

Supporting Information

Discovery of New Benzothiazole-Based Inhibitors of Breakpoint Cluster Region-Abelson Kinase Including the T315I Mutant

*Seunghye Hong^{a+}, Jinhee Kim^{a+}, Sun-Mi Yun^{b+}, Hyunseung Lee^b, Yoonsu Park^a, Soon-Sun Hong^{*b},
and Sungwoo Hong^{*a}*

^aDepartment of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 305-701, Korea, ^bDepartment of Biomedical Sciences, College of Medicine, Inha University, Incheon, 400-712, Korea.

I. Kinase Selectivity	S2
II. Comparison of Effect of Core on Enzyme Potency	S4
III. Anti-proliferative Effects of Selected Compounds	S5
IV. Cell Cycle Analysis	S5

Appendix I

Spectral Copies of ¹H- and ¹³C-NMR, HRMS Data Obtained in this Study	S6
---	----

Table S1. Kinase affinity of compound **9a**. Panel of 96 Kinases were tested at 1 μ M in a high-throughput binding assay (Ambit Bioscience).

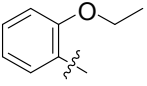
KINOMEScan Gene Symbol	Entrez Gene Symbol	Percent Control (POC)
ABL1(E255K)-phosphorylated	ABL1	4.6
ABL1(T315I)-phosphorylated	ABL1	4.5
ABL1-phosphorylated	ABL1	5
ACVR1B	ACVR1B	100
ADCK3	CABC1	100
AKT1	AKT1	67
AKT2	AKT2	100
ALK	ALK	100
AURKA	AURKA	100
AURKB	AURKB	100
AXL	AXL	85
BMPR2	BMPR2	100
BRAF	BRAF	100
BRAF(V600E)	BRAF	100
BTK	BTK	100
CDK11	CDK19	100
CDK2	CDK2	100
CDK3	CDK3	96
CDK7	CDK7	62
CDK9	CDK9	100
CHEK1	CHEK1	100
CSF1R	CSF1R	100
CSNK1D	CSNK1D	86
CSNK1G2	CSNK1G2	100
DCAMKL1	DCLK1	100
DYRK1B	DYRK1B	95
EGFR	EGFR	100
EGFR(L858R)	EGFR	100
EPHA2	EPHA2	100
ERBB2	ERBB2	100
ERBB4	ERBB4	100
ERK1	MAPK3	100
FAK	PTK2	100

FGFR2	FGFR2	100
FGFR3	FGFR3	91
FLT3	FLT3	94
GSK3B	GSK3B	100
IGF1R	IGF1R	100
IKK-alpha	CHUK	100
IKK-beta	IKBKB	100
INSR	INSR	91
JAK2(JH1domain-catalytic)	JAK2	100
JAK3(JH1domain-catalytic)	JAK3	86
JNK1	MAPK8	100
JNK2	MAPK9	100
JNK3	MAPK10	100
KIT	KIT	79
KIT(D816V)	KIT	93
KIT(V559D,T670I)	KIT	100
LKB1	STK11	100
MAP3K4	MAP3K4	100
MAPKAPK2	MAPKAPK2	100
MARK3	MARK3	100
MEK1	MAP2K1	100
MEK2	MAP2K2	100
MET	MET	100
MKNK1	MKNK1	100
MKNK2	MKNK2	71
MLK1	MAP3K9	100
p38-alpha	MAPK14	100
p38-beta	MAPK11	100
PAK1	PAK1	93
PAK2	PAK2	91
PAK4	PAK4	94
PCTK1	CDK16	100
PDGFRA	PDGFRA	79
PDGFRB	PDGFRB	16
PDPK1	PDPK1	67
PIK3C2B	PIK3C2B	100
PIK3CA	PIK3CA	100

PIK3CG	PIK3CG	93
PIM1	PIM1	100
PIM2	PIM2	74
PIM3	PIM3	100
PKAC-alpha	PRKACA	75
PLK1	PLK1	100
PLK3	PLK3	87
PLK4	PLK4	94
PRKCE	PRKCE	82
RAF1	RAF1	100
RET	RET	96
RIOK2	RIOK2	100
ROCK2	ROCK2	100
RSK2(Kin.Dom.1-N-terminal)	RPS6KA3	58
SNARK	NUAK2	100
SRC	SRC	72
SRPK3	SRPK3	100
TGFBR1	TGFBR1	100
TIE2	TEK	100
TRKA	NTRK1	100
TSSK1B	TSSK1B	96
TYK2(JH1domain-catalytic)	TYK2	73
ULK2	ULK2	100
VEGFR2	KDR	98
YANK3	STK32C	100
ZAP70	ZAP70	93

Table S2. Comparison of Effect of Benzoxazole Core on Enzyme Potency

Ar	X	Abl wt IC ₅₀ (nM)	Abl T315I IC ₅₀ (nM)
	N-H	18.8	6.22
	O	40.8	6.12
	S	0.06	0.11

	N-H	1.61	2.28
	O	N.D	11.6
	S	0.03	0.064

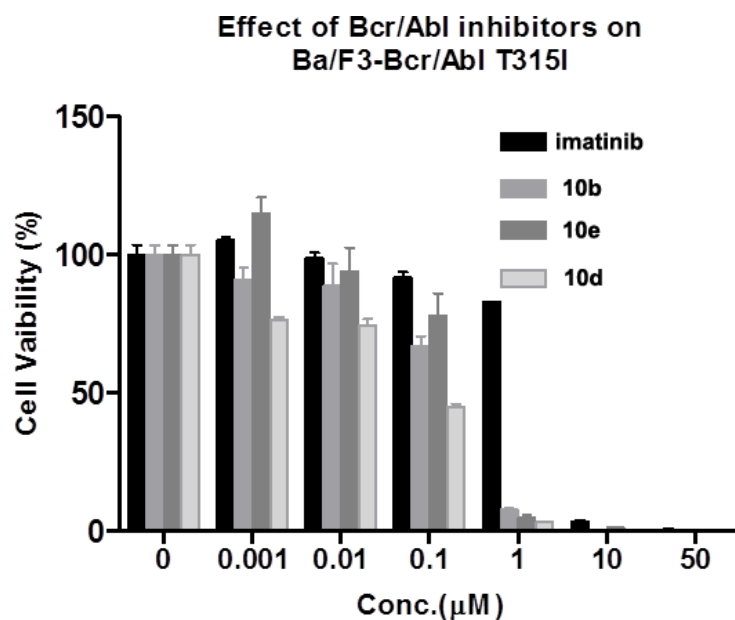


Figure S1. Anti-proliferative Effects of Selected Compounds on Bcr-Abl Transformed Ba/F3 Cells.

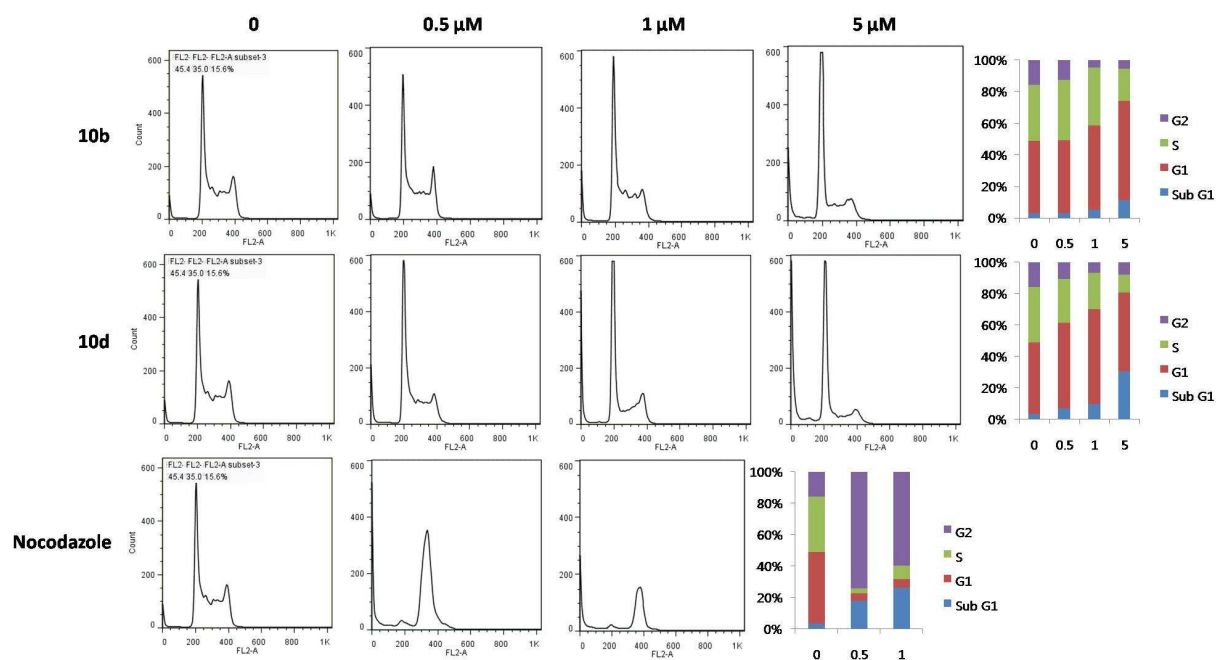
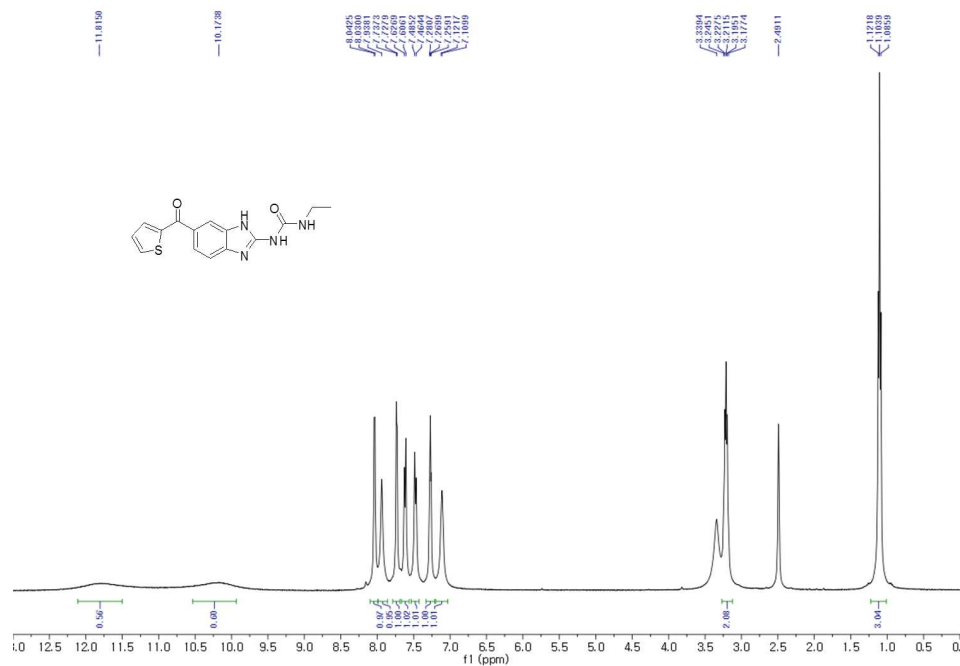


Figure S2. Cell cycle analysis of **10b**, **10d** and nocodazole.

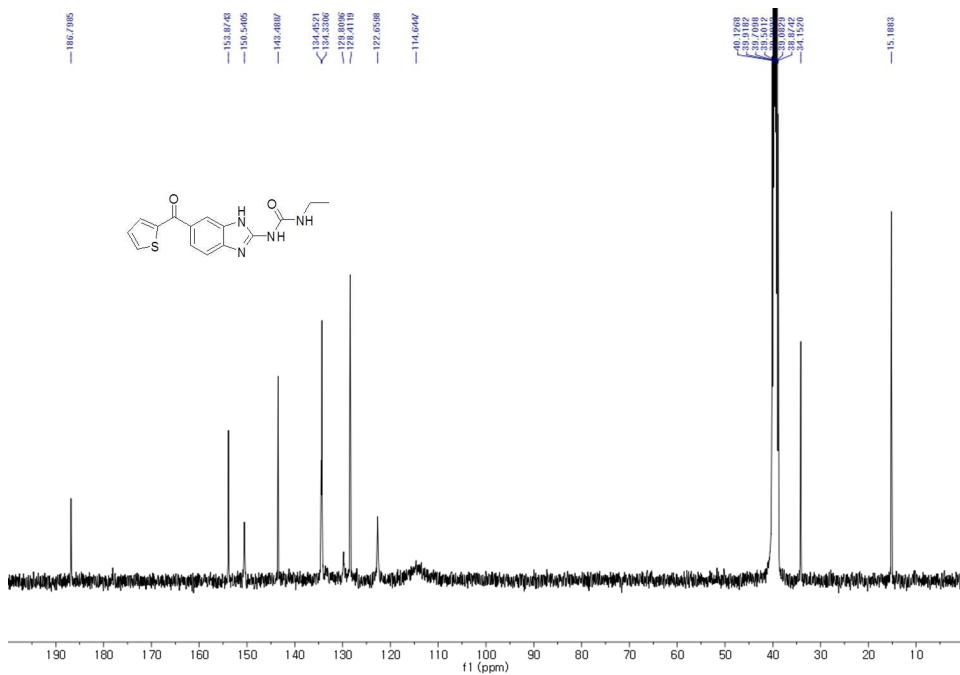
Appendix I

Spectral Copies of ^1H , ^{13}C NMR, HRMS, and HPLC

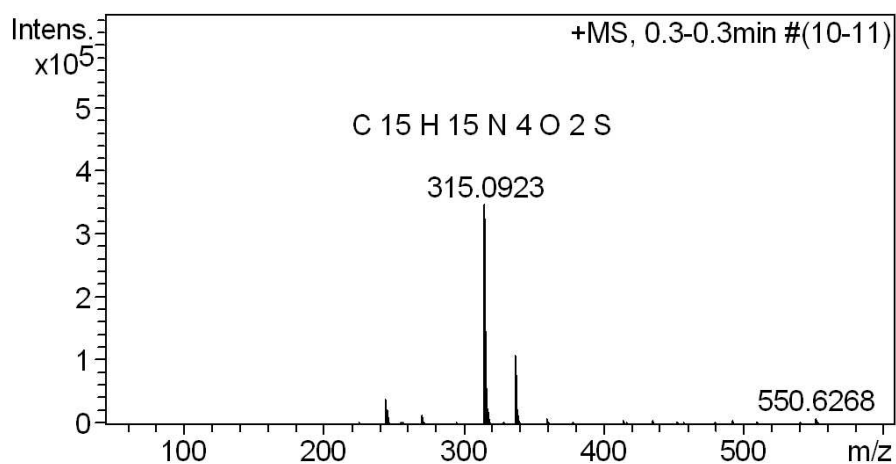
1-Ethyl-3-(5-(thiophene-2-carbonyl)-1H-benzo[d]imidazol-2-yl)urea (1).



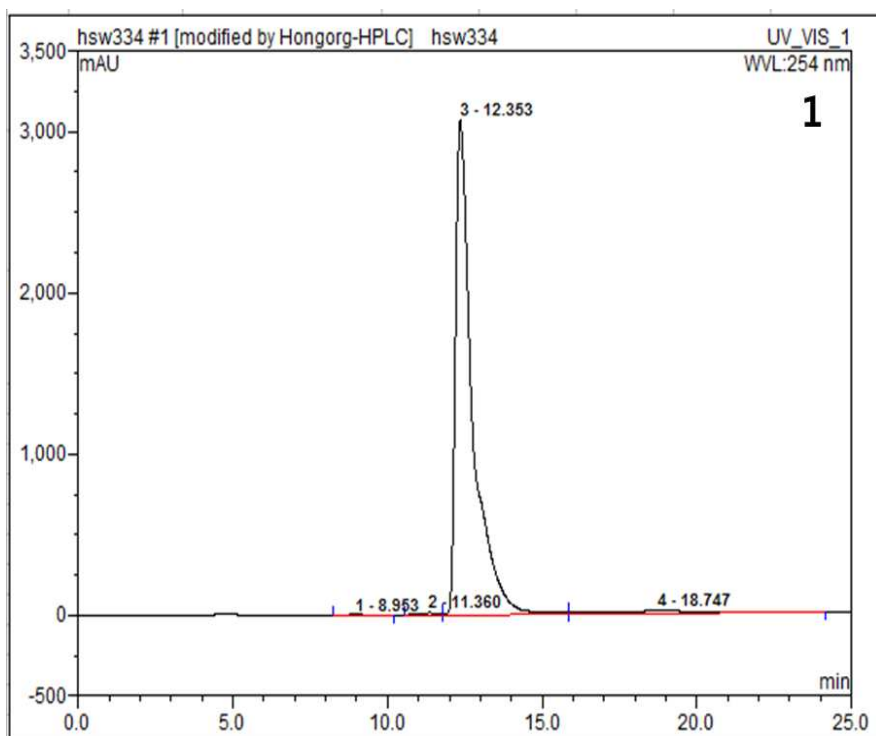
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆



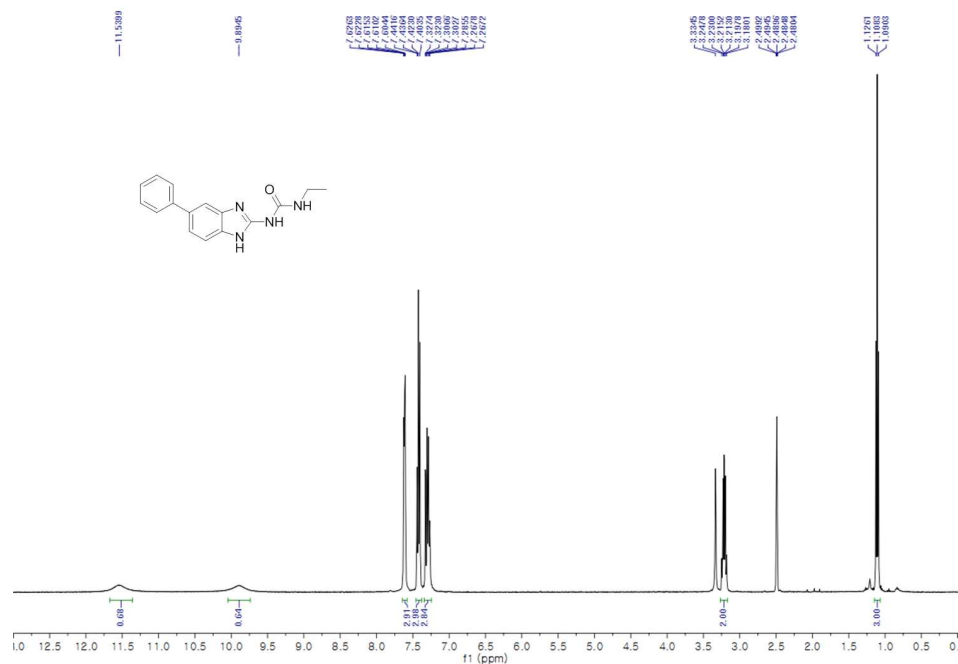
HRMS



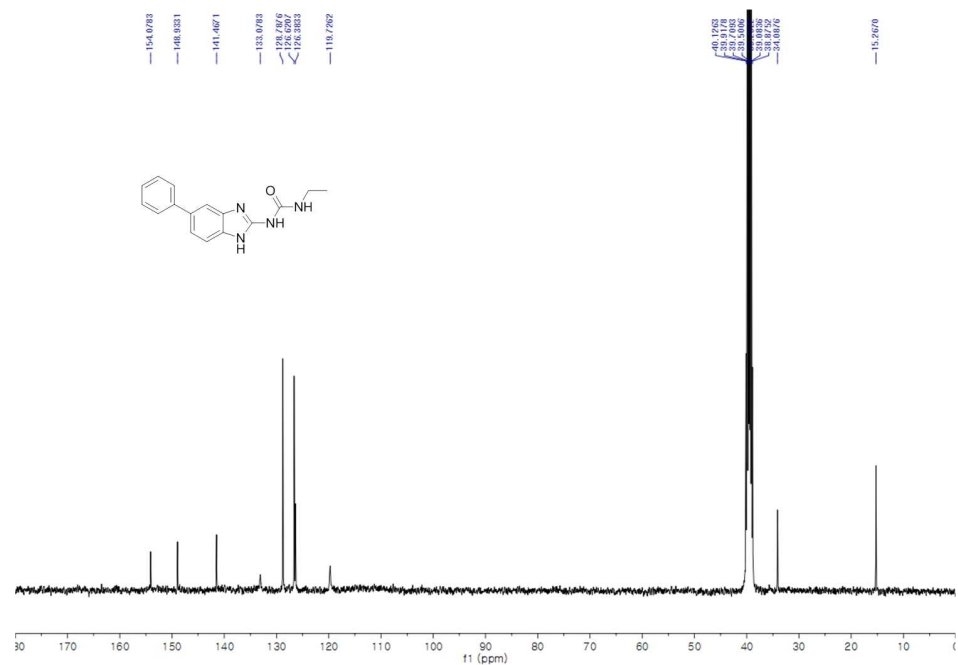
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	8.95	n.a.	2.476	2.010	0.10	n.a.	BMB*
2	11.36	n.a.	10.813	8.659	0.43	n.a.	BM *
3	12.35	n.a.	3066.387	1957.469	96.67	n.a.	M *
4	18.75	n.a.	12.527	56.857	2.81	n.a.	MB*
Total:			3092.203	2024.995	100.00	0.000	

HPLC-Purity

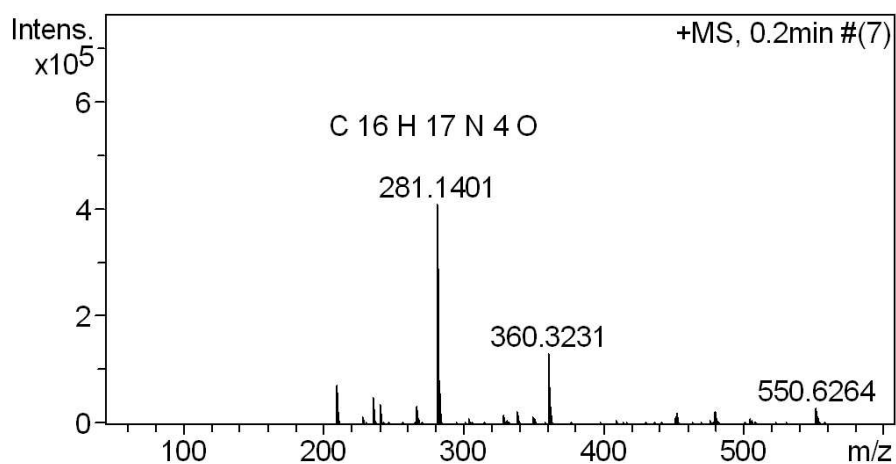
1-Ethyl-3-(6-phenyl-1H-benzo[d]imidazol-2-yl)urea (2).



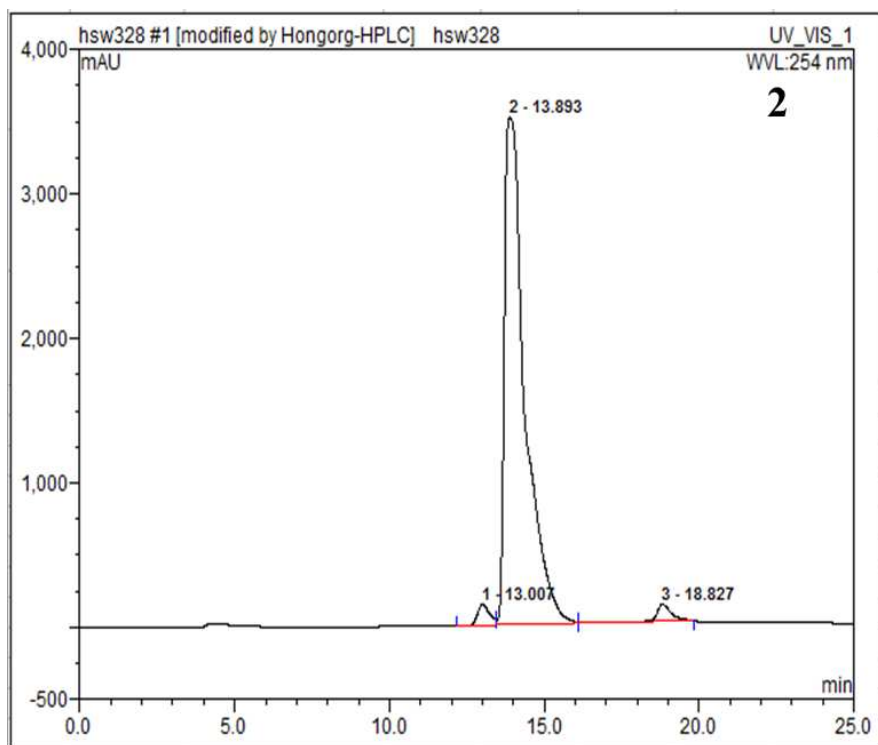
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆



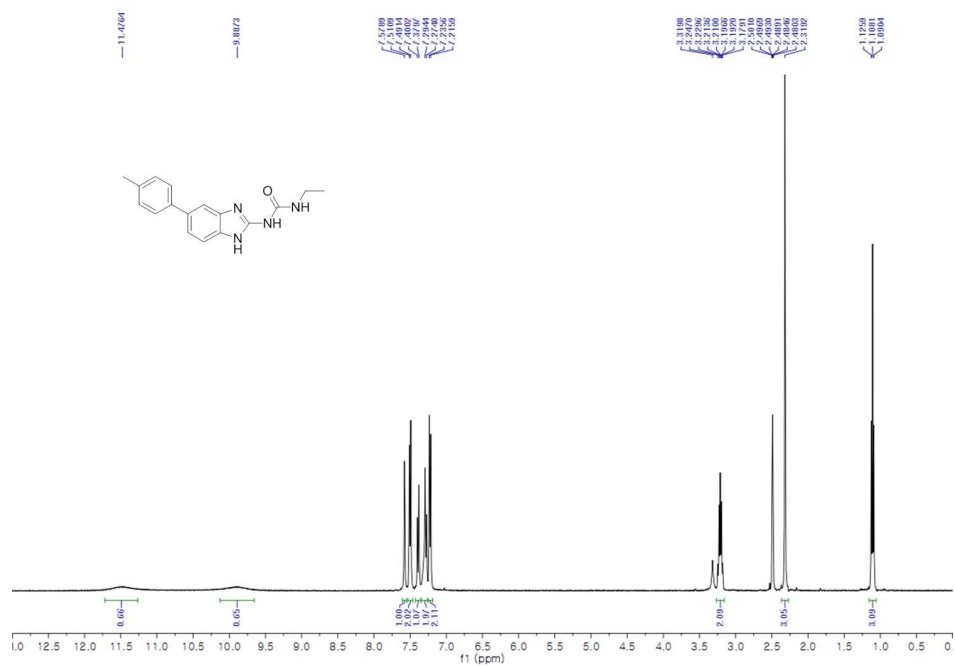
HRMS



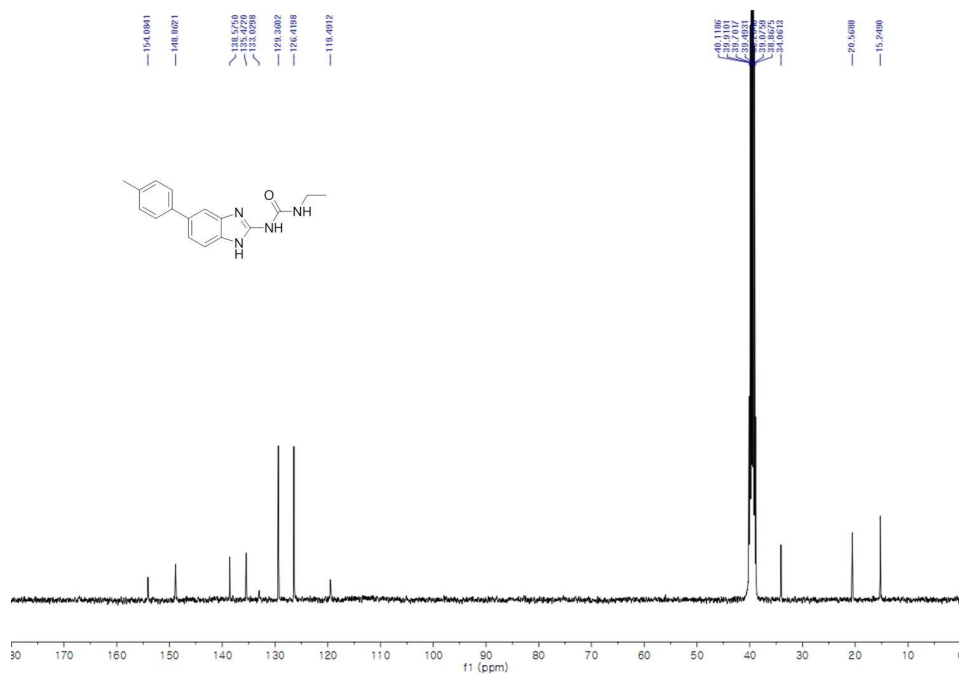
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13.01	n.a.	139.782	62.055	2.21	n.a.	BM *
2	13.89	n.a.	3506.634	2683.812	95.44	n.a.	M *
3	18.83	n.a.	117.235	66.224	2.35	n.a.	MB*
Total:			3763.651	2812.091	100.00	0.000	

HPLC-Purity

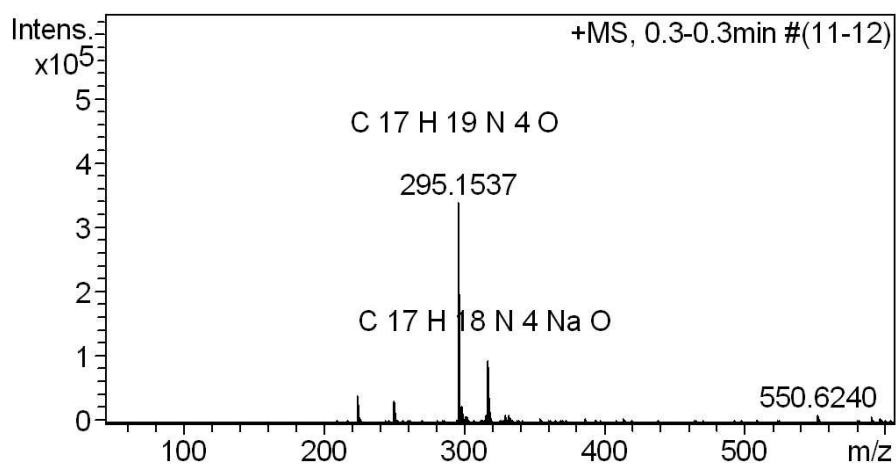
1-Ethyl-3-(5-*p*-tolyl-1*H*-benzo[*d*]imidazol-2-yl)urea (5a).



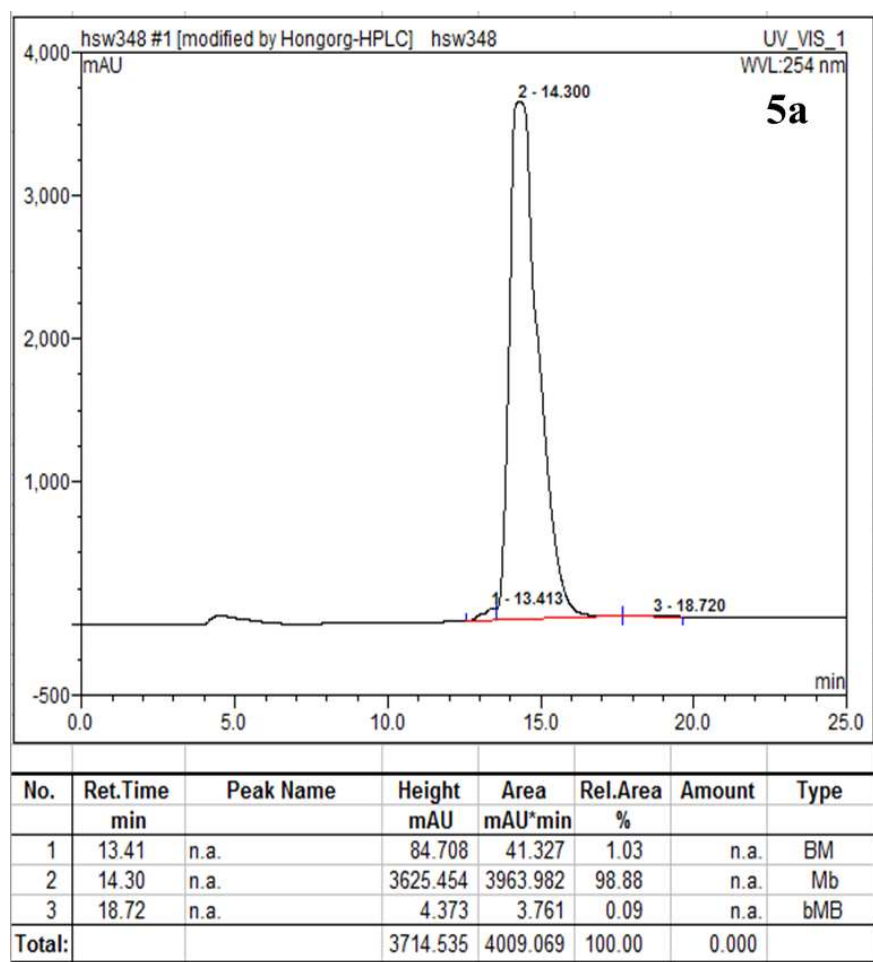
400 MHz, ^1H NMR in DMSO- d_6



100 MHz, ^{13}C NMR in DMSO- d_6

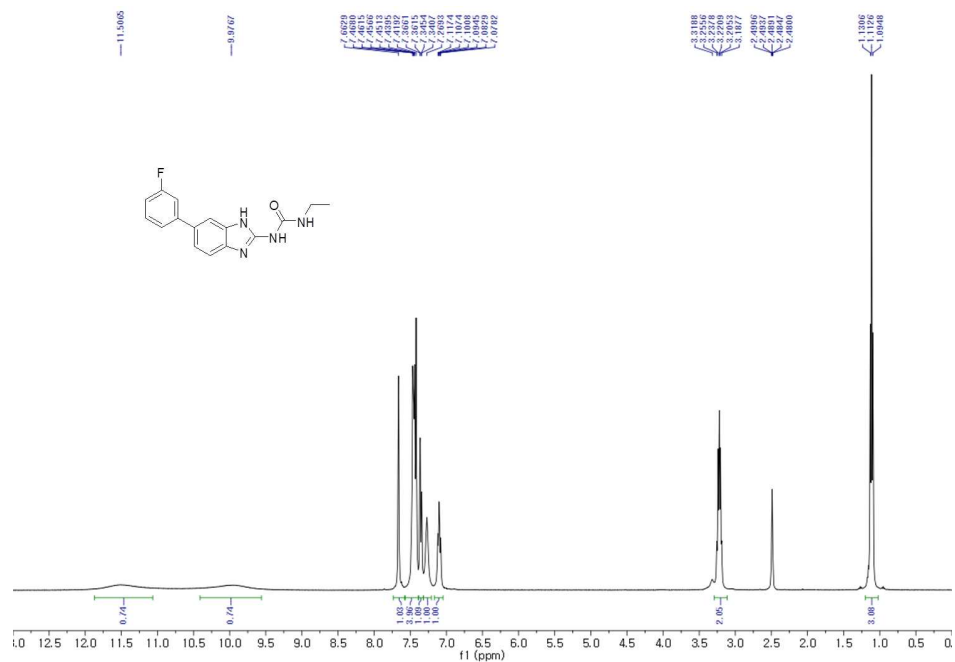


HRMS

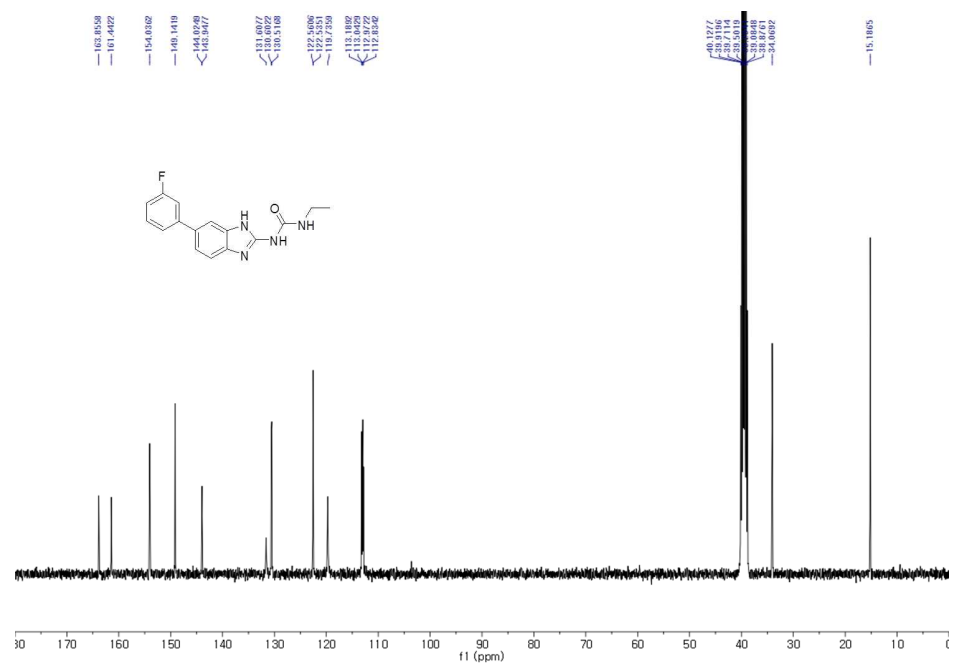


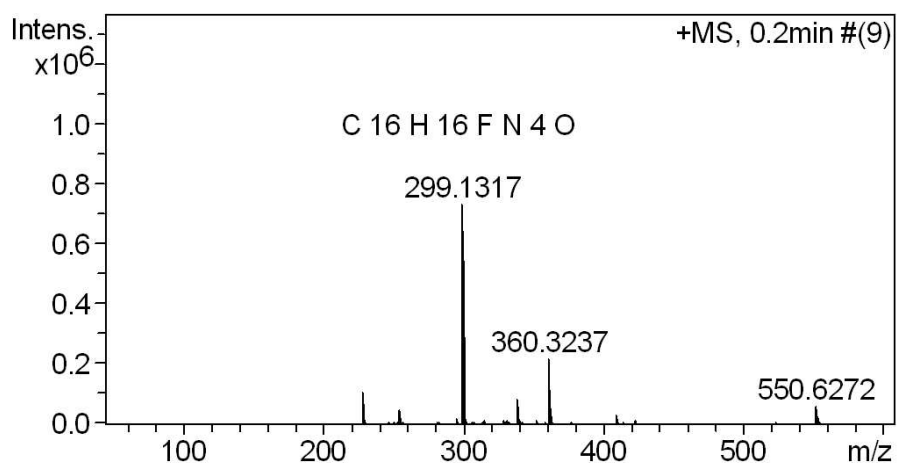
HPLC-Purity

1-Ethyl-3-(6-(3-fluorophenyl)-1H-benzo[d]imidazol-2-yl)urea (5b).

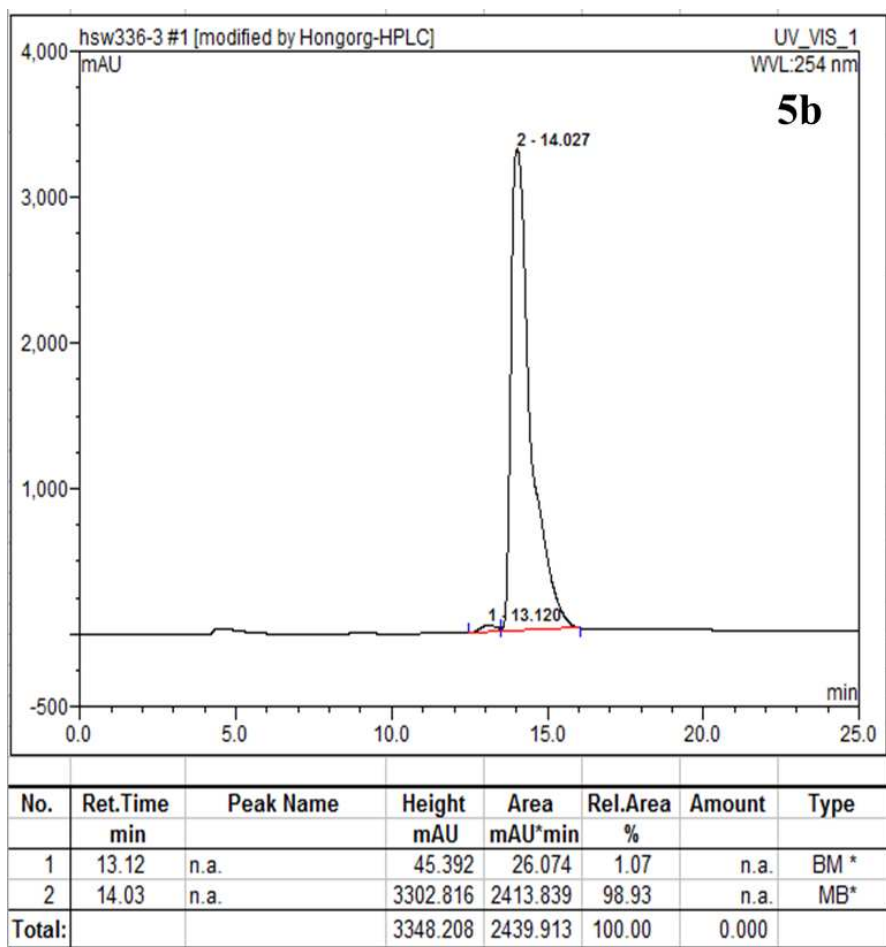


400 MHz, ¹H NMR in DMSO-*d*₆



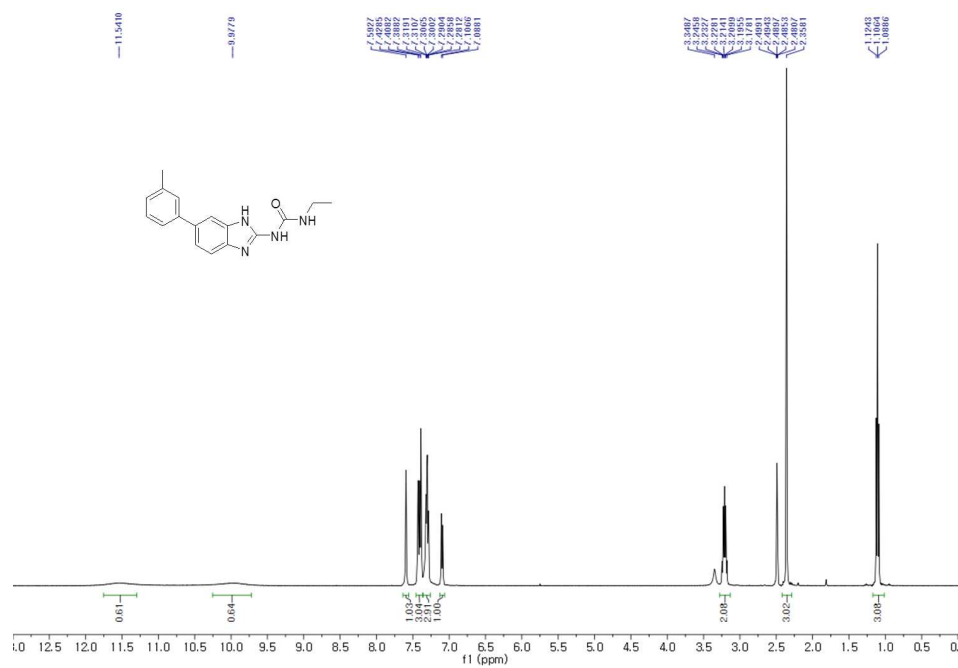


HRMS

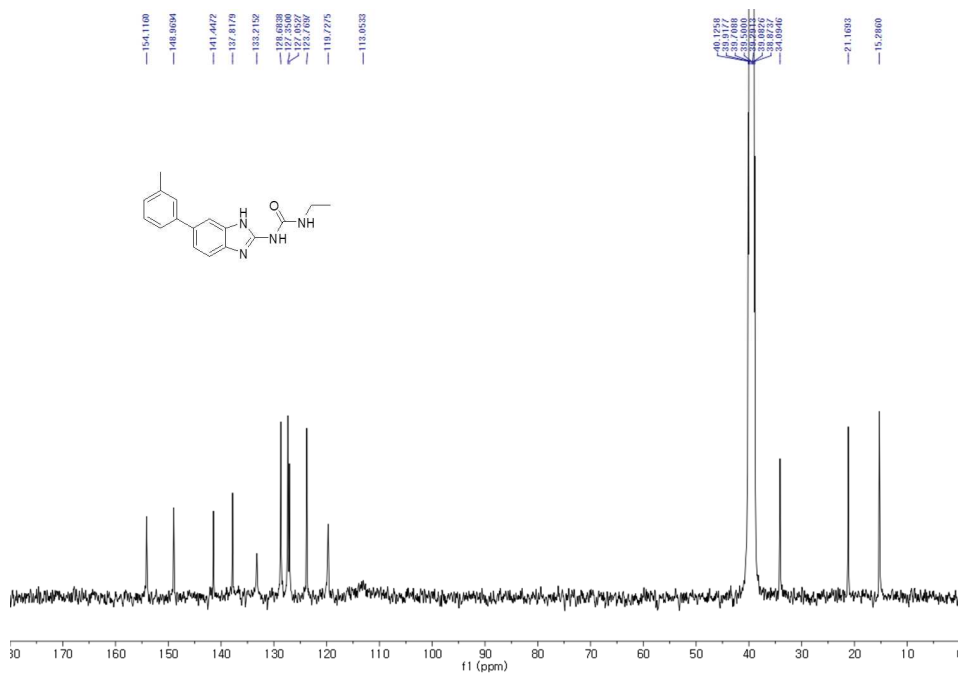


HPLC-Purity

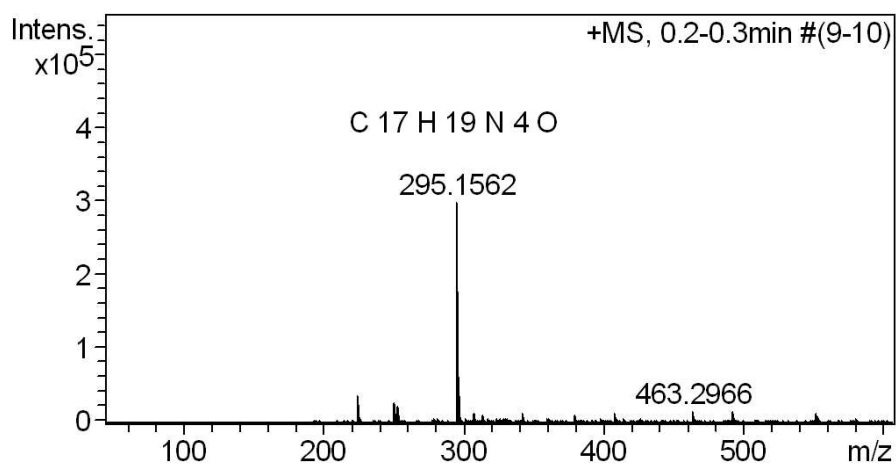
1-Ethyl-3-(6-*m*-tolyl-1*H*-benzo[*d*]imidazol-2-yl)urea (5c).



