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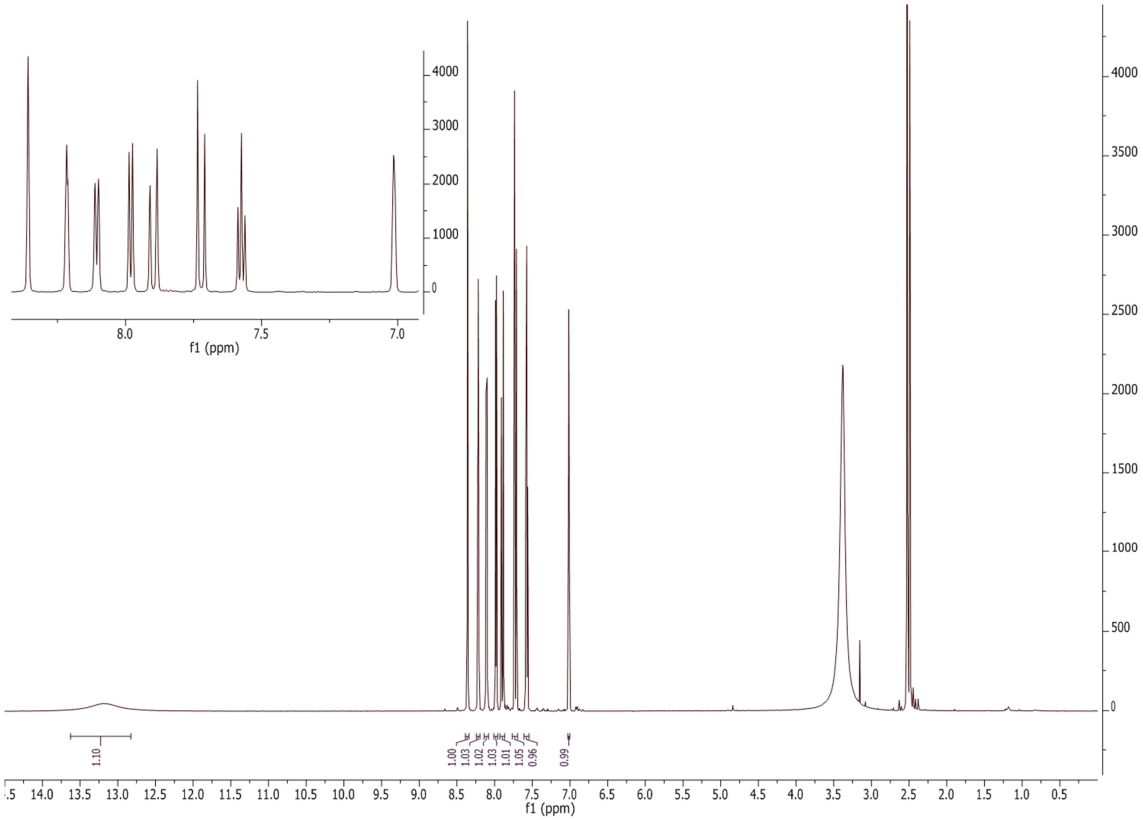
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ADDENDUM

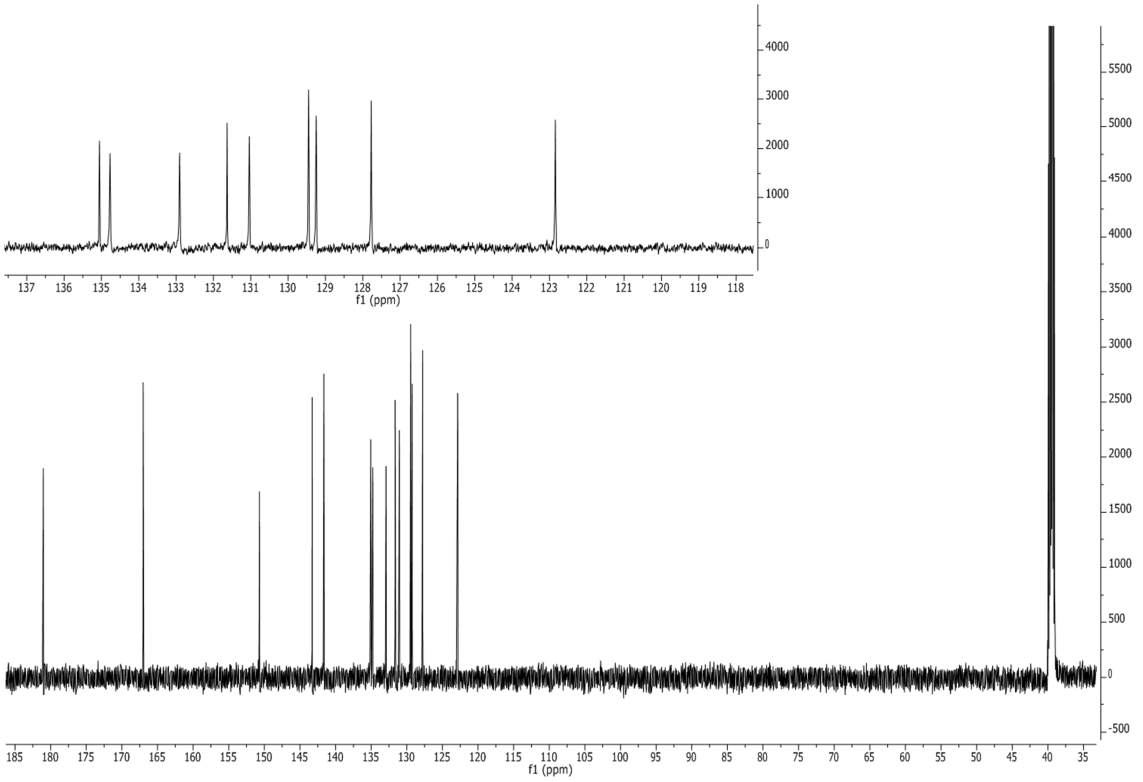
- List of selected ^{1}H NMR and ^{13}C NMR spectra
- List of mass spectrometry data
- List of IR spectra
- List of HPLC data
- IC_{50} values obtained during radioligand binding assays
- *In vivo d*ata tables
- Structures of compounds SJR1 – SJR5 used in QSAR study

3-[(1*E*)-3-(5-methylthiophen-2-yl)-3-oxoprop-1-en-1-yl]benzoic acid (37f)

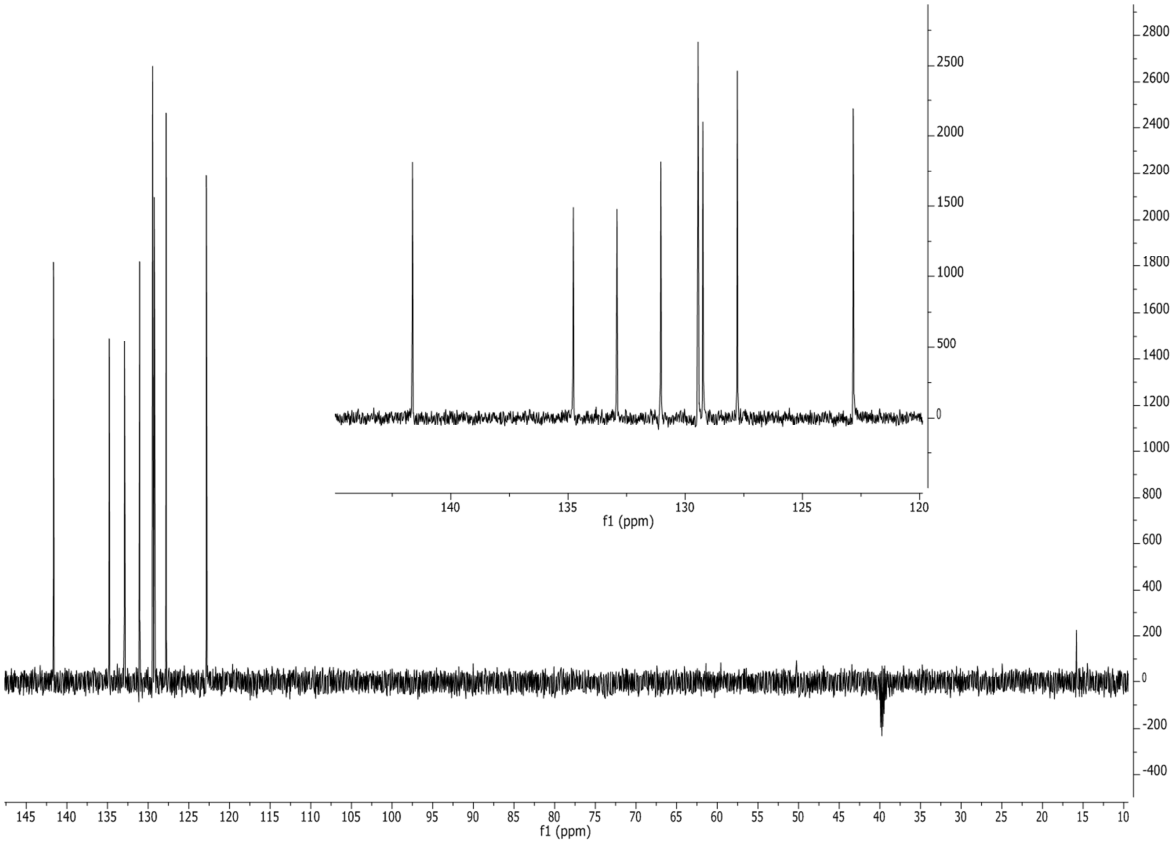
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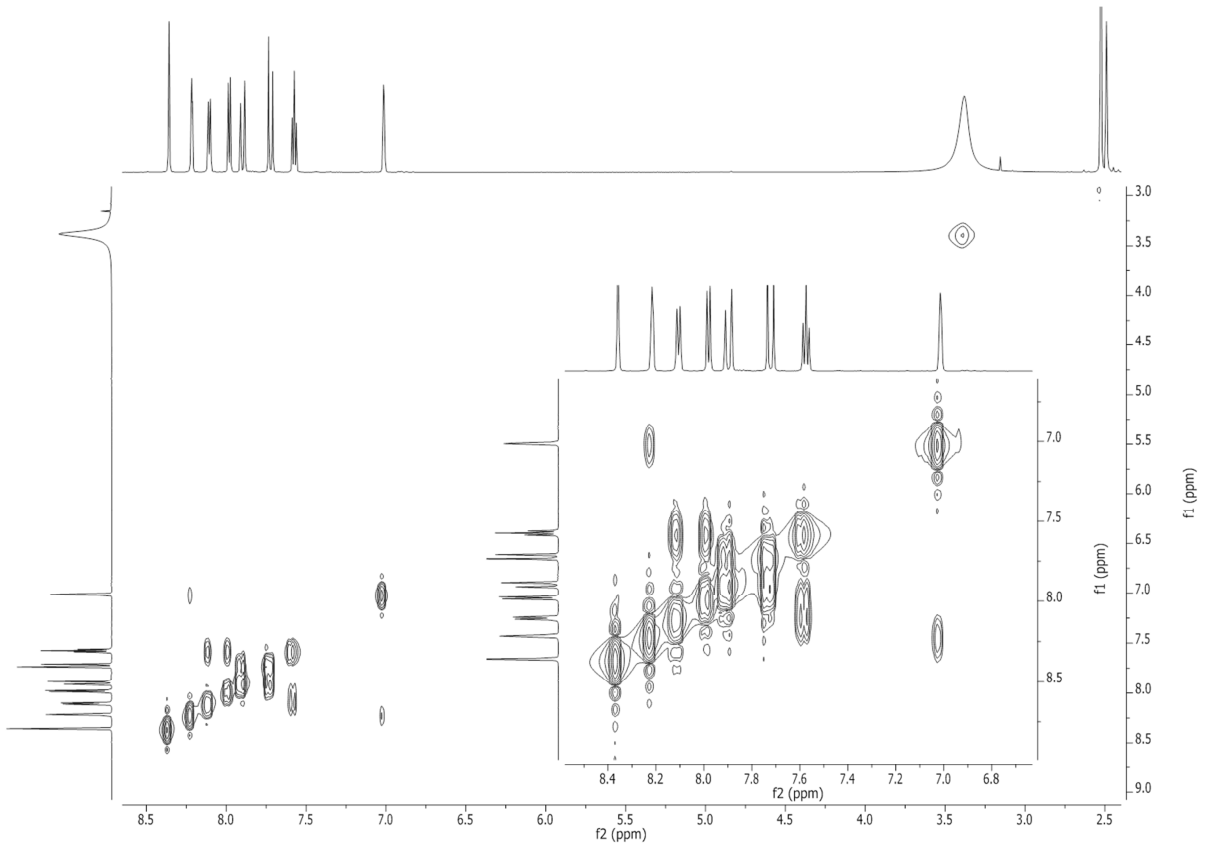
^{13}C NMR



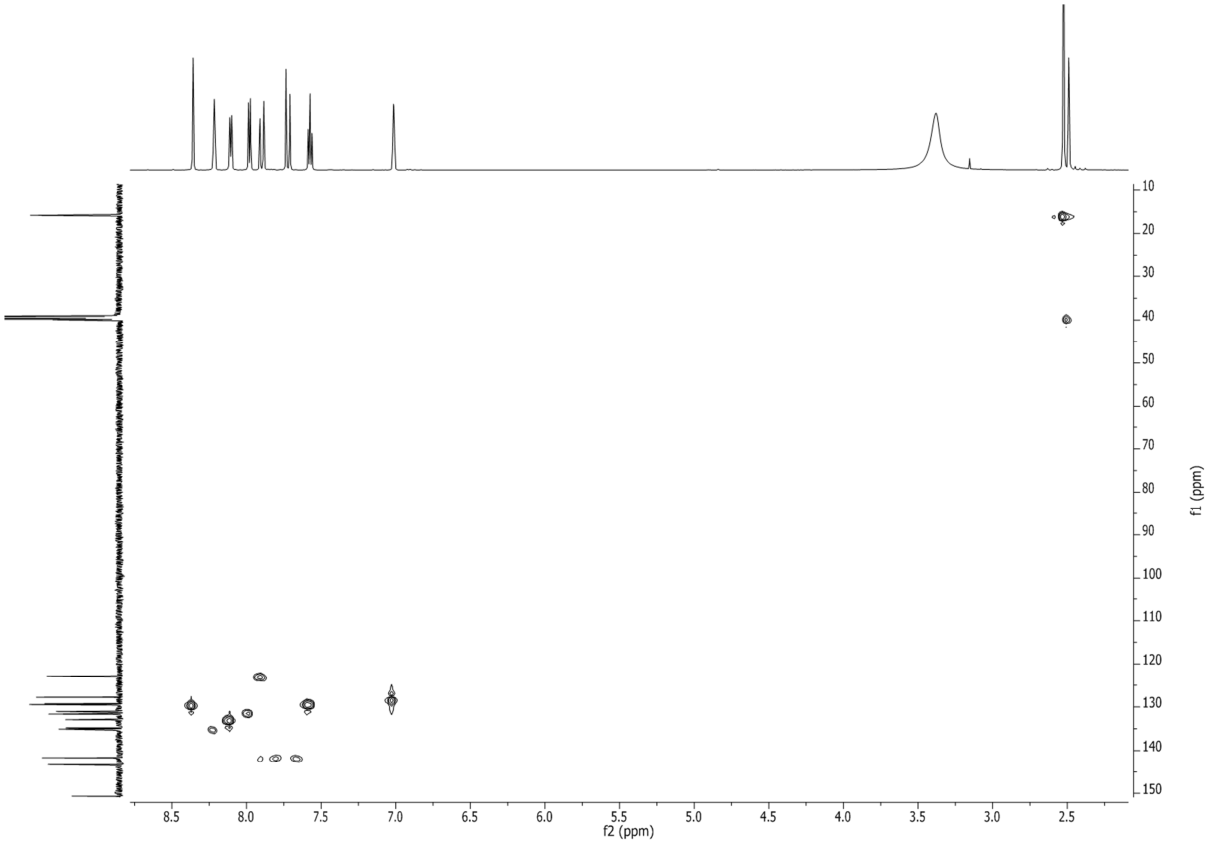
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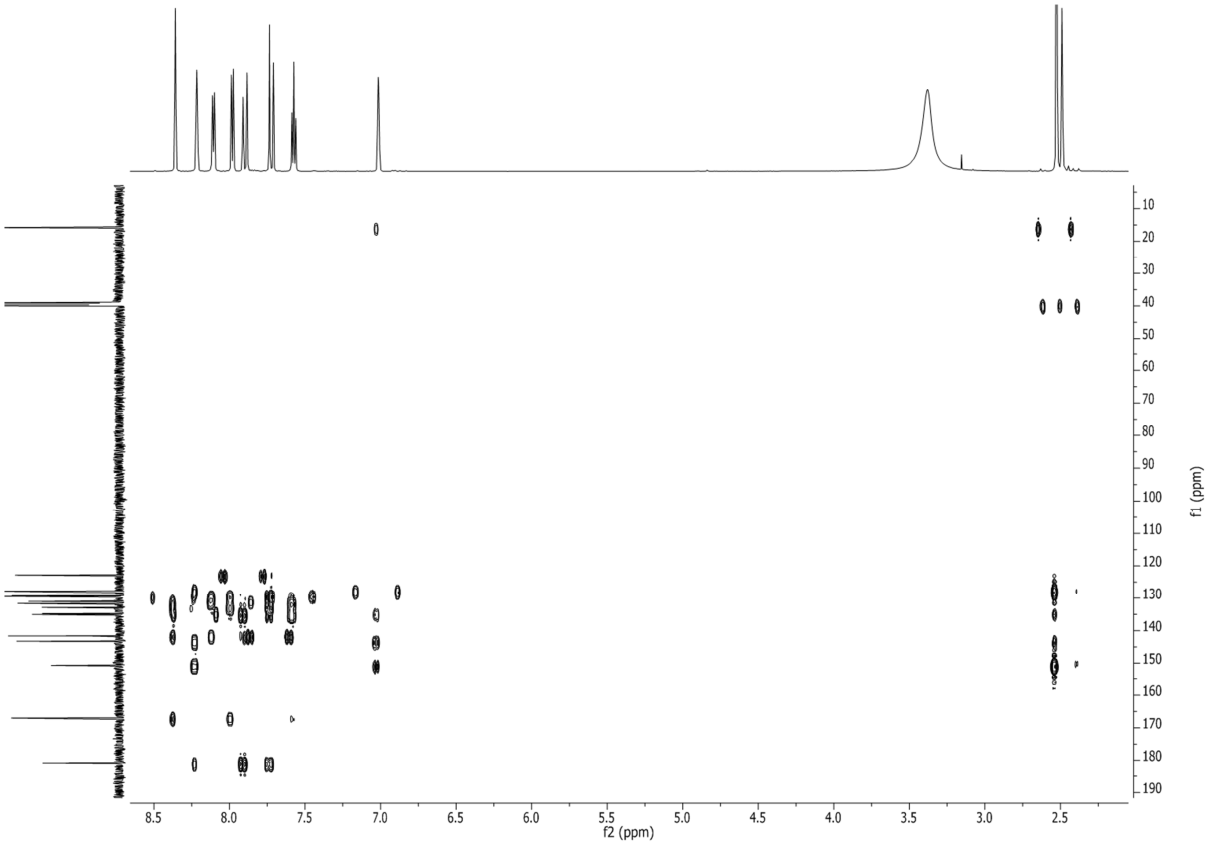
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HSQC

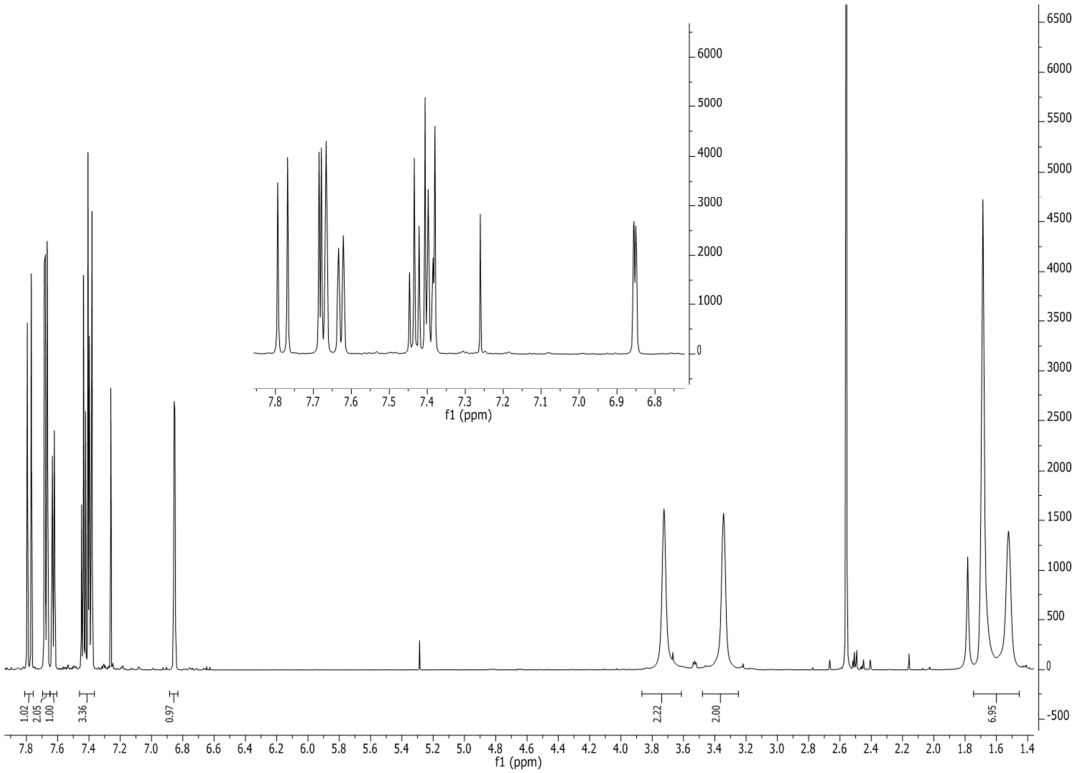


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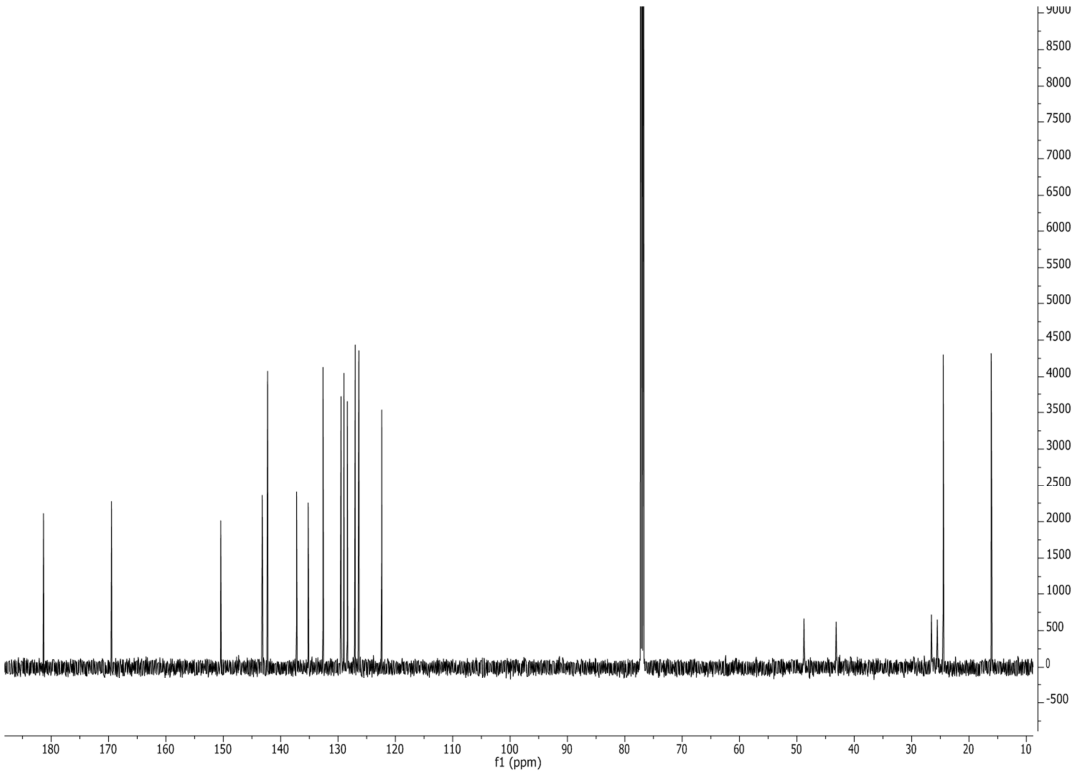


(2*E*)-1-(5-methylthiophen-2-yl)-3-[3-(piperidine-1-carbonyl)phenyl]prop-2-en-1-one (38f)

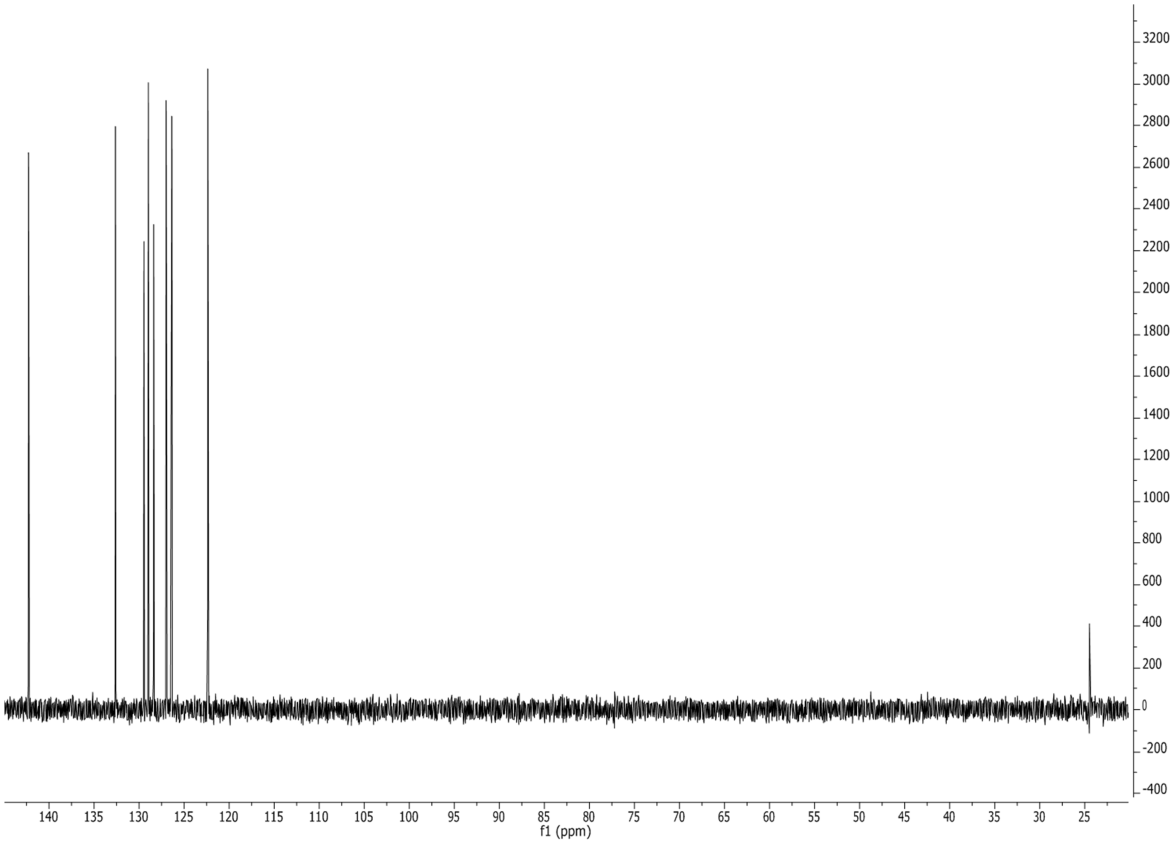
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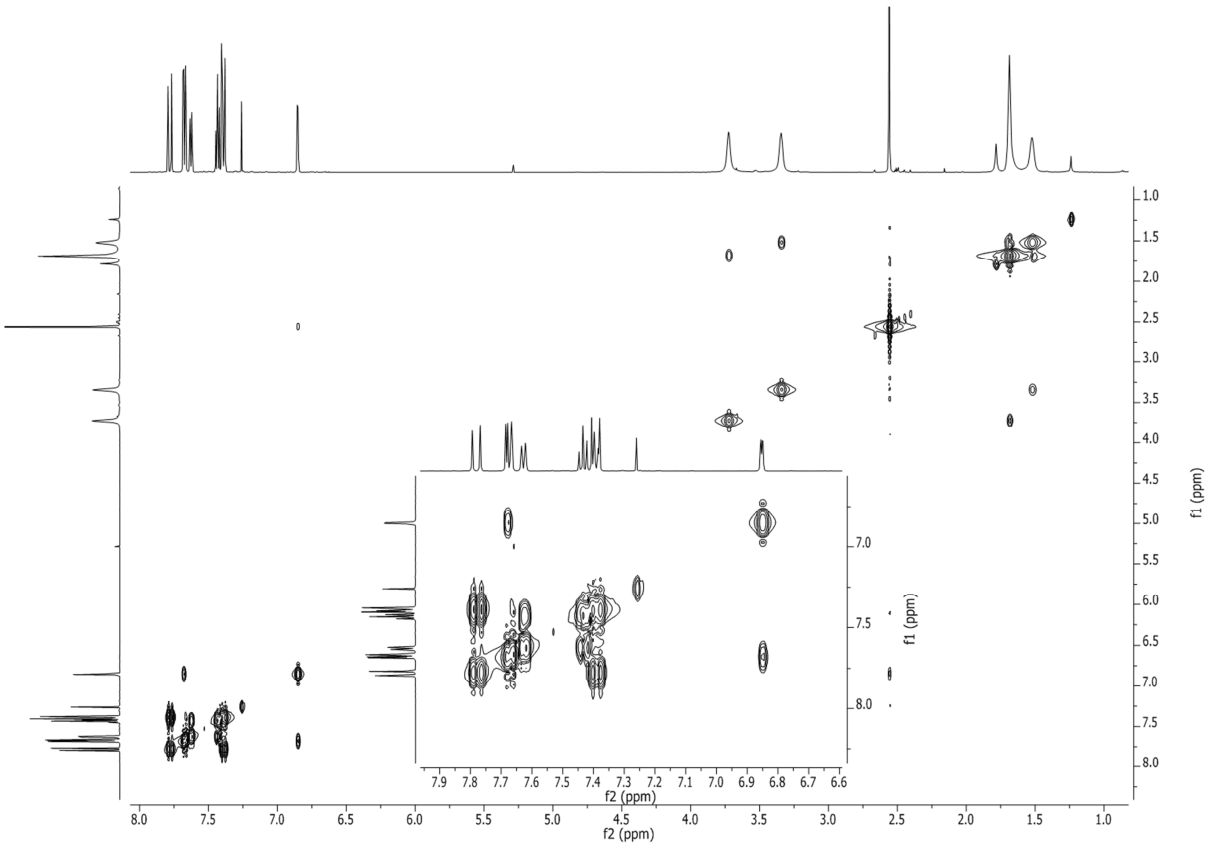
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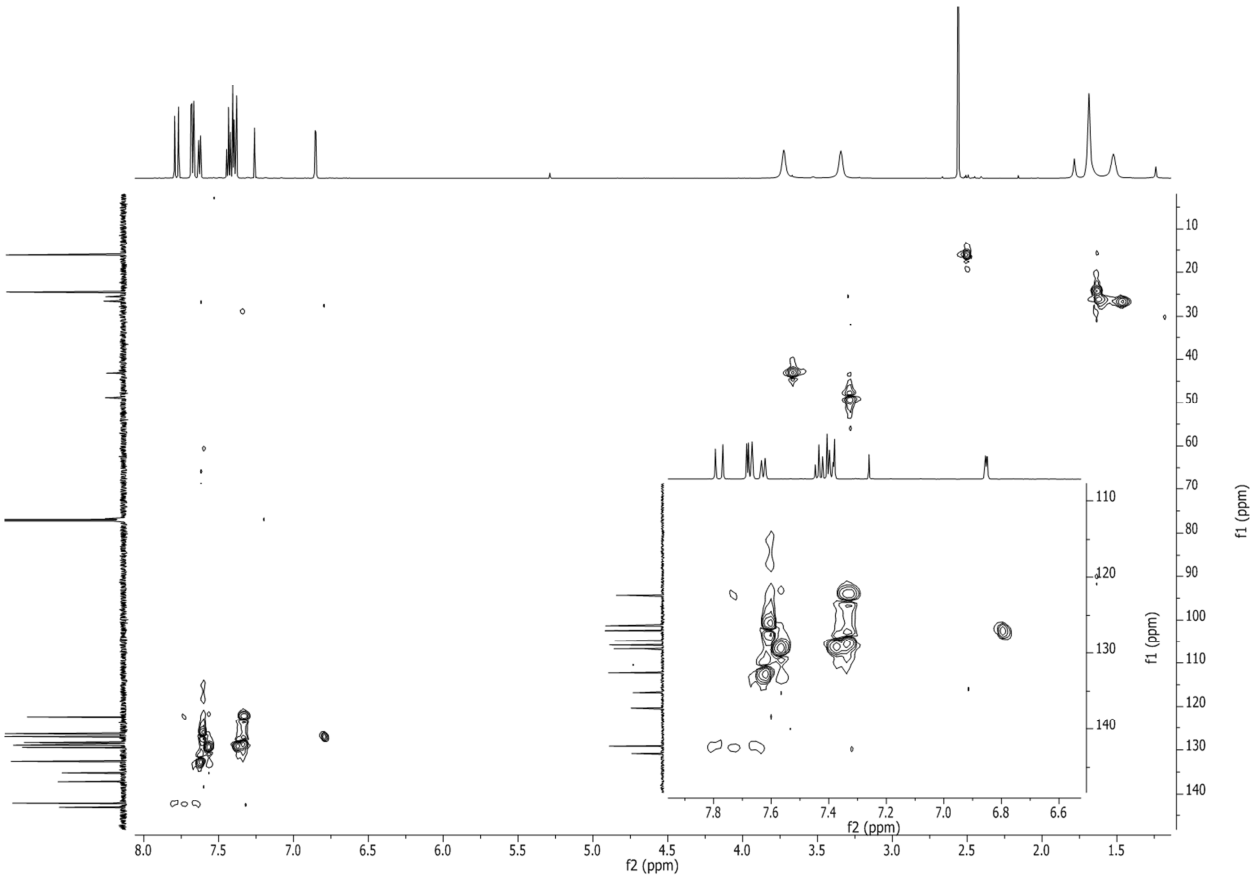
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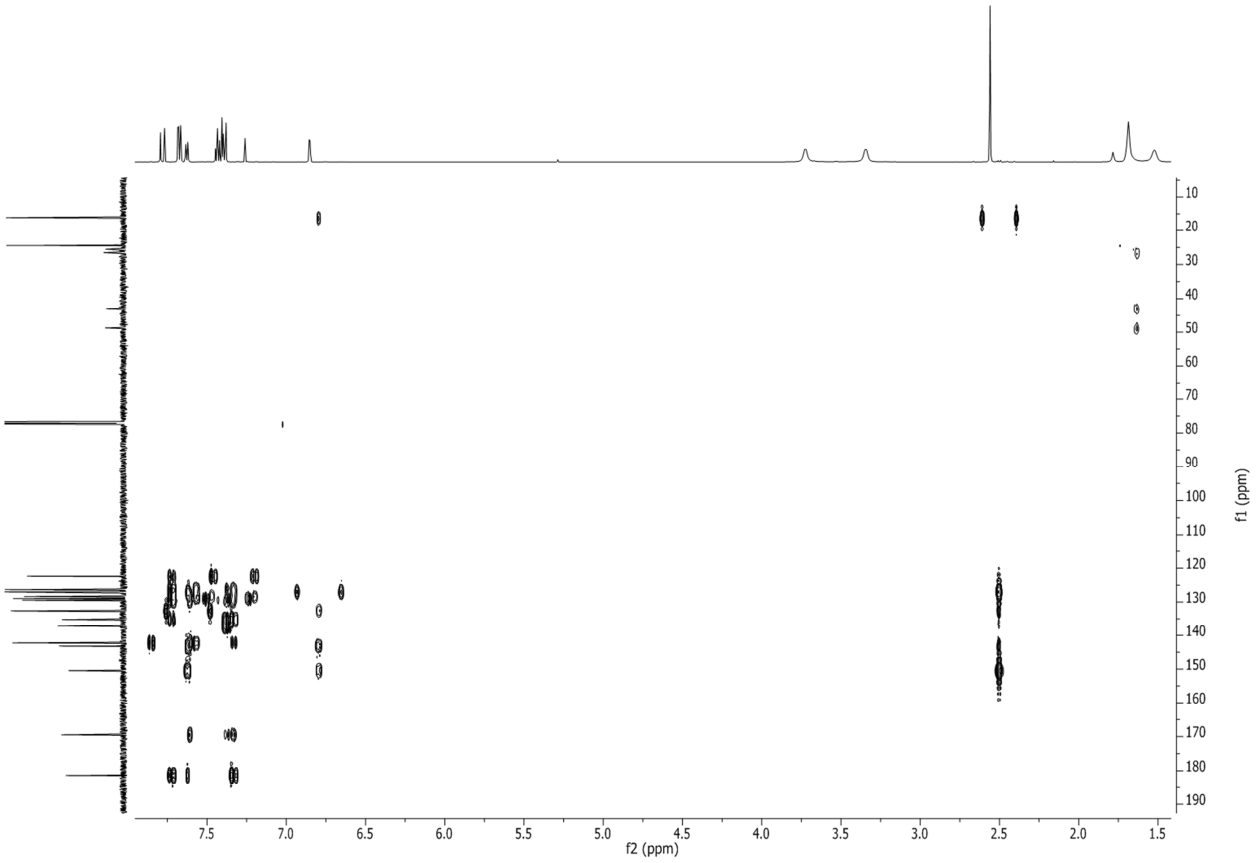
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HSQC

