

## Supporting Information

### Identification of Novel 2,4,5-Trisubstituted Pyrimidines as Potent Dual Inhibitors of Plasmodial *PfGSK3/PfPK6* with Activity Against Blood Stage Parasites *in vitro*

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**Table S1. Ligand efficiency values of IKK16 and best performing analogues**

Compound	<sup>a</sup> LE
IKK16	0.26
9g	0.28
18i	0.29
18j	0.30
18n	0.29
18r	0.30
23a	0.32
23b	0.33
23c	0.33
23d	0.34
23e	0.35
23f	0.34
23g	0.35

<sup>a</sup>Ligand efficiency was calculated as follows:  $PPK6$  pIC<sub>50</sub>/number of heavy atoms in the molecule

**Table S2. Physicochemical properties of IKK16 and 23b-f**

Compound	<sup>a</sup> Kinetic solubility (μg/mL)	<sup>b</sup> Effective permeability (P <sub>e</sub> ) (cm/s)	<sup>c</sup> CLogP	<sup>e</sup> PSA (Polar surface area)
IKK16	30	2.08 x10 <sup>-6</sup>	5.27	61.87
23b	56.3	1.36 x10 <sup>-6</sup>	5.09	63.07
23c	19.43	1.30 x10 <sup>-6</sup>	5.08	62.56
23d	55.28	<1.75 x10 <sup>-7</sup>	5.21	64.36
23e	0.93	<sup>d</sup> N/A	4.34	83.04
23f	0.5	N/A	4.16	83.04

<sup>a</sup>Kinetic solubility analysis was carried out in phosphate buffered saline solution (PBS) at pH 7.4 from 10 mM DMSO stock solutions.

<sup>b</sup>Permeability analysis was performed using a chamber separated by an immobilized artificial phospholipid membrane layer into a donor and an acceptor well. <sup>c</sup>ClogP and PSA were calculated using the QikProp ADME prediction software from Schrodinger Maestro version 12.9.137. <sup>d</sup>N/A: Below limit of quantitation in acceptor well

**Table S3. Calculated LogD values of 9f and 9g**

Compound	CLogD
<b>9f</b>	2
<b>9g</b>	2.7

cLogD values were calculated using Chemaxon

**Table S4. Liver stage activity of 23b-e with associated host cell cytotoxicity**

Compound	<i>P. berghei</i> liver stage <sup>a</sup> EC <sub>50</sub> (μM)	HepG2 <sup>b</sup> CC <sub>50</sub> (μM)
<b>23b</b>	5.2	9.3
<b>23c</b>	2.4	10.5
<b>23d</b>	2.8	5.1
<b>23e</b>	3.4	4.9

<sup>a</sup>EC<sub>50</sub> values are presented as mean values of two experiments performed in duplicate. <sup>b</sup>CC<sub>50</sub> was determined using the CellTiter-Fluor assay. Values are presented as the mean of two experiments performed in triplicate.

**Table S5. PDB codes of the HsCDK2 and HsGSK-3β used as templates for the model building of *Pf*PK6 and *Pf*GSK-3**

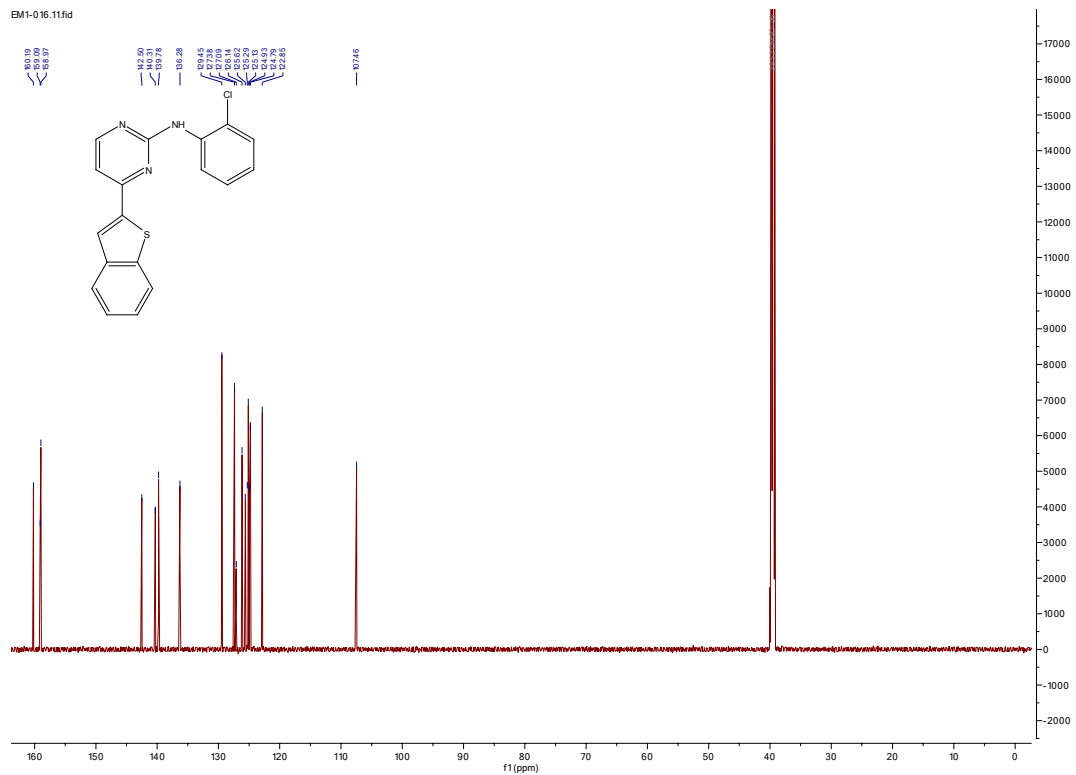
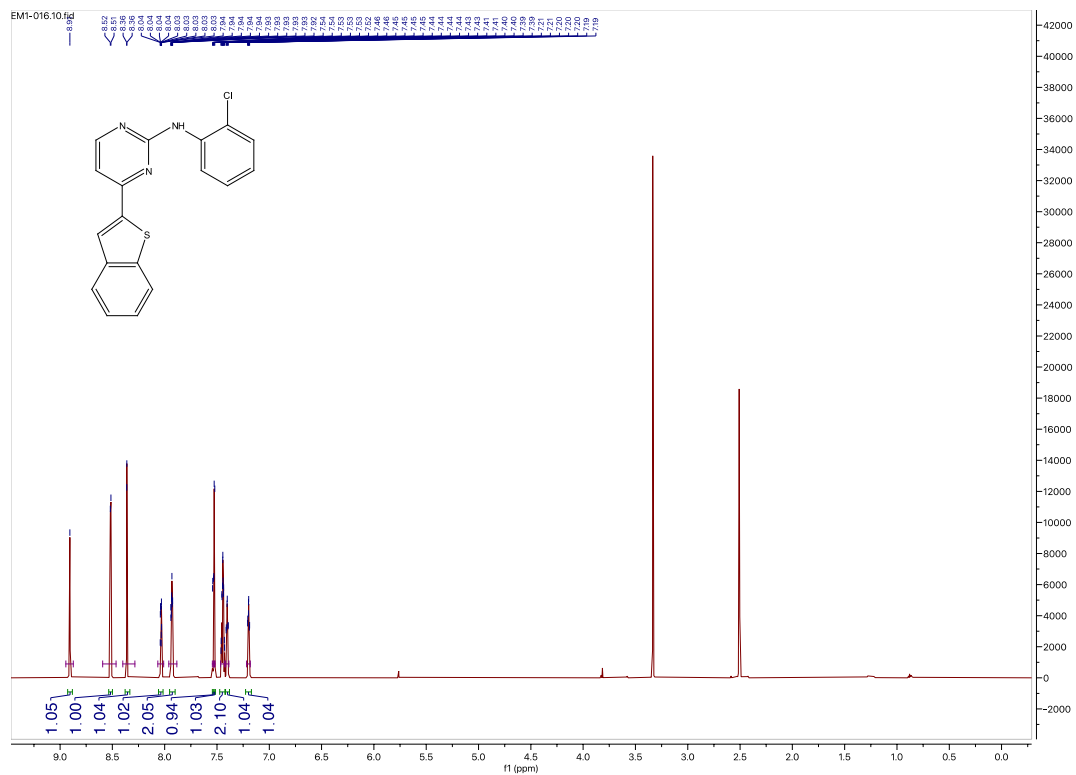
<b><i>Pf</i>PK6</b>		
PDB ID	Resolution	% Identity
1h24	2.70 Å	40.85
1oiu	2.00 Å	40.85
4eom	2.10 Å	40.13
1vyw	2.30 Å	40.07
1e9h	2.50 Å	39.81
<b><i>Pf</i>GSK-3</b>		
PDB ID	Resolution	% Identity
1r0e	2.25 Å	57.45
5air	2.53 Å	55.16
2o5k	3.20 Å	54.97
4afj	1.98 Å	54.68
3eb0	2.65 Å	49.33







# 4-(Benzo[b]thiophen-2-yl)-N-(2-chlorophenyl)pyrimidin-2-amine (4d)

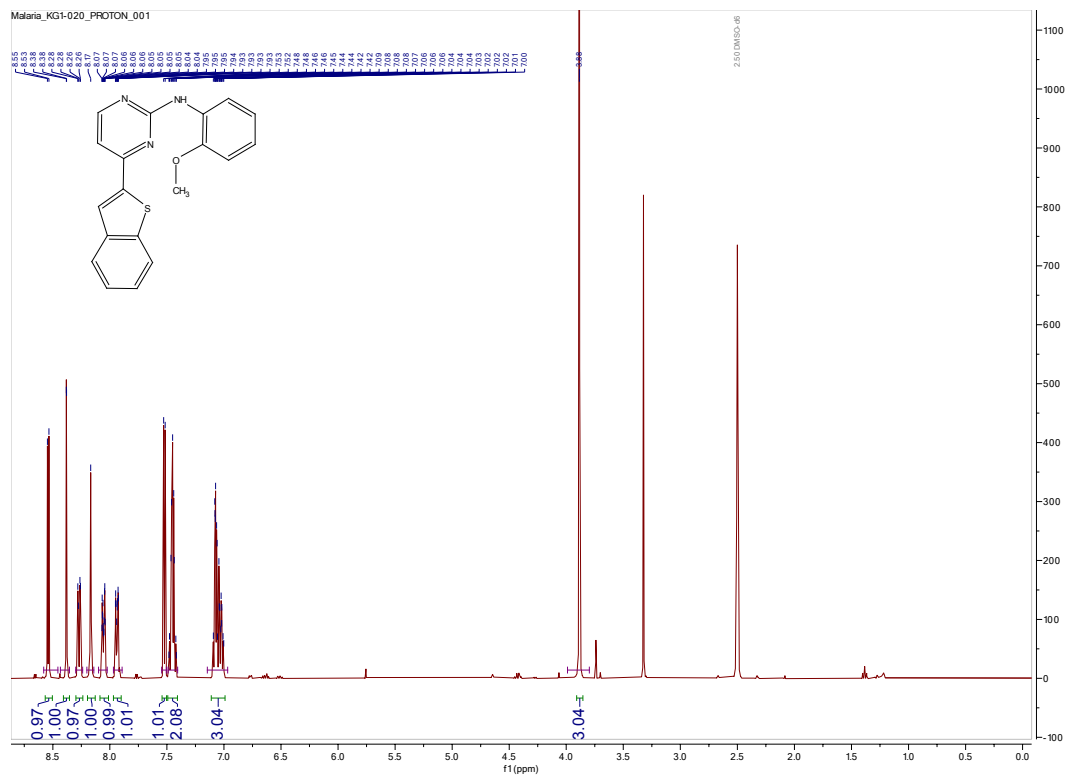








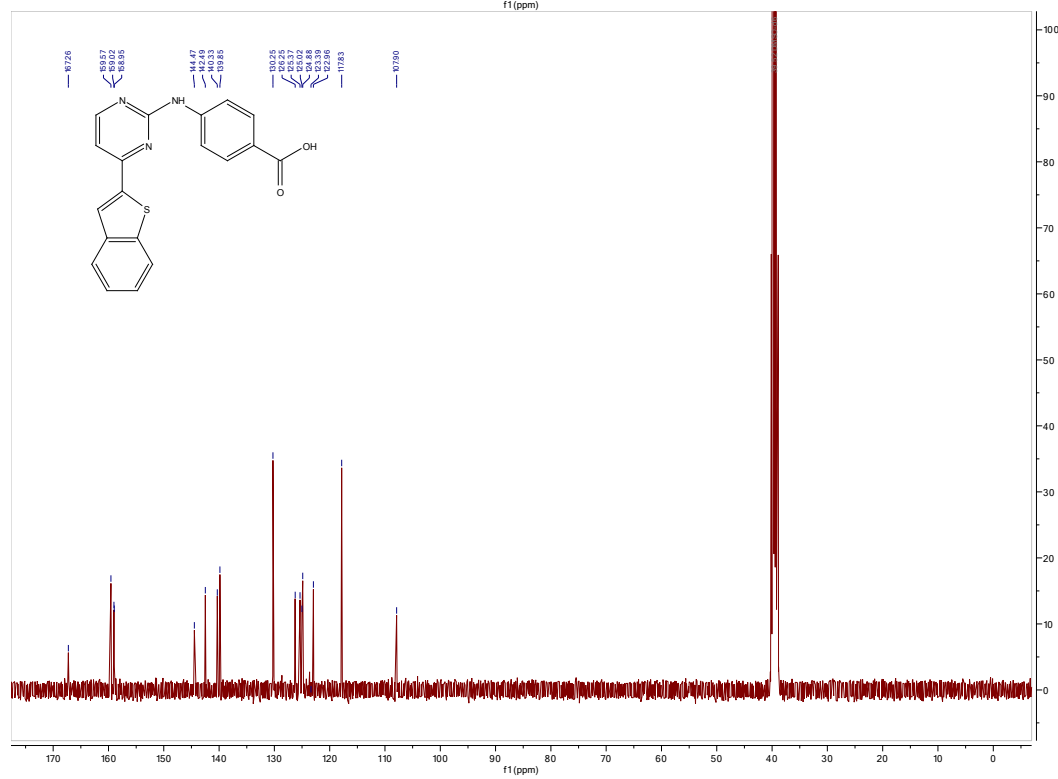
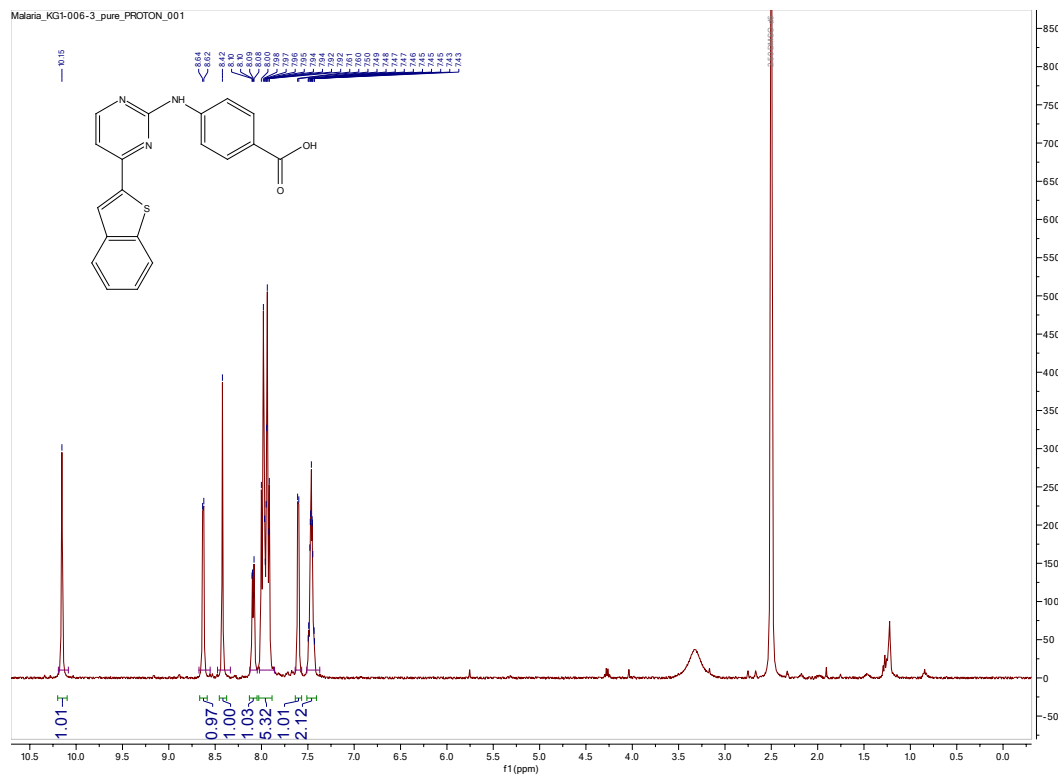
# 4-(Benzo[b]thiophen-2-yl)-N-(2-methoxyphenyl)pyrimidin-2-amine (4g)





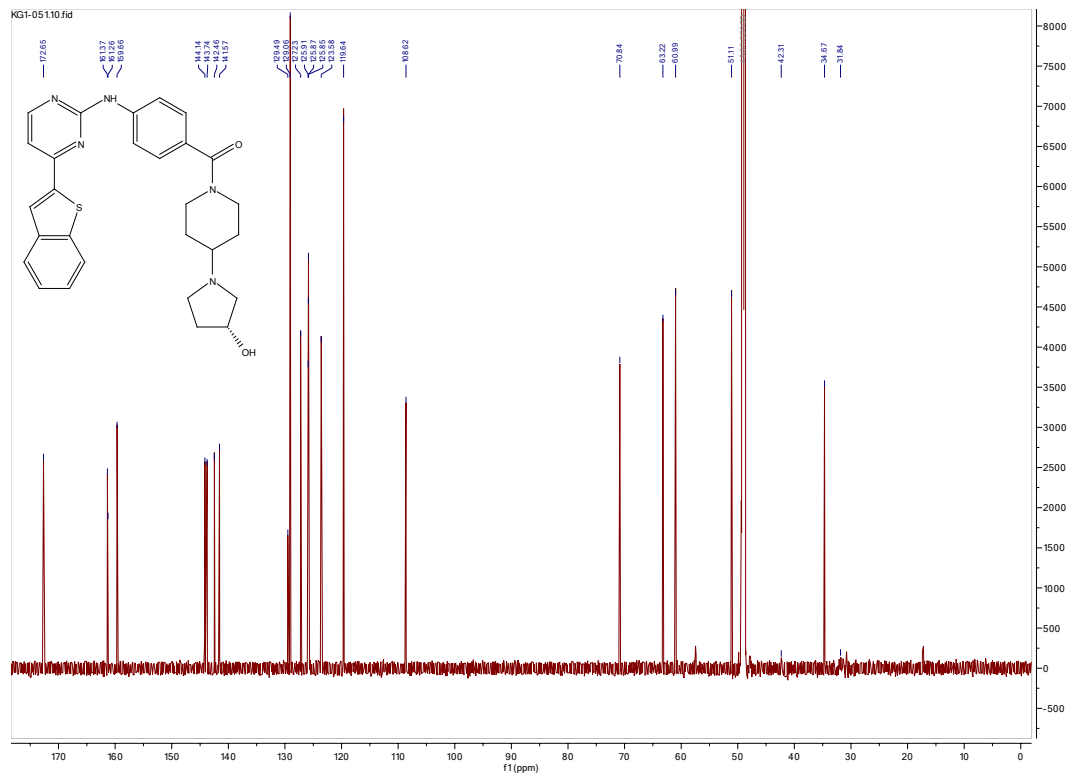
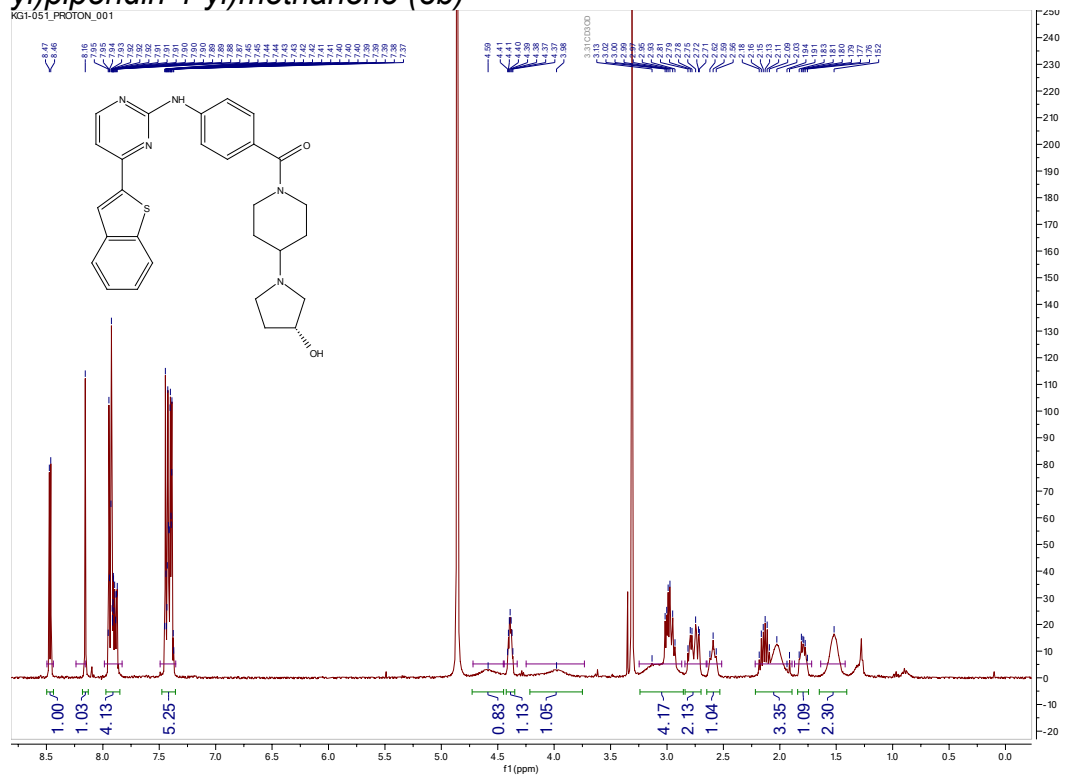


# 4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)benzoic acid (6)





**(R)-4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(3-hydroxypyrrolidin-1-yl)piperidin-1-yl)methanone (8b)**



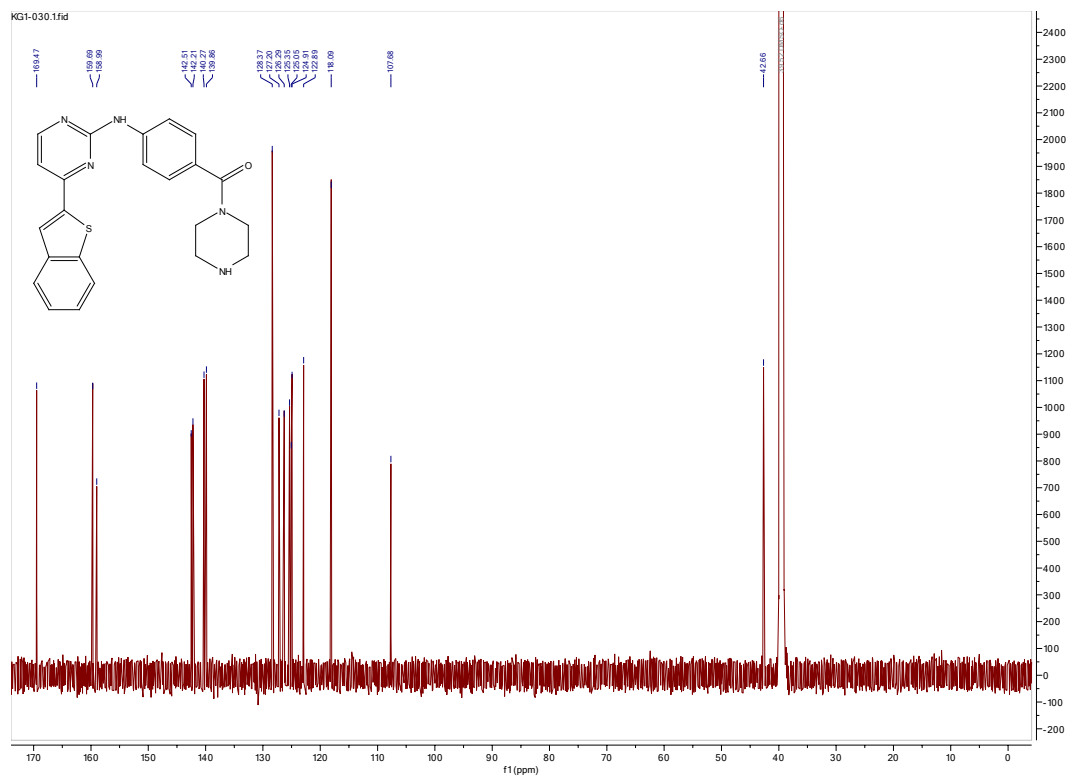
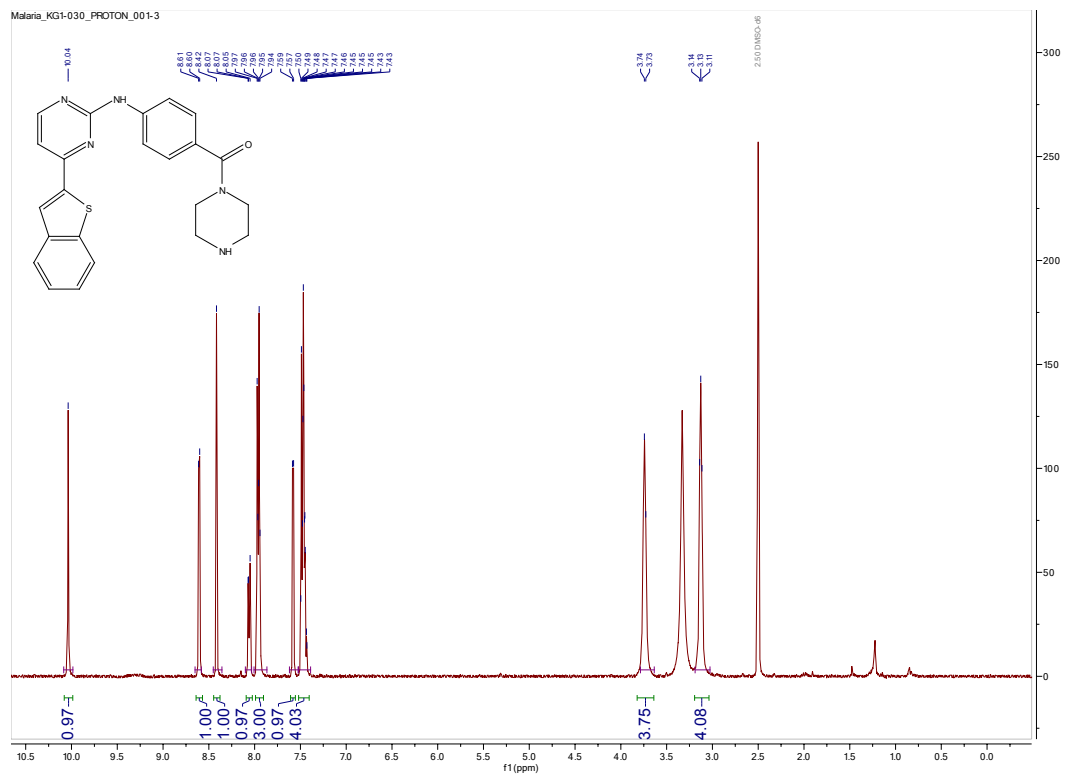




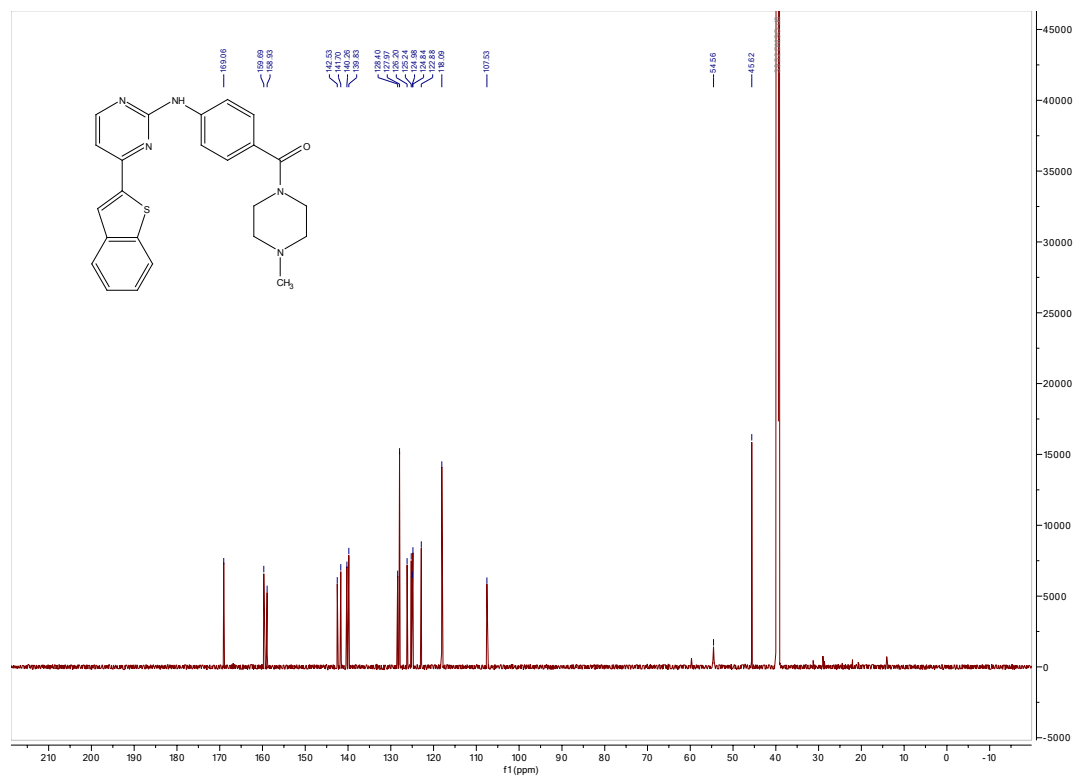
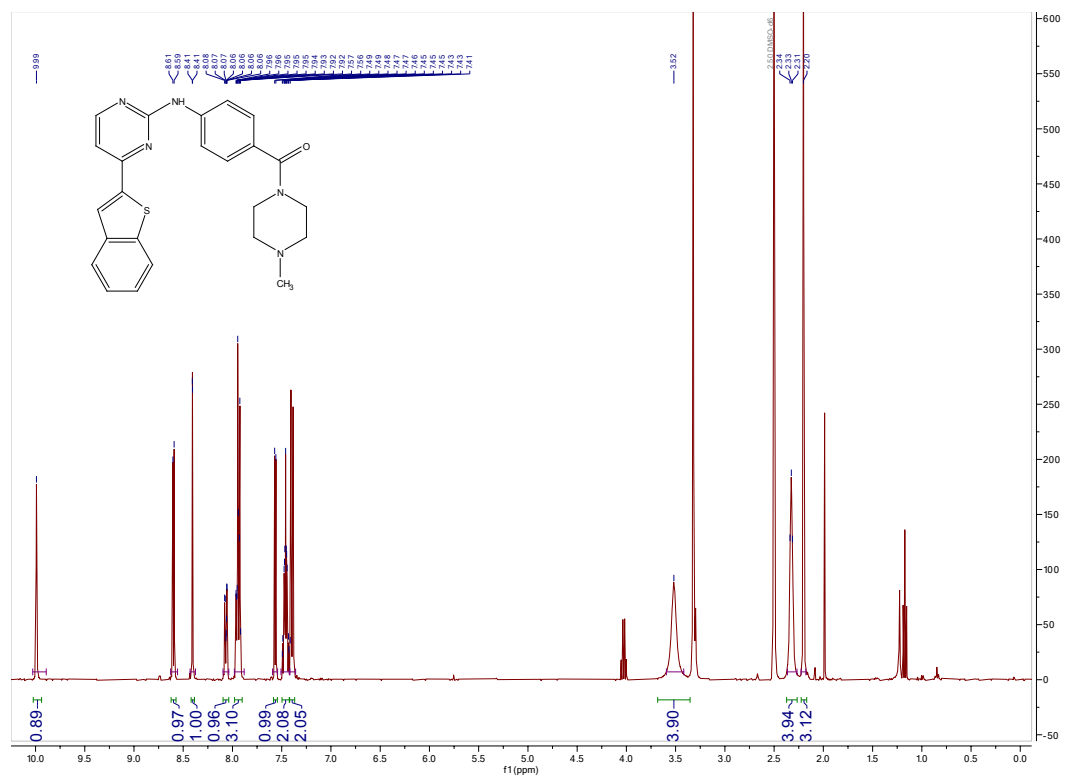




**4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(piperazin-1-yl)methanone (9c)**



4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-methylpiperazin-1-yl)methanone (9d)

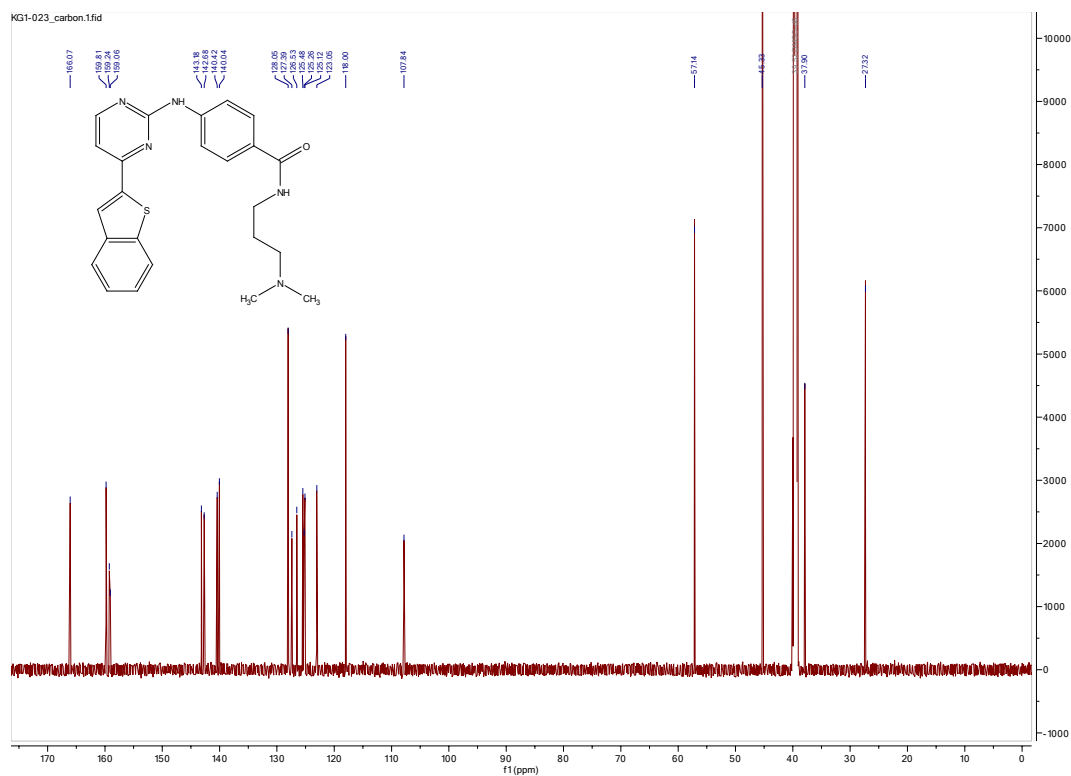
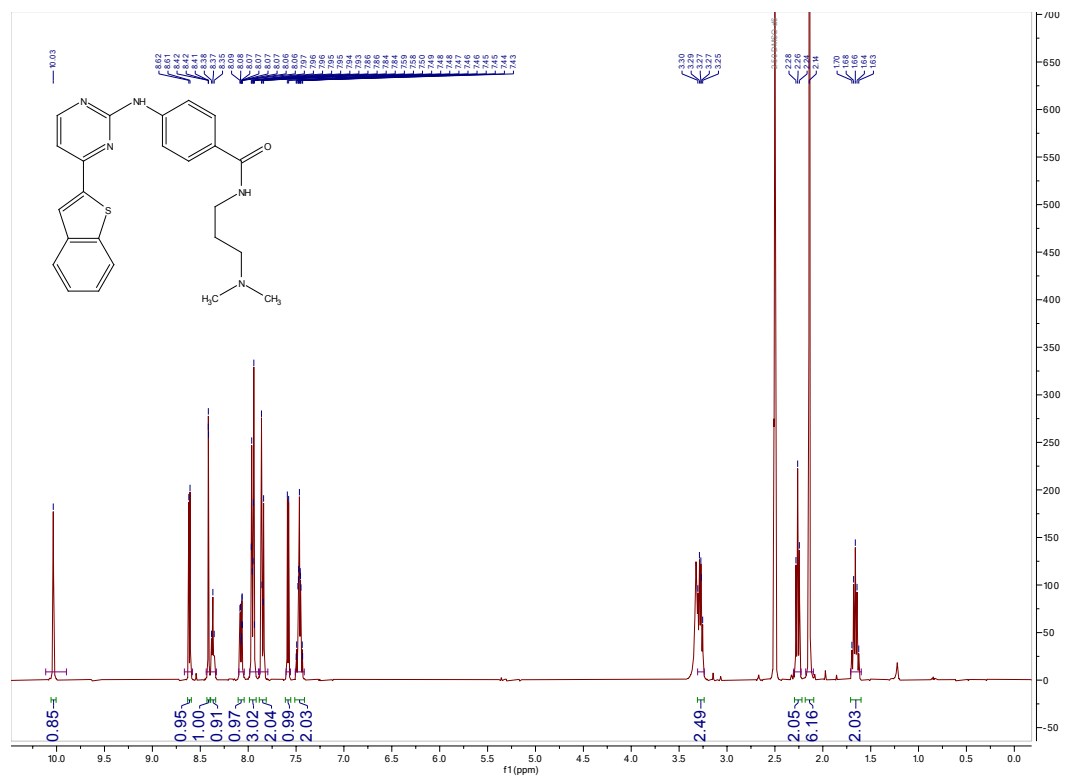








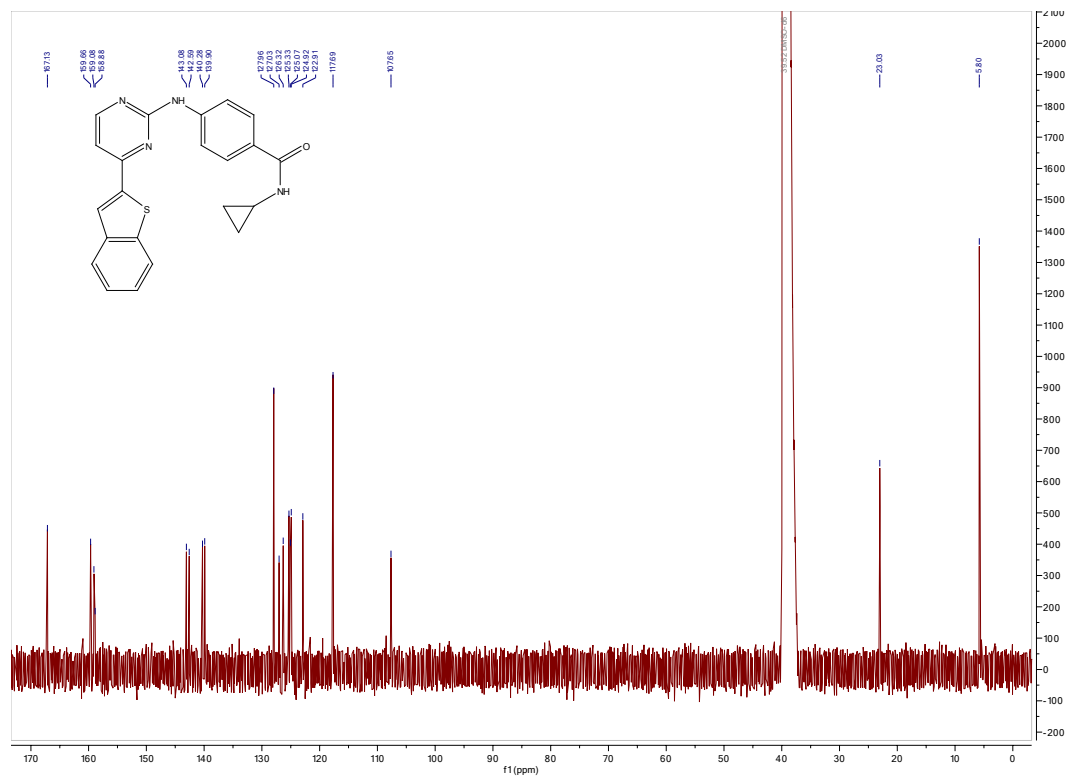
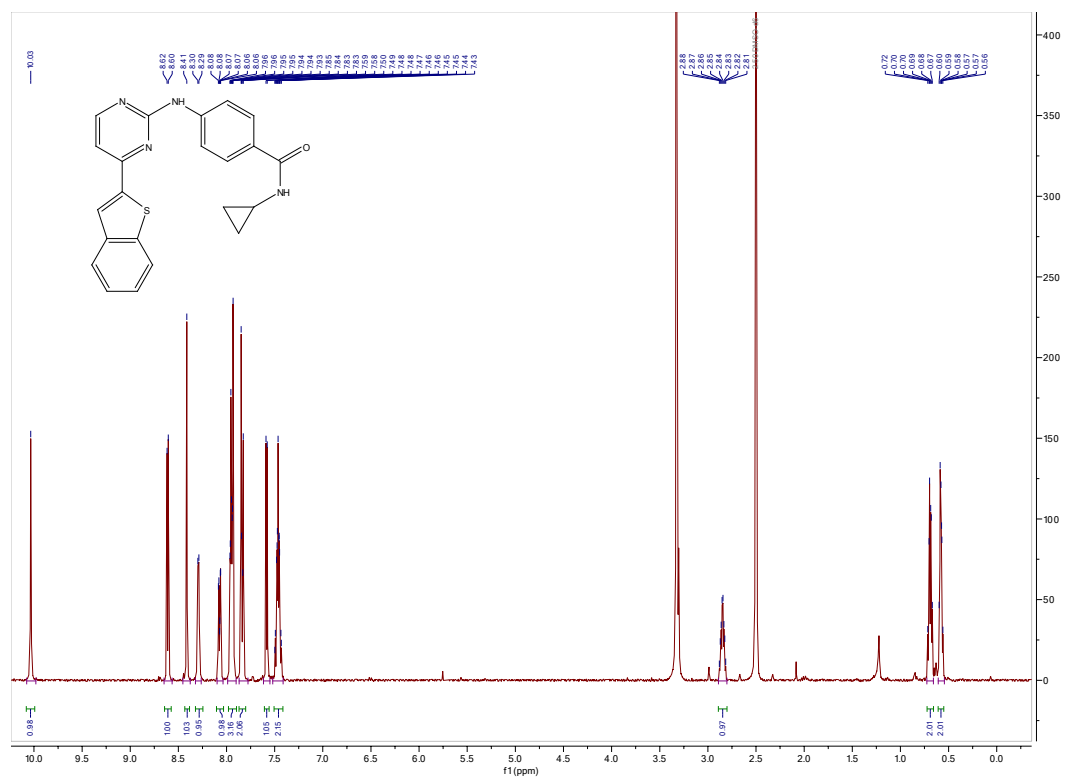
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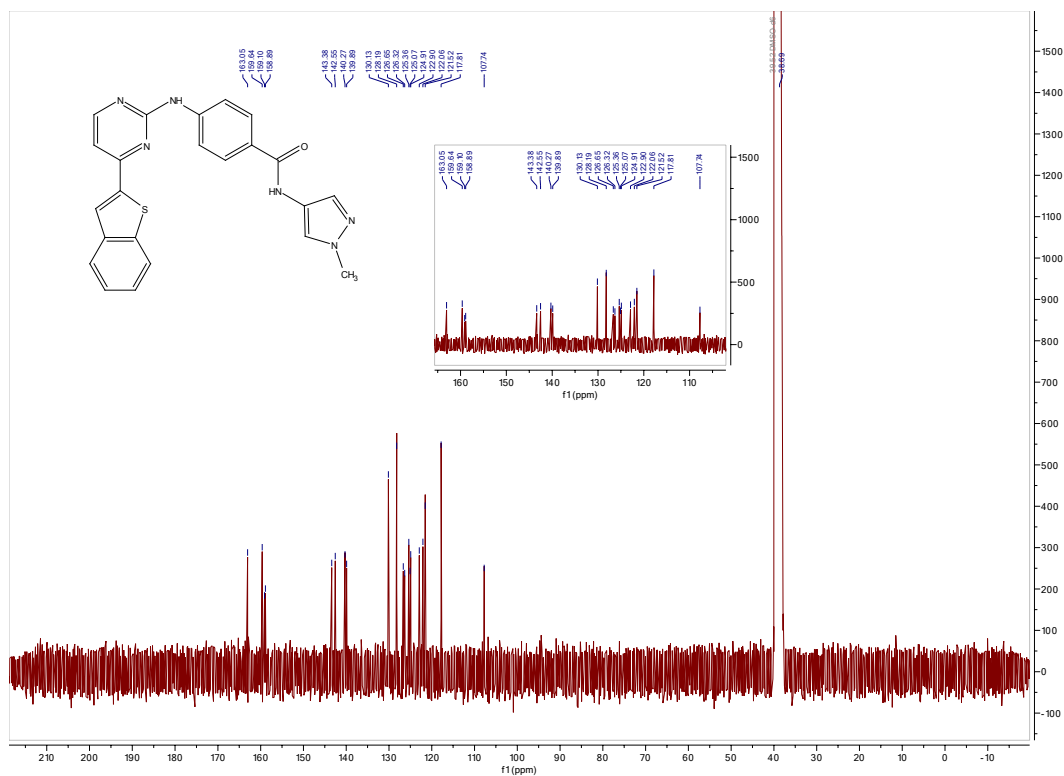
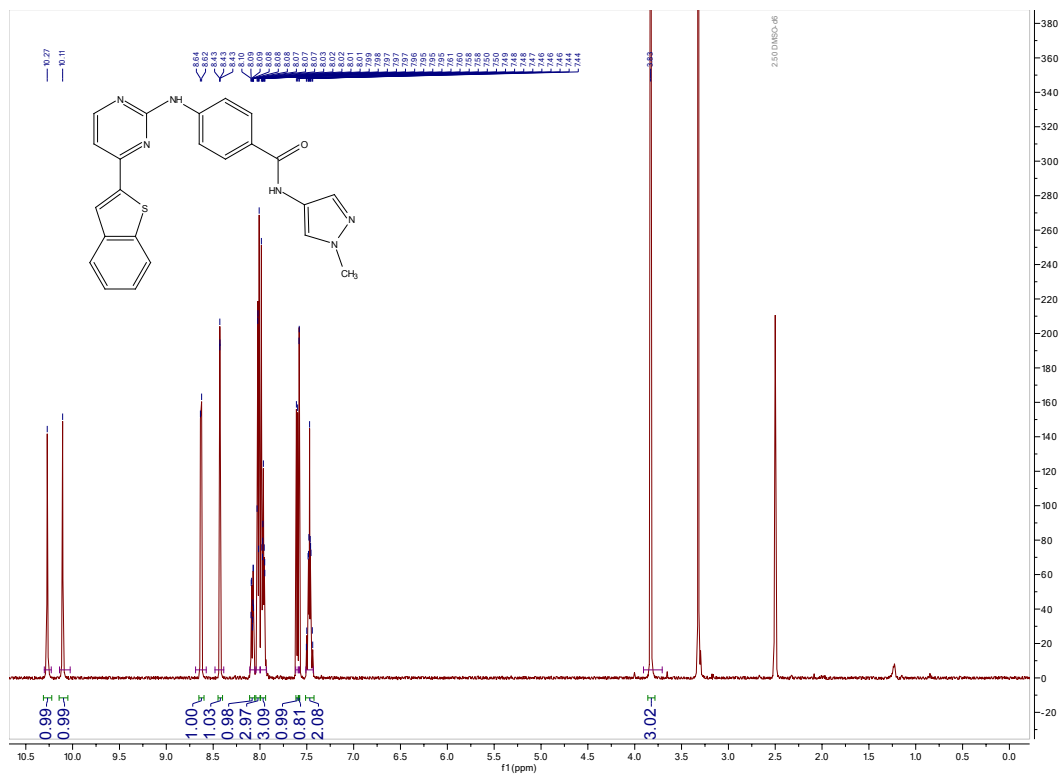




