

Supporting Information

Organophosphorus-catalyzed Diaza-Wittig reaction: Application to the synthesis of pyridazines

Hassen Bel Abed,^a Oscar Mammoliti,^b Omprakash Bande,^a Guy Van Lommen^b and Piet Herdewijn^{*a}

^aRega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium

^bGalapagos NV, Laboratory of Medicinal Chemistry, Generaal De Wittelaan L11 A3, B-2800 Mechelen, Belgium

Table of Contents

¹H and ¹³C NMR spectra

| | |
|---|-----|
| ¹ H and ¹³ C NMR spectra for methyl 2-diazo-3-oxobutanoate | S2 |
| ¹ H and ¹³ C NMR spectra for methyl 2-diazo-3-oxopentanoate | S3 |
| ¹ H and ¹³ C NMR spectra for 2-Diazo-1-phenylbutane-1,3-dione | S4 |
| ¹ H and ¹³ C NMR spectra for 1e | S5 |
| ¹ H and ¹³ C NMR spectra for 1f | S6 |
| ¹ H and ¹³ C NMR spectra for 1h | S7 |
| ¹ H and ¹³ C NMR spectra for 1i | S8 |
| ¹ H and ¹³ C NMR spectra for 1j | S9 |
| ¹ H and ¹³ C NMR spectra for 4-hydroxy-1-phenylsulfonyl-4-(thiophene-2-yl)-2-butanone | S10 |
| ¹ H and ¹³ C NMR spectra for 2e | S11 |
| ¹ H and ¹³ C NMR spectra for 2f | S12 |
| ¹ H and ¹³ C NMR spectra for 2g | S13 |
| ¹ H and ¹³ C NMR spectra for 2h | S14 |
| ¹ H and ¹³ C NMR spectra for 2i | S15 |
| ¹ H and ¹³ C NMR spectra for 2j | S16 |
| ¹ H and ¹³ C NMR spectra for 2n | S17 |

LC/MS analysis

| | |
|--------------------------------|--------|
| LC/MS analysis for 2a-o | S18-25 |
|--------------------------------|--------|

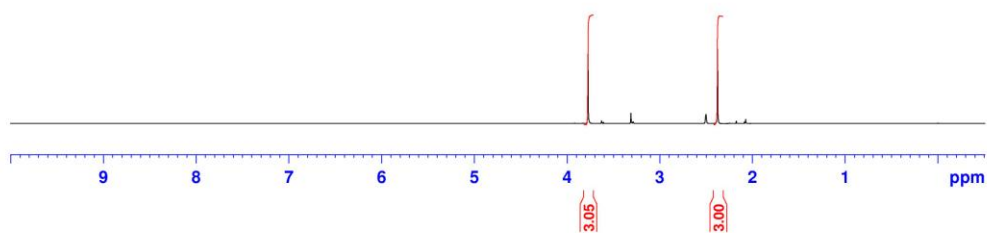
¹H AND ¹³C NMR SPECTRA

Methyl 2-diazo-3-oxobutanoate proton spectrum (500 MHz) in DMSO-d6



Methyl 2-diazo-3-oxobutanoate

3.774
3.312
2.502
2.377



Methyl 2-diazo-3-oxobutanoate carbon spectrum (125 MHz) in DMSO-d6

189.27

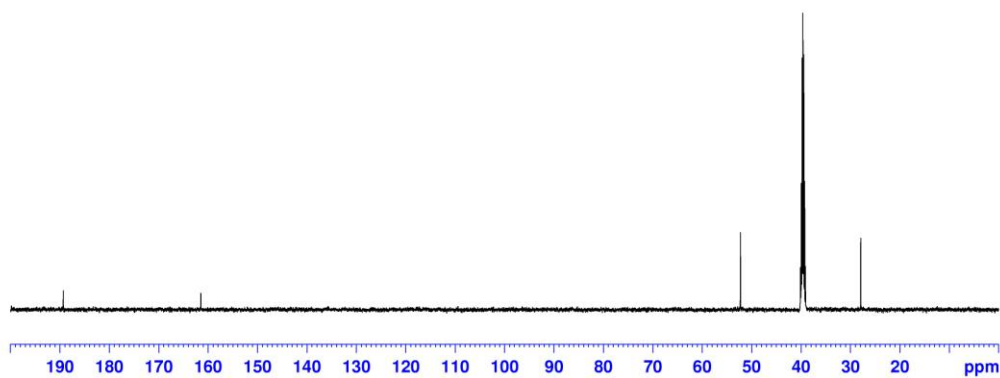
161.48



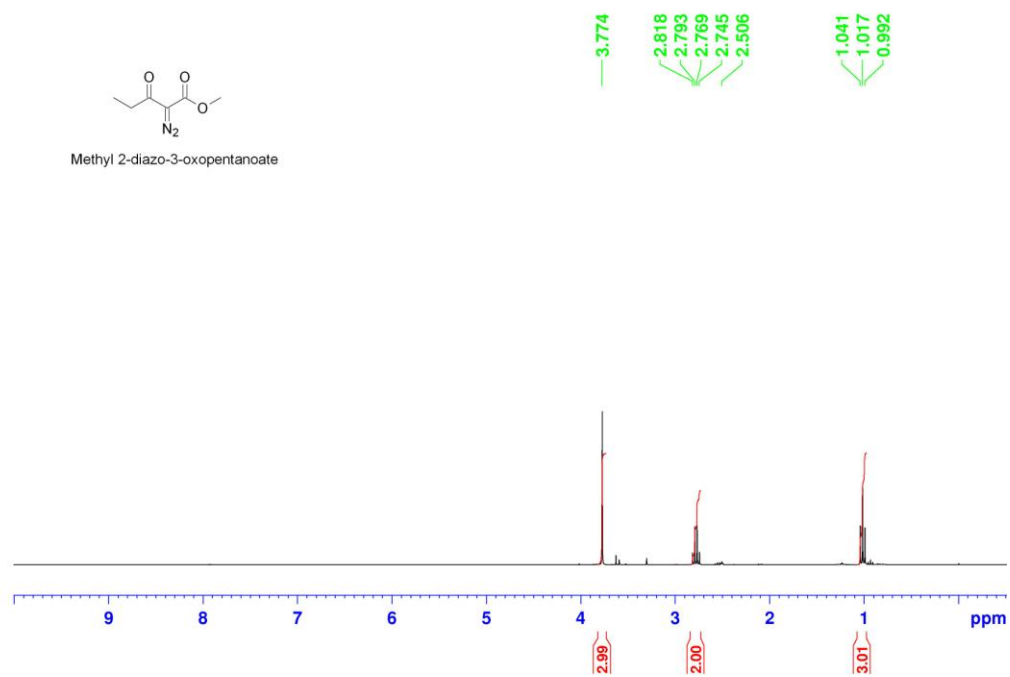
Methyl 2-diazo-3-oxobutanoate

52.26

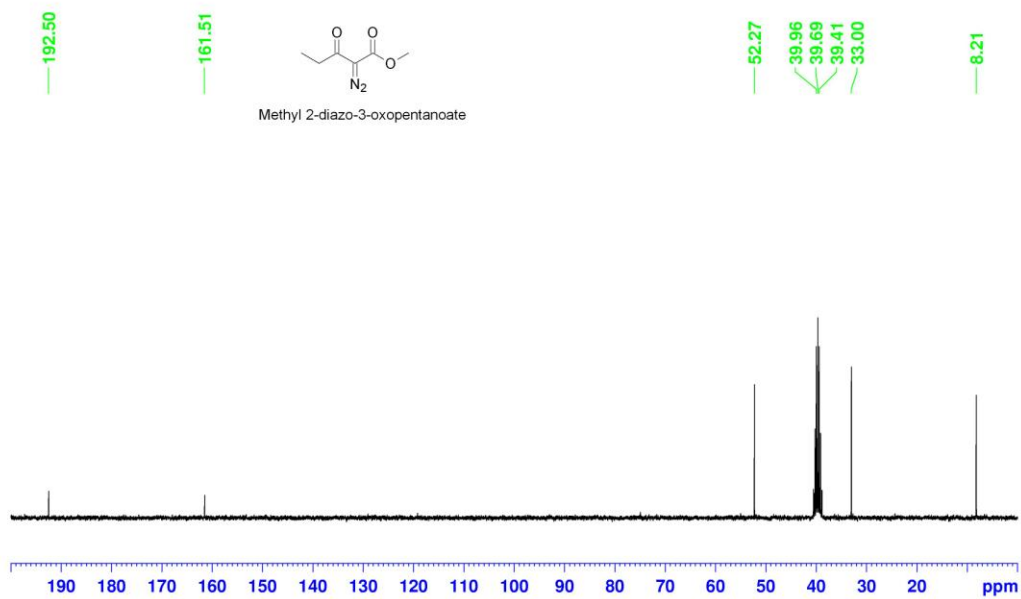
27.91



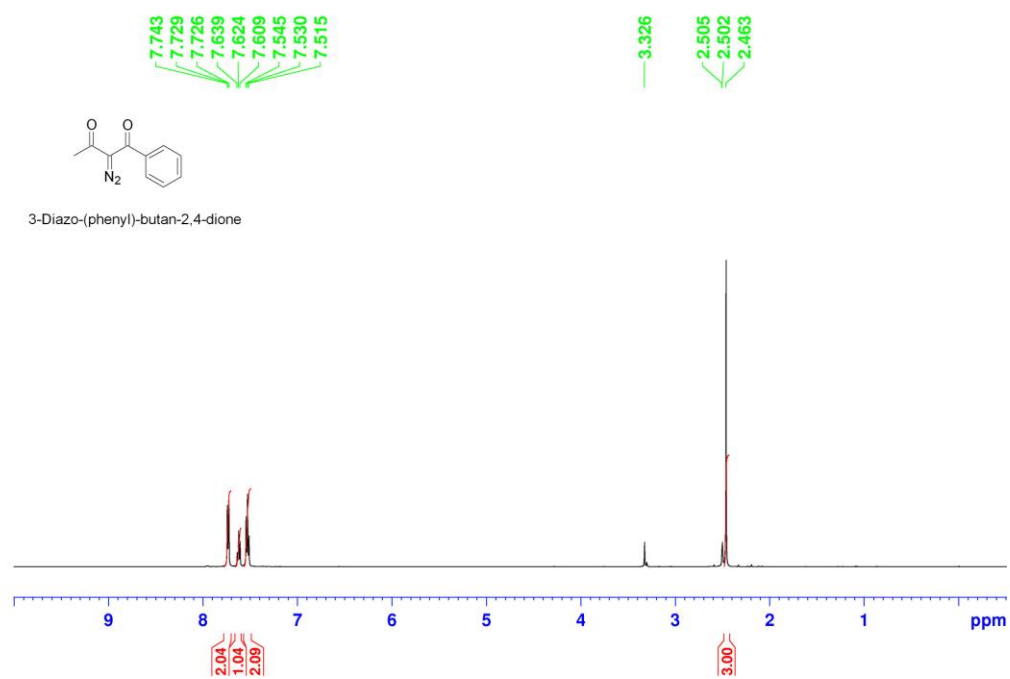
Methyl 2-diazo-3-oxopentanoate carbon spectrum (300 MHz) in DMSO-d6



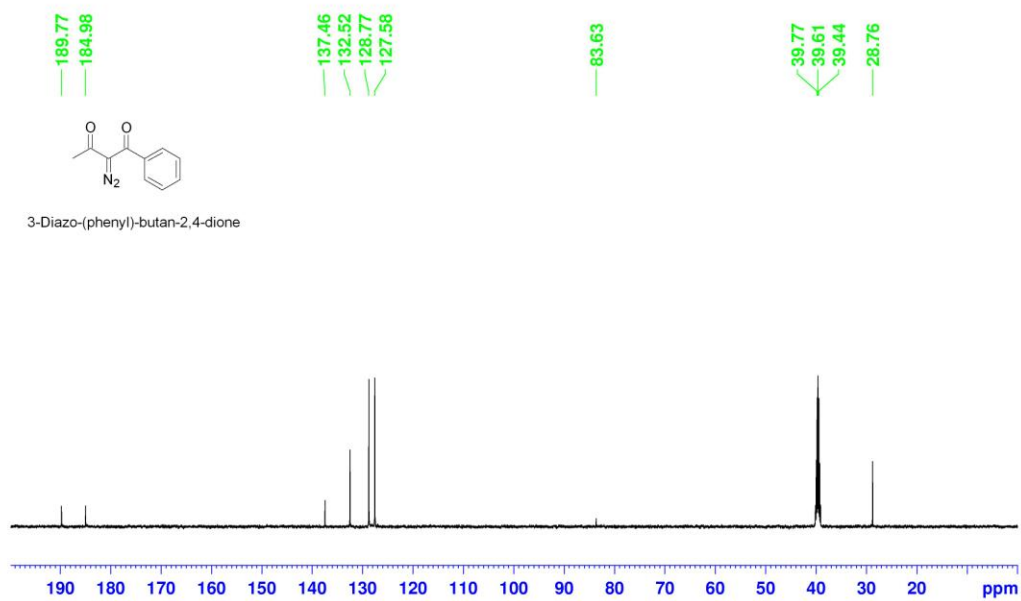
Methyl 2-diazo-3-oxopentanoate carbon spectrum (75 MHz) in DMSO-d6