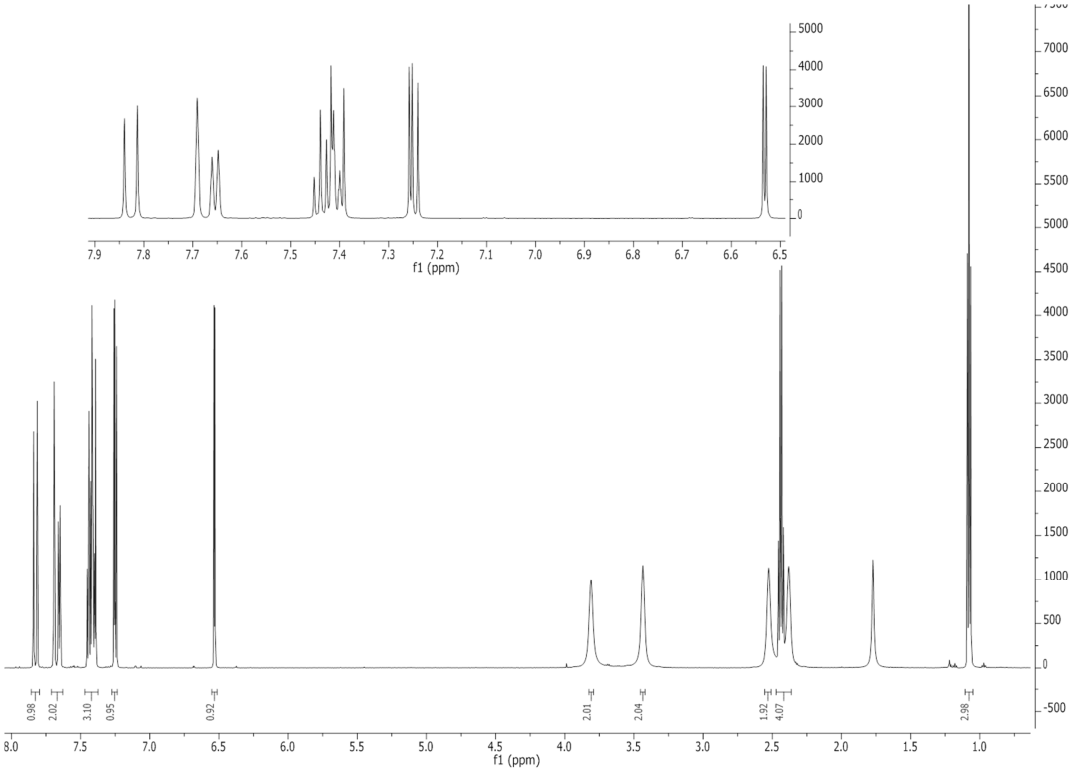


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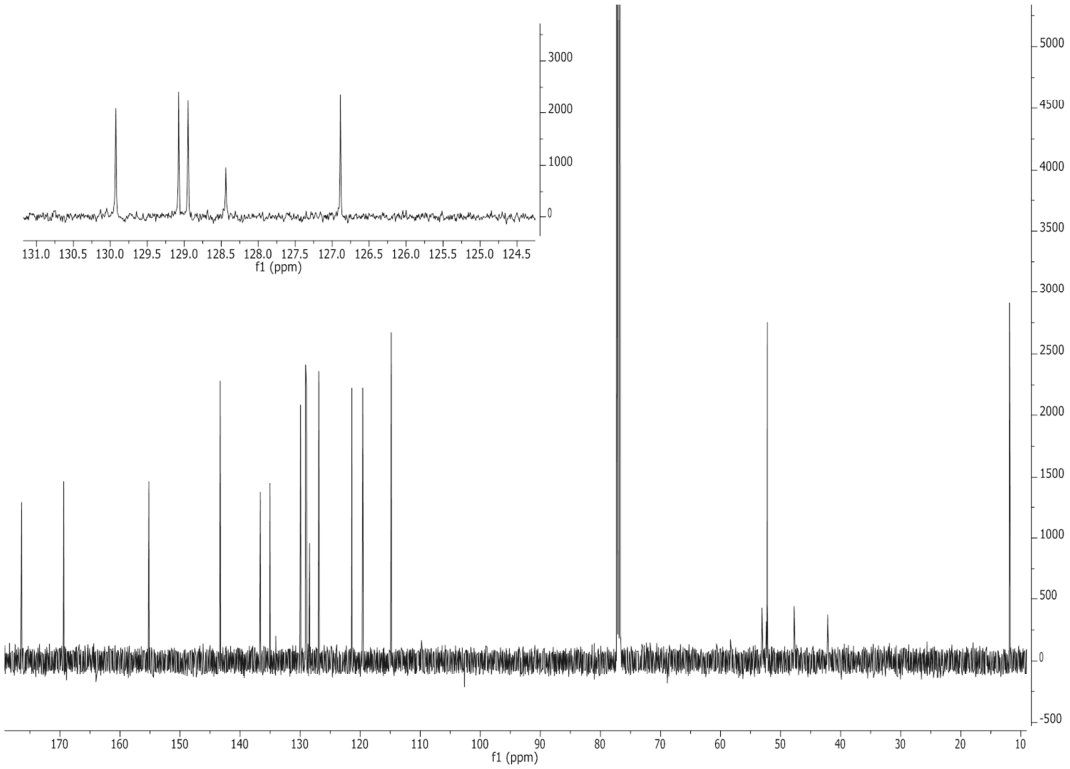


(2E)-1-(5-bromofuran-2-yl)-3-[3-(4-ethylpiperazine-1-carbonyl)phenyl]prop-2-en-1-one (38k)

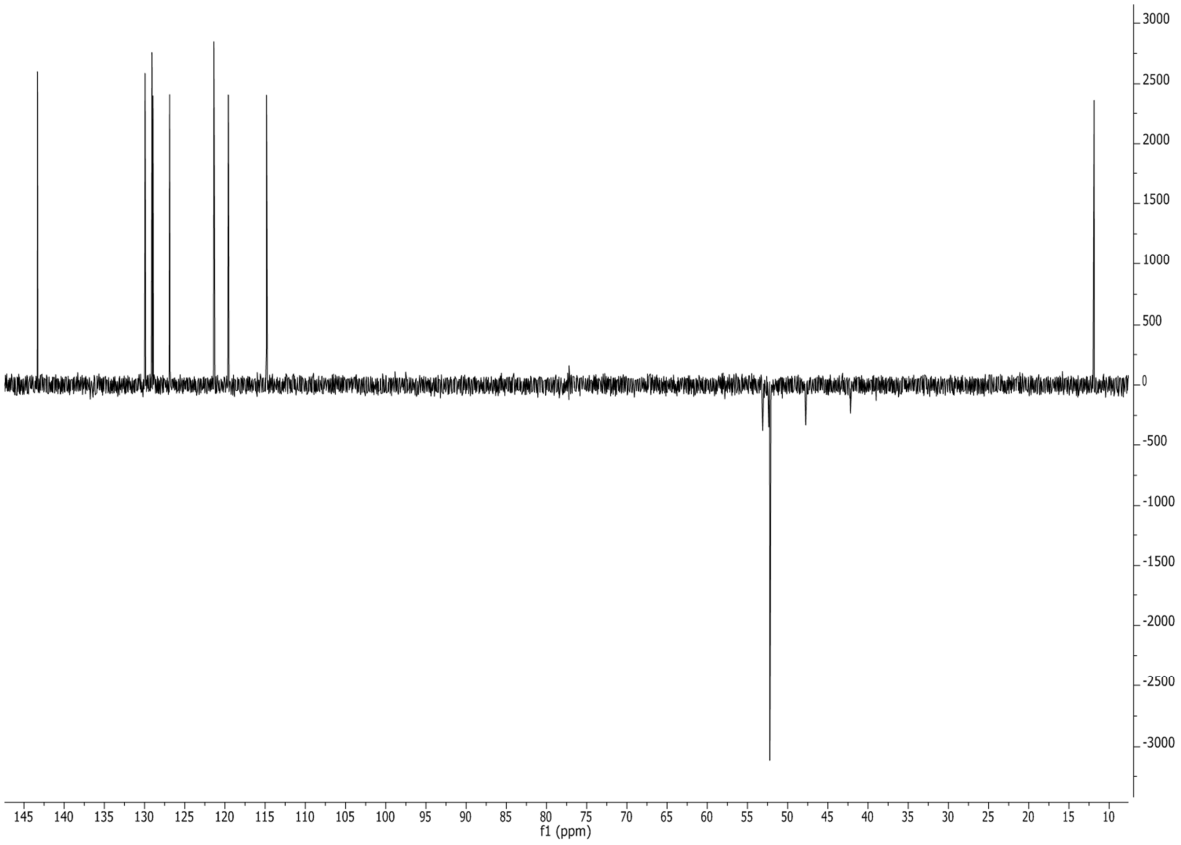
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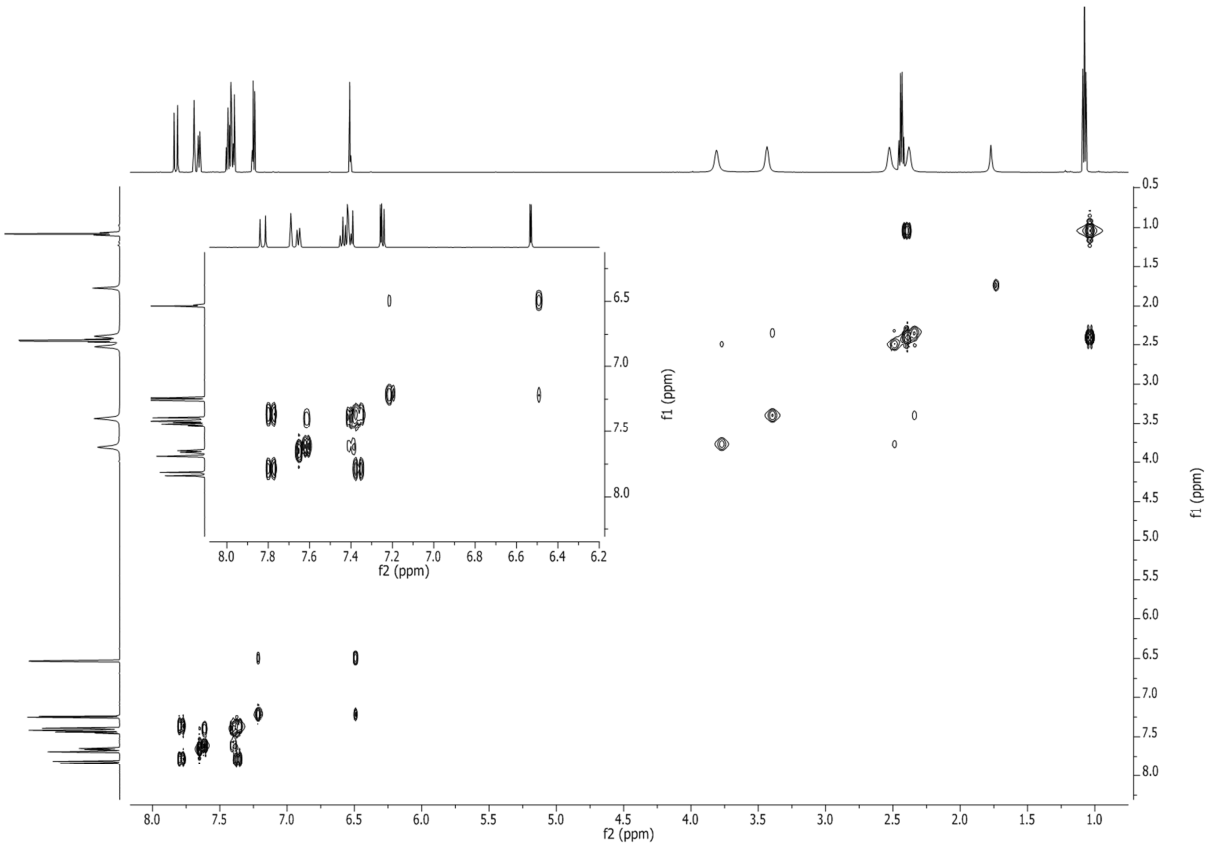
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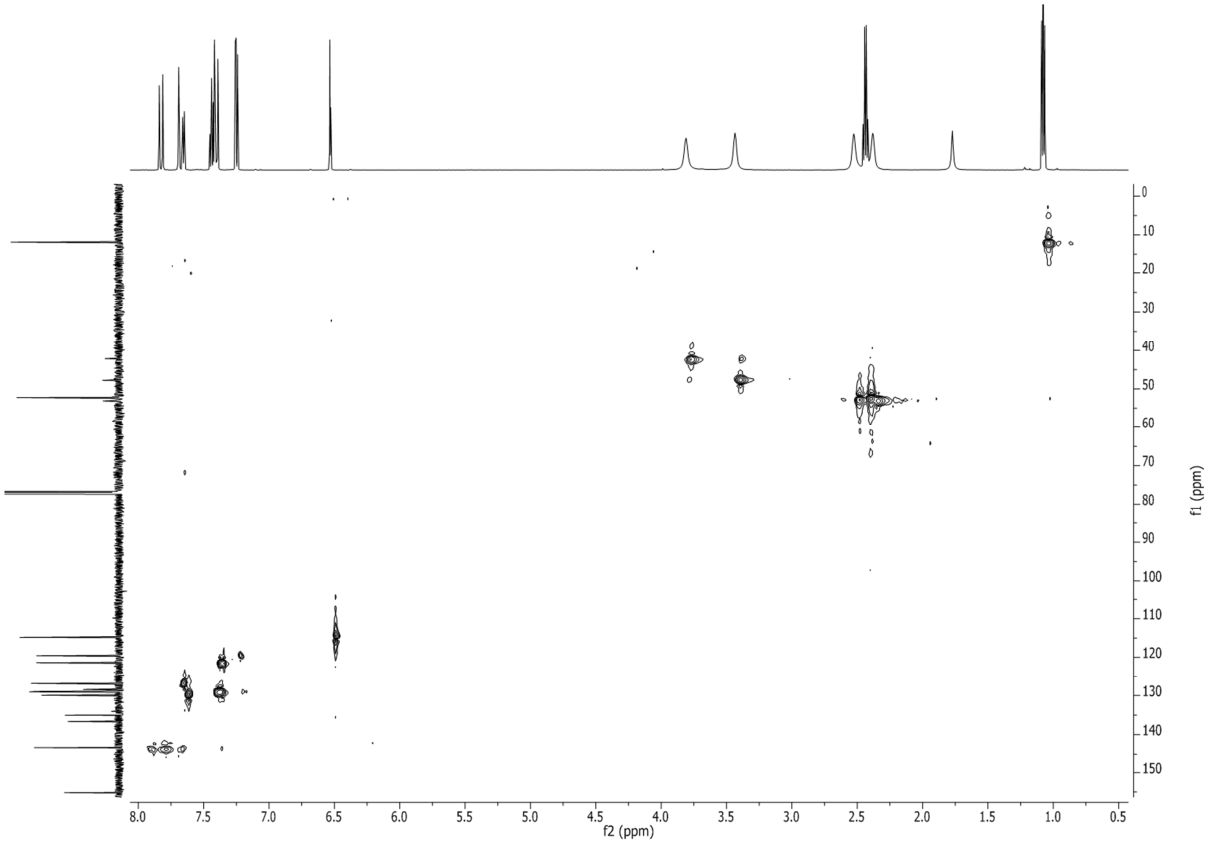
DEPT 135



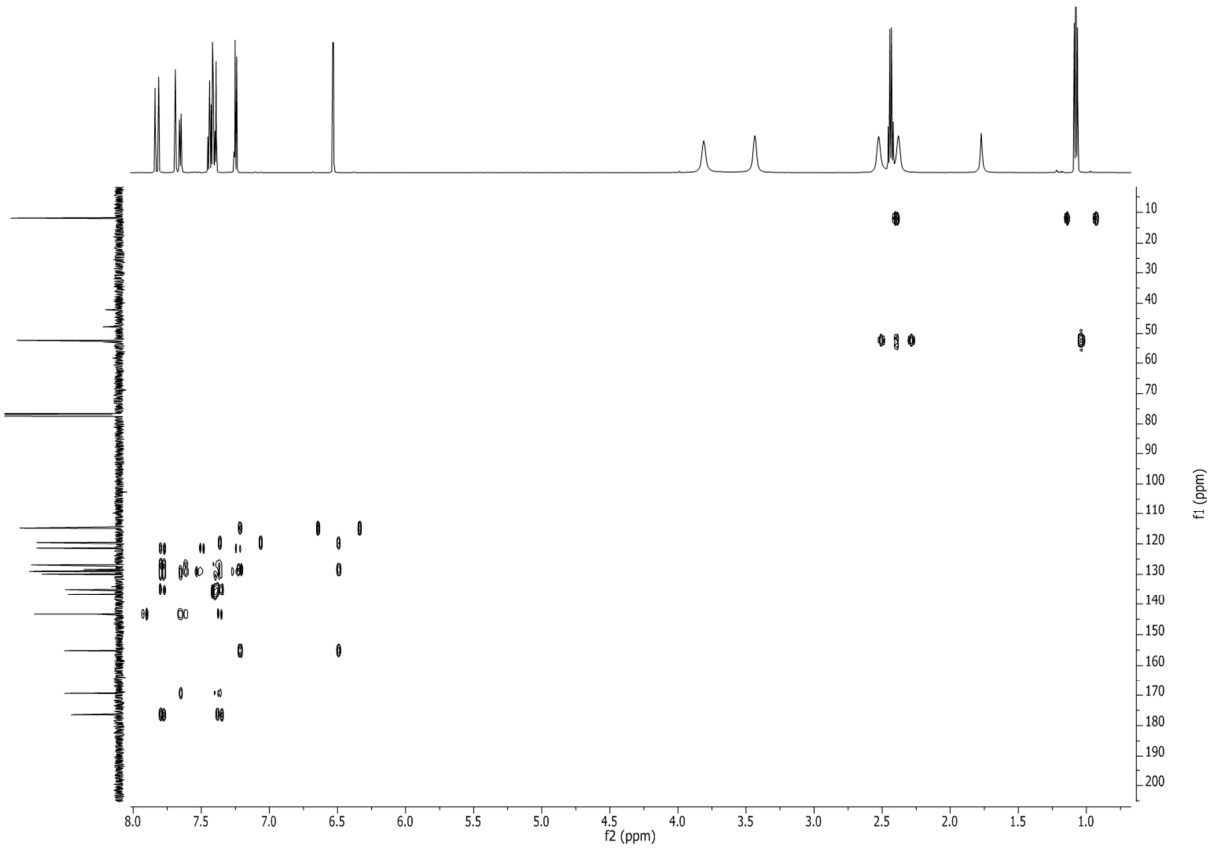
COSY



HSQC

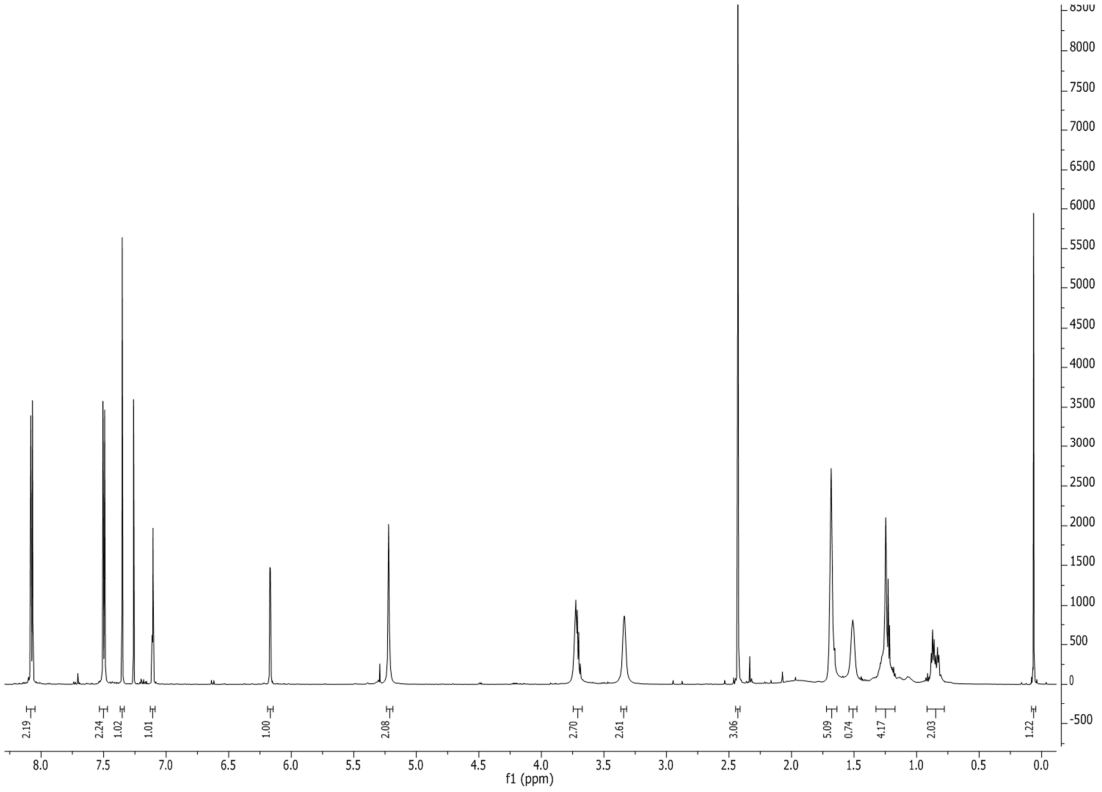


HMBC

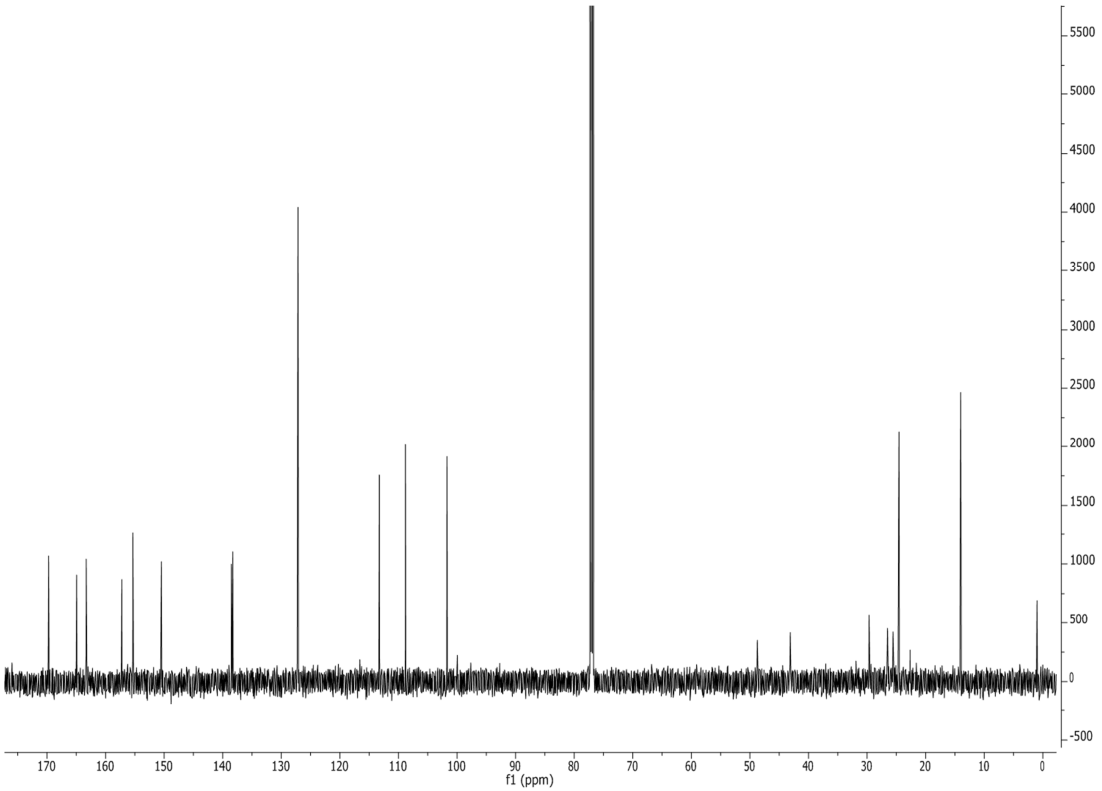


4-(5-methylfuran-2-yl)-6-[4-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39a)

^{1}H NMR

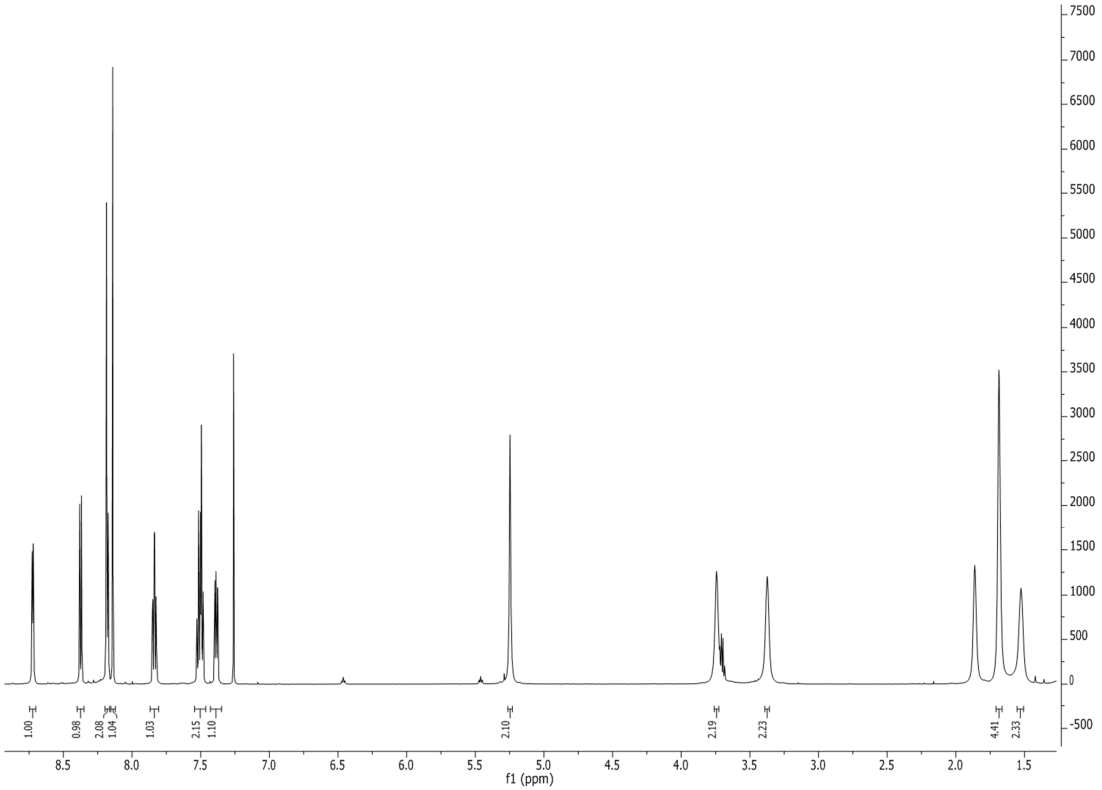


^{13}C NMR

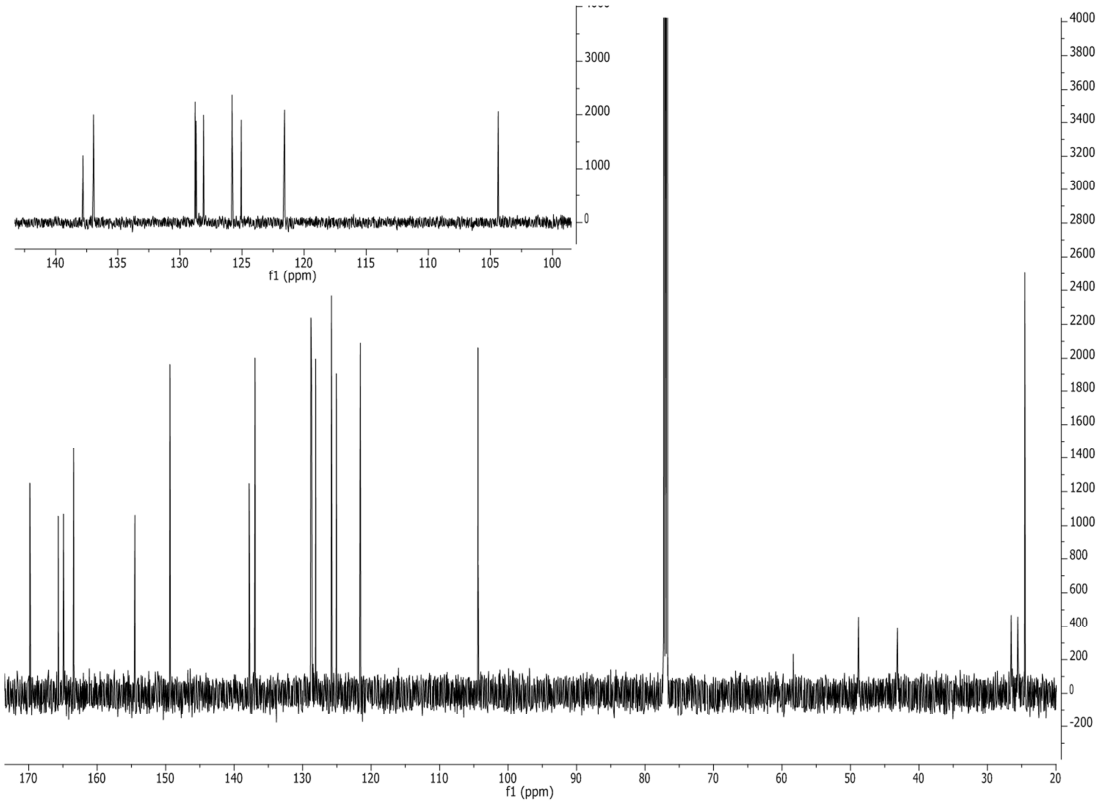


4-[3-(piperidine-1-carbonyl)phenyl]-6-(pyridin-2-yl)pyrimidin-2-amine (39b)

^{1}H NMR

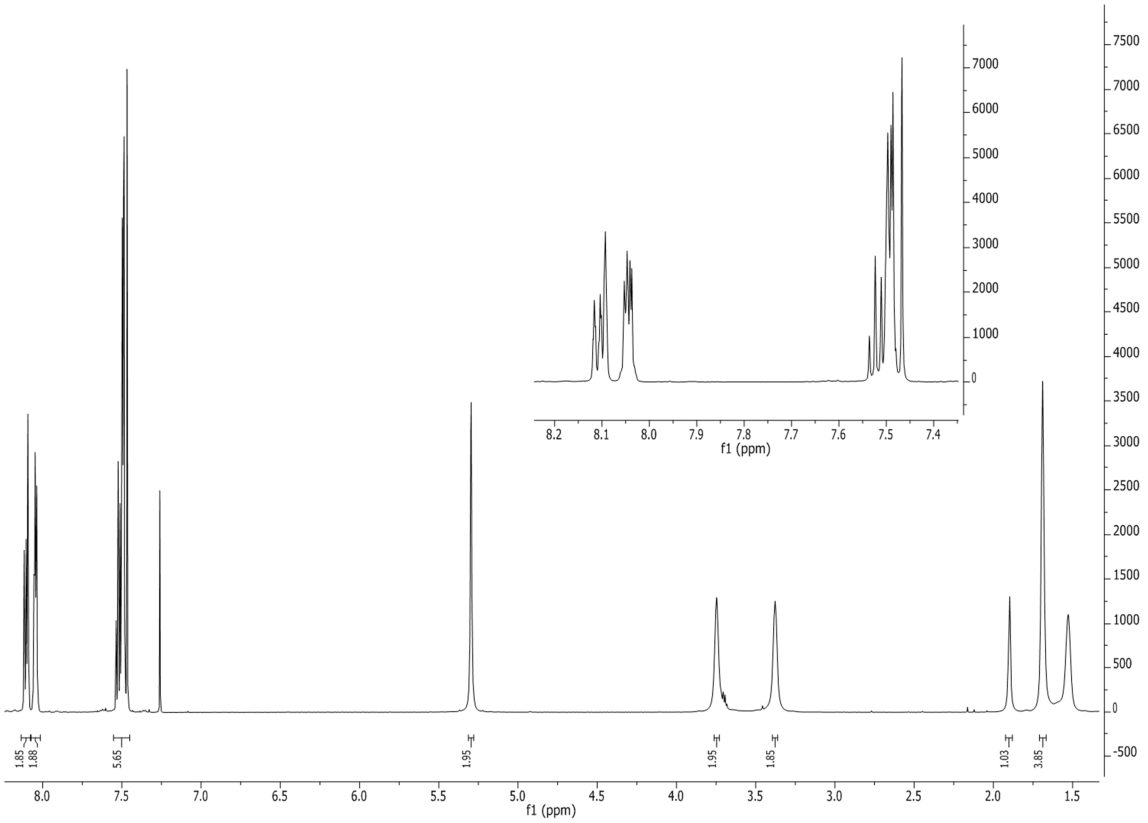


^{13}C NMR

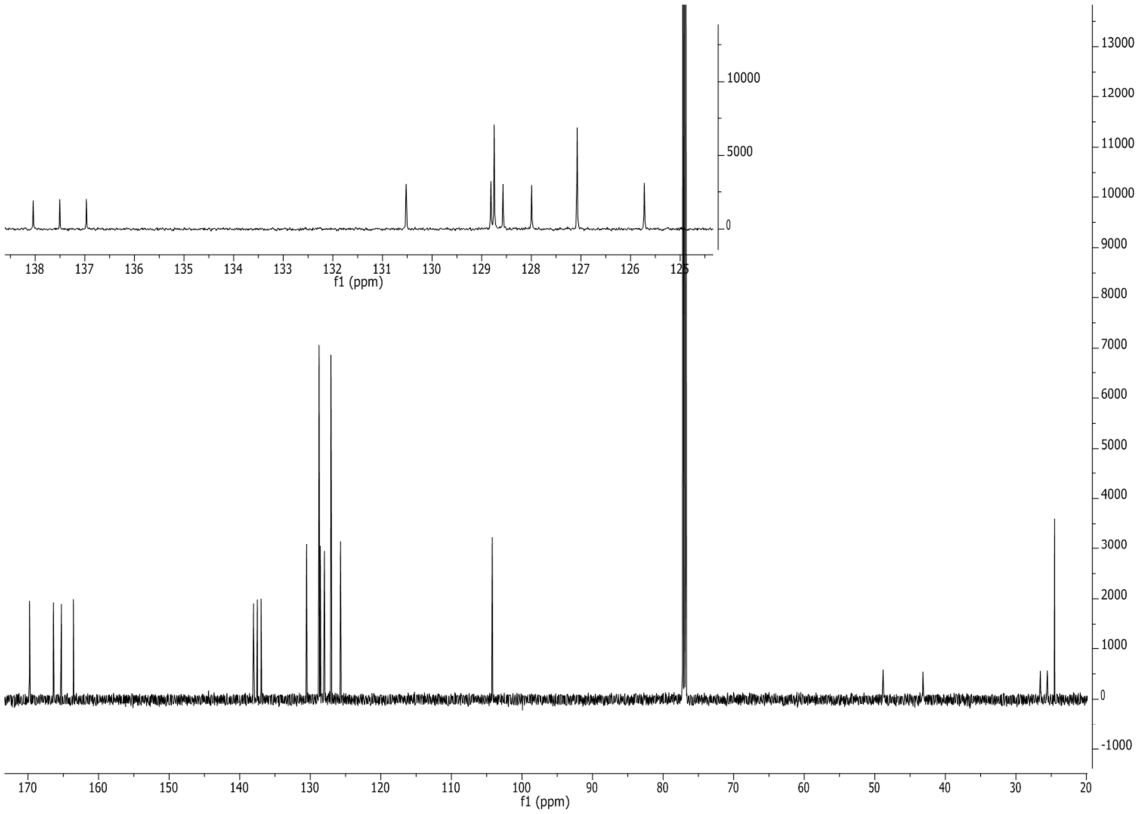


4-phenyl-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39c)