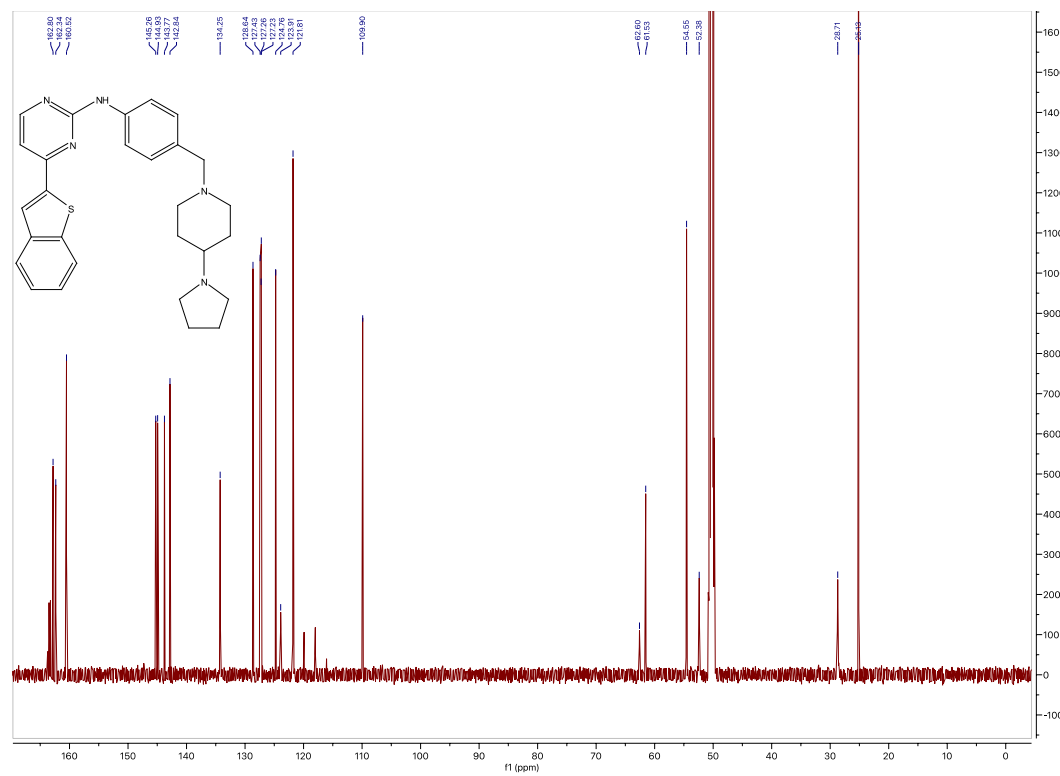
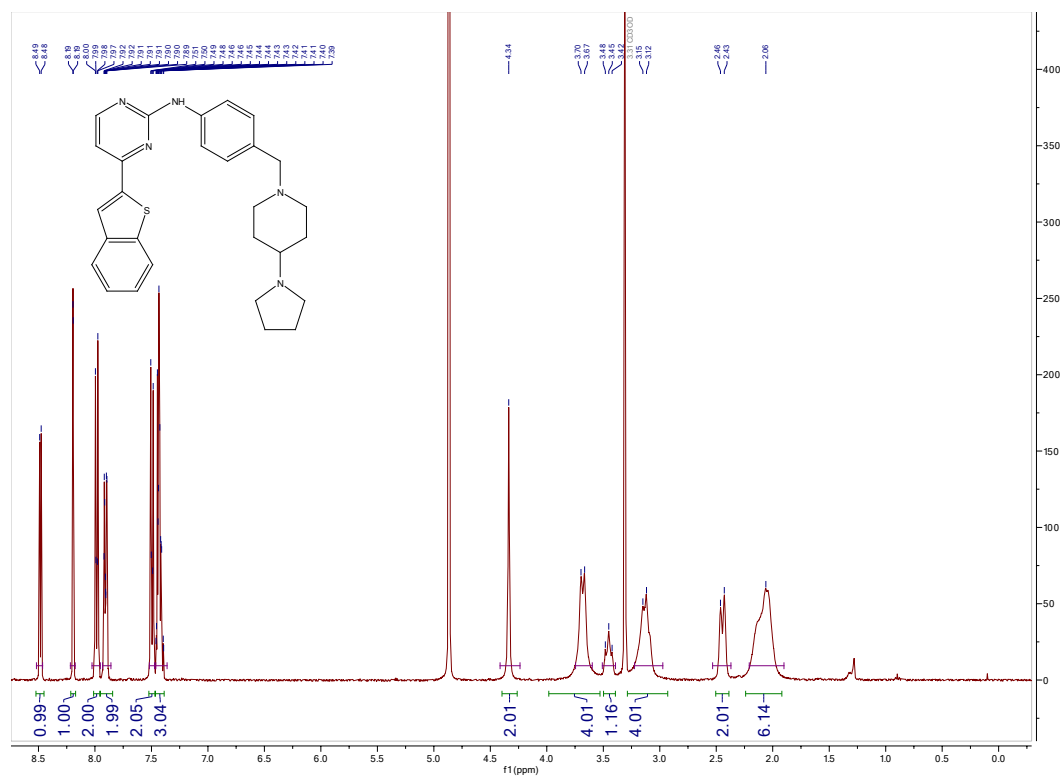
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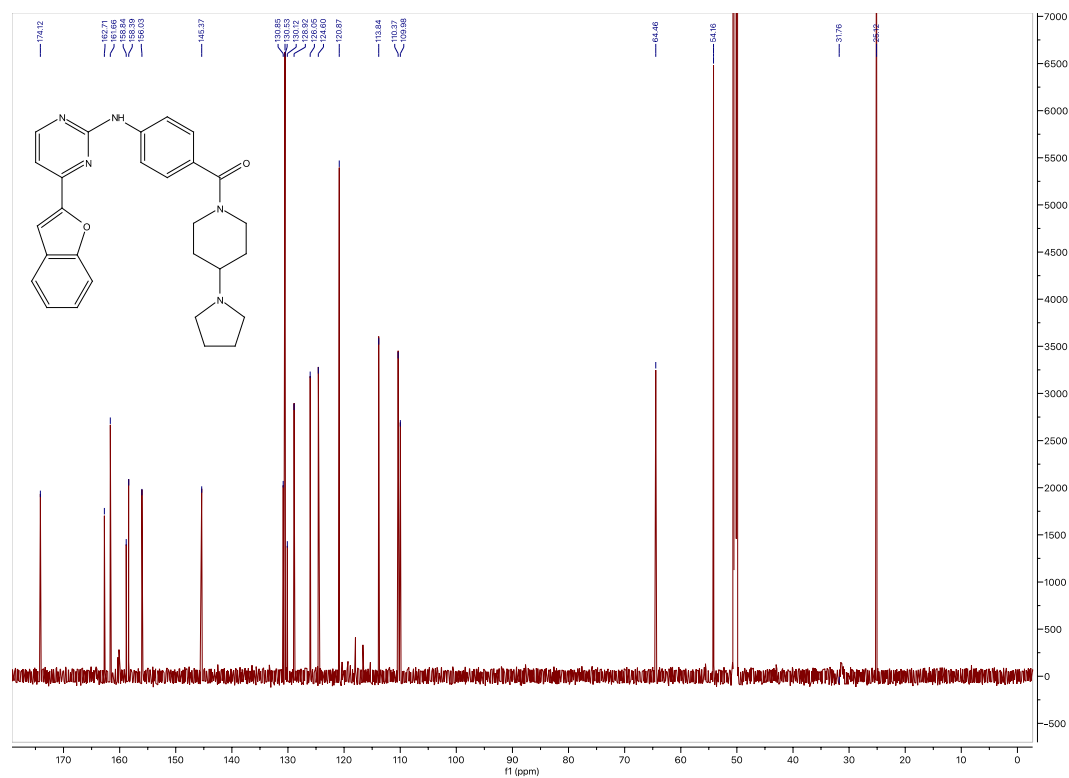
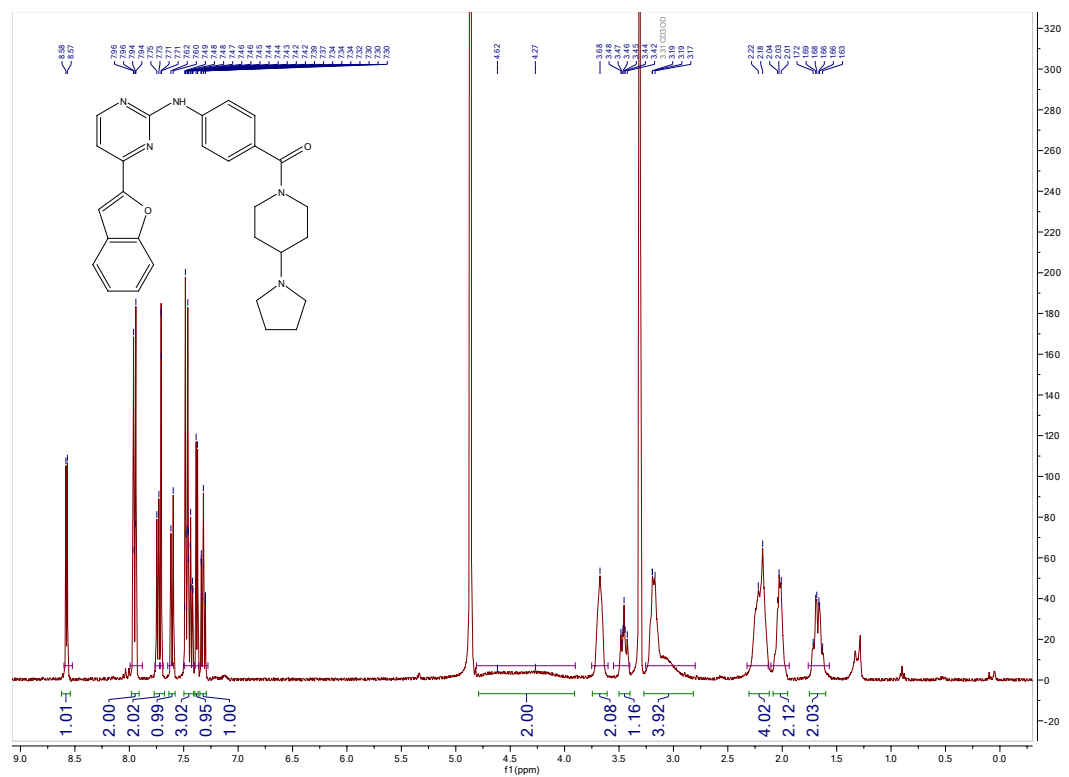
4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-(1-methyl-1H-pyrazol-4-yl)benzamide (9k)



4-(Benzo[b]thiophen-2-yl)-N-(4-((4-(pyrrolidin-1-yl)piperidin-1-yl)methyl)phenyl)pyrimidin-2-amine (12)

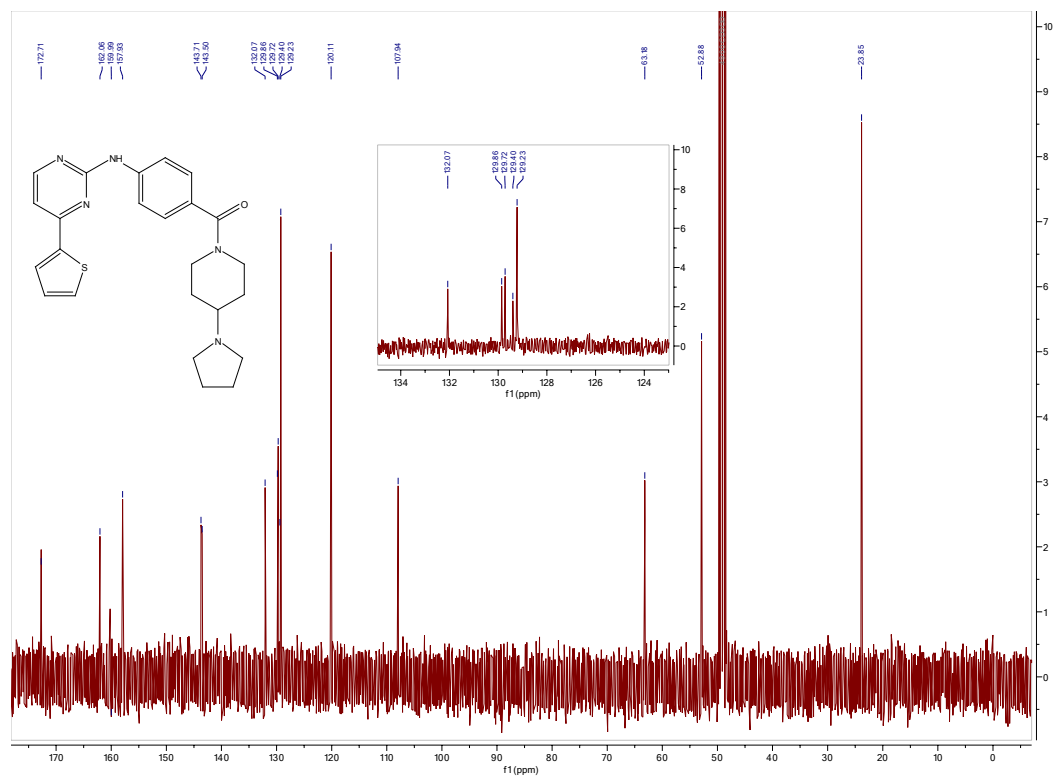
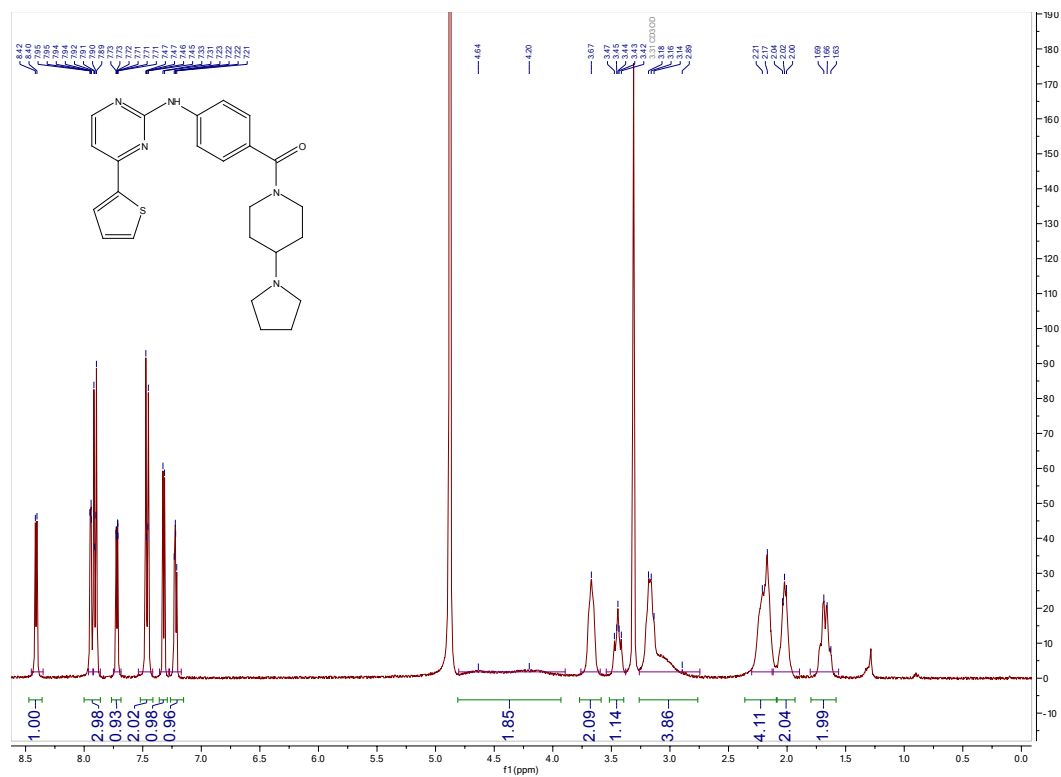


4-((4-(Benzofuran-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18a)





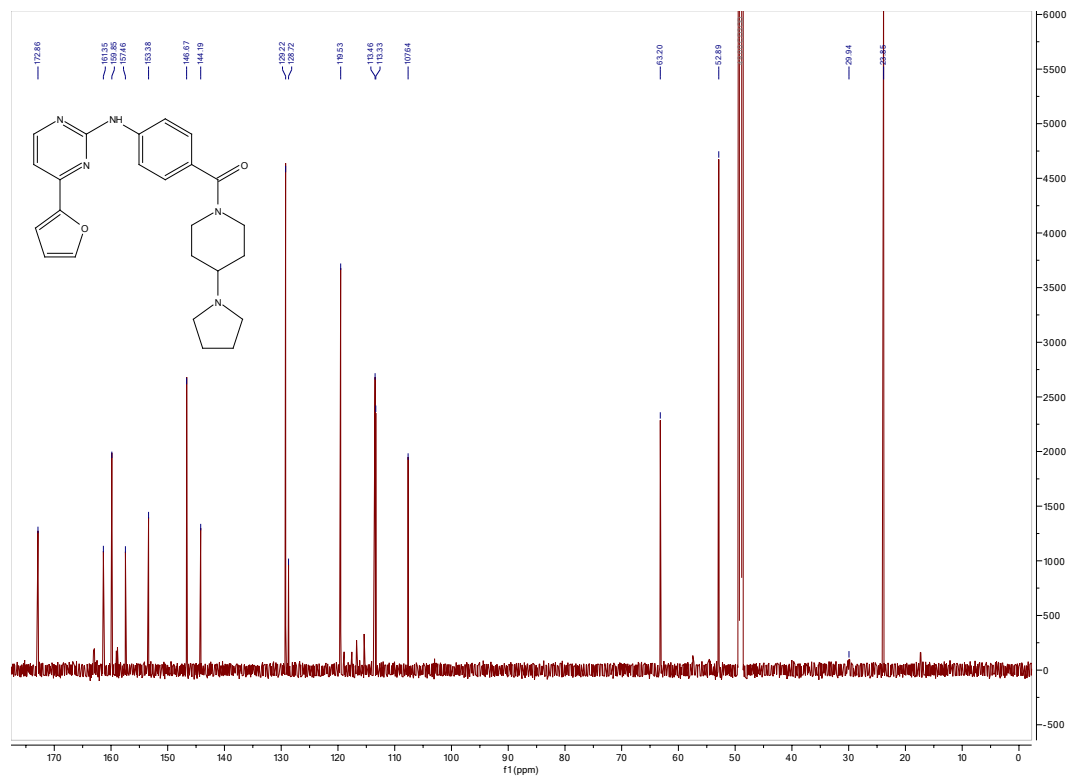
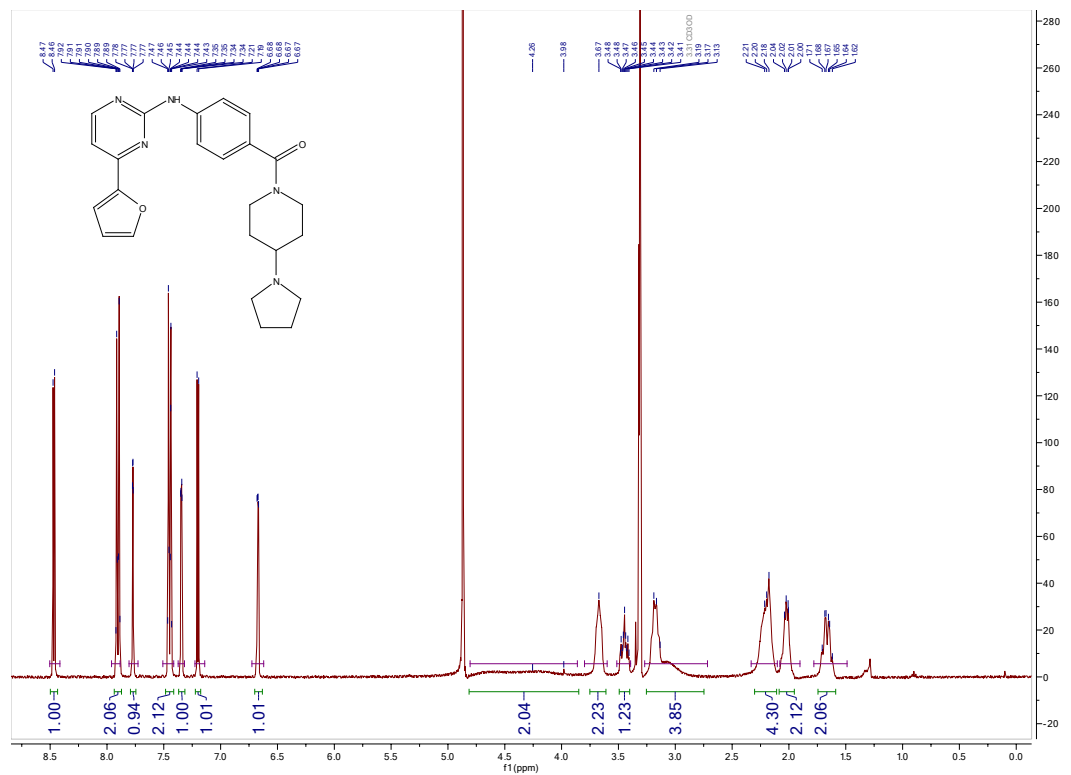
(4-(Pyrrolidin-1-yl)piperidin-1-yl)(4-((4-(thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)methanone (18c)



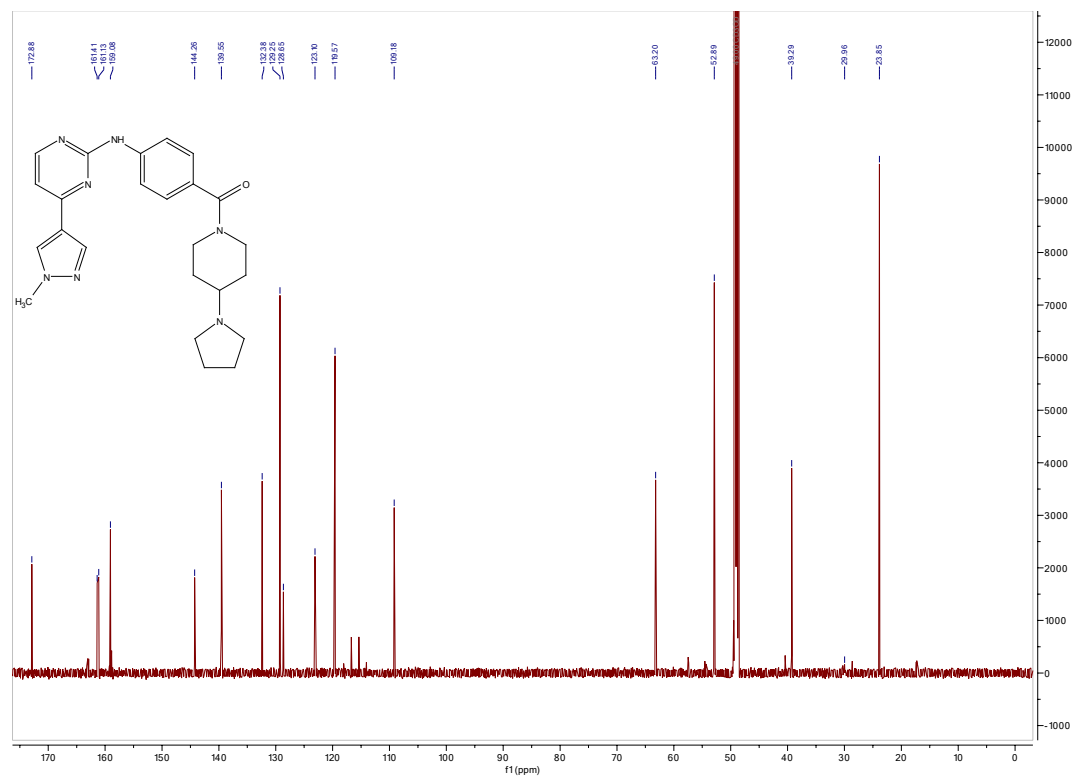
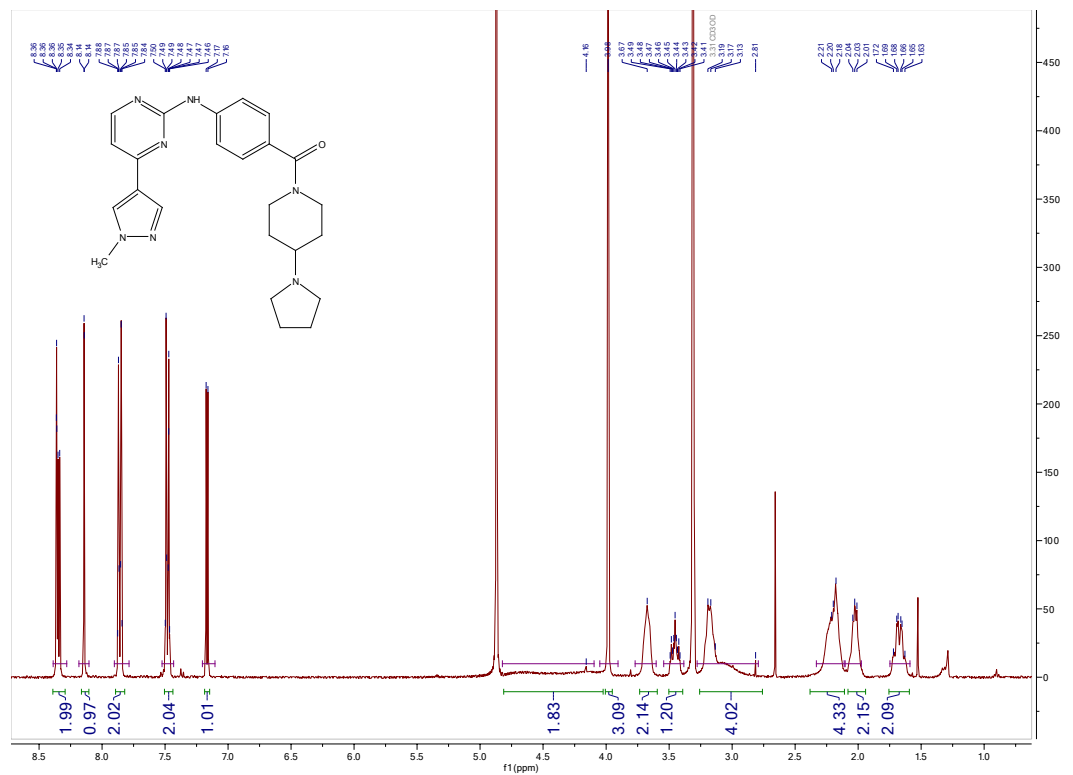




(4-((4-(Furan-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18e)



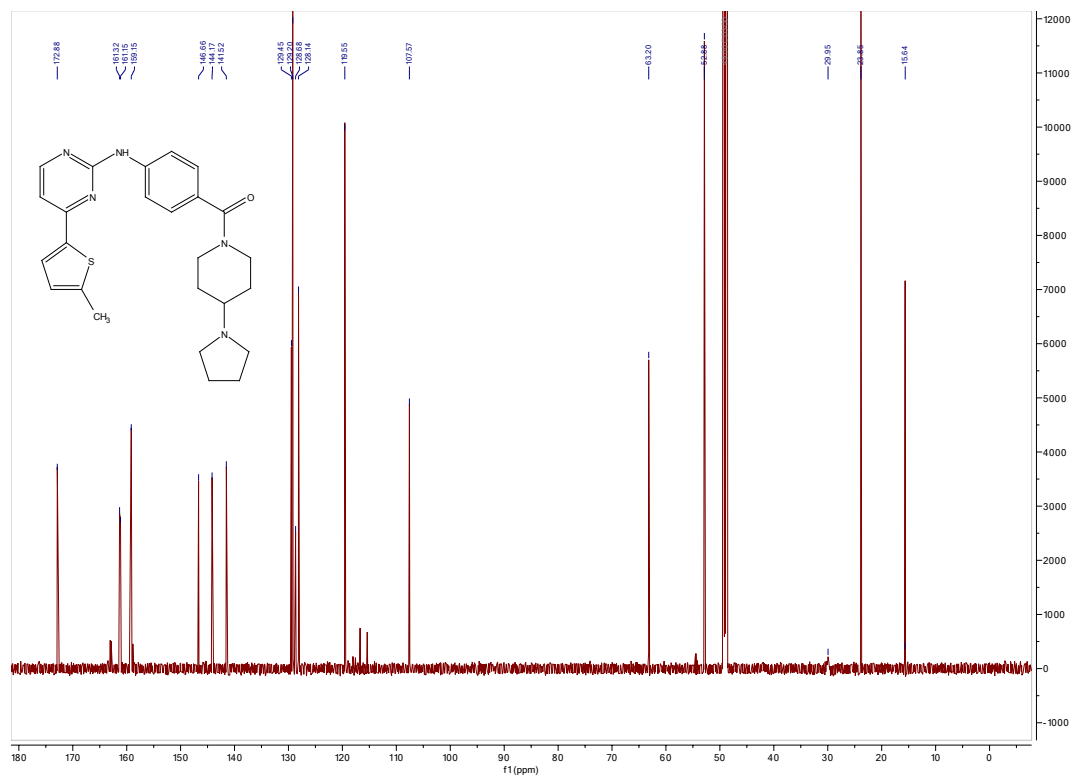
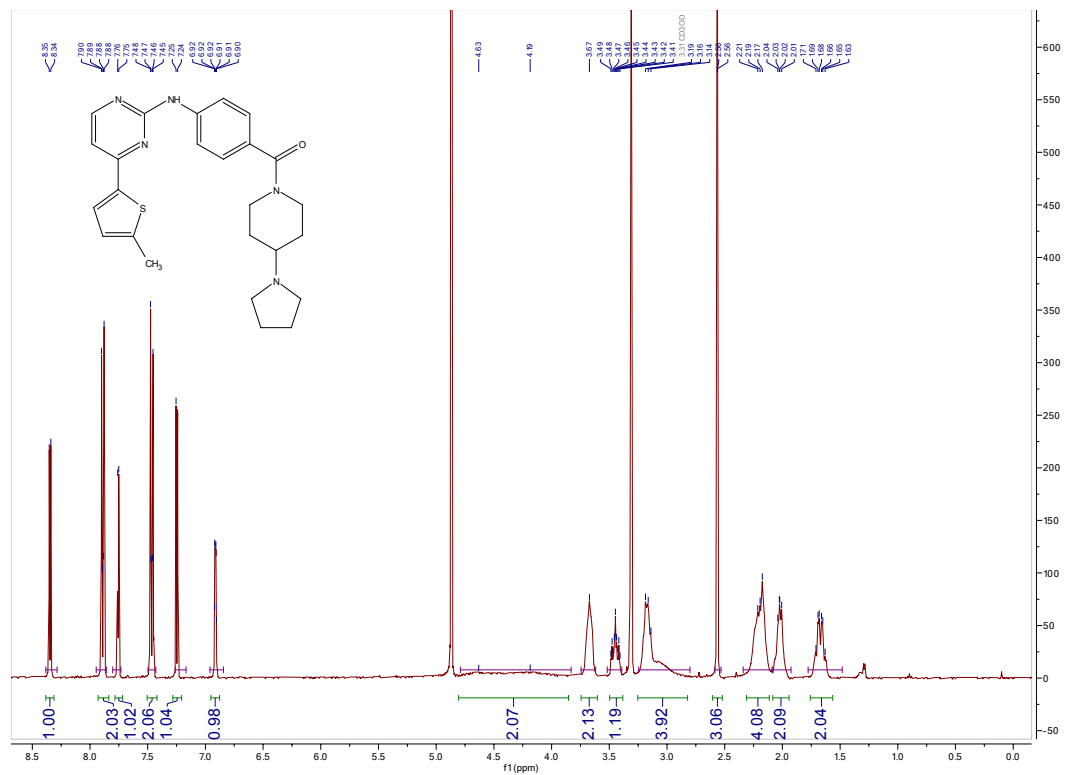
**(4-((4-(1-Methyl-1H-pyrazol-4-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18f)**



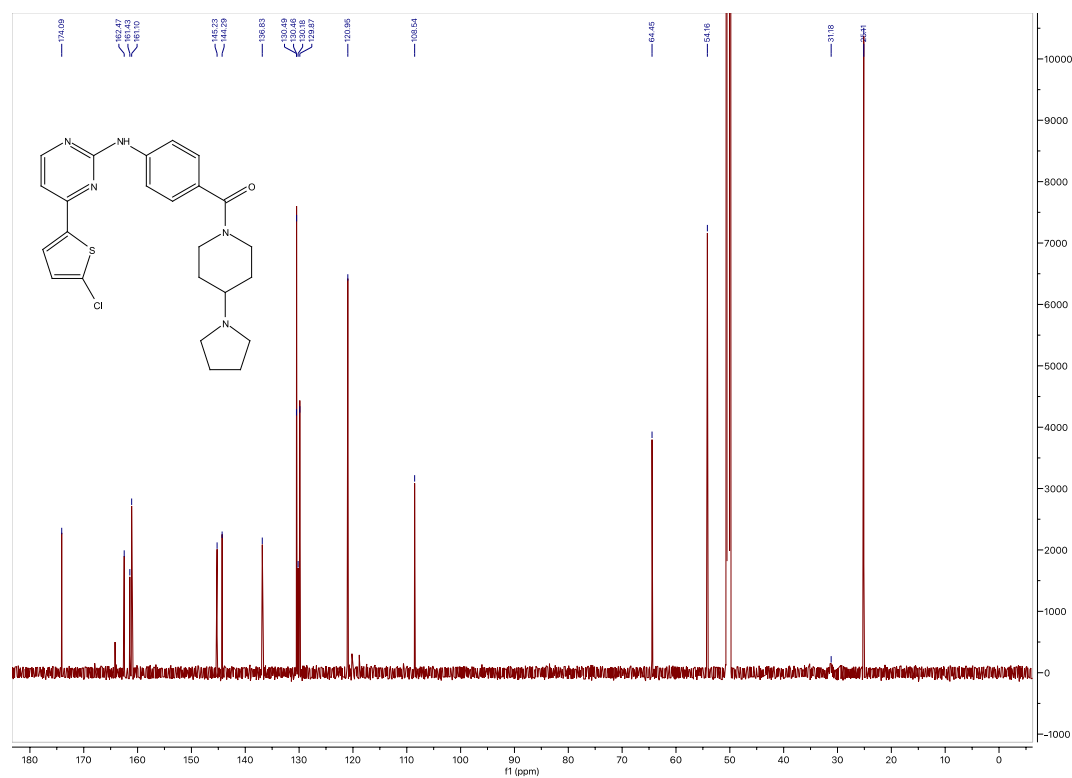
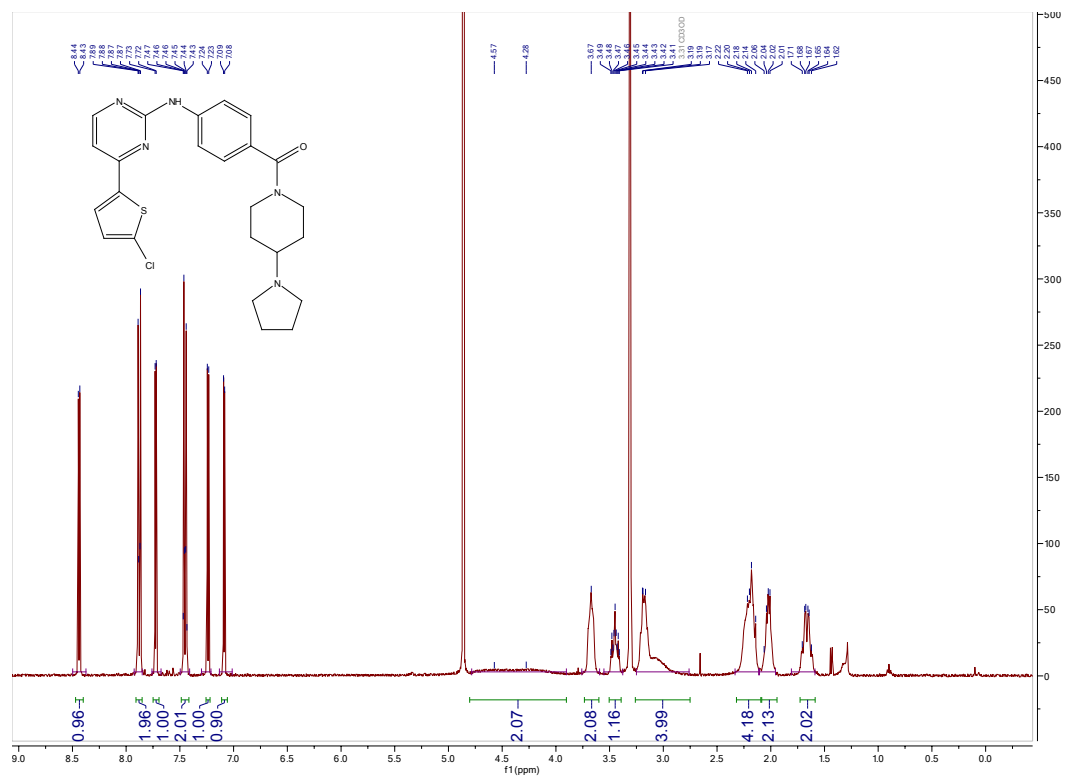




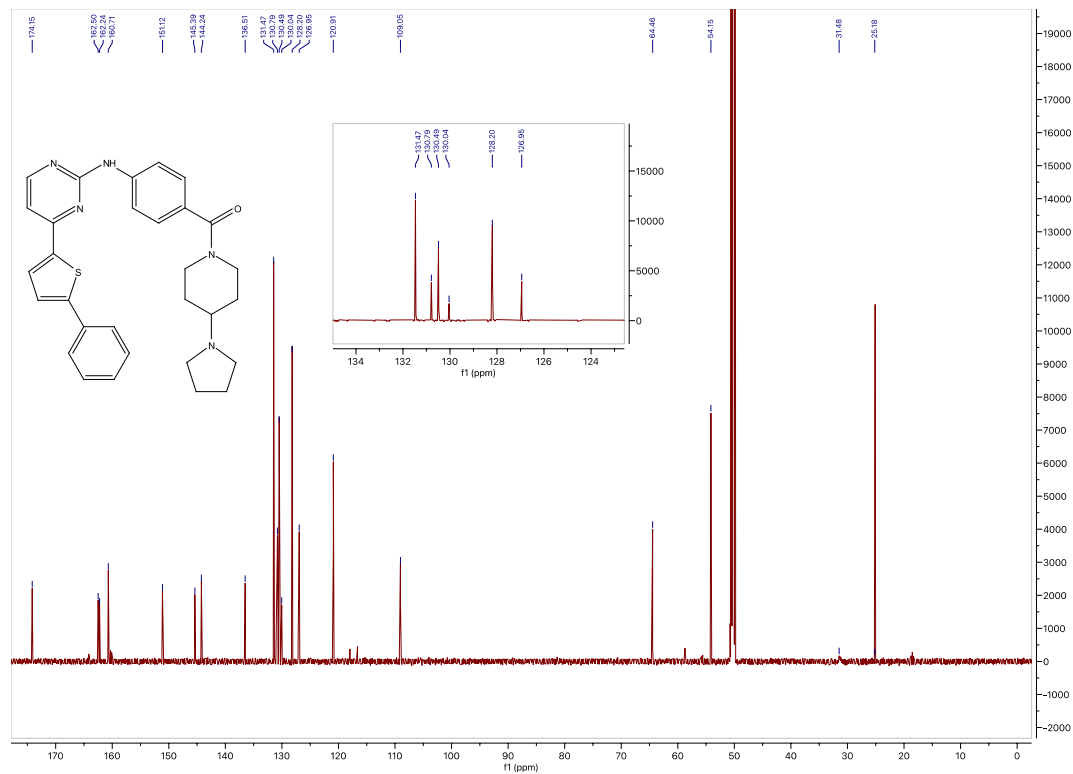
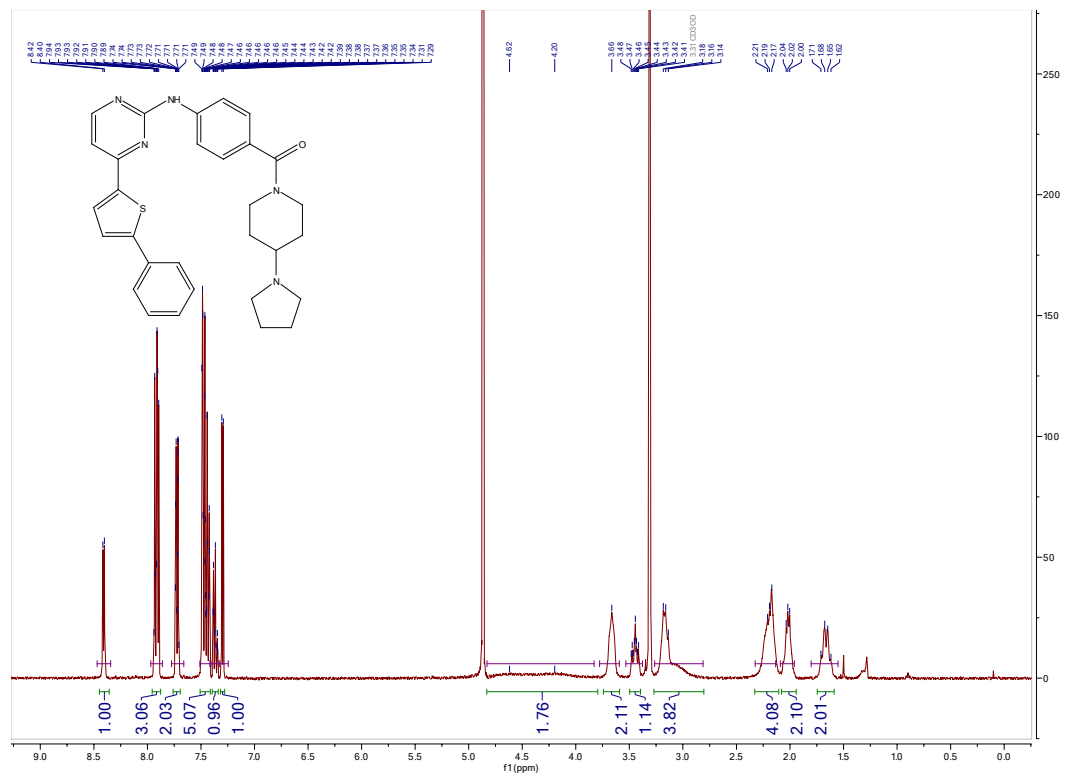
**(4-((4-(5-Methylthiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(3-pyrrolidin-1-yl)piperidin-1-yl)methanone (18i)**



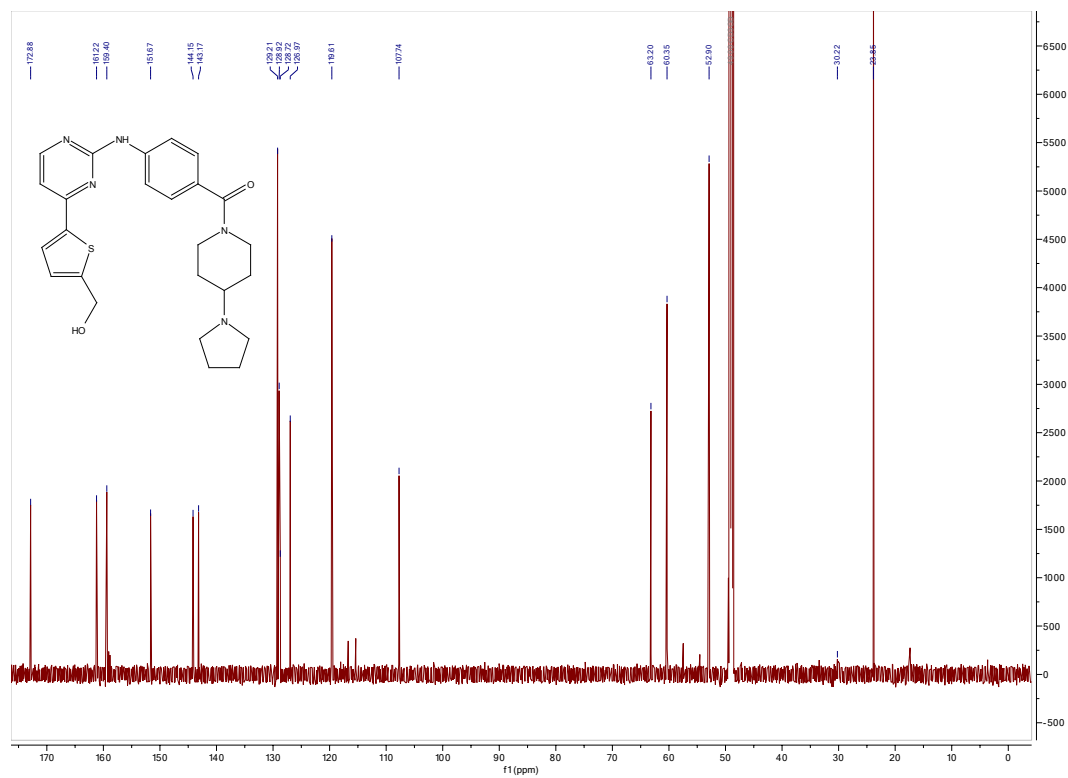
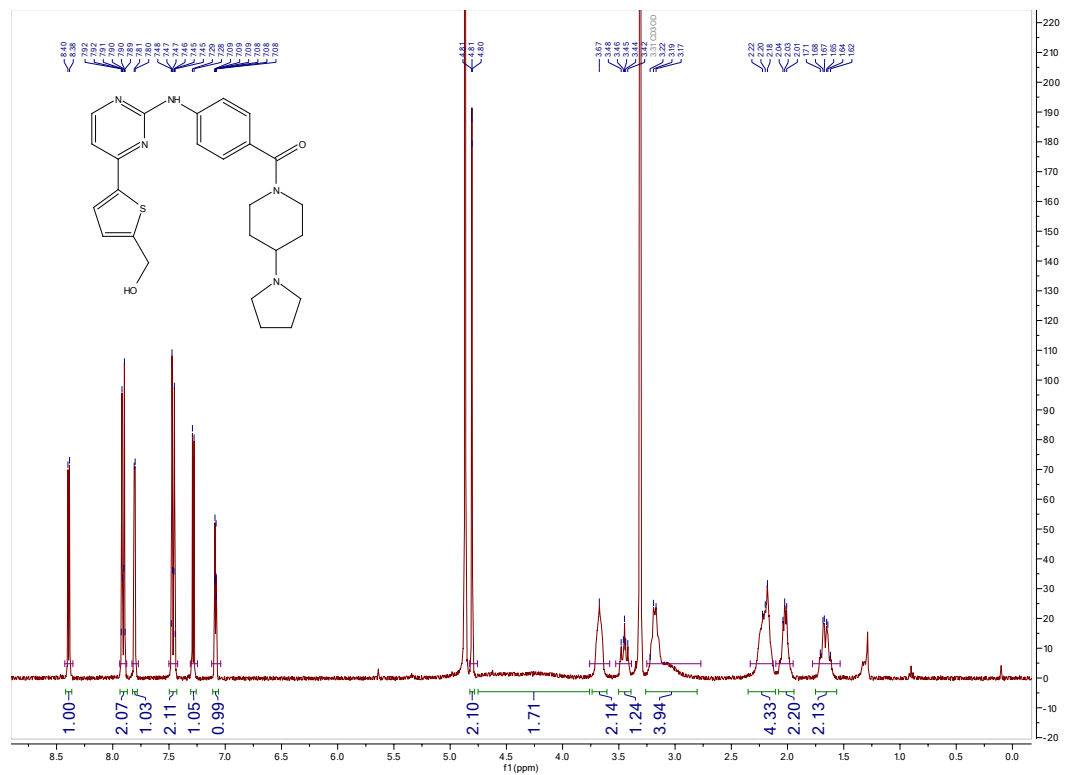
*4-((4-(5-Chlorothiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18j)*



