Supporting Information

N-Nosyl-O-Bromoethyl Hydroxylamine Acts as Multifunctional Formaldehyde, Formaldimine, and 1,2-Oxazetidine Surrogate for the C-C and C-O Bond-Forming Reactions

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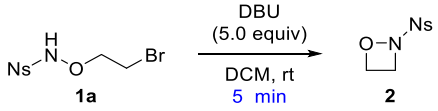
1. General information

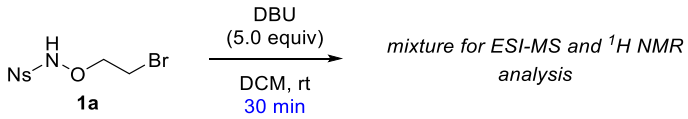
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All solvents employed in the reactions were distilled from appropriate drying agents prior to use. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 GF254 plates. Visualization on TLC was achieved by use of UV light (254 nm). Flash column chromatography was performed using Tsingdao silica gel. ^{1}H and ^{13}C NMR spectra were recorded on Agilent 400MR DD2 (400 MHz) spectrometer or Agilent 600MR DD2 (600 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and tetramethylsilane (TMS) or the residual solvent peak was used as an internal reference: ^{1}H NMR (TMS, δ 0.00; $CDCl_3$, δ 7.26; 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 obtained on a Bruker Daltonics SolariX 7.0 Tesla Fourier Transform Ion Cyclotron Resonance (FT-ICR analyzer) Mass Spectrometer using the electrospray ionization (ESI) technique. Reactions carried out at elevated temperature were heated using an oil bath.

2. Detection of the intermediates by ESI-HRMS and ^{1}H NMR analysis



To a solution of **1a** (33 mg, 0.1 mmol, 1.0 equiv) in DCM (1 mL) was added dropwise of DBU (76 mg, 0.5 mmol, 5.0 equiv) at room temperature. The reaction mixture was stirred at the same temperature for 5 min, then the solution was quenched with saturated NH_4Cl solution (3 mL). The organic layer was separated and the aqueous layer was extracted with DCM (3 mL x 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 3/1) to afford the product 1,2-oxazetidine **2** (15 mg, 60% yield) as a white solid. ^{1}H NMR

(600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.5 Hz, 2H), 8.22 (d, *J* = 8.5 Hz, 2H), 4.78 (t, *J* = 8.2 Hz, 2H), 4.54 (t, *J* = 8.2 Hz, 2H). The spectral data of **2** was consistent with that reported in the literature.[1]



To a solution of **1a** (33 mg, 0.1 mmol, 1.0 equiv) in DCM (1 mL) was added dropwise of DBU (76 mg, 0.5 mmol, 5.0 equiv) at room temperature. After stirring at room temperature for 30 minutes, an aliquot of reaction solution was taken out and diluted with methanol. Then, the mixture was immediately subjected to mass spectra analysis. The ESI-HRMS data was acquired and recorded on a 7 Tesla SolariX FT-ICR mass spectrometer (Bruker Daltonics, Bremen, Germany). By analyzing the data, we assigned the plausible structures of four species **S1-S4** as following (**Figure S1**). They all should derive from a Ns-$NHCH_2OCH_3$ precursor, indicating that the formaldimine [H_2C=N-Ns] intermediate might be formed in the reaction mixture.

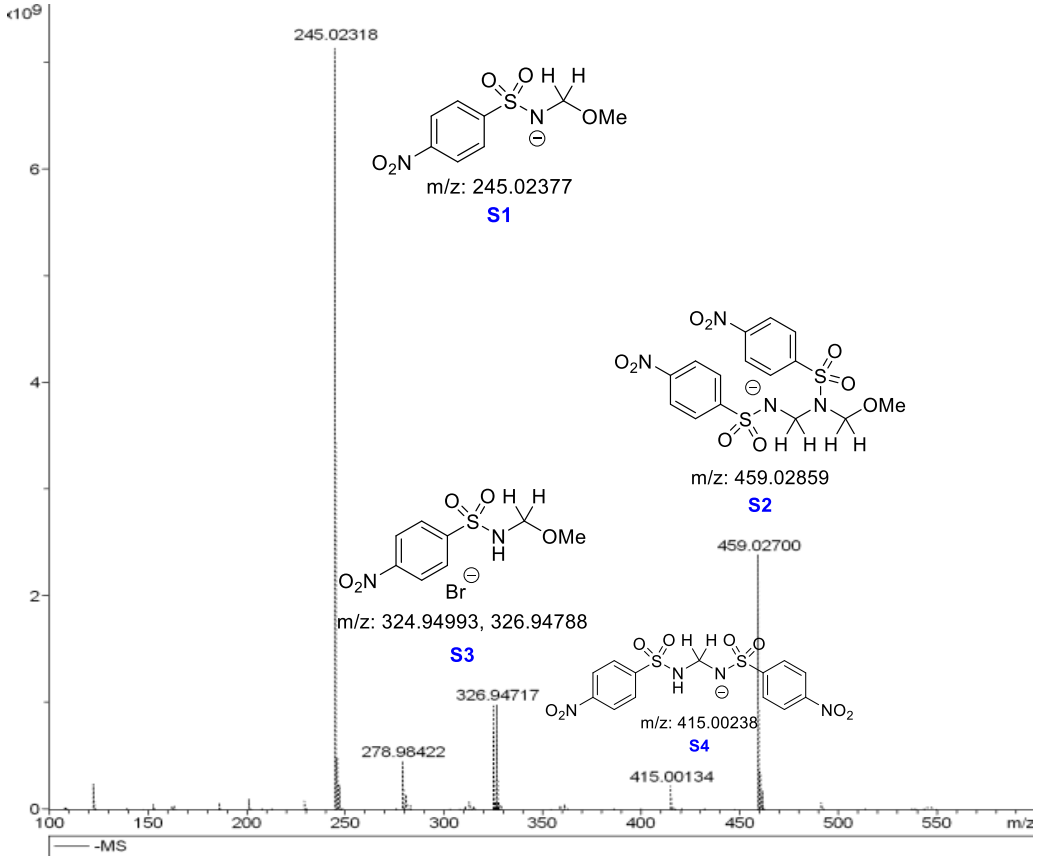


Figure S1. ESI-HRMS data of the reaction mixture (in CH_3OH).

To further confirm the structures of the above **S1-S4**, the reaction mixture was subjected to the mass spectra analysis in CD_3OD solvent (**Figure S2**). Again, the ESI-HRMS data were consistent with the above assigned structures.

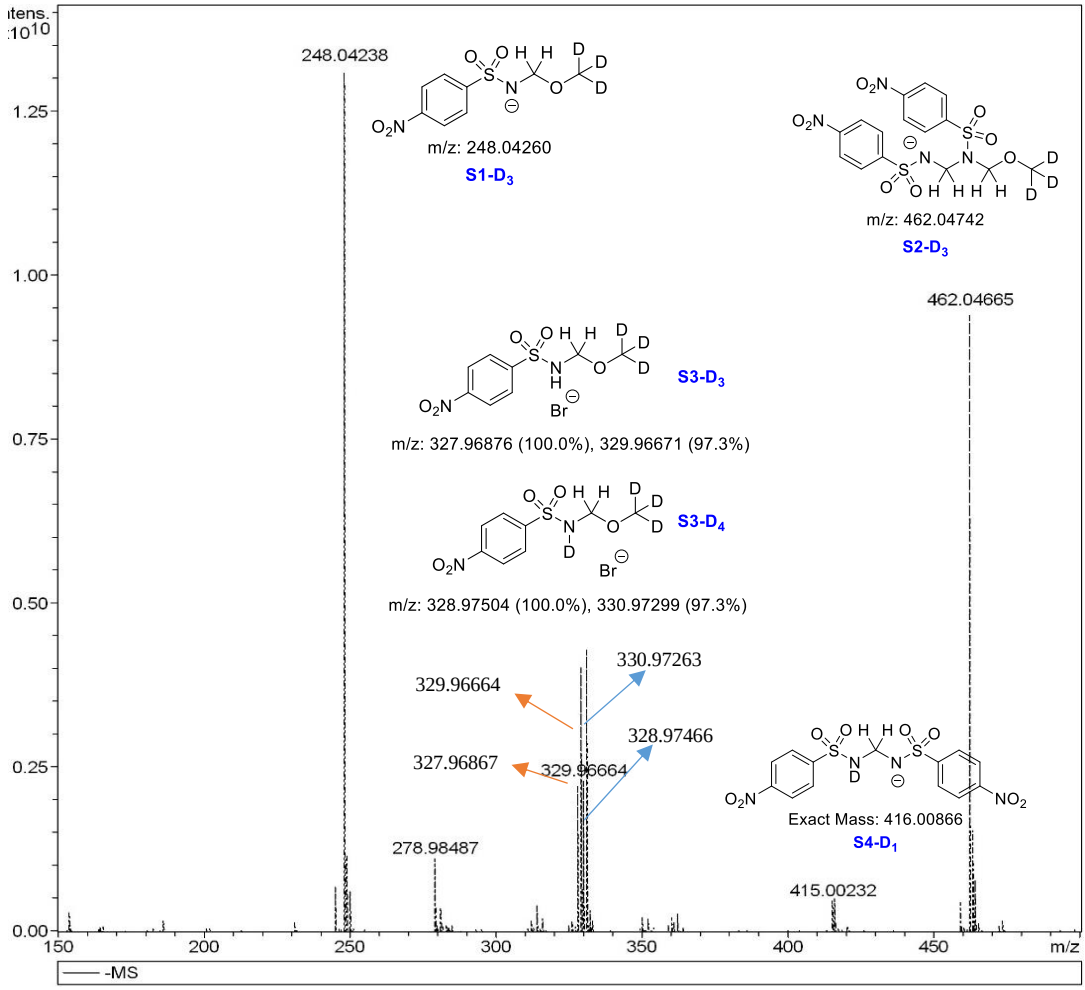


Figure S2. ESI-HRMS data of the reaction mixture (in CD_3OD).

Meanwhile, to gain details of the reaction process, hydroxylamine **1a** (1.0 equiv) and DBU (5.0 equiv) were dissolved in $CDCl_3$. Then the ^1H NMR spectra of the mixture were recorded at 1 min, 5 min, and 30 min, respectively. As shown in **Figure S3**, a large amount of 1,2-oxazetidine **2** was rapidly generated just after 1 min of the reaction, and the starting material **1a** was almost fully converted to compound **2** after 5 min the reaction. However, when the reaction was extended to 30 min, compound **1a** was finally degraded to nosylamide.

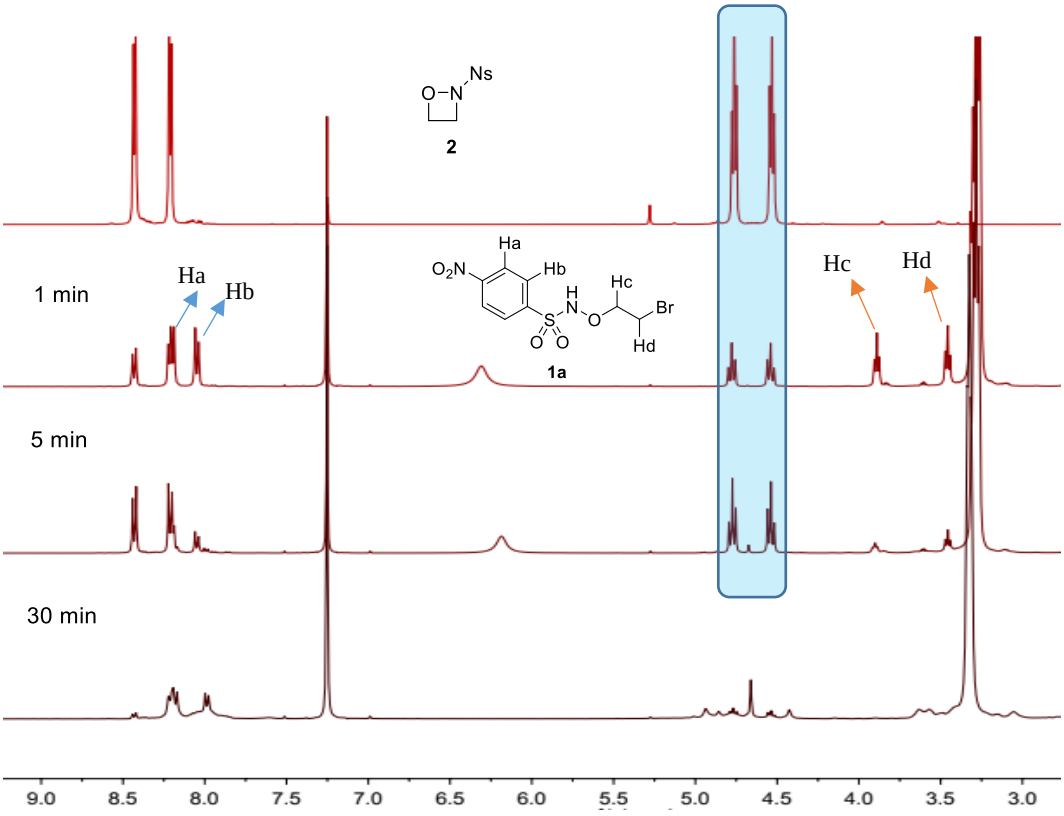


Figure S3. ^{1}H NMR spectra of the reaction mixture (in $CDCl_3$).

The final product nosylamide was isolated and identified by ^{1}H NMR spectra. The whole fragmentation process could also be clearly monitored by TLC method (**Figure S4**).

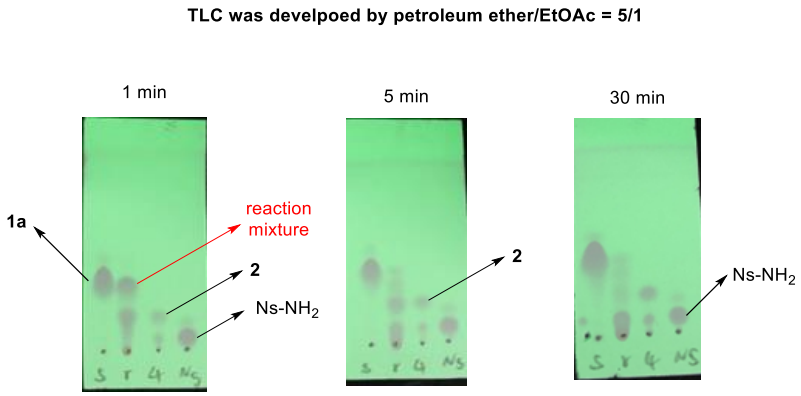
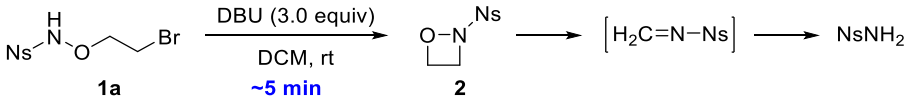


Figure S4. Detection of the intermediates by TLC analysis.

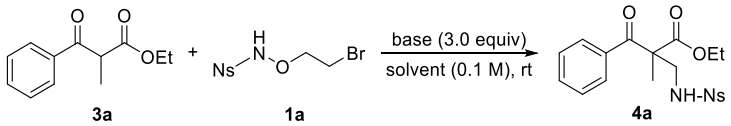
According to the above data and observation, we deduced that *N*-nosyl-*O*-bromoethyl hydroxylamine **1a** rapidly generated the four-membered 1,2-oxazetidine **2** within 5 minutes of the reaction. Then compound **2** probably could in situ generate the formaldimine [H_2C=N-Ns] intermediate in the presence of DBU

base. This intermediate is also highly unstable, which could be finally decomposed to nosylamide.



3. Optimization of the reaction conditions

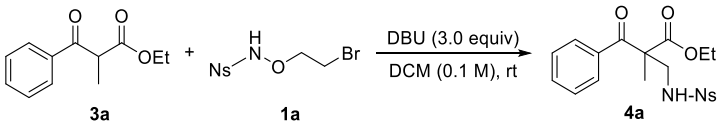
Table S1. Screening of the bases and solvents[a]



entry	Base	solvent	t (h)	yield (%)[b]
1	K_2CO_3 (50%)	DMF	24	47
2	Cs_2CO_3 (50%)	DMF	4	73
3	CsOH (50%)	DMF	4	54
4	K_2CO_3 (s)	DMF	24	35
5	Cs_2CO_3 (s)	DMF	4	71
6	CsOH (s)	DMF	4	60
7	DBU	DMF	1	78
8	TMG	DMF	1	75
9	DBU	DCM	1	85
10	Pyridine	DCM	24	0
11	TEA	DCM	24	0[c]
12	DBU	PhMe	4	51
13	DBU	Ethyl acetate	4	72
14	DBU	THF	4	63
15	DBU	CH_3CN	4	69

[a]Reaction conditions: **1a** (0.10 mmol), **3a** (0.20 mmol) and base (0.30 mmol) in indicated solvent. [b]Isolated yield. [c]1,2-Oxazetidine was formed.

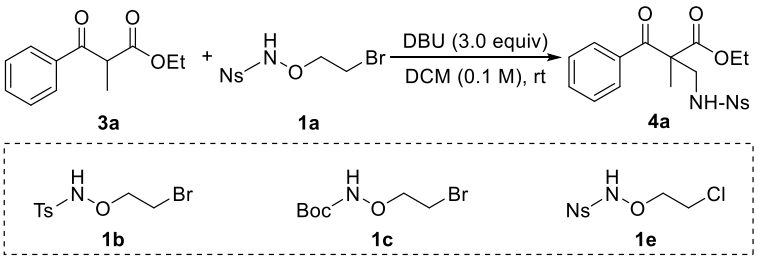
Table S2. Screening of other reaction parameters[a]



entry	**3a**:**1a**	T (°C)	t (h)	yield (%)[b]
1	2.5 : 1	rt	1	84
2	2 : 1	rt	1	85
3	1.5 : 1	rt	1	81
4	1 : 1	rt	1	60
5	1 : 1.5	rt	1	34
6	2 : 1	0	24	68
7	2 : 1	40	1	59

[a]Reaction conditions: **1a**, **3a** and DBU (3.0 equiv) in DCM. [b]Isolated yield.

Table S3. Screening of hydroxylamines[a]



entry	substrates	base	solvent	t (h)	yield (%)[b]
1	**1a**	DBU	DCM	1	85
2	**1b**	DBU	DCM	24	0[c]
3	**1b**	CsOH	DMF	24	0
4	**1b**	^{t}BuOK	THF	24	0[d]
5	**1c**	DBU	DCM	24	0
6	**1c**	CsOH	DMF	24	0
7	**1c**	^{t}BuOK	THF	24	0[c]
8	**1e**	DBU	DCM	1	72
9	**1e**	CsOH	DMF	1	46
10	**1e**	^{t}BuOK	THF	24	0[d]

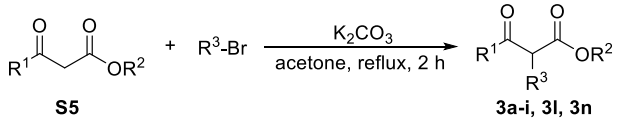
[a]Reaction conditions: **1** (0.10 mmol), **3a** (0.2 mmol) and base (0.30 mmol) in indicated solvent. [b]Isolated yield. [c]1,2-Oxazetidine was formed. [d]Decomposition of the starting materials.

4. General procedure for the preparation of nucleophile substrates

4.1. General procedure for the preparation of *β*-keto esters 3

Compounds **3j**, **3m**, **3p** are commercial available. Other known carbonyl substrates were prepared as following procedures.

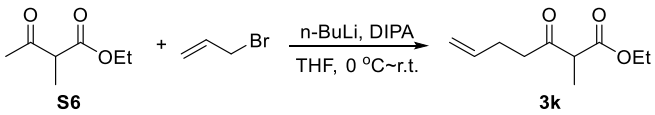
4.1.1 Method A: preparation of *β*-keto esters 3a-i, 3l, and 3n[2]



A mixture of **S5** (3 ~ 20 mmol, 1.0 equiv) and anhydrous K_2CO_3 (1.5 equiv) in acetone was stirred at room temperature for five minutes. Then, methyl iodide or corresponding bromide (2.0 equiv) was added carefully. The reaction mixture was heated to refluxed in an oil bath until the completion of the reaction as monitored by TLC. After the mixture was cooled to room temperature, the precipitate was filtered off and the solvent was removed under vacuum. The crude mixture was purified by column chromatography (petroleum ether/EtOAc = 200/1 ~ 20/1) to afford the

products **3a-i**, **3l** and **3n** in 48-92% yields.

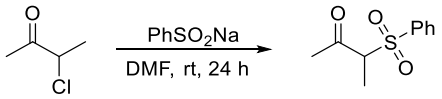
4.1.2 Method B: preparation of *β*-keto ester 3k[3]



S6 **3k**

Diisopropylamine (22 mmol, 2.2 equiv) was dissolved in dry tetrahydrofuran (40 mL) and the solution cooled to 0 ℃. n-Butyllithium (22 mmol, 2.2 equiv., 2.5 M solution in n-hexane) was slowly added and the reaction mixture was stirred at room temperature for 30 minutes and afterwards cooled to 0 ℃. *β*-ketoester **S6** (10 mmol, 1.0 equiv) was dissolved in dry tetrahydrofuran (5 mL) and slowly added to the solution. The reaction mixture was stirred for 15 minutes after which allyl bromide (12 mmol, 1.2 equiv) was added. The solution was allowed to stir at 0 ℃ for 30 minutes and at room temperature for 90 minutes. The reaction mixture was quenched with saturated ammonium chloride (20 mL) and extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo. The crude mixture was purified by column chromatography (petroleum ether/EtOAc = 50/1) to afford the product **3k** as a colorless oil (550 mg, 30% yield).

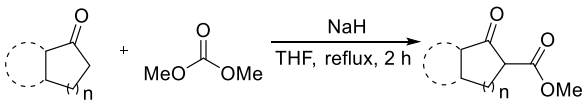
4.1.3 Method C: preparation of *β*-keto ester 3o[4]



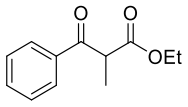
S7 **3o**

To a solution of α-haloketone **S7** (10 mmol, 1.0 equiv) in DMF (20 mL) was added sodium benzenesulfinate (10 mmol, 1.0 equiv) in one portion and the reaction mixture was stirred at room temperature for 24 h. The reaction was stopped by the addition of water (30 mL) and extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (20 mL), dried with $NaSO_4$ and the solvent was removed under reduced pressure. The crude mixture was purified by column chromatography (petroleum ether/EtOAc = 10/1) to afford the product **3o** as a white solid (1.71 g, 81% yield).

4.1.4 Method D: preparation of *β*-keto esters 3q-u[5]

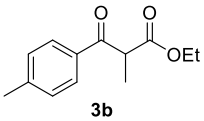


To a suspension of NaH (2.1 equiv) in THF (50 mL) was added dimethyl carbonate (5.0 equiv) at room temperature. The mixture was stirred for 5 minutes and then ketone **S8** (3 ~ 20 mmol, 1.0 equiv) in THF (30 mL) was added dropwise. The reaction mixture was heated to refluxed in an oil bath until the completion of the reaction as monitored by TLC. The resulting mixture was then cooled to 0 ℃ and 1 M HCl was added until the solution became neutral. The mixture was then poured into water (30 mL) and extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuum. The crude mixture was purified by column chromatography (petroleum ether/EtOAc = 200/1 ~ 100/1) to afford the products **3q-u** in 70-88% yields.



3a

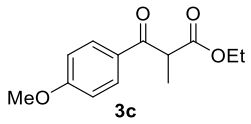
Following the general method A, **3a** was obtained by flash column chromatography (petroleum ether/EtOAc = 200/1) as a colorless oil (1.9 g, 92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 1.44 (d, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H). The spectral data of **3a** was consistent with that reported in the literature.[6]



3b

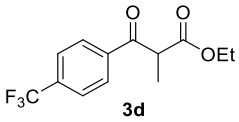
Following the general method A, **3b** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (363 mg, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz,

2H), 4.35 (q, *J* = 7.1 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 1.47 (d, *J* = 7.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). The spectral data of **3b** was consistent with that reported in the literature.[6]



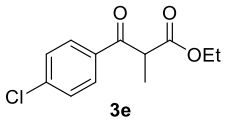
3c

Following the general method A, **3c** was obtained by flash column chromatography (petroleum ether/EtOAc = 50/1) as a colorless oil (1.07 g, 91% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 1.47 (d, *J* = 7.1 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). The spectral data of **3c** was consistent with that reported in the literature.[7]



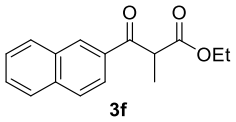
3d

Following the general method A, **3d** was obtained by flash column chromatography (petroleum ether/EtOAc = 30/1) as a colorless oil (1.02 g, 74% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.50 (d, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H). The spectral data of **3d** was consistent with that reported in the literature.[8]



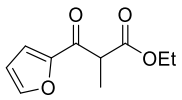
3e

Following the general method A, **3e** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (323 mg, 67% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 4.31 (q, *J* = 7.0 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.48 (d, *J* = 7.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). The spectral data of **3e** was consistent with that reported in the literature.[9]



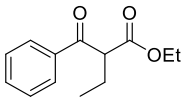
3f

Following the general method A, **3f** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (910 mg, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.04 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.94 – 7.85 (m, 2H), 7.65 –7.54 (m, 2H), 4.54 (q, *J* = 7.1 Hz, 1H), 4.21 – 4.11 (m, 2H), 1.56 (d, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). The spectral data of **3f** was consistent with that reported in the literature.[10]



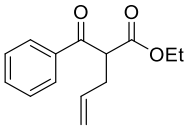
3g

Following the general method A, **3g** was obtained by flash column chromatography (petroleum ether/EtOAc = 20/1) as a colorless oil (456 mg, 86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 – 7.57 (m, 1H), 7.30 – 7.24 (m, 1H), 6.55 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.22 – 4.08 (m, 3H), 1.46 (d, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H). The spectral data of **3g** was consistent with that reported in the literature.[6]



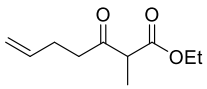
3h

Following the general method A, **3h** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (1.9 g, 86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 9.3 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 4.25 – 4.09 (m, 3H), 2.09 – 1.98 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H). The spectral data of **3h** was consistent with that reported in the literature.[9]



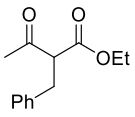
3i

Following the general method A, **3i** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (3.3 g, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 5.88 – 5.73 (m, 1H), 5.16 – 4.96 (m, 2H), 4.39 (t, *J* = 7.2 Hz, 1H), 4.17 – 4.09 (m, 2H), 2.83 – 2.70 (m, 2H), 1.16 (t, *J* = 7.1 Hz, 3H). The spectral data of **3i** was consistent with that reported in the literature.[10]



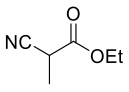
3k

Following the general method B, **3k** was obtained by flash column chromatography (petroleum ether/EtOAc = 50/1) as a colorless oil (550 mg, 30% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.91 – 5.69 (m, 1H), 5.08 – 4.94 (m, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.51 (q, *J* = 7.1 Hz, 1H), 2.76 – 2.52 (m, 2H), 2.42 – 2.25 (m, 2H), 1.33 (d, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). The spectral data of **3k** was consistent with that reported in the literature.[3]



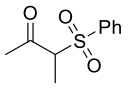
3l

Following the general method A, **3l** was obtained by flash column chromatography (petroleum ether/EtOAc = 50/1) as a colorless oil (1.25 g, 57% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.14 (m, 5H), 4.14 (q, *J* = 7.7 Hz, 2H), 3.78 (t, *J* = 7.6 Hz, 1H), 3.16 (d, *J* = 7.7 Hz, 2H), 2.18 (s, 3H), 1.19 (t, *J* = 7.7 Hz, 3H). The spectral data of **3l** was consistent with that reported in the literature.[11]



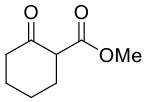
3n

Following the general method A, **3n** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (621 mg, 48% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.27 (q, *J* = 7.1 Hz, 2H), 3.54 (q, *J* = 7.4 Hz, 1H), 1.59 (d, *J* = 7.4 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). The spectral data of **3n** was consistent with that reported in the literature.[12]



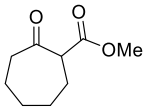
3o

Following the general method C, **3o** was obtained by flash column chromatography (petroleum ether/EtOAc = 10/1) as a white solid (1.71 g, 81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 4.16 (q, *J* = 7.0 Hz, 1H), 2.41 (s, 3H), 1.37 (d, *J* = 6.9 Hz, 3H). The spectral data of **3o** was consistent with that reported in the literature.[4]



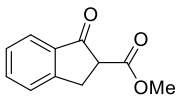
3q

Following the general method D, **3q** was obtained by flash column chromatography (petroleum ether/EtOAc = 200/1) as a colorless oil (2.3 g, 74% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.16 (s, 1H), 3.75 (s, 3H), 2.32 – 2.17 (m, 3H), 1.76 – 1.54 (m, 5H). The spectral data of **3q** was consistent with that reported in the literature.[13]



3r

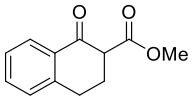
Following the general method D, **3r** was obtained by flash column chromatography (petroleum ether/EtOAc = 200/1) as a colorless oil (357 mg, 70% yield, keto/enol form = 2.8/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.65 (s, 0.26H), 3.75 – 3.68 (m, 3H), 3.54 (dd, *J* = 10.4, 4.0 Hz, 0.7H), 2.68 – 2.50 (m, 1.2H), 2.46 – 2.31 (m, 1.21H), 2.16 – 2.03 (m, 0.73H), 2.01 – 1.76 (m, 3H), 1.77 – 1.65 (m, 0.75H), 1.65 – 1.51 (m, 1.27H), 1.52 – 1.35 (m, 2H). The spectral data of **3r** was consistent with that reported in the literature.[13]



3s

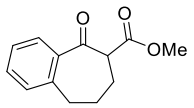
Following the general method D, **3s** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a brown solid (1.56 g, 82%

yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.3 Hz, 1H), 3.80 – 3.69 (m, 4H), 3.60 – 3.47 (m, 1H), 3.37 (dd, *J* = 17.3, 8.3 Hz, 1H). The spectral data of **3s** was consistent with that reported in the literature.[14]



3t

Following the general method D, **3t** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a pale yellow oil (3.6 g, 88% yield, keto/enol form = 1/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.41 (s, 0.5H), 8.04 (d, *J* = 7.7 Hz, 0.58H), 7.85 – 7.75 (m, 0.49H), 7.49 (t, *J* = 7.5 Hz, 0.61H), 7.37 – 7.21 (m, 2H), 7.17 (d, *J* = 7.2 Hz, 0.42H), 3.82 (s, 1.4H), 3.78 (s, 1.6H), 3.63 (dd, *J* = 10.6, 4.6 Hz, 0.49H), 3.13 – 2.93 (m, 1.26H), 2.81 (t, *J* = 7.6 Hz, 1H), 2.62 – 2.42 (m, 1.43H), 2.43 – 2.30 (m, 0.52H). The spectral data of **3t** was consistent with that reported in the literature.[14]

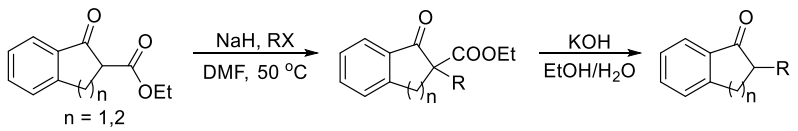


3u

Following the general method D, **3u** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a pale yellow oil (471 mg, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.61 (s, 1H), 7.62 (dd, *J* = 6.5, 2.5 Hz, 1H), 7.39 – 7.28 (m, 2H), 7.25 – 7.17 (m, 1H), 3.82 (s, 1.44H), 3.78 (s, 1.56H),2.64 (t, *J* = 6.6 Hz, 2H), 2.19 – 2.02 (m, 4H). The spectral data of **3u** was consistent with that reported in the literature.[14]

4.2 General procedure for the preparation of *α*-substituted ketones 5

4.2.1 Method E: preparation of *α*-substituted ketones 5a-b and 5d-i[15]



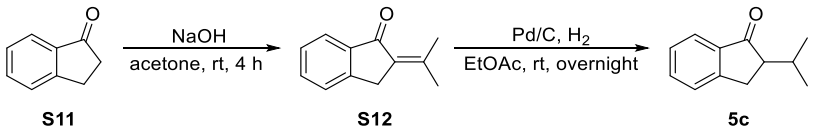
S9 **S10** **5a-b, 5d-i**

To a solution of **S9** (5 ~ 23 mmol, 1.0 equiv) in dry DMF (12 mL) was added

NaH (60% in oil, 10 mmol, 2.0 equiv), the solution was stirred at room temperature for 30 minutes and methyl iodide (15 mmol, 3.0 equiv) was added. The reaction was stirred at 50 ℃ in an oil bath for 3h. After completion, the reaction mixture was cooled, quenched with a saturated NH_4Cl aqueous solution (15 mL) and the product was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was used in the next step without further purification.