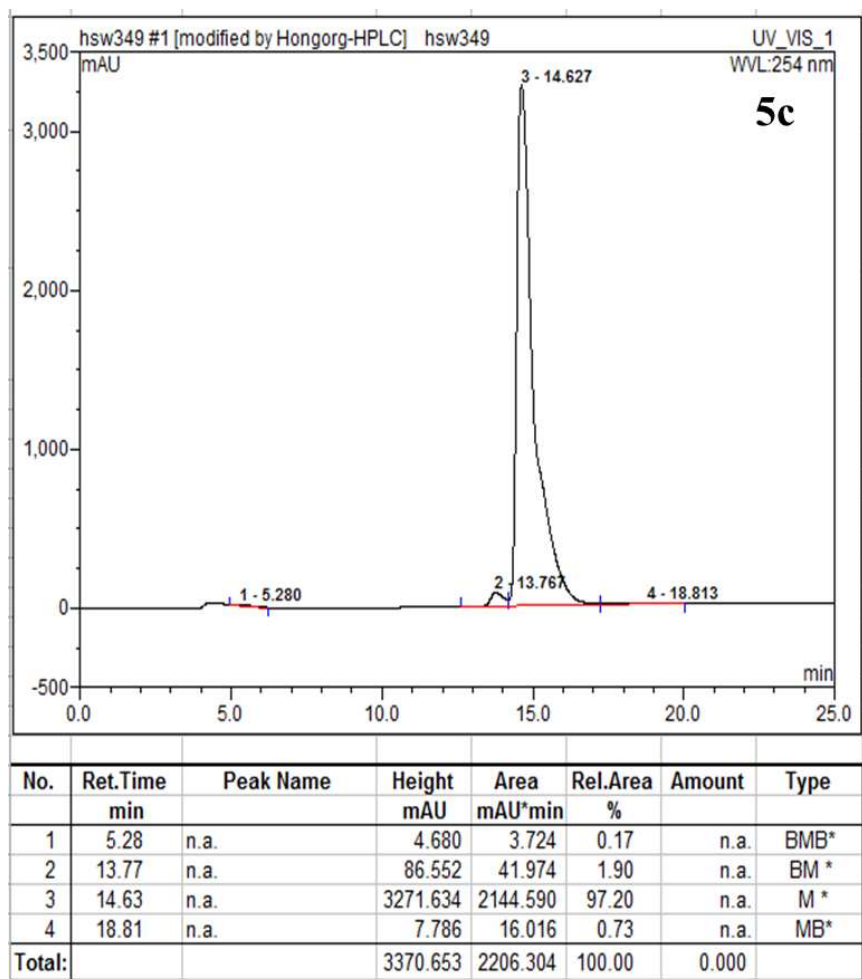
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ^{13}C NMR in DMSO- d_6

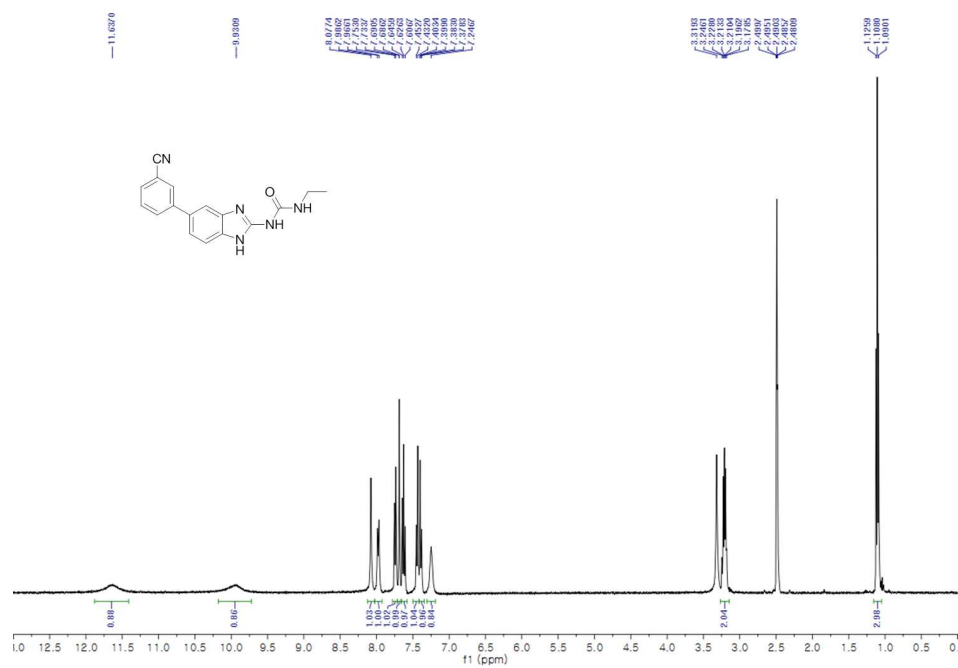


HRMS

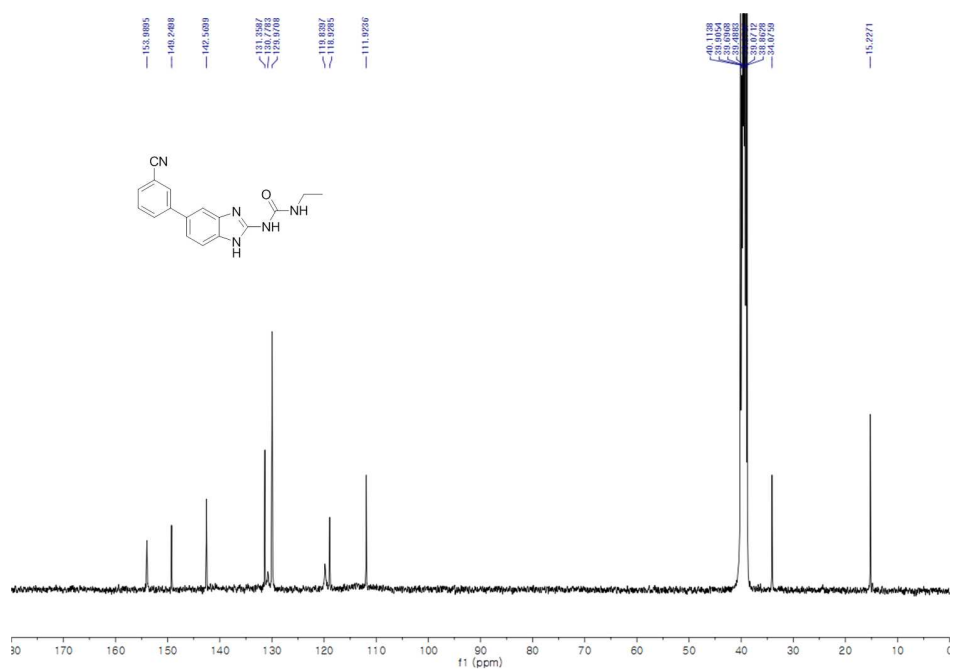


HPLC-Purity

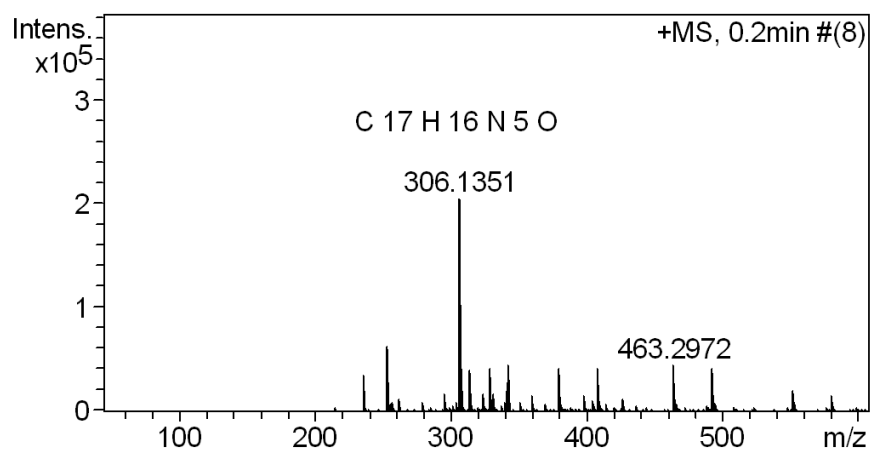
1-(5-(3-Cyanophenyl)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5d).



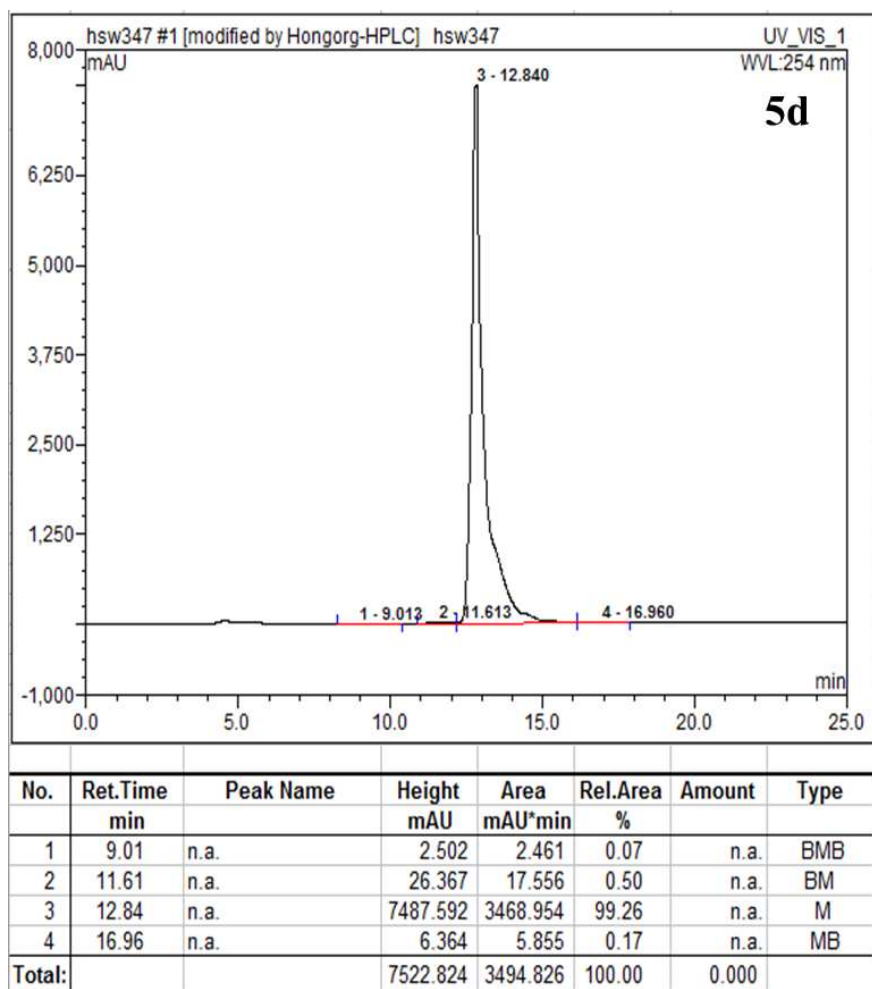
400 MHz, ^1H NMR in DMSO- d_6



100 MHz, ^{13}C NMR in DMSO- d_6

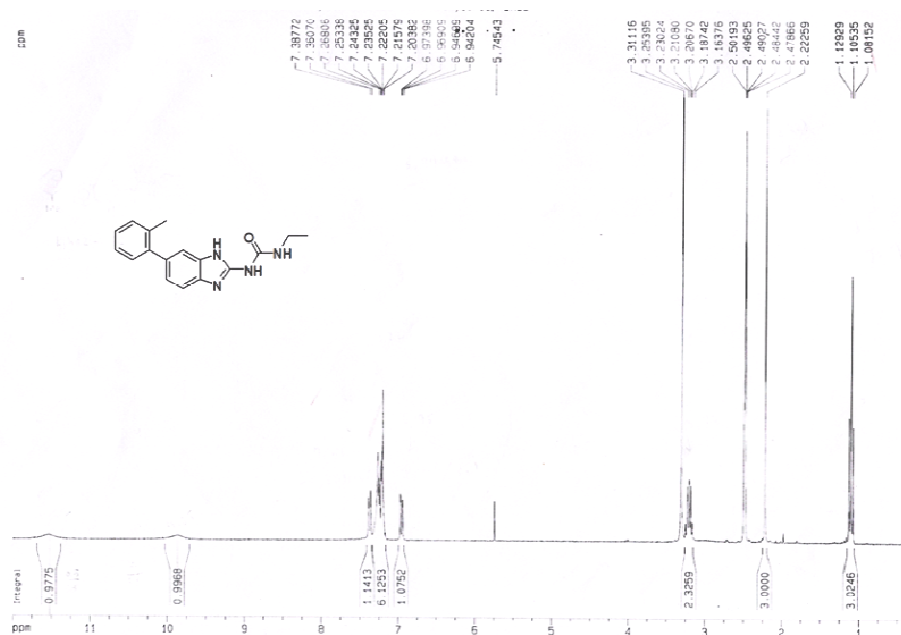


HRMS

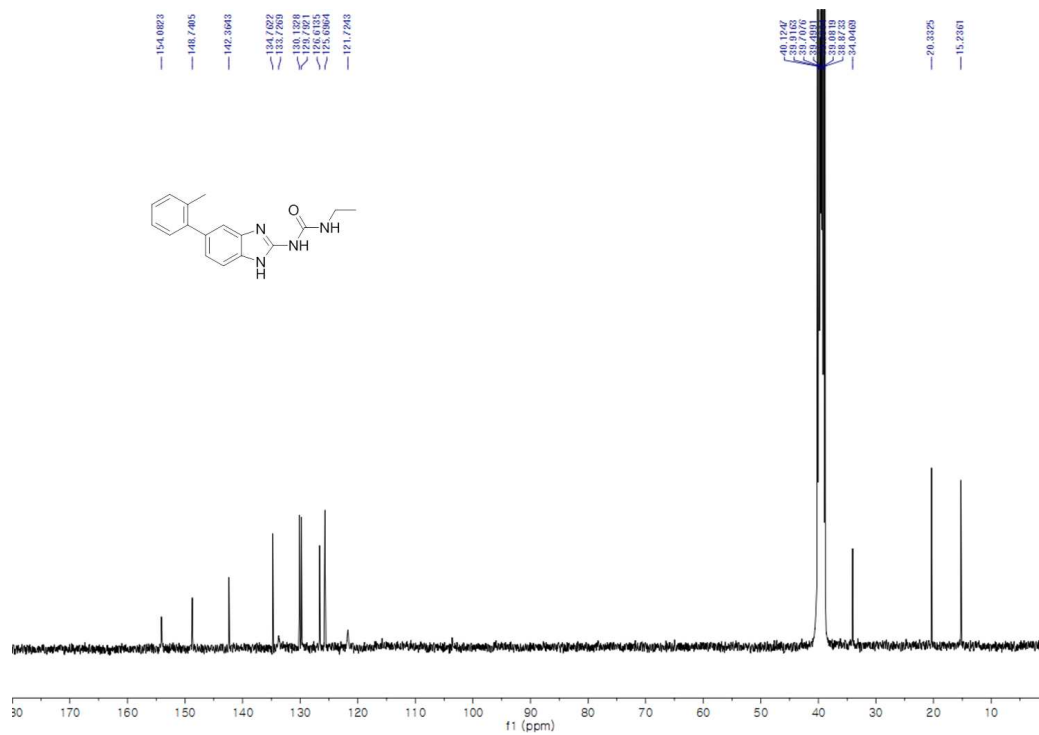


HPLC-Purity

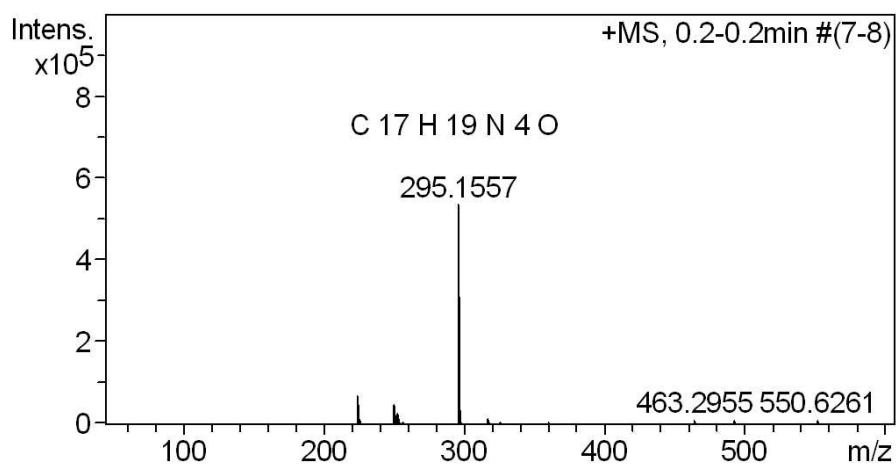
1-Ethyl-3-(5-o-tolyl-1H-benzo[d]imidazol-2-yl)urea (5e).



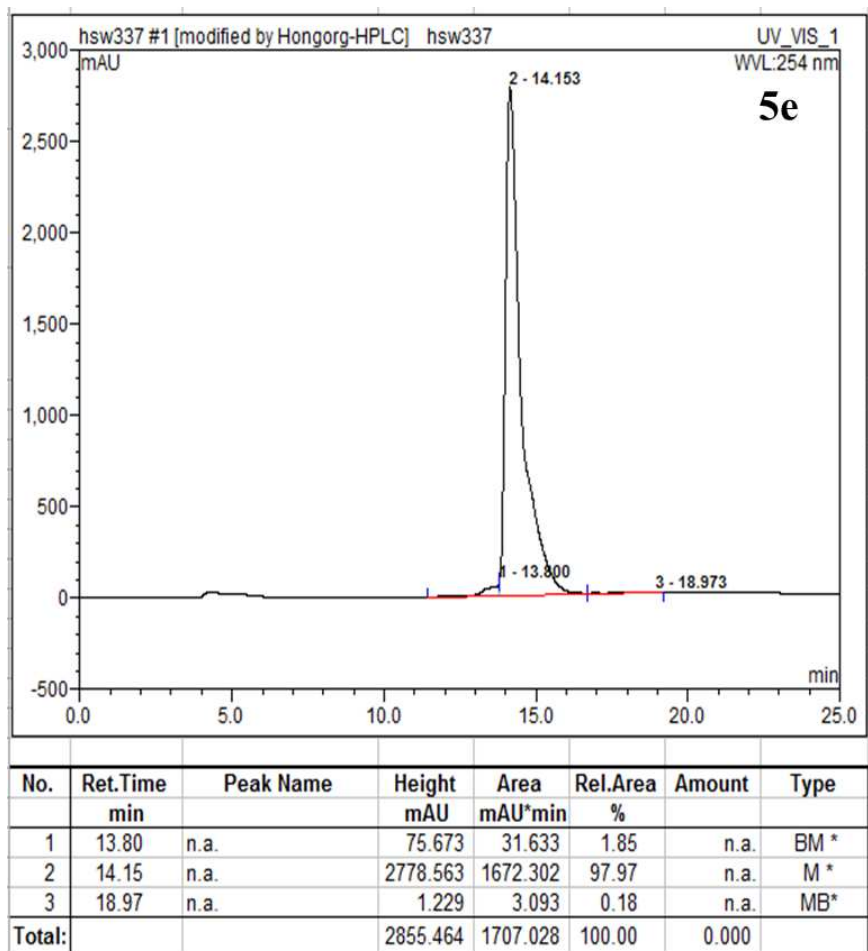
300 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆

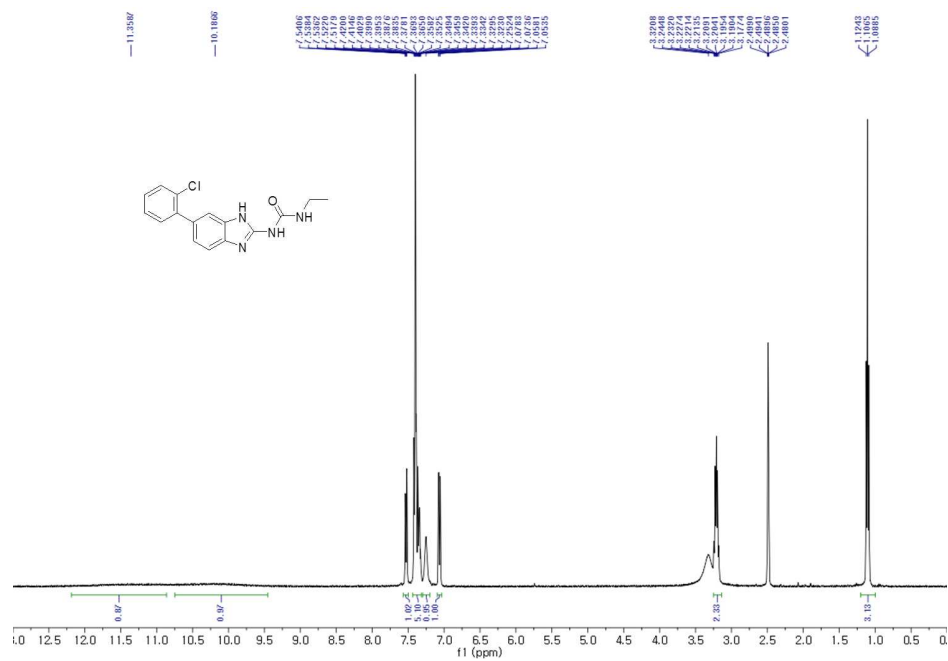


HRMS

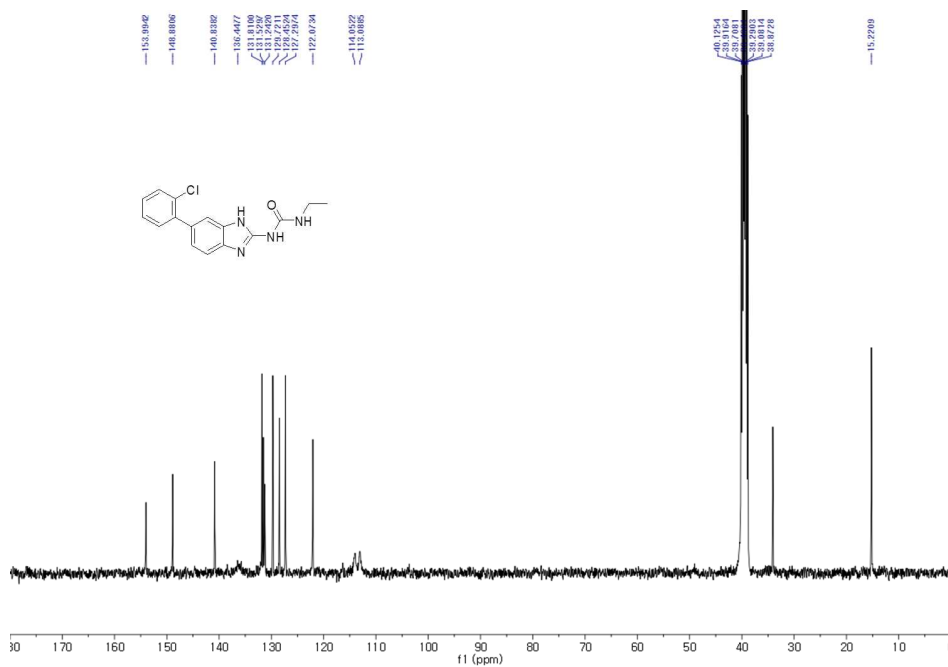


HPLC-Purity

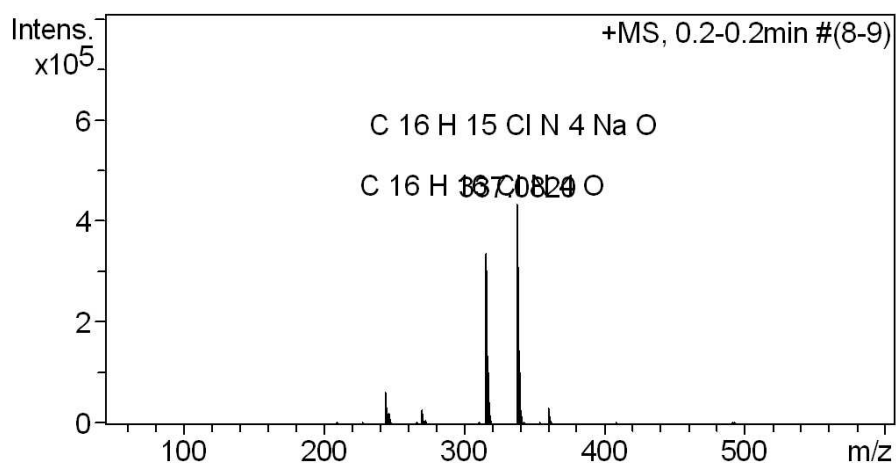
1-(6-(2-Chlorophenyl)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5f).



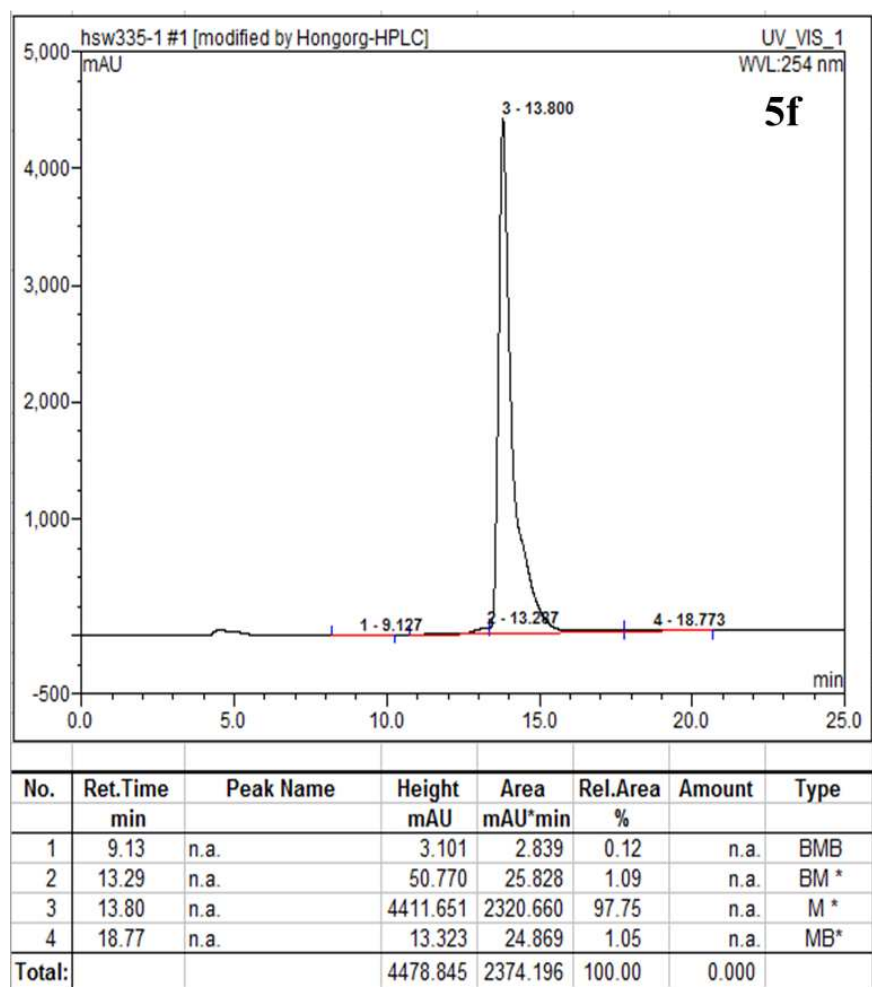
400 MHz, ^1H NMR in DMSO- d_6



100 MHz, ^{13}C NMR in DMSO- d_6



HRMS



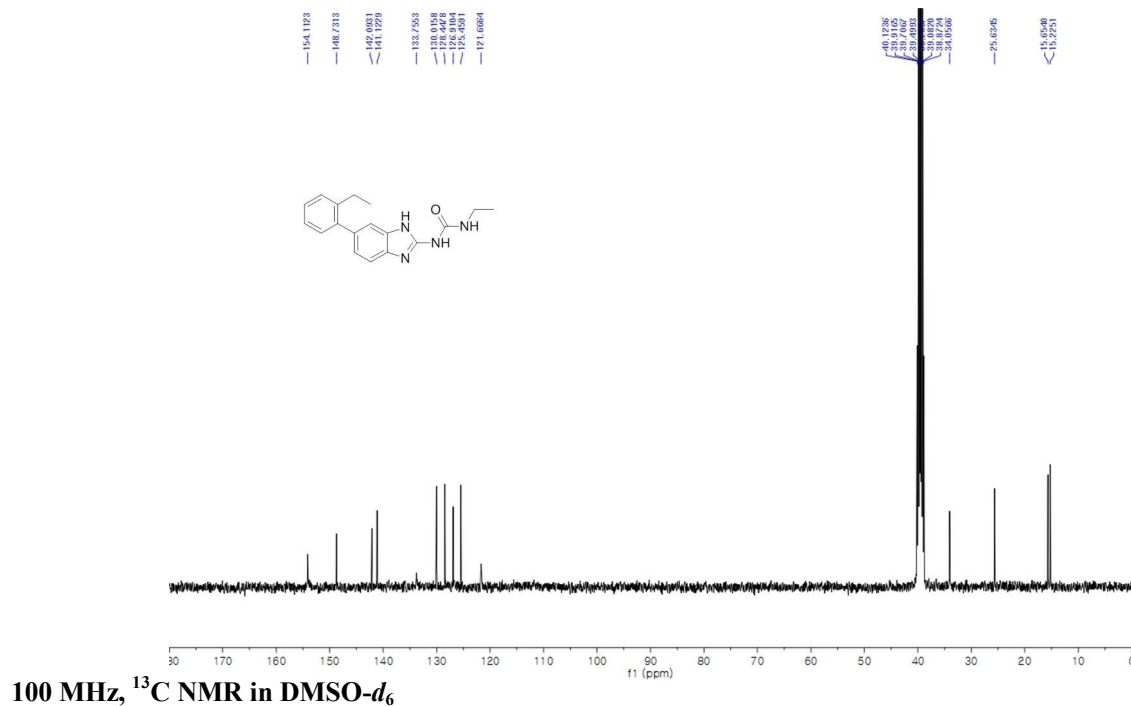
HPLC-Purity

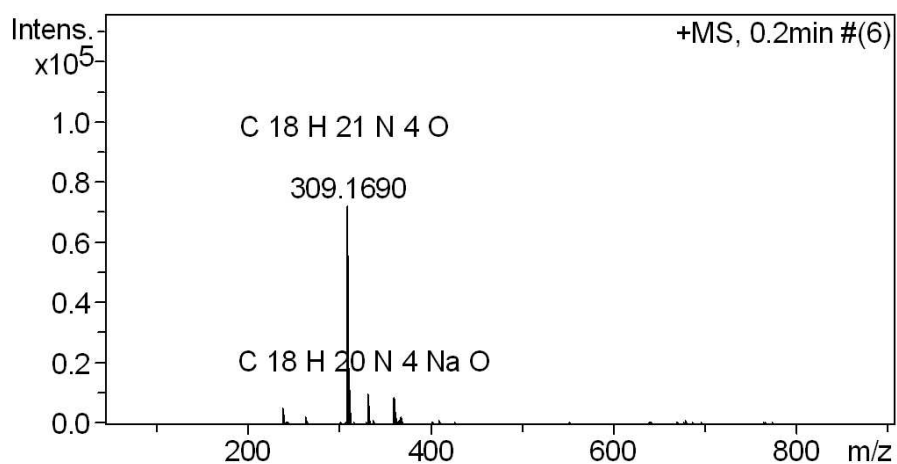
Chemical Structure:

CCNC(=O)Nc1ccc(cc1Cc2ccccc2)c3nc[nH]3

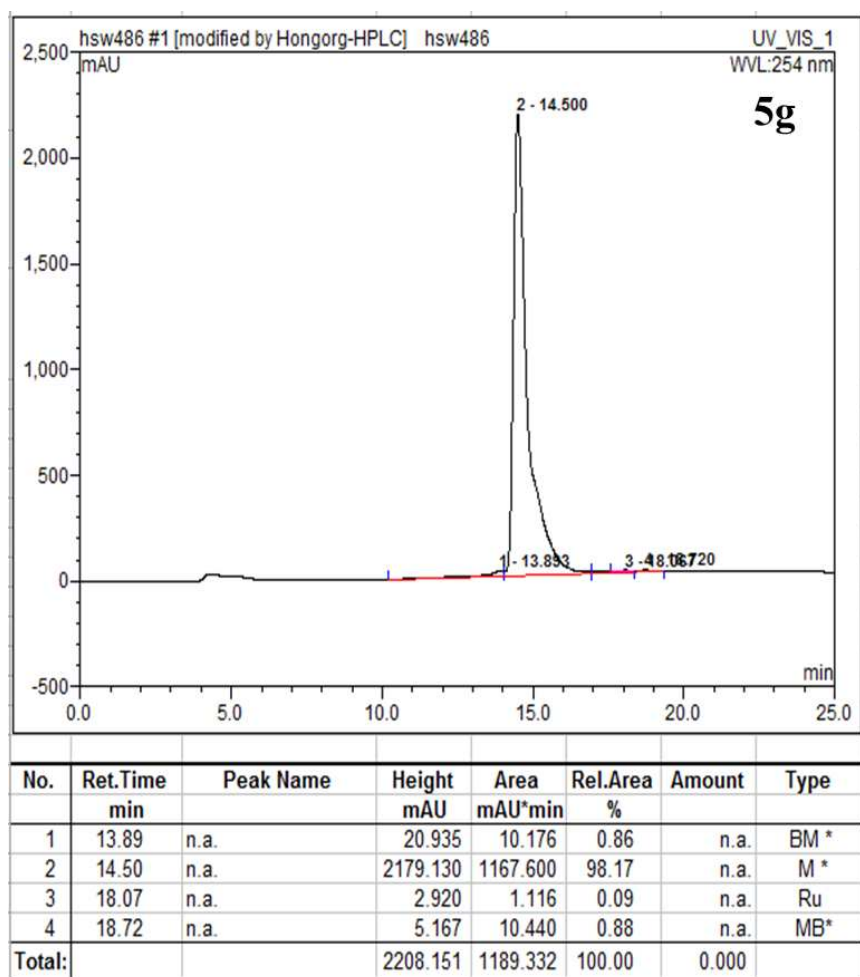
¹H NMR Data (DMSO-*d*₆, 300 MHz):

Chemical Shift (ppm)	Multiplicity	Integration
~11.4	broad singlet	0.49
~10.0	broad singlet	0.40
7.5 - 7.8	multiplet	1.84, 1.84, 1.44, 1.00
~3.2	singlet	2.10
~2.5	singlet	2.00
~1.2	singlet	3.05, 3.05



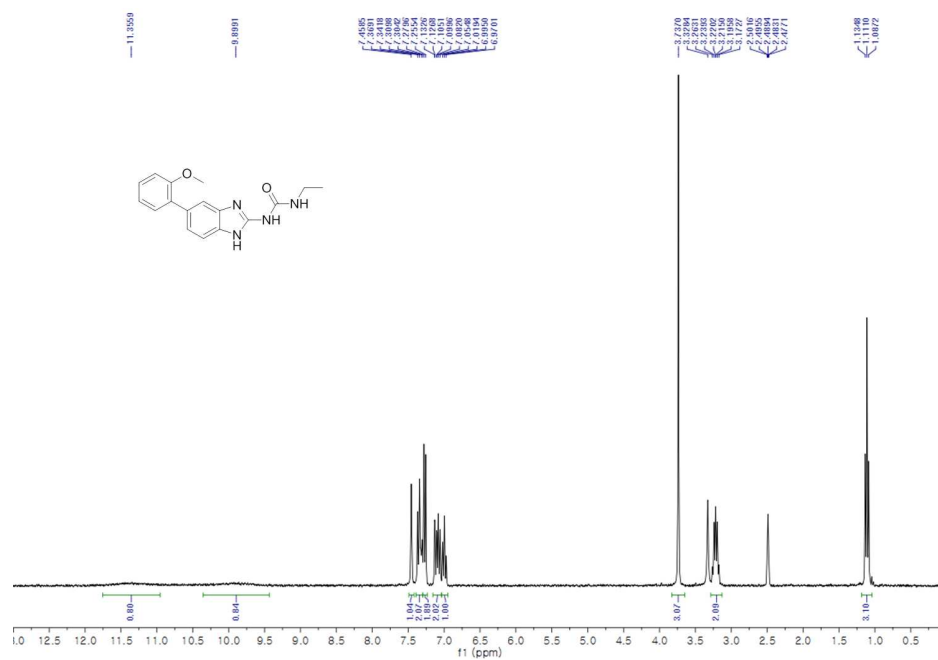


HRMS

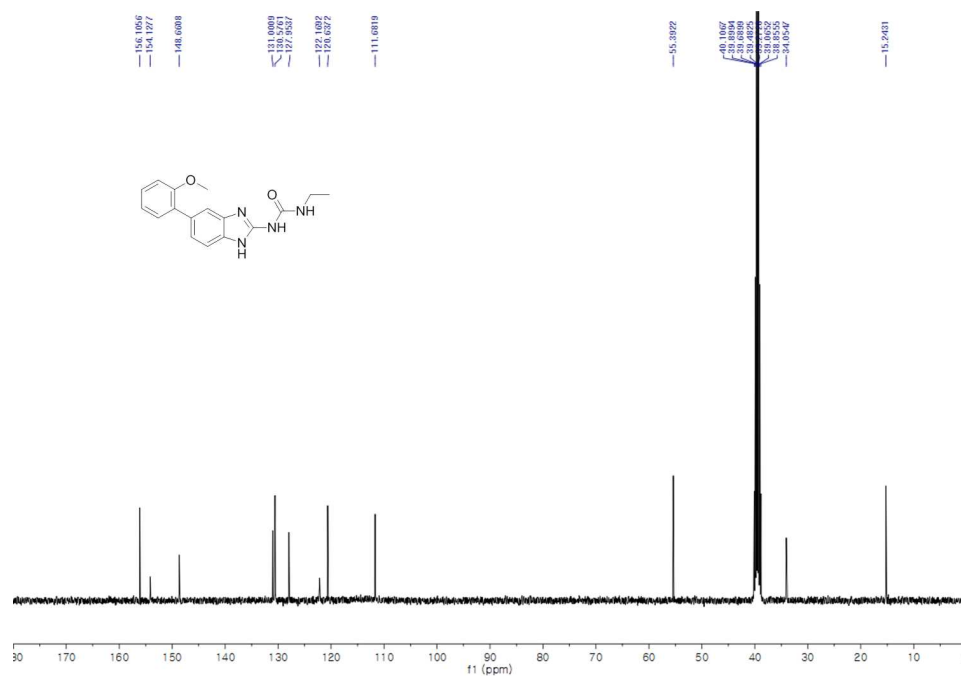


HPLC-Purity

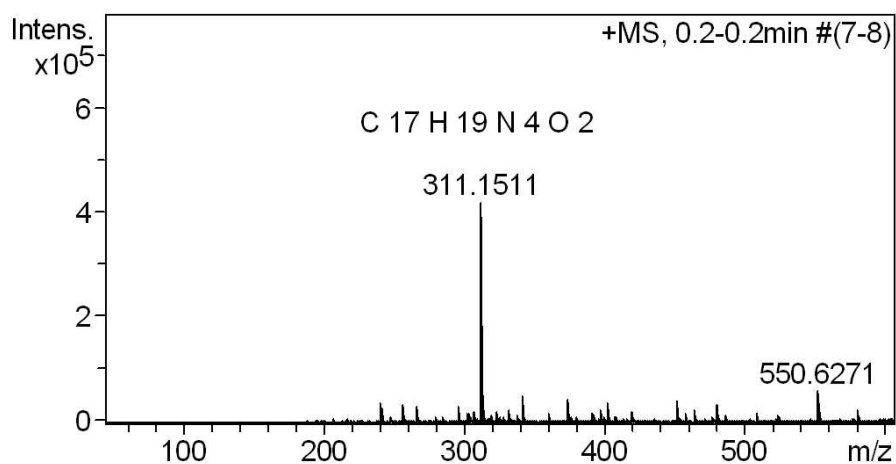
1-Ethyl-3-(5-(2-methoxyphenyl)-1H-benzo[d]imidazol-2-yl)urea (5h).



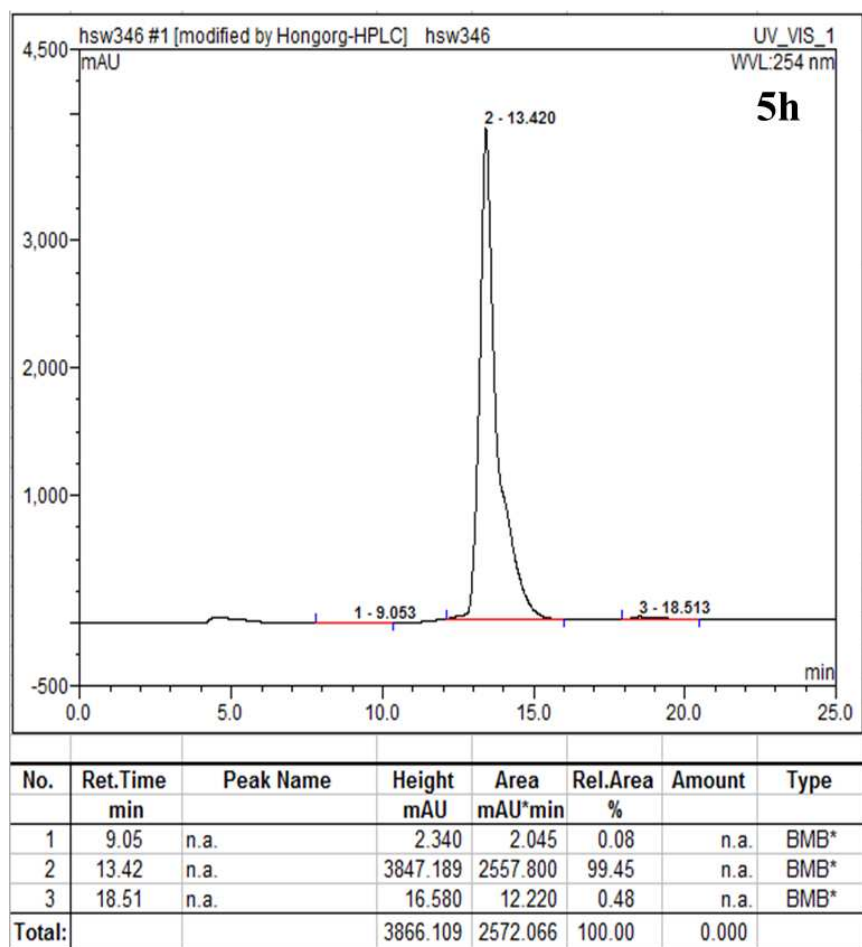
300 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆

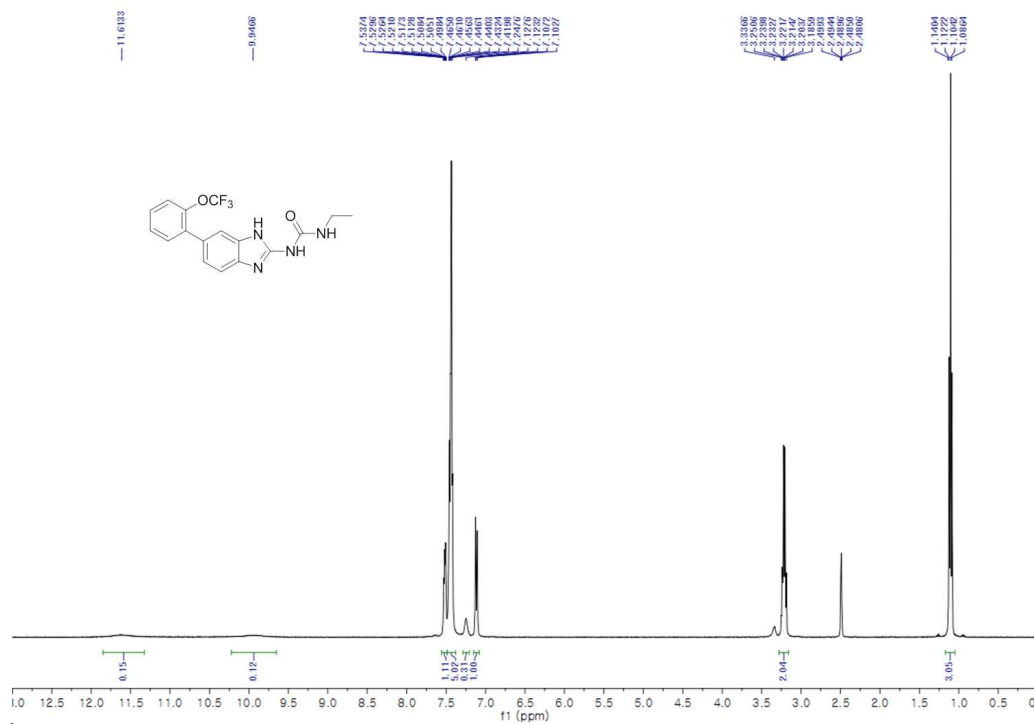


HRMS

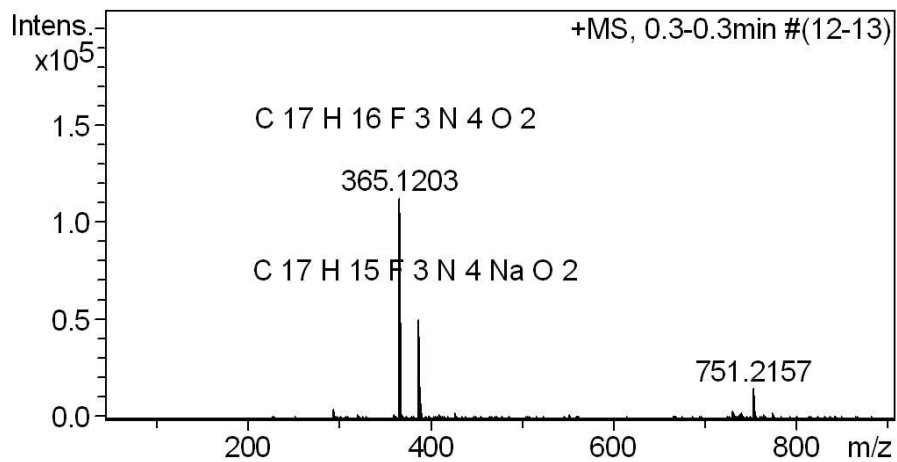


HPLC-Purity

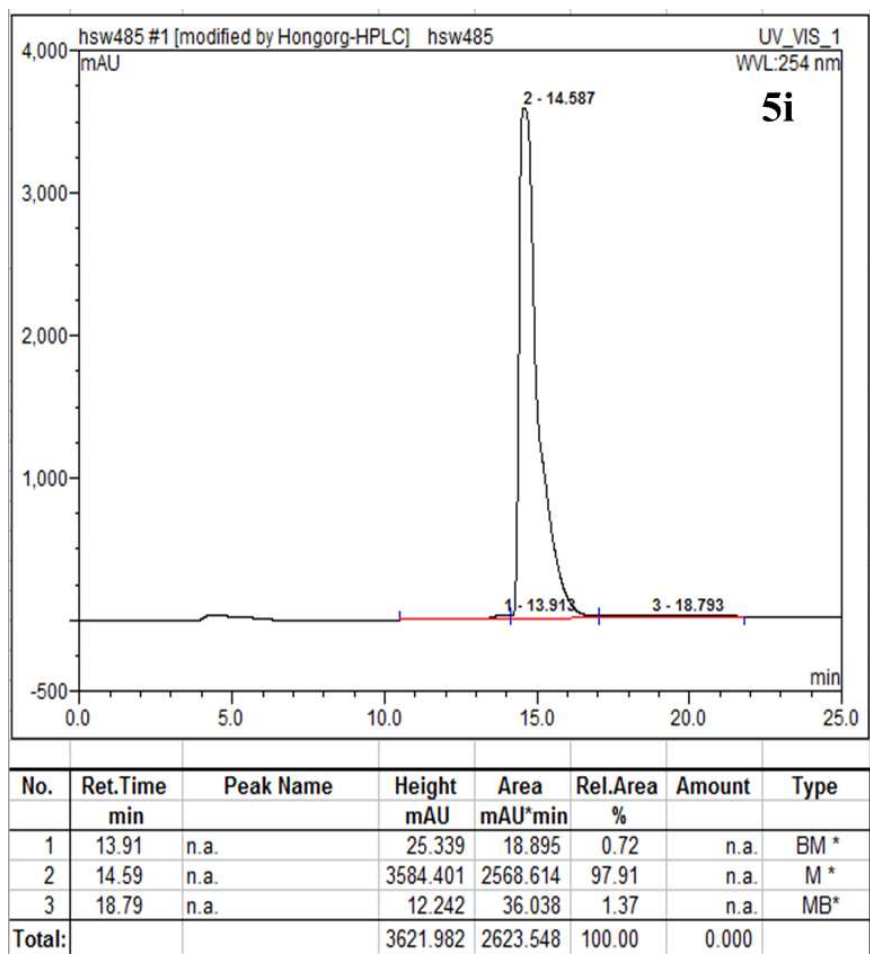
1-Ethyl-3-(6-(2-(trifluoromethoxy)phenyl)-1H-benzo[d]imidazol-2-yl)urea (5i).