**(4-((4-(5-Phenylthiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18k)**

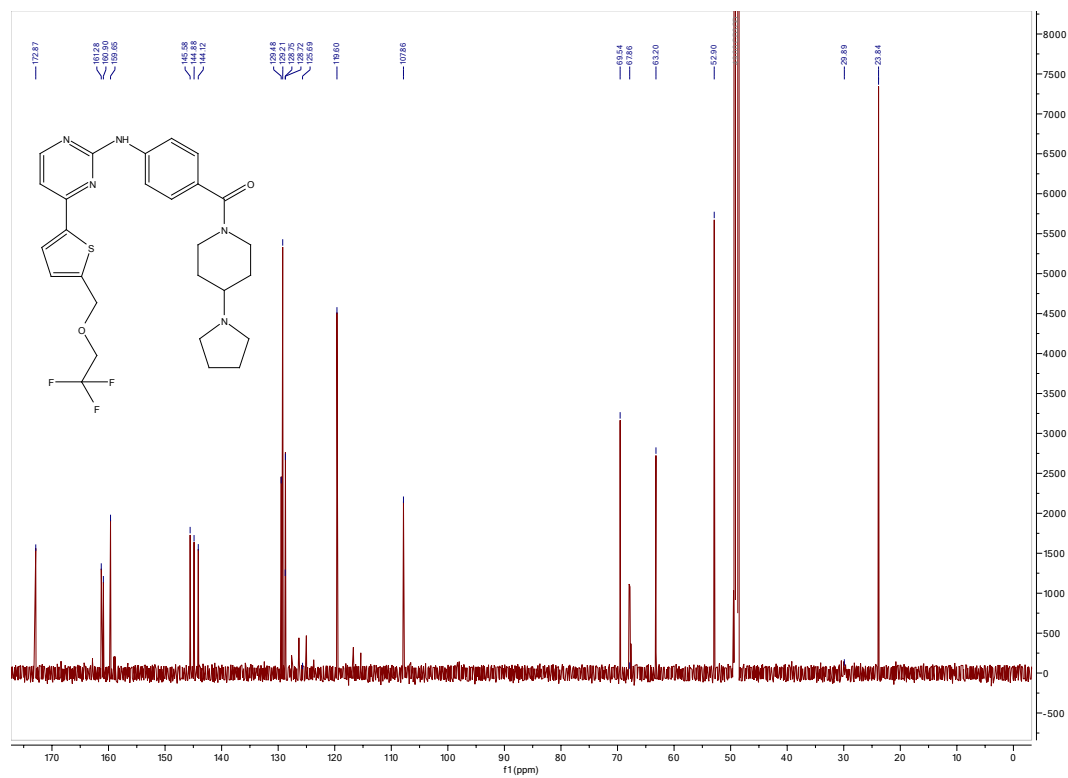
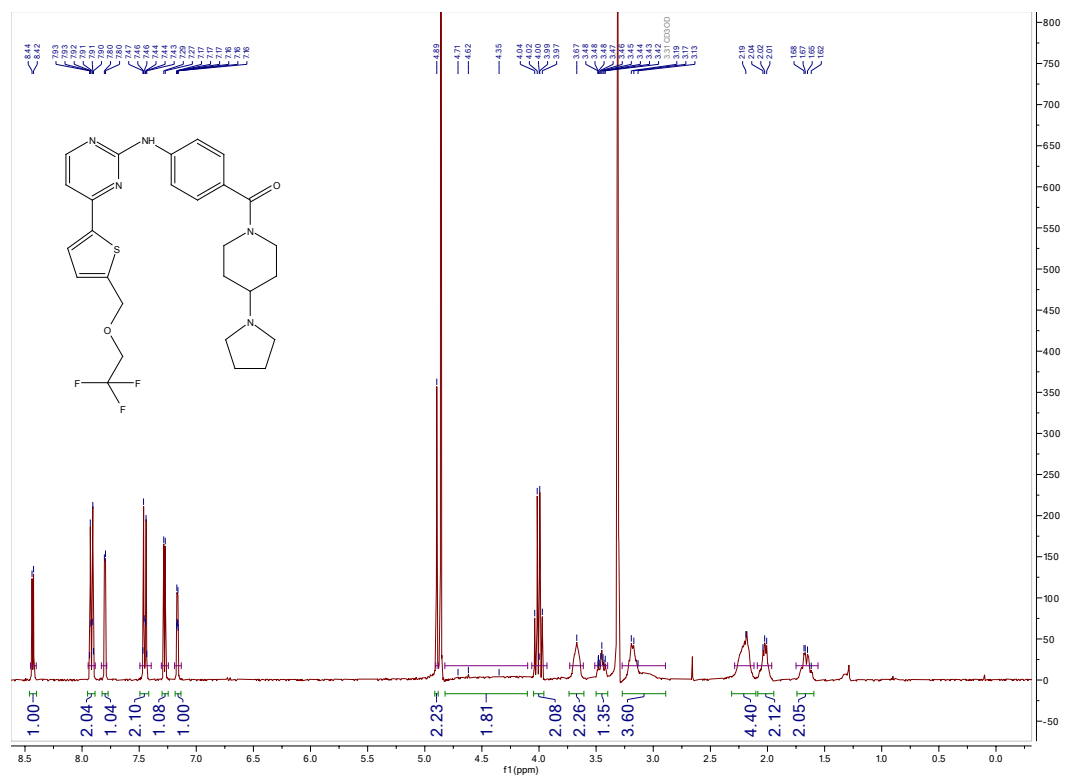


**(4-((4-(5-(Hydroxymethyl)thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18)**

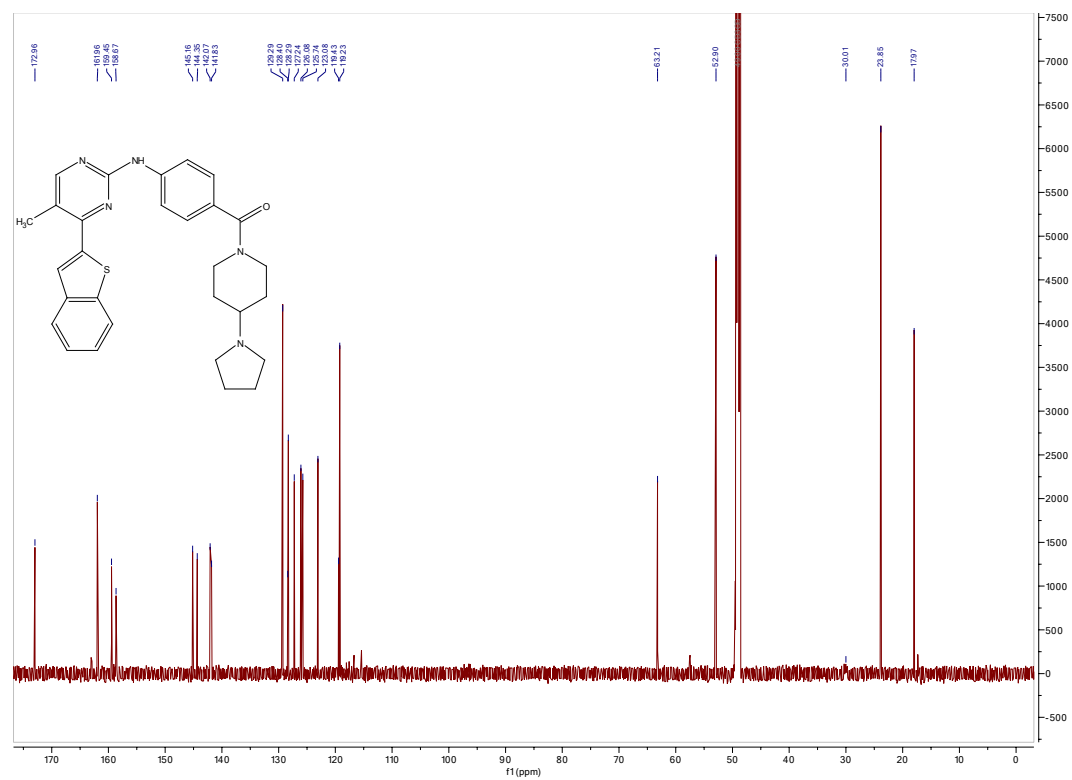
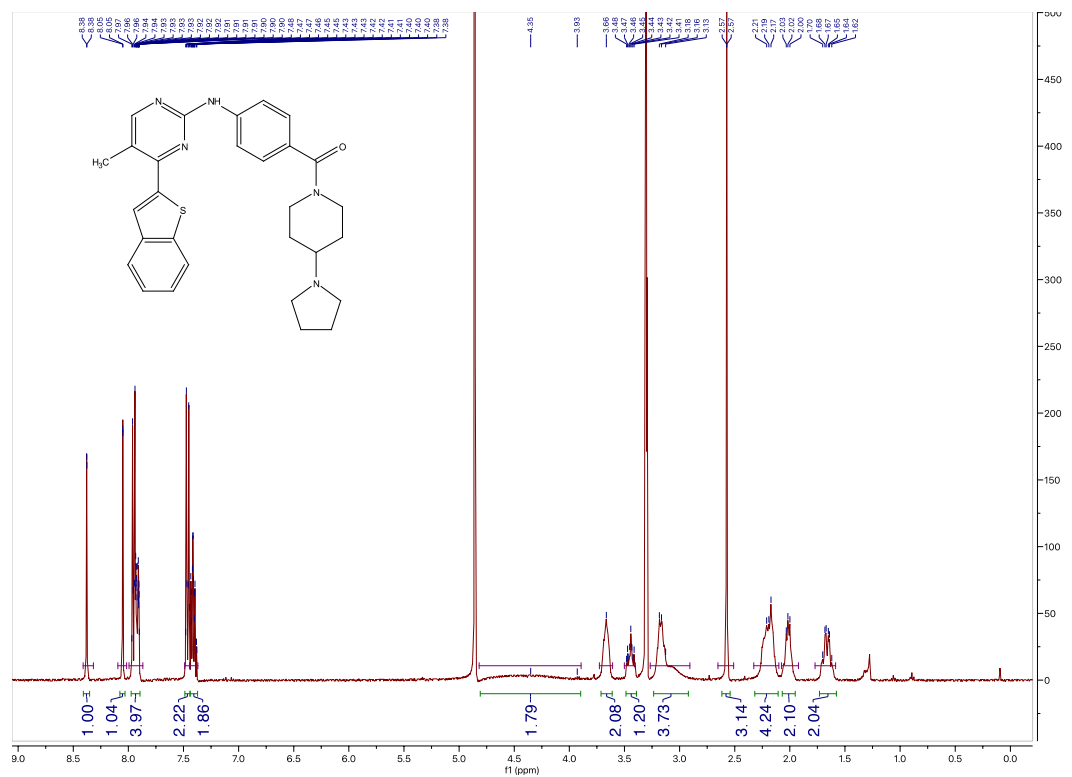




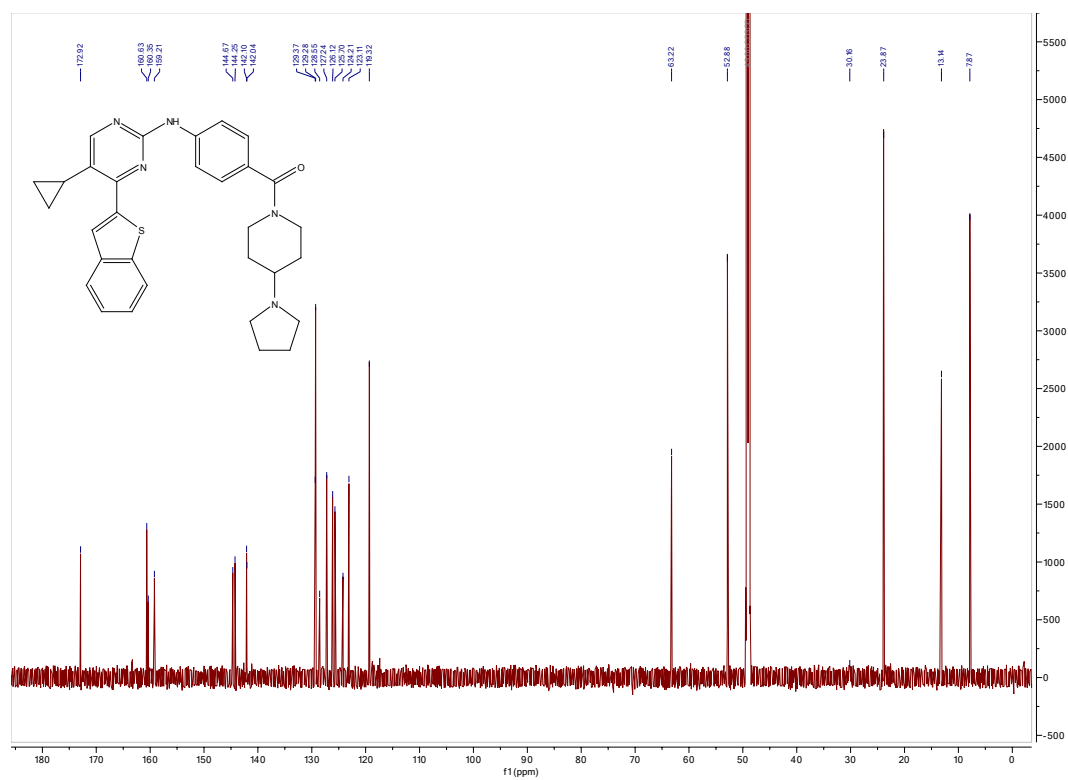
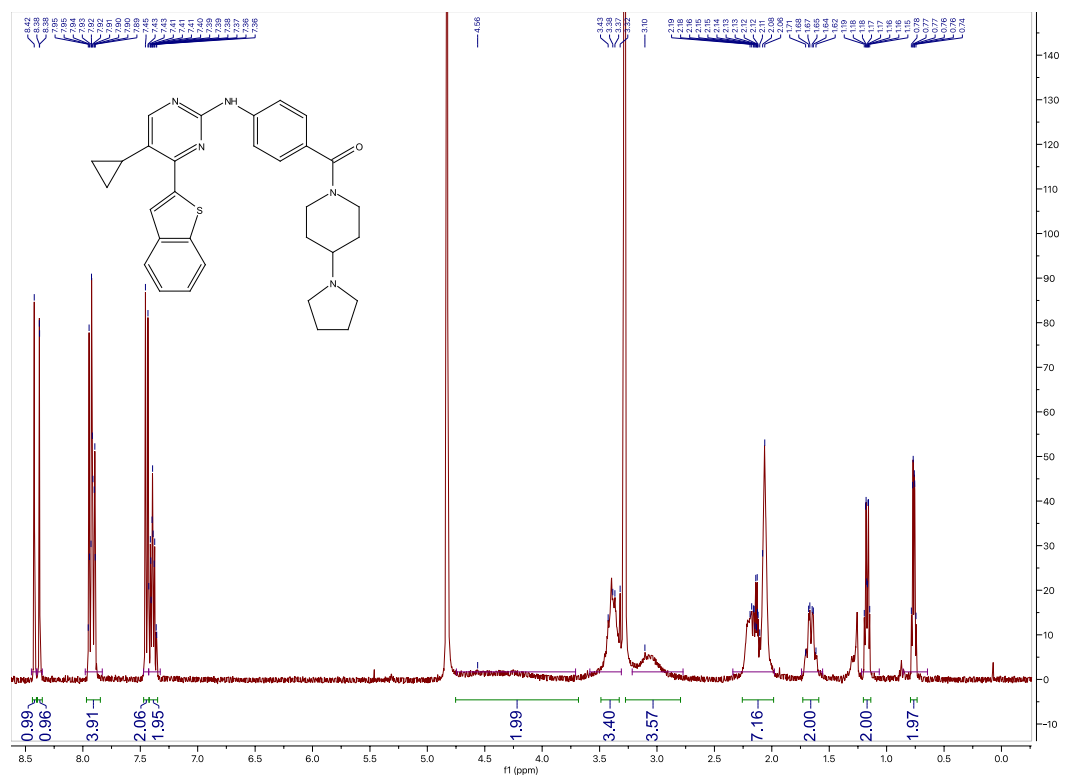
(4-(Pyrrolidin-1-yl)piperidin-1-yl)(4-((4-(5-((2,2,2-trifluoroethoxy)methyl)thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)methanone (18m)



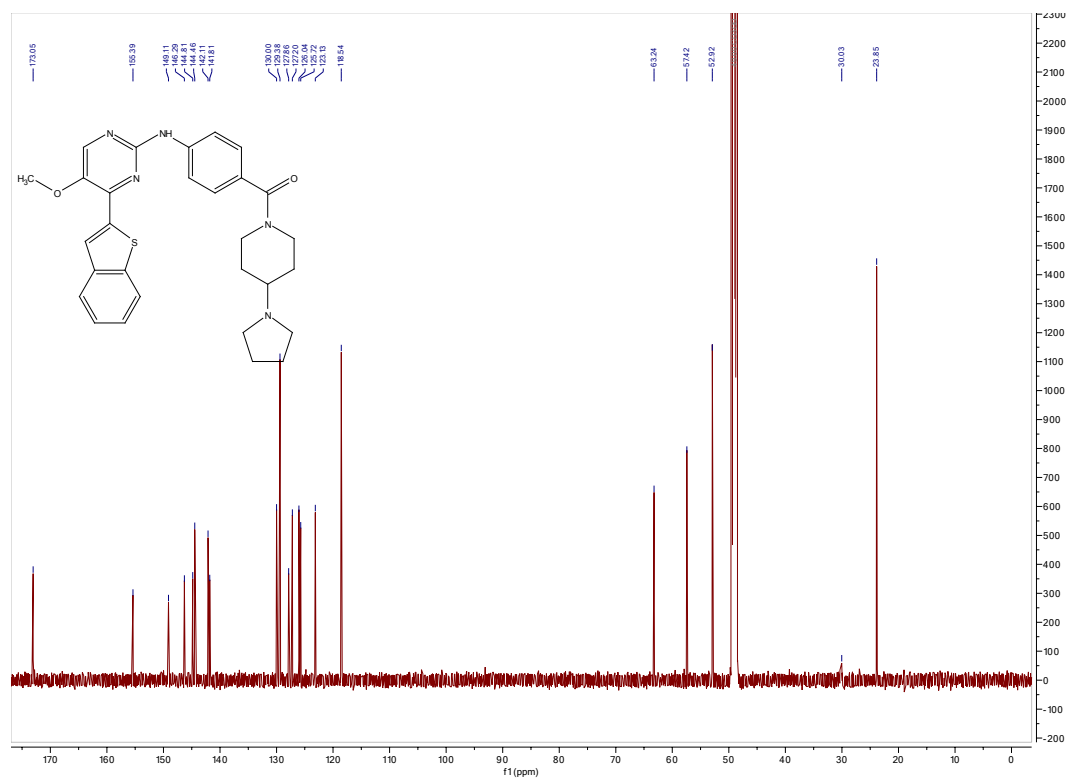
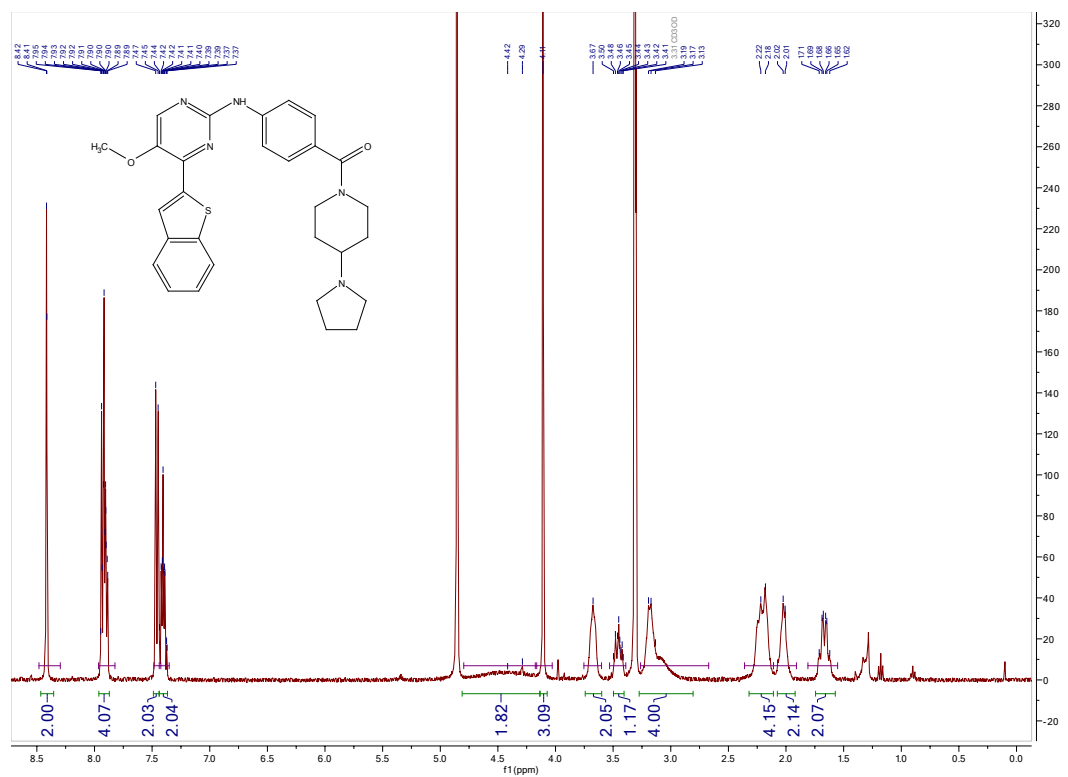
**4-((4-(Benzo[b]thiophen-2-yl)-5-methylpyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18n)**



**4-((4-(Benzo[b]thiophen-2-yl)-5-cyclopropylpyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18o)**



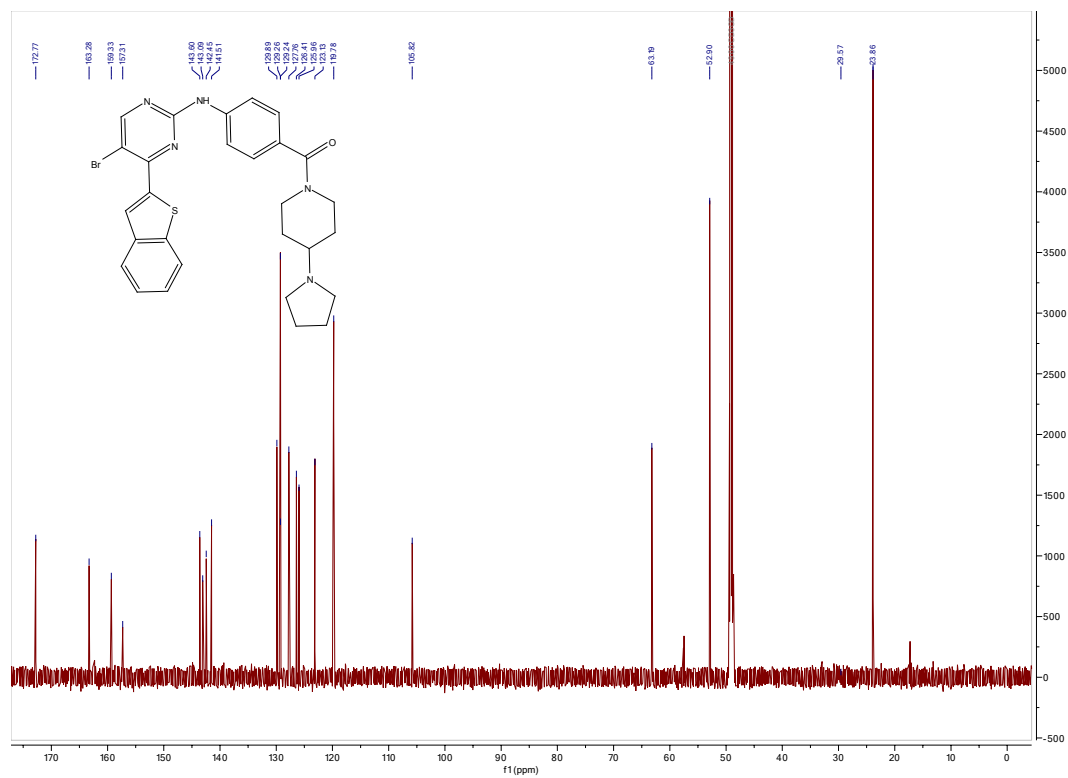
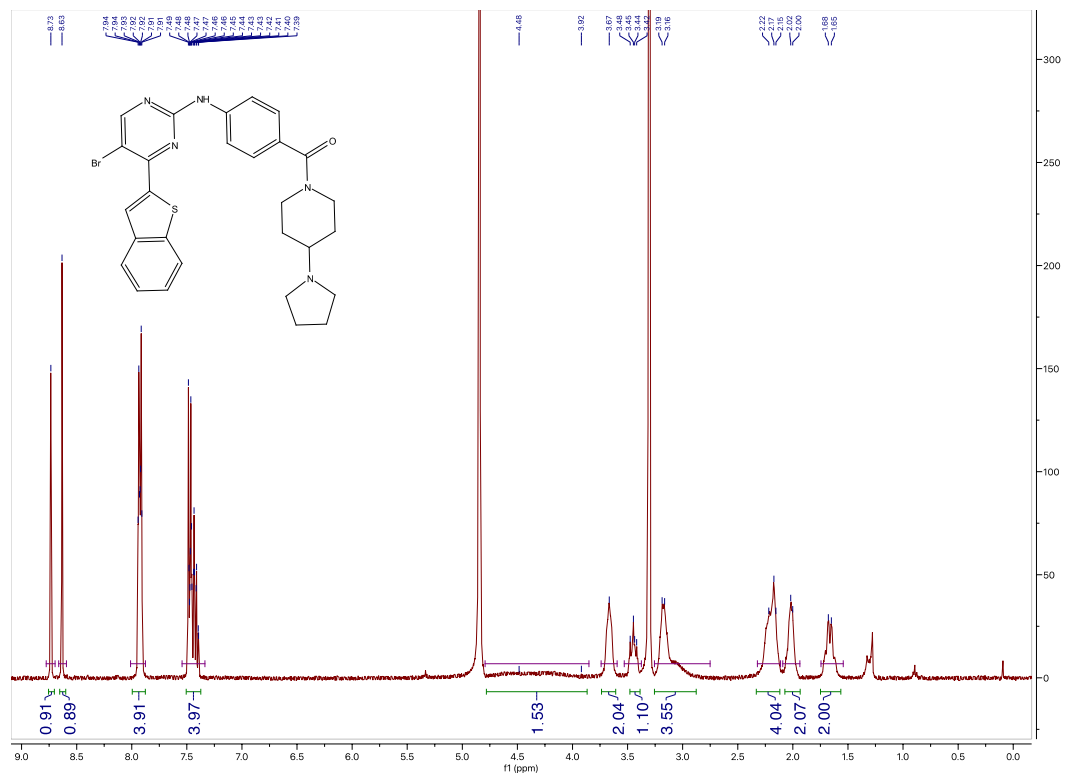
**4-((4-(Benzo[b]thiophen-2-yl)-5-methoxypyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18p)**







**4-((4-(Benzo[b]thiophen-2-yl)-5-bromopyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18s)**



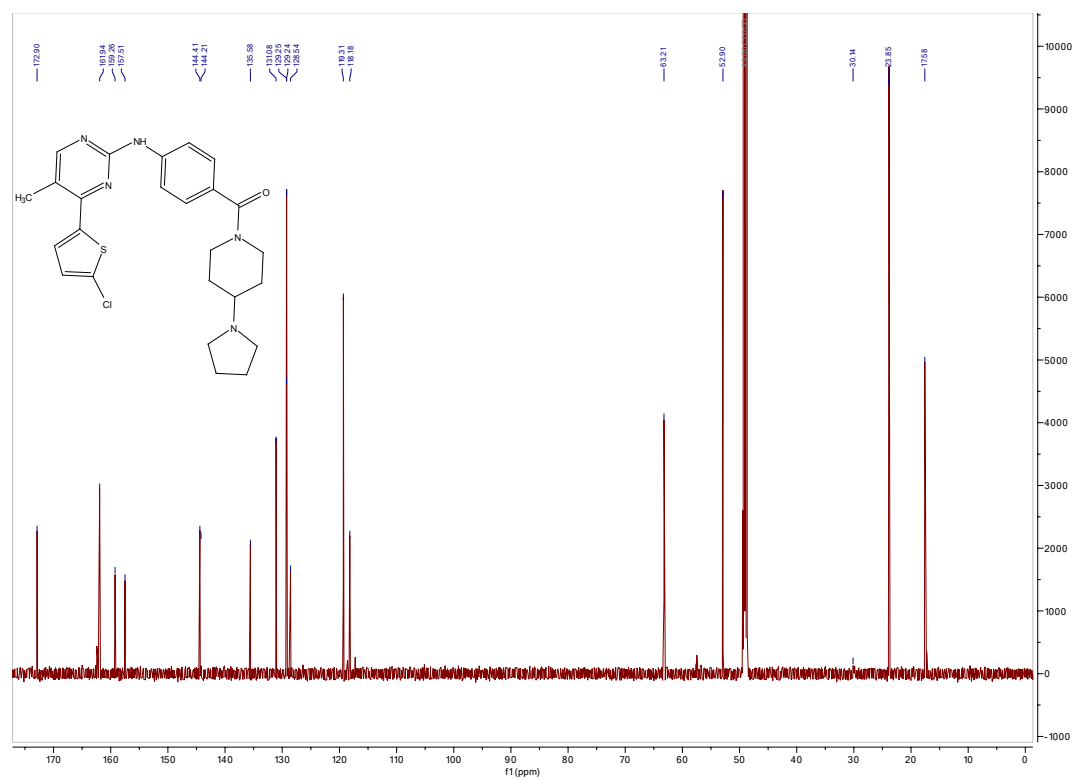
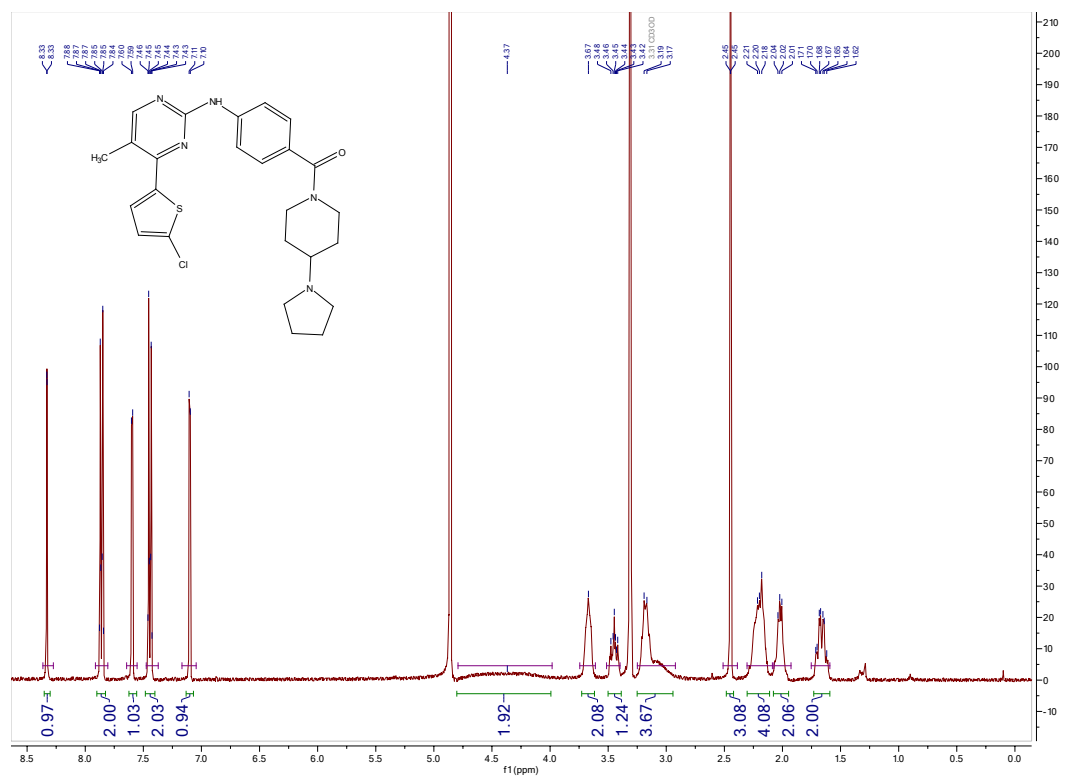




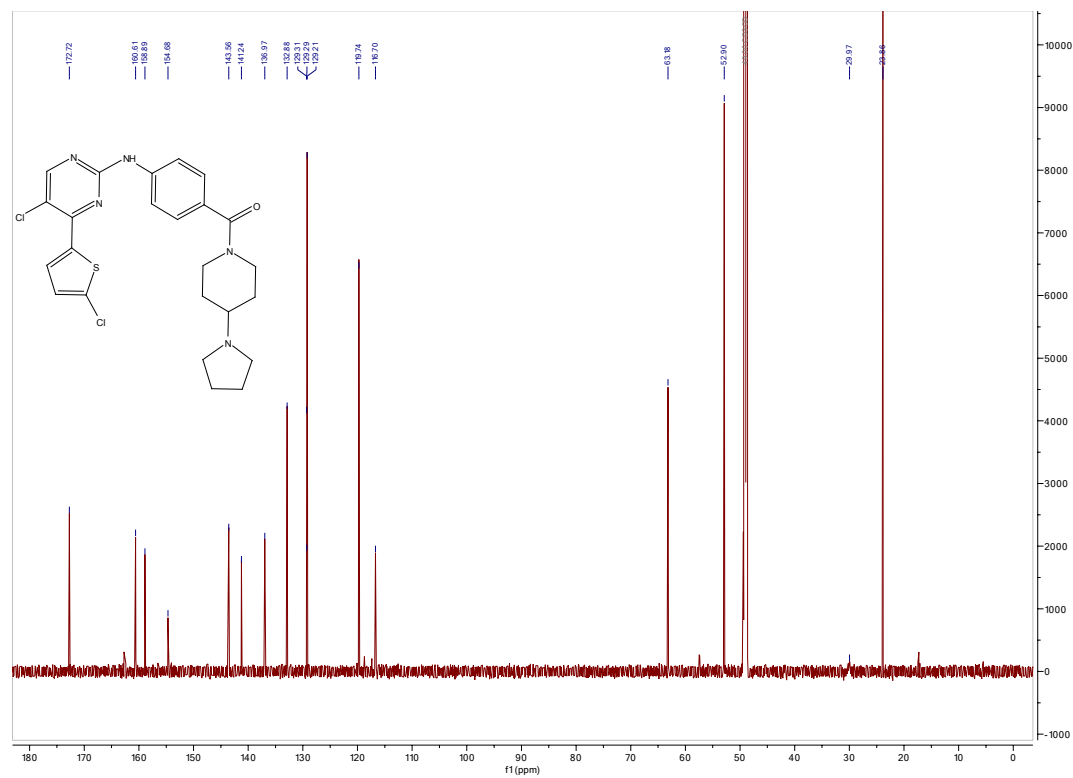
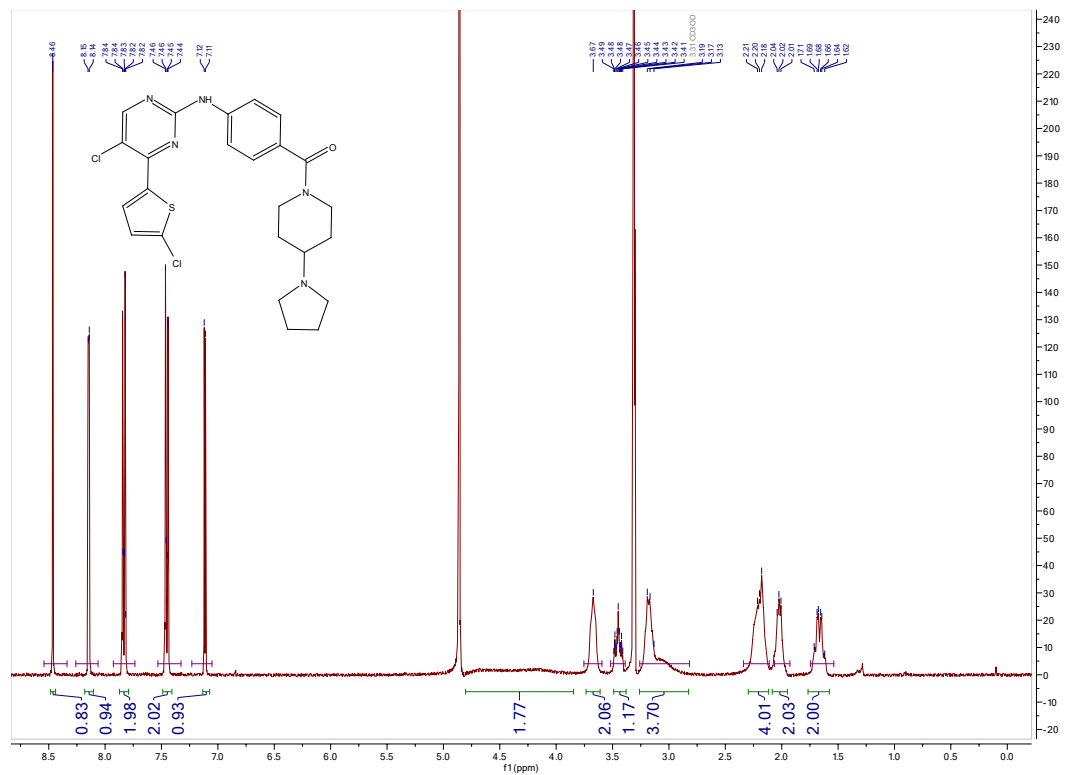




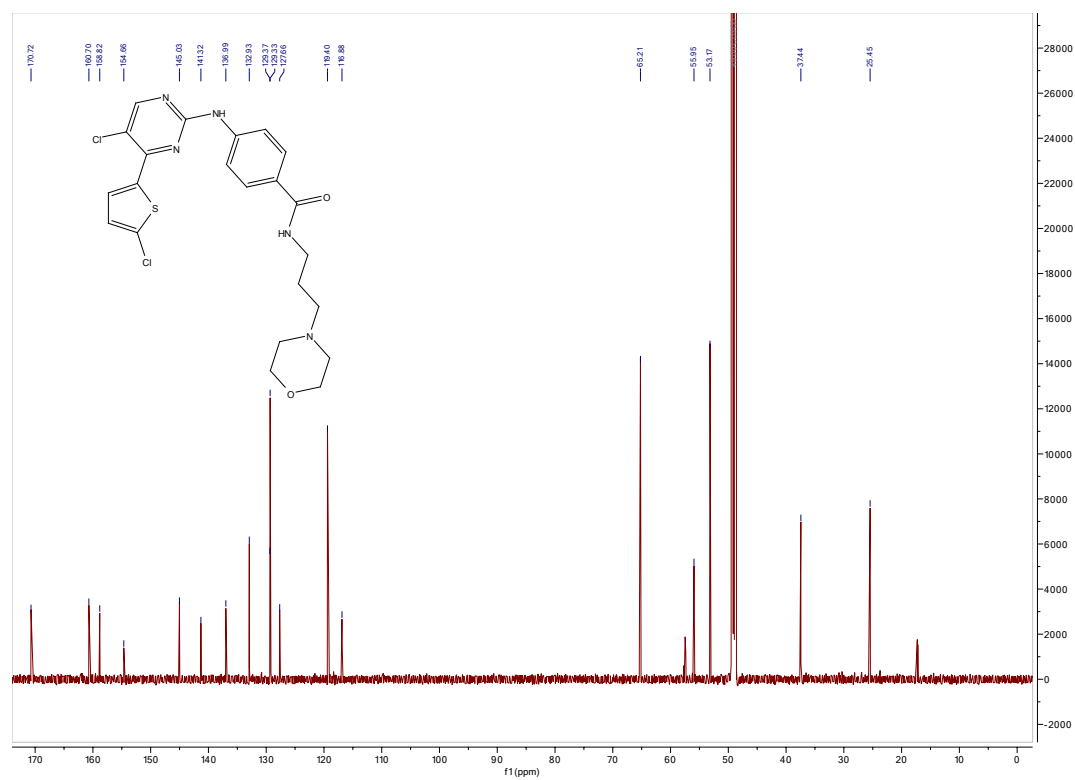
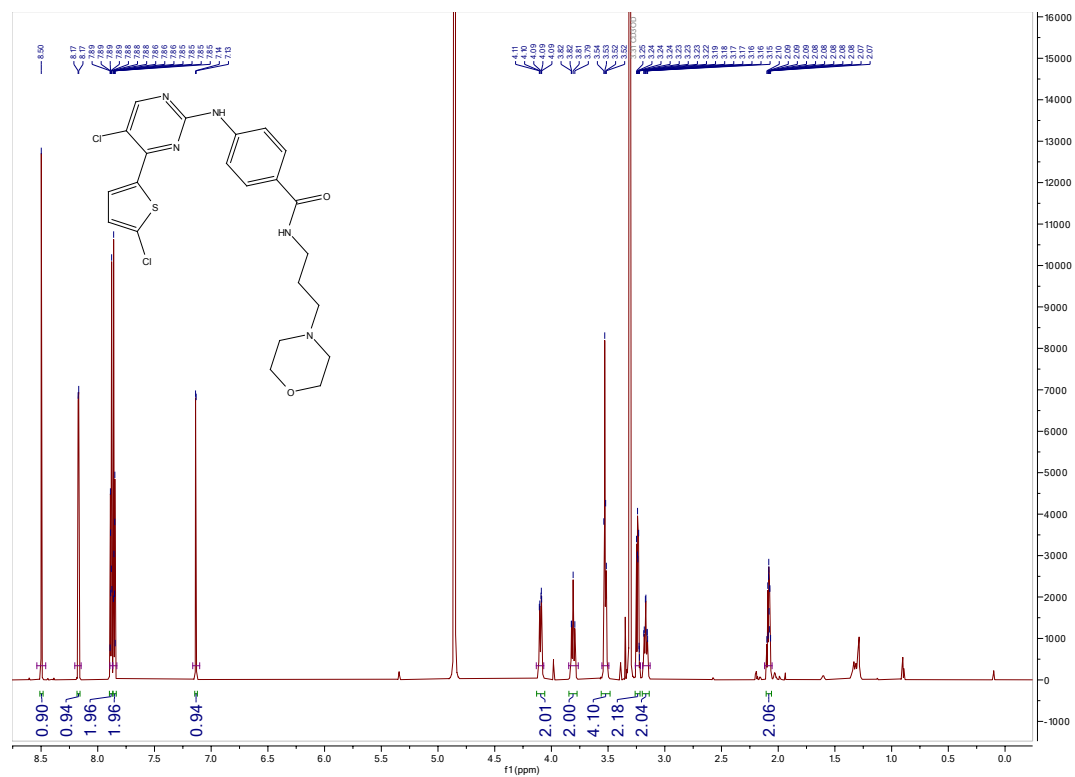
**(4-((4-(5-Chlorothiophen-2-yl)-5-methylpyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (23c)**



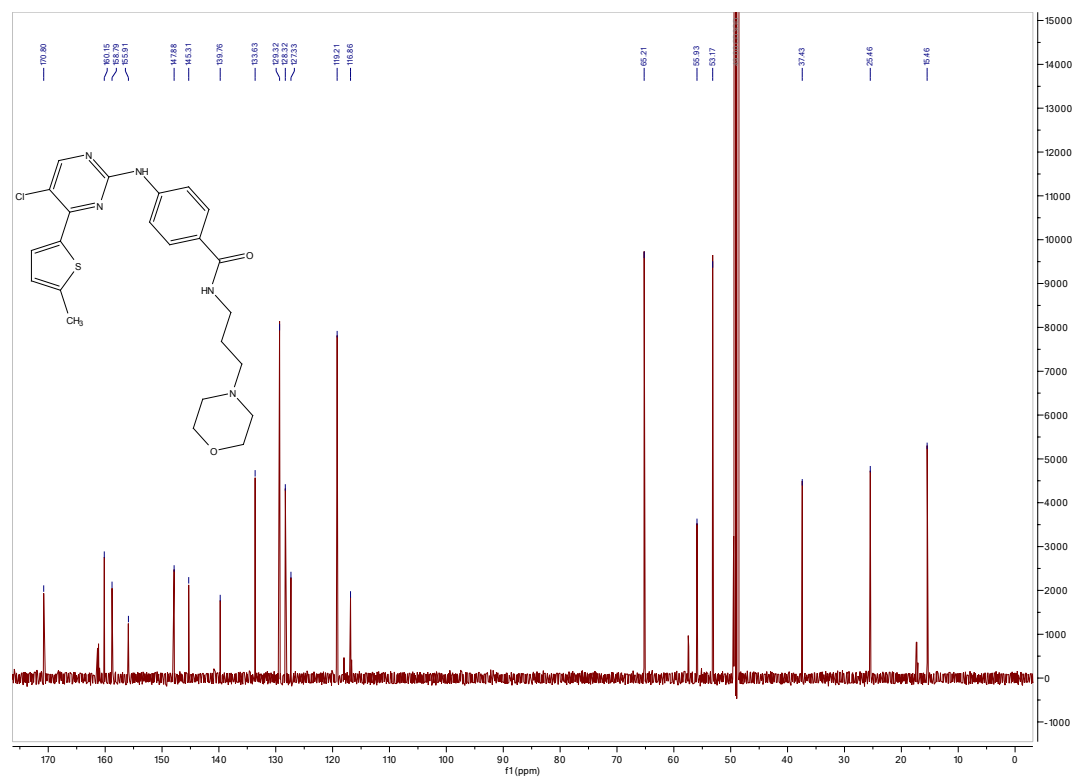
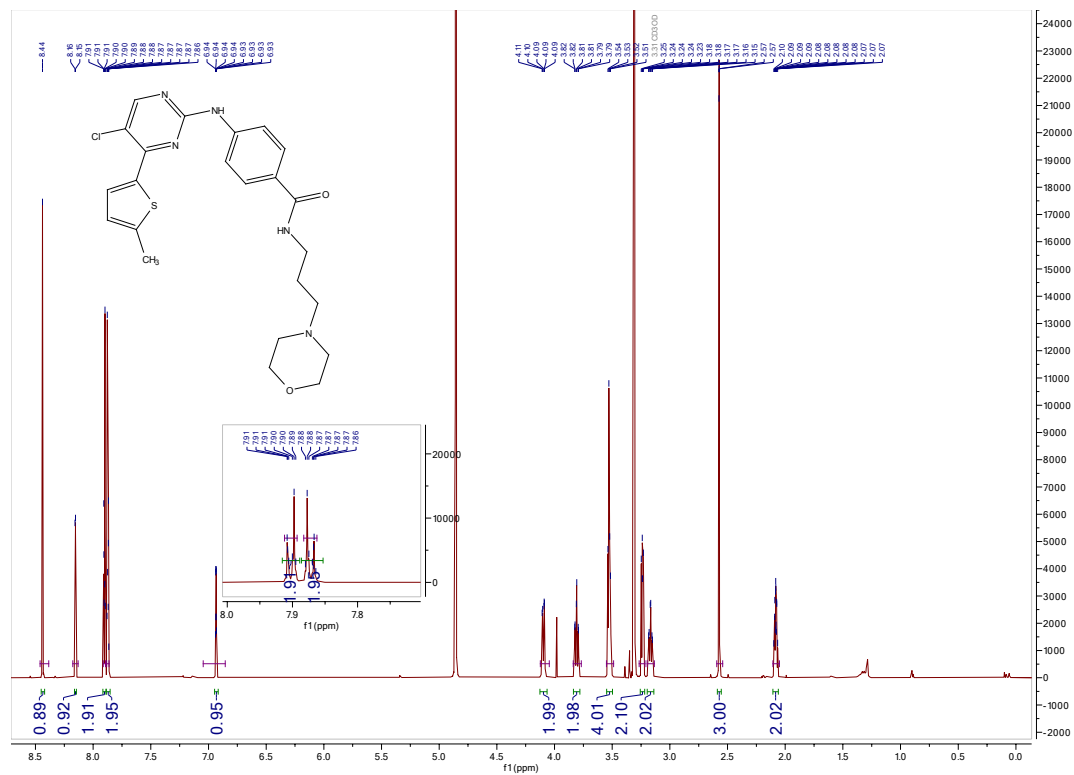
**4-((5-Chloro-4-(5-chlorothiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (23d)**



