Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Annulation–Retro-Claisen Cascade of Bifunctional Peroxides for the Synthesis of Lactone Natural Products

Qianlan Xu, Jialin Li, Xuemin Li, and Lin Hu*

Chongqing Key Laboratory of Natural Product Synthesis and Drug Research, School of Pharmaceutical Sciences, Chongqing University, Chongqing 401331, China

*Corresponding: lhu@cqu.edu.cn

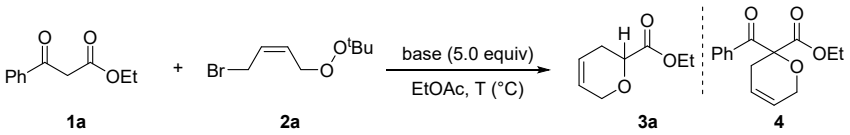
Table of Contents

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. ^{1}H and ^{13}C NMR spectra were recorded on Agilent 400MR DD2 (400 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; acetone-d_6 δ 2.05), ^{13}C NMR ($CDCl_3$, δ 77.0; acetone-d_6 δ 29.84, 206.26). 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) were acquired on a 7 Tesla SolariX FT-ICR MS (Bruker Daltonics, Bremen, Germany) with an ESI source.

2. Optimization of the tandem reaction

Table S1. Screening of the temperature and bases[a]

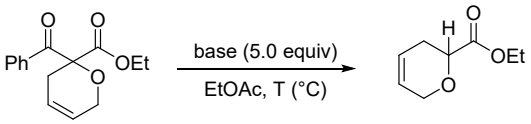


1a **2a** **3a** **4**

entry	base	T (°C)	time (h)	yield (%)[b]
1	Cs_2CO_3	40	24	8[c]
2	Cs_2CO_3	50	24	10[c]
3	Cs_2CO_3	60	24	20[c]
4	Cs_2CO_3	70	24	29[c]
5	Cs_2CO_3	80	24	41
6	Cs_2CO_3	90	12	43
7	Cs_2CO_3	100	12	40
8	Cs_2CO_3	110	12	37
9	Cs_2CO_3	120	12	35
10	50% aq. Cs_2CO_3	90	12	13[c]
11	CsOH	90	4	28[c]
12	KOH	90	4	26[c]
13	LiOH	90	24	8[c, d]
14	NaOH	90	4	23[c]
15	K_2CO_3	90	24	5[c, d]
16	K_3PO_4	90	24	16[c]
17	$K_3PO_4·7H_2O$	80	24	43
18	$K_3PO_4·7H_2O$	90	12	50
19	$K_3PO_4·7H_2O$	100	12	41
20	50% aq. K_3PO_4	90	24	11[c]

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.1 mmol), and base (5.0 equiv, 0.5 mmol) in EtOAc (1 mL).
[b] Isolated yield of **3a**. [c] Intermediate **4** as major product. [d] Starting materials left

Table S2. The influence of base on retro-Claisen reaction

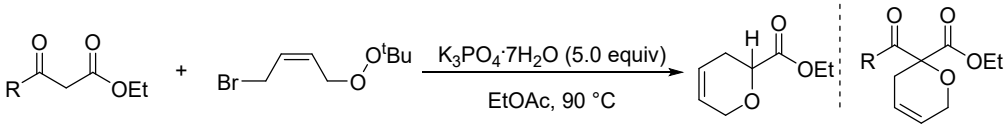


4 **3a**

entry	base	T (°C)	time (h)	yield (%)[b]
1	$K_3PO_4·7H_2O$	90	12	61
2	K_3PO_4	90	12	19[c]
3	50% aq K_3PO_4	90	12	12[c]
4	Cs_2CO_3	90	12	35

[a] Reaction conditions: **4** (0.1 mmol), and base (5.0 equiv, 0.5 mmol) in EtOAc (1 mL).
[b] Isolated yield of **3a**. [c] Starting material was left

Table S3. Screening of the substrates[a]



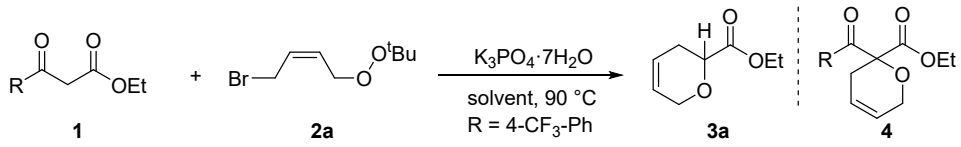
1 **2a** **3a** **4**

1a: R = Ph **1b:** R = Me **1c:** R = 4-MeO-Ph **1d:** R = 4-CF_3-Ph
1e: R = 4-NO_2-Ph **1f:** R = 4-Cl-Ph **1g:** R = 4-CN-Ph

entry	substrate	**1 : 2a**	base	T (°C)	time (h)	yield (%)[b]
1	**1a**	1 : 1.5	$K_3PO_4·7H_2O$	90	12	60
2	**1a**	1 : 2	$K_3PO_4·7H_2O$	90	12	56
3	**1a**	1.5 : 1	$K_3PO_4·7H_2O$	90	12	46
4	**1b**	1 : 1.5	$K_3PO_4·7H_2O$	90	12	15[c]
5	**1c**	1 : 1.5	$K_3PO_4·7H_2O$	90	12	20[c]
6	**1d**	1 : 1.5	$K_3PO_4·7H_2O$	90	12	65
7	**1e**	1 : 1.5	$K_3PO_4·7H_2O$	90	12	55
8	**1f**	1 : 1.5	$K_3PO_4·7H_2O$	90	12	62
9	**1g**	1 : 1.5	$K_3PO_4·7H_2O$	90	12	52

[a] Reaction conditions: **1** (0.1 mmol), base ($K_3PO_4·7H_2O$, 5 equiv, 0.5 mmol) in EtOAc (1 mL).
[b] Isolated yield of **3a**. [c] Intermediate **4** as major product.

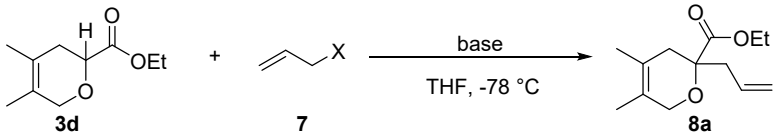
Table S4. Further optimization[a]



entry	base	equiv	solvent	T (°C)	**1 : 2a**	time (h)	yield (%)[b]
1	$K_3PO_4·7H_2O$	5.0	EA	90	1 : 1.5	12	65
2	$K_3PO_4·7H_2O$	7.0	EA	90	1 : 1.5	12	60
3	$K_3PO_4·7H_2O$	10.0	EA	90	1 : 1.5	12	62
4	$K_3PO_4·7H_2O$	5.0	THF	90	1 : 1.5	3	19[d]
5	$K_3PO_4·7H_2O$	5.0	DCM	90	1 : 1.5	12	10[c]
6	$K_3PO_4·7H_2O$	5.0	DMF	90	1 : 1.5	4	0[d]
7	$K_3PO_4·7H_2O$	5.0	MeCN	90	1 : 1.5	8	16[d]

[a] Reaction conditions: **1** (0.1 mmol), **2a** (0.15 mmol), and $K_3PO_4·7H_2O$ in solvent (1mL) .
[b] Isolated yield of **3a**. [c] Intermediate **4** as major product. [d] Peroxide was decomposed.

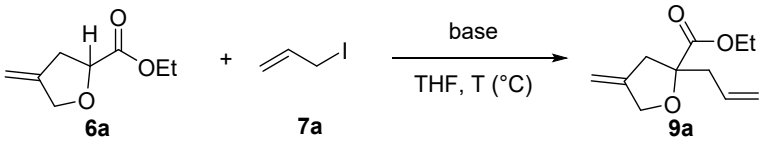
Table S5. Optimization of the alkylation reaction of 3d and 7[a]



entry	X	base	equiv of base	**3d : 7**	T (°C)	solvent	time (min)	yield (%)[b]
1	Br	t-BuOK (1.0 M)	1	1 : 1	-78	THF	10	0[c]
2	Br	LDA (1.0 M)	1	1 : 1	-78	THF	10	30
3	Br	NaHMDS (1.0 M)	1	1 : 1	-78	THF	10	35
4	Br	LiHMDS (1.0 M)	1	1 : 1	-78	THF	10	25
5	Br	KHMDS (1.0 M)	1	1 : 1	-78	THF	10	32
6	I	NaHMDS (1.0 M)	1	1 : 1	-78	THF	10	37
7	I	NaHMDS (0.5 M)	1	1 : 1	-78	THF	10	40
8	I	NaHMDS (0.05 M)	1	1 : 1	-78	THF	10	54
9	I	NaHMDS (0.03 M)	1	1 : 1	-78	THF	10	51
10	I	NaHMDS (0.05 M)	1	1 : 1	-65	THF	10	50
11	I	NaHMDS (0.05 M)	1	1 : 1	-55	THF	10	43
12	I	NaHMDS (0.05 M)	1	1 : 1	-20	THF	10	0[c]
13	I	NaHMDS (0.05 M)	1.5	1 : 1	-78	THF	10	48
14	I	NaHMDS (0.05 M)	1	1 : 1.5	-78	THF	10	56
15	I	NaHMDS (0.05 M)	1	1.5 : 1	-78	THF	10	41
16	I	NaHMDS (0.05 M)	1	1 : 2	-78	THF	10	60
17	I	NaHMDS (0.05 M)	1	1 : 2	-78	PhMe	10	30
18	I	NaHMDS (0.05 M)	1	1 : 2	-78	Et_2O	10	23
19	I	NaHMDS (0.05 M)	1	1 : 2	-78	CH_2Cl_2	10	15[d]
20	I	NaHMDS (0.05 M)	1	1 : 2	-78	DMF	10	0[c]

[a] Reaction conditions: **3d** (0.1 mmol), **7** and base in solvent (2 mL). [b] Isolated yield. [c] **3d** was decomposed.
[d] Starting materials left.

Table S6. Optimization of the alkylation reaction of 6a and 7a[a]

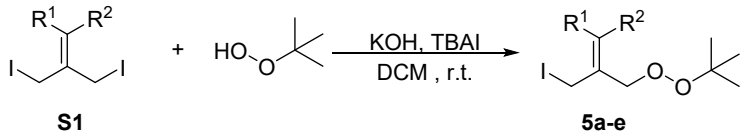


entry	base (equiv)	T (°C)	time (min)	yield (%)[b]
1	NaHMDS	-78	10	22%
2	LiHMDS	-78	10	45%
3	LiHMDS	-65	10	57%
4	LiHMDS	-55	10	30%

[a] Reaction conditions: **6a** (0.1 mmol), **7a** (0.2 mmol) and base (0.1 mmol, 0.05 M in THF, 2mL) in THF (2 mL). [b] Isolated yield.

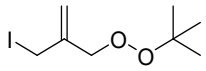
3. Preparation of the substrates

3.1 Preparation of the peroxides



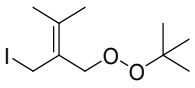
To a solution of the **S1**[1] (0.8 mmol ~ 2.0 mmol, 1.0 equiv), *tert*-butyl hydroperoxide (5.5 M solution in hexane, 0.8 mmol ~ 2.0 mmol, 1.0 equiv), and tetrabutylammonium iodide (0.1 equiv) in DCM (8 mL ~ 20 mL) was added powder KOH (1.0 equiv). The resulting solution was stirred at room temperature for 24 h. After completion, the reaction was quenched by water (10 mL). The organic layer was separated, and the aqueous layer was extracted with DCM (3 x 20 mL). The combined organic layer was washed with brine (20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether / EtOAc = 200 : 1) to give peroxides **5a-e** as light yellow oils in 50-65% yields.

"Caution! organic peroxides are potentially explosive. All the reactions relating to these compounds should be cautiously conducted in fume hood with a safety shield. Meanwhile, 2-iodomethylallyl peroxides 5 should be stored in a −20 °C fridge and protected from the light."



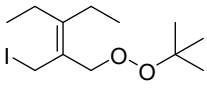
5a

Following the general procedure (11.5 mmol scale), **5a** was obtained as a light yellow oil (700 mg, 56% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.41 (s, 1H), 5.19 (s, 1H), 4.57 (s, 2H), 4.01 (s, 2H), 1.24 (s, 9H). The spectral data of **5a** was consistent with that reported in the literature.[2]



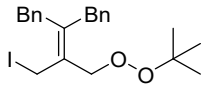
5b

Following the general procedure (3.57 mmol scale), **5b** was obtained as a light yellow oil (147 mg, 47% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.56 (s, 2H), 4.08 (s, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.25 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 140.2, 126.2, 80.4, 72.4, 26.4, 21.5, 21.0, 8.5. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{10}H_{19}INaO_2$: 321.0322; Found: 321.0320.



5c

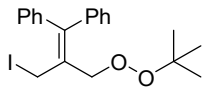
Following the general procedure (11.5 mmol scale), **5c** was obtained as a light yellow oil (948 mg, 51% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.56 (s, 2H), 4.09 (s, 2H), 2.20 – 2.08 (m, 4H), 1.25 (s, 9H), 1.08 (t, *J* = 7.6 Hz, 3H), 0.97 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 150.8, 125.8, 80.3, 72.0, 26.4, 25.3, 13.0, 11.6, 8.0. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{12}H_{23}INaO_2$: 349.0635; Found: 349.0639.



5d

Following the general procedure (2.9 mmol scale), **5d** was obtained as a light yellow oil (490 mg, 54% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33 – 7.18 (m, 6H), 7.16 (d, *J* = 7.4 Hz, 2H), 7.10 (d, *J* = 7.4 Hz, 2H), 4.79 (s, 2H), 4.24 (s, 2H), 3.44 (s,

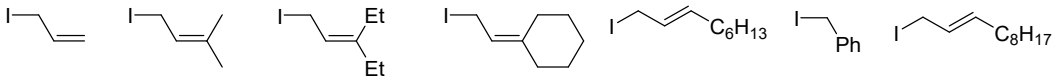
2H), 3.42 (s, 2H), 1.29 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 142.0, 138.8, 137.8, 130.9, 128.7, 128.5, 128.5, 128.5, 126.3, 126.2, 80.3, 71.9, 37.4, 37.1, 26.4, 6.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{22}H_{27}INaO_2$: 473.0948; Found: 473.0940.



5e

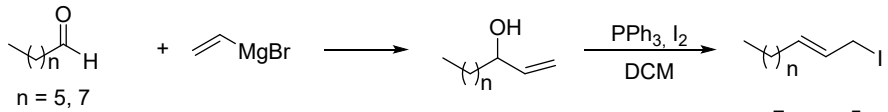
Following the general procedure (4.35 mmol scale), **5e** was obtained as a light yellow oil (440 mg, 44% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 – 7.17 (m, 10H), 4.71 (s, 2H), 4.22 (s, 2H), 1.26 (s, 9H). The spectral data of **5e** was consistent with that reported in the literature.[1]

3.2 Substrates 7a-g were prepared as following procedure



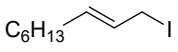
7a **7b** **7c** **7d** **7e** **7f** **7g**

Note: substrates **7a** and **7f** were commercial available, substrates **7b-d** were prepared according to the reported method.[3] Substrates **7e** and 7**g** were prepared according to the following procedure.[4]



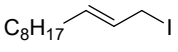
To a solution of aldehyde **S2** (10 mmol, 1.0 equiv) in dry THF (50 mL) was added vinylmagnesium bromide (1.0 M in THF, 15 mmol, 1.5 equiv) dropwise at 0 °C. The mixture was stirred for 2 h at 0 °C and 1 h at room temperature. The reaction was quenched with 20 mL saturated NH_4Cl, extracted with EtOAc (3 x 50 mL), and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo to give the allylic alcohol as a viscous oil, which was used for the next step directly without further purification.

To a solution of PPh_3 (15 mmol, 1.5 equiv) in CH_2Cl_2 (15 mL) was added iodine (15 mmol, 1.5 equiv), and the mixture stirred at room temperature for 5 min. A solution of the crude allylic alcohol (10 mmol, 1.0 equiv) in CH_2Cl_2 (30 mL) was added, and the mixture stirred at room temperature overnight. The reaction mixture was extracted with CH_2Cl_2 (3 x 50 mL) and washed with saturated $Na_2S_2O_3$ solution (20 mL), saturated sodium hydrogen carbonate solution (20 mL) and brine (20 mL). The organic layer was dried with Na_2SO_4 filtered, and concentrated in vacuo. Purification of the crude residue by silica gel flash column chromatography (petroleum ether) afforded **7e** and 7**g** in 49-57% yields.



7e

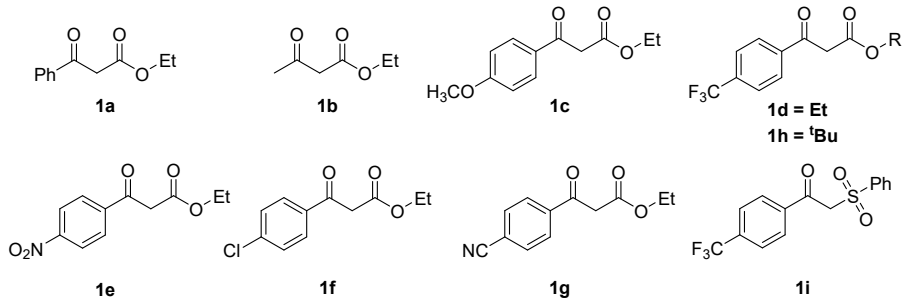
Following the general procedure, **7e** was obtained as a light yellow oil (1.4 g, 57% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.73 – 5.68 (m, 2H), 3.89 – 3.85 (m, 2H), 2.05 – 1.98 (m, 2H), 1.36 – 1.20 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H). The spectral data of **7e** was consistent with that reported in the literature.[5]



7g

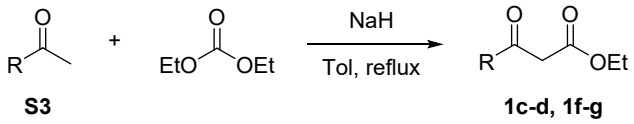
Following the general procedure, **7g** was obtained as a light yellow oil (1.36 g, 49% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.72 – 5.69 (m, 2H), 3.88 – 3.87 (m, 2H), 2.02 – 1.99 (m, 2H), 1.30 – 1.26 (m, 12H), 0.88 (t, *J* = 6.6 Hz, 3H). The spectral data of **7g** was consistent with that reported in the literature.[5]

3.3 Substrates 1a-k were prepared as following procedure



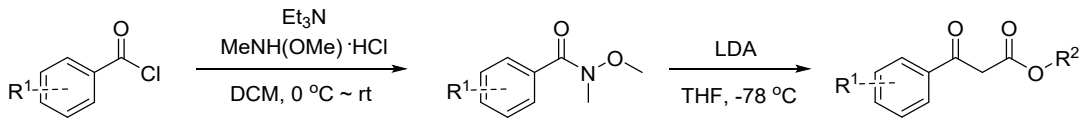
1a **1b** **1c** **1d = Et** **1h = ^{t}Bu** **1e** **1f** **1g** **1i**

Note: substrates **1a** and **1b** were commercial available, substrates **1c-d**, **1f-g** were prepared according to the following method A; substrates **1e**, **1h** were prepared according to the following method B; substrate **1i** was prepared according to the following method C.



S3 **1c-d, 1f-g**

Method A: To a dried three-necked flask equipped with a dropping funnel, a condenser, and a magnetic stirrer was added NaH (1.1 g, 28 mmol, 60 wt% in mineral oil), diethyl carbonate (2.4 mL, 20 mmol, 2.0 equiv), and toluene (10 mL). The mixture was heated to reflux. A solution of ketone **S3** (10 mmol, 1.0 equiv) in toluene (5 mL) was added dropwise from the dropping funnel over 10 min. 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 (3 x 20 mL). 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 **1c-d** and **1f-g** in 60-73% yields.

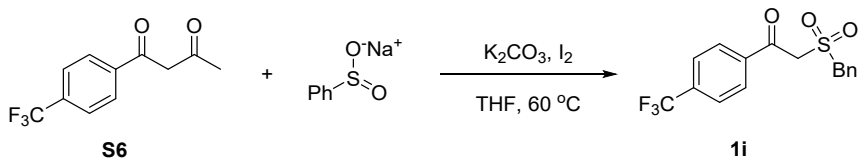


S4 **S5** **1e, 1h**

Method B: 50 mL of the dried round bottom flask was taken, and *N,O*-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 mmol, 2.1 equiv) and **S4** (10 mmol, 1.0 equiv) at 0 °C. After the addition was completed, the reaction

mixture was warmed to room temperature and stirred for 3 hours. After the reaction was completed as monitored by TLC plate, the reaction was quenched with 10 mL of NH_4Cl, the organic phase was separated and the aqueous phase was extracted with DCM (3 x 15 mL). The organic phase was combined, washed with brine, dried over Na_2SO_4. The solvent was removed by vacuum, which was used for the next step without further purification.

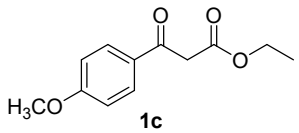
n-Butyllithium (2.5 M in hexane, 3.1 equiv) was added at -78 °C to THF solution (0.1 M) containing diisopropylamine (3.0 equiv) in a round-bottomed flask filled with N_2. After 30 min at 0 °C, the medium was recooled to -78 °C and freshly distilled *tert*-Butyl acetate (3.0 equiv) was added. After stirred for 30 min at -78 °C, **S5** (1.0 equiv) was added at this temperature. After 1 hour, the reaction was quenched at room temperature with a saturated solution of $NaHCO_3$, and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were then washed with a saturated solution of NH_4Cl. The organic layer was washed with 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 products **1e** and **1h** in 62-70% yields.