300 MHz, ^1H NMR in DMSO- d_6

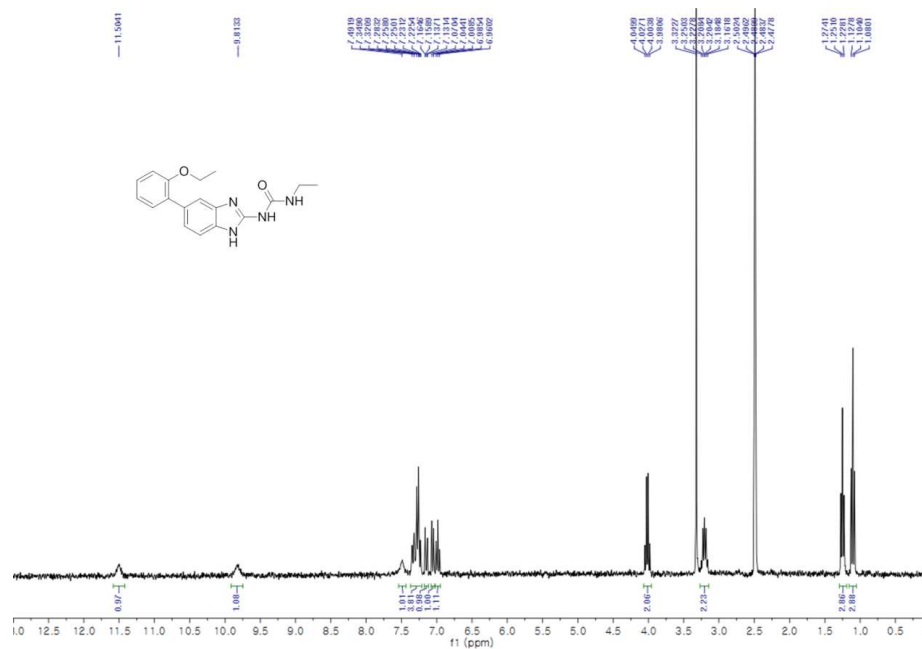


HRMS

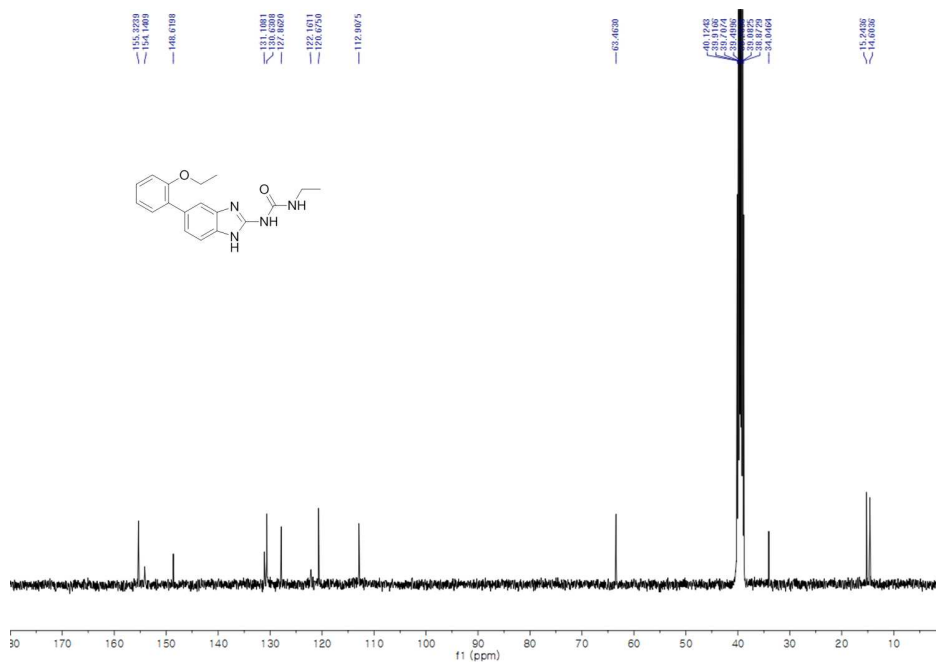


HPLC-Purity

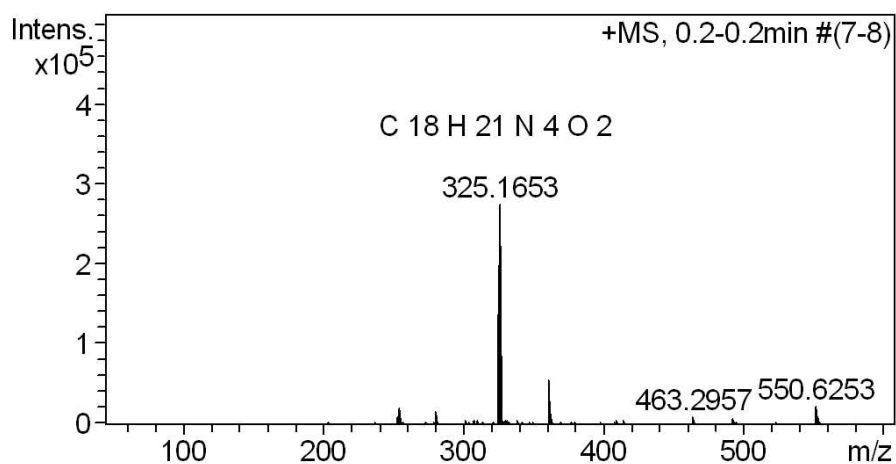
1-(5-(2-Ethoxyphenyl)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5j).



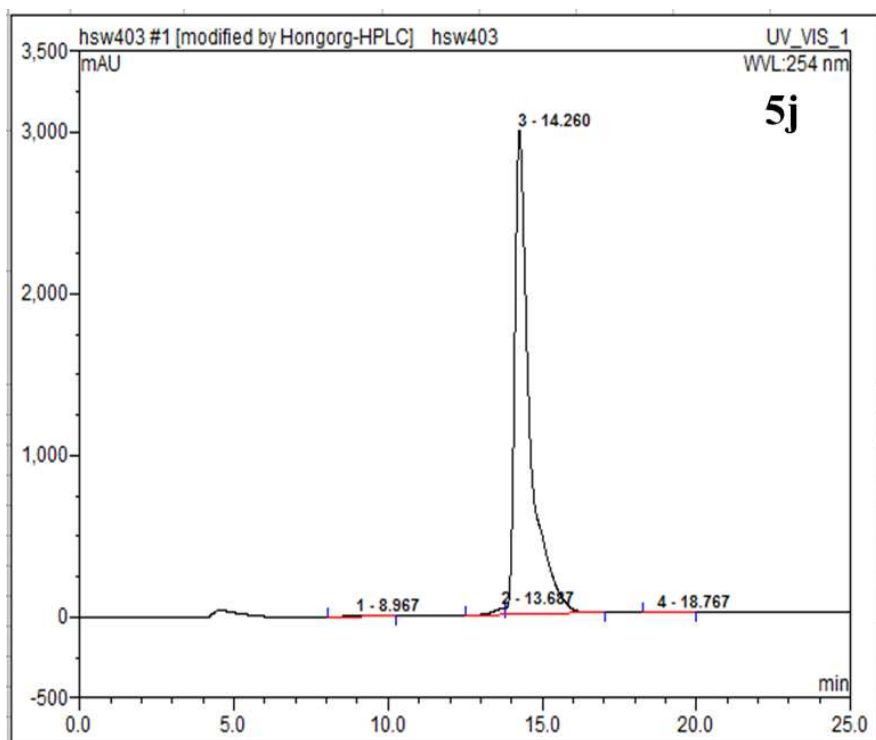
300 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆



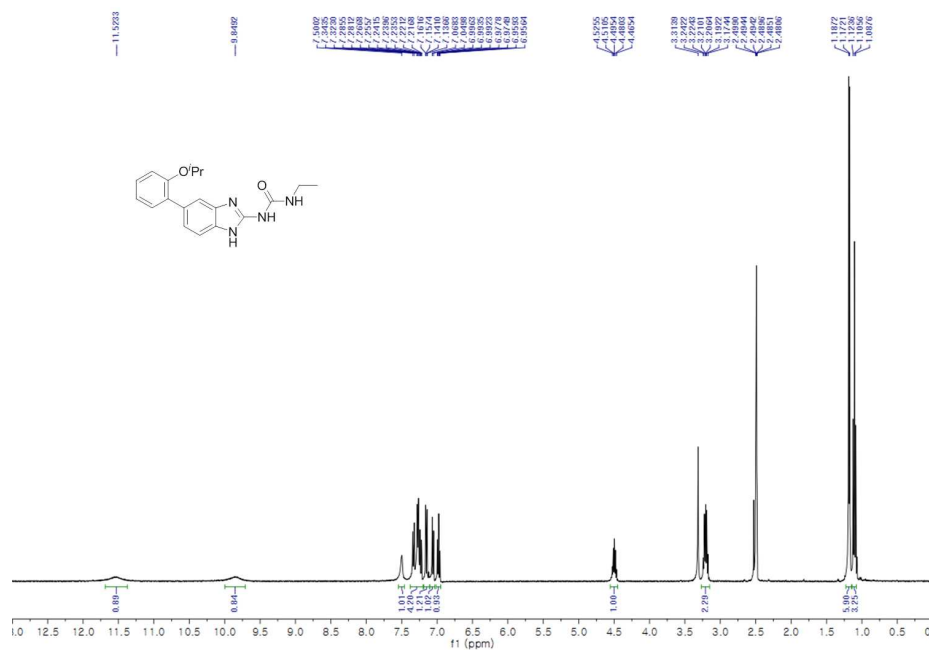
HRMS



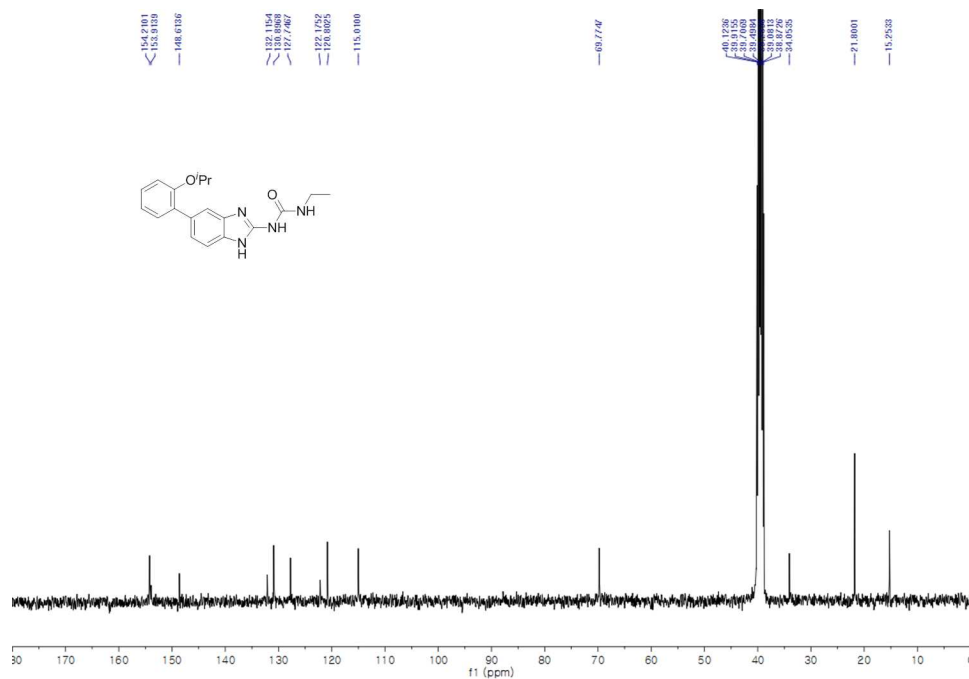
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	8.97	n.a.	2.607	2.578	0.15	n.a.	BMB
2	13.69	n.a.	34.981	14.513	0.85	n.a.	BM
3	14.26	n.a.	2988.768	1693.127	98.92	n.a.	MB
4	18.77	n.a.	1.670	1.439	0.08	n.a.	BMB
Total:			3028.025	1711.657	100.00	0.000	

HPLC-Purity

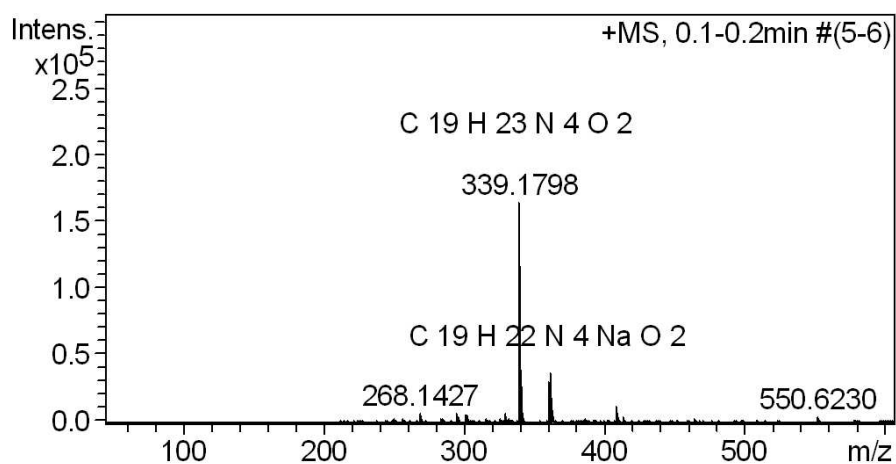
1-Ethyl-3-(5-(2-isopropoxyphenyl)-1H-benzo[d]imidazol-2-yl)urea (5k).



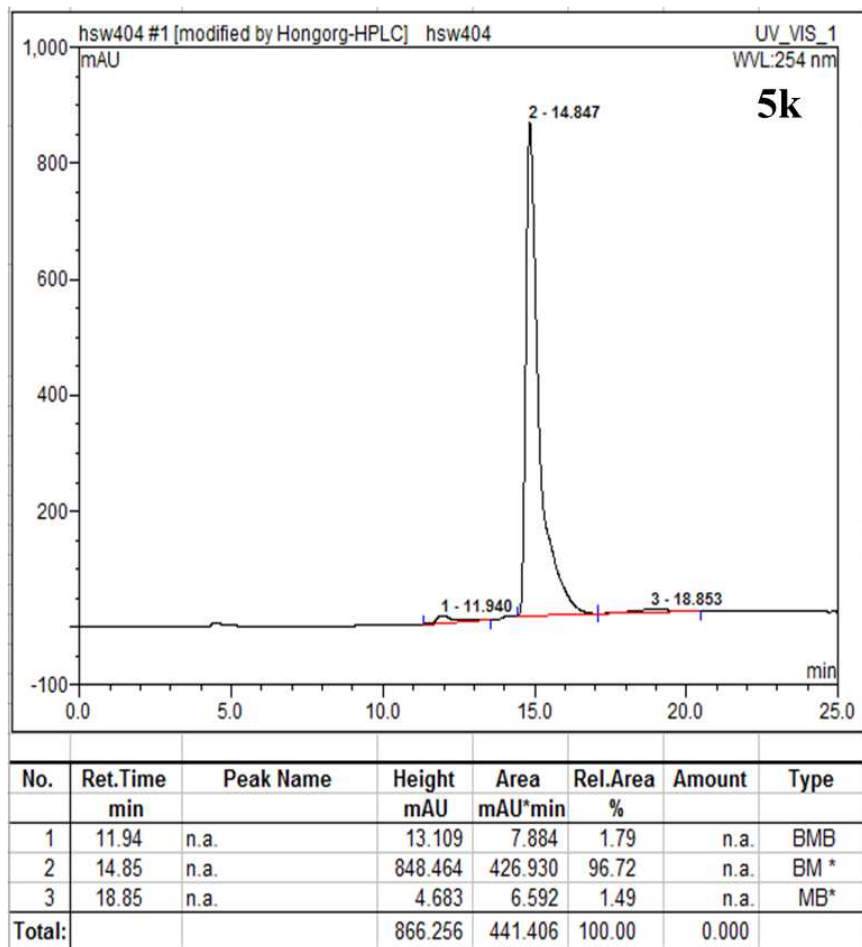
400 MHz, ^1H NMR in DMSO- d_6



100 MHz, ^{13}C NMR in DMSO- d_6

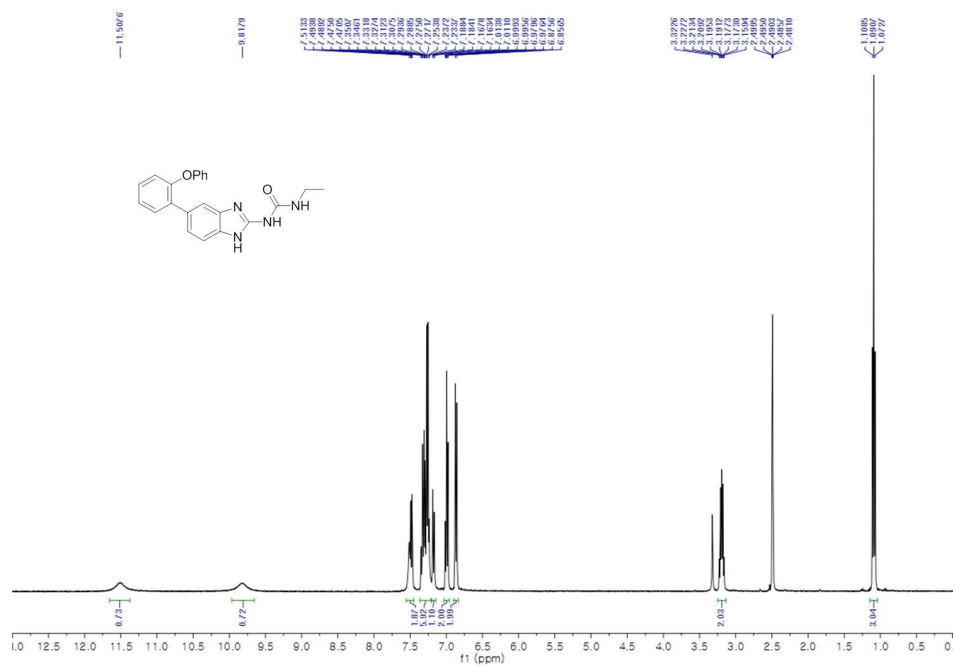


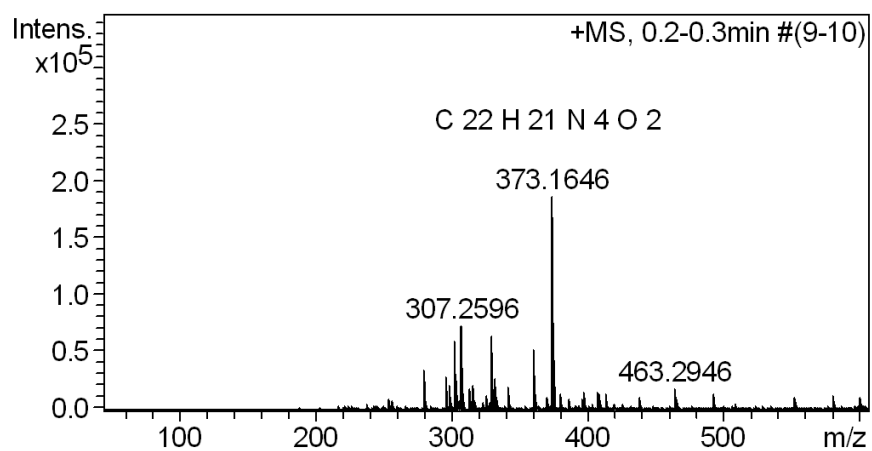
HRMS



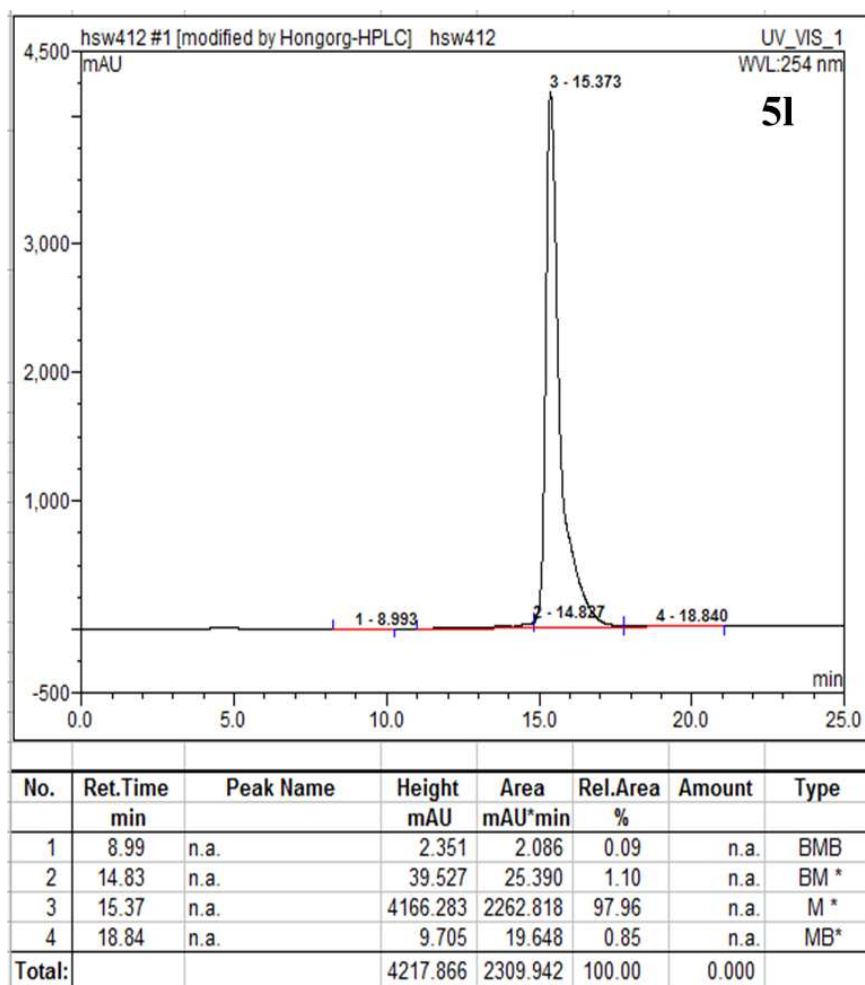
HPLC-Purity

1-Ethyl-3-(5-(2-phenoxyphenyl)-1H-benzo[d]imidazol-2-yl)urea (5l).



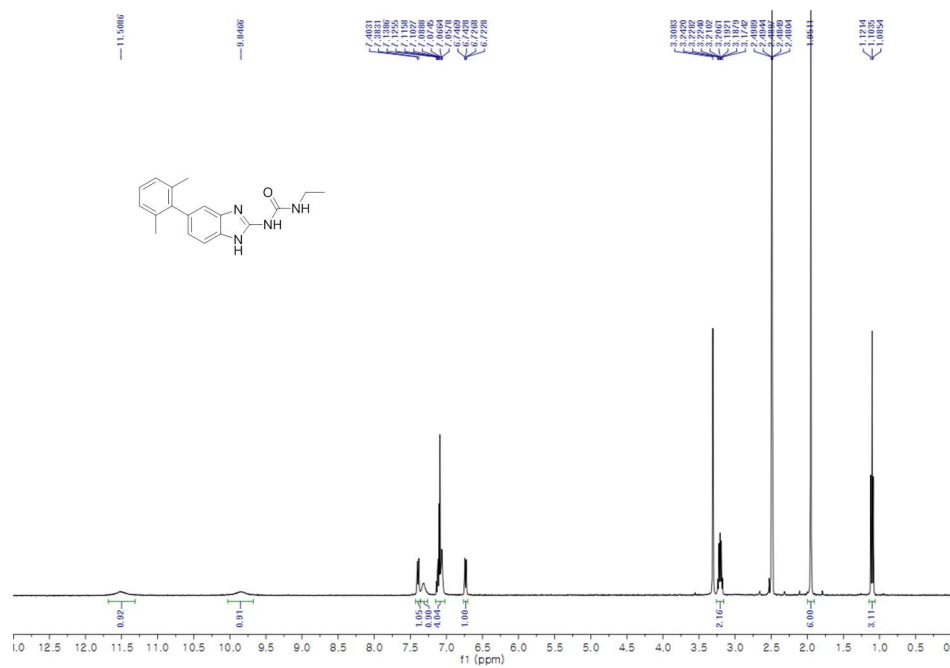


HRMS

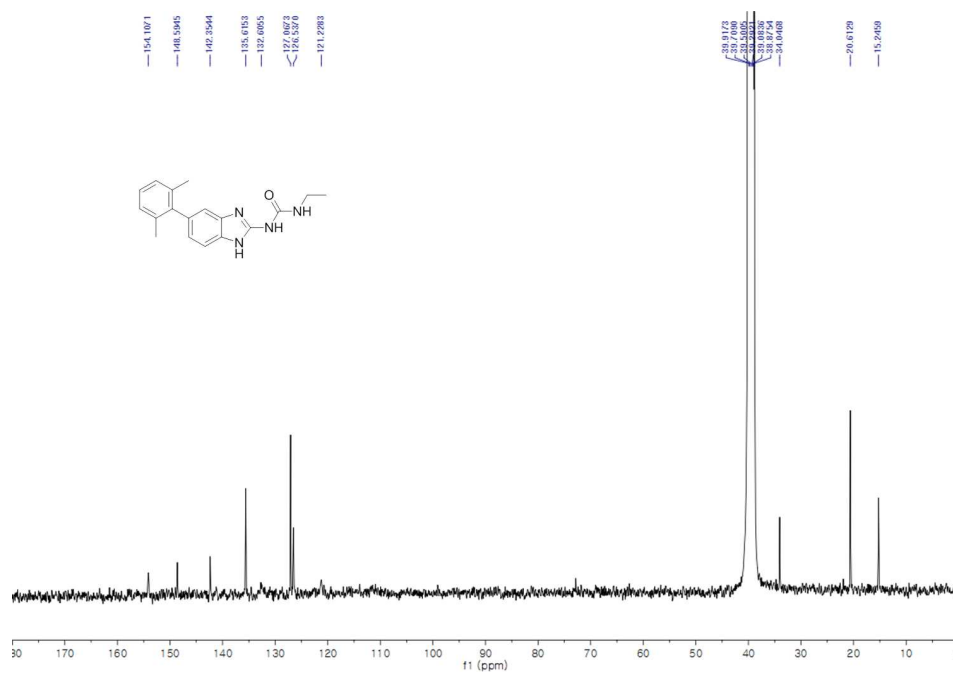


HPLC-Purity

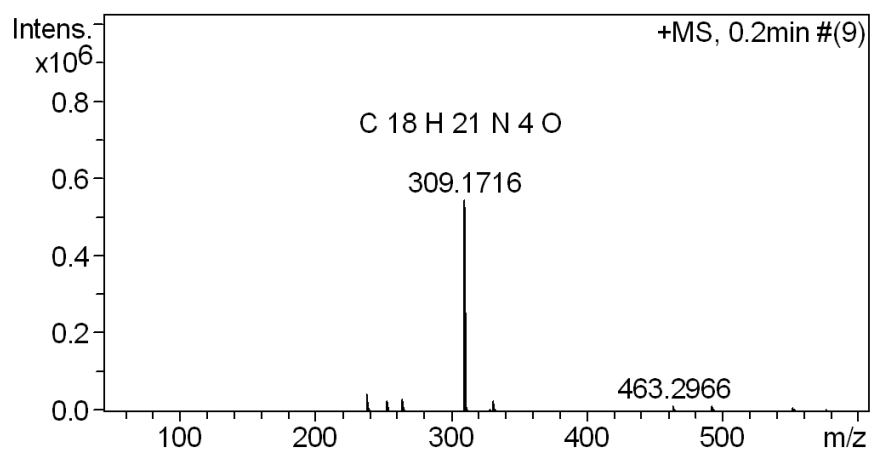
1-(5-(2,6-Dimethylphenyl)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5m).



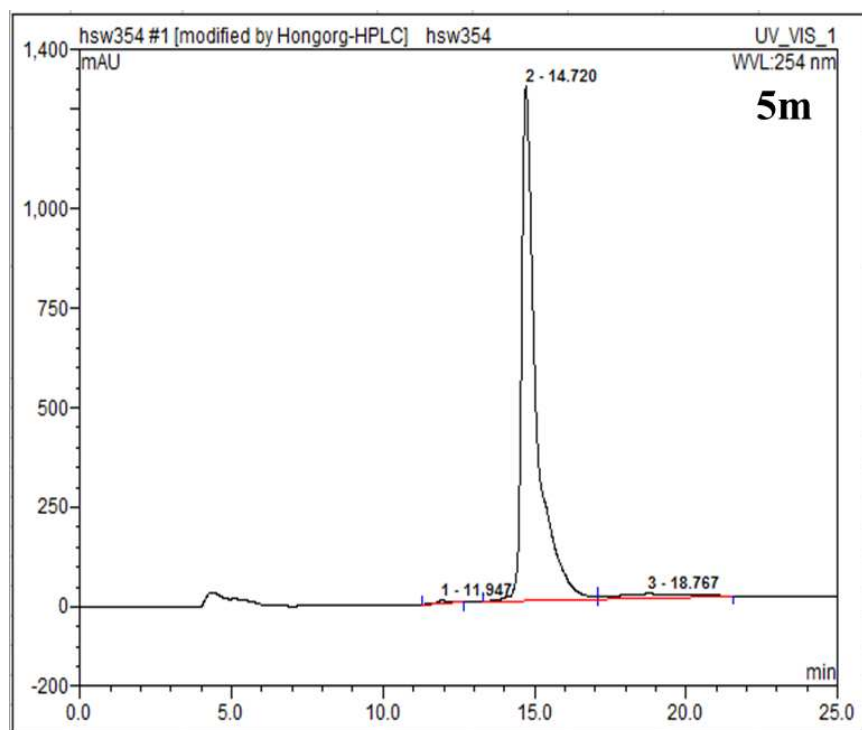
400 MHz, ^1H NMR in DMSO- d_6



100 MHz, ^{13}C NMR in DMSO- d_6



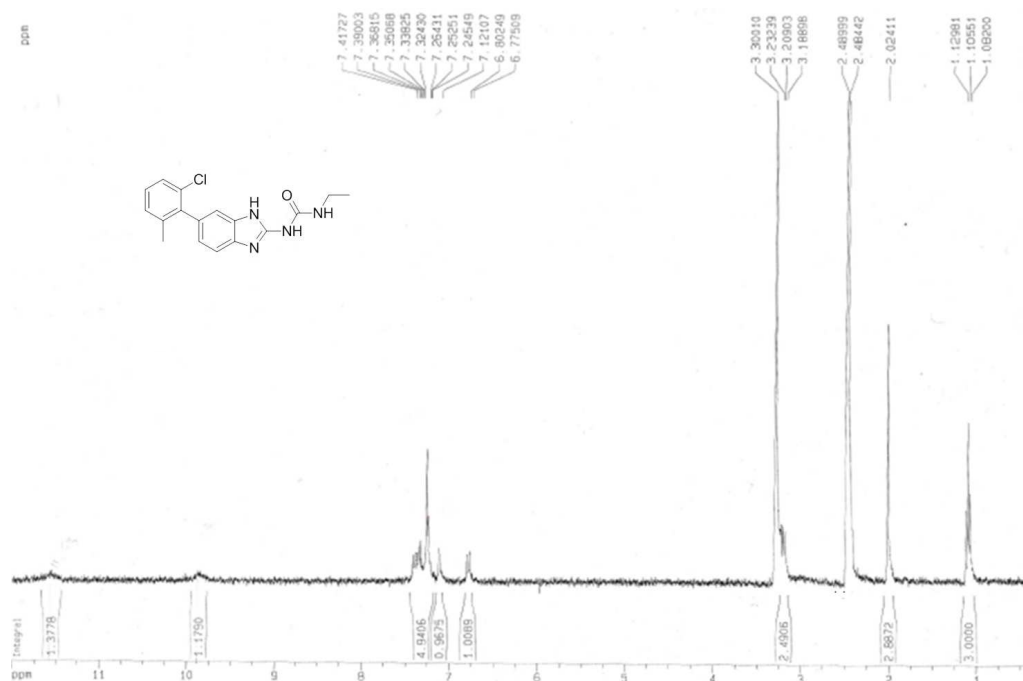
HRMS



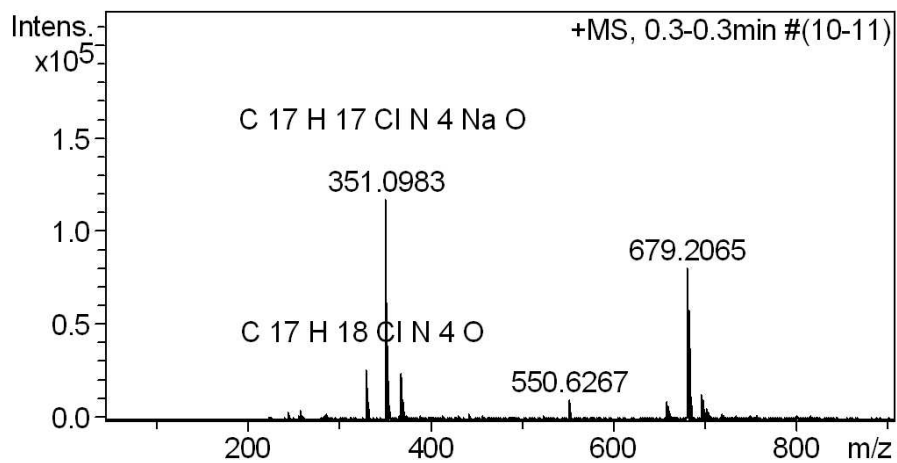
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	11.95	n.a.	7.586	3.444	0.46	n.a.	BMB
2	14.72	n.a.	1293.849	723.135	96.27	n.a.	BM *
3	18.77	n.a.	10.097	24.551	3.27	n.a.	MB*
Total:			1311.532	751.130	100.00	0.000	

HPLC-Purity

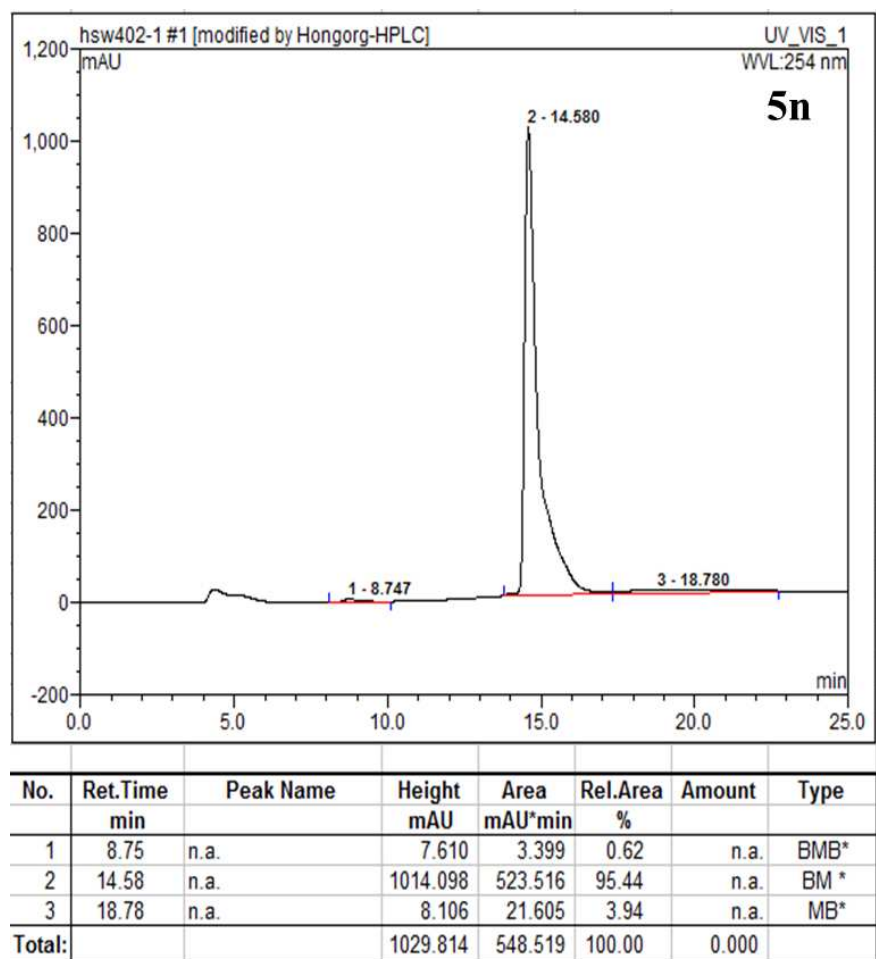
1-(5-(2-Chloro-6-methylphenyl)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5n).



300 MHz, ¹H NMR in DMSO-*d*₆

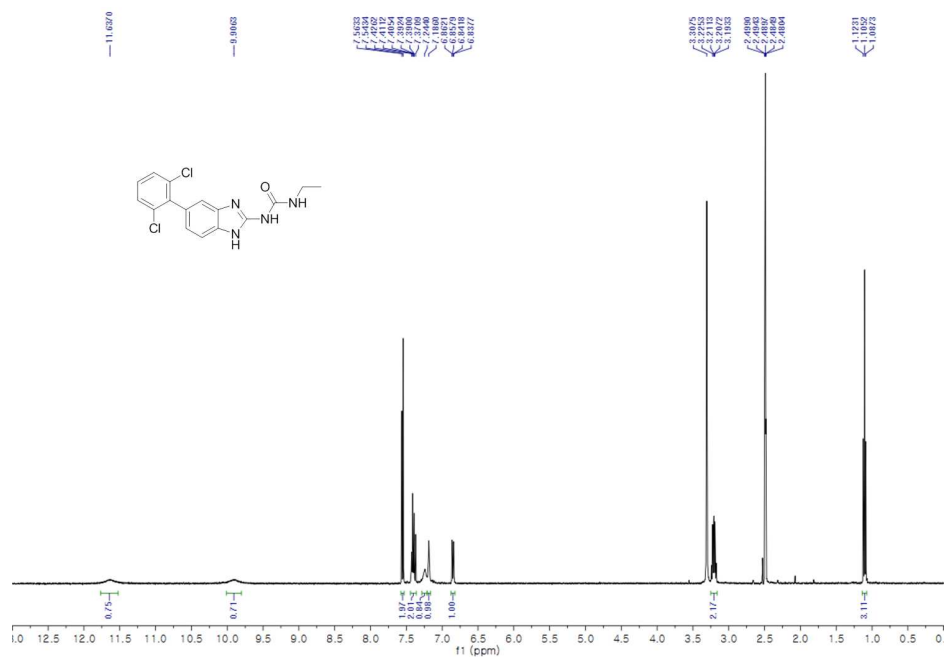


HRMS

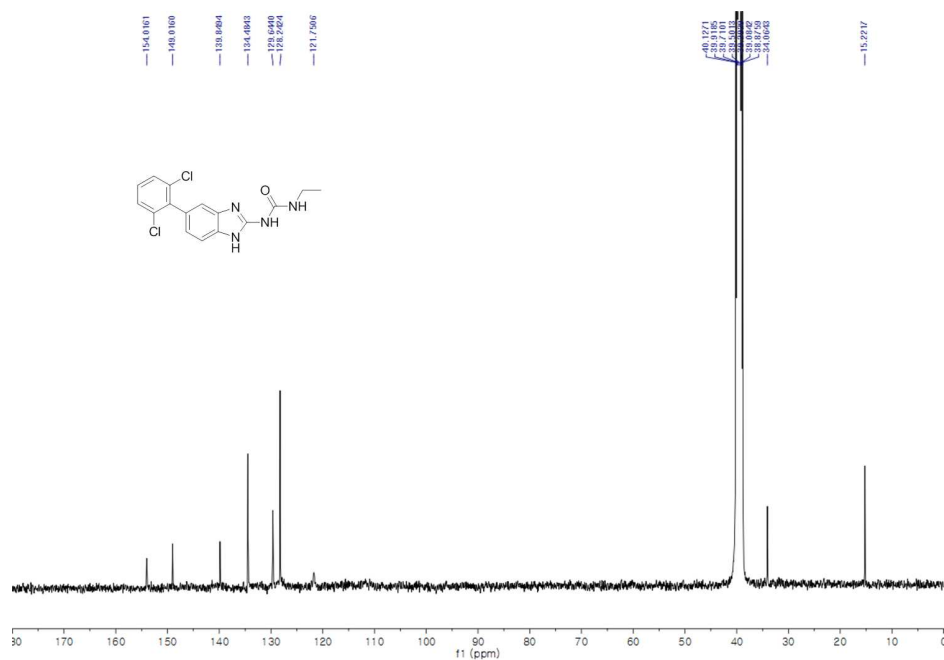


HPLC-Purity

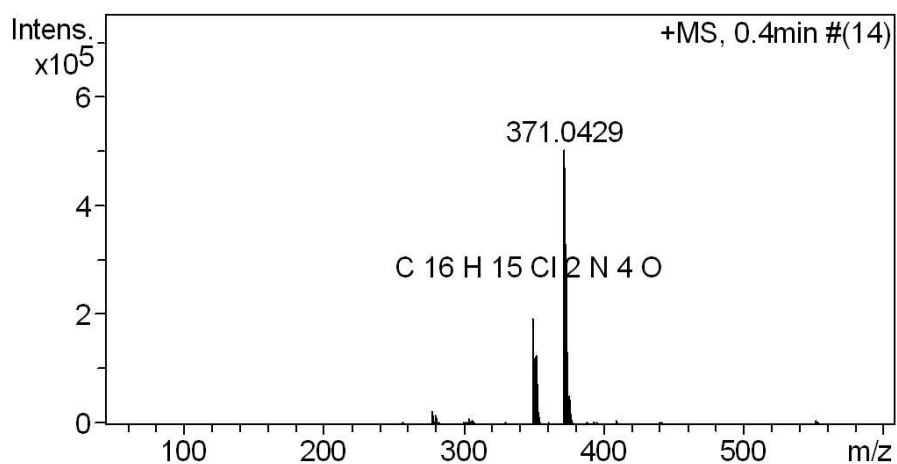
1-(5-(2,6-Dichlorophenyl)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5o)



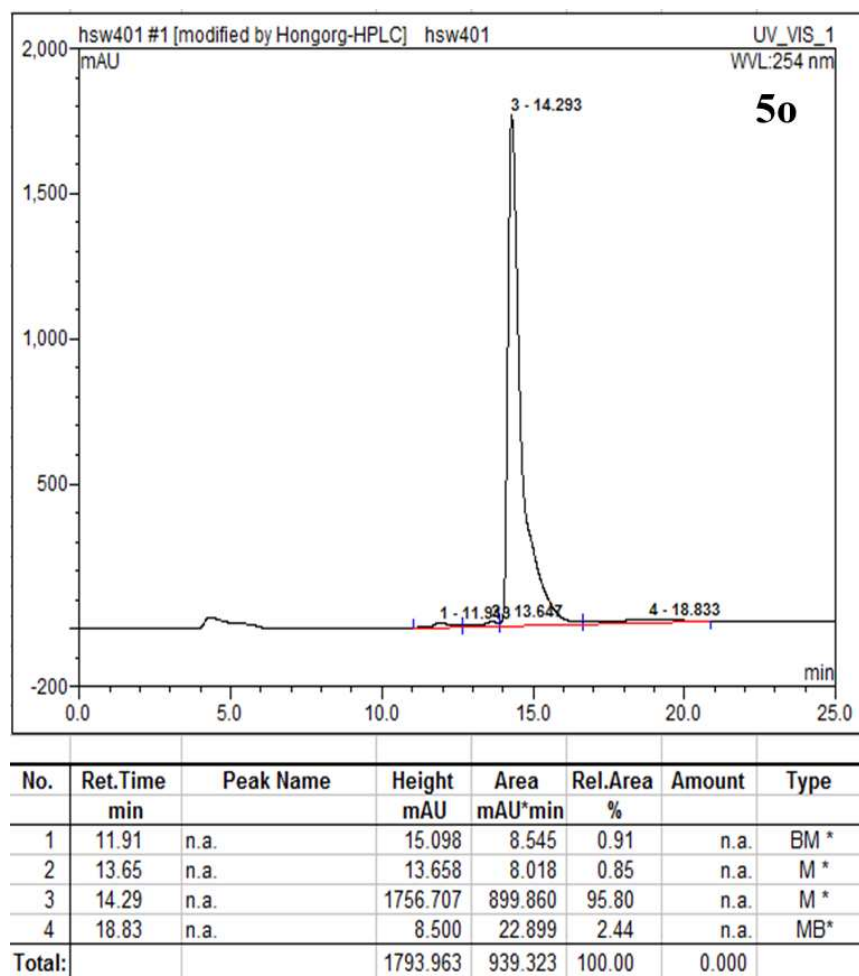
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆

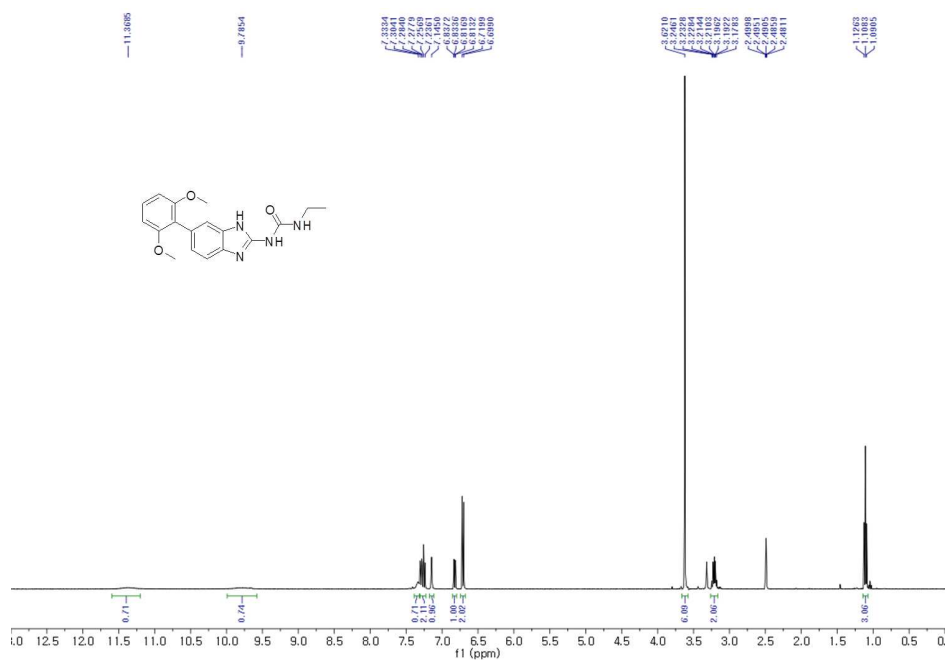


HRMS

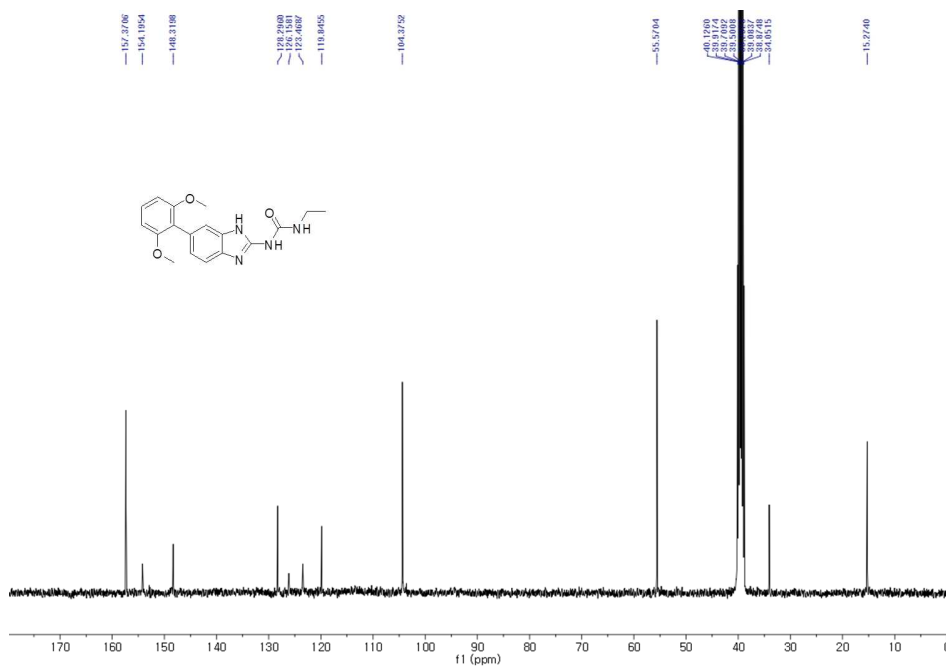


HPLC-Purity

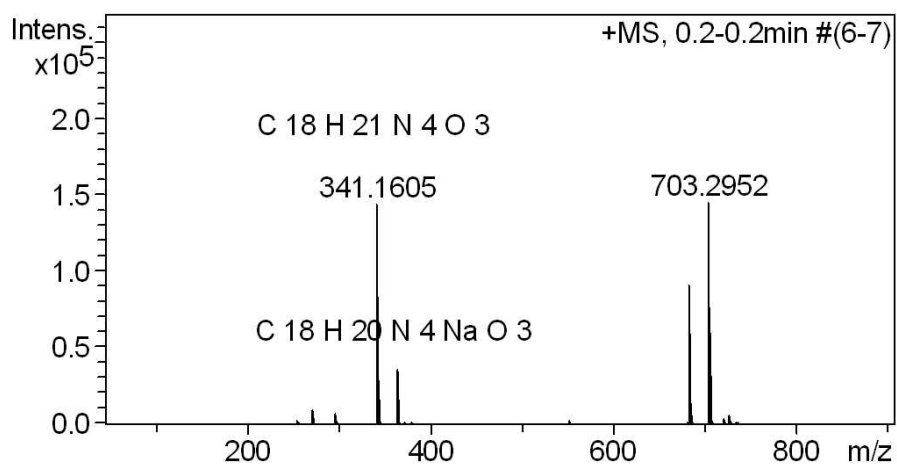
1-(6-(2,6-Dimethoxyphenyl)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5p).