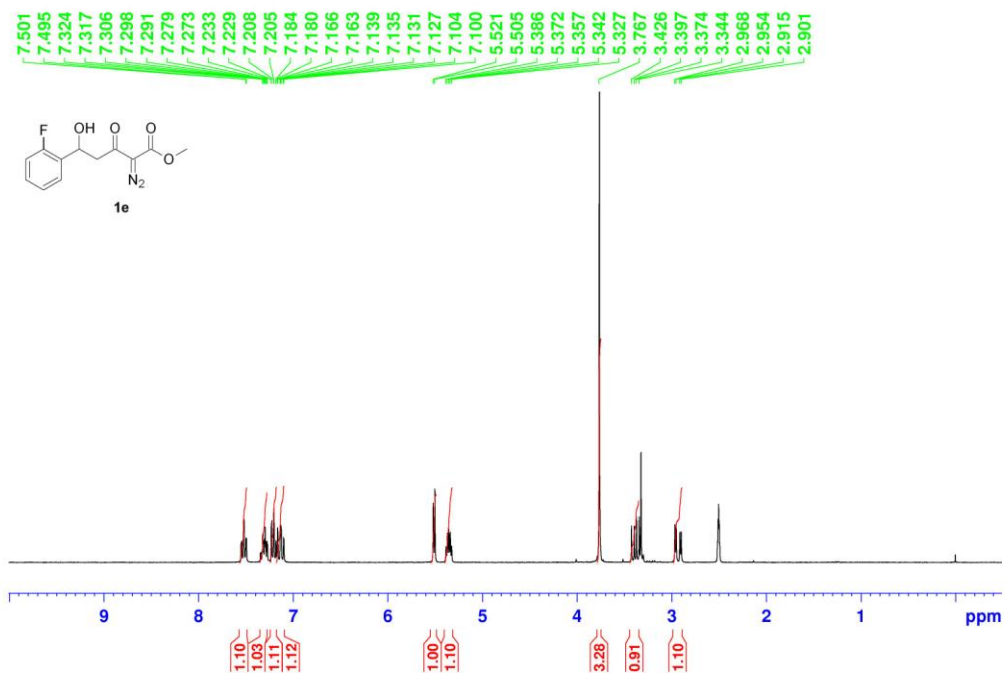
3-diazo-(phenyl)-butan-2,4-dione proton spectrum (500 MHz) in DMSO-d6



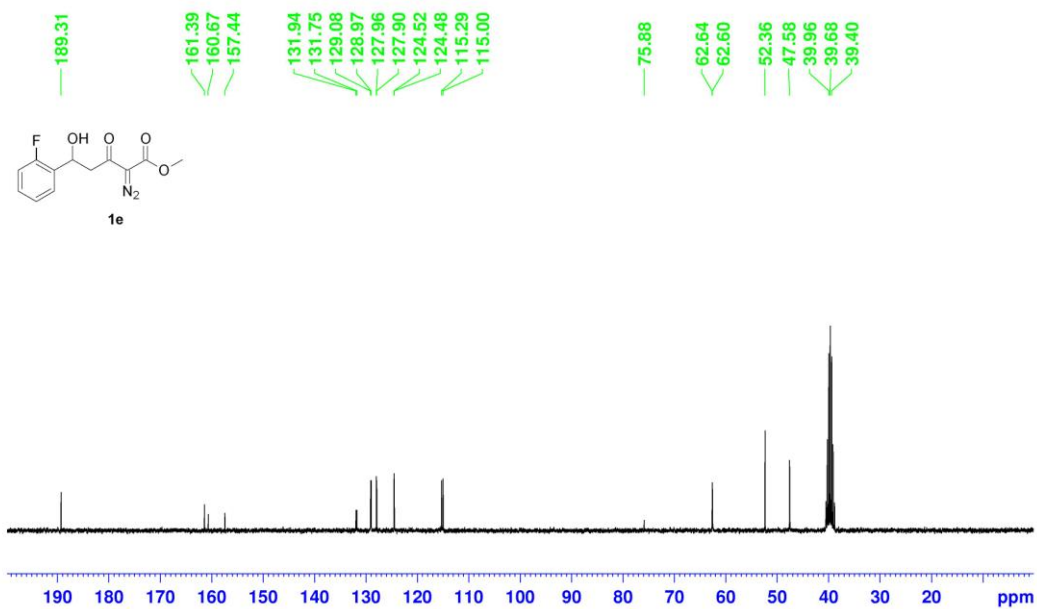
3-diazo-(phenyl)-butan-2,4-dione carbon spectrum (125 MHz) in DMSO-d6



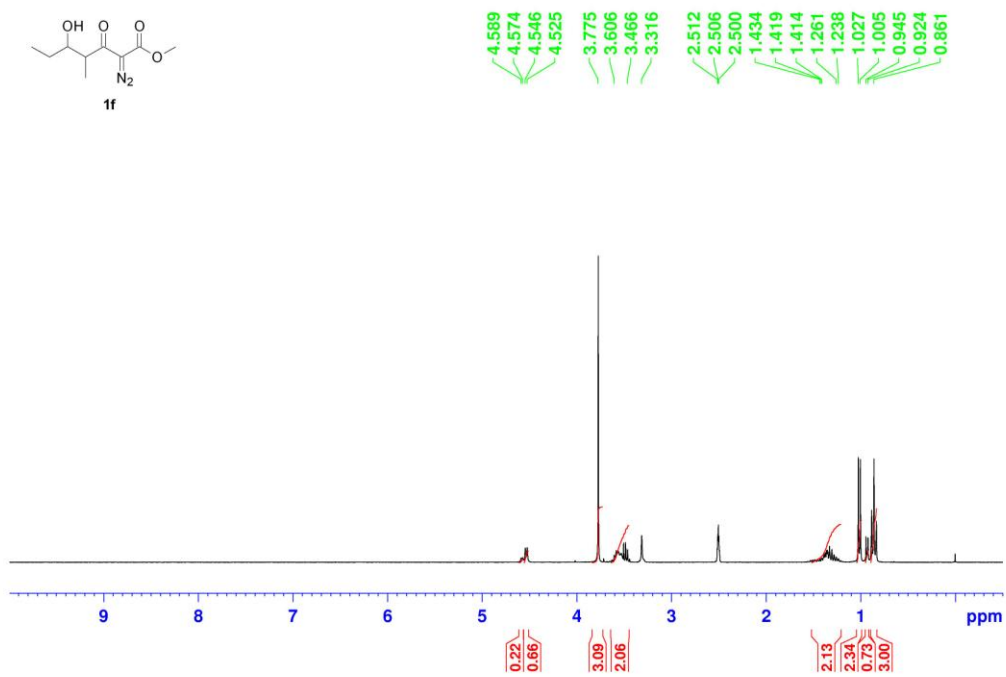
1e proton spectrum (300 MHz) in DMSO-d6



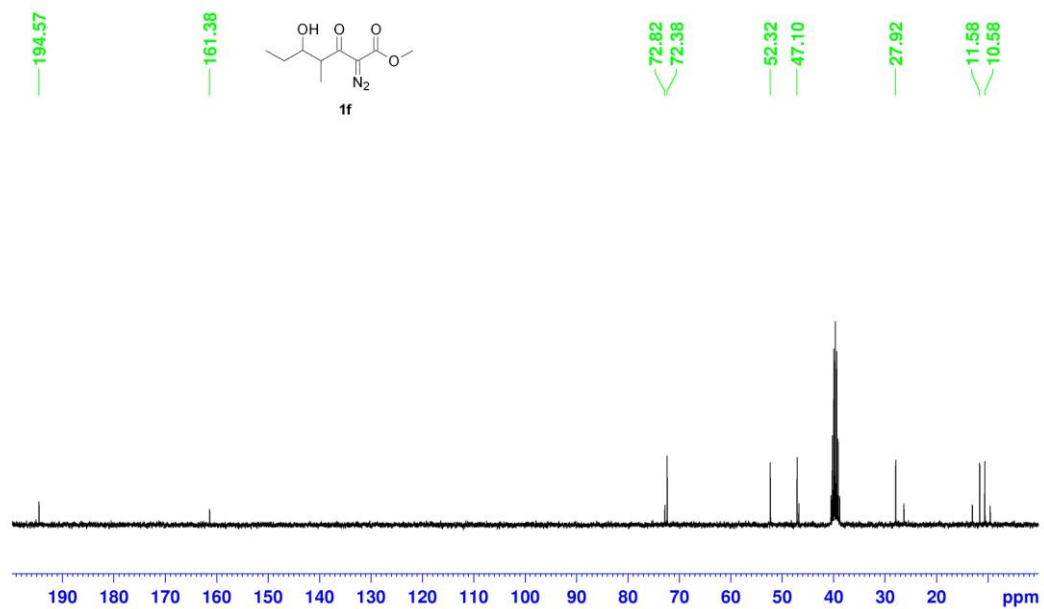
1e carbon spectrum (75 MHz) in DMSO-d6



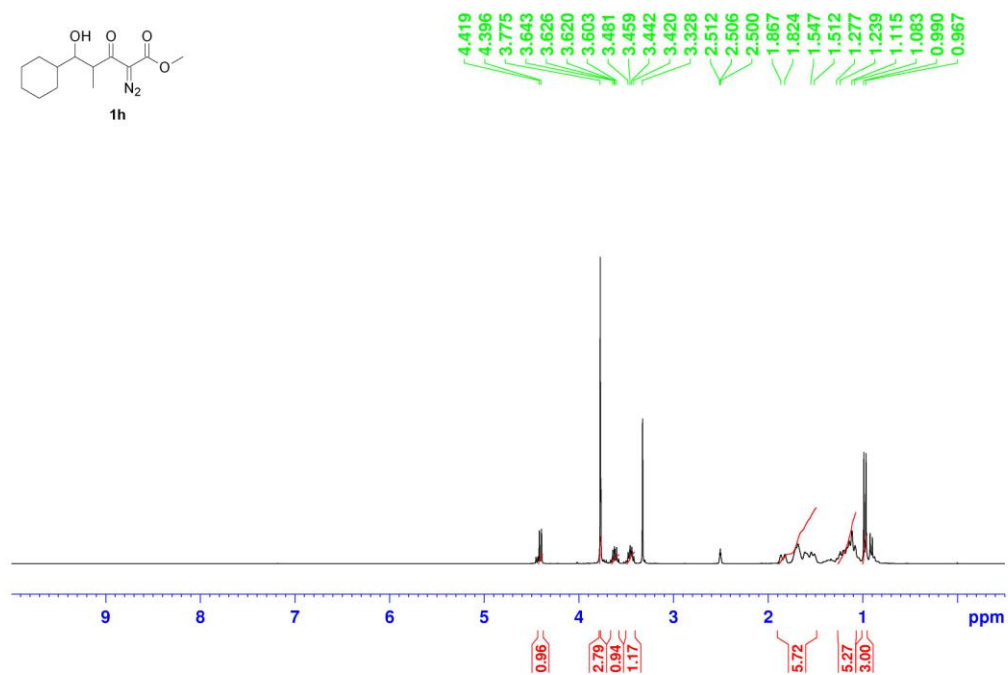
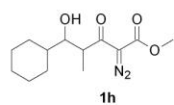
1f proton spectrum (300 MHz) in DMSO-d6



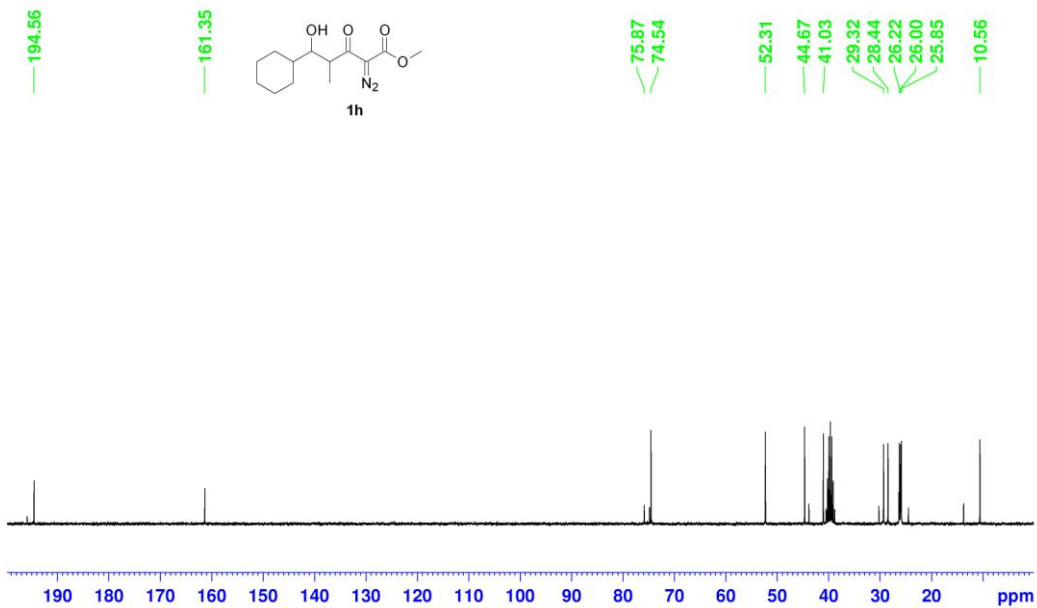
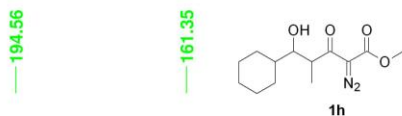
1f carbon spectrum (75 MHz) in DMSO-d6



