Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Rh (III)-Catalyzed Redox-Neutral C-H Alkylation Reaction with Allylic Alcohols by Using a Traceless Oxidizing Directing Group

Yubo Wang,[ab] Yu Chen,[*a] Yaxi Yang[b] and Bing Zhou[*b]

[a] College of Chemistry and Materials Science, South-Central University for Nationalities, Wuhan 430074, PR China

[b] Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Shanghai 201203, PR China

Corresponding Author

* E-mail: chenyuwh888@126.com; zhoubing@simm.ac.cn

Table of contents:

General methods:

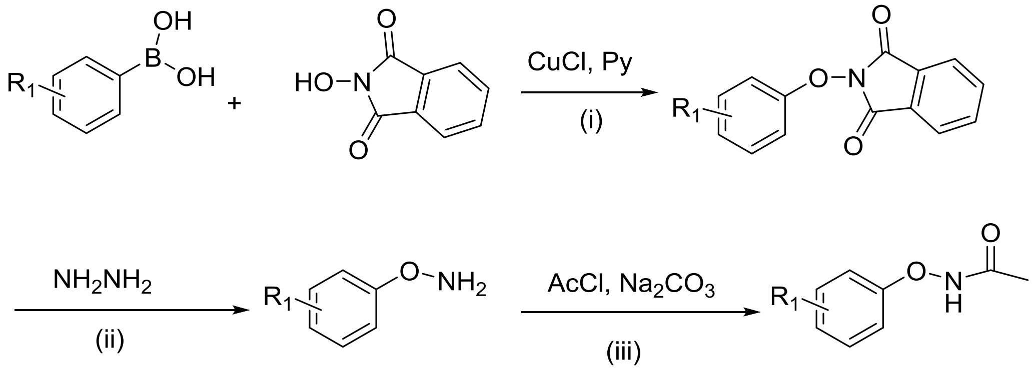
Mass spectra and high-resolution mass spectra were measured on a Finnigan MAT-95 mass spectrometer. ^{1}H and ^{13}C NMR spectra were determined on Bruker AM-300, Bruker AM-400, Bruker AM-500 instruments using tetramethylsilane as internal reference. Datas are presented as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, br d = broad doublet, t = triplet, m = multiplet), J = coupling constant in hertz (Hz). Silica gel 60H (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China) was used for general chromatography.

Materials:

All reagents were purchased from commercial sources, such as *Strem Chemicals*, *Adamas-beta*, *Sigma-Aldrich*, *J&K* and *TCI*, which were used without further purification, unless otherwise indicated. $[Cp^{*}RhCl_2]_2$[S1], the starting materials **1**[S2] and allylic alcohol **2**[S3] were synthesized according to published procedures.

General procedure for the synthesis of N-phenoxyacetamides:

Method A:



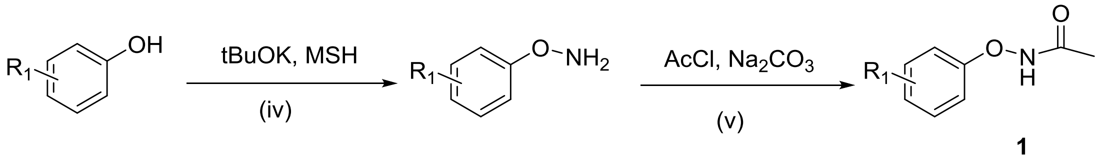
1

(i) *N*-aryloxyphthalimides were prepared following a published procedure reported: In a reaction flask, a mixture of *N*-hydroxyphthalimide (1.0 equiv), arylboronic acid (2.0 equiv), CuCl (1.0 equiv), freshly activated 4Å molecular sieves (250 mg/mmol) and pyridine (1.1 equiv) in 1,2-dichloroethane (DCE, 0.2 M) were stirred at room temperature. The reaction flask was open to atmosphere. After 24-48 h, the reaction mixture became green as the reaction proceeded. 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 *N*-aryloxyphthalimides.

(ii) Hydrazine monohydrate (4.0 equiv., 51%-64%) was added to the solution of *N*-aryloxyphthalimide (1.0 equiv.) in DCM (0.25 M). The reaction was stirred at room temperature overnight. $MgSO_4$ was added to the mixture and the suspension was stirred for additional 10 minutes. The precipitate was filtered off and washed with DCM. The filtrate was concentrated and the resulting oil *N*-aryloxyamines was directly used without further purification.

(iii) *N*-aryloxyamine (1.0 equiv.) was dissolved in ether (0.2 M).The flask was cooled in an ice bath, to which acyl chloride (1.1 eq.) was slowly added. The ice bath was allowed to warm to room temperature and the mixture was stirred for 3 h at room temperature. The reaction was quenched with saturated $NaHCO_3$ and extracted with EtOAc. The organic phase was washed three times with saturated $NaHCO_3$ and dried over $NaSO_4$.The solvent was evaporated under reduced pressure. The crude product was purified by recrystallization from EtOAc/PE to afford the desired *N*-aryloxyacetamide **1** as colorless crystals.

Method B:

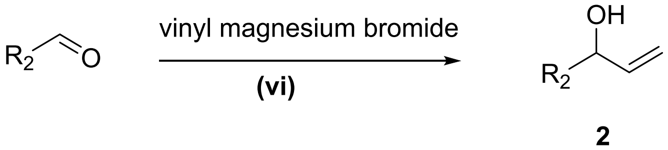


1

(iv) Phenols (1.0 equiv.) was dissolved in methanol (0.25 M), and then potassium tert-butoxide (1.0 equiv.) was added. The mixture was allowed to stir for 0.5 h under N_2 atmosphere. The methanol was removed, and the residue was taken up in DCM. Then the freshly prepared *O*-mesitylsulfonylhydroxylamine (MSH, 1.0 equiv.) was added under ice cooling. The mixture was allowed to stir for 1 h, dichloromethane was then removed under reduce pressure to afford the corresponding *N*-aryloxyamine.

(v) *N*-aryloxyamine (1.0 equiv.) was dissolved in ether (0.2 M).The flask was cooled in an ice bath, to which acyl chloride (1.1 eq.) was slowly added. The ice bath was allowed to warm to room temperature and the mixture was stirred for 3 h at room temperature. The reaction was quenched with saturated $NaHCO_3$ and extracted with EtOAc. The organic phase was washed three times with saturated $NaHCO_3$ and dried over $NaSO_4$.The solvent was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography to give the *N*-aryloxyacetamide **1**.

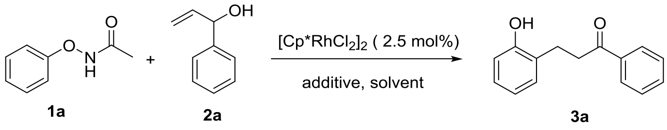
General procedure for the synthesis of allylic alcohol



2

(vi) Aldehyde (1.0 equiv.) was dissolved in dry THF (20 mL). The solution was cooled to 0 ℃ and vinyl magnesium bromide (1 M in THF, 1.2 equiv.) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 4 h. The reaction was quenched by addition of sat. aq. NH_4Cl (equal volume), the phases were separated and the aqueous phase was extracted with EtOAc (3 × equal volume). The combined organic phases were washed with brine, dried over Na_2SO_4. The solvent was evaporated under reduced pressure and purified by silica gel column chromatography to give the allylic alcohol **2**.

Table S1. Optimization of reaction conditions.[a]

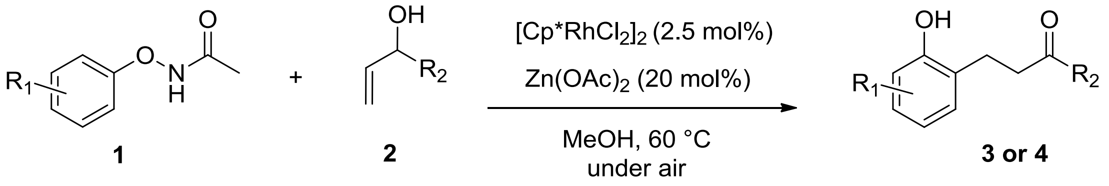


entry	additive	solvent	yield%[b]
1	CsOAc	MeOH	27
2	KOAc	MeOH	19
3	$Cu(OAc)_2$	MeOH	10
4	AgOAc	MeOH	30
5	**$Zn(OAc)_2$**	**MeOH**	**90**
6	$Zn(OAc)_2$	DCE	12

7	$Zn(OAc)_2$	Toluene	15
8	$Zn(OAc)_2$	DMF	55
9	$Zn(OAc)_2$	Dioxane	60
10	$Zn(OAc)_2$	Acetone	69
11[c]	$Zn(OAc)_2$	MeOH	84
12	-	MeOH	0
13[d]	$Zn(OAc)_2$	MeOH	0
14	$AgSbF_6$	MeOH	40

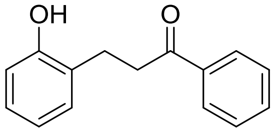
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %) and additive (20 mol %) in solvent (1.0 mL) at 60 ℃ for 8 h, [b] Isolated yields. [c] 1.25 mol% $[Cp^*RhCl_2]_2$ and 10 mol% $Zn(OAc)_2$ were used. [d] No $[Cp^*RhCl_2]_2$ was used.

General Procedures for Rh(III)-Catalyzed C-H alkylation with allylic alcohols



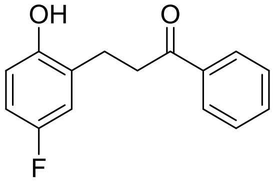
$[Cp^*RhCl_2]_2$ (2.5 mol %), $Zn(OAc)_2$ (20 mol%), *N*-aryloxyacetamide **1** (0.2 mmol), allylic alcohol **2** (0.3 mmol, 1.5 equiv) and MeOH (1 mL) were added into a test tube under air. The reaction mixture was stirred at 60 ^{o}C for 8 h. After the completion of the reaction (monitored by TLC) the reaction mixture was cooled to room temperature, and diluted with DCM and passed through a short silica gel (100 − 200 mesh size) bed, and repeatedly washed with DCM (20 mL × 3 times). The combined organic layers were concentrated under reduced pressure and the crude product was purified on a silica gel column directly to give the corresponding product **3** or **4**.

Spectroscopic data of all final Compounds



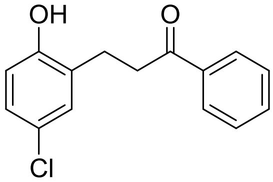
3a

The title compound was obtained in 90% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.01 (s, 1H), 7.98 (m, 2H), 7.61 – 7.54 (m, 1H), 7.48 – 7.42 (m, 2H), 7.16 – 7.09 (m, 2H), 6.93 (dd, *J* = 8.1, 0.8 Hz, 1H), 6.87 (td, *J* = 7.4, 1.2 Hz, 1H), 3.48 – 3.43 (t, *J* = 6.0 Hz, 2H), 3.08 – 3.00 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 202.2, 154.6, 136.2, 133.9, 130.7, 128.8, 128.5, 128.1, 127.9, 40.5, 23.5. HRMS (ESI$^+$): calcd for $C_{15}H_{15}O_2$ [M+H]$^+$ 227.1067, found 227.1065.



3b

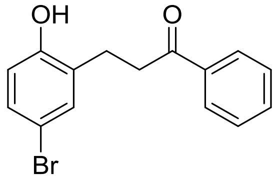
The title compound was obtained in 81% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.07 – 7.91 (m, 3H), 7.64 – 7.58 (m, 1H), 7.52 – 7.44 (m, 2H), 6.94 – 6.73 (m, 3H), 3.48 (dd, *J* = 6.5, 5.3 Hz, 2H), 3.08 – 2.95 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 201.8, 157.0 (d, *J* = 236.2 Hz), 150.5, 135.9, 133.9, 129.1 (d, *J* = 6.25 Hz), 128.7, 128.4, 118.5 (d, *J* = 8.75 Hz), 116.4 (d, *J* = 22.5 Hz), 114.3 (d, *J* = 22.5 Hz), 40.2, 23.5. HRMS (ESI$^+$): calcd for $C_{15}H_{14}FO_2$ [M+H]$^+$ 245.0972, found 245.0976.



3c

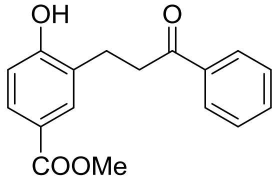
The title compound was obtained in 76% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.23 (s, 1H), 7.97 (m, 2H), 7.61 – 7.56 (m, 1H), 7.49 – 7.42 (m, 2H), 7.09 (d, *J* = 2.6 Hz, 1H), 7.06 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 3.49

– 3.40 (m, 2H), 3.03 – 2.94 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.1, 153.4, 135.9, 134.2, 130.3, 129.6, 128.7, 128.5, 127.9, 125.3, 119.1, 40.4, 23.4. HRMS (ESI$^+$): calcd for $C_{15}H_{14}ClO_2$ [M+H]$^+$ 261.0677, found 261.0671.



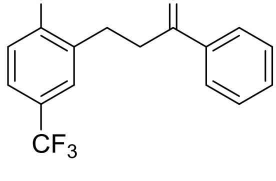
3d

The title compound was obtained in 83% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.26 (brs, 1H), 7.97 (m, 2H), 7.63 – 7.55 (m, 1H), 7.46 (m, 2H), 7.24 (d, J = 2.5 Hz, 1H), 7.19 (dd, J = 8.6, 2.5 Hz, 1H), 6.81 (d, J = 8.6 Hz, 1H), 3.49 – 3.41 (m, 2H), 3.01 – 2.95 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.1, 153.9, 135.9, 134.2, 133.2, 130.9, 130.2, 128.8, 128.5, 119.7, 112.6, 40.4, 23.3. HRMS (ESI$^+$): calcd for $C_{15}H_{14}BrO_2$ [M+H]$^+$ 305.0172, found 305.0169.



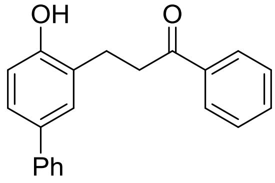
3e

The title compound was obtained in 84% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.82 (s, 1H), 8.02 – 7.94 (m, 2H), 7.86 (d, J = 2.1 Hz, 1H), 7.80 (dd, J = 8.5, 2.2 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 6.93 (d, J = 8.5 Hz, 1H), 3.87 (s, 3H), 3.53 – 3.44 (m, 2H), 3.11 – 3.02 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.4, 167.2, 159.3, 135.9, 134.2, 132.9, 130.2, 128.9, 128.5, 127.7, 122.5, 117.6, 51.9, 40.4, 23.4. HRMS (ESI$^+$): calcd for $C_{17}H_{17}O_4$ [M+H]$^+$ 285.1121, found 285.1129.



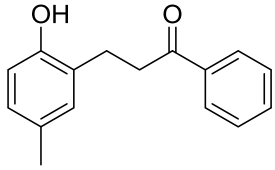
3f

The title compound was obtained in 83% yield as an amorphous solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.06 – 7.94 (m, 2H), 7.63 (ddd, J = 6.8, 4.0, 1.3 Hz, 1H), 7.52 (m, 3H), 7.39 (dd, J = 8.4, 2.0 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 3.36 – 3.29 (t, J = 7.6 Hz,, 2H), 2.93 (t, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.8, 159.1, 136.9, 133.6, 129.1, 128.6, 128.3, 127.4 (q, J = 4.0 Hz), 125.3 (d, J = 269 Hz), 124.9 (q, J = 4.0 Hz), 119.8 (q, J = 31 Hz), 115.4, 37.9, 24.8. HRMS (ESI$^+$): calcd for $C_{16}H_{14}F_3O_2$ [M+H]$^+$ 295.0940, found 295.0935.



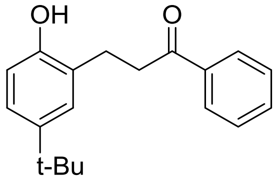
3g

The title compound was obtained in 90% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.13 (s, 1H), 8.00 (m, 2H), 7.61 – 7.56 (m, 1H), 7.54 (m, 2H), 7.45 (m, 2H), 7.43 – 7.38 (m, 2H), 7.36 (m, 2H), 7.32 – 7.27 (m, 1H), 7.02 – 6.97 (m, 1H), 3.54 – 3.48 (m, 2H), 3.13 – 3.08 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.2, 154.3, 141.1, 136.2, 134.0, 129.5, 128.8, 128.5, 128.2, 126.9, 126.8, 126.7, 118.1, 40.6, 23.7. HRMS (ESI$^+$): calcd for $C_{21}H_{19}O_2$ [M+H]$^+$ 303.1380, found 303.1383.



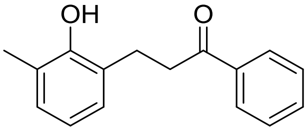
3h

The title compound was obtained in 74% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.98 (m, 2H), 7.78 (s, 1H), 7.61 – 7.53 (m, 1H), 7.45 (m, 2H), 6.92 (m, 2H), 6.82 (d, J = 8.0 Hz, 1H), 3.44 (m, 2H), 3.00 (m, 2H), 2.25 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.1, 152.3, 136.3, 133.8, 131.2, 129.9, 128.8, 128.6, 128.5, 127.6, 117.4, 40.6, 23.6, 20.6. HRMS (ESI$^+$): calcd for $C_{16}H_{17}O_2$ [M+H]$^+$ 241.1223, found 241.1222.



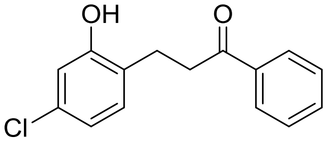
3i

The title compound was obtained in 77% yield as an amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.4 Hz, 2H), 7.83 (s, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.18 – 7.10 (m, 2H), 6.86 (d, *J* = 8.1 Hz, 1H), 3.50 – 3.42 (m, 2H), 3.09 – 2.98 (m, 2H), 1.29 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.1, 152.2, 143.5, 136.3, 133.8, 128.8, 128.5, 127.5, 127.1, 125.0, 116.9, 40.7, 34.1, 31.7, 24.1. HRMS (ESI$^+$): calcd for $C_{19}H_{23}O_2$ $[M+H]^+$ 283.1693, found 283.1694.



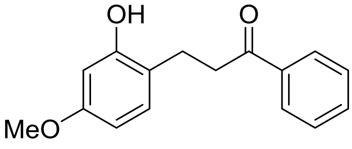
3j

The title compound was obtained in 72% yield as an amorphous solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.99 (m, 2H), 7.60 – 7.55 (m, 1H), 7.45 (m, 2H), 6.99 (m, 2H), 6.78 (m, 1H), 3.49 – 3.41 (m, 2H), 3.07 – 3.01 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.3, 152.9, 136.2, 133.9, 129.3, 128.8, 128.5, 128.2, 127.4, 126.3, 120.3, 40.7, 23.5, 16.6. HRMS (ESI$^+$): calcd for $C_{16}H_{17}O_2$ $[M+H]^+$ 241.1223, found 241.1228.



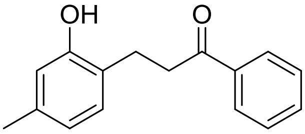
3k

The title compound was obtained in 76% yield as an amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.97 (m, 2H), 7.63 – 7.53 (m, 1H), 7.46 (m, 2H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.83 (dd, *J* = 8.1, 2.1 Hz, 1H), 3.48 – 3.37 (m, 2H), 3.02 – 2.93 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 155.5, 135.9, 134.2, 133.1, 131.5, 128.9, 128.5, 126.5, 120.9, 118.0, 40.2, 22.9. HRMS (ESI$^+$): calcd for $C_{15}H_{14}ClO_2$ [M+H]$^+$ 261.0677, found 261.0671.



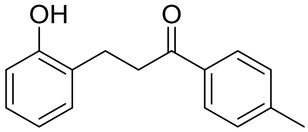
3l

The title compound was obtained in 64% yield as an amorphous solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H), 7.98 (m, 2H), 7.70 – 7.57 (m, 1H), 7.56 – 7.47 (m, 2H), 6.98 (t, J = 8.1 Hz, 1H), 6.52 – 6.40 (m, 2H), 3.72 (s, 3H), 3.12 – 3.02 (m, 2H), 2.92 – 2.81 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 200.4, 158.6, 156.3, 136.9, 133.5, 129.2, 128.4, 127.4, 115.2, 108.6, 102.3, 55.9, 38.4, 18.9. HRMS (ESI$^+$): calcd for $C_{16}H_{17}O_3$ [M+H]$^+$ 257.1172, found 257.1177.



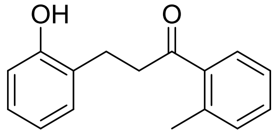
3m

The title compound was obtained in 70% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 – 7.97 (m, 2H), 7.95 (s, 1H), 7.63 – 7.56 (m, 1H), 7.47 (m, 2H), 7.04 (d, J = 7.7 Hz, 1H), 6.78 (s, 1H), 6.71 (d, J = 7.7 Hz, 1H), 3.47 – 3.44 (m, 2H), 3.05 – 3.02 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 203.5, 155.7, 139.4, 137.6, 135.1, 131.8, 130.0, 129.7, 126.1, 122.9, 119.4, 41.9, 24.6, 22.4. HRMS (ESI$^+$): calcd for $C_{16}H_{17}O_2$ [M+H]$^+$ 241.1223, found 241.1228.



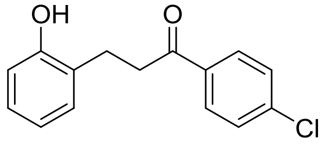
4a

The title compound was obtained in 85% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.17 (s, 1H), 7.88 (d, J = 8.3 Hz, 2H), 7.24 (m, 2H), 7.11 (m, 2H), 6.92 (dd, J = 8.5, 1.1 Hz, 1H), 6.86 (td, J = 7.5, 1.2 Hz, 1H), 3.46 – 3.41 (m, 2H), 3.05 – 3.01 (m, 2H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 201.8, 154.7, 144.9, 133.7, 130.7, 129.5, 128.6, 128.1, 128.0, 120.8, 117.6, 40.4, 23.5, 21.8. HRMS (ESI$^+$): calcd for $C_{16}H_{17}O_2$ [M+H]$^+$ 241.1223, found 241.1218.



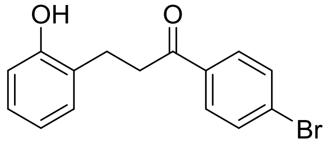
4b

The title compound was obtained in 76% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (s, 1H), 7.69 (dd, J = 8.2, 1.2 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.25 (m, 2H), 7.14 – 7.09 (m, 2H), 6.92 (dd, J = 8.5, 1.2 Hz, 1H), 6.86 (td, J = 7.4, 1.2 Hz, 1H), 3.40 – 3.36 (m, 2H), 3.04 – 3.00 (m, 2H), 2.49 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.9, 154.6, 139.1, 136.7, 132.4, 132.2, 130.7, 129.2, 128.1, 127.9, 125.9, 120.8, 117.5, 43.0, 23.9, 21.9. HRMS (ESI$^+$): calcd for $C_{16}H_{17}O_2$ [M+H]$^+$ 241.1223, found 241.1222.



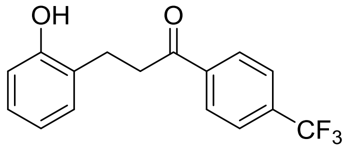
4c

The title compound was obtained in 79% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.95 – 7.84 (d, J = 8.6 Hz, 2H), 7.71 (s, 1H), 7.42 (d, J = 8.6 Hz, 2H), 7.17 – 7.07 (m, 2H), 6.91 (dd, J = 8.5, 1.0 Hz, 1H), 6.86 (td, J = 7.5, 1.1 Hz, 1H), 3.40 (m, 2H), 3.05 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.8, 154.5, 140.4, 134.6, 130.7, 129.8, 129.1, 128.2, 127.7, 120.9, 117.5, 40.4, 23.6. HRMS (ESI$^+$): calcd for $C_{15}H_{14}ClO_2$ [M+H]$^+$ 261.0677, found 261.0673.



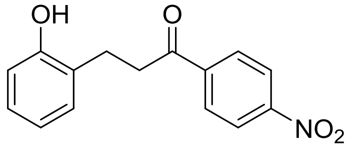
4d

The title compound was obtained in 81% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.86 – 7.78 (m, 2H), 7.70 (s, 1H), 7.62 – 7.55 (m, 2H), 7.16 – 7.07 (m, 2H), 6.91 (dd, J = 8.5, 1.1 Hz, 1H), 6.86 (td, J = 7.5, 1.1 Hz, 1H), 3.44 – 3.32 (m, 2H), 3.07 – 2.98 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 201.0, 154.5, 134.9, 132.1, 130.7, 129.9, 129.1, 128.2, 127.6, 120.9, 117.4, 40.4, 23.7. HRMS (ESI$^+$): calcd for $C_{15}H_{14}BrO_2$ [M+H]$^+$ 305.0172, found 305.0168.



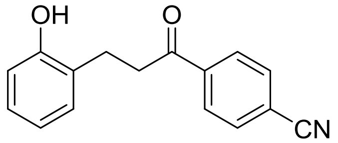
4e

The title compound was obtained in 75% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.08 (d, J = 8.2 Hz, 2H), 7.72 (d, J = 8.3 Hz, 2H), 7.37 (s, 1H), 7.16 – 7.08 (m, 2H), 6.92 – 6.85 (m, 2H), 3.45 (t, J = 6.2 Hz, 2H), 3.06 (t, J = 6.2 Hz, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.9, 154.4, 138.9, 134.9 (q, J = 32.5 Hz), 130.7, 128.8, 128.2, 127.4, 126.9 (q, J = 218.8 Hz), 125.8 (q, J = 3.75 Hz), 121.0, 117.3, 40.6, 23.7. HRMS (ESI$^+$): calcd for $C_{16}H_{14}F_3O_2$ [M+H]$^+$ 295.0940, found 295.0934.



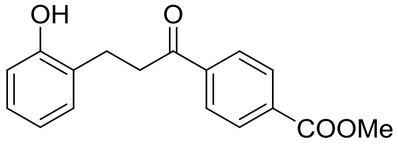
4f

The title compound was obtained in 60% yield as an amorphous solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 1H), 8.36 – 8.30 (m, 2H), 8.23 – 8.14 (m, 2H), 7.12 (dd, J = 7.5, 1.4 Hz, 1H), 7.02 (td, J = 7.8, 1.7 Hz, 1H), 6.80 (d, J = 7.6 Hz, 1H), 6.71 (td, J = 7.4, 1.0 Hz, 1H), 3.38 – 3.34 (m, 2H), 2.88 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.3, 155.6, 150.3, 141.6, 130.3, 129.8, 127.6, 127.2, 124.3, 119.4, 115.3, 39.2, 24.9. HRMS (ESI$^+$): calcd for $C_{15}H_{12}NO_4$ [M-H]$^+$ 270.0772, found 270.0775.



