Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

A Formal (3+2) Annulation-Cannizzaro Cascade of Bifunctional Peroxides for the Synthesis of Dihydrofurans

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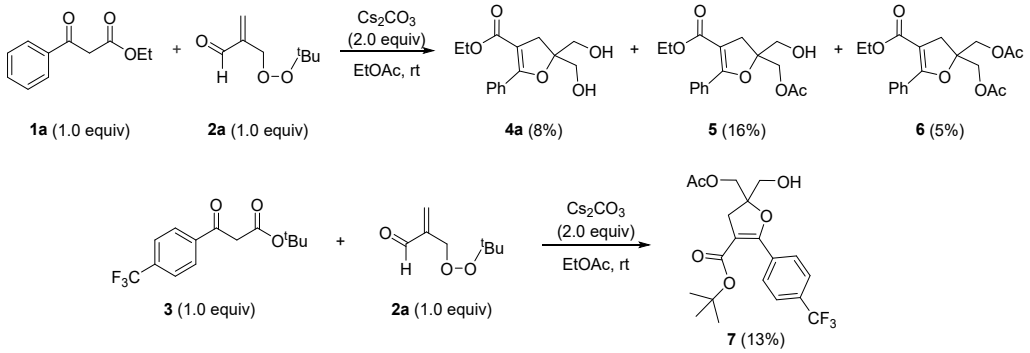
Table of Contents

1. General Information

Unless otherwise stated, all reagents obtained from Adamas, Accela, or Acros were used without further purification. All solvents employed in the reactions were distilled from appropriate drying agents prior to use. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 GF254 plates. Visualization on TLC was achieved by use of UV light (254 nm). Flash column chromatography was performed using Tsingdao silica gel. ^{1}H and ^{13}C NMR spectra were recorded on Agilent 400MR DD2 (400 MHz) spectrometer or Agilent 600MR DD2 (600 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and tetramethylsilane (TMS) or the residual solvent peak was used as an internal reference: ^{1}H NMR (TMS, δ 0.00; $CDCl_3$, δ 7.26; CD_3OD, δ 3.31), ^{13}C NMR ($CDCl_3$, δ 77.16; CD_3OD, δ 49.00). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz) and integration. High resolution mass spectra (HRMS) data were acquired on AB SCIEX TripleTOF 6600 mass spectrometer (AB SCIEX, USA) or Agilent 6546 Q-TOF mass spectrometer (Agilent Technologies, USA) with an ESI source.

2. Optimization of the reaction

Isolation and identification of the new products



Data of compound **5**: **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.79 - 7.70 (m, 2H), 7.47 - 7.34 (m, 3H), 4.36 (d, *J* = 11.7 Hz, 1H), 4.31 (d, *J* = 11.8 Hz, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.75 (s, 2H), 3.05 (d, *J* = 15.5 Hz, 1H), 2.96 (d, *J* = 15.5 Hz, 1H), 2.26 (br, s, 1H), 2.11 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (150 MHz, $CDCl_3$)** δ 171.2, 165.0, 164.0, 130.6, 129.7, 129.4, 127.7, 102.6, 87.0, 64.8, 64.3, 60.0, 36.2, 20.9, 14.3. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{17}H_{21}O_6$: 321.1333; Found: 321.1335.

^{1}H-^{1}H COSY correlations of compound 5:

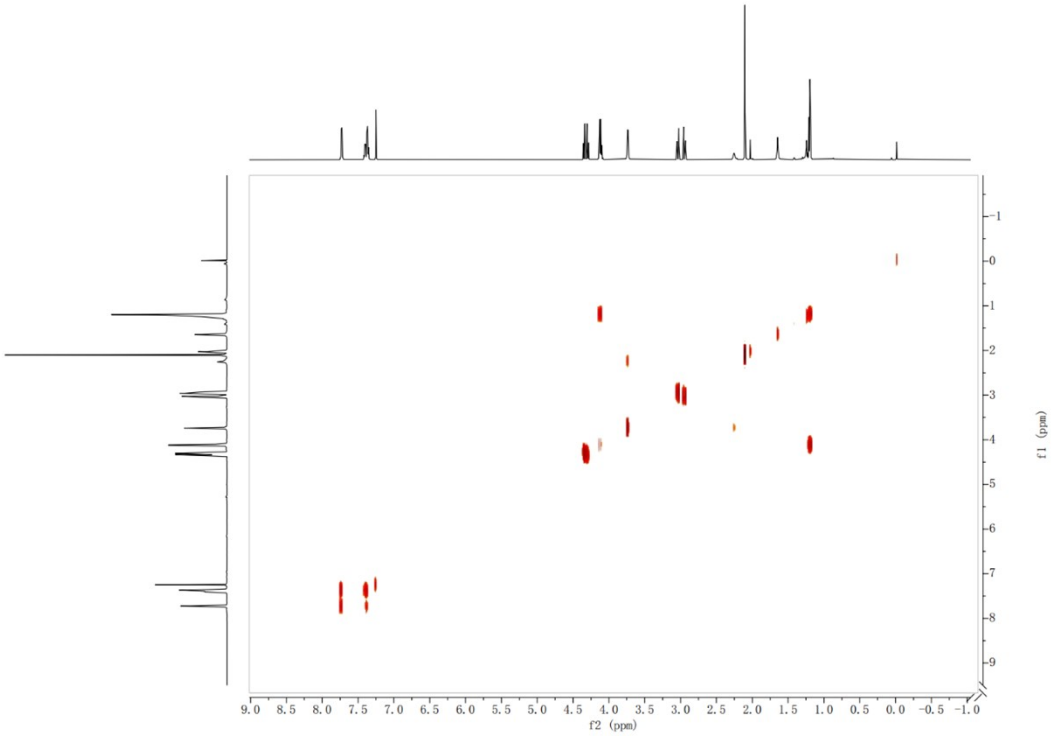


Figure S1. COSY spectrum of compound 5

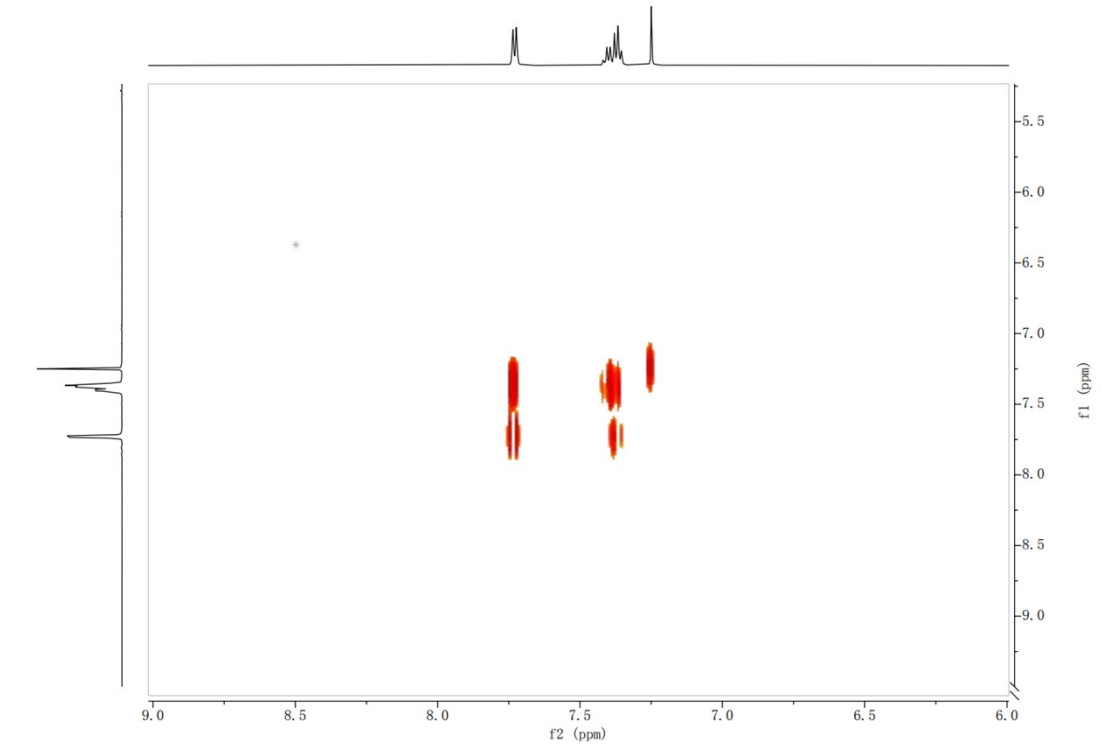


Figure S2. Enlarged view of COSY spectra of 5 (6.0 – 9.0 ppm)

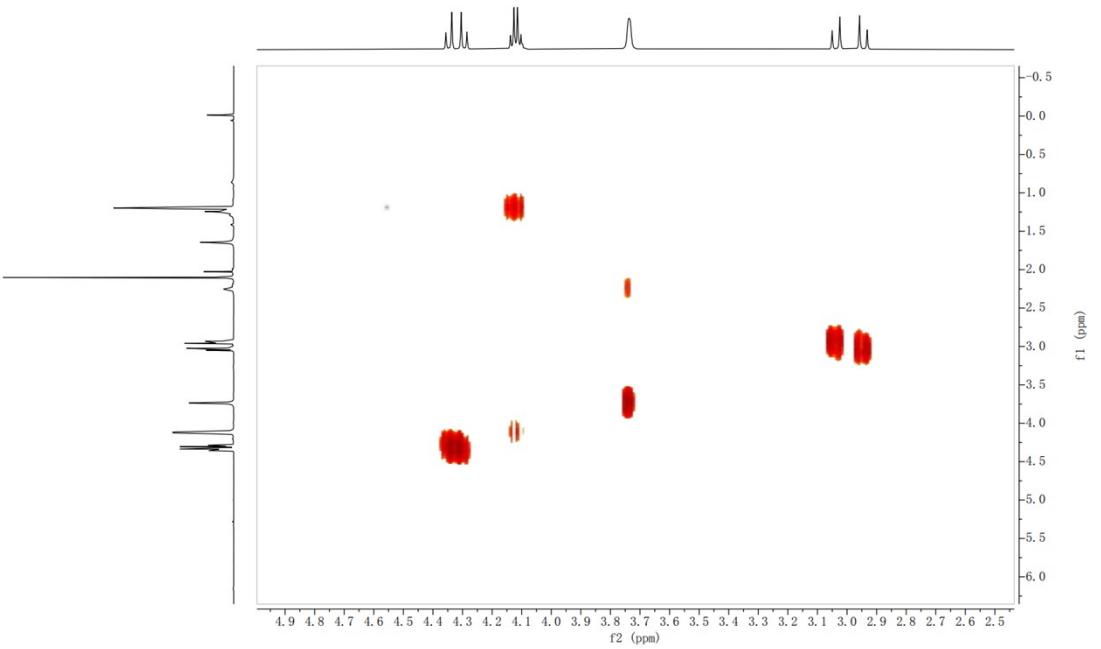


Figure S3. Enlarged view of COSY spectra of 5 (2.5 – 5.0 ppm)

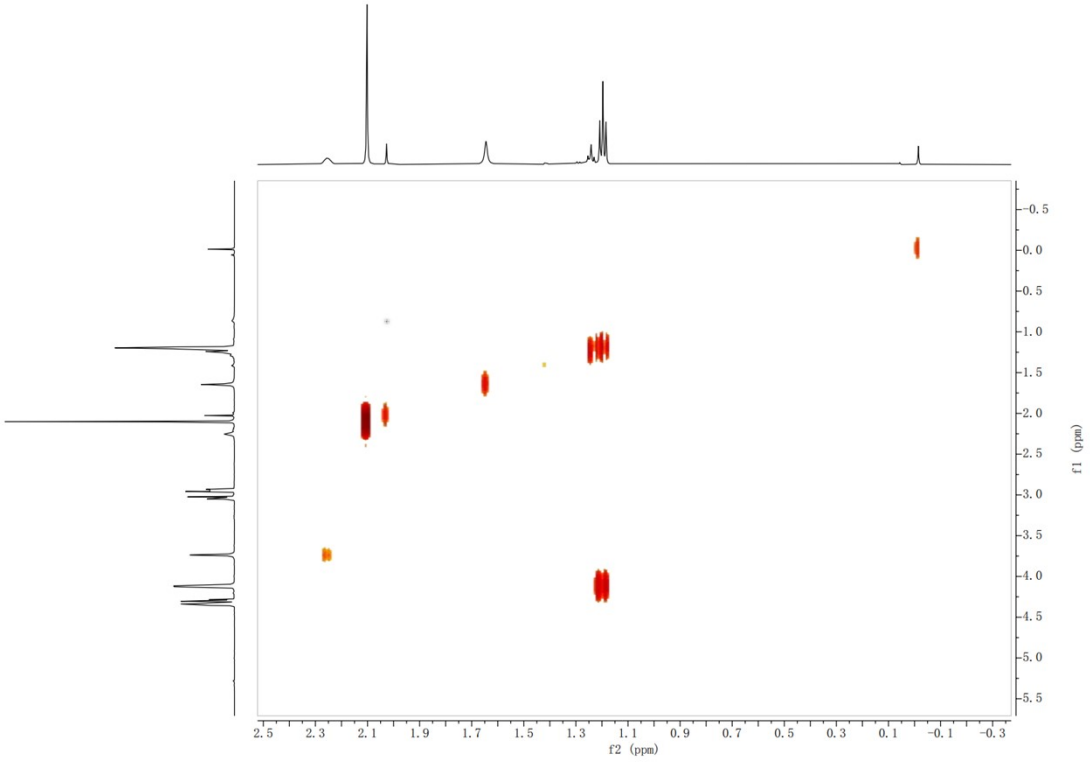


Figure S4. Enlarged view of COSY spectra of 5 (0.0 – 2.5 ppm)

^{1}H-^{13}C HSQC correlations of compound 5:

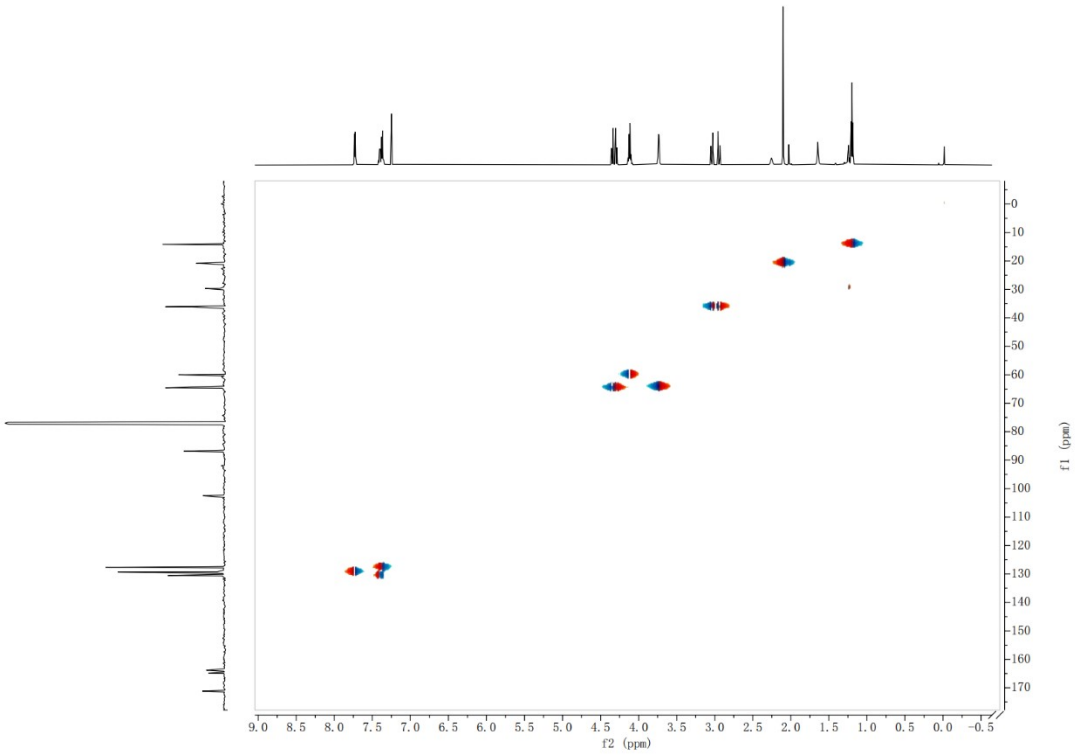


Figure S5. HSQC spectrum of compound 5

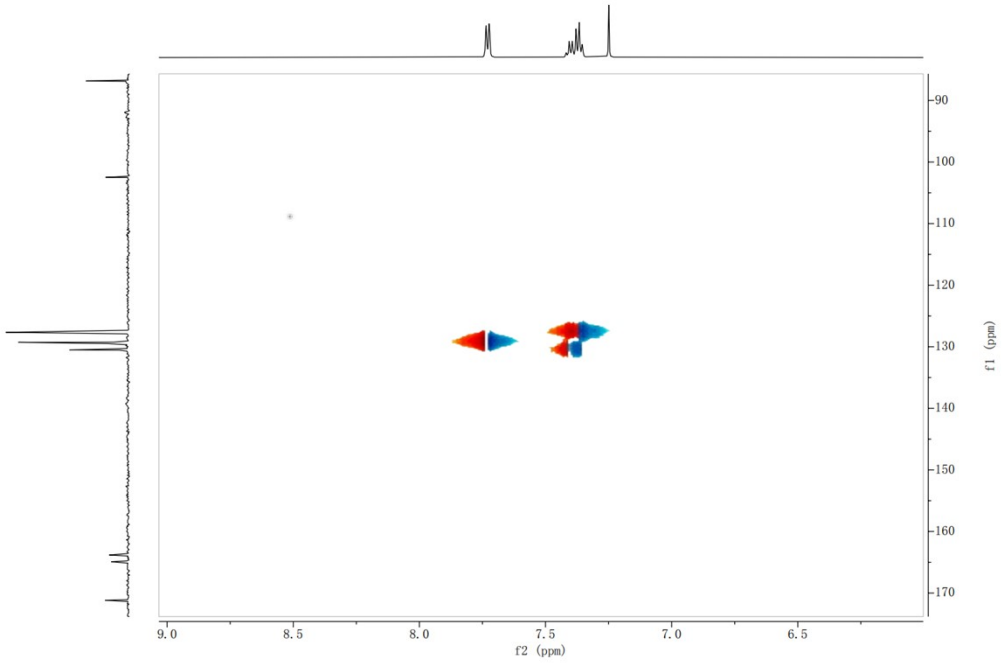


Figure S6. Enlarged view of HSQC spectra of 5 (6.0 – 9.0 and 85 – 175 ppm)

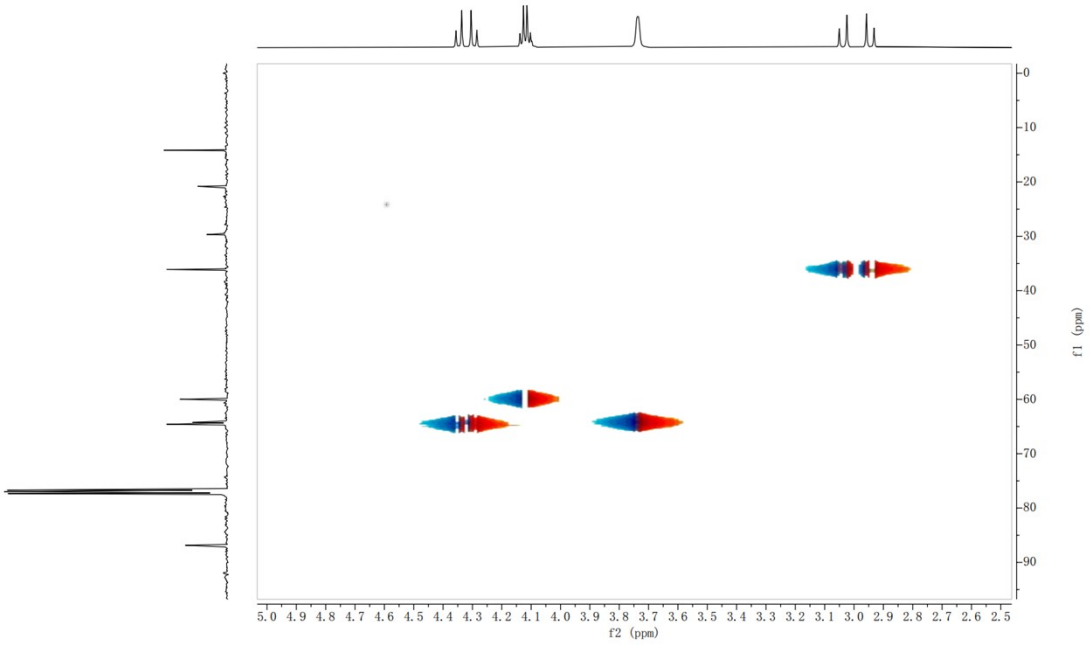


Figure S7. Enlarged view of HSQC spectra of 5 (2.5 – 5.0 and 0 – 100 ppm)

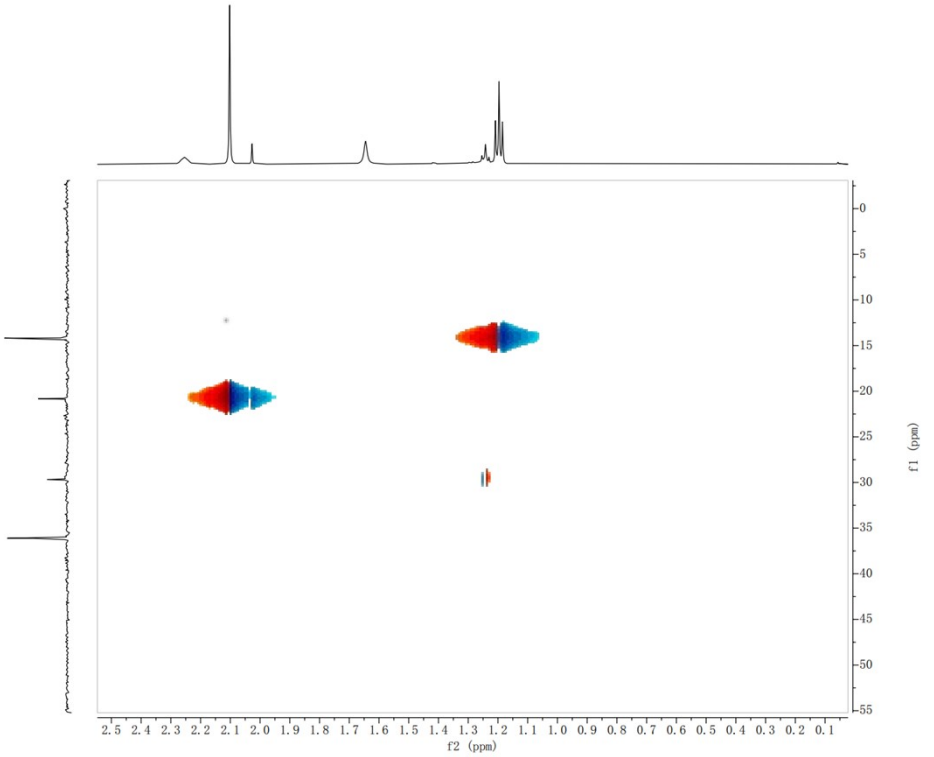


Figure S8. Enlarged view of HSQC spectra of 5 (0.0 – 2.5 and 0 – 55 ppm)

^{1}H-^{13}C HMBC correlations of compound 5:

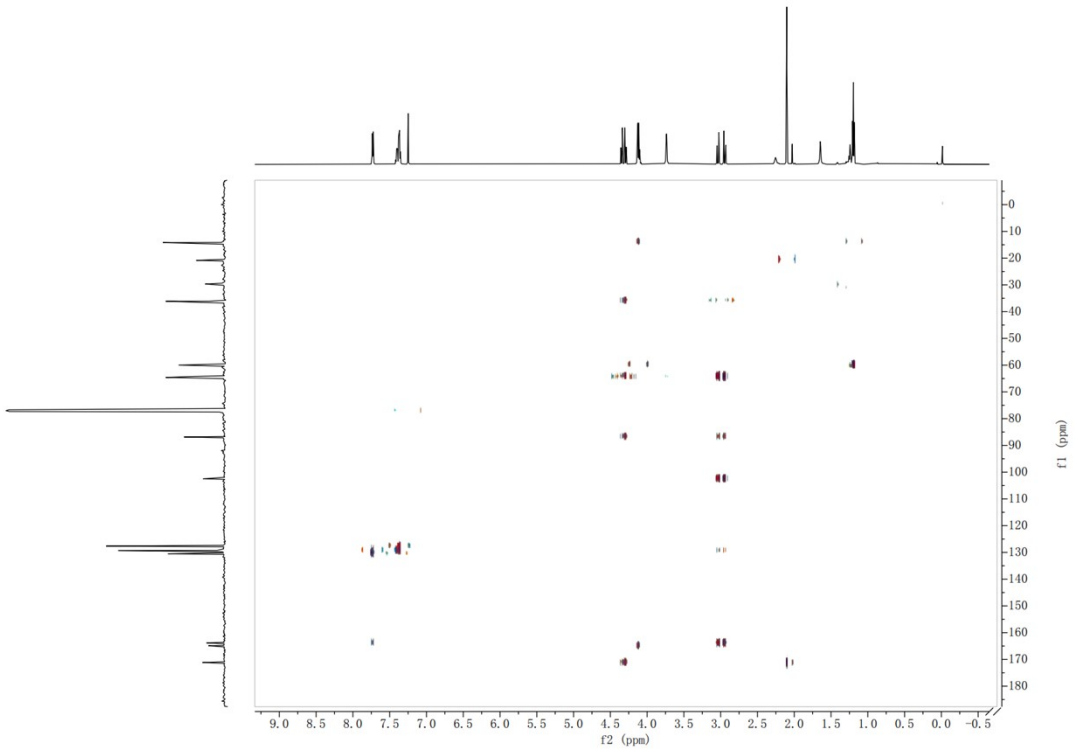


Figure S9. HMBC spectrum of compound 5

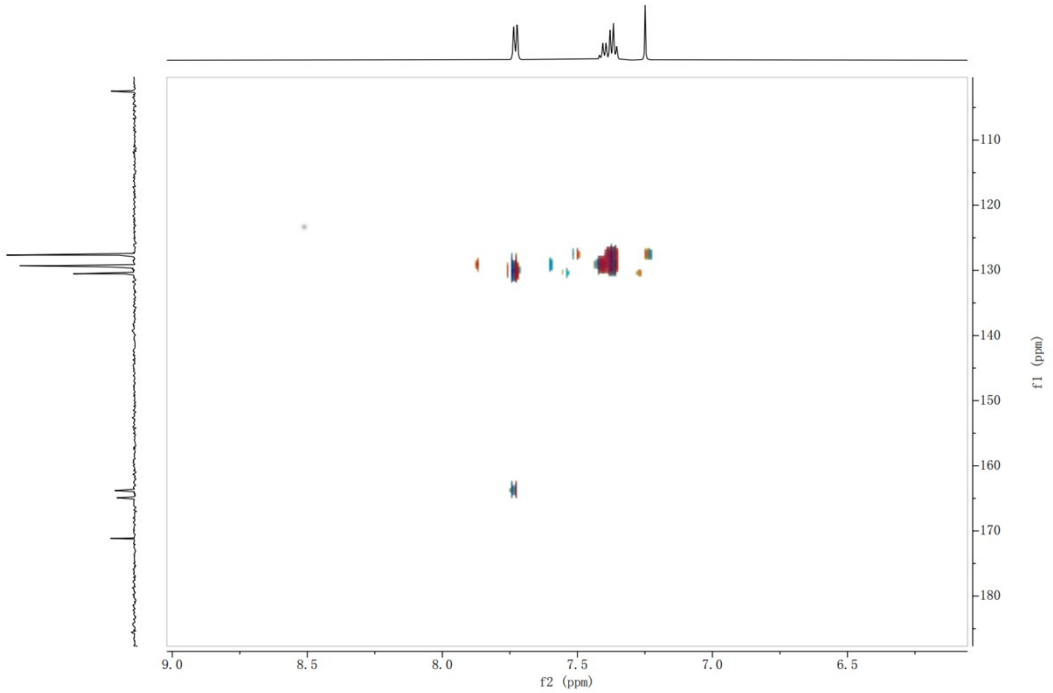


Figure S10. Enlarged view of HMBC spectra of 5 (6.0 – 9.0 and 100 – 190 ppm)

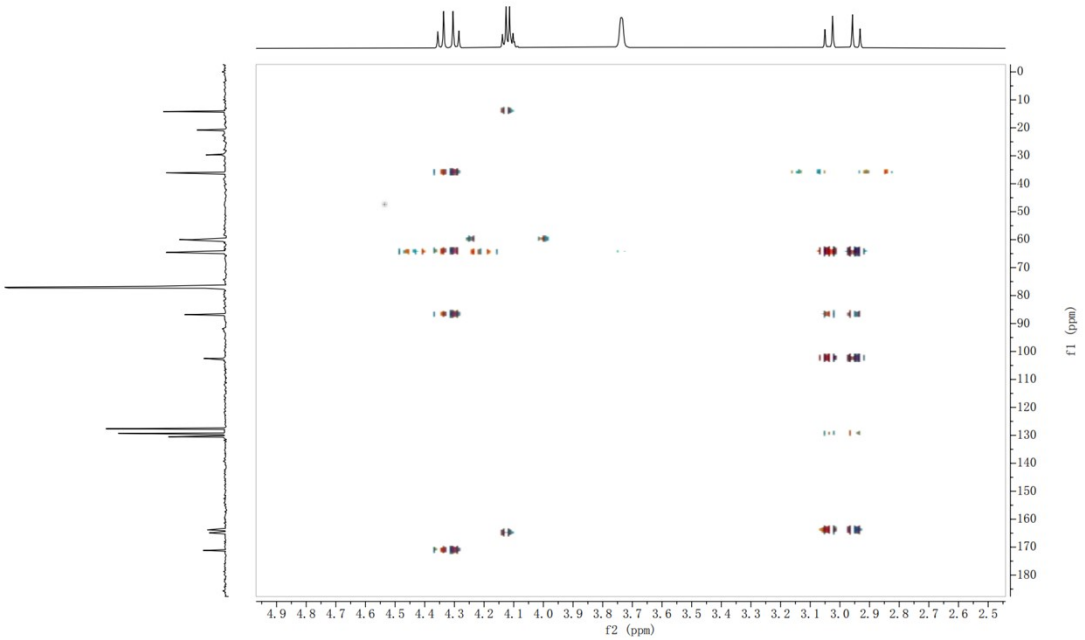


Figure S11. Enlarged view of HMBC spectra of 5 (2.5 – 5.0 and 0 – 190 ppm)

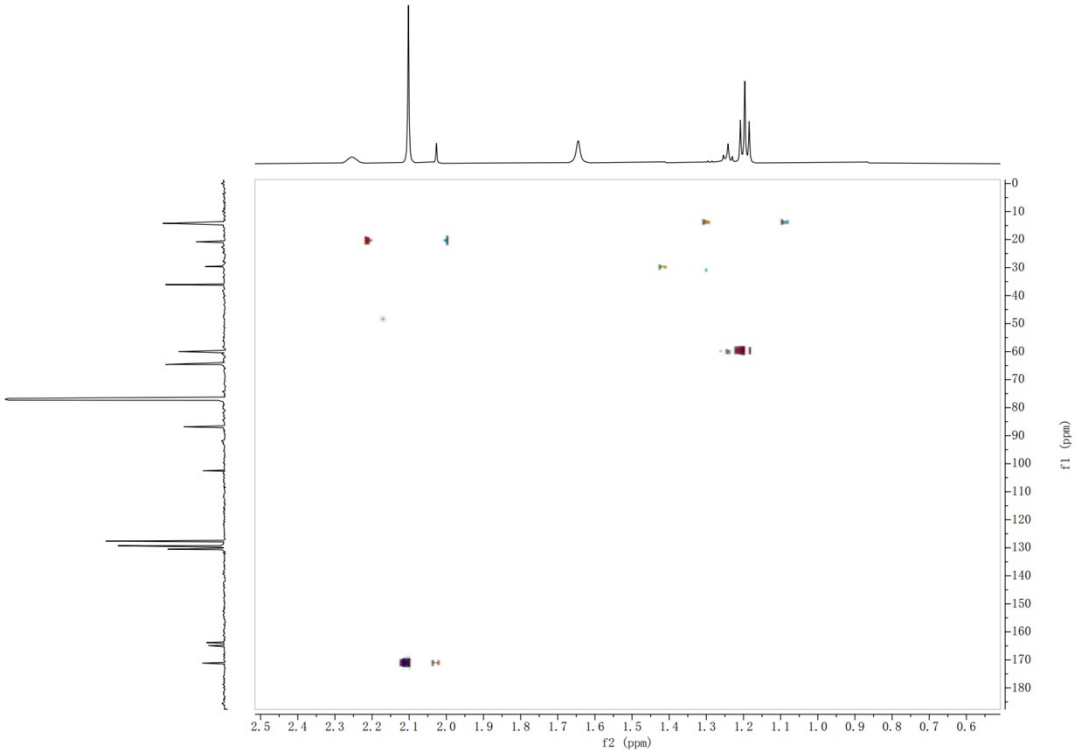
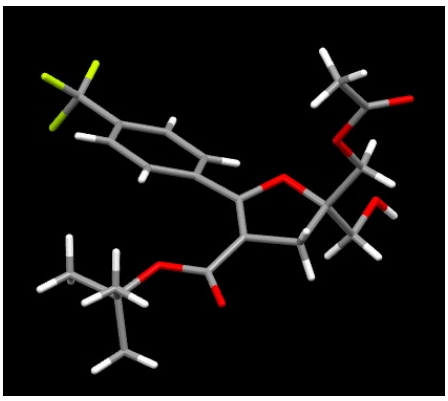


Figure S12. Enlarged view of HMBC spectra of 5 (0.5 – 2.5 and 0 – 190 ppm)

Data of compound **6**: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (dd, *J* = 8.2, 1.7 Hz, 2H), 7.43 - 7.31 (m, 3H), 4.30 (d, *J* = 11.7 Hz, 2H), 4.26 (d, *J* = 11.7 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.02 (s, 2H), 2.10 (s, 6H), 1.18 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ170.8, 165.0, 164.2, 130.7, 129.4, 127.8, 102.2, 84.8, 64.9, 60.2, 36.7, 20.8, 14.2. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{19}H_{23}O_7$: 363.1439; Found: 363.1434.

Data of compound **7**: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 4.34 (s, 2H), 3.76 (s, 2H), 3.04 (d, *J* = 15.9 Hz, 1H), 2.91 (d, *J* = 15.9 Hz, 1H), 2.13 (s, 3H), 1.40 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.3, 164.1, 161.2, 133.5, 131.9 (d, *J* = 32.2 Hz), 129.9, 124.7, 105.8, 87.1, 80.8, 64.7, 64.1, 36.5, 28.2, 20.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{20}H_{23}F_3NaO_6$: 439.1339; Found: 439.1346.

X-ray data for compound **7** are as follows:



CCDC: 2301447(the ellipsoid is 50% probability)

Table S1. Crystal data and structure refinement for 7

Identification code	20211115-XQL-05-92-1
Empirical formula	$C_{20}H_{23}F_3O_6$
Formula weight	416.38
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	6.1686(4)
b/Å	40.158(2)
c/Å	8.3757(7)
α/°	90
β/°	98.900(6)
γ/°	90
Volume/Å^3	2049.8(2)
Z	4
ρ_{calc}g/cm^3	1.349
μ/mm^{-1}	0.116
F(000)	872.0
Crystal size/mm^3	0.38 × 0.35 × 0.24
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.762 to 57.722
Index ranges	$-5 \le h \le 8$, $-50 \le k \le 29$, $-10 \le l \le 7$
Reflections collected	8311
Independent reflections	4646 [R_{int} = 0.0345, R_{sigma} = 0.0720]
Data/restraints/parameters	4646/0/268
Goodness-of-fit on F^2	1.046
Final R indexes [I>=2σ (I)]	R_1 = 0.0894, wR_2 = 0.2242
Final R indexes [all data]	R_1 = 0.1482, wR_2 = 0.2697
Largest diff. peak/hole / e Å^{-3}	0.64/-0.36

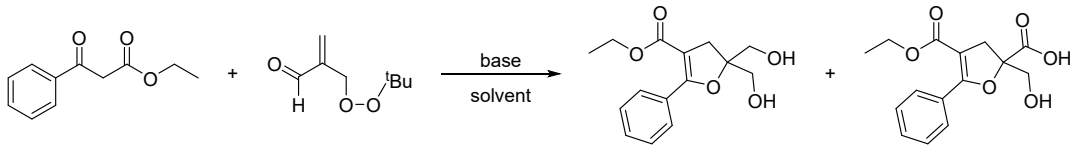
Table S2. Bond Lengths for 7

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O4	C8	1.361(4)	C11	C12	1.379(5)
O4	C4	1.466(4)	C12	C14	1.371(5)
O6	C16	1.323(5)	C12	C13	1.485(5)
O6	C17	1.478(5)	F1	C13	1.301(5)
O2	C3	1.430(5)	F3	C13	1.248(5)
O2	C2	1.345(6)	C15	C14	1.385(5)
O5	C16	1.202(5)	C7	C16	1.460(5)
O3	C5	1.405(6)	C7	C6	1.500(5)
C9	C8	1.481(5)	C4	C3	1.507(6)
C9	C10	1.382(5)	C4	C6	1.542(5)
C9	C15	1.388(5)	C4	C5	1.496(6)
O1	C2	1.202(6)	C17	C18	1.514(6)
C8	C7	1.354(5)	C17	C19	1.504(7)
F2	C13	1.343(6)	C17	C20	1.508(7)
C11	C10	1.389(5)	C2	C1	1.477(7)

Table S3. Bond Angles for 7

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C8	O4	C4	109.0(3)	C5	C4	C6	111.8(4)
C16	O6	C17	121.9(3)	C12	C14	C15	120.2(4)
C2	O2	C3	114.2(4)	O6	C16	C7	115.1(3)
C10	C9	C8	122.8(3)	O5	C16	O6	123.9(4)
C10	C9	C15	119.1(3)	O5	C16	C7	121.0(4)
C15	C9	C8	117.9(3)	F2	C13	C12	111.4(4)
O4	C8	C9	110.9(3)	F1	C13	F2	99.2(4)
C7	C8	O4	113.5(3)	F1	C13	C12	114.6(4)
C7	C8	C9	135.6(3)	F3	C13	F2	103.3(5)
C12	C11	C10	119.6(3)	F3	C13	C12	115.7(4)
C9	C10	C11	120.6(3)	F3	C13	F1	110.7(5)
C11	C12	C13	119.5(4)	O2	C3	C4	110.4(3)
C14	C12	C11	120.3(4)	O6	C17	C18	109.5(4)
C14	C12	C13	120.2(4)	O6	C17	C19	109.8(4)
C14	C15	C9	120.3(3)	O6	C17	C20	103.0(3)
C8	C7	C16	133.2(4)	C19	C17	C18	112.6(4)
C8	C7	C6	108.5(3)	C19	C17	C20	111.3(5)
C16	C7	C6	118.3(3)	C20	C17	C18	110.2(5)
O4	C4	C3	107.1(3)	C7	C6	C4	103.4(3)
O4	C4	C6	104.5(3)	O2	C2	C1	112.3(4)
O4	C4	C5	106.9(3)	O1	C2	O2	122.2(5)
C3	C4	C6	115.0(4)	O1	C2	C1	125.5(5)
C5	C4	C3	110.9(4)	O3	C5	C4	109.7(4)

Table S4. Screening of base, solvent, and temperature

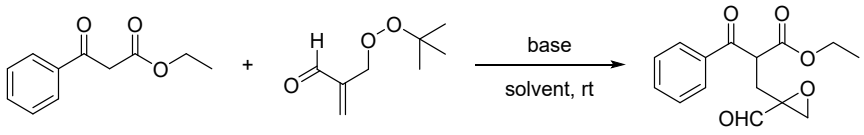


1a (1.0 equiv) **2a** (1.0 equiv) **4a** **8a**

Entry	Base	Equiv.	Sol.	Temp.(°C)	Time	Yield of **4a** (%)	Yield of **8a** (%)
1	Cs_2CO_3	2.0	EtOAc	rt	1 h	8	23
2	K_3PO_4	2.0	EtOAc	rt	2 h	5	15
3	KOH	2.0	EtOAc	rt	20 min	13	34
4	NaOH	2.0	EtOAc	rt	20 min	10	27
5	KOH	2.0	THF	rt	20min	29	31
6	KOH	2.0	DCM	rt	20 min	45	43
7	KOH	2.0	$CHCl_3$	rt	25 min	37	27
8	KOH	2.0	PhMe	rt	30 min	28	30
9	KOH	2.0	MeCN	rt	20 min	31	26
10	KOH	2.0	Et_2O	rt	25 min	33	35
11	KOH	1.0	DCM	rt	25 min	20	15
12	KOH	3.0	DCM	rt	15 min	37	35
13	KOH	2.0	DCM	0	30 min	32	35
14	KOH	2.0	DCM	-10	55 min	12	8
15	$CsOH•H_2O$	2.0	DCM	rt	20 min	38	32
16	NaOH	2.0	DCM	rt	30 min	31	29
17	LiOH	2.0	DCM	rt	30 min	25	19
18	KO^tBu	2.0	DCM	rt	30 min	23	22
19	LiO^tBu	2.0	DCM	rt	30 min	25	21

Conditions: **1** (0.1 mmol), **2** (0.1 mmol) and base in indicated solvent (1 mL) and temperature.