^{1}H NMR

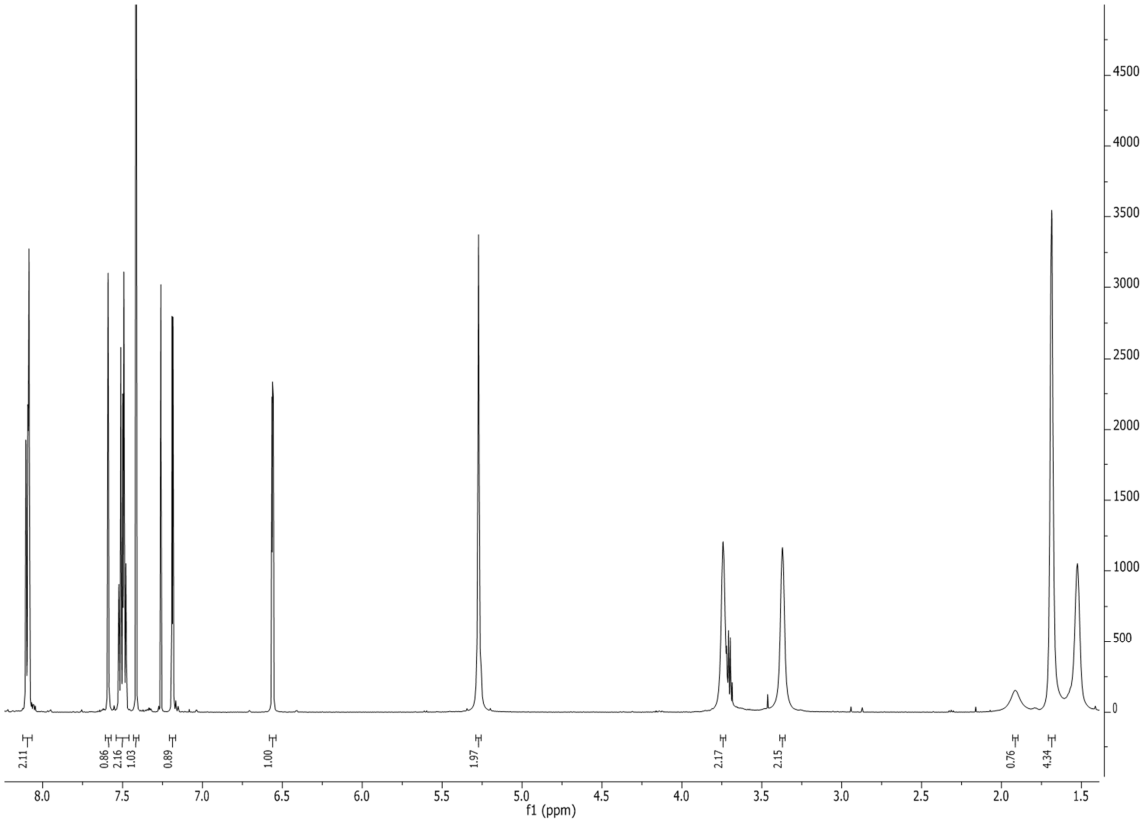


^{13}C NMR

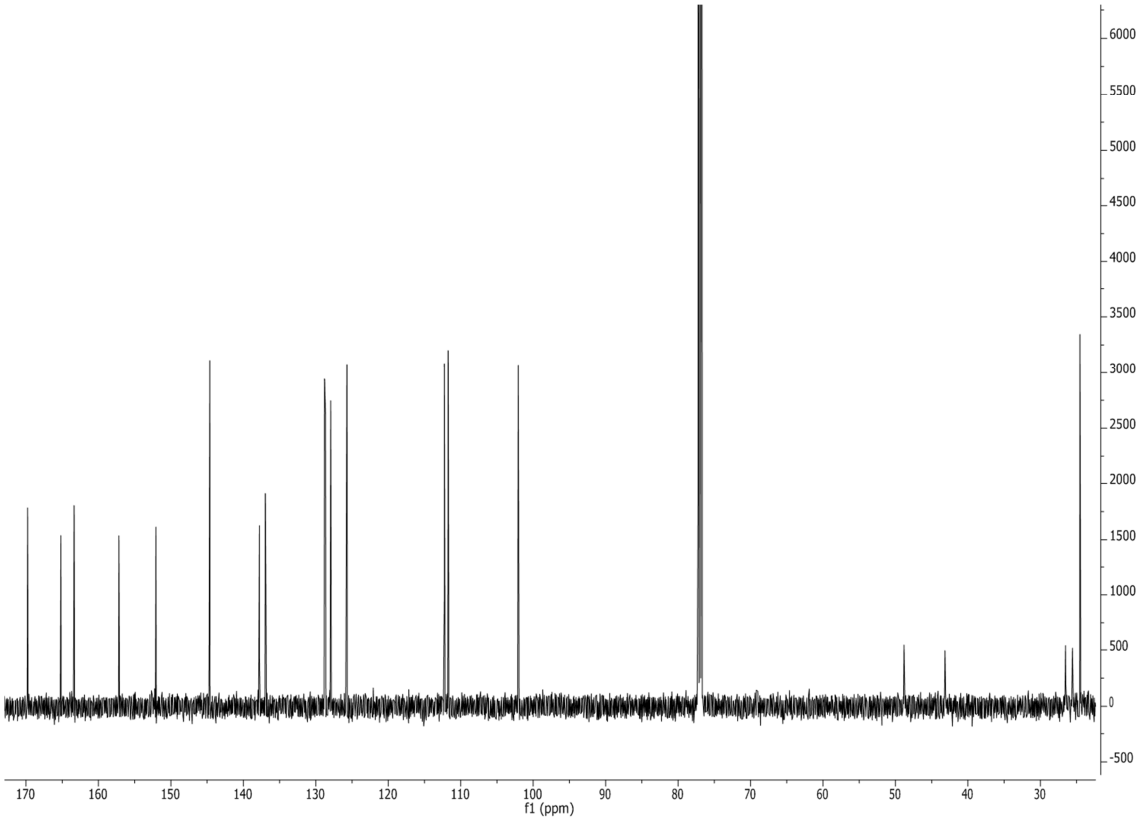


4-(furan-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39d)

^{1}HNMR

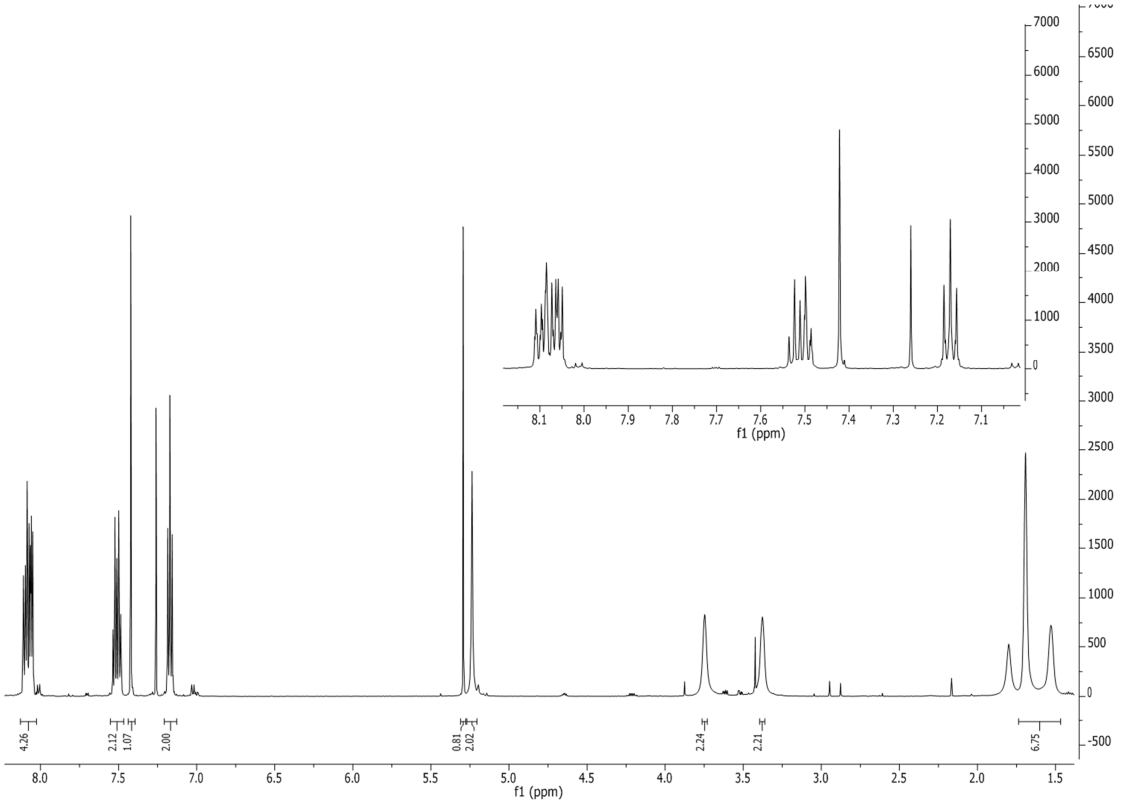


^{13}C NMR

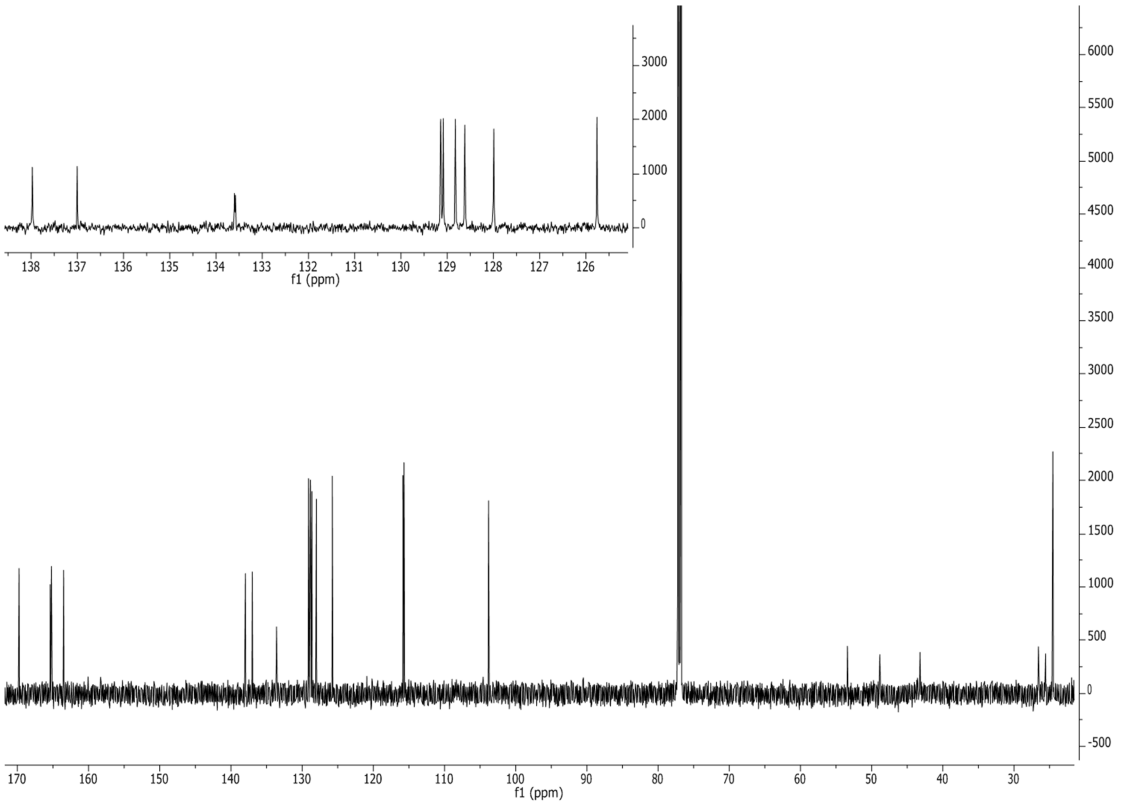


4-(4-fluorophenyl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39e)

^{1}H NMR

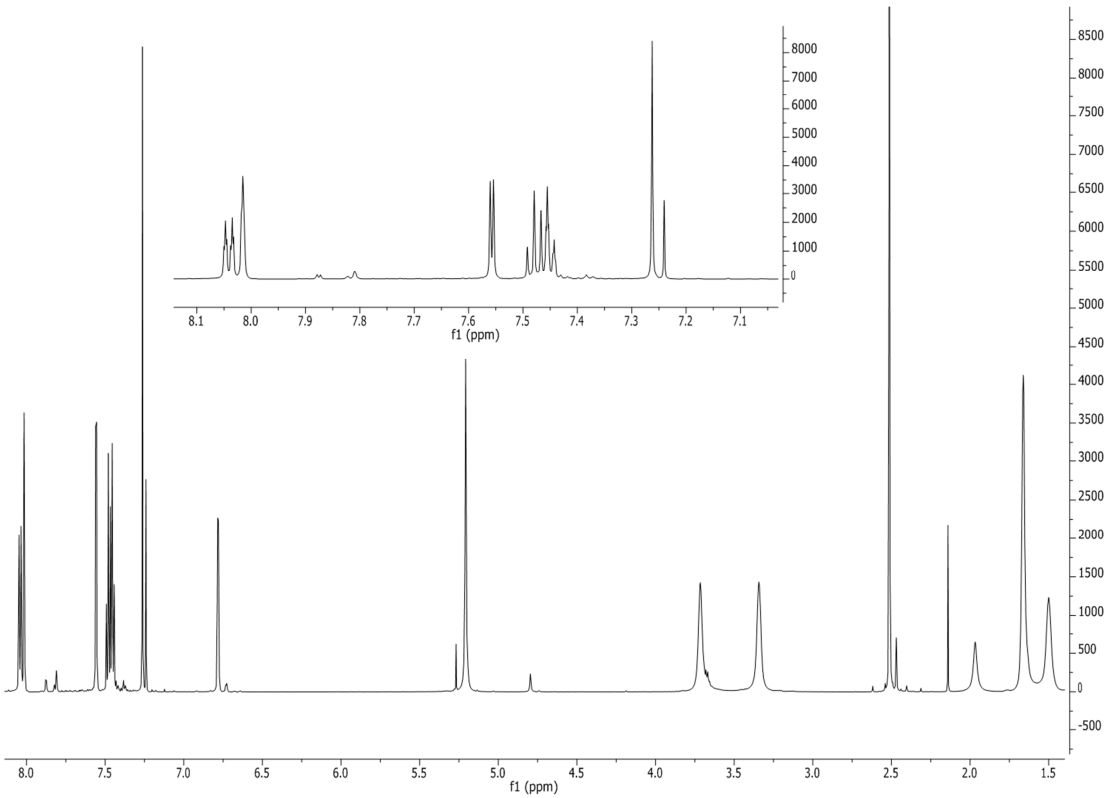


^{13}C NMR

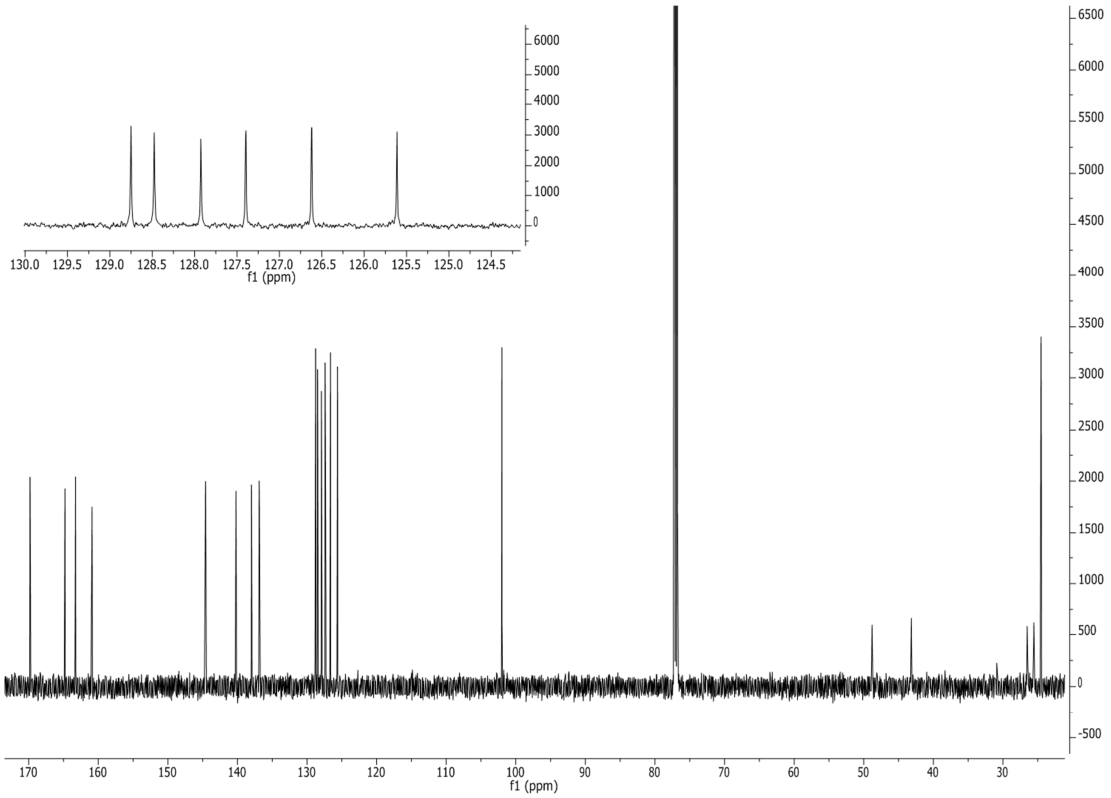


4-(5-methylthiophen-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39f)

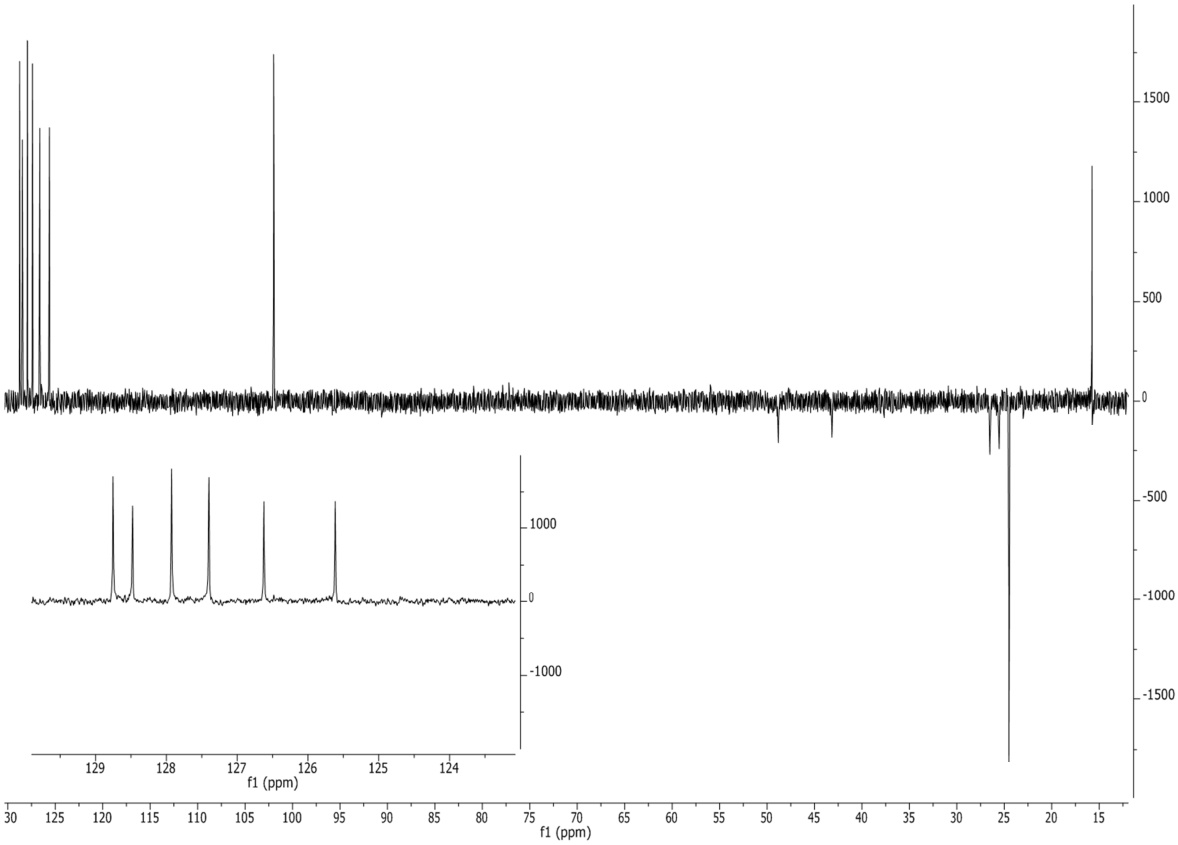
^{1}H NMR



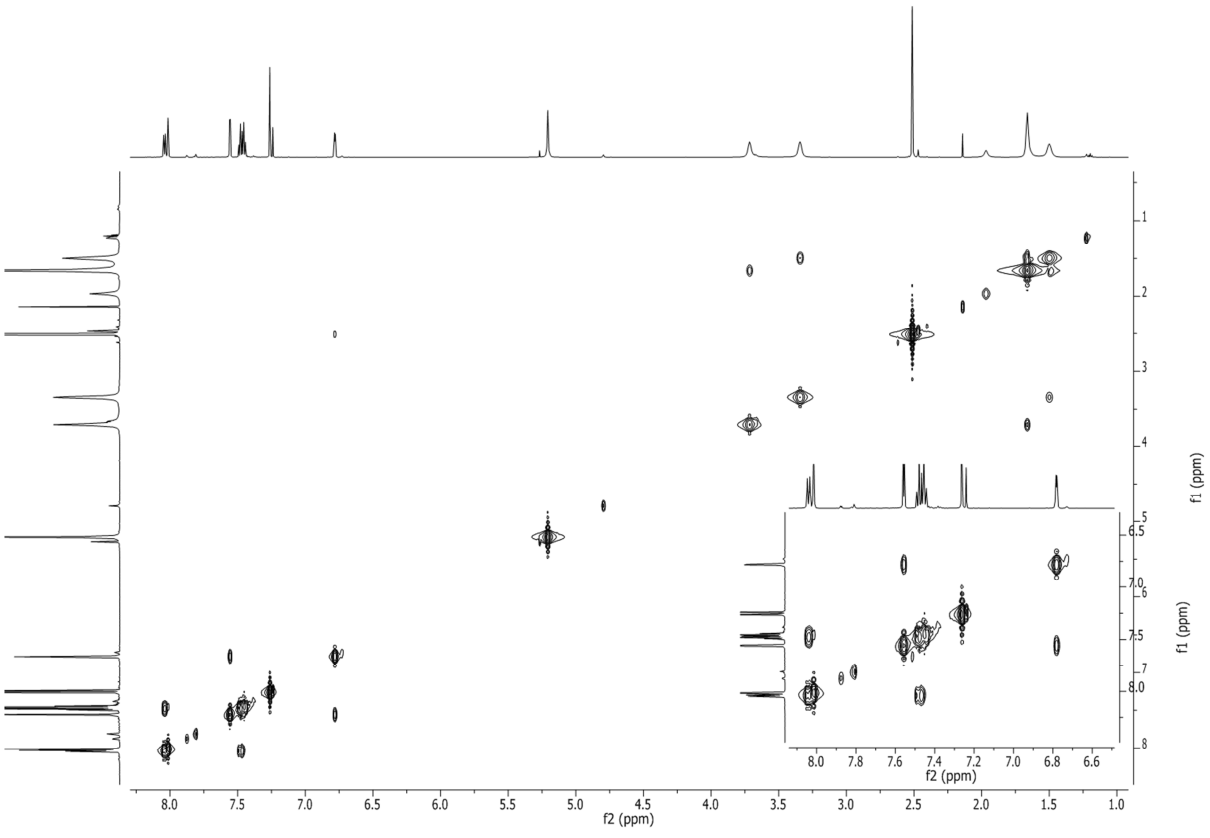
^{13}C NMR



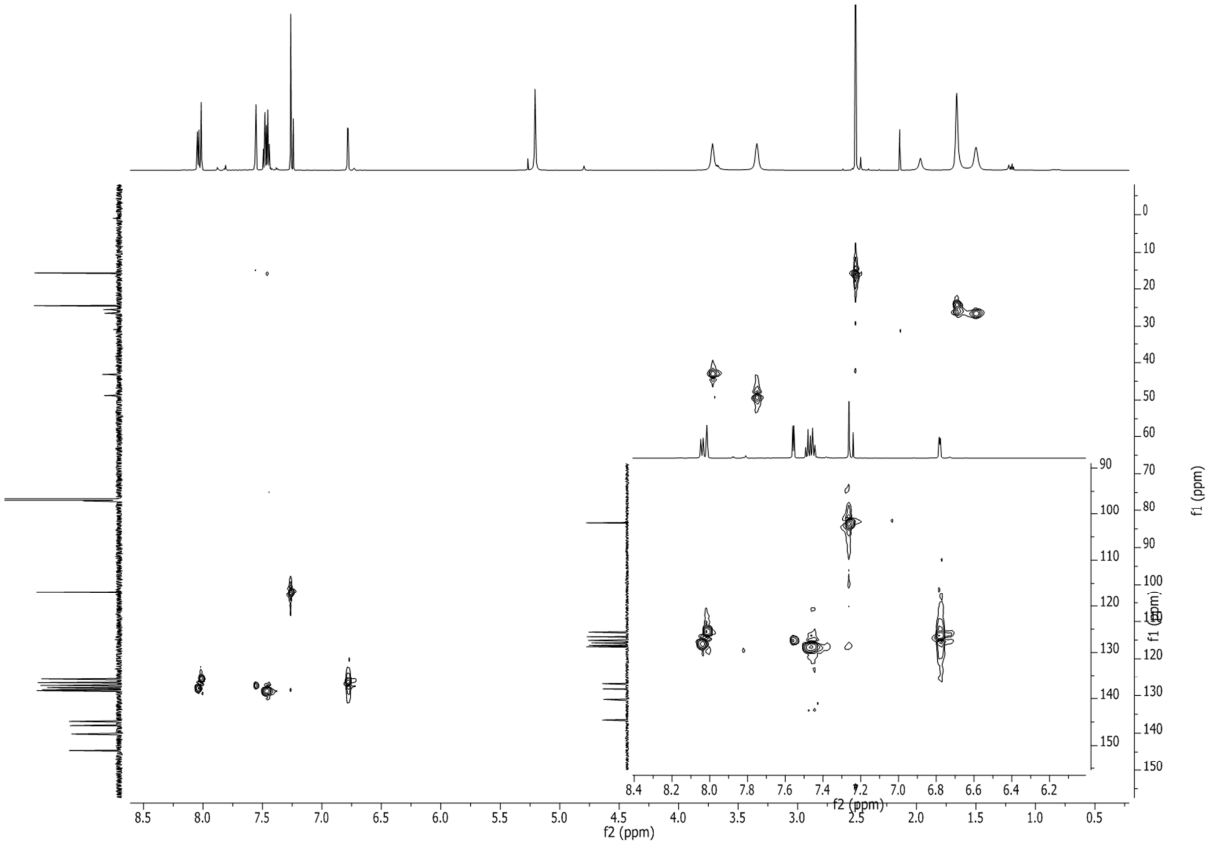
DEPT 135



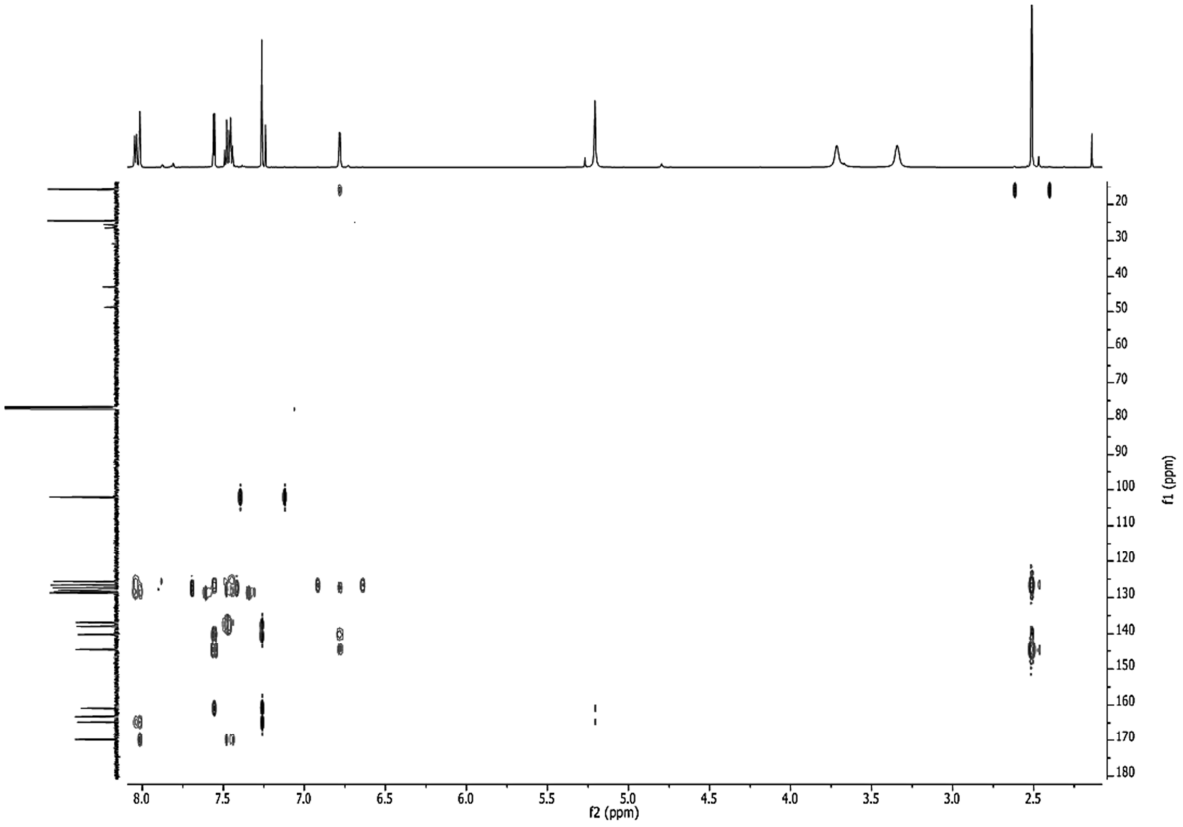
COSY



HSQC

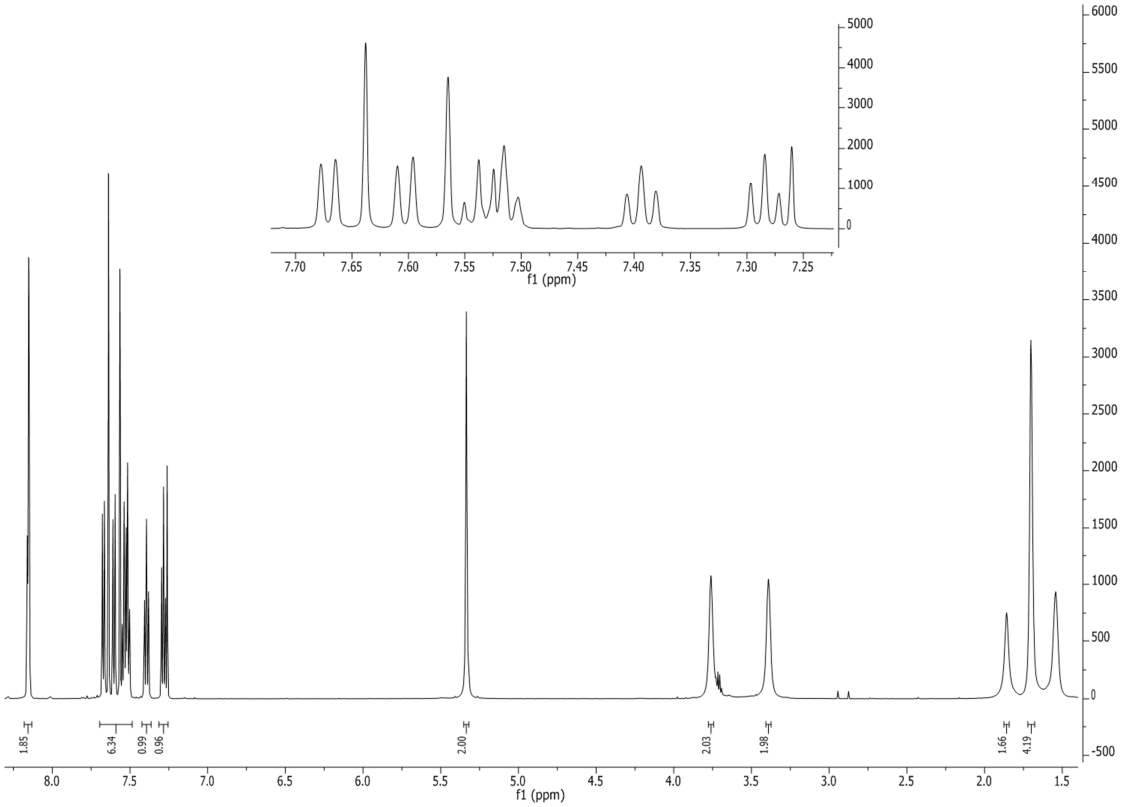


HMBC

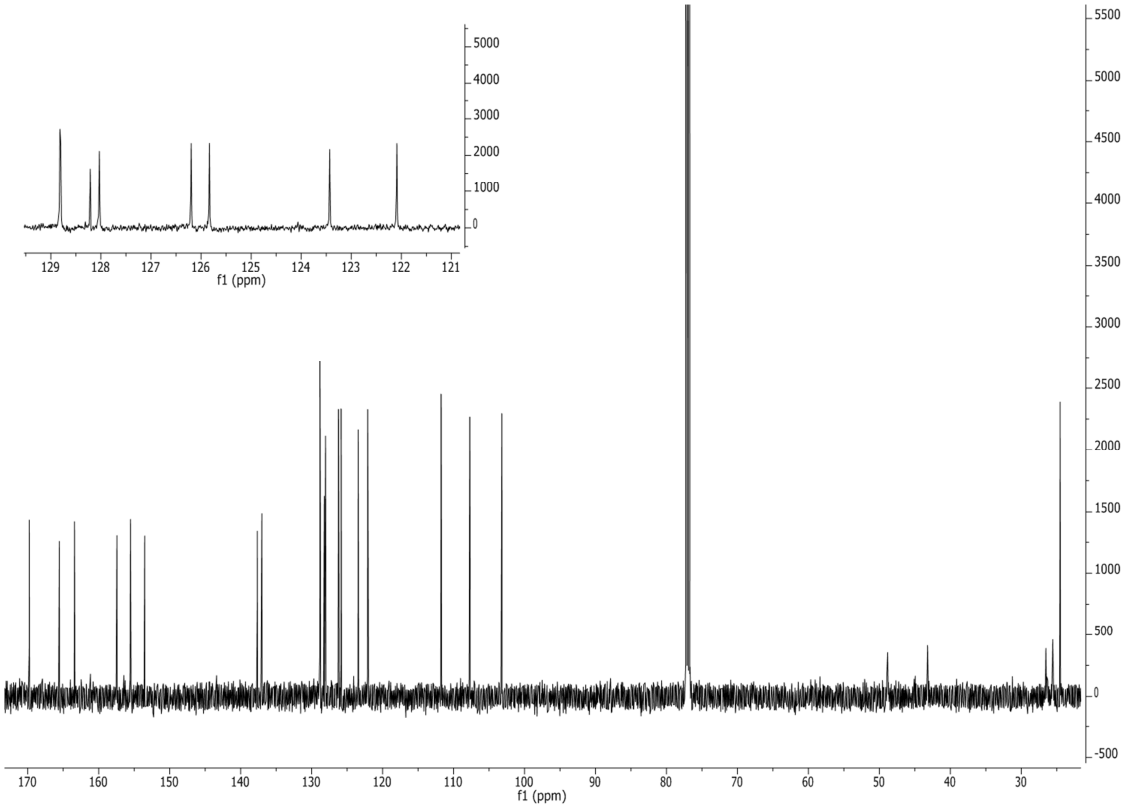


4-(1-benzofuran-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39g)