S6 **1i**

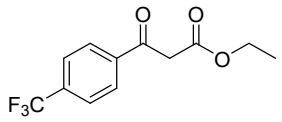
Method C: To a round bottom flask charged with **S6** (2.6 mmol, 1.0 equiv), sodium benzenesulfinate dihydrate (508 mg, 3.1 mmol, 1.2 equiv), K_2CO_3 (539 mg, 3.9 mmol, 1.5 equiv), and iodine (1.3 g, 5.2 mmol, 2.0 equiv) was added THF (11 mL). This mixture was stirred at room temperature overnight until the complete consumption of the starting material as monitored by TLC. A solution of Na_2SO_3 (1.3 g, 8.7 mmol) in H_2O (11 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 ethyl acetate (3 x 10 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 **1i** (544 mg, 65% yield).



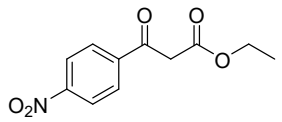
1c

Following the general method A, **1c** was obtained as a light yellow oil in 1:11 mixture of enol and keto form (1.62 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 **1c** was consistent with that reported in the literature.[2]



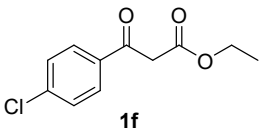
1d

Following the general method A, **1d** was obtained as a yellow oil in 1:2 mixture of enol and keto form (1.56 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 **1d** was consistent with that reported in the literature.[2]



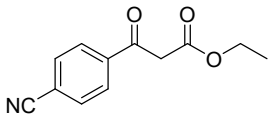
1e

Following the general method B, **1e** was obtained as a white solid in 1:4 mixture of enol and keto form (1.47 g, 62% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.57 (s, 0.25H), 8.34 (m, 2H), 8.28 (m. 2H), 5.77 (s, 0.25H), 4.23 (q, *J* = 8.0 Hz. 2H), 4.04 (s, 2H). 1.26 (t, *J* = 8.0 Hz, 3H). The spectral data of **1e** was consistent with that reported in the literature.[2]



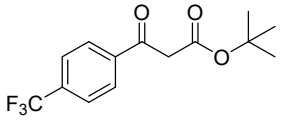
1f

Following the general method A, **1f** was obtained as a light yellow oil in 1:5 mixture of enol and keto form (1.47 g, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.57 (s, 0.2H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 5.63 (s, 0.2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). The spectral data of **1f** was consistent with that reported in the literature.[2]



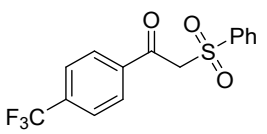
1g

Following the general method A, **1g** was obtained as a light yellow oil in 1:3 mixture of enol and keto form (1.37 g, 63% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.55 (s, 0.3H), 8.10 – 7.99 (m, 2H), 7.83 – 7.77 (m, 2H), 5.72 (s, 0.3H), 4.18 (q, *J* = 14.3, 7.2 Hz, 2H), 4.00 (s, 2H), 1.34 (t, *J* = 7.3 Hz, 3H). The spectral data of **1g** was consistent with that reported in the literature.[2]



1h

Following the general method B, **1h** was obtained as a pink solid in 1:10 mixture of enol and keto form (1.95 g, 68% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.71 (s, 0.1H), 8.04 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 5.63 (s, 0.1H), 3.91 (s, 2H), 1.42 (s, 9H). The spectral data of **1h** was consistent with that reported in the literature.[6]

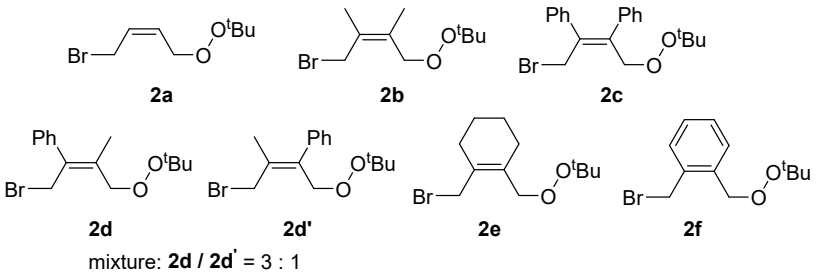


1i

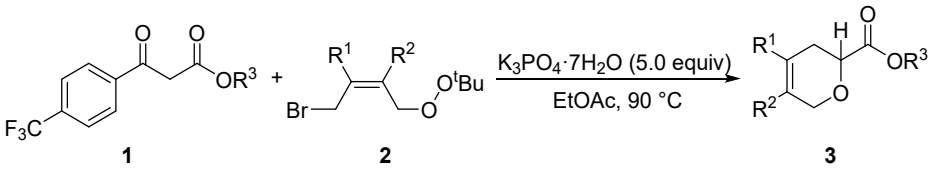
Following the general method C, **1i** was obtained as a white solid (544mg, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.27 – 7.99 (m, 2H), 7.91 (dt, *J* = 12.8, 7.1 Hz, 2H), 7.82 – 7.72 (m, 2H), 7.69 (d, *J* = 6.6 Hz, 1H), 7.59 (dd, *J* = 15.0, 9.4 Hz, 2H), 4.77 (s, 2H). The spectral data of **1i** was consistent with that reported in the literature.[7]

4. General procedure for the tandem reactions

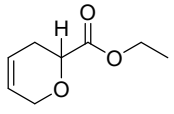
4.1 General procedure for the tandem reactions of peroxides 2a-f with 1d, 1h-i



Note: peroxides **2a-f** were prepared according to the reported method.[8]

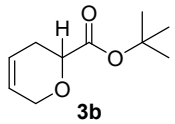


To a solution of substrates **1d**, **1h-i** (0.2 mmol, 1.0 equiv) and peroxides **2a-f** (0.3 mmol, 1.5 equiv) in ethyl acetate (2 mL) was added $K_3PO_4·7H_2O$ solid (338 mg, 1.0 mmol, 5.0 equiv) at room temperature. The resulting solution was vigorously stirred at 90 °C for 12 h. After completion of the reaction as monitored by the TLC, the reaction mixture was diluted with ethyl acetate (5 mL) and water (5 mL). The ethyl acetate layer was separated and the aqueous layer was extracted with EtOAc (3 x 5 mL). The combined extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 100 : 1 ~ 50 : 1) to afford the desired dihydropyrans products **3a-i** in 61-75% yields.



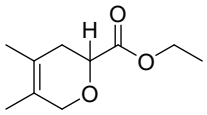
3a

Following the general procedure, **3a** was prepared from **1d** and **2a** and obtained as a light yellow oil (20.3 mg, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.89 – 5.79 (m, 1H), 5.78 – 5.67 (m, 1H), 4.37 (d, *J* = 16.5 Hz, 1H), 4.26 – 4.19 (m, 4H), 2.40 – 2.30 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.4, 126.0, 122.9, 72.1, 65.6, 61.1, 27.7, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_8H_{12}NaO_3$: 179.0679; Found: 179.0675.



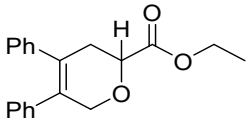
3b

Following the general procedure, **3b** was prepared from **1h** and **2a** and obtained as a light yellow oil (25.0 mg, 68% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.83 – 5.80 (m, 1H), 5.77 – 5.67 (m, 1H), 4.35 (d, *J* = 16.6 Hz, 1H), 4.21 (d, *J* = 16.6 Hz, 1H), 4.09 (dd, *J* = 8.3, 5.3 Hz, 1H), 2.35 – 2.29 (m, 2H), 1.47 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.6, 126.1, 123.0, 81.5, 72.3, 65.4, 28.0, 27.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{10}H_{16}NaO_3$: 207.0992; Found: 207.0993.



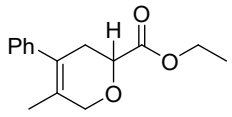
3c

Following the general procedure, **3c** was prepared from **1d** and **2b** and obtained as a light yellow oil (27.6 mg, 75% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.30 – 4.14 (m, 3H), 4.07 (q, *J* = 15.6 Hz, 2H), 2.38 – 2.14 (m, 2H), 1.65 (s, 3H), 1.52 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.5, 124.2, 122.4, 72.8, 69.2, 61.0, 33.0, 18.2, 14.2, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{10}H_{16}NaO_3$: 207.0992; Found: 207.0991.

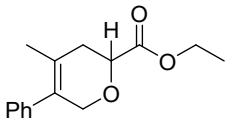


3d

Following the general procedure, **3d** was prepared from **1d** and **2c** and obtained as a yellow solid (40.6 mg, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.16 – 7.11 (m, 6H), 7.08 – 6.96 (m, 4H), 4.71 (d, *J* = 16.4 Hz, 1H), 4.56 – 4.43 (m, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.90 – 2.73 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.2, 140.5, 137.8, 133.7, 130.8, 129.0, 128.7, 128.1, 127.9, 127.0, 126.7, 73.0, 69.2, 61.3, 32.8, 14.3. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{20}H_{20}NaO_3$: 331.1305; Found: 331.1307. **Melting point:** 49.5-49.9 °C.



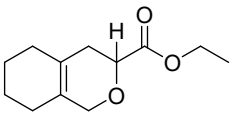
3e



3f

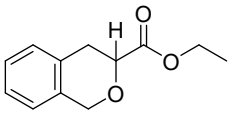
Following the general procedure, **3e** and **3f** were prepared from **1d** and peroxide mixture **2d** and **2d'** (3 : 1). The formed products were separable and the combined yields were 71%. The major product **3e** was obtained as a light yellow solid (26.6 mg, 54% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 – 7.31 (m, 3H), 7.18 (d, *J* = 7.3 Hz, 2H), 4.39 – 4.33 (m, 1H), 4.32 – 4.18 (m, 4H), 2.63 – 2.60 (m, 2H), 1.55 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.3, 141.0, 128.5, 128.2, 127.8, 126.8, 73.0, 69.2, 61.1, 32.9, 15.2, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{18}NaO_3$: 269.1148; Found: 269.1139. **Melting point:** 58.7-59.1 °C.

The minor product **3f** was obtained as a light yellow solid (8.4 mg, 17% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36 – 7.32 (m, 2H), 7.29 – 7.25 (m, 1H), 7.16 – 7.10 (m, 2H), 4.52 – 4.43 (m, 1H), 4.37 – 4.24 (m, 4H), 2.55 – 2.30 (m, 2H), 1.64 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.4, 138.2, 131.2, 128.7, 128.3, 127.1, 125.9, 72.8, 69.3, 61.2, 32.9, 19.6, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{18}NaO_3$: 269.1148; Found: 269.1139. **Melting point:** 59.8-60.1 °C.



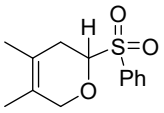
3g

Following the general procedure, **3g** was prepared from **1d** and **2e** and obtained as a white solid (31.1 mg, 74% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.27 – 4.17 (m, 3H), 4.06 (q, *J* = 15.5 Hz, 2H), 2.24 – 2.12 (m, 2H), 1.91 – 1.85 (m, 2H), 1.83 – 1.63 (m, 4H), 1.59 – 1.45 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.6, 126.9, 124.8, 72.9, 68.5, 61.0, 29.2, 24.8, 22.5, 22.3, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{12}H_{18}NaO_3$: 233.1148; Found: 233.1147. **Melting point:** 30.1-30.6 °C.



3h

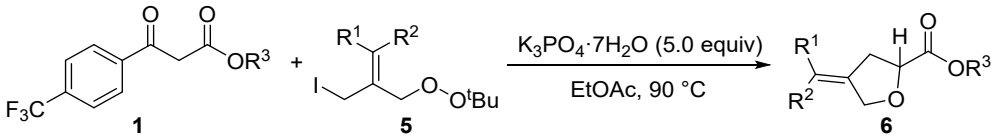
Following the general procedure, **3h** was prepared from **1d** and **2f** and obtained as a light yellow oil (25.2 mg, 61% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24 – 7.10 (m, 3H), 7.06 – 6.96 (m, 1H), 5.01 (d, *J* = 15.0 Hz, 1H), 4.87 (d, *J* = 15.0 Hz, 1H), 4.37 (dd, *J* = 8.6, 5.9 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.13 – 3.04 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.1, 133.6, 131.6, 128.7, 126.7, 126.4, 124.2, 73.3, 67.9, 61.3, 30.8, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{12}H_{14}NaO_3$: 229.0835; Found: 229.0836.



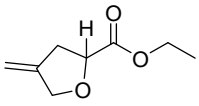
3i

Following the general procedure, **3i** was prepared from **1i** and **2b** and obtained as a white solid (32.7 mg, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.94 (d, *J* = 7.6 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 2H), 4.64 (dd, *J* = 8.4, 4.7 Hz, 1H), 4.15 (d, *J* = 15.3 Hz, 1H), 4.00 (d, *J* = 15.3 Hz, 1H), 2.52 – 2.33 (m, 2H), 1.67 (s, 3H), 1.50 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 136.3, 133.9, 129.5, 128.9, 123.8, 121.2, 88.8, 69.4, 28.0, 18.3, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{16}NaO_3S$: 275.0712; Found: 275.0704. **Melting point:** 64.3-64.5 °C.

4.2 General procedure for the tandem reactions of peroxides 5a-e with 1d, 1h-i

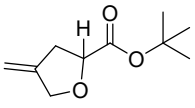


To a solution of substrates **1d**, **1h-i** (0.2 mmol, 1.0 equiv) and peroxides **5a-e** (0.3 mmol, 1.5 equiv) in ethyl acetate (2 mL) was added $K_3PO_4·7H_2O$ solid (338 mg, 1.0 mmol, 5.0 equiv) at room temperature. The resulting solution was vigorously stirred at 90 °C for 12 h. After completion of the reaction as monitored by the TLC, the reaction mixture was diluted with ethyl acetate (5 mL) and water (5 mL). The ethyl acetate layer was separated and the aqueous layer was extracted with EtOAc (3 x 5 mL). The combined extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 100 : 1 ~ 50 : 1) to afford the desired dihydropyrans products **6a-g** in 63-74% yields.



6a

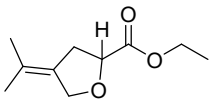
Following the general procedure, **6a** was prepared from **1d** and **5a** and obtained as a light yellow oil (20.6 mg, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.04 (s, 1H), 4.97 (s, 1H), 4.62 – 4.50 (m, 2H), 4.39 (d, *J* = 12.9 Hz, 1H), 4.25 – 4.17 (m, 2H), 2.92 (dd, *J* = 15.9, 8.4 Hz, 1H), 2.70 (dd, *J* = 15.9, 8.4 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.4, 145.1, 105.4, 77.2, 71.5, 61.1, 36.4, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_8H_{12}NaO_3$: 179.0679; Found: 179.0676.



6b

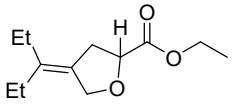
Following the general procedure, **6b** was prepared from **1h** and **5a** and obtained as a light yellow oil (24.7 mg, 67% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.02 (s, 1H), 4.95 (s, 1H), 4.54 (d, *J* = 12.9 Hz, 1H), 4.47 (dd, *J* = 8.3, 5.1 Hz, 1H), 4.37 (d, *J* = 12.9 Hz, 1H), 2.88 (dd, *J* = 15.9, 8.4 Hz, 1H), 2.65 (dd, *J* = 15.9, 8.4 Hz, 1H), 1.47 (s,

9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.6, 145.5, 105.0, 81.4, 77.5, 71.4, 36.4, 27.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{10}H_{16}NaO_3$: 207.0992; Found: 207.0992.



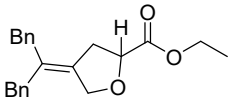
6c

Following the general procedure, **6c** was prepared from **1d** and **5b** and obtained as a light yellow oil (27.2 mg, 74% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.64 – 4.47 (m, 2H), 4.36 (d, *J* = 12.2 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.81 (dd, *J* = 15.1, 8.0 Hz, 1H), 2.60 (dd, *J* = 15.1, 8.0 Hz, 1H), 1.65 (s, 3H), 1.57 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.7, 129.0, 122.5, 77.5, 70.5, 61.0, 34.1, 21.5, 20.9, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{10}H_{16}NaO_3$: 207.0992; Found: 207.0990.



6d

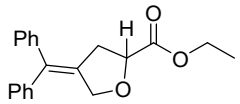
Following the general procedure, **6d** was prepared from **1d** and **5c** and obtained as a light yellow oil (29.7 mg, 70% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.55 (dd, *J* = 8.3, 5.7 Hz, 2H), 4.38 (d, *J* = 12.4 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.83 (dd, *J* = 15.7, 8.3 Hz, 1H), 2.61 (dd, *J* = 15.8, 5.3 Hz, 1H), 2.01 (q, *J* = 7.5 Hz, 2H), 1.91 (q, *J* = 7.5 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.95 (q, *J* = 7.5 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.7, 134.3, 128.4, 77.3, 70.0, 61.0, 33.5, 25.8, 25.5, 14.2, 12.4, 12.3. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{12}H_{20}NaO_3$: 235.1305; Found: 235.1304.



6e

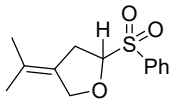
Following the general procedure, **6e** was prepared from **1d** and **5d** and obtained as a light yellow oil (47.7 mg, 71% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 – 7.17

(m, 6H), 7.12 – 7.04 (m, 4H), 4.80 (d, *J* = 12.8 Hz, 1H), 4.69 (dd, *J* = 8.3, 5.1 Hz, 1H), 4.61 (d, *J* = 12.8 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.30 (s, 2H), 3.18 (s, 2H), 3.05 (dd, *J* = 16.0, 8.3 Hz, 1H), 2.86 (dd, *J* = 16.0, 5.1 Hz, 1H), 1.31 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.5, 139.0, 138.8, 133.7, 128.9, 128.6, 128.5, 128.5, 126.2, 126.2, 77.5, 70.5, 61.2, 38.7, 38.4, 34.5, 14.2. **HRMS (ESI)** m/z: [M + Na]$^+$ Calcd for $C_{22}H_{24}NaO_3$: 359.1618; Found: 359.1618.



6f

Following the general procedure, **6f** was prepared from **1d** and **5e** and obtained as a yellow solid (44.4 mg, 72% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.03 (m, 10H), 4.71 (d, *J* = 13.6 Hz, 1H), 4.65 – 4.58 (m, 1H), 4.51 (d, *J* = 13.6 Hz, 1H), 4.33 – 4.11 (m, 2H), 3.07 (dd, *J* = 16.5, 8.1 Hz, 1H), 2.84 (dd, *J* = 16.5, 5.1 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.3, 141.7, 141.3, 135.7, 134.2, 128.7, 128.5, 128.3, 127.1, 126.9, 77.1, 71.3, 61.1, 36.0, 14.2. **HRMS (ESI)** m/z: [M + Na]$^+$ Calcd for $C_{20}H_{20}NaO_3$: 331.1305; Found: 331.1305. **Melting point:** 64.5-64.8 ^{o}C.

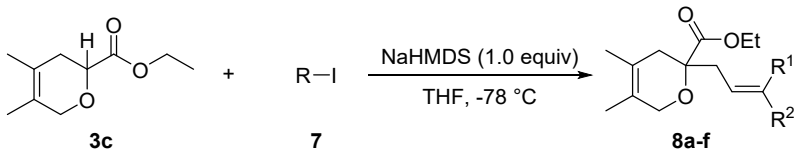


6g

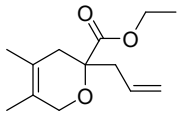
Following the general procedure, **6g** was prepared from **1i** and **5b** and obtained as a white solid (31.8 mg, 63% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.93 (d, *J* = 7.5 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.57 (t, *J* = 7.3 Hz, 2H), 5.04 (d, *J* = 8.5 Hz, 1H), 4.63 (d, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 11.7 Hz, 1H), 3.26 (dd, *J* = 16.7, 7.8 Hz, 1H), 2.90 (dd, *J* = 16.7, 7.8 Hz, 1H), 1.69 (s, 3H), 1.54 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 136.7, 133.9, 129.3, 129.0, 126.9, 123.7, 95.0, 71.9, 29.6, 21.6, 21.1. **HRMS (ESI)** m/z: [M + Na]$^+$ Calcd for $C_{13}H_{16}NaO_3S$: 275.0712; Found: 275.0704. **Melting point:** 67.8-68.4 ^{o}C.

5. General procedure for the alkylation reactions

5.1 General procedure for the alkylation of iodides 7 with 3c

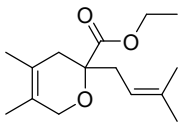


To a solution of the **3c** (36.8 mg, 0.2 mmol, 1.0 equiv) in dry THF (4 mL) at N_2 atmosphere was added iodides **7** (0.4 mmol, 2.0 equiv) at -78 ^oC. Then, a solution of NaHMDS (0.05 M in THF, 4 mL, 1.0 equiv) was slowly added to the mixture, and the reaction was kept stirring at -78 ^oC for 10 minutes. After completion, the reaction mixture was quenched with saturated NH_4Cl solution (5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether / EtOAc = 50 : 1) to afford the the products **8a-f** in 52-65% yields.



