Supplementary Information

Palladium-catalyzed enantioselective carbonylation toward N-N axially chiral amides

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1. General Information

Unless otherwise noted, all chemicals were purchased from commercial suppliers and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a 600 MHz spectrometer (150 MHz for ^{13}C NMR). NMR experiments are reported in units, parts per million (ppm), and were referenced to $CDCl_3$ (7.26 or 77.0 ppm) and DMSO (2.50 or 39.5 ppm) as the internal standard. The coupling constants J are given in Hertz. Column chromatography was performed using EM silica gel 60 (200−300 mesh). ABsciex5600plusQTOF HR mass spectrometer equipped with an ESI source was used for analysis.

2. Experimental Procedures

2.1 General procedure (0.1 mmol scale)

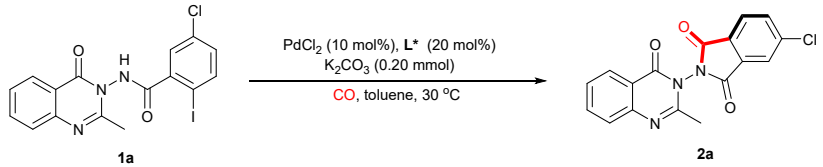
An oven-dried 25 mL Schlenk tube charged with **1a** (0.1 mmol), Pd(bpy)Cl_2 (10 mol%, 3.3 mg), **L3** (20 mol%, 8.8 mg), DABCO (0.2 mmol, 22.40 mg),5 Å MS (160 mg), and Hantzsch ester (0.12 mmol, 30.4 mg), 1.5 mL of toluene added. Then, the tube was vacuumed and refilled with CO and was placed in 30 ^{o}C oil-bath for 48 h. The crude reaction mixture was concentrated in vacuo and the residue was purified by silica gel flash column chromatography to afford the corresponding products.

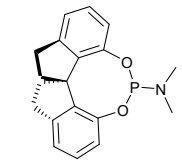
2.2 General procedure (1.0 mmol scale)

An oven-dried 50 mL Schlenk tube charged with **1a** (1.0 mmol), Pd(bpy)Cl_2 (10 mol%, 33.0 mg), **L3** (20 mol%, 88.0 mg), DABCO (2.0 mmol, 224.0 mg),5 Å MS (1.6 g), and Hantzsch ester (1.2 mmol, 304.0 mg), 15 mL of toluene added. Then, the tube was vacuumed and refilled with CO and was placed in 30 ^{o}C oil-bath for 60 h. The crude reaction mixture was concentrated in vacuo and the residue was purified by silica gel flash column chromatography to afford the corresponding products in 65% yield and 81% ee.

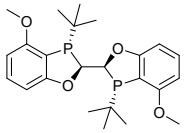
2.3 Detailed Information of Conditions Optimization for 2a[a]

Table S1:

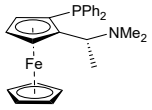




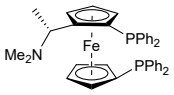
L1, 25%, 20% ee



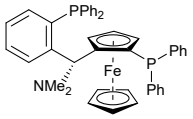
L2, 42%, 30% ee



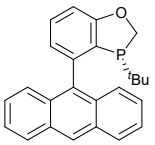
L3, 33%, 68% ee



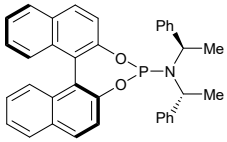
L4, 20%, 27 ee



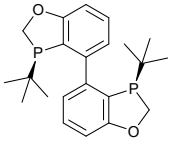
L5, 26%, 10% ee



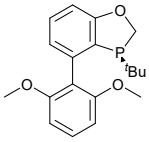
L6, N,R



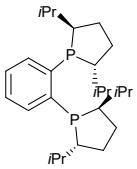
L7, 32%, 11% ee



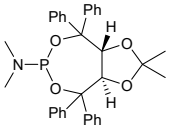
L8, 15%, 18% ee



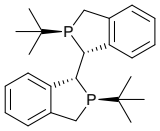
L9, N,R



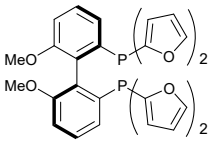
L10, N,R



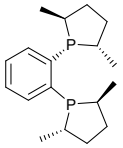
L11, 25%, 10% ee



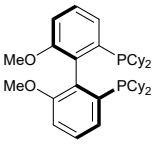
L12, N,R



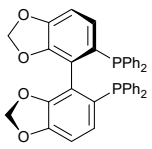
L13, N,R



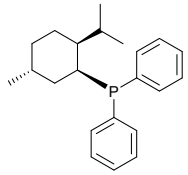
L14, N,R



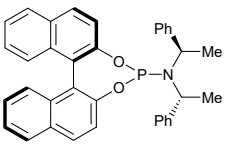
L15, trace



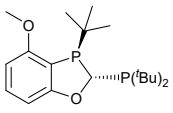
L16, N,R



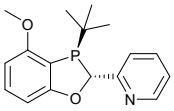
L17, N,R



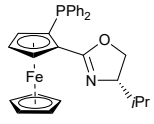
L18, 40%, <10% ee



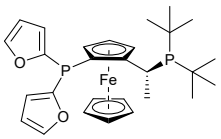
L19, trace



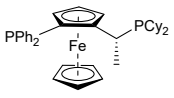
L20, N,R



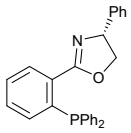
L21, N,R



L22, N,R

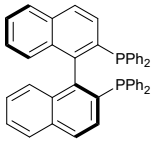


L23, N,R

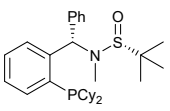


L24, N,R

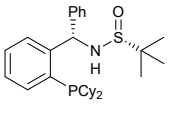
L25, N,R



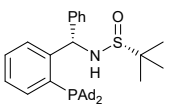
L26, N, R



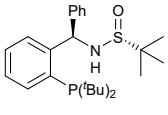
L27, N, R



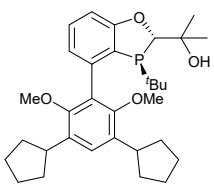
L28, 50%, 5%, ee



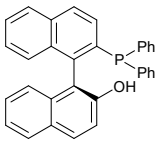
L29, N, R



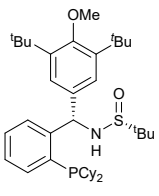
L30, N, R



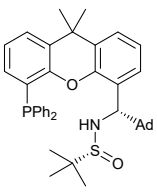
L31, N, R



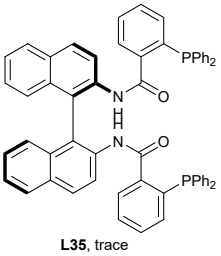
L32, N, R



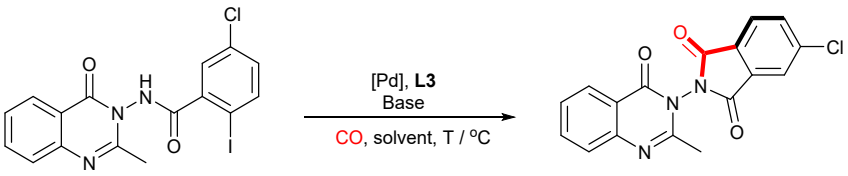
L33, 30%, 9% ee



L34, 33%, 5%, ee



L35, trace



1a **2a**

Entry	Catalyst	Base	Solvent	T / °C	Yield / %	ee / %
1	$Pd(OAc)_2(PPh_3)_2$	K_2CO_3	Ph-Me	30	36	65
2	$Pd(PivO)_2$	K_2CO_3	Ph-Me	30	41	57
3	$Pd(acac)_2$	K_2CO_3	Ph-Me	30	35	63
4	$Pd(PPh_3)_2Cl_2$	K_2CO_3	Ph-Me	30	26	59
5	$Pd(dppf)Cl_2$	K_2CO_3	Ph-Me	30	21	--
6	$Pd(TMEDA)Cl_2$	K_2CO_3	Ph-Me	30	27	77
7	$Pd(MeCN)_2Cl_2$	K_2CO_3	Ph-Me	30	37	9
8	$Pd(dppp)Cl_2$	K_2CO_3	Ph-Me	30	trace	--
9	$Pd(PCy_3)_2Cl_2$	K_2CO_3	Ph-Me	30	N, R	--
10	$PdCl_2$	K_2CO_3	Ph-Me	30	33	68
11	$Pd(OAc)_2$	K_2CO_3	Ph-Me	30	55	77
12	$Pd_2(dba)_3$	K_2CO_3	Ph-Me	30	58	71
13	$Pd(hfac)_2$	K_2CO_3	Ph-Me	30	43	37
14	$Pd(TFA)_2$	K_2CO_3	Ph-Me	30	31	72
15	$RhCl(PPh_3)_3$	K_2CO_3	Ph-Me	30	N, R	--
16	$FeSO_4$	K_2CO_3	Ph-Me	30	N, R	--
17	$CuCl_2$	K_2CO_3	Ph-Me	30	N, R	--
18	CuI	K_2CO_3	Ph-Me	30	N, R	--
19	Ag(OAc)	K_2CO_3	Ph-Me	30	N, R	--
20	$[Ir(ppy)_2Cl]_2$	K_2CO_3	Ph-Me	30	N, R	--
21	$Pd(bpy)Cl_2$	K_2CO_3	Ph-Me	30	30	78
22	$Pd(bpy)Cl_2$	pyridine	Ph-Me	30	26	57
23	$Pd(bpy)Cl_2$	DBU	Ph-Me	30	N, R	--
24	$Pd(bpy)Cl_2$	KOtBu	Ph-Me	30	trace	--

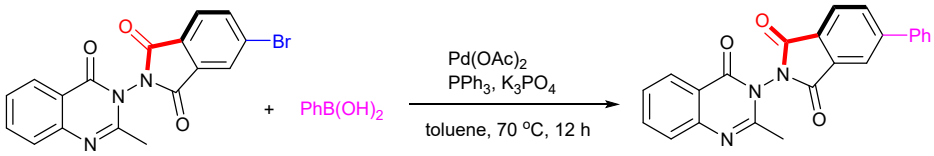
25	$Pd(bpy)Cl_2$	NaOtBu	Ph-Me	30	trace	--
26	$Pd(bpy)Cl_2$	NaOH	Ph-Me	30	trace	--
27	$Pd(bpy)Cl_2$	Na_2CO_3	Ph-Me	30	38	53
28	$Pd(bpy)Cl_2$	Cs_2CO_3	Ph-Me	30	36	69
29	$Pd(bpy)Cl_2$	Et_3N	Ph-Me	30	< 10	73
30	$Pd(bpy)Cl_2$	DIPEA	Ph-Me	30	13	51
31[b]	$Pd(bpy)Cl_2$	DABCO	Ph-Me	30	46 (77)[b]	81 (81)[b]
32	$Pd(bpy)Cl_2$	DABCO	MeCN	30	trace	--
33	$Pd(bpy)Cl_2$	DABCO	MTBE	30	20	57
34	$Pd(bpy)Cl_2$	DABCO	DCB	30	27	60
35	$Pd(bpy)Cl_2$	DABCO	MeOH	30	trace	--
36	$Pd(bpy)Cl_2$	DABCO	DCM	30	60	30
37	$Pd(bpy)Cl_2$	DABCO	acetone	30	< 10	51
38	$Pd(bpy)Cl_2$	DABCO	Ph-CF_3	30	47	66
39	$Pd(bpy)Cl_2$	DABCO	Ph-F	30	50	67
40	$Pd(bpy)Cl_2$	DABCO	Ph-Cl	30	48	73
41	$Pd(bpy)Cl_2$	DABCO	Ph-Br	30	44	60
42	$Pd(bpy)Cl_2$	DABCO	o-Xylene	30	49	60
43	$Pd(bpy)Cl_2$	DABCO	Mesitylene	30	36	71
44	$Pd(bpy)Cl_2$	DABCO	$CHCl_3$	30	33	70
45	$Pd(bpy)Cl_2$	DABCO	Et_2O	30	trace	--
46	$Pd(bpy)Cl_2$	DABCO	DME	30	-	-
47	$Pd(bpy)Cl_2$	DABCO	Ph-Me: DMSO (1:1)	30	22	61
48	$Pd(bpy)Cl_2$	DABCO	Ph-Me: MeCN (1:1)	30	45	67
49	$Pd(bpy)Cl_2$	DABCO	Ph-Me: acetone (1:1)	30	36	73
50	$Pd(bpy)Cl_2$	DABCO	Ph-Me: DCM (1:1)	30	47	71
51	$Pd(bpy)Cl_2$	DABCO	Ph-Me: DMF (1:1)	30	N, R	--
52	$Pd(bpy)Cl_2$	DABCO	Ph-Me: DMA (1:1)	30	N, R	--
53	$Pd(bpy)Cl_2$	DABCO	Ph-Me	40	44	77
54	$Pd(bpy)Cl_2$	DABCO	Ph-Me	50	43	73
55	$Pd(bpy)Cl_2$	DABCO	Ph-Me	60	47	69

$Pd(bpy)Cl_2$	DABCO	Ph-Me	70	49	65

[a] **Reaction conditions**: **1a** (0.10 mmol), Cat (10 mol%), ligand (20 mol%), base (0.20 mmol), 5 Å MS (160 mg), solvent (1.5 mL) at 30 °C for 48 h, in CO, isolated yield. [b] Hantzsch ester (0.12 mmol).

3. Synthetic application

3.1 Derivatization of 3ad



3ad, 81% ee

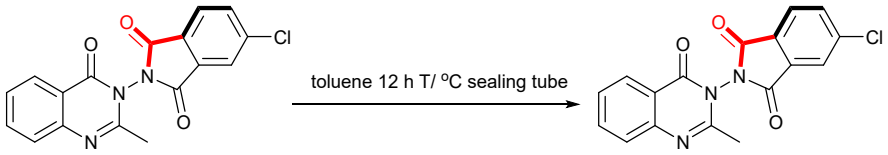
7, 72%, 73% ee

A dried 25 mL Schlenk tube was charged with **3ad** (0.10 mmol, 38.4 mg), $PhB(OH)_2$ (0.15 mmol, 18.3 mg), $Pd(OAc)_2$ (0.01 mmol, 2.3 mg) and PPh_3 (0.02 mmol, 5.3 mg), K_3PO_4 (0.25 mmol, 53.1 mg), 1.5 mL of toluene added by syringe. The reaction tube was vacuumed and refilled with N_2 for 3 times, and was placed in 70 °C oil-bath for 12 h. The crude reaction mixture was concentrated in vacuo and the residue was purified by silica gel flash column chromatography to afford the corresponding products **7**.

3.2 Stability on racemization of product 3aa

We investigated the racemization temperature of this axially chiral (*Ra*)-5-Chloro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione **3aa** scaffold.

Table S2: stability on racemization of product **3aa**



3aa, 81% ee

Entry	T / (°C)	Time (h)	ee of recovered 3aa (%)
1	90	12	81
2	100	12	81
3	110	12	79
4	120	12	77
5	130	12	75
6	140	12	67
7	150	12	65

4. DFT (density functional theory) calculations

4.1 Rotational Energy Barriers of Compound 3aa

DFT calculations were performed using ORCA 5.0.1 packages.[1] Equilibrium structures and transitions states were fully optimized using M06-2X[2] density functional method with the def2-SVP basis sets,[3] while single point energies were computed at RI-PWPB95(D3BJ)/def2TZVPP level[4] with the SMD solvation model.[5] Frequency analyses at 298 K were performed on M06-2X/def2-SVP optimized geometries to obtain thermodynamic corrections and to confirm the nature of the stationary points as equilibrium structures (with all real frequencies) or transition states (with only one imaginary frequency), and relative free energies, ΔG_{298}, were reported in these cases. Saddle points were connected to minima in the usual way with intrinsic reaction coordinate (IRC) calculations.[6]

Table S3. Zero-point energies (*ZPE*), enthalpy corrections (*ΔH*), free energy corrections (*ΔG*) of stationary points computed at the M062X/def2-SVP level, with single point electronic energies (*E*), enthalpies (*H*) and free energies (*G*) computed at the RI-PWPB95(D3BJ)/def2TZVPP (SMD: toluene) // M062X/def2-SVP level. All numbers are in hartrees.

Structure	*ZPE*	Δ*H*	Δ*G*	*E*	*H*	*G*
I-GS	0.246154	0.265580	0.200923	-1503.453910	-1503.434484	-1503.499141
I-TS	0.245285	0.263655	0.201645	-1503.397159	-1503.378789	-1503.440799

4.2 Cartesian Coordinates

1-GS			
C	5.32475641517340	-1.93678709995562	0.18984190641610
C	6.00417461288338	-0.74826426199650	-0.12783767029210
C	5.31030608918442	0.43105153058645	-0.34234372053338
C	3.90710625619017	0.45394848310265	-0.24426532448095
C	3.23632769773133	-0.74239169443671	0.07394094773820
C	3.94386008485068	-1.93307368756721	0.29026085407166
N	3.24179876876556	1.65025779340108	-0.46380562625367

C	1.96430394098850	1.67616093442545	-0.37309968014792
N	1.21863288126322	0.53997231452932	-0.06161806164242
C	1.77475302699981	-0.73826231011599	0.18107676643768
N	-0.13761157959771	0.61020686368091	0.02448754282264
C	-0.96449508593570	0.13246264646859	-1.01849463326077
C	-2.31284141027692	-0.01252466723513	-0.38844267496725
C	-2.20876313484441	0.28062654006924	0.96943276248851
C	-0.79245094301343	0.63090067095606	1.28092838710977
C	-3.51578922269978	-0.37155716326013	-0.97349083681430
C	-4.62833356288477	-0.42707854710601	-0.12776764619877
C	-4.53745779292266	-0.13627398678203	1.23928739124329
C	-3.31378118427973	0.22451445523921	1.80584976839929
O	1.05782082167605	-1.67221471587714	0.44154944251130
O	-0.26826607978192	0.89852311968810	2.31923649580576
O	-0.60836372945712	-0.07181972319413	-2.13893442351764
Cl	-6.16578697631044	-0.86730265662527	-0.79034574653314
C	1.19119589002825	2.93696206138301	-0.60174736913770
H	5.88484425024559	-2.85690623839134	0.35865373075466
H	7.09268146280129	-0.75415785020439	-0.20573145444700
H	5.81882319623121	1.36308697408151	-0.58884016300245
H	3.37724656371607	-2.83180050184829	0.53766446485282
H	-3.59384617227771	-0.60286946014619	-2.03598423734946
H	-5.43925328685040	-0.19384341717645	1.84904917602324
H	-3.22529858405846	0.45288648144667	2.86864633674517
H	0.61298243768554	3.20308909041639	0.29492423757253
H	1.90752232826408	3.73087118529234	-0.83201818680105
H	0.48831902051258	2.81113183715157	-1.43776175561265
1-TS			
C	-5.53820446094922	-1.39868726251899	0.61208872006047
C	-5.89987307561236	-0.10727980226038	1.02639840536804
C	-5.05238552154402	0.97211798036442	0.82033082836210

C	-3.80106294035544	0.76762110091589	0.21915954960126
C	-3.43685520697697	-0.53263729328199	-0.16759538763697
C	-4.31122996009330	-1.61093391810011	-0.00081817205066
N	-2.98694523288872	1.83860448761488	-0.11124537612924
C	-1.76312897154366	1.63065308943995	-0.42552444192099
N	-1.21776337404346	0.32335146225402	-0.32624776658195
C	-2.10399430968801	-0.72178742776849	-0.76805434325279
N	0.15233469652364	0.08703496975593	-0.35582501913652
C	1.07983932826550	1.00979739181477	0.20318982515736
C	2.40223377208186	0.32014223114288	0.14844866432056
C	2.17404060854844	-1.02653236343680	-0.08659965666632
C	0.69892553015294	-1.23690442194979	-0.14511185421048
C	3.67097278081904	0.83100155777831	0.36163389106082
C	4.72373775478673	-0.08846064043013	0.30248089149296
C	4.50778743490452	-1.45216918328430	0.06735399405636
C	3.21314024625788	-1.94371173764138	-0.11613490413499
O	-1.76369100310151	-1.59825711073483	-1.50804841863805
O	0.10132942444219	-2.24067803350826	0.07621691295279
O	0.83528123273946	2.07708583692870	0.68343678423507
Cl	6.34410334974597	0.47270544334576	0.54219355589466
C	-1.00490590121235	2.73460776733714	-1.11435822857934
H	-6.22443216907811	-2.23166276006057	0.76840208206691
H	-6.86986842683189	0.05267938019155	1.50022017754279
H	-5.33424548478794	1.98828184885374	1.09674704232829
H	-3.99623263271959	-2.59912755656917	-0.33949339067900
H	3.84683791911303	1.88642389869280	0.56929568278449
H	5.36854186045960	-2.12057060689160	0.04271167737106
H	3.02451424292051	-3.00586401656997	-0.27514244196738
H	-0.14682136168023	2.35500264832059	-1.68093628816399
H	-1.71678918460386	3.20630809178097	-1.80224640436594
H	-0.65086096405064	3.48194994847446	-0.39756059054140

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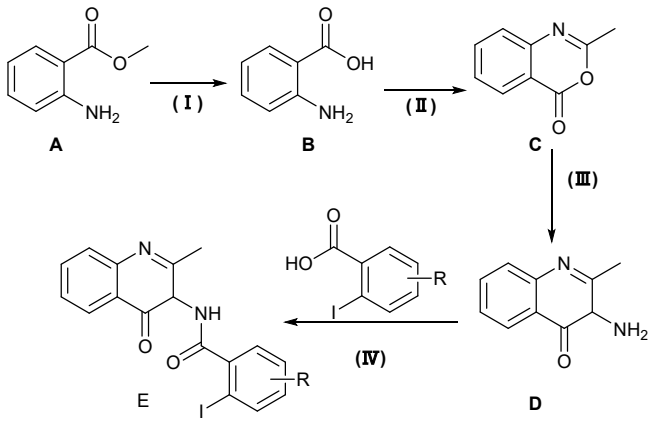
6 (a) H. P. Hratchian and H. B. Schlegel, *J. Chem. Phys*., 2004, **120**, 9918-9924; (b) H. P. Hratchian and H. B. Schlegel, *J. Chem. Theory Comput*., 2005, **1***,* 61-69.

5. Preparation of Starting Materials

5.1 Preparation of starting material with 3aa-3af and 3ak-3ar



(I) To a mixture of water and ethanol (100 mL) was added **A** (40 mmol). Subsequently, NaOH (120 mmol) was introduced, and the reaction was stirred at 60 °C for 5 h. After the reaction was completed, the reaction was extracted with ethyl acetate (3 times). The aqueous phase was collected, and an appropriate amount of HCl was added. The mixture was then extracted with ethyl acetate (20 mL × 3), and the organic layers were combined, the organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo to afford yellow solid **B**.

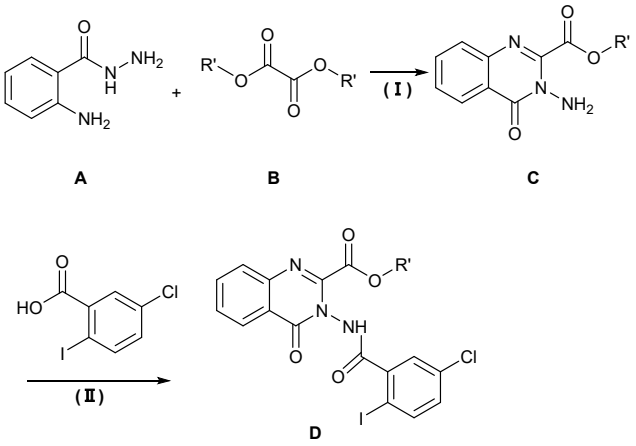
(II) Compound **B** (20 mmol) was added to a 100 mL pear-shaped flask, followed by acetic anhydride (200 mmol). The mixture was refluxed for 5 hours. After the reaction was completed, the reaction was washed with sodium carbonate until the acetic anhydride was thoroughly removed. The solution was concentrated under vacuum and purified by column chromatography (silica gel, petroleum ether/EtOAc, 5:1) to yield white solid **C**.

(III) Compound **C** (10 mmol) was added to a 100 mL pear-shaped flask, followed by ethanol (20 mL) and hydrazine hydrate (11 mmol). The mixture was refluxed for 3 h. After the reaction was completed, the crude product was purified by silica gel flash column chromatography to afford (silica gel, petroleum ether/EtOAc, 5:1) to afford white solid **D**.

(IV) To a dry round-bottom flask equipped with a magnetic stir bar were added 2-

iodobenzoic acid with substituents (10 mmol) and thionyl chloride (10 mL). The mixture was refluxed at 80 °C for 30 minutes. After concentration under vacuum and further drying under high vacuum for 30 minutes, compound **D** (10 mmol) dissolved in pyridine was added under N_2. The mixture was refluxed at 115 °C for 30 minutes. Upon the reaction was completed, water was poured into the reaction mixture, and the solution was extracted with ethyl acetate (20 mL × 3), The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by silica gel flash column chromatography to afford (silica gel, petroleum ether/ EtOAc, 5:1) the corresponding products **E** as a white solid.

5.2 Preparation of starting material with 3ag-3aj.

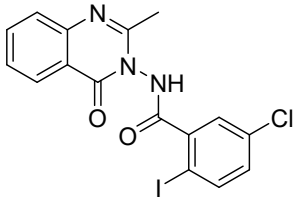


(I) Compound **A** (10 mmol) was added to a 100 mL Schlenk tube, followed by **B** (50 mmol) The mixture was refluxed for 8 h. After the reaction was completed, the crude product was purified by silica gel flash column chromatography to afford **C**.

(**II**) To a dry round-bottom flask equipped with a magnetic stir bar were added 5-chloro-2-iodobenzoic acid (10 mmol) and thionyl chloride (10 mL). The mixture was refluxed at 80 °C for 30 minutes. After concentration under vacuum and further drying under high vacuum for 30 minutes, compound **C** (5 mmol) dissolved in pyridine was added under N_2. The mixture was refluxed at 115 °C for 30 minutes. Upon the reaction was completed, water was poured into the reaction mixture, and the solution was extracted with ethyl acetate (20 mL × 3), The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by silica gel flash column

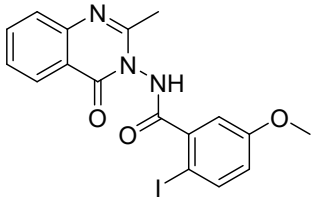
chromatography to afford (silica gel, petroleum ether/ EtOAc, 5:1) the corresponding products **D** as a white solid.

5-Chloro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1a)



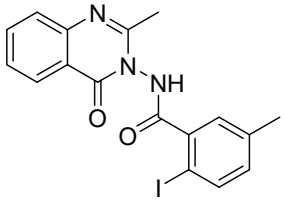
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid (265 mg, 60% yield) : mp 235.3-237.1 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.52 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.80-7.77 (m, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 2.4 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 6.81 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 2.76 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.0, 158.2, 153.8, 146.9, 142.4, 135.5, 135.5, 131.5, 128.0, 127.5, 127.4, 127.2, 126.0, 125.1, 120.5, 21.2.; MS (EI) 438 (M^+); HRMS (ESI) *m/z* calcd for $C_{16}H_{12}ClIN_3O_2^+$ $(M+H)^+$ 439.9657, found 439.9651; IR: 3311, 3085, 2917, 1704, 773.

2-Iodo-5-methoxy-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1b):



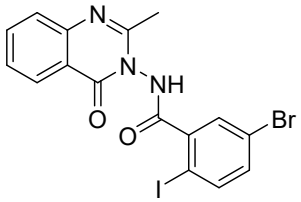
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (280 mg, 64% yield) : mp 202.1-205.3 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.89 (s, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.77 (t, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.17 (d, *J* = 3.0 Hz, 1H), 6.58 (dd, J_1 = 8.4 Hz, J_2 = 3.0 Hz, 1H), 3.74 (s, 3H), 2,77 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 164.3, 158.4, 154.2, 146.9, 135.4, 132.6, 127.5, 127.3, 127.1, 126.5, 121.7, 121.4, 120.6, 109.0, 56.3, 21.2.; MS (EI) 435 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{15}IN_3O_3^+$ $(M+H)^+$ 436.0153, found 436.0153; IR: 3203, 3012, 2946, 1698, 1020

2-Iodo-5-methyl-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1c):



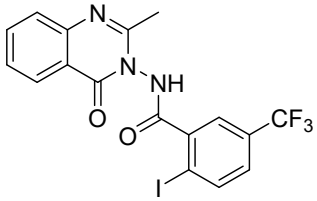
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (315 mg, 75% yield) : mp 140.1-143.0 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.60 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.88 (dd, J_1 = 16.2 Hz, J_2 = 7.8 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.50 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 2.60 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.4, 164.1, 158.3, 154.2, 147.1, 146.8, 135.9, 135.4, 130.2, 127.4, 127.4, 127.1, 125.0, 124.5, 120.5, 22.2, 21.1.;MS (EI) 419 (M+); HRMS (ESI) m/z calcd for $C_{17}H_{15}IN_3O_2^+$ $(M+H)^+$ 420.0203, found 420.0200; IR: 3473, 3133, 2919, 1700, 1384.

5-Bromo-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1d):



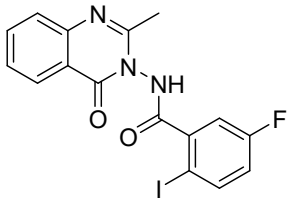
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid (300 mg, 62% yield) : mp 236.0-239.2°C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.78 (s, 1H), 8.16 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.90-7.87 (m, 1H), 7.77 (d, J = 2.4 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.58 (t, J = 7 .8 Hz, 1H), 7.55 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.9, 158.89, 155.8, 146.6, 141.7, 140.9, 135.3, 135.0, 131.2, 127.1, 126.9, 126.4, 121.3, 120.4, 92.5, 21.6.; MS (EI) 482 (M^+); HRMS (ESI) *m/z* calcd for $C_{16}H_{12}BrIN_3O_2^+$ $(M+H)^+$ 483.9152, found 483.9152; IR: 3309, 3077, 2979, 1700, 696.

2-Iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-5-(trifluoromethyl)benzamide (1e):



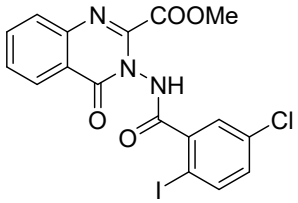
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid (350 mg, 74% yield) : mp 243.9-244.1 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.86 (s, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.88 (d, J = 6.6 Hz, 1H), 7.70 (d, J = 7.8 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.2, 158.9, 155.7, 146.6, 141.1, 140.2, 135.3, 128.7 (q, J = 31.5 Hz) , 128.5 (q, J = 4.5 Hz), 127.0, 127.0, 126.5, 124.9 (q, J = 3.0 Hz), 123.7 (q, J = 271.5 Hz), 120.5, 99.7, 21.6; MS (EI) 472 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{12}F_3IN_3O_2^+$ $(M+H)^+$ 473.9921, found 473.9920; IR: 3307, 3068, 2973, 1698, 825.

5-Fluoro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1f):



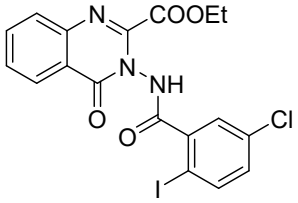
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid 247 mg, 58% yield) : mp 223.8-225.3 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.75 (s, 1H), 8.16 (d, J = 7.8 Hz, 1H), 8.04 (dd, J_1 = 9.0Hz, J_2 = 5.4 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.58 (t, J = 7.2 Hz, 1H), 7.48 (dd, J_1 = 8.4 Hz, J_2 = 3.0 Hz, 1H), 7.27 (td, J_1 = 9.0 Hz, J_2 = 3.0 Hz, 1H), 2.60 (s, 3H); 13C NMR (150 MHz, DMSO-d6) δ 167. 0, 161.3 (d, J = 246.0 Hz), 158.8, 155.8, 146.6, 141.8 (d, J = 27.5 Hz), 140.7 (d, J = 6.0 Hz), 135.2, 127.0, 127.0, 126.5, 120.5, 119.7 (d, J = 21 Hz), 116.4 (d, J = 24.0 Hz), 87.6 (d, J = 4.5 Hz), 21.5; MS (EI) 422 (M^+); HRMS (ESI) m/z calcd for $C_{16}H_{12}FIN_3O_2^+$ $(M+H)^+$ 423.9953, found 423.9952; IR: 3316, 3056, 2964, 1704, 811.

Methyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1g):



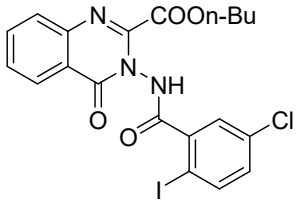
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid (215 mg, 44% yield) : mp 213.6-216.3 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 12.07 (s, 1H), 8.27 (d, J = 7.8 Hz, 1H), 8.01 (t, J = 9.0 H, 2H), 7.86 (d, J = 8.4 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.52 (d, J = 2.4 Hz, 1H), 7.43 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 3.99 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.0, 160.0, 158.0, 147.3, 145.4, 141.7, 140.0, 135.9, 133.0, 132.2, 129.1, 128.6, 128.2, 126.9, 121.8, 91.8, 53.9.; MS (EI) 482 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{11}ClIN_3O_4^+$ $(M+H)^+$ 483.9556, found 483.9556; IR: 3272, 3081, 2852, 1712, 1305.

Ethyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1h):



Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (225 mg, 45% yield) : mp 235.0-235.9 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 2.06 (s, 1H), 8.27 (d, J = 7.8 Hz, 1H), 8.03-7.99 (m, 2H), 7.87 (t, J = 8.4 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.52 (d, J = 3.0 Hz, 1H), 7.42 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 4.49-4.41 (m, 2H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.9, 159.6, 158.0, 147.5, 145.5, 141.8, 139.7, 135.9, 133.0, 132.3, 129.1, 128.6, 128.1, 126.8, 121.7, 91.8, 63.2, 13.9; MS (EI) 496 (M^+); HRMS (ESI) *m/z* calcd for $C_{13}H_{14}ClIN_3O_4^+$ $(M+H)^+$ 497.9712, found 497.9712; IR: 3274, 3087, 2979, 1714, 1374.

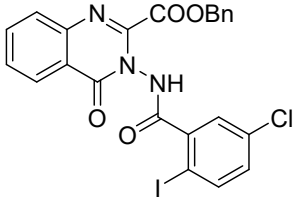
Butyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1i):



Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid (220 mg, 42% yield) : mp 172.2-173.7 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 12.05 (s, 1H), 8.27 (d, J = 7.8 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.51 (d, J = 2.4 Hz, 1H), 7.43 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 4.46-

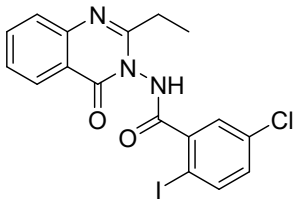
4.42 (m, 1H), 4.39-4.35 (m, 1H), 1.71-1.66 (m, 2H), 1.40-1.34 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.9, 159.7, 157.9, 147.6, 145.5, 141.9, 139.6, 135.9, 132.9, 132.4, 129.1, 128.6, 128.2, 126.8, 121.8, 91.9, 66.7, 29.9, 18.4, 13.5; MS (EI) 524 (M^+); HRMS (ESI) *m/z* calcd for $C_{20}H_{18}ClIN_3O_4^+$ $(M+H)^+$ 526.0025, found 526.0025; IR: 3247, 3087, 2956, 1716, 1467.

Benzyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1j):



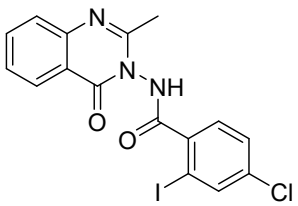
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid (225 mg, 40% yield) : mp 207.1-209.7 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 12.05 (s, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.2 Hz, 1H), 7.47 (d, J = 7.8 Hz, 2H), 7.47-7.33 (m, 5H), 5.52-5.43 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.1, 159.4, 158.0, 147.3, 145.4, 141.8, 139.7, 135.9, 134.6, 133.0, 132.3, 129.1, 128.6, 128.6, 128.5, 128.5, 128.2, 126.9, 121.7, 91.9, 68.4.; MS (EI) 558 (M^+); HRMS (ESI) *m/z* calcd for $C_{23}H_{16}ClIN_3O_4^+$ $(M+H)^+$ 559.9869, found 559.9869; IR: 3199, 3072, 2962, 1704, 1376.