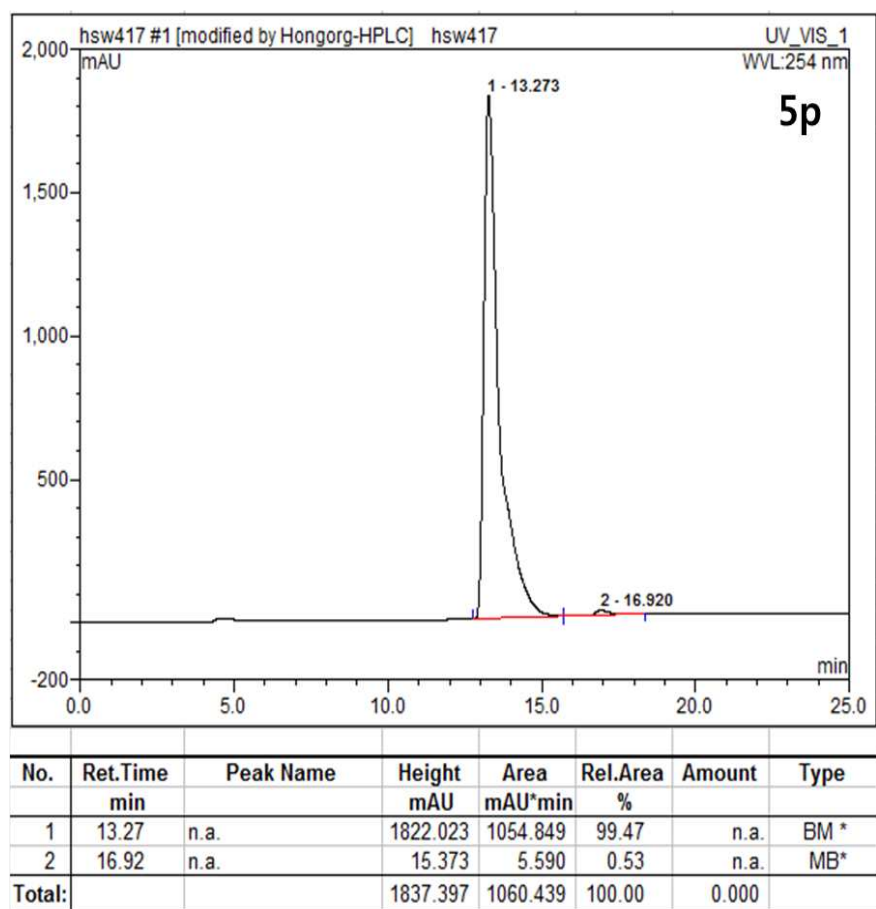
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ^{13}C NMR in DMSO- d_6

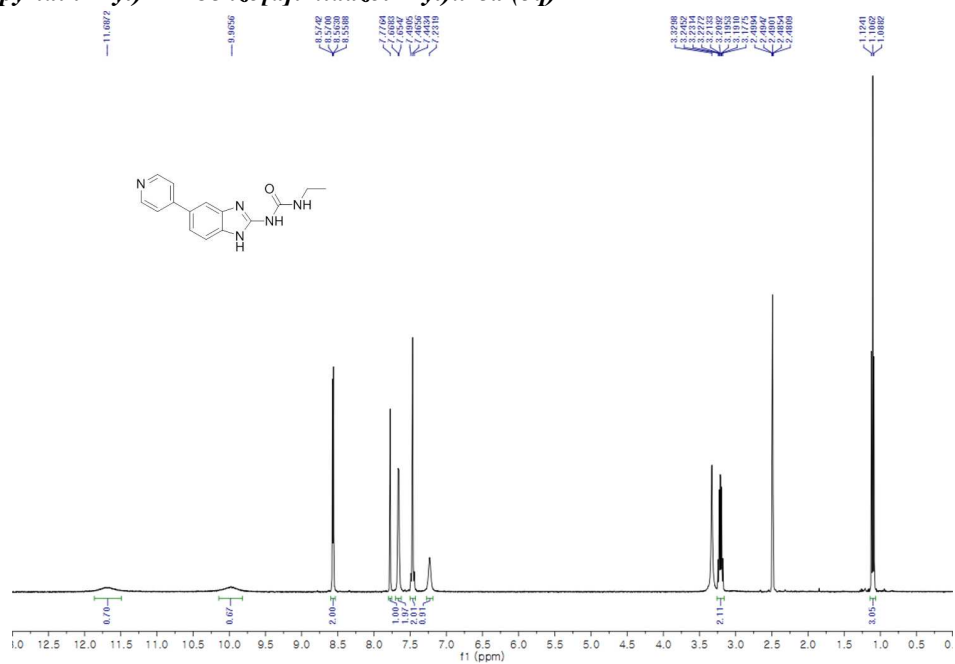


HRMS

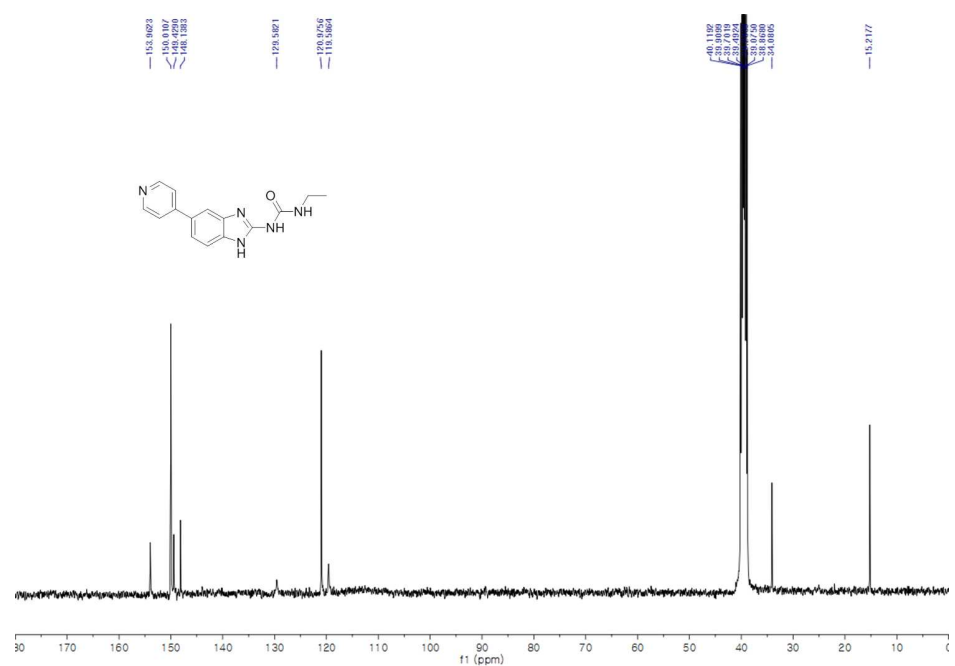


HPLC-Purity

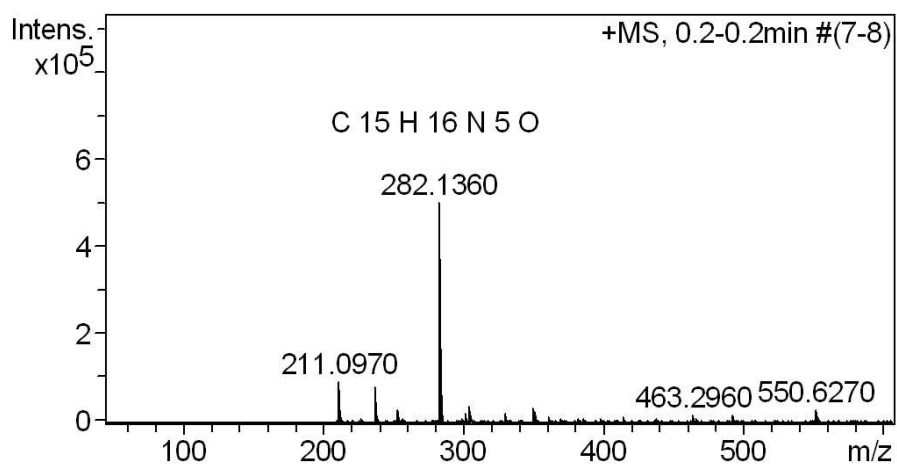
1-Ethyl-3-(5-(pyridin-4-yl)-1H-benzod[imidazol-2-yl)urea (5q)



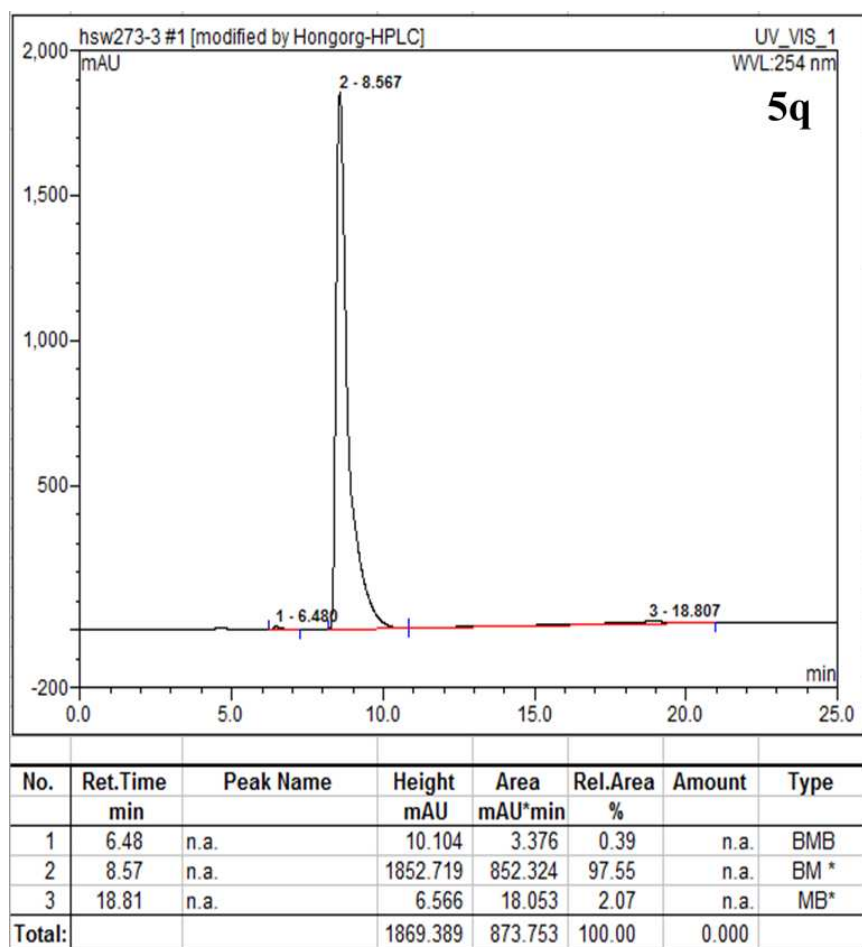
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆

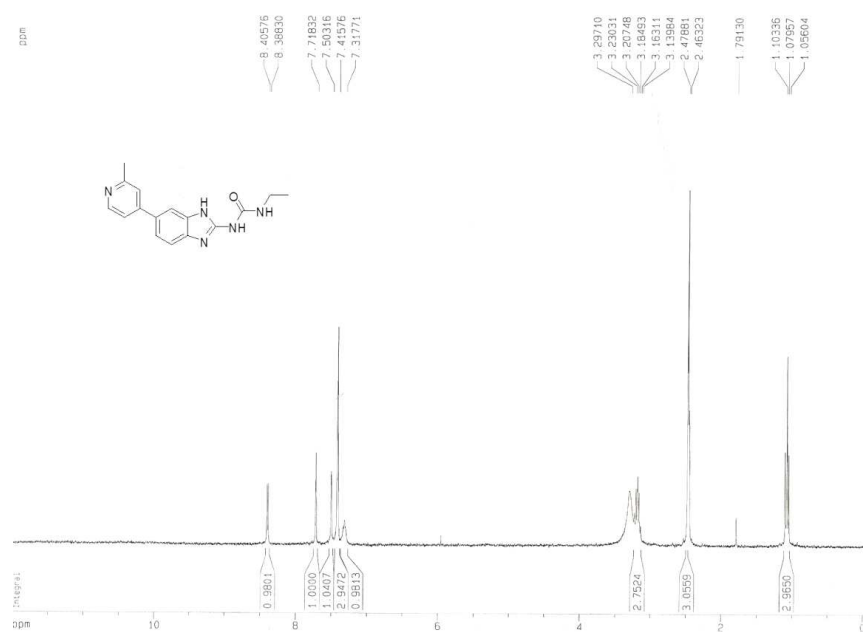


HRMS

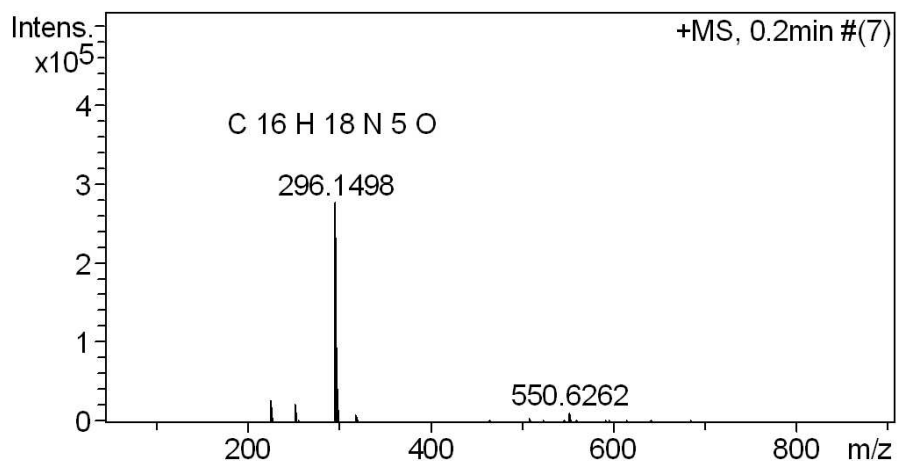


HPLC-Purity

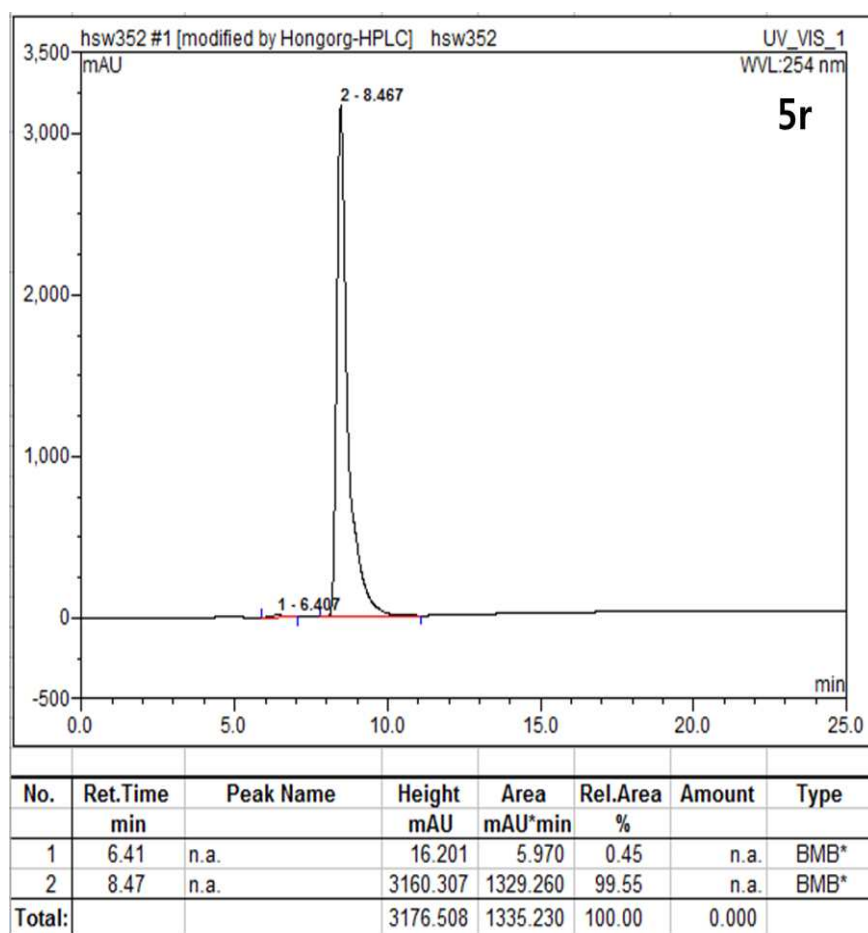
1-Ethyl-3-(6-(2-methylpyridin-4-yl)-1H-benzo[d]imidazol-2-yl)urea (5r).



300 MHz, ¹H NMR in DMSO-*d*₆

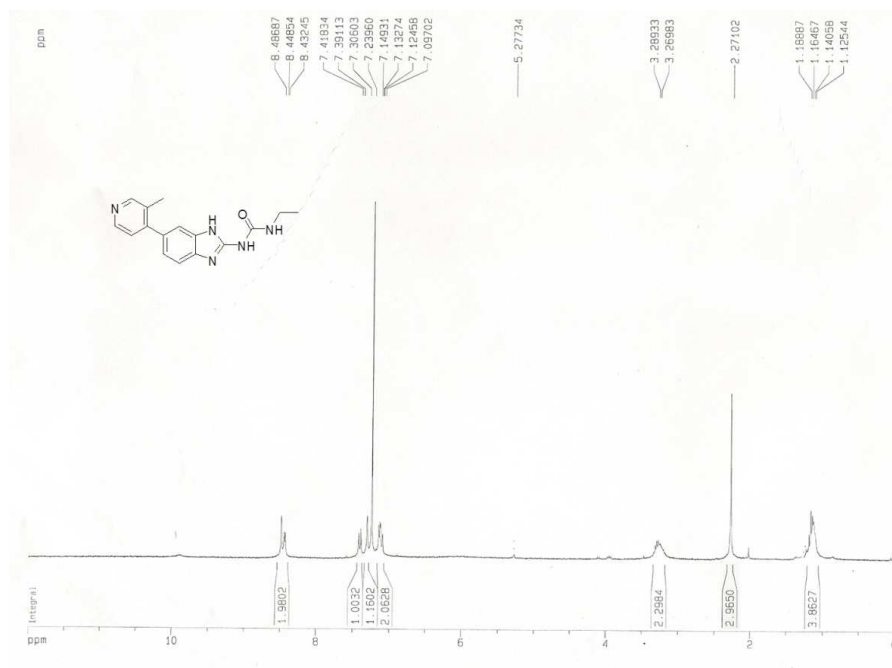


HRMS

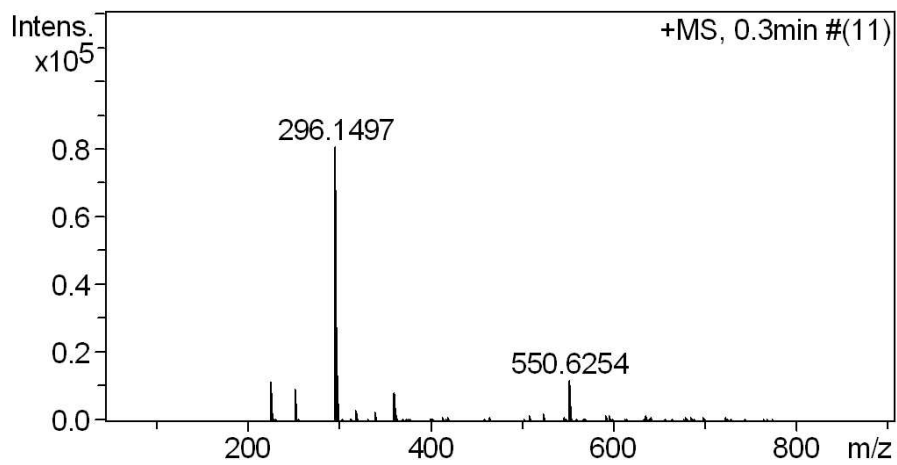


HPLC-Purity

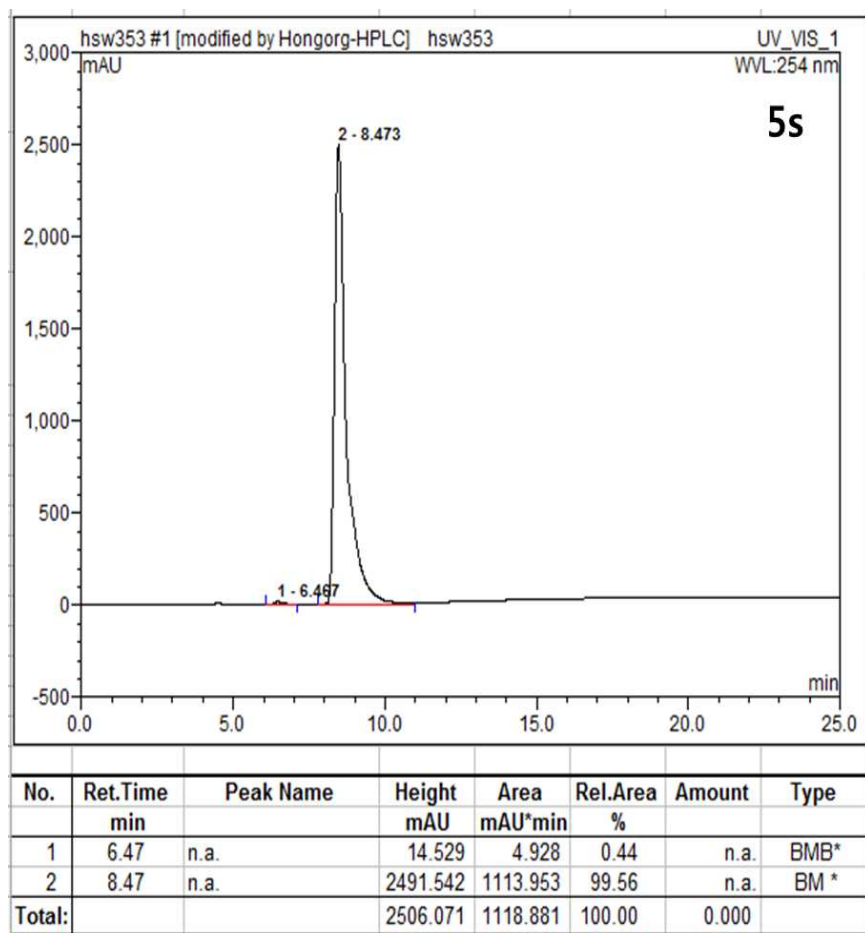
1-Ethyl-3-(6-(3-methylpyridin-4-yl)-1H-benzo[d]imidazol-2-yl)urea (5s).



300 MHz, ^1H NMR in CDCl_3

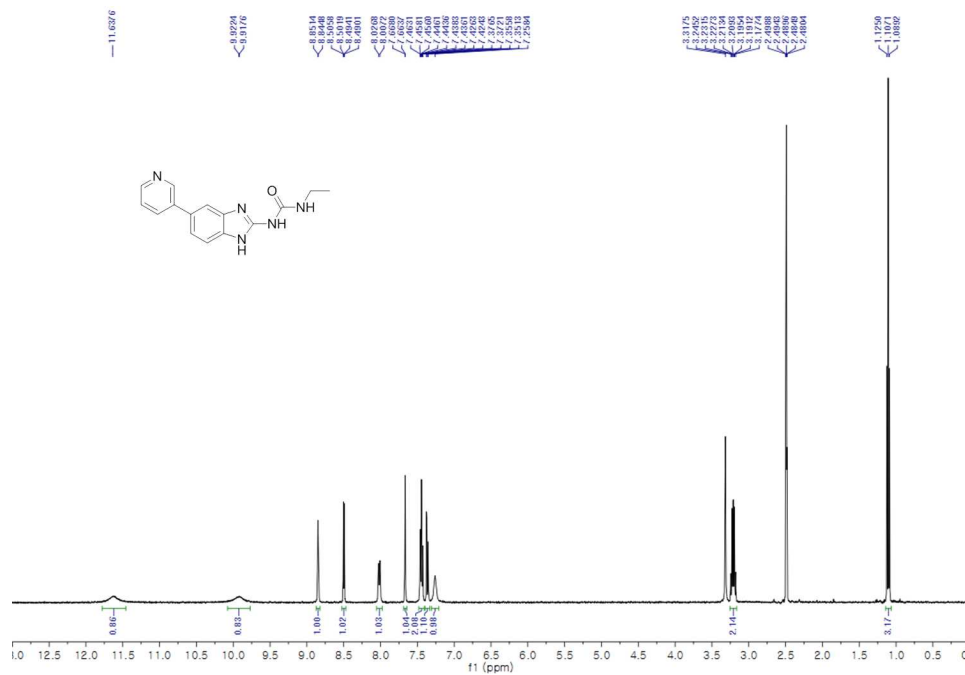


HRMS

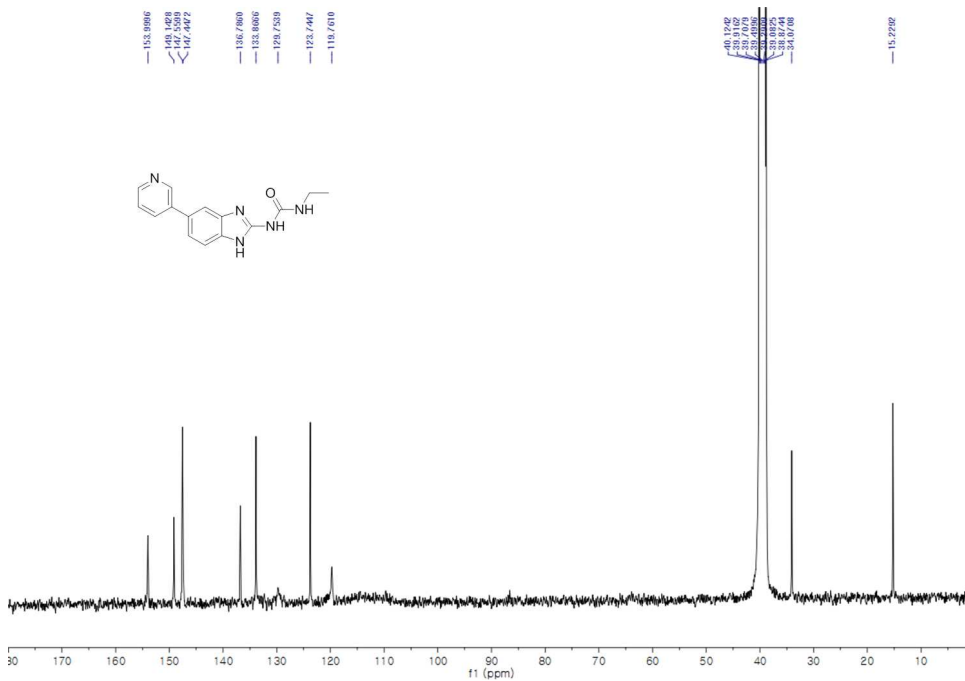


HPLC-Purity

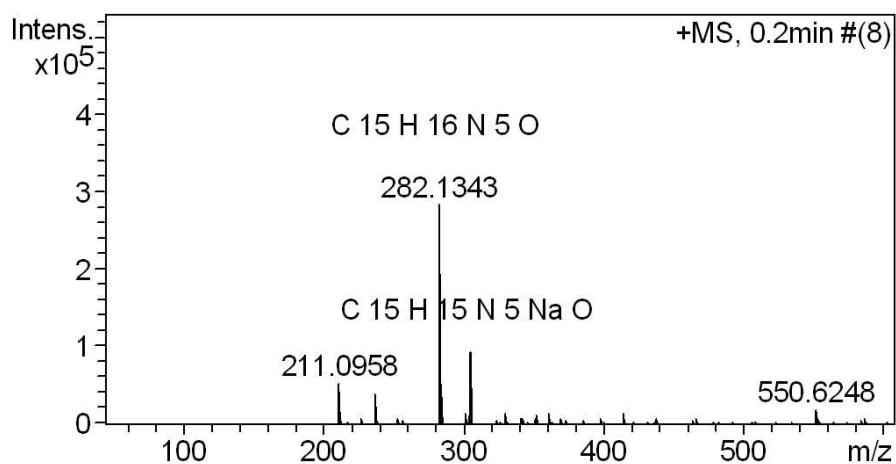
1-Ethyl-3-(6-(pyridin-3-yl)-1H-benzo[d]imidazol-2-yl)urea (5t).



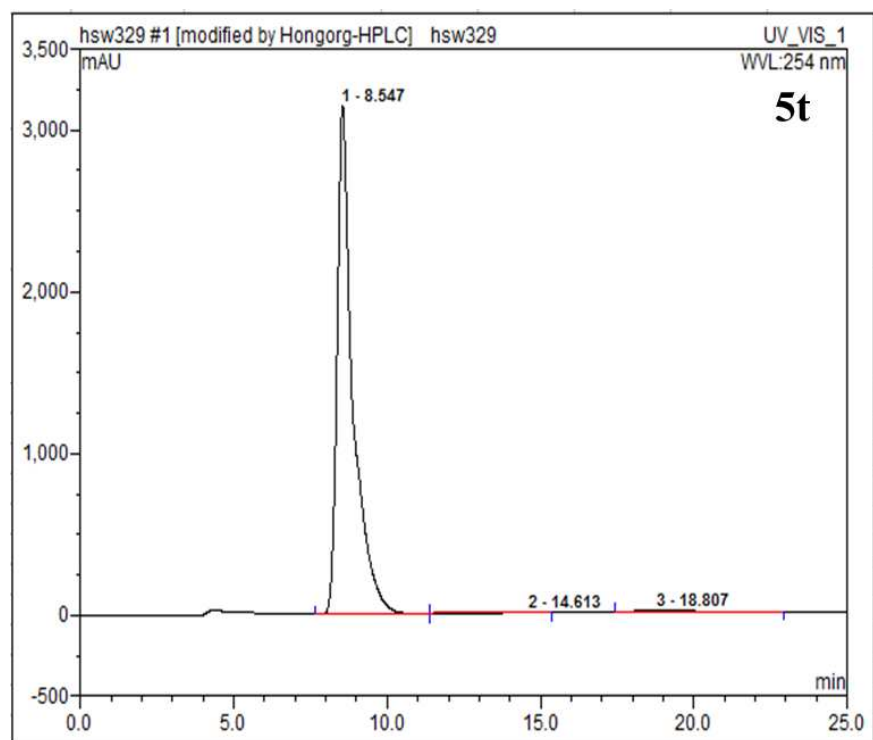
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆



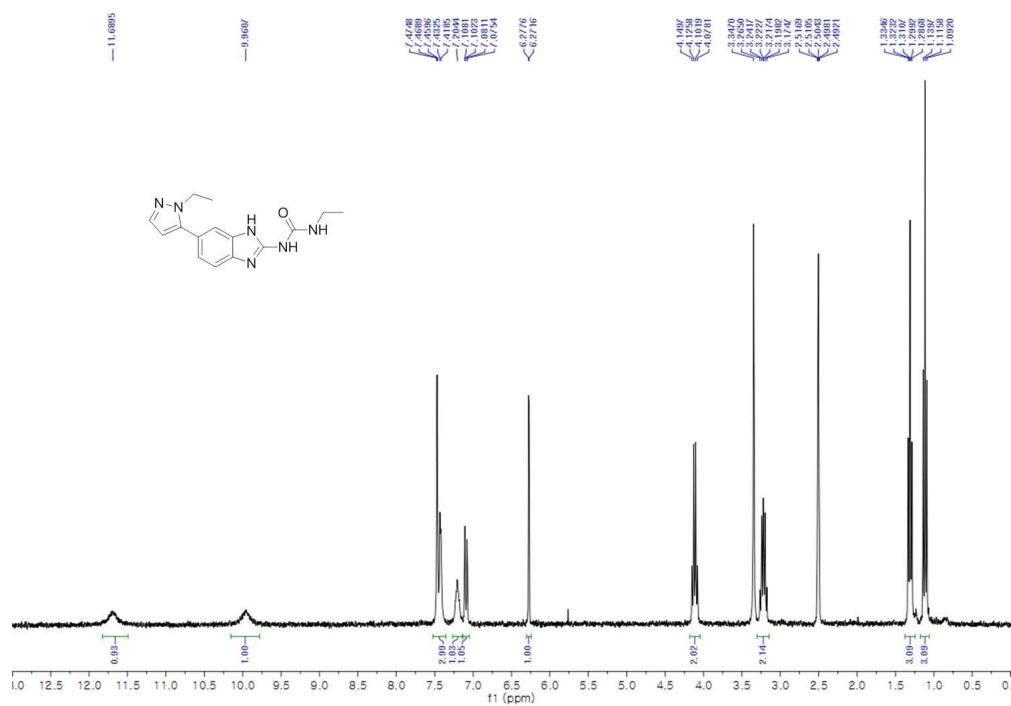
HRMS



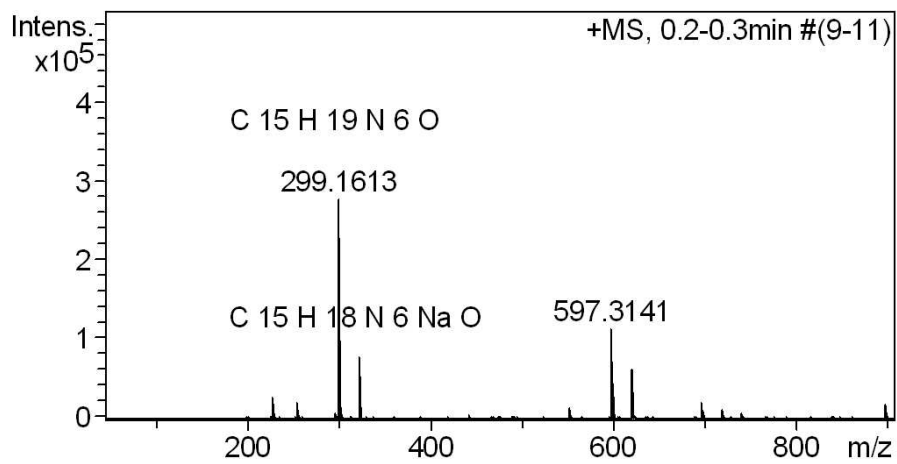
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.55	n.a.	3141.194	1875.220	99.30	n.a.	BM *
2	14.61	n.a.	2.588	0.647	0.03	n.a.	MB*
3	18.81	n.a.	6.120	12.662	0.67	n.a.	BMB*
Total:			3149.901	1888.529	100.00	0.000	

HPLC-Purity

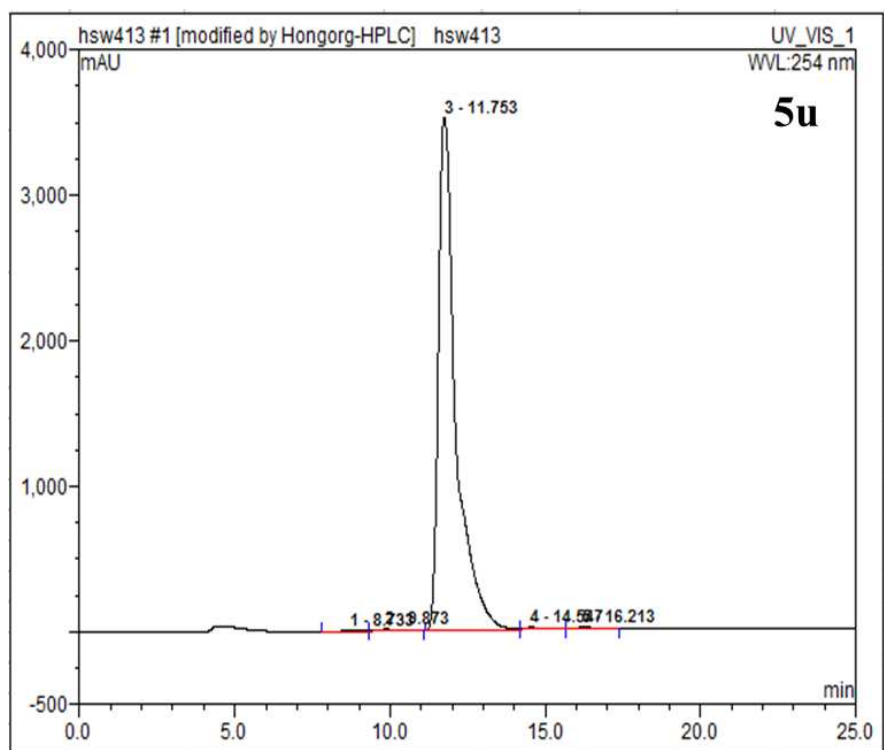
1-Ethyl-3-(6-(1-ethyl-1H-pyrazol-5-yl)-1H-benzo[d]imidazol-2-yl)urea (5u).



300 MHz, ¹H NMR in DMSO-*d*₆



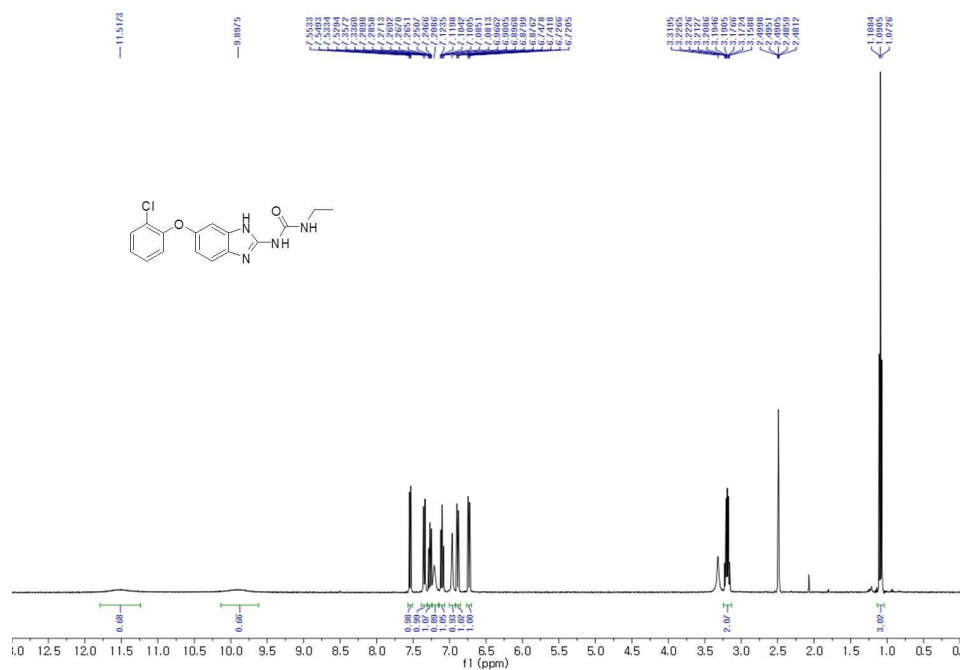
HRMS



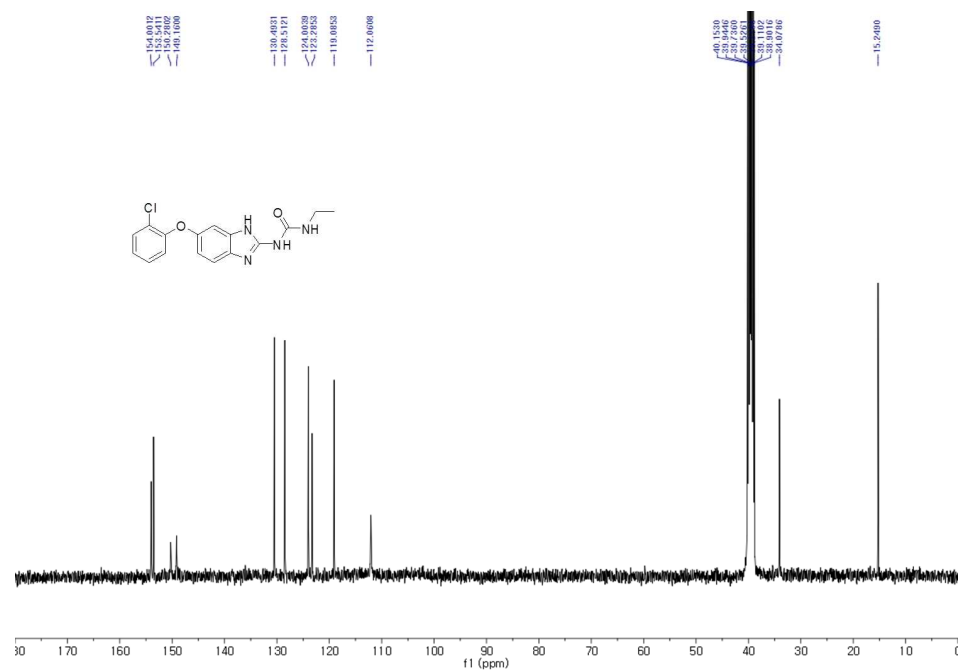
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	8.73	n.a.	3.913	3.236	0.14	n.a.	BM
2	9.87	n.a.	13.124	9.257	0.40	n.a.	MB
3	11.75	n.a.	3525.058	2298.319	98.88	n.a.	BM *
4	14.55	n.a.	14.153	6.777	0.29	n.a.	M *
5	16.21	n.a.	10.930	6.777	0.29	n.a.	MB*
Total:			3567.178	2324.366	100.00	0.000	

HPLC-Purity

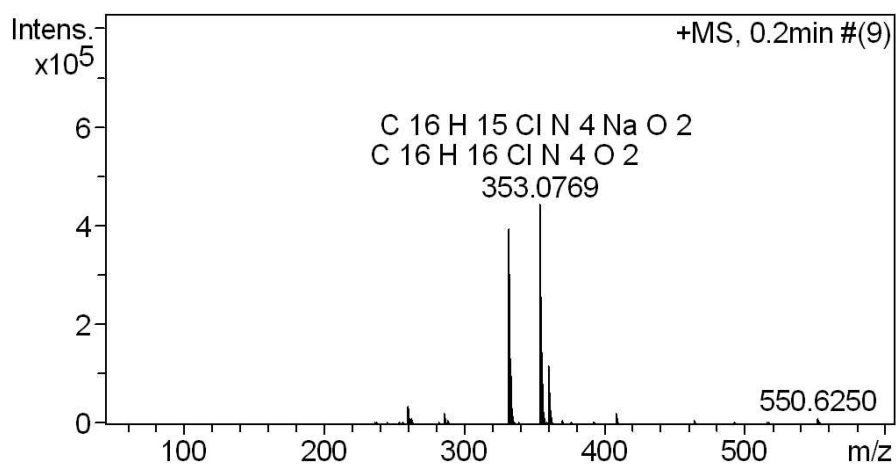
1-(5-(2-Chlorophenoxy)-1H-benzo[d]imidazol-2-yl)-3-ethylurea (5v)



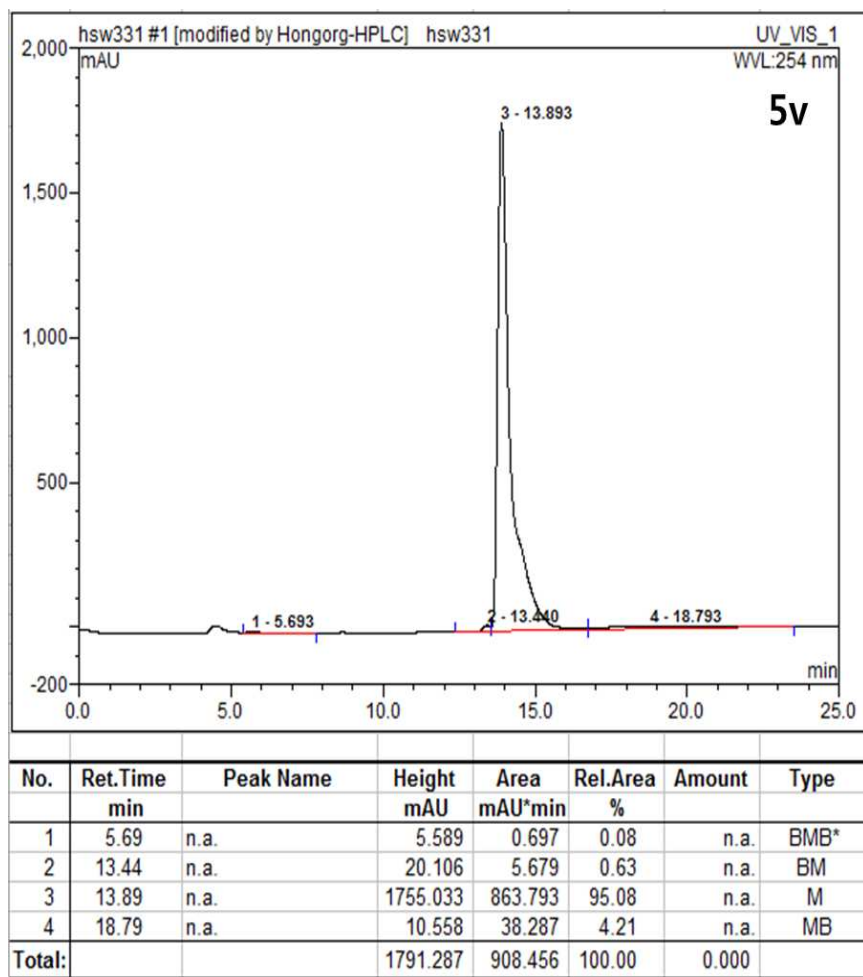
400 MHz, ¹H NMR in DMSO-*d*₆



400 MHz, ^1H NMR in DMSO- d_6

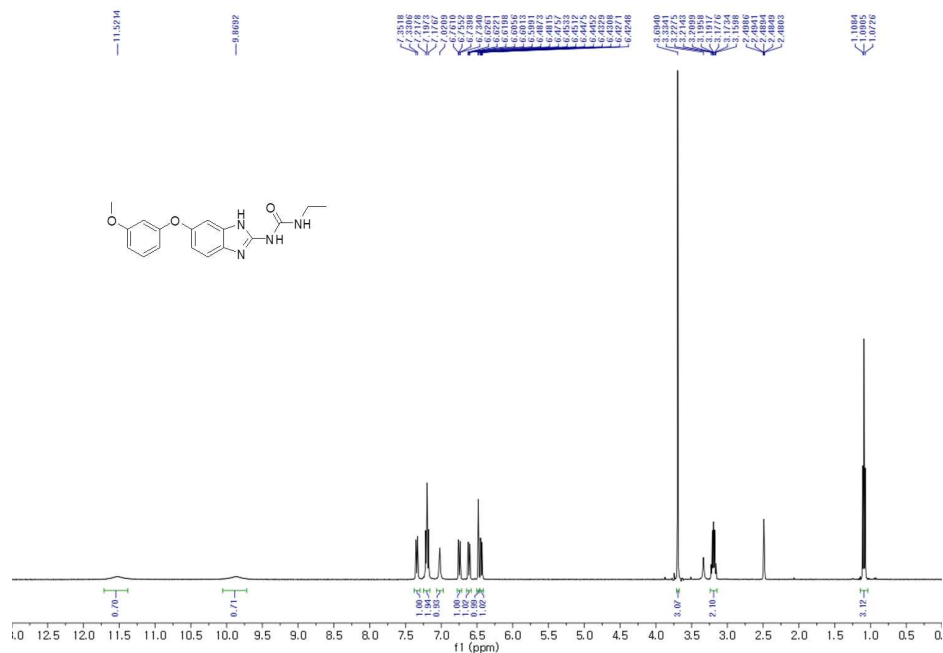


HRMS

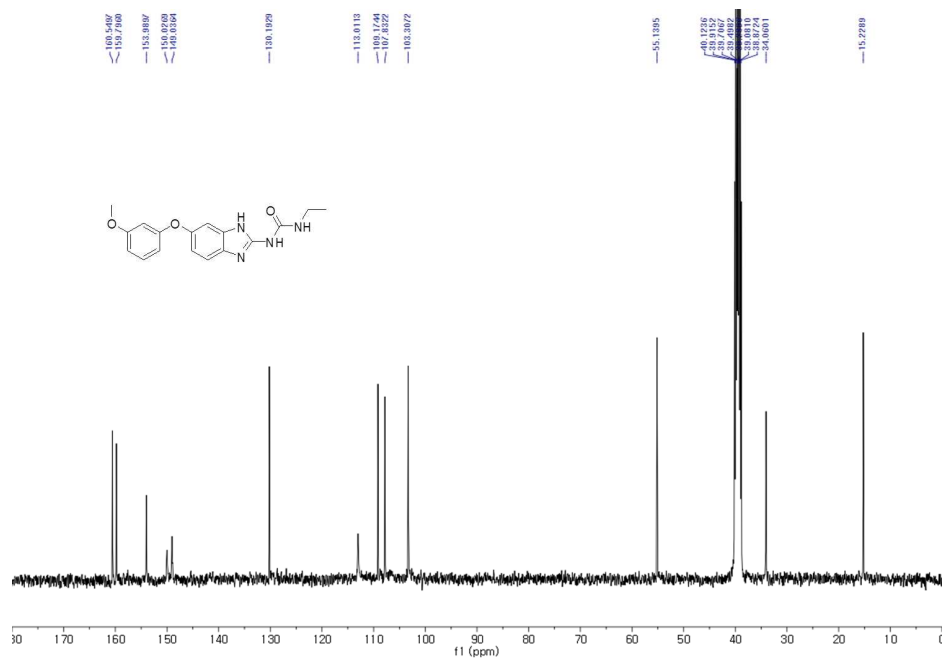


HPLC-Purity

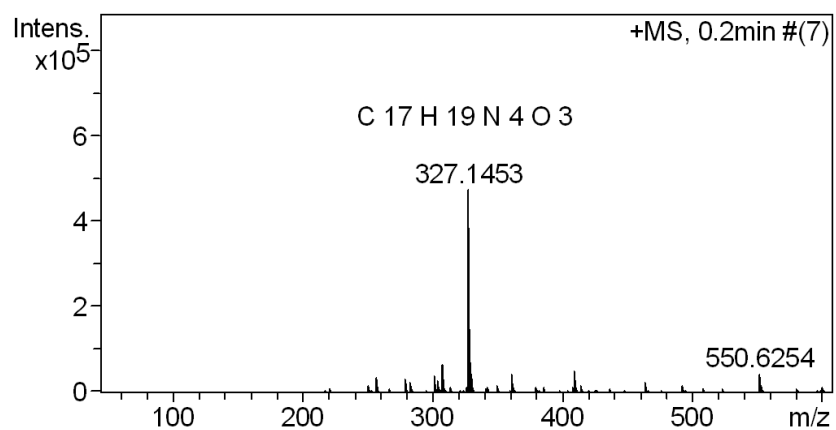
1-Ethyl-3-(5-(3-methoxyphenoxy)-1H-benzo[d]imidazol-2-yl)urea (5w)