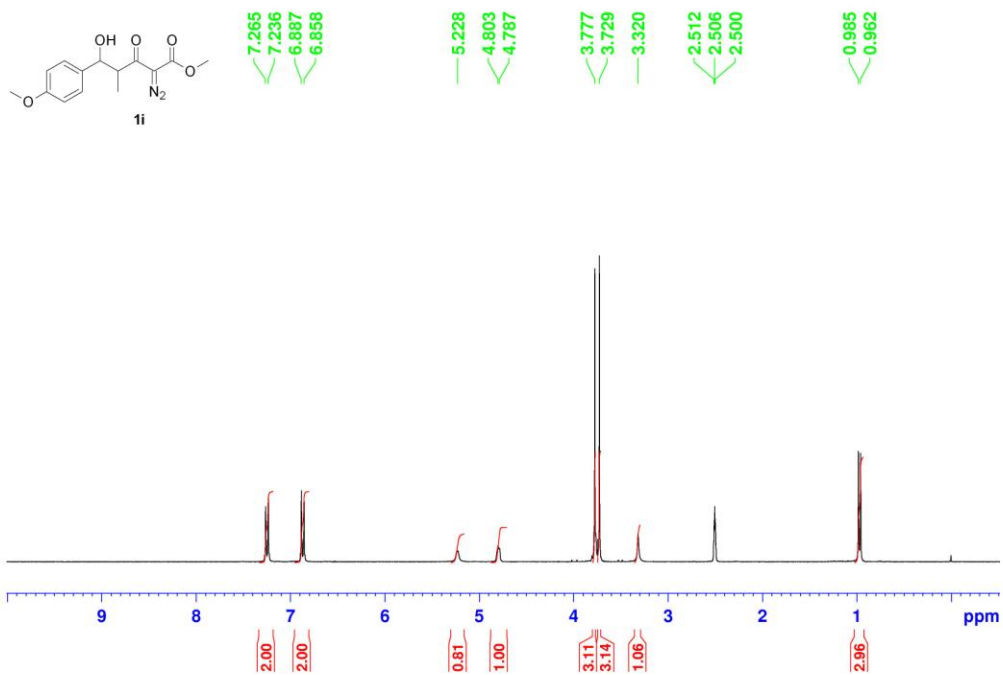
1h proton spectrum (300 MHz) in DMSO-d6



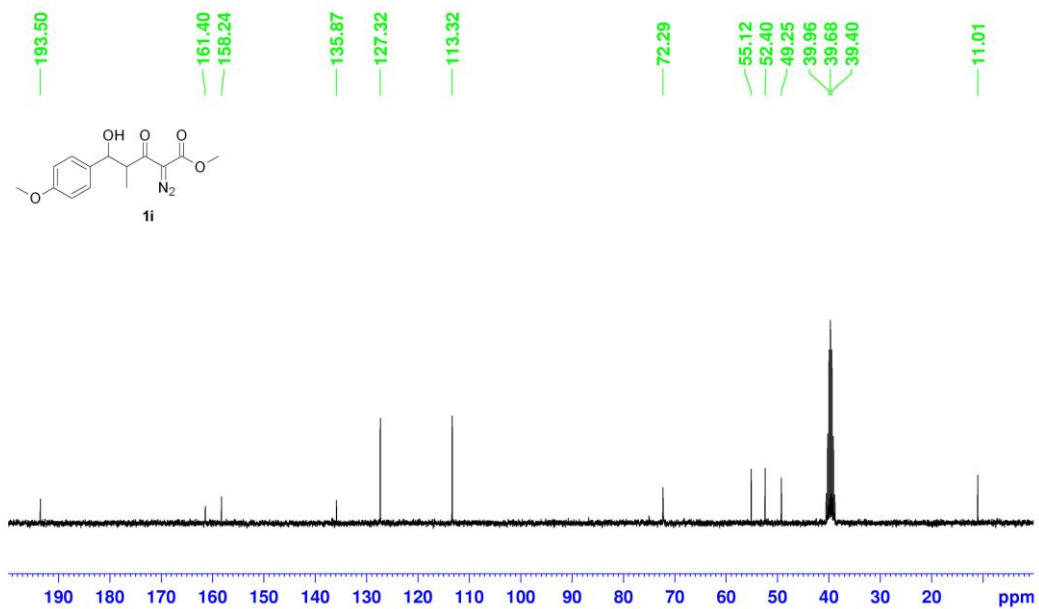
1h carbon spectrum (75 MHz) in DMSO-d6



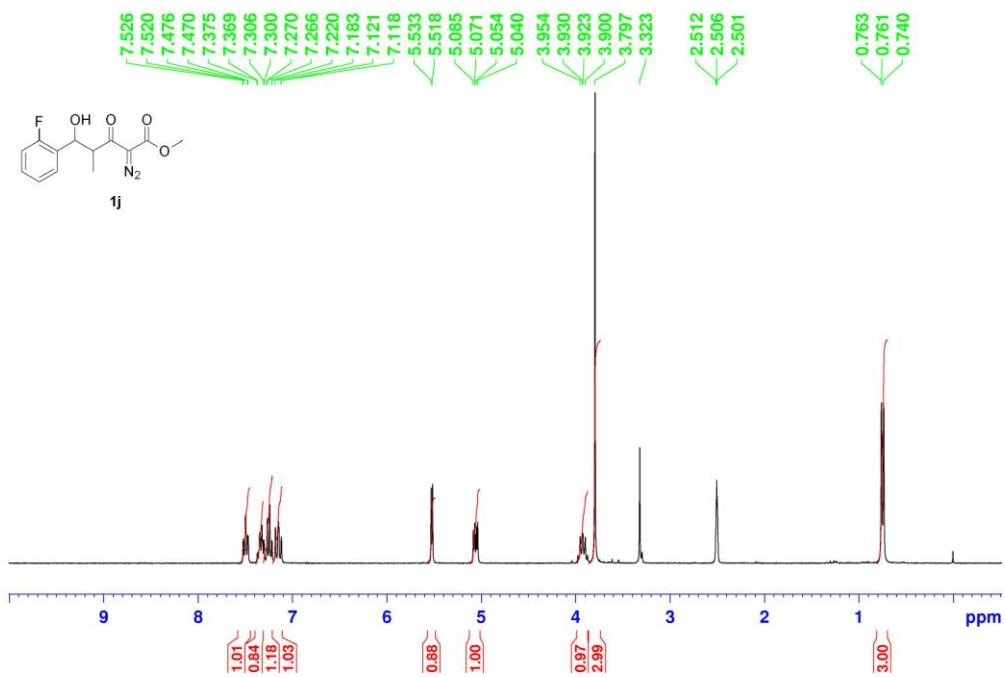
1i proton spectrum (300 MHz) in DMSO-d6



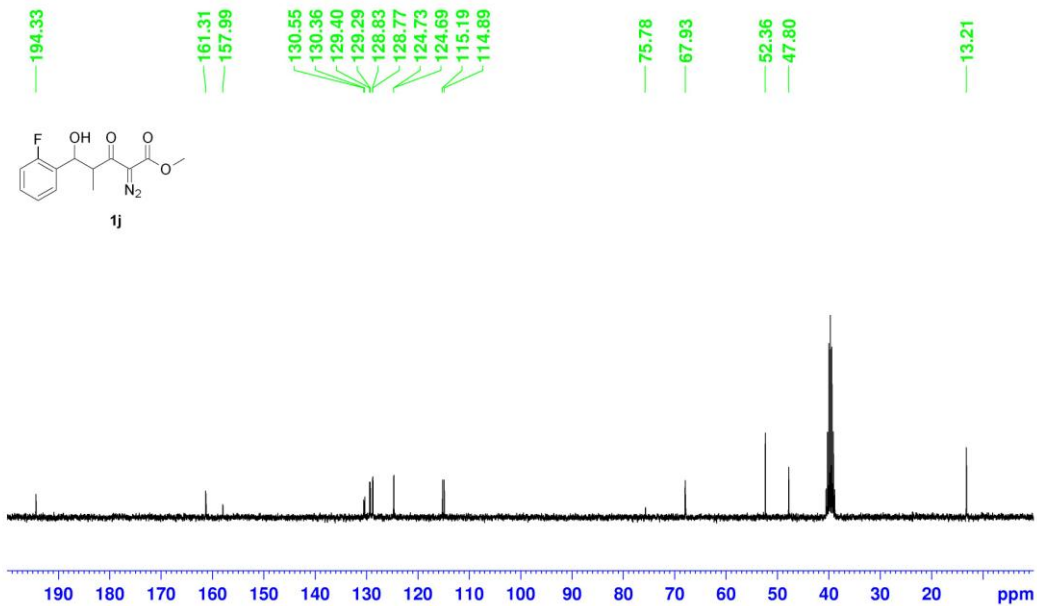
1i carbon spectrum (75 MHz) in DMSO-d6



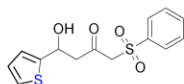
1j proton spectrum (300 MHz) in DMSO-d6



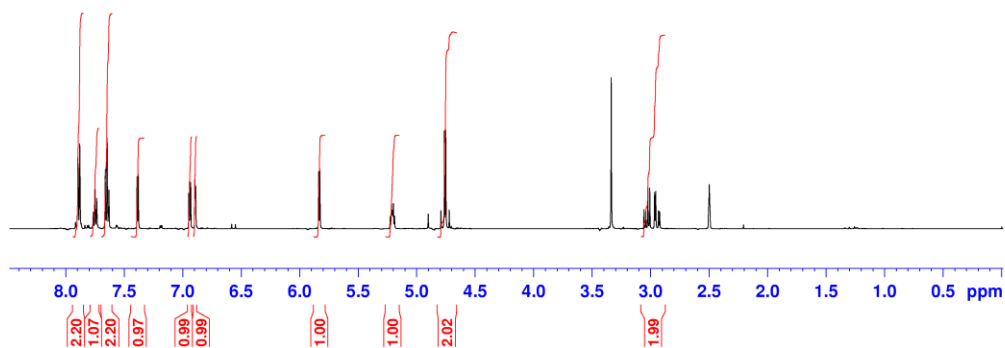
1j carbon spectrum (75 MHz) in DMSO-d6



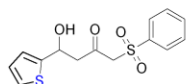
4-hydroxy-1-phenylsulfonyl-4-(thiophene-2-yl)-2-butanone proton spectrum (500 MHz) in DMSO-d6



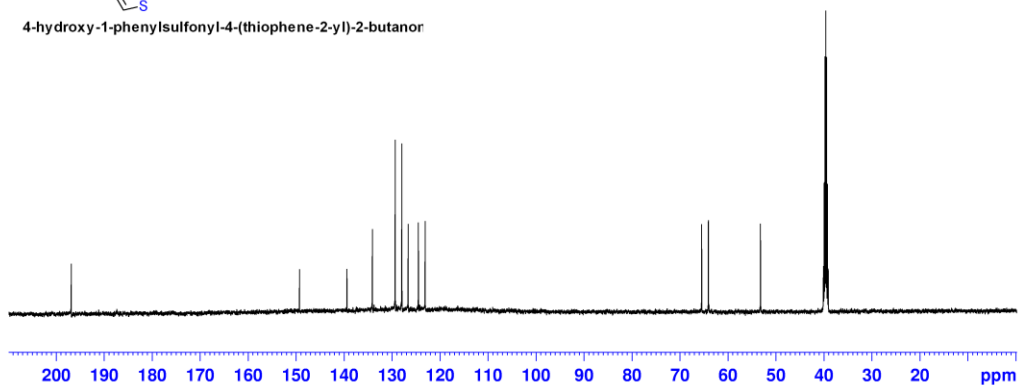
4-hydroxy-1-phenylsulfonyl-4-(thiophene-2-yl)-2-butanone