4-((5-Chloro-4-(5-chlorothiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-morpholinopropyl)benzamide (23e)



4-((5-Chloro-4-(5-methylthiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-morpholinopropyl)benzamide (23f)

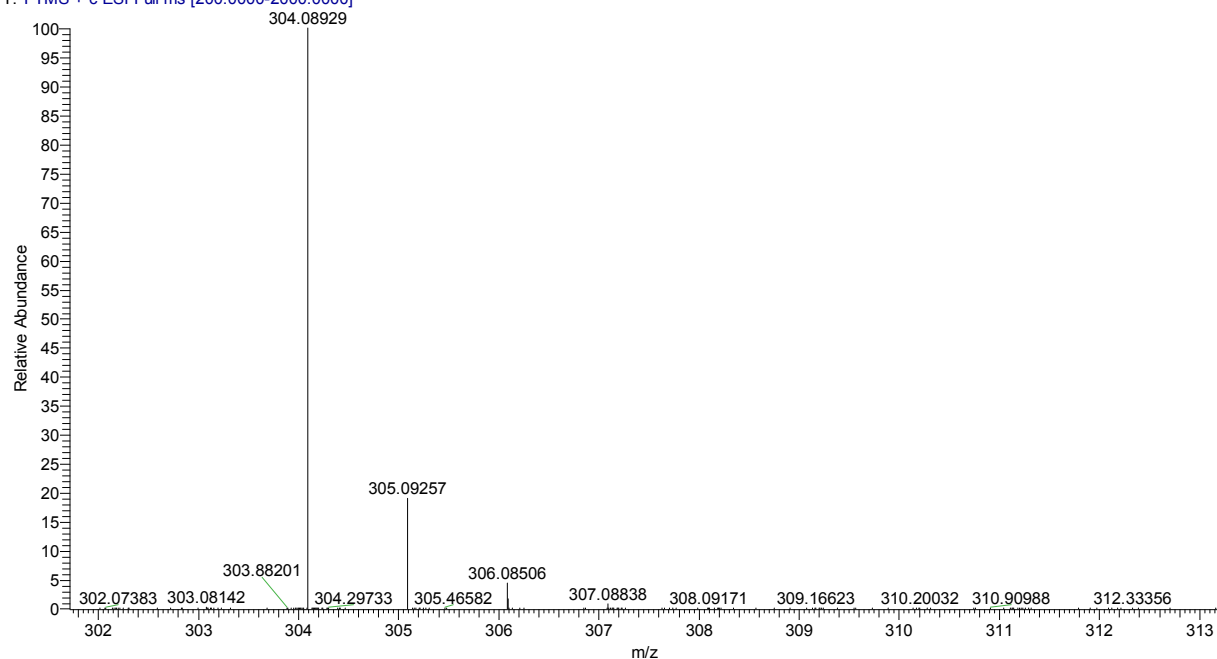




## HRMS spectra of compounds submitted for biological screening

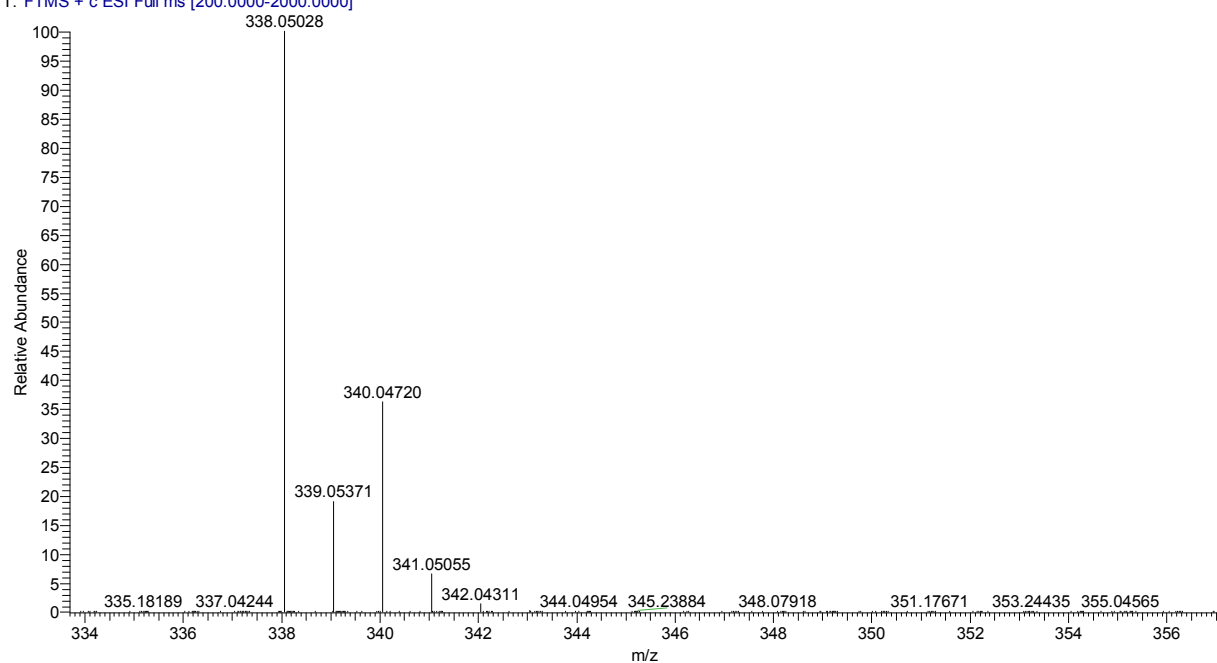
### 4-(Benzo[b]thiophen-2-yl)-N-phenylpyrimidin-2-amine (4a)

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### 4-(Benzo[b]thiophen-2-yl)-N-(4-chlorophenyl)pyrimidin-2-amine (4b)

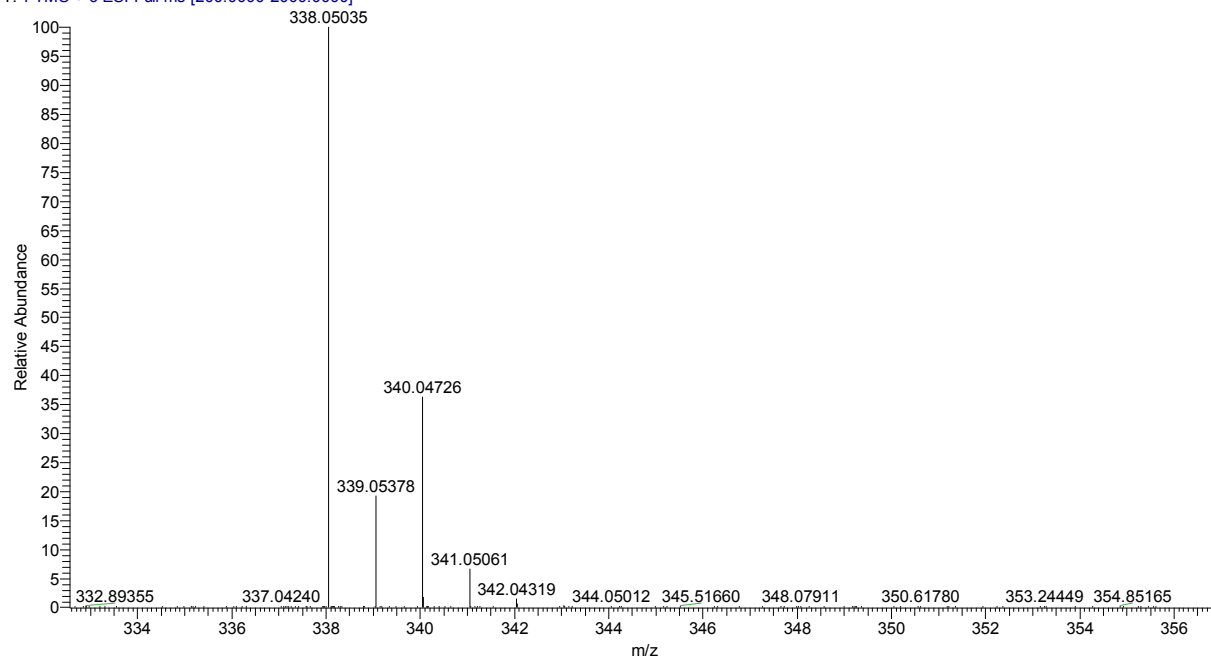
KG-09 #1313-1372 RT: 5.67-5.93 AV: 60 NL: 1.14E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]





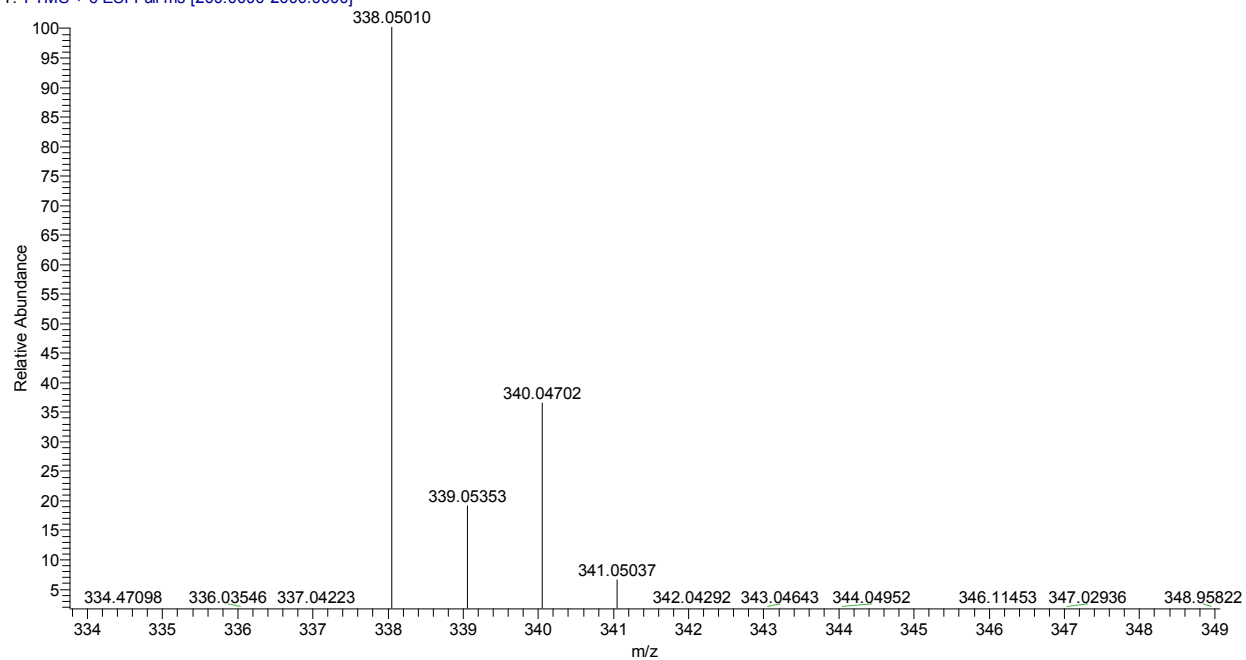
### 4-(Benzo[b]thiophen-2-yl)-N-(3-chlorophenyl)pyrimidin-2-amine (4c)

KG-12 #1313-1372 RT: 5.67-5.93 AV: 60 NL: 1.85E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



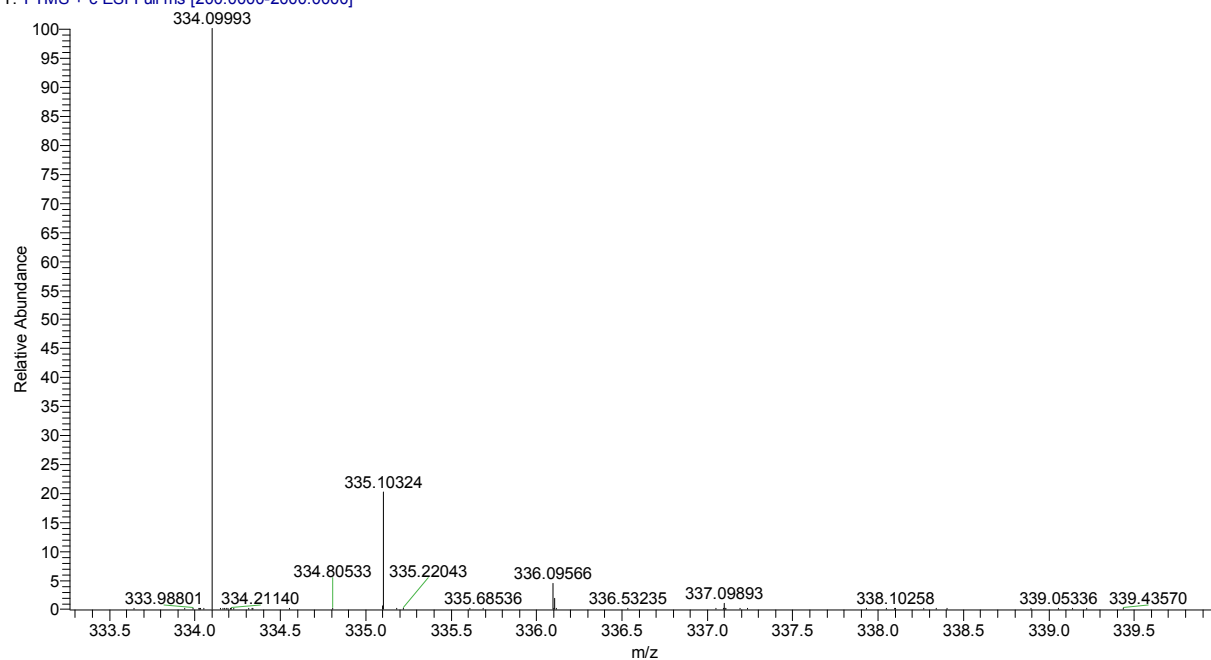
### 4-(Benzo[b]thiophen-2-yl)-N-(2-chlorophenyl)pyrimidin-2-amine (4d)

KG-16 #1365-1402 RT: 5.90-6.06 AV: 38 NL: 2.29E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



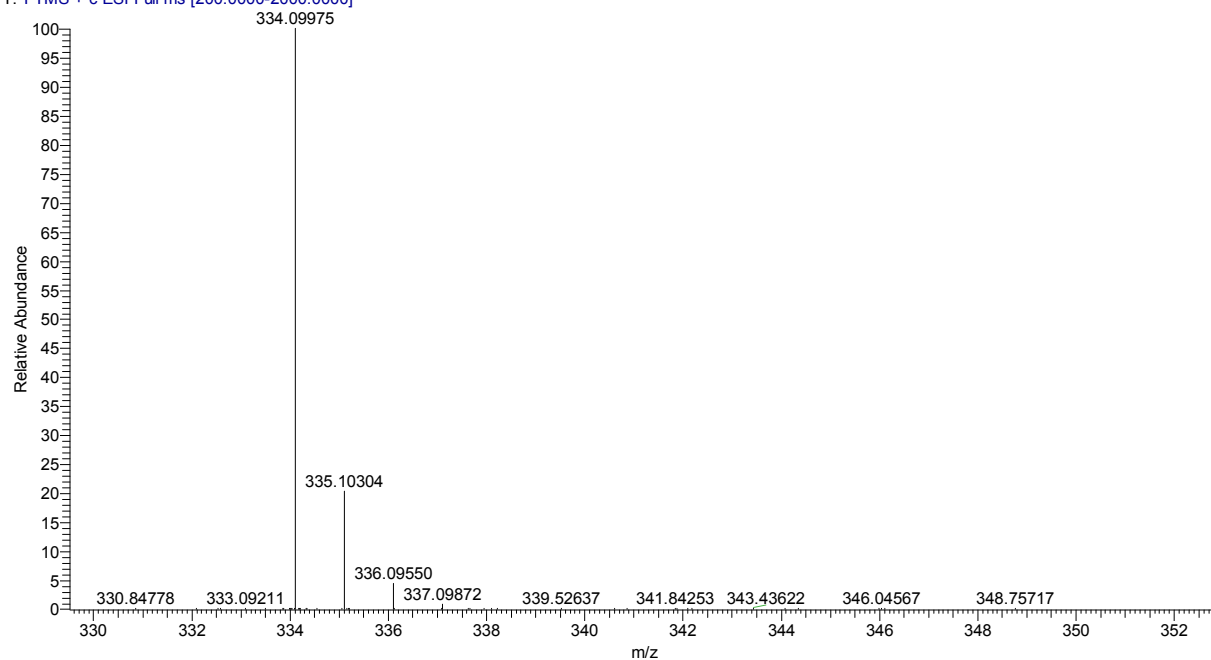
### 4-(Benzo[b]thiophen-2-yl)-N-(4-methoxyphenyl)pyrimidin-2-amine (4e)

KG-18 #1193-1236 RT: 5.15-5.34 AV: 44 NL: 1.03E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



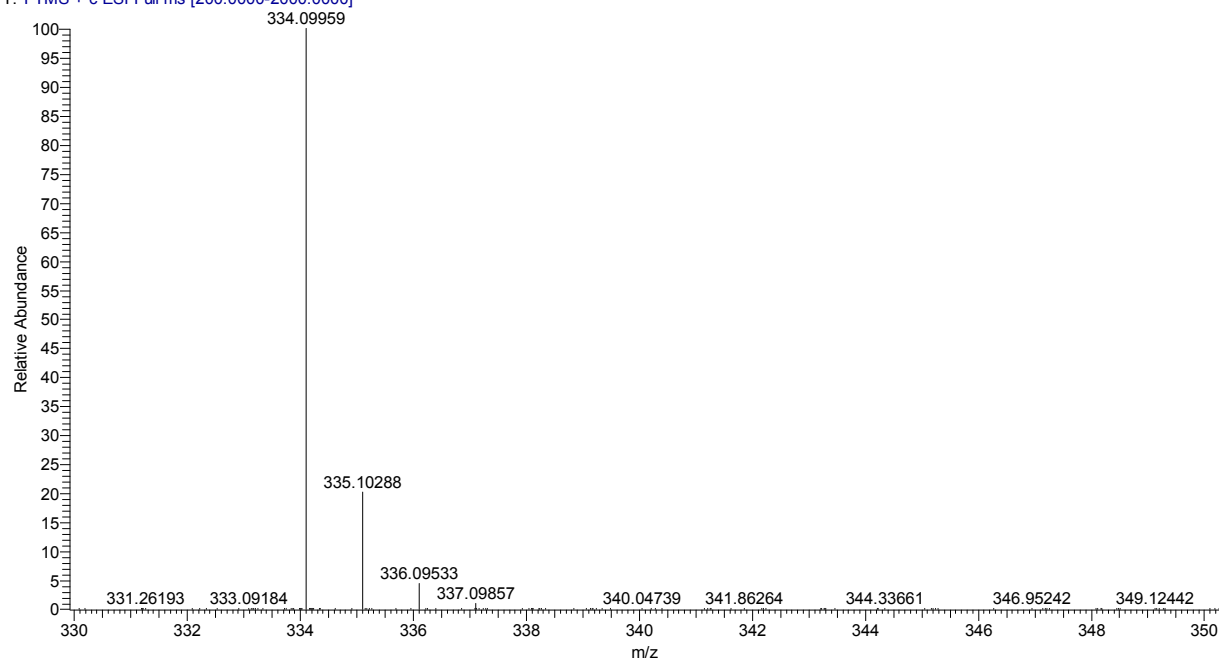
### 4-(Benzo[b]thiophen-2-yl)-N-(3-methoxyphenyl)pyrimidin-2-amine (4f)

KG-19 #1214-1252 RT: 5.25-5.41 AV: 39 NL: 4.98E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



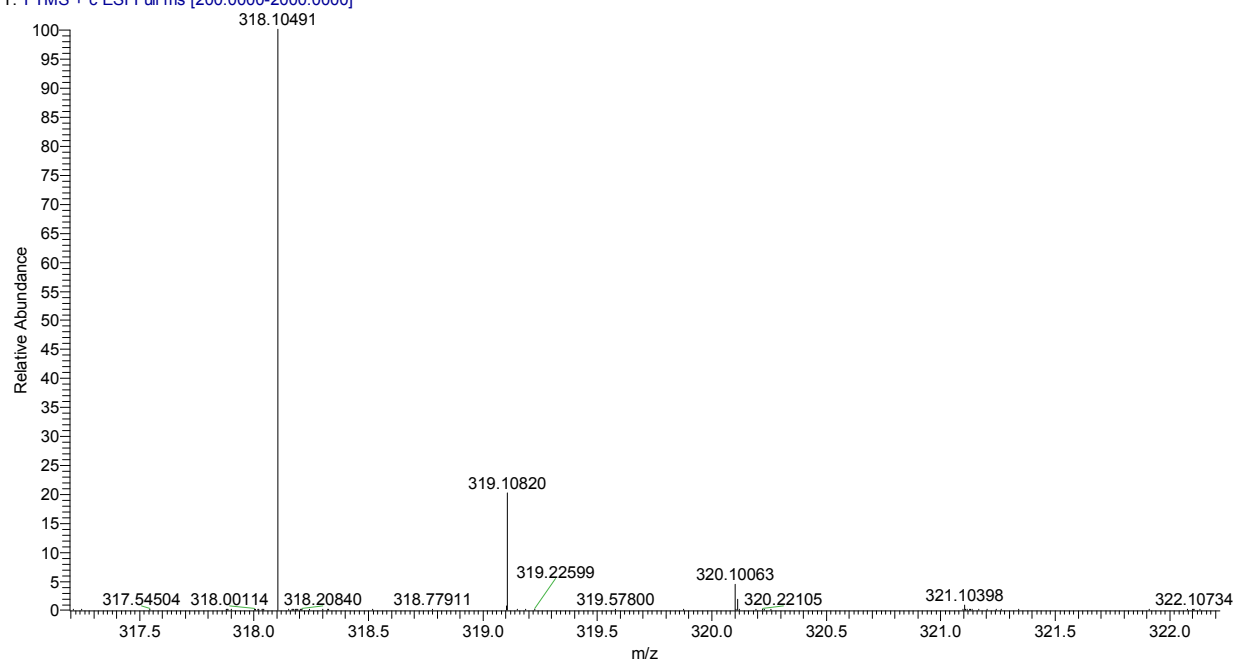
### 4-(Benzo[b]thiophen-2-yl)-N-(2-methoxyphenyl)pyrimidin-2-amine (4g)

KG-20 #1301-1351 RT: 5.62-5.84 AV: 51 NL: 5.90E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



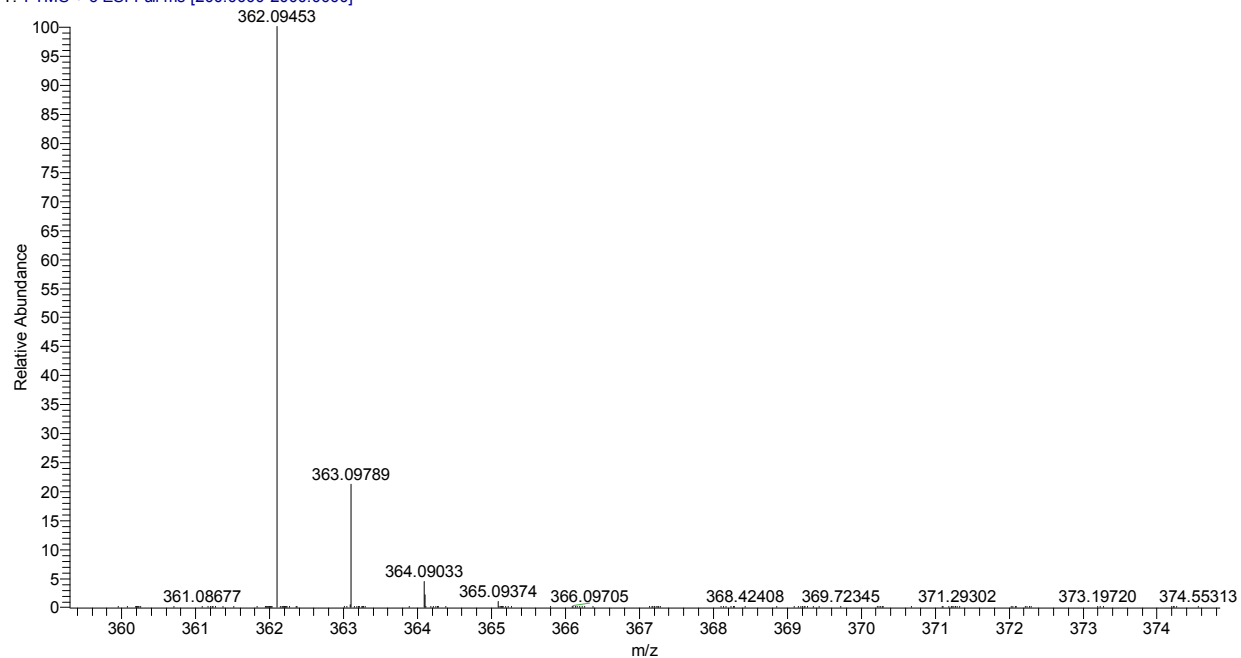
### 4-(Benzo[b]thiophen-2-yl)-N-benzylpyrimidin-2-amine (4h)

KG-8 #1166-1226 RT: 5.04-5.30 AV: 61 NL: 2.79E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



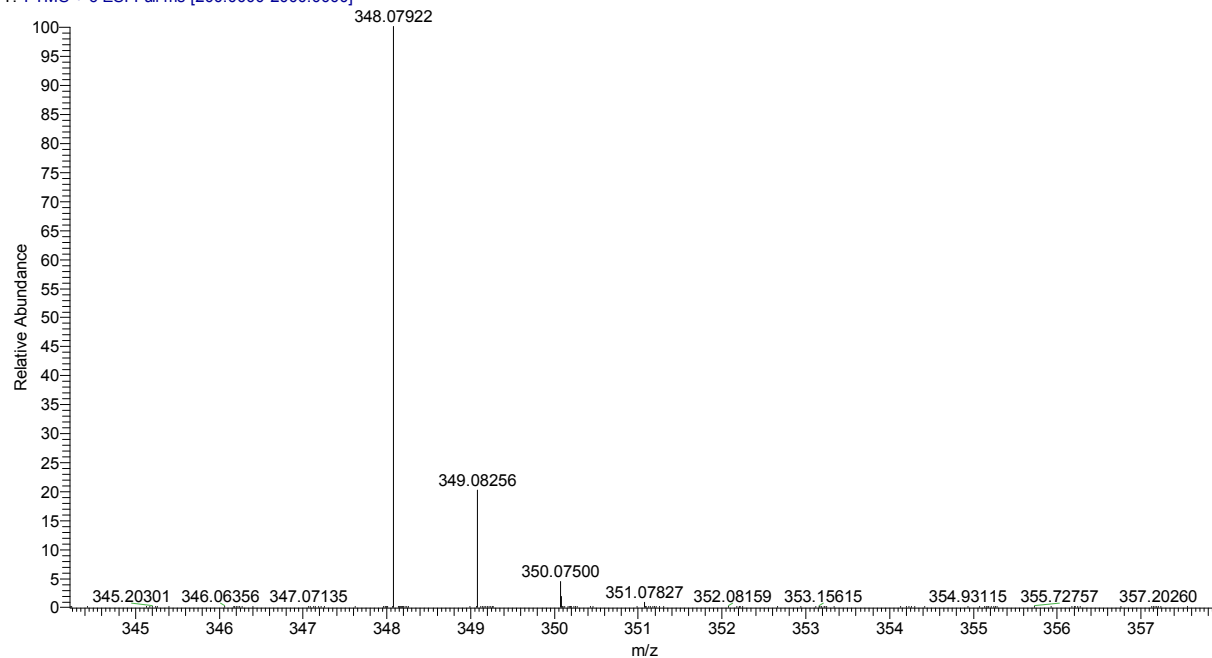
### 4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)benzoate (5)

KG-05 #1209-1260 RT: 5.22-5.45 AV: 52 NL: 2.70E9  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



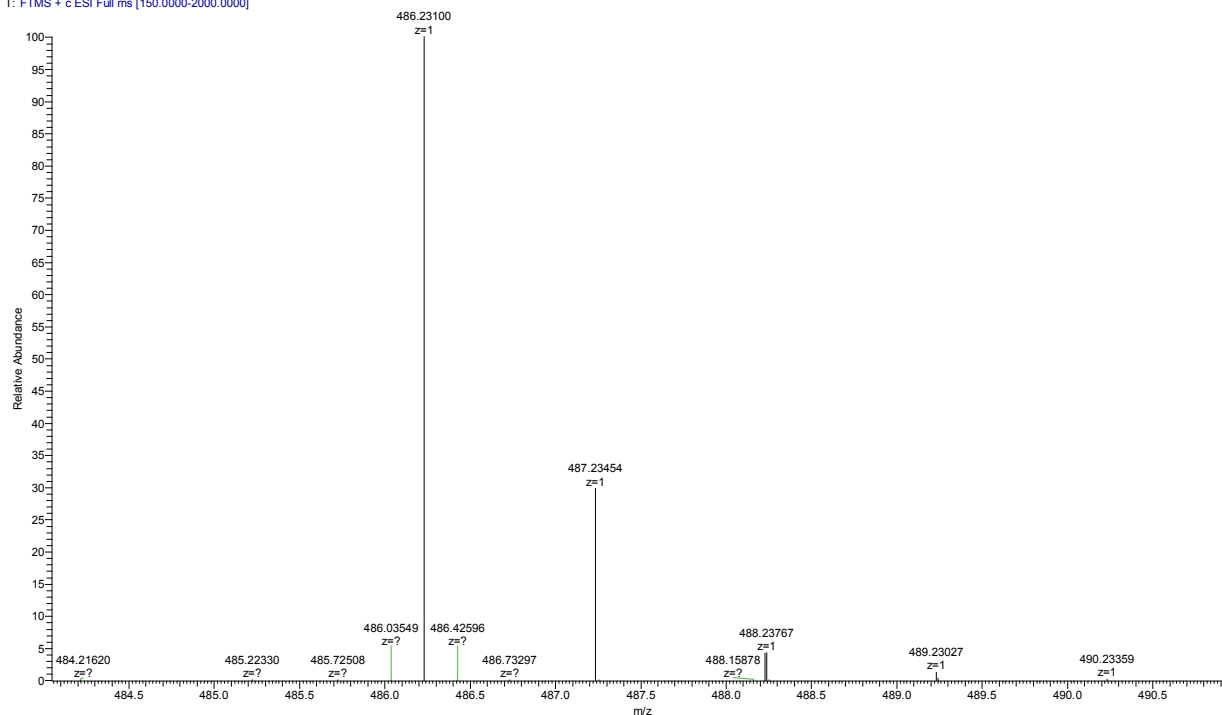
### 4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)benzoic acid (6)

KG-06 #1031-1083 RT: 4.45-4.68 AV: 53 NL: 3.18E8  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



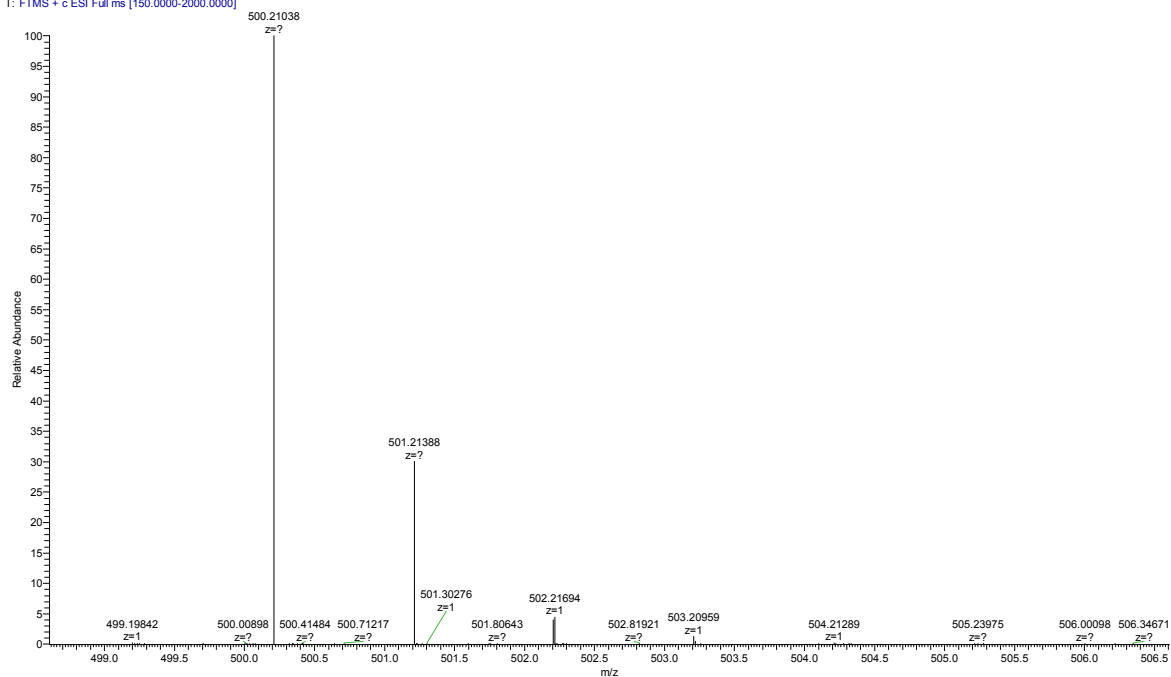
**4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(methyl(propyl)amino)piperidin-1-yl)methanone (8a)**

K50B #987-1004 RT: 4.26-4.34 AV: 18 NL: 1.01E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]

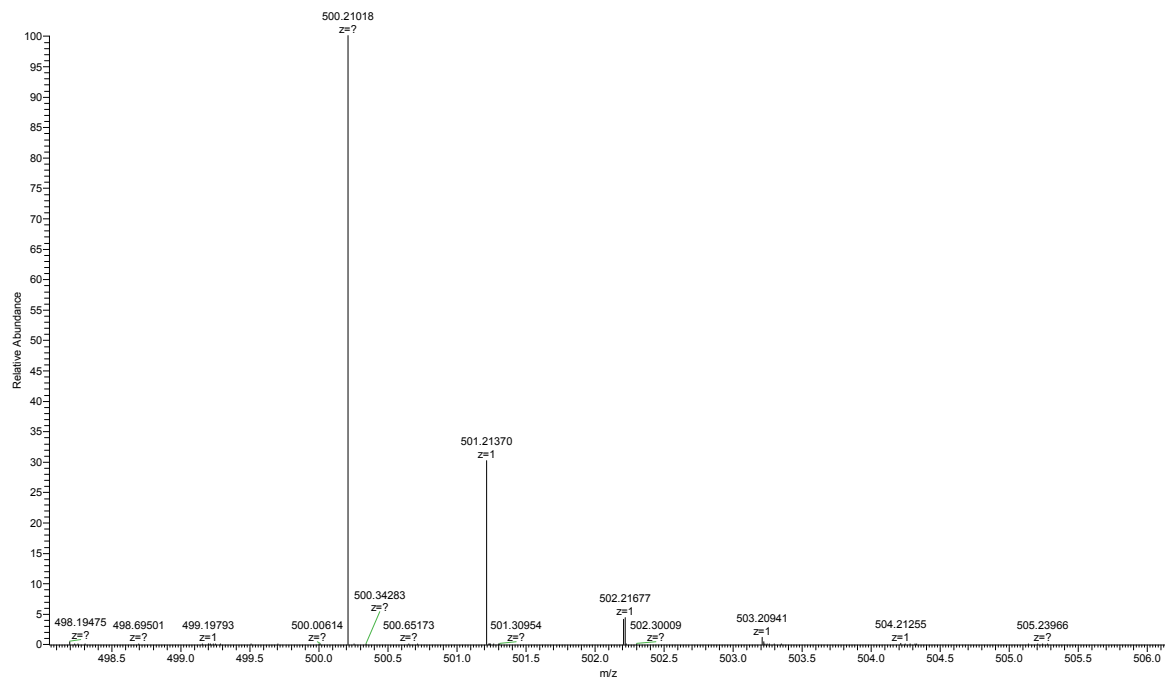


**(R)-4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(3-hydroxypyrrolidin-1-yl)piperidin-1-yl)methanone (8b)**

K51 #927-970 RT: 4.01-4.19 AV: 44 NL: 5.17E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]

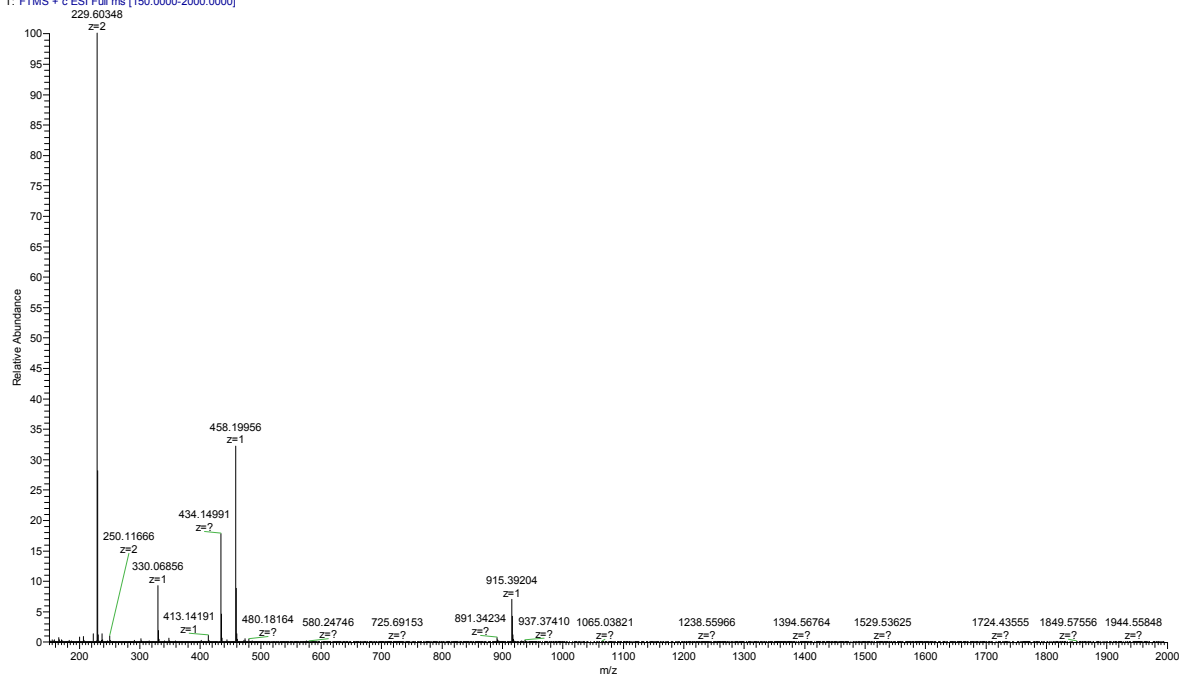


**(S)-4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(3-hydroxypyrrolidin-1-yl)piperidin-1-yl)methanone (8c, KG1-052)**



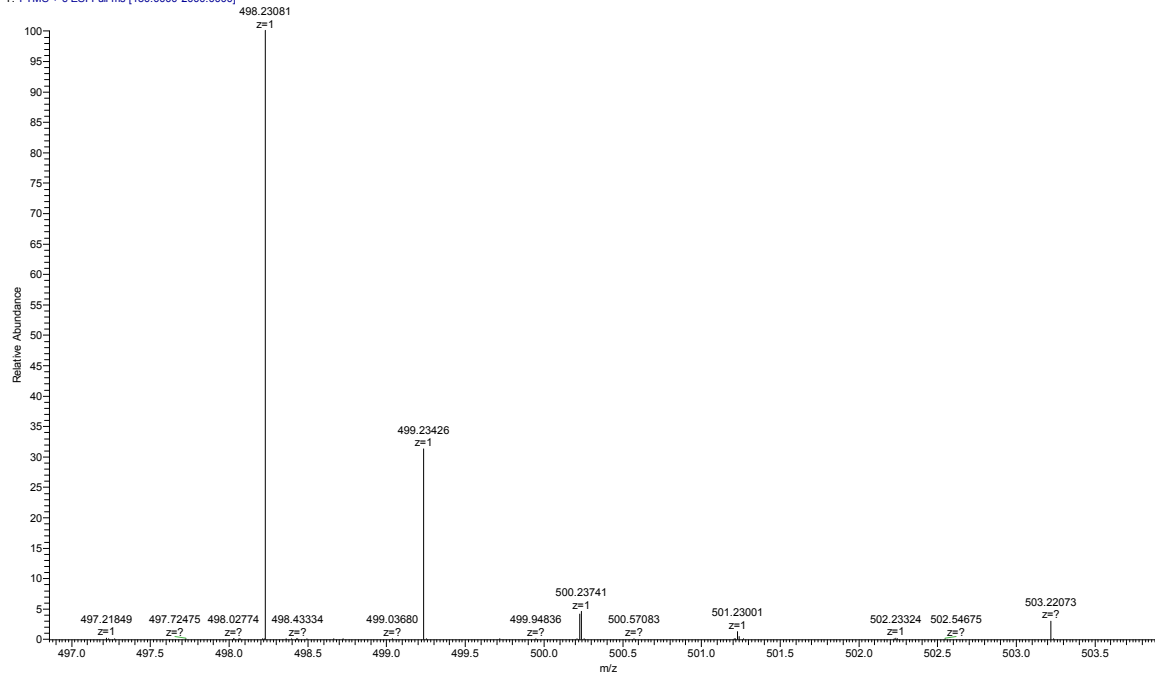
**4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(dimethylamino)piperidin-1-yl)methanone (9a)**

K21 #942-976 RT: 4.07-4.22 AV: 35 NL: 1.64E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



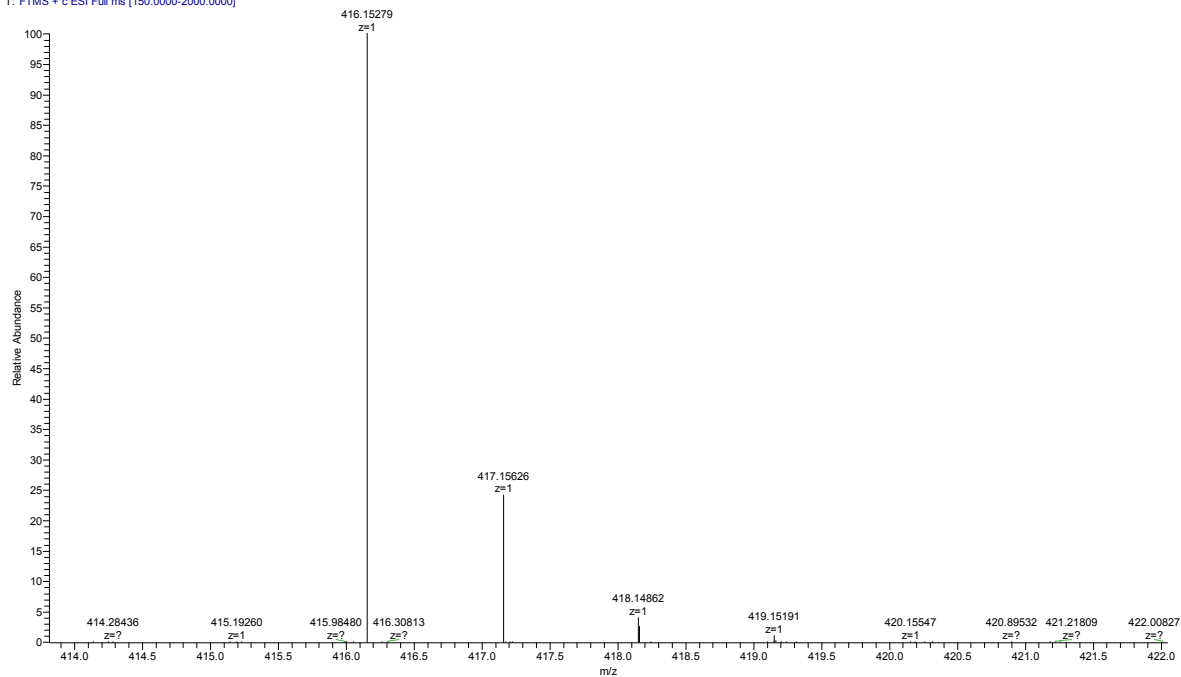
**[1,4'-Bipiperidin]-1'-yl(4-((4-(benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)methanone (9b)**

K48 #974-1008 RT: 4.21-4.36 AV: 35 NL: 1.12E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



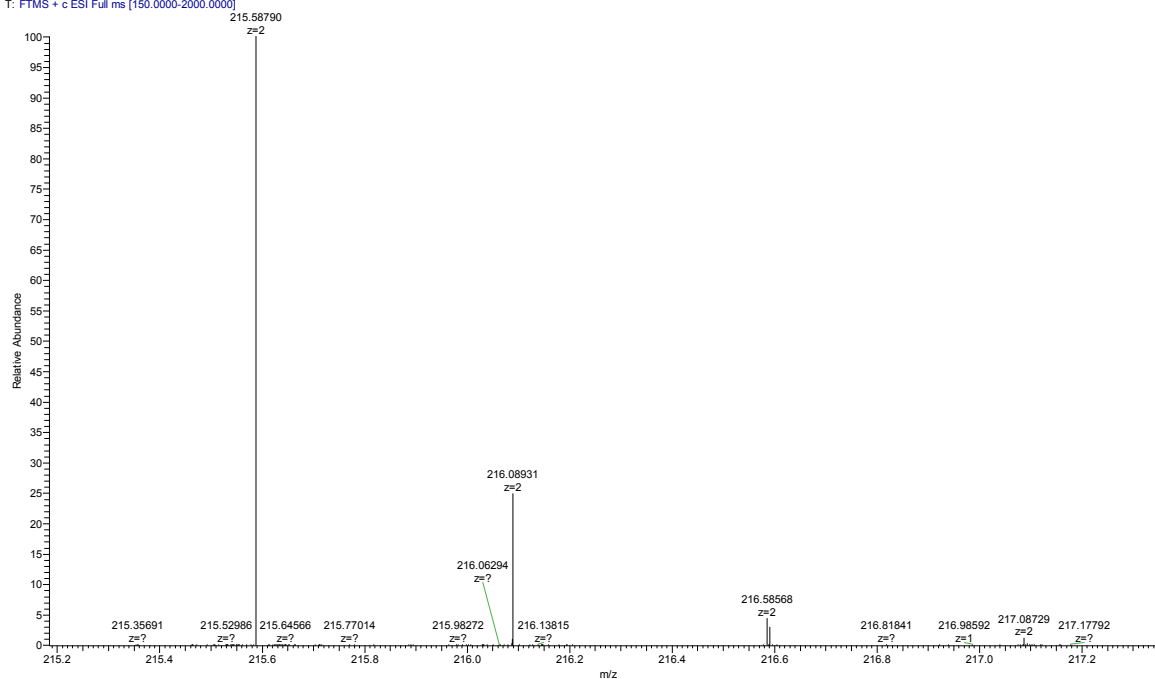
**(4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(piperazin-1-yl)methanone (9c)**

K30 #924-941 RT: 3.99-4.07 AV: 18 NL: 4.45E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



