

Supporting information

Robust leishmanicidal upshot of some new diphenyl triazine-based molecules

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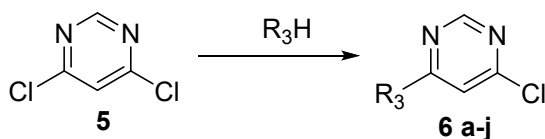
e-mail: nhoda@jmi.ac.in

1. General procedure for the synthesis of compounds 6a–6j (Scheme S1)

A mixture of 4,6-dichloropyrimidine **5** (10 mmol), different amines (**R₃**) (10 mmol) and K₂CO₃ (13 mmol) in anhydrous dimethylformamide (DMF) in round bottom flask was refluxed at 100 °C overnight. The reaction completion as well as formation of desired product was preliminarily confirmed by TLC. The reaction mixture was cooled to room temperature and diluted by ethyl acetate (100 mL) and the organic layer was washed with water and then with brine solution. The organic layer was dried over sodium sulphate, concentrated and purified by column chromatography using 15–20% EtOAc/Hexane to obtain compounds **6a–6j**.

Scheme S1.

Scheme 2.



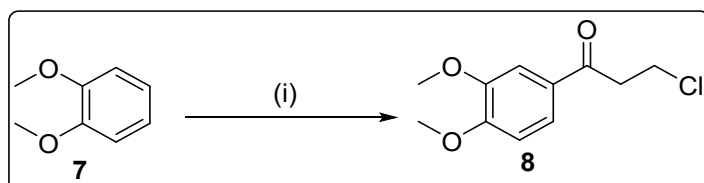
- 6a; R₃H = morpholine
6b; R₃H = 4-methylpiperidine
6c; R₃H = piperidine
6d; R₃H = 2-(piperazin-1-yl)nicotinonitrile
6e; R₃H = 7-chloro-4-(piperazin-1-yl)quinoline
6f; R₃H = 5-methyl-7-(piperazin-1-yl)-[1,2,4]triazolo[1,5-a]pyrimidine
6g; R₃H = 1-(2-methoxyphenyl)piperazine
6h; R₃H = 1-ethylpiperazine
6i; R₃H = 1-(4-nitrophenyl)piperazine
6j; R₃H = 1-(4-fluorophenyl)piperazine

Reagents and conditions: K₂CO₃, DMF, reflux 100 °C, overnight.

2. General procedure for the synthesis of compound **8** (Scheme S2)

A mixture of aluminium chloride (5.3 g, 39.7 mol) and 25 mL DCM was allowed for stirring at room temperature. 3-chloropropionyl chloride (5.5 g, 43.3 mol) dissolved in 20 mL DCM was added dropwise to the stirring solution of AlCl₃. After half an hour 1,2-dimethoxybenzene (5.0 g, 36.1 mol) was added to the reaction mixture and the mixture was allowed for stirring for 24 h at room temperature. On the completion of the reaction, the reaction mixture was poured into ice-cold water and the organic part was extracted with DCM (50 mL x 3). The organic layer was washed with sodium bicarbonate and brine solutions and was dried over Na₂SO₄. The crude product **8** was purified by column chromatography using ethyl acetate hexane 25:75.

Scheme S2.

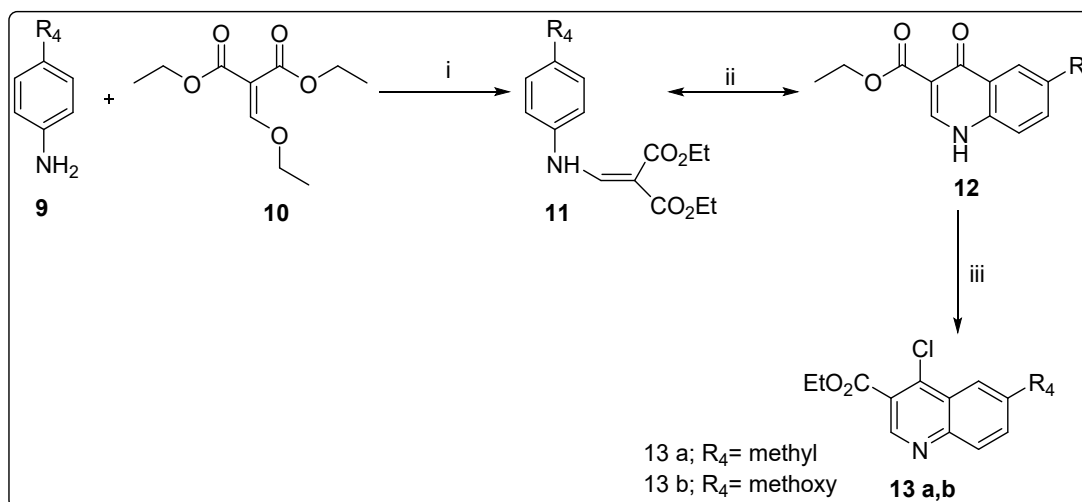


Reagents and conditions: (i) 3-chloropropionyl chloride, AlCl₃, CH₂Cl₂, 24h, room temperature

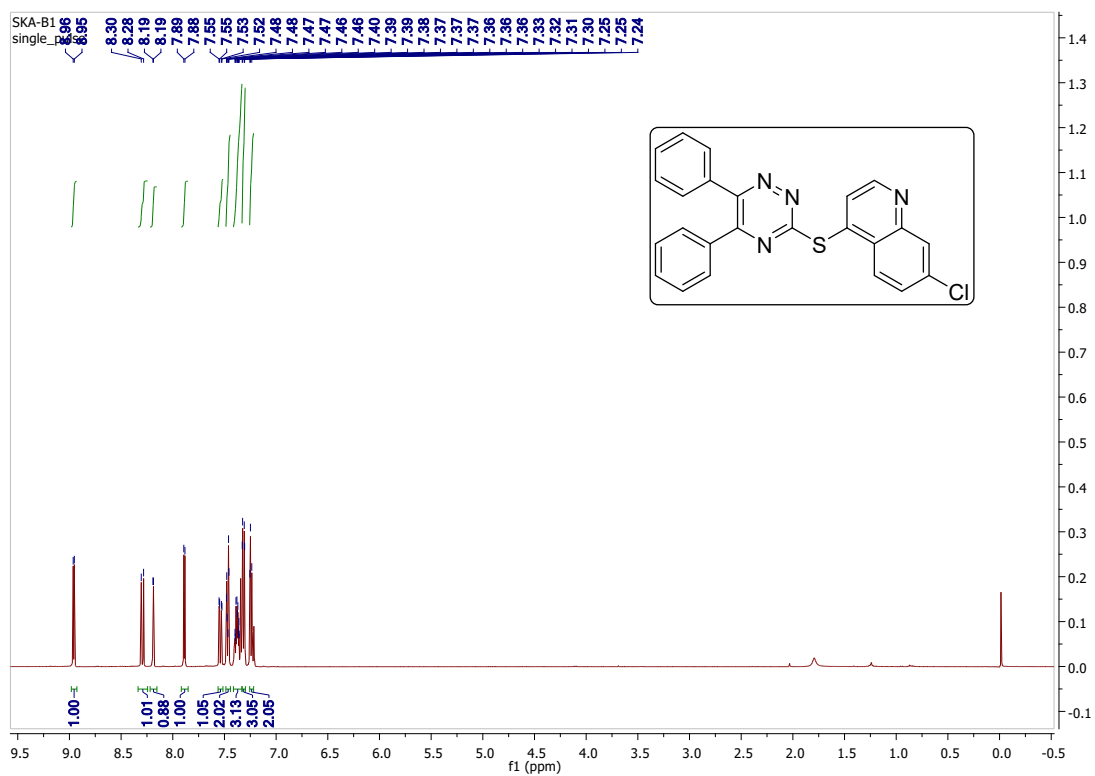
3. General procedure for the synthesis of compounds 13a and 13b (Scheme S3)

A solution of **3** (85 mmol) in POCl₃ (1.34 mole) could reflux for 18 h. On the completion of the reaction, the reaction mixture was cooled and concentrated under vacuum. The resulting brown oil was obtained in CH₂Cl₂ (500 mL) and was washed with water (250 mL x 3). The organic extract received was dried through Na₂SO₄ and concentrated in vacuum to give a brown oil. The crude product (**5a–5d**) was chromatographed on silica gel eluting with 15% EtOAc/Hexane.[1]

Scheme S3.



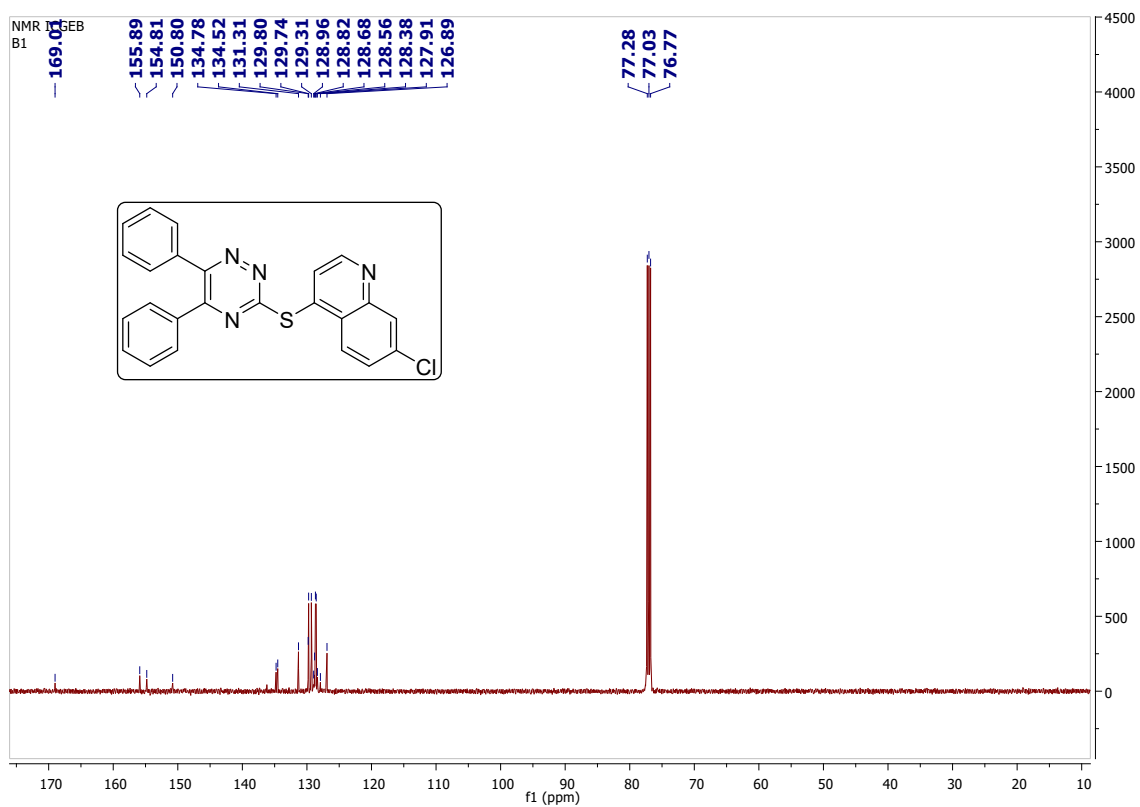
Reagents and conditions. (i) Benzene, 83 °C reflux, 1.5h (ii) Acetic acid, 110 C reflux 4-5h; (iii) POCl₃, 110 C, 18h.



Spe

central data of the synthesized compounds

Figure S1: ¹H NMR spectrum of Molecule (T1)



Generic Display Report

Analysis Info

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Method 20170112_pos_50-1000.m
Sample Name B1-1
Comment

Acquisition Date 2/10/2019 1:27:24 PM

Operator Bruker07
Instrument micrOTOF-Q

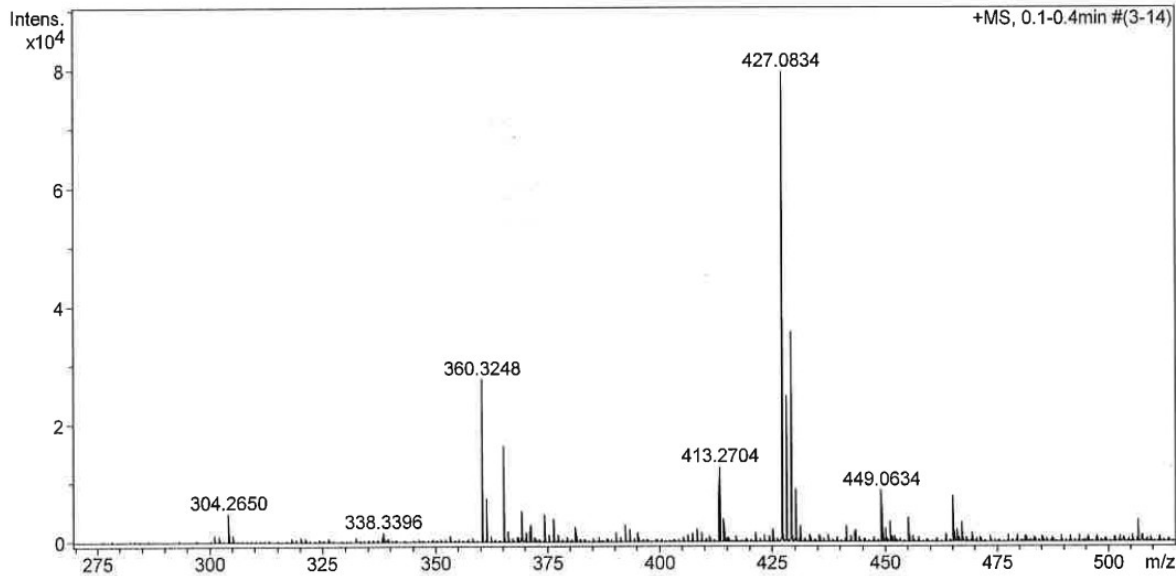
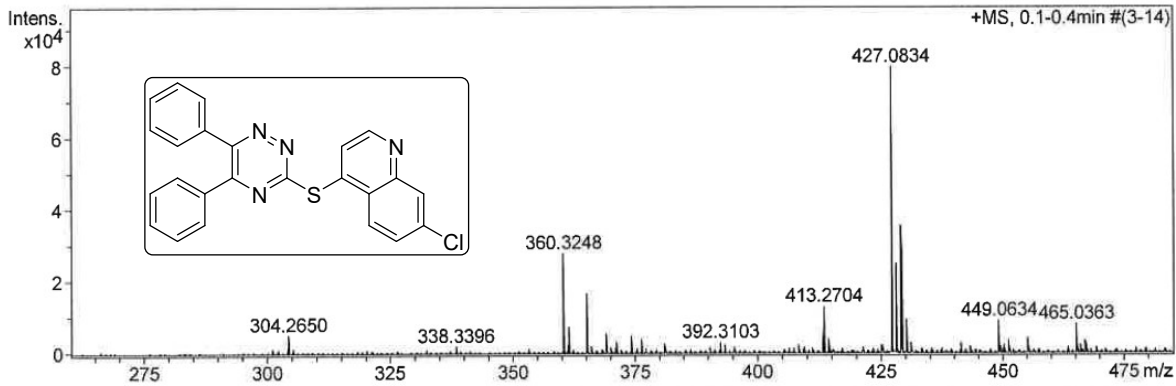
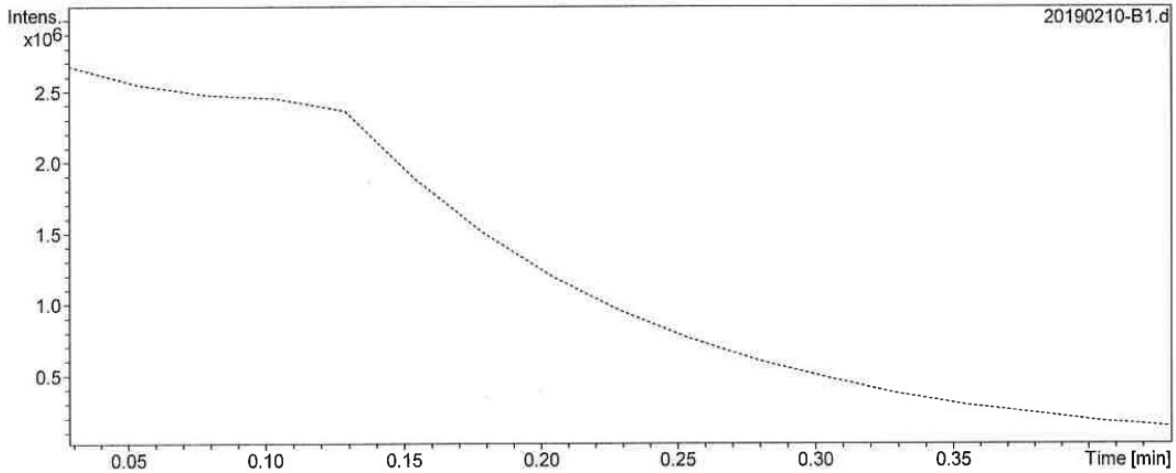


Figure S3: Mass spectrum of Molecule (T1)

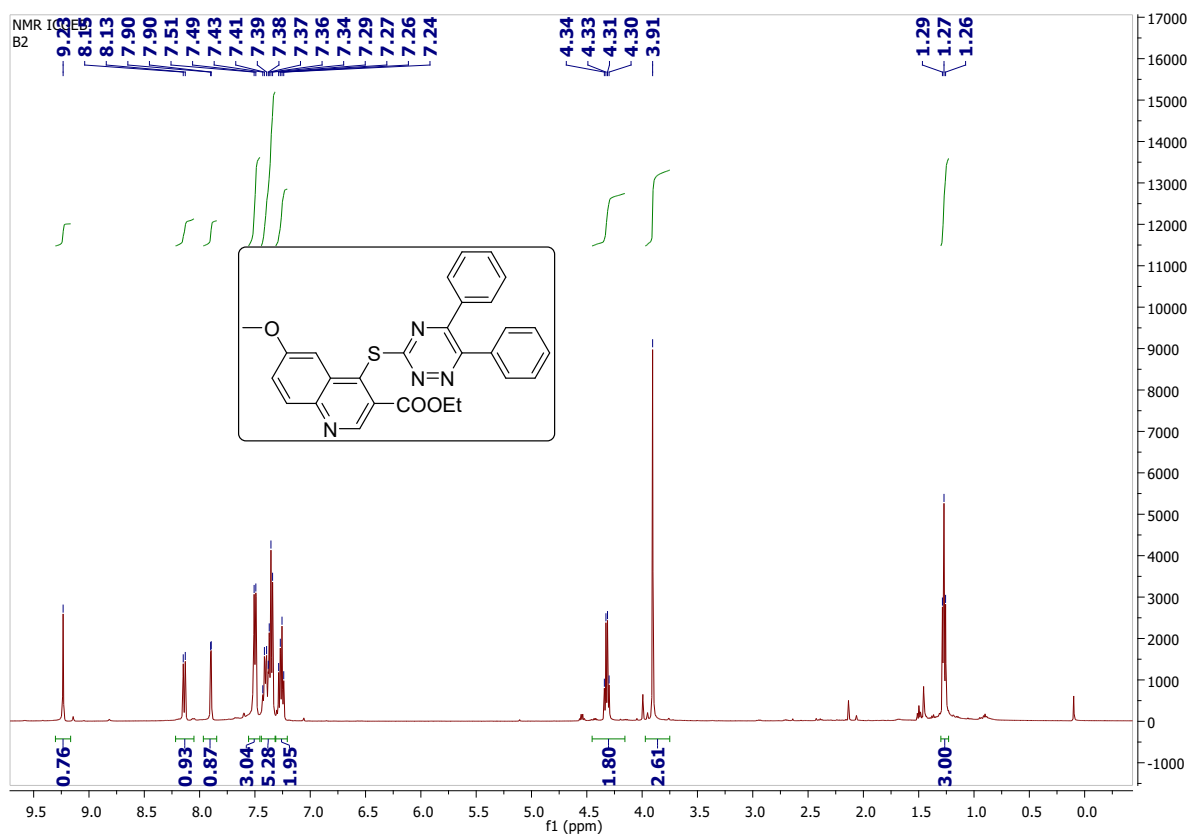


Figure S4: ¹H NMR spectrum of Molecule (T2)