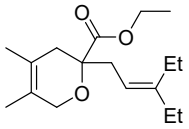
8a

Following the general procedure, **8a** was prepared from **3c** and **7a** and obtained as a light yellow oil (26.9 mg, 60% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.86 – 5.76 (m, 1H), 5.15 – 5.01 (m, 2H), 4.29 – 4.10 (m, 3H), 3.98 (d, *J* = 16.0 Hz, 1H), 2.48 (d, *J* = 7.1 Hz, 2H), 2.40 (d, *J* = 16.7 Hz, 1H), 2.13 (d, *J* = 16.7 Hz, 1H), 1.63 (s, 3H), 1.49 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.1, 132.2, 123.1, 121.9, 118.5, 78.2, 66.7, 60.8, 43.1, 36.5, 18.5, 14.3, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{20}NaO_3$: 247.1305; Found: 247.1296.



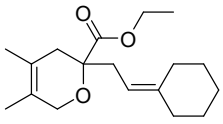
8b

Following the general procedure, **8b** was prepared from **3c** and **7b** and obtained as a light yellow oil (27.2 mg, 54% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.17 (t, *J* = 7.3 Hz, 1H), 4.21 – 4.14 (m, 3H), 3.97 (d, *J* = 15.8 Hz, 1H), 2.51 – 2.35 (m, 3H), 2.11 (d, *J* = 16.4 Hz, 1H), 1.70 (s, 3H), 1.64 (s, 3H), 1.59 (s, 3H), 1.50 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.4, 134.8, 123.1, 122.1, 117.5, 78.7, 66.7, 60.8, 37.3, 36.5, 25.9, 18.5, 17.9, 14.3, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{24}NaO_3$: 275.1618; Found: 275.1609.



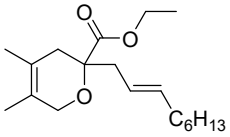
8c

Following the general procedure, **8c** was prepared from **3c** and **7c** and obtained as a light yellow oil (32.4 mg, 58% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.13 (t, *J* = 7.3 Hz, 1H), 4.24 – 4.11 (m, 3H), 3.97 (d, *J* = 15.9 Hz, 1H), 2.54 – 2.37 (m, 3H), 2.12 (d, *J* = 16.7 Hz, 1H), 2.02 (q, *J* = 7.5 Hz, 4H), 1.64 (s, 3H), 1.50 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.95 (dt, *J* = 16.7, 7.5 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.3, 145.9, 123.1, 122.2, 115.5, 78.6, 66.7, 60.7, 36.7, 36.5, 29.3, 23.1, 18.5, 14.3, 13.7, 13.0, 12.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{28}NaO_3$: 303.1931; Found: 303.1919.



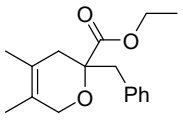
8d

Following the general procedure, **8d** was prepared from **3c** and **7d** and obtained as a light yellow oil (32.7 mg, 56% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.11 (t, *J* = 7.5 Hz, 1H), 4.25 – 4.09 (m, 3H), 3.97 (d, *J* = 15.8 Hz, 1H), 2.52 – 2.36 (m, 3H), 2.13 – 2.08 (m, 5H), 1.64 (s, 3H), 1.55 – 1.40 (m, 9H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.4, 142.9, 123.0, 122.2, 114.1, 78.7, 66.7, 60.7, 37.3, 36.4, 36.2, 28.8, 28.5, 27.7, 26.8, 18.5, 14.3, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{18}H_{28}NaO_3$: 315.1931; Found: 315.1917.



8e

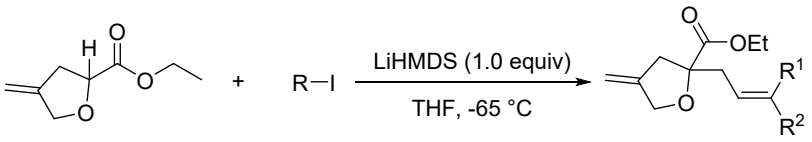
Following the general procedure, **8e** was prepared from **3c** and **7e** and obtained as a light yellow oil (32.0 mg, 52% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.51 – 5.35 (m, 2H), 4.21 – 4.14 (m, 3H), 3.97 (d, *J* = 15.8 Hz, 1H), 2.50 – 2.32 (m, 3H), 2.10 (d, *J* = 16.5 Hz, 1H), 2.00 (d, *J* = 6.6 Hz, 1H), 1.96 (d, *J* = 6.6 Hz, 1H), 1.63 (s, 3H), 1.49 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 11H), 0.87 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.2, 134.9, 123.1, 123.0, 122.0, 78.6, 66.7, 60.7, 42.0, 36.4, 32.6, 31.7, 29.3, 28.8, 22.6, 18.5, 14.3, 14.1, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{32}NaO_3$: 331.2244; Found: 331.2232.



8f

Following the general procedure, **8f** was prepared from **3c** and **7f** and obtained as a light yellow oil (35.6 mg, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36 – 7.09 (m, 5H), 4.22 (d, *J* = 15.6 Hz, 1H), 4.14 – 3.96 (m, 3H), 3.01 (s, 2H), 2.39 (d, *J* = 16.5 Hz, 1H), 2.15 (d, *J* = 16.5 Hz, 1H), 1.61 (s, 3H), 1.47 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.1, 135.8, 130.3, 127.9, 126.7, 123.1, 122.1, 79.1, 66.9, 60.7, 45.0, 36.4, 18.5, 14.1, 13.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{22}NaO_3$: 297.1461; Found: 297.1449.

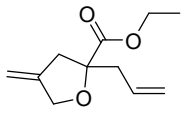
5.2 General procedure for the alkylation of iodides 7 with 6a



6a **7** **9a-f**

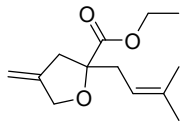
To a solution of the **6a** (31.2 mg, 0.2 mmol, 1.0 equiv) in dry THF (4 mL) at N_2 atmosphere was added iodides **7** (0.2 mmol, 2.0 equiv) at -65 °C. Then a solution of LiHMDS (0.05 M in THF, 2 mL, 1.0 equiv) was slowly added to the mixture, and the

reaction was kept stirring at -65 °C for 10 minutes. After completion, the solution mixture was quenched with saturated NH_4Cl solution (5 mL) and extracted with EtOAc (3 x 5 mL), The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether / EtOAc = 50 : 1) to afford the the products **9a-f** in 51-63% yields



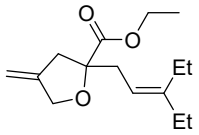
9a

Following the general procedure, **9a** was prepared from **6a** and **7a** and obtained as a light yellow oil (22.4 mg, 57% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.86 – 5.75 (m, 1H), 5.17 – 5.07 (m, 2H), 4.99 (s, 1H), 4.92 (s, 1H), 4.46 (s, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.91 (d, *J* = 16.0 Hz, 1H), 2.70 – 2.47 (m, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.5, 145.7, 132.2, 118.9, 105.3, 86.3, 71.4, 61.2, 41.6, 41.1, 14.3. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{11}H_{16}NaO_3$: 219.0992; Found: 219.0987.



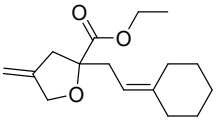
9b

Following the general procedure, **9b** was prepared from **6a** and **7b** and obtained as a light yellow oil (23.7 mg, 53% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.15 (t, *J* = 6.7 Hz, 1H), 4.98 (s, 1H), 4.90 (s, 1H), 4.45 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.91 (d, *J* = 15.9 Hz, 1H), 2.64 –2.54 (m, 2H), 2.49 – 2.43 (m, 1H), 1.70 (s, 3H), 1.61 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.8, 146.2, 135.3, 117.8, 105.0, 87.0, 71.3, 61.1, 41.2, 36.0, 25.9, 17.9, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{20}NaO_3$: 247.1305; Found: 247.1296.



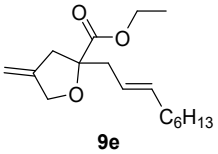
9c

Following the general procedure, **9c** was prepared from **6a** and **7c** and obtained as a light yellow oil (31.7 mg, 63% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.12 (t, *J* = 7.2 Hz, 1H), 4.98 (s, 1H), 4.91 (s, 1H), 4.45 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.92 (d, *J* = 15.9 Hz, 1H), 2.69 – 2.42 (m, 3H), 2.03 (dq, *J* = 14.1, 7.5 Hz, 4H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.96 (q, *J* = 7.6 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.8, 146.4, 146.2, 115.7, 105.0, 86.9, 71.3, 61.0, 41.1, 35.4, 29.3, 23.2, 14.2, 13.0, 12.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{24}NaO_3$: 275.1618; Found: 275.1608.



9d

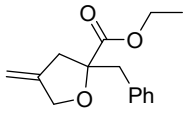
Following the general procedure, **9d** was prepared from **6a** and **7d** and obtained as a light yellow oil (29.0 mg, 55% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.11 (t, *J* = 7.4 Hz, 1H), 4.98 (s, 1H), 4.91 (s, 1H), 4.45 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.91 (d, *J* = 15.9 Hz, 1H), 2.69 – 2.53 (m, 2H), 2.47 (dd, *J* = 14.4, 7.1 Hz, 1H), 2.12 – 2.08 (m, 4H), 1.55 – 1.41 (m, 6H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.8, 146.2, 143.4, 114.3, 105.0, 87.0, 71.3, 61.1, 41.0, 37.3, 34.9, 28.9, 28.5, 27.8, 26.8, 14.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{16}H_{24}NaO_3$: 287.1618; Found: 287.1608.



9e

Following the general procedure, **9e** was prepared from **6a** and **7e** and obtained as a light yellow oil (28.6 mg, 51% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.55 – 5.48 (m, 1H), 5.46 – 5.34 (m, 1H), 4.98 (s, 1H), 4.90 (s, 1H), 4.45 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.91 – 2.87 (m, 1H), 2.68 – 2.41 (m, 3H), 2.03 – 1.95 (m, 2H), 1.33 – 1.20 (m, 11H), 0.87 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.7, 146.0, 135.3,

123.3, 105.1, 86.9, 71.4, 61.1, 41.0, 40.6, 32.6, 31.7, 29.3, 28.8, 22.6, 14.3, 14.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{28}NaO_3$: 303.1931; Found: 303.1919.

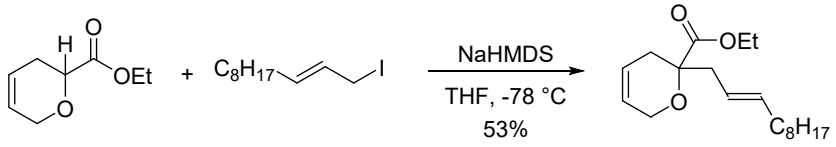


9f

Following the general procedure, **9f** was prepared from **6a** and **7f** and obtained as a light yellow oil (30.5 mg, 62% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 – 7.18 (m, 5H), 4.96 (s, 1H), 4.88 (s, 1H), 4.45 (s, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.22 (d, *J* = 13.9 Hz, 1H), 3.05 (d, *J* = 13.9 Hz, 1H), 2.94 (d, *J* = 15.9 Hz, 1H), 2.61 (d, *J* = 15.9 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.6, 145.6, 135.9, 130.2, 128.1, 126.7, 105.2, 87.2, 71.4, 61.2, 42.9, 41.4, 14.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{18}NaO_3$: 269.1148; Found: 269.1139.

6. Total Synthesis of the natural products

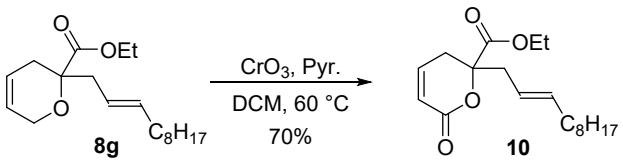
6.1 Synthesis of (±)-tanikolide 12



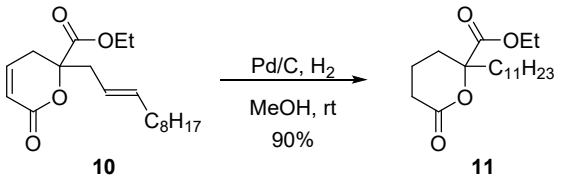
3a **7g** **8g**

To a solution of the **3a** (1.56 g, 10.0 mmol, 1.0 equiv) in dry THF (100 mL) at N_2 atmosphere was added allylic iodide **7g** (20.0 mmol, 2.0 equiv) at -78 °C. Then, a solution of NaHMDS (0.05 M in THF, 1.0 equiv) was slowly added to the mixture, and the reaction was kept stirring at -78 °C for 10 minutes. After completion, the reaction was quenched with saturated NH_4Cl solution (20 mL) and extracted with EtOAc (3 x 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether / EtOAc = 50 : 1) to afford the product **8g** (1.63 g, 53% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.80 – 5.75 (m, 1H), 5.70 – 5.66 (m, 1H), 5.54 – 5.36 (m, 2H), 4.47 – 4.41 (m, 1H), 4.24 – 4.15 (m, 3H), 2.59 – 2.38 (m, 3H), 2.25 –

2.16 (m, 1H), 2.01 – 1.96 (m, 2H), 1.33 – 1.18 (m, 15H), 0.87 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.0, 134.9, 125.2, 123.0, 122.3, 77.7, 63.0, 60.8, 42.1, 32.5, 31.8, 31.1, 29.4, 29.3, 29.2, 29.1, 22.6, 14.3, 14.0. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{32}NaO_3$: 331.2244; Found: 331.2230.

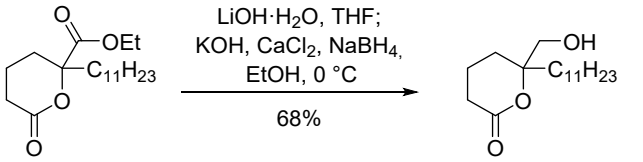


To a solution of pyridine (0.94 mL, 11.7 mmol, 18.0 equiv) and CrO_3 (714 mg, 7.2 mmol, 11.0 equiv) in CH_2Cl_2 (13 mL) was stirred for 20 minutes at 0 °C, whereupon a solution of compound **8g** (200 mg, 0.65 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL) was added slowly for 5 minutes and then refluxed at 60 °C for 12 h. After completion of the reaction as monitored by the TLC. The solution was filtered through a pad of celite and of the diatomite was subsequently washed with 50 mL of CH_2Cl_2. Then the filtrate was washed with saturated $NaHCO_3$ (3 x 10 mL) and 2 M HCl (2 x 10 mL) and brine (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 10 : 1 ~ 5 : 1) to afford product **10** (146.7 mg, 70% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.77 – 6.73(m, 1H), 6.02 – 5.99 (m, 1H), 5.60 – 5.48 (m, 2H), 4.19 (q, *J* = 7.1, 6.6 Hz, 2H), 2.97 – 2.44 (m, 4H), 2.00 (q, *J* = 7.7, 7.1 Hz, 2H), 1.35 – 1.23 (m, 15H), 0.88 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.4, 162.9, 142.9, 136.7, 121.6, 121.6, 84.3, 62.2, 41.1, 32.5, 31.8, 31.1, 29.4, 29.2, 29.1, 22.6, 14.1, 14.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{30}NaO_4$: 345.2036; Found: 345.2031.



To a solution of **10** (80 mg, 0.25 mmol) in MeOH (2.5 mL) was added 5% Pd/C (16 mg, 20 wt%) and the mixture was stirred for 12 h at room temperature under H_2

atmosphere (balloon). The reaction was filtered through a pad of celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 5 : 1) to afford **11** (76.1 mg, 94% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.27 – 4.17 (m, 2H), 2.61 (dd, *J* = 18.7, 6.4 Hz, 1H), 2.45 (dd, *J* = 18.7, 6.4 Hz, 1H), 2.23 – 2.10 (m, 1H), 2.03 – 1.71 (m, 3H), 1.32 – 1.18 (m, 23H), 0.87 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.0, 170.3, 86.1, 62.0, 38.8, 31.9, 30.5, 29.6, 29.5, 29.5, 29.3, 28.8, 23.0, 22.7, 17.2, 14.2, 14.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{34}NaO_4$: 349.2349; Found: 349.2347.

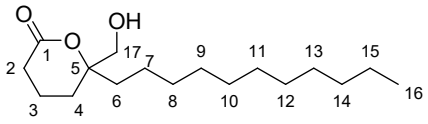


11 **(±)-Tanikolide (12)**

To a cold (0 °C) mixture of **11** (80 mg, 0.25 mmol) and THF / H_2O (1:1, 3 mL) was added $LiOH{\cdot}H_2O$ (11.8 mg, 0.28 mmol). The mixture was stirred at same temperature for 4 h. After completion of the reaction, the mixture was acidified (pH = 2-3) with 2 M HCl, and then extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, and the volatiles were evaporated to give the crude product was sufficiently pure and used directly in the next reaction. A mixture of KOH (32.5 mg, 0.58 mmol), $CaCl_2$ (129 mg, 1.16 mmol) and the crude product (50 mg, 0.145 mmol) in anhydrous EtOH (2.5 mL) was cooled to 0 °C, then $NaBH_4$ (44 mg, 1.16 mmol) was added in one portion. After stirring at room temperature for 26 h, the mixture was cooled to 0 °C, acidified (pH = 1) with 2 M HCl, and stirred at room temperature for additional 14 h. The volatiles were evaporated and the residue was diluted with saturated NaCl solution. The aqueous solution was extracted with EtOAc (3 x 15 mL). The combined organic layers were separated, dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 1 : 1) to provide **12** (47.4 mg, 68% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.65 (d, *J* = 11.9 Hz, 1H), 3.54 (d, *J* = 11.9 Hz, 1H), 2.48 (q, *J* = 6.2 Hz, 2H), 2.08 – 1.54 (m, 8H), 1.33 – 1.25 (m, 16H), 0.87 (t, *J* =

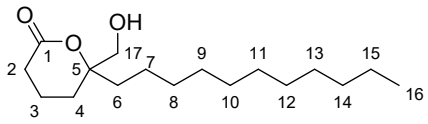
6.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.7, 86.5, 67.5, 36.6, 31.9, 30.0, 29.8, 29.6, 29.6, 29.5, 29.4, 29.3, 26.6, 23.4, 22.7, 16.6, 14.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{32}NaO_3$: 307.2244; Found: 307.2251. The spectral data of **12** was consistent with that reported in the literature.[9]

Table S7. Comparison of ^{1}H NMR data of synthetic 12 and natural tanikolide



H	Natural[9]	Synthetic
2	2.48 (m, 2H)	2.48 (q, *J* = 6.2 Hz, 2H)
3-15	1.94 – 1.85 (m, 3H) 1.75 – 1.71 (m, 2H) 1.63 (m, 1H) 1.34 (m, 1H) 1.29 (m 1H) 1.28 (m,2H) 1.26 (bs, 14H)	2.08 – 1.54 (m, 8H) 1.33 – 1.25 (m, 16H)
16	0.88 (t, *J* = 7.1 Hz, 3H)	0.87 (t, *J* = 6.7 Hz, 3H)
17	3.66 (dd, *J* = 12, 6.4 Hz, 1H) 3.56 (dd, *J* = 12, 6.4 Hz, 1H)	3.65 (d, *J* = 11.9 Hz, 1H) 3.54 (d, *J* = 11.9 Hz, 1H)

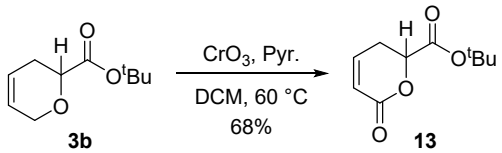
Table S8. Comparison of ^{13}C NMR data of synthetic 12 and natural tanikolide



C	Natural[9]	Synthetic
1	171.6	171.7
2	29.7	30.0
3	16.6	16.6
4	26.6	26.6

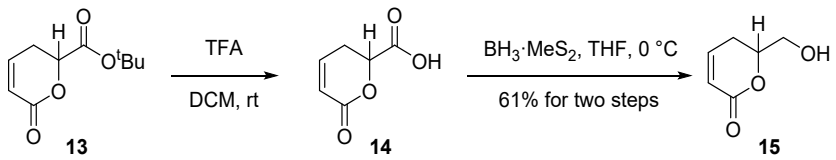
5	86.4	86.5
6	36.6	36.6
7	23.4	23.4
8	29.9	29.8
9	29.6	29.6
10	29.5	29.6
11	29.5	29.5
12	29.4	29.4
13	29.3	29.3
14	31.8	31.9
15	22.6	22.7
16	14.1	14.1
17	67.5	67.5

6.2 Synthesis of (±)-goniothalamins 18 and 19



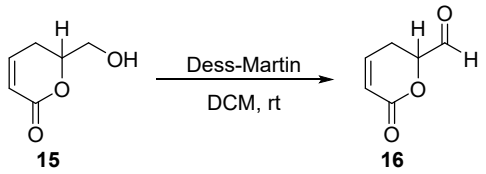
To a solution of pyridine (9.4 mL, 117.0 mmol, 18.0 equiv) and CrO_3 (7.1 g, 71.5 mmol, 11.0 equiv) in CH_2Cl_2 (60 mL) was stirred for 20 minutes at 0 °C, whereupon a solution of compound **3b** (1.2 g, 6.5 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added slowly for 5 minutes and then refluxed at 60 °C for 12 h. After completion of the reaction as monitored by the TLC, the solution was filtered through a pad of celite and of the diatomite was subsequently washed with 100 mL of CH_2Cl_2. Then the filtrate was washed with saturated $NaHCO_3$ (3 x 30 mL) and 2 M HCl (2 x 30 mL) and brine (30 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 5 : 1) to afford product **13** (876.1 mg, 68% yield) as a white solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.85 – 6.75 (m, 1H), 6.05 (d, *J*

= 9.9 Hz, 1H), 4.92 (t, *J* = 5.7 Hz, 1H), 2.84 – 2.67 (m, 2H), 1.47 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.1, 162.0, 142.4, 122.0, 83.4, 74.6, 27.8, 26.5. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{10}H_{14}NaO_4$: 221.0784; Found: 221.0775. **Melting point:** 87.5-87.9 °C.

