Supplementary Information

Photoinduced Four-component Intramolecular Cyclization/Hydroxytrifluoromethylation Cascade: Facile Access to Polyfunctionalized 3,4-Dihydroquinazolinones

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SUPPLEMENTARY INFORMATION

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1. Experimental Section

All reagents and solvents were used from commercial sources unless otherwise stated. All raw materials are obtained from commercial sources. All experiments were conducted in the air. All the reactions were monitored by thin-layer chromatography (TLC). TLC was performed on pre-coated silica gel plates (Qingdao Haiyang Chemical Co., Ltd, China). Column chromatography was performed on silica gel (240-400 mesh) with petroleum ether and ethyl acetate as eluent. ^{1}H and ^{13}C NMR (400 and 100 MHz) spectra were recorded on a Bruker Avance 400 MHz using $CDCl_3$ and DMSO-d_6 as solvent with tetramethylsilane as the internal standard. Melting points are determined using an WRS-1B apparatus and are uncorrected. High resolution mass spectra were obtained with the Q-TOF-Premier mass spectrometer. Reactions were monitored by TLC and visualized with ultraviolet light.

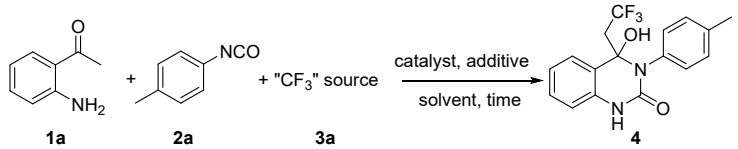
General Procedure (4 as an example)

2-Aminoacetophenone (40.5 mg, 0.3 mmol), *p*-Tolyl isocyanate (43.9 mg, 0.33 mmol), Togni II reagent (114 mg, 0.36 mmol) and Methylene Blue trihydrate (1.0 mg, 1 mol%) were added to a solution of THF/H_2O (5 mL/1 mL) , the reaction mixture was stirred in a 10 mL sealed tube at room temperature for 12 h. The reaction was monitored by TLC. Once the reaction was completed, the reaction mixture was treated with H_2O (15.0 mL) and DCM (8.0 mL). The organic and aqueous layers were then separated, and the aqueous layer was extracted with DCM (3 x 8 mL). The combined organic extracts were dried (Na_2SO_4), then the solvent was removed under reduced pressure and the remaining residue was purified by column chromatography. Compound **4** (267 mg, 80% yield) was obtained as a white solid.

2. Optimization of reaction conditions

2-Aminoacetophenone (**1a**, 40.5 mg, 0.3 mmol), *p*-Tolyl isocyanate (**2a**, 43.9 mg, 0.33 mmol), trifluoromethylation reagent (0.36 mmol) and photocatalyst dissolved in the solvent were added to a 10 mL sealed tube containing a magnetic stirring bar. The resulting solution was degassed using three freeze-pump-thaw cycles and the tube was finally backfilled with argon. The samples were irradiated with the respective light source for the mentioned time. The reaction was monitored by TLC. Once the reaction was completed, the reaction mixture was treated with H_2O (15.0 mL) and DCM (8.0 mL). The organic and aqueous layers were then separated, and the aqueous layer was extracted with DCM (3 x 8 mL). The combined organic extracts were dried (Na_2SO_4), then the solvent was removed under reduced pressure and the remaining residue was purified by column chromatography. The yield of **4** was the isolated yield.

Table S1. Optimization of reaction conditions[a]



1a 2a 3a 4

Entry	CF_3 source	catalyst	additive	solvent	time (h)	yield[b] (%)
1	Togni's II	MB (10 mol %)	-	THF/H_2O (5:1)	12	59
2	CF_3SO_2Na	MB (10 mol %)	-	THF/H_2O (5:1)	12	17
3	Togni's II	Rose Bengal (10 mol %)	-	THF/H_2O (5:1)	12	31
4	Togni's II	Eosin Y (10 mol %)	-	THF/H_2O (5:1)	12	31
5	Togni's II	$Ir(ppy)_3$ (10 mol %)	-	THF/H_2O (5:1)	12	37
6	Togni's II	Mes-$Acr^+BF_4^-$ (10 mol %)	-	THF/H_2O (5:1)	12	32
7	Togni's II	Mes-$Acr^+ClO_4^-$ (10 mol %)	-	THF/H_2O (5:1)	12	35
8	Togni's II	MB (10 mol %)	-	MeCN/H_2O (5:1)	12	28
9	Togni's II	MB (10 mol %)	-	MeOH/H_2O (5:1)	12	17
10	Togni's II	MB (10 mol %)	-	EtOH/H_2O (5:1)	12	21
11	Togni's II	MB (10 mol %)	-	DCE/H_2O (5:1)	12	55
12	Togni's II	MB (10 mol %)	-	DCM/H_2O (5:1)	12	57
13	Togni's II	MB (10 mol %)	-	1,4-dioxane/H_2O (5:1)	12	35
14	Togni's II	MB (10 mol %)	-	THF/H_2O (4:2)	12	59
15	Togni's II	MB (10 mol %)	-	THF/H_2O (3:3)	12	63
16	Togni's II	MB (5 mol %)	-	THF/H_2O (3:3)	12	61
17	Togni's II	MB (1 mol %)	-	THF/H_2O (3:3)	12	61

18	Togni's II	MB (1 mol %)	-	THF/H_2O (3:3)	12	55 [c]
19	Togni's II	MB (1 mol %)	-	THF/H_2O (3:3)	12	58 [d]
20	Togni's II	MB (1 mol %)	NaOH	THF/H_2O (3:3)	12	< 5
21	Togni's II	MB (1 mol %)	DBU	THF/H_2O (3:3)	12	N.D.
22	Togni's II	MB (1 mol %)	K_2CO_3	THF/H_2O (3:3)	12	< 5
23	Togni's II	MB (1 mol %)	K_3PO_4	THF/H_2O (3:3)	12	11
24	Togni's II	MB (1 mol %)	TEA	THF/H_2O (3:3)	12	10
25	Togni's II	MB (1 mol %)	DMAP	THF/H_2O (3:3)	12	24
26	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	12	73
27	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	12	80 [e]
28	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	12	80[e, f]
29	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	12	N.D. [g]
30	Togni's II	MB (1 mol %)	1M HCl	THF/H_2O (3:3)	12	65
31	Togni's II	MB (1 mol %)	TFA	THF/H_2O (3:3)	12	61
32	Togni's II	MB (1 mol %)	TfOH	THF/H_2O (3:3)	12	59
33	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	4	37 [e]
34	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	8	59 [e]
35	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	18	80 [e]
36	Togni's II	MB (1 mol %)	AcOH	THF/H_2O (3:3)	24	79 [e]
37	Togni's II	MB (1 mol %)	AcOH	DMSO/H_2O (3:3)	12	74 [e]
38	Togni's II	MB (1 mol %)	AcOH	DMF/H_2O (3:3)	12	80 [e]
39	Togni's II	MB (1 mol %)	AcOH	DCE/H_2O (3:3)	12	47 [e]
40	Togni's II	MB (1 mol %)	AcOH	Acetone/H_2O (3:3)	12	39 [e]
41	Togni's II	MB (1 mol %)	AcOH	DMF/H_2O (4:2)	12	83 [e]
42	**Togni's II**	**MB (1 mol %)**	**AcOH**	**DMF/H_2O (5:1)**	**12**	**87 [e]**

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.33 mmol), **3a** (0.36 mmol), catalyst, additive (0.3 mmol) and solvent (6 mL) irradiated with 8 W white bulb at the indicated reaction conditions. [b]Isolated yield. [c]irradiated with 5 W 635 nm LEDs. [d]irradiated with 8 W 635 nm LEDs. [e]N_2 atmosphere. [f]irradiated with 16 W white bulb. [g]Without light.

3. Cyclic voltammetry analyses

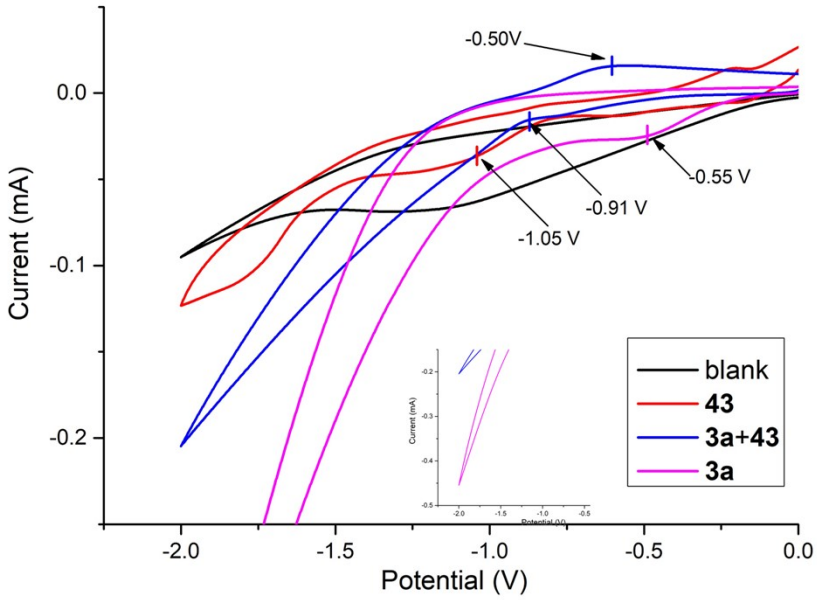


Fig. S1. Cyclic voltammetry experiments[a].

[a]Test conditions: Cyclic voltammograms of 0.1M $^{n}Bu_4NBF_4$ solution in THF at room temperature: (a) blank; (b) blank + **43**(0.1 M); (c) blank + **3a**(0.1 M) + **43**(0.1 M); (d) blank + **3a**(0.1 M). The voltammogram was obtained at a scan rate of 50 mV/s with glass carbon as the working electrode, Pt wire, and Ag/Ag^+ as the counter and reference electrode.

4. On/Off light-illumination experiments

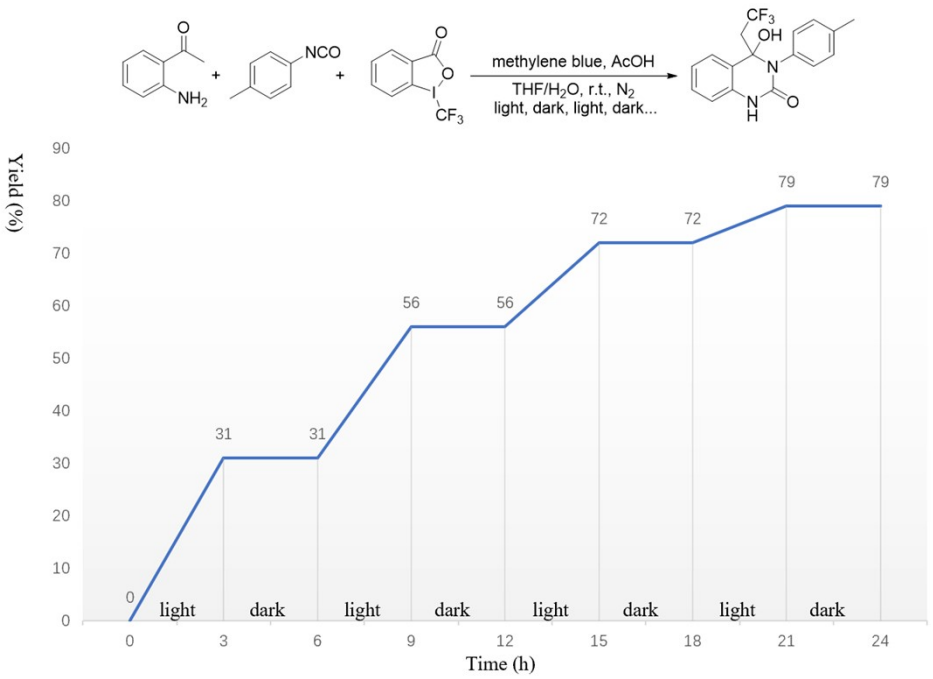


Fig. S2. On/Off light-illumination experiments

The On/Off light-illumination experiments were also carried out under the standard conditions, and the result demonstrated that the continuous irradiation of visible-light is essential for the present procedure.

5. The Computational Calculations

5.1. Computational Details

Density functional theory (DFT) calculations were performed with Gaussian 16. [1] The geometry of each species was optimized using the B3LYP functional[2] and the 6-311G(d,p) basis set with the SMD[3] solvation model for THF. Frequency calculations were also conducted at the same level of theory to obtain vibrational frequencies to determine the identity of stationary points as intermediates or transition states, as well as obtaining the thermal corrections to enthalpy ($H_{correction}$) and free energy ($G_{correction}$) at the temperature of 298 K. All DFT calculations were with an ultrafine integration grid. All structural figures were generated with CYLview[4]. Distances in structural figures are shown in Å and energies are in kcal/mol.

5.2. DFT-computed Gibbs free-energy profiles for benzyl isocyanate[a].

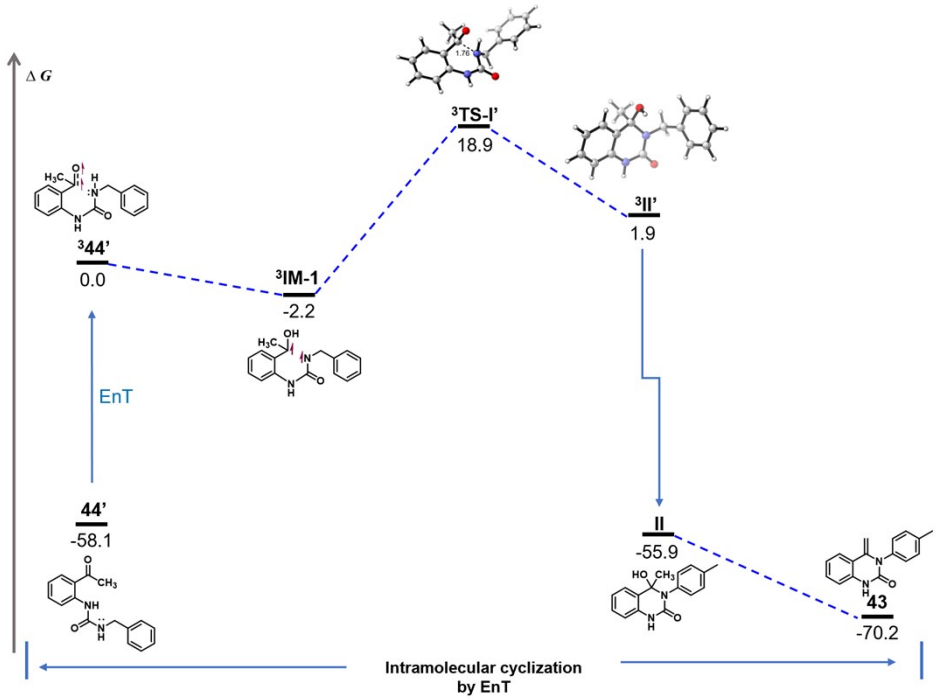
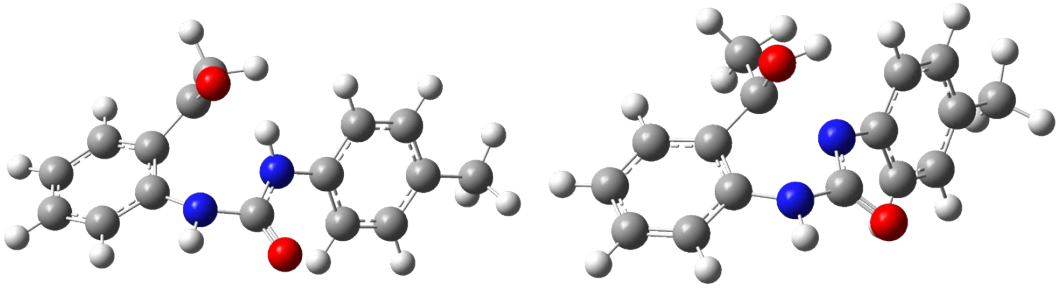


Fig. S3. DFT-computed Gibbs free-energy profiles for benzyl isocyanate[a].

[a]Values are in kcal mol^{-1}, obtained at the B3LYP/6-311G (d, p), SMD (THF) level of theory for the intramolecular cyclization reaction sequence.

5.3. IRC Scan data



P1 **P41**

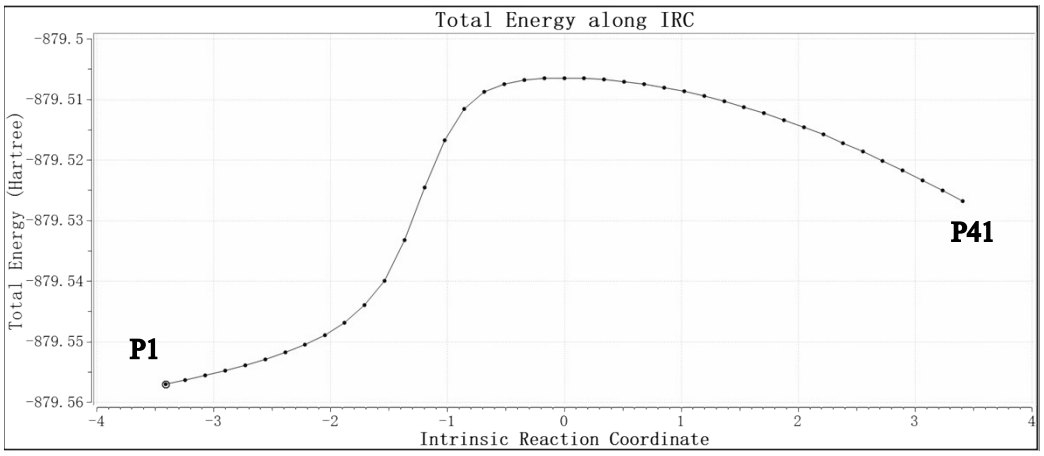
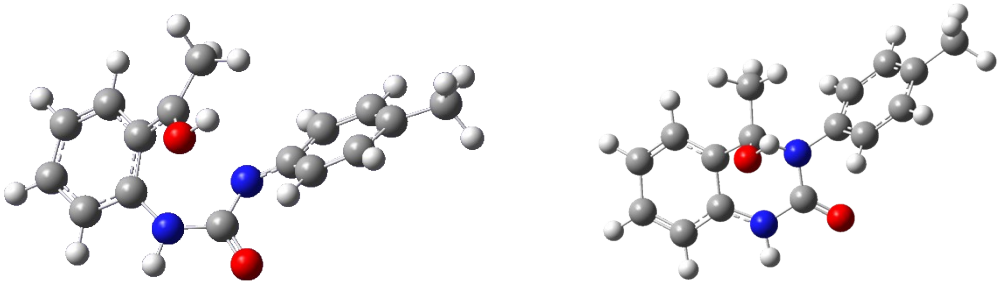


Figure S4. IRC scan of **TS-1**.



P1 **P41**

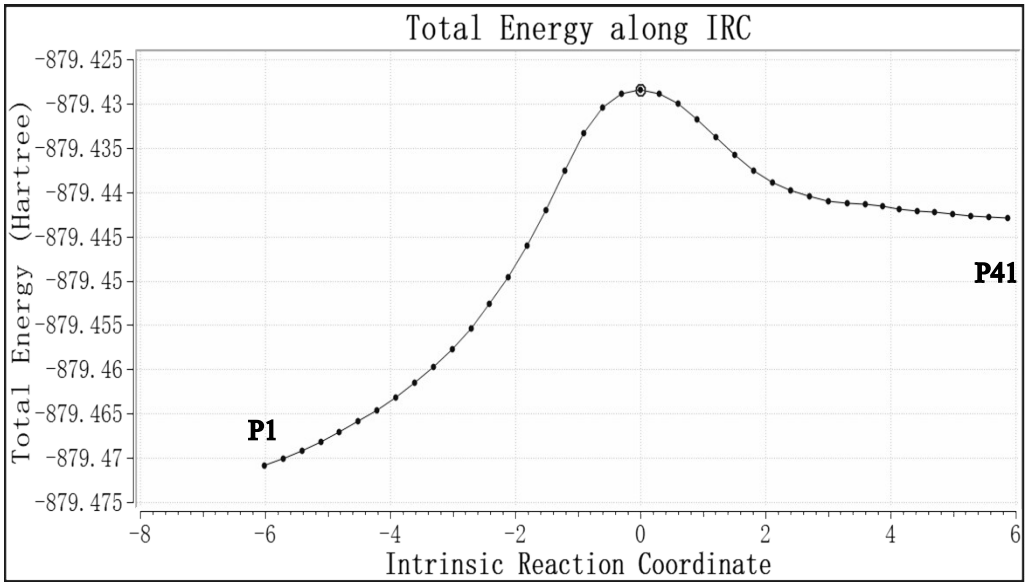
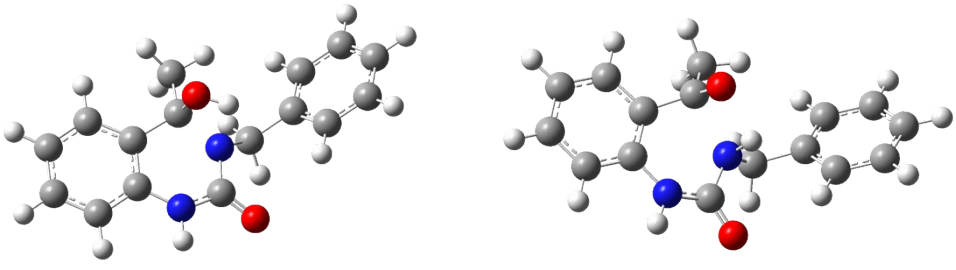


Figure S5. IRC scan of ^{3}TS-1.



P1 **P41**

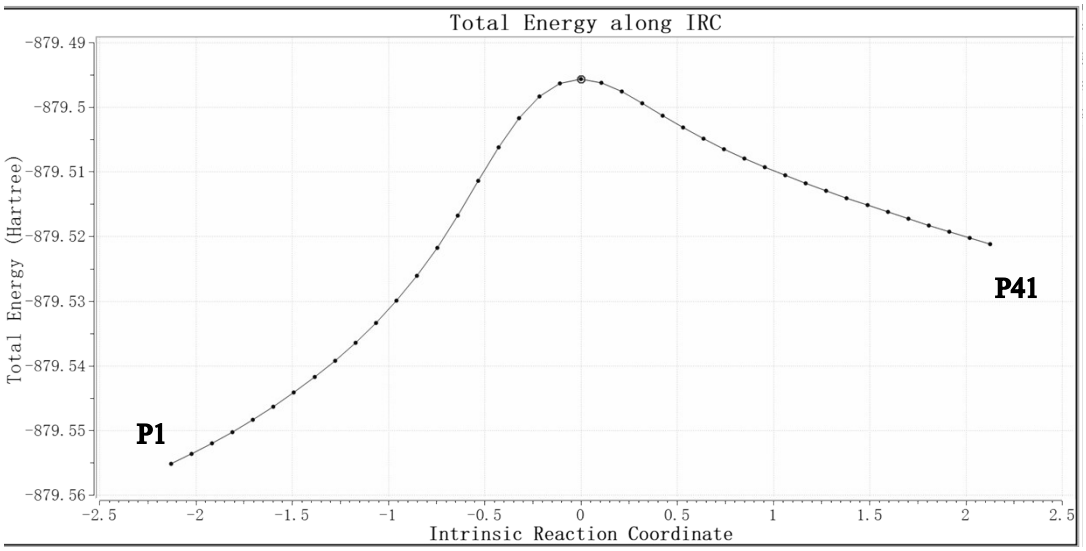


Figure S6. IRC scan of ^{3}TS-1'.

5.4. Cartesian Coordinates and Energies of Calculated Structures

1a			
E[B3LYP/6-311G(d,p)/SMD(THF)]= -440.38988784			
Zero-point correction=0.153503			
Thermal correction to Energy=0.162839			
Thermal correction to Enthalpy=0.163783			
Thermal correction to Gibbs Free Energy=0.119017			
C	−1.7478080	0.6324750	−0.9503300
C	−0.3747320	0.7232540	−0.8524250
C	0.2446500	1.7972170	−0.1659040
C	−0.5912570	2.8003440	0.4233040
C	−1.9908150	2.6644890	0.2992370
C	−2.5759000	1.6066510	−0.3704940
H	−2.1876130	−0.2043460	−1.4828670
H	0.2598250	−0.0343390	−1.3015730
H	−2.6294370	3.4175070	0.7431200
H	−3.6537810	1.5318110	−0.4478440
C	−0.0122280	3.9557270	1.1352970
O	1.2053300	4.1125760	1.2513750
C	−0.9380460	4.9918080	1.7451090
H	−1.5993170	4.5432090	2.4916820
H	−0.3271690	5.7574940	2.2219600
H	−1.5683180	5.4586970	0.9831110
N	1.5967530	1.8365030	−0.0750900
H	2.1524490	1.1600230	−0.5733190
H	2.0264540	2.6416240	0.3586640

2a
E[B3LYP/6-311G(d,p)/SMD(THF)]= **-439.174397487**
Zero-point correction=0.130631
Thermal correction to Energy=0.139579
Thermal correction to Enthalpy=0.140524
Thermal correction to Gibbs Free Energy=0.095317

C	−1.4830410	0.2484440	0.0204360
C	−0.1032330	0.3026080	0.2369890
C	0.6118370	1.4866130	0.0722000
C	−0.0521240	2.6497960	−0.3170080
C	−1.4345380	2.6178440	−0.5392930
C	−2.1317510	1.4287290	−0.3702810
H	0.4258090	−0.5948410	0.5401140
H	1.6813950	1.5174830	0.2427740
H	−1.9513740	3.5219320	−0.8418910
H	−3.2029050	1.4171880	−0.5456350
C	−2.2584370	−1.0330350	0.1981380
H	−1.6066700	−1.8525120	0.5075360
H	−3.0409670	−0.9201350	0.9554260
H	−2.7527080	−1.3285810	−0.7330020
N	0.6922260	3.8265250	−0.4751240
C	0.5479770	4.9801810	−0.7758600
O	0.5401720	6.1196050	−1.0503910

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E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.576779978**
Zero-point correction=0.289155
Thermal correction to Energy=0.307535
Thermal correction to Enthalpy=0.308479
Thermal correction to Gibbs Free Energy=0.238711

C	−0.2292600	0.5643620	−1.6018530
C	−0.9702690	−0.1568460	−0.6501360
C	−2.1498310	0.4359960	−0.1045240
C	−2.5035880	1.7322580	−0.5239570
C	−1.7533230	2.4371790	−1.4496780
C	−0.6147120	1.8374160	−1.9909390
H	0.6443770	0.1128690	−2.0489900
H	−3.3956550	2.1906000	−0.1185410
H	−2.0527010	3.4325240	−1.7548710
H	−0.0220720	2.3632860	−2.7314630
C	−3.0261500	−0.2816930	0.8586420
O	−2.8637870	−1.4706340	1.1293410
C	−4.1617660	0.4668440	1.5240050
H	−4.6302140	−0.1974010	2.2491270
H	−3.8063310	1.3683510	2.0293830
H	−4.9106740	0.7732920	0.7878940
N	−0.6054110	−1.4386790	−0.2487180
H	−1.3675630	−1.9594230	0.1808060
C	0.5046390	−2.2221110	−0.5577670
N	1.7377320	−1.6078690	−0.6487550
H	2.4328810	−2.2312530	−1.0396330
C	2.2654100	−0.5048590	0.0721850
C	3.4134830	0.1162990	−0.4349500
C	1.7266010	−0.0450780	1.2764870
C	4.0047750	1.1720830	0.2483960
H	3.8414060	−0.2374180	−1.3672400
C	2.3200940	1.0269770	1.9401450

H	0.8541110	−0.5229580	1.7025080
C	3.4654520	1.6574870	1.4462640
H	4.8985220	1.6316420	−0.1620980
H	1.8850080	1.3678610	2.8742160
O	0.3828180	−3.4255530	−0.7290730
C	4.0925110	2.8270270	2.1638800
H	5.1817990	2.7355150	2.2004000
H	3.8648330	3.7709170	1.6556470
H	3.7240300	2.9077490	3.1889150

TSI

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.506501197**
Zero-point correction= 0.285133
Thermal correction to Energy= 0.302734
Thermal correction to Enthalpy= 0.303678
Thermal correction to Gibbs Free Energy= 0.238766

C	−0.3020180	−0.5436080	0.4122790
C	0.9780930	−0.0900890	0.8209960
C	1.1581040	1.1814290	1.3217180
C	0.0577270	2.0515820	1.3979490
C	−1.1821940	1.6676680	0.9258170
C	−1.3812680	0.3843480	0.3767870
H	1.8087230	−0.7845040	0.8084400
H	2.1328640	1.4980340	1.6718780
H	0.1852690	3.0495760	1.8021840
H	−2.0096370	2.3692440	0.9264240
C	−0.5056220	−1.9447510	0.1810010
N	−2.1177760	−1.7797510	−1.5598970
C	−2.8521880	−0.6469000	−1.4333500
N	−2.5768940	0.1260310	−0.2587370
H	−3.2236830	0.9060780	−0.2278090
O	−3.7549650	−0.2274420	−2.1547340
O	−1.5681180	−2.5470840	0.7250410
H	−2.1851930	−2.5780030	−0.0767480
C	0.5722310	−2.8407270	−0.3072530
H	0.9980720	−3.3796010	0.5490750
H	0.1265820	−3.5994300	−0.9567690
H	1.3627240	−2.3169680	−0.8410750
C	−2.0554930	−2.4205800	−2.8045660
C	−1.9701710	−3.8232140	−2.8327410
C	−1.9897110	−1.7398690	−4.0373590
C	−1.8246020	−4.5137350	−4.0338430
H	−2.0394150	−4.3714470	−1.8992820
C	−1.8411110	−2.4389260	−5.2271220
H	−2.0607130	−0.6602490	−4.0544340
C	−1.7565800	−3.8393070	−5.2557500
H	−1.7687500	−5.5979230	−4.0177970
H	−1.7904440	−1.8850380	−6.1602570
C	−1.6135200	−4.5799520	−6.5620650
H	−0.7740880	−4.1946750	−7.1497700

H	−1. 4483110	−5. 6471320	−6. 3981100
H	−2. 5121860	−4. 4732270	−7. 1797870

II

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.573235913**
Zero-point correction=0.290489
Thermal correction to Energy=0.307862
Thermal correction to Enthalpy=0.308806
Thermal correction to Gibbs Free Energy=0.244343

C	−2. 6583300	0. 3219700	1. 4634160
C	−1. 3354500	0. 2795450	1. 0467470
C	−0. 7866850	1. 3670240	0. 3538460
C	−1. 5569810	2. 5034950	0. 0805200
C	−2. 8873500	2. 5216890	0. 5070970
C	−3. 4404610	1. 4465740	1. 1964360
H	−3. 0787290	−0. 5223590	1. 9983900
H	−0. 7154770	−0. 5873310	1. 2497500
H	−3. 5099120	3. 3803090	0. 2914990
H	−4. 4751130	1. 4840350	1. 5164540
N	0. 5338310	1. 3298280	−0. 0724500
H	1. 0858520	0. 5024620	0. 1071470
C	1. 2516300	2. 4182220	−0. 5156090
O	2. 4521470	2. 3368540	−0. 7325350
N	0. 5268140	3. 5919130	−0. 6546380
C	1. 2761860	4. 7164080	−1. 1652660
C	1. 8052380	5. 6545930	−0. 2807890
C	1. 4759420	4. 8820050	−2. 5367120
C	2. 5122550	6. 7526140	−0. 7636020
H	1. 6589330	5. 5215080	0. 7849990
C	2. 1802150	5. 9856070	−3. 0123370
H	1. 0943500	4. 1409600	−3. 2289840
C	2. 7108060	6. 9395200	−2. 1365490
H	2. 9155730	7. 4759200	−0. 0621290
H	2. 3260670	6. 1018710	−4. 0815630
C	3. 5031460	8. 1139130	−2. 6546070
H	3. 1528930	8. 4279130	−3. 6409060
H	3. 4367230	8. 9691810	−1. 9779780
H	4. 5637900	7. 8556200	−2. 7521450
C	−0. 9587860	3. 6288340	−0. 7544060
C	−1. 4660640	5. 0089620	−0. 3252620
H	−1. 0393040	5. 7893290	−0. 9572040
H	−2. 5491700	5. 0528820	−0. 4333730
H	−1. 2029750	5. 2211640	0. 7123340
O	−1. 3752000	3. 3641420	−2. 1048550
H	−1. 2305690	4. 1679730	−2. 6214570

43

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-803.107031286**
Zero-point correction=0.263105
Thermal correction to Energy=0.278898

Thermal correction to Enthalpy=0.279842
Thermal correction to Gibbs Free Energy=0.217576

C	−2. 0326350	−0. 2184310	−0. 0135940
C	−0. 6852040	−0. 2654030	−0. 3932770
C	0. 0658890	0. 8997910	−0. 4194290
C	−0. 5195770	2. 1172210	−0. 0608620
C	−1. 8560290	2. 1575990	0. 3116390
C	−2. 6441930	0. 9970890	0. 3338830
H	−0. 2430840	−1. 2190230	−0. 6610400
H	1. 1087680	0. 8596040	−0. 7127980
H	0. 0657330	3. 0290970	−0. 0688650
H	−2. 2930760	3. 1055430	0. 5972490
N	−2. 7853960	−1. 3843300	0. 0226540
H	−2. 3483560	−2. 2636780	−0. 2175870
C	−4. 0811820	−1. 4816920	0. 4705520
N	−4. 6825600	−0. 2780480	0. 8263360
C	−6. 0469080	−0. 3675250	1. 2905400
C	−7. 0992310	−0. 3775900	0. 3766780
C	−6. 3111890	−0. 4272530	2. 6546300
C	−8. 4108180	−0. 4556250	0. 8328210
H	−6. 8878880	−0. 3278230	−0. 6853930
C	−7. 6289240	−0. 5038220	3. 1028140
H	−5. 4891580	−0. 4173600	3. 3613390
C	−8. 6989840	−0. 5200670	2. 2028560
H	−9. 2242220	−0. 4687370	0. 1142040
H	−7. 8260980	−0. 5556740	4. 1685210
C	−10. 1259690	−0. 6103970	2. 6837230
H	−10. 7184550	0. 2374460	2. 3255930
H	−10. 6091940	−1. 5200800	2. 3127130
H	−10. 1782960	−0. 6227360	3. 7742080
O	−4. 6541920	−2. 5561230	0. 5446430
C	−4. 0771570	1. 0056730	0. 7015030
C	−4. 7833450	2. 1311400	0. 9144880
H	−5. 8270360	2. 1126670	1. 1897130
H	−4. 3179800	3. 1001300	0. 8118560

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E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.474725992**
Zero-point correction=0.285021
Thermal correction to Energy=0.303876
Thermal correction to Enthalpy=0.304820
Thermal correction to Gibbs Free Energy=0.233806

C	−0. 2269330	0. 5658500	−1. 6569560
C	−0. 9506650	−0. 1349530	−0. 6725760
C	−2. 1919360	0. 4378750	−0. 0655070
C	−2. 4564940	1. 7869420	−0. 4154840
C	−1. 7020740	2. 4537330	−1. 3669470
C	−0. 5939670	1. 8456970	−2. 0311370
H	0. 6324940	0. 0900110	−2. 1107920
H	−3. 2908630	2. 3018480	0. 0415460
H	−1. 9711770	3. 4737360	−1. 6218790

H	−0.0435420	2.3862180	−2.7887530
C	−3.0475250	−0.3217780	0.8026790
O	−2.8314660	−1.5501800	1.0722060
C	−4.2571540	0.3453580	1.4230400
H	−4.7490190	−0.3785720	2.0731960
H	−3.9876870	1.2246290	2.0186110
H	−4.9758560	0.6758600	0.6645940
N	−0.5828110	−1.3476540	−0.1763130
H	−1.3687710	−1.7844550	0.3727620
C	0.4963260	−2.1956410	−0.5315010
N	1.7529230	−1.6612650	−0.5475320
H	2.4373040	−2.2994290	−0.9363520
C	2.2853290	−0.5256610	0.1248370
C	3.3934930	0.1110210	−0.4419050
C	1.7785230	−0.0592810	1.3397810
C	3.9801990	1.1979520	0.1968330
H	3.7902800	−0.2475370	−1.3857310
C	2.3642540	1.0428910	1.9568670
H	0.9358070	−0.5513530	1.8082380
C	3.4743980	1.6908100	1.4053730
H	4.8403160	1.6774740	−0.2592640
H	1.9525010	1.3955190	2.8969440
O	0.2639130	−3.3606810	−0.8000250
C	4.1250300	2.8583680	2.1042560
H	4.9433450	2.5225020	2.7516060
H	4.5481860	3.5663610	1.3872290
H	3.4104940	3.3945450	2.7331170

^{3}IM-1

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.490467544**
Zero-point correction= 0.286086
Thermal correction to Energy= 0.304504
Thermal correction to Enthalpy= 0.305449
Thermal correction to Gibbs Free Energy= 0.237078