5-Chloro-*N*-(2-ethyl-4-oxoquinazolin-3(4*H*)-yl)-2-iodobenzamide (1k):



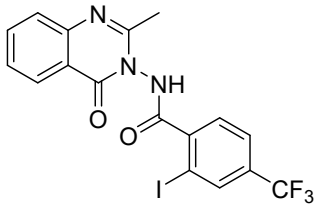
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (305 mg, 67% yield) : mp 237.5-240.3 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.71 (s, 1H), 8.18 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.92-7.89 (m, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.67 (J = 3 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.44 (dd, J_1 = 8.4 Hz, 1H, J_2 = 2.4 Hz, 1H), 3.00-2.85 (m, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.2, 159.0, 158.9, 146.5, 141.4, 140.9, 135.2, 133.1, 132.1, 128.6, 127.3, 126.9, 126.4, 120.4, 91.7, 26.6, 10.7; MS (EI) 452 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{14}ClIN_3O_2^+$ $(M+H)^+$ 453.9814, found 458.9812; IR: 3155, 2988,2952, 1687, 1605, 1375, 1100.

4-Chloro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1l):



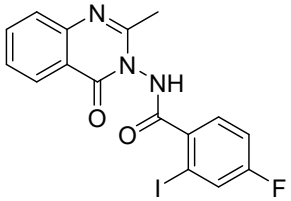
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (330 mg, 75% yield) : mp 220.9-223.7 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.71 (s, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 2.4 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.73-7.66 (m, 3H), 7.57 (t, J = 7.2 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.4, 158.8, 155.8, 146.5, 138.7, 137.9, 135.8, 135.2, 130.1, 128.3, 127.0, 126.9, 126.4, 120.5, 94.7, 21.5; MS (EI) 438 (M^+); HRMS (ESI) *m/z* calcd for $C_{16}H_{12}ClIN_3O_2^+$ $(M+H)^+$ 439.9657, found 439.9654; IR: 3318, 3083, 2969, 1698, 775.

2-Iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-4-(trifluoromethyl)benzamide (1m):



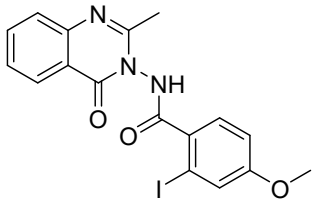
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (206 mg, 63% yield) : mp 250.4-252.0 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.83 (s, 1H), 8.34 (s, 1H), 8.16 (d, J = 7.8 Hz, 1H), 8.02 (d, J = 7.8 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.4, 158.8, 155.7, 146.6, 143.3 ,135.9 (q, J = 4.5 Hz), 135.2, 131.8 (q, J = 31.5 Hz), 129.6, 127.0 0 127.0, 126.5, 125.3 (q, J = 4.5 Hz), 122.7 (q, J = 270.0 Hz), 120.5, 94.3, 21.6; MS (EI) 472 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{12}F_3IN_3O_2^+$ $(M+H)^+$ 473.9921, found 473.9919; IR: 3241, 3093, 2983, 1710, 690.

4-Fluoro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1n):



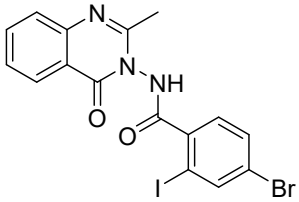
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (275 mg, 65% yield) : mp 219.2-220.9 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.66 (s, 1H), 8.16 (d, J = 7.8 Hz, 1H), 7.93 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.90-7.87 (m, 1H), 7.73-7.71 (m, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.50 (td, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.5, 162.4 (d, J = 252.0 Hz), 158.8, 155.9, 146.6, 135.6 (d, J = 3.0 Hz), 135.2, 130.7 (d, J = 9.0 Hz), 127.0, 126.9, 126.7 (d, J = 24.0 Hz), 126.5, 120.6, 115.4 (d, J = 21.0 Hz) 94.5 (d, J = 9.0 Hz), 21.6; MS (EI) 422 (M^+); HRMS (ESI) *m/z* calcd for $C_{16}H_{12}FIN_3O_2^+$ $(M+H)^+$ 423.9953, found 423.9953; IR: 3502, 3068, 2817, 1685, 863.

2-Iodo-4-methoxy-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1o):



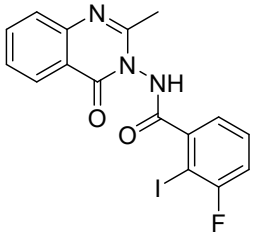
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a white solid (220 mg, 50% yield) : mp 191.3-193.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.28 (s, 1H), 7.95 (dd , J_1 = 1.2 Hz, J_2 = 7.8 Hz, 1H), 7.74-7.72 (m, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.38 (t, J = 7.8 Hz, 1H), 7.20 (d, J = 2.4 Hz, 1H), 6.69 (dd, J_1 =2.4 Hz, J_2 = 8.4 Hz, 1H), 3.70 (s, 3H), 2.70 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.9, 161.3, 160.6, 155.5, 147.0, 135.0, 130.3, 129.8, 127.1, 126.9, 126.5, 125.8, 120.5, 113.6, 93.1, 55.5, 22.0; MS (EI) 435 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{15}IN_3O_3^+$ $(M+H)^+$ 436.0153, found 436.0153; IR: 3203, 3012, 2946, 1698, 1020.

4-Bromo-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1p):



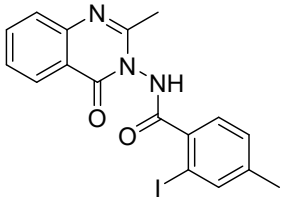
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (290 mg, 60% yield) : mp 266.8-269.1 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.71 (s, 1H), 8.23 (s, 1H), 8.15 (d, J =7.8 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.84 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.60-7.56 (m, 2H), 2.59 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.5, 158.8, 155.8, 146.5, 141.3, 138.3, 135.2, 131.2, 130.4, 127.0, 126.9, 126.5, 124.5, 120.5, 95.9, 21.5; MS (EI) 482 (M^+); HRMS (ESI) *m/z* calcd for $C_{16}H_{12}BrIN_3O_2^+$ $(M+H)^+$ 483.9152, found 483.9151; IR: 3320, 3085, 2904, 1700, 694.

3-Fluoro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1q):



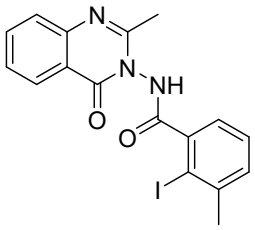
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (260 mg, 61% yield) : mp 131.6-132.3 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.73 (s, 1H), 8.16 (d, J = 7.8 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.65-7.61 (m, 1H), 7.58 (t, J = 7.2 Hz, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.47 (t, J = 8.4 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.2, 161.5 (d, J = 241.5 Hz), 158.8, 155.8, 146.6, 141.4, 135.2, 130.8 (d, J = 9.0 Hz), 127.0, 127.0, 125.0 (d, J = 4.5 Hz), 120.6, 117.5(d, J = 24.0 Hz)), 82.6, 82.5 (d, J = 28.5 Hz), 21.6; MS (EI) 422 (M^+); HRMS (ESI) *m/z* calcd for $C_{16}H_{12}FIN_3O_2^+$ $(M+H)^+$ 423.9953, found 423.9953; IR: 3459, 3158, 2935, 1664, 848.

2-Iodo-4-methyl-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1r):



Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (288 mg, 69% yield) : mp 203.2-205.2 ^{o}C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 11.55 (s, 1H), 8.16 (d, J = 7.8 Hz, 1H), 7.58-7.55 (m, 2H), 7.69 (d, J = 7.8 Hz, 1H), 7.57 (t, J =7.8 Hz, 2H), 7.43 (d, J = 7.8 Hz, 1H), 2.58 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.9, 158.9, 156.0, 146.6, 142.5, 141.0, 136.1, 135.1, 128.8, 128.7, 127.0, 126.9, 126.5, 120.6, 93.5, 21.5, 20.2; MS (EI) 419 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{15}IN_3O_2^+$ $(M+H)^+$ 420.0203, found 420.0201; IR: 3183, 3004, 2927, 1720, 1376.

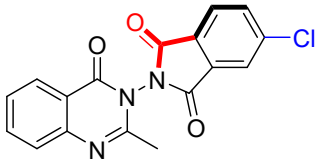
2-Iodo-3-methyl-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl) benzamide (1s):



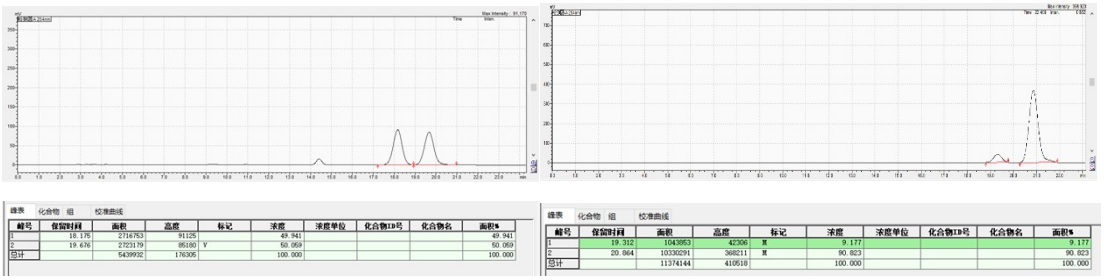
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 5:1) gave the product as a yellow solid (210 mg,50 % yield) : mp 120.1-128.6 ^{o}C; ^{1}H NMR (DMSO-d_6, 600 MHz), δ 11.58 (s, 1H), 8.16 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 7.90-7.87 (m, 1H), 7.69 (d, J = 7.8Hz,1H), 7.59-7.56 (m, 1H), 7.52-7.50 (m, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.44 (dd, J_1 = 7.2 Hz, J_2 = 2.4 Hz, 1H), 2.62 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.7, 158.9, 156.0, 146.6, 142.6, 140.8, 135.1, 131.4, 128.3, 127.0, 126.9, 126.5, 126.2, 120.6, 99.7, 28.5, 21.7; MS (EI) 419 (M^+); HRMS (ESI) m/z calcd for $C_{17}H_{15}IN_3O_2^+$ $(M+H)^+$ 420.0203, found 420.0202; IR: 3455, 3156, 2910, 1622,1380.

6. Characterization Data for the Products

(*Ra*)-5-Chloro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3aa):



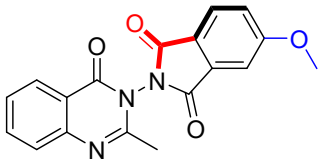
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (26.21 mg, 77% yield) as a yellow solid: mp 203.6-205.1 °C; $[\alpha]_D^{25}$ = -13.60 (c = 0.10 in MeCN, 81% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.22 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 1.8 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.86 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.83-7.80 (m, 1H), 7.72(d, J = 8.4 Hz, 1H), 7.50 (t, J = 7.2 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.3, 163.0, 158.2, 153.8, 146.9, 142.4, 135.5, 135.5, 131.5, 127.9, 127.5, 127.4, 127.2, 126.0, 125.1, 120.5, 21.2; MS (EI) 339 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{11}ClN_3O_3^+$ $(M+H)^+$ 340.0483, found 340.0483. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 19.3 min, t (major) = 20.8 min; IR: 3095, 2925, 1747, 1698, 730.



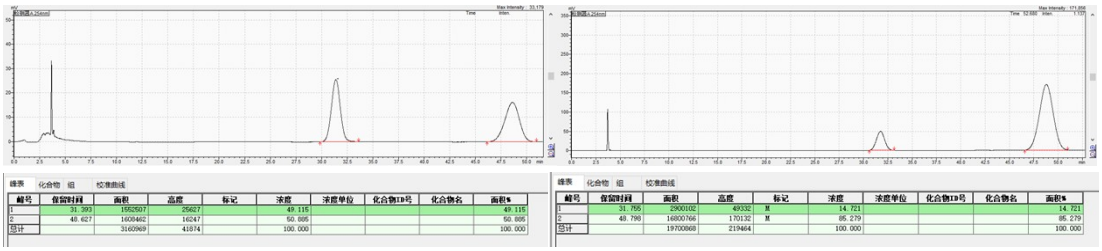
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	18.175	2716753	91125	49.941	49.941
2	19.676	2723179	85180	50.059	50.059
Total		5439932	176305	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	19.312	1043853	42306	9.177	9.177
2	20.864	10330291	368211	90.823	90.823
Total		11374144	410518	100.000	100.000

(*Ra*)-5-Methoxy-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ab):



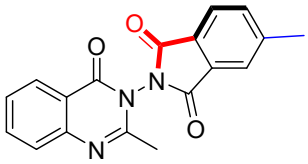
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (19.5 mg, 56% yield) as a yellow solid: mp 188.3-190.7 °C; $[\alpha]_D^{25}$ = -5.60 (c = 0.10 in MeCN, 71% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.22 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.81-7.79 (m, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 2.4 Hz, 1H), 7.32 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 3.98 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.4, 164.1, 158.3, 154.2, 147.1, 146.9, 135.9, 135.3, 130.2, 127.4, 127.3, 127.3, 127.1, 125.1, 124.5, 120.6, 22.2, 21.2; MS (EI) 335 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{14}ClN_3O_4^+$ $(M+H)^+$ 336.0979, found 336.0979. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA =80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 31.7 min, t (major) = 48.8 min; IR: 3012, 2925, 1749, 1698, 1089.



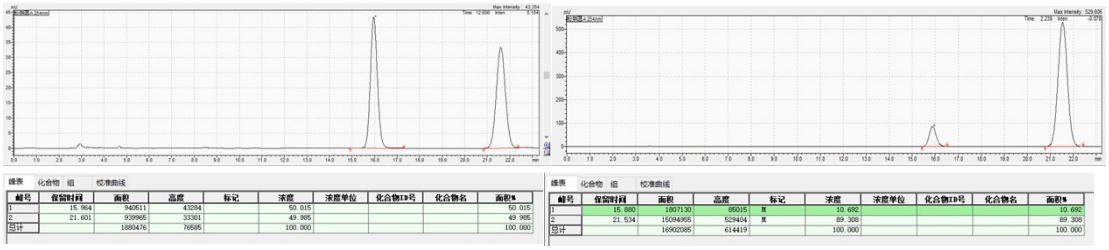
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	31.393	1552507	25627	49.115	49.115
2	48.627	1608462	16247	50.885	50.885
Total		3160969	41874	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	31.755	2900102	49332	14.721	14.721
2	48.798	16800766	170132	85.279	85.279
Total		19700868	219464	100.000	100.000

(*Ra*)-5-Methyl-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ac):



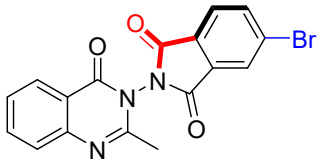
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (27.9 mg, 87% yield) as a yellow solid: mp 164.4-165.9 °C; $[\alpha]_D^{25}$ = 55.60 (c = 0.10 in MeCN, 79% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.21 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.81 (s, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.48 (t, J = 7.2 Hz, 1H), 2.58 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.4, 164.2, 158.3, 154.2, 147.1, 146.9, 136.0, 135.3, 130.3, 127.4, 127.4, 127.1, 125.1, 124.6, 120.6, 22.2, 21.2; MS (EI) 319 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{14}N_3O_3^+$ $(M+H)^+$ 320.1030, found 320.1029. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 15.9 min, t (major) = 21.5 min; IR: 3014, 2927, 1749, 1704, 1384.



NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	15.964	940511	43284	50.015	50.015
2	21.601	939965	33301	49.985	49.985
Total		1880476	76585	100.000	100.000

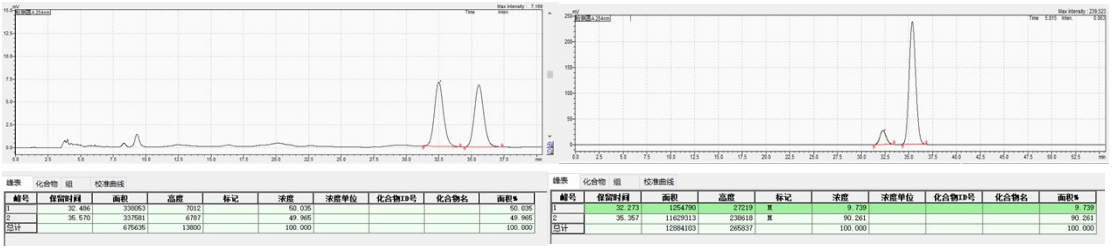
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	15.880	1807130	85015	10.692	10.692
2	21.534	1509404	529404	89.308	89.308
Total		16902085	614419	100.000	100.000

(*Ra*)-5-Bromo-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ad):



Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (28.9 mg, 75% yield) as a yellow solid: mp 189.3-190.7 °C; $[\alpha]_D^{25}$ = -141.0 (c = 0.20 in MeCN, 81% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.21 (d, J = 8.4 Hz, 1H), 8.15 (s, 1H), 8.03 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.82 (t, J = 7.8 Hz,1H), 7.71 (d, J = 8.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 163.0, 158.2, 153.7, 146.8, 138.4,

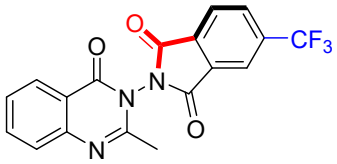
135.5, 131.5, 130.6, 128.3, 128.0, 127.5, 127.4, 127.3, 125.9, 120.5, 21.1; MS (EI) 382 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{11}FN_3O_3^+$ $(M+H)^+$ 383.9978, found 383.9977. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 32.3 min, t (major) = 35.4 min; IR: 3062, 2929, 1749, 1697 ,692.



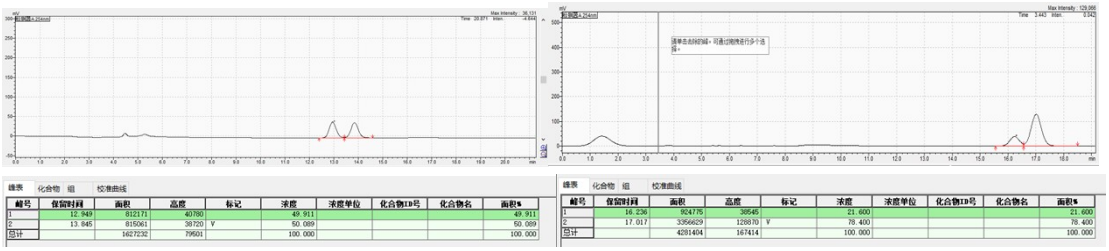
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	32.486	338053	7012	50.035	50.035
2	35.570	337581	6787	49.965	49.965
Total		675635	13800	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	32.273	1254790	27219	9.739	9.739
2	35.357	11629313	238618	90.261	90.261
Total		12884103	265837	100.000	100.000

(*Ra*)-2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)-5-(trifluoromethyl)isoindoline-1,3-dione (3ae):



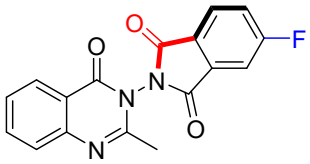
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (10.3 mg, 28% yield) as a yellow solid: mp 80.2-83.2 °C; $[\alpha]_D^{25}$ = -35.4 (c = 0.10 in MeCN, 57% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.29 (s, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 8.18 (s, 2H), 7.83 (t, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.9, 162.8, 158.1, 153.5, 146.8, 137.5 (q, *J* = 34.5 Hz), 135.6, 132.7, 132.5 (q, *J* = 3.0 Hz), 130.7, 127.6, 127.4, 127.4, 125.3, 122.7 (q, *J* = 271.5 Hz), 121.9 (q, *J* = 4.5 Hz) 120.4, 21.2; MS (EI) 373 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{11}F_3N_3O_3^+$ $(M+H)^+$ 374.0747, found 374.0747. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 90/10, 1.0 mL/min, λ = 254 nm, t (minor) = 14.2 min, t (major) = 17.0 min; IR: 3089, 2925, 1702, 771.



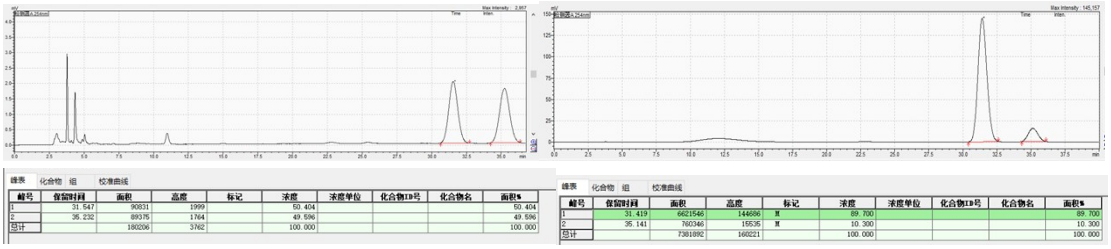
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	12.949	812171	40780	49.911	49.911
2	13.845	815061	38720	50.089	50.089
Total		1627232	79501	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	16.236	924775	38545	21.600	21.600
2	17.017	3356629	128870	78.400	78.400
Total		4281404	167414	100.000	100.000

(*Ra*)-5-Fluoro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3af):



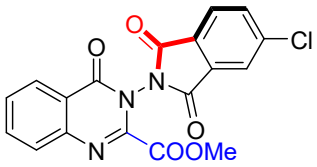
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (22.5 mg, 70% yield) as a yellow solid: mp 190.2-195.7 °C; $[\alpha]_D^{25}$ = -68.30 (c = 0.20 in MeCN, 79% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.29 (s, 1H), 8.22 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 8.17 (d, J = 1.2 Hz, 2H), 7.84-7.82 (m, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.0 (d, J = 258.0 Hz), 163.1, 163.0, 163.0, 158.2, 153.9, 146.9, 135.4, 132.7 (d, J = 10.5 Hz), 127.5, 127.4 (d, J = 4.5 Hz), 127.3 (d, J = 4.5 Hz), 125.8 (d, J = 3.0 Hz), 125.1 (d, J = 24.0 Hz), 120.5, 112.5 (d, J = 25.5 Hz), 21.1; MS (EI) 323 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{11}FN_3O_3^+$ $(M+H)^+$ 324.0779, found 324.0778. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 31.4 min, t (major) = 35.1 min; IR: 3073, 2919, 1752, 1702, 927.



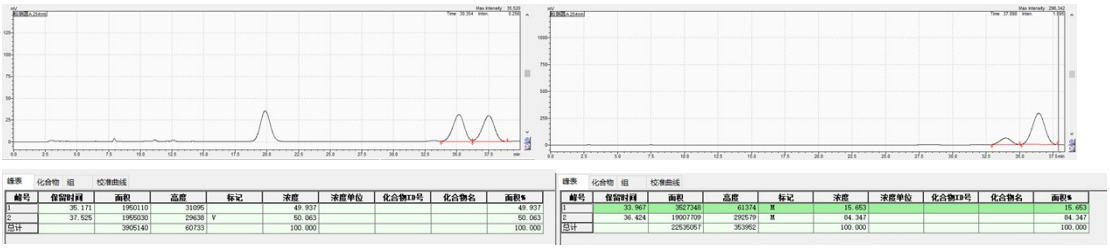
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	31.547	90831	1999	50.404	50.404
2	35.232	89375	1764	49.596	49.596
Total		180206	3762	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	31.419	6621546	144686	89.700	89.700
2	35.141	760346	15535	10.300	10.300
Total		160221	160221	100.000	100.000

(*Ra*)-Methyl 3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3ag):



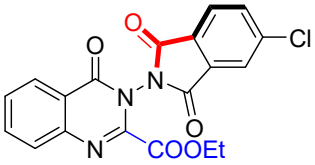
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (17.0 mg, 45% yield) as a yellow solid: mp 186.2-189.1 °C; $[\alpha]_D^{25}$ = 4.20 (c = 0.10 in MeCN, 69% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.21 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.99 (d, J = 2.4 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.85 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.83-7.80 (m, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.3, 163.0, 158.1, 153.8, 146.8, 142.4, 138.4, 135.6, 135.4, 131.5, 127.9, 127.5, 127.4, 127.3, 125.9, 125.0, 120.5, 21.2; MS (EI) 383 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{11}ClN_3O_5^+$ $(M+H)^+$ 384.0382, found 384.0382. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 22.2 min, t (major) = 31.9 min; IR: 3100, 2925, 1712, 1211, 1380.



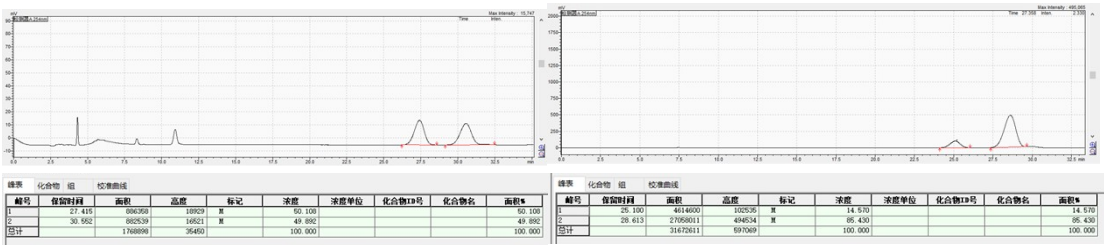
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	35.171	1950110	31095	49.937	49.937
2	37.525	1955030	29638	50.063	50.063
Total		3905140	60733	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	33.967	3527348	61374	15.653	15.653
2	36.424	19007709	292579	84.347	84.347
Total		22535057	353952	100.000	100.000

(*Ra*)-Ethyl-3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3ah):



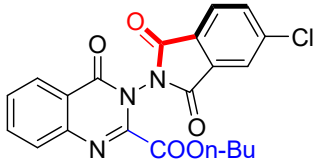
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (26.5 mg, 67% yield) as a yellow solid: mp 189.5-192,0 °C; $[\alpha]_D^{25}$ = 13.60 (c = 0.20 in MeCN, 71% ee); ^{1}H NMR (DMSO-d_6, 600 MHz) δ8.31 (d, J = 1.8 Hz, 1H), 8.26 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.14 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 8.10 (t, J = 7.2 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.82 (t, J = 7.8 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.5, 162.1, 158.4, 157.0, 144.8, 144.0, 141.5, 137.0, 136.3, 130.6, 130.4, 128.9, 127.3, 127.3, 126.8, 125.2, 120.8, 63.6, 13.5; MS (EI) 397 (M^+); HRMS (ESI) *m/z* calcd for $C_{19}H_{13}ClN_3O_5^+$ $(M+H)^+$ 398.0538, found 398.0535. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 25.1 min, t (major) = 28.6 min; IR: 3075, 2927, 1749, 1716, 1338, 1267.



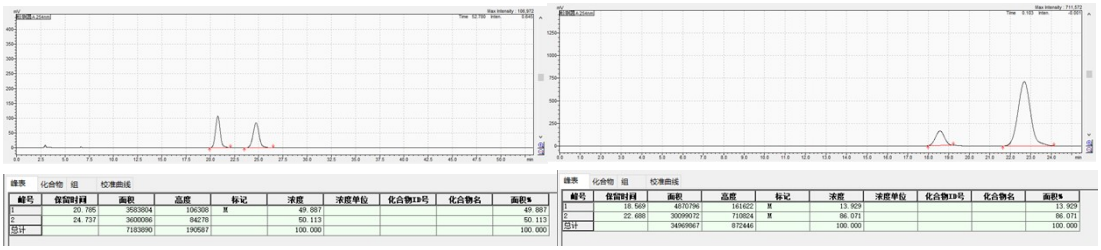
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	27.415	886358	18929	50.108	50.108
2	30.552	882539	16521	49.892	49.892
Total			35450	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	25.100	4614600	102535	14.570	14.570
2	28.613	27058011	494534	65.430	65.430
Total		31672611	597069	100.000	100.000

(Ra)-Butyl 3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3ai):



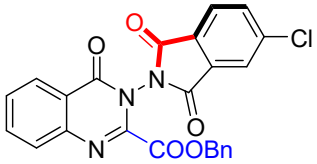
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (31.4 mg, 74% yield) as a yellow solid: mp 189.6-193.6 °C; $[\alpha]_D^{25}$ = 12.20 (c = 0.10 in MeCN, 73% ee); 1H NMR (DMSO-d_6, 600 MHz) δ 8.31 (d, J = 1.8 Hz, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.14 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 8.09 (t, J = 8.4 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.81 (t, J = 7.8 Hz, 1H), 4.28 (t, J = 6.6 Hz, 2H), 1.51-1.46 (m, 2H), 1.22 (q, J = 7.2 Hz, 2H), 0.76 (t, J = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.5, 162.2, 158.5, 156.9, 144.9, 144.2, 141.6, 137.0, 136.4, 130.6, 130.3, 128.9, 127.2, 127.3, 126.7, 125.3, 120.8, 67.1, 29.7, 18.3, 13.3; MS (EI) 425 (M^+); HRMS (ESI) *m/z* calcd for $C_{21}H_{17}ClN_3O_5^+$ $(M+H)^+$ 426.0851, found 426.0851. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 18.5 min, t (major) = 22.7 min; IR: 3102, 2964, 1751, 1714, 1467, 1261.



NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	20.785	3583804	106308	49.887	49.887
2	24.737	3600086	84278	50.113	50.113
Total		7183890	190587	100.000	100.000

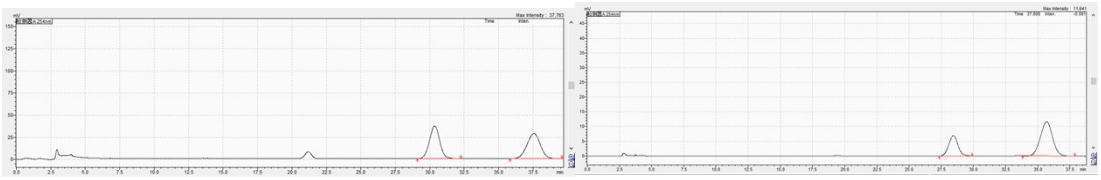
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	18.569	4870796	161622	13.929	13.929
2	22.688	30099072	710824	86.071	86.071
Total		34969867	872446	100.000	100.000

(*Ra*)-Benzyl 3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3aj):



Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (27.5 mg, 60% yield) as a yellow solid: mp 190.0-193.2 °C; $[\alpha]_D^{25}$ = 25.0 (c = 0.10 in MeCN, 37% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.31 (d, J = 6.0 Hz, 1H), 7.94 (d, J = 6.0 Hz, 1H), 7.91-7.8 (m, 1H), 7.80-7.78 (m, 2H), 7.66-7.63 (m, 1H), 7.27-7.26 (m, 5H), 7.2-7.19 (m, 2H), 5.31 (dd, J_1 = 6.0 Hz, J_2 = 12.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.3, 162.0, 158.6, 157.6, 145.4, 143.7, 141.9, 135.8, 135.1, 133.9, 131.2, 129.6, 129.2, 128.8, 128.7, 128.5, 127.2, 127.6, 125.7, 124.9, 122.1, 68.9; MS (EI) 459 (M^+); HRMS (ESI) *m/z* calcd for $C_{24}H_{15}ClN_3O_5^+$ $(M+H)^+$ 460.0695, found 460.0693. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 28.4 min, t (major) = 35.7 min; IR:

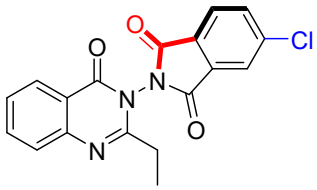
3081, 2929, 1754, 1700, 1259.



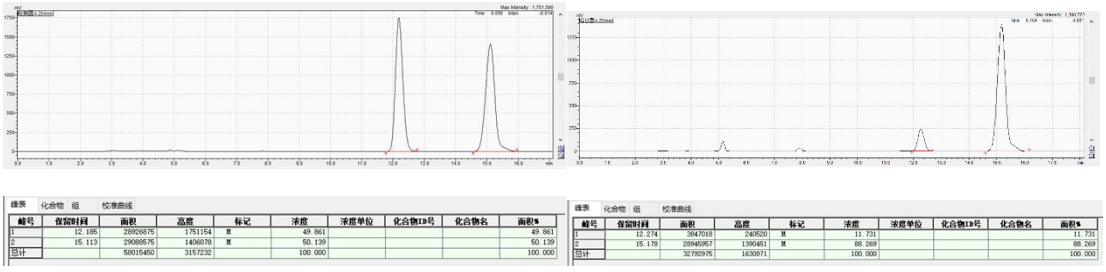
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	30.361	1921092	36853	50.006	50.006
2	37.564	1920664	28444	49.994	49.994
Total		65296	65296	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	28.441	348366	6932	31.195	31.195
2	35.686	768375	11655	68.805	68.805
Total		1116741	18586	100.000	100.000

(*Ra*)-5-chloro-2-(2-ethyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ak):



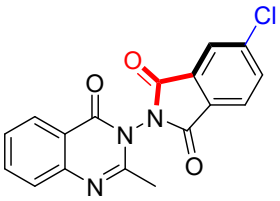
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (19.2 mg, 54% yield) as a yellow solid: mp 195.3-198.4°C; $[\alpha]_D^{25}$ = 22.04 (c = 0.10 in MeCN, 77% ee); ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.27 (d, J = 1.8 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H),8.13-8.12 (m, 2H), 8.12-8.10 (m, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 2.79 (q, J = 7.8 Hz, 2H), 1.22 (t, J = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6)) δ 164.0, 163.8, 158. 5, 158.1, 146.7, 141.5, 136.7, 136.4, 131.8, 128.4, 128.2, 128.2, 127.2, 127.0, 125.3, 119.8, 26.3, 10.8; MS (EI) 353 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{13}ClN_3O_3^+$ $(M+H)^+$ 354.0640, found 354.0641. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 12.2 min, t (major) = 15.1 min; IR: 3092, 3080, 2991, 2935, 1748, 1700, 1605, 1345, 1280.



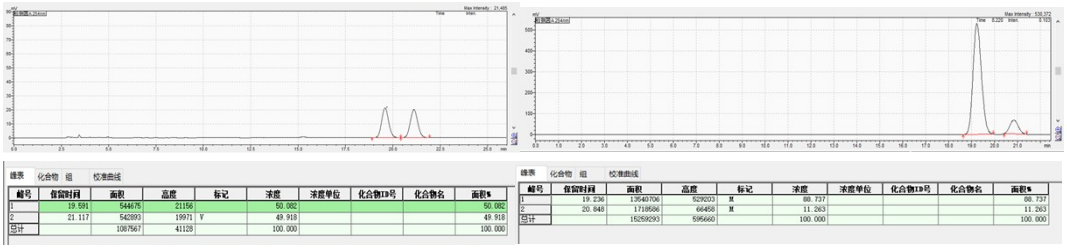
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.Area·%
1	12.185	28926875	1751154	49.861	49.861
2	15.113	29088575	1406078	50.139	50.139
Total		58015450	3157232	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.Area·%
1	12.274	3847018	240520	11.731	11.731
2	15.178	28945957	1390451	88.269	88.269
Total		32792975	32792975	100.000	100.000

(*Sa*)-4-Chloro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3al):



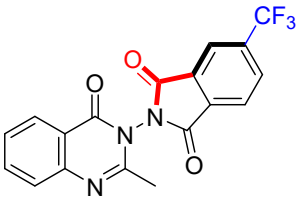
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (21.9 mg, 64% yield) as a yellow solid: mp 192.5-197.4°C; $[\alpha]_D^{25}$ = -33.4 (c = 0.10 in MeCN, 77% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.20 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.98 (d, J = 1.8 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.85 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.83-7.80 (m, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.3, 163.0, 158.1, 153.7, 146.8, 142.3, 135.5, 135.5, 131.5, 127.9, 127.5, 127.4, 127.2, 125.9, 125.0, 120.4, 21.2; MS (EI) 339 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{11}ClN_3O_3^+$ $(M+H)^+$ 340.0483, found 340.0482. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 19.2 min, t (major) = 20.8 min; IR: 3064, 2923, 1749, 1700, 779.