The crude **S10** was dissolved in EtOH/H_2O (5/1, 22 mL). After adding KOH (12.5 mmol, 2.5 equiv), the reaction mixture was heated to reflux in an oil bath for 2 hours. The residue was neutralized with a saturated NH_4Cl aqueous solution (10 mL), the volatiles were removed under vacuum, and the resulting aqueous layer was extracted with EtOAc (20 mL× 3). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash chromatography (petroleum ether/EtOAc = 300/1 ~ 100/1) to afford **5a-b, 5d-i** in 30-81% overall yields.

4.2.2 Method F: preparation of α-substituted ketone 5c[16]

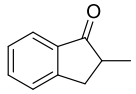


S11 **S12** **5c**

To a solution of **S11** (1.32 g, 10.0 mmol) in anhydrous acetone (20 mL), NaOH (132 mg, 3.3 mmol) was added. The mixture was stirred at room temperature for 4 h and then neutralized with 1 N HCl. Acetone was removed by distillation, after adding water (20 mL) and EtOAc (30 mL), the mixture was partitioned. The organic layer was washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuum. The residue was purified by flash chromatography (petroleum ether/EtOAc = 80/1) to afford **S12**.

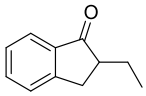
To a solution of **S12** (1.44 g, 10 mmol) in EtOAc (20 mL), 10% Pd/C (20% weight of compound **S12**) was added. The mixture was stirred overnight under a hydrogen atmosphere at room temperature. Insoluble materials were removed by

filtration and washed with EtOAc. The filtrate was evaporated to dryness under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc = 30/1) to afford **5c** in 35% overall yield.



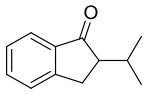
5a

Following the general method E, **5a** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (314 mg, 43% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 3.43 – 3.32 (m, 1H), 2.76 – 2.63 (m, 2H), 1.29 (dd, *J* = 7.2, 1.2 Hz, 3H). The spectral data of **5a** was consistent with that reported in the literature.[17]



5b

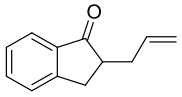
Following the general method E, **5b** was otained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (320 mg, 40% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 3.32 (dd, *J* = 17.2, 7.9 Hz, 1H), 2.82 (dd, *J* = 17.2, 3.9 Hz, 1H), 2.67 – 2.57 (m, 1H), 2.05 – 1.90 (m, 1H), 1.60 – 1.46 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H). The spectral data of **5b** was consistent with that reported in the literature.[17]



5c

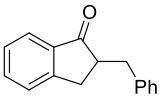
Following the general method F, **5c** was obtained by flash column chromatography (petroleum ether/EtOAc = 30/1) as a colorless oil (610 mg, 35% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.0 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 1H), 3.10 (dd, *J* = 17.4, 8.1 Hz, 1H), 2.89 (dd, *J* = 17.5, 4.0 Hz, 1H), 2.62 (dt, *J* = 8.3, 4.2 Hz, 1H), 2.46 – 2.30 (m, 1H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H). The spectral data of **5c** was

consistent with that reported in the literature.[16]



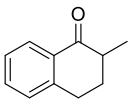
5d

Following the general method E, **5d** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (258 mg, 30% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 5.87 – 5.72 (m, 1H), 5.16 – 5.00 (m, 2H), 3.28 (dd, *J* = 17.3, 7.7 Hz, 1H), 2.86 (dd, *J* = 17.3, 3.8 Hz, 1H), 2.81 – 2.64 (m, 2H), 2.32 – 2.19 (m, 1H). The spectral data of **5d** was consistent with that reported in the literature.[18]



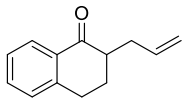
5e

Following the general method E, **5e** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (378 mg, 34% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.1 Hz, 1H), 7.45 – 7.34 (m, 2H), 7.34 – 7.19 (m, 5H), 3.44 – 3.37 (m, 1H), 3.17 (dd, *J* = 17.3, 7.5 Hz, 1H), 3.07 – 2.95 (m, 1H), 2.92 – 2.82 (m, 1H), 2.75 – 2.59 (m, 1H). The spectral data of **5e** was consistent with that reported in the literature.[15]



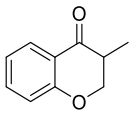
5f

Following the general method E, **5f** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (288 mg, 36% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 3.07 – 2.87 (m, 2H), 2.62 – 2.48 (m, 1H), 2.22 – 2.07 (m, 1H), 1.91 – 1.76 (m, 1H), 1.25 (d, *J* = 6.8, 3H). The spectral data of **5f** was consistent with that reported in the literature.[9]



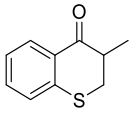
5g

Following the general method E, **5g** was obtained by flash column chromatography (petroleum ether/EtOAc = 300/1) as a colorless oil (3.45 g, 81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 8.2 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 5.91 – 5.76 (m, 1H), 5.15 – 5.03 (m, 2H), 2.98 (dd, *J* = 7.8, 4.5 Hz, 2H), 2.81 – 2.70 (m, 1H), 2.59 – 2.47 (m, 1H), 2.32 – 2.16 (m, 2H), 1.93 – 1.77 (m, 1H). The spectral data of **5g** was consistent with that reported in the literature.[19]



5h

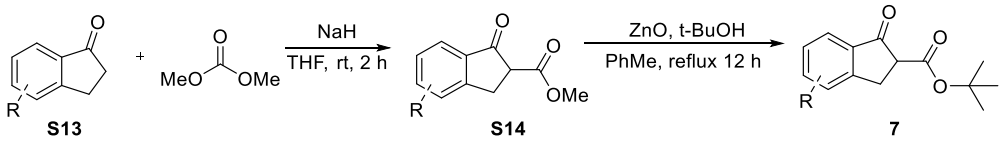
Following the general method E, **5h** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (393 mg, 40% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.9, 1H), 7.51 – 7.42 (m, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 4.50 (dd, *J* = 11.3, 5.1 Hz, 1H), 4.20 – 4.10 (m, 1H), 2.93 – 2.80 (m, 1H), 1.22 (d, *J* = 7.0 Hz, 3H). The spectral data of **5h** was consistent with that reported in the literature.[20]



5i

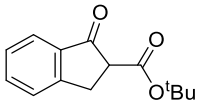
Following the general method E, **5i** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (348 mg, 39% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 3.19 – 3.06 (m, 2H), 2.99 – 2.86 (m, 1H), 1.34 (d, *J* = 6.9 Hz, 3H). The spectral data of **5i** was consistent with that reported in the literature.[20]

4.3. General procedure for the preparation of indanone carboxylates 7



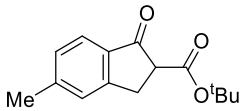
To a suspension of NaH (2.1 equiv) in THF (50 mL) were sequentially added dimethyl carbonate (5.0 equiv) and a catalytic amount of potassium *tert*-butoxide (0.1 equiv) at room temperature. The mixture was stirred for 5 min and then ketone **S13** (1.0 equiv) in THF (30 mL) was added dropwise. The reaction was stirred at room temperature until the completion of the reaction as monitored by ^{1}H NMR. The resulting thick mixture was then cooled to 0 ℃ and 1 M HCl was added until the solution became neutral. The mixture was then poured into water (30 mL), extracted with EtOAc (30 mL x 3), washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuum to afford crude **S14**.

To a flask equipped with a Dean-Stark trap and reflux condenser was added above crude **S14** (1.0 equiv), *tert*-butanol (10 equiv), ZnO (0.2 equiv) and toluene (60 mL). The mixture was heated to reflux in an oil bath until complete conversion. After the mixture was cooled to room temperature, the precipitate was filtered off and the solvent was removed under vacuum. Then the residue was purified by column chromatography (petroleum ether/EtOAc = 100/1 ~ 10/1) to afford the products **7a-l** in 32-67% yields.



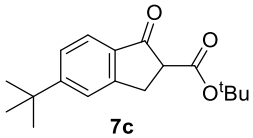
7a

Following the general procedure starting from 1-indanone (10 mmol scale), **7a** was obtained as a pale purple oil (1.4 g, 62% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 100/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.7 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 3.62 (dd, *J* = 8.3, 3.9 Hz, 1H), 3.54 – 3.45 (m, 1H), 3.33 (dd, *J* = 17.1, 8.2 Hz, 1H), 1.49 (s, 9H). The spectral data of **7a** was consistent with that reported in the literature.[1]



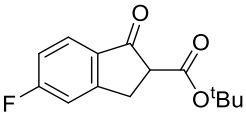
7b

Following the general procedure starting from 5-methyl-1-indanone (6 mmol scale), **7b** was obtained as a white solid (990 mg, 67% yield) following flash silica gel chromatography (petroleumether/EtOAc = 100/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 3.60 (dd, *J* = 8.2, 3.9 Hz, 1H), 3.43 (dd, *J* = 17.1, 3.7 Hz, 1H), 3.27 (dd, *J* = 17.2, 8.2 Hz, 1H), 2.43 (s, 3H), 1.48 (s, 9H). The spectral data of **7b** was consistent with that reported in the literature.[1]



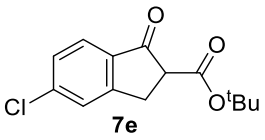
7c

Following the general procedure starting from 5-tert-butyl-indan-1-one (15 mmol scale), **7c** was obtained as a pale purple solid (2.4 g, 56% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 100/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 1H), 7.48 (s, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 3.59 (dd, *J* = 8.1, 3.9 Hz, 1H), 3.46 (dd, *J* = 17.0, 3.3 Hz, 1H), 3.29 (dd, *J* = 17.1, 8.2 Hz, 1H), 1.48 (s, 9H), 1.34 (s, 9H). The spectral data of **7c** was consistent with that reported in the literature.[1]



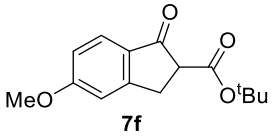
7d

Following the general procedure starting from 5-fluoro-1-indanone (10 mmol scale), **7d** was obtained as a pale yellow solid (1.23 g, 49% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 40/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.1, 5.5 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.08 (t, *J* = 8.3 Hz, 1H), 3.63 (dd, *J* = 8.1, 3.8 Hz, 1H), 3.48 (dd, *J* = 17.7, 3.6 Hz, 1H), 3.30 (dd, *J* = 17.4, 8.2 Hz, 1H), 1.48 (s, 9H). The spectral data of **7d** was consistent with that reported in the literature.[1]



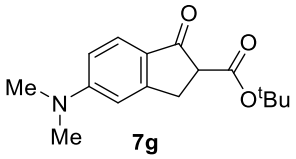
7e

Following the general procedure starting from 5-chloro-1-indanone (10 mmol scale), **7e** was obtained as a pale purple solid (1.65 g, 62% yield) following flash silica gel hromatography (petroleum ether/EtOAc = 40/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 3.62 (dd, *J* = 8.1, 3.7 Hz, 1H), 3.52 – 3.40 (m, 1H), 3.30 (dd, *J* = 17.4, 8.2 Hz, 1H), 1.48 (s, 9H). The spectral data of **7e** was consistent with that reported in the literature.[1]



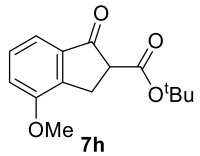
7f

Following the general procedure starting from 5-methoxy-1-indanone (10 mmol scale), **7f** was obtained as a white solid (1.34 g, 51% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 50/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 9.0 Hz, 1H), 6.93 – 6.81 (m, 2H), 3.84 (s, 3H), 3.56 (dd, *J* = 8.0, 3.7 Hz, 1H), 3.40 (dd, *J* = 17.2, 3.1 Hz, 1H), 3.23 (dd, *J* = 17.2, 8.1 Hz, 1H), 1.45 (s, 9H). The spectral data of **7f** was consistent with that reported in the literature.[1]



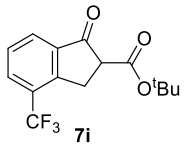
7g

Following the general procedure starting from 5-dimethylamino-1-indanone (10 mmol scale), **7g** was obtained as a yellow solid (1.38 g, 50% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 10/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.8 Hz, 1H), 6.66 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.56 (s, 1H), 3.55 (dd, *J* = 8.2, 3.9 Hz, 1H), 3.43 – 3.30 (m, 1H), 3.18 (dd, *J* = 17.0, 8.2 Hz, 1H), 3.08 (s, 6H), 1.48 (s, 9H). The spectral data of **7g** was consistent with that reported in the literature.[1]



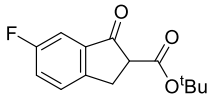
7h

Following the general procedure starting from 4-methoxy-1-indanone (10 mmol scale), **7h** was obtained as a white solid (1.44 g, 55% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 50/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 7.05 – 6.99 (m, 1H), 3.91 (s, 3H), 3.59 (dd, *J* = 7.7, 3.5 Hz, 1H), 3.47 – 3.15 (m, 2H), 1.48 (s, 9H). The spectral data of **7h** was consistent with that reported in the literature.[1]



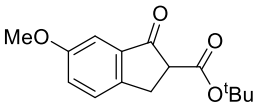
7i

Following the general procedure starting from 4-methoxy-1-indanone (10 mmol scale), **7i** was obtained as a white solid (1.08 g, 36% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 50/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 – 7.78 (m, 1H), 7.73 – 7.52 (m, 1H), 7.50– 7.37 (m, 1H), 3.67 – 3.41 (m, 3H), 1.58 – 1.42 (m, 9H). The spectral data of **7i** was consistent with that reported in the literature.[21]



7j

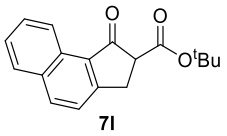
Following the general procedure starting from 6-fluoro-1-indanone (10 mmol scale), **7j** was obtained as a yellow oil (1.65 g, 66% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 100/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (dd, 1H), 7.40 – 7.27 (m, 2H), 3.65 (dd, *J* = 8.2, 3.8 Hz, 1H), 3.48 – 3.38 (m, 1H), 3.28 (dd, *J* = 17.1, 8.1 Hz, 1H), 1.47 (s, 9H). The spectral data of **7j** was consistent with that reported in the literature.[1]



7k

Following the general procedure starting from 6-methoxy-1-indanone (10 mmol

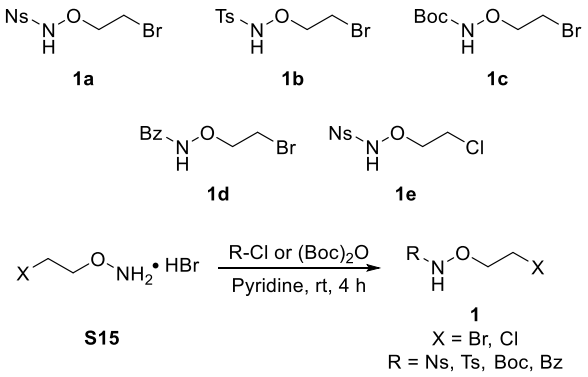
scale), **7k** was obtained as a white solid (1.50 g, 57% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 50/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.3 Hz, 1H), 7.20 – 7.13 (m, 2H), 3.80 (s, 3H), 3.61 (dd, *J* = 8.0, 3.7 Hz, 1H), 3.44 – 3.30 (m, 1H), 3.24 (dd, *J* = 16.8, 8.0 Hz, 1H), 1.47 (s, 9H). The spectral data of **7k** was consistent with that reported in the literature.[1]



7l

Following the general procedure starting from 2,3-dihydro-1H-cyclop-enta[a]naphthalen-1-one (10 mmol scale), **7l** was obtained as a white solid (903 mg, 32% yield) following flash silica gel chromatography (petroleum ether/EtOAc = 100/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 8.3 Hz, 1H), 8.04 (t, *J* = 9.4 Hz, 1H), 7.88 (t, *J* = 7.7 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.54 (dd, *J* = 18.4, 8.0 Hz, 2H), 3.73 (dd, *J* = 7.8, 3.5 Hz, 1H), 3.58 (dd, *J* = 17.5, 3.1 Hz, 1H), 3.39 (dd, *J* = 17.6, 7.8 Hz, 1H), 1.52 (s, 9H). The spectral data of **7l** was consistent with that reported in the literature.[1]

5. General procedure for the preparation of hydroxylamines 1



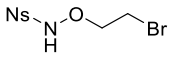
1a **1b** **1c** **1d** **1e**

S15

1
X = Br, Cl
R = Ns, Ts, Boc, Bz

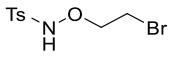
To a solution of **S15**[22] (1.0 equiv) in pyridine (25 mL), R-Cl or $(Boc)_2O$ (1.5 equiv) was added in three portions at 0 ^oC. The resulting brown suspension was warmed to rt and stirred for 4 h. After completion, the reaction mixture was poured into 1.0 M HCl solution and extracted with EtOAc (25 mL x 3). The organic solvents were combined, washed with saturated $NaHCO_3$ (20 mL) and H_2O (20 mL), dried

over Na_2SO_4 and concentrated. The residue was purified by column chromatography (petroleum ether/EtOAc = 6/1) to afford **1a-1e** in 37-58% yields.



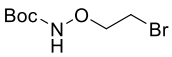
1a

Following the general procedure described above (18 mmol scale), **1a** was obtained by flash column chromatography (petroleum ether/EtOAc = 6/1) as a yellow solid (3.4 g, 58% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.6 Hz, 2H), 8.16 (d, *J* = 8.6 Hz, 2H), 7.44 (s, 1H), 4.32 (t, *J* = 5.7 Hz, 2H), 3.56 (t, *J* = 5.7 Hz, 2H). The spectral data of **1a** was consistent with that reported in the literature.[1]



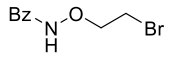
1b

Following the general procedure described above (5 mmol scale), **1b** was obtained by flash column chromatography (petroleum ether/EtOAc = 6/1) as a yellow solid (735 mg, 50% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 6.99 (s, 1H), 4.29 (t, *J* = 5.8 Hz, 2H), 3.56 (t, *J* = 5.8 Hz, 2H), 2.46 (s, 3H). The spectral data of **1b** was consistent with that reported in the literature.[23]



1c

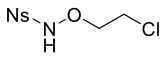
Following the general procedure described above (6.3 mmol scale), **1c** was obtained by flash column chromatography (petroleum ether/EtOAc = 6/1) as a colorless oil (562 mg, 37% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (s, 1H), 4.13 (t, *J* = 6.3 Hz, 2H), 3.53 (t, *J* = 6.3 Hz, 2H), 1.47 (s, 9H). The spectral data of **1c** was consistent with that reported in the literature.[23]



1d

Following the general procedure described above (5.6 mmol scale), **1d** was obtained by flash column chromatography (petroleum ether/EtOAc = 100/1) as a colorless oil (700 mg, 51% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.47 (s, 1H), 7.74 (d, *J* = 7.4 Hz, 2H), 7.52 (t, *J* = 6.9 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 2H), 4.31 (t, *J* = 5.6 Hz,

2H), 3.59 (t, *J* = 5.6 Hz, 2H). The spectral data of **1d** was consistent with that reported in the literature.[23]

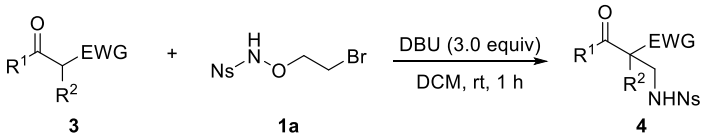


1e

Following the general procedure described above (13.7 mmol scale), **1e** was obtained by flash column chromatography (petroleum ether/EtOAc = 6/1) as a yellow solid (1.62 g , 42% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.7 Hz, 2H), 8.16 (d, *J* = 8.7 Hz, 2H), 7.31 (s, 1H), 4.35 – 4.23 (m, 2H), 3.80 – 3.68 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.9, 141.7, 130.1, 124.3, 76.9, 40.9. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_8H_8ClN_2O_5S$ 278.9848; Found 278.9842. **Melting point:** 100.6-102.5 °C.

6. General procedure for the C-C bond-forming reactions

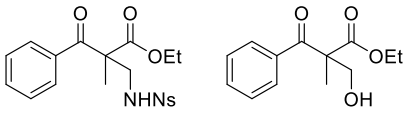
6. 1 General procedure for the preparation of aminomethyl products 4



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

To a solution of *β*-keto esters **3** (0.4 mmol, 2.0 equiv) and DBU (91 mg, 0.6 mmol, 3.0 equiv) in DCM (1 mL) was added the solution of **1a** (65 mg, 0.2 mmol, 1.0 equiv) in DCM (1 mL) dropwise at room temperature over 10 minutes. The reaction mixture was stirred at the same temperature for 1 h. After completion, the reaction was quenched with saturated NH_4Cl (2 mL). The organic layer was separated, and the aqueous layer was extracted with DCM (5 mL x 3). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 8/1 ~ 5/1) to afford the products **4a-u** in 65-93% yields.

Note: A rough range of 10% to 50% of *α*-hydroxymethyl products were usually formed in the above Mannich reaction process. Substrates **3a**, **3c**, **3g**, **3k**, and **3t**, which produced the corresponding *α*-hydroxymethyl products **4a'**, **4c'**, **4g'**, **4k'**, and **4t'**, were exemplified in the following section.

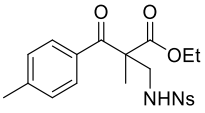


4a **4a'**

Following the general procedure described above, **4a** (major product, white solid, 71 mg, 85% yield) and **4a'** (minor product, colorless oil, 8 mg, 17% yield) were obtained by flash column chromatography (petroleum ether/EtOAc = 8/1 ~ 6/1).

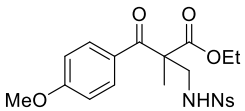
Data for product **4a**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 7.76 (d, 2H), 7.55 (t, 1H), 7.42 (t, 2H), 5.62 (t, *J* = 6.8 Hz, 1H), 4.29 – 4.06 (m, 2H), 3.57 – 3.32 (m, 2H), 1.60 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.5, 171.8, 150.0, 146.0, 134.3, 133.5, 128.8, 128.6, 128.2, 124.4, 62.3, 57.7, 49.0, 19.7, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{20}N_2NaO_7S$ 443.0883; Found 443.0872. **Melting point:** 150.3-151.4 °C.

Data for product **4a'**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.99 (m, 2H), 2.78 (s, 1H), 1.61 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.0, 172.8, 135.3, 133.0, 128.7, 128.5, 67.9, 61.7, 59.0, 18.8, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{16}NaO_4$ 259.0941; Found 259.0933.

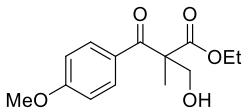


4b

Following the general procedure described above, **4b** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (70 mg, 81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.4 Hz, 2H), 8.04 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 5.68 (t, *J* = 6.7 Hz, 1H), 4.21 – 4.09 (m, 2H), 3.51 – 3.36 (m, 2H), 2.38 (s, 3H), 1.58 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.9, 171.9, 149.9, 146.0, 144.6, 131.6, 129.3, 128.9, 128.2, 124.4, 62.3, 57.6, 49.0, 21.6, 19.8, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{20}H_{22}N_2NaO_7S$ 457.1040; Found 457.1053. **Melting point:** 166.3-168.0 °C.



4c

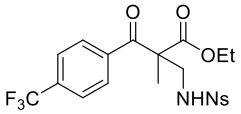


4c'

Following the general procedure described above, **4c** (major product, white solid, 70 mg, 78% yield) and **4c'** (minor product, colorless oil, 14 mg, 27% yield) were obtained by flash column chromatography (petroleum ether/EtOAc = 5/1).

Data for product **4c**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.6 Hz, 2H), 8.04 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 5.61 (t, *J* = 6.8 Hz, 1H), 4.24 – 4.09 (m, 2H), 3.86 (s, 3H), 3.50 – 3.32 (m, 2H), 1.59 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.8, 172.0, 163.8, 145.0, 146.1, 131.3, 128.2, 126.9, 124.4, 113.8, 62.3, 57.4, 55.5, 49.1, 19.9, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{20}H_{22}N_2NaO_8S$ 473.0989; Found 473.1001. **Melting point:** 163.2-164.3 ^oC.

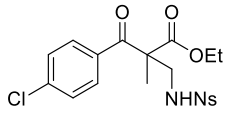
Data for product **4c'**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.00 (d, *J* = 11.2 Hz, 1H), 3.93 (d, *J* = 11.2 Hz, 1H), 3.85 (s, 3H), 2.90 (s, 1H), 1.59 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.2, 173.0, 163.4, 131.1, 127.9, 113.7, 67.9, 61.6, 58.6, 55.4, 18.9, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{14}H_{18}NaO_5$ 289.1046; Found 289.1039.



4d

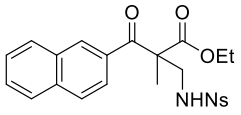
Following the general procedure described above, **4d** was obtained by flash column chromatography (petroleum ether/EtOAc = 5/1) as a white solid (72 mg, 74% yield). **^{1}H NMR** (400 MHz, acetone-d_6) δ 8.45 (d, *J* = 8.8 Hz, 2H), 8.14 (d, *J* = 8.8 Hz, 2H), 7.99 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.10 (s, 1H), 4.24 – 4.06 (m, 2H), 3.68 – 3.54 (m, 2H), 1.62 (s, 3H), 1.07 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, acetone-d_6) δ 196.6, 171.9, 151.0, 147.4, 139.2, 134.3 (q, $^2J_{C\text{-}F}$ = 32.6 Hz), 130.0, 129.2, 126.6 (q, $^3J_{C\text{-}F}$ = 7.6 Hz), 125.3, 124.7 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 62.7, 58.8, 49.3, 19.8, 13.9. **HRMS (ESI)** m/z: $[M - H]^-$ Calcd for $C_{20}H_{18}F_3N_2O_7S$ 487.0792; Found

487.0787. **Melting point:** 169.4-170.8 °C.



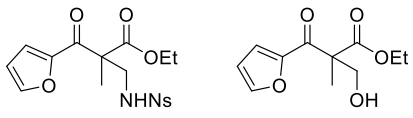
4e

Following the general procedure described above, **4e** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (76 mg, 83% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.4 Hz, 2H), 8.04 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 5.69 – 5.62 (m, 1H), 4.24 – 4.09 (m, 2H), 3.51 – 3.36 (m, 2H), 1.57 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.2, 171.5, 150.0, 146.0, 140.1, 132.5, 130.2, 129.0, 128.2, 124.4, 62.5, 57.8, 48.9, 19.6, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{19}ClN_2NaO_7S$ 477.0494; Found 477.0507. **Melting point:** 167.2-168.5 °C.



4f

Following the general procedure described above, **4f** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (82 mg, 87% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 – 8.21 (m, 3H), 8.03 (d, *J* = 8.5 Hz, 2H), 7.94 – 7.74 (m, 4H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 5.76 (t, *J* = 6.8 Hz, 1H), 4.25 – 4.11 (m, 2H), 3.61 – 3.46 (m, 2H), 1.68 (s, 3H), 1.07 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.1, 171.9, 149.9, 145.9, 135.4, 132.1, 131.5, 130.6, 129.6, 129.0, 128.4, 128.1, 127.6, 127.1, 124.3, 124.1, 62.3, 57.8, 49.0, 19.9, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{23}H_{22}N_2NaO_7S$ 493.1040; Found 493.1039. **Melting point:** 142.0-143.5 °C.



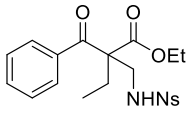
4g **4g'**

Following the general procedure described above, **4g** (major product, white solid, 53 mg, 65% yield) and **4g'** (minor product, colorless oil, 14 mg, 32% yield) were obtained by flash column chromatography (petroleum ether/EtOAc = 5/1).

Data for product **4g**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.8 Hz, 2H),

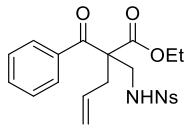
8.02 (d, *J* = 8.8 Hz, 2H), 7.53 (s, 1H), 7.23 (d, *J* = 3.6 Hz, 1H), 6.56 – 6.50 (m, 1H), 5.62 (t, *J* = 6.8 Hz, 1H), 4.23 – 4.04 (m, 2H), 3.43 (d, *J* = 6.3 Hz, 2H), 1.56 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 186.0, 171.0, 150.9, 149.9, 146.5, 146.0, 128.2, 124.4, 119.1, 112.7, 62.0, 57.1, 47.8, 18.5, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{18}N_2NaO_8S$ 433.0676; Found 433.0686. **Melting point:** 163.1-165.4 °C.

Data for product **4g'**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.32 – 7.18 (d, *J* = 3.5 Hz, 1H), 6.53 (d, *J* = 3.4 Hz, 1H), 4.24 – 4.08 (m, 2H), 4.03 – 3.91 (m, 2H), 2.80 (t, *J* = 6.8 Hz, 1H), 1.56 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 187.3, 172.1, 151.5, 146.1, 118.4, 112.4, 66.7, 61.5, 58.5, 17.5, 13.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{11}H_{14}NaO_5$ 249.0733; Found 249.0727.



4h

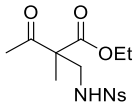
Following the general procedure described above, **4h** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (70 mg, 80% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.4 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 5.37 – 5.25 (m, 1H), 4.24 – 4.06 (m, 2H), 3.60 (dd, *J* = 13.1, 5.6 Hz, 1H), 3.45 (dd, *J* = 13.1, 7.8 Hz, 1H), 2.29 – 2.06 (m, 2H), 1.08 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.9, 171.6, 150.0, 145.7, 135.1, 133.4, 128.6, 128.3, 128.2, 124.4, 62.1, 61.4, 45.8, 25.8, 13.7, 8.0. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{20}H_{22}N_2NaO_7S$ 457.1040; Found 457.1051. **Melting point:** 132.0-132.8 °C.



4i

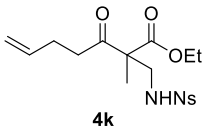
Following the general procedure described above, **4i** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (76 mg, 85% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.8 Hz, 2H), 8.00 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 7.1 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 5.54 –

5.39 (m, 1H), 5.35 (t, *J* = 6.6 Hz, 1H), 5.06 – 4.93 (m, 2H), 4.25 – 4.09 (m, 2H), 3.59 (dd, *J* = 13.2, 5.0 Hz, 1H), 3.45 (dd, *J* = 13.3, 7.5 Hz, 1H), 2.91 (dd, *J* = 14.8, 7.1 Hz, 1H), 2.82 (dd, *J* = 14.8, 7.9 Hz, 1H), 1.10 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.3, 171.1, 150.0, 145.7, 135.0, 133.5, 130.5, 128.6, 128.5, 128.2, 124.4, 120.7, 62.4, 60.7, 46.5, 37.6, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{21}H_{22}N_2NaO_7S$ 469.1040; Found 469.1049. **Melting point:** 145.6-146.4 °C.

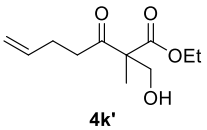


4j

Following the general procedure described above, **4j** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (63 mg, 88% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.9 Hz, 2H), 8.03 (d, *J* = 9.0 Hz, 2H), 5.56 (t, *J* = 6.9 Hz, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.34 – 3.19 (m, 2H), 2.19 (s, 3H), 1.44 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 205.6, 171.0, 150.0, 145.7, 128.2, 124.4, 62.2, 59.8, 47.3, 26.5, 18.2, 13.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{14}H_{18}N_2NaO_7S$ 381.0727; Found 381.0733. **Melting point:** 115.2-116.8 °C.



4k

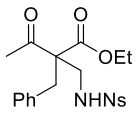


4k'

Following the general procedure described above, **4k** (major product, colorless oil, 58 mg, 73% yield) and **4k'** (minor product, colorless oil, 21 mg, 50% yield) were obtained by flash column chromatography (petroleum ether/EtOAc = 8/1).

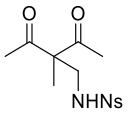
Data for product **4k**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.5 Hz, 2H), 8.03 (d, *J* = 8.6 Hz, 2H), 5.82 – 5.66 (m, 1H), 5.51 (t, *J* = 6.9 Hz, 1H), 5.07 – 4.91 (m, 2H), 4.18 (q, *J* = 6.3, 5.7 Hz, 2H), 3.34 – 3.20 (m, 2H), 2.66 – 2.48 (m, 2H), 2.37 – 2.19 (m, 2H), 1.44 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.9, 171.0, 150.0, 145.7, 136.4, 128.2, 124.4, 115.7, 62.2, 59.6, 47.5, 38.0, 27.5, 18.1, 13.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{22}N_2NaO_7S$ 421.1040; Found 421.1047.

Data for product **4k'**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.87 – 5.70 (m, 1H), 5.09 – 4.91 (m, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.87 (d, *J* = 11.4 Hz, 1H), 3.80 (d, *J* = 11.4 Hz, 1H), 2.84 – 2.49 (m, 3H), 2.38 – 2.26 (m, 2H), 1.38 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 207.7, 172.4, 136.9, 115.4, 66.6, 61.6, 61.1, 38.4, 27.5, 17.1, 14.0. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{11}H_{18}NaO_4$ 237.1097; Found 237.1092.