C	0.3092440	0.4714880	−0.2790120
C	1.1548080	1.0376310	0.7291240
C	1.6206700	0.3132770	1.8083730
C	1.2775530	−1.0355640	1.9582770
C	0.4736210	−1.6293030	0.9856810
C	−0.0045110	−0.9249140	−0.1160100
H	1.4179840	2.0849280	0.6538210
H	2.2494500	0.8013870	2.5455990
H	1.6334260	−1.6134100	2.8028220
H	0.2245730	−2.6829070	1.0607530
C	−0.1304460	1.3135260	−1.3382180
N	−2.7491040	−0.8010550	−0.8609070
C	−1.9973110	−1.8938290	−1.3214100
N	−0.6499480	−1.7148090	−1.1342990
H	−0.1073230	−2.5023130	−1.4675780
O	−2.4587180	−2.8405210	−1.9439210
O	−1.2144130	1.0582700	−2.0984640

H	−1.8384050	0.4482310	−1.6260550
C	0.5270650	2.6083660	−1.7002190
H	1.5970400	2.6128200	−1.4881240
H	0.3857220	2.7845220	−2.7701250
H	0.0736720	3.4606820	−1.1738880
C	−3.9528720	−0.9275500	−0.2954750
C	−4.6824500	0.2777300	−0.0387950
C	−4.5529230	−2.1666990	0.1090470
C	−5.9168670	0.2437080	0.5683990
H	−4.2302990	1.2164240	−0.3364830
C	−5.7863060	−2.1728080	0.7144780
H	−4.0294410	−3.0933050	−0.0787390
C	−6.5020790	−0.9777430	0.9585250
H	−6.4509710	1.1694230	0.7524250
H	−6.2263490	−3.1176990	1.0160070
C	−7.8557430	−1.0234780	1.6017860
H	−7.8493550	−1.6670680	2.4866720
H	−8.1974780	−0.0293440	1.8939810
H	−8.5941020	−1.4449990	0.9090420

^{3}TS-1

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.428460479**
Zero-point correction= 0.284126
Thermal correction to Energy= 0.302014
Thermal correction to Enthalpy= 0.302958
Thermal correction to Gibbs Free Energy= 0.237187

C	−0.6507680	−0.8268030	0.0148430
C	−1.4927360	0.2624090	−0.0310610
C	−2.8678520	0.0937790	0.2202420
C	−3.3891840	−1.2009970	0.7379930
C	−2.5522350	−2.3265020	0.5535650
C	−1.2256270	−2.1483090	0.2333080
H	0.4070340	−0.7278640	−0.1881170
H	−1.1302300	1.2398370	−0.3363830
H	−2.9264390	−3.3231980	0.7545320
H	−0.5784490	−3.0155540	0.1597940
N	−3.7810300	1.0422960	−0.1223990
H	−3.4376210	1.9515710	−0.4130450
C	−5.1898980	0.9347840	−0.2334440
O	−5.8085510	1.9580140	−0.5237610
N	−5.6790880	−0.3250670	−0.0583460
C	−7.0810110	−0.4843520	0.0145420
C	−7.9079210	0.2998140	0.8404270
C	−7.6722150	−1.5253460	−0.7138630
C	−9.2700800	0.0412830	0.9257630
H	−7.4814040	1.1278480	1.3928230
C	−9.0387890	−1.7749900	−0.6235950
H	−7.0440970	−2.1320000	−1.3565940
C	−9.8649270	−0.9995900	0.1970430
H	−9.8882630	0.6632300	1.5664400
H	−9.4709210	−2.5849780	−1.2027960

C	−11.3489050	−1.2528630	0.2840400
H	−11.6226510	−2.1885000	−0.2081170
H	−11.6842530	−1.3047710	1.3244160
H	−11.9149790	−0.4463850	−0.1953430
C	−4.6981020	−1.2024840	1.3298800
C	−5.3910400	−2.5118820	1.5815420
H	−4.8772850	−3.0421560	2.3898510
H	−6.4235660	−2.3480750	1.8968710
H	−5.3980250	−3.1435860	0.6930380
O	−4.8262850	−0.2783790	2.3532130
H	−5.7476970	−0.2744690	2.6512620

III

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-1140.83707422**
Zero-point correction=0.278593
Thermal correction to Energy=0.298272
Thermal correction to Enthalpy=0.299216
Thermal correction to Gibbs Free Energy=0.227347

C	−2.1843600	−0.2391150	−0.0803250
C	−0.8428520	−0.2704910	−0.4412230
C	−0.0775500	0.8958540	−0.3929950
C	−0.6710520	2.0942840	0.0157140
C	−2.0090640	2.1337740	0.3757200
C	−2.8149410	0.9634470	0.3508490
H	−0.4039540	−1.2087960	−0.7643630
H	0.9677080	0.8675830	−0.6768960
H	−0.0846590	3.0056370	0.0495050
H	−2.4428730	3.0788600	0.6724650
N	−2.9670100	−1.3891960	−0.1459700
H	−2.5480380	−2.2496340	−0.4739320
C	−4.2717380	−1.5074420	0.2657680
N	−4.8607280	−0.3222560	0.7174370
C	−6.1709820	−0.4654920	1.3136460
C	−7.3085370	−0.5126990	0.5105320
C	−6.2913890	−0.5697540	2.6966170
C	−8.5613360	−0.6578690	1.0964100
H	−7.2094400	−0.4367910	−0.5650210
C	−7.5521430	−0.7094910	3.2743330
H	−5.4027340	−0.5442420	3.3174440
C	−8.7067140	−0.7555260	2.4867230
H	−9.4415860	−0.6971240	0.4627340
H	−7.6362190	−0.7912060	4.3529660
C	−10.0737990	−0.8979730	3.1075920
H	−10.6617710	0.0166770	2.9758970
H	−10.6365990	−1.7120250	2.6413420
H	−10.0061410	−1.1007150	4.1782500
O	−4.8630340	−2.5729060	0.2427880
C	−4.1835910	0.9231240	0.7181230
C	−4.9618460	2.1536310	1.0787580
H	−4.3385910	2.8567020	1.6351140

C	−5. 5237700	2. 9228380	−0. 1043160
F	−6. 2627610	3. 9778830	0. 3176810
F	−4. 5651510	3. 4233160	−0. 9178490
F	−6. 3313450	2. 1680890	−0. 8851980
H	−5. 8147190	1. 9164190	1. 7138600

III'

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-1140.78735467**
Zero-point correction=0.275752
Thermal correction to Energy=0.295778
Thermal correction to Enthalpy=0.296722
Thermal correction to Gibbs Free Energy=0.225908

C	−2. 0059800	−0. 1938000	−0. 0774310
C	−0. 6089770	−0. 2806630	−0. 0980060
C	0. 1576440	0. 8579800	0. 1137750
C	−0. 4567060	2. 0868650	0. 3575820
C	−1. 8461050	2. 1676390	0. 3771010
C	−2. 6328890	1. 0355390	0. 1576420
H	−0. 1390350	−1. 2419770	−0. 2753550
H	1. 2391750	0. 7837300	0. 0943750
H	0. 1400160	2. 9755420	0. 5248730
H	−2. 3275940	3. 1223980	0. 5530690
N	−2. 7912200	−1. 3244100	−0. 2780850
H	−2. 3304950	−2. 2101130	−0. 4385140
C	−4. 1131420	−1. 4326490	0. 1047270
N	−4. 7406320	−0. 2353530	0. 4198260
C	−6. 0551230	−0. 3262770	1. 0162580
C	−7. 1860850	−0. 5488650	0. 2316850
C	−6. 1913220	−0. 2241420	2. 4007610
C	−8. 4392830	−0. 6476640	0. 8283520
H	−7. 0841780	−0. 6486180	−0. 8412930
C	−7. 4501460	−0. 3183390	2. 9895140
H	−5. 3096570	−0. 0857030	3. 0154250
C	−8. 5959390	−0. 5276000	2. 2146980
H	−9. 3102600	−0. 8256220	0. 2058080
H	−7. 5397390	−0. 2382670	4. 0680150
C	−9. 9616530	−0. 6036300	2. 8499380
H	−10. 4371000	0. 3837340	2. 8722190
H	−10. 6236710	−1. 2706850	2. 2924640
H	−9. 9023620	−0. 9608550	3. 8806920
O	−4. 6676300	−2. 5169600	0. 1754170
C	−4. 1591750	1. 1069830	0. 1030960
H	−5. 5686460	2. 7351740	0. 7799240
H	−4. 2776760	2. 2248140	2. 0294250
C	−4. 6993310	2. 1465490	1. 0373450
C	−4. 5760340	1. 4891750	−1. 3481360
F	−4. 0369230	2. 6688040	−1. 7236460
F	−4. 1818440	0. 5660680	−2. 2489470
F	−5. 9150120	1. 6161080	−1. 4797490

IV-1

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-1140.69088778**
Zero-point correction=0.282096
Thermal correction to Energy=0.301116
Thermal correction to Enthalpy=0.302061
Thermal correction to Gibbs Free Energy=0.233542

C	−2. 1710790	−0. 2678030	−0. 0046840
C	−0. 8380520	−0. 2784320	−0. 4315420
C	−0. 1484810	0. 9144770	−0. 5029710
C	−0. 7618780	2. 1349330	−0. 1538400
C	−2. 0707410	2. 1567990	0. 2595480
C	−2. 8186740	0. 9494940	0. 3392380
H	−0. 3686240	−1. 2192200	−0. 6928860
H	0. 8851320	0. 9105930	−0. 8283460
H	−0. 1964560	3. 0562150	−0. 2078830
H	−2. 5255330	3. 0999020	0. 5240360
N	−2. 8817070	−1. 4323730	0. 0917790
H	−2. 4293440	−2. 3065790	−0. 1614560
C	−4. 1735750	−1. 5540650	0. 5218300
N	−4. 7941390	−0. 2962630	0. 8661110
C	−6. 1552050	−0. 4304010	1. 3841490
C	−7. 2242500	−0. 5059870	0. 5010710
C	−6. 3417470	−0. 5303470	2. 7592070
C	−8. 5085260	−0. 6620730	1. 0131420
H	−7. 0588830	−0. 4445760	−0. 5668360
C	−7. 6332280	−0. 6845630	3. 2525040
H	−5. 4933990	−0. 4927950	3. 4322650
C	−8. 7360810	−0. 7494620	2. 3915730
H	−9. 3460440	−0. 7210770	0. 3268810
H	−7. 7839300	−0. 7625560	4. 3236510
C	−10. 1331790	−0. 8896230	2. 9373840
H	−10. 5564200	0. 0939010	3. 1703590
H	−10. 7959500	−1. 3688240	2. 2139330
H	−10. 1426410	−1. 4760500	3. 8587630
O	−4. 7661500	−2. 5970130	0. 6150550
C	−4. 1719790	0. 8893270	0. 7602580
C	−4. 9356470	2. 1381630	1. 1210330
H	−4. 2821110	2. 8219360	1. 6623590
C	−5. 5000360	2. 9036550	−0. 0706090
F	−6. 1602220	3. 9898640	0. 3682560
F	−4. 5483110	3. 3297700	−0. 9264590
F	−6. 3672210	2. 1639790	−0. 7904040
H	−5. 7810020	1. 9044490	1. 7637100

IV-2

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-1140.69089454**
Zero-point correction=0.282079
Thermal correction to Energy=0.301122
Thermal correction to Enthalpy=0.302066
Thermal correction to Gibbs Free Energy=0.233357

C	2. 1998960	0. 8684620	2. 7394440
C	3. 5672960	0. 7655900	2. 4118710
C	4. 3150330	1. 8837750	2. 1049750

C	3.6966790	3.1394340	2.1202640
C	2.3165410	3.2707450	2.4324440
C	1.5826120	2.0945660	2.7507370
H	1.6373790	-0.0223890	2.9871200
H	4.0428080	-0.2081130	2.4058320
H	5.3674970	1.8099260	1.8587840
H	0.5347380	2.1561150	3.0045420
C	1.7518810	4.5720730	2.4252060
N	2.5236250	5.6415880	2.1712830
N	4.4094570	4.2712020	1.8347180
H	5.3948140	4.1855220	1.6007930
C	3.9273580	5.5503590	1.8444840
O	4.5853540	6.5292230	1.6067550
C	0.2904350	4.7927660	2.7226720
H	0.1102290	5.8143490	3.0484850
H	-0.0241080	4.1247830	3.5242310
C	-0.6411450	4.5477190	1.5408430
F	-1.9112630	4.7777740	1.9177830
F	-0.5830680	3.2839660	1.0724330
F	-0.3722330	5.3608690	0.4997500
C	2.0212020	7.0132210	2.2427660
C	1.6069750	7.6565650	1.0821590
C	2.0152790	7.6613170	3.4721520
C	1.1575970	8.9689680	1.1666260
H	1.6335530	7.1412410	0.1306900
C	1.5599730	8.9758550	3.5371790
H	2.3617250	7.1517250	4.3634420
C	1.1228970	9.6491450	2.3914590
H	0.8311650	9.4737590	0.2638340
H	1.5509160	9.4852710	4.4942900
C	0.6191800	11.0670850	2.4646530
H	0.8025570	11.5046300	3.4473760
H	1.1032150	11.6955330	1.7119640
H	-0.4583440	11.1065590	2.2733410

IV'

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-1140.65364164**
Zero-point correction=0.282019
Thermal correction to Energy=0.300297
Thermal correction to Enthalpy=0.301241
Thermal correction to Gibbs Free Energy=0.236235

C	-2.1801340	-0.2358120	-0.2438770
C	-0.8042330	-0.4116570	-0.0970040
C	-0.0642820	0.5263380	0.6137340
C	-0.6894390	1.6363230	1.1791970
C	-2.0631290	1.8081320	1.0310880
C	-2.8211080	0.8732240	0.3266550
H	-0.3266660	-1.2802510	-0.5362320
H	1.0044600	0.3867740	0.7260700
H	-0.1112630	2.3691860	1.7284360

H	−2.5386610	2.6855890	1.4514560
N	−2.9261680	−1.1795890	−0.9760570
H	−2.4209760	−1.8811070	−1.5055980
C	−4.2696730	−1.3495690	−0.9238860
N	−4.9101820	−0.3262370	−0.1353650
C	−5.9654020	−0.5469860	0.6631450
C	−6.9275760	−1.5636070	0.6202710
C	−6.0122290	0.4859790	1.7232180
C	−8.0475950	−1.3897250	1.4037350
H	−6.8494460	−2.3841740	−0.0762090
C	−7.3261820	0.6839100	2.3785860
H	−5.4132400	−0.0077560	2.5202940
C	−8.2996270	−0.2535250	2.2555050
H	−8.8270950	−2.1427580	1.3364750
H	−7.4469950	1.5440450	3.0276330
C	−9.6266770	−0.1558020	2.9570690
H	−10.4482400	−0.1667580	2.2346460
H	−9.7732750	−1.0068130	3.6290270
H	−9.6946480	0.7614840	3.5431010
O	−4.8926030	−2.2554180	−1.4257270
C	−4.3066600	1.0282670	0.0598850
H	−4.5716680	2.1178640	1.9579640
C	−5.1820250	1.6621070	1.1842270
C	−4.5233760	1.8341880	−1.2533420
F	−4.1119140	3.1024510	−1.0841330
F	−3.8467580	1.3177420	−2.2943340
F	−5.8239180	1.8662510	−1.6032910
H	−5.8425460	2.4237240	0.7742710

4a

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-1216.7061989**
Zero-point correction=0.295750
Thermal correction to Energy=0.316422
Thermal correction to Enthalpy=0.317366
Thermal correction to Gibbs Free Energy=0.244847

C	−2.5748720	−1.5386730	0.0729150
C	−3.9078660	−1.9233040	−0.1103470
C	−4.8445200	−0.9874390	−0.5284060
C	−4.4573050	0.3292480	−0.7765960
C	−3.1293060	0.7054840	−0.5909430
C	−2.1718760	−0.2163540	−0.1582540
H	−4.1928530	−2.9542360	0.0707880
H	−5.8763610	−1.2891890	−0.6688180
H	−5.1828090	1.0615450	−1.1100560
H	−2.8518940	1.7344280	−0.7770660
N	−1.6209330	−2.4626760	0.4744180
H	−1.9071920	−3.4153080	0.6558740
C	−0.2598470	−2.2831150	0.3684420
N	0.1469850	−0.9999010	0.0051830
C	1.5802480	−0.8158380	−0.0717410
C	2.3069360	−0.3148930	1.0062070

C	2.2440970	-1.1517100	-1.2528160
C	3.6855470	-0.1390770	0.8920550
H	1.7937150	-0.0564280	1.9231190
C	3.6202500	-0.9825550	-1.3531540
H	1.6761030	-1.5425840	-2.0893490
C	4.3664070	-0.4707450	-0.2827810
H	4.2396670	0.2579150	1.7363610
H	4.1233430	-1.2488970	-2.2774620
C	5.8599980	-0.2966710	-0.4010870
H	6.2728800	0.2068680	0.4752580
H	6.3614000	-1.2654000	-0.4990040
H	6.1217780	0.2914140	-1.2860600
O	0.5172940	-3.2048560	0.5544900
C	-0.7364060	0.1601770	0.2016570
C	-0.2107630	1.3508810	-0.6602750
H	-0.8056290	1.4498230	-1.5665610
C	-0.1824220	2.7055290	0.0078970
F	0.0363660	3.6736330	-0.9145250
F	-1.3482900	3.0336670	0.6331750
F	0.7914350	2.8291820	0.9320120
H	0.8149690	1.1692930	-0.9742250
O	-0.6736870	0.4595210	1.6121600
H	-1.4130210	1.0419050	1.8323760

4a'

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-1216.69281245**
Zero-point correction=0.295395
Thermal correction to Energy=0.316488
Thermal correction to Enthalpy=0.317432
Thermal correction to Gibbs Free Energy=0.244704

C	-1.9883940	-0.1771090	0.0001500
C	-0.5903290	-0.2527380	-0.0176200
C	0.1647590	0.9090730	0.0596080
C	-0.4653970	2.1494020	0.1660960
C	-1.8548600	2.2176660	0.1818520
C	-2.6333480	1.0613890	0.0916200
H	-0.1123000	-1.2238950	-0.0862730
H	1.2470580	0.8457100	0.0446490
H	0.1202200	3.0584320	0.2343900
H	-2.3315040	3.1852970	0.2628380
N	-2.7574920	-1.3338270	-0.0645620
H	-2.2861060	-2.2264450	-0.1208850
C	-4.0786840	-1.4132770	0.3229260
N	-4.7255270	-0.1964080	0.4999490
C	-6.0561170	-0.2779260	1.0676650
C	-7.1672140	-0.5302730	0.2621860
C	-6.2231620	-0.1579280	2.4459510
C	-8.4319590	-0.6351530	0.8317340
H	-7.0411470	-0.6523240	-0.8058450
C	-7.4941020	-0.2627580	3.0080270
H	-5.3573900	0.0214090	3.0699160

C	−8.6201190	−0.4984160	2.2131090
H	−9.2862880	−0.8353310	0.1927480
H	−7.6087050	−0.1685110	4.0830900
C	−9.9990510	−0.5952890	2.8164690
H	−9.9523250	−0.6990280	3.9025480
H	−10.5889650	0.3005100	2.5926430
H	−10.5487320	−1.4511830	2.4147500
O	−4.6198880	−2.4909010	0.5090040
C	−4.1609340	1.0921370	0.0250880
C	−4.7461130	2.2769060	0.8216560
C	−4.5687420	1.3011580	−1.4670910
F	−3.9739040	2.3880080	−2.0062090
F	−4.2311540	0.2450700	−2.2327780
F	−5.9016630	1.4828180	−1.6167850
H	−5.8353260	2.2069520	0.8173470
H	−4.4740130	3.2080730	0.3142330
O	−4.2258540	2.2406460	2.1412340
H	−4.8200860	2.7547910	2.6994450

^{3}44’

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.471446263**
Zero-point correction=0.286700
Thermal correction to Energy=0.305013
Thermal correction to Enthalpy=0.305957
Thermal correction to Gibbs Free Energy=0.236027

C	1.5610100	1.7529610	0.7619090
C	1.8041160	0.3976760	0.4685710
C	2.9518420	−0.0181150	−0.3905600
C	3.6506160	1.0520970	−1.0080600
C	3.3644810	2.3770220	−0.7131730
C	2.3363580	2.7544470	0.1967640
H	0.7474910	2.0039740	1.4311420
H	4.4529020	0.8351240	−1.7004170
H	3.9546710	3.1533930	−1.1895620
H	2.1566730	3.7961200	0.4244320
C	3.3169870	−1.3953310	−0.5708000
O	2.7176610	−2.3485250	0.0311460
C	4.4591340	−1.7429410	−1.5020950
H	4.5509570	−2.8287770	−1.5385050
H	4.2948480	−1.3711570	−2.5196180
H	5.4113980	−1.3254430	−1.1552410
N	1.0148400	−0.6208960	0.9017780
H	1.4854940	−1.5532220	0.7515050
C	−0.0900280	−0.5773660	1.8093730
N	−1.1542000	0.1668730	1.4335760
H	−1.9000910	0.1810380	2.1185220
O	−0.0214310	−1.2195280	2.8425130
C	−1.4858640	0.6827180	0.0980220
H	−1.4020930	1.7723620	0.0895910
H	−0.7539910	0.2893160	−0.6070610
C	−2.8845000	0.2759010	−0.3199770

C	−3.8862700	1.2385140	−0.4655390
C	−3.1951700	−1.0674780	−0.5652530
C	−5.1753990	0.8704680	−0.8528550
H	−3.6557910	2.2823570	−0.2778250
C	−4.4807290	−1.4369770	−0.9500730
H	−2.4269080	−1.8263760	−0.4581320
C	−5.4751290	−0.4678100	−1.0948440
H	−5.9425420	1.6290830	−0.9632680
H	−4.7071690	−2.4802760	−1.1409220
H	−6.4762700	−0.7564790	−1.3954440

^{3}IM-1'

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.462316467**
Zero-point correction=0.287459
Thermal correction to Energy=0.305759
Thermal correction to Enthalpy=0.306703
Thermal correction to Gibbs Free Energy=0.236899

C	0.4602130	−0.2574620	−0.1605470
C	1.7286970	−0.5712620	−0.7324940
C	2.8662990	0.1321070	−0.3910850
C	2.8188690	1.2675720	0.4796020
C	1.5806400	1.7666230	0.8125840
C	0.3791080	1.1293290	0.4002280
H	1.8286600	−1.4581580	−1.3447060
H	3.8249700	−0.2002070	−0.7758990
H	3.7265660	1.7764890	0.7738390
H	1.4977080	2.7277380	1.3128950
C	−0.5290410	−1.2756150	0.0443020
N	−2.6218950	1.0183610	−0.6685960
C	−1.8889600	2.1053270	−0.4329430
N	−0.7428610	1.9336950	0.4424990
H	−0.5193120	2.8596190	0.7968450
O	−2.0947930	3.2407550	−0.8378470
O	−1.5937270	−1.0543640	0.6891310
H	−2.4119250	0.1852020	−0.1050260
C	−0.2928180	−2.6626200	−0.5225430
H	0.5806710	−3.1434200	−0.0691520
H	−1.1736290	−3.2693930	−0.3120000
H	−0.1287910	−2.6455620	−1.6053230
C	−3.8034820	1.0443480	−1.5295850
H	−3.8326990	0.0970020	−2.0718800
H	−3.6710910	1.8468250	−2.2556750
C	−5.0995050	1.2368200	−0.7627380
C	−5.8622160	0.1323930	−0.3710740
C	−5.5442230	2.5197570	−0.4217670
C	−7.0444230	0.3026540	0.3485380
H	−5.5288820	−0.8671500	−0.6325460
C	−6.7253240	2.6923630	0.2968910
H	−4.9576170	3.3822090	−0.7186790
C	−7.4786130	1.5838800	0.6843470
H	−7.6261250	−0.5638790	0.6438650

H	−7. 0599580	3. 6922700	0. 5516370
H	−8. 3990600	1. 7186180	1. 2418780

^{3}TS'

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.420601946**
Zero-point correction=0.285529
Thermal correction to Energy=0.302845
Thermal correction to Enthalpy=0.303789
Thermal correction to Gibbs Free Energy=0.238873

C	−0. 6507680	−0. 8268030	0. 0148430
C	−1. 4927360	0. 2624090	−0. 0310610
C	−2. 8678520	0. 0937790	0. 2202420
C	−3. 3891840	−1. 2009970	0. 7379930
C	−2. 5522350	−2. 3265020	0. 5535650
C	−1. 2256270	−2. 1483090	0. 2333080
H	0. 4070340	−0. 7278640	−0. 1881170
H	−1. 1302300	1. 2398370	−0. 3363830
H	−2. 9264390	−3. 3231980	0. 7545320
H	−0. 5784490	−3. 0155540	0. 1597940
N	−3. 7810300	1. 0422960	−0. 1223990
H	−3. 4376210	1. 9515710	−0. 4130450
C	−5. 1898980	0. 9347840	−0. 2334440
O	−5. 8085510	1. 9580140	−0. 5237610
N	−5. 6790880	−0. 3250670	−0. 0583460
C	−7. 0810110	−0. 4843520	0. 0145420
C	−7. 9079210	0. 2998140	0. 8404270
C	−7. 6722150	−1. 5253460	−0. 7138630
C	−9. 2700800	0. 0412830	0. 9257630
H	−7. 4814040	1. 1278480	1. 3928230
C	−9. 0387890	−1. 7749900	−0. 6235950
H	−7. 0440970	−2. 1320000	−1. 3565940
C	−9. 8649270	−0. 9995900	0. 1970430
H	−9. 8882630	0. 6632300	1. 5664400
H	−9. 4709210	−2. 5849780	−1. 2027960
C	−11. 3489050	−1. 2528630	0. 2840400
H	−11. 6226510	−2. 1885000	−0. 2081170
H	−11. 6842530	−1. 3047710	1. 3244160
H	−11. 9149790	−0. 4463850	−0. 1953430
C	−4. 6981020	−1. 2024840	1. 3298800
C	−5. 3910400	−2. 5118820	1. 5815420
H	−4. 8772850	−3. 0421560	2. 3898510
H	−6. 4235660	−2. 3480750	1. 8968710
H	−5. 3980250	−3. 1435860	0. 6930380
O	−4. 8262850	−0. 2783790	2. 3532130
H	−5. 7476970	−0. 2744690	2. 6512620

II'

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-879.444816152**
Zero-point correction=0.287163
Thermal correction to Energy=0.304739
Thermal correction to Enthalpy=0.305683

Thermal correction to Gibbs Free Energy=0.240092

C	−4. 7947420	−0. 0634910	−0. 7195880
C	−3. 8987560	0. 9970240	−0. 6515120
C	−2. 6064530	0. 7890780	−0. 1856990
C	−2. 1226070	−0. 5758180	0. 2130250
C	−3. 0787970	−1. 6259090	0. 1909540
C	−4. 3538270	−1. 4016760	−0. 2462870
H	−5. 8080930	0. 0753210	−1. 0697760
H	−4. 2065410	2. 0049940	−0. 9147710
H	−2. 7735750	−2. 6144230	0. 5127590
H	−5. 0729030	−2. 2136550	−0. 2477330
N	−1. 7094720	1. 7935500	0. 0425140
H	−1. 9888300	2. 7557790	−0. 1114040
C	−0. 4256890	1. 6719470	0. 5858910
O	0. 1883090	2. 6963890	0. 8764480
N	0. 0629740	0. 4050620	0. 7378970
C	−0. 6401350	−0. 8111450	0. 1986930
C	−0. 1453610	−1. 1082450	−1. 2332420
H	0. 9326060	−1. 2906430	−1. 2440240
H	−0. 6627840	−1. 9892660	−1. 6208430
H	−0. 3530430	−0. 2641620	−1. 8939420
O	−0. 3742980	−1. 9121640	1. 0468180
H	0. 3901650	−2. 3876480	0. 6983750
C	1. 3502070	0. 2518010	1. 4326890
H	1. 4743410	1. 1514460	2. 0348530
H	1. 2614270	−0. 5953820	2. 1115440
C	2. 5676580	0. 0713150	0. 5413800
C	2. 9574530	1. 0733060	−0. 3569690
C	3. 3374310	−1. 0926640	0. 6233930
C	4. 0835780	0. 9070030	−1. 1586470
H	2. 3773920	1. 9875020	−0. 4156130
C	4. 4687430	−1. 2604290	−0. 1767820
H	3. 0536060	−1. 8736370	1. 3226360
C	4. 8425480	−0. 2617560	−1. 0727360
H	4. 3745640	1. 6928250	−1. 8475150
H	5. 0545830	−2. 1700530	−0. 0993080
H	5. 7202460	−0. 3890330	−1. 6968960

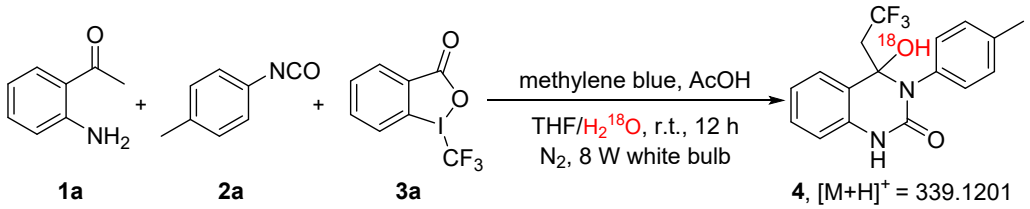
[1]43’

E[B3LYP/6-311G(d,p)/SMD(THF)]= **-803.023909912**
Zero-point correction=0.260693
Thermal correction to Energy=0.27645
Thermal correction to Enthalpy=0.277394
Thermal correction to Gibbs Free Energy=0.215162

C	2. 5881200	0. 3930300	0. 3819200
C	3. 8811150	0. 2625110	0. 8685990
C	4. 6101400	−0. 9048100	0. 6147460
C	4. 0300960	−1. 9370020	−0. 1304860
C	2. 7383960	−1. 8139710	−0. 6203390
C	1. 9729470	−0. 6416110	−0. 3797790
H	4. 3163240	1. 0733890	1. 4436790

H	5.6194870	-1.0023010	0.9966220
H	4.5924460	-2.8429450	-0.3283180
H	2.2951030	-2.6178720	-1.1966940
N	1.8348360	1.5426660	0.6159420
H	2.2373010	2.2922430	1.1624390
C	0.5486870	1.7713920	0.1885780
N	-0.0235780	0.7499810	-0.5596230
O	-0.0386590	2.8113150	0.4604450
C	0.6544210	-0.4575610	-0.8543320
C	-0.0315800	-1.4723590	-1.6553990
H	-0.5697540	-2.2910520	-1.1860840
H	0.0405960	-1.4781540	-2.7403770
C	-1.3878260	0.9751880	-1.0732160
H	-1.4232520	0.6202510	-2.1036590
H	-1.5339590	2.0542660	-1.0797900
C	-2.4843190	0.3112130	-0.2595500
C	-3.3388090	-0.6220920	-0.8531120
C	-2.6836900	0.6480910	1.0852020
C	-4.3693520	-1.2128570	-0.1211610
H	-3.1973780	-0.8879570	-1.8957260
C	-3.7078220	0.0549820	1.8190860
H	-2.0414840	1.3864000	1.5520220
C	-4.5539030	-0.8783880	1.2184080
H	-5.0234750	-1.9350540	-0.5976800
H	-3.8507110	0.3262700	2.8595290
H	-5.3524580	-1.3377690	1.7905740

6. HRMS for O^{18} labeling experiments



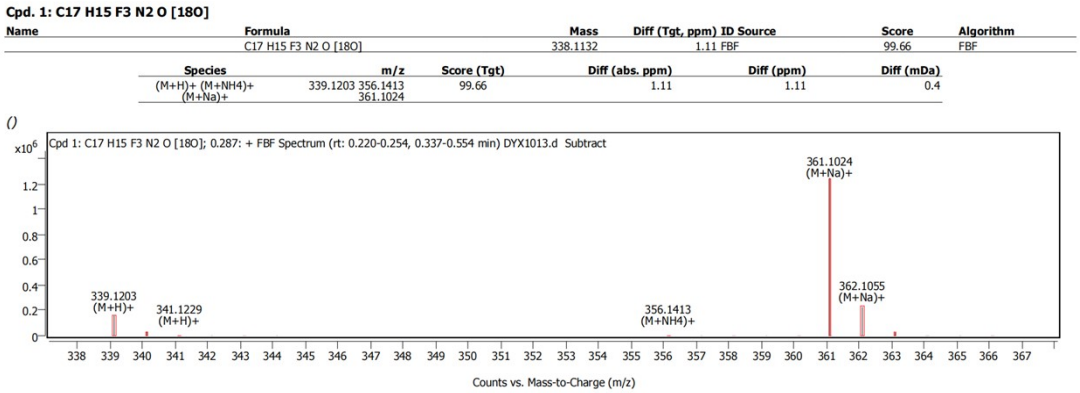
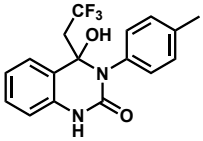
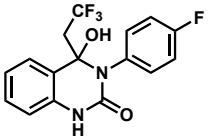


Fig. S7. HRMS for O^{18} labeling experiments.

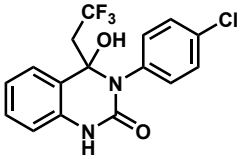
8. Data of compounds



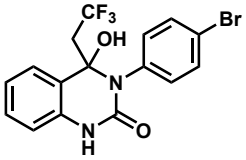
4-hydroxy-3-(*p*-tolyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (4): White solid; mp 211.7-218.3 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.79 (s, 1H), 10.06 (s, 1H), 8.67 (dd, *J* = 8.7, 1.1 Hz, 1H), 8.24 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.88 – 7.79 (m, 1H), 7.72 – 7.62 (m, 2H), 7.40 – 7.29 (m, 3H), 4.74 (q, *J* = 10.7 Hz, 2H), 2.50 (s, 3H). **^{13}C NMR (100 MHz, DMSO-d_6) δ** 195.09, 152.72, 142.21, 137.47, 135.43, 132.07, 131.55, 129.60, 125.52**(q, *J* = 275 Hz)**, 121.47, 121.33, 120.69, 119.23, 43.05**(q, *J* = 27 Hz)**, 20.83.**^{19}F NMR (376 MHz, DMSO-d_6) δ -60.88. HRMS (ESI): calcd. for $C_{17}H_{16}F_3N_2O_2$ [M+H]$^+$ 337.1158; found 337.1155.**



3-(4-fluorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (5): White solid; mp 225.6-232.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.58 (s, 1H), 9.94 (s, 1H), 8.46 – 8.40 (m, 1H), 8.01 – 7.98 (m, 1H), 7.65 – 7.59 (m, 1H), 7.56 – 7.50 (m, 2H), 7.17 – 7.09 (m, 3H), 4.49 (q, *J* = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.22, 158.02 (d, *J* = 238 Hz), 152.76, 142.09, 136.37 (d, *J* = 3.0 Hz), 135.50, 132.12, 129.73, 125.51 (q, *J* = 275 Hz), 121.47, 120.83 (d, *J* = 8.0 Hz), 120.63, 115.74 (d, *J* = 22 Hz), 43.06 (q, *J* = 27 Hz).^{19}F NMR (376 MHz, DMSO-d_6) δ -60.88, -120.91. HRMS (ESI): calcd. for $C_{16}H_{13}F_4N_2O_2$ [M+H]$^+$ 341.0908; found 341.0905.

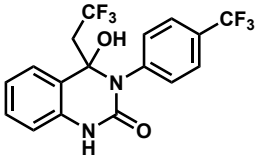


3-(4-chlorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1*H*)-one (6): White solid; mp 196.2-198.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 10.05 (s, 1H), 8.41 (dd, *J* = 8.6, 1.2 Hz, 1H), 8.01 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.63 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.39 – 7.31 (m, 2H), 7.14 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 4.50 (q, *J* = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.41, 152.62, 141.88, 139.08, 135.50, 132.12, 129.08, 126.25, 125.51 (q, *J* = 275 Hz), 121.63, 121.58, 120.70, 120.57, 43.07 (q, *J* = 25 Hz).^{19}F NMR (376 MHz, DMSO-d_6) δ -60.87. HRMS (ESI): calcd. for $C_{16}H_{13}ClF_3N_2O_2$ [M+H]$^+$ 357.0612; found 357.0617.

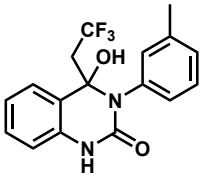


3-(4-bromophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (7): White solid; mp 215.8-220.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 10.05 (s, 1H), 8.41 (d, *J* = 8.5 Hz, 1H), 8.01 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.63 (ddd, *J* = 8.6, 7.1, 1.6 Hz, 1H), 7.53 – 7.43 (m, 4H), 7.19 – 7.08 (m, 1H), 4.50 (q, *J* = 10.7 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$) δ** 195.24, 152.60, 141.86, 139.51, 135.50, 132.12, 131.98, 125.52**(q, *J* = 272 Hz),** 121.65, 121.61, 120.98, 120.71, 114.18,

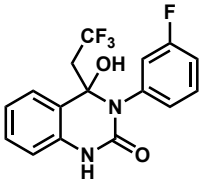
43.07 (q, J = 26 Hz). ^{19}**F NMR (376 MHz, DMSO-d_6) δ -60.88. HRMS (ESI): calcd. for $C_{16}H_{13}BrF_3N_2O_2$ [M+H]$^+$ 401.0107; found 401.0110.**



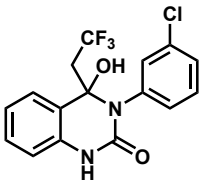
4-hydroxy-4-(2,2,2-trifluoroethyl)-3-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-2(1H)-one (8): White solid; mp 212.9-222.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.66 (s, 1H), 10.32 (s, 1H), 8.43 (d, J = 8.6 Hz, 1H), 8.05 – 7.99 (m, 1H), 7.73 (t, J = 9.0 Hz, 2H), 7.66 (d, J = 8.6 Hz, 2H), 7.51 – 7.21 (m, 1H), 7.19 – 7.07 (m, 1H), 4.51 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.27, 152.59, 142.73 (q, J = 226 Hz), 135.51, 132.13, 126.86, 126.50 (q, J = 3 Hz), 125.23 (q, J = 222 Hz), 123.65, 122.62 (q, J = 31 Hz), 121.89, 121.80, 120.82, 43.08 (q, J = 27 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.17, -60.91. HRMS (ESI): calcd. for $C_{17}H_{13}F_6N_2O_2$ [M+H]$^+$ 391.0876; found 391.0870.