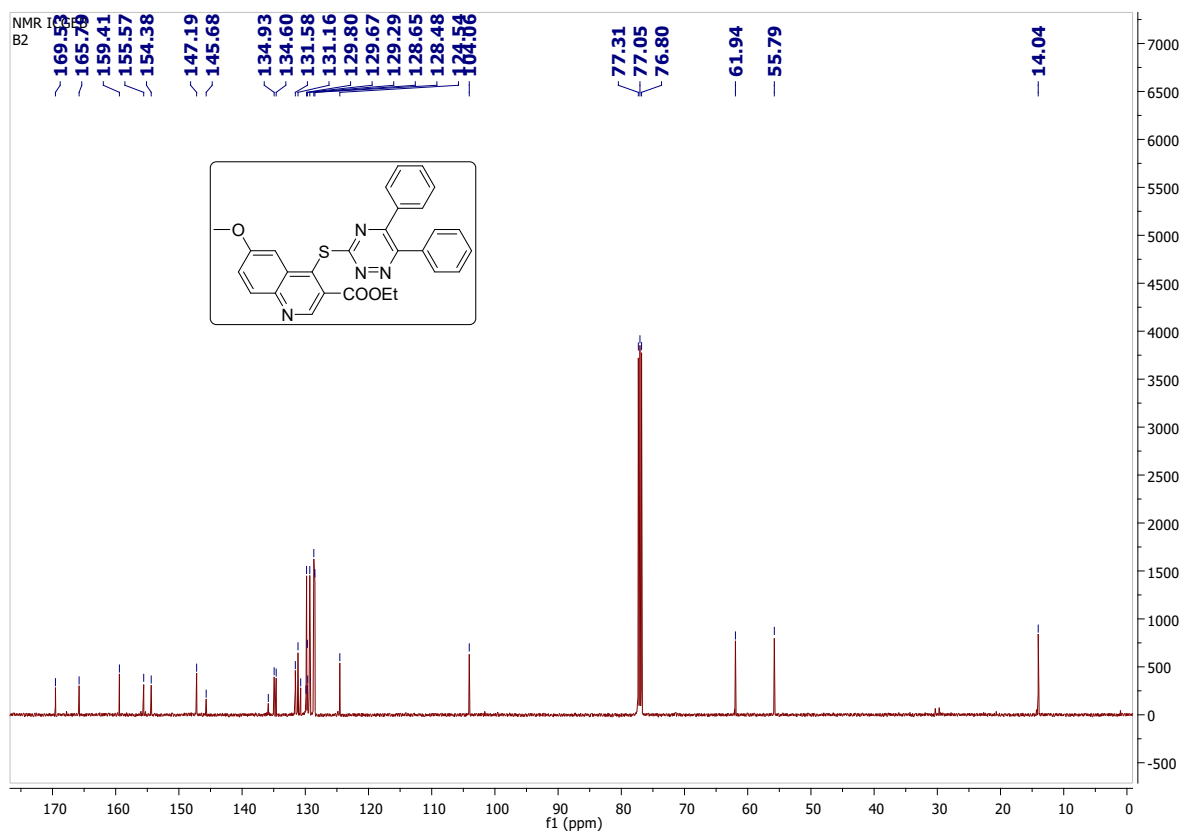


Figure S5: ¹³C NMR spectrum of Molecule (T2)

Generic Display Report

Analysis Info

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Method 20170112_pos_50-1000.m
Sample Name B2-1
Comment

Acquisition Date 2/10/2019 1:41:00 PM

Operator Bruker07
Instrument micrOTOF-Q

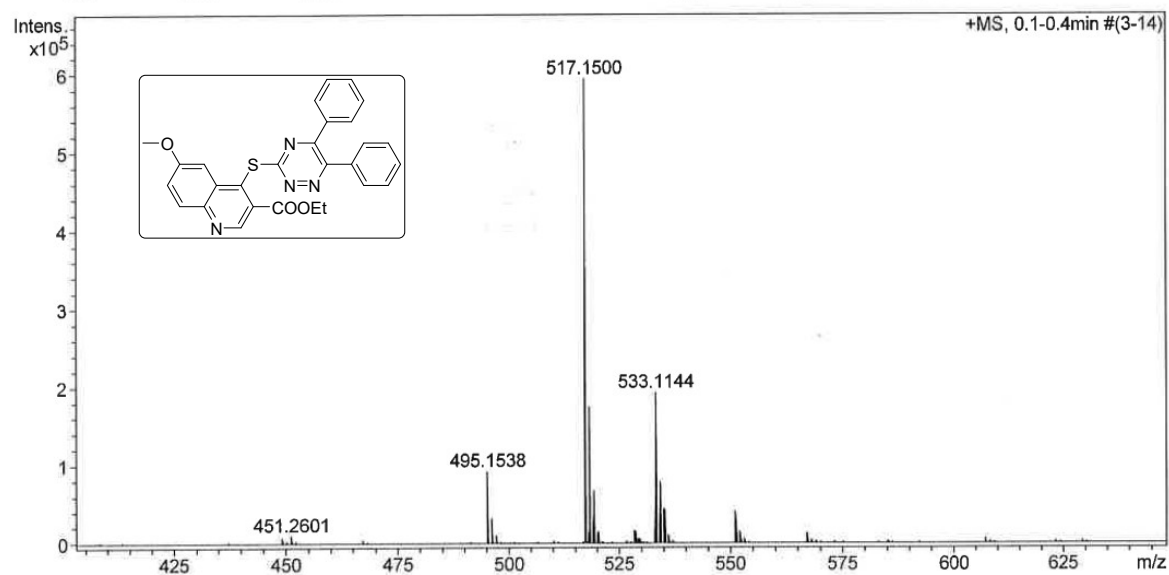
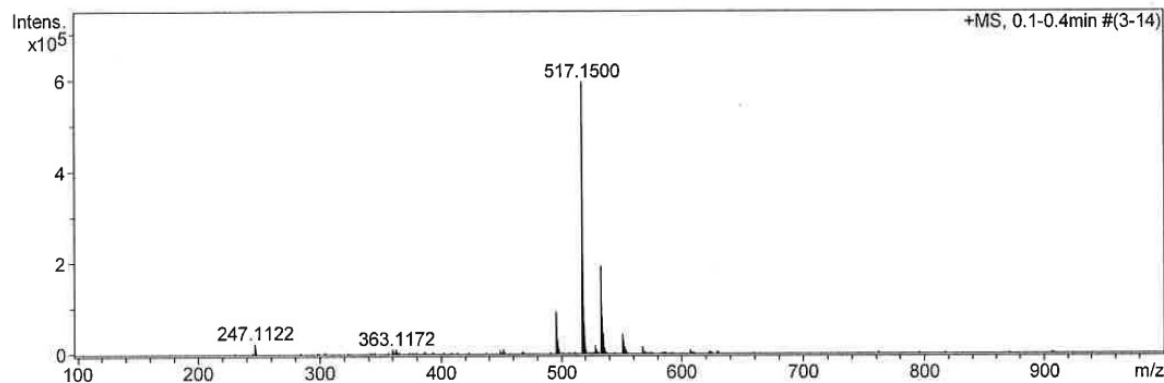
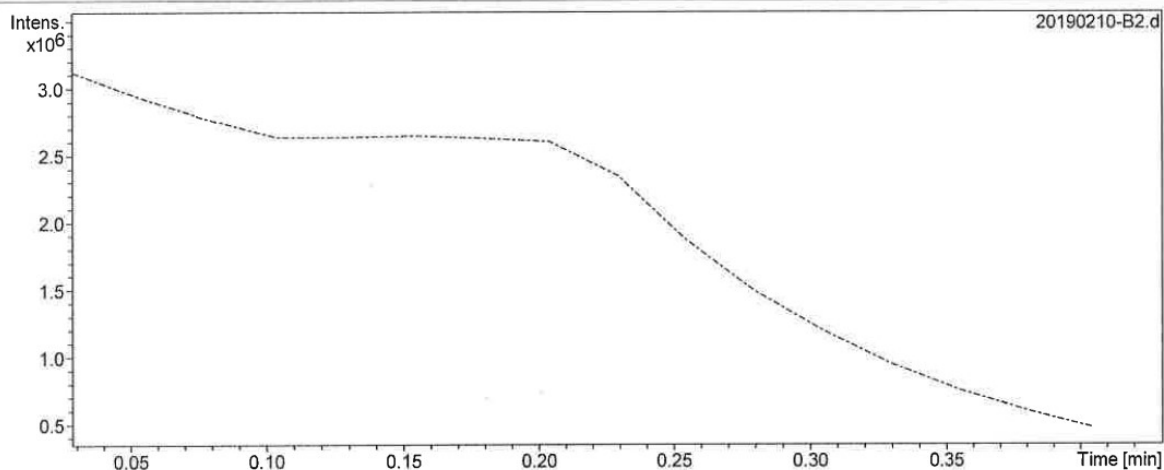


Figure S6: Mass spectrum of Molecule (T2)

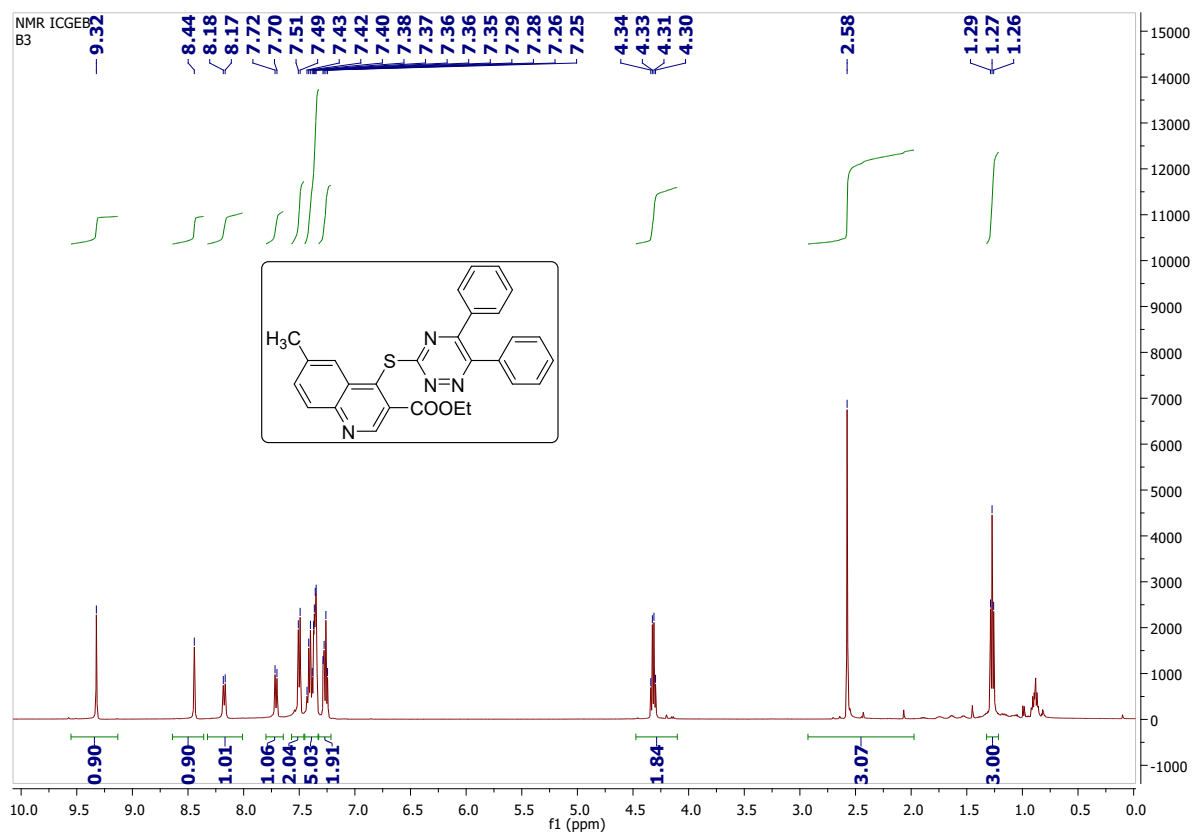


Figure S7: ¹H NMR spectrum of Molecule (T3)

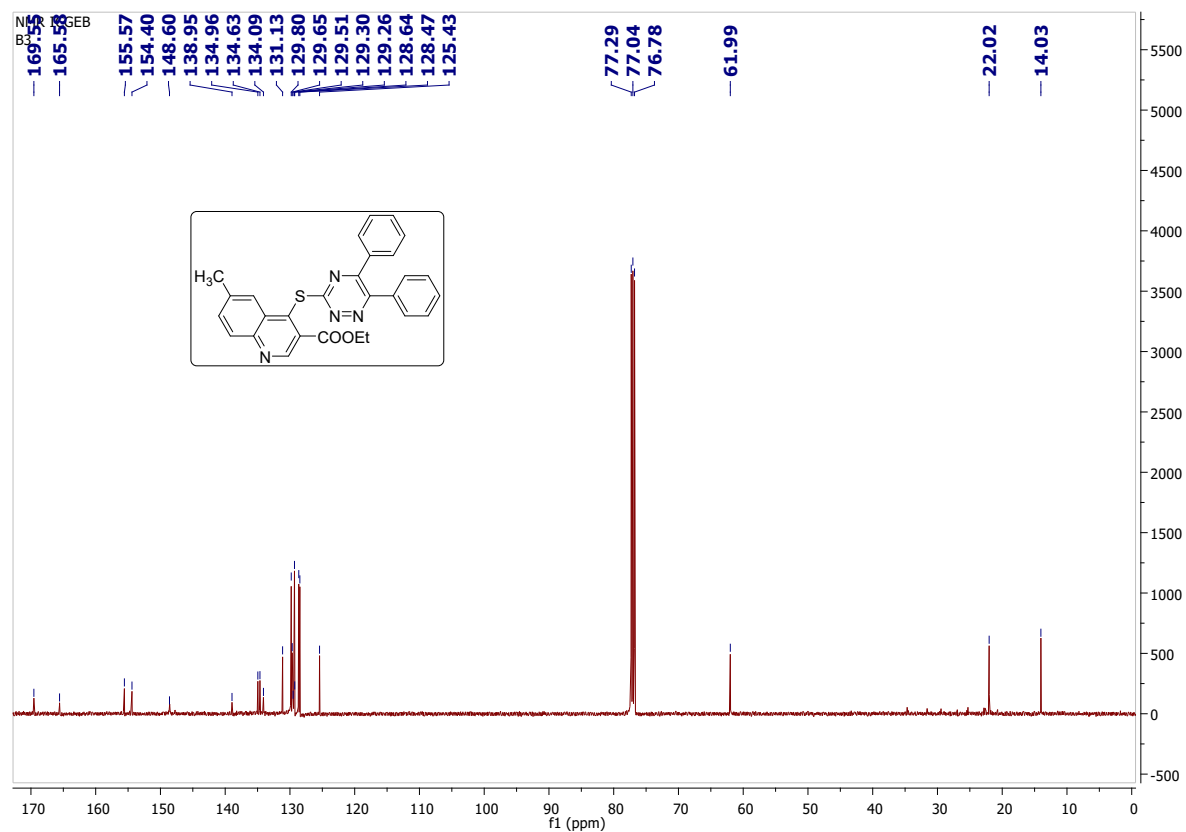


Figure S8: ¹³C NMR spectrum of Molecule (T3)

Generic Display Report

Analysis Info

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Sample Name B3-1
Comment

Acquisition Date 2/10/2019 1:57:22 PM

Operator Bruker07
Instrument micrOTOF-Q

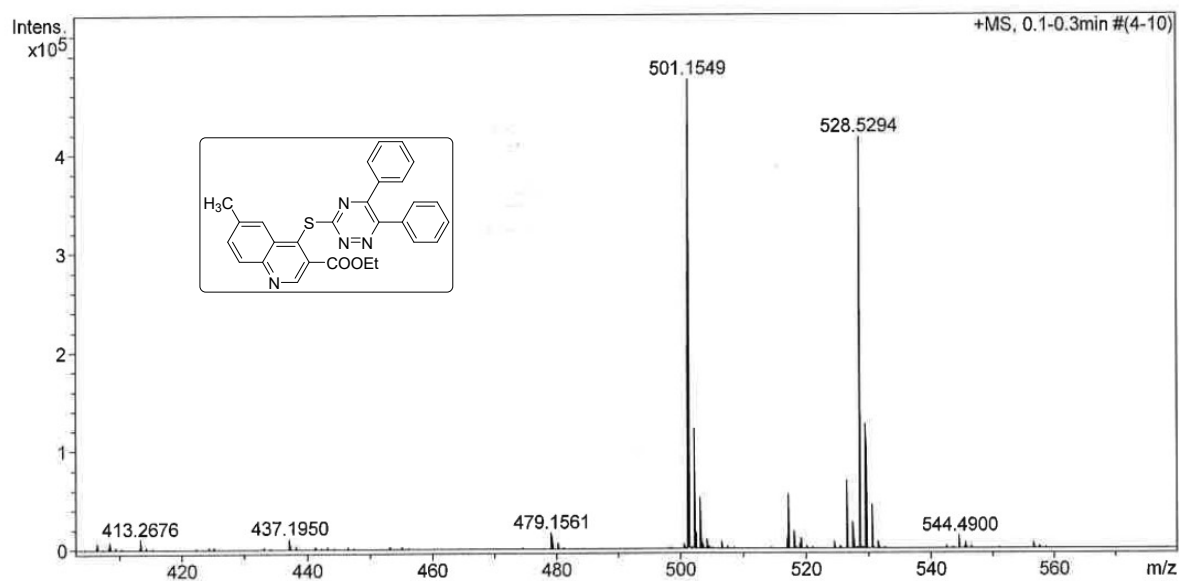
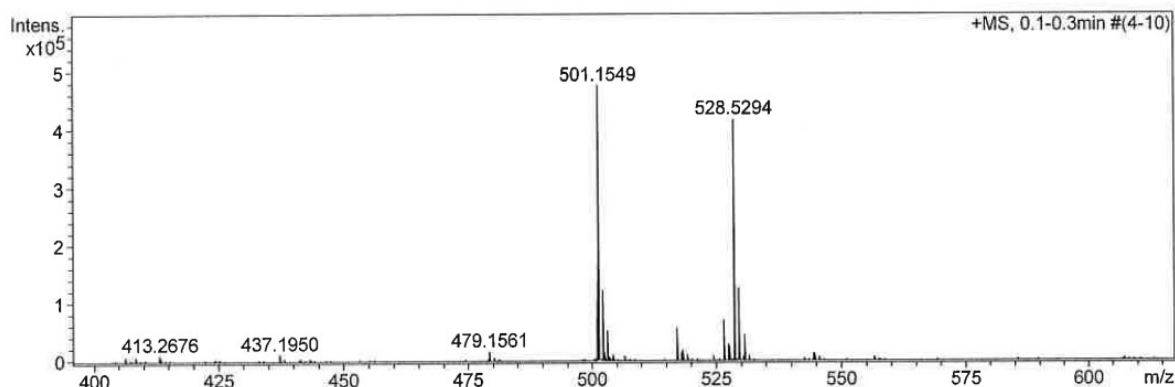
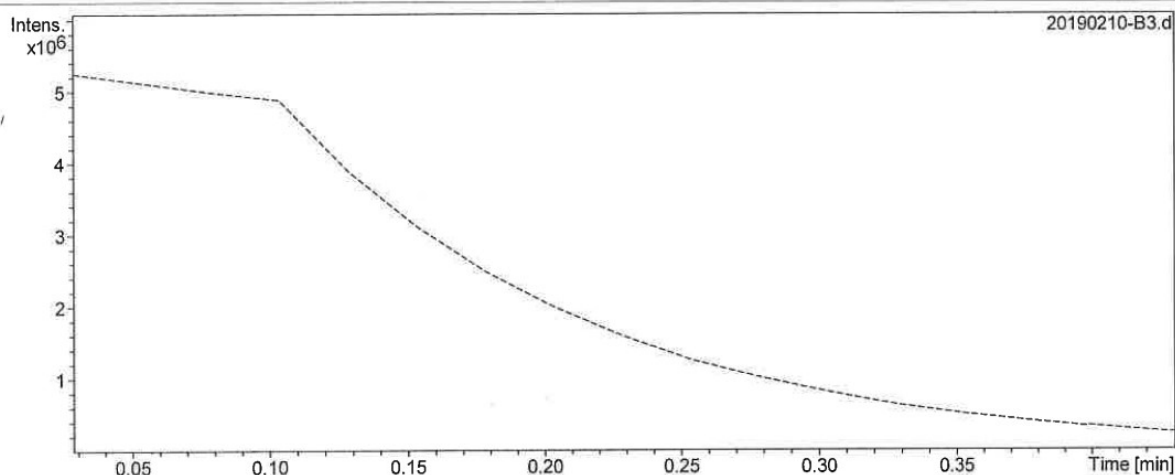


Figure S9: Mass spectrum of Molecule (T3)

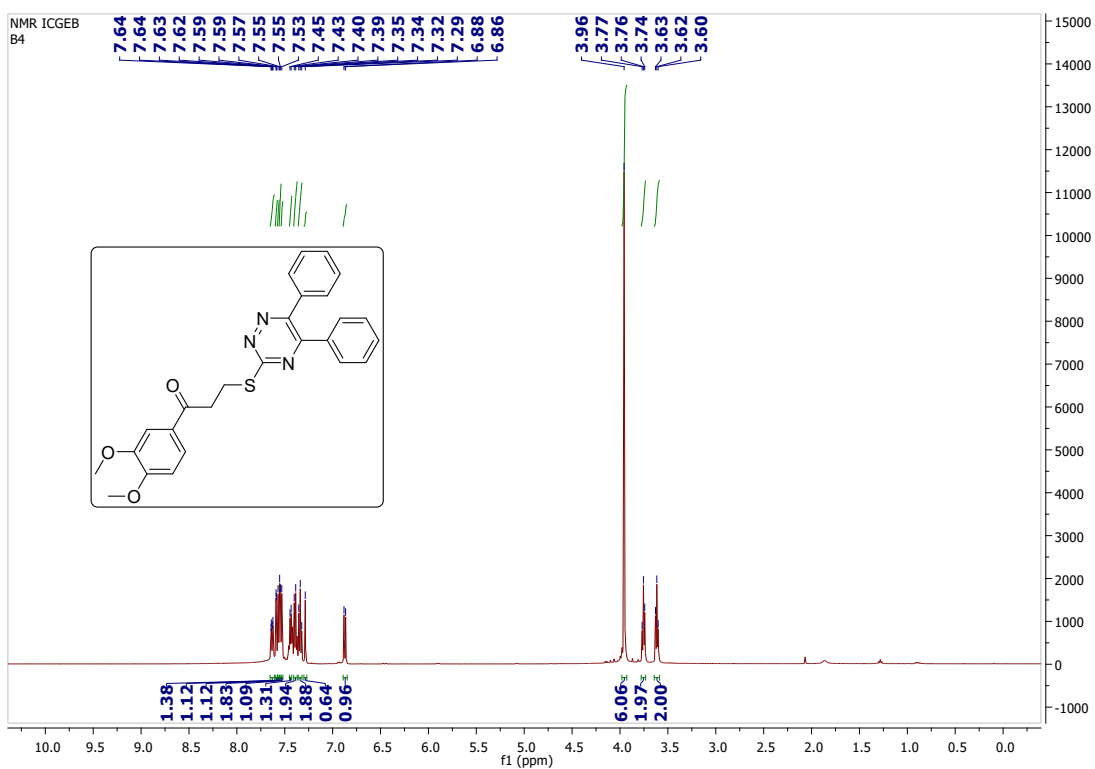


Figure S10: ^1H NMR spectrum of Molecule (T4)