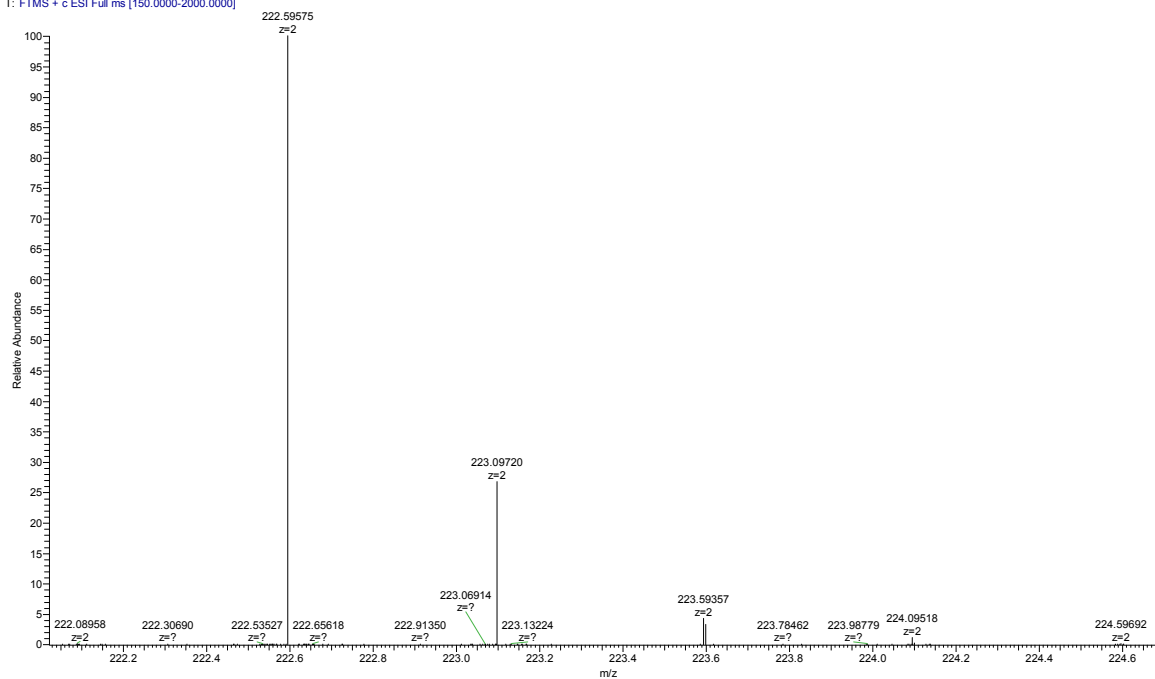
**4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-methylpiperazin-1-yl)methanone (9d)**

K22 #925-980 RT: 4.00-4.23 AV: 56 NL: 2.26E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



**4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-(1-methylpiperidin-4-yl)benzamide (9e)**

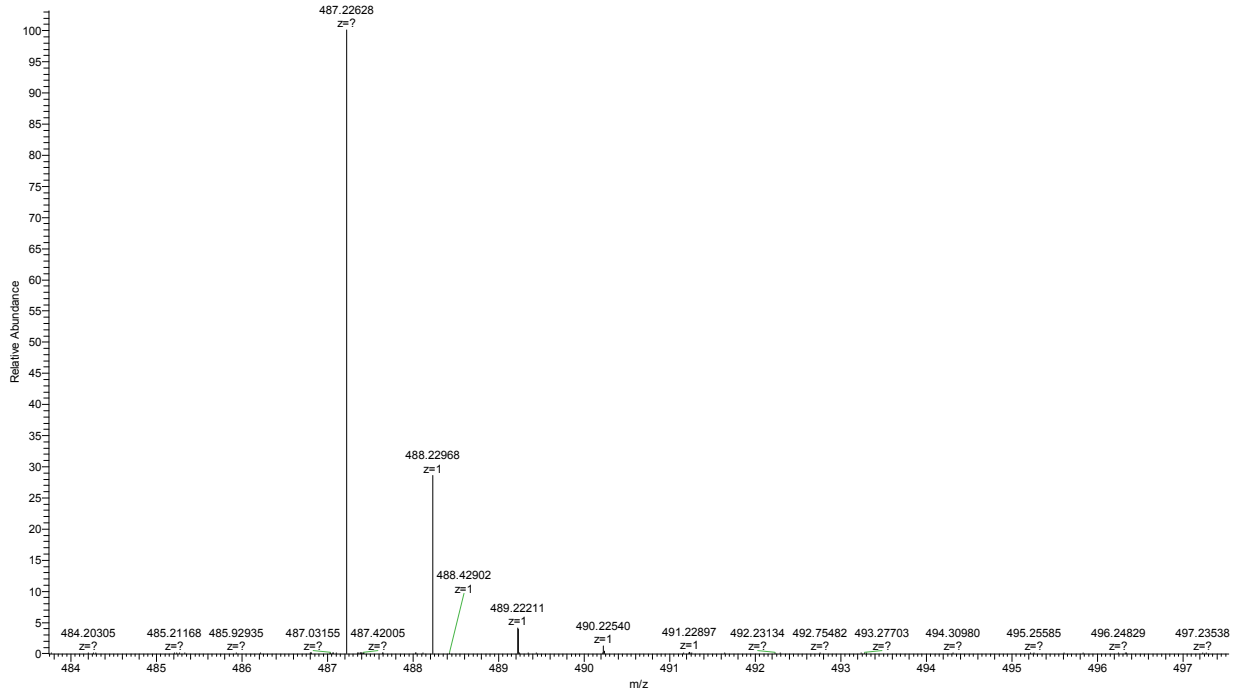
K24 #945-982 RT: 4.08-4.24 AV: 38 NL: 1.55E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]





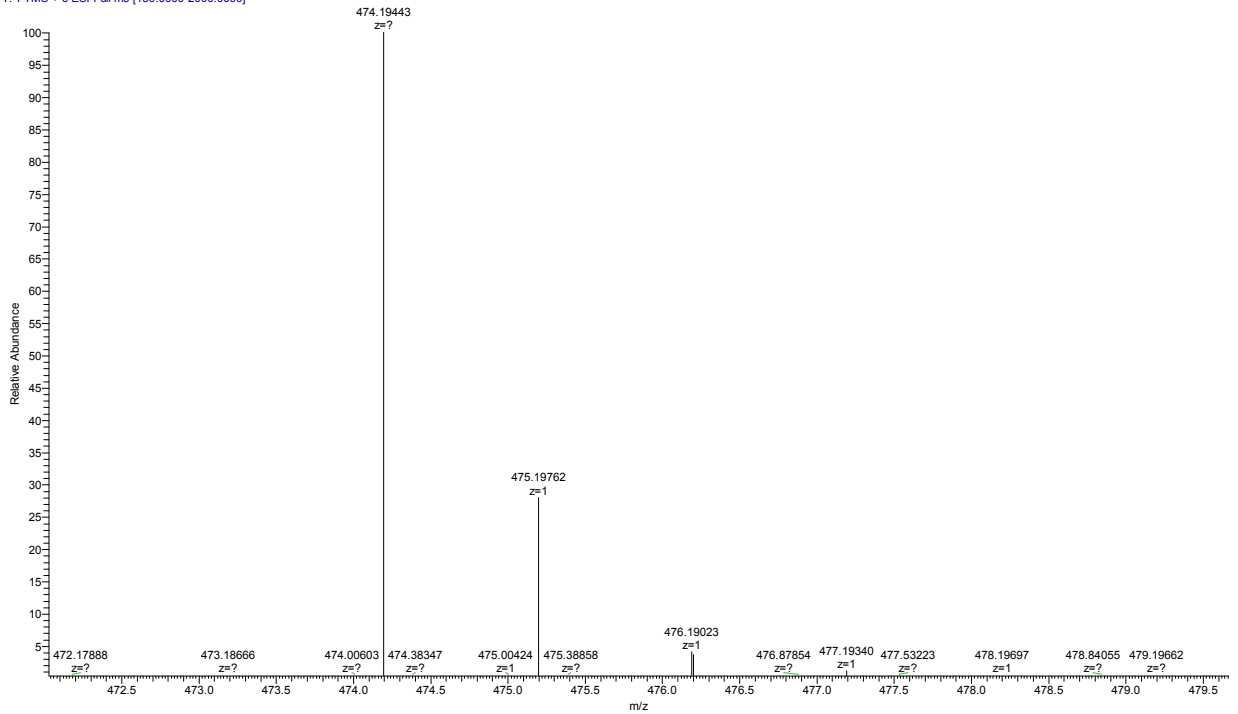
4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-(4-methylpiperazin-1-yl)propyl)benzamide (9f)

K47 #880-911 RT: 3.80-3.94 AV: 32 NL: 2.04E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



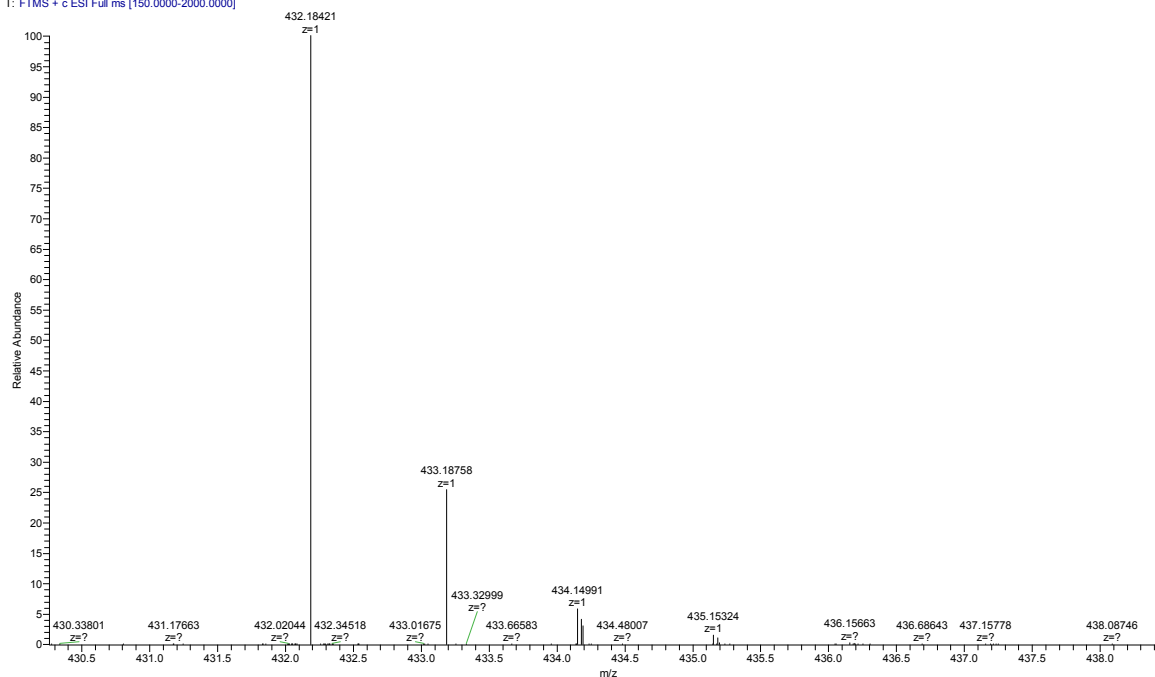
4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-morpholinopropyl)benzamide (9g)

K27 #945-1006 RT: 4.08-4.35 AV: 62 NL: 3.14E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



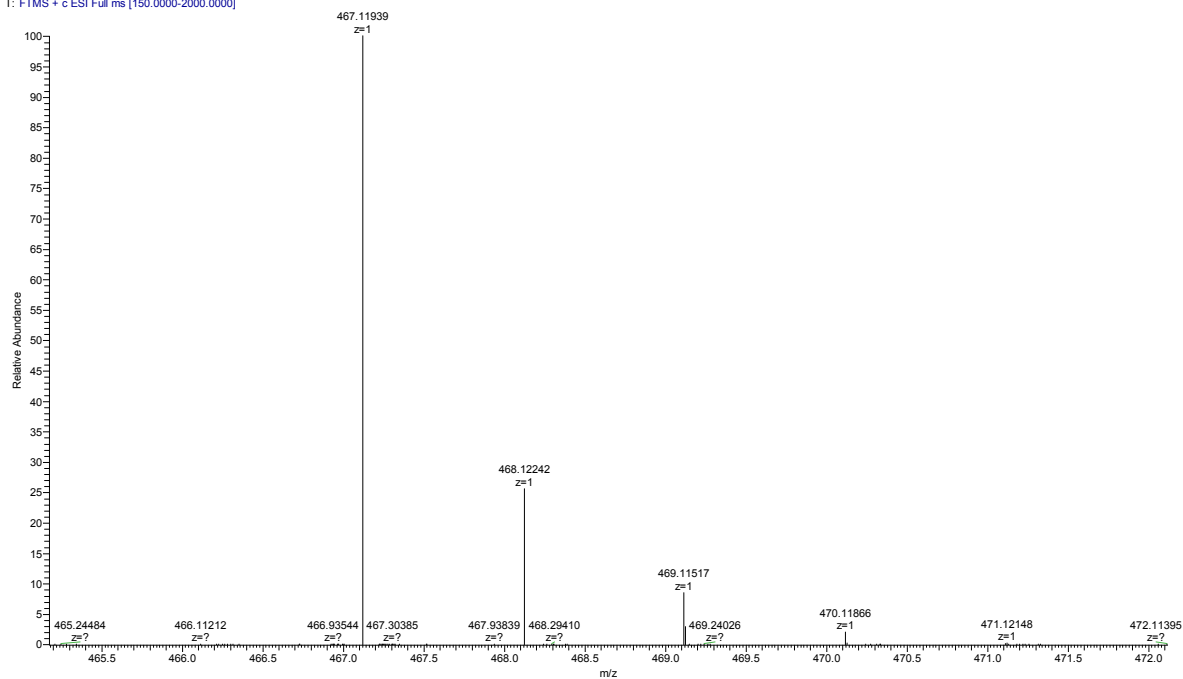
### 4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-(dimethylamino)propyl)benzamide (9h)

K23 #955-1000 RT: 4.13-4.32 AV: 46 NL: 1.96E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



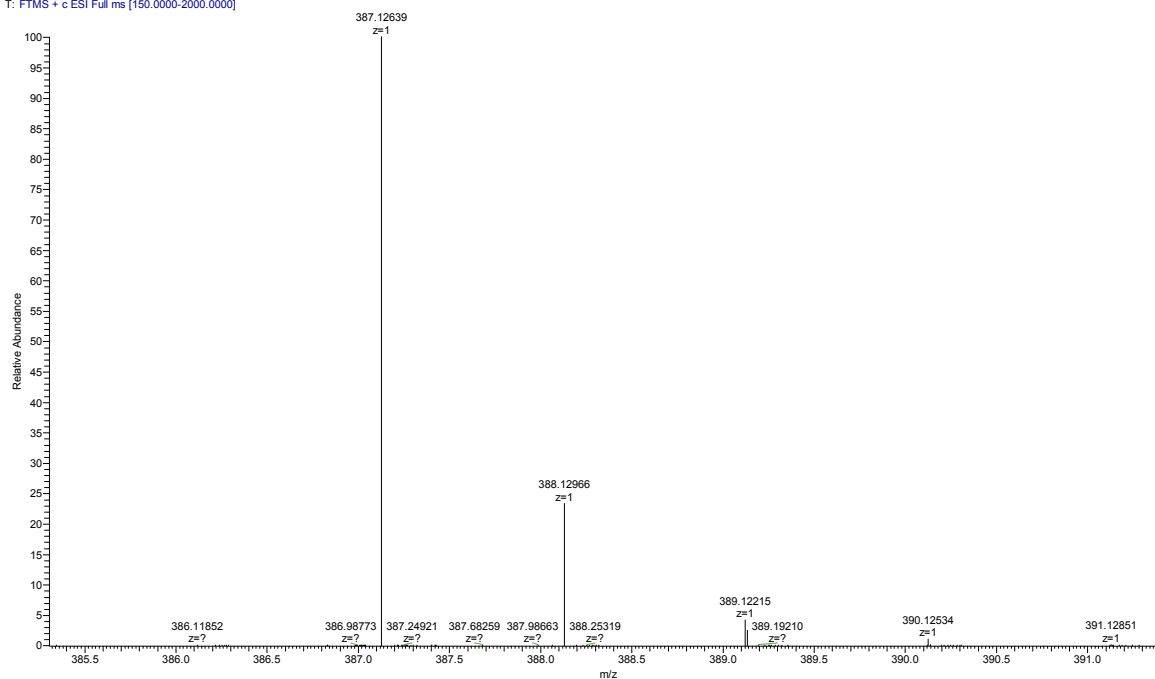
### 4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-(methylsulfonyl)propyl)benzamide (9i)

K31 #1109-1152 RT: 4.79-4.98 AV: 44 NL: 1.96E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



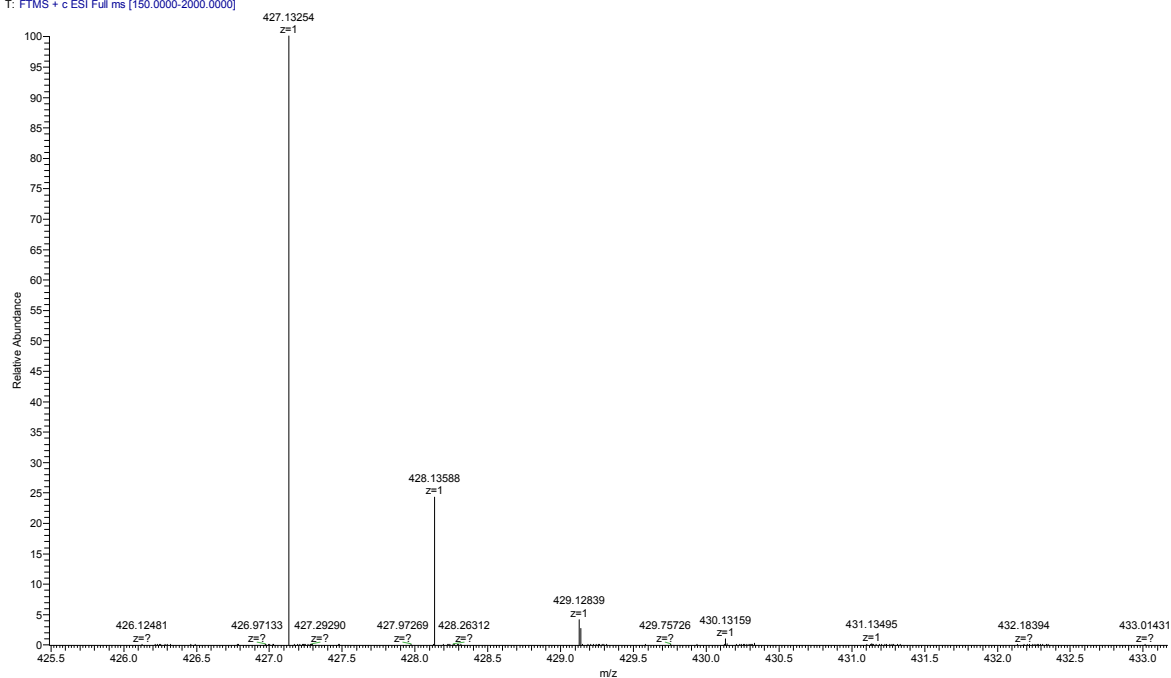
### 4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-cyclopropylbenzamide (9j)

K25 #1202-1236 RT: 5.19-5.34 AV: 35 NL: 1.39E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



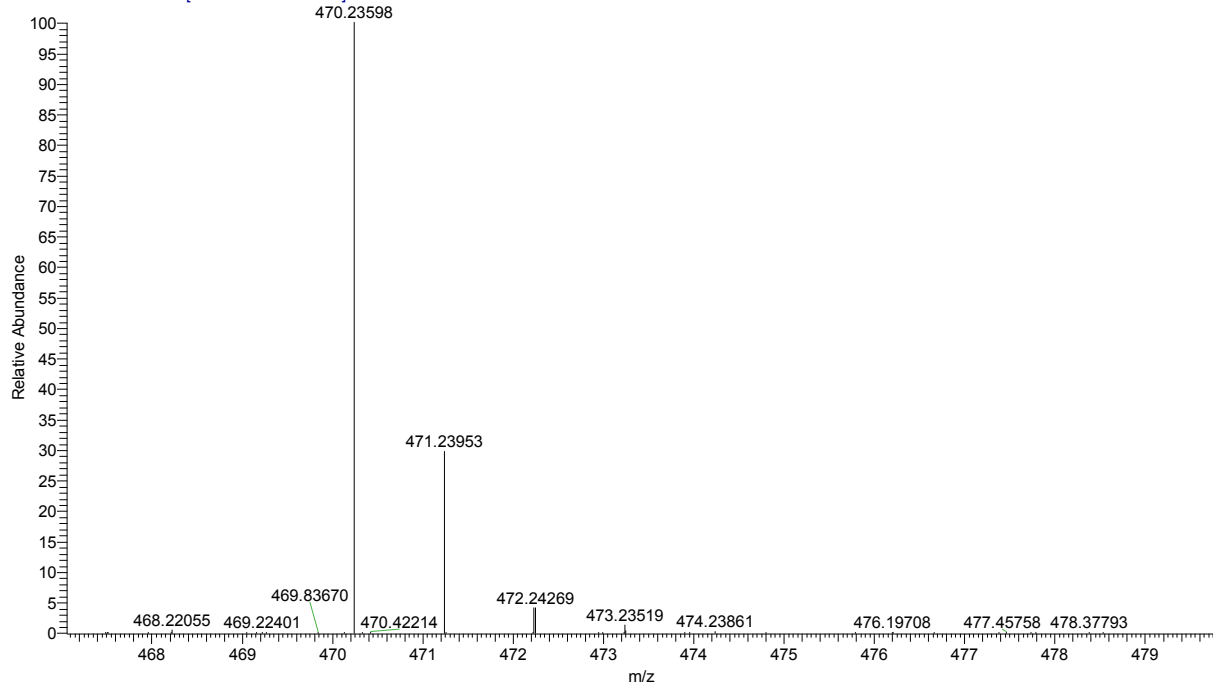
### 4-((4-(Benzo[b]thiophen-2-yl)pyrimidin-2-yl)amino)-N-(1-methyl-1H-pyrazol-4-yl)benzamide (9k)

K32 #1154-1196 RT: 4.99-5.17 AV: 43 NL: 1.23E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



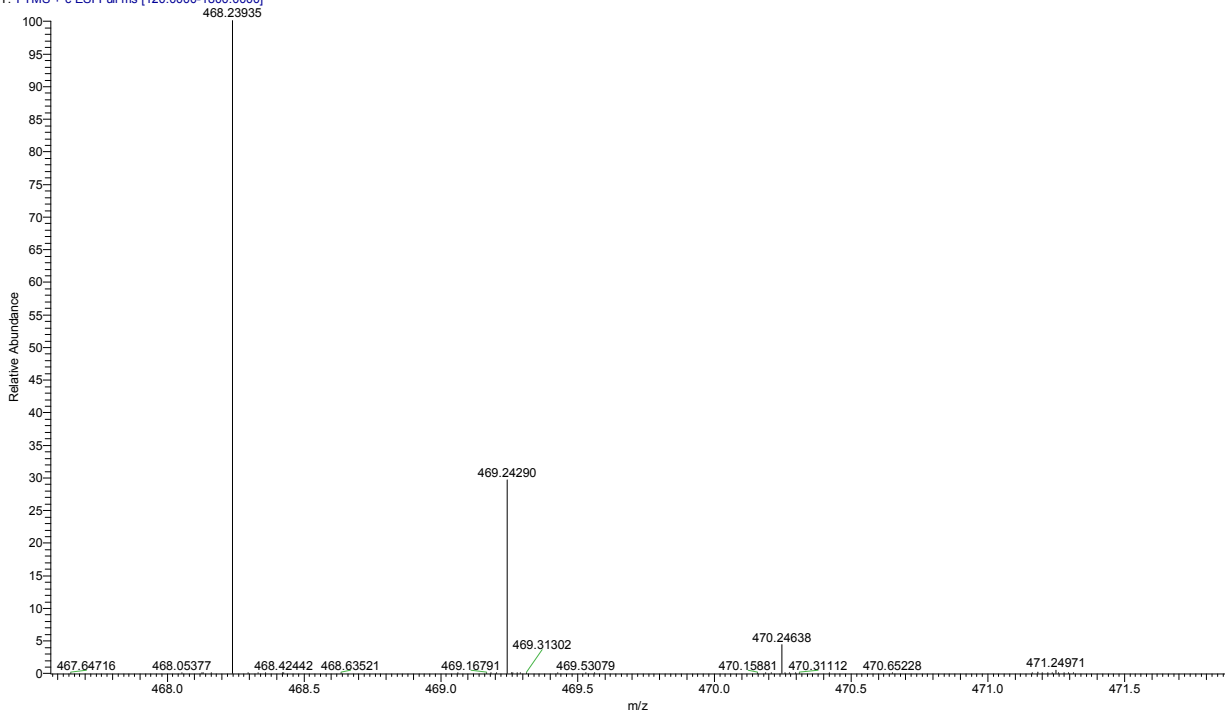
**4-(Benzo[b]thiophen-2-yl)-N-(4-((4-(pyrrolidin-1-yl)piperidin-1-yl)methyl)phenyl)pyrimidin-2-amine (12)**

KG-35 #722-782 RT: 3.12-3.38 AV: 61 NL: 3.30E8  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



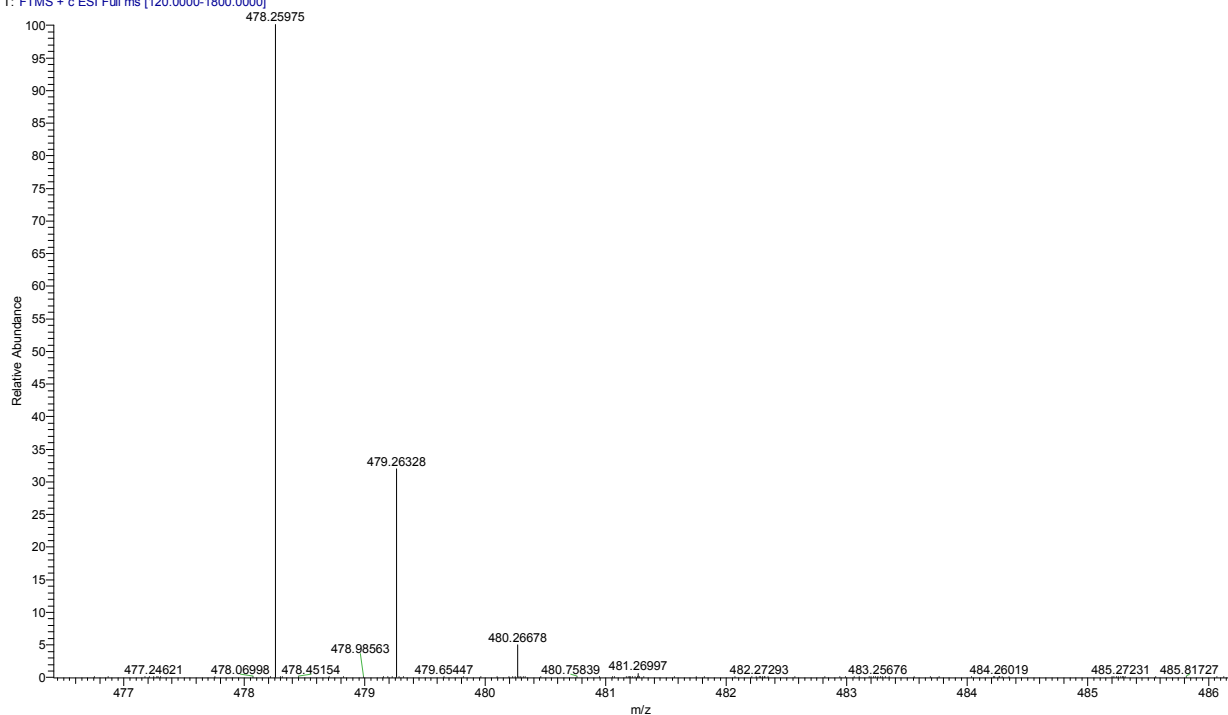
**4-((4-(Benzofuran-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18a)**

K6 #843-920 RT: 3.64-3.98 AV: 78 NL: 3.32E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



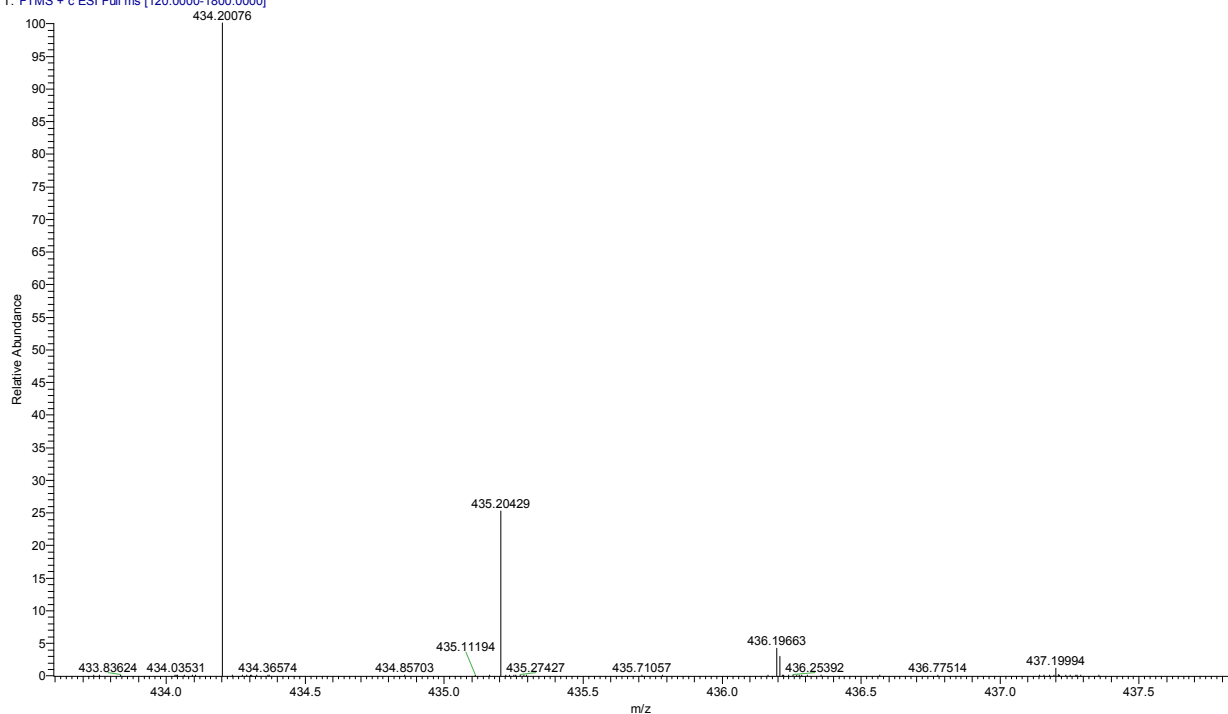
**(4-((4-(Naphthalen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18b)**

K33 #862-939 RT: 3.72-4.06 AV: 78 NL: 4.41E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



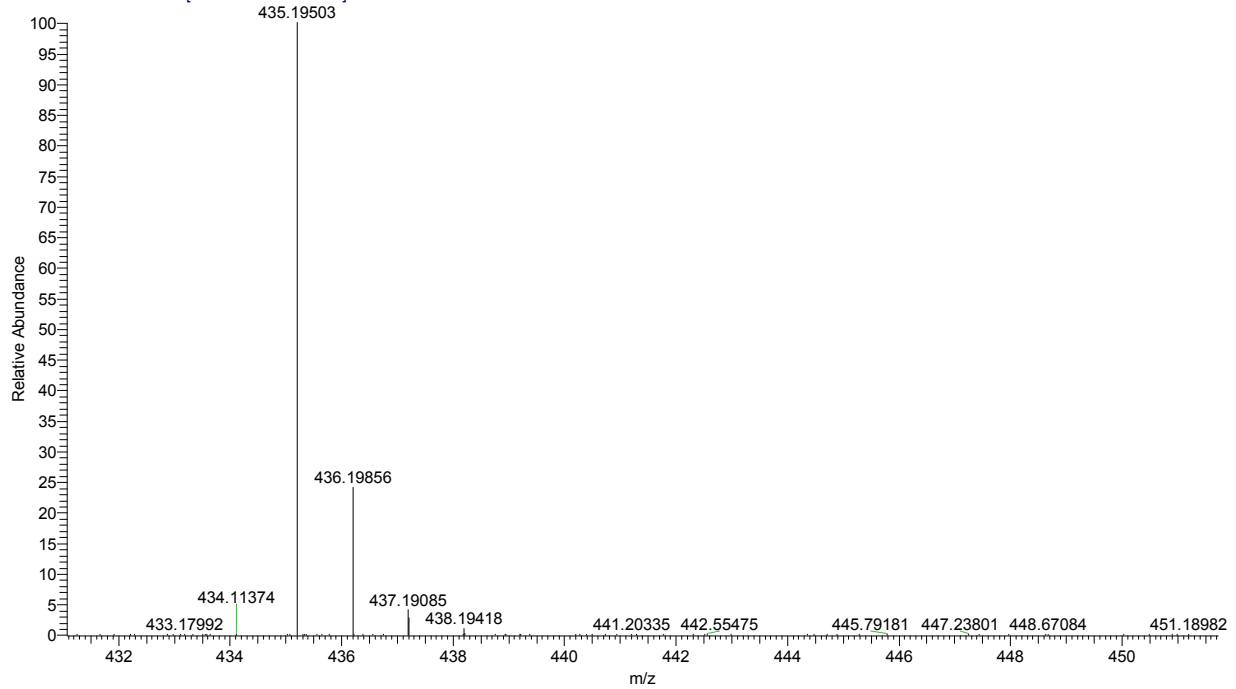
**(4-(Pyrrolidin-1-yl)piperidin-1-yl)(4-((4-(thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)methanone (18c)**

K4 #707-802 RT: 3.05-3.47 AV: 96 NL: 1.95E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



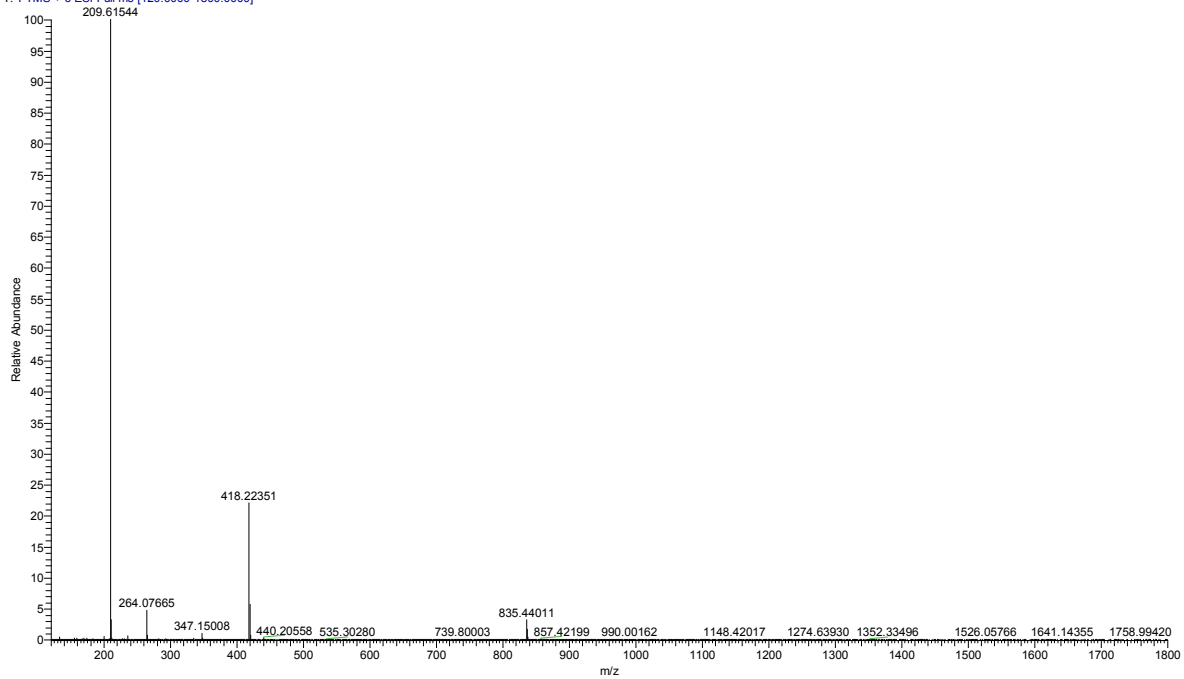
**(4-(Pyrrolidin-1-yl)piperidin-1-yl)(4-((4-(thiazol-2-yl)pyrimidin-2-yl)amino)phenyl)methanone (18d)**

KG-65 #638-715 RT: 2.76-3.09 AV: 78 NL: 3.34E8  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



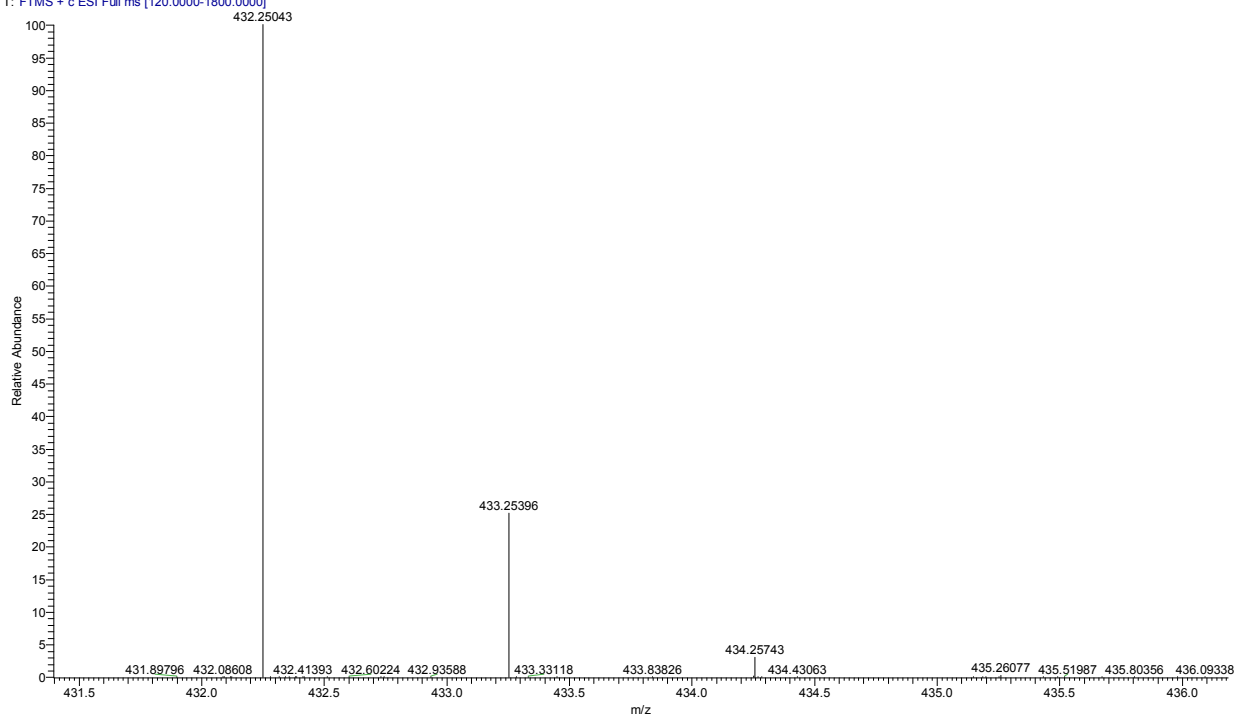
**(4-((4-(Furan-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18e)**

K24 #691-749 RT: 2.99-3.24 AV: 59 NL: 2.33E9  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



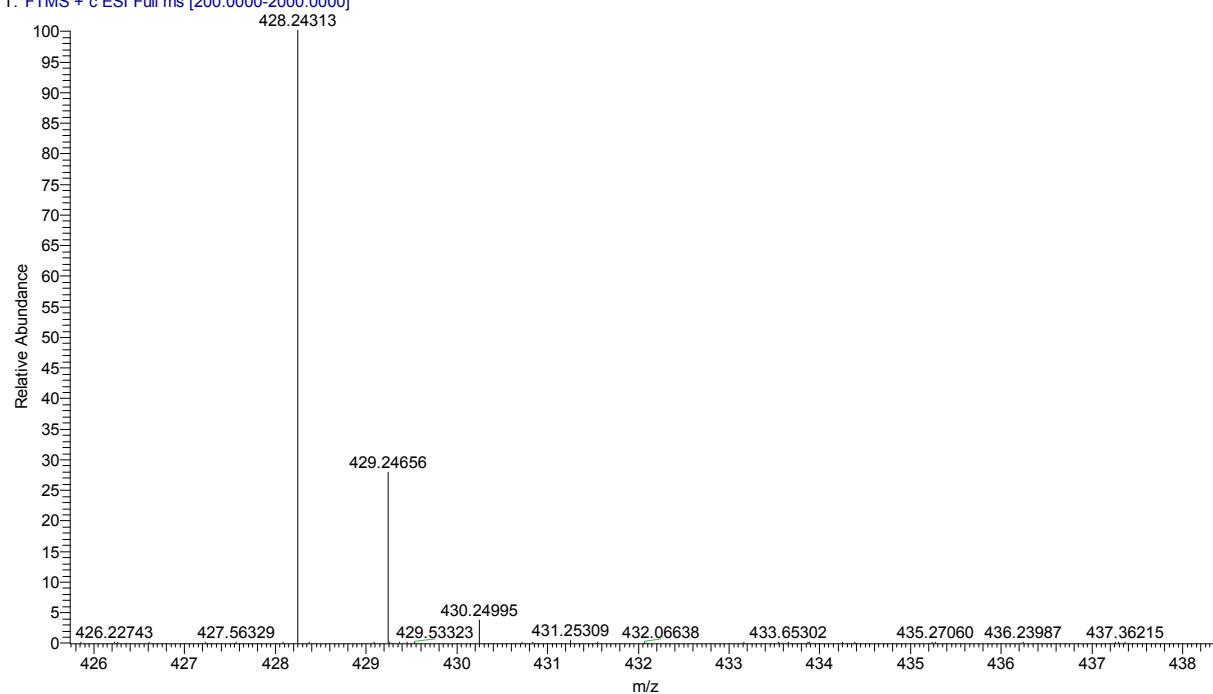
***4-((4-(1-Methyl-1H-pyrazol-4-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18f)***

K30 #586-655 RT: 2.53-2.83 AV: 70 NL: 1.62E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



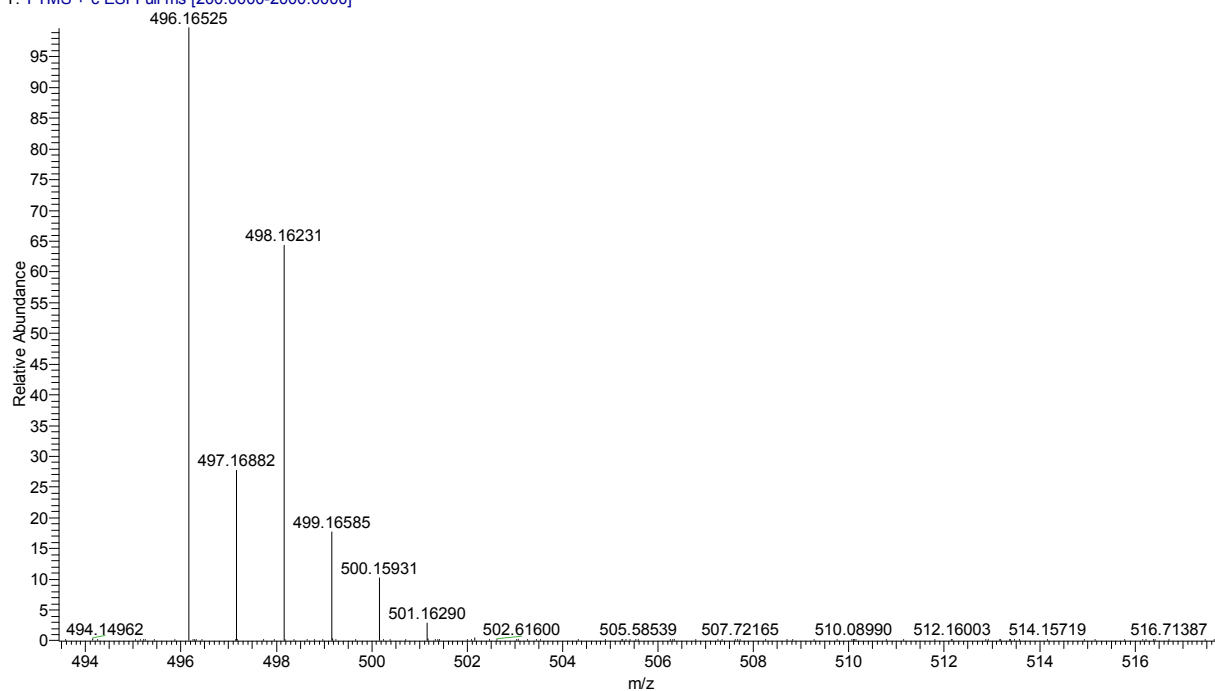
***4-((4-Phenylpyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18g)***

KG-62 #748-798 RT: 3.23-3.45 AV: 51 NL: 3.83E8  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



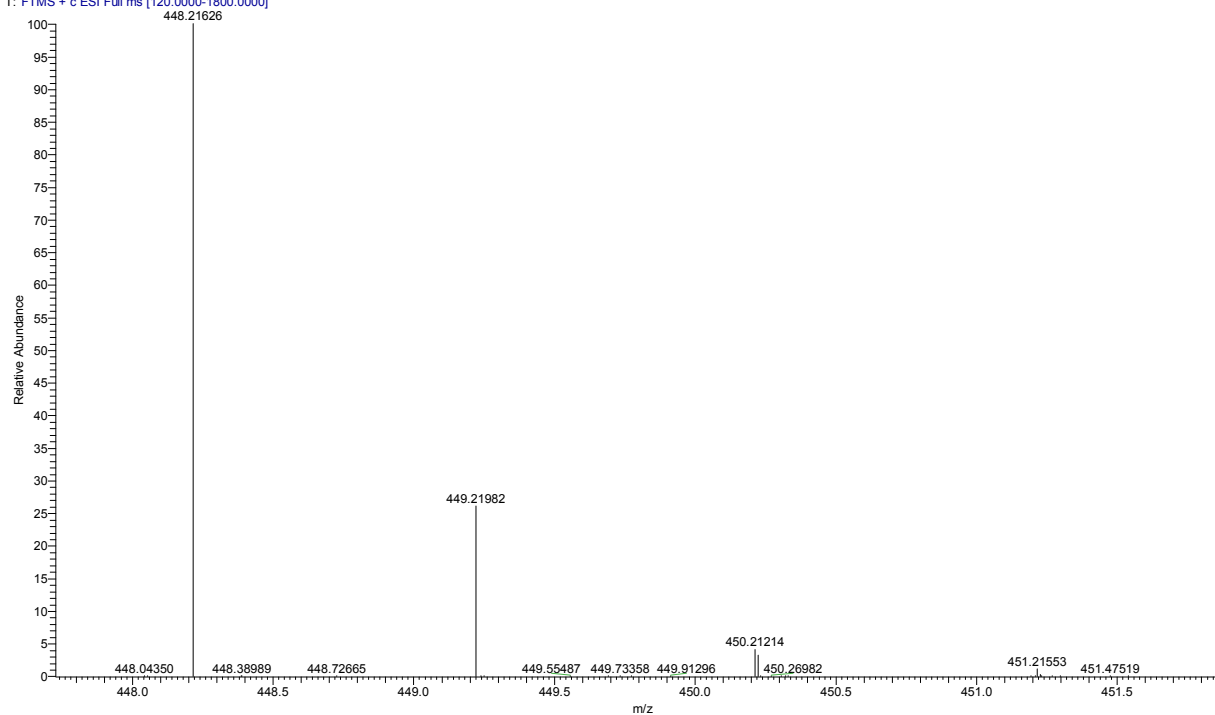
**(4-((4-(3,4-Dichlorophenyl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18h)**