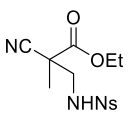
4l

Following the general procedure described above, **4l** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (75 mg, 86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.9 Hz, 2H), 7.98 (d, *J* = 8.9 Hz, 2H), 7.25 – 7.18 (m, 3H), 7.09 – 7.00 (m, 2H), 5.24 (t, 1H), 4.32 – 4.17 (m, 2H), 3.38 – 3.14 (m, 4H), 2.25 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 204.5, 170.4, 150.1, 145.3, 134.3, 129.7, 128.7, 128.2, 127.6, 124.4, 64.4, 62.4, 45.4, 37.9, 27.9, 13.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{20}H_{22}N_2NaO_7S$ 457.1040; Found 457.1050. **Melting point:** 76.2-78.0 ^{o}C.



4m

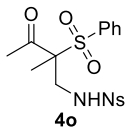
Following the general procedure described above, **4m** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (53 mg, 80% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.7 Hz, 2H), 5.61 – 5.52 (m, 1H), 3.23 (d, *J* = 6.8 Hz, 2H), 2.17 (s, 6H), 1.44 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 207.2, 150.1, 145.4, 128.2, 124.5, 65.6, 47.1, 26.8, 17.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{16}N_2NaO_6S$ 351.0621; Found 351.0626. **Melting point:** 133.3-134.8 ^{o}C.



4n

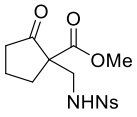
Following the general procedure described above, **4n** was obtained by flash

column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (61 mg, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.7 Hz, 2H), 8.07 (d, *J* = 8.6 Hz, 2H), 5.81 (t, *J* = 6.7 Hz, 1H), 4.26 (q, *J* = 7.4, 6.9 Hz, 2H), 3.48 (dd, *J* = 13.6, 6.1 Hz, 1H), 3.41 (dd, *J* = 13.6, 6.3 Hz, 1H), 1.62 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.6, 150.2, 145.5, 128.3, 124.5, 118.1, 63.7, 48.2, 44.6, 20.8, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}N_3NaO_6S$ 364.0574; Found 364.0578. **Melting point:** 128.1-129.5 °C.



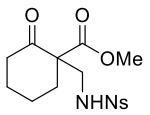
4o

Following the general procedure described above, **4o** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (78 mg, 91% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.80 – 7.63 (m, 3H), 7.55 (t, *J* = 7.7 Hz, 2H), 5.34 (t, *J* = 6.7 Hz, 1H), 3.48 (dd, *J* = 13.6, 6.3 Hz, 1H), 3.30 (dd, *J* = 13.5, 6.9 Hz, 1H), 2.43 (s, 3H), 1.75 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 202.7, 150.2, 145.3, 135.1, 134.2, 129.8, 129.3, 128.2, 124.5, 75.7, 45.1, 28.3, 15.4. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{18}N_2NaO_7S_2$ 449.04476; Found 449.04484. **Melting point:** 158.9-160.8 °C.



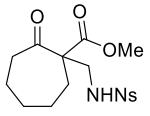
4p

Following the general procedure described above, **4p** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (60 mg, 84% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.7 Hz, 2H), 8.02 (d, *J* = 8.8 Hz, 2H), 5.67 (t, *J* = 6.8 Hz, 1H), 3.68 (s, 3H), 3.30 – 3.14 (m, 2H), 2.58 – 2.19 (m, 4H), 2.17 – 1.93 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 213.6, 171.4, 150.0, 145.6, 128.2, 124.5, 59.9, 53.0, 45.0, 38.1, 31.7, 19.5. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{14}H_{16}N_2NaO_7S$ 379.0570; Found 379.0580. **Melting point:** 93.5-94.7 °C.



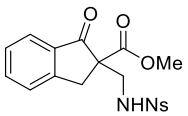
4q

Following the general procedure described above, **4q** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (63 mg, 85% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.4 Hz, 2H), 8.03 (d, *J* = 8.5 Hz, 2H), 5.64 – 5.46 (m, 1H), 3.73 (s, 3H), 3.26 (dd, *J* = 12.7, 8.4 Hz, 1H), 3.11 (dd, *J* = 12.7, 5.2 Hz, 1H), 2.70 – 2.54 (m, 1H), 2.51 – 2.33 (m, 2H), 2.11 – 1.95 (m, 1H), 1.88 – 1.74 (m, 1H), 1.66 – 1.57 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 209.1, 170.7, 150.0, 145.8, 128.2, 124.4, 61.4, 53.0, 47.3, 40.7, 34.1, 26.9, 21.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{18}N_2NaO_7S$ 393.0727; Found 393.0733. **Melting point:** 152.1-153.6 °C.



4r

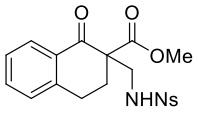
Following the general procedure described above, **4r** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (58 mg, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H), 8.02 (d, *J* = 8.8 Hz, 2H), 5.73 – 5.65 (m, 1H), 3.70 (s, 3H), 3.33 – 3.19 (m, 2H), 2.79 – 2.68 (m, 1H), 2.54 – 2.43 (m, 1H), 2.10 – 1.99 (m, 1H), 1.96 – 1.85 (m, 1H), 1.85 – 1.70 (m, 2H), 1.69 – 1.48 (m, 3H), 1.41 – 1.28 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 210.2, 171.4, 149.9, 145.8, 128.2, 124.4, 62.7, 52.8, 47.4, 42.5, 31.5, 29.8, 25.7, 24.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}N_2NaO_7S$ 407.0883; Found 407.0892. **Melting point:** 165.4-166.5 °C.



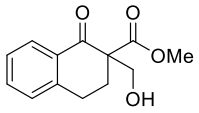
4s

Following the general procedure described above, **4s** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (75 mg, 93% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.5 Hz, 2H), 8.01 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.43

(t, *J* = 7.5 Hz, 1H), 5.77 – 5.70 (m, 1H), 3.65 (s, 3H), 3.58 – 3.48 (m, 3H), 3.30 (dd, *J* = 13.0, 8.8 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.3, 171.2, 153.2, 150.1, 145.5, 136.2, 134.4, 128.2, 126.8, 125.1, 124.5, 60.1, 53.2, 46.5, 35.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{18}H_{16}N_2NaO_7S$ 427.0570; Found 427.0577. **Melting point:** 144.1-146.0 °C.



4t

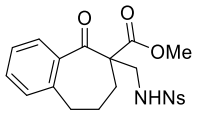


4t'

Following the general procedure described above, **4t** (major product, white solid, 69 mg, 82% yield) and **4t'** (minor product, colorless oil, 14 mg, 29% yield) were obtained by flash column chromatography (petroleum ether/EtOAc = 8/1 ~ 5/1).

Data for product **4t**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.7 Hz, 2H), 8.04 (d, *J* = 8.7 Hz, 2H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 5.88 – 5.79 (m, 1H), 3.65 (s, 3H), 3.51 (dd, *J* = 12.6, 8.7 Hz, 1H), 3.30 (dd, *J* = 12.7, 4.6 Hz, 1H), 3.05 – 2.98 (m, 2H), 2.51 (dt, *J* = 13.7, 4.7 Hz, 1H), 2.30 (dt, *J* = 13.6, 7.7 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.4, 171.1, 150.0, 145.7, 143.1, 134.5, 131.2, 128.9, 128.3, 127.9, 127.1, 124.4, 58.0, 53.0, 46.9, 29.9, 25.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{19}H_{18}N_2NaO_7S$ 441.0727; Found 441.0737. **Melting point:** 177.0-178.4 °C.

Data for product **4t'**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.20 (m, 1H), 4.02 (dd, *J* = 11.3, 3.4 Hz, 1H), 3.90 (t, *J* = 10.6 Hz, 1H), 3.72 (s, 3H), 3.28 (dd, *J* = 9.9, 4.1 Hz, 1H), 3.08 – 2.90 (m, 2H), 2.45 (dt, *J* = 13.7, 4.6 Hz, 1H), 2.23 – 2.12 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.2, 171.7, 143.2, 134.0, 131.8, 128.8, 127.8, 127.0, 66.3, 59.2, 52.6, 29.2, 25.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{14}NaO_4$ 257.0784; Found 257.0777.

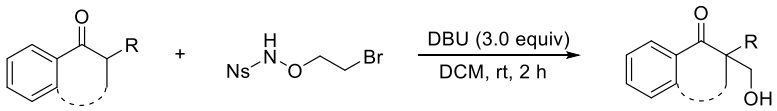


4u

Following the general procedure described above, **4u** was obtained by flash

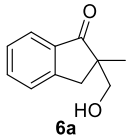
column chromatography (petroleum ether/EtOAc = 8/1) as a white solid (62 mg, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.2 Hz, 2H), 8.05 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 5.78 – 5.74 (m, 1H), 3.59 (s, 3H), 3.48 – 3.33 (m, 2H), 2.98 – 2.86 (m, 1H), 2.86 – 2.74 (m, 1H), 2.38 – 2.27 (m, 1H), 2.07 – 1.89 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 204.3, 171.3, 150.0, 145.8, 138.8, 138.7, 132.2, 129.4, 128.2, 126.7, 124.5, 62.0, 52.9, 47.9, 33.0, 30.1, 22.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{20}H_{20}N_2NaO_7S$ 455.0883; Found 455.0893. **Melting point:** 189.1-190.7 ^oC.

6.2 General procedure for the preparation of hydroxylmethyl products 6



5 **1a** **6**

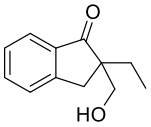
To a solution of α-substituted ketone **5** (0.2 mmol, 1.0 equiv) and DBU (91 mg, 0.6 mmol, 3.0 equiv) in DCM (1 mL) was added the solution of **1a** (98 mg, 0.3 mmol, 1.5 equiv) in DCM (1 mL) dropwise at room temperature over 10 minutes. The reaction mixture was stirred at the same temperature for 2 h. After completion, the solution was quenched with saturated NH_4Cl (2 mL). The organic layer was separated, and the aqueous layer was extracted with DCM (5 mL x 3). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 8/1 ~ 5/1) to afford the products **6a-i** in 61-91% yields.



6a

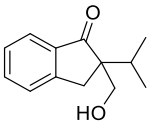
Following the general procedure described above, **6a** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a colorless oil (32 mg, 91% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.4 Hz,

1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.3 Hz, 1H), 3.82 (d, *J* = 10.7 Hz, 1H), 3.61 (d, *J* = 10.7 Hz, 1H), 3.25 (d, *J* = 17.2 Hz, 1H), 2.88 (d, *J* = 17.2 Hz, 1H), 2.48 (s, 1H), 1.23 (s, 3H). The spectral data of **6a** was consistent with that reported in the literature.[24]



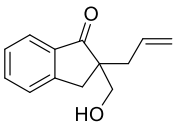
6b

Following the general procedure described above, **6b** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a colorless oil (32 mg, 85% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 3.85 (d, *J* = 10.7 Hz, 1H), 3.61 (d, *J* = 10.8 Hz, 1H), 3.12 – 2.94 (m, 2H), 2.46 (s, 1H), 1.81 – 1.61 (m, 2H), 0.80 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 211.6, 153.9, 136.7, 135.2, 127.4, 126.5, 123.8, 66.5, 54.8, 34.9, 26.5, 8.5. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{12}H_{14}NaO_2$ 213.0886; Found 213.0878.



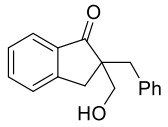
6c

Following the general procedure described above, **6c** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a colorless oil (34 mg, 83% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 3.93 – 3.84 (m, 1H), 3.61 (d, *J* = 10.8 Hz, 1H), 3.08 (d, *J* = 17.6 Hz, 1H), 2.73 (d, *J* = 17.6 Hz, 1H), 2.51 (dd, *J* = 8.6, 3.5 Hz, 1H), 2.41 (hept, *J* = 6.8 Hz, 1H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.67 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 212.7, 154.4, 136.9, 135.1, 127.4, 126.3, 123.7, 66.0, 57.7, 31.6, 29.6, 17.6, 17.5. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{16}NaO_2$ 227.1043; Found 227.1041.



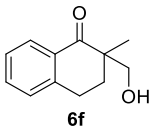
6d

Following the general procedure described above, **6d** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a colorless oil (37 mg, 91% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 1H), 5.68 – 5.53 (m, 1H), 5.09 (d, *J* = 16.9 Hz, 1H), 5.00 (d, *J* = 10.1 Hz, 1H), 3.83 (d, *J* = 10.9 Hz, 1H), 3.62 (d, *J* = 10.9 Hz, 1H), 3.12 – 2.98 (m, 2H), 2.57 (s, 1H), 2.48 – 2.34 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 210.7, 153.7, 136.3, 135.2, 132.8, 127.4, 126.5, 123.9, 118.8, 66.6, 54.2, 38.1, 34.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{13}H_{14}NaO_2$ 225.0886; Found 225.0884.



6e

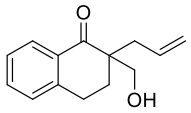
Following the general procedure described above, **6e** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a colorless oil (44 mg, 88% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.38 – 7.24 (m, 2H), 7.24 – 7.10 (m, 5H), 3.83 (d, *J* = 10.9 Hz, 1H), 3.62 (d, *J* = 10.9 Hz, 1H), 3.15 (d, *J* = 17.4 Hz, 1H), 3.05 (d, *J* = 13.5 Hz, 1H), 2.97 (d, *J* = 13.5 Hz, 1H), 2.82 (d, *J* = 17.4 Hz, 1H), 2.68 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 211.1, 153.5, 136.7, 136.1, 135.2, 130.2, 128.1, 127.4, 126.5, 126.4, 124.0, 66.5, 55.1, 38.6, 34.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{16}NaO_2$ 275.1043; Found 275.1042.



6f

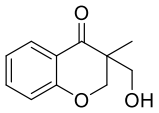
Following the general procedure described above, **6f** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a colorless oil (24 mg, 63% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 3.82 – 3.57 (m, 2H), 3.16 (ddd, *J* = 17.2, 12.0, 5.0 Hz, 1H), 2.94 (dt, *J* = 17.4, 4.3 Hz, 1H), 2.85 (t, *J* = 6.6 Hz, 1H), 2.23 (td, *J* = 12.8, 5.1 Hz, 1H), 1.82 – 1.71 (m, 1H), 1.23 (s, 3H). The spectral data of

6f was consistent with that reported in the literature.[25]



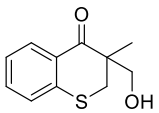
6g

Following the general procedure described above, 6**g** was obtained by flash column chromatography (petroleum ether/EtOAc = 8/1) as a colorless oil (26 mg, 61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 5.91 – 5.72 (m, 1H), 5.25 – 5.09 (m, 2H), 3.79 – 3.61 (m, 2H), 3.13 (ddd, *J* = 16.9, 11.4, 5.1 Hz, 1H), 2.99 – 2.84 (m, 2H), 2.50 (dd, *J* = 14.0, 6.9 Hz, 1H), 2.34 (dd, *J* = 13.9, 8.0 Hz, 1H), 2.05 (ddd, *J* = 13.7, 11.4, 5.1 Hz, 1H), 1.93 (dt, *J* = 13.8, 4.5 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 203.8, 143.5, 133.7, 132.7, 131.4, 128.8, 127.7, 126.8, 119.0, 66.3, 49.0, 34.7, 27.8, 24.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{14}H_{16}NaO_2$ 239.1043; Found 239.1042.



6h

Following the general procedure described above, **6h** was obtained by flash column chromatography (petroleum ether/EtOAc = 5/1) as a colorless oil (31 mg, 81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.08 – 6.85 (m, 2H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.18 (d, *J* = 11.5 Hz, 1H), 3.93 (dd, *J* = 11.1, 6.6 Hz, 1H), 3.59 (dd, *J* = 11.2, 6.3 Hz, 1H), 2.29 (t, *J* = 6.3 Hz, 1H), 1.23 (s, 3H). The spectral data of **6h** was consistent with that reported in the literature.[26]

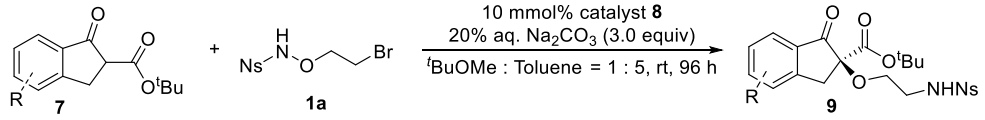


6i

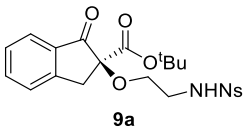
Following the general procedure described above, **6i** was obtained by flash column chromatography (petroleum ether/EtOAc = 5/1) as a colorless oil (26 mg, 62% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 3.98 (dd, *J* = 11.3, 6.7 Hz, 1H),

3.66 – 3.57 (m, 2H), 2.78 (d, *J* = 13.6 Hz, 1H), 2.57 (t, *J* = 6.7 Hz, 1H), 1.33 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.0, 141.6, 133.3, 129.9, 129.7, 127.2, 124.8, 67.8, 45.8, 34.7, 17.6. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{11}H_{12}NaO_2S$ 231.0450; Found 231.0449.

7. General procedure for the catalytic asymmetric reactions of indanone carboxylates 7 with hydroxylamine 1a

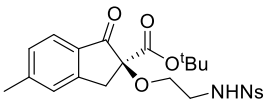


To a solution of *tert*-butyl indanone carboxylate substrates **7** (0.24 mmol, 1.2 equiv), hydroxylamine **1a** (0.2 mmol, 1.0 equiv), and catalyst **8** (16 mg, 0.02mmol, 0.1 equiv) in ^{t}BuOMe/toluene (2 mL, v/v = 1/5) was added 20% aq. Na_2CO_3 (318 uL, 0.6 mmol, 3.0 equiv) at room temperature. The reaction mixture was stirred at the same temperature for 96 h. After completion, the solution was quenched with saturated NH_4Cl (2 mL) and extracted with EtOAc (3 mL x 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 10/1 ~ 5/1) to afford the products **9a-l** in 50-67% yield and 90-97% ee. The absolute configuration of products **9** was determined to be the *S* by comparing their specific rotation value with the reported data in the literature.[1]



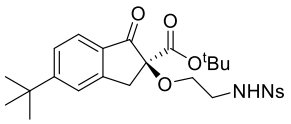
Following the general procedure described above, **9a** was obtained by flash silica chromatography (PE/EtOAc = 10/1) as a white solid (56 mg, 60% yield). The compound was determined to be 91% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 °C; t(major) = 23.9 min, t(minor) = 32.2. $[\alpha]_D^{25}$ = -10.9 (c = 1.05, $CHCl_3$); Reported data from Lit.[1]: $[\alpha]_D^{25}$ = -9.6 (c = 0.8, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.6 Hz, 2H), 8.08 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.5 Hz,

1H), 7.47 – 7.38 (m, 2H), 6.24 (s, 1H), 3.88 – 3.67 (m, 2H), 3.47 (d, *J* = 17.2 Hz, 1H), 3.29 – 3.16 (m, 2H), 3.07 (d, *J* = 17.2 Hz, 1H), 1.37 (s, 9H). The spectral data of **9a** was consistent with that reported in the literature.[1]



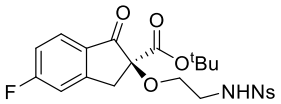
9b

Following the general procedure described above, 9**b** was obtained by flash silica chromatography (petroleum ether/EtOAc = 10/1) as a white solid (48 mg, 51% yield). The compound was determined to be 90% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 ℃; t(major) = 20.5 min, t(minor) = 25.8 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.25 – 7.17 (m, 2H), 6.20 (s, 1H), 3.91 – 3.66 (m, 2H), 3.41 (d, *J* = 17.2 Hz, 1H), 3.30 – 3.16 (m, 2H), 2.99 (d, *J* = 17.2 Hz, 1H), 2.46 (s, 3H), 1.38 (s, 9H). The spectral data of **9b** was consistent with that reported in the literature.[1]



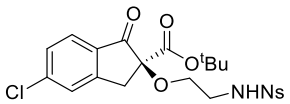
9c

Following the general procedure described above, **9c** was obtained by flash silica chromatography (petroleum ether/EtOAc = 10/1) as a colorless oil (63 mg, 59% yield). The compound was determined to be 90% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak AD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 ℃; t(major) = 19.7 min, t(minor) = 23.5 min. $[\alpha]_D^{25}$ = 4.2 (c = 0.4, $CHCl_3$); Reported data from Lit.[1]: $[\alpha]_D^{25}$ = 3.1 (c = 0.5, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.1 Hz, 2H), 8.08 (d, *J* = 8.1 Hz, 2H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.37 (m, 2H), 6.28 (s, 1H), 3.84 – 3.65 (m, 2H), 3.45 (d, *J* = 17.1 Hz, 1H), 3.27 – 3.14 (m, 2H), 3.03 (d, *J* = 17.1 Hz, 1H), 1.38 (s, 9H), 1.36 (s, 9H). The spectral data of **9c** was consistent with that reported in the literature.[1]



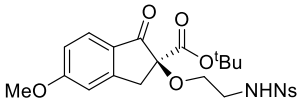
9d

Following the general procedure described above, **9d** was obtained by flash silica chromatography (petroleum ether/EtOAc = 8/1) as a white solid (52 mg, 53% yield). The compound was determined to be 90% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 75/25, 1.0 mL/min, 254 nm, 47 bar, 25 ℃; t(major) = 14.1 min, t(minor) = 22.8 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.7 Hz, 2H), 8.09 (d, *J* = 8.7 Hz, 2H), 7.77 (dd, *J* = 7.9, 5.4 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.16 (s, 1H), 3.89 – 3.66 (m, 2H), 3.47 (d, *J* = 17.4 Hz, 1H), 3.31 – 3.15 (m, 2H), 3.08 (d, *J* = 17.4 Hz, 1H), 1.38 (s, 9H). The spectral data of **9d** was consistent with that reported in the literature.[1]



9e

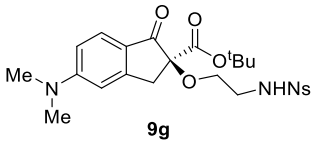
Following the general procedure described above, **9e** was obtained by flash silica chromatography (petroleum ether/EtOAc = 8/1) as a white solid (64 mg, 63% yield). The compound was determined to be 90% ee by HPLC analysis. HPLC conditions: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41bar, 25 ℃; t(major) = 27.5 min, t(minor) = 39.0 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.6 Hz, 2H), 8.08 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.52 – 7.32 (m, 2H), 6.17 (s, 1H), 3.86 – 3.68 (m, 2H), 3.45 (d, *J* = 17.4 Hz, 1H), 3.29 – 3.15 (m, 2H), 3.07 (d, *J* = 17.4 Hz, 1H), 1.38 (s, 9H). The spectral data of **9e** was consistent with that reported in the literature.[1]



9f

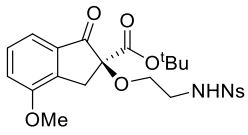
Following the general procedure described above, **9f** was obtained by flash silica chromatography (petroleum ether/EtOAc = 8/1) as a white solid (57 mg, 56% yield). The compound was determined to be 90% ee by HPLC analysis. **HPLC conditions**:

Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 ℃; t(major) = 35.7 min, t(minor) = 44.8 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.6 Hz, 2H), 8.08 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.84 (s, 1H), 6.22 (s, 1H), 3.91 (s, 3H), 3.87 – 3.64 (m, 2H), 3.44 (d, *J* = 17.2 Hz, 1H), 3.27 – 3.15 (m, 2H), 2.98 (d, *J* = 17.2 Hz, 1H), 1.39 (s, 9H). The spectral data of **9f** was consistent with that reported in the literature.[1]



9g

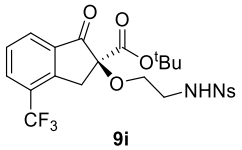
Following the general procedure described above (1.0 equiv of 50% aq. Cs_2CO_3 was used), **9g** was obtained by flash silica chromatography (petroleum ether/EtOAc = 5/1) as a yellow solid (70 mg, 67% yield). The compound was determined to be 96% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm, 50 bar, 25 ℃; t(major) = 24.1 min, t(minor) = 31.4 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.8 Hz, 2H), 8.7 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 1H), 6.75 – 6.62 (m, 1H), 6.46 (s, 1H), 6.31 (s, 1H), 3.82 – 3.67 (m, 2H), 3.34 (d, *J* = 17.0 Hz, 1H), 3.27 – 3.18 (m, 2H), 3.12 (s, 6H), 2.85 (d, *J* = 17.0 Hz, 1H), 1.39 (s, 9H). The spectral data of **9g** was consistent with that reported in the literature.[1]



9h

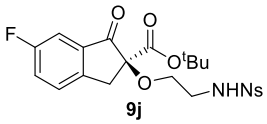
Following the general procedure described above, **9h** was obtained by flash silica chromatography (petroleum ether/EtOAc = 8/1) as a white solid (48mg, 50% yield). The compound was determined to be 90% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak AD-H, Hexane/*i*-PrOH = 75/25, 1.0 mL/min, 254 nm, 51 bar, 25 ℃; t(major) = 14.5 min, t(minor) = 20.9 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.6 Hz, 2H), 8.06 (d, *J* = 8.6 Hz, 2H), 7.42 – 7.29 (m, 2H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.25– 6.17 (m, 1H), 3.90 (s, 3H), 3.85 – 3.65 (m, 2H), 3.35 – 3.17 (m, 3H), 2.81 (d, *J* = 17.6 Hz, 1H), 1.38 (s, 9H). The spectral data of **9h** was consistent with that reported

in the literature.[1]



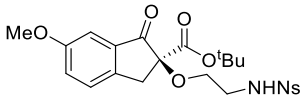
9i

Following the general procedure described above, **9i** was obtained by flash silica chromatography (petroleum ether/EtOAc = 12/1) as a colorless oil (72 mg, 66% yield). The compound was determined to be 95% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 93/7, 1.0 mL/min, 254 nm, 39 bar, 25 ℃; t(major) = 47.5 min, t(minor) = 53.9 min. $[\alpha]_D^{25}$ = -12.2 (c = 0.7, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.91 (t, *J* = 8.3 Hz, 2H), 7.57 (t, *J* = 7.7 Hz, 1H), 6.14 (s, 1H), 3.89– 3.70 (m, 2H), 3.60 (d, *J* = 17.8 Hz, 1H), 3.29 – 3.14 (m, 3H), 1.36 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.1, 168.7, 149.9, 148.5 (q, $^3J_{C\text{-}F}$ = 2.5 Hz), 146.0, 135.5, 132.4 (q, $^2J_{C\text{-}F}$ = 5.5 Hz), 128.8, 128.5, 128.4, 128.2, 124.2, 123.4 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 84.6, 84.0, 65.1, 43.4, 38.1, 27.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{23}H_{23}F_3N_2NaO_8S$ 567.1019; Found 567.1041.



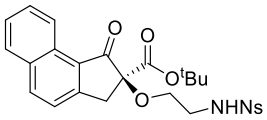
9j

Following the general procedure described above, **9j** was obtained by flash silica chromatography (petroleum ether/EtOAc = 8/1) as a white solid (57 mg, 58% yield). The compound was determined to be 93% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 ℃; t(major) = 31.2 min, t(minor) = 40.9 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.8 Hz, 2H), 8.09 (d, *J* = 8.8 Hz, 2H), 7.49 – 7.31 (m, 3H), 6.20 (t, *J* = 4.4 Hz, 1H), 3.90 – 3.69 (m, 2H), 3.44 (d, *J* = 17.0 Hz, 1H), 3.25 – 3.19 (m, 2H), 3.04 (d, *J* = 17.0 Hz, 1H), 1.38 (s, 9H). The spectral data of **9j** was consistent with that reported in the literature.[1]



9k

Following the general procedure described above, **9k** was obtained by flash silica chromatography (petroleum ether/EtOAc = 8/1) as a white solid (60 mg, 59% yield). The compound was determined to be 90% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 ℃; t(major) = 30.4 min, t(minor) = 41.2 min. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.6 Hz, 2H), 8.08 (d, *J* = 8.5 Hz, 2H), 7.40 – 7.18 (m, 2H), 7.14 (s, 1H), 6.25 (s, 1H), 3.89 – 3.68 (m, 5H), 3.39 (d, *J* = 16.8 Hz, 1H), 3.30 – 3.16 (m, 2H), 2.98 (d, *J* = 16.9 Hz, 1H), 1.37 (s, 9H). The spectral data of **9k** was consistent with that reported in the literature.[1]



9l

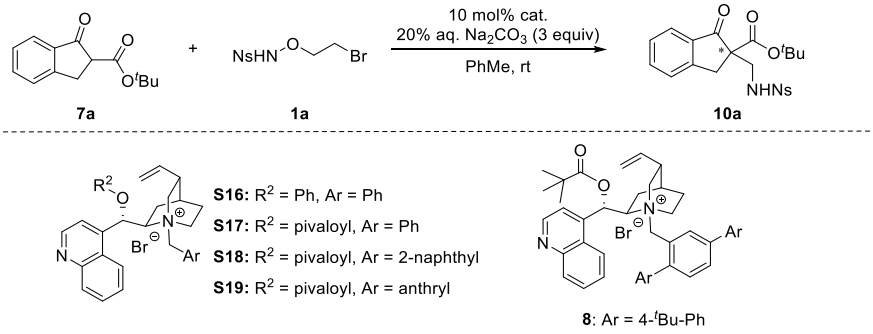
Following the general procedure described above, **9l** was obtained by flash silica chromatography (petroleum ether/EtOAc = 10/1) as a white solid (64 mg, 61% yield). The compound was determined to be 97% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 88/12, 1.0 mL/min, 254 nm, 39 bar, 25 ℃; t(major) = 47.6 min, t(minor) = 54.5 min. $[\alpha]_D^{25}$ = 21.4 (c = 2.21, $CHCl_3$); Reported data from Lit.[1]: $[\alpha]_D^{25}$ = 19.1 (c = 2.25, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.97 (d, *J* = 8.3 Hz, 1H), 8.29 (d, *J* = 8.8 Hz, 2H), 8.15 – 8.05 (m, 3H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 6.27 (s, 1H), 3.95 – 3.73 (m, 2H), 3.59 (d, *J* = 17.4 Hz, 1H), 3.31 – 3.11 (m, 3H), 1.39 (s, 9H). The spectral data of **9l** was consistent with that reported in the literature.[1]

8 General procedure for the catalytic asymmetric Mannich reactions

8.1 Screening of the reaction conditions

The following catalysts **S16-S19** and **8** were known compounds and were prepared from literature.[1]

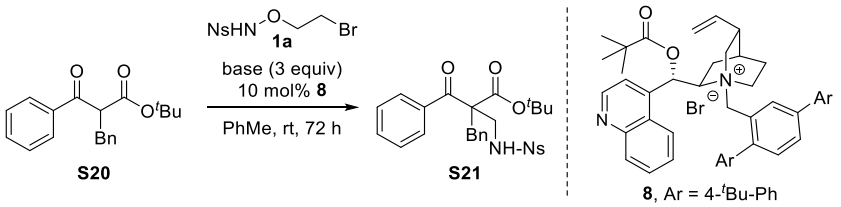
Table S4. Catalyst screening for reaction of 7a and 1a[a]



entry	T (°C)	t (h)	Cat.	base	yield of **10a** (%)[b]	ee of **10a** (%)[c]
1	rt	96	**S16**	20% aq Na_2CO_3	25	8
2	rt	96	**S17**	20% aq Na_2CO_3	20	15
3	rt	96	**S18**	20% aq Na_2CO_3	22	26
4	rt	96	**S19**	20% aq Na_2CO_3	29	33
5	rt	96	**8**	20% aq Na_2CO_3	45	42

[a]Reaction conditions: **1a** (0.1 mmol), **7a** (0.12 mmol), catalyst (10 mol%) and base (0.3 mmol) indicated temperature. [b]Isolated yield. [c]Determined by HPLC analysis.

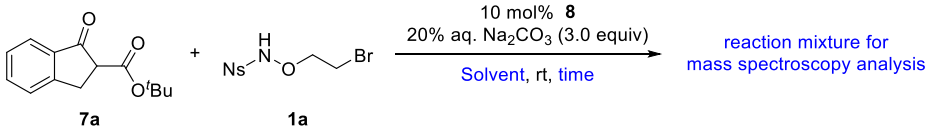
Table S5. Initial results for reaction of benzoyl acetate and 1a[a]



entry	T (°C)	base	yield (%)[b]	ee (%)[c]
1	rt	Cs_2CO_3 (50%)	0	0
2	rt	KOH (50%)	21	5

[a]Reaction conditions: **1a** (0.1 mmol), **S20** (0.12 mmol), catalyst (10 mol%) and base (0.3 mmol) indicated temperature. [b]Isolated yield. [c]Determined by HPLC analysis.

8.2 Investigation of the solvent effect via mass and NMR spectroscopy



To a solution of *tert*-butyl indanone carboxylate **7a** (56 mg, 0.24 mmol, 1.2 equiv), hydroxylamine **1a** (65 mg, 0.2 mmol, 1.0 equiv), and catalyst **8** (16 mg,

0.02mmol, 0.1 equiv) in toluene or toluene/^{t}BuOMe (v/v = 5/1) (2 mL) was added 20% aq. Na_2CO_3 (318 uL, 0.6 mmol, 3.0 equiv) at room temperature. After stirring at room temperature for 12 h, 48 h, and 64 h, an aliquot of reaction solution was taken out from toluene or toluene/^{t}BuOMe solvents. Then, the mixture was subjected to mass spectroscopy analysis. The recorded ESI-MS data and assigned structures of possible compounds were demonstrated in following **Figures S5-6**.

