(*98 pages*)

Supporting Information For

Synthesis of 2-Aminobenzofurans via Base-Mediated [3+2] Annulation of *N*-Phenoxy Amides with *gem*-Difluoroalkenes

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Supporting Information

Contents

I. General

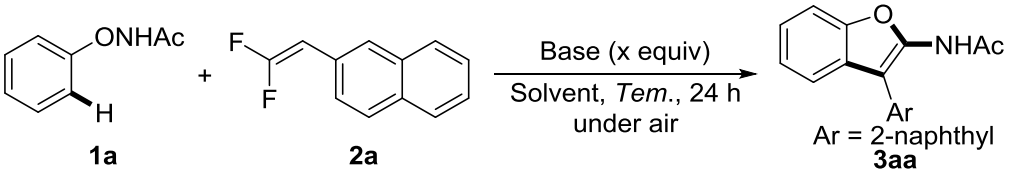
NMR spectra were recorded on JEOL 400 NMR (^{1}H 400 MHz; ^{13}C 100 MHz) in DMSO-d_6, $CDCl_3$ or CD_3OD. Abbreviations for data quoted are s, singlet; brs, broad singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale (DMSO-d_6: δ_H = 2.50 ppm, δ_C = 39.52 ppm; $CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm; CD_3OD: δ_H = 3.31 ppm, δ_C = 49.00 ppm). Mass spectra and high-resolution mass spectra were measured on an agilent TOF-G6230B mass spectrometer and Thermo-DFS mass spectrometer. Thin-layer chromatographs were done on pre-coated silica gel 60 F254 plates (Merck). Silica gel 60H (200-300 mesh) and preparative TLC (200x200 mm, 0.2-0.25 mm in thickness) manufactured by Qingdao Haiyang Chemical Group Co. (China) were used for general chromatography. The chemicals were purchased from commercial suppliers and were dried and purified when necessary. *N*-phenoxy amides[S1] and the *gem*-difluoroalkene substrates[S2] were prepared according to published procedures. No attempts were made to optimize yields for substrate synthesis.

II. Experimental Information and Characterization Data

Optimization studies:

The mixture of *N*-phenoxyacetamide **1a** (0.1 mmol, 1.0 equiv), 2-(2,2-difluorovinyl)naphthalene **2a** (0.15 mmol, 1.5 equiv) and additive (0.1 mmol, 1.0 equiv) in the solvent (1 mL) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, it was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified by preparative TLC (eluent: PE/EA = 2/1, R_f = 0.4) to give the desired 2-aminobenzofuran product **3aa**.

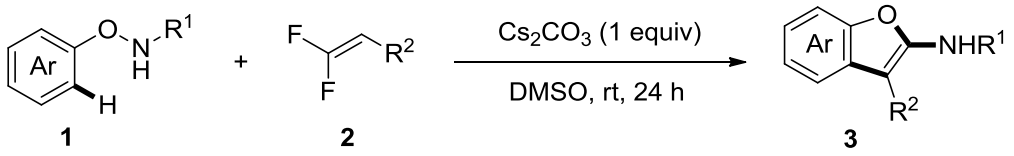
Table S1 Optimized Reaction Conditions Screening[a]



Entry	Base (equiv)	Additive (equiv)	Solvent	*Tem.* (^{o}C)	Yield[b] (%)
1	CsOAc (1)	-	DMF	40	40
2	NaOAc (1)	-	DMF	40	13
3	KOAc (1)	-	DMF	40	25
4	Cs_2CO_3 (1)	-	DMF	40	52
5	K_3PO_4 (1)	-	DMF	40	27
6	KOPiv (1)	-	DMF	40	45
7	DMBCO (1)	-	DMF	40	13
8	Et_3N (1)	-	DMF	40	trace
9	2 M-NH_3·MeOH (1)	-	DMF	40	trace
10	Ph_3P (1)	-	DMF	40	n.r.
11	Cs_2CO_3 (1)	-	MeOH	40	n.r.
12	Cs_2CO_3 (1)	-	TFE	40	n.r.
13	Cs_2CO_3 (1)	-	THF	40	20
14	Cs_2CO_3 (1)	-	CH_3CN	40	43
15	Cs_2CO_3 (1)	-	toluene	40	n.r.
16	Cs_2CO_3 (1)	-	DCM	40	n.r.
17	Cs_2CO_3 (1)	-	DMSO	40	60
18	Cs_2CO_3 (1)	-	DMA	40	53
19	Cs_2CO_3 (1)	-	pyridine	40	32
20	Cs_2CO_3 (1)	-	acetone	40	trace
21	Cs_2CO_3 (1)	-	HMPA	40	43
22[c]	Cs_2CO_3 (1)	-	DMSO	40	32
23[d]	Cs_2CO_3 (1)	-	DMSO	40	53
24	Cs_2CO_3 (1)	-	DMSO	rt	72
25	Cs_2CO_3 (1)	-	DMSO	60	53
26	Cs_2CO_3 (0.2)	LiOH (3)	DMSO	rt	14
27	Cs_2CO_3 (0.2)	$NaHCO_3$ (3)	DMSO	rt	46
28	Cs_2CO_3 (0.2)	$Ca(OH)_2$ (3)	DMSO	rt	64
29[e]	Cs_2CO_3 (1)	H_2O (0.5 mL)	DMSO	rt	30
30	Cs_2CO_3 (2)	-	DMSO	rt	44
31	Cs_2CO_3 (0.5)	-	DMSO	rt	51

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol) and base in solvent (0.1 M) for 24 h without exclusion of air or moisture. [b] Isolated yields were report. [c] **2a** (1.2 equiv). [d] **2a** (2.0 equiv). [e] The reaction was conducted in a mixed solvent of DMSO/H_2O (1/1, 0.1 M).

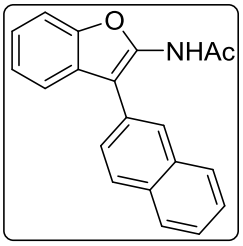
General procedure for the synthesis of 2-aminobenzofurans:



The mixture of *N*-aryloxyacetamide **1** (0.2 mmol, 1.0 equiv), *gem*-difluoroalkene **2** (0.3 mmol, 1.5 equiv) and Cs_2CO_3 (0.2 mmol, 1.0 equiv) in DMSO (2.0 mL) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, the solvent was removed under reduced pressure, and the resulted mixture was purified by preparative TLC to afford the corresponding 2-aminobenzofuran derivatives **3.**

Characterization of products:

***N*-(3-(naphthalen-2-yl)benzofuran-2-yl)acetamide (3aa)**



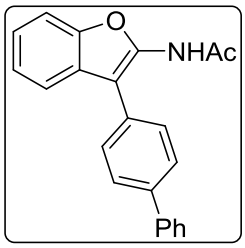
This compound was obtained in 72% yield (43.3 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 2/1, R_f = 0.4.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.50 (brs, 1H), 8.16 (s, 1H), 8.06-8.00 (m, 2H), 7.99-7.94 (m, 1H), 7.83 (d, *J* = 7.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.60-7.53 (m, 2H), 7.43-7.33 (m, 2H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.4, 151.2, 144.0, 133.2, 132.1, 128.6, 128.4, 128.0, 127.6, 127.3, 126.7, 126.5, 126.3, 126.0, 124.8, 123.4, 120.0, 111.8, 111.3, 22.8.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{16}NO_2$: 302.1176; found: 302.1166.

***N*-(3-([1,1'-biphenyl]-4-yl)benzofuran-2-yl)acetamide (3ab)**



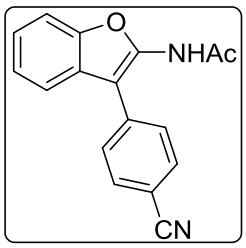
This compound was obtained in 54% yield (35.2 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 2/1, R_f = 0.5.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.47 (brs, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.77-7.73 (m, 3H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.52-7.48 (m, 2H), 7.42-7.33 (m, 3H), 2.09 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.7, 151.3, 143.8, 139.7, 139.2, 130.2, 129.2, 128.6, 127.7, 127.3, 126.7, 124.9, 123.5, 120.0, 111.8, 111.4, 22.8.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{18}NO_2$: 328.1332; found: 328.1322.

***N*-(3-(4-isocyanophenyl)benzofuran-2-yl)acetamide (3ac)**



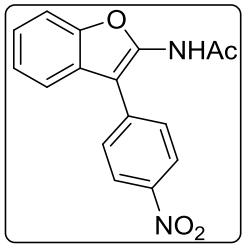
This compound was obtained in 47% yield (25.9 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 2/1, R_f = 0.3.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.58 (brs, 1H), 7.96 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.43-7.34 (m, 2H), 2.07 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.1, 151.1, 144.8, 136.3, 132.8, 129.5, 128.7, 126.5, 125.0, 123.7, 119.6, 118.9, 112.8, 111.4, 109.7, 22.8.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{13}N_2O_2$: 277.0972; found: 277.0965.

***N*-(3-(4-nitrophenyl)benzofuran-2-yl)acetamide (3ad)**



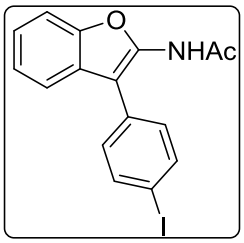
This compound was obtained in 51% yield (30.2 mg, in 0.2 mmol scale) as yellow solid. Eluent: DCM/EA = 30/1, R_f = 0.6.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.66 (brs, 1H), 8.35 (d, *J* = 8.8 Hz, 2H), 7.87 (d, *J* = 8.7 Hz, 2H), 7.79-7.75 (m, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.44-7.34 (m, 2H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 169.9, 151.1, 146.1, 145.2, 138.4, 128.9, 126.5, 125.1, 124.1, 123.7, 119.6, 111.4, 109.6, 22.8.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}N_2O_4$: 297.0870; found: 297.0863.

***N*-(3-(4-iodophenyl)benzofuran-2-yl)acetamide (3ae)**



This compound was obtained in 67% yield (50.5 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 2/1, R_f = 0.5.

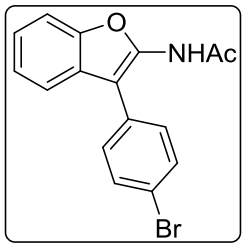
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.43 (brs, 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.41-7.36 (m, 3H), 7.31 (t, *J* = 7.3 Hz, 1H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.3, 151.1, 143.8, 137.7, 130.6, 130.1, 126.8, 124.8, 123.4, 119.7, 111.3, 111.0, 93.5, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}INO_2$: 377.9985; found: 377.9974.

Scale-up synthesis of compound 3ae: The mixture of *N*-phenoxyacetamides **1a** (2 mmol, 1.0 equiv), 1-(2,2-difluorovinyl)-4-iodobenzene **2e** (3 mmol, 1.5 equiv) and Cs_2CO_3 (2 mmol, 1.0 equiv) in DMSO (17.0 mL) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, the mixture was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified with silica gel column chromatography (eluent: PE/EA = 2/1, R_f = 0.4) to afford the corresponding 2-aminobenzofuran derivative **3ae** in 64% (0.483 g) isolated yield.

***N*-(3-(4-bromophenyl)benzofuran-2-yl)acetamide (3af)**



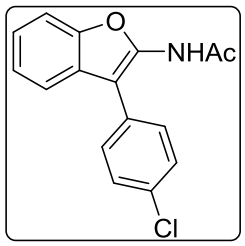
This compound was obtained in 75% yield (49.4 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 3/1, R_f = 0.45.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.43 (brs, 1H), 7.72-7.67 (m, 3H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.41-7.36 (m, 1H), 7.34-7.30 (m, 1H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.3, 151.1, 143.9, 131.9, 130.3, 130.0, 126.9, 124.8, 123.4, 120.5, 119.7, 111.3, 110.9, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}BrNO_2$: 330.0124; found: 330.0113.

***N*-(3-(4-chlorophenyl)benzofuran-2-yl)acetamide (3ag)**



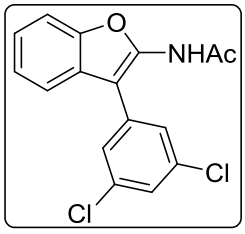
This compound was obtained in 70% yield (39.8 mg, in 0.2 mmol scale) as orange solid. Eluent: PE/EA = 3/1, R_f = 0.45.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.46 (brs, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.63-7.55 (m, 5H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 2.07 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.3, 151.1, 143.9, 132.0, 130.0, 129.7, 129.0, 126.9, 124.8, 123.4, 119.7, 111.3, 110.9, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}ClNO_2$: 286.0629; found: 286.0620.

***N*-(3-(3,5-dichlorophenyl)benzofuran-2-yl)acetamide (3ah)**



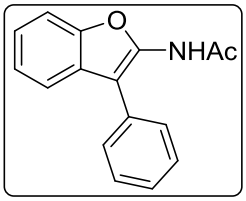
This compound was obtained in 64% yield (40.8 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 5/1, R_f = 0.25.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.57 (brs, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.64-7.57 (m, 4H), 7.42-7.31 (m, 2H), 2.07 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.1, 151.0, 144.7, 134.6, 129.4, 127.0, 126.5, 125.0, 123.7, 119.5, 112.8, 111.3, 109.3, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{12}Cl_2NO_2$: 320.0240; found: 320.0230.

***N*-(3-phenylbenzofuran-2-yl)acetamide (3ai)**



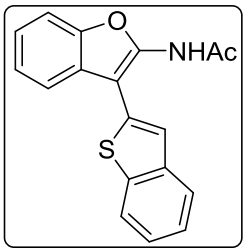
This compound was obtained in 54% yield (27.1 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 3/1, R_f = 0.35.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.41 (brs, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.62-7.57 (m, 3H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.42-7.36 (m, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.6, 151.2, 143.6, 131.0, 129.0, 128.0, 127.5, 127.2, 124.7, 123.3, 119.8, 112.2, 111.2, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{14}NO_2$: 252.1019; found: 252.1013.

***N*-(3-(benzo[b]thiophen-2-yl)benzofuran-2-yl)acetamide (3aj)**



This compound was obtained in 50% yield (30.7 mg, in 0.2 mmol scale) as red solid. Eluent: PE/EA = 5/1, R_f = 0.25.

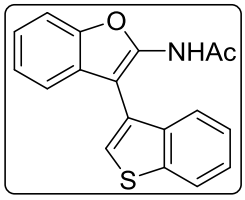
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.64 (brs, 1H), 8.09 (d, *J* = 6.8 Hz, 1H), 8.01 (d, *J* = 7.7 Hz, 1H), 7.94-7.92 (m, 2H), 7.66-7.62 (m, 1H), 7.47-7.42 (m, 2H), 7.41-7.35

(m, 2H), 2.18 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.5, 151.2, 144.6, 139.6, 138.4, 132.5, 126.1, 125.3, 124.7, 124.6, 123.8, 123.7, 122.2, 121.9, 120.4, 111.4, 107.3, 22.9.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}NO_2S$: 308.0740; found: 308.0730.

_N_-(3-(benzo[b]thiophen-3-yl)benzofuran-2-yl)acetamide (3ak)



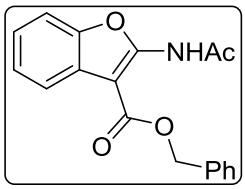
This compound was obtained in 65% yield (39.9 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.45.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.44 (brs, 1H), 8.09 (d, *J* = 7.2 Hz, 1H), 7.89 (s, 1H), 7.62 (t, *J* = 7.2 Hz, 2H), 7.46-7.35 (m, 5H), 7.28 (t, *J* = 7.5 Hz, 1H), 1.97 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.0, 151.2, 144.6, 139.6, 137.6, 128.0, 126.2, 125.9, 124.6, 124.4, 123.22, 123.18, 122.6, 120.0, 111.2, 105.8, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}NO_2S$: 308.0740; found: 308.0731.

benzyl 2-acetamidobenzofuran-3-carboxylate (3al)



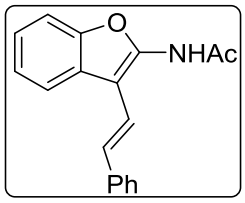
This compound was obtained in 80% yield (49.3 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 5/1, R_f = 0.3.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.69 (brs, 1H), 7.85-7.81 (m, 1H), 7.61-7.58 (m, 1H), 7.51-7.47 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.38-7.32 (m, 3H), 5.36 (s, 2H), 2.11 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 168.3, 162.6, 153.7, 150.0, 136.1, 128.6, 128.2, 128.1, 124.9, 124.6, 124.5, 120.7, 111.2, 98.0, 65.8, 23.4.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_4$: 310.1074; found: 310.1064.

(*E*)-*N*-(3-styrylbenzofuran-2-yl)acetamide (3am)



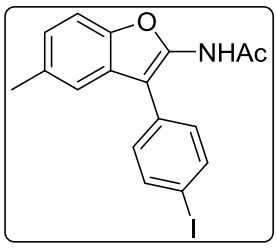
This compound was obtained in 52% yield (28.7 mg, in 0.2 mmol scale) as brown solid. Eluent: PE/EA = 3/1, R_f = 0.3.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.59 (brs, 1H), 8.12-8.09 (m, 1H), 7.64 (d, *J* = 7.5 Hz, 2H), 7.57-7.54 (m, 1H), 7.42-7.34 (m, 4H), 7.29 (d, *J* = 5.4 Hz, 1H), 7.27-7.25 (m, 1H), 7.18 (d, *J* = 17.2 Hz, 1H), 2.15 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 169.3, 151.2, 146.4, 137.5, 128.7, 127.9, 127.4, 126.1, 125.9, 124.4, 123.5, 121.0, 118.5, 111.1, 107.2, 23.0.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_2$: 278.1176; found: 278.1174.

***N*-(3-(4-iodophenyl)-5-methylbenzofuran-2-yl)acetamide (3be)**



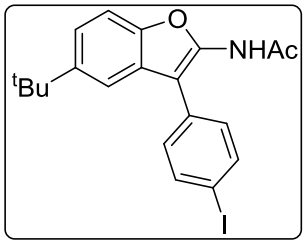
This compound was obtained in 63% yield (49.3 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.5.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.39 (brs, 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.47-7.44 (m, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 1H), 2.40 (s, 3H), 2.05 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.3, 149.5, 143.8, 137.7, 132.4, 130.8, 130.1, 126.9, 125.9, 119.4, 110.8, 93.3, 22.7, 21.1.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{15}INO_2$: 392.0142; found: 392.0131.

***N*-(5-(*tert*-butyl)-3-(4-iodophenyl)benzofuran-2-yl)acetamide (3ce)**



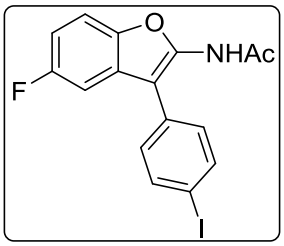
This compound was obtained in 77% yield (66.4 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 3/1, R_f = 0.55.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.39 (brs, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 7.46-7.41 (m, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 2.04 (s, 3H), 1.32 (s, 9H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.3, 149.4, 146.0, 143.9, 137.8, 130.8, 130.1, 126.4, 122.6, 115.3, 111.4, 110.6, 93.4, 34.6, 31.6, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{21}INO_2$: 434.0611; found: 434.0601.

***N*-(5-fluoro-3-(4-iodophenyl)benzofuran-2-yl)acetamide (3de)**



This compound was obtained in 50% yield (39.5 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 3/1, R_f = 0.4.

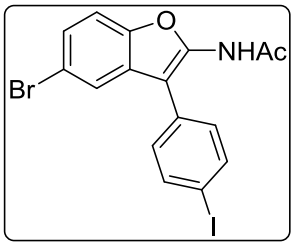
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.52 (brs, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.63 (dd, *J* = 9.0, 4.2 Hz, 1H), 7.45 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.21 (td, *J* = 9.2, 2.6 Hz, 1H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.1, 158.9 (d, *J* = 235.7 Hz), 147.4, 145.6, 137.8, 130.1, 130.0, 127.8 (d, *J* = 10.2 Hz), 112.6 (d, *J* = 9.4 Hz), 112.3 (d, *J* = 26.9 Hz), 111.2, 105.6 (d, *J* = 25.5 Hz), 93.7, 22.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ -119.29.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{12}FINO_2$: 395.9891; found: 395.9882.

***N*-(5-bromo-3-(4-iodophenyl)benzofuran-2-yl)acetamide (3ee)**



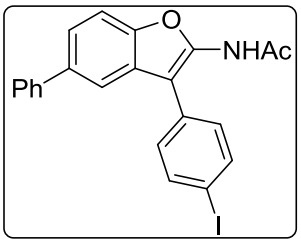
This compound was obtained in 60% yield (54.6 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.4.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.54 (brs, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 1.9 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.51 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.38 (d, *J* = 8.3 Hz, 2H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.1, 149.9, 145.2, 137.8, 130.1, 129.9, 129.1, 127.5, 122.0, 115.9, 113.4, 110.4, 93.8, 22.8.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{12}BrINO_2$: 455.9091; found: 455.9079.

***N*-(3-(4-iodophenyl)-5-phenylbenzofuran-2-yl)acetamide (3fe)**



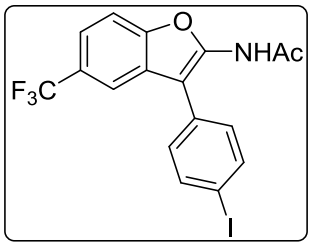
This compound was obtained in 51% yield (46.2 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 3/1, R_f = 0.55.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.49 (brs, 1H), 7.89-7.84 (m, 3H), 7.71-7.64 (m, 4H), 7.49-7.43 (m, 4H), 7.35 (t, *J* = 7.4 Hz, 1H), 2.07 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.3, 150.8, 144.5, 140.6, 137.8, 136.1, 130.5, 130.2, 128.9, 127.5, 127.2, 124.0, 117.7, 111.6, 111.3, 93.5, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{17}INO_2$: 454.0298; found: 454.0288.

***N*-(3-(4-iodophenyl)-5-(trifluoromethyl)benzofuran-2-yl)acetamide (3ge)**



This compound was obtained in 62% yield (55.3 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.3.

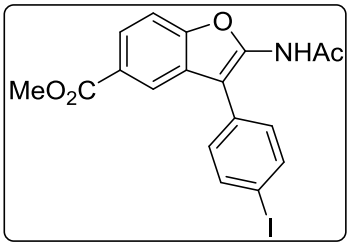
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.63 (brs, 1H), 7.94 (s, 1H), 7.91-7.86 (m, 2H), 7.83 (d, *J* = 8.6 Hz, 1H), 7.71 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 2H), 2.07 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.1, 152.7, 145.9, 137.9, 130.2, 129.7, 127.3, 124.6 (q, *J* = 270.7 Hz), 124.5 (q, *J* = 31.6 Hz), 121.8, 117.0, 112.3, 110.9, 94.0, 22.7.

^{19}F NMR (376 MHz, CDCl$_3$): δ -60.91.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{12}F_3INO_2$: 445.9859; found: 445.9846.

methyl 2-acetamido-3-(4-iodophenyl)benzofuran-5-carboxylate (3he)



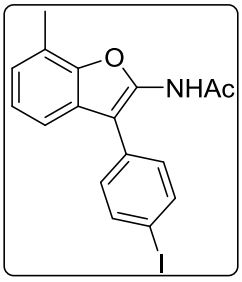
This compound was obtained in 39% yield (33.9 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.25.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.57 (brs, 1H), 8.21 (d, *J* = 1.6 Hz, 1H), 7.99 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 2H), 3.86 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.2, 166.1, 153.7, 145.3, 137.9, 130.1, 129.9, 127.2, 126.1, 125.1, 121.1, 111.6, 111.1, 94.0, 52.2, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{15}INO_4$: 436.0040; found: 436.0030.

***N*-(3-(4-iodophenyl)-7-methylbenzofuran-2-yl)acetamide (3ie)**



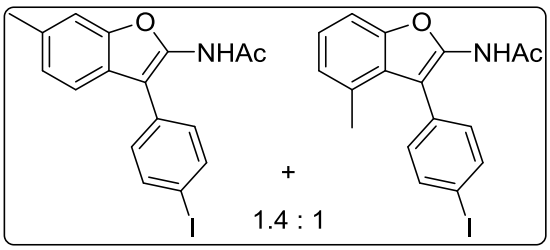
This compound was obtained in 51% yield (39.8 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.55.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.42 (brs, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.49 (dd, *J* = 6.6, 2.1 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.22-7.19 (m, 2H), 2.46 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.4, 150.1, 143.6, 137.7, 130.9, 130.0, 126.4, 125.7, 123.5, 120.9, 117.2, 111.6, 93.4, 22.7, 14.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{15}INO_2$: 392.0142; found: 392.0133.

***N*-(3-(4-iodophenyl)-6-methylbenzofuran-2-yl)acetamide (3je) and *N*-(3-(4-iodophenyl)-4-methylbenzofuran-2-yl)acetamide (3je')**



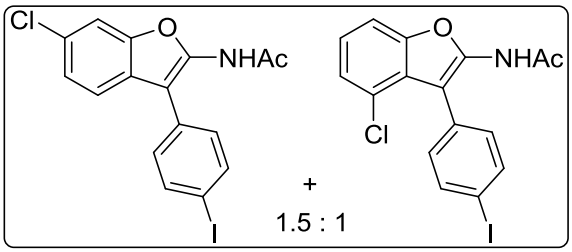
This compound was obtained in 68% yield (53.2 mg, in 0.2 mmol scale) as light yellow solid. An inseparable mixture of two regioisomers was obtained and the ratio was determined to be 1.4 : 1 by ^{1}H-NMR analysis. Eluent: PE/EA = 3/1, R_f = 0.5.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.38 (brs, 1H), 10.13 (s, 0.7H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 1.4H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.40-7.37 (m, 3.4H), 7.25-7.20 (m, 2.4H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 7.4 Hz, 0.7H), 2.43 (s, 3H), 2.12 (s, 2.1H), 2.06 (s, 3H), 1.96 (s, 2.1H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.5, 170.3, 151.5, 151.1, 143.8, 143.1, 137.7, 136.9, 134.6, 132.4, 131.6, 131.0, 130.8, 130.0, 126.0, 124.6, 124.3, 119.3, 111.3, 111.1, 108.8, 94.1, 93.3, 22.7, 22.5, 21.2, 19.4.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{15}INO_2$: 392.0142; found: 392.0128.

***N*-(6-chloro-3-(4-iodophenyl)benzofuran-2-yl)acetamide (3ke) and *N*-(4-chloro-3-(4-iodophenyl)benzofuran-2-yl)acetamide (3ke')**



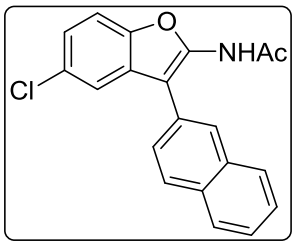
This compound was obtained in 56% yield (46.0 mg, in 0.2 mmol scale) as light yellow solid. An inseparable mixture of two regioisomers was obtained and the ratio was determined to be 1.5 : 1 by ^{1}H-NMR analysis. Eluent: PE/EA = 3/1, R_f = 0.55.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.51 (brs, 1H), 10.31 (brs, 0.65H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 1.3H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.60-7.57 (m, 0.65H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.36-7.32 (m, 1.65H), 7.31-7.28 (m, 0.65H), 7.23 (d, *J* = 8.2 Hz, 1.3H), 2.06 (s, 3H), 1.98 (s, 2H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.4, 170.2, 151.8, 151.2, 145.5, 144.6, 137.8, 136.6, 132.7, 130.0, 129.9, 129.3, 125.9, 125.5, 124.7, 124.6, 124.3, 123.8, 120.8, 111.7, 110.9, 110.5, 94.3, 93.8, 22.7, 22.5.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{12}ClINO_2$: 411.9596; found: 411.9589.

***N*-(5-chloro-3-(naphthalen-2-yl)benzofuran-2-yl)acetamide (3la)**



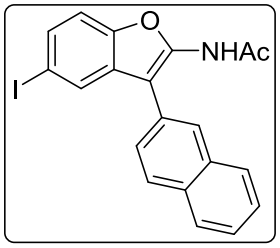
This compound was obtained in 62% yield (41.5 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.3.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.62 (brs, 1H), 8.17 (s, 1H), 8.06-8.01 (m, 2H), 7.98-7.93 (m, 1H), 7.80 (d, *J* = 2.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.58-7.52 (m, 2H), 7.42 (dd, *J* = 8.7, 2.0 Hz, 1H), 2.09 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.2, 149.7, 145.6, 133.2, 132.2, 129.0, 128.5, 128.1, 128.0, 127.9, 127.6, 126.9, 126.5, 126.4, 125.9, 124.7, 119.3, 112.9, 111.4, 22.8.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{15}ClNO_2$: 336.0786; found: 336.0776.

***N*-(5-iodo-3-(naphthalen-2-yl)benzofuran-2-yl)acetamide (3ma)**



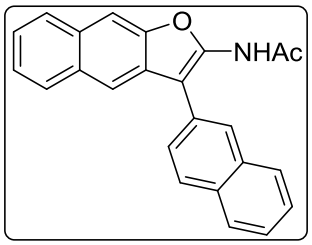
This compound was obtained in 57% yield (48.6 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.4.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.58 (brs, 1H), 8.13 (s, 1H), 8.07-8.02 (m, 3H), 7.99-7.94 (m, 1H), 7.71-7.66 (m, 2H), 7.59-7.53 (m, 2H), 7.49 (d, *J* = 8.5 Hz, 1H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.2, 150.5, 144.9, 138.0, 133.2, 133.1, 132.2, 130.1, 128.5, 128.1, 128.0, 127.6, 126.9, 126.5, 126.4, 125.9, 115.6, 113.7, 87.6, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{15}INO_2$: 428.0142; found: 428.0127.

***N*-(3-(naphthalen-2-yl)naphtho[2,3-b]furan-2-yl)acetamide (3na)**



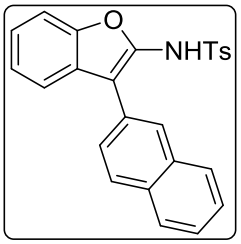
This compound was obtained in 73% yield (51.2 mg, in 0.2 mmol scale) as dark green solid. Eluent: PE/EA = 3/1, R_f = 0.3.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.27 (brs, 1H), 8.13-8.07 (m, 2H), 8.06-8.02 (m, 2H), 8.00-7.96 (m, 1H), 7.91 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.64-7.57 (m, 2H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 1.98 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.7, 148.6, 143.8, 133.0, 132.5, 130.4, 129.6, 129.2, 128.7, 128.2, 128.0, 127.9, 127.8, 127.4, 126.62, 126.55, 126.2, 125.8, 124.5, 122.4, 121.2, 115.1, 112.3, 22.6.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{18}NO_2$: 352.1332; found: 352.1320.

4-methyl-N-(3-(naphthalen-2-yl)benzofuran-2-yl)benzenesulfonamide (3oa)



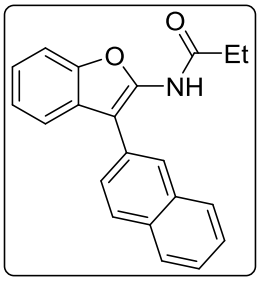
This compound was obtained in 59% yield (48.5 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 3/1, R_f = 0.45.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 11.12 (brs, 1H), 7.95-7.91 (m, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.60 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.57-7.53 (m, 3H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.42-7.38 (m, 1H), 7.34-7.30 (m, 1H), 6.97 (d, *J* = 8.2 Hz, 2H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 151.3, 143.1, 142.2, 137.7, 133.0, 132.1, 129.2, 128.0, 127.9, 127.6, 127.5, 127.2, 127.1, 126.4, 126.3, 126.2, 125.3, 123.4, 120.2, 114.3, 111.3, 20.8.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{20}NO_3S$: 414.1158; found: 414.1145.

***N*-(3-(naphthalen-2-yl)benzofuran-2-yl)propionamide (3pa)**



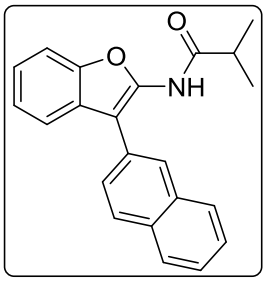
This compound was obtained in 66% yield (41.5 mg, in 0.2 mmol scale) as orange solid. Eluent: PE/EA = 2/1, R_f = 0.6.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.44 (brs, 1H), 8.16 (s, 1H), 8.05-7.94 (m, 3H), 7.85-7.82 (m, 1H), 7.73 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.59-7.52 (m, 2H), 7.43-7.33 (m, 2H), 2.45-2.29 (m, 2H), 1.13-1.05 (m, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 174.1, 151.3, 144.1, 133.2, 132.1, 128.6, 128.3, 127.9, 127.6, 127.3, 126.7, 126.5, 126.2, 126.0, 124.7, 123.4, 119.9, 111.8, 111.3, 28.6, 9.5.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{18}NO_2$: 316.1332; found: 316.1324.

***N*-(3-(naphthalen-2-yl)benzofuran-2-yl)isobutyramide (3qa)**



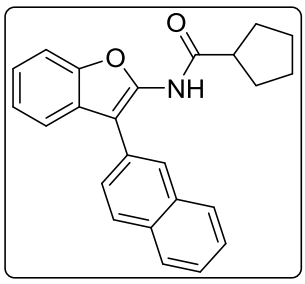
This compound was obtained in 60% yield (39.5 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 5/1, R_f = 0.45.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.39 (brs, 1H), 8.12 (s, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.98-7.94 (m, 2H), 7.84 (d, *J* = 7.1 Hz, 1H), 7.72 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.59-7.52 (m, 2H), 7.43-7.33 (m, 2H), 2.64 (p, *J* = 6.7 Hz, 1H), 1.12 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 177.1, 151.3, 144.1, 133.2, 132.1, 128.6, 128.2, 127.8, 127.6, 127.3, 126.5, 126.2, 126.0, 124.8, 123.4, 120.0, 112.1, 111.3, 34.2, 19.1.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{20}NO_2$: 330.1489; found: 330.1478.

***N*-(3-(naphthalen-2-yl)benzofuran-2-yl)cyclopentanecarboxamide (3ra)**



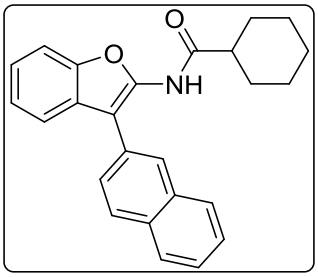
This compound was obtained in 66% yield (46.9 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 5/1, R_f = 0.45.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.41 (brs, 1H), 8.13 (s, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.98-7.95 (m, 2H), 7.87-7.82 (m, 1H), 7.72 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.59-7.52 (m, 2H), 7.43-7.33 (m, 2H), 2.83 (p, *J* = 7.6 Hz, 1H), 1.92-1.46 (m, 8H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 176.3, 151.3, 144.2, 133.2, 132.1, 129.5, 128.2, 127.8, 127.6, 127.3, 126.6, 126.5, 126.2, 126.0, 124.7, 123.3, 119.9, 112.8, 111.2, 44.3, 29.7, 25.6.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{22}NO_2$: 356.1645; found: 356.1635.

***N*-(3-(naphthalen-2-yl)benzofuran-2-yl)cyclohexanecarboxamide (3sa)**



This compound was obtained in 79% yield (58.3 mg, in 0.2 mmol scale) as light yellow solid. Eluent: PE/EA = 5/1, R_f = 0.45.

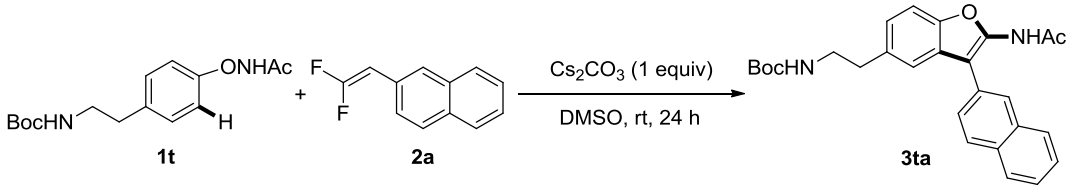
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.35 (brs, 1H), 8.12 (s, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.98-7.95 (m, 2H), 7.85-7.82 (m, 1H), 7.71 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.59-7.52 (m, 2H), 7.42-7.33 (m, 2H), 2.42-2.36 (m, 1H), 1.85-1.61 (m, 5H), 1.46-1.20 (m, 5H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 176.1, 151.3, 144.2, 133.2, 132.1, 128.7, 128.2, 127.8, 127.6, 127.3, 126.6, 126.5, 126.2, 126.0, 124.7, 123.3, 119.9, 112.1, 111.2, 43.9, 28.8, 25.3, 25.1.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{24}NO_2$: 370.1802; found: 370.1793.

III. Synthetic Applications

Late-stage C-H modification of natural products:



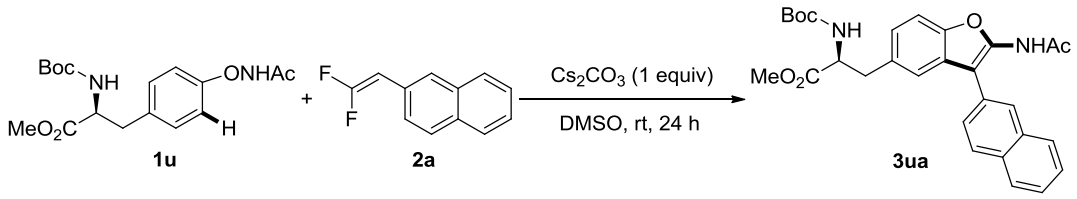
The mixture of dopamine derivative **1t** (0.2 mmol, 1.0 equiv), 2-(2,2-difluorovinyl)naphthalene **2a** (0.3 mmol, 1.5 equiv) and Cs_2CO_3 (0.2 mmol, 1.0 equiv) in DMSO (2.0 mL) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, the mixture was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified by preparative TLC (Eluent: PE/EA =

3/1, R_f = 0.25) to afford the desired product **3ta** in 62% (55.1 mg) isolated yield as light yellow solid.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.48 (brs, 1H), 8.16 (s, 1H), 8.06-8.00 (m, 2H), 7.99-7.94 (m, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H), 7.58-7.54 (m, 2H), 7.53 (d, *J* = 8.7 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 6.90-6.83 (m, 1H), 3.20 (q, *J* = 5.9 Hz, 2H), 2.83 (t, *J* = 7.0 Hz, 2H), 2.08 (s, 3H), 1.29 (s, 9H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.4, 155.6, 150.0, 144.1, 134.6, 133.2, 132.1, 128.8, 128.3, 128.0, 127.6, 127.4, 126.8, 126.4, 126.2, 126.1, 125.6, 119.7, 111.8, 110.9, 77.4, 42.0, 35.4, 28.2, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{29}N_2O_4$: 445.2122; found: 445.2110.

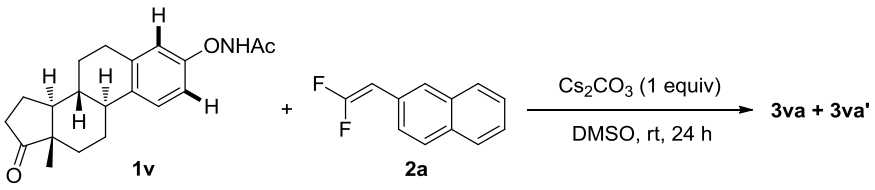


The mixture of tyrosine derivative **1u** (0.2 mmol, 1.0 equiv), 2-(2,2-difluorovinyl)naphthalene **2a** (0.3 mmol, 1.5 equiv) and Cs_2CO_3 (0.2 mmol, 1.0 equiv) in DMSO (2.0 mL) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, the mixture was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified by preparative TLC (Eluent: PE/EA = 2/1, R_f = 0.3) to afford the desired product **3ua** in 58% (58.3 mg) isolated yield as light yellow solid.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.48 (brs, 1H), 8.15 (s, 1H), 8.06-7.95 (m, 3H), 7.74-7.70 (m, 2H), 7.60-7.55 (m, 2H), 7.54-7.50 (m, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 4.28-4.21 (m, 1H), 3.63 (s, 3H), 3.15 (dd, *J* = 13.7, 4.7 Hz, 1H), 2.97 (dd, *J* = 13.6, 10.4 Hz, 1H), 2.07 (s, 3H), 1.22 (s, 9H).

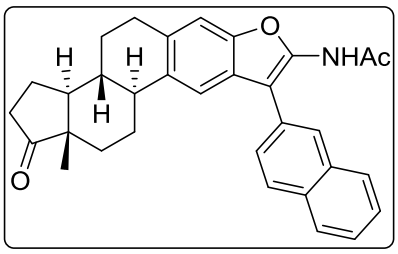
^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 172.6, 170.3, 155.4, 150.2, 144.1, 133.2, 132.6, 132.1, 128.7, 128.3, 128.0, 127.6, 127.2, 126.7, 126.4, 126.3, 126.0, 125.9, 120.5, 111.7, 110.9, 78.2, 55.5, 51.8, 36.5, 28.0, 22.7.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{29}H_{30}N_2O_6Na$: 525.1996; found:525.1978.



The mixture of estrone derivative **1v** (0.2 mmol, 1.0 equiv), 2-(2,2-difluorovinyl)naphthalene **2a** (0.3 mmol, 1.5 equiv) and Cs_2CO_3 (0.2 mmol, 1.0 equiv) in DMSO (2.0 mL) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, the mixture was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified by preparative TLC to afford the desired product **3va** and **3va'**.

***N*-((3aS,3bR,10bS,12aS)-12a-methyl-9-(naphthalen-2-yl)-1-oxo-2,3,3a,3b,4,5,10b,11,12,12a-decahydro-1H-cyclopenta[7,8]phenanthro[2,3-b]furan-8-yl)acetamide (3va)**



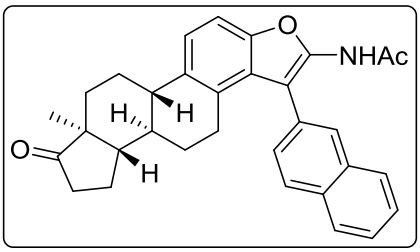
This compound was obtained in 37% yield (35.3 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 2/1, R_f = 0.25.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.41 (brs, 1H), 8.10 (s, 1H), 8.04-7.98 (m, 2H), 7.95 (d, *J* = 5.2 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.62 (s, 1H), 7.56-7.53 (m, 2H), 7.30 (s, 1H), 3.01-2.95 (m, 2H), 2.46-2.38 (m, 2H), 2.32 (t, *J* = 10.6 Hz, 1H), 2.06 (s, 3H), 1.97-1.93 (m, 2H), 1.76 (d, *J* = 12.1 Hz, 1H), 1.55-1.32 (m, 7H), 0.80 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 219.6, 170.3, 149.9, 143.4, 135.4, 133.9, 133.2, 132.0, 128.9, 128.4, 128.0, 127.6, 126.6, 126.4, 126.2, 126.1, 125.2, 115.7, 111.8, 110.5, 49.8, 47.3, 43.8, 37.7, 35.4, 31.3, 29.3, 26.0, 25.7, 22.7, 21.2, 13.5.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{32}NO_3$: 478.2377; found: 478.2372.

***N*-((5bS,7aS,10aS,10bR)-7a-methyl-1-(naphthalen-2-yl)-8-oxo-5b,7,7a,8,9,10,10a, 10b,11,12-decahydro-6H-cyclopenta[7,8]phenanthro[2,1-b]furan-2-yl)acetamide (3va')**



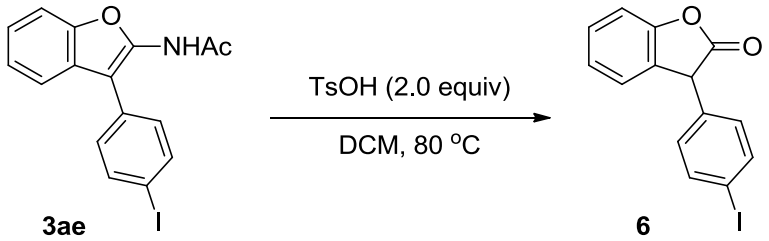
This compound was obtained in 27% yield (25.8 mg, in 0.2 mmol scale) as yellow solid. Eluent: PE/EA = 2/1, R_f = 0.25.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.09 (brs, 1H), 7.97-7.89 (m, 4H), 7.57-7.54 (m, 2H), 7.51 (d, *J* = 8.6 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 2.67-2.60 (m, 1H), 2.43-2.38 (m, 2H), 2.31-2.25 (m, 1H), 2.04 (d, *J* = 12.4 Hz, 1H), 1.90 (s, 3H), 1.80-1.75 (m, 2H), 1.71-1.65 (m, 1H), 1.53-1.38 (m, 6H), 1.14-1.08 (m, 1H), 0.80 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 219.6, 149.3, 144.2, 134.0, 132.6, 132.2, 130.1, 129.9, 128.3, 128.0, 127.9, 127.6, 127.2, 126.4, 126.3, 125.9, 122.3, 114.1, 108.6, 49.4, 47.2, 44.2, 37.4, 35.4, 31.5, 27.5, 26.2, 25.5, 22.5, 21.0, 13.5.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{32}NO_3$: 478.2377; found: 478.2370.

Derivatizations of compound 3ae:



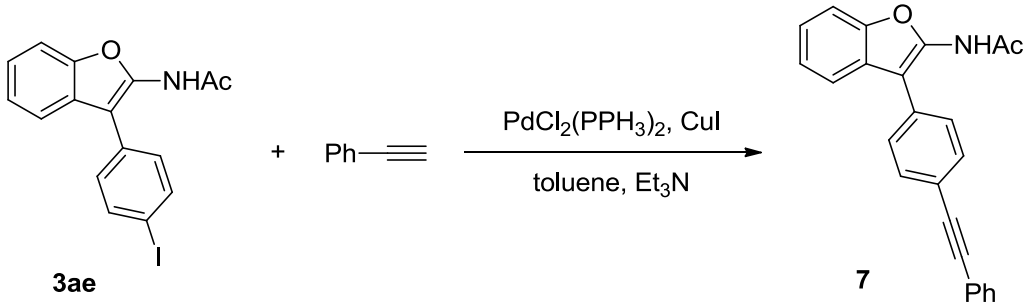
The mixture of *N*-(3-(4-iodophenyl)benzofuran-2-yl)acetamide **3ae** (0.1 mmol, 1.0 equiv), and TsOH·H_2O (0.2 mmol, 2.0 equiv) in DCM (2.5 mL) was stirred at 80 °C for 12 h without exclusion of air or moisture. Afterwards, the reaction mixture was concentrated and purified by preparative TLC (Eluent: PE/EA = 3/1, R_f = 0.8) to afford the desired product **6** in 63% (21.1 mg) isolated yield as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.40-7.36 (m, 1H),

7.21-7.17 (m, 3H), 6.98 (d, *J* = 8.3 Hz, 2H), 4.84 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 154.1, 138.4, 134.8, 130.3, 129.8, 126.5, 125.4, 124.8, 111.2, 94.2, 49.4.