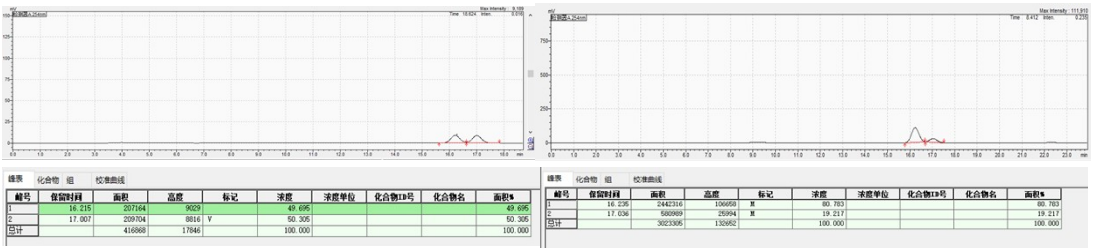
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	19.591	544675	21156	50.082	50.082
2	21.117	542893	19971	49.918	49.918
Total		1087567	41128	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	19.236	13540706	529203	88.737	88.737
2	20.848	1718586	66458	11.263	11.263
Total		15259293	595660	100.000	100.000

(*Sa*)-2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)-4-(trifluoromethyl)isoindoline-1,3-dione (3am):



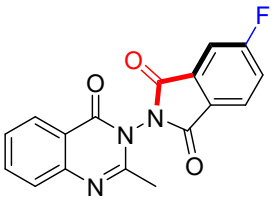
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (17.7 mg, 47% yield) as a yellow solid: mp 116.1-119.8 °C; $[\alpha]_D^{25}$ = 5.20 (c = 0.20 in MeCN, 61% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.21 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 8.03 (q, J = 4.2 Hz, 1H), 7.83-7.80 (m, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.70 (dd, J_1 = 7.2 Hz, J_2 = 2.4 Hz, 1H), 7.56 (td, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.51-7.48 (m, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.9, 162.8, 158.1, 153.5, 146.8, 137.5 (q, J = 34.5 Hz), 135.6, 132.7, 132.5 (q, J = 3.0 Hz), 130.7, 127.6, 127.4, 127.4, 125.3, 122.7 (q, J = 271 Hz), 121.9 (q, J = 3.0 Hz), 120.4, 21.1; MS (EI) 373 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{11}F_3N_3O_3^+$ $(M+H)^+$ 374.0747, found 374.0745.The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 16.2 min, t (major) = 17.0 min; IR: 3083, 2929, 1731, 1679, 771.



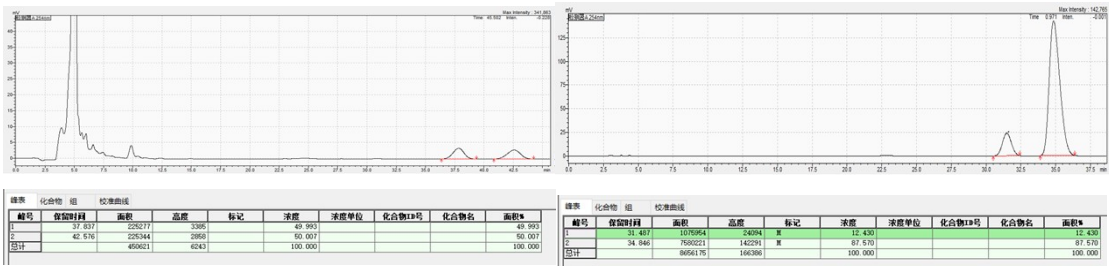
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	16.215	207164	9029	49.695	49.695
2	17.007	209704	8816	50.305	50.305
Total		416868	17846	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	16.235	2442316	106658	80.783	80.783
2	17.036	580989	25994	19.217	19.217
Total		3023305	132652	100.000	100.000

(*Sa*)-4-Fluoro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3an):



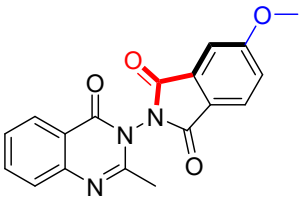
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (22.3 mg, 69% yield) as a yellow solid: mp 181.1-185.0 °C; $[\alpha]_D^{25}$ = -57.40 (c = 0.20 in MeCN, 75% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.21 (d, J = 7.8 Hz, 1H), 8.04 (dd, J_1 = 7.8 Hz, J_2 = 4.2 Hz, 1H), 7.83-7.80 (m, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.69 (dd, J_1 = 6.6 Hz, J_2 = 2.4 Hz, 1H), 7.56 (td, J_1 = 9.0 Hz, J_2 = 2.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7 (d, J = 259.5 Hz),163.1, 163.0, 163.0, 158.2, 153.8, 146.9, 135.5, 132.8 (d, J = 9.0 Hz), 127.5, 127.3, (d, J = 6.0 Hz), 127.3 (d, J = 3.0 Hz), 125.8 (d, J = 3.0 Hz), 122.7 (d, J = 24.0 Hz), 120.4, 112.5 (d, J = 25.5 Hz), 21.1; MS (EI) 323 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{11}FN_3O_3^+$ $(M+H)^+$ 324.0779, found 324.0778. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 31.5 min, t (major) = 34.8 min; IR: 3064, 2921, 1752, 1702, 925.



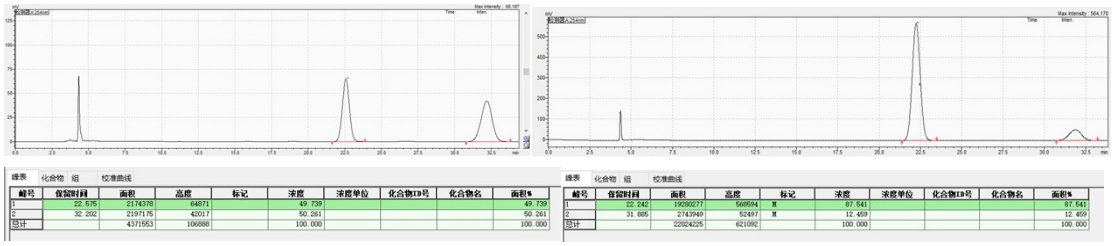
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	37.837	225277	3385	49.993	49.993
2	42.576	225344	2858	50.007	50.007
Total		450621	6243	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	31.487	1075954	24094	12.430	12.430
2	34.846	7580221	142291	87.570	87.570
Total		8656175	166386	100.000	100.000

(*Sa*)-4-Methoxy-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ao):



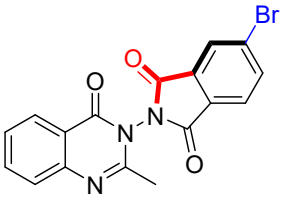
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (19.4 mg, 58% yield) as a yellow solid: mp 187.6-192.5 °C; $[\alpha]_D^{25}$ = -23.8 (c = 0.10 in MeCN, 75% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.21 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.80 (t, J = 7.8 Hz, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.47 (d, J =2.4 Hz, 1H), 7.32 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 3.97 (s, 3H). 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 164.2, 163.9, 158.4, 154.2, 146.9, 135.4, 132.5, 127.4, 127.4, 127.1, 126.5, 121.8, 121.4, 120.6, 109.0, 56.3, 21.2; MS (EI) 335 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{14}ClN_3O_4^+$ $(M+H)^+$ 336.0979, found 336.0978. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 22.2 min, t (major) = 31.9 min; IR: 3008, 2925, 1749, 1704, 1091.



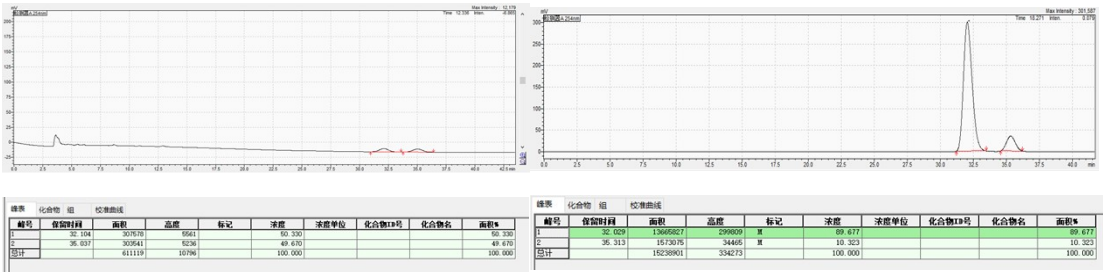
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	22.575	2174378	64871	49.739	49.739
2	32.202	2197175	42017	50.261	50.261
Total		4371553	106888	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	22.242	19280277	568594	87.541	87.541
2	31.885	2743949	52497	12.459	12.459
Total		22024225	621092	100.000	100.000

(*Sa*)-4-Bromo-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ap):



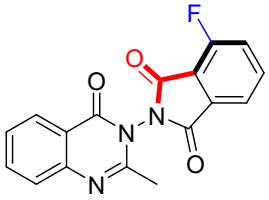
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (22.8 mg, 59% yield) as a yellow solid: mp 187.9-193.3 °C; $[\alpha]_D^{25}$ = 20.40 (c = 0.20 in MeCN, 80% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.17 (d, J = 7.8 Hz, 1H), 8.16 (s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.81 (t, J = 7.8 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.50 (t, J = 7.2 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 162.9, 158.2, 153.7, 146.8, 138.5, 135.5, 131.4, 130.6, 128.3, 127.9, 127.5, 127.4, 127.3, 125.9, 120.5, 21.1; MS (EI) 382 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{10}FN_3O_3^+$ $(M+H)^+$ 383.9978, found 383.9978. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 32.0 min, t (major) = 34.3 min; IR: 3089, 2925, 1745, 1700, 692.



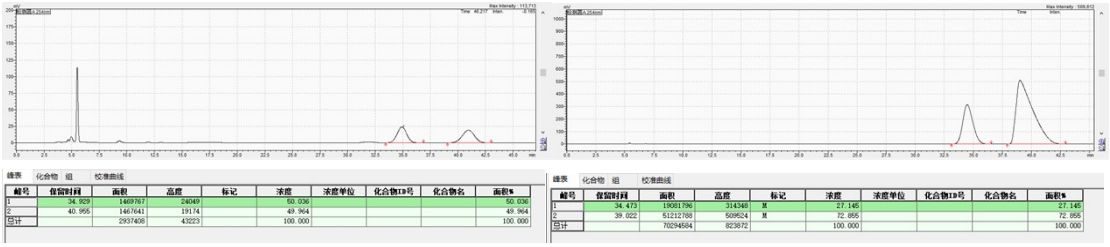
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	32.104	307578	5561	50.330	50.330
2	35.037	303541	5236	49.670	49.670
Total		611119	10796	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	32.029	13665827	299809	89.677	89.677
2	35.313	1573075	34465	10.323	10.323
Total		15238901	334273	100.000	100.000

(*Sa*)-3-Fluoro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3aq):



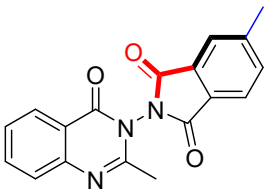
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (22.3 mg, 69% yield) as a yellow solid: mp 173.0-176.7 °C; $[\alpha]_D^{25}$ = 11.40 (c = 0.20 in MeCN, 46% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.21 (d, J = 7.8 Hz, 1H), 7.91-7.87 (m, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.54 (t, J = 8.4 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H),2.5 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.1 (d, J = 3.0 Hz), 160.7, 158.2, 158.1 (d, J = 256.5 Hz), 153.8, 146.8, 138.1 (d, J = 7.5 Hz), 135.5, 131.7, 127.4, 127.4, 127.2, 123.7 (d, J = 19.5 Hz), 120.9 (d, J = 3.0 Hz), 120.4, 116.2, 21.1; MS (EI) 323 (M^+); HRMS (ESI) *m/z* calcd for $C_{17}H_{11}FN_3O_3^+$ $(M+H)^+$ 324.0779, found 324.0778. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 34.4 min, t (major) = 39.0 min; IR: 3075, 2923, 1743, 1710, 906.



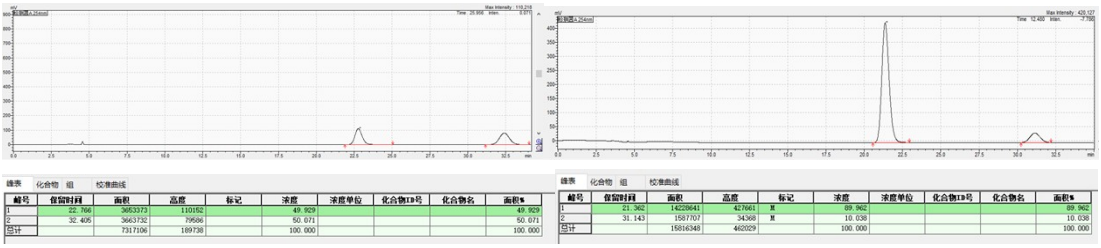
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	34.929	1469767	24049	50.036	50.036
2	40.955	1467641	19174	49.964	49.964
Total		2937408	43223	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	34.473	19081796	314348	27.145	27.145
2	39.022	51212788	509524	72.855	72.855
Total		70294584	823872	100.000	100.000

(*Sa*)-4-Methyl-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ar):



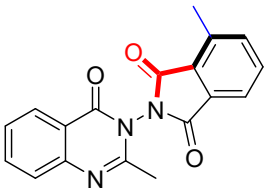
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (25.5 mg, 80% yield) as a yellow solid: mp 212.5-217.7 °C; $[\alpha]_D^{25}$ = 43.20 (c = 0.10 in MeCN, 80% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.21 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 7.2 Hz, 1H), 7.81 (s, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.71 (d, J =8.4 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.48 (t, J = 7.2 Hz, 1H), 2.58 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.3, 164.2, 158.3, 154.2, 147.1, 146.9, 135.9, 135.3, 130.2, 127.4, 127.3, 127.3, 127.1, 125.1, 124.5, 120.5, 22.2, 21.1; MS (EI) 319 (M^+); HRMS (ESI) *m/z* calcd for $C_{18}H_{14}N_3O_3^+$ $(M+H)^+$ 320.1030, found 320.1028. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 21.4 min, t (major) = 31.1 min; IR:3019, 2925, 1751, 1704, 1384.



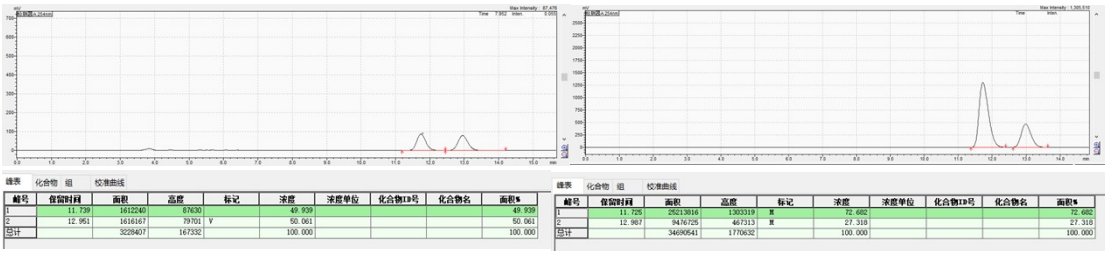
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	22.766	3653373	110152	49.929	49.929
2	32.405	3663732	79586	50.071	50.071
Total		7317106	189738	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	21.362	14228641	427661	89.962	89.962
2	31.143	1587707	34368	10.038	10.038
Total		15816348	462029	100.000	100.000

(*Sa*)-3-Methyl-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3as):



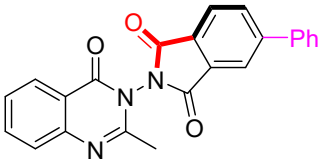
Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (11.8 mg, 37% yield) as a yellow solid: mp 129.0-134.2 °C; $[\alpha]_D^{25}$ = -41.80 (c = 0.10 in MeCN, 45% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ8.22 (dd, J_1 = 1.2 Hz, J_2 = 7.8 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.83-7.80 (m, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 2.76 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.7, 164.2, 158.3, 154.2, 146.9, 139.6, 137.7, 135.4, 134.9, 130.3, 127.4, 127.3, 127.1, 126.8, 122.3, 120.6, 21.2, 17.9; MS (EI) 319 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{14}N_3O_3^+$ $(M^+H)^+$ 320.1030, found 320.1028. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 11.7 min, t (major) = 12.9 min; IR: 3191, 2923, 1743. 1700, 1374.



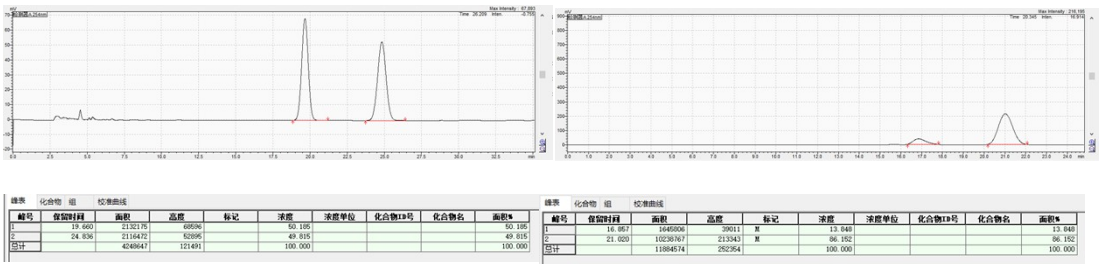
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	11.739	1612240	87630	49.939	49.939
2	12.951	1616167	79701	50.061	50.061
Total		3228407	167332	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	11.725	25213816	1303319	72.682	72.682
2	12.987	9476725	467313	27.318	27.318
Total		34690541	1770632	100.000	100.000

(*Ra*)-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-5-(phenylethynyl)isoindoline-1,3-dione (7):



Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 10:1) gave the product (27.4 mg, 72% yield) as a yellow solid mp 178.0-179.8 °C; $[\alpha]_D^{25}$ = -58.80 (c = 0.10 in MeCN, 45% ee); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.23 (d, *J* = 8.4 Hz, 2H), 8.08 (s, 2H), 7.82 (t, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 2H), 2.53 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.3, 163.1, 157.3, 153.6, 148.0, 145.8, 137.6, 134.5, 134.4, 132.9, 129.7, 128.4, 128.1, 127.2, 126.4, 126.4, 126.1, 124.1, 122.1, 119.5, 20.2; MS (EI) 382 (M^+); HRMS (ESI) m/z calcd for $C_{23}H_{16}N_3O_3^+$ $(M^+H)^+$ 382.1186, found 382.1187. The enantiomeric ratio was determined by Daicel Chiralcel AD-H (0.46 cm × 25 cm), Hexanes/IPA = 80/20, 1.0 mL/min, λ = 254 nm, t (minor) = 32.2 min, t (major) = 38.2 min; IR: 3089, 2964, 1749, 1702, 1261.

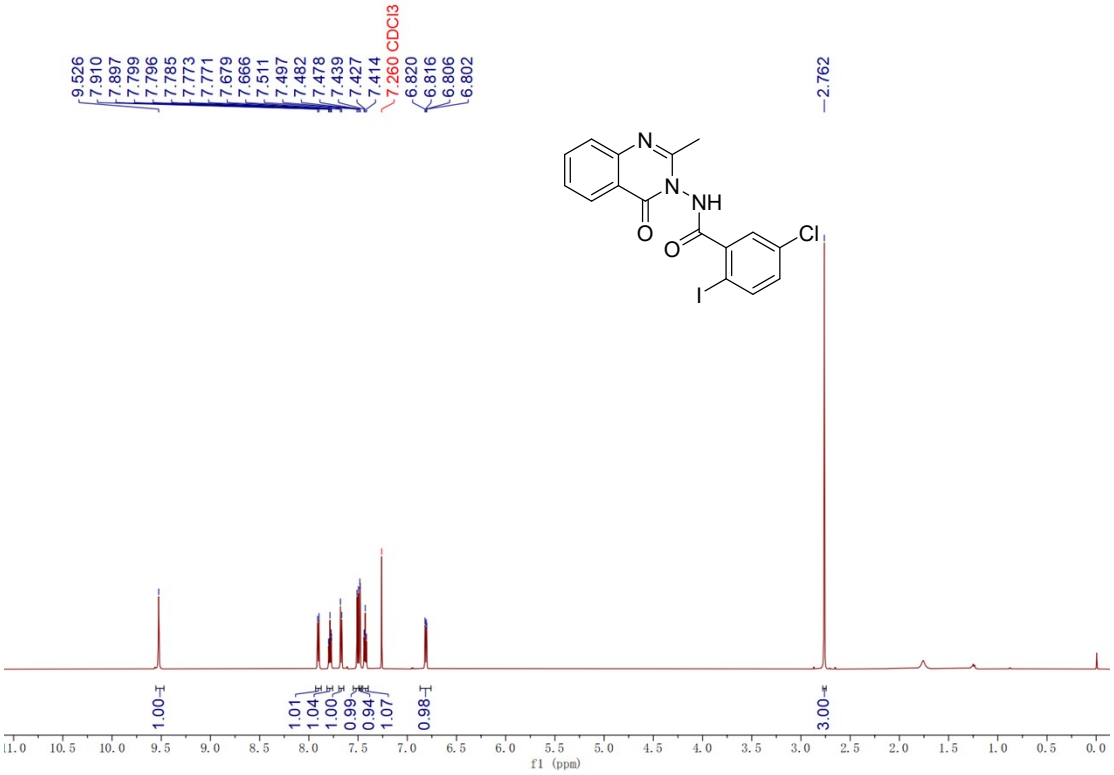


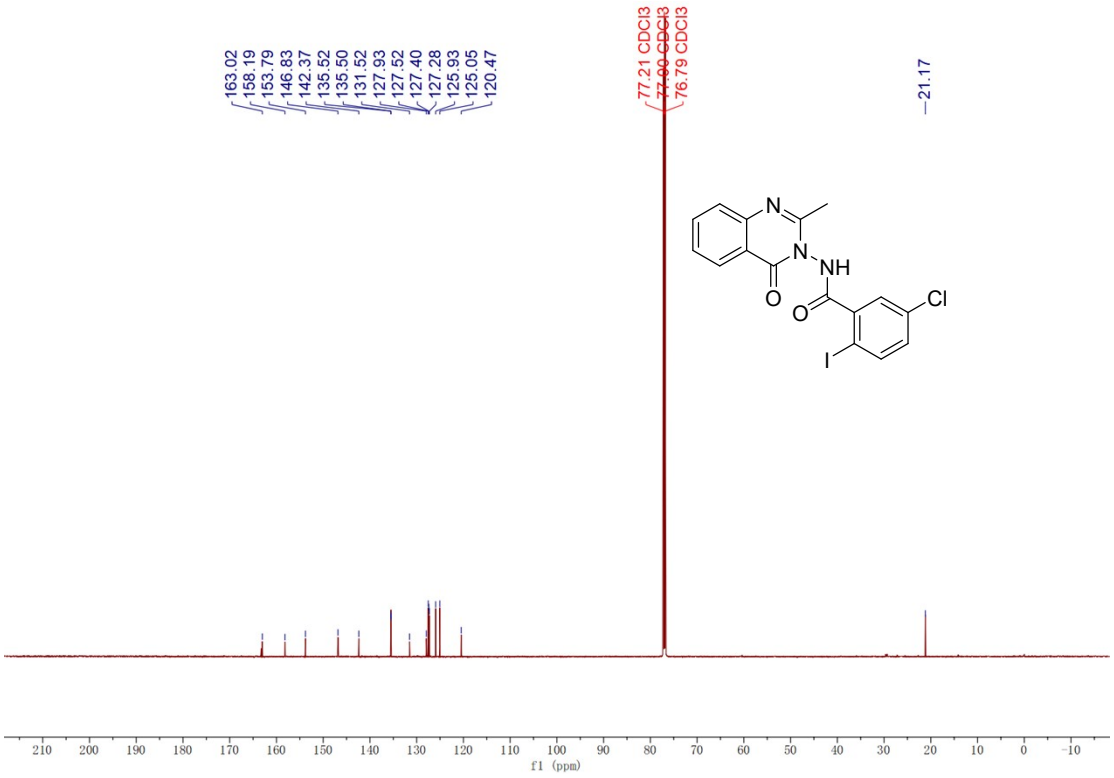
NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	19.660	2132174	68596	50.185	50.185
2	24.836	2116472	52895	49.815	49.815
Total		4248647	121491	100.000	100.000

NO.	Ret·Time	Area·(uAU*min)	Height·(uAU)	Potency	Rel.·Area·%
1	16.857	1645806	39011	13.848	13.848
2	20.020	10238767	213343	86.152	86.152
Total		11884574	252354	100.000	100.000

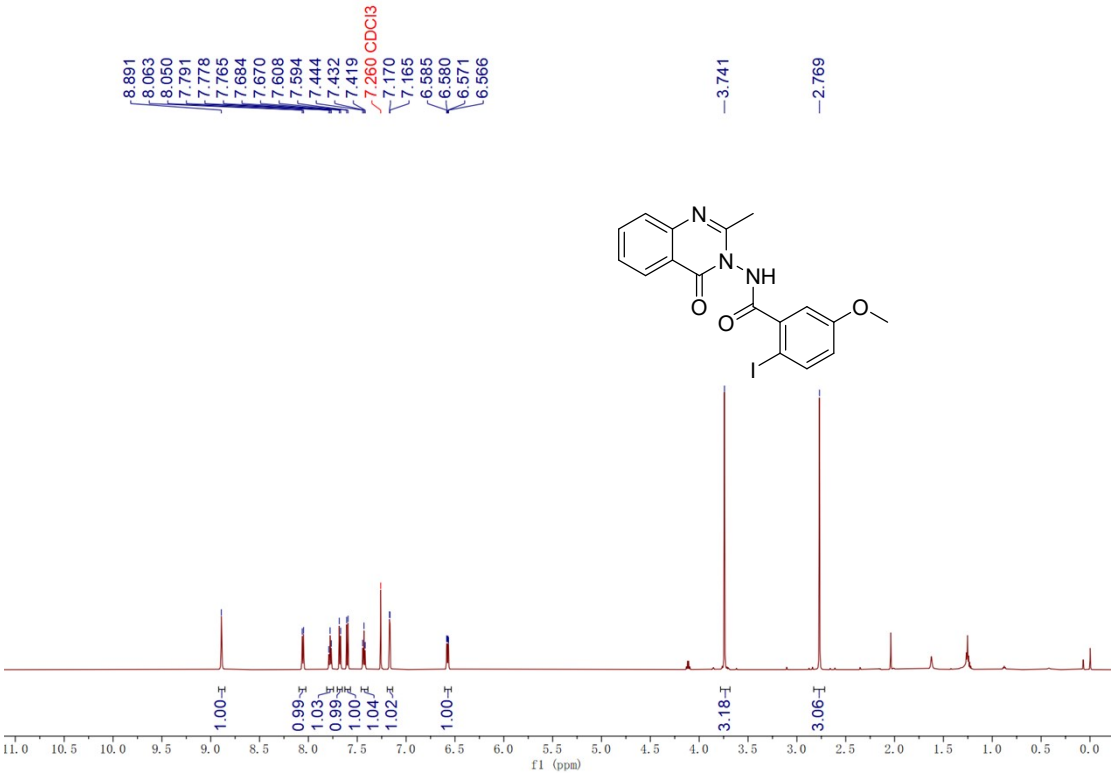
7. Copies of the ^{1}H NMR and ^{13}C NMR Spectra.

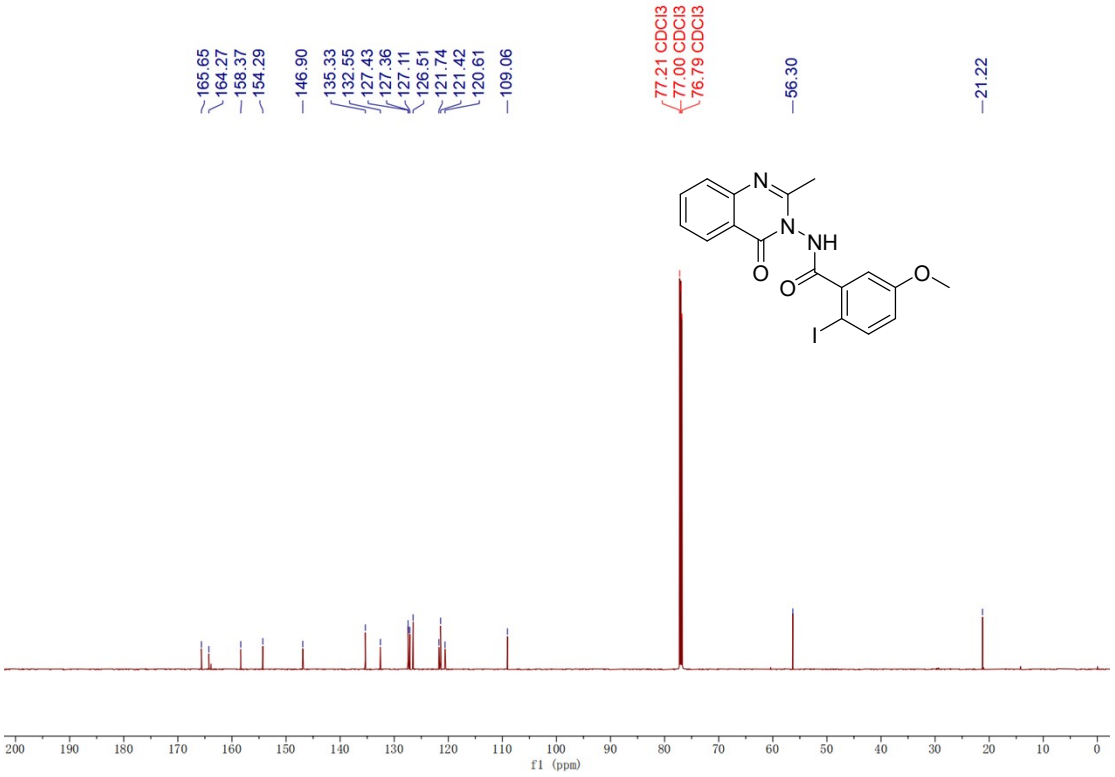
5-Chloro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1a)



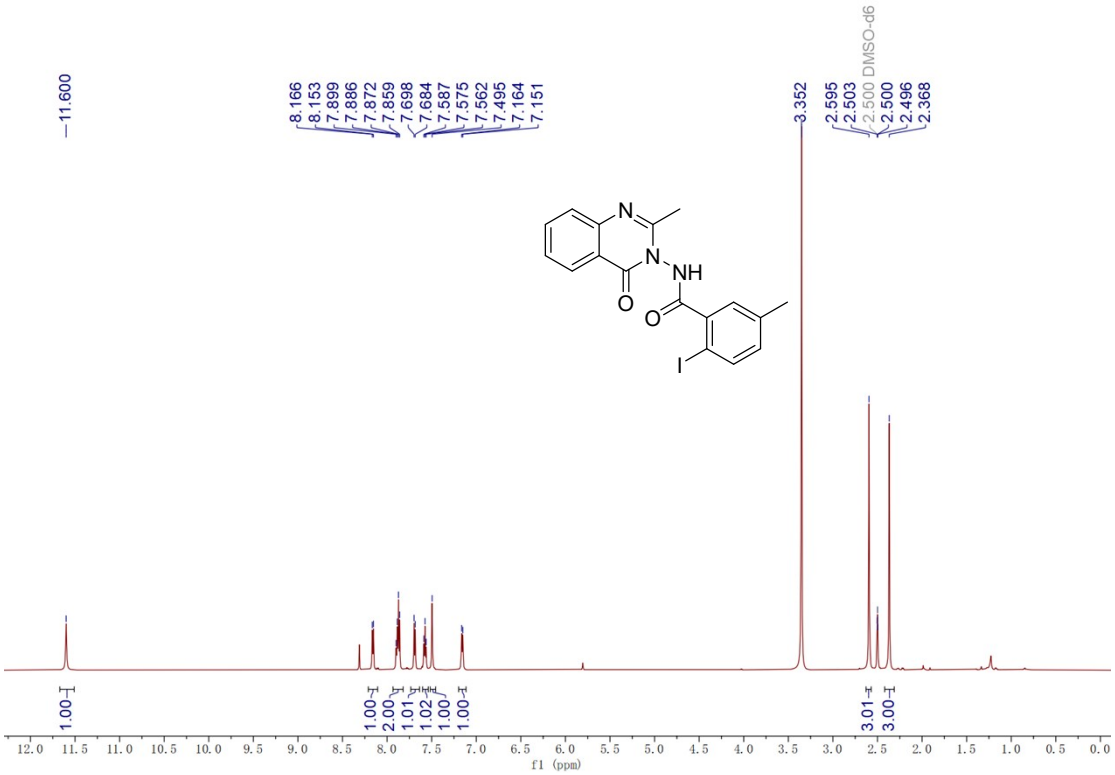


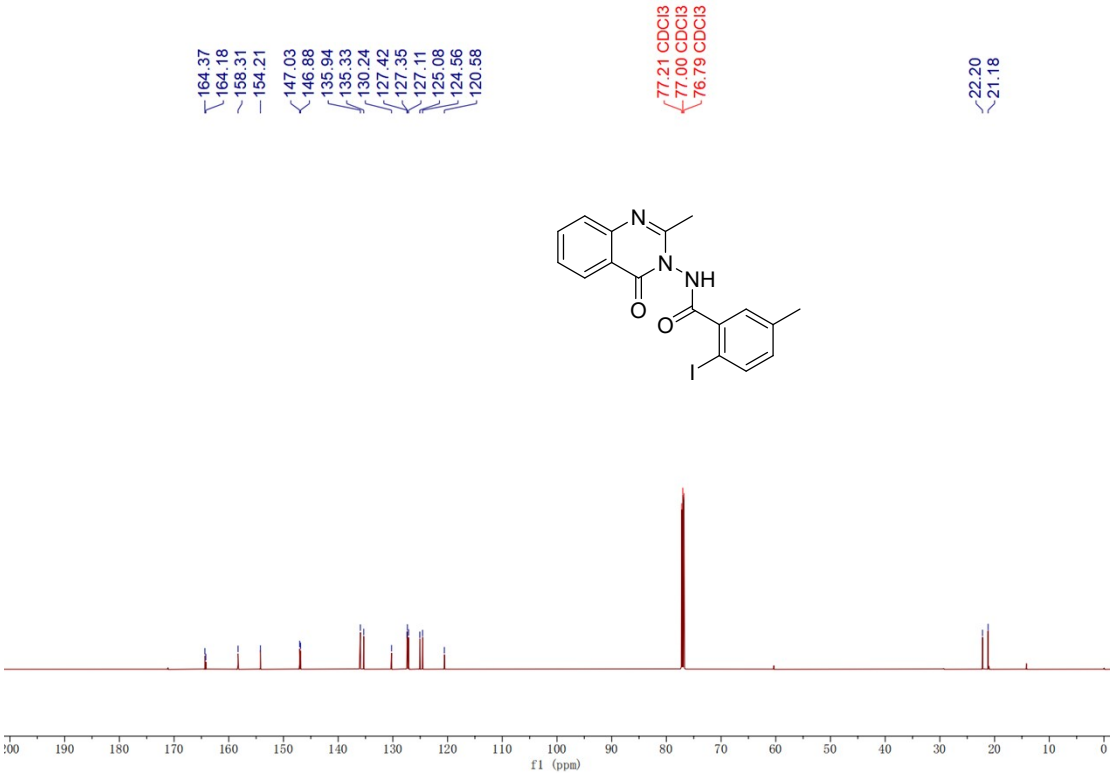
2-Iodo-5-methoxy-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1b)