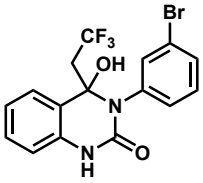
4-hydroxy-3-(m-tolyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (9): White solid; mp 196.2-198.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 9.84 (s, 1H), 8.42 (dt, J = 8.6, 1.5 Hz, 1H), 8.00 (dd, J = 8.1, 1.6 Hz, 1H), 7.61 (ddd, J = 8.6, 7.0, 1.5 Hz, 1H), 7.38 (d, J = 2.2 Hz, 1H), 7.31 (d, J = 8.2 Hz, 1H), 7.21 – 7.09 (m, 2H), 6.82 (d, J = 7.4 Hz, 1H), 4.48 (t, J = 10.7 Hz, 2H), 2.28 (s, 3H). ^{13}**C NMR (100 MHz, $CDCl_3$) δ** 195.06, 152.70, 142.11, 139.99, 138.32, 135.42, 132.07, 129.03, **125.52 (q, J = 276 Hz)**, 123.43, 121.55, 121.41, 120.73, 119.70, 116.33, 43.46, **42.80 (q, J = 26 Hz)**. ^{19}**F NMR (376 MHz, DMSO-d_6) δ -60.87. HRMS (ESI): calcd. for $C_{17}H_{16}F_3N_2O_2$ [M+H]$^+$ 337.1158; found 337.1162.**



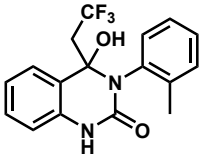
3-(3-fluorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (10): White solid; mp 187.1-192.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 10.13 (s, 1H), 8.48 – 8.36 (m, 1H), 8.03 – 7.95 (m, 1H), 7.72 – 7.59 (m, 1H), 7.57 – 7.44 (m, 1H), 7.36 – 7.27 (m, 1H), 7.25 – 7.20 (m, 1H), 7.17 – 7.10 (m, 1H), 6.84 – 6.76 (m, 1H), 4.50 (q, J = 10.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.24, 162.78 (d, J = 240 Hz), 152.61, 141.96 (d, J = 11 Hz), 141.76, 135.50, 132.11, 130.76 (d, J = 10 Hz), 125.50 (q, J = 275 Hz), 121.73, 121.68, 120.77, 114.75 (d, J = 3 Hz), 109.02 (d, J = 21 Hz), 105.73 (d, J = 26 Hz), 43.08 (q, J = 27 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.90, -112.18. HRMS (ESI): calcd. for $C_{16}H_{13}F_4N_2O_2$ [M+H]$^+$ 341.0908; found 341.0912.



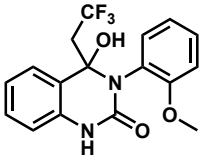
3-(3-chlorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (11): White solid; mp 224.3-227.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 10.13 (s, 1H), 8.40 (d, J = 8.5 Hz, 1H), 8.00 (dd, J = 8.2, 1.5 Hz, 1H), 7.75 (t, J = 2.0 Hz, 1H), 7.63 (ddd, J = 8.6, 7.2, 1.5 Hz, 1H), 7.47 – 7.29 (m, 2H), 7.16 – 7.10 (m, 1H), 7.04 (dt, J = 7.8, 1.5 Hz, 1H), 4.50 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.25, 152.61, 141.69, 141.65, 141.53, 135.49, 133.60, 132.10, 130.86, 125.50 (q, J = 275 Hz), 122.31, 121.77, 120.76, 118.42, 117.40, 43.08 (q, J = 26 Hz).^{19}F NMR (376 MHz, DMSO-d_6) δ -60.89. HRMS (ESI): calcd. for $C_{16}H_{13}ClF_3N_2O_2$ [M+H]$^+$ 357.0612; found 357.0615.



3-(3-bromophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (12): White solid; mp 222.0-225.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.62 (s, 1H), 10.10 (s, 1H), 8.45 – 8.36 (m, 1H), 8.01 (dd, J = 8.1, 1.6 Hz, 1H), 7.94 – 7.84 (m, 1H), 7.67 – 7.58 (m, 1H), 7.41 (dd, J = 8.2, 1.9 Hz, 1H), 7.25 (t, J = 8.0 Hz, 1H), 7.21 – 7.05 (m, 2H), 4.50 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.28, 152.58, 141.79, 141.74, 135.52, 132.13, 131.17, 125.50 (q, J = 275 Hz), 125.21, 122.12, 121.76, 121.66, 121.28, 120.73, 117.78, 43.08 (q, J = 26 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.89. HRMS (ESI): calcd. for $C_{16}H_{13}BrF_3N_2O_2$ [M+H]$^+$ 401.0107; found 401.0103.

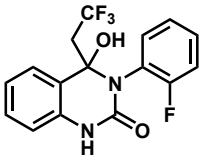


4-hydroxy-3-(o-tolyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (13): White solid; mp 212.7-215.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 9.11 (s, 1H), 8.30 (dd, J = 8.6, 1.2 Hz, 1H), 7.96 (dd, J = 8.3, 1.5 Hz, 1H), 7.58 (ddd, J = 8.6, 7.2, 1.6 Hz, 1H), 7.44 (dd, J = 8.2, 1.5 Hz, 1H), 7.20 (dd, J = 8.0, 1.7 Hz, 1H), 7.17 – 7.08 (m, 2H), 7.04 (td, J = 7.4, 1.3 Hz, 1H), 4.44 (q, J = 10.7 Hz, 2H), 2.24 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 194.71, 153.43, 141.88, 137.11, 135.16, 131.80, 131.67, 130.78, 125.50 (q, J = 275 Hz), 125.04, 124.89, 122.33, 121.48, 121.11, 43.10 (q, J = 27 Hz), 17.61.^{19}F NMR (376 MHz, DMSO-d_6) δ -60.86. HRMS (ESI): calcd. for $C_{17}H_{16}F_3N_2O_2$ [M+H]$^+$ 337.1158; found 337.1166.

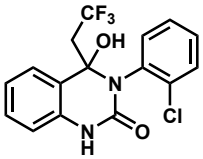


4-hydroxy-3-(2-methoxyphenyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (14): White solid; mp 215.5-218.7 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.23 (s, 1H), 9.12 (s, 1H),

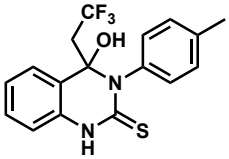
8.08 – 8.04 (m, 1H), 7.92 – 7.84 (m, 2H), 7.60 – 7.54 (m, 1H), 7.13 (td, J = 7.6, 1.2 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.93 – 6.85 (m, 1H), 4.39 (q, J = 10.8 Hz, 2H), 3.86 (s, 3H). ^{13}**C NMR (100 MHz, CDCl$_3$) δ 193.89, 153.22, 149.94, 140.52, 134.50, 131.13, 128.34, 125.60 (q,** *J* **= 229Hz), 123.73, 122.27, 122.05, 121.68, 120.79, 111.53, 56.11, 43.21 (q,** *J* **= 26Hz).** ^{19}**F NMR (376 MHz, DMSO-d_6) δ -60.87. HRMS (ESI): calcd. for $C_{17}H_{16}F_3N_2O_3$ [M+H]$^+$ 353.1108; found 353.1107.**



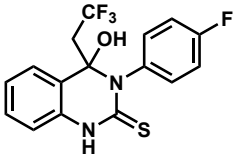
3-(2-fluorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (15): White solid; mp 221.4-226.4 °C; ^{1}**H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 9.72 (s, 1H), 8.26 – 8.17 (m, 1H), 7.97 (dd,** *J* **= 8.1, 1.6 Hz, 1H), 7.94 – 7.81 (m, 1H), 7.68 – 7.56 (m, 1H), 7.29 – 7.19 (m, 1H), 7.18 – 7.11 (m, 2H), 7.11 – 6.98 (m, 1H), 4.45 (q,** *J* **= 10.7 Hz, 2H).** ^{13}**C NMR (100 MHz, CDCl$_3$) δ 194.51, 153.87 (d,** *J* **= 242 Hz), 152.97, 141.00, 135.00, 131.67, 127.28 (d,** *J* **= 11 Hz), 125.50 (q,** *J* **= 274 Hz), 124.83 (d,** *J* **= 4 Hz), 124.41 (d,** *J* **= 7 Hz), 123.62, 123.12, 122.00, 121.68, 115.81 (d,** *J* **= 19 Hz), 43.17 (q,** *J* **= 26 Hz).** ^{19}**F NMR (376 MHz, DMSO-d_6) δ -60.90, -126.28. HRMS (ESI): calcd. for $C_{17}H_{16}F_3N_2O_2$ [M+H]$^+$ 341.0908; found 341.0905.**



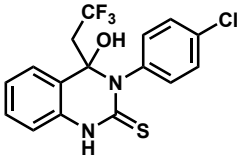
3-(2-chlorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (16): White solid; mp 220.9-223.8 °C; ^{1}**H NMR (400 MHz, DMSO-d_6) δ** 10.46 (s, 1H), 9.44 (s, 1H), 8.19 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.97 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.80 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.60 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H), 7.48 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.32 (td, *J* = 7.8, 1.6 Hz, 1H), 7.15 (dtd, *J* = 9.4, 7.5, 1.4 Hz, 2H), 4.45 (q, *J* = 10.8 Hz, 2H). ^{13}**C NMR (100 MHz, CDCl$_3$) δ** 194.41, 153.16, 140.78, 135.99, 134.88, 131.50, 129.91, 127.86, 126.01, 125.58, 125.56, 125.48 **(q,** *J* **= 275Hz),** 123.64, 122.13, 121.85, 43.18**(q,** *J* **= 26 Hz).** ^{19}**F NMR (376 MHz, DMSO-d_6) δ -60.89. HRMS (ESI): calcd. for $C_{16}H_{13}ClF_3N_2O_2$ [M+H]$^+$ 357.0612; found 357.0617.**



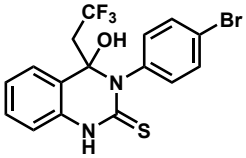
4-hydroxy-3-(p-tolyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-2(1H)-thione (21): White solid; mp 211.3-214.1 °C; ^{1}**H NMR (400 MHz, DMSO-d_6) δ 10.52 (s, 1H), 9.78 (s, 1H), 8.41 (dd,** *J* **= 8.6, 1.2 Hz, 1H), 7.99 (dd,** *J* **= 8.2, 1.6 Hz, 1H), 7.61 (ddd,** *J* **= 8.6, 7.1, 1.6 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.15 – 7.06 (m, 3H), 4.47 (q,** *J* **= 10.7 Hz, 2H), 2.25 (s, 3H).** ^{13}**C NMR (100 MHz, CDCl$_3$) δ 195.00, 152.75, 142.18, 137.45, 135.39, 132.03, 131.59, 129.58, 125.56 (q,** *J* **= 275 Hz), 121.60, 121.35, 120.73, 119.30, 43.07 (q,** *J* **= 26 Hz), 20.82.** ^{19}**F NMR (376 MHz, DMSO-d_6) δ -60.86. HRMS (ESI): calcd. for $C_{17}H_{16}F_3N_2OS$ [M+H]$^+$ 353.0930; found 353.0935.**



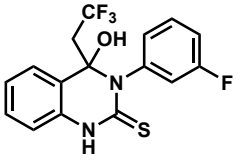
3-(4-fluorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-2(1H)-thione (22): White solid; mp 219.1-222.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.60 (s, 1H), 9.95 (s, 1H), 8.45 – 8.39 (m, 1H), 8.02 – 7.94 (m, 2H), 7.77 – 7.70 (m, 1H), 7.65 – 7.60 (m, 1H), 7.53 – 7.50 (m, 1H), 7.28 – 7.18 (m, 1H), 7.11 (dd, J = 6.0, 1.9 Hz, 1H), 4.50 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.20, 158.03 (d, J = 237 Hz), 152.76, 142.11, 136.37 (d, J = 3 Hz), 135.50, 129.73, 129.03, 125.51 (q, J = 274 Hz), 121.46, 120.83 (d, J = 8 Hz), 120.63, 115.74 (d, J = 22 Hz), 43.06 (q, J = 25 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.87, -120.89. HRMS (ESI): calcd. for $C_{16}H_{13}F_4N_2OS$ [M+H]$^+$ 357.0679; found 357.0677.



3-(4-chlorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-2(1H)-thione (23): White solid; mp 212.6-215.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 10.05 (s, 1H), 8.42 (dd, J = 8.6, 1.8 Hz, 1H), 8.02 (d, J = 1.5 Hz, 1H), 7.66 – 7.60 (m, 1H), 7.58 – 7.52 (m, 2H), 7.38 – 7.33 (m, 2H), 7.16 – 7.10 (m, 1H), 4.50 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.24, 152.62, 141.88, 139.08, 137.36, 135.51, 132.12, 129.73, 129.09, 125.51 (q, J = 274 Hz), 121.63, 121.04, 120.58, 43.07 (q, J = 27 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.87. HRMS (ESI): calcd. for $C_{16}H_{13}ClF_3N_2OS$ [M+H]$^+$ 373.0384; found 373.0387.

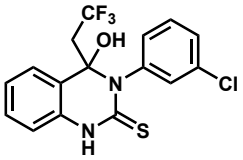


3-(4-bromophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-2(1H)-thione (24): White solid; mp 215.4-220.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.60 (s, 1H), 10.04 (s, 1H), 8.41 (dd, J = 8.5, 1.3 Hz, 1H), 7.97 – 7.94 (m, 1H), 7.67 – 7.58 (m, 2H), 7.48 (d, J = 2.1 Hz, 3H), 7.17 – 7.09 (m, 1H), 4.49 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.79, 152.14, 141.40, 139.06, 135.05, 131.67, 131.52, 125.06 **(q, J = 273 Hz)**, 121.19, 121.15, 120.52, 120.25, 113.73, 42.62**(q, J = 26 Hz)**. **^{19}F NMR (376 MHz, DMSO-d_6) δ -60.88. HRMS (ESI): calcd. for $C_{16}H_{13}BrF_3N_2OS$ [M+H]$^+$ 416.9879; found 416.9875.**

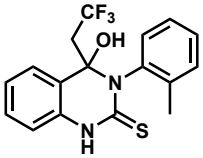


3-(3-fluorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-2(1H)-thione (25): White solid; mp 189.9-192.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.62 (s, 1H), 10.14 (s, 1H), 8.44 – 8.38 (m, 1H), 7.97 – 7.93 (m, 1H), 7.67 – 7.59 (m, 2H), 7.56 – 7.52 (m, 1H), 7.36 – 7.28 (m, 1H), 7.18 – 7.11 (m, 1H), 6.85 – 6.77 (m, 1H), 4.50 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.25, 162.77 (d, J = 239 Hz), 152.61, 141.95 (d, J = 12 Hz), 141.73, 135.51, 133.34, 132.10, 131.20, 130.77 (d, J = 9 Hz), 125.50 (q, J = 275 Hz), 121.76, 120.78, 114.76 (d, J = 2 Hz),

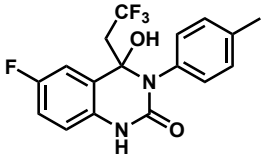
109.04 (d, J = 21 Hz), 105.73 (d, J = 23 Hz), 43.08 (q, J = 26 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.88, -112.16. HRMS (ESI): calcd. for $C_{16}H_{13}F_4N_2OS$ $[M+H]^+$ 357.0679; found 353.0677.



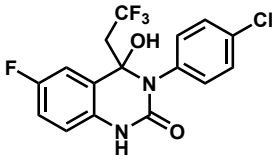
3-(3-chlorophenyl)-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-2(1H)-thione (26): White solid; mp 224.1-227.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.60 (s, 1H), 10.10 (s, 1H), 8.40 (d, J = 8.5 Hz, 1H), 7.97 – 7.91 (m, 1H), 7.75 (d, J = 2.1 Hz, 1H), 7.66 – 7.60 (m, 1H), 7.38 (dd, J = 7.6, 2.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.05 (dd, J = 7.7, 2.1 Hz, 1H), 4.49 (q, J = 10.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.22, 152.60, 141.76, 141.65, 137.34, 135.51, 133.62, 132.89, 132.10, 125.48 (q, J = 275 Hz), 122.31, 121.74, 120.74, 118.45, 117.40, 43.08 (q, J = 26 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.86. HRMS (ESI): calcd. for $C_{16}H_{13}ClF_3N_2OS$ $[M+H]^+$ 373.0384; found 373.0388.



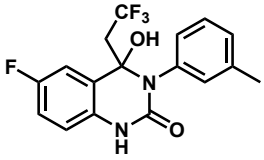
4-hydroxy-3-(o-tolyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-2(1H)-thione (27): White solid; mp 221.5-224.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.49 (s, 1H), 9.13 (s, 1H), 8.35 – 8.29 (m, 1H), 7.98 (dd, J = 8.1, 1.6 Hz, 1H), 7.64 – 7.55 (m, 1H), 7.46 (dd, J = 8.0, 1.5 Hz, 1H), 7.22 (dd, J = 7.5, 1.6 Hz, 1H), 7.19 – 7.02 (m, 3H), 4.46 (q, J = 10.7 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.74 (q, J = 2 Hz), 153.42, 141.94, 137.10, 135.19, 131.83, 131.70, 130.78, 126.48, 125.74 (q, J = 275 Hz), 125.07, 124.90, 122.22 (q, J = 2 Hz), 121.44, 121.09, 43.59, 42.83 (q, J = 26 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.87. HRMS (ESI): calcd. for $C_{17}H_{16}F_3N_2OS$ $[M+H]^+$ 353.0930; found 353.0933.



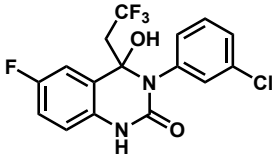
6-fluoro-4-hydroxy-3-(p-tolyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (34): White solid; mp 217.5-218.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.27 (s, 1H), 9.77 (s, 1H), 8.36 (dd, J = 9.4, 5.2 Hz, 1H), 7.85 (dd, J = 9.9, 3.0 Hz, 1H), 7.54 – 7.45 (m, 1H), 7.42 – 7.37 (m, 2H), 7.13 – 7.05 (m, 2H), 4.49 (q, J = 10.6 Hz, 2H), 2.25 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.17, 162.39, 156.24 (d, J = 238 Hz), 152.81, 138.26, 137.40, 131.59, 129.61, 125.45 (q, J = 303 Hz), 123.17 (d, J = 7.5 Hz), 122.37 (d, J = 22.5 Hz), 119.22, 117.42 (d, J = 24 Hz), 43.24 (q, J = 36 Hz), 20.82. ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.02, -121.29. HRMS (ESI): calcd. for $C_{17}H_{15}F_4N_2O_2$ $[M+H]^+$ 355.1064; found 355.1061.



3-(4-chlorophenyl)-6-fluoro-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (35): White solid; mp 206.3-206.7 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.34 (s, 1H), 10.02 (s, 1H), 8.36 (dd, J = 9.4, 5.2 Hz, 1H), 7.87 (dd, J = 9.9, 3.0 Hz, 1H), 7.57 – 7.51 (m, 3H), 7.36 – 7.33 (m, 2H), 4.50 (q, J = 10.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.32, 156.38 (d, J = 238 Hz), 152.70, 139.01, 137.93 (d, J = 2 Hz), 129.10, 128.79, 126.27, 125.75 (q, J = 193 Hz), 123.16 (d, J = 7 Hz), 122.43 (d, J = 23 Hz), 120.54, 117.53 (d, J = 23 Hz), 43.28 (q, J = 17 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.03, -120.89. HRMS (ESI): calcd. for $C_{16}H_{12}ClF_4N_2O_2$ $[M+H]^+$ 375.0518 found 375.0521.



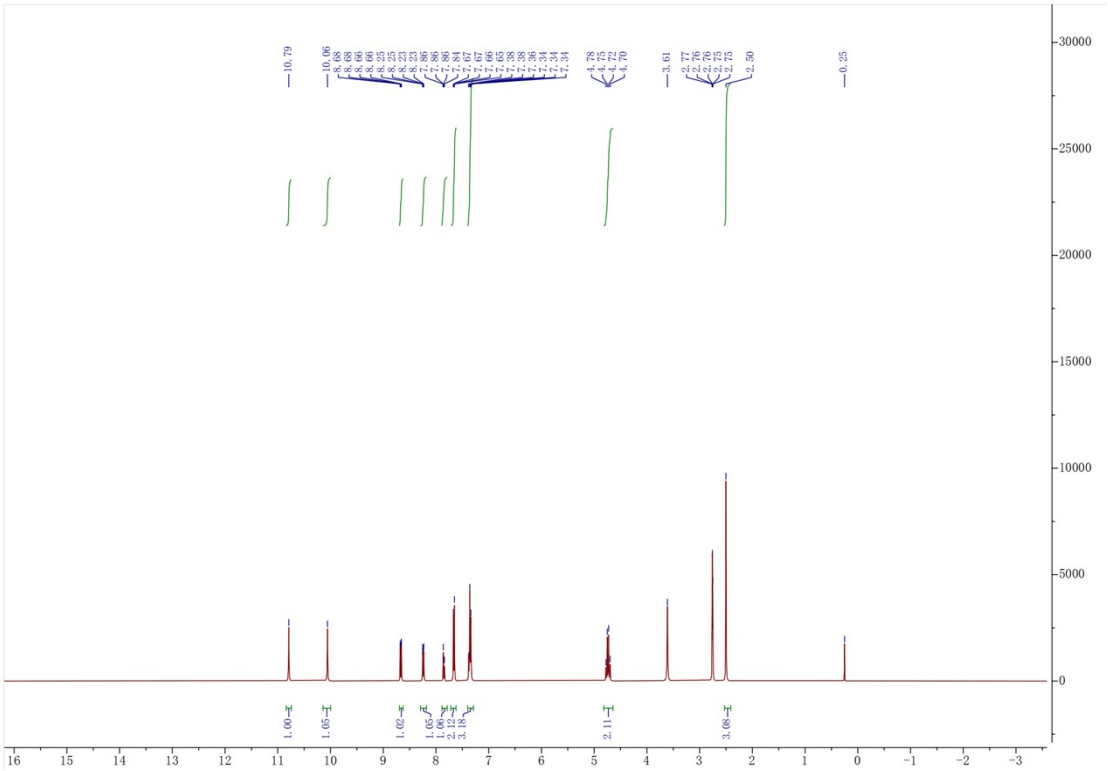
6-fluoro-4-hydroxy-3-(m-tolyl)-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (36): White solid; mp 214.5-216.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (s, 1H), 9.81 (s, 1H), 8.36 (dd, J = 9.4, 5.2 Hz, 1H), 7.85 (dd, J = 9.9, 3.0 Hz, 1H), 7.52 (ddd, J = 9.3, 7.8, 3.1 Hz, 1H), 7.35 (d, J = 2.0 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.16 (d, J = 7.8 Hz, 1H), 6.82 (d, J = 7.4 Hz, 1H), 4.49 (q, J = 10.7 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.16, 156.28 (d, J = 238 Hz), 152.79, 139.92, 138.35, 138.14, 129.05, 125.36 (q, J = 275 Hz), 123.46, 123.21 (d, J = 7.5 Hz), 122.35 (d, J = 21 Hz), 119.69, 117.43 (d, J = 24 Hz), 116.31, 43.28 (q, J = 27 Hz), 20.77. ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.02, -121.18. HRMS (ESI): calcd. for $C_{17}H_{15}F_4N_2O_2$ $[M+H]^+$ 355.1064 found 355.1069.



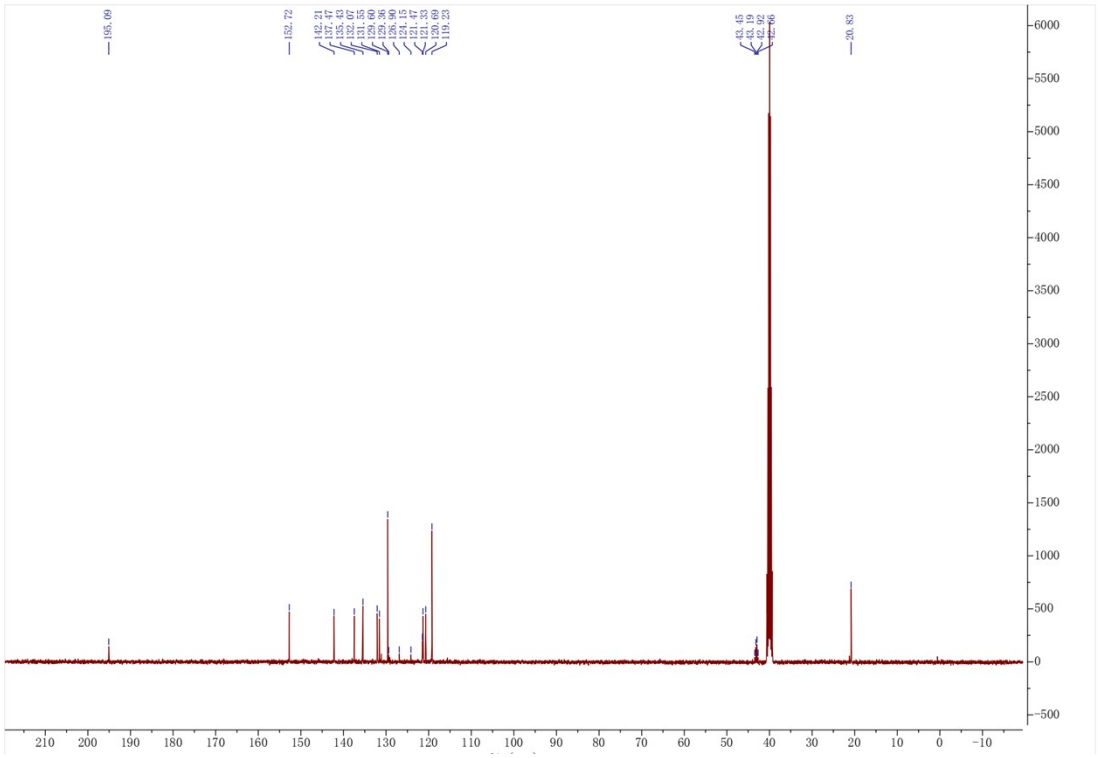
3-(3-chlorophenyl)-6-fluoro-4-hydroxy-4-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2(1H)-one (37): White solid; mp 204.2-204.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.35 (s, 1H), 10.09 (s, 1H), 8.36 (dd, J = 9.4, 5.2 Hz, 1H), 7.87 (dd, J = 9.9, 3.0 Hz, 1H), 7.74 (t, J = 2.0 Hz, 1H), 7.58 – 7.50 (m, 1H), 7.38 – 7.28 (m, 2H), 7.05 (dt, J = 7.4, 1.8 Hz, 1H), 4.50 (q, J = 10.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.35, 156.46 (d, J = 238 Hz), 152.68, 141.58, 137.76 (d, J = 2 Hz), 133.61, 130.88, 125.34 (q, J = 275 Hz), 123.22 (d, J = 8 Hz), 122.53, 122.32, 118.39, 117.55 (d, J = 24 Hz), 117.37, 43.29 (q, J = 27 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.04, -120.72. HRMS (ESI): calcd. for $C_{16}H_{12}ClF_4N_2O_2$ $[M+H]^+$ 375.0518 found 375.0515.