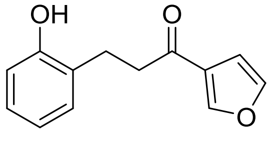
4g

The title compound was obtained in 63% yield as an amorphous solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.11 (d, J = 8.5 Hz, 2H), 7.99 (d, J = 8.5 Hz, 2H), 7.12 (m, 1H), 7.06 – 6.97 (m, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.71 (t, *J* = 7.3 Hz, 1H), 3.37 – 3.27 (m, 2H), 2.87 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.0, 155.2, 139.7, 132.8, 129.8, 128.6, 127.1, 126.8, 118.9, 118.2, 115.1, 114.8, 38.5, 24.6. HRMS (ESI$^+$): calcd for $C_{16}H_{14}NO_2$ [M+H]$^+$ 252.1019, found 252.1014.



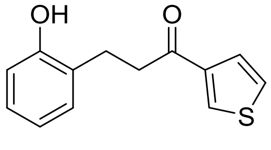
4h

The title compound was obtained in 77% yield as an amorphous solid. ^{1}H NMR (400 MHz, DMSO) δ 9.40 (s, 1H), 8.14 – 8.02 (m, 4H), 7.12 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.01 (td, *J* = 7.8, 1.7 Hz, 1H), 6.80 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.71 (td, *J* = 7.4, 1.1 Hz, 1H), 3.89 (s, 3H), 3.35 – 3.30 (m, 2H), 2.87 (t, *J* = 7.6 Hz, 2H).^{13}C NMR (100 MHz, DMSO) δ 199.7, 166.0, 155.6, 140.3, 133.5, 130.3, 129.9, 128.6, 127.5, 127.3, 119.3, 115.3, 52.9, 38.9, 25.0. HRMS (ESI$^+$): calcd for $C_{17}H_{17}O_4$ [M+H]$^+$ 285.1121, found 285.1119.



4i

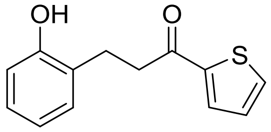
The title compound was obtained in 79% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.06 (s, 1H), 7.80 (s, 1H), 7.43 (m, 1H), 7.13 – 7.09 (m, 2H), 6.90 (d, *J* = 7.7 Hz, 1H), 6.87 – 6.83 (m, 1H), 6.75 (dd, *J* = 1.9, 0.8 Hz, 1H), 3.22 (m, 2H), 2.99 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 196.6, 154.2, 147.9, 144.3, 130.4, 128.1, 127.6, 127.0, 120.7, 117.4, 108.5, 41.8, 23.3. HRMS (ESI$^+$): calcd for $C_{13}H_{13}O_3$ [M+H]$^+$ 227.0859, found 227.0855.



4j

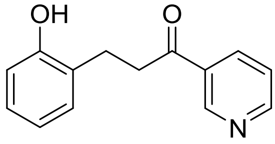
The title compound was obtained in 81% yield as an amorphous solid. ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.10 (dd, J = 2.9, 1.2 Hz, 1H), 7.98 (brs, 1H), 7.53 (dd, J = 5.1, 1.3 Hz, 1H), 7.30 (dd, J = 5.1, 2.9 Hz, 1H), 7.17 – 7.06 (m, 2H), 6.92 (dd, J = 8.5, 1.1 Hz, 1H), 6.86 (td, J = 7.4, 1.2 Hz, 1H), 3.36 (t, 2H), 3.01 (t, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.3, 154.6, 141.4, 133.1, 130.7, 128.1, 127.8, 126.9, 126.7, 120.8, 117.5, 41.6, 23.6. HRMS (ESI$^+$): calcd for $C_{13}H_{13}O_2S$ [M+H]$^+$ 233.0631, found 233.0625.



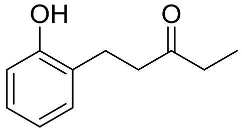
4k

The title compound was obtained in 80% yield as an amorphous solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, J = 3.8, 1.1 Hz, 1H), 7.75 (brs, 1H), 7.65 (dd, J = 4.9, 1.1 Hz, 1H), 7.15 – 7.08 (m, 3H), 6.91 (dd, J = 8.5, 1.2 Hz, 1H), 6.86 (td, J = 7.4, 1.2 Hz, 1H), 3.43 – 3.34 (m, 2H), 3.05 – 2.99 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.7, 154.6, 143.2, 134.6, 133.0, 130.7, 128.4, 128.2, 127.7, 120.9, 117.5, 40.9, 24.4. HRMS (ESI$^+$): calcd for $C_{13}H_{13}O_2S$ [M+H]$^+$ 233.0631, found 233.0625.



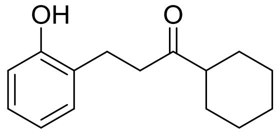
4l

The title compound was obtained in 61% yield as an amorphous solid. ^1H NMR (400 MHz, $CDCl_3$) δ 9.22 (d, J = 1.7 Hz, 1H), 8.77 (d, J = 5.9 Hz, 1H), 8.41 (brs,1H), 8.28 (dt, J = 8.0, 1.9 Hz, 1H), 7.44 (dd, J = 7.9, 4.8 Hz, 1H), 7.14 (dd, J = 7.5, 1.6 Hz, 1H), 7.09 (td, J = 7.8, 1.5 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.84 (t, J = 7.4 Hz, 1H), 3.42 (t, J = 6.7 Hz, 2H), 3.07 (t, J = 6.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.2, 154.8, 153.5, 149.7, 136.1, 132.1, 130.7, 128.1, 127.3, 124.1, 120.7, 116.7, 40.2, 24.7. HRMS (ESI$^+$): calcd for $C_{14}H_{14}NO_2$ [M+H]$^+$ 228.1019, found 228.1014.



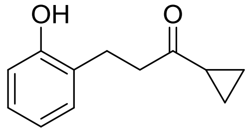
4m

The title compound was obtained in 65% yield as an amorphous solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.32 (s, 1H), 7.00 (m, 2H), 6.77 (dd, *J* = 8.0, 0.9 Hz, 1H), 6.69 (td, *J* = 7.4, 1.1 Hz, 1H), 2.75 – 2.59 (m, 4H), 2.42 (q, *J* = 7.3 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 211.0, 155.5, 130.1, 127.6, 127.4, 119.2, 115.1, 42.0, 35.3, 24.7, 8.1. HRMS (ESI$^+$): calcd for $C_{11}H_{15}O_2$[M+H]$^+$ 179.1067, found 179.1065.



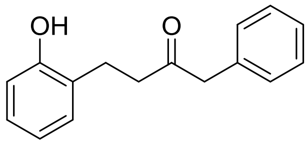
4n

The title compound was obtained in 71% yield as an amorphous solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (brs, 1H), 7.15 – 7.10 (m, 1H), 7.06 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.91 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.86 (td, *J* = 7.4, 1.2 Hz, 1H), 2.95 – 2.90 (m, 2H), 2.85 (dd, *J* = 7.2, 4.9 Hz, 2H), 2.36 (m, 1H), 1.79 (m, 4H), 1.37 – 1.17 (m, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 217.5, 154.6, 130.6, 128.0, 127.9, 120.7, 117.6, 50.8, 42.5, 28.6, 25.8, 25.7, 23.3. HRMS (ESI$^+$): calcd for $C_{15}H_{21}O_2$[M+H]$^+$ 233.1536, found 233.1532.



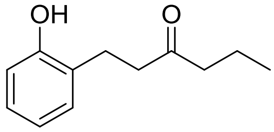
4o

The title compound was obtained in 72% yield as oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.21 (s, 1H), 7.14 (td, *J* = 7.8, 1.6 Hz, 1H), 7.08 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.92 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.87 (td, *J* = 7.4, 1.1 Hz, 1H), 3.13 – 3.07 (m, 2H), 2.92 – 2.82 (m, 2H), 1.96 (m, 1H), 1.13 – 1.08 (m, 2H), 0.98 – 0.91 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 214.3, 154.7, 130.7, 128.1, 127.9, 120.6, 117.8, 45.4, 23.4, 20.8, 12.2. HRMS (ESI$^+$): calcd for $C_{12}H_{15}O_2$ [M+H]$^+$ 191.1067, found 191.1066.



4p

The title compound was obtained in 76% yield as oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.32 (s, 1H), 7.29 (m, 2H), 7.23 (m, 1H), 7.19 – 7.14 (m, 2H), 7.00 (m, 2H), 6.76 (m, 1H), 6.68 (m, 1H), 3.75 (s, 2H), 2.78 – 2.72 (m, 2H), 2.72 – 2.66 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 207.7, 155.2, 135.0, 129.8, 129.7, 128.4, 127.1, 127.0, 126.6, 118.9, 114.9, 48.9, 41.7, 24.3. HRMS (ESI$^+$): calcd for $C_{16}H_{17}O_2$ [M+H]$^+$ 241.1223, found 241.1217.

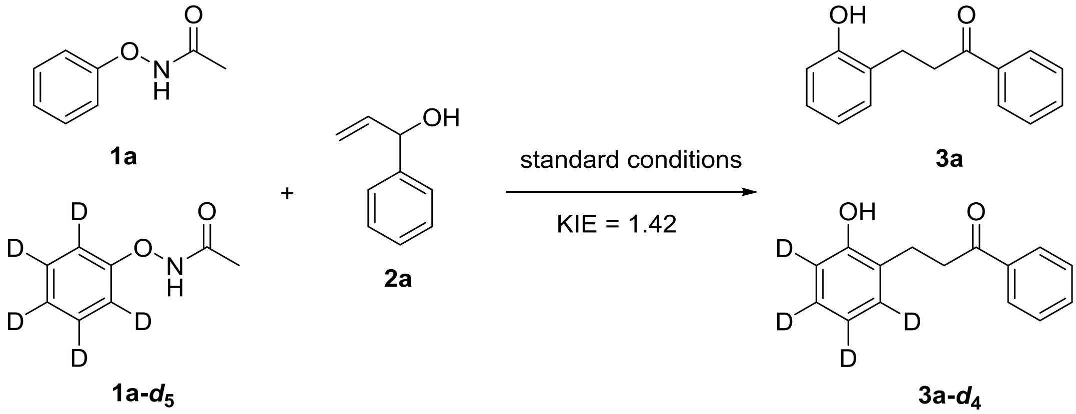


4q

The title compound was obtained in 68% yield as an amorphous solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.31 (s, 1H), 7.07 – 6.91 (m, 2H), 6.77 (dd, J = 8.0, 1.0 Hz, 1H), 6.69 (td, J = 7.4, 1.2 Hz, 1H), 2.75 – 2.60 (m, 4H), 2.39 (t, J = 7.2 Hz, 2H), 1.47 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 210.1, 155.1, 129.6, 127.1, 126.9, 118.8, 114.8, 43.7, 41.8, 24.2, 16.7, 13.6. HRMS (ESI$^+$): calcd for $C_{12}H_{17}O_2$ [M+H]$^+$ 193.1223, found 193.1218.

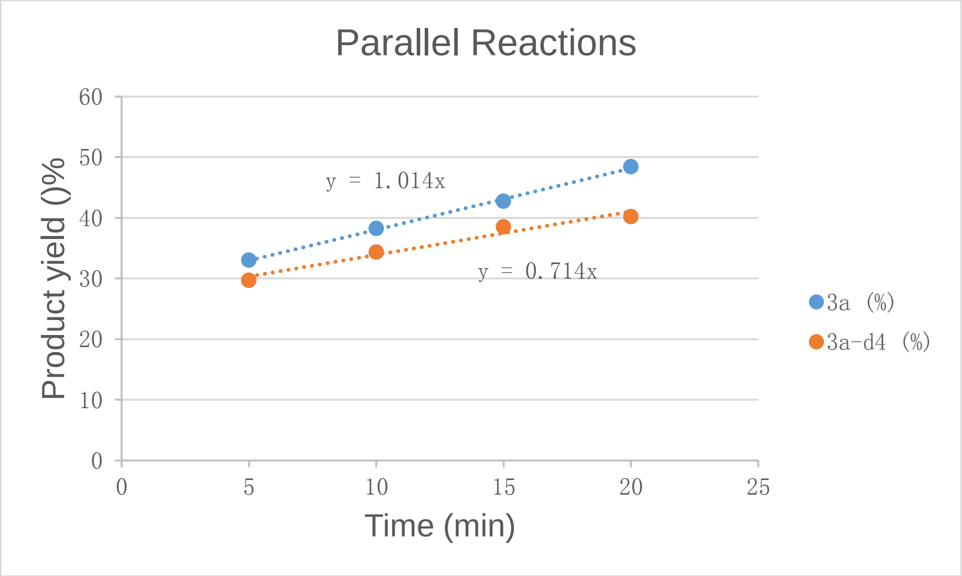
Mechanic Studies

General procedure for estimation of the KIE:

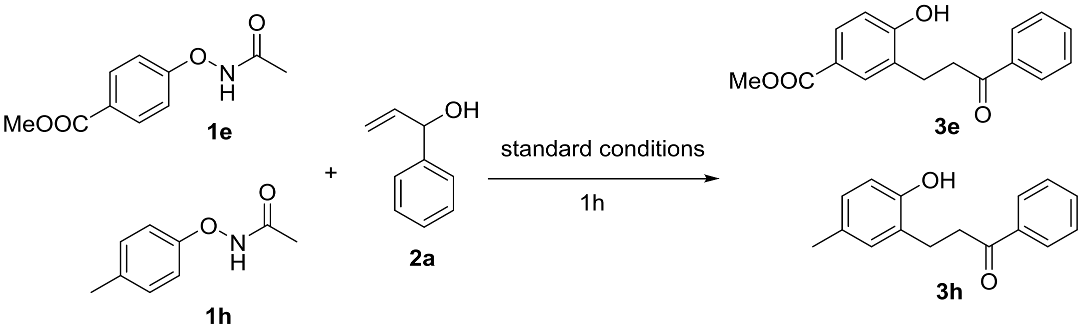


To two separate pressure tubes were charged with $[Cp^{*}RhCl_2]_2$ (0.01 mmol, 0.05 equiv.), $Zn(OAc)_2$ (0.04 mmol, 0.2 equiv.), **2a** (0.3 mmol, 1.5 equiv.), **1a** (0.2 mmol, 1 equiv.) or **1a-*d*$_5$** (0.2 mmol, 1 equiv.), and MeOH (1 mL). The two reaction mixtures were stirred at 60℃ in an oil bath. The solvent was rapidly carried out at 5, 10, 15 and 20 minutes. The samples were filtered over a plug of celite and evaporated under reduced pressure, added 1,2-dibromoethane (EDB) as internal substance. KIE value (k_H/k_D) was determined on the basis of ^{1}H NMR analysis.

Time/(min)	5	10	15	20
3a/(%)	33	38.2	42.7	48.4
3a-*d*$_4$/(%)	29.7	34.3	38.5	40.2



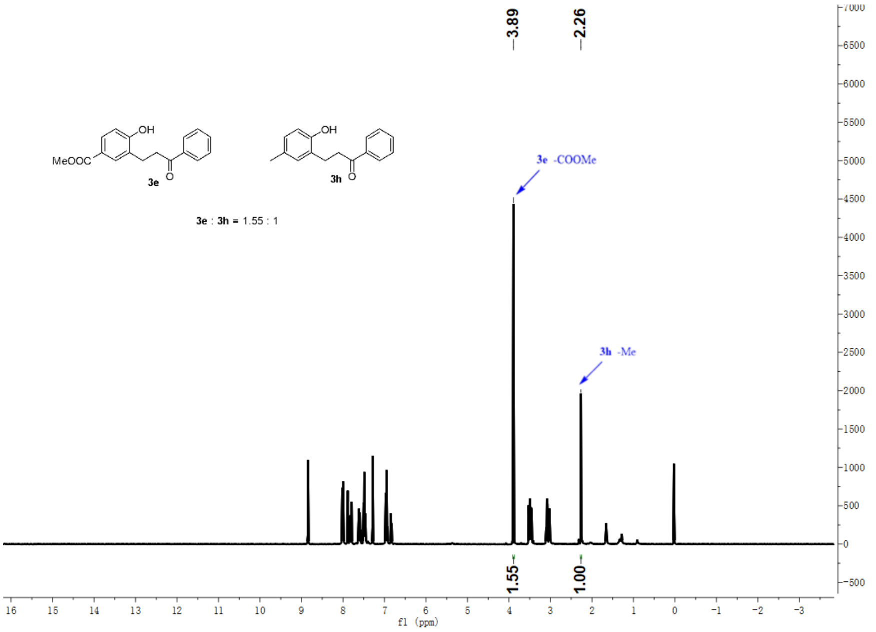
Intermolecular Competition Experiment:



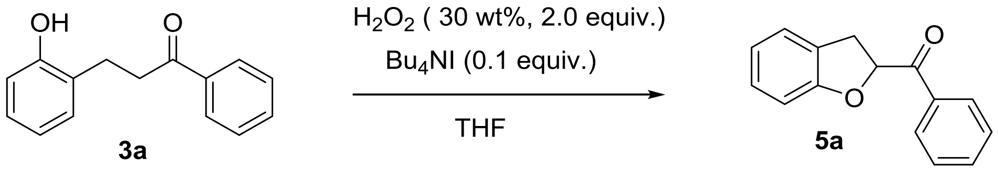
3e : **3h** = 1.55 : 1

An equimolar mixture of **1e** (0.1 mmol, 1 equiv.) and **1h** (0.1 mmol, 1 equiv.) were allowed to react with **2a** (0.15 mmol, 1.5 equiv.) in MeOH (1 mL) in the presence of

$[Cp^*RhCl_2]_2$ (0.05 mmol, 0.05 equiv.) and $Zn(OAc)_2$ (0.02 mmol, 0.2 equiv.). The reaction was stopped after 1 h, and the product generated was isolated by using column chromatography and was analyzed by ^{1}H-NMR. Product: **1.55:1**.



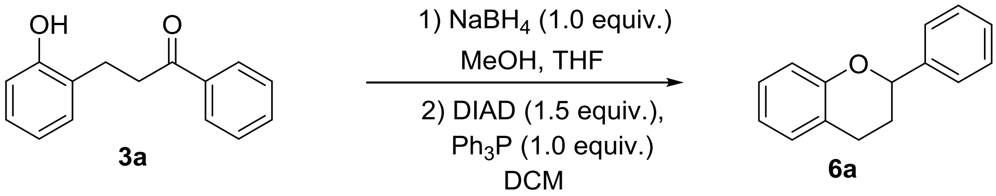
Procedure for Derivatization of 3a



To a stirring mixture of **3a** (1.0 mmol) and Bu_4NI (0.10 mmol) in THF (5.0 mL) was added 30 wt% hydrogen peroxide (2.0 mmol) at room temperature. The reaction was monitored by TLC analysis. After 5 h, the resulting mixture was poured into water (10 mL), and the aqueous phase was extracted with EtOAc (twice). The combined organic layers were washed with saturated Na_2SO_3 solution, brine, and water. The organic layers were dried over Na_2SO_4 and solvents were removed in *vacuo*. The crude residue was purified by silica gel column chromatography to give **5a** in 78% yield as a white amorphous solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.2, 1.0 Hz, 2H), 7.65 – 7.60 (m, 1H), 7.51 (m, 2H), 7.21 – 7.13 (m, 2H), 6.92 – 6.87 (m, 2H), 5.95 (dd, J = 9.5, 8.4 Hz, 1H), 3.58 (d, J = 9.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.6, 159.1, 134.6, 133.8, 129.2, 128.9, 128.5, 125.2, 124.9, 121.3, 109.9, 82.7, 32.7. HRMS (ESI$^+$): calcd for

$C_{15}H_{13}O_2[M+H]^+$ 225.0910, found 225.0908.



1) To a stirring mixture of **3a** (1.0 mmol) in THF (2 mL) and MeOH (2 mL) at 0 ℃ was added $NaBH_4$ (1.0 mmol). The reaction mixture was warmed to r.t. and stirred for 1 h. After cooling to 0 ℃, EtOAc (5 mL) was added and then the reaction was quenched with AcOH (0.5 mL). The organic layer was removed and the aqueous layer was extracted with EtOAc (5mL). The organic layers were combined and washed with brine. The organic solution was dried with Na_2SO_4, filtered and concentrated in *vacuo*. This crude residue was used in the following step without further purification.

2) The crude material was then dissolved in DCM (2 mL) and Ph_3P (1.5 mmol) was added. To this mixture was added DIAD (1.0 mmol) in DCM (1 mL) slowly at rome temperature. The reaction mixture was then stirred at rome temperature overnight, filtered and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give **6a** in 83% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H), 7.17 – 7.10 (m, 2H), 6.88 (m, 2H), 4.62 (dd, J = 10.4, 3.5 Hz, 1H), 2.96 (ddd, J = 14.2, 10.7, 6.1 Hz, 1H), 2.74 (ddd, J = 14.2, 6.4, 4.1 Hz, 1H), 2.11 (m, 1H), 2.00 – 1.87 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7, 144.0, 130.7, 128.7, 128.0, 127.8, 127.3, 125.9, 120.9, 116.4, 73.2, 39.5, 26.1. HRMS (ESI$^+$): calcd for $C_{15}H_{15}O$ $[M+H]^+$ 211.1117, found 221.1112.

Reference:

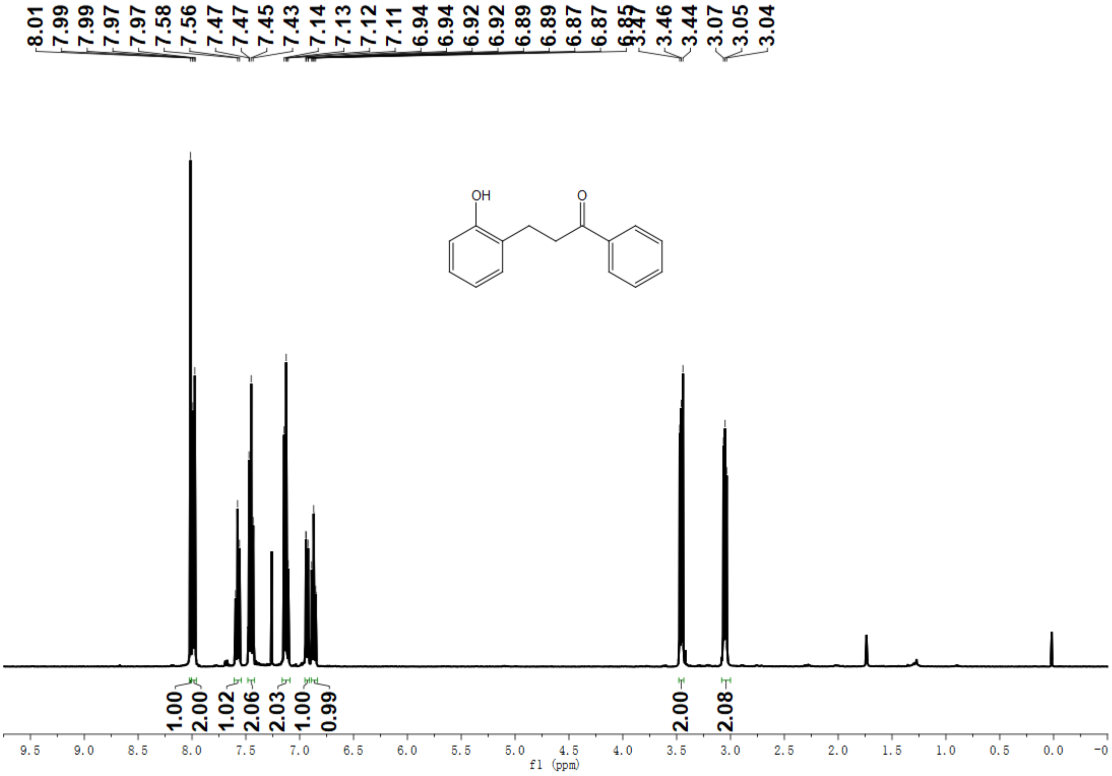
S1: K. Fujita, Y. Takahashi, M. Owaki, K. Yamamoto and R. Yamaguchi, *Org. Lett.*, 2004, **6**, 2785.

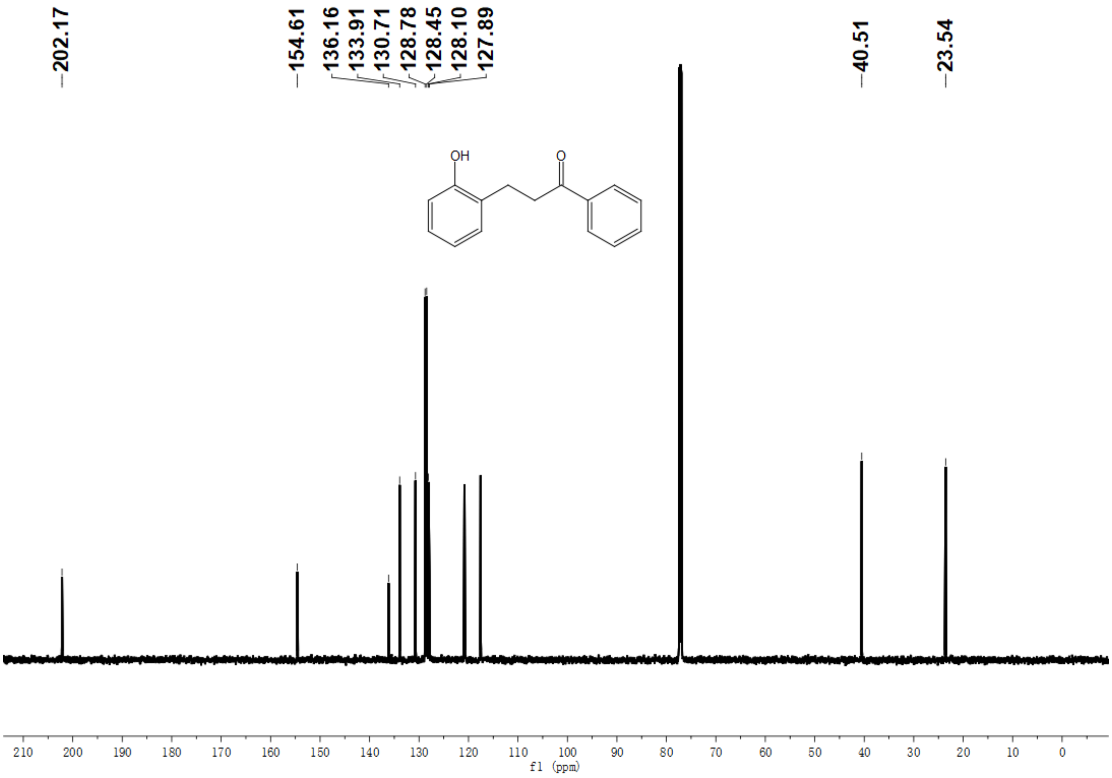
S2: B.-J. Li, J.-B. Lan, D. Wu and J.-S. You, *Angew. Chem. Int. Ed.*, 2016, **127**, 14214.

S3: Y.-Y. Jiang, J.-Y. Han, C.-Z. Yu, S. O. Vass, P. F. Searle, P. Browne, R. J. Knox and L.-Q. Hu, *J. Med. Chem.*, 2006, **49**, 4333.