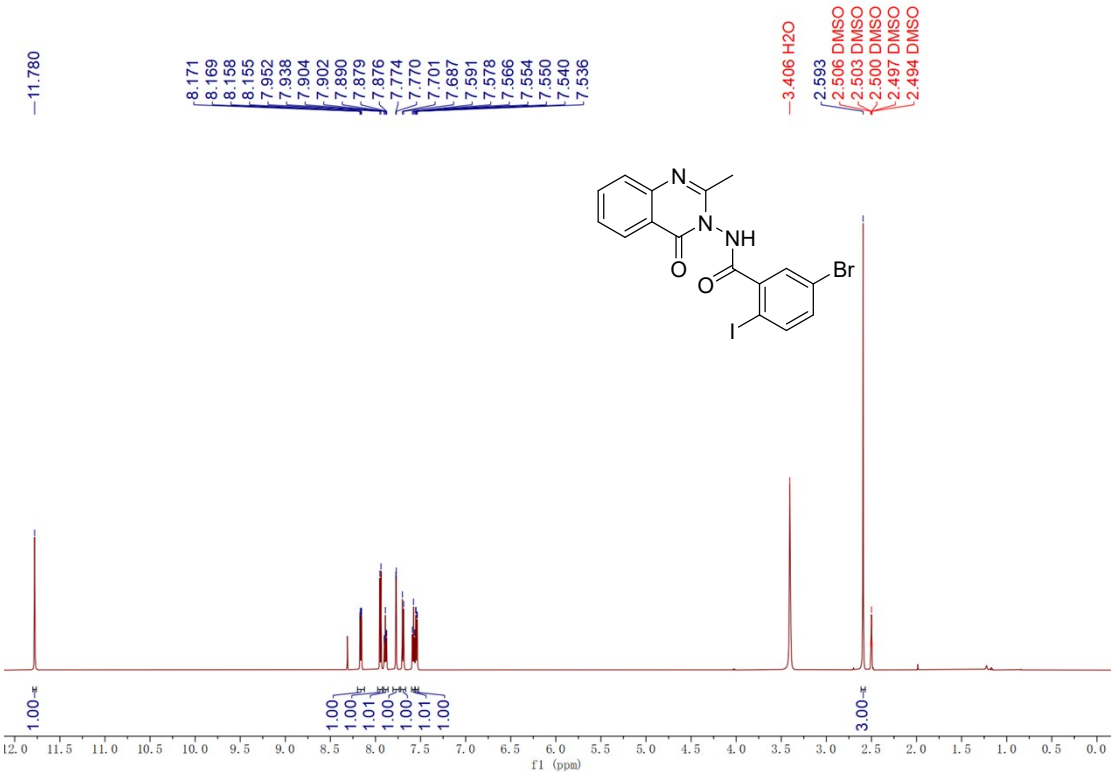


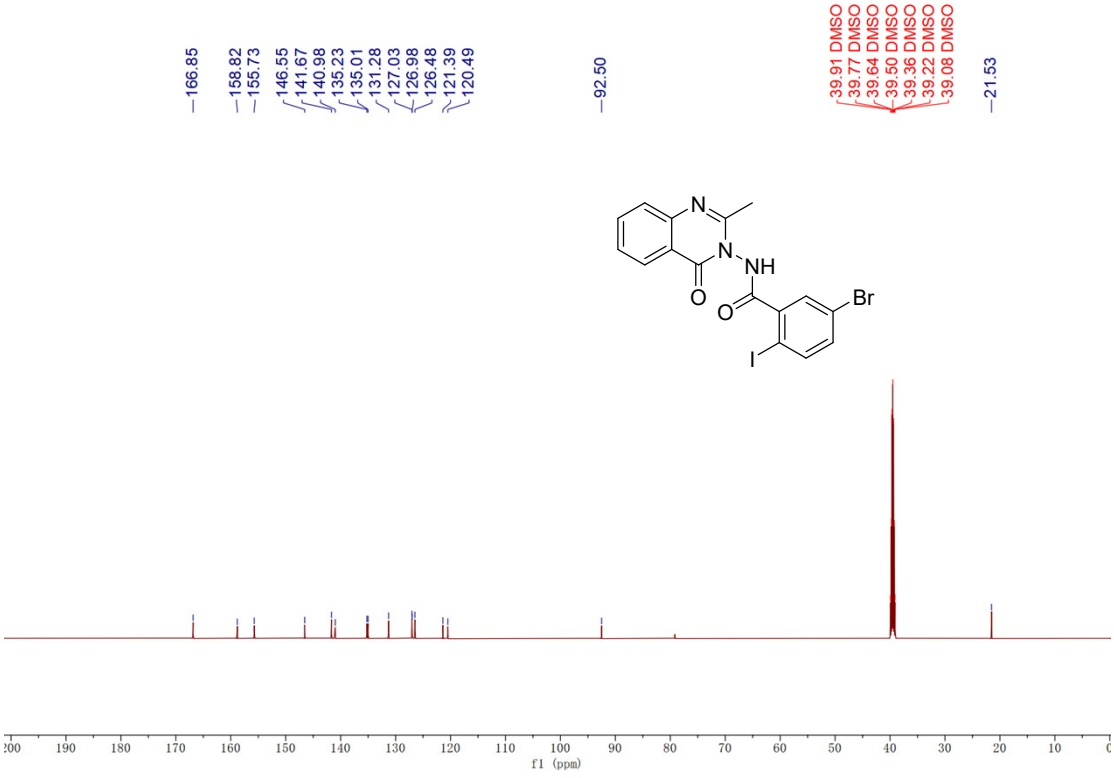
2-Iodo-5-methyl-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1c)



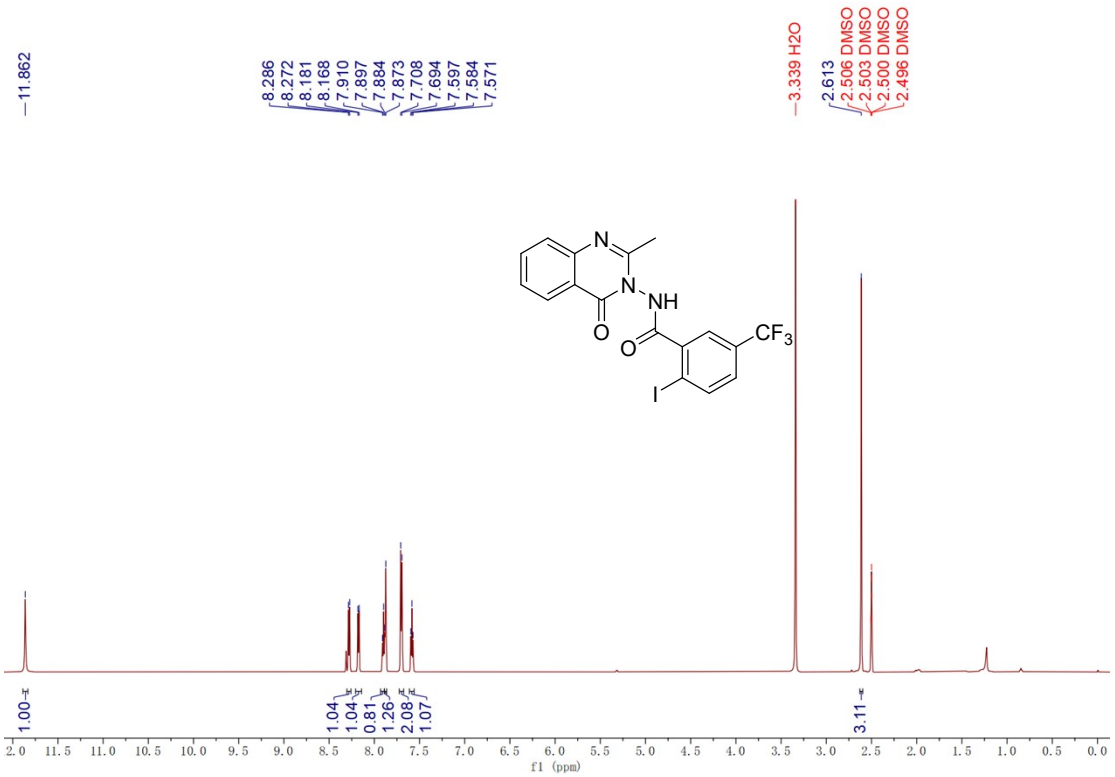


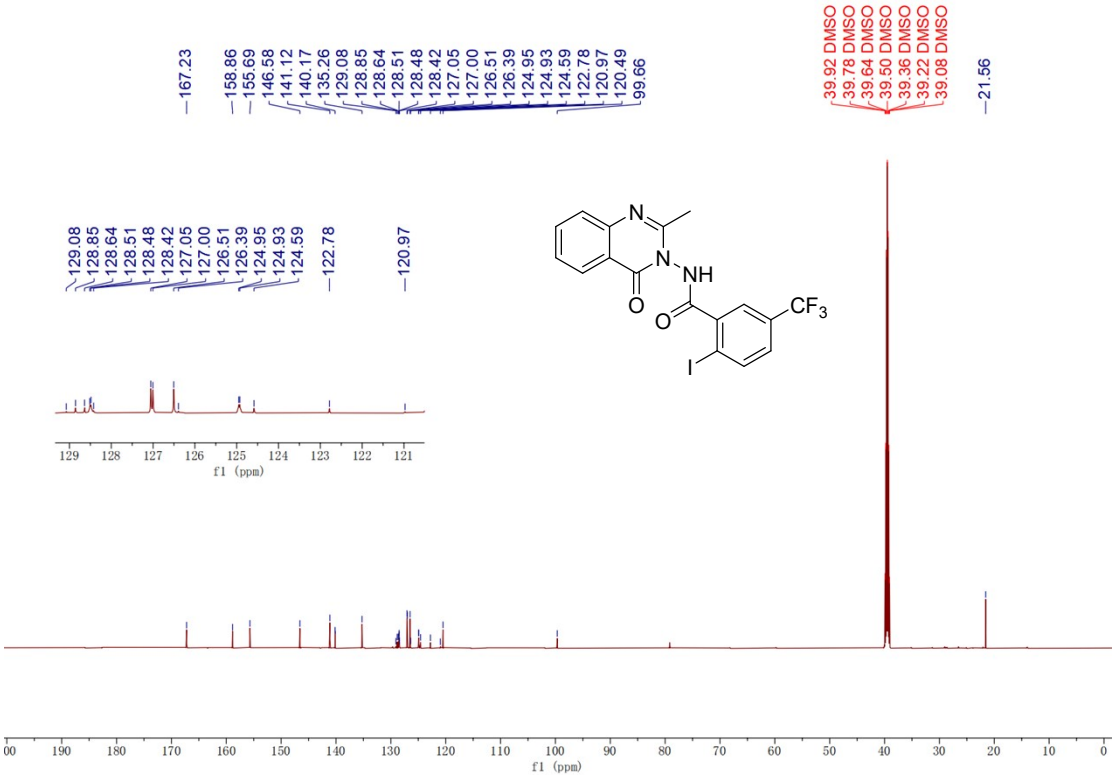
5-Bromo-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1d)



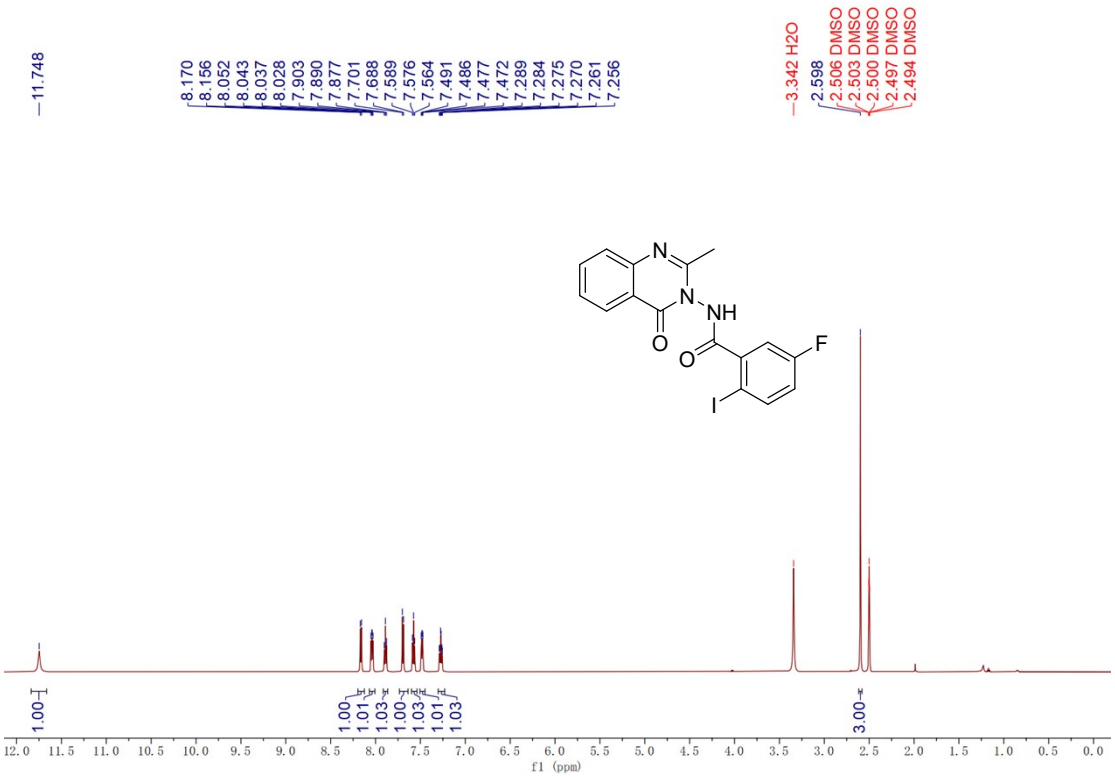


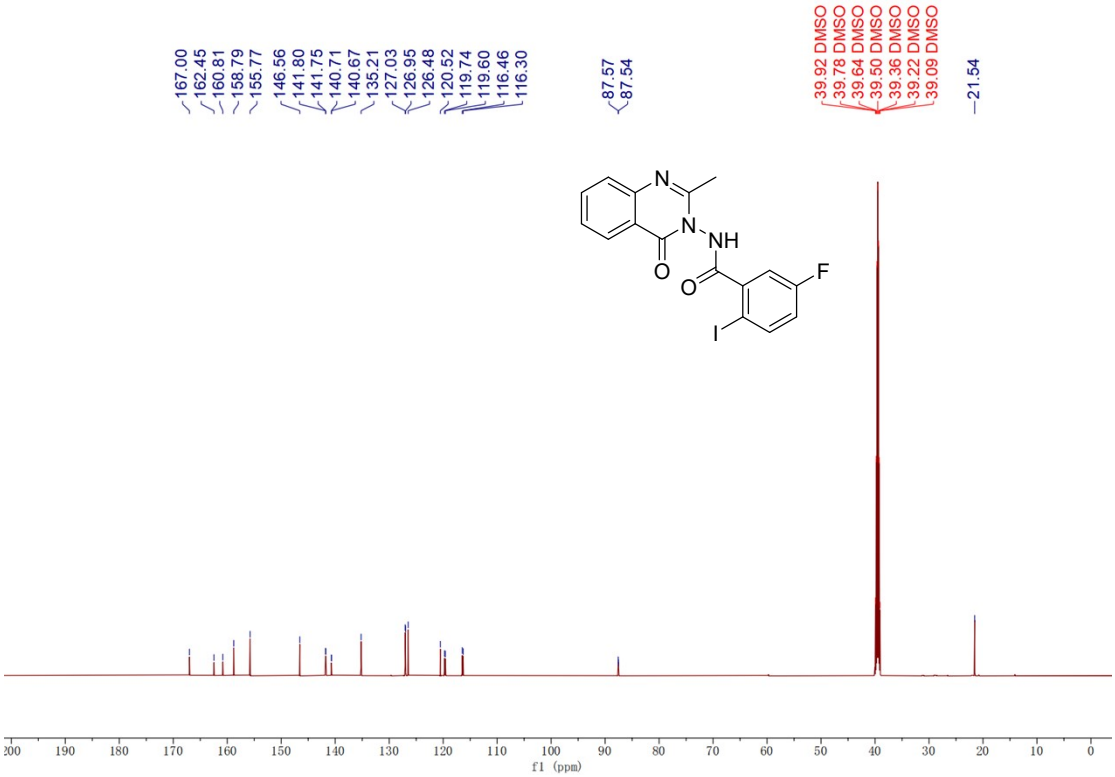
2-Iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-5-(trifluoromethyl)benzamide (1e)



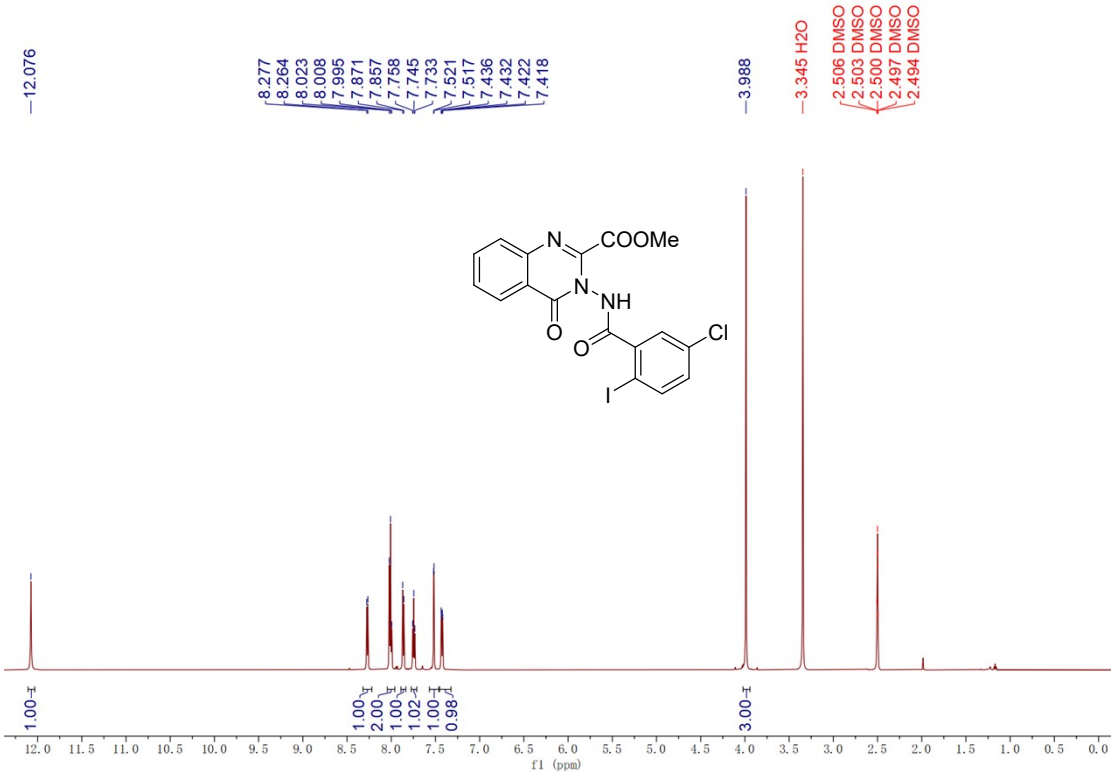


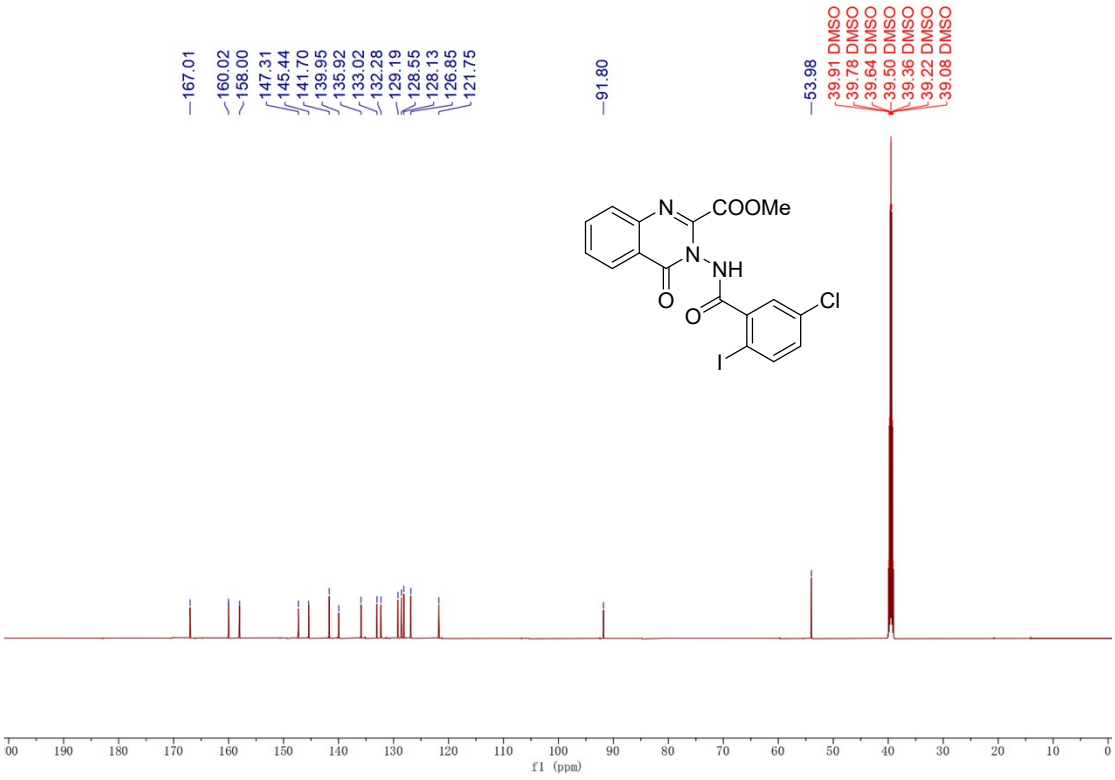
5-Fluoro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1f)



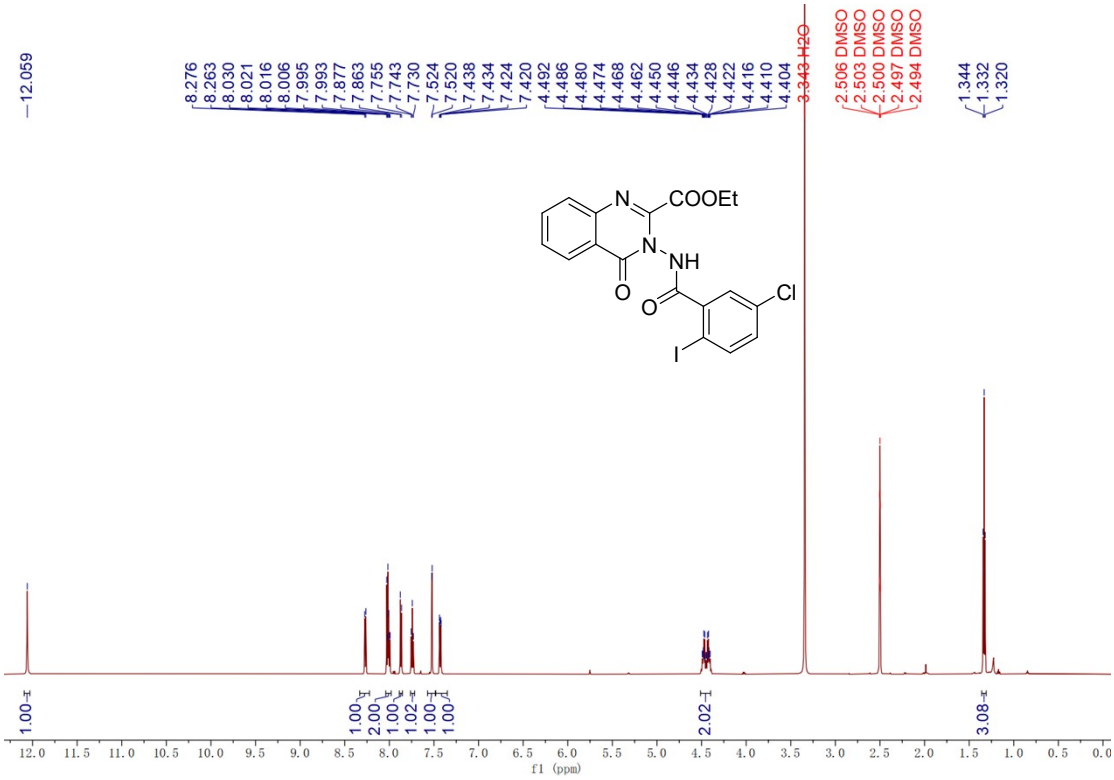


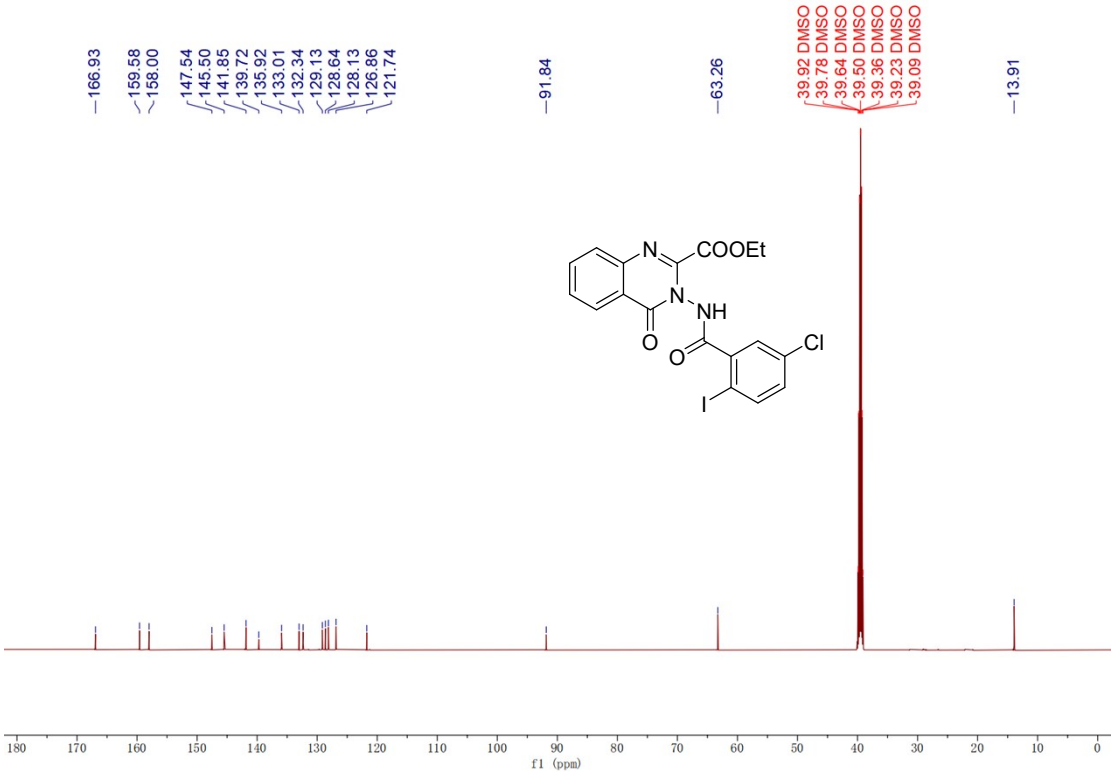
Methyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1g)



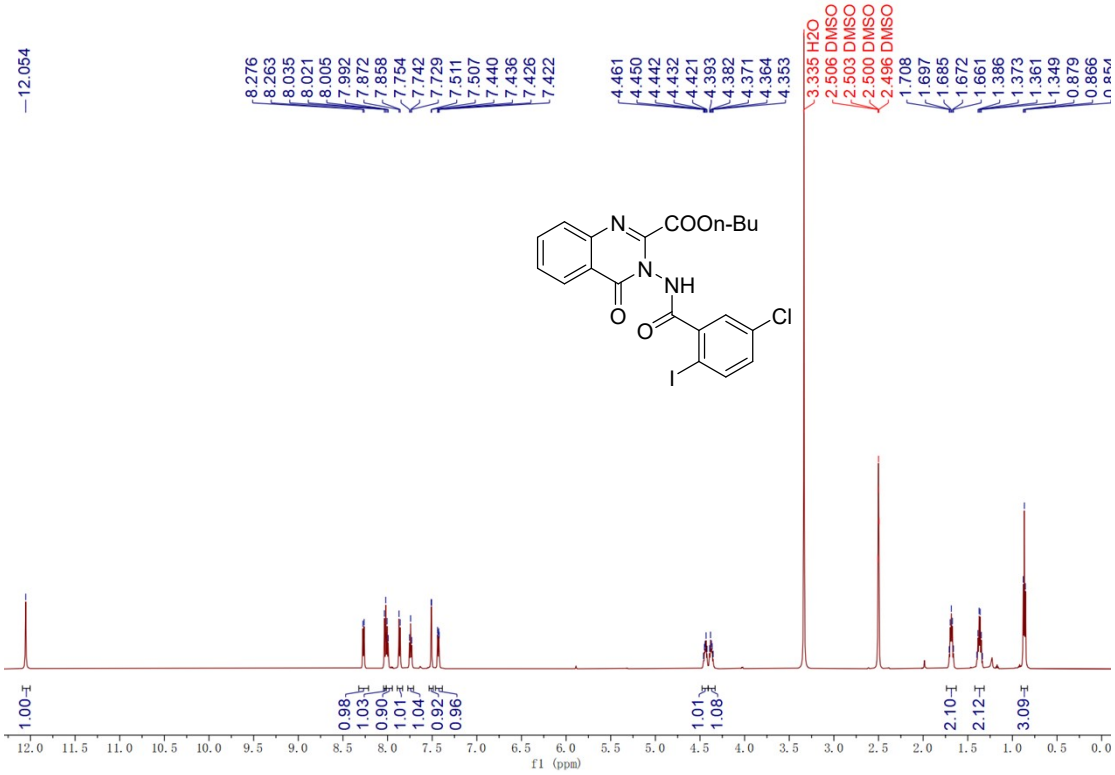


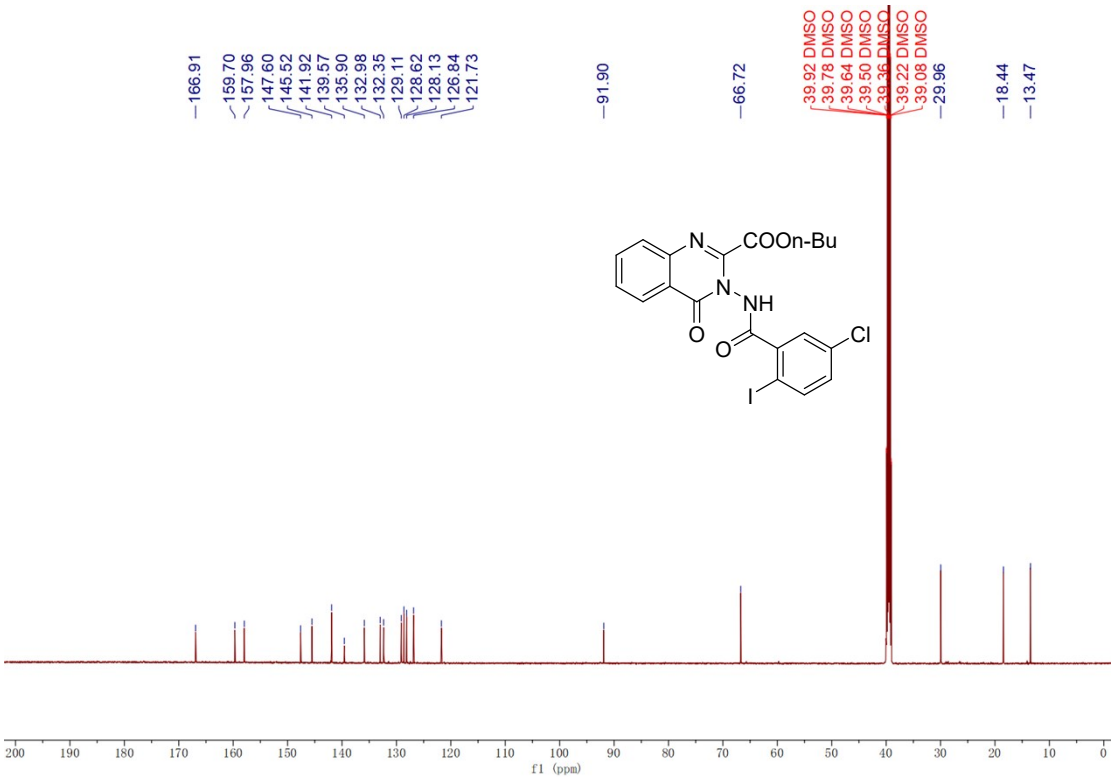
Ethyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1h)



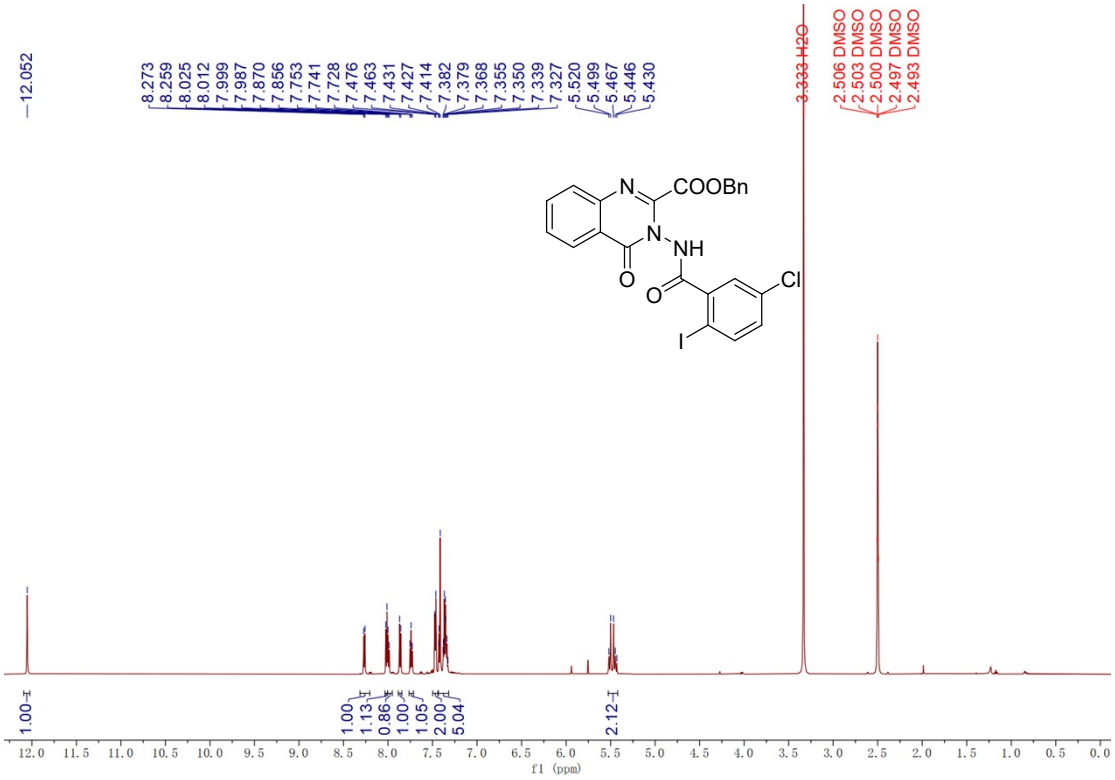


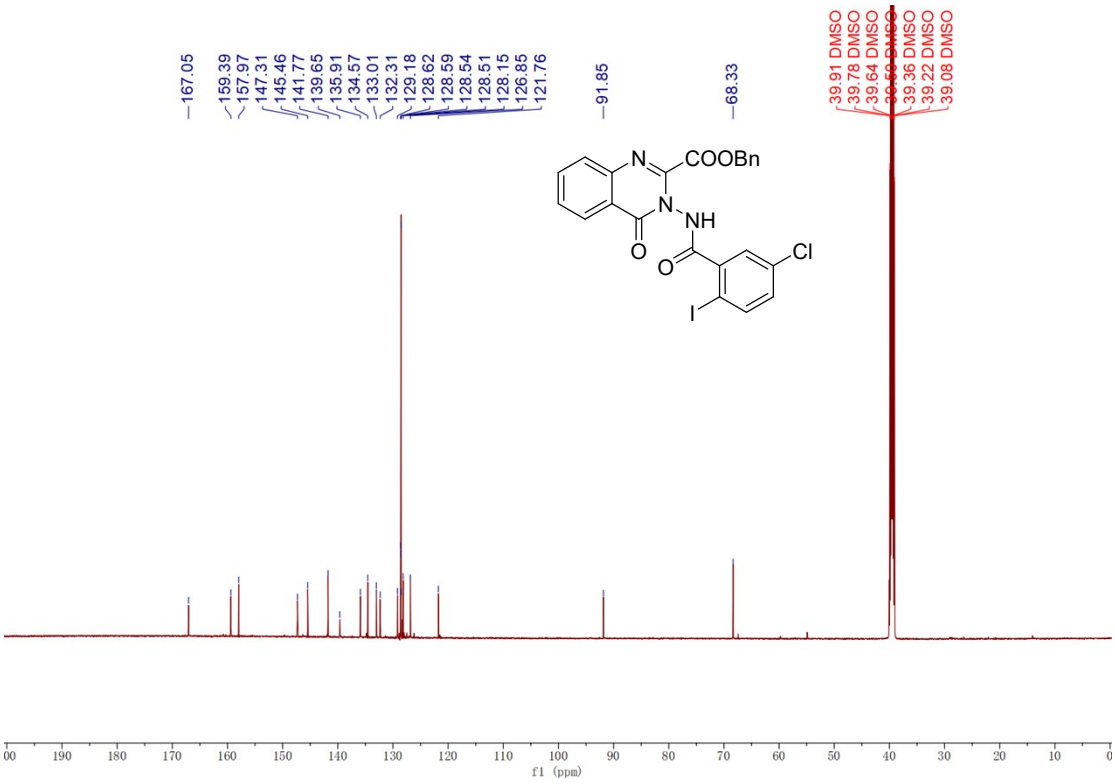
Butyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1i)