7.Copies of all NMR spectra

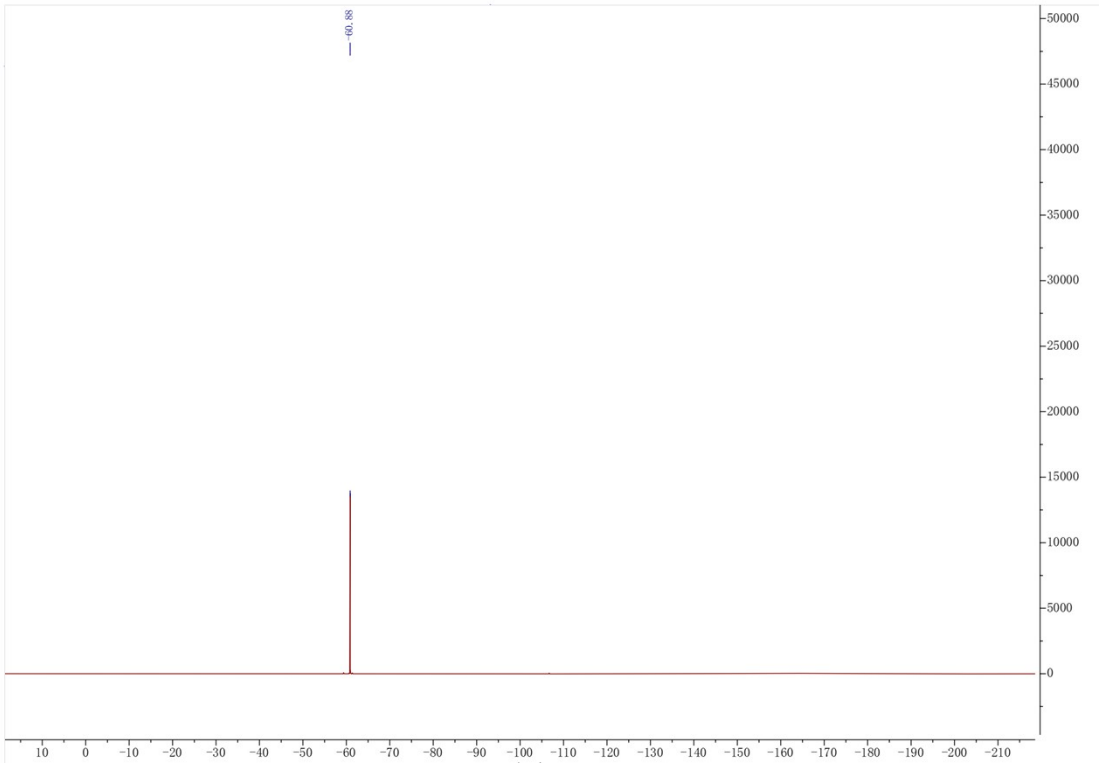
^{1}H NMR (400 MHz, DMSO-d_6) of 4



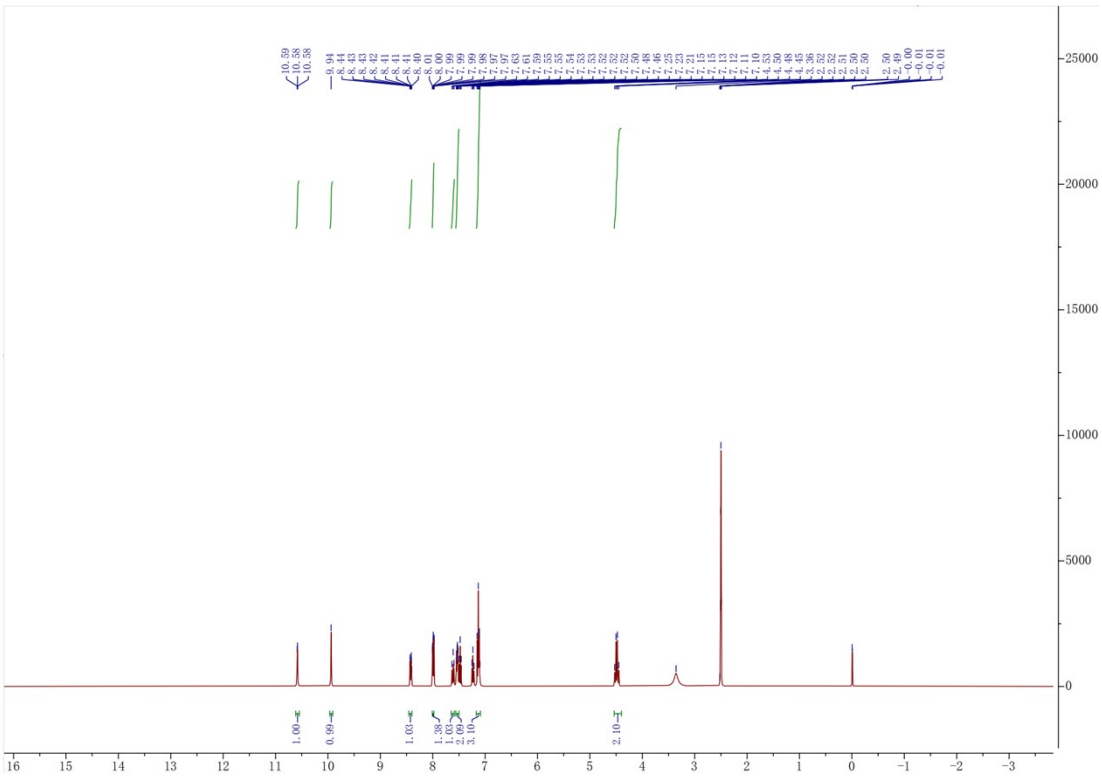
^{13}C NMR (100 MHz, DMSO-d_6) of 4



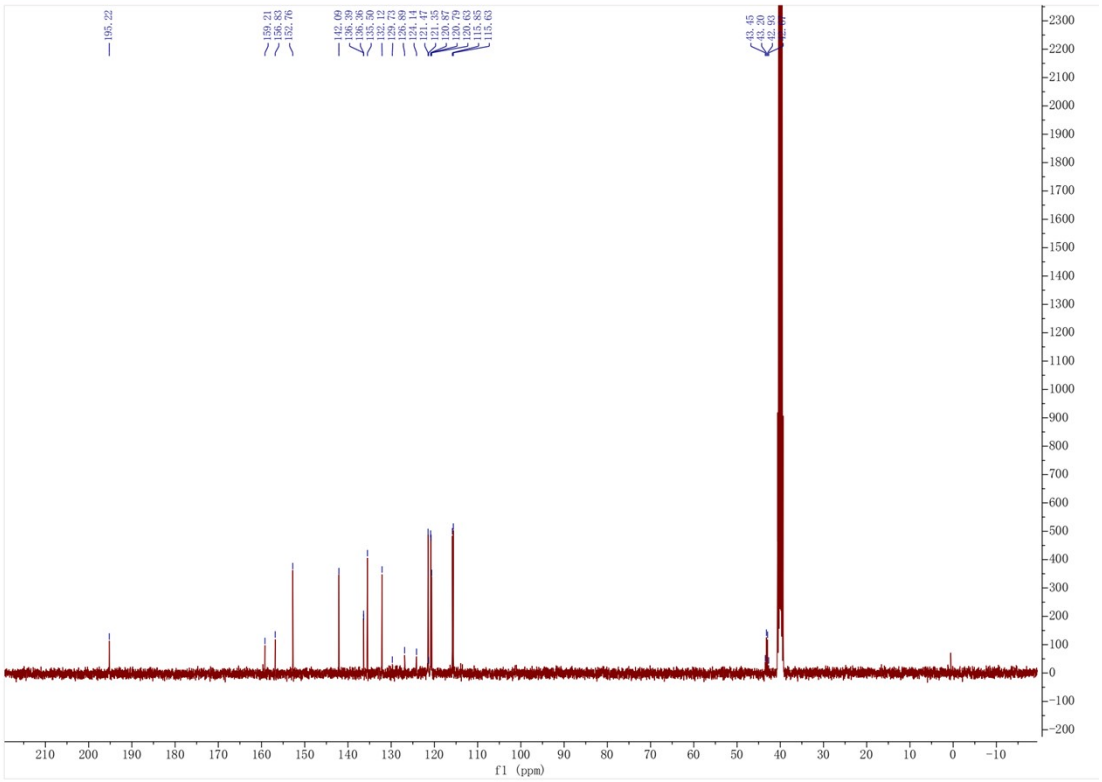
^{19}F NMR (376 MHz, DMSO-d_6) of 4



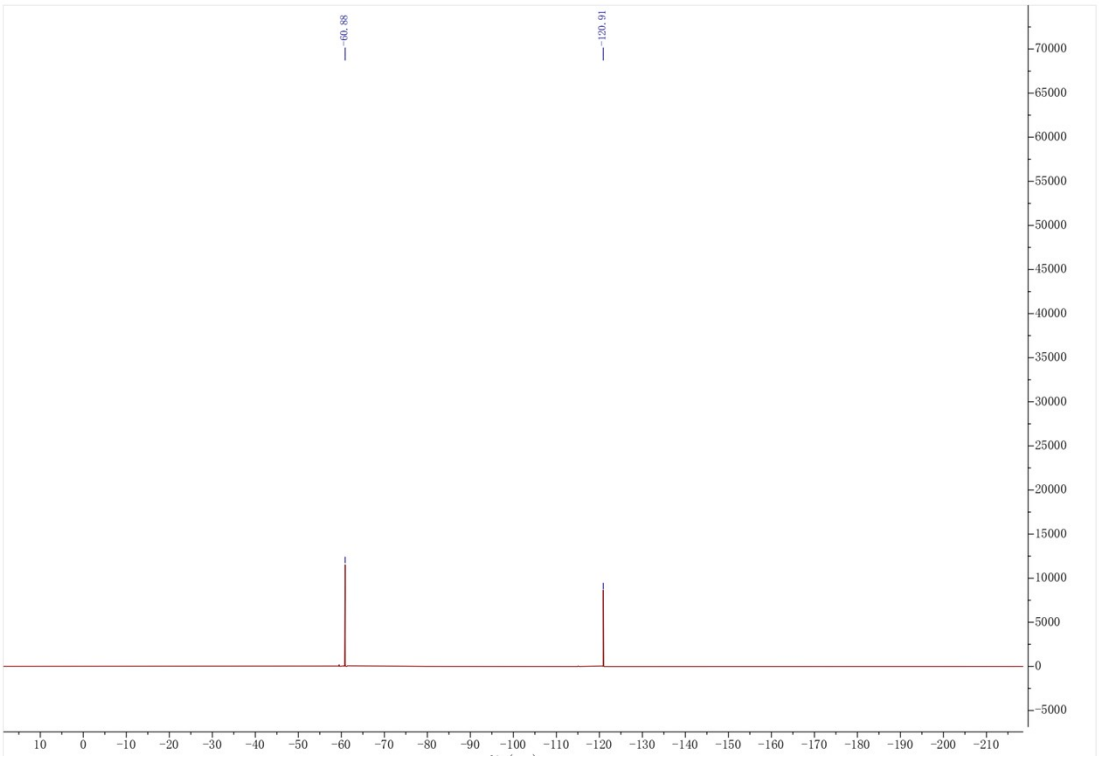
^{1}H NMR (400 MHz, DMSO-d_6) of 5



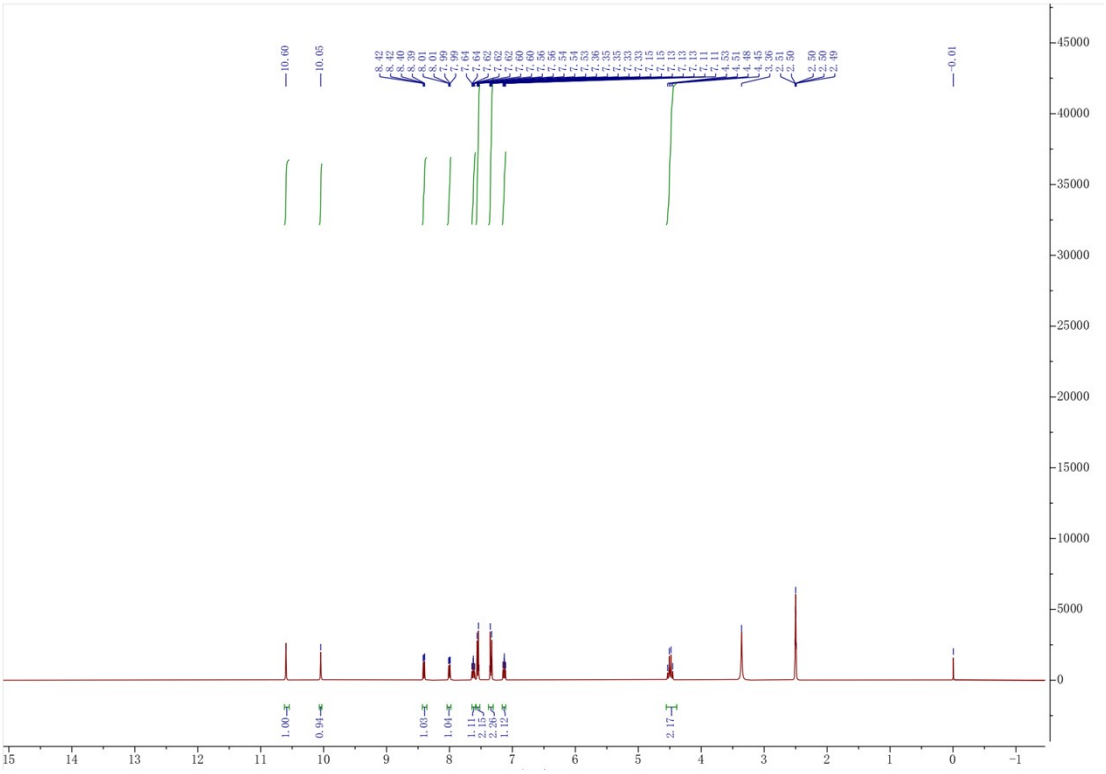
^{13}C NMR (100 MHz, DMSO-d_6) of 5



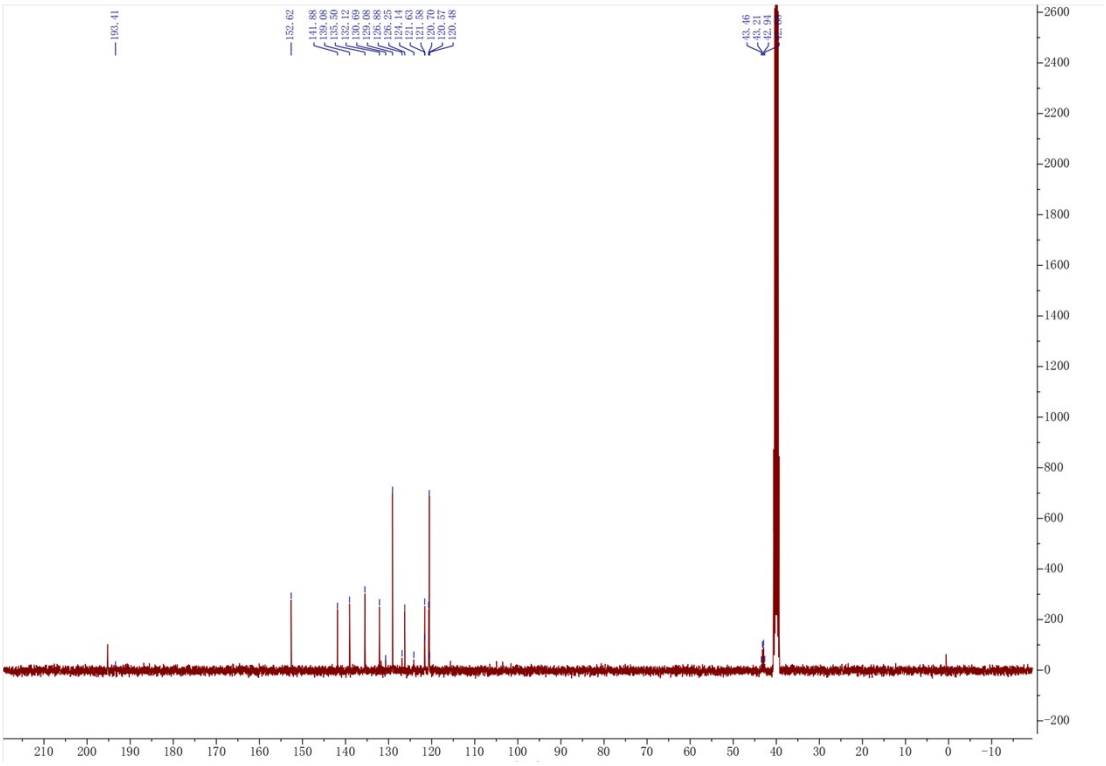
^{19}F NMR (376 MHz, DMSO-d_6) of 5



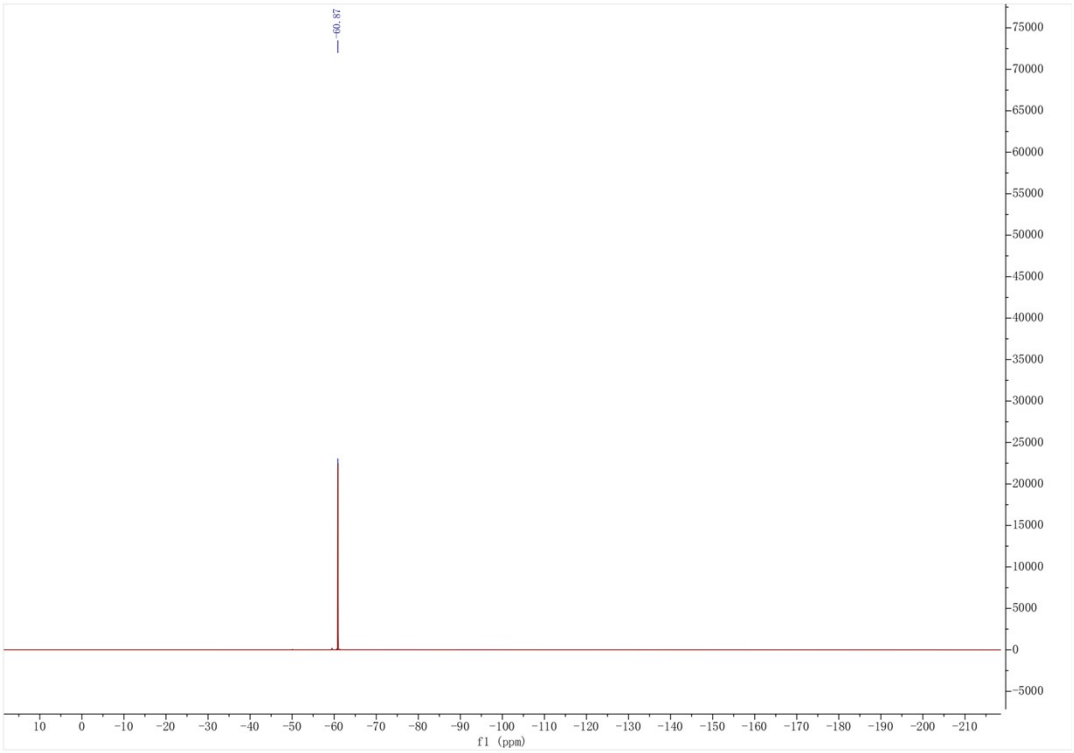
^{1}H NMR (400 MHz, DMSO-d_6) of 6



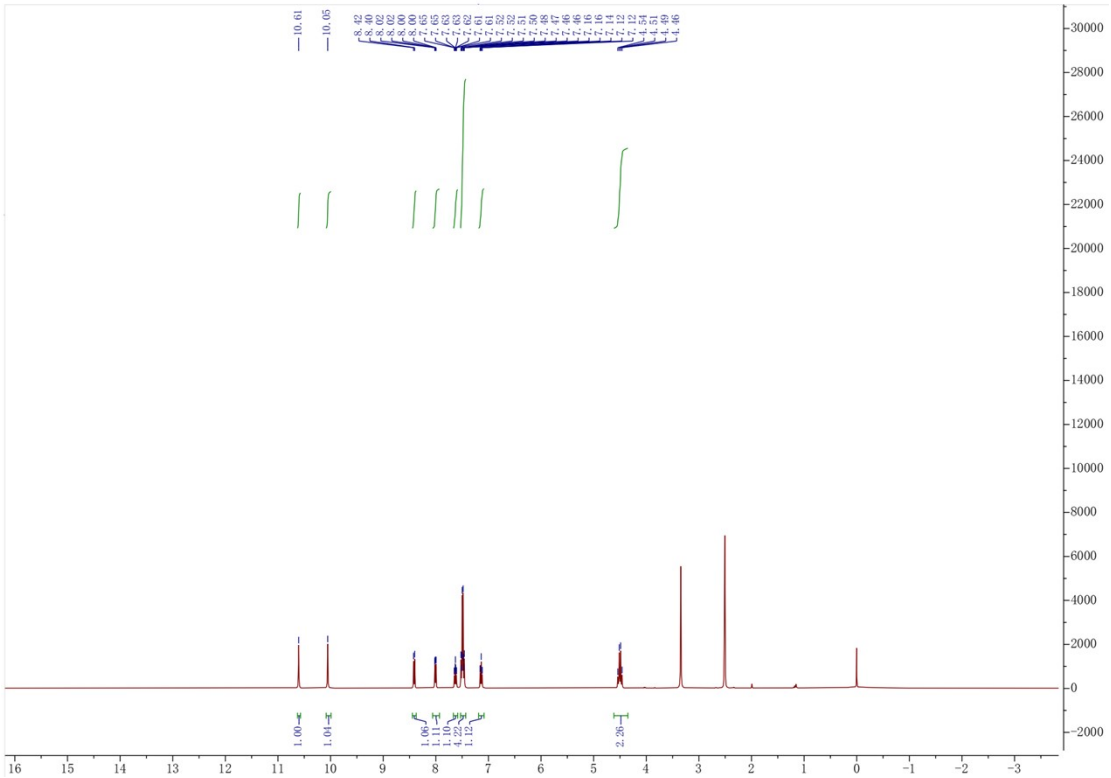
^{13}C NMR (100 MHz, DMSO-d_6) of 6



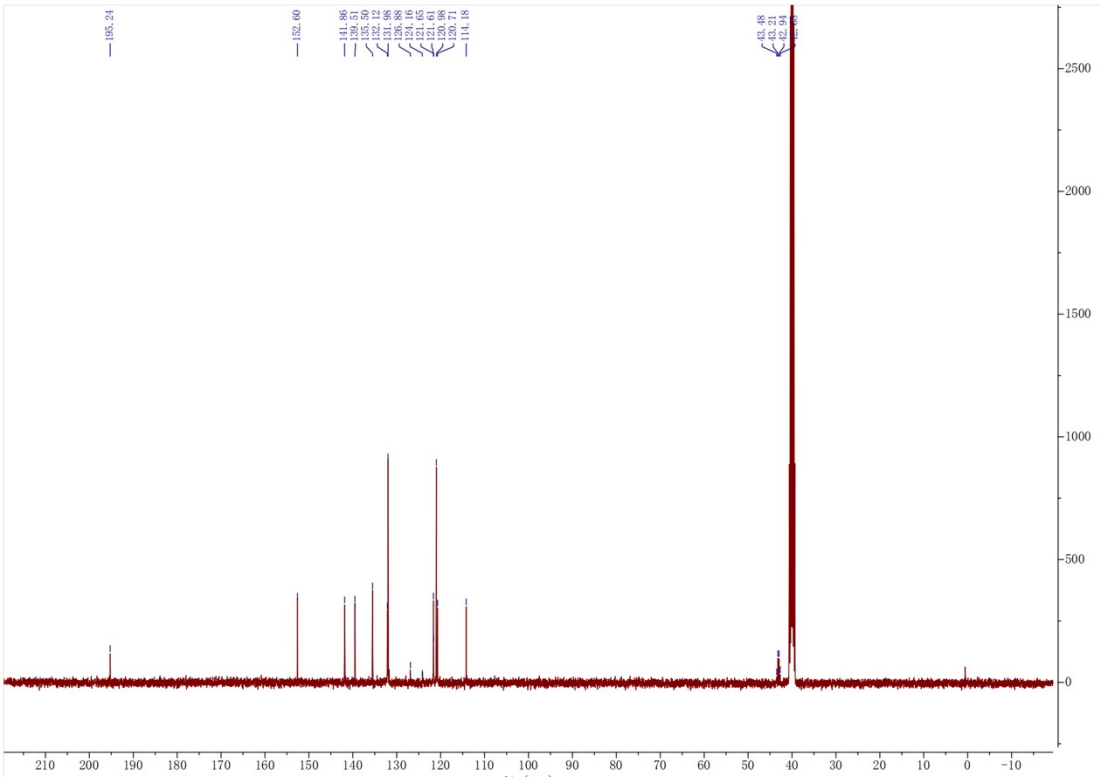
^{19}F NMR (376 MHz, DMSO-d_6) of 6



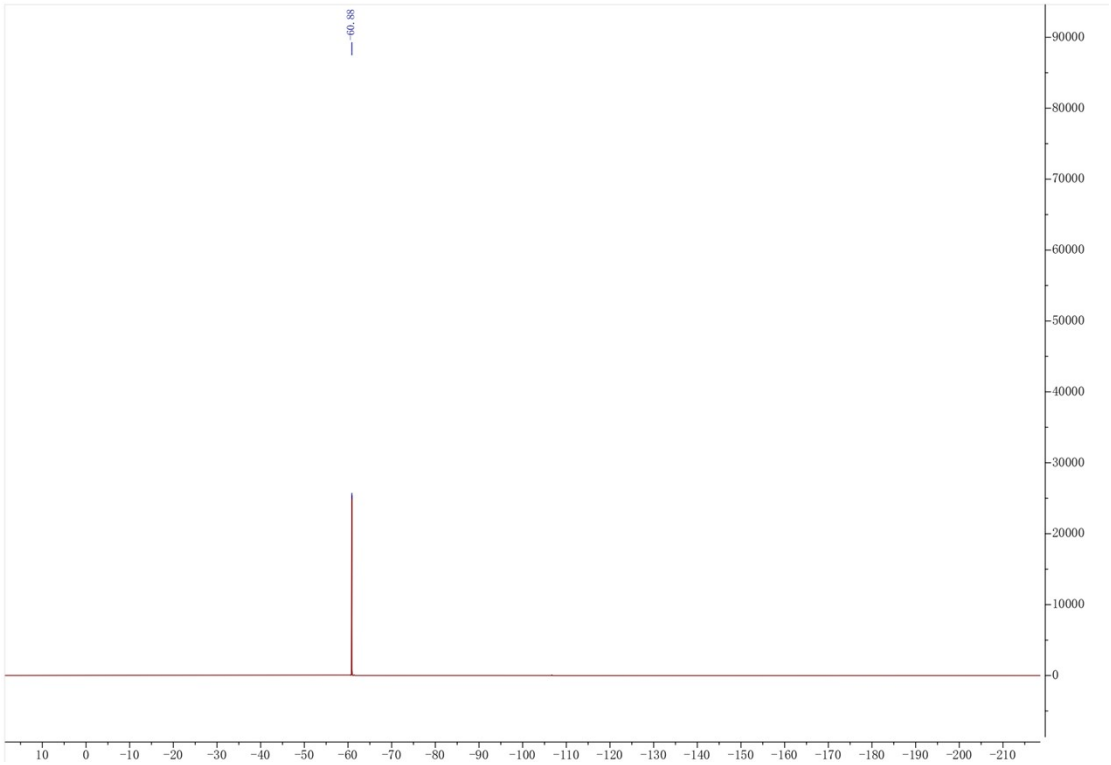
^{1}H NMR (400 MHz, DMSO-d_6) of 7



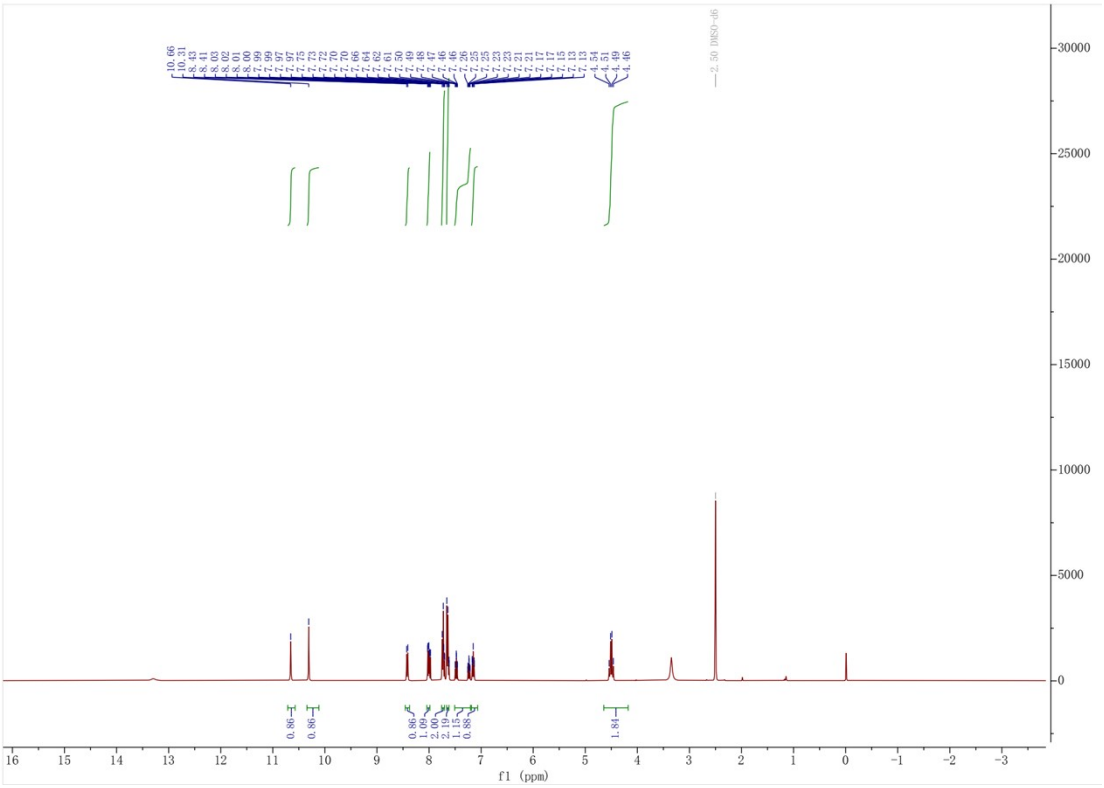
^{13}C NMR (100 MHz, DMSO-d_6) of 7



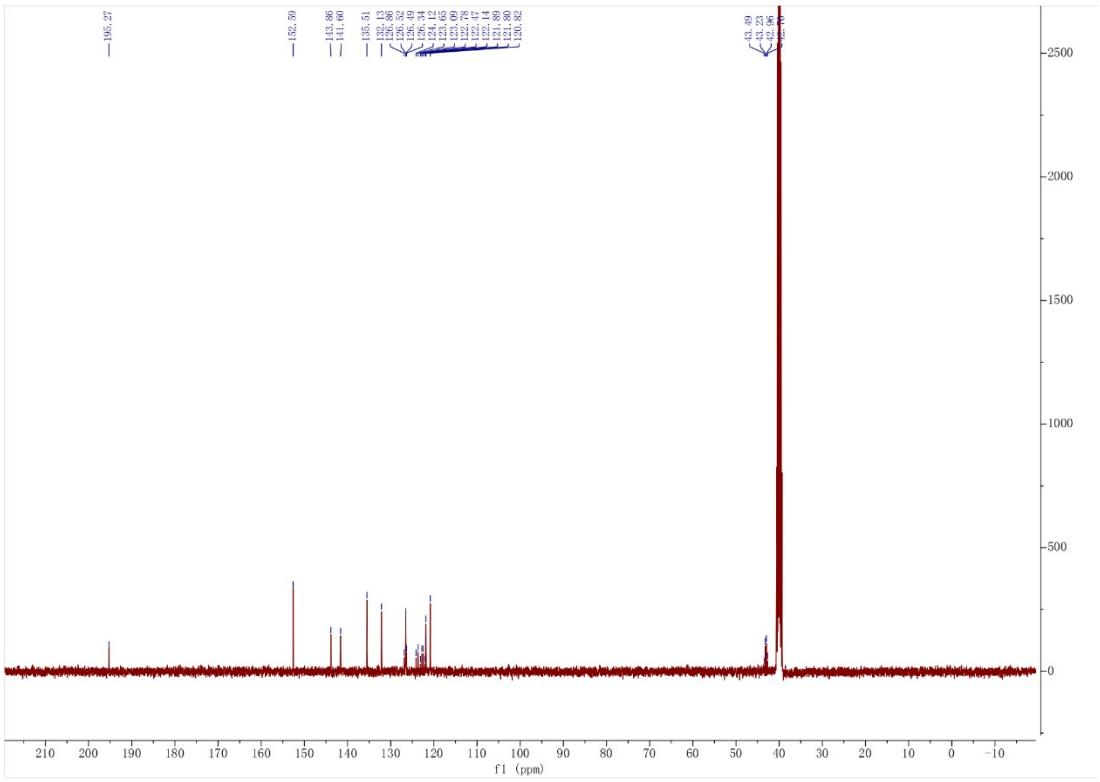
^{19}F NMR (376 MHz, DMSO-d_6) of 7



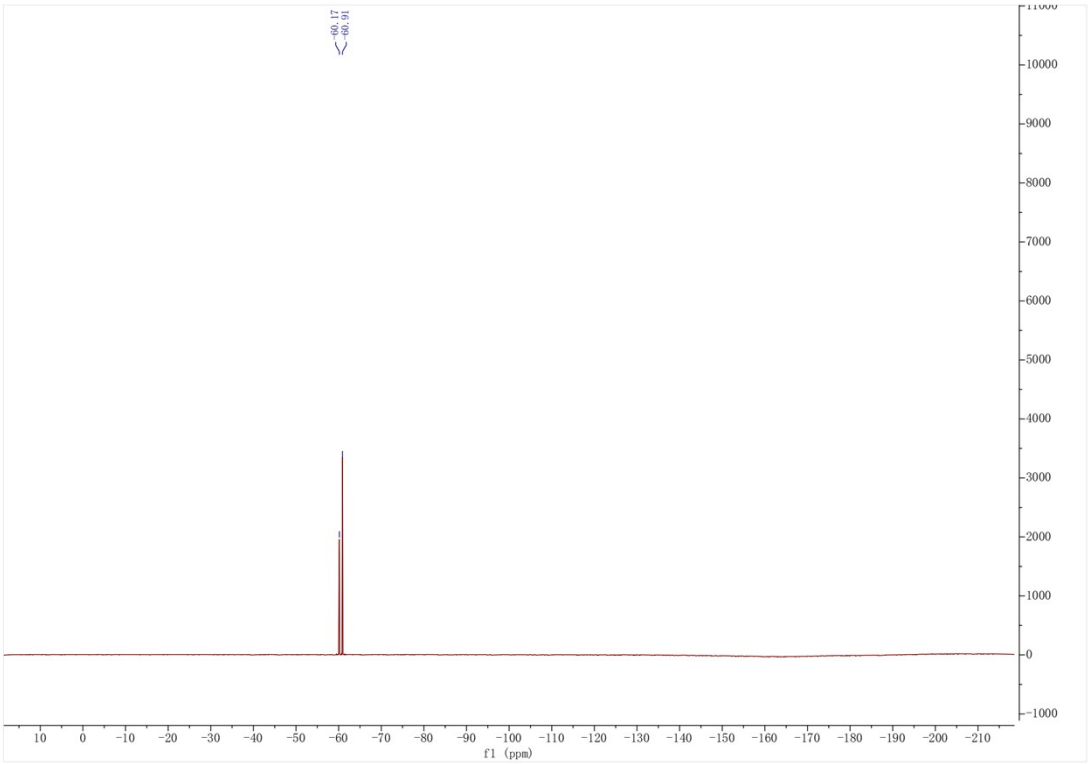
^{1}H NMR (400 MHz, DMSO-d_6) of 8



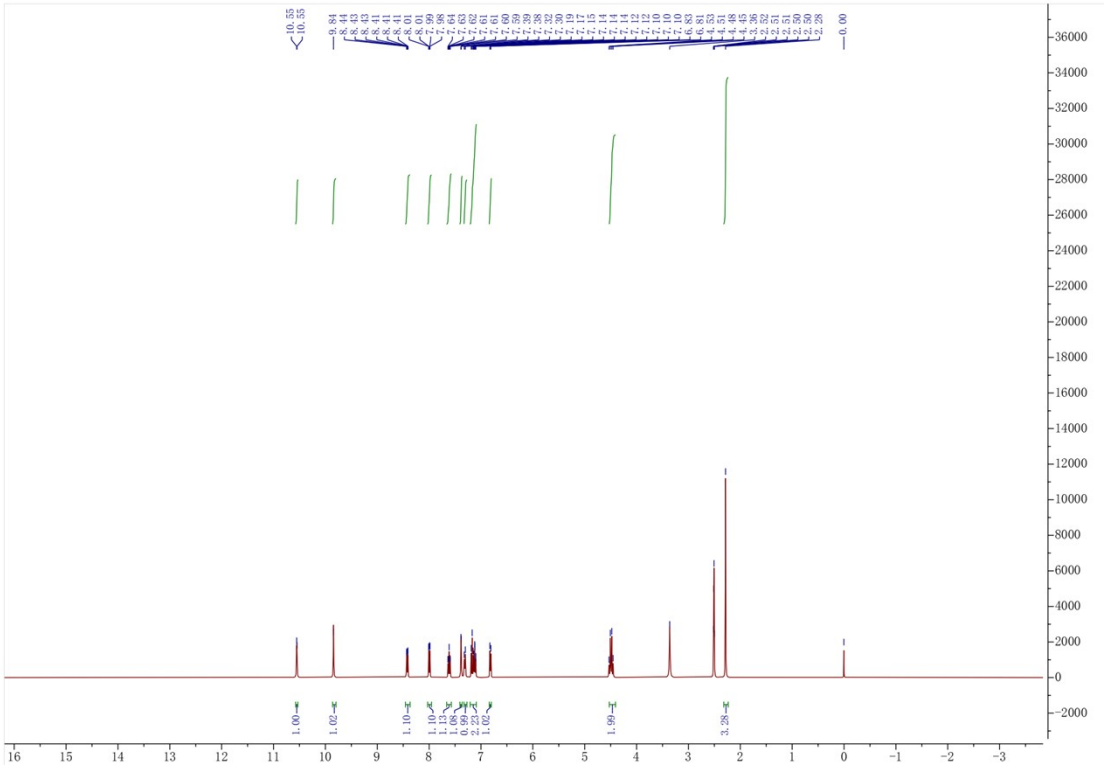
^{13}C NMR (100 MHz, DMSO-d_6) of 8



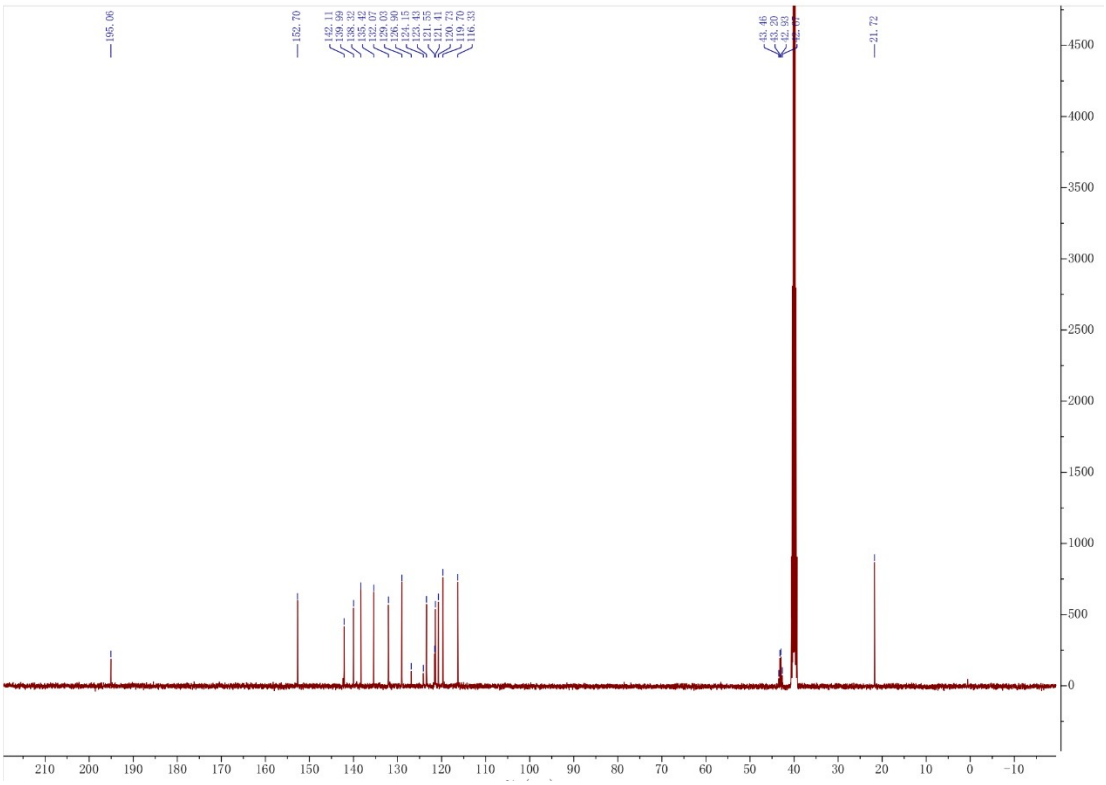
^{19}F NMR (376 MHz, DMSO-d_6) of 8



^{1}H NMR (400 MHz, DMSO-d_6) of 9



^{13}C NMR (100 MHz, DMSO-d_6) of 9



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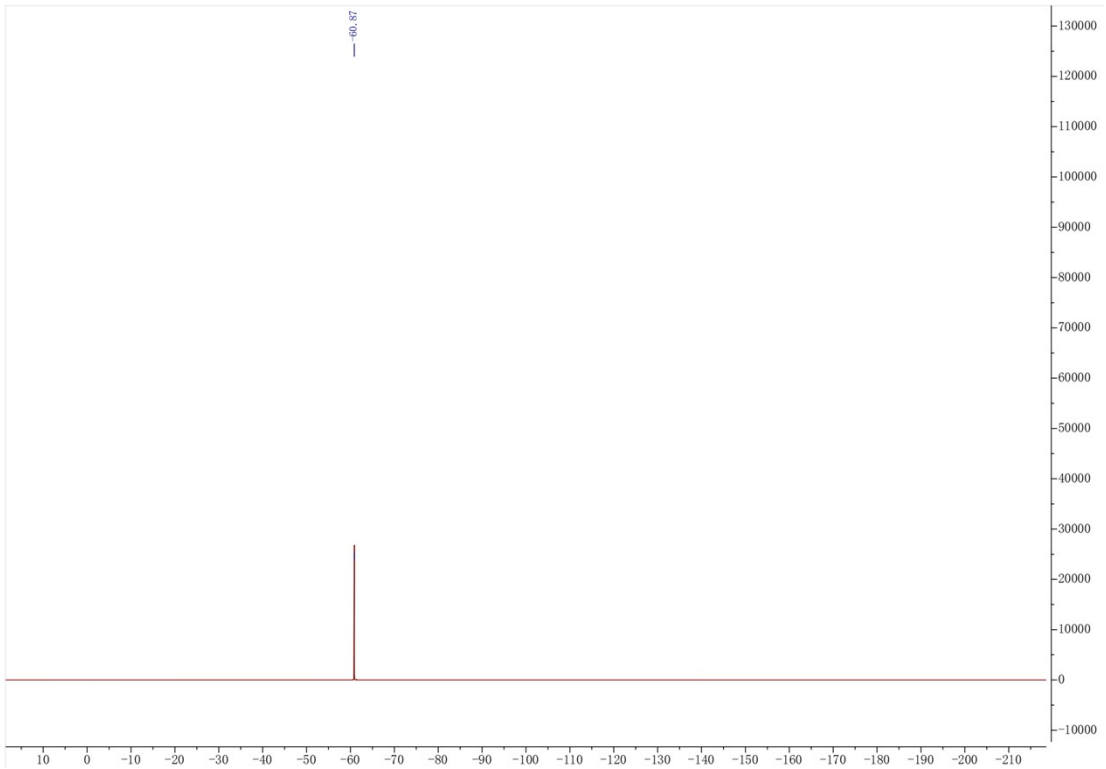
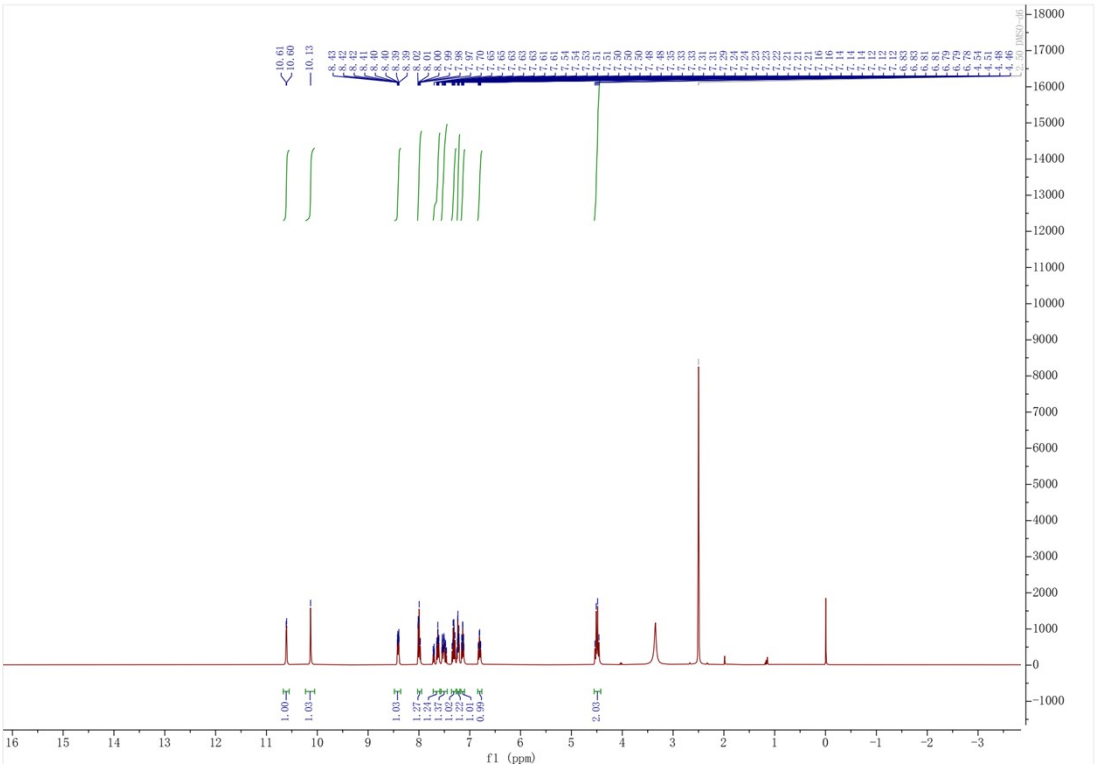