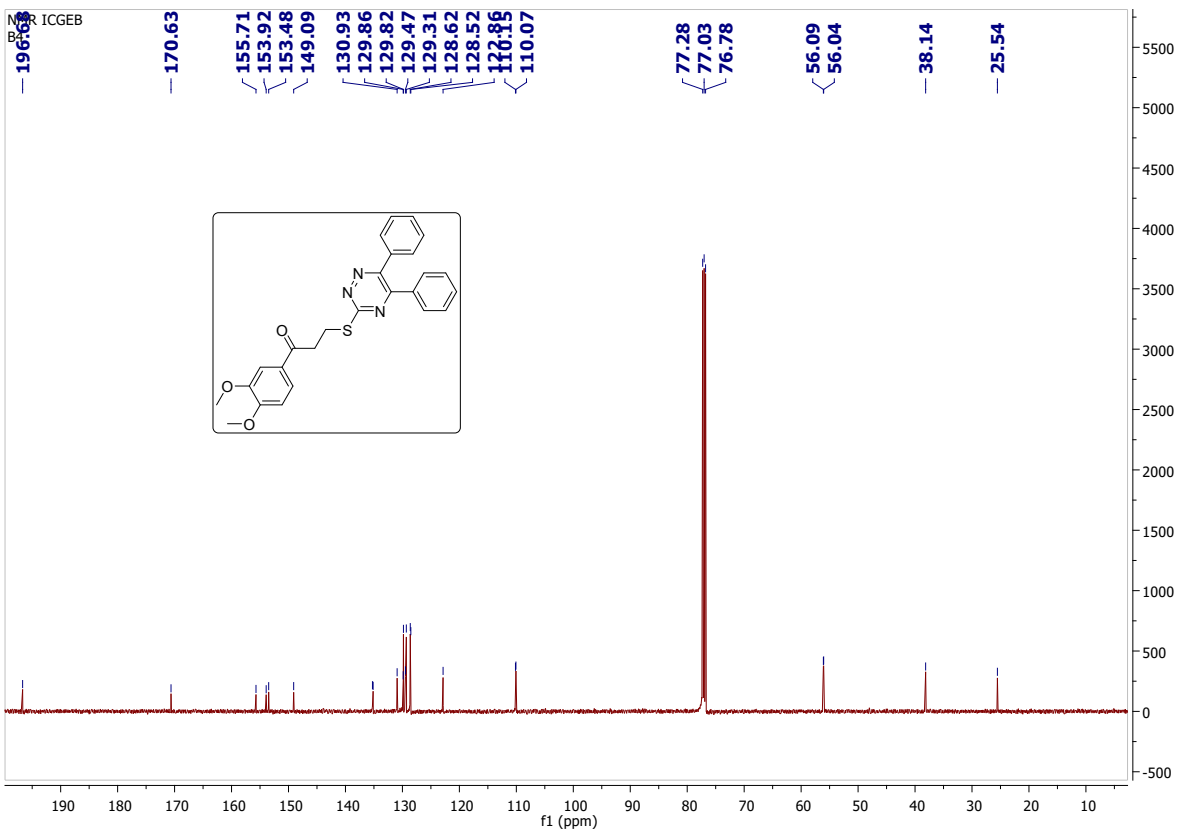


Figure S11: ^{13}C NMR spectrum of Molecule (T4)

Generic Display Report

Analysis Info

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Method 20170112_pos_50-1000.m
Sample Name B4-1
Comment

Acquisition Date 2/10/2019 2:08:08 PM

Operator Bruker07
Instrument micrOTOF-Q

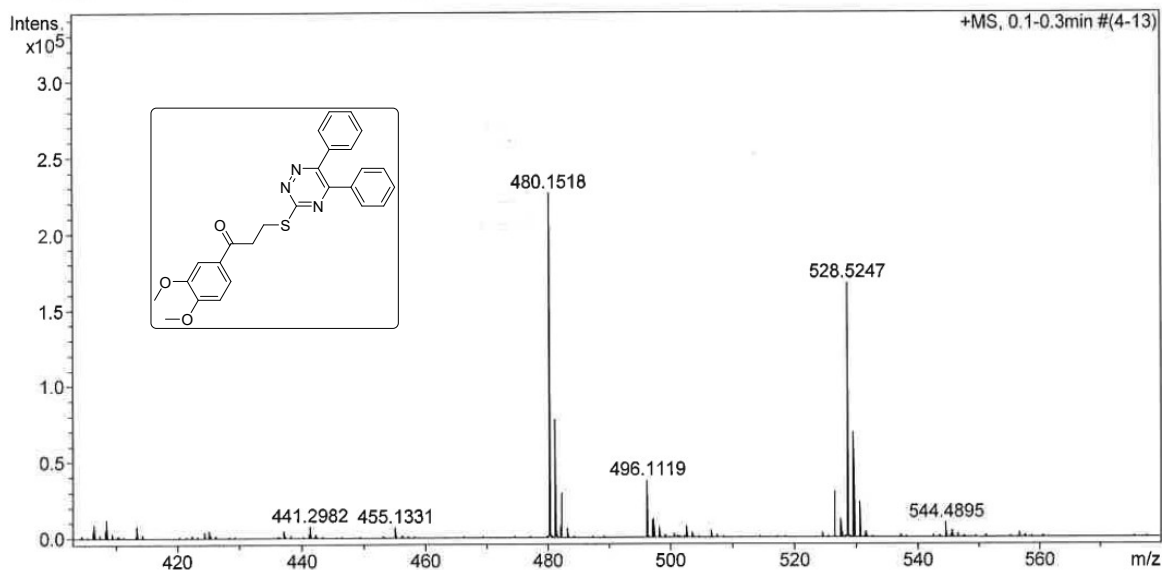
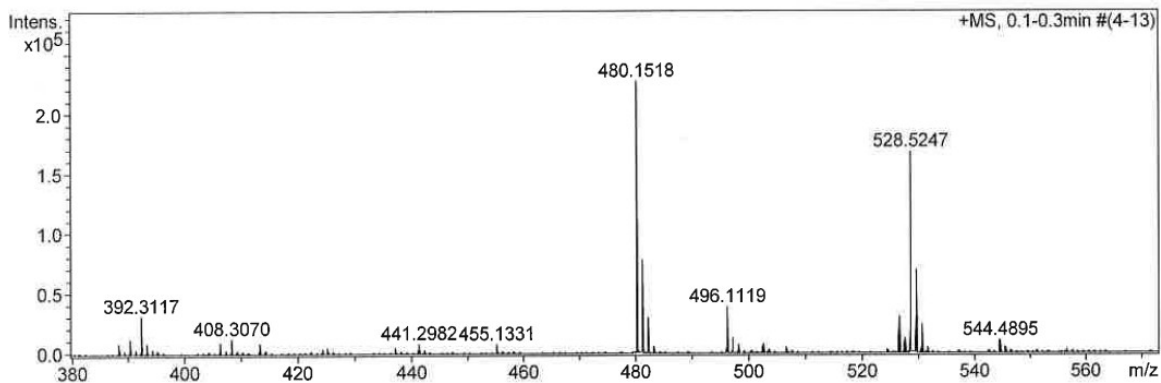
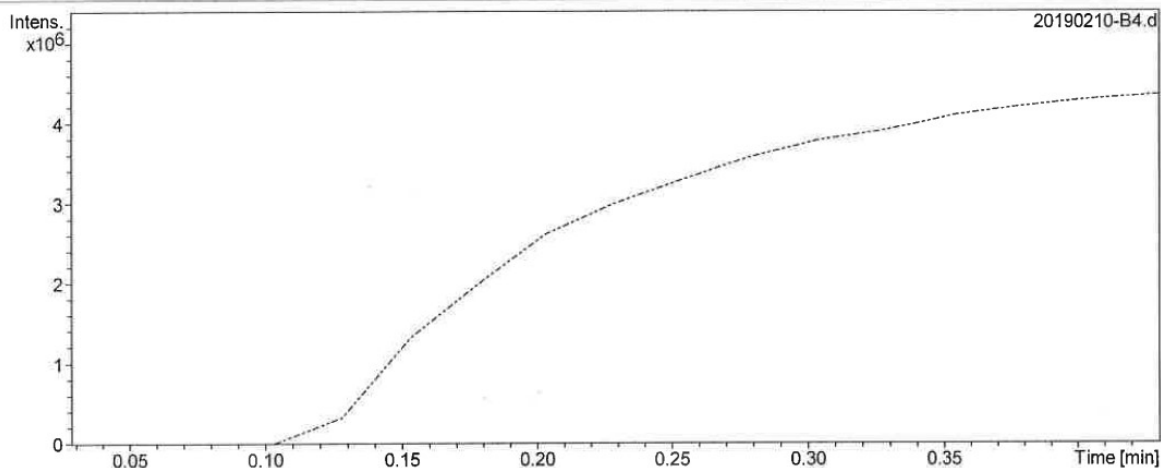


Figure S12: Mass spectrum of Molecule (T4)

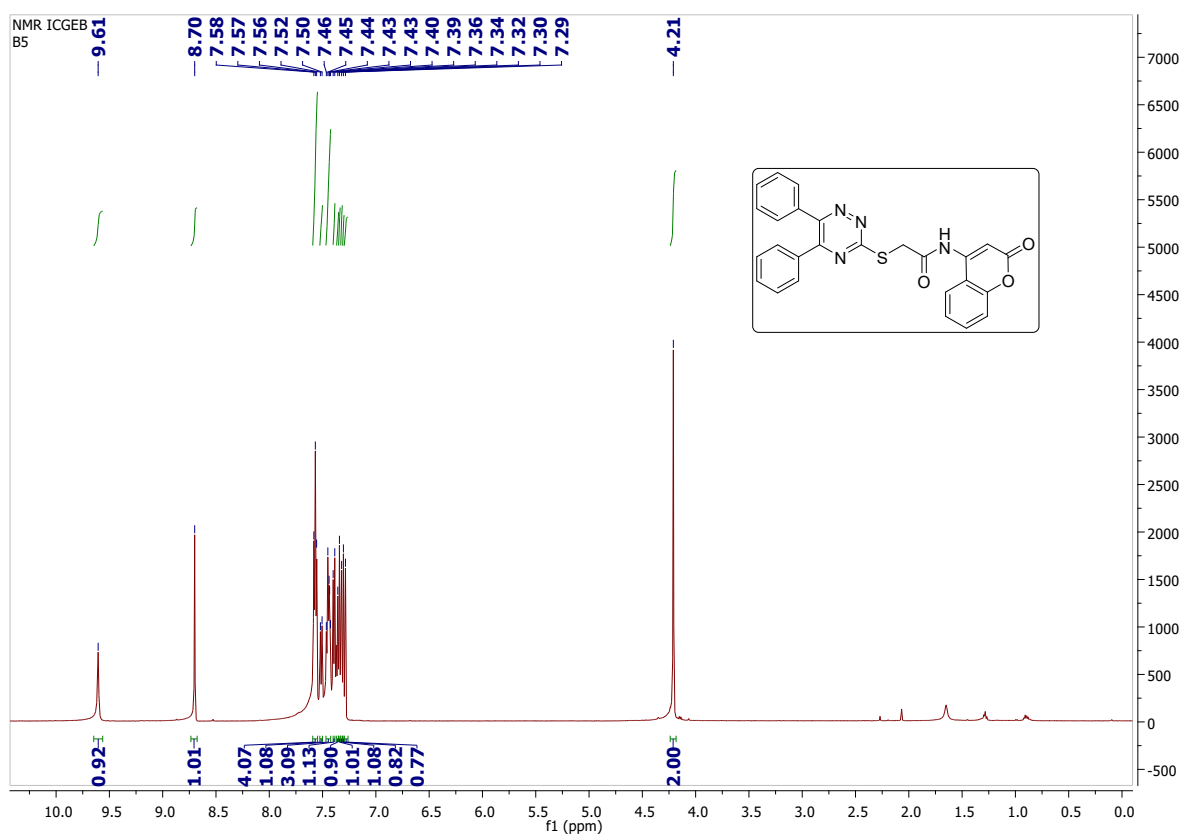


Figure S13: ¹H NMR spectrum of Molecule (T5)

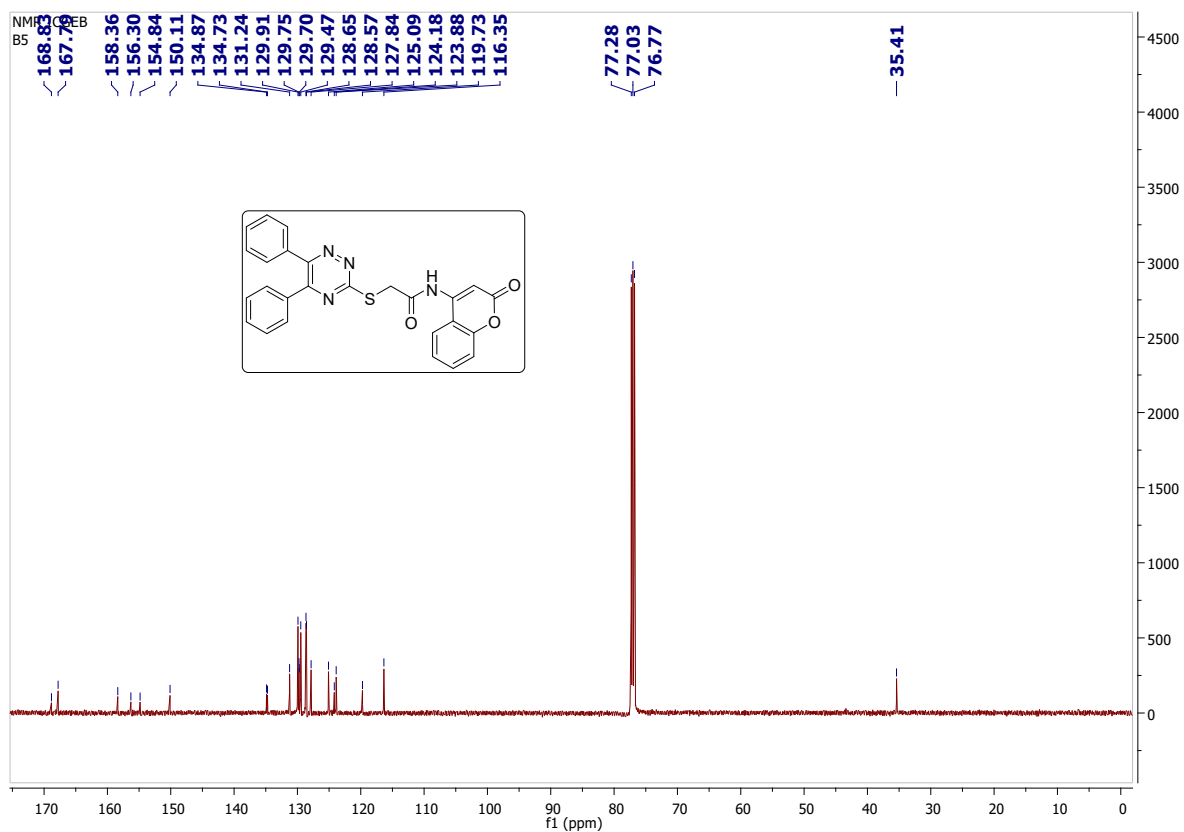


Figure S14: ¹³C NMR spectrum of Molecule (T5)

Generic Display Report

Analysis Info

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Method 20170112_pos_50-1000.m
Sample Name B5-1
Comment

Acquisition Date 2/10/2019 2:15:21 PM

Operator Bruker07
Instrument micrOTOF-Q

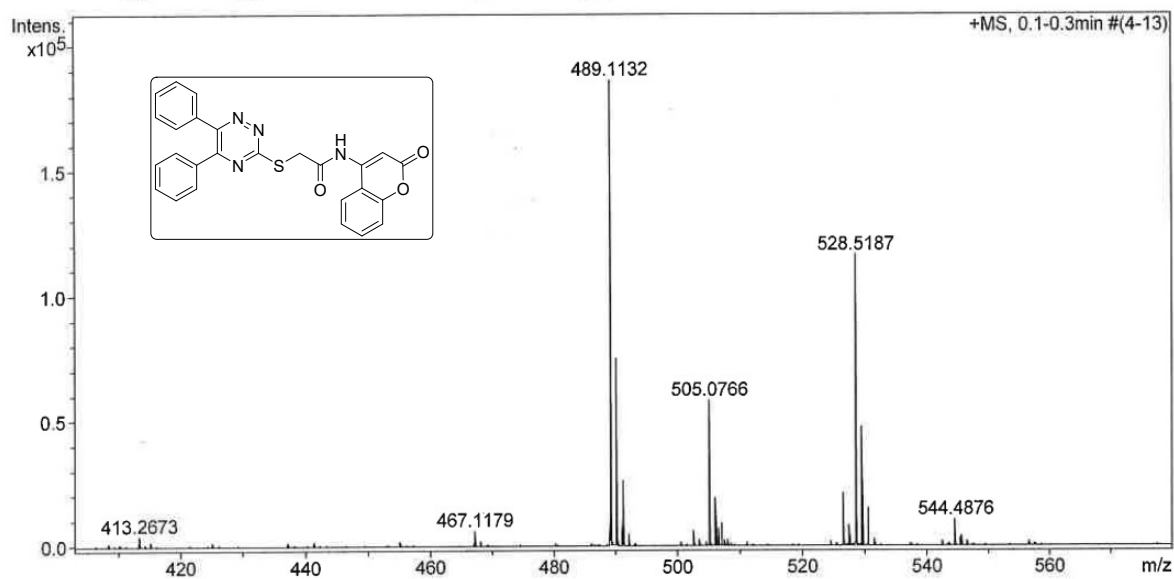
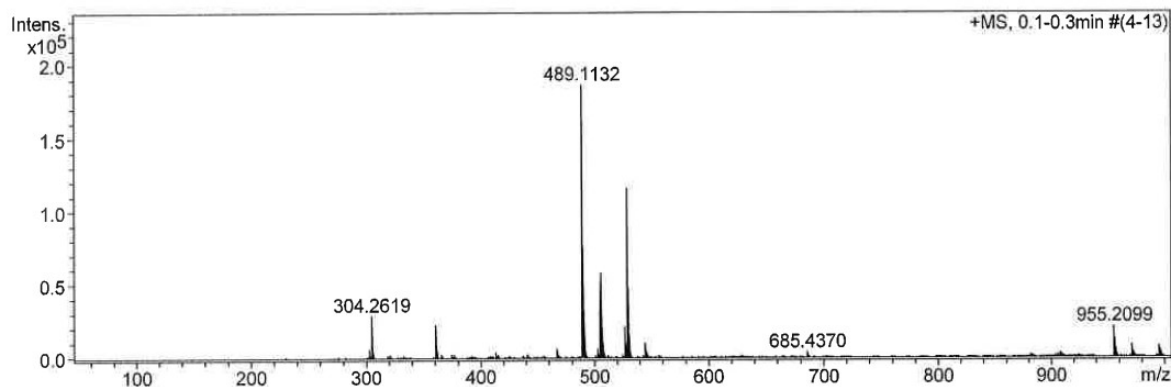
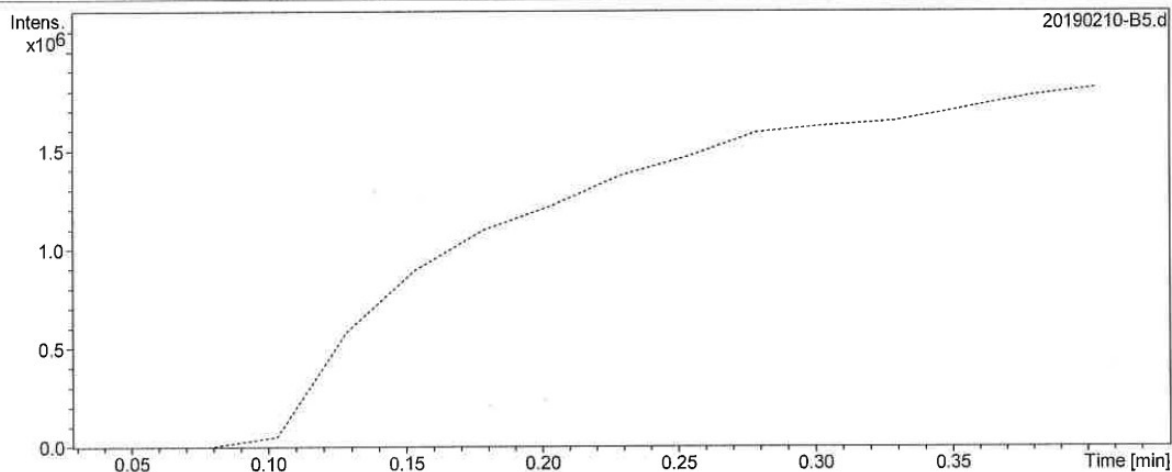