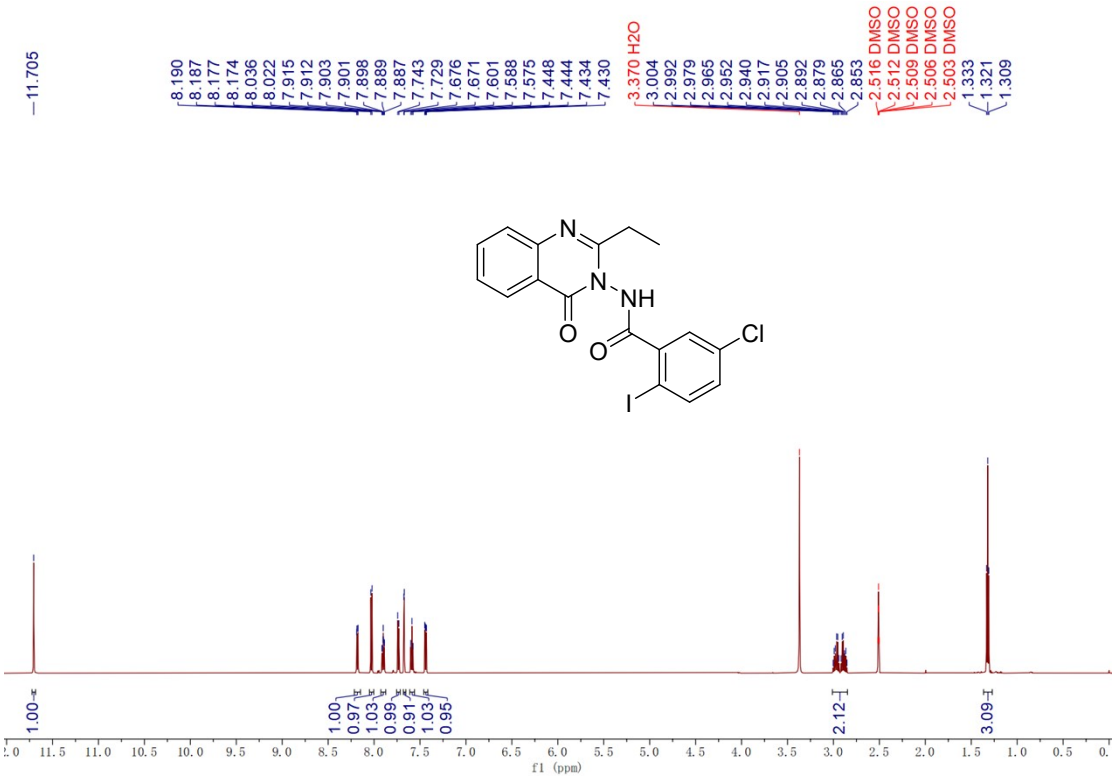


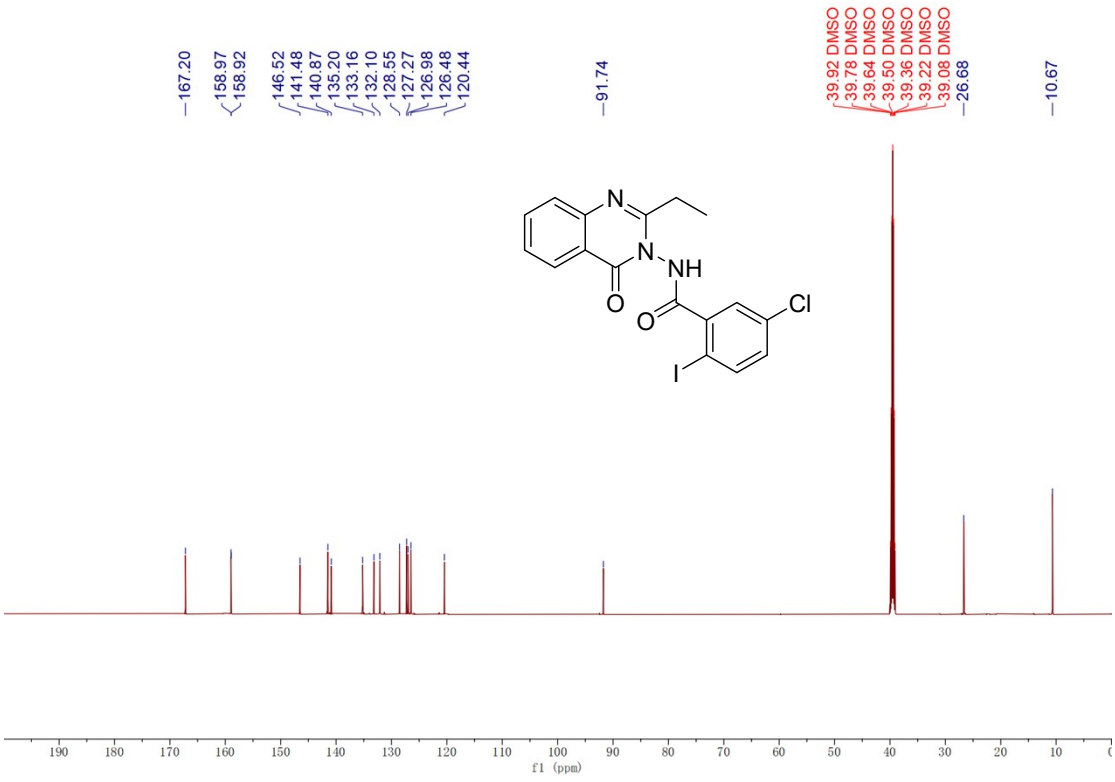
Benzyl 3-(5-chloro-2-iodobenzamido)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (1j)



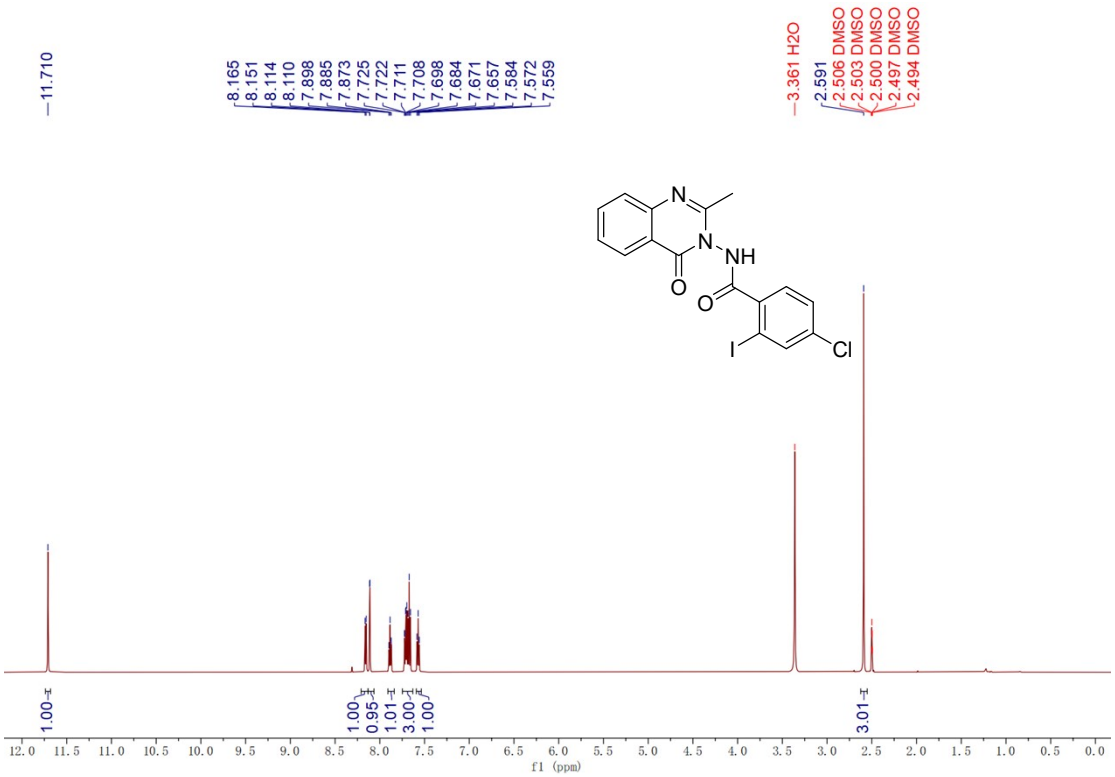


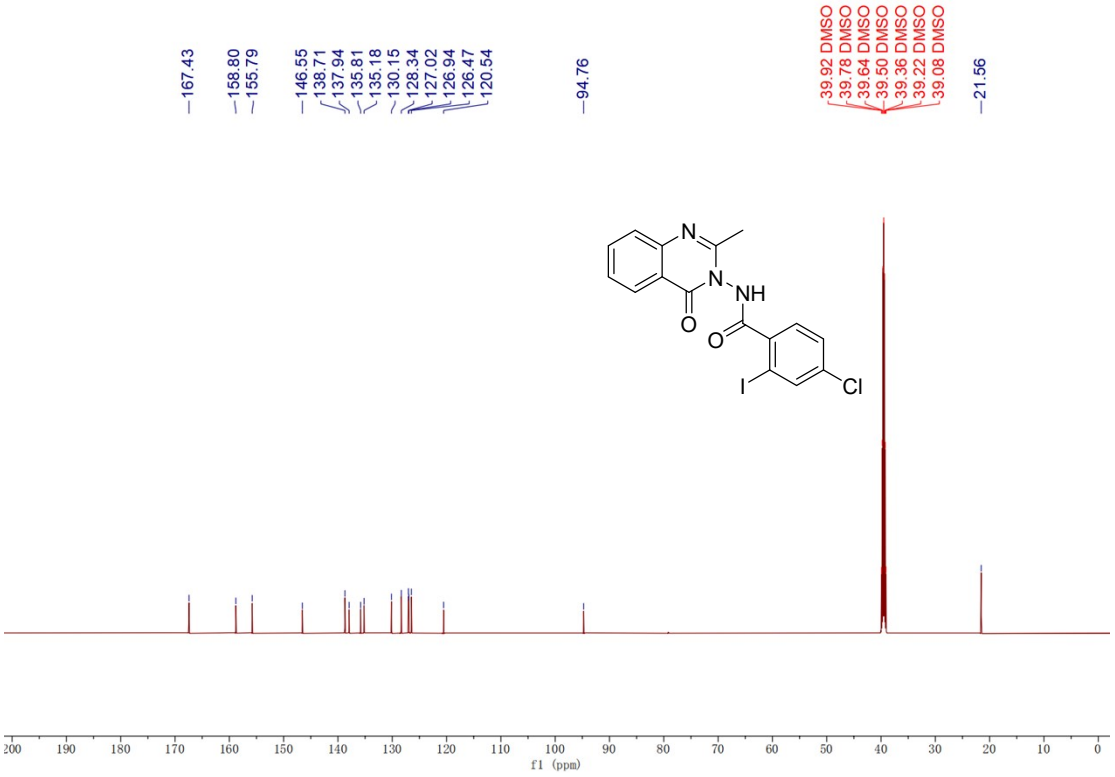
5-Chloro-*N*-(2-ethyl-4-oxoquinazolin-3(4*H*)-yl)-2-iodobenzamide (1k):



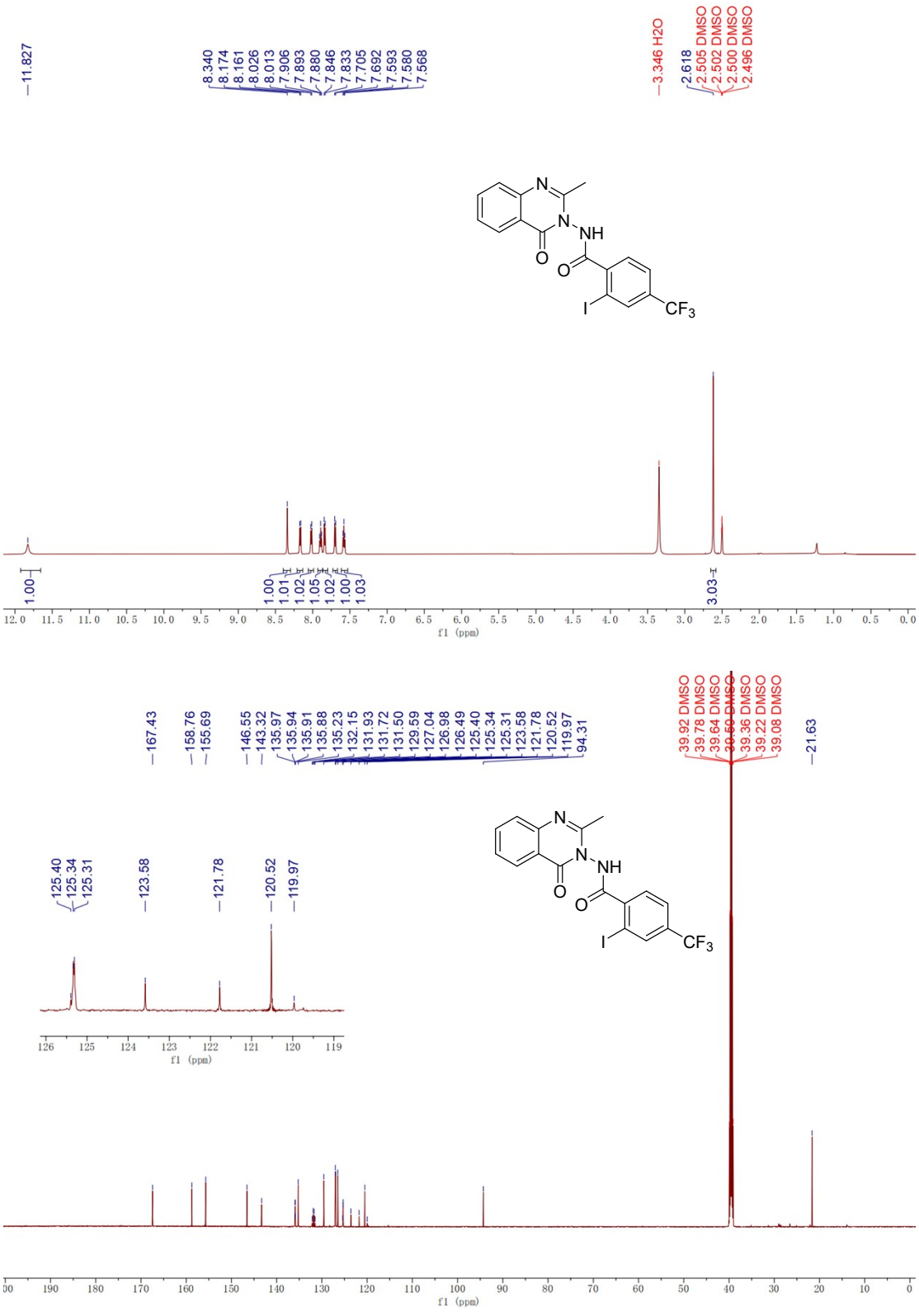


4-Chloro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1l)

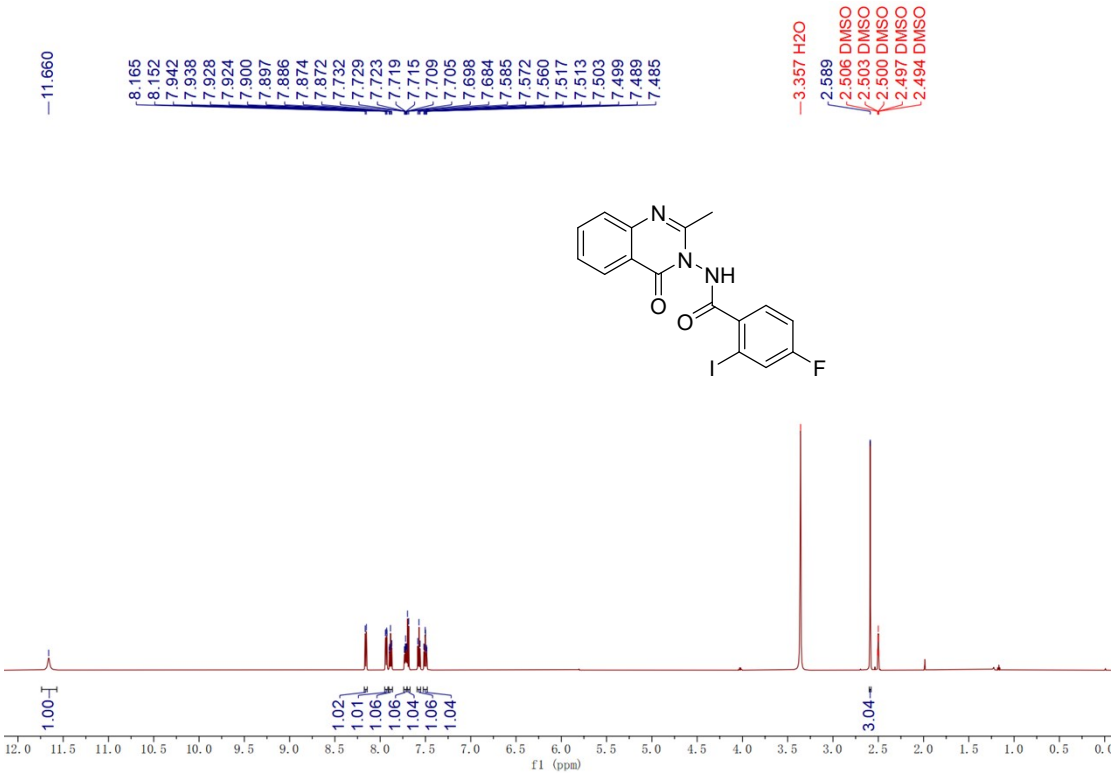


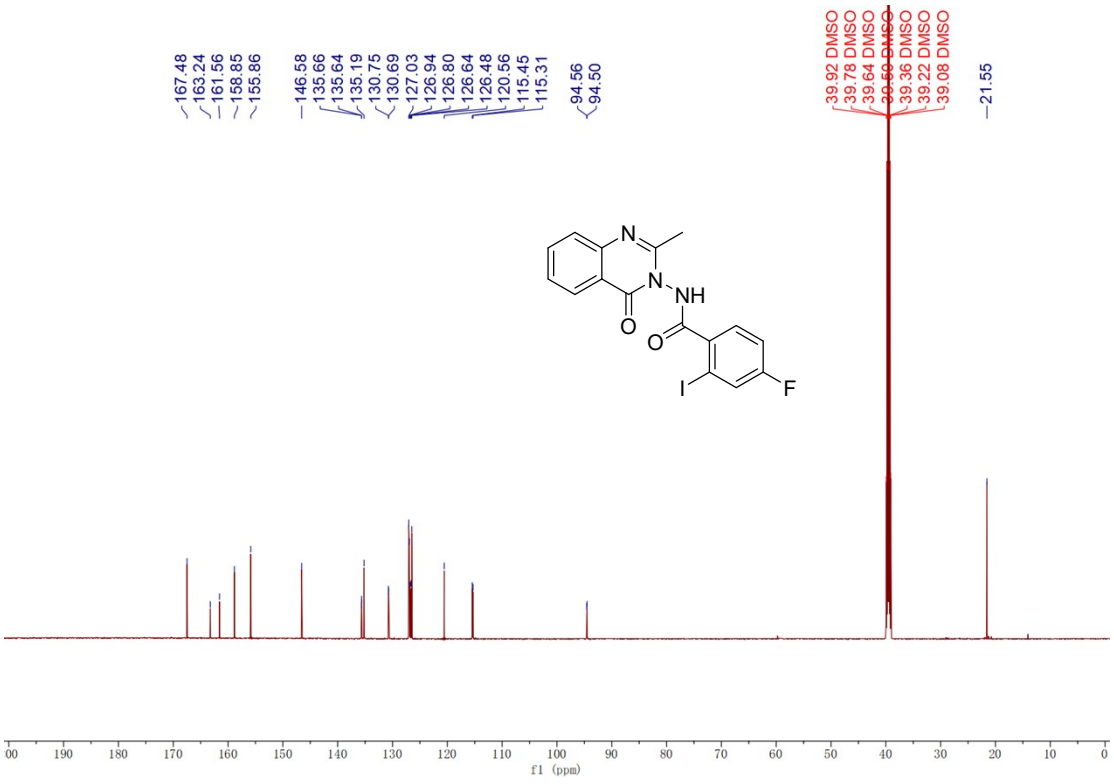


2-Iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-4-(trifluoromethyl)benzamide (m)

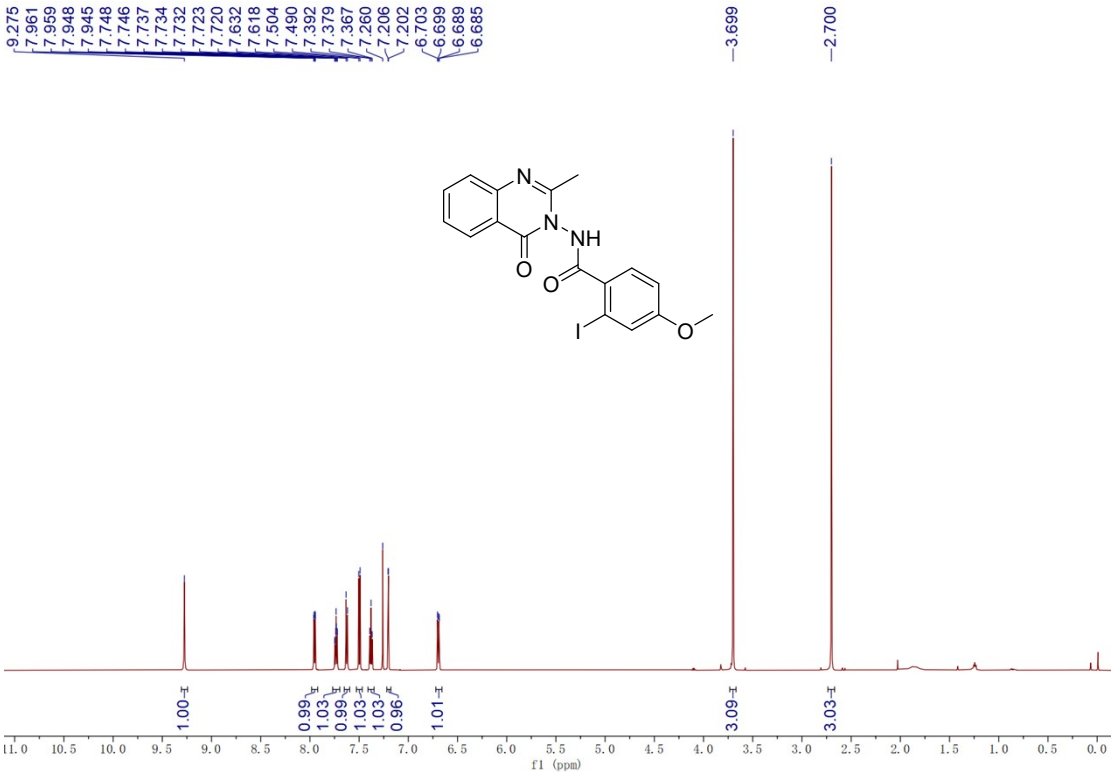


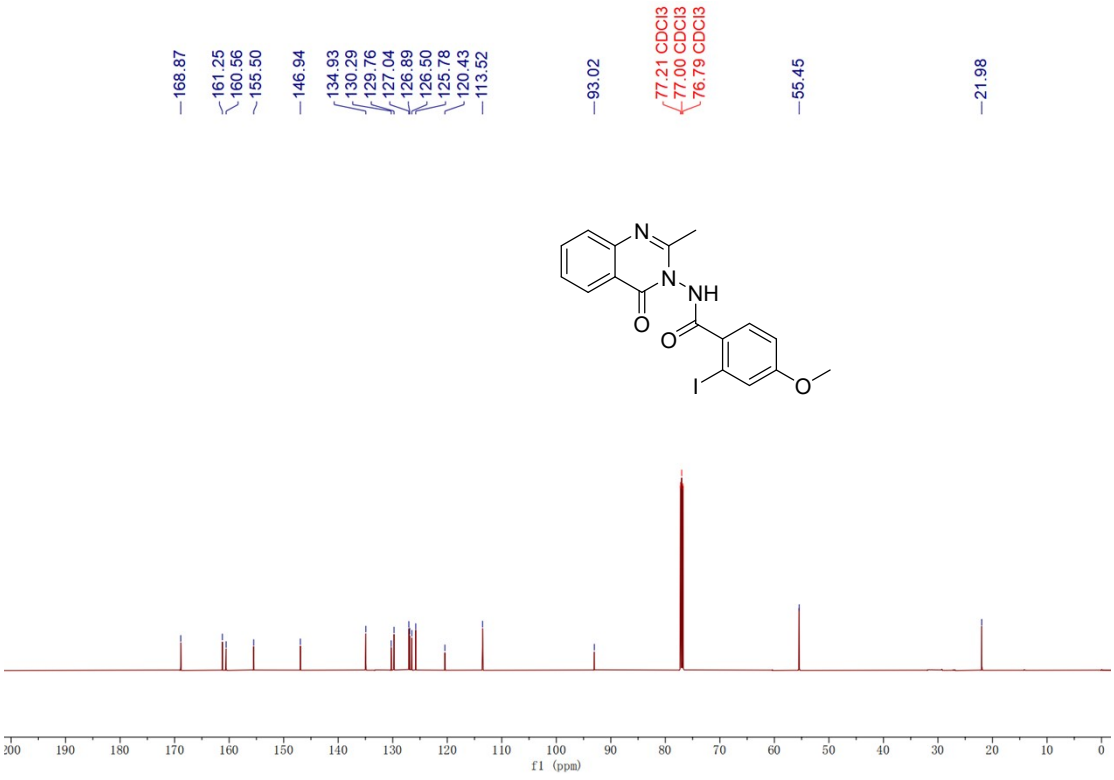
4-Fluoro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1n)



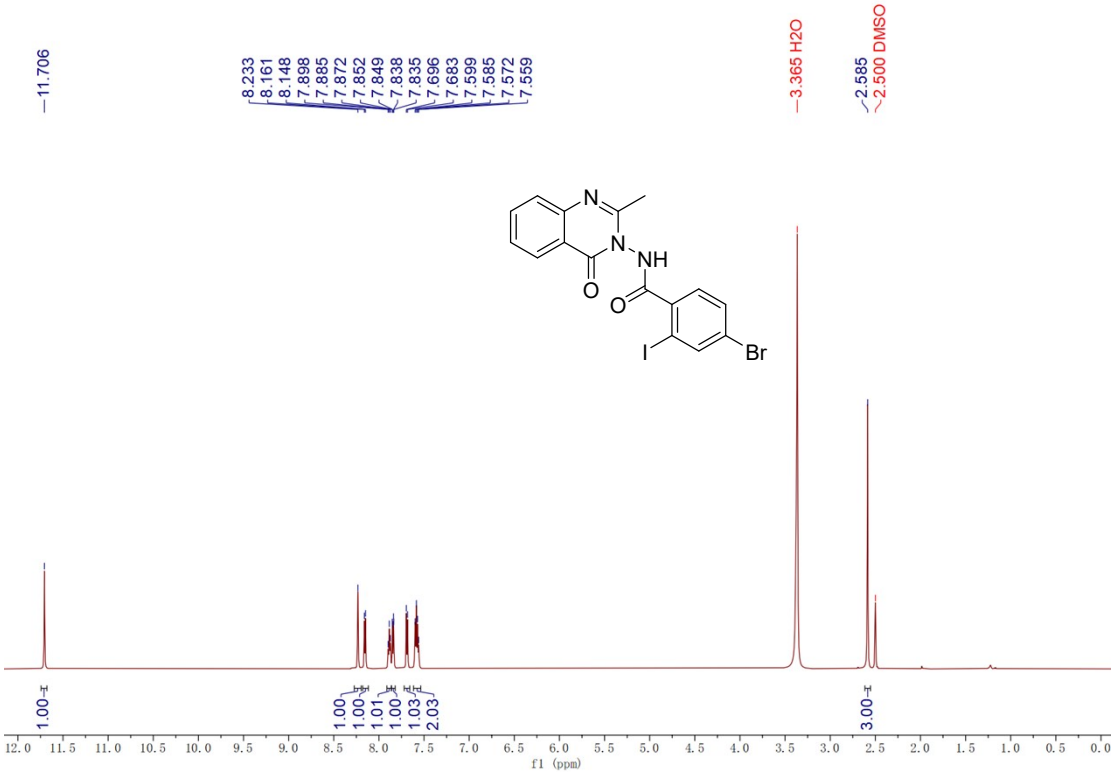


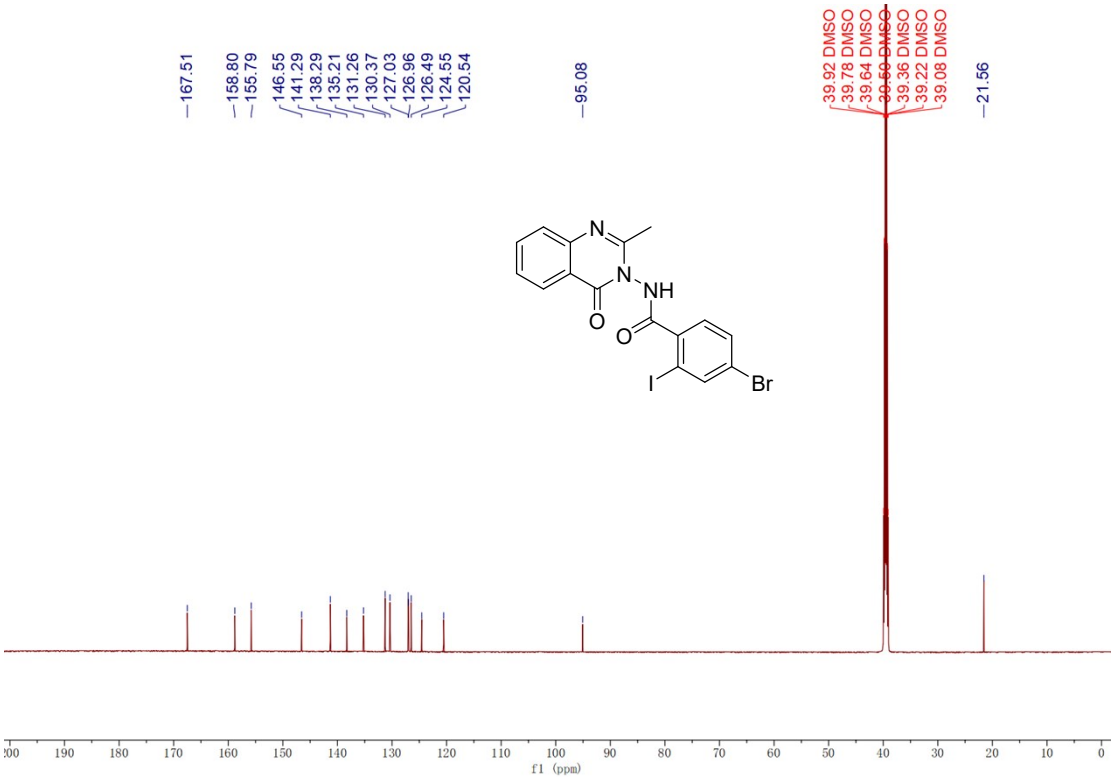
2-Iodo-4-methoxy-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1o)



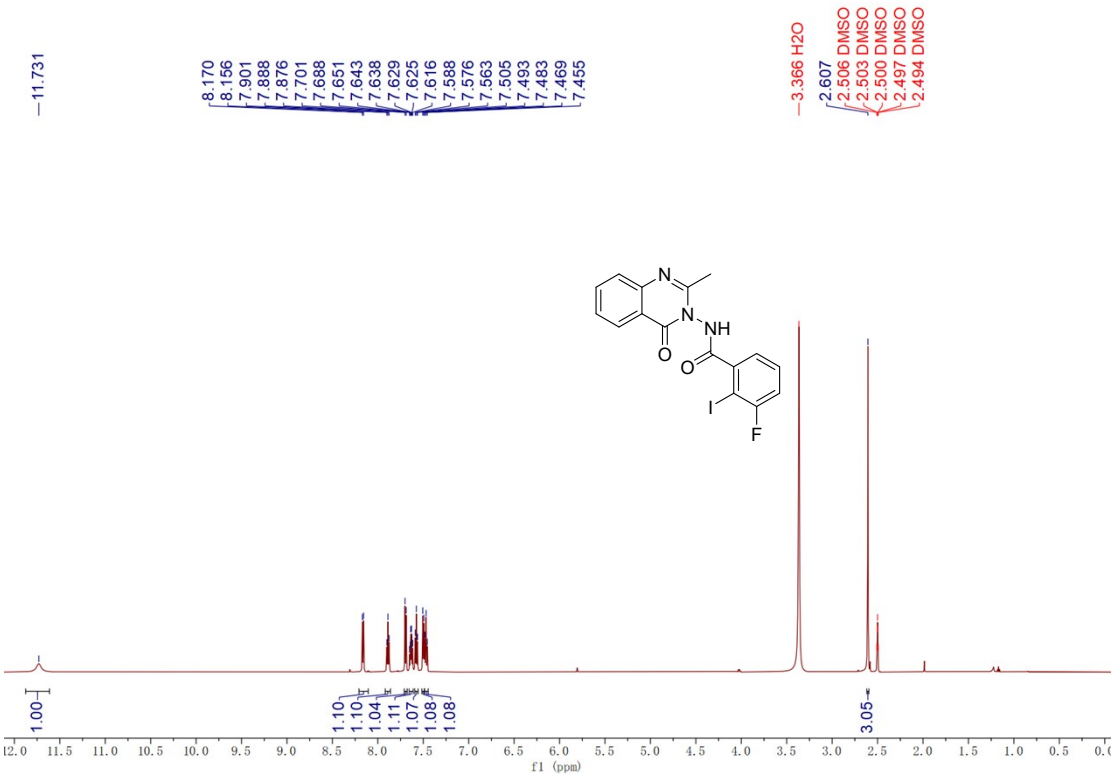


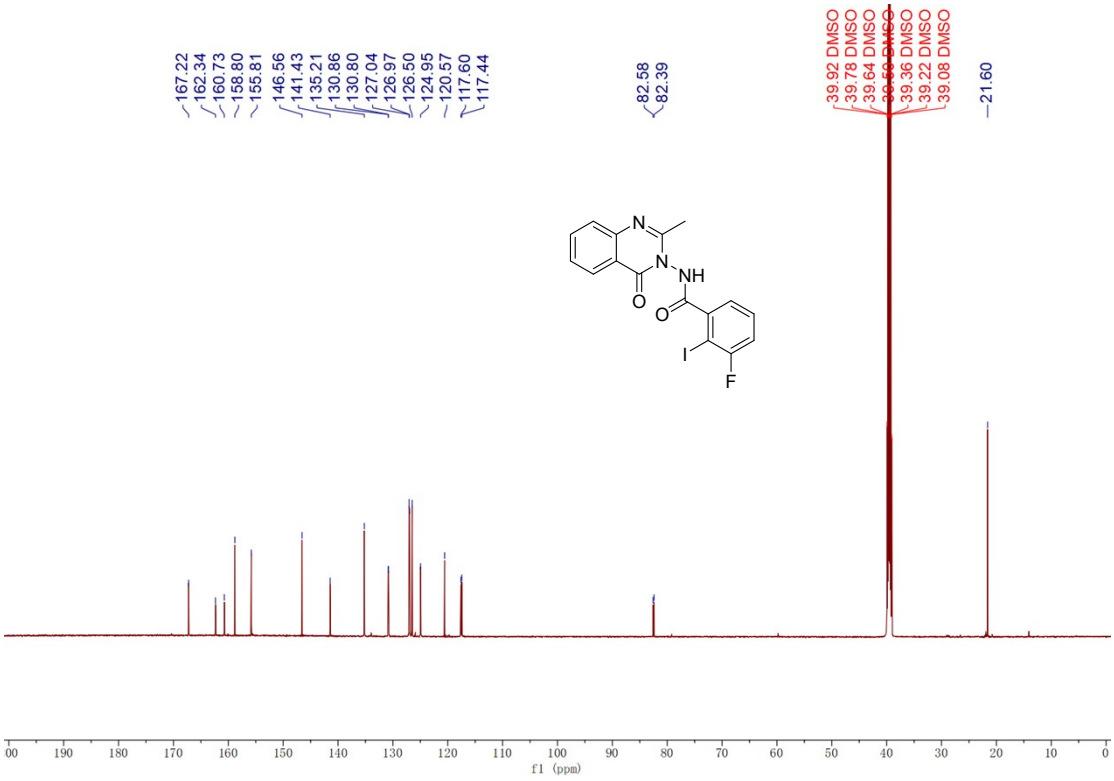
4-Bromo-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1p)