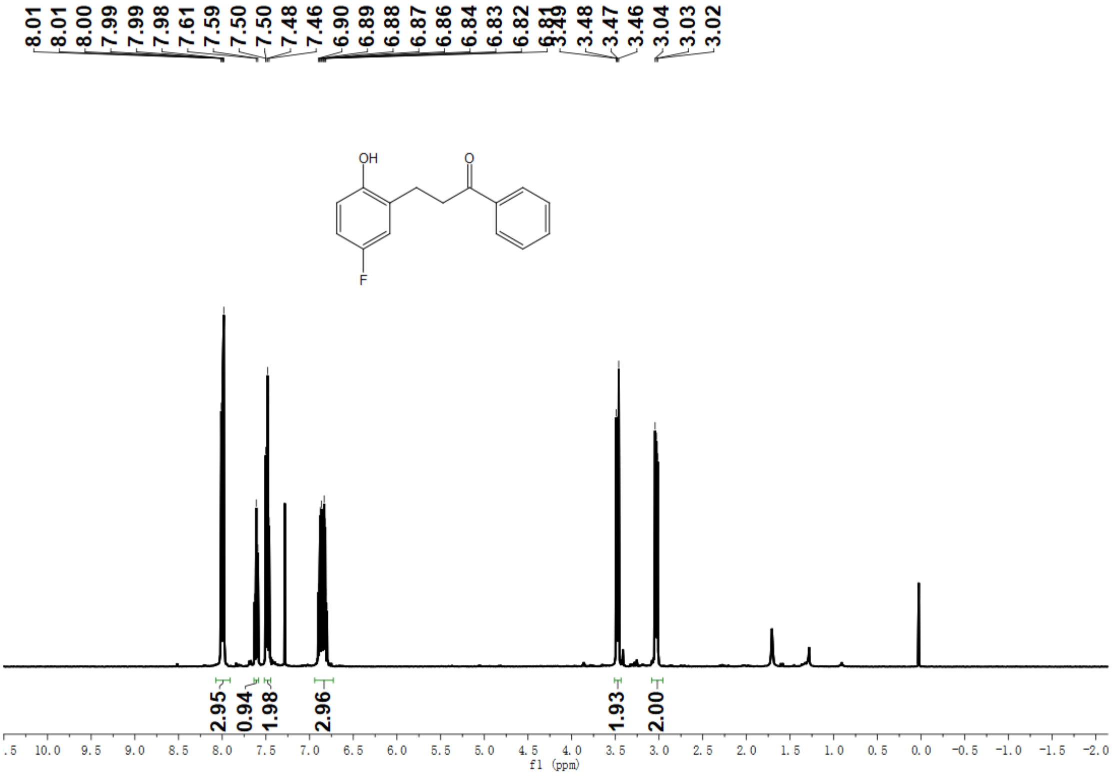
Copies of NMR Spectra Data

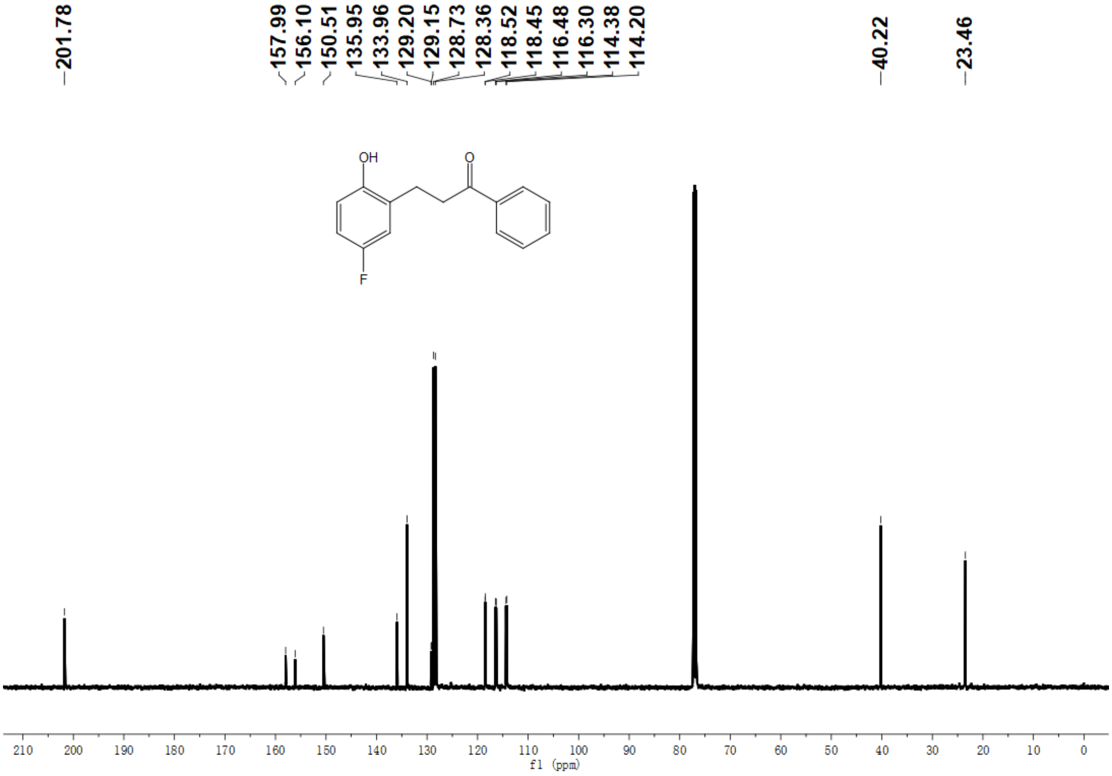
^{1}H and ^{13}C NMR Spectra of Compound **3a**



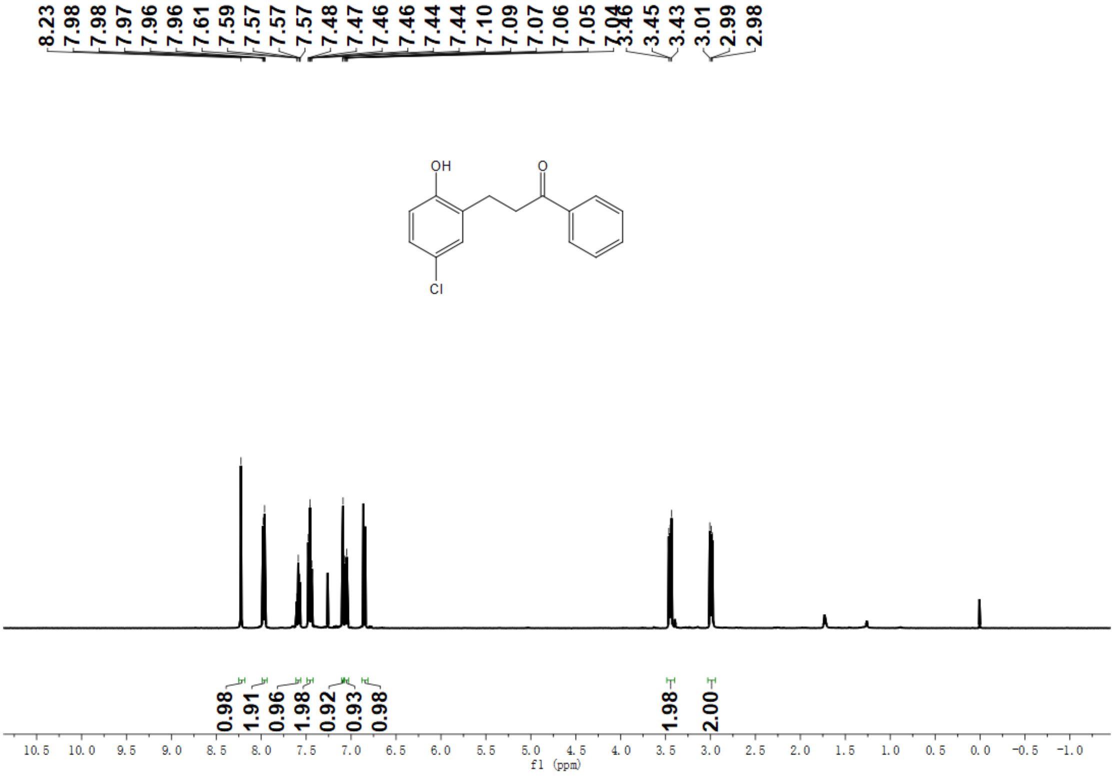


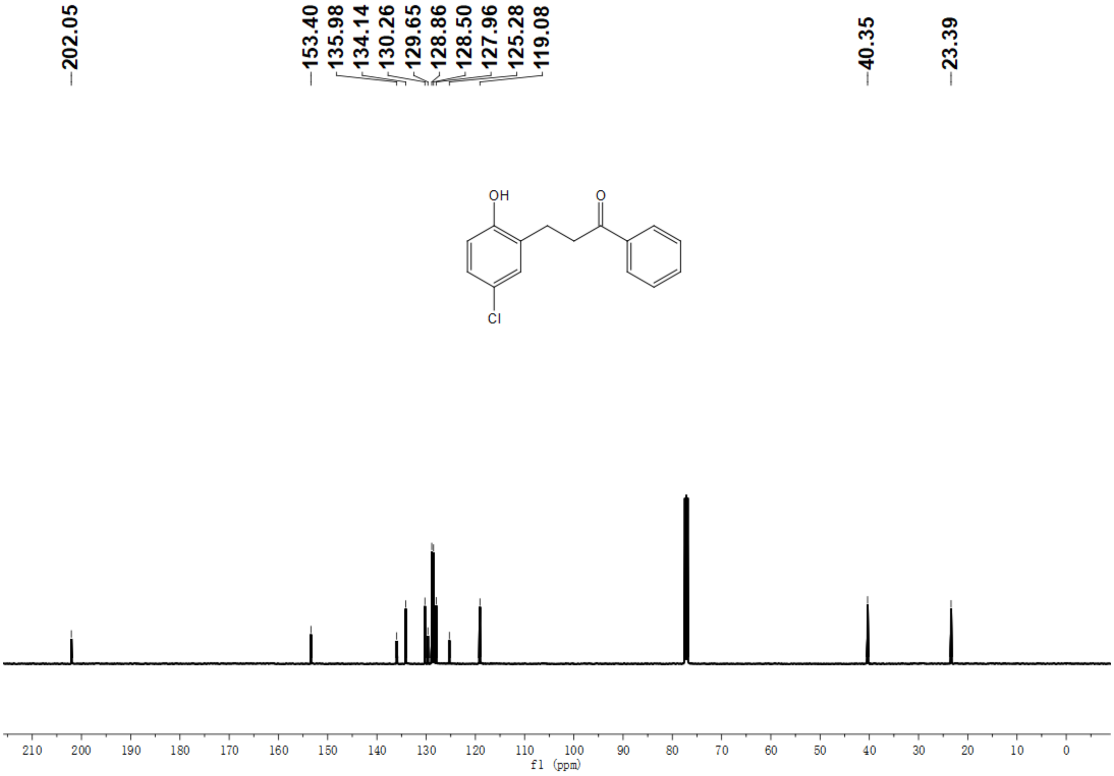
^{1}H and ^{13}C NMR Spectra of Compound **3b**



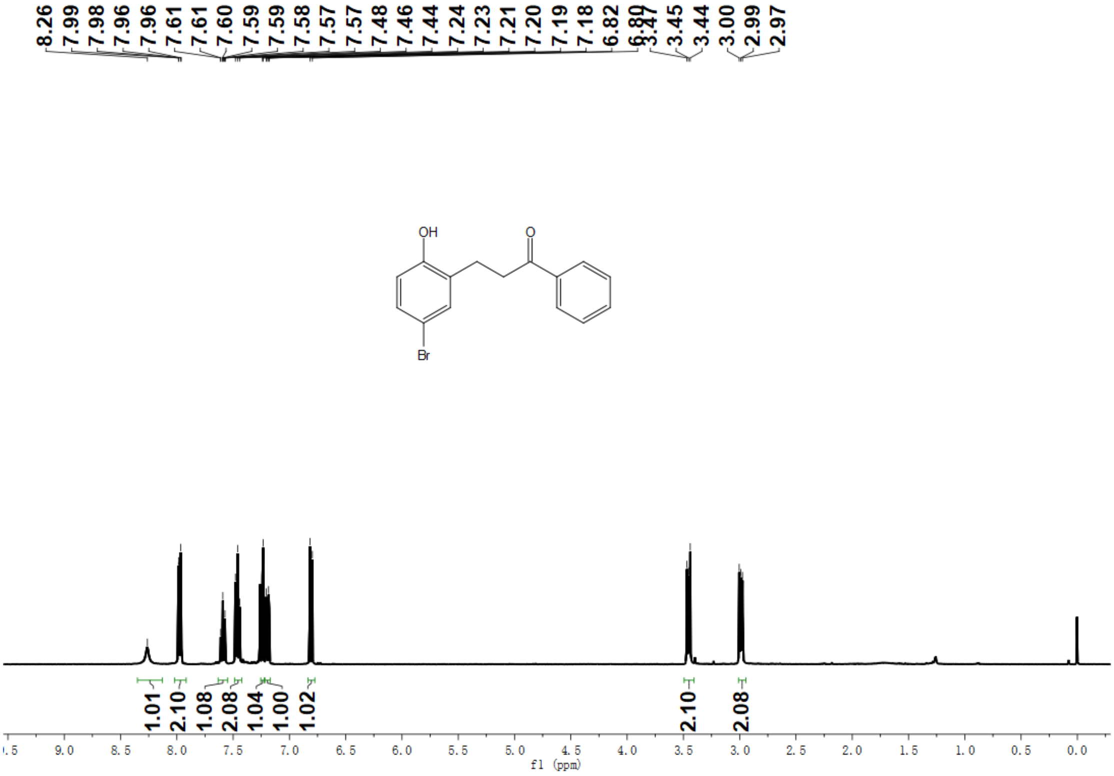


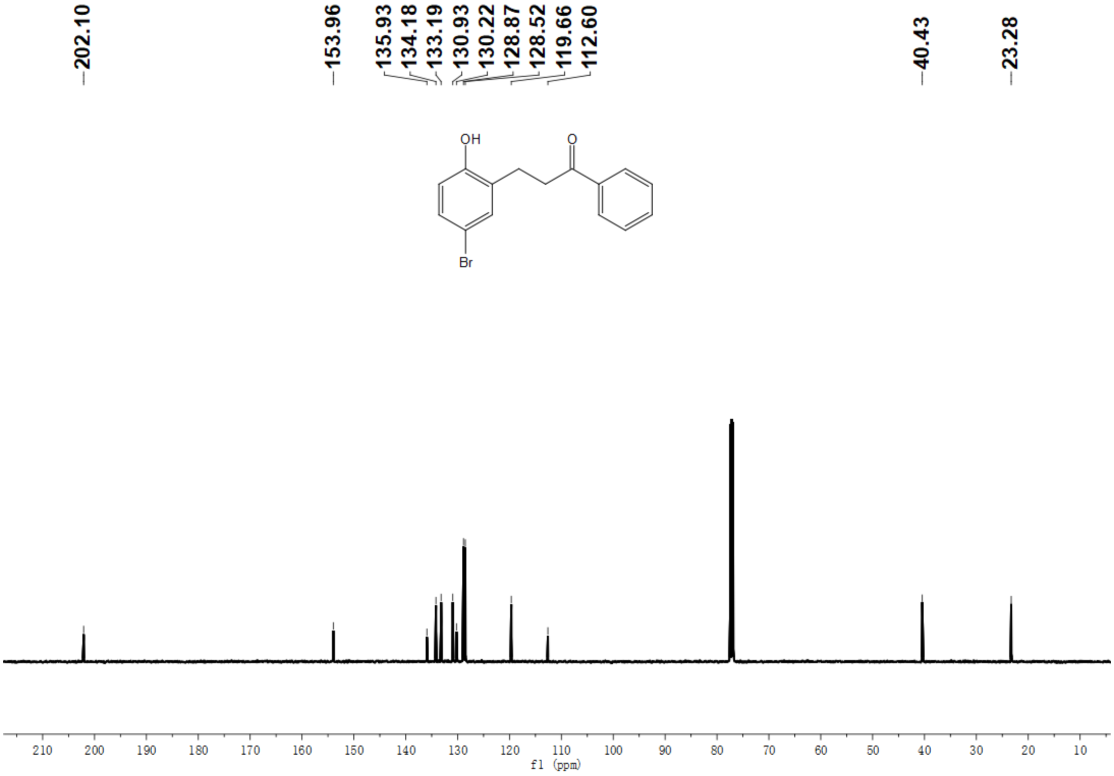
^{1}H and ^{13}C NMR Spectra of Compound **3c**



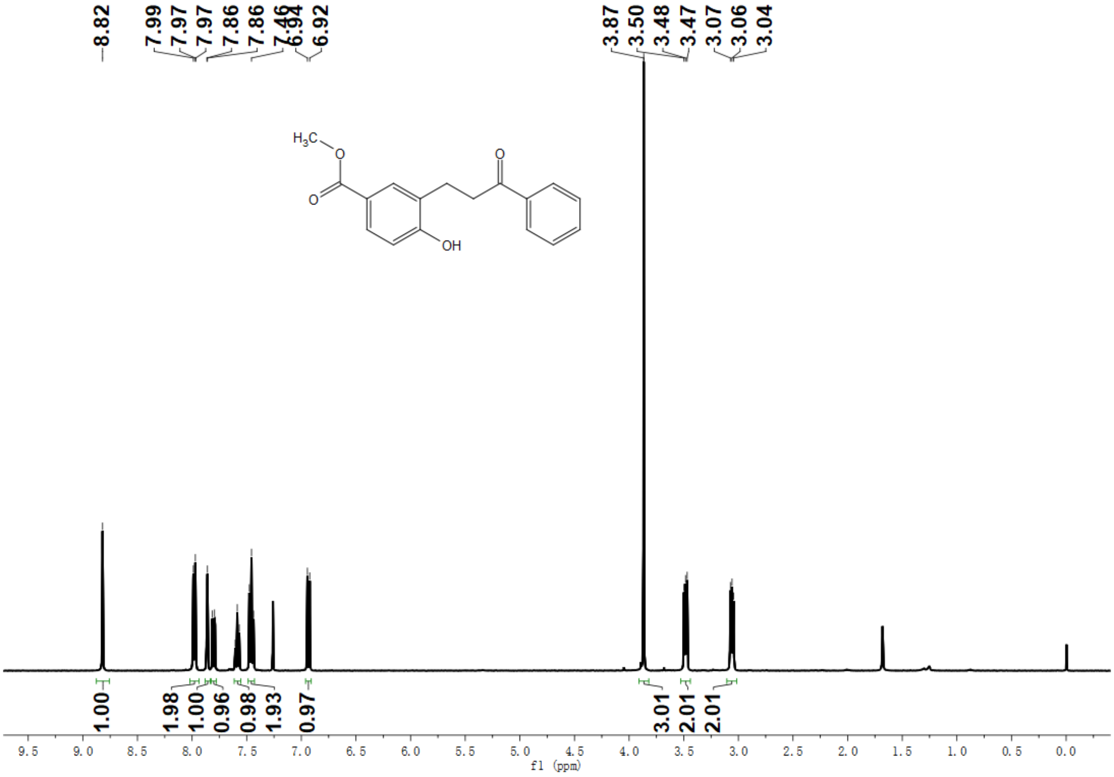


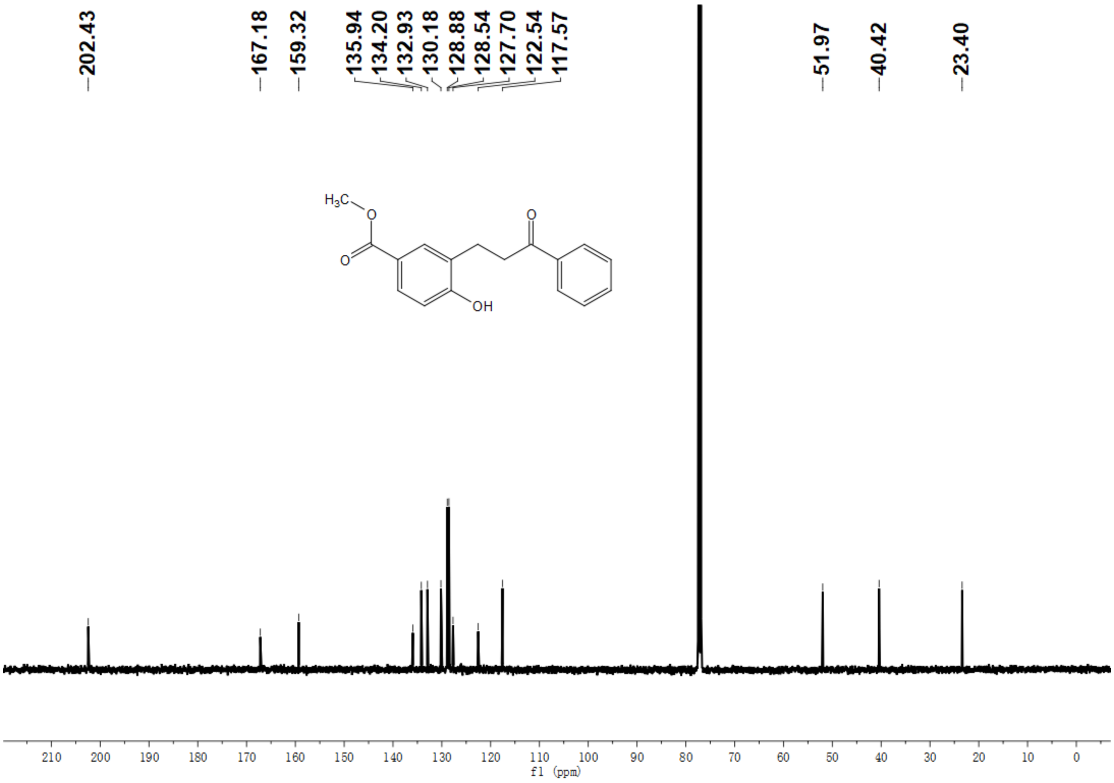
^{1}H and ^{13}C NMR Spectra of Compound **3d**



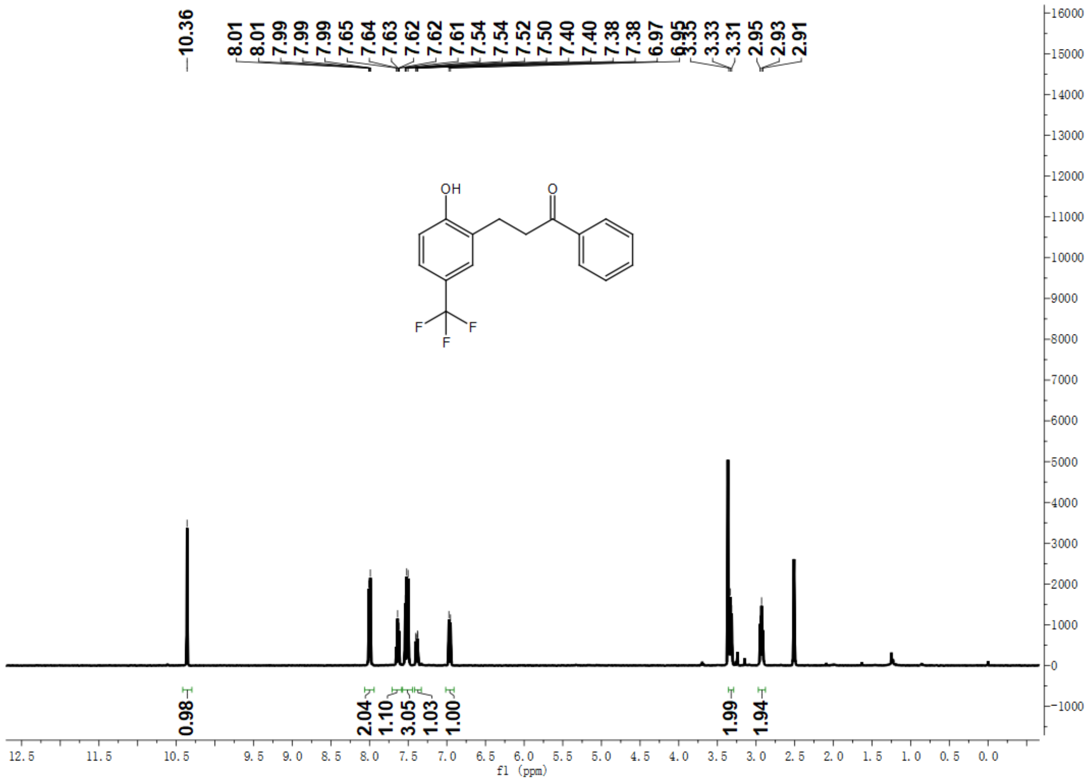


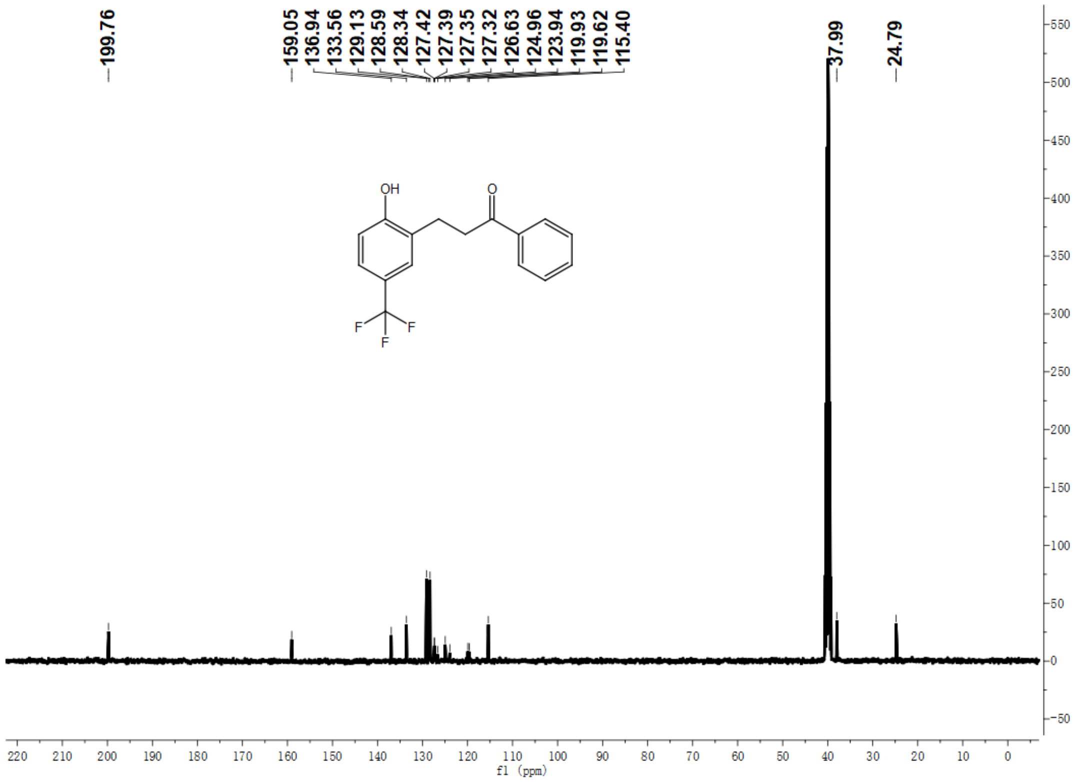
^{1}H and ^{13}C NMR Spectra of Compound **3e**