Table S5. Optimization of the epoxidation reaction conditions



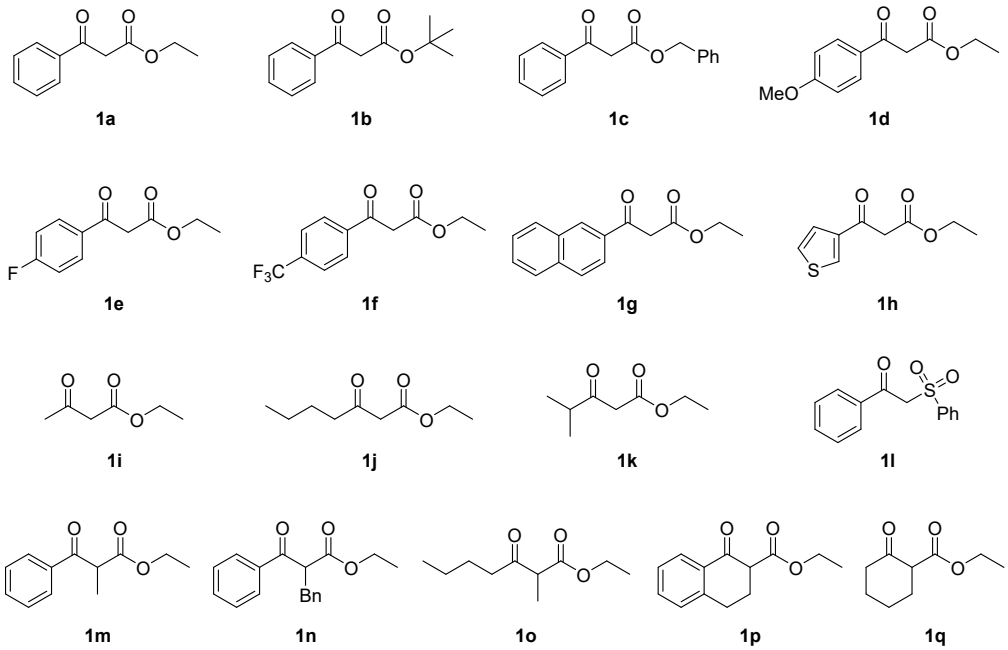
1a (1.0 equiv) **2a** (1.0 equiv) **12a**

Entry	Base	Equiv.	Sol.	Time	Yield of **12a** (%)
1	Et_3N	2.0	DCM	6 h	40
2	DABCO	2.0	DCM	1 h	39
3	Na_2CO_3	2.0	DCM	24 h	21
4	K_2CO_3	2.0	DCM	30 min	81
5	K_3PO_4	2.0	DCM	20 min	65
6	K_2CO_3	2.0	PhMe	30 min	75
7	K_2CO_3	2.0	MeCN	20 min	63
8	K_2CO_3	2.0	DMF	30 min	55
9	K_2CO_3	1.0	DCM	45 min	77
10	K_2CO_3	3.0	DCM	20 min	69

Conditions: **1** (0.1 mmol), **2** (0.1 mmol) and base in indicated solvent (1 mL) and temperature; **12a** was isolated as a pair of 1:1 diasteromers.

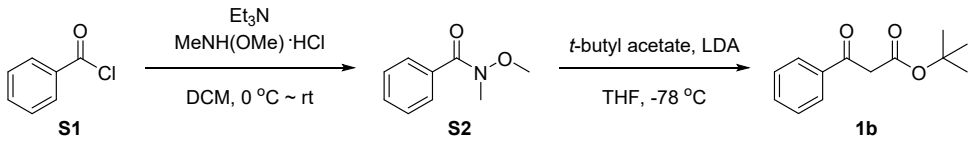
3. Preparation of the substrates

3.1 Preparation of *β*-keto esters



Note: Compounds **1a**, **1i-k** and **1q** are commercial available. Other *β*-keto esters are known compounds and were prepared as following procedure.

Method A: preparation of 1b.

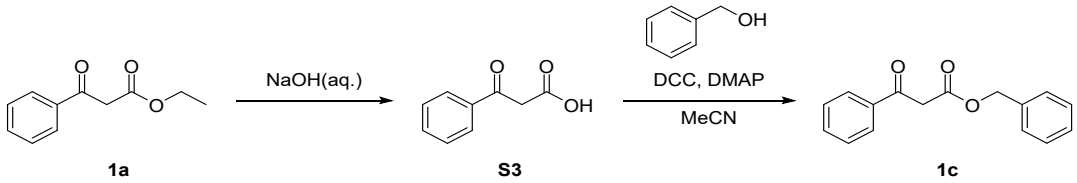


50 mL of the dried round bottom flask was taken, and dimethylhydroxylamine hydrochloride (1.02 g, 10.5 mmol, 1.05 equiv) in dry DCM (24 mL) was treated dropwise with triethylamine (2.9 mL, 21.0 mmol, 2.1 equiv) and **S1** (1.2mL, 10.0 mmol, 1.0 equiv) at 0 °C. After the addition was completed, the system was returned to room temperature, stirred for 3 h, and the reaction progress was monitored by TLC plate. After the reaction was completed, the reaction was quenched with 10 mL sat. aq. NH_4Cl, the organic phase was separated and the aqueous phase was extracted with DCM (15 mL × 3). The organic phase was combined, washed with brine, dried over Na_2SO_4. The solvent was removed by vacuum and the mixture was purified by column chromatography on silica gel (petroleum ether / EtOAc = 5:1) to give product **S2** in

85% yield.

n-Butyllithium (1.2 M in hexane, 3.1 equiv) was added at -78 °C to a THF solution (0.1 M) containing diisopropylamine (3.0 equiv) in a round-bottomed flask flushed with argon. After 30 min at 0 °C, the medium was recooled to -78 °C and freshly distilled tert-butyl acetate (3.0 equiv) was added. After 30 min at -78 °C, **S2** (1.0 equiv) was added at this temperature. After 1 h, the reaction was quenched at room temperature with sat. aq. $NaHCO_3$, and the mixture extracted with EtOAc (20 mL × 3). The combined organic layer was washed with sat. aq. NH_4Cl (20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether / EtOAc = 50:1) to give product **1b** in 92% yield.

Method B: preparation of 1c.

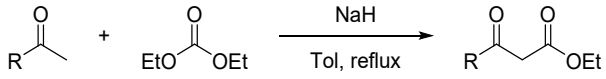


1a **S3** **1c**

An aqueous sodium hydroxide solution (1.0 M, 50 mL) was added to ethylbenzoylacetate (8.7 mL, 50.0 mmol). This mixture was stirred overnight at room temperature then transferred to a separating funnel. It was washed with DCM (3 × 10 mL) and the aqueous layer acidified to pH 1 by the addition of 2.0 M HCl. The precipitate was collected by suction filtration and dried under vacuum to yield benzoylacetic acid **S3** (6.3 g, 39.0 mmol, 78%), which was used without further purification.

A solution of acid **S3** (1.640 g, 10.0 mmol) and the benzyl alcohol (10.0 mmol) in acetonitrile (20 mL) was prepared. To this solution was added a solution of dicyclohexylcarbodiimide (2.1 g, 10.0 mmol) and 4-dimethylaminopyridine (61 mg, 0.5 mmol) in acetonitrile (10 mL) under rapid stirring. This mixture was stirred overnight at room temperature. Then the mixture was directly purified by column chromatography on silica gel (petroleum ether / EtOAc = 50:1) to give product **1c** in 85% yield.

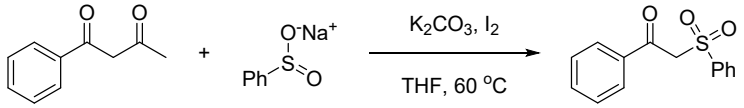
Method C: preparation of 1d-h and 1p.



S4 **1d-h, 1p**

To a dried three-necked flask equipped with a dropping funnel, a condenser, and a magnetic stirrer was added NaH (1.1 g, 28.0 mmol, 2.8 equiv, 60% in mineral oil), diethyl carbonate (2.4 mL, 20.0 mmol, 2.0 equiv.), and toluene (10 mL). The mixture was heated to reflux. A solution of ketone **S4** (10.0 mmol, 1.0 equiv.) in toluene (5 mL) was added dropwise from the dropping funnel over 1-2 h. After the addition, the mixture was heated to reflux until the evolution of hydrogen ceased (15-20 min). When the reaction was cooled to room temperature, glacial acetic acid (3 mL) was added dropwise and a heavy, pasty solid appeared. Ice-water was added until the solid was dissolved completely. The toluene layer was separated, and the aqueous layer was extracted with EtOAc (20 mL × 3). The combined organic layer was washed with water (20 mL) and brine (20 mL), then dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (petroleum ether / EtOAc = 40:1 ~ 20:1) to give the corresponding *β*-keto esters **1d-h** and **1p** in 60-77% yields (Note: THF solvent was used in case of **1p**).

Method D: preparation of 1l.

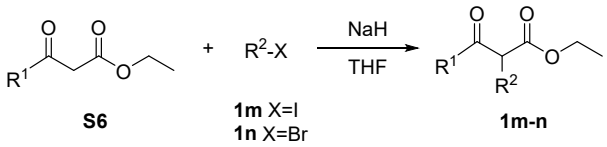


S5 **1l**

To a round bottom flask charged with **S5** (10.0 mmol, 1.0 equiv), sodium benzenesulfinate dihydrate (2.0 g, 12.0 mmol, 1.2 equiv), K_2CO_3 (2.1 g, 15.0 mmol, 1.5 equiv), and iodine (5.0 g, 20.0 mmol, 2.0 equiv) was added THF (50 mL). This mixture was stirred at room temperature overnight until the complete consumption of the starting material as monitored by TLC. A solution of Na_2SO_3 (5.0 g, 34.0 mmol) in H_2O (50 mL) was added to the mixture and then the reaction was stirred at 60 °C for 4 h. Upon completion of the reaction, the solution was extracted with EtOAc (3 × 40 mL), and the organic layer was separated, dried and concentrated to give a residue, which

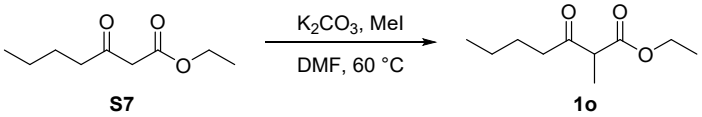
was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 9:1) to afford the desired *β*-keto sulfonate product **1l** in 65% yield.

Method E: preparation of 1m-n.

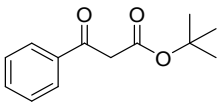


To a suspension of NaH (0.4 g, 10.0 mmol, 1.0 equiv, 60% in mineral oil) in dry THF (20 mL) was added dropwise **S6** (10.0 mmol, 1.0 equiv). When the gas evolution stopped, alkyl halide (10.0 mmol, 1.0 equiv) was added slowly. The reaction mixture was stirred for a further 20 h at room temperature then quenched with sat. aq. NH_4Cl (30 mL). The phases were separated and the aqueous phase further extracted with EtOAc (3 × 20 mL). The combined organic layer was dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (petroleum ether / EtOAc = 40:1 ~ 20:1) to give the corresponding *β*-keto esters **1m-n** in 85-90% yields.

Method F: preparation of 1o.

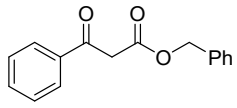


The mixture of **S7** (30.0 mmol, 1.0 equiv), K_2CO_3 (45.0 mmol, 1.5 equiv) and methyl iodide (33.0 mmol, 1.1 equiv) in dry DMF (30 mL) was heated under an argon atmosphere at 60 °C for 4 h. The reaction mixture was then poured into water and the aqueous layer was extracted with EtOAc (3 × 50 mL). The organic layer was washed with water, brine and dried over anhydrous Na_2SO_4. Evaporation of solvent and purification by flash column chromatography on silica gel (petroleum ether / EtOAc = 20:1) afforded the product **1o** in 77% yield.



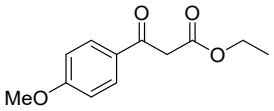
Following the general method A, **1b** was obtained as a yellow oil in 3:10 mixture of enol and keto form (10.0 mmol scale, 2.0 g, 92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$)

δ 12.72 (s, 0.3H), 7.94 (d, *J* = 7.4 Hz, 2H), 7.76 (d, *J* = 8.8 Hz, 0.6H), 7.59 (t, *J* = 7.4 Hz, 0.9H), 7.53 - 7.35 (m, 3H), 5.58 (s, 0.3H), 3.90 (s, 2H), 1.54 (s, 3H), 1.43 (s, 9H). The spectral data of **1b** was consistent with that reported in the literature.[1]



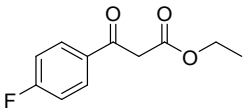
1c

Following the general method B, **1c** was obtained as a yellow oil in 3:10 mixture of enol and keto form (10.0 mmol scale, 2.2 g, 85% yield).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.48 (s, enol), 7.90 (d, *J* = 8.0 Hz, enol), 7.86 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 7.9 Hz, enol), 7.51 (t, *J* = 7.5 Hz, 1H), 7.44–7.24 (m, 7H), 5.68 (s, enol), 5.19 (s, enol), 5.13 (s, 2H), 3.98 (s, 2H). The spectral data of **1c** was consistent with that reported in the literature.[2]



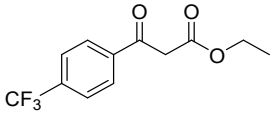
1d

Following the general method C, **1d** was obtained as a light yellow oil in 1:11 mixture of enol and keto form (10.0 mmol scale, 1.6 g, 73% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.63 (s, 0.09H), 7.93 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 5.58 (s, 0.09H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 2H), 3.87 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). The spectral data of **1d** was consistent with that reported in the literature.[3]



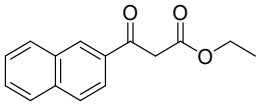
1e

Following the general method C, **1e** was obtained as a light yellow oil in 1:4 mixture of enol and keto form (10.0 mmol scale, 1.6 g, 75% yield). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 12.61 (s, 0.25H), 7.98 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.15 (t, *J* = 8.5 Hz, 2H), 5.59 (s, 0.25H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). The spectral data of **1e** was consistent with that reported in the literature.[3]



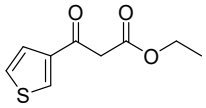
1f

Following the general method C, **1f** was obtained as a yellow oil in 1:2 mixture of enol and keto form (10.0 mmol scale, 1.6 g, 60% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.56 (s, 0.5H), 8.06 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 1H), 5.72 (s, 0.5H), 4.29 (q, *J* = 7.1 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 2H), 1.35 (t, *J* = 7.1 Hz, 1.5H), 1.26 (t, *J* = 7.1 Hz, 3H). The spectral data of **1f** was consistent with that reported in the literature.[3]



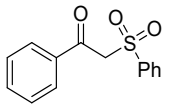
1g

Following the general method C, **1g** was obtained as a light yellow solid in 1:4 mixture of enol and keto form (10.0 mmol scale, 1.6 g, 62% yield). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 12.67 (s, 0.25H), 8.46 (s, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.98 (d, *J* = 8.6 Hz, 1H), 7.90 (dd, *J* = 15.8, 8.3 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 5.81 (s, 0.25H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.12 (s, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). The spectral data of **1g** was consistent with that reported in the literature.[3]



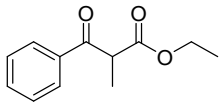
1h

Following the general method C, **1h** was obtained as a light yellow oil in keto form (10.0 mmol scale, 1.5 g, 76% yield). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.72 (d, *J* = 3.8 Hz, 1H), 7.68 (d, *J* = 4.9 Hz, 1H), 7.13 (t, *J* = 4.4 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.90 (s, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). The spectral data of **1h** was consistent with that reported in the literature.[3]



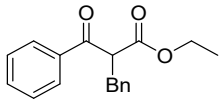
1l

Following the general method D, **1l** was obtained as a yellow solid (10.0 mmol scale, 1.7 g, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 (d, *J* = 7.8 Hz, 4H), 7.67 - 7.59 (m, 2H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 4.74 (s, 2H). The spectral data of **1l** was consistent with that reported in the literature.[3]



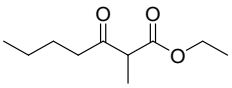
1m

Following the general method E, **1m** was obtained as a yellow oil (10.0 mmol scale, 1.9 g, 90% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.98 (d, *J* = 7.1 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.49-7.45 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.49 (d, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H). The spectral data of **1m** was consistent with that reported in the literature.[4]



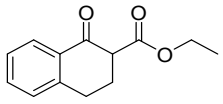
1n

Following the general method E, **1n** was obtained as a colorless oil (10.0 mmol scale, 2.4 g, 85% yield). **^{1}H NMR (600 MHz, $CDCl_3$)**. δ 7.96 (d, *J* = 7.98 Hz, 2H), 7.56 (t, *J* = 7.26 Hz, 1H), 7.45 (d, *J* = 7.50 Hz, 2H), 7.23 - 7.27 (m,5H), 7.19 (t, *J* = 7.08 Hz, 1H), 4.62 (t, *J* = 7.26 Hz, 1H), 4.11 (q, *J* = 6.96 Hz, 2H), 3.30 - 3.37 (m, 2H), 1.11 (t, *J* = 7.02 Hz, 3H). The spectral data of **1n** was consistent with that reported in the literature.[5]



1o

Following the general method F, **1o** was obtained as a yellow oil (10.0 mmol scale, 1.4 g, 77% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**. δ 4.17 (q, *J* = 7.0 Hz, 2H), 3.50 (q, *J* = 7.2 Hz, 1H), 2.64 - 2.39 (m, 2H), 1.63 - 1.50 (m, 2H), 1.37 - 1.21 (m, 8H), 0.89 (t, *J* = 7.3 Hz, 3H). The spectral data of **1o** was consistent with that reported in the literature.[6]

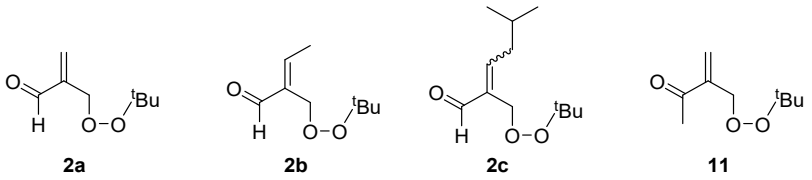


1p

Following the general method C, **1p** was obtained as a light brown oil (10.0 mmol scale, 1.7 g, 77% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**.δ12.49 (1H, s), 8.05 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.80 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.49 (td, J = 7.5, 1.5 Hz, 1H), 7.34 - 7.26 (m, 2H), 7.26 - 7.24 (m, 1H), 4.28 (q, 4H), 4.30 - 4.22 (m, 2H), 3.62 - 3.58 (dd, *J* = 10.4, 4.7 Hz, 1H), 3.10-2.94 (m, 2H), 2.83 - 2.79 (m, 2H), 2.59 - 2.55 (m, 2H), 2.52 -

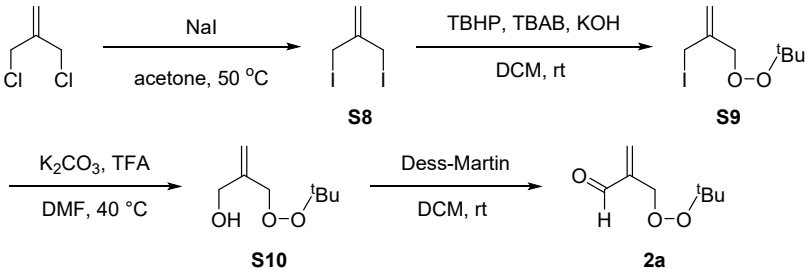
2.46 (m, 1H), 2.40 - 2.32 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H). The spectral data of **1p** was consistent with that reported in the literature.[7]

3.2 Preparation of the peroxides



2a **2b** **2c** **11**

Method A: preparation of 2a.



S8 **S9** **S10** **2a**

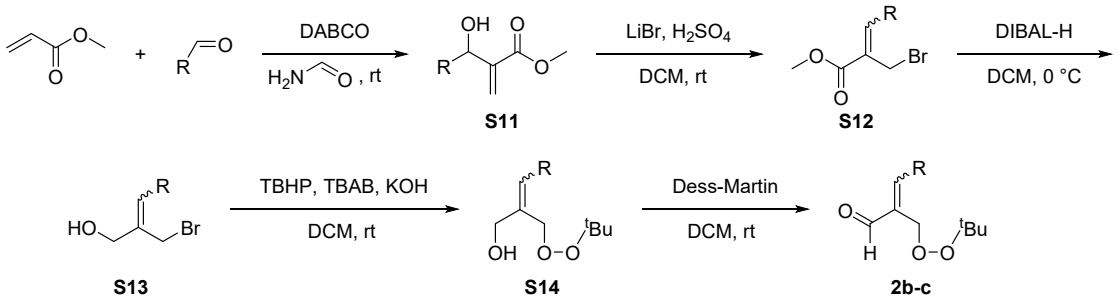
S8 and **S9** were prepared according to literature report.[3]

To a solution of **S9** (2.0 g, 7.4 mmol, 1.0 equiv) in DMF (74 mL) was added K_2CO_3 (2.6 g, 18.5 mmol, 2.5 equiv) and TFA (1.4 mL, 18.5 mmol, 2.5 equiv) at room temperature. The mixture was heated to 40 °C and stirred for 3.5 h. After completion, EtOAc (300 mL) was added and the mixture was washed with brine (100 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 10:1) to afford the compound **S10** (889 mg, 75% yield) as a colorless oil.

To a solution of the **S10** (889 mg, 5.5 mmol, 1.0 equiv) in DCM (55 mL) was added Dess-Martin reagent (3.5 g, 8.3 mmol, 1.5 equiv) at room temperature. The reaction mixture was stirred for 1 h. After completion, the solution was quenched with sat. aq. $NaHCO_3$ (100 mL). The organic layer was separated, the aqueous layer was extracted with DCM (20 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 30:1) to afford the product **2a** (713 mg, 81% yield) as a colorless oil. **^{1}H NMR (400**

MHz, $CDCl_3$) δ 9.57 (d, *J* = 1.0 Hz, 1H), 6.56 (s, 1H), 6.20 (s, 1H), 4.65 (s, 2H), 1.22 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 193.1, 144.9, 135.8, 80.7, 70.5, 26.2. **HRMS (ESI)** m/z: $[M + K]^+$ Calcd for $C_8H_{14}KO_3$: 197.0575; Found: 197.0507.

Method B: preparation of 2b-c.



Following a literature procedure[8], methyl acrylate (10.0 mmol, 1.0 equiv), aldehyde (12.0 mmol, 1.2 equiv), formamide (1.0 mmol, 0.1 equiv) and DABCO (3.0 mmol, 0.3 equiv) were stirred at room temperature for 1~3 days. After completion, the reaction was directly submitted to flash silica gel chromatography (petroleum ether / EtOAc = 2:1 - 1:1) to afford the MBH adduct **S11** in 85-92% yields.

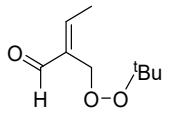
LiBr (3.0 equiv) was added to a solution of the appropriate MBH adduct **S11** (1.0 equiv) in anhydrous DCM (1.0 M) at room temperature. After cooling to 0 °C, 98 % H_2SO_4 (1.5 equiv) was rapidly added. And then the reaction was allowed to warm to room temperature and stir for 15-20 h. After completion, the solution was quenched with sat. aq. Na_2CO_3. The organic layer was separated, the aqueous layer was extracted with DCM, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 70:1) to afford the product **S12** in 67-82% yields.[8]

To a solution of the **S12** (1.0 equiv) in anhydrous DCM (0.1 M) was added DIBAl-H (3.0 equiv) dropwise under a N_2 atmosphere at 0 °C. After 1 h, added MeOH dropwise to quench the reaction. Then the mixture was added sat. aq. Rochelle's salt at room temperature and stir for 1 h. After completion, the solution was filtered through a pad of celite and washed with DCM. The filtrate was washed with brine, dried over

Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 10:1) to afford the compound **S13** in 65-77% yields.

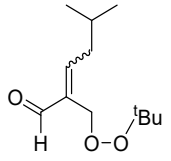
To a solution of the **S13** (1.0 equiv), tert-butyl hydroperoxide (3.1 M solution in hexane, 1.0 equiv) and TBAB (0.1 equiv) in DCM (0.1 M) was added powder KOH (1.0 equiv). The resulting solution was stirred at room temperature for 2-4 h. After completion, the reaction was quenched by water. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 10:1) to afford the compound **S14** in 85-89% yields.

To a solution of the **S14** (1.0 equiv) in DCM (0.1 M) was added Dess-Martin reagent (1.5 equiv) at room temperature. The reaction mixture was stirred for 1 h. After completion, the solution was quenched with sat. aq. $NaHCO_3$. The organic layer was separated, the aqueous layer was extracted with DCM, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 30:1) to afford the products **2b**-**c** in 62-75% yields.



2b

Following the above procedure, **2b** was obtained as a light yellow oil (65 mg, 75% yield).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.44 (s, 1H), 6.88 (q, *J* = 7.1 Hz, 1H), 4.68 (s, 2H), 2.13 (d, *J* = 7.0 Hz, 3H), 1.22 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 193.5, 155.6, 138.7, 80.6, 65.4, 26.4, 15.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_9H_{16}NaO_3$: 195.0992; Found: 195.1022.

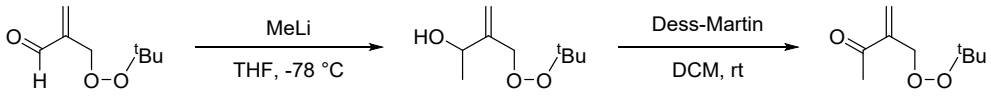


2c

Following the above procedure, **2c** was obtained as a colorless oil (66 mg, 62%

yield).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.44 (s, 0.8H), 9.41 (s, 0.2H), 6.78 (t, *J* = 7.6 Hz, 0.8H), 6.71 (t, *J* = 7.6 Hz, 0.2H), 4.65 (s, 1.5H), 4.09 (s, 0.5H), 2.40 (t, *J* = 7.2 Hz, 2H), 1.84 (m, 1H), 0.97 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 193.5, 192.0, 159.5, 157.4, 140.5, 138.1, 80.6, 65.8, 38.3, 38.2, 28.4, 28.2, 26.4, 22.7, 22.6, 19.9. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{23}O_3$: 215.1642; Found: 215.1648.

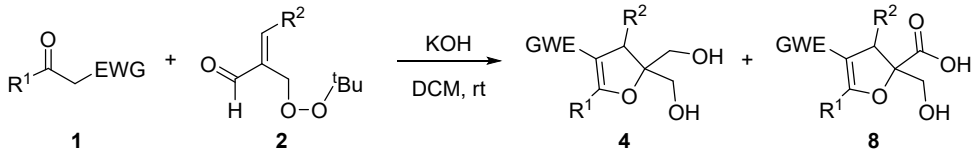
Method C: preparation of 10.



To a solution of the **2a** (158 mg, 1.0 mmol, 1.0 equiv) in anhydrous THF (10 mL) was added MeLi (2.5 equiv) dropwise under a N_2 atmosphere at -78 °C. After 1 h, quench the reaction by sat. aq. NH_4Cl (10 mL). The mixture was extracted with EtOAc (5 mL × 3), dried over Na_2SO_4 and concentrated in vacuum to afford the crude product **S15** (170 mg) without further purification.

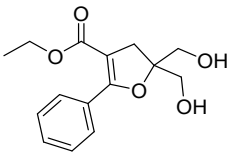
To a solution of the crude compound **S15** (170 mg, 1.0 mmol, 1.0 equiv) in DCM (10 mL) was added Dess-Martin reagent (636 mg, 1.5 mmol, 1.5 equiv) at room temperature. The reaction mixture was stirred for 1 h. After completion, the solution was quenched with sat. aq. $NaHCO_3$ (20 mL). The organic layer was separated, the aqueous layer was extracted with DCM (10 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 30:1) to afford the product **10** (115 mg, 67% overall yield of two steps) as a light yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.18 (s, 1H), 6.09 (s, 1H), 4.65 (s, 2H), 2.34 (s, 3H), 1.22 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.7, 143.9, 127.5, 80.7, 72.8, 26.4, 26.0. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_9H_{16}NaO_3$: 195.0992; Found: 195.0990.

4. General procedure for the synthesis of dihydrofurans



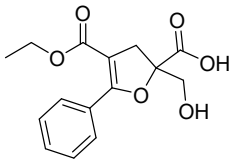
To a solution of **1** (0.2 mmol, 1.0 equiv) and **2** (0.2 mmol, 1.0 equiv) in DCM (1 mL) was added powder KOH (22 mg, 0.4 mmol, 2.0 equiv) at room temperature. The reaction mixture was stirred for 10-60 min. After completion, the reaction was quenched by water (2 mL) and extracted with DCM (3 mL × 3). The separated aqueous layer was left for further acidification (see below). The separated organic layers were collected, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 3:1 ~ 2:1) to afford the alcohol products **4** in 29-45% yields.

Additionally, the above mentioned aqueous layer was treated with 2.0 M HCl to adjust the pH to 2~3 and extracted with DCM (3 mL × 3). The combined organic phase was dried and concentrated. The solid residue was triturated with petroleum ether / diethyl ether (10: 1) and filtered to afford the carboxylic acid products **8b-8e** and **8g** in 42-29% yields. While in case of slurry residue, the carboxylic acid products **8a**, **8f**, and **8h-n** were purified by flash silica gel chromatography (DCM / MeOH = 15:1 ~ 5:1) in 43-27% yields.



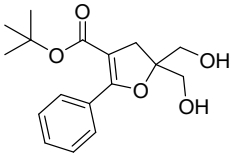
4a

Following the general procedure, **4a** was obtained as a colorless oil (0.2 mmol scale, 25 mg, 45% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 - 7.70 (m, 2H), 7.45 - 7.33 (m, 3H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.85 - 3.79 (m, 4H), 2.95 (s, 2H), 2.38 (br, s, 2H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.1, 163.8, 130.5, 129.7, 129.3, 127.6, 102.8, 88.5, 65.1, 60.0, 35.8, 14.2. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{19}O_5$: 279.1227; Found: 279.1217.



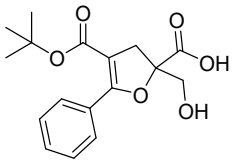
8a

Following the general procedure, **8a** was obtained as a colorless oil (0.2 mmol scale, 25 mg, 43% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.86 - 7.79 (m, 2H), 7.45 - 7.33 (m, 3H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.93 (d, *J* = 11.7 Hz, 1H), 3.84 (d, *J* = 11.7 Hz, 1H), 3.28 (d, *J* = 15.3 Hz, 1H), 3.12 (d, *J* = 15.3 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 178.7, 167.0, 166.9, 131.9, 131.2, 130.7, 128.5, 102.8, 92.0, 67.2, 60.9, 38.6, 14.5. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{15}H_{15}O_6$: 291.0863; Found: 291.0817.



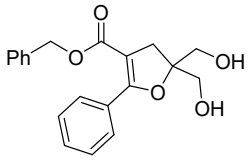
4b

Following the general procedure, **4b** was obtained as a colorless oil (0.2 mmol scale, 24 mg, 39% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.74 - 7.67 (m, 2H), 7.41 - 7.34 (m, 3H), 3.88 - 3.82 (m, 4H), 2.93 (s, 2H), 1.64 (br, s, 2H), 1.39 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.6, 162.80 130.3, 129.4, 127.8, 104.8, 88.2, 80.4, 65.4, 36.3, 28.3. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{17}H_{21}O_5$: 305.1383; Found: 305.1332.



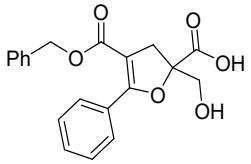
8b

Following the general procedure, **8b** was obtained as a yellow solid (0.2 mmol scale, 27 mg, 42% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.78 - 7.71 (m, 2H), 7.44 - 7.34 (m, 3H), 3.92 (d, *J* = 11.7 Hz, 1H), 3.83 (d, *J* = 11.7 Hz, 1H), 3.24 (d, *J* = 15.4 Hz, 1H), 3.08 (d, *J* = 15.4 Hz, 1H), 1.35 (s, 9H). **^{13}C NMR (100 MHz, CD_3OD)** δ 178.8, 166.4, 165.7, 132.1, 131.0, 130.7, 128.5, 104.5, 90.8, 81.2, 66.7, 38.9, 28.5. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{17}H_{19}O_6$: 319.1176; Found: 319.1121. **Melting point:** 190.3 – 191.2 ℃.



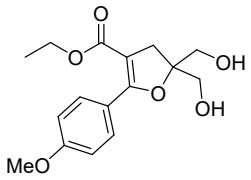
4c

Following the general procedure, **4c** was obtained as a white oil (0.2 mmol scale, 24 mg, 35% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 - 7.66 (m, 2H), 7.47 - 7.21 (m, 9H), 5.12 (s, 2H), 3.88 - 3.82 (m, 4H), 3.00 (s, 2H), 1.84 (br, s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.0, 164.7, 136.2, 130.6, 129.8, 129.4, 128.5, 128.5, 128.2, 128.1, 128.1, 127.8, 102.6, 88.8, 65.9, 65.0, 35.9. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{20}H_{21}O_5$: 341.1384; Found: 341.1382.



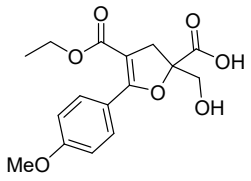
8c

Following the general procedure, **8c** was obtained as a white solid (0.2 mmol scale, 28 mg, 39% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.79 (d, *J* = 7.4 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.36 - 7.18 (m, 7H), 5.08 (s, 2H), 3.92 (d, *J* = 11.8 Hz, 1H), 3.83 (d, *J* = 11.7 Hz, 1H), 3.31 (d, *J* = 15.3 Hz, 1H), 3.17 (d, *J* = 15.3 Hz, 1H). **^{13}C NMR (100 MHz, CD_3OD)** δ 177.7, 167.1, 166.3, 137.7, 131.5, 131.3, 130.7, 130.5, 129.4, 129.0, 129.0, 128.5, 102.6, 91.0, 66.6, 38.6. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{20}H_{17}O_6$: 353.1019; Found: 353.0958. **Melting point:** 132.1 – 133.4 ℃.



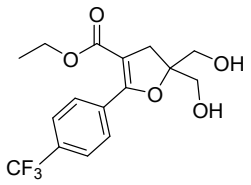
4d

Following the general procedure, **4d** was obtained as a colorless oil (0.2 mmol scale, 27 mg, 43% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.90 - 3.73 (m, 7H), 2.92 (s, 2H), 2.32 (br, s, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.5, 163.8, 161.5, 131.3, 122.1, 113.2, 101.5, 88.1, 65.3, 60.0, 55.5, 36.1, 14.4. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}O_6$: 309.1333; Found: 309.1333.



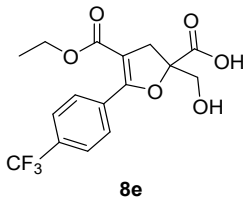
8d

Following the general procedure, **8d** was obtained as a white solid (0.2 mmol scale, 26 mg, 41% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.86 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 4.12 (q, *J* = 6.8 Hz, 2H), 3.96 (d, *J* = 12.0 Hz, 1H), 3.85 - 3.82 (m, 4H), 3.23 (d, *J* = 15.6 Hz, 1H), 3.15 (d, *J* = 15.5 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 179.1, 167.0, 166.6, 162.9, 132.6, 123.9, 113.8, 101.3, 91.0, 66.9, 60.8, 55.8, 38.8, 14.6. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}O_7$: 323.1125; Found: 323.1125. **Melting point:** 181.4 – 182.1 ℃.



4e

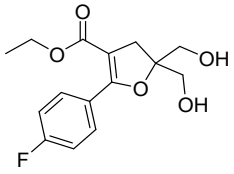
Following the general procedure, **4e** was obtained as a colorless oil (0.2 mmol scale, 21 mg, 30% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.88 - 3.82 (m, 4H), 2.99 (s, 2H), 2.23 (br, s, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.0, 162.3, 133.4, 132.2 (d, *J* = 32.8 Hz), 129.9, 124.7 (q, *J* = 3.8 Hz), 124.0 (d, *J* = 271.9 Hz), 104.6, 89.1, 65.2, 60.4, 36.0, 14.3. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}F_3O_5$: 347.1100; Found: 347.1105.



8e

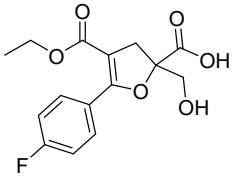
Following the general procedure, **8e** was obtained as a yellow solid (0.2 mmol scale, 24 mg, 33% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 8.02 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.94 (d, *J* = 11.8 Hz, 1H), 3.85 (d, *J* = 11.8 Hz, 1H), 3.33 (d, *J* = 15.7 Hz, 1H), 3.16 (d, *J* = 15.7 Hz, 1H), 1.17 (t, *J* = 7.1

Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 178.9, 166.4, 164.6, 135.6, 132.6 (q, *J* = 32.4 Hz), 131.4, 125.5 (q, *J* = 271.6 Hz), 125.3 (q, *J* = 3.8 Hz), 104.7, 91.9, 66.7, 61.1, 38.7, 23.5, 14.5. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{16}H_{15}F_3NaO_6$: 383.0713; Found: 383.0723. **Melting point:** 121.1 - 122.4 ℃.



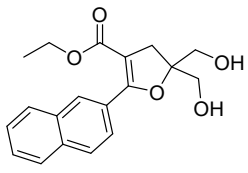
4f

Following the general procedure, **4f** was obtained as a colorless oil (0.2 mmol scale, 24 mg, 40% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.78 (dd, *J* = 8.1, 5.9 Hz, 2H), 7.03 (t, *J* = 8.6 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.85 - 3.71 (m, 4H), 3.00 - 2.75 (m, 4H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.3, 164.0 (d, *J* = 251.5 Hz), 163.0, 131.8 (d, *J* = 8.6 Hz), 126.0 (d, *J* = 3.3 Hz), 114.8 (d, *J* = 21.7 Hz), 102.7, 88.6, 65.0, 60.2, 36.0, 14.3. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}FO_5$: 297.1132; Found: 297.1126.



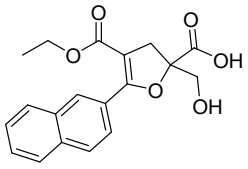
8f

Following the general procedure, **8f** was obtained as a colorless oil (0.2 mmol scale, 23 mg, 37% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.96 - 7.88 (m, 2H), 7.11 (t, *J* = 8.8 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.95 (d, *J* = 11.9 Hz, 1H), 3.84 (d, *J* = 11.7 Hz, 1H), 3.26 (d, *J* = 15.6 Hz, 1H), 3.16 (d, *J* = 15.5 Hz, 1H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 174.7, 166.3, 165.3 (d, *J* = 249.0 Hz), 165.1, 133.2 (d, *J* = 8.6 Hz), 127.4 (d, *J* = 3.1 Hz), 115.5 (d, *J* = 22.0 Hz), 102.9, 90.1, 66.2, 61.1, 38.4, 14.5. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}FO_6$: 311.0925; Found: 311.0919.



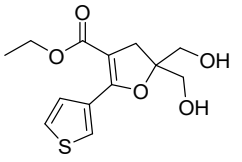
4g

Following the general procedure, **4g** was obtained as a light yellow oil (0.2 mmol scale, 22 mg, 33% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.31 (s, 1H), 7.91 - 7.80 (m, 4H), 7.55 - 7.47 (m, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.92 - 3.86 (m, 4H), 3.02 (s, 2H), 2.01 (br, s, 2H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.3, 163.8, 134.3, 132.5, 129.9, 128.9, 127.8, 127.5, 127.3, 126.5, 126.2, 103.3, 88.6, 65.4, 60.1, 36.2, 14.4. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}O_5$: 329.1384; Found: 329.1381.



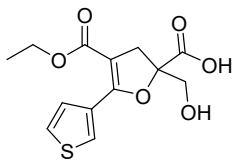
8g

Following the general procedure, **8g** was obtained as a light yellow solid (0.2 mmol scale, 20 mg, 29% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 8.43 (s, 1H), 7.96 - 7.80 (m, 4H), 7.54 - 7.51 (m, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.97 (d, *J* = 11.8 Hz, 1H), 3.86 (d, *J* = 11.8 Hz, 1H), 3.33 (d, *J* = 15.4 Hz, 1H), 3.20 (d, *J* = 15.4 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 178.2, 167.0, 166.7, 135.6, 133.8, 131.1, 129.7, 129.1, 128.6, 128.3, 127.8, 127.7, 127.3, 103.1, 91.8, 67.1, 61.0, 38.8, 14.6. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{19}H_{19}O_6$: 343.1176; Found: 343.1177. **Melting point:** 211.8 – 212.7 ℃.