HRMS (ESI) *m/z*: $[M-H]^-$ Calcd for $C_{14}H_8IO_2$: 334.9574; found: 334.9572.



The mixture of *N*-(3-(4-iodophenyl)benzofuran-2-yl)acetamide **3ae** (0.1 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (5 mol %) and CuI (10 mol %) was added into a dry three-necked flask under an N_2 atmosphere. Afterwards, phenylacetylene (0.1 mmol, 1.0 equiv), Et_3N (0.08 mL) and toluene (0.67mL) was injected and the reaction was stirred at 65 ^oC for 6 h. Then, the reaction mixture was diluted with H_2O and extracted by Ethyl acetate for three times. The combined organic phases was washed by diluted hydrochloric acid solution to remove the Et_3N. The solvent was concentrated and purified by preparative TLC (Eluent: PE/EA = 3/1, R_f = 0.45) to afford the desired product **7** in 75% (26.3 mg) isolated yield as light yellow solid.

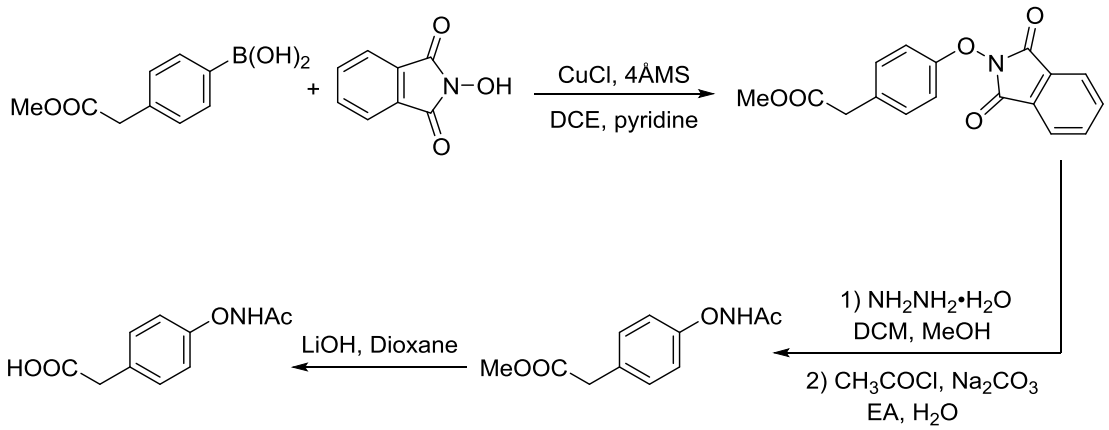
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.68 (brs, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.69-7.66 (m, 4H), 7.62-7.56 (m, 3H), 7.46-7.43 (m, 3H), 7.41-7.37 (m, 1H), 7.35-7.31 (m, 1H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 170.4, 151.2, 144.2, 137.7, 131.9, 131.4, 130.1, 128.9, 128.8, 128.2, 126.9, 124.8, 123.4, 122.3, 121.1, 119.8, 111.3, 89.9, 89.2, 22.7.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{18}NO_2$: 352.1332; found: 352.1320.

On-DNA synthesis:

Synthesis of 2-(4-(acetamidooxy)phenyl)acetic acid:



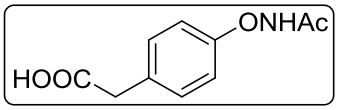
The title *N*-phenoxyacetamide was synthesized according to a reported procedure[S1]: In a reaction flask, a mixture of (4-(acetoxymethyl)phenyl)boronic acid (1.0 equiv), *N*-hydroxyphthalimide (1.2 equiv), CuCl (1.0 equiv), freshly activated 4 Å molecular sieves (250 mg/mmol) and pyridine (1.1 equiv) in 1,2-dichloroethane (0.33 M) was stirred at room temperature under an air atmosphere. The reaction mixture turned to green as the reaction proceeded and monitored by TLC. Afterwards, silica gel was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel to afford desired methyl 2-(4-((1,3-dioxoisoindolin-2-yl)oxy)phenyl)acetate.

Hydrazine monohydrate (3.0 equiv) was added to the solution of methyl 2-(4-((1,3-dioxoisoindolin-2-yl)oxy)phenyl)acetate (1.0 equiv) in 10% MeOH in $CHCl_3$ (0.1 M). The reaction was allowed to stir at room temperature for about 2 h and monitored by TLC. Afterwards, the precipitate was filtered off and washed with DCM. The filtrate was concentrated under reduce pressure to afford the resulting oil, which was directed used for the next step without purification.

The product of previous step (1.0 equiv) was added to a biphasic mixture of Na_2CO_3 (1.2 equiv) in EtOAc/H_2O (2/1, 0.6 M). The resulting solution was cooled to 0 ^oC followed by the dropwise addition of acyl chloride (2.0 equiv). After stirring at room temperature overnight, the reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The organic phase was washed twice with sat. $NaHCO_3$ after which it was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by recrystallization from EtOAc/PE to give desired methyl

2-(4-(acetamidooxy)phenyl)acetate as white crystals.

LiOH (1.2 equiv, 1 M in H_2O) was added to the solution of Methyl 2-(4-(acetamidooxy)phenyl)acetate (1.0 equiv) in dioxane. The reaction was allowed to stir at room temperature for about 4 h. Afterwards, diluted HCl solution (1 M) was added to neutralize the excess base, the reaction mixture was extracted with EtOAc, dried over Na_2SO_4, and filtered. The filtrate was concentrated under reduce pressure to afford the 2-(4-(acetamidooxy)phenyl)acetic acid as white soild. (Eluent: EA/MeOH = 10/1. R_f = 0.5)

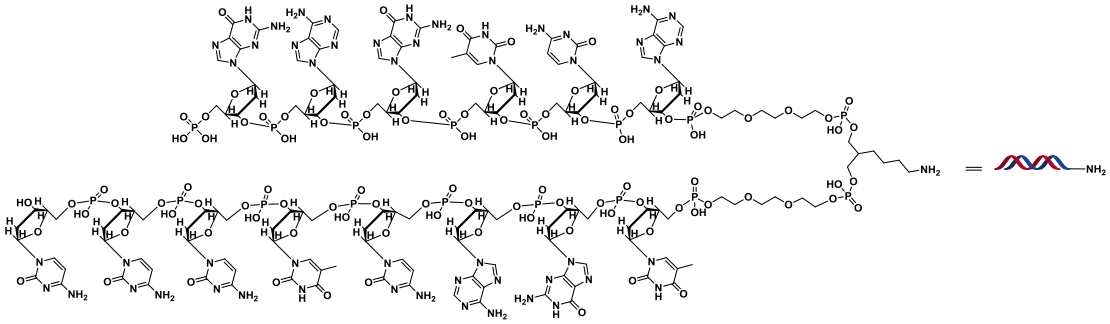


^{1}H NMR (400 MHz, CD_3OD): δ 7.23 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 3.55 (s, 2H), 2.00 (s, 3H).

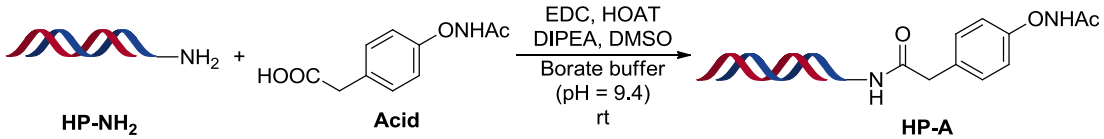
^{13}C NMR (100 MHz, CD_3OD): δ 175.6, 170.5, 159.9, 131.5, 130.6, 114.2, 41.0, 19.3

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_{12}NO_4$: 210.0761; found: 210.0764.

DNA headpiece HP-NH_2 (5′/5Phos/GAGTCA/iSp9/iUniAmM/iSp9/TGACTCCC-3′) (MW: 4937.23)

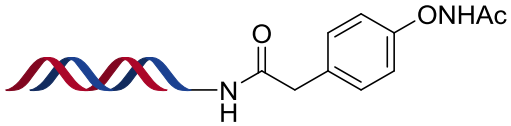


General procedure for the synthesis of DNA-conjugated *N*-phenoxyacetamide:

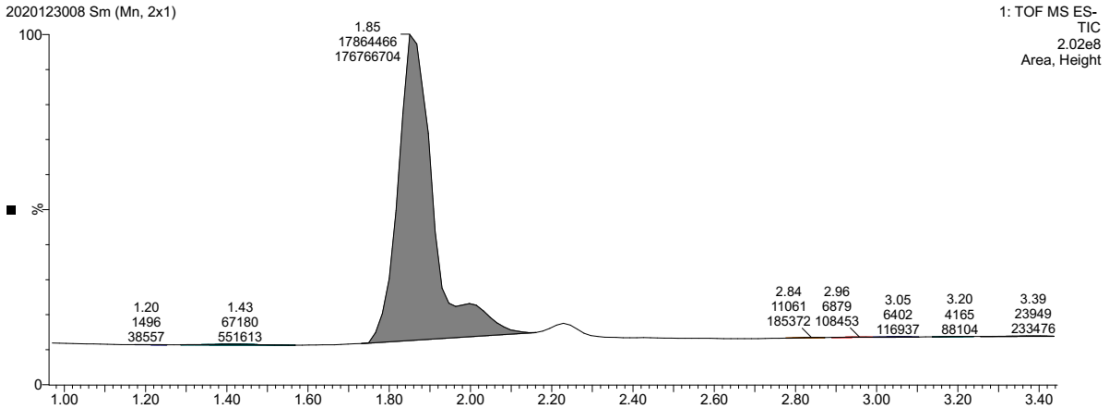


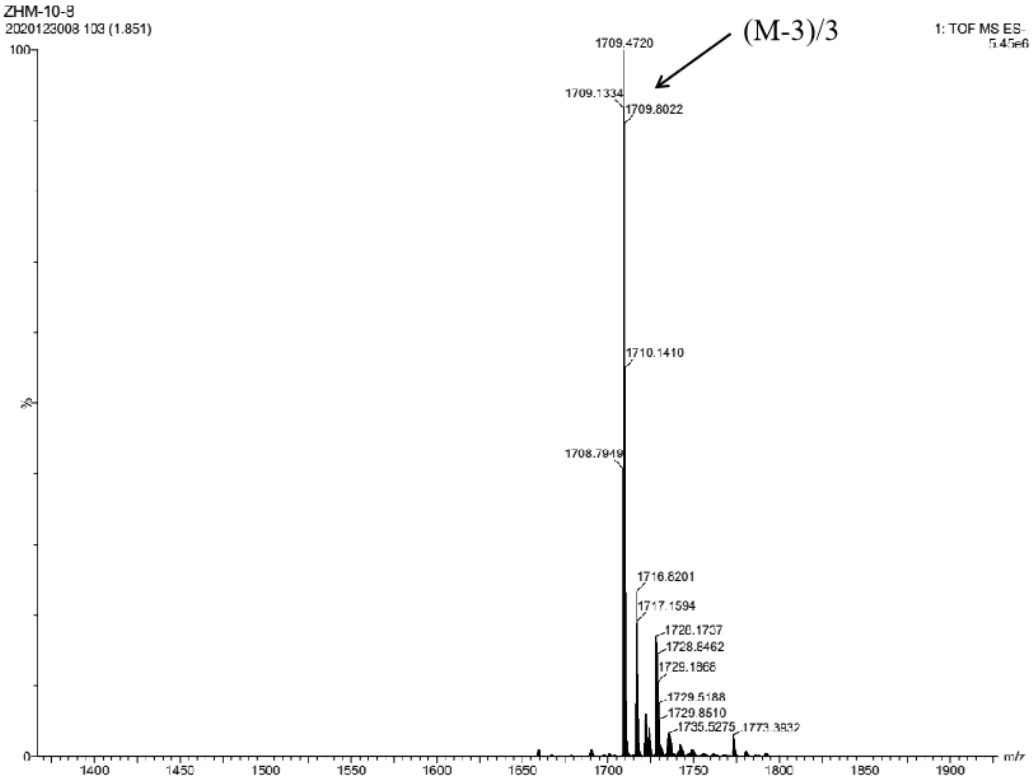
The acid (20.83 μL, 120 mM in DMSO), HOAT (400 μL, 120 mM in DMSO), EDC (400 μL, 600 mM in DMSO) and DIPEA (400 μL, 600mM in DMSO) was mixed together and incubate for 10 min at room temperature, after that the solution of DNA headpiece (50 nmol, dissolved in 100 μL of borate buffer (pH 9.4)) was added

to the mixture. The resulted mixture was vortexed and stood at 25 ^{o}C overlight. 5 M NaCl aqueous solution/cold ethanol (1/30) (25 mL) were sequentially added, and stored at -80 ^{o}C for at least 1 h. The mixture was centrifuged at 4 ^{o}C for 30 min at 12000 rpm to remove the supernatant. The resulting pellet was re-dissolved in ddH_2O (100 μL), which was used in following reaction without further purification.

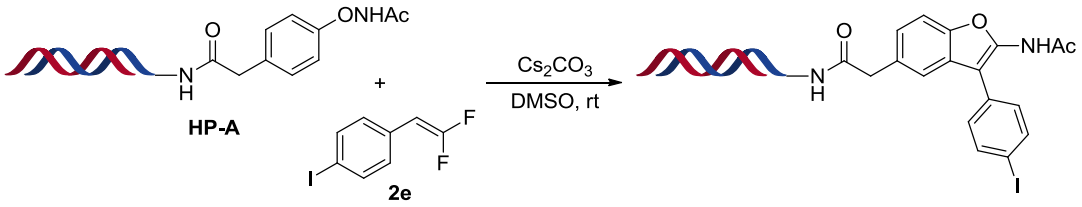


Calculated Molecular Weight: 1708.4294
Found Molecular Weight: 1709.4720

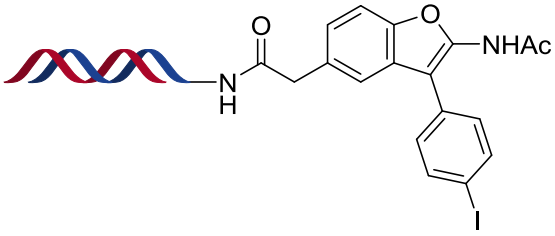




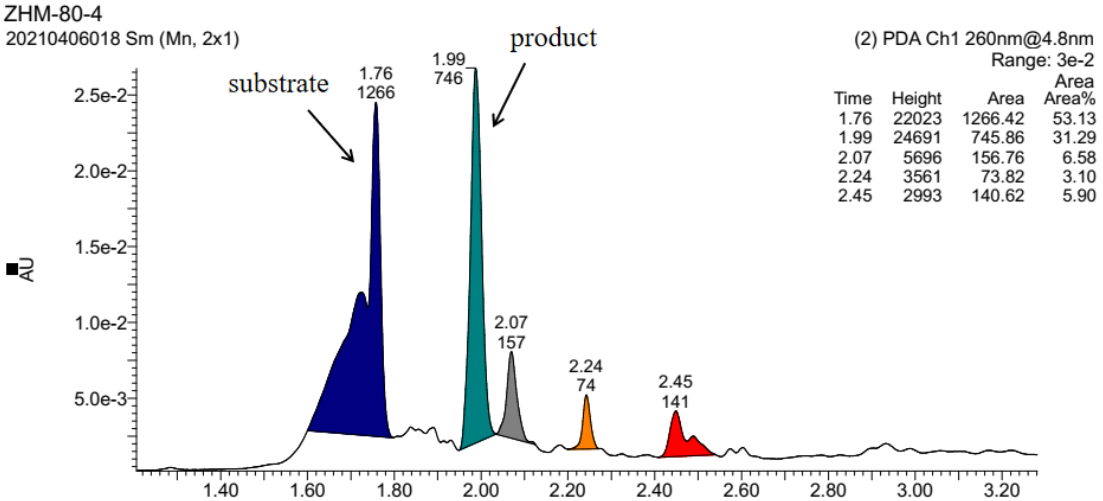
General Procedures for the on-DNA [3+2] annulation reactions:

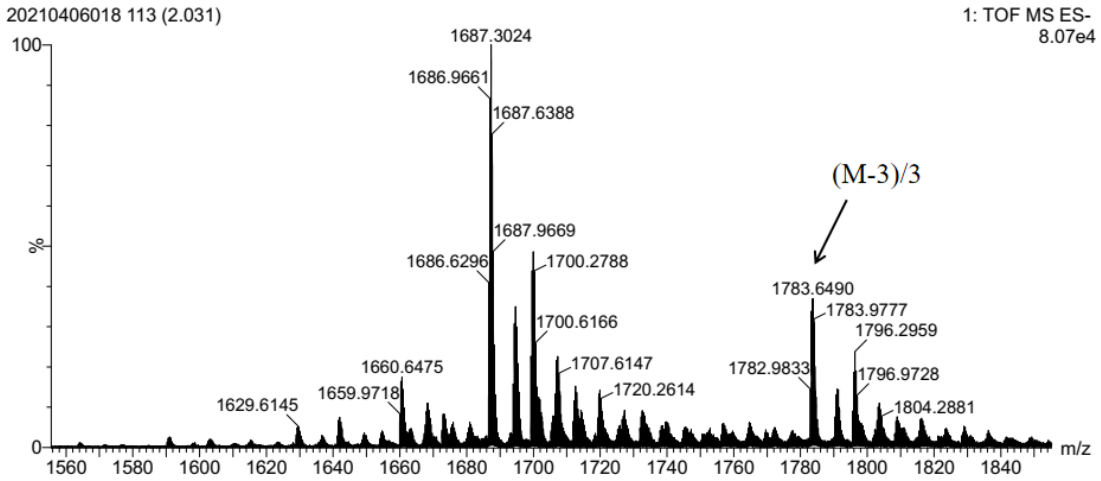


To a solution of **HP-A** (4 μL, 0.5 mM in ddH_2O) in 20 μL DMSO was added *gem*-difluoroalkene **2e** (4 μL, 500 mM in DMA) and Cs_2CO_3 (4 μL, 200 mM in ddH_2O). The resulting mixture was vortexed and stood at room temperature for 17 hours. After that, 300 equiv of scavenger sodium diethyldithiocarbamic acid (3.2 μL, 500 mM in ddH2O) was added to the mixture, and heated at 60 ^{o}C for 30 minutes. The reaction mixture was next centrifuged at 4 ^{o}C for 30 min at 12,000 rpm, and the resulted supernatant was collected. To the supernatant, 5 M NaCl aqueous solution/cold ethanol (1/30) (25 mL) were sequentially added, and stored at -80 ^{o}C for 1 h. The sample was centrifuged for 30 minutes at 4 ^{o}C in a microcentrifuge at 12,000 rpm to remove the supernatant. The resulting pellet (precipitate) was re-dissolved in ddH_2O (100 μL) for LC-MS detection.



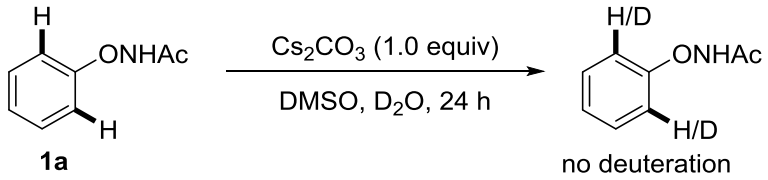
Calculated Molecular Weight: 1783.7387
Found Molecular Weight: 1783.6490



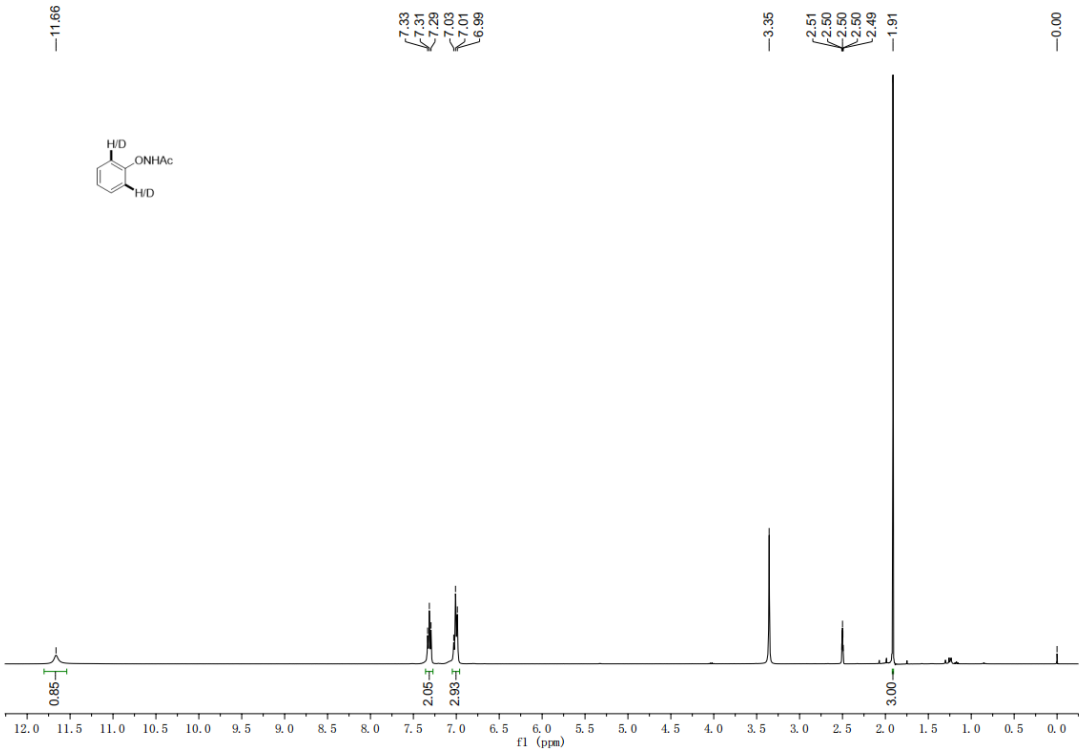


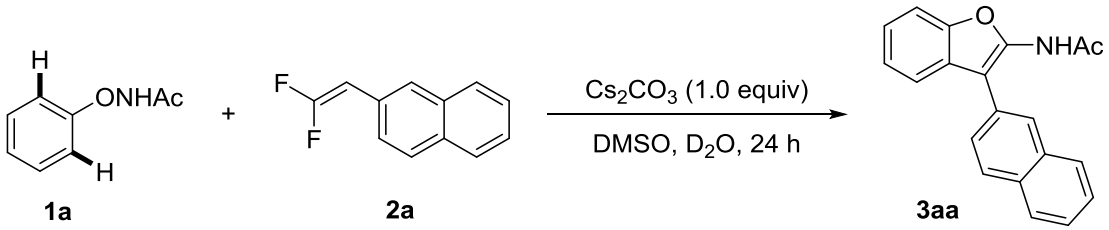
IV. Mechanistic Studies

Deuterium labeling experiment:



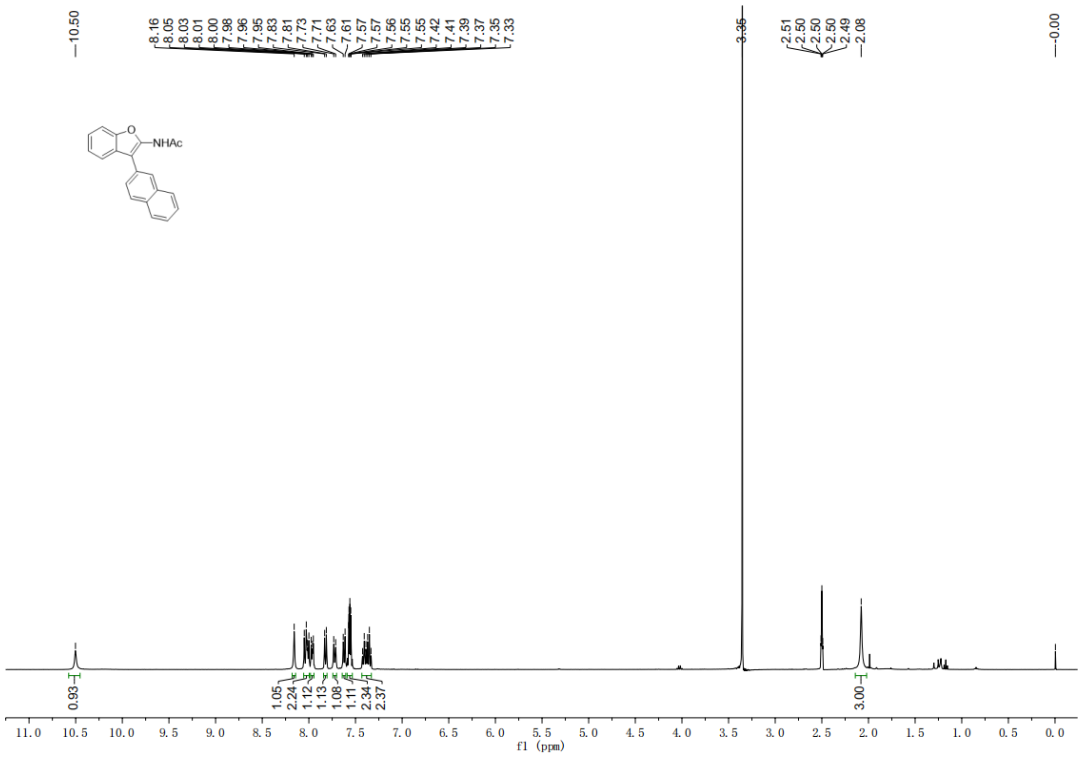
N-phenoxyacetamide **1a** (0.2 mmol) was dissolved in DMSO (1.6 mL) and D_2O (0.4 mL) in the presence of Cs_2CO_3 (0.2 mmol). The reaction was conducted under the standard condition for 24 h, afterwards, **1a** was recovered by flash column chromatography on silica gel (Eluent: PE/EA = 2/1) in 71% yield and was analyzed by ^{1}H-NMR spectroscopy. No deuteration was detected by ^{1}H-NMR analysis.



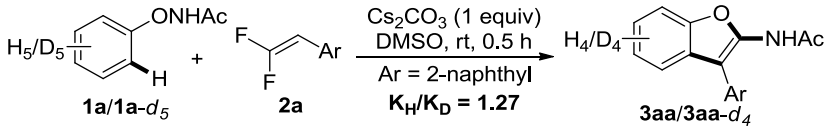


1a **2a** **3aa**

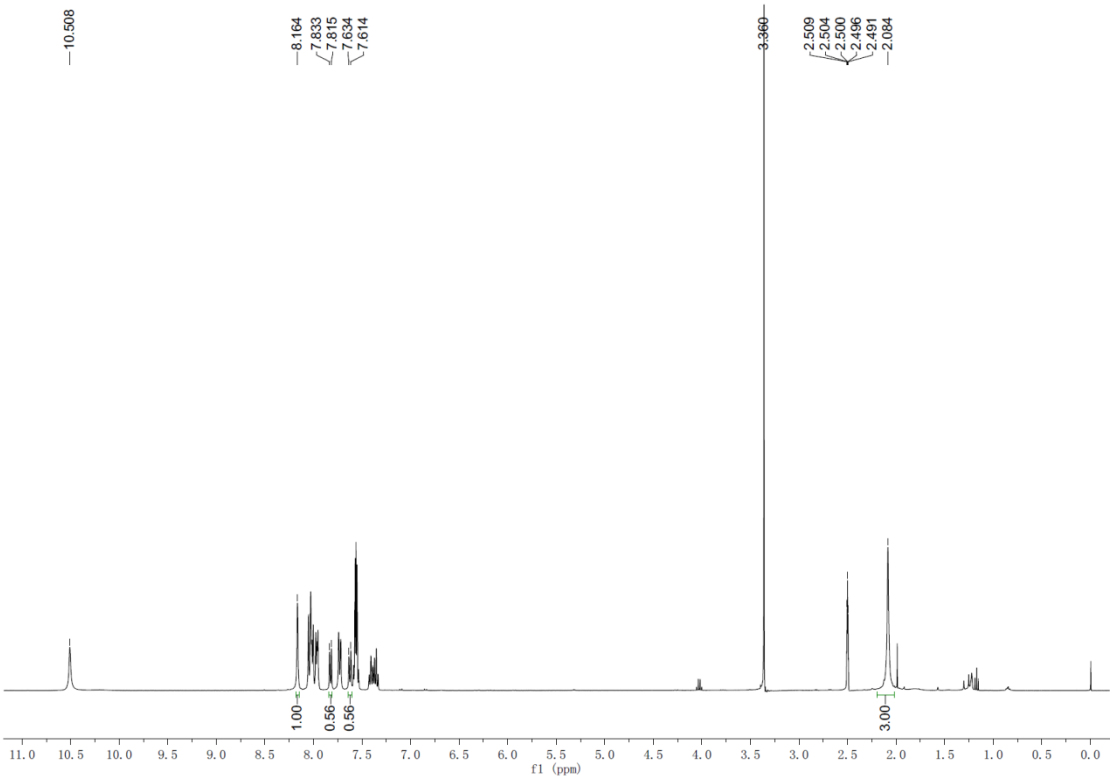
The mixture of *N*-phenoxyacetamide **1a** (0.2 mmol, 1.0 equiv), 2-(2,2-difluorovinyl)naphthalene **2a** (0.3 mmol, 1.5 equiv) and Cs_2CO_3 (0.2 mmol, 1.0 equiv) in DMSO (1.6 mL) and D_2O (0.4 mL) was stirred under the standard conditions for 24 h. Afterwards, the mixture was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified by preparative TLC (eluent: PE/EA = 2/1) to afford the desired product **3aa** in 56% yield. The deuterium incorporation was analyzed by ^{1}H-NMR spectroscopy. The result showed that no deuteration was observed at the *ortho* position of the directing group.



Kinetic isotope studies:

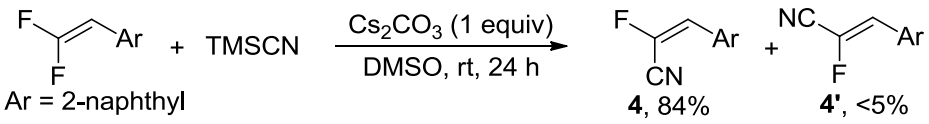


An equimolar mixture of **1a** (0.1 mmol, 1.0 equiv) and **1a-*d*$_5$** (0.1 mmol, 1.0 equiv) was allowed to react with **2a** (0.1 mmol, 1.0 equiv) in DMSO (0.5 mL) in the presence of Cs_2CO_3 (0.1 mmol, 1.0 equiv). The reaction was stopped after 0.5 h, and the product was isolated by preparative TLC and analyzed by ^{1}H-NMR spectroscopy (DMSO, 400 MHz). The singlet and doublet at δ: 2.08 (3H) and 7.62 (0.56H) were used for calculation and an average value of k_H/k_D = 1.27 was obtained.

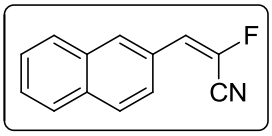


Another two parallel KIE experiments were performed by treating 1 equiv of **1a** or 1 equiv of **1a-*d*$_5$** with 1.0 equiv of **2a** separately under the standard conditions for 0.5 h. Afterwards, the two reactions were purified by preparative TLC to afford the corresponding product **3aa** in 20% and 19% yield, respectively. Thus give an KIE value of k_H/k_D = 1.05.

Control experiments:



The mixture of *gem*-difluoroalkene **2a** (0.2 mmol, 1 equiv), TMSCN (0.3 mmol, 1.5 equiv) and Cs_2CO_3 (1 equiv) in DMSO (0.1 M) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, the mixture was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified by preparative TLC (eluent: PE, R_f = 0.5) to afford the corresponding product **4** in 84% (33.0 mg) yield along with trace amount of **4'**.

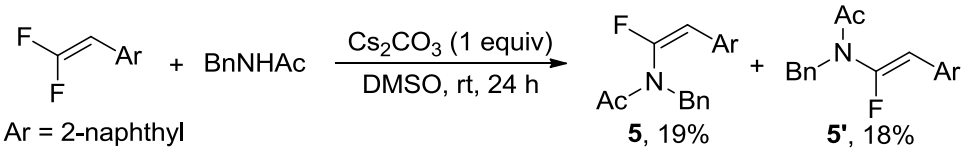


^{1}H NMR (**400 MHz**, **$CDCl_3$**): δ 7.97 (s, 1H), 7.88-7.81 (m, 3H), 7.71 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.58-7.50 (m, 2H), 7.18 (d, *J* = 16.9 Hz, 1H).

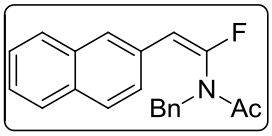
^{13}C NMR (**100 MHz**, **$CDCl_3$**): δ 134.1, 133.1, 131.3 (d, *J* = 239.3 Hz), 129.6 (d, *J* = 4.0 Hz), 129.2, 128.6, 127.9, 127.8, 127.2, 126.3 (d, *J* = 24.2 Hz), 125.6 (d, *J* = 7.1 Hz), 124.2 (d, *J* = 1.0 Hz), 112.8 (d, *J* = 47.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.86 (d, *J* = 17.9 Hz).

HRMS (ESI) calculated for $C_{13}H_9FN$ ($[M+H]^+$): 198.0714; found: 198.0711.



The mixture of *gem*-difluoroalkene **2a** (0.2 mmol, 1 equiv), *N*-benzylacetamide (0.3 mmol, 1.5 equiv) and Cs_2CO_3 (1 equiv) in DMSO (0.1 M) was stirred at room temperature for 24 h without exclusion of air or moisture. Afterwards, the mixture was diluted with Ethyl acetate and extracted by H_2O for three times, and once with saturated brine. Then, the reaction mixture was concentrated and purified by preparative TLC to afford the corresponding product **5** and **5'**.



This compound was obtained in 19% yield (12.2 mg) as yellow oil. Eluent: PE/EA= 10/1 , R_f = 0.5.

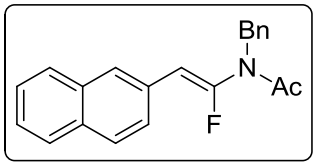
^{1}H NMR (**400 MHz**, **$CDCl_3$**): δ 7.78 (dd, *J* = 5.9, 3.3 Hz, 1H), 7.73-7.68 (m, 2H), 7.51-7.45 (m, 3H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.32-7.23 (m, 3H), 7.17 (d, *J* = 8.7 Hz, 1H), 6.29 (d, *J* = 8.2 Hz, 1H), 4.76 (s, 2H), 2.14 (s, 3H).

^{13}C NMR (**100 MHz**, **$CDCl_3$**): δ 170.7 (d, *J* = 4.0 Hz), 150.8 (d, *J* = 267.7 Hz), 136.2,

133.5, 132.9, 129.4, 128.8, 128.7, 128.6, 128.2, 128.1, 127.7, 127.4 (d, *J* = 4.1 Hz), 126.7 (d, *J* = 3.0 Hz), 124.4 (d, *J* = 1.0 Hz), 107.3 (d, *J* = 43.4 Hz), 49.5 (d, *J* = 2.0 Hz), 21.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ - 77.51.

HRMS (ESI) calculated for $C_{21}H_{19}FNO$ ($[M+H]^+$): 320.1445; found: 320.1441.



This compound was obtained in 18% yield (11.2 mg) as yellow oil. Eluent: PE/EA= 10/1, R_f = 0.4.

^{1}H NMR (**400 MHz**, **$CDCl_3$**): δ 7.85-7.76 (m, 4H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.51-7.44 (m, 2H), 7.38-7.27 (m, 5H), 5.62 (d, *J* = 29.1 Hz, 1H), 4.82 (s, 2H), 2.30 (s, 3H).

^{13}C NMR (**100 MHz**, **$CDCl_3$**): δ 170.9 (d, *J* = 4.0 Hz), 150.1 (d, *J* = 280.8 Hz), 136.7, 133.4, 132.9, 129.3 (d, *J* = 7.1 Hz), 128.9, 128.7, 128.4, 128.33, 128.25, 128.22, 127.9, 127.7, 126.7, 126.6, 126.1 (d, *J* = 8.1 Hz), 108.3 (d, *J* = 23.2 Hz), 50.6, 22.0.

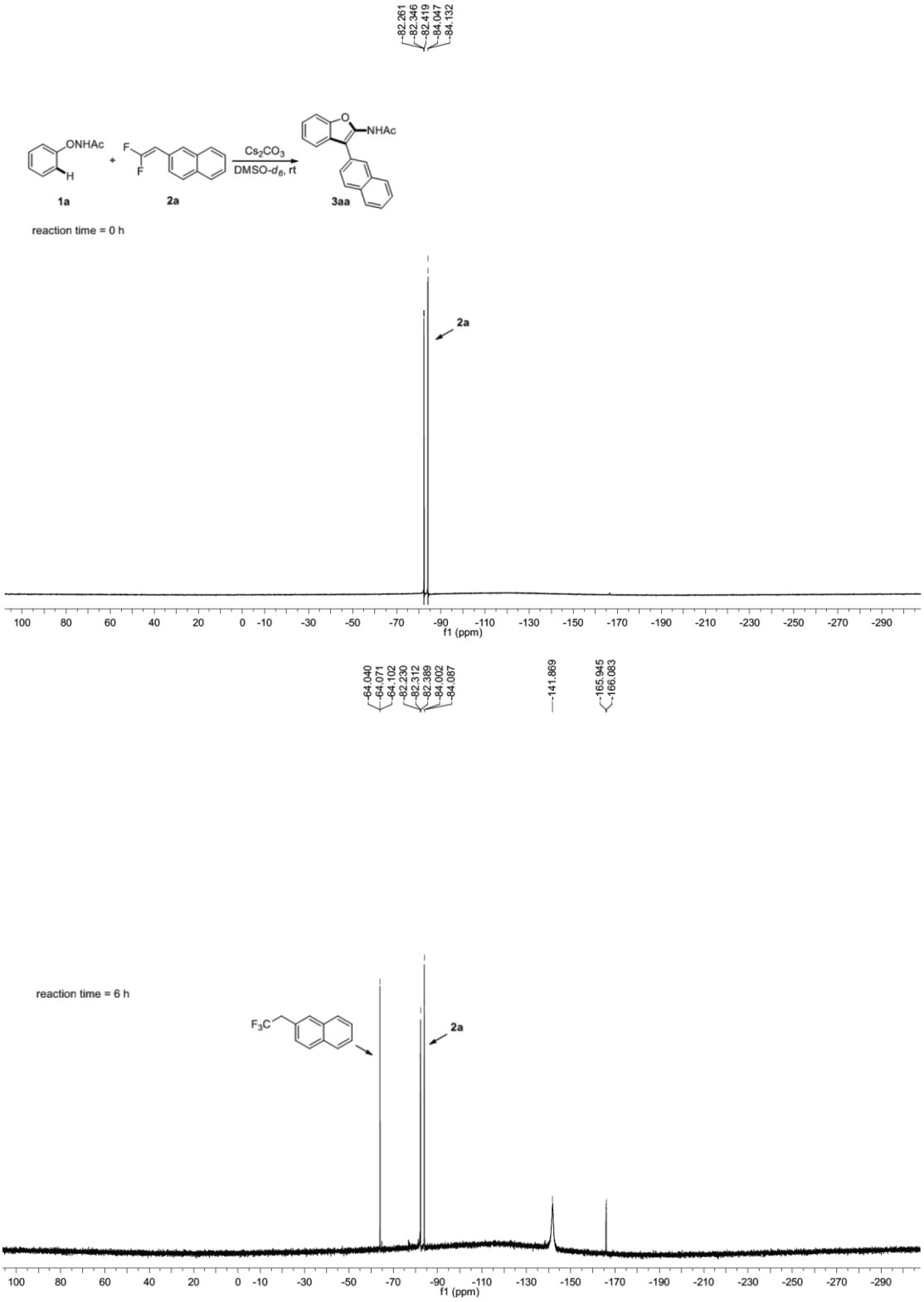
^{19}F NMR (376 MHz, $CDCl_3$): δ -82.11 (d, *J* = 30.8 Hz).

HRMS (ESI) calculated for $C_{21}H_{19}FNO$ ($[M+H]^+$): 320.1445; found: 320.1439.

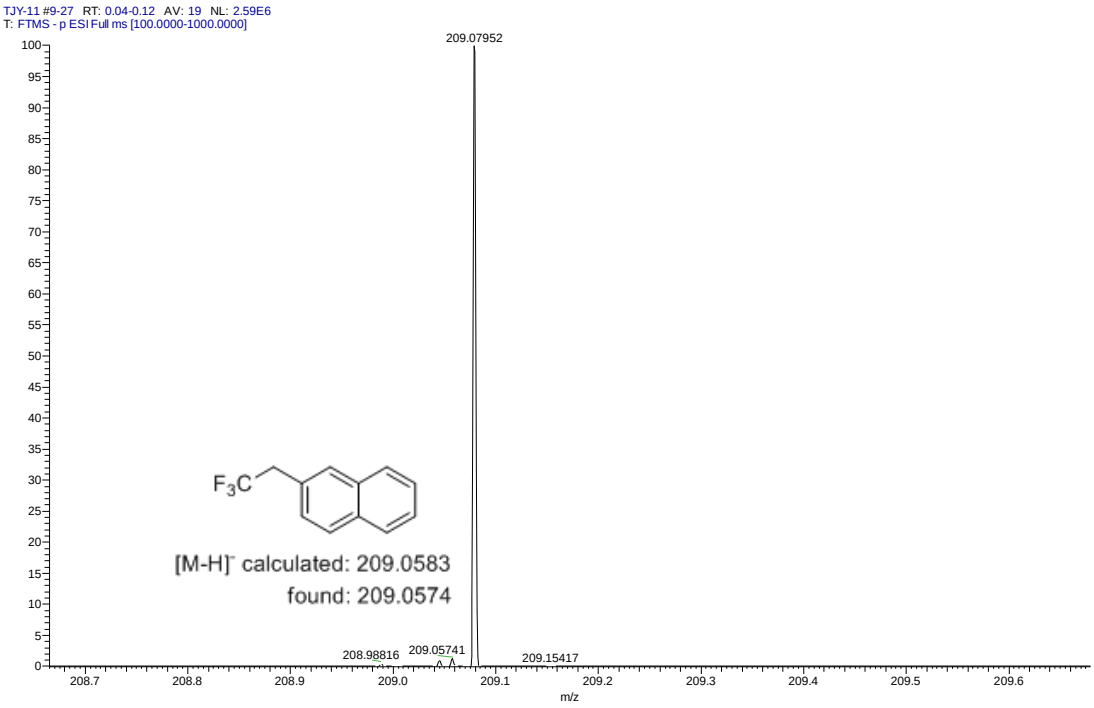
Detection of F^-:

N-phenoxyacetamide **1a** (0.1 mmol, 1.0 equiv), 2-(2,2-difluorovinyl)naphthalene **2a** (0.15 mmol, 1.5 equiv) and Cs_2CO_3 (0.1 mmol, 1.0 equiv) were dissolved in DMSO-d_6 (1.0 mL), the resulted mixture was analyzed by ^{19}F-NMR. Then, the mixture was stirred under the standard conditions for 6 h. Afterwards, the crude mixture was analyzed by ^{19}F-NMR and HRMS. As a result, 2-(2,2,2-trifluoroethyl)naphthalene was detected by HRMS, which probably derived from the addition of F^- to *gem*-difluoroalkene substrate **2a**. Several new signals were also detected in ^{19}F NMR spectrum (δ -141.87, -165.95, -166.08), which was in consistence with the signal of fluorine anion.

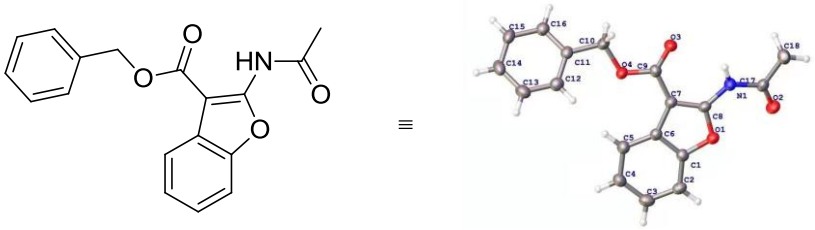
^{19}F-NMR of the crude mixture:



HRMS of 2-(2,2,2-trifluoroethyl)naphthalene:



V. X-Ray Crystallographic Data (CCDC2072717)



Experimental: A suitable crystal was selected and on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 149.98(10) K during data collection. Using Olex2,[S3] the structure was solved with the SHELXT structure solution program using Intrinsic Phasing[S4] and refined with the SHELXL refinement package using Least Squares minimization.[S5]

Crystal structure determination of [ckf]:

Crystal Data for $C_{18}H_{15}NO_4$ (M =309.31 g/mol): triclinic, space group P-1 (no. 2), a = 10.0306(6) Å, b = 12.3755(8) Å, c = 13.4817(10) Å, α = 110.230(7) °, β = 99.614(5) °, γ = 101.993(5) °, V = 1483.09(19) Å^3, Z = 4, T = 149.98(10) K, μ(Mo Kα) = 0.099 mm^{-1}, $Dcalc$ = 1.385 g/cm^3, 10482 reflections measured (4.3° ≤ 2Θ ≤

50 °), 5209 unique (R_{int} = 0.0265, R_{sigma} = 0.0458) which were used in all calculations. The final R_1 was 0.0456 (I > 2σ(I)) and wR_2 was 0.1192 (all data).