Figure S15: Mass spectrum of Molecule (T5)

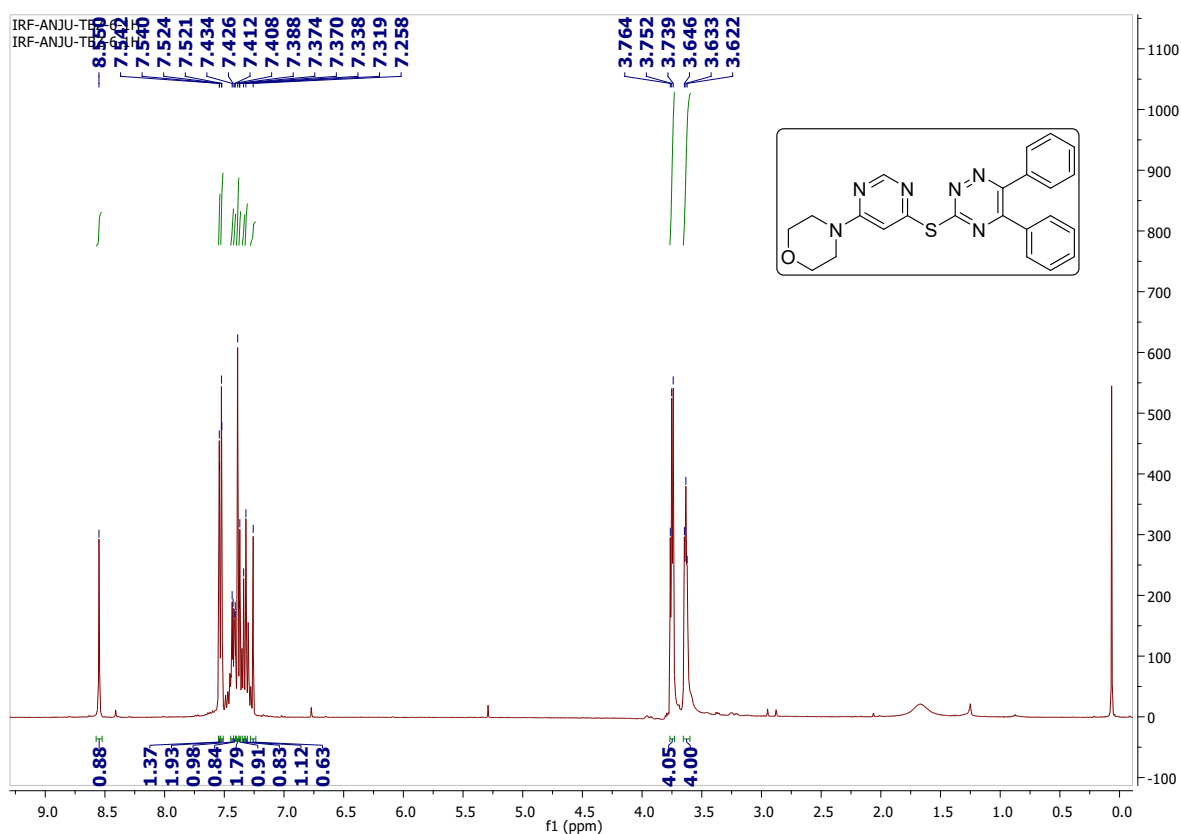


Figure S16: ¹H NMR spectrum of Molecule (T6)

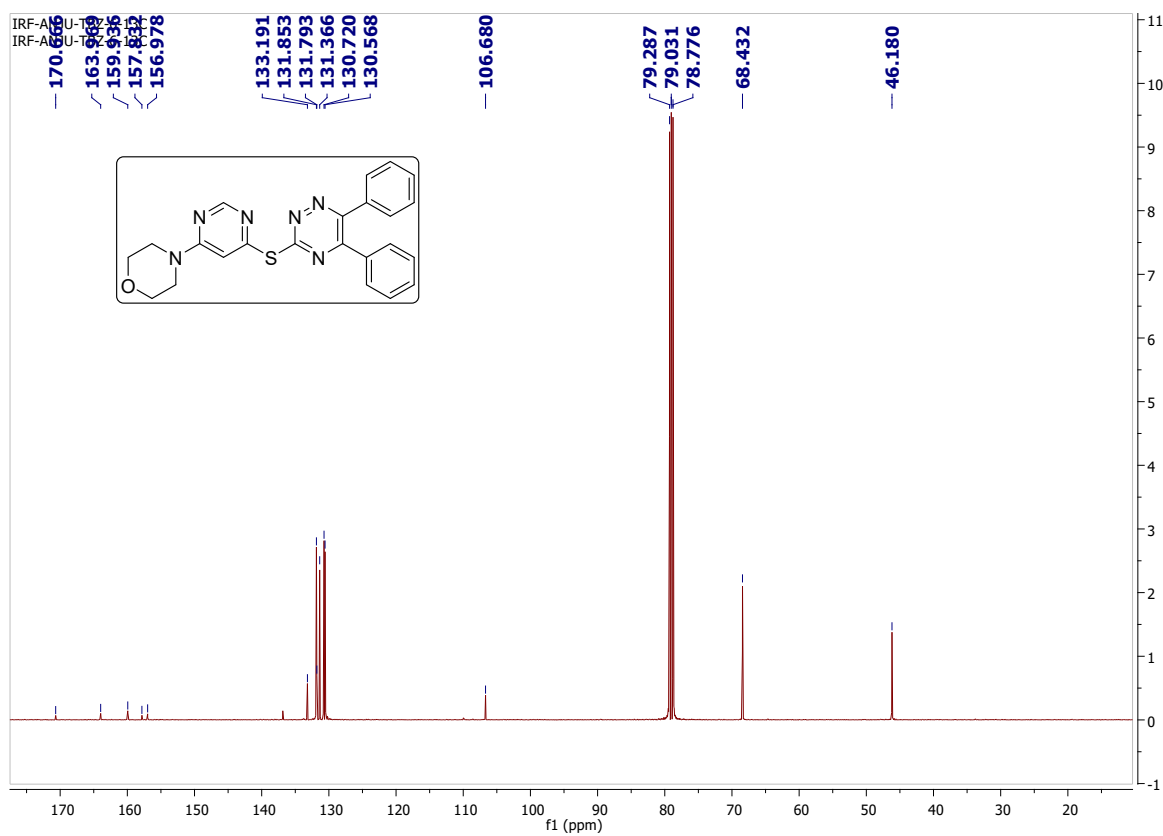


Figure S17: ¹³C NMR spectrum of Molecule (T6)

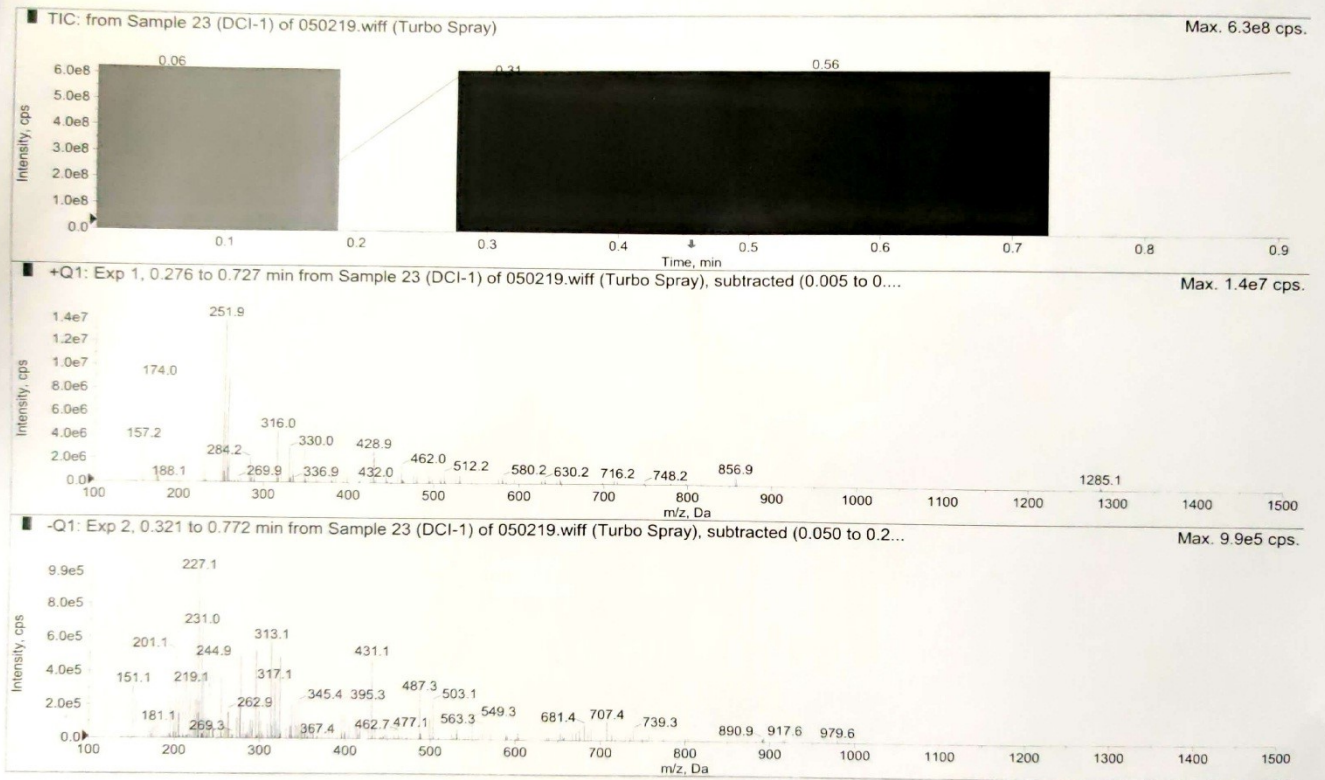


Figure S18: Mass spectrum of Molecule (T6)

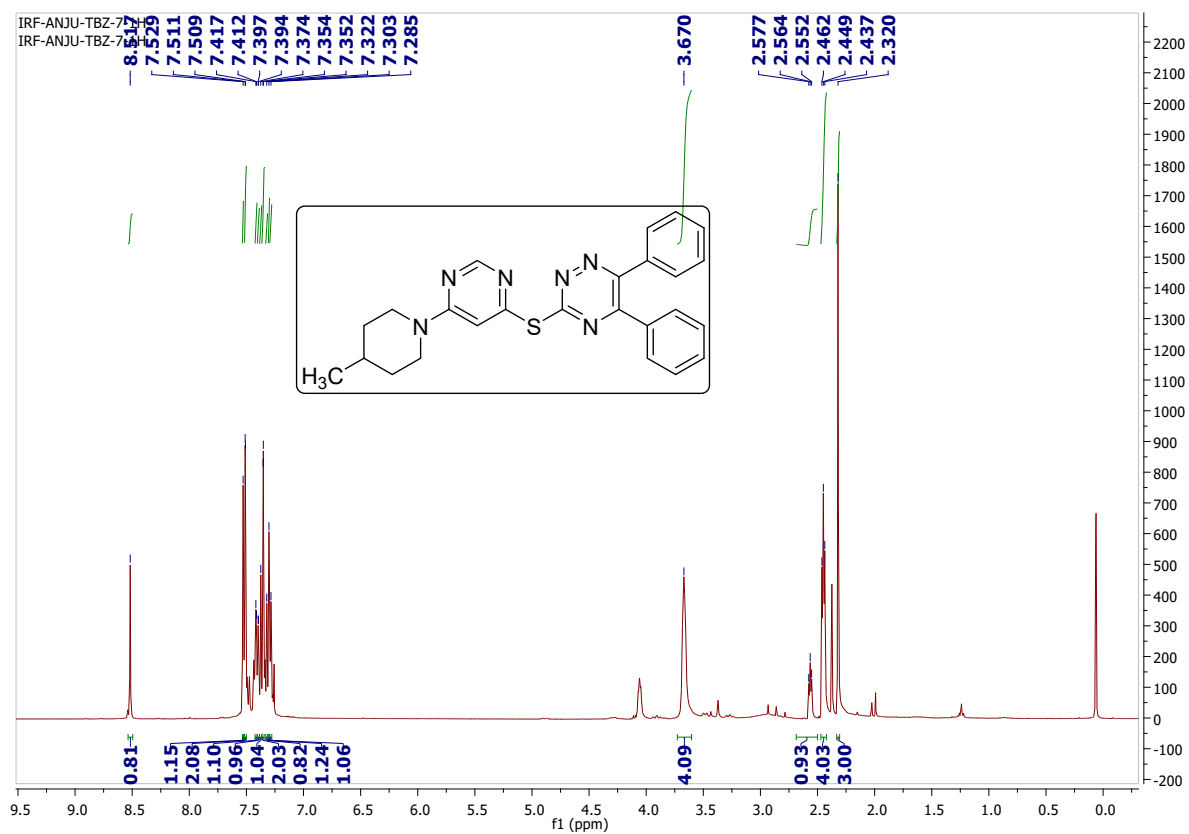


Figure S19: ¹H NMR spectrum of Molecule (T7)

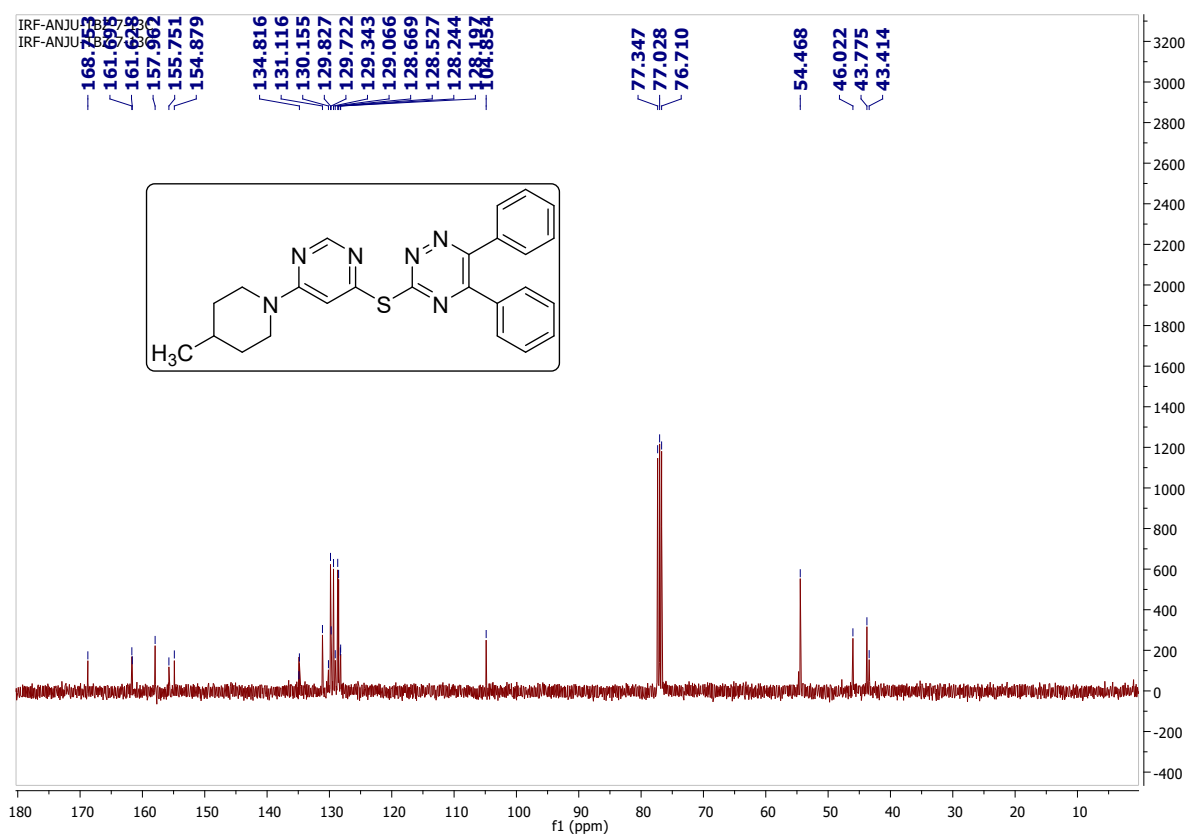


Figure S20: ¹³C NMR spectrum of Molecule (T7)

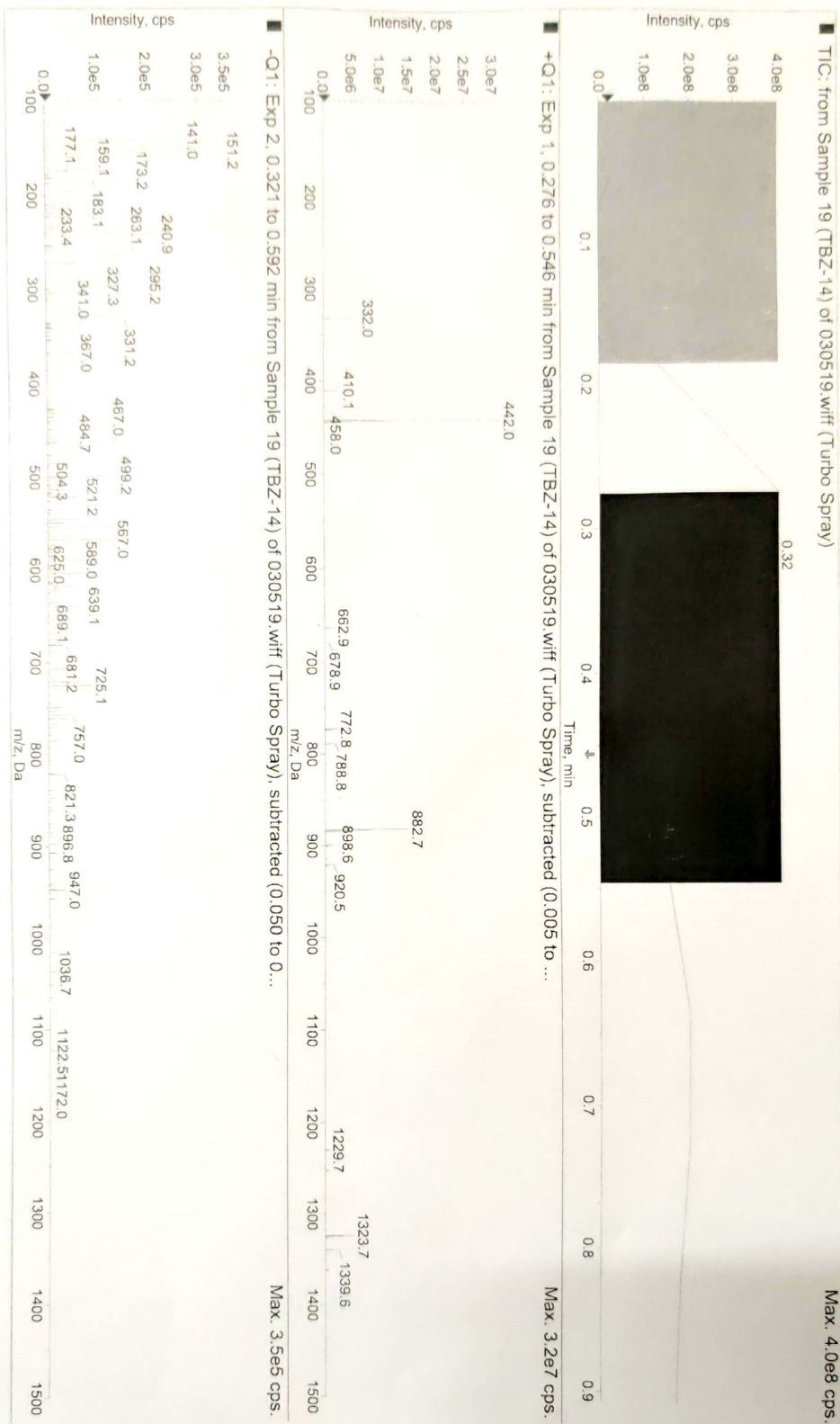


Figure S21: Mass spectrum of Molecule (T7)