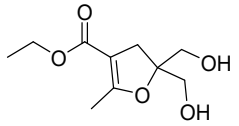
4h

Following the general procedure, **4h** was obtained as a yellow oil (0.2 mmol scale, 26 mg, 45% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 (d, *J* = 3.8 Hz, 1H), 7.49 (d, *J* = 5.1 Hz, 1H), 7.10 - 7.08 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 4H), 2.98 (s, 2H), 2.09 (br, s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.3, 157.4, 132.4, 131.2, 130.3, 127.3, 101.3, 88.7, 65.2, 60.2, 36.0, 14.6. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}O_5S$: 285.0791; Found: 285.0790.



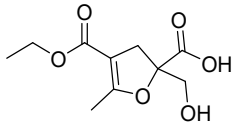
8h

Following the general procedure, **8h** was obtained as a yellow oil (0.2 mmol scale, 24 mg, 40% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 8.19 (dd, *J* = 3.9, 1.3 Hz, 1H), 7.63 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.11 (dd, *J* = 5.1, 3.8 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.94 (d, *J* = 11.8 Hz, 1H), 3.83 (d, *J* = 11.7 Hz, 1H), 3.27 (d, *J* = 15.7 Hz, 1H), 3.16 (d, *J* = 15.7 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 177.4, 166.6, 159.7, 133.6, 132.3, 131.5, 127.8, 101.0, 90.8, 66.7, 61.0, 38.7, 14.78. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{15}O_6S$: 299.0584; Found: 299.0584.



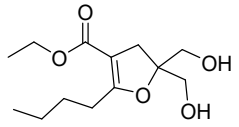
4i

Following the general procedure, **4i** was obtained as a colorless oil (0.2 mmol scale, 13 mg, 30% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.15 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 4H), 2.69 (s, 2H), 2.27 (br, s, 2H), 2.20 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.8, 166.1, 102.5, 89.3, 65.4, 59.8, 34.4, 14.5, 14.3. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{10}H_{16}NaO_5$: 239.0890; Found: 239.0898.



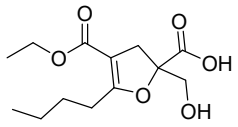
8i

Following the general procedure, **8i** was obtained as a colorless oil (0.2 mmol scale, 12 mg, 27% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 4.14 (q, *J* = 7.1 Hz, 2H), 3.83 (d, *J* = 11.7 Hz, 1H), 3.72 (d, *J* = 11.7 Hz, 1H), 3.01 (d, *J* = 14.7 Hz, 1H), 2.89 (d, *J* = 14.8 Hz, 1H), 2.23 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 179.4, 169.4, 167.7, 102.4, 91.8, 67.0, 60.7, 37.1, 14.8, 14.4. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{10}H_{13}O_6$: 229.0707; Found: 229.0718.



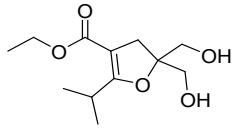
4j

Following the general procedure, **4j** was obtained as a colorless oil (0.2 mmol scale, 22 mg, 43% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.14 (q, *J* = 7.1 Hz, 2H), 3.75 - 3.69 (m, 4H), 2.75 - 2.37 (m, 6H), 1.56 - 1.49 (m, 2H), 1.39 - 1.24 (m, 6H), 0.90 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, CDCl3)** δ 170.5, 166.0, 101.7, 88.8, 65.0, 59.6, 34.3, 29.1, 27.5, 22.4, 14.3, 13.8. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{23}O_5$: 259.1540; Found: 259.1529.



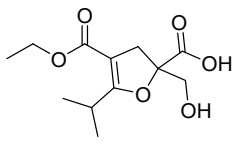
8j

Following the general procedure, **8j** was obtained as a colorless oil (0.2 mmol scale, 24 mg, 44% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 4.14 (q, *J* = 7.1 Hz, 2H), 3.83 (d, *J* = 11.6 Hz, 1H), 3.72 (d, *J* = 11.6 Hz, 1H), 3.03 (d, *J* = 14.9 Hz, 1H), 2.89 (d, *J* = 14.9 Hz, 1H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.63 - 1.59 (m, 2H), 1.47 - 1.32 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 177.4, 173.0, 167.4, 102.0, 91.0, 66.6, 60.7, 37.0, 30.0, 28.5, 23.4, 14.7, 14.1. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{13}H_{19}O_6$: 271.1176; Found: 271.1137.



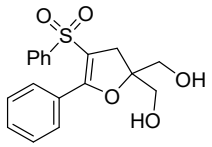
4k

Following the general procedure, **4k** was obtained as a colorless oil (0.2 mmol scale, 20 mg, 40% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.15 (q, *J* = 7.1 Hz, 2H), 3.75 - 3.69 (s, 4H), 3.65 - 3.58 (m, 1H), 2.69 (s, 2H), 2.19 (br, s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.6, 166.0, 100.4, 88.7, 65.2 59.7, 34.4, 27.0, 19.7, 14.5. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{12}H_{19}O_5$: 243.1227; Found: 243.1201.



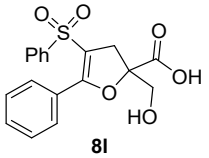
8k

Following the general procedure, **8k** was obtained as a colorless oil (0.2 mmol scale, 21 mg, 40% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 4.14 (q, *J* = 7.1 Hz, 2H), 3.81 (d, *J* = 11.6 Hz, 1H), 3.72 (d, *J* = 11.7 Hz, 1H), 3.63 - 3.53 (m, 1H), 3.09 - 2.98 (m, 1H), 2.90 - 2.81 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.17 (dd, *J* = 9.2, 6.9 Hz, 6H). **^{13}C NMR (100 MHz, CD_3OD)** δ 176.8, 176.4, 167.2, 100.3, 90.5, 66.3, 60.7, 36.9, 28.2, 19.8, 19.7, 14.7. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{12}H_{17}O_6$: 257.1019; Found: 257.0982.



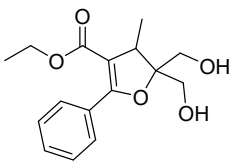
4l

Following the general procedure, **4l** was obtained as a yellow oil (0.2 mmol scale, 24 mg, 35% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 - 7.68 (m, 2H), 7.69 - 7.63 (m, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.51 - 7.34 (m, 5H), 3.81 - 3.75 (m, 4H), 3.00 (s, 2H), 2.01 (br, s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 163.1, 141.8, 133.1, 131.3, 129.7, 129.2, 128.3, 128.0, 127.1, 111.1, 89.4, 64.9, 36.5. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}O_5S$: 347.0948; Found: 347.0950.



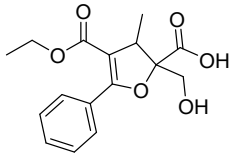
8l

Following the general procedure, **8l** was obtained as a yellow oil (0.2 mmol scale, 20 mg, 28% yield). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.75 - 7.69 (m, 4H), 7.62 - 7.55 (m, 1H), 7.52 - 7.43 (m, 3H), 7.40 - 7.36 (m, 2H), 3.86 (d, *J* = 12.0 Hz, 1H), 3.76 (d, *J* = 11.9 Hz, 1H), 3.32 (d, *J* = 14.8 Hz, 1H), 3.22 (d, *J* = 14.8 Hz, 1H). **^{13}C NMR (100 MHz, CD_3OD)** δ 177.9, 165.6, 143.2, 134.1, 131.8, 130.8, 130.2, 128.6, 127.8, 110.6, 92.0, 66.5, 39.0. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{18}H_{17}O_6S$: 361.0740; Found: 361.0743.



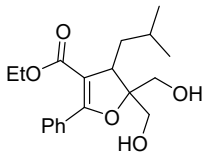
4m

Following the general procedure, **4m** was obtained as a colorless oil (0.2 mmol scale, 24 mg, 41% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.72 - 7.64 (m, 2H), 7.47 - 7.32 (m, 3H), 4.19 - 4.06 (m, 2H), 4.04 (d, *J* = 11.8 Hz, 1H), 3.95 (d, *J* = 11.8 Hz, 1H), 3.89 (d, *J* = 11.5 Hz, 1H), 3.73 (d, *J* = 11.5 Hz, 1H), 3.25 (q, *J* = 7.0 Hz, 1H), 2.51 (br, s, 1H), 1.80 (br, s, 1H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ165.2, 163.4, 130.6, 130.2, 129.5, 127.8, 109.1, 89.4, 64.7, 62.3, 60.0, 42.3, 14.4, 14.2. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}O_5$: 293.1384; Found: 293.1387.



8m

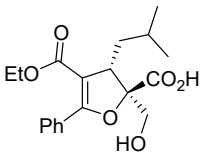
Following the general procedure, **8m** was obtained as a colorless oil (0.2 mmol scale, 23 mg, 37% yield, dr = 2:1). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.95 - 7.71 (m, 2H), 7.50 - 7.32 (m, 3H), 4.20 - 4.02 (m, 2.9H), 3.96 (d, *J* = 11.5 Hz, 0.7H), 3.89 - 3.78 (m, 0.4H), 3.62 (q, *J* = 5.8, 0.7H), 3.20 (q, *J* = 7.2 Hz, 0.3H), 1.31 - 1.26 (m, 3H), 1.14 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, CD_3OD)** δ 175.5, 166.7, 166.3, 166.2, 165.7, 131.6, 131.5, 131.4, 131.0, 130.8, 128.5, 128.5, 109.0, 108.8, 94.7, 92.5, 66.4, 63.4, 61.0, 45.7, 44.0, 16.3, 14.5, 14.4. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{16}H_{18}NaO_6$: 329.0996; Found: 329.0987.



4n

Following the general procedure, **4n** was obtained as a colorless oil (0.2 mmol scale, 19 mg, 29% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76 - 7.64 (m, 2H), 7.45 - 7.30 (m, 3H), 4.18 - 3.95 (m, 4H), 3.88 (d, *J* = 11.4 Hz, 1H), 3.70 (d, *J* = 11.5 Hz, 1H), 3.24 (dd, *J* = 8.3, 4.4 Hz, 1H), 2.64 (br, s, 2H), 1.59 (td, *J* = 10.5, 8.8, 5.2 Hz, 2H), 1.47 (dt, *J* = 9.8, 5.3 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.95 (dd, *J* = 12.2, 6.3 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.4, 163.2, 130.6, 130.1, 129.7, 127.7, 108.8, 90.1, 64.7,

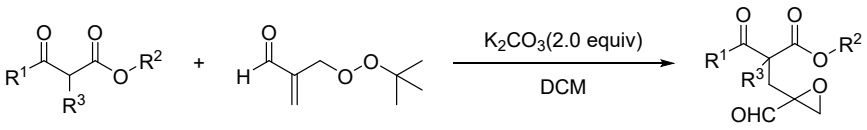
62.5, 60.0, 45.0, 38.7, 26.7, 23.6, 22.3, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{26}NaO_5$: 357.1673; Found: 357.1684.



8n

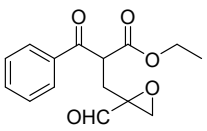
Following the general procedure, **8n** was obtained as a yellow oil (0.2 mmol scale, 19 mg, 27% yield, dr > 20:1, relative configuration). **^{1}H NMR (400 MHz, CD_3OD)** δ 7.84 (d, *J* = 7.2 Hz, 2H), 7.43 - 7.35 (m, 3H), 4.19 (d, *J* = 11.7 Hz, 1H), 4.12 - 3.97 (m, 3H), 3.55 (dd, *J* = 7.7, 5.0 Hz, 1H), 1.76 - 1.56 (m, 1H), 1.46 - 1.24 (m, 2H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.98 (dd, *J* = 10.0, 6.5 Hz, 1H). **^{13}C NMR (100 MHz, CD_3OD)** δ 175.7, 166.9, 166.3, 131.6, 131.2, 130.8, 128.4, 108.7, 93.4, 63.6, 61.0, 48.4, 40.4, 27.6, 23.6, 22.8, 14.4. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{24}NaO_6$: 371.1466; Found: 371.1468.

5. General procedure for the synthesis of epoxides



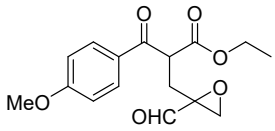
1 **2a** **12**

To a solution of **1** (0.2 mmol, 1.0 equiv) and **2a** (31.6 mg, 0.2 mmol, 1.0 equiv) in DCM (1 mL) was added powder K_2CO_3 (55.2 mg, 0.4 mmol, 2.0 equiv) at room temperature. The reaction mixture was stirred for 30 min. After completion, the solution was quenched with sat. aq. NH_4Cl (1 mL) and extracted with DCM (2 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 10 : 1) to afford the epoxide products **12** in 52-81% yields.



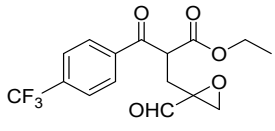
12a

Following the general procedure, **12a** was obtained as a colorless oil (0.2 mmol scale, 45 mg, 81% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (d, *J* = 3.5 Hz, 1H), 8.03 - 7.97 (m, 2H), 7.62 - 7.57 (m, 1H), 7.51 - 7.45 (m, 2H), 4.65 (ddd, *J* = 13.5, 8.1, 6.4 Hz, 1H), 4.20 - 4.03 (m, 2H), 3.14 - 2.98 (m, 2H), 2.68 (ddd, *J* = 41.9, 14.8, 7.3 Hz, 1H), 2.57 - 2.38 (m, 1H), 1.16 (td, *J* = 7.1, 5.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.5, 198.4, 194.3, 194.2, 169.3, 169.2, 135.8, 135.7, 133.9, 128.9, 128.8, 62.0, 61.9, 59.5, 59.4, 50.9, 50.3, 49.7, 49.6, 27.3, 27.0, 14.0, 14.0. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}O_5$: 277.1071; Found: 277.1046.



12b

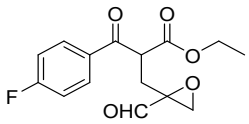
Following the general procedure, **12b** was obtained as a colorless oil (0.2 mmol scale, 46 mg, 75% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (s, 1H), 8.04 - 7.96 (m, 2H), 6.97 - 6.93 (m, 2H), 4.63 - 4.58 (m, 1H), 4.17 - 4.09 (m, 2H), 3.87 (d, *J* = 2.2 Hz, 3H), 3.11 - 3.01 (m, 2H), 2.64 (ddd, *J* = 30.1, 14.8, 7.4 Hz, 1H), 2.48 (ddd, *J* = 22.5, 14.8, 7.1 Hz, 1H), 1.17 (td, *J* = 7.1, 4.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.5, 198.4, 192.7, 192.6, 169.5, 169.4, 164.2, 131.4, 131.3, 128.9, 128.8, 114.1, 61.9, 61.8, 59.5, 59.4, 55.7, 50.8, 50.4, 49.3, 27.4, 27.1, 14.0. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}O_6$: 307.1176; Found: 307.1171.



12c

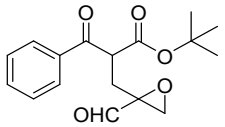
Following the general procedure, **12c** was obtained as a colorless oil (0.2 mmol scale, 49 mg, 71% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.83 (d, *J* = 9.8 Hz, 1H), 8.11 (dd, *J* = 11.9, 8.3 Hz, 2H), 7.75 (dd, *J* = 8.5, 4.5 Hz, 2H), 4.63 (dt, *J* = 18.1, 7.4 Hz, 1H), 4.15 (q, *J* = 6.7, 6.2 Hz, 2H), 3.13 - 3.03 (m, 2H), 2.73 (ddd, *J* = 46.9, 14.8, 7.2 Hz, 1H), 2.47 (ddd, *J* = 35.5, 14.8, 7.2 Hz, 1H), 1.16 (td, *J* = 7.1, 4.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.4, 198.3, 193.6, 193.3, 168.8, 168.7, 138.6, 135.2, 134.9, 129.3, 129.1, 126.0 (q, *J* = 3.8 Hz), 123.6 (q, *J* = 273.1 Hz), 62.2, 62.2, 59.4,

59.3, 51.0, 50.4, 50.1, 50.0, 27.2, 27.0, 14.0, 13.9. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}F_3O_5$: 345.0944; Found: 345.0942.



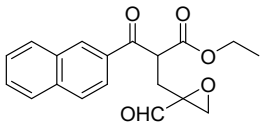
12d

Following the general procedure, **12d** was obtained as a colorless oil (0.2 mmol scale, 43 mg, 73% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.82 (d, *J* = 5.1 Hz, 1H), 8.07 - 8.00 (m, 2H), 7.17 - 7.11 (m, 2H), 4.59 (dt, *J* = 14.9, 7.2 Hz, 1H), 4.16 - 4.09 (m, 2H), 3.06 (dt, *J* = 13.9, 4.8 Hz, 2H), 2.67 (ddd, *J* = 43.3, 14.8, 7.2 Hz, 1H), 2.45 (ddd, *J* = 30.7, 14.8, 7.2 Hz, 1H), 1.15 (td, *J* = 7.0, 4.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.5, 198.4, 192.7, 192.5, 169.1, 169.0, 167.5, 165.0, 132.3, 131.7, 131.6, 131.5, 116.2, 116.0, 62.0, 62.0, 59.4, 59.3, 50.9, 50.3, 49.7, 49.6, 27.2, 27.0, 14.0. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}FO_5$: 295.0976; Found: 295.0973.



12e

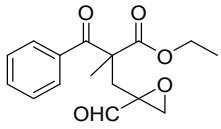
Following the general procedure, **12e** was obtained as a colorless oil (0.2 mmol scale, 48 mg, 79% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.85 (s, 1H), 8.00 - 7.95 (m, 2H), 7.59 - 7.56 (m, 1H), 7.49 - 7.44 (m, 2H), 4.54 - 4.50 (m, 1H), 3.09 - 3.02 (m, 2H), 2.69 (dd, *J* = 14.8, 6.7 Hz, 0.5H), 2.59 - 2.49 (m, 1H), 2.39 (dd, *J* = 14.8, 8.0 Hz, 0.5H), 1.31 (d, *J* = 7.7 Hz, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.6, 198.3, 194.6, 194.6, 168.3, 168.2, 136.2, 133.6, 128.8, 128.8, 82.6, 82.5, 59.5, 59.4, 50.9, 50.8, 50.8, 50.2, 27.8, 27.8, 27.1, 26.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{20}NaO_5$: 327.1203; Found: 327.1212.



12f

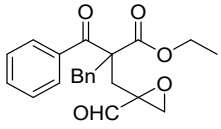
Following the general procedure, **12f** was obtained as a colorless oil (0.2 mmol scale, 48 mg, 74% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.86 (d, *J* = 1.6 Hz, 1H), 8.58 (dd, *J* = 19.8, 2.0 Hz, 1H), 8.09 - 7.96 (m, 2H), 7.93 - 7.87 (m, 2H), 7.65 - 7.55 (m, 2H), 4.85 - 4.79 (m, 1H), 4.14 (qt, *J* = 7.0, 4.3 Hz, 2H), 3.16 - 3.02 (m, 2H),

2.74 (ddd, *J* = 39.2, 14.8, 7.3 Hz, 1H), 2.56 (ddd, *J* = 32.1, 14.7, 7.1 Hz, 1H), 1.16 (td, *J* = 7.1, 5.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.5, 198.4, 194.2, 194.1, 169.4, 169.3, 136.0, 133.2, 133.2, 132.6, 131.0, 130.9, 130.0, 129.1, 128.9, 127.9, 127.1, 124.3, 124.2, 62.0, 61.9, 59.5, 59.4, 50.9, 50.4, 49.8, 27.5, 27.2, 14.0. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{19}H_{19}O_5$: 327.1227; Found: 327.1214.



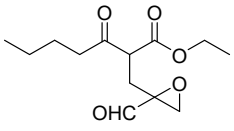
12g

Following the general procedure, **12g** was obtained as a colorless oil (0.2 mmol scale, 41 mg, 71% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (d, *J* = 2.4 Hz, 1H), 7.86 - 7.73 (m, 2H), 7.55 - 7.46 (m, 1H), 7.42 - 7.38 (m, 2H), 4.18 - 4.02 (m, 2H), 3.09 - 2.92 (m, 3H), 2.53 (d, *J* = 15.0 Hz, 0.5H), 2.41 (d, *J* = 15.0 Hz, 0.5H), 1.58 (d, *J* = 3.7 Hz, 3H), 1.07 (td, *J* = 7.2, 5.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.0, 197.9, 197.4, 197.3, 173.4, 173.3, 135.8, 135.8, 132.8, 132.6, 128.7, 128.6, 128.6, 128.6, 77.4, 62.0, 61.9, 59.5, 59.4, 56.5, 56.2, 51.3, 51.0, 33.8, 33.8, 22.2, 22.1, 13.7. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}O_5$: 291.1227; Found: 291.1218.



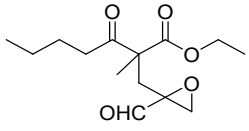
12h

Following the general procedure, **12h** was obtained as a colorless oil (0.2 mmol scale, 45 mg, 61% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.81 (d, *J* = 38.9 Hz, 1H), 7.76 (dd, *J* = 48.5, 7.8 Hz, 2H), 7.50 - 7.36 (m, 3H), 7.31 - 6.85 (m, 5H), 4.34 - 3.88 (m, 2H), 3.70 - 3.33 (m, 2H), 3.15 - 2.85 (m, 3H), 2.46 (d, *J* = 15.2 Hz, 0.5H), 2.25 (d, *J* = 15.4 Hz, 0.5H), 0.96 (dt, *J* = 22.7, 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.4, 198.1, 197.9, 196.3, 172.6, 137.6, 135.8, 135.6, 132.9, 132.4, 130.7, 130.6, 128.9, 128.7, 128.4, 128.3, 127.2, 127.2, 62.1, 61.7, 61.5, 60.8, 59.7, 59.7, 50.8, 41.3, 40.8, 31.9, 31.6, 13.5, 13.5. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}O_5$: 367.1540; Found: 367.1548.



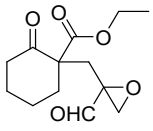
12i

Following the general procedure, **12i** was obtained as a colorless oil (0.2 mmol scale, 33 mg, 65% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.82 (d, *J* = 3.4 Hz, 1H), 4.22 - 4.15 (m, 2H), 3.71 (q, *J* = 7.0 Hz, 1H), 3.04 (d, *J* = 3.4 Hz, 2H), 2.67 - 2.44 (m, 3H), 2.28 (ddd, *J* = 39.3, 14.8, 7.2 Hz, 1H), 1.61 - 1.52 (m, 2H), 1.34 - 1.24 (m, 5H), 0.89 (td, *J* = 7.3, 2.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 204.2, 204.0, 198.3, 198.2, 169.2, 169.1, 61.9, 61.8, 59.5, 59.5, 54.4, 54.2, 50.6, 50.3, 42.1, 41.9, 26.0, 25.9, 25.7, 22.2, 14.1, 14.12, 13.9. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{21}O_5$: 257.1384; Found: 257.1377.



12j

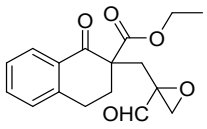
Following the general procedure, **12j** was obtained as a colorless oil (0.2 mmol scale, 38 mg, 70% yield, dr = 1:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.80 (d, *J* = 2.6 Hz, 1H), 4.23 - 4.11 (m, 2H), 3.05 - 2.96 (m, 2H), 2.81 (d, *J* = 14.8 Hz, 1H), 2.54 - 2.41 (m, 2H), 2.33 (dd, *J* = 14.7, 9.4 Hz, 1H), 1.53 (h, *J* = 7.6 Hz, 2H), 1.43 - 1.21 (m, 8H), 0.88 (td, *J* = 7.3, 3.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 207.1, 206.9, 198.2, 198.0, 172.6, 172.4, 61.8, 61.7, 59.6, 59.3, 58.4, 57.9, 52.0, 51.3, 38.1, 37.8, 31.6, 31.1, 26.1, 26.0, 22.3, 20.6, 20.4, 14.1, 14.0, 14.0, 13.9. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{14}H_{23}O_5$: 271.1540; Found: 271.1537.



12k

Following the general procedure, **12k** was obtained as a colorless oil (0.2 mmol scale, 26 mg, 52% yield, dr = 1:2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.86 (d, *J* = 17.3 Hz, 1H), 4.18 (m, 2H), 3.10 - 2.90 (m, 2H), 2.76 (d, *J* = 14.6 Hz, 0.5H), 2.64 - 2.40 (m, 3H), 2.11 - 1.96 (m, 1.5H), 1.80 - 1.47 (m, 5H), 1.30 - 1.23 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 207.5, 207.3, 198.2, 198.1, 171.8, 171.3, 61.9, 61.8, 59.5, 59.4, 59.4, 51.6,

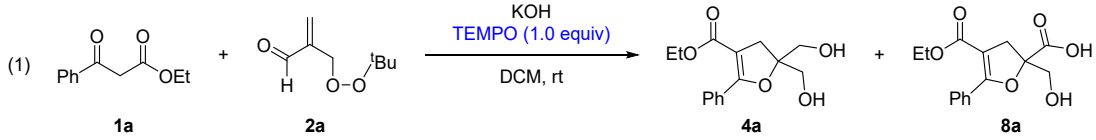
51.2, 40.8, 40.8, 37.4, 37.2, 31.9, 31.6, 27.6, 27.0, 22.4, 22.2, 14.0. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{19}O_5$: 255.1227; Found: 255.1226.



12l

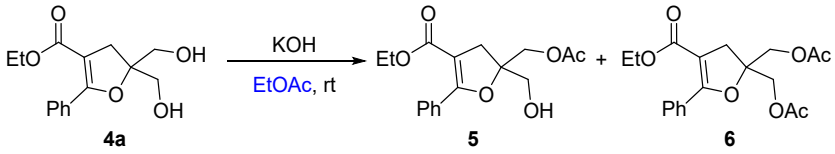
Following the general procedure, **12l** was obtained as a colorless oil (0.2 mmol scale, 34 mg, 57% yield, dr = 1:2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.90 (d, *J* = 22.2 Hz, 1H), 8.02 (dd, *J* = 11.5, 8.2 Hz, 1H), 7.50 - 7.41 (m, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 4.19 - 4.06 (m, 2H), 3.27 - 2.82 (m, 5H), 2.76 - 2.58 (m, 1H), 2.51 - 2.43 (m, 1H), 2.40 (d, *J* = 14.4 Hz, 1H), 2.21 - 2.07 (m, 1H), 1.14 (dt, *J* = 20.7, 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.1, 198.0, 194.8, 171.9, 171.2, 143.1, 142.9, 133.8, 133.5, 132.3, 131.9, 128.8, 128.7, 128.3, 128.1, 126.9, 61.8, 59.7, 59.3, 56.4, 56.2, 52.7, 51.3, 33.3, 32.1, 31.1, 30.8, 26.3, 26.0, 14.0, 14.0. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}O_5$: 303.1227; Found: 303.1225.

6. Mechanistic investigations



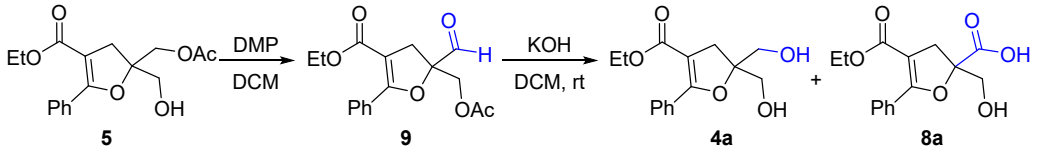
To a solution of **1a** (19.2 mg, 0.1 mmol, 1.0 equiv) and **2a** (15.8 mg, 0.1 mmol, 1.0 equiv), and TEMPO (15.6 mg, 0.1 mmol, 1.0 equiv) in DCM (1 mL) was added powder KOH (11.2 mg, 0.2 mmol, 2.0 equiv) at room temperature. The reaction mixture was stirred for 1 h. After completion, the reaction was quenched by water (2 mL) and extracted with DCM (3 mL × 3). Combined the organic phase, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 3:1 ~ 2:1) to afford the alcohol product **4a** in 38% yield. Additionally, the aqueous phase of step1 was added 2.0 M HCl to adjust pH to 2~3 and extracted with DCM (2 mL × 3). The combined organic phase was dried and concentrated to give a residue, which was purified by flash silica gel chromatography

(DCM / MeOH = 15:1 ~ 5:1) to afford the carboxylic acid product **8a** in 35% yield.

(2) 

4a **5** **6**

To a solution of **4a** (27.8 mg, 0.1 mmol, 1.0 equiv) in EtOAc (1 mL) was added powder KOH (11.2 mg, 0.2 mmol, 2.0 equiv) at room temperature. The reaction mixture was stirred for 20 min. After completion, the solution was quenched with sat. aq. NH_4Cl (1 mL) and extracted with diethyl ether (2 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 50:1 ~ 30:1) to afford the products **5** (17 mg, 53% yield) and **6** (4 mg, 10% yield).

(3) 

5 **9** **4a** **8a**

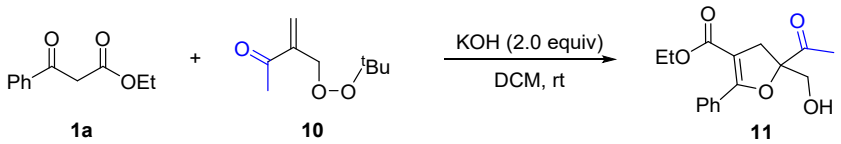
20 min: **5** (R = Ac) / **4a** (R = H) **8a**

1 h: **4a** **8a**

To a solution of **5** (64 mg, 0.2 mmol, 1.0 equiv) in DCM (2 mL) was added Dess-Martin reagent (127 mg, 0.3 mmol, 1.5 equiv) to at room temperature. The mixture was stirred for 1 h and quenched with sat. aq. $NaHCO_3$ (5 mL). The organic layer was separated, and the aqueous layer was extracted with DCM (2 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 20:1) to afford the aldehyde product **9** (39 mg, 62% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.80 (s, 1H), 7.82 (dd, *J* = 8.3, 1.6 Hz, 2H), 7.50 - 7.36 (m, 3H), 4.56 - 4.39 (m, 2H), 4.14 (q, *J* = 7.1 Hz, 3H), 3.29 (d, *J* = 16.0 Hz, 1H), 3.06 (d, *J* = 16.0 Hz, 1H), 2.09 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.5, 170.4, 164.0, 163.8, 130.9, 129.4, 128.8, 127.8, 102.2, 89.0, 64.6, 60.2, 36.1, 20.6, 14.1. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}O_6$: 319.1177; Found: 319.1187.

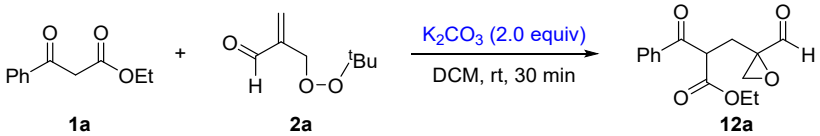
To a solution of **9** (39 mg, 0.12 mmol, 1.0 equiv) in DCM (2 mL) was added powder KOH (14 mg, 0.24 mmol, 2.0 equiv) at room temperature. The reaction process

was monitored by TLC, and the products **4a**, **5** and **8a** could be detected at 20 min. When the reaction mixture was prolonged to 1 h, only the products **4a** and **8a** could be detected. Then, the reaction mixture was quenched by water (2 mL) and extracted with DCM (3 mL × 3). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 2:1) to afford the alcohol product **4a** (11 mg, 34% yield). Additionally, the aqueous phase was treated with 2.0 M HCl to adjust the pH to 2~3 and extracted with DCM (3 mL × 3). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (DCM / MeOH = 15:1 ~ 5:1) to afford the carboxylic acid product **8a** (13 mg, 37% yield).

(4) 

1a **10** **11**

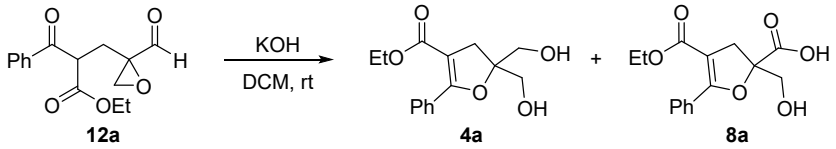
To a solution of **1a** (19.2 mg, 0.1 mmol, 1.0 equiv) and **10** (17.2 mg, 0.1 mmol, 1.0 equiv) in DCM (1 mL) was added powder KOH (11.2 mg, 0.2 mmol, 2.0 equiv) at room temperature. The reaction mixture was stirred for 30 min. After completion, the solution was quenched with sat. aq. NH_4Cl (1 mL) and extracted with DCM (2 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 5:1) to afford the product **11** (20 mg, 70% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 - 7.79 (m, 2H), 7.47 - 7.40 (m, 3H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.00 - 3.75 (m, 2H), 3.25 - 3.06 (m, 2H), 2.38 (s, 3H), 2.18 (br, s, 1H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 210.0, 164.5, 163.5, 131.0, 129.4, 129.3, 128.0 102.8, 92.6, 66.0, 60.3, 37.6, 27.0, 14.3. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}O_5$: 291.1227; Found: 291.1241.

(5) 

1a **2a** **12a**

To a solution of **1a** (38.4 mg, 0.2 mmol, 1.0 equiv) and **2a** (31.6 mg, 0.2 mmol, 1.0 equiv) in DCM (1 mL) was added K_2CO_3 (55.2 mg, 0.4 mmol, 2.0 equiv) at room

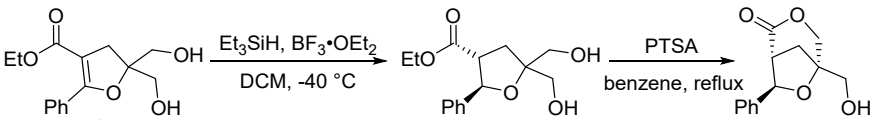
temperature. The reaction mixture was stirred for 30 min. After completion, the solution was quenched with sat. aq. NH_4Cl (1 mL) and extracted with DCM (2 mL × 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 10:1) to afford the epoxide product **12a** (45 mg, 81% yield, dr = 1:1).

(6) 

12a **4a** **8a**

To a solution of **12a** (55 mg, 0.2 mmol, 1.0 equiv) in DCM (1 mL) was added powder KOH (22 mg, 0.4 mmol, 2.0 equiv) at room temperature. The reaction mixture was stirred for 30 min. After completion, the reaction was quenched by water (2 mL) and extracted with DCM (3 mL × 3). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether / EtOAc = 2:1) to afford the alcohol product **4a** (18 mg, 33% yield). Additionally, the aqueous phase was treated with 2.0 M HCl to adjust the pH to 2~3 and extracted with DCM (3 mL × 3). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (DCM / MeOH = 15:1 ~ 5:1) to give carboxylic acid product **8a** (17 mg, 30% yield).

7. Synthetic applications

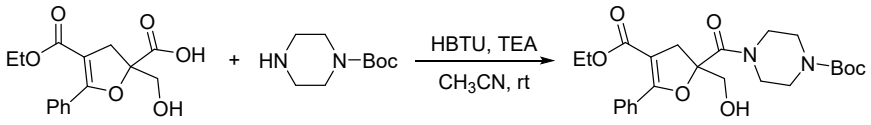


4a **17** **18**

A 5 mL flask equipped with a stirrer bar was charged with **4a** (56 mg, 0.2 mmol, 1.0 equiv) followed by the addition of dry DCM (2 mL). The resulting mixture was stirred at −40 °C for 20 min, and subsequently, triethylsilane (90 μL, 0.56 mmol, 2.8 equiv) and $BF_3{\cdot}OEt_2$ (90 μL, 0.64 mmol, 3.2 equiv) were added. The mixture was stirred at −40 °C until the consumption of **4a** and then the mixture was warmed up to room temperature. Finally, triethylamine (90 μL, 0.6 mmol, 3.0 equiv) and water (2

mL) were added. The mixture was extracted with DCM (3 × 2 mL), and the combined organic phase was dried with Na_2SO_4 and removed under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether / EtOAc = 3:1) to afford the tetrahydrofuran **17** (43 mg, 77% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33 (m, 5H), 5.13 (d, *J* = 9.6 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.78 - 3.65 (m, 4H), 3.09 (q, *J* = 9.6 Hz, 1H), 2.53 - 1.68 (m, 4H), 1.18 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.3, 139.7, 128.7, 128.5, 126.4, 85.7, 83.6, 65.9, 65.6, 61.1, 52.6, 35.3, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}NaO_5$: 303.1203; Found: 303.1206.

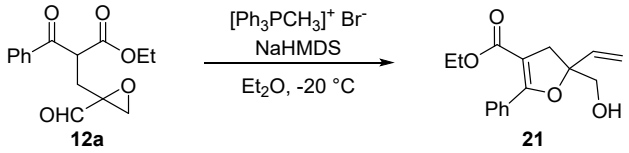
A solution of **17** (43 mg, 0.15 mmol, 1.0 equiv) and PTSA (1.2 mg, 0.007 mmol, 0.05 equiv) in benzene (2 mL) was refluxed at 90 °C overnight. After completion, the reaction was quenched with solid Na_2CO3 and filtered. Then the filtrate was concentrated in vacuum. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 5 : 1) to afford **18** (25 mg, 72% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.42 - 7.28 (m, 5H), 5.43 (s, 1H), 4.47 (dd, *J* = 11.5, 2.1 Hz, 1H), 4.34 (d, *J* = 11.5 Hz, 1H), 3.97 (s, 2H), 3.19 (d, *J* = 4.1 Hz, 1H), 2.16 (m, 2H), 2.03 (d, *J* = 11.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.6, 140.6, 128.7, 128.2, 125.2, 82.6, 82.0, 76.8, 64.2, 50.3, 28.9. **HRMS (ESI)** m/z: $[M + MeOH + Na]^+$ Calcd for $C_{14}H_{18}NaO_5$: 289.1047; Found: 289.1061.



8a **19** **20**

A solution of **8a** (58 mg, 0.2 mmol, 1.0 equiv), **19** (45 mg, 0.24 mmol, 1.2 equiv) and HBTU (91 mg, 0.24 mmol, 1.2 equiv) in CH_3CN (2 mL) was added TEA (83 μL, 0.6 mmol, 3.0 equiv) at room temperature. The reaction mixture was stirred for 30 min. After completion, the solution was added 2.0 M NaOH to adjust pH to 12~13 and extracted with EtOAc (3 mL × 3). The combined organic layer was dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (petroleum ether / EtOAc = 2:1) to afford **20** (69 mg, 75% yield) as a yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.79 (d, *J* = 7.4 Hz, 2H), 7.49 - 7.36 (m, 3H),

4.16 (qd, *J* = 7.1, 4.2 Hz, 2H), 3.92 (d, *J* = 11.5 Hz, 1H), 3.82 - 3.12 (m, 12H), 1.45 (s, 9H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.3, 164.5, 162.7, 154.6, 131.1, 129.3, 129.0, 128.0, 103.1, 88.2, 80.6, 66.4, 60.4, 43.3, 38.7, 38.5, 28.5, 14.3. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{24}H_{32}N_2NaO_7$: 483.2102; Found: 483.2105.



To a suspension of $[Ph_3PCH_3]Br$ (86 mg, 0.24 mmol, 1.2 equiv) in dry THF (1 mL) was added a solution of NaHMDS (2.0 M, 0.15 mL, 0.3 mmol, 1.5 equiv) at room temperature. The mixture was stirred for 1 h and a solution of aldehyde **12a** (55 mg, 0.2 mmol, 1.0 equiv) in dry THF (1 ml) was added at -20 °C. The reaction mixture was stirred overnight at the same temperature and quenched with sat. aq. NH_4Cl. The mixture was extracted with diethyl ether (3 × 2 mL) and the extract was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. Purification of the residue by column chromatography on silica gel (petroleum ether / EtOAc = 10:1) to afford 38 mg of the product **21** in 70% yield as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (dd, *J* = 7.9, 1.9 Hz, 2H), 7.40 (m, 3H), 5.95 (dd, *J* = 17.3, 10.9 Hz, 1H), 5.46 (d, *J* = 17.3 Hz, 1H), 5.31 (d, *J* = 11.0 Hz, 1H), 4.12 (q, *J* = 7.0 Hz, 2H), 3.73 (t, *J* = 11.0 Hz, 2H), 3.22 (d, *J* = 15.3 Hz, 1H), 2.98 (d, *J* = 15.3 Hz, 1H), 1.92 (br, s, 1H), 1.20 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.2, 163.8, 137.8, 130.6, 130.0, 129.5, 127.8, 115.8, 102.5, 88.9, 67.2, 60.0, 38.4, 14.3. **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}O_4$: 275.1278; Found: 275.1273.