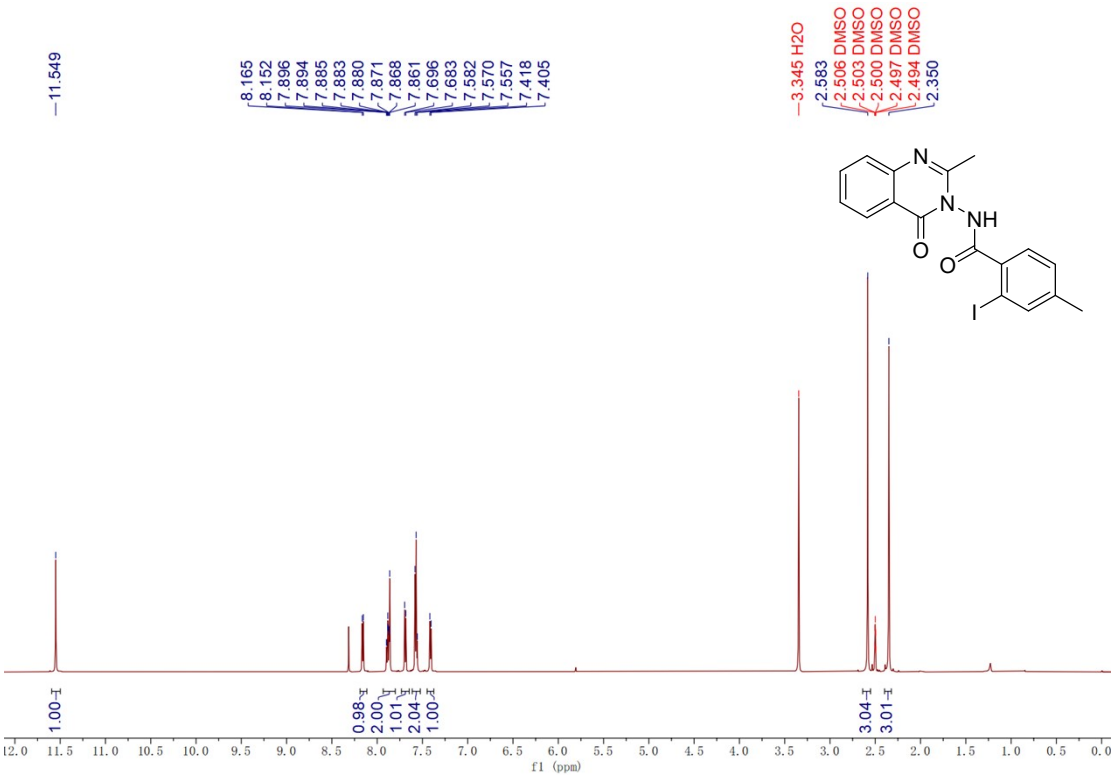


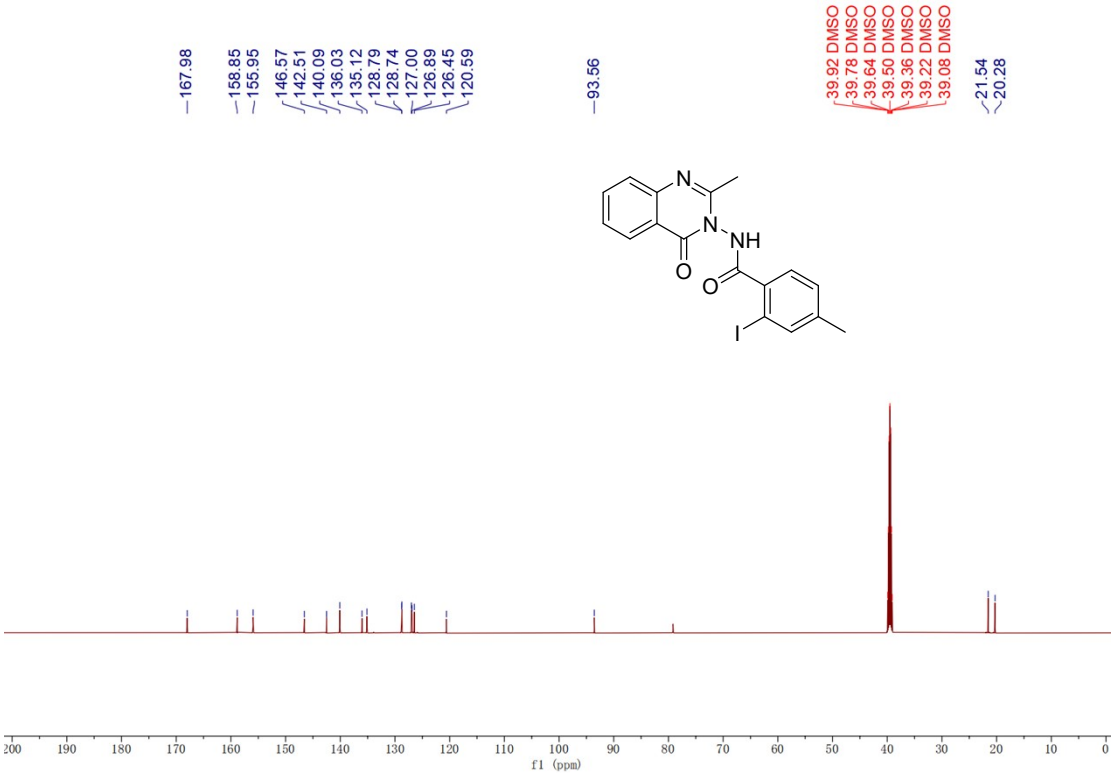
3-Fluoro-2-iodo-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1q)



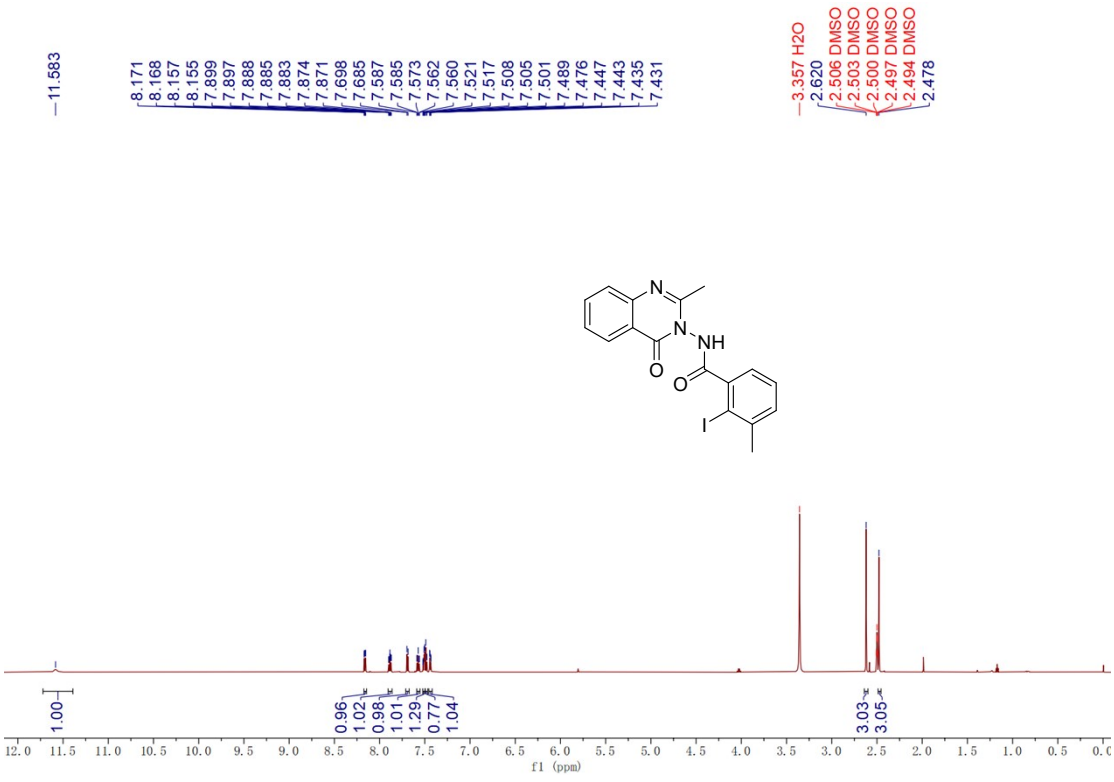


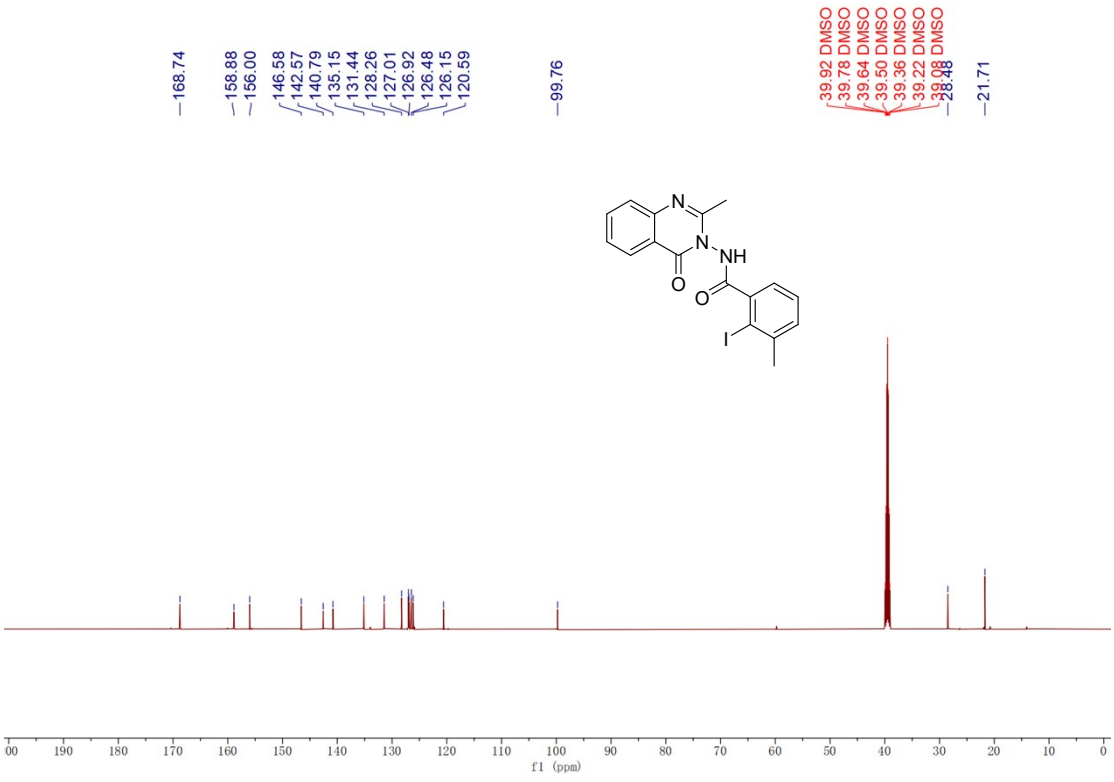
2-Iodo-4-methyl-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1r)





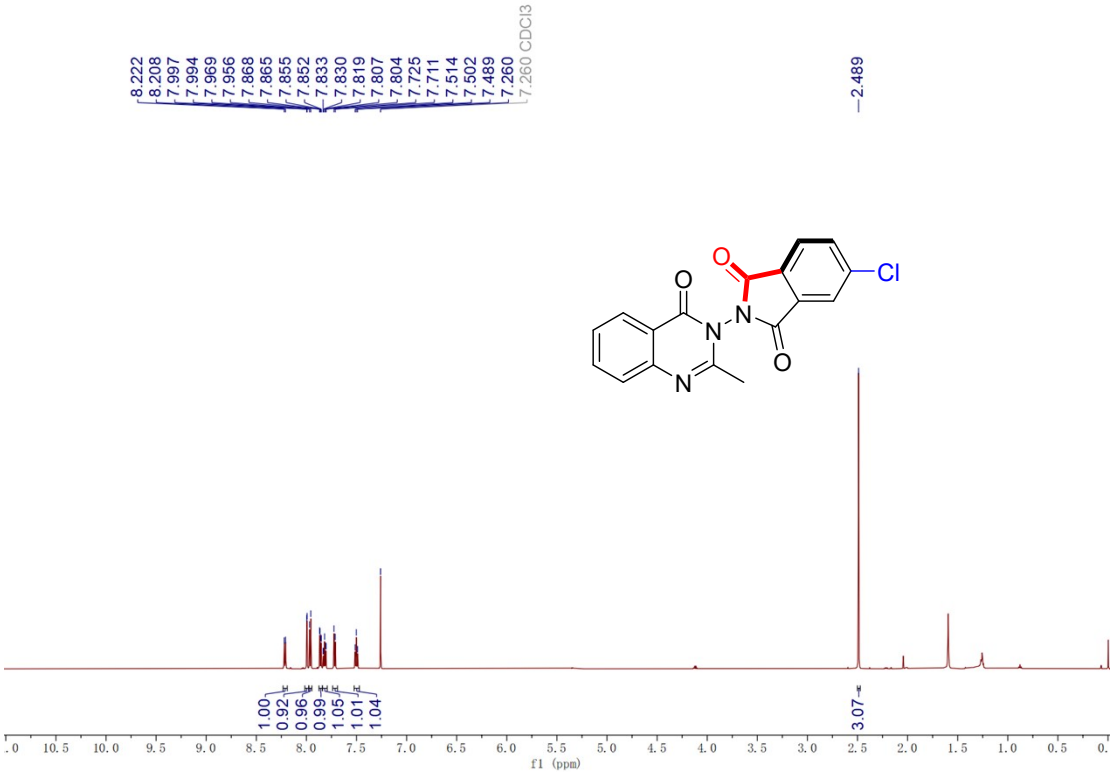
4-Iodo-3-methyl-*N*-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzamide (1s)

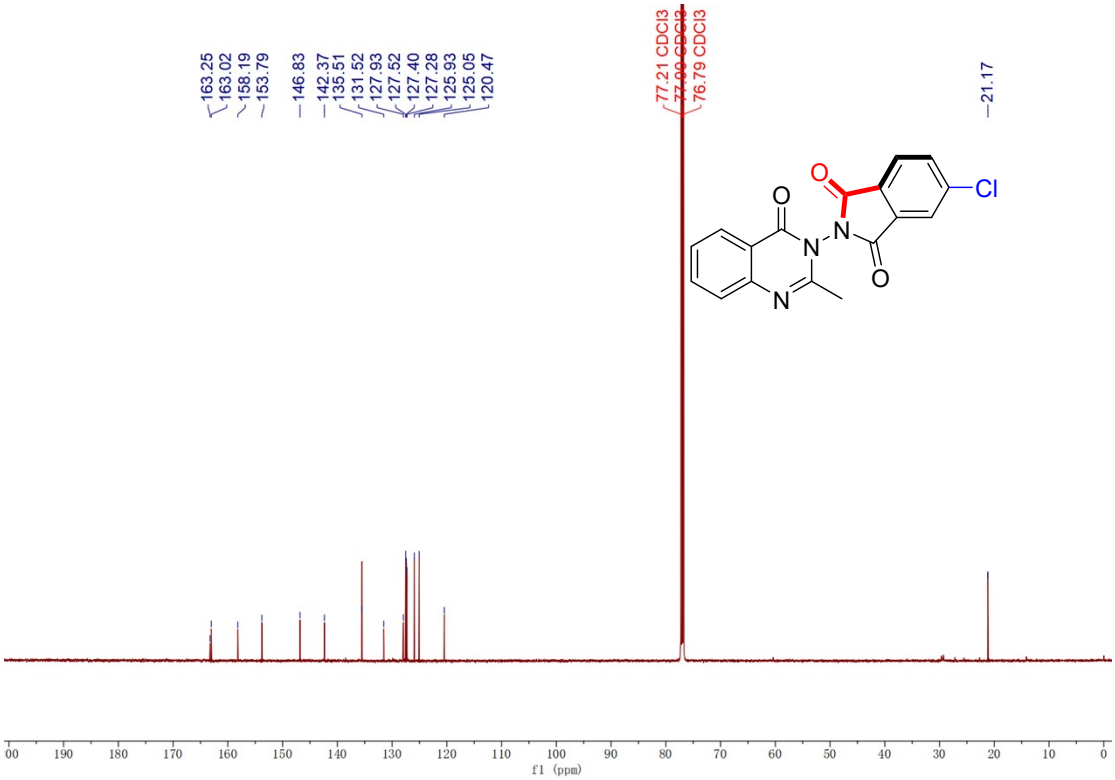




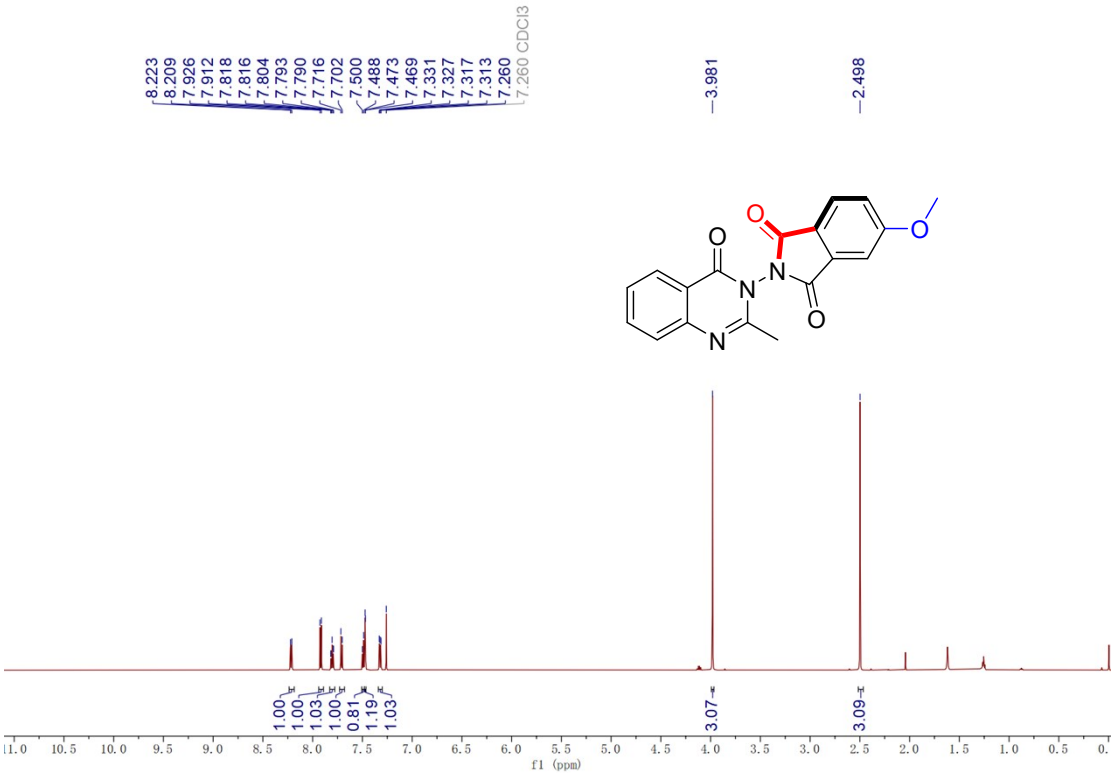
Characterization Data for the Products

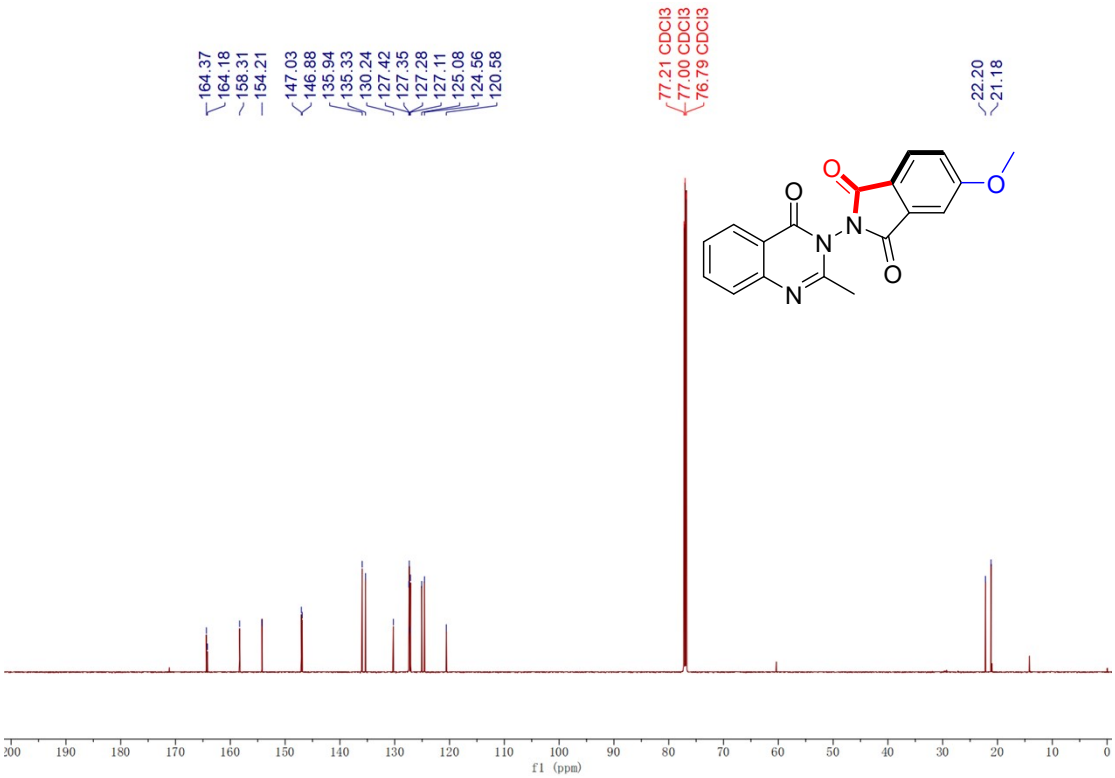
(*Ra*)-5-Chloro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3aa)

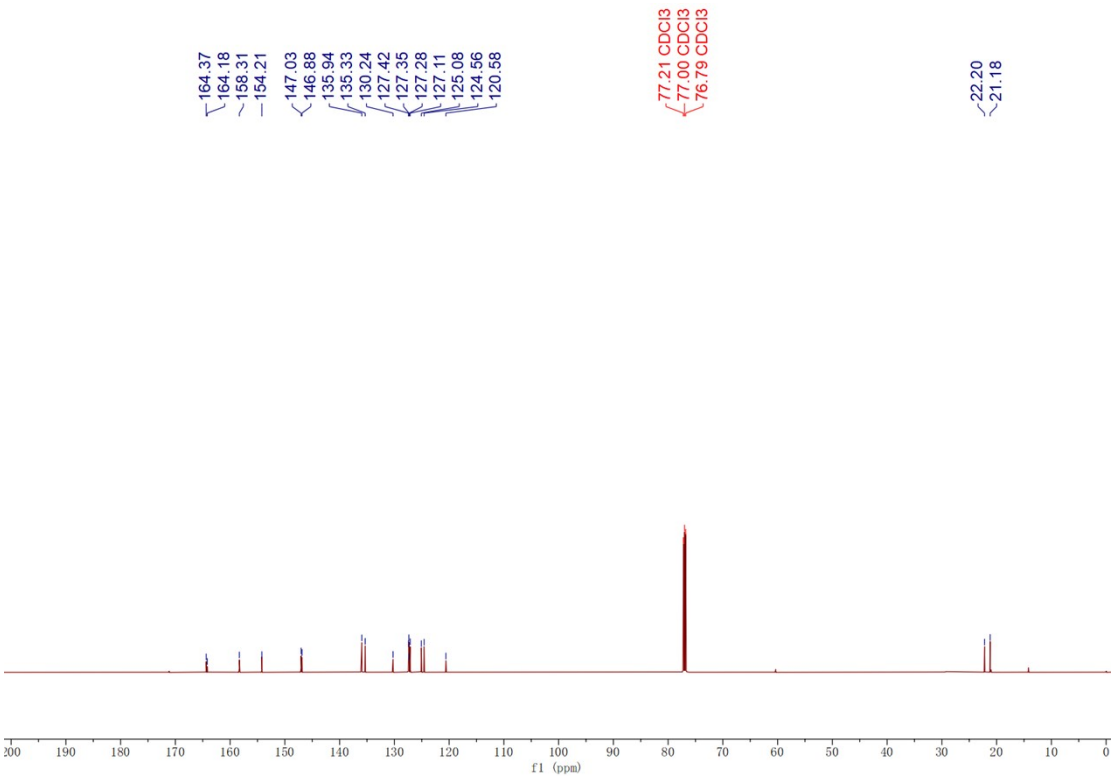




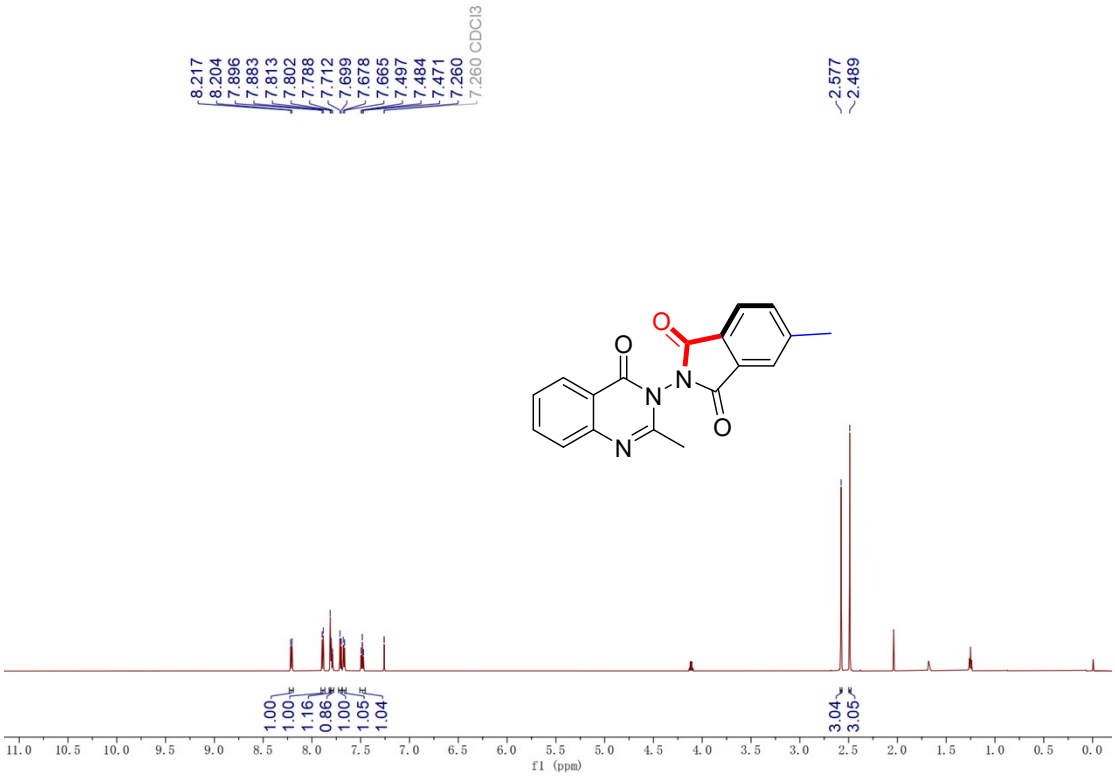
(*Ra*)-5-Methoxy-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ab)

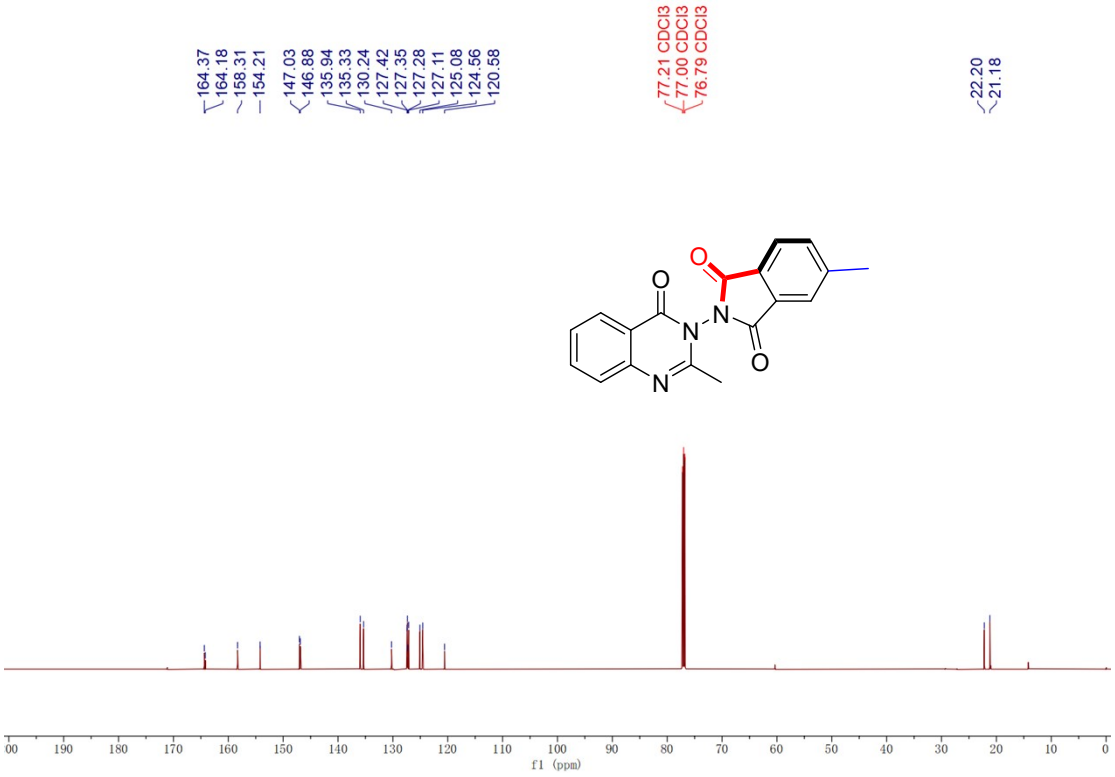




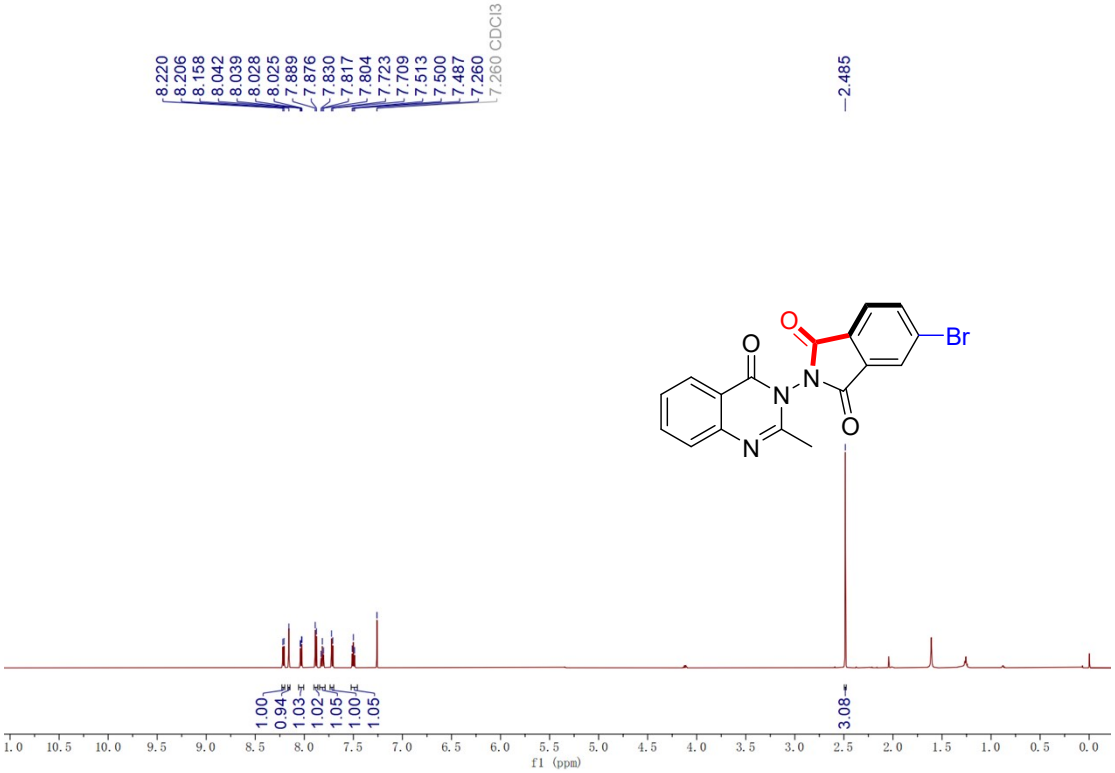

164.37
164.18
158.31
154.21
147.03
146.88
135.94
135.33
130.24
127.42
127.35
127.28
127.11
125.08
124.56
120.58
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
22.20
21.18
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

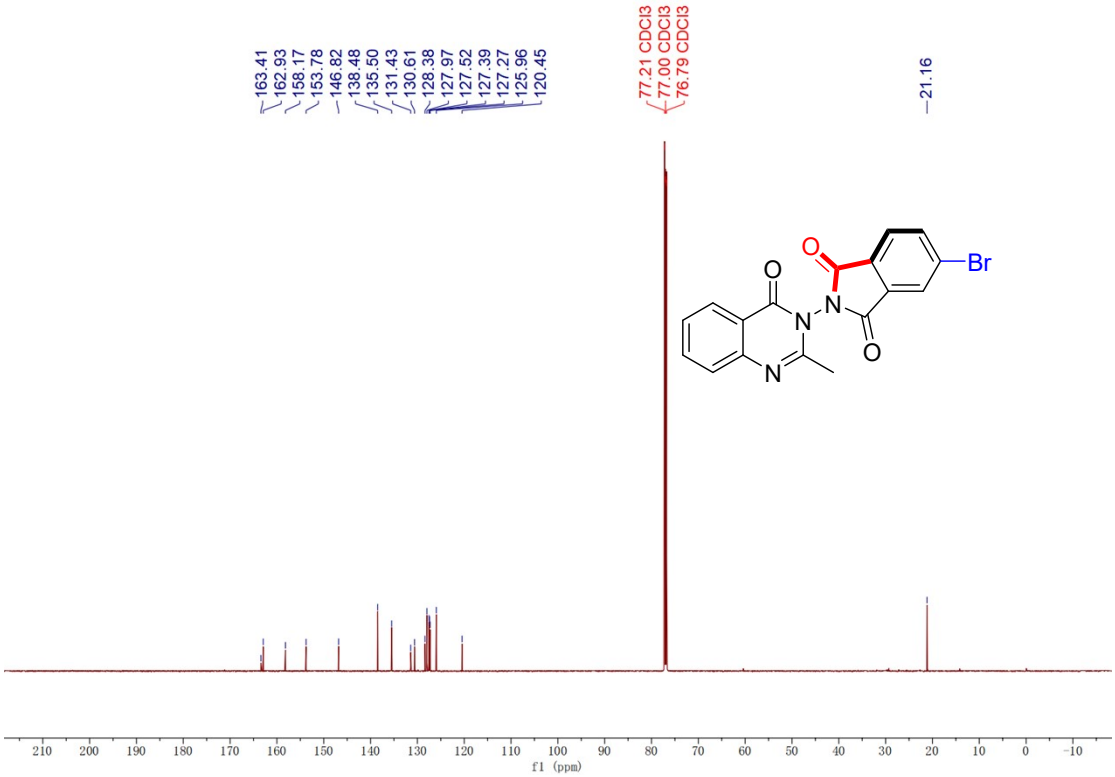
(*Ra*)-5-Methyl-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ac)