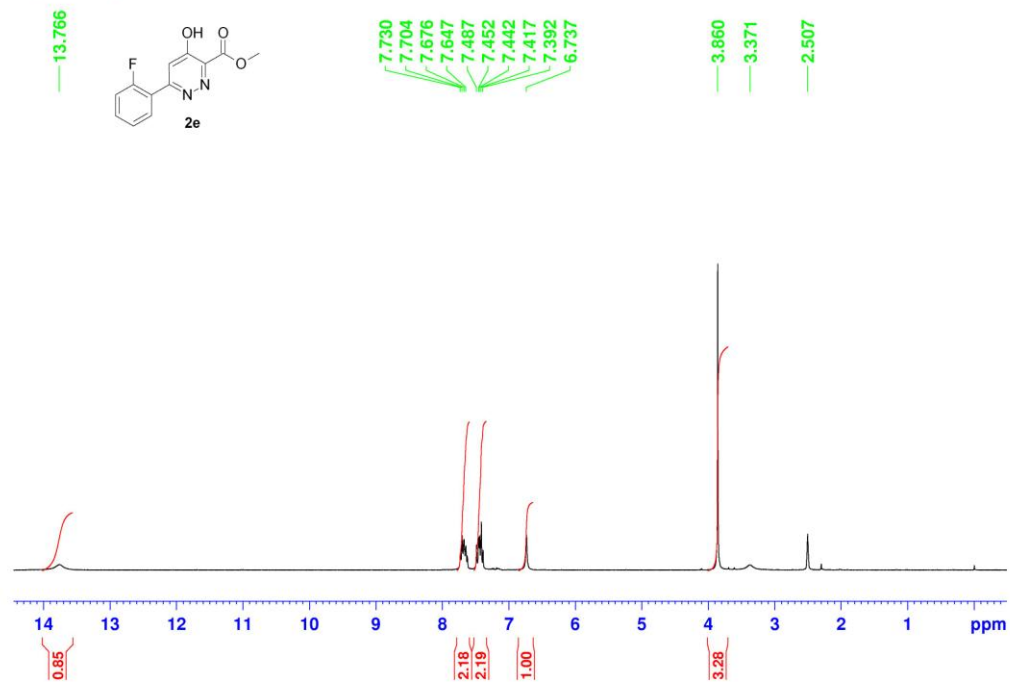
4-hydroxy-1-phenylsulfonyl-4-(thiophene-2-yl)-2-butanone carbon spectrum (125 MHz) in DMSO-d6



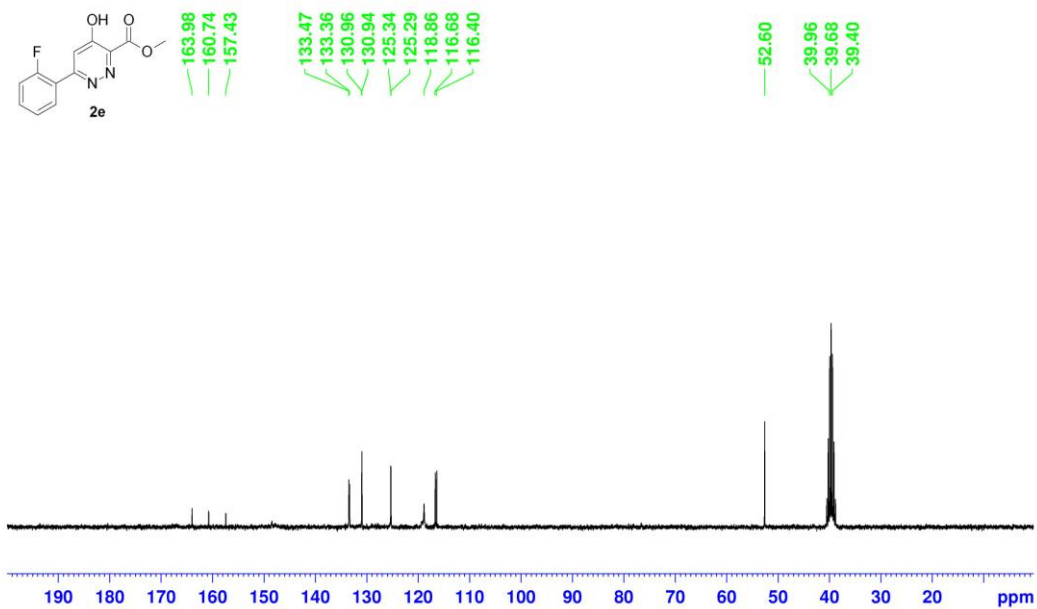
4-hydroxy-1-phenylsulfonyl-4-(thiophene-2-yl)-2-butanone