8. References

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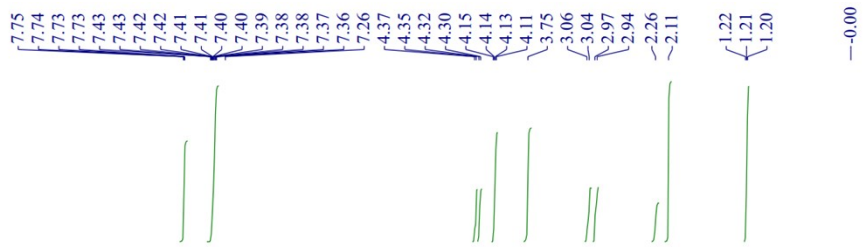
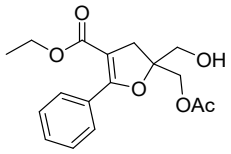
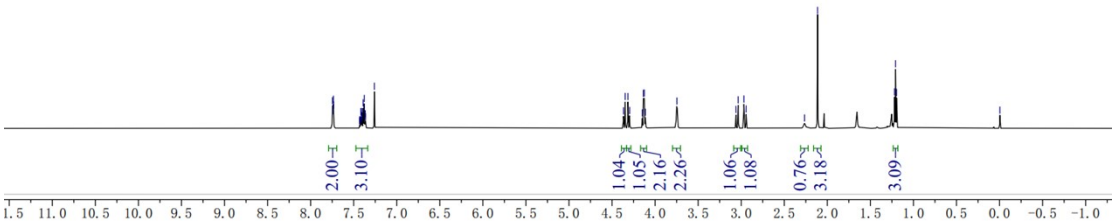
9. NMR spectra for new compounds

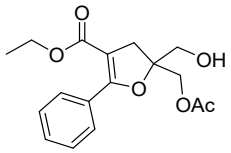




5

^{1}H NMR (600 MHz, $CDCl_3$)





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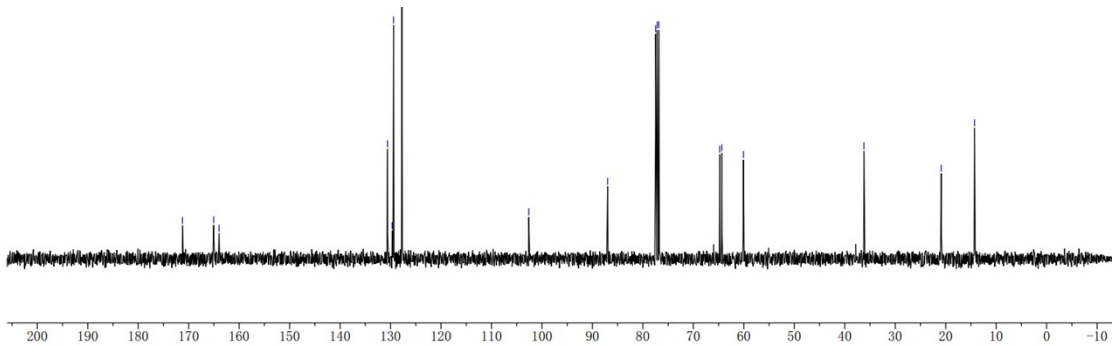

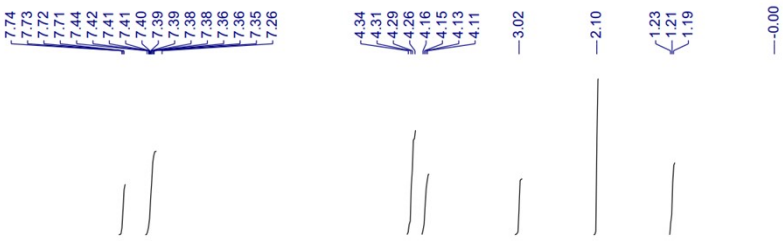

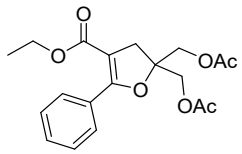

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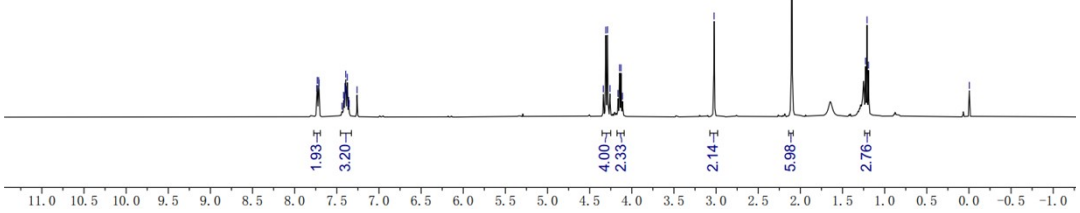
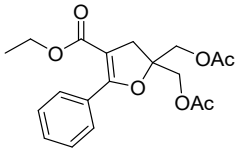
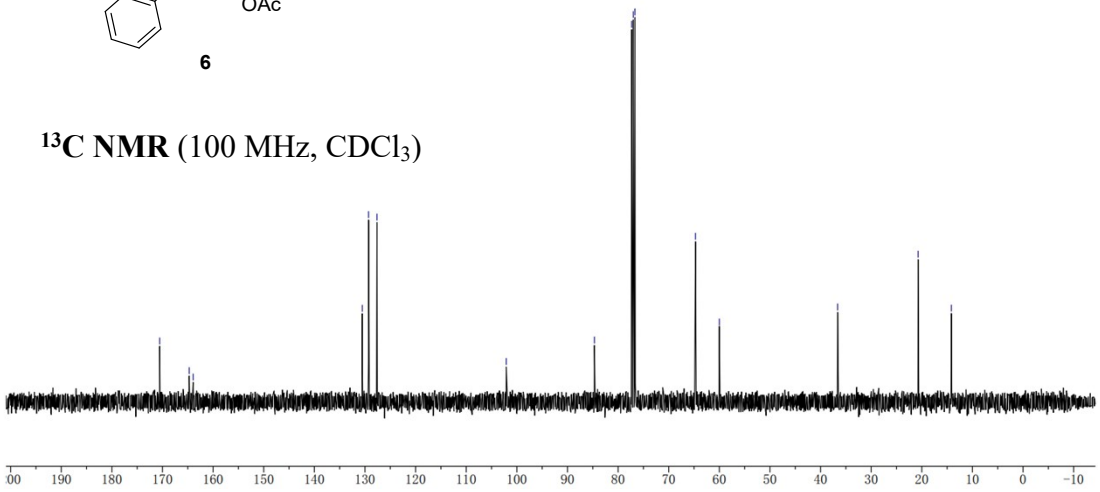
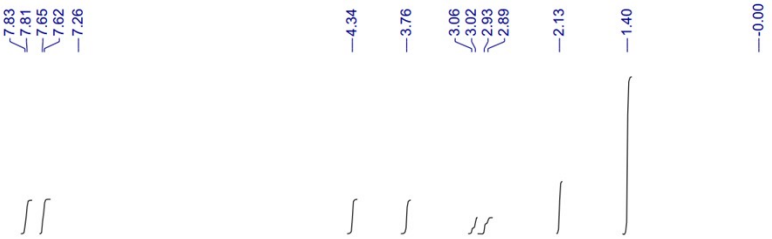


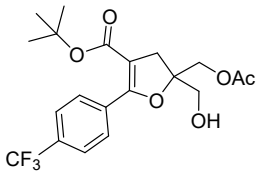


6

^{13}C NMR (100 MHz, $CDCl_3$)







7

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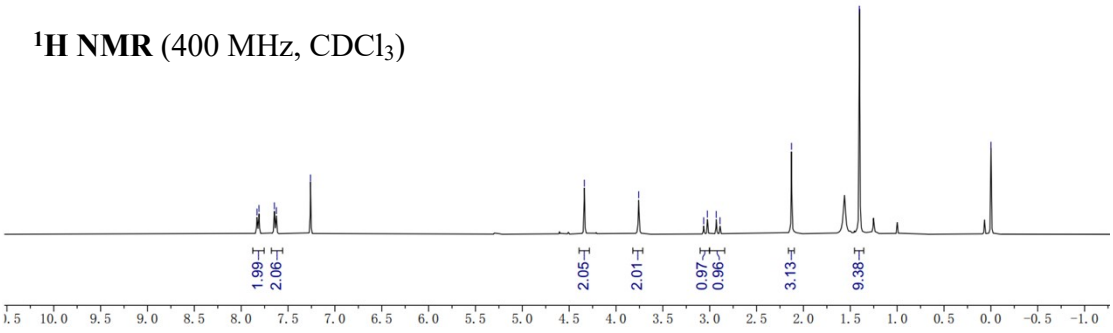

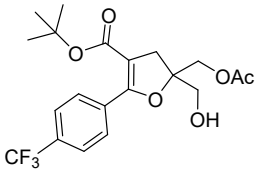

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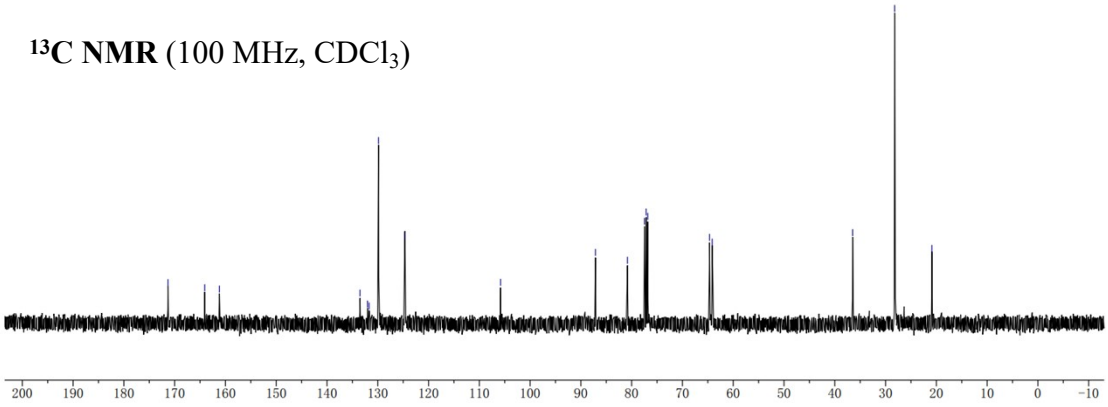
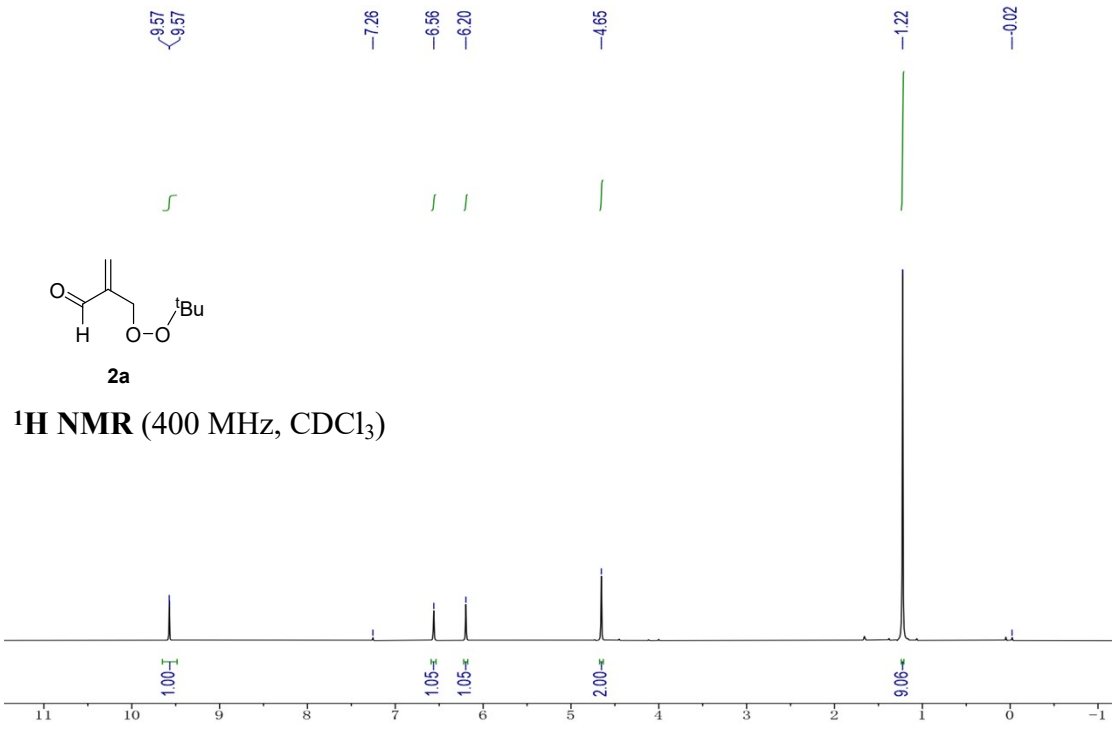
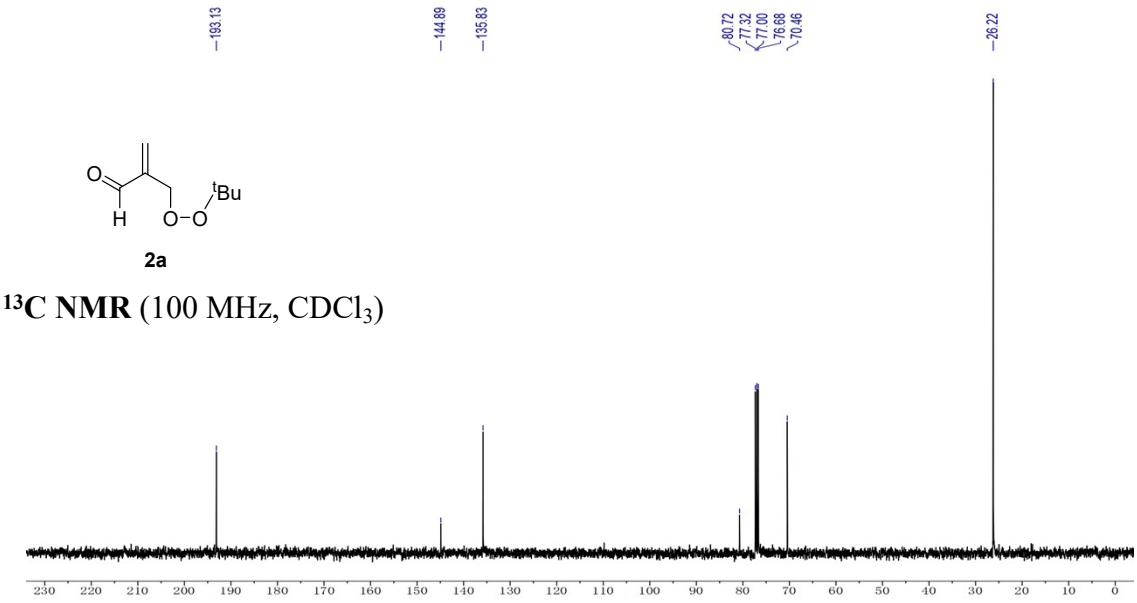




2a

^{1}H NMR (400 MHz, $CDCl_3$)



2a

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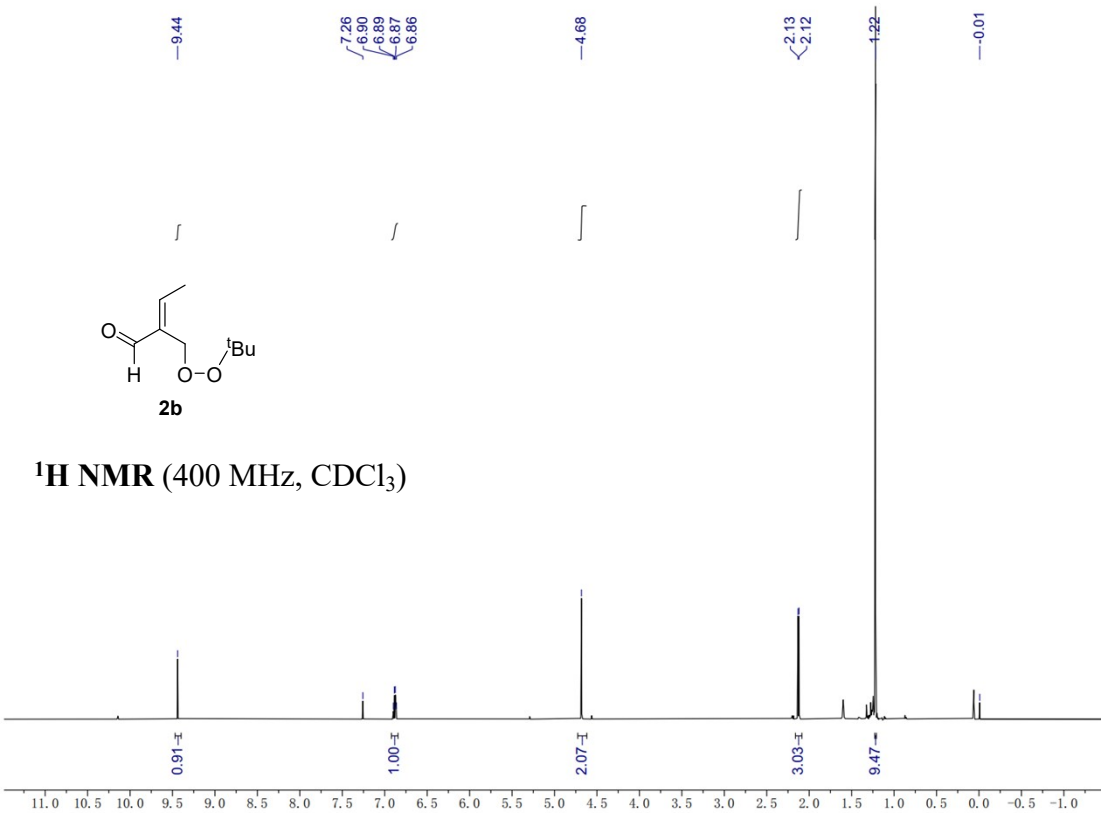

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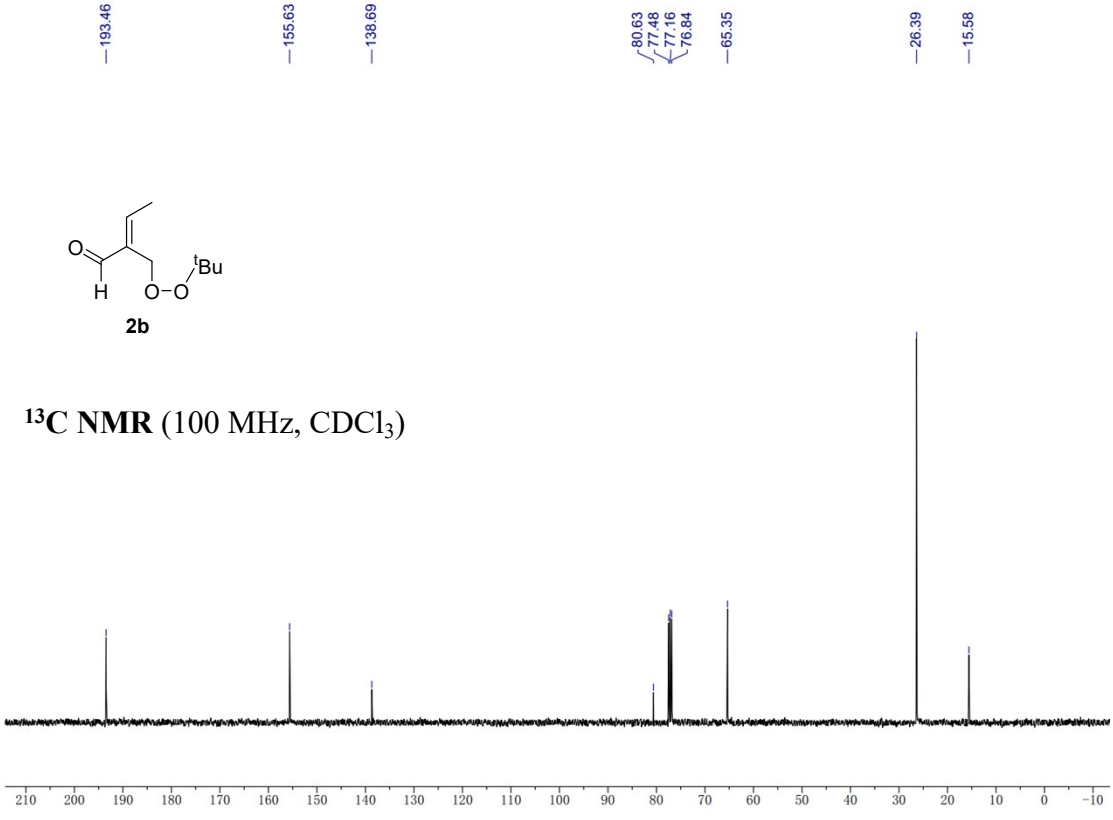

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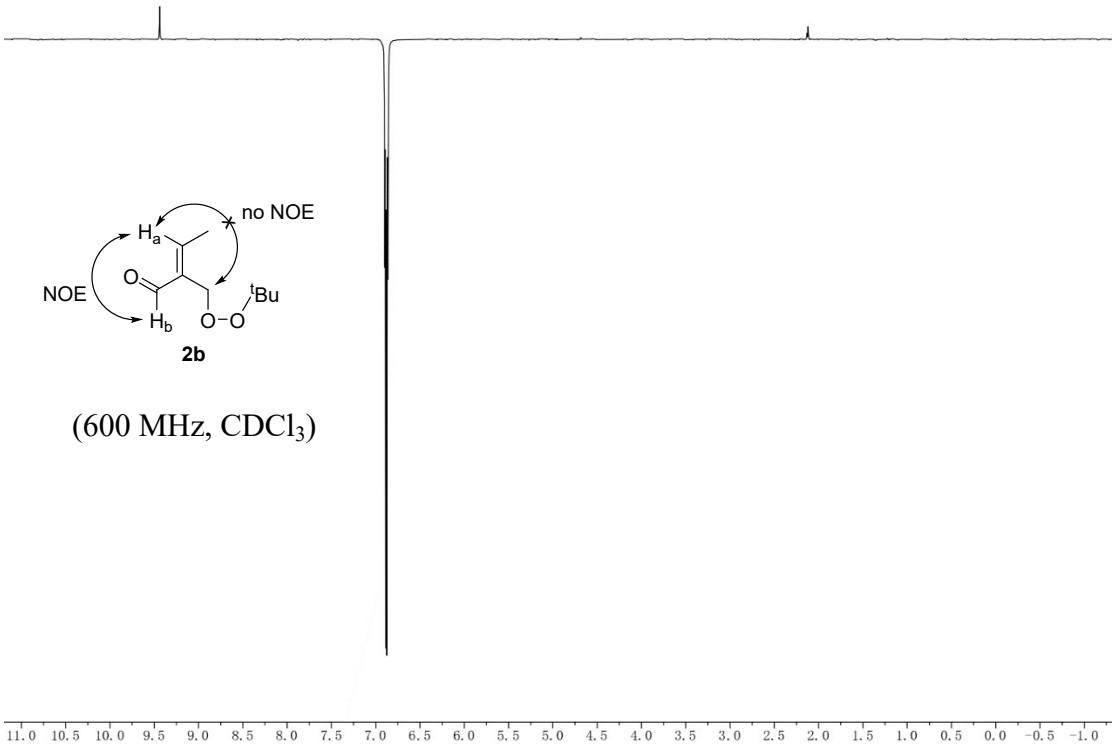

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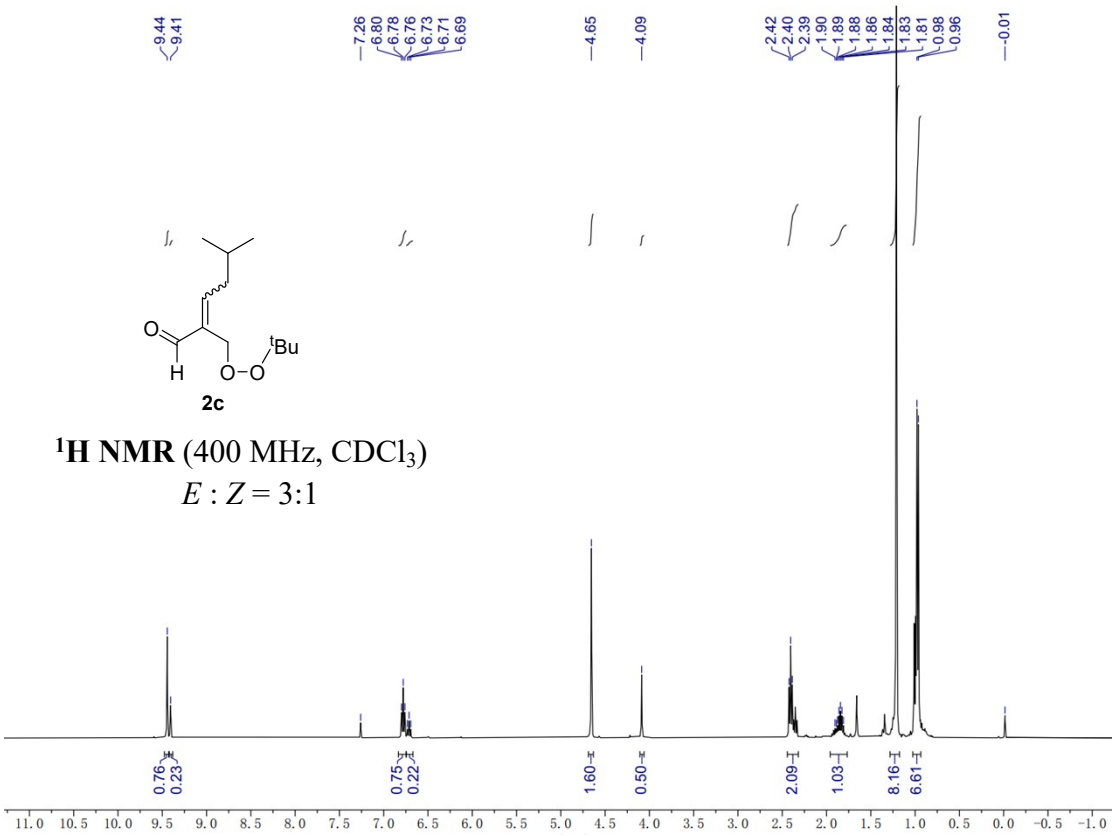

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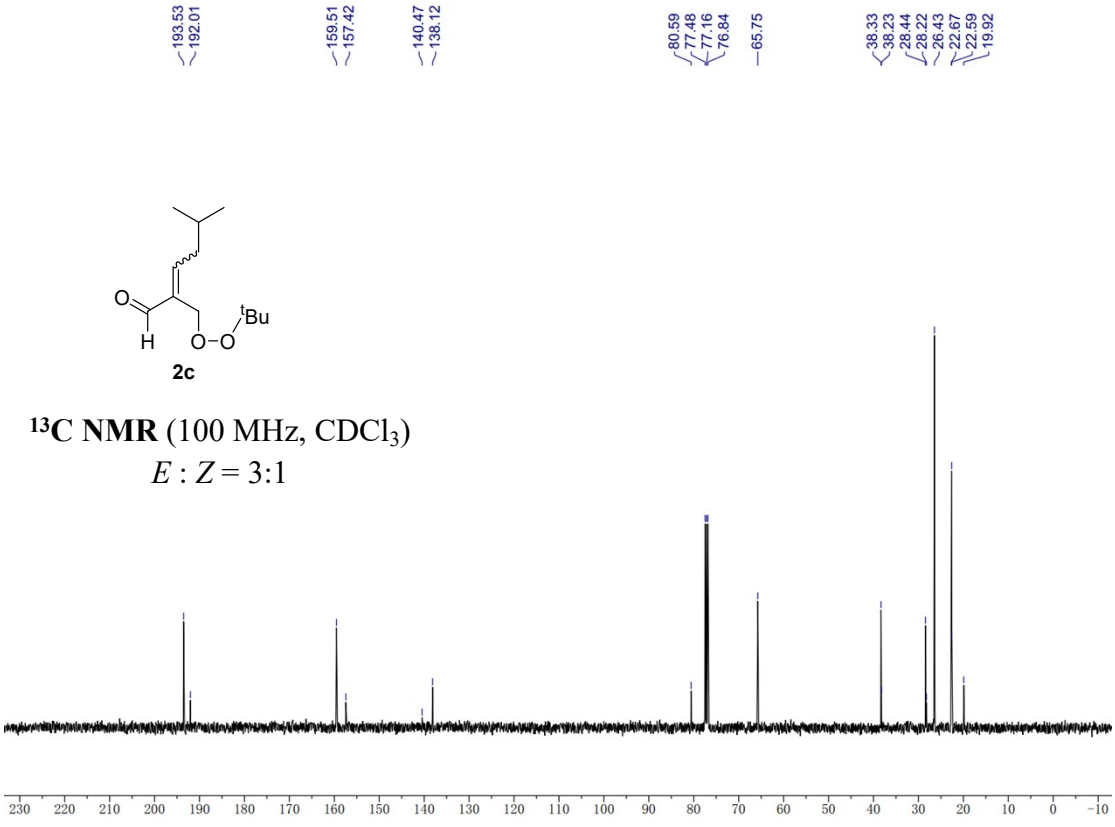

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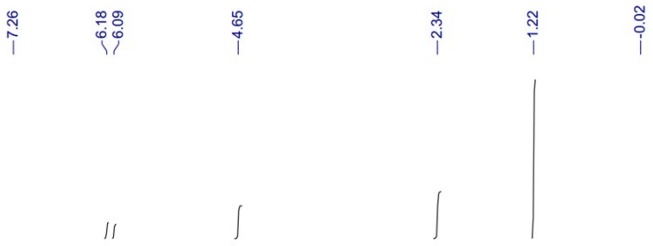

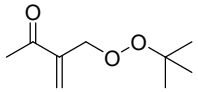

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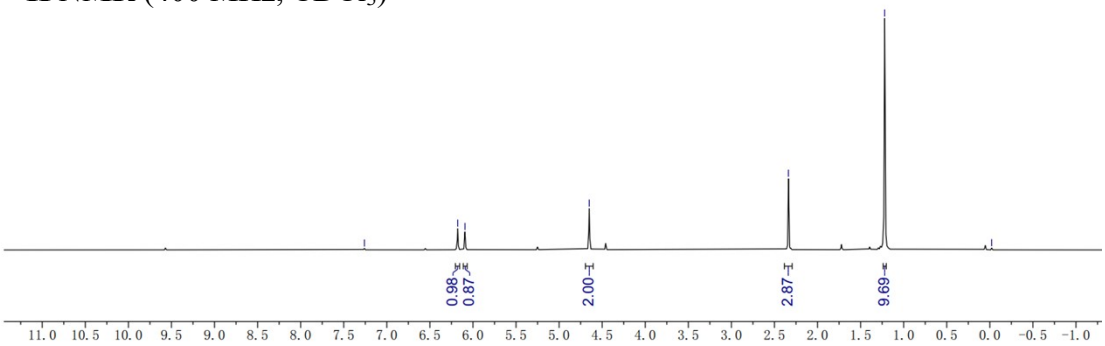

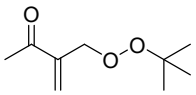

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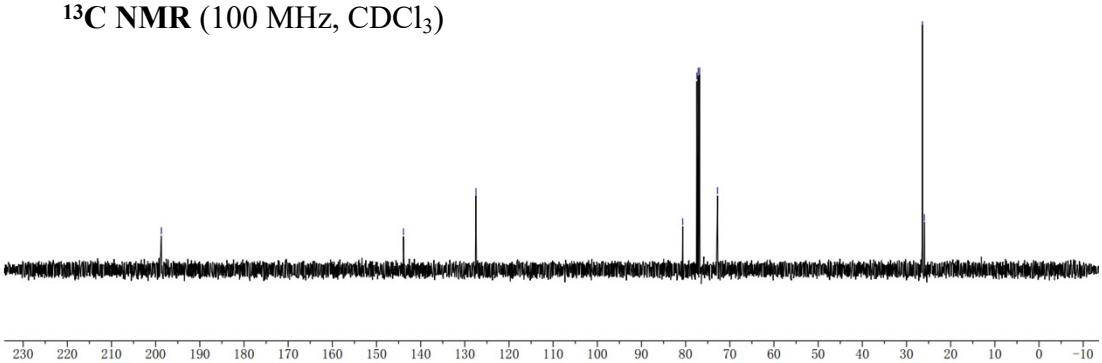

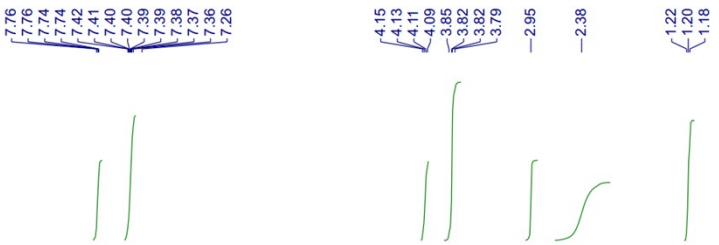

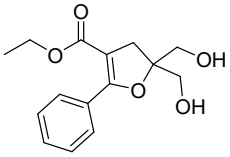

4a

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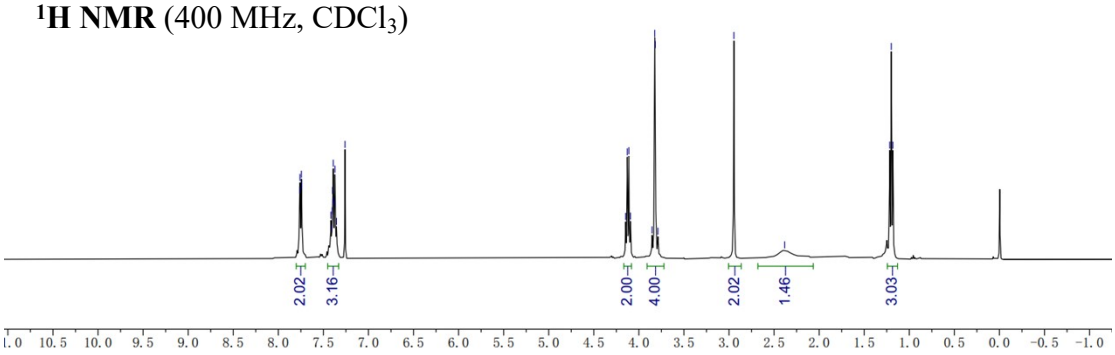

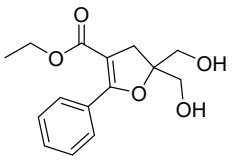

4a

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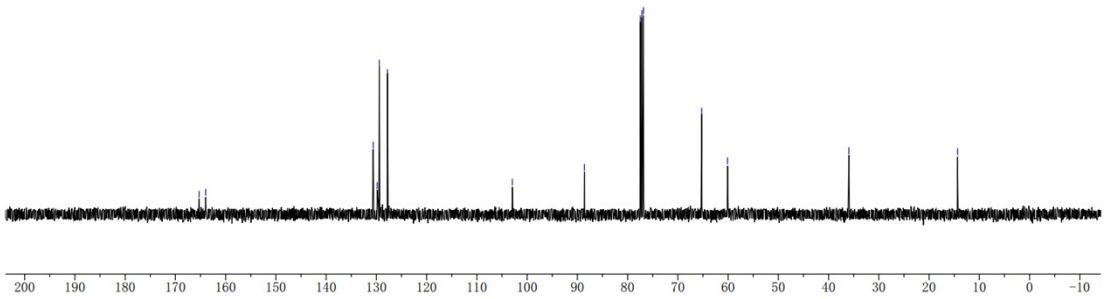

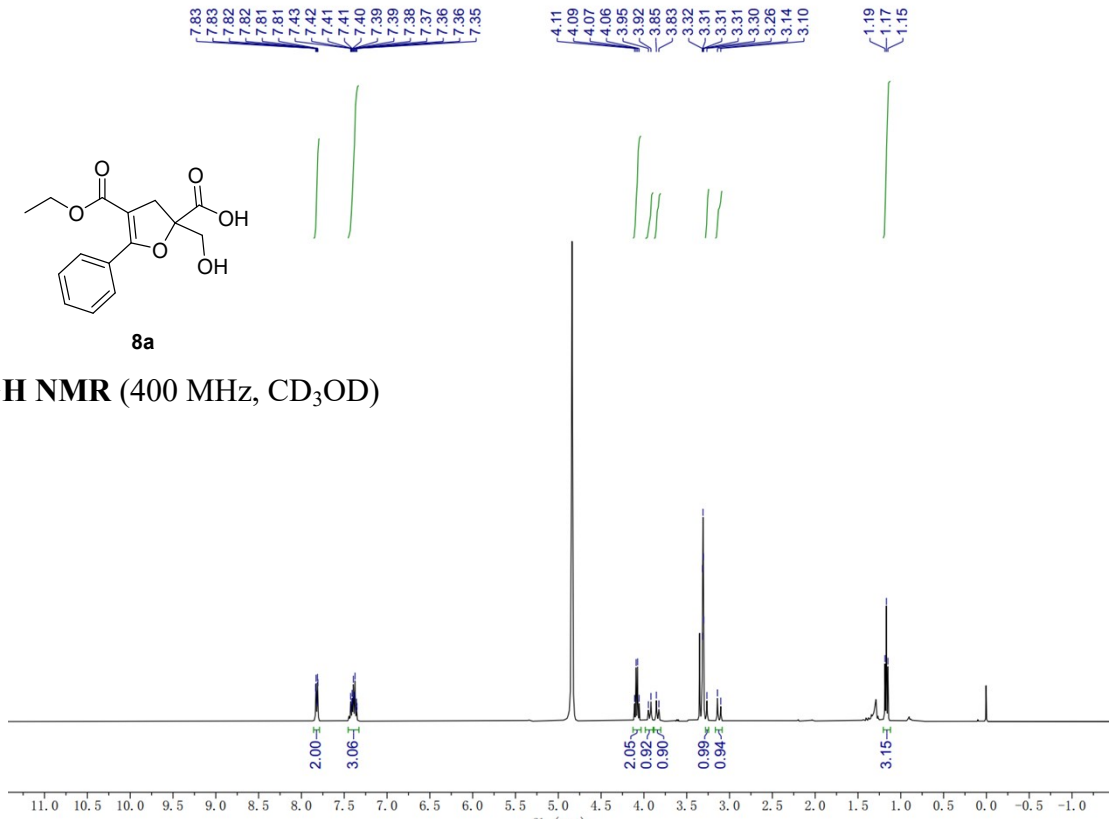

8a

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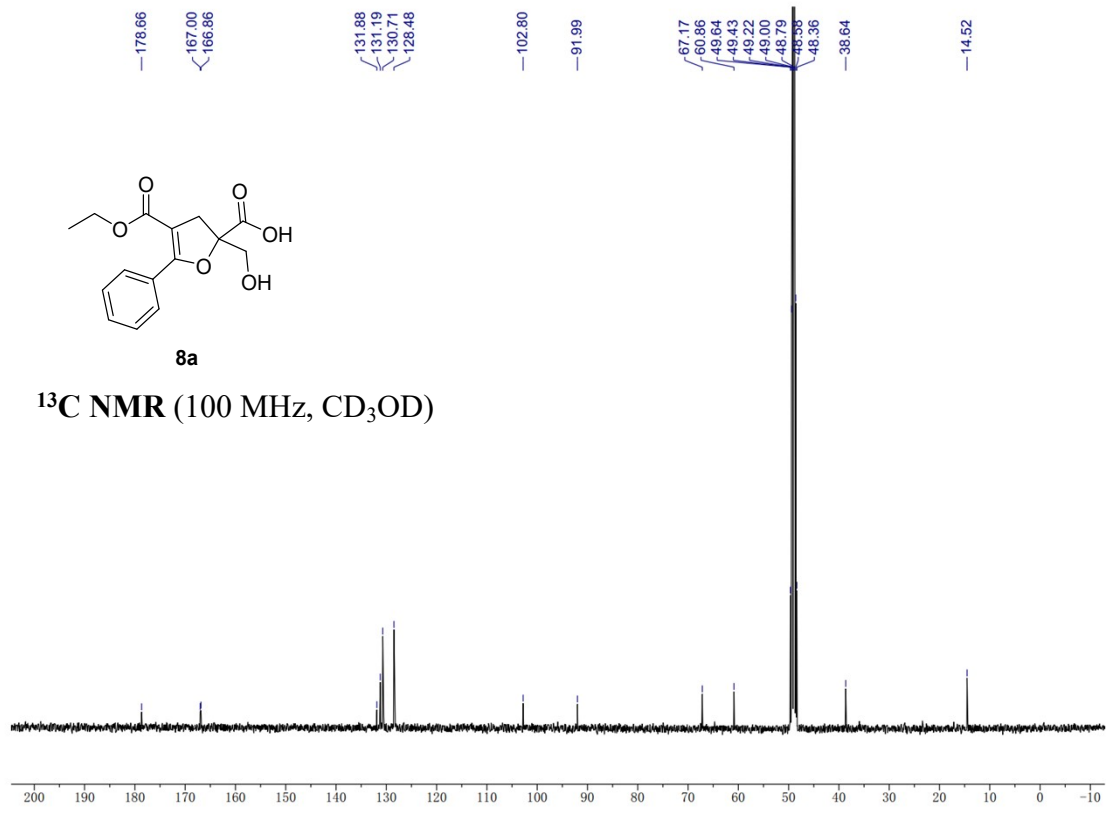

8a

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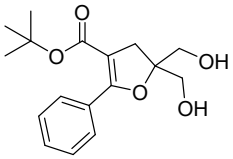
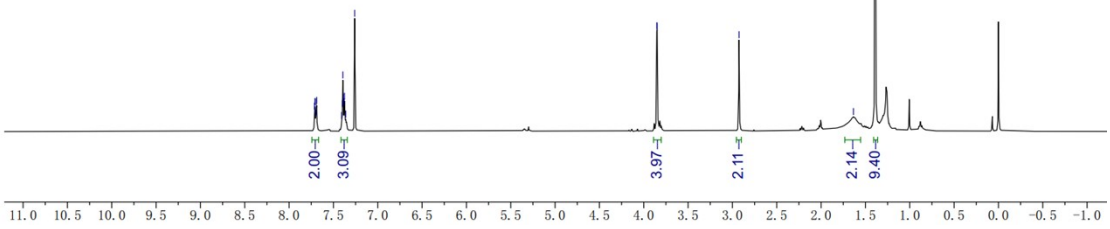
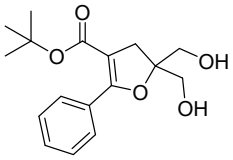