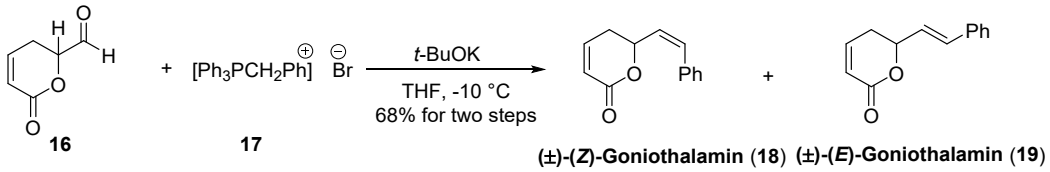


To a solution of **13** (600 mg, 3.0 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added TFA (3.0 mL) dropwise. The reaction mixture was allowed to warm up to room temperature and stirred for 2 hours. The mixture was concentrated under reduced pressure, and the crude acid **14** was sufficiently pure and used directly in next step. **^{13}H NMR (400 MHz, acetone-d_6)** δ 6.95 (dt, *J* = 9.1, 4.1 Hz, 1H), 5.95 (d, *J* = 9.9 Hz, 1H), 5.14 (t, *J* = 5.5 Hz, 1H), 2.91 (ddt, *J* = 19.0, 6.1, 2.8 Hz, 1H), 2.75 (dt, *J* = 18.8, 5.0 Hz, 1H). **^{13}C NMR (100 MHz, acetone-d_6)** δ 206.4, 162.6, 144.4, 122.1, 74.7, 27.2. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_6H_5O_4$: 141.0193; Found: 141.0187. **Melting point:** 113.5-114.0 °C.

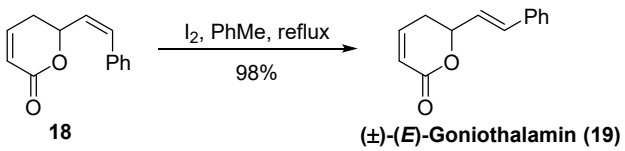
BH_3·Me_2S (0.6 mL, 10.0 M in THF, 6.0 mmol) was added dropwise to a solution of the crude acid **14** in THF (30 mL) at 0 °C. The mixture was allowed to warm up to room temperature and stirred for another 1 ~ 2 h. After completion of the reaction as monitored by the TLC. MeOH (15 mL) was then added to the mixture dropwise, and the solvent was removed. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 3 : 1 ~ 1 : 1) to afford **15** (234.5 mg, 61% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.96 – 6.92 (m, 1H), 6.04 (d, *J* = 9.8 Hz, 1H), 4.58 – 4.52 (m, 1H), 3.89 (dd, *J* = 12.4, 3.2 Hz, 1H), 3.75 (dd, *J* = 12.4, 3.2 Hz, 1H), 2.74 (br s, 1H), 2.65 – 2.56 (m, 1H), 2.35 – 2.28 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.0, 145.5, 120.9, 78.4, 63.8, 25.2. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_6H_7O_3$: 127.0401; Found: 127.0401.



Compound **15** (128.1 mg, 1.0 mmol) was dissolved in 5 mL of CH_2Cl_2 and Dess-Martin reagent (848.3 mg, 2.0 mmol) were added to the solution. The solution was stirred at room temperature for 30 min. The reaction mixture was diluted with 10 mL of Et_2O. The solution was filtered through a pad of celite and of the diatomite was subsequently washed with 50 mL of Et_2O. The organic fraction was concentrated and the crude aldehyde **16** was used directly in next step without further purification.



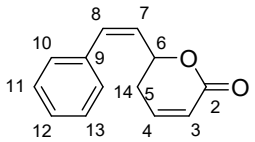
A solution of **17** (1.7 g, 3.9 mmol) in THF (10 mL) was cooled to -10 °C, and *t*-BuOK (2.9 mL, 1.0 M in THF, 2.9 mmol) was added. The mixture was stirred for 30 minutes to obtain an orange solution, and then the crude aldehyde **16** in 2 mL THF was dropwise added. After stirring for 30 minutes at -10 °C, the reaction was quenched quickly with H_2O (5 mL), and then extracted with EtOAc (3 × 20 mL). The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated, the residue was purified by flash chromatography on silica gel (petroleum ether / EtOAc = 10 : 1 ~ 7 : 1) to give **18** (114.1 mg, 57% yield) and **19** (22.0 mg, 11% yield) as a colorless oil. Data of compound **18**: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 – 7.24 (m, 5H), 6.90 (ddd, *J* = 9.9, 5.5, 3.0 Hz, 1H), 6.77 (d, *J* = 11.5 Hz, 1H), 6.05 (d, *J* = 9.8 Hz, 1H), 5.83 (dd, *J* = 11.5, 9.3 Hz, 1H), 5.30 (td, *J* = 9.8, 4.8 Hz, 1H), 2.60 – 2.38 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 163.9, 144.6, 135.6, 134.8, 128.6, 128.5, 127.9, 127.8, 121.6, 74.1, 29.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{12}NaO_2$: 223.0730; Found: 223.0731. The spectral data of **18** was consistent with that reported in the literature.[10]



18 **(±)-(*E*)-Goniothalamin (19)**

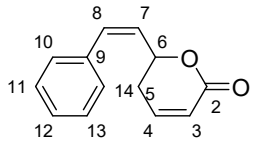
A solution of **18** (35 mg, 0.17 mmol) and I_2 (17.7 mg, 0.07 mmol) in toluene (2 mL) was refluxed at 120 °C for 2 hours. After completion, the reaction mixture was diluted with H_2O (5 mL), and then extracted with EtOAc (3 x 5 mL). The organic layer was washed with saturated $Na_2S_2O_3$ (5 mL) and brine (5 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 5 : 1) to afford **19** (34.3 mg, 98% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 – 7.24 (m, 5H), 7.00 – 6.87 (m, 1H), 6.73 (d, *J* = 16.1 Hz, 1H), 6.28 (dd, *J* = 15.9, 6.3 Hz, 1H), 6.09 (d, *J* = 9.9 Hz, 1H), 5.10 (ddd, *J* = 8.5, 7.2, 5.8 Hz, 1H), 2.56 – 2.53 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 163.9, 144.6, 135.7, 133.1, 128.7, 128.3, 126.7, 125.6, 121.7, 77.9, 29.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{12}NaO_2$: 223.0730; Found: 223.0731. The spectral data of **19** was consistent with that reported in the literature.[10]

Table S9. Comparison of ^{1}H NMR data of synthetic 18 and natural (*Z*)-goniothalamin



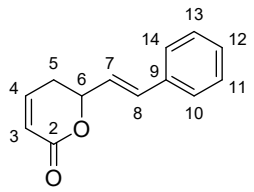
H	Natural[10]	Synthetic
3	6.03 (ddd, *J* = 9.8, 2.4, 1.2 Hz)	6.05 (d, *J* = 9.8 Hz, 1H)
4	6.85 (ddd, *J* = 9.8, 5.6, 2.9 Hz, 1H)	6.90 (ddd, *J* = 9.9, 5.5, 3.0 Hz, 1H)
5	2.47 (m, 2H)	2.60 – 2.38 (m, 2H)
6	5.28 (td, *J* = 9.9, 4.6 Hz, 1H)	5.30 (td, *J* = 9.8, 4.8 Hz, 1H),
7	5.81(dd, *J* = 11.5, 9.3 Hz, 1H)	5.83 (dd, *J* = 11.5, 9.3 Hz, 1H)
8	6.75 (d, *J* = 11.5 Hz, 1H)	6.77 (d, *J* = 11.5 Hz, 1H)
10-14	7.34 – 7.27 (m, 5H)	7.40 – 7.24 (m, 5H)

Table S10. Comparison of ^{13}C NMR data of synthetic 18 and natural (*Z*)-goniothalamin



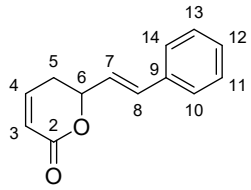
C	Natural[10]	Synthetic
2	163.8	163.9,
3	121.7	121.6
4	144.4	144.6
5	29.8	29.7
6	74.1	74.1
7	128.6	128.5
8	134.8	134.8
9	135.7	135.6
10-14	128.6	128.6, 127.9, 127.8

Table S11. Comparison of ^{1}H NMR data of synthetic 19 and natural (*E*)-goniothalamin



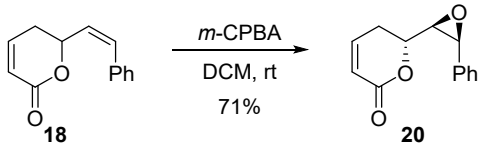
H	Natural[10]	Synthetic
3	6.08 (dt, *J* = 10, 1.5 Hz, 1H)	6.09 (d, *J* = 9.9 Hz, 1H)
4	6.91 (ddd, *J* = 9.8, 6.3, 2.4 Hz, 1H)	7.00 – 6.87 (m, 1H)
5	2.53 (m, 2H)	2.56 – 2.53 (m, 2H)
6	5.09 (m, 1H)	5.10 (ddd, *J* = 8.5, 7.2, 5.8 Hz, 1H)
7	6.26 (dd, *J* = 16.0, 6.3 Hz, 1H)	6.28 (dd, *J* = 15.9, 6.3 Hz, 1H)
8	6.71 (d, *J* = 16.1 Hz, 1H,)	6.73 (d, *J* = 16.1 Hz, 1H)
10-14	7.40 −7.28 (m, 5H)	7.43 – 7.24 (m, 5H)

Table S12. Comparison of ^{13}C NMR data of synthetic 19 and natural (*E*)-goniothalamin



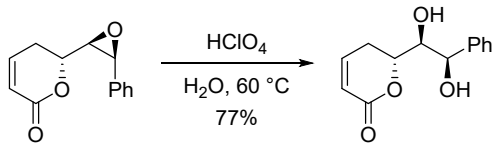
C	Natural[10]	Synthetic
2	163.8	163.9
3	121.8	121.7
4	144.6	144.6
5	29.9	29.9
6	77.9	77.9
7	125.7	125.6
8	133.2	133.1
9	135.8	135.7
10-14	128.7, 128.4, 126.7	128.7, 128.3, 126.7

6.3 Synthesis of (±)-7-*epi*-goniodiole 21



Compound **18** (31 mg, 0.15 mmol) was dissolved in 2 mL of CH_2Cl_2, then *m*-CPBA (106.9 mg, 0.62 mmol) were added to the solution at 0 °C. The reaction was stirred at room temperature for 6 hours. After completion, the reaction mixture was diluted with 10 mL of Et_2O and 10 mL of saturated $NaHCO_3$ solution. The organic phase was separated and the aqueous layer was extracted with EtOAc (5 x 10 mL). The organic layer was washed with 20% $Na_2S_2O_3$ solution and brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 5 : 1) to give **20** (23.0 mg, 71%). The diastereoselectivity for this reaction was determined to be 7:1 on the basis

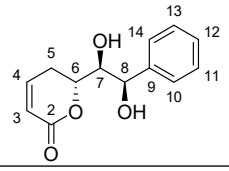
of crude ^{1}H NMR analysis. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42 – 7.28 (m, 5H), 6.87 (ddd, *J* = 9.3, 5.6, 2.9 Hz, 1H), 5.96 (d, *J* = 9.8 Hz, 1H), 4.27 (d, *J* = 3.9 Hz, 1H), 3.88 (ddd, *J* = 10.3, 8.2, 4.5 Hz, 1H), 3.45 (dd, *J* = 8.2, 3.9 Hz, 1H), 2.64 – 2.61 (m, 1H), 2.56 – 2.50 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.6, 144.3, 133.5, 128.5, 128.3, 126.4, 121.5, 73.1, 58.1, 57.6, 27.0. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{12}NaO_3$: 239.0679; Found: 239.0682.



20 **(±)-7-*epi*-Goniodiol (21)**

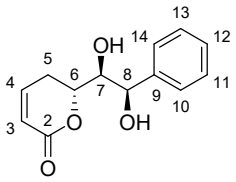
A suspension of compound **20** (30 mg, 0.14 mmol) in distilled H_2O (2.4 mL) and $HClO_4$ (0.14 mmol) was stirred at 60 °C for 3 h. The mixture was extracted with EtOAc (2 x 5 mL), and the organic phase was washed with brine (5 mL), dried over Na_2SO_4, concentrated. The mixture of diastereomers product could be separated and was purified by silica gel flash column chromatography (petroleum ether / Et_2O = 1 : 1 ~ 1 : 2) to afford **21** (25.2 mg, 77%) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.28 (m, 5H), 6.91 (ddd, *J* = 10.7, 7.2, 4.7, 3.5 Hz, 1H), 5.98 (dd, *J* = 9.7, 2.8 Hz, 1H), 4.90 (d, *J* = 4.4 Hz, 1H), 4.41 (dt, *J* = 11.4, 4.9 Hz, 1H), 3.95 (dd, *J* = 5.2, 4.2 Hz, 1H), 2.60 (ddt, *J* = 17.2, 11.7, 2.7 Hz, 1H), 2.48 (dt, *J* = 18.7, 5.1 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 163.9, 145.7, 140.1, 128.8, 128.3, 126.4, 120.9, 77.3, 76.1, 71.9, 24.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{14}NaO_4$: 257.0784; Found: 257.0773. The spectral data of **21** was consistent with that reported in the literature.[11]

Table S13. Comparison of ^{1}H NMR data of synthetic 21 and natural 7-*epi*-goniodiol



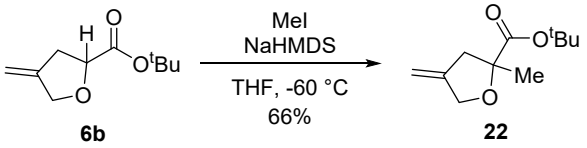
H	natural[11]	Synthetic
3	5.99 (dd, *J* = 9.7, 1.0 Hz, 1H)	5.98 (d, *J* = 9.7 Hz, 1H)
4	6.92 (m, 1H)	6.91 (ddd, *J* = 10.7, 7.2, 4.7, 3.5 Hz, 1H)
5	2.60 (m, 1H), 2.49 (ddd, *J* = 18.8, 5.2, 4.9 Hz, 1H)	2.60 (ddt, *J* = 17.2, 11.7, 2.7 Hz, 1H), 2.48 (dt, *J* = 18.7, 5.1 Hz, 1H)
6	4.41 (ddd, J = 10.9, 5.5, 5.2 Hz, 1H)	4.41 (dt, *J* = 11.4, 4.9 Hz, 1H)
7	3.94 (m, 1H)	3.95 (dd, *J* = 5.2, 4.2 Hz, 1H)
8	4.90 (d, *J* = 4.2 Hz, 1H)	4.90 (d, *J* = 4.4 Hz, 1H)
10-14	7.38 – 7.31 (m, 5H)	7.46 – 7.28 (m, 5H)

Table S14. Comparison of ^{13}C NMR data of synthetic 21 and natural 7-*epi*-goniodiol

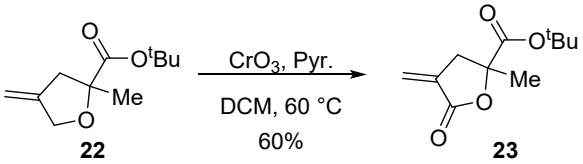


C	natural[11]	Synthetic
2	163.9	163.9,
3	120.9	120.9
4	145.7	145.7
5	24.9	24.9
6	77.3	77.3
7	71.9	71.9
8	76.1	76.1
9	140.2	140.1
10-14	128.7, 128.3, 126.4	128.8, 128.3, 126.4

6.4 Synthesis of (±)-plakolide A 28

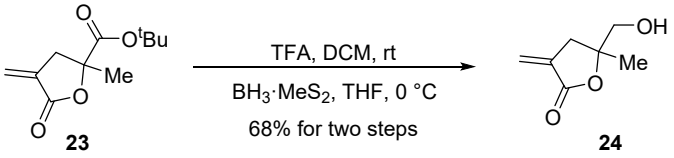


To a solution of the **6b** (1.26 g, 6.8 mmol, 1.0 equiv) in dry THF (70 mL) at N_2 atmosphere at -60 °C. Then, a solution of NaHMDS (2.0 M in THF, 1.0 equiv) was slowly added to the mixture, and the reaction was kept stirring at -60 °C for 10 minutes. Then methyl iodide (13.6 mmol, 2.0 equiv) was added, and the reaction was kept stirring at -60 °C for 2 hour. After completion, the solution was quenched with saturated NH_4Cl (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether / EtOAc = 50 : 1) to afford the the product **22** (888.6 mg, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.98 (s, 1H), 4.90 (s, 1H), 4.45 (s, 2H), 2.90 (d, *J* = 15.8 Hz, 1H), 2.46 (d, *J* = 15.8 Hz, 1H), 1.48 (s, 3H), 1.45 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.5, 146.7, 104.8, 84.0, 81.3, 71.3, 43.2, 27.9, 23.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{11}H_{18}NaO_3$: 221.1148; Found: 221.1152.



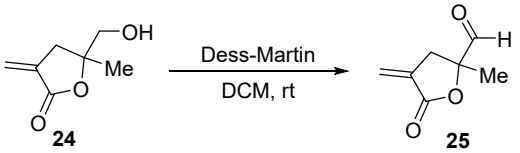
To a solution of pyridine (5.3 mL, 65.3 mmol, 18.0 equiv) and CrO_3 (4.0 g, 39.6 mmol, 11.0 equiv) in CH_2Cl_2 (30 mL) was stirred for 20 minutes at 0 °C, whereupon a solution of compound **22** (720 mg, 3.6 mmol, 1.0 equiv) in CH_2Cl_2 (6 mL) was added slowly for 5 minutes and then refluxed at 60 °C for 12 h. After completion of the reaction as monitored by the TLC, the solution was filtered through a pad of celite and of the diatomite was subsequently washed with 100 mL of CH_2Cl_2. Then the filtrate was washed with saturated $NaHCO_3$ (3 x 20 mL) and 2 M HCl (2 x 20 mL) and brine (20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and

concentrated in vacuum. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 5 : 1) to afford product **23** (458.5 mg, 60% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.24 (s, 1H), 5.63 (s, 1H), 3.16 (d, *J* = 17.2 Hz, 1H), 2.77 (d, *J* = 17.2 Hz, 1H), 1.62 (s, 3H), 1.45 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.2, 169.2, 133.9, 122.3, 83.1, 81.1, 38.7, 27.7, 23.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{11}H_{16}NaO_4$: 235.0941; Found: 235.0933.

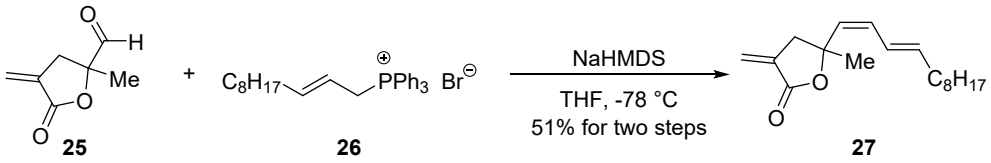


To a solution of **23** (212.2 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added TFA (1.0 mL) dropwise. The reaction mixture was allowed to warm up to room temperature and stirred for 2 hours. The mixture was concentrated under reduced pressure, and the crude free acid was sufficiently pure and used directly in next step.

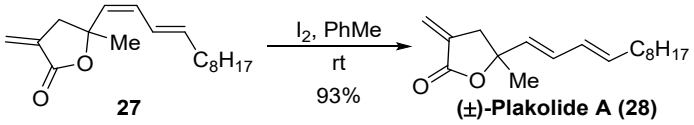
$BH_3·Me_2S$ (0.2 mL, 10 M in THF, 2.0 mmol) was added dropwise to a solution of the crude acid in THF (10 mL) at 0 °C. The mixture was allowed to warm up to room temperature and stirred for another 1 ~ 2 h. After completion of the reaction as monitored by the TLC, MeOH (5 mL) was then added to the mixture dropwise, and the solvent was removed. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 3 : 1 ~ 1 : 1) to afford **24** (96.6 mg, 68% yield) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.22 (s, 1H), 5.63 (s, 1H), 3.70 (d, *J* = 12.1 Hz, 1H), 3.51 (d, *J* = 12.1 Hz, 1H), 3.06 (d, *J* = 17.1 Hz, 1H), 2.61 (d, *J* = 17.2 Hz, 1H), 2.34 (br s, 1H), 1.38 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.0, 135.5, 122.4, 83.5, 68.1, 35.6, 23.4. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_7H_{10}NaO_3$: 165.0522; Found: 165.0525.