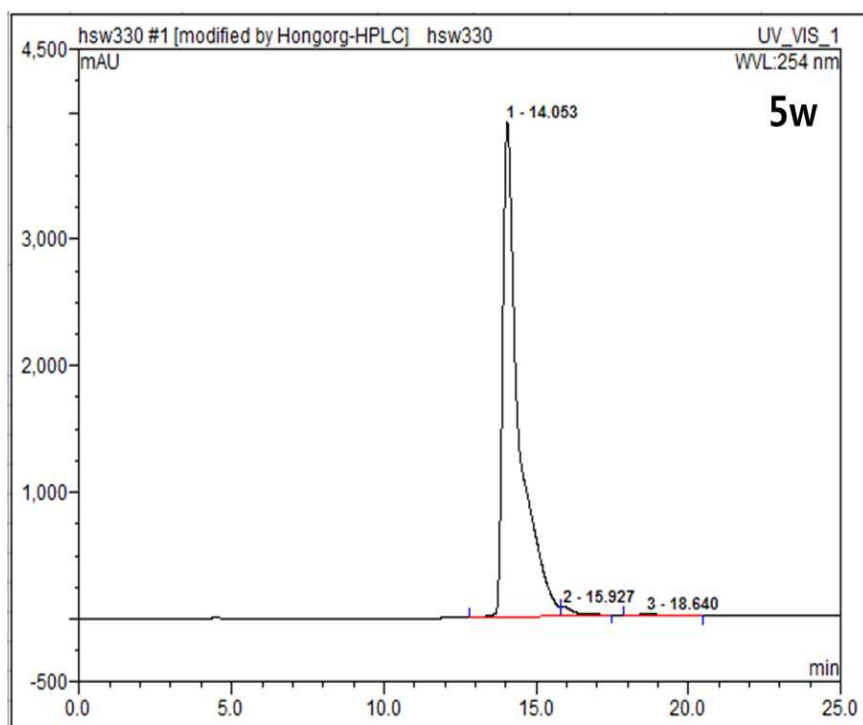
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆



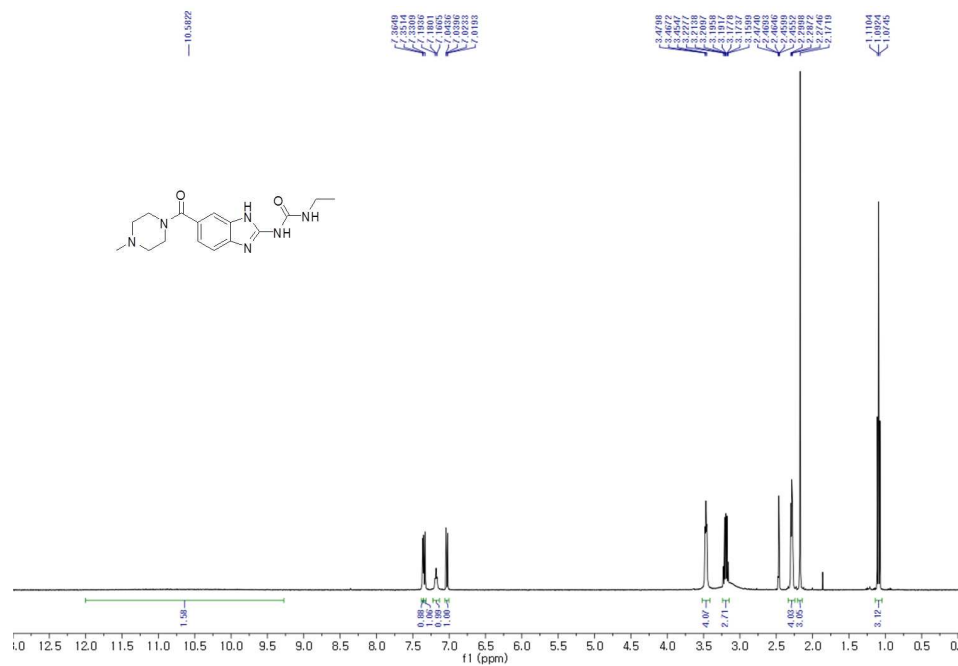
HRMS



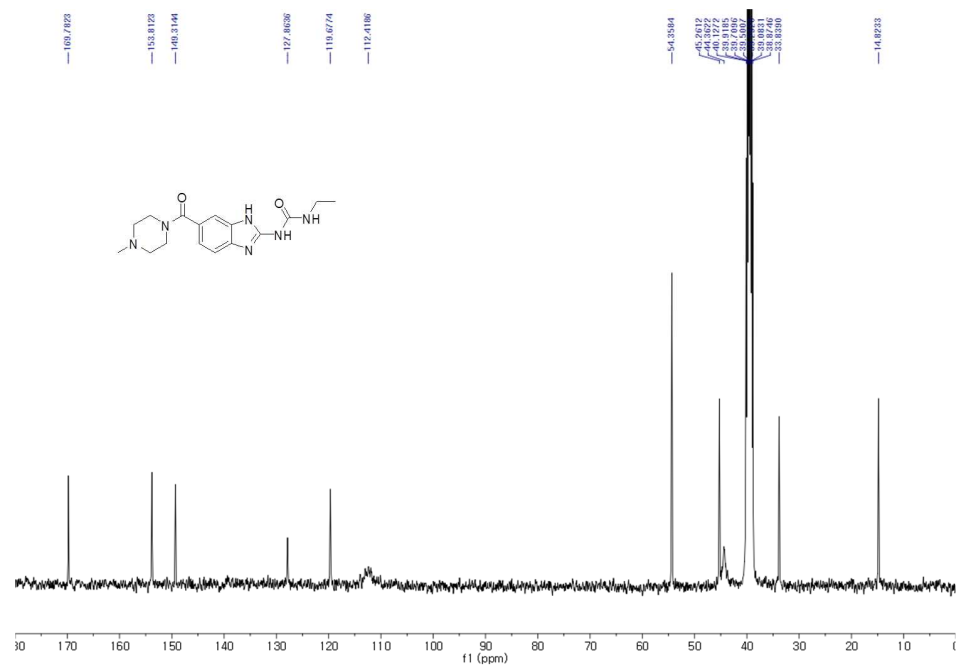
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	14.05	n.a.	3906.194	2410.877	98.42	n.a.	BM
2	15.93	n.a.	67.555	34.355	1.40	n.a.	MB
3	18.64	n.a.	4.957	4.454	0.18	n.a.	BMB
Total:			3978.707	2449.685	100.00	0.000	

HPLC-Purity

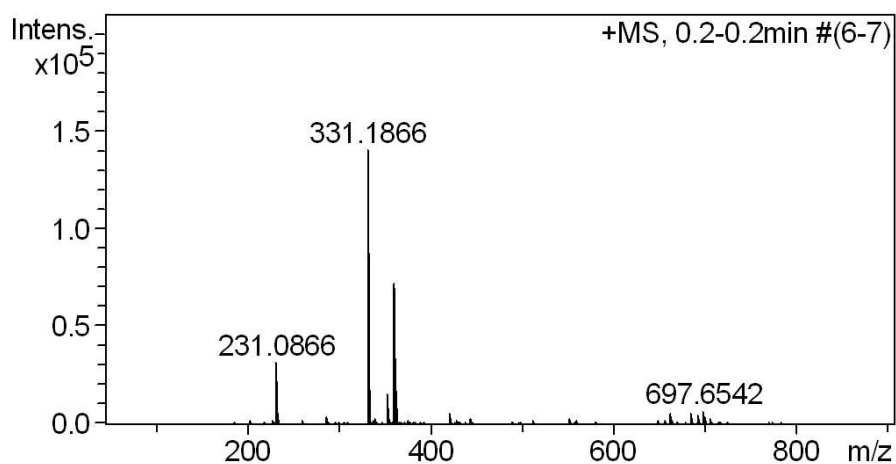
1-Ethyl-3-(6-(4-methylpiperazine-1-carbonyl)-1H-benzo[d]imidazol-2-yl)urea (5x).



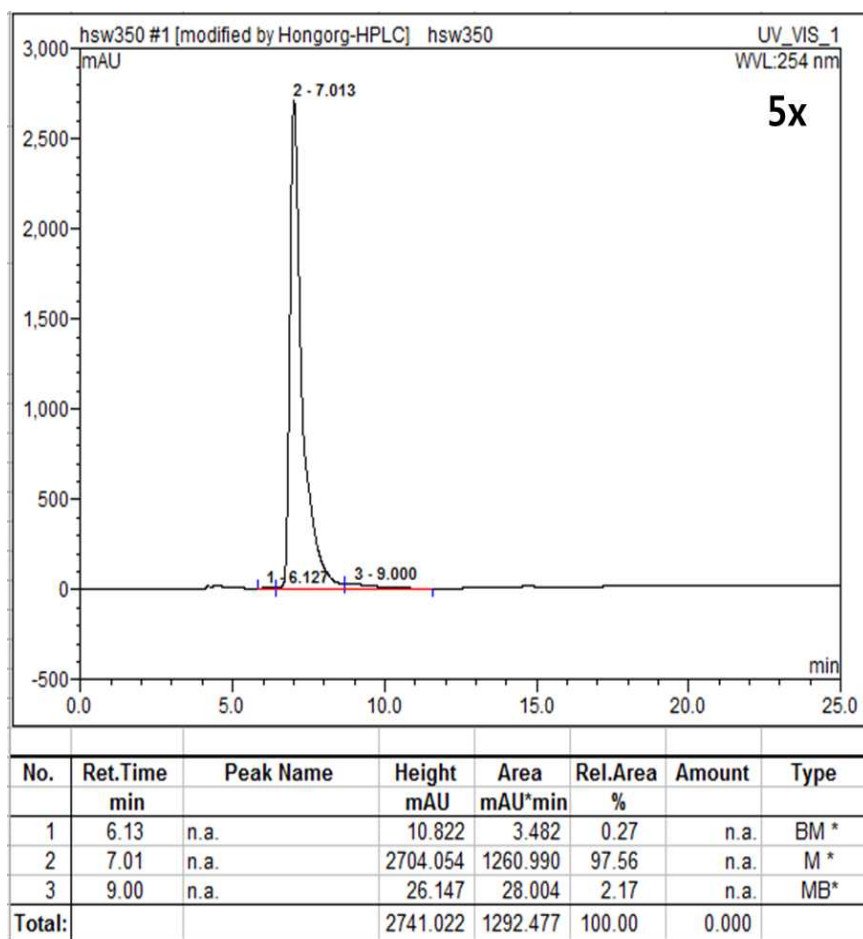
400 MHz, ^1H NMR in $\text{DMSO-}d_6$



100 MHz, ^{13}C NMR in DMSO- d_6

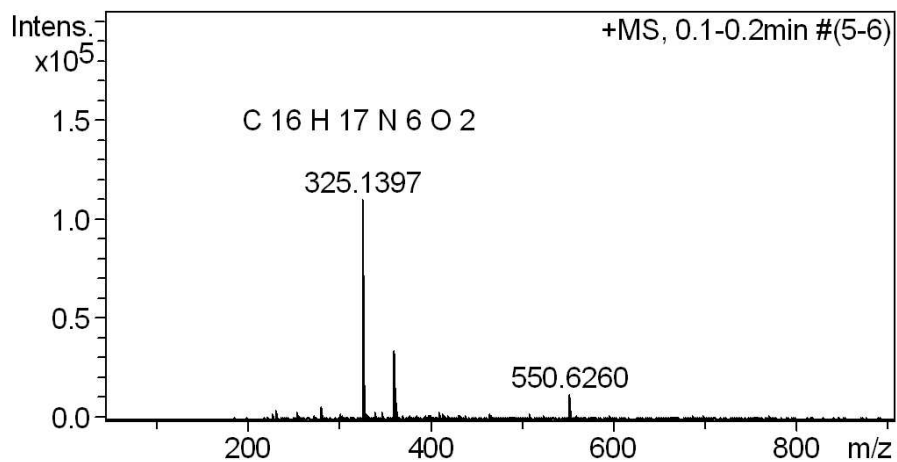
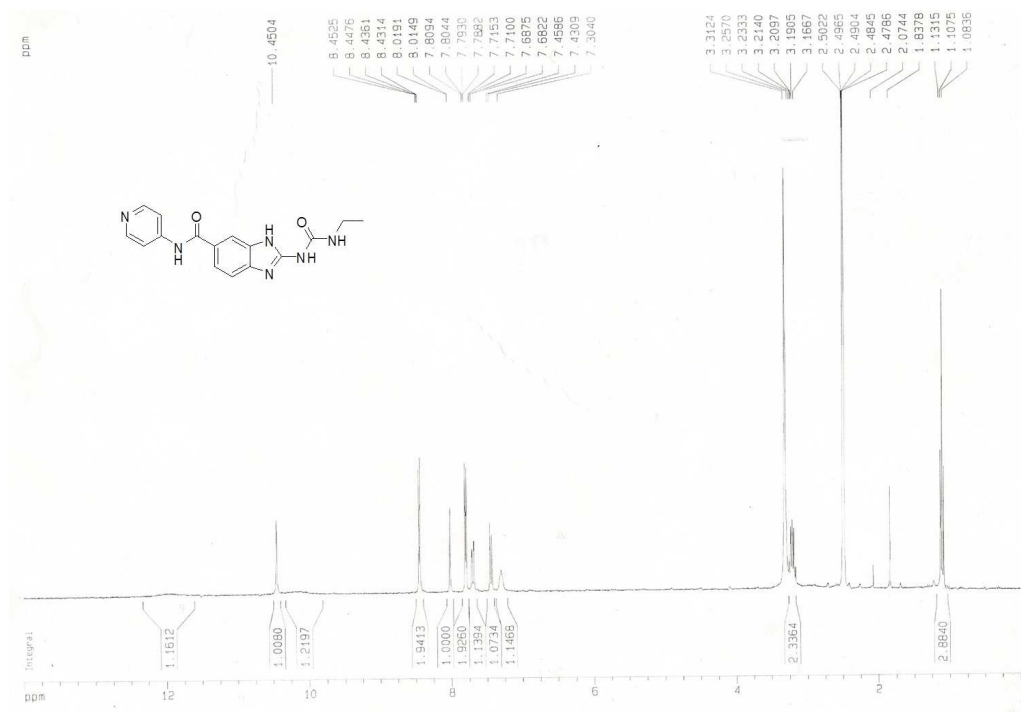


HRMS

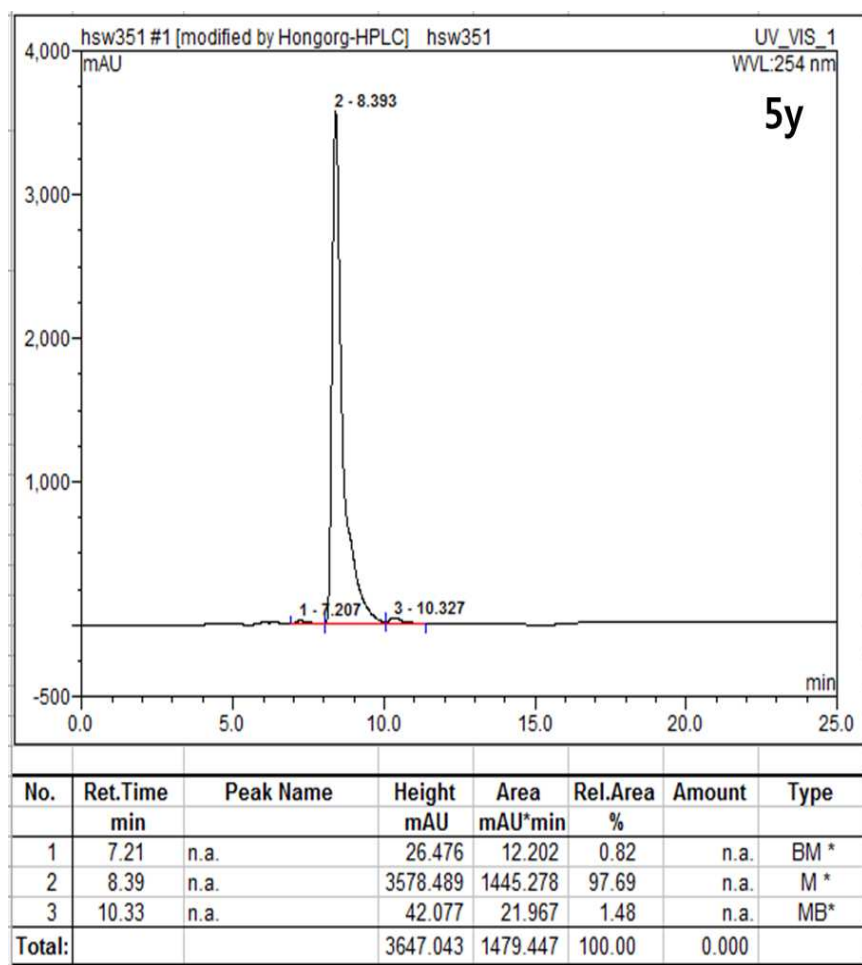


HPLC-Purity

2-(3-Ethylureido)-N-(pyridin-4-yl)-1H-benzo[d]imidazole-6-carboxamide (5y).

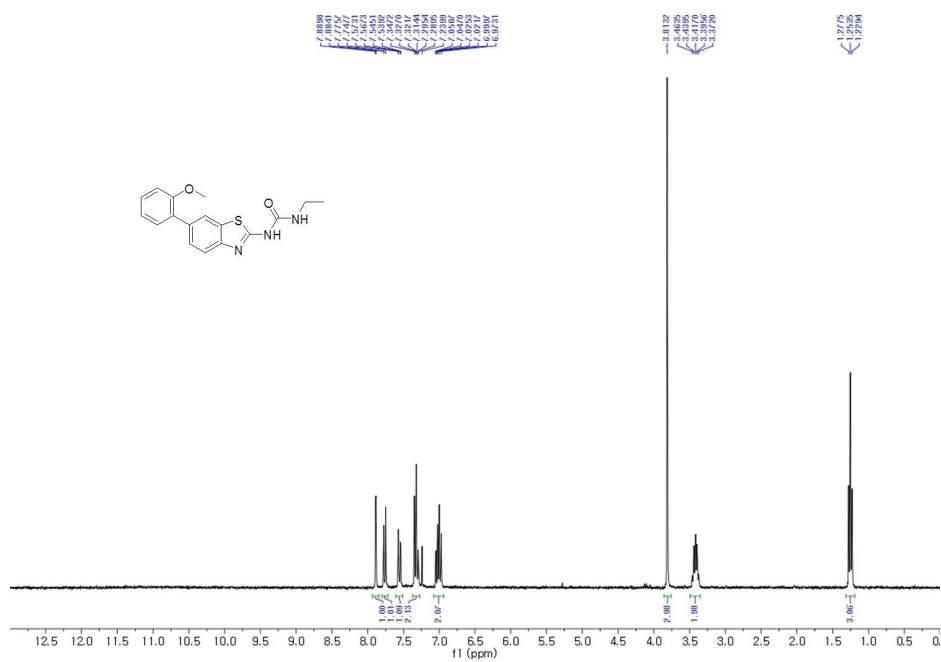


HRMS

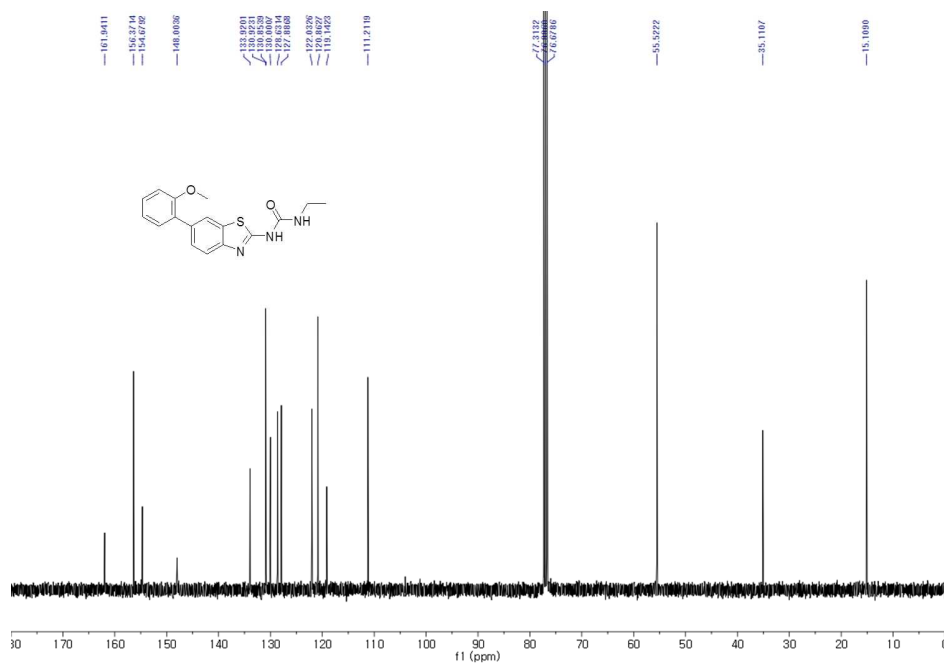


HPLC-Purity

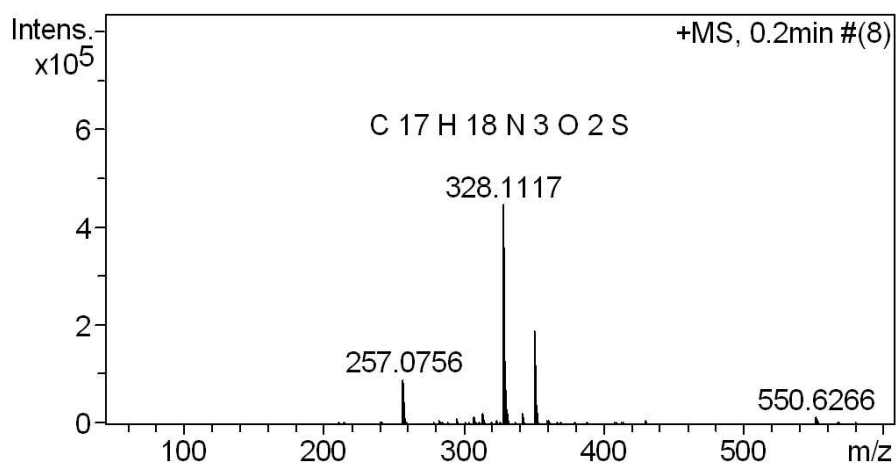
1-Ethyl-3-(6-(2-methoxyphenyl)benzo[d]thiazol-2-yl)urea (9a)



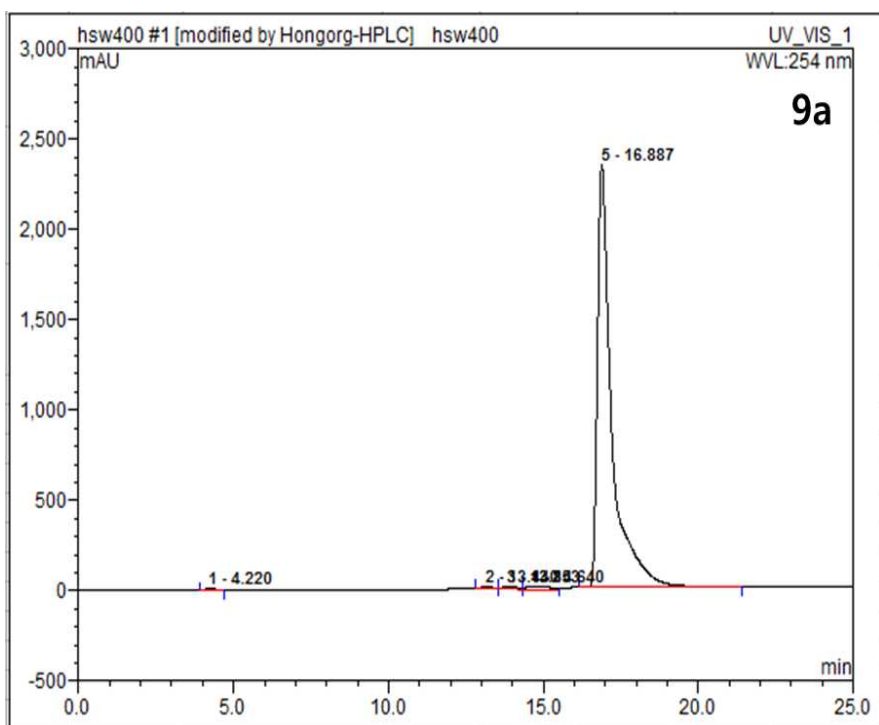
300 MHz, ^1H NMR in CDCl_3



100 MHz, ^{13}C NMR in CDCl_3



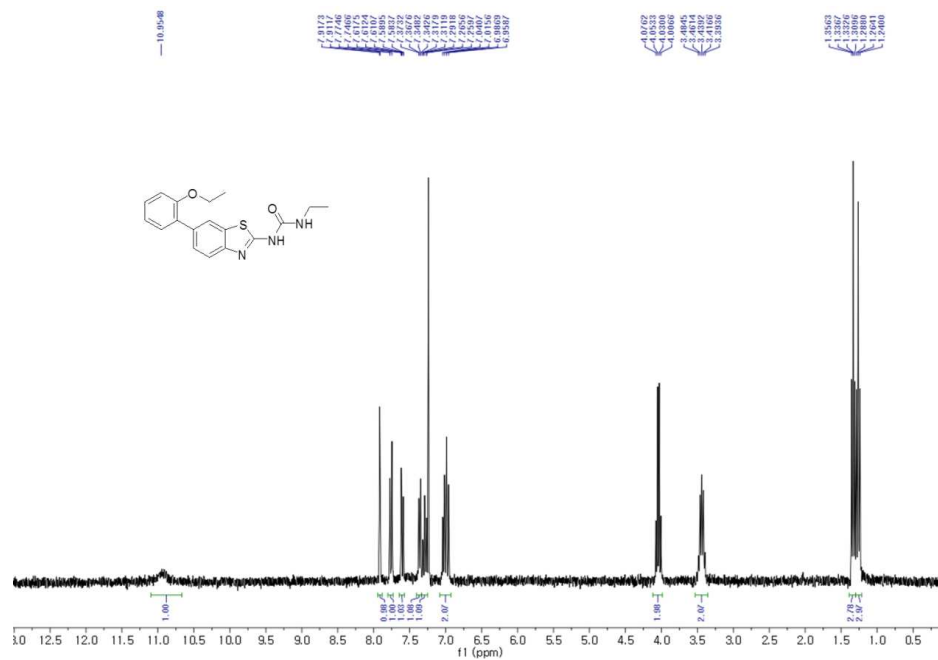
HRMS



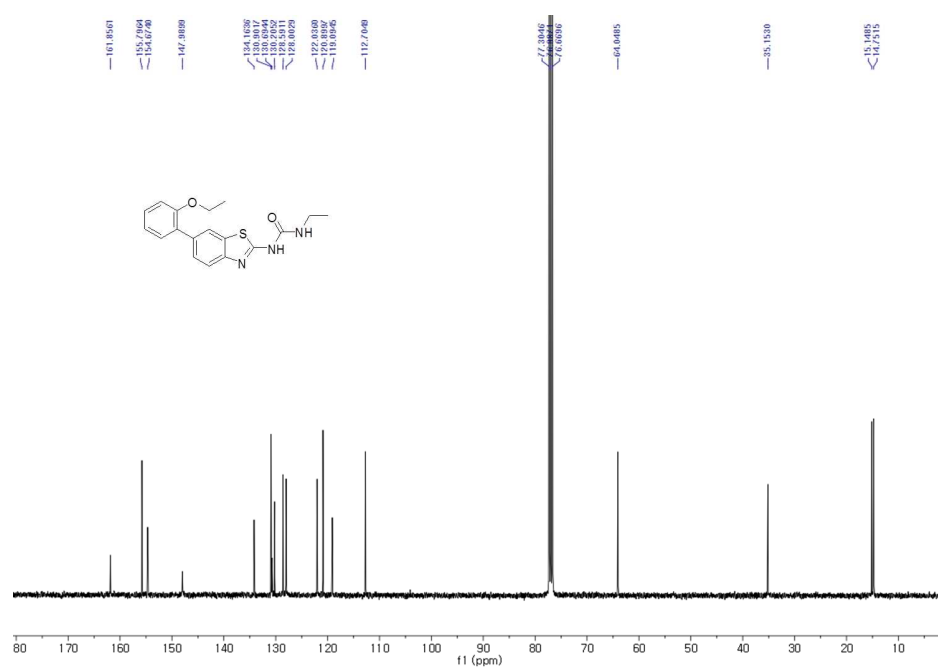
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	4.22	n.a.	7.851	3.034	0.24	n.a.	BMB
2	13.14	n.a.	10.038	4.839	0.38	n.a.	BM *
3	13.85	n.a.	13.398	9.248	0.72	n.a.	M *
4	14.64	n.a.	19.525	20.306	1.57	n.a.	M *
5	16.89	n.a.	2340.678	1252.407	97.10	n.a.	BMB*
Total:			2391.490	1289.834	100.00	0.000	

HPLC-Purity

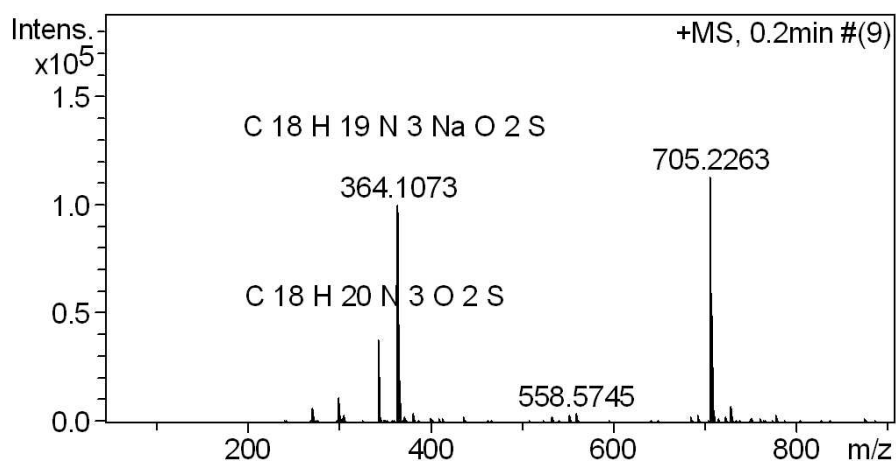
1-(6-(2-Ethoxyphenyl)benzo[d]thiazol-2-yl)-3-ethylurea (9b).



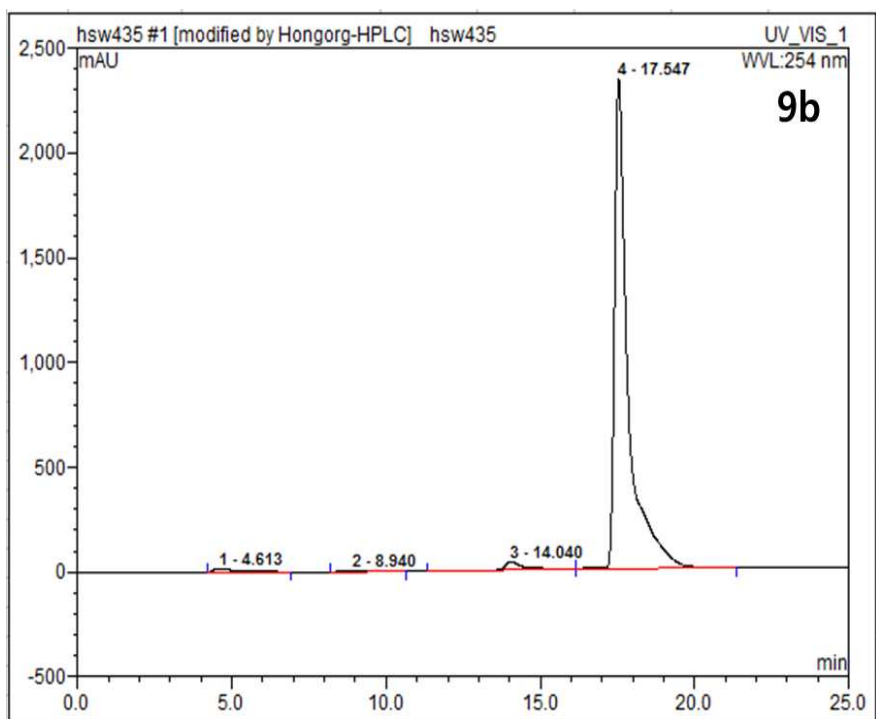
300 MHz, ¹H NMR in CDCl₃



100 MHz, ¹³C NMR in CDCl₃



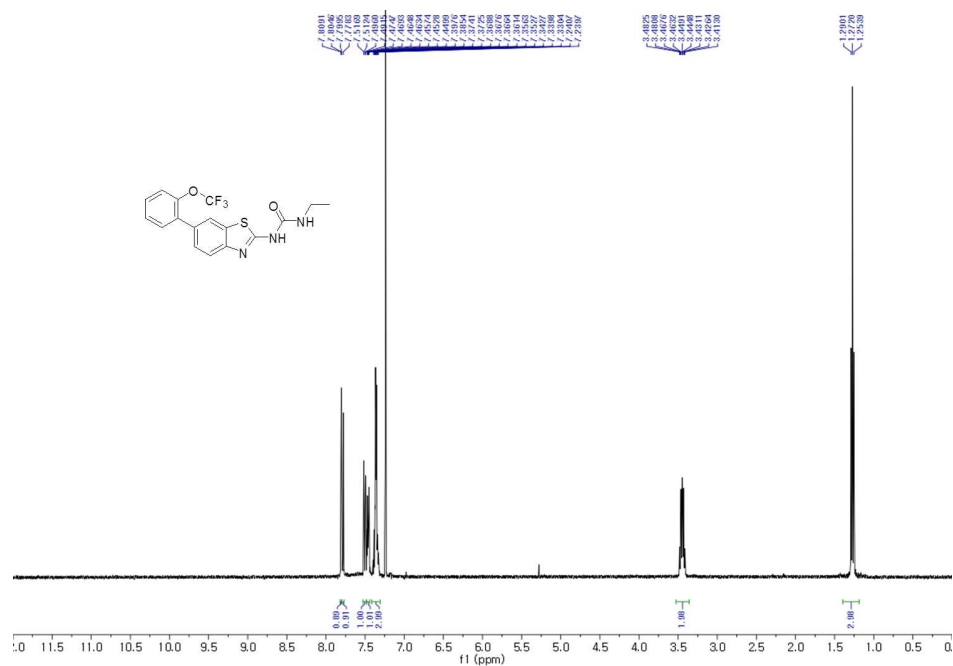
HPLC



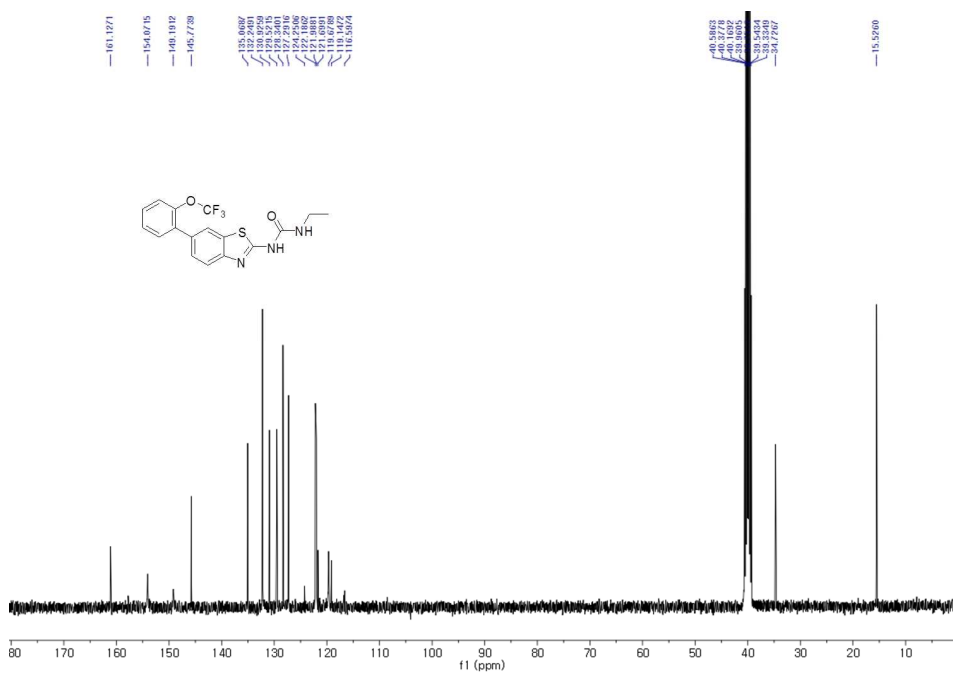
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	4.61	n.a.	14.980	12.689	1.02	n.a.	BMB*
2	8.94	n.a.	3.120	2.898	0.23	n.a.	BMB
3	14.04	n.a.	40.425	34.833	2.79	n.a.	BM *
4	17.55	n.a.	2334.921	1196.880	95.96	n.a.	MB*
Total:			2393.446	1247.301	100.00	0.000	

HPLC-Purity

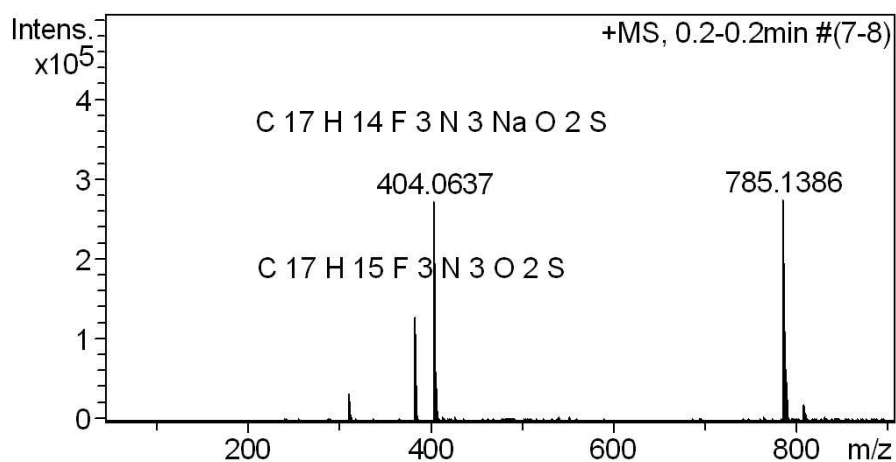
1-Ethyl-3-(6-(2-(trifluoromethoxy)phenyl)benzo[d]thiazol-2-yl)urea (9c).



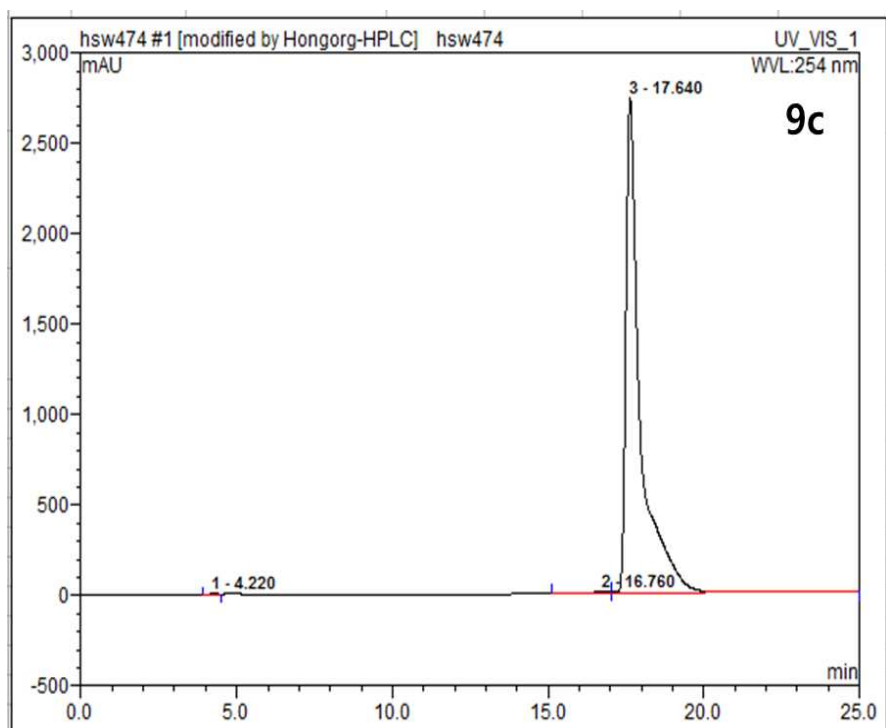
400 MHz, ¹H NMR in CDCl₃



100 MHz, ¹³C NMR in DMSO-*d*₆



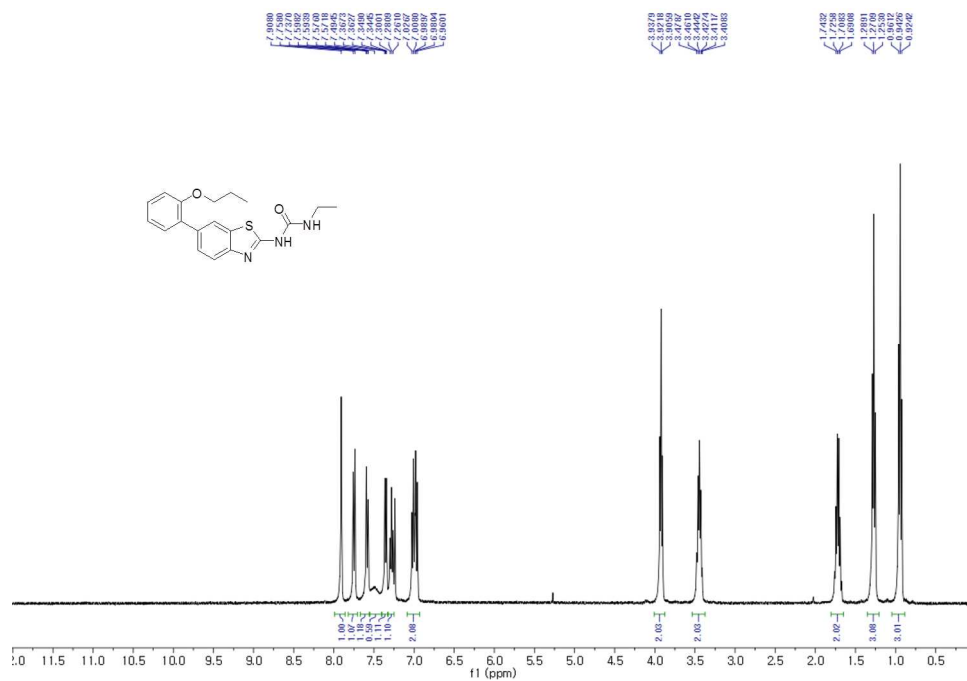
HRMS



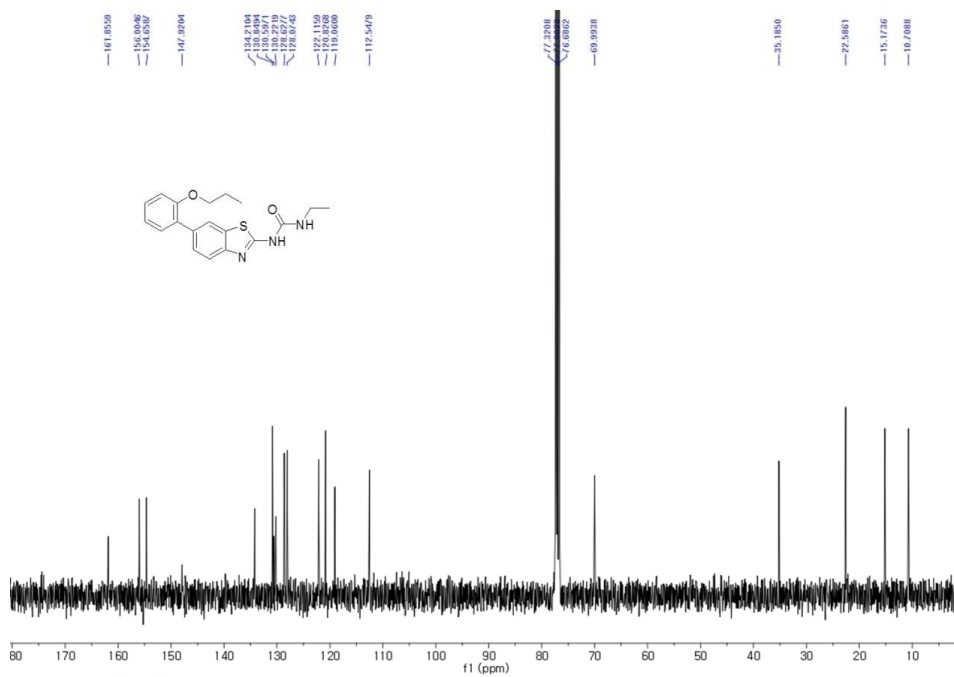
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.22	n.a.	5.330	1.611	0.11	n.a.	BMB*
2	16.76	n.a.	9.005	5.021	0.34	n.a.	BM *
3	17.64	n.a.	2733.124	1468.761	99.55	n.a.	MB*
Total:			2747.459	1475.393	100.00	0.000	

HPLC-Purity

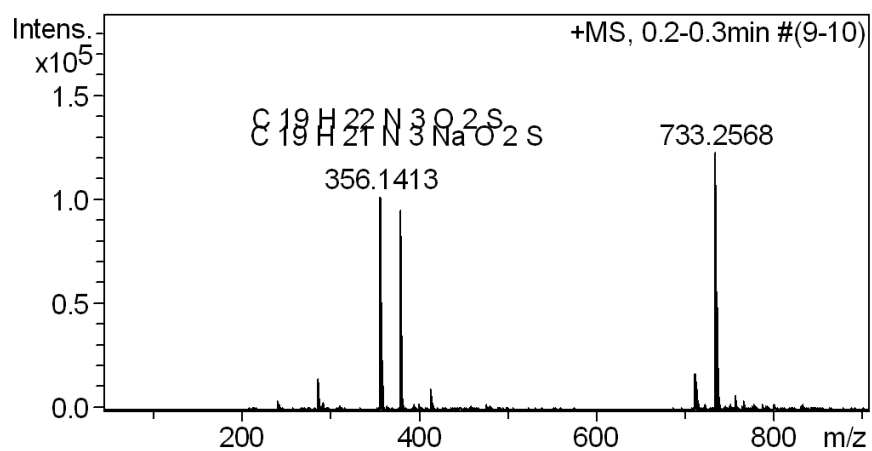
1-Ethyl-3-(6-(2-propoxyphenyl)benzo[d]thiazol-2-yl)urea (9d).