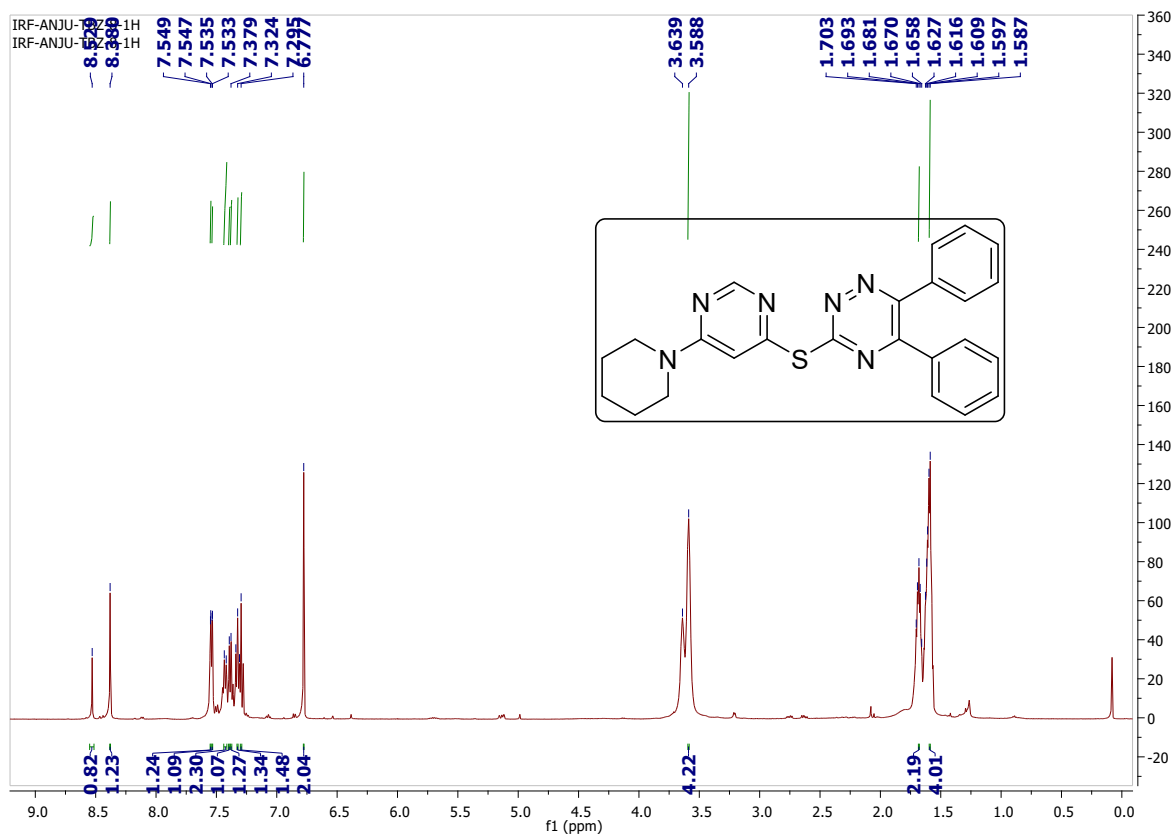


Figure S22: ¹H NMR spectrum of Molecule (T8)

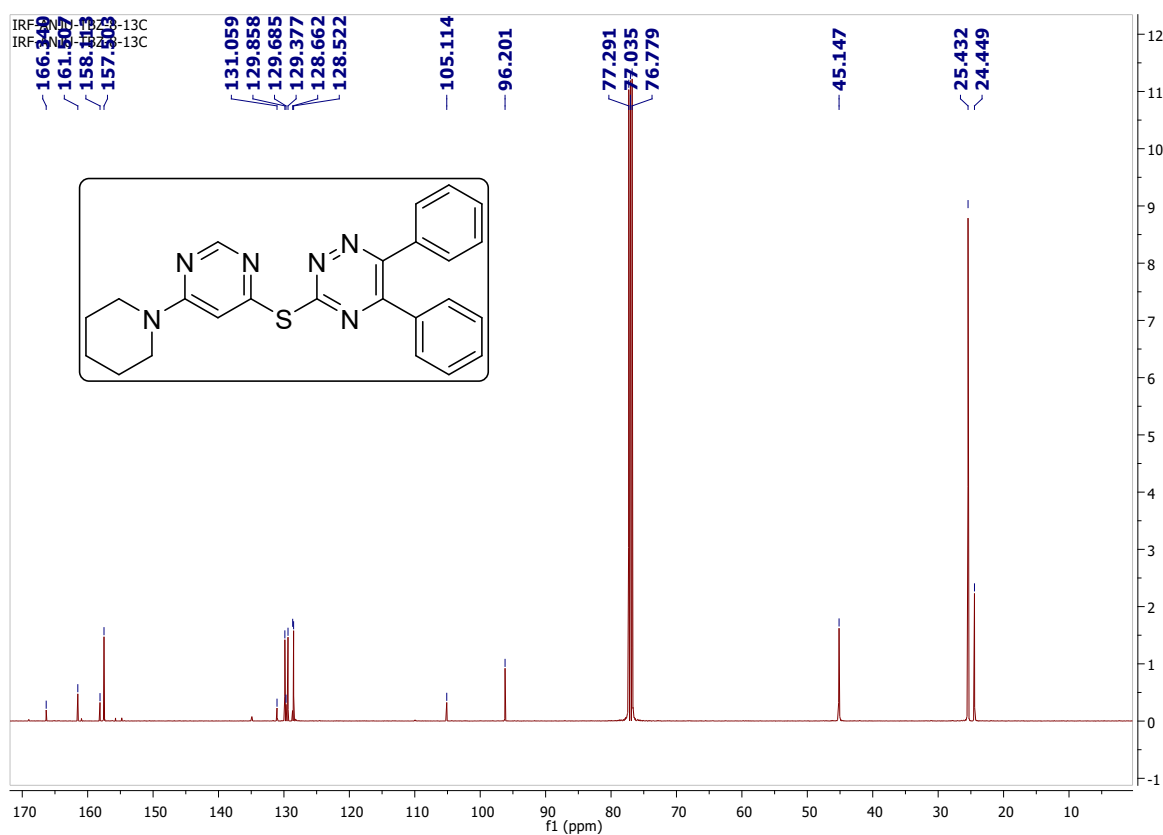


Figure S23: ¹³C NMR spectrum of Molecule (T8)

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INSTRUMENT ID : UPLC-MS-03

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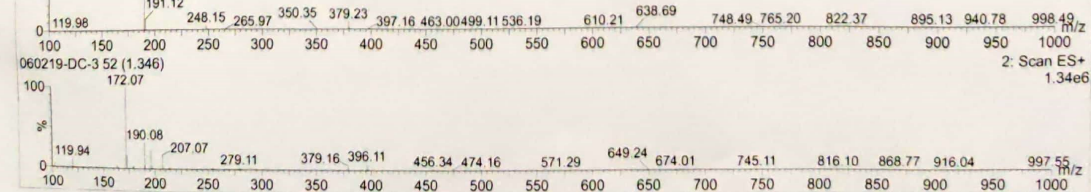
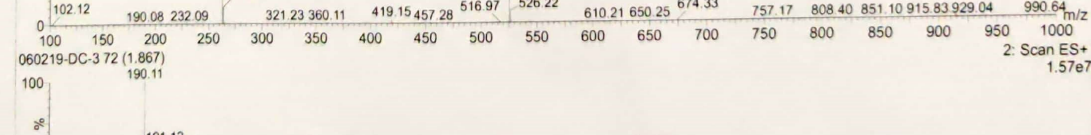
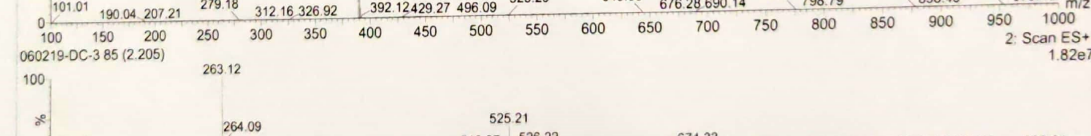
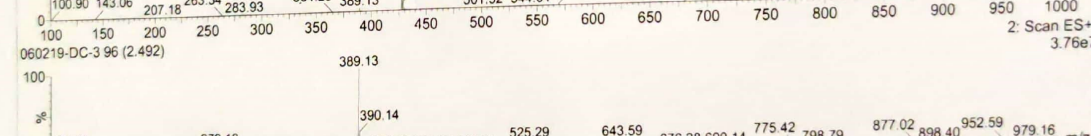
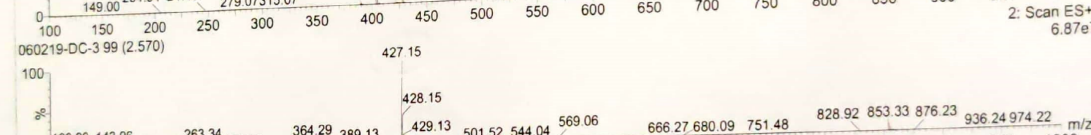
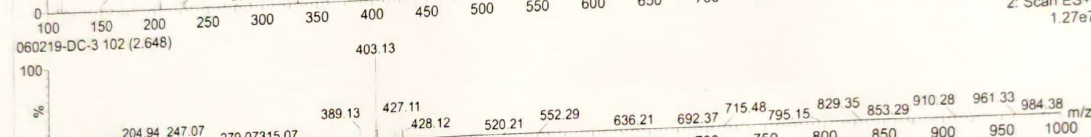
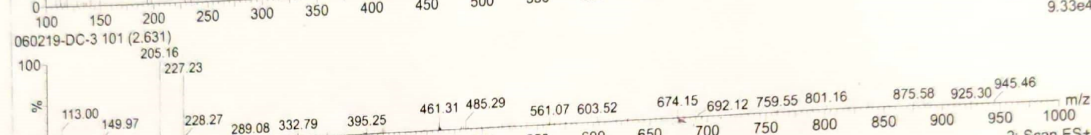
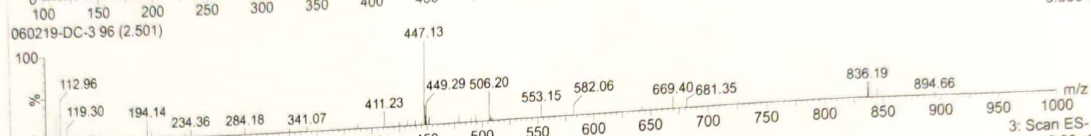
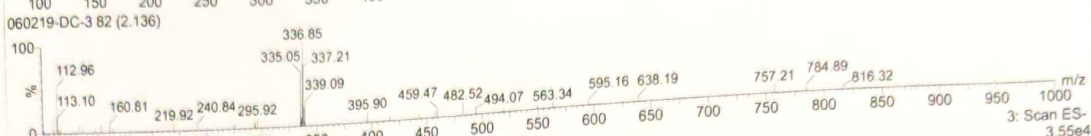
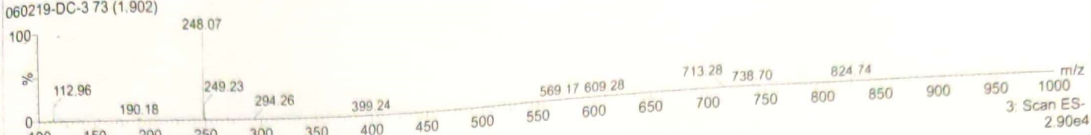
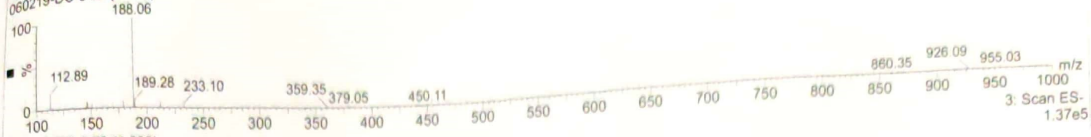


Figure S24: Mass spectrum of Molecule (T8)

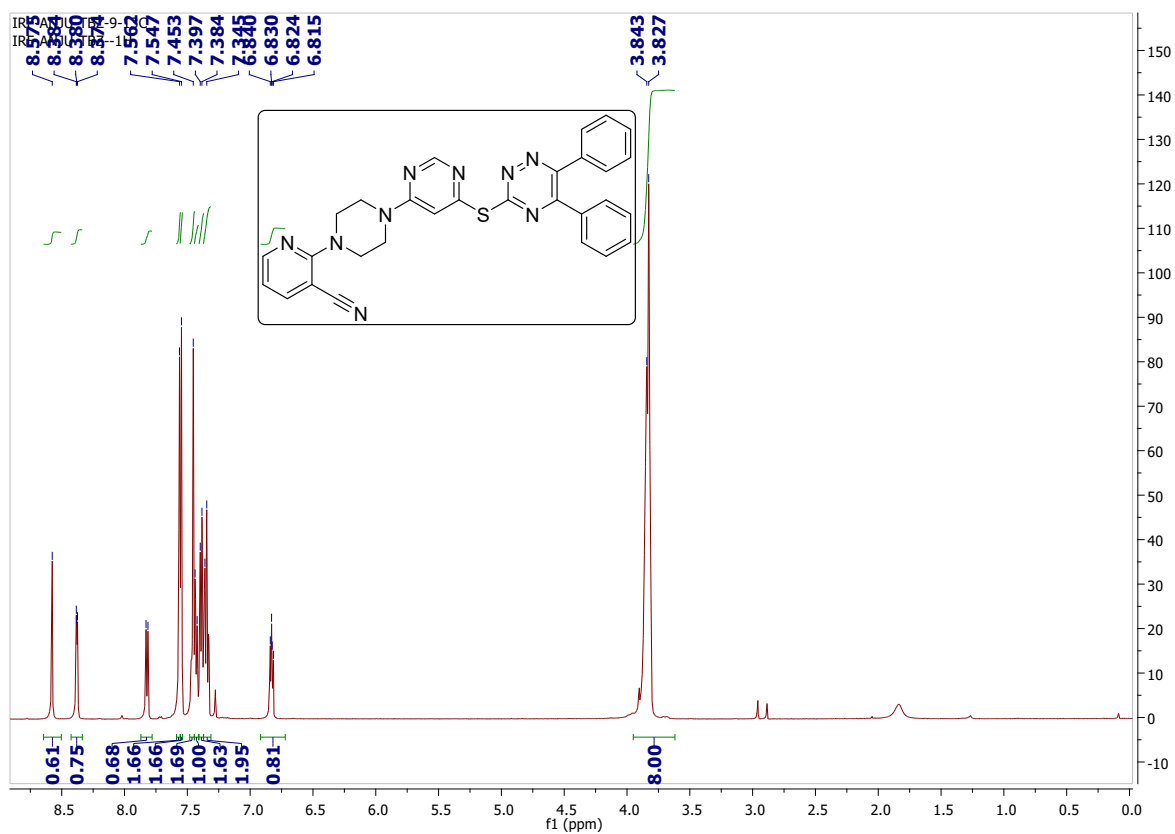


Figure S25: ^1H NMR spectrum of Molecule (T9)

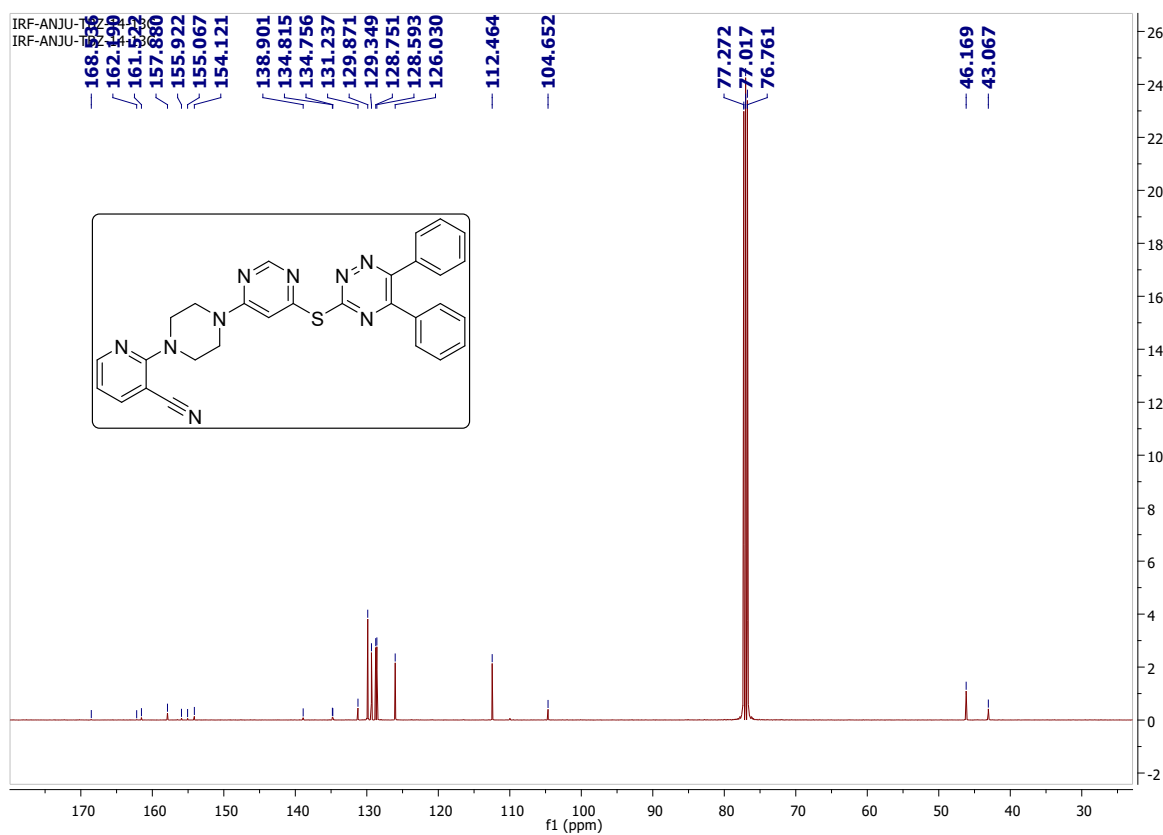


Figure S26: ^{13}C NMR spectrum of Molecule (T9)

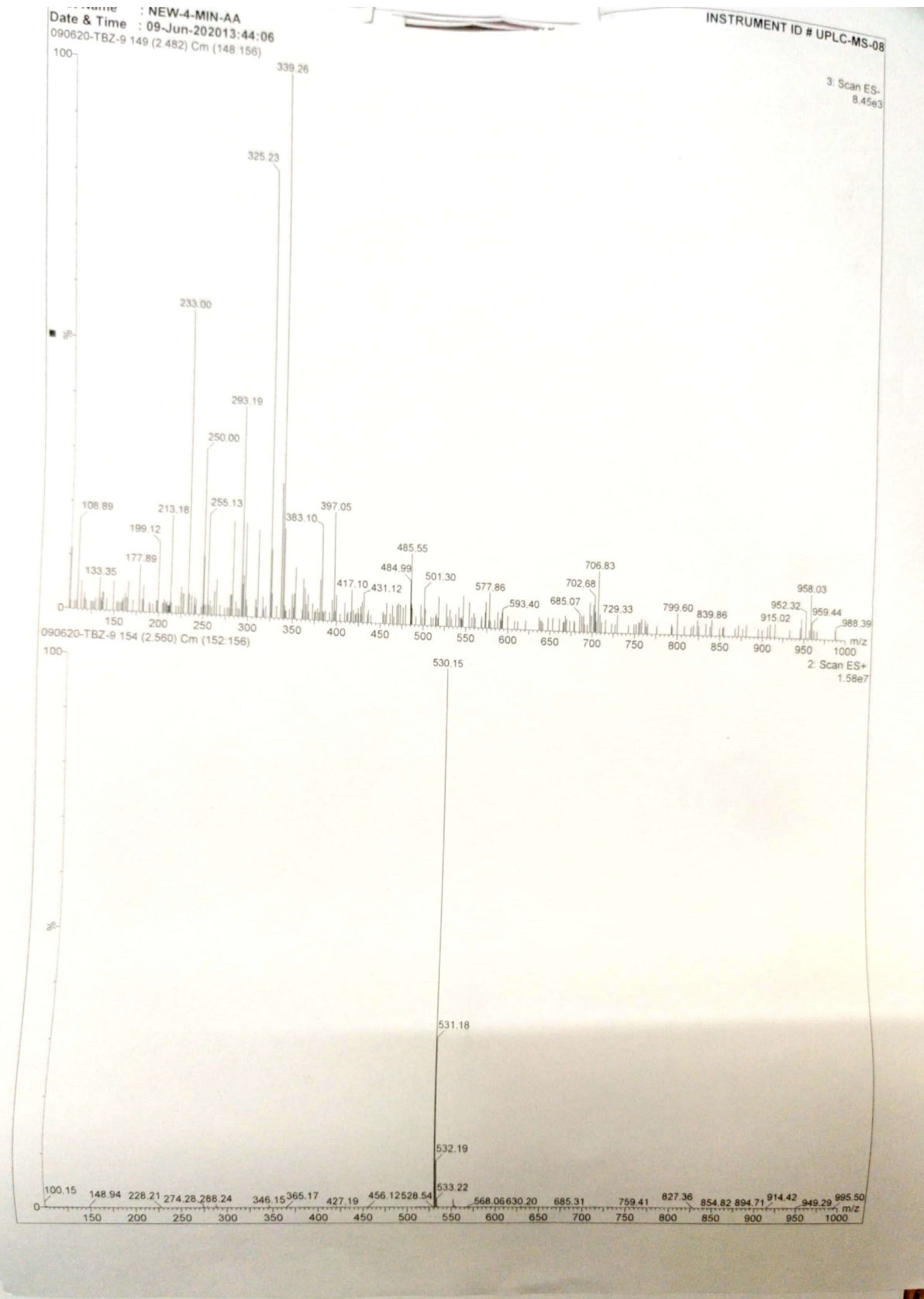


Figure S27: Mass spectrum of Molecule (T9)