^{1}H NMR

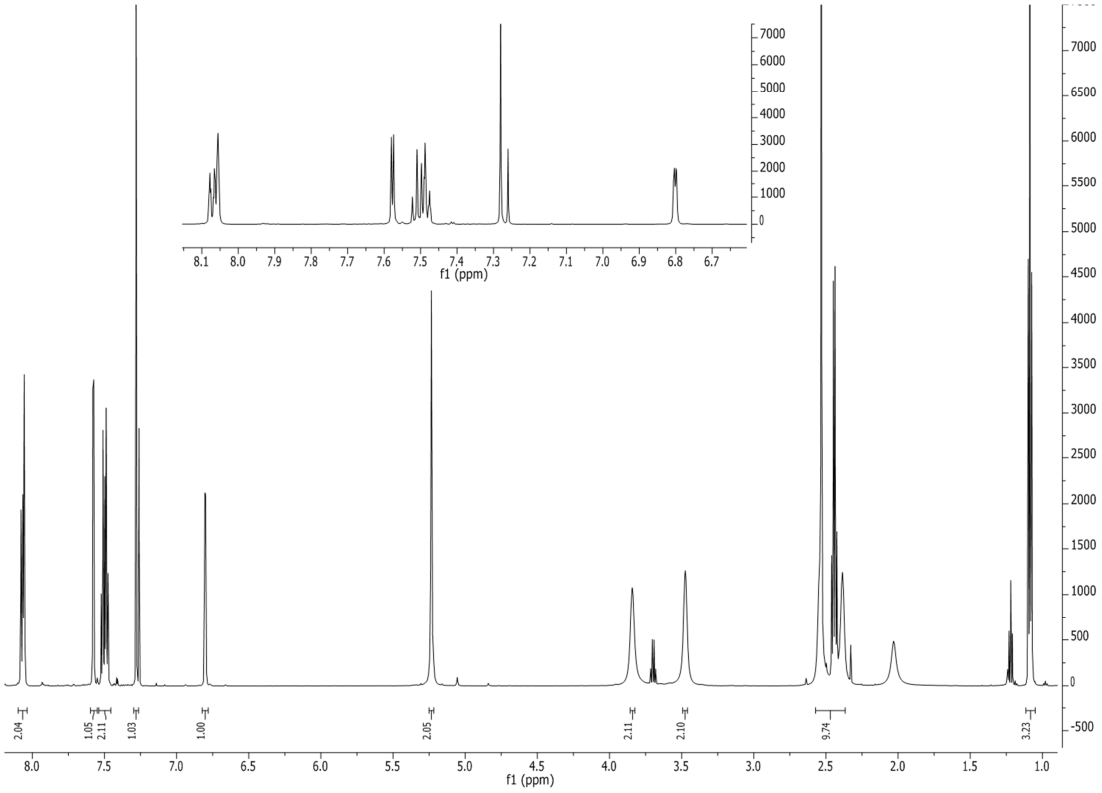


^{13}C NMR

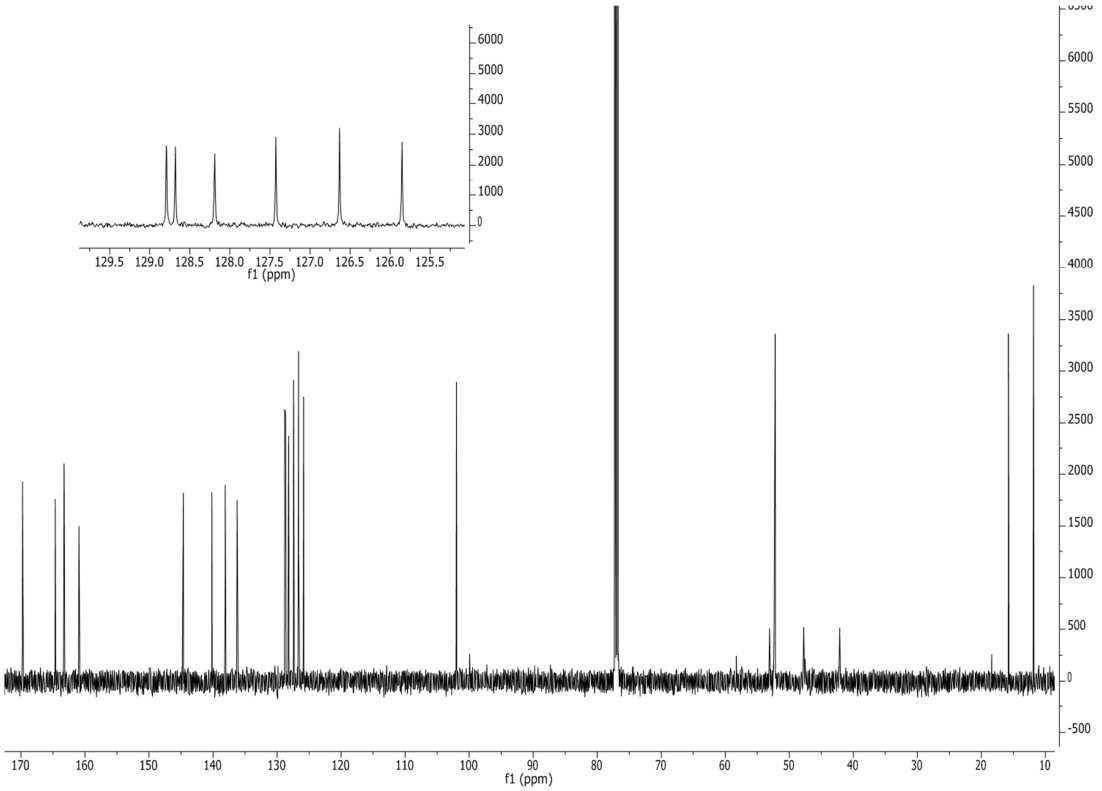


4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(5-methylthiophen-2-yl)pyrimidin-2-amine (39h)

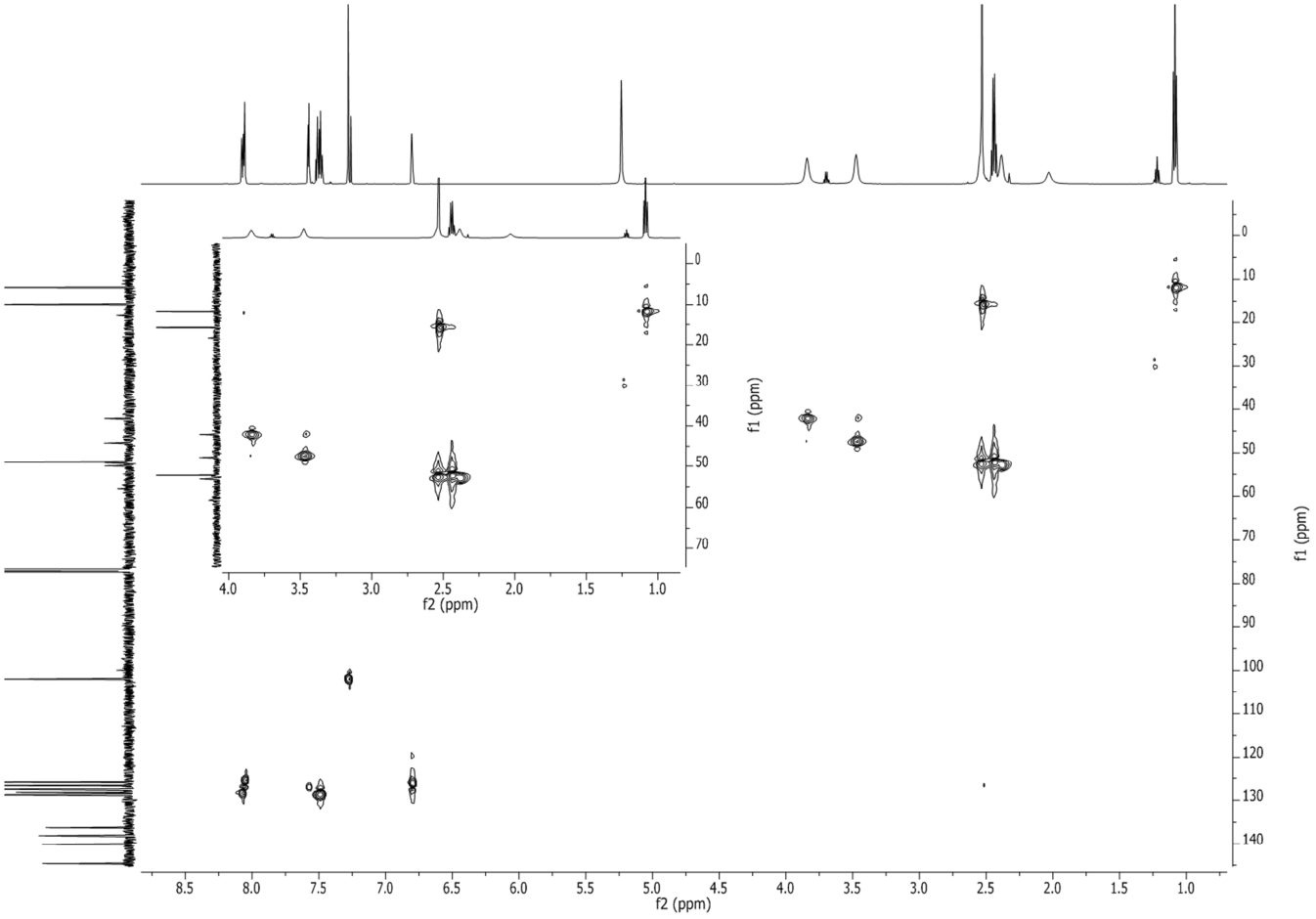
^{1}H NMR



^{13}C NMR

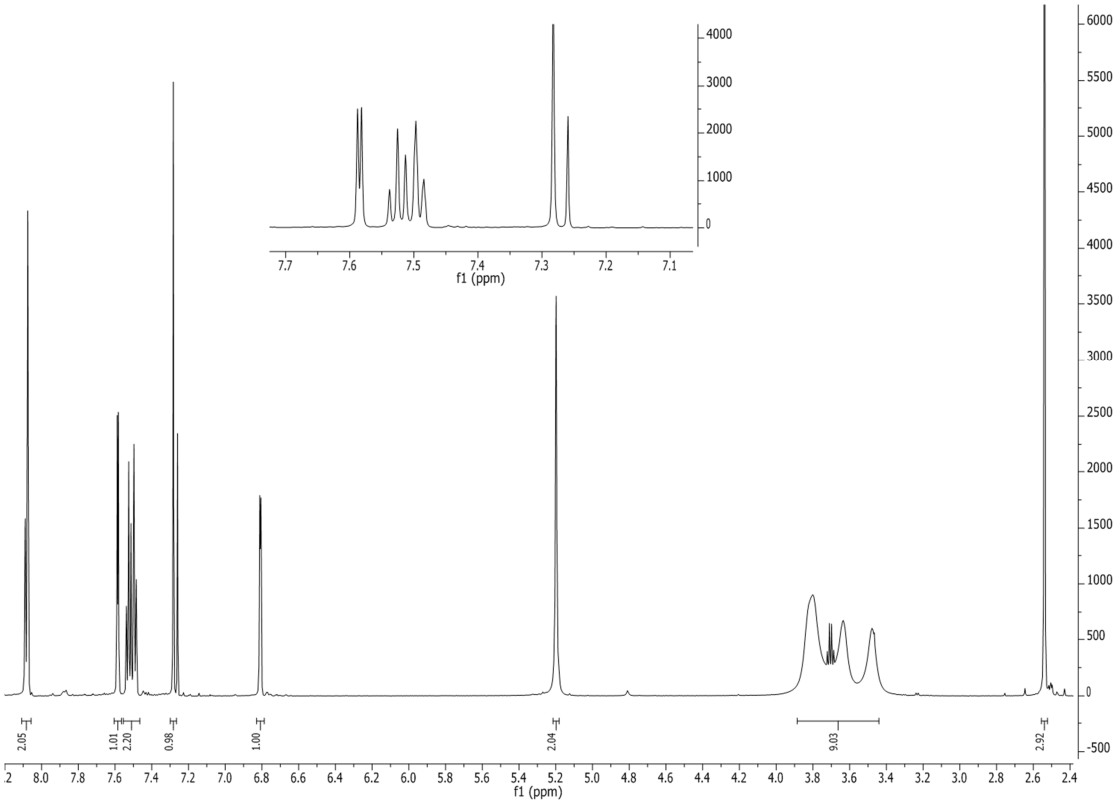


HSQC

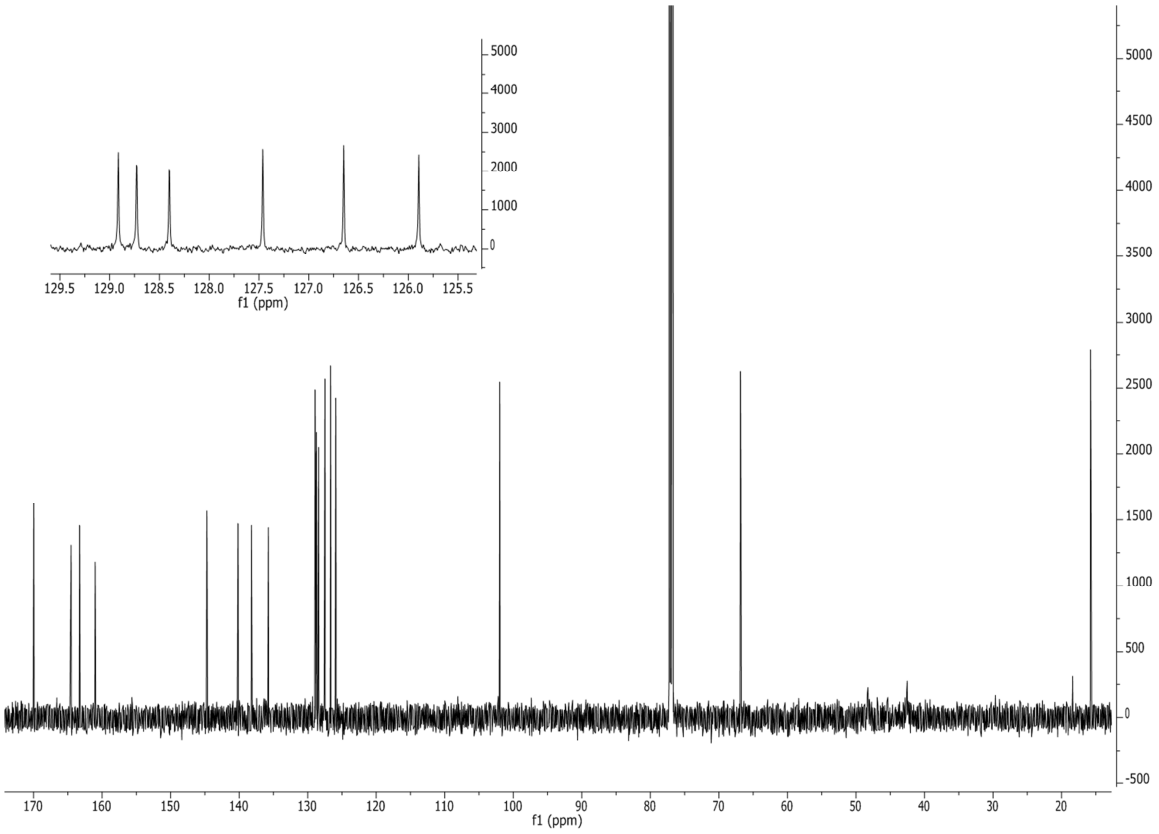


4-(5-methylthiophen-2-yl)-6-[3-(morpholine-4-carbonyl)phenyl]pyrimidin-2-amine (39i)

^{1}H NMR

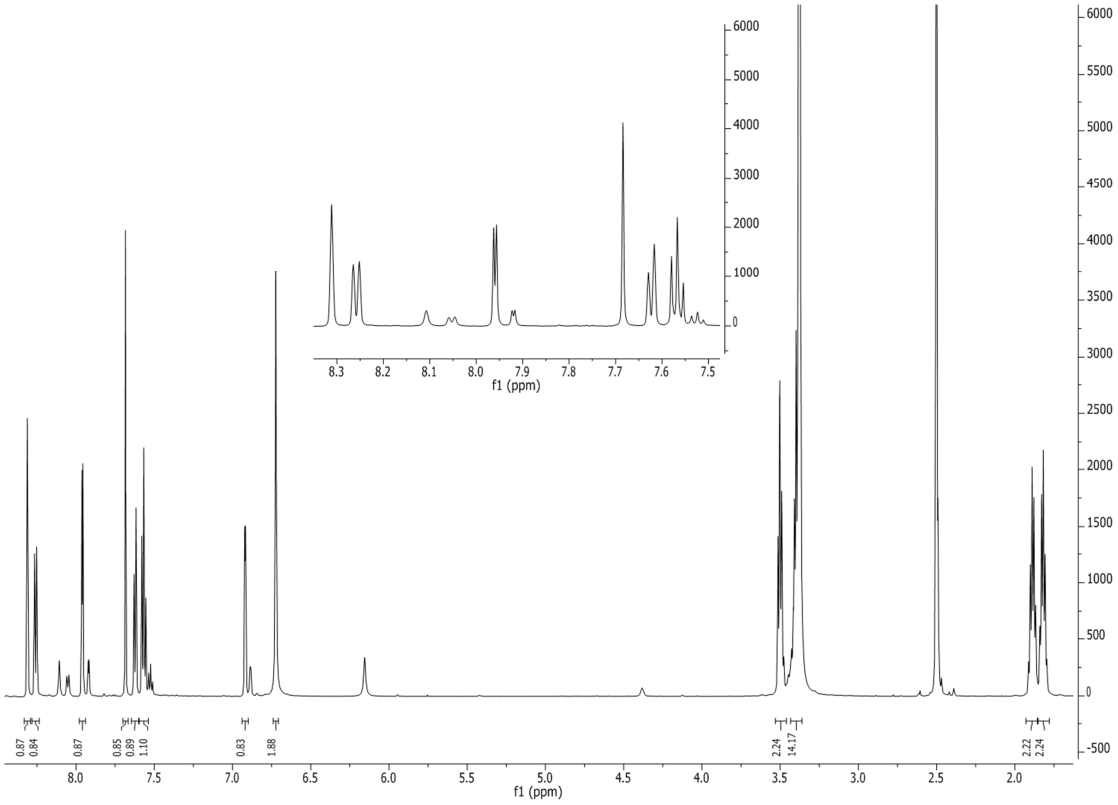


^{13}C NMR

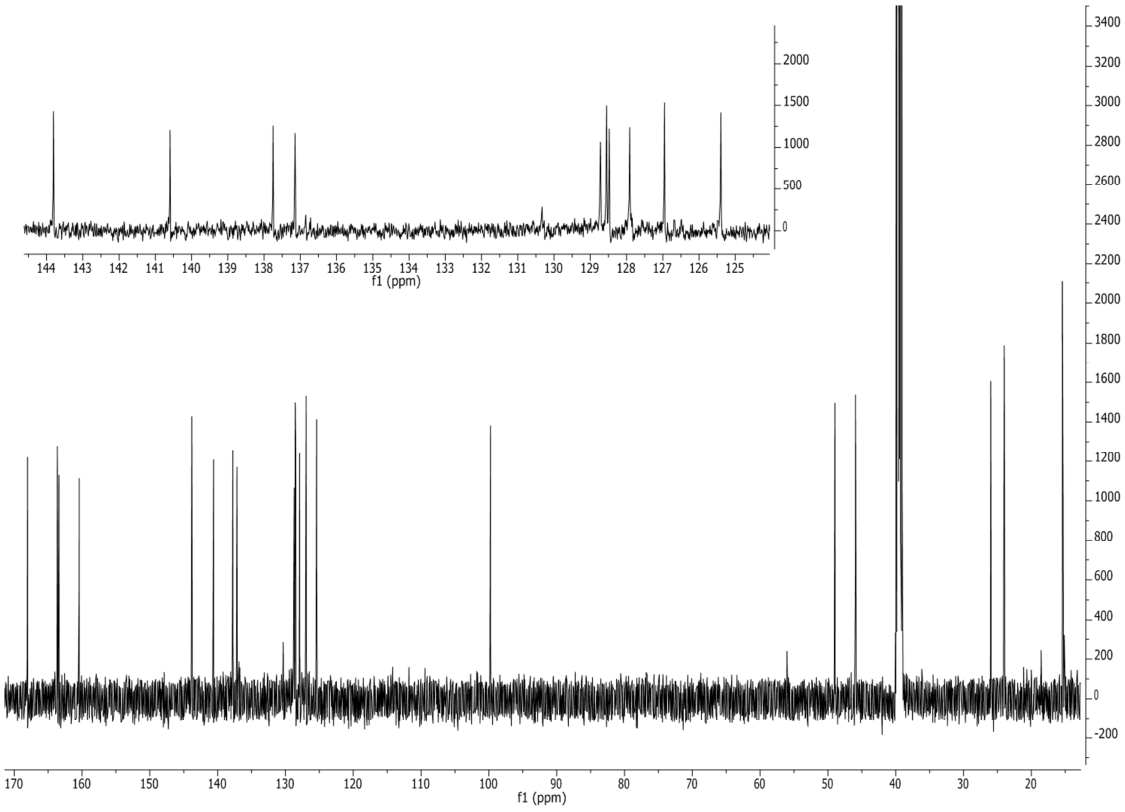


4-(5-methylthiophen-2-yl)-6-[3-(pyrrolidine-1-carbonyl)phenyl]pyrimidin-2-amine (39j)

^{1}H NMR

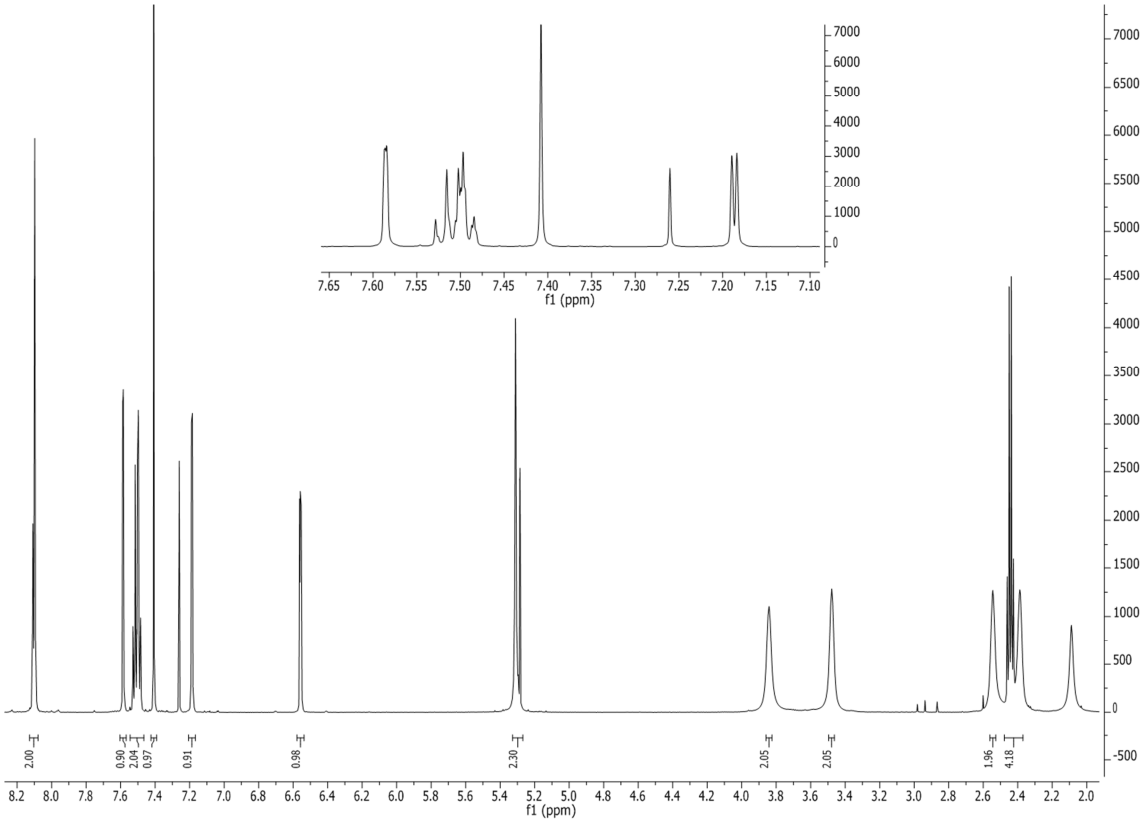


^{13}C NMR

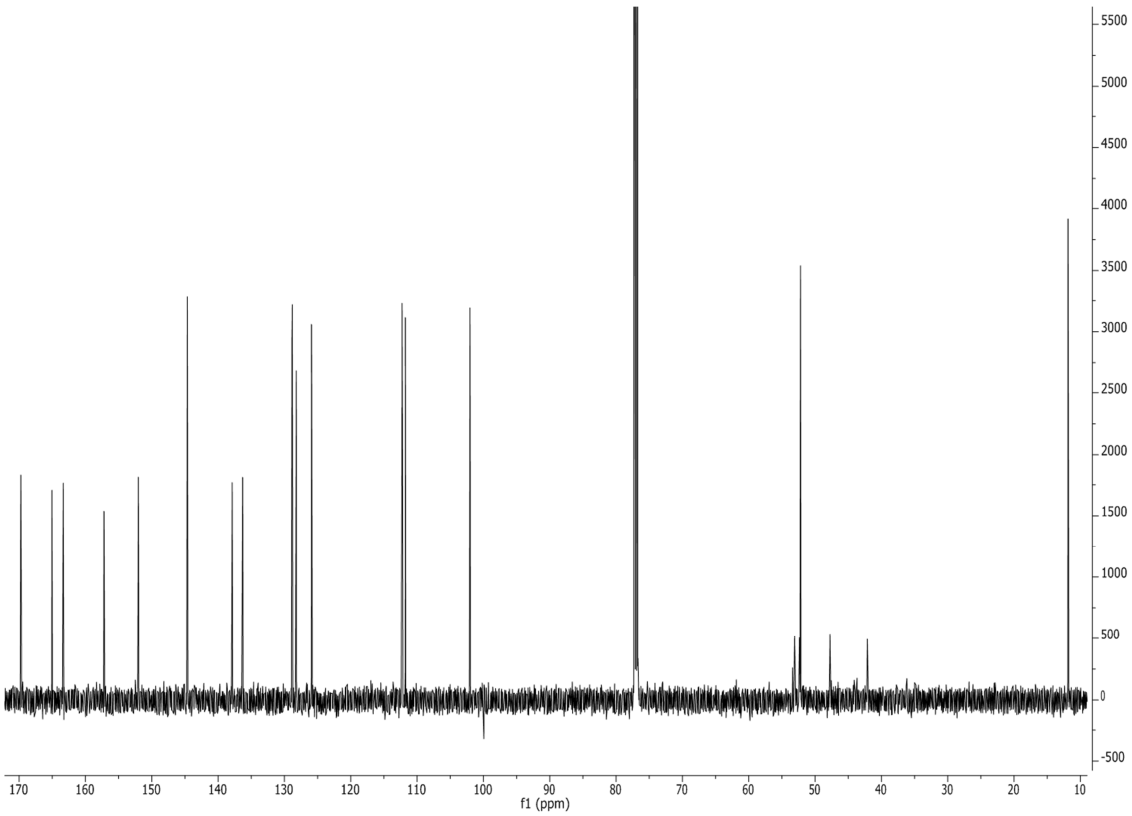


4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(furan-2-yl)pyrimidin-2-amine (39k)