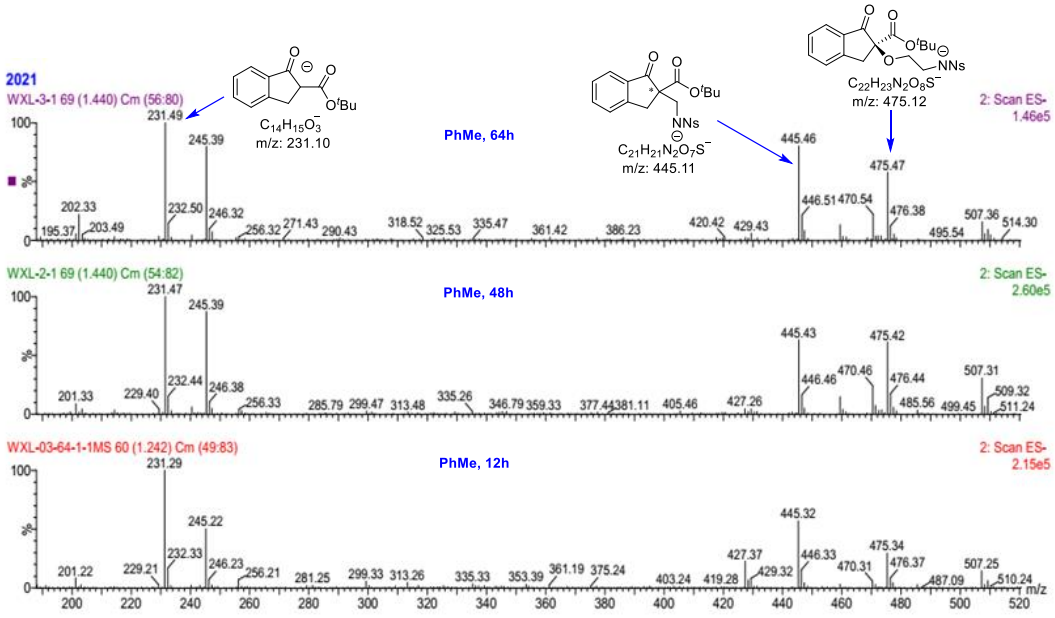


Figure S5. ESI-MS data of the reaction mixture (toluene as solvent)

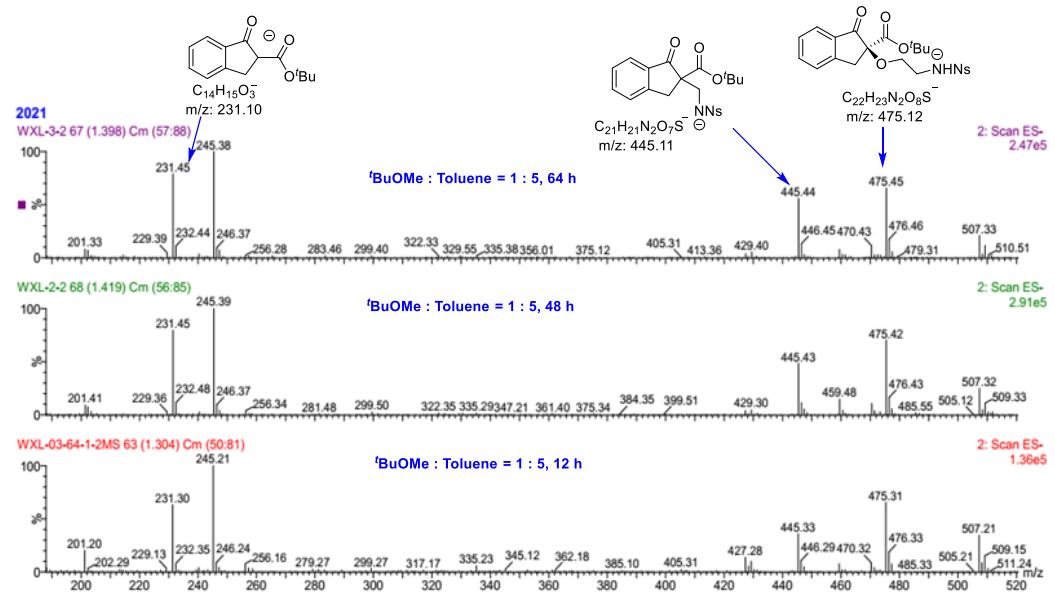
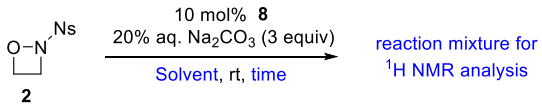


Figure S6. ESI-MS data of the reaction mixture (toluene/^{t}BuOMe as solvents)



To a solution of 1,2-oxazetidine **2** (12 mg, 0.05 mmol, 1.0 equiv) and catalyst **8** (4 mg, 0.005 mmol, 0.1 equiv) in toluene or toluene/^{t}BuOMe (v/v = 5/1) (0.5 mL) was added 20% aq. Na_2CO_3 (80 uL, 0.15 mmol, 3.0 equiv), the reaction mixture was stirred at room temperature. After stirring at room temperature for 12 h, 48 h, and 72 h, the crude reaction mixture was subjected to ^{1}H NMR analysis (mesitylene was used as internal standard). The ^{1}H NMR spectra were shown in following **Figures S7-14**.

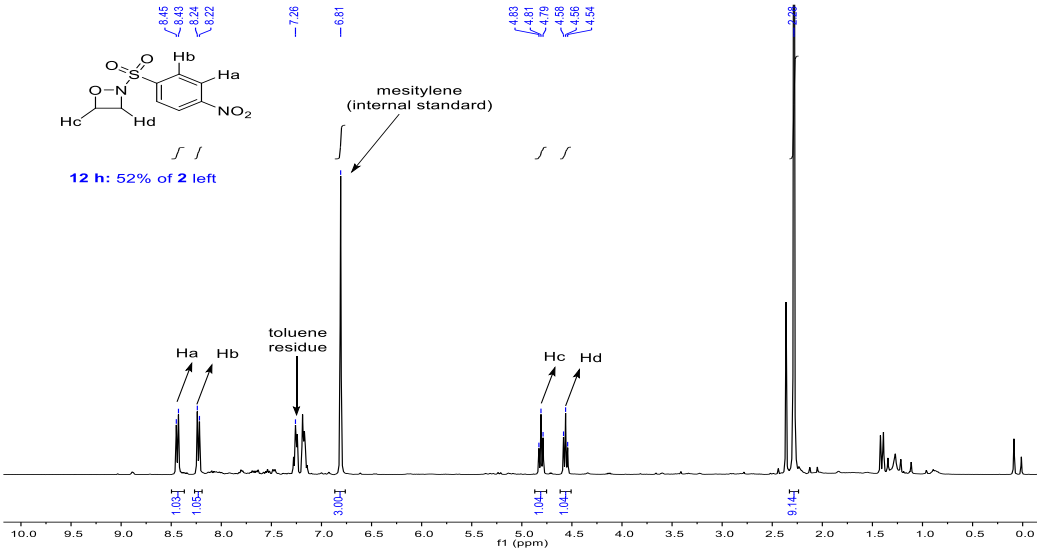


Figure S7. Crude ^{1}H NMR of compound 2 (toluene as solvent, 12 h)

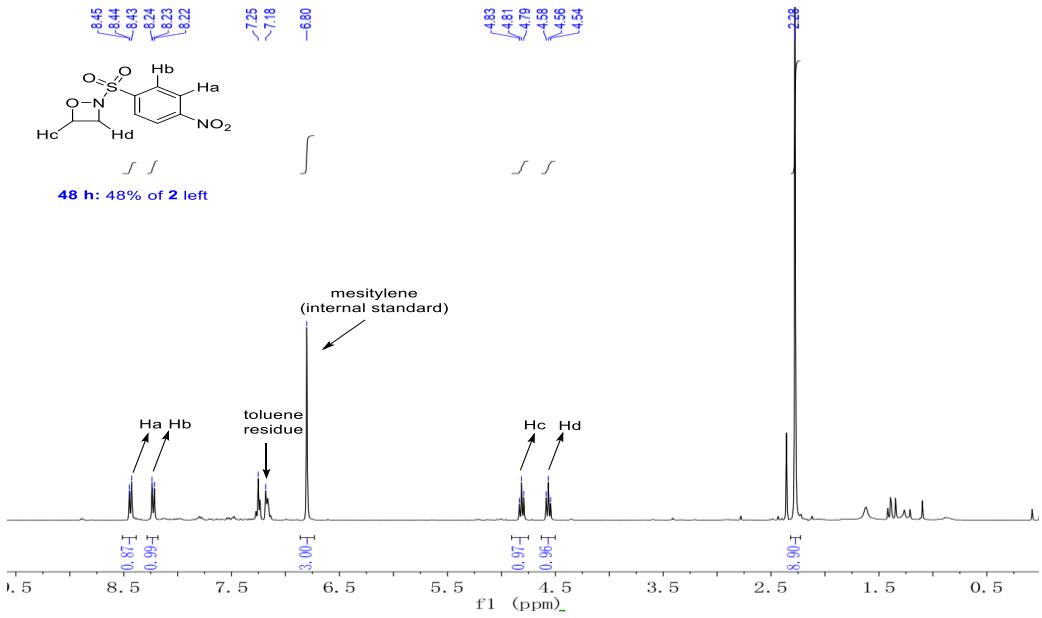


Figure S8. Crude ^{1}H NMR of compound 2 (toluene as solvent, 48 h)

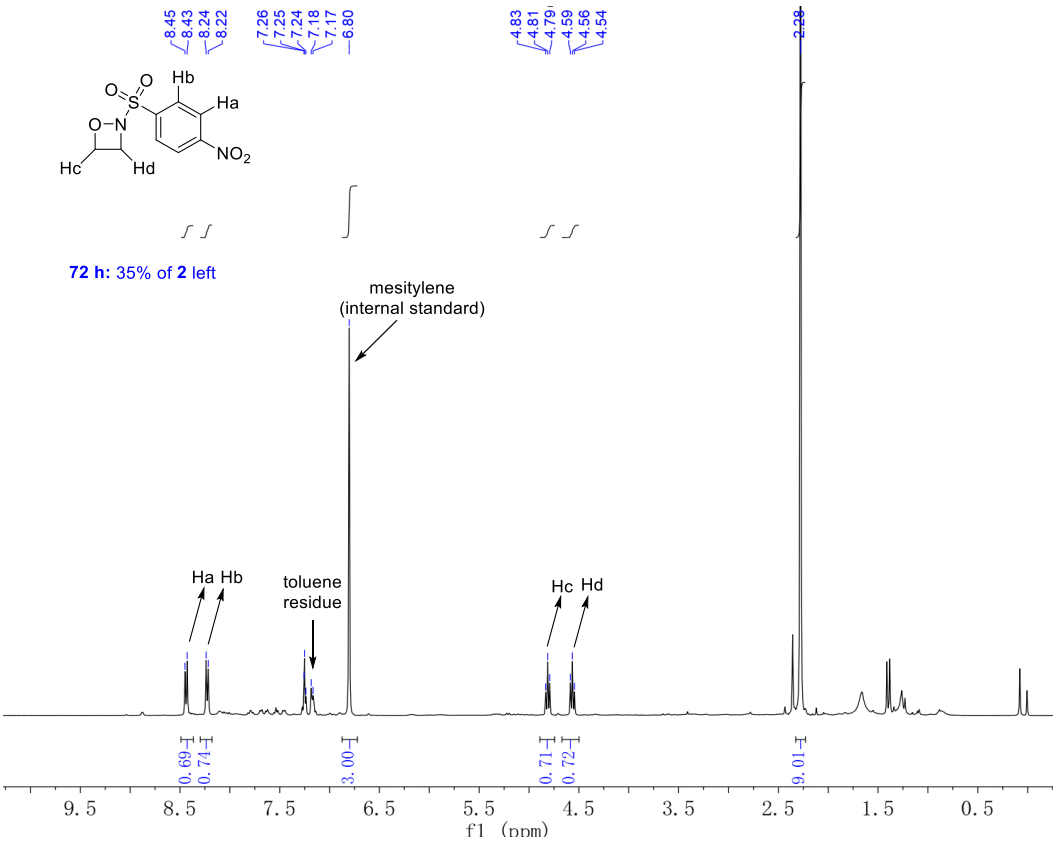


Figure S9. Crude ^{1}H NMR of compound 2 (toluene as solvent, 72 h)

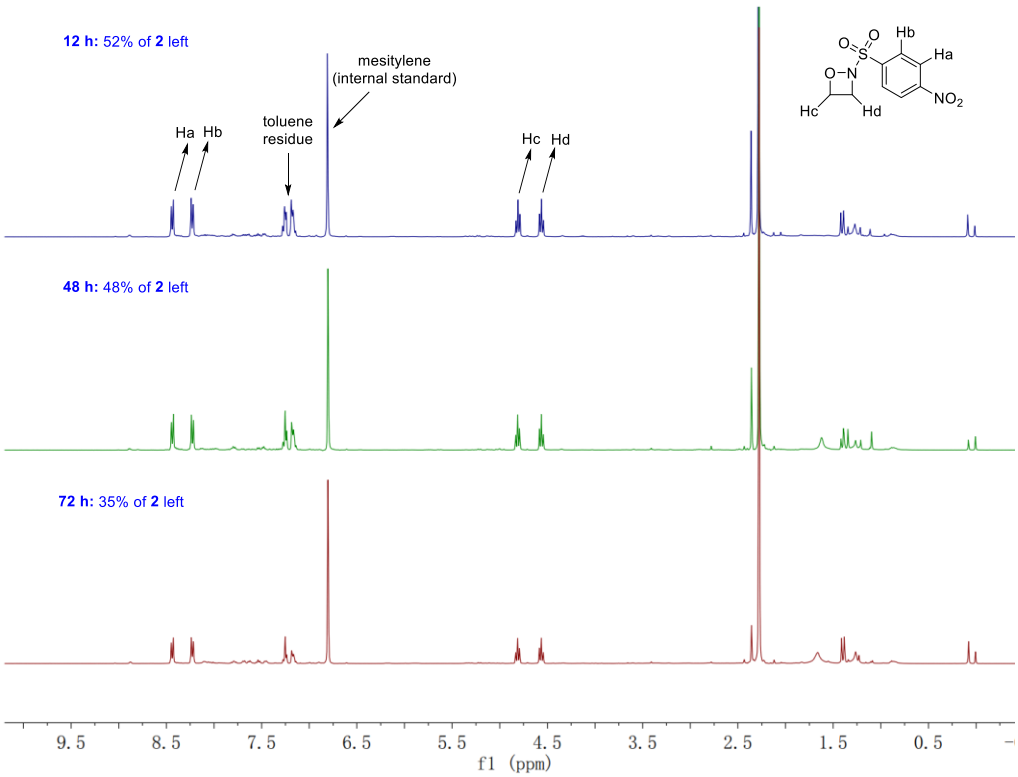


Figure S10. Comparison of the crude ^{1}H NMR (toluene as solvent)

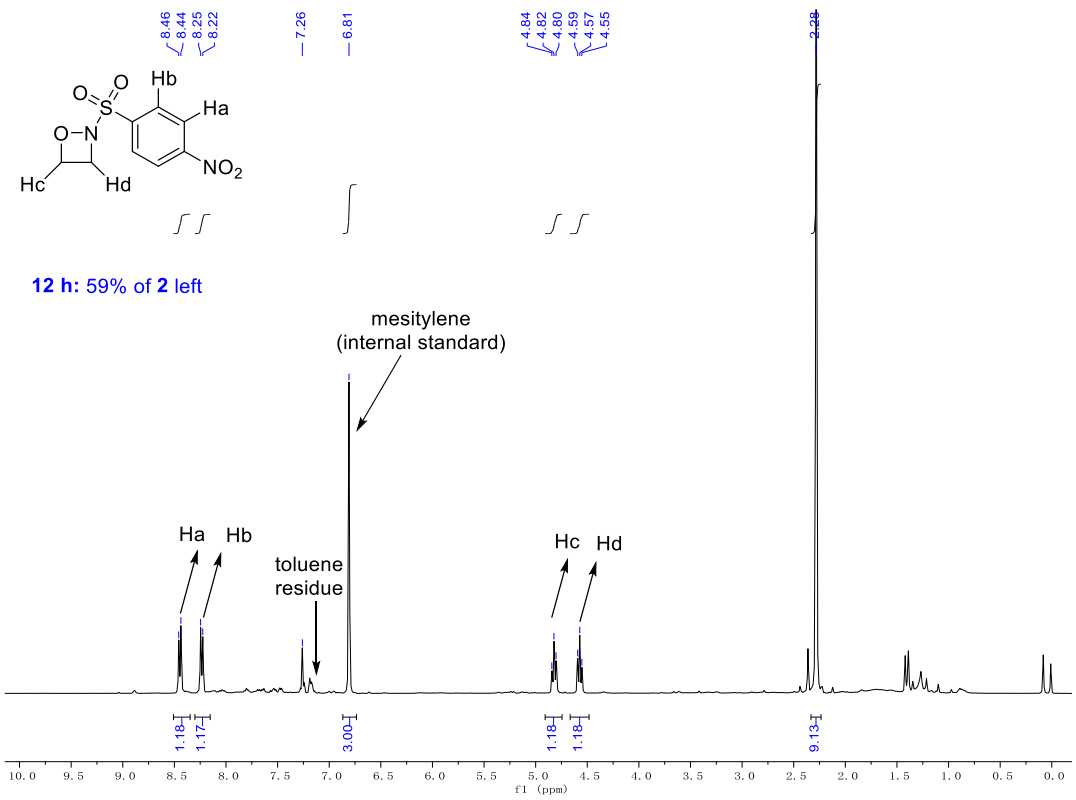


Figure S11. Crude ^{1}H NMR of compound 2 (^{t}BuOMe/Toluene as solvents, 12 h)

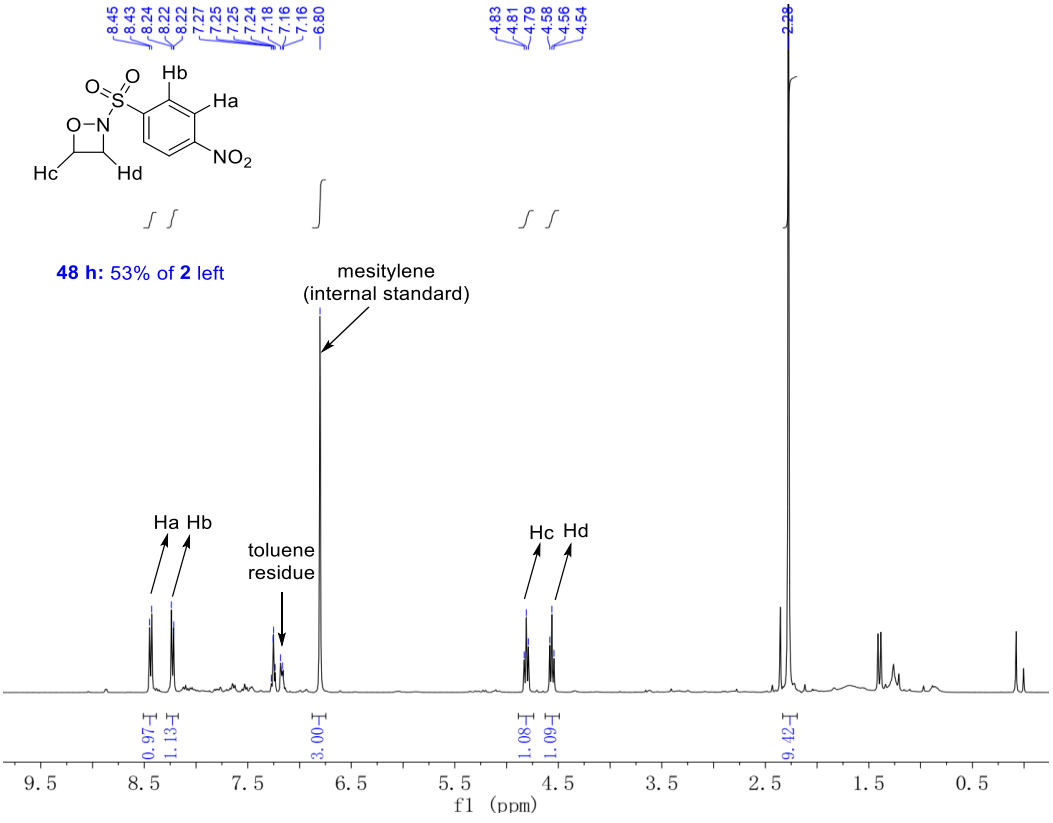


Figure S12. Crude ^{1}H NMR of compound 2 (^{t}BuOMe/Toluene as solvents, 48 h)

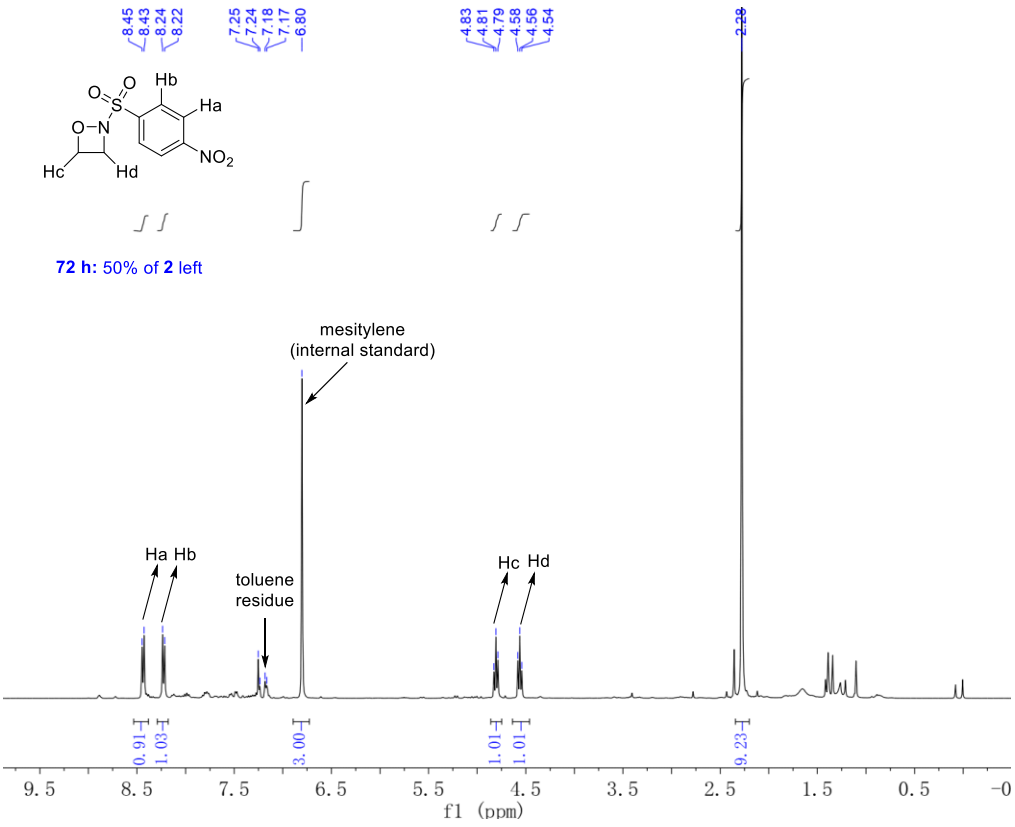


Figure S13. Crude ^{1}H NMR of compound 2 (^{t}BuOMe/Toluene as solvents, 72 h)

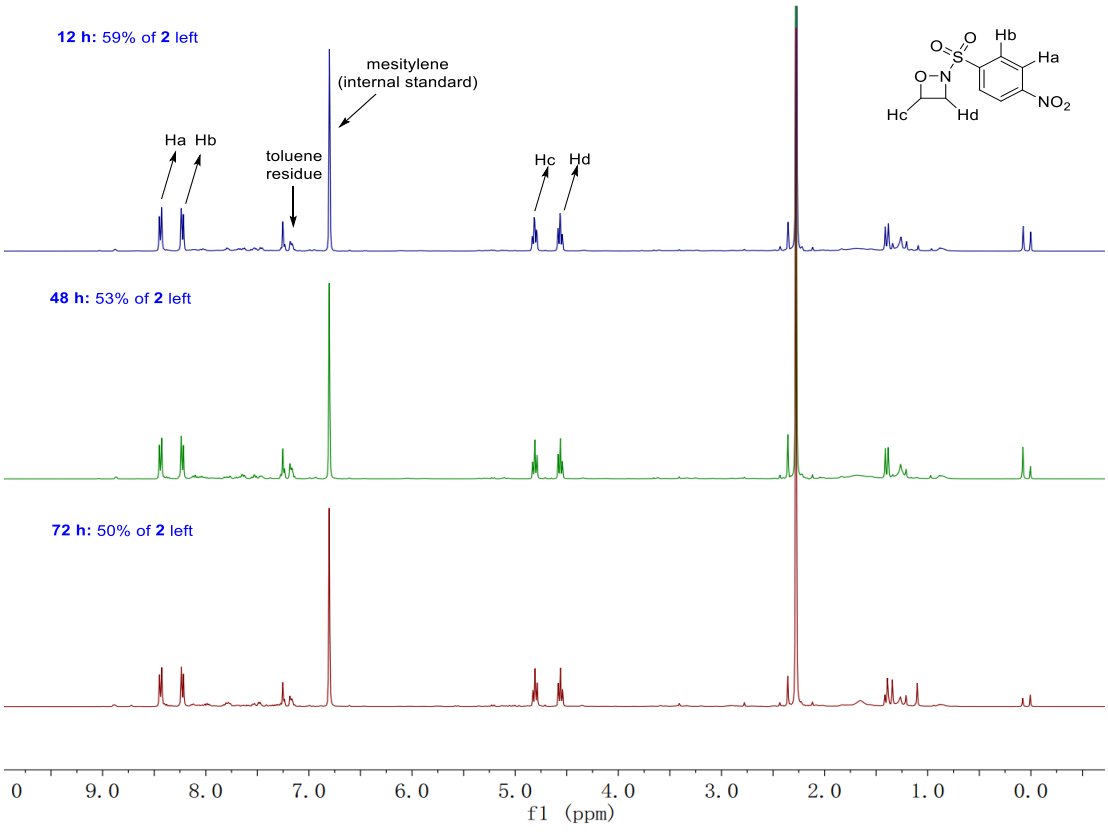
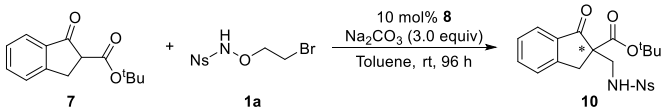


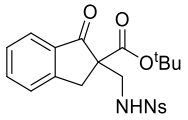
Figure S14. Comparison of the crude ^{1}H NMR (^{t}BuOMe/Toluene as solvents)

8.3 General procedure for catalytic asymmetric Mannich reactions



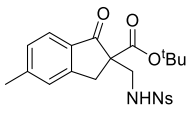
7 1a 10

To a solution of *tert*-butyl indanone carboxylate substrates **7** (0.24 mmol, 1.2 equiv), hydroxylamine **1a** (0.2 mmol, 1.0 equiv), and catalyst **8** (16 mg, 0.02mmol, 0.1 equiv) in toluene (2 mL) was added 20% aq. Na_2CO_3 (318 uL, 0.6 mmol, 3.0 equiv) at room temperature. The reaction mixture was stirred at the same temperature for 96 h. After completion, the solution was quenched with saturated NH_4Cl (2 mL) and extracted with EtOAc (3 mL x 3), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 10/1 ~ 5/1) to afford the products **10a-d** in 40-45% yield and 42-56% ee.



10a

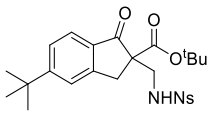
Following the general procedure described above, **10a** was obtained by flash silica chromatography (petroleum ether/EtOAc = 10/1) as a white solid (40 mg, 45% yield). The compound was determined to be 42% ee by HPLC analysis. **HPLC conditions:** Daicel Chiralpak AD-H, Hexane/*i*-PrOH = 70/30, 1.0 mL/min, 254 nm, 55 bar, 25 ^oC; t(major) = 13.9 min, t(minor) = 26.8 min. $[\alpha]_D^{25}$ = -12.6 (c = 0.3, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.5 Hz, 2H), 8.00 (d, *J* = 8.5 Hz, 2H), 7.77 – 7.63 (m, 2H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 1H), 5.67 (dd, *J* = 9.3, 4.4 Hz, 1H), 3.45 (d, *J* = 19.2 Hz, 3H), 3.22 (dd, *J* = 12.8, 9.1 Hz, 1H), 1.33 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.8, 170.2, 153.1, 150.1, 145.5, 135.9, 134.6, 128.2, 128.1, 126.7, 124.9, 124.5, 83.4, 60.6, 46.5, 35.9, 27.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{21}H_{22}N_2NaO_7S$ 469.1040; Found 469.1045. **Melting point:** 153.2-154.5 ^oC.



10b

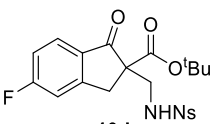
Following the general procedure described above, **10b** was obtained by flash

silica chromatography (petroleum ether/EtOAc = 10/1) as a white solid (40 mg, 43% yield). The compound was determined to be 56% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 ℃; t(major) = 19.8 min, t(minor) = 23.5 min. $[\alpha]_D^{25}$ = -27.4 (c = 1.25, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H), 8.00 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.31 (s, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 5.64 (dd, *J* = 8.9, 4.1 Hz, 1H), 3.41 (s, 3H), 3.21 (dd, *J* = 12.7, 9.2 Hz, 1H), 2.47 (s, 3H), 1.33 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.2, 170.3, 153.6, 150.1, 147.5, 145.6, 132.4, 129.4, 128.2, 127.0, 124.7, 124.5, 83.3, 60.7, 46.6, 35.8, 27.7, 22.2. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{22}H_{24}N_2NaO_7S$ 483.1209; Found 483.1196. **Melting point**: 161.7-162.6 ^oC.



10c

Following the general procedure described above, **10c** was obtained by flash silica chromatography (petroleum ether/EtOAc = 10/1) as a white solid (45 mg, 45% yield). The compound was determined to be 48% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 ℃; t(major) = 11.7 min, t(minor) = 15.8 min. $[\alpha]_D^{25}$ = -21.6 (c = 1.15, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.6 Hz, 2H), 8.00 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.54 – 7.40 (m, 2H), 5.68 (dd, *J* = 8.6, 3.9 Hz, 1H), 3.50 – 3.32 (m, 3H), 3.22 (dd, *J* = 12.5, 9.3 Hz, 1H), 1.37 (s, 9H), 1.34 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.3, 170.3, 160.5, 153.5, 150.1, 145.5, 132.2, 128.2, 126.0, 124.5, 123.2, 83.3, 60.8, 46.6, 36.0, 35.7, 31.1, 27.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{25}H_{30}N_2NaO_7S$ 525.1666; Found 525.1676. **Melting point:** 158.4-159.3 ^oC.



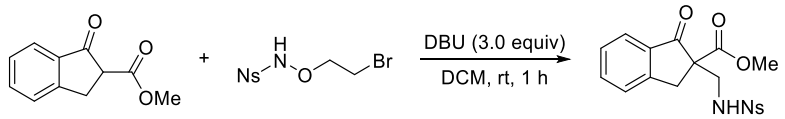
10d

Following the general procedure described above, **10d** was obtained by flash

silica chromatography (petroleum ether/EtOAc = 10/1) as a white solid (37mg, 40% yield). The compound was determined to be 52% ee by HPLC analysis. **HPLC conditions**: Daicel Chiralpak OD-H, Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 41 bar, 25 °C; t(major) = 21.3 min, t(minor) = 25.8 min. $[\alpha]_D^{25}$ = -19.1 (c = 2.12, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.7 Hz, 2H), 8.01 (d, *J* = 8.8 Hz, 2H), 7.75 (dd, *J* = 8.5, 5.2 Hz, 1H), 7.23 – 7.05 (m, 2H), 5.62 (dd, *J* = 8.9, 4.4 Hz, 1H), 3.55 – 3.38 (m, 3H), 3.22 (dd, *J* = 12.8, 9.1 Hz, 1H), 1.33 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.9, 169.7, 167.8 (d, $^1J_{C\text{-}F}$ = 258.2 Hz), 156.2 (d, $^3J_{C\text{-}F}$ = 10.4 Hz), 150.1, 145.4, 131.1, 128.2, 127.3 (d, $^3J_{C\text{-}F}$ = 11.5 Hz), 124.5, 116.6 (d, $^2J_{C\text{-}F}$ = 24.2 Hz), 113.5 (d, $^2J_{C\text{-}F}$ = 23.0 Hz), 83.6, 61.0, 46.3, 35.7, 27.7. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{21}H_{21}FN_2NaO_7S$ 487.0956; Found 487.0951. **Melting point:** 155.6-156.6 °C.