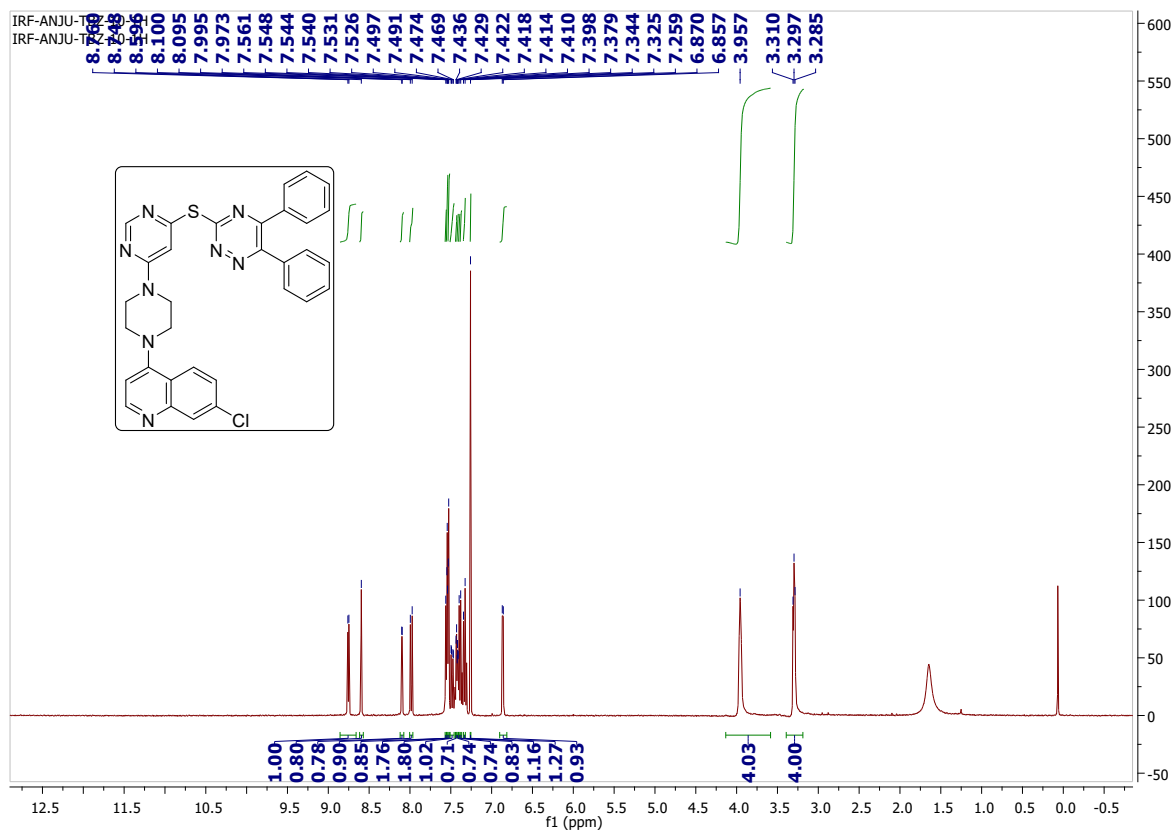


Figure S28: ^1H NMR spectrum of Molecule (T10)

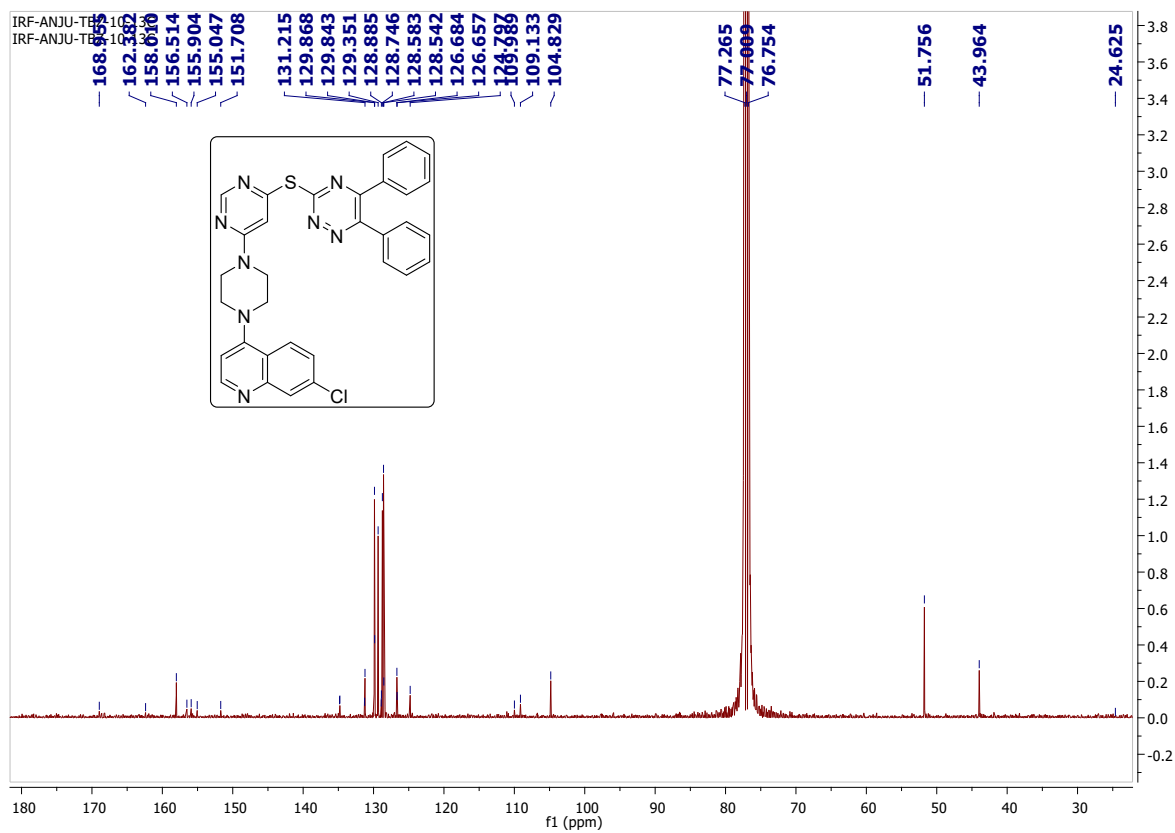


Figure S29: ^{13}C NMR spectrum of Molecule (T10)

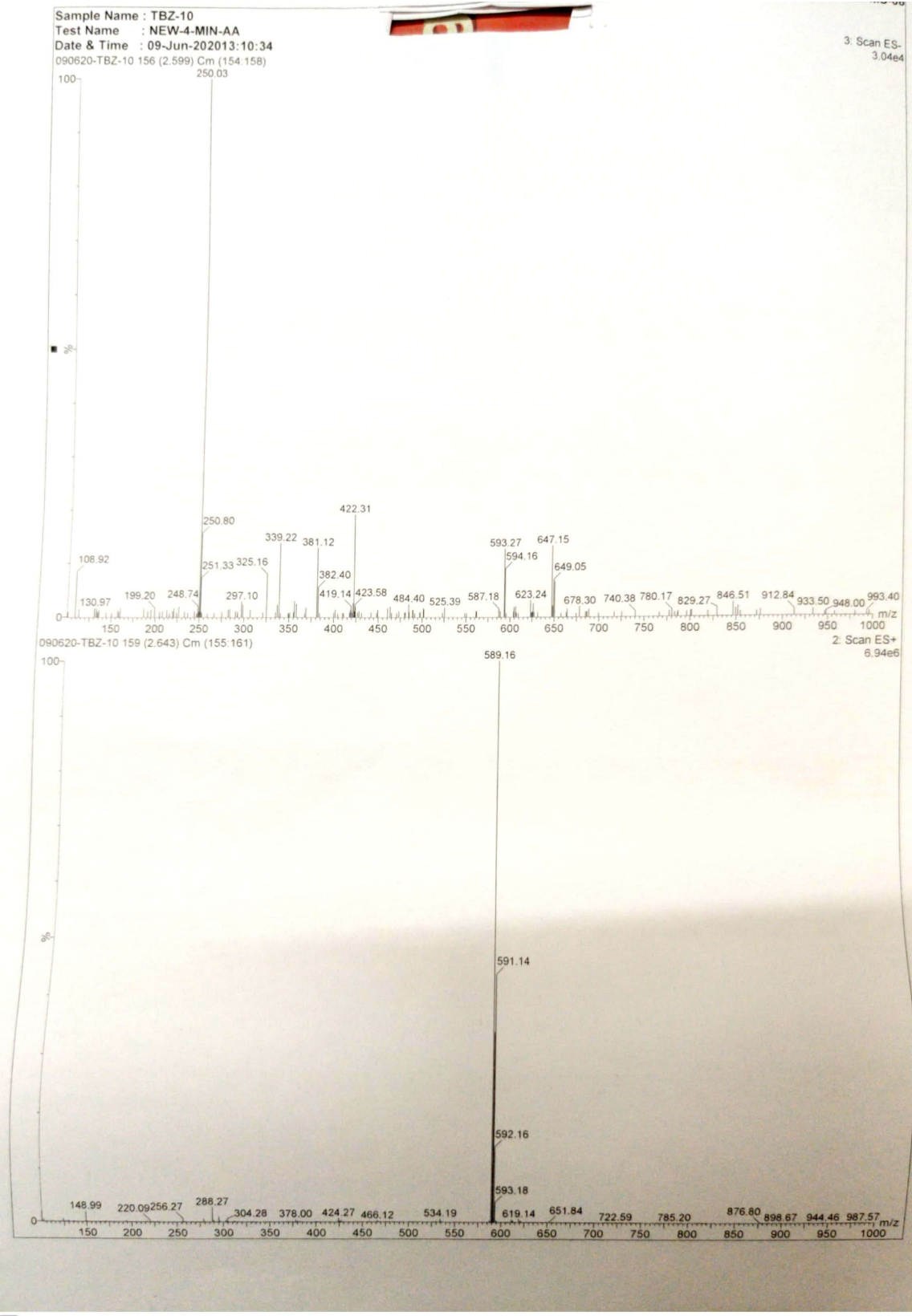


Figure S30: Mass spectrum of Molecule (T10)

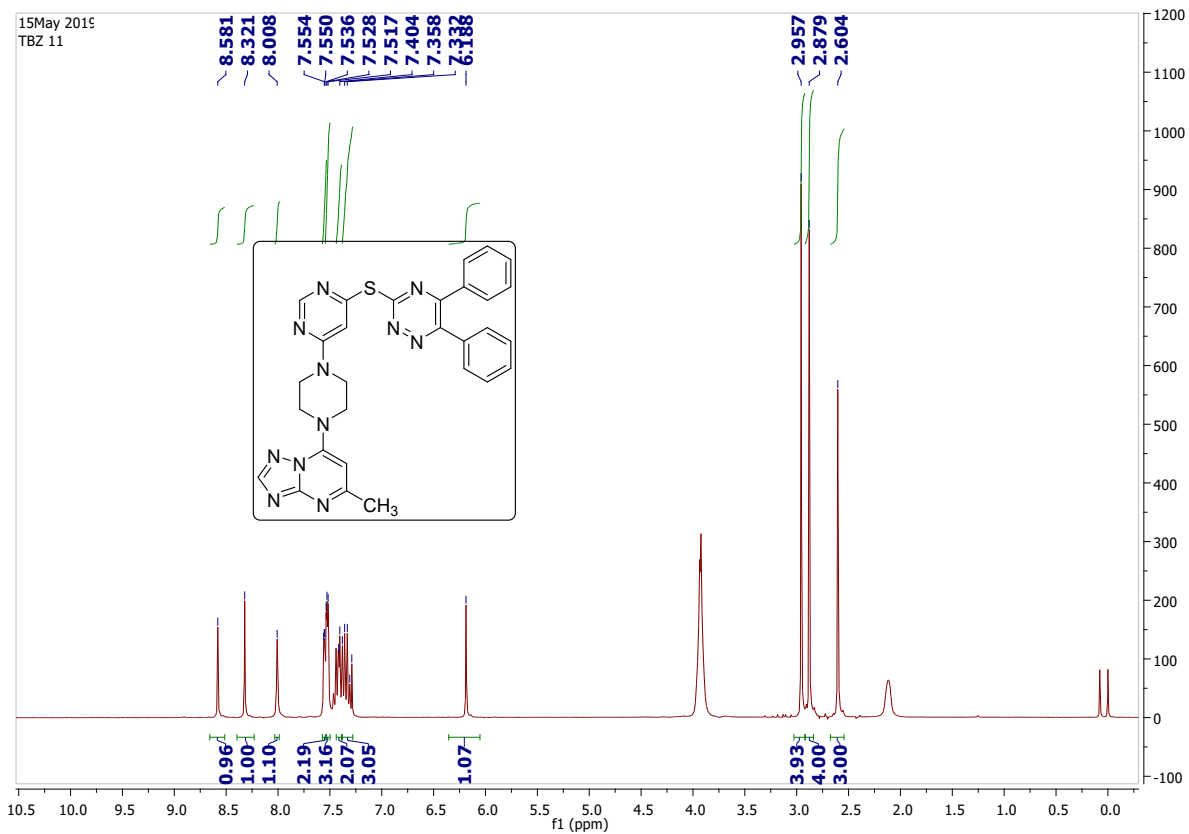


Figure S31: ^1H NMR spectrum of Molecule (T11)

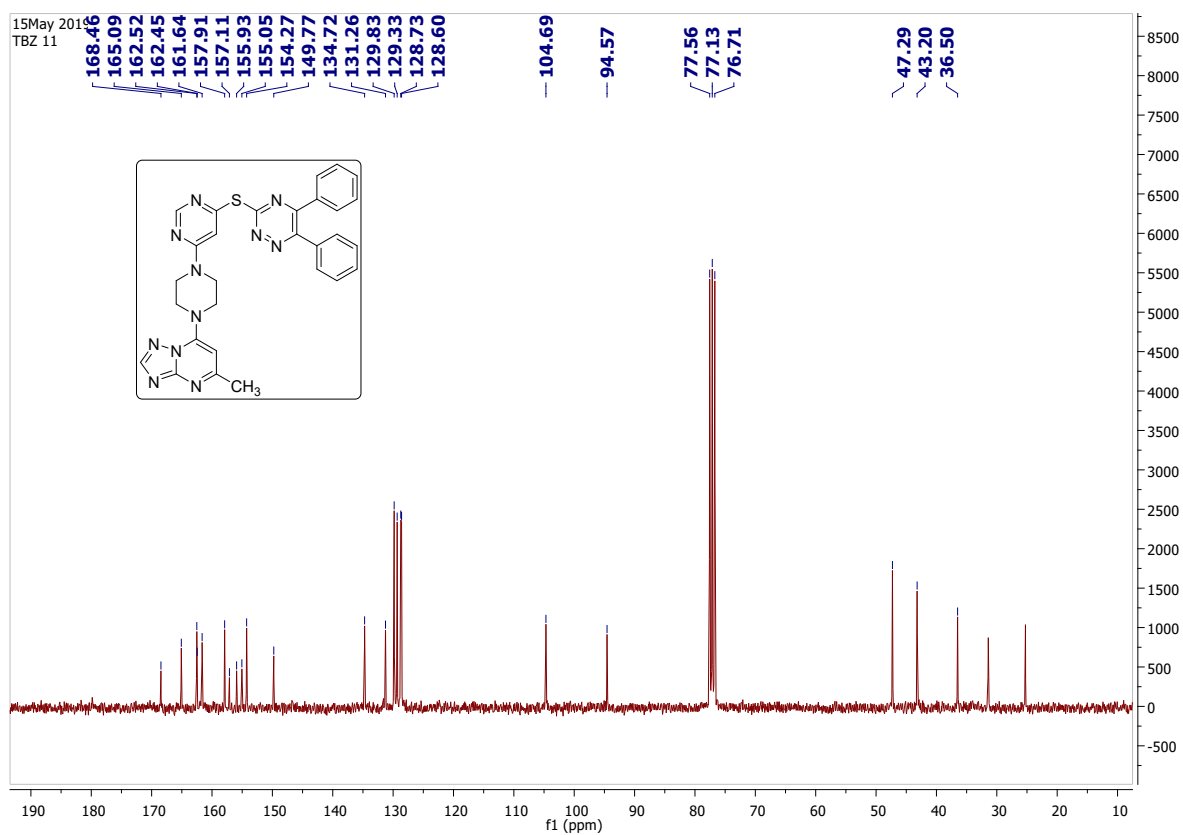


Figure S32: ^{13}C NMR spectrum of Molecule (T11)

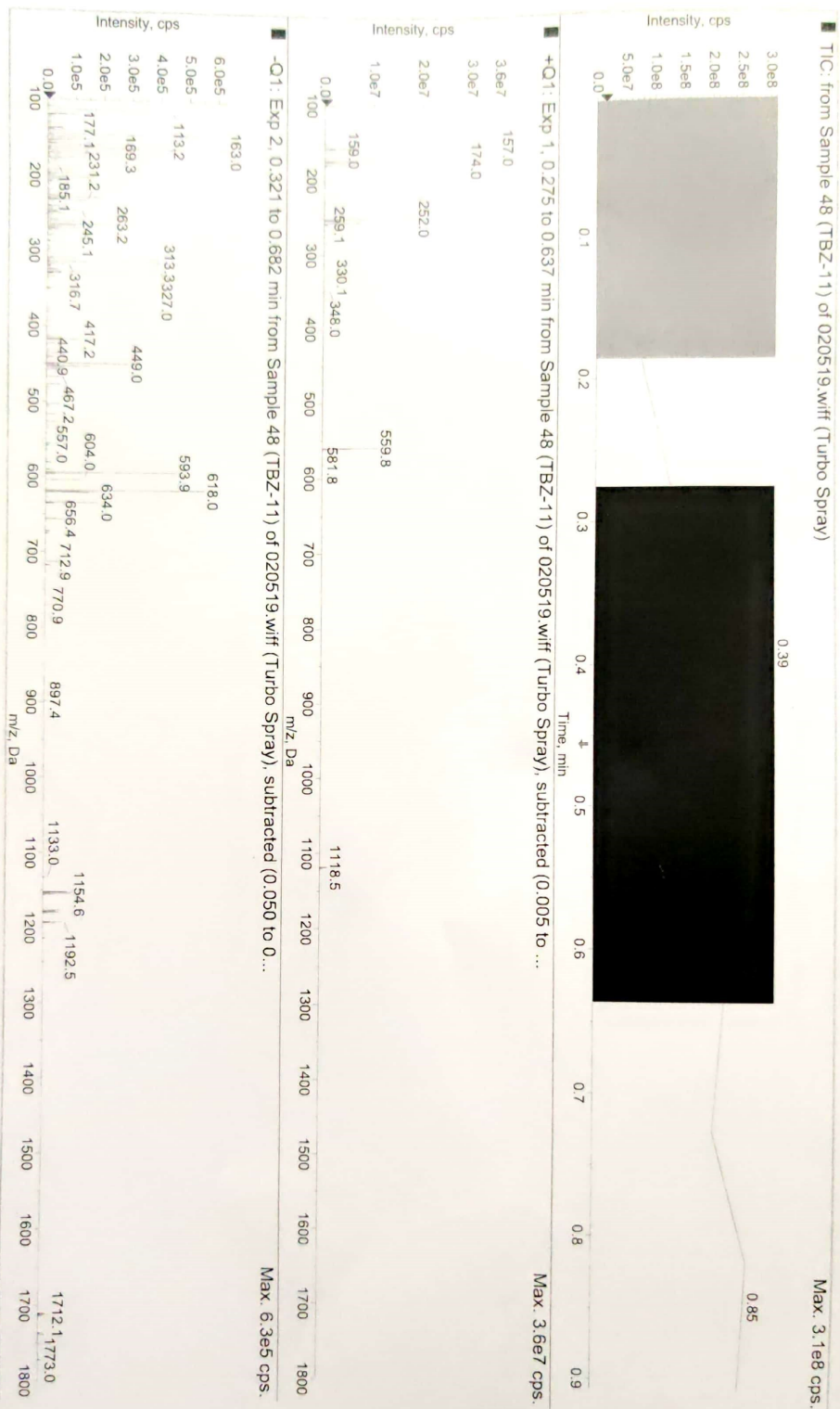


Figure S33: Mass spectrum of Molecule (T11)