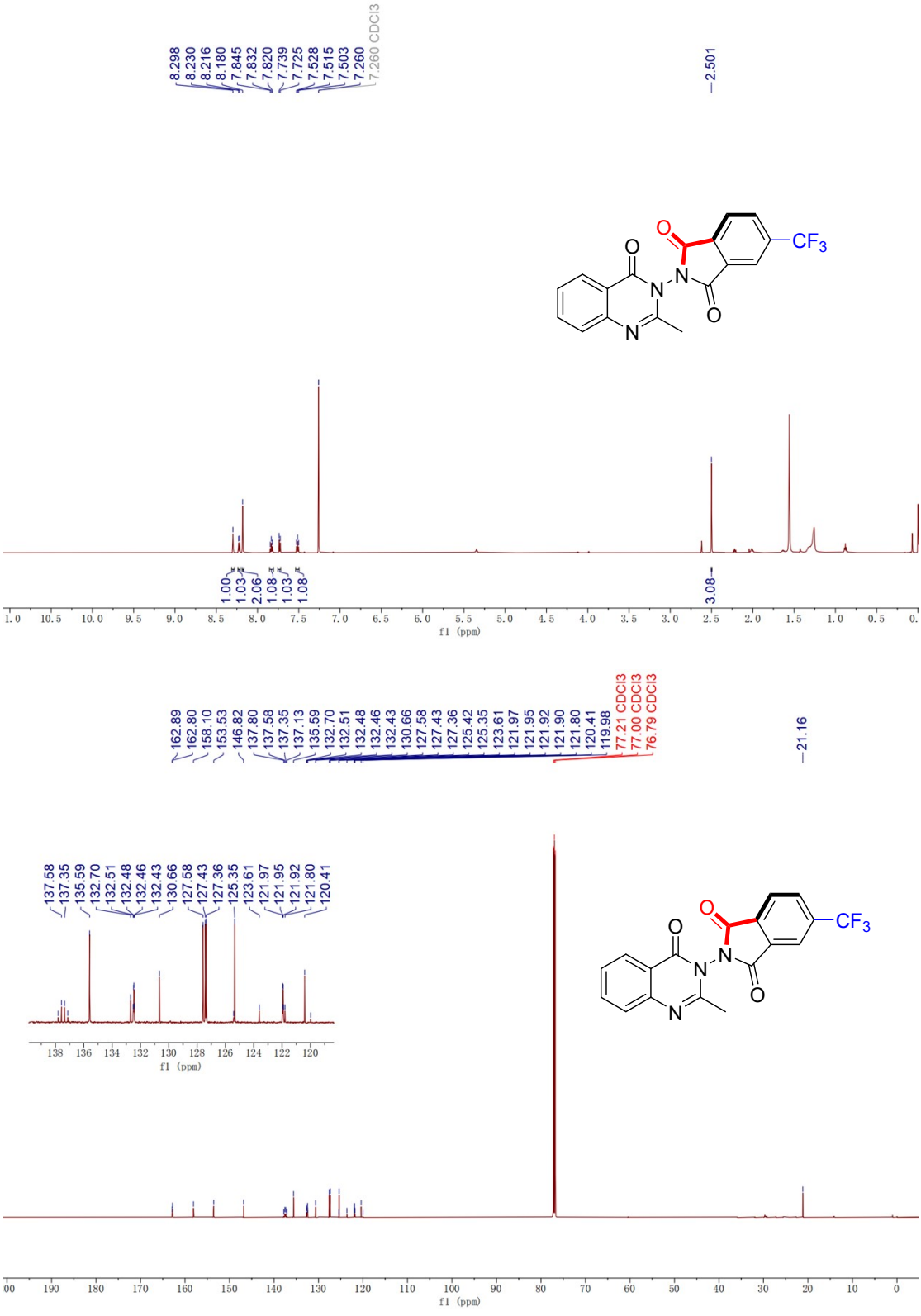


(*Ra*)-5-Bromo-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ad)

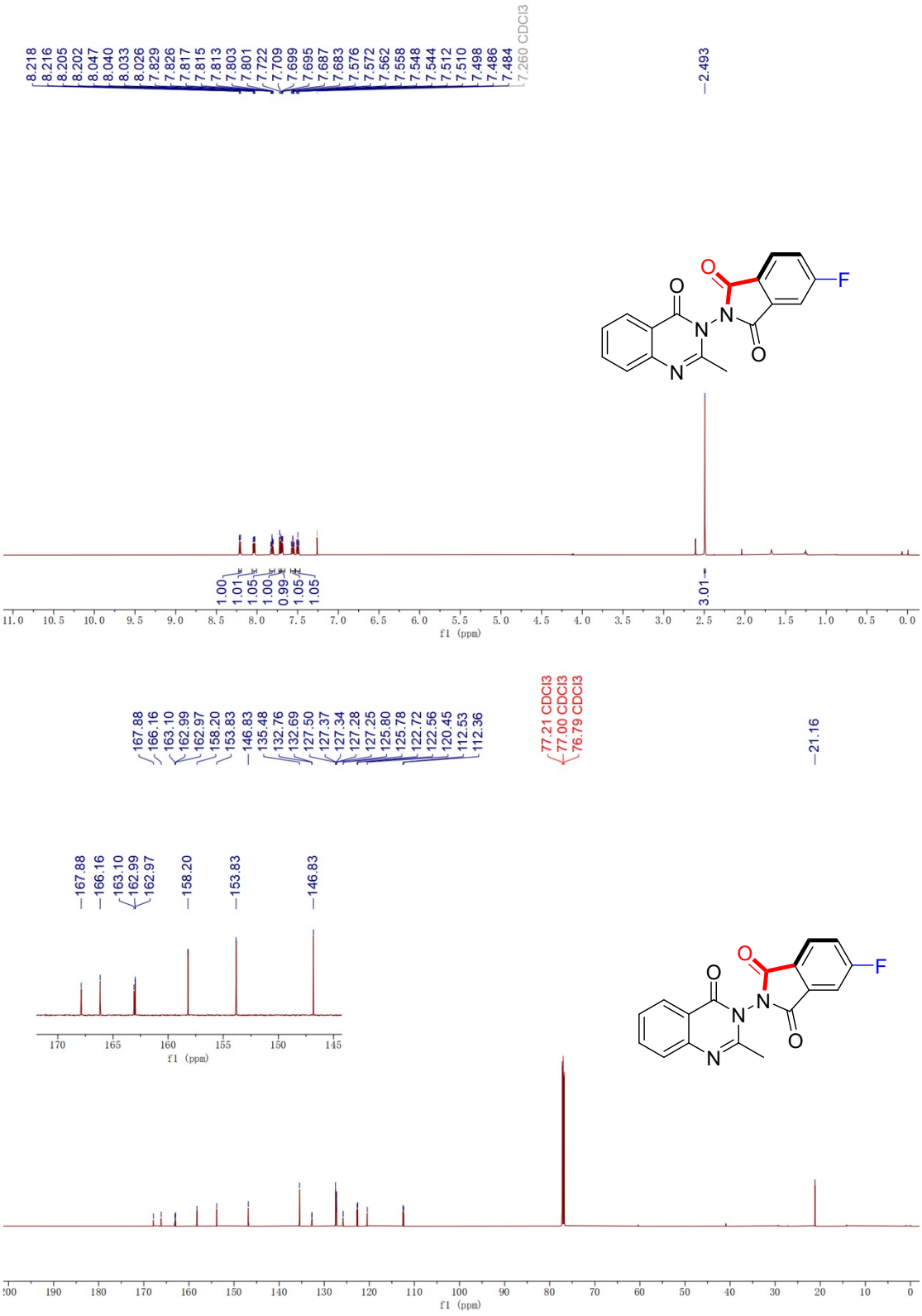




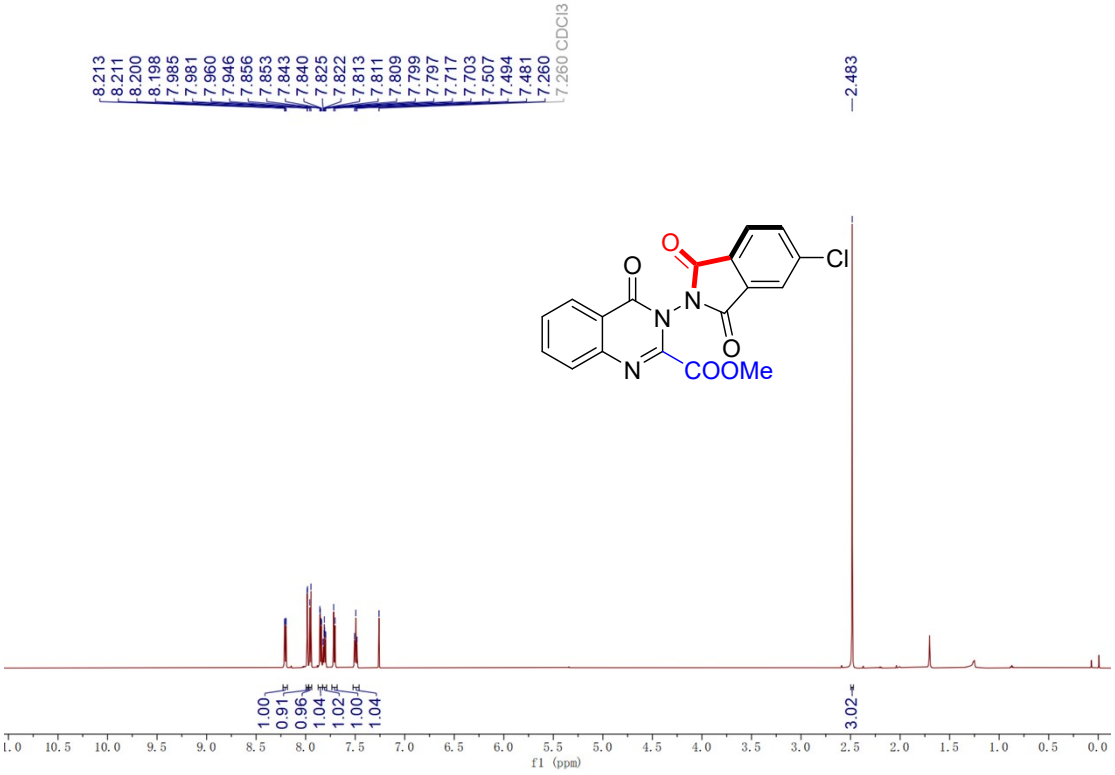
(*Ra*)-2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)-5-(trifluoromethyl)isoindoline-1,3-dione (3ae)

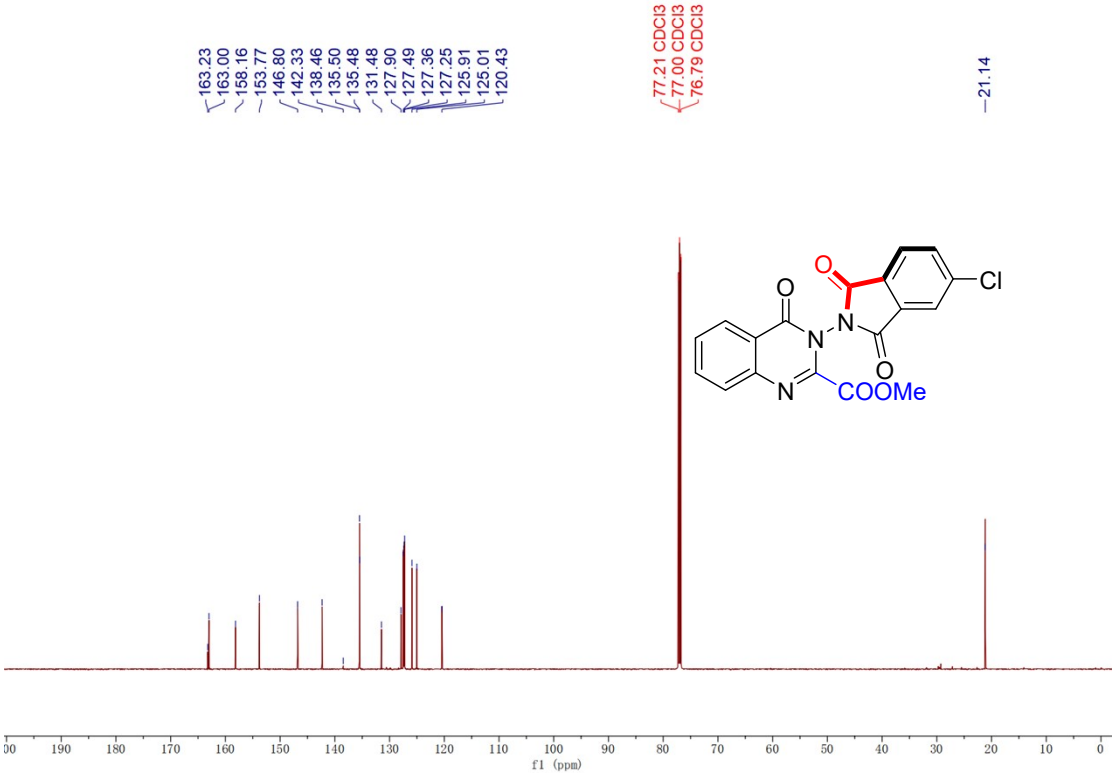


(*Ra*)-5-Fluoro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3af)

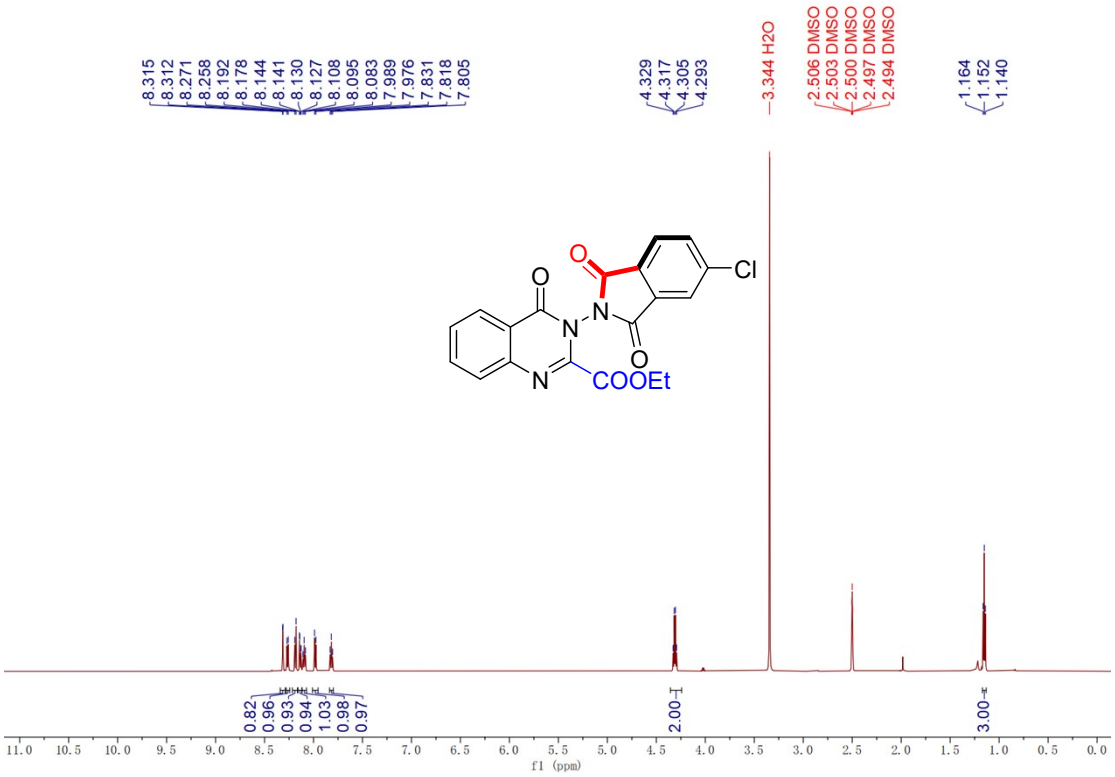


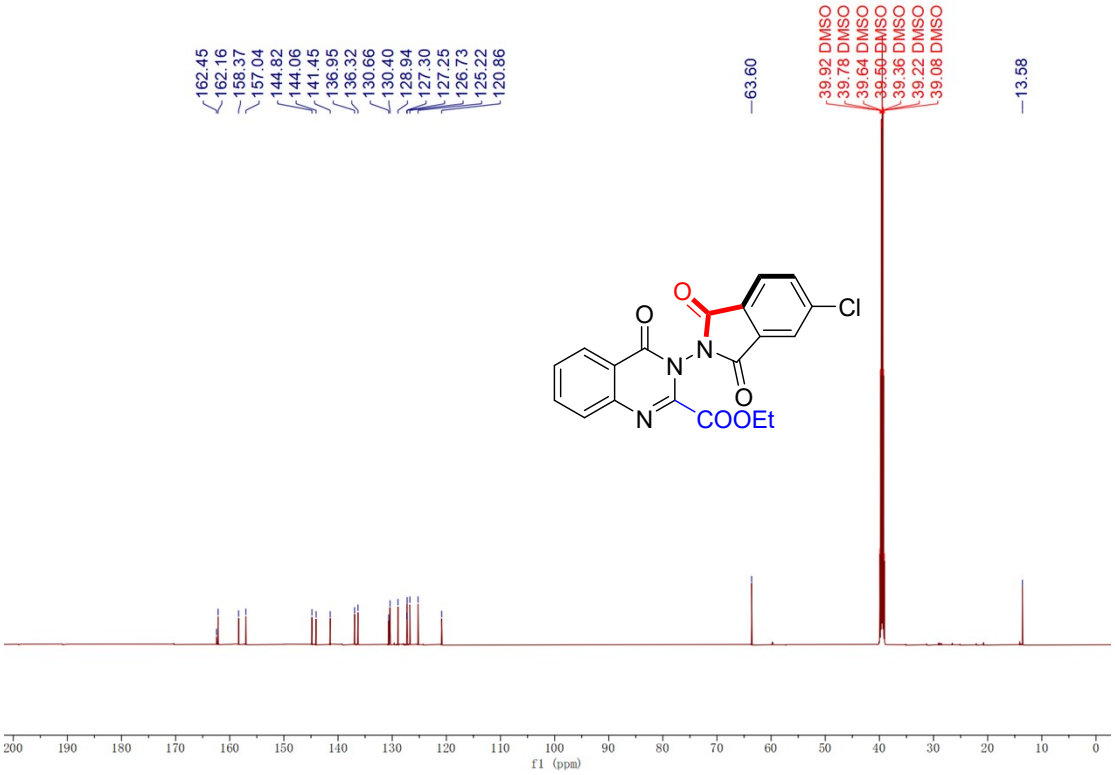
(Ra)-Methyl 3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3ag)



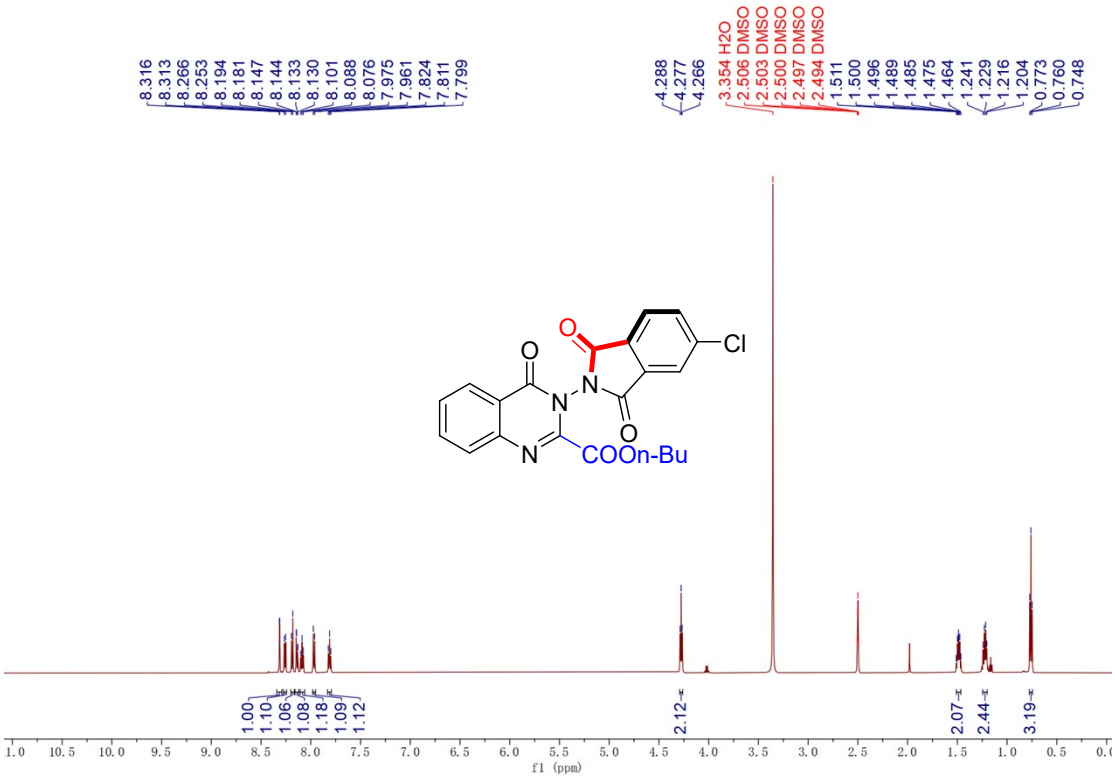


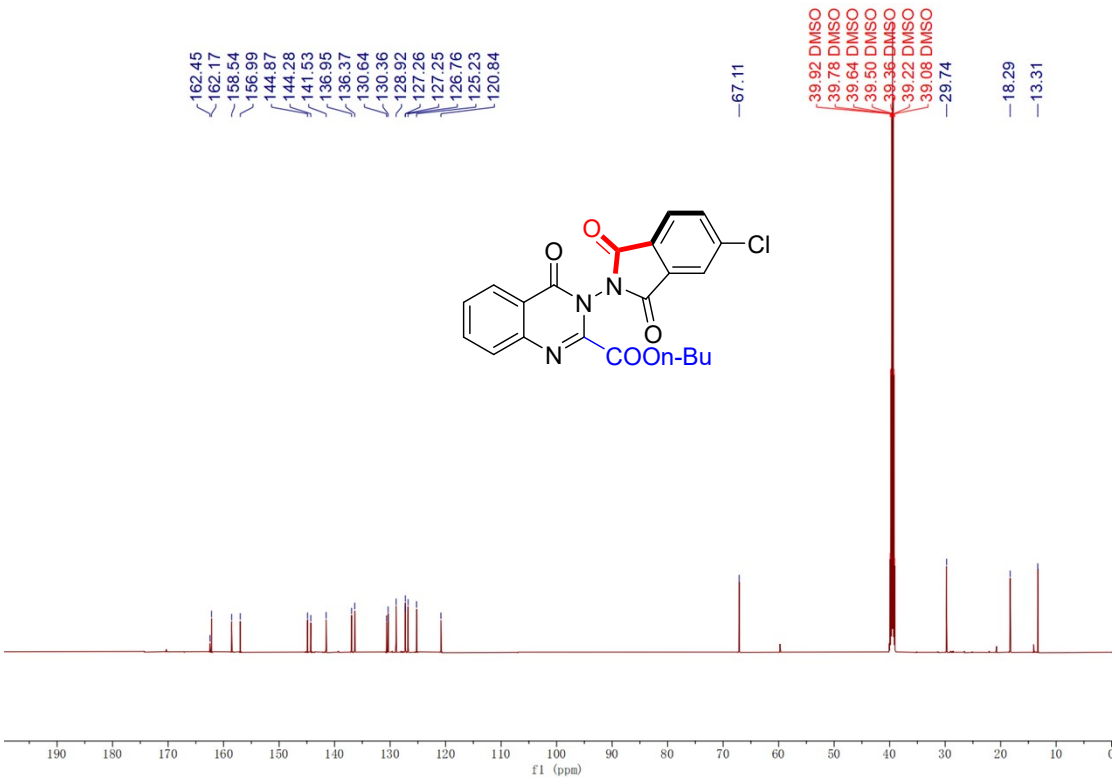
(*Ra*)-Ethyl 3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3ah)



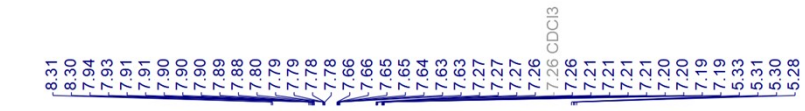


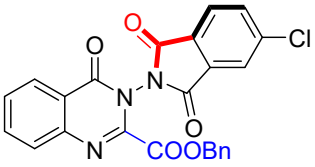
(*Ra*)-Butyl 3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3ai)

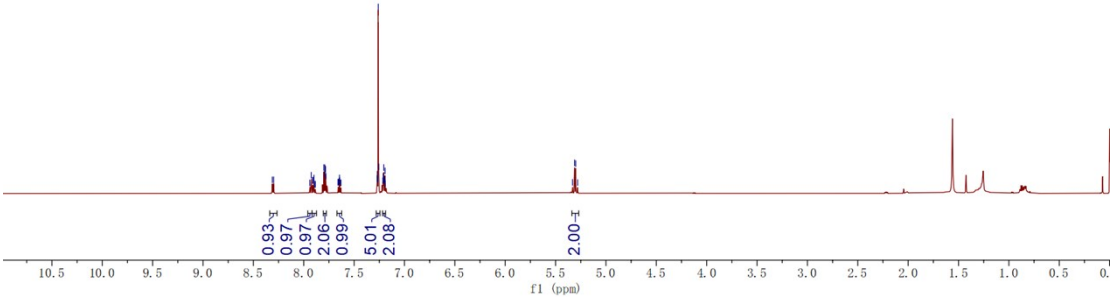


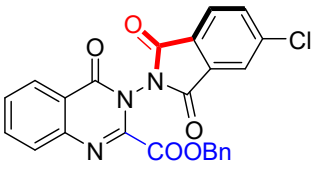


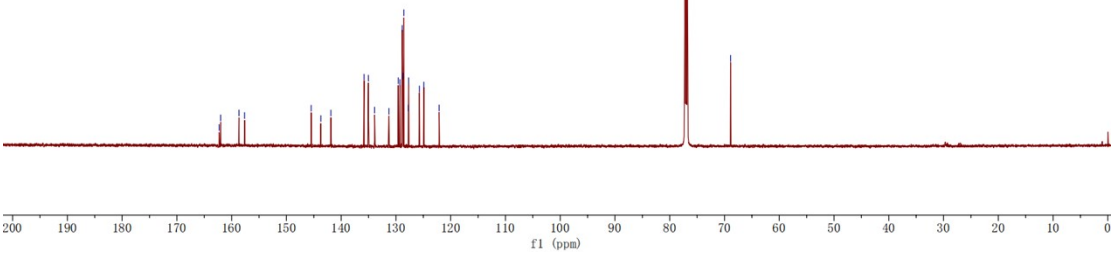
(*Ra*)-Benzyl 3-(5-chloro-1,3-dioxoisoindolin-2-yl)-4-oxo-3,4-dihydroquinazoline-2-carboxylate (3aj)



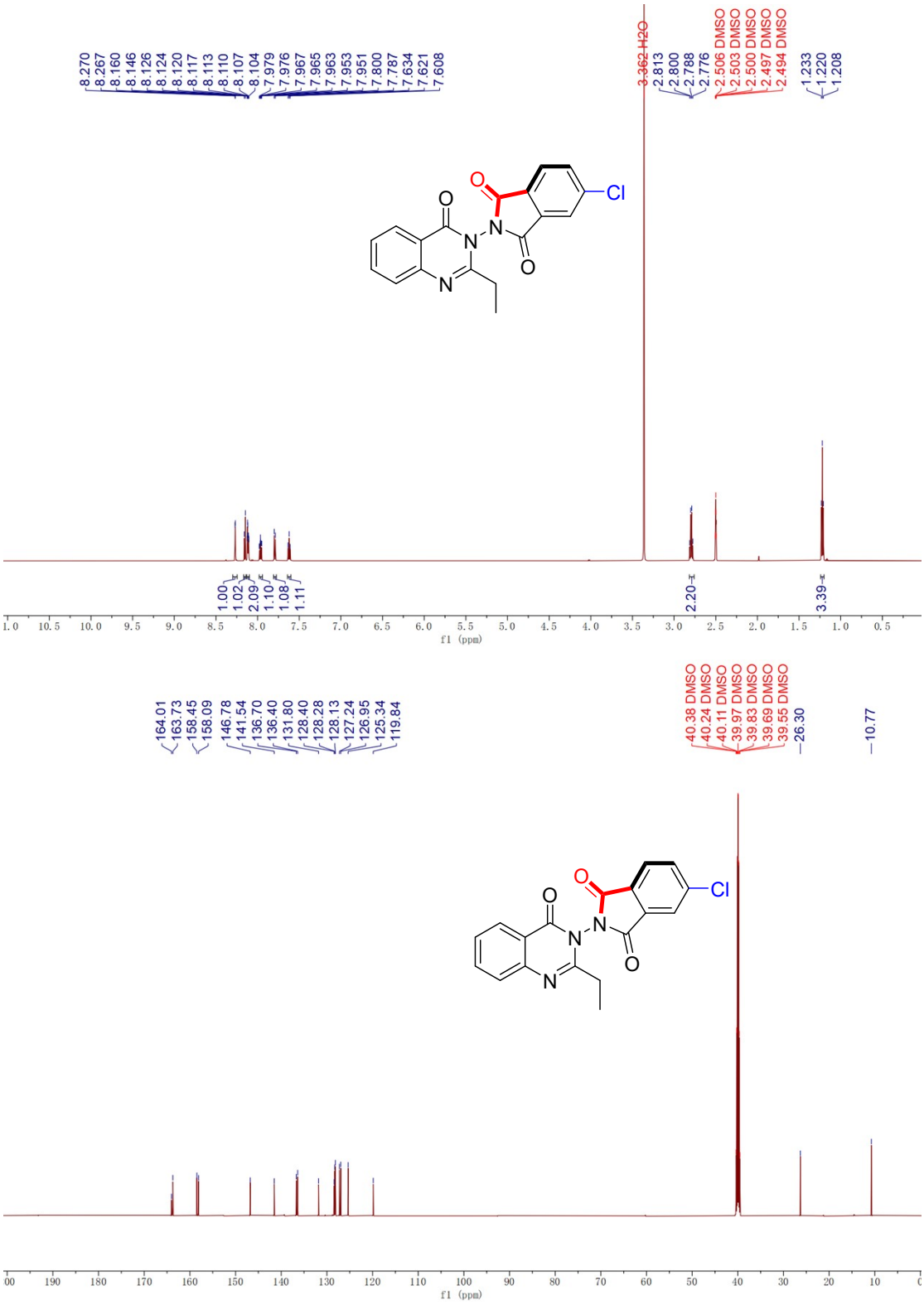




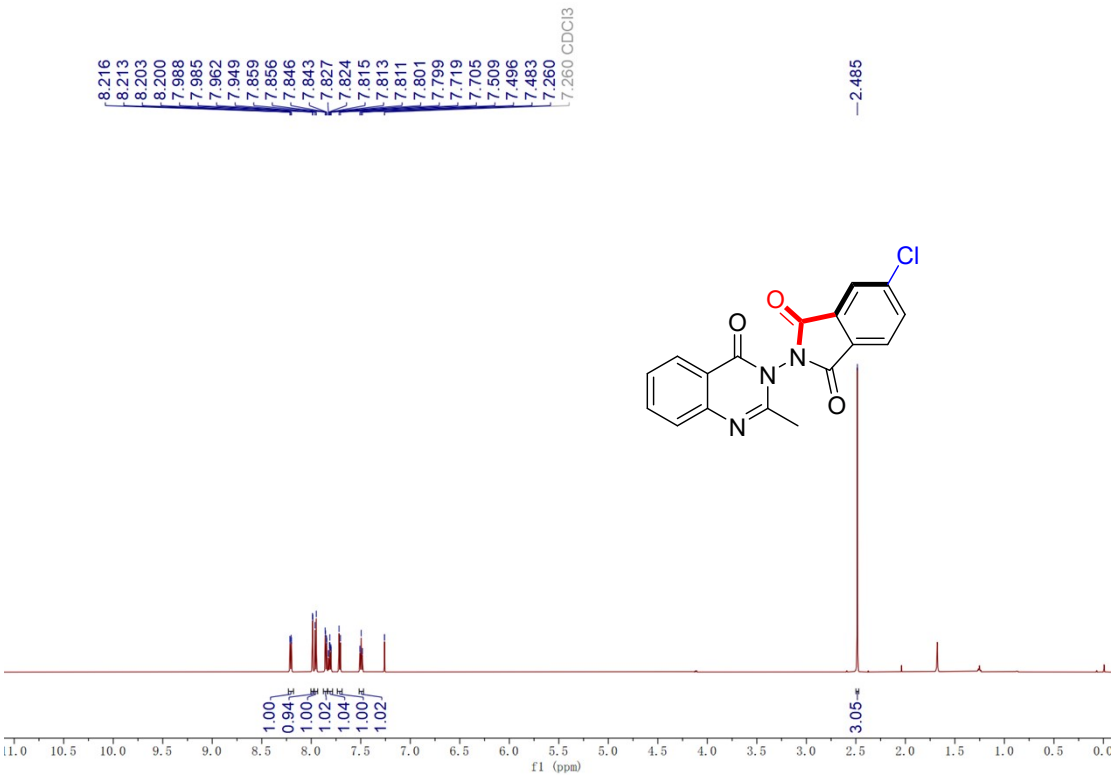


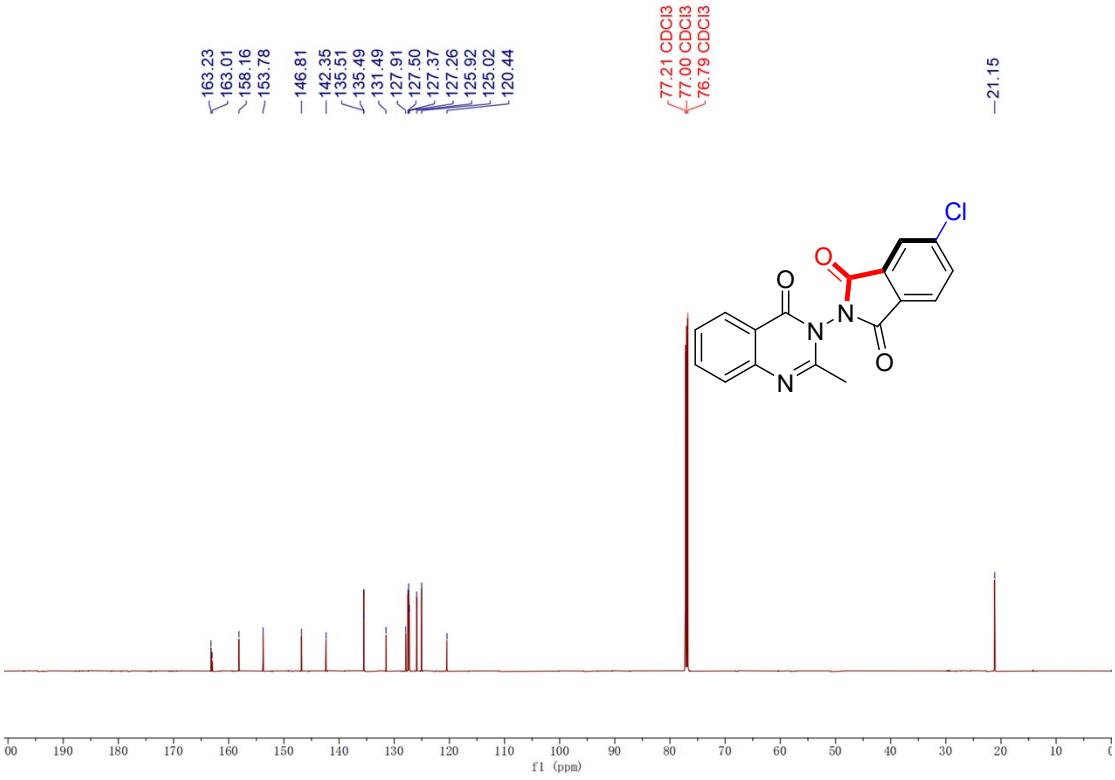


(*Ra*)-5-Chloro-2-(2-ethyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ak):