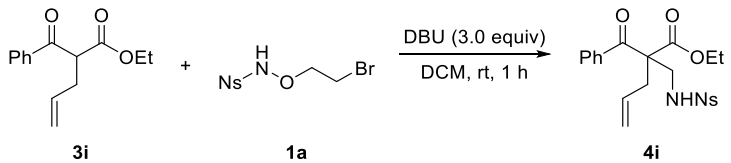
9. Gram-scale synthesis and synthetic applications

9.1 Gram-scale synthesis of compounds 4s, 4i, and 6b



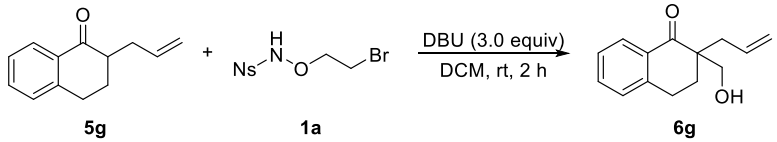
3s **1a** **4s**

To a solution of **3s** (1.9 g, 10 mmol, 2.0 equiv) and DBU (2.3 g, 15 mmol, 3.0 equiv) in DCM (25 mL) was added the solution of **1a** (1.6 g, 5 mmol, 1.0 equiv) in DCM (25 mL) at room temperature over 10 minutes. The reaction mixture was stirred at the same temperature for 1 h. After completion, the solution was quenched with saturated NH_4Cl (20 mL) and extracted with DCM (40 mL x 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 8/1) to afford the product **4s** as a white solid (1.83 g, 91% yield).



3i **1a** **4i**

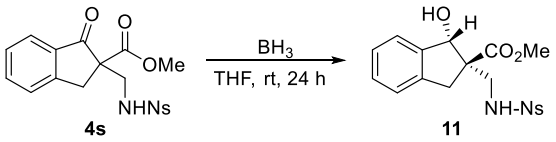
To a solution of **3i** (1.86 g, 8 mmol, 2.0 equiv) and DBU (1.81 g, 12 mmol, 3.0 equiv) in DCM (20 mL) was added the solution of **1a** (1.3 g, 4 mmol, 1.0 equiv) in DCM (20 mL) at room temperature over 10 minutes. The reaction mixture was stirred at the same temperature for 1 h. After completion, the solution was quenched with saturated NH_4Cl (20 mL) and extracted with DCM (30 mL x 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 8/1) to afford the product **4i** as a white solid (1.4 g, 78% yield).



5g **1a** **6g**

To a solution of α-substituted ketone **5g** (1.86 g, 10 mmol, 1.0 equiv) and DBU (4.54 g, 30 mmol, 3.0 equiv) in DCM (30 mL) was added the solution of **1a** (4.88 g, 15 mmol, 1.5 equiv) in DCM (30 mL) at room temperature over 10 min. The reaction mixture was stirred at the same temperature for 2 h. After completion, the solution was quenched with saturated NH_4Cl (20 mL) and extracted with DCM (30 mL x 3). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 8/1) to afford the product **6g** as a colorless oil (1.13 g, 52% yield).

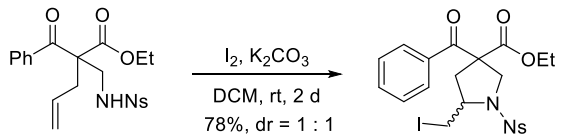
9.2 Synthetic applications



4s **11**

To a solution of **4s** (81 mg, 0.2 mmol, 1.0 equiv) in anhydrous THF (2 mL) was added dropwise of borane (1.0 M solution in THF, 0.4 mL, 0.4 mmol, 2.0 equiv) at room temperature under an N_2 atmosphere. After stirring for 24 h at the same temperature, the mixture was quenched with EtOH (2 mL) and concentrated. The residue was diluted with H_2O (3 mL) and extracted with EtOAc (5 mL x 3). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuum. The

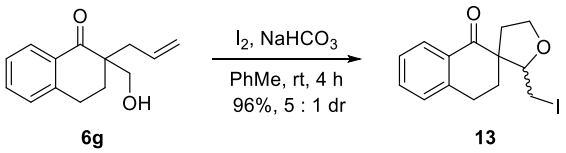
residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 5/1) to afford the product **11** as a white solid (50 mg, 61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.6 Hz, 2H), 7.97 (d, *J* = 8.6 Hz, 2H), 7.39 – 7.30 (m, 1H), 7.30 – 7.21 (m, 2H), 7.20 – 7.08 (m, 1H), 5.82 – 5.73 (m, 1H), 5.72 – 5.65 (m, 1H), 3.73 (s, 3H), 3.42 – 3.28 (m, 2H), 3.23 (d, *J* = 16.4 Hz, 1H), 3.13 – 2.97 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.8, 149.9, 145.6, 141.3, 138.2, 128.9, 128.2, 127.5, 124.7, 124.4, 124.2, 79.2, 58.3, 52.8, 45.7, 38.1. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{18}H_{18}N_2NaO_7S$ 429.0727; Found 429.0730. **Melting point:** 110.3-112.1 °C.



4i **12**

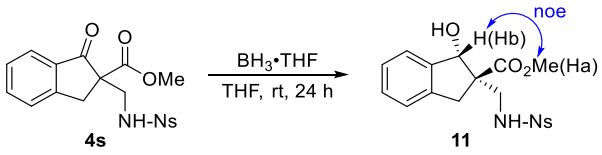
K_2CO_3 (83 mg, 0.6 mmol, 3.0 equiv) and I_2 (152 mg, 0.6 mmol, 3.0 equiv) were added to a solution of the **4i** (89 mg, 0.2 mmol, 1.0 equiv) in DCM (4 mL) at room temperature. The reaction mixture was stirred at the same temperature for 2 days. Then, a saturated aqueous solution of $Na_2S_2O_3$ (5 mL) was added, the phases were separated and the aqueous phase was extracted with DCM (5 mL x 3). The organic phases were combined, washed with brine (3mL), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 8/1) to afford the product **12** as a white solid (89 mg, 78% yield, dr = 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.44 – 8.34 (m, 1H), 8.11 – 8.01 (m, 2H), 7.81 – 7.71 (m, 2H), 7.63 – 7.52 (m, 1H), 7.52 – 7.39 (m, 2H), 7.40 – 7.30 (m, 1H), 4.40 (dd, *J* = 12.2, 2.5 Hz, 0.56H), 4.20 (dd, *J* = 12.0, 2.4 Hz, 0.36H), 4.17 – 4.00 (m, 2.56H), 3.97 – 3.79 (m, 1.39H), 3.73 – 3.63 (m, 0.57H), 3.61 – 3.47 (m, 1H), 3.46 – 3.36 (m, 0.38H), 3.06 – 2.83 (m, 1H), 2.37 (ddd, *J* = 13.6, 7.8, 2.7 Hz, 0.4H), 2.22 (ddd, *J* = 13.5, 8.0, 2.6 Hz, 0.56H), 1.03 – 0.88 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.2, 191.8, 170.8, 170.0, 150.2, 150.1, 143.9, 142.4, 134.3, 134.1, 133.9, 132.4, 128.9, 128.7, 128.7, 128.6, 128.5, 128.4, 124.4, 124.1, 62.5, 62.5, 62.1, 61.3, 60.5, 60.2, 54.8, 54.7, 40.6, 40.0, 13.6, 13.5, 11.6, 10.9. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{21}H_{21}IN_2NaO_7S$ 595.0006; Found 595.0019. **Melting point:** 111.7-113.5

°C.



$NaHCO_3$ (50 mg, 0.6 mmol, 3.0 equiv) and I_2 (127 mg, 0.5 mmol, 2.5 equiv) were added to a solution of **6g** (43 mg, 0.2 mmol, 1.0 equiv) in PhMe (2 mL) at room temperature. The reaction mixture was stirred at the same temperature for 4 h. Then, a saturated aqueous solution of $Na_2S_2O_3$ (5 mL) was added, the phases were separated and the aqueous phase was extracted with DCM (5 mL x 3). The organic phases were combined, washed with brine (3mL), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 15/1) to afford the product **13** as a brown oil (66 mg, 96% yield, dr = 5:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 6.9 Hz, 1H), 7.31 (t, *J* = 7.1 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 4.37 – 4.26 (m, 0.18H), 4.25 – 4.10 (m, 1.94H), 3.93 (d, *J* = 8.8 Hz, 0.89H), 3.85 (d, *J* = 8.9 Hz, 0.18H), 3.42 – 3.25 (m, 2H), 3.07 – 2.91 (m, 2H), 2.57 (dd, *J* = 12.6, 6.4 Hz, 0.95H), 2.33 (dd, *J* = 12.9, 7.5 Hz, 0.15H), 2.26 – 2.19 (m, 2H), 2.09 (dd, *J* = 12.9, 7.1 Hz, 0.17H), 1.59 (dd, *J* = 12.6, 8.9 Hz, 0.9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.1, 198.3, 143.0, 143.0, 133.6, 131.4, 131.0, 128.6, 128.0, 126.8, 79.5, 78.5 , 75.2, 75.1, 54.6, 42.1, 40.7, 33.4, 32.4, 26.7, 26.1, 10.2, 8.5. **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{14}H_{15}INaO_2$ 365.0009; Found: 365.0010.

10. Determination of the relative configuration of compound 11



NOE analysis was used to determine the relative configuration of compound **11**. As shown in **Figure S15**, when selecting to irradiate Ha (OMe) proton signal in compound **11**, a clear NOE effect between Hb and Ha (OMe) was observed. This result indicated the protons of Hb and Ha (CO_2Me) are on the same side of the ring,

namely, they are mutually *cis* to each other.

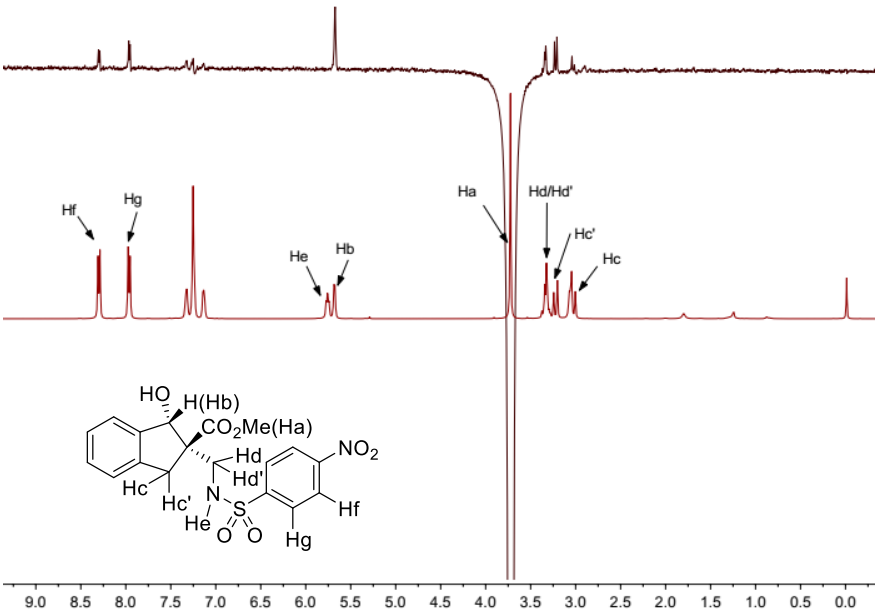


Figure S15. Comparison of the ^{1}H NMR and NOE spectra of compound 11

11. References

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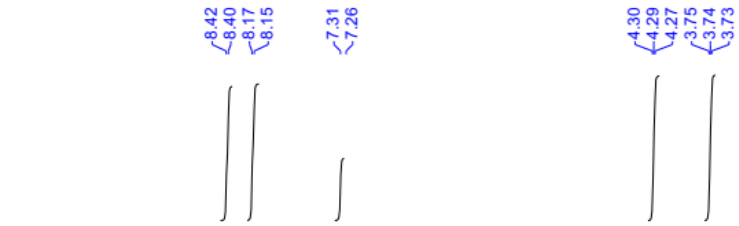
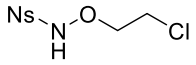
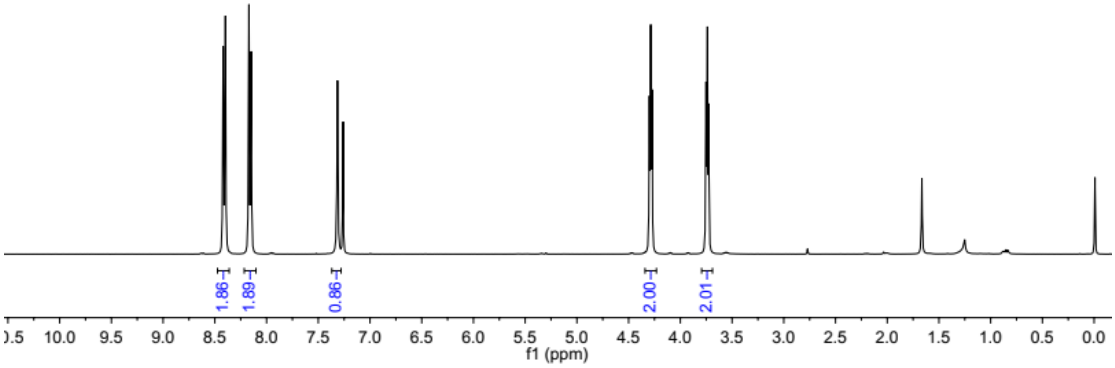
12. Spectra data for the new compounds



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



1e



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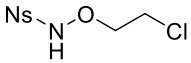

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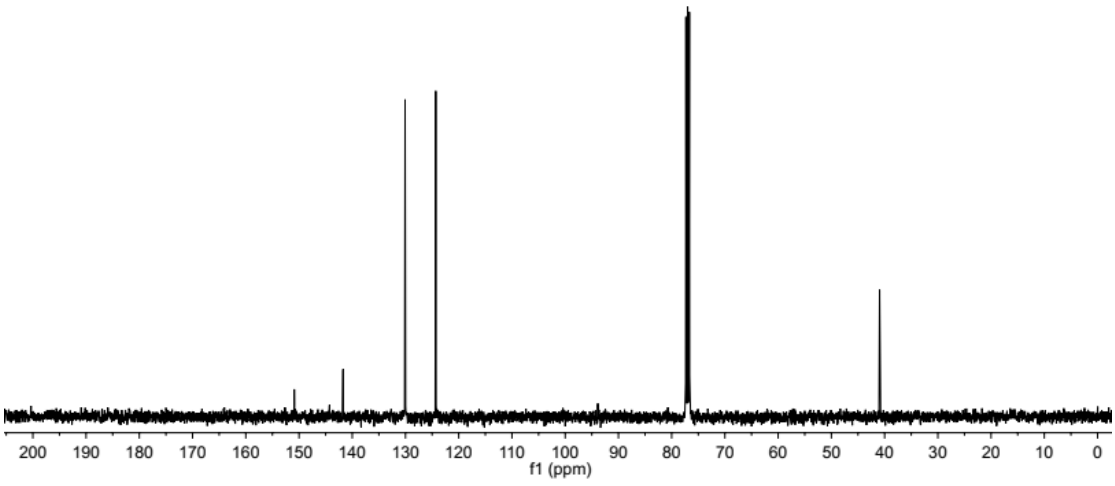

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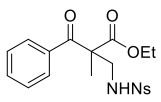
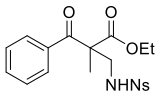
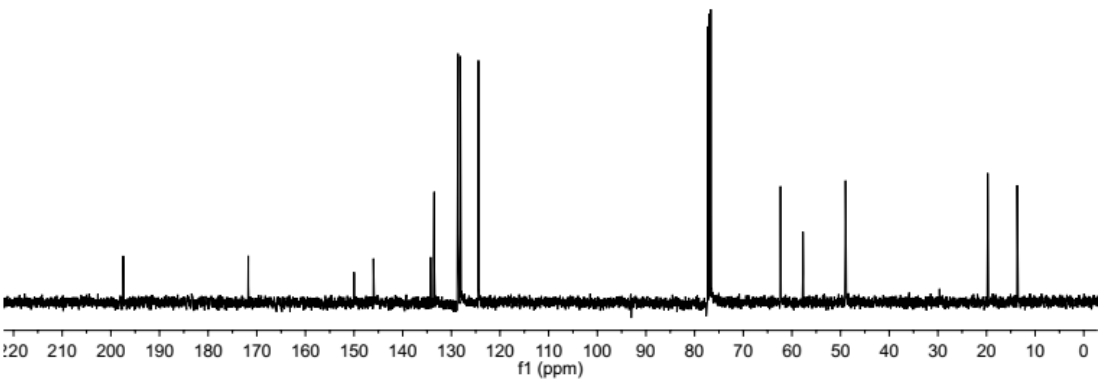


4a

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



4a



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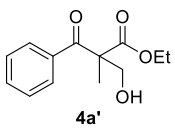

4a'

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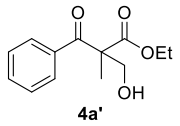

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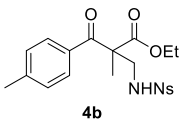

4b

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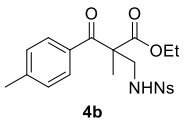

4b

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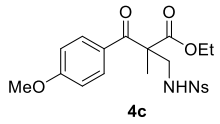

4c

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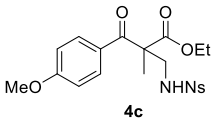

4c

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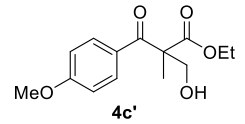

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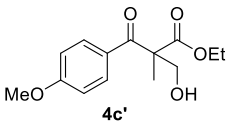

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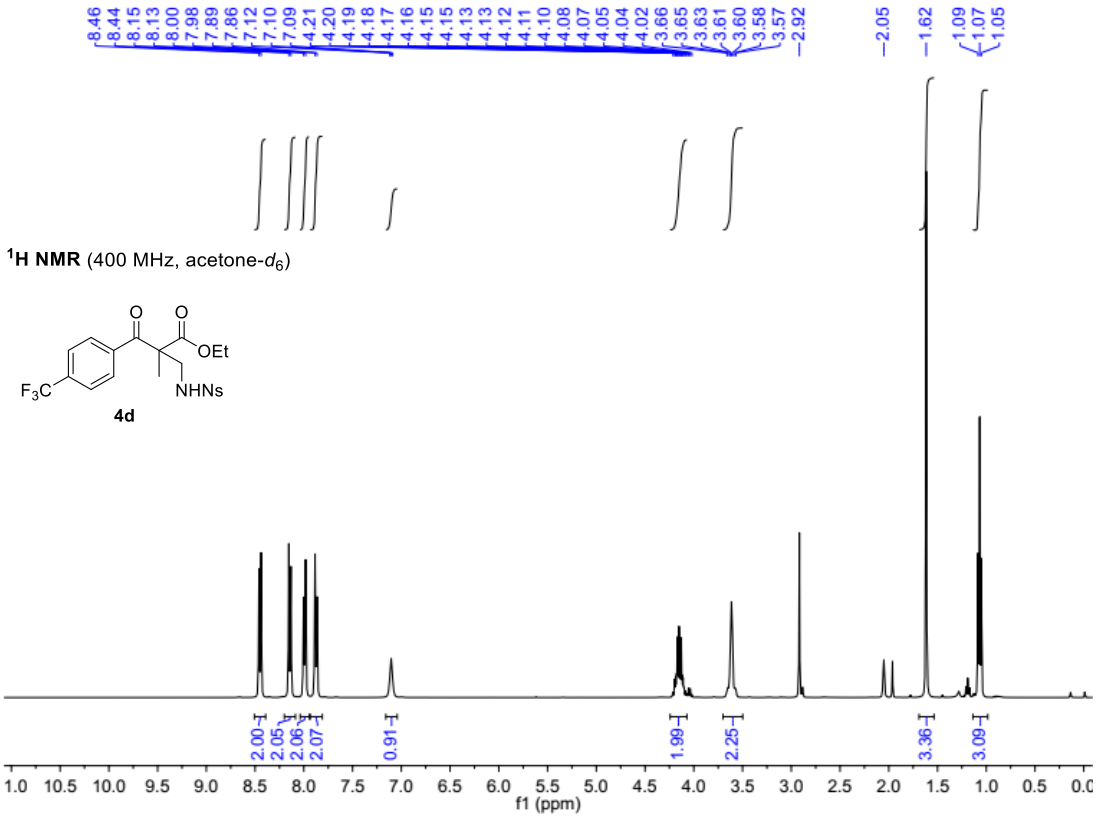

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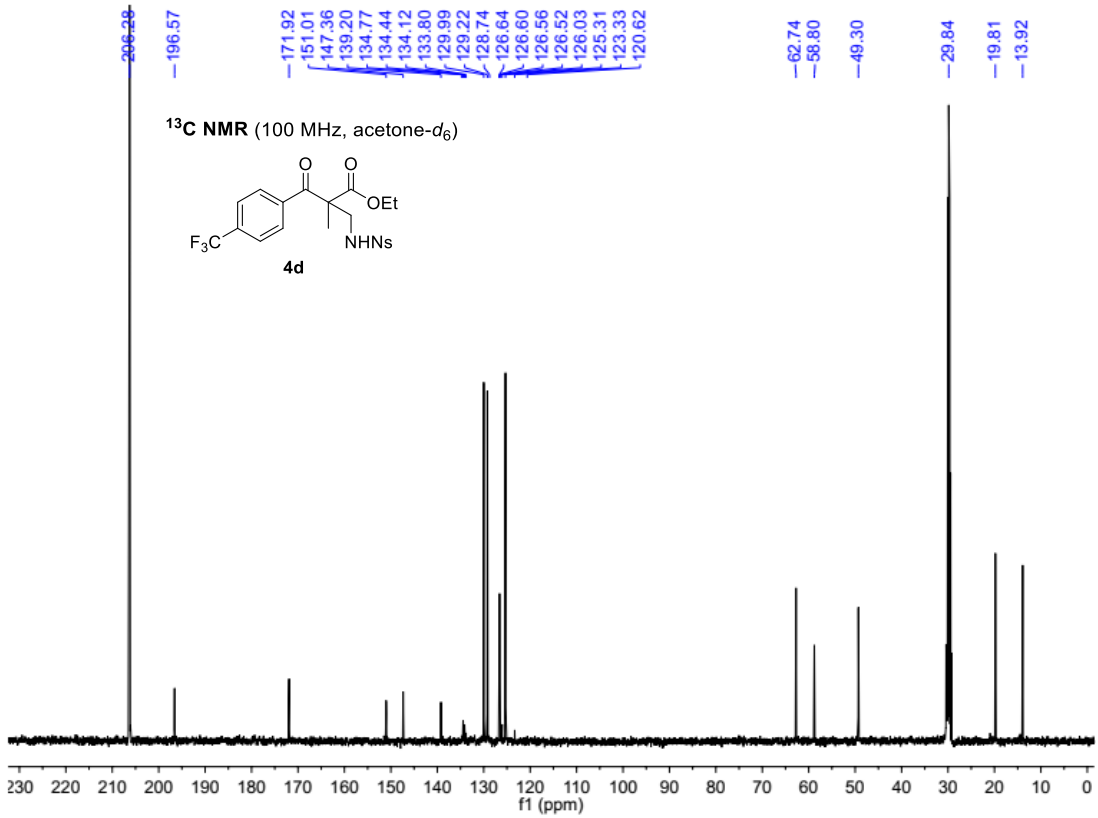
4d



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

4d

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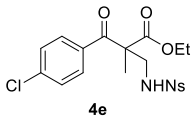

4e

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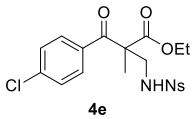

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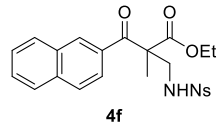

4f

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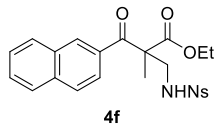

4f

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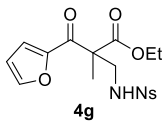

4g

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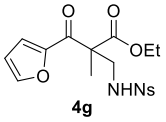

4g

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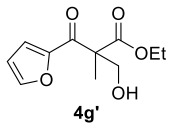

4g'

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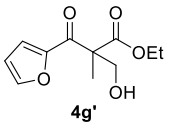
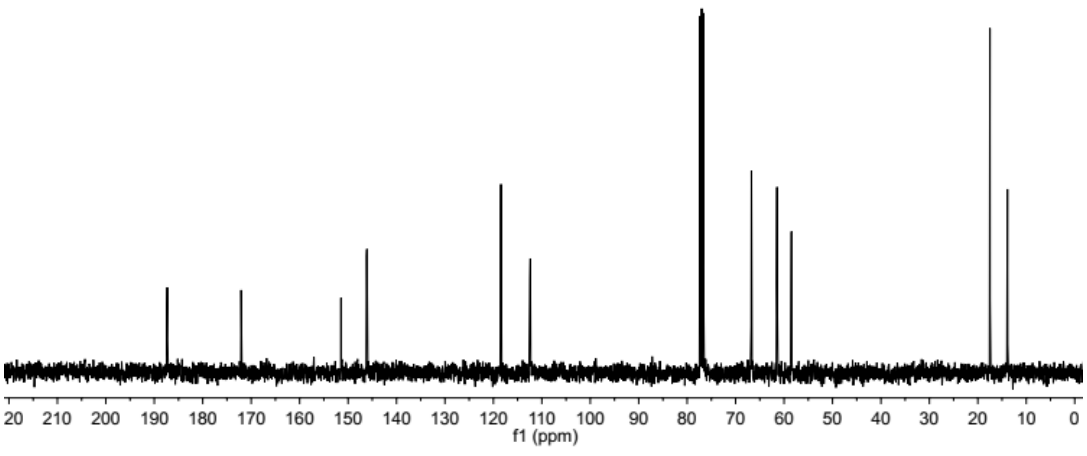
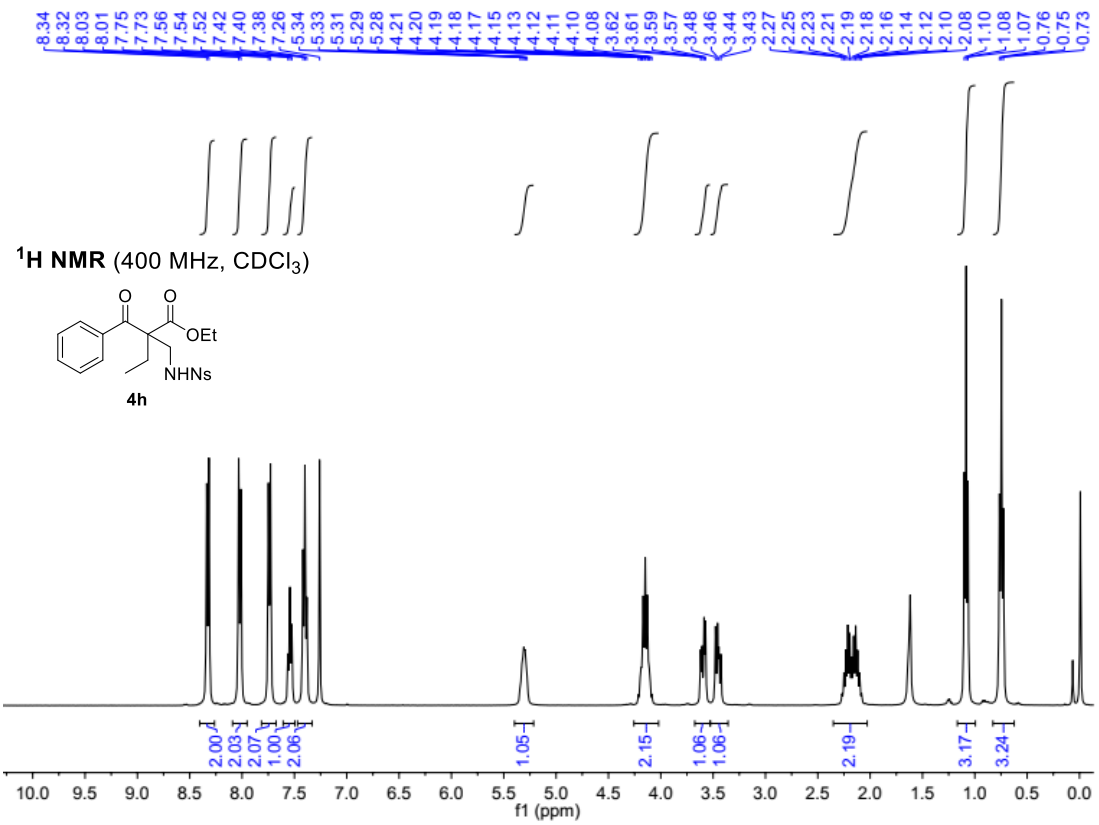
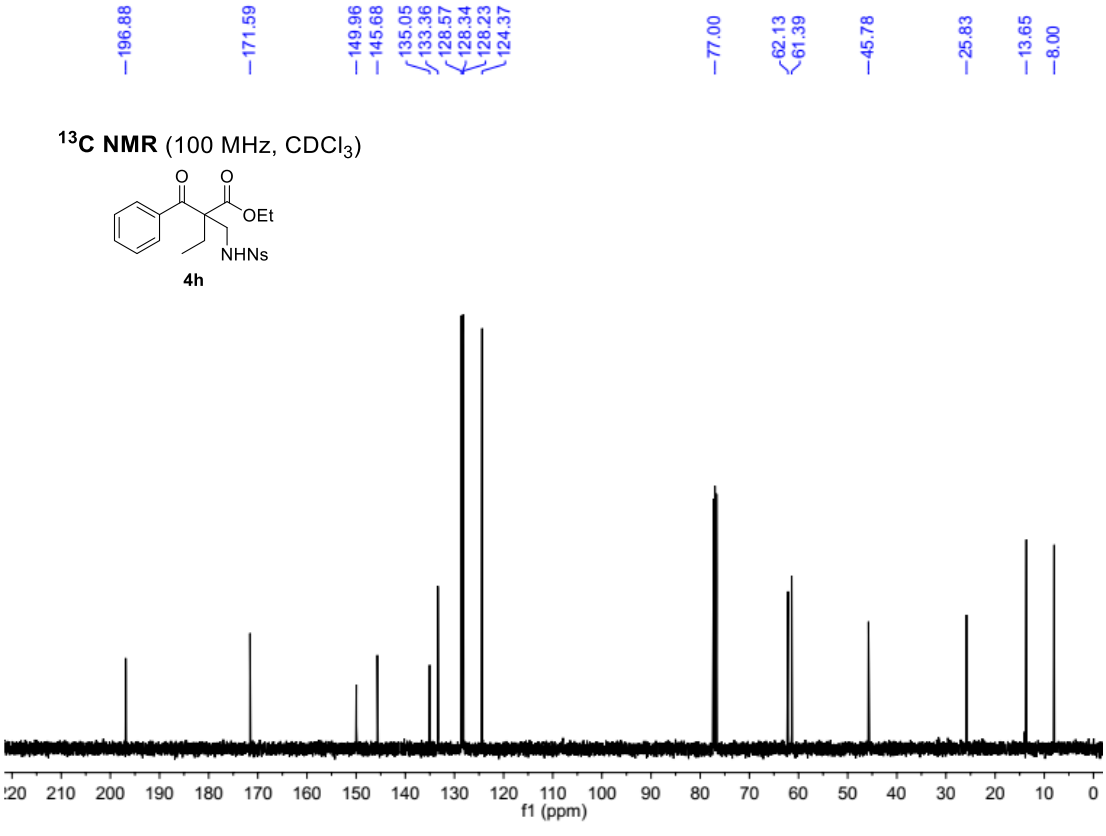


4g'




8.34
8.32
8.03
8.01
7.75
7.73
7.56
7.54
7.52
7.42
7.40
7.38
7.26
5.34
5.33
5.31
5.29
5.28
4.21
4.20
4.19
4.18
4.17
4.15
4.13
4.12
4.11
4.10
4.08
3.62
3.61
3.59
3.57
3.48
3.46
3.44
3.43
2.27
2.25
2.23
2.21
2.19
2.18
2.16
2.14
2.12
2.10
2.08
1.10
1.08
1.07
0.76
0.75
0.73
1H NMR (400 MHz, CDCl3)
O
O
OEt
NHNs
4h
2.00
2.03
2.07
1.00
2.06
1.05
2.15
1.06
1.06
2.19
3.17
3.24
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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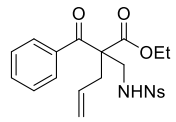
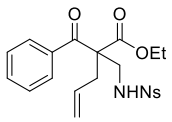
171.59
149.96
145.68
135.05
133.36
128.57
128.34
128.23
124.37
77.00
62.13
61.39
45.78
25.83
13.65
8.00
13C NMR (100 MHz, CDCl3)
O
O
OEt
NHNs
4h
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

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



4i

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



4i

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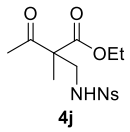

4j

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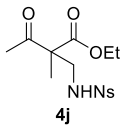

4j

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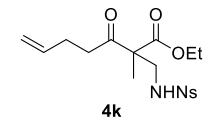

4k

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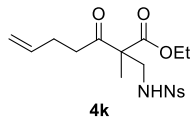

4k

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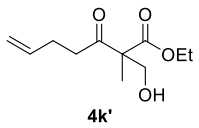

4k'