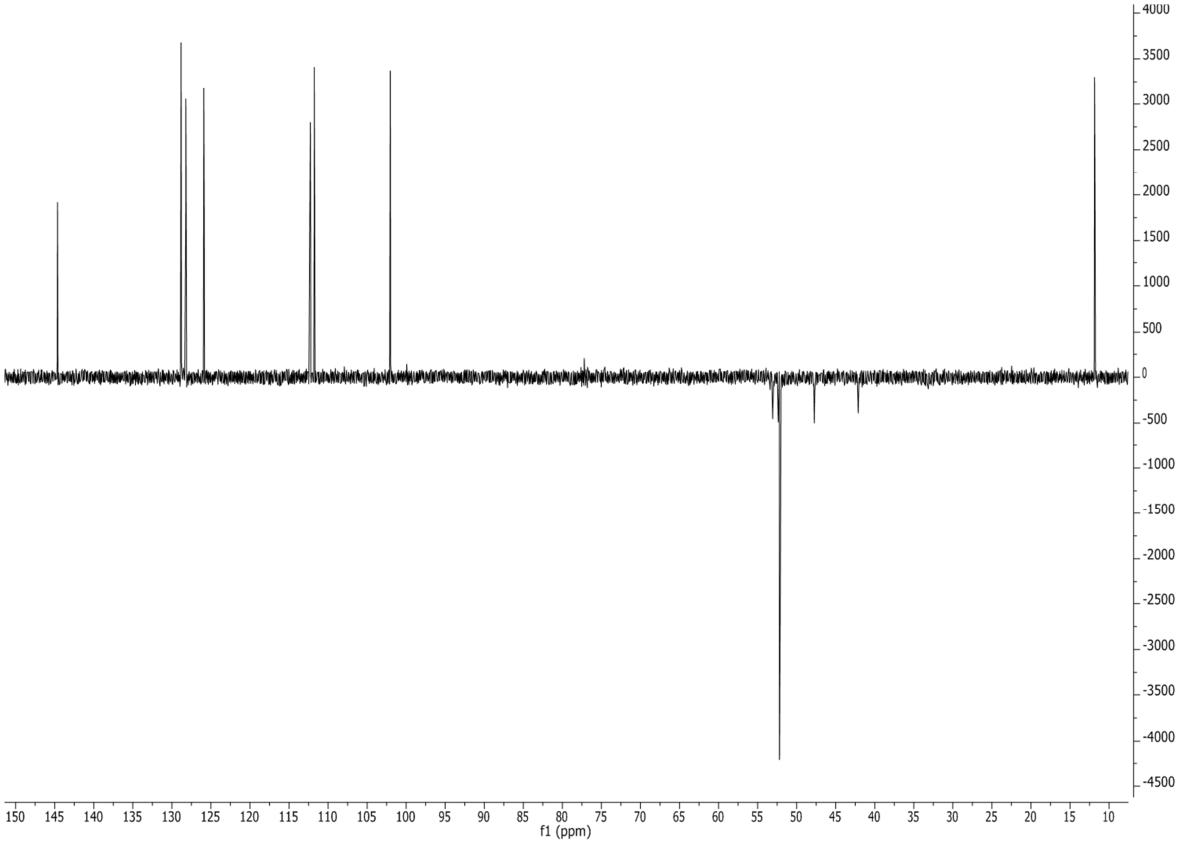
^{1}H NMR



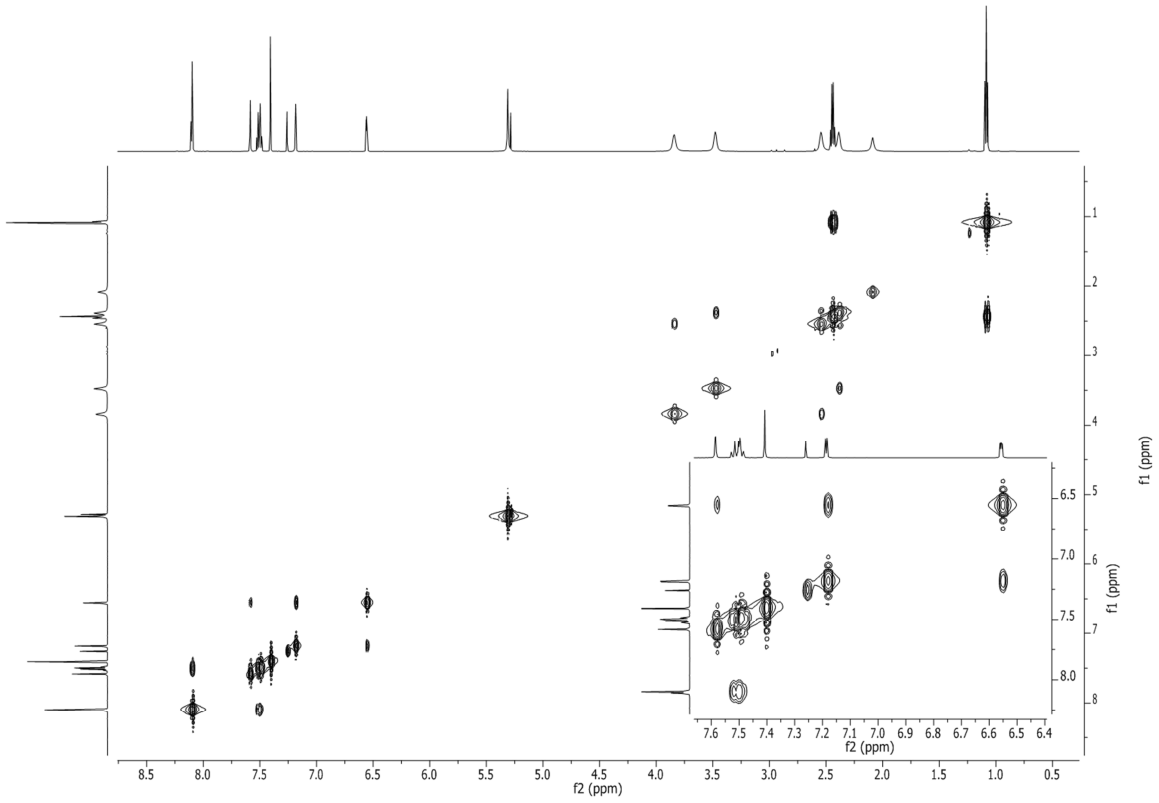
^{13}C NMR



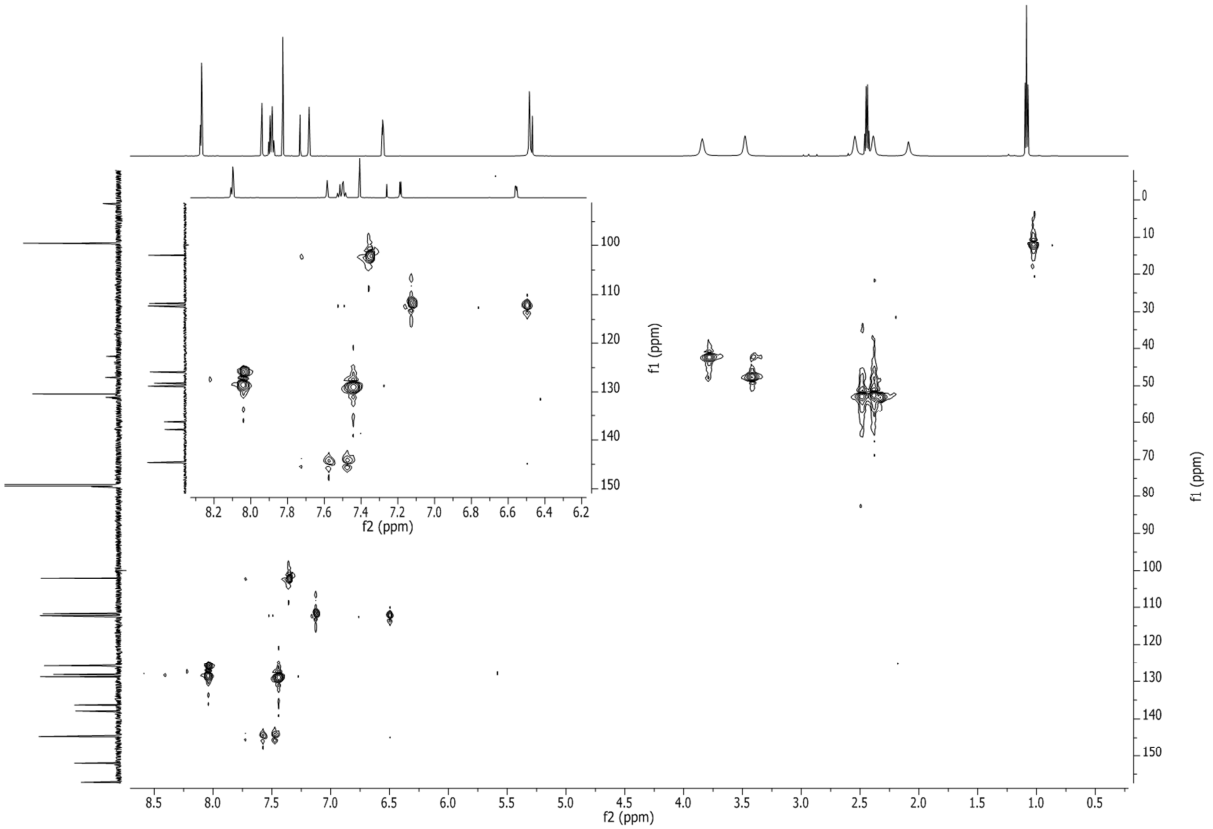
DEPT 135



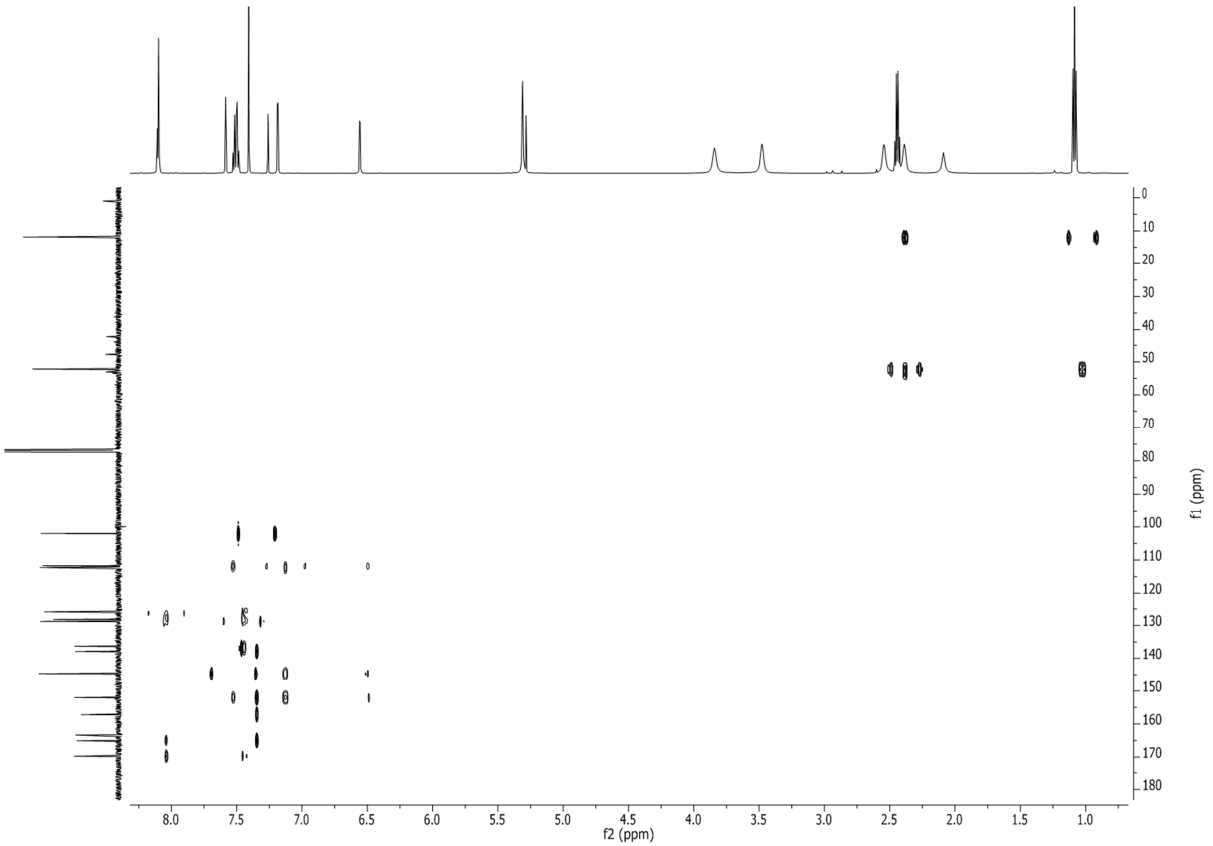
COSY



HSQC

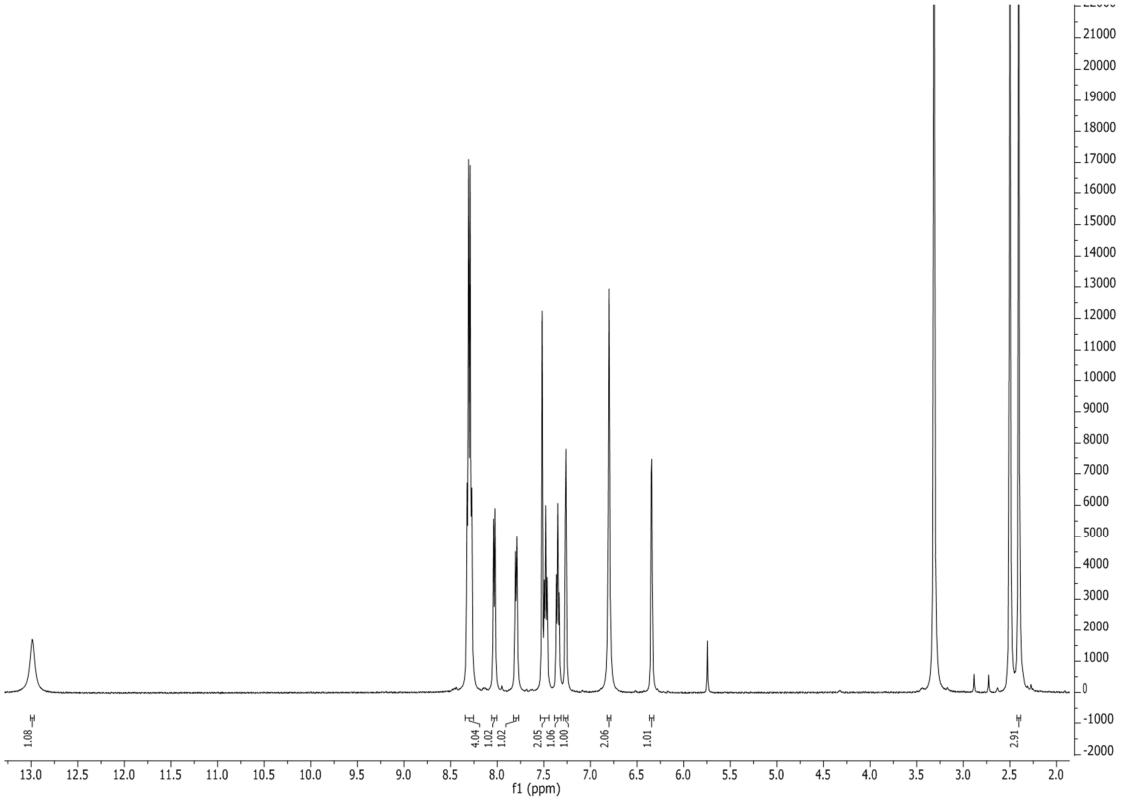


HMBC

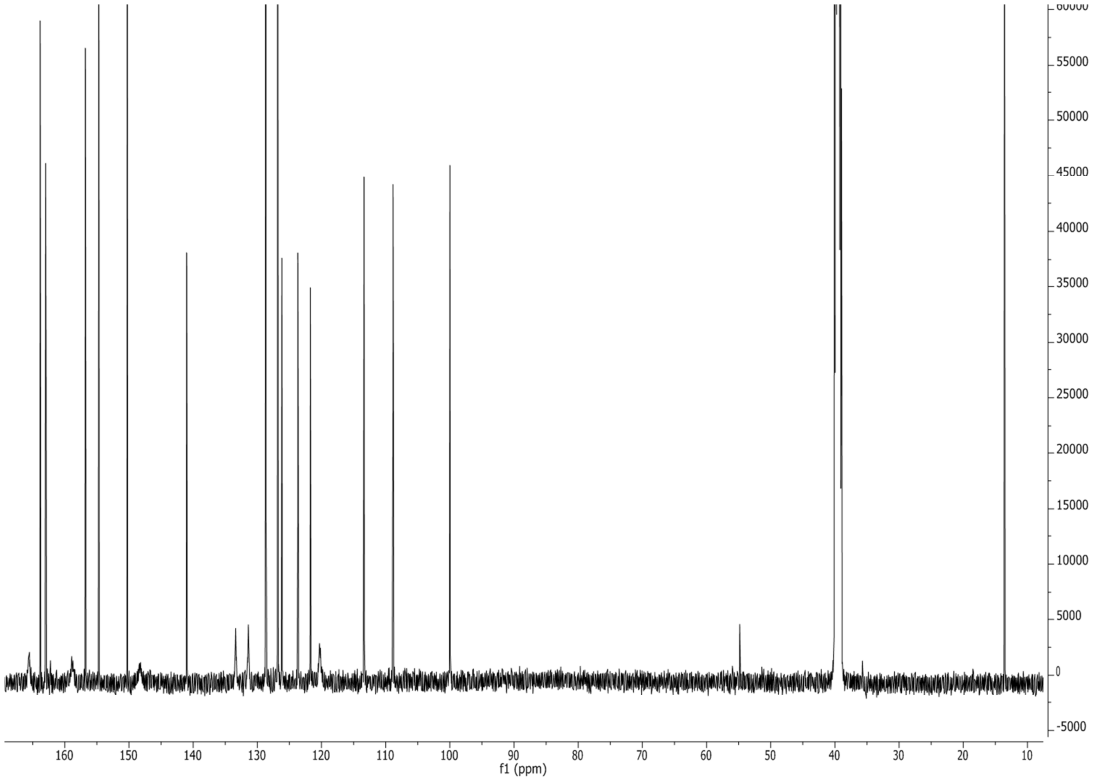


4-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-(1,3-benzothiazol-2-yl)benzamide (39l)

^{1}H NMR

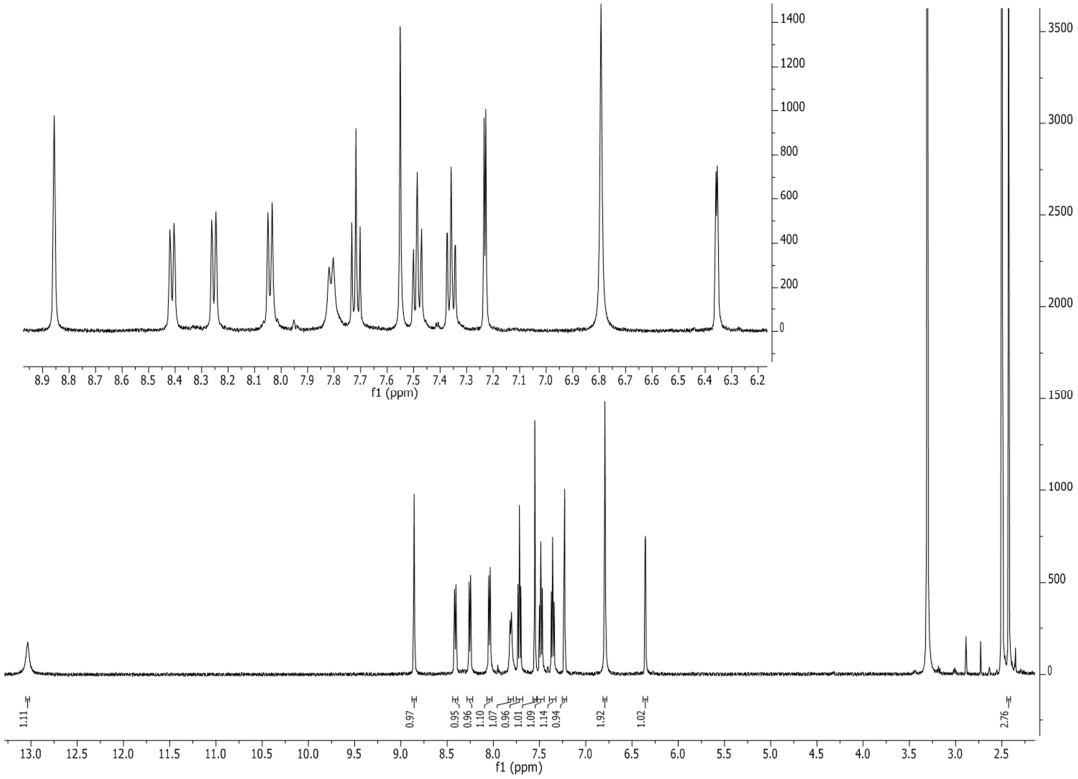


^{13}C NMR

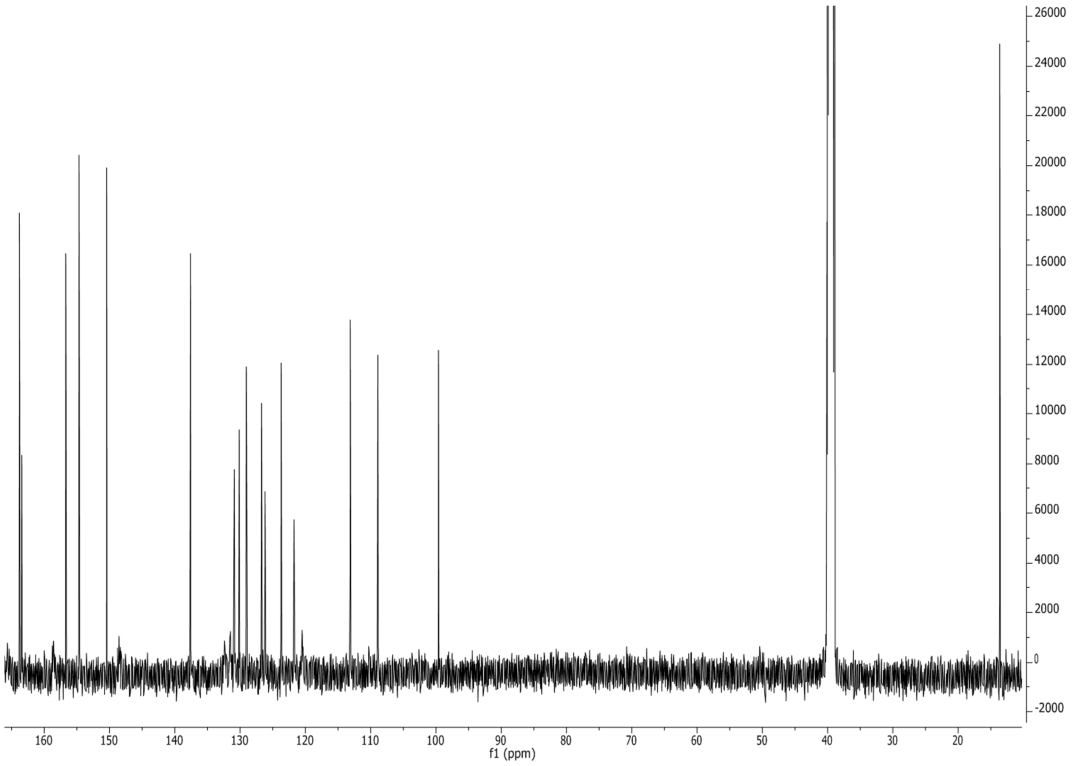


3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl}-N-(1,3-benzothiazol-2-yl)benzamide (39m)

^{1}H NMR

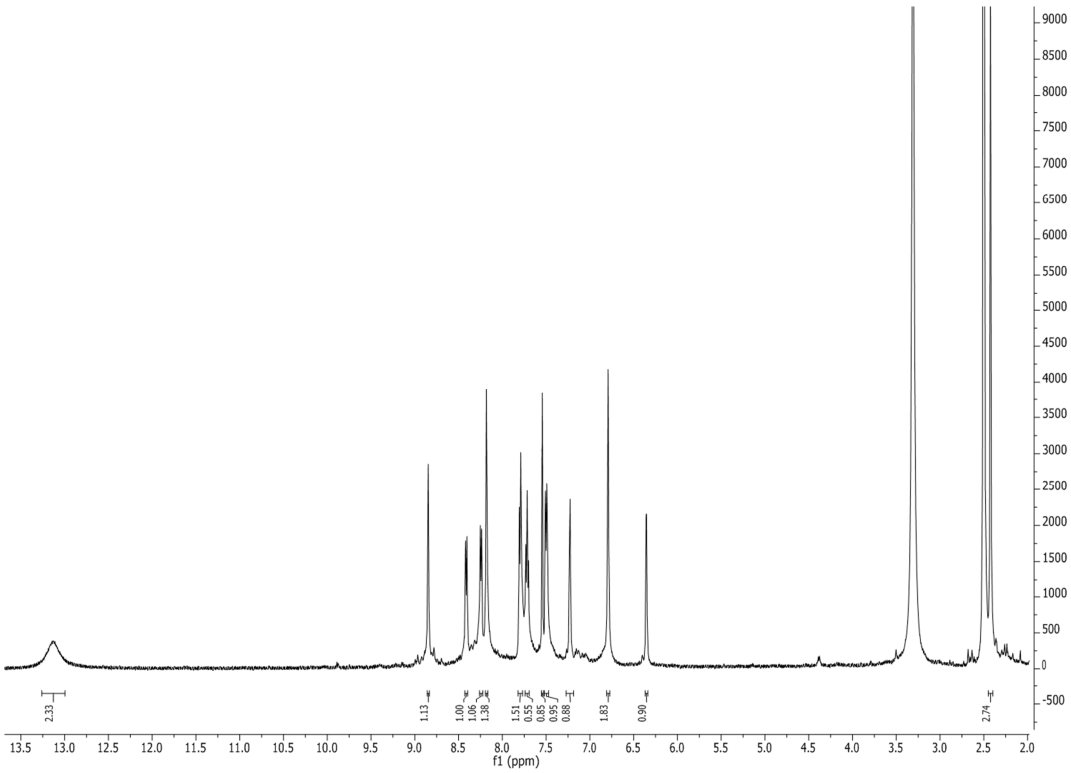


^{13}C NMR

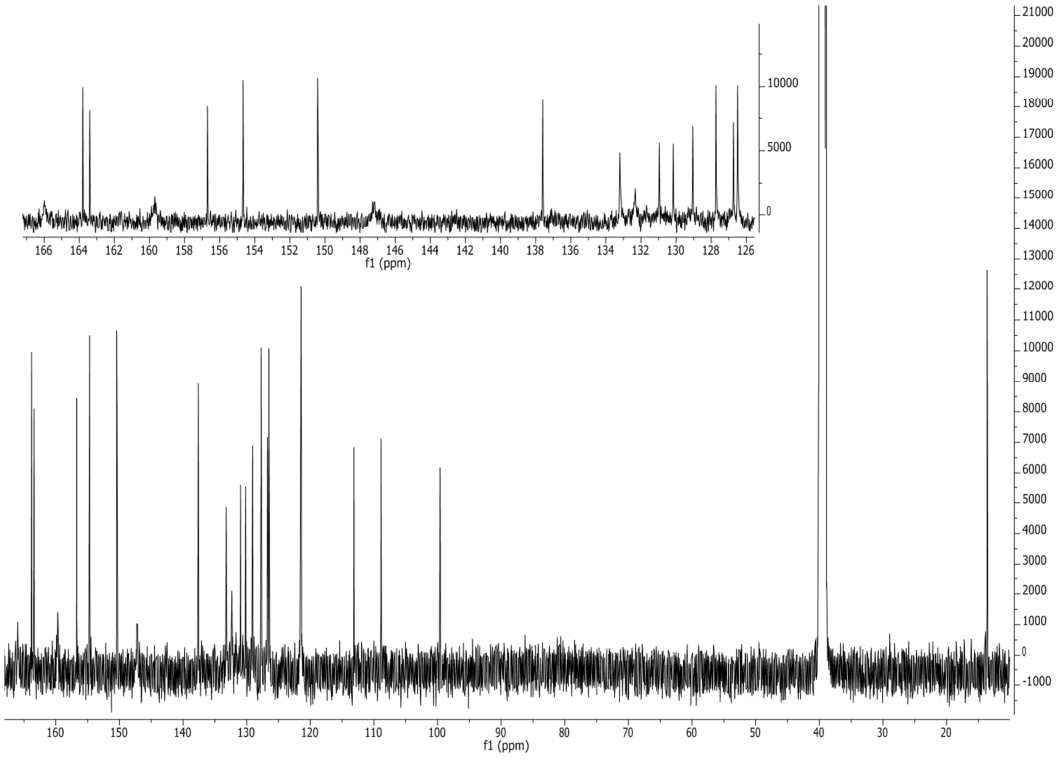


3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-6-chloro-1,3-benzothiazol-2-yl)benzamide (39n)

^{1}H NMR

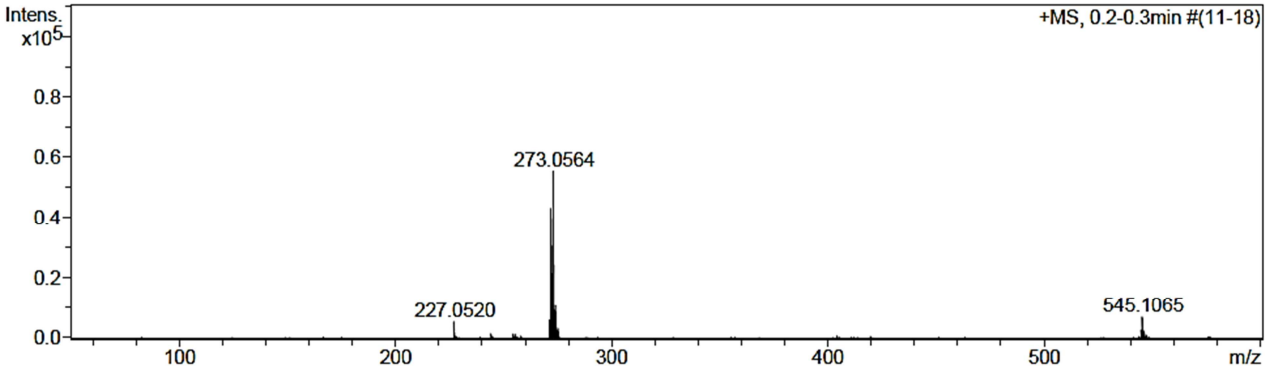


^{13}C NMR



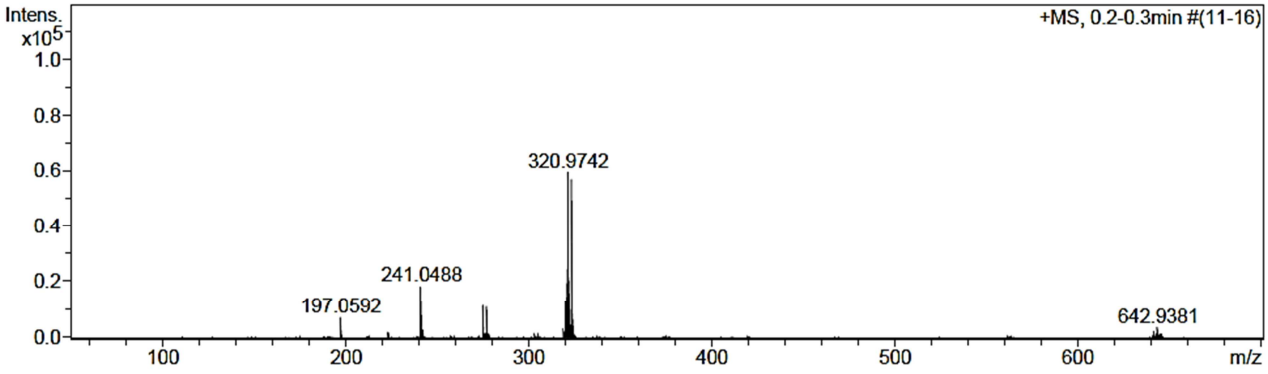
Mass spectra

3-[(1*E*)-3-(5-methylthiophen-2-yl)-3-oxoprop-1-en-1-yl]benzoic acid (37f)



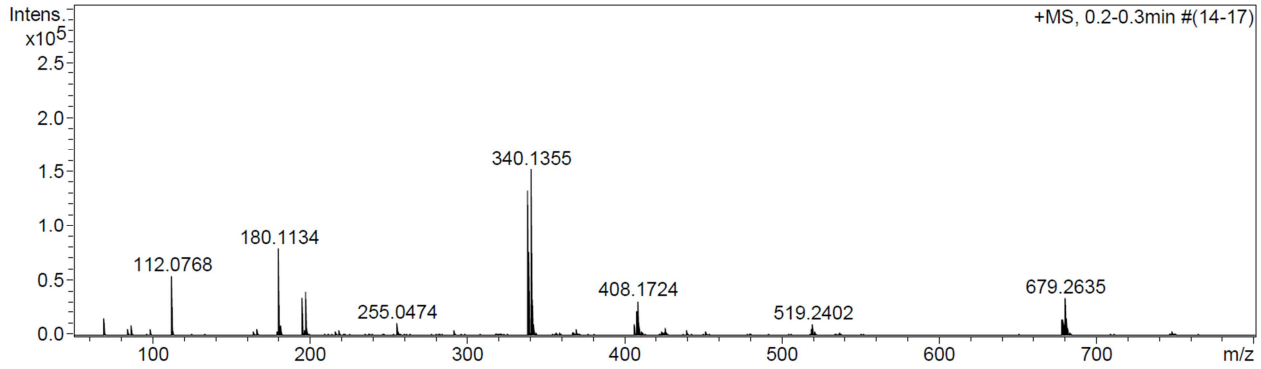
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
273.0565	$C_{15}H_{13}O_3S$	100	273.0580	1.5	5.5	10.1	9.5	ok	even

3-[(1*E*)-3-(5-bromofuran-2-yl)-3-oxoprop-1-en-1-yl]benzoic acid (37h)



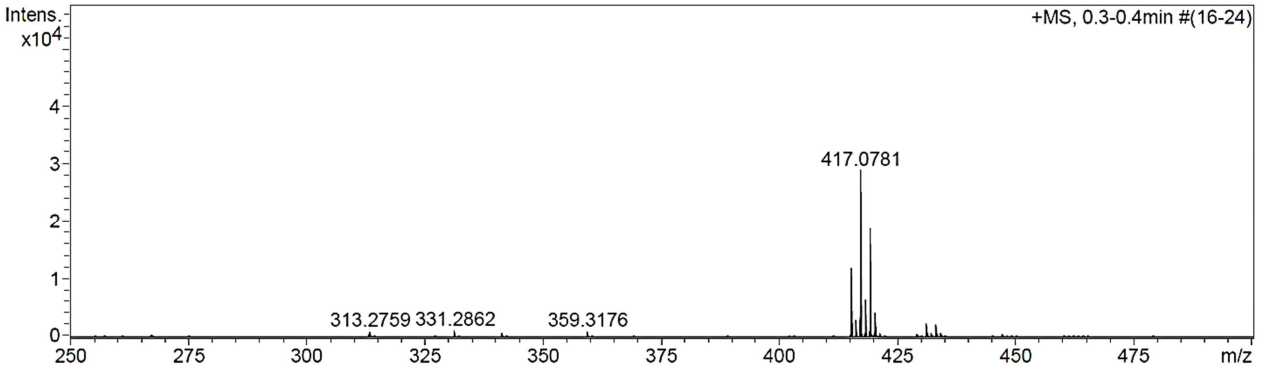
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
320.9740	$C_{14}H_{10}BrO_4$	100.0	320.9757	1.5	4.6	86.5	9.5	ok	even

(2*E*)-1-(5-methylthiophen-2-yl)-3-[3-(piperidine-1-carbonyl)phenyl]prop-2-en-1-one (38f)



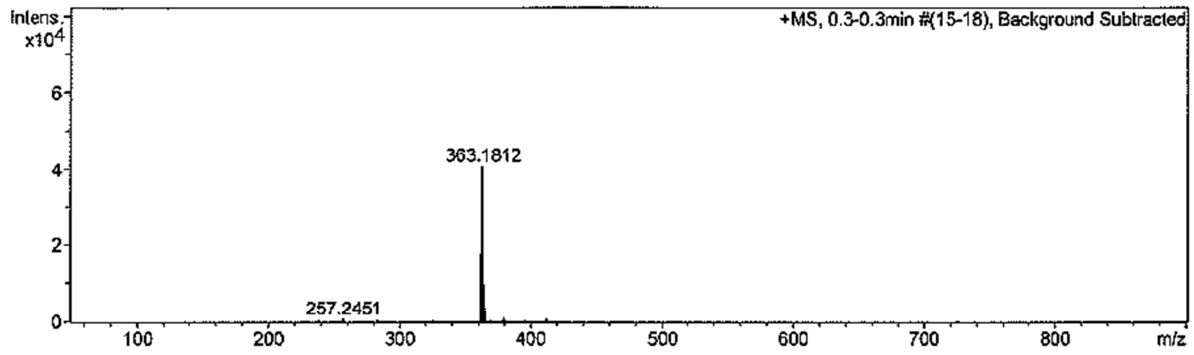
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
339.1267	$C_{20}H_{21}NO_2S$	100.00	339.1288	2.0	5.9	467.1	11.0	ok	odd

(2E)-1-(5-bromofuran-2-yl)-3-[3-(4-ethylpiperazine-1-carbonyl)phenyl]prop-2-en-1-one (38k)



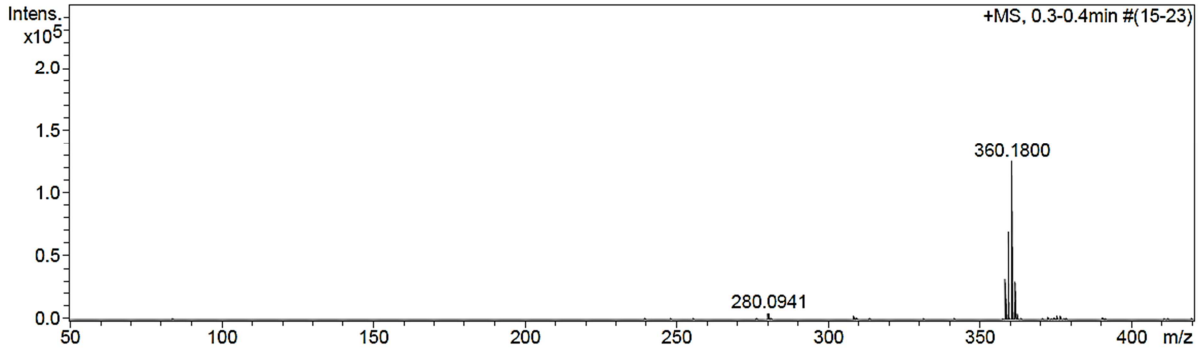
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
416.0718	$C_{20}H_{21}BrN_2O_3$	28.93	416.0730	1.2	2.9	665.1	11.0	ok	odd

4-(5-methylfuran-2-yl)-6-[4-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39a)



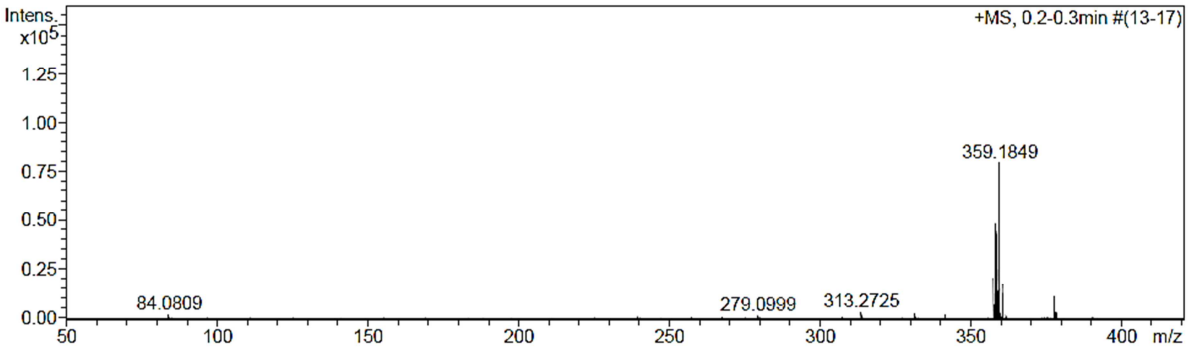
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
363.1812	$C_{21}H_{23}N_4O_2$	100.0	0.3	363.1821	3.4	3.4	12.5	ok	even