KG-63 #880-944 RT: 3.80-4.08 AV: 65 NL: 2.33E8  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



**(4-((4-(5-Methylthiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18i)**

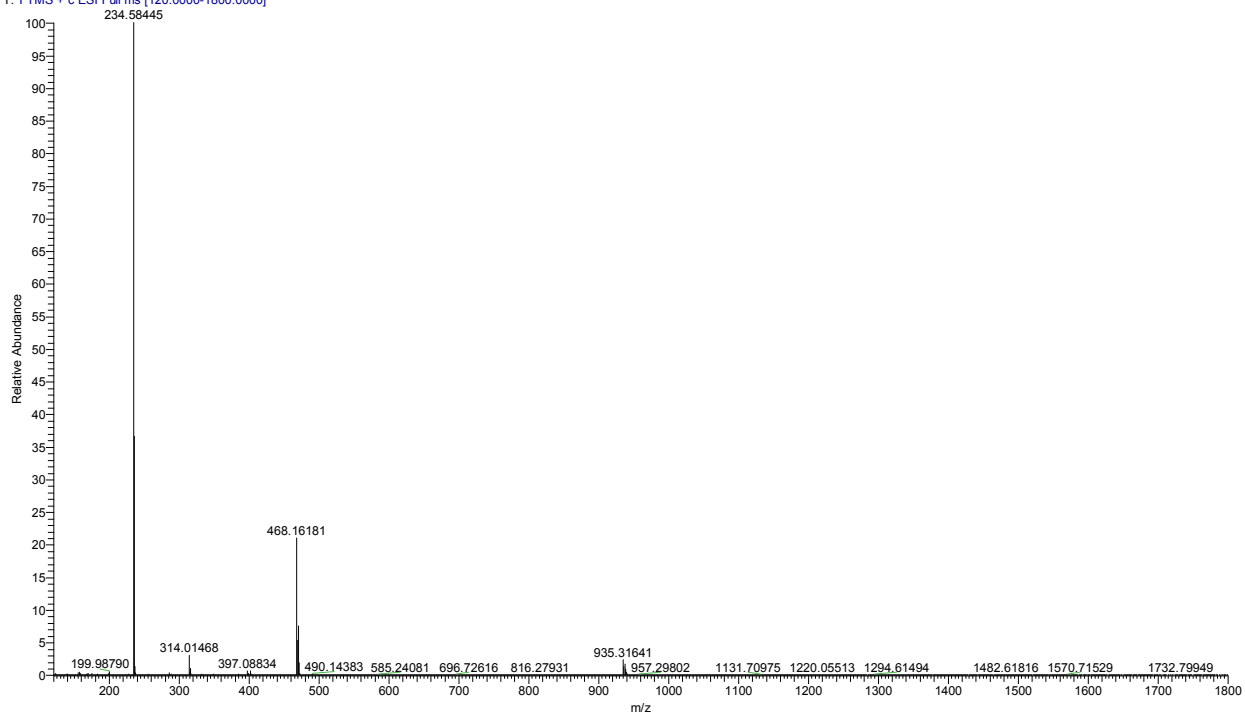
K10 #770-837 RT: 3.33-3.62 AV: 68 NL: 3.70E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]





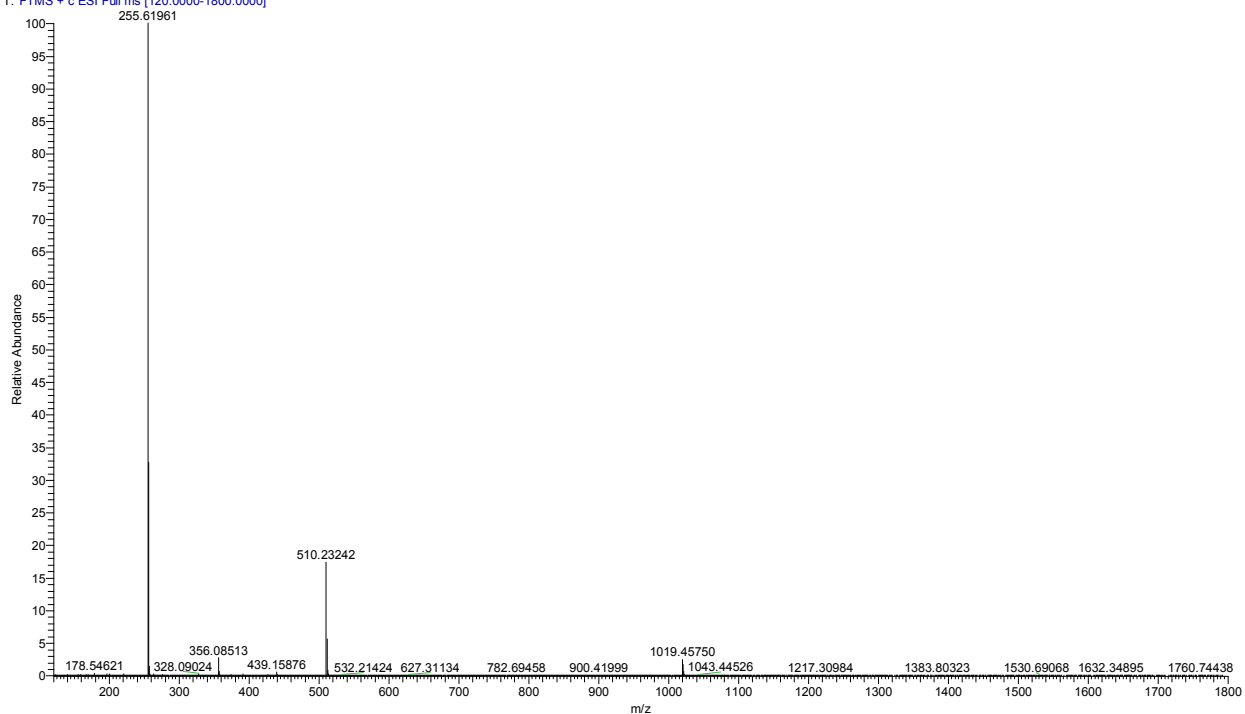
**(4-((4-(5-Chlorothiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18j)**

K11 #797-879 RT: 3.44-3.80 AV: 63 NL: 1.72E9  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



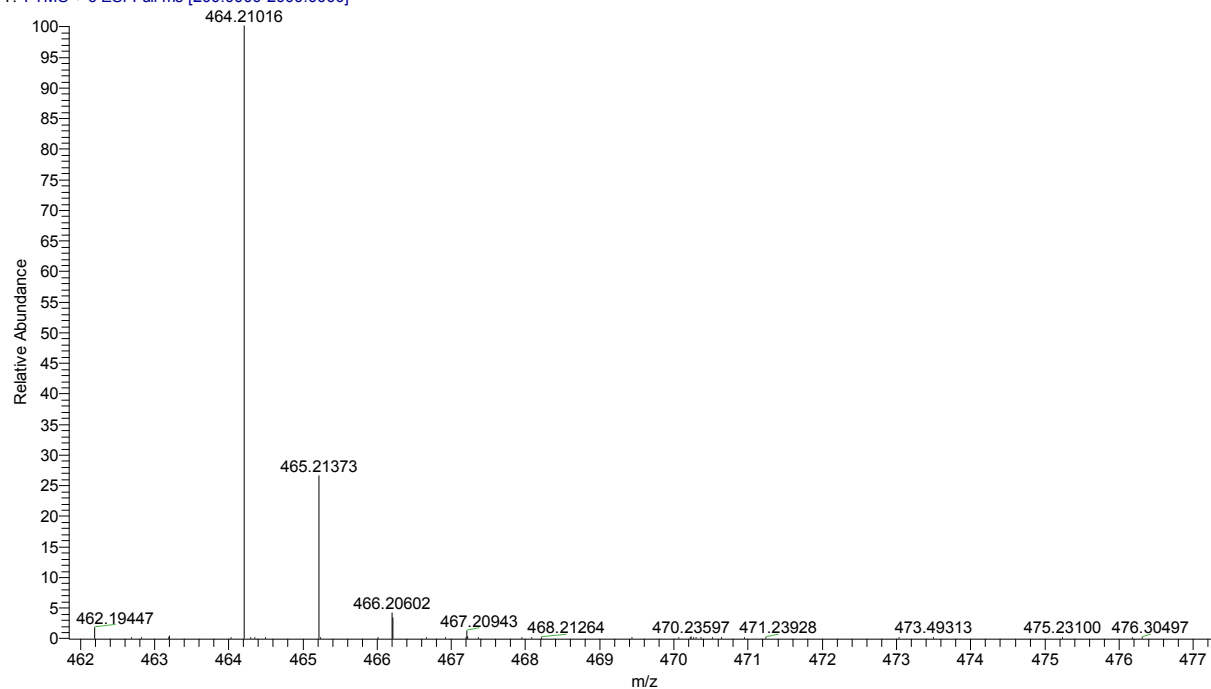
**(4-((4-(5-Phenylthiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18k)**

K23 #886-956 RT: 3.83-4.13 AV: 71 NL: 2.75E9  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



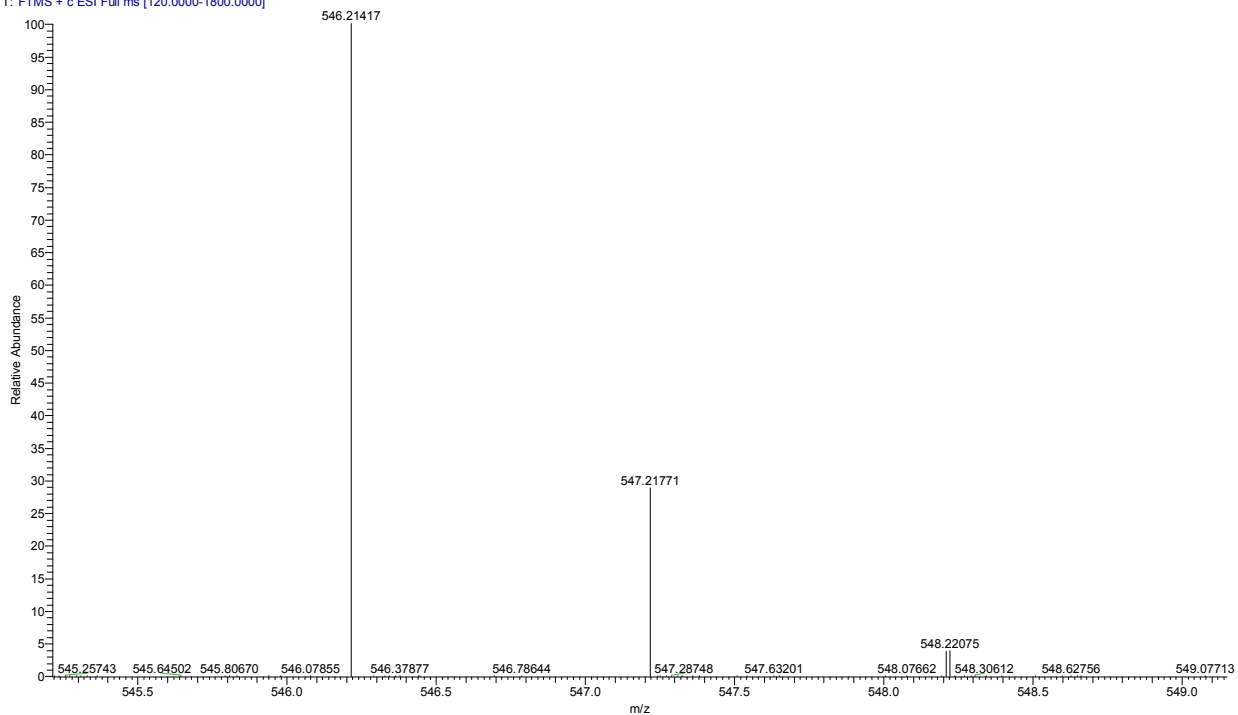
**4-((4-(5-(Hydroxymethyl)thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18l)**

KG-37 #627-664 RT: 2.71-2.87 AV: 38 NL: 1.78E8  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



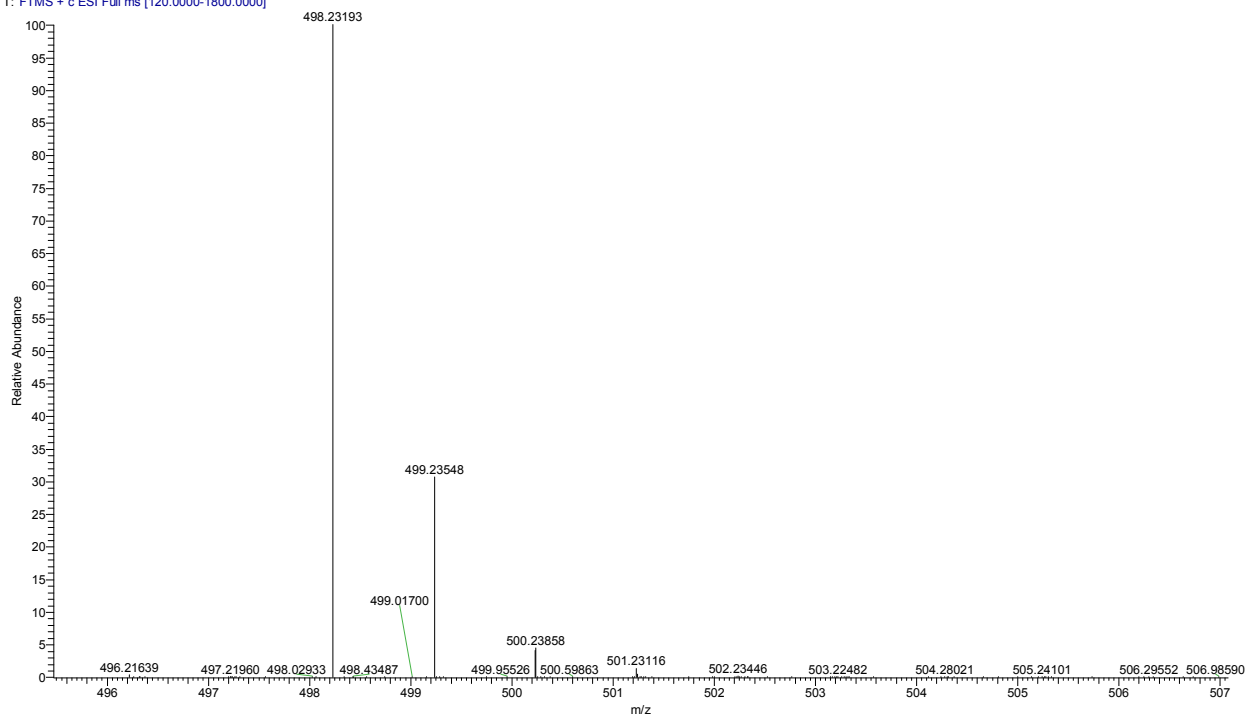
**4-(Pyrrolidin-1-yl)piperidin-1-yl)(4-((4-(5-((2,2-trifluoroethoxy)methyl)thiophen-2-yl)pyrimidin-2-yl)amino)phenyl)methanone (18m)**

K29 #824-901 RT: 3.56-3.89 AV: 78 NL: 1.68E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



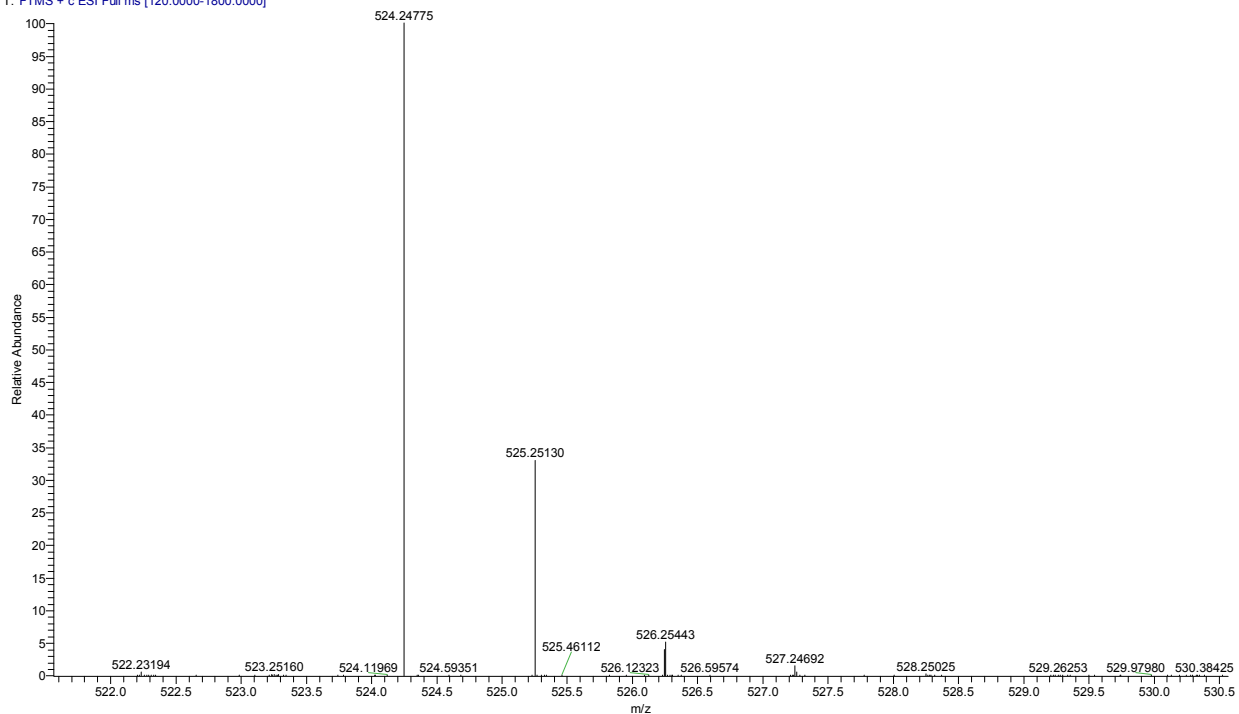
**(4-((4-(Benzo[b]thiophen-2-yl)-5-methylpyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18n)**

K15 #876-941 RT: 3.79-4.07 AV: 66 NL: 6.21E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



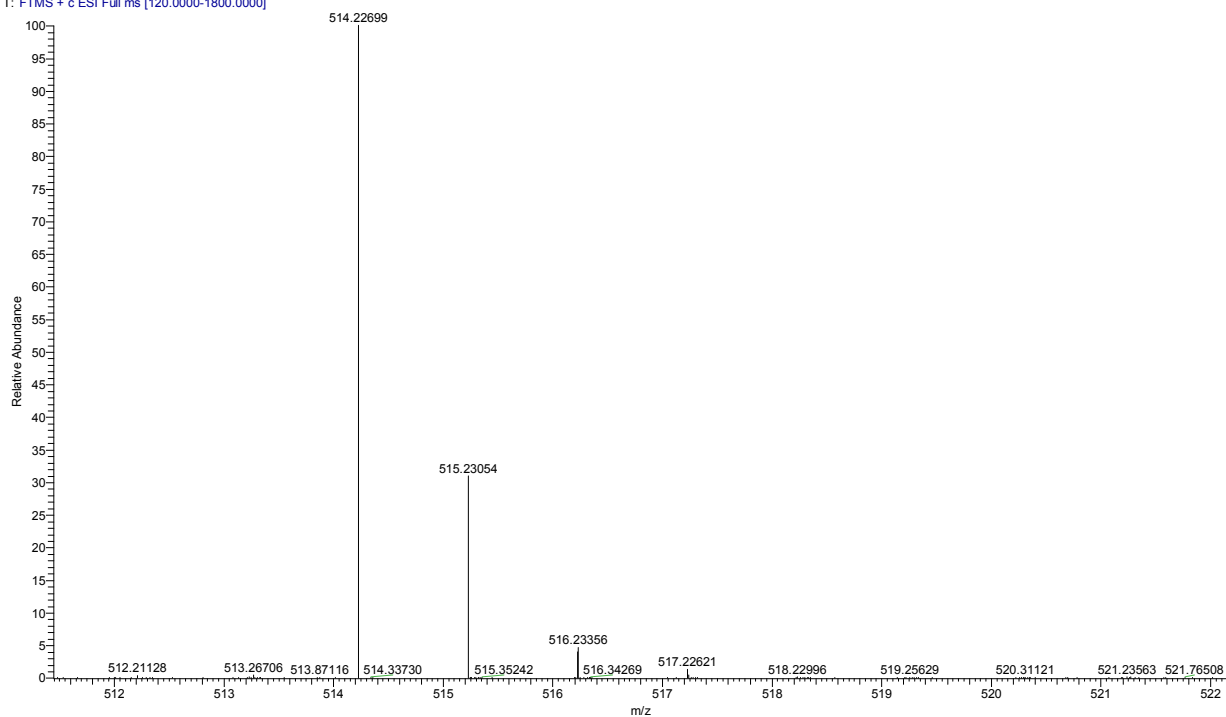
**(4-((4-(Benzo[b]thiophen-2-yl)-5-cyclopropylpyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18o)**

K16 #928-993 RT: 4.01-4.29 AV: 66 NL: 1.73E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



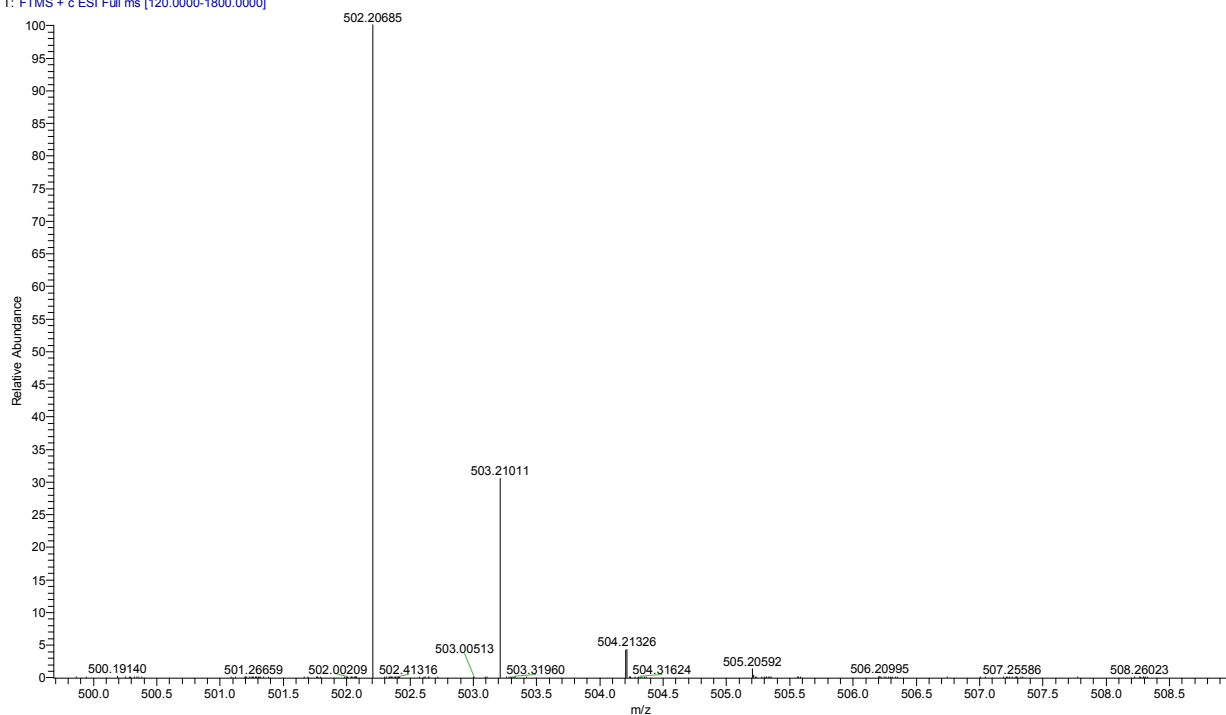
**4-((4-(Benzo[b]thiophen-2-yl)-5-methoxypyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18p)**

K31 #889-938 RT: 3.84-4.05 AV: 50 NL: 1.18E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



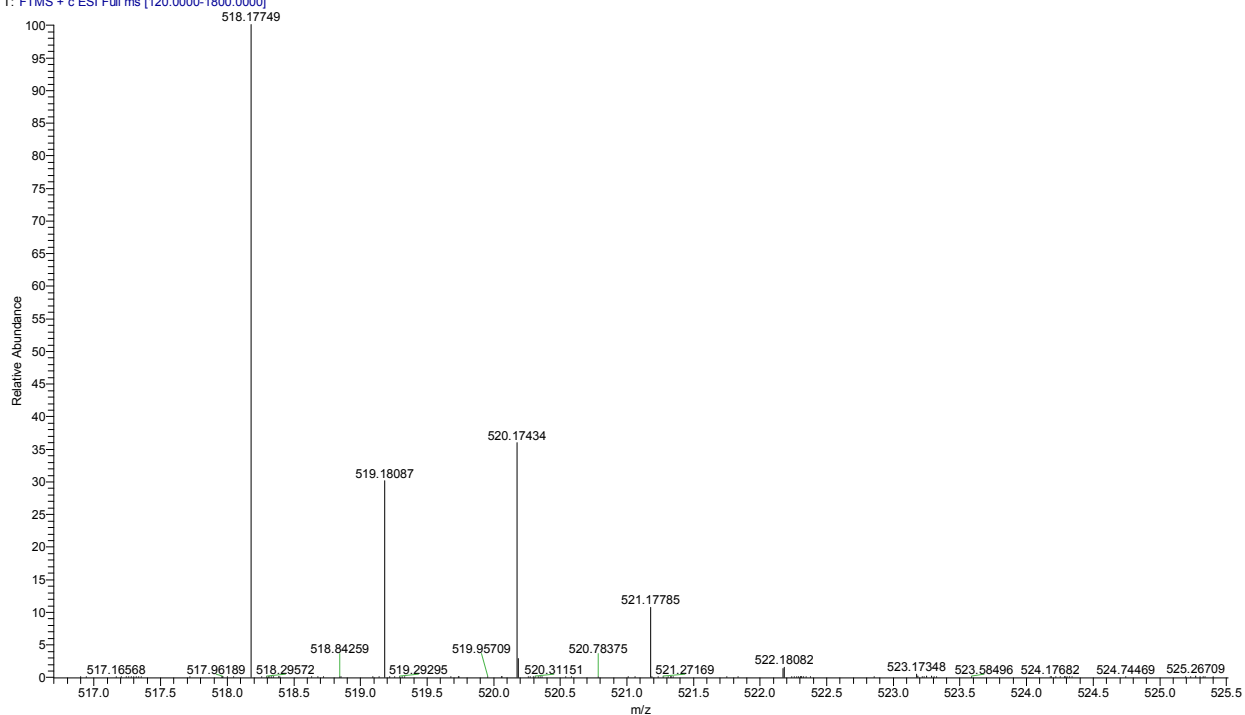
**4-((4-(Benzo[b]thiophen-2-yl)-5-fluoropyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18q)**

K19 #901-957 RT: 3.89-4.14 AV: 57 NL: 4.64E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



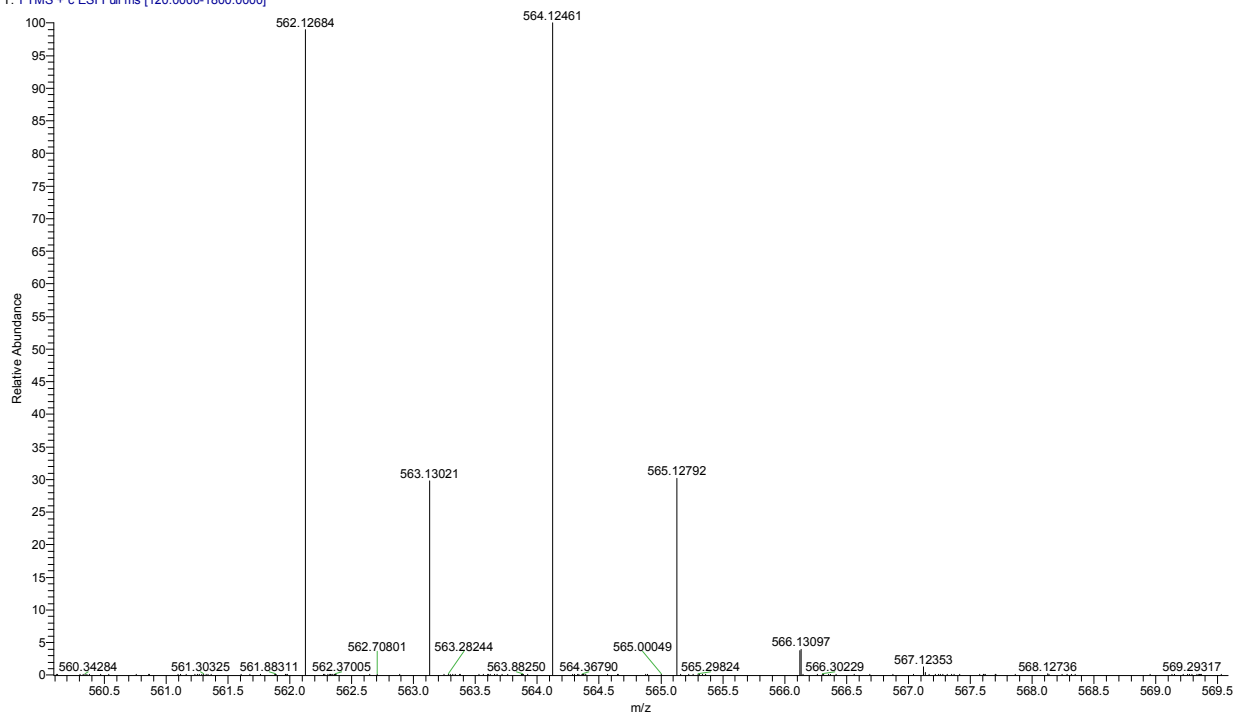
**(4-((4-(Benzo[b]thiophen-2-yl)-5-chloropyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18r)**

K20 #938-989 RT: 4.05-4.27 AV: 52 NL: 2.49E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



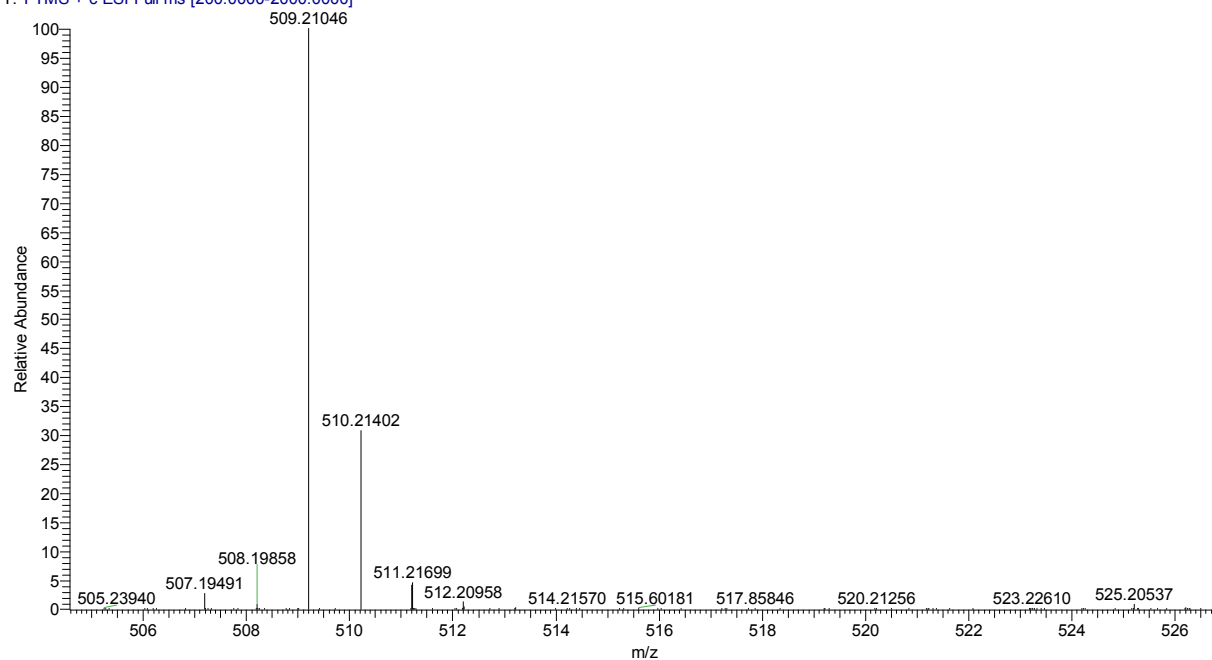
**(4-((4-(Benzo[b]thiophen-2-yl)-5-bromopyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (18s)**

K057 #944-1004 RT: 4.08-4.34 AV: 61 NL: 4.32E8  
T: FTMS + c ESI Full ms [120.0000-1800.0000]



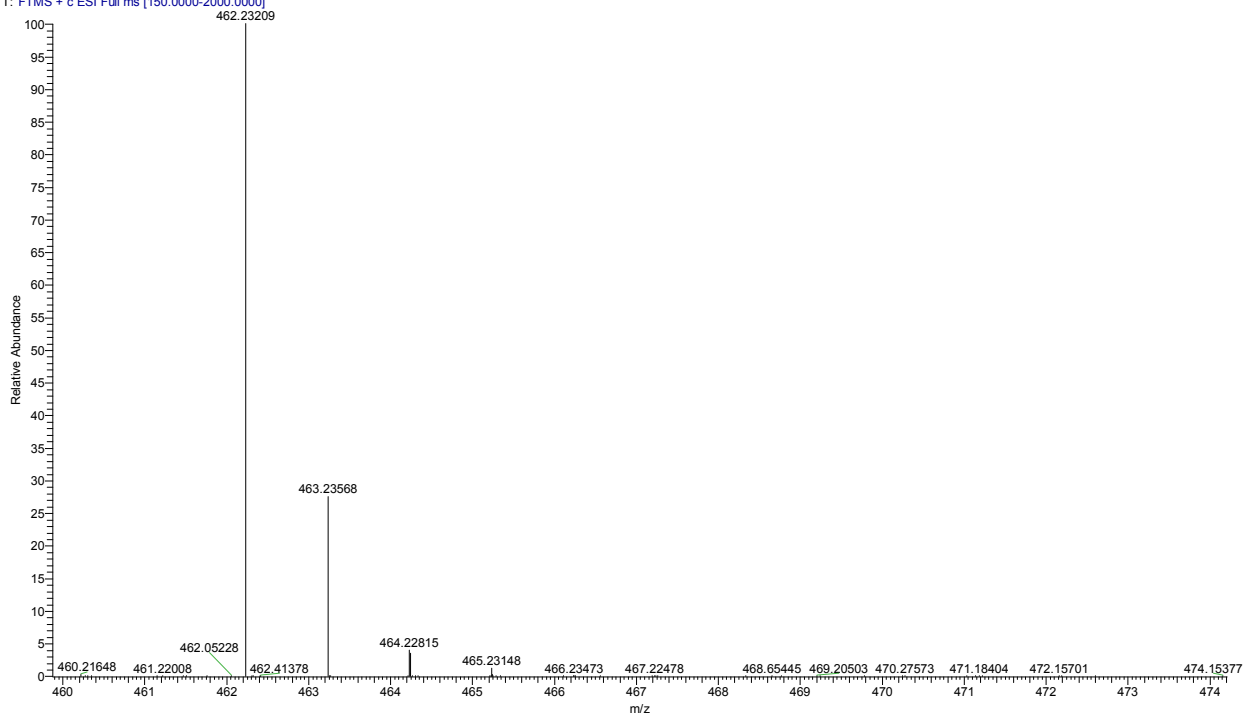
**4-(Benzo[b]thiophen-2-yl)-2-((4-(4-(pyrrolidin-1-yl)piperidine-1-carbonyl)phenyl)amino)pyrimidine-5-carbonitrile (18t)**

KG-61 #857-910 RT: 3.70-3.93 AV: 54 NL: 2.80E8  
T: FTMS + c ESI Full ms [200.0000-2000.0000]



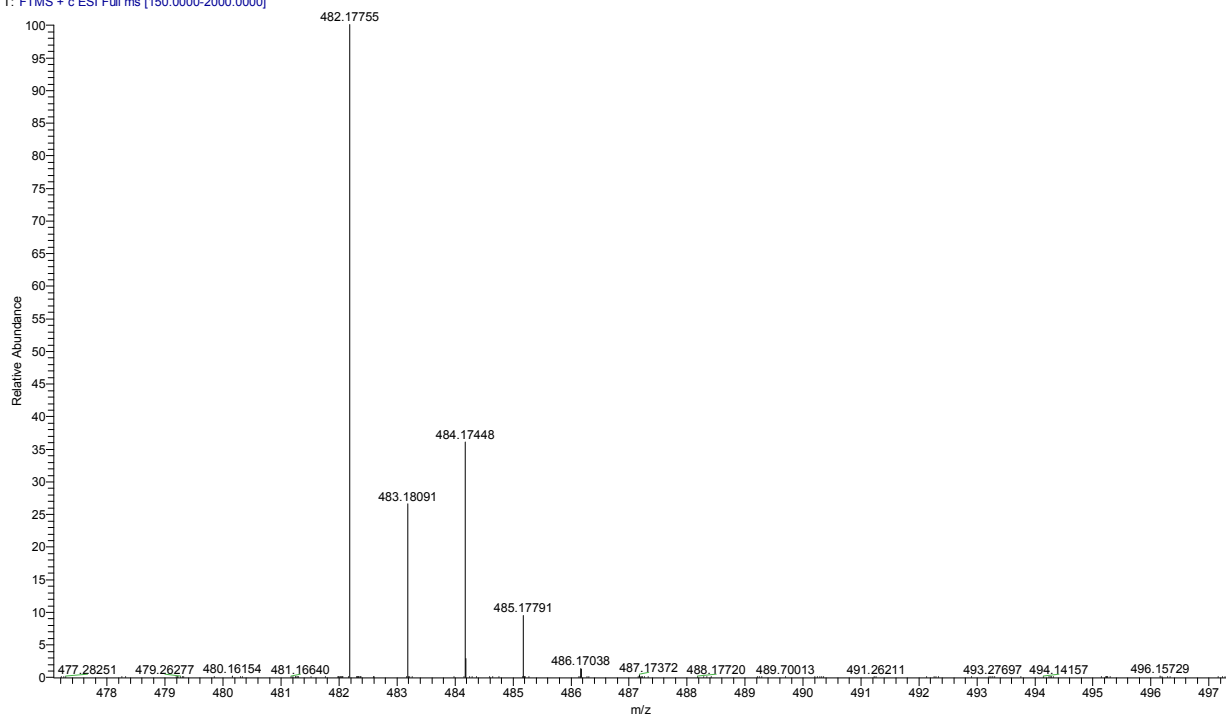
**(4-((5-Methyl-4-(5-methylthiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (23a)**

KG52 #788-852 RT: 3.40-3.68 AV: 65 NL: 3.42E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



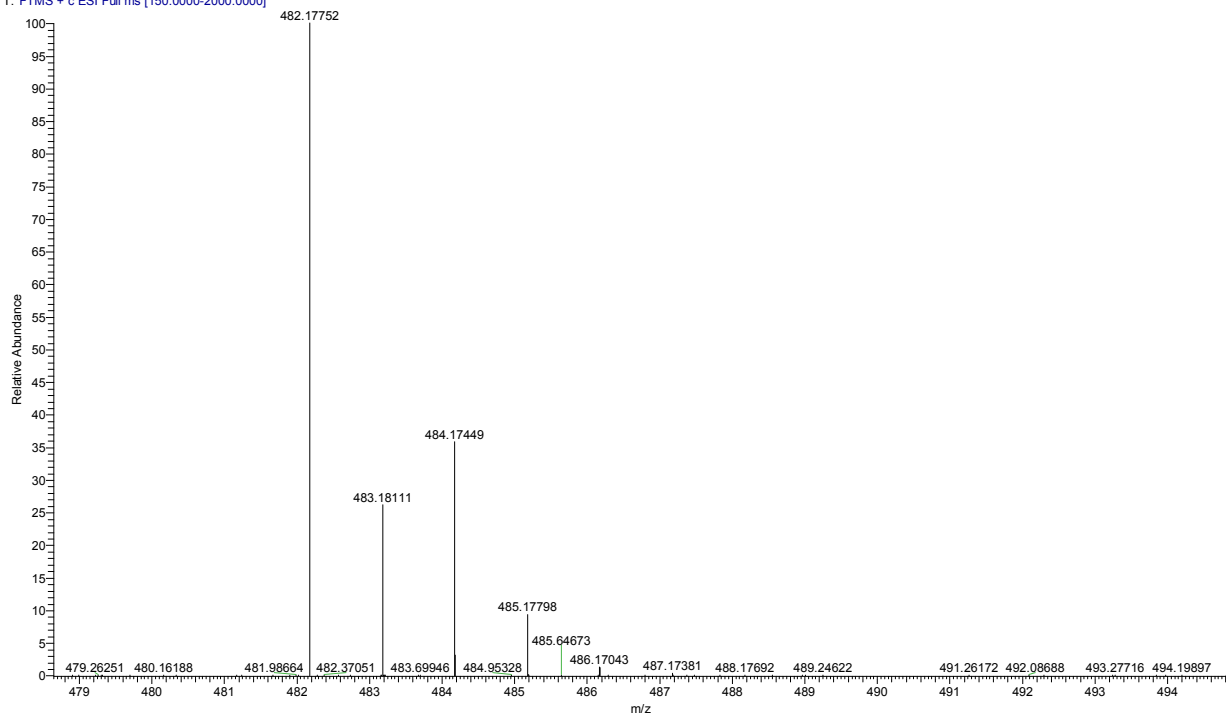
***4-((5-Chloro-4-(5-methylthiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (23b)***

KG50 #854-914 RT: 3.69-3.95 AV: 61 NL: 1.17E9  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



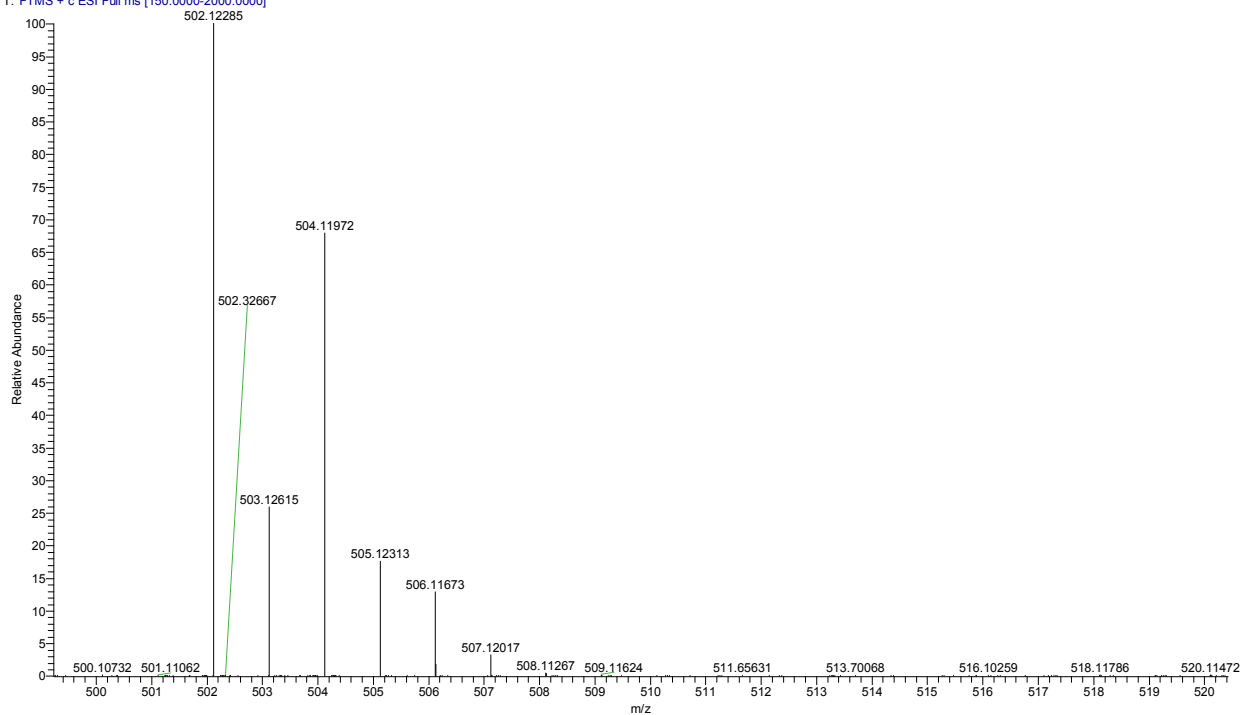
***4-((4-(5-Chlorothiophen-2-yl)-5-methylpyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (23c)***

KG53 #826-881 RT: 3.57-3.81 AV: 56 NL: 2.78E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



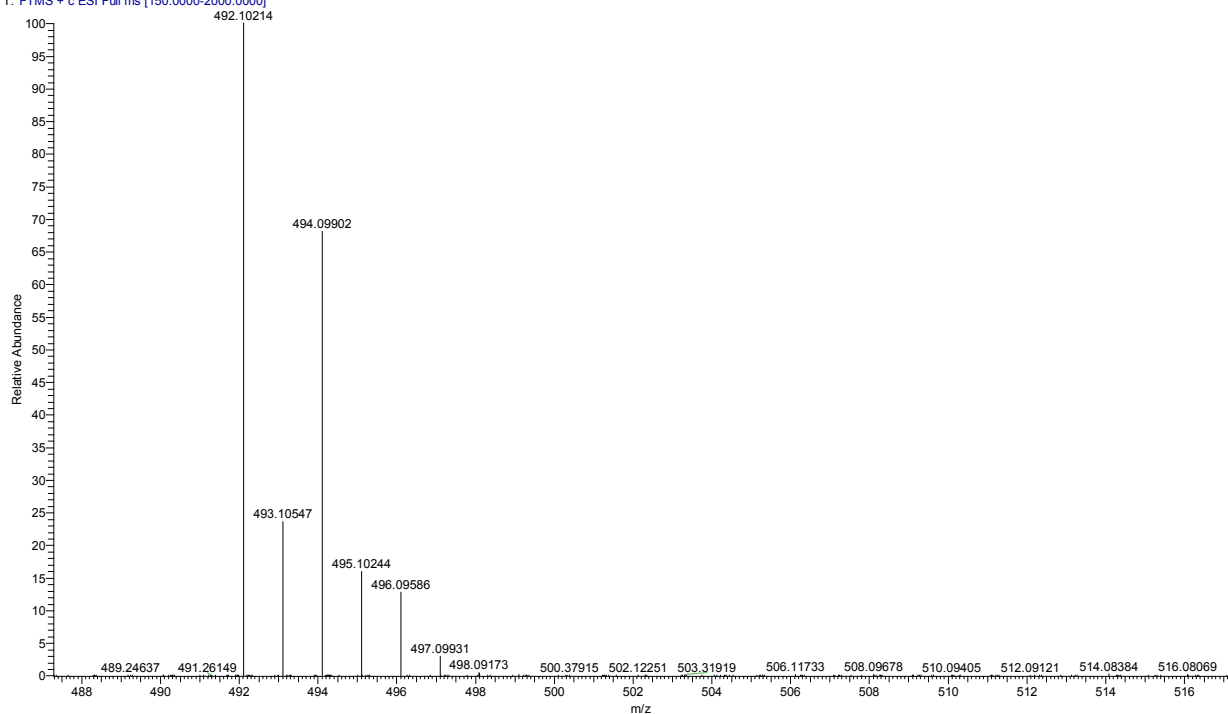
**4-((5-Chloro-4-(5-chlorothiophen-2-yl)pyrimidin-2-yl)amino)phenyl)(4-(pyrrolidin-1-yl)piperidin-1-yl)methanone (23d)**