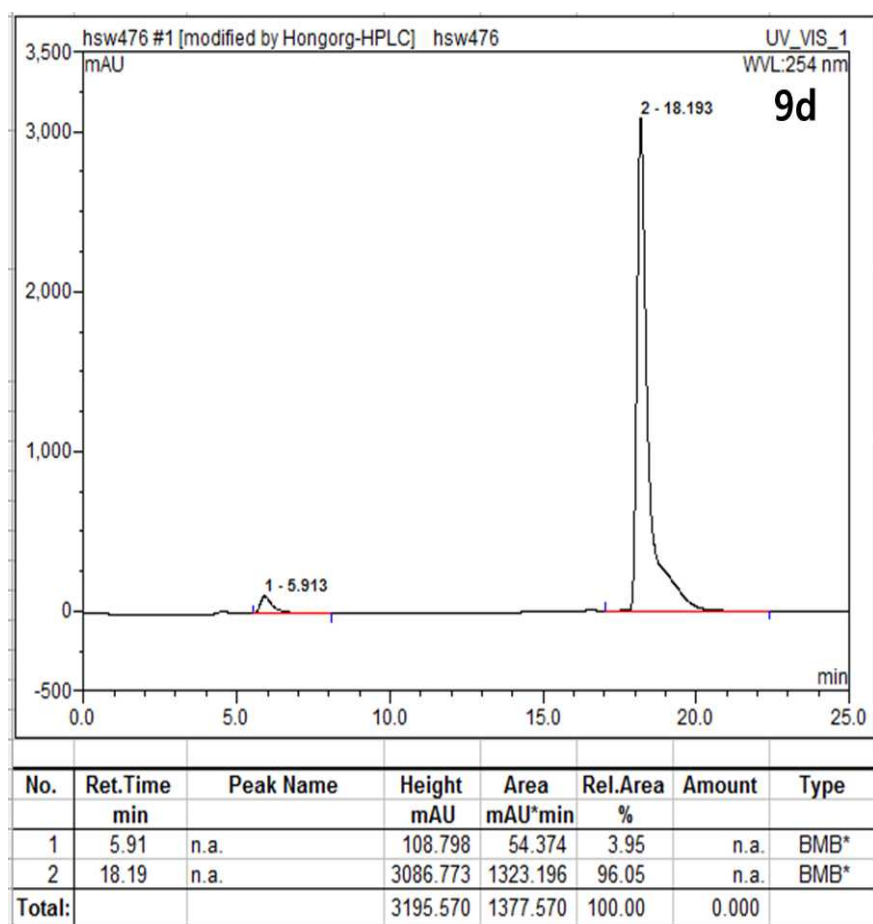
400 MHz, ¹H NMR in CDCl₃



100 MHz, ¹³C NMR in CDCl₃

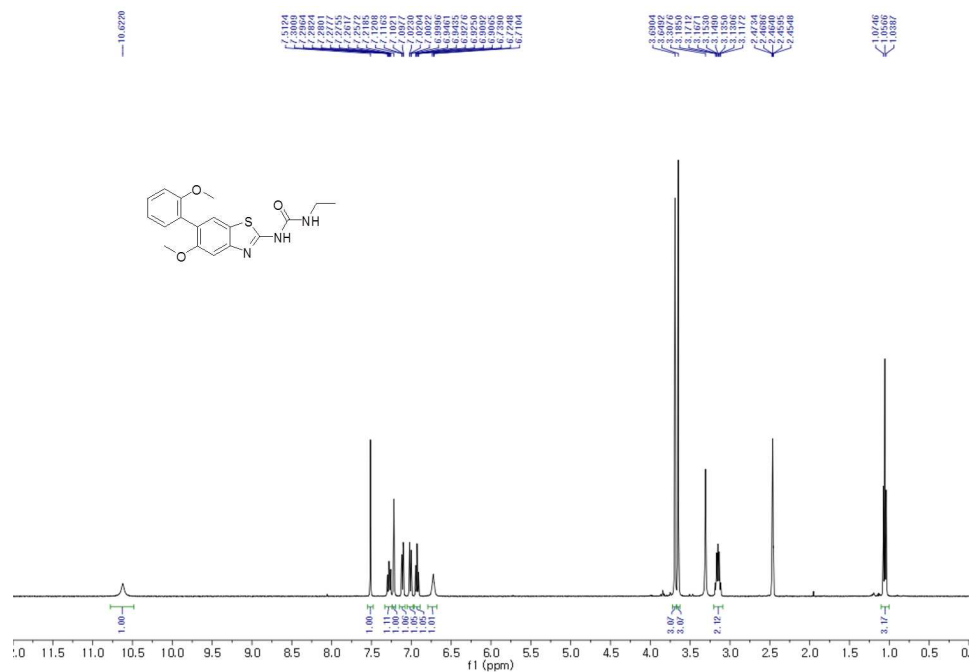


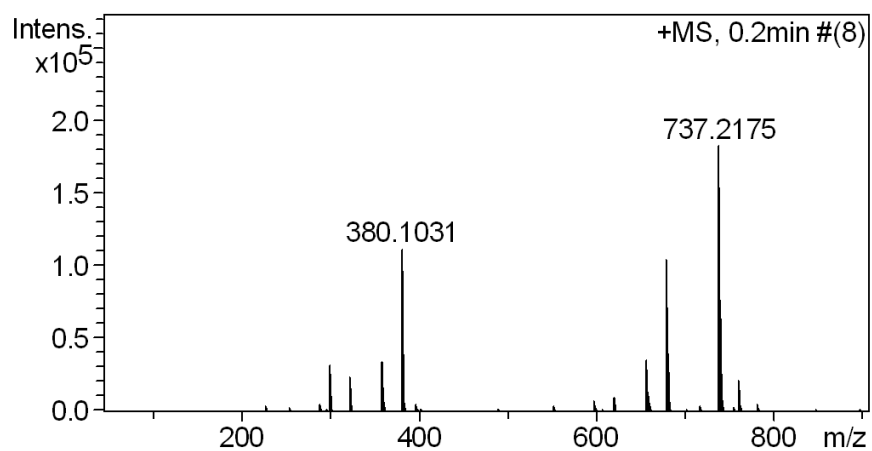
HRMS



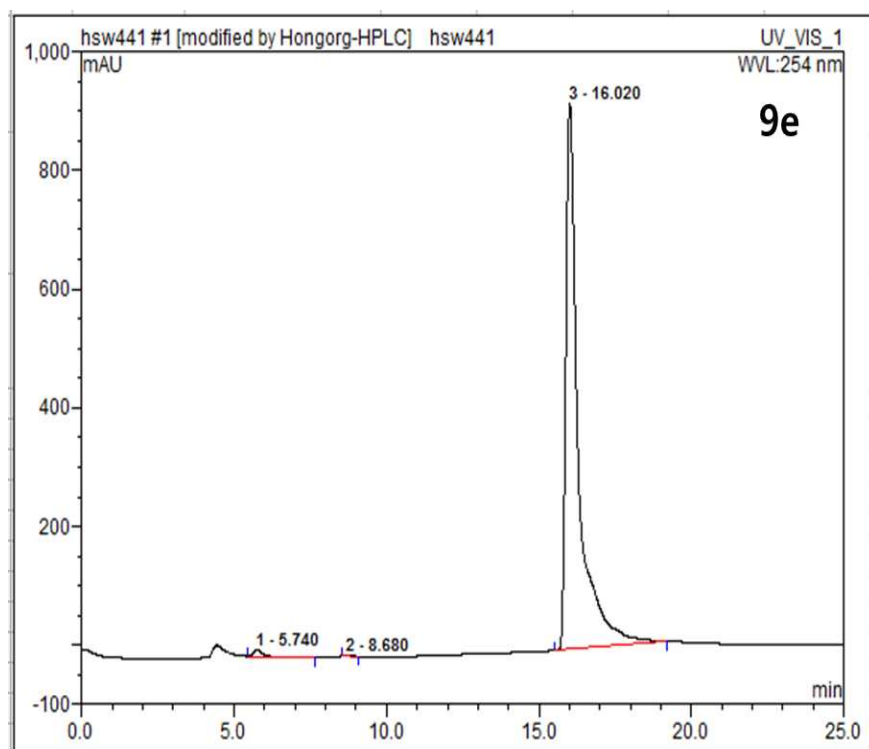
HPLC-Purity

1-Ethyl-3-(5-methoxy-6-(2-methoxyphenyl)benzo[d]thiazol-2-yl)urea (9e).





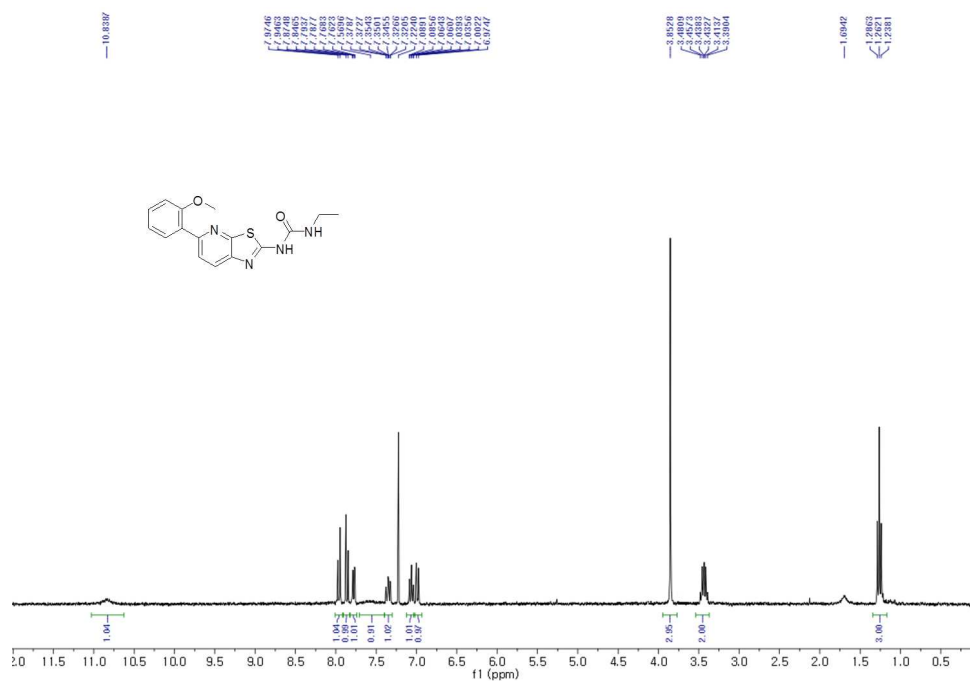
HRMS



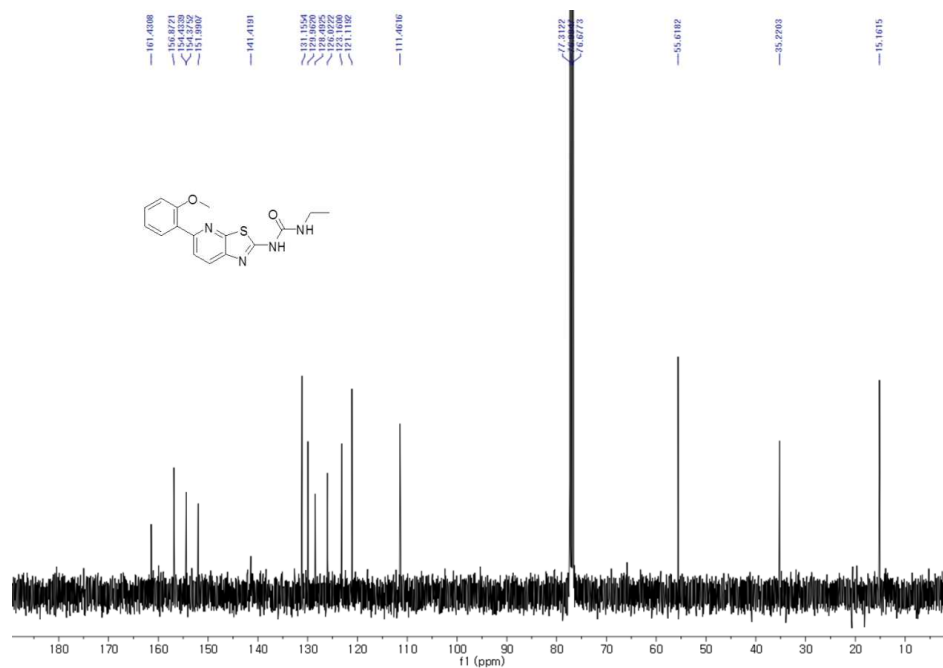
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.74	n.a.	10.970	3.356	0.76	n.a.	BMB*
2	8.68	n.a.	0.393	0.127	0.03	n.a.	BMB*
3	16.02	n.a.	919.869	440.459	99.22	n.a.	BMB*
Total:			931.232	443.942	100.00	0.000	

HPLC-Purity

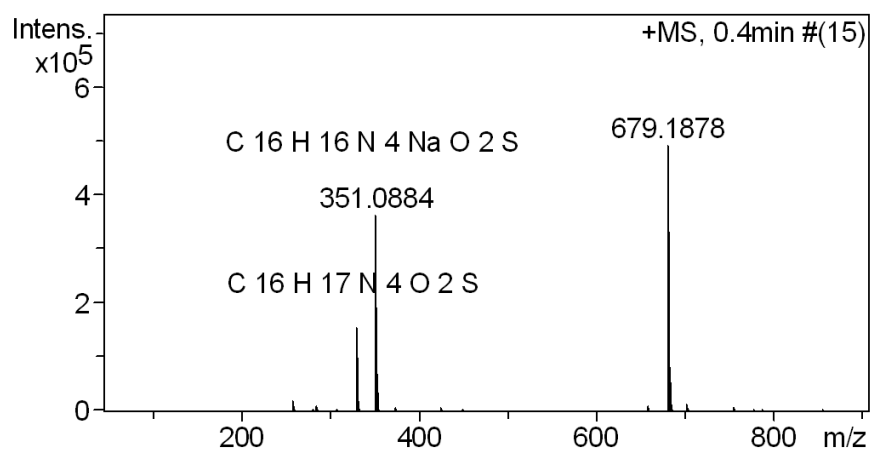
1-Ethyl-3-(5-(2-methoxyphenyl)thiazolo[5,4-b]pyridin-2-yl)urea (9f).



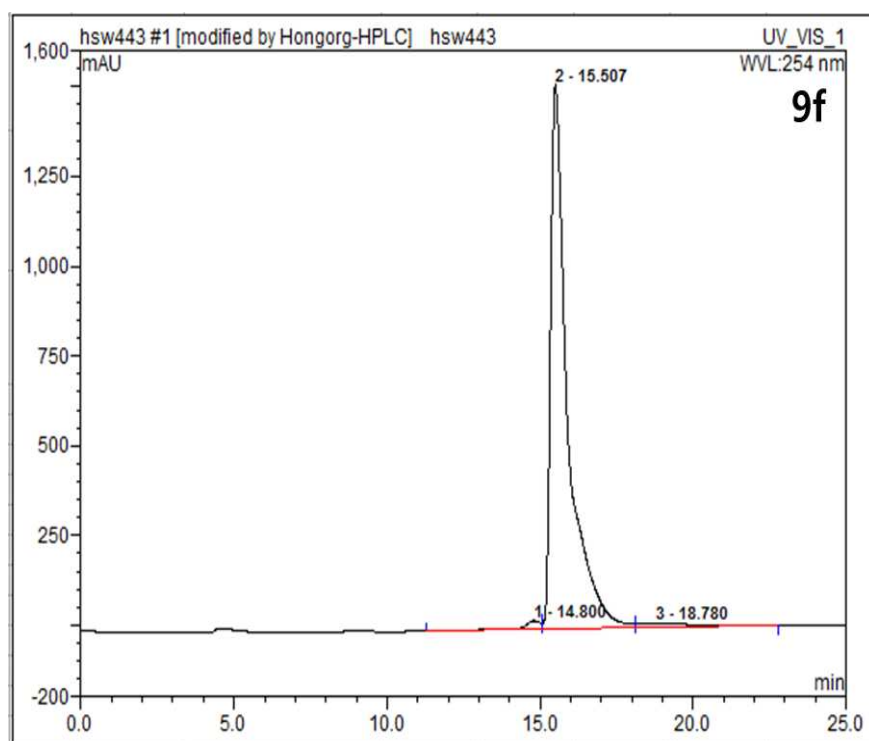
400 MHz, ¹H NMR in CDCl₃



100 MHz, ¹³C NMR in CDCl₃



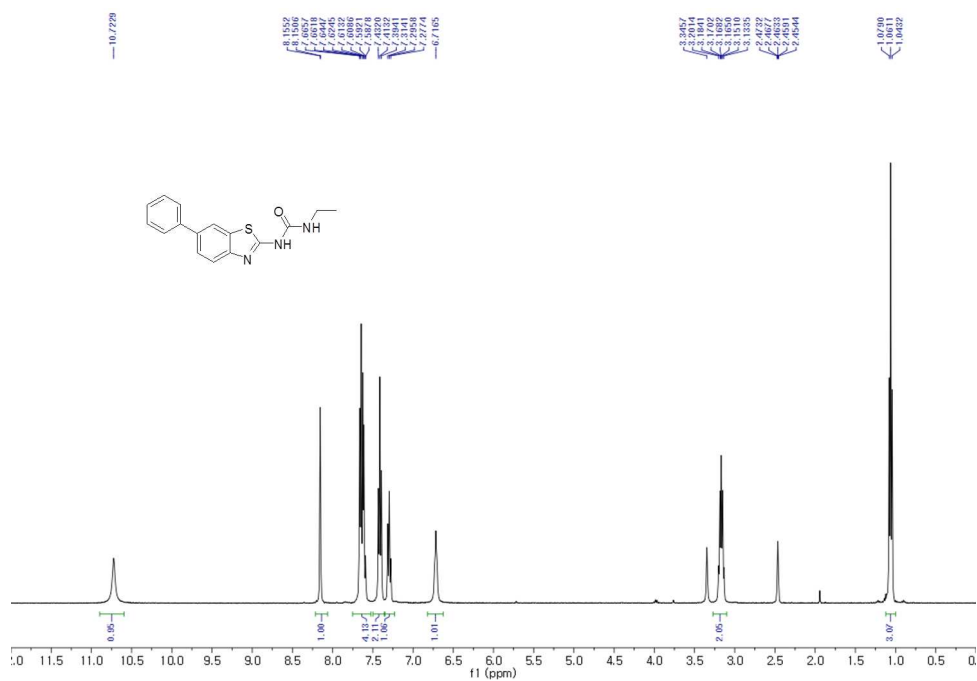
HRMS



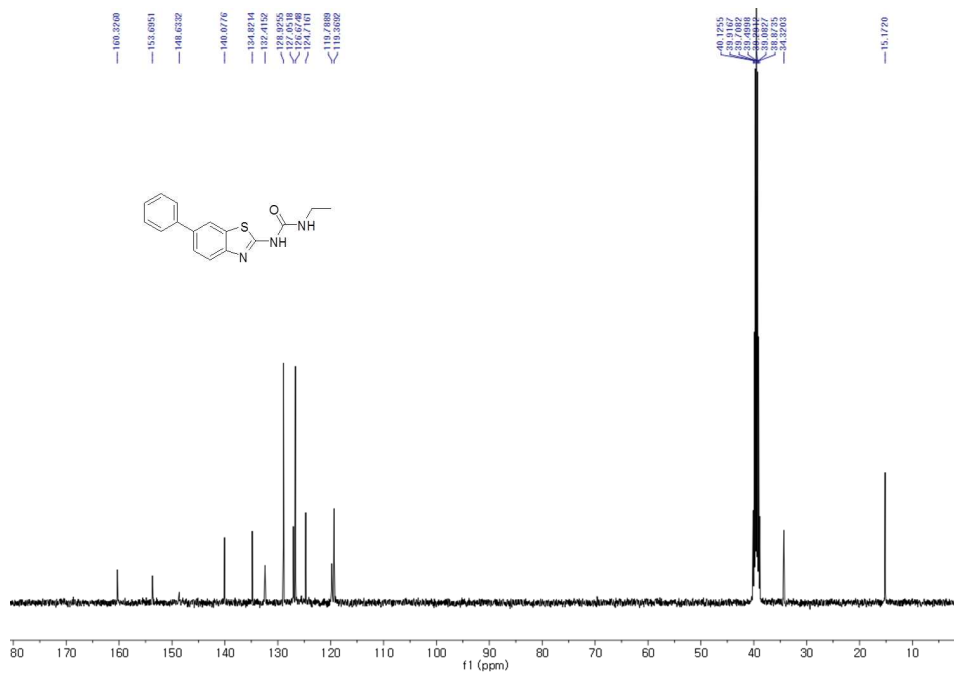
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	14.80	n.a.	23.565	16.239	1.59	n.a.	BM *
2	15.51	n.a.	1514.667	980.345	96.16	n.a.	M *
3	18.78	n.a.	9.900	22.870	2.24	n.a.	MB*
Total:			1548.132	1019.454	100.00	0.000	

HPLC-Purity

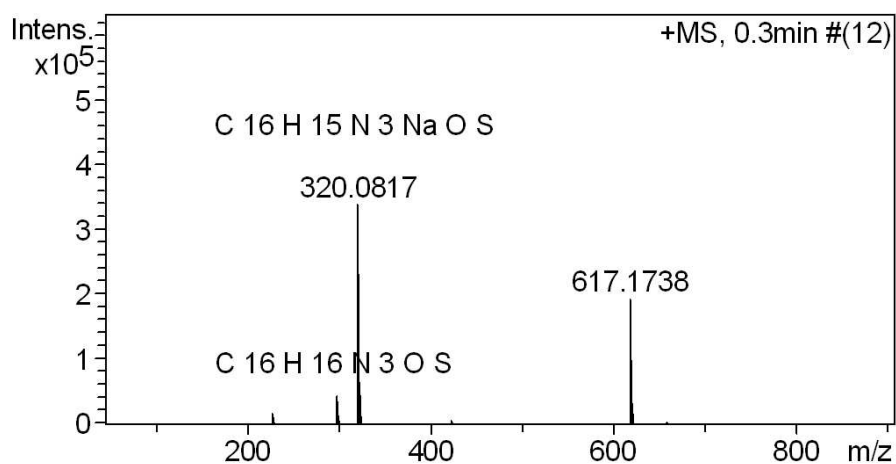
1-Ethyl-3-(6-phenylbenzo[d]thiazol-2-yl)urea (9g).



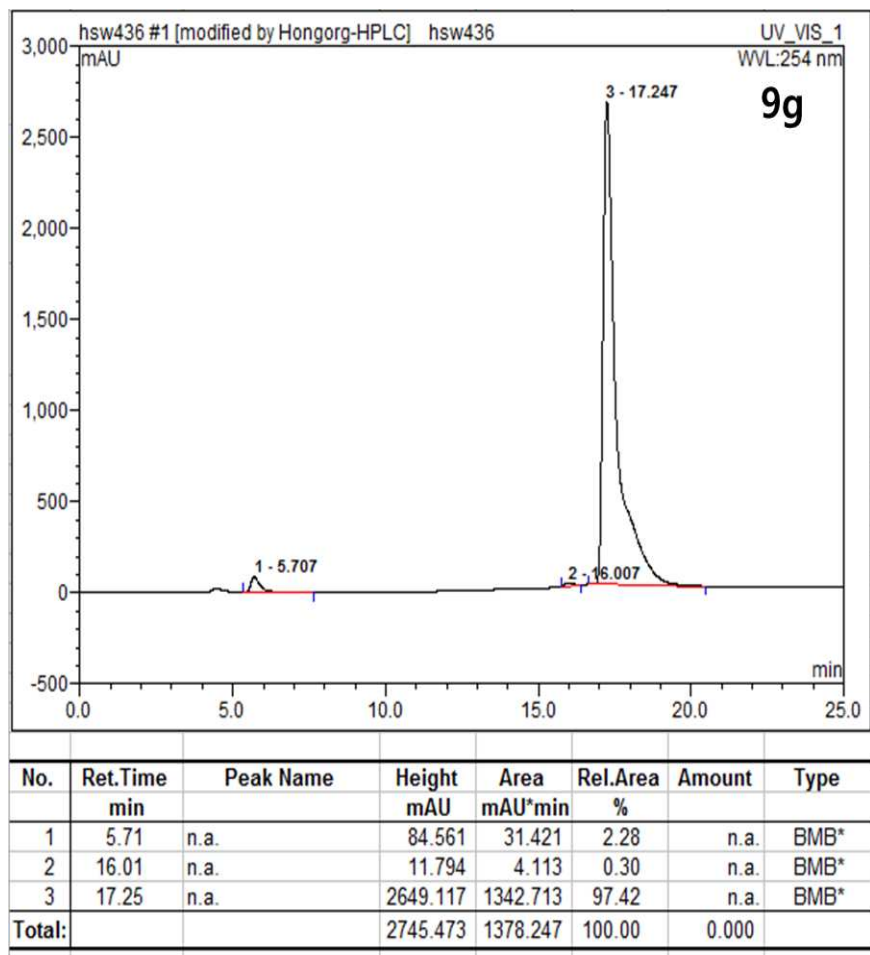
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆

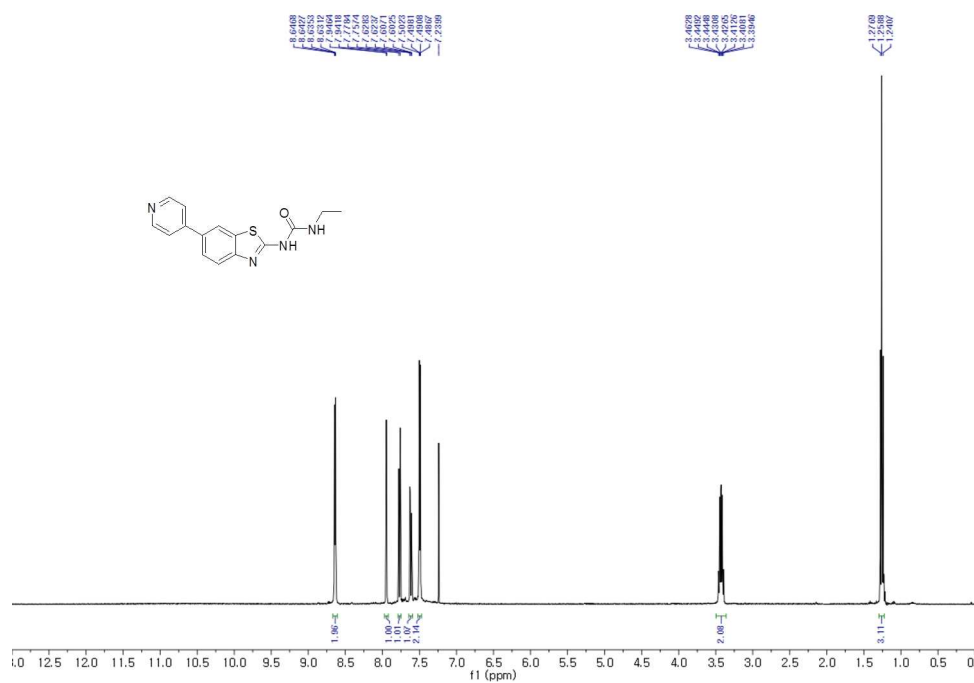


HRMS

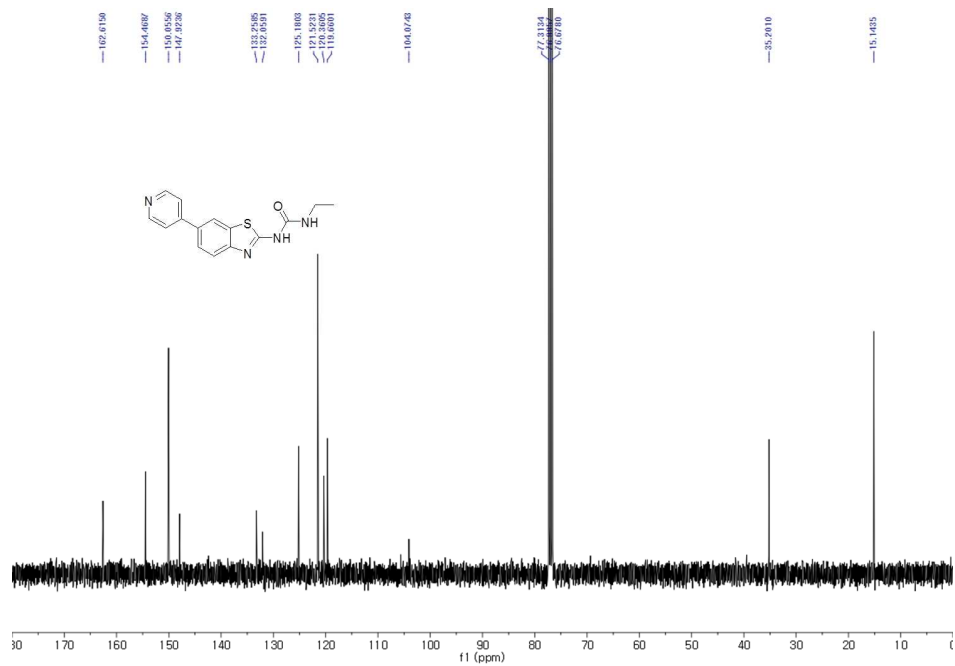


HPLC-Purity

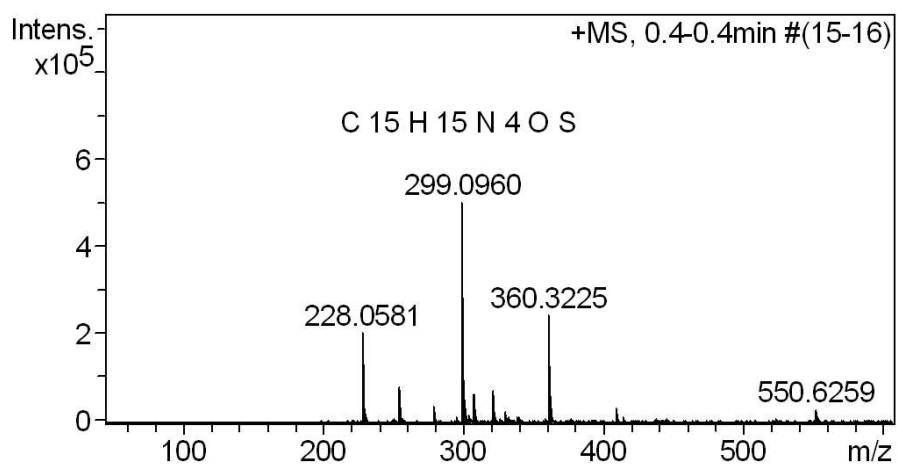
1-Ethyl-3-(6-(pyridin-4-yl)benzo[d]thiazol-2-yl)urea (9h).



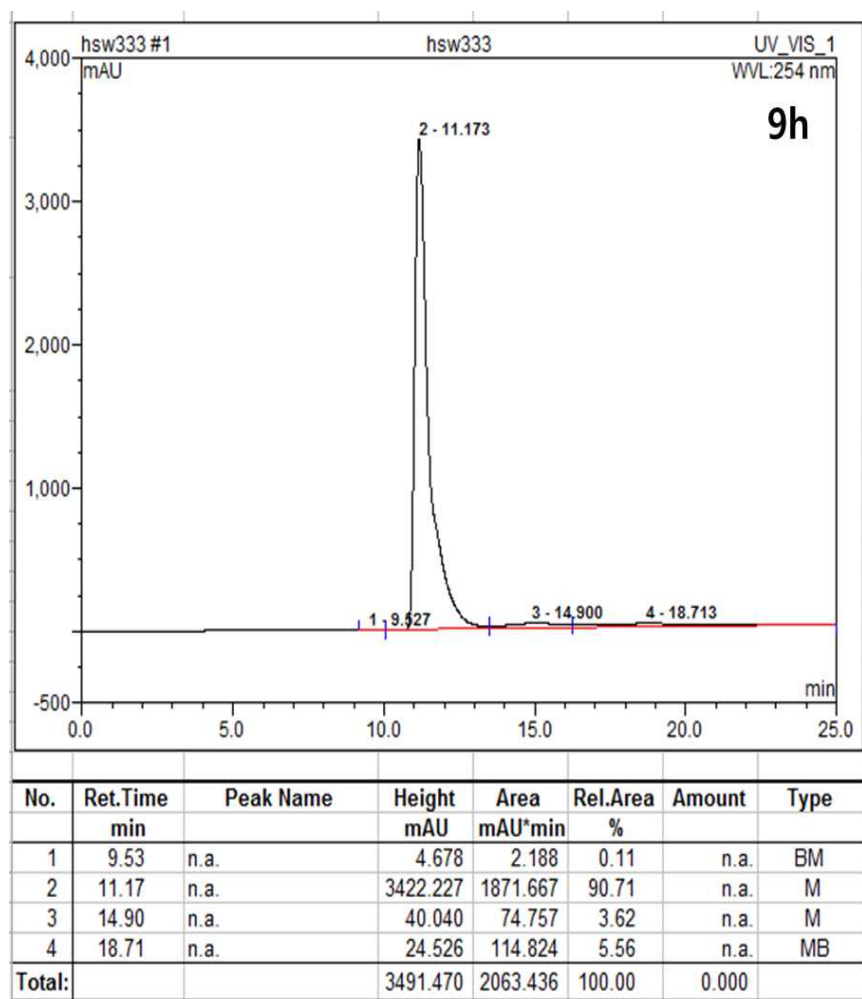
400 MHz, ^1H NMR in CDCl_3



100 MHz, ^1H NMR in CDCl_3

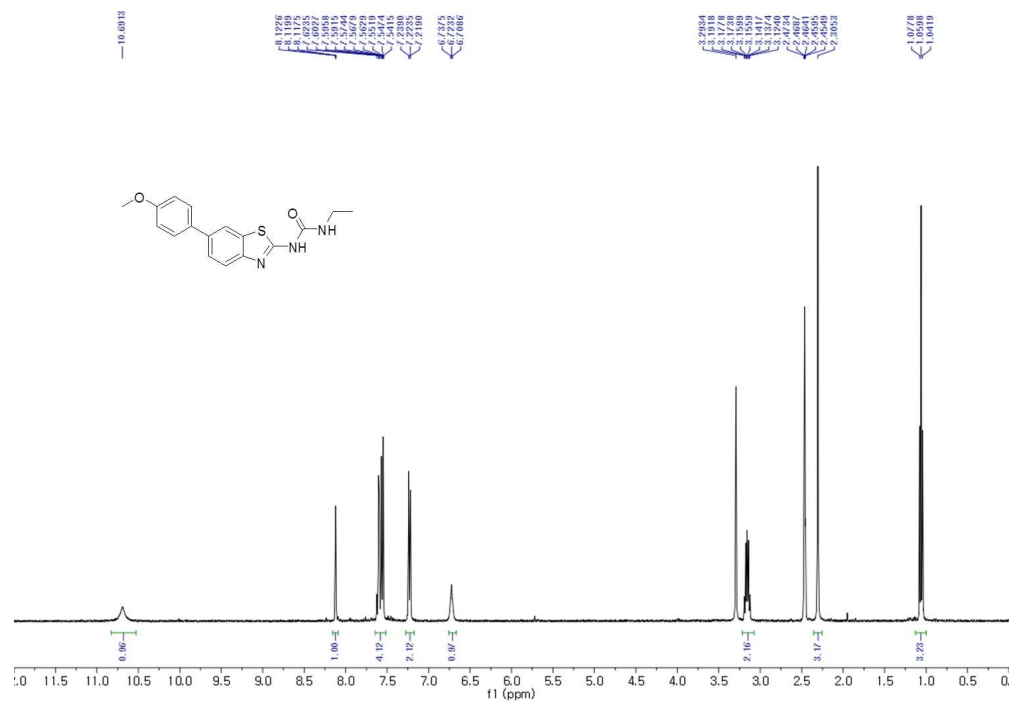


HRMS

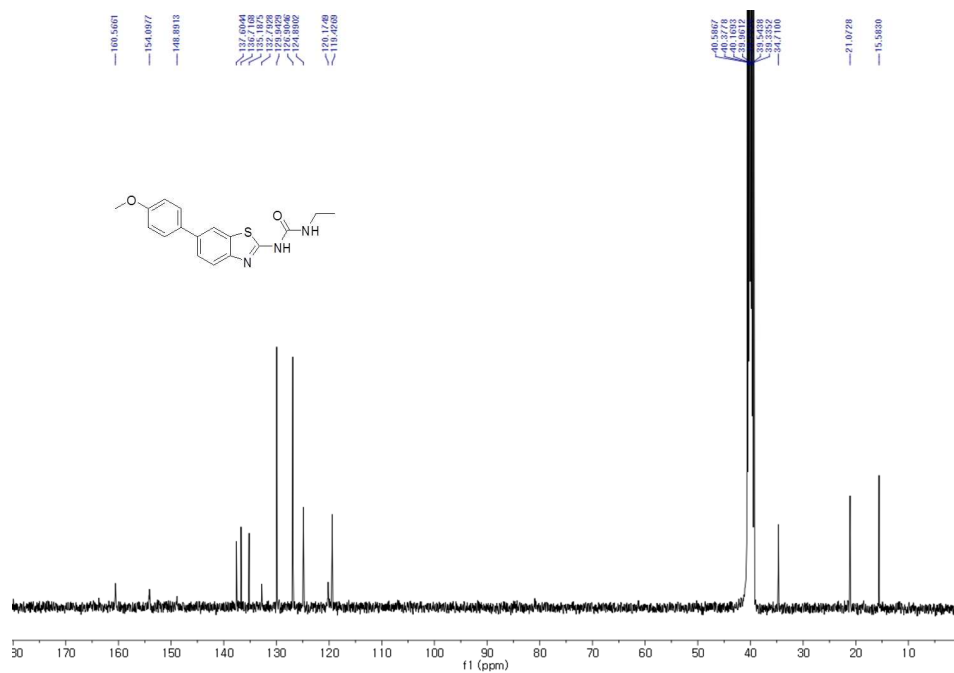


HPLC-Purity

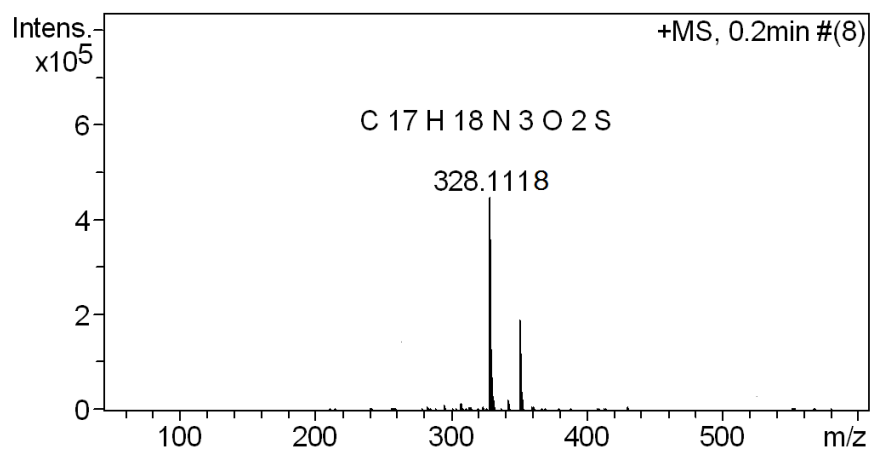
1-Ethyl-3-(6-(4-methoxyphenyl)benzo[d]thiazol-2-yl)urea (9i).



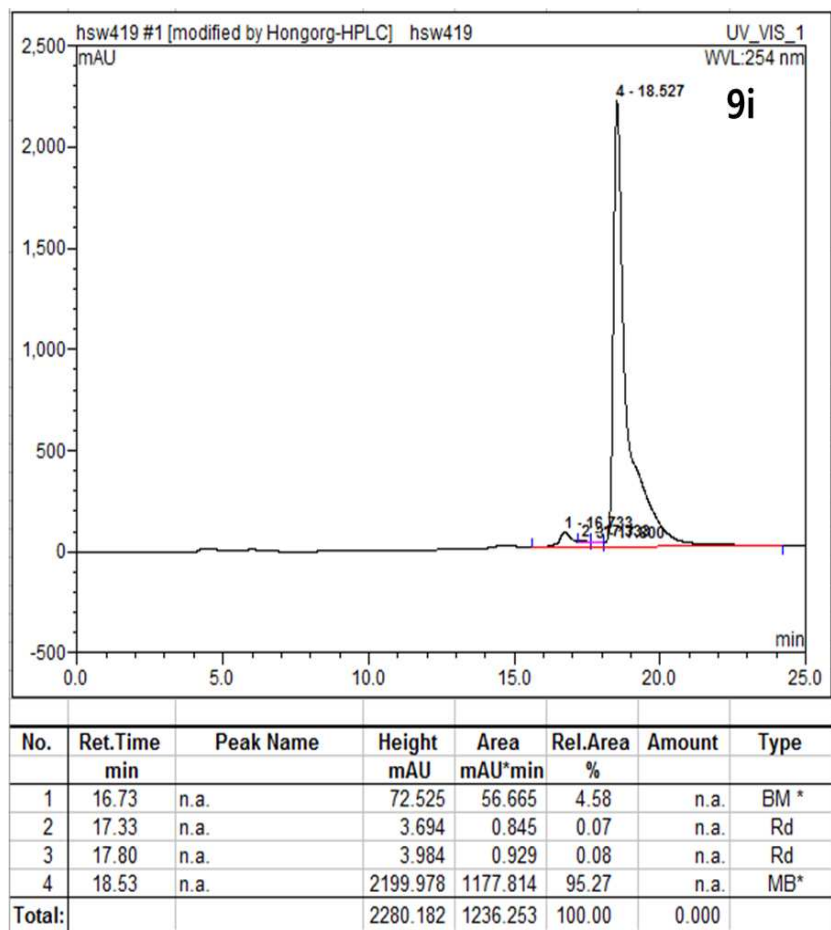
400 MHz, ¹H NMR in DMSO-*d*₆



100 MHz, ¹³C NMR in DMSO-*d*₆

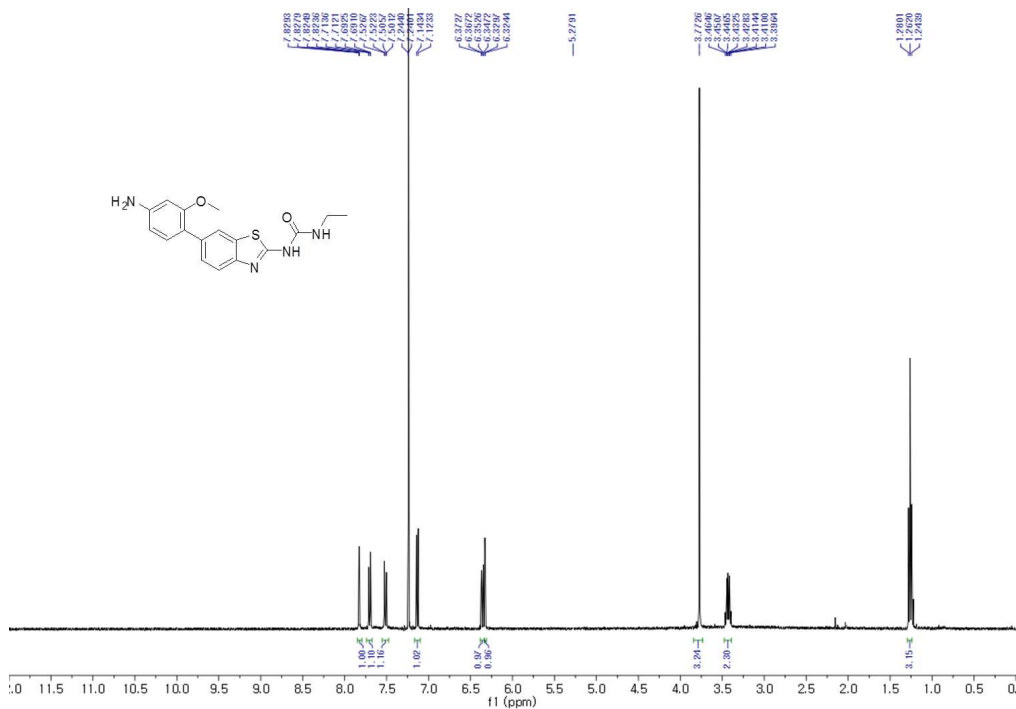


HRMS

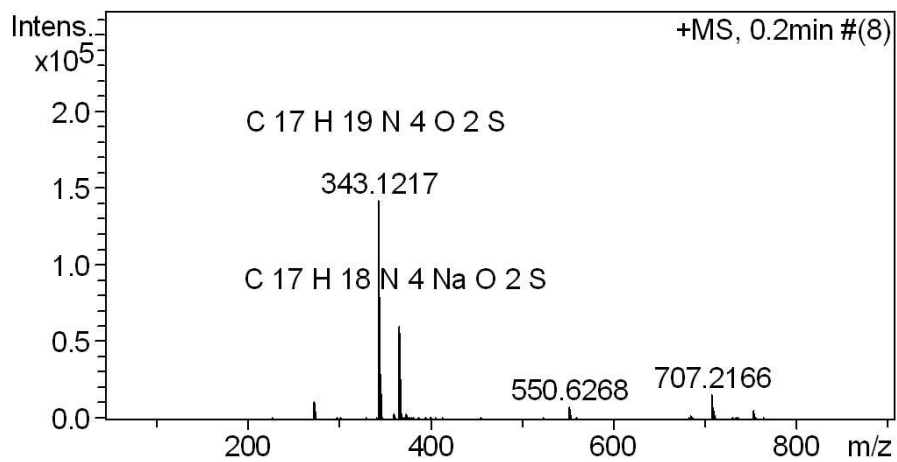


HPLC-Purity

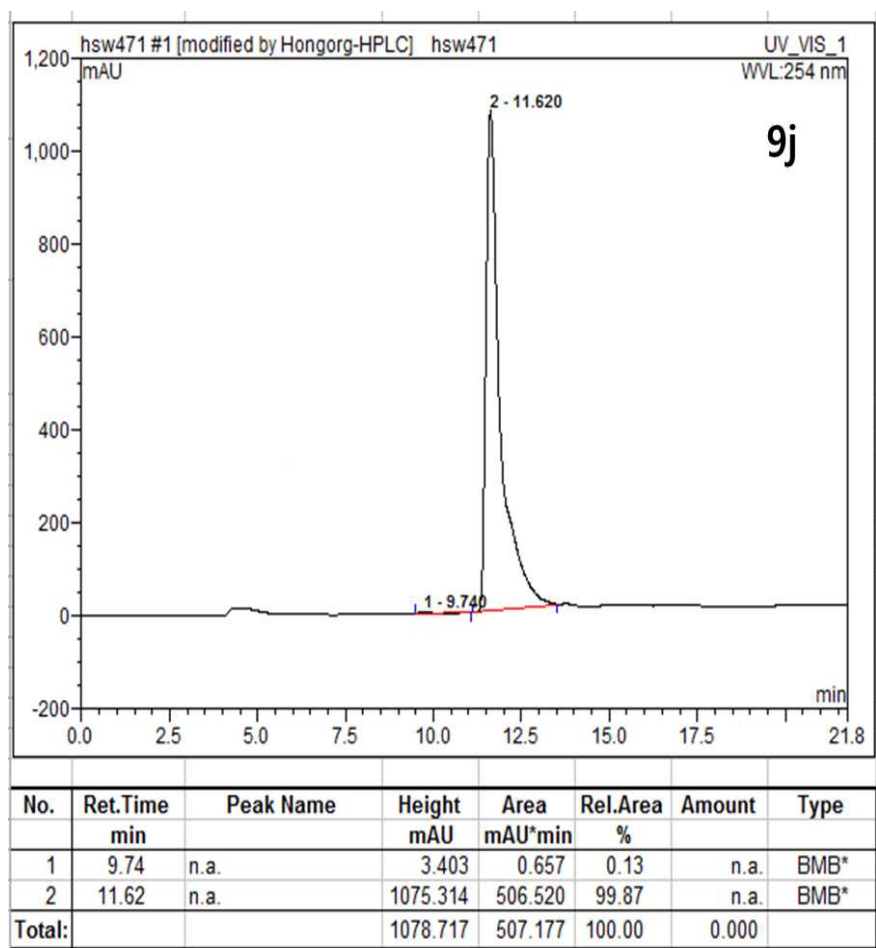
1-(6-(4-Amino-2-methoxyphenyl)benzo[d]thiazol-2-yl)-3-ethylurea (9j).



400 MHz, ¹H NMR in CDCl₃

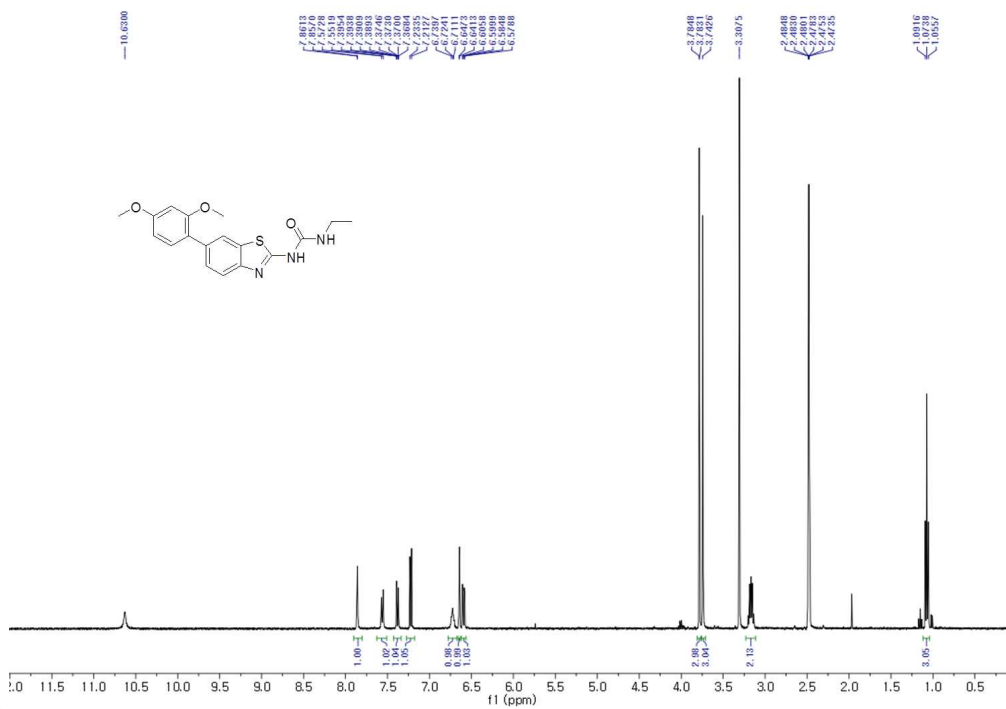


HRMS

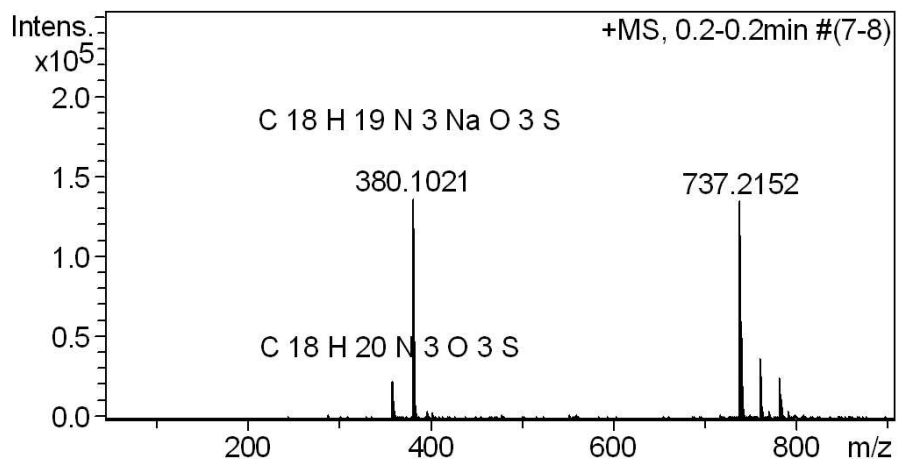


HPLC-Purity

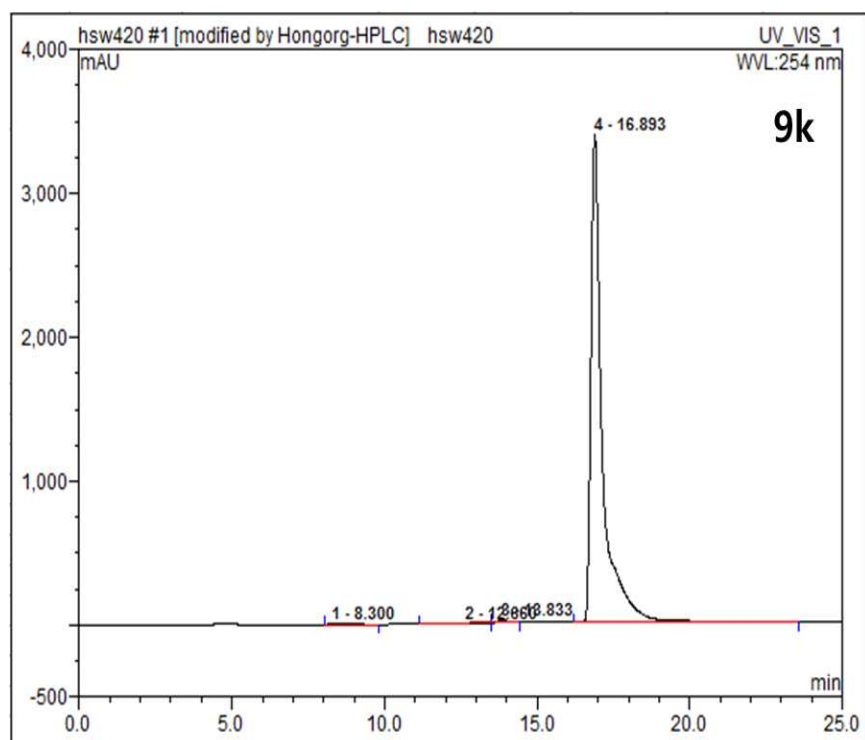
1-(6-(2,4-Dimethoxyphenyl)benzo[d]thiazol-2-yl)-3-ethylurea (9k).