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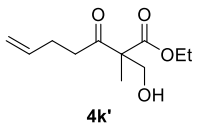
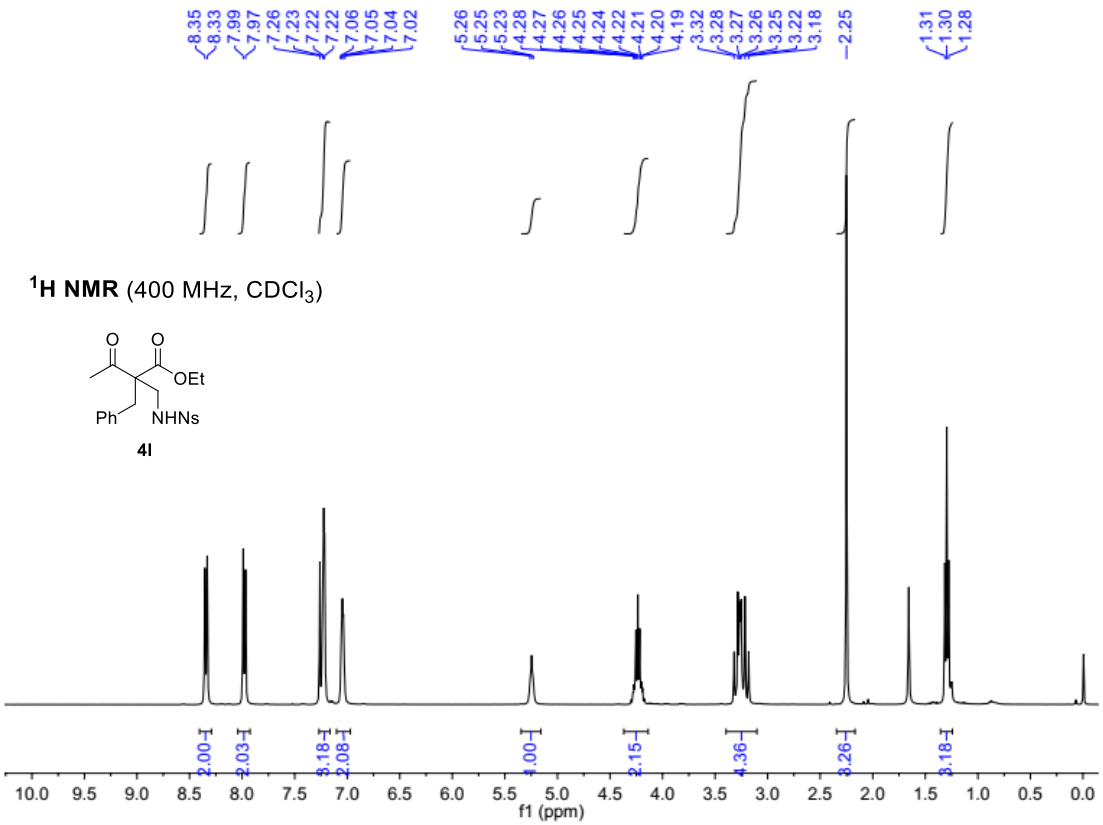
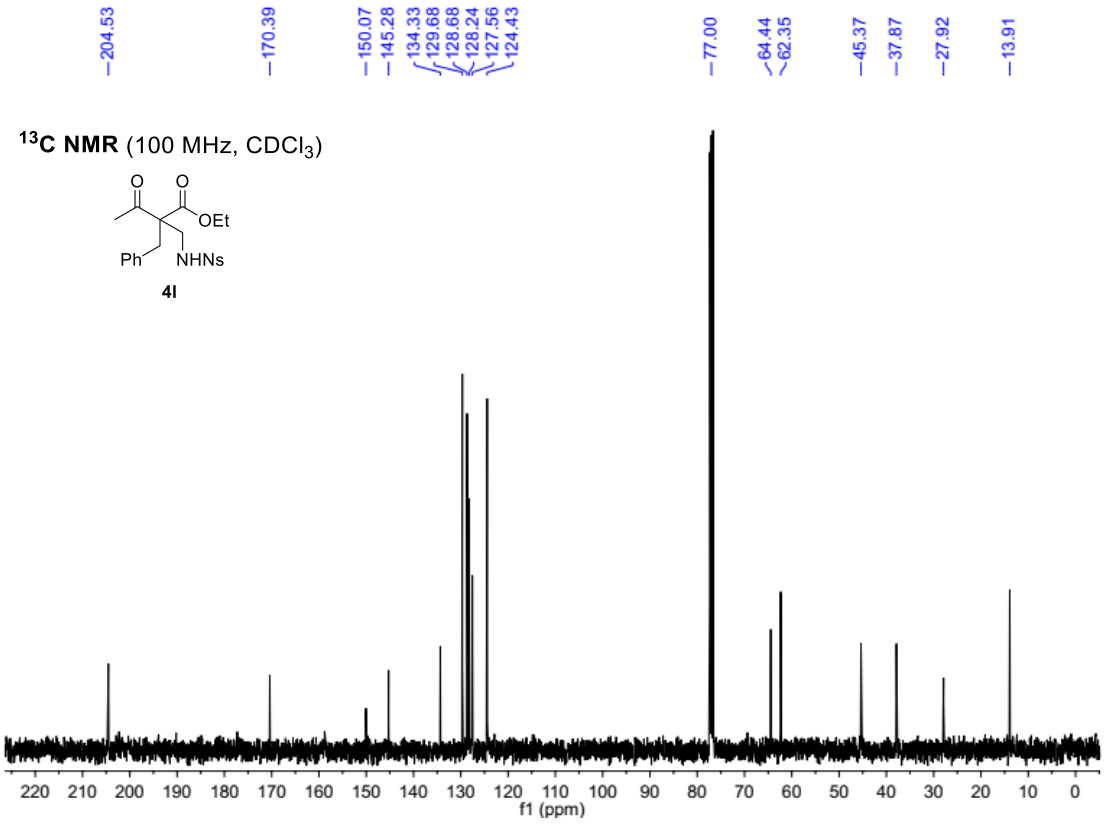


4k'



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

4l



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

4l

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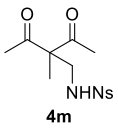

4m

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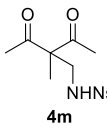

4m

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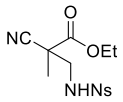
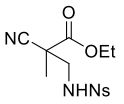


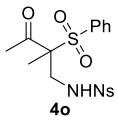
4n

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



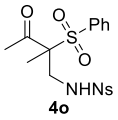
4n

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



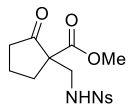
4o

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



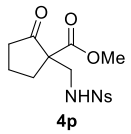
4o

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



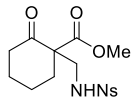
4p

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



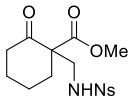
4p

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

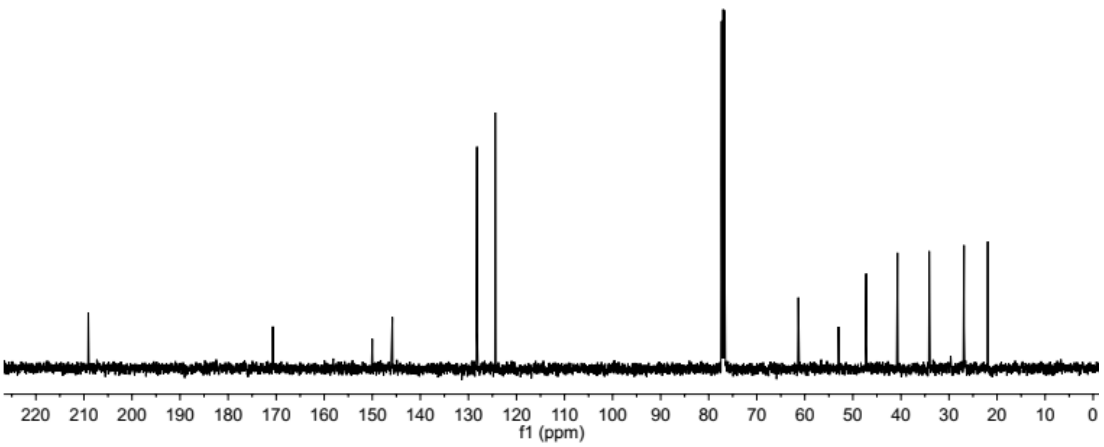


4q

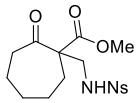
^{13}C NMR (100 MHz, $CDCl_3$)



4q

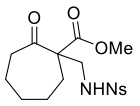


^{1}H NMR (400 MHz, $CDCl_3$)



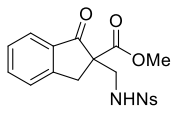
4r

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



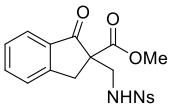
4r

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



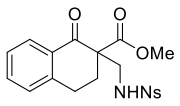
4s

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



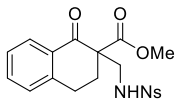
4s

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



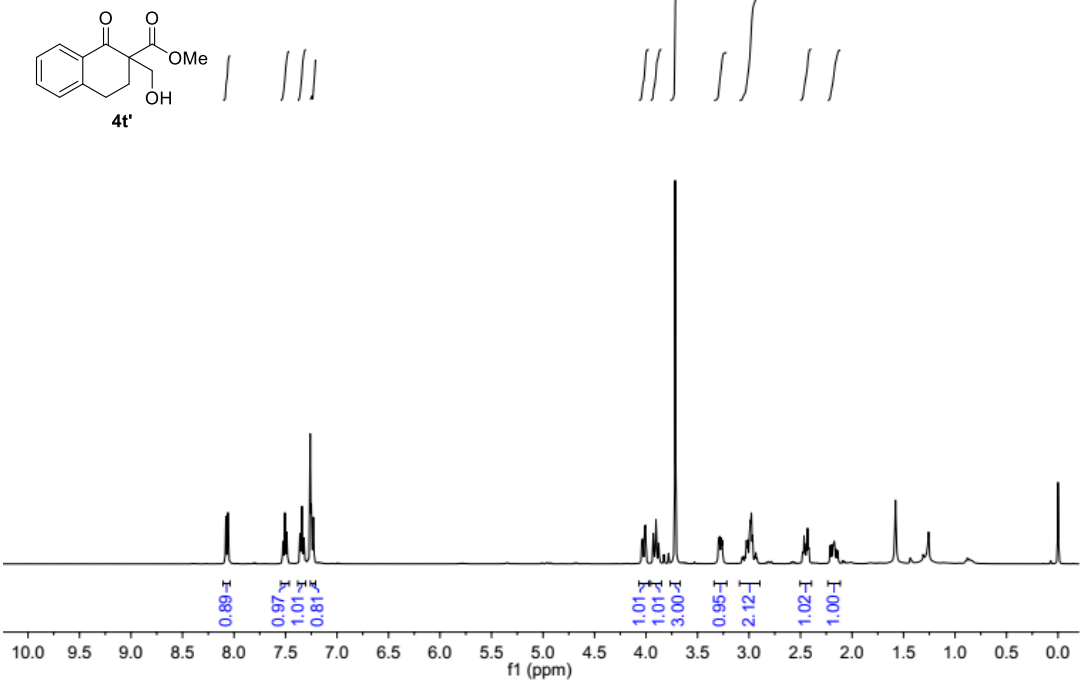
4t

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



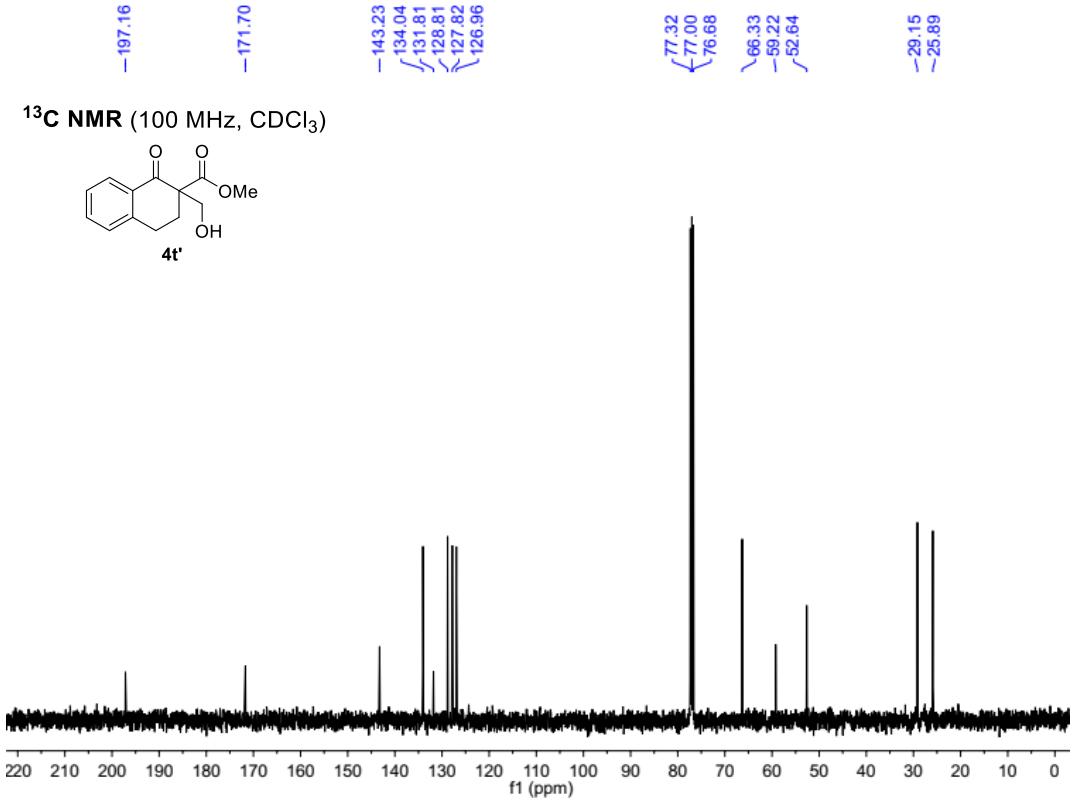
4t

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



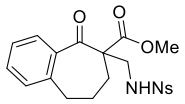
4t'

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



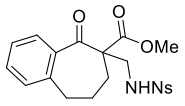
4t'

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

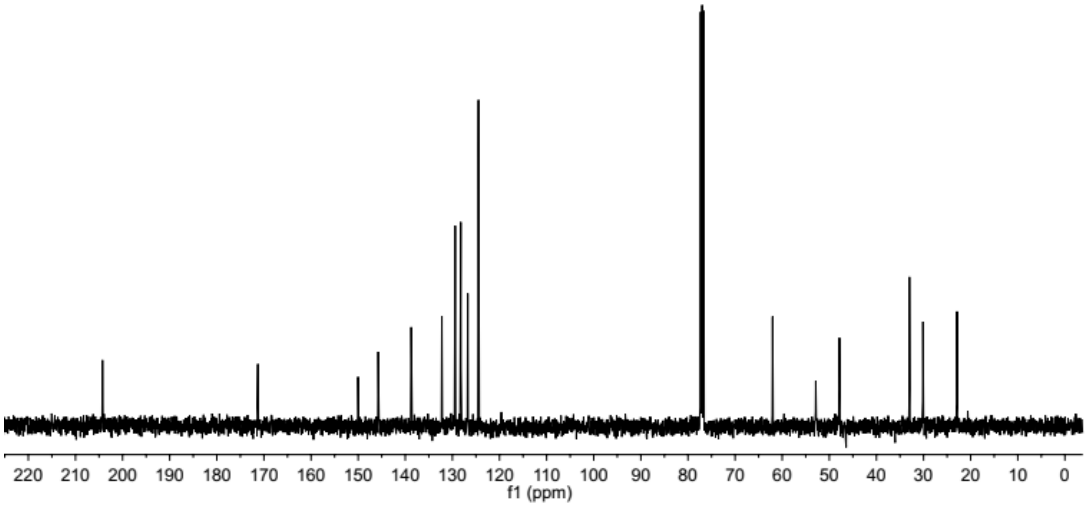


4u

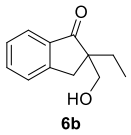
^{13}C NMR (100 MHz, $CDCl_3$)



4u

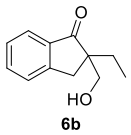


^{1}H NMR (400 MHz, $CDCl_3$)

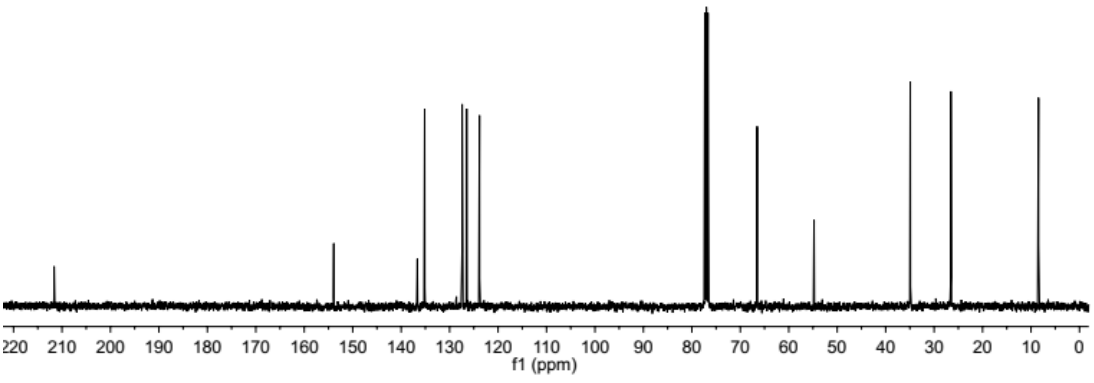


6b

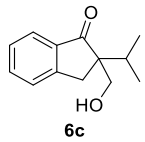
^{13}C NMR (100 MHz, $CDCl_3$)



6b

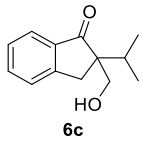


^{1}H NMR (400 MHz, $CDCl_3$)

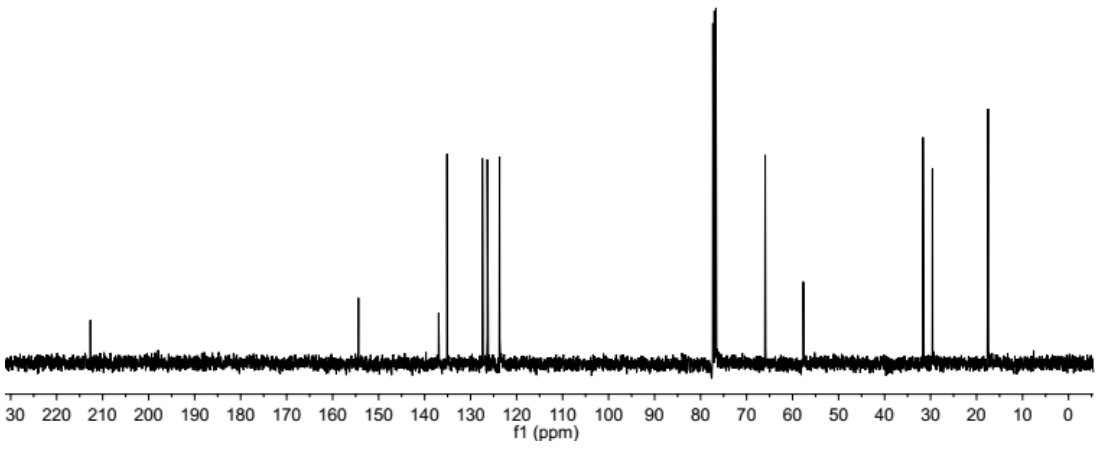


6c

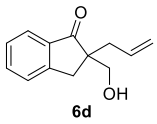
^{13}C NMR (100 MHz, $CDCl_3$)



6c

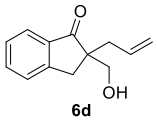


^{1}H NMR (400 MHz, $CDCl_3$)



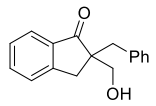
6d

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



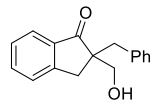
6d

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



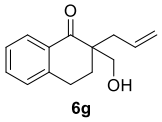
6e

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



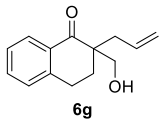
6e

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

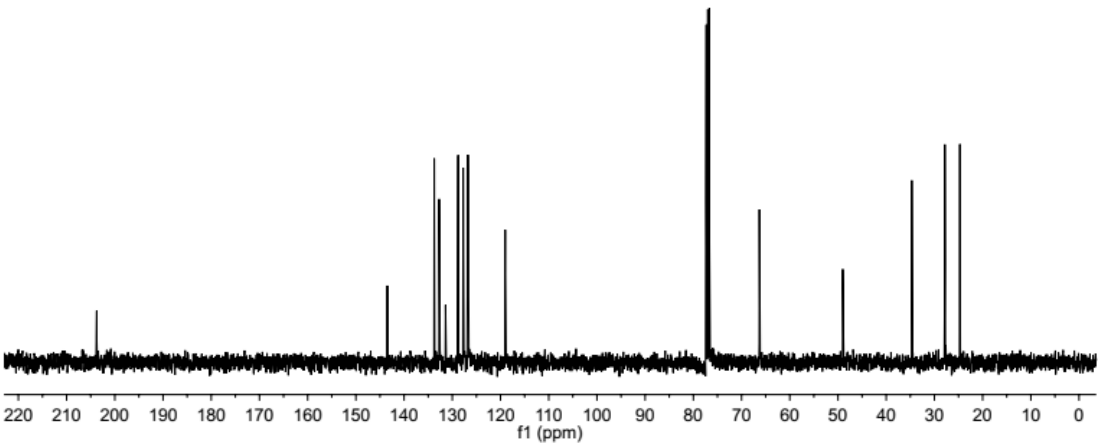


6g

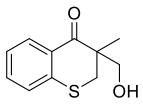
^{13}C NMR (100 MHz, $CDCl_3$)



6g

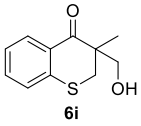


^{1}H NMR (400 MHz, $CDCl_3$)



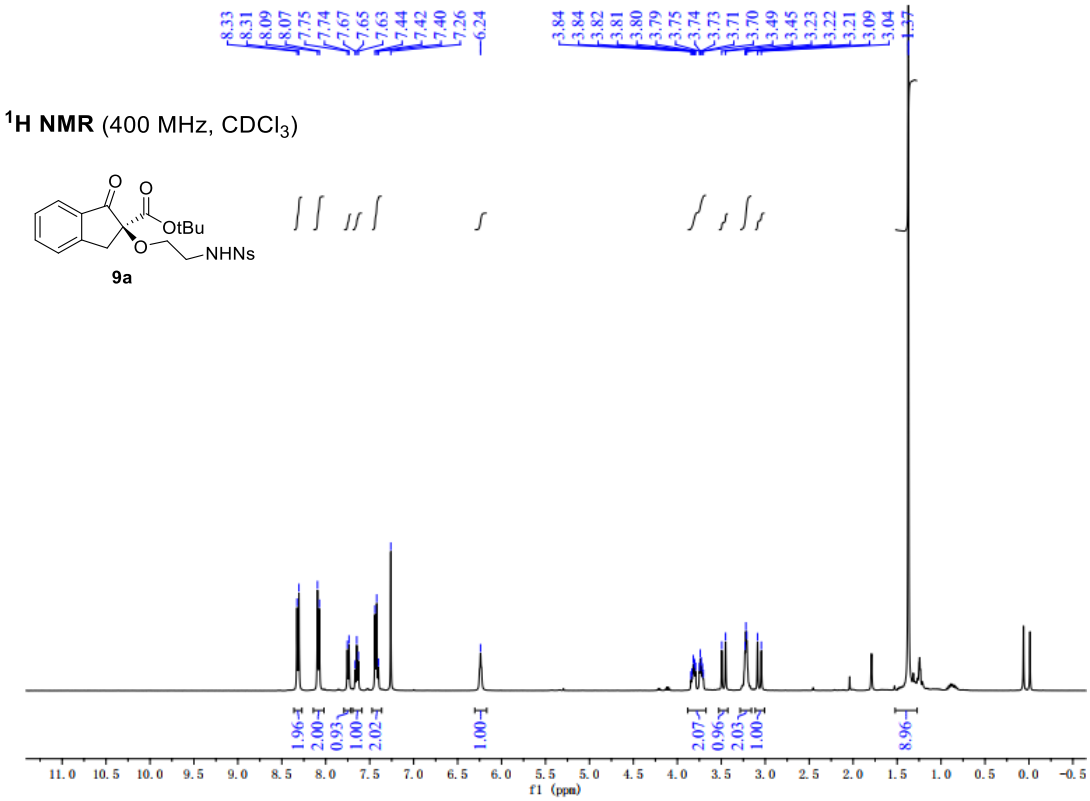
6i

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



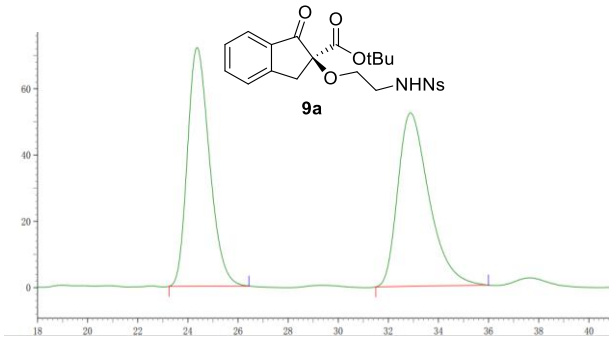
6i

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



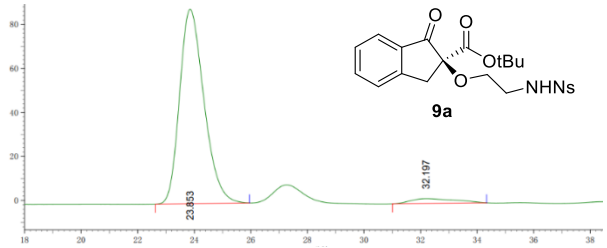
HPLC spectrum of compound **9a**:

Racemate:

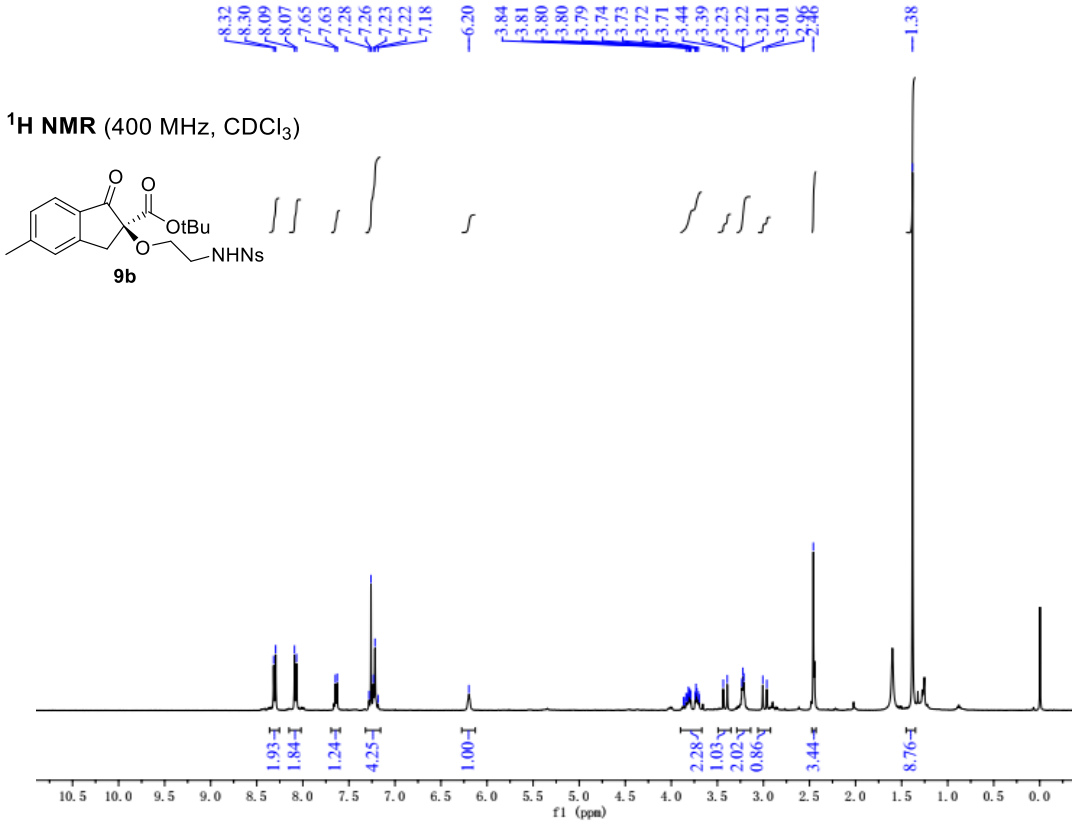


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	24.363	288118	17631015	49.254
2	32.883	209217	18164732	50.746

Enantioselective:

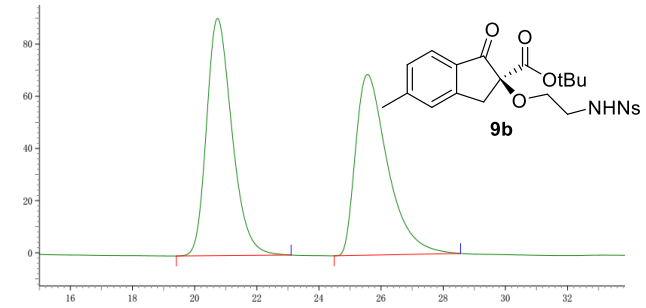


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	23.853	353678	21217754	95.655
2	32.197	8861	963833	4.345



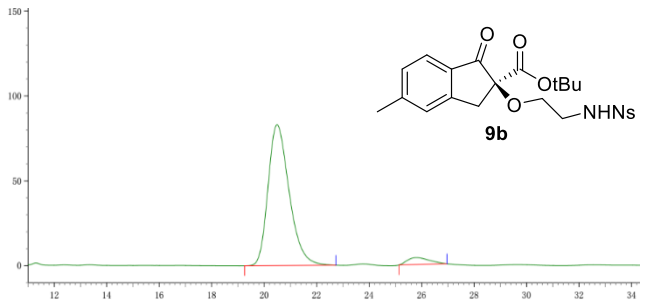
HPLC spectrum of compound **9b**:

Racemate:



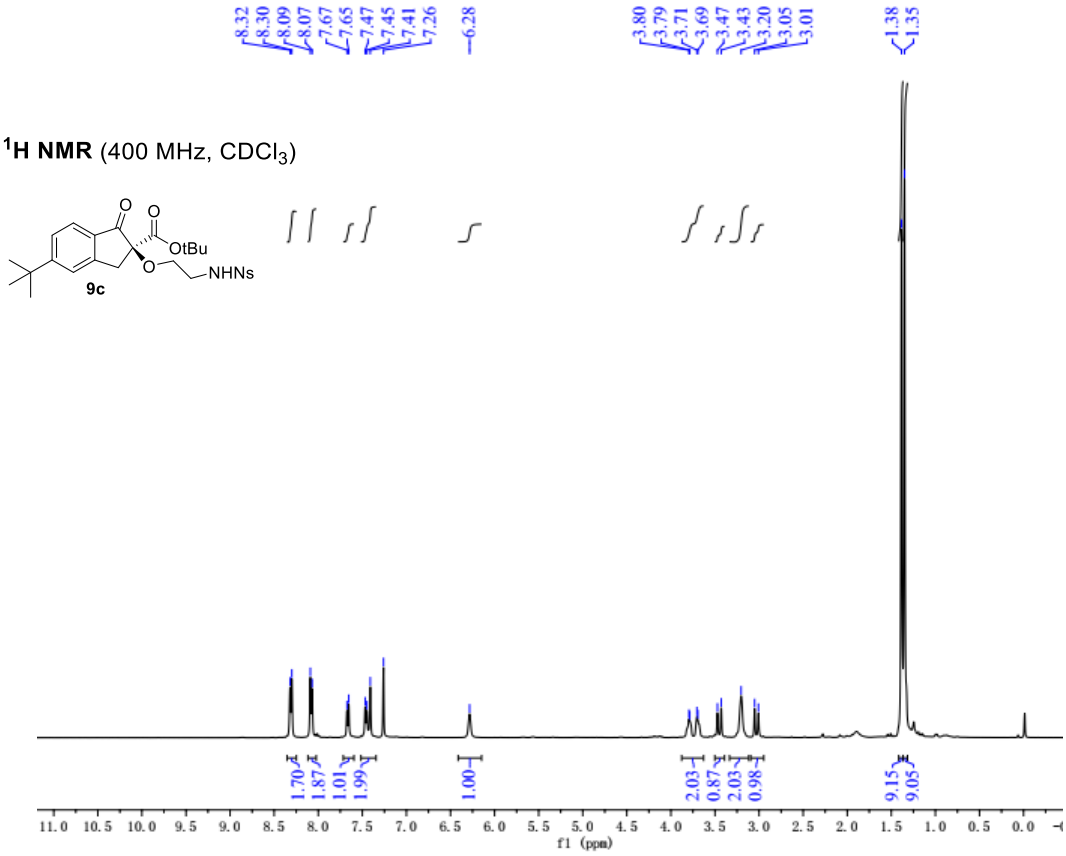
Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	20.737	363957	20710714	50.928
2	25.563	277312	19955777	49.072