KG51 #883-942 RT: 3.82-4.07 AV: 60 NL: 9.31E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



**4-((5-Chloro-4-(5-chlorothiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-morpholinopropyl)benzamide (23e)**

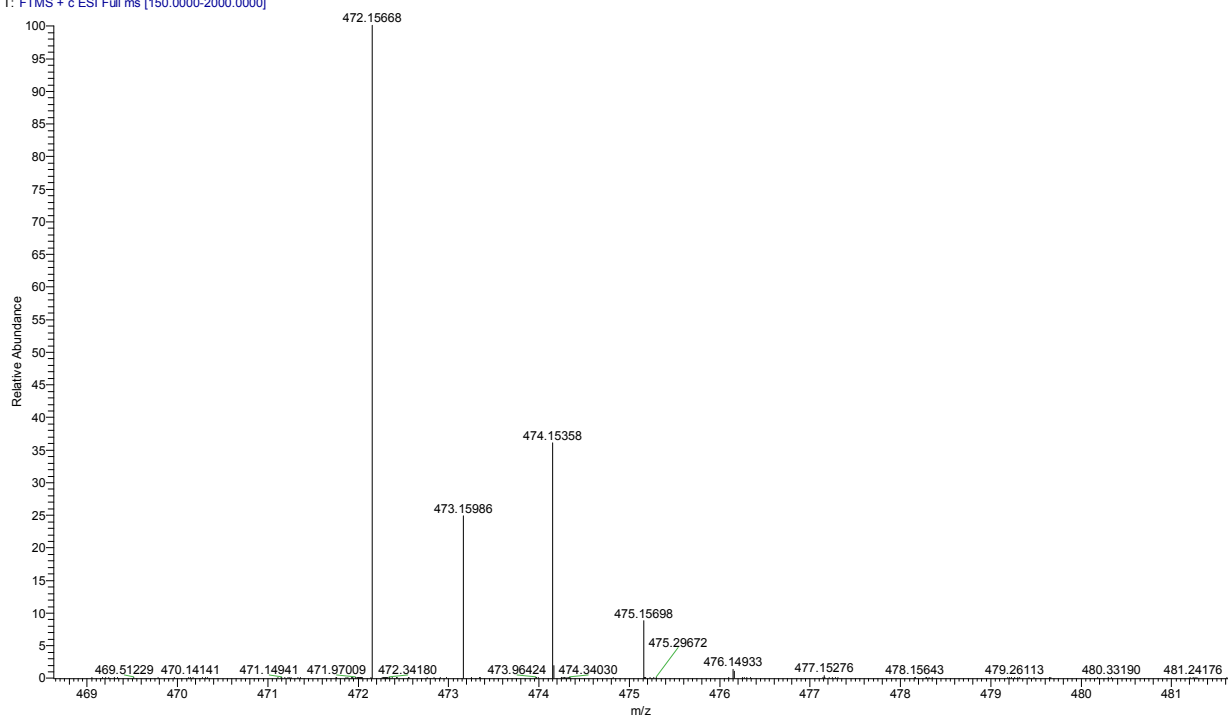
KG70 #888-950 RT: 3.84-4.11 AV: 63 NL: 2.83E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]





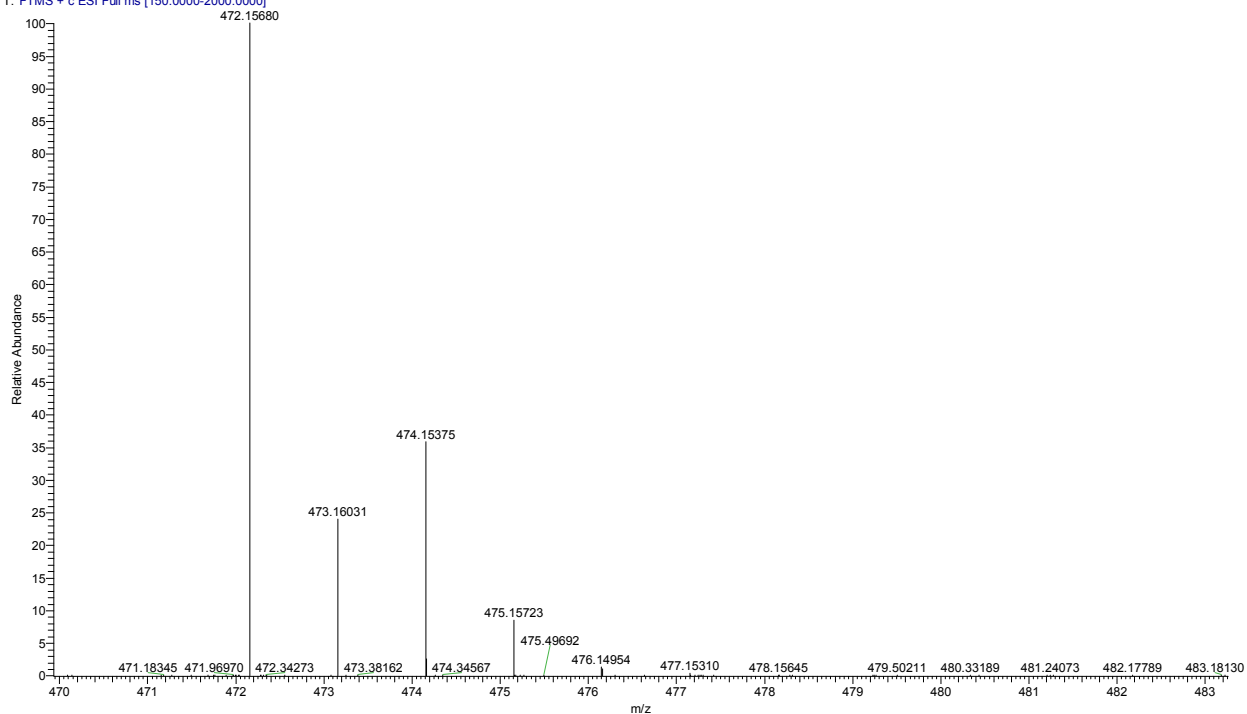
**4-((5-Chloro-4-(5-methylthiophen-2-yl)pyrimidin-2-yl)amino)-N-(3-morpholinopropyl)benzamide (23f)**

KG69 #858-945 RT: 3.71-4.08 AV: 88 NL: 7.24E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]



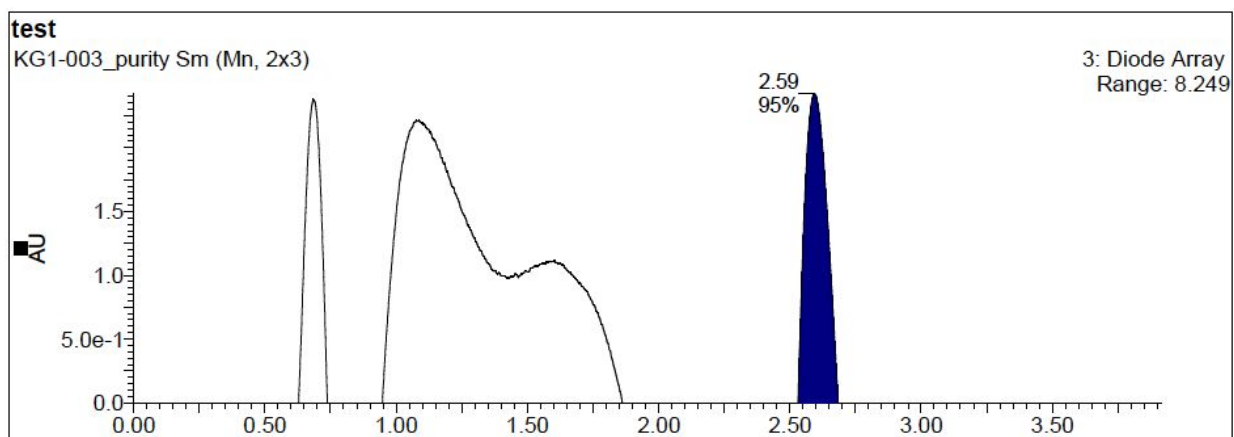
**4-((4-(5-Chlorothiophen-2-yl)-5-methylpyrimidin-2-yl)amino)-N-(3-morpholinopropyl)benzamide (23g)**

KG68 #823-884 RT: 3.56-3.82 AV: 62 NL: 4.97E8  
T: FTMS + c ESI Full ms [150.0000-2000.0000]

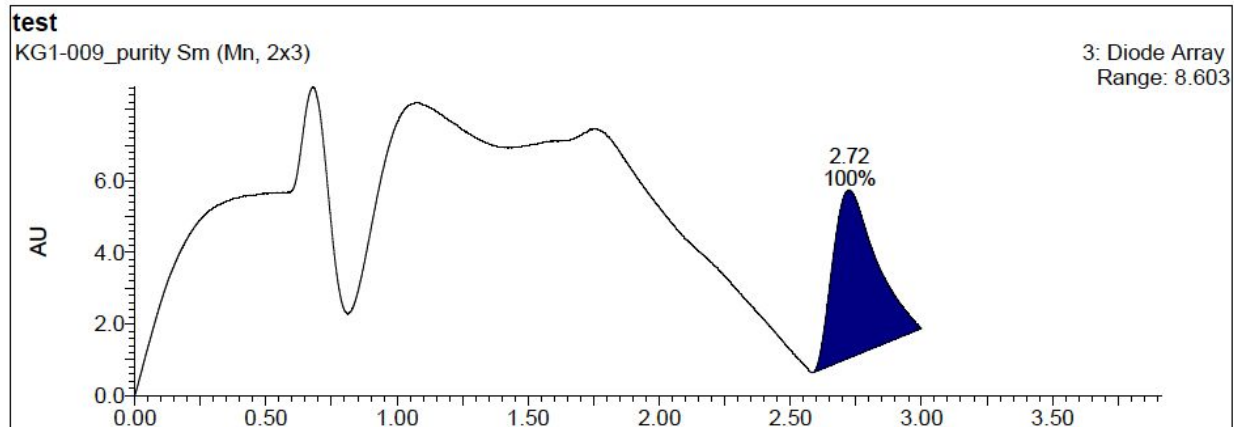


## HPLC traces of compounds submitted for biological screening

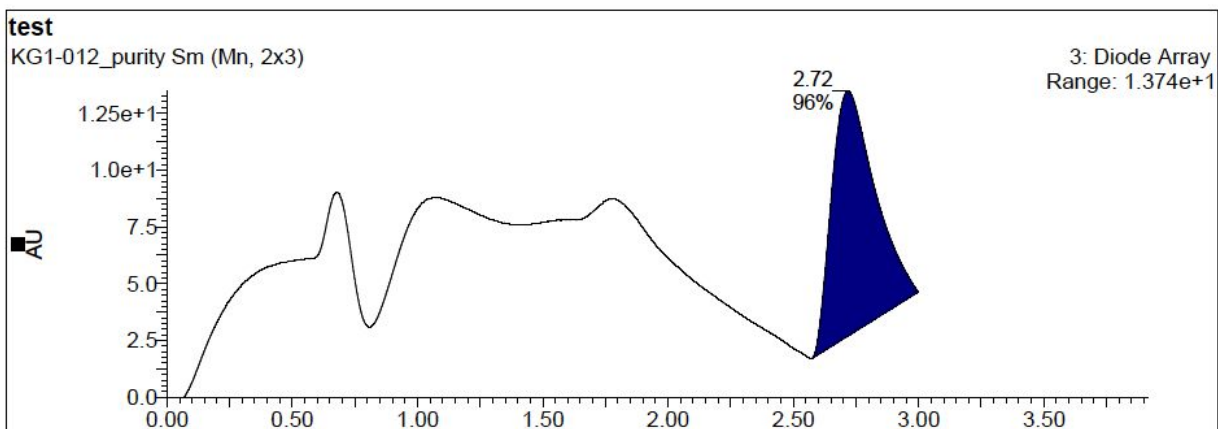
4a



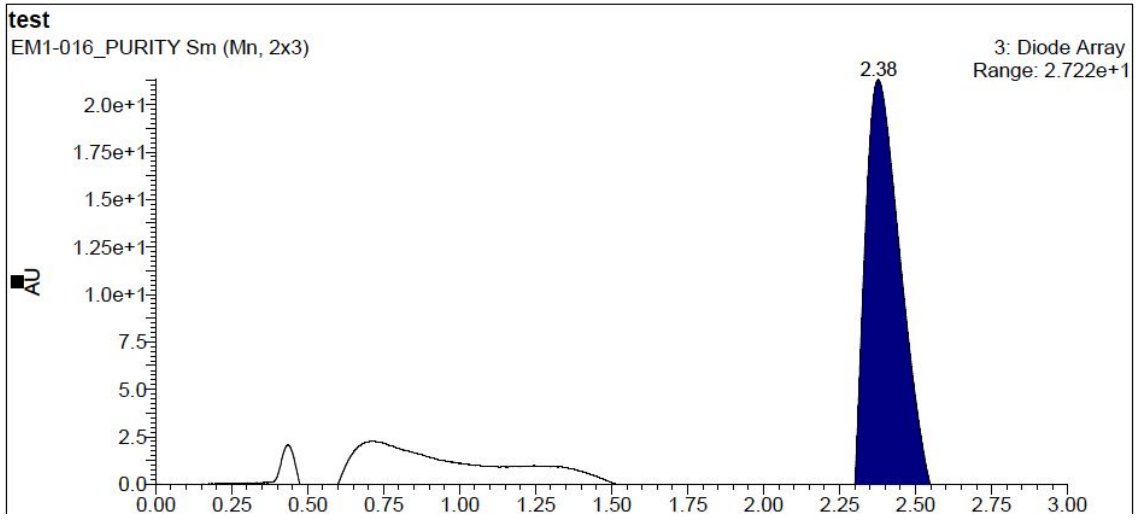
4b



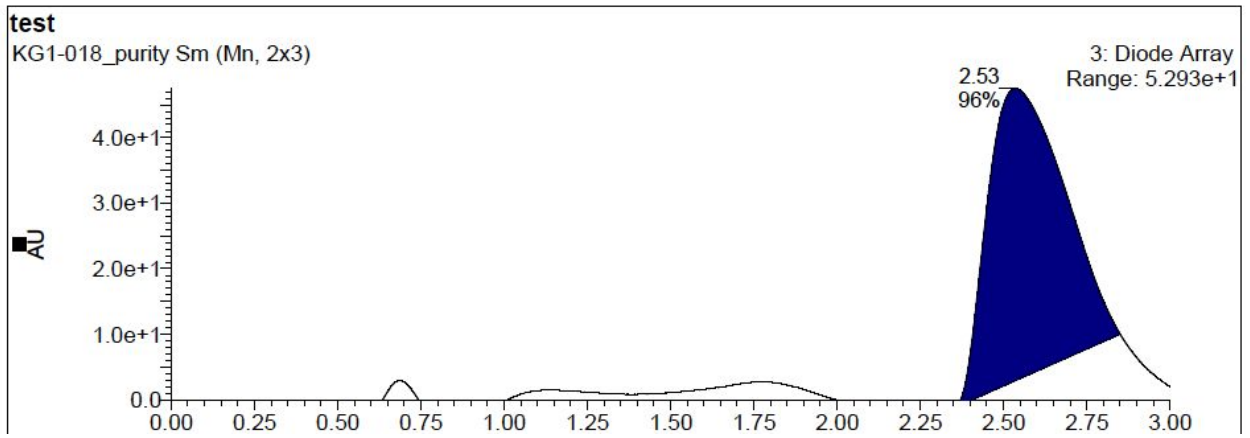
4c



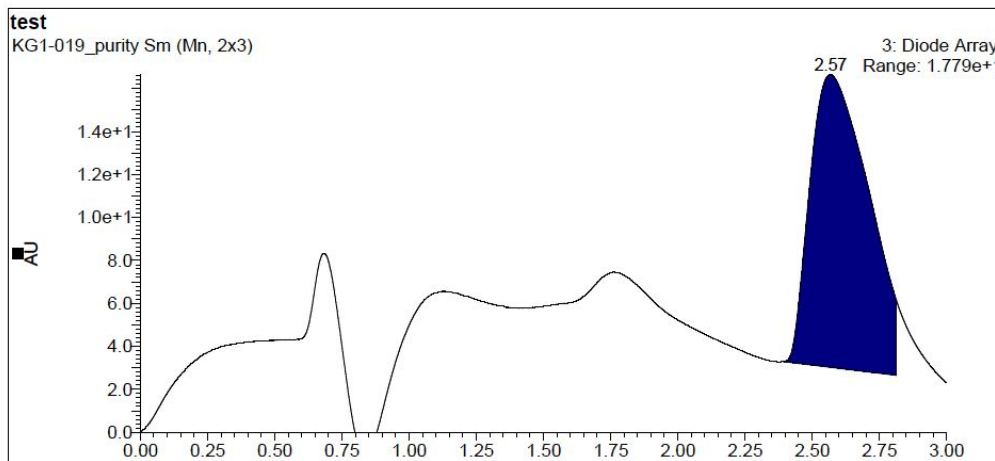
4d



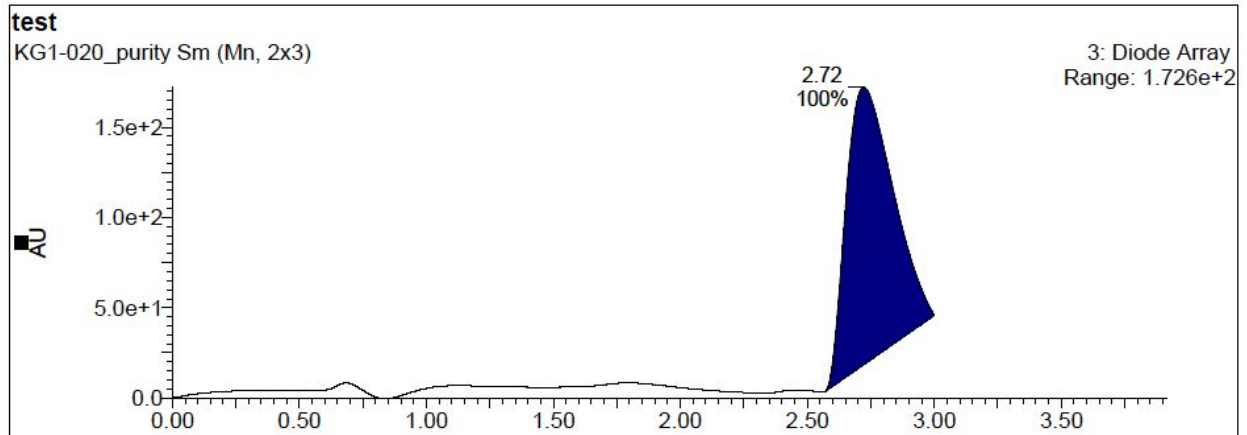
4e



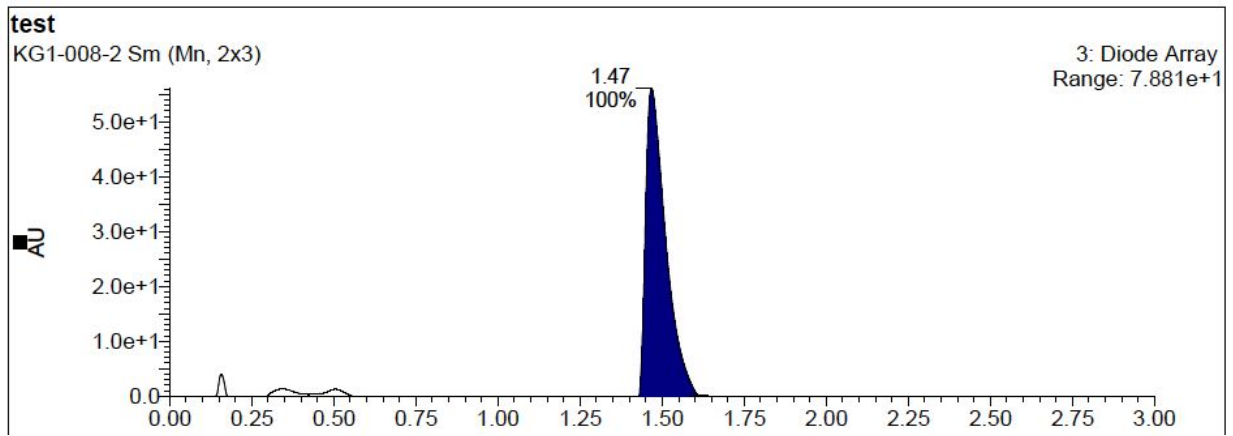
4f



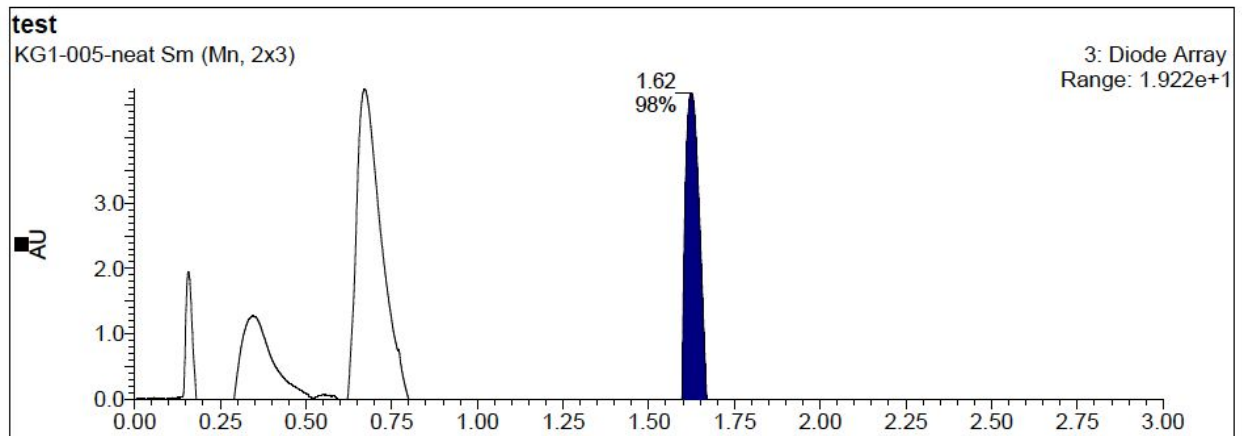
### 4g



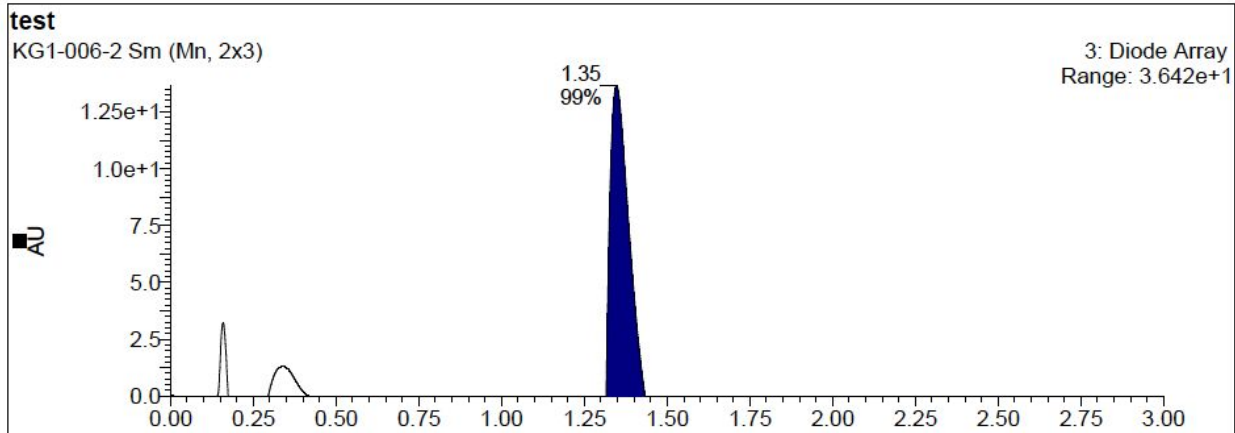
### 4h



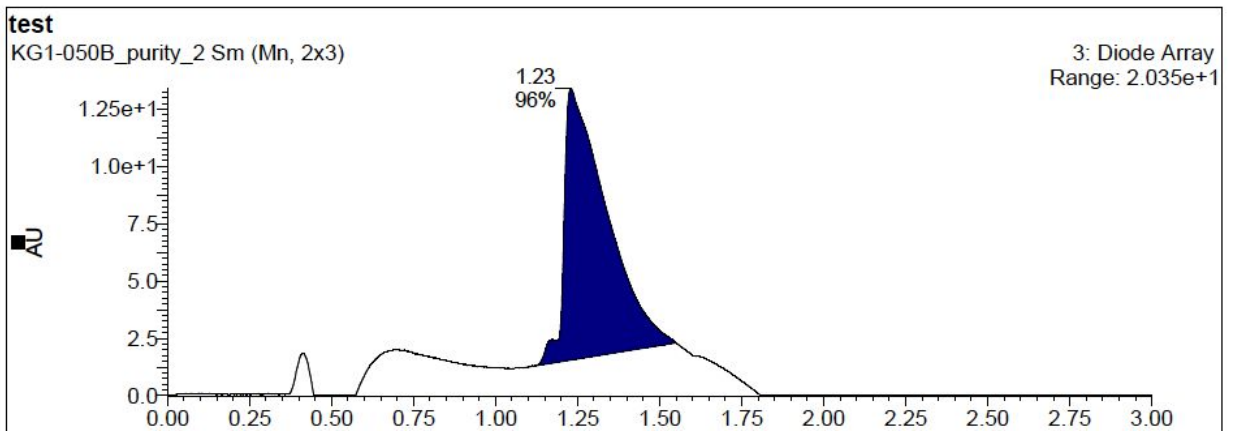
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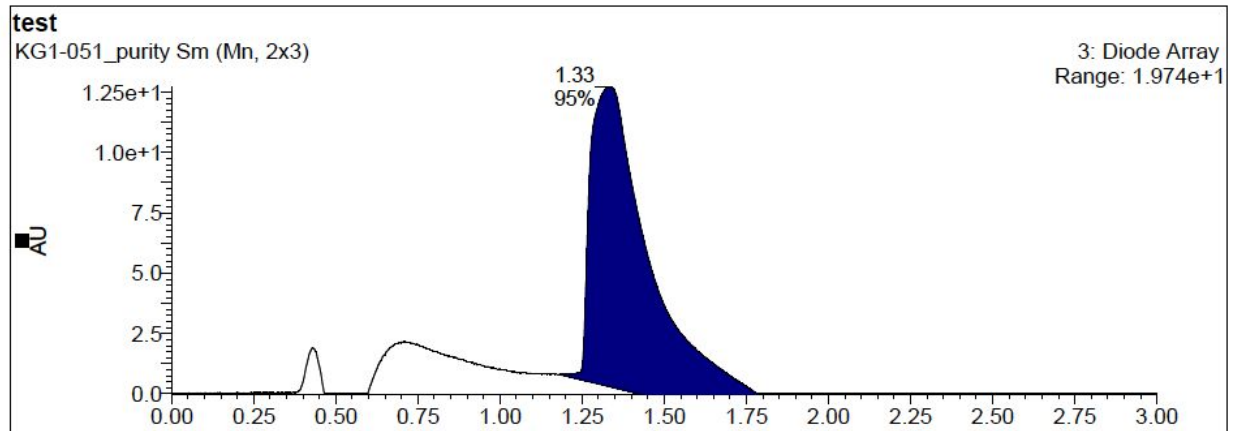
6