Table S2 **Crystal data and structure refinement for ckf.**

Identification code	ckf
Empirical formula	$C_{18}H_{15}NO_4$
Formula weight	309.31
Temperature/K	149.98(10)
Crystal system	triclinic
Space group	P-1
a/Å	10.0306(6)
b/Å	12.3755(8)
c/Å	13.4817(10)
α/°	110.230(7)
β/°	99.614(5)
γ/°	101.993(5)
Volume/Å^3	1483.09(19)
Z	4
ρ_{calc}g/cm^3	1.385
μ/mm^{-1}	0.099
F(000)	648.0
Crystal size/mm^3	0.14 × 0.12 × 0.11
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.3 to 50
Index ranges	-11 ≤ h ≤ 11, -12 ≤ k ≤ 14, -16 ≤ l ≤ 16
Reflections collected	10482
Independent reflections	5209 [R_{int} = 0.0265, R_{sigma} = 0.0458]
Data/restraints/parameters	5209/0/418
Goodness-of-fit on F^2	1.040
Final R indexes [I>=2σ (I)]	R_1 = 0.0456, wR_2 = 0.1058
Final R indexes [all data]	R_1 = 0.0637, wR_2 = 0.1192
Largest diff. peak/hole / e Å^{-3}	0.26/-0.19

Refinement model description:

Table S3 **Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for ckf. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.**

Atom	*x*	*y*	*z*	U(eq)
O1	4176.7(12)	8924.6(11)	5303.1(9)	30.2(3)

Table S3 **Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for ckf. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.**

Atom	*x*	*y*	*z*	U(eq)
O2	4688.2(15)	9875.8(13)	7550.9(10)	43.7(4)
O3	6826.7(14)	6694.4(12)	5470.7(10)	36.7(3)
O4	5645.0(13)	5655.5(11)	3693.6(9)	32.0(3)
N1	5933.6(15)	8763.6(14)	6583.1(11)	31.2(4)
C1	3532.5(18)	8315.7(16)	4185.9(14)	27.6(4)
C2	2513.3(18)	8620.2(17)	3605.5(15)	31.7(4)
C3	2000.4(19)	7889.3(18)	2501.9(15)	35.9(5)
C4	2488(2)	6917.3(18)	2028.2(15)	35.5(5)
C5	3516.0(19)	6628.3(17)	2623.4(14)	32.3(5)
C6	4049.5(17)	7352.7(16)	3738.9(14)	26.2(4)
C7	5077.7(18)	7368.2(16)	4642.5(14)	26.6(4)
C8	5094.3(18)	8328.5(16)	5536.0(14)	26.9(4)
C9	5939.5(19)	6567.8(17)	4668.8(14)	28.3(4)
C10	6457(2)	4805.7(17)	3603.2(14)	32.3(4)
C11	6128.6(17)	3979.2(17)	2420.4(14)	28.1(4)
C12	5826.3(18)	4378.6(18)	1586.0(15)	34.3(5)
C13	5589(2)	3613(2)	499.2(16)	39.9(5)
C14	5642(2)	2451(2)	240.4(16)	39.8(5)
C15	5928.8(19)	2044.8(18)	1061.6(15)	37.0(5)
C16	6176.9(18)	2812.3(17)	2151.6(15)	31.8(4)
C17	5724(2)	9521.1(17)	7538.7(15)	31.5(4)
C18	6880(2)	9830.6(19)	8540.0(15)	40.3(5)
O5	8948.1(12)	8907.2(11)	5242.4(10)	32.1(3)
O6	9448.1(16)	9893.5(15)	7451.7(11)	54.0(4)
O7	11538.3(14)	6667.0(12)	5437.4(10)	37.7(3)
O8	10548.2(13)	5707.2(11)	3623.8(9)	31.1(3)
N2	10535.3(16)	8593.0(14)	6527.5(11)	33.9(4)
C19	11362(2)	9545(2)	8495.0(15)	45.8(6)
C20	10352(2)	9382.7(18)	7468.9(15)	35.5(5)
C21	9834.5(18)	8283.6(16)	5466.1(14)	28.4(4)
C22	9925.7(18)	7402.7(16)	4556.2(14)	27.8(4)
C23	9002.1(18)	7475.7(16)	3643.4(14)	27.6(4)
C24	8620.6(19)	6874.9(17)	2503.5(14)	32.1(5)
C25	7667.0(19)	7231.8(18)	1902.4(15)	35.0(5)
C26	7100.1(19)	8141.6(18)	2399.9(15)	35.5(5)
C27	7476.4(19)	8757.6(17)	3525.3(15)	33.4(5)

Table S3 **Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for ckf. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.**

Atom	*x*	*y*	*z*	U(eq)
C28	8427.7(18)	8397.4(16)	4105.0(14)	27.6(4)
C29	10756.8(18)	6586.6(17)	4602.5(14)	28.2(4)
C30	11286(2)	4810.8(17)	3593.8(14)	31.6(4)
C31	11029.7(18)	3993.5(16)	2420.2(14)	27.2(4)
C32	12087.6(19)	3519.1(17)	2075.9(15)	33.8(5)
C33	11880(2)	2772.8(18)	989.8(15)	37.2(5)
C34	10611(2)	2489.8(18)	241.9(15)	36.9(5)
C35	9554(2)	2950.4(18)	578.9(15)	37.0(5)
C36	9754.3(19)	3697.1(17)	1658.2(14)	32.3(4)

Table S4 **Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for ckf. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.**

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	32.2(7)	30.0(7)	29.5(7)	9.9(6)	6.6(6)	15.4(6)
O2	53.9(9)	49.3(9)	36.5(8)	14.5(7)	14.7(7)	34.7(8)
O3	42.5(8)	39.3(8)	27.8(7)	9.7(6)	2.6(6)	22.5(6)
O4	35.2(7)	29.6(8)	28.4(7)	5.7(6)	2.9(6)	17.7(6)
N1	31.8(8)	34.0(10)	26.3(8)	6.9(7)	5.7(7)	16.5(7)
C1	26.7(9)	28.4(11)	27.2(10)	10.7(9)	6.3(8)	8.0(8)
C2	31.0(10)	31.7(11)	38.8(11)	16.8(10)	11.4(9)	15.1(8)
C3	31.4(10)	42.7(13)	38.9(12)	21.4(10)	6.5(9)	14.1(9)
C4	37.5(11)	39.3(12)	27.0(10)	11.4(9)	2.5(9)	13.5(9)
C5	33.0(10)	34.3(12)	29.4(10)	10.2(9)	7.4(9)	13.8(9)
C6	27.3(9)	25.4(10)	27.8(10)	11.1(8)	8.3(8)	9.3(8)
C7	27.3(9)	27.2(11)	27.5(10)	10.7(9)	8.2(8)	11.6(8)
C8	27.3(9)	27.9(11)	30.6(10)	13.8(9)	8.8(8)	13.4(8)
C9	30.3(10)	29.9(11)	24.8(10)	9.7(9)	7.3(8)	10.9(8)
C10	35.8(10)	29.8(11)	31.3(10)	8.8(9)	5.8(9)	17.4(9)
C11	23.6(9)	28.7(11)	29.8(10)	8.1(9)	6.2(8)	9.4(8)
C12	33.1(10)	33.4(11)	37.2(11)	14.0(10)	8.7(9)	11.3(9)
C13	39.1(11)	52.8(14)	31.6(11)	18.0(11)	7.0(9)	20.8(10)
C14	35.2(11)	50.7(14)	26.6(10)	3.9(10)	3.9(9)	21.2(10)
C15	34.9(10)	30.3(11)	37.8(11)	3.0(10)	4.5(9)	15.1(9)
C16	29.9(10)	31.7(11)	32.5(10)	10.5(9)	6.5(8)	11.1(8)
C17	40.7(11)	26.9(11)	29.8(10)	10.6(9)	11.5(9)	14.7(9)

Table S4 **Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for ckf. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.**

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C18	47.2(12)	38.6(12)	29.4(11)	7.9(10)	6.6(9)	12.9(10)
O5	35.9(7)	32.3(8)	30.4(7)	10.3(6)	7.5(6)	19.0(6)
O6	67.1(10)	71.8(12)	36.0(8)	16.6(8)	17.0(8)	51.2(9)
O7	45.9(8)	40.2(9)	25.7(7)	7.8(6)	2.2(6)	24.2(7)
O8	37.0(7)	30.5(7)	26.5(7)	7.5(6)	6.1(6)	19.6(6)
N2	42.7(9)	35.7(10)	24.8(8)	6.9(8)	6.3(7)	24.9(8)
C19	65.1(14)	46.2(14)	29.7(11)	12.4(11)	10.3(10)	29.4(11)
C20	45.4(12)	34.8(12)	32.4(11)	13.7(9)	12.5(9)	21.5(10)
C21	30.0(10)	27.9(11)	30.0(10)	12.1(9)	6.7(8)	13.7(8)
C22	28.3(9)	29.2(11)	27.1(10)	10.1(9)	7.3(8)	12.3(8)
C23	25.5(9)	29.7(11)	28.6(10)	12.2(9)	7.1(8)	8.7(8)
C24	31.6(10)	33.6(11)	29.6(10)	9.5(9)	8.0(9)	11.1(8)
C25	34.9(10)	39.7(12)	27.4(10)	13.0(9)	2.2(9)	9.7(9)
C26	31.3(10)	38.3(12)	38.8(11)	19.0(10)	3.5(9)	11.5(9)
C27	31.6(10)	33.0(12)	41.3(12)	17.5(10)	9.8(9)	15.6(8)
C28	26.1(9)	29.6(11)	25.8(10)	9.5(9)	5.6(8)	9.0(8)
C29	29.3(10)	30.3(11)	23.8(10)	8.0(9)	7.6(8)	10.3(8)
C30	37.3(10)	30.7(11)	31.3(10)	11.9(9)	8.9(9)	19.1(9)
C31	32.2(10)	23.8(10)	27.5(10)	10.1(8)	8.4(8)	11.5(8)
C32	33.4(10)	35.0(12)	31.3(10)	9.2(9)	5.7(9)	15.4(9)
C33	40.6(11)	39.8(12)	34.0(11)	10.1(10)	14.4(9)	21.2(9)
C34	47.4(12)	35.0(12)	27.2(10)	8.6(9)	10.4(9)	15.4(9)
C35	35.7(11)	38.0(12)	31.5(11)	9.5(10)	2.2(9)	11.0(9)
C36	29.5(10)	32.2(11)	34.9(11)	9.4(9)	10.1(9)	13.5(8)

Table S5 **Bond Lengths for ckf.**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.393(2)	O5	C21	1.354(2)
O1	C8	1.355(2)	O5	C28	1.396(2)
O2	C17	1.210(2)	O6	C20	1.210(2)
O3	C9	1.220(2)	O7	C29	1.219(2)
O4	C9	1.340(2)	O8	C29	1.338(2)
O4	C10	1.444(2)	O8	C30	1.449(2)
N1	C8	1.371(2)	N2	C20	1.377(2)
N1	C17	1.386(2)	N2	C21	1.364(2)
C1	C2	1.377(2)	C19	C20	1.496(3)

Table S5 **Bond Lengths for ckf.**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C6	1.384(3)	C21	C22	1.362(2)
C2	C3	1.384(3)	C22	C23	1.453(2)
C3	C4	1.382(3)	C22	C29	1.447(3)
C4	C5	1.382(3)	C23	C24	1.399(2)
C5	C6	1.397(2)	C23	C28	1.386(3)
C6	C7	1.450(2)	C24	C25	1.390(3)
C7	C8	1.363(2)	C25	C26	1.383(3)
C7	C9	1.449(3)	C26	C27	1.384(3)
C10	C11	1.501(2)	C27	C28	1.374(2)
C11	C12	1.391(3)	C30	C31	1.497(2)
C11	C16	1.376(3)	C31	C32	1.386(3)
C12	C13	1.390(3)	C31	C36	1.390(2)
C13	C14	1.373(3)	C32	C33	1.387(2)
C14	C15	1.378(3)	C33	C34	1.379(3)
C15	C16	1.392(2)	C34	C35	1.374(3)
C17	C18	1.500(3)	C35	C36	1.381(2)

Table S6 **Bond Angles for ckf.**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C8	O1	C1	105.48(14)	C21	O5	C28	105.22(14)
C9	O4	C10	117.07(13)	C29	O8	C30	116.51(13)
C8	N1	C17	128.28(16)	C21	N2	C20	128.77(17)
C2	C1	O1	124.85(17)	O6	C20	N2	122.12(18)
C2	C1	C6	124.53(17)	O6	C20	C19	123.83(18)
C6	C1	O1	110.62(16)	N2	C20	C19	114.05(17)
C1	C2	C3	115.65(18)	O5	C21	N2	119.05(16)
C4	C3	C2	121.43(18)	O5	C21	C22	113.40(15)
C5	C4	C3	122.09(18)	C22	C21	N2	127.54(17)
C4	C5	C6	117.52(18)	C21	C22	C23	105.18(16)
C1	C6	C5	118.77(17)	C21	C22	C29	123.00(16)
C1	C6	C7	105.47(15)	C29	C22	C23	131.77(16)
C5	C6	C7	135.75(17)	C24	C23	C22	135.83(17)
C8	C7	C6	105.64(16)	C28	C23	C22	105.69(15)
C8	C7	C9	124.05(16)	C28	C23	C24	118.47(17)
C9	C7	C6	130.31(16)	C25	C24	C23	117.57(18)
O1	C8	N1	118.53(16)	C26	C25	C24	121.96(18)
O1	C8	C7	112.80(15)	C25	C26	C27	121.41(19)

Table S6 **Bond Angles for ckf.**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C7	C8	N1	128.62(17)	C28	C27	C26	115.77(18)
O3	C9	O4	123.43(17)	C23	C28	O5	110.50(15)
O3	C9	C7	125.02(17)	C27	C28	O5	124.70(17)
O4	C9	C7	111.55(15)	C27	C28	C23	124.81(17)
O4	C10	C11	108.56(14)	O7	C29	O8	123.27(18)
C12	C11	C10	121.45(17)	O7	C29	C22	124.38(17)
C16	C11	C10	119.56(16)	O8	C29	C22	112.33(15)
C16	C11	C12	118.94(17)	O8	C30	C31	107.84(14)
C13	C12	C11	120.46(19)	C32	C31	C30	119.56(16)
C14	C13	C12	120.11(19)	C32	C31	C36	118.70(16)
C13	C14	C15	119.80(18)	C36	C31	C30	121.74(16)
C14	C15	C16	120.21(19)	C31	C32	C33	120.55(17)
C11	C16	C15	120.47(18)	C34	C33	C32	120.12(18)
O2	C17	N1	122.31(17)	C35	C34	C33	119.64(17)
O2	C17	C18	123.98(17)	C34	C35	C36	120.58(18)
N1	C17	C18	113.70(17)	C35	C36	C31	120.41(17)

Table S7 **Torsion Angles for ckf.**

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O1	C1	C2	C3	-179.42(15)	O5	C21	C22	C23	0.54(19)
O1	C1	C6	C5	179.52(14)	O5	C21	C22	C29	-176.98(14)
O1	C1	C6	C7	0.17(18)	O8	C30	C31	C32	145.16(16)
O4	C10	C11	C12	33.5(2)	O8	C30	C31	C36	-34.6(2)
O4	C10	C11	C16	-148.94(15)	N2	C21	C22	C23	-178.37(16)
C1	O1	C8	N1	177.23(14)	N2	C21	C22	C29	4.1(3)
C1	O1	C8	C7	-0.43(18)	C20	N2	C21	O5	9.1(3)
C1	C2	C3	C4	0.3(2)	C20	N2	C21	C22	-172.04(18)
C1	C6	C7	C8	-0.41(17)	C21	O5	C28	C23	-0.34(18)
C1	C6	C7	C9	179.04(17)	C21	O5	C28	C27	179.51(16)
C2	C1	C6	C5	0.0(3)	C21	N2	C20	O6	2.7(3)
C2	C1	C6	C7	-179.29(16)	C21	N2	C20	C19	-177.24(17)
C2	C3	C4	C5	-0.5(3)	C21	C22	C23	C24	178.50(19)
C3	C4	C5	C6	0.5(3)	C21	C22	C23	C28	-0.71(18)
C4	C5	C6	C1	-0.3(2)	C21	C22	C29	O7	-6.4(3)
C4	C5	C6	C7	178.79(18)	C21	C22	C29	O8	172.15(15)
C5	C6	C7	C8	-179.59(18)	C22	C23	C24	C25	179.97(18)
C5	C6	C7	C9	-0.1(3)	C22	C23	C28	O5	0.65(18)

Table S7 **Torsion Angles for ckf.**

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C6	C1	C2	C3	0.0(2)	C22	C23	C28	C27	-179.19(16)
C6	C7	C8	O1	0.53(19)	C23	C22	C29	O7	176.85(17)
C6	C7	C8	N1	-176.83(16)	C23	C22	C29	O8	-4.6(3)
C6	C7	C9	O3	176.47(16)	C23	C24	C25	C26	-0.3(3)
C6	C7	C9	O4	-3.5(2)	C24	C23	C28	O5	-178.72(14)
C8	O1	C1	C2	179.60(16)	C24	C23	C28	C27	1.4(3)
C8	O1	C1	C6	0.14(17)	C24	C25	C26	C27	1.1(3)
C8	N1	C17	O2	2.1(3)	C25	C26	C27	C28	-0.7(3)
C8	N1	C17	C18	-178.97(16)	C26	C27	C28	O5	179.54(15)
C8	C7	C9	O3	-4.2(3)	C26	C27	C28	C23	-0.6(3)
C8	C7	C9	O4	175.83(15)	C28	O5	C21	N2	178.87(14)
C9	O4	C10	C11	-171.29(14)	C28	O5	C21	C22	-0.15(19)
C9	C7	C8	O1	-178.97(14)	C28	C23	C24	C25	-0.9(2)
C9	C7	C8	N1	3.7(3)	C29	O8	C30	C31	-174.23(14)
C10	O4	C9	O3	-1.4(2)	C29	C22	C23	C24	-4.3(3)
C10	O4	C9	C7	178.60(14)	C29	C22	C23	C28	176.51(17)
C10	C11	C12	C13	177.02(16)	C30	O8	C29	O7	1.2(2)
C10	C11	C16	C15	-177.53(16)	C30	O8	C29	C22	-177.29(14)
C11	C12	C13	C14	0.5(3)	C30	C31	C32	C33	-179.15(16)
C12	C11	C16	C15	0.1(3)	C30	C31	C36	C35	179.34(17)
C12	C13	C14	C15	0.1(3)	C31	C32	C33	C34	-0.4(3)
C13	C14	C15	C16	-0.6(3)	C32	C31	C36	C35	-0.4(3)
C14	C15	C16	C11	0.5(3)	C32	C33	C34	C35	0.0(3)
C16	C11	C12	C13	-0.6(3)	C33	C34	C35	C36	0.2(3)
C17	N1	C8	O1	21.1(3)	C34	C35	C36	C31	0.0(3)
C17	N1	C8	C7	-161.63(18)	C36	C31	C32	C33	0.6(3)

Table S8 **Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for ckf.**

Atom	*x*	*y*	*z*	U(eq)
H1	6685.92	8537.3	6655.92	37
H2	2190.52	9274.33	3933.5	38
H3	1312.99	8055.69	2069.9	43
H4	2112.1	6442.81	1285.45	43
H5	3840.42	5975.88	2293.43	39
H10A	6217.09	4345.82	4035.41	39
H10B	7457.31	5228.79	3876.06	39

Table S8 **Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for ckf.**

Atom	*x*	*y*	*z*	U(eq)
H12	5782.46	5163.49	1756.68	41
H13	5394.3	3888.51	-53.68	48
H14	5485.14	1938.95	-486.91	48
H15	5956.55	1255.42	887.06	44
H16	6376.71	2534.16	2701.98	38
H18A	7761.99	10214.58	8451.85	61
H18B	6939.74	9109.55	8640.79	61
H18C	6679.22	10365.87	9168.36	61
H2A	11179	8248.05	6620.99	41
H19A	12310.68	9856.67	8470.52	69
H19B	11258.03	8783.7	8557.22	69
H19C	11167.11	10097.75	9115.8	69
H24	8991.57	6259.03	2160.34	39
H25	7402.24	6847.34	1143.01	42
H26	6452.09	8343.92	1968.89	43
H27	7108.82	9376.16	3867.66	40
H30A	10938.21	4355.39	4002.79	38
H30B	12289.24	5196.33	3919.65	38
H32	12943.71	3702.78	2577.45	41
H33	12598.16	2462.66	765.53	45
H34	10471.14	1989.86	-486.72	44
H35	8696.62	2757.57	75.69	44
H36	9031.23	4003.51	1876.53	39

VI. DFT Calculation Details

Computational details:

Density functional theory (DFT) calculations were performed by using Gaussian 09 quantum chemical package.[S6] The geometries of all reported reactants, intermediates, transition states, and products were optimized at the M06[S7] level of density functional theory with a standard 6-311++G(d,p) basis set using SMD[S8] solvation model (solvent = DMSO). Frequency analysis was conducted at the same level of theory to verify the stationary points to be real minima or saddle points and to obtain the thermodynamic energy corrections. The energies presented in this paper are the Gibbs free energies

with thermodynamic corrections which were calculated under standard conditions (1 atm and 298.15 K) (denoted as Δ*G* for clarity).

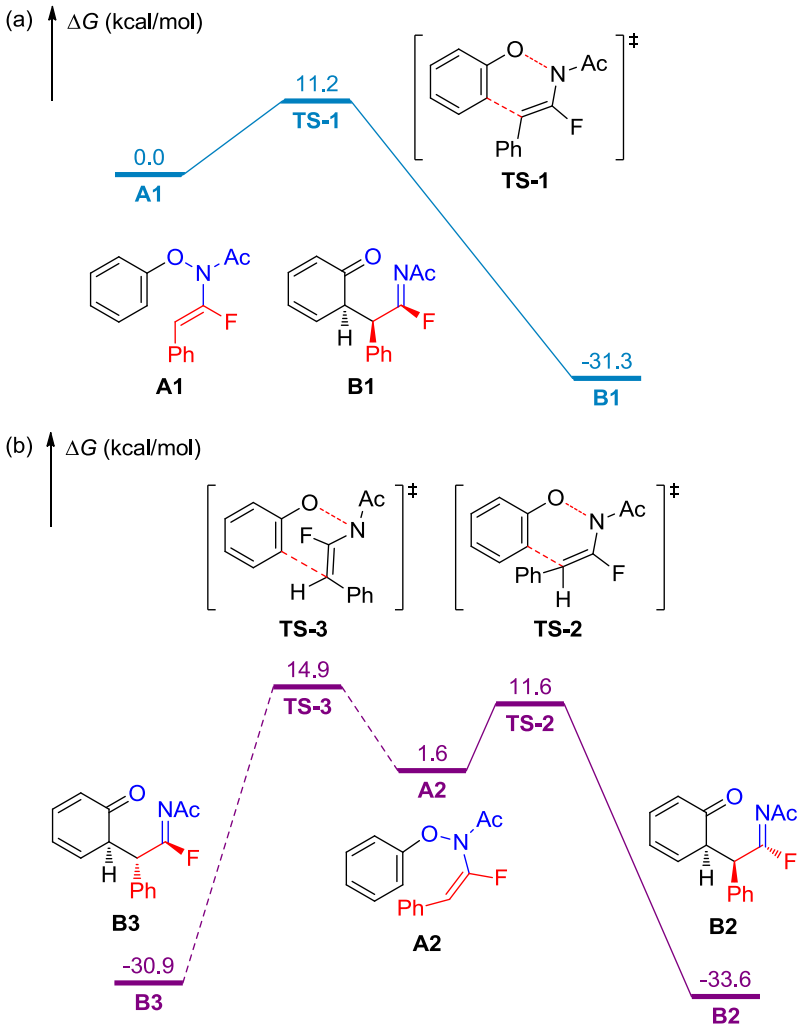


Figure S1 Computed Gibbs free energy changes of the [3,3]-σ rearrangement process

Various energy values for the reported species:

Table S9 Thermodynamic energy corrections and energies with corrections (in Hartree) of the reported species.

Species	corr. to ZPE	corr. to *E*	corr. to *H*	corr. to *G*	ZPE	*E*	*H*	*G*
A1	0.262307	0.280063	0.281007	0.213912	-922.487169	-922.469414	-922.468470	-922.535565
TS-1	0.260554	0.277821	0.278765	0.214318	-922.471504	-922.454237	-922.453293	-922.517739
B1	0.263039	0.280582	0.281526	0.216506	-922.538971	-922.521429	-922.520484	-922.585504
A2	0.262094	0.279577	0.280521	0.216205	-922.487198	-922.469715	-922.468771	-922.533087

TS-2	0.259788	0.277226	0.278171	0.213861	-922.471217	-922.453779	-922.452834	-922.517144
B2	0.263152	0.280770	0.281714	0.216381	-922.542285	-922.524668	-922.523723	-922.589057
TS-3	0.260014	0.277391	0.278335	0.213409	-922.465292	-922.447915	-922.446971	-922.511898
B3	0.263194	0.280950	0.281894	0.215232	-922.536916	-922.519160	-922.518215	-922.584878

Cartesian coordinates of the optimized structures:

A1

C	3.66618800	2.82613200	-0.28002100
C	3.76631700	2.33550300	1.01768400
C	3.12392500	1.16126900	1.37602500
C	2.38517800	0.47615400	0.42008200
C	2.27482200	0.94362700	-0.87930100
C	2.92154200	2.12729200	-1.21888100
H	4.16747000	3.74864000	-0.55573600
H	4.34603500	2.87350600	1.76180600
H	3.18792500	0.76549000	2.38519700
H	1.69972800	0.39571800	-1.61782300
H	2.83908100	2.50002500	-2.23559800
O	1.81735500	-0.70471000	0.86820600
N	0.87864600	-1.25676200	-0.01151800
C	1.23239700	-2.46224700	-0.62229700
O	0.37325600	-3.13849300	-1.14009100
C	2.68703400	-2.78722700	-0.60444900
H	3.29268200	-1.94033800	-0.93948700
H	3.00329900	-3.03479800	0.41370300
H	2.85984000	-3.64582400	-1.25354400
C	-0.43860800	-0.94049400	0.30987300
C	-1.20100800	-0.11107400	-0.39490900
H	-0.70273400	0.31549700	-1.26184000
C	-2.58646200	0.28637600	-0.18466300
C	-3.14721100	1.17870700	-1.10706800
C	-3.38555000	-0.16843900	0.87324700
C	-4.45962300	1.60480200	-0.98188800
H	-2.53631600	1.53671000	-1.93206800
C	-4.69795000	0.25964300	0.99415000
H	-2.98386400	-0.85985900	1.60427800
C	-5.24080800	1.14590900	0.07113200
H	-4.87400500	2.29712400	-1.70868100
H	-5.30397000	-0.10253600	1.81945100
H	-6.26998500	1.47721200	0.17277500
F	-0.86685400	-1.55991200	1.43010800

TS-1 (Imaginary frequency = -395.78 cm^{-1})

C	-1.49347600	2.87769000	0.25884800
C	-1.15989700	2.07175200	1.34119000
C	0.08137000	1.45790000	1.38733400
C	1.01603300	1.67059500	0.36176100
C	0.65992200	2.47188800	-0.73641300
C	-0.58148900	3.07839800	-0.77756900
H	-2.47097600	3.34911900	0.21607800
H	-1.87626100	1.91057400	2.14166900
H	0.35860100	0.80856300	2.21433600
H	1.37878800	2.59752100	-1.54186000
H	-0.85165500	3.70488100	-1.62242200
O	2.20142300	1.08411200	0.41506200
N	2.12031800	-0.45704800	-0.44758000
C	3.36707300	-1.07128900	-0.31495600
O	3.45530700	-2.25807900	-0.54929000
C	4.52574600	-0.19681600	0.01031900
H	4.52716800	0.70026600	-0.61248800
H	4.46231000	0.13575700	1.05049800
H	5.44568900	-0.76421500	-0.13551200
C	0.96389300	-1.05352700	-0.15727700
C	-0.17879100	-0.74091700	-0.81582100
H	-0.00383500	-0.18136600	-1.73110000
C	-1.55953900	-1.00376700	-0.48763000
C	-2.52872000	-0.47079300	-1.35213300
C	-1.98815500	-1.68261800	0.66538900
C	-3.87941800	-0.60384600	-1.07610400
H	-2.20420400	0.05899300	-2.24435700
C	-3.33862700	-1.81185900	0.93515100
H	-1.26337100	-2.10207500	1.35255200
C	-4.28731500	-1.27346800	0.07009300
H	-4.61490400	-0.18282200	-1.75460000
H	-3.65823000	-2.33678800	1.83033800
H	-5.34523800	-1.37772000	0.29222200
F	0.92315600	-1.78284000	0.98649400

B1

C	-2.14680800	2.79749200	-1.14917000
C	-1.81590200	3.48806800	0.07590500
C	-0.84735400	3.06202800	0.91364100
C	-0.10675300	1.84201600	0.63845300
C	-0.25251000	1.26844000	-0.75901500
C	-1.43972300	1.72643300	-1.52995600
H	-2.97679900	3.15977000	-1.74699200
H	-2.39470400	4.37061300	0.33774300

H	-0.65113800	3.55943400	1.85931200
H	0.60770800	1.73920700	-1.27924400
H	-1.67111200	1.19223700	-2.44921600
O	0.63299500	1.31359600	1.45568700
N	2.41924000	-0.13815700	-0.75764200
C	3.67844500	-0.43374000	-0.21113100
O	4.37765100	-1.29731500	-0.68282100
C	4.06833900	0.46263500	0.91591000
H	3.98531200	1.50927900	0.60646800
H	3.37209400	0.32138100	1.75002500
H	5.08731100	0.24787600	1.24047500
C	1.34889600	-0.58044300	-0.29425200
C	-0.01274700	-0.24507200	-0.84570900
H	0.07150800	-0.46735400	-1.91919500
C	-1.12637800	-1.11106500	-0.30071600
C	-1.18367500	-2.44413700	-0.70881600
C	-2.09592600	-0.63979300	0.57811700
C	-2.17835500	-3.28966900	-0.24329300
H	-0.43350700	-2.81856600	-1.40294700
C	-3.09843000	-1.48429500	1.04320100
H	-2.08955800	0.39358600	0.91510800
C	-3.14126200	-2.80976100	0.63737900
H	-2.20619300	-4.32416500	-0.57261200
H	-3.84928400	-1.09867800	1.72660700
H	-3.92496200	-3.46751800	1.00166600
F	1.35048200	-1.45945300	0.72112100

A2

C	2.43404300	2.58276500	-0.32532800
C	1.68441200	3.02899900	0.75451200
C	0.36727300	2.61348000	0.91133800
C	-0.18609600	1.76516600	-0.03223400
C	0.54302200	1.31621700	-1.12331400
C	1.86062000	1.72726100	-1.26067100
H	3.46624000	2.89954100	-0.43937900
H	2.12682100	3.69419300	1.48992500
H	-0.23304900	2.93681300	1.75661700
H	0.09259300	0.64147900	-1.84479900
H	2.44314000	1.37675700	-2.10791000
O	-1.51968600	1.41432200	0.15277200
N	-1.71262000	0.02291600	0.04705800
C	-2.68210000	-0.40667000	-0.85711700
O	-3.10009000	-1.54061100	-0.77077100
C	-3.09588400	0.58342100	-1.89040400

H	-2.23167200	1.04113300	-2.37888100
H	-3.67357800	1.38905600	-1.42635800
H	-3.71601900	0.07564800	-2.62949500
C	-1.48020700	-0.63039300	1.25750500
C	-0.38810900	-1.29447600	1.60733500
H	-0.33382000	-1.62805000	2.64210100
C	0.75479300	-1.57935600	0.73661400
C	2.04497700	-1.43027000	1.25196400
C	0.59980800	-1.99926700	-0.58609900
C	3.15450500	-1.65801500	0.45147700
H	2.17129200	-1.11985700	2.28658000
C	1.71092800	-2.23762600	-1.38135500
H	-0.39679600	-2.15404600	-0.98933000
C	2.99010400	-2.05996100	-0.86886100
H	4.15149900	-1.52647500	0.86170900
H	1.57684500	-2.56897000	-2.40711700
H	3.85857700	-2.24608300	-1.49383800
F	-2.46978600	-0.43210000	2.15806500

TS-2 (Imaginary frequency = -419.30 cm^{-1})

C	2.37278600	2.33333900	-0.20654900
C	1.49191700	2.57678500	0.83440300
C	0.14974600	2.24105500	0.69736800
C	-0.31857600	1.68605400	-0.50685000
C	0.58982000	1.44287400	-1.55584700
C	1.91709400	1.77343400	-1.40735100
H	3.42408500	2.58353700	-0.09637400
H	1.84974400	3.01454800	1.76148200
H	-0.56338000	2.42870700	1.49571000
H	0.21567800	0.98411000	-2.46758500
H	2.61812700	1.59435800	-2.21741200
O	-1.58945700	1.35954800	-0.63397400
N	-1.79473200	-0.33153000	-0.07681600
C	-3.07978000	-0.73718000	-0.44452300
O	-3.56428700	-1.69706000	0.11669900
C	-3.72058700	-0.02260400	-1.58061700
H	-3.02759700	0.07720900	-2.41914100
H	-4.00604000	0.98888100	-1.27784100
H	-4.60969500	-0.57583400	-1.88551800
C	-1.33040500	-0.37758200	1.16551600
C	-0.03874000	-0.57922900	1.52433100
H	0.20854400	-0.32829200	2.55491800
C	1.03326500	-1.13936400	0.72638500
C	2.34735500	-0.90300900	1.15048100

C	0.82523100	-1.91026500	-0.42747400
C	3.42561900	-1.38936600	0.42497800
H	2.51395700	-0.32497400	2.05644500
C	1.90228100	-2.40283300	-1.13920900
H	-0.18642300	-2.12705600	-0.75490300
C	3.20594000	-2.13673900	-0.72293100
H	4.43822800	-1.18958500	0.76231600
H	1.72946100	-3.00668000	-2.02510500
H	4.04666500	-2.52655400	-1.28917500
F	-2.16623100	0.07735600	2.14282500

B2

C	3.20093500	1.62887100	0.62963500
C	2.16020700	1.19674600	1.34923400
C	0.75588800	1.34207800	0.87521300
C	0.57867600	1.92791100	-0.51723400
C	1.76847600	2.38353600	-1.21227500
C	2.99320400	2.23145600	-0.66899600
H	4.21519700	1.53255900	1.00355400
H	2.30300700	0.73260100	2.32322000
H	0.27489600	2.07939200	1.54156800
H	1.62905500	2.82293400	-2.19590400
H	3.86769500	2.56363000	-1.22317900
O	-0.54194600	2.01663000	-1.00115700
N	-2.15240100	-0.59135400	0.00851200
C	-3.52707000	-0.39554200	-0.20133000
O	-4.35076000	-1.01748600	0.42413500
C	-3.82811500	0.56774600	-1.29986100
H	-3.29369700	0.27675000	-2.20965000
H	-3.46014800	1.56125000	-1.01993000
H	-4.90134800	0.60748300	-1.49037400
C	-1.46450800	0.13944200	0.74501300
C	-0.01188200	0.00586300	1.06182400
H	0.01847300	-0.19587300	2.14327100
C	0.65872700	-1.14732400	0.35568200
C	1.24307600	-2.15821000	1.11383900
C	0.76129700	-1.20528600	-1.03443100
C	1.91752900	-3.20764700	0.50176800
H	1.17213100	-2.11873800	2.19853600
C	1.43776100	-2.25049300	-1.64711700
H	0.30186400	-0.43778600	-1.65065300
C	2.01833300	-3.25463000	-0.88127700
H	2.36670800	-3.98774300	1.10943000
H	1.50812600	-2.28289300	-2.73042400

H	2.54556800	-4.07243100	-1.36373700
F	-2.03492000	1.13756700	1.45586000

TS-3 (Imaginary frequency = -365.51 cm^{-1})

C	2.19576400	3.36571800	0.10610600
C	3.14256400	2.33616400	0.10130600
C	2.79617300	1.08098400	-0.34869800
C	1.49397300	0.83705900	-0.83427000
C	0.54031000	1.87011100	-0.78659400
C	0.90162200	3.13235000	-0.33510300
H	2.47638000	4.35238400	0.46263700
H	4.15152700	2.52905100	0.45349600
H	3.51183400	0.26205100	-0.35718300
H	-0.46119200	1.66671000	-1.15468000
H	0.16939600	3.93405500	-0.32386300
O	1.17769300	-0.33995100	-1.32957000
N	0.59081900	-1.46462400	-0.00846200
C	1.38940500	-2.60994500	-0.01628700
O	1.30465000	-3.37707600	0.91969700
C	2.21886000	-2.86384400	-1.22511300
H	1.64242300	-2.71214400	-2.13996600
H	3.05842000	-2.16279700	-1.25559600
H	2.59827200	-3.88564300	-1.17944800
C	0.29970400	-0.77533700	1.08345200
C	-0.81800400	-0.03603600	1.30469100
H	-0.80015300	0.56812700	2.21002000
C	-2.04669500	-0.00236600	0.54708300
C	-3.10977700	0.73455900	1.09373100
C	-2.24359000	-0.65332900	-0.68256000
C	-4.33150500	0.80786500	0.44748600
H	-2.96322500	1.24599300	2.04172200
C	-3.46714400	-0.57577500	-1.32284600
H	-1.42820300	-1.20819900	-1.13241100
C	-4.51410900	0.15148000	-0.76335700
H	-5.14309100	1.37894100	0.88771000
H	-3.60767400	-1.08223800	-2.27310600
H	-5.46998200	0.20951800	-1.27540900
F	1.28727600	-0.65613000	2.01779200

B3

C	-0.49176600	3.66179700	-0.15129500
C	0.83547400	3.95965000	0.34553100
C	1.85094100	3.07854200	0.26072700
C	1.65620400	1.78436800	-0.37214800

C	0.22646900	1.35152000	-0.65435900
C	-0.78147100	2.45013300	-0.63672800
H	-1.24568500	4.44201400	-0.11904500
H	1.01041400	4.94022600	0.78149000
H	2.85409400	3.32299800	0.59793400
H	0.22826000	0.84686200	-1.63014800
H	-1.78012700	2.21761900	-0.99757900
O	2.58486200	1.04064800	-0.65009600
N	0.91596600	-1.80991600	-0.23311600
C	1.89770300	-2.80382100	-0.06654900
O	1.66384100	-3.80612200	0.56248000
C	3.17175200	-2.51661200	-0.78434700
H	2.97049200	-2.21178400	-1.81544300
H	3.67100300	-1.67356900	-0.29300000
H	3.82392700	-3.39083100	-0.76695700
C	0.81453400	-0.81772900	0.51048100
C	-0.19788100	0.28716400	0.41447600
H	-0.19941100	0.79582500	1.38741700
C	-1.58636600	-0.25529100	0.16172200
C	-2.53133400	-0.19368700	1.18147200
C	-1.95058000	-0.80464000	-1.06663200
C	-3.81795300	-0.68022400	0.98509000
H	-2.25538400	0.24158100	2.13913300
C	-3.23551600	-1.28919700	-1.26379800
H	-1.23094300	-0.85584500	-1.87898800
C	-4.17303200	-1.22935000	-0.23872900
H	-4.54434500	-0.62495000	1.79067200
H	-3.50777800	-1.71403500	-2.22569000
H	-5.17873500	-1.60777400	-0.39671600
F	1.65108400	-0.64787400	1.55668700

VII. References

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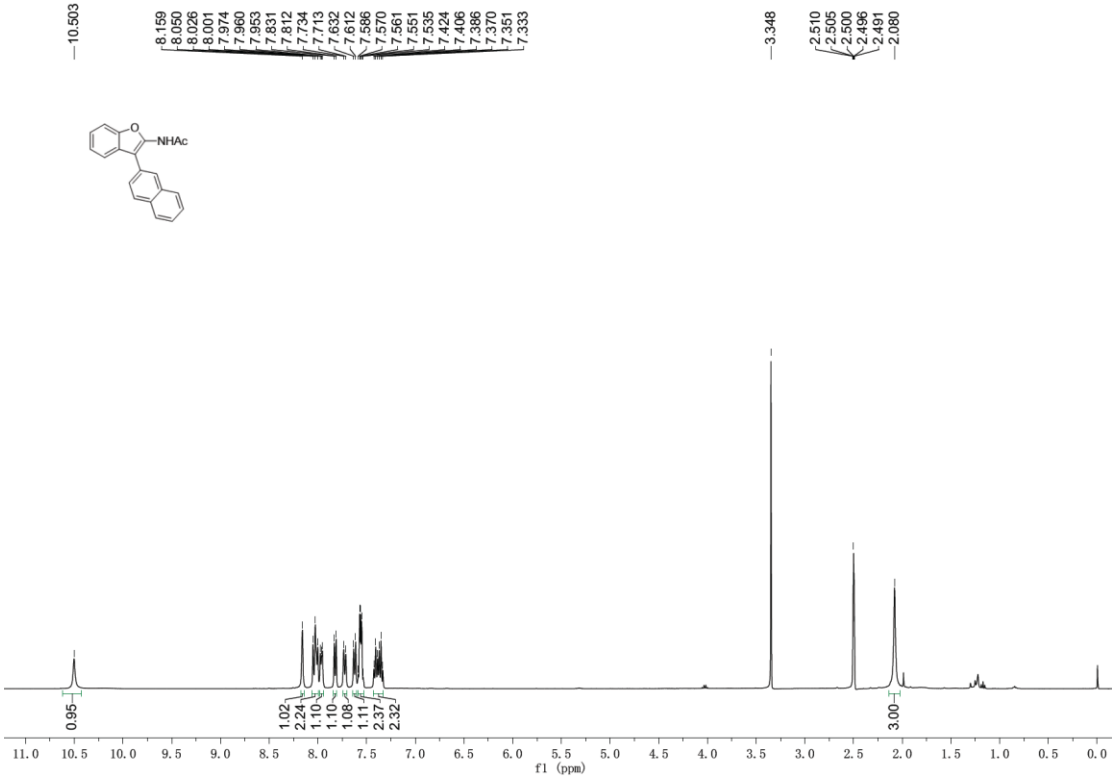
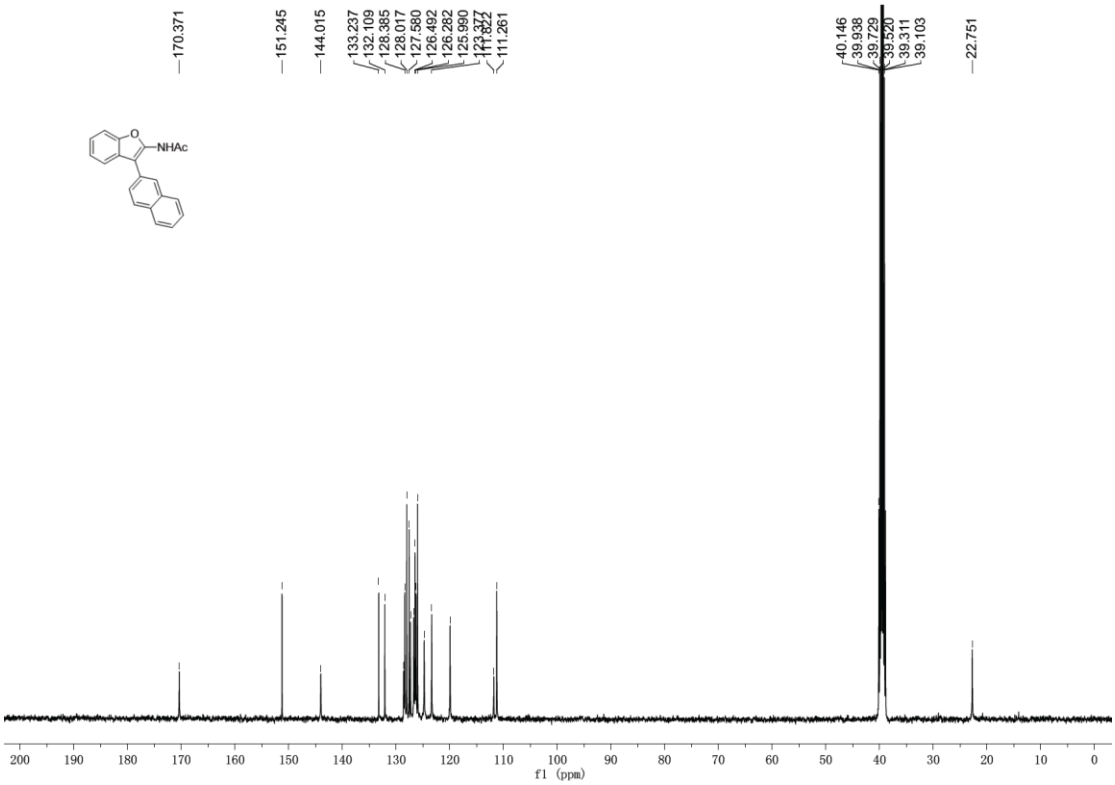
VIII. Copies of ^{1}H and ^{13}C NMR Spectra

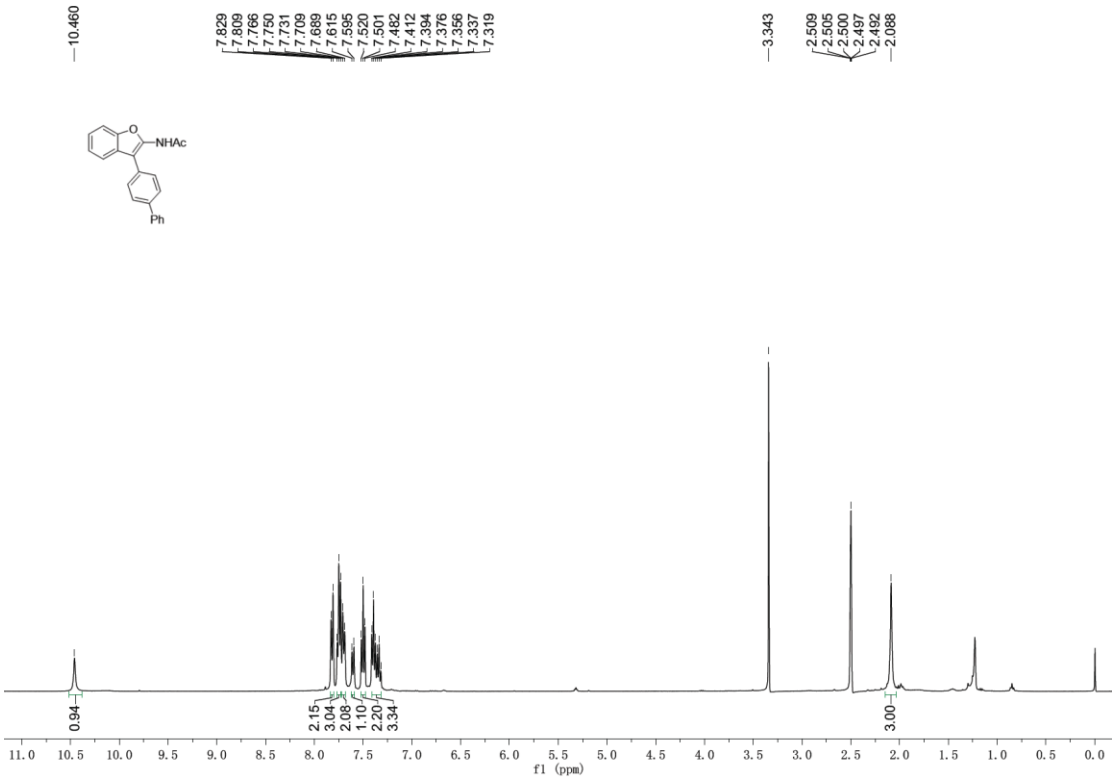
3aa-^{1}H NMR (400 Hz, DMSO-d_6)