4b

^{1}H NMR (400 MHz, $CDCl_3$)





4b

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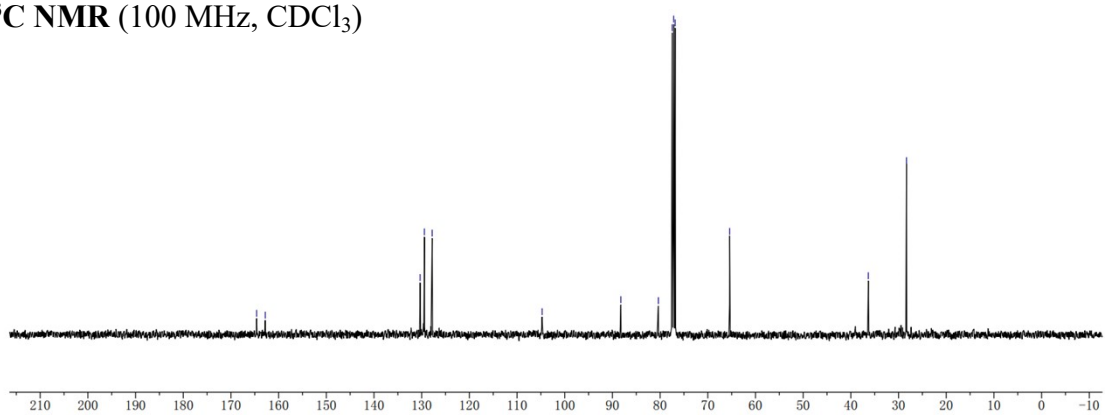
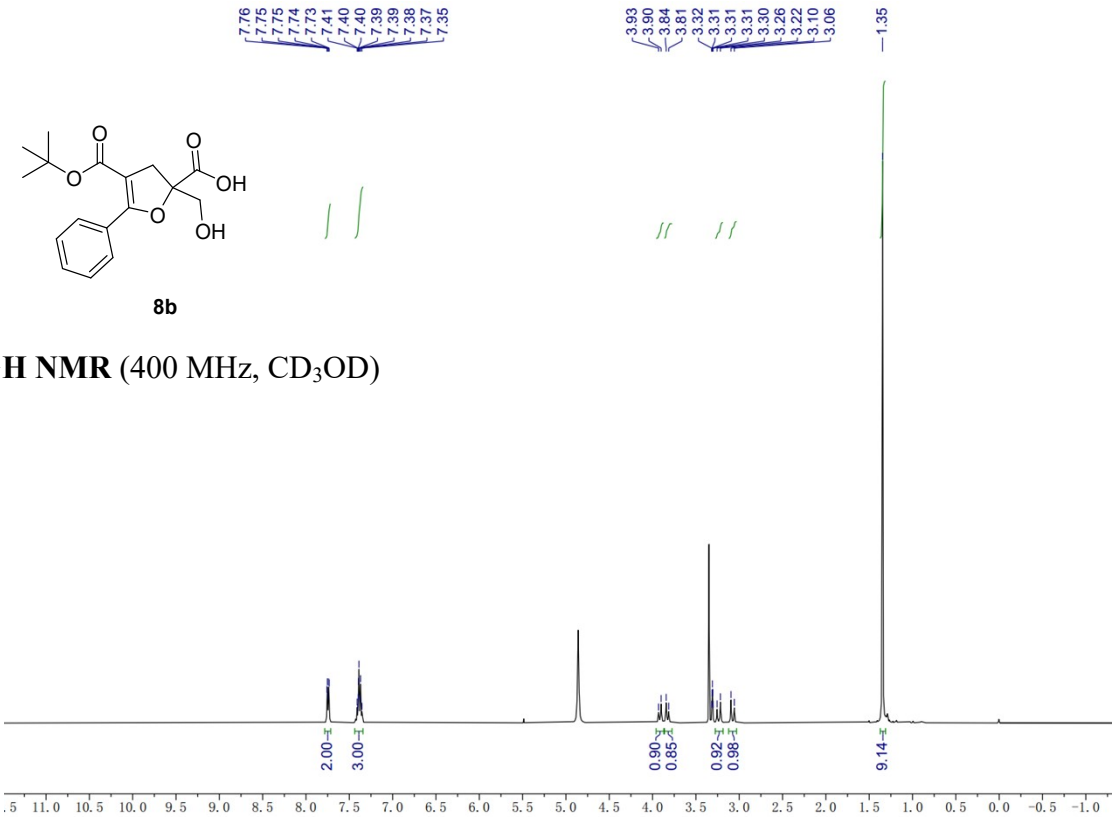
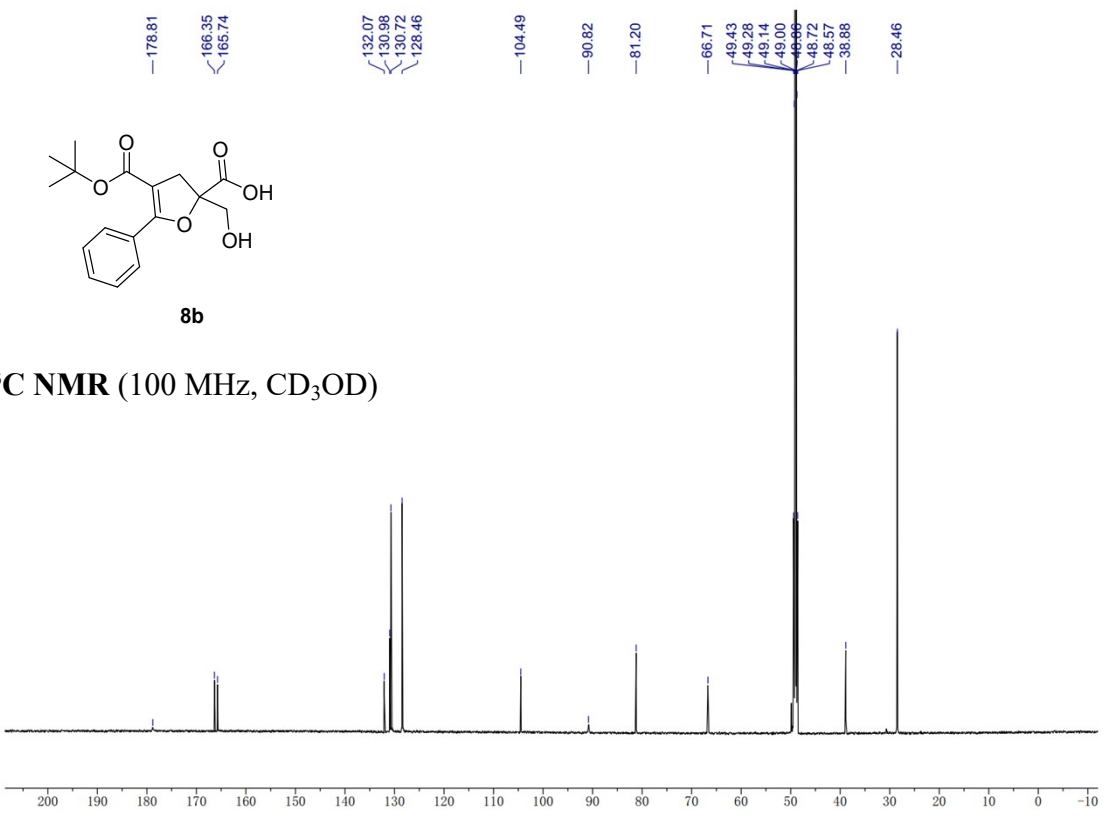




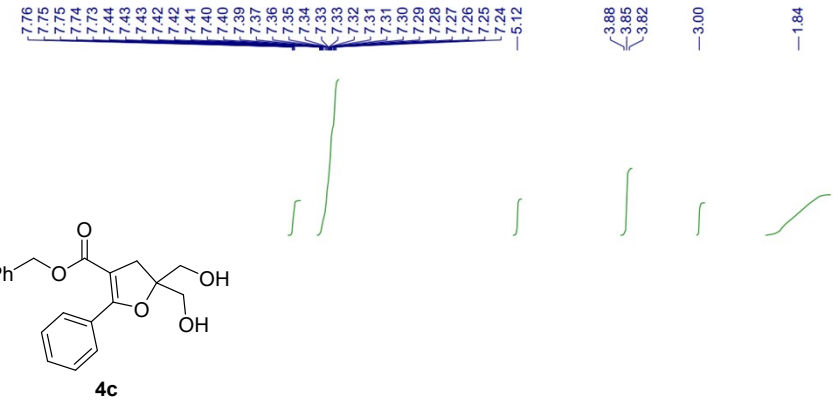
8b

^{1}H NMR (400 MHz, CD_3OD)



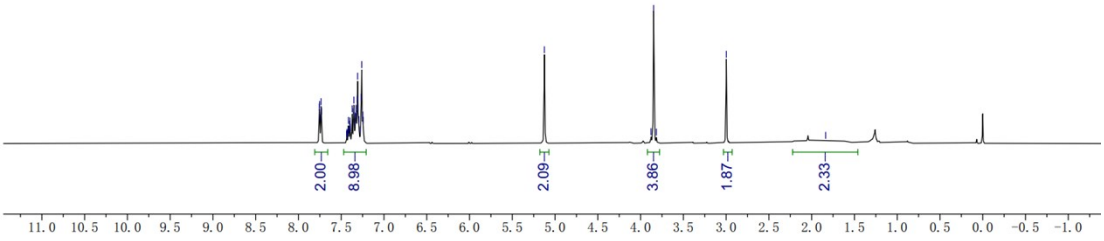
8b

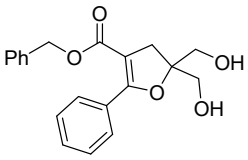
^{13}C NMR (100 MHz, CD_3OD)



4c

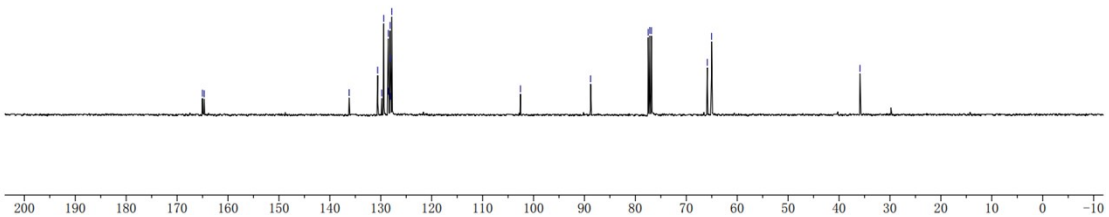
^{1}H NMR (400 MHz, $CDCl_3$)

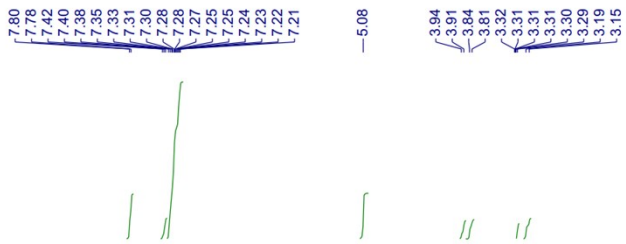


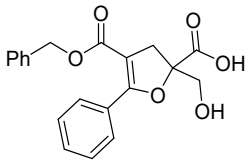


4c

^{13}C NMR (100 MHz, $CDCl_3$)

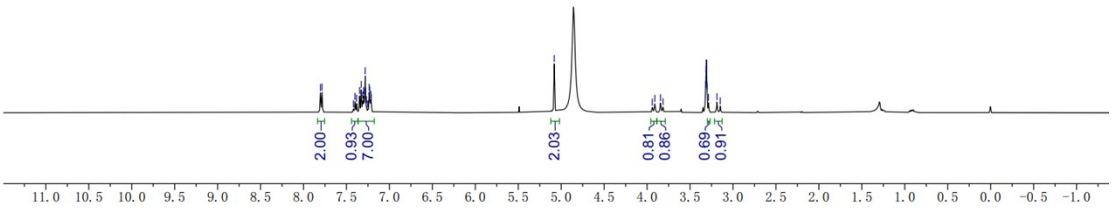


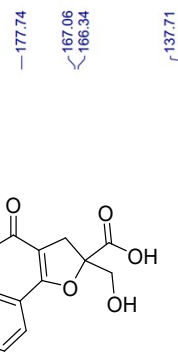




8c

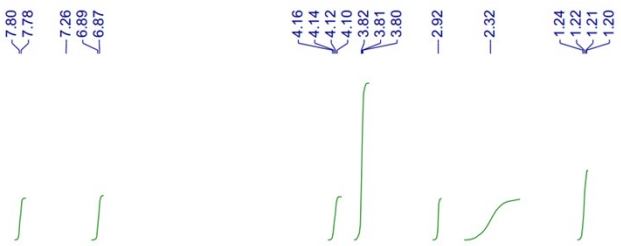
^{1}H NMR (400 MHz, CD_3OD)

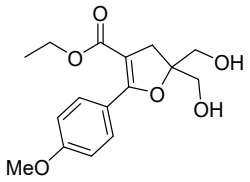




8c

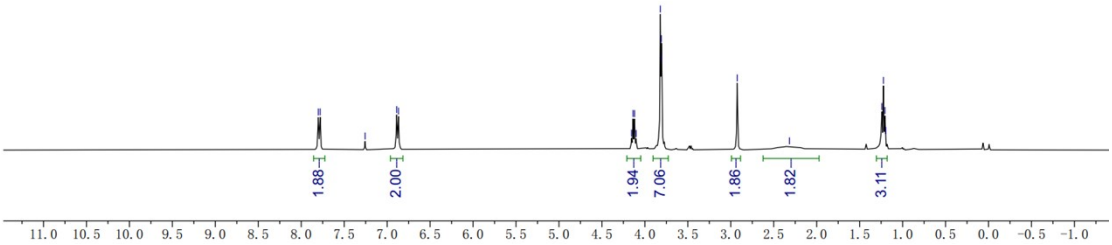
^{13}C NMR (100 MHz, CD_3OD)

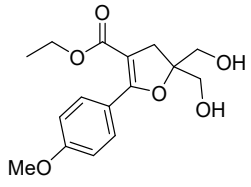




4d

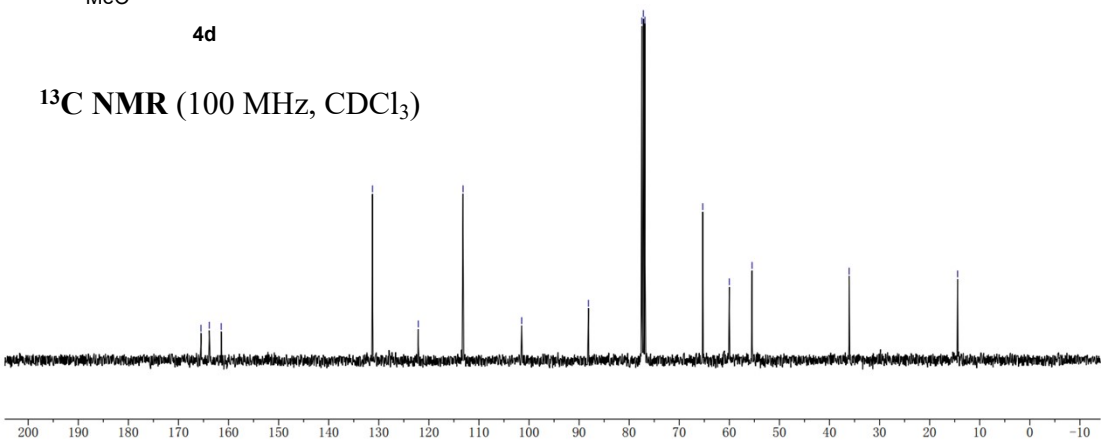
^{1}H NMR (400 MHz, $CDCl_3$)

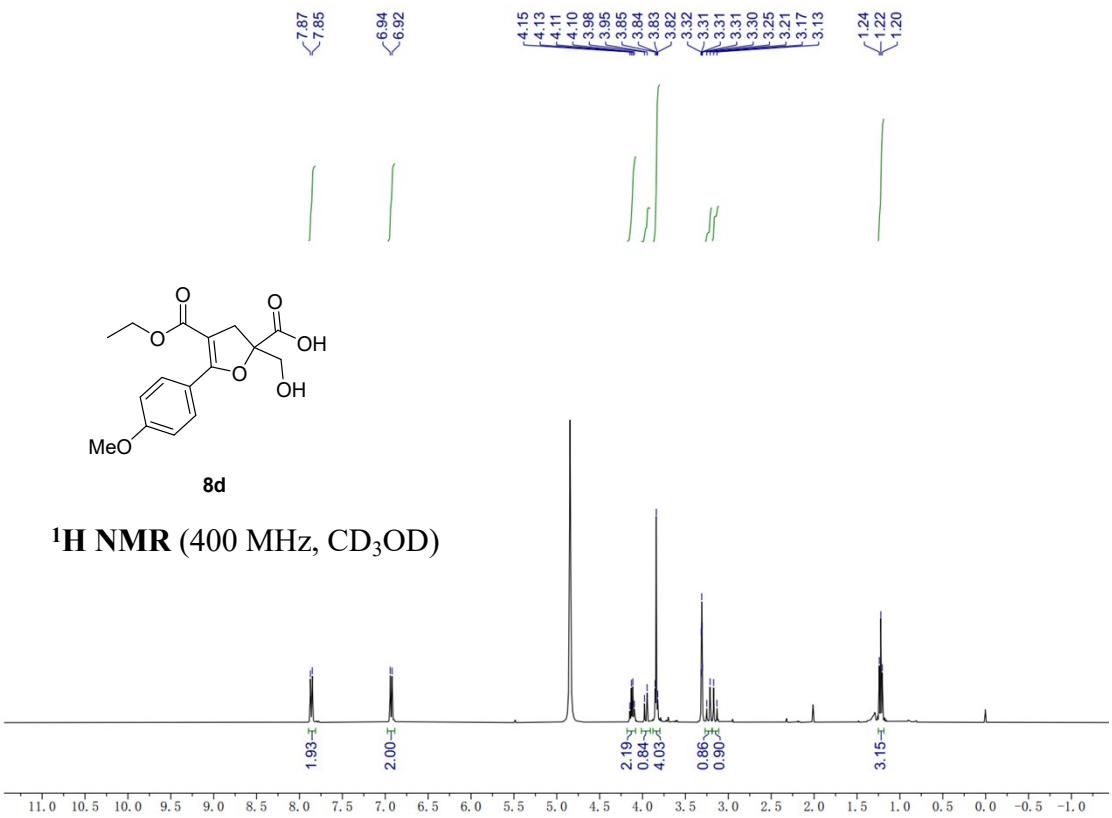




4d

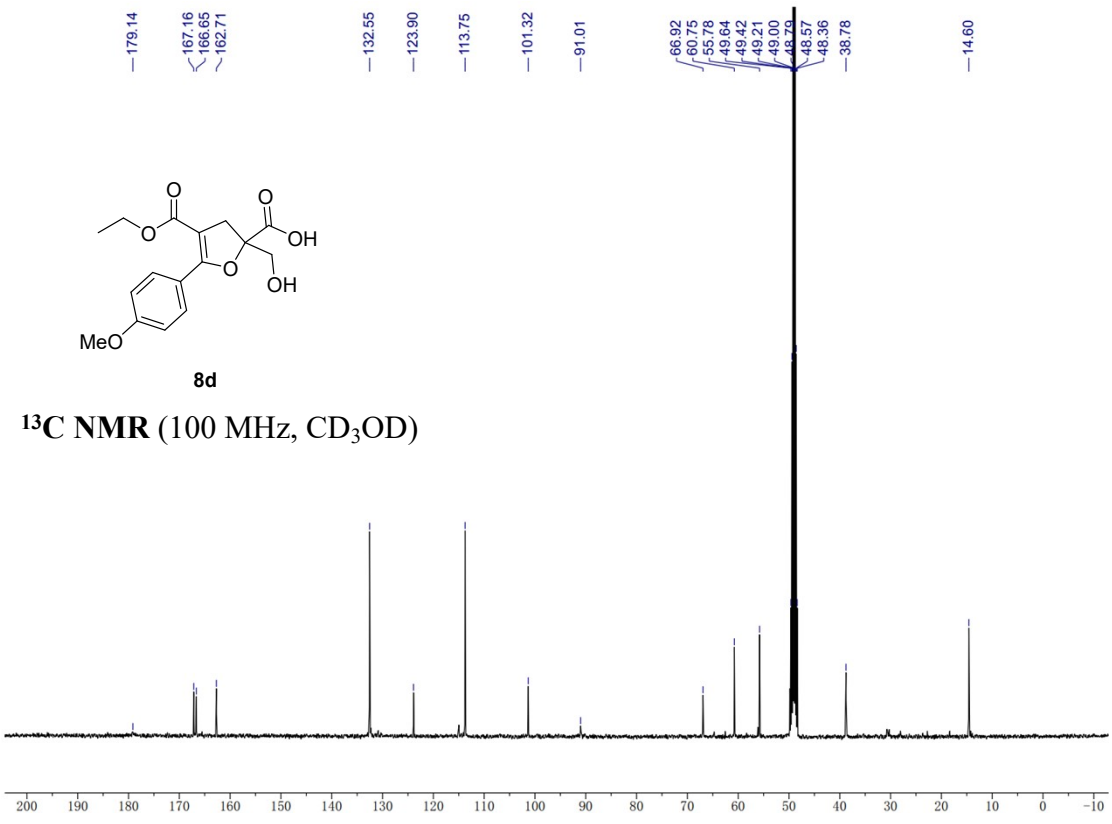
^{13}C NMR (100 MHz, $CDCl_3$)





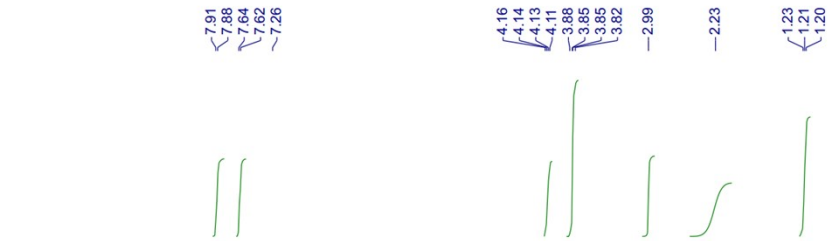
8d

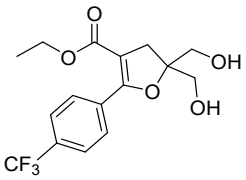
^{1}H NMR (400 MHz, CD_3OD)



8d

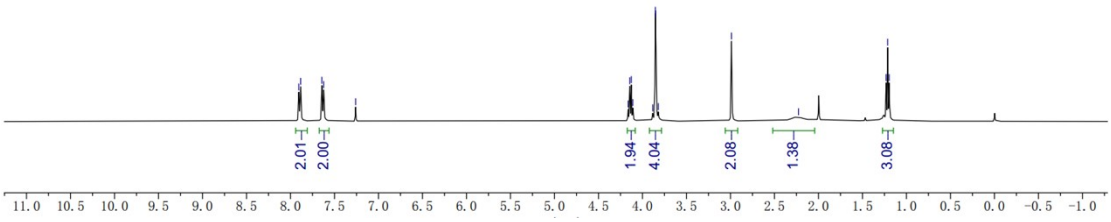
^{13}C NMR (100 MHz, CD_3OD)

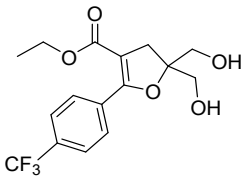




4e

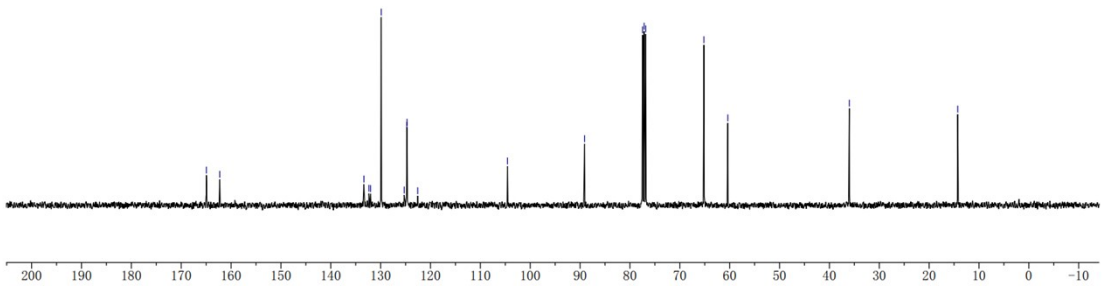
^{1}H NMR (400 MHz, $CDCl_3$)

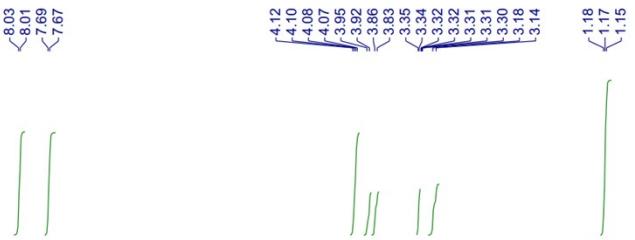


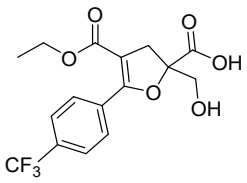


4e

^{13}C NMR (100 MHz, $CDCl_3$)

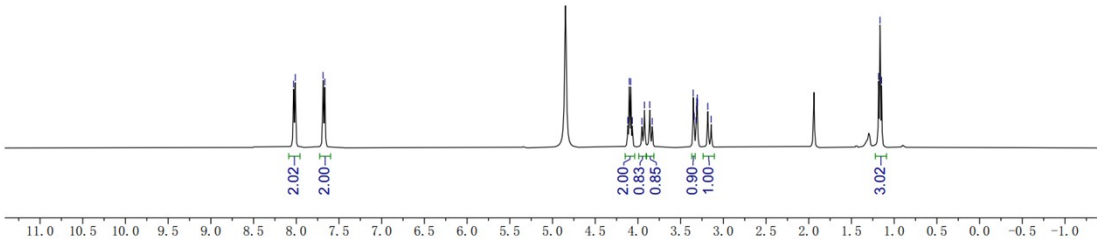


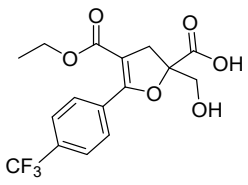




8e

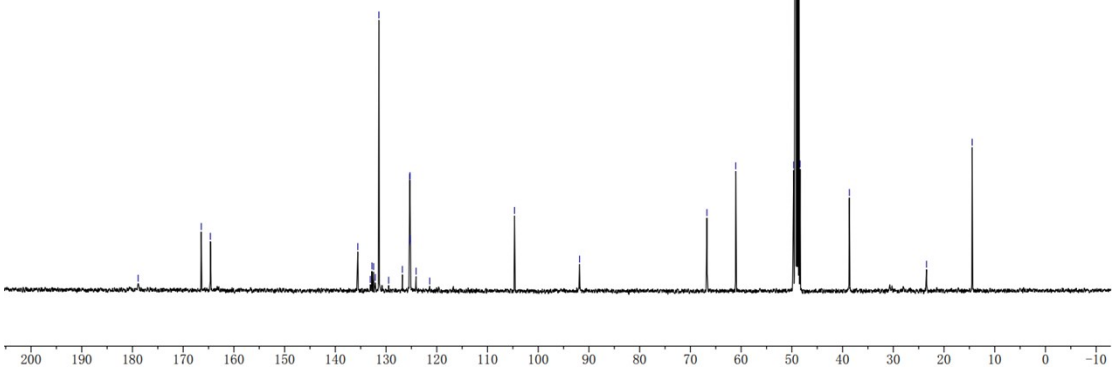
[1]H NMR (400 MHz, CD_3OD)

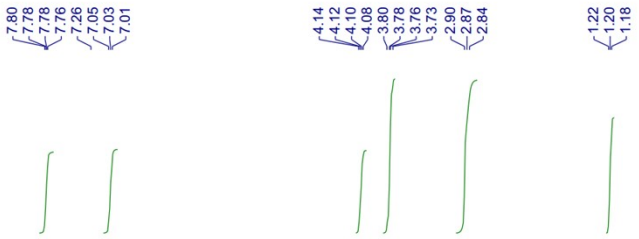


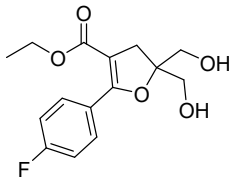


8e

[13]C NMR (100 MHz, CD_3OD)

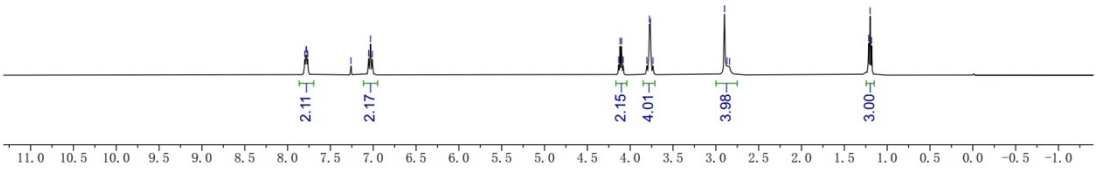


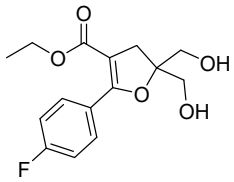




4f

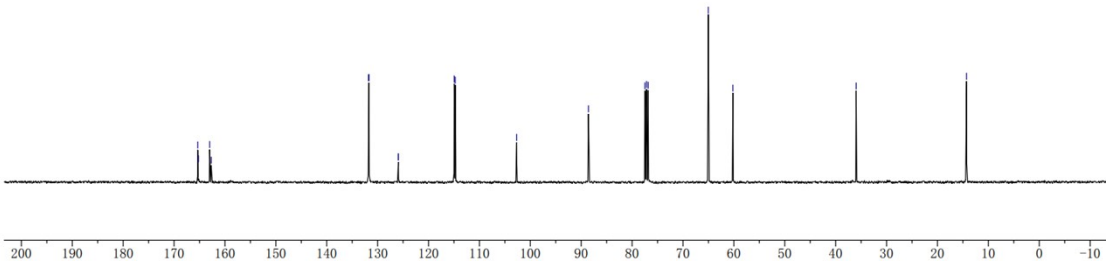
^{1}H NMR (400 MHz, $CDCl_3$)

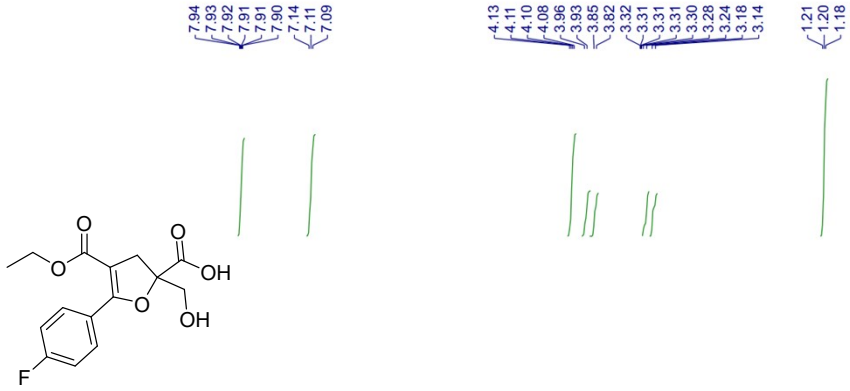




4f

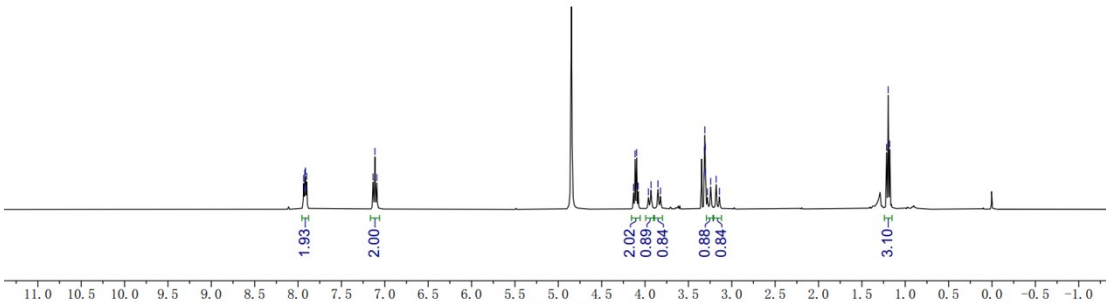
^{13}C NMR (100 MHz, $CDCl_3$)

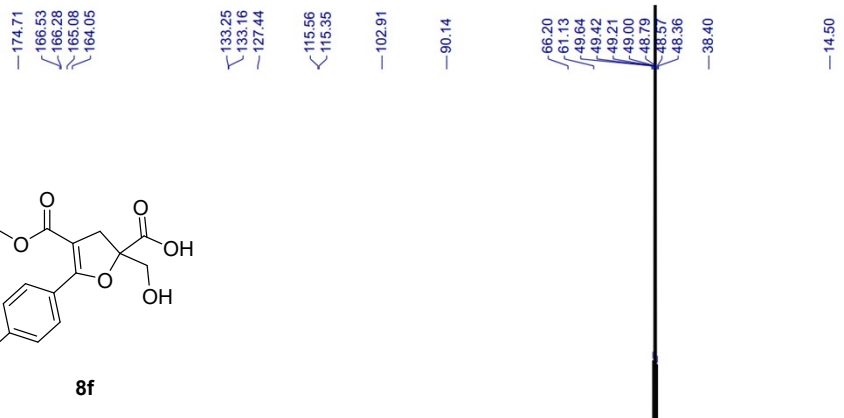




8f

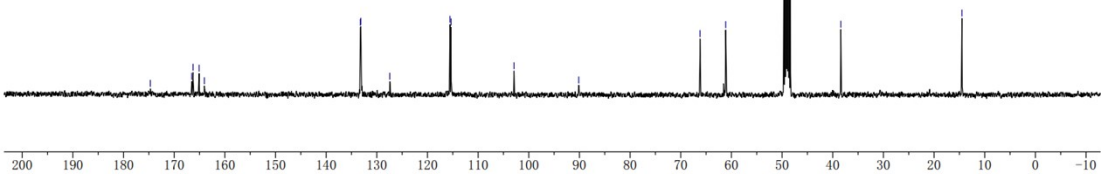
^{1}H NMR (400 MHz, CD_3OD)

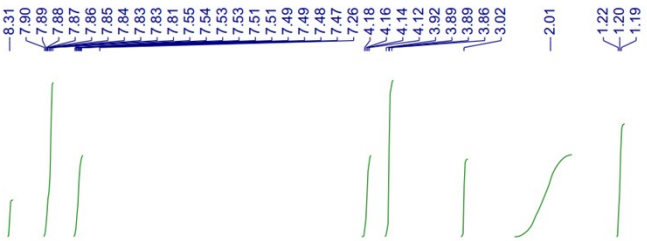


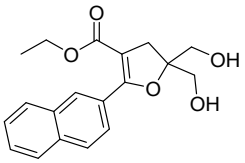


8f

^{13}C NMR (100 MHz, CD_3OD)

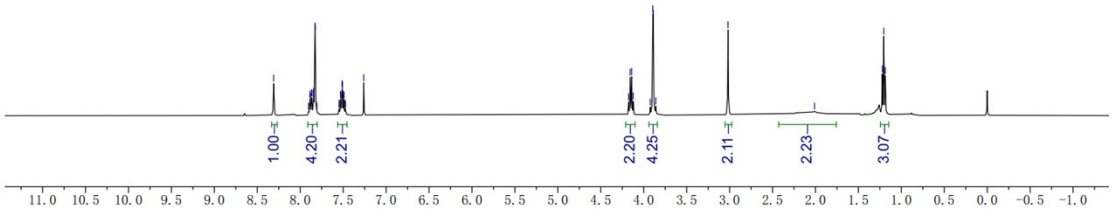


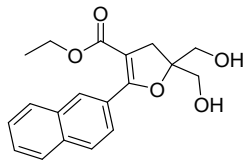




4g

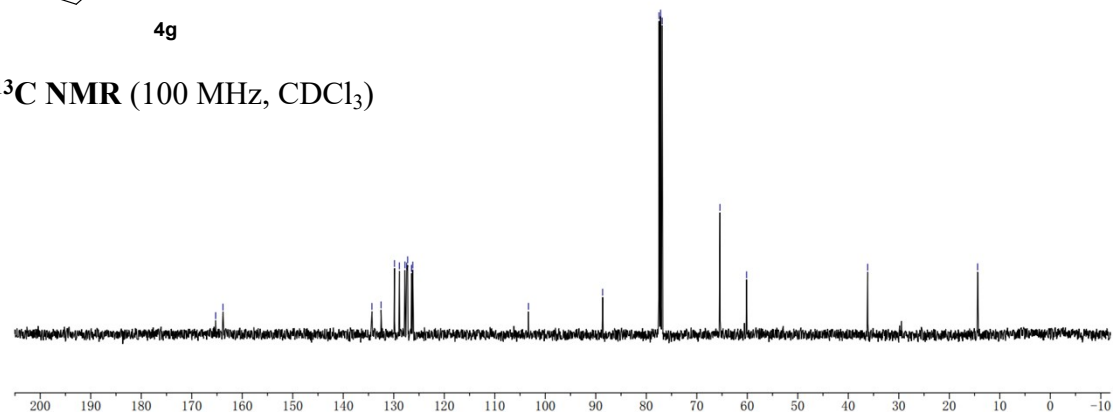
^{1}H NMR (400 MHz, $CDCl_3$)

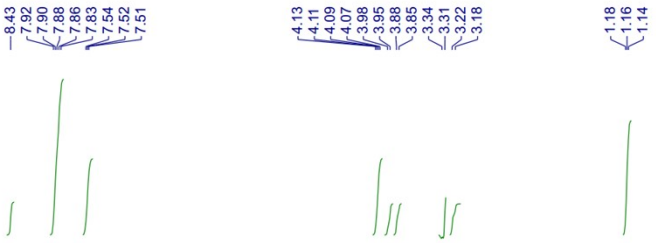


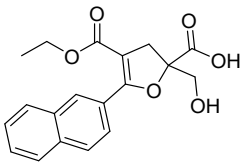


4g

^{13}C NMR (100 MHz, $CDCl_3$)

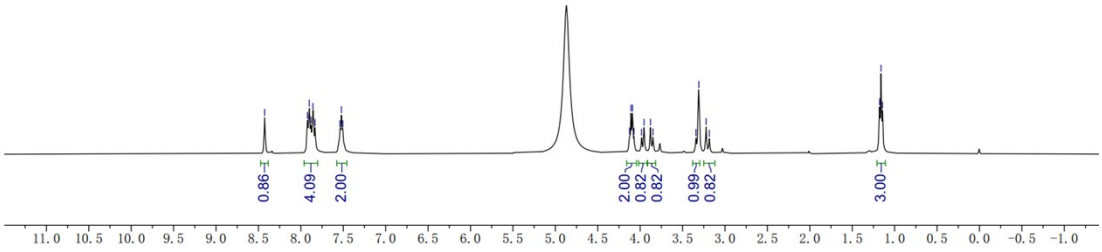


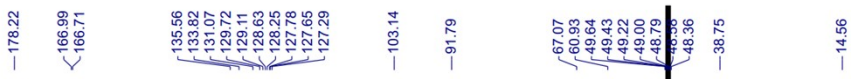


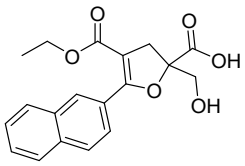


8g

^{1}H NMR (400 MHz, CD_3OD)

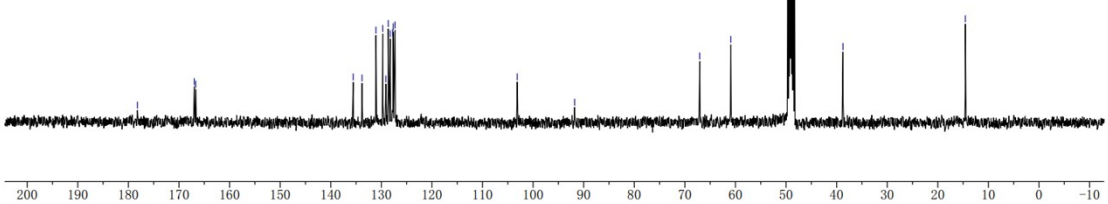


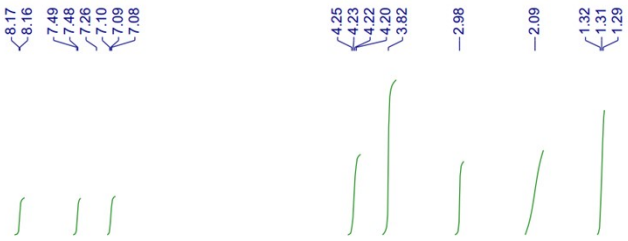


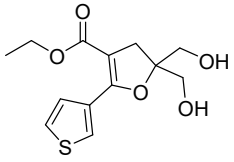


8g

^{13}C NMR (100 MHz, CD_3OD)

