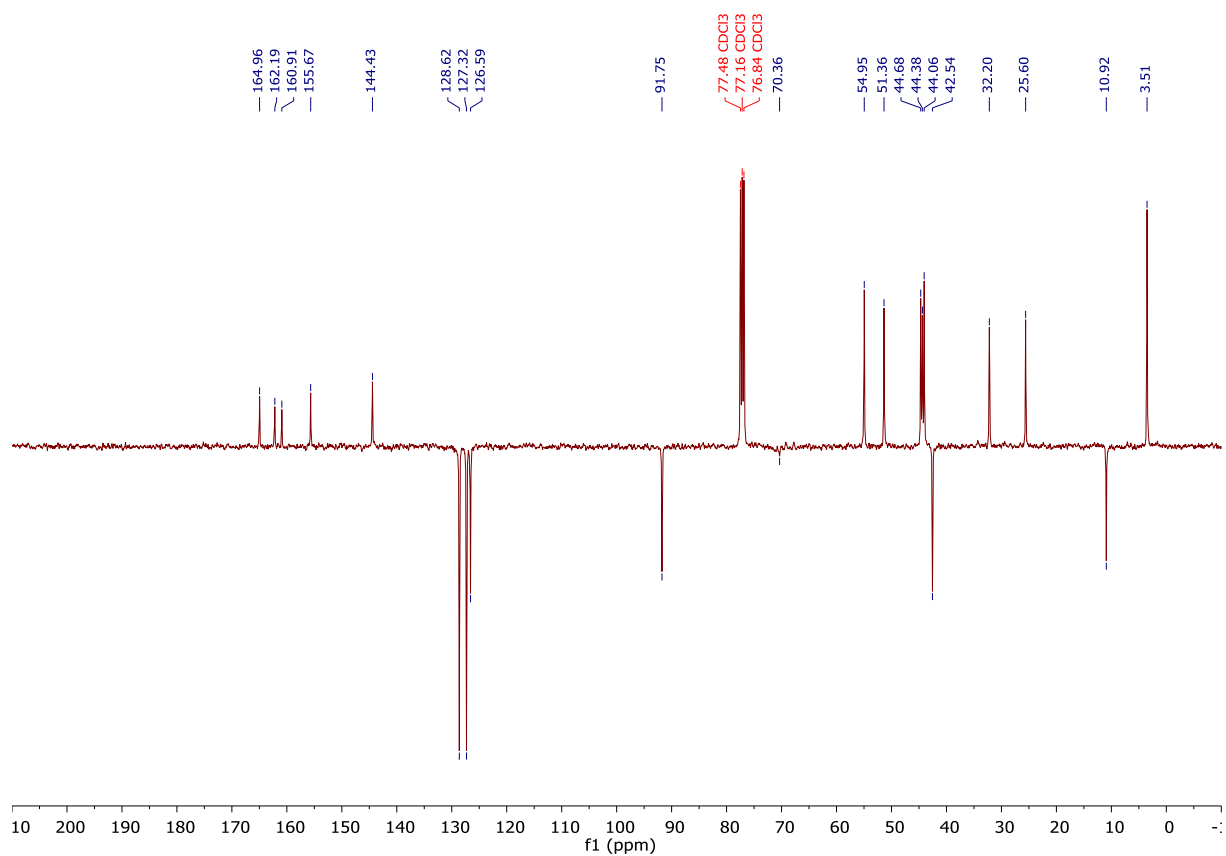


¹H-NMR: 106**¹³C-NMR**

¹H-NMR: 107

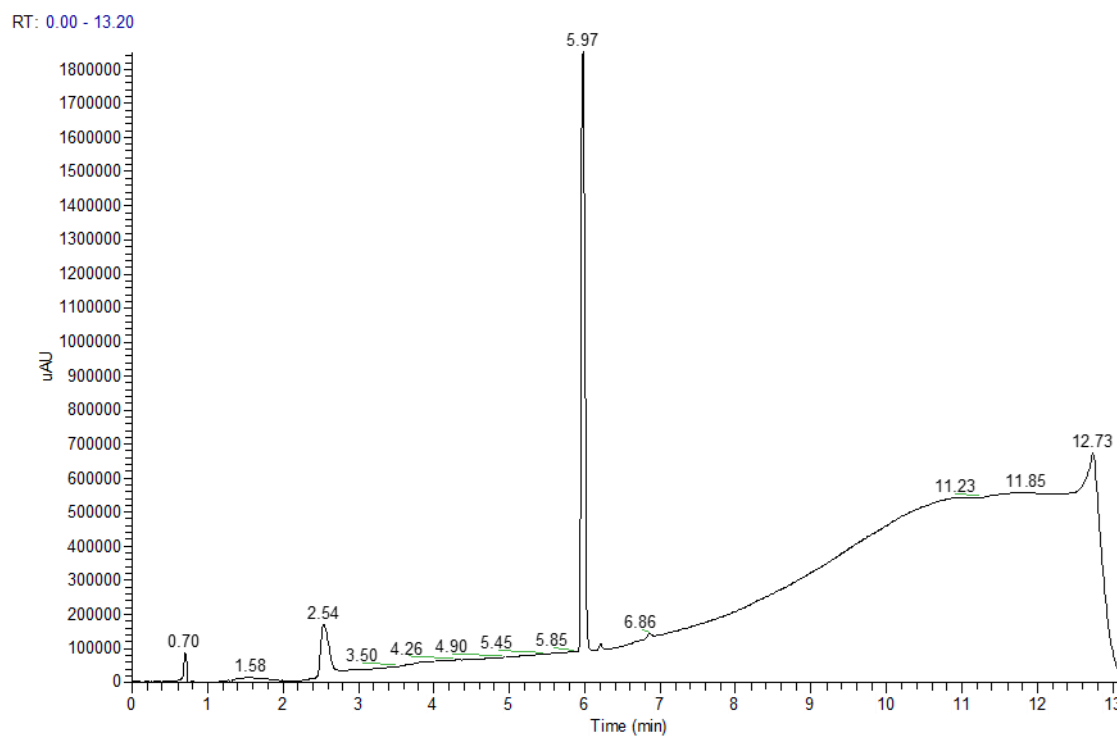


¹³C-NMR



HPLC-traces:

(S,S)-1, LEI-401: 10-90% (CH₃CN in H₂O + 0.1% TFA), RT = 5.97 min, Purity: >95%.



2: 10-90% (CH₃CN in H₂O + 0.1% TFA), RT = 6.12 min, Purity: >95%.