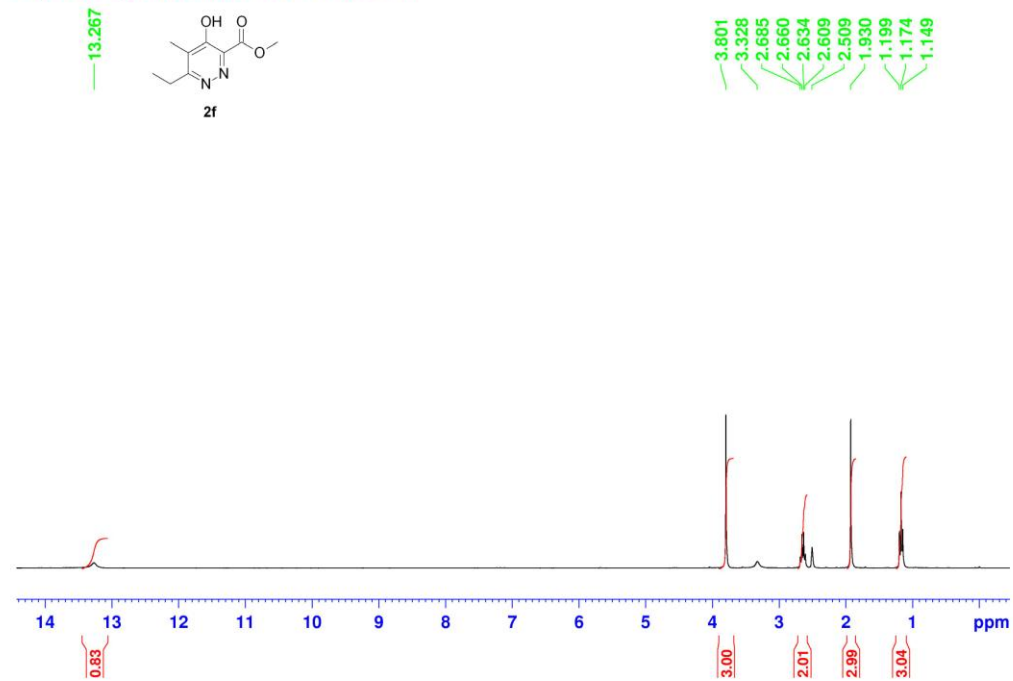
2e proton spectrum (300 MHz) in DMSO-d6



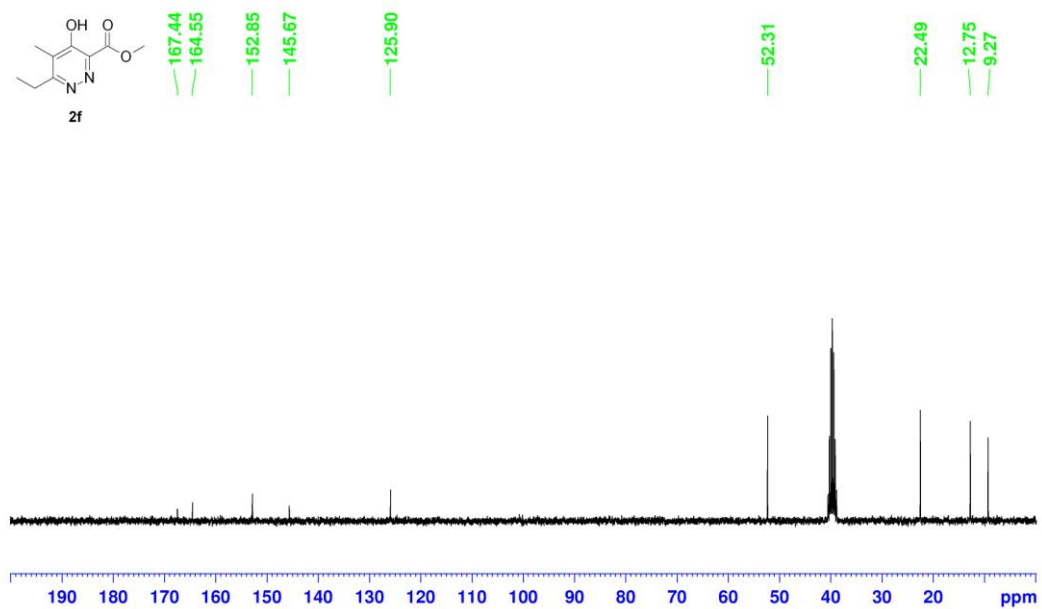
2e carbon spectrum (75 MHz) in DMSO-d6



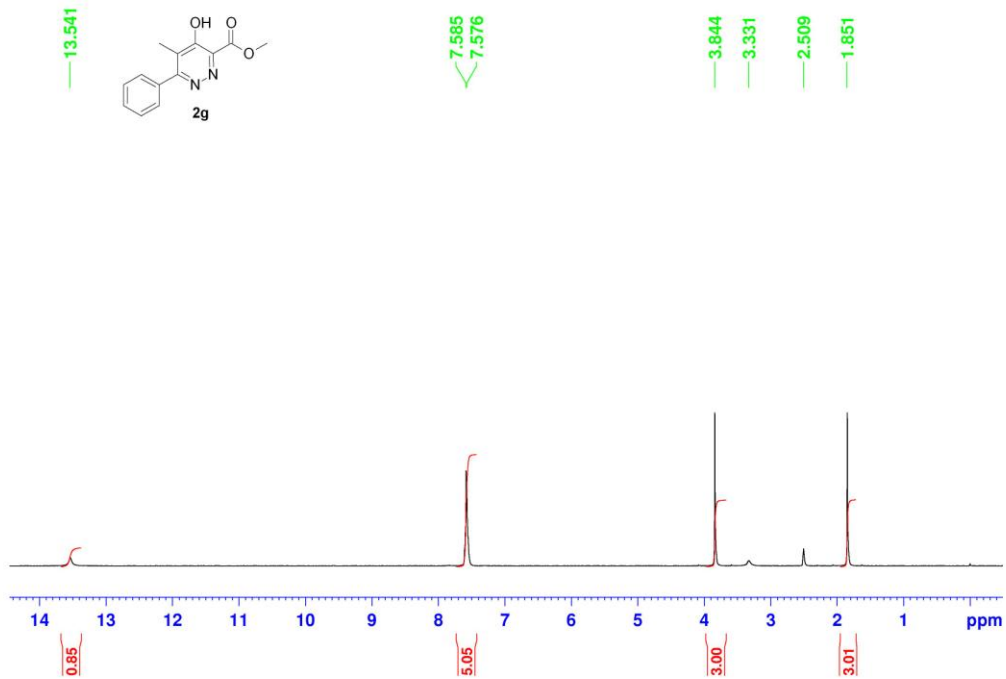
2f proton spectrum (300 MHz) in DMSO-d6



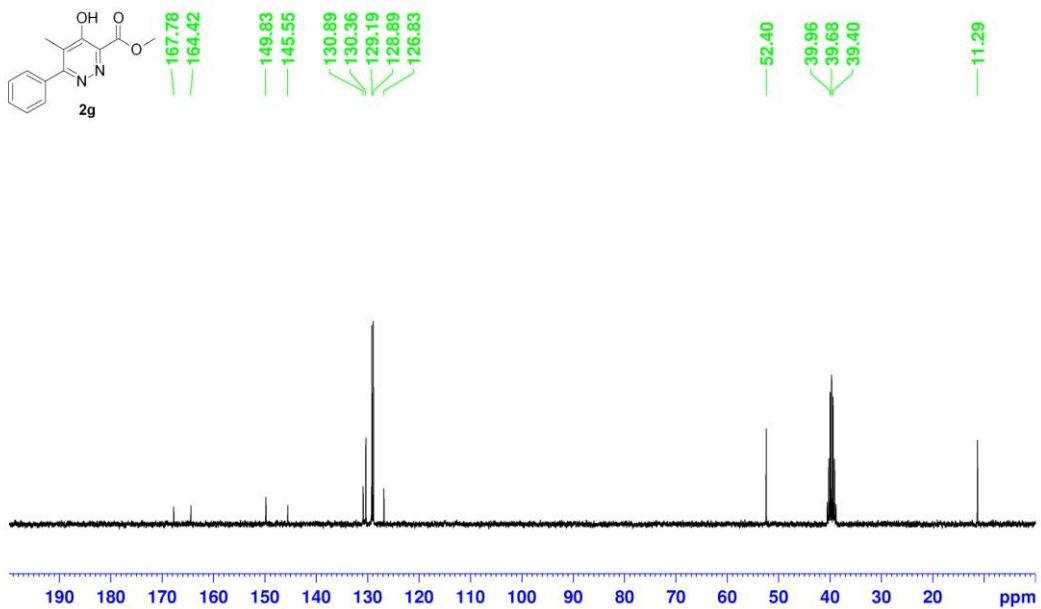
2f carbon spectrum (75 MHz) in DMSO-d6



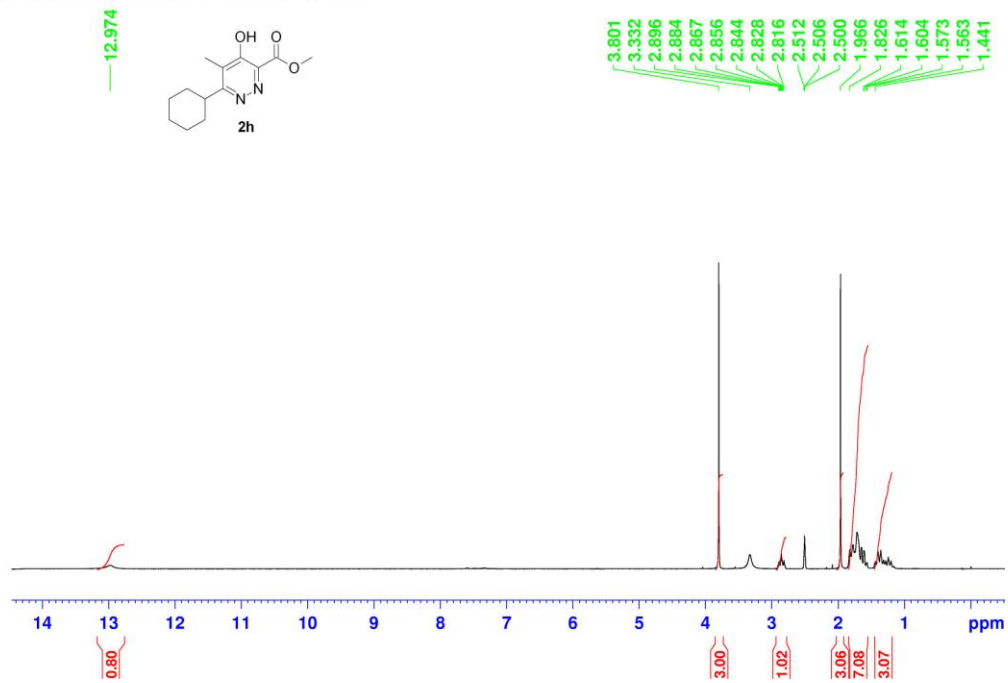
2g proton spectrum (300 MHz) in DMSO-d6



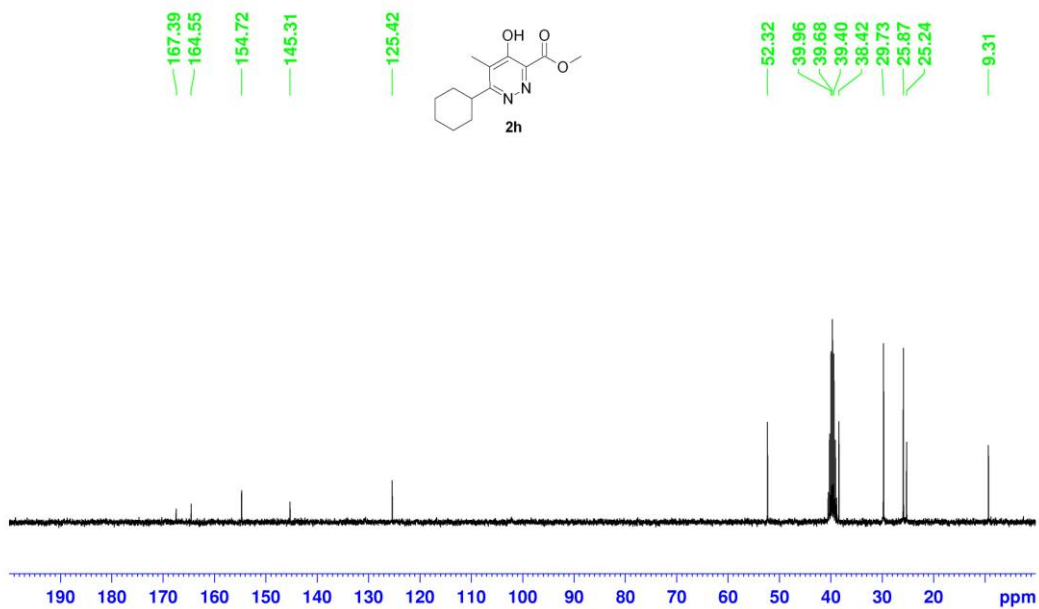
2g carbon spectrum (75 MHz) in DMSO-d6



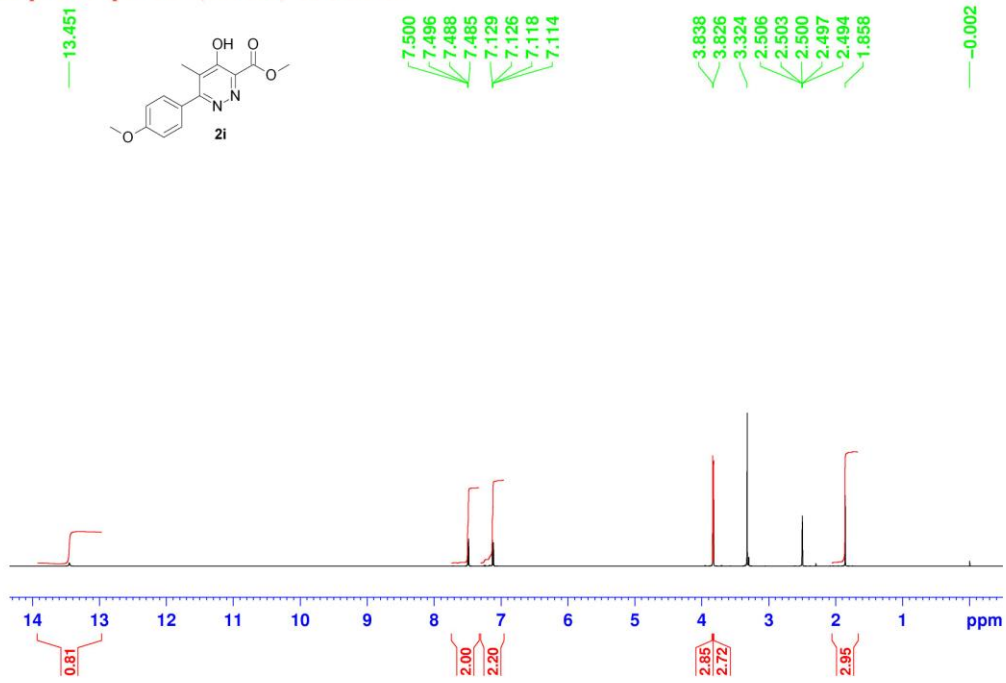
2h proton spectrum (300 MHz) in DMSO-d6



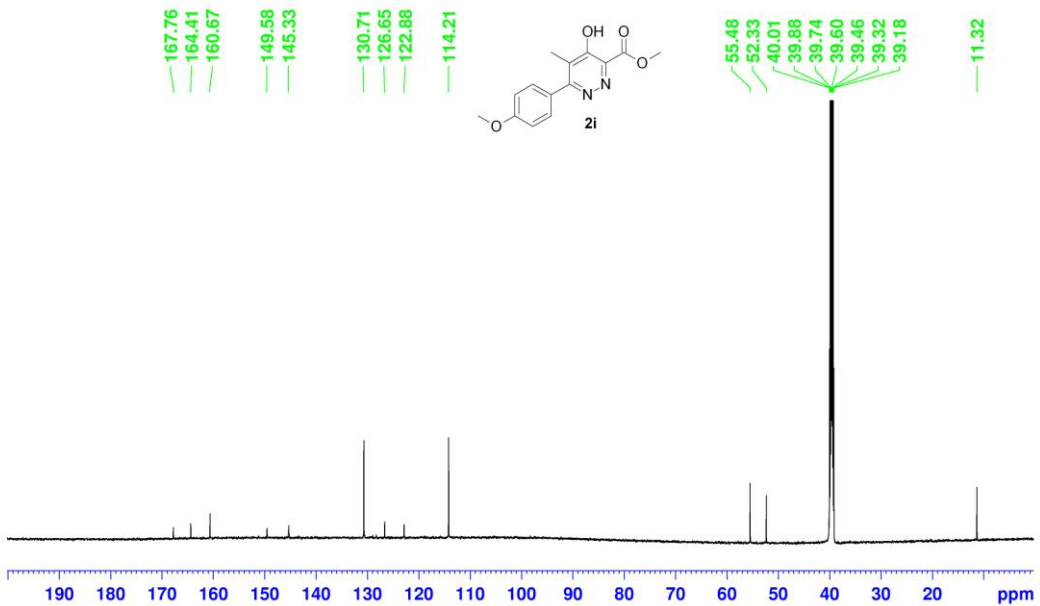
2h carbon spectrum (75 MHz) in DMSO-d6



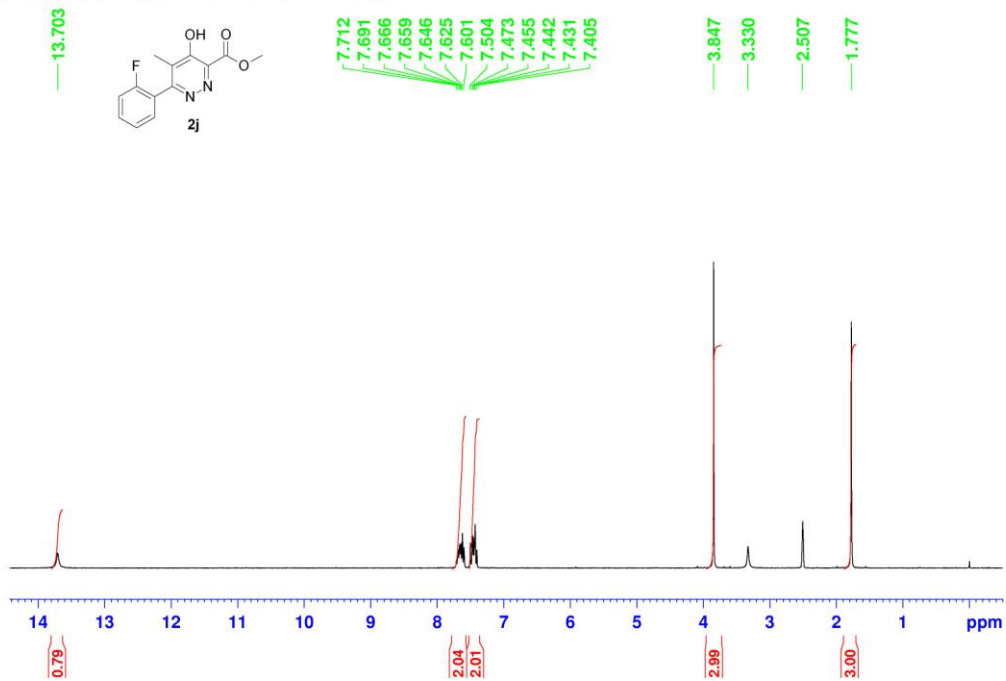
2i proton spectrum (600 MHz) in DMSO-d6



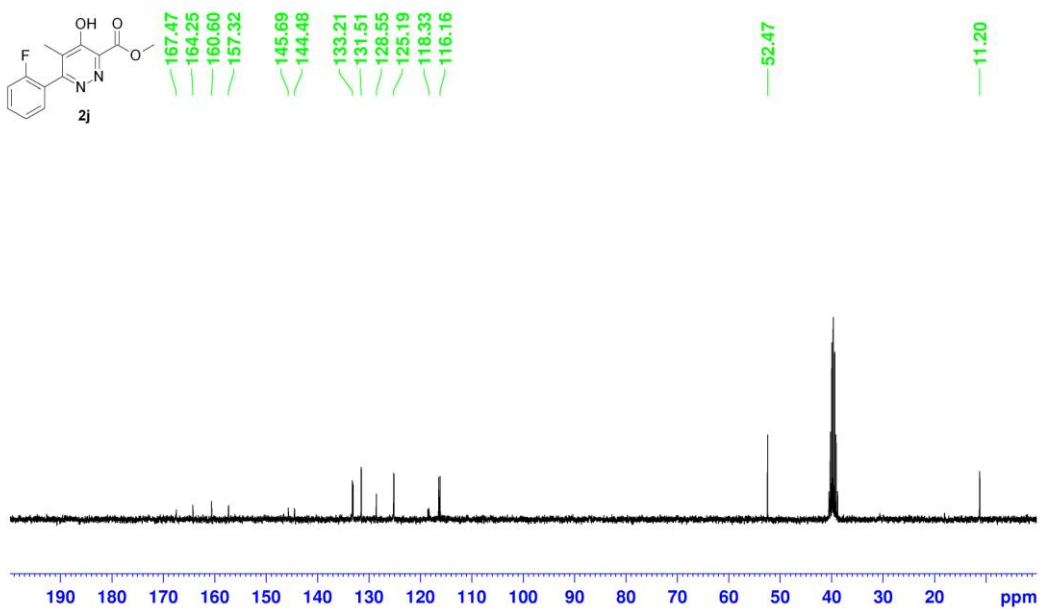
2i carbon spectrum (150 MHz) in DMSO-d6



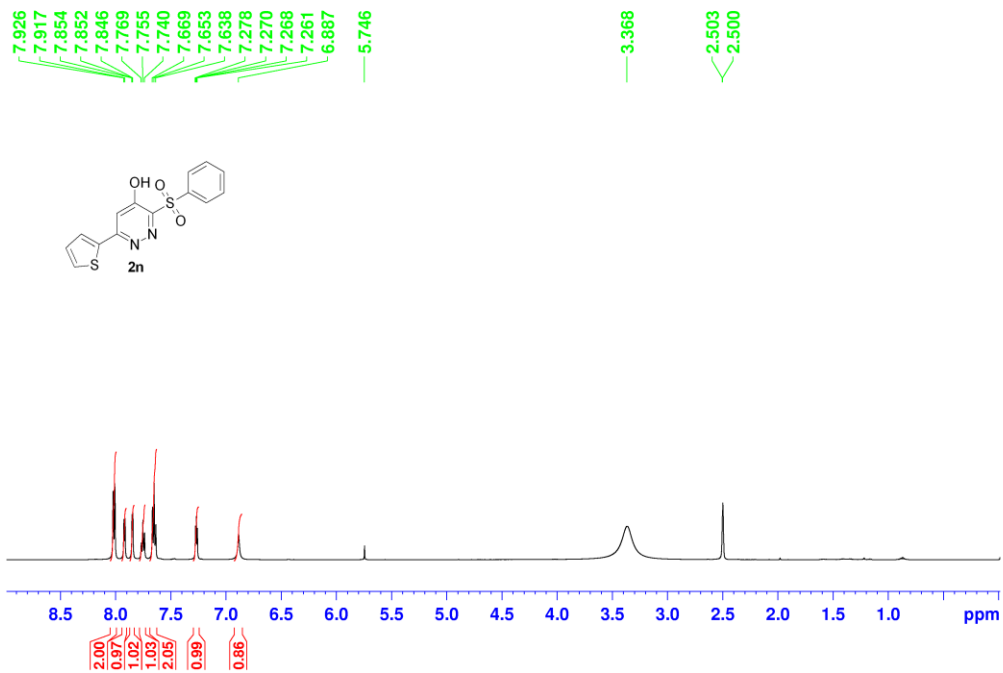
2j proton spectrum (300 MHz) in DMSO-d6



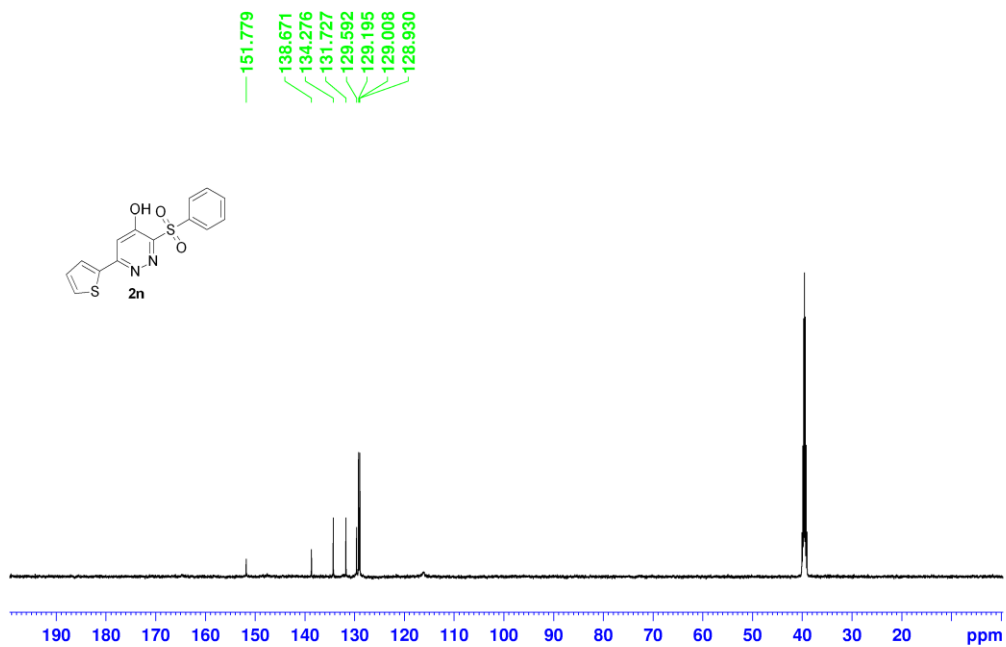
2j carbon spectrum (75 MHz) in DMSO-d6



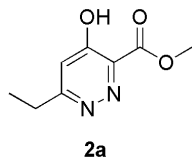