Compound **24** (28.4 mg, 0.2 mmol) was dissolved in CH_2Cl_2 (2 mL) and Dess-Martin reagent (170.7 mg, 0.4 mmol) were added to the solution. The solution was stirred at room temperature for 0.5 hours. The reaction mixture was diluted with 5 mL of Et_2O. The solution was filtered through a pad of celite and subsequent washing of the diatomite with 20 mL of Et_2O. The organic fraction was concentrated and the crude aldehyde **25** was used directly in next step without further purification.



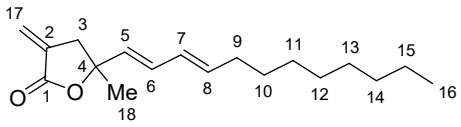
A solution of **26** (99 mg, 0.2 mmol) in THF (2 mL) was cooled to -78 °C, and NaHMDS (0.15 mL, 2.0 M in THF, 0.3 mmol) was added. The mixture was stirred for 30 min to obtain an orange solution, and then the aldehyde **25** in 1 mL THF was dropwise added. After stirring for 30 minutes at -78 °C, the reaction was diluted with EtOAc (5 mL), and then the organic layer was removed under reduced pressure, and the crude product was purified by flash chromatography (petroleum ether / EtOAc = 50 : 1) to give **27** (28.2 mg, 51% yield, *Z,E* / *E,E* = 9 : 1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.38 (ddd, *J* = 15.0, 11.6, 1.6 Hz, 1H), 6.24 (t, *J* = 2.9 Hz, 1H), 5.96 (q, *J* = 11.1, 10.5 Hz, 1H), 5.75 (dt, *J* = 14.3, 6.8 Hz, 1H), 5.63 (t, *J* = 2.5 Hz, 1H), 5.43 (d, *J* = 11.7 Hz, 1H), 3.04 (dt, *J* = 16.6, 2.8 Hz, 1H), 2.94 (dt, *J* = 16.6, 2.5 Hz, 1H), 2.12 (q, *J* = 7.3, 7.1 Hz, 2H), 1.57 (s, 3H), 1.34 – 1.20 (m, 12H), 0.88 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.6, 139.5, 135.3, 130.2, 125.4, 122.2, 83.4, 42.2, 32.9, 31.9, 29.4, 29.3, 29.2, 29.1, 28.8, 22.7, 14.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{18}H_{28}NaO_2$: 299.1982; Found: 299.1978.



A solution of **27** (10 mg, 0.04 mmol) and I_2 (3.6 mg, 0.01 mmol) in toluene (1 mL) was stirred at room temperature for 1 hours, the reaction mixture was diluted with H_2O (5 mL), and then extracted with EtOAc (3 × 5 mL). The organic layer was

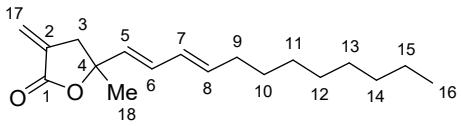
washed with saturated $Na_2S_2O_3$ (5 mL) and brine (5 mL) and dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether / EtOAc = 20 : 1) to afford plakolide A **28** as a colorless oil (9.3 mg, 93% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.22 (dd, *J* = 15.3, 10.6 Hz, 1H), 6.21 (t, *J* = 2.6 Hz, 1H), 5.98 (dd, *J* = 15.3, 10.2 Hz, 1H), 5.76 (dt, *J* = 15.0, 7.2 Hz, 1H), 5.62 (d, *J* = 15.2 Hz, 1H), 5.61 (t, *J* = 2.6 Hz, 1H), 2.91 (dt, *J* = 16.6, 2.7 Hz, 1H), 2.79 (dt, *J* = 16.6, 2.7 Hz, 1H), 2.06 (q, *J* = 7.3, 7.1 Hz, 2H), 1.51 (s, 3H), 1.32 – 1.15 (m, 12H), 0.87 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.8, 137.4, 135.3, 132.2, 129.6, 128.7, 122.3, 82.4, 40.8, 32.7, 31.9, 29.4, 29.2, 29.2, 29.1, 27.1, 22.7, 14.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{18}H_{28}NaO_2$: 299.1982; Found: 299.1978. The spectral data of **28** was consistent with that reported in the literature.[12]

Table S15. Comparison of ^{1}H NMR data of synthetic 28 and natural plakolide A



H	Natural[12]	Synthetic
3	2.89 (dt, *J* = 16.5, 2.4 Hz, 1H)	2.91 (dt, *J* = 16.6, 2.7 Hz, 1H)
	2.77 (dt, *J* = 16.5, 2.4 Hz, 1H)	2.79 (dt, *J* = 16.6, 2.7 Hz, 1H)
5	5.58 (d, *J* = 15.4 Hz, 1H)	5.62 (d, *J* = 15.2 Hz, 1H)
6	6.21 (dd, *J* = 15.4, 10.4 Hz, 1H)	6.21 (t, *J* = 15.2 Hz, 1H),
7	5.97 (dd, *J* = 15.0, 10.4 Hz, 1H)	5.98 (dd, *J* = 15.3, 10.2 Hz, 1H)
8	5.73 (dt, *J* = 15.0, 6.9 Hz, 1H)	5.76 (dt, *J* = 15.0, 7.2 Hz, 1H)
9	2.05 (dt, *J* = 7.2, 6.9 Hz, 2H)	2.06 (q, *J* = 7.3, 7.1 Hz, 2H)
10-15	1.33 (m, 2H) 1.15 (m, 10H)	1.32 – 1.15 (m, 12H)
16	0.85 (t, *J* = 7.2 Hz, 3H)	0.87 (t, *J* = 6.6 Hz, 3H)

Table S16. Comparison of ^{13}C NMR data of synthetic 28 and natural plakolide A



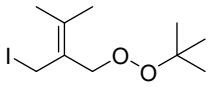
C	Natural[12]	Synthetic
1	169.8	169.8
2	135.4	135.3
3	40.8	40.8
4	82.4	82.4
5	132.2	132.2
6	129.7	129.6
7	128.7	128.7
8	137.4	137.4
9	32.7	32.7
10	29.4	29.4
11	29.3	29.2
12	29.2	29.2
13	29.1	29.1
14	31.9	31.9
15	22.7	22.7
16	14.1	14.1
17	122.3	122.3
18	27.1	27.1

7. References

1. M. Gao, Y. Luo, Q. Xu, Y. Zhao, X. Gong, Y. Xia and L. Hu, *Angew. Chem. Int. Ed.,* 2021, **60**, 19813.
2. M. Gao, Y. Zhao, C. Zhong, S. Liu, P. Liu, Q. Yin and L. Hu, *Org. Lett.,* 2019, ***21***, 5679.
3. B.Xu and U. K. Tambar, *Angew. Chem., Int. Ed.,* 2017, **56**, 9868.
4. A. A. Khan, S. H. Chee, B. L. Stocker and Mattie S. M. Timmer, *Eur. J. Org. Chem*., 2012, **5**, 995.
5. B. Xu and U. K. Tambar, *J. Am. Chem. Soc.,* 2016, **138**, 12073.
6. P. A. Peixoto, A. Boulangé, S. Leleu and X. Franck, *Eur. J. Org. Chem*., 2013, **16**, 3316.
7. Y. Xiong, J. Weng and G. Lu, *Adv. Synth. Catal.,* 2018, **360**, 1611.
8. C. Zhong, Q. Yin, Y. Zhao, Q. Li and L. Hu, *Chem. Commun.,* 2020, **56**, 13189.
9. I. P. Singh, K. E. Milligan and W. H. Gerwick, *J. Nat. Prod.,* 1999, **62**, 1333.
10. M. Mohideen, S. Zulkepli, N. K. Nik-Salleh, M. Zulkefeli, J. F. F. A. Weber and A. F. M. M. Rahman, *Arch. Pharm. Res*., 2013*,* **36**, 812.
11. T. Yoshida, S. Yamauchi, R. Tago, M. Maruyama, K. Akiyama, T. Sugahara, T. Kishida and Y. Koba, *Biosci. Biotechnol. Biochem.,* 2008, **72**, 2342.
12. S. P. Gunasekera, R. A. Isbrucker, R. E. Longley, A. E. Wright, S. A. Pomponi and J. K. Reed, *J. Nat. Prod.,* 2004, **67**, 110.

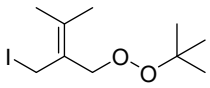
8. NMR Spectra for New Compounds

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

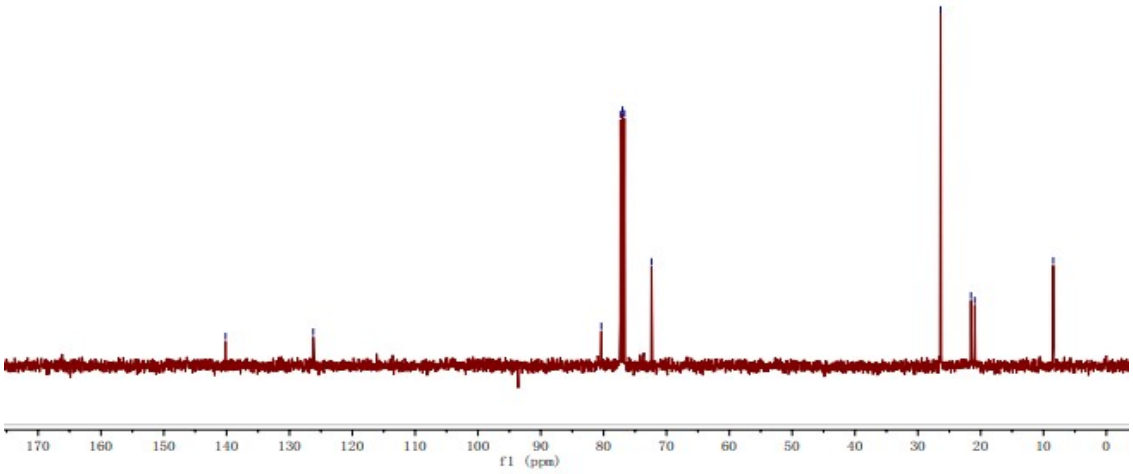


5b

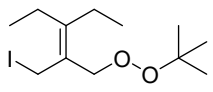
^{13}C NMR (100 MHz, $CDCl_3$)



5b

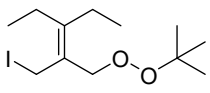


^{1}H NMR (400 MHz, $CDCl_3$)



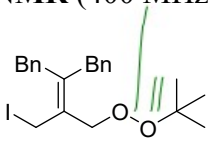
5c

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

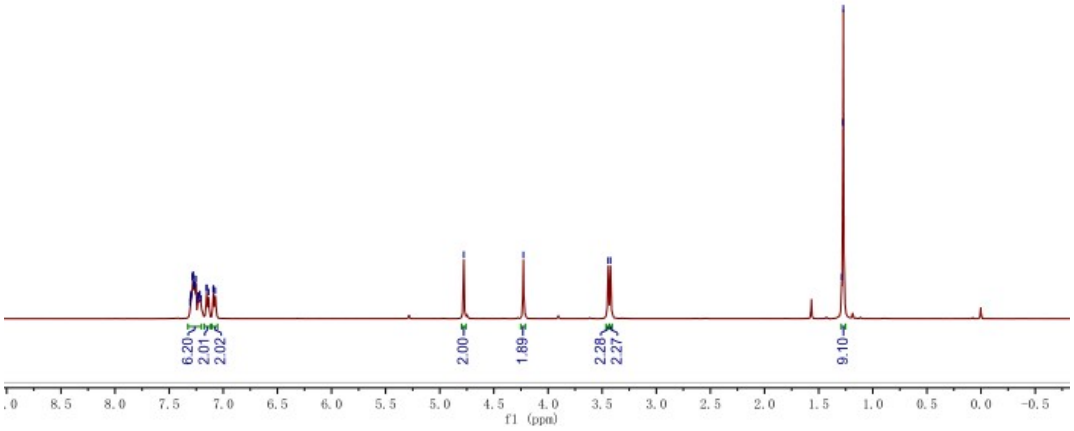


5c

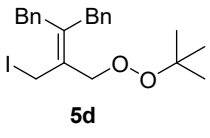
^{1}H NMR (400 MHz, $CDCl_3$)



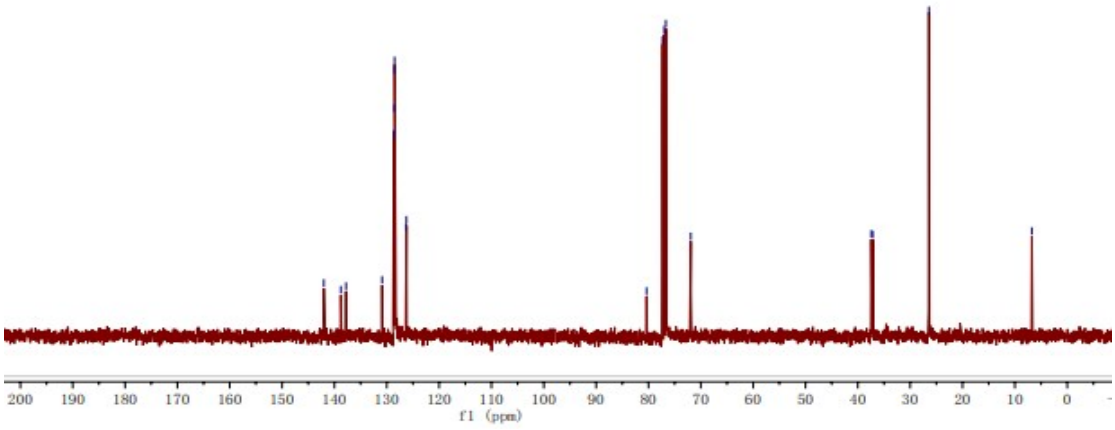
5d



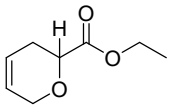
^{13}C NMR (100 MHz, $CDCl_3$)



5d

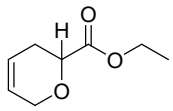


^{1}H NMR (400 MHz, $CDCl_3$)



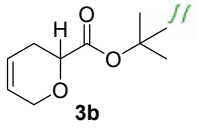
3a

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



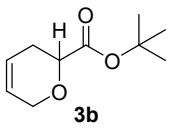
3a

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



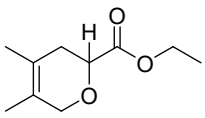
3b

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



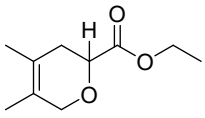
3b

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

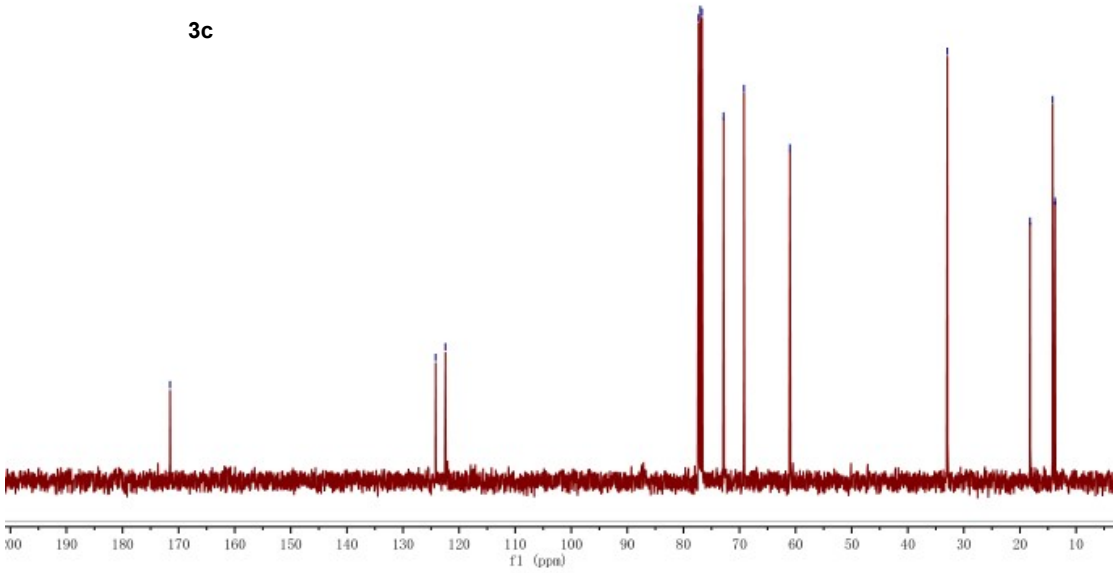


3c

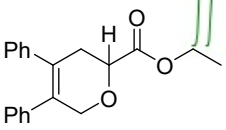
^{13}C NMR (100 MHz, $CDCl_3$)



3c

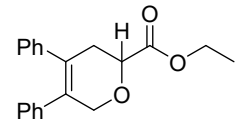


^{1}H NMR (400 MHz, $CDCl_3$)



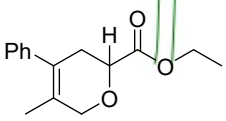
3d

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



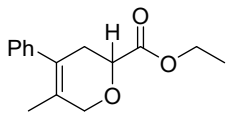
3d

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



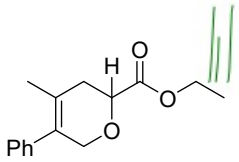
3e

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

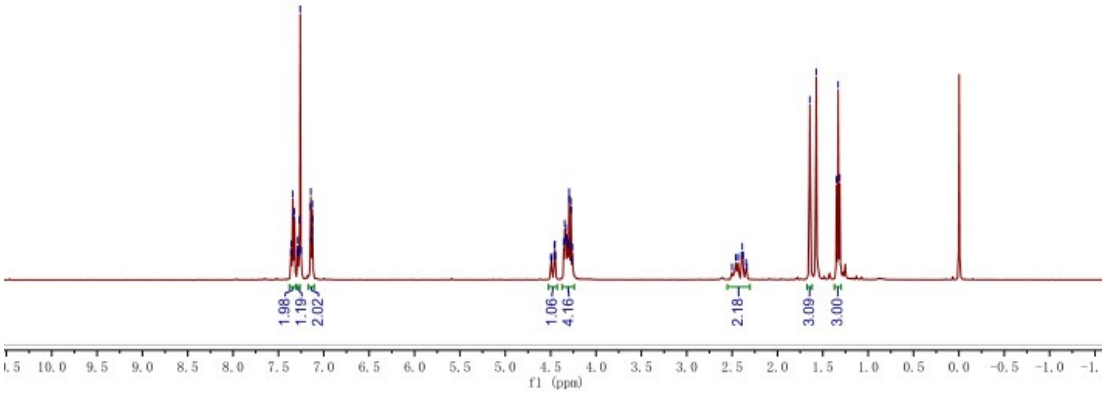


3e

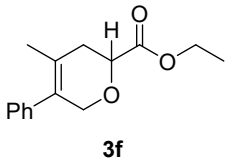
^{1}H NMR (400 MHz, $CDCl_3$)



3f

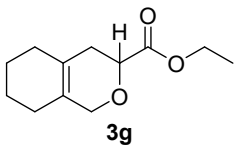


^{13}C NMR (100 MHz, $CDCl_3$)



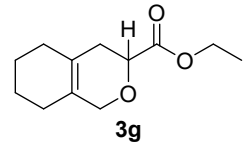
3f

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



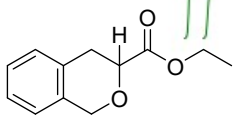
3g

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



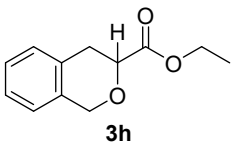
3g

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



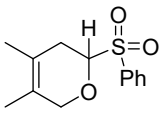
3h

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

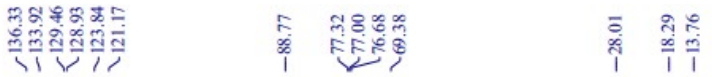


3h

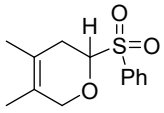
^{1}H NMR (400 MHz, $CDCl_3$)



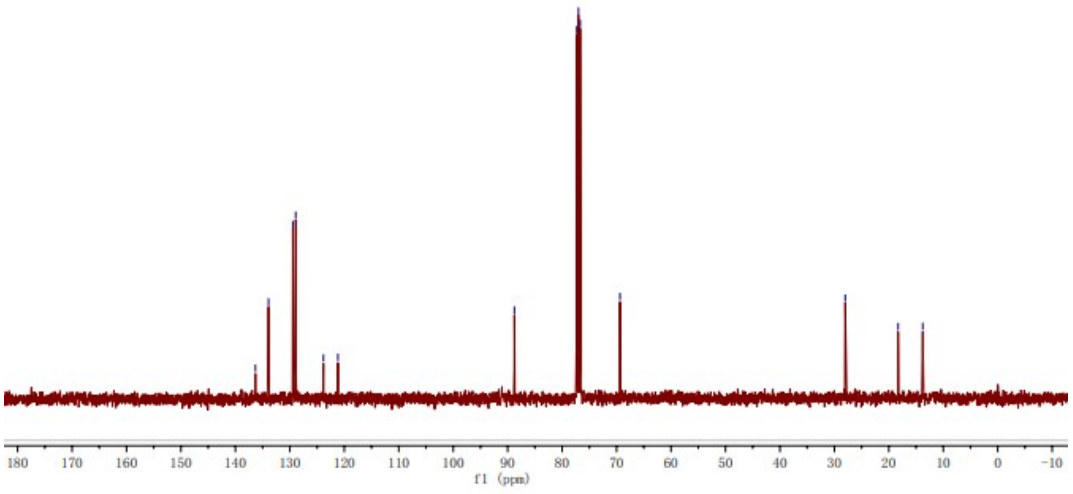
3i



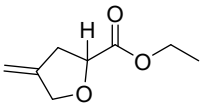
^{13}C NMR (100 MHz, $CDCl_3$)