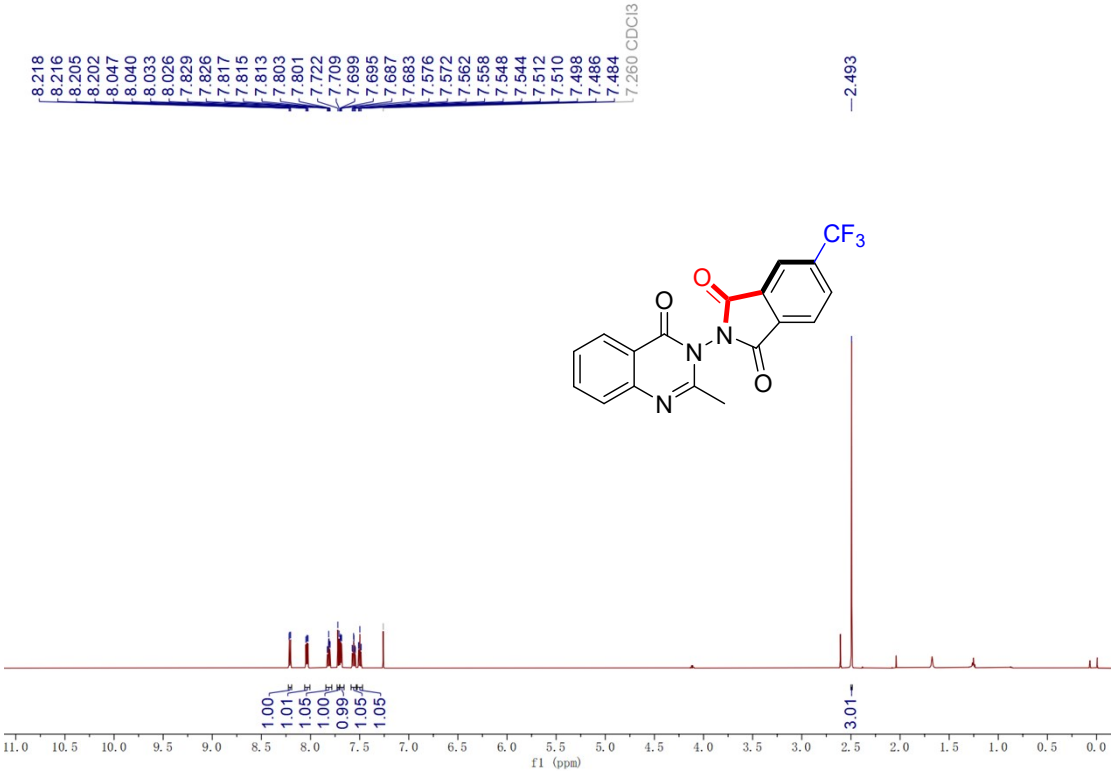


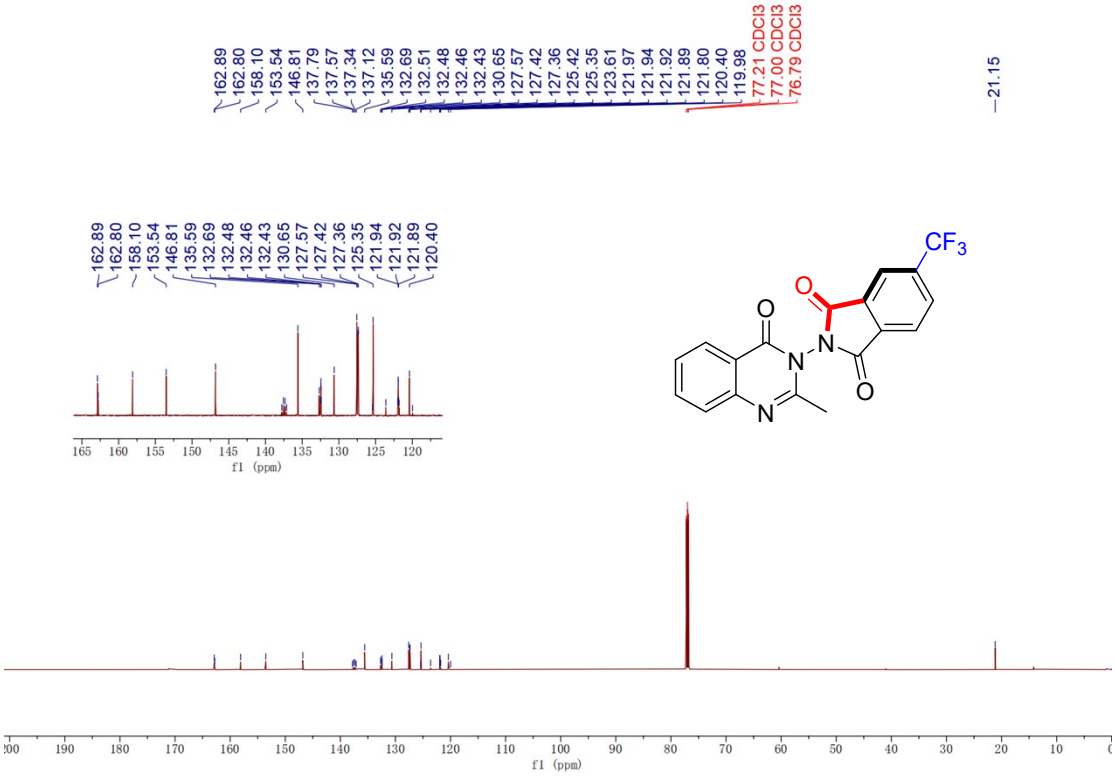
(*Sa*)-4-Chloro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ak)



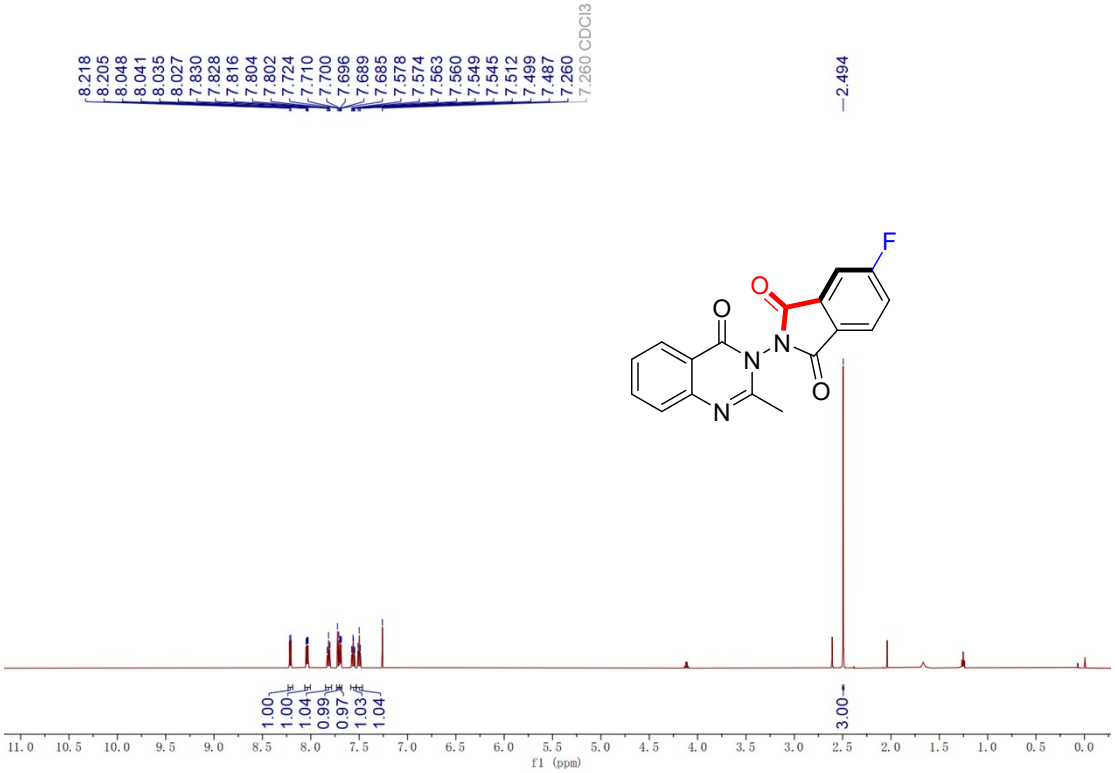


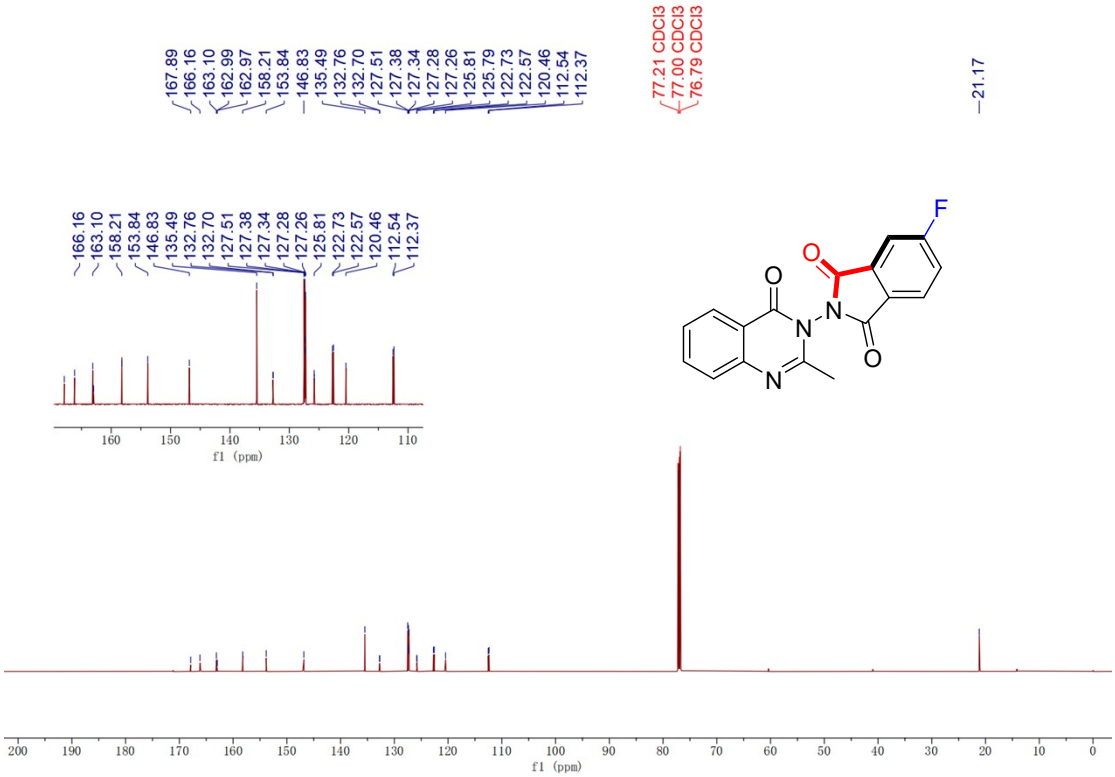
(*Sa*)-2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)-4-(trifluoromethyl)isoindoline-1,3-dione (3al)

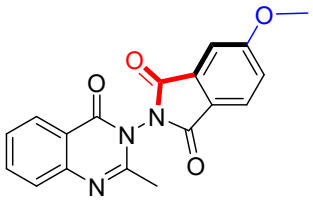


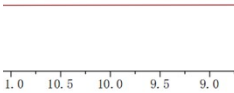


(*Sa*)-4-Fluoro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3am)

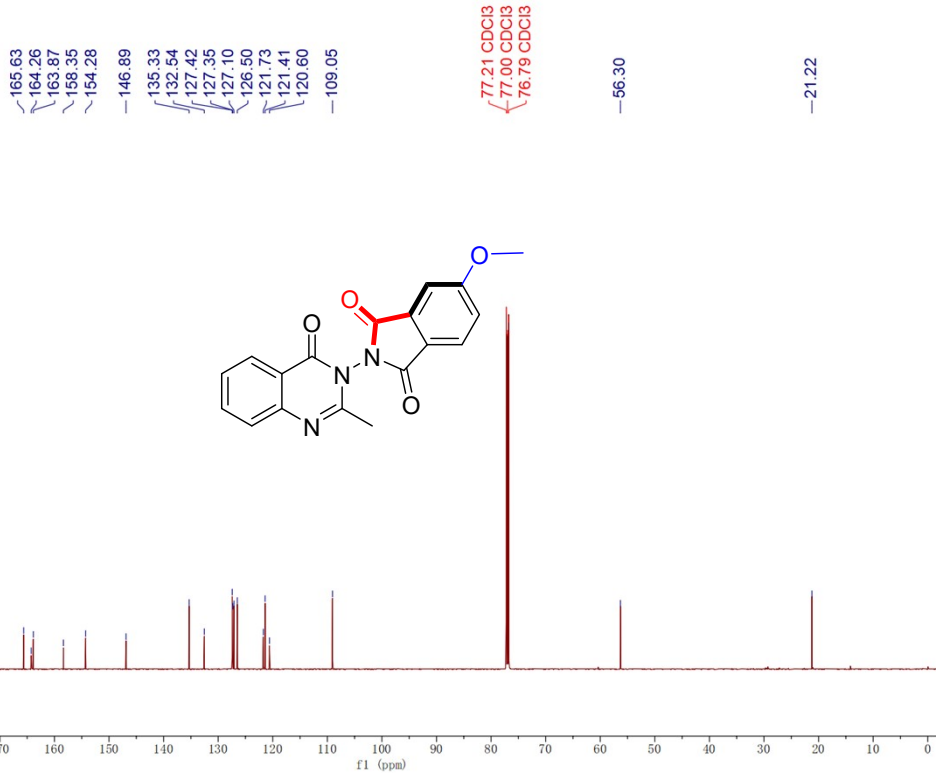




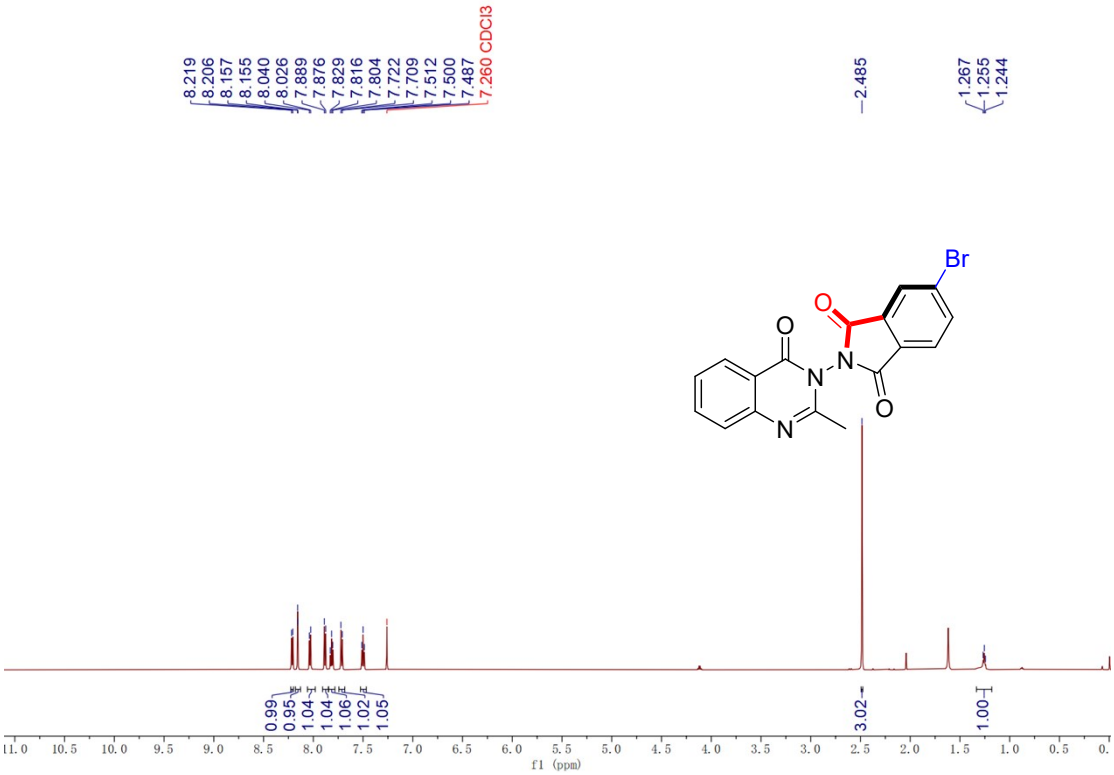


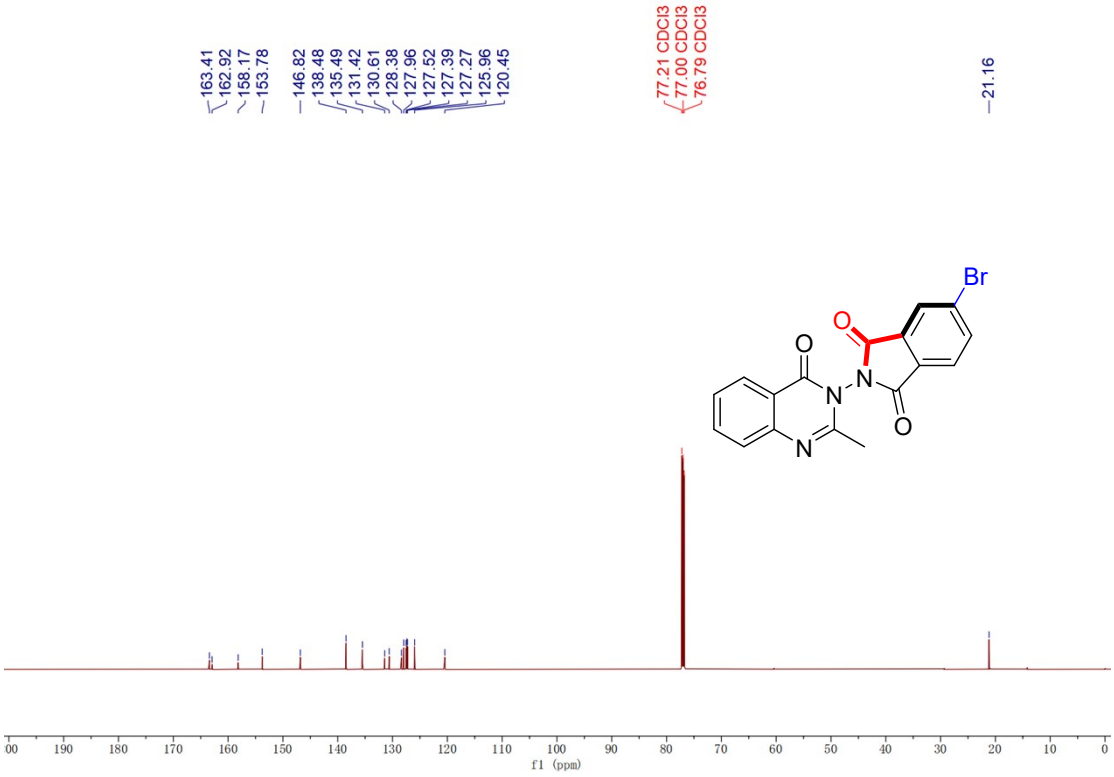


(*Sa*)-4-Methoxy-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3an)

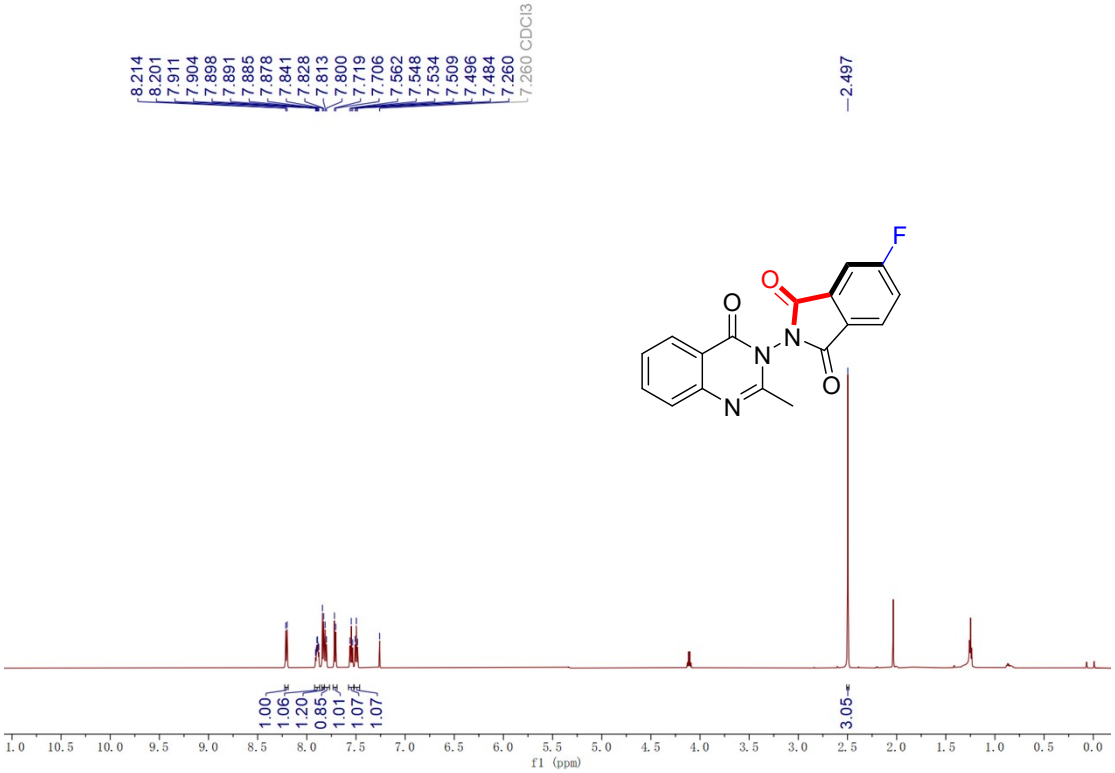


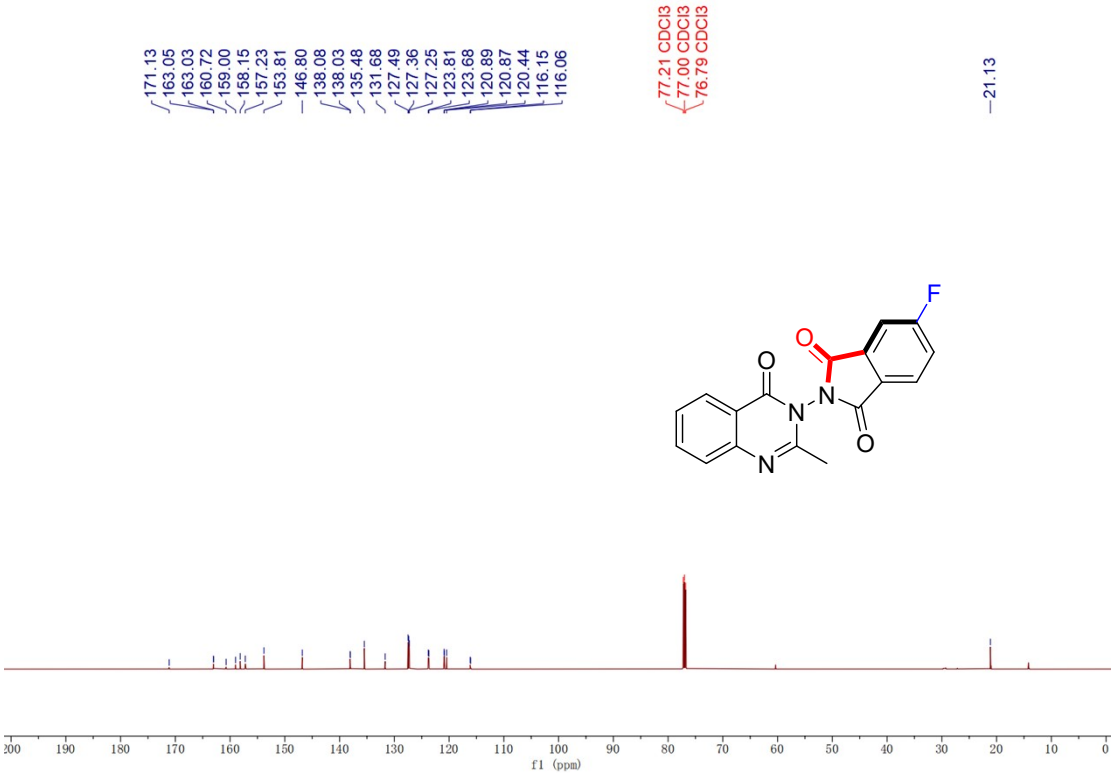
(*Sa*)-4-Bromo-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ao)



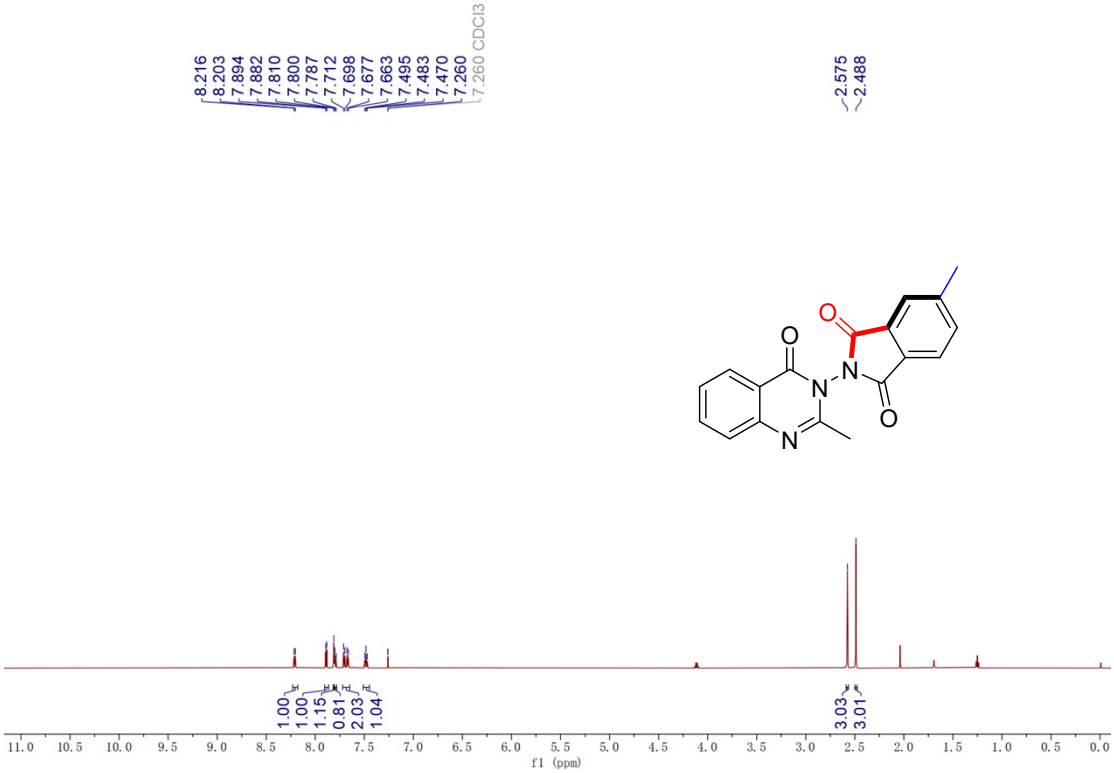


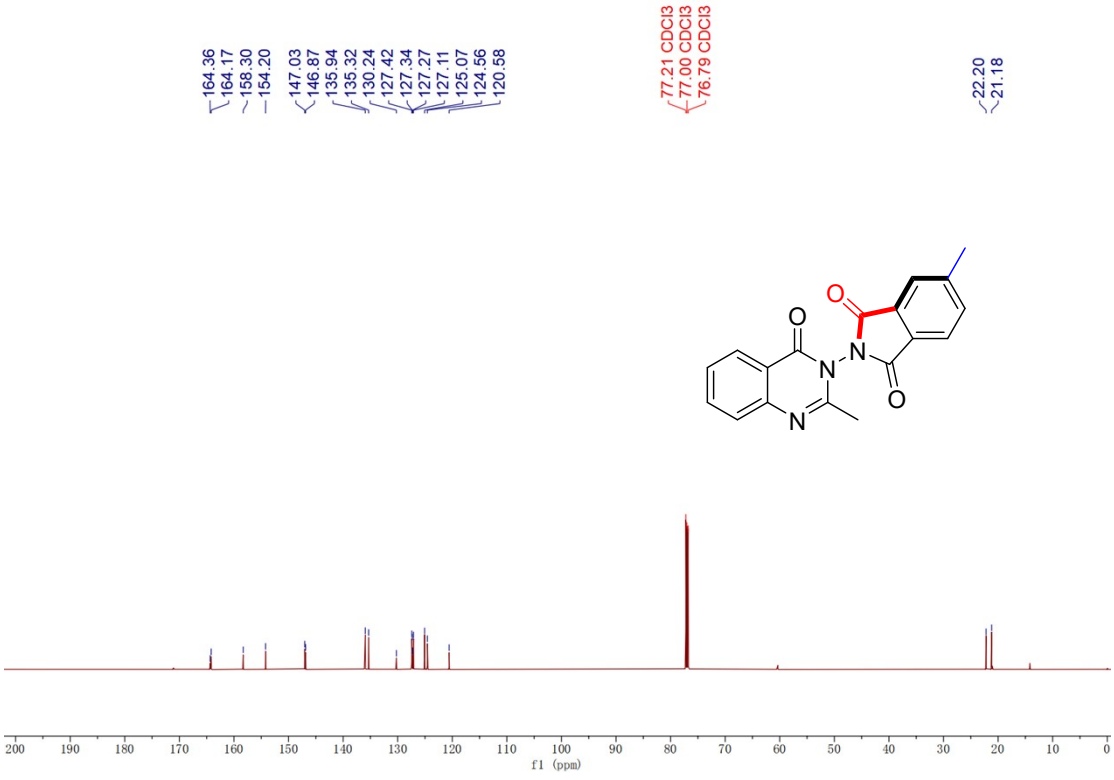
(*Sa*)-3-Fluoro-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ap)



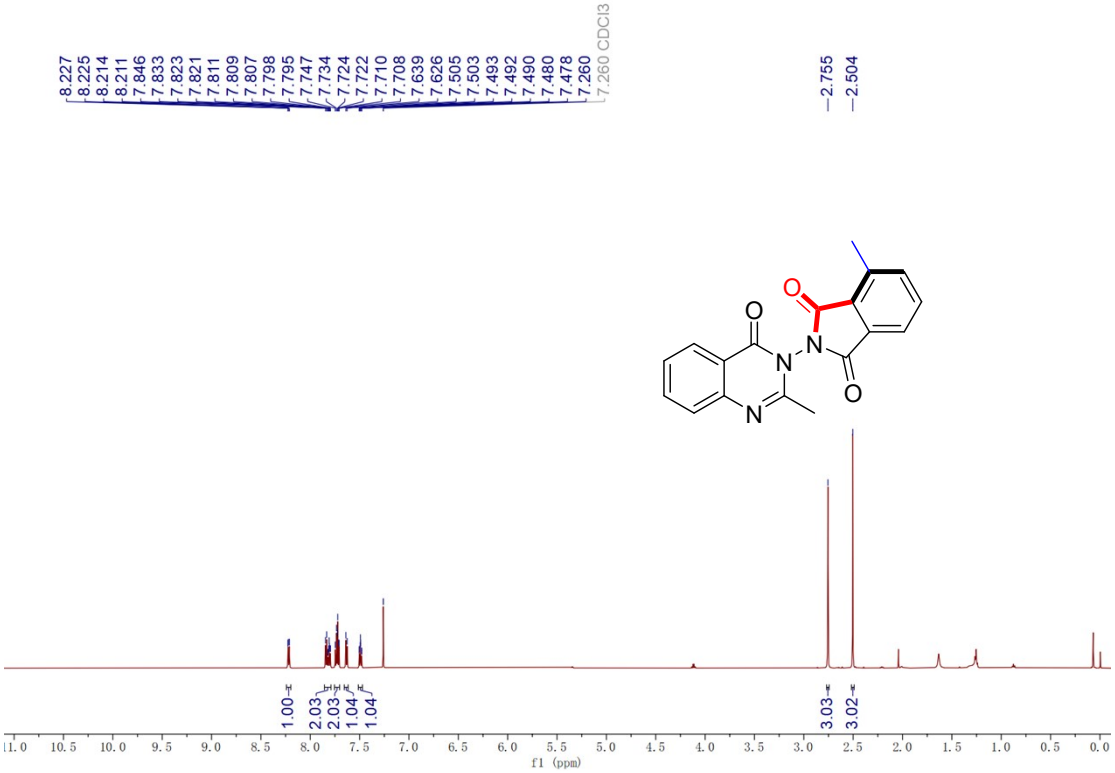


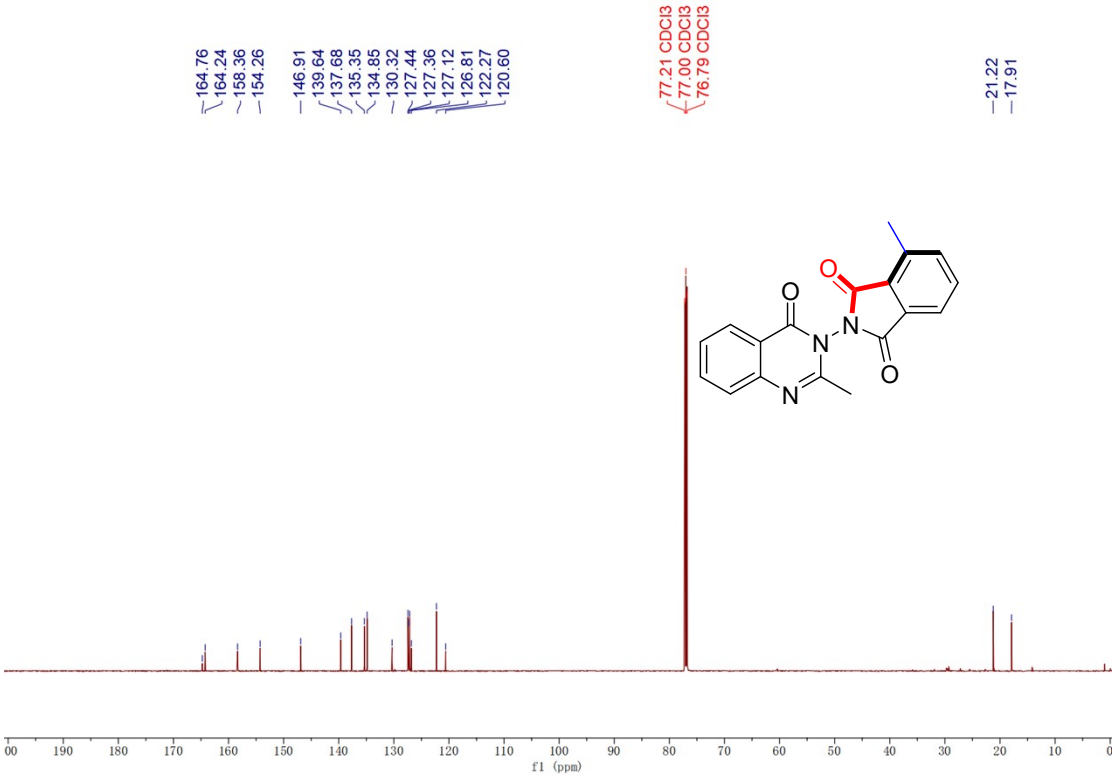
(*Sa*)-4-Methyl-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3aq)





(*Sa*)-3-Methyl-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)isoindoline-1,3-dione (3ar)





(*Ra*)-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-5-(phenylethynyl)isoindoline-1,3-dione (7)