^{1}H NMR (400 MHz, DMSO-d_6) of 10



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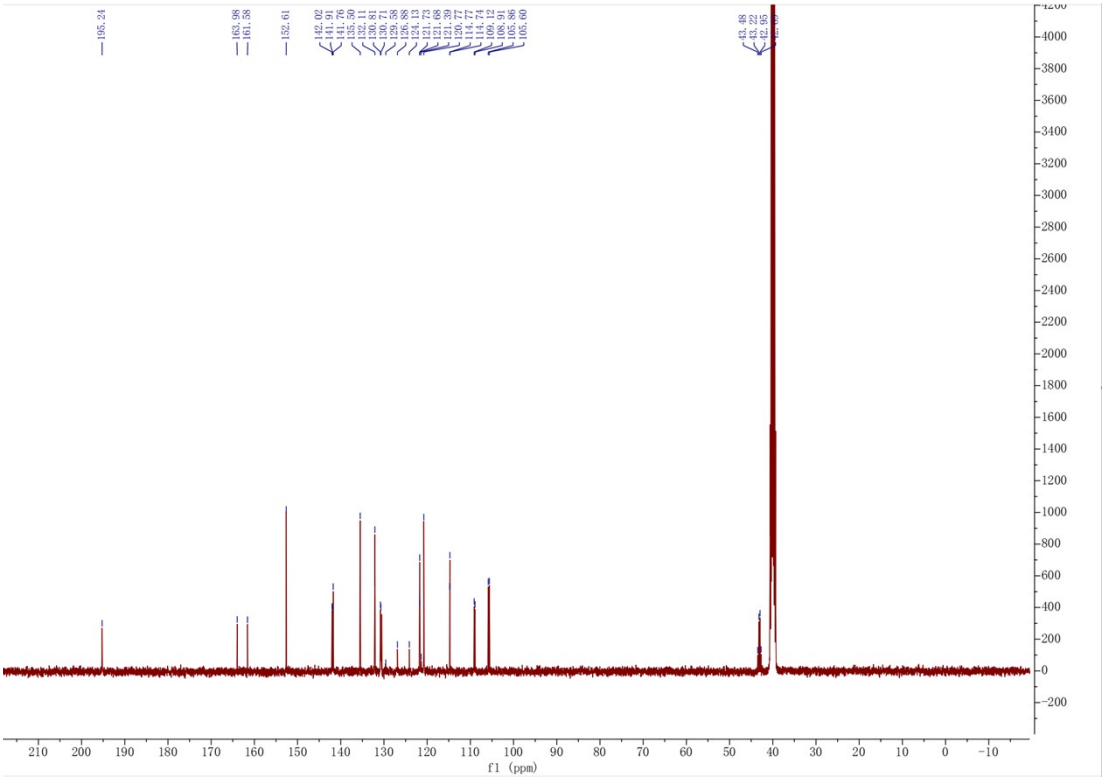
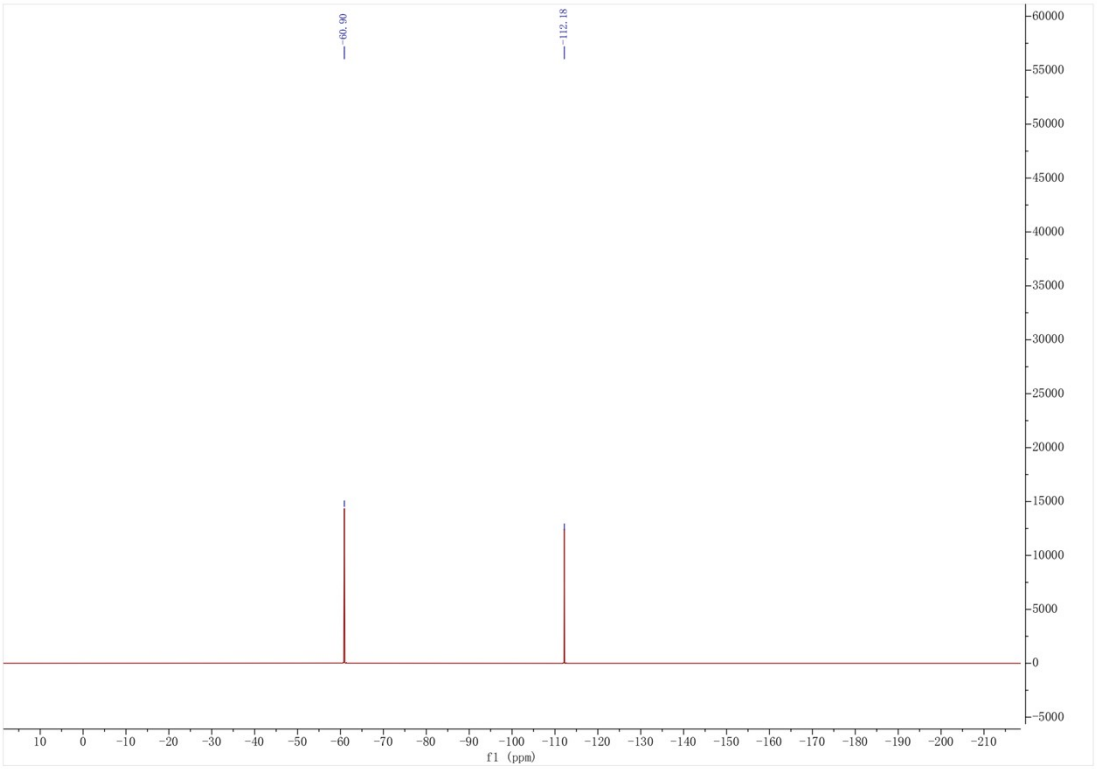
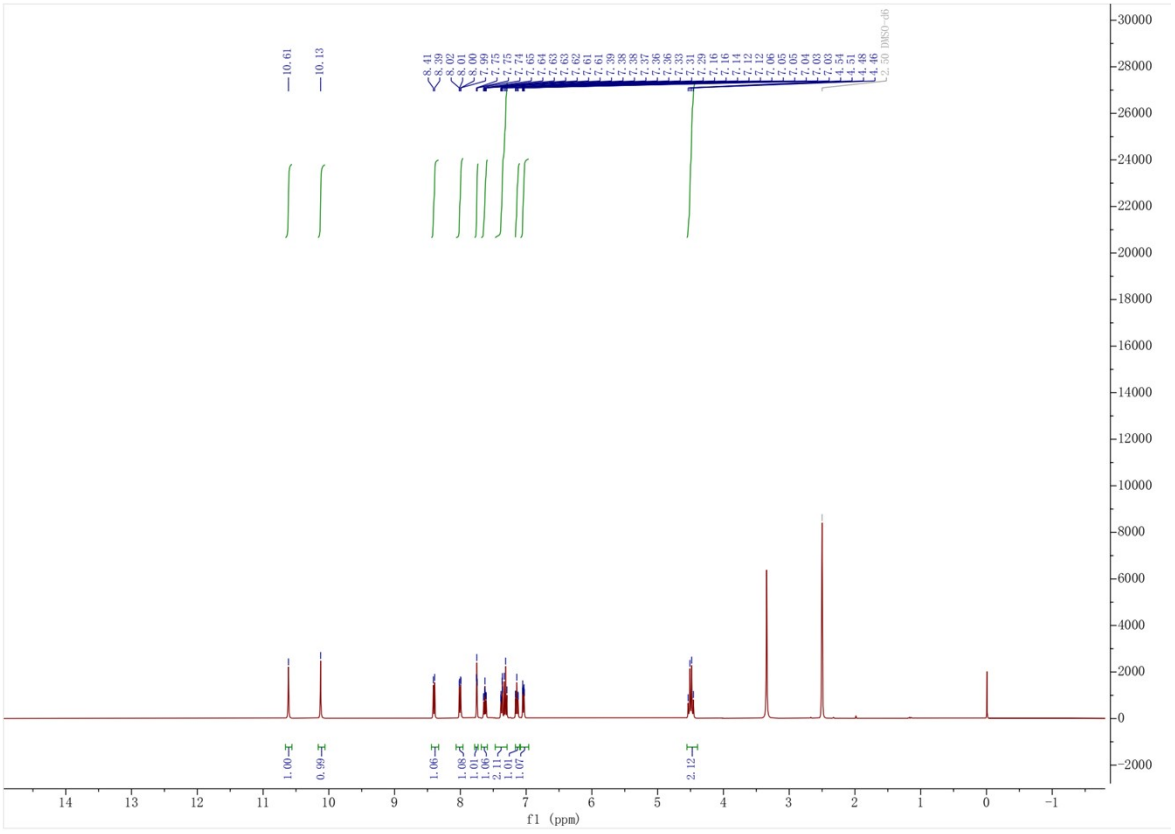