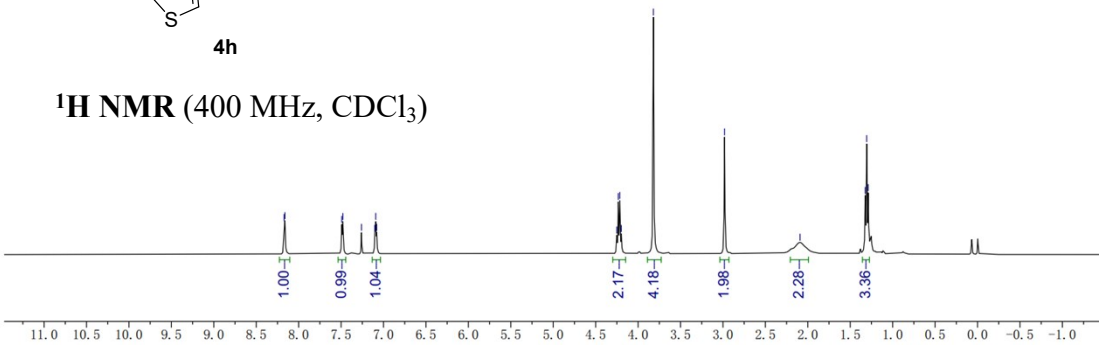


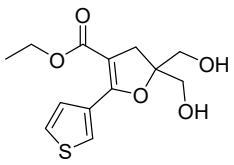




4h

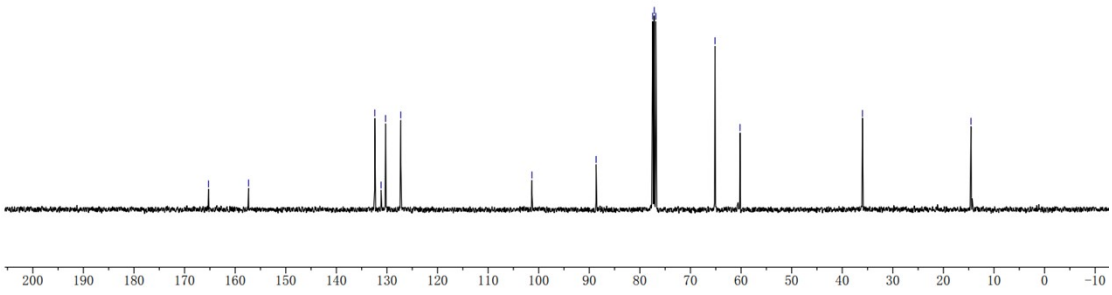
^{1}H NMR (400 MHz, $CDCl_3$)

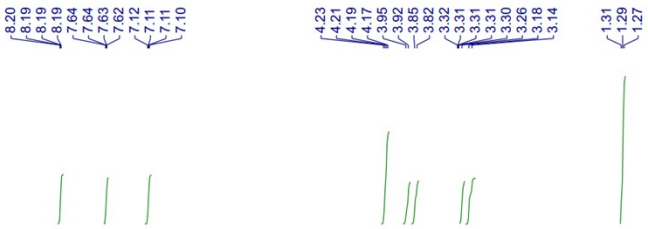


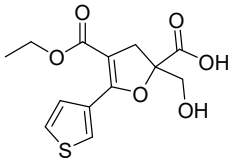


4h

^{13}C NMR (100 MHz, $CDCl_3$)

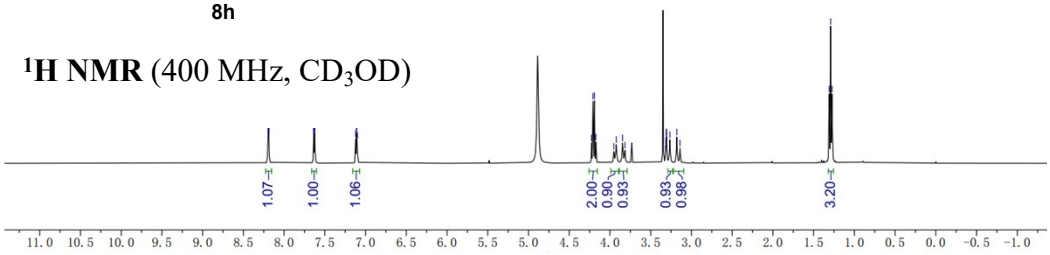


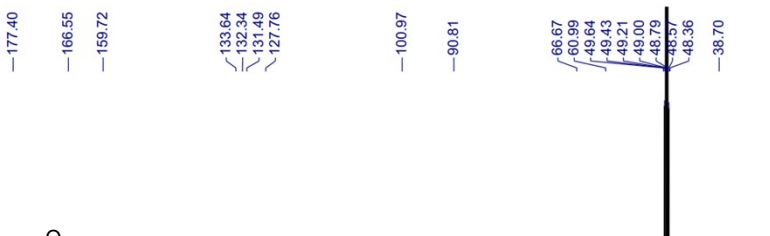


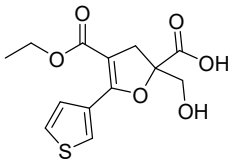


8h

^{1}H NMR (400 MHz, CD_3OD)

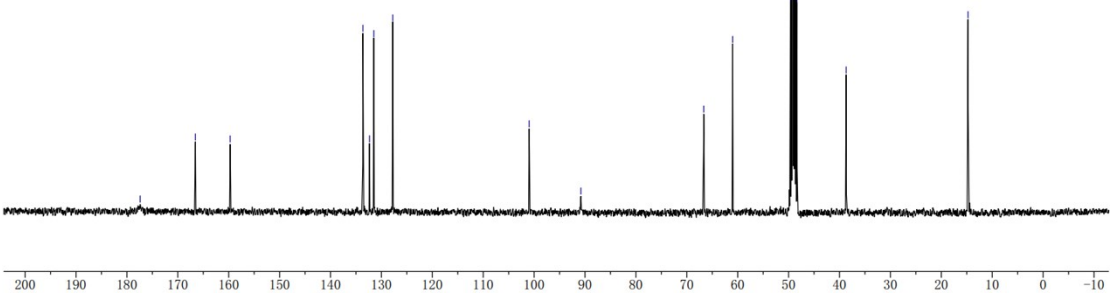


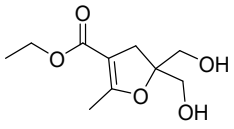




8h

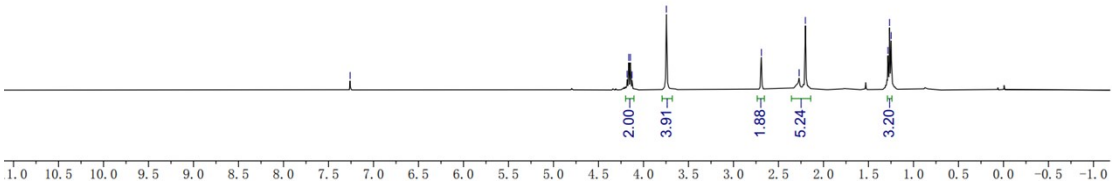
^{13}C NMR (100 MHz, CD_3OD)

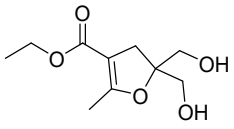




4i

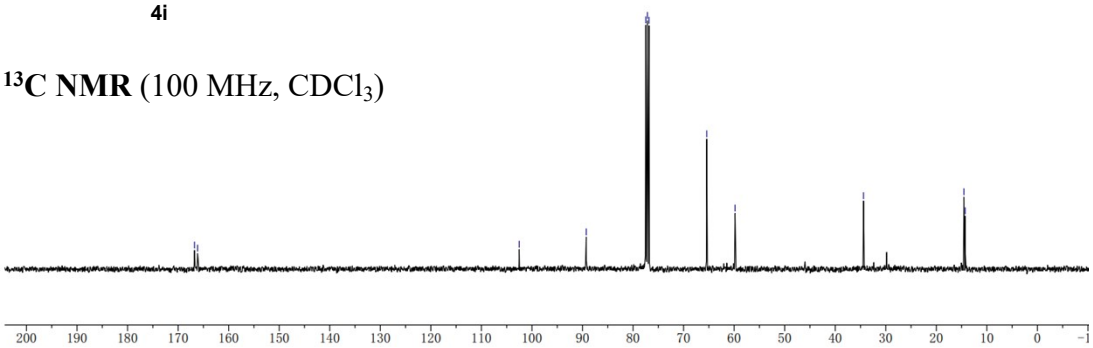
^{1}H NMR (400 MHz, $CDCl_3$)

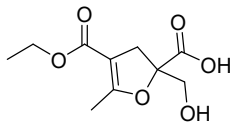




4i

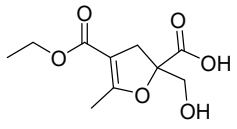
^{13}C NMR (100 MHz, $CDCl_3$)





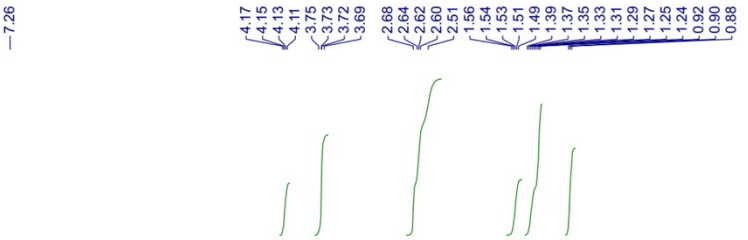
8i

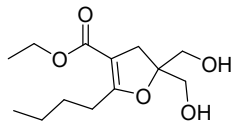
^{1}H NMR (400 MHz, CD_3OD)



8i

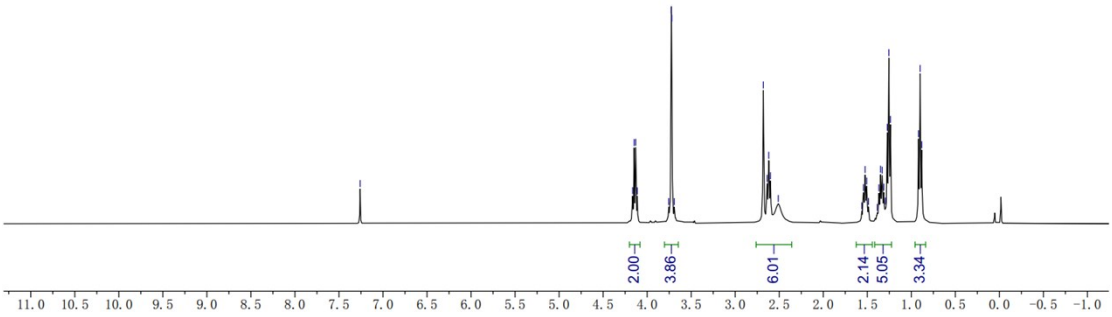
^{13}C NMR (100 MHz, CD_3OD)

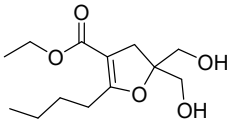




4j

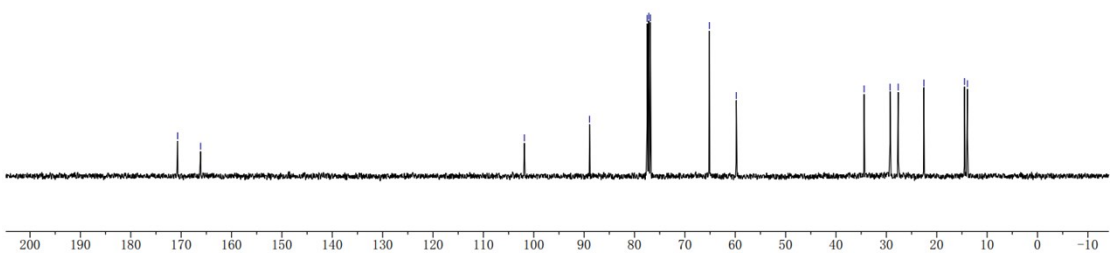
^{1}H NMR (400 MHz, $CDCl_3$)

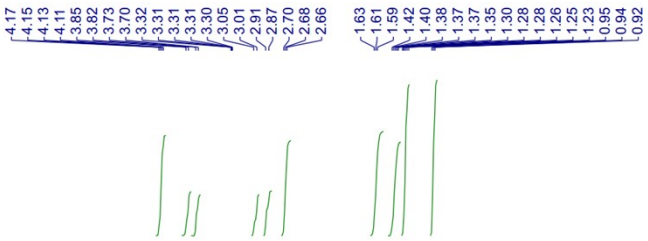


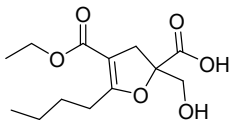


4j

^{13}C NMR (100 MHz, $CDCl_3$)

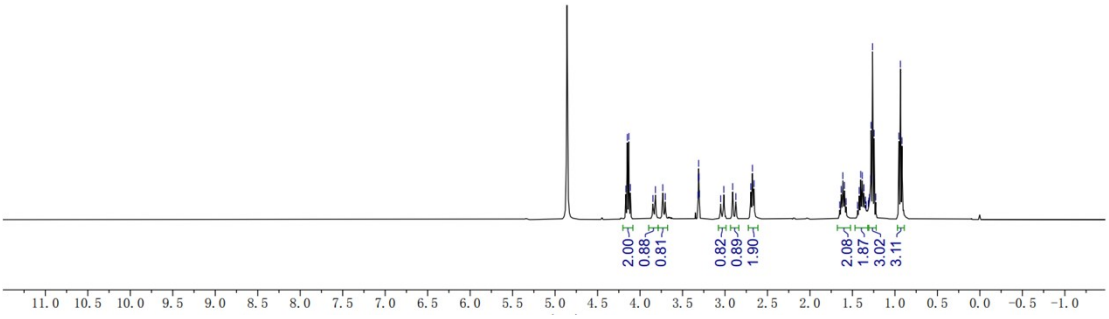


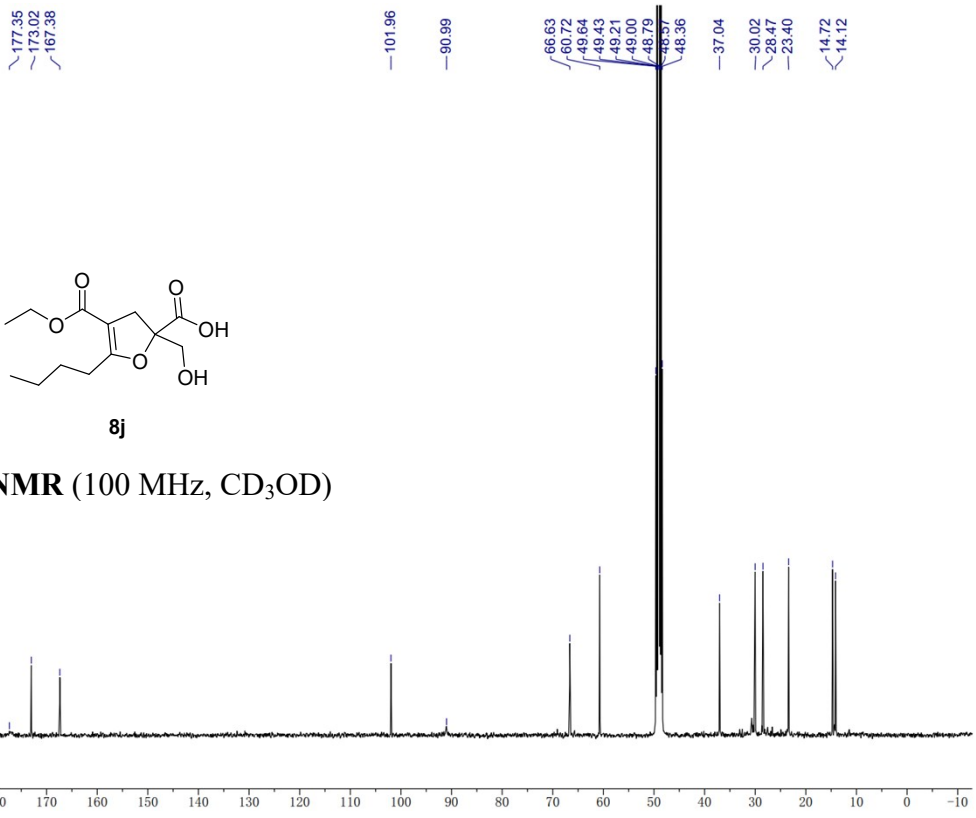




8j

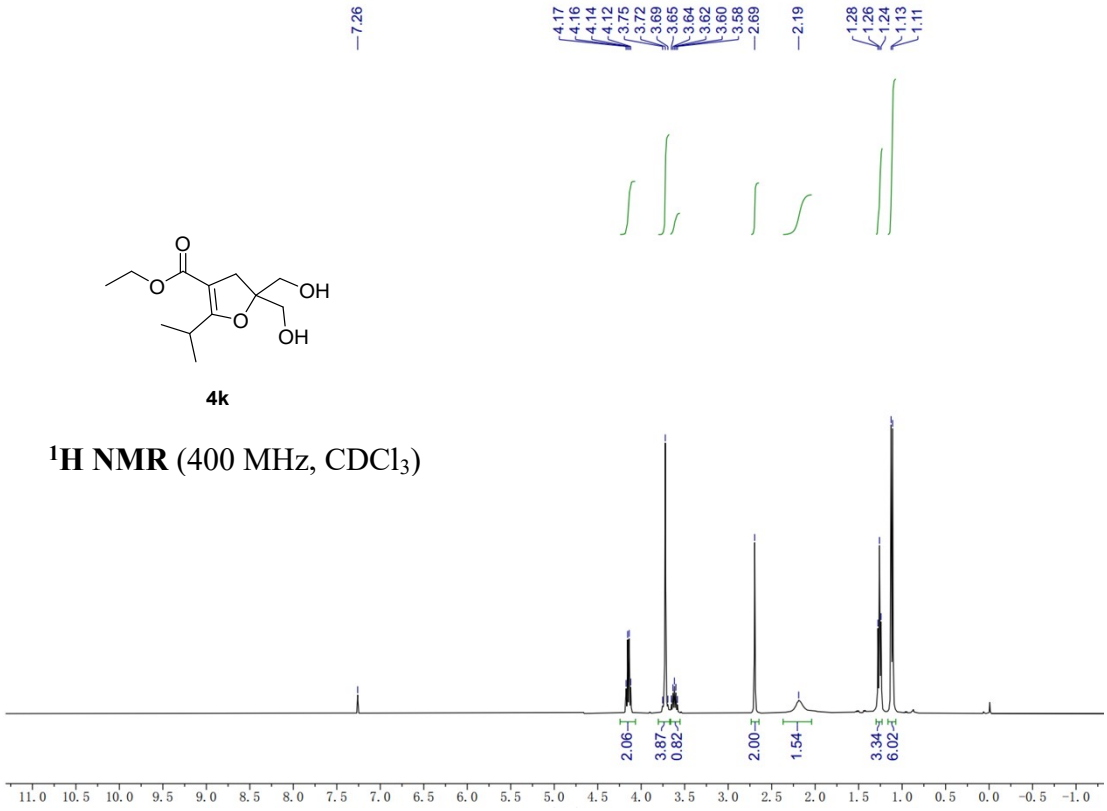
^{1}H NMR (400 MHz, CD_3OD)





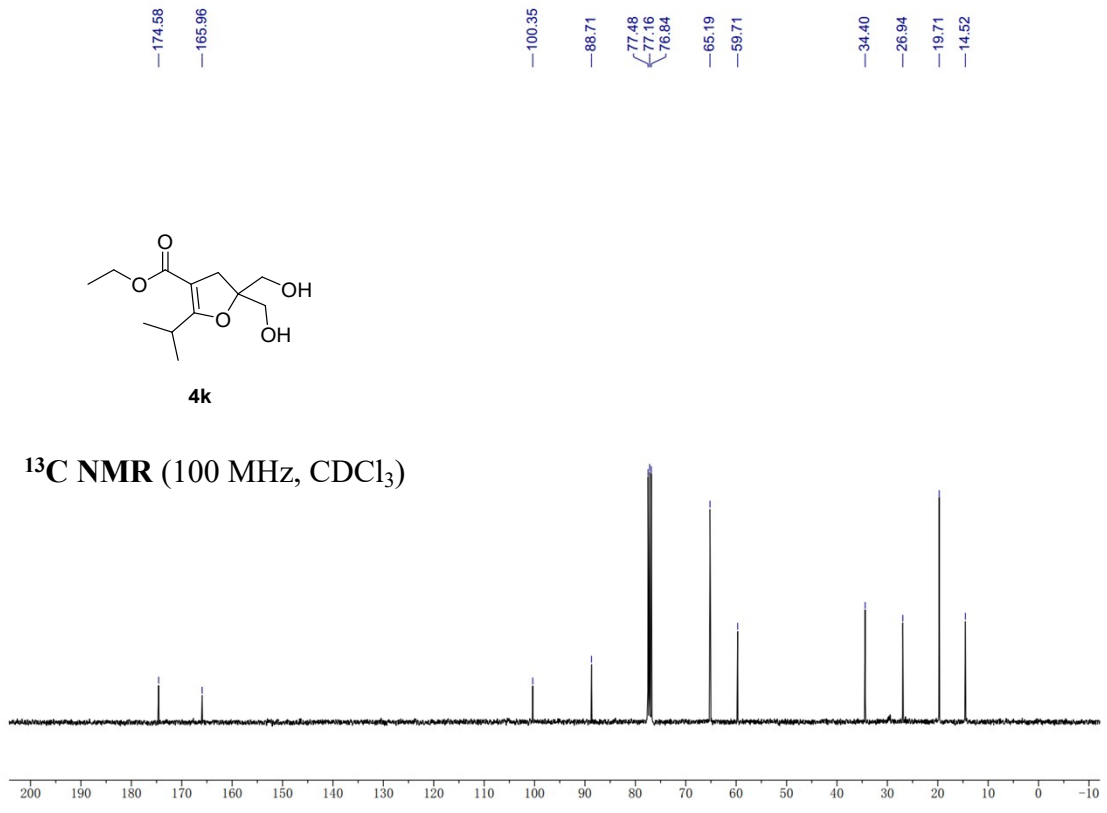
8j

^{13}C NMR (100 MHz, CD_3OD)



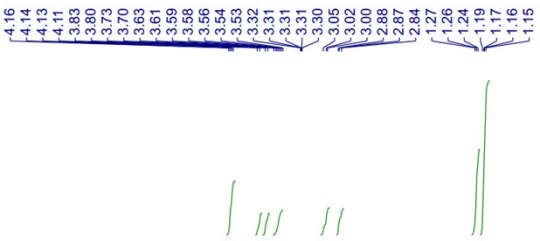
4k

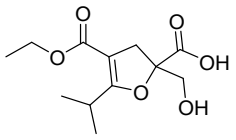
^{1}H NMR (400 MHz, $CDCl_3$)



4k

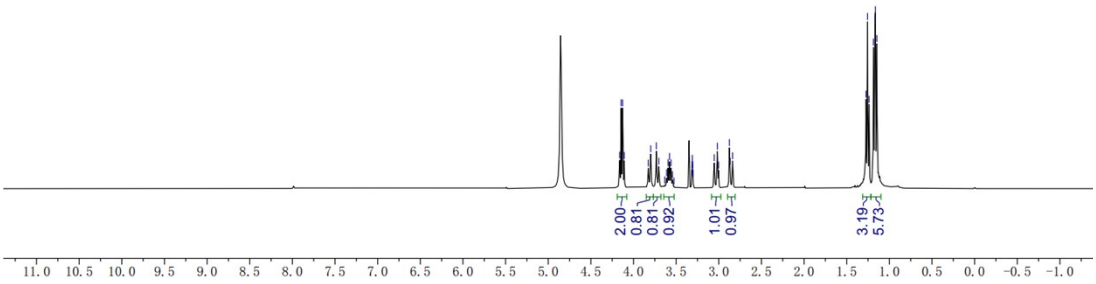
^{13}C NMR (100 MHz, $CDCl_3$)

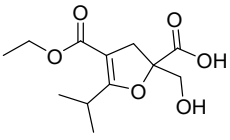




8k

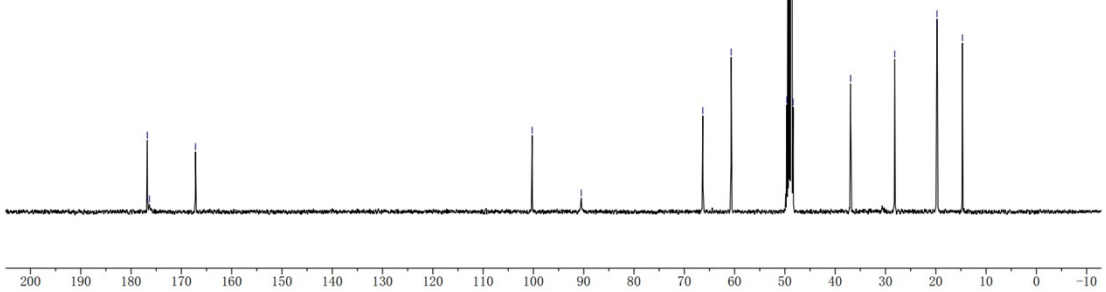
^{1}H NMR (400 MHz, CD_3OD)

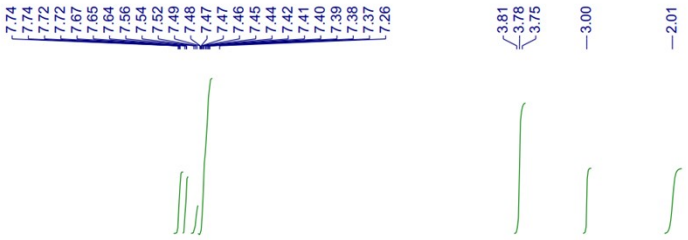


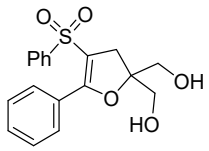


8k

^{13}C NMR (100 MHz, CD_3OD)

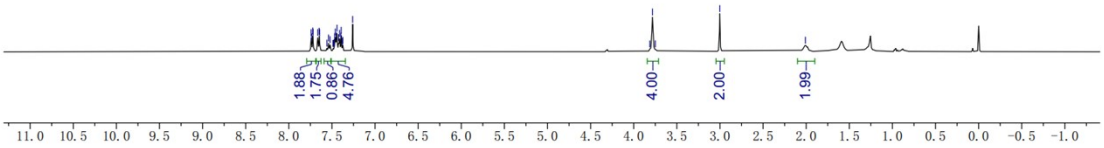


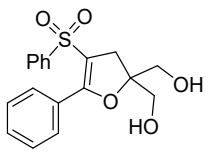




4l

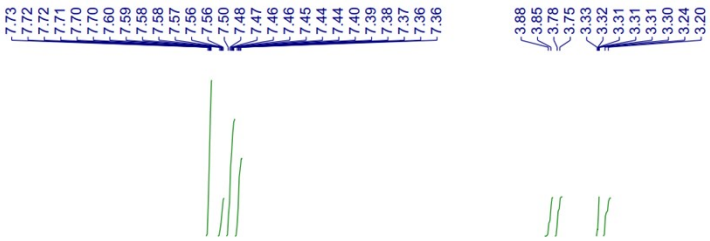
^{1}H NMR (400 MHz, $CDCl_3$)

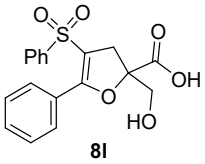




4l

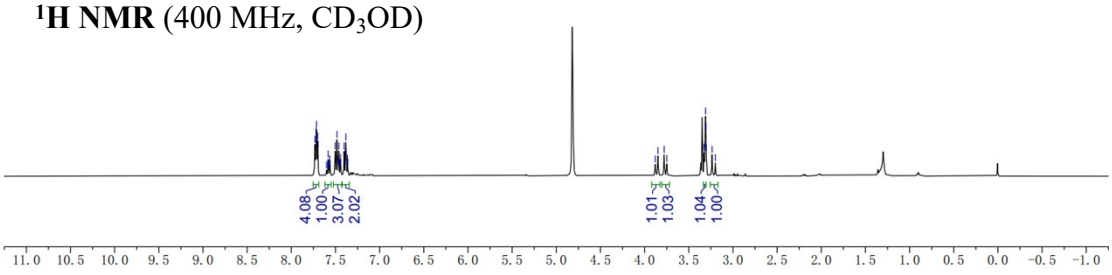
^{13}C NMR (100 MHz, $CDCl_3$)

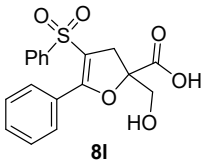




8l

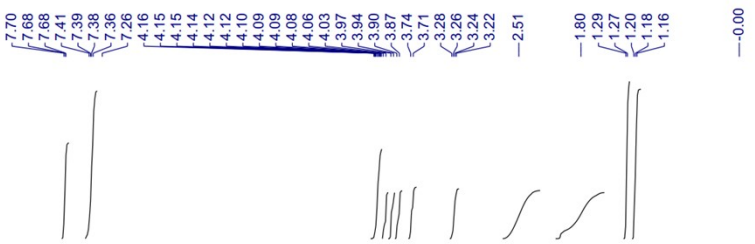
^{1}H NMR (400 MHz, CD_3OD)

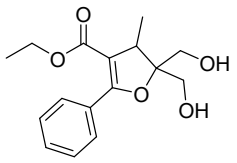




8l

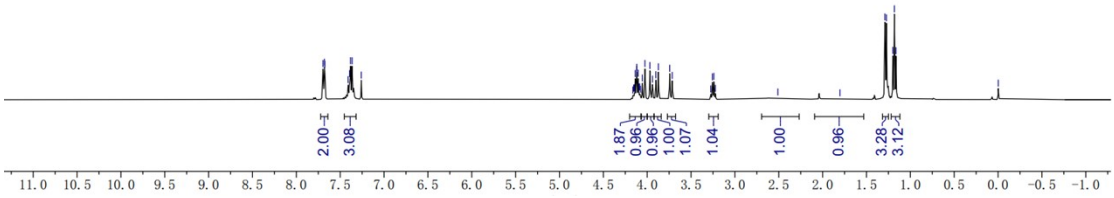
^{13}C NMR (100 MHz, CD_3OD)

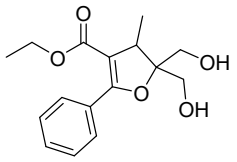




4m

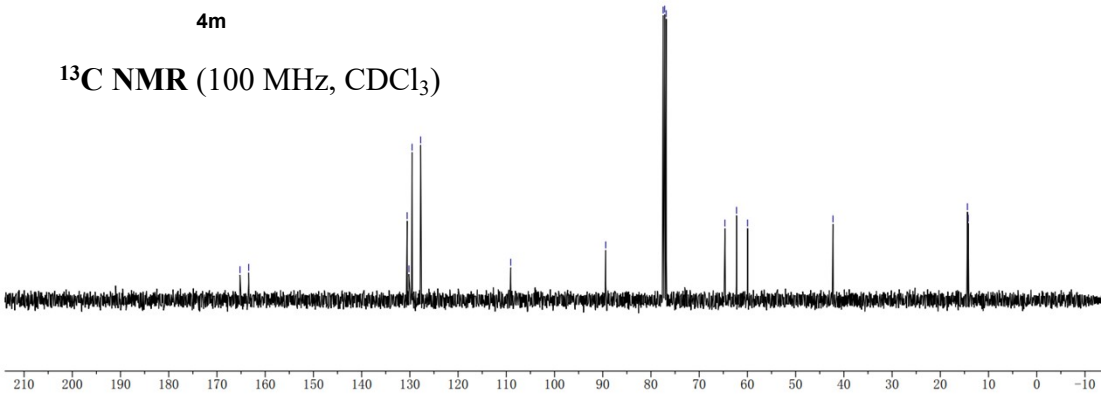
^{1}H NMR (400 MHz, $CDCl_3$)

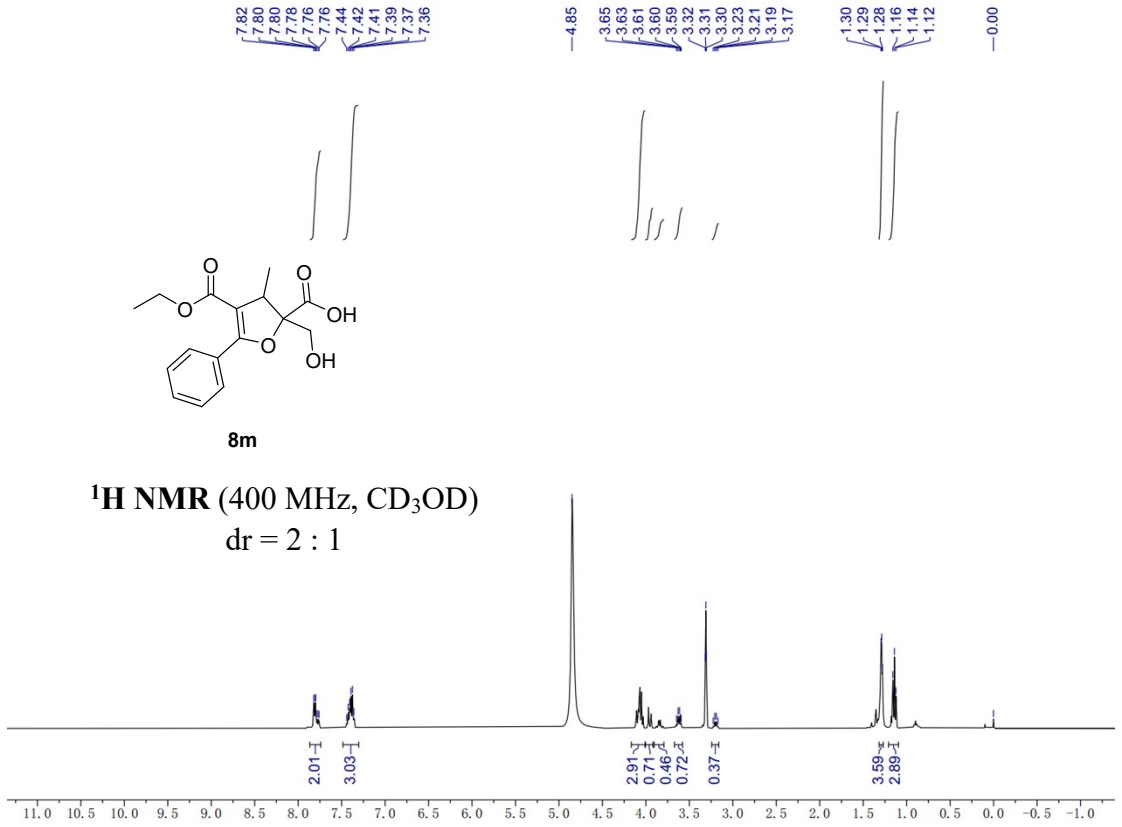




4m

^{13}C NMR (100 MHz, $CDCl_3$)

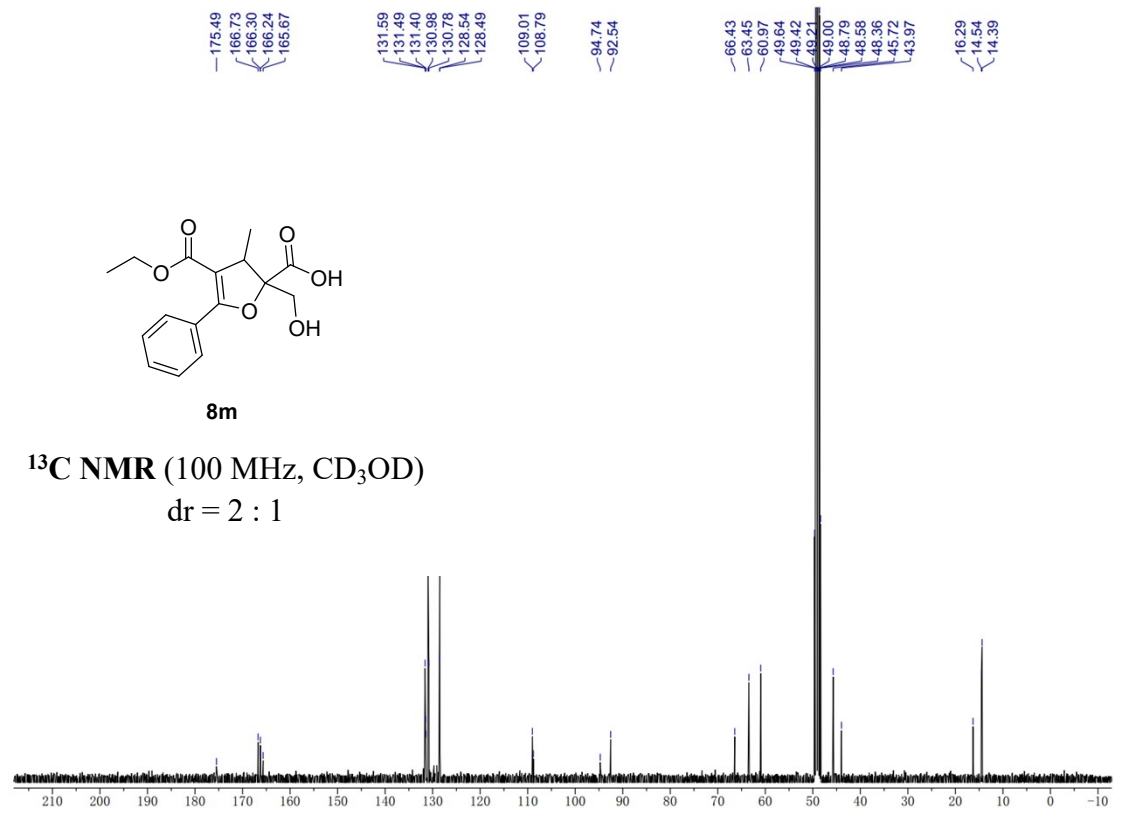




8m

^{1}H NMR (400 MHz, CD_3OD)

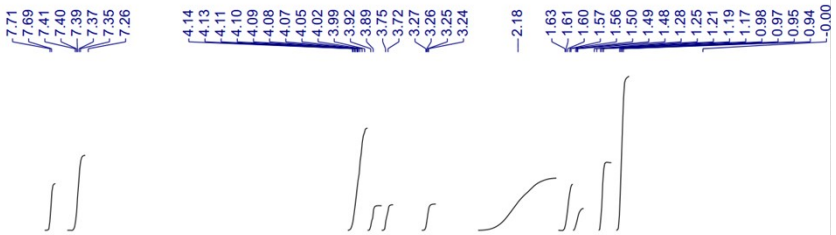
dr = 2 : 1

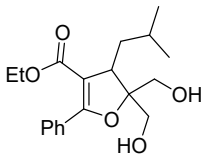


8m

^{13}C NMR (100 MHz, CD_3OD)

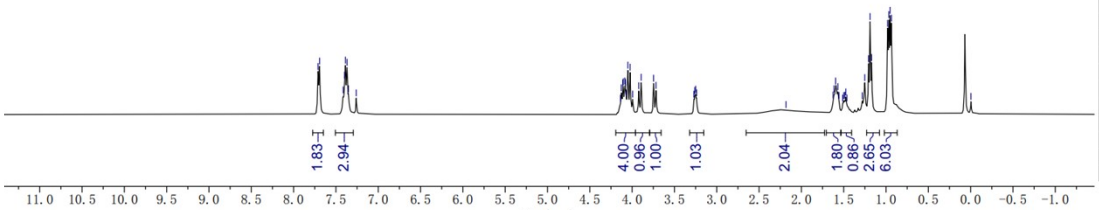
dr = 2 : 1

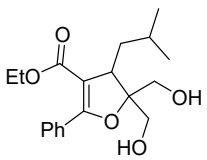




4n

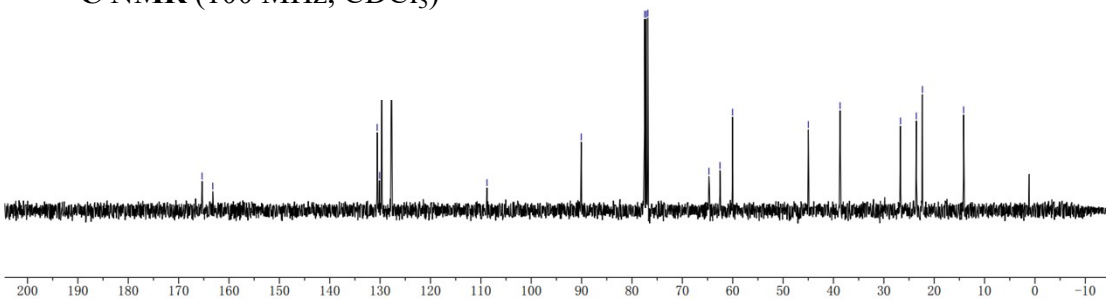
^{1}H NMR (400 MHz, $CDCl_3$)