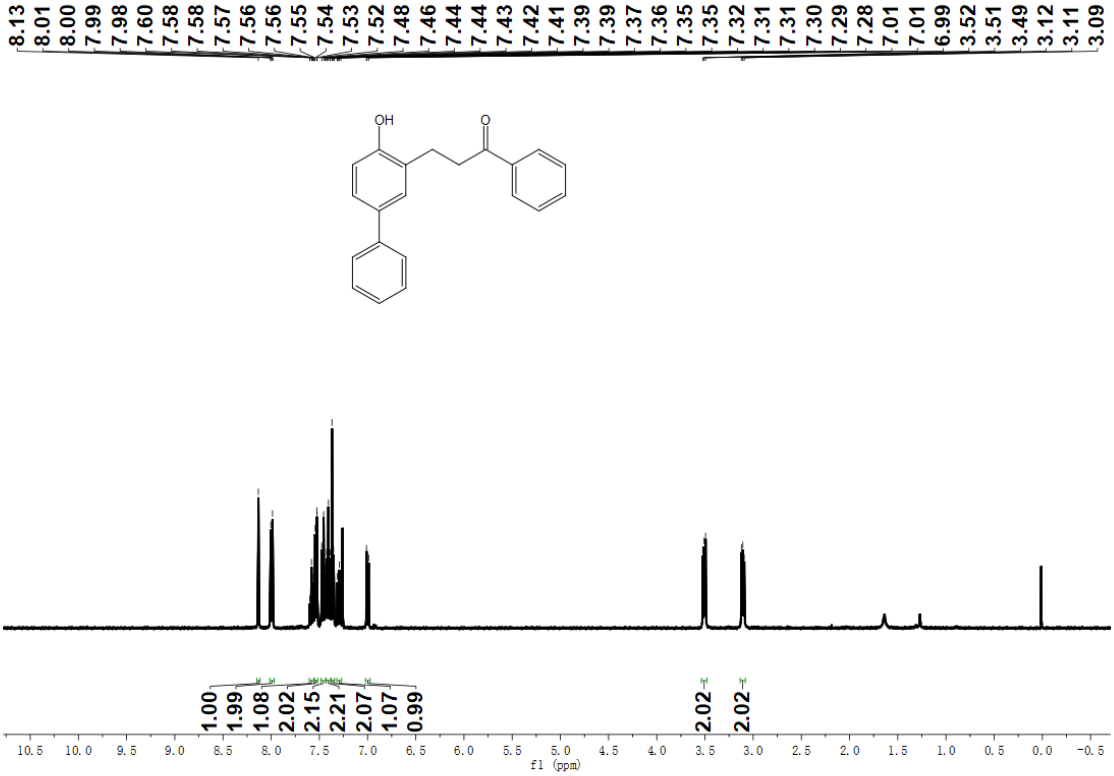


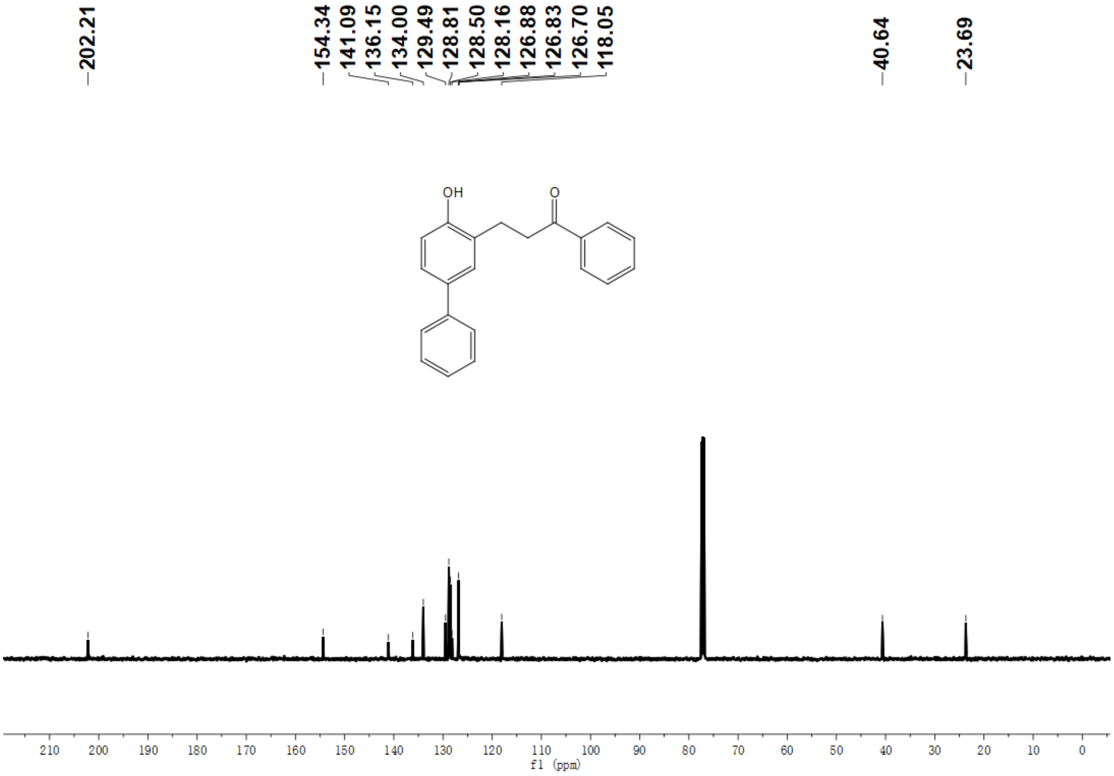
^1H and ^{13}C NMR Spectra of Compound **3f**



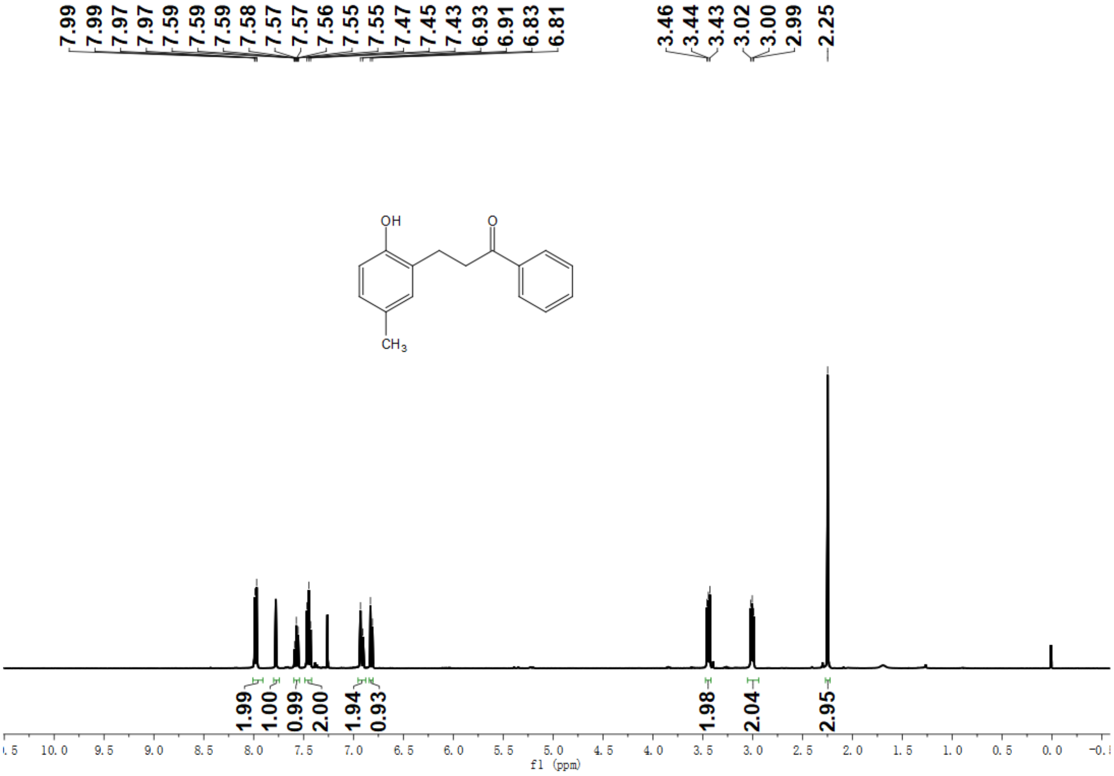


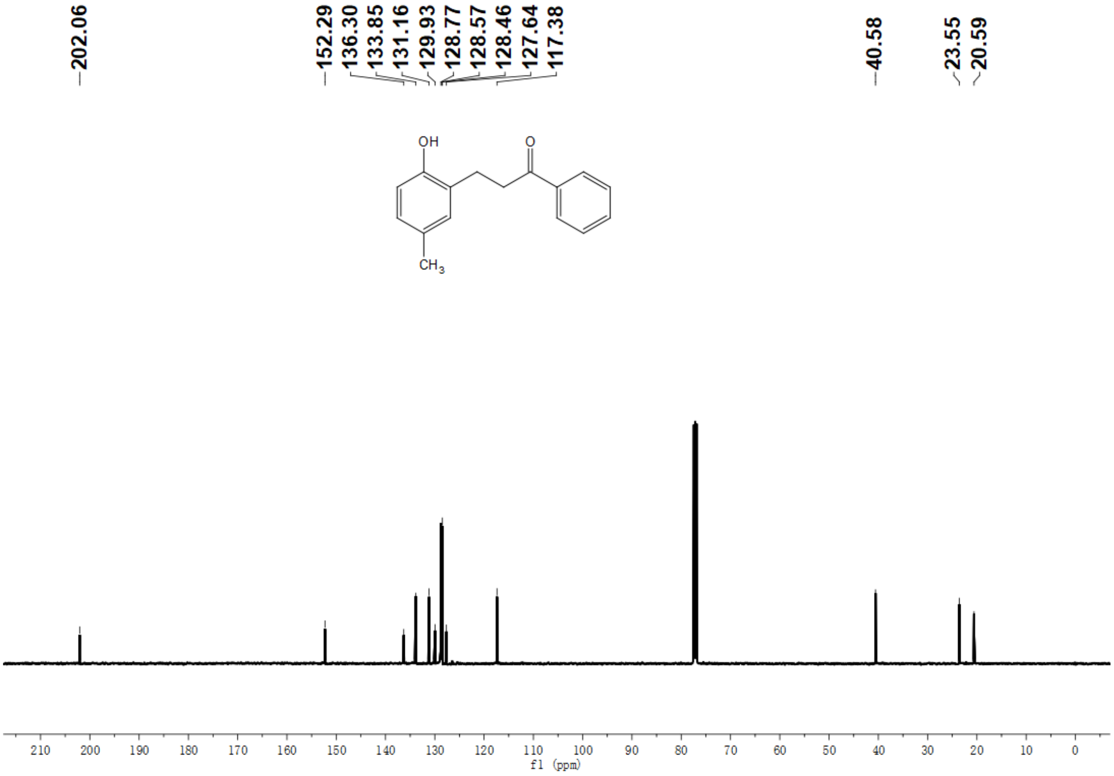
^{1}H and ^{13}C NMR Spectra of Compound **3g**



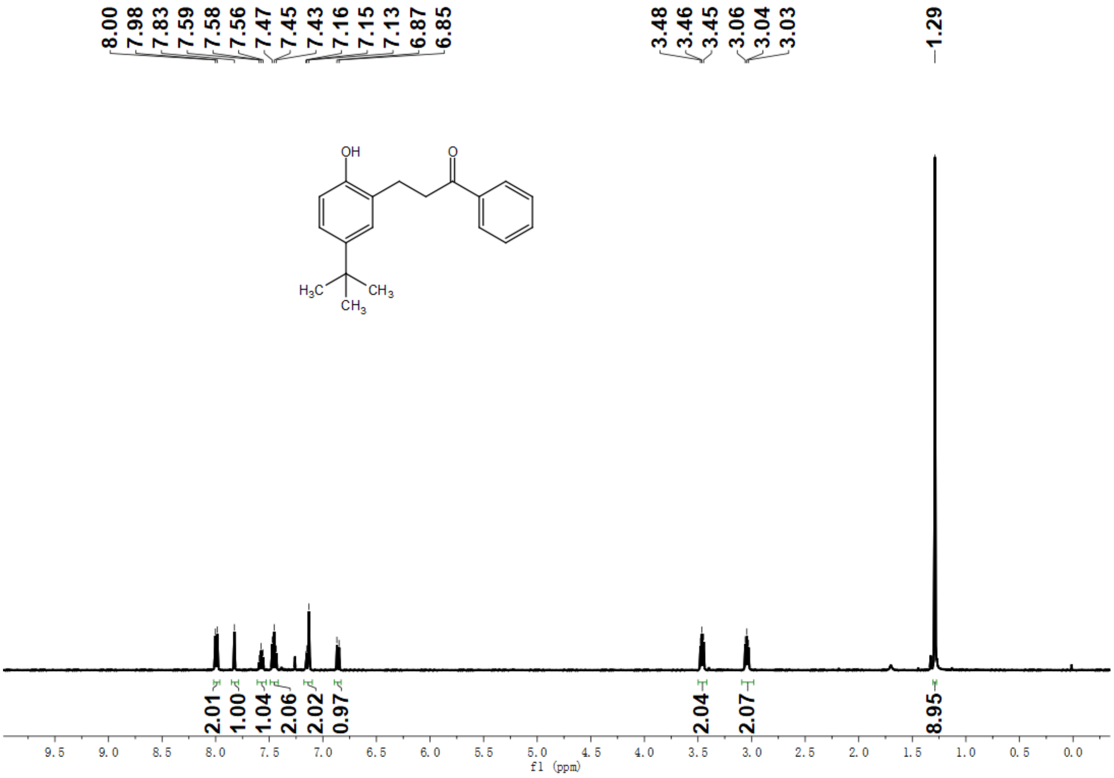


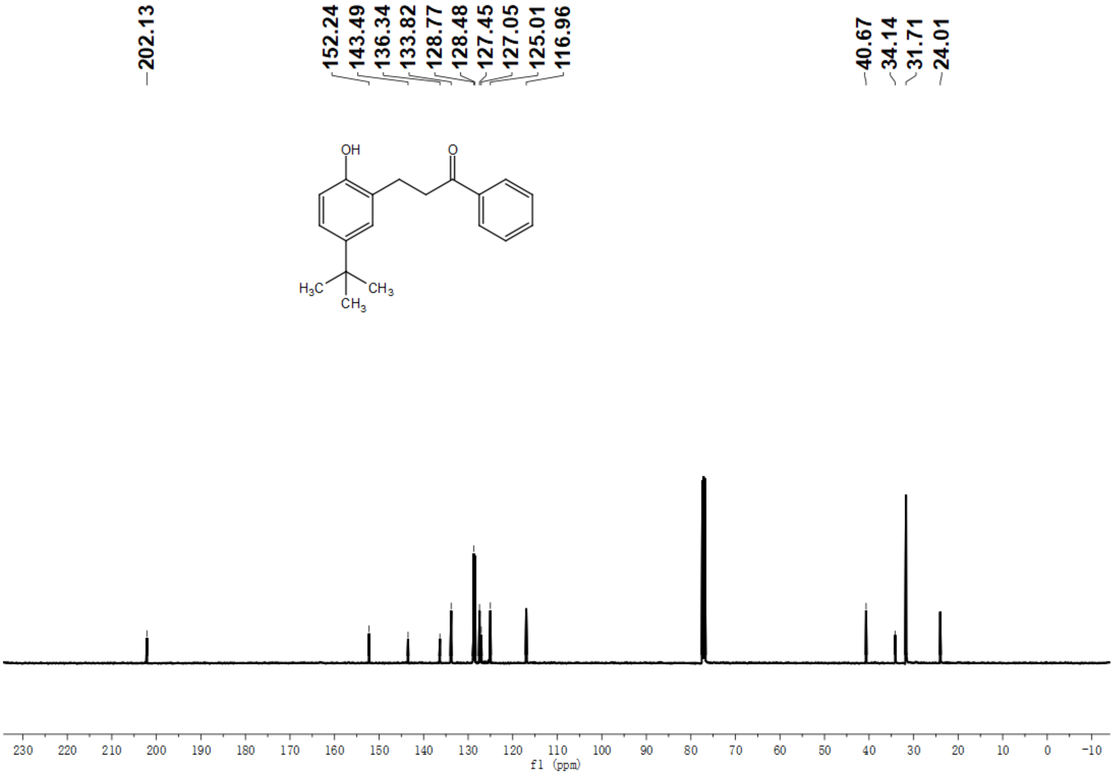
^{1}H and ^{13}C NMR Spectra of Compound **3h**



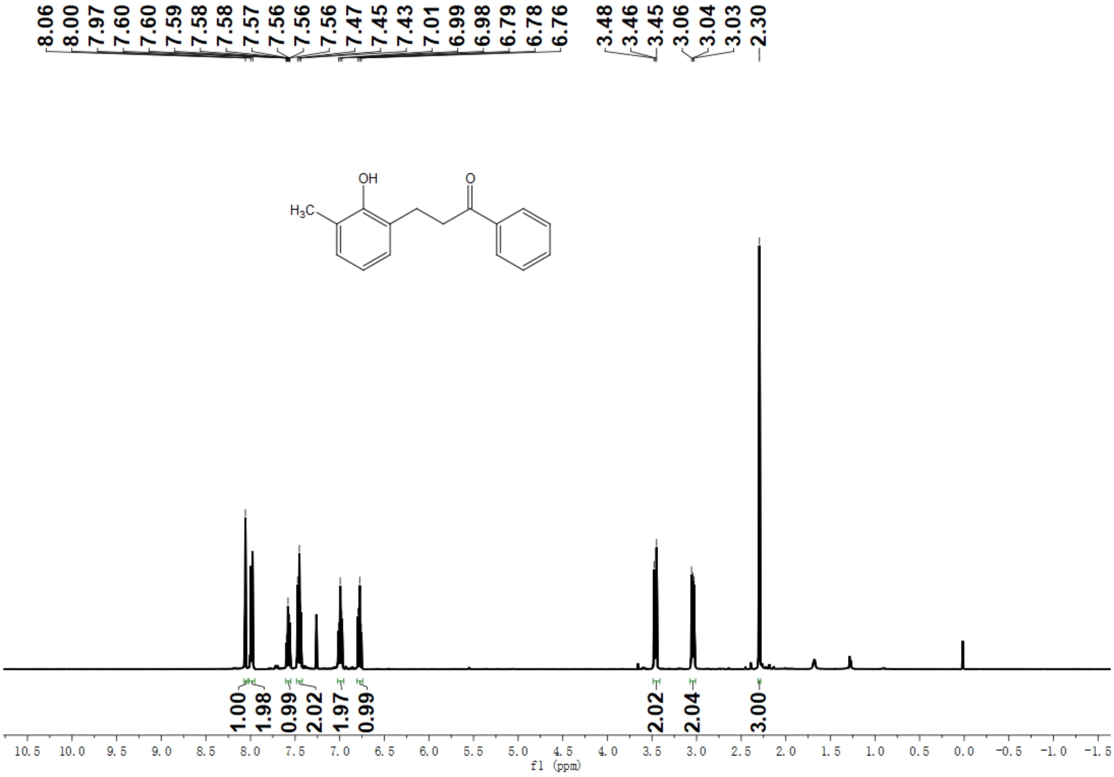


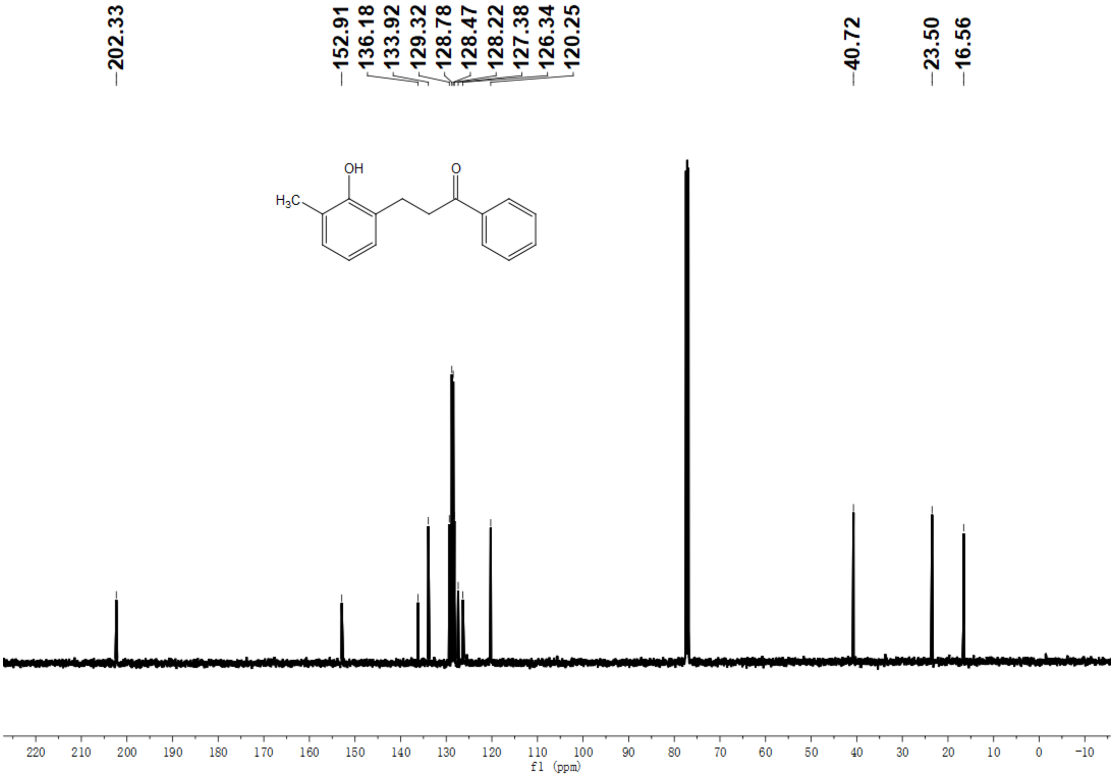
^{1}H and ^{13}C NMR Spectra of Compound **3i**



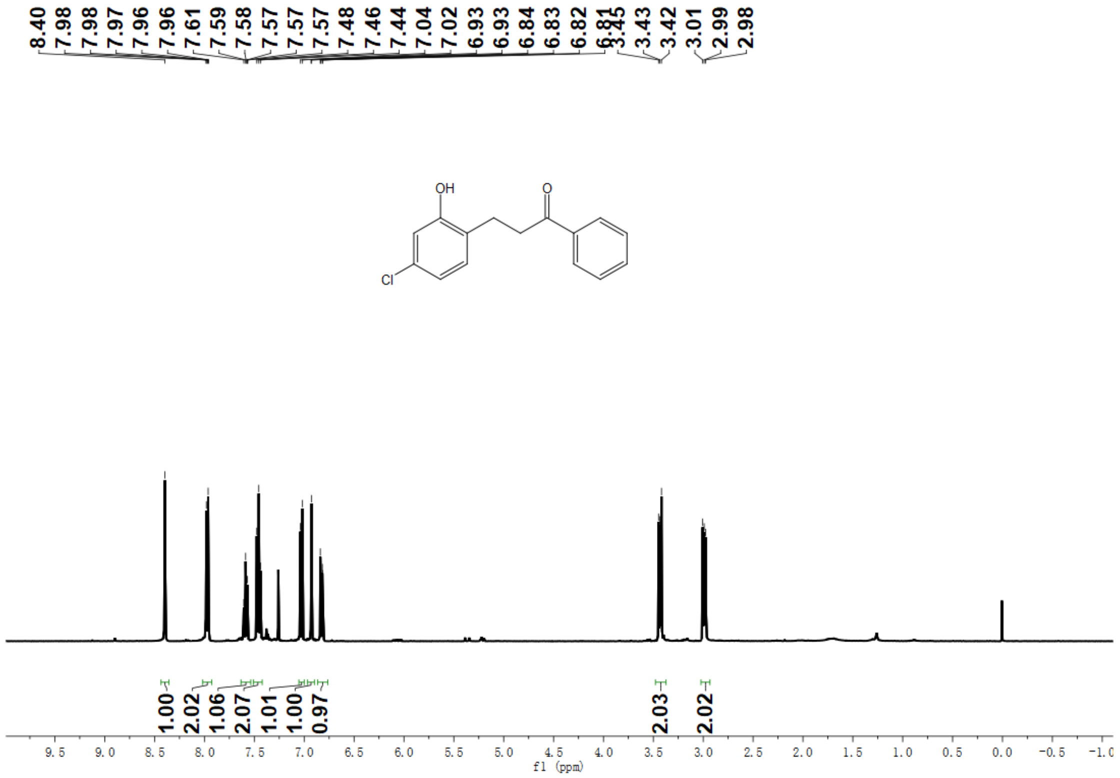


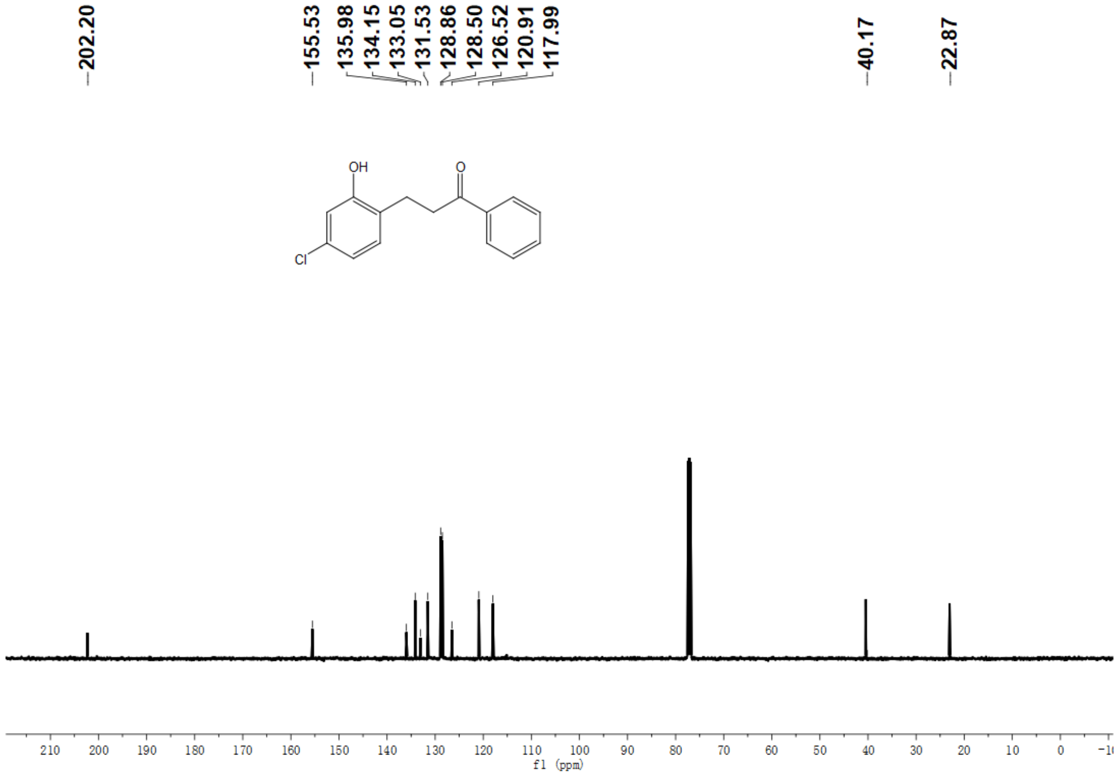
^{1}H and ^{13}C NMR Spectra of Compound **3j**