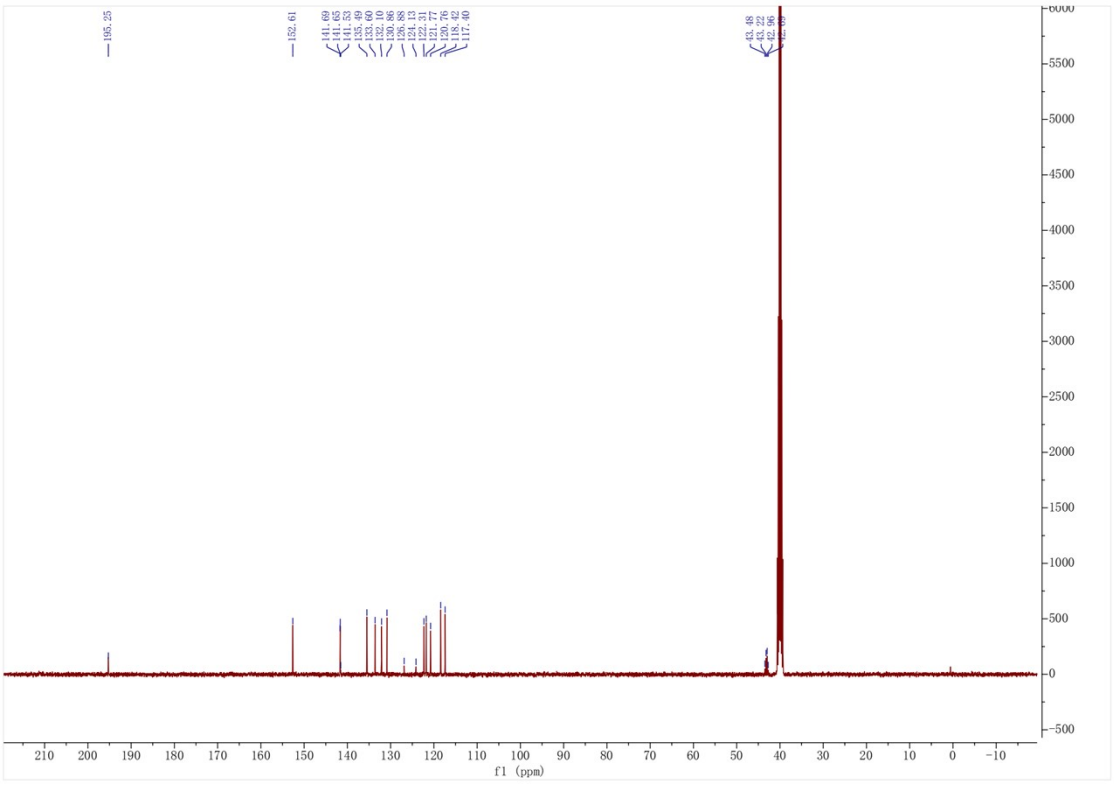
^{19}F NMR (376 MHz, DMSO-d_6) of 10



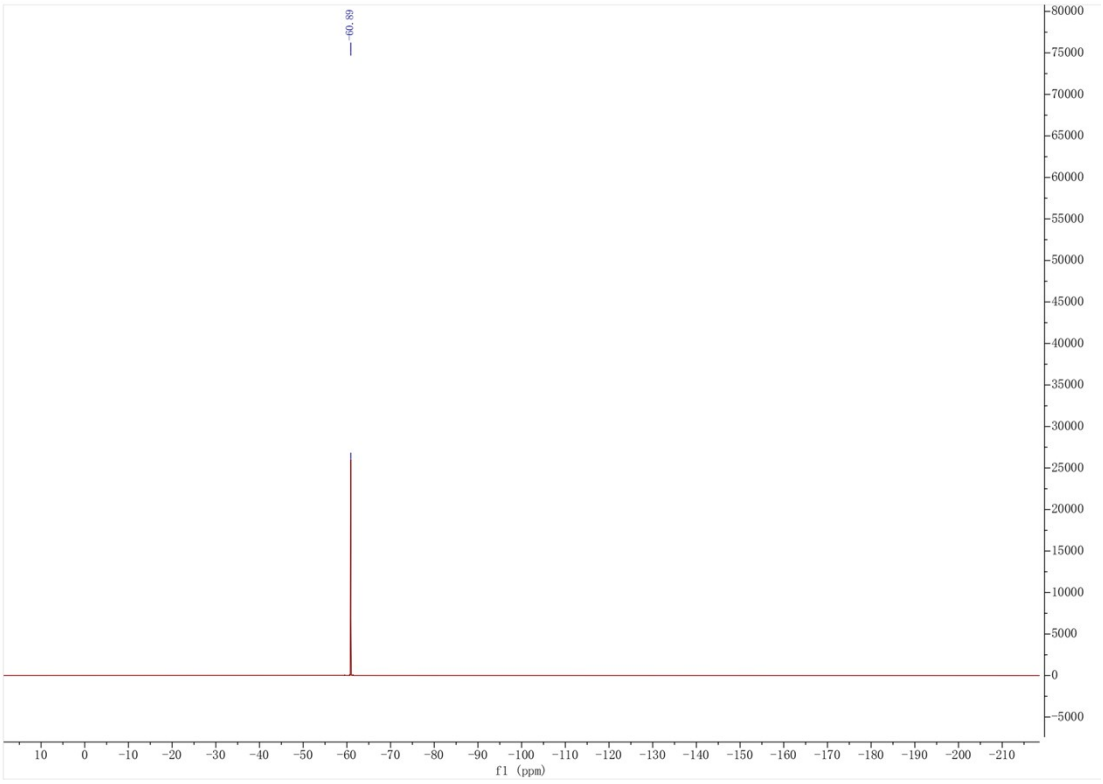
^{1}H NMR (400 MHz, DMSO-d_6) of 11



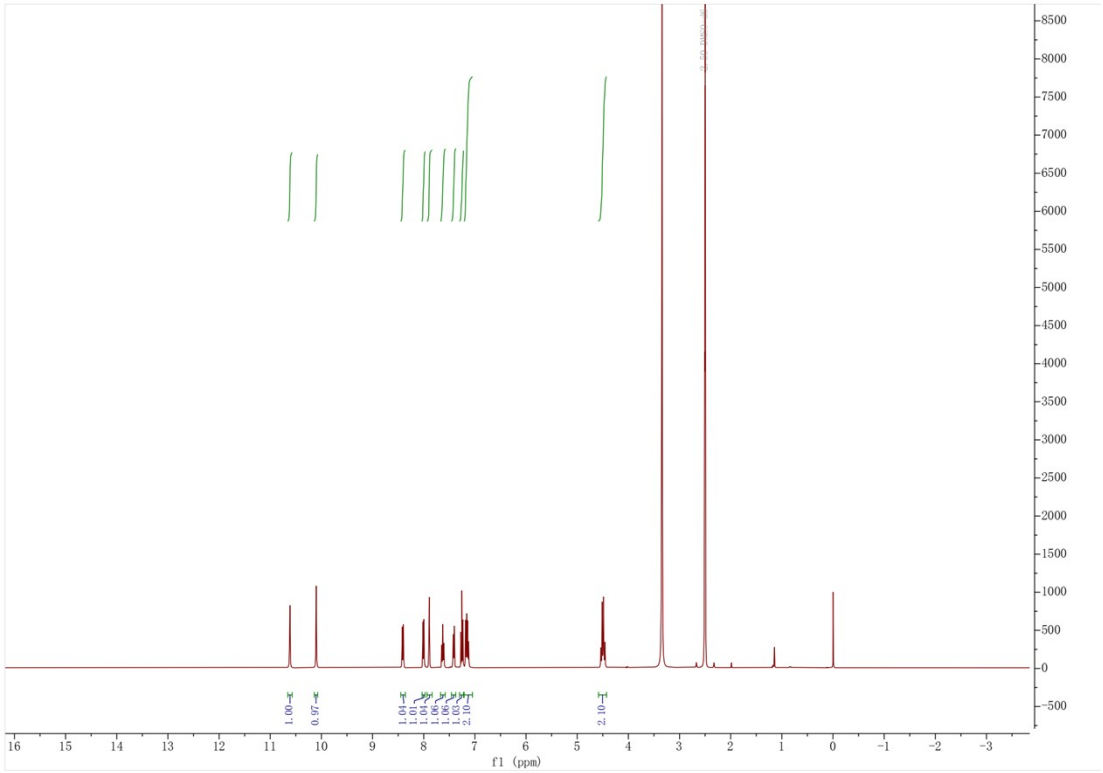
^{13}C NMR (100 MHz, DMSO-d_6) of 11



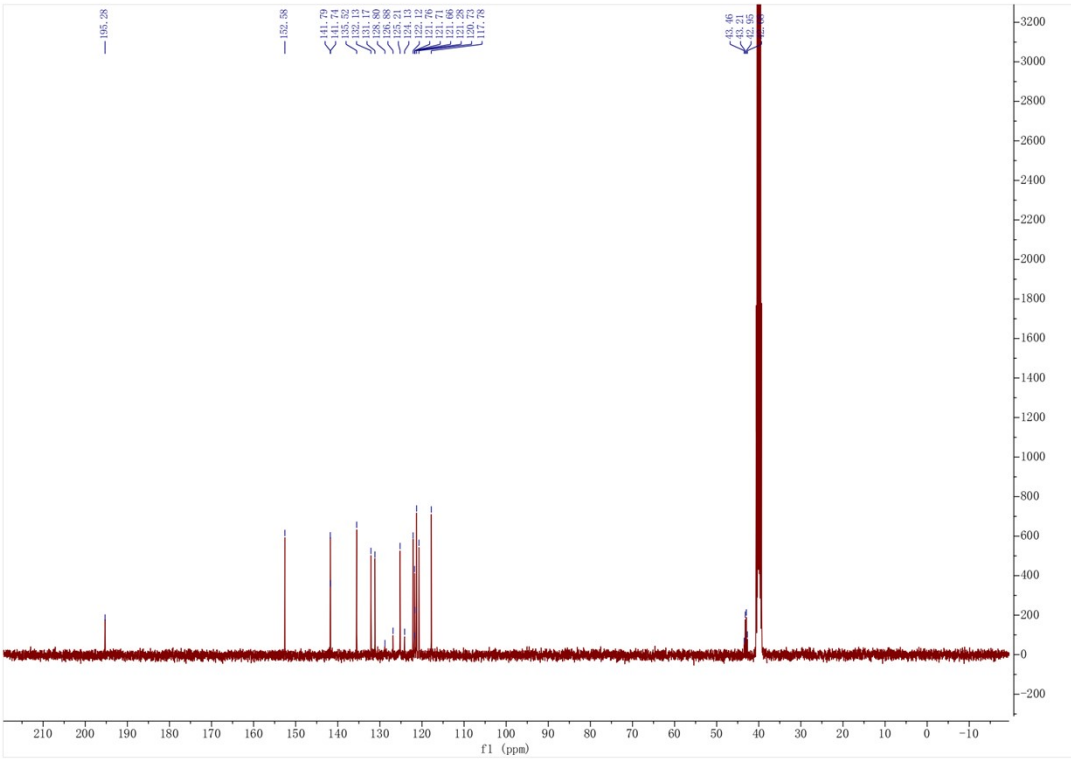
^{19}F NMR (376 MHz, DMSO-d_6) of 11



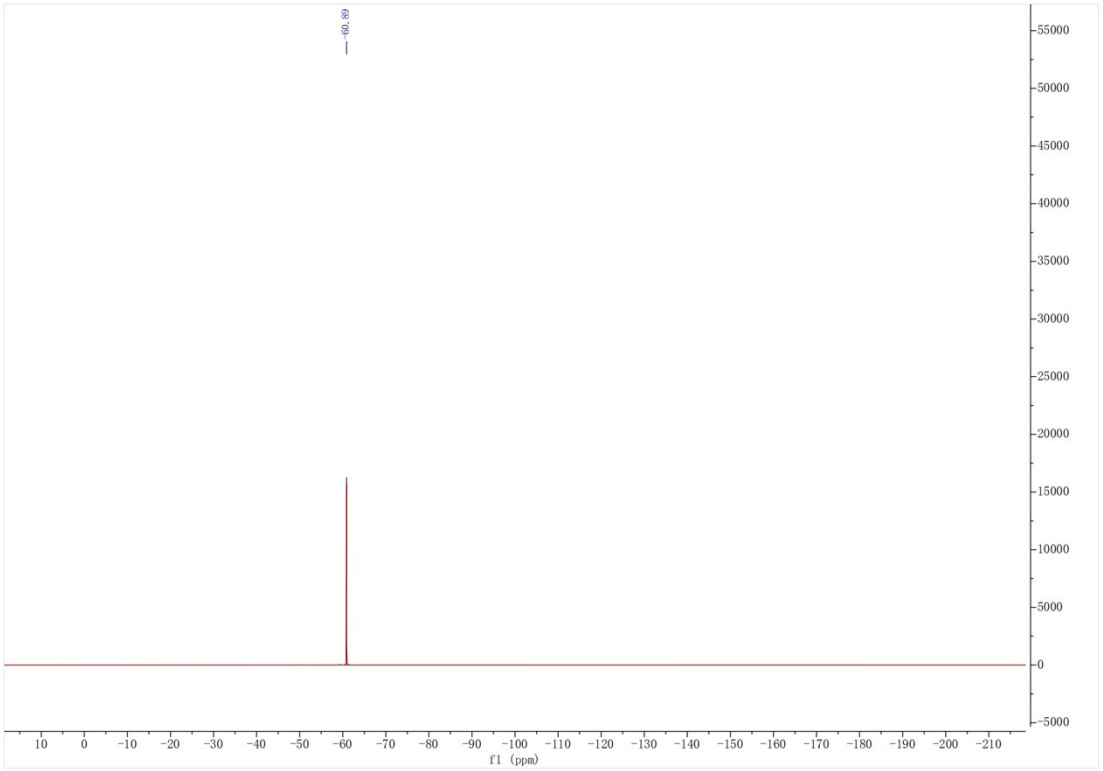
^{1}H NMR (400 MHz, DMSO-d_6) of 12



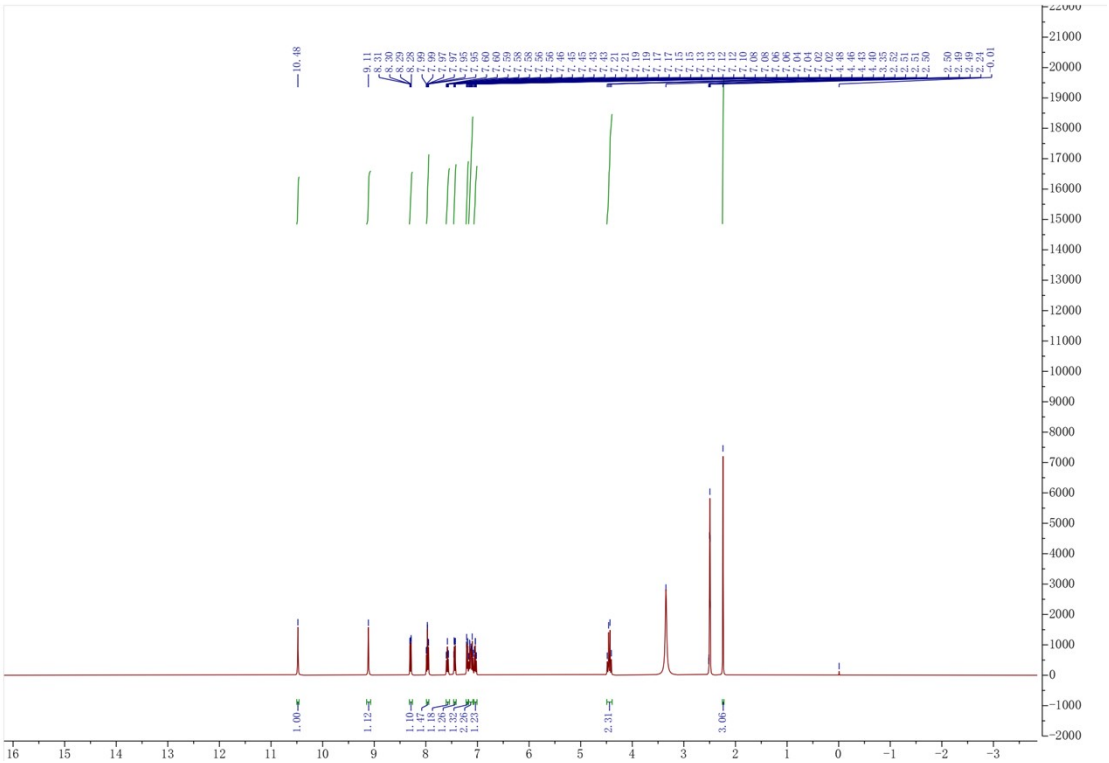
^{13}C NMR (100 MHz, DMSO-d_6) of 12



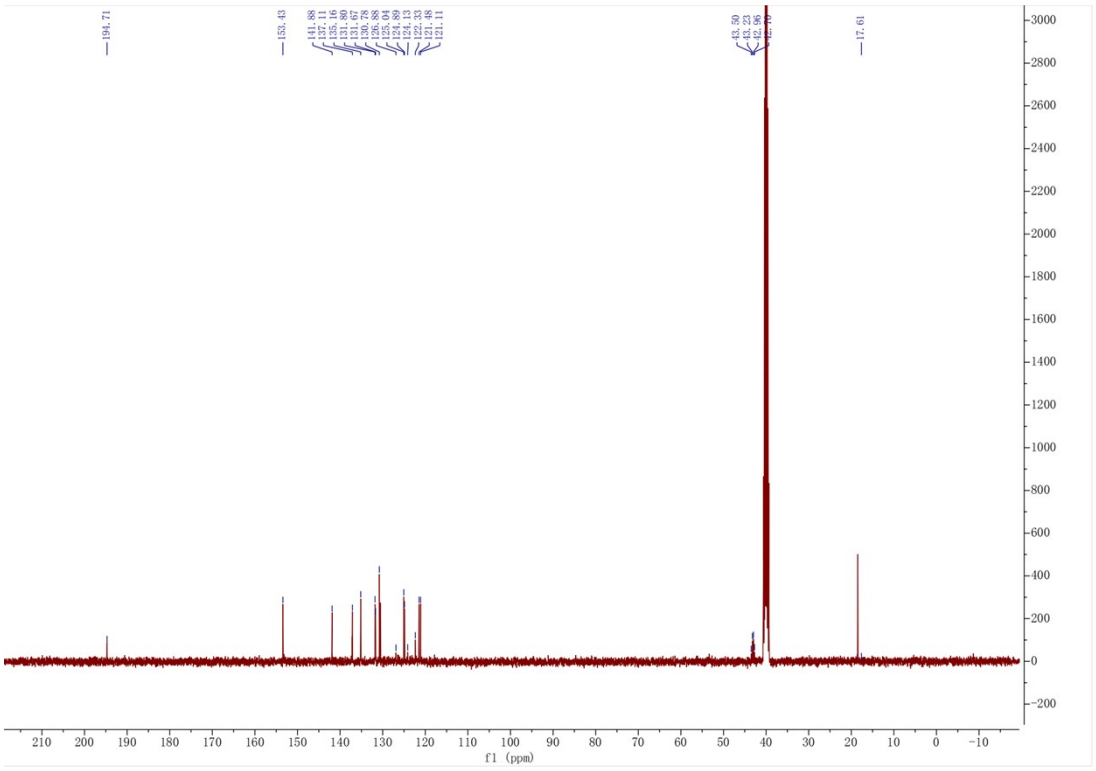
^{19}C NMR (376 MHz, DMSO-d_6) of 12



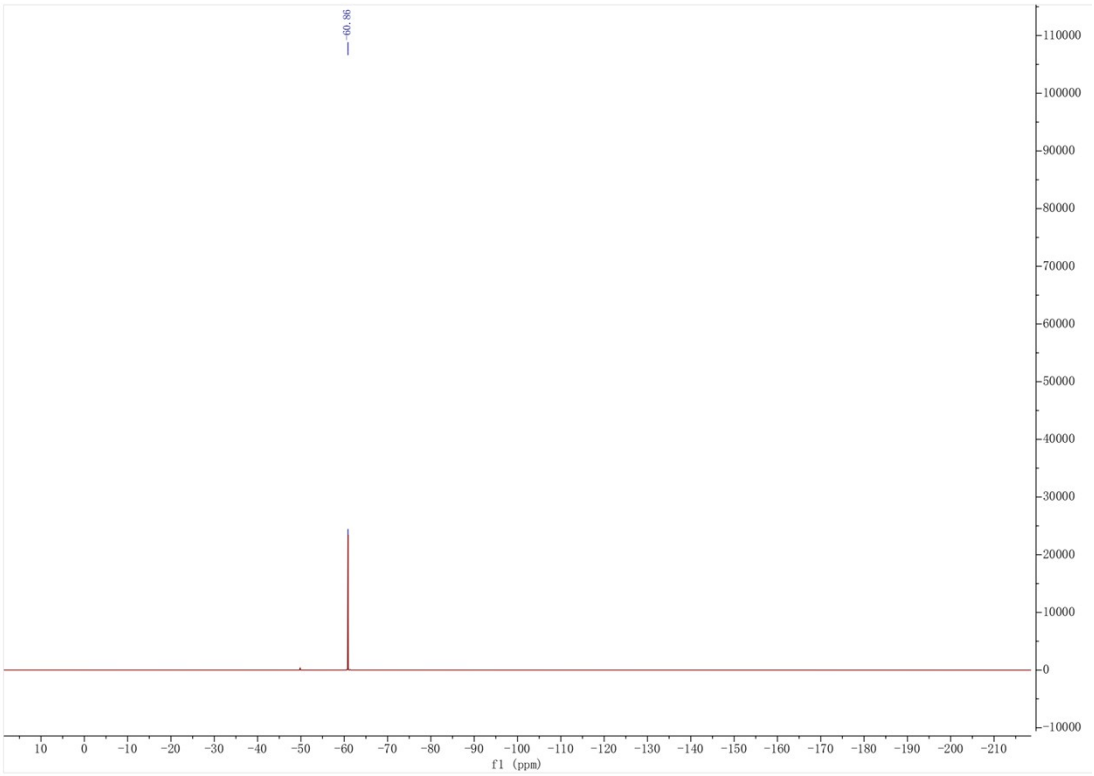
^{1}H NMR (400 MHz, DMSO-d_6) of 13



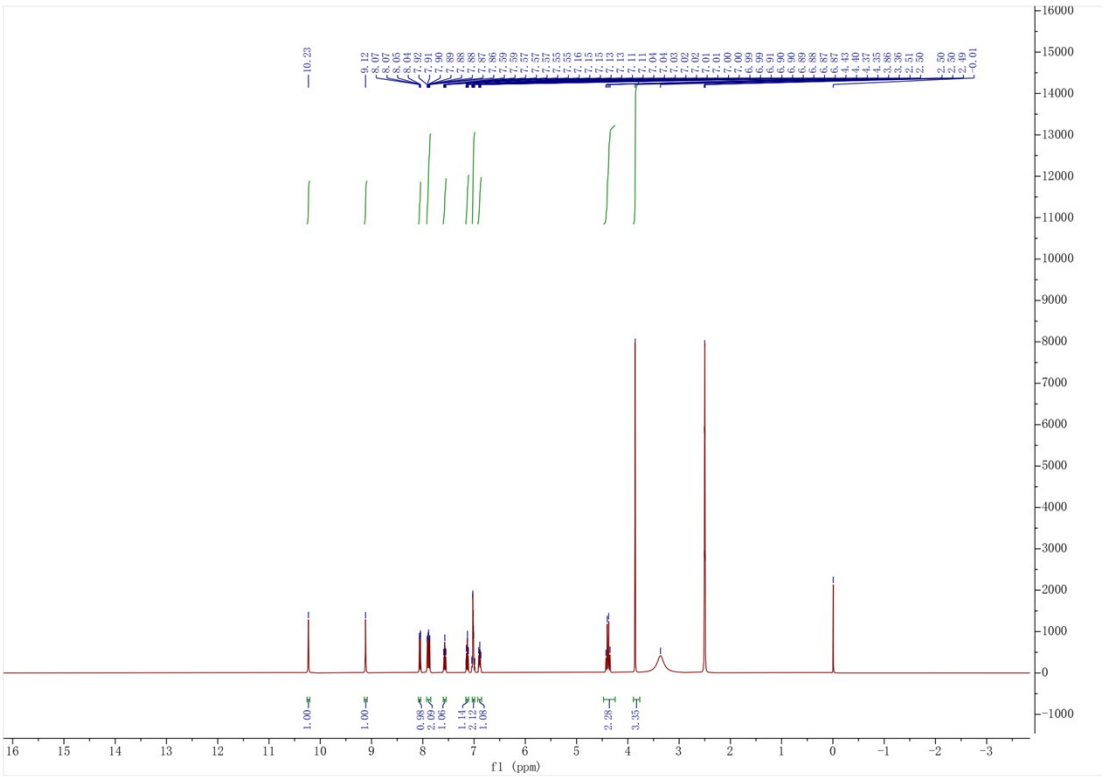
^{13}C NMR (100 MHz, DMSO-d_6) of 13



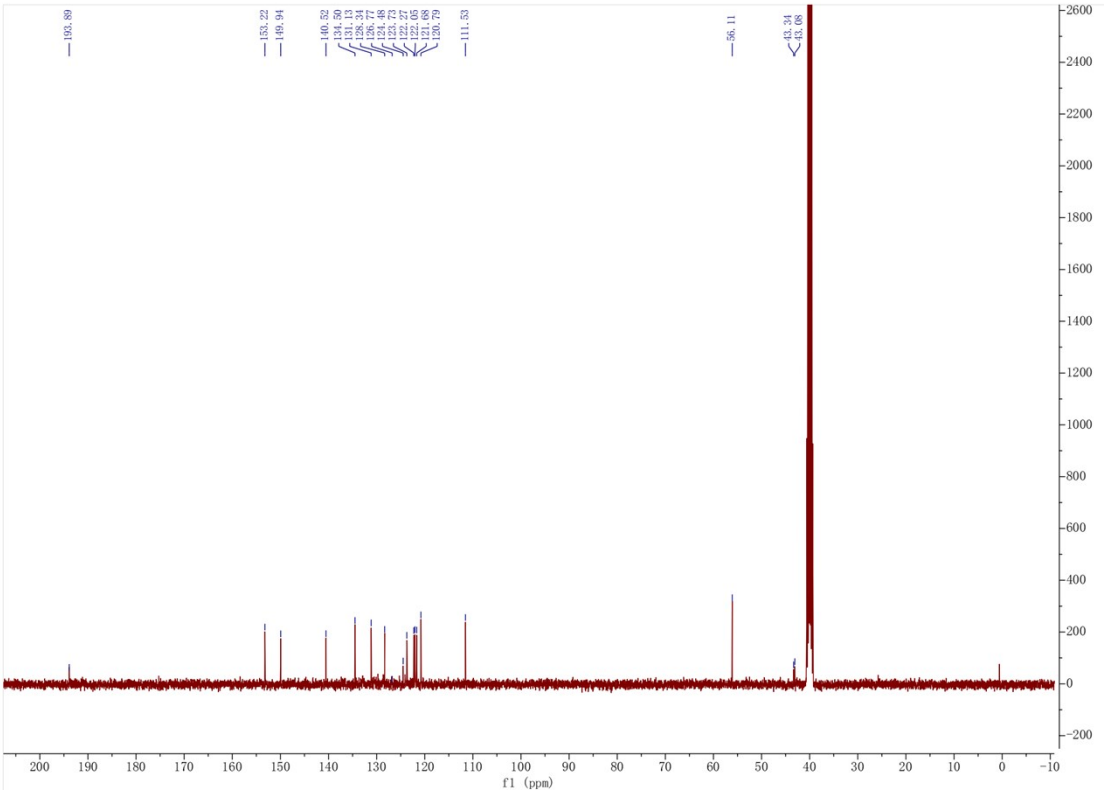
^{19}F NMR (376 MHz, DMSO-d_6) of 13



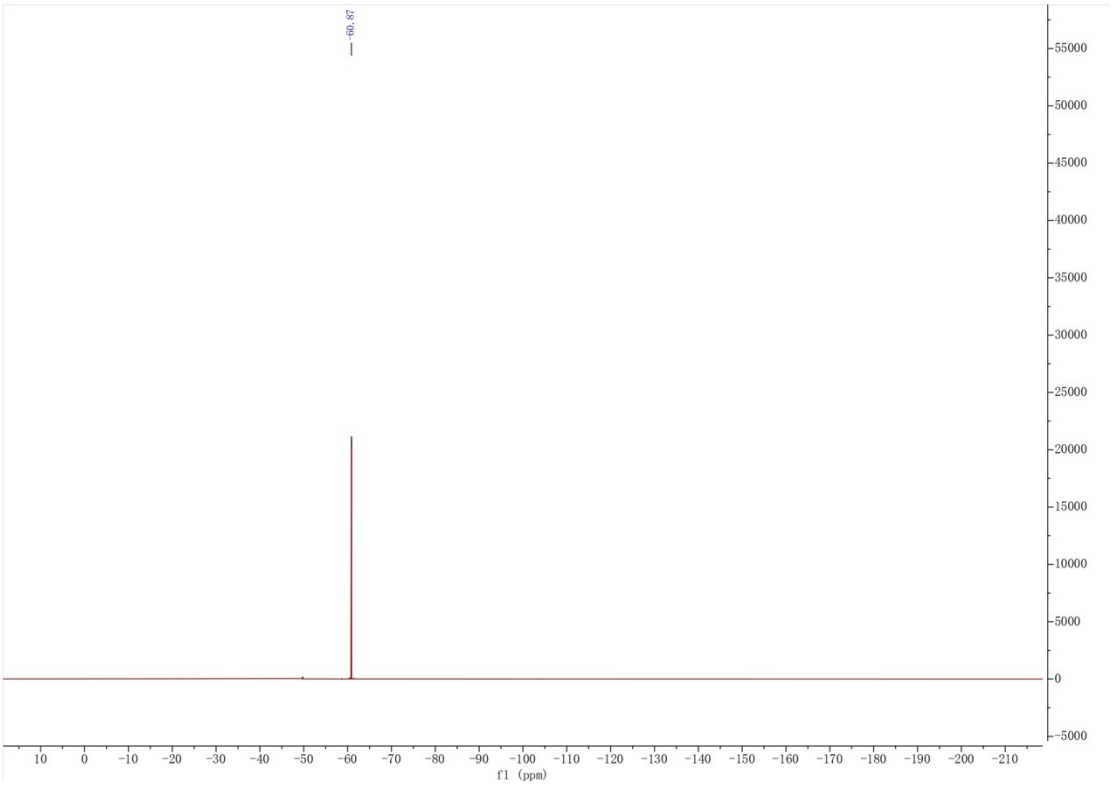
^{1}H NMR (400 MHz, DMSO-d_6) of 14



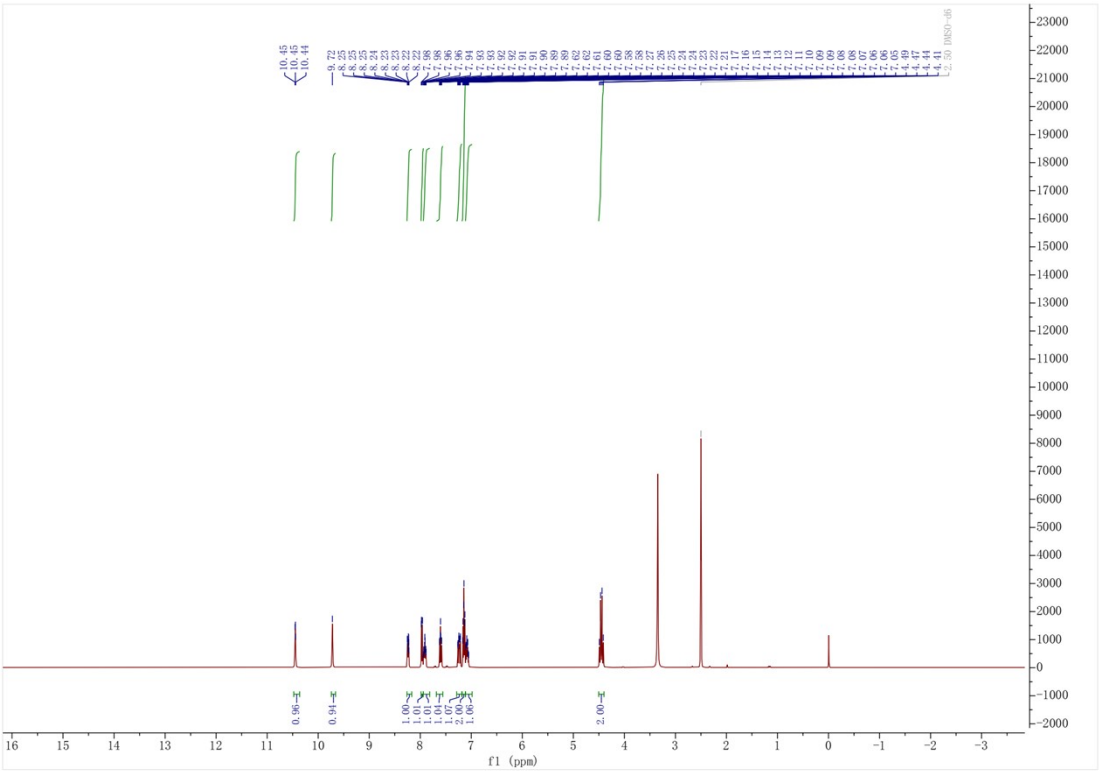
^{13}C NMR (100 MHz, DMSO-d_6) of 14



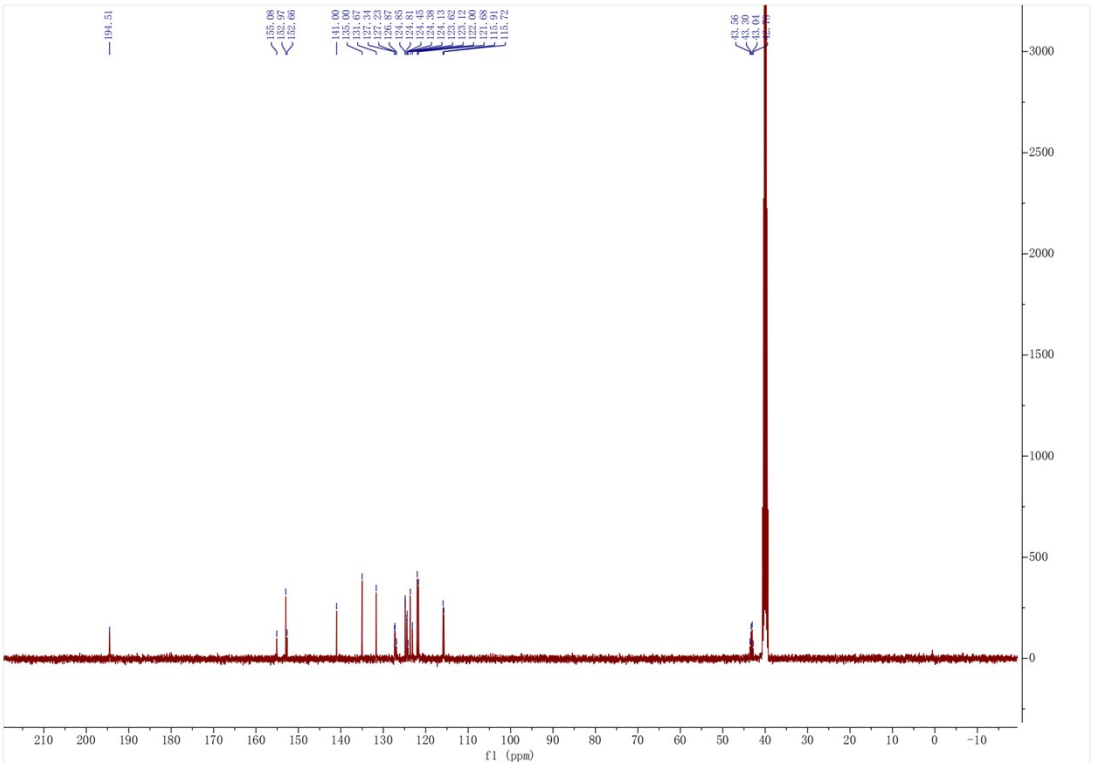
^{19}F NMR (376 MHz, DMSO-d_6) of 14



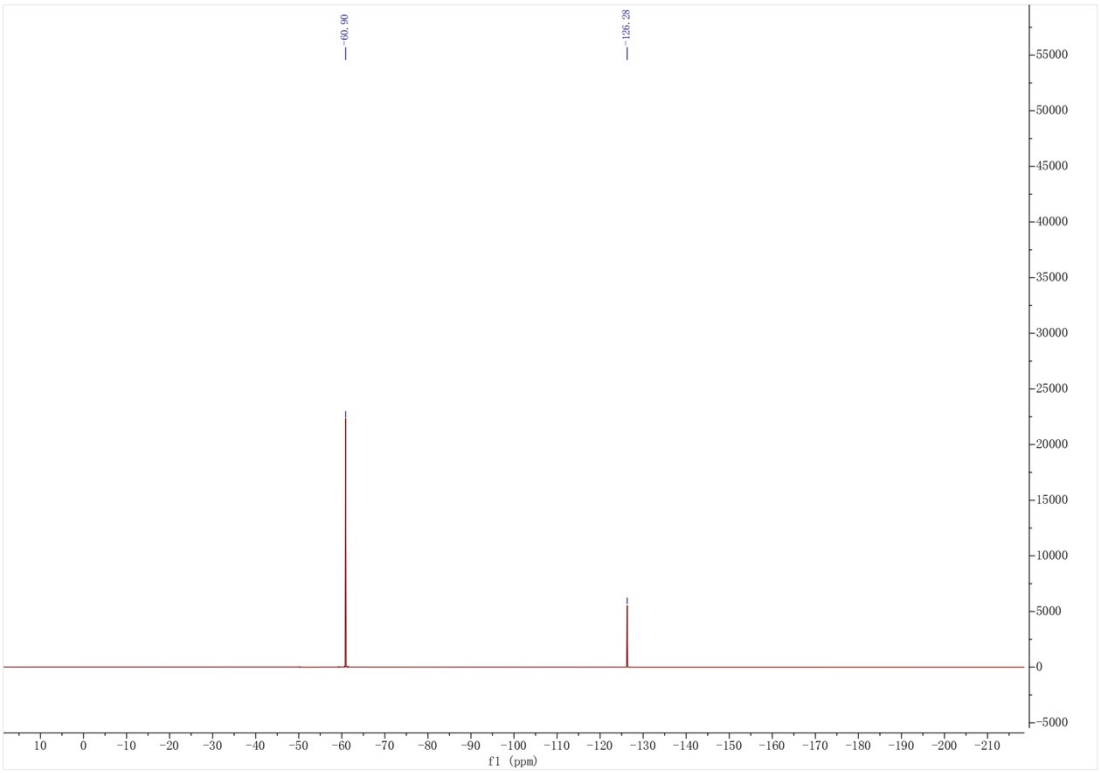
^{1}H NMR (400 MHz, DMSO-d_6) of 15



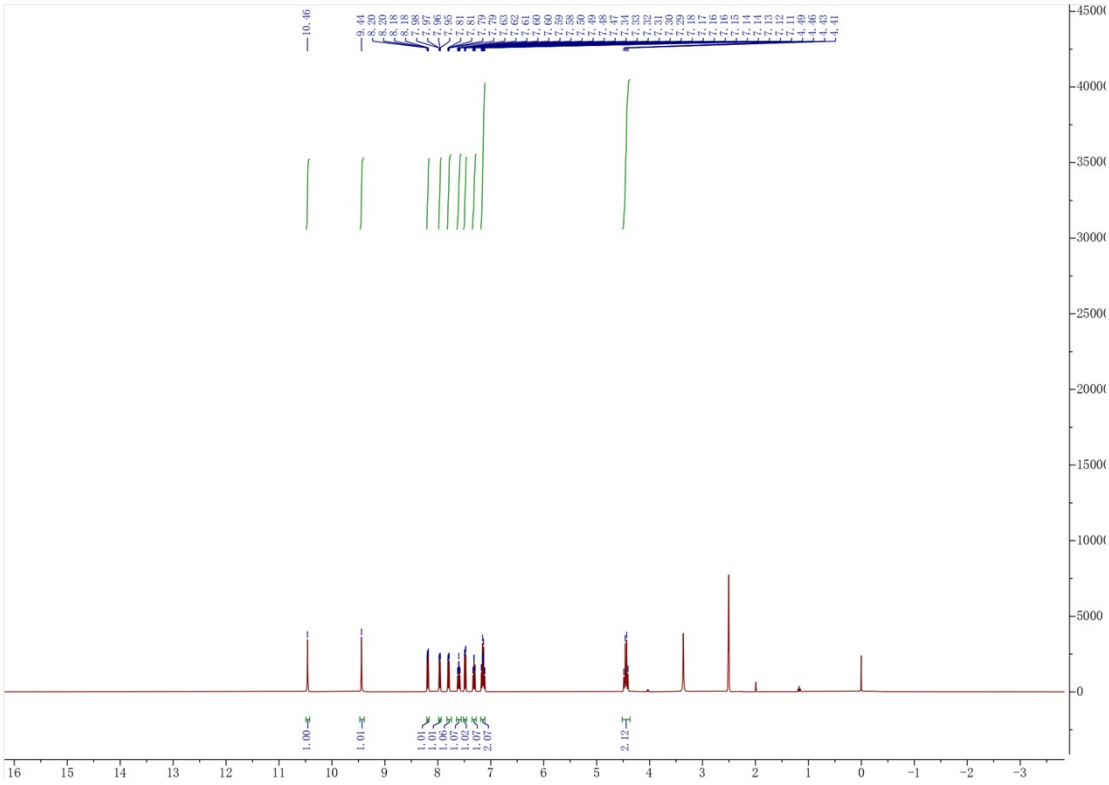
^{13}C NMR (100 MHz, DMSO-d_6) of 15



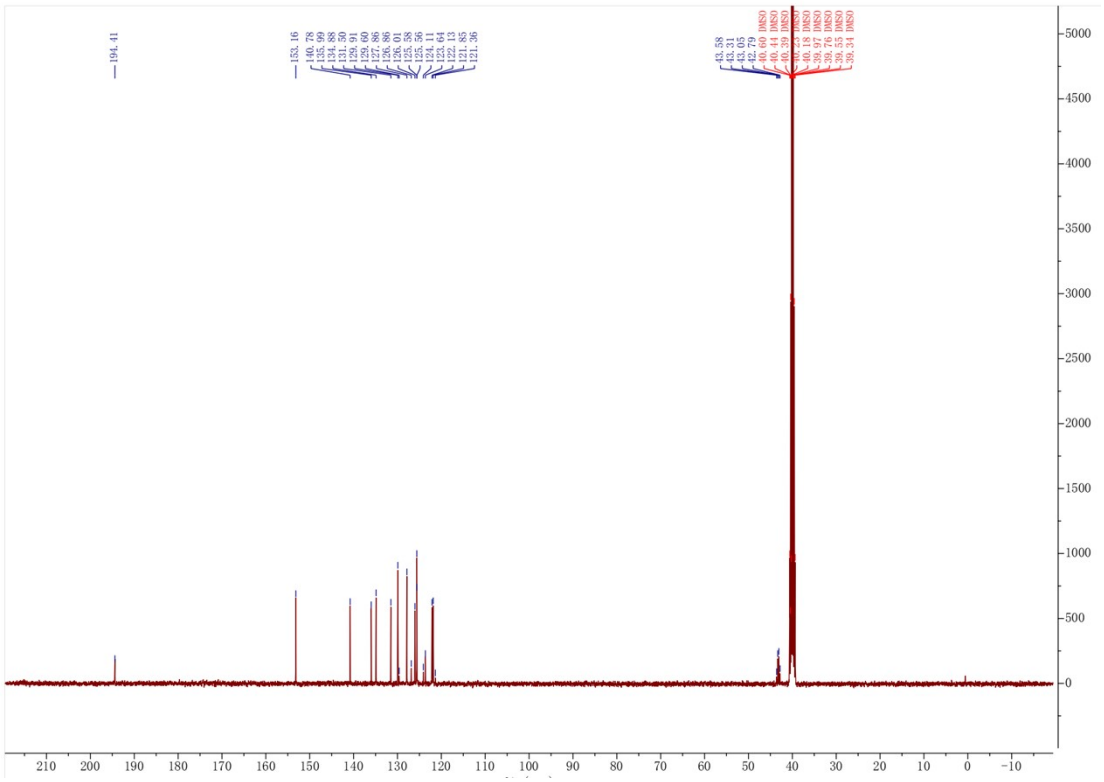
^{19}F NMR (376 MHz, DMSO-d_6) of 15



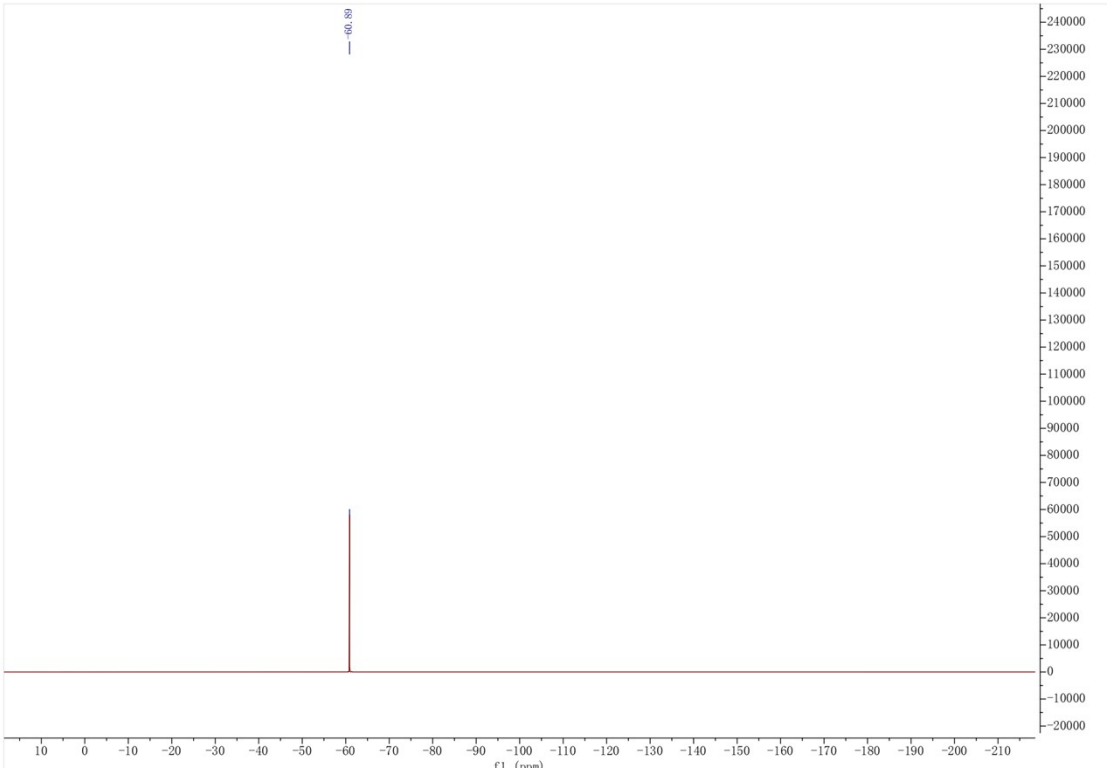
^{1}H NMR (400 MHz, DMSO-d_6) of 16



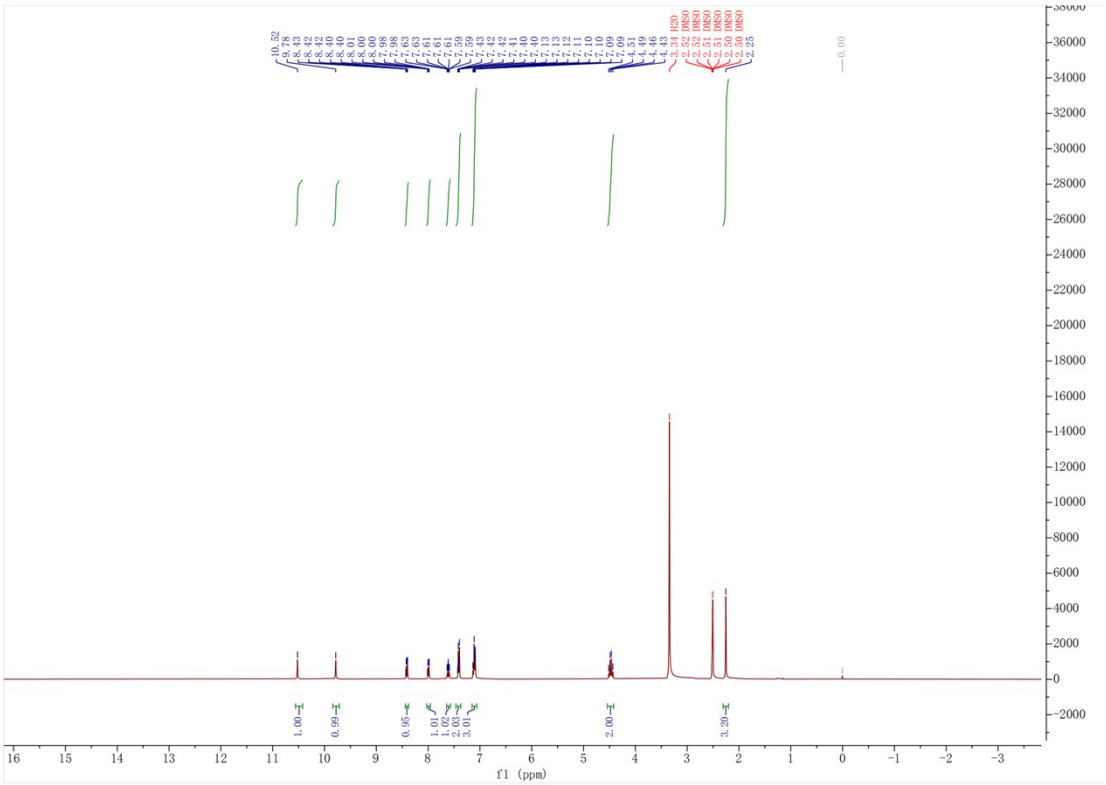
^{13}C NMR (100 MHz, DMSO-d_6) of 16



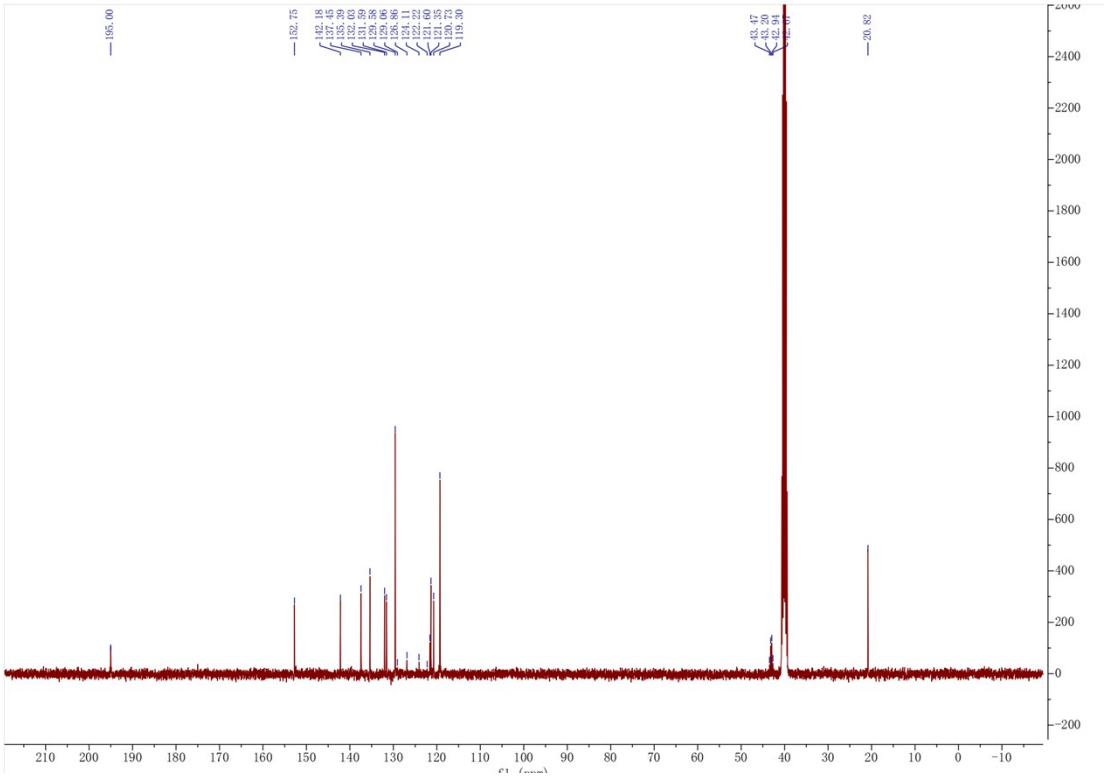
^{19}F NMR (376 MHz, DMSO-d_6) of 16