3aa-^{13}C NMR (100 Hz, DMSO-d_6)



3ab-^{1}H NMR (400 Hz, DMSO-d_6)



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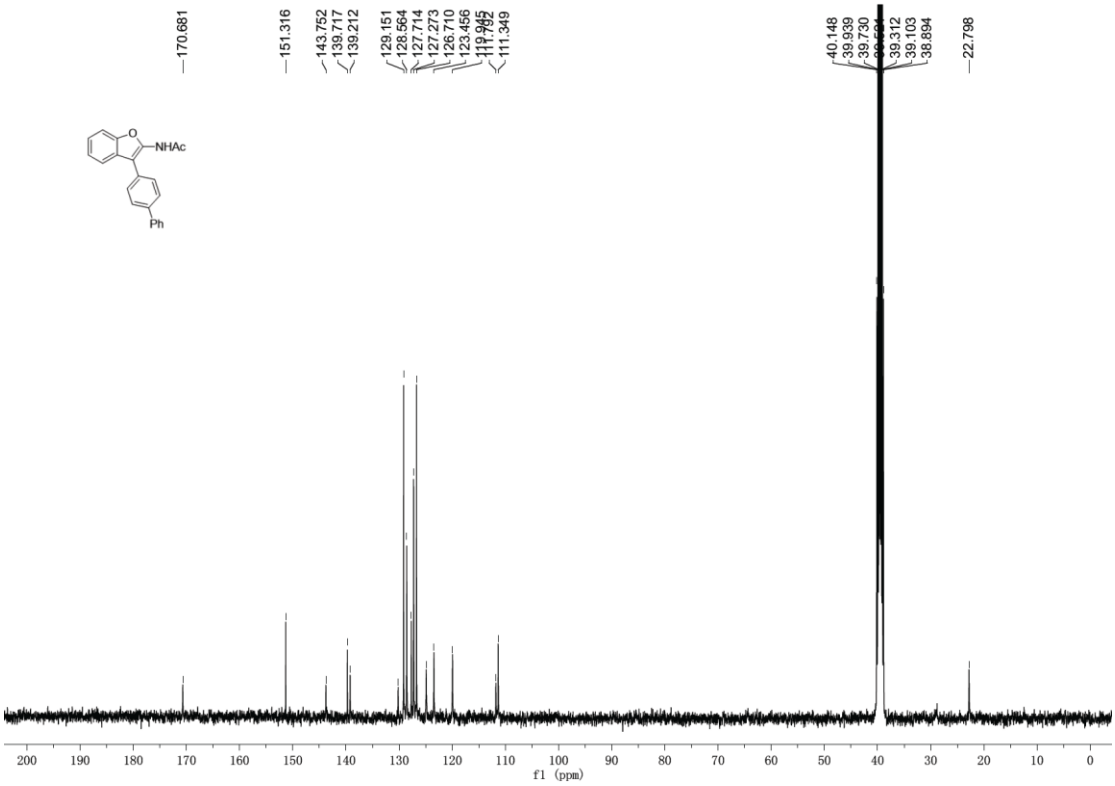
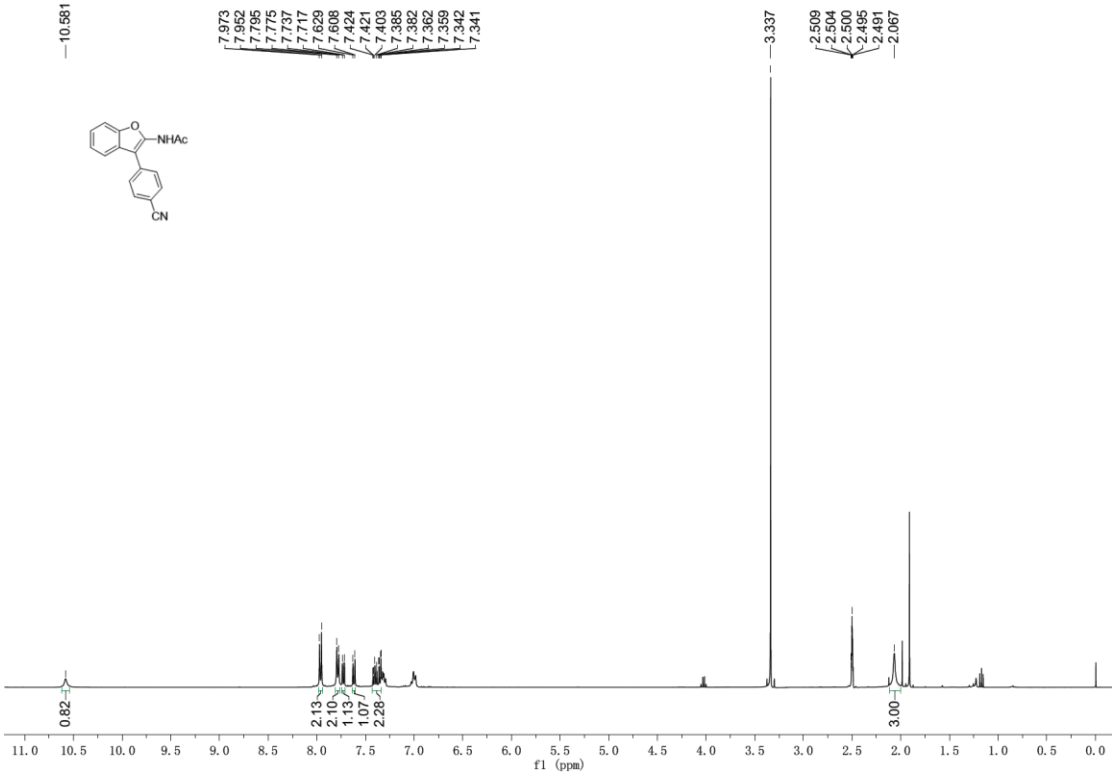


3ac-^{1}H NMR (400 Hz, DMSO-d_6)



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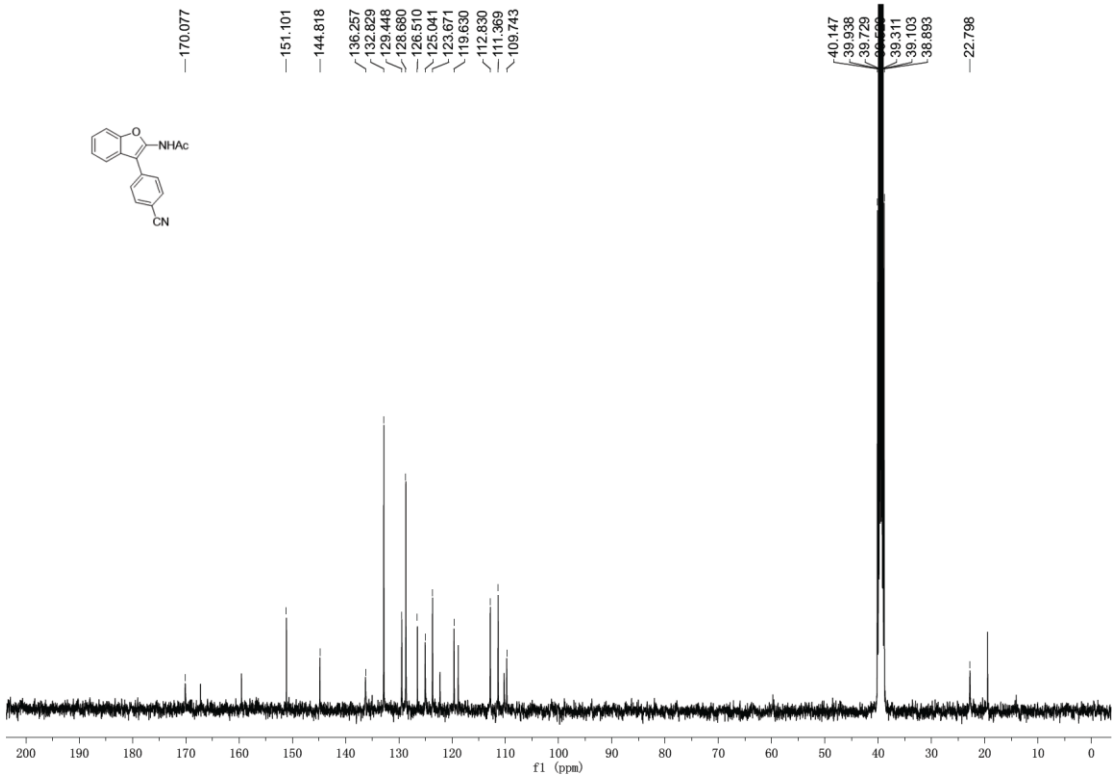

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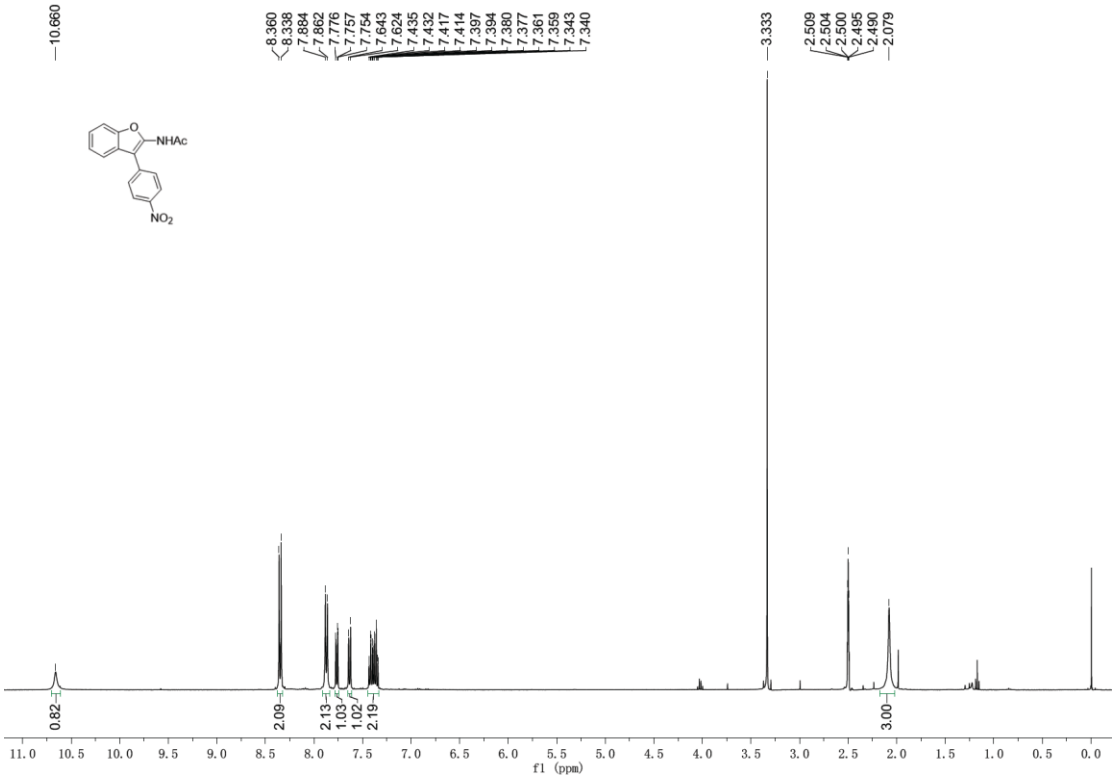

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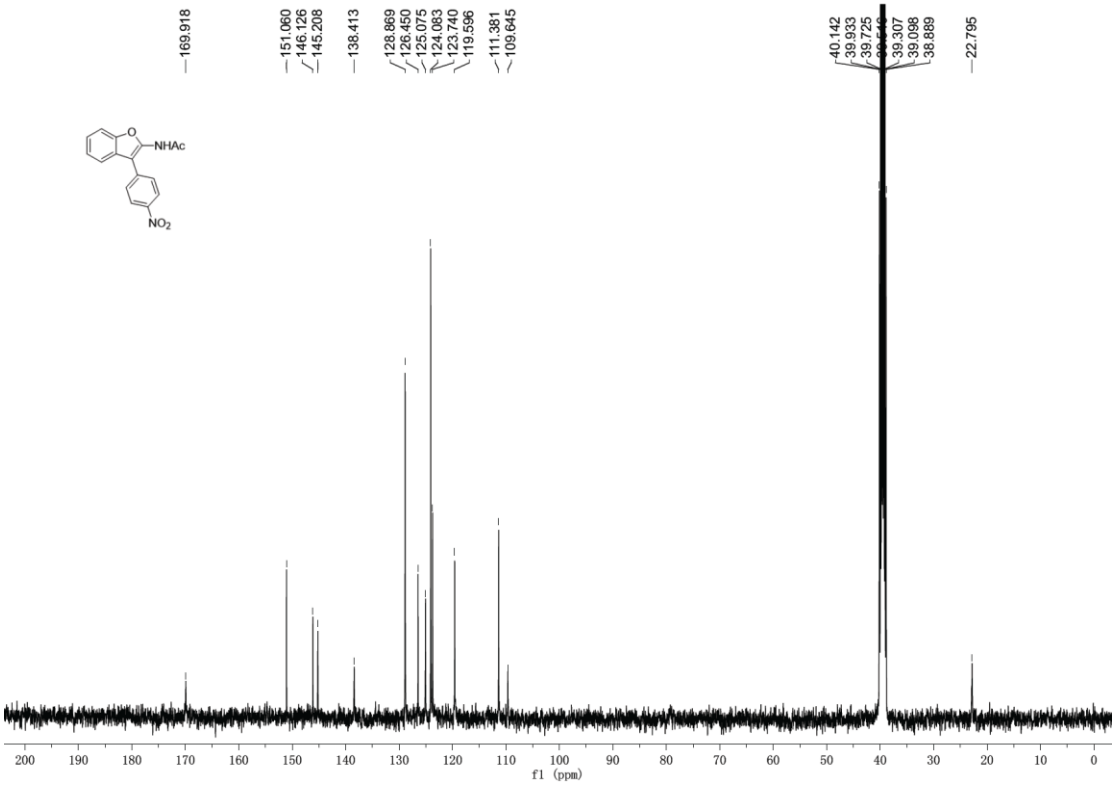
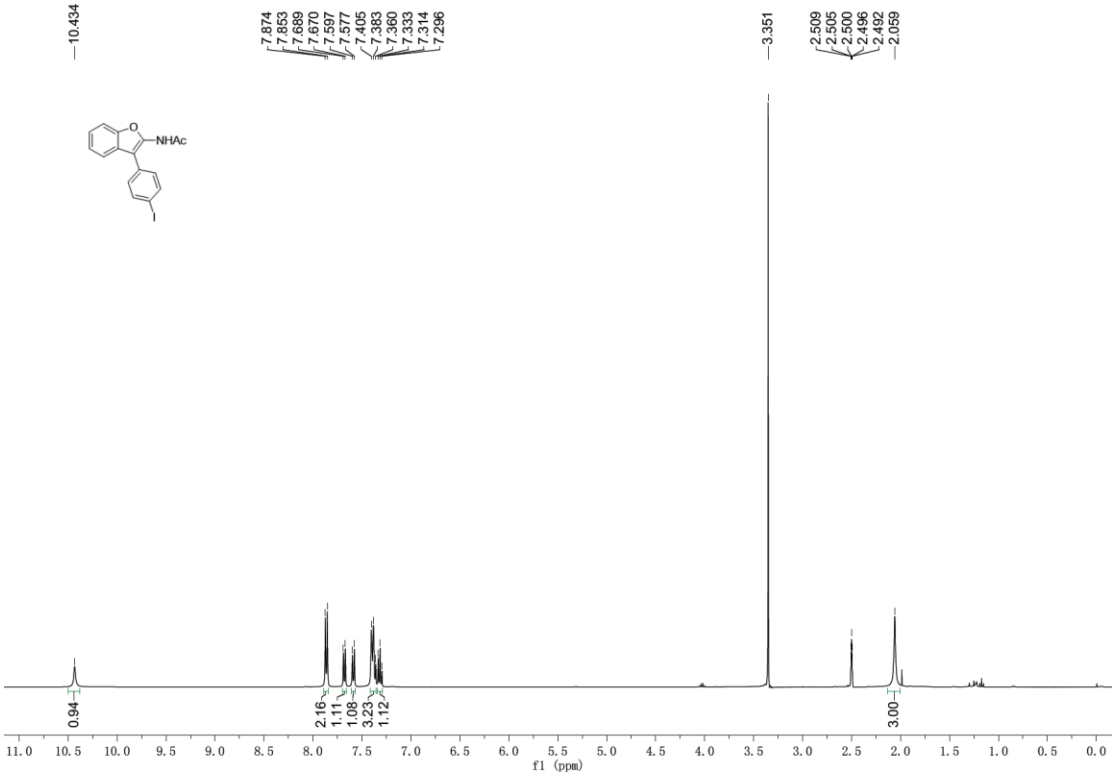


3ae-^{1}H NMR (400 Hz, DMSO-d_6)



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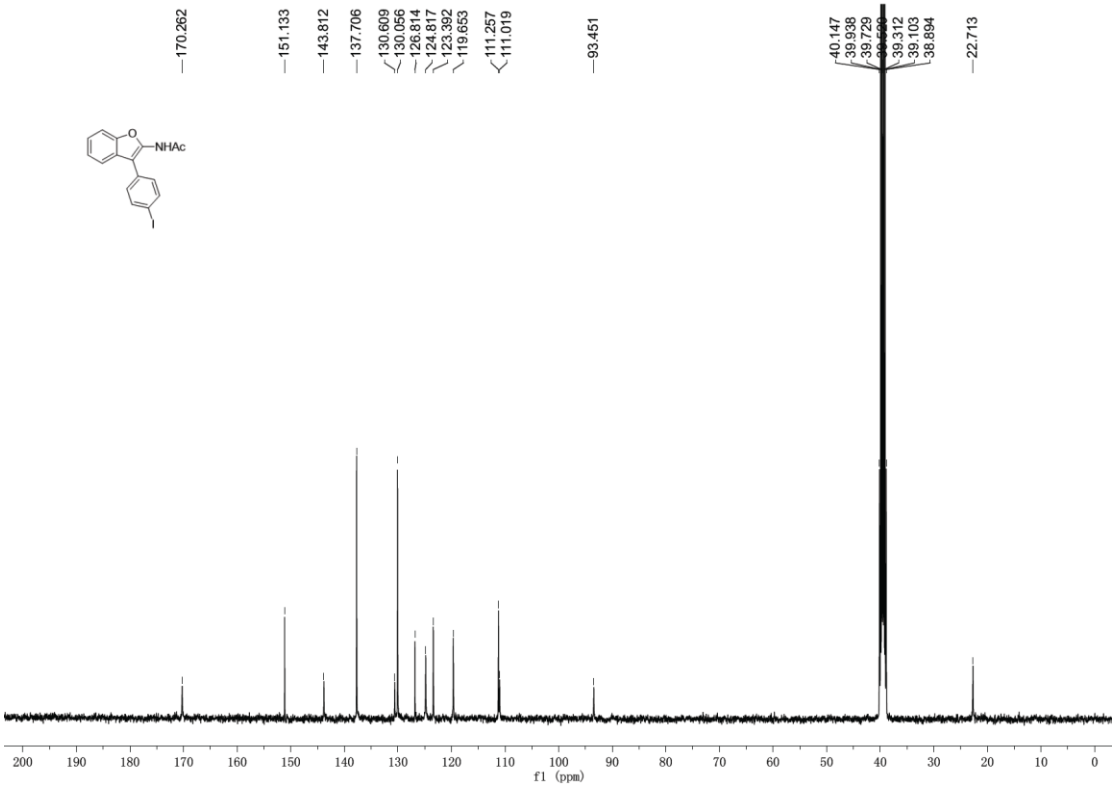
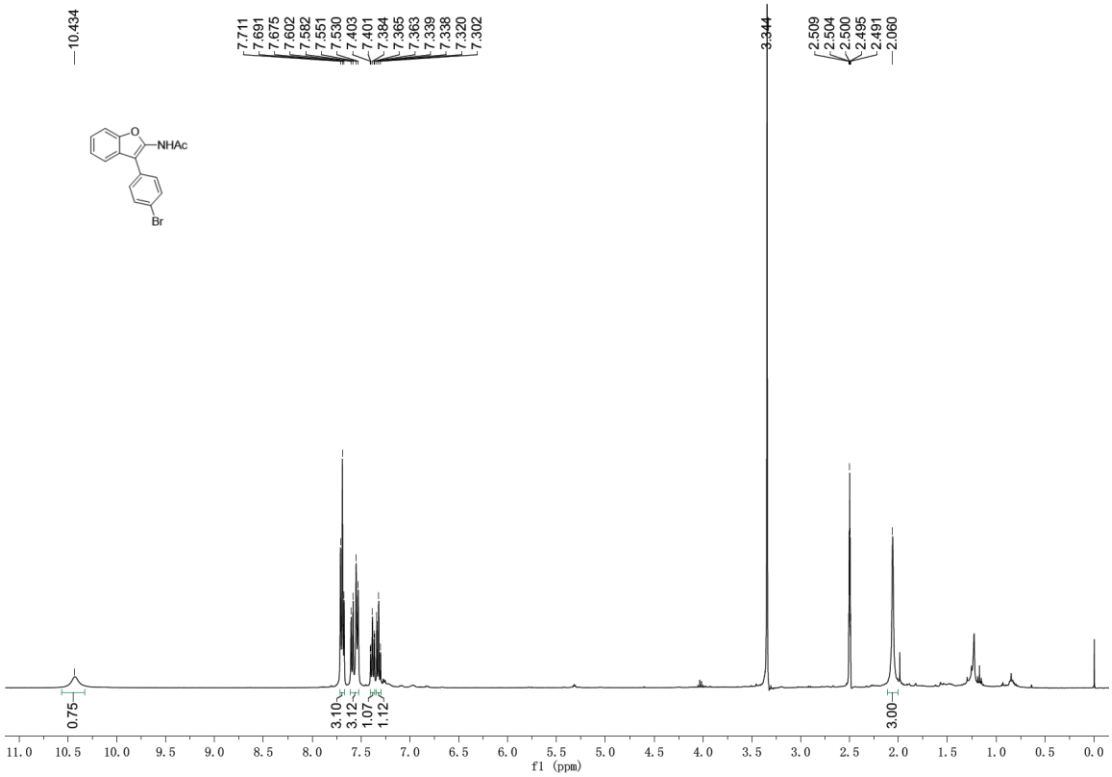
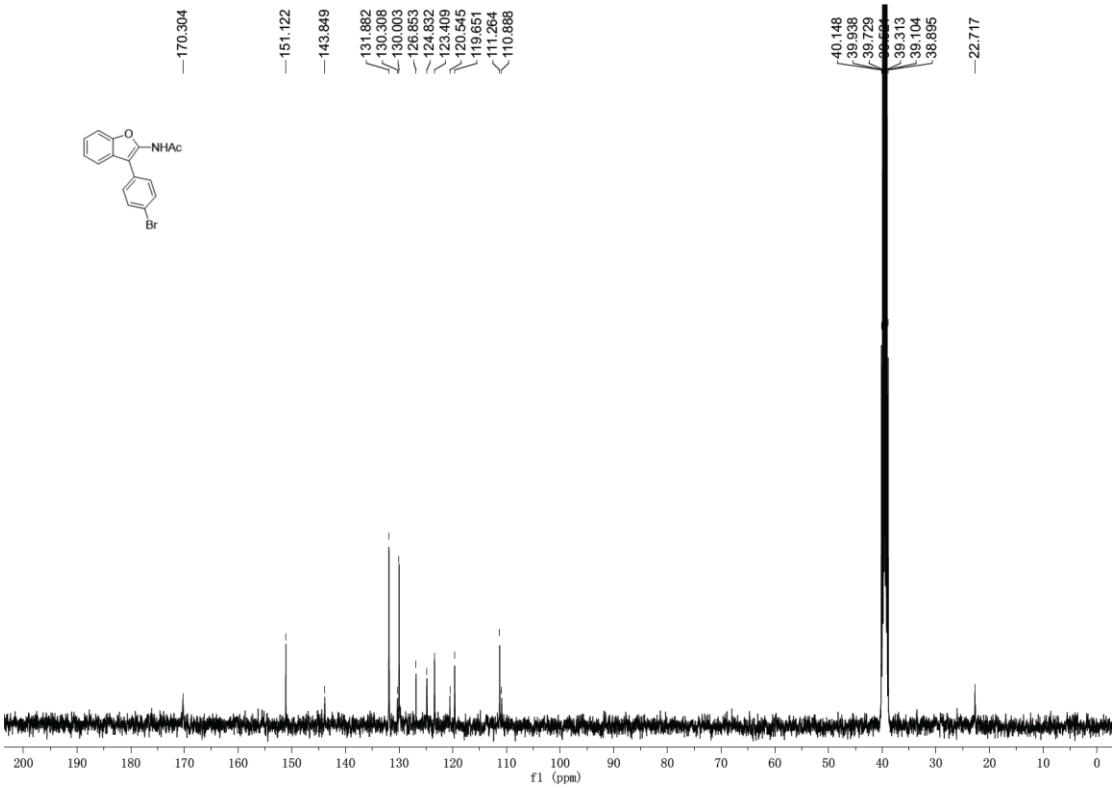


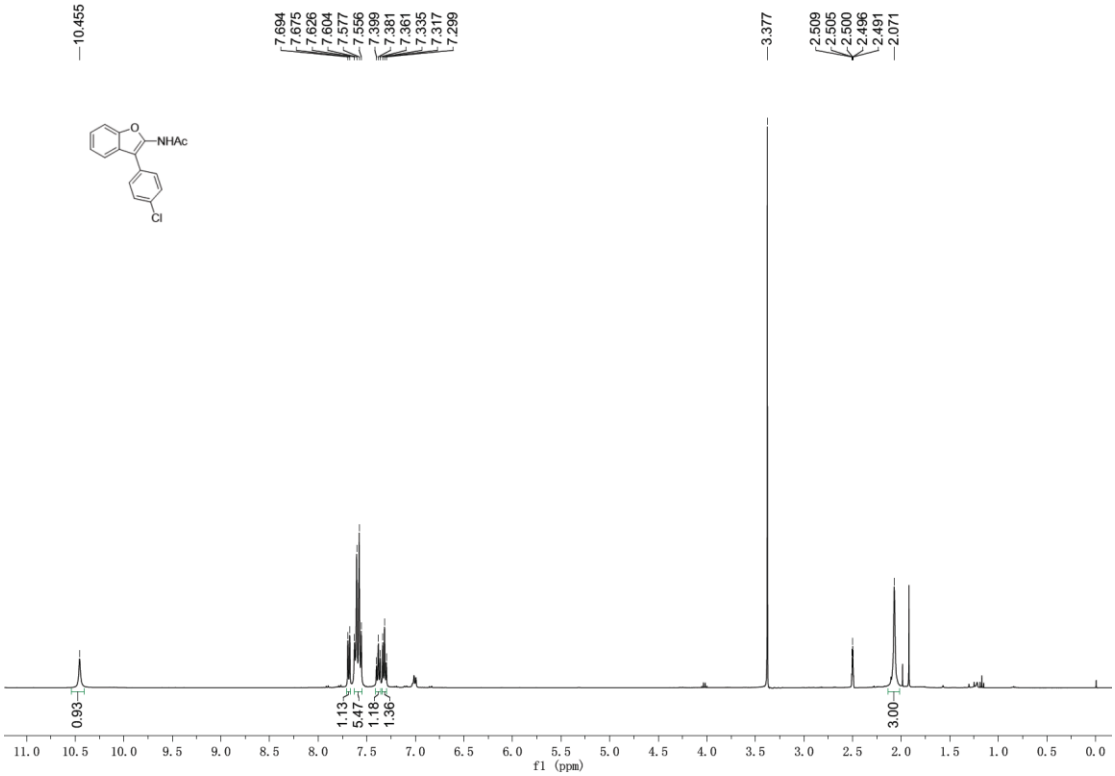
3af-^{1}H NMR (400 Hz, DMSO-d_6)



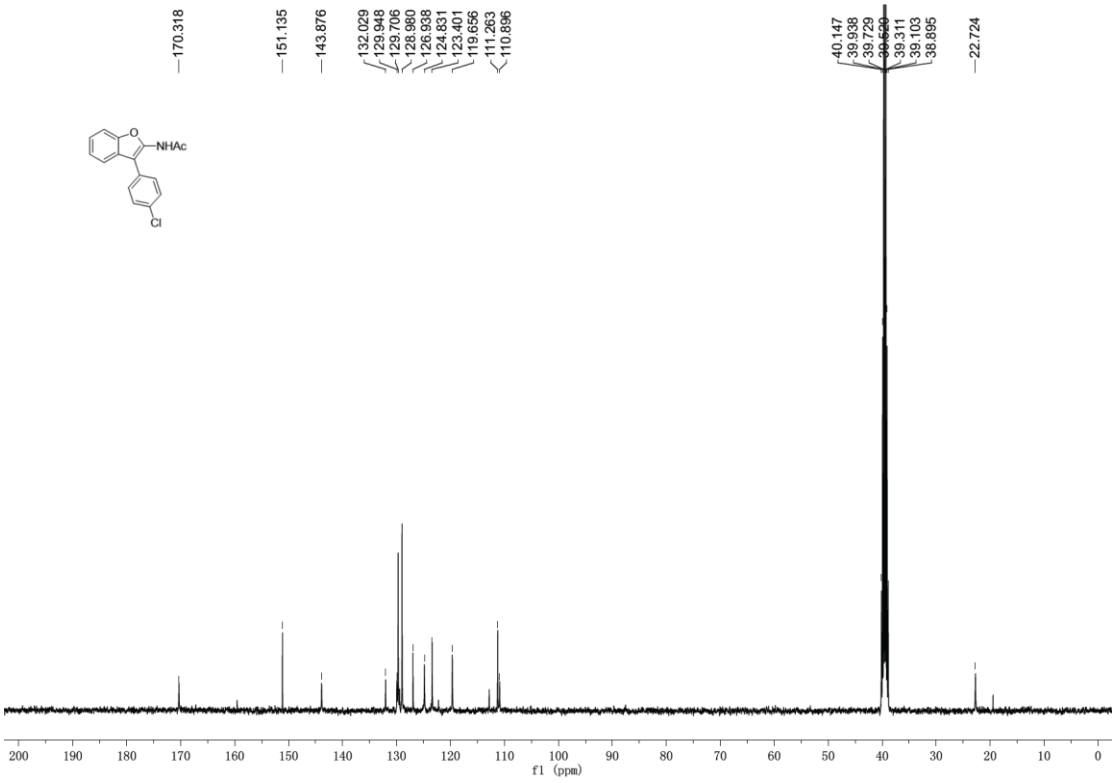
3af-^{13}C NMR (100 Hz, DMSO-d_6)



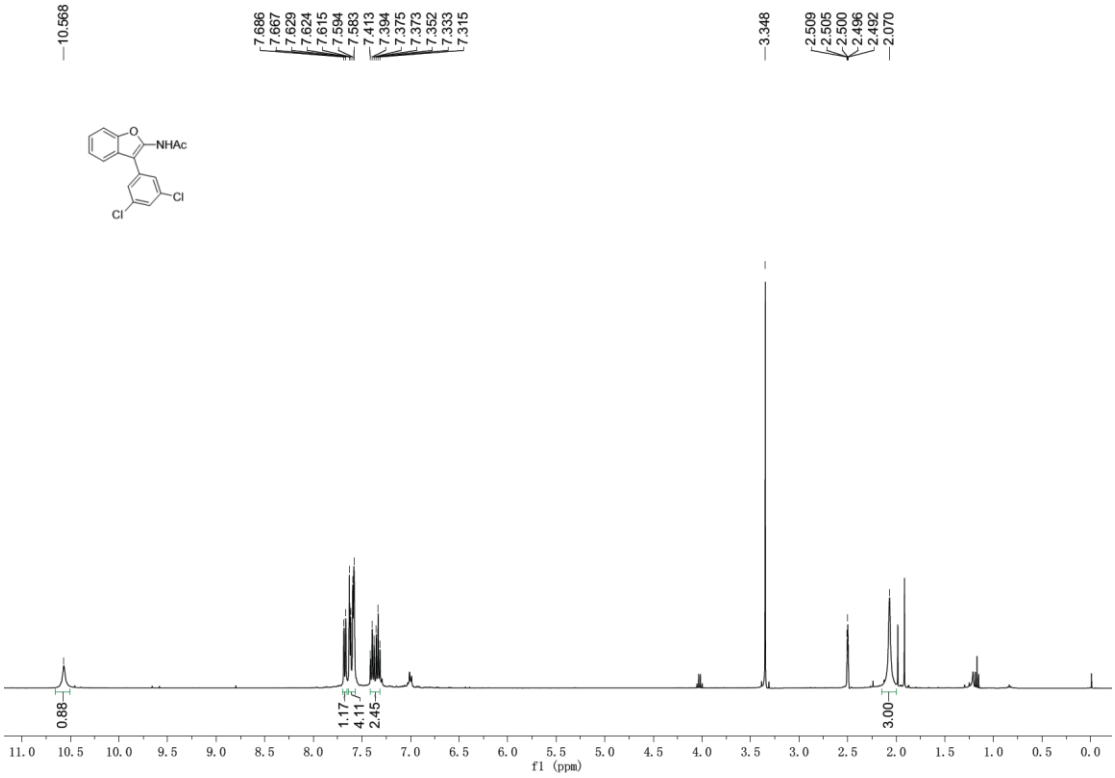
3ag-^{1}H NMR (400 Hz, DMSO-d_6)



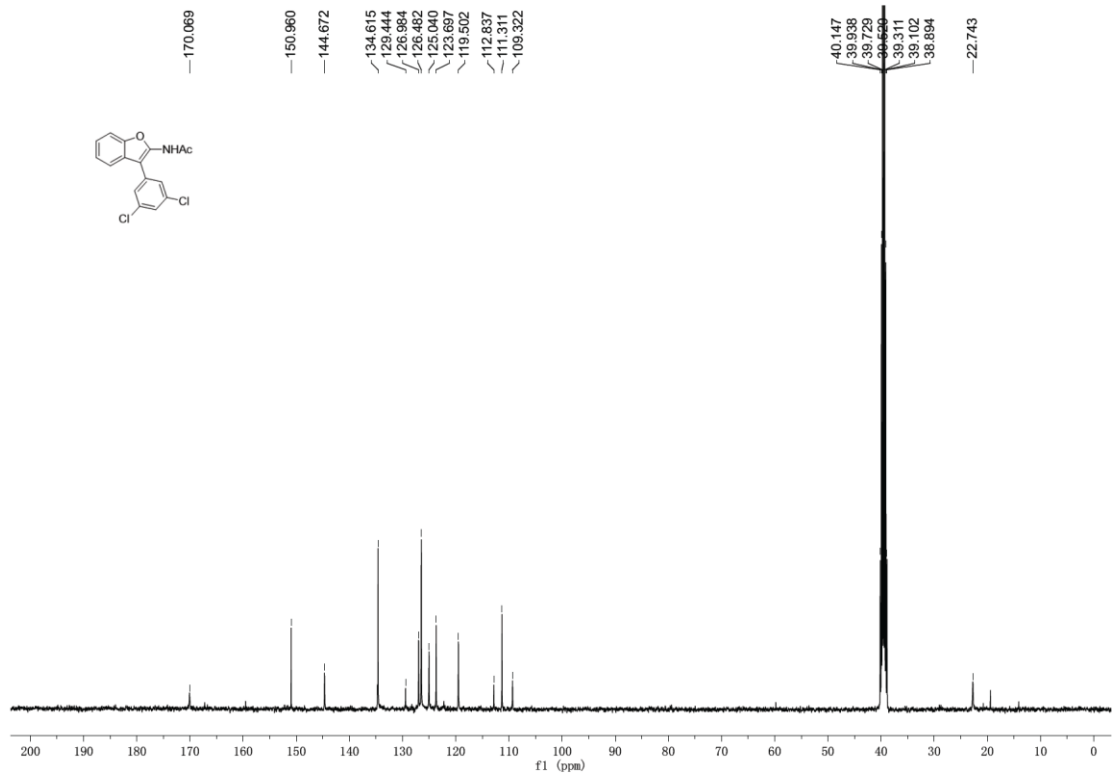
3ag-^{13}C NMR (100 Hz, DMSO-d_6)



3ah-^{1}H NMR (400 Hz, DMSO-d_6)



3ah-^{13}C NMR (100 Hz, DMSO-d_6)



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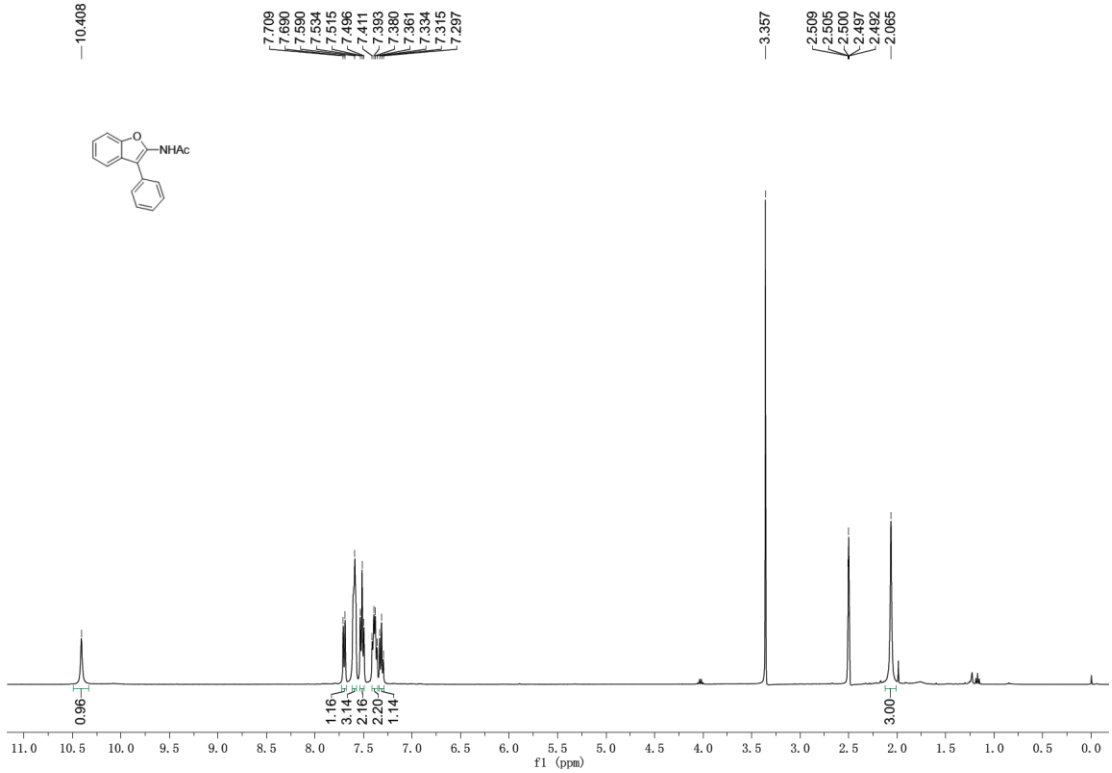
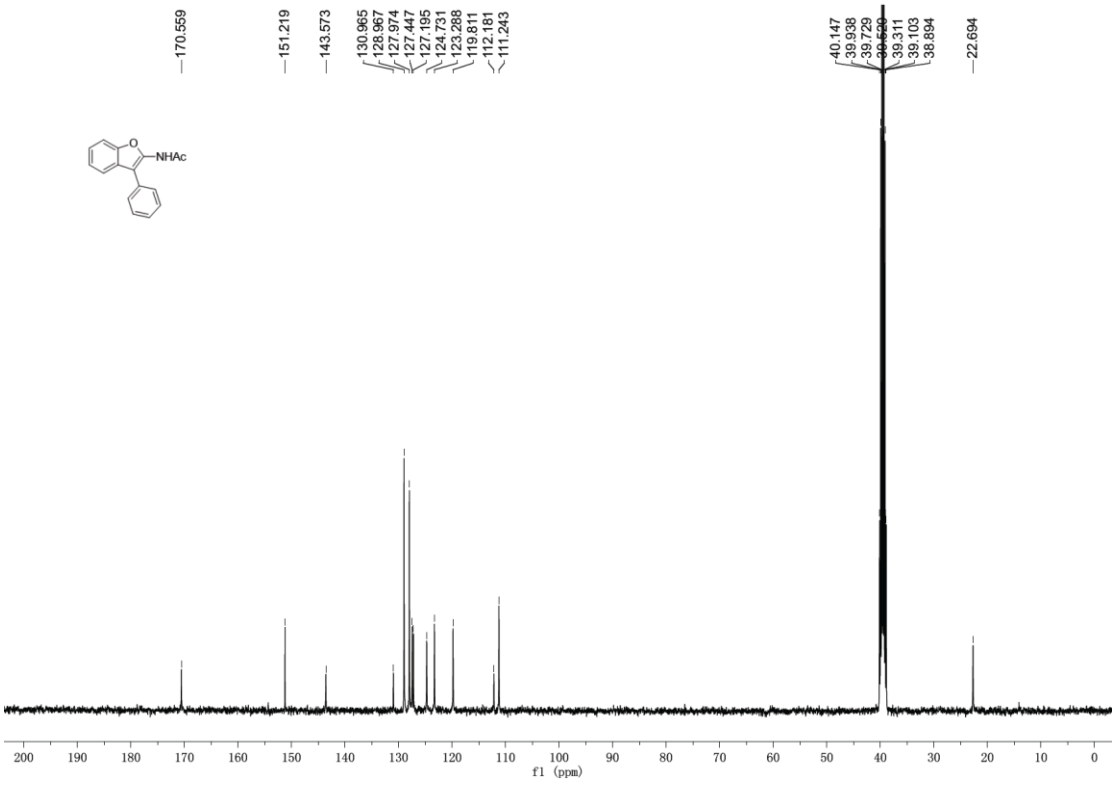
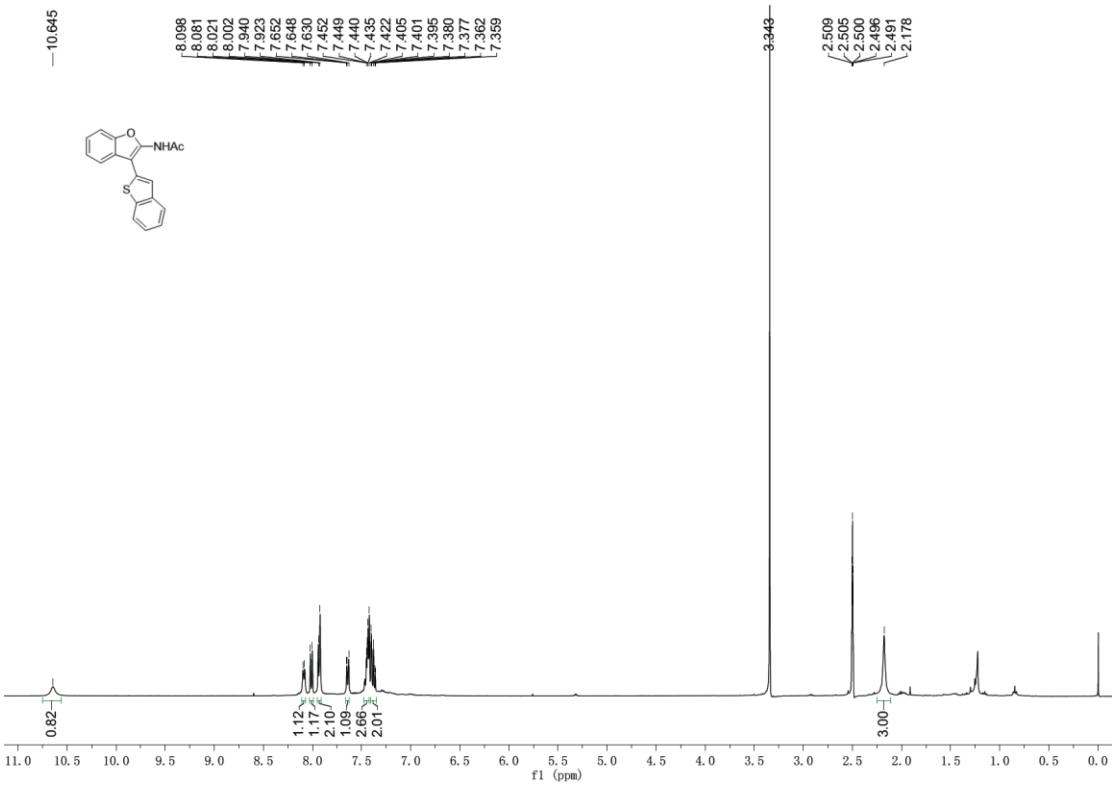


3ai-^{13}C NMR (100 Hz, DMSO-d_6)



3aj-^{1}H NMR (400 Hz, DMSO-d_6)