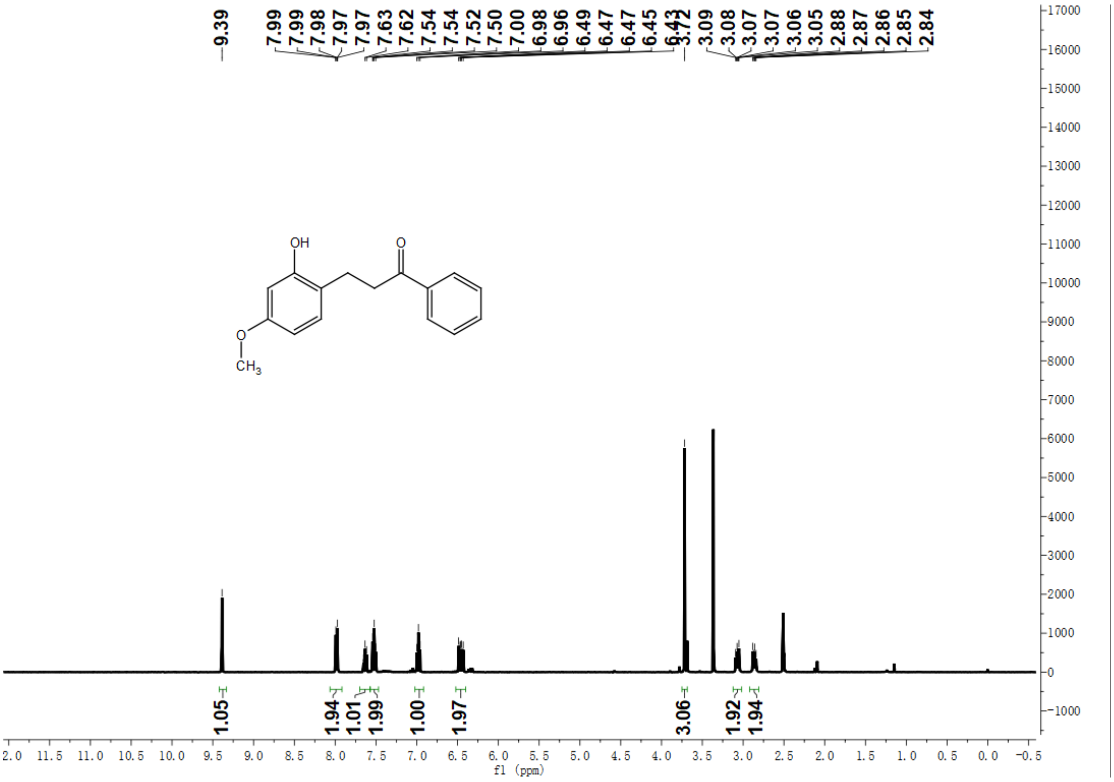


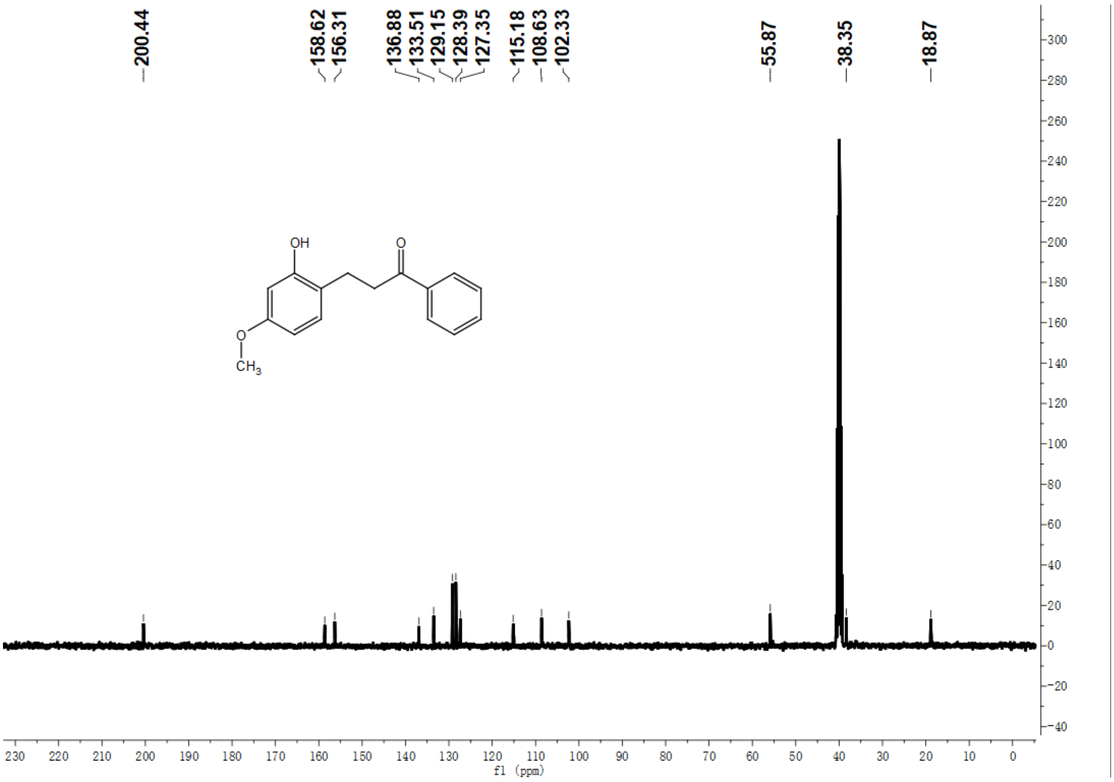
^{1}H and ^{13}C NMR Spectra of Compound **3k**



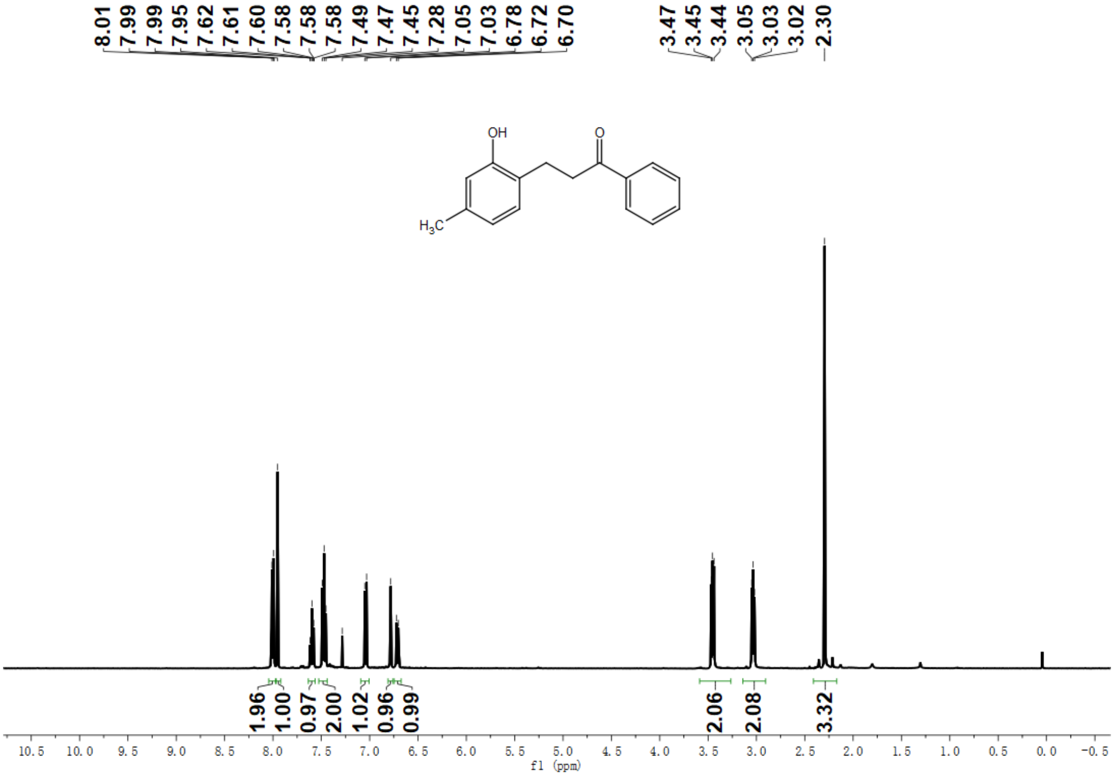


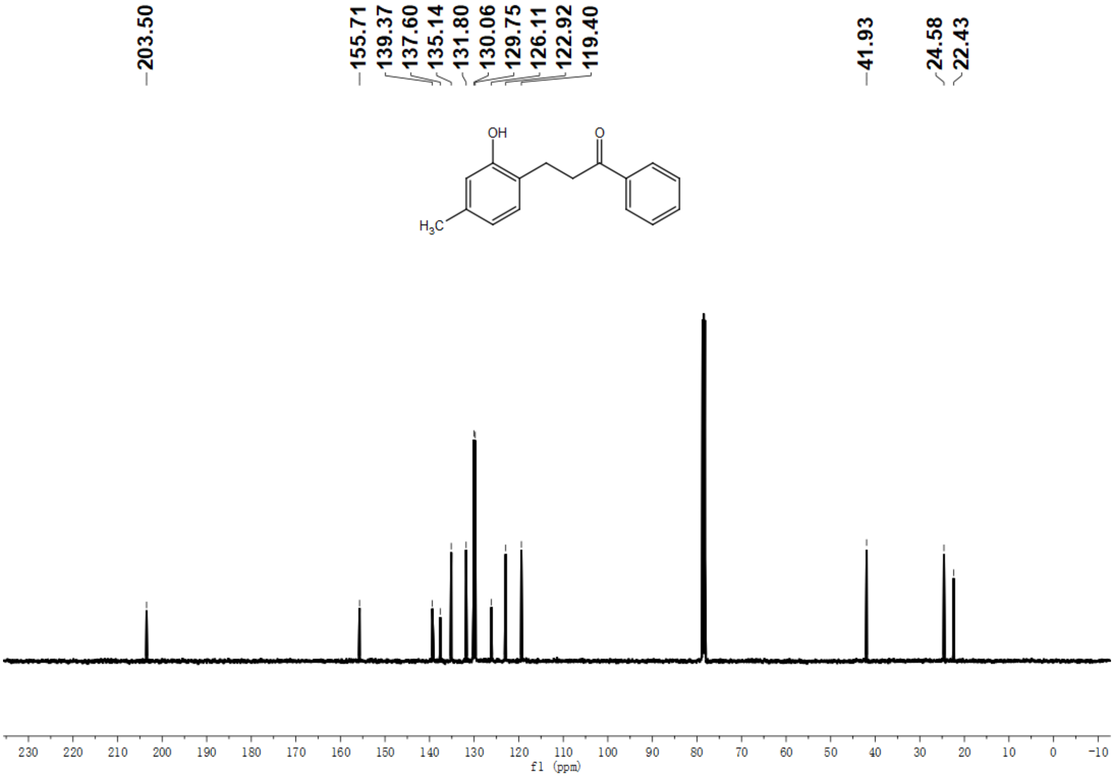
^{1}H and ^{13}C NMR Spectra of Compound **3l**



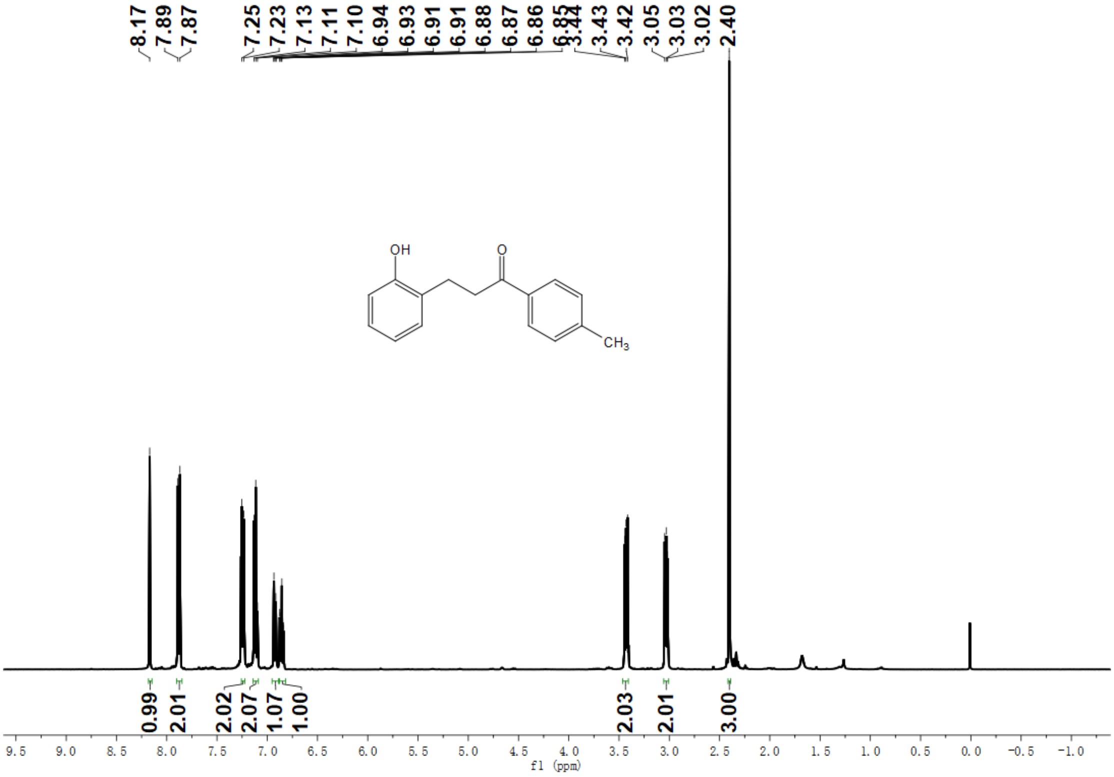


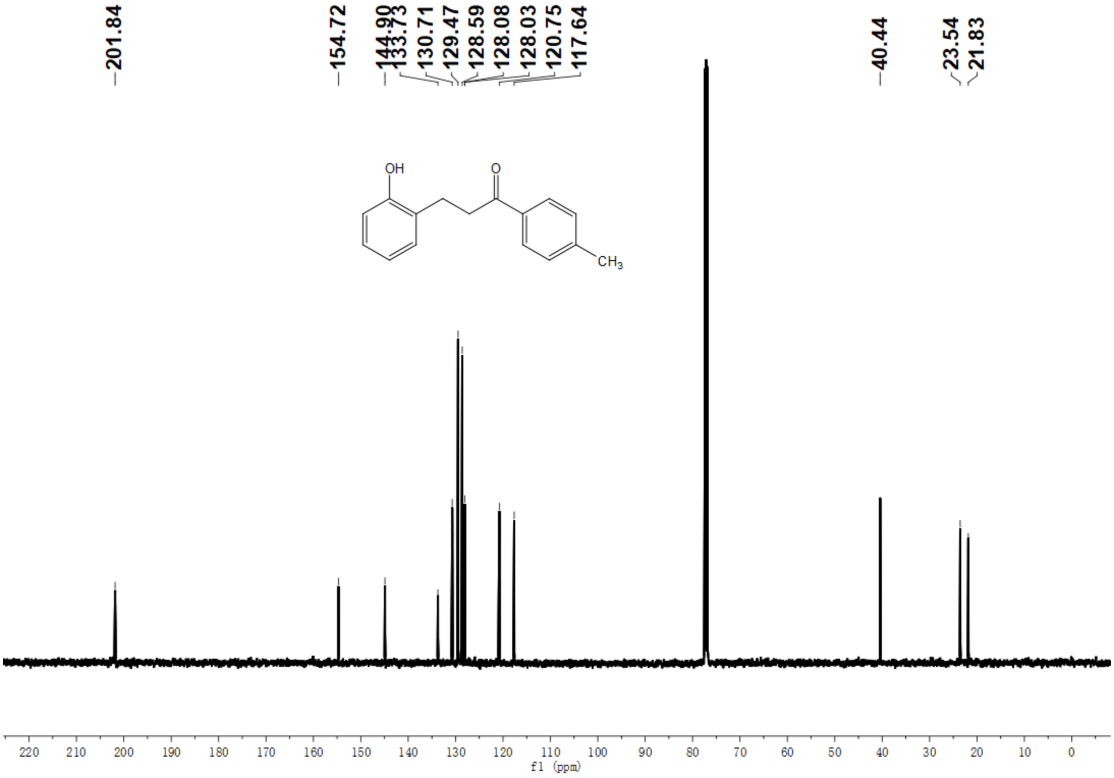
^{1}H and ^{13}C NMR Spectra of Compound **3m**



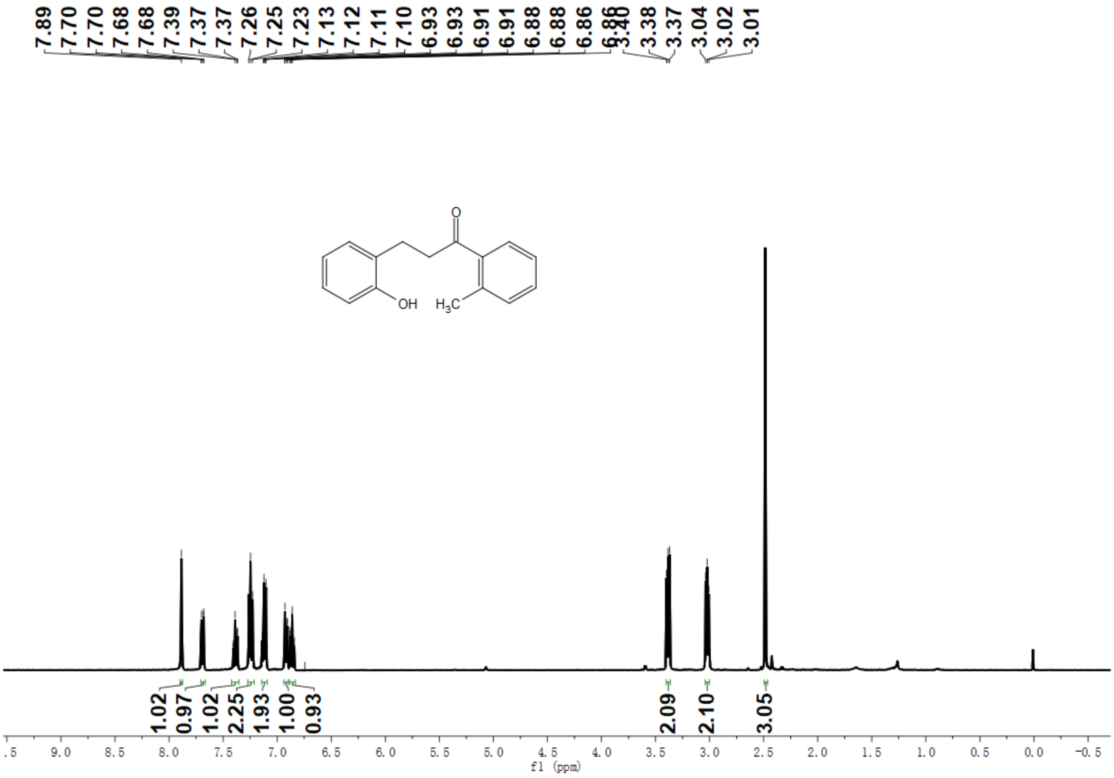


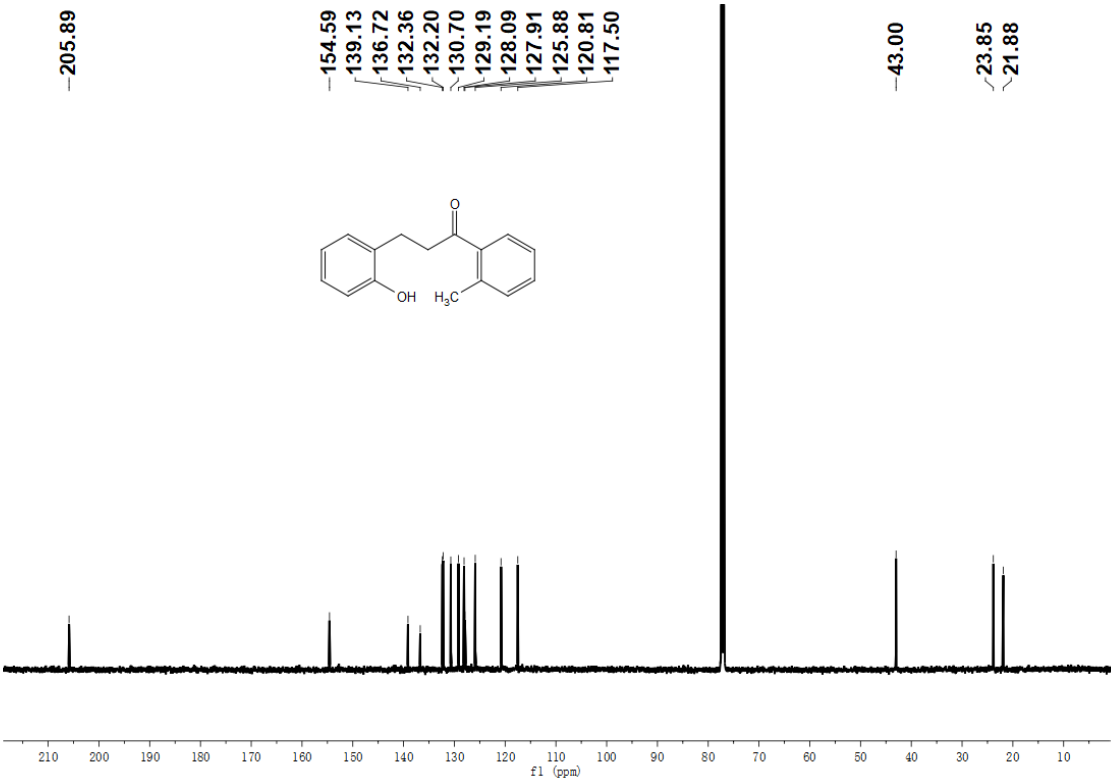
^{1}H and ^{13}C NMR Spectra of Compound **4a**



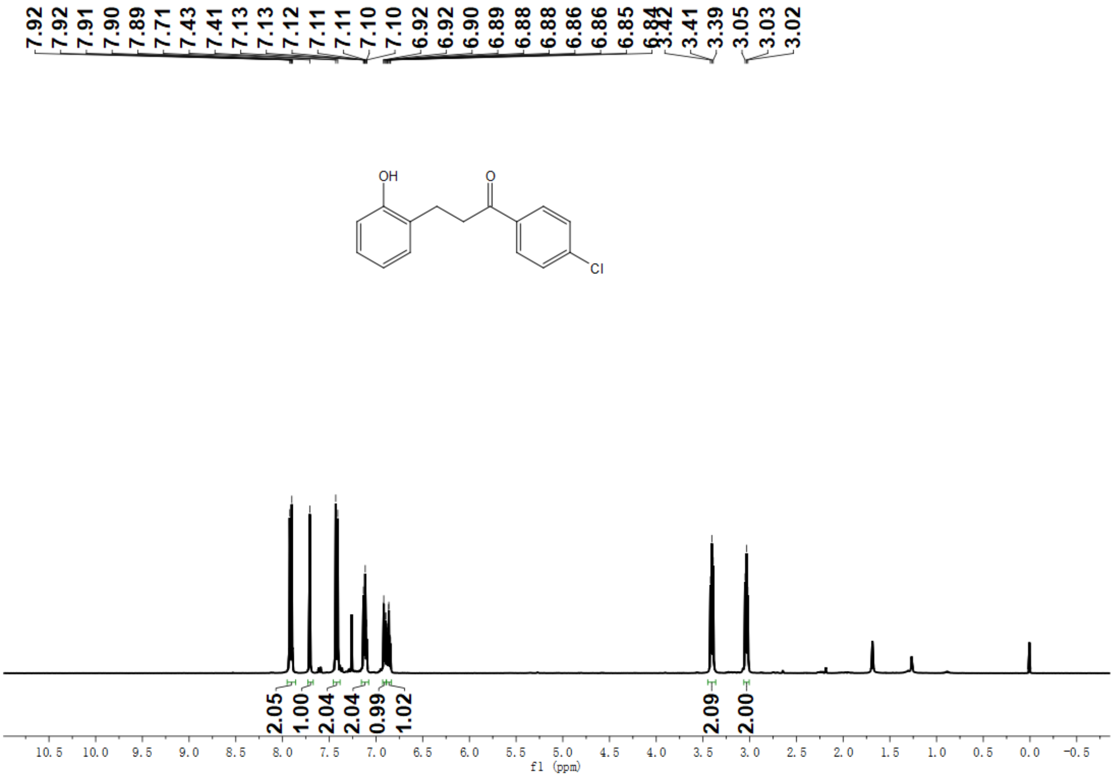


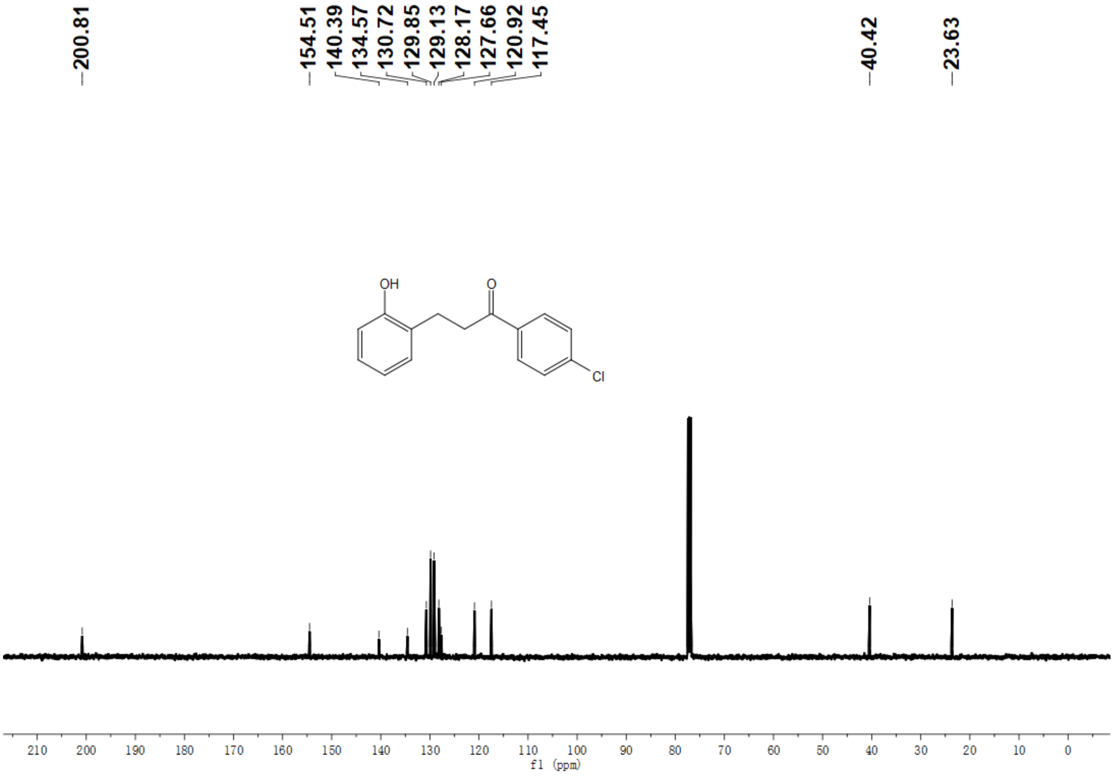
^{1}H and ^{13}C NMR Spectra of Compound **4b**