3i

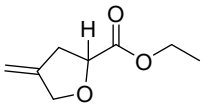


^{1}H NMR (400 MHz, $CDCl_3$)



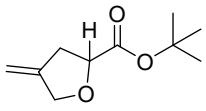
6a

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



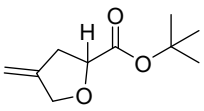
6a

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



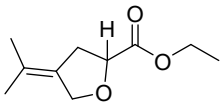
6b

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



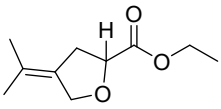
6b

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



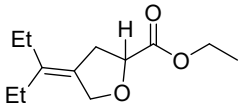
6c

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



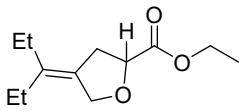
6c

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



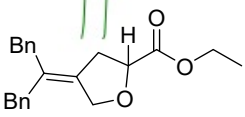
6d

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

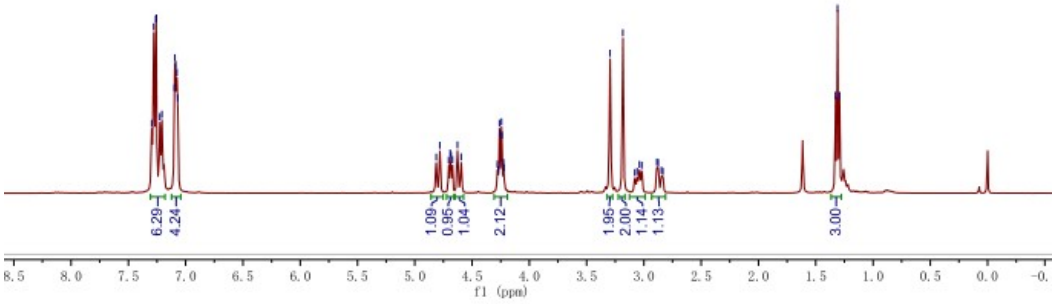


6d

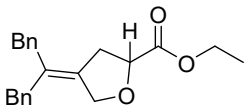
^{1}H NMR (400 MHz, $CDCl_3$)



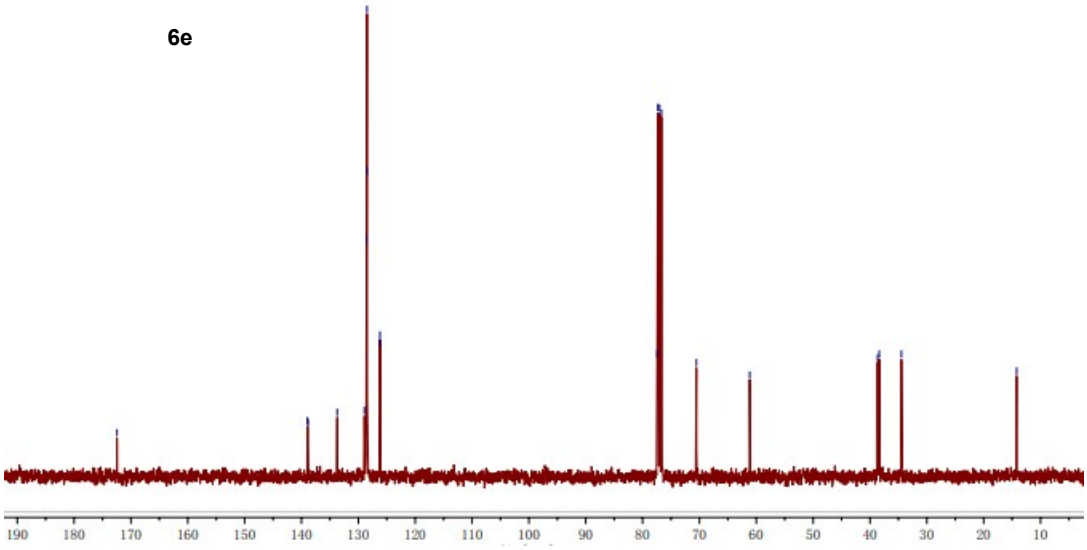
6e



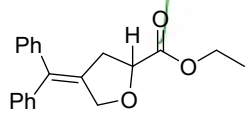
^{13}C NMR (100 MHz, $CDCl_3$)



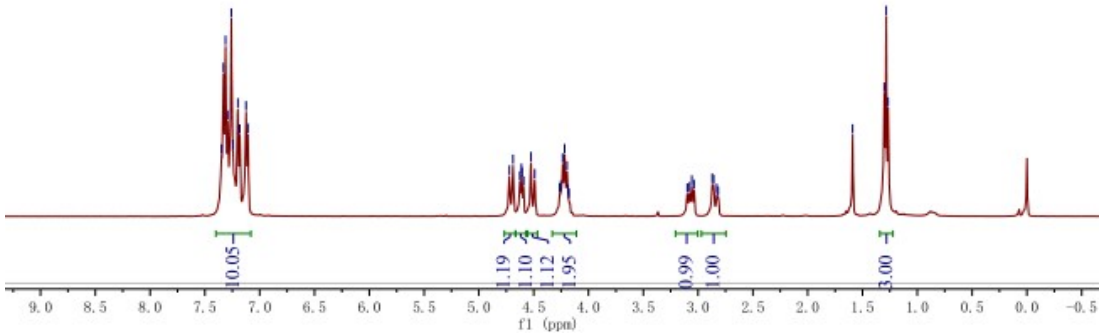
6e



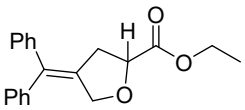
^{1}H NMR (400 MHz, $CDCl_3$)



6f

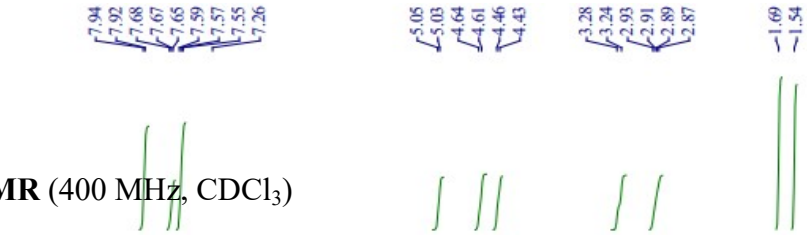


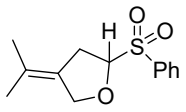
^{13}C NMR (100 MHz, $CDCl_3$)



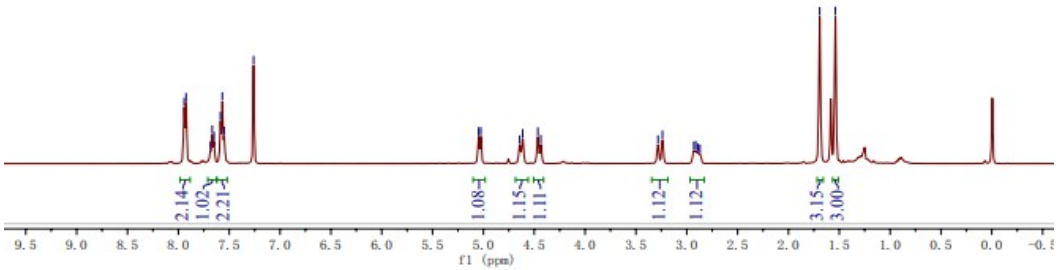
6f

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

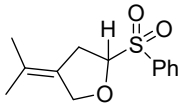




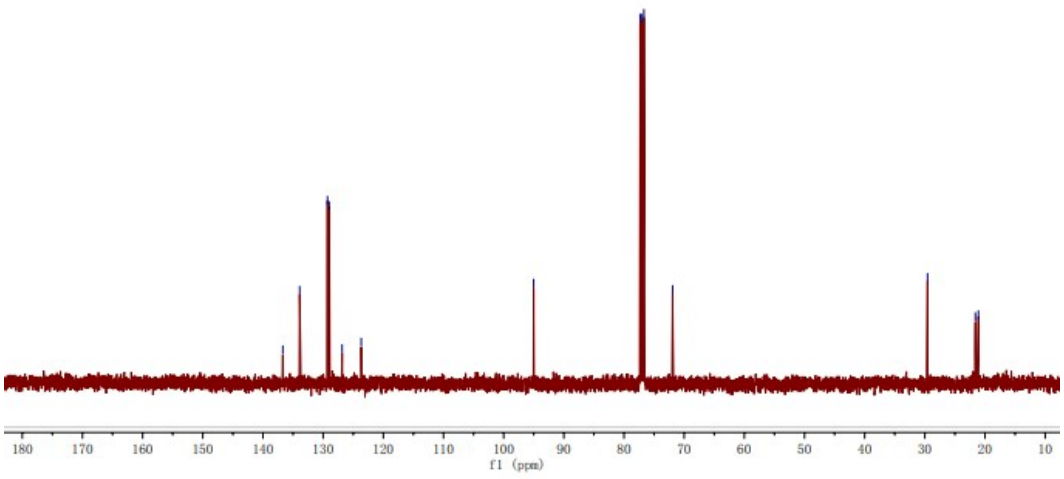
6g



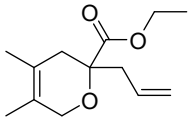
^{13}C NMR (100 MHz, $CDCl_3$)



6g

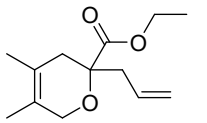


^{1}H NMR (400 MHz, $CDCl_3$)



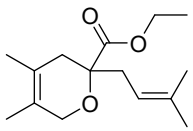
8a

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



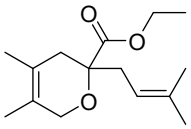
8a

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



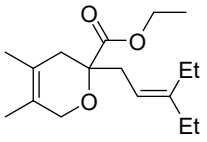
8b

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



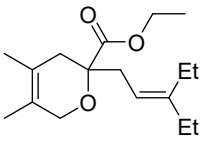
8b

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

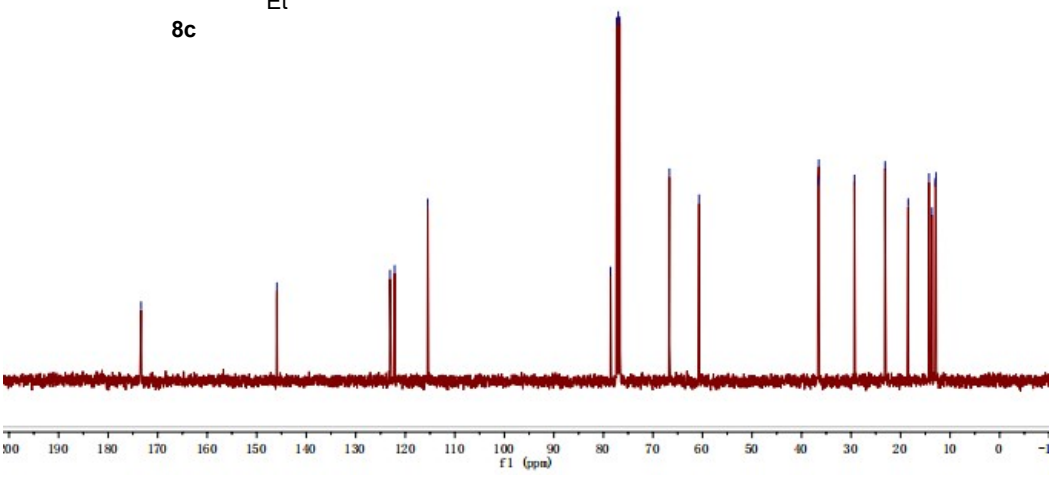


8c

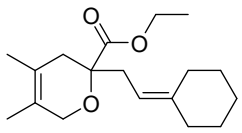
^{13}C NMR (100 MHz, $CDCl_3$)



8c

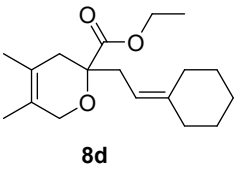


^{1}H NMR (400 MHz, $CDCl_3$)