2n proton spectrum (500 MHz) in DMSO-d6



2n carbon spectrum (125 MHz) in DMSO-d6

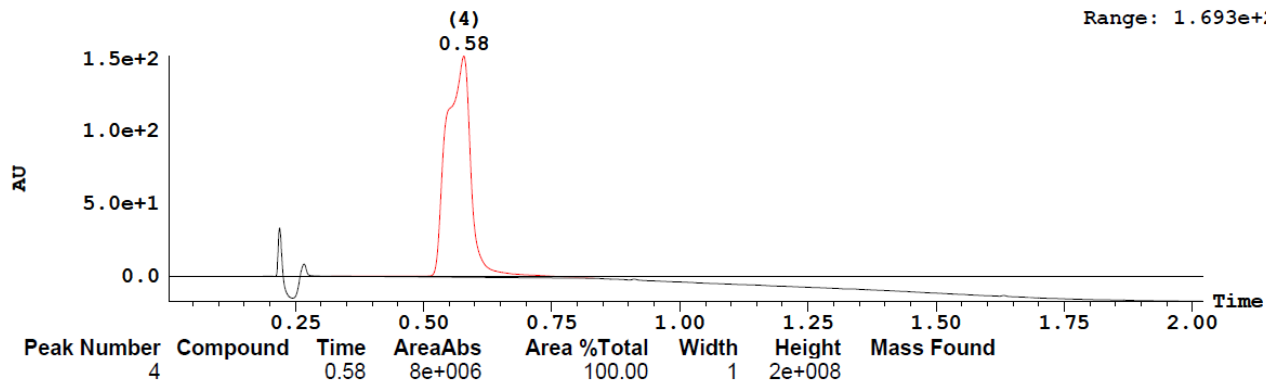


LC/MS ANALYSIS

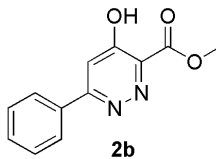
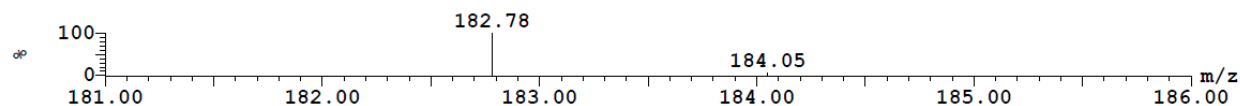


UV Detector: TIC

1.521e+2
Range: 1.693e+2

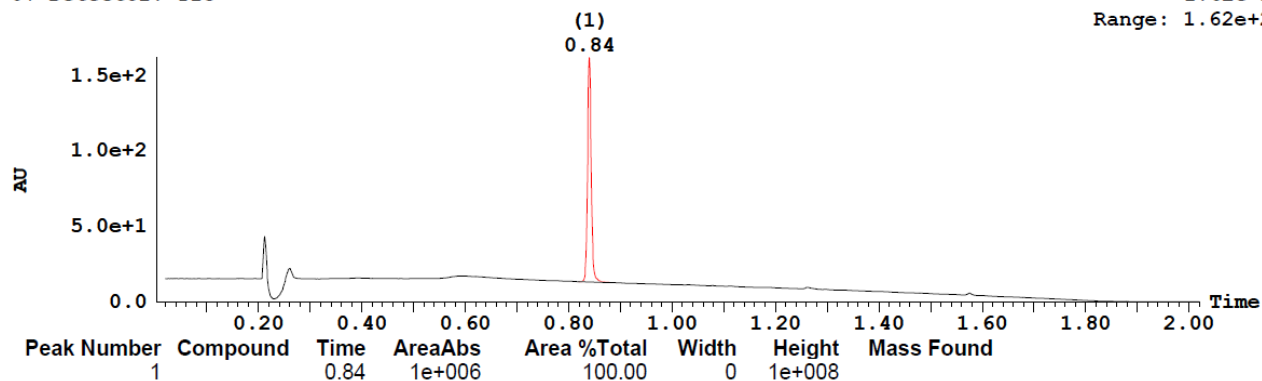


Peak ID Compound Time Mass Found
4 0.58
SAMPLE: 2:42 Combine (135:140) 1.1e+008

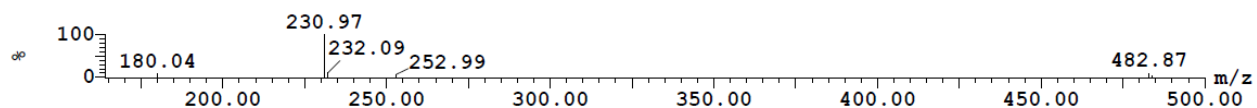


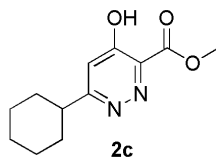
UV Detector: TIC

1.62e+2
Range: 1.62e+2



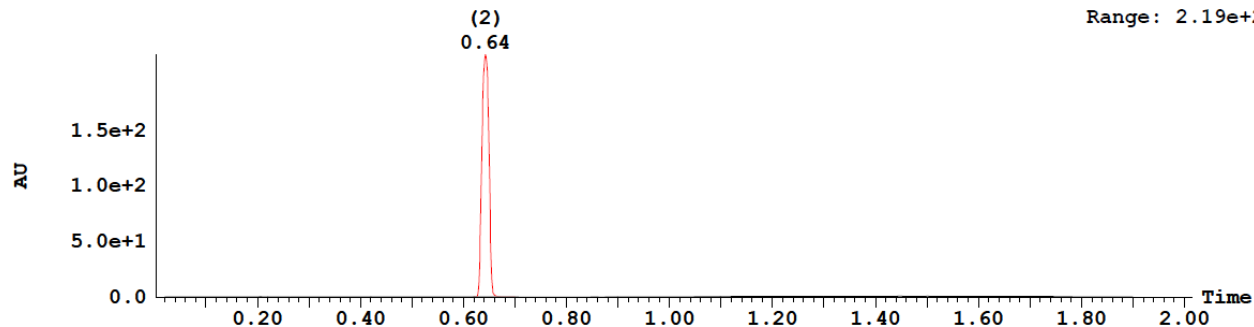
Peak ID Compound Time Mass Found
1 0.84
SAMPLE: 1:12 Combine (198:202) 4.3e+007





UV Detector: TIC

2.19e+2
Range: 2.19e+2

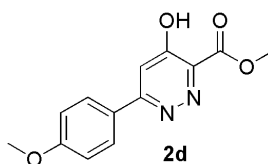
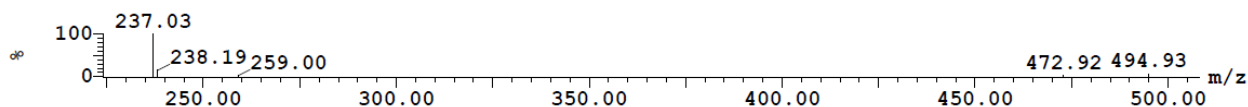


| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|-------------|----------|------|---------|-------------|-------|--------|------------|
| 2 | | 0.64 | 3e+006 | 100.00 | 0 | 2e+008 | |

Peak ID Compound Time Mass Found
2 0.64

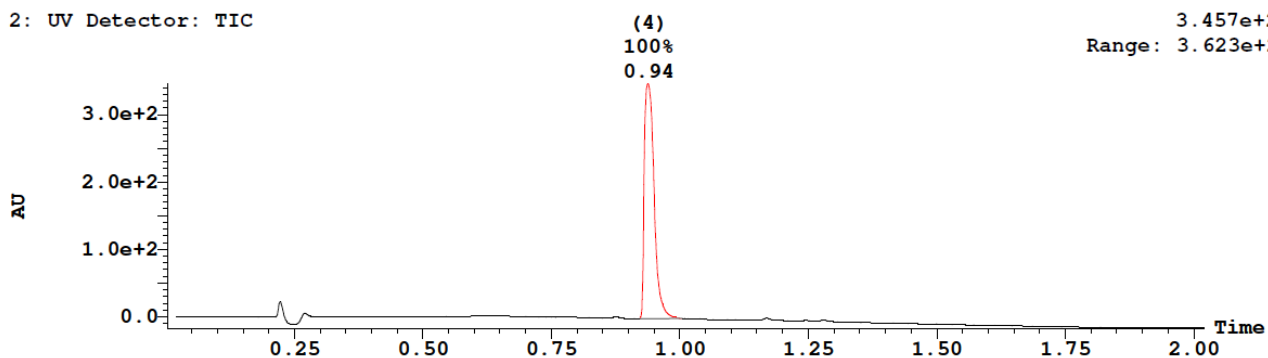
SAMPLE: 2:30 Combine (151:155)