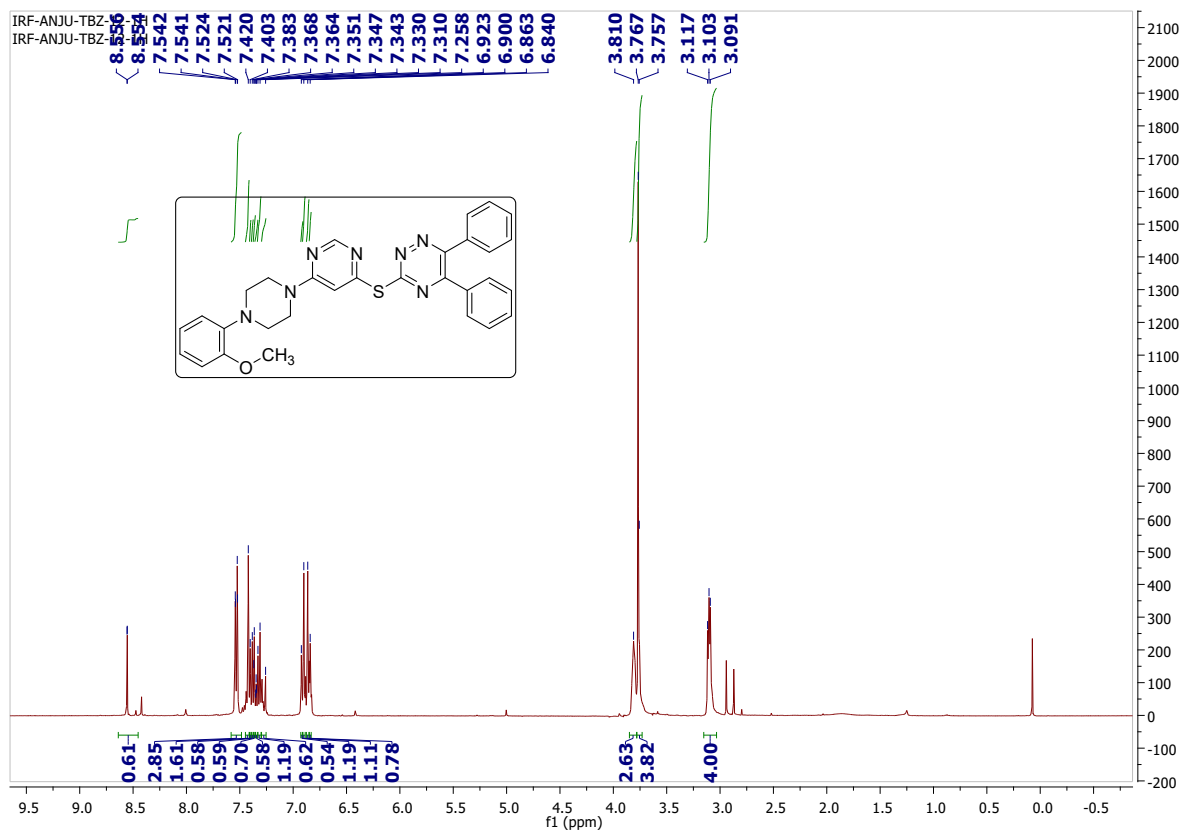


Figure S34: ¹H NMR spectrum of Molecule (T12)

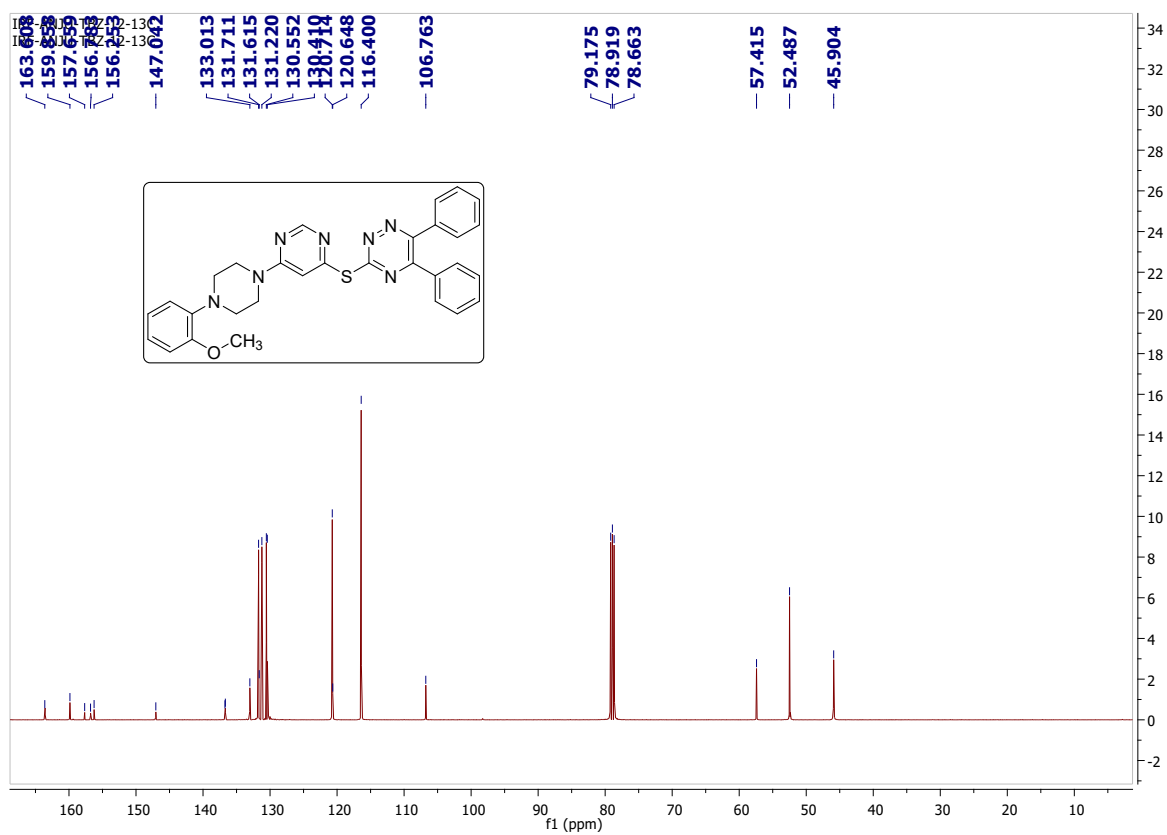
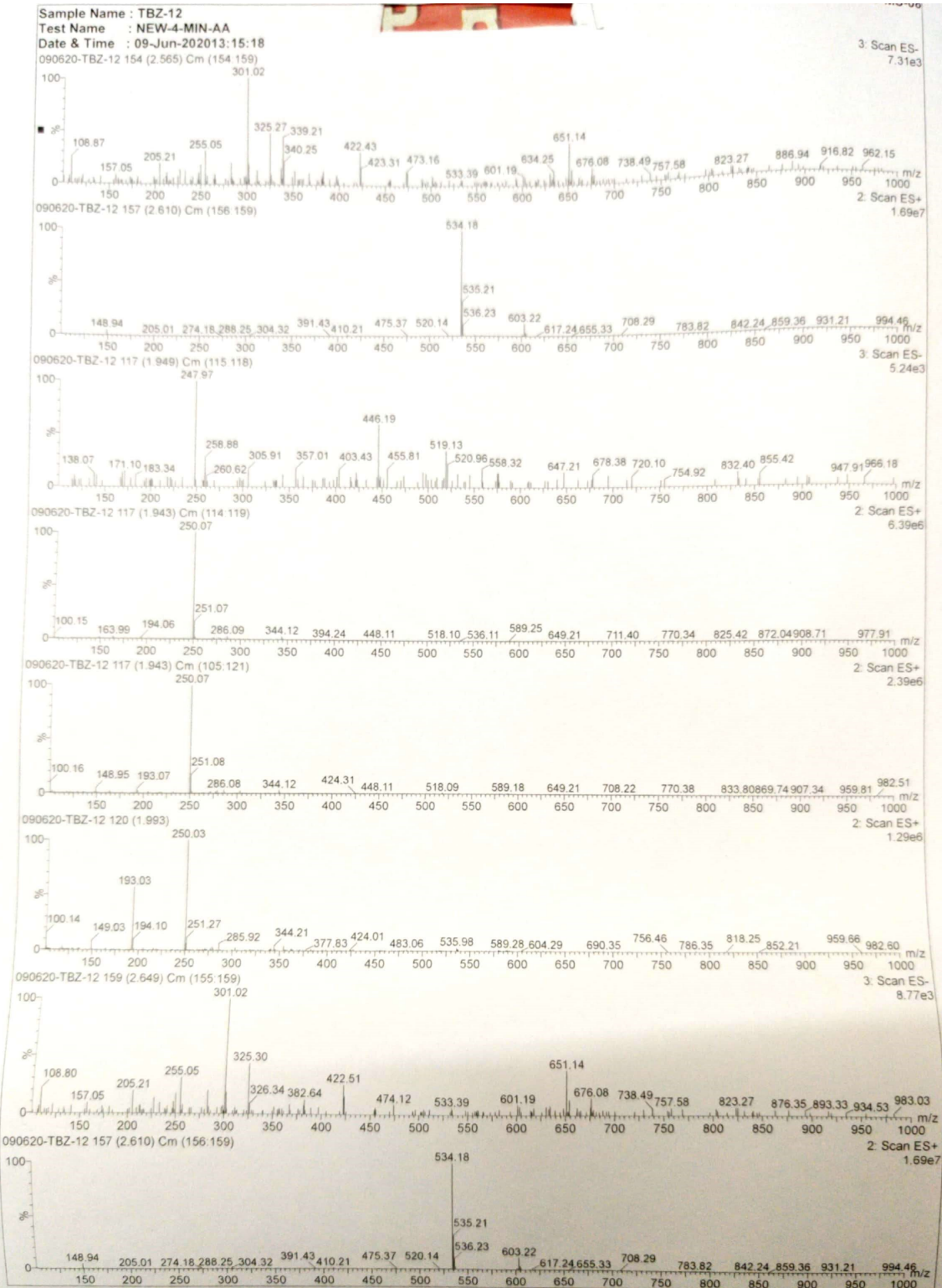


Figure S35: ¹³C NMR spectrum of Molecule (T12)



CS Scanned with CamScanner

Figure S36: Mass spectrum of Molecule (T12)

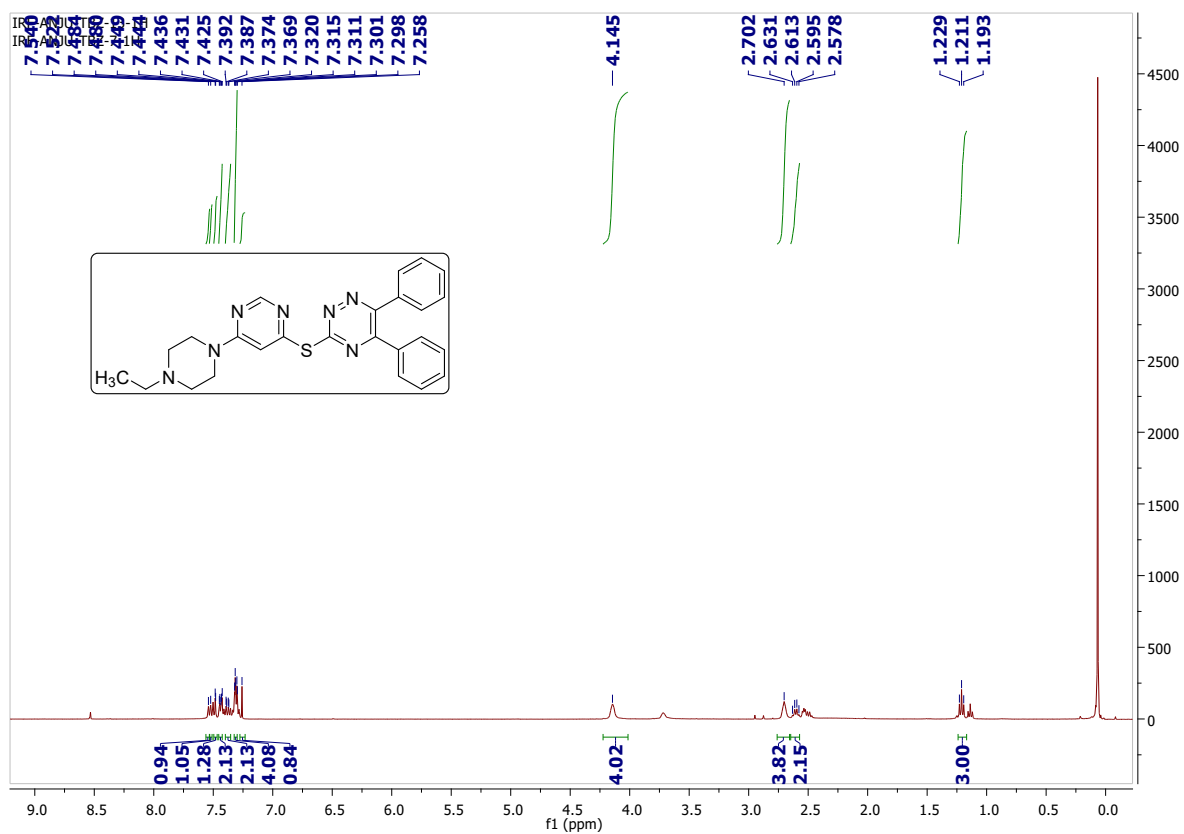


Figure S37: ¹H NMR spectrum of Molecule (T13)

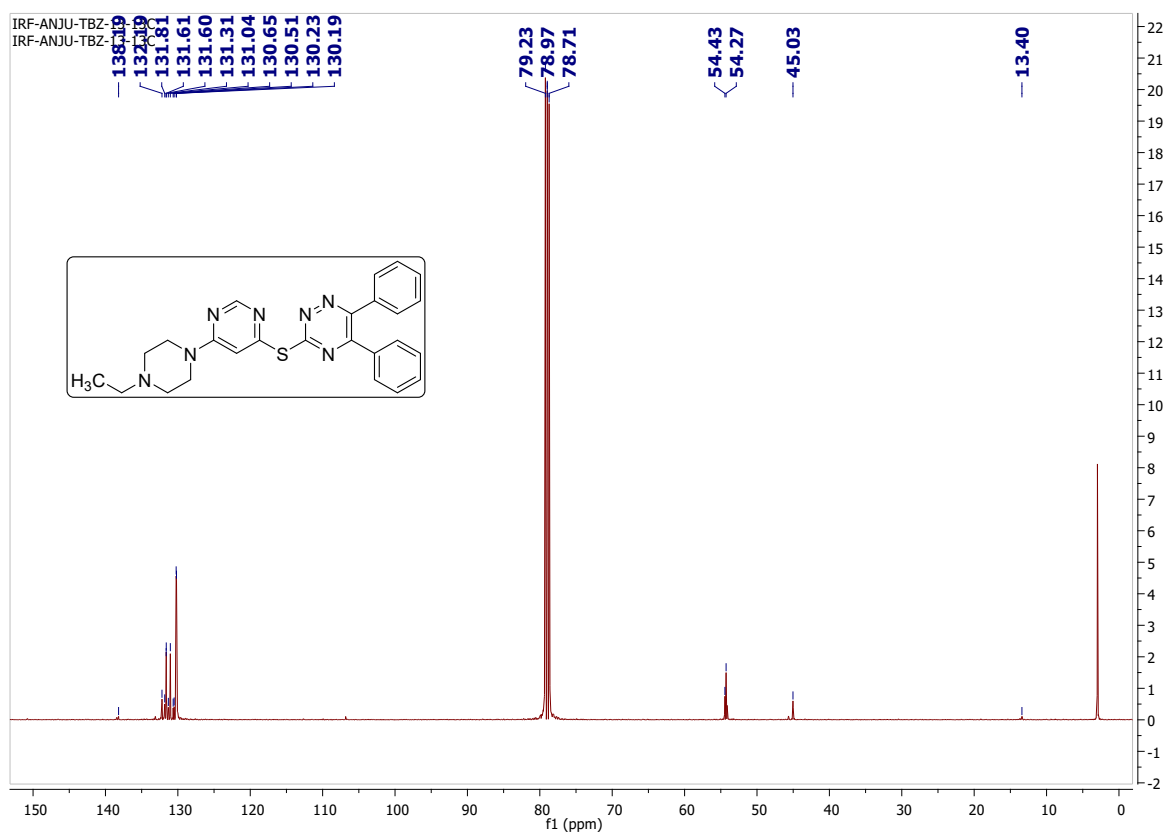


Figure S38: ¹³C NMR spectrum of Molecule (T13)

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Test Name : NEW-4-MIN-AA
Date & Time : 09-Jun-2020 13:39:20
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INSTRUMENT ID # UPLC-MS-08

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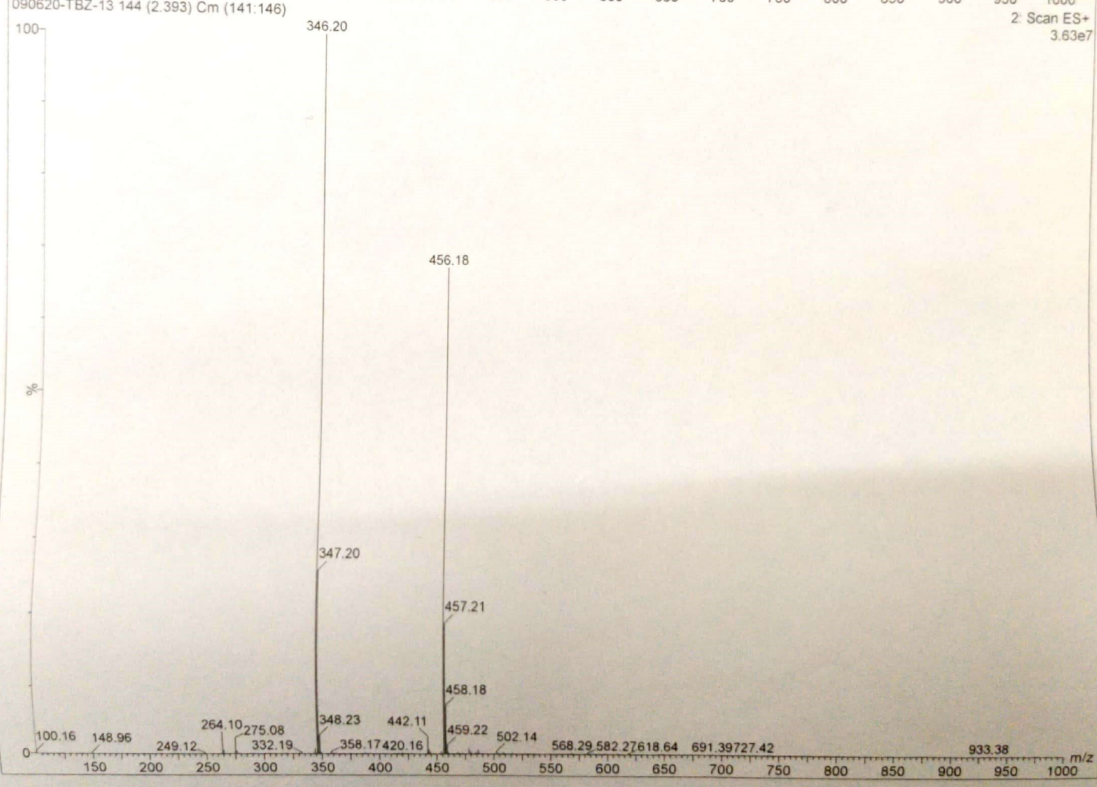
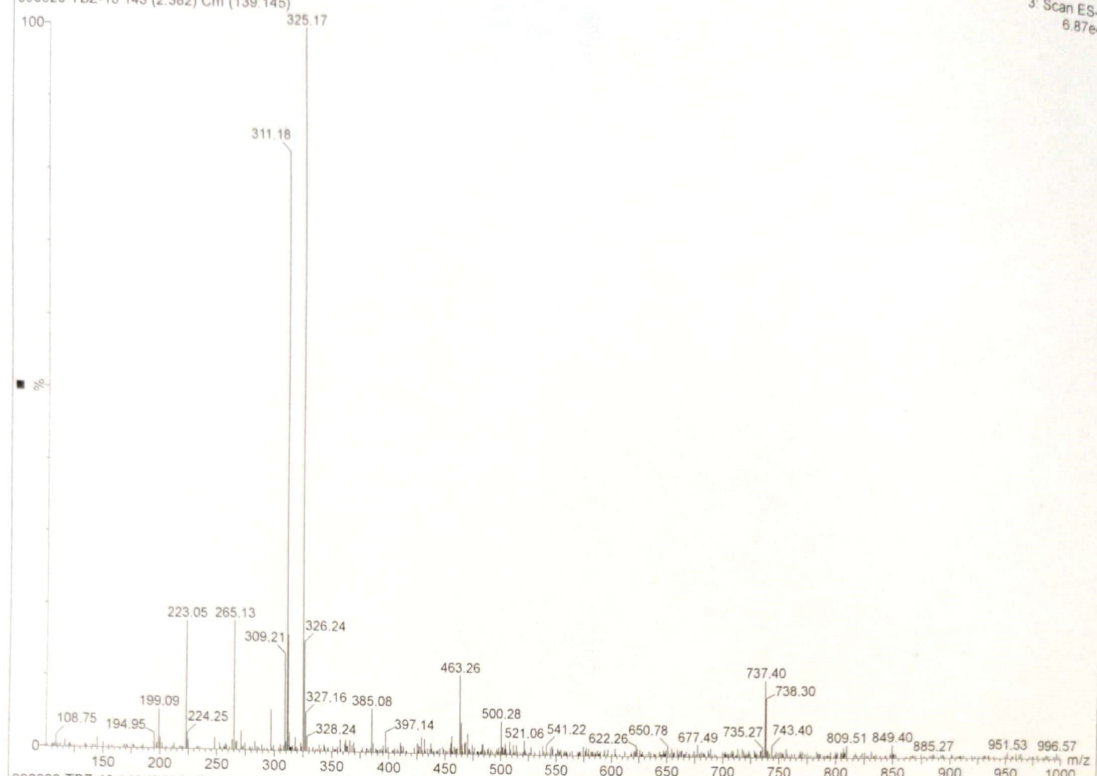


Figure S39: Mass spectrum of Molecule (T13)