4-[3-(piperidine-1-carbonyl)phenyl]-6-(pyridin-2-yl)pyrimidin-2-amine (39b)



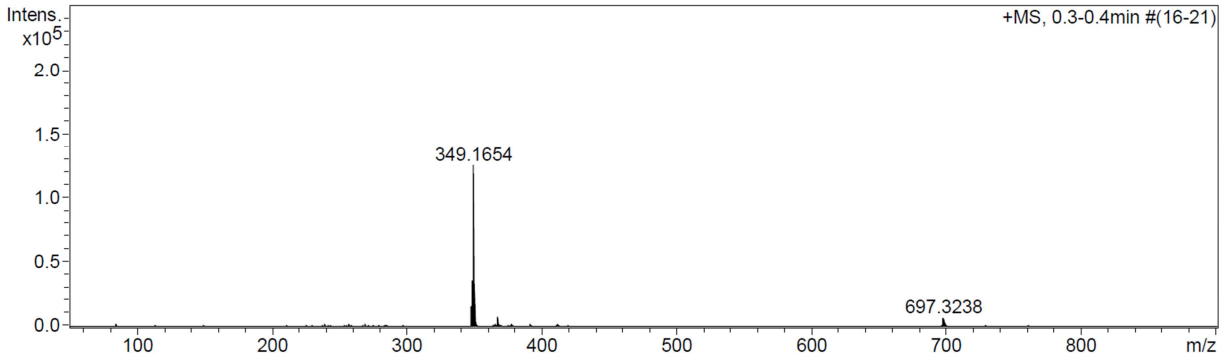
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
359.1724	$C_{21}H_{21}N_5O$	100.00	359.1754	3.1	8.5	514.5	13.5	ok	even

4-phenyl-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39c)



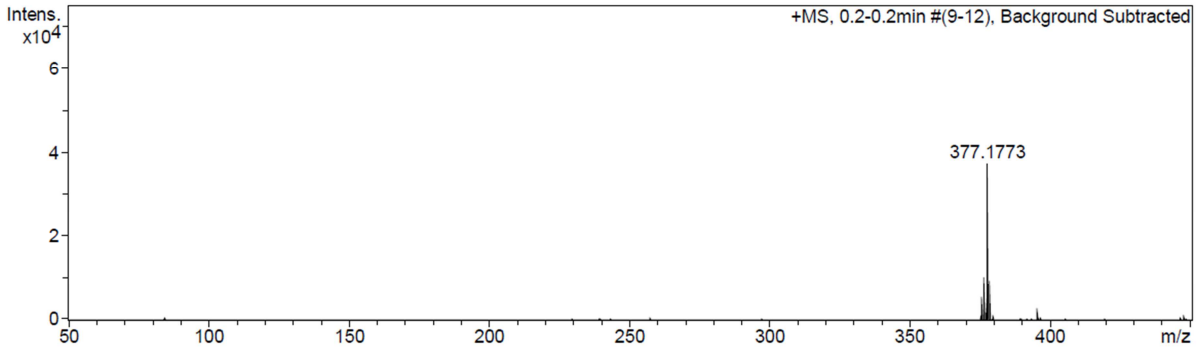
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
359.1849	$C_{22}H_{23}N_4O$	37.65	359.1866	1.7	4.8	14.7	13.5	ok	even

4-(furan-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39d)



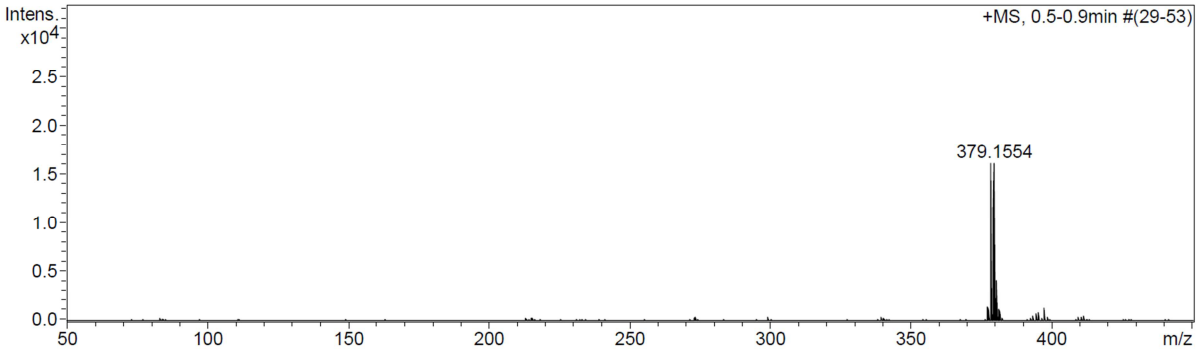
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
348.1581	$C_{20}H_{20}N_4O_2$	100.0	348.1586	0.7	1.9	617.8	13.0	ok	odd

4-(4-fluorophenyl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39e)



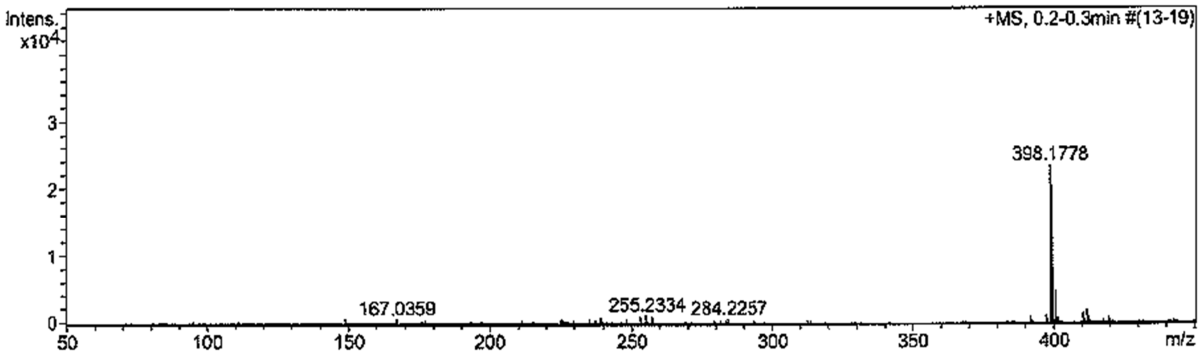
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
377.1773	$C_{22}H_{22}FN_4O$	100.00	377.1772	-0.0	-0.1	2.2	13.5	ok	even

4-(5-methylthiophen-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39f)



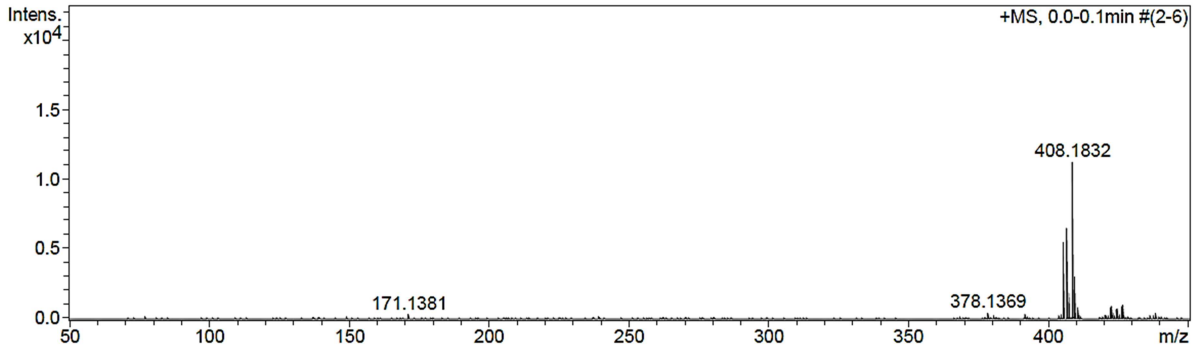
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
378.1489	$C_{21}H_{22}N_4OS$	100.0	378.1509	1.9	5.1	387.2	13.0	ok	odd

4-(1-benzofuran-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39g)



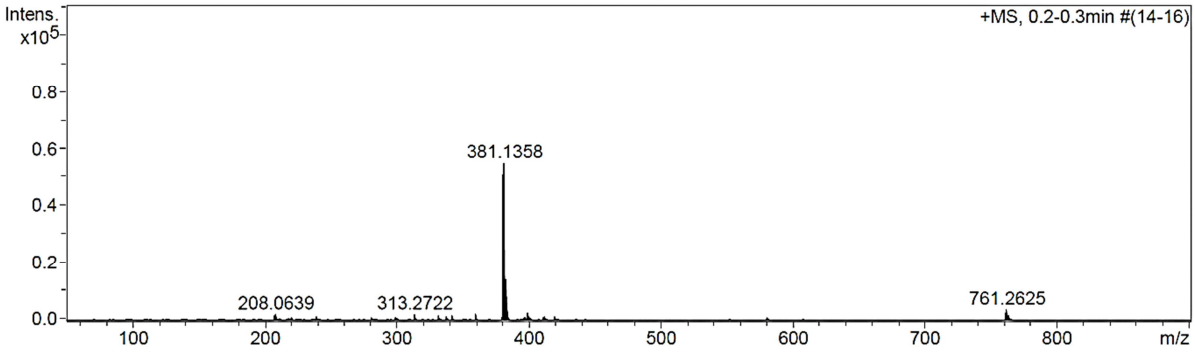
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
398.1778	$C_{24}H_{22}N_4O_2$	0.0	398.1767	-4.1	-10.2	361.2	16.0	ok	odd

4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(5-methylthiophen-2-yl)pyrimidin-2-amine (39h)



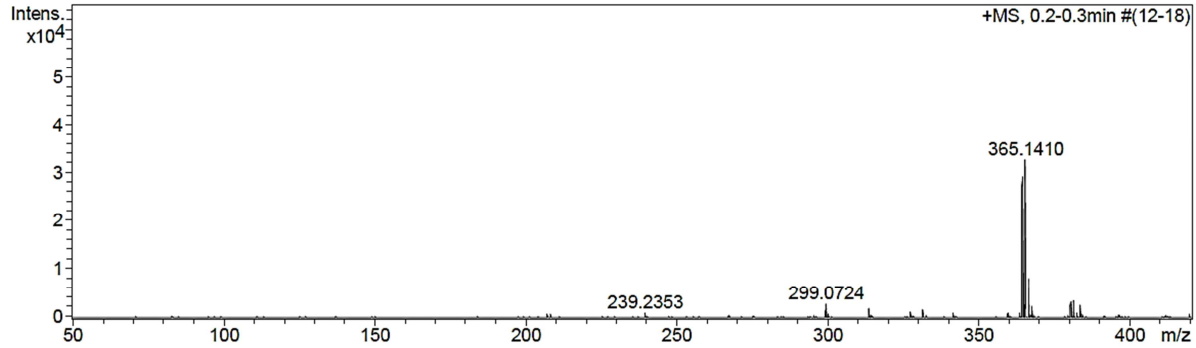
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
408.1832	$C_{22}H_{26}N_5OS$	81.71	408.1853	2.0	4.9	7.5	12.5	ok	even

4-(5-methylthiophen-2-yl)-6-[3-(morpholine-4-carbonyl)phenyl]pyrimidin-2-amine (39i)



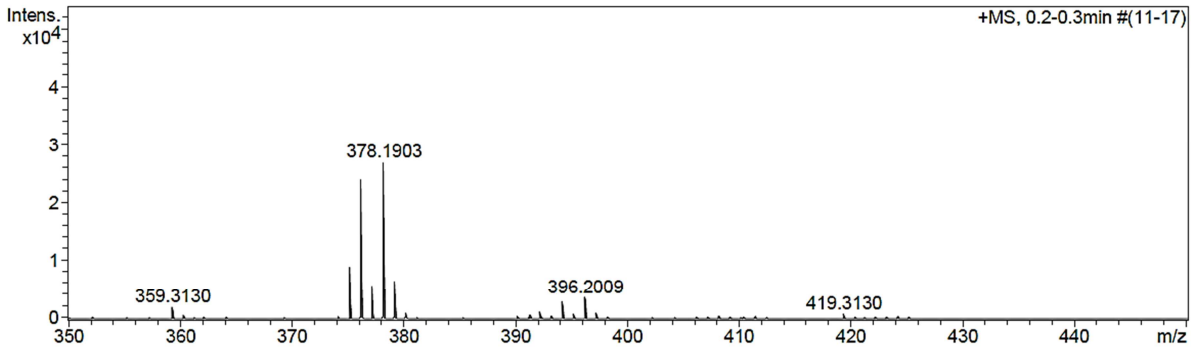
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
380.1290	$C_{20}H_{20}N_4O_2S$	1.55	380.1301	1.2	3.1	393.8	13.0	ok	odd

4-(5-methylthiophen-2-yl)-6-[3-(pyrrolidine-1-carbonyl)phenyl]pyrimidin-2-amine (39j)



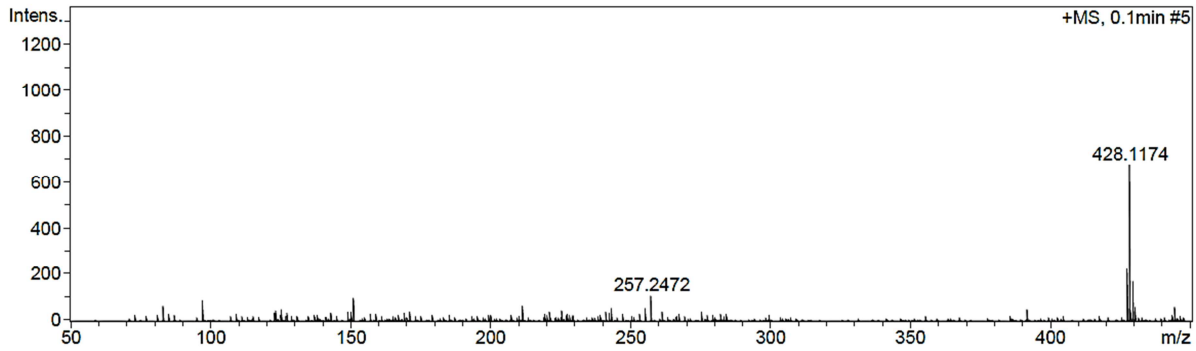
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
365.1410	$C_{20}H_{21}N_4OS$	41.27	365.1431	2.0	5.6	6.8	12.5	ok	even

4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(furan-2-yl)pyrimidin-2-amine (39k)



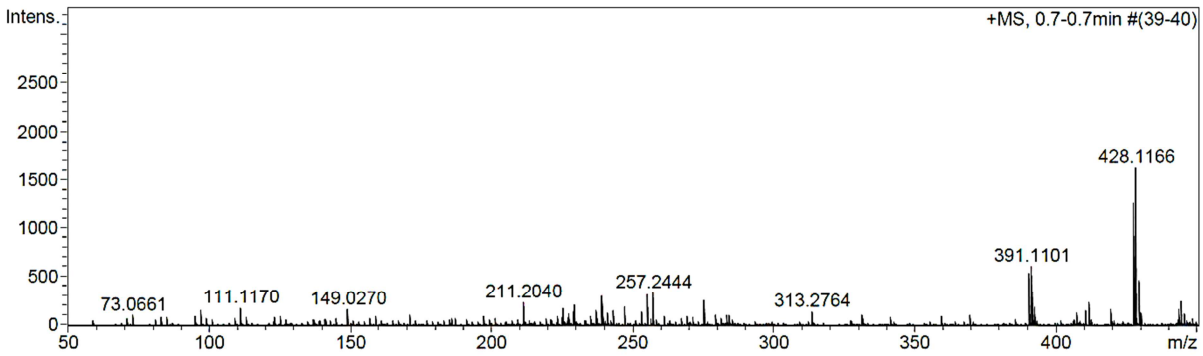
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
378.1903	$C_{21}H_{24}N_5O_2$	39.94	378.1898	-0.6	-15	9.5	13.5	ok	even

4-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-(1,3-benzothiazol-2-yl)benzamide (39l)



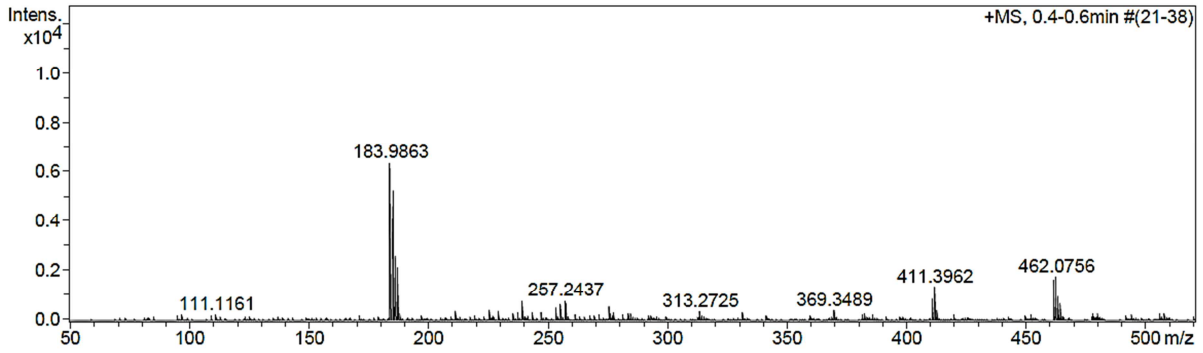
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
428.1174	$C_{23}H_{18}N_5O_2S$	100.00	428.1176	0.2	0.5	44.9	17.5	ok	even

3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl}-N-(1,3-benzothiazol-2-yl)benzamide (39m)



Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
428.1166	$C_{23}H_{18}N_5O_2S$	100.00	428.1176	1.0	2.4	9.2	17.5	ok	even

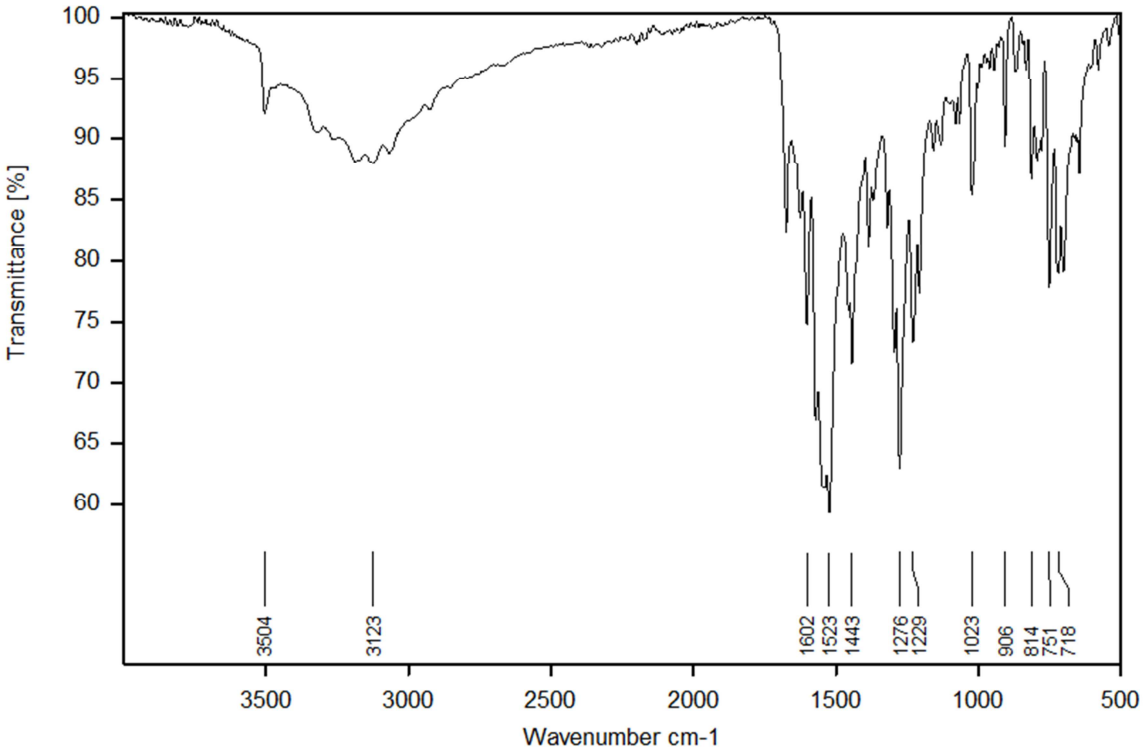
3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-6-chloro-1,3-benzothiazol-2-yl)benzamide (39n)



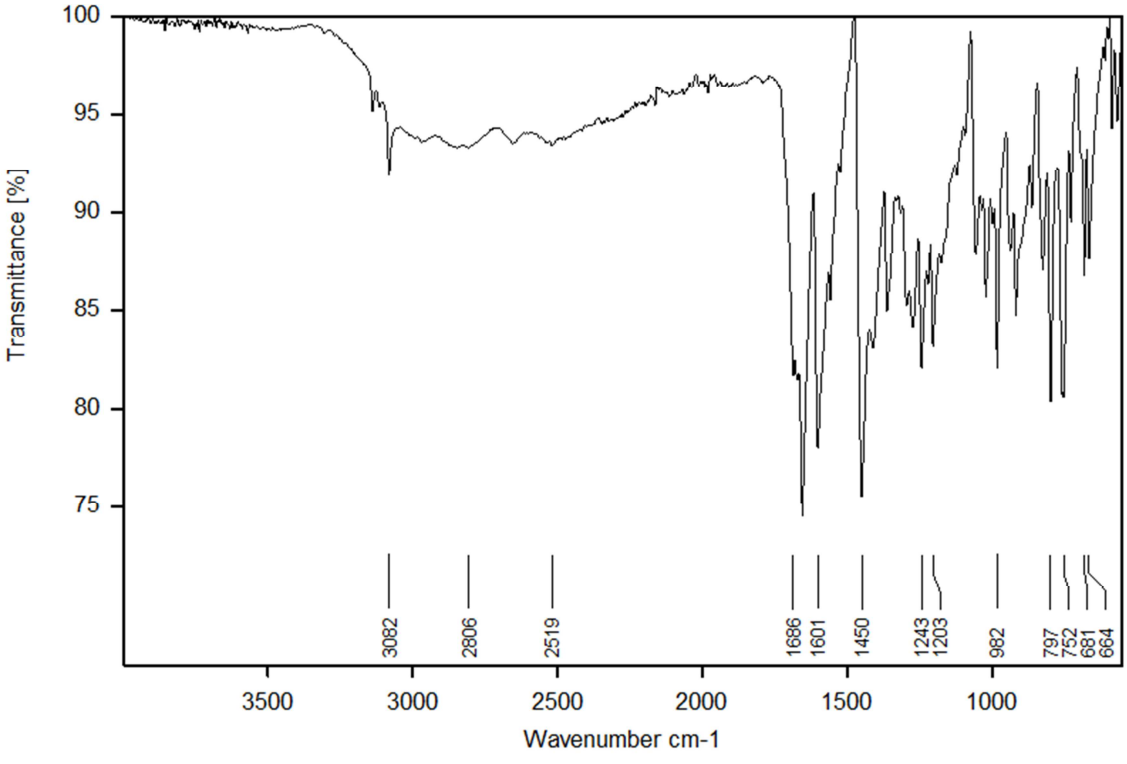
Meas. m.z	Formula	Score	m/z	Err [mDa]	Err [ppm]	mSima	Rdb	N-rule	e⁻Conf
462.0756	$C_{23}H_{17}ClN_5O_2S$	100.0	462.0752	-0.3	-0.7	106.7	22.5	even	ok

IR Spectra

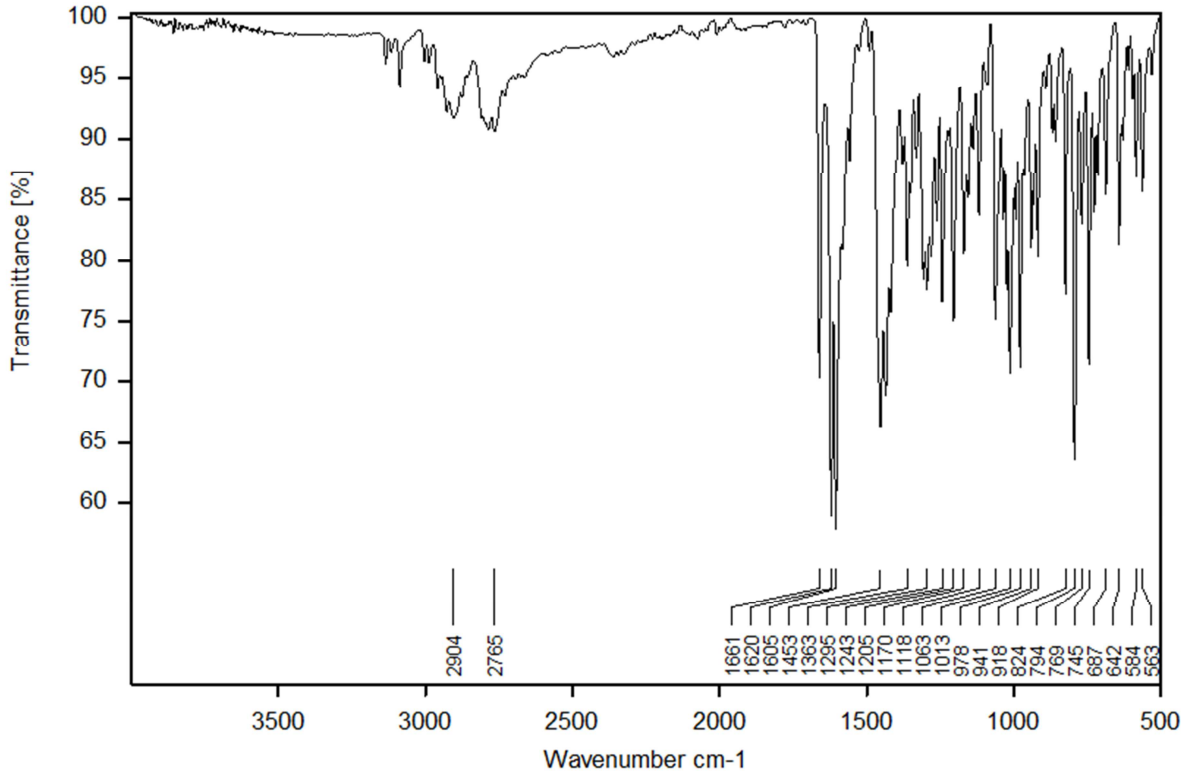
3-[(1*E*)-3-(5-methylthiophen-2-yl)-3-oxoprop-1-en-1-yl]benzoic acid (37f)



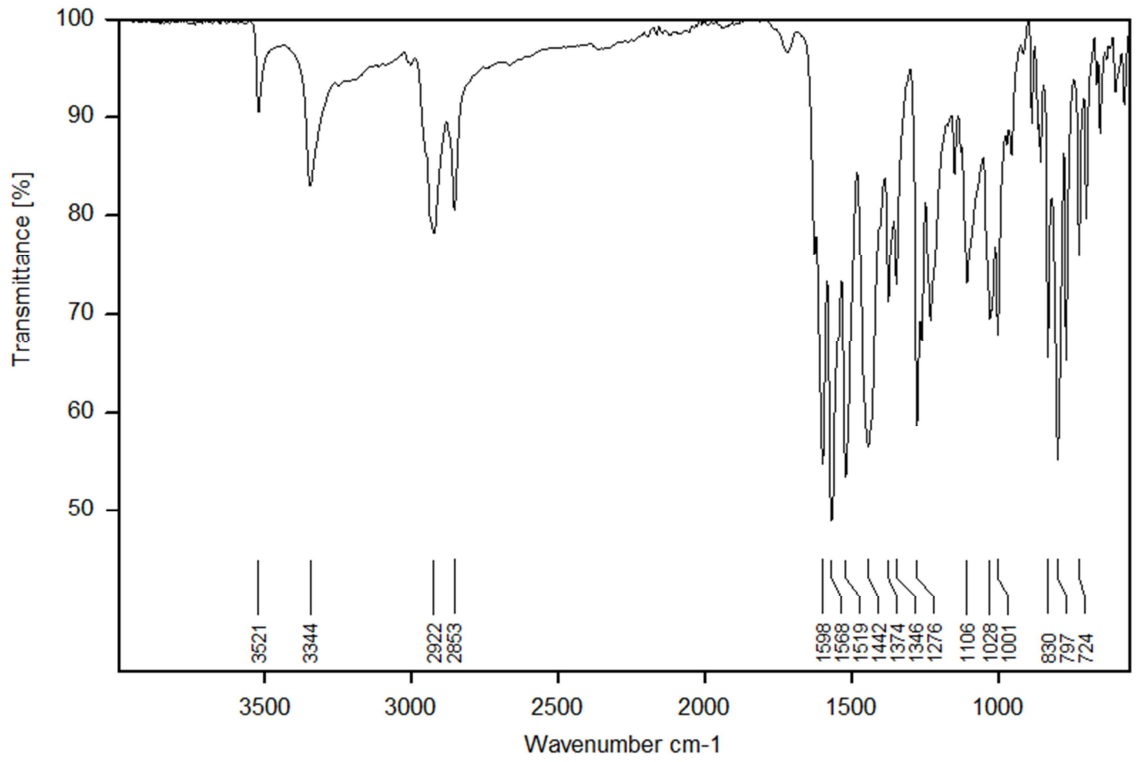
(2*E*)-1-(5-methylthiophen-2-yl)-3-[3-(piperidine-1-carbonyl)phenyl]prop-2-en-1-one (38f)



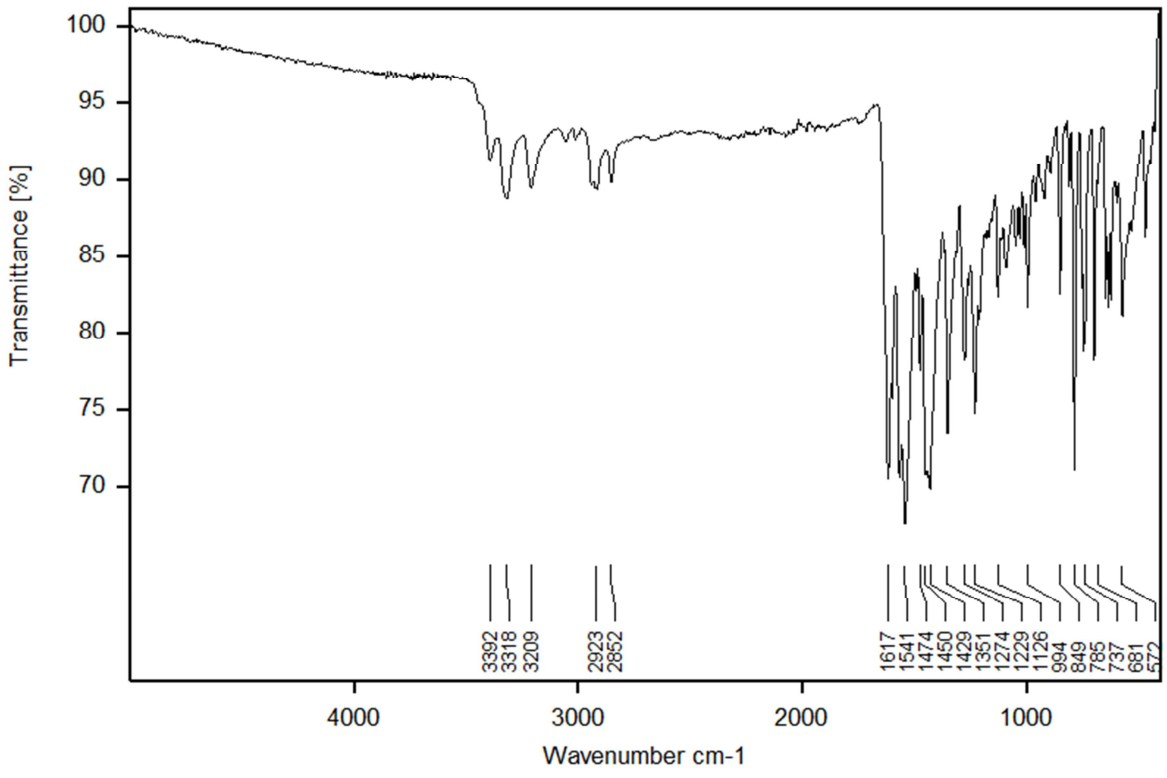
(2E)-1-(5-bromofuran-2-yl)-3-[3-(4-ethylpiperazine-1-carbonyl)phenyl]prop-2-en-1-one (38k)



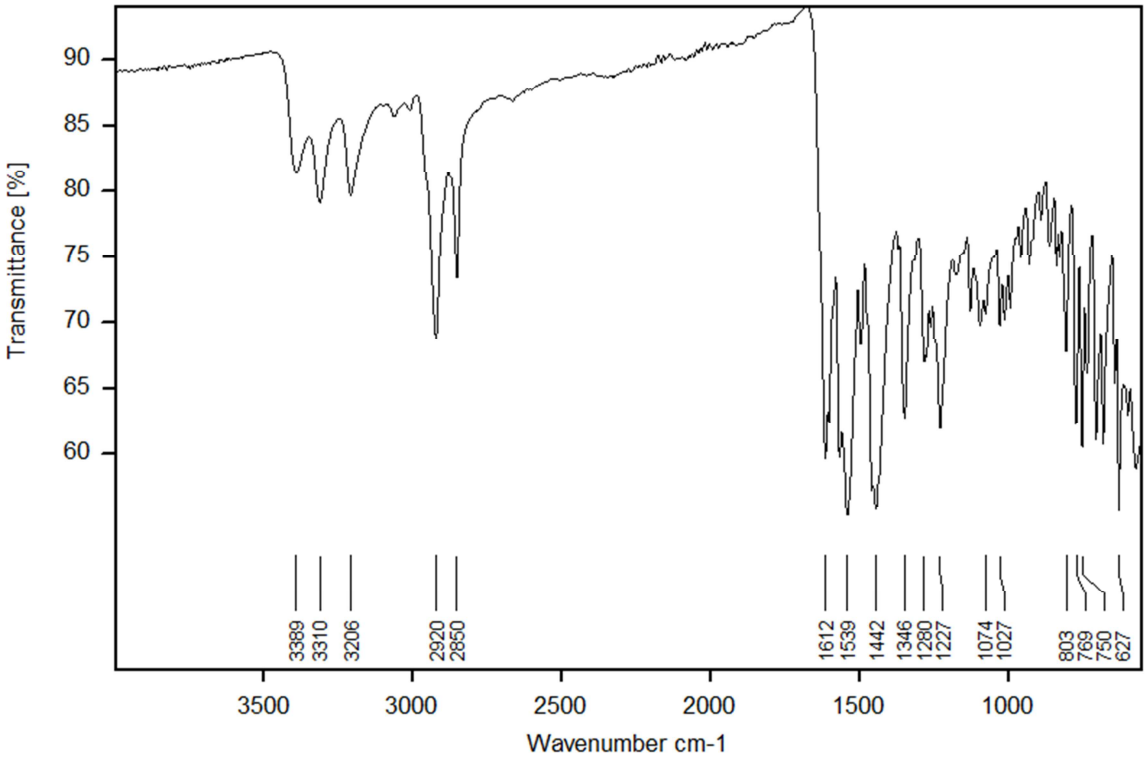
4-(5-methylfuran-2-yl)-6-[4-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39a)