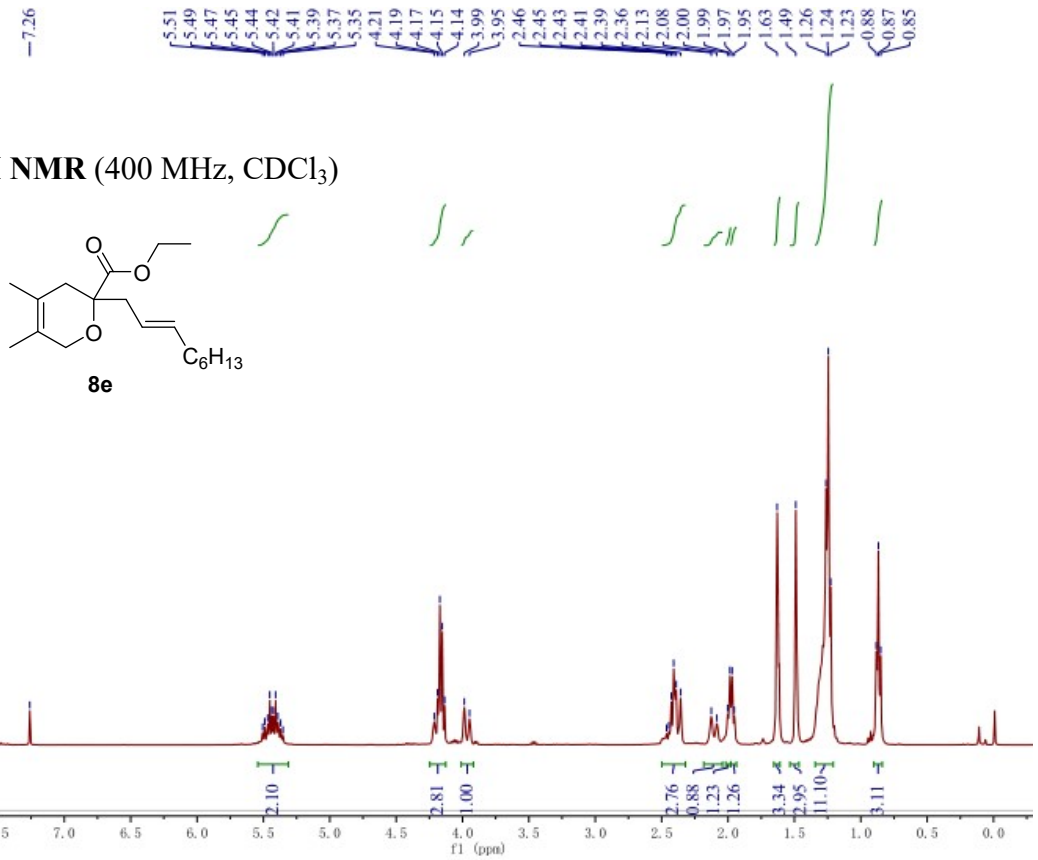
8d

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



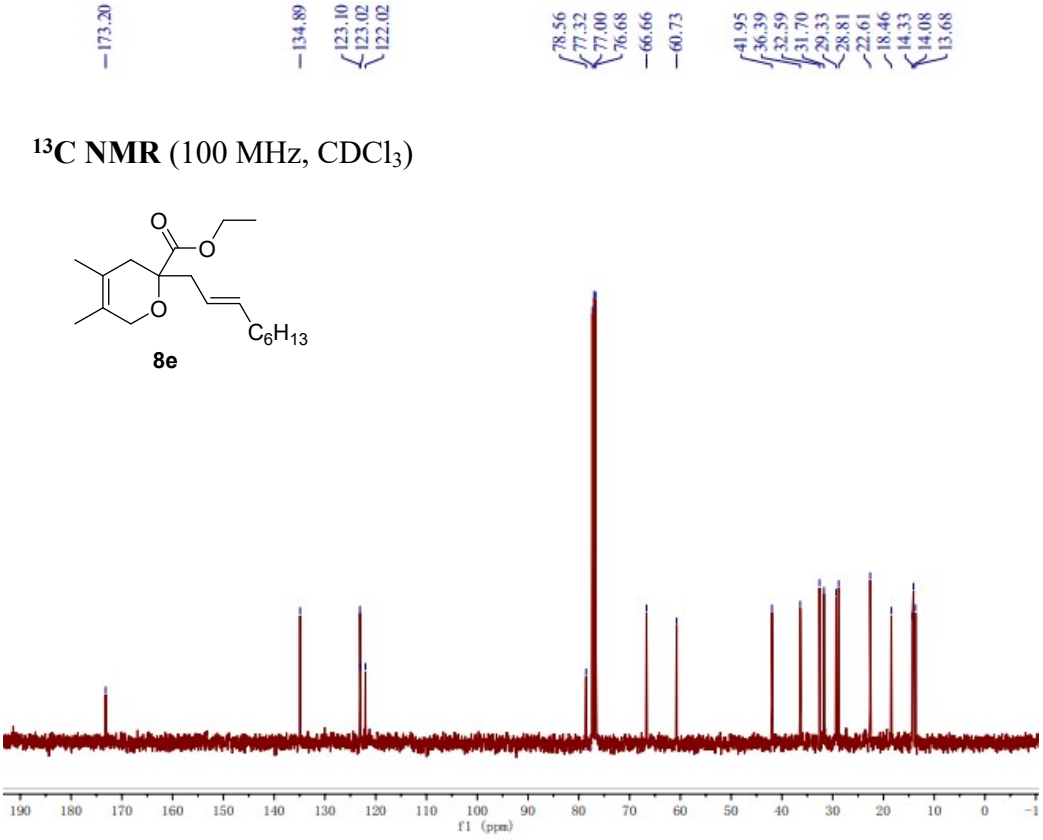
8d

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



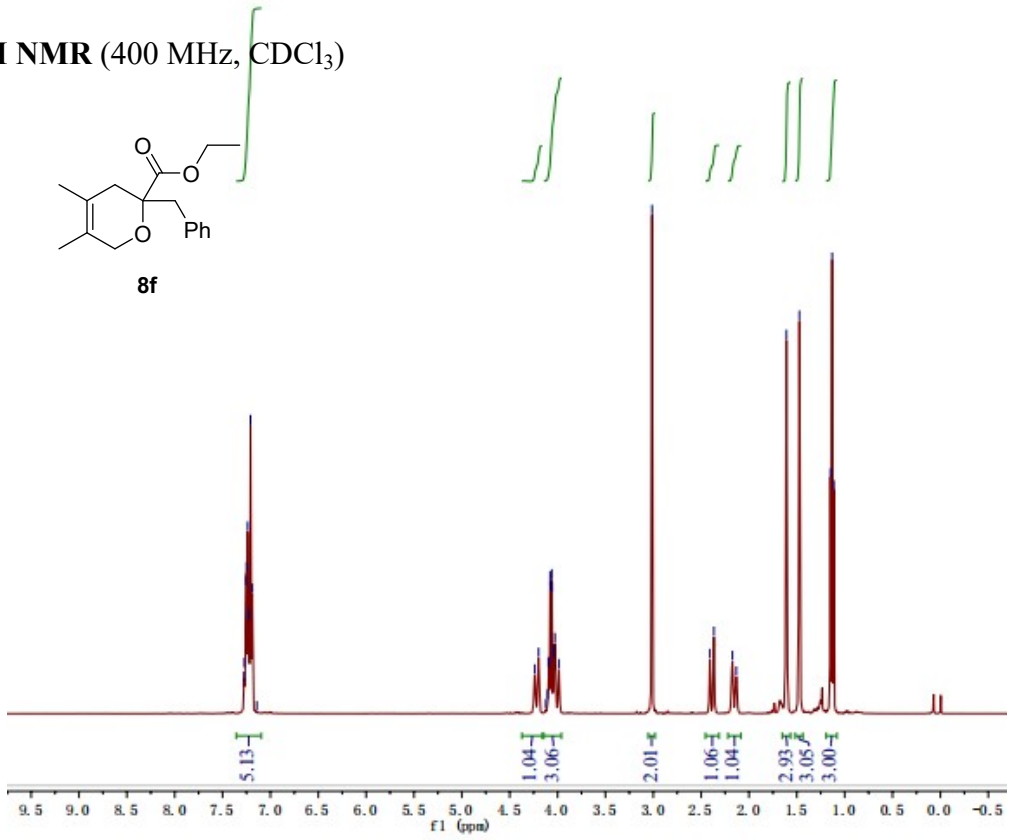
8e

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



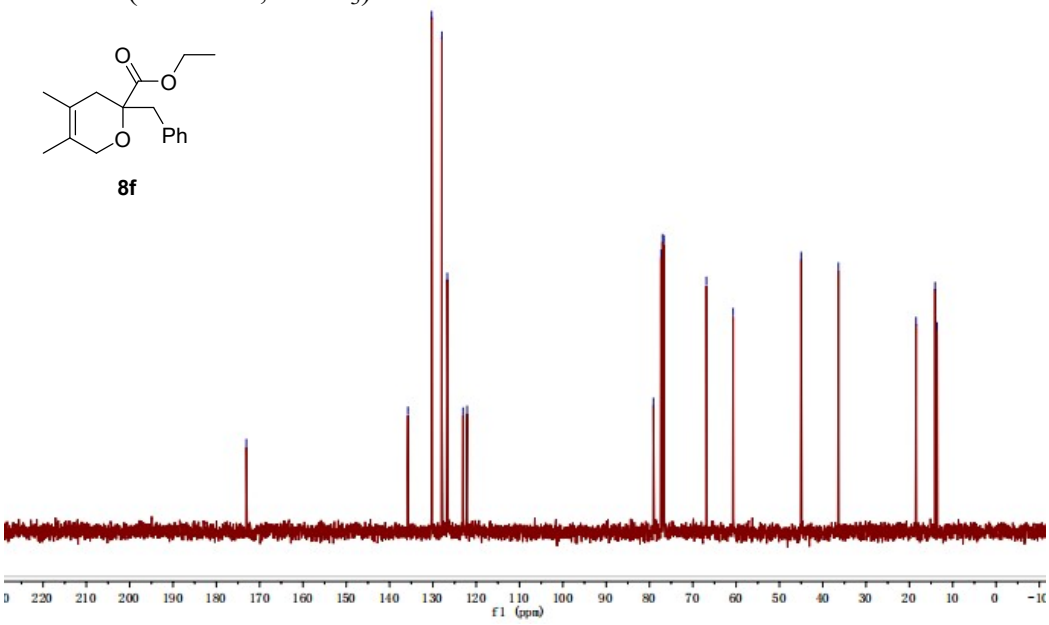
8e

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



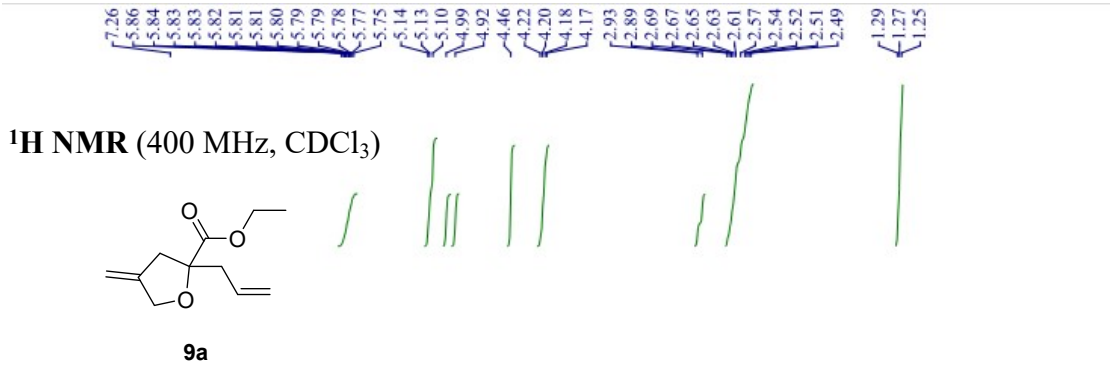
8f

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

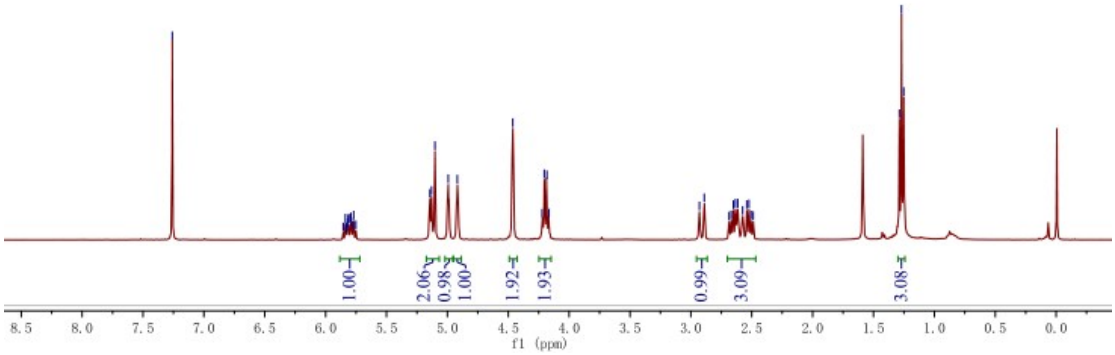


8f

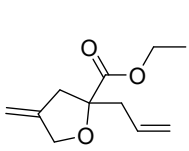
^{1}H NMR (400 MHz, $CDCl_3$)



9a

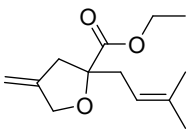


^{13}C NMR (100 MHz, $CDCl_3$)



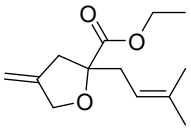
9a

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



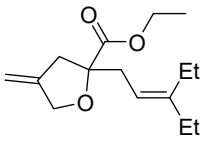
9b

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



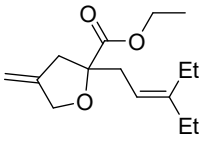
9b

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



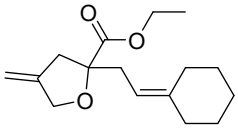
9c

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



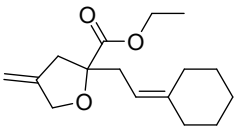
9c

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



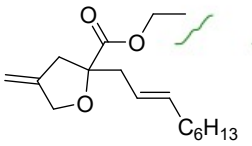
9d

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

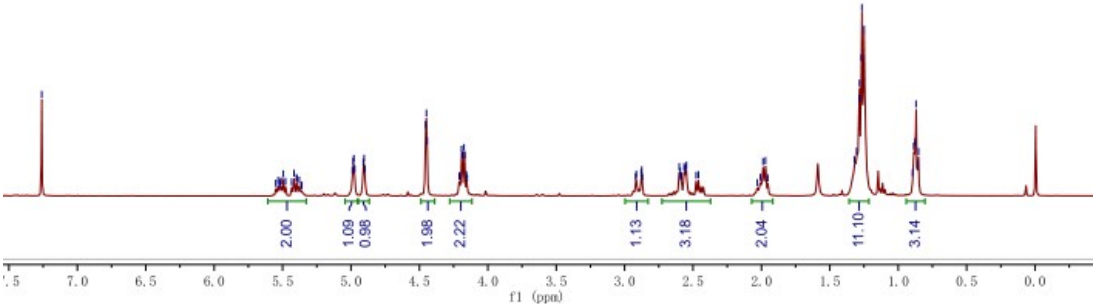


9d

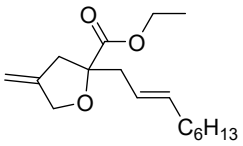
^{13}H NMR (400 MHz, $CDCl_3$)



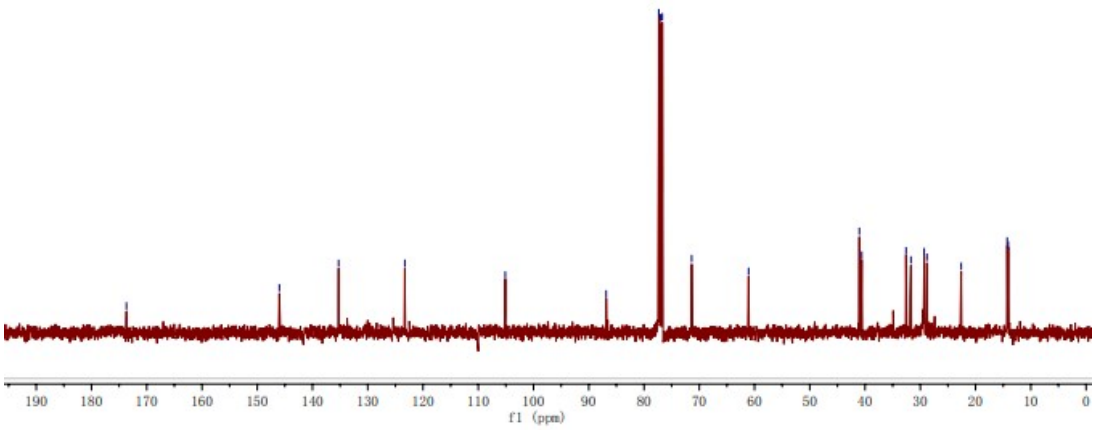
9e



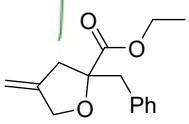
^{13}C NMR (100 MHz, $CDCl_3$)



9e

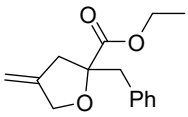


^{1}H NMR (400 MHz, $CDCl_3$)

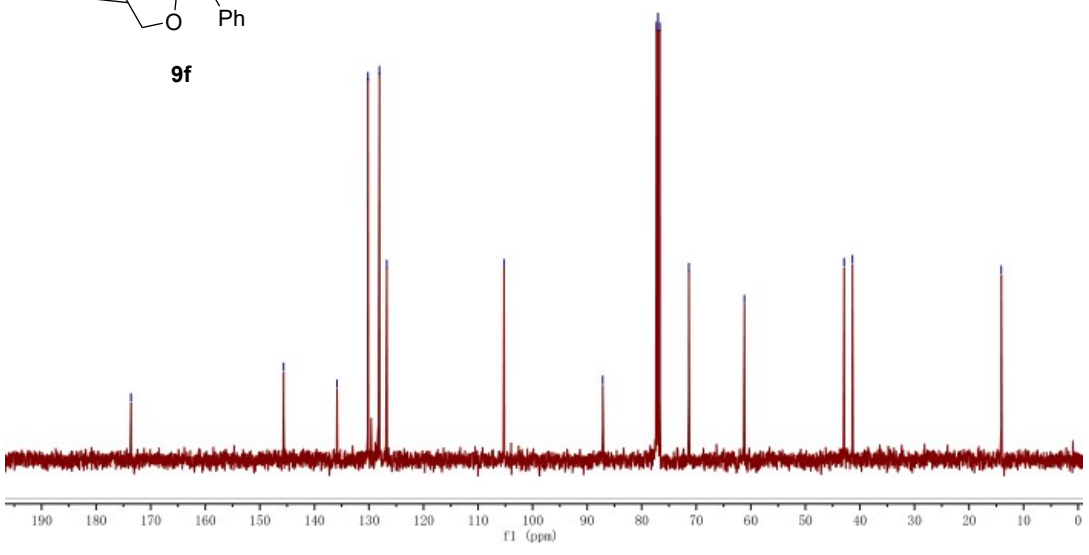


9f

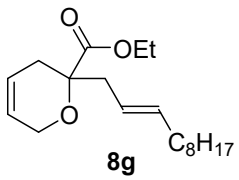
^{13}C NMR (100 MHz, $CDCl_3$)



9f

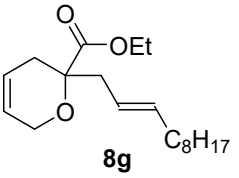


^{1}H NMR (400 MHz, $CDCl_3$)

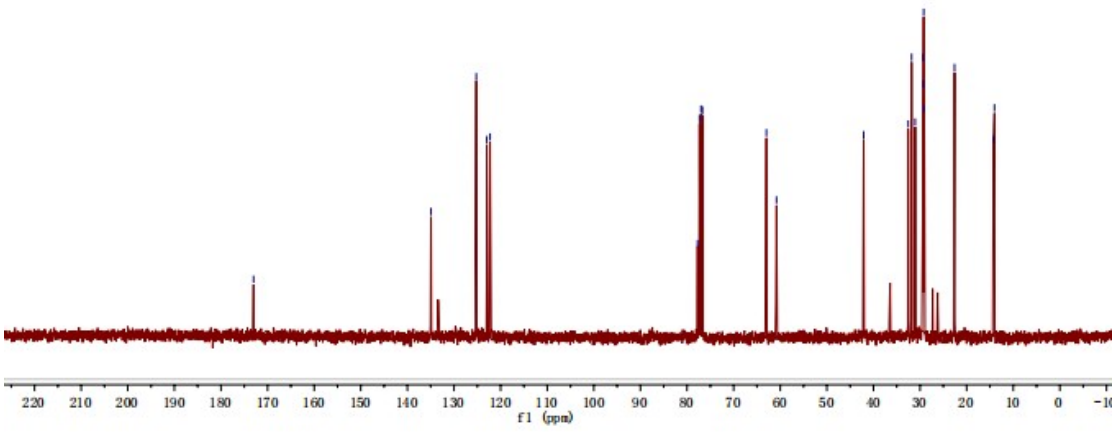


8g

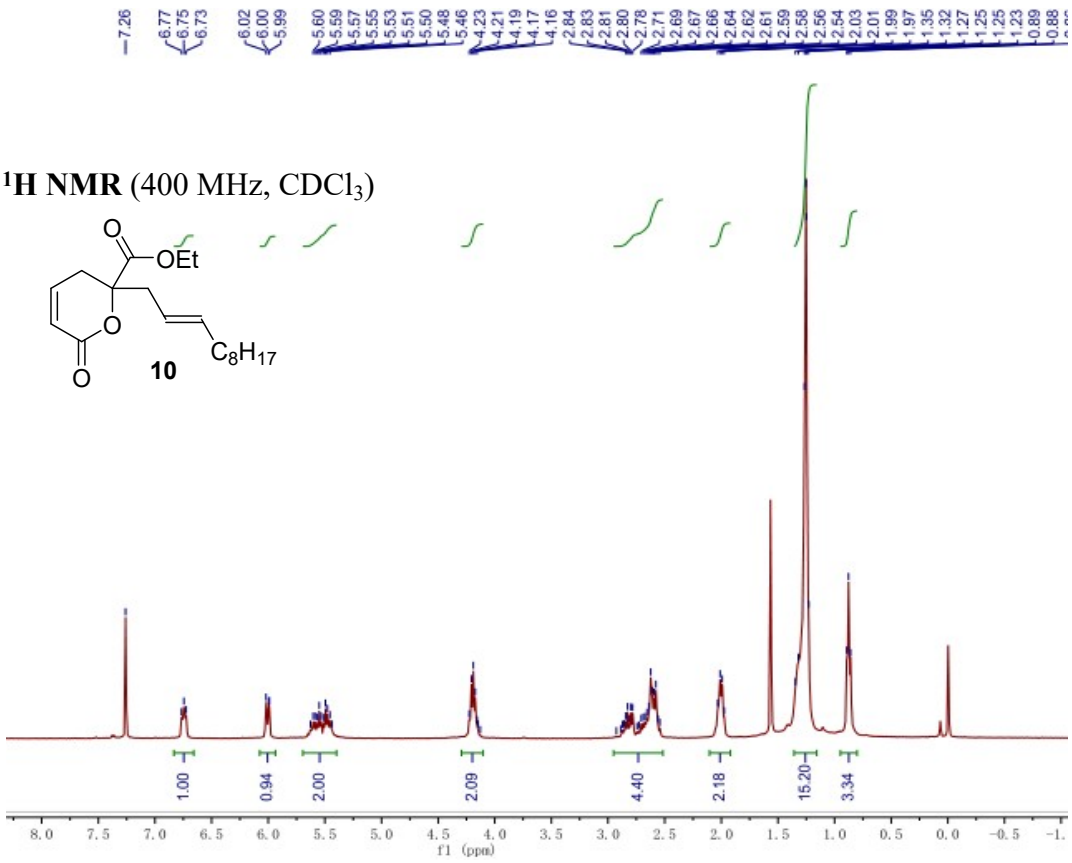
^{13}C NMR (100 MHz, $CDCl_3$)



8g

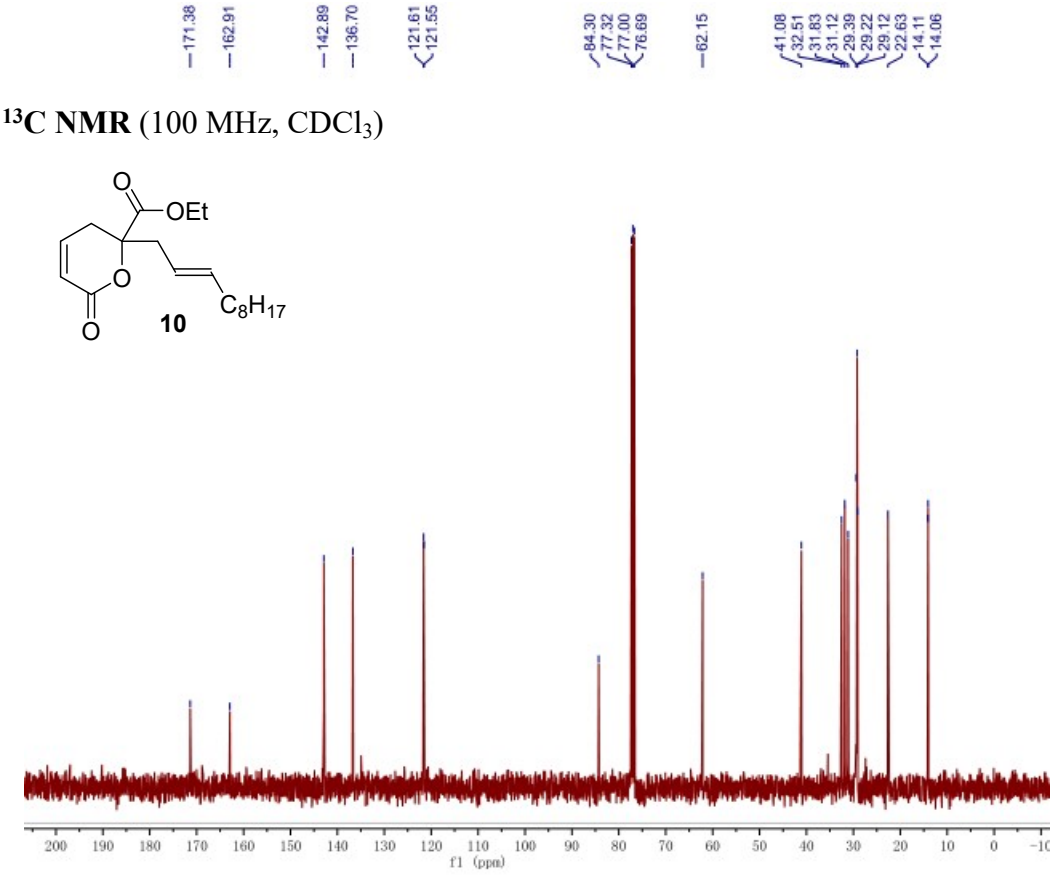


^{1}H NMR (400 MHz, $CDCl_3$)



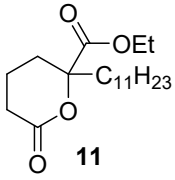
10

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



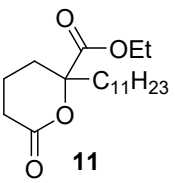
10

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



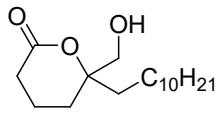
11

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



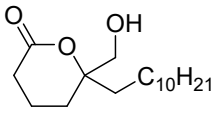
11

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



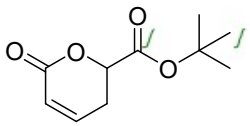
12

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



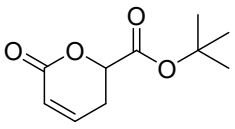
12

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



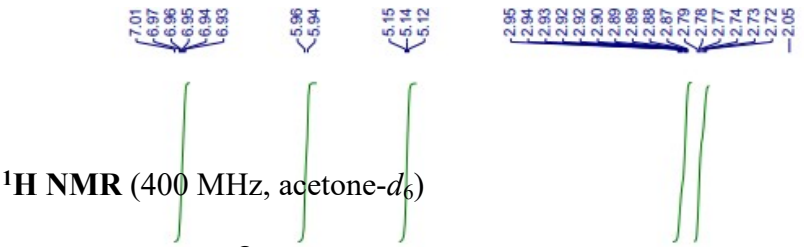
13

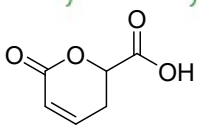
^{13}C NMR (100 MHz, $CDCl_3$)



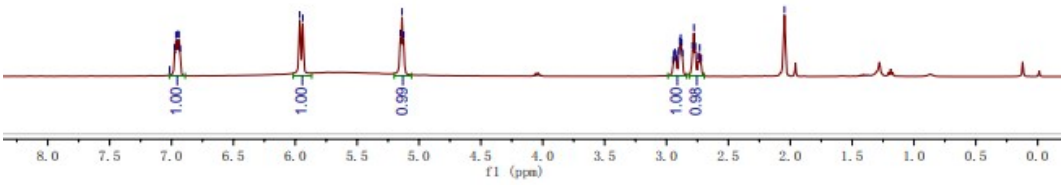
13

^{1}H NMR (400 MHz, acetone-d_6)