1.2e+008



2: UV Detector: TIC

3.457e+2
Range: 3.623e+2

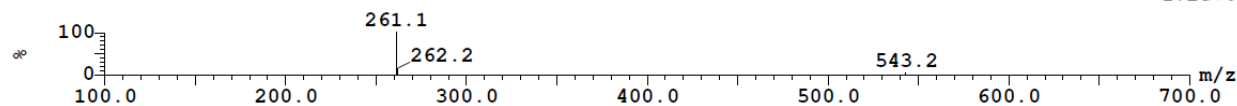


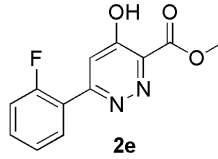
| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|-------------|----------|------|---------|-------------|-------|--------|------------|
| 4 | | 0.94 | 8e+006 | 100.00 | 0 | 3e+008 | |

Peak ID Compound Time Mass Found
4 0.94

4: (Time: 0.94) Combine (220:225)

1: MS ES+
1.2e+008

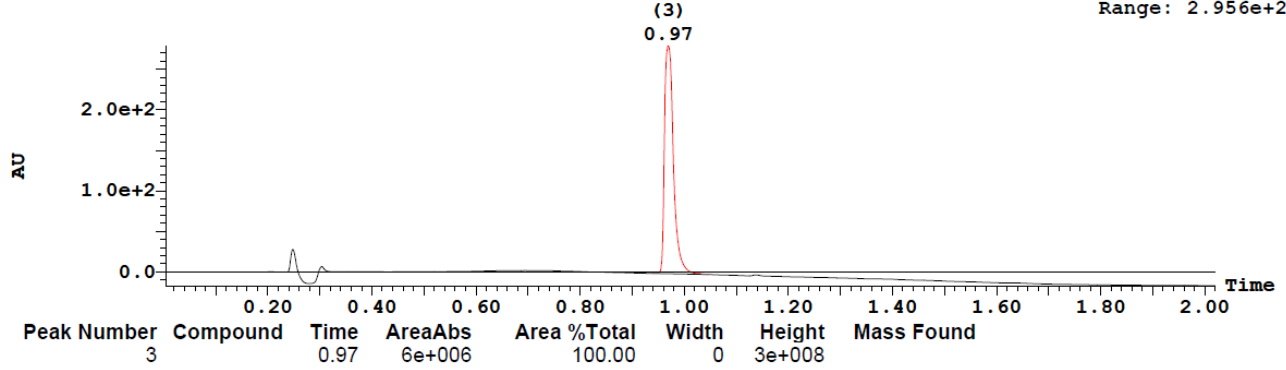




UV Detector: TIC

2.788e+2

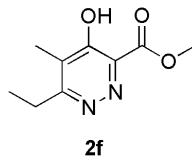
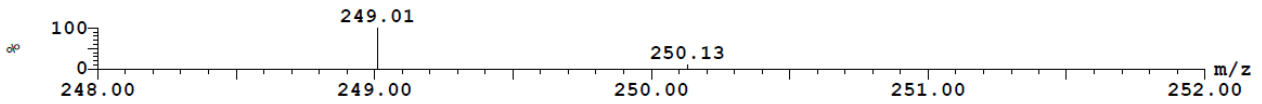
Range: 2.956e+2



Peak ID Compound Time Mass Found

3 0.97

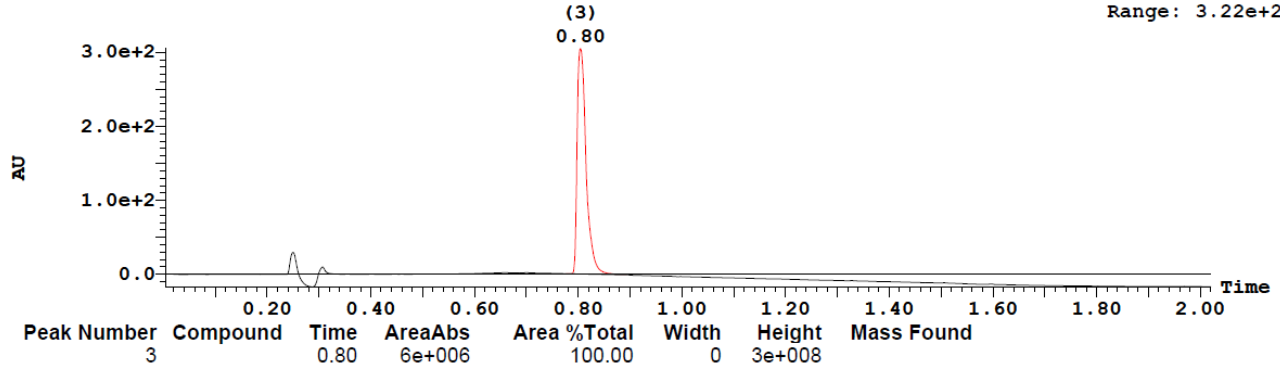
SAMPLE: 1:5 Combine (227:232) 8.3e+007



UV Detector: TIC

3.051e+2

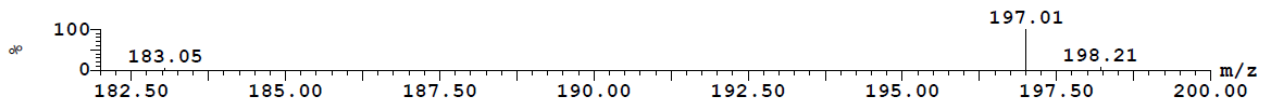
Range: 3.22e+2

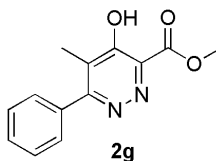


Peak ID Compound Time Mass Found

3 0.80

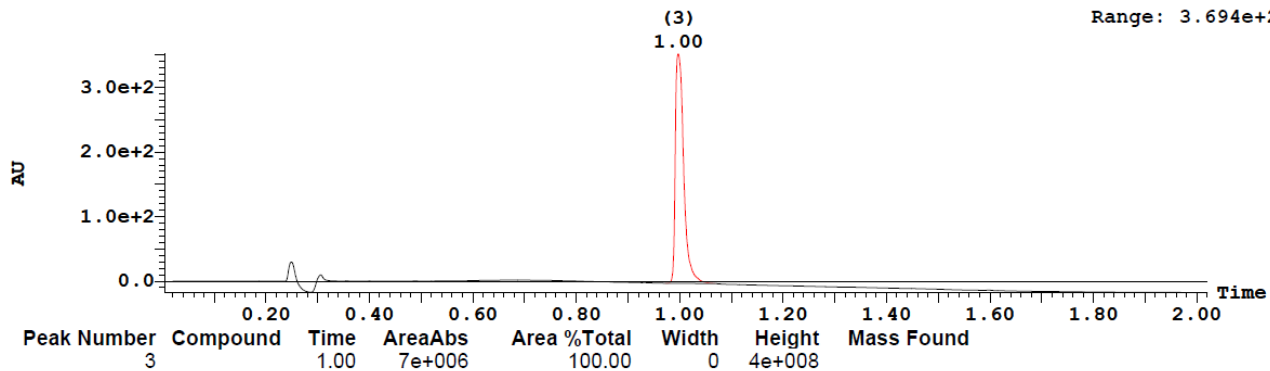
SAMPLE: 1:4 Combine (188:193) 1.1e+008





UV Detector: TIC

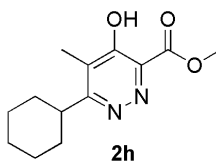
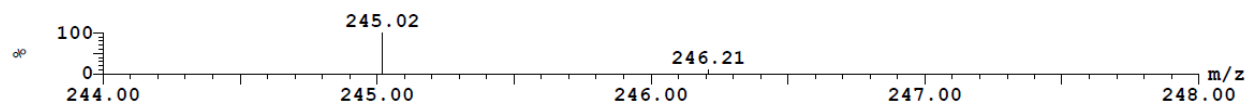
3.519e+2
Range: 3.694e+2



Peak ID Compound Time Mass Found
3 1.00

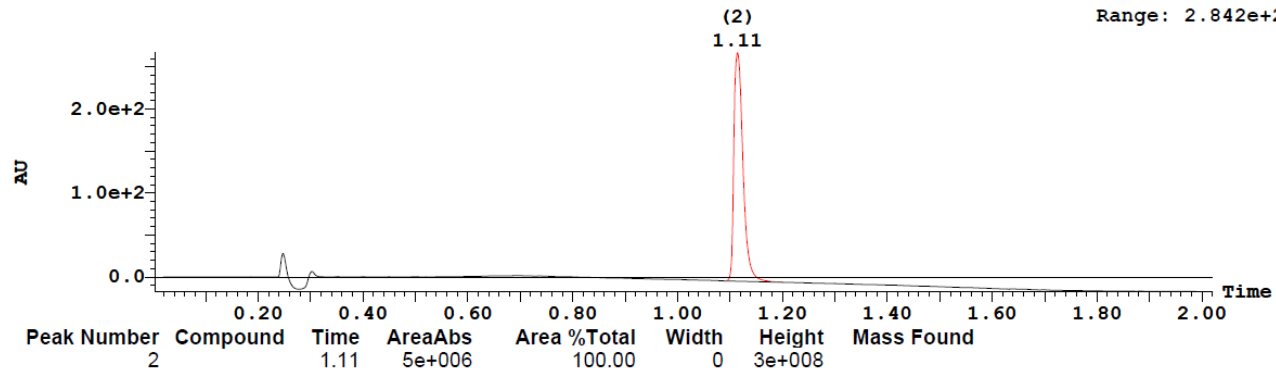
SAMPLE: 1:5 Combine (234:239)

1.1e+008



UV Detector: TIC

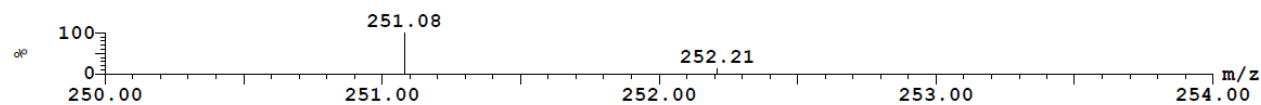
2.67e+2
Range: 2.842e+2

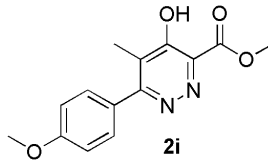


Peak ID Compound Time Mass Found
2 1.11

SAMPLE: 1:6 Combine (262:267)

1.1e+008

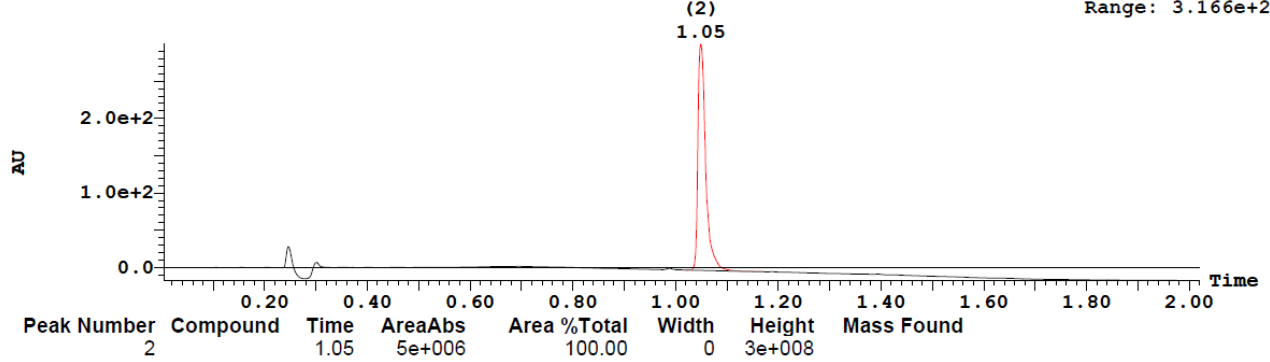




UV Detector: TIC

2.994e+2

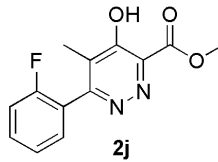
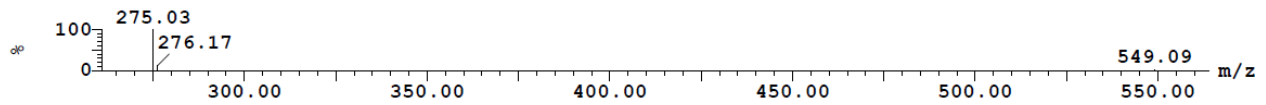
Range: 3.166e+2



Peak ID Compound Time Mass Found

SAMPLE: 1:3 Combine (246:251)