400 MHz, ¹H NMR in DMSO-*d*₆



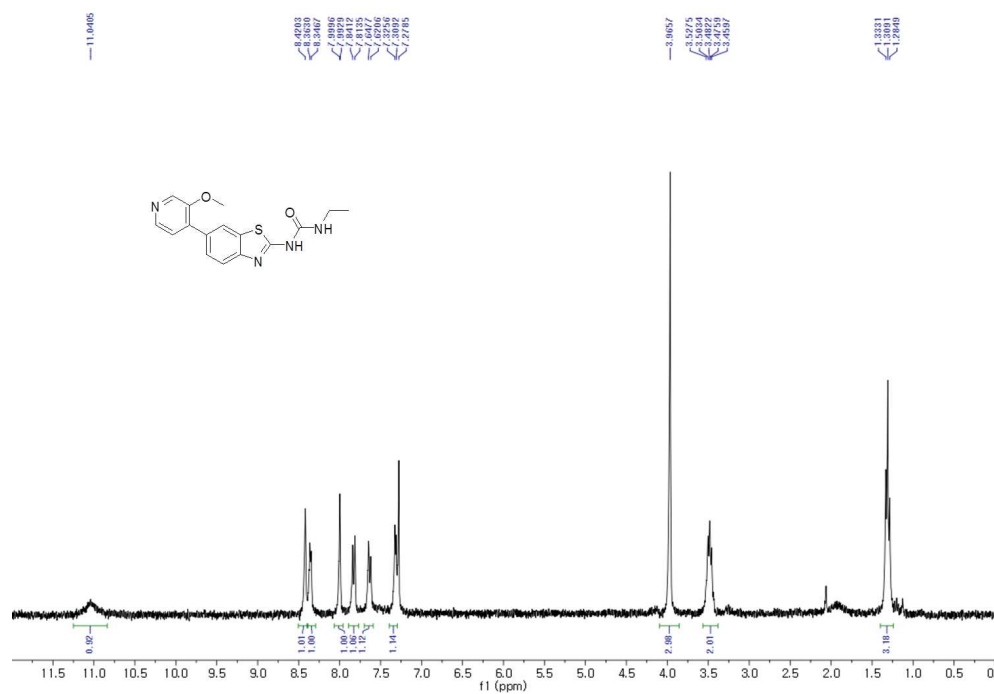
HRMS



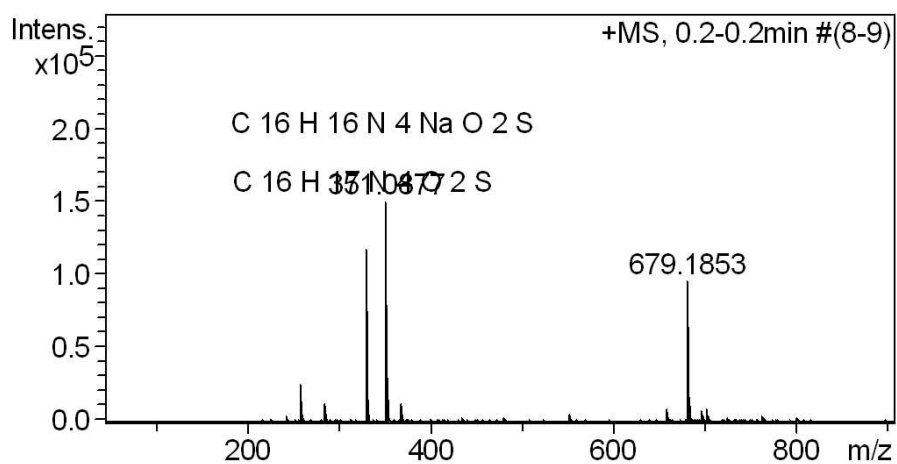
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	8.30	n.a.	10.877	5.145	0.34	n.a.	BMB
2	12.66	n.a.	2.760	2.741	0.18	n.a.	BM
3	13.83	n.a.	18.637	6.151	0.41	n.a.	MB
4	16.89	n.a.	3385.674	1478.196	99.06	n.a.	BMB
Total:			3417.948	1492.233	100.00	0.000	

HPLC-Purity

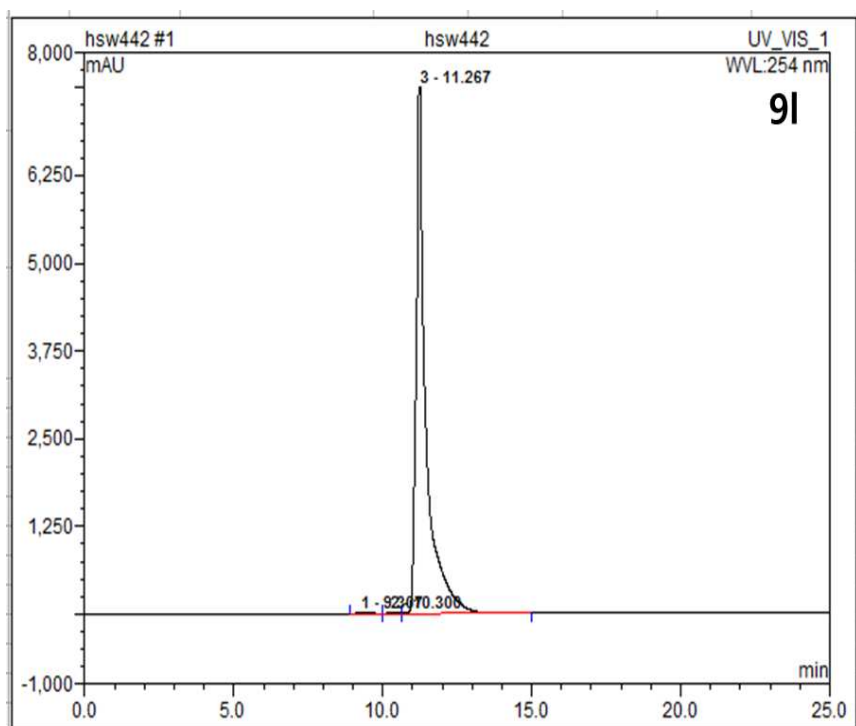
1-Ethyl-3-(6-(3-methoxypyridin-4-yl)benzo[d]thiazol-2-yl)urea (9l).



300 MHz, ¹H NMR in CDCl₃



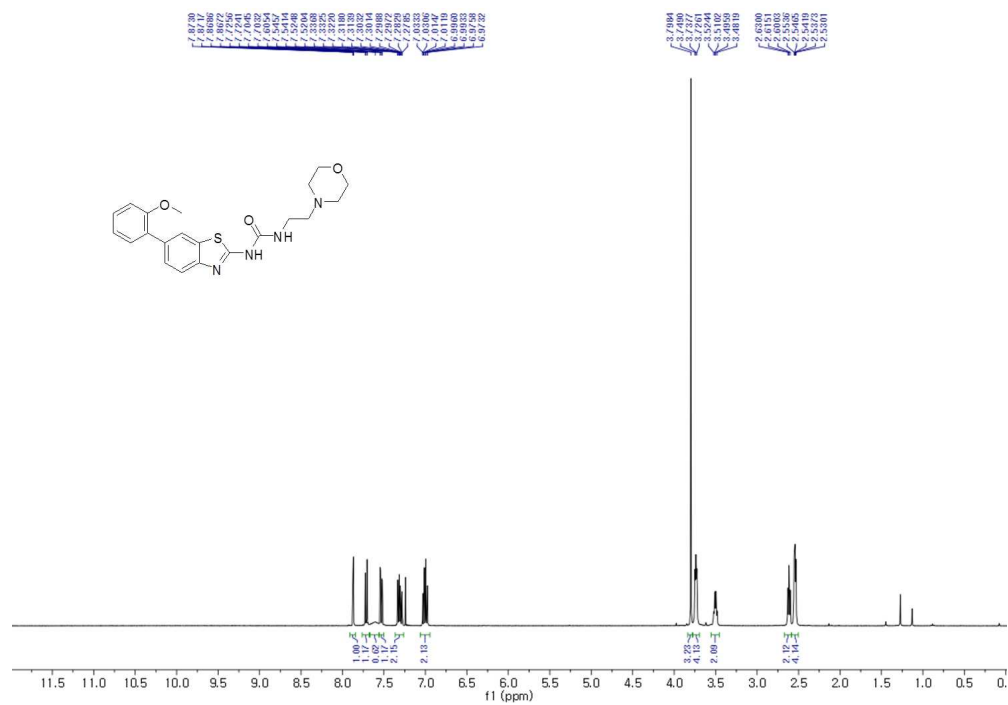
HRMS



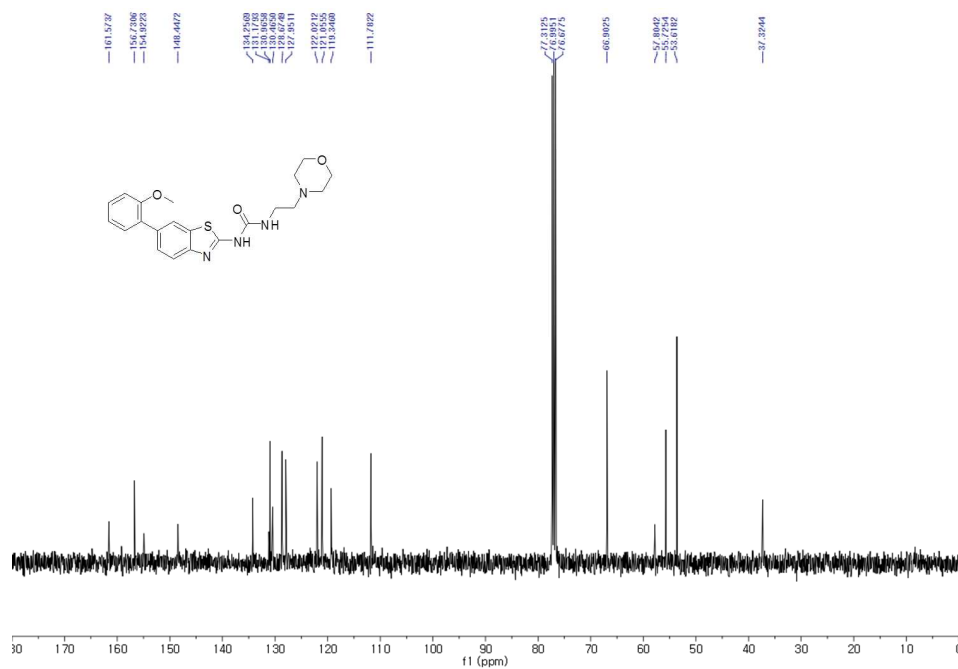
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.31	n.a.	33.325	14.388	0.50	n.a.	BM
2	10.30	n.a.	11.369	4.914	0.17	n.a.	M
3	11.27	n.a.	7491.918	2872.243	99.33	n.a.	MB
Total:			7536.611	2891.545	100.00	0.000	

HPLC-Purity

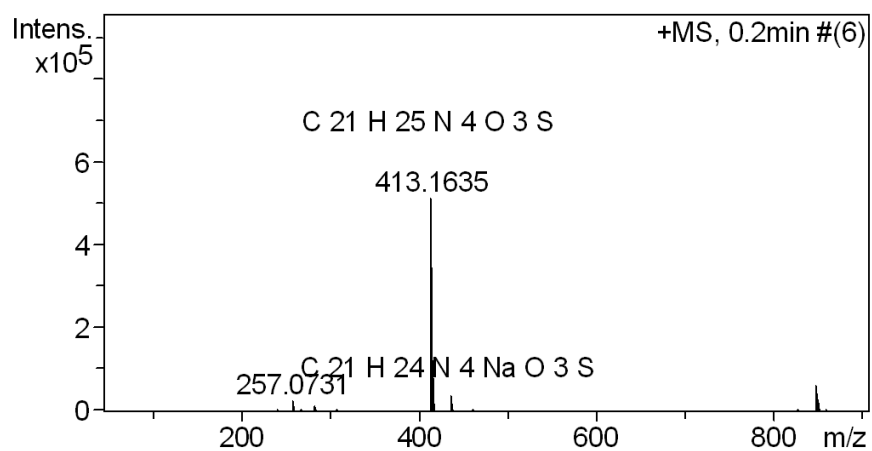
1-(6-(2-Methoxyphenyl)benzo[d]thiazol-2-yl)-3-(2-morpholinoethyl)urea (10a).



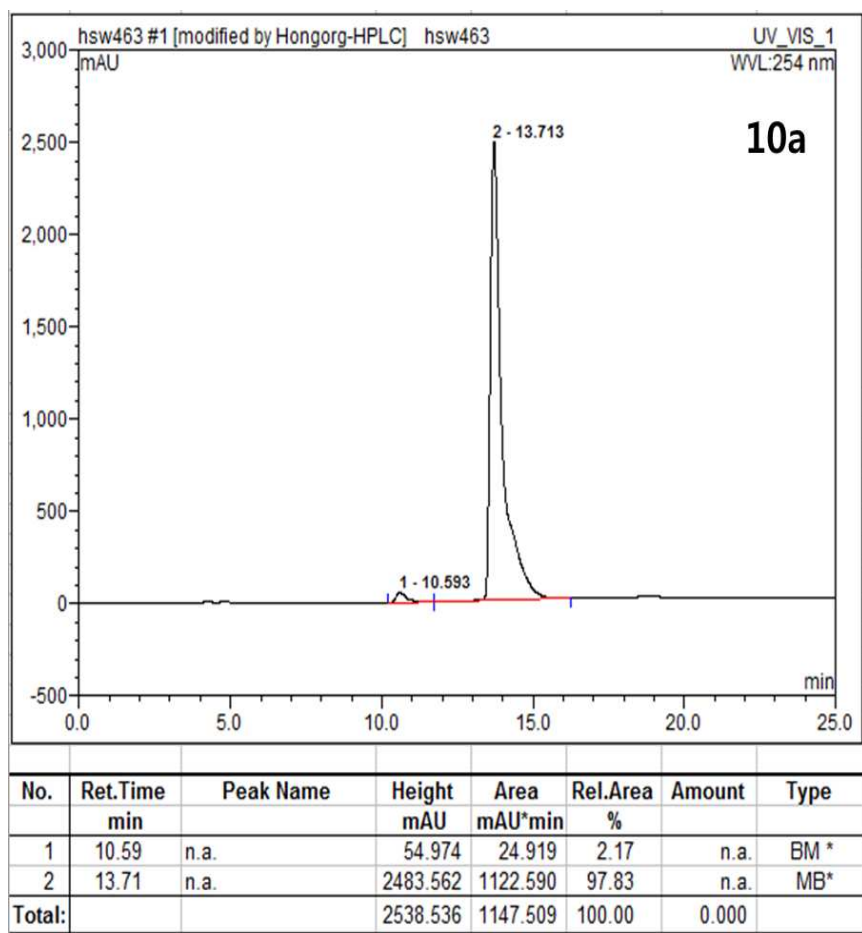
400 MHz, ¹H NMR in CDCl₃



100 MHz, ¹³C NMR in CDCl₃

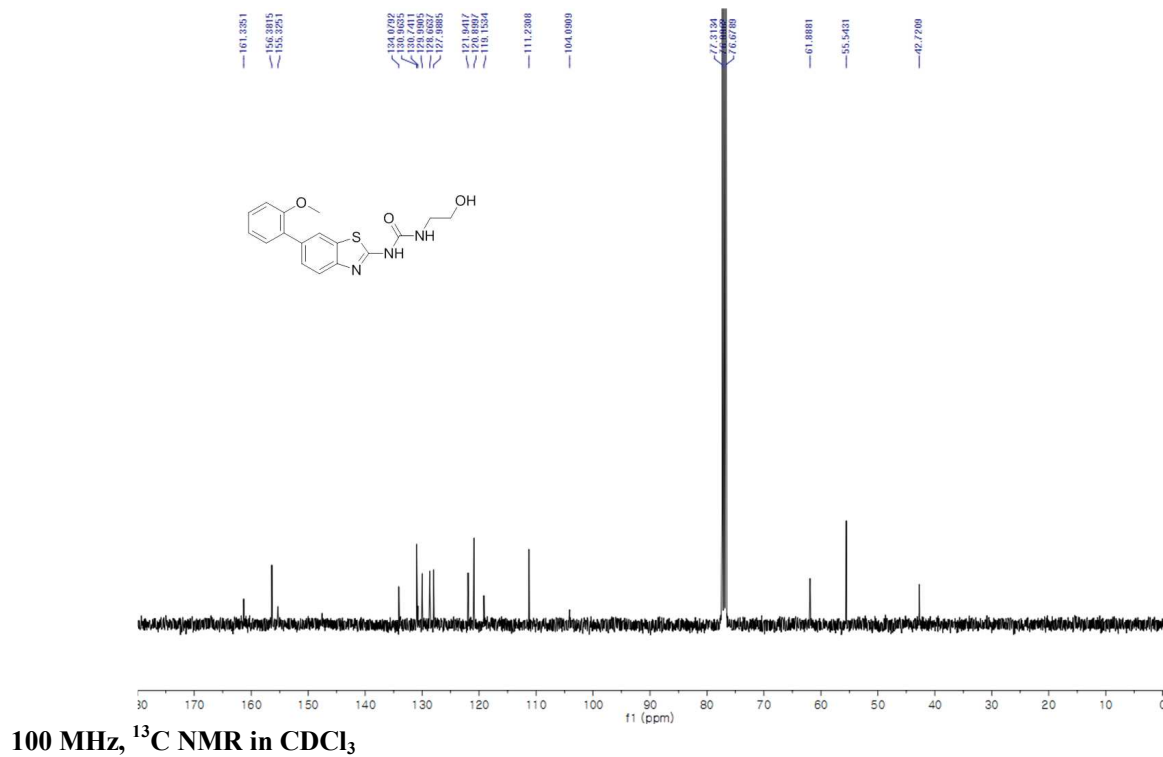
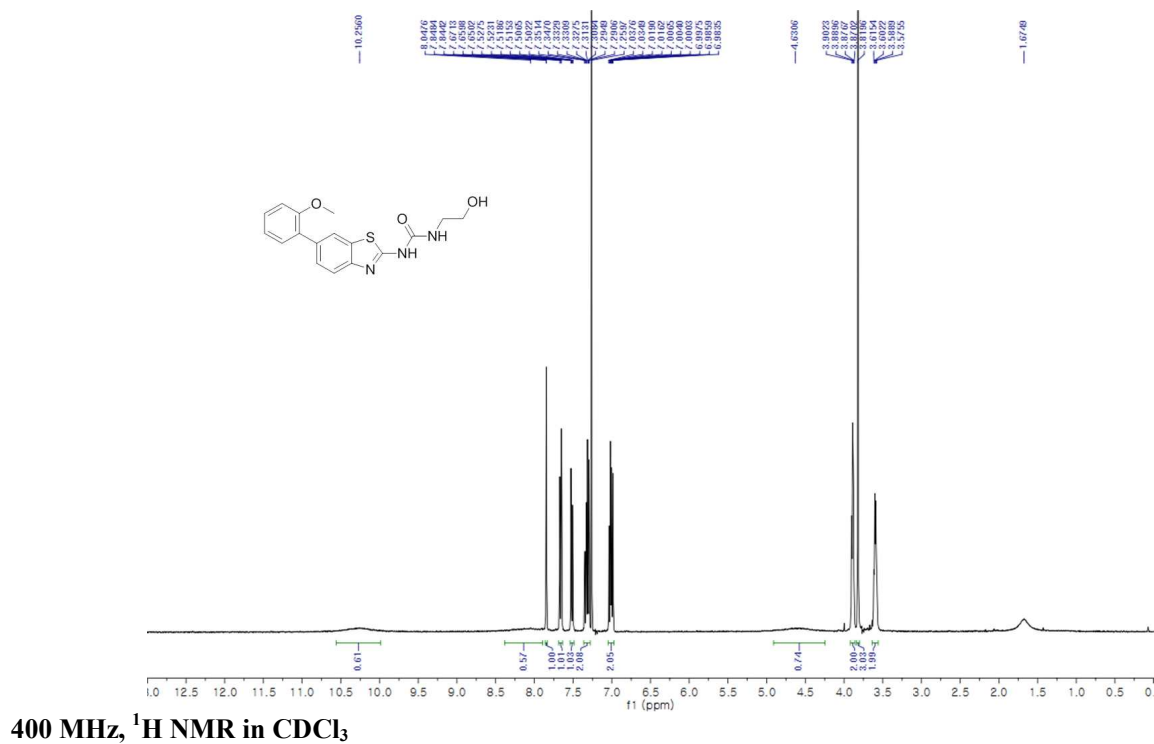


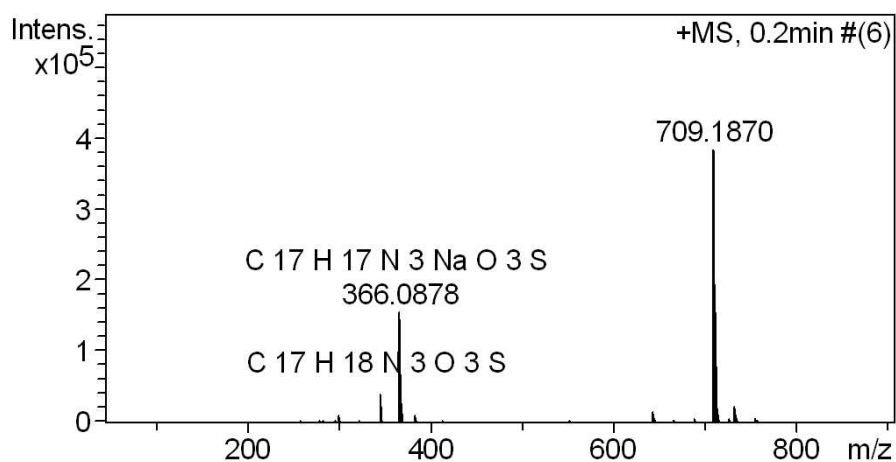
HRMS



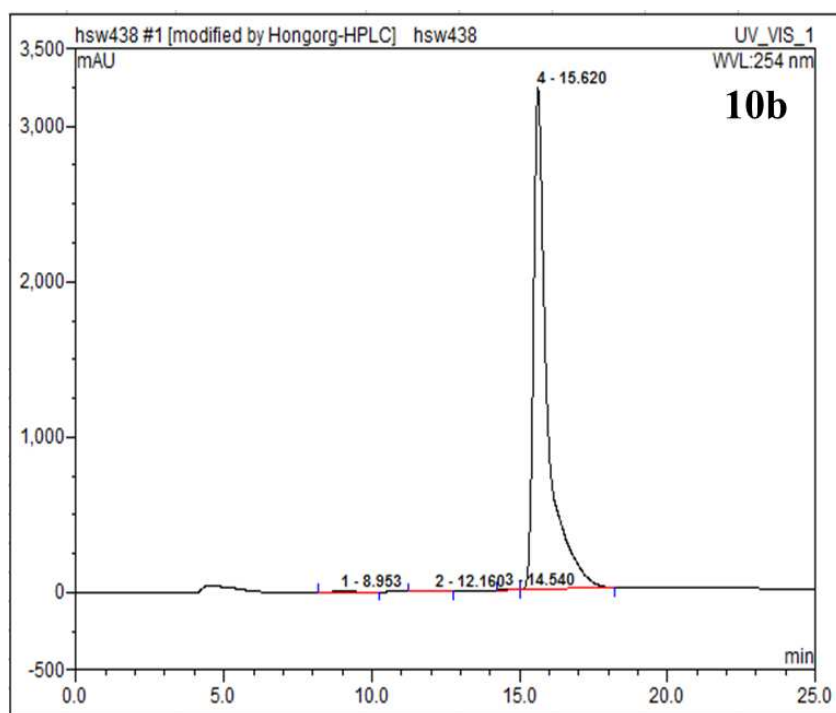
HPLC-Purity

1-(2-Hydroxyethyl)-3-(6-(2-methoxyphenyl)benzo[d]thiazol-2-yl)urea (10b).





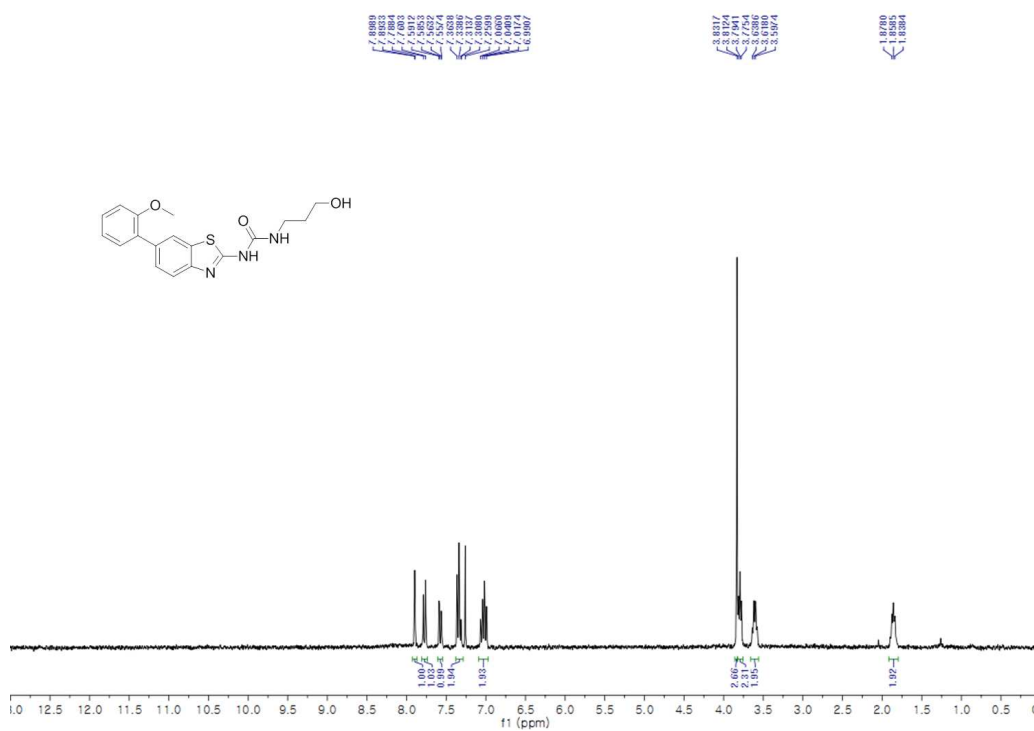
HRMS



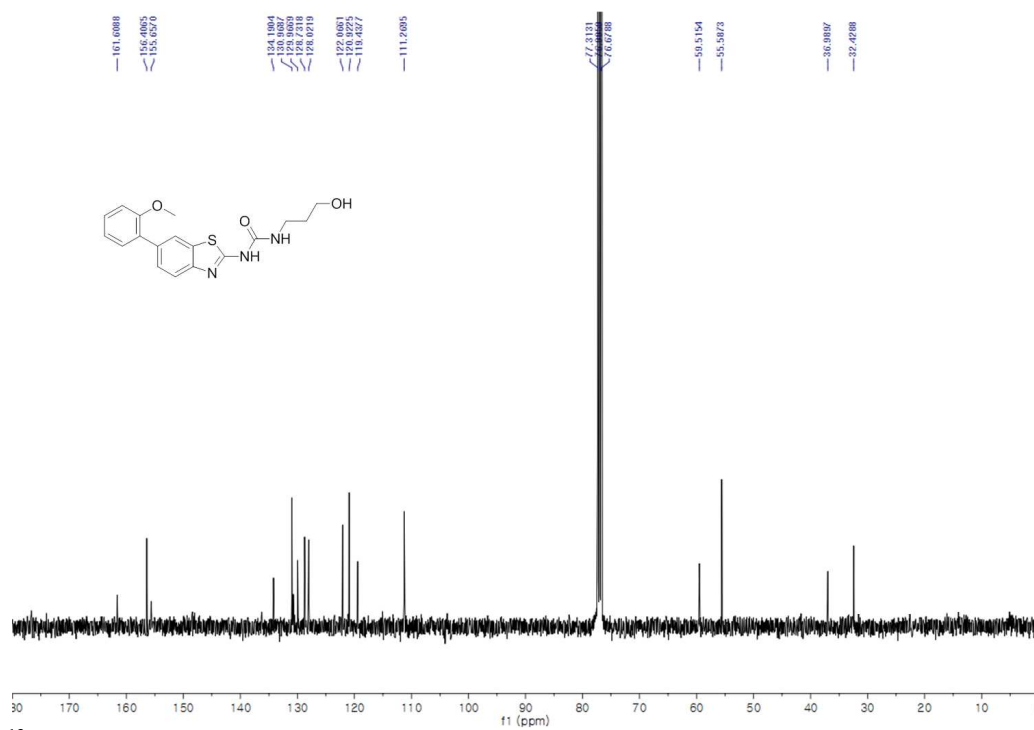
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	8.95	n.a.	2.733	2.457	0.14	n.a.	BMB
2	12.16	n.a.	3.228	2.284	0.13	n.a.	BMB
3	14.54	n.a.	5.895	2.018	0.12	n.a.	BMB*
4	15.62	n.a.	3231.205	1748.408	99.61	n.a.	bMB
Total:			3243.061	1755.169	100.00	0.000	

HPLC-Purity

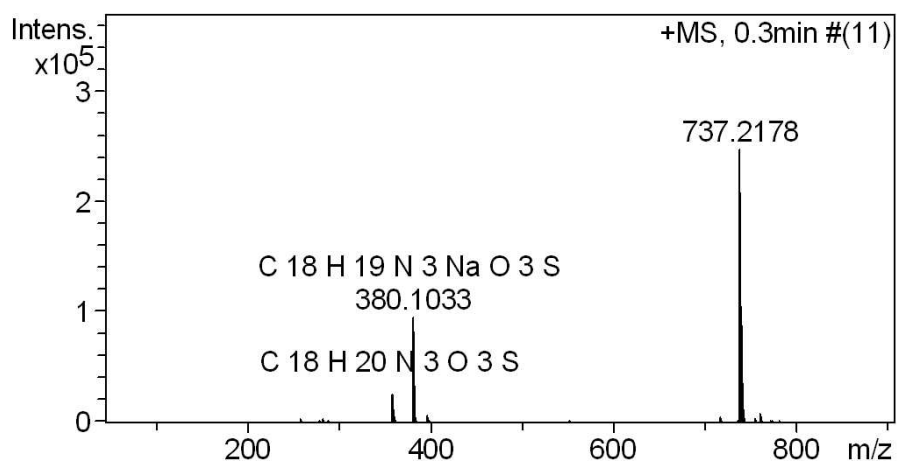
1-(3-Hydroxypropyl)-3-(6-(2-methoxyphenyl)benzo[d]thiazol-2-yl)urea (10c).



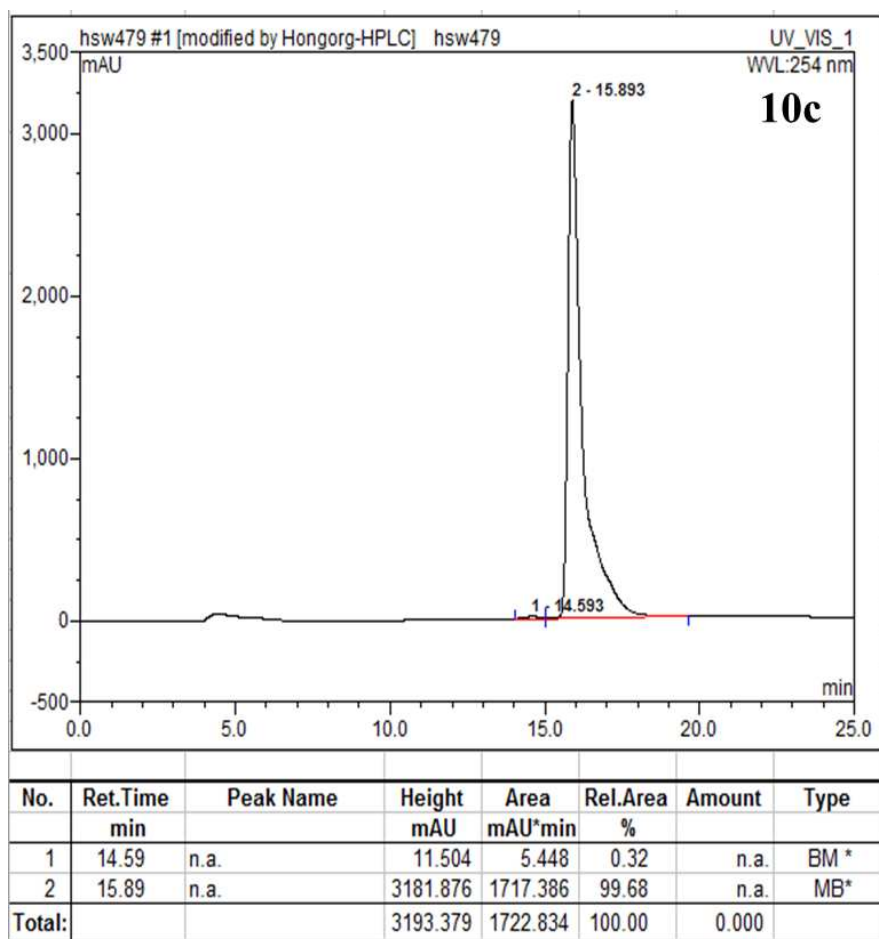
300 MHz, ¹H NMR in CDCl₃



100 MHz, ¹³C NMR in CDCl₃

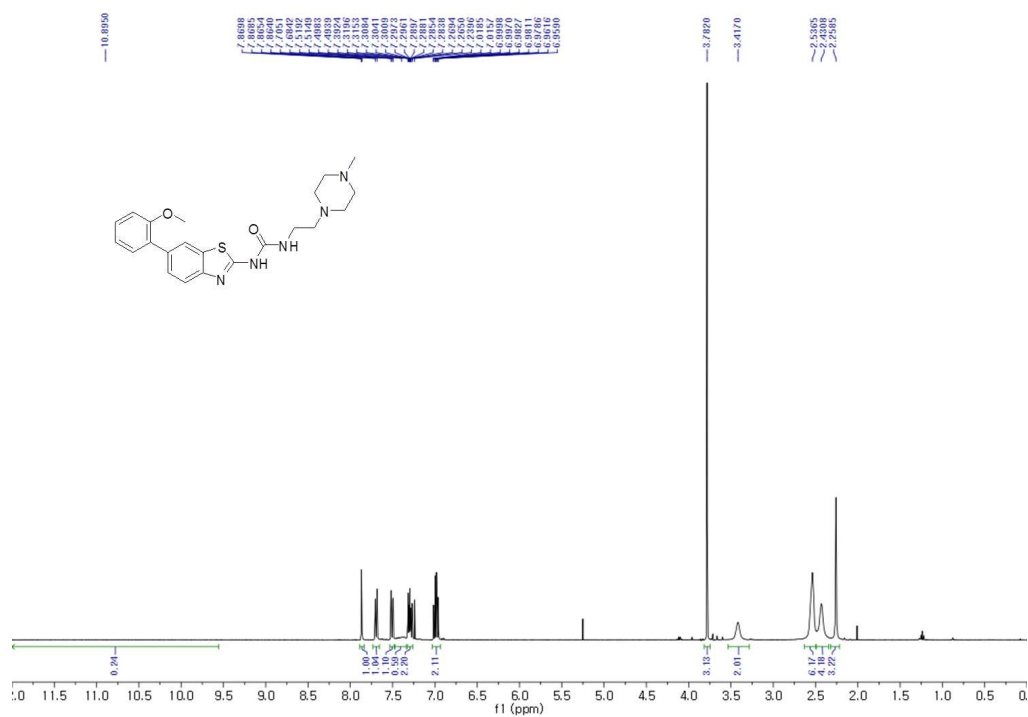


HRMS

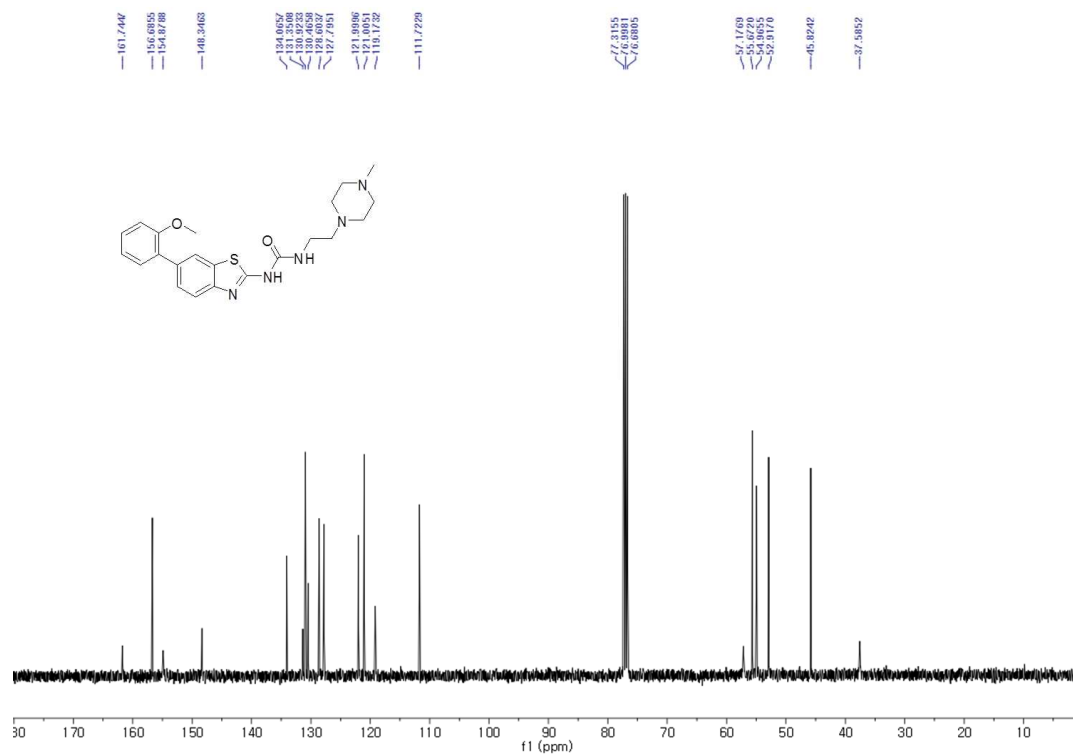


HPLC-Purity

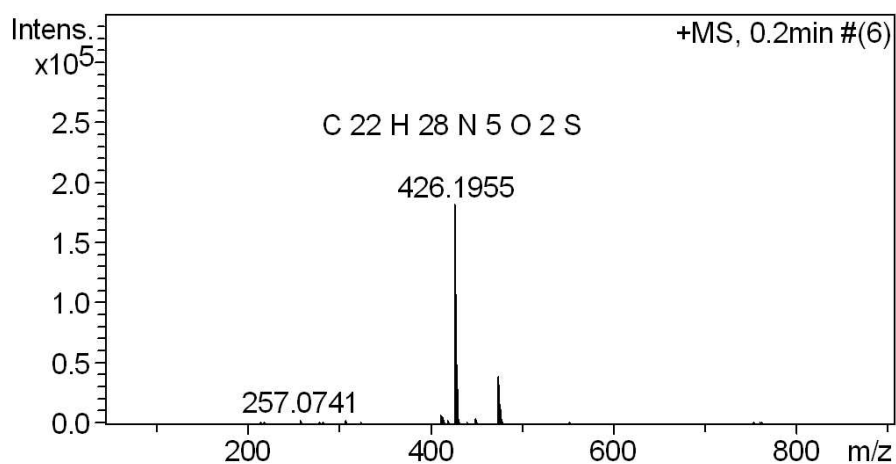
1-(6-(2-Methoxyphenyl)benzo[d]thiazol-2-yl)-3-(2-(4-methylpiperazin-1-yl)ethyl)urea (10d).



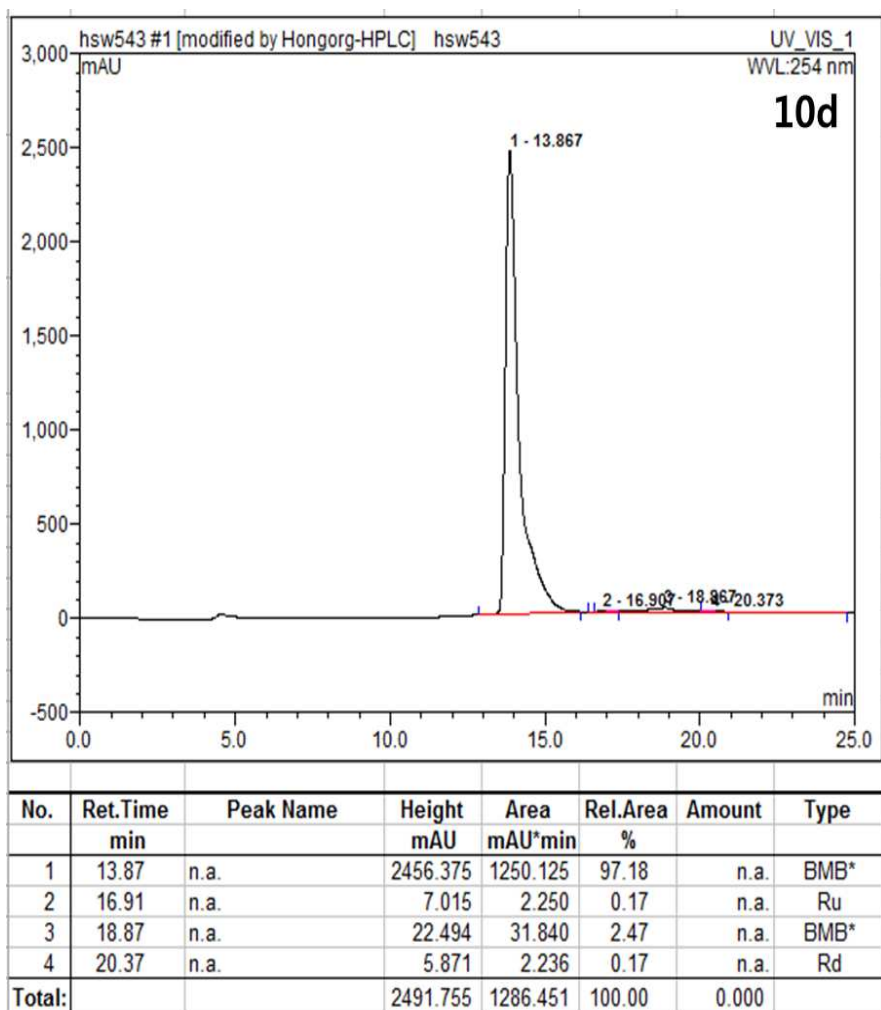
400 MHz, ¹H NMR in CDCl₃



100 MHz, ¹³C NMR in CDCl₃

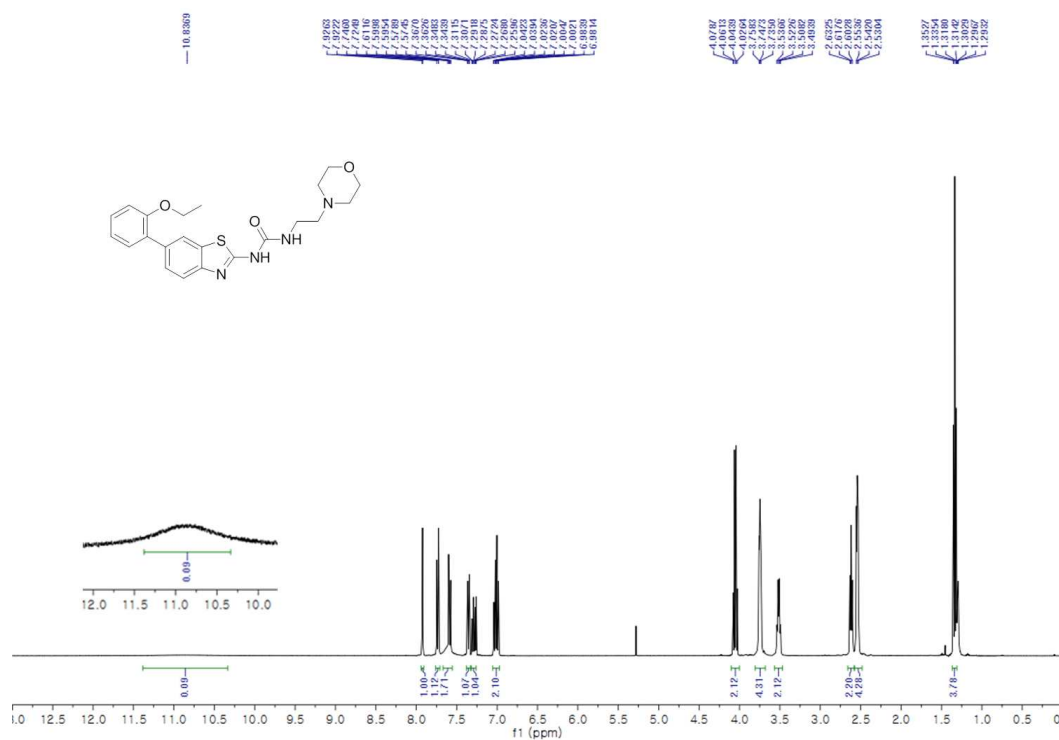


HRMS

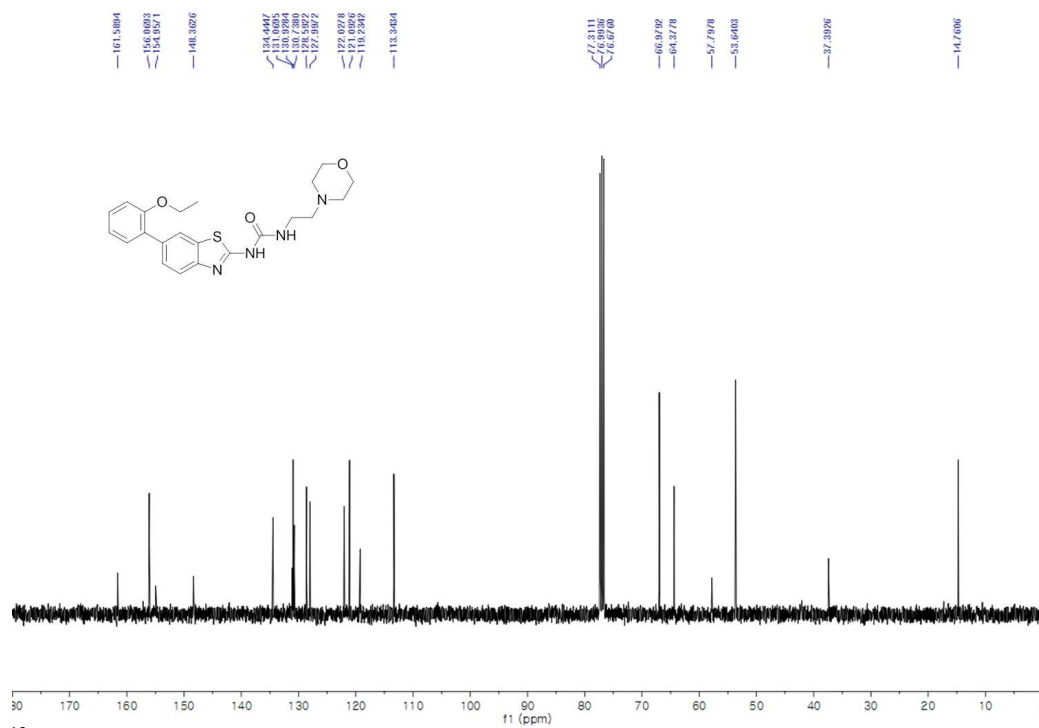


HPLC-Purity

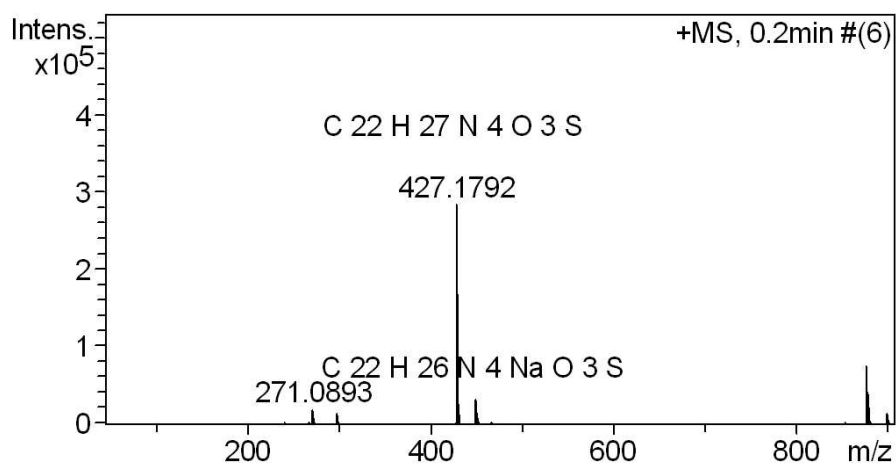
1-(6-(2-Ethoxyphenyl)benzo[d]thiazol-2-yl)-3-(2-morpholinoethyl)urea (10e).