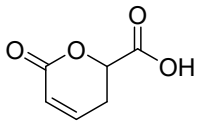




14

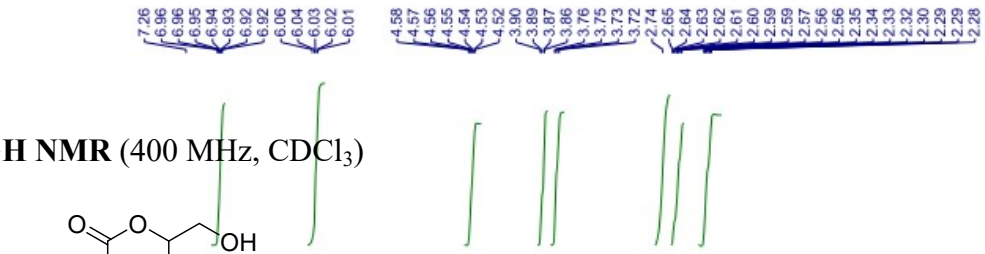


^{13}C NMR (100 MHz, acetone-d_6)

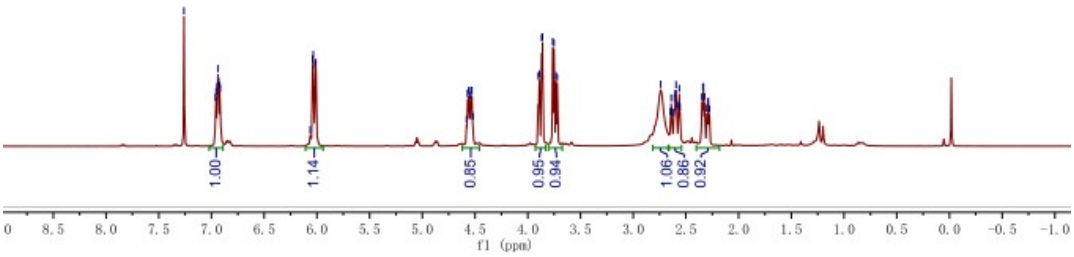


14

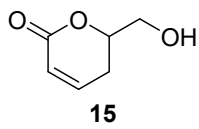
^{1}H NMR (400 MHz, $CDCl_3$)



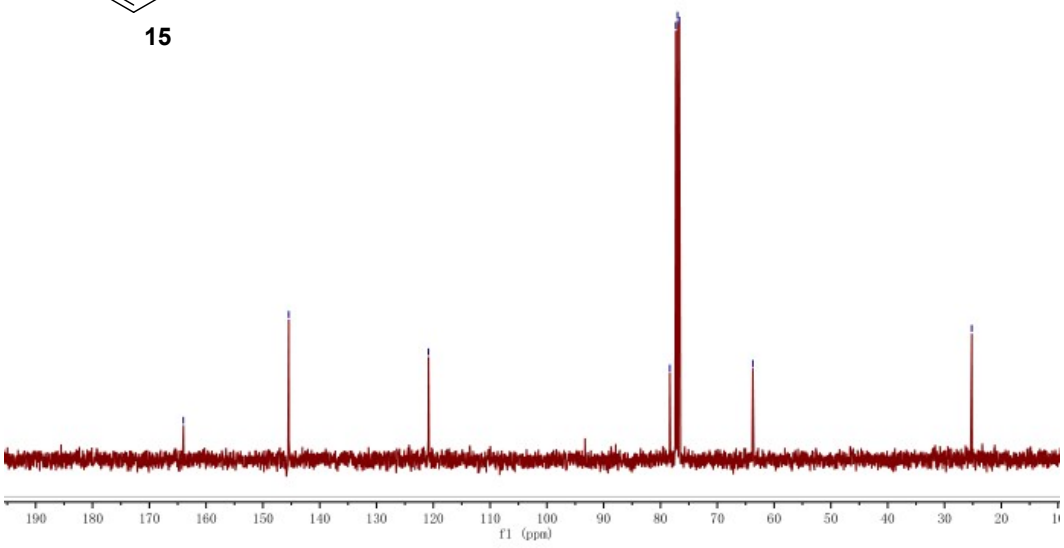
15



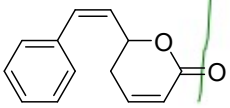
^{13}C NMR (100 MHz, $CDCl_3$)



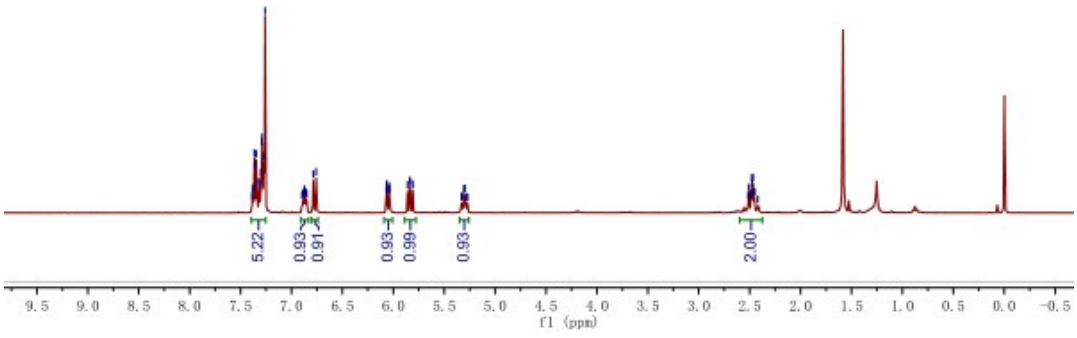
15



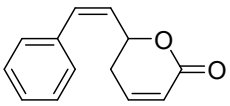
^{1}H NMR (400 MHz, $CDCl_3$)



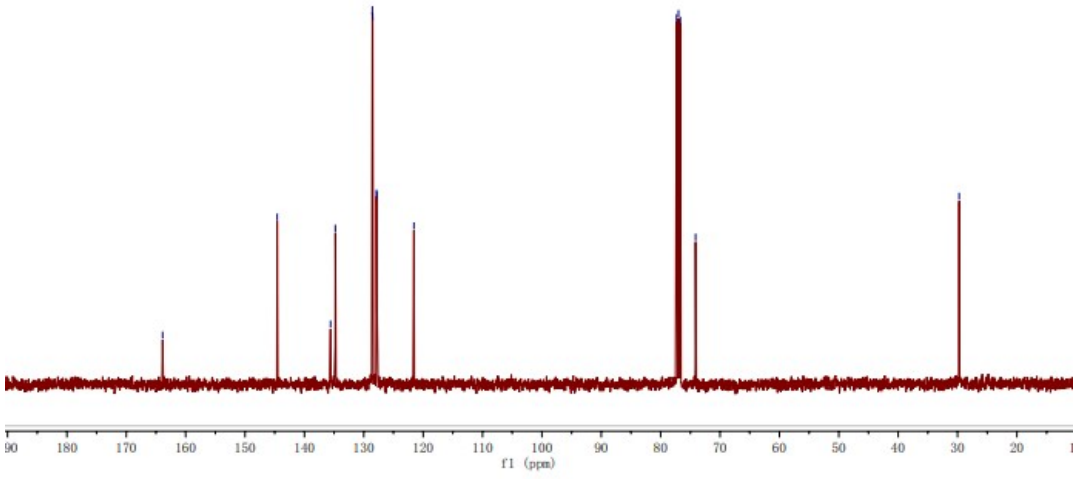
18



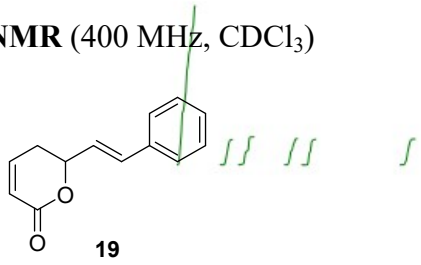
^{13}C NMR (100 MHz, $CDCl_3$)



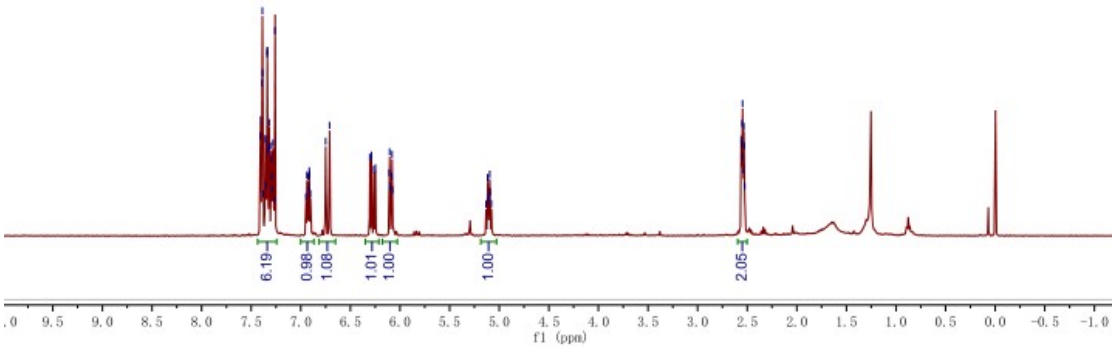
18



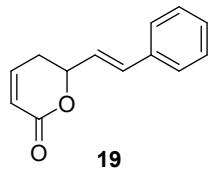
^{1}H NMR (400 MHz, $CDCl_3$)



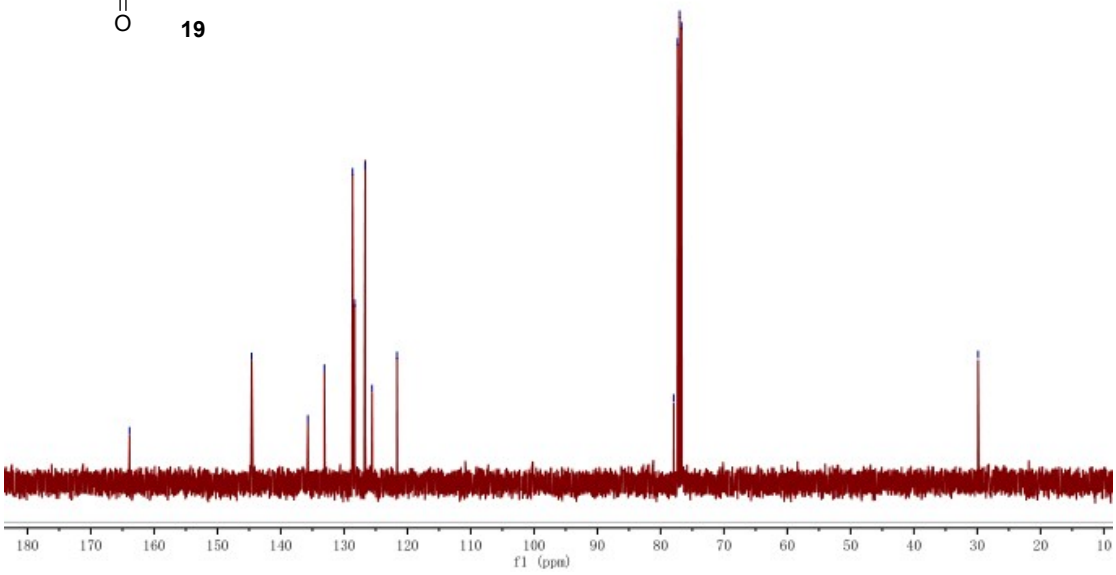
19



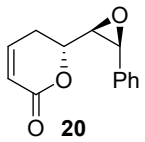
^{13}C NMR (100 MHz, $CDCl_3$)



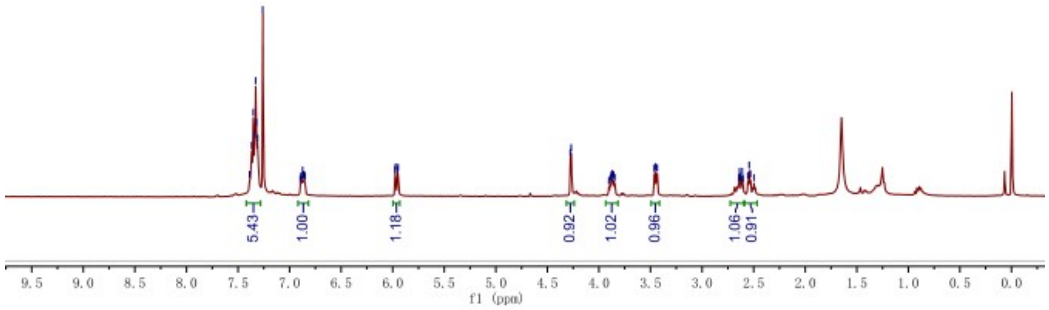
19



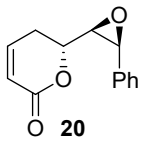
^{1}H NMR (400 MHz, $CDCl_3$)



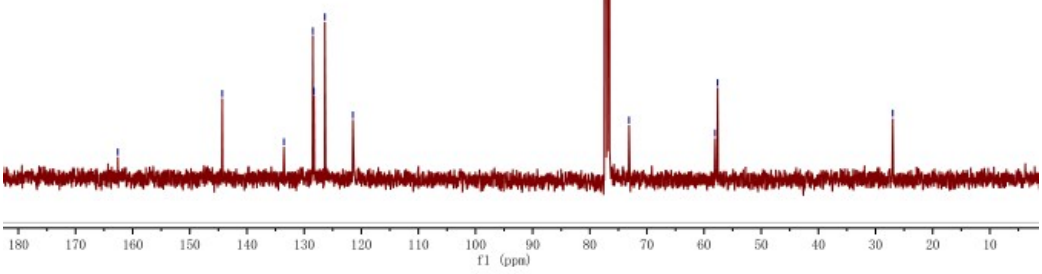
20



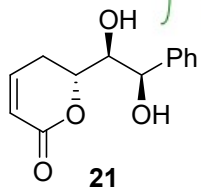
^{13}C NMR (100 MHz, $CDCl_3$)



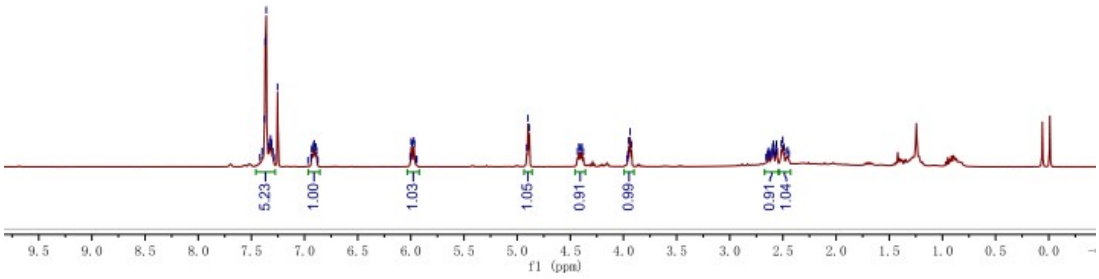
20



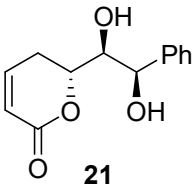
^{1}H NMR (400 MHz, $CDCl_3$)



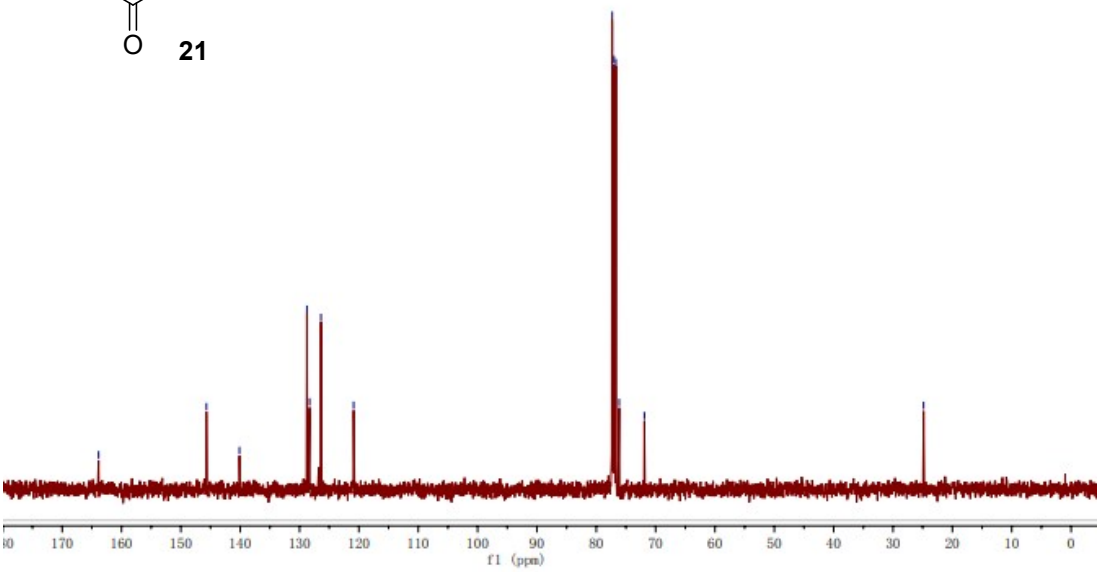
21



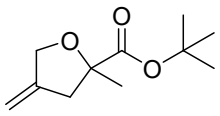
^{13}C NMR (100 MHz, $CDCl_3$)



21

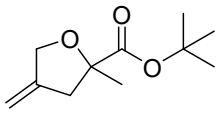


^{1}H NMR (400 MHz, $CDCl_3$)



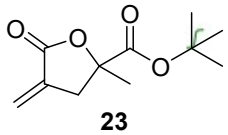
22

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



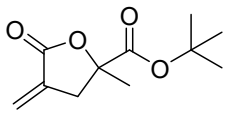
22

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



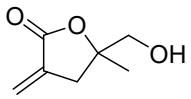
23

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



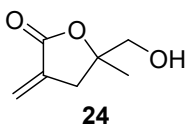
23

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

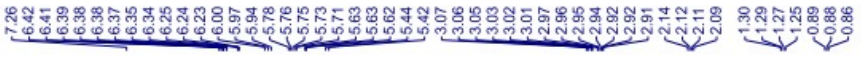


24

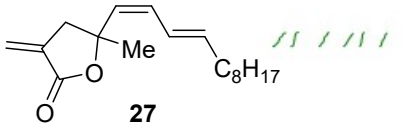
^{13}C NMR (100 MHz, $CDCl_3$)



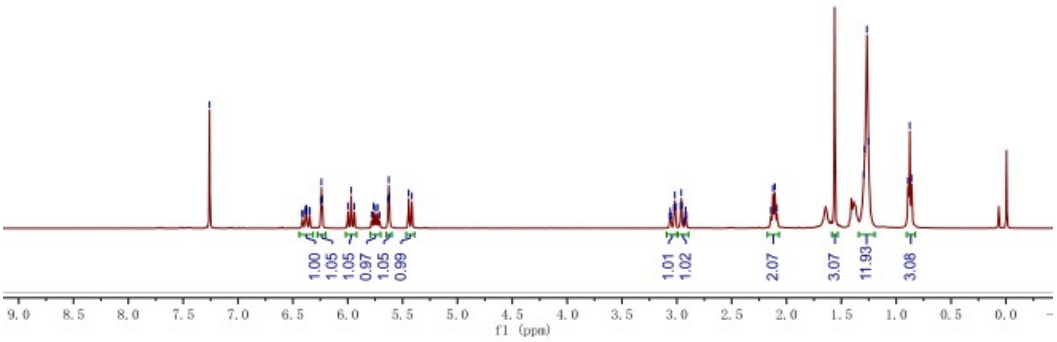
24



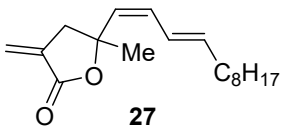
^{1}H NMR (400 MHz, $CDCl_3$)



27

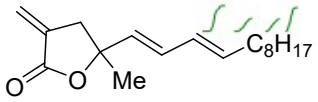


^{13}C NMR (100 MHz, $CDCl_3$)

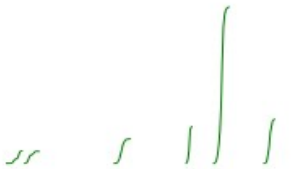


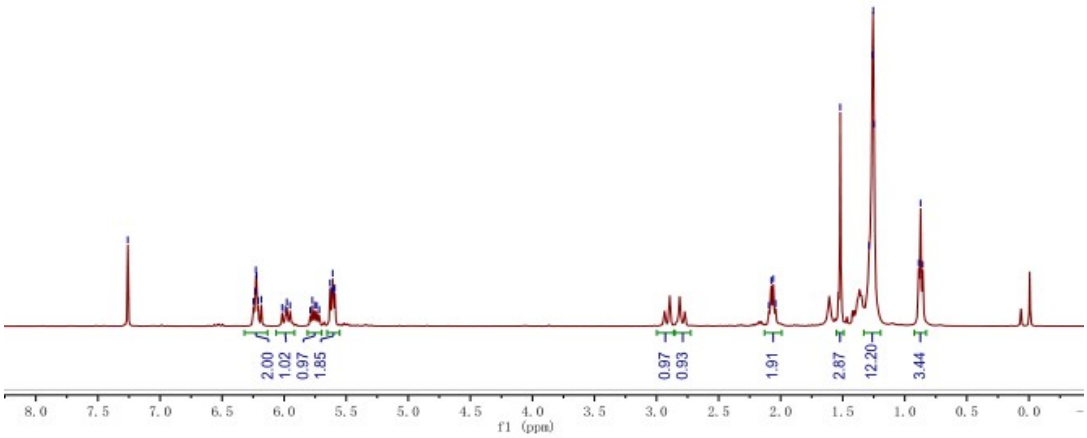
27

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

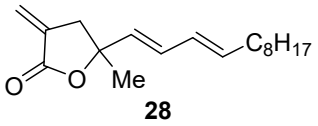


28





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



28