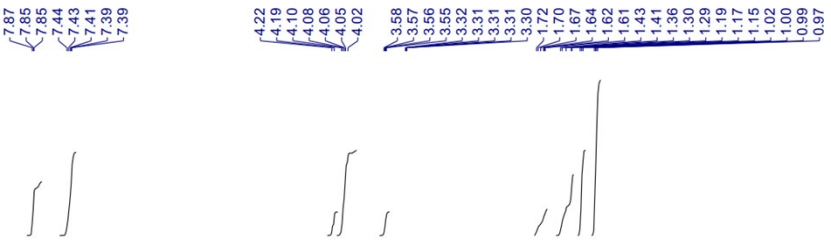


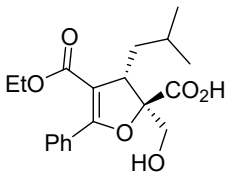


4n

^{13}C NMR (100 MHz, $CDCl_3$)



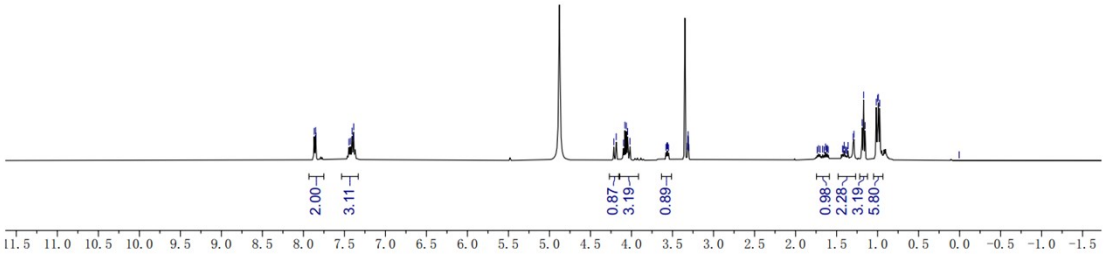


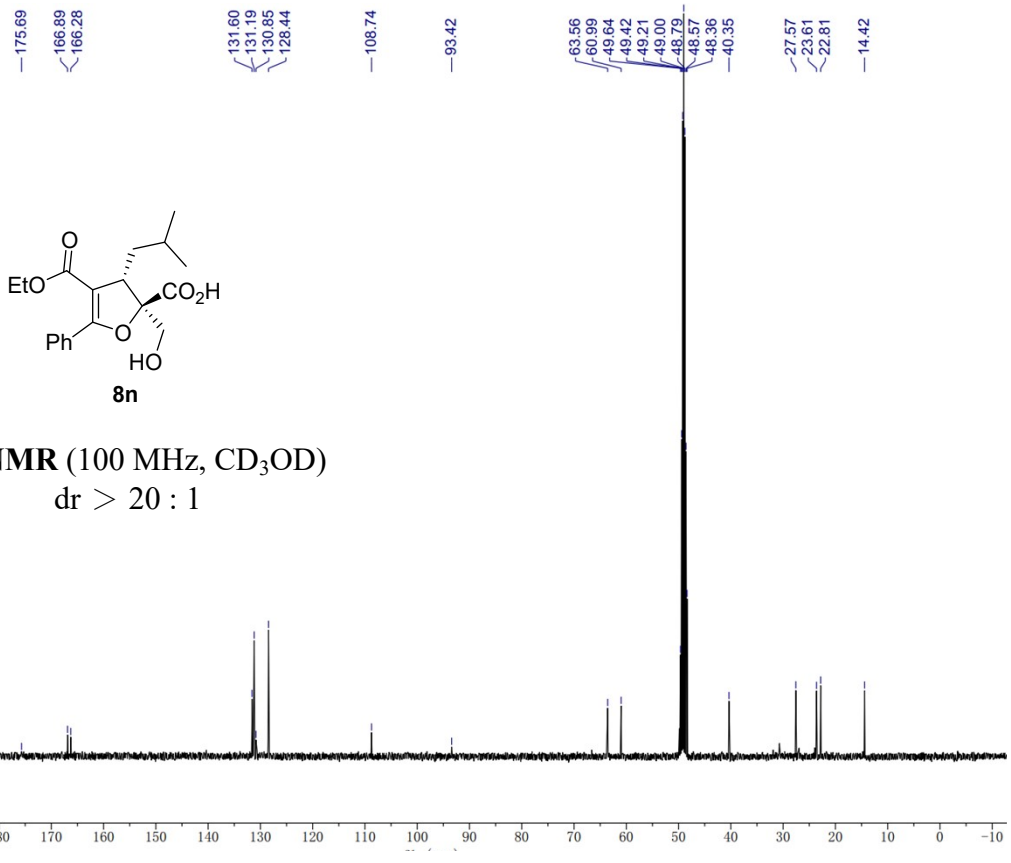


8n

^{1}H NMR (400 MHz, CD_3OD)

dr > 20 : 1

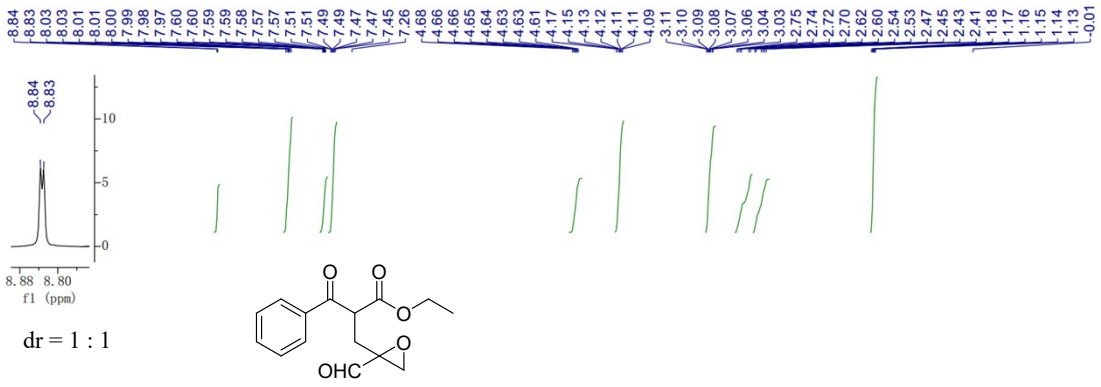




8n

^{13}C NMR (100 MHz, CD_3OD)

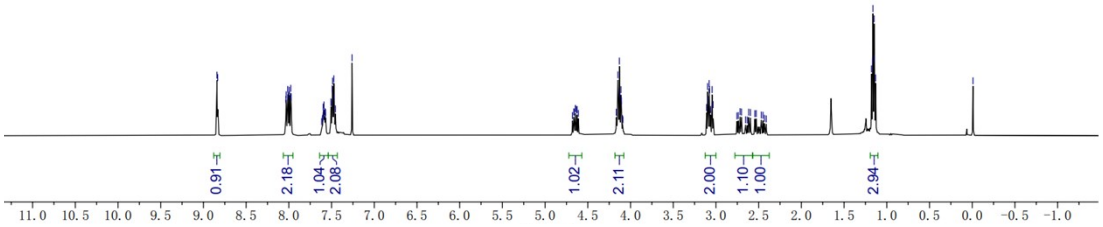
dr > 20 : 1

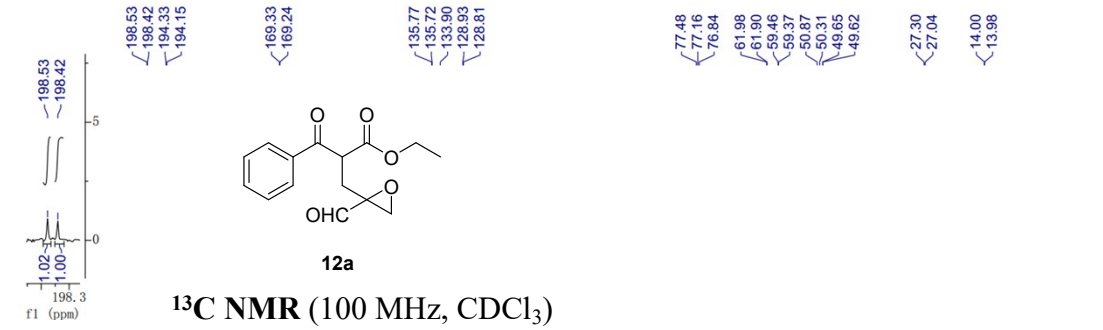


dr = 1 : 1

12a

^{1}H NMR (400 MHz, $CDCl_3$)

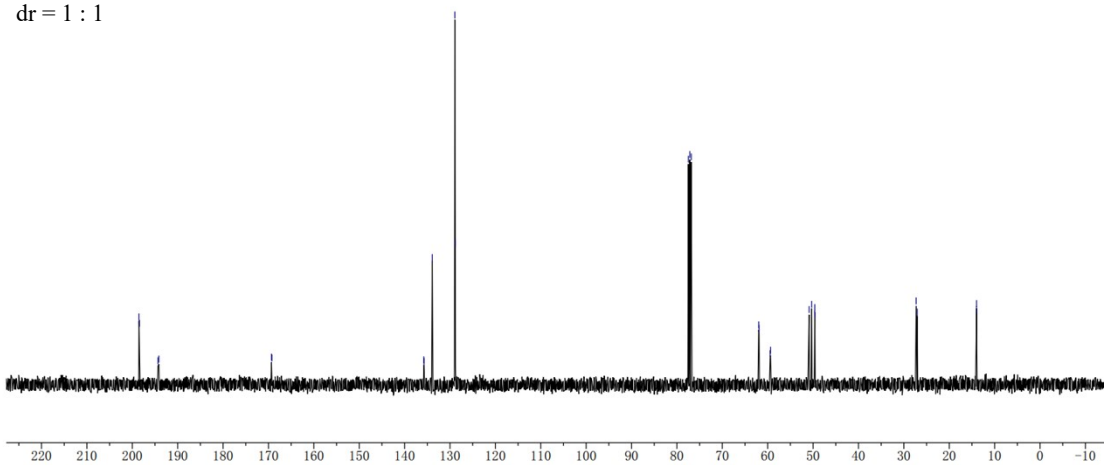


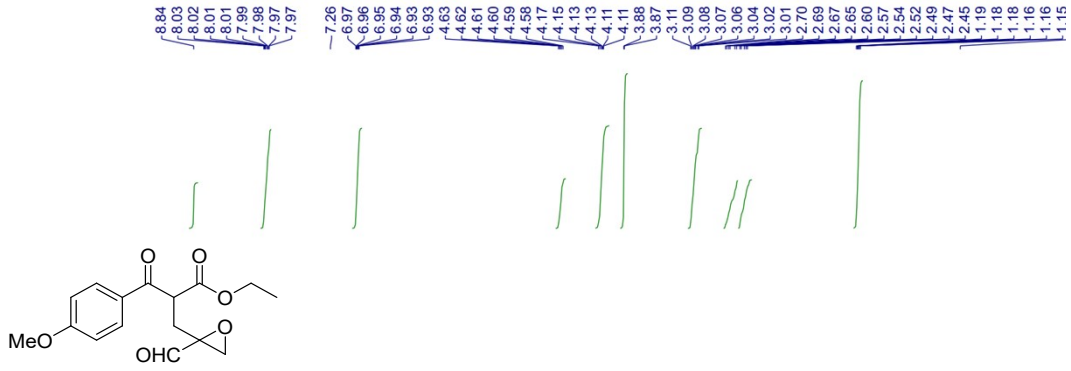


12a

^{13}C NMR (100 MHz, $CDCl_3$)

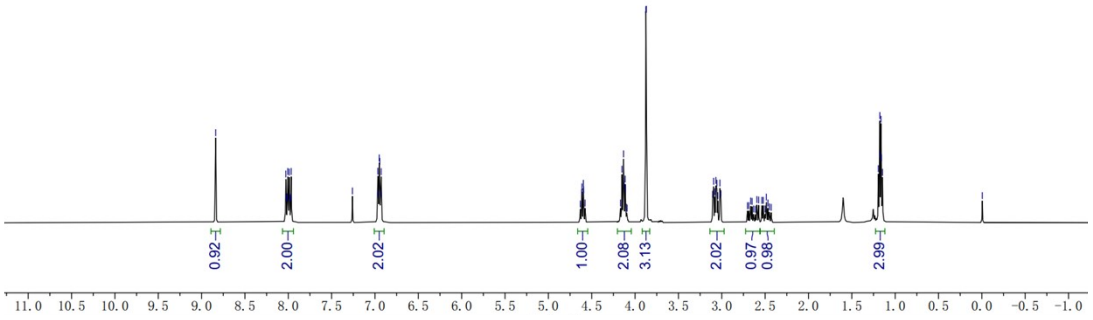
dr = 1 : 1

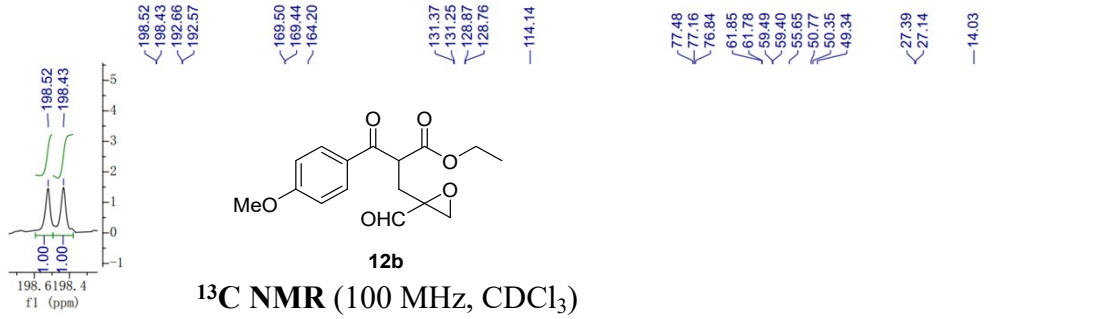




12b

^{1}H NMR (400 MHz, $CDCl_3$)

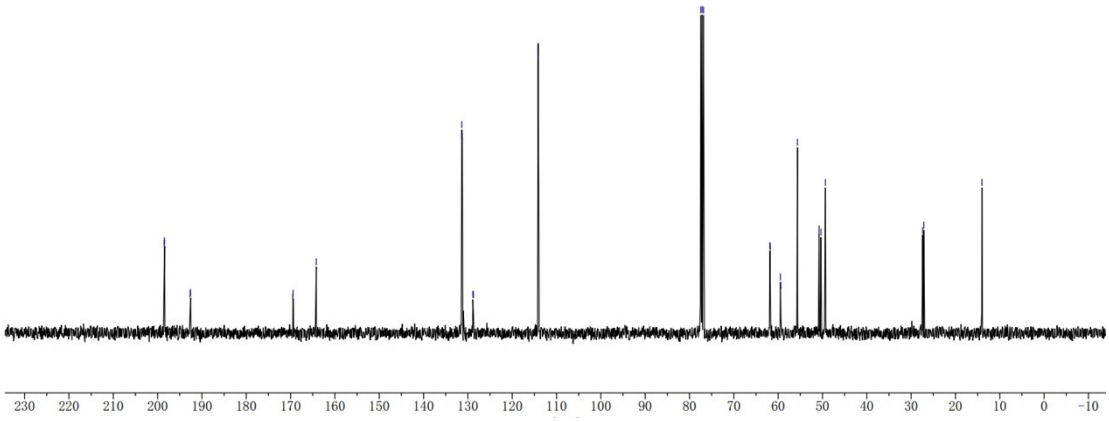


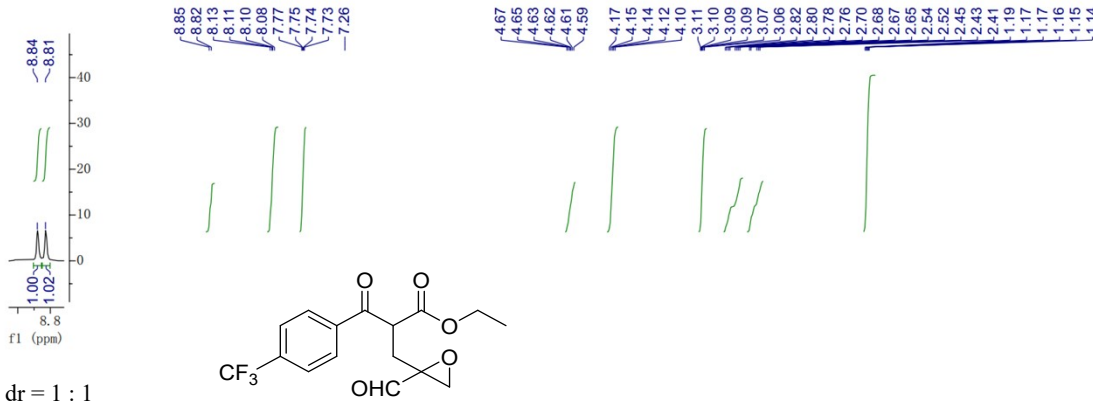


12b

^{13}C NMR (100 MHz, $CDCl_3$)

dr = 1 : 1

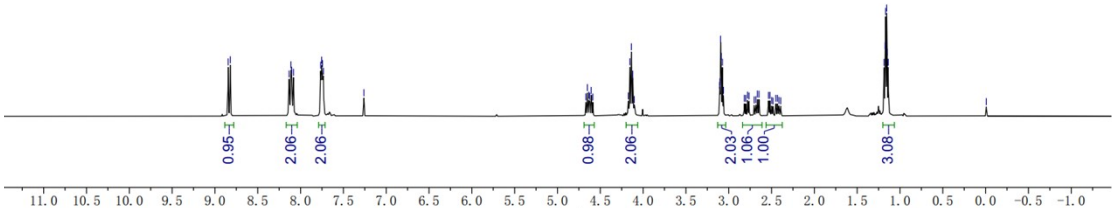


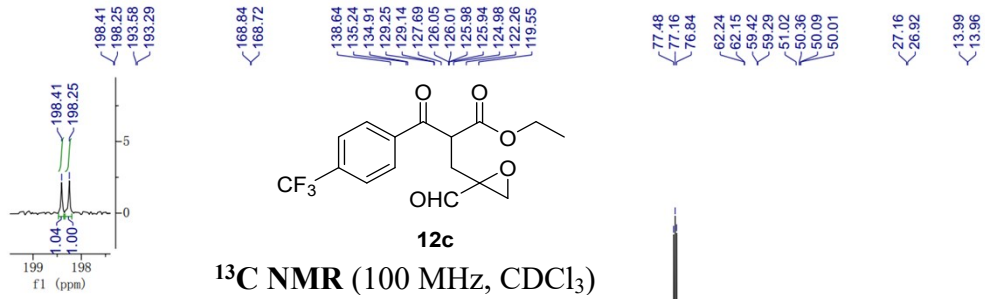


dr = 1 : 1

12c

^{1}H NMR (400 MHz, $CDCl_3$)

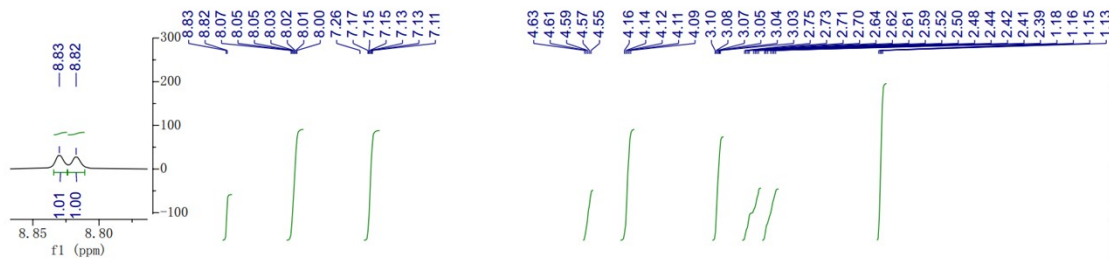




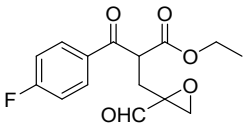
12c

^{13}C NMR (100 MHz, $CDCl_3$)

dr = 1 : 1

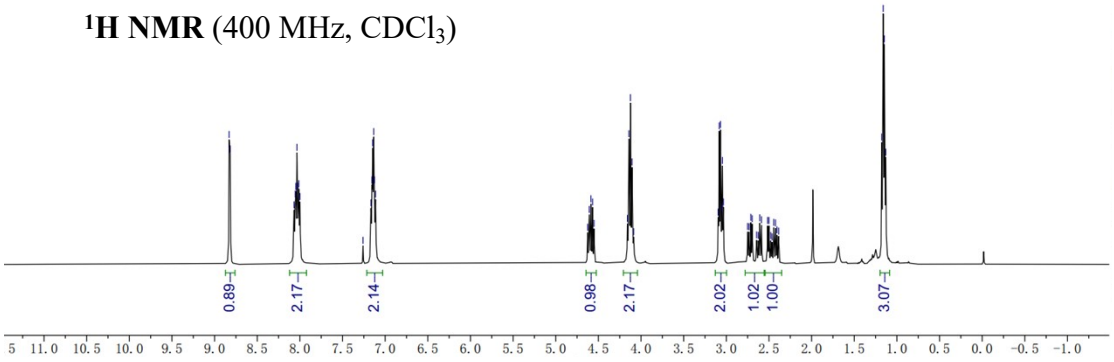


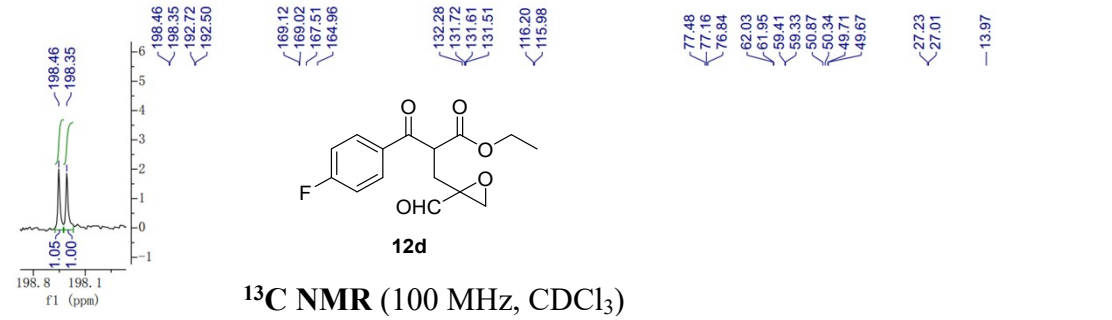
dr = 1 : 1



12d

^{1}H NMR (400 MHz, $CDCl_3$)

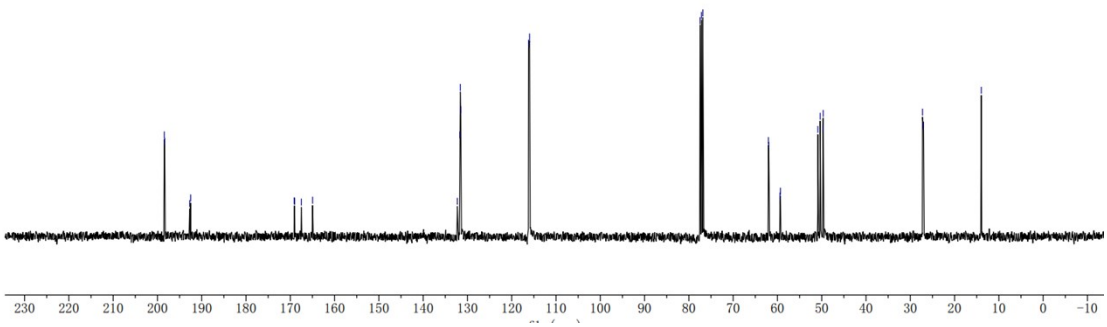


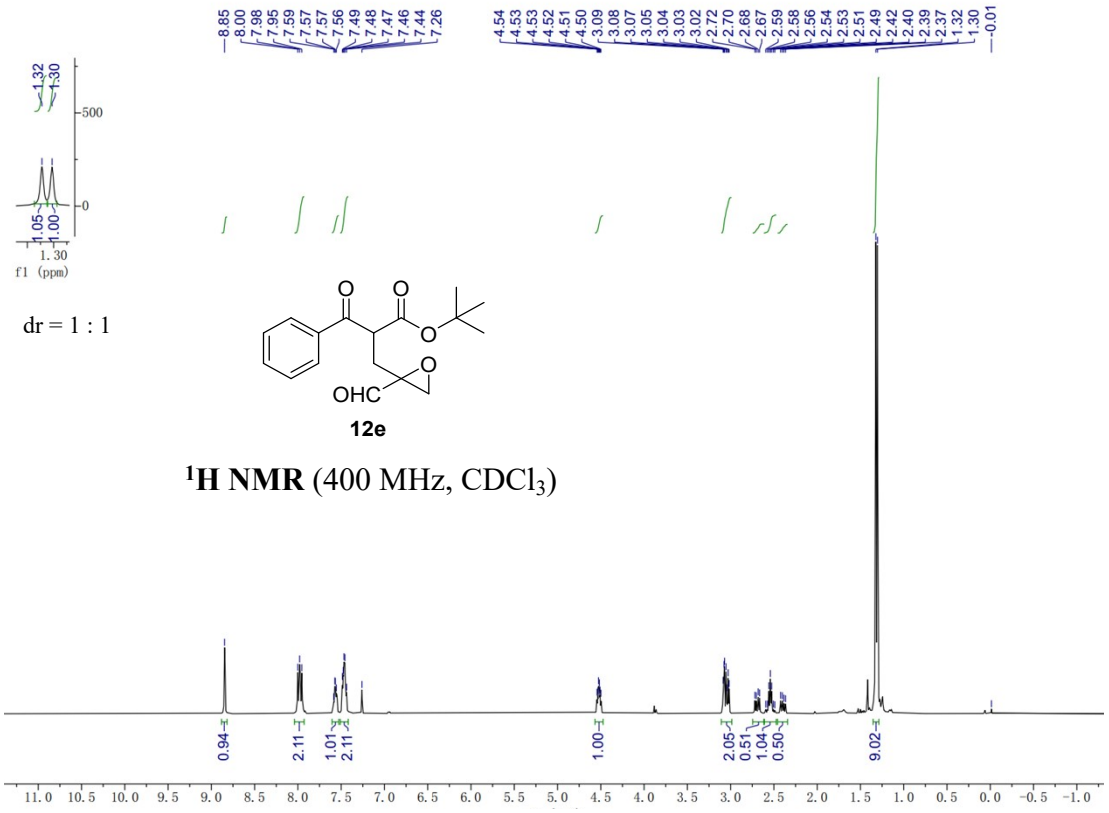


12d

^{13}C NMR (100 MHz, $CDCl_3$)

dr = 1 : 1

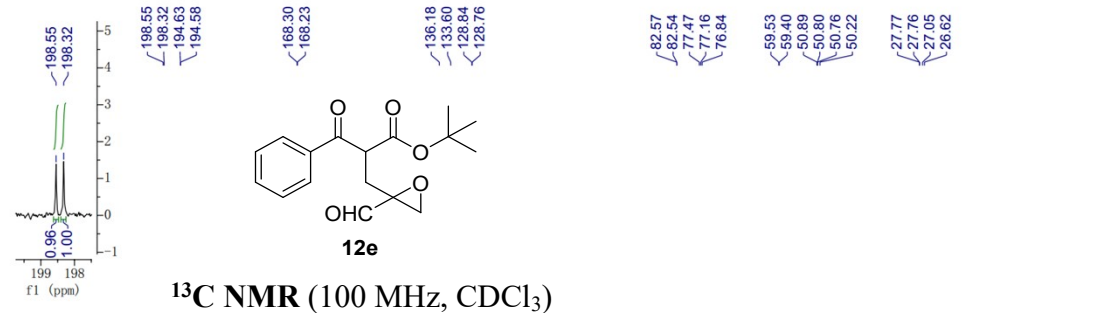




dr = 1 : 1

12e

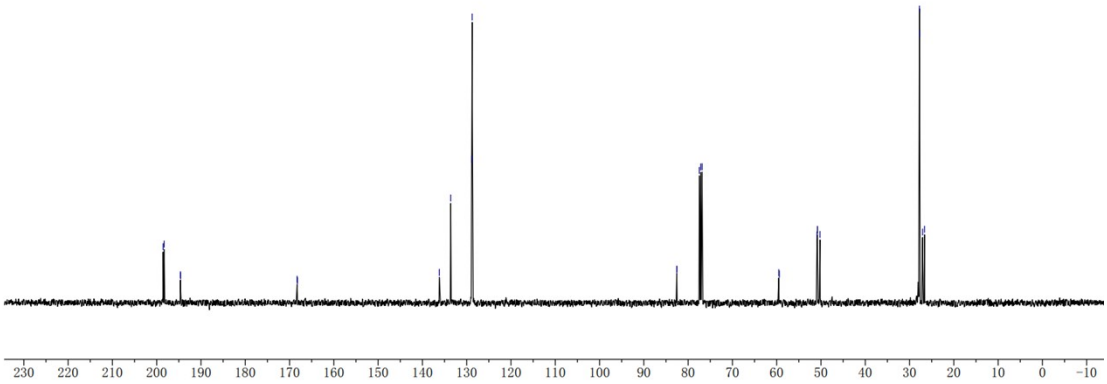
^{1}H NMR (400 MHz, $CDCl_3$)



12e

^{13}C NMR (100 MHz, $CDCl_3$)

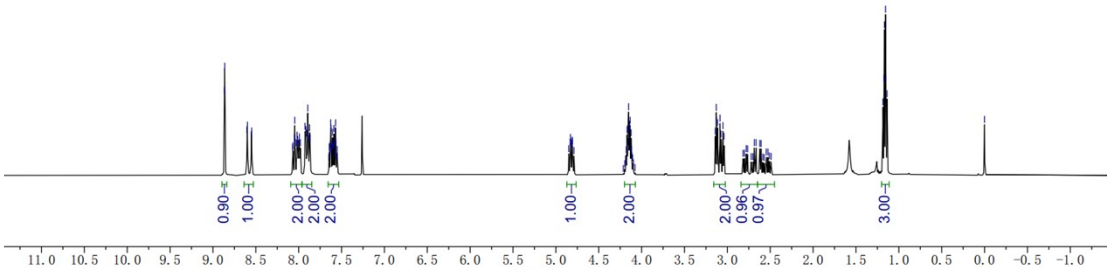
dr = 1 : 1

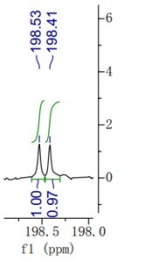


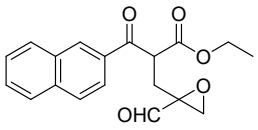
12f

dr = 1 : 1

^{1}H NMR (400 MHz, $CDCl_3$)



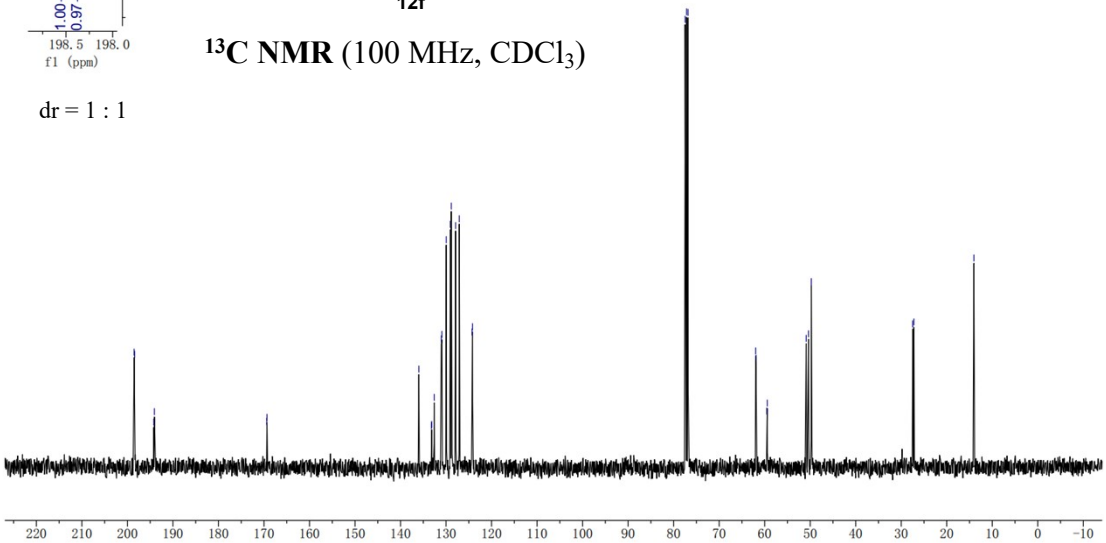


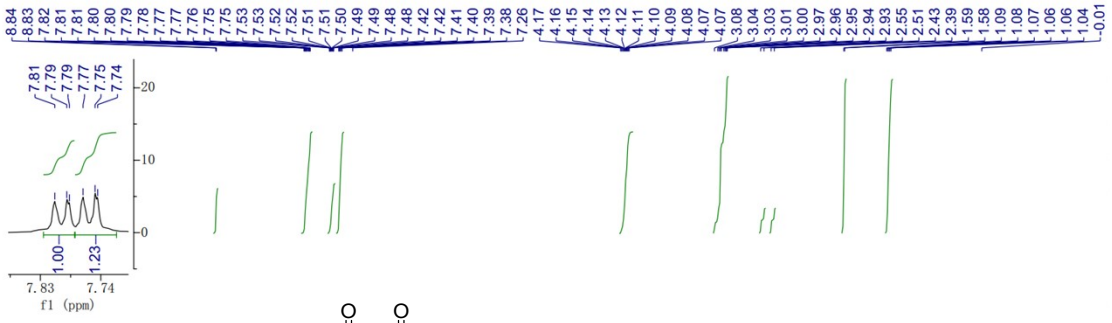


12f

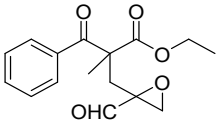
^{13}C NMR (100 MHz, $CDCl_3$)

dr = 1 : 1



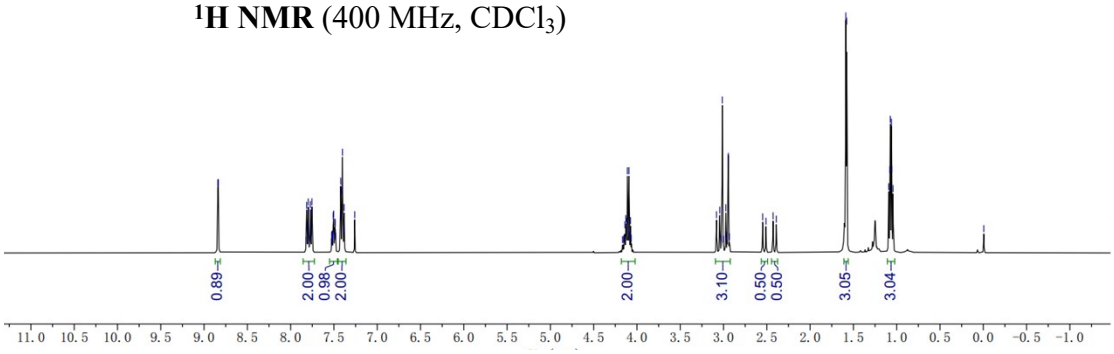


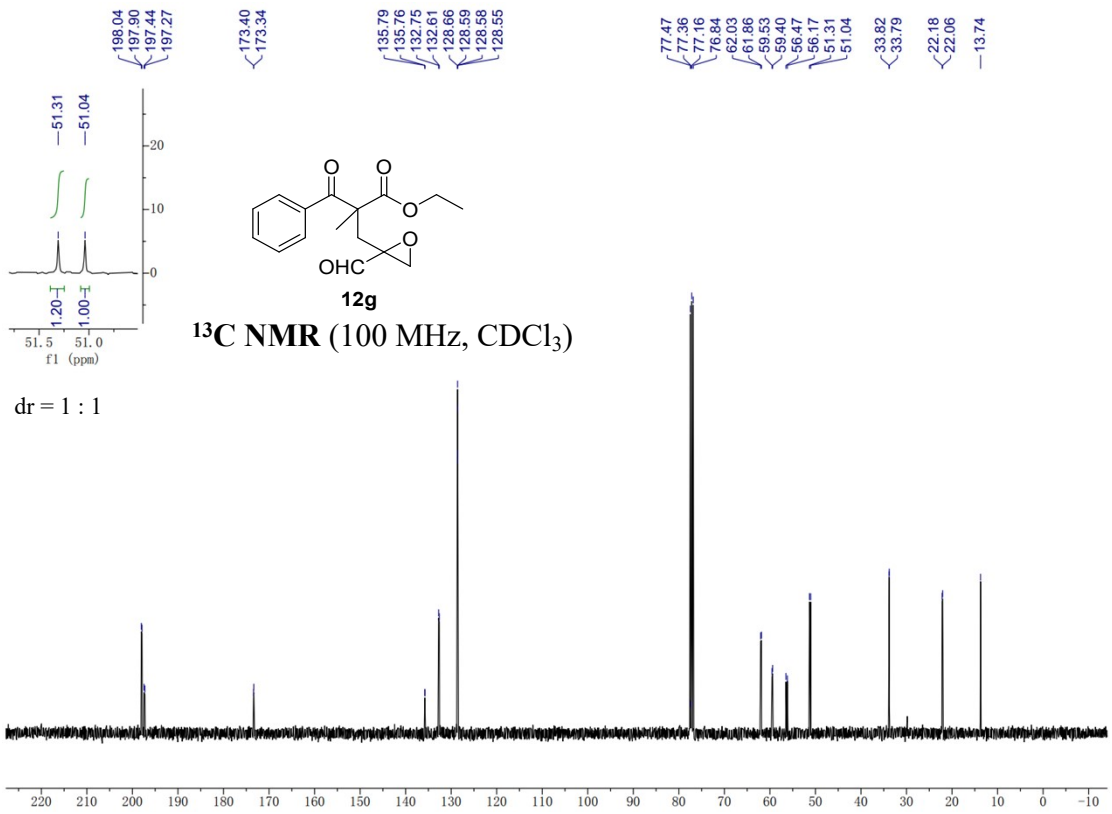
dr = 1 : 1



12g

^{1}H NMR (400 MHz, $CDCl_3$)

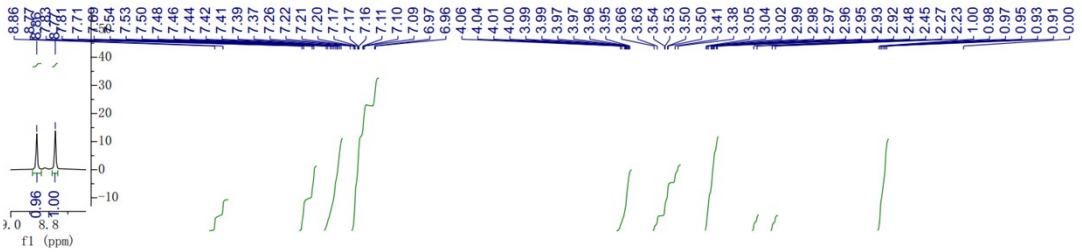




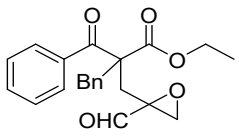
12g

^{13}C NMR (100 MHz, $CDCl_3$)

dr = 1 : 1

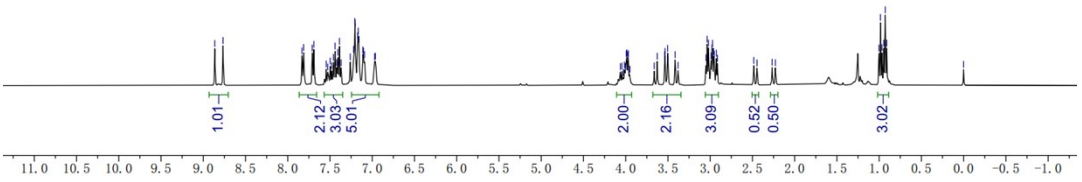


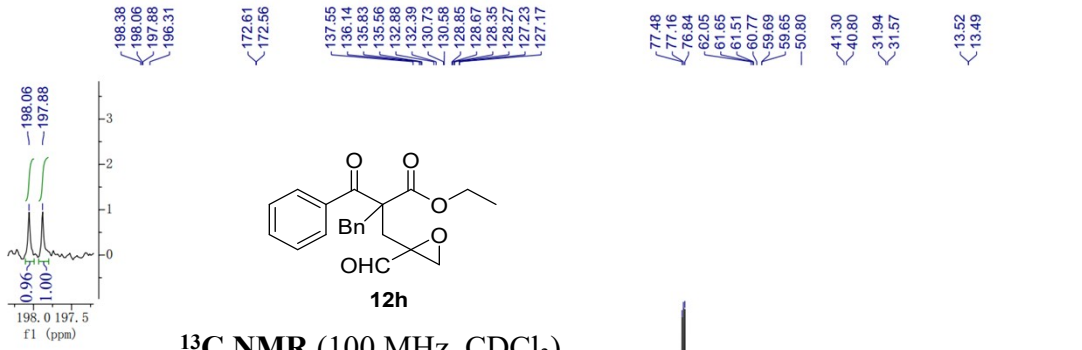
dr = 1 : 1



12h

^{1}H NMR (400 MHz, $CDCl_3$)