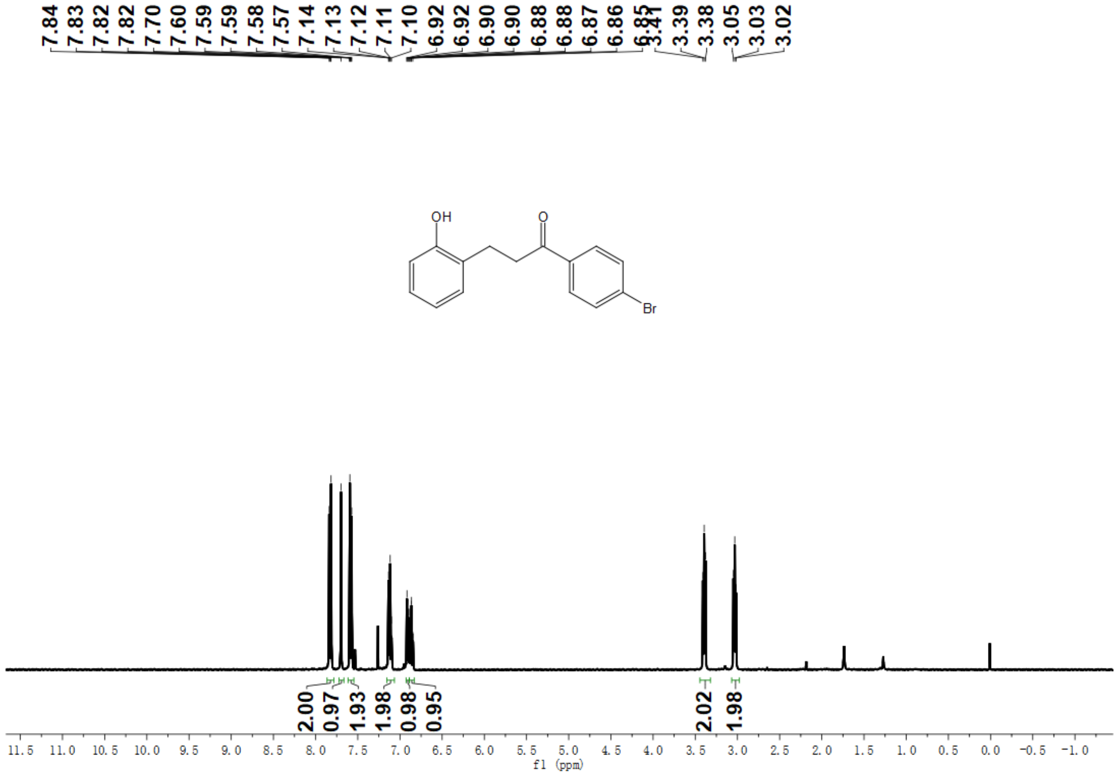


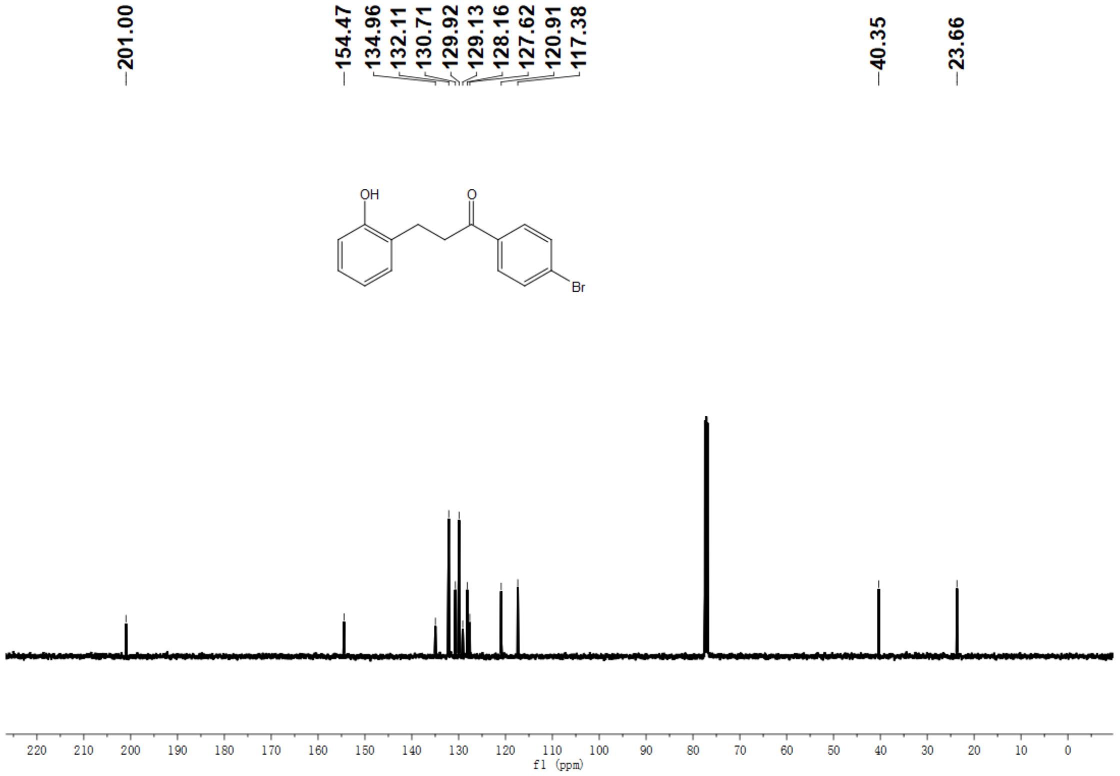
^{1}H and ^{13}C NMR Spectra of Compound **4c**



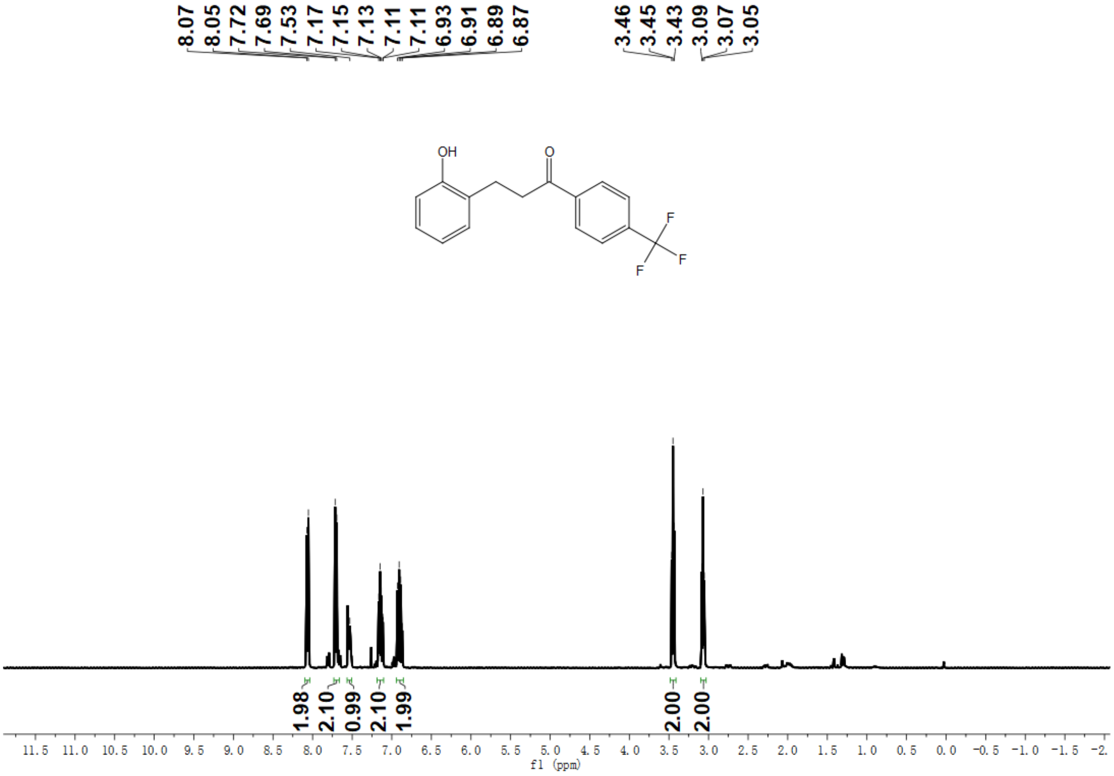


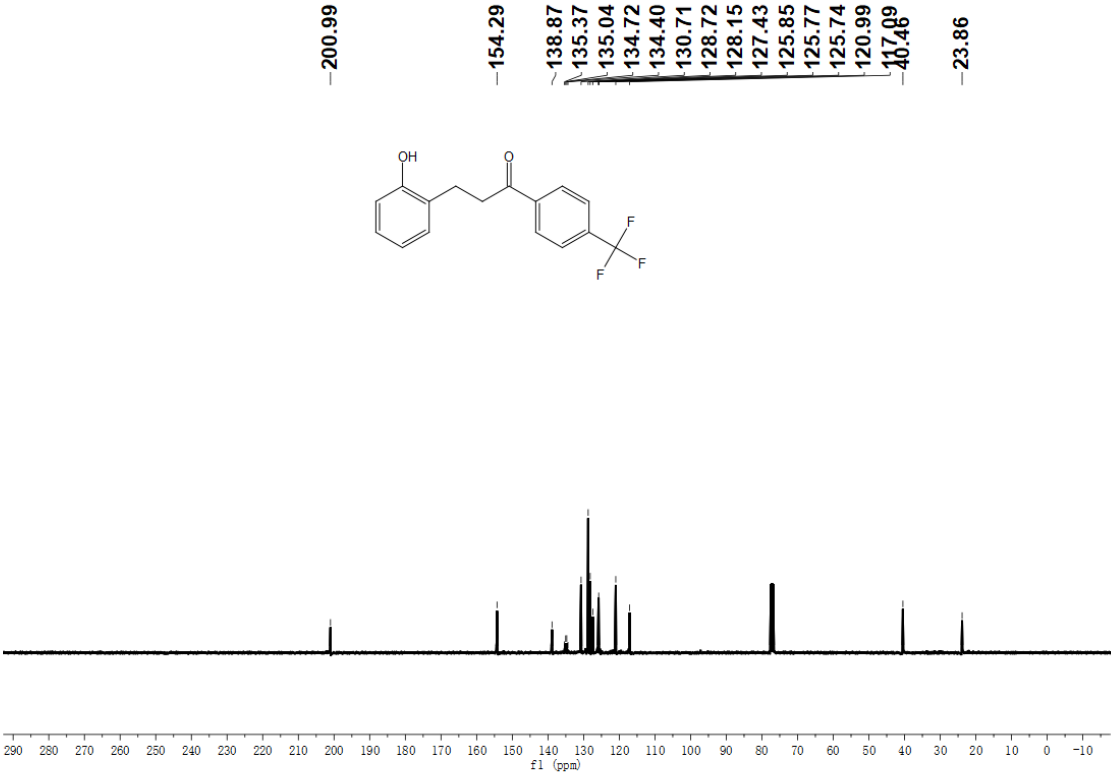
^{1}H and ^{13}C NMR Spectra of Compound **4d**



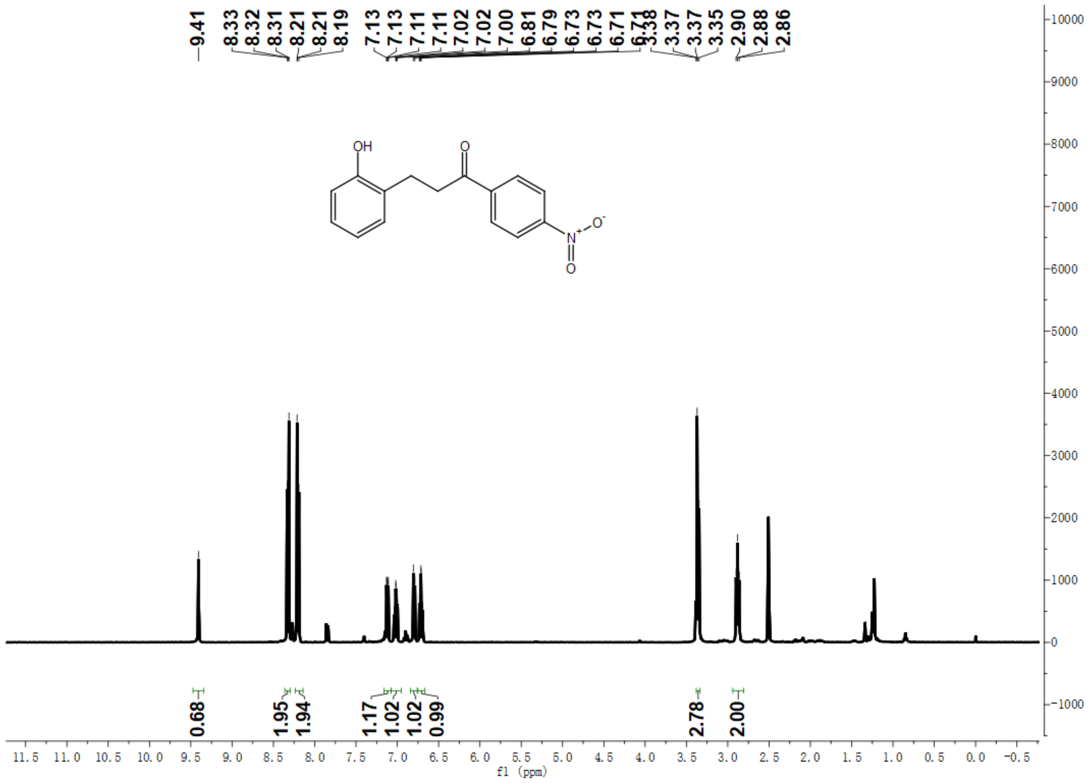


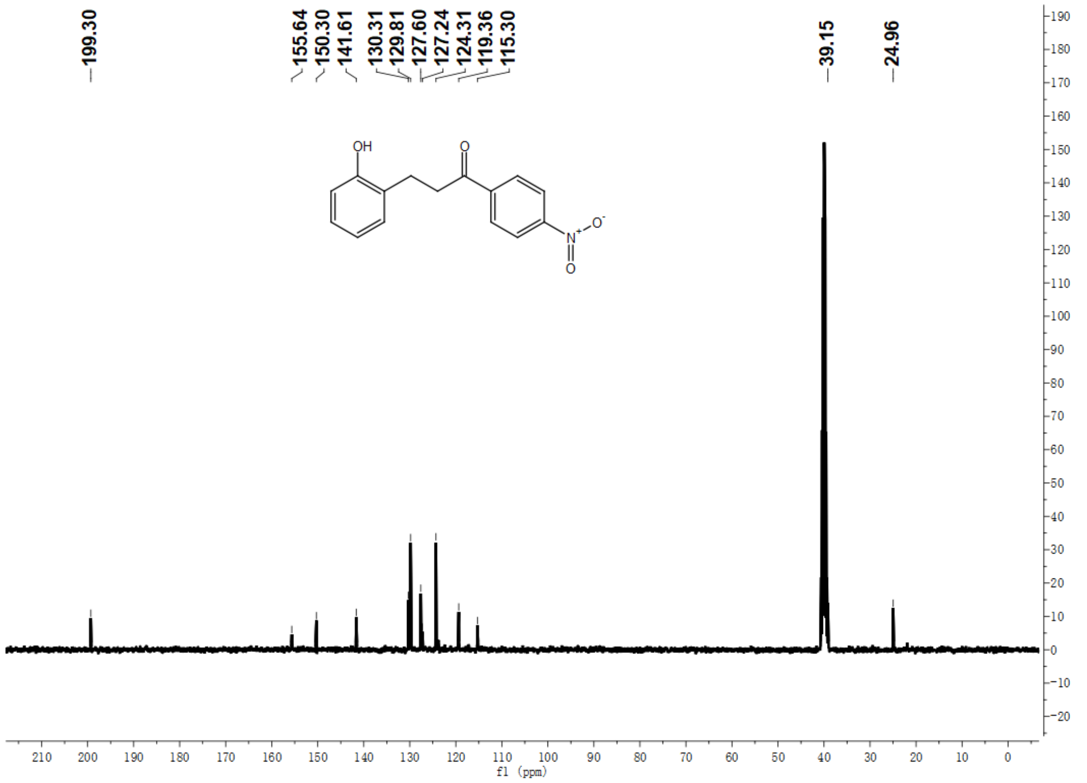
^{1}H and ^{13}C NMR Spectra of Compound **4e**



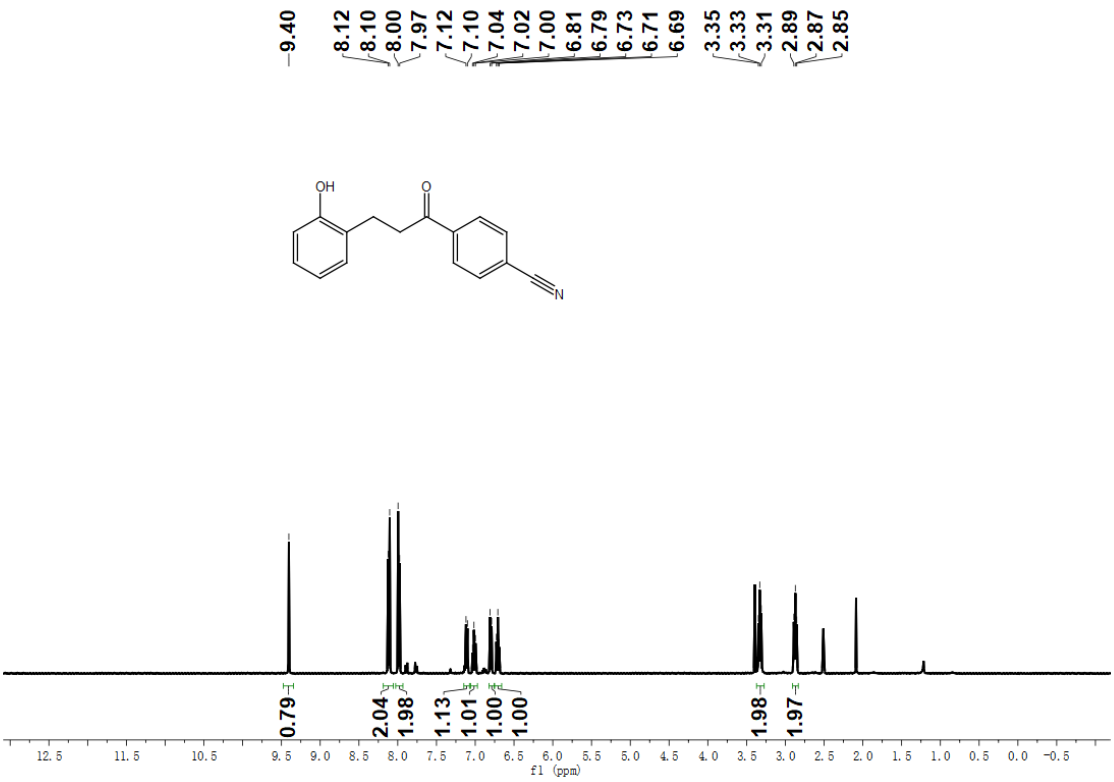


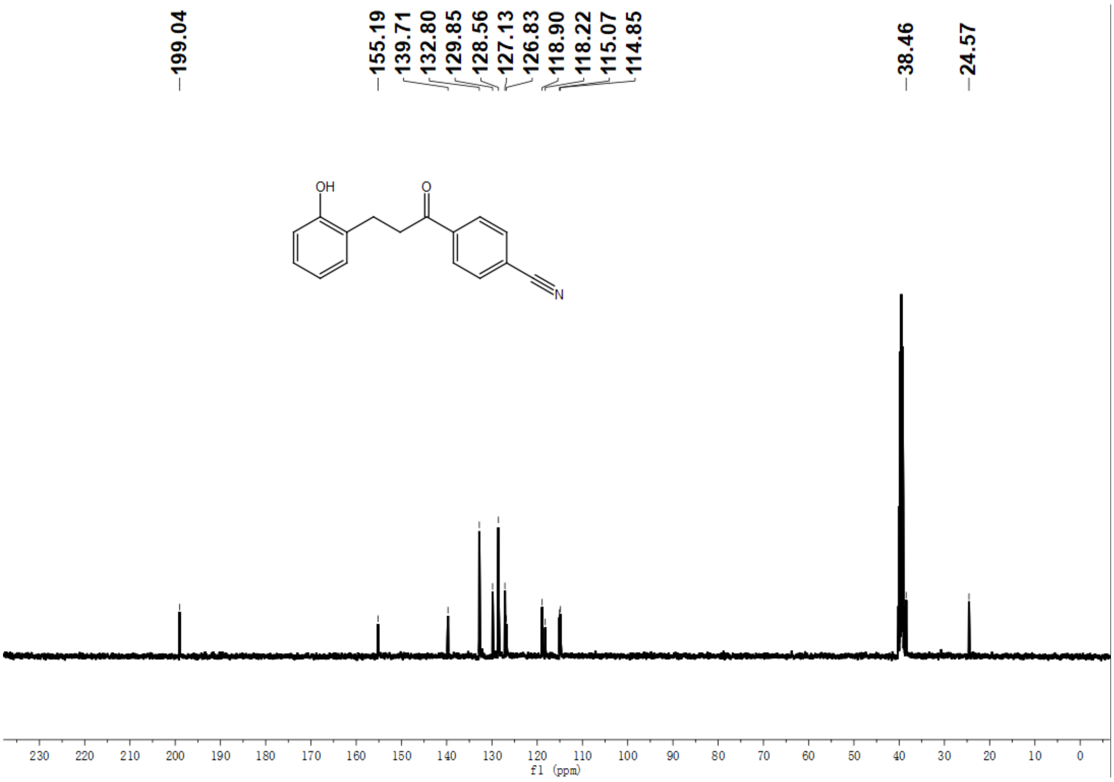
^{1}H and ^{13}C NMR Spectra of Compound **4f**



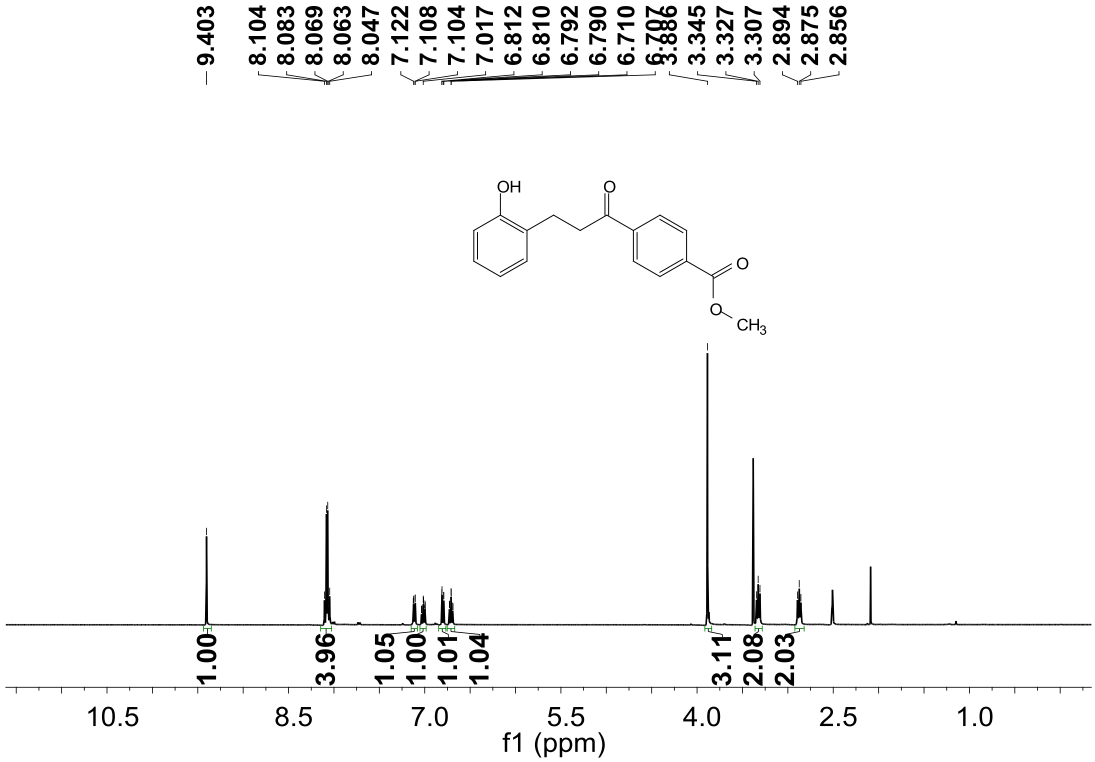


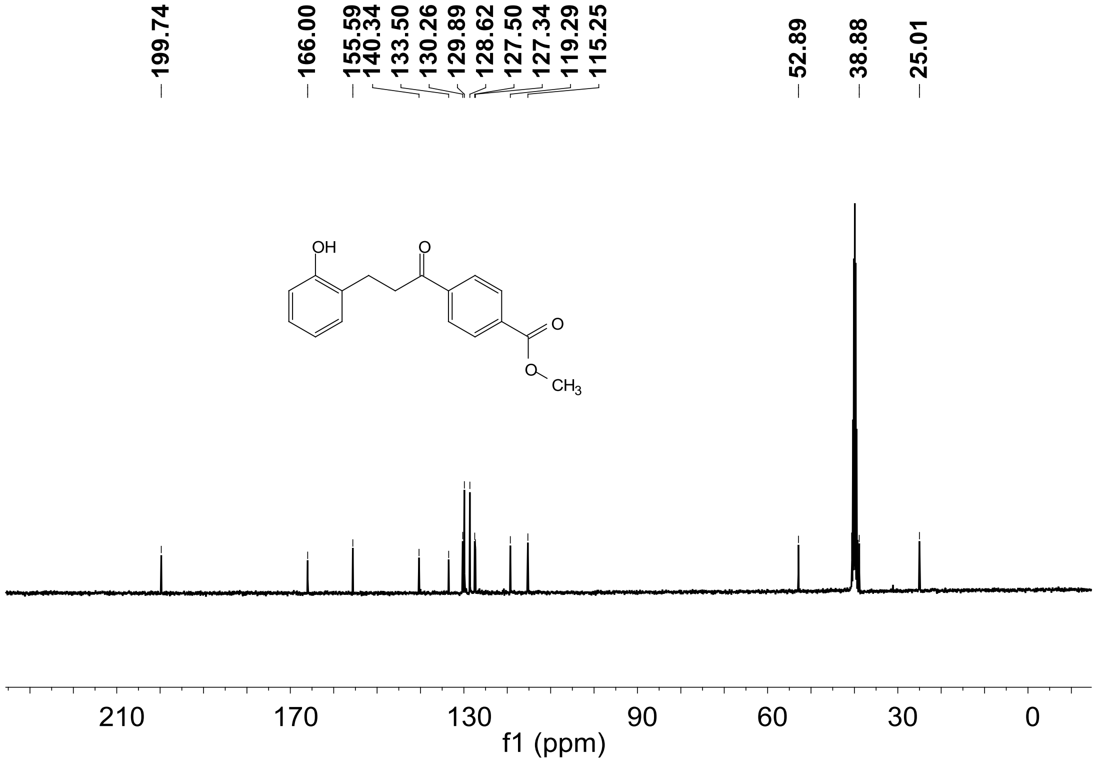
^{1}H and ^{13}C NMR Spectra of Compound **4g**