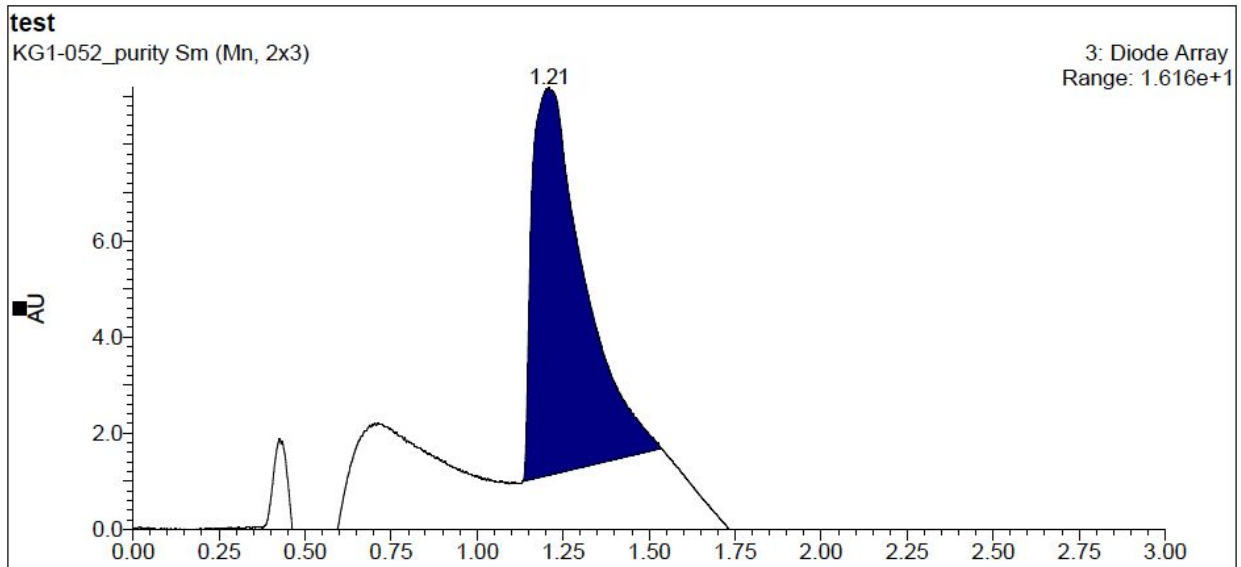
8a



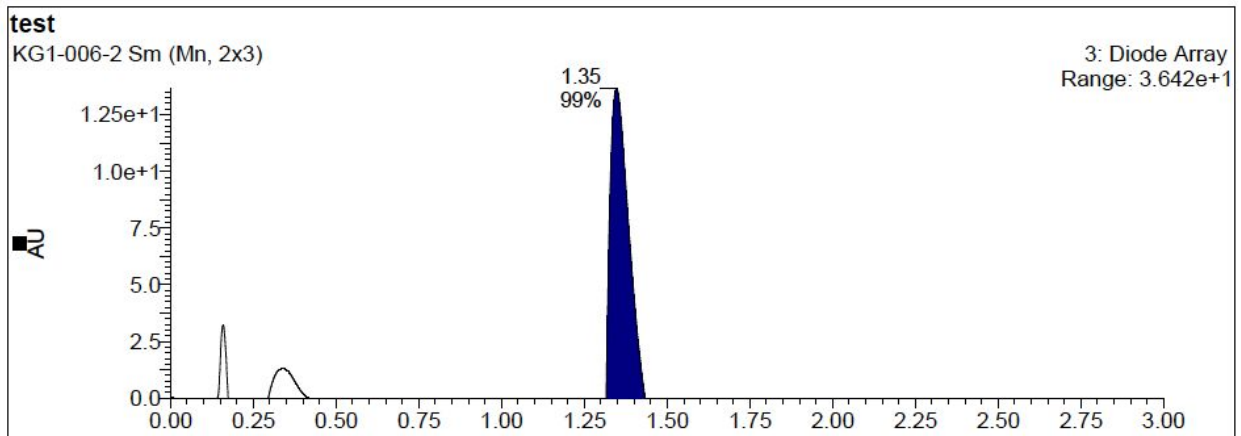
8b



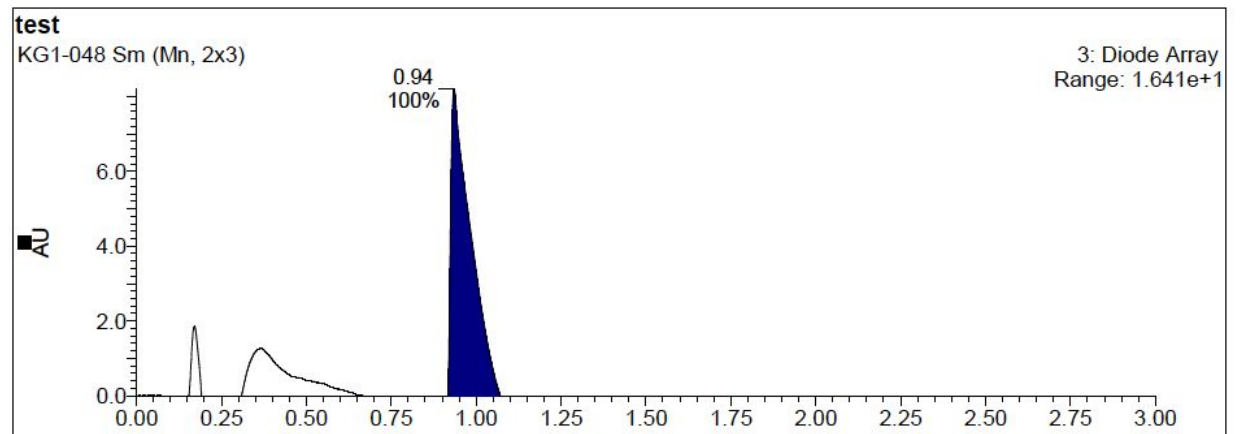
8c



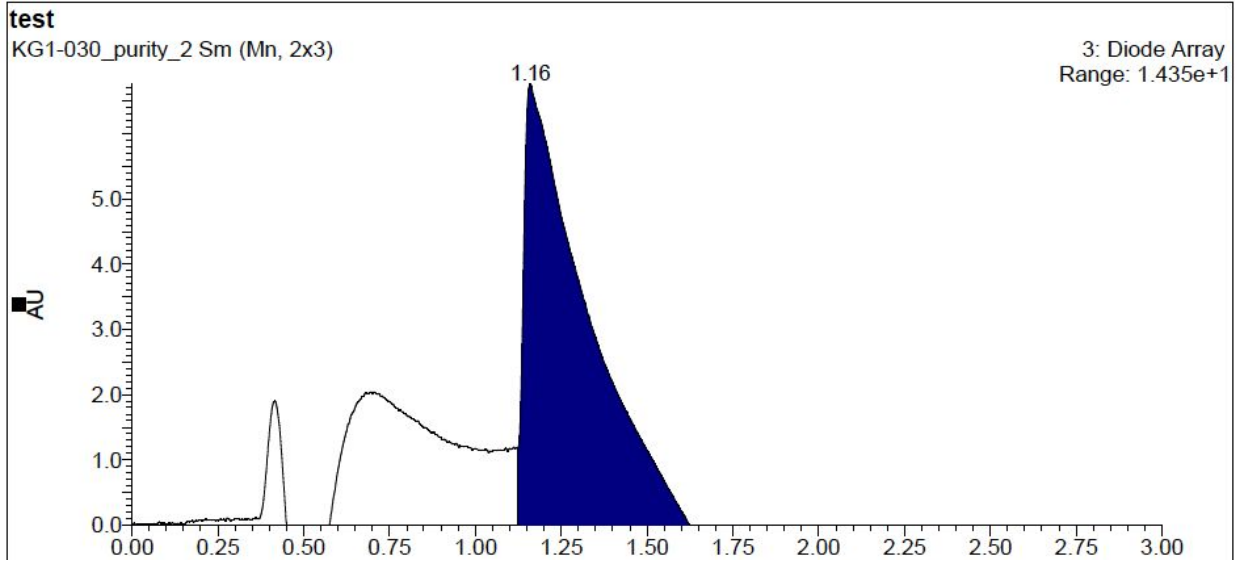
9a



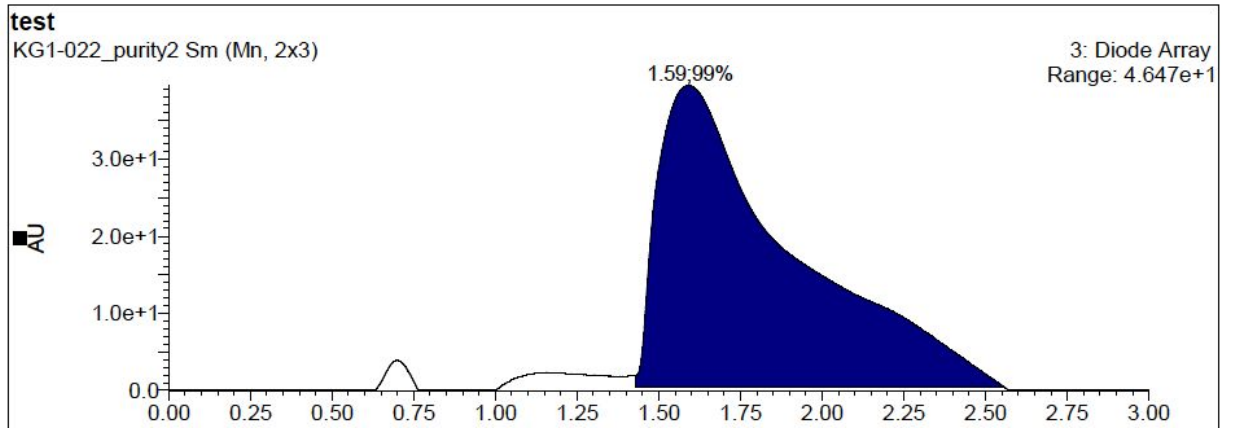
9b



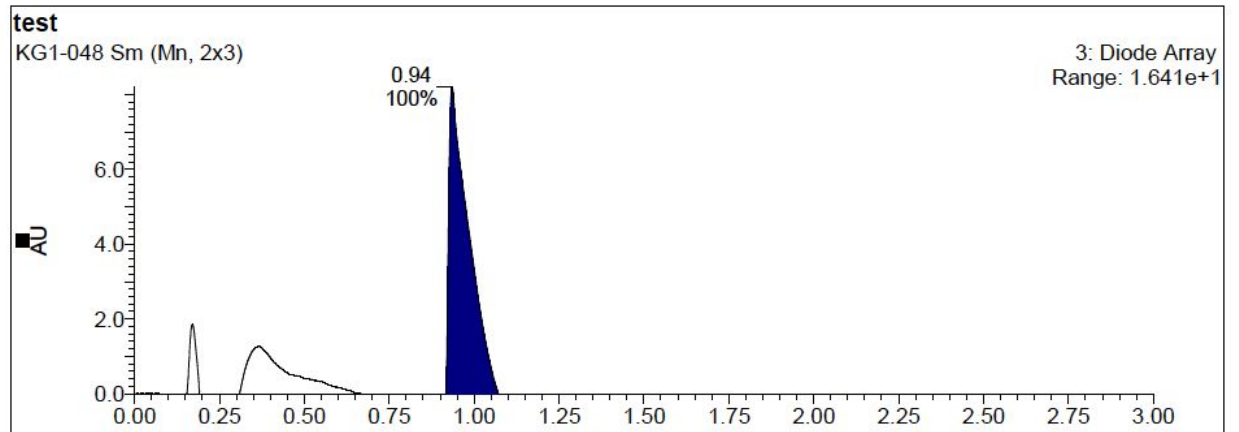
9c



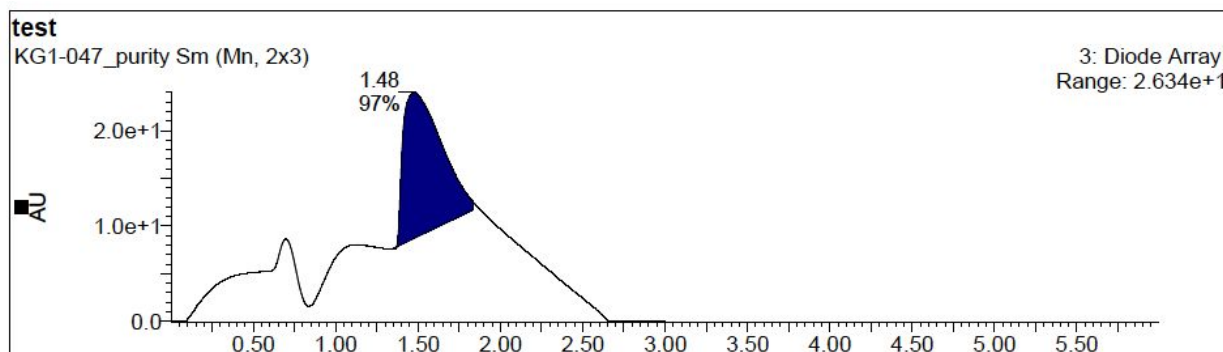
9d



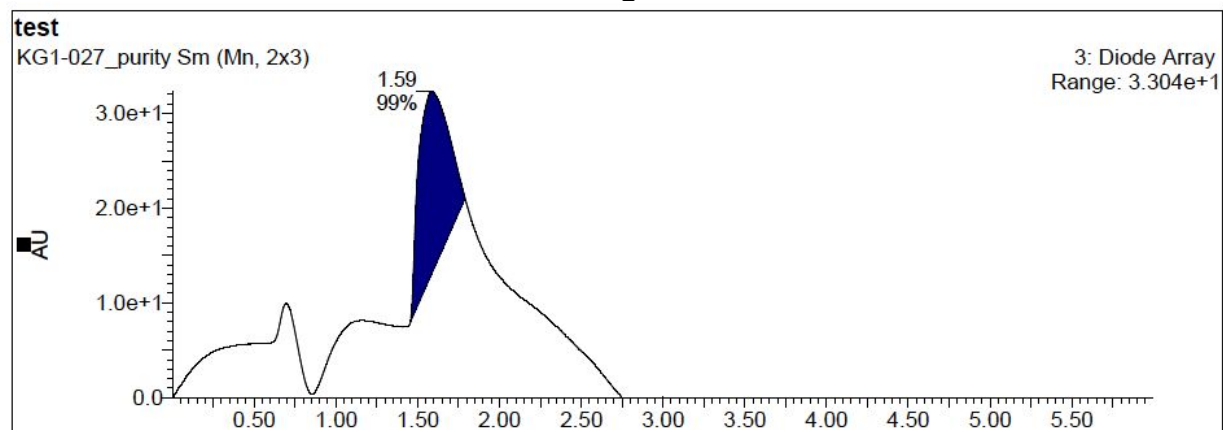
9e



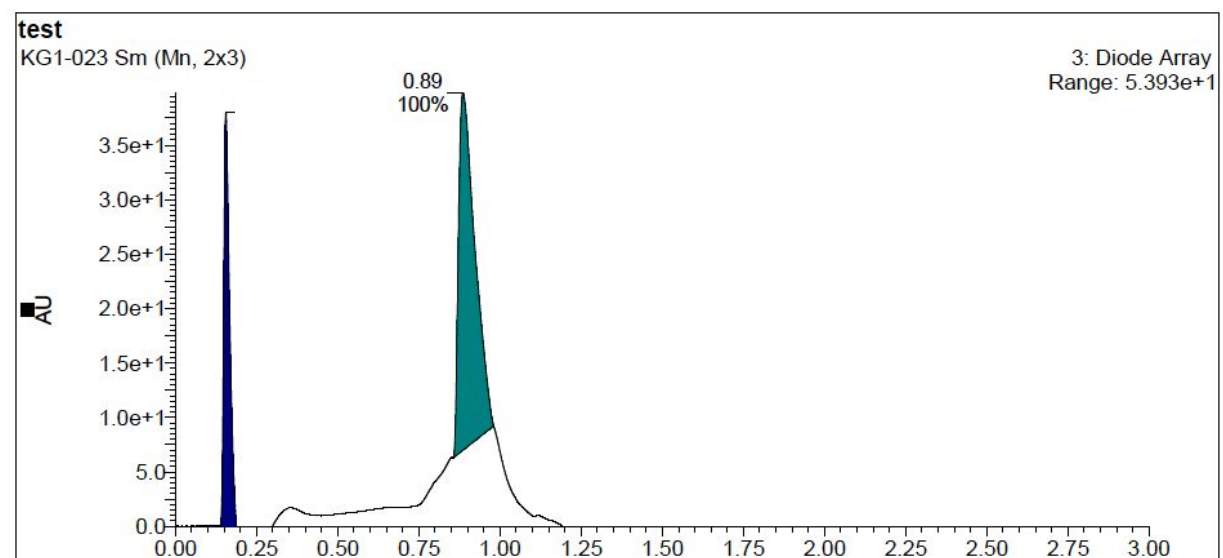
9f



9g

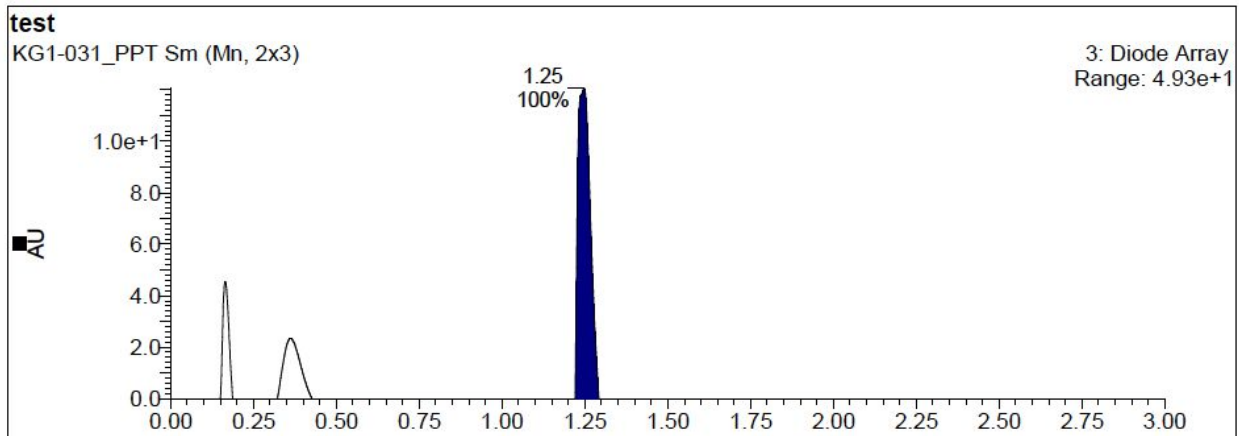


9h

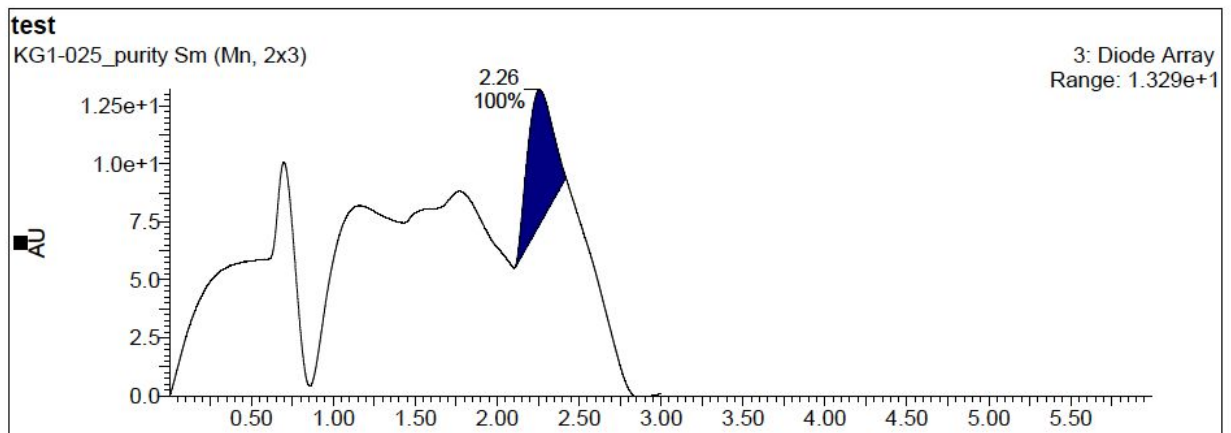




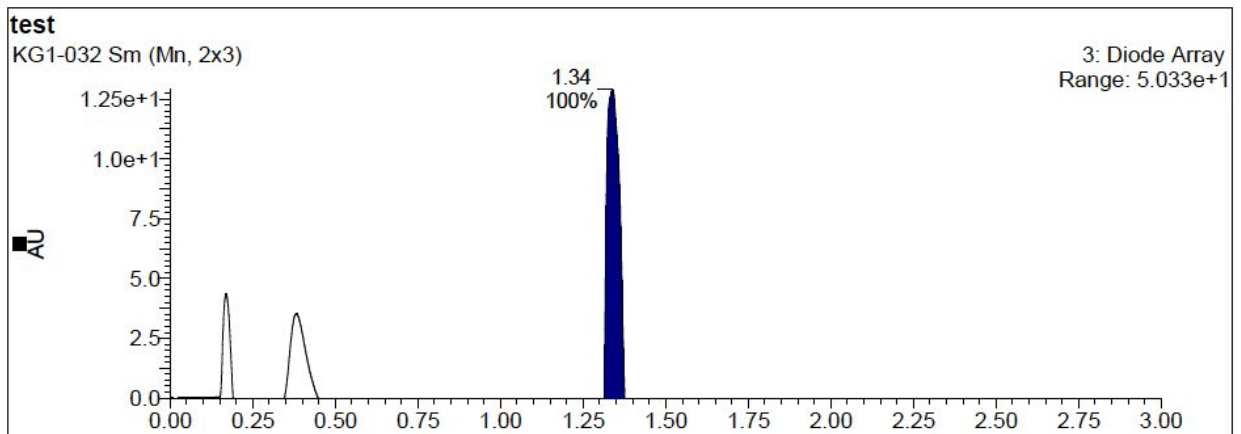
9i



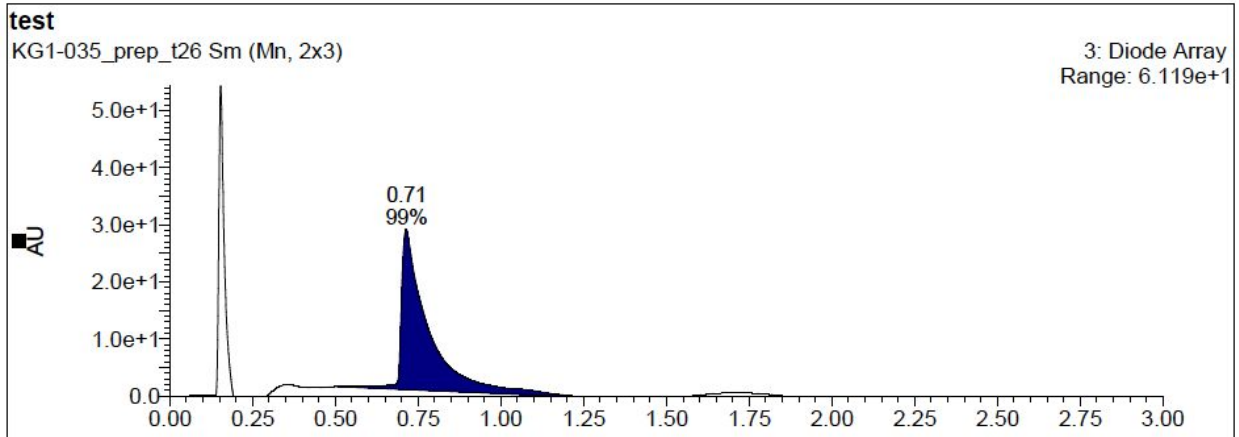
9j



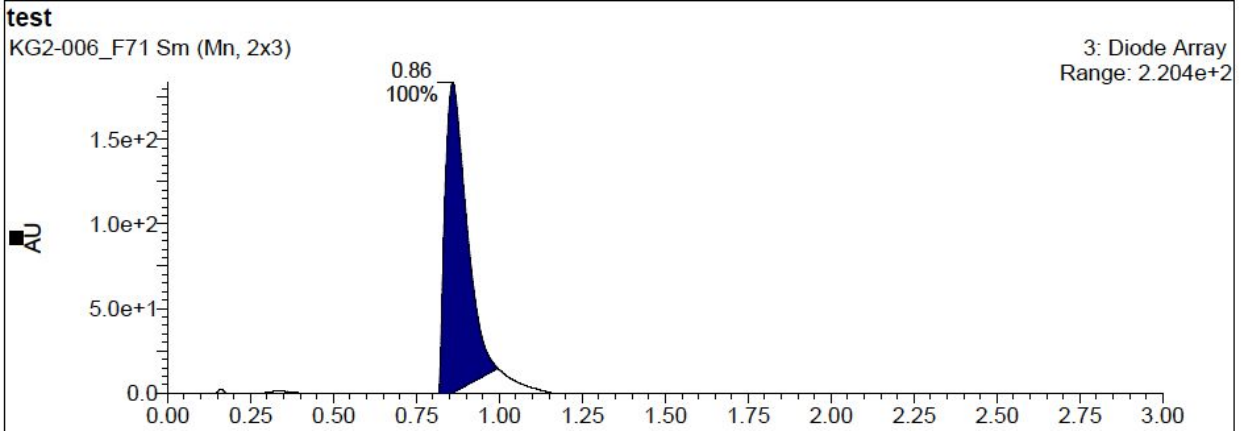
9k



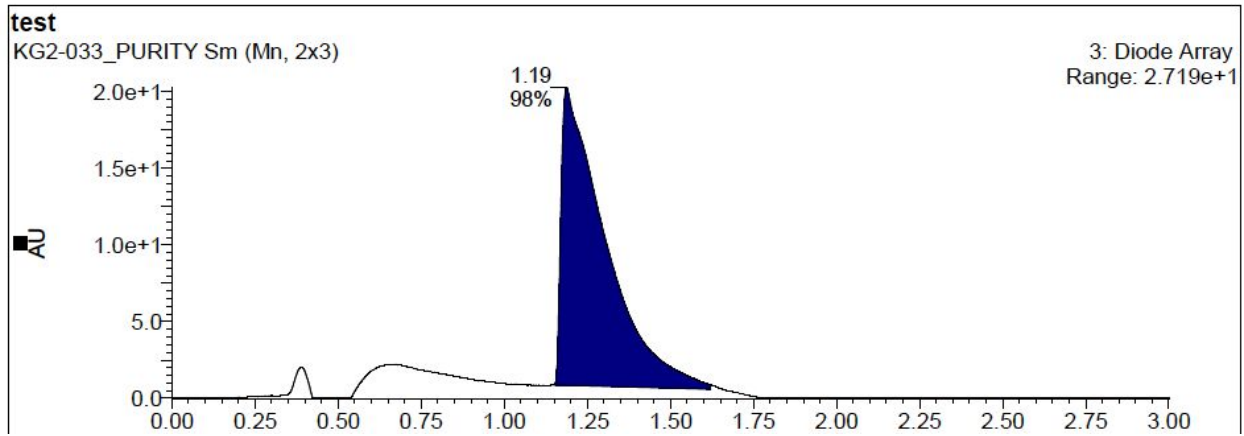
12



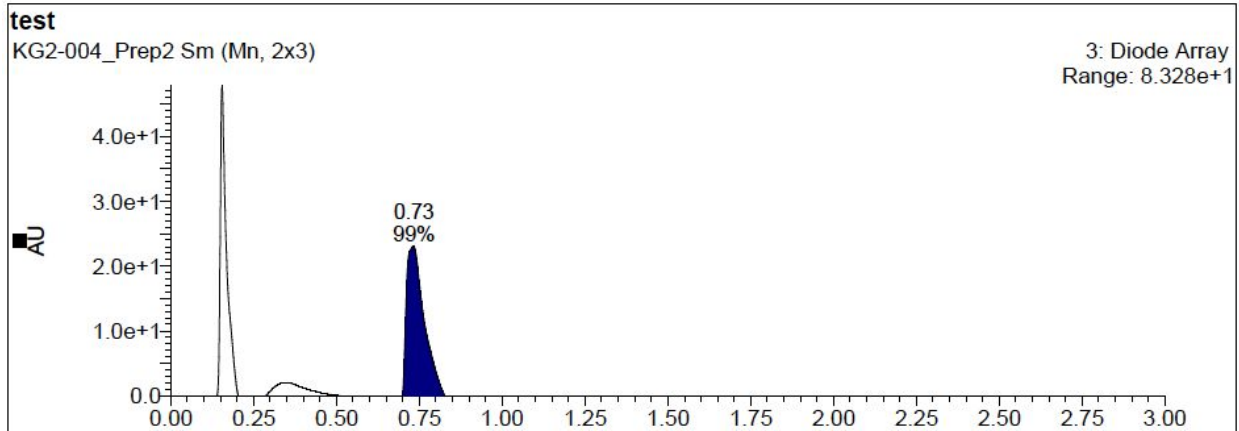
18a



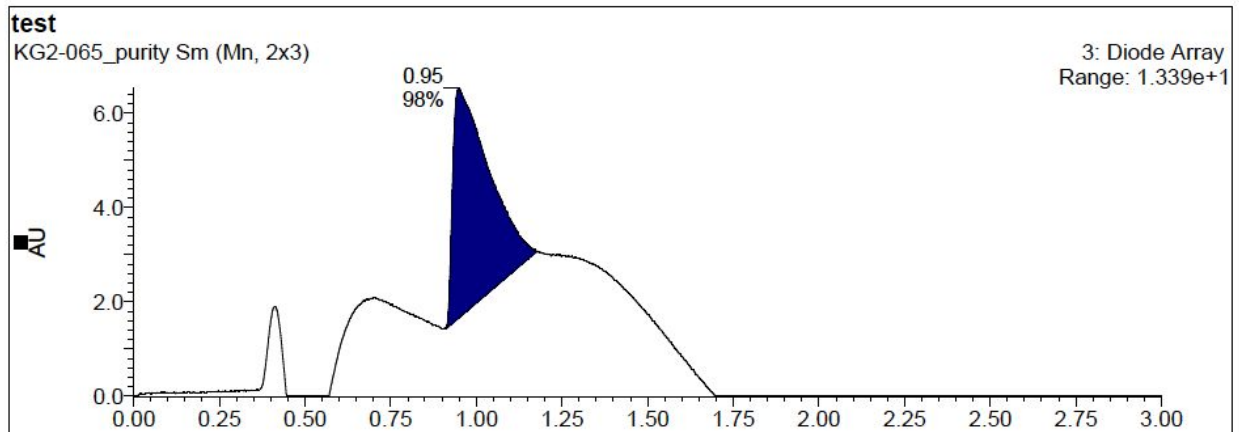
18b



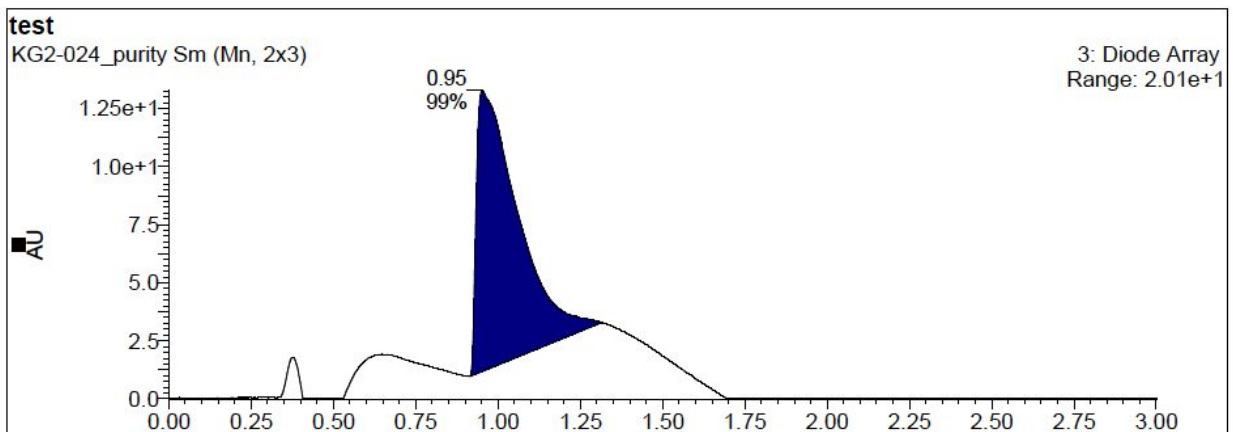
18c



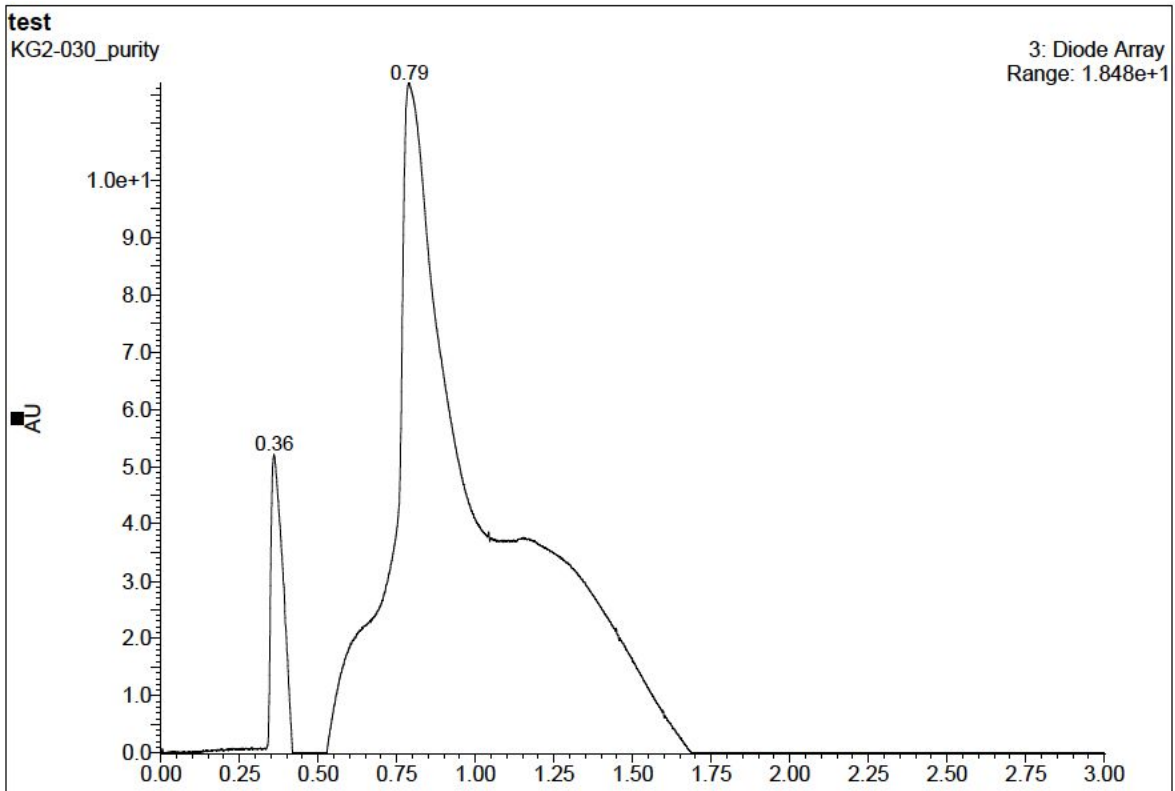
18d



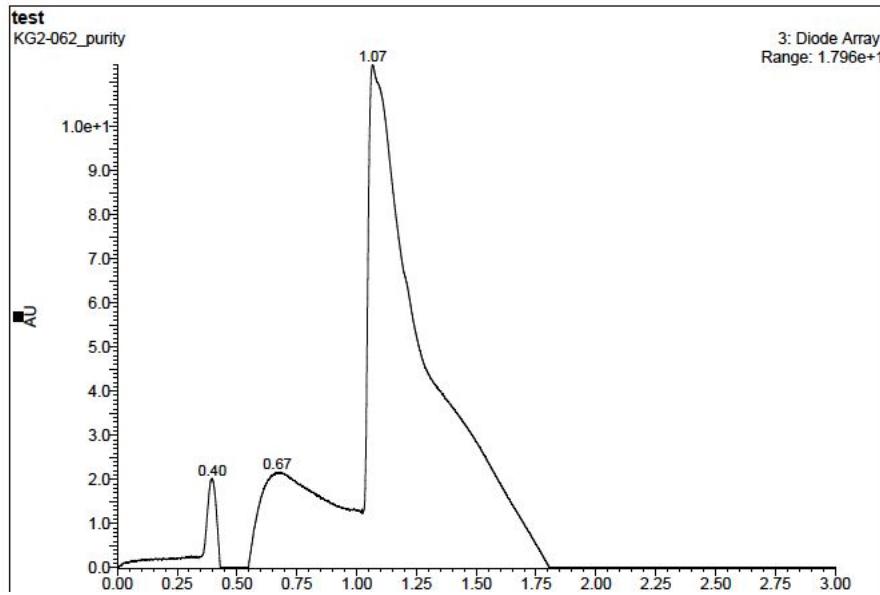
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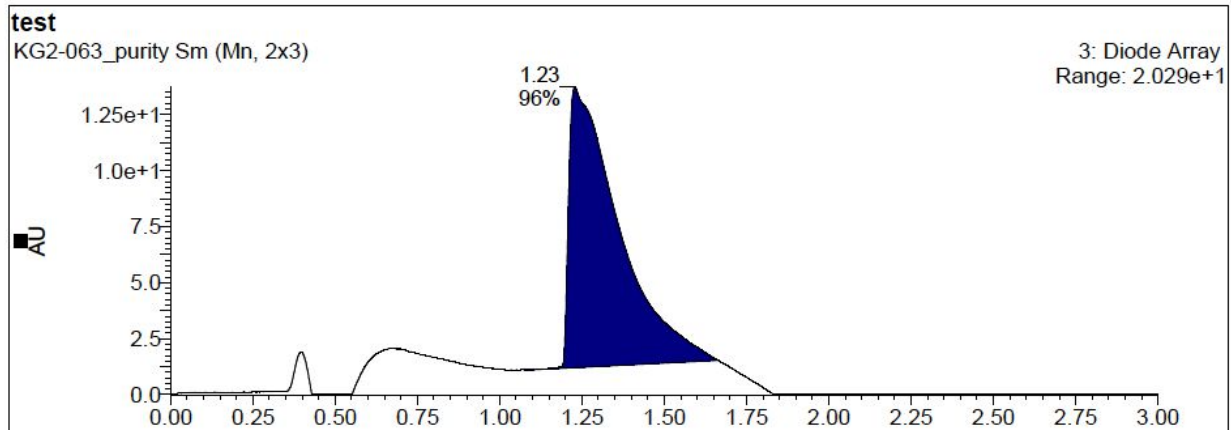
18f



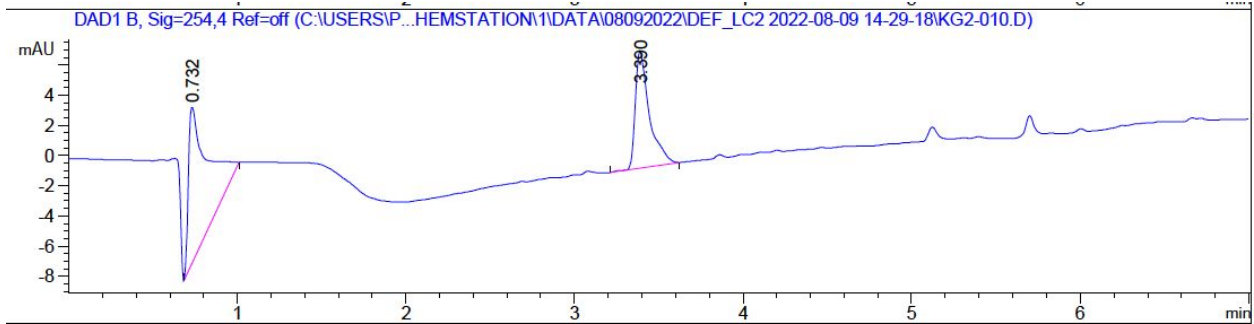
18g



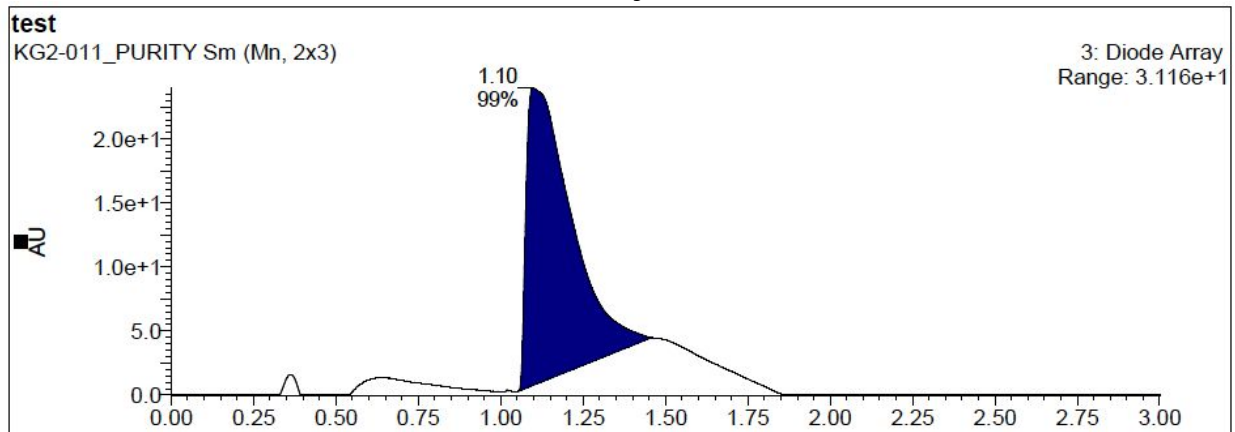
### 18h



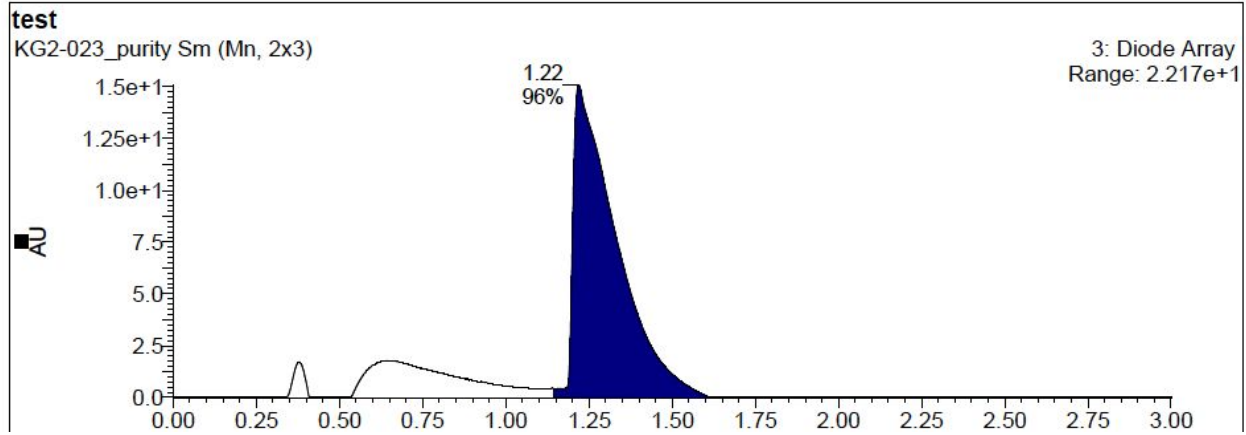
### 18i



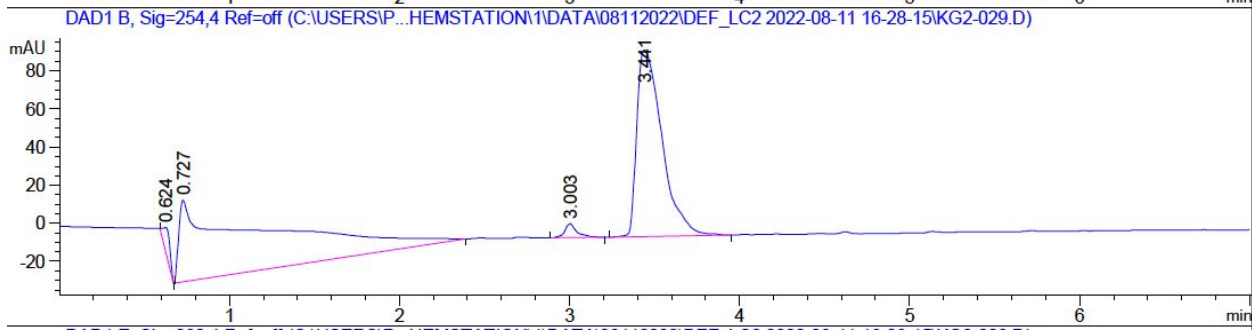
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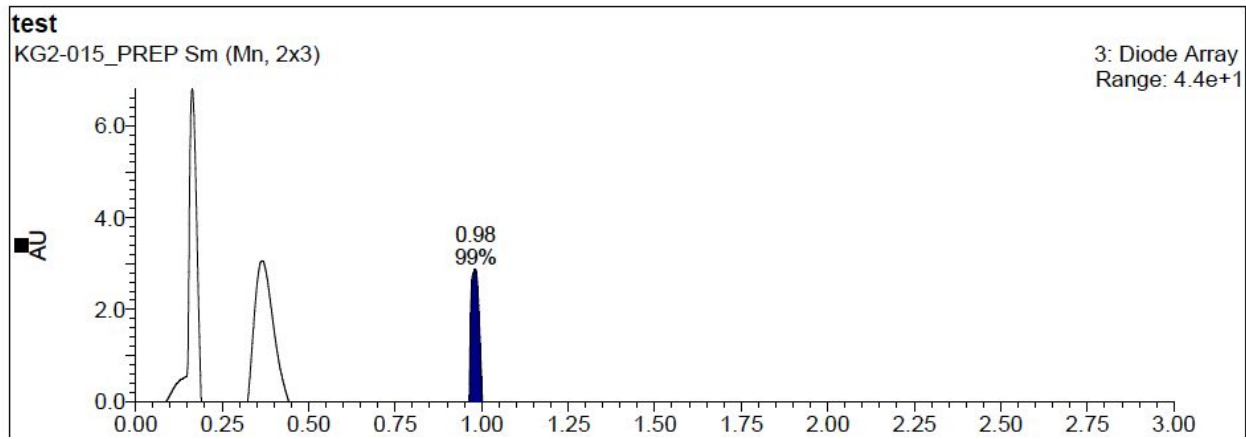
### 18k



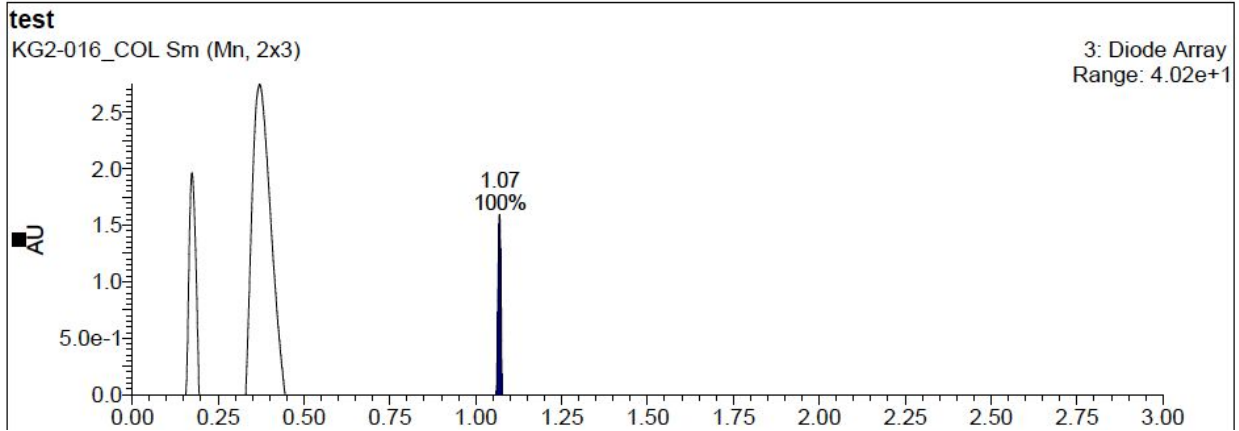
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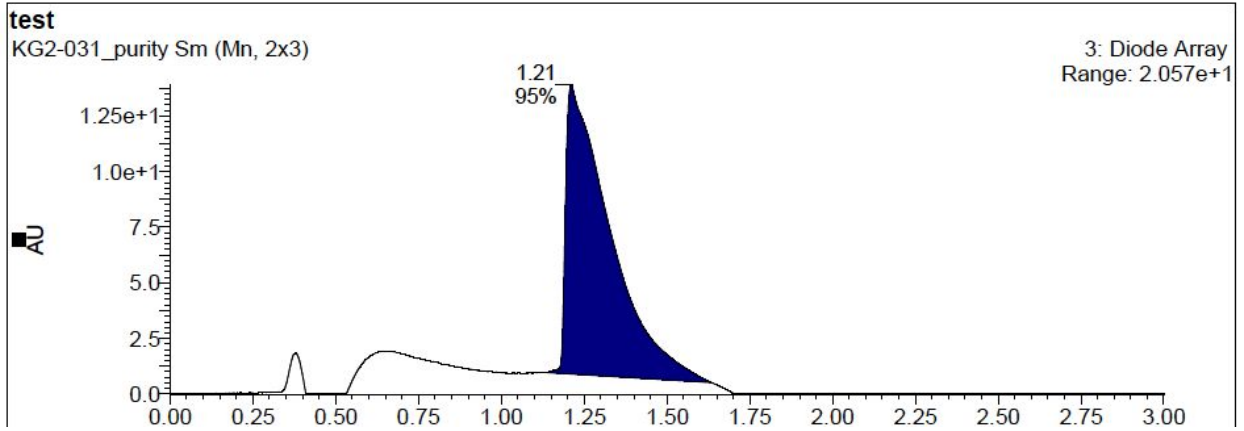
### 18n



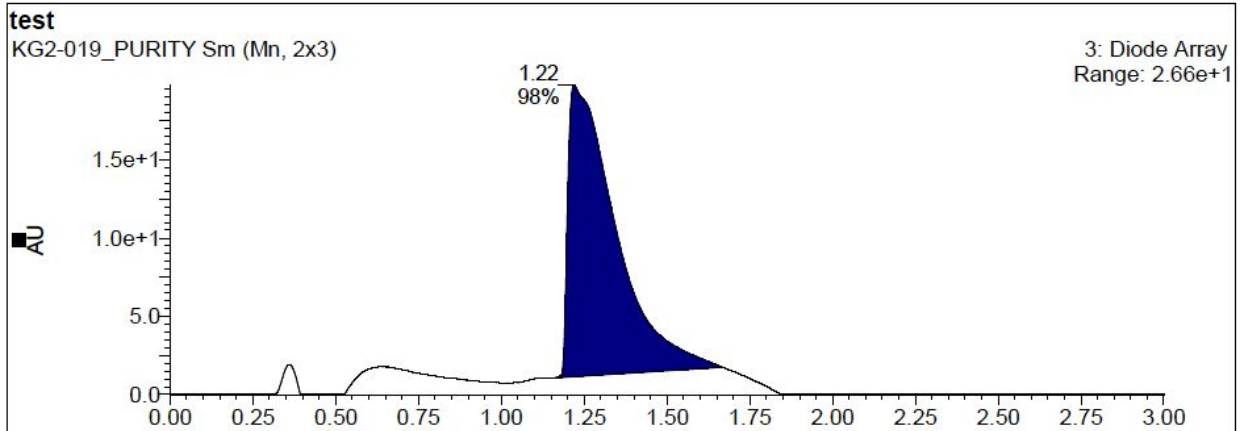
### 18o



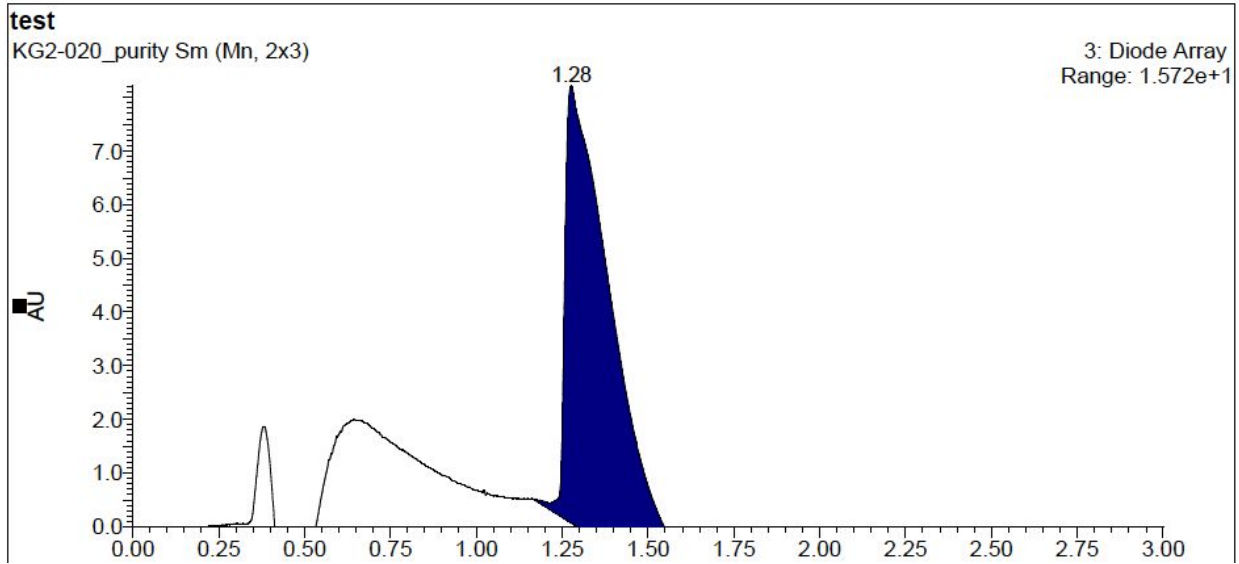
### 18p



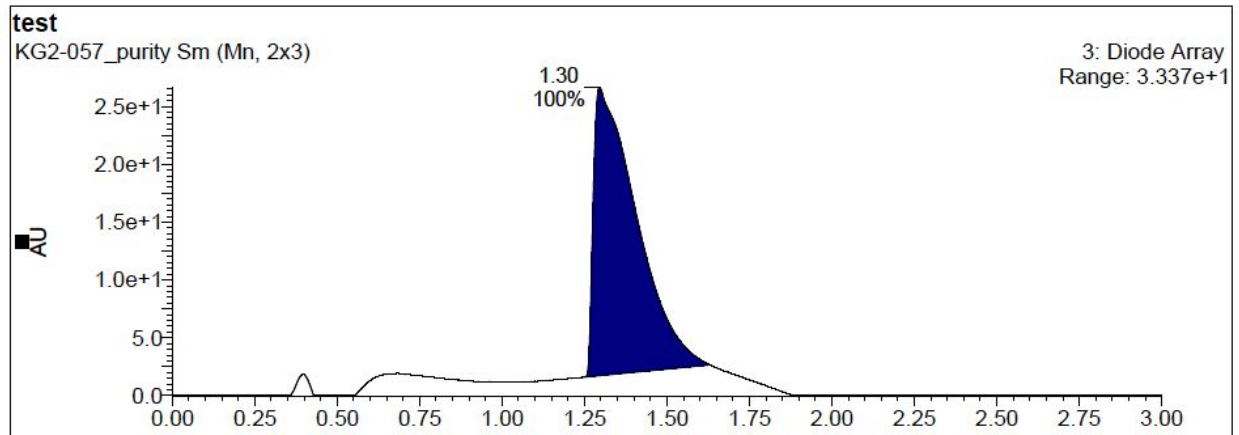
### 18q



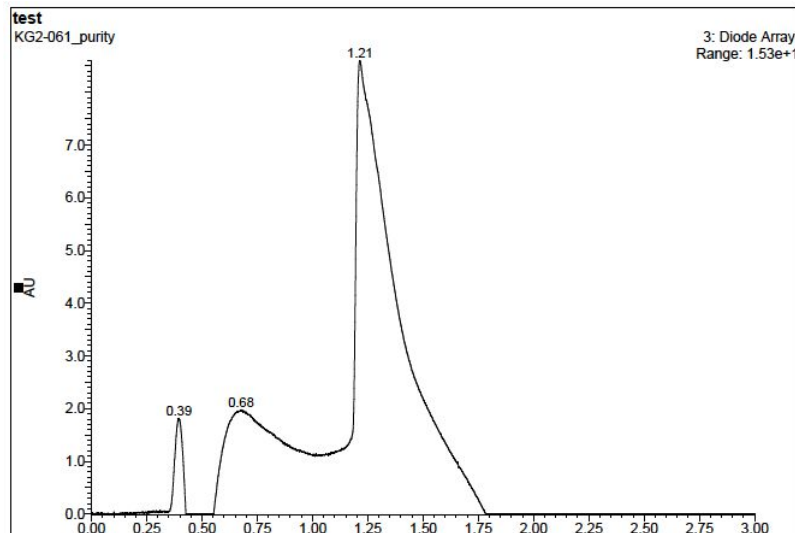
### 18r



### 18s

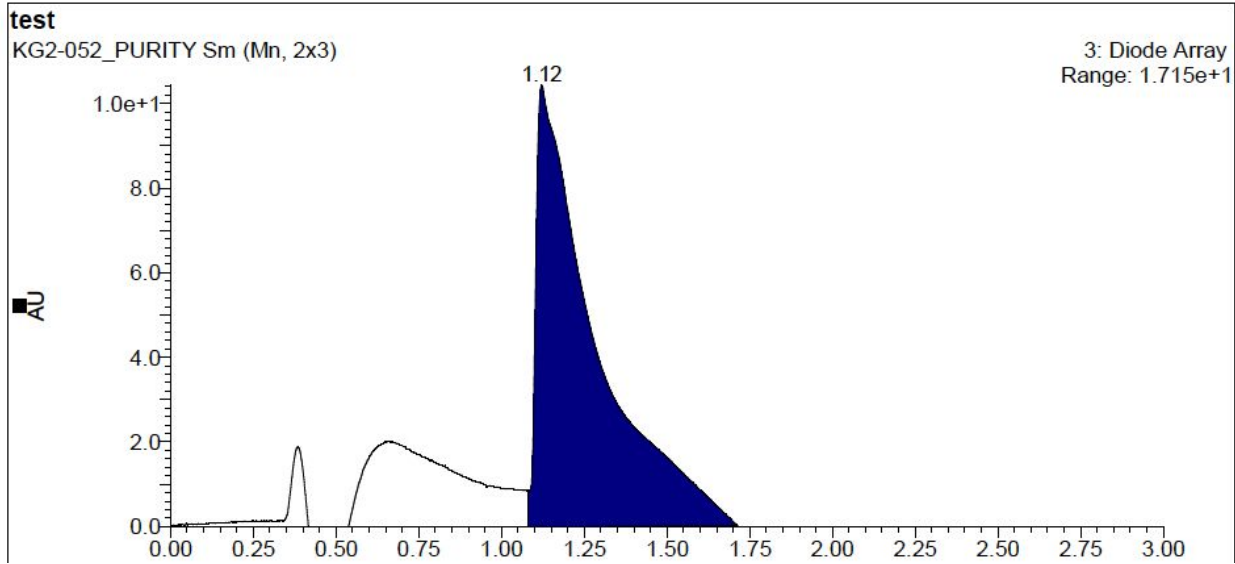


### 18t

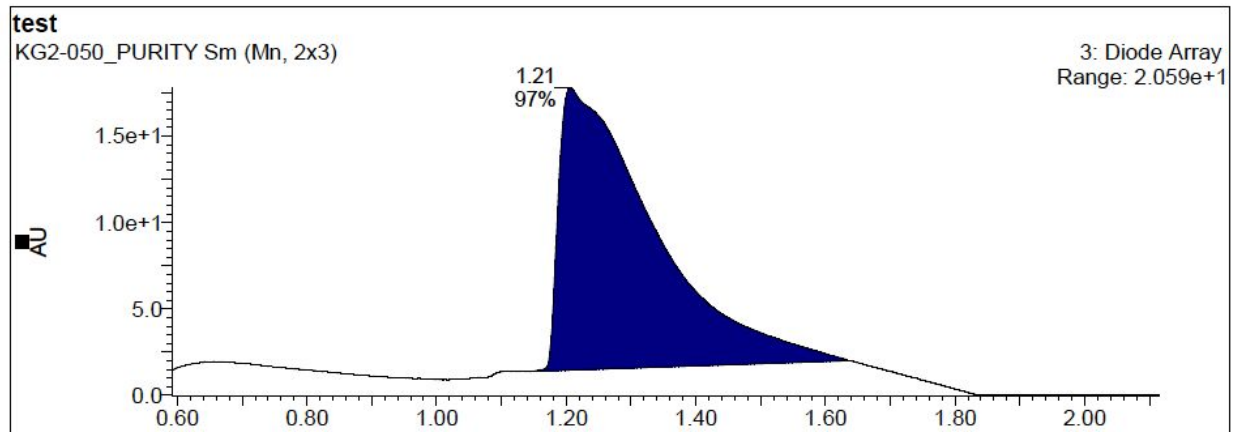




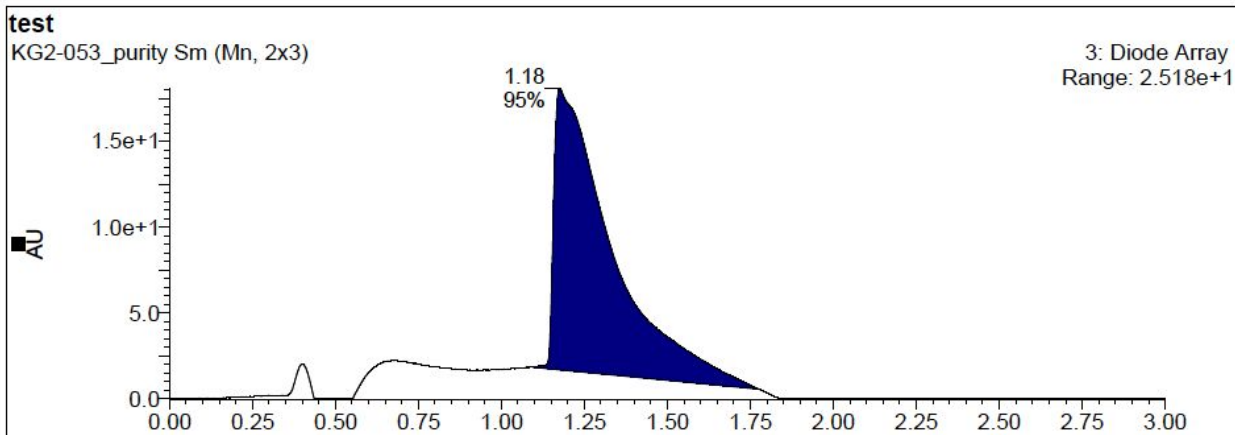
**23a**



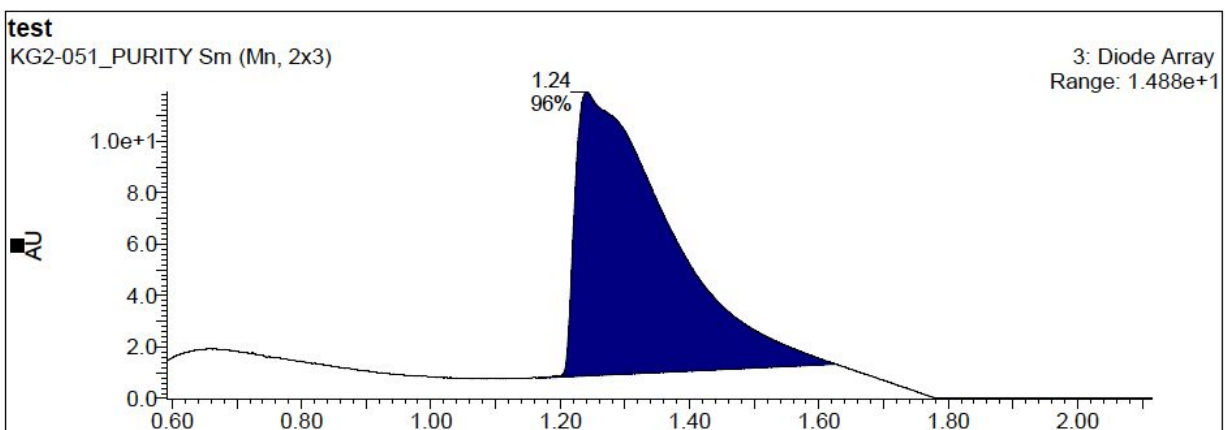
**23b**



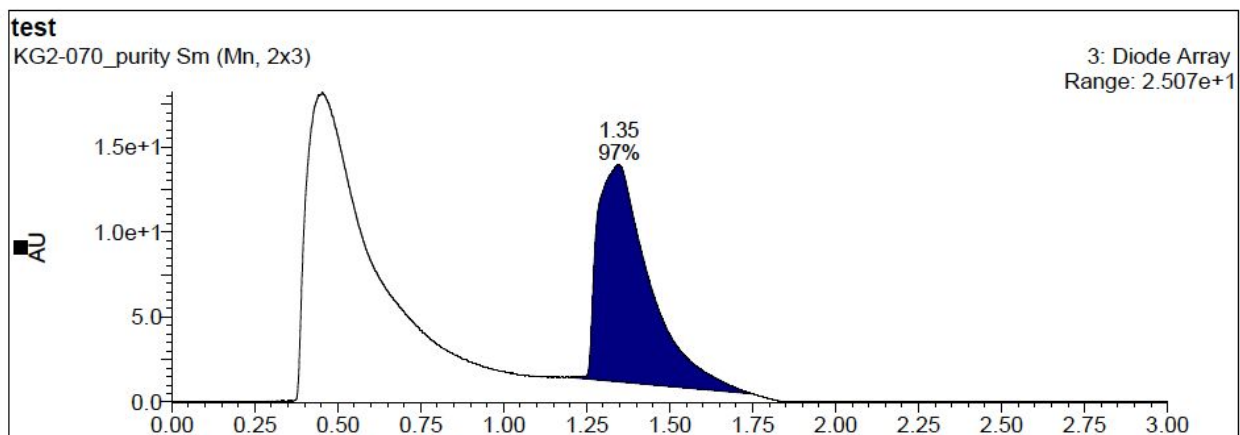
**23c**



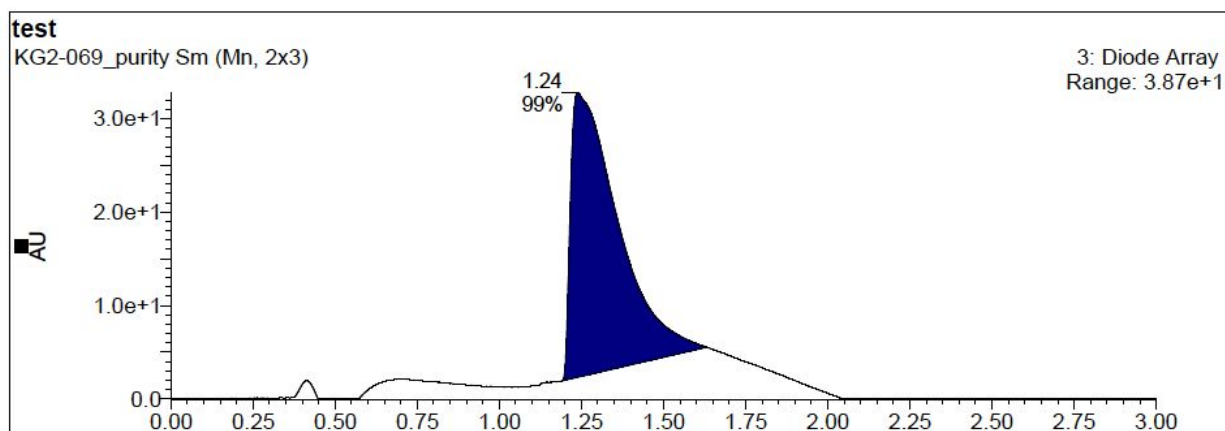
### 23d



### 23e



### 23f



# 23g