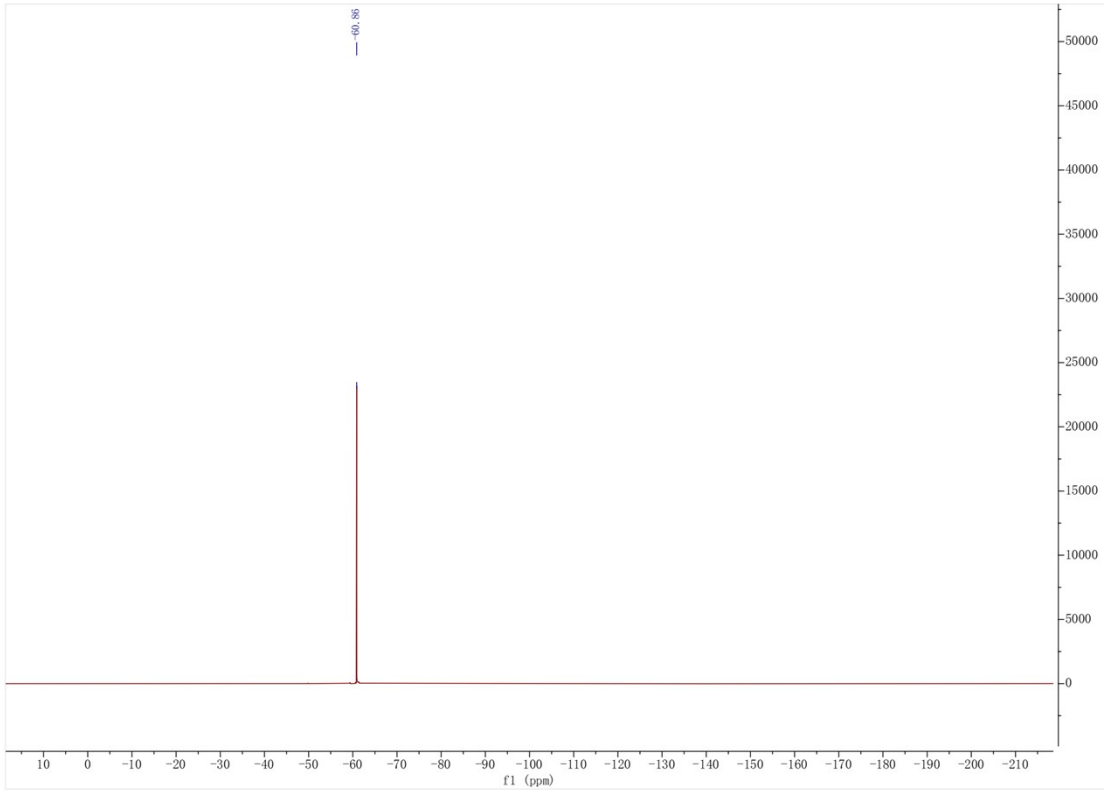
^{1}H NMR (400 MHz, DMSO-d_6) of 21



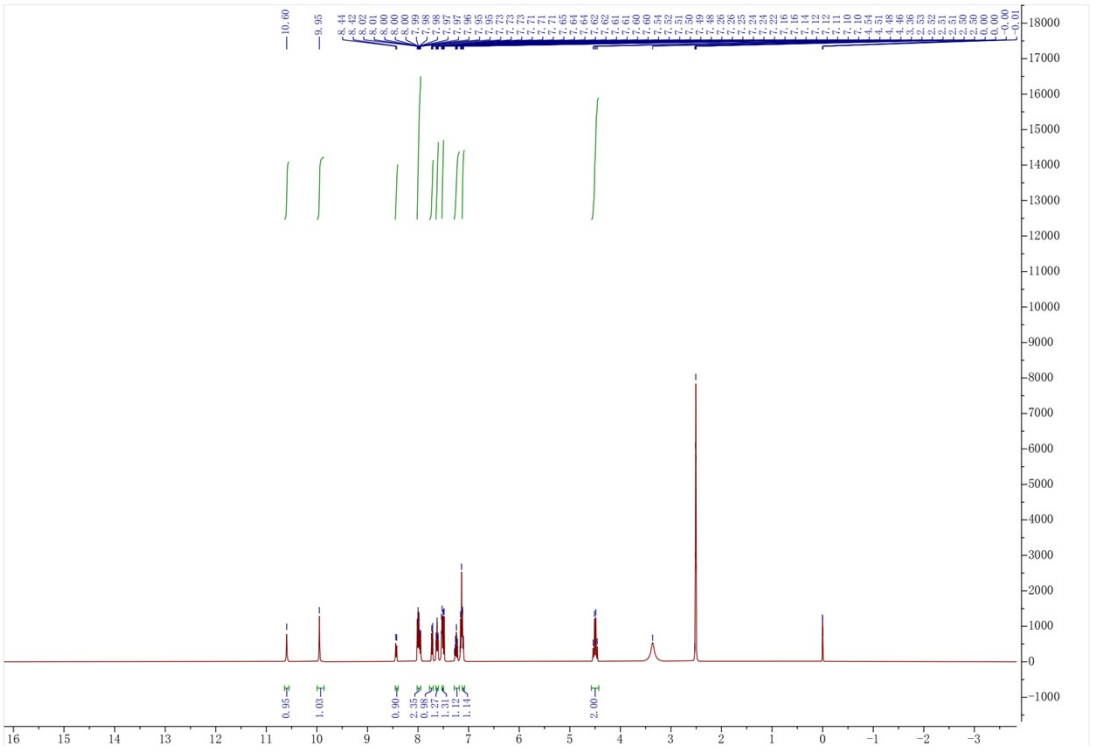
^{13}C NMR (100 MHz, DMSO-d_6) of 21



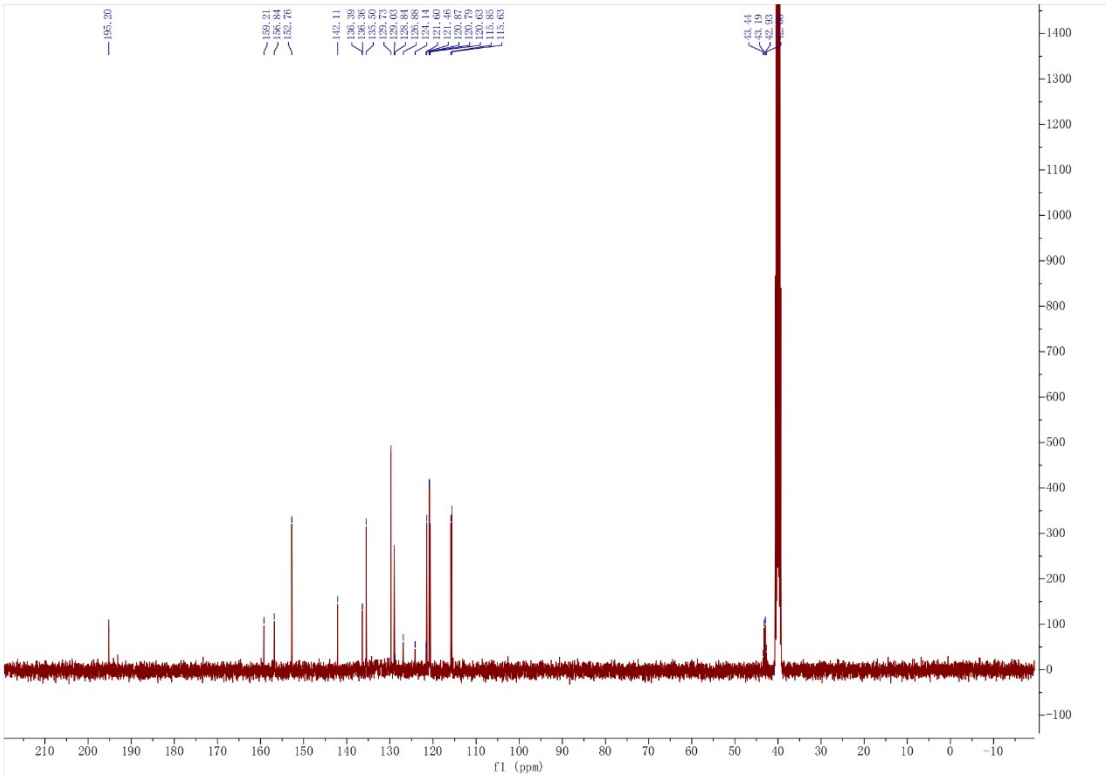
^{19}F NMR (376 MHz, DMSO-d_6) of 21



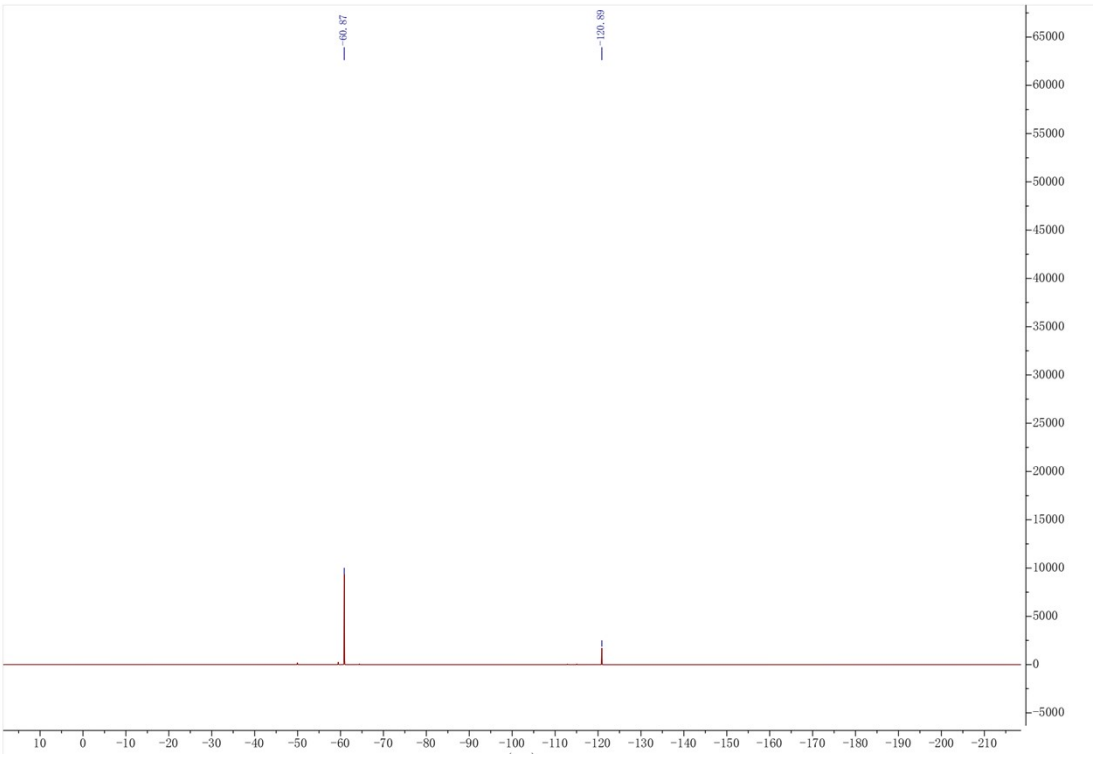
^{1}H NMR (400 MHz, DMSO-d_6) of 22



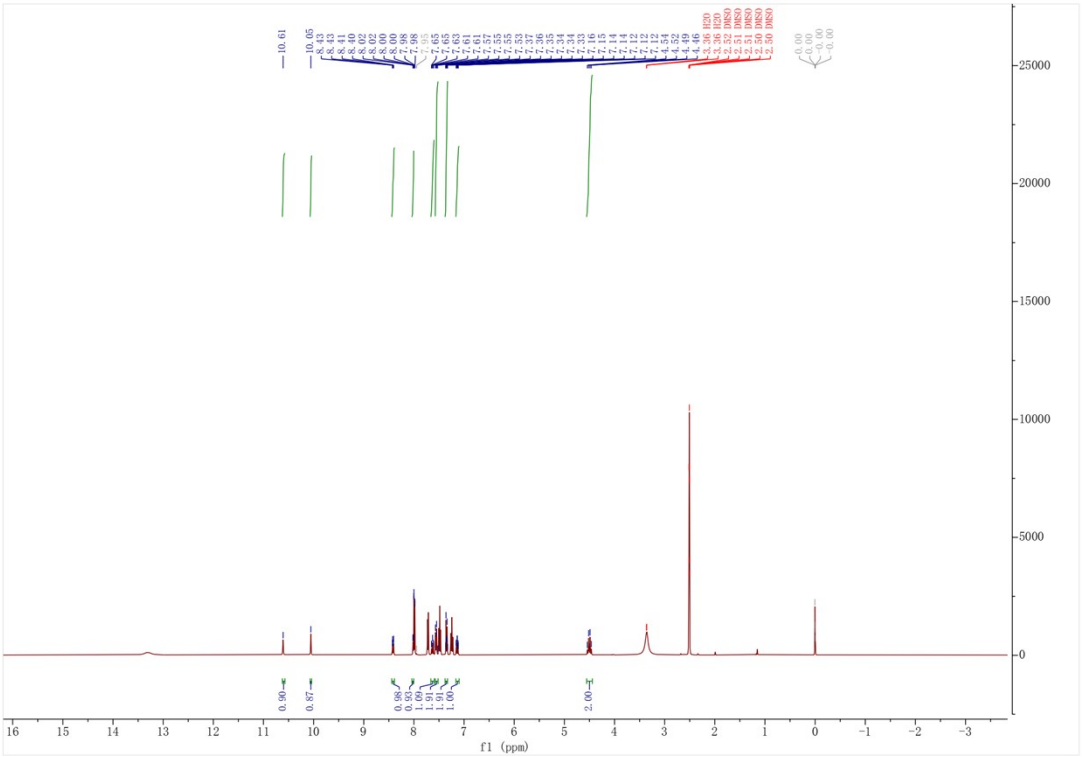
^{13}C NMR (100 MHz, DMSO-d_6) of 22



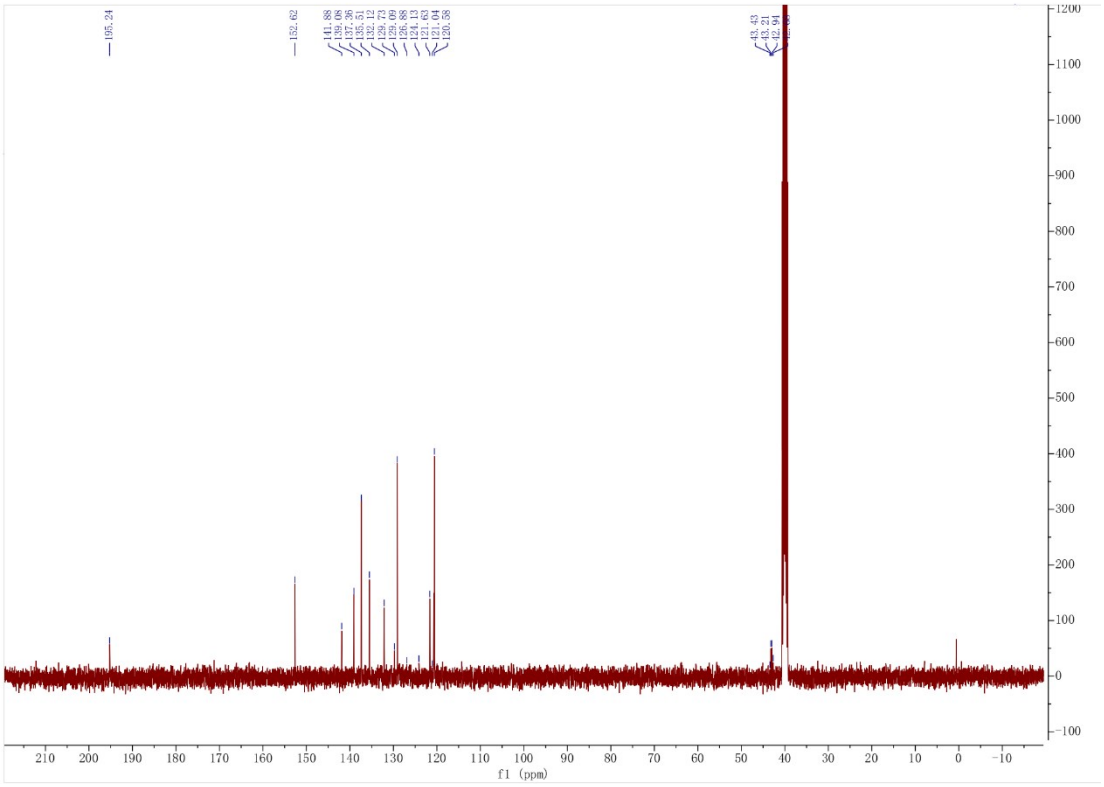
^{19}F NMR (376 MHz, DMSO-d_6) of 22



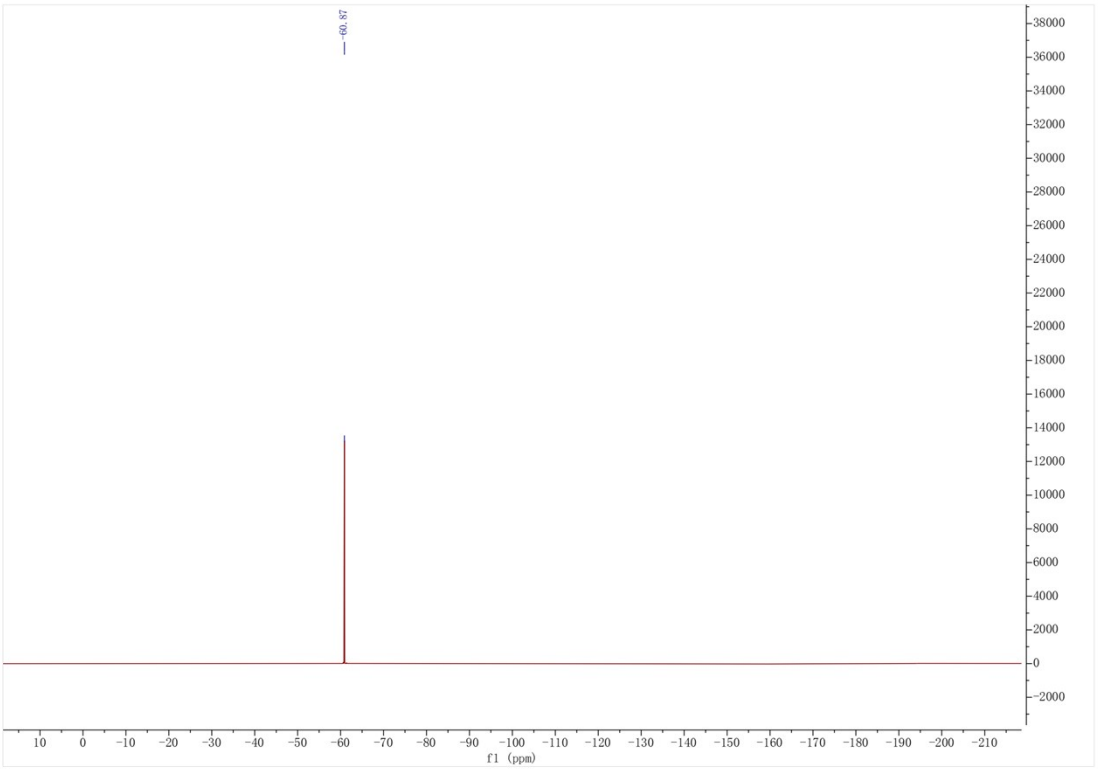
^{1}H NMR (400 MHz, DMSO-d_6) of 23



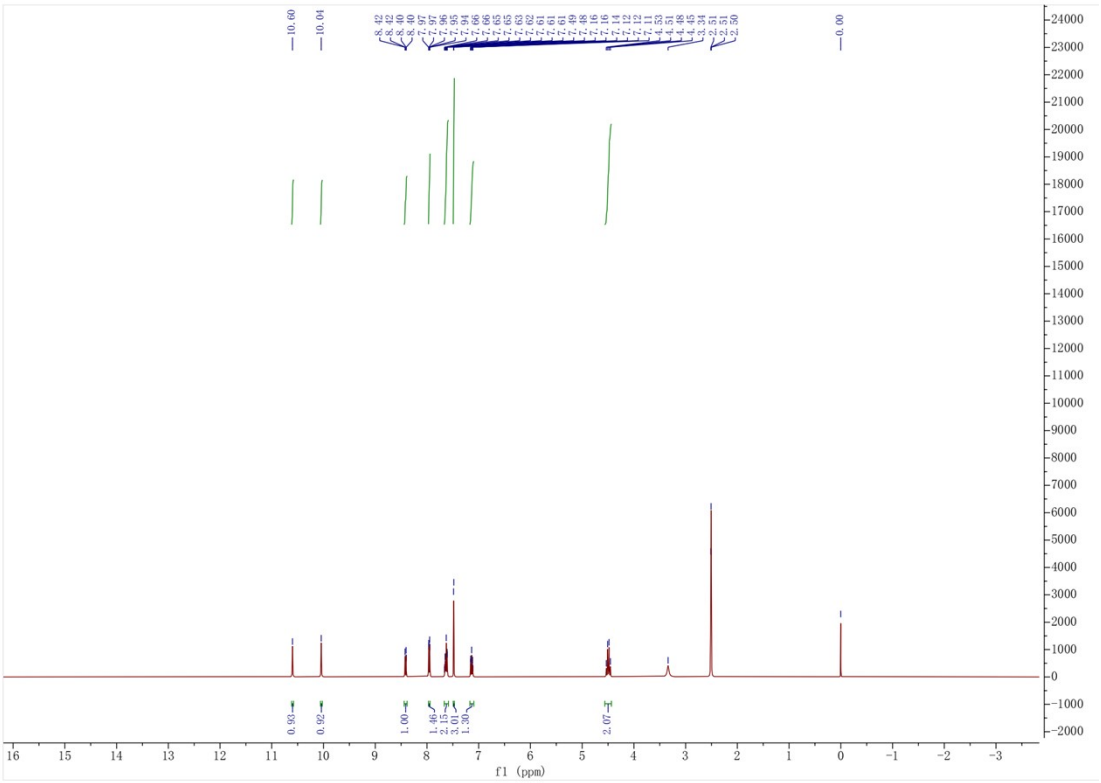
^{13}C NMR (100 MHz, DMSO-d_6) of 23



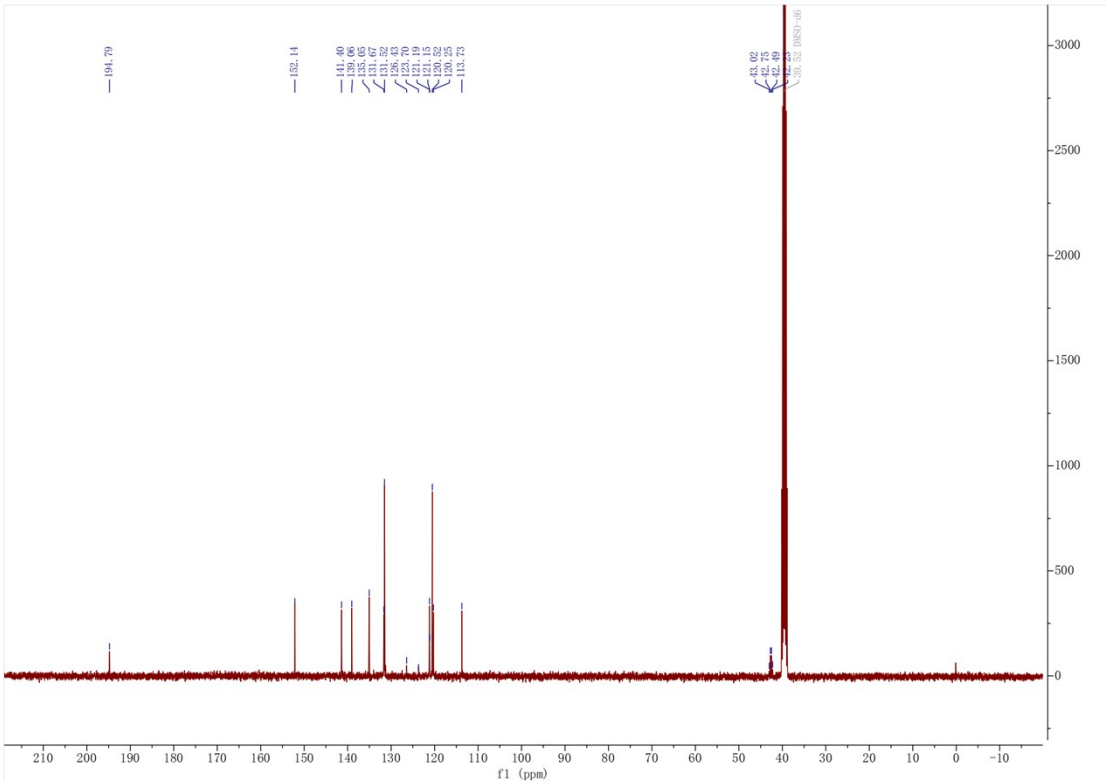
^{19}F NMR (376 MHz, DMSO-d_6) of 23



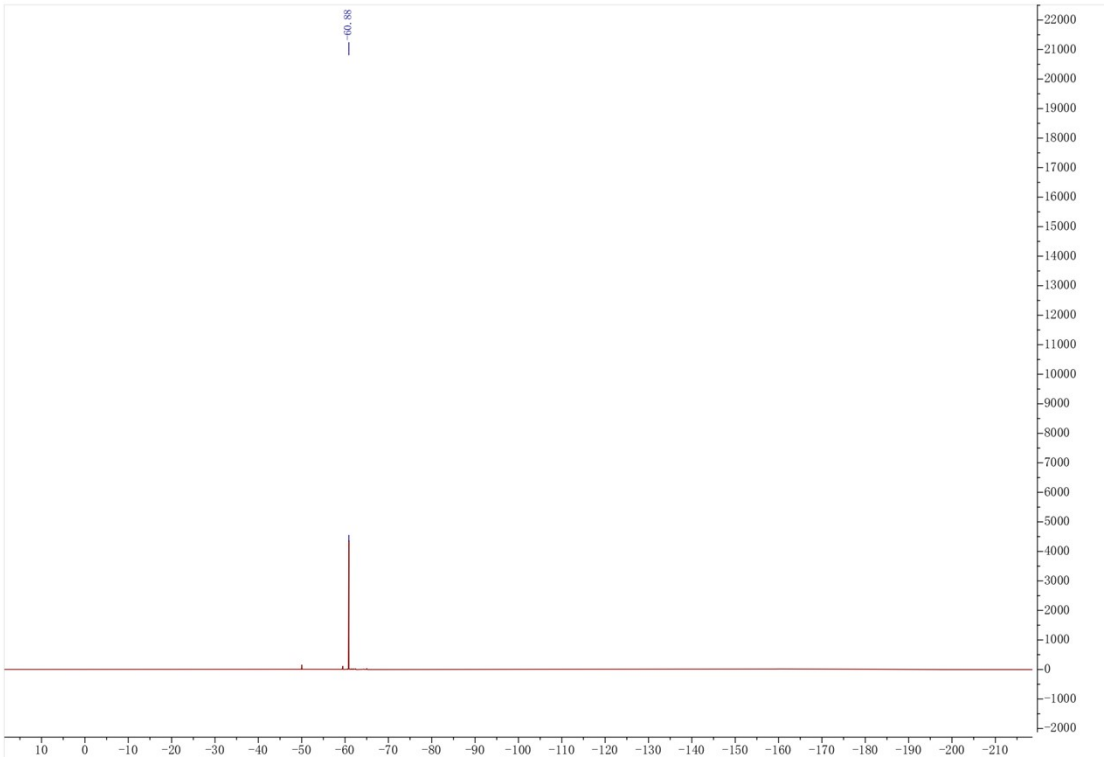
^{1}H NMR (400 MHz, DMSO-d_6) of 24



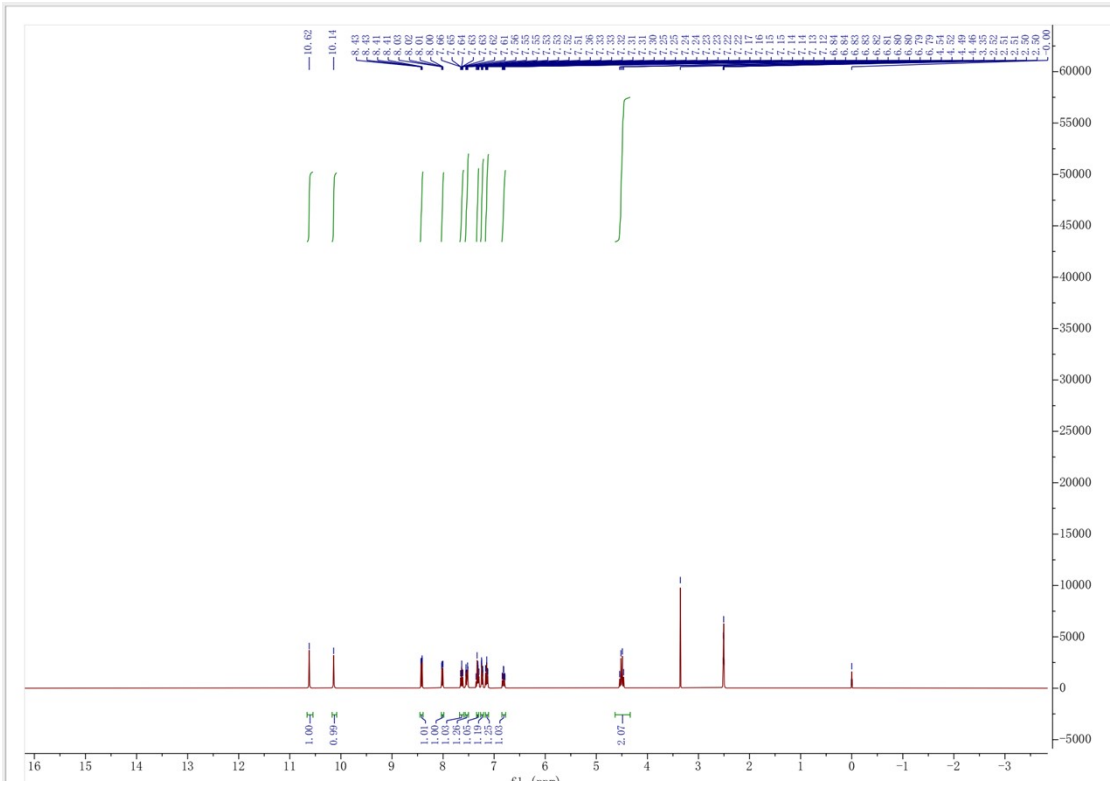
^{13}C NMR (100 MHz, DMSO-d_6) of 24



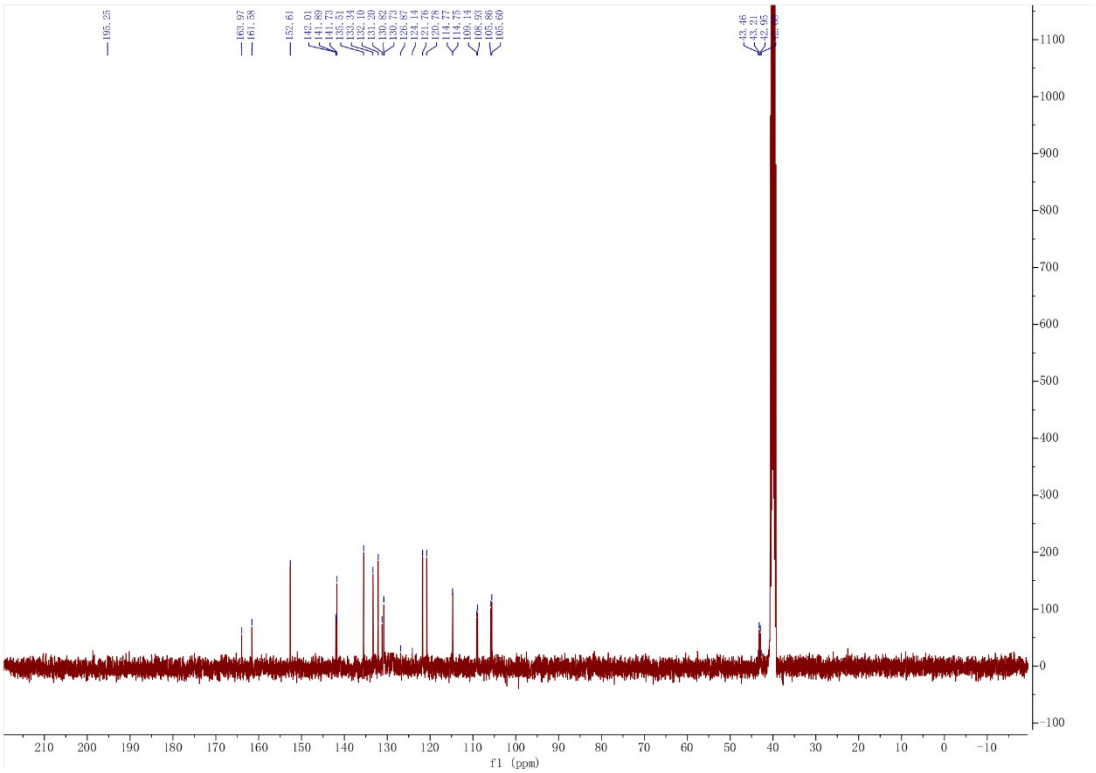
^{19}F NMR (376 MHz, DMSO-d_6) of 24



^{1}H NMR (400 MHz, DMSO-d_6) of 25



^{13}C NMR (100 MHz, DMSO-d_6) of 25



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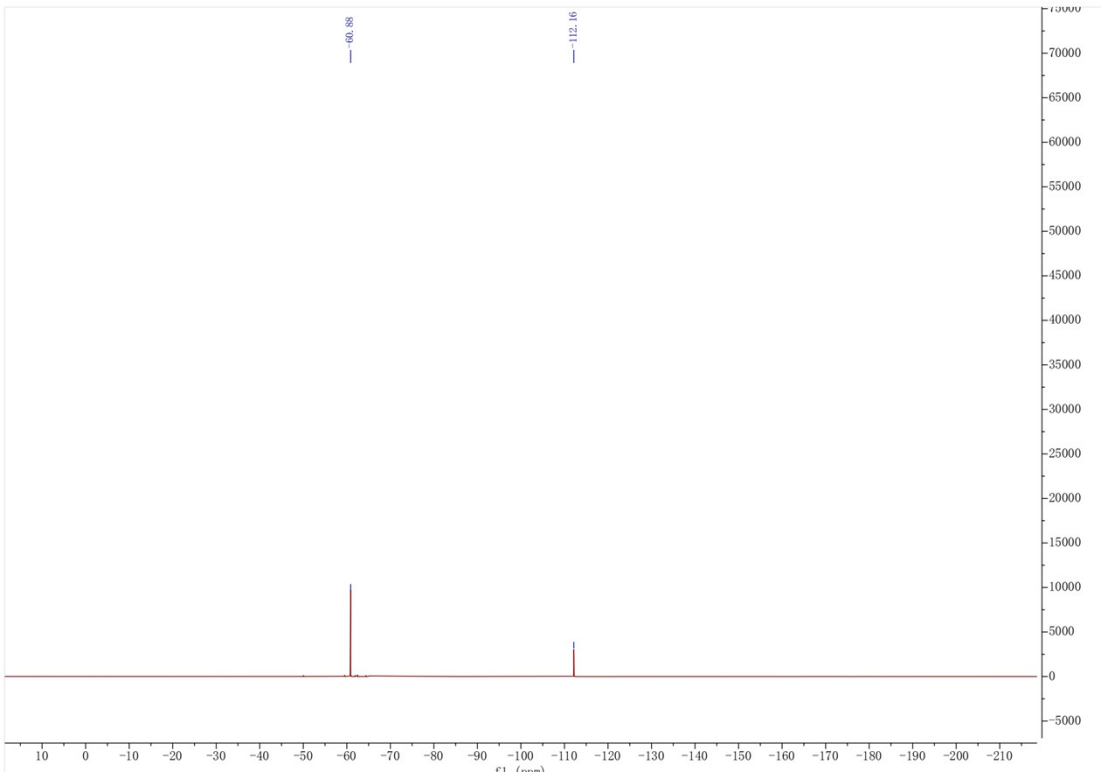
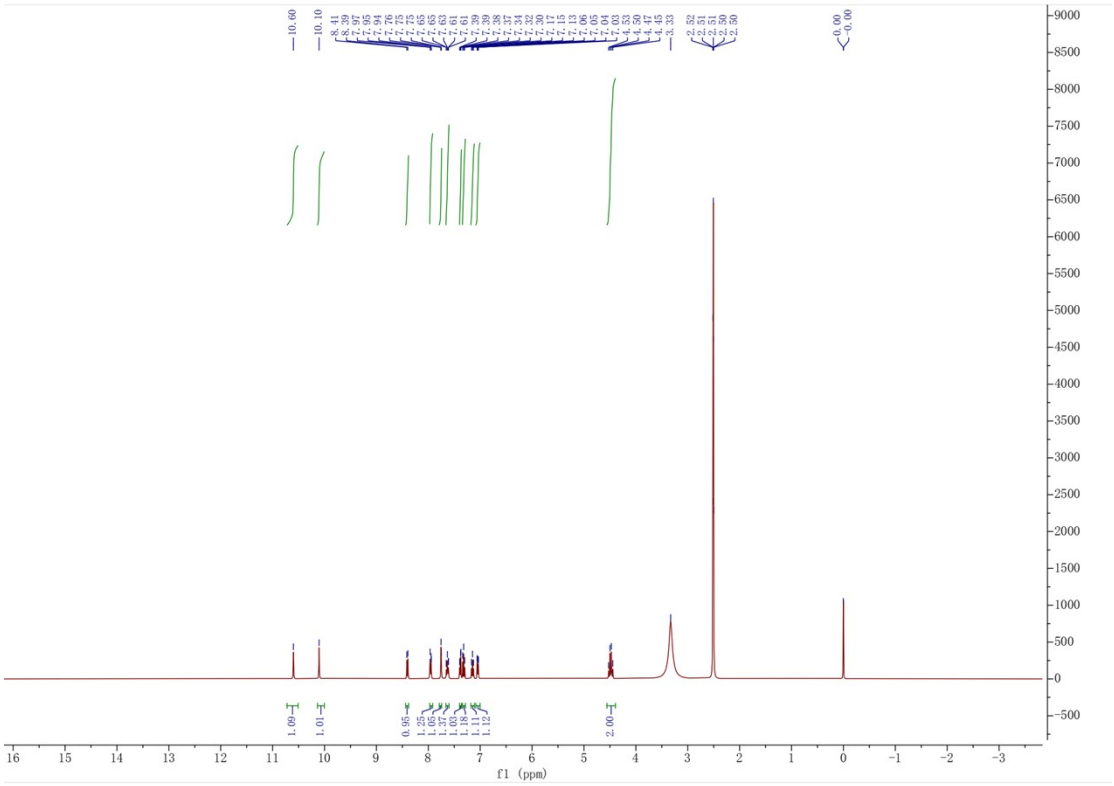
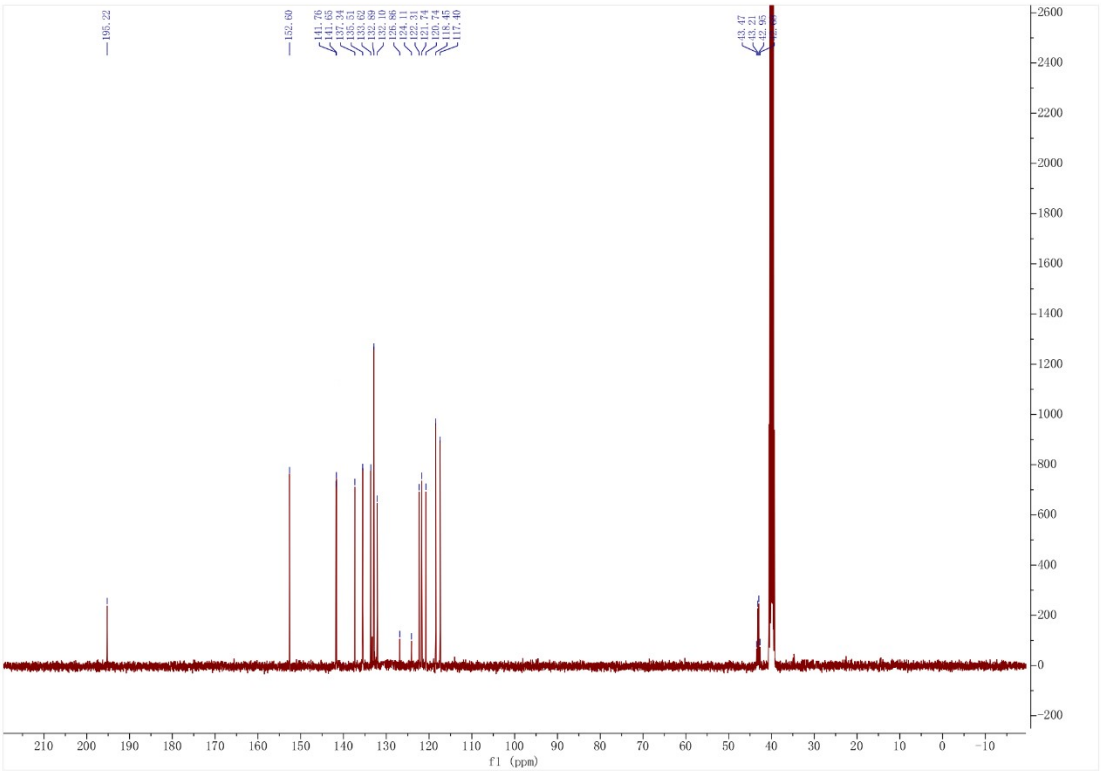


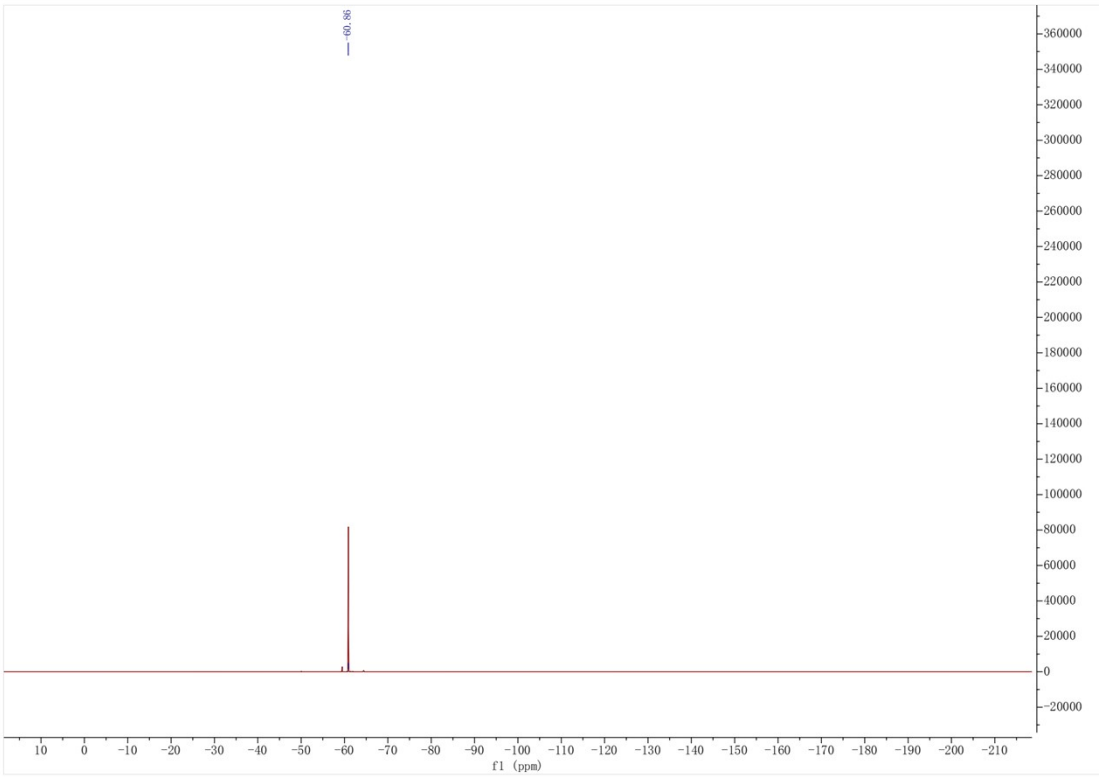
^{1}H NMR (400 MHz, DMSO-d_6) of 26



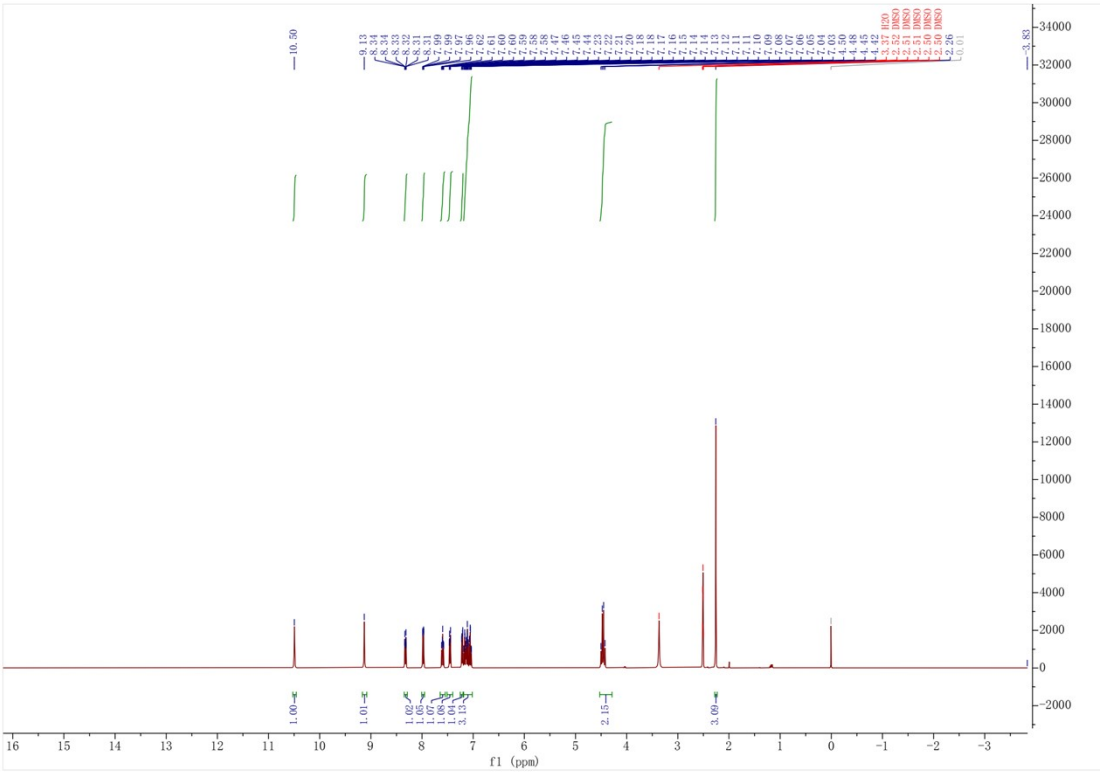
^{13}C NMR (100 MHz, DMSO-d_6) of 26



^{19}F NMR (376 MHz, DMSO-d_6) of 26



^{1}H NMR (400 MHz, DMSO-d_6) of 27



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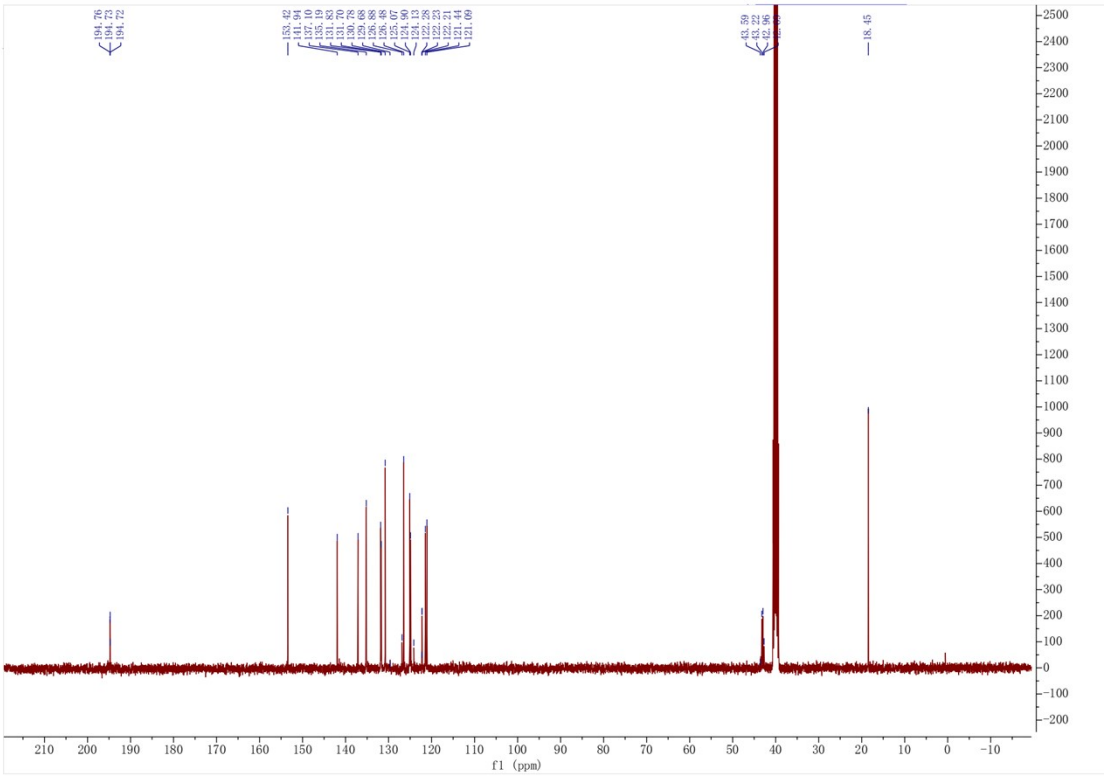