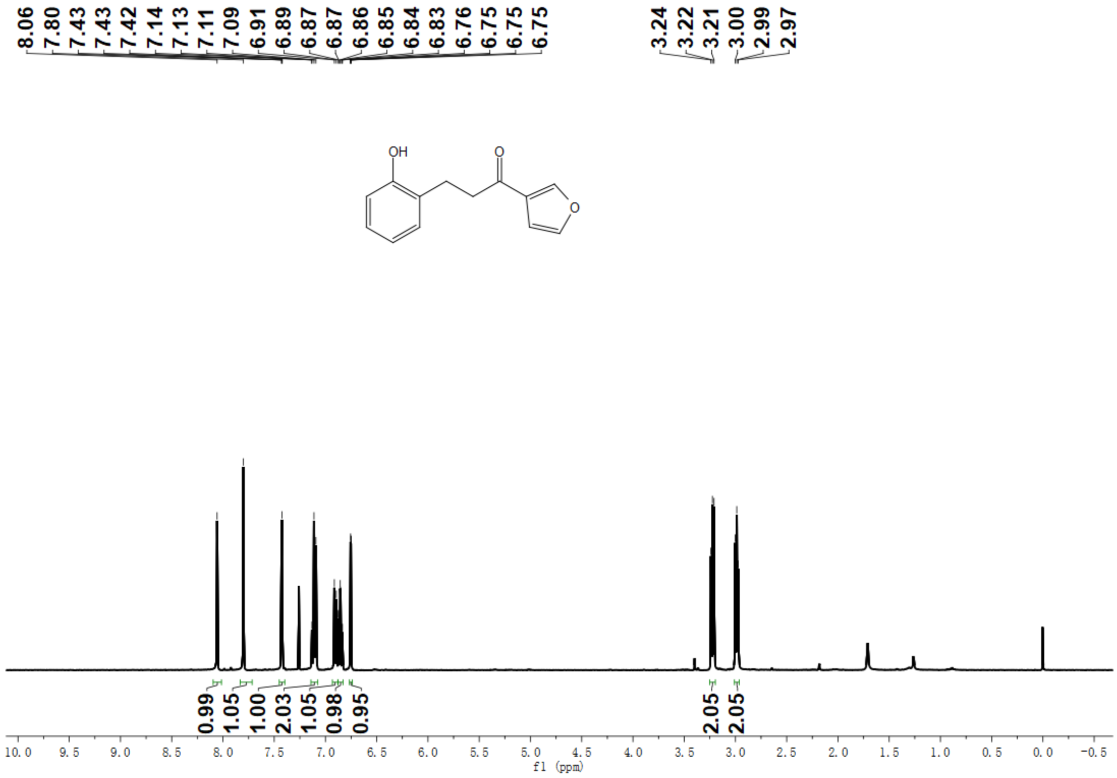


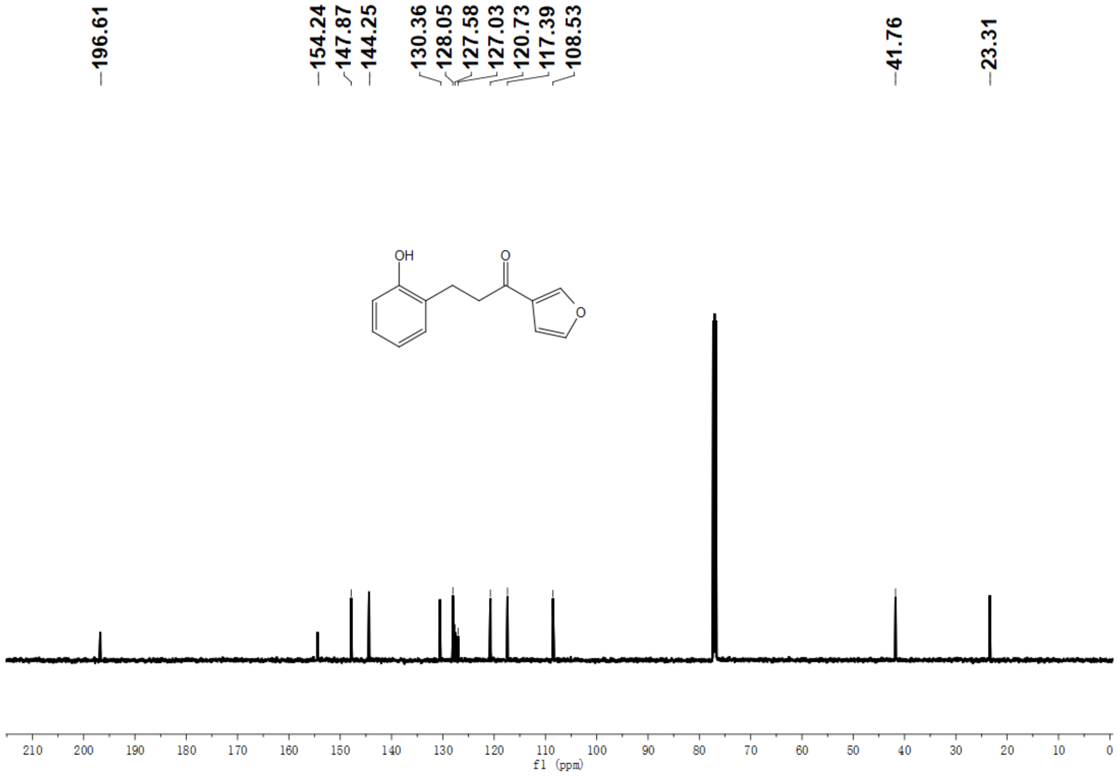
^{1}H and ^{13}C NMR Spectra of Compound **4h**



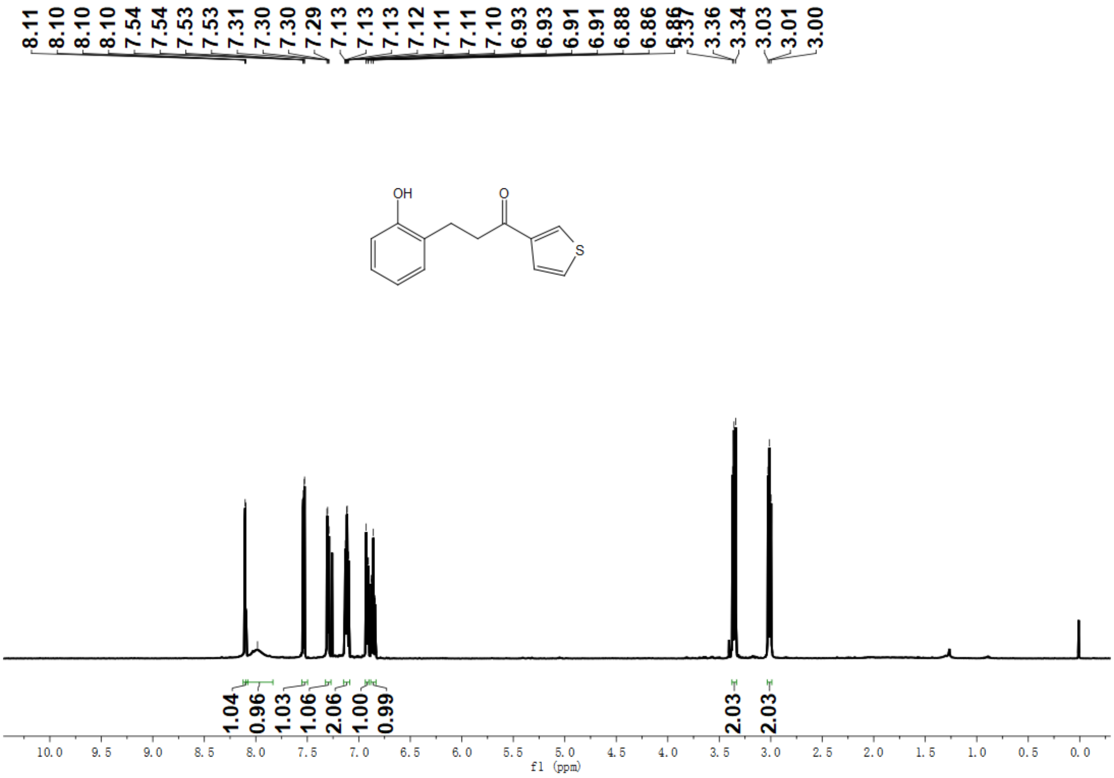


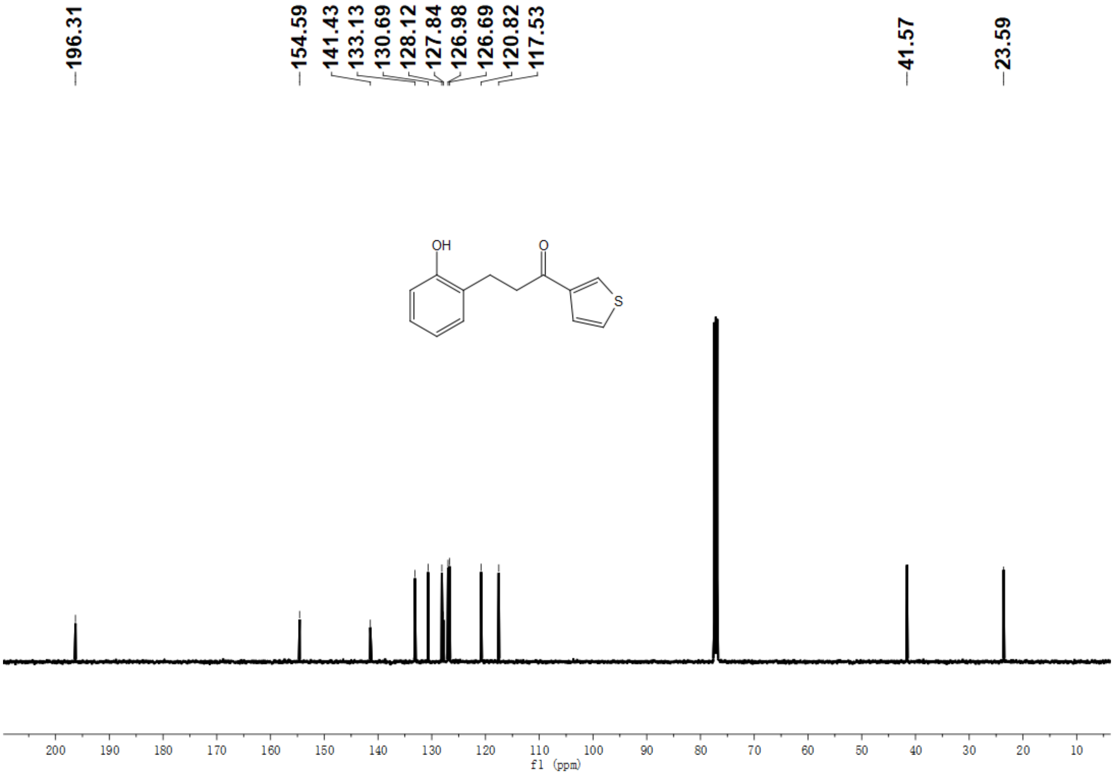
^{1}H and ^{13}C NMR Spectra of Compound **4i**



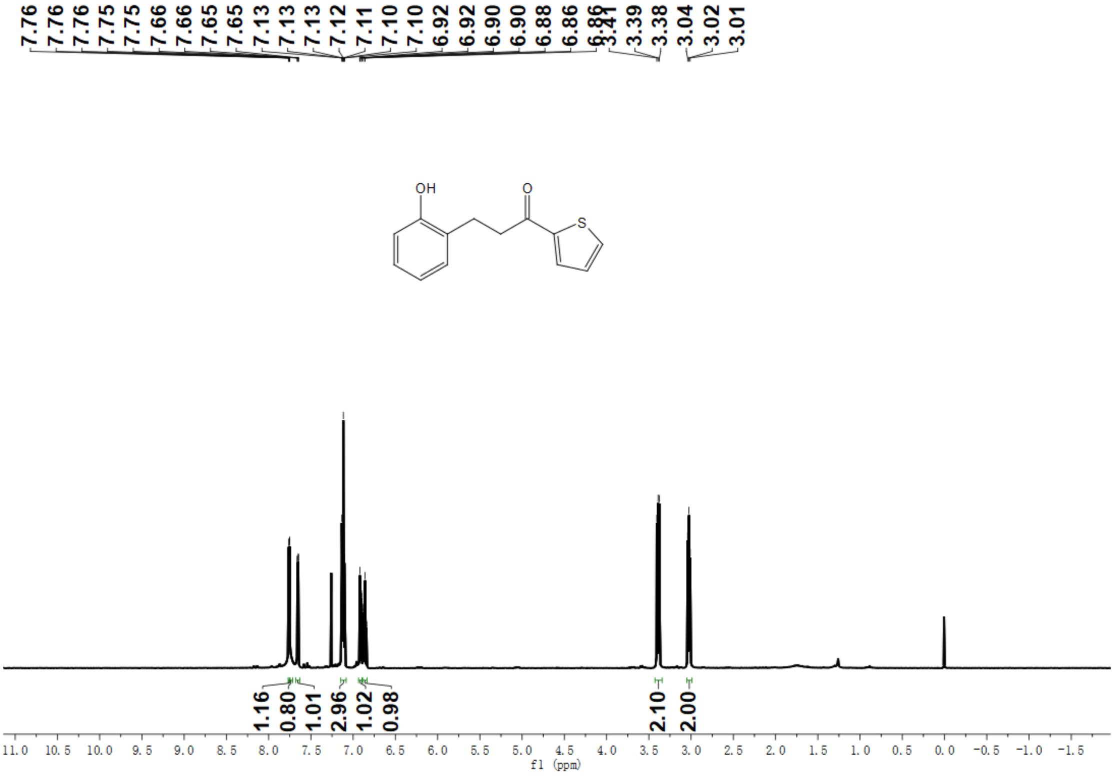


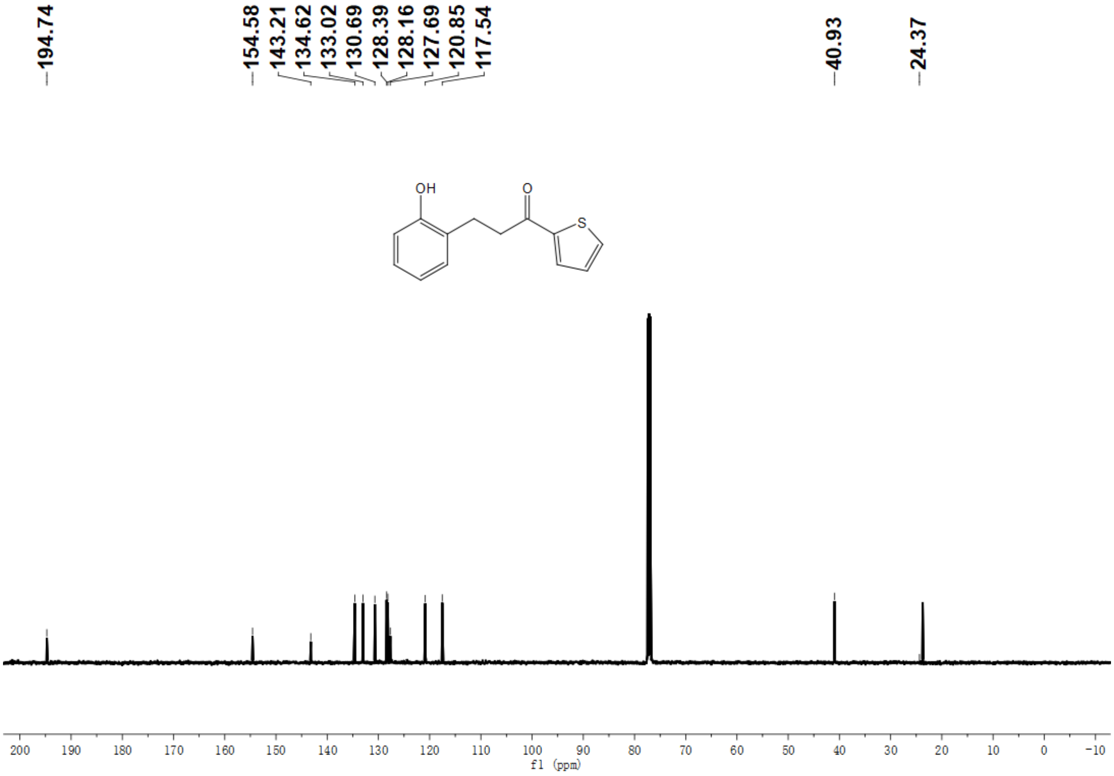
^{1}H and ^{13}C NMR Spectra of Compound **4j**



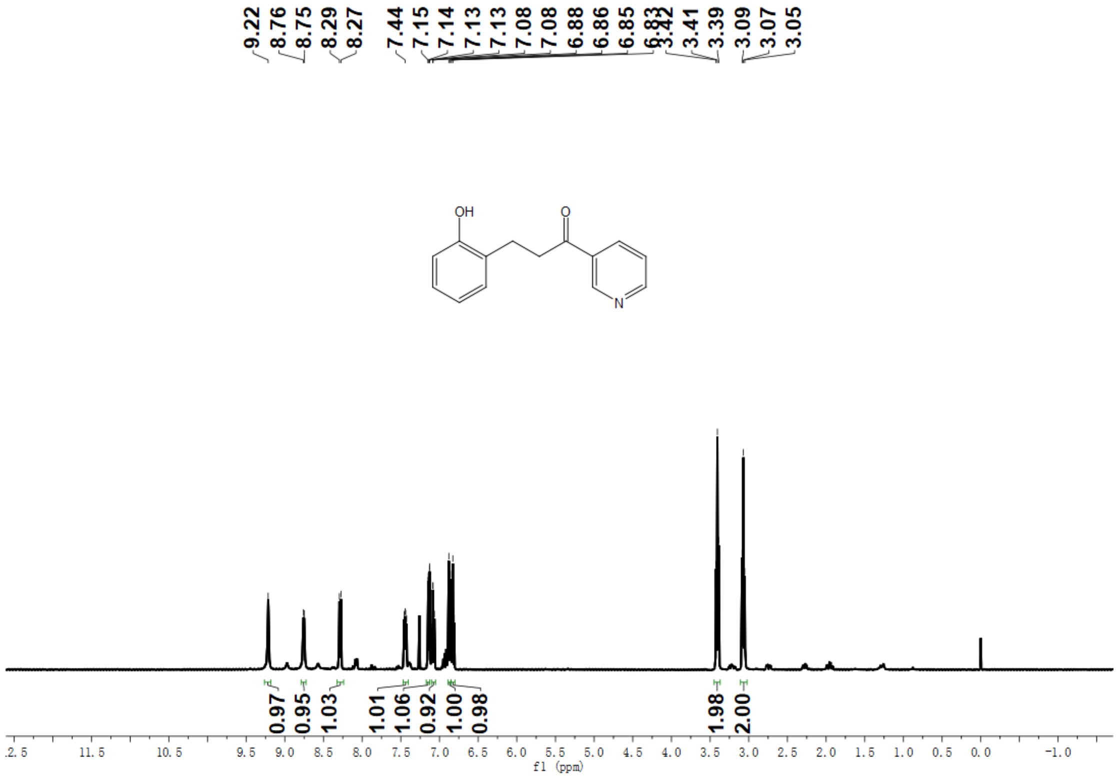


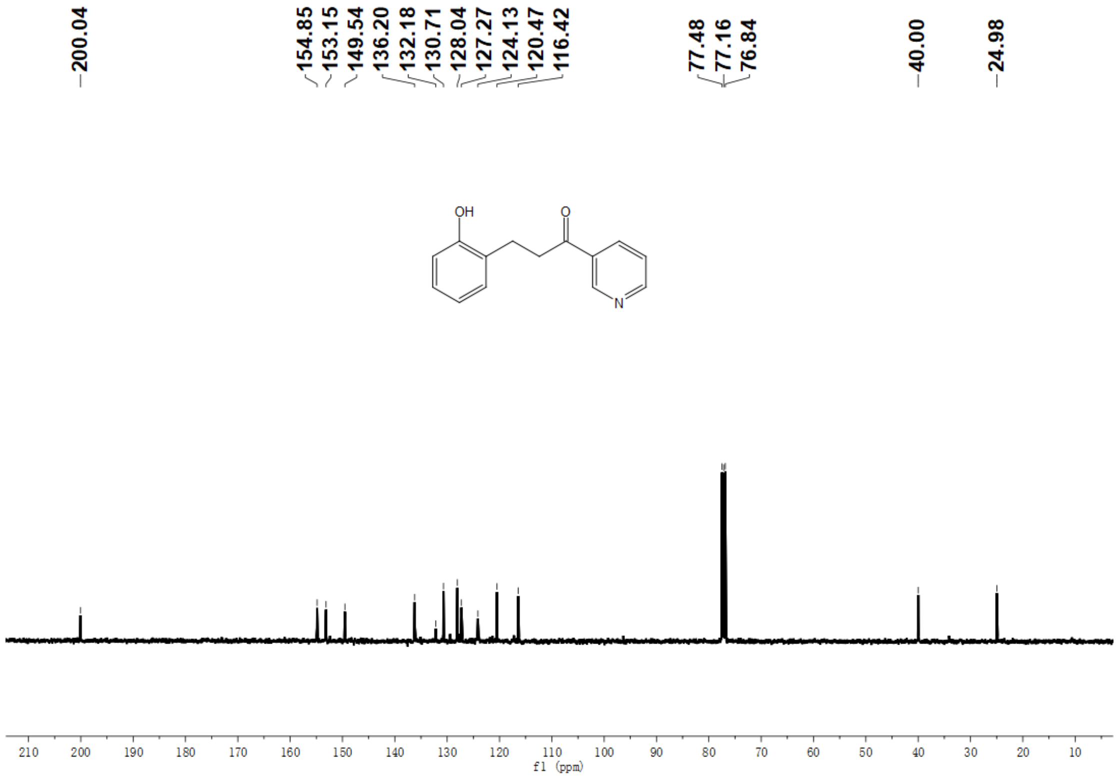
^{1}H and ^{13}C NMR Spectra of Compound **4k**



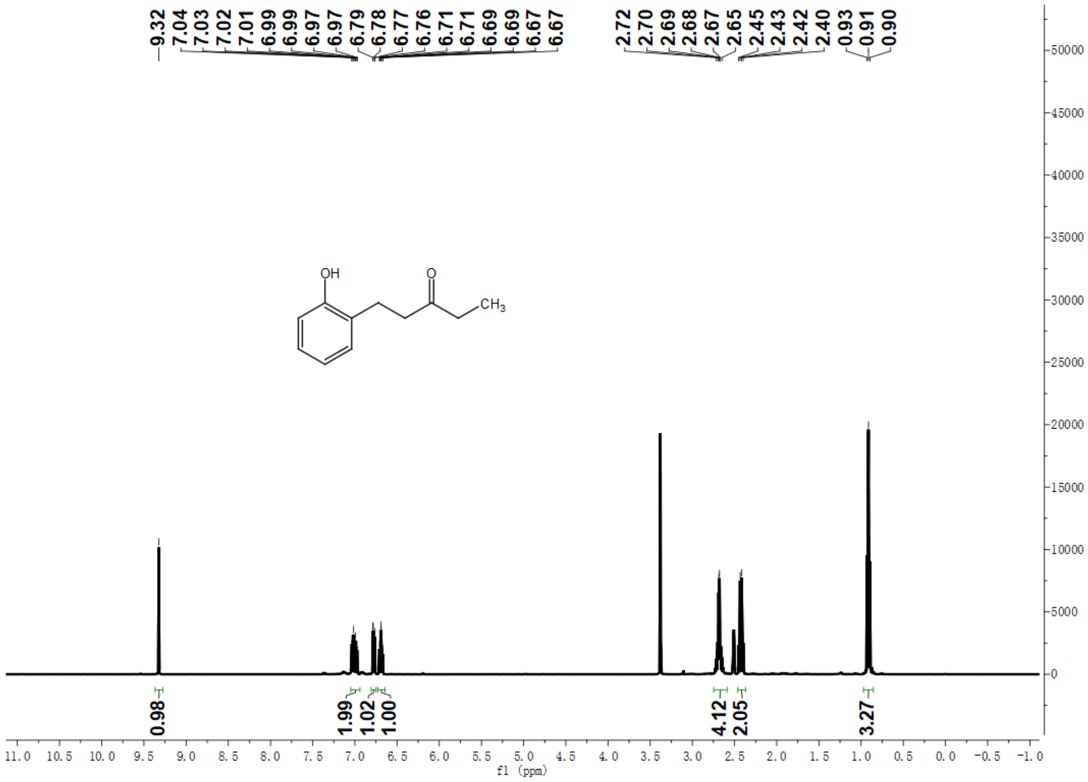


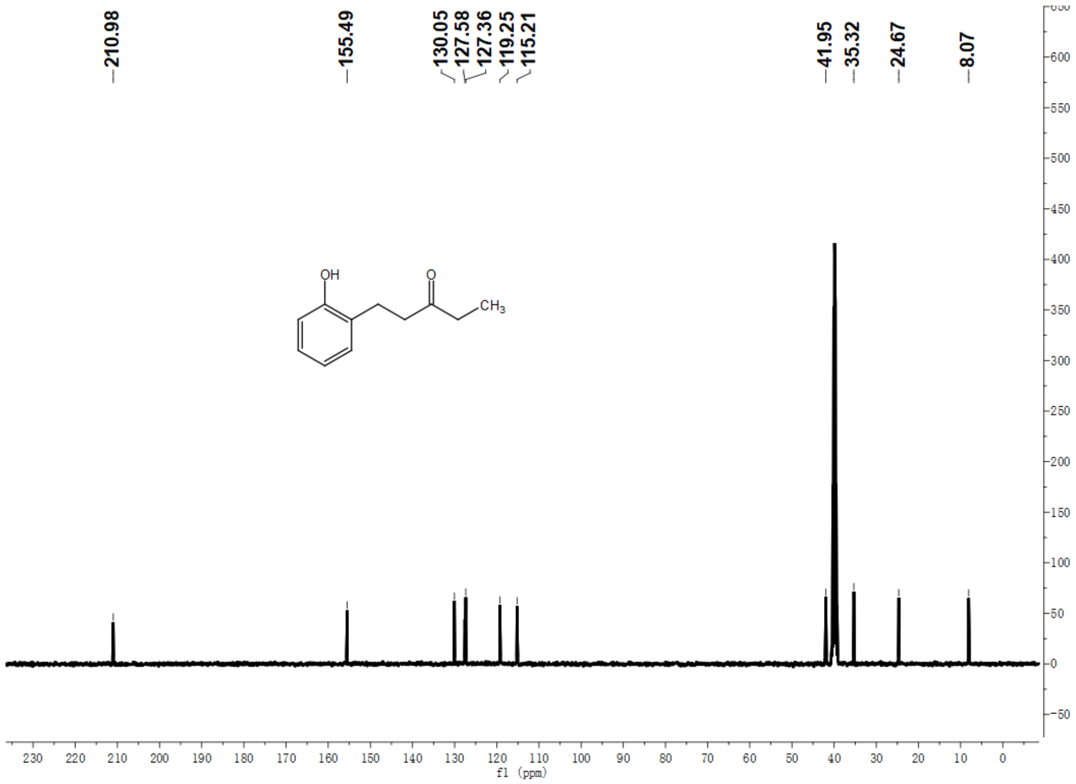
^{1}H and ^{13}C NMR Spectra of Compound **4l**