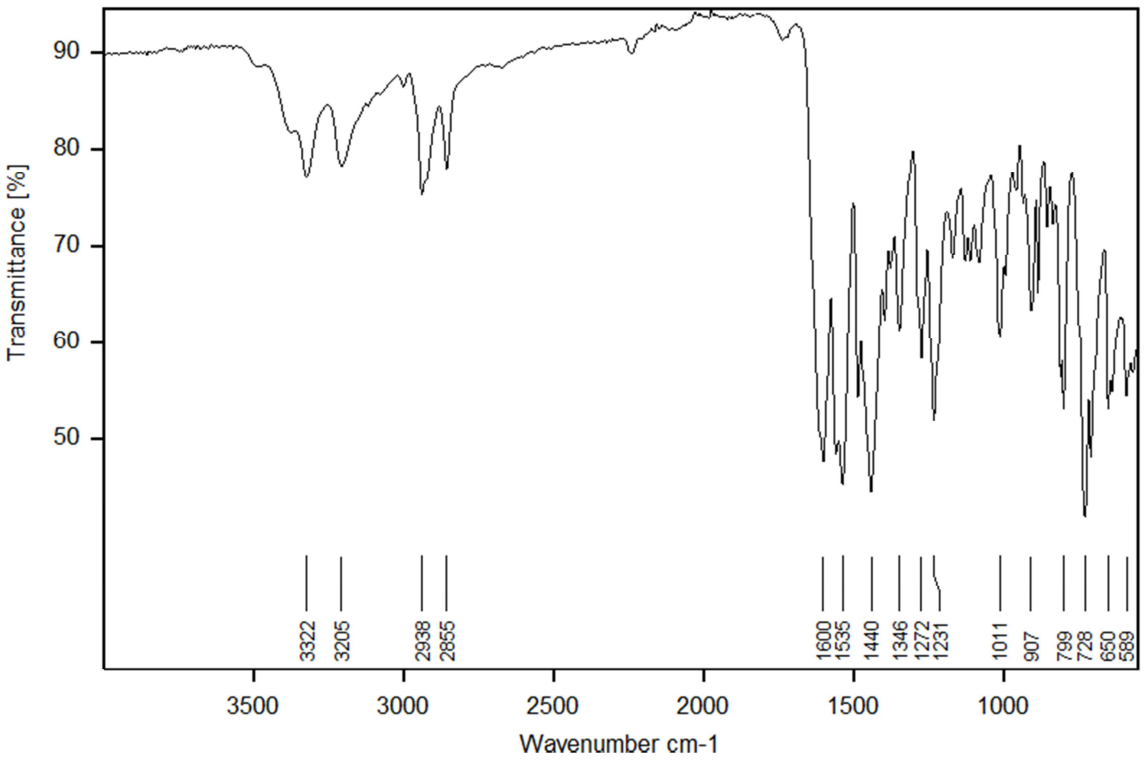
4-[3-(piperidine-1-carbonyl)phenyl]-6-(pyridin-2-yl)pyrimidin-2-amine (39b)



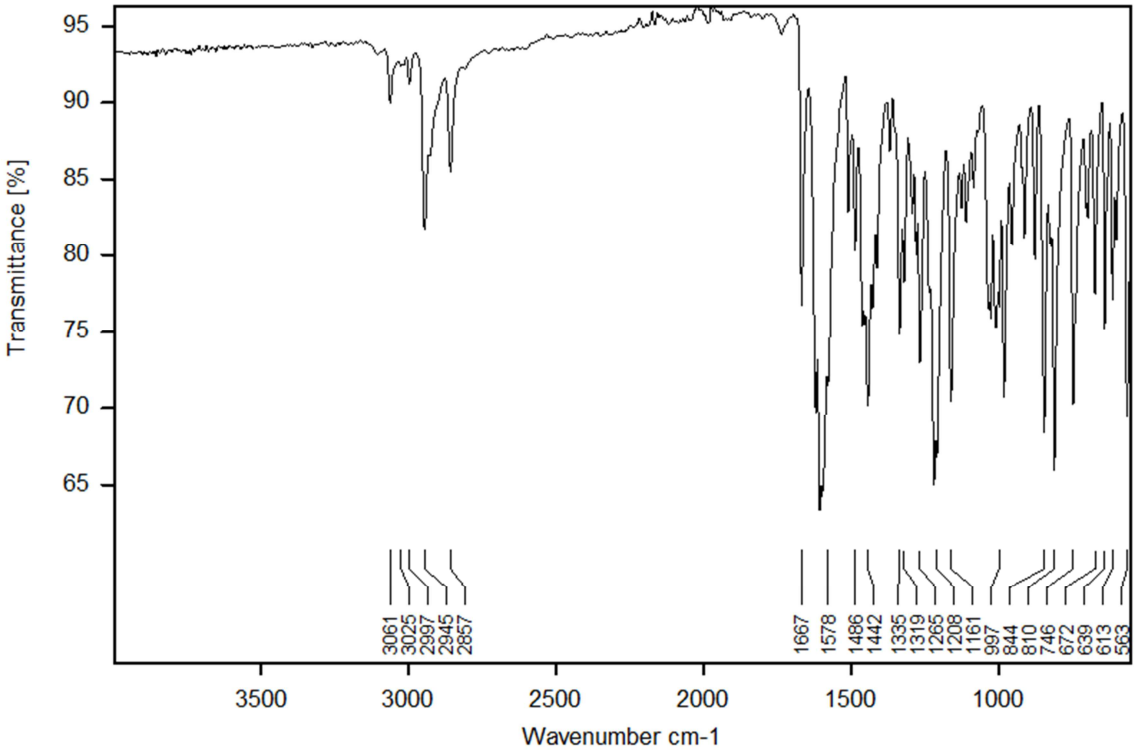
4-phenyl-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39c)



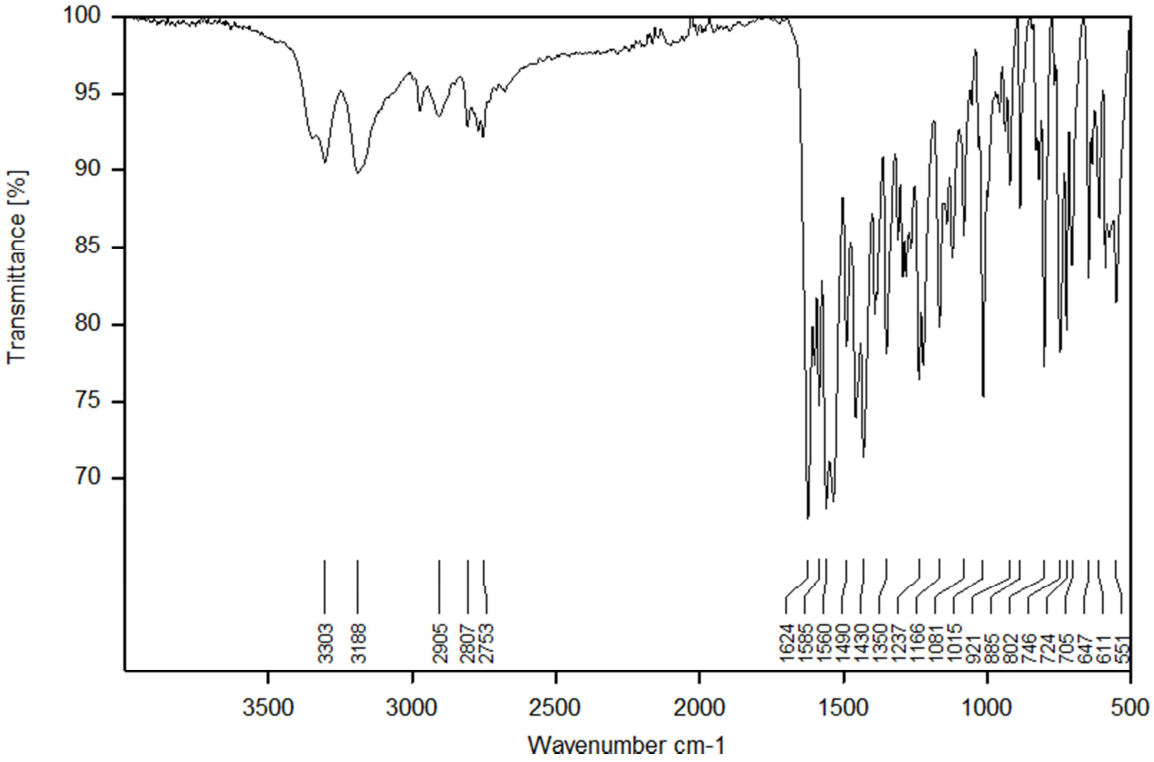
4-(furan-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39d)



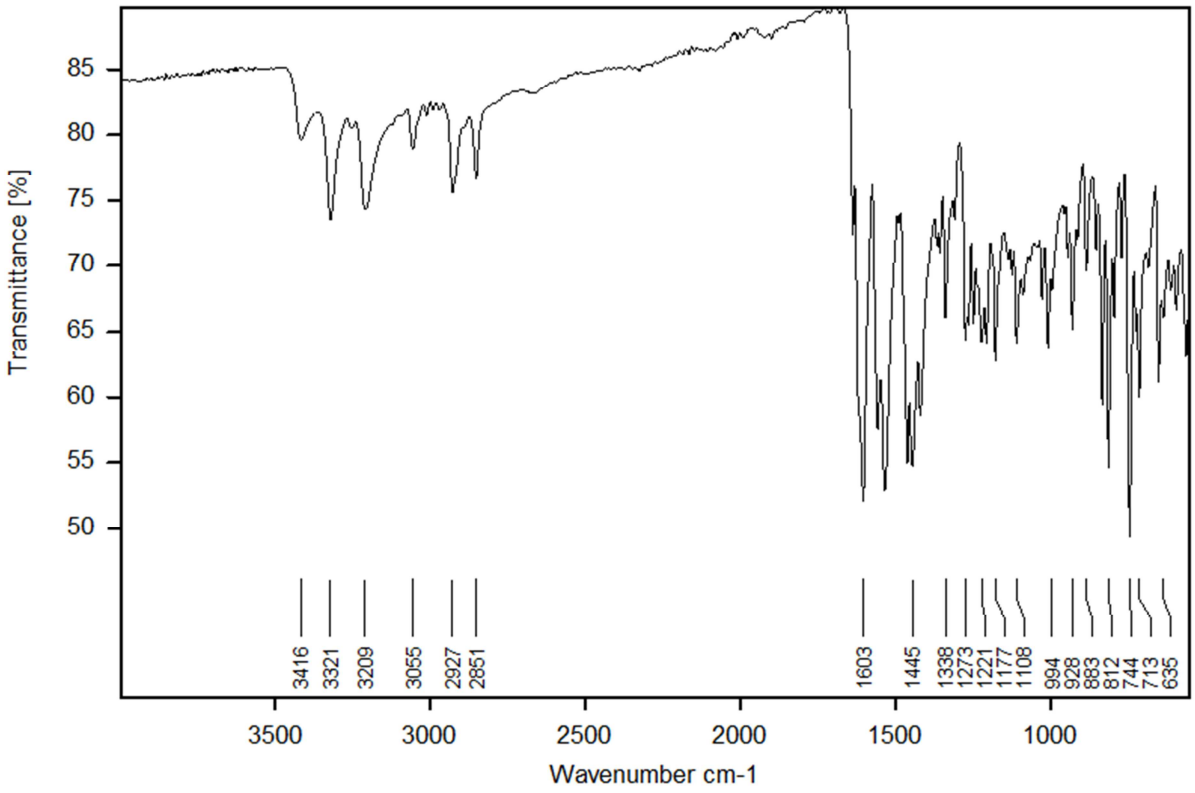
4-(4-fluorophenyl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39e)



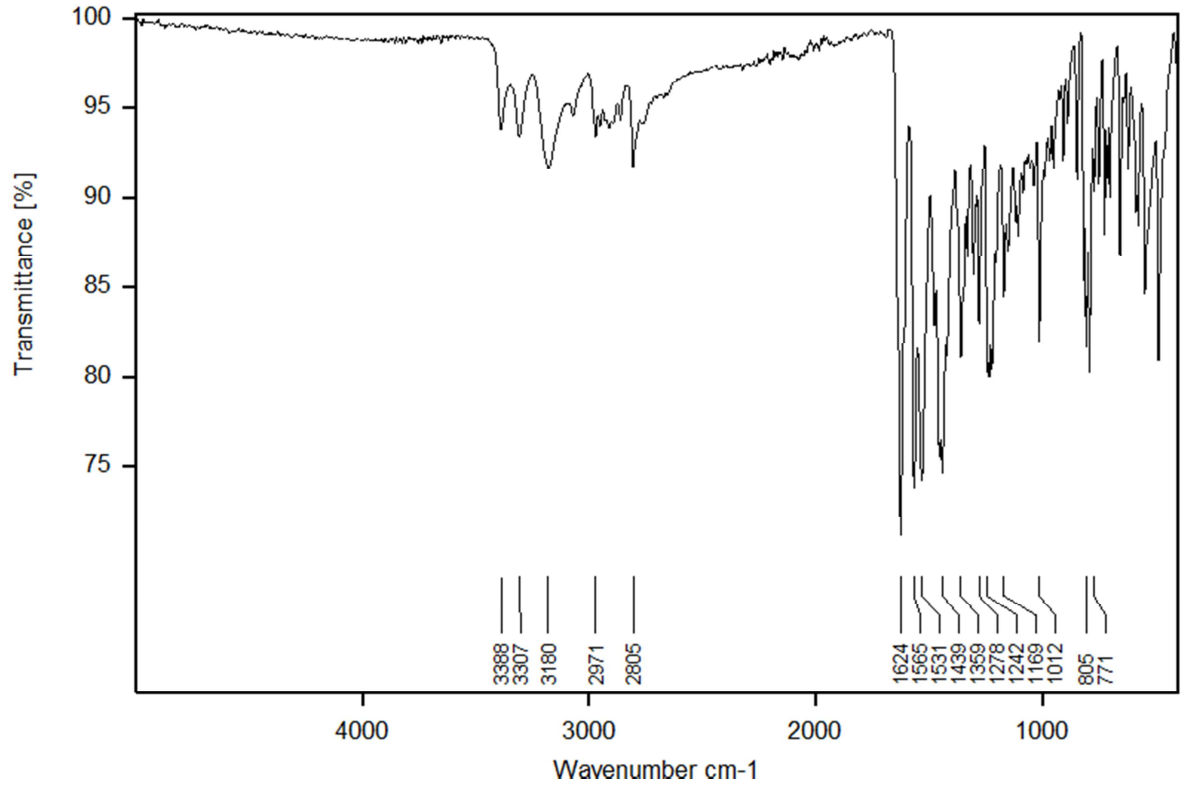
4-(5-methylthiophen-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39f)



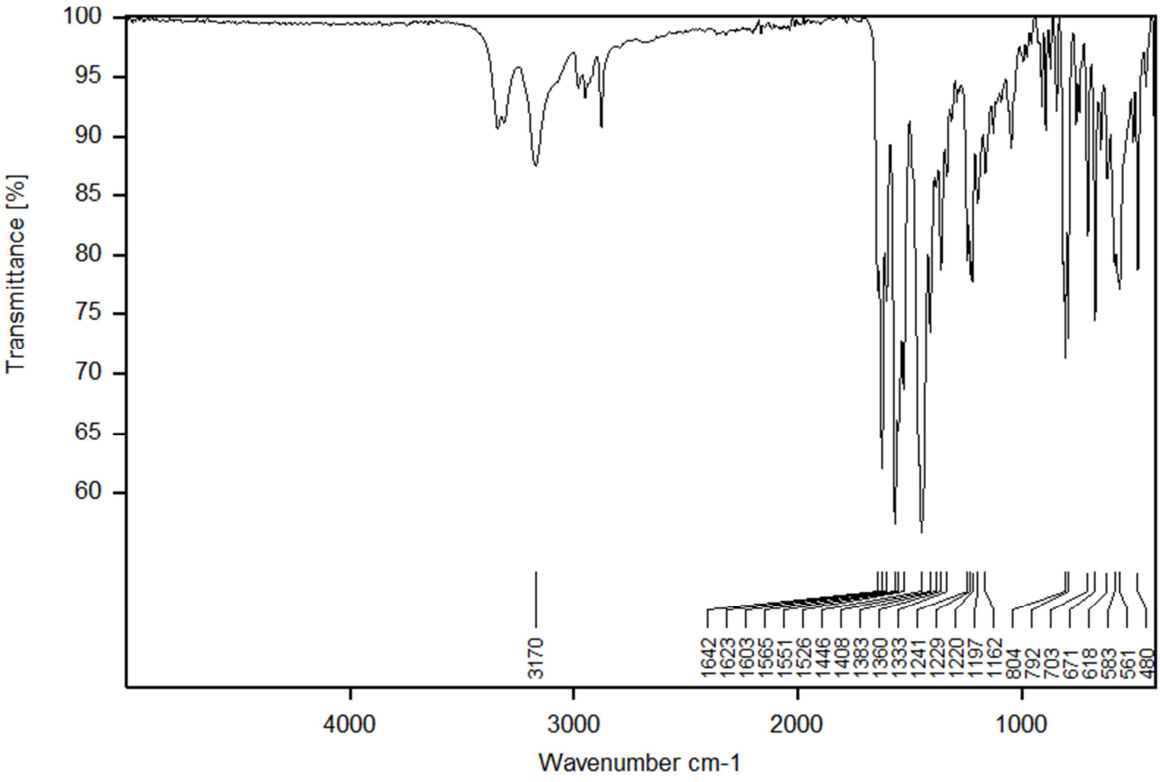
4-(1-benzofuran-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39g)



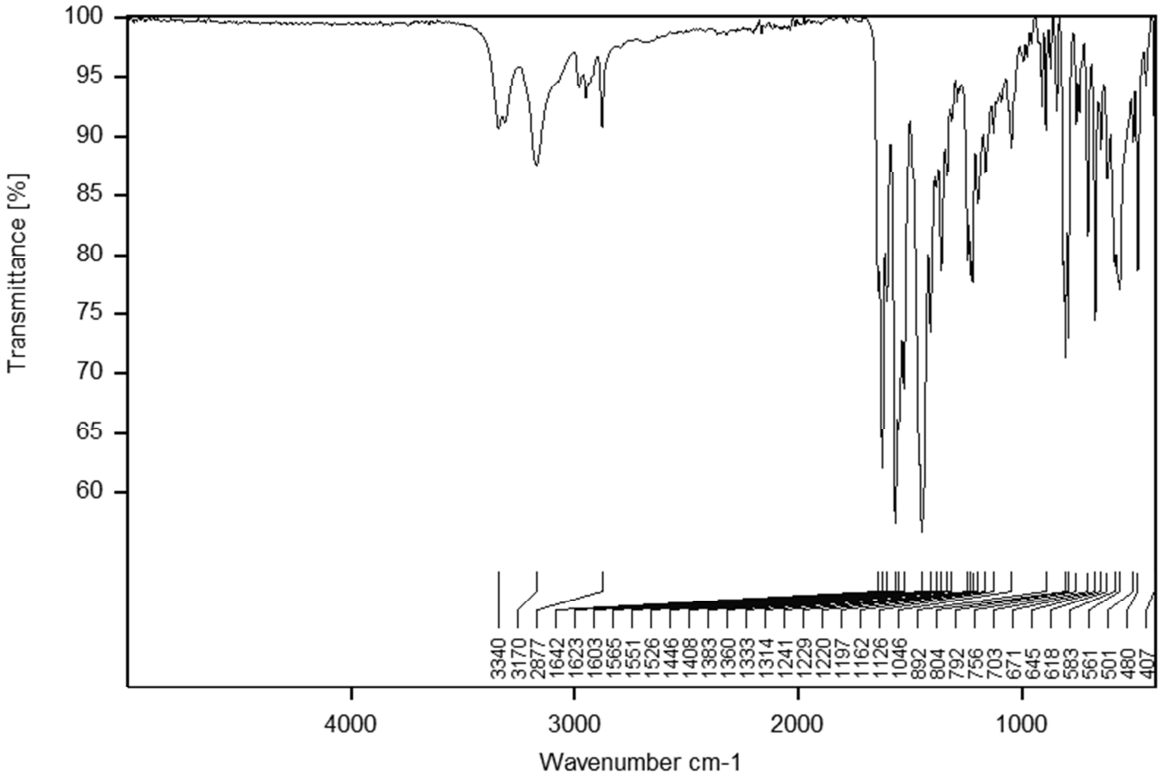
4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(5-methylthiophen-2-yl)pyrimidin-2-amine (39h)



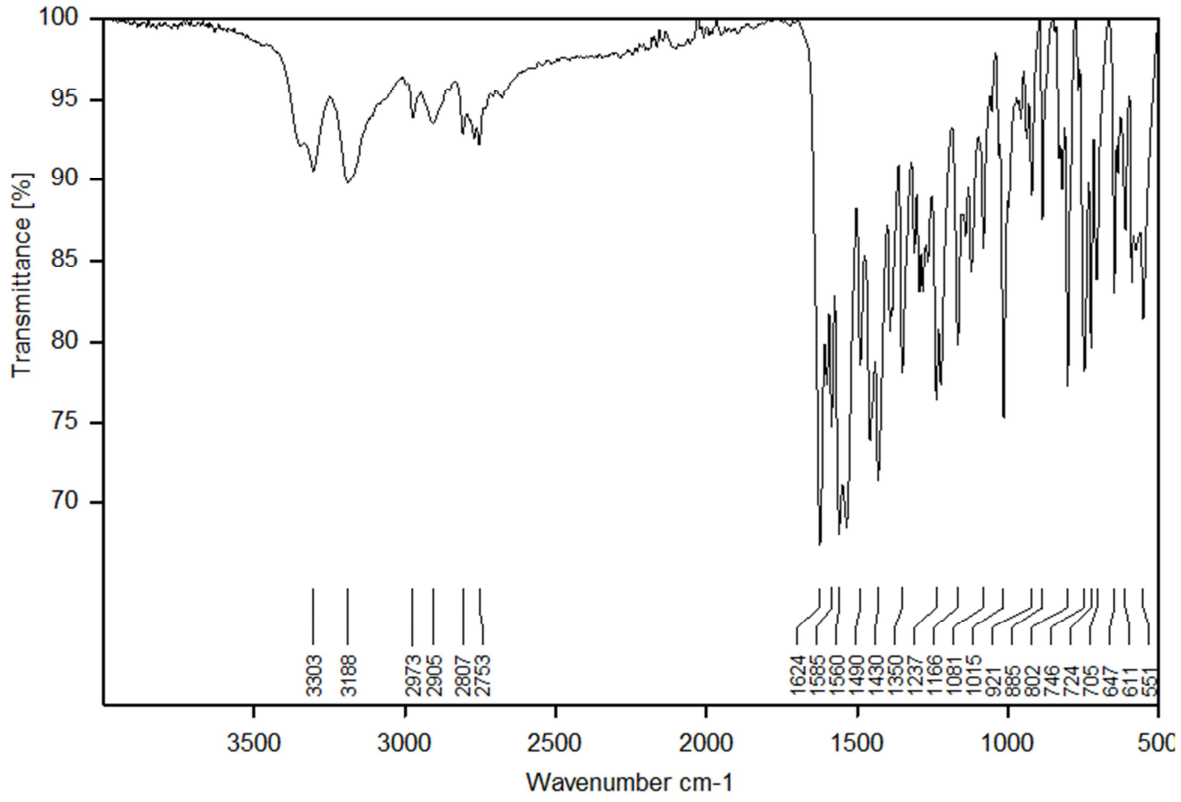
4-(5-methylthiophen-2-yl)-6-[3-(morpholine-4-carbonyl)phenyl]pyrimidin-2-amine (39i)



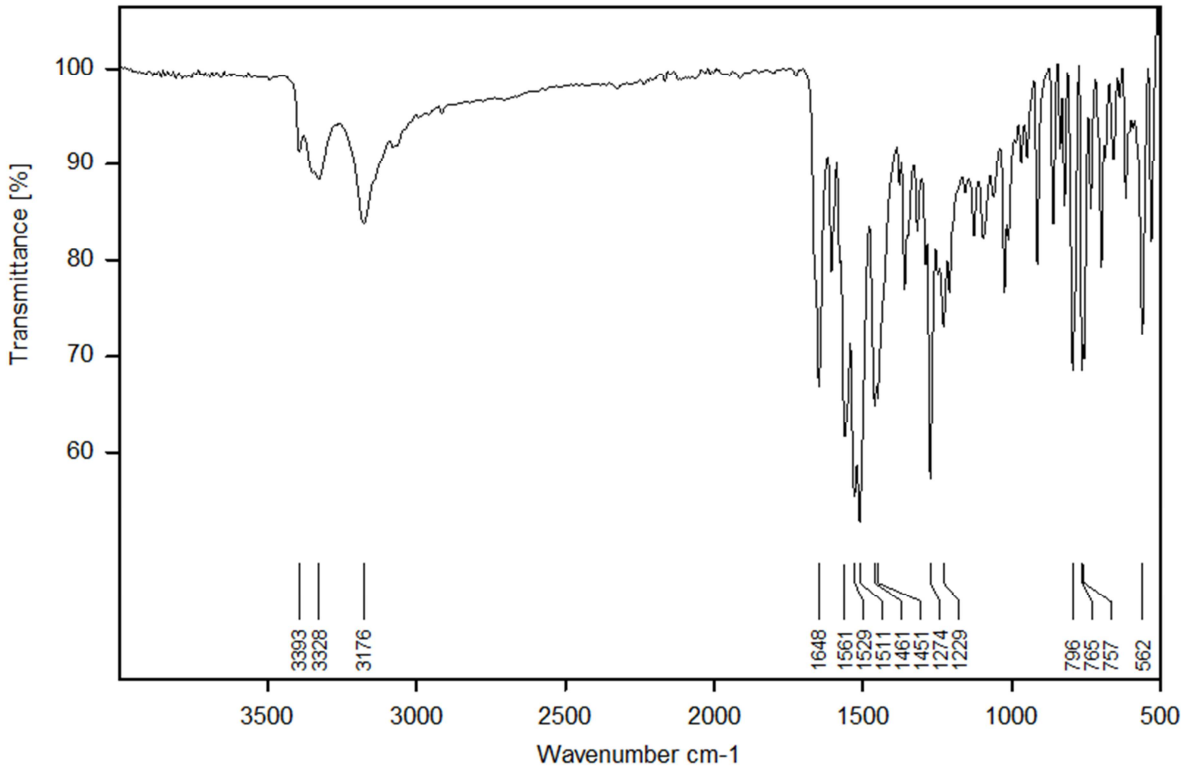
4-(5-methylthiophen-2-yl)-6-[3-(pyrrolidine-1-carbonyl)phenyl]pyrimidin-2-amine (39j)



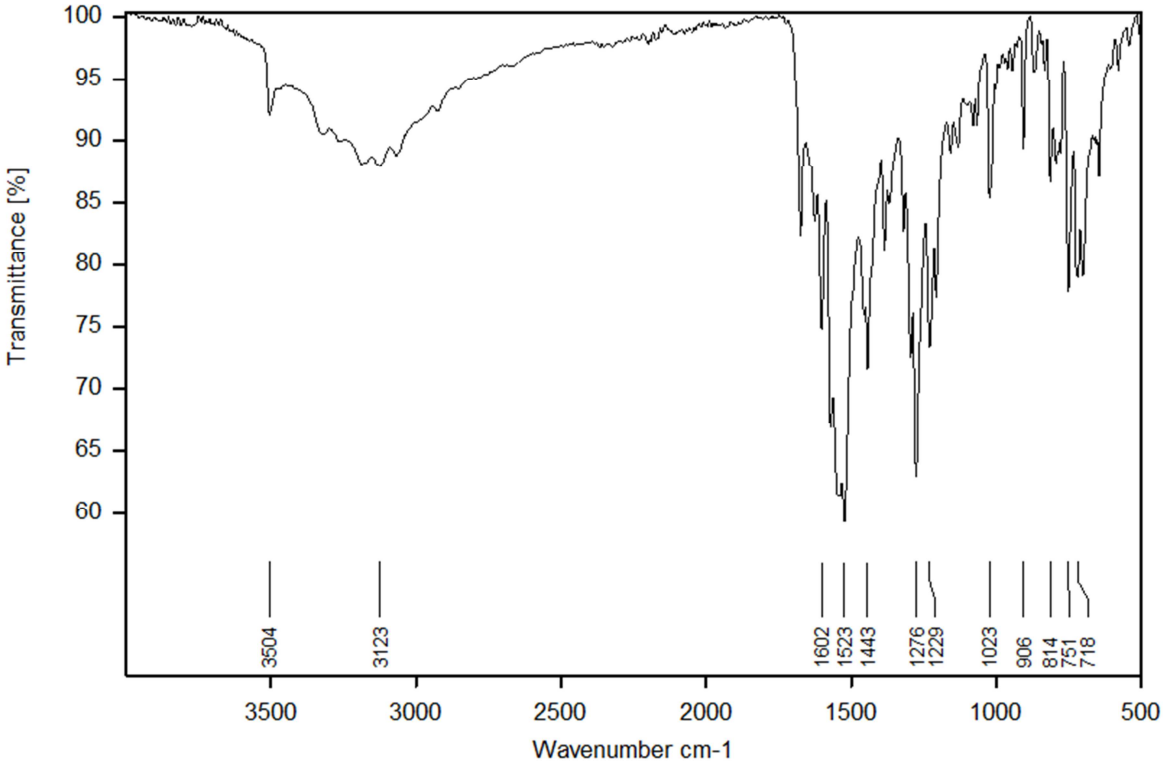
4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(furan-2-yl)pyrimidin-2-amine (39k)



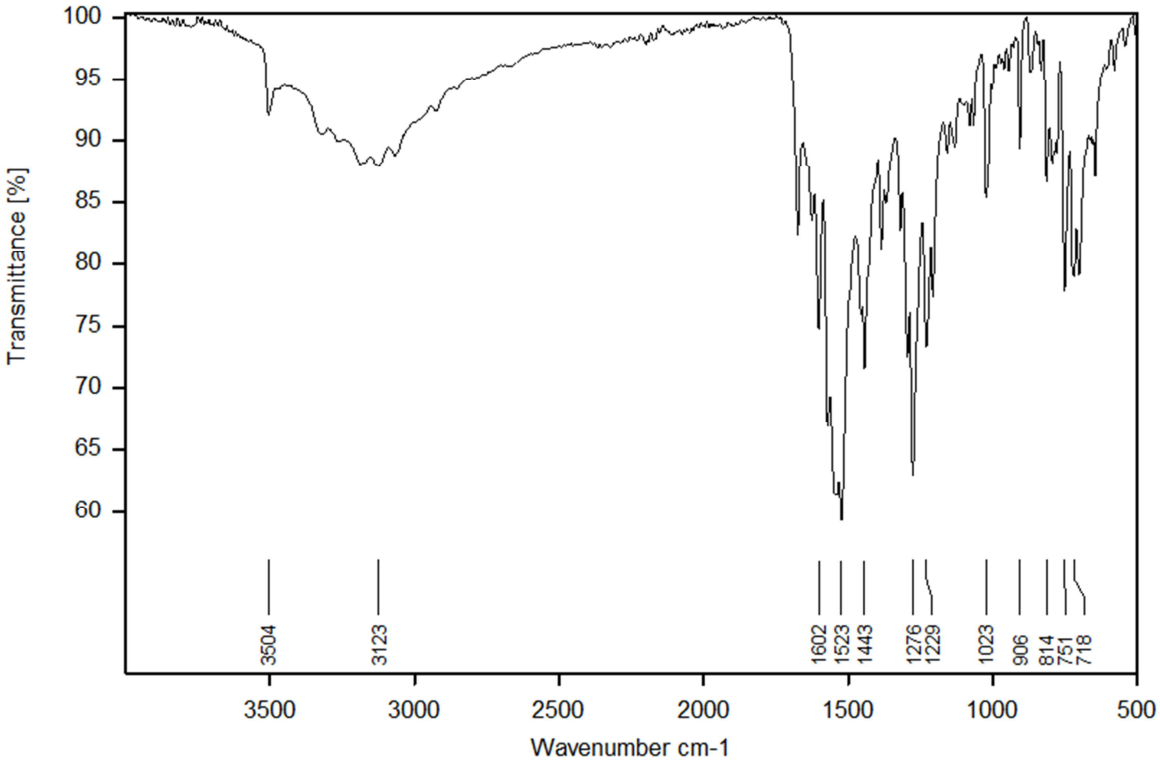
4-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-(1,3-benzothiazol-2-yl)benzamide (39l)



3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl}-N-(1,3-benzothiazol-2-yl)benzamide (39m)

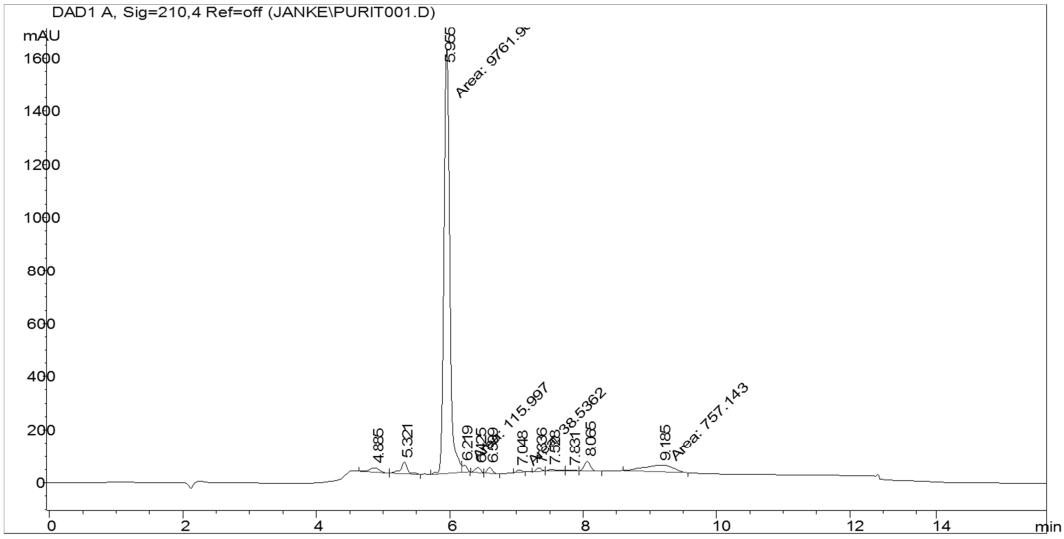


3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-6-chloro-1,3-benzothiazol-2-yl)benzamide (39n)