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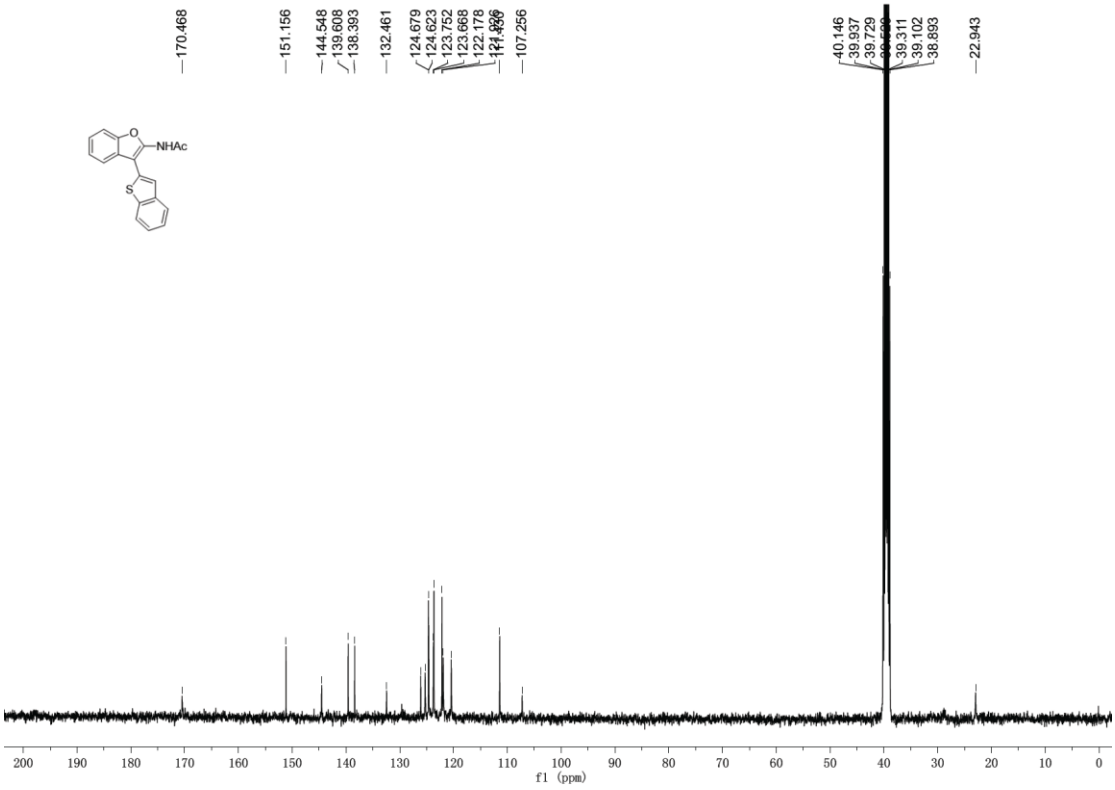
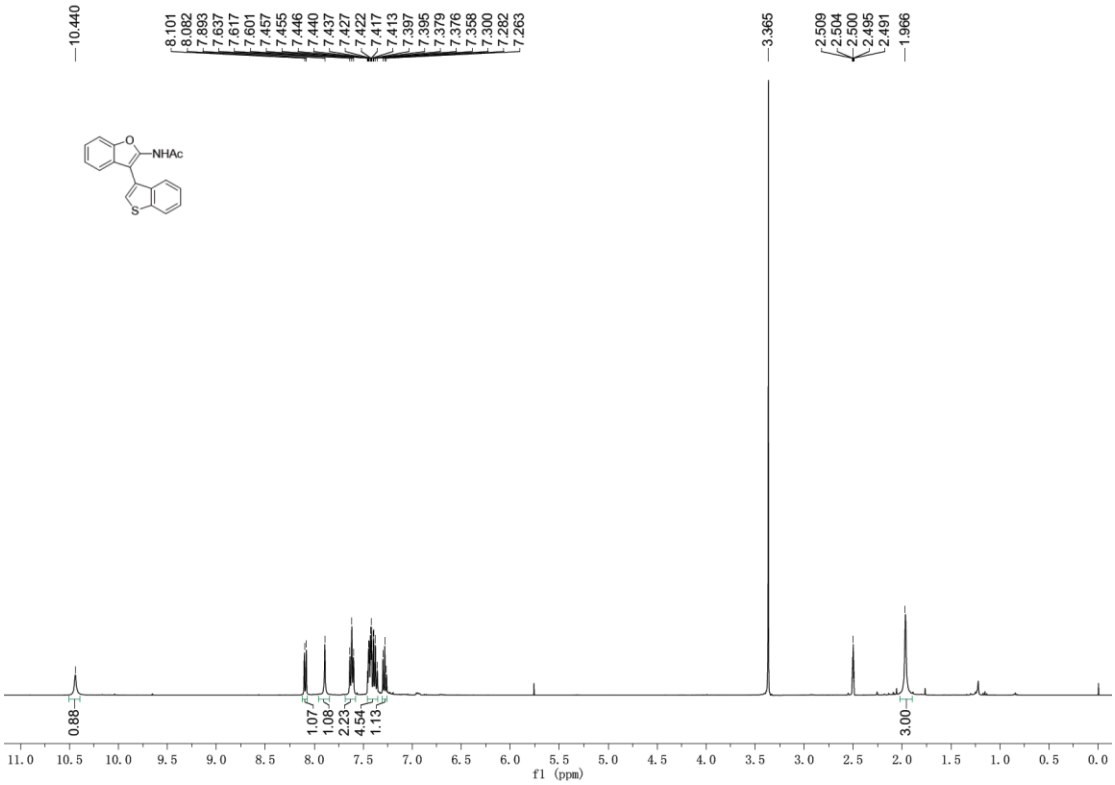
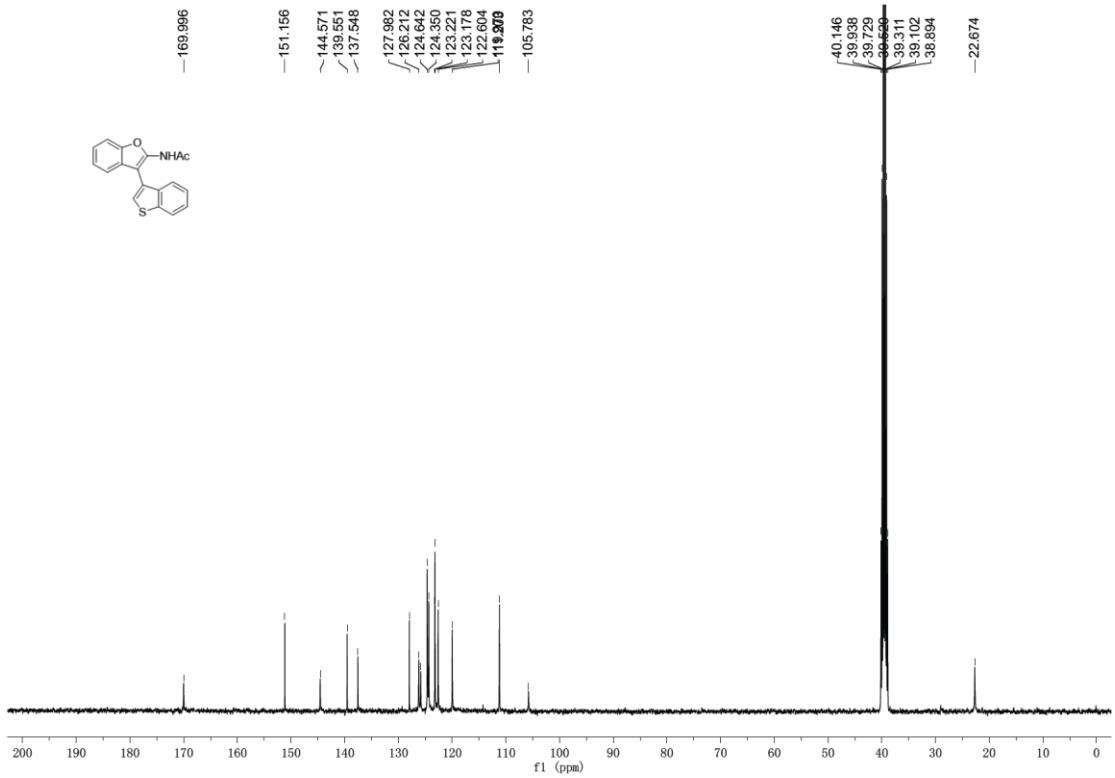


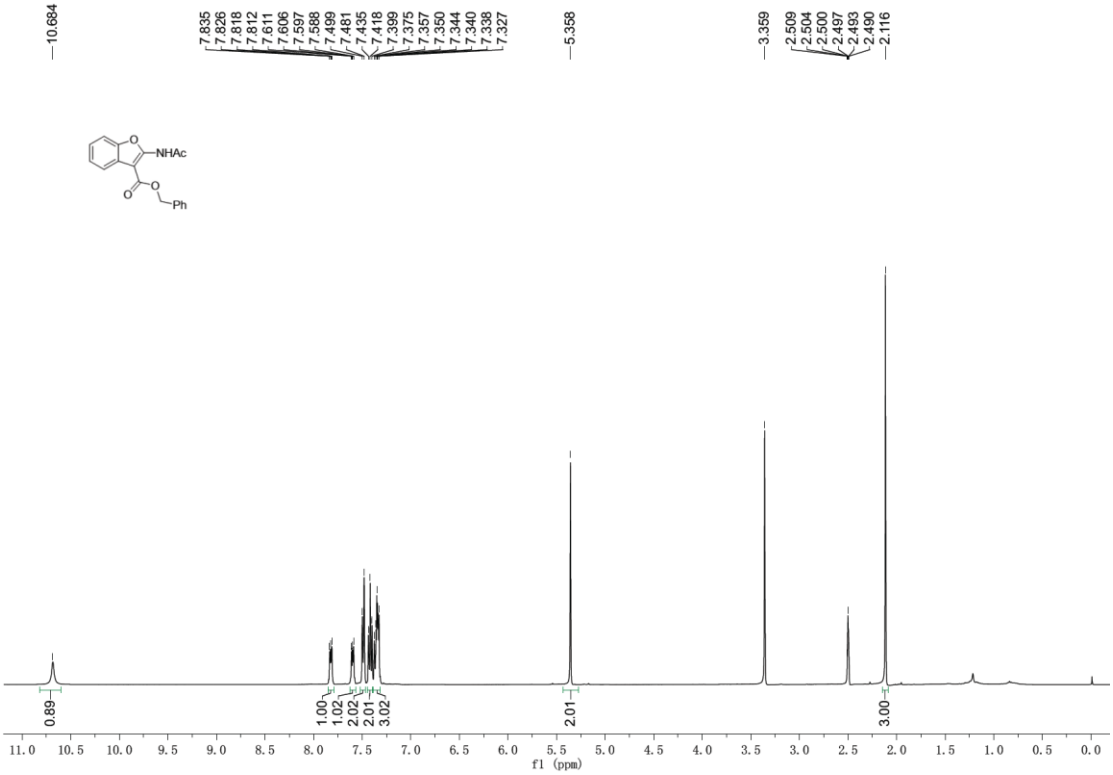
3ak-^{1}H NMR (400 Hz, DMSO-d_6)



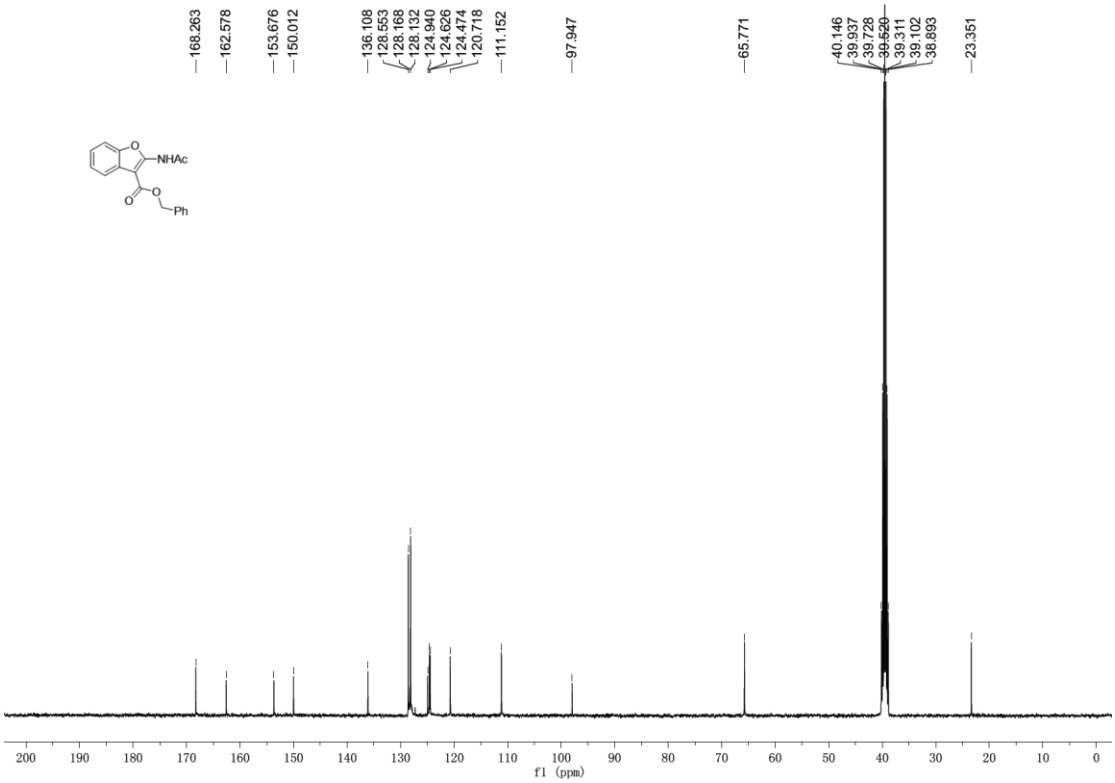
3ak-^{13}C NMR (100 Hz, DMSO-d_6)



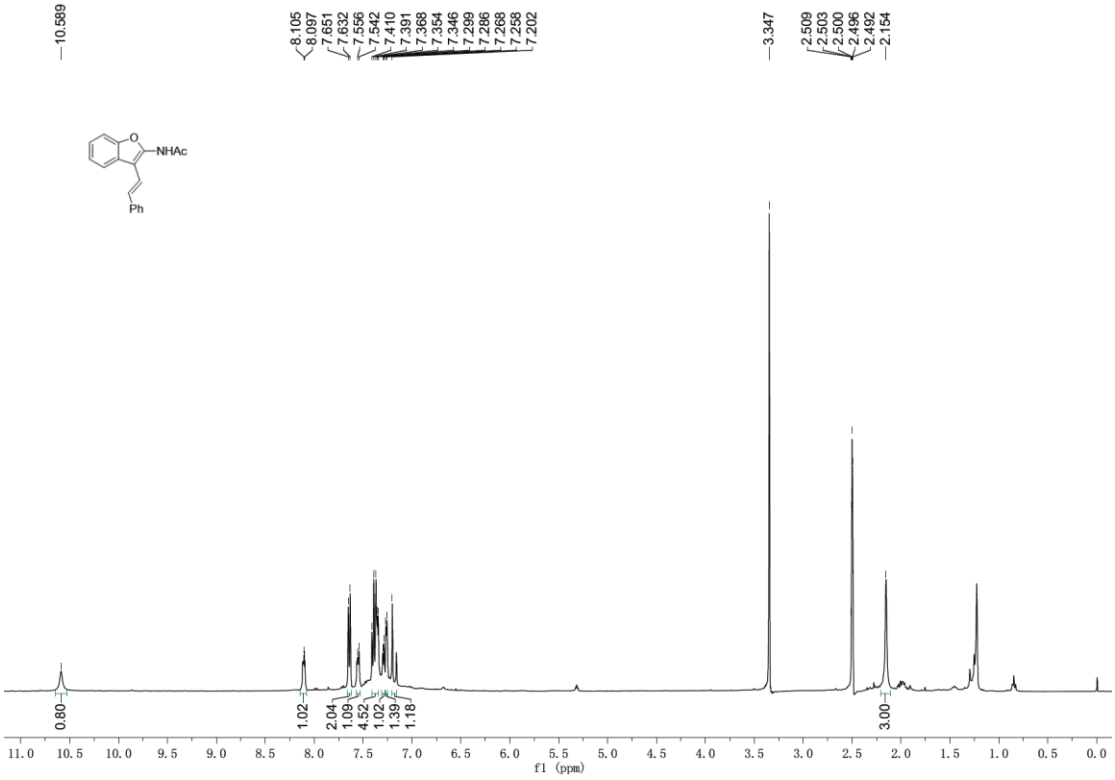
3al-^{1}H NMR (400 Hz, DMSO-d_6)



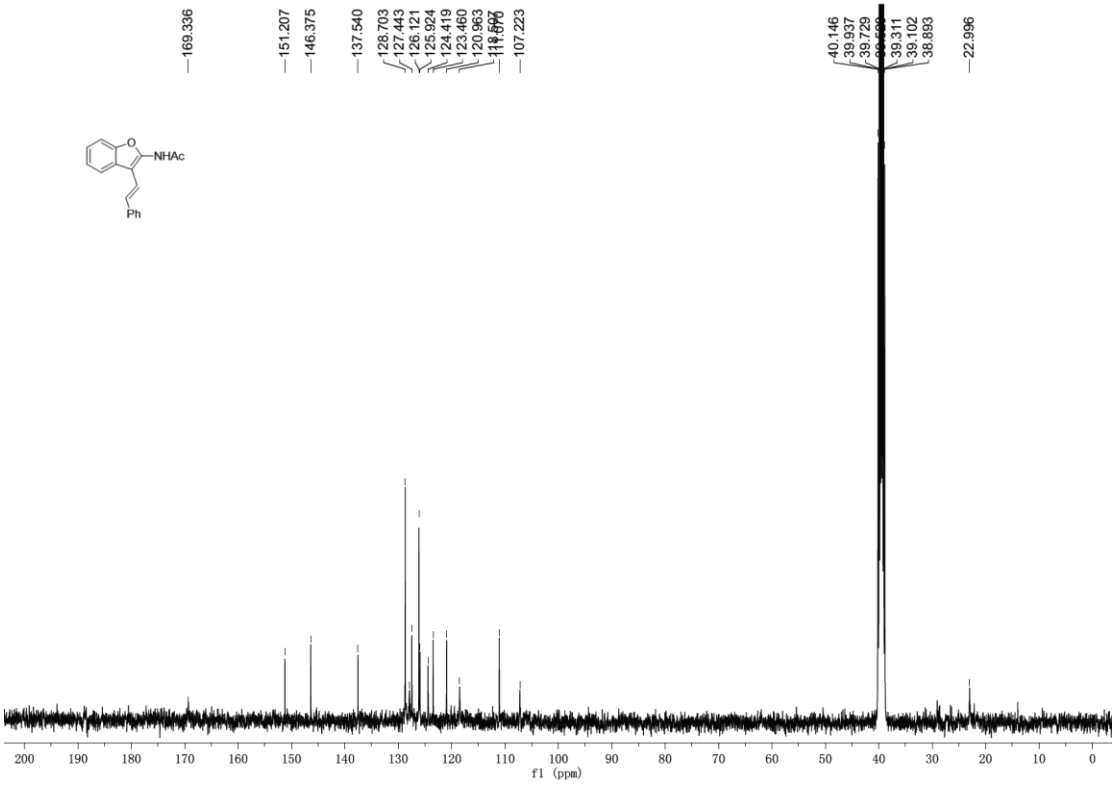
3al-^{13}C NMR (100 Hz, DMSO-d_6)



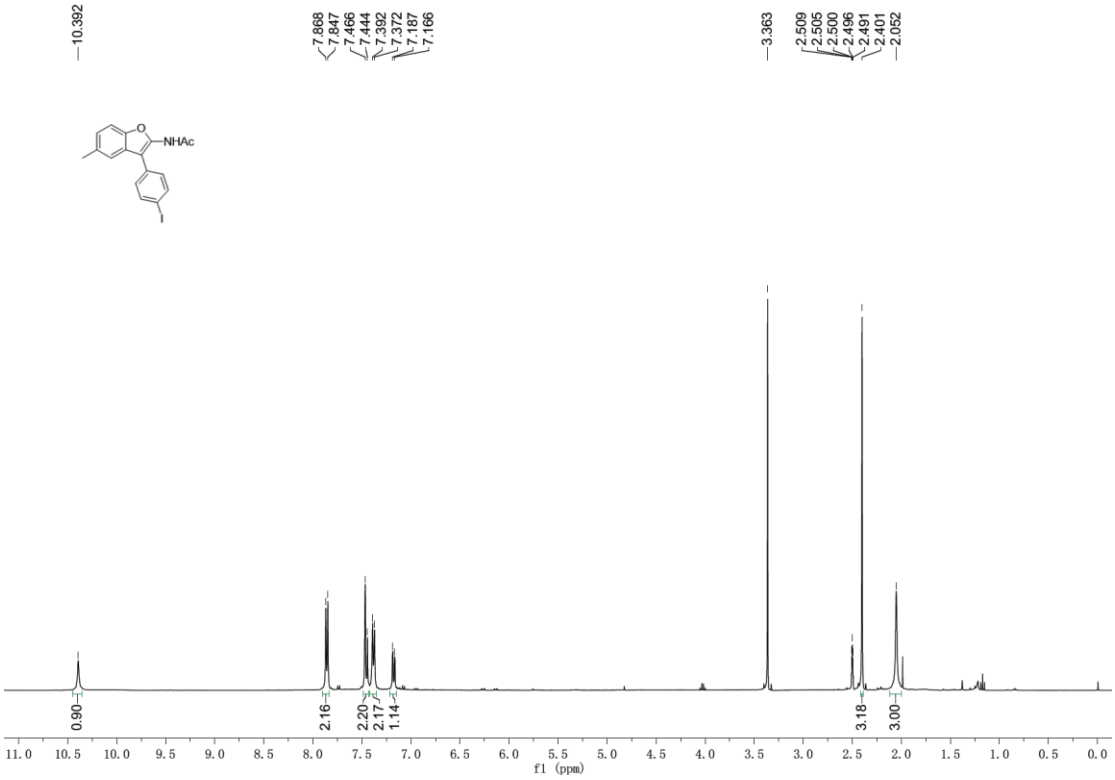
3am-^{1}H NMR (400 Hz, DMSO-d_6)



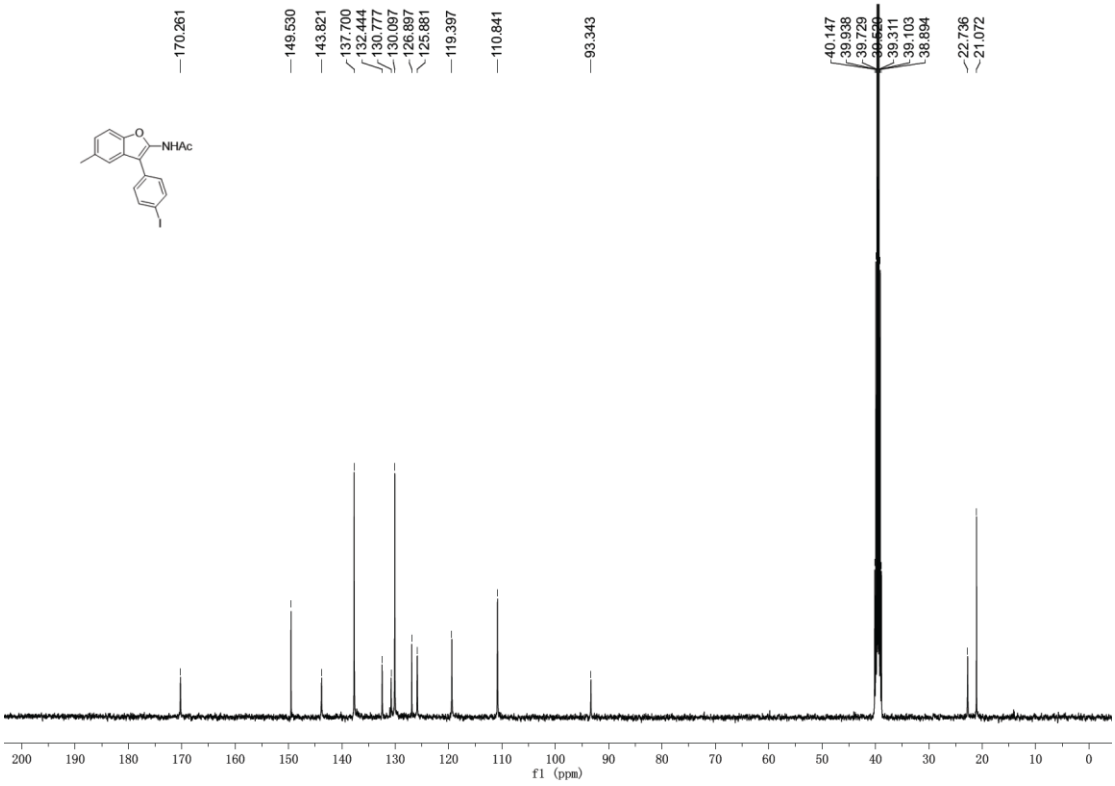
3am-^{13}C NMR (100 Hz, DMSO-d_6)



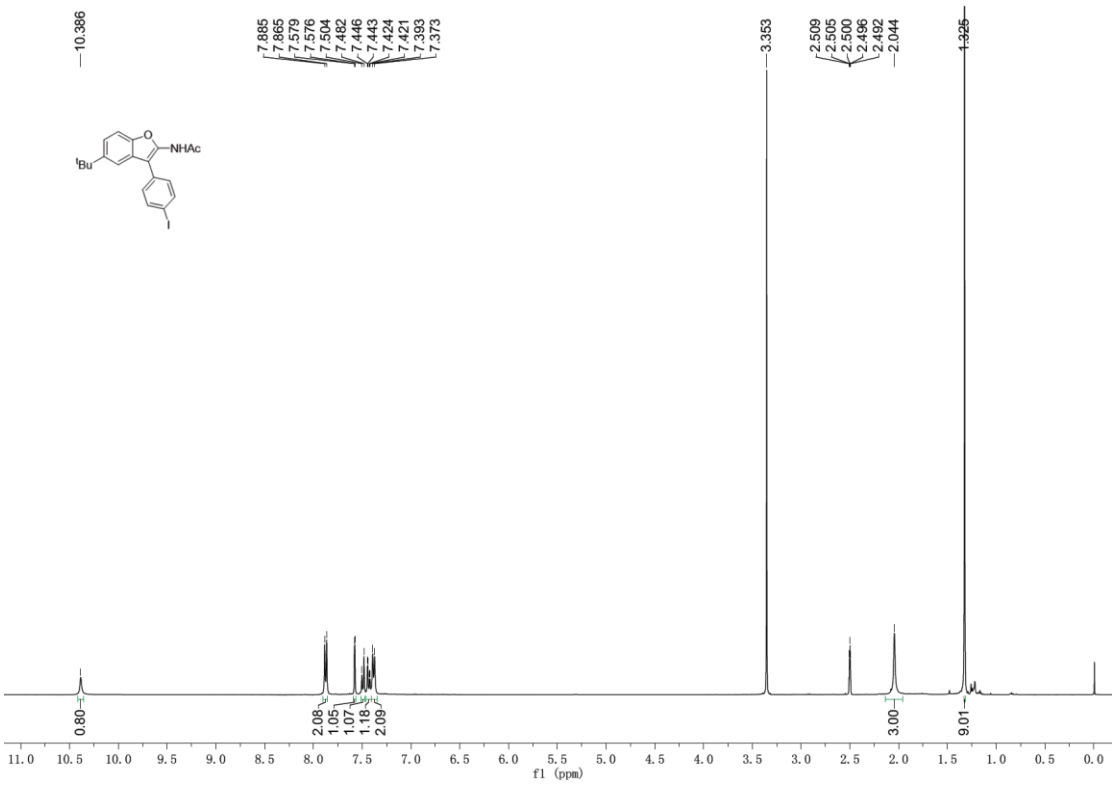
3be-^{1}H NMR (400 Hz, DMSO-d_6)



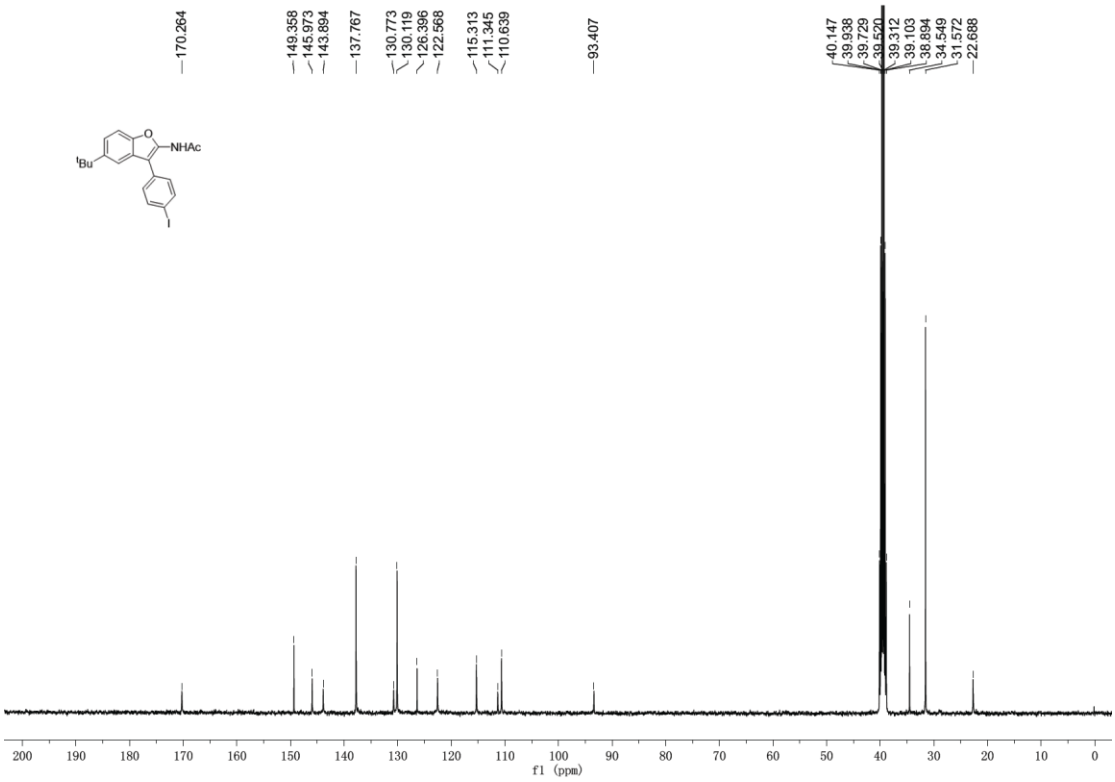
3be-^{13}C NMR (100 Hz, DMSO-d_6)



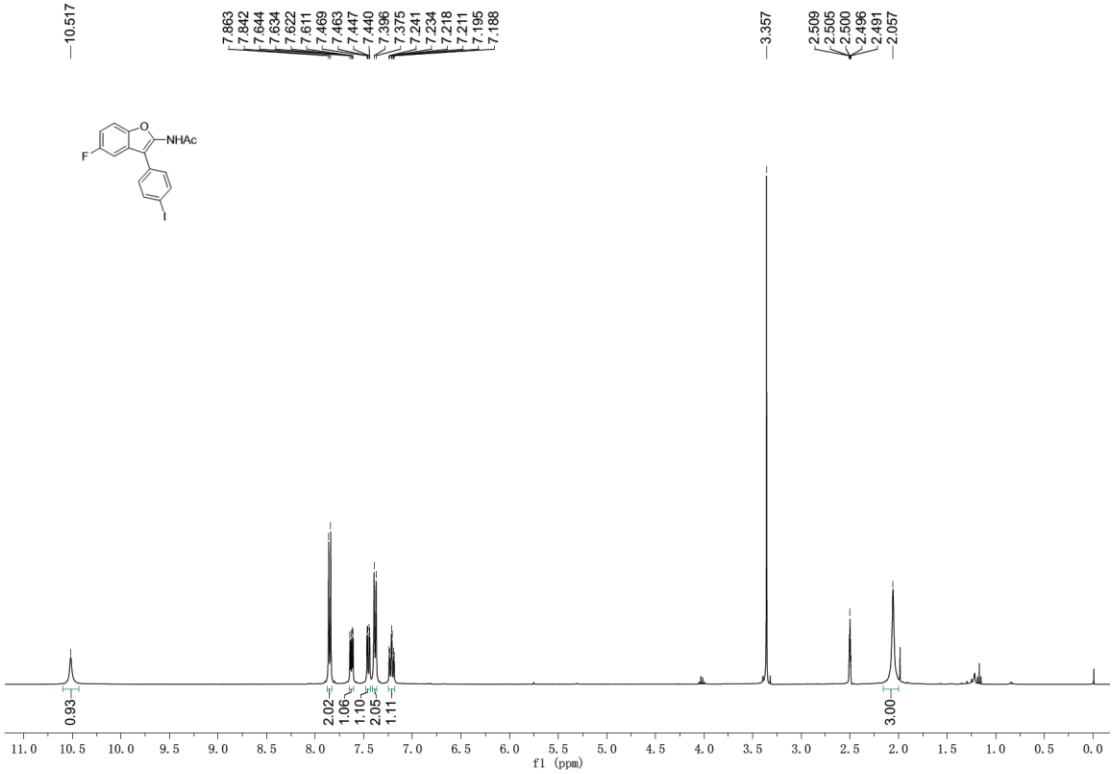
3ce-^{1}H NMR (400 Hz, DMSO-d_6)



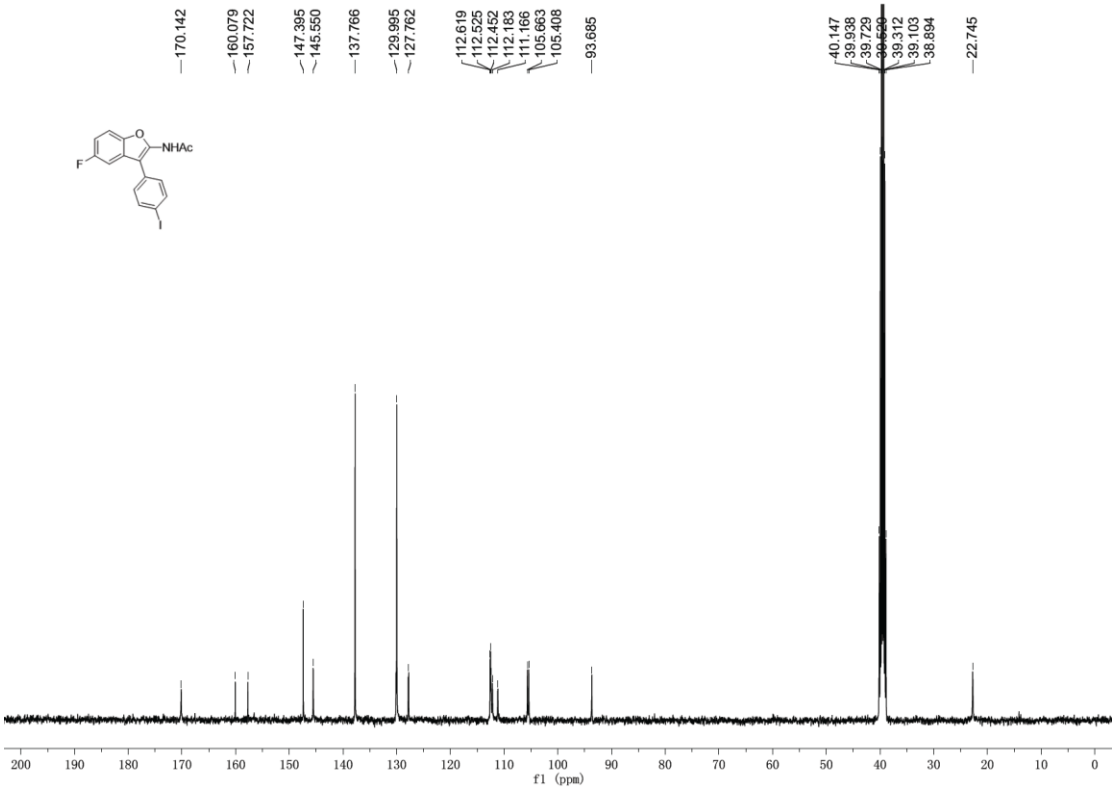
3ce-^{13}C NMR (100 Hz, DMSO-d_6)



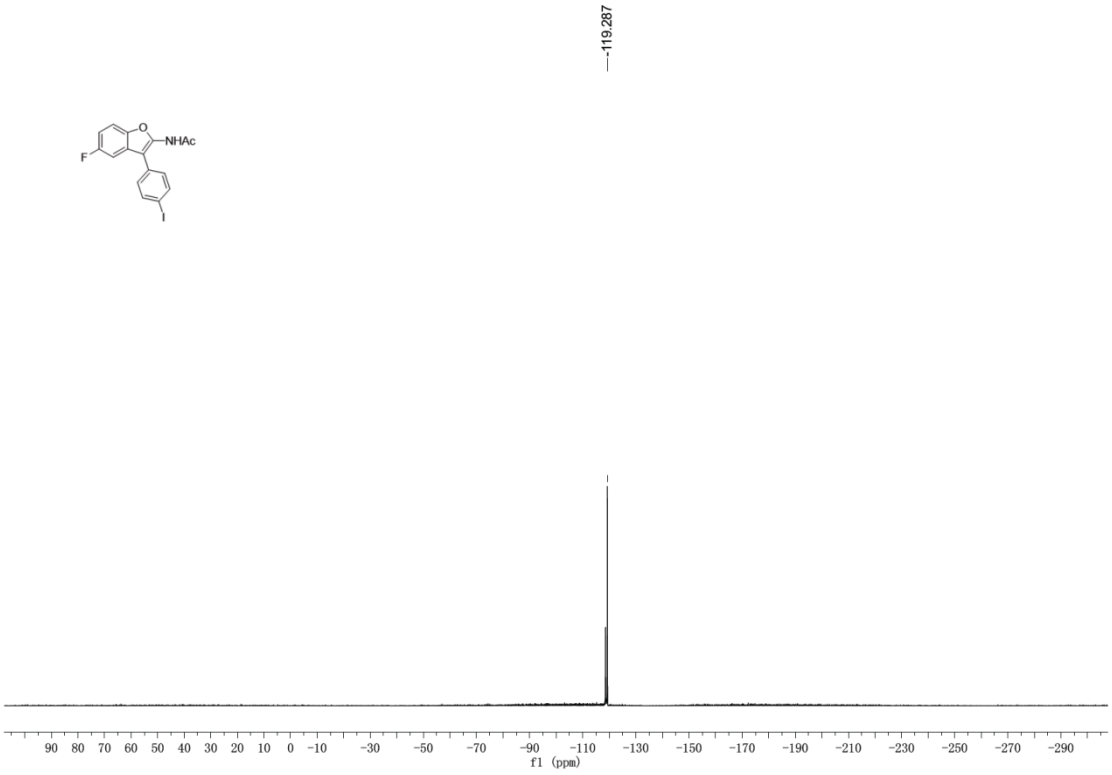
3de-^{1}H NMR (400 Hz, DMSO-d_6)



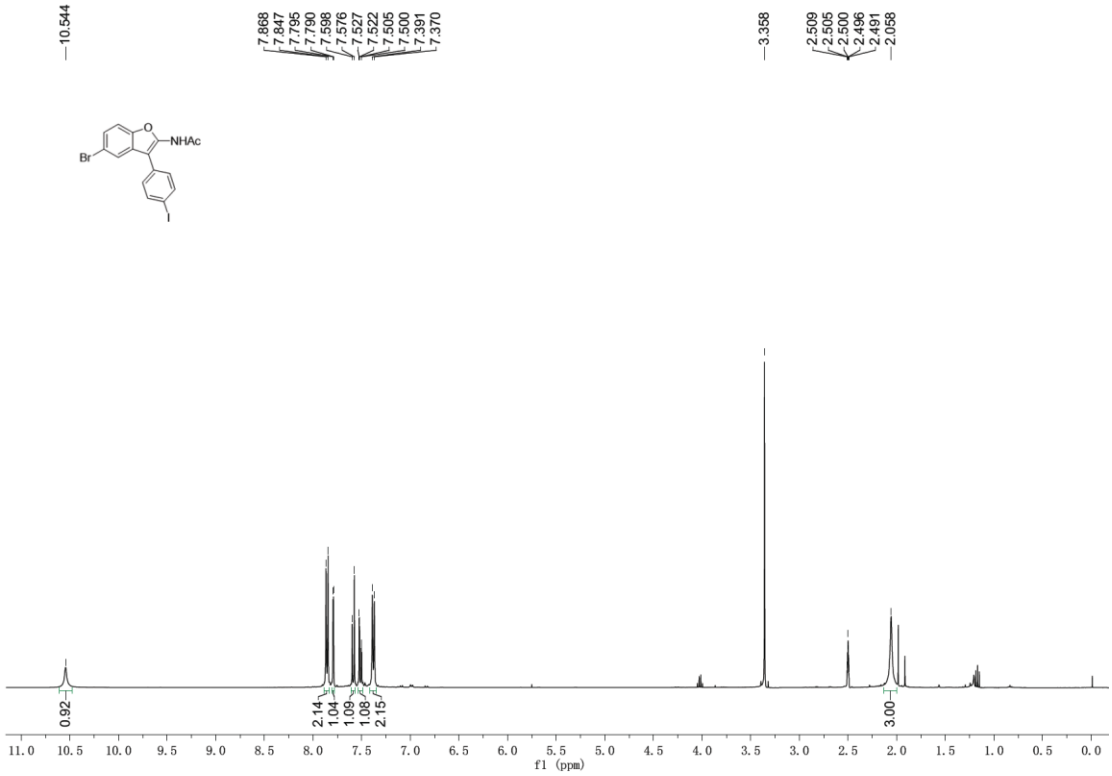
3de-^{13}C NMR (100 Hz, DMSO-d_6)



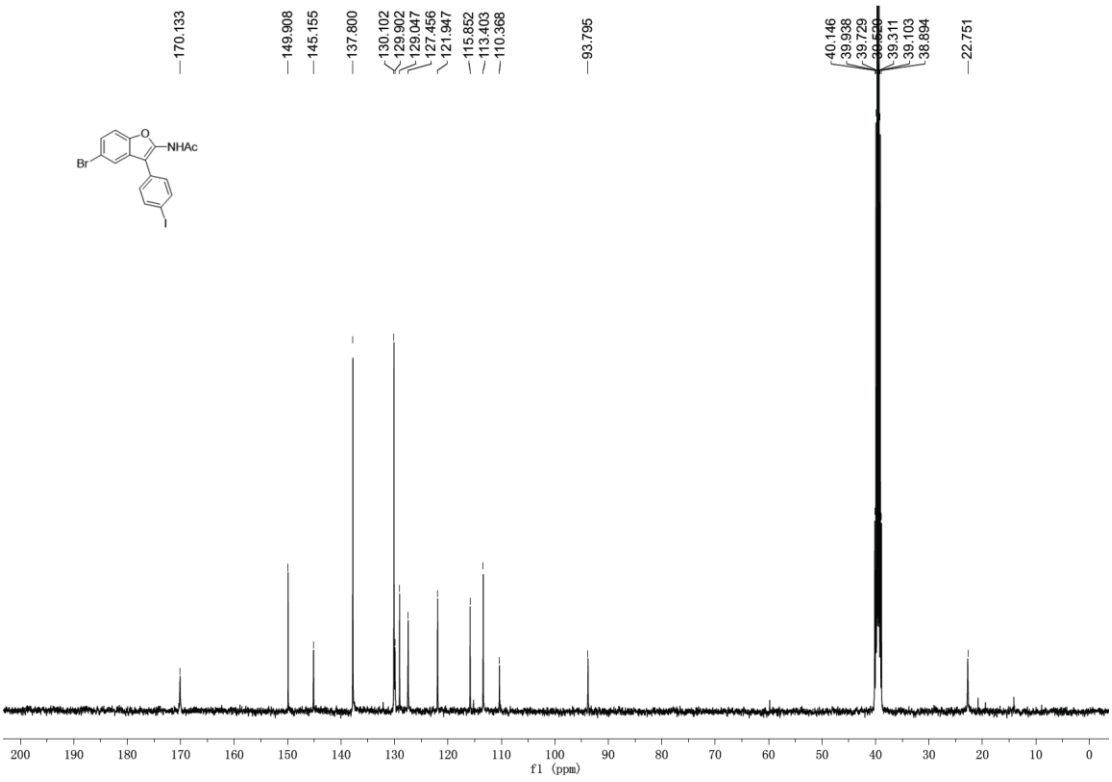
3de-^{19}F NMR (376 Hz, $CDCl_3$)



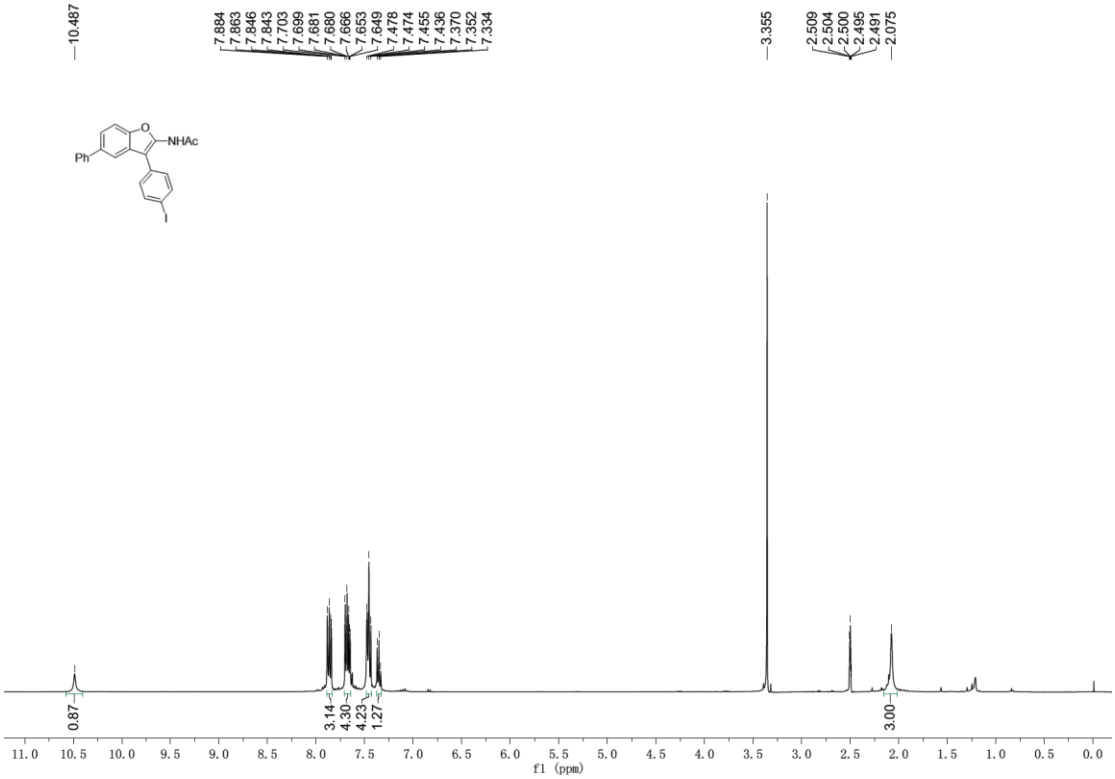
3ee-^{1}H NMR (400 Hz, DMSO-d_6)