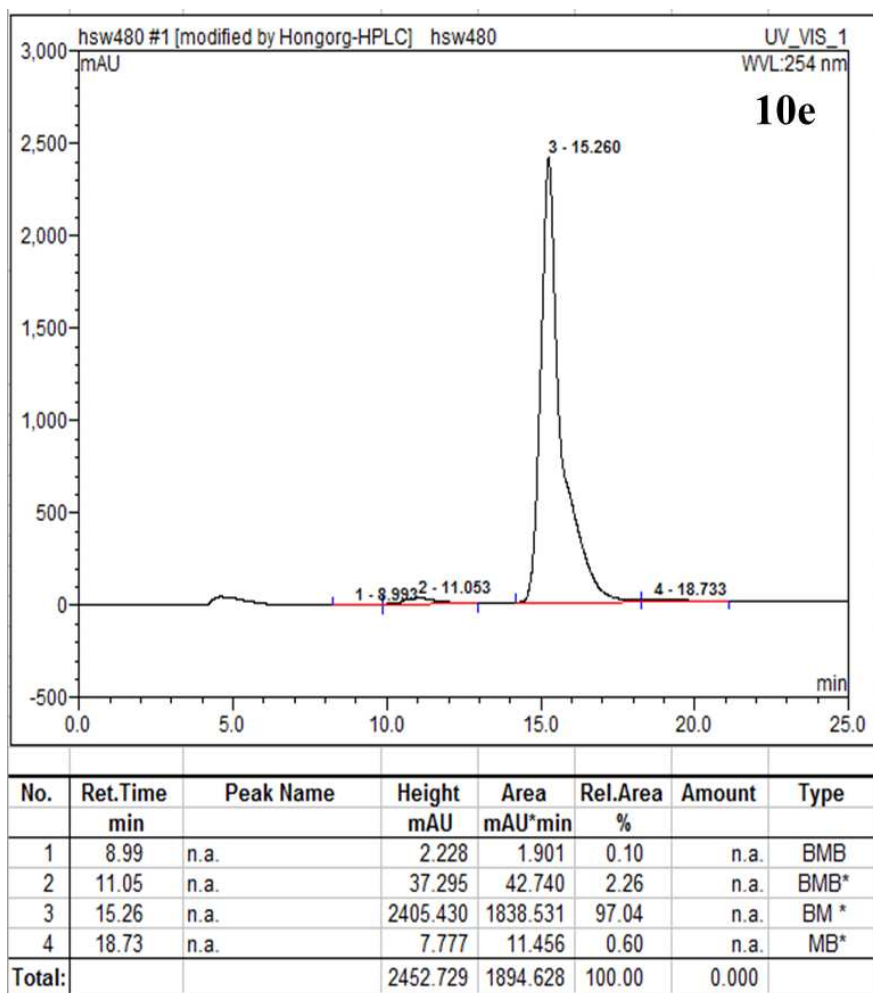
400 MHz, ¹H NMR in CDCl₃, 55 °C



100 MHz, ¹³C NMR in CDCl₃, 55 °C

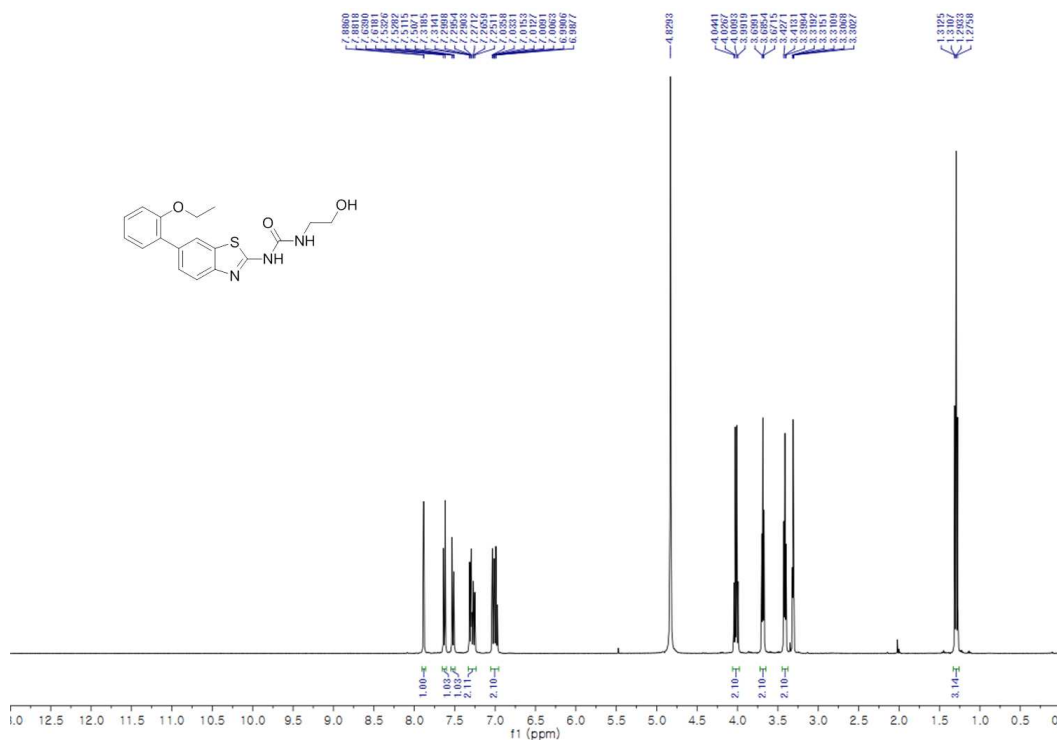


HRMS

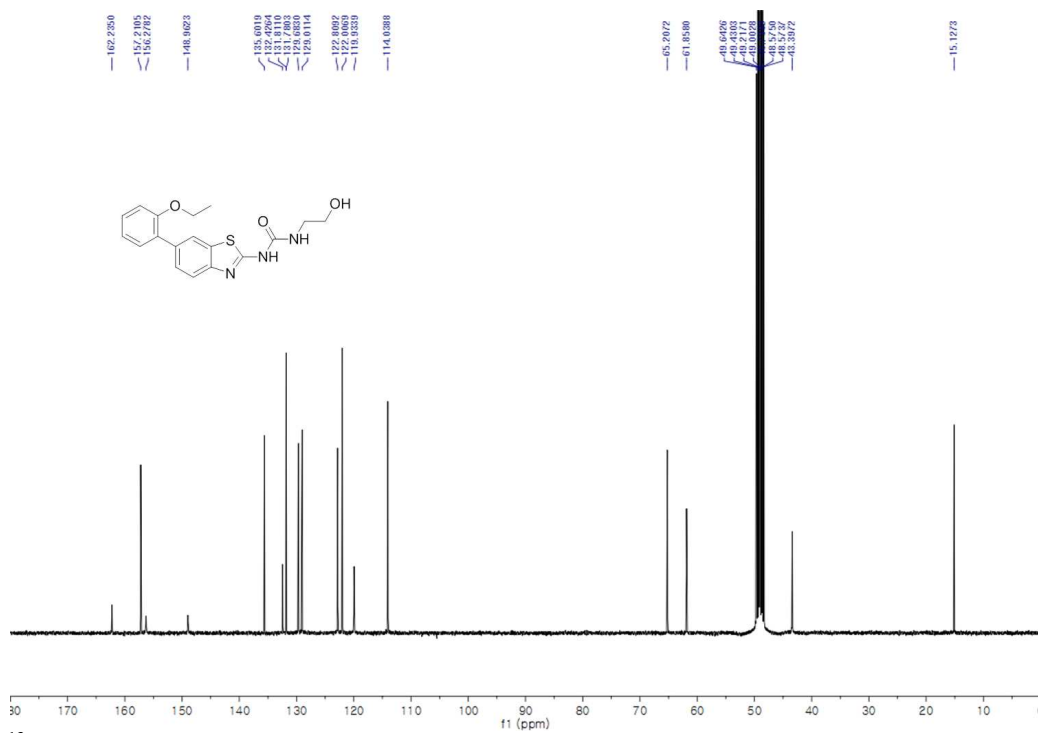


HPLC-Purity

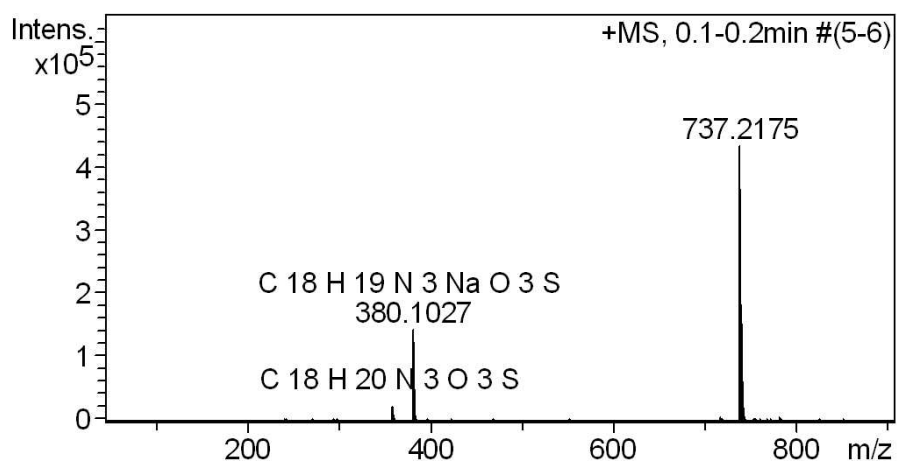
1-(6-(2-Ethoxyphenyl)benzo[d]thiazol-2-yl)-3-(2-hydroxyethyl)urea (10f).



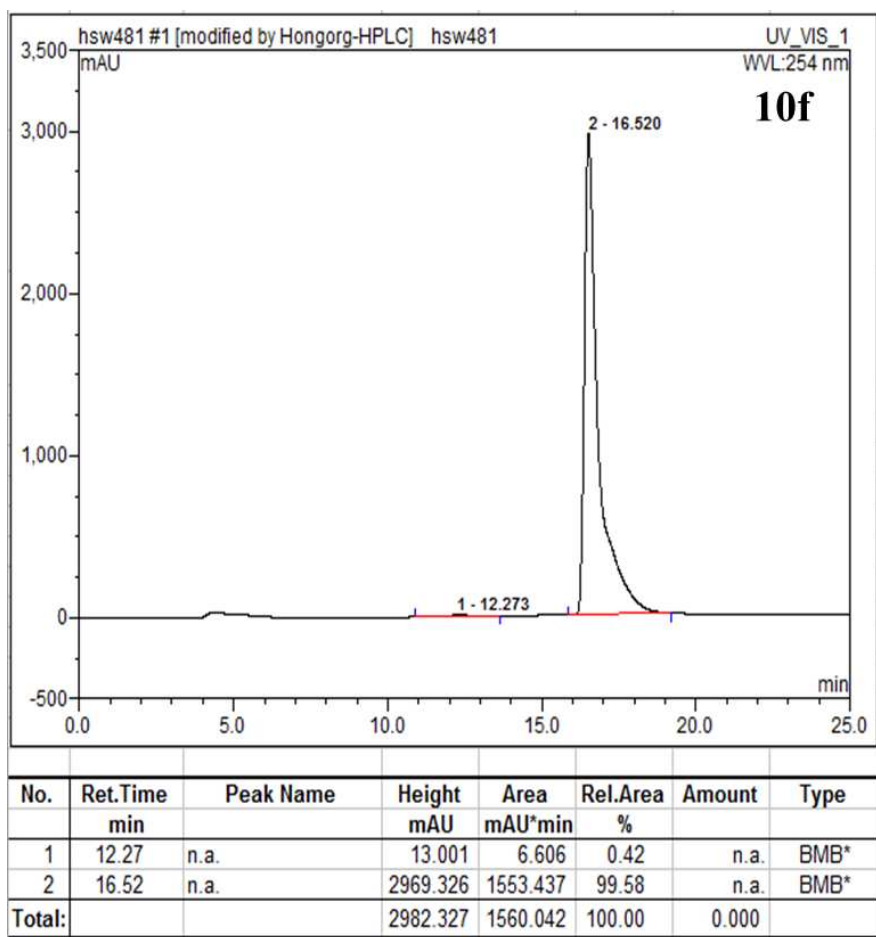
400 MHz, ^1H NMR in MeOD- d_4



100 MHz, ^{13}C NMR in MeOD- d_4

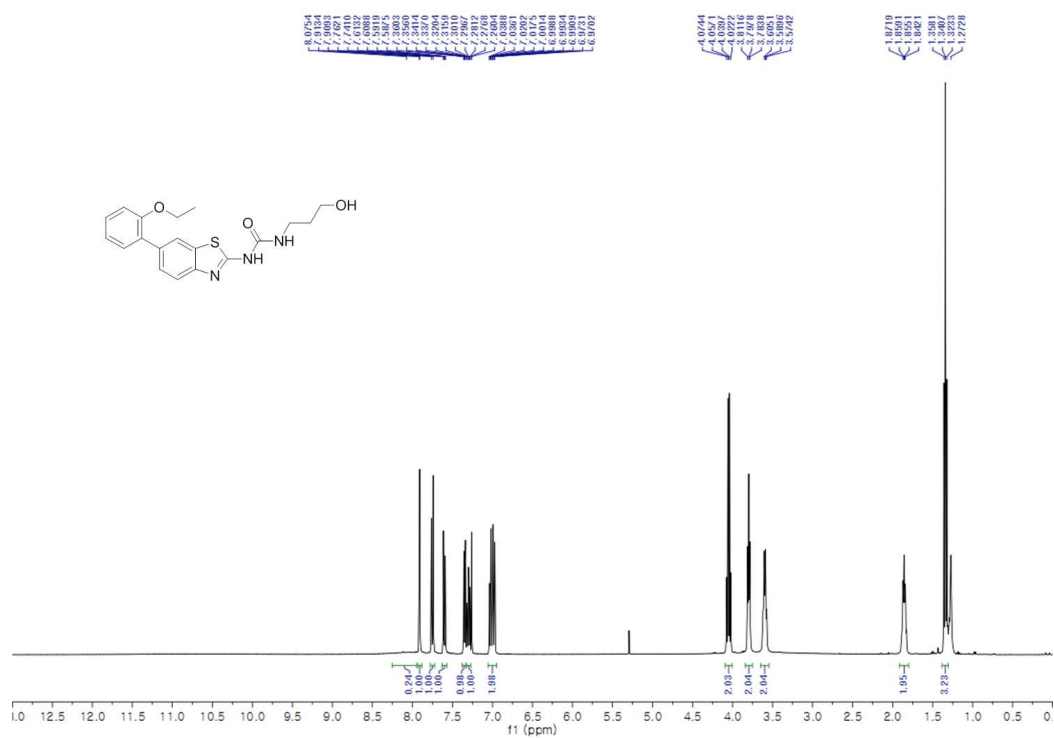


HRMS

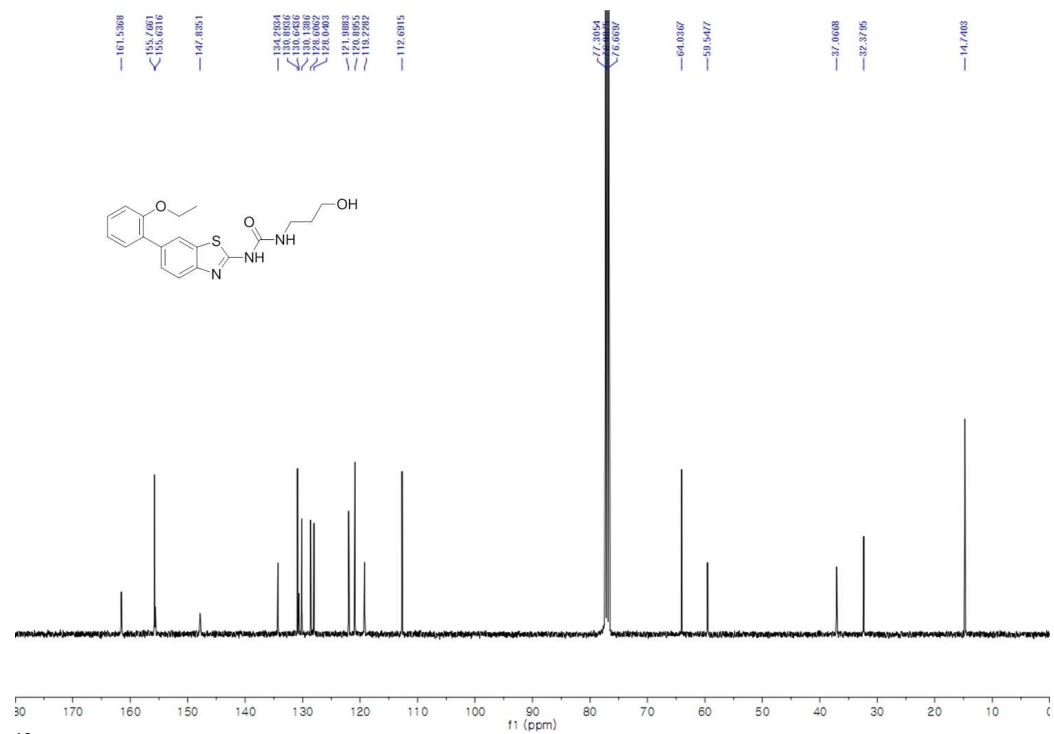


HPLC-Purity

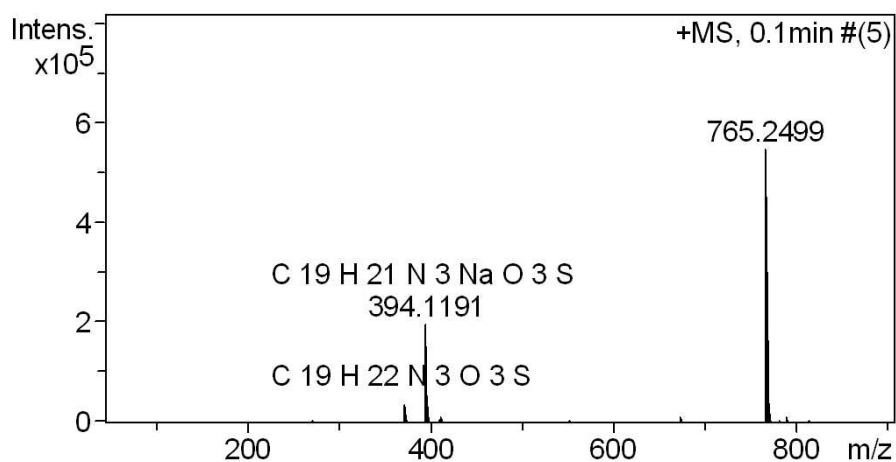
1-(6-(2-Ethoxyphenyl)benzo[d]thiazol-2-yl)-3-(3-hydroxypropyl)urea (10g).



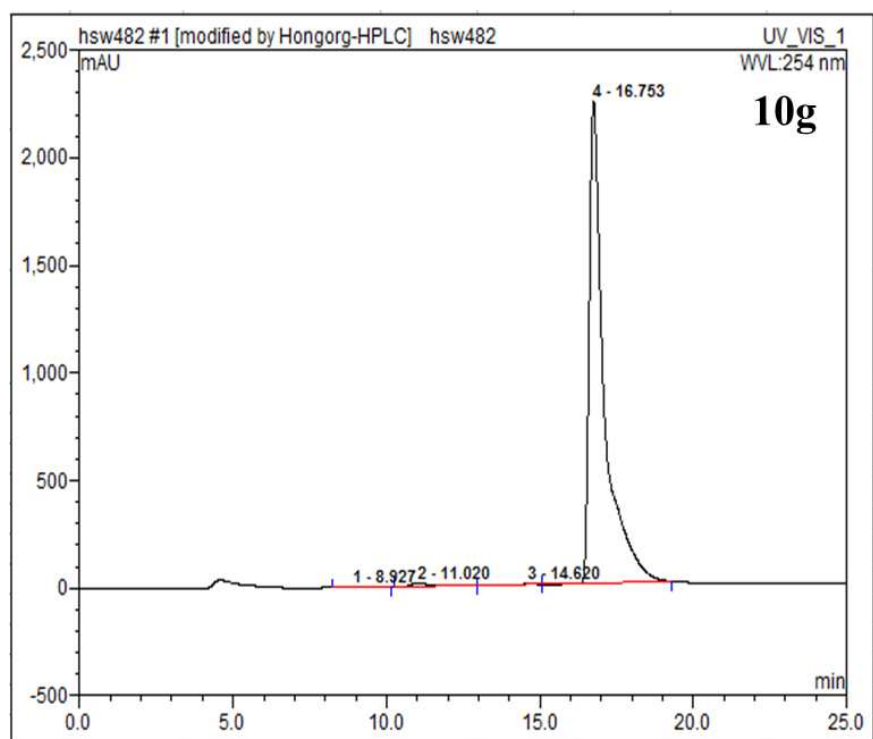
400 MHz, ^1H NMR in CDCl_3



100 MHz, ^{13}C NMR in CDCl_3



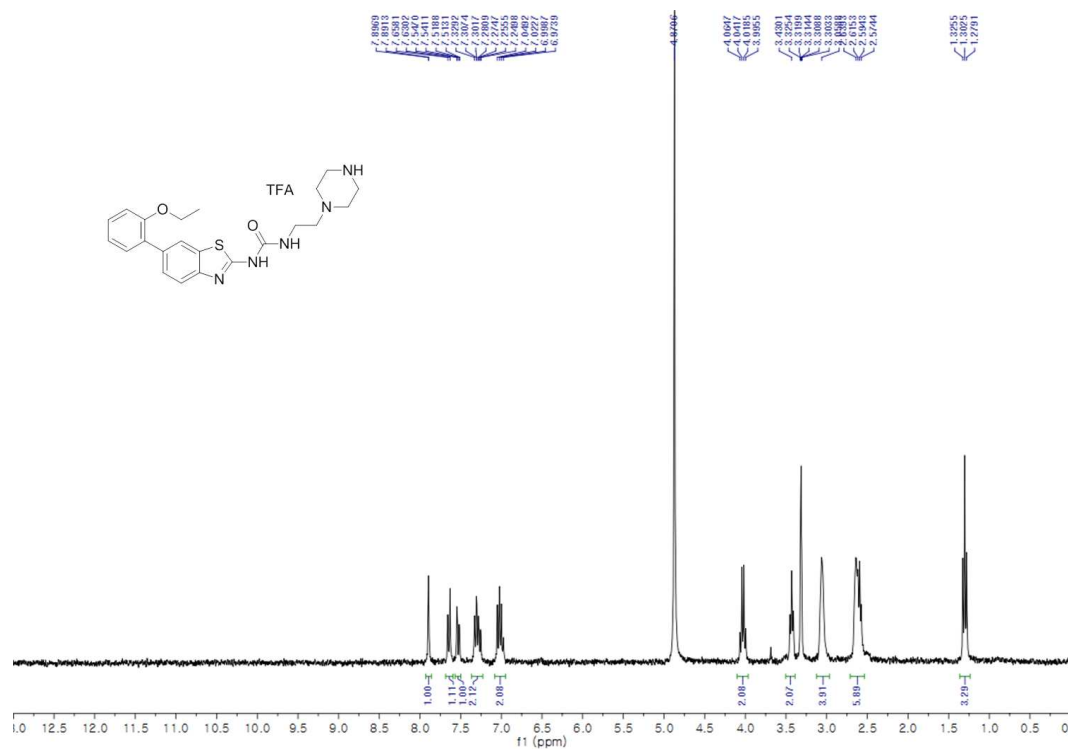
HRMS



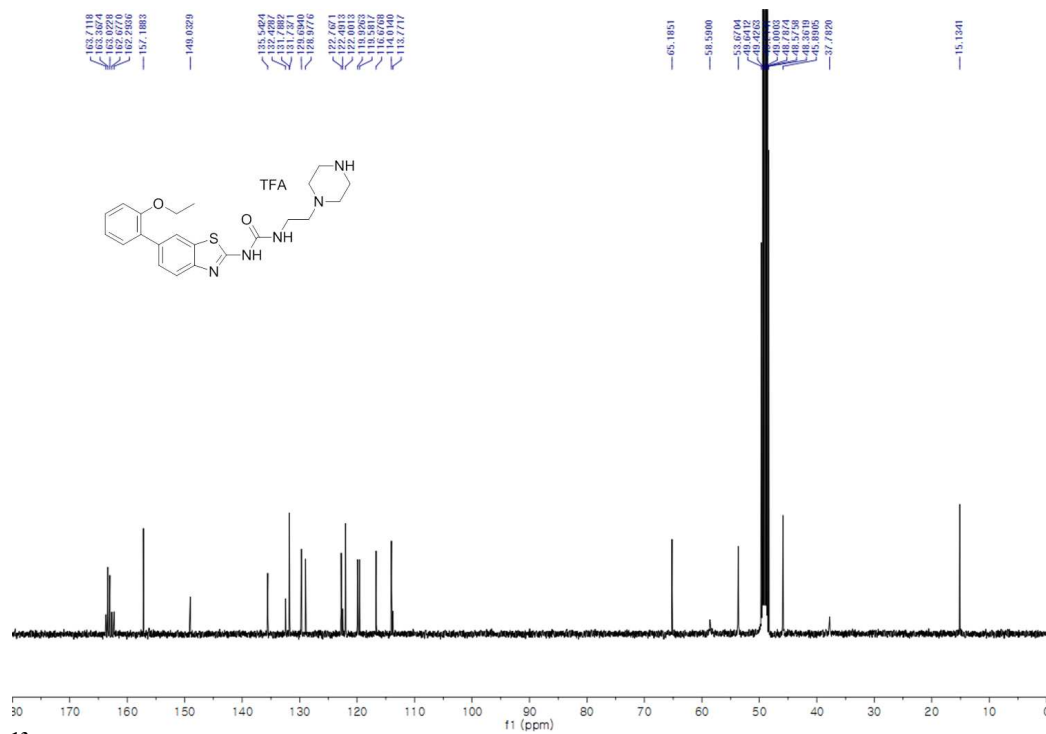
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.93	n.a.	2.436	2.066	0.16	n.a.	BMB
2	11.02	n.a.	18.562	14.942	1.16	n.a.	BMb*
3	14.62	n.a.	3.221	0.326	0.03	n.a.	bM *
4	16.75	n.a.	2239.138	1268.857	98.65	n.a.	MB*
Total:			2263.357	1286.192	100.00	0.000	

HPLC-Purity

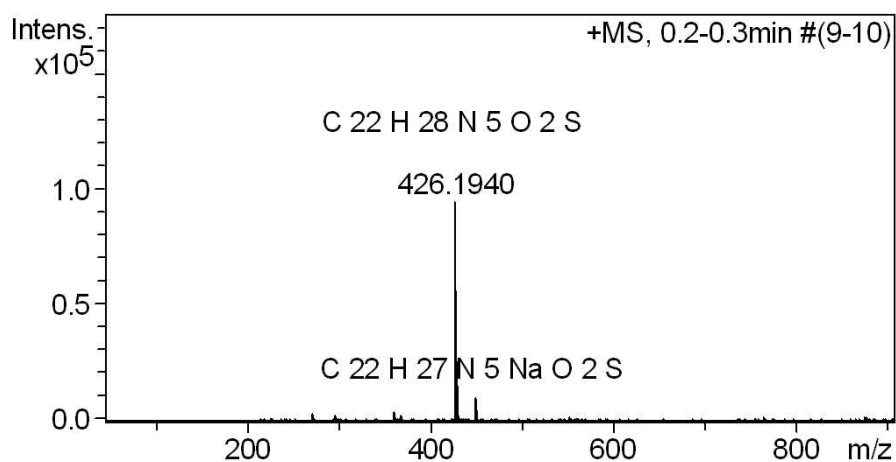
1-(6-(2-Ethoxyphenyl)benzo[d]thiazol-2-yl)-3-(2-(piperazin-1-yl)ethyl)urea (10h).



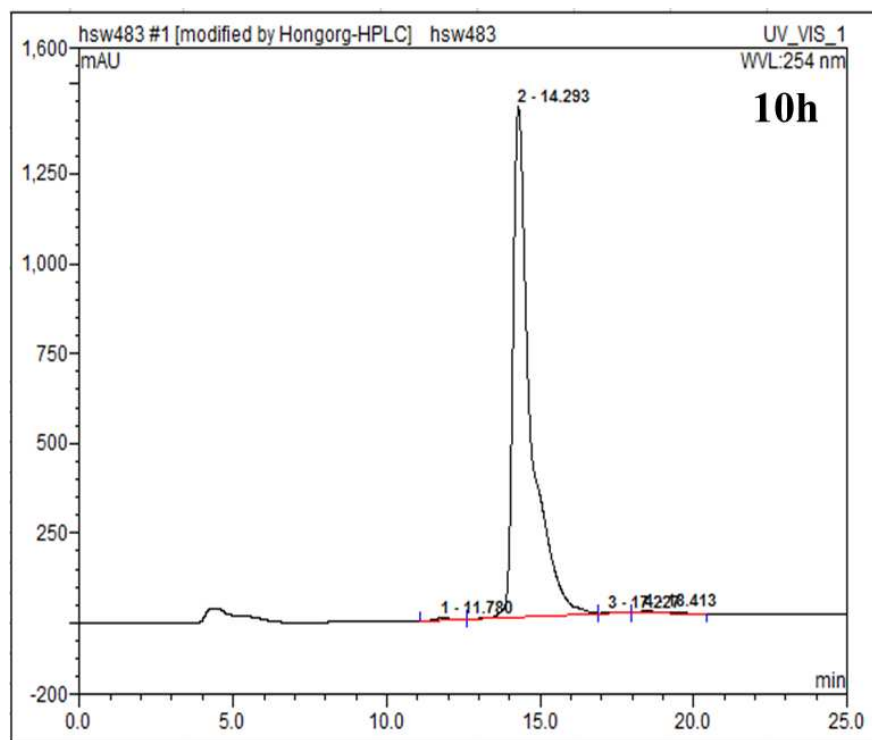
400 MHz, ¹H NMR in MeOD-d₄



100 MHz, ¹³C NMR in MeOD-d₄



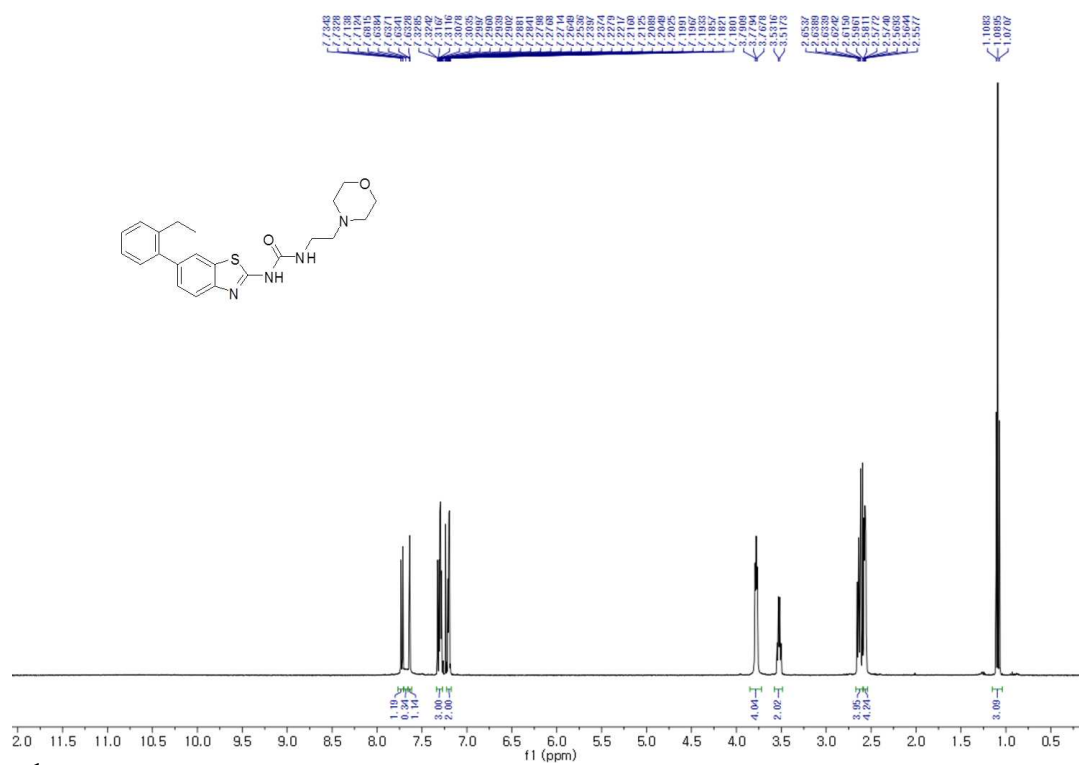
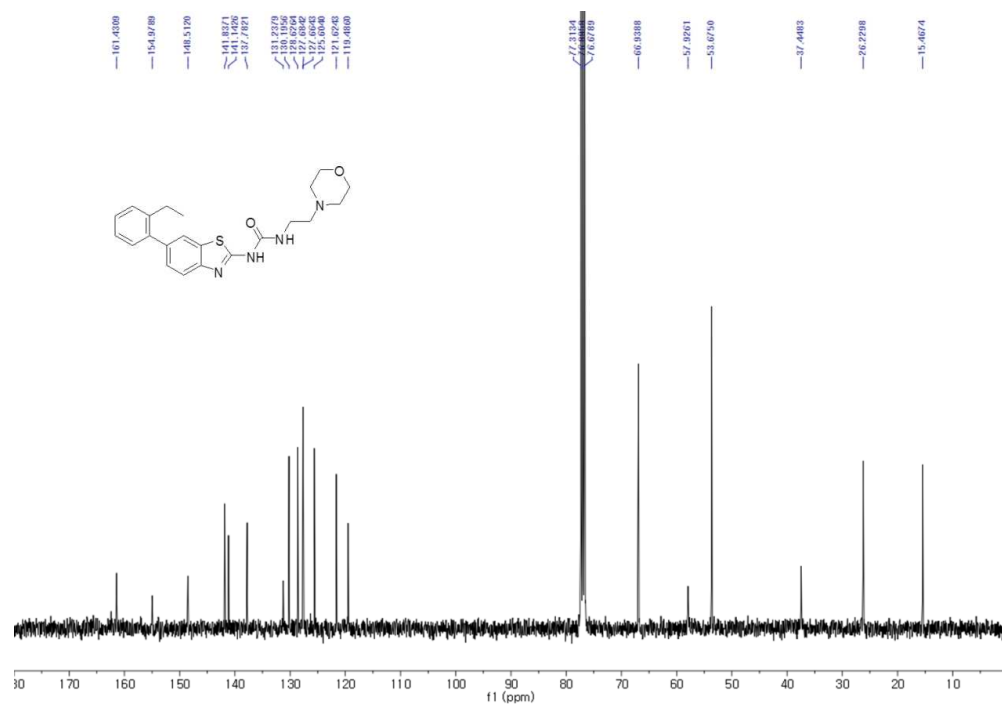
HRMS



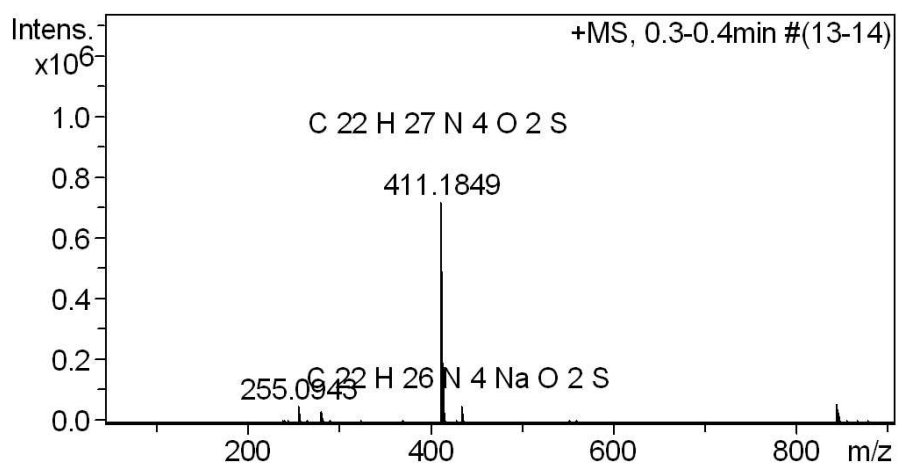
No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	11.78	n.a.	5.782	4.238	0.44	n.a.	BM
2	14.29	n.a.	1421.650	953.558	98.70	n.a.	M
3	17.23	n.a.	4.631	2.444	0.25	n.a.	Mb*
4	18.41	n.a.	7.264	5.907	0.61	n.a.	bMB
Total:			1439.326	966.148	100.00	0.000	

HPLC-Purity

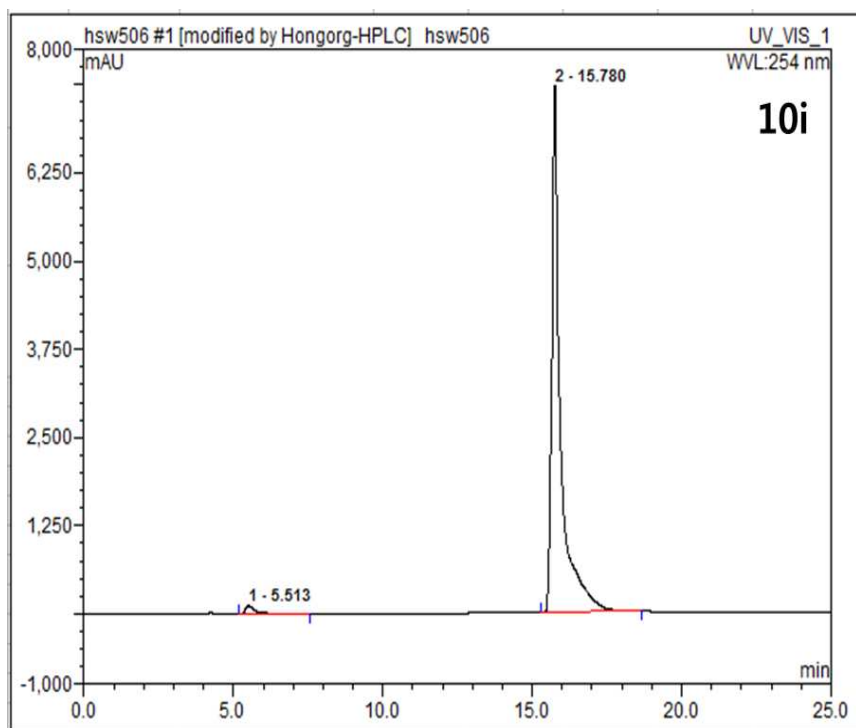
1-(6-(2-Ethylphenyl)benzo[d]thiazol-2-yl)-3-(2-morpholinoethyl)urea (10i).

400 MHz, ¹H NMR in CDCl₃

100 MHz, ^{13}C NMR in CDCl_3



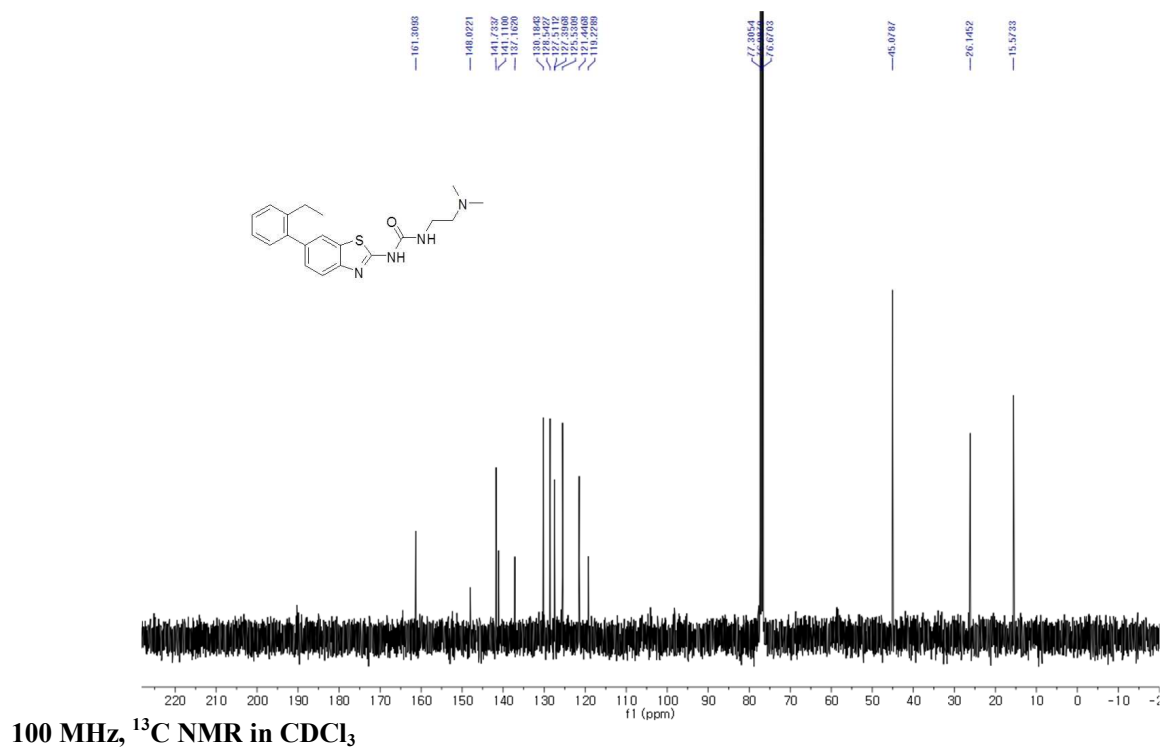
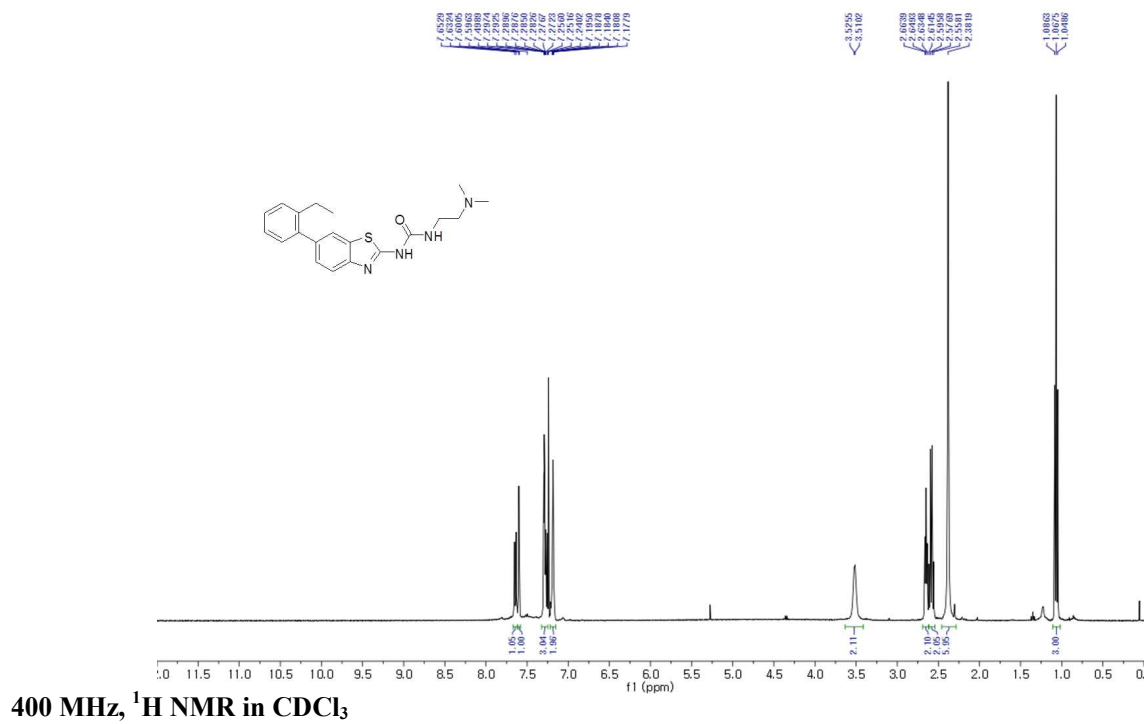
HRMS

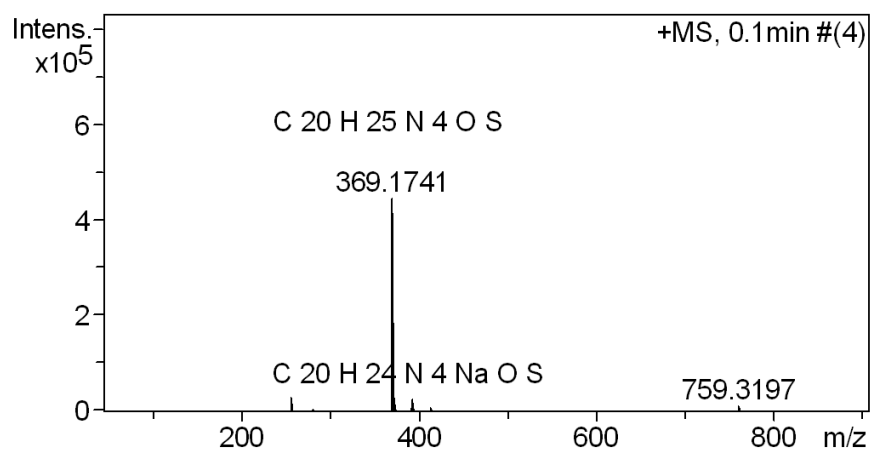


No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	5.51	n.a.	112.236	41.746	1.65	n.a.	BMB*
2	15.78	n.a.	7471.244	2487.875	98.35	n.a.	BMB*
Total:			7583.480	2529.621	100.00	0.000	

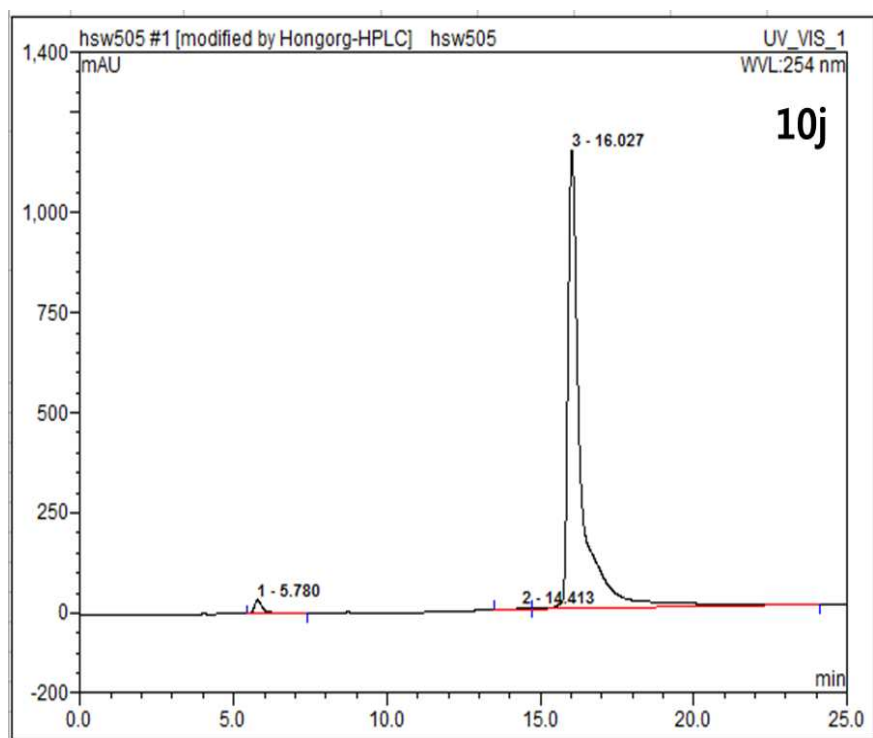
HPLC-Purity

1-(2-(Dimethylamino)ethyl)-3-(6-(2-ethylphenyl)benzo[d]thiazol-2-yl)urea (10j).





HRMS



No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	5.78	n.a.	34.781	11.738	2.04	n.a.	BMB
2	14.41	n.a.	5.086	2.261	0.39	n.a.	BM
3	16.03	n.a.	1143.995	562.428	97.57	n.a.	MB
Total:			1183.863	576.427	100.00	0.000	

HPLC-Purity