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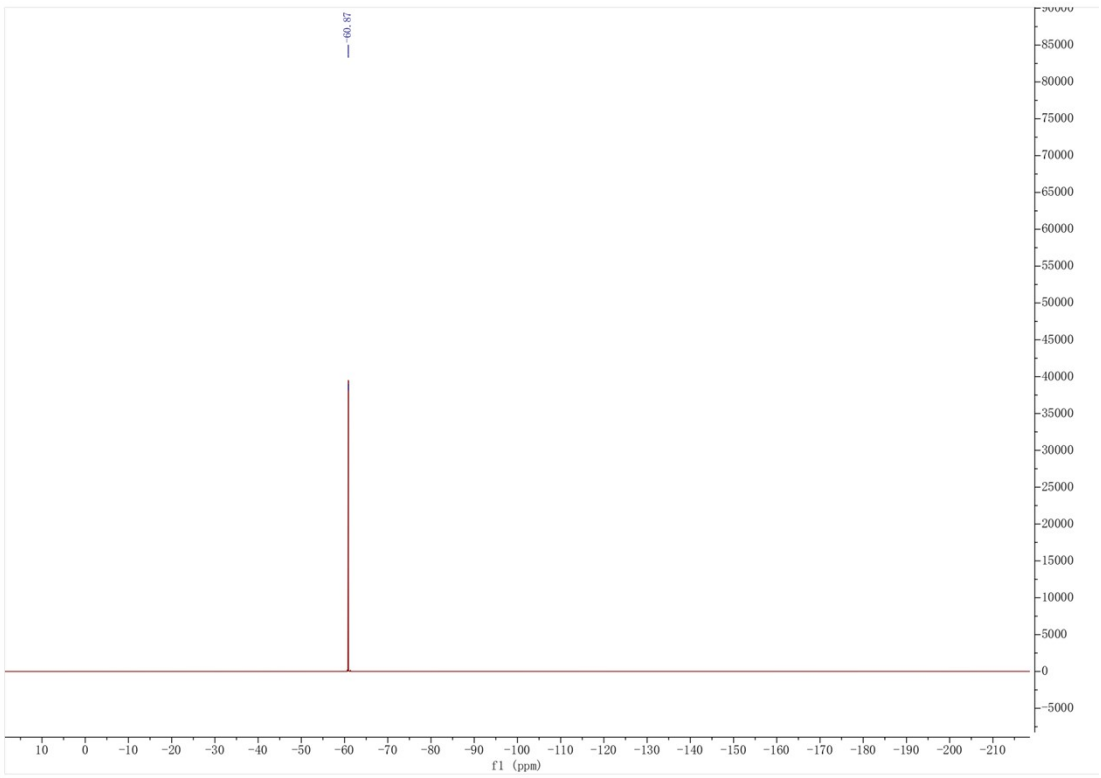
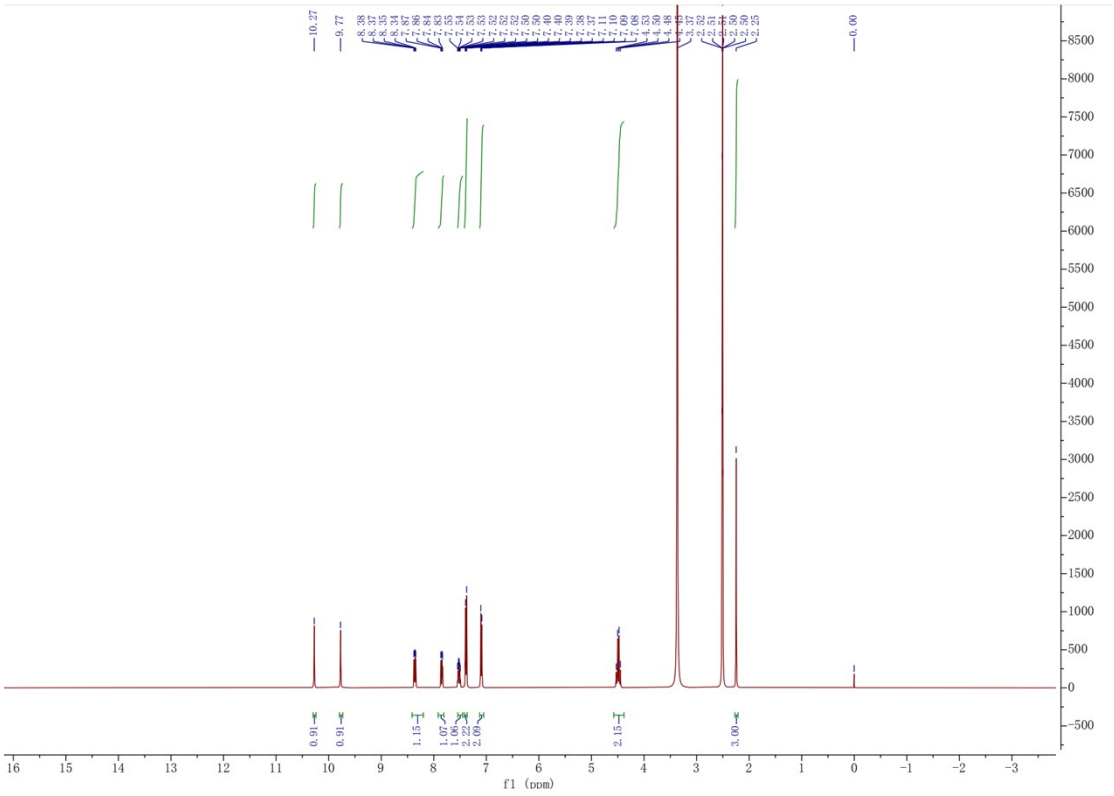
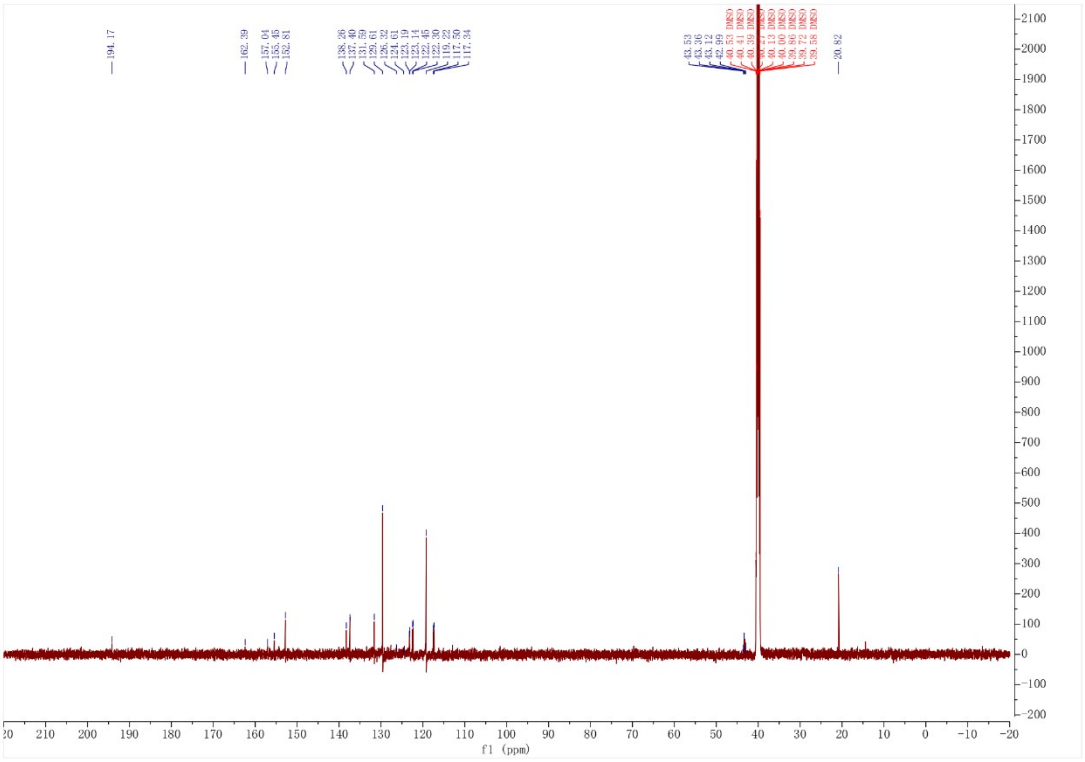


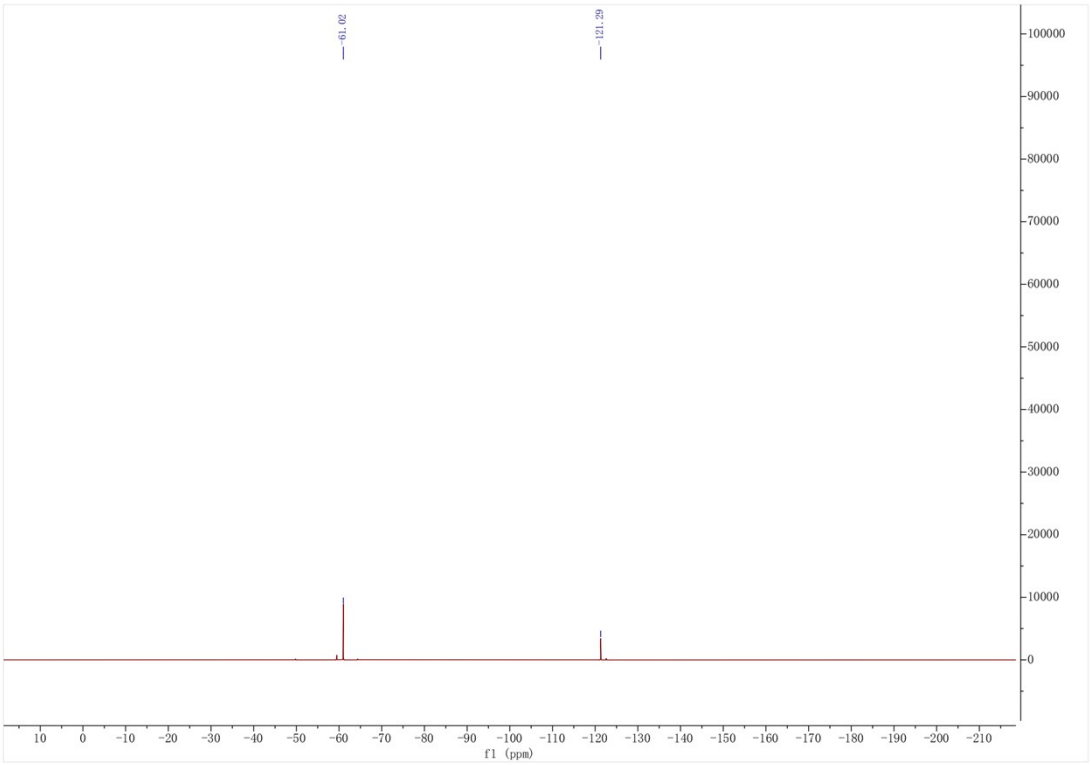
^{1}H NMR (400 MHz, DMSO-d_6) of 34



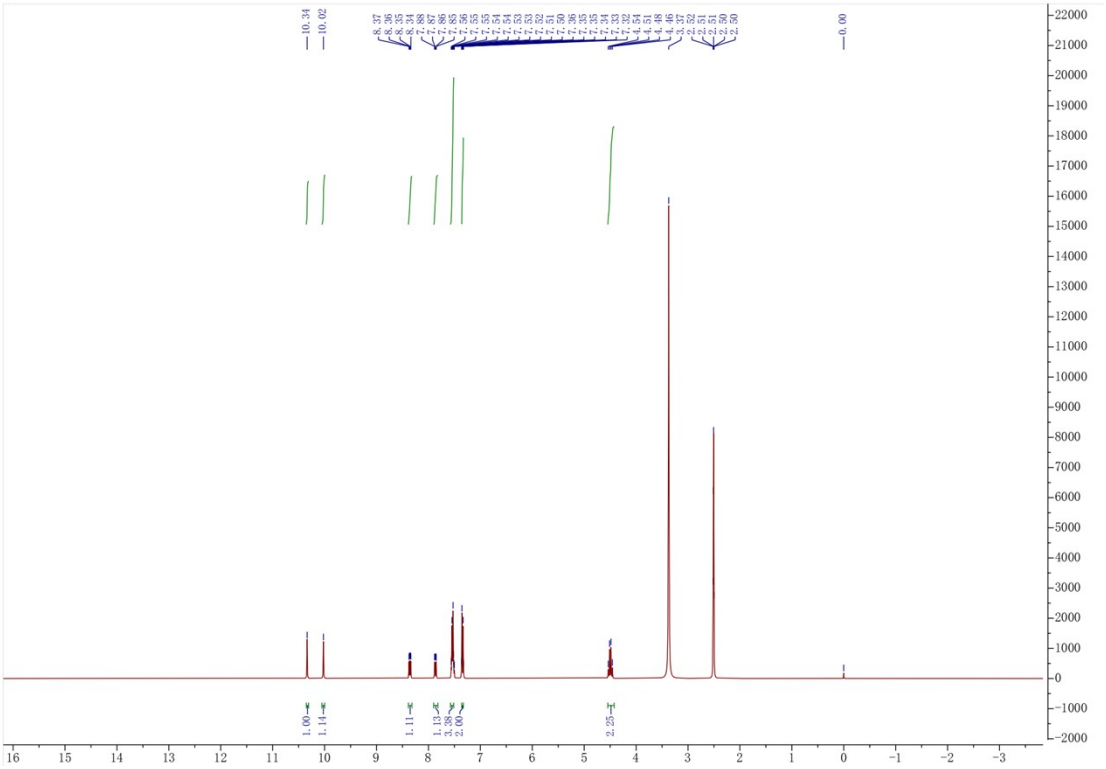
^{13}C NMR (150 MHz, DMSO-d_6) of 34



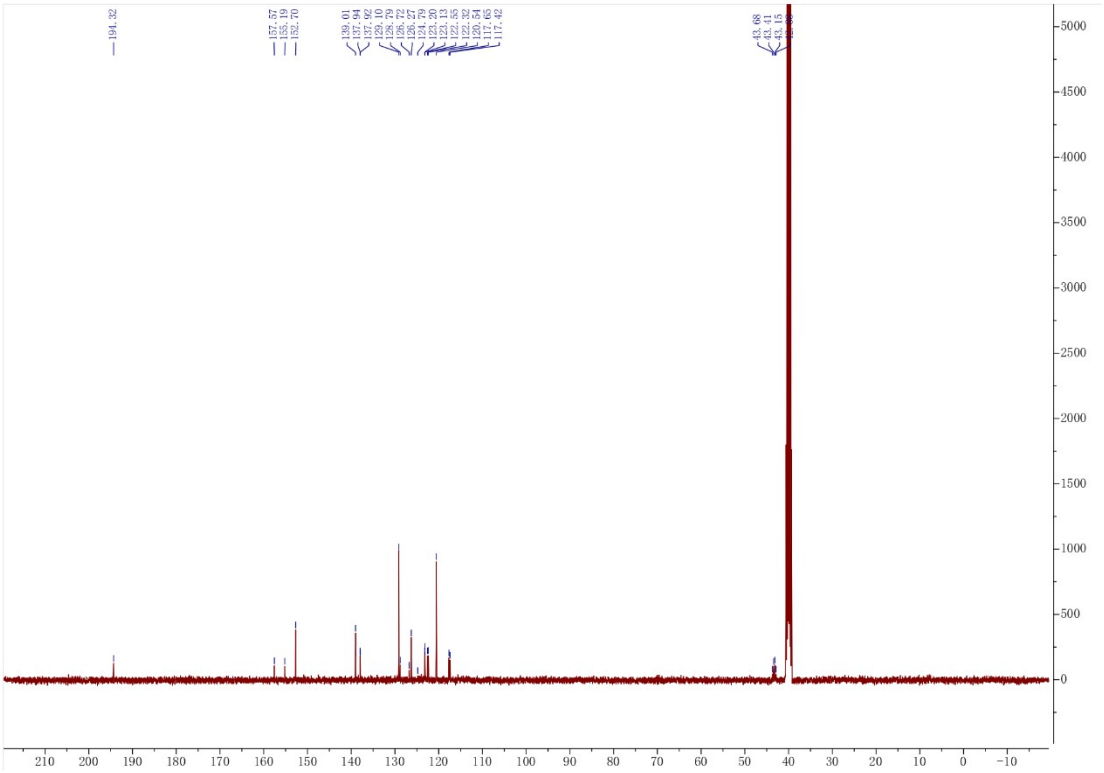
^{19}F NMR (378 MHz, DMSO-d_6) of 34



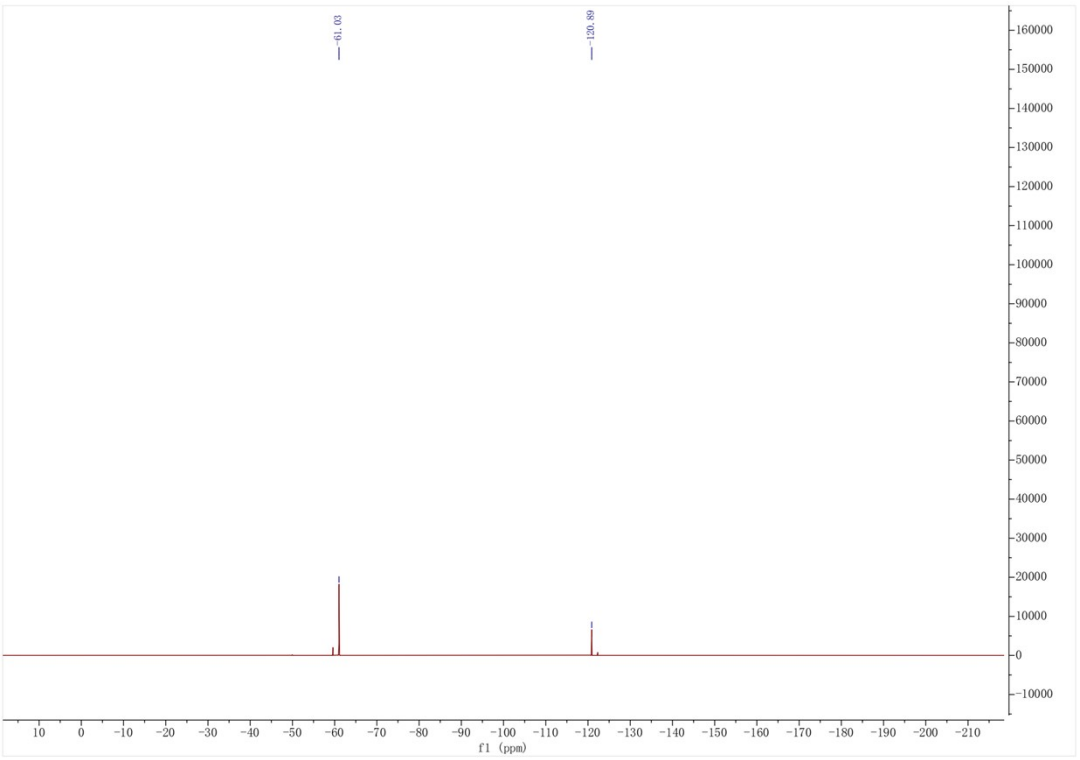
^{1}H NMR (400 MHz, DMSO-d_6) of 35



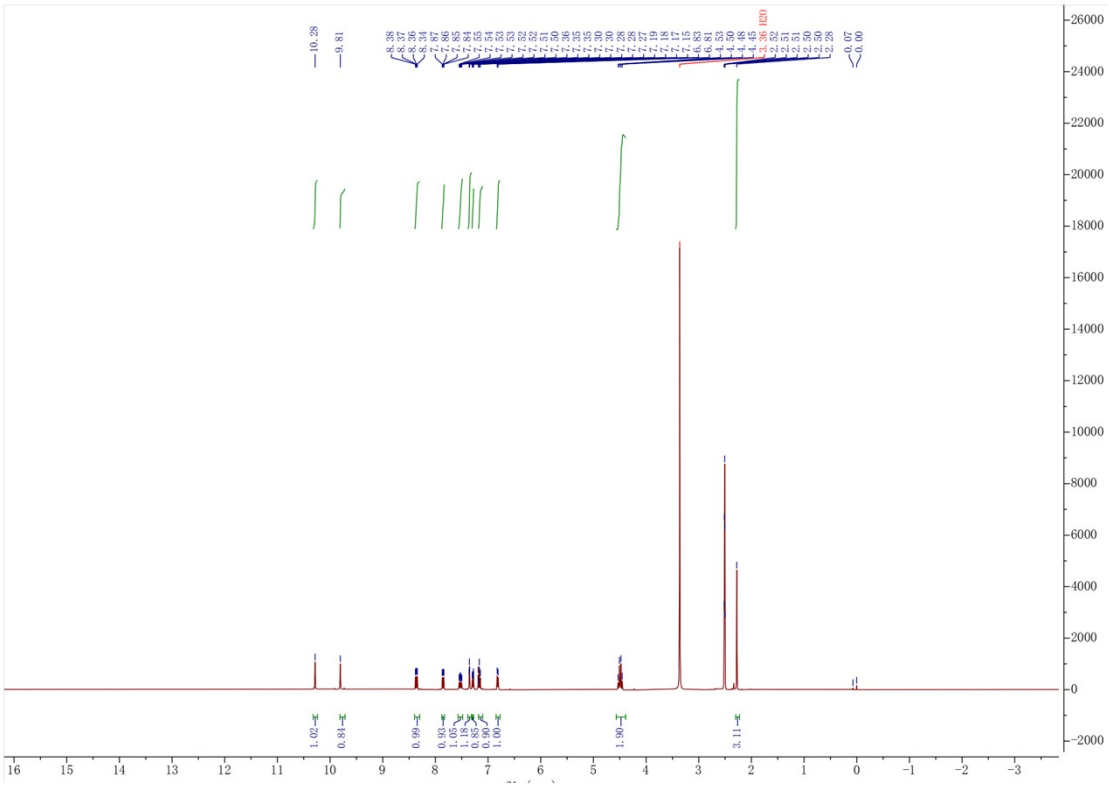
^{13}C NMR (100 MHz, DMSO-d_6) of 35



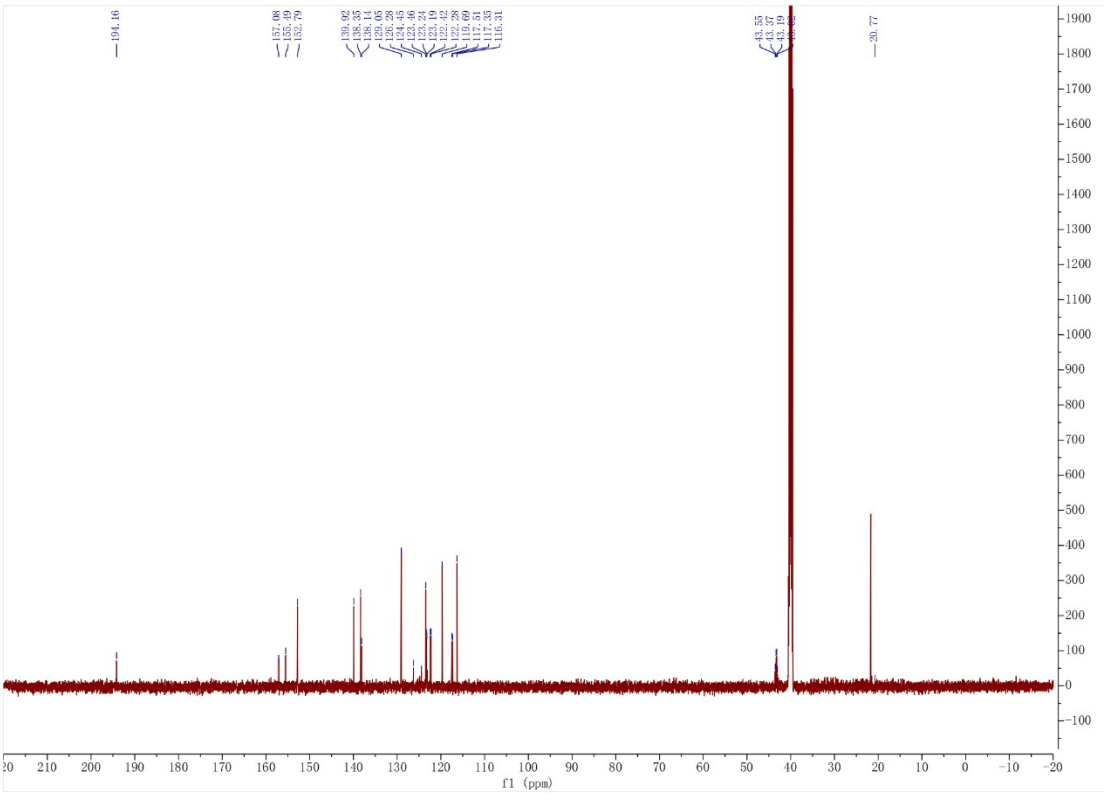
^{19}F NMR (378 MHz, DMSO-d_6) of 35



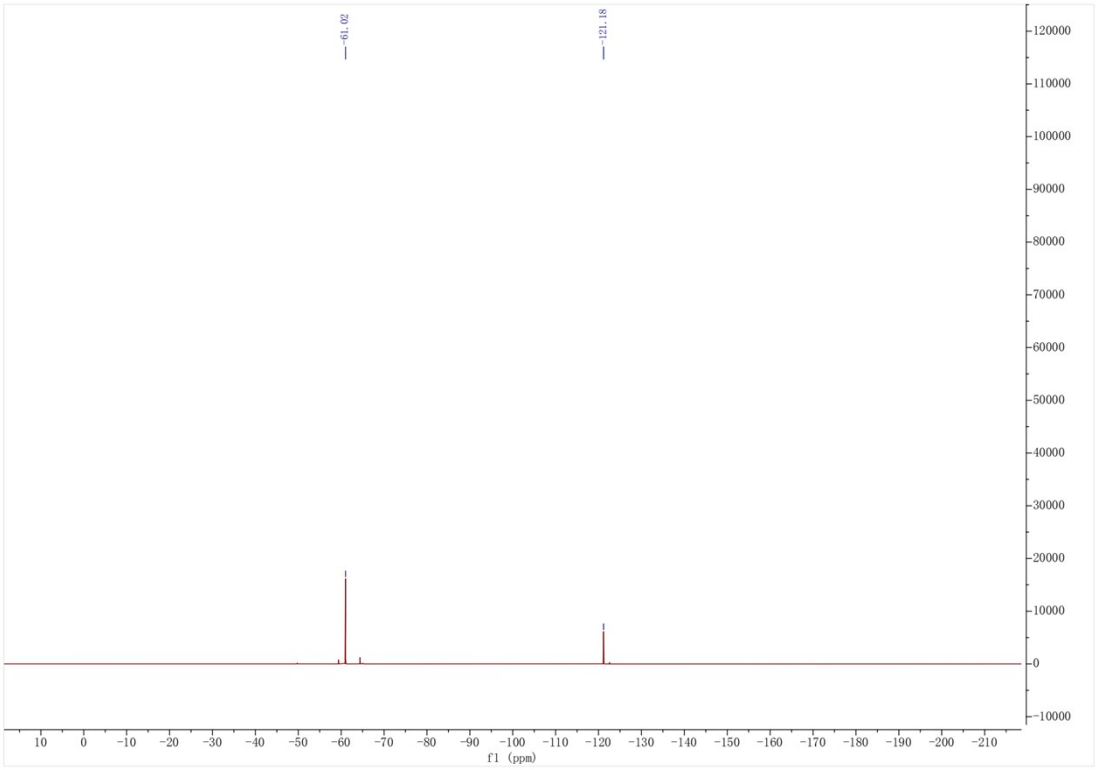
^{1}H NMR (400 MHz, DMSO-d_6) of 36



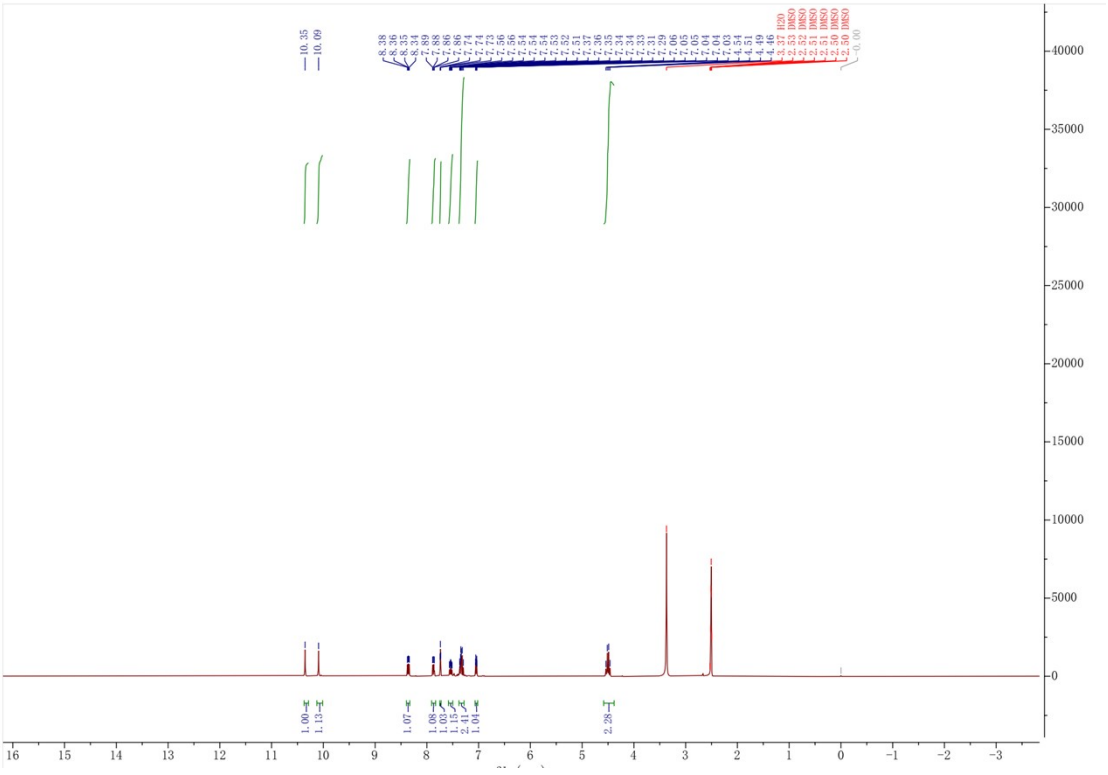
^{13}C NMR (150 MHz, DMSO-d_6) of 36



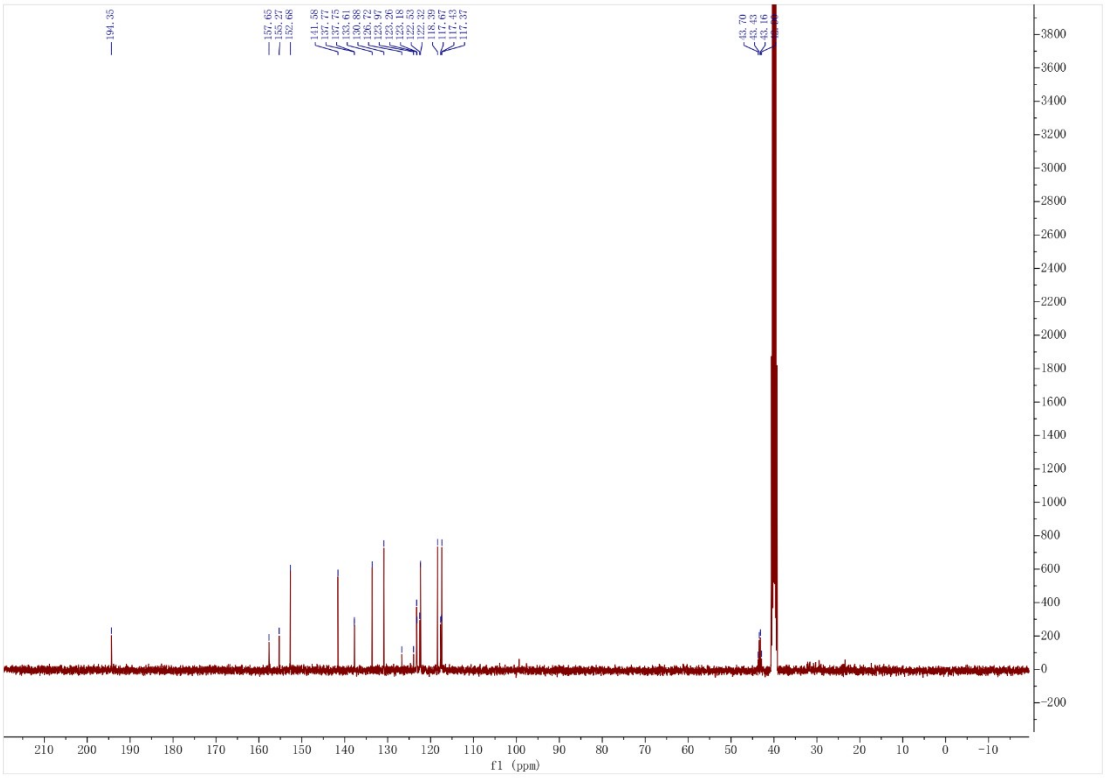
^{19}F NMR (378 MHz, DMSO-d_6) of 36



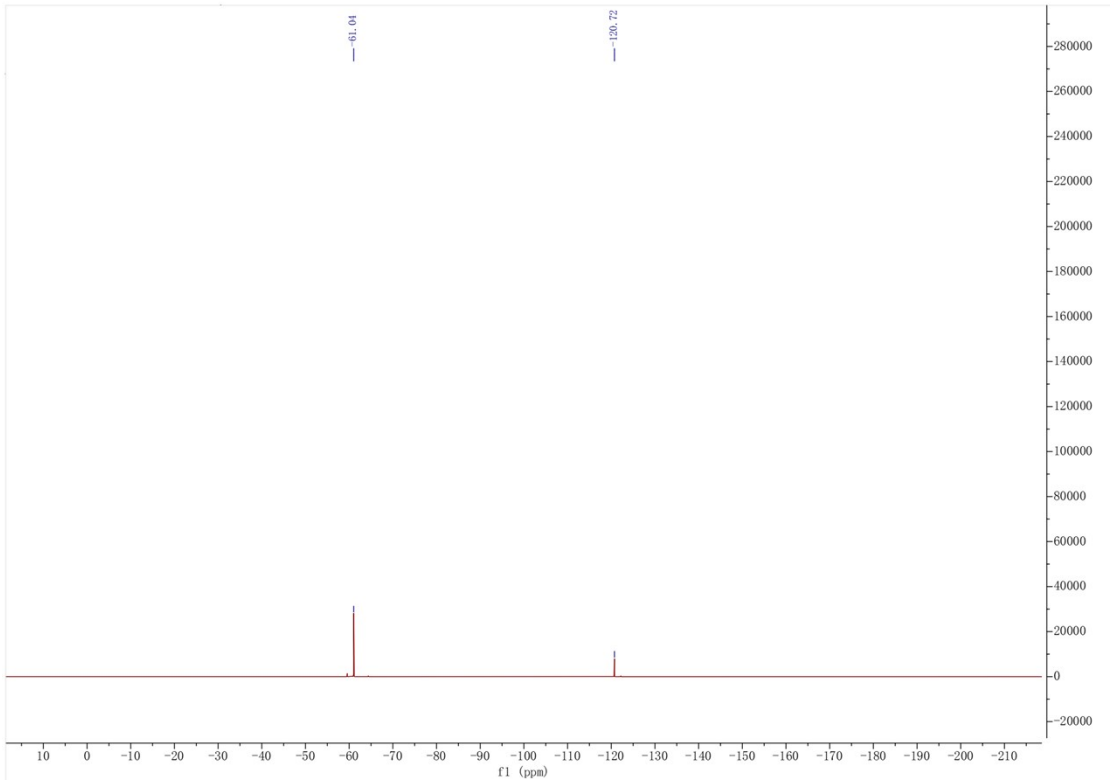
^{1}H NMR (400 MHz, DMSO-d_6) of 37



^{13}C NMR (100 MHz, DMSO-d_6) of 37



^{19}F NMR (378 MHz, DMSO-d_6) of 37



1. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.
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