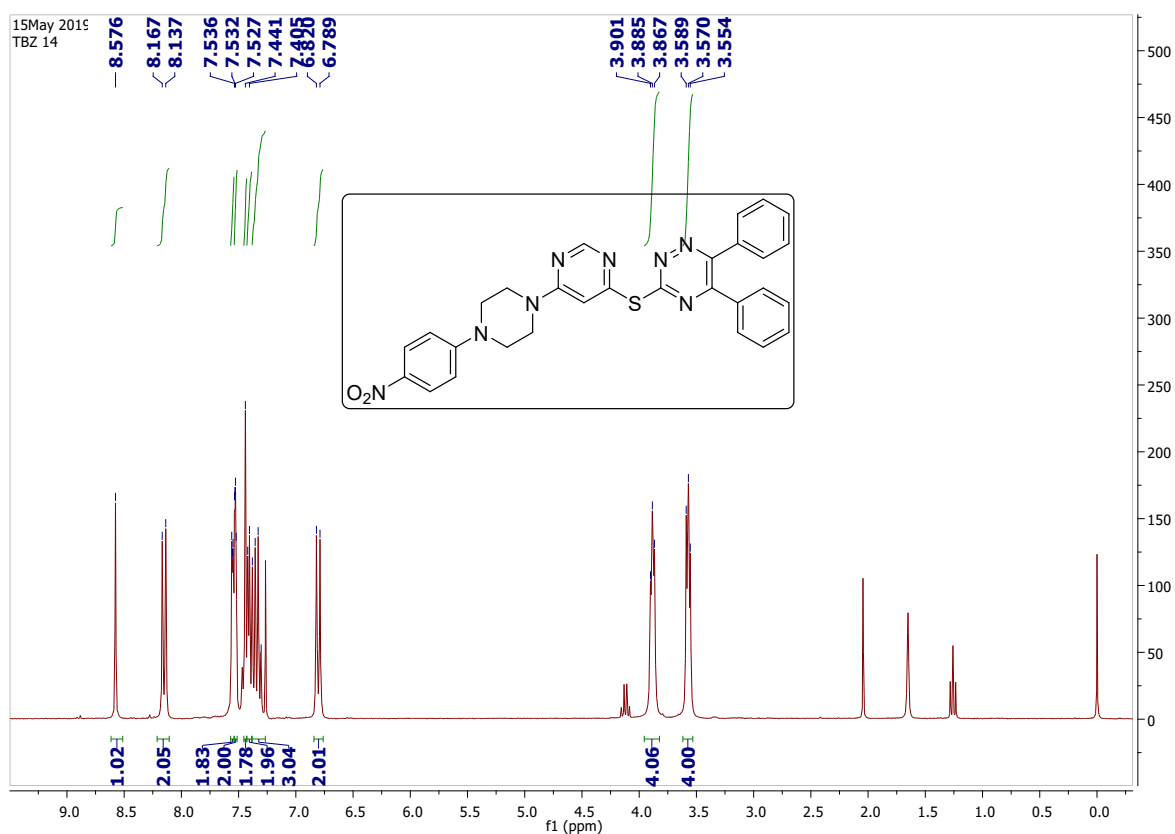


Figure S40: ^1H NMR spectrum of Molecule (T14)

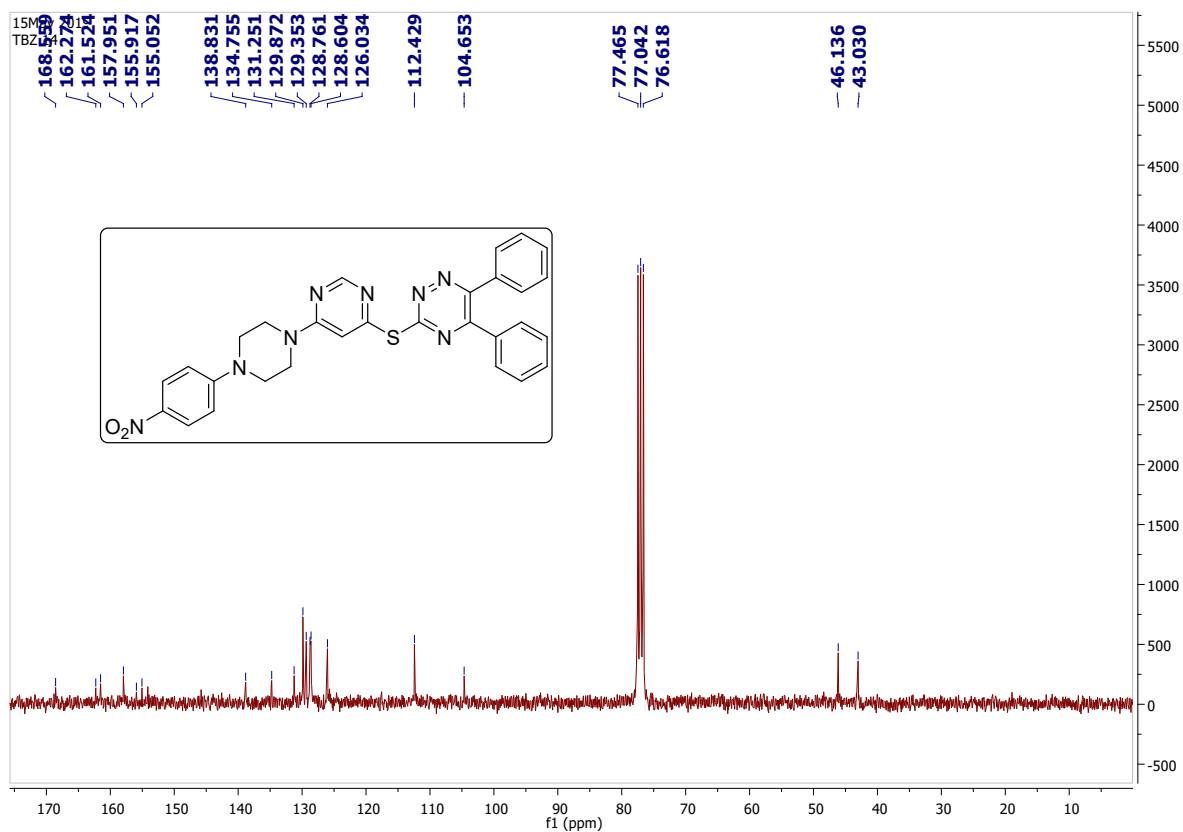


Figure S41: ^{13}C NMR spectrum of Molecule (T14)

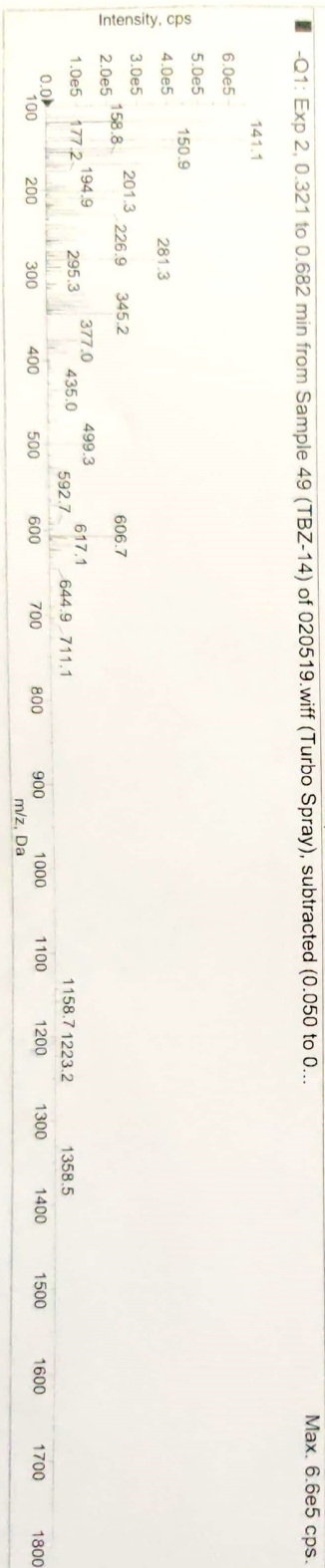
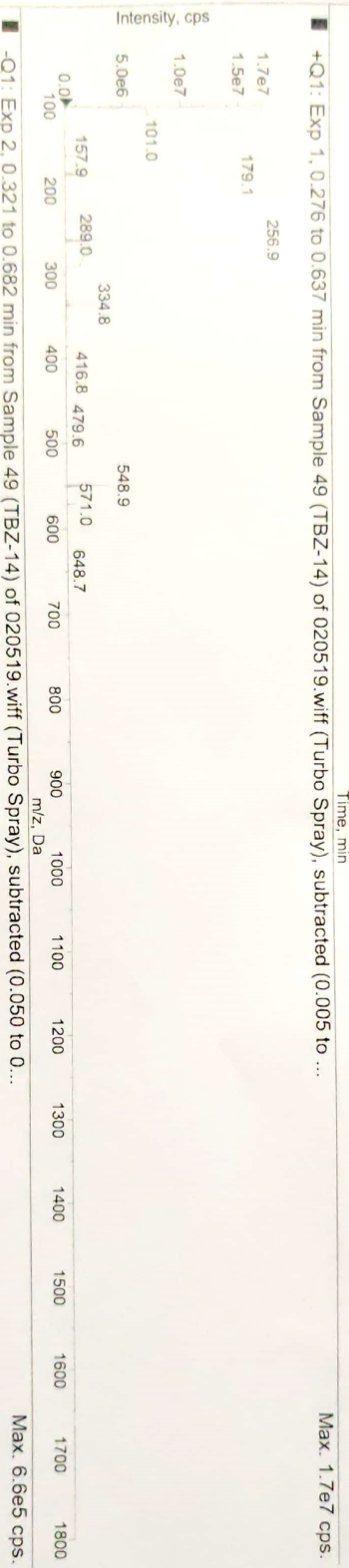
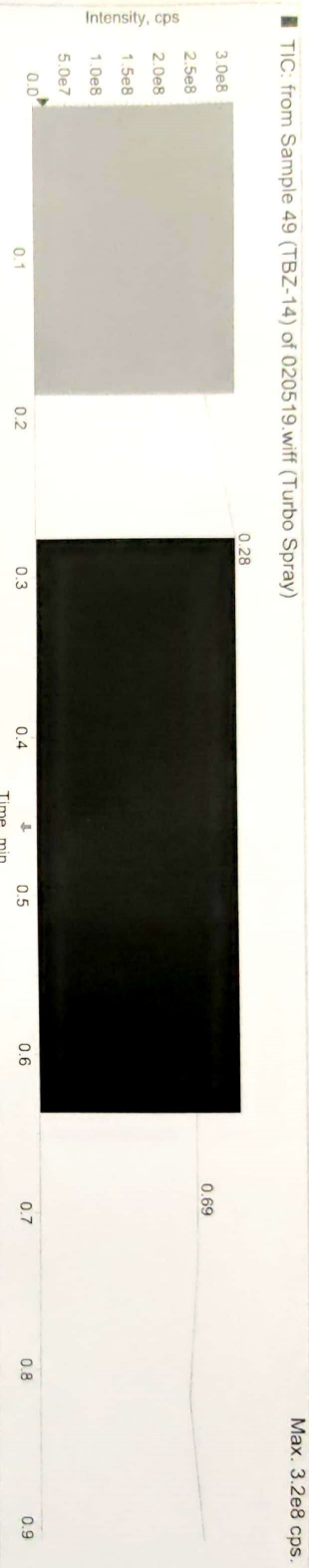


Figure S42: Mass spectrum of Molecule (T14)

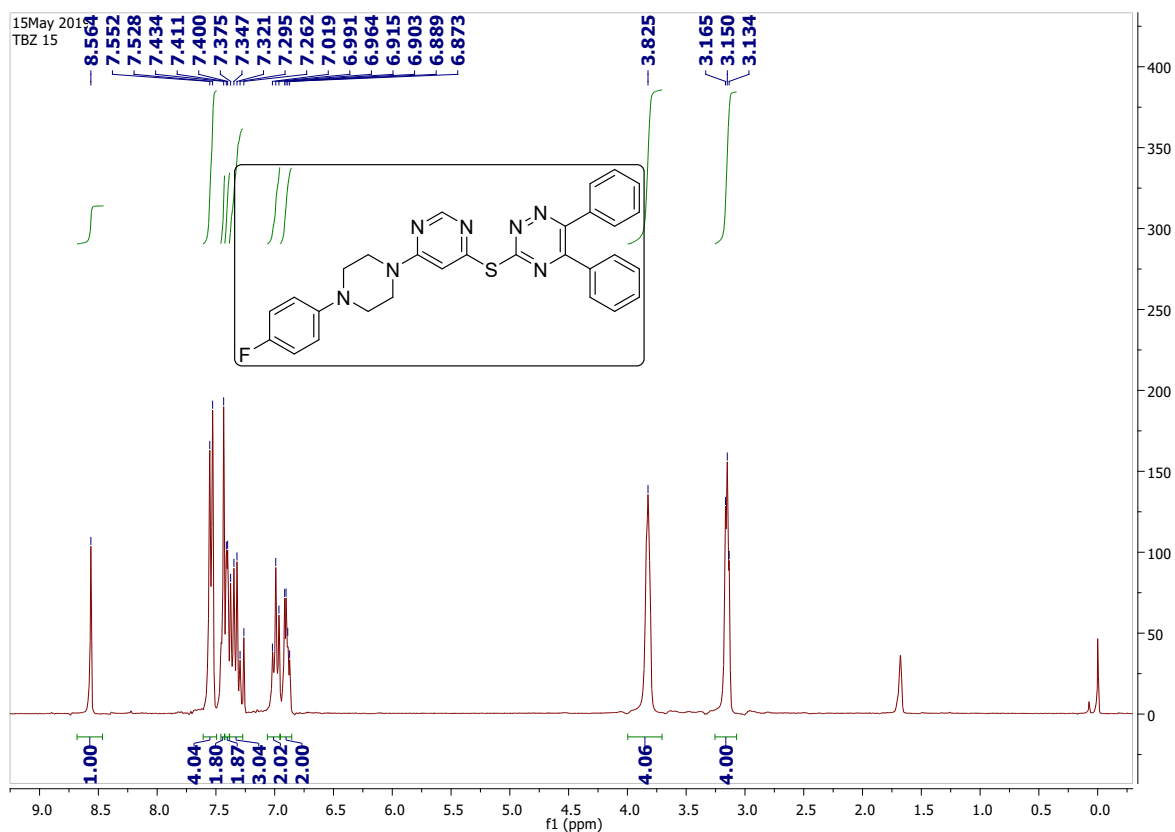


Figure S43: ¹H NMR spectrum of Molecule (T15)

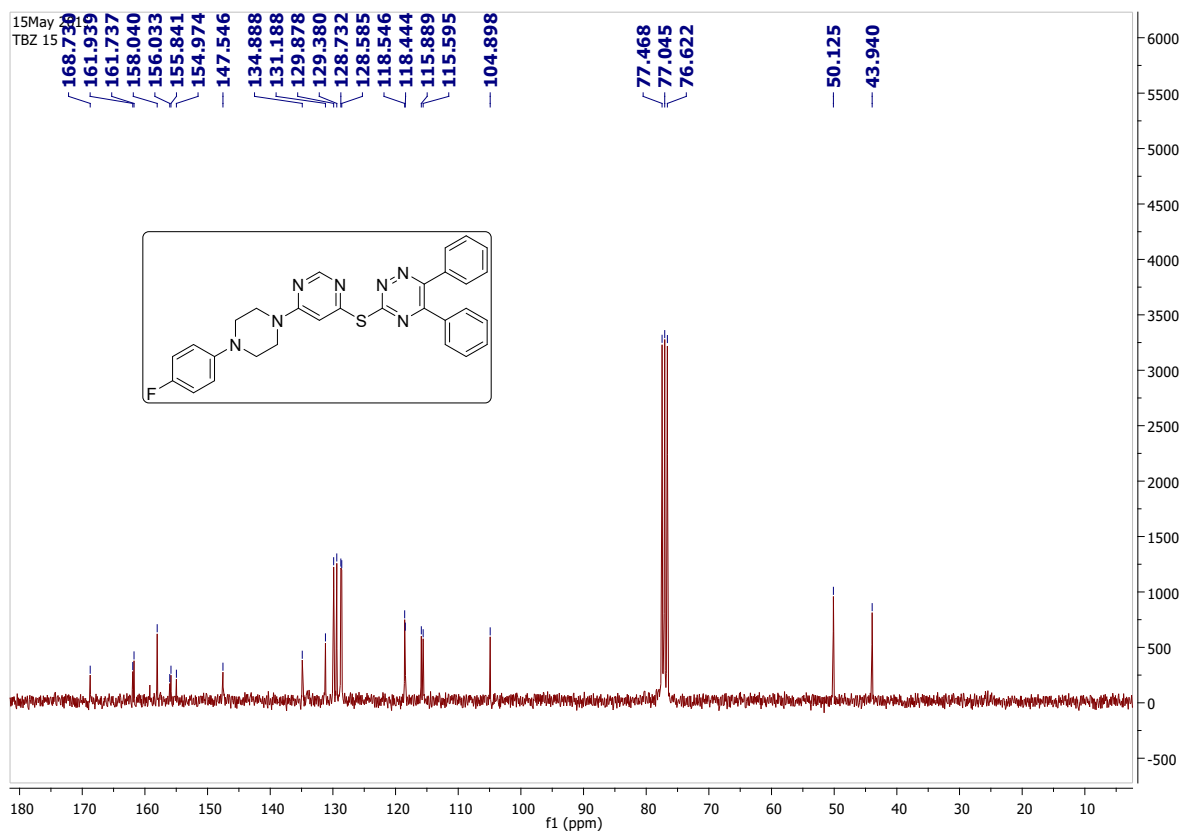


Figure S44: ¹³C NMR spectrum of Molecule (T15)

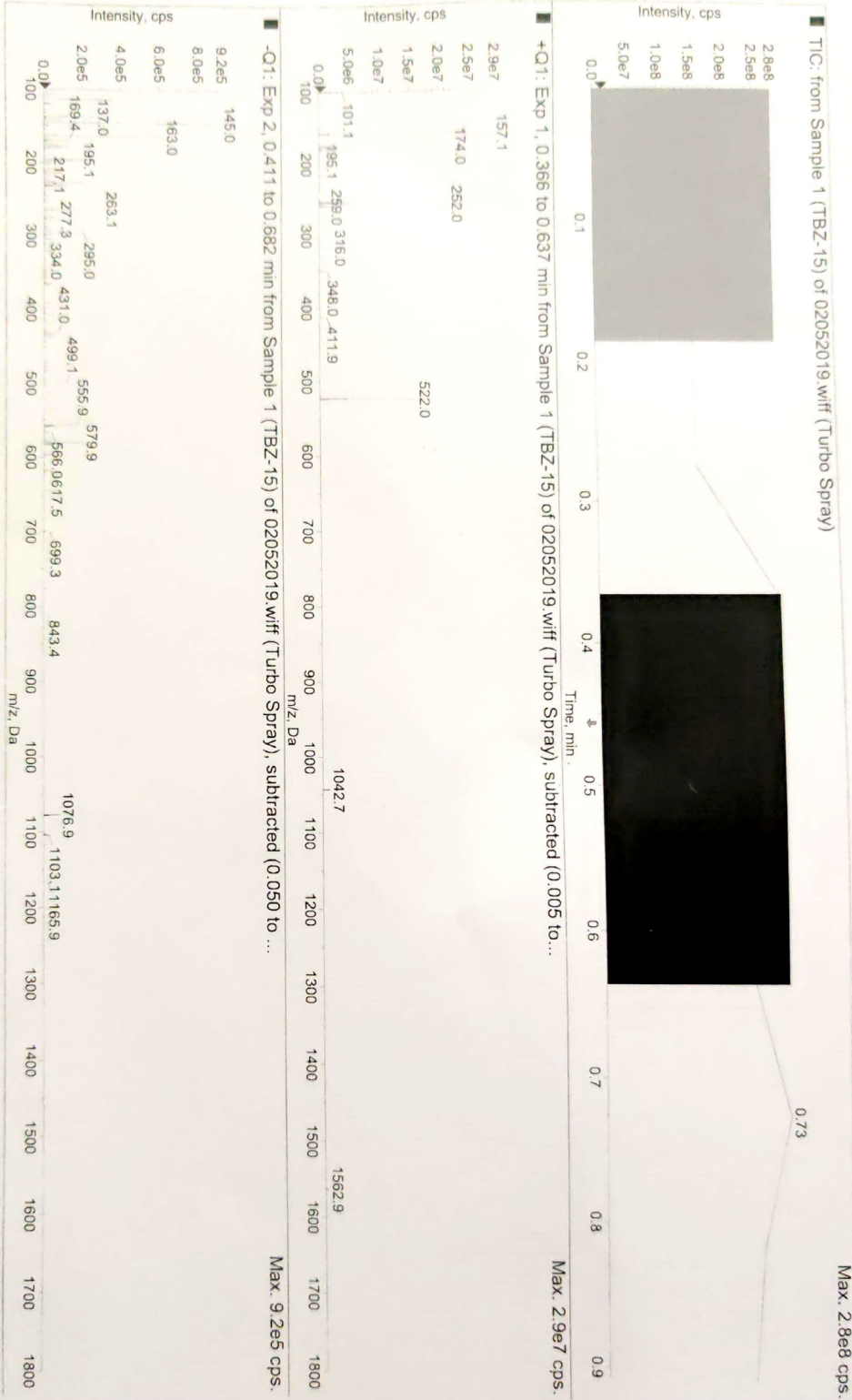


Figure S45: Mass spectrum of Molecule (T15)

References

- [1] J. Kumar, P. Meena, A. Singh, E. Jameel, M. Maqbool, M. Mobashir, et al., Synthesis and screening of triazolopyrimidine scaffold as multi-functional agents for Alzheimer's disease therapies, *European Journal of Medicinal Chemistry*. (2016).
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