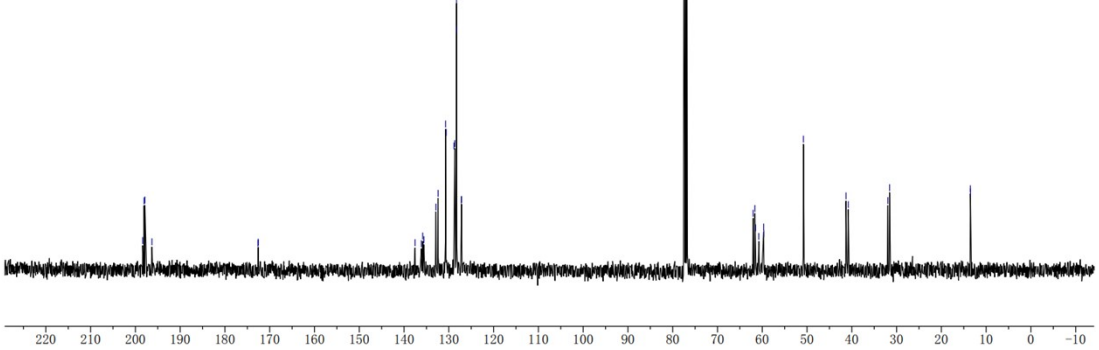


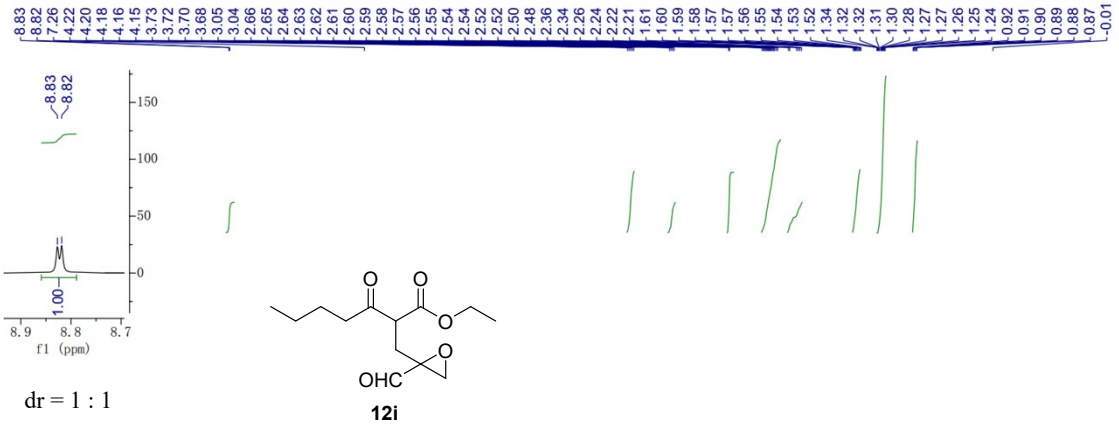


12h

^{13}C NMR (100 MHz, $CDCl_3$)

dr = 1 : 1

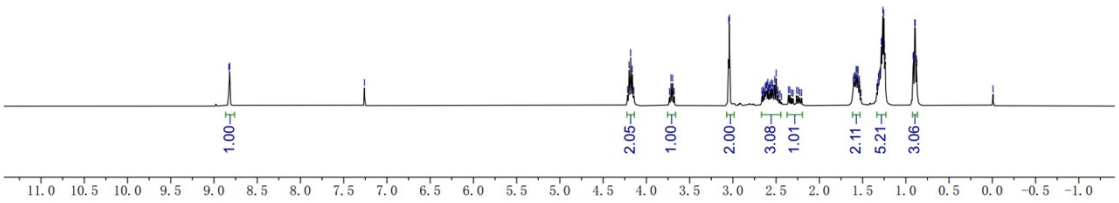


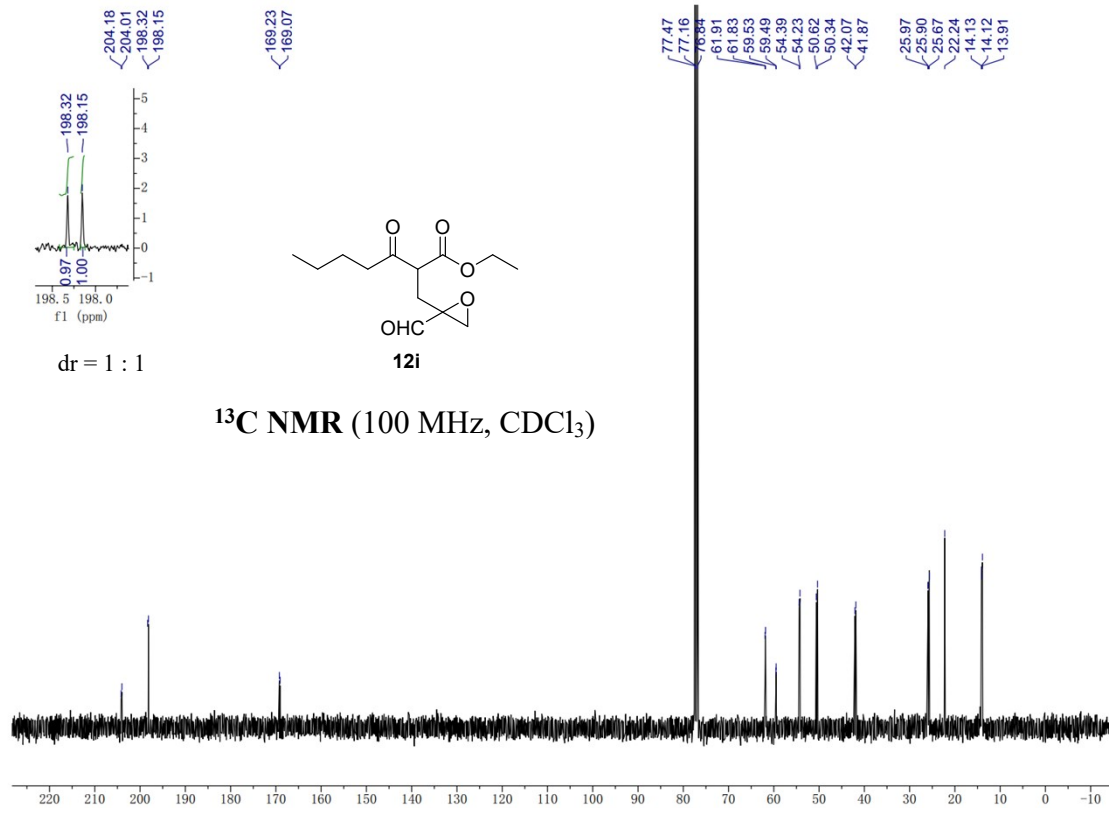


dr = 1 : 1

12i

^{1}H NMR (400 MHz, $CDCl_3$)

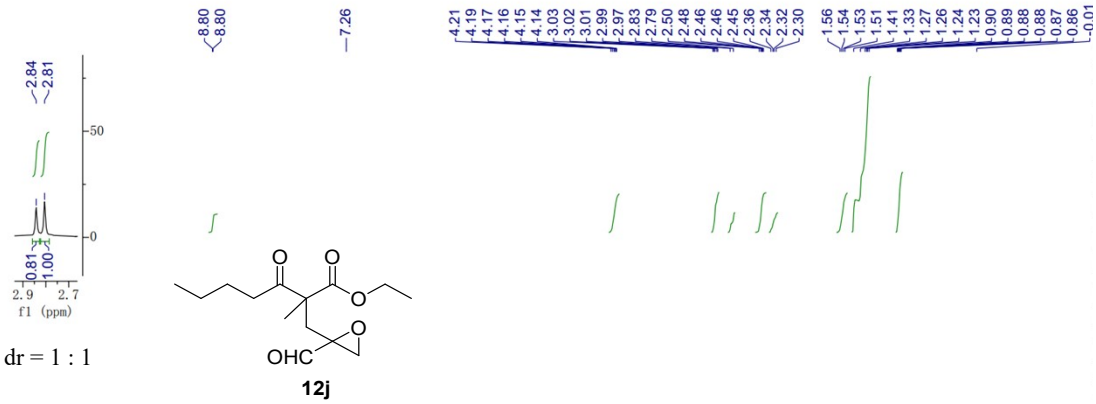




dr = 1 : 1

12i

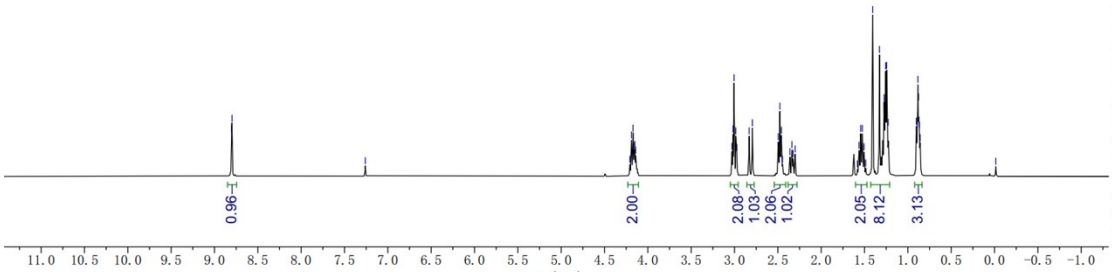
^{13}C NMR (100 MHz, $CDCl_3$)

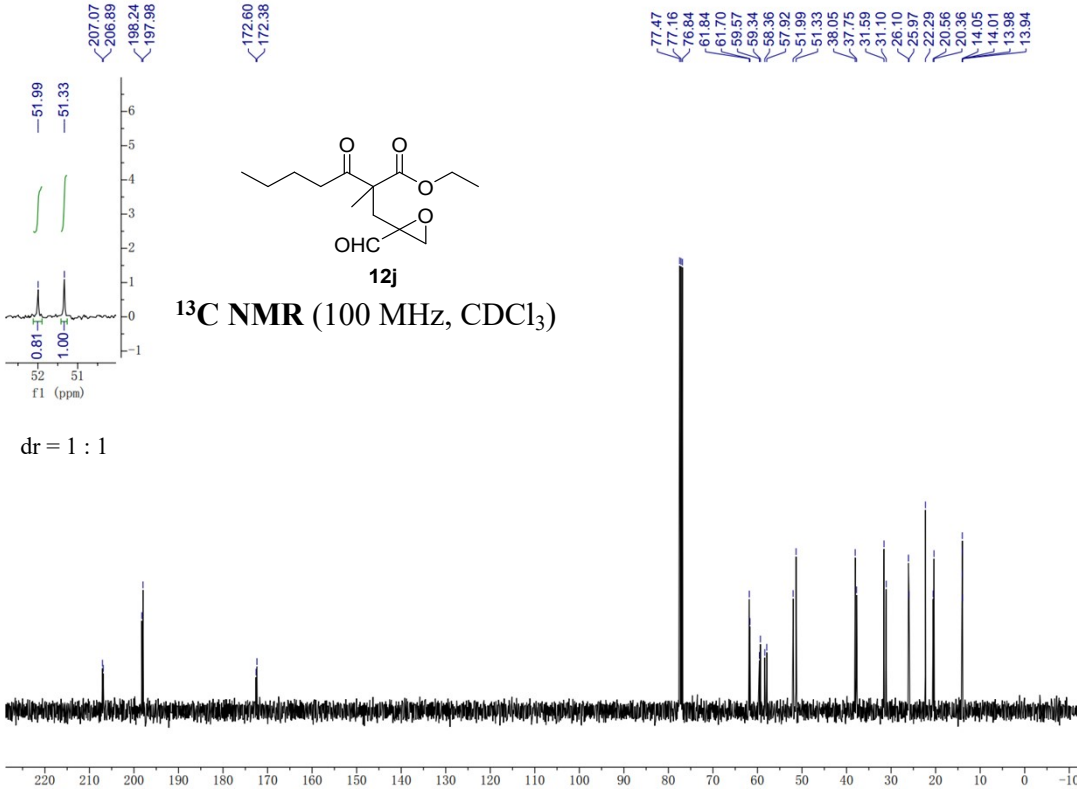


dr = 1 : 1

12j

^{1}H NMR (400 MHz, $CDCl_3$)

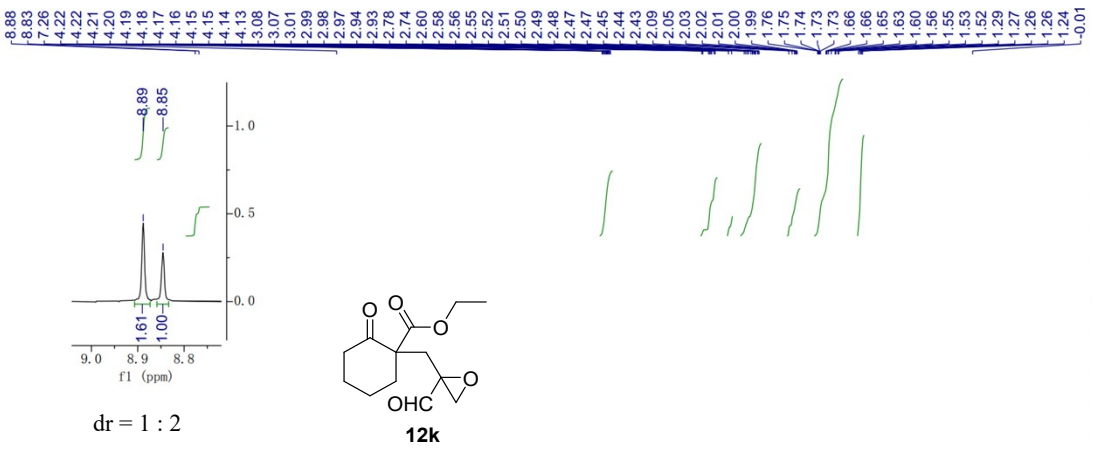




dr = 1 : 1

12j

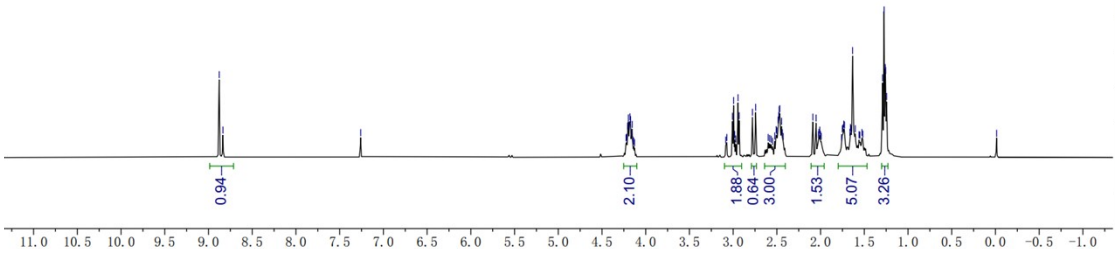
^{13}C NMR (100 MHz, $CDCl_3$)



dr = 1 : 2

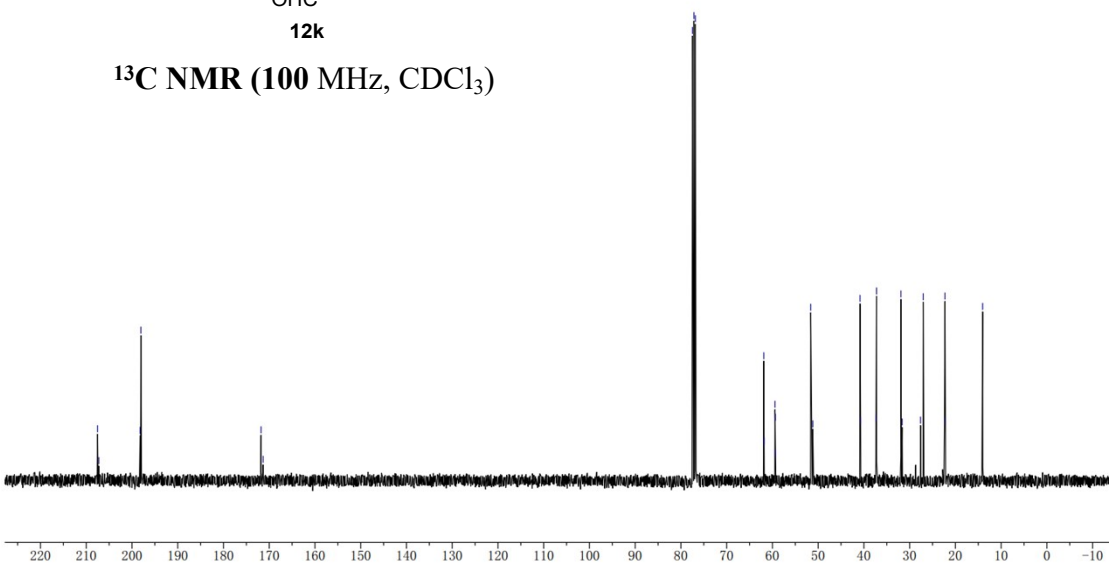
12k

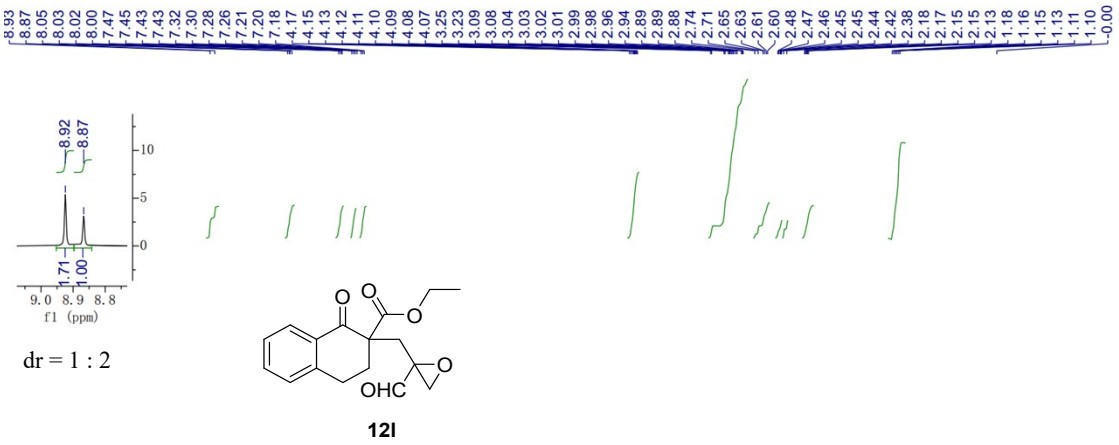
^{1}H NMR (400 MHz, $CDCl_3$)



12k

^{13}C NMR (100 MHz, $CDCl_3$)

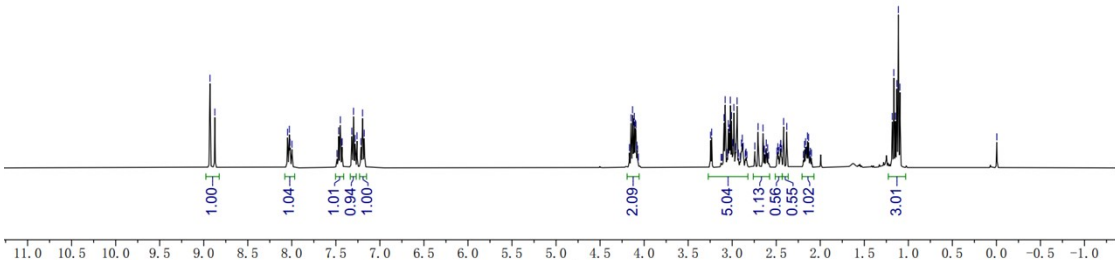


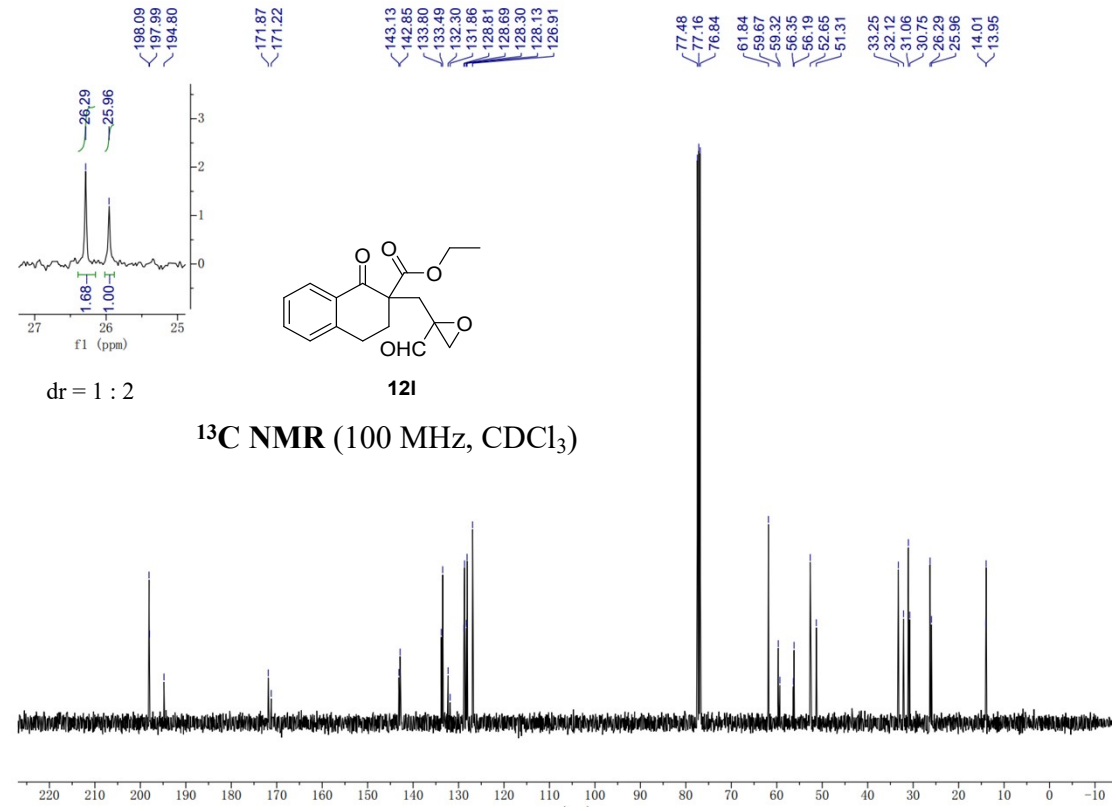


dr = 1 : 2

12l

^{1}H NMR (400 MHz, $CDCl_3$)





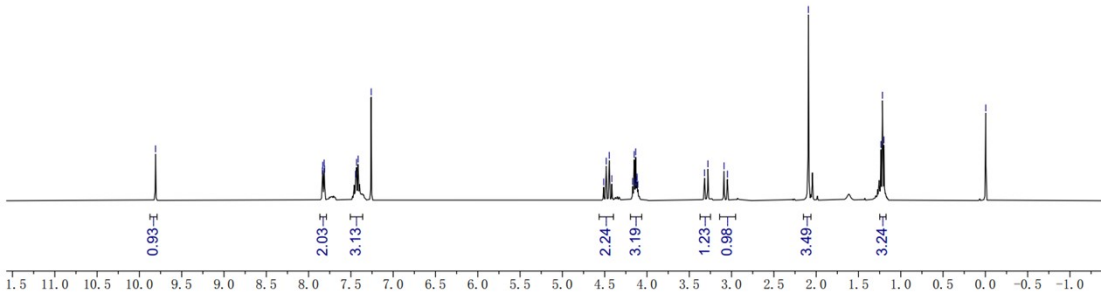
dr = 1 : 2

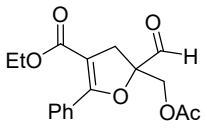
12l

^{13}C NMR (100 MHz, $CDCl_3$)

9

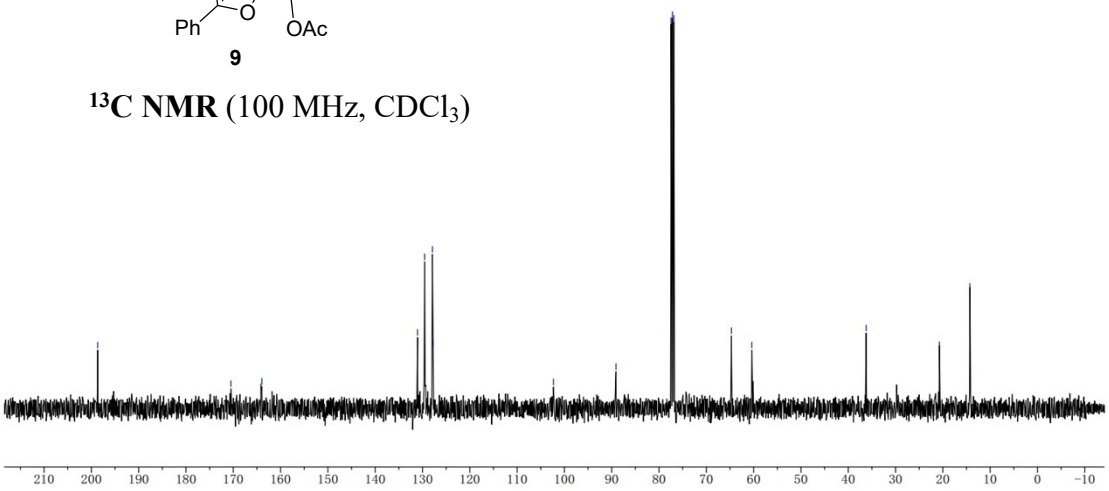
^{1}H NMR (400 MHz, $CDCl_3$)

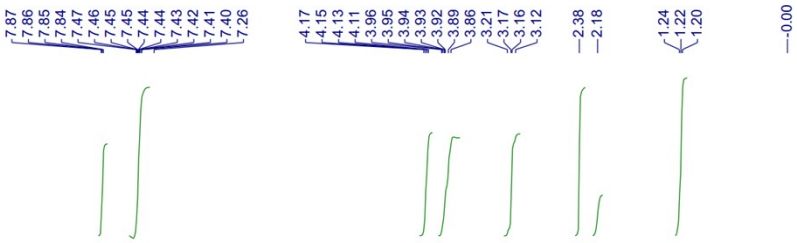


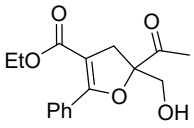


9

^{13}C NMR (100 MHz, $CDCl_3$)

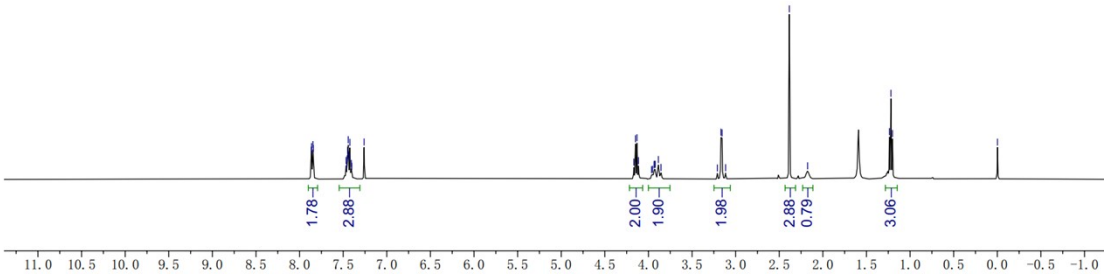


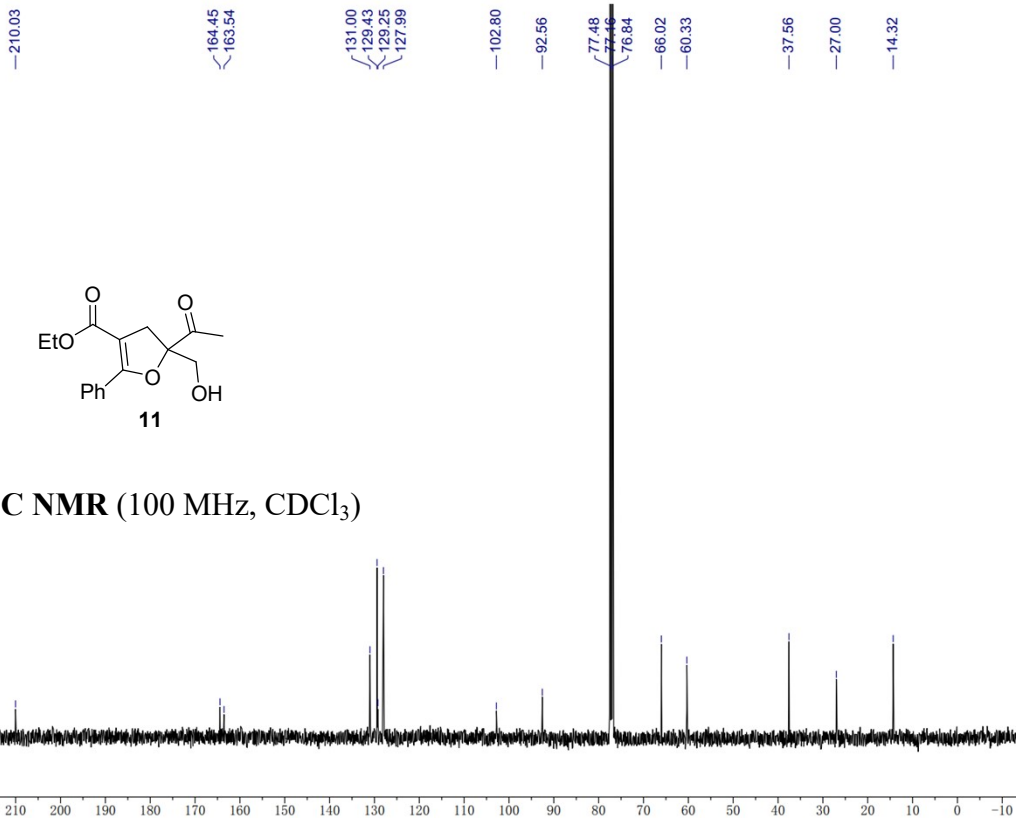




11

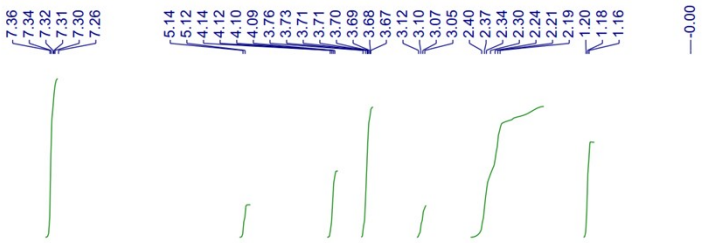
^{1}H NMR (400 MHz, $CDCl_3$)

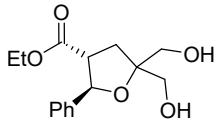




11

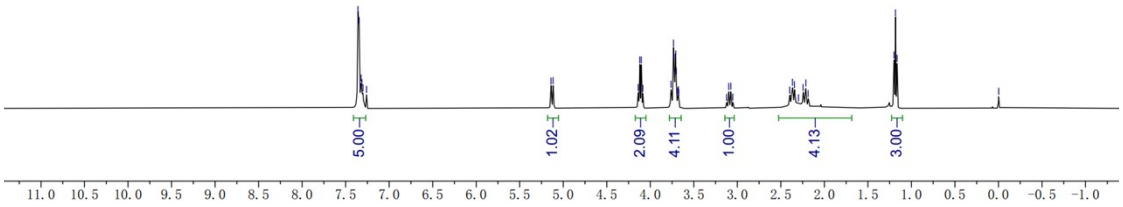
^{13}C NMR (100 MHz, $CDCl_3$)

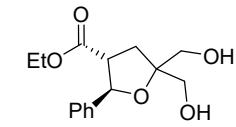




17

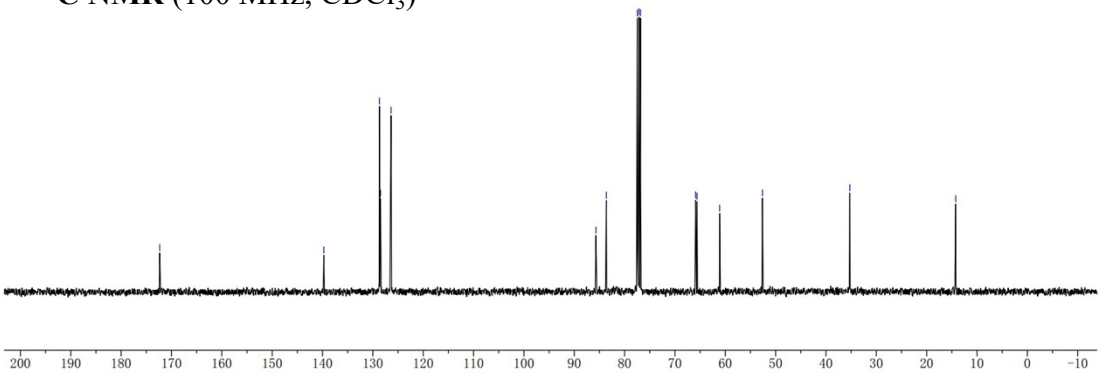
^{1}H NMR (400 MHz, $CDCl_3$)

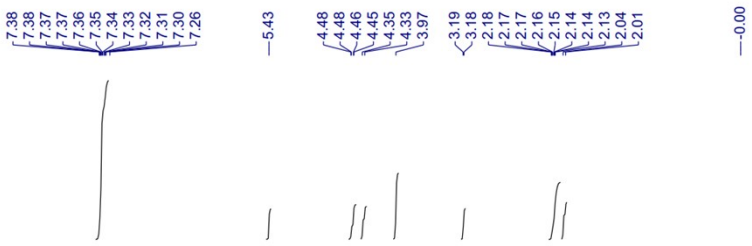


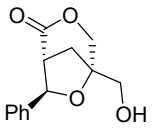


17

^{13}C NMR (100 MHz, $CDCl_3$)

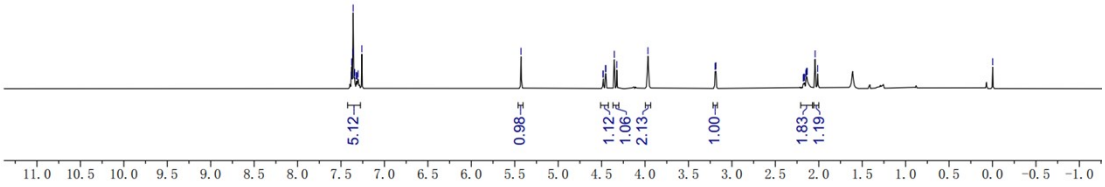


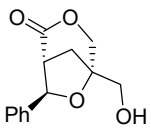




18

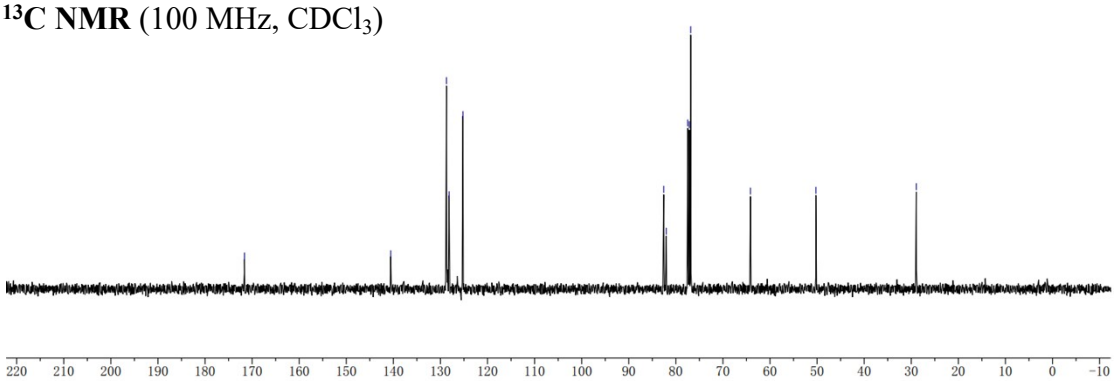
^{1}H NMR (400 MHz, $CDCl_3$)

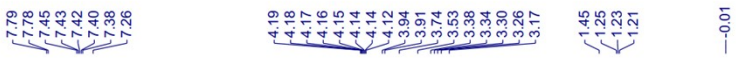


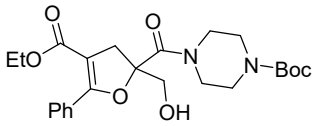


18

^{13}C NMR (100 MHz, $CDCl_3$)

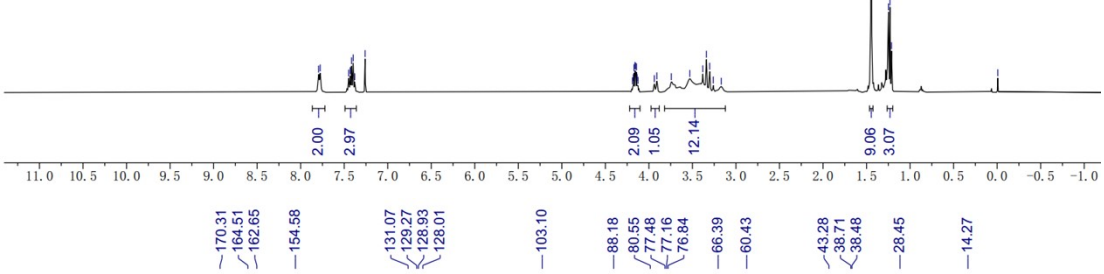


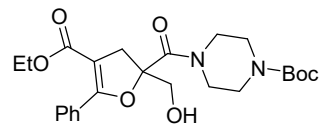




20

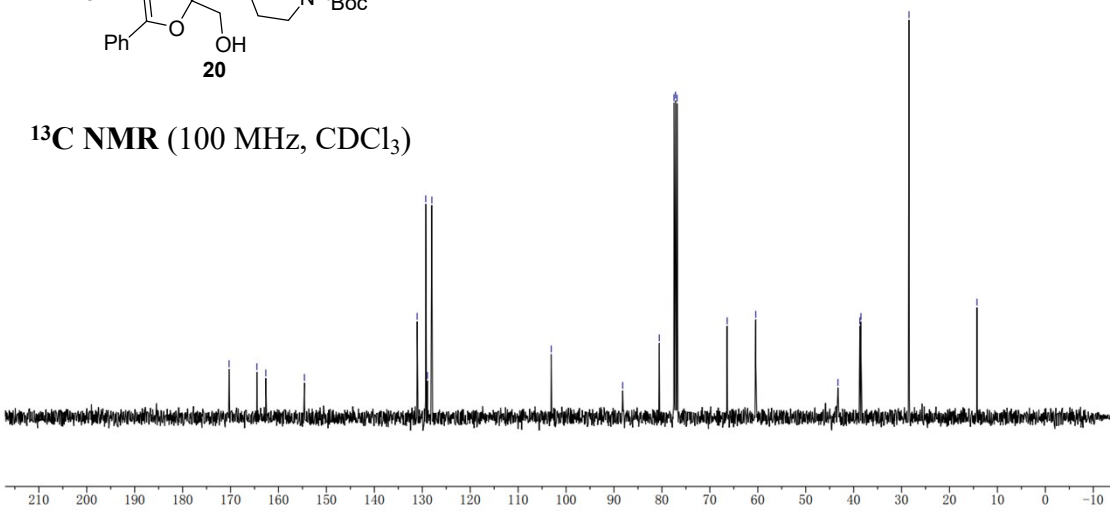
^{1}H NMR (400 MHz, $CDCl_3$)

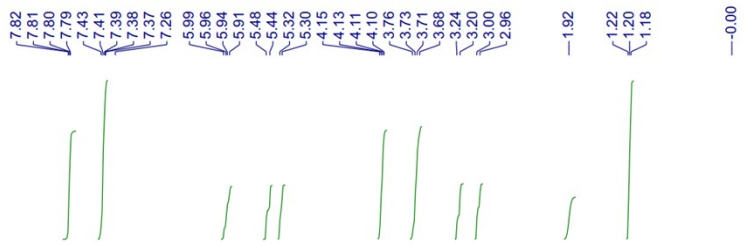


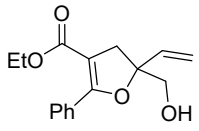


20

^{13}C NMR (100 MHz, $CDCl_3$)

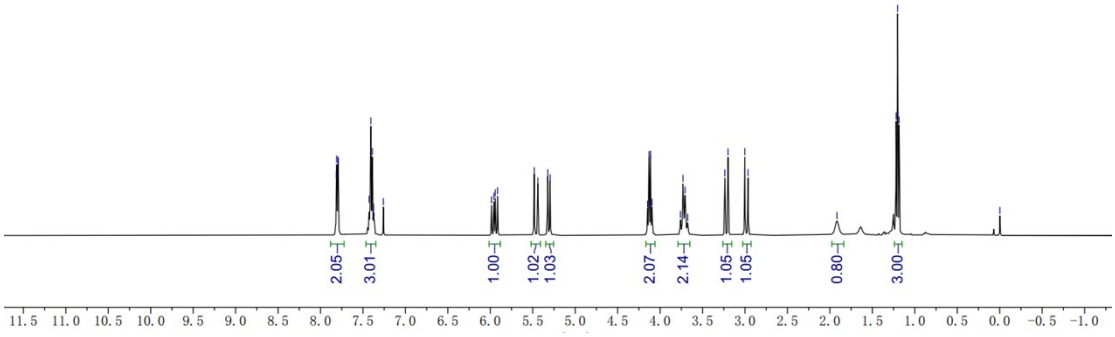


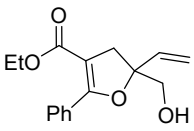




21

^{1}H NMR (400 MHz, $CDCl_3$)





21

^{13}C NMR (100 MHz, $CDCl_3$)