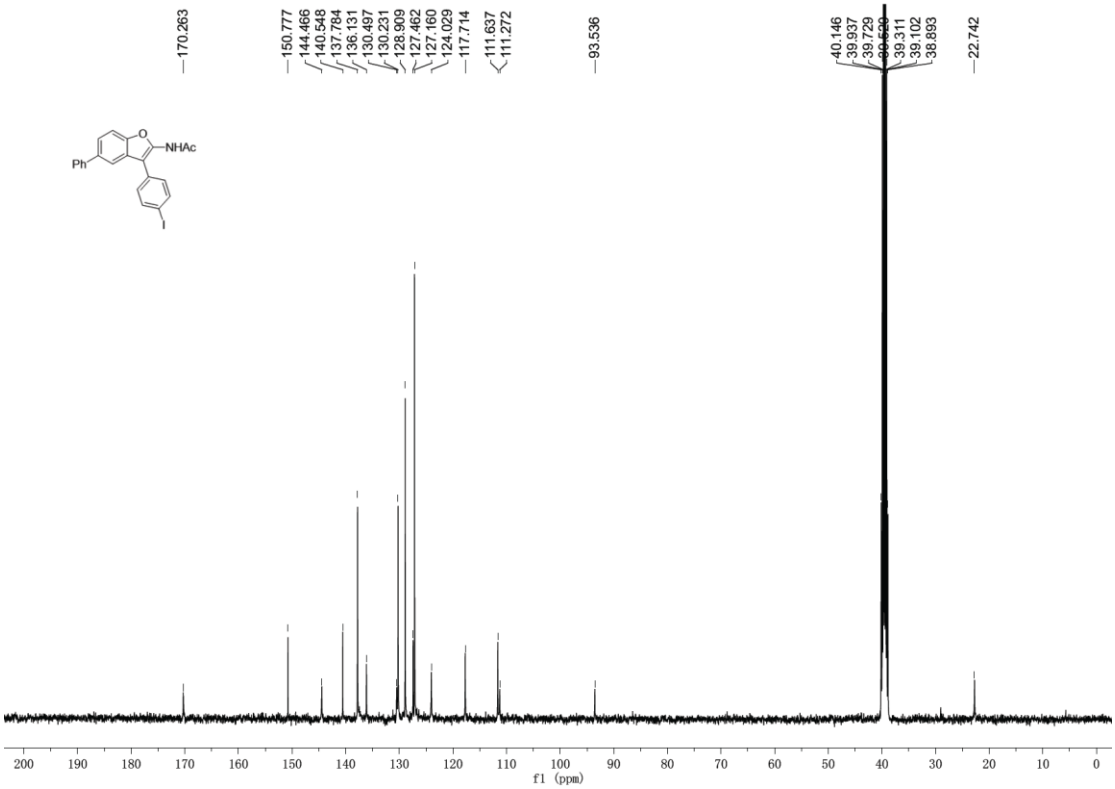
3ee-^{13}C NMR (100 Hz, DMSO-d_6)



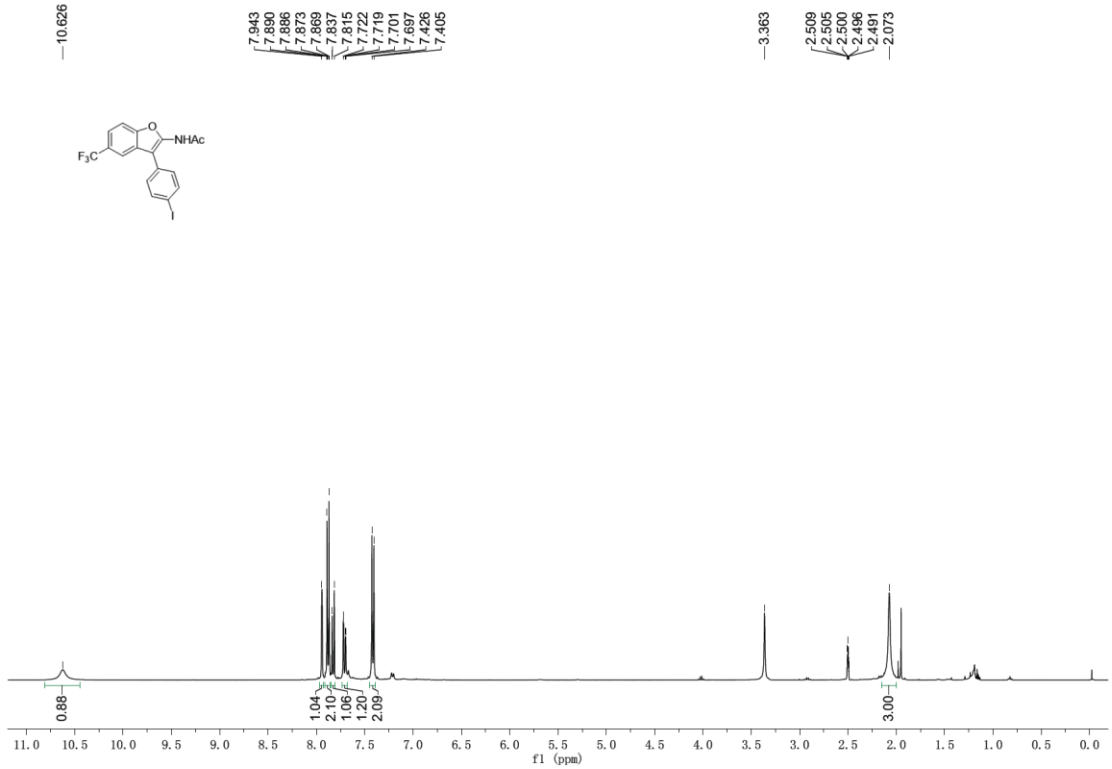
3fe-^{1}H NMR (400 Hz, DMSO-d_6)



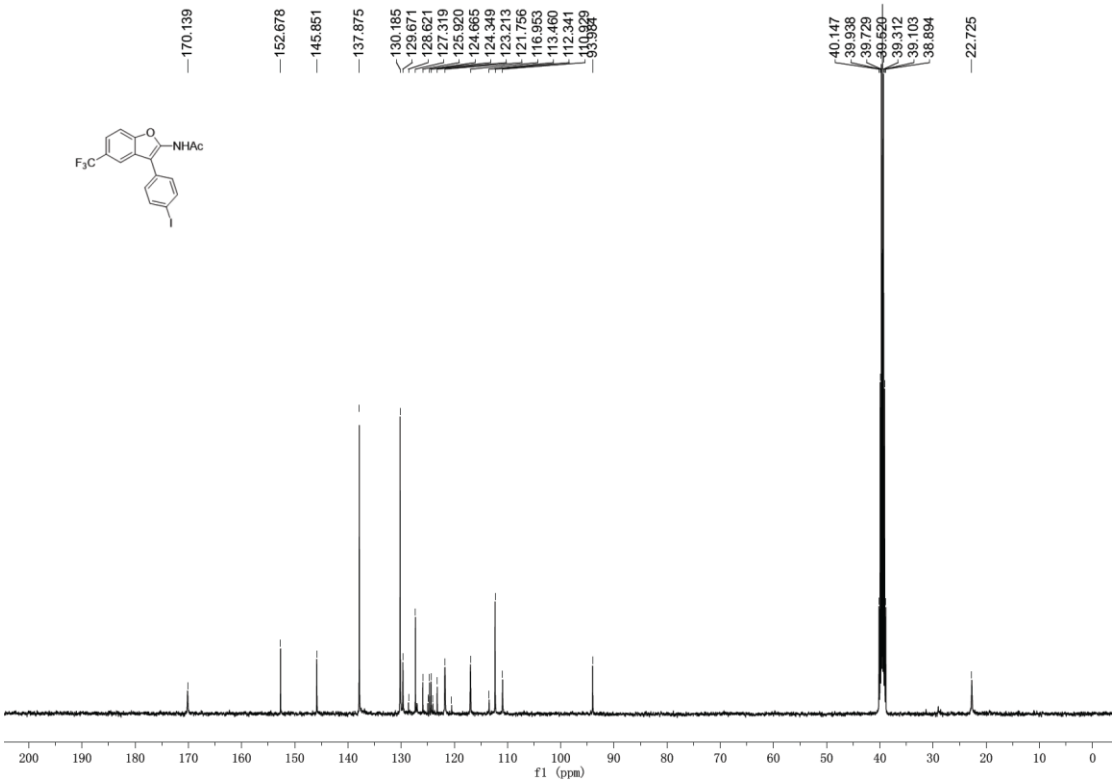
3fe-^{13}C NMR (100 Hz, DMSO-d_6)



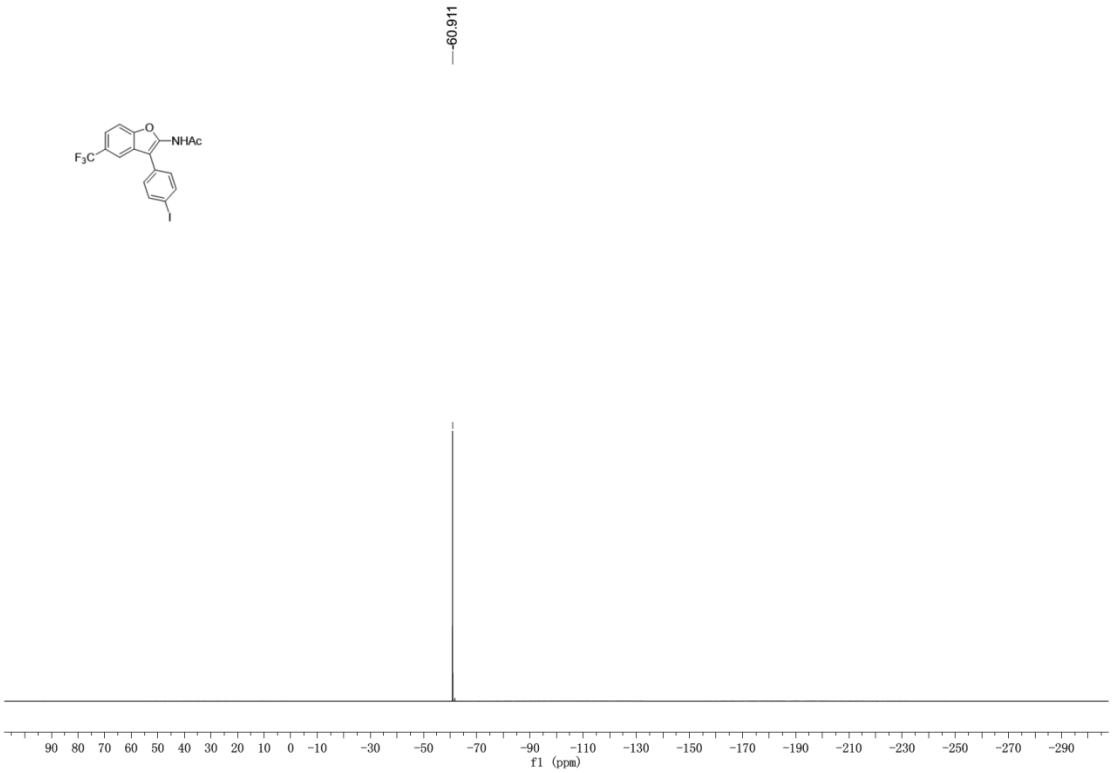
3ge-^{1}H NMR (400 Hz, DMSO-d_6)



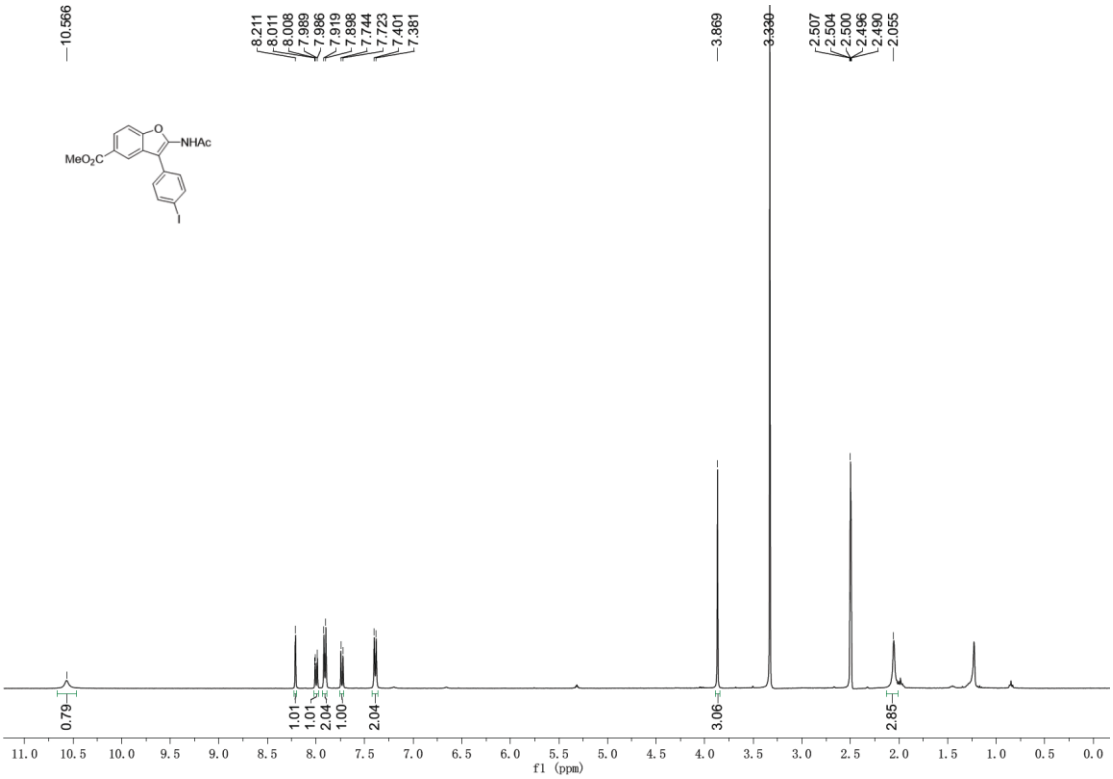
3ge-^{13}C NMR (100 Hz, DMSO-d_6)



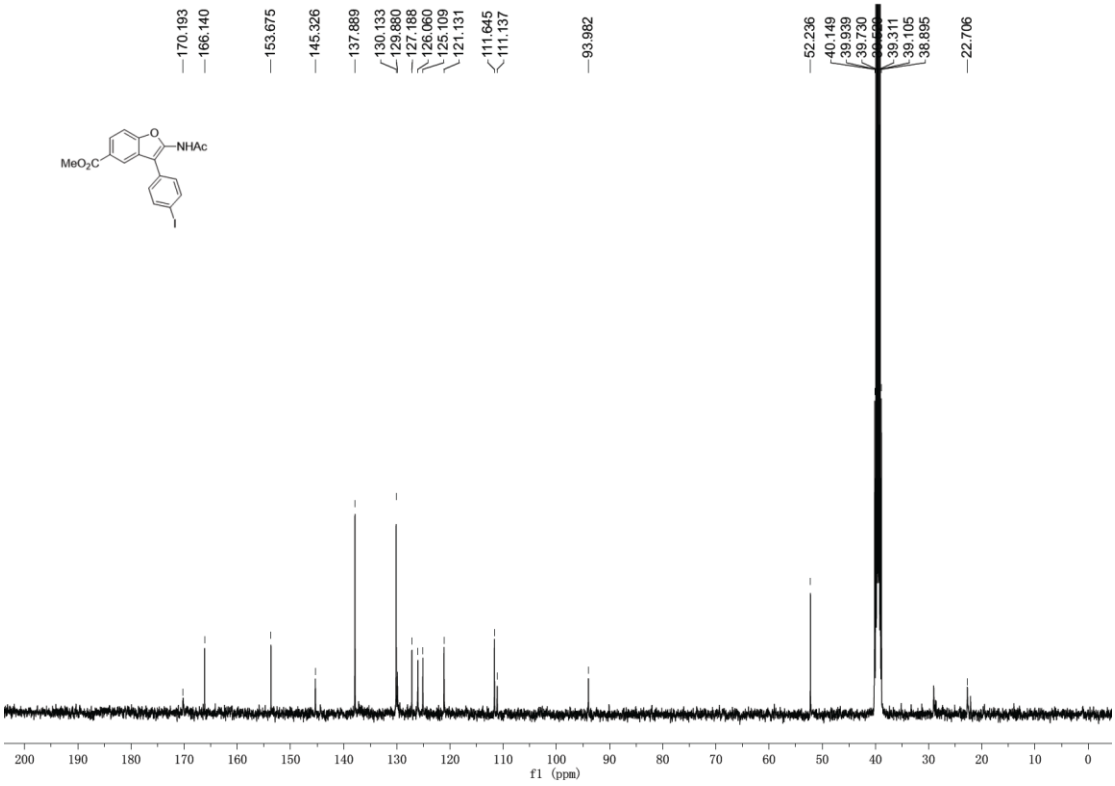
3ge-^{19}F NMR (376 Hz, $CDCl_3$)



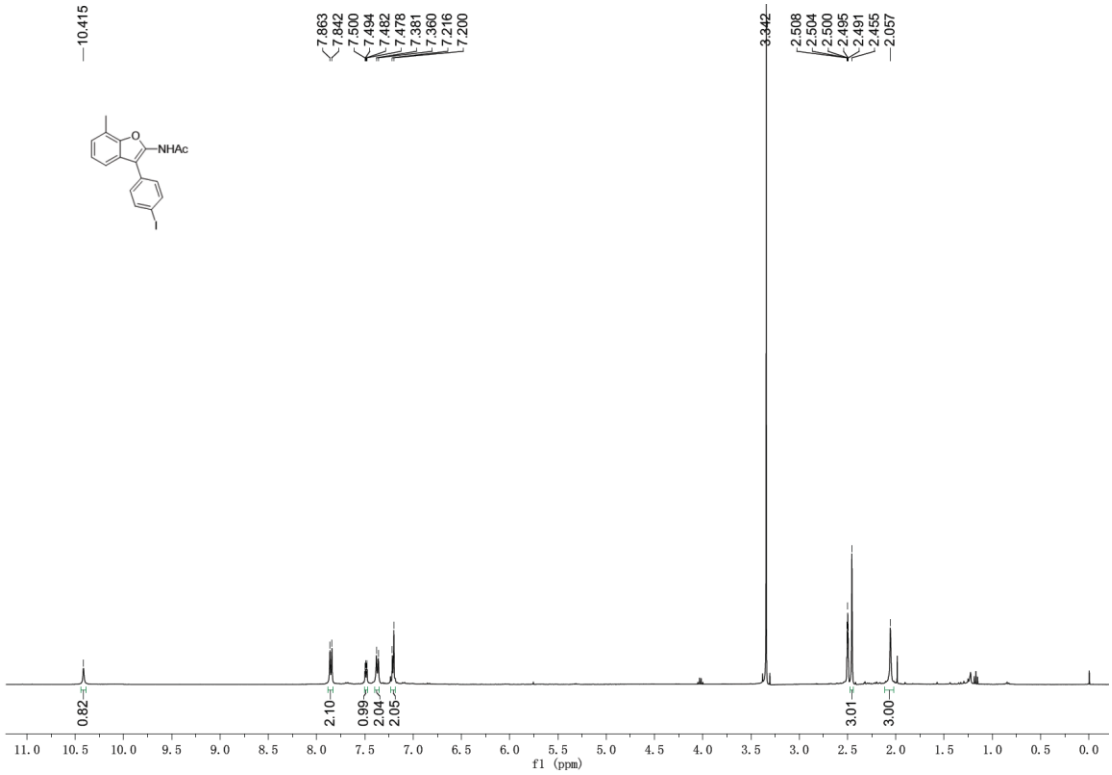
3he-^{1}H NMR (400 Hz, DMSO-d_6)



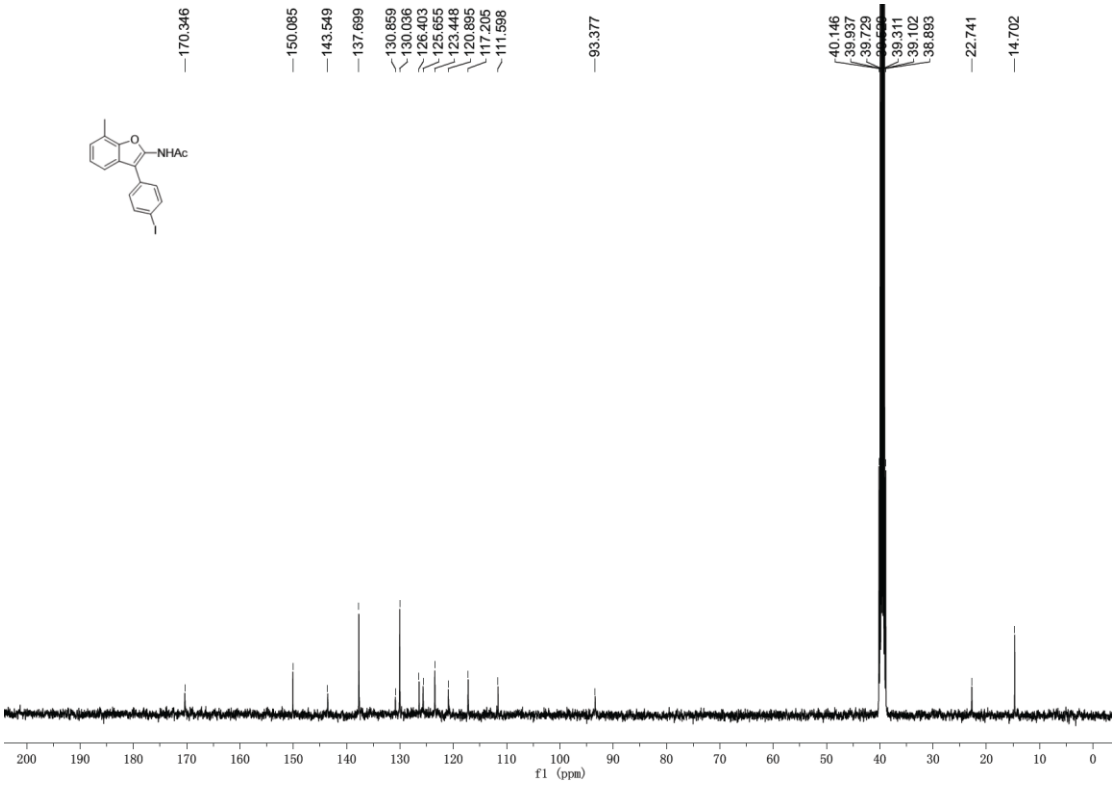
3he-^{13}C NMR (100 Hz, DMSO-d_6)



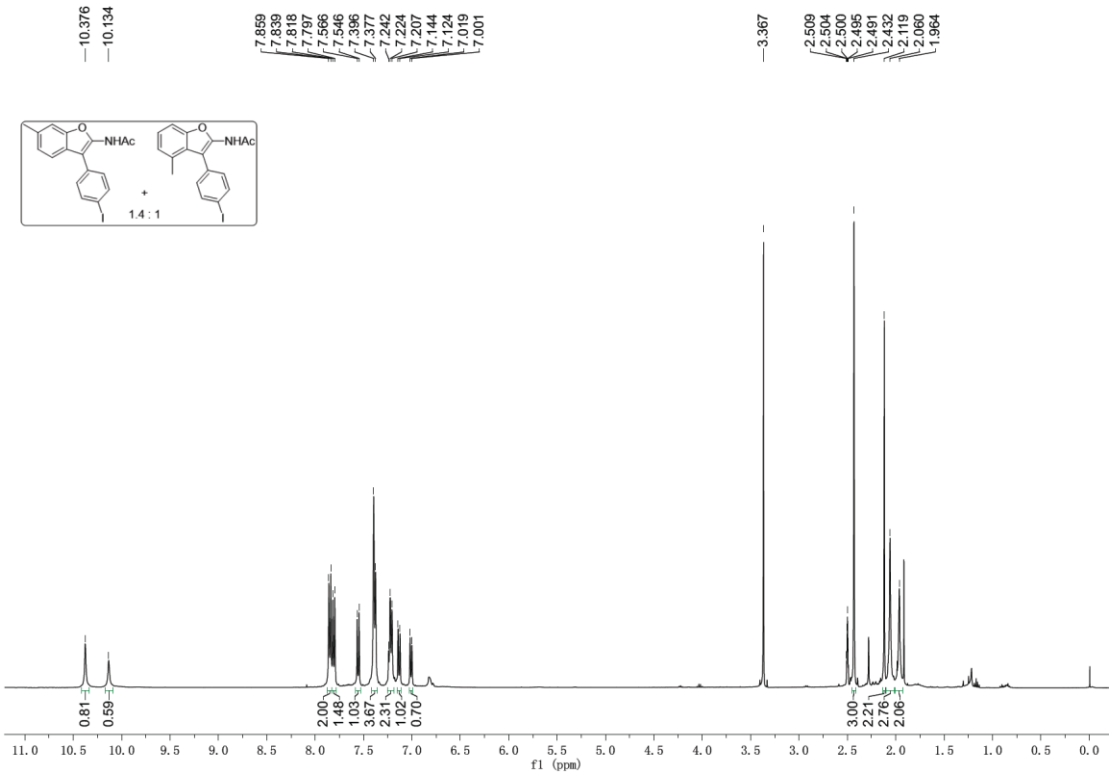
3ie-^{1}H NMR (400 Hz, DMSO-d_6)



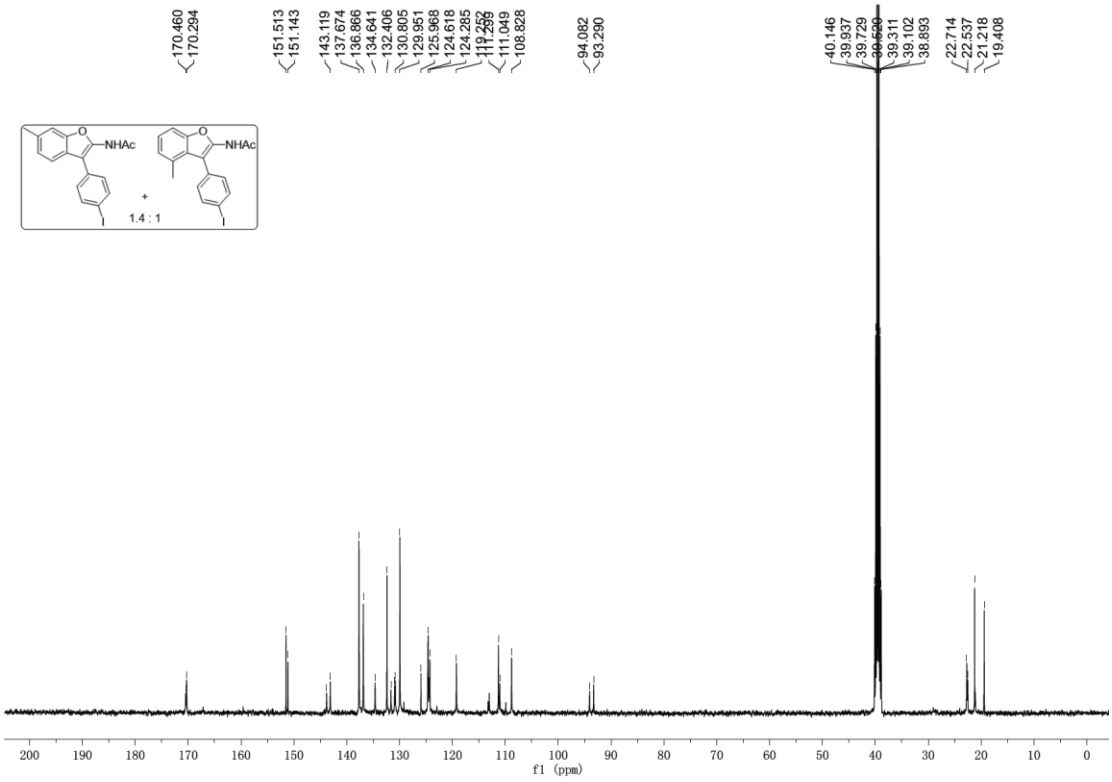
3ie-^{13}C NMR (100 Hz, DMSO-d_6)



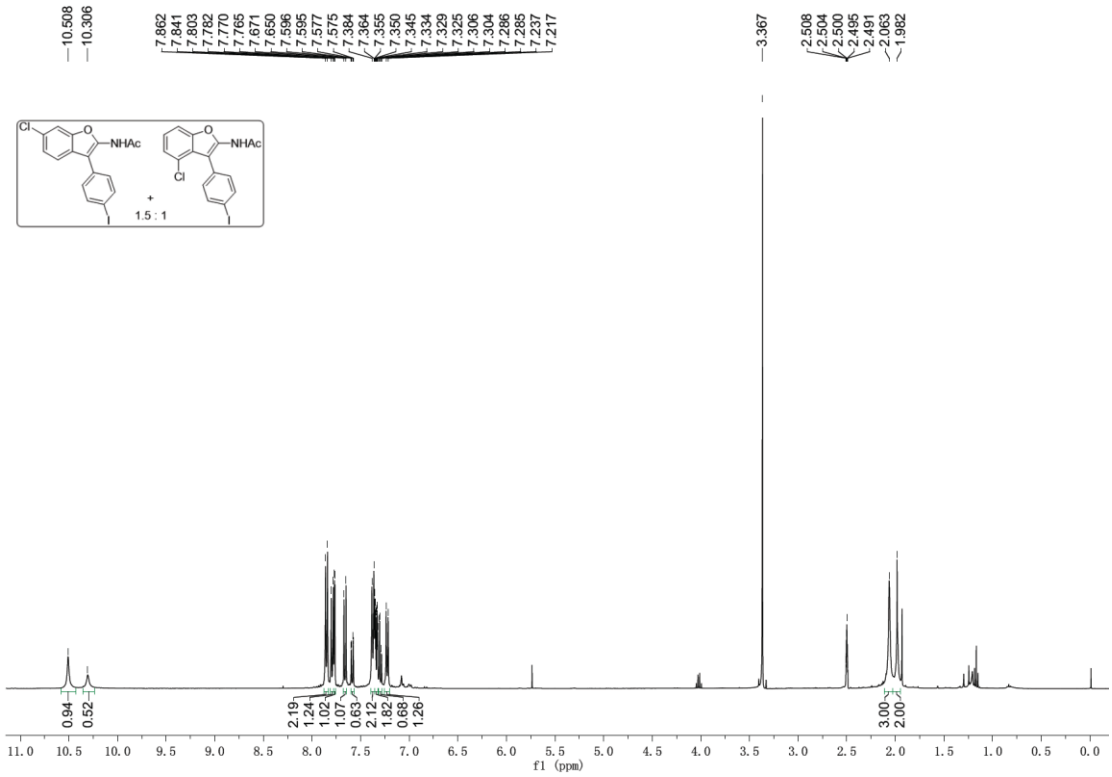
3je & 3je'-^{1}H NMR (400 Hz, DMSO-d_6)



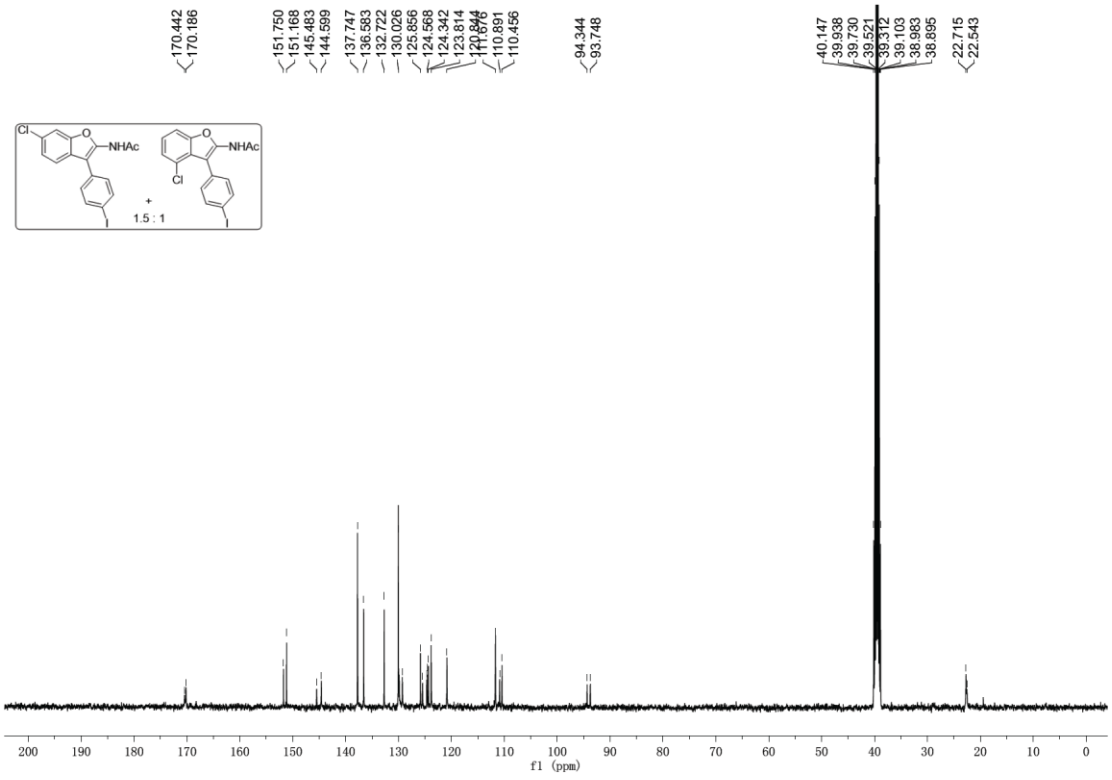
3je & 3je'-^{13}C NMR (100 Hz, DMSO-d_6)



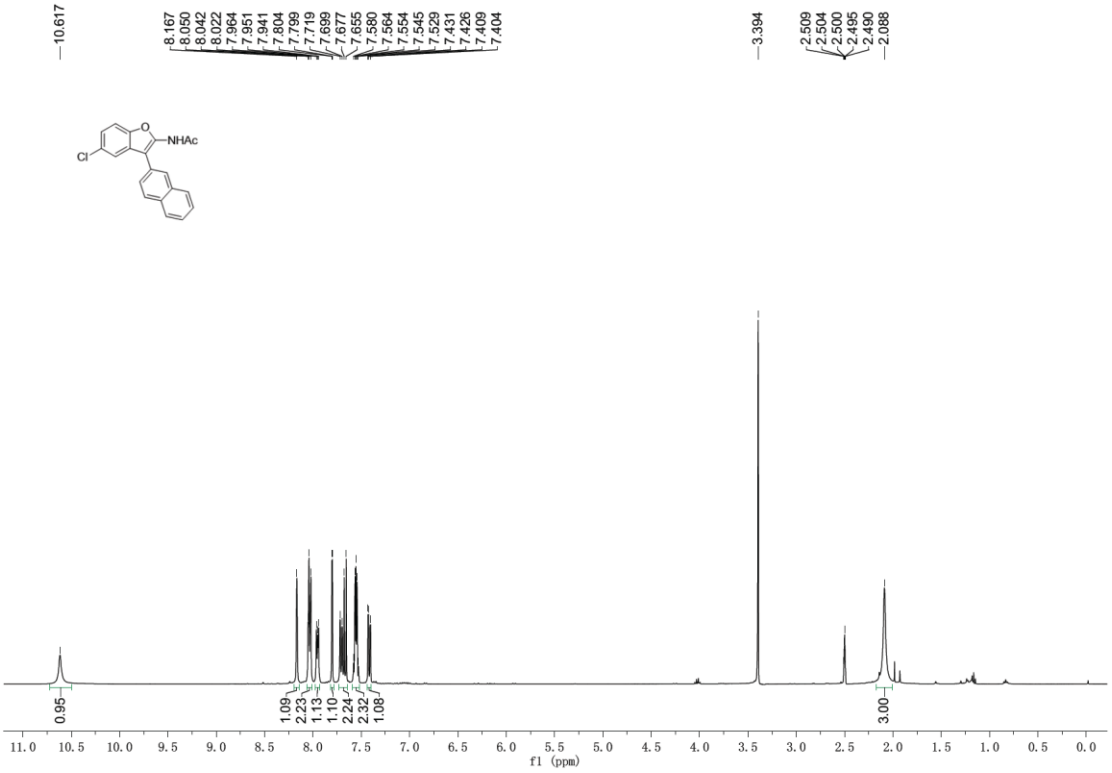
3ke & 3ke'-^{1}H NMR (400 Hz, DMSO-d_6)



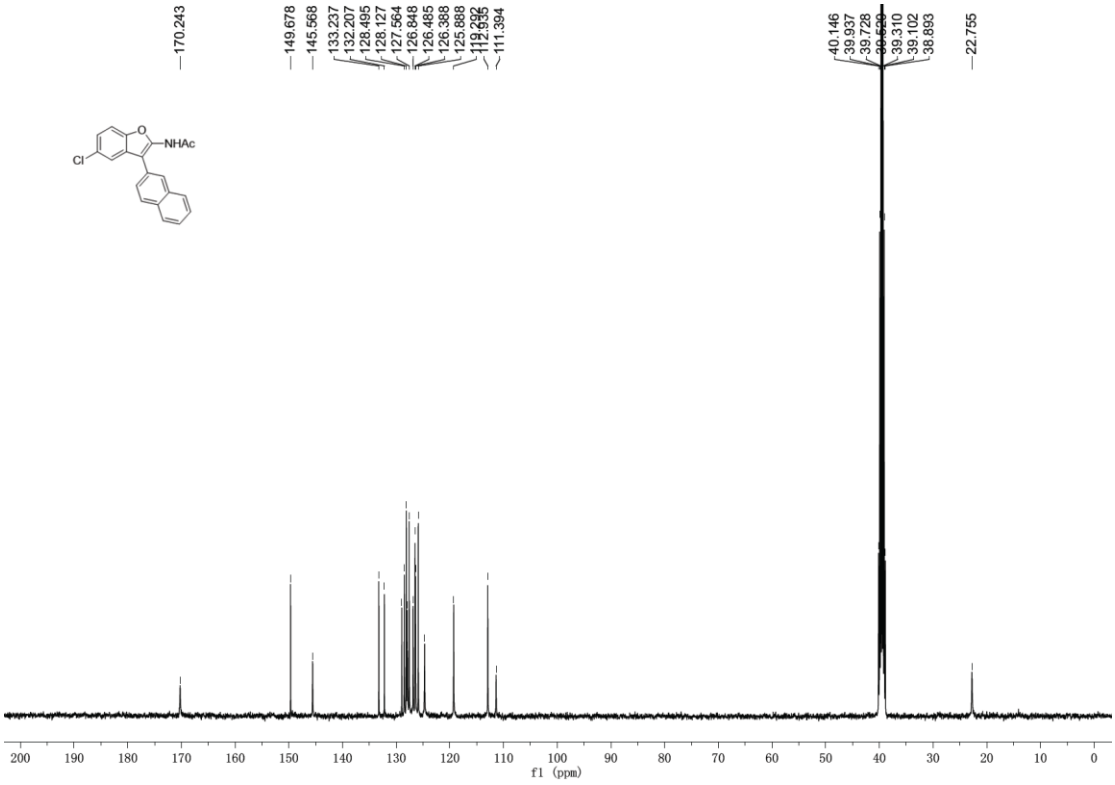
3ke & 3ke'-^{13}C NMR (100 Hz, DMSO-d_6)



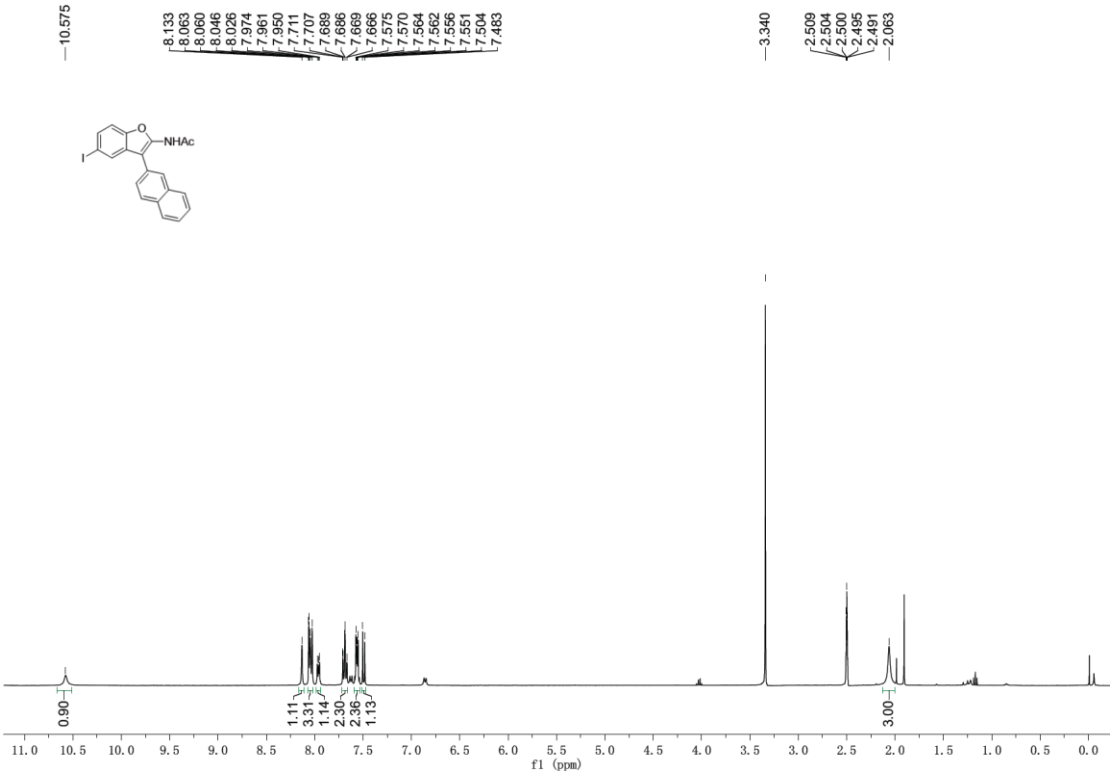
3la-^{1}H NMR (400 Hz, DMSO-d_6)



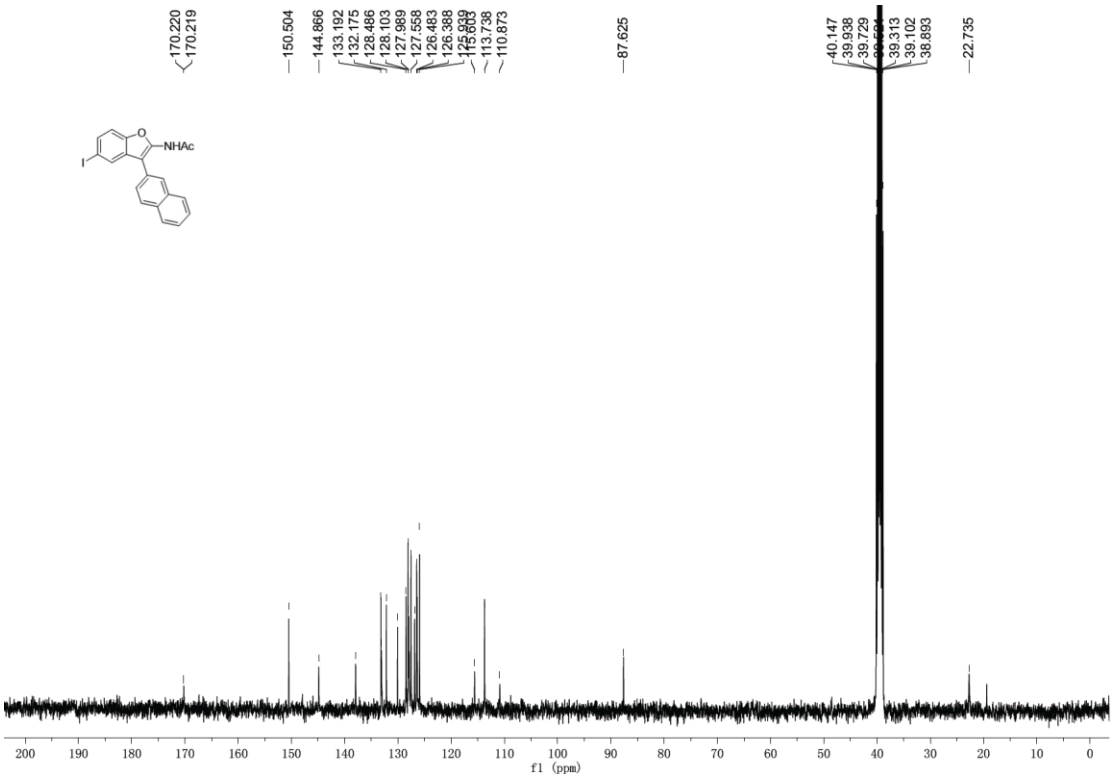
3la-^{13}C NMR (100 Hz, DMSO-d_6)



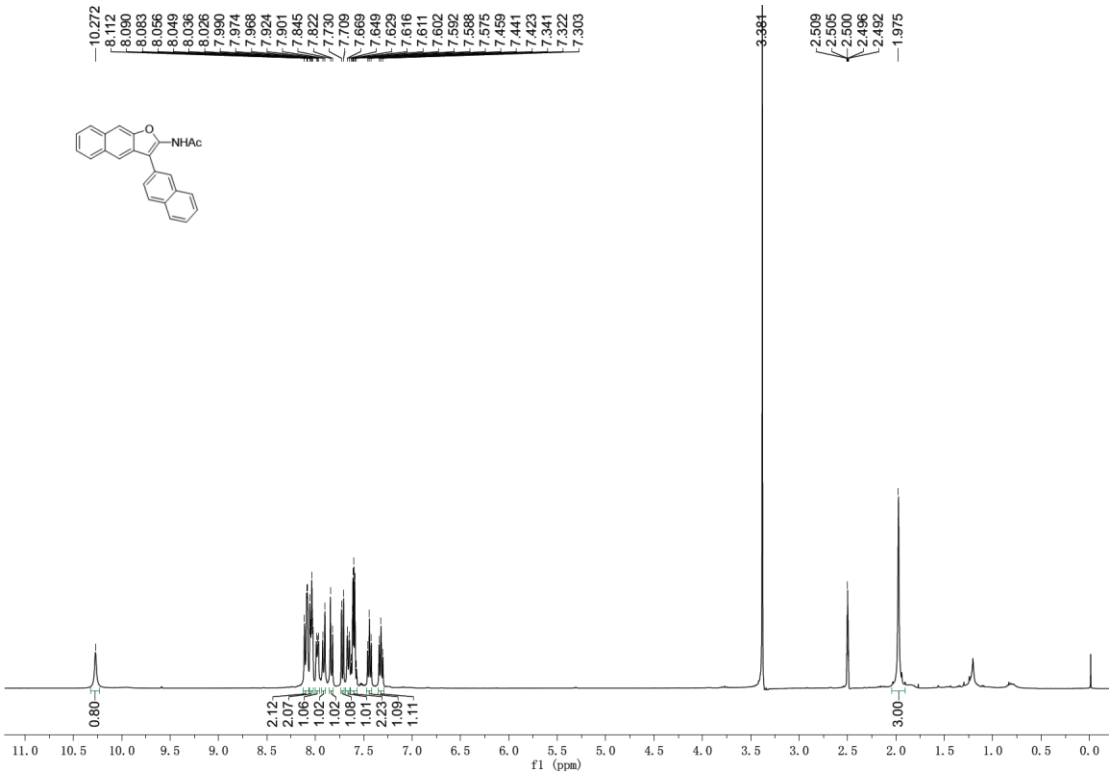
3ma-^{1}H NMR (400 Hz, DMSO-d_6)