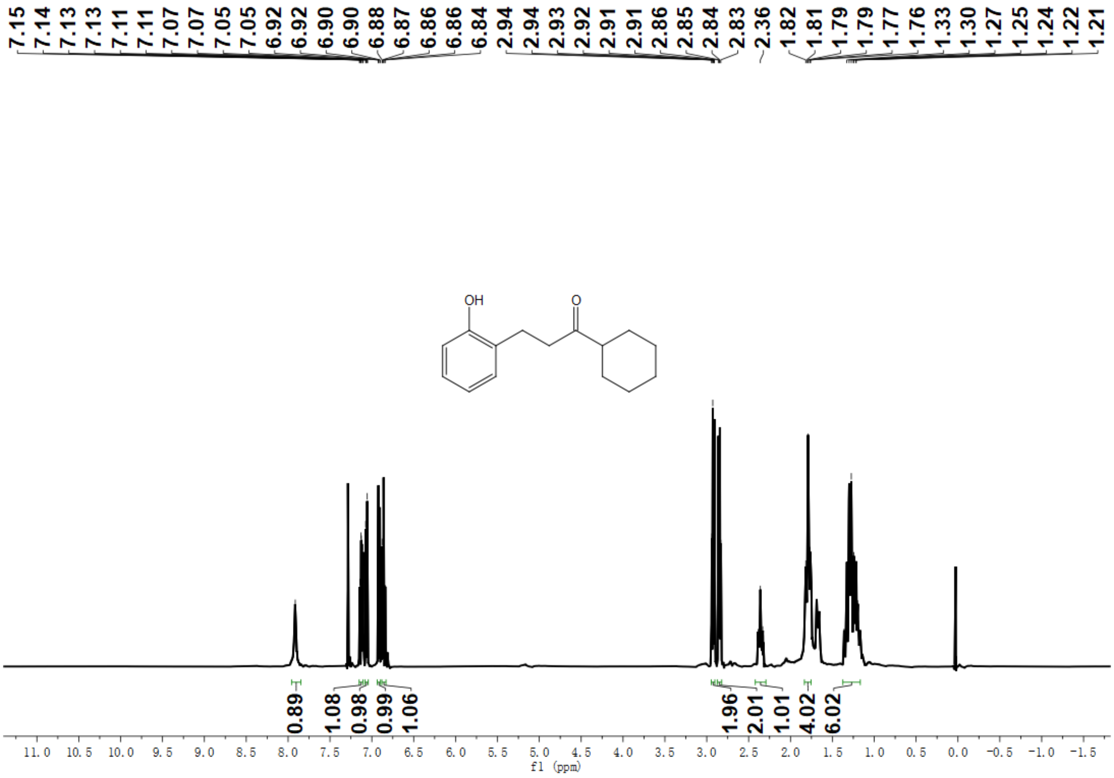


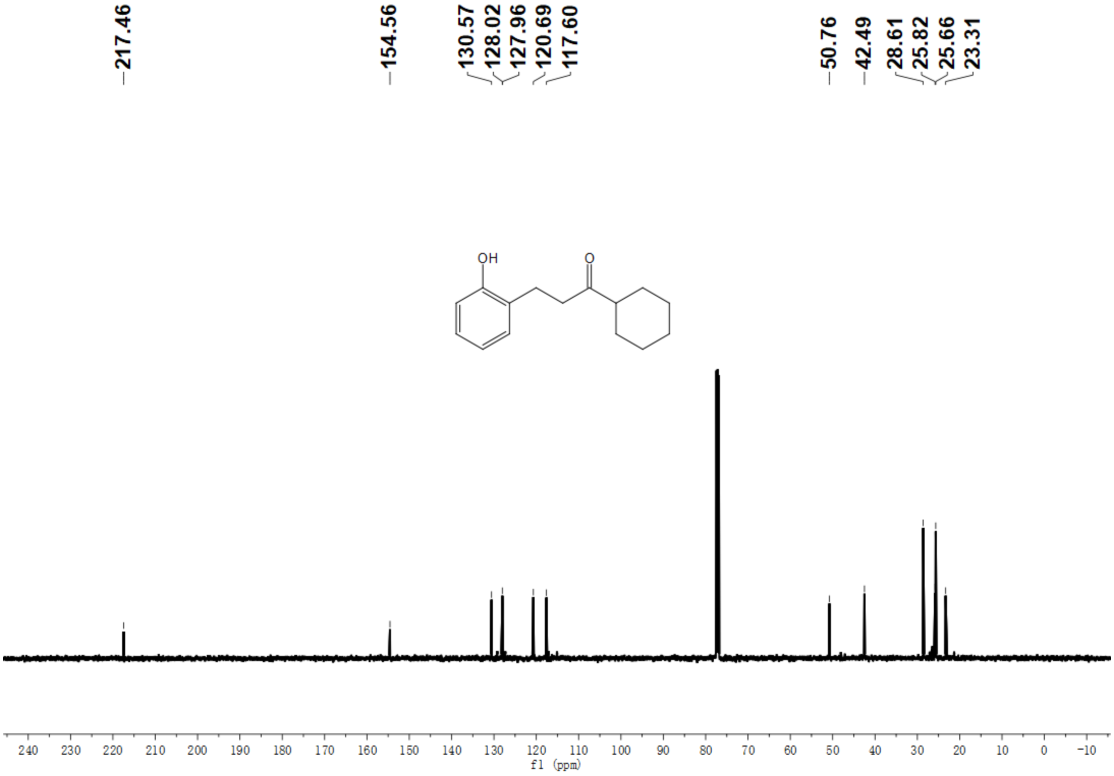
^{1}H and ^{13}C NMR Spectra of Compound **4m**



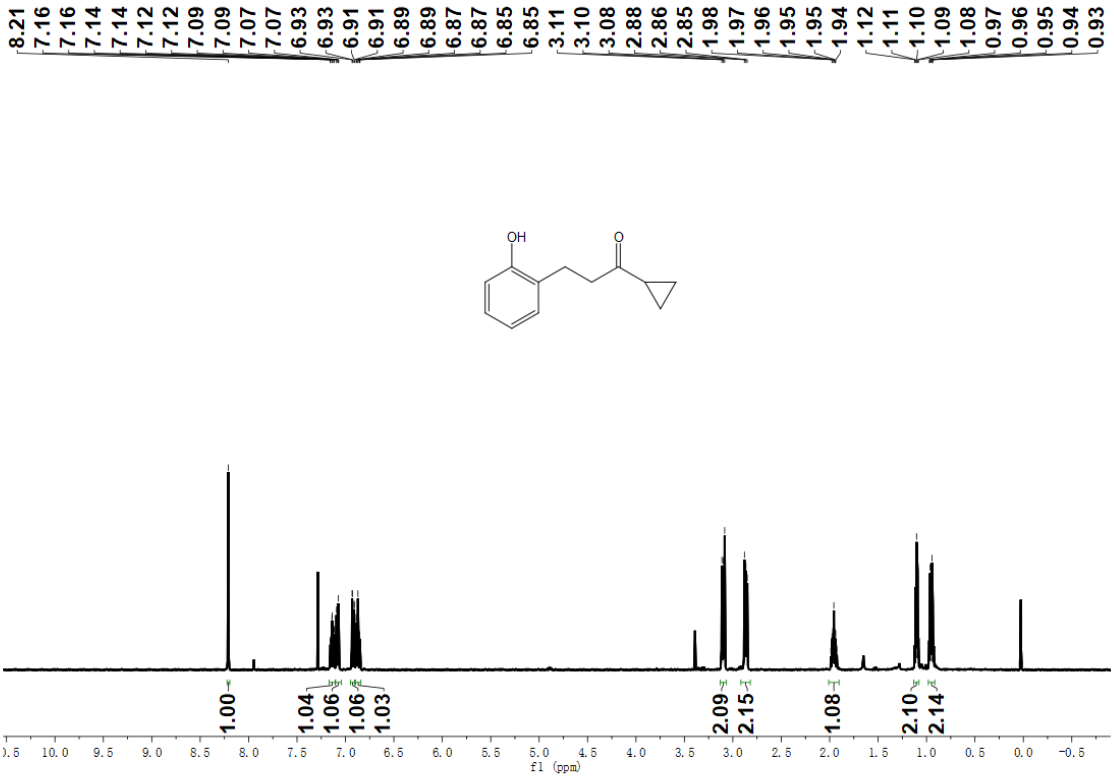


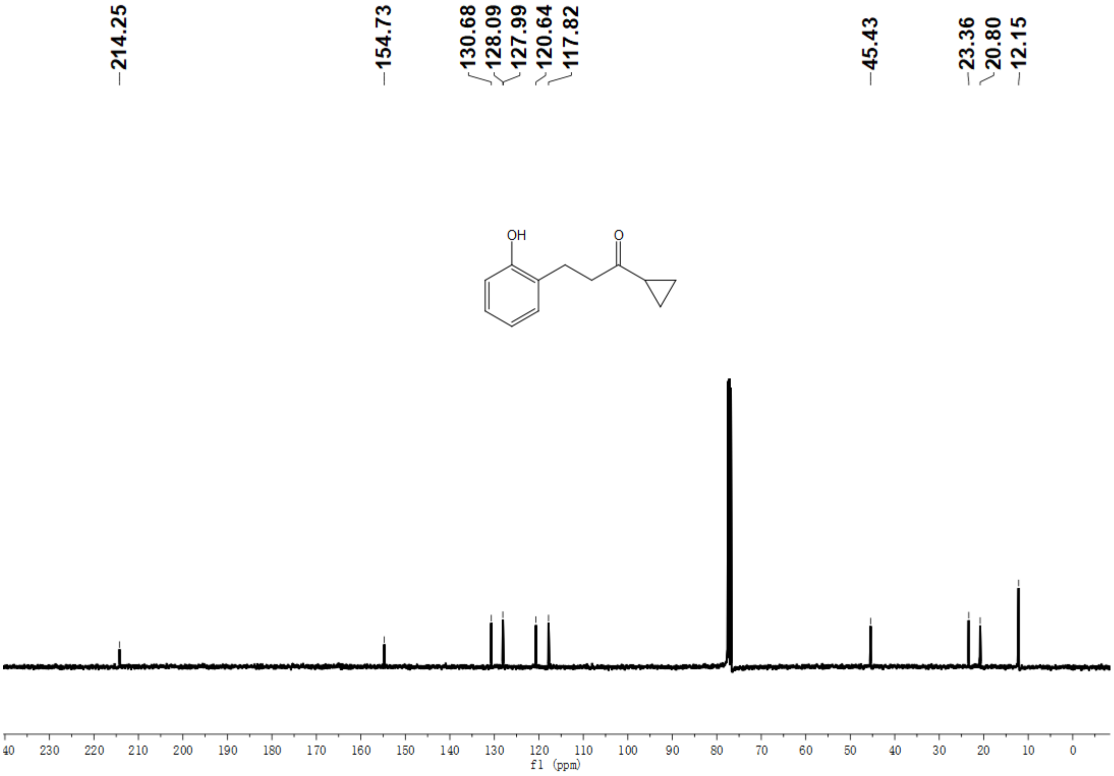
^{1}H and ^{13}C NMR Spectra of Compound **4n**



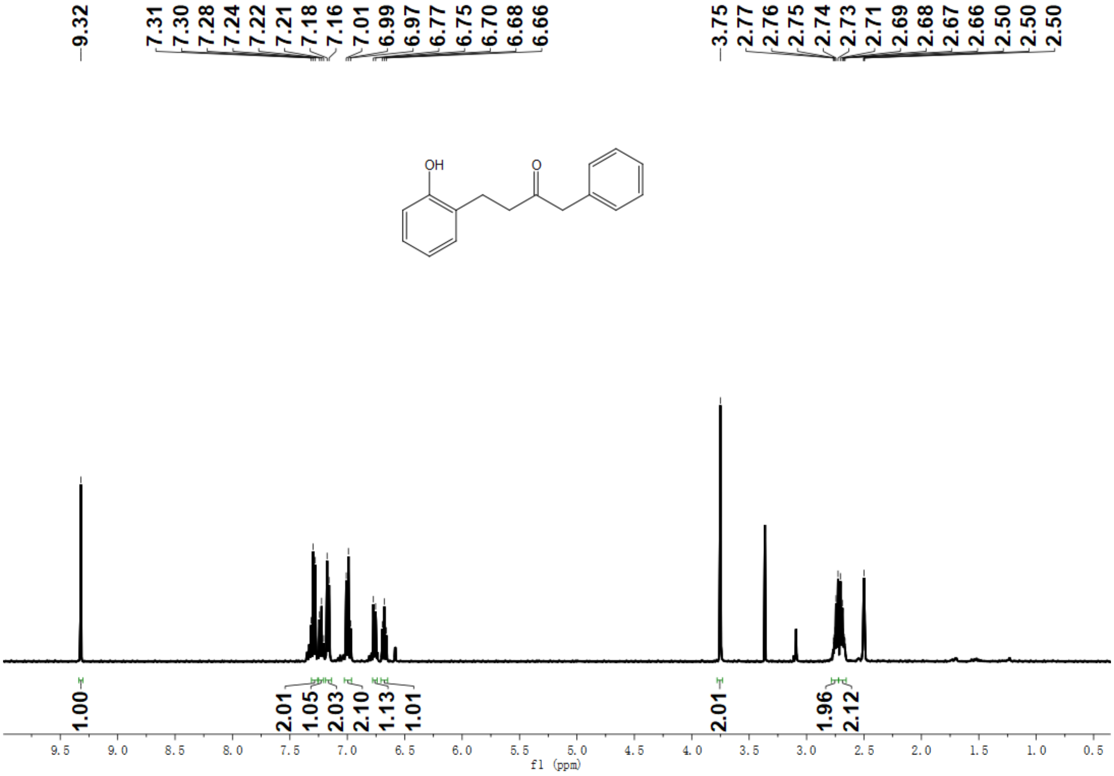


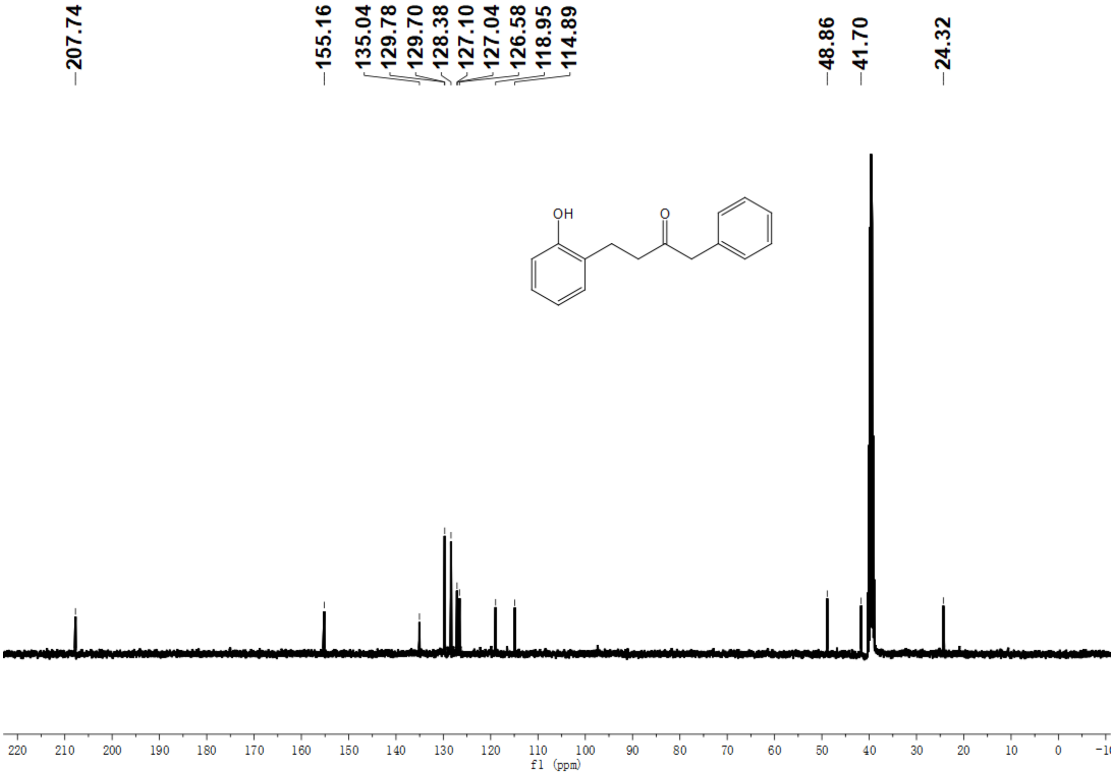
^{1}H and ^{13}C NMR Spectra of Compound **4o**



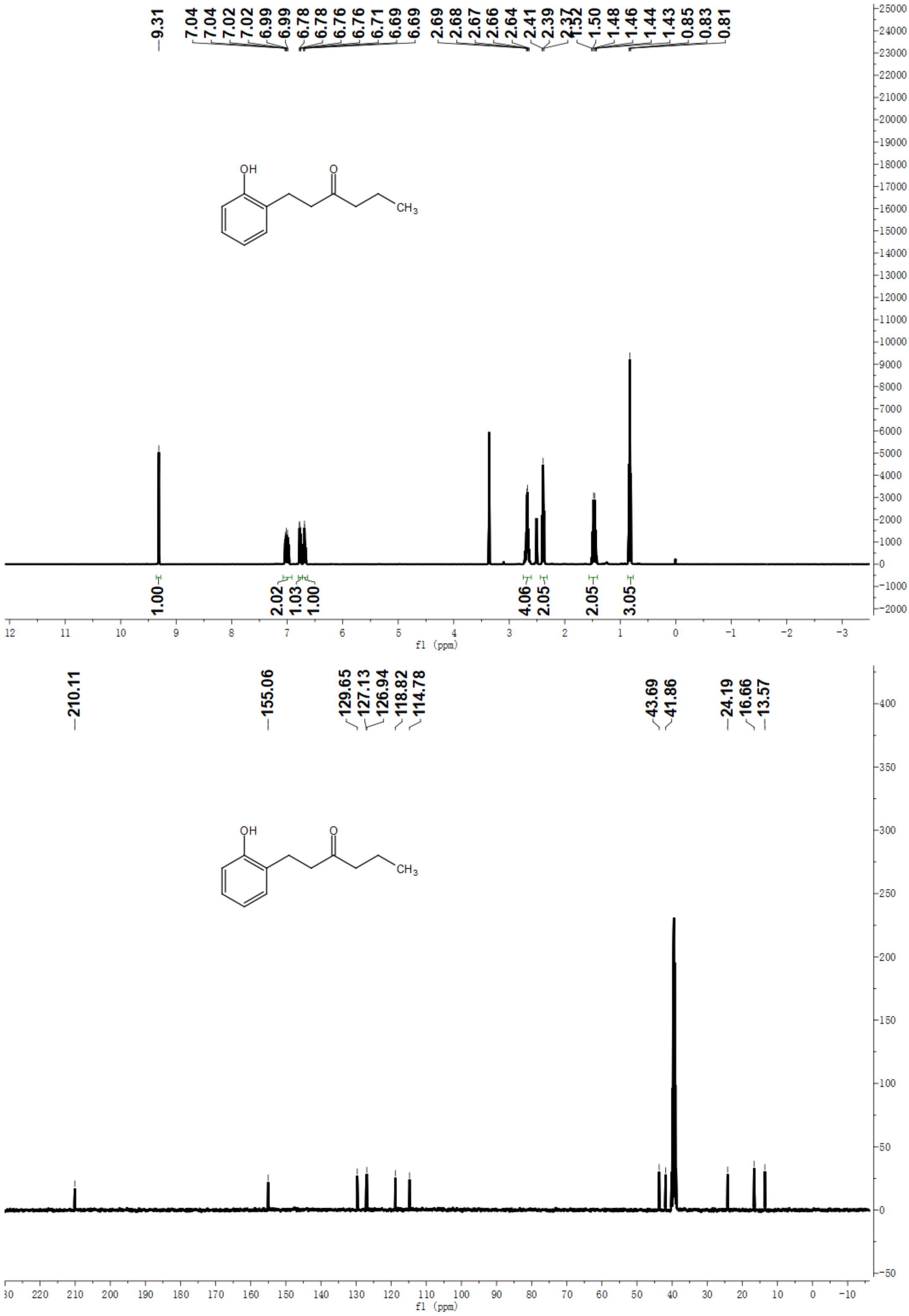


^{1}H and ^{13}C NMR Spectra of Compound **4p**

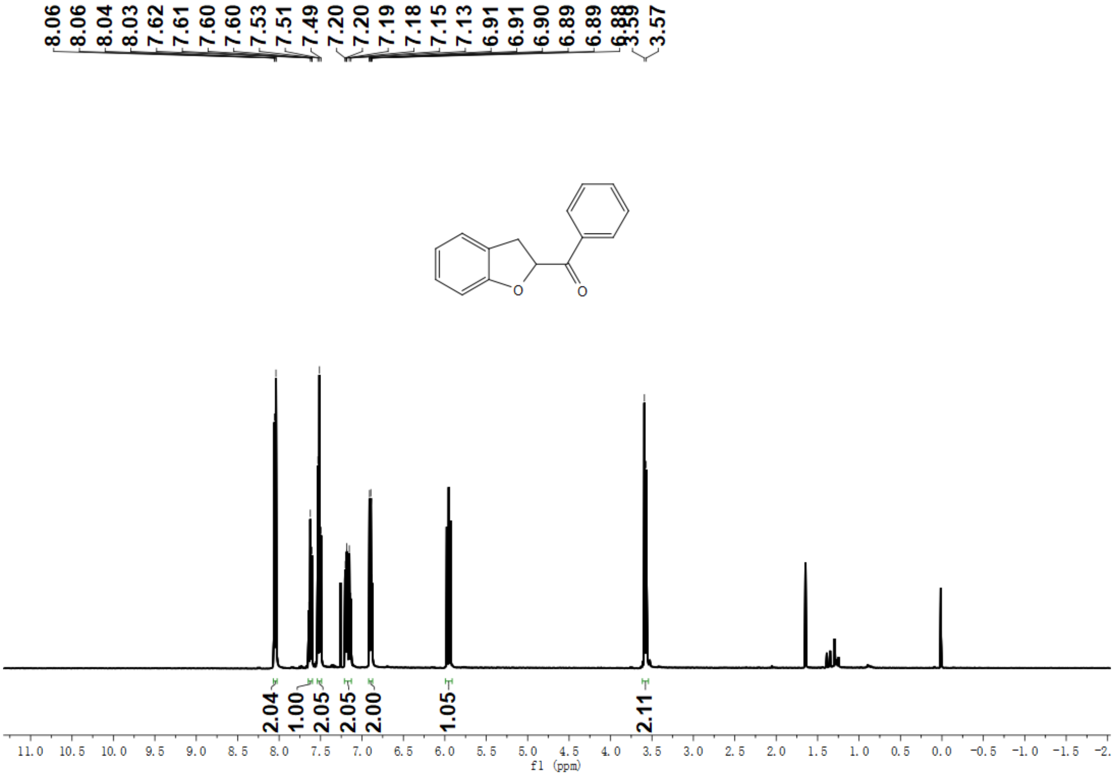


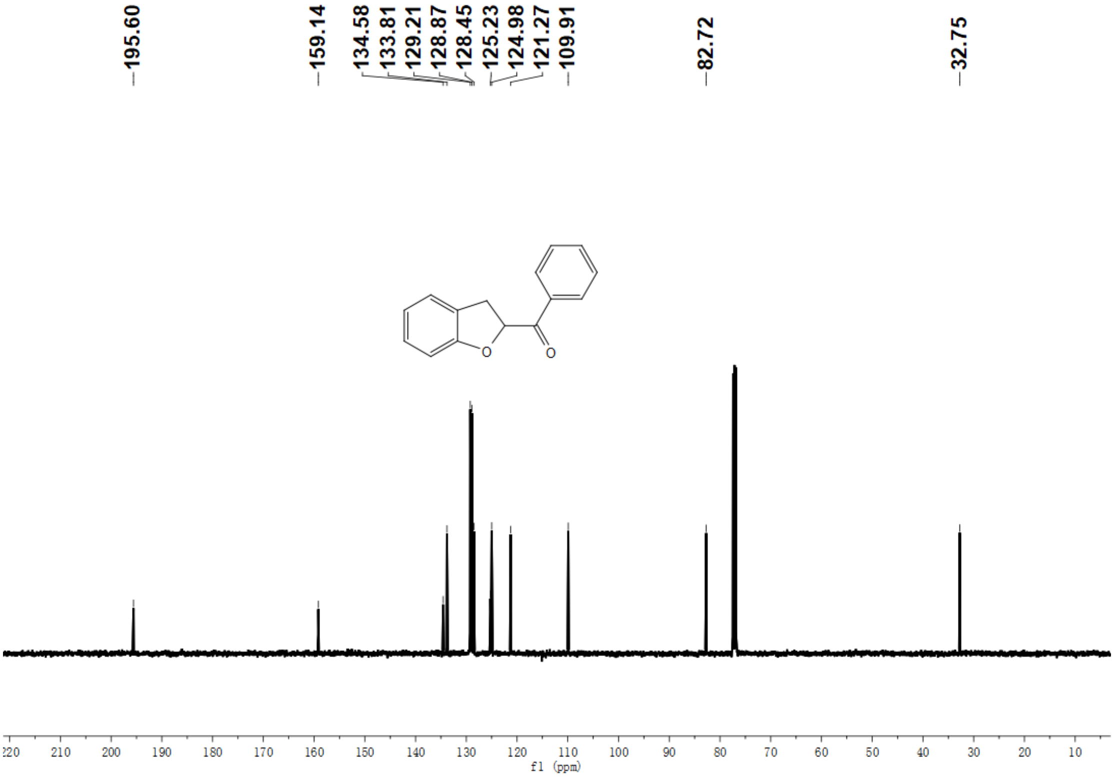


^{1}H and ^{13}C NMR Spectra of Compound **4q**



^{1}H and ^{13}C NMR Spectra of Compound **5a**





^{1}H and ^{13}C NMR Spectra of Compound **6a**