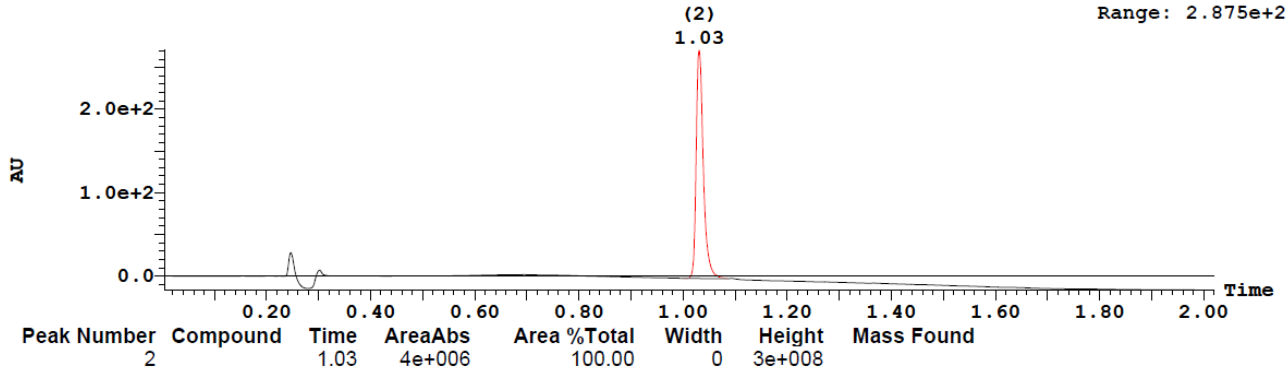
9.8e+007



UV Detector: TIC

2.709e+2

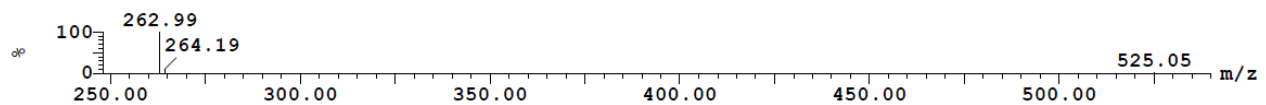
Range: 2.875e+2

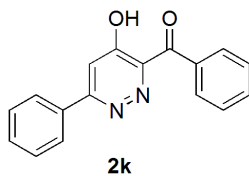


Peak ID Compound Time Mass Found

SAMPLE: 1:2 Combine (242:247)

8.0e+007

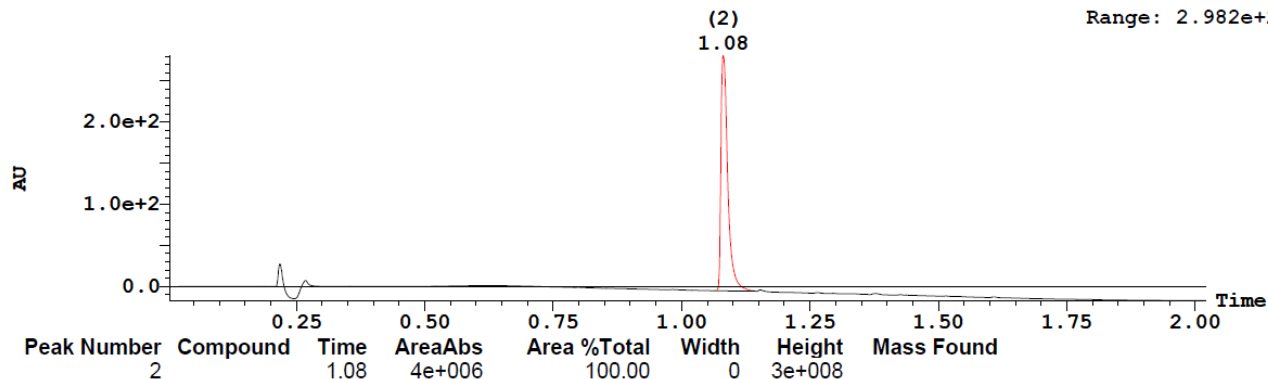




UV Detector: TIC

2.811e+2

Range: 2.982e+2

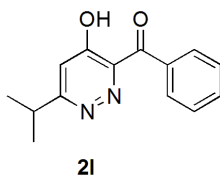
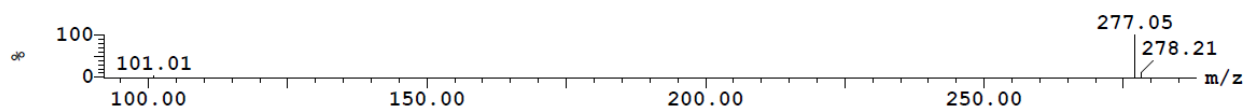


Peak ID Compound Time Mass Found

2 1.08

SAMPLE: 2:13 Combine (254:259)

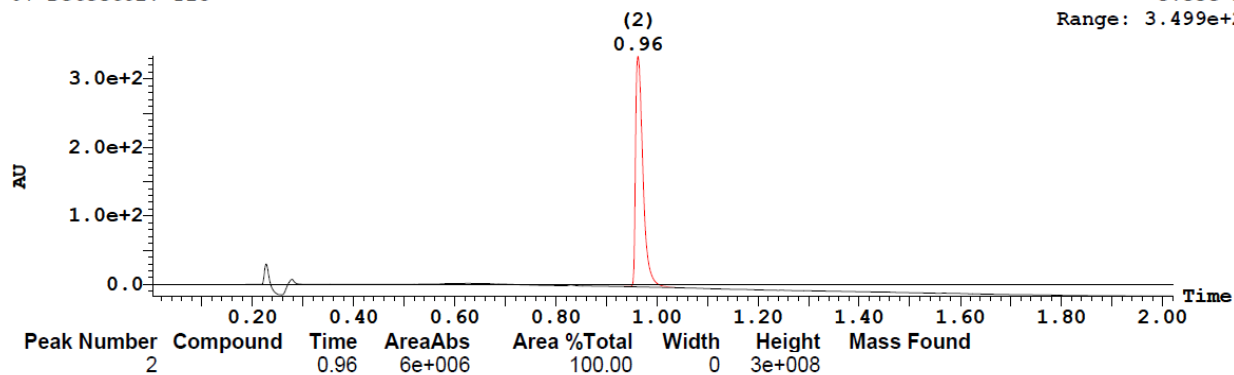
5.8e+007



UV Detector: TIC

3.33e+2

Range: 3.499e+2

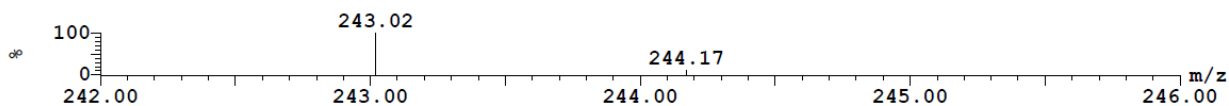


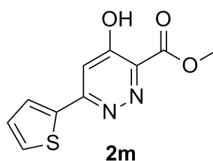
Peak ID Compound Time Mass Found

2 0.96

SAMPLE: 1:37 Combine (226:231)

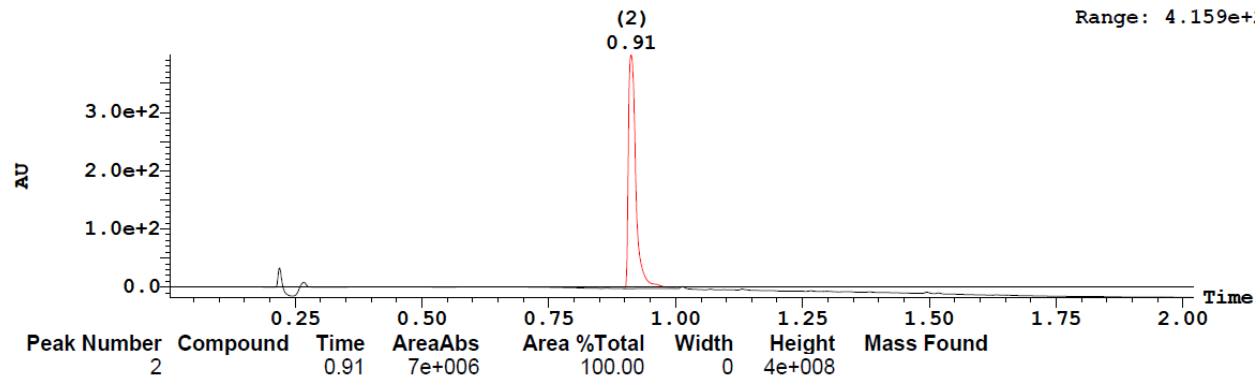
1.1e+008





UV Detector: TIC

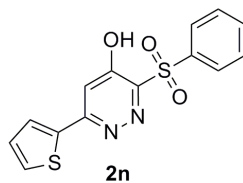
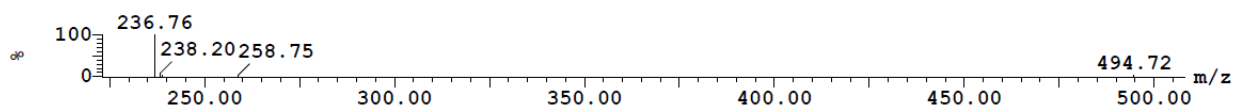
3.988e+2
Range: 4.159e+2



Peak ID Compound Time Mass Found
2 0.91

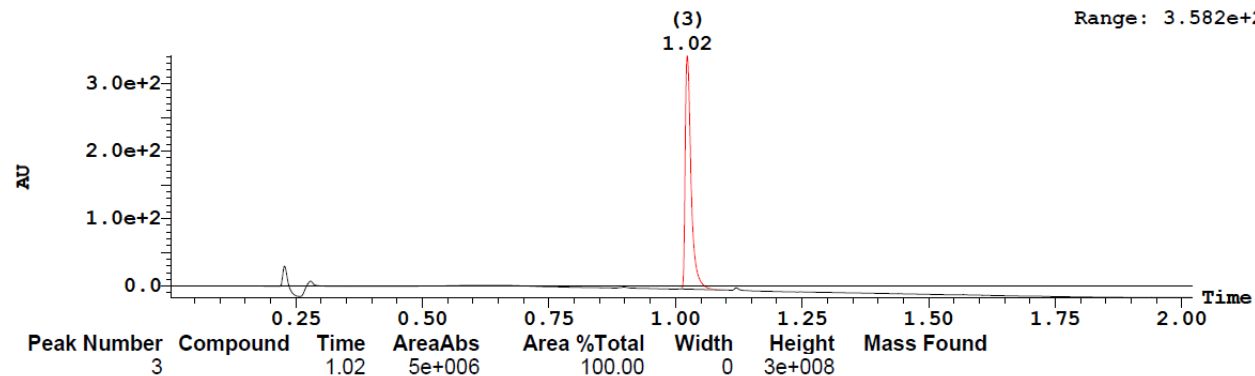
SAMPLE: 2:41 Combine (214:219)

9.9e+007



UV Detector: TIC

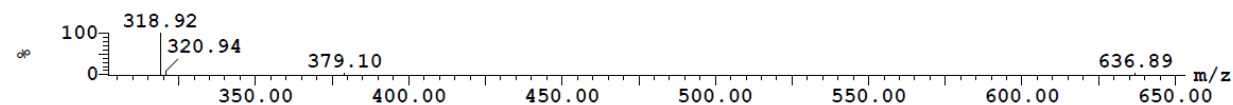
3.413e+2
Range: 3.582e+2

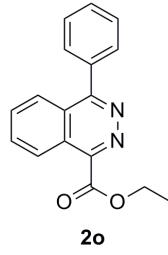


Peak ID Compound Time Mass Found
3 1.02

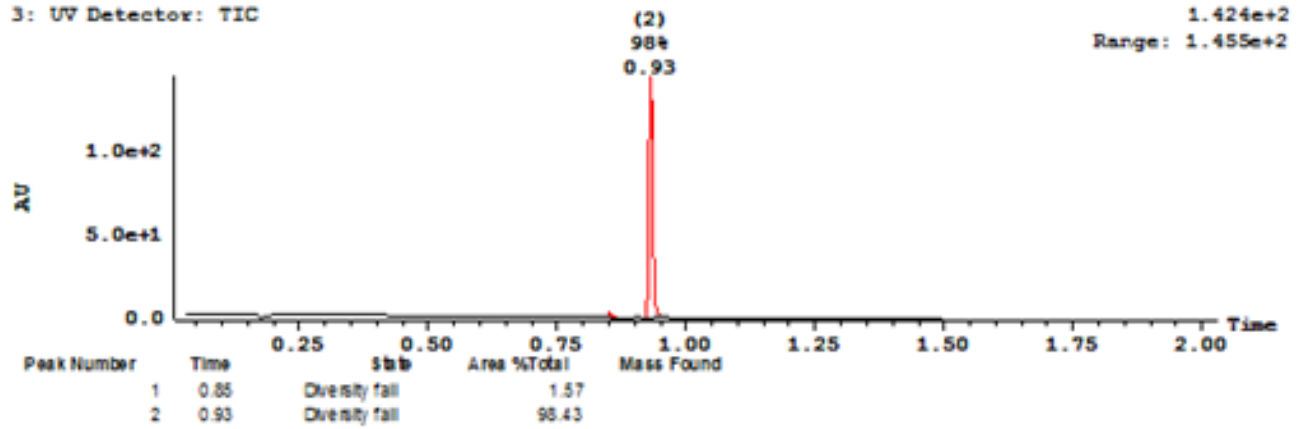
SAMPLE: 1:36 Combine (240:245)

2.6e+007





3: UV Detector: TIC



| Peak ID | Time | Mass Found | BPM | State |
|---------|------|------------|-----|----------------|
| 2 | 0.93 | | 279 | Diversity fail |

2: (Time: 0.93) Combine (54)

1:MS ES+
3.2e+007