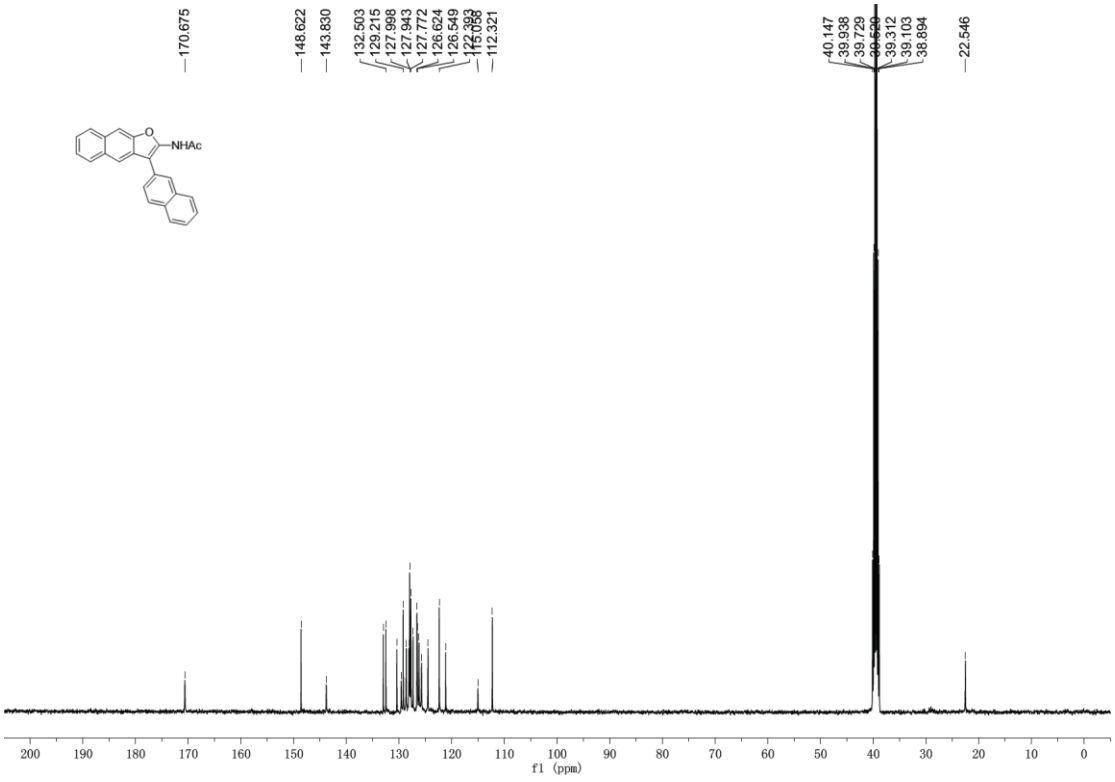
3ma-^{13}C NMR (100 Hz, DMSO-d_6)



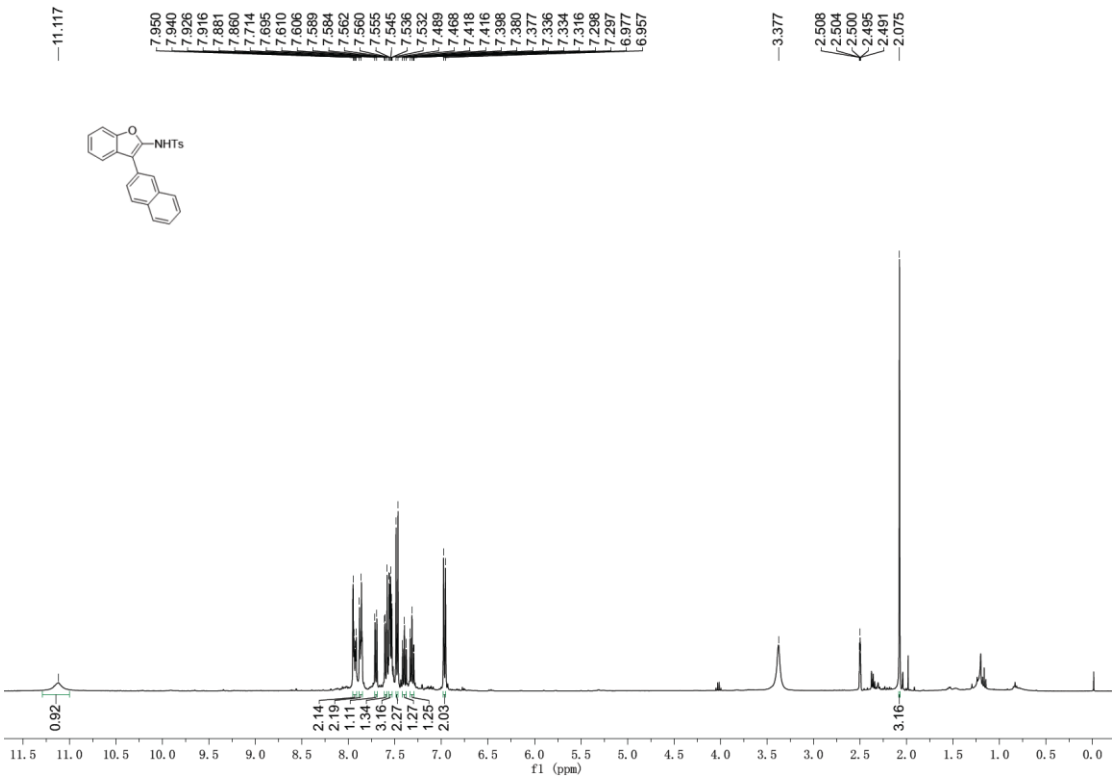
3na-^{1}H NMR (400 Hz, DMSO-d_6)



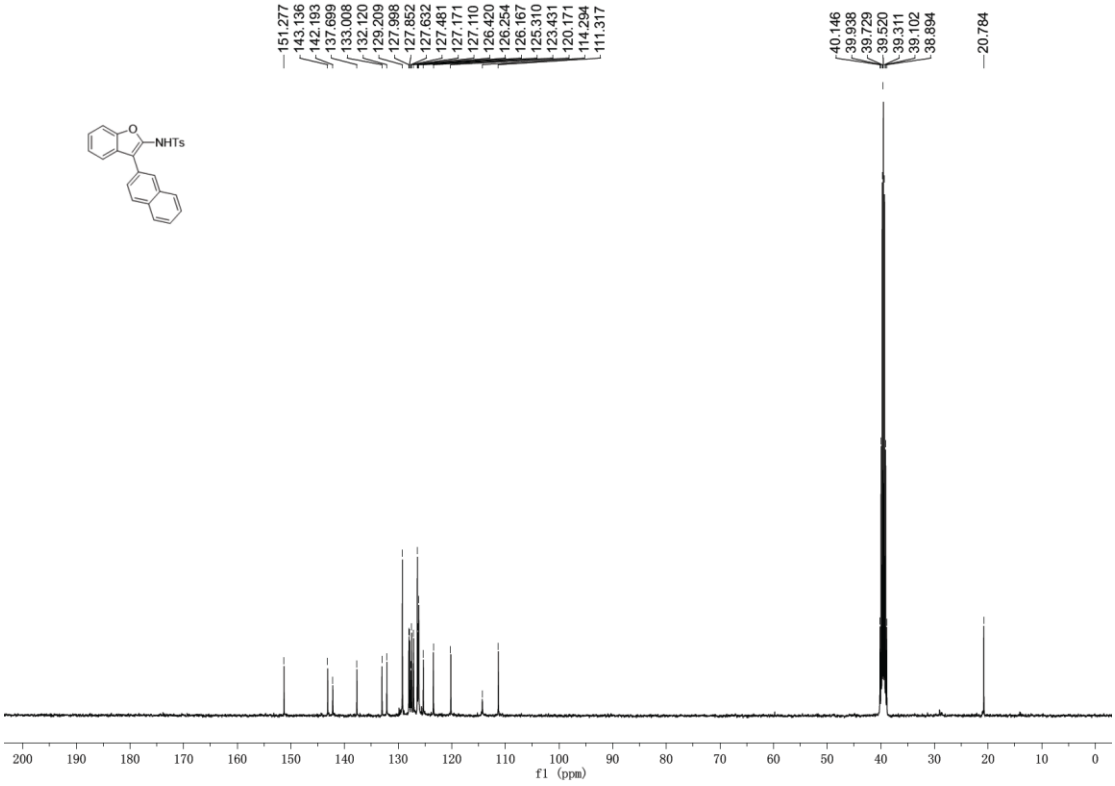
3na-^{13}C NMR (100 Hz, DMSO-d_6)



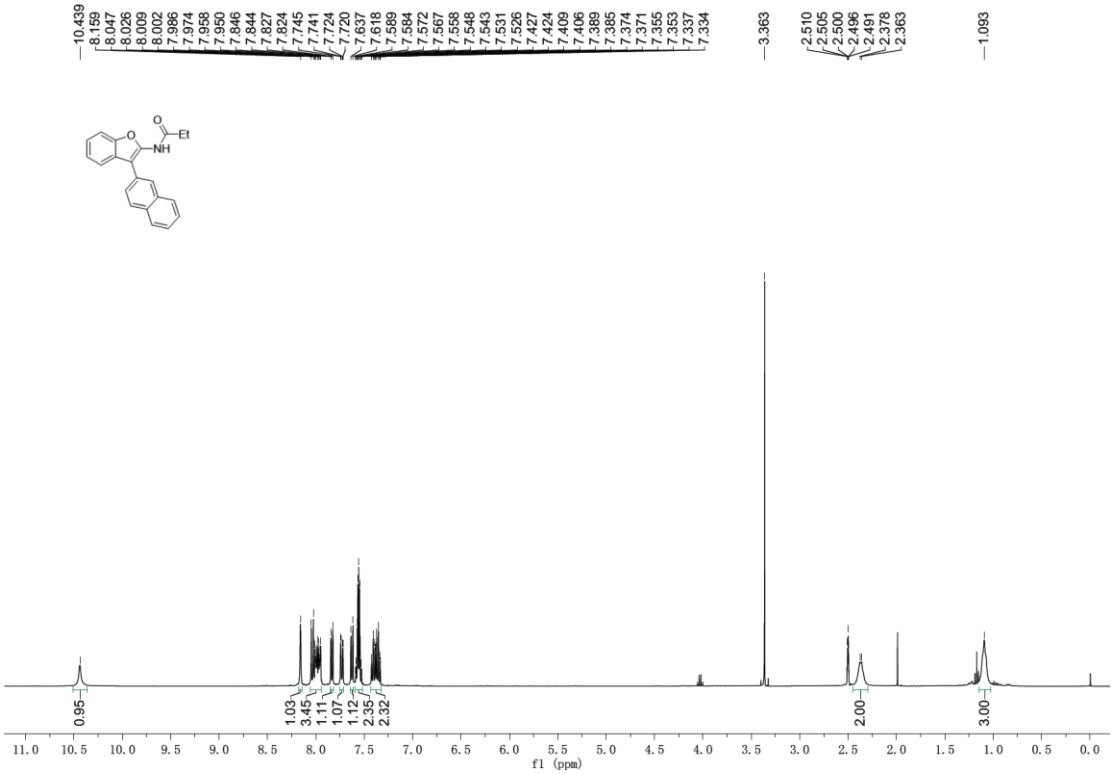
3oa-^{1}H NMR (400 Hz, DMSO-d_6)



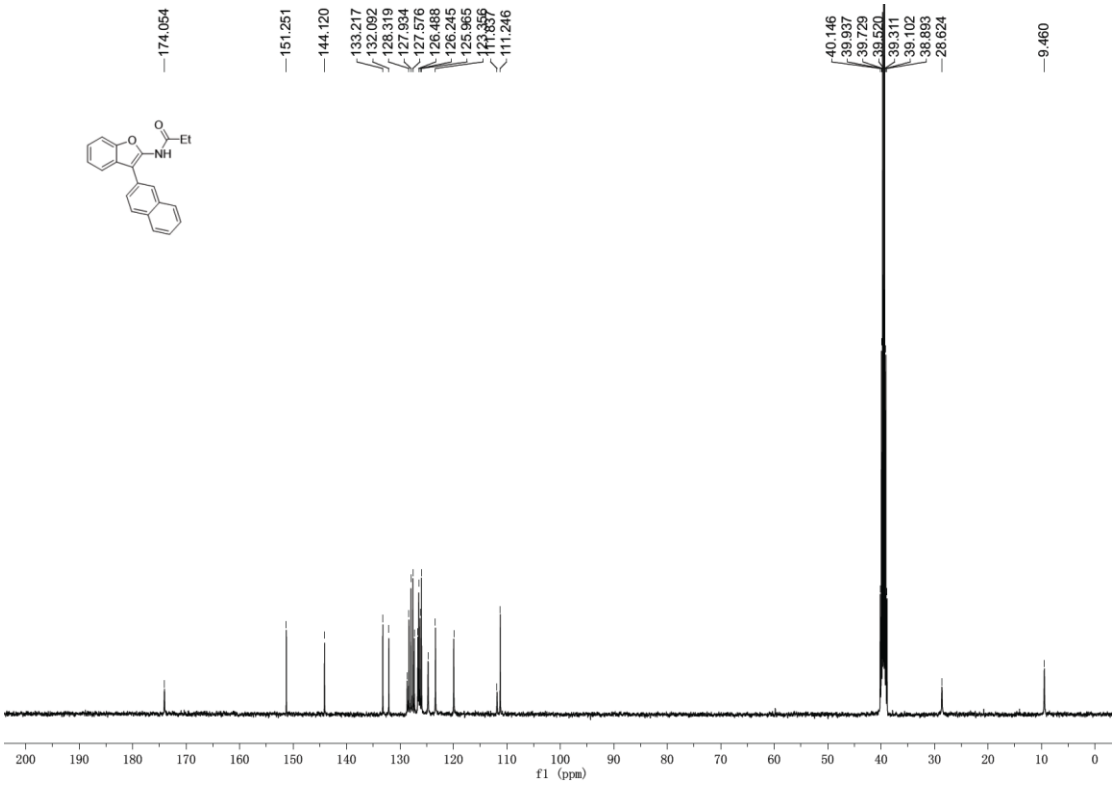
3oa-^{13}C NMR (100 Hz, DMSO-d_6)



3pa-^{1}H NMR (400 Hz, DMSO-d_6)



3pa-^{13}C NMR (100 Hz, DMSO-d_6)



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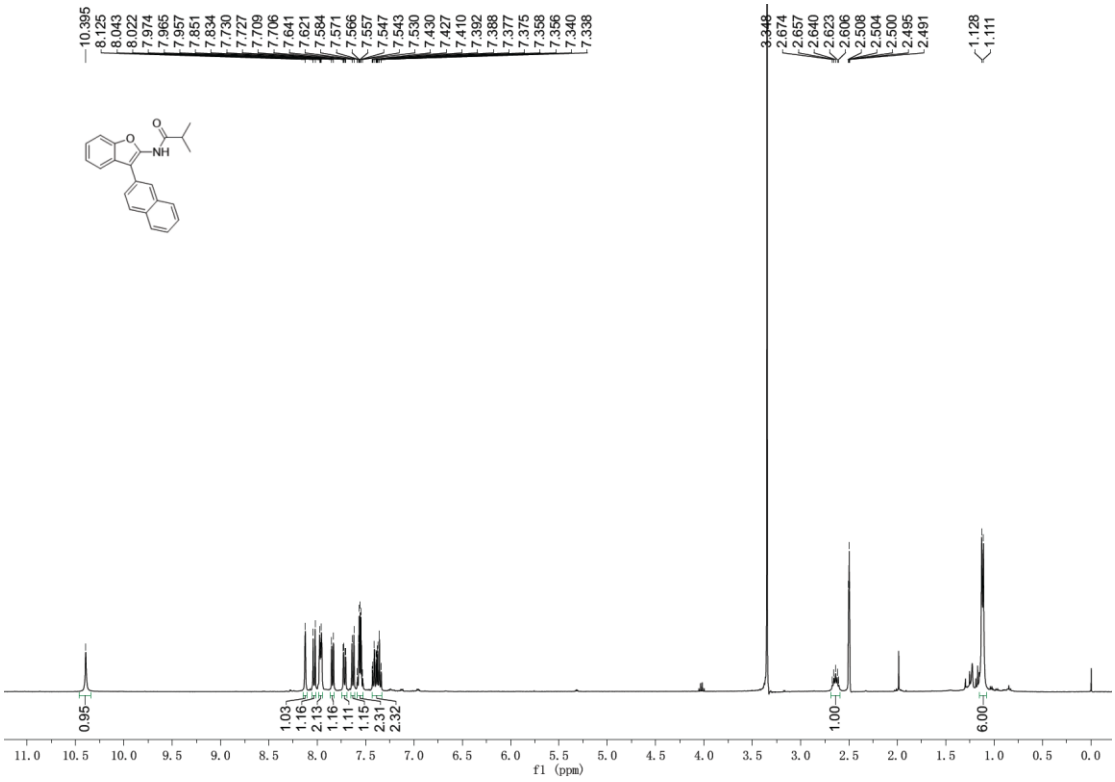

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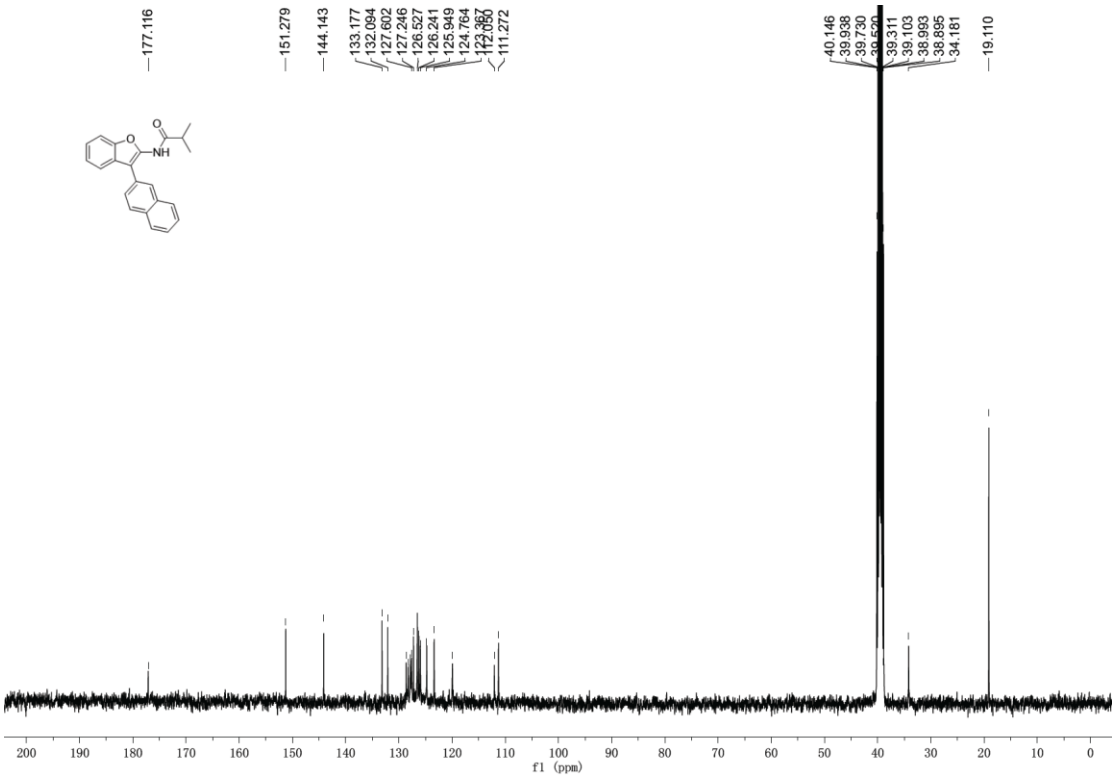
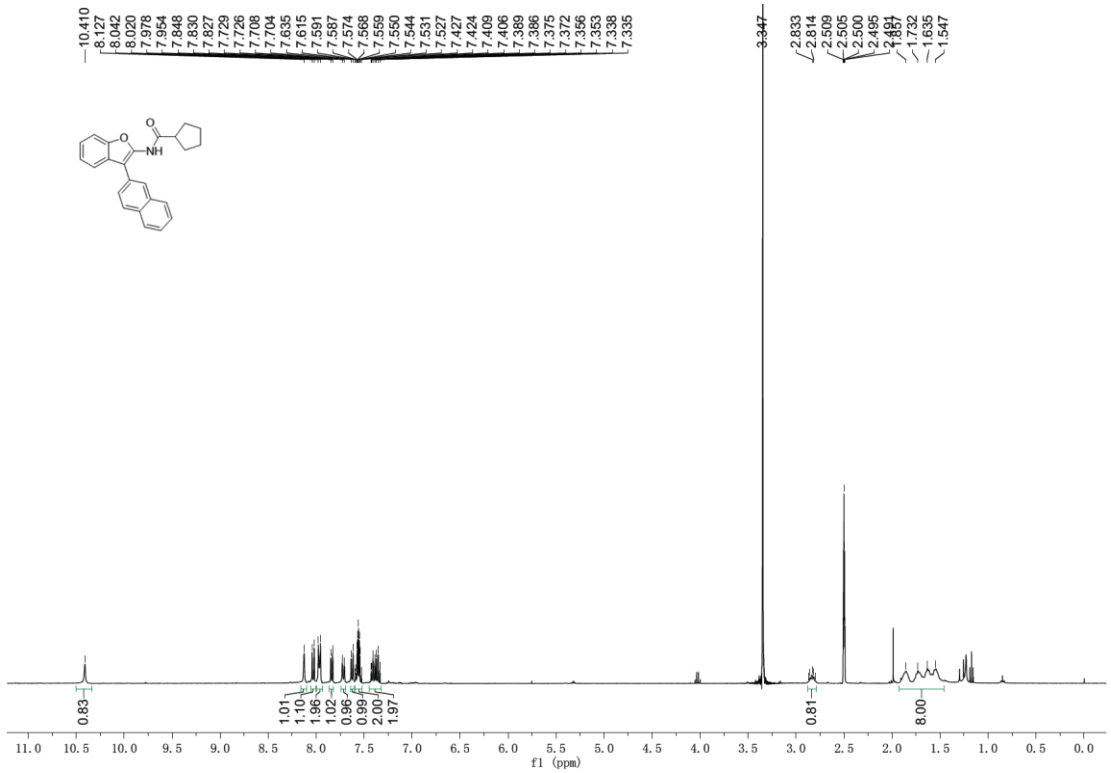
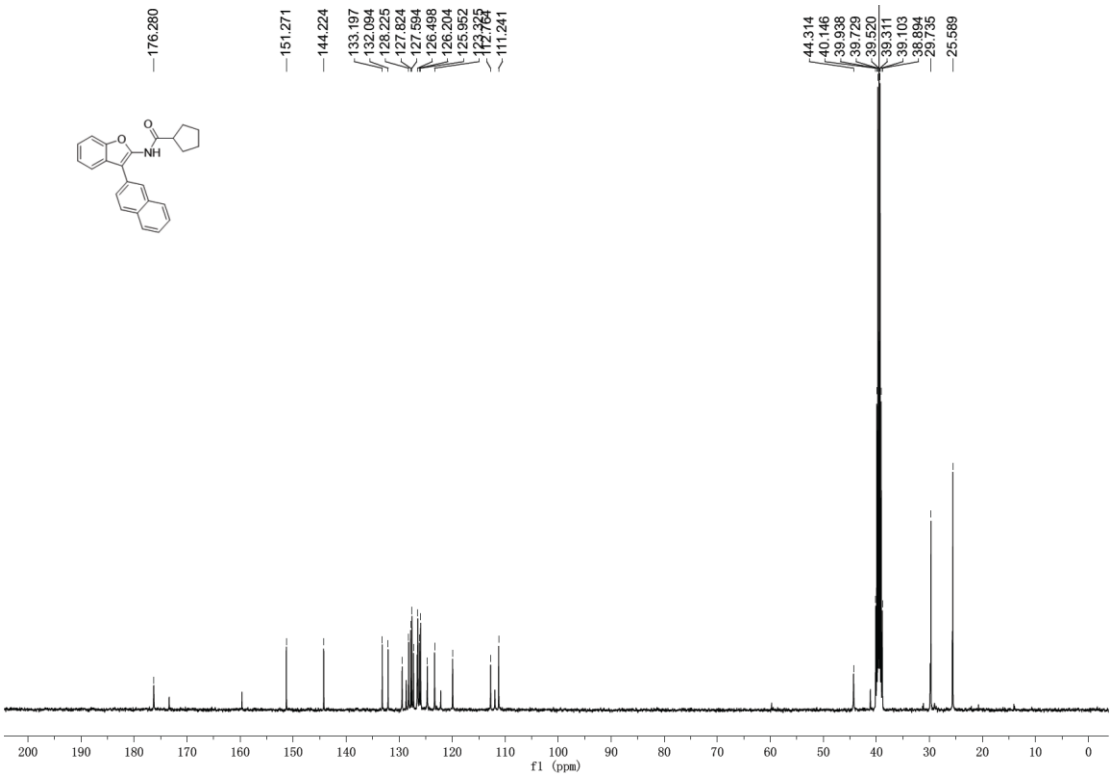


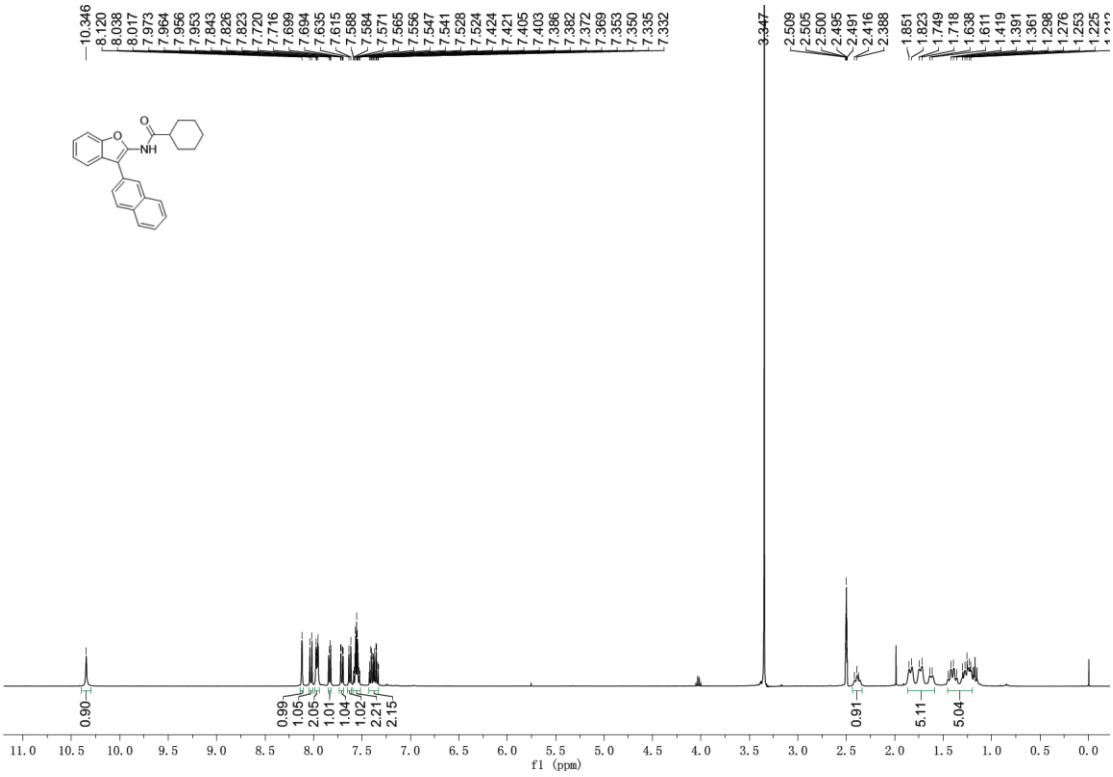
3ra-^{1}H NMR (400 Hz, DMSO-d_6)



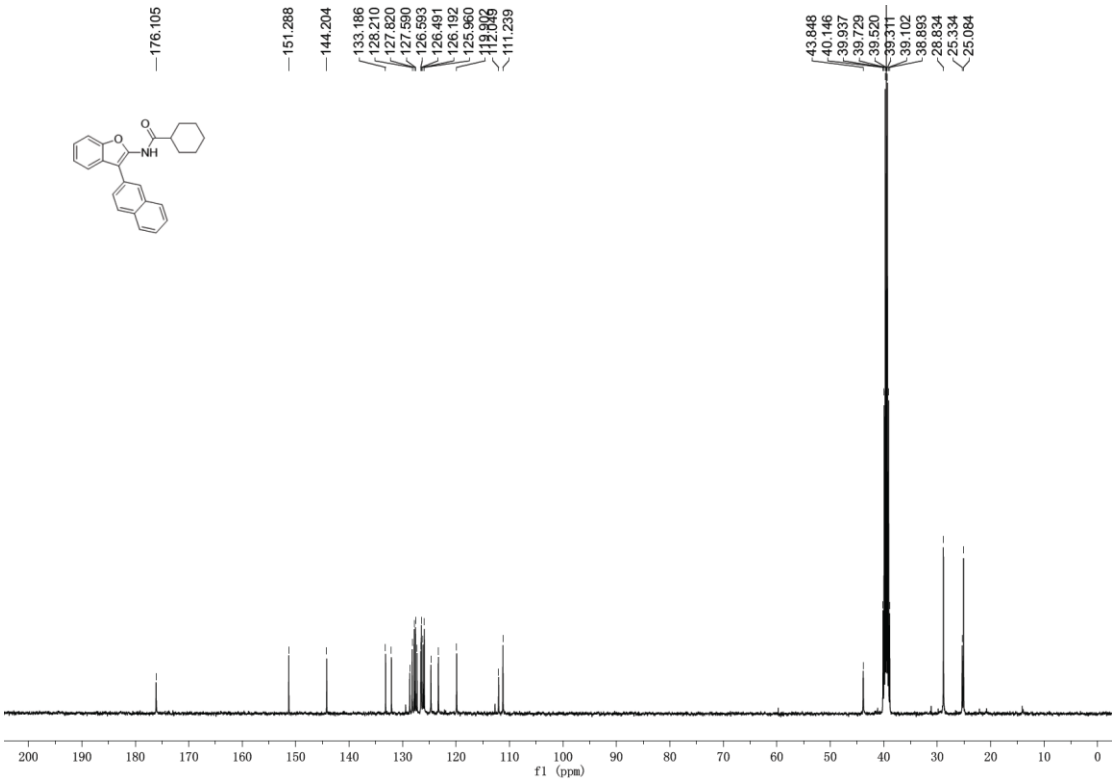
3ra-^{13}C NMR (100 Hz, DMSO-d_6)



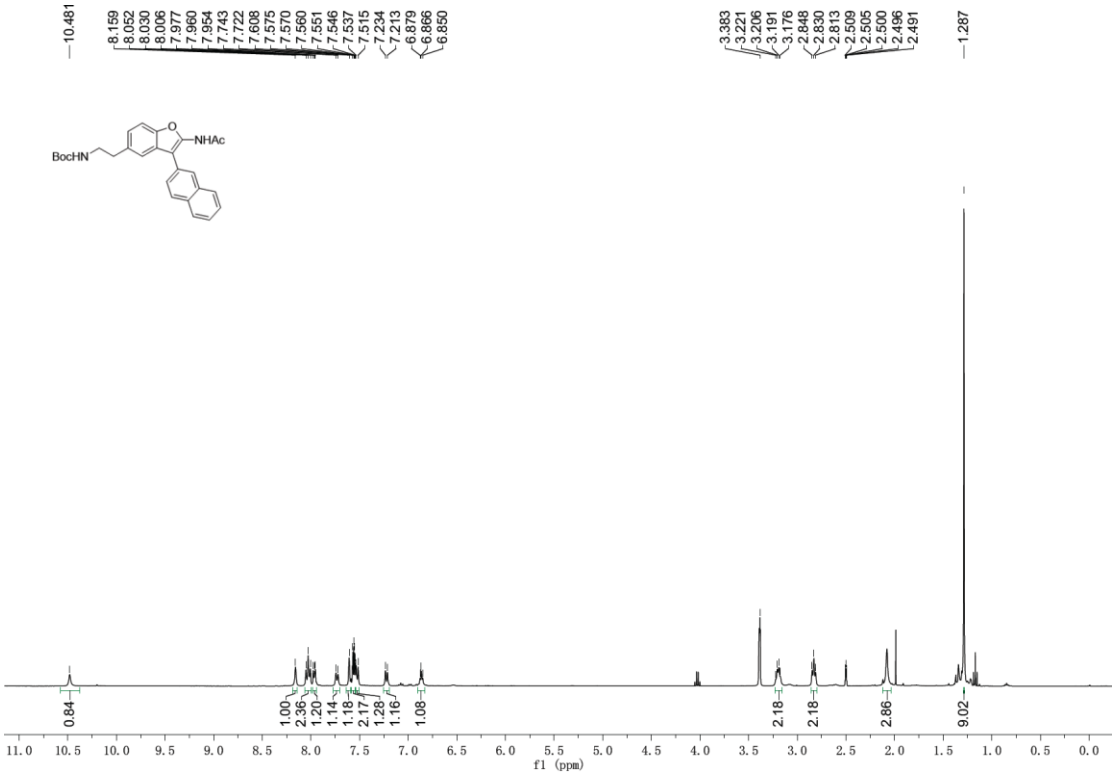
3sa-^{1}H NMR (400 Hz, DMSO-d_6)



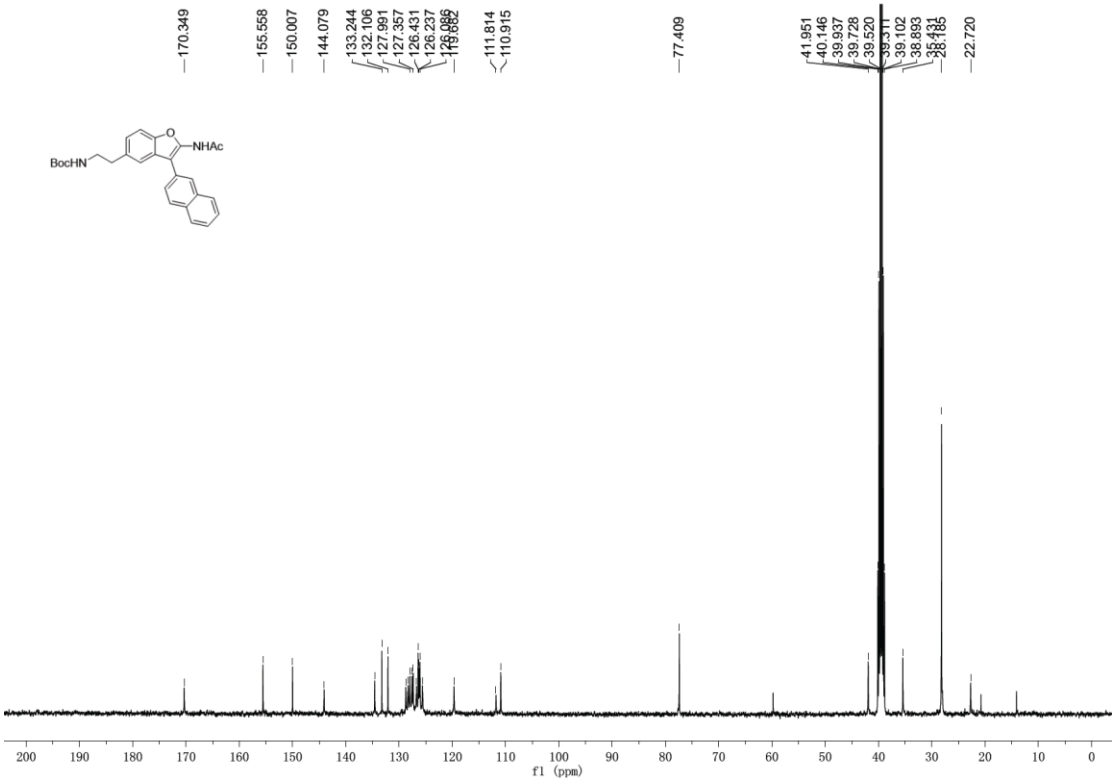
3sa-^{13}C NMR (100 Hz, DMSO-d_6)



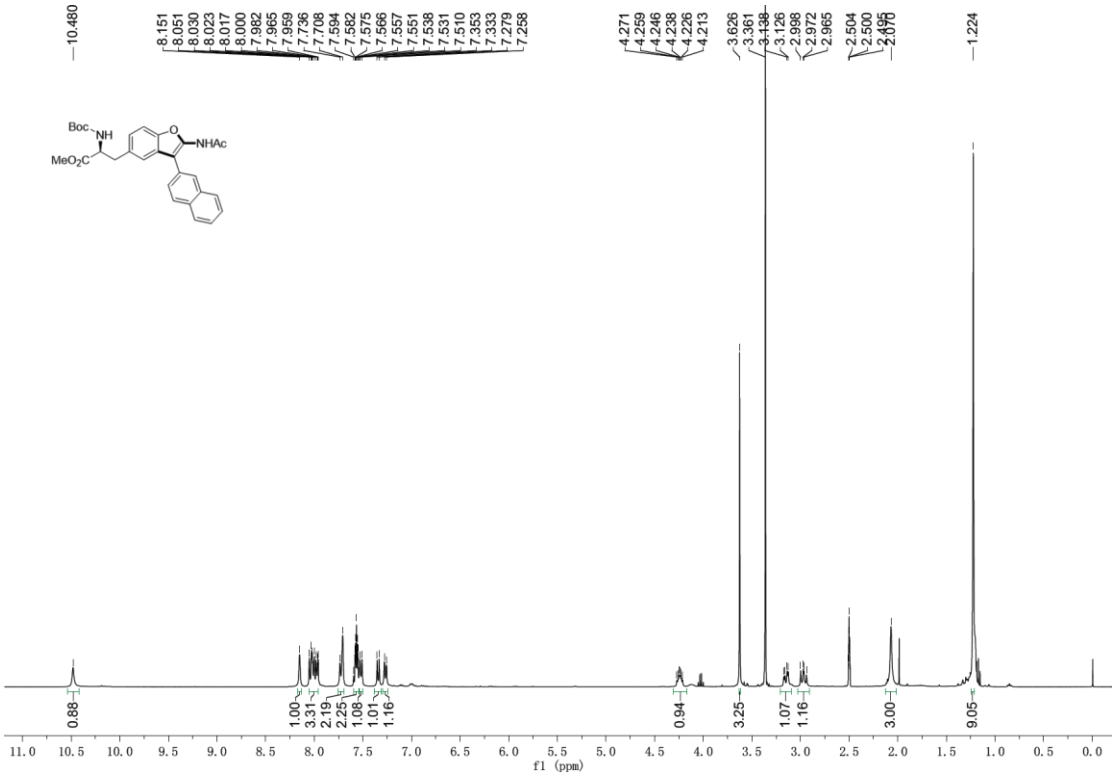
3ta-^{1}H NMR (400 Hz, DMSO-d_6)



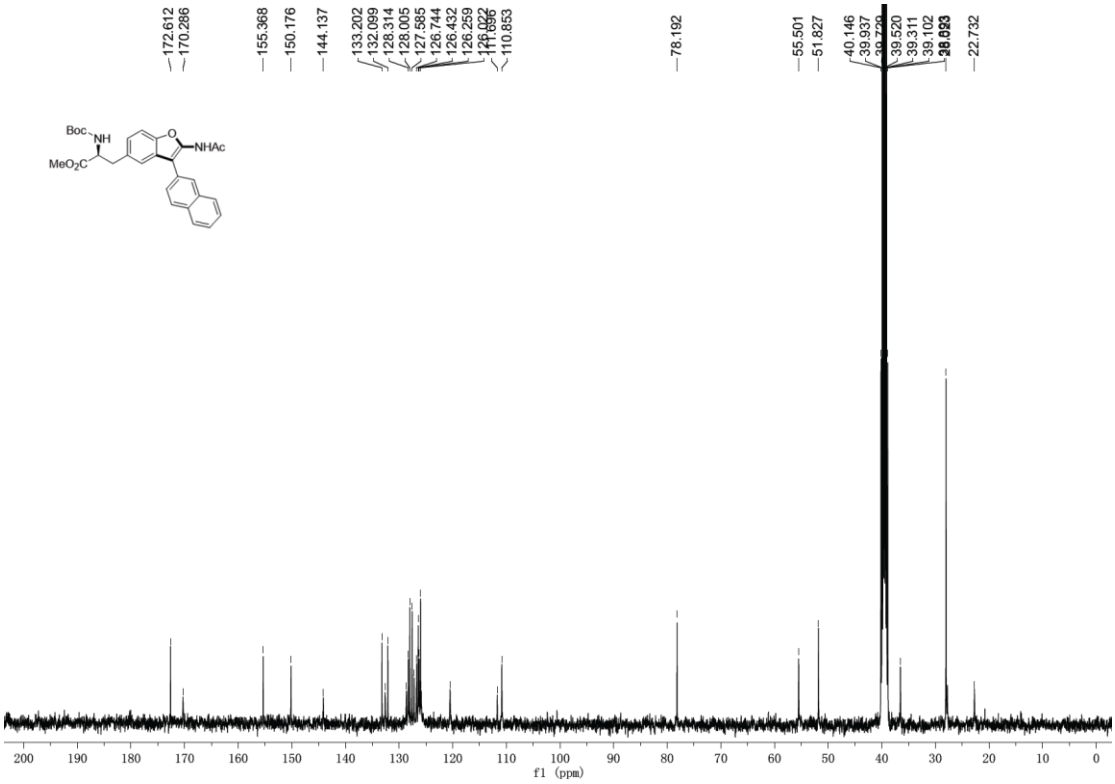
3ta-^{13}C NMR (100 Hz, DMSO-d_6)



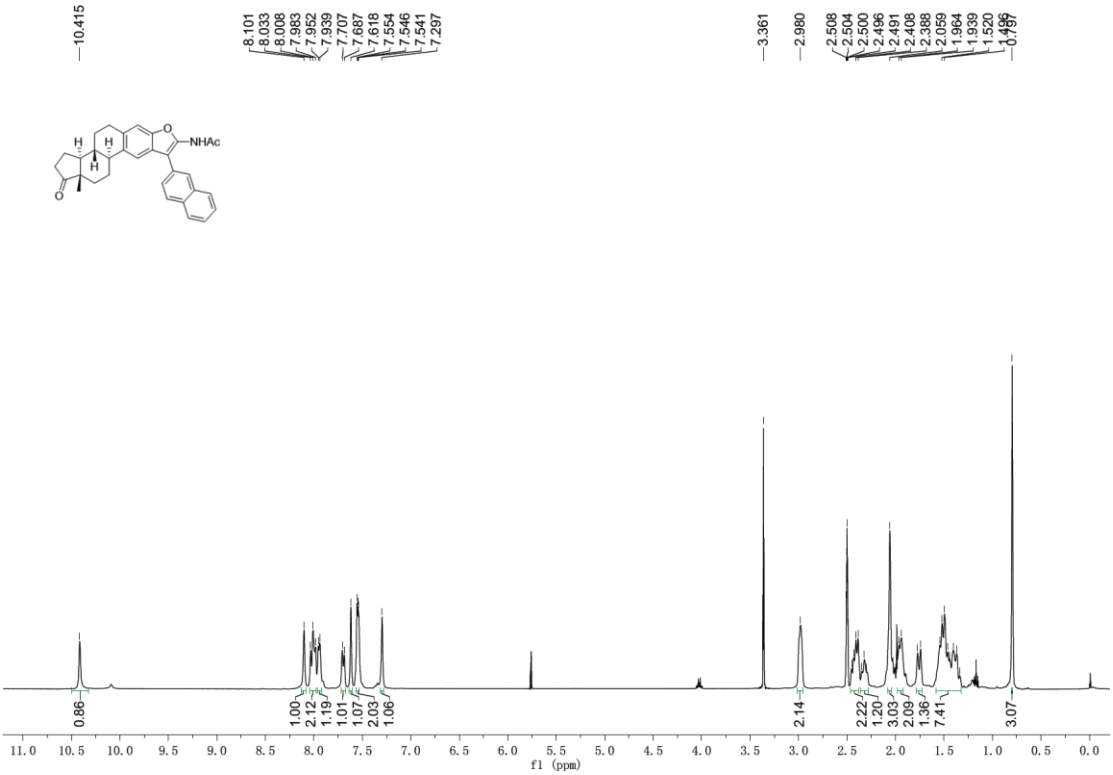
3ua-^{1}H NMR (400 Hz, DMSO-d_6)