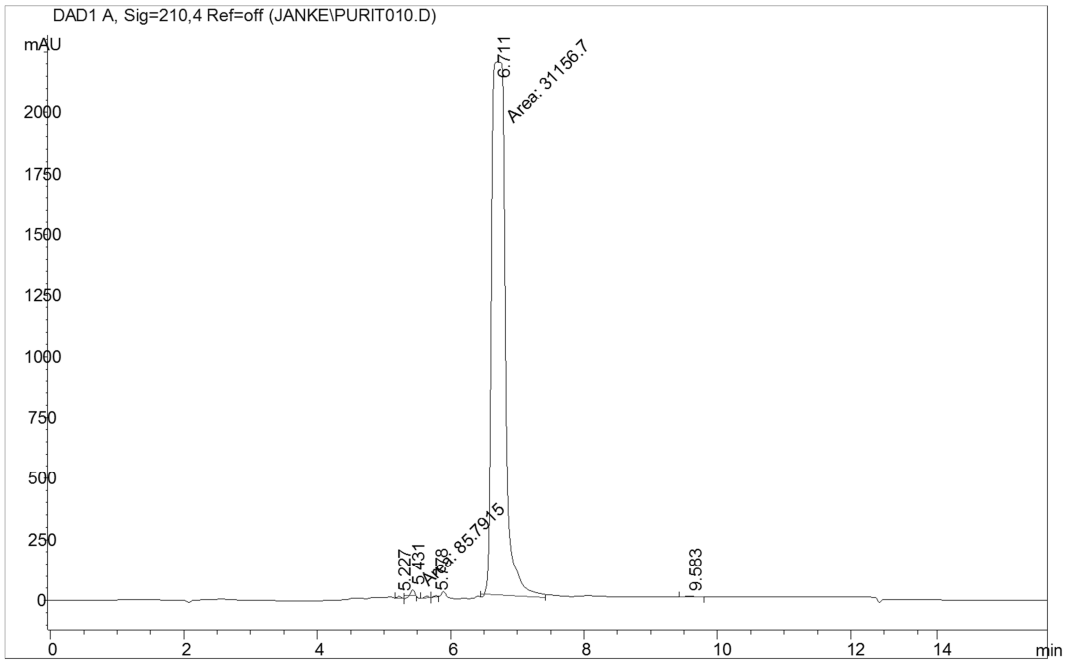


HPLC Chromatograms

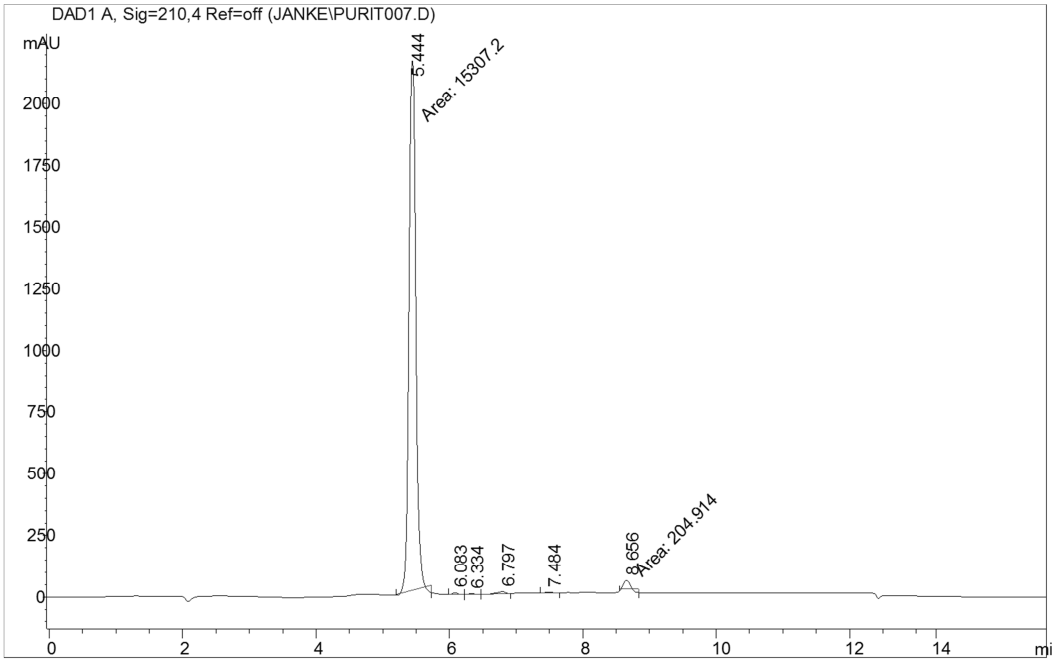
4-(5-methylfuran-2-yl)-6-[4-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39a)



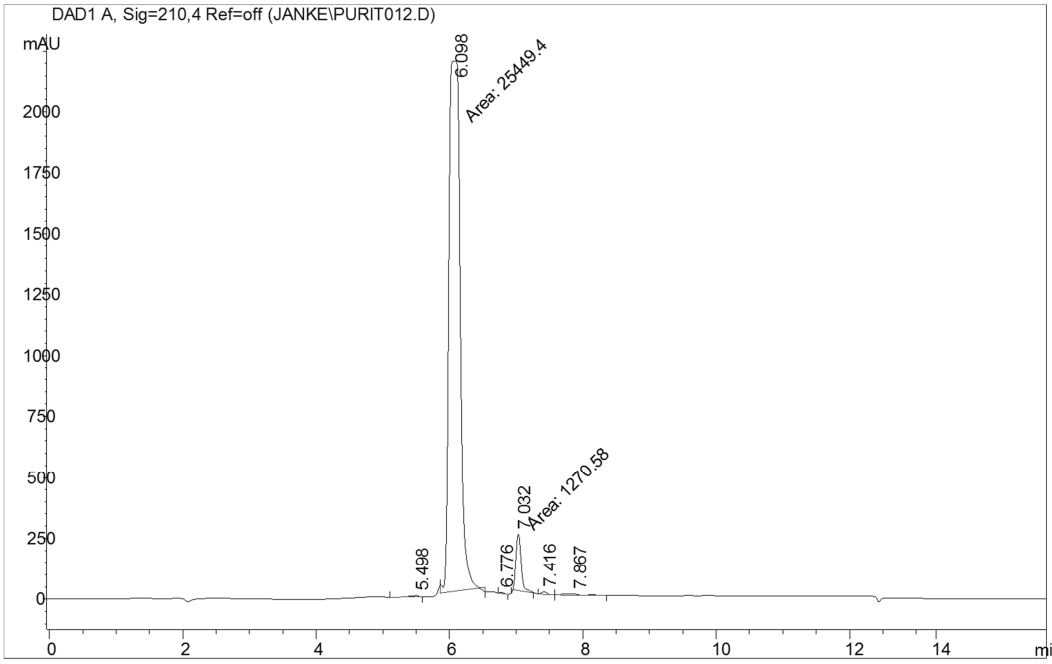
4-[3-(piperidine-1-carbonyl)phenyl]-6-(pyridin-2-yl)pyrimidin-2-amine (39b)



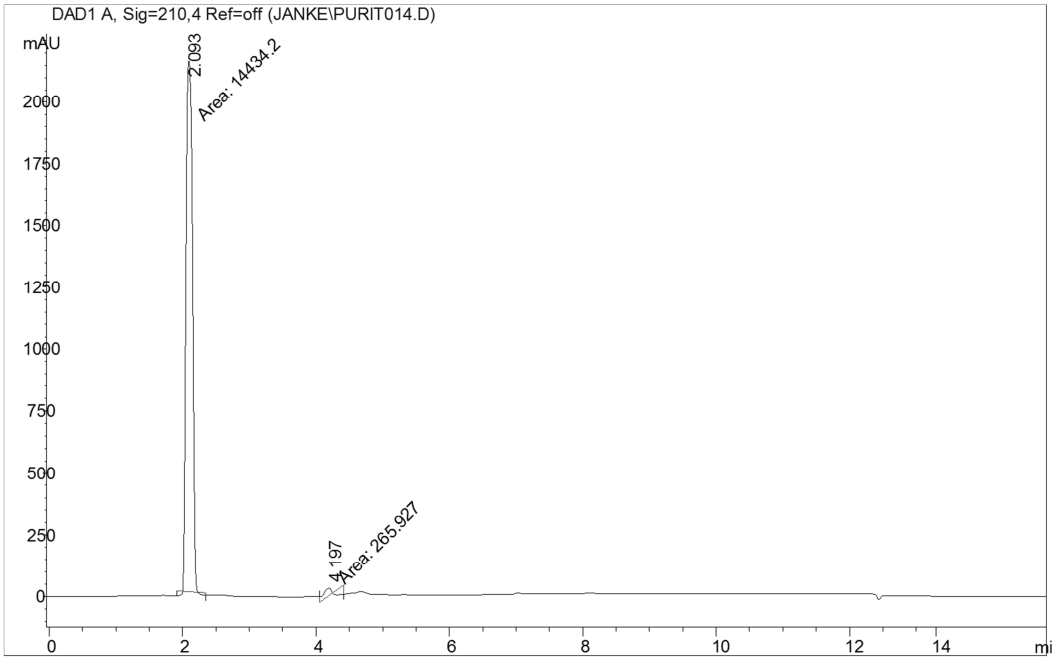
4-phenyl-6-[3-(piperidine-1- carbonyl)phenyl]pyrimidin-2-amine (39c)



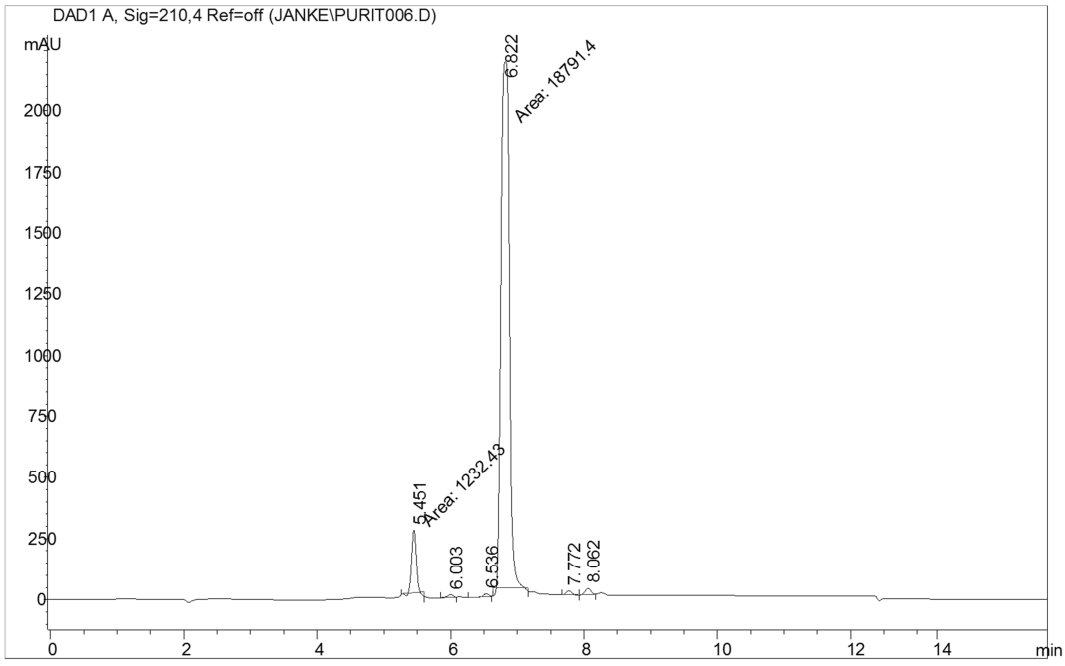
4-(furan-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39d)



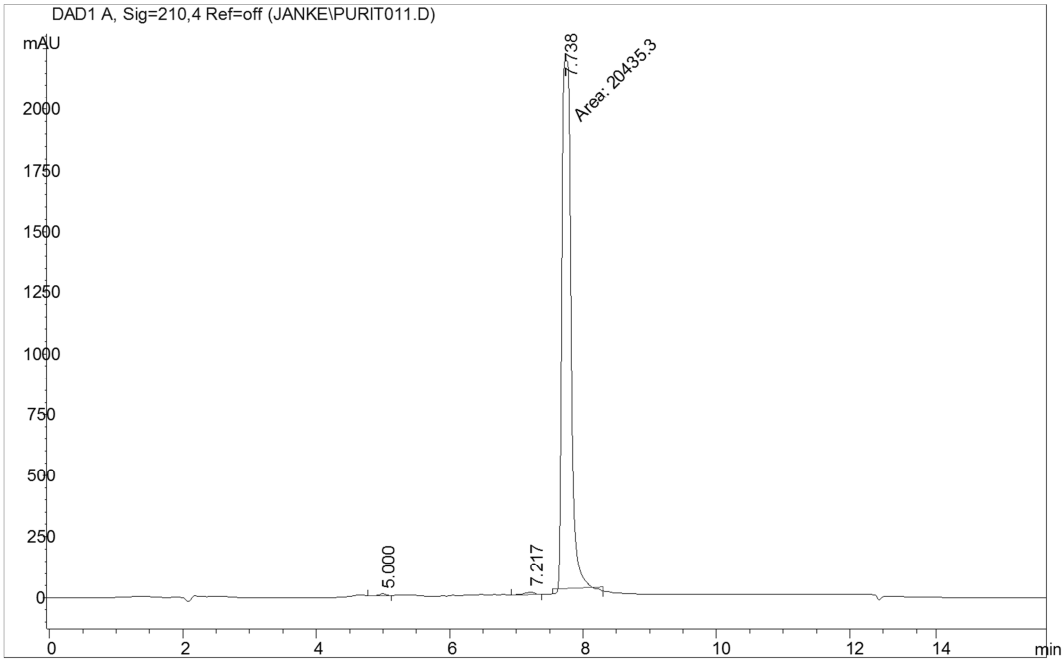
4-(4-fluorophenyl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39e)



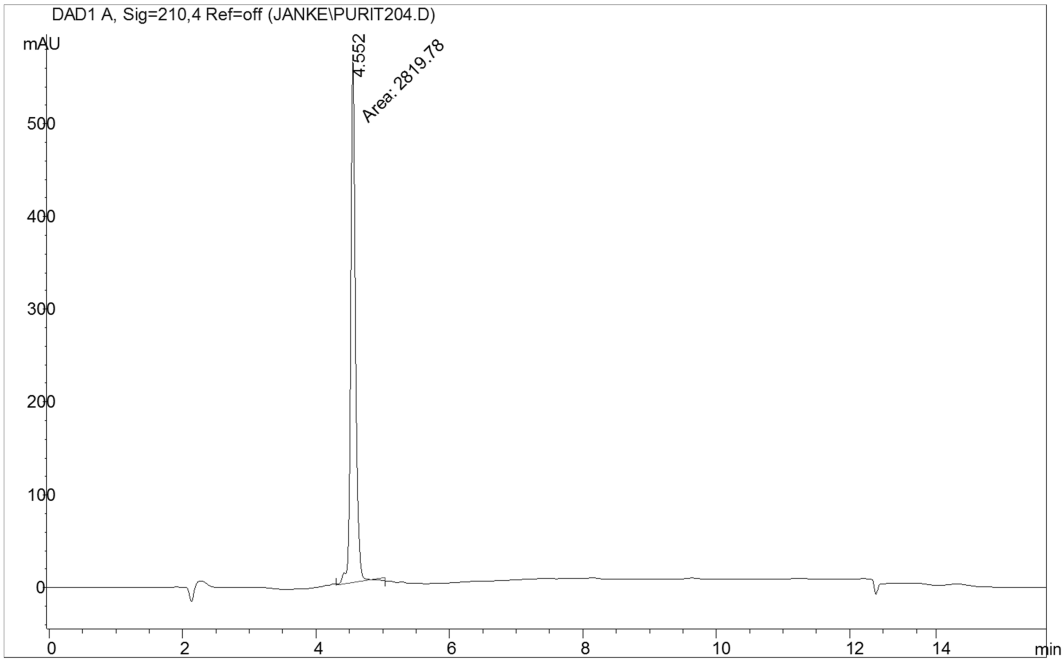
4-(5-methylthiophen-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39f)



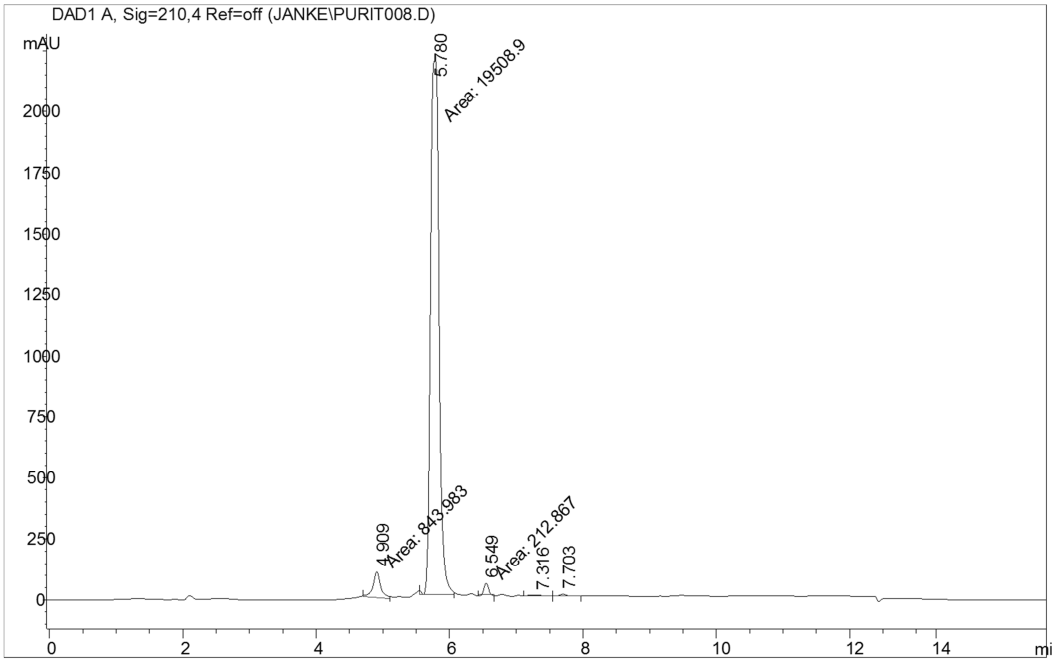
4-(1-benzofuran-2-yl)-6-[3-(piperidine-1-carbonyl)phenyl]pyrimidin-2-amine (39g)



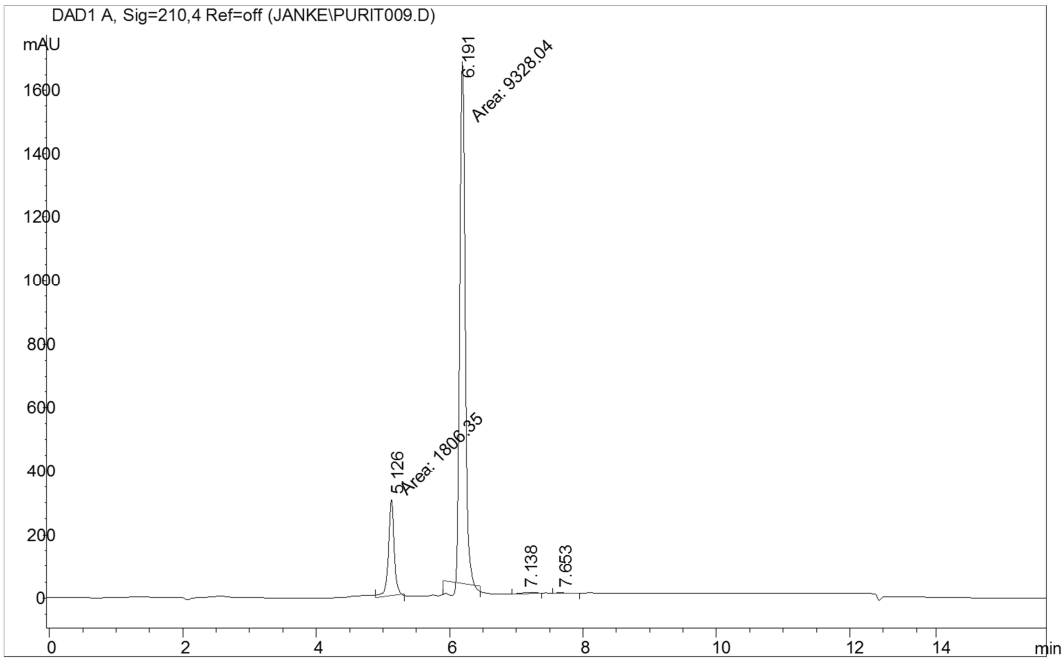
4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(5-methylthiophen-2-yl)pyrimidin-2-amine (39h)



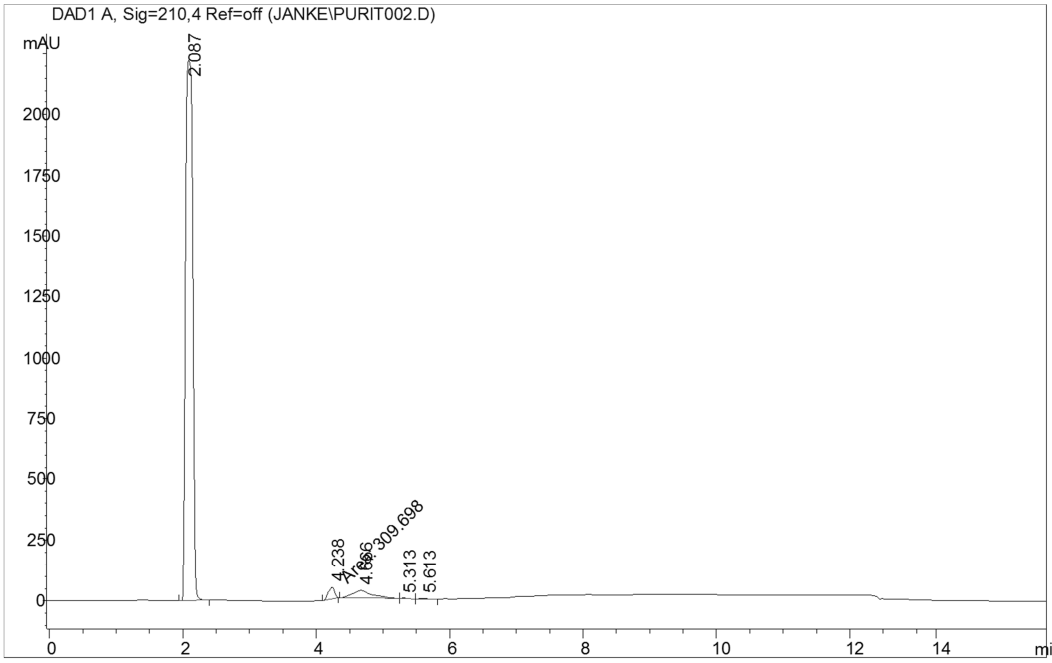
4-(5-methylthiophen-2-yl)-6-[3-(morpholine-4-carbonyl)phenyl]pyrimidin-2-amine (39i)



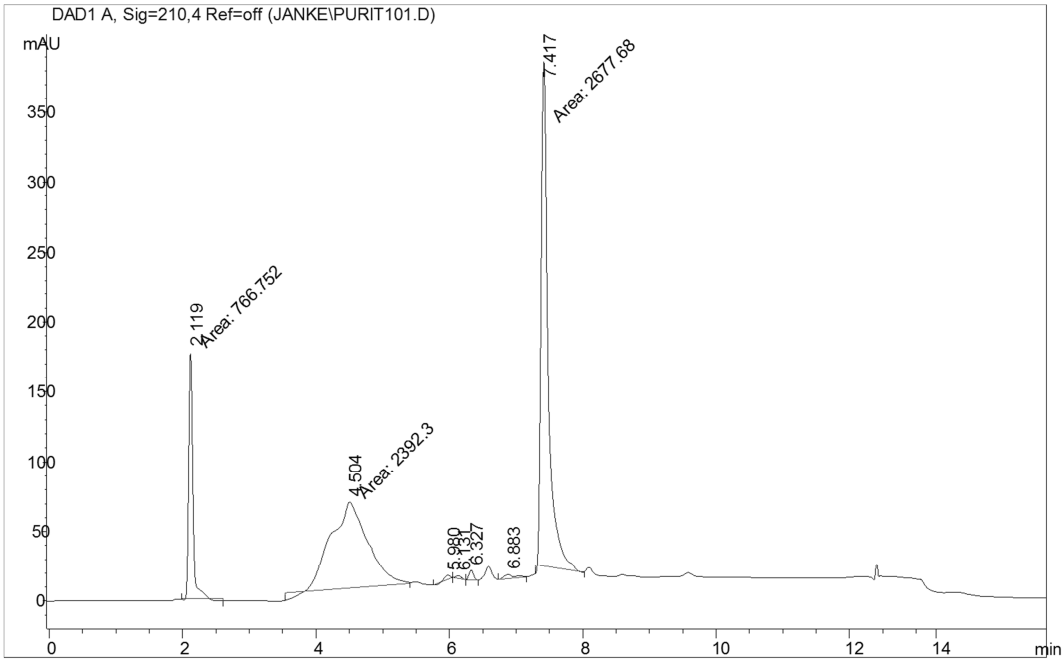
4-(5-methylthiophen-2-yl)-6-[3-(pyrrolidine-1-carbonyl)phenyl]pyrimidin-2-amine (39j)



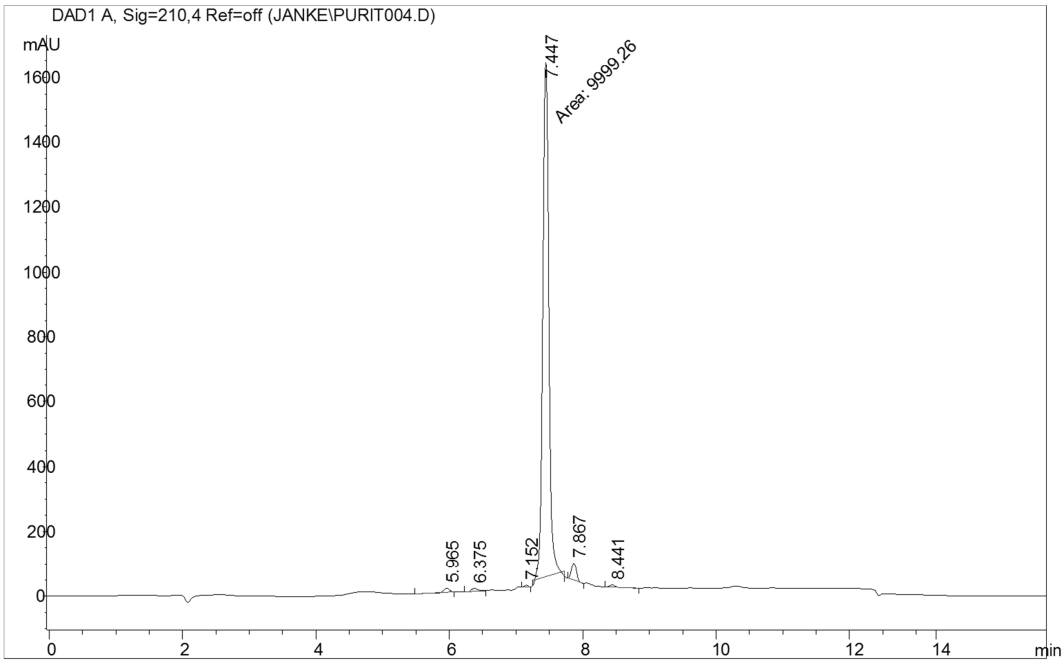
4-[3-(4-ethylpiperazine-1-carbonyl)phenyl]-6-(furan-2-yl)pyrimidin-2-amine (39k)



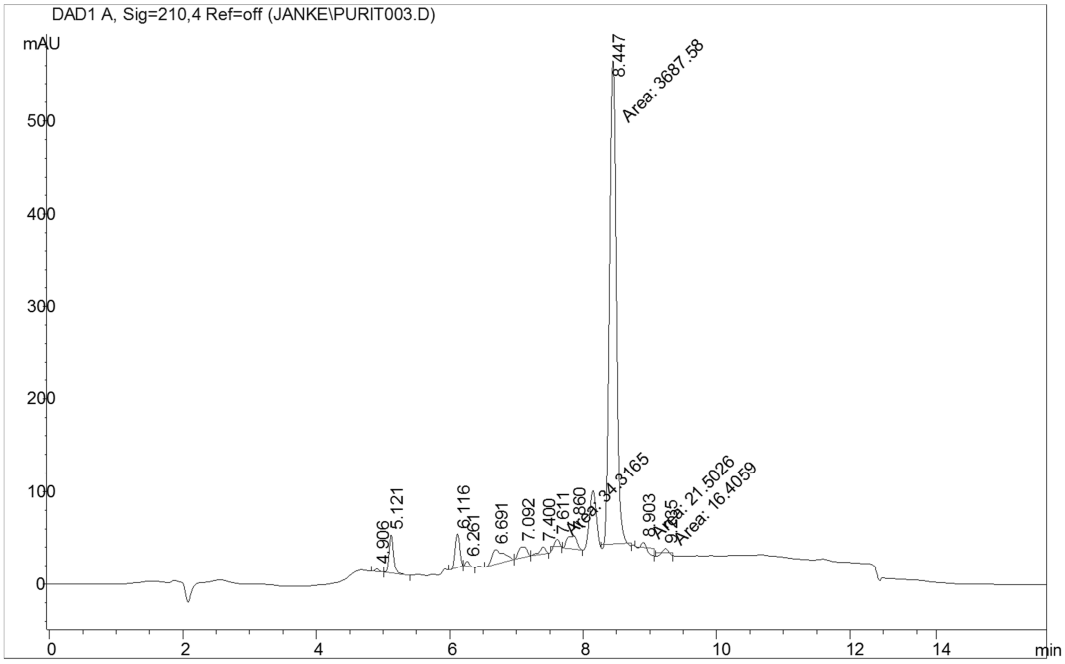
4-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-(1,3-benzothiazol-2-yl)benzamide (39l)



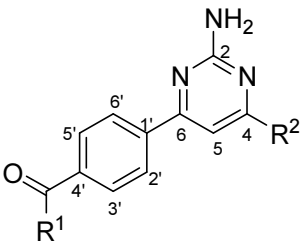
3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl}-N-(1,3-benzothiazol-2-yl)benzamide (39m)



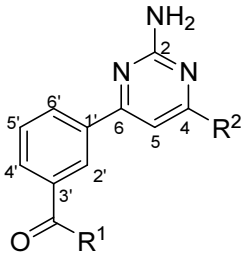
3-[2-amino-6-(5-methylfuran-2-yl)pyrimidin-4-yl]-N-6-chloro-1,3-benzothiazol-2-yl)benzamide (39n)



IC_{50} values obtained during Radioligand binding assays



39a, **39l 39b** - **39k**,



39m - **39n**

	R^1	R^2	$A_{2A}IC_{50}$ (nM)	A_1IC_{50} (nM)
39a	1-piperidinyl	2-(5-methylfuranyl)	20656 ± 2773	2601 ± 38.5
39l	1,3-benzothiazol-2-amine	2-(5-methylfuranyl)	191437 ± 16114	78.0 ± 3.24
39b	1-piperidinyl	2-pyridinyl	10.3 ± 0.87	21.0 ± 1.18
39c	1-piperidinyl	phenyl	5.37 ± 0.60	1.32 ± 0.10
39d	1-piperidinyl	2-furanyl	5.61 ± 0.85	10.7 ± 1.56
39e	1-piperidinyl	4-fluorophenyl	20.0 ± 1.03	3.53 ± 0.34
39f	1-piperidinyl	2-(5-methylthienyl)	0.65 ± 0.28	2.97 ± 0.31
39g	1-piperidinyl	2-benzofuranyl	69.3 ± 1.72	15.0 ± 3.46
39h	4-ethyl-1-piperazinyl	2-(5-methylthienyl)	37.4 ± 1.23	22.9 ± 1.45
39i	morpholinyl	2-(5-methylthienyl)	27.2 ± 10.8	9.06 ± 2.13
39j	pyrrolidinyl	2-(5-methylthienyl)	147 ± 0.70	22.3 ± 4.13
39k	4-ethyl-1-piperazinyl	2-furanyl	13.6 ± 0.10	170 ± 7.85
39m	1,3-benzothiazol-2-amine	2-(5-methylfuranyl)	670115 ± 6252	556 ± 46.5
39n	6-chloro-1,3-benzothiazol-2-amine	2-(5-methylfuranyl)	38447 ± 64.5	380 ± 26.7

In Vivo Data tables

Istradefylline (KW 6002) after 90 minutes:

Control group receiving haloperidol (5 mg/kg) and DMSO:

Test animal	Time measured (seconds)
1	120
2	120
3	120
4	60
5	120
6	57
7	120
8	120
9	120
10	120

Group 2 receiving haloperidol (5 mg/kg) and 0.4 mg/kg KW 6002:

Test animal	Time measured (seconds)
1	14
2	28
3	10
4	22
5	69
6	18
7	12
8	25
9	15
10	15

Group 3 receiving haloperidol (5 mg/kg) and 2 mg/kg KW 6002:

Test animal	Time measured (seconds)
1	0
2	11
3	11
4	9
5	9
6	7
7	9
8	0
9	8
10	17

Compound 39f at 90 min and 180 min:

Control group receiving haloperidol (5 mg/kg) and DMSO:

Test animal	Time measured (seconds)	Time measured (seconds)
1	120	120
2	120	68
3	120	97
4	120	78
5	120	106
6	120	120
7	120	120
8	72	48
9	120	120
10	120	120

Group 2 receiving haloperidol (5 mg/kg) and 0.4 mg/kg compound 39f:

Test animal	Time measured (seconds)	Time measured (seconds)
1	28	120
2	120	120
3	120	120
4	110	100
5	120	25
6	117	120
7	120	120
8	120	120
9	120	120
10	37	51

Group 3 receiving haloperidol (5 mg/kg) and 2 mg/kg compound 39f:

Test animal	Time measured (seconds)	Time measured (seconds)
1	38	47
2	103	46
3	120	36
4	120	60
5	22	75
6	120	120
7	120	87
8	120	34
9	120	76
10	5	22

Compound 39c after 90 minutes:

Control group receiving haloperidol (5 mg/kg) and DMSO:

Test animal	Time measured (seconds)
1	120
2	120
3	120
4	25
5	120
6	120
7	120
8	58
9	102
10	49

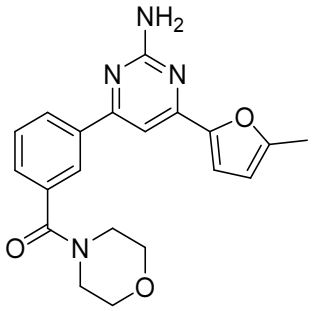
Group 2 receiving haloperidol (5 mg/kg) and 0.4 mg/kg compound 39c:

Test animal	Time measured (seconds)
1	19
2	11
3	120
4	19
5	16
6	15
7	24
8	20
9	29
10	120

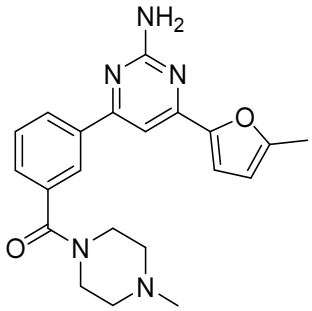
Group 3 receiving haloperidol (5 mg/kg) and 2 mg/kg compound 39c:

Test animal	Time measured (seconds)
1	4
2	18
3	0
4	25
5	40
6	20
7	3
8	8
9	18
10	20

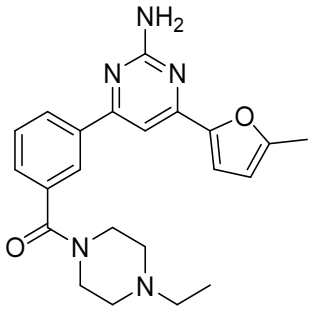
Structures of compounds SJR1 - 5 used in QSAR study (Robinson, 2013)



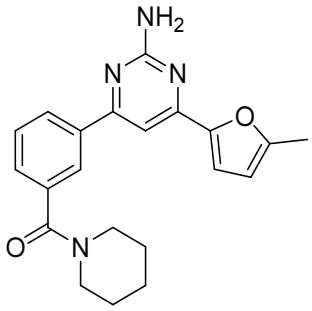
SJR1*



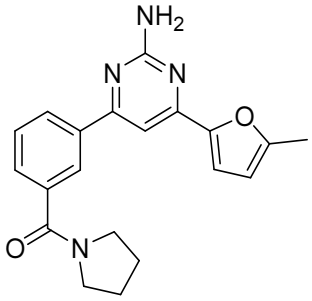
SJR2*



SJR3*



SJR4*



SJR5*