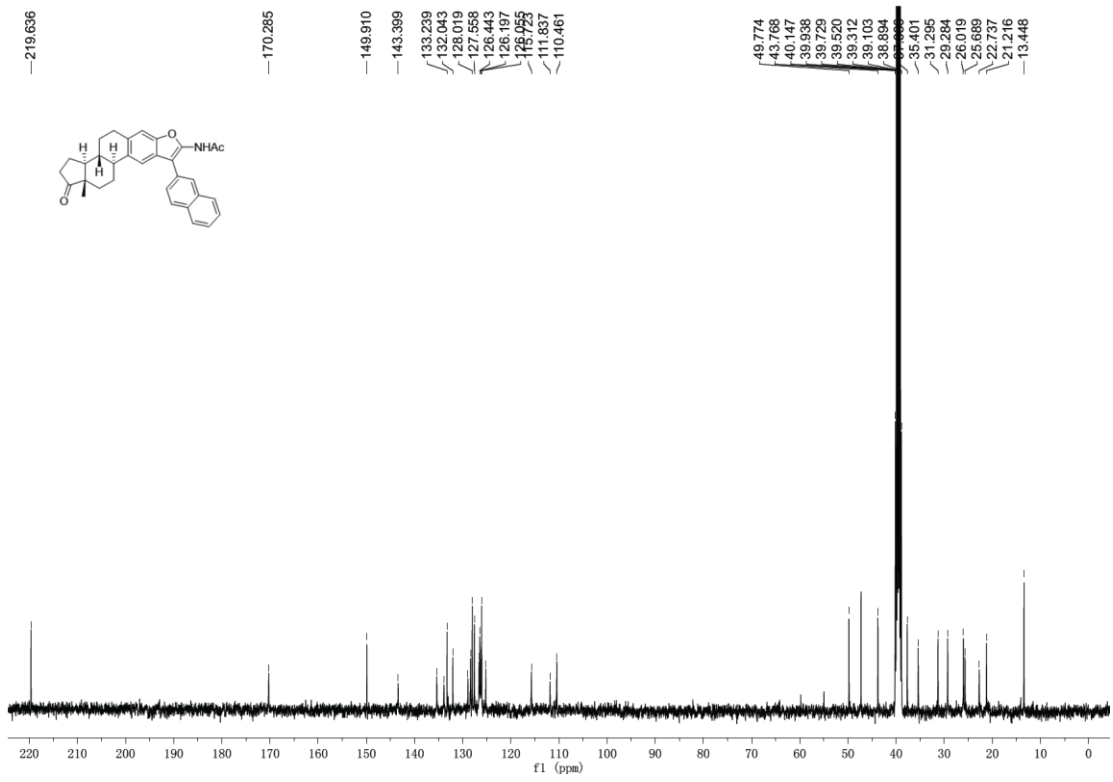
3ua-^{13}C NMR (100 Hz, DMSO-d_6)



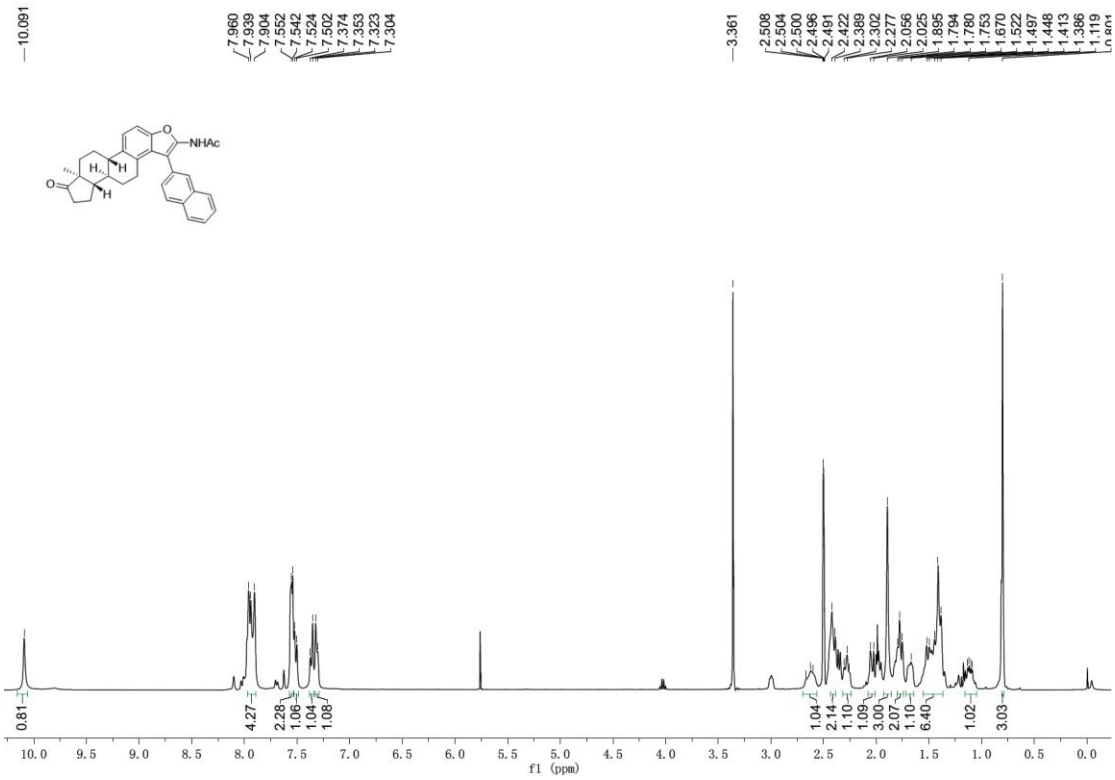
3va-^{1}H NMR (400 Hz, DMSO-d_6)



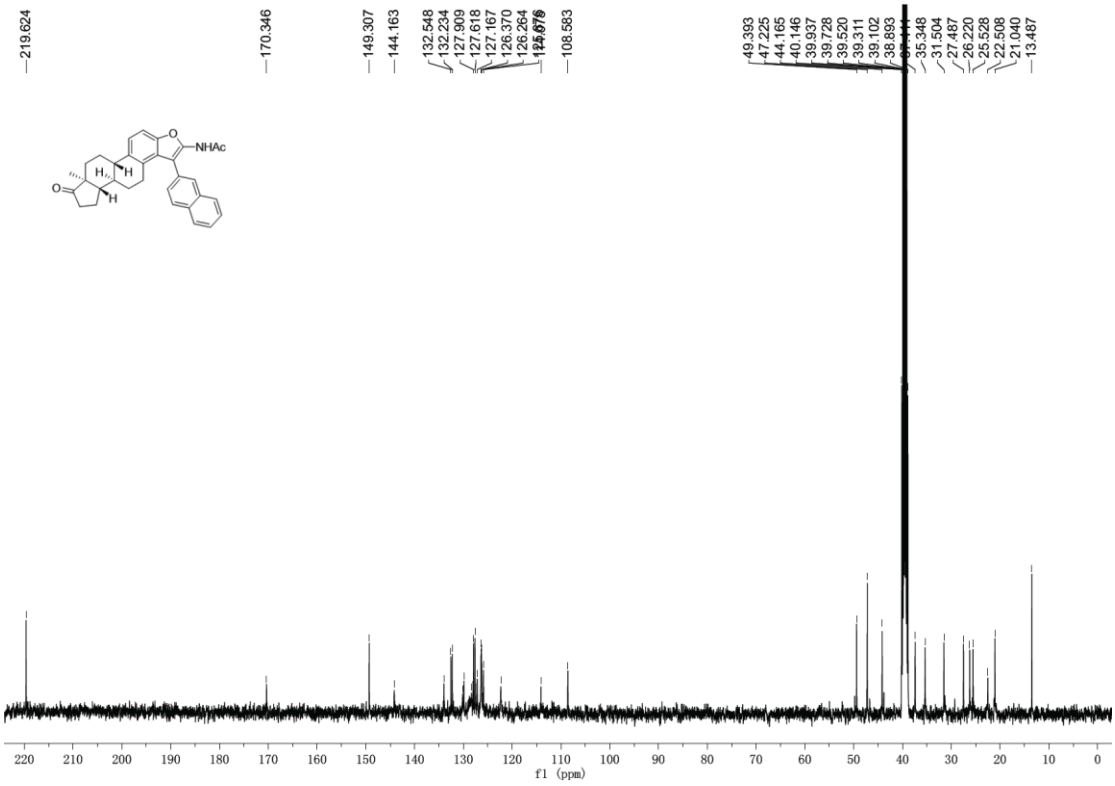
3va-^{13}C NMR (100 Hz, DMSO-d_6)



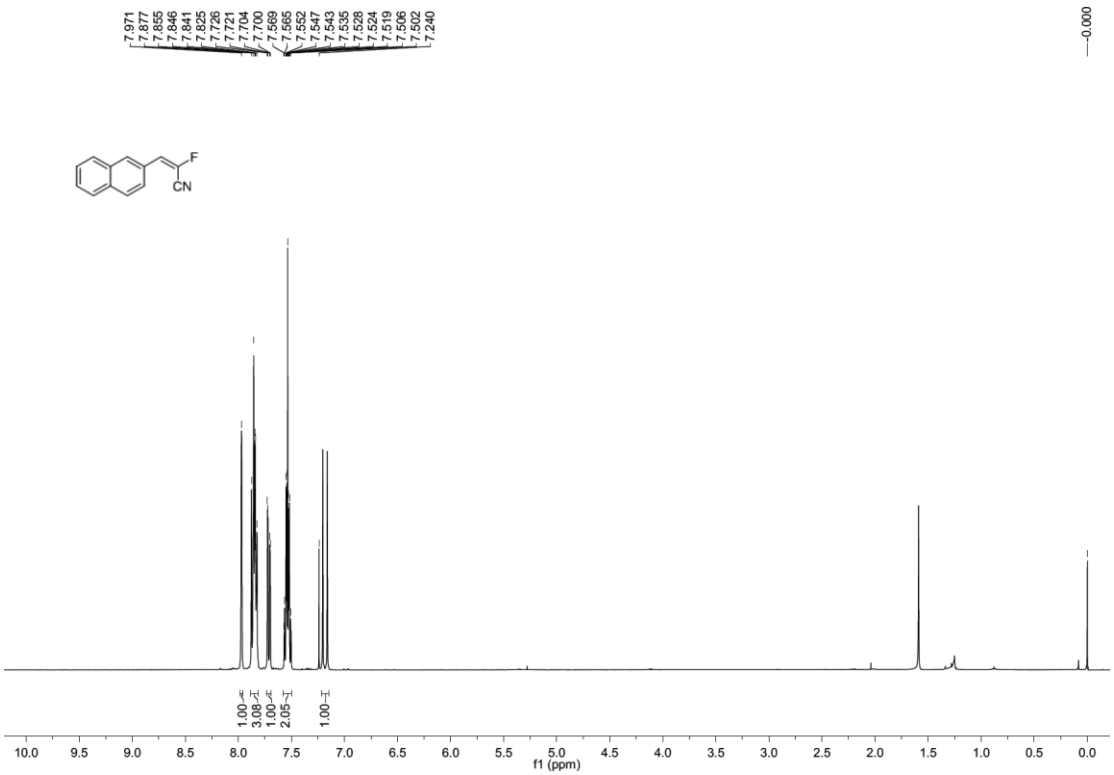
3va'-^{1}H NMR (400 Hz, DMSO-d_6)



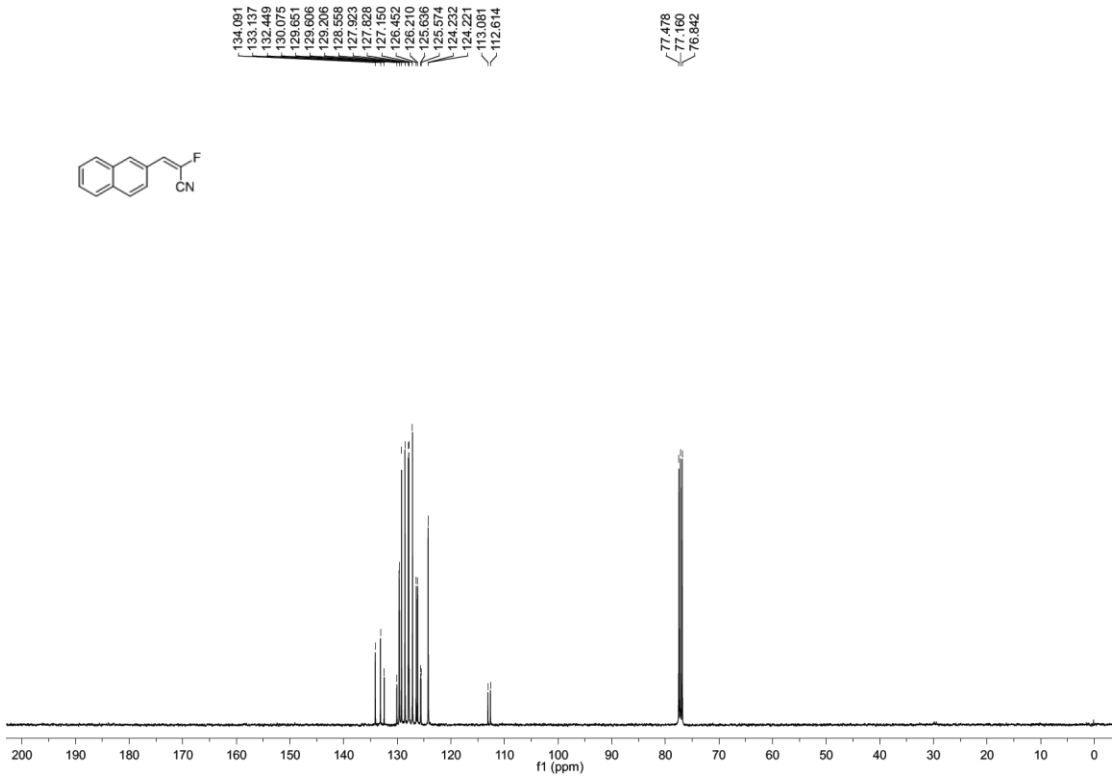
3va'-^{13}C NMR (100 Hz, DMSO-d_6)



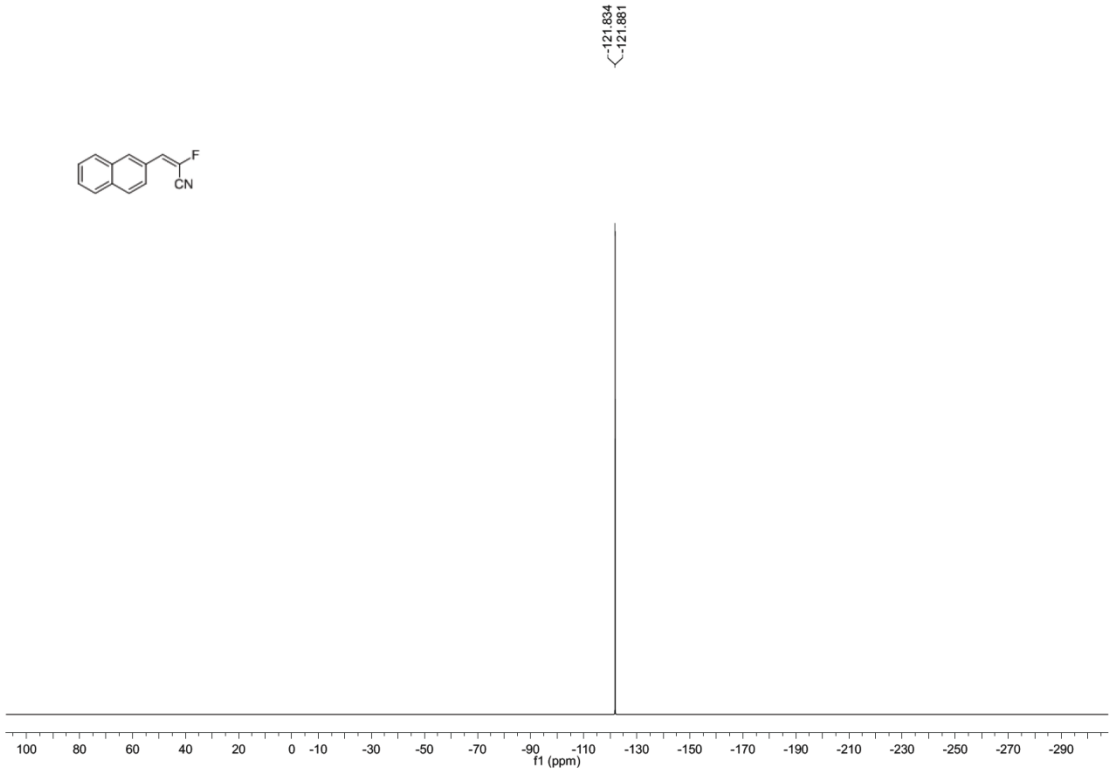
4-^{1}H NMR (400 Hz, $CDCl_3$)



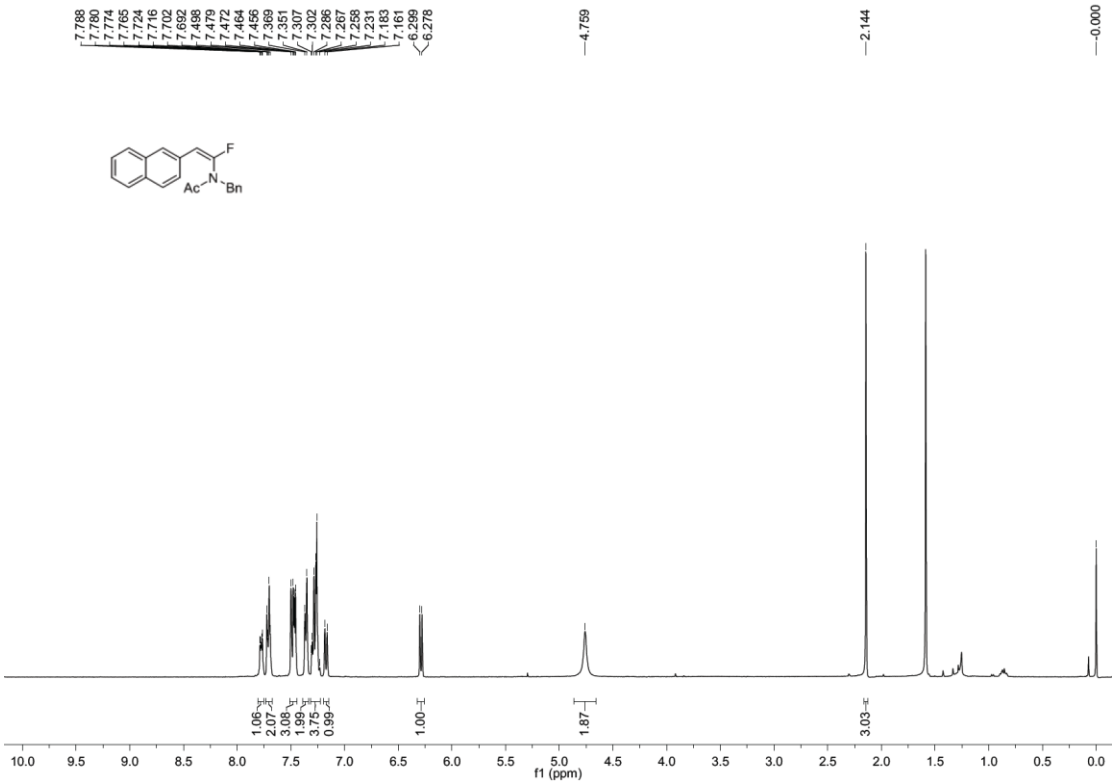
4-^{13}C NMR (100 Hz, $CDCl_3$)



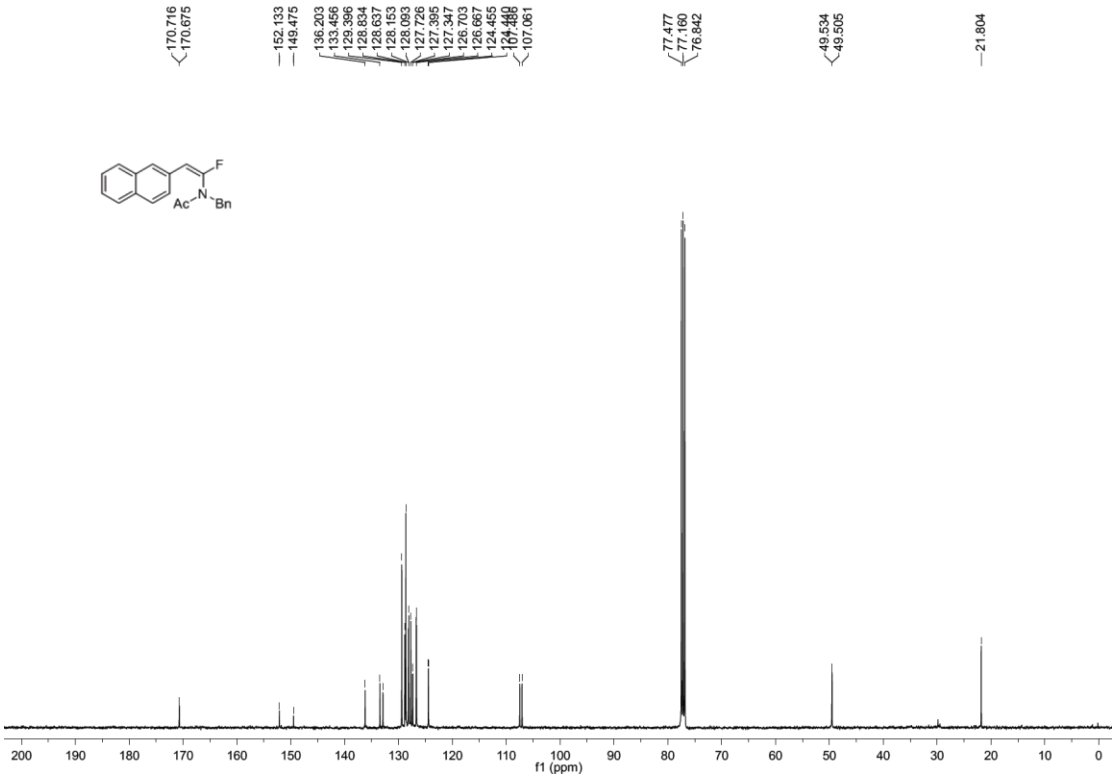
4-^{19}F NMR (376 Hz, $CDCl_3$)



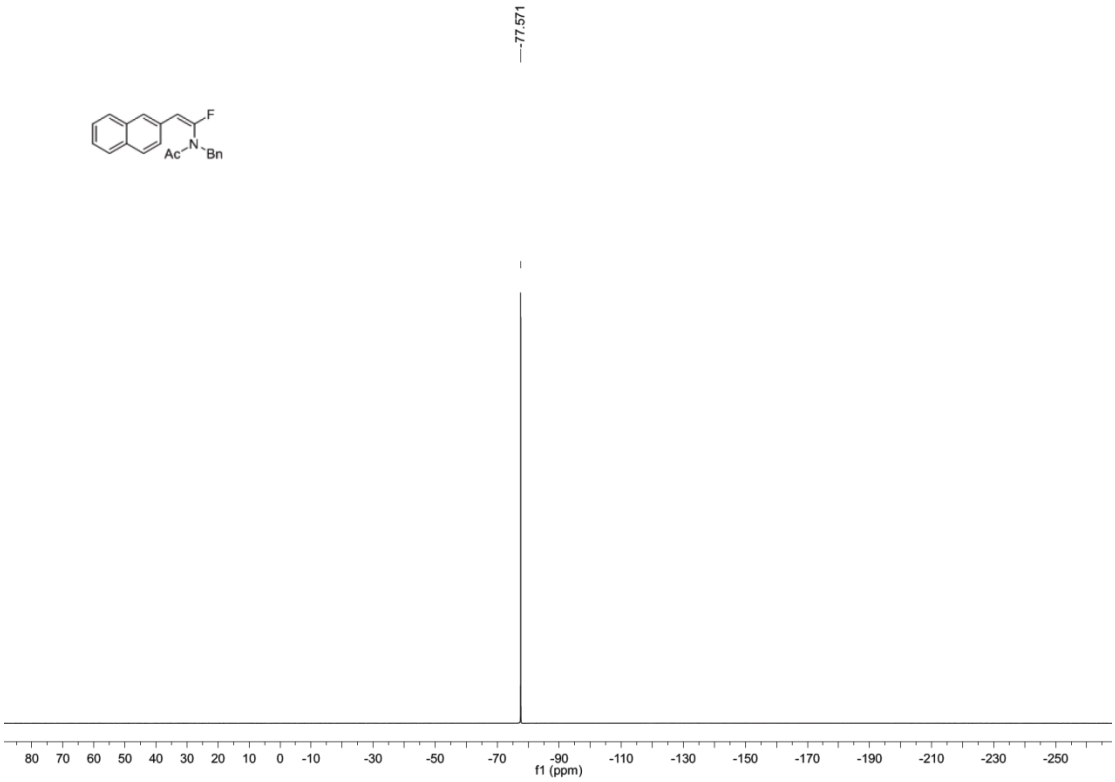
5-^{1}H NMR (400 Hz, $CDCl_3$)



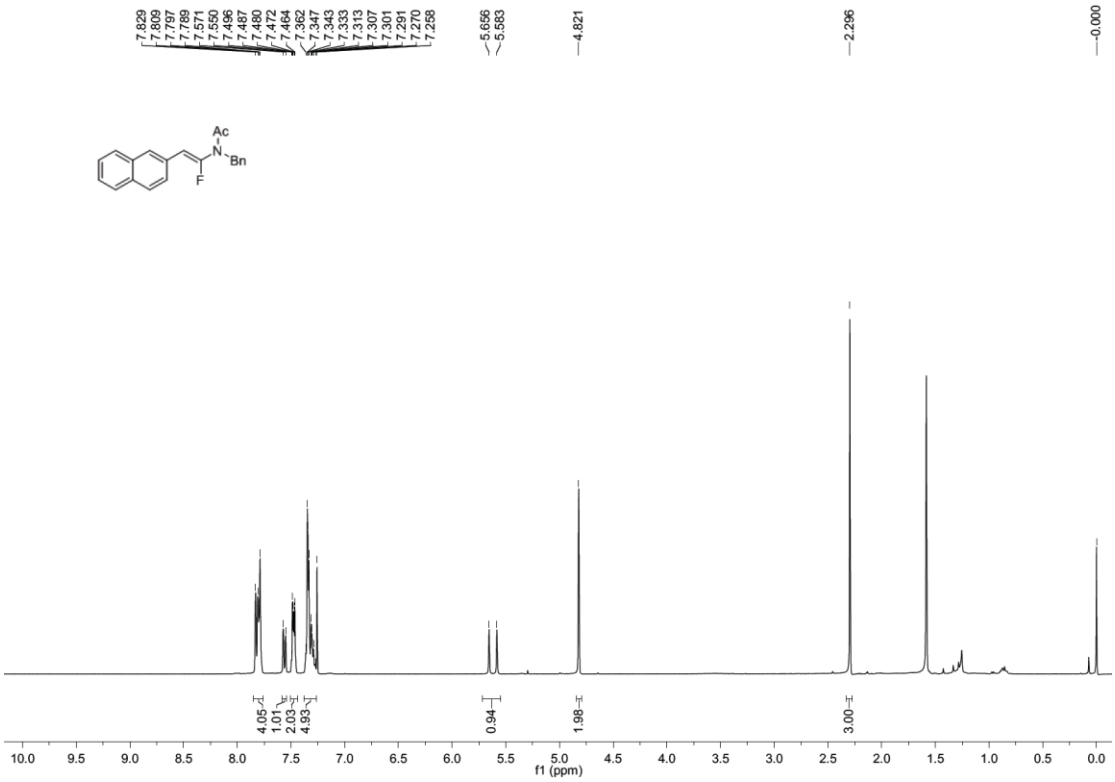
5-^{13}C NMR (100 Hz, $CDCl_3$)



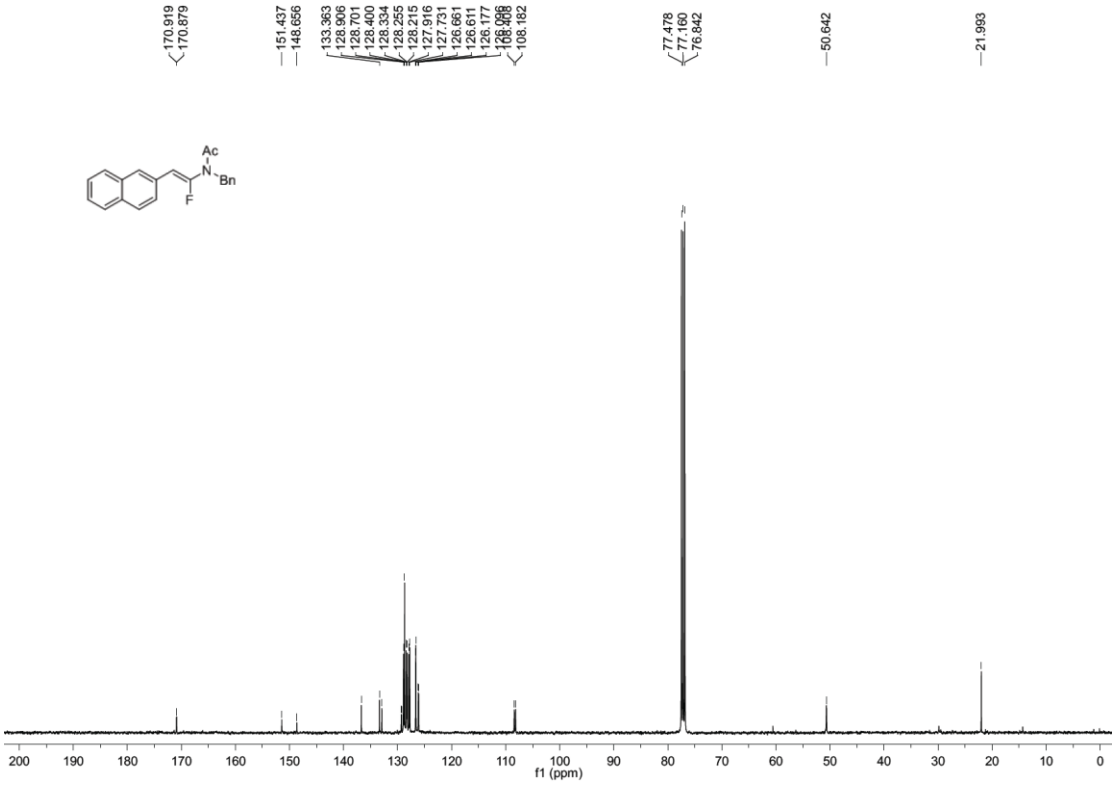
5-^{19}F NMR (376 Hz, $CDCl_3$)



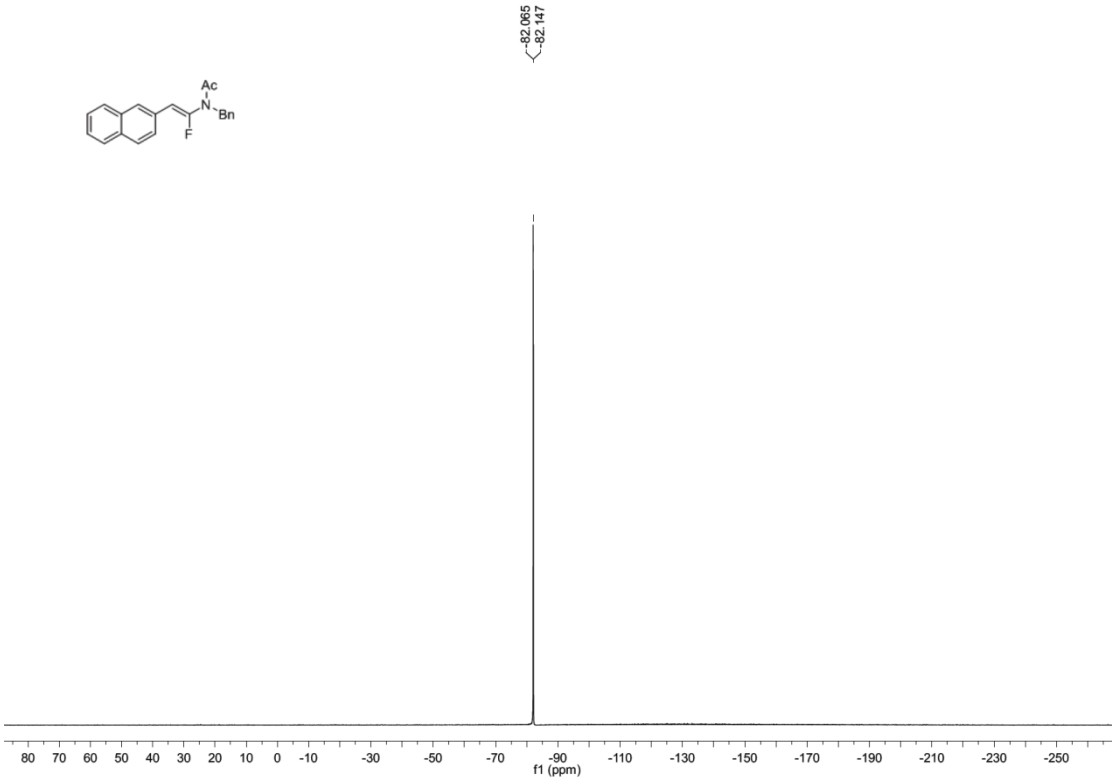
5'-^{1}H NMR (400 Hz, $CDCl_3$)



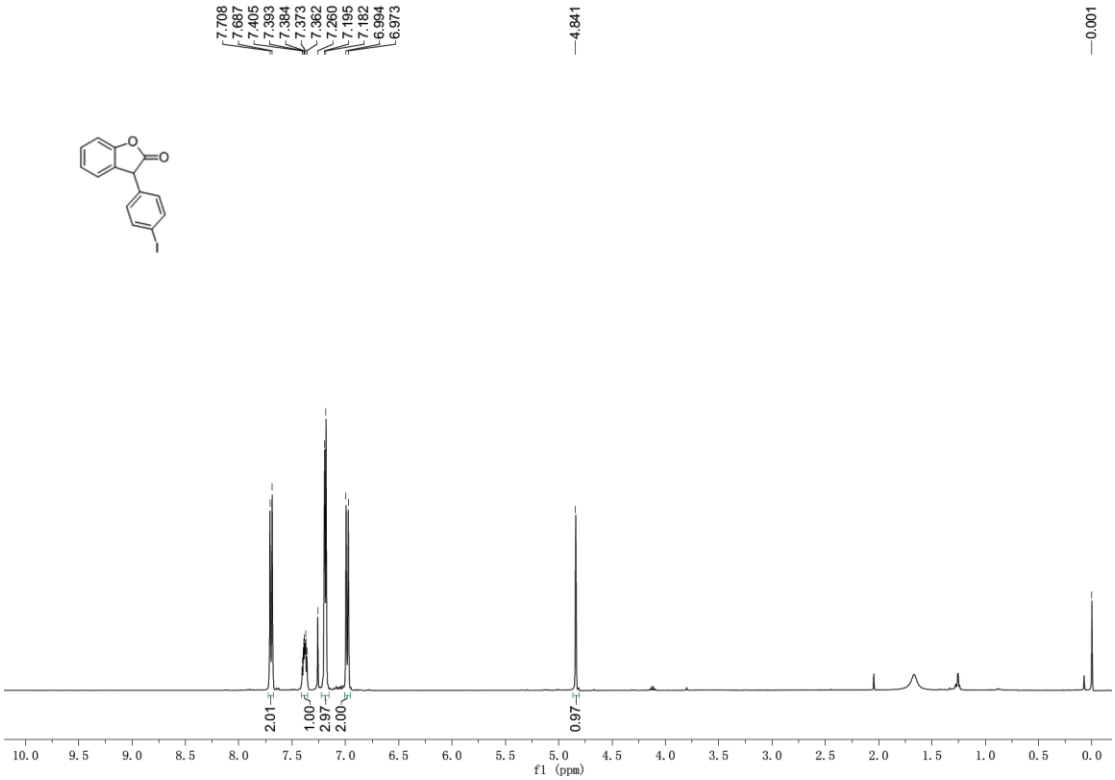
5'-^{13}C NMR (100 Hz, $CDCl_3$)



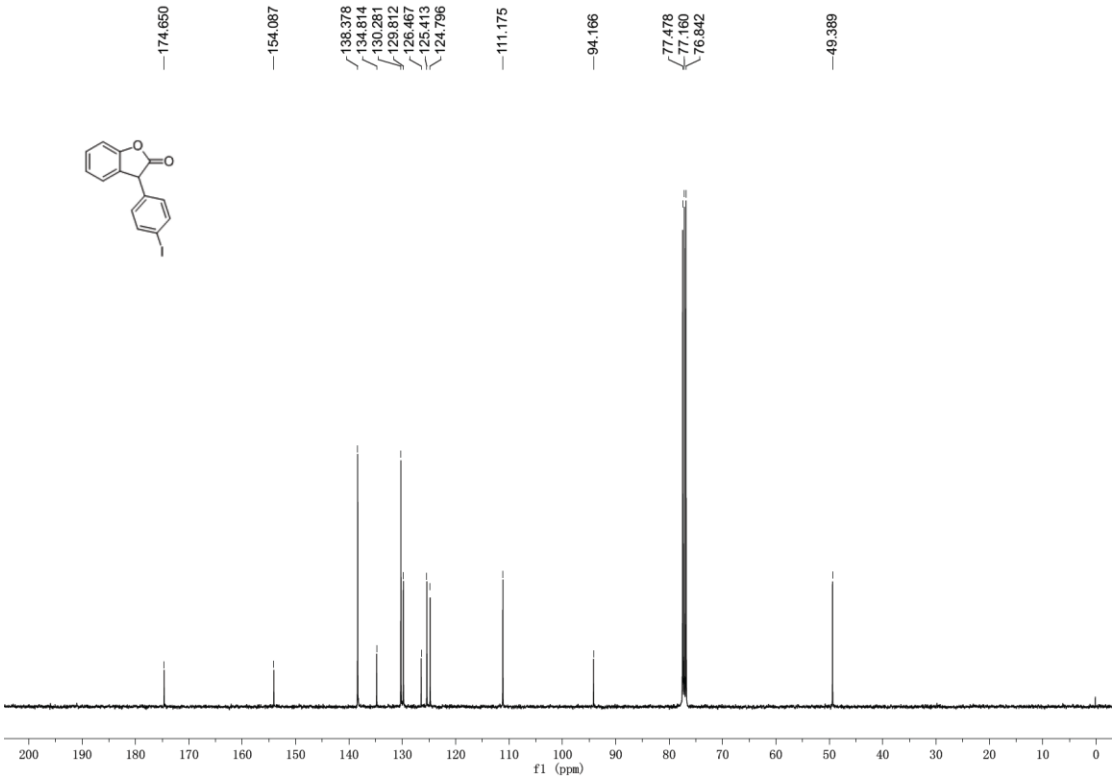
5'-^{19}F NMR (376 Hz, $CDCl_3$)



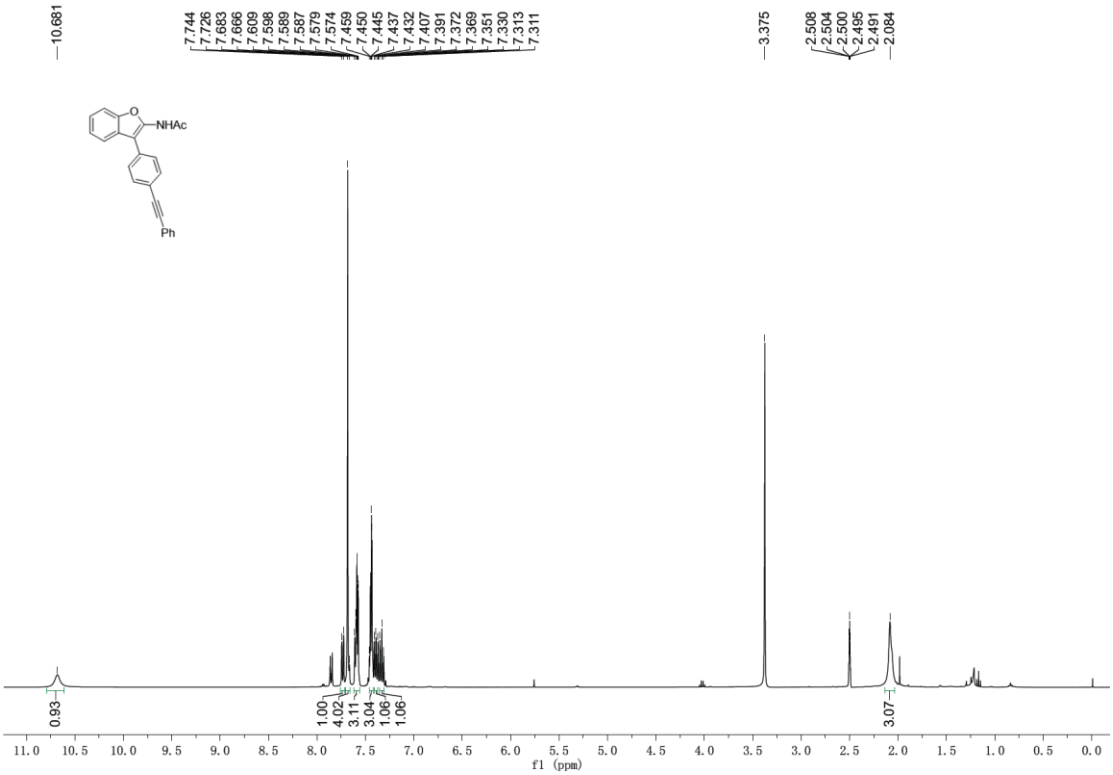
6-^{1}H NMR (400 Hz, $CDCl_3$)



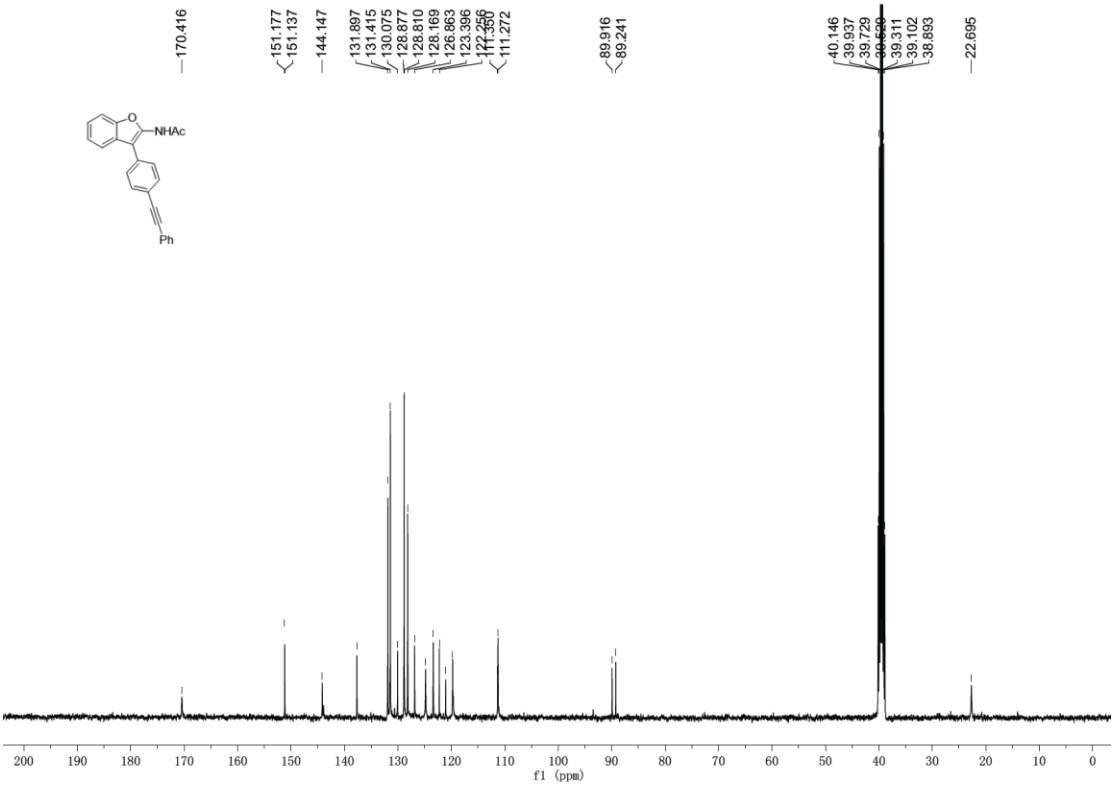
6-^{13}C NMR (100 Hz, $CDCl_3$)



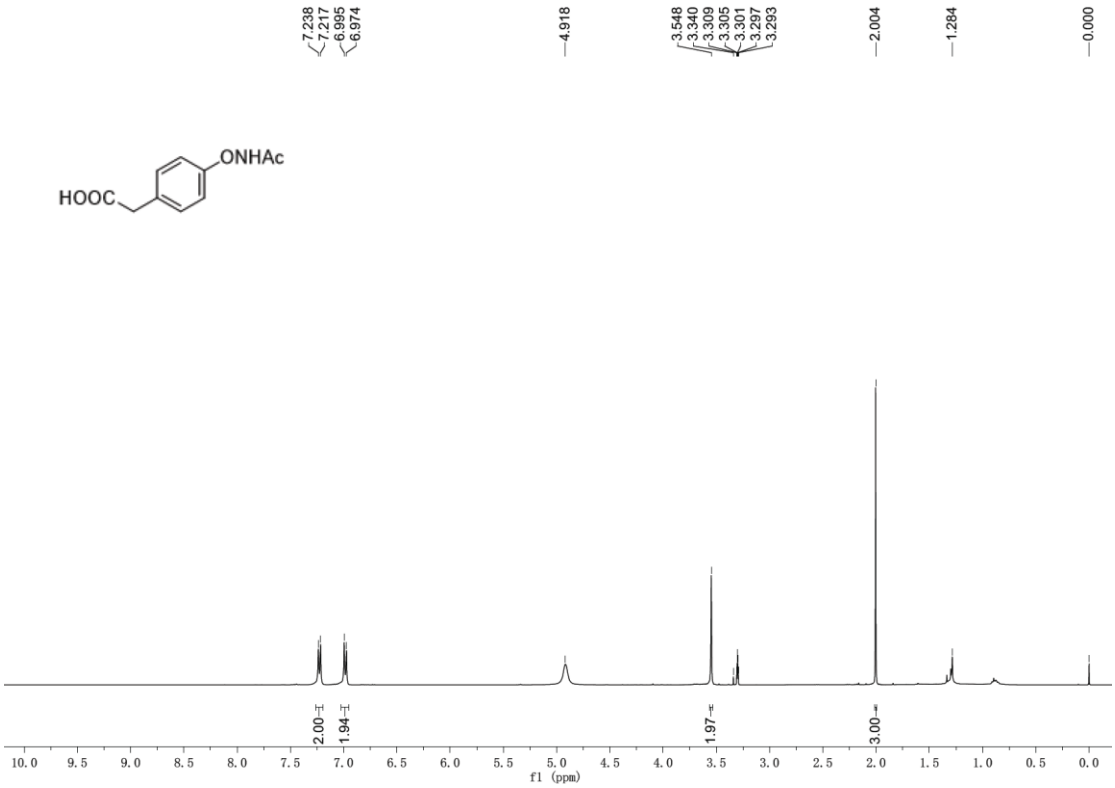
7-^{1}H NMR (400 Hz, DMSO-d_6)



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



2-(4-(acetamidooxy)phenyl)acetic acid -^{1}H NMR (400 Hz, CD_3OD)



2-(4-(acetamidooxy)phenyl)acetic acid -^{13}C NMR (100 Hz, CD_3OD)