Enantioselective:



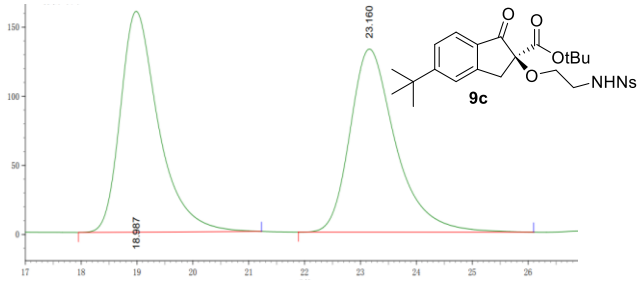
Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	20.490	331992	18594680	95.182
2	25.797	16130	941333	4.818

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



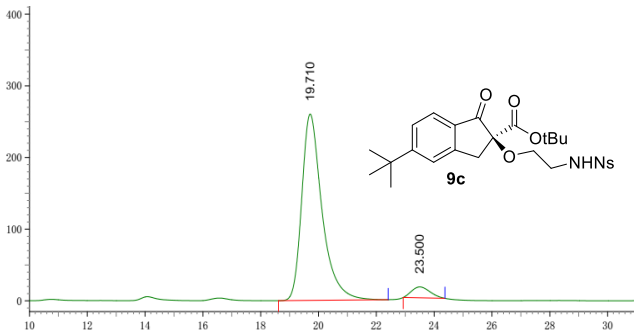
HPLC spectrum of compound **9c**:

Racemate:

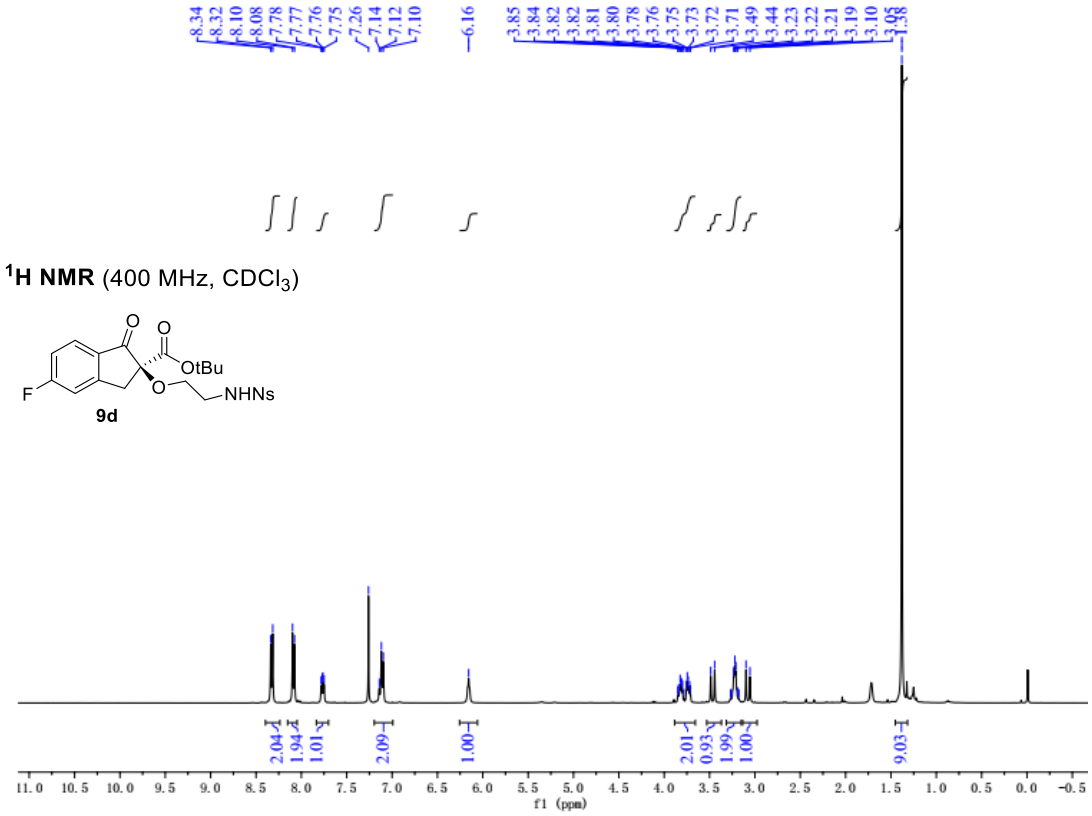


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	18.987	638915	30288506	50.183
2	23.160	529871	30067386	49.817

Enantioselective:



Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	19.710	1040320	50723618	94.972
2	23.500	60946	2685605	5.028

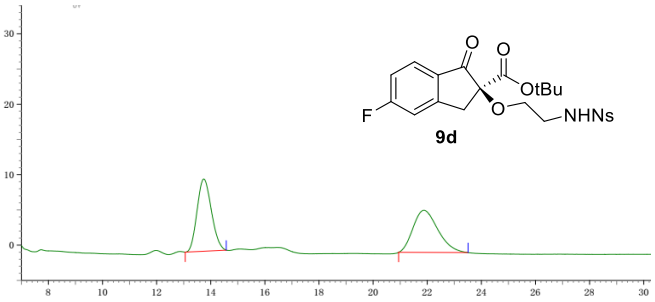


^{1}H NMR (400 MHz, $CDCl_3$)

9d

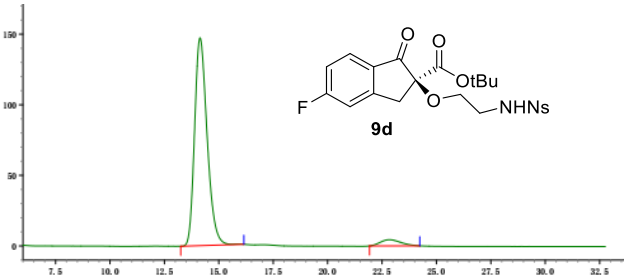
HPLC spectrum of compound **9d**:

Racemate:

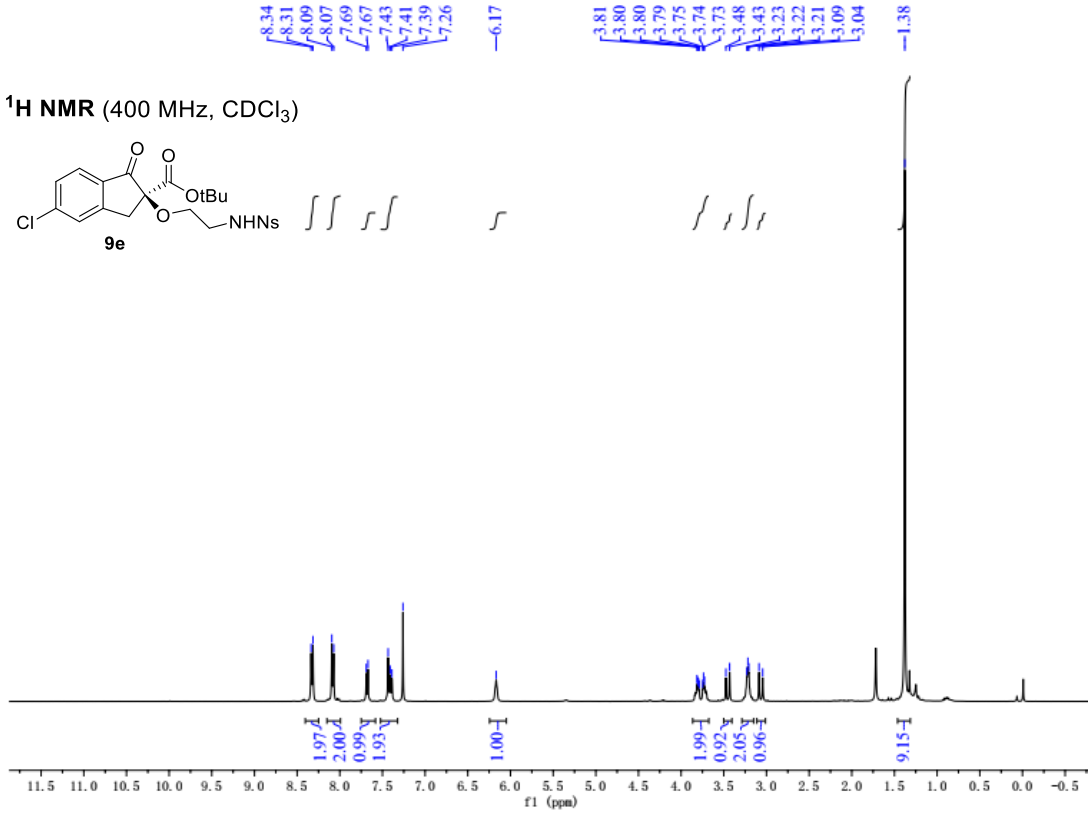


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	13.740	41015	1508263	49.607
2	21.877	23902	1532169	50.393

Enantioselective:

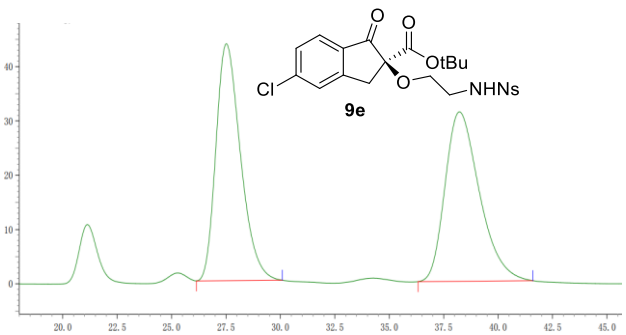


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	14.137	588817	23573132	95.369
2	22.833	17499	1144726	4.631



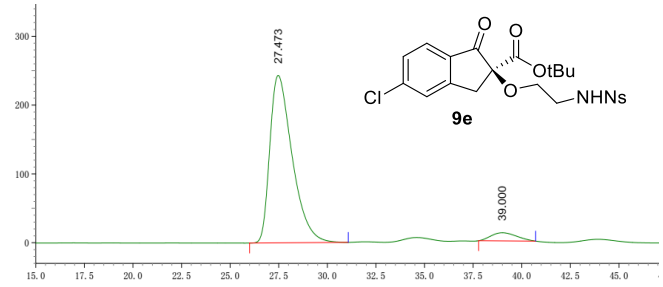
HPLC spectrum of compound **9e**:

Racemate:



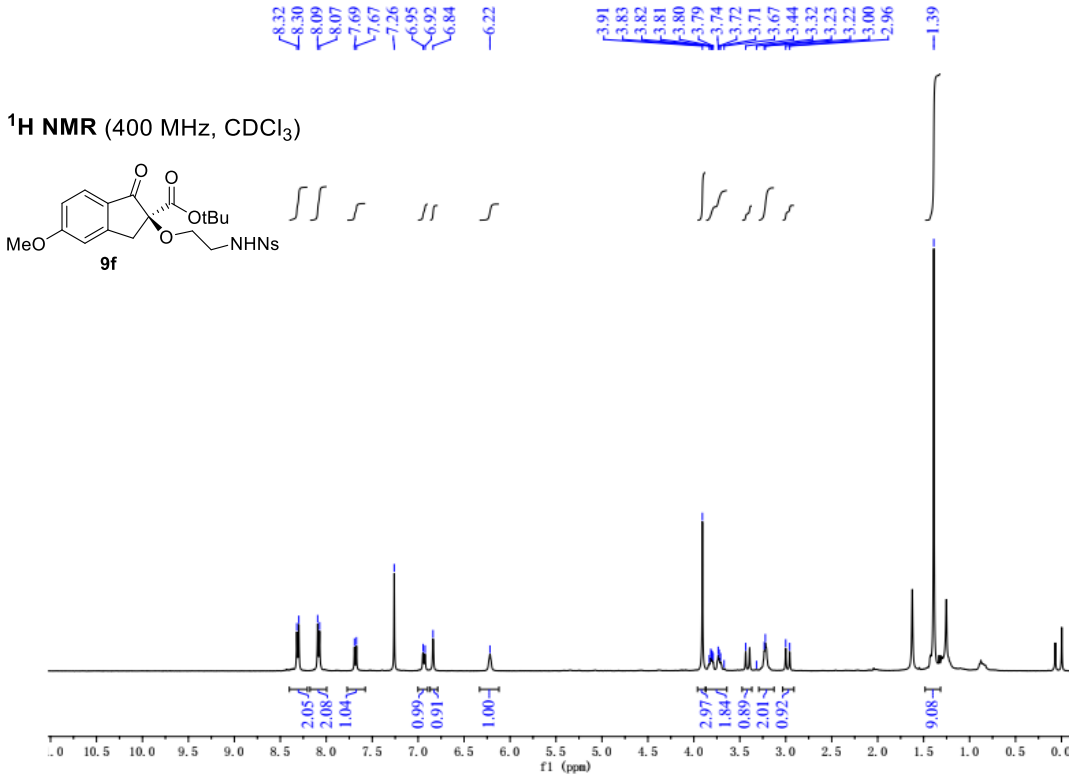
Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	27.517	174434	13735774	50.050
2	38.220	124785	13708350	49.950

Enantioselective:



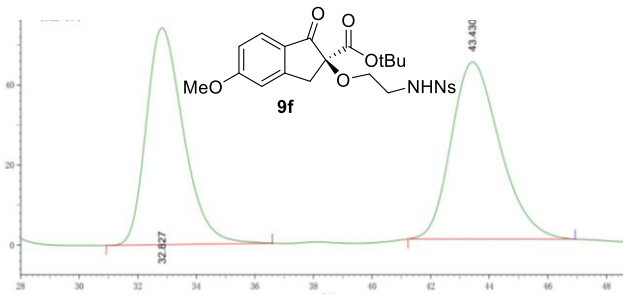
Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	27.473	973693	77980569	94.720
2	39.000	47327	4347014	5.280

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



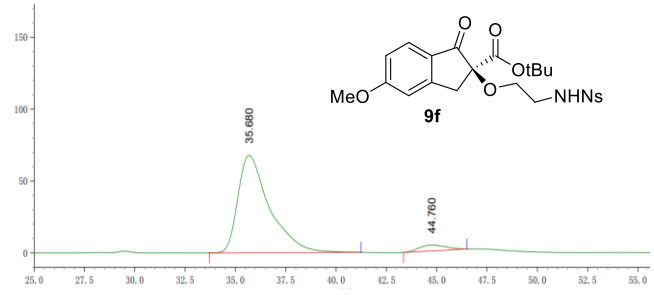
HPLC spectrum of compound **9f**:

Racemate:

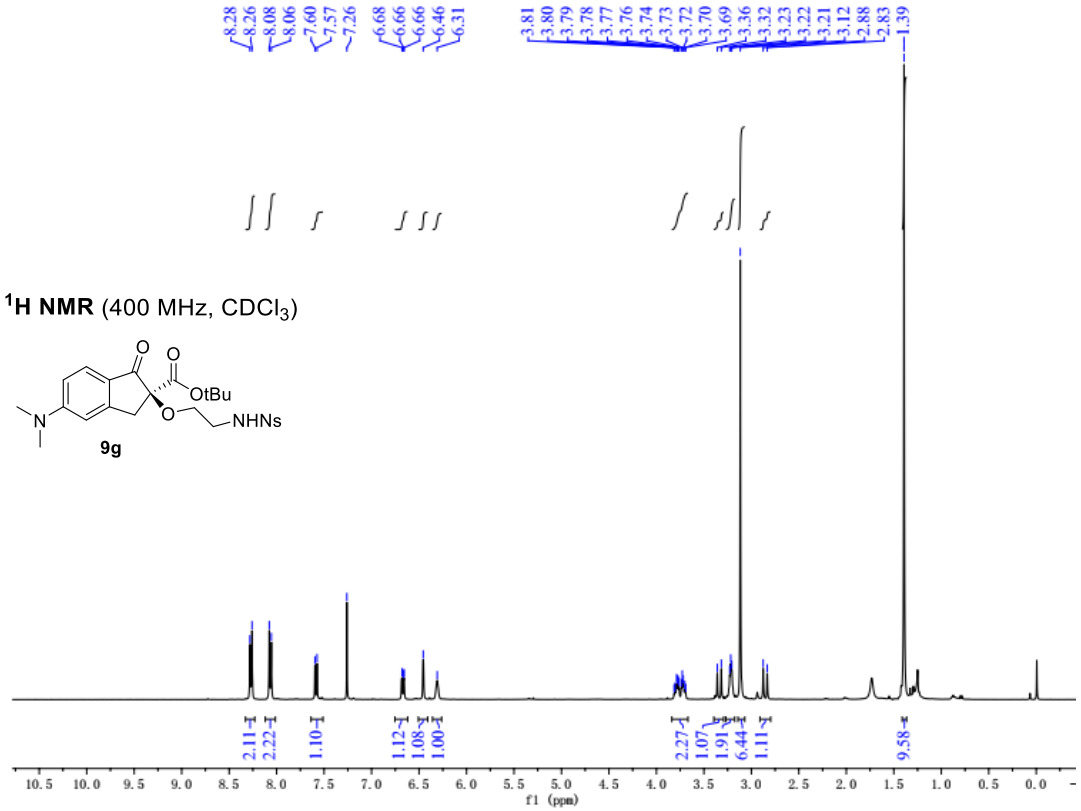


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	32.827	216747	19150323	48.308
2	43.430	176895	20491545	51.692

Enantioselective:



Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	35.680	270931	29548104	95.123
2	44.760	16289	1515024	4.877

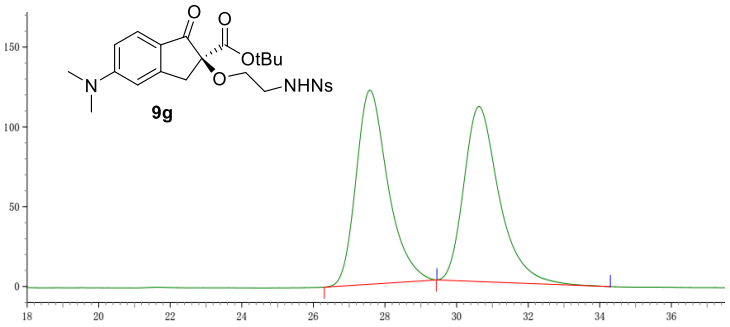


^{1}H NMR (400 MHz, $CDCl_3$)

9g

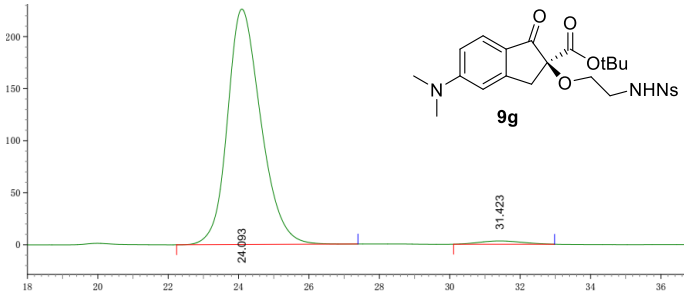
HPLC spectrum of compound **9g**:

Racemate:

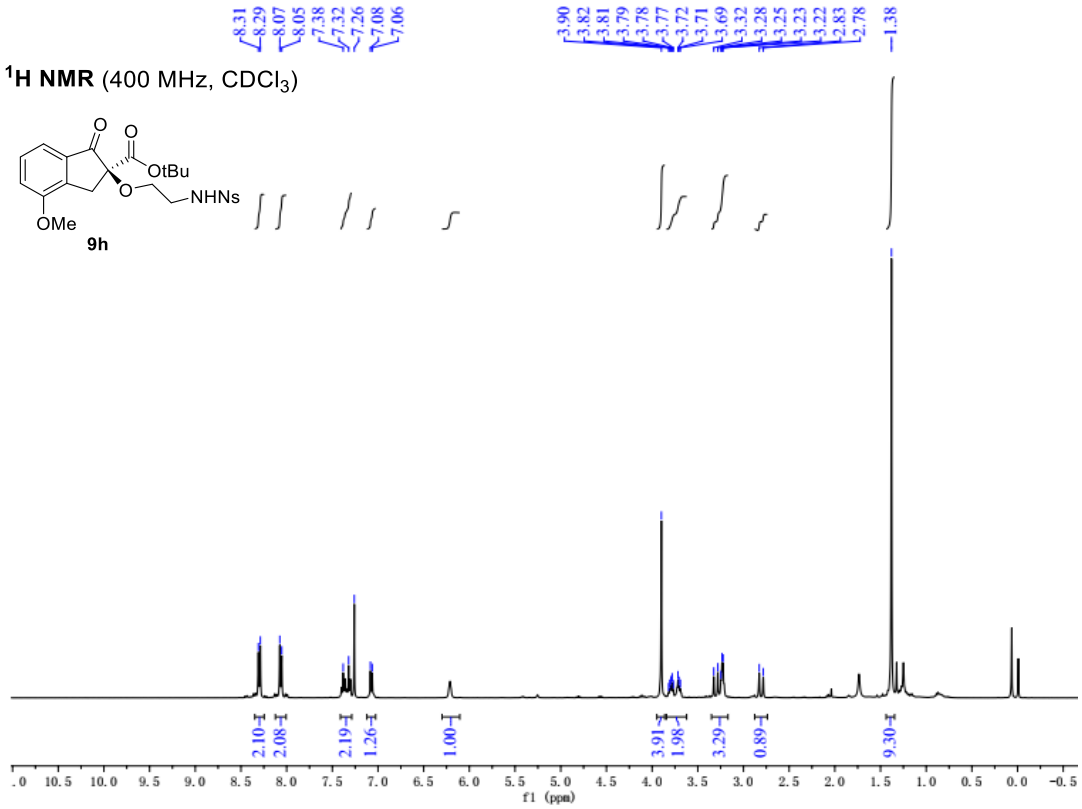


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	27.580	486443	30148700	50.052
2	30.623	438846	30085744	49.948

Enantioselective:

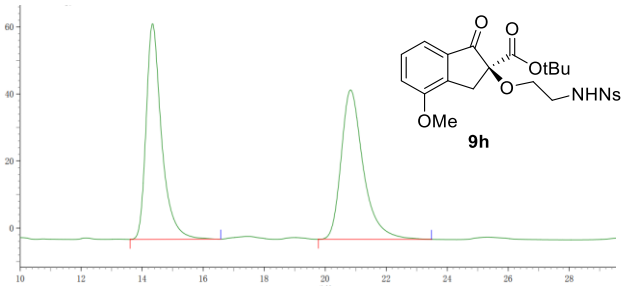


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	24.093	904868	59751731	98.263
2	31.423	12509	1056468	1.737



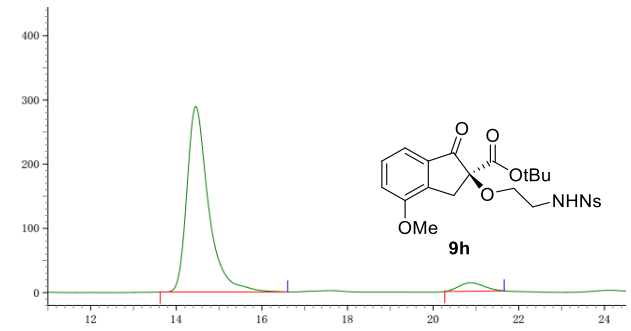
HPLC spectrum of compound **9h**:

Racemate:

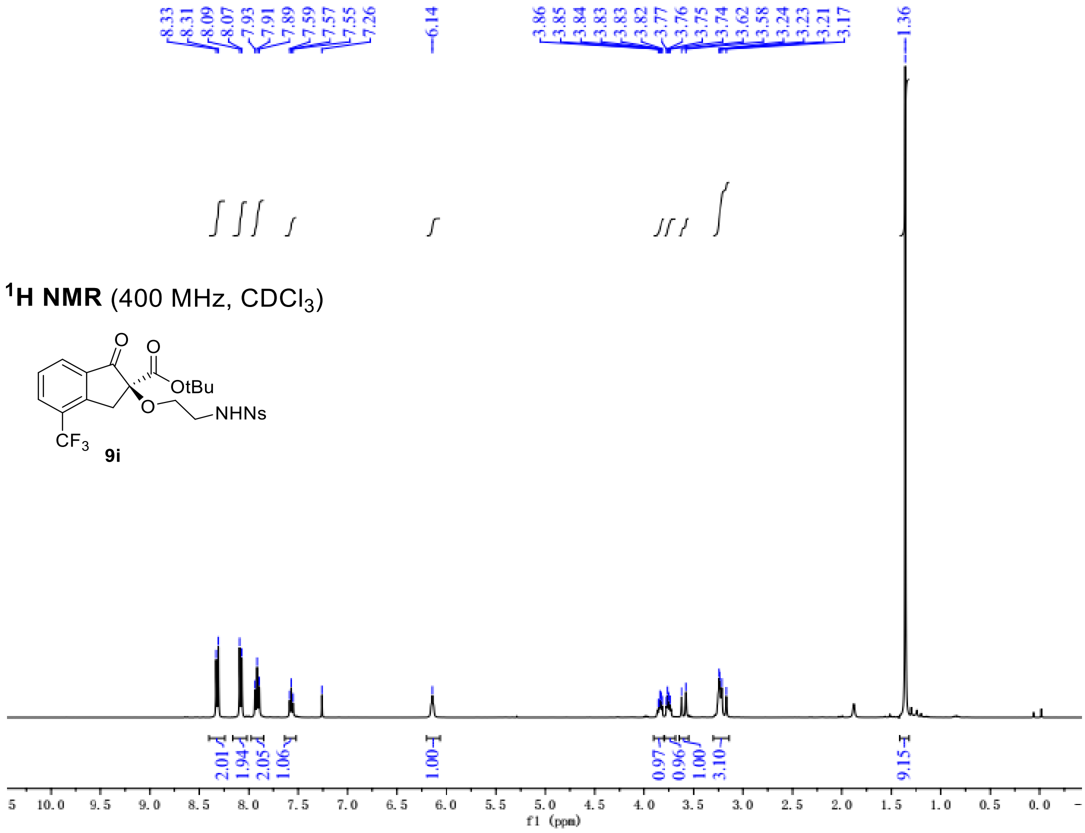


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	14.340	257297	9047533	50.149
2	20.833	178258	8993914	49.851

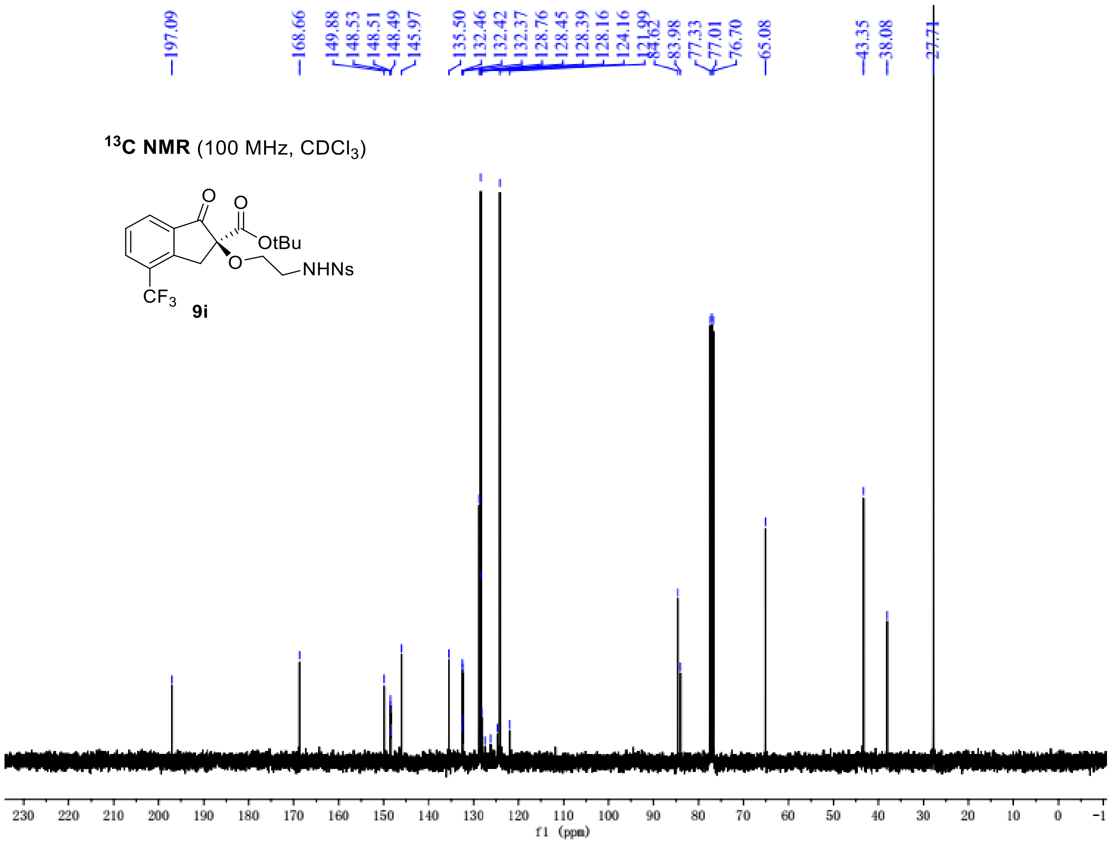
Enantioselective:



Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	14.457	1156347	40504886	94.934
2	20.877	53051	2161484	5.066



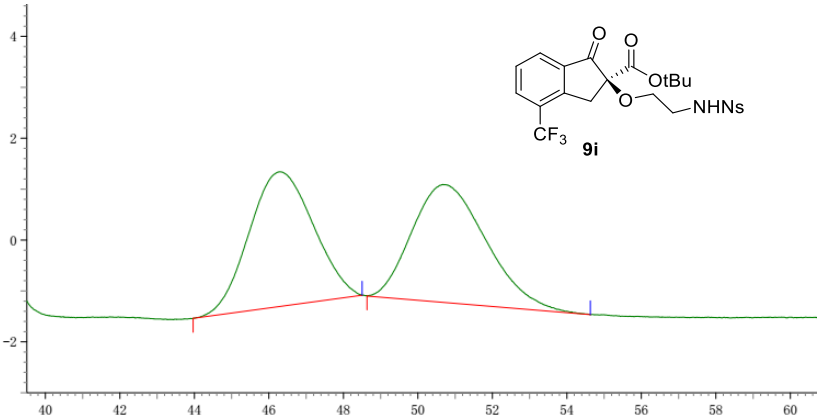
^{1}H NMR (400 MHz, CDCl$_3$)
O
O
OtBu
O
NHNs
CF$_3$
9i



^{13}C NMR (100 MHz, CDCl$_3$)
O
O
OtBu
O
NHNs
CF$_3$
9i

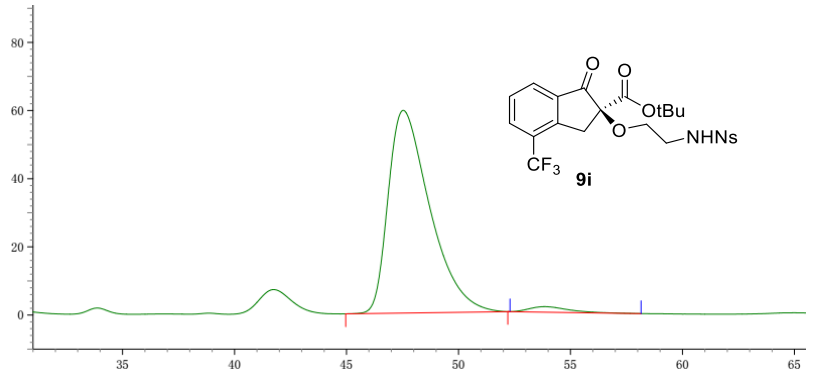
HPLC spectrum of compound **9i**:

Racemate:

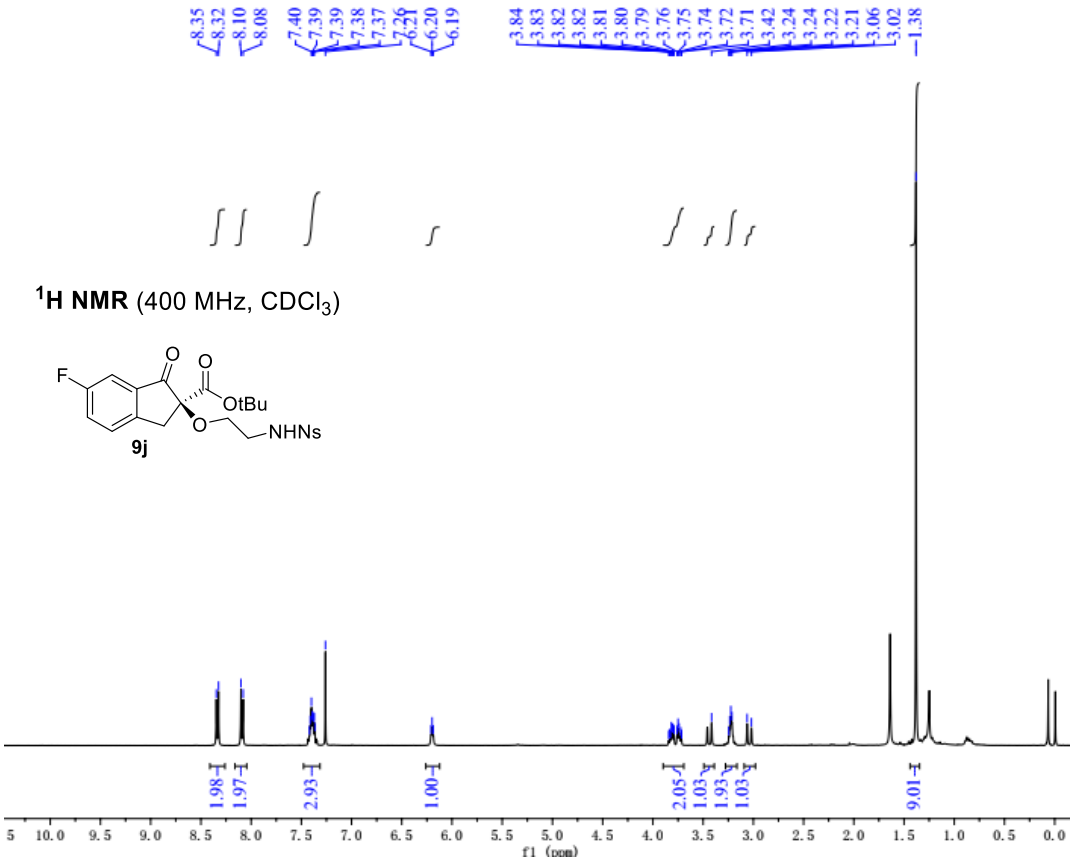


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	46.290	10587	1267384	49.648
2	50.667	9260	1285335	50.352

Enantioselective:

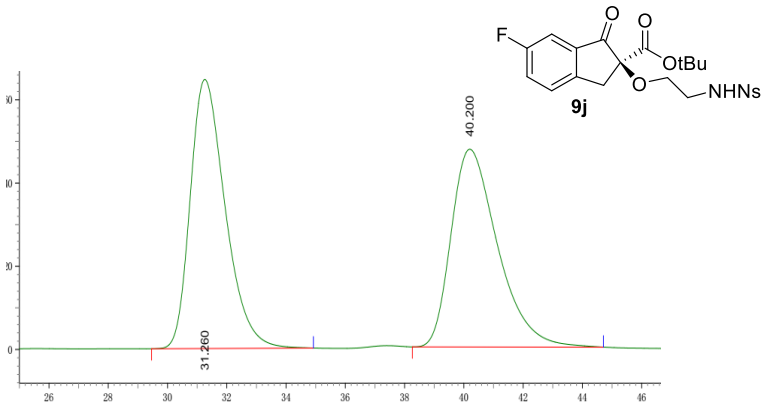


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	47.530	237898	30818934	97.483
2	53.863	6500	795758	2.517



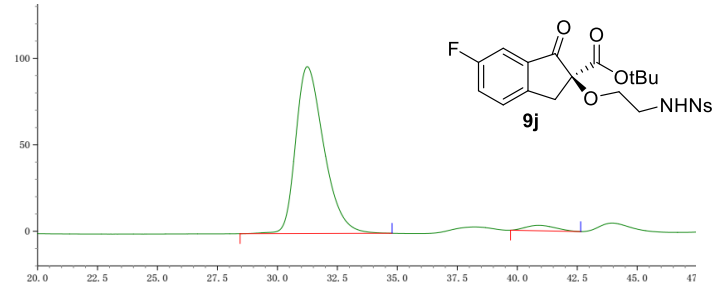
HPLC spectrum of compound **9j**:

Racemate:

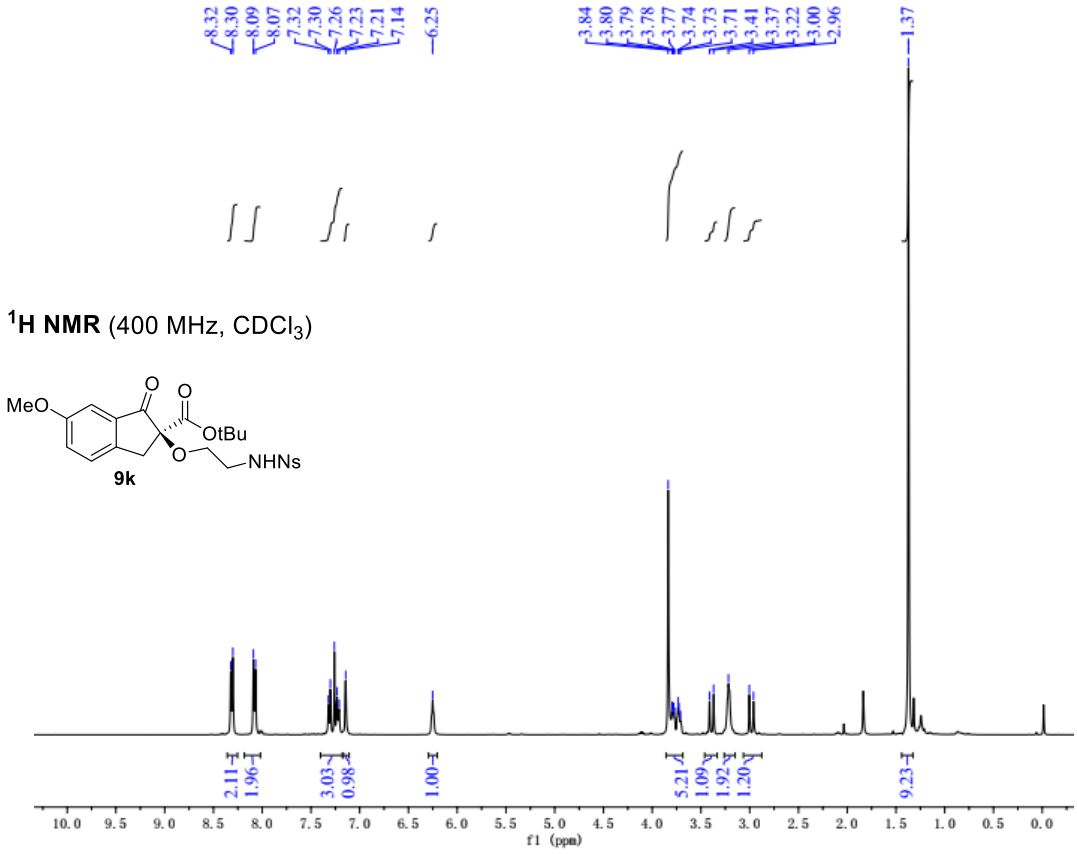


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	31.260	258639	21227054	50.557
2	40.200	190103	20759430	49.443

Enantioselective:



Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	31.243	385970	31548559	96.675
2	40.893	12475	1084957	3.325

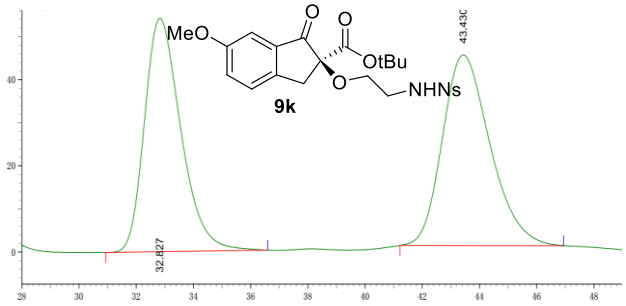


^{1}H NMR (400 MHz, $CDCl_3$)

9k

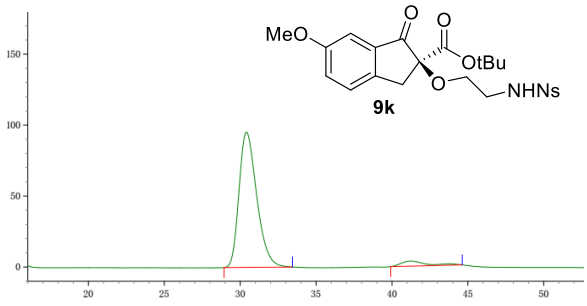
HPLC spectrum of compound **9k**:

Racemate:

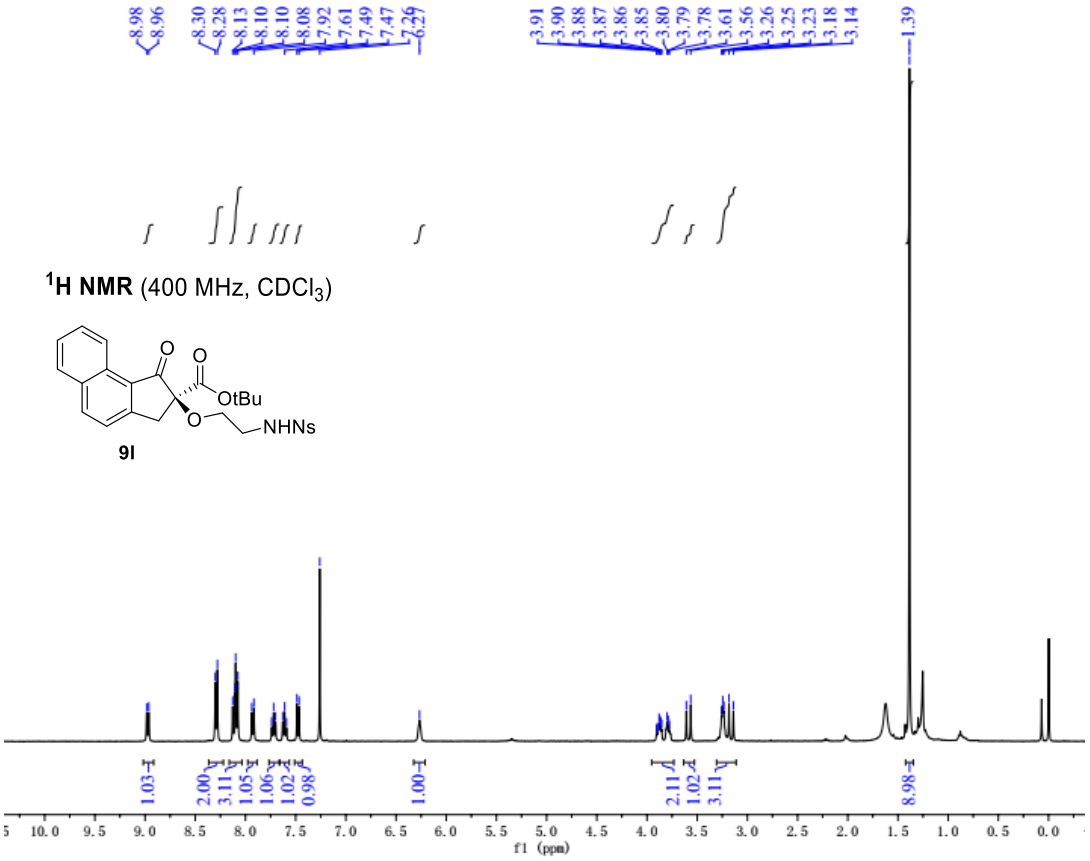


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	32.827	216747	19150323	48.308
2	43.430	176895	20491545	51.692

Enantioselective:

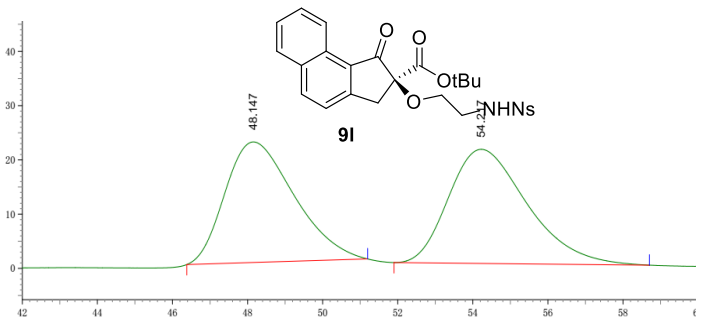


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	30.413	381315	30985121	94.842
2	41.220	14404	1685164	5.158



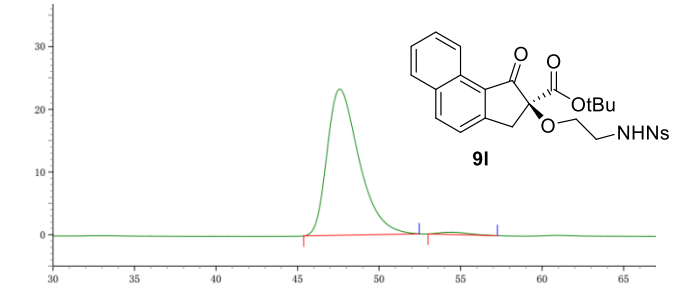
HPLC spectrum of compound **9l** :

Racemate:

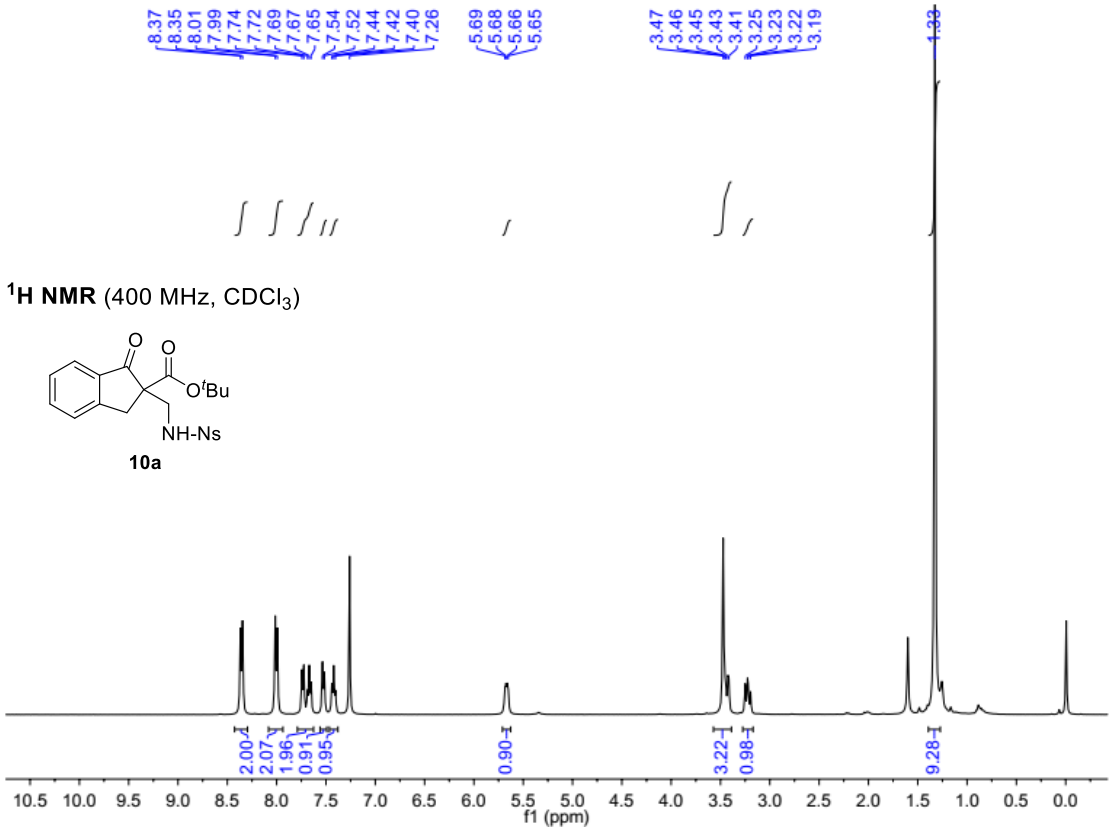


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	48.147	88904	11376455	48.203
2	54.217	84171	12224662	51.797

Enantioselective:

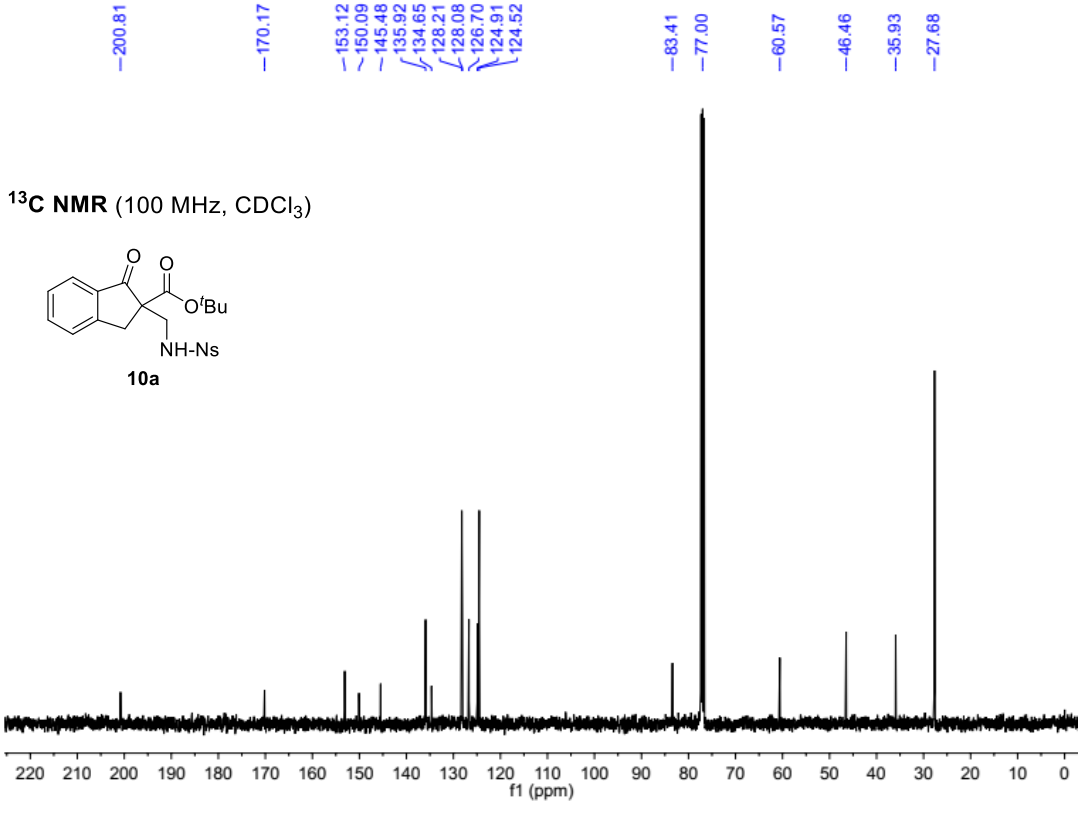


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	47.583	93200	12756344	98.611
2	54.483	1458	179650	1.389



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

10a

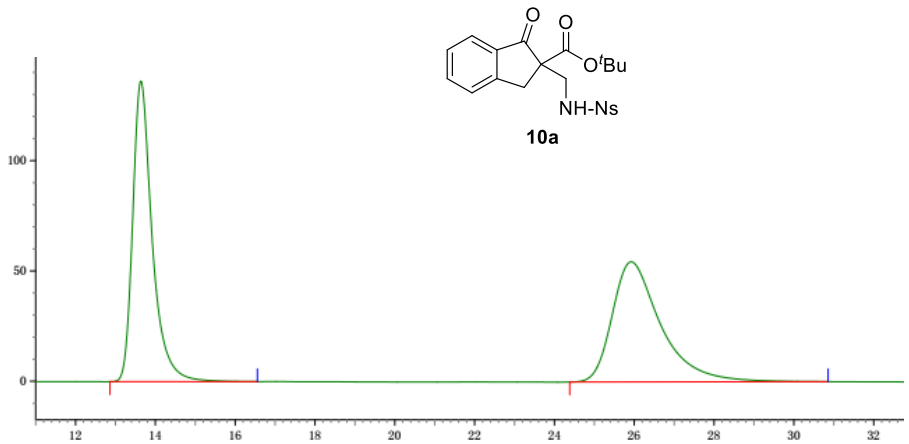


^{13}C NMR (100 MHz, $CDCl_3$)

10a

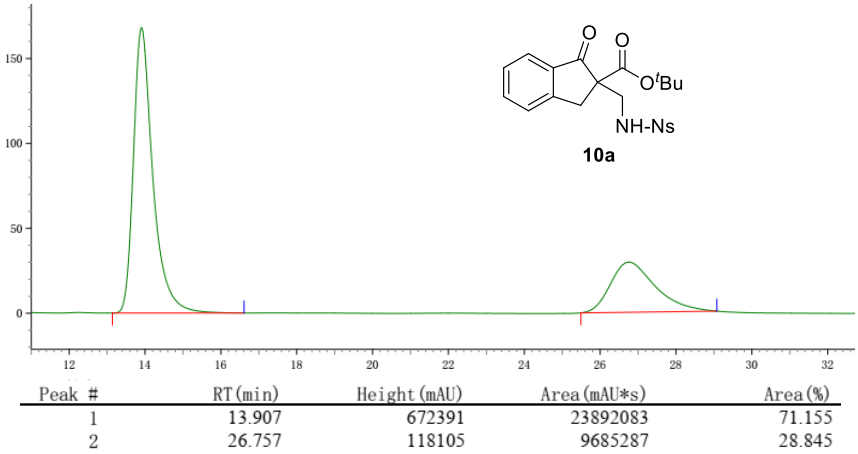
HPLC spectrum of compound **10a**:

Racemate:



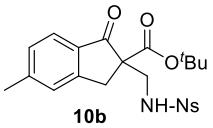
Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	13.637	544963	18518105	50.147
2	25.923	217860	18409568	49.853

Enantioselective:



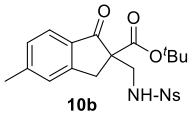
Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	13.907	672391	23892083	71.155
2	26.757	118105	9685287	28.845

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



10b

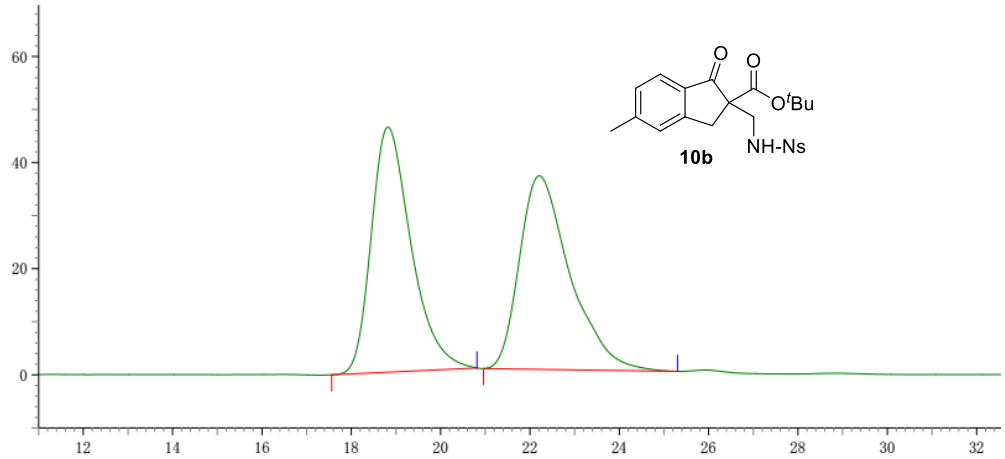
^{13}C NMR (100 MHz, $CDCl_3$)



10b

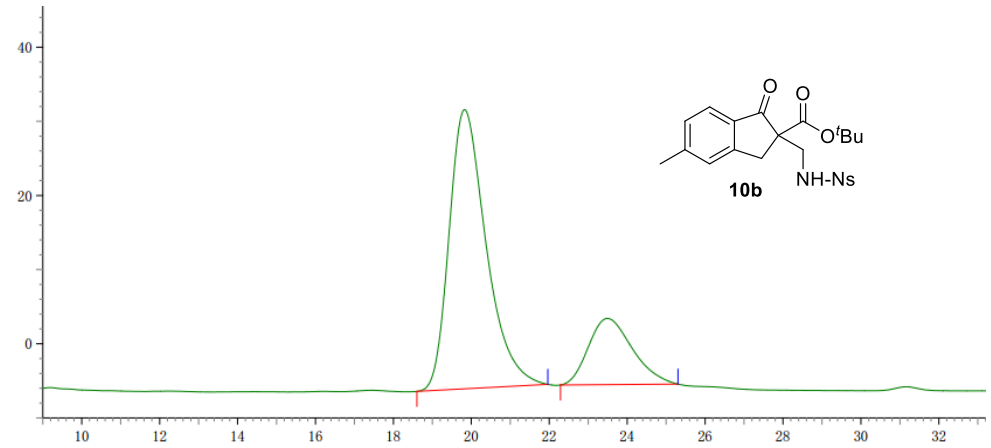
HPLC spectrum of compound **10b**:

Racemate:

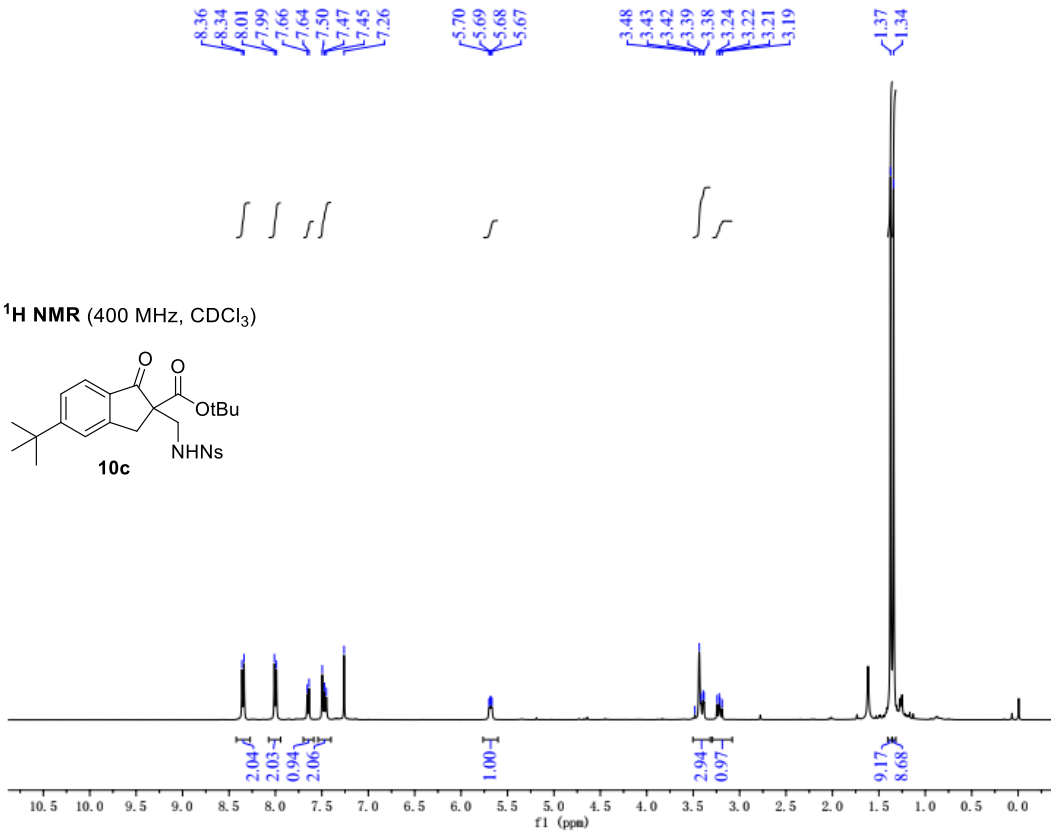


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	18.820	184853	11469401	50.007
2	22.210	145973	11466003	49.993

Enantioselective:

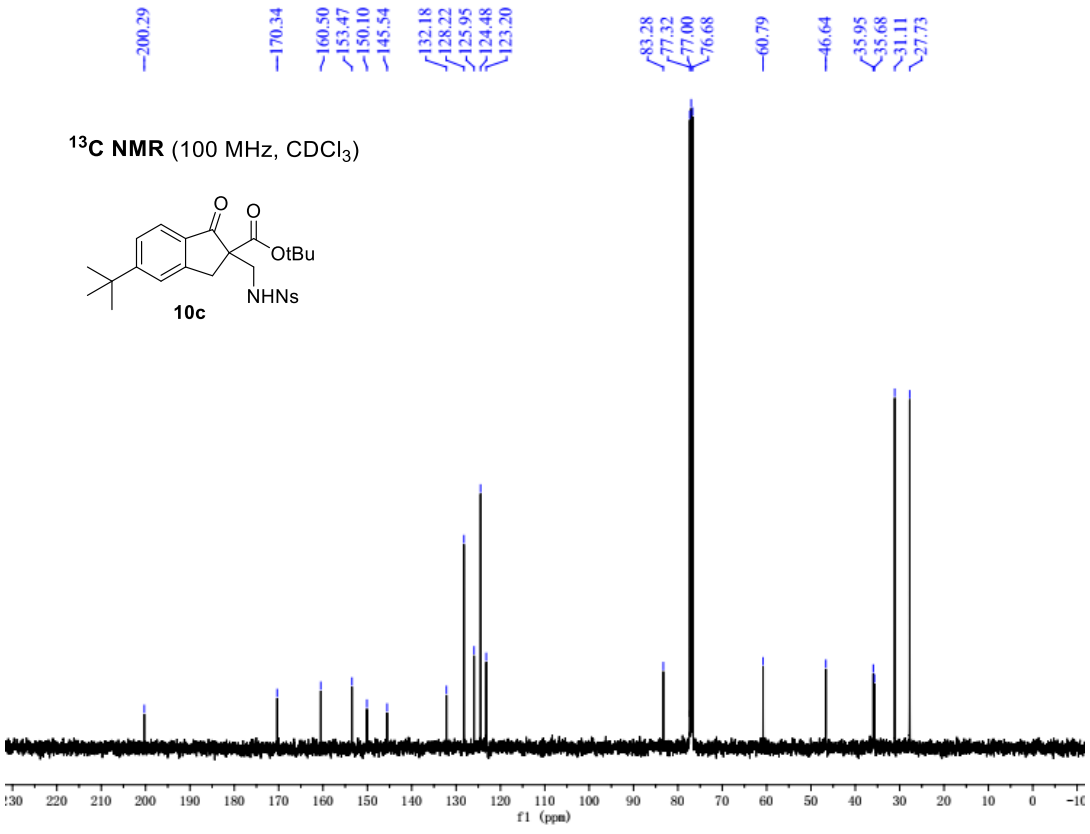


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	19.827	150681	9938124	78.049
2	23.487	35712	2795065	21.951



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

10c

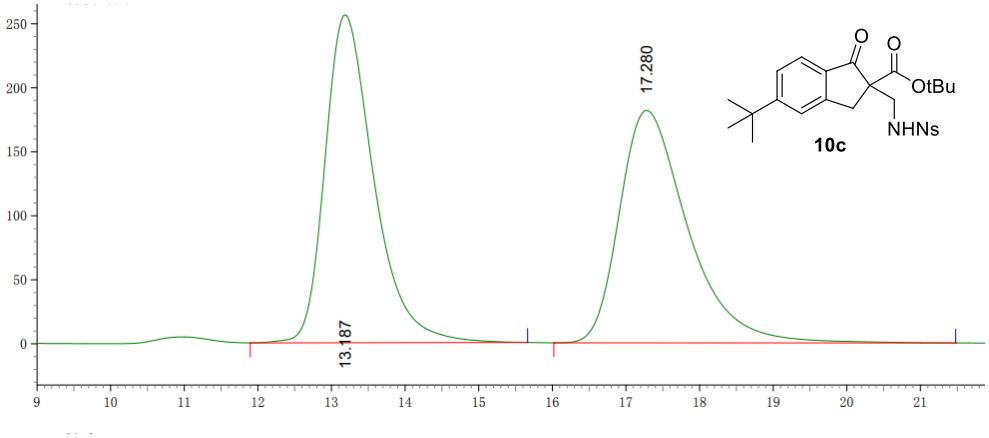


^{13}C NMR (100 MHz, $CDCl_3$)

10c

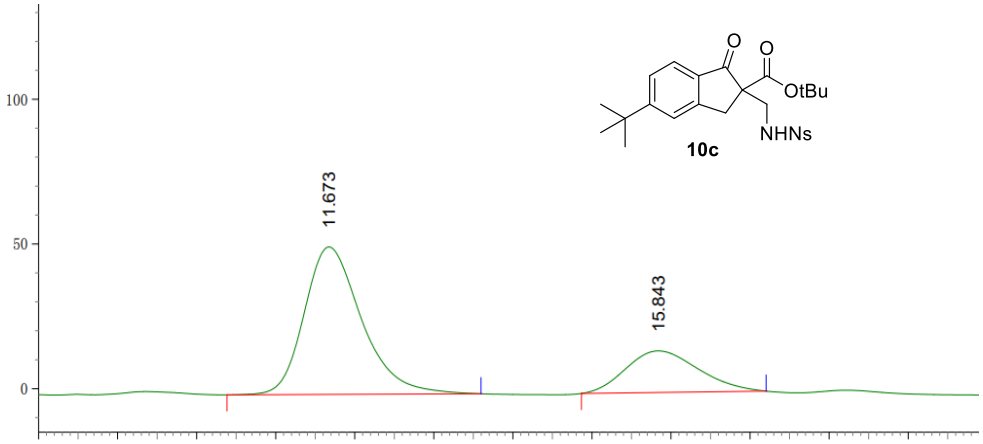
HPLC spectrum of compound **10c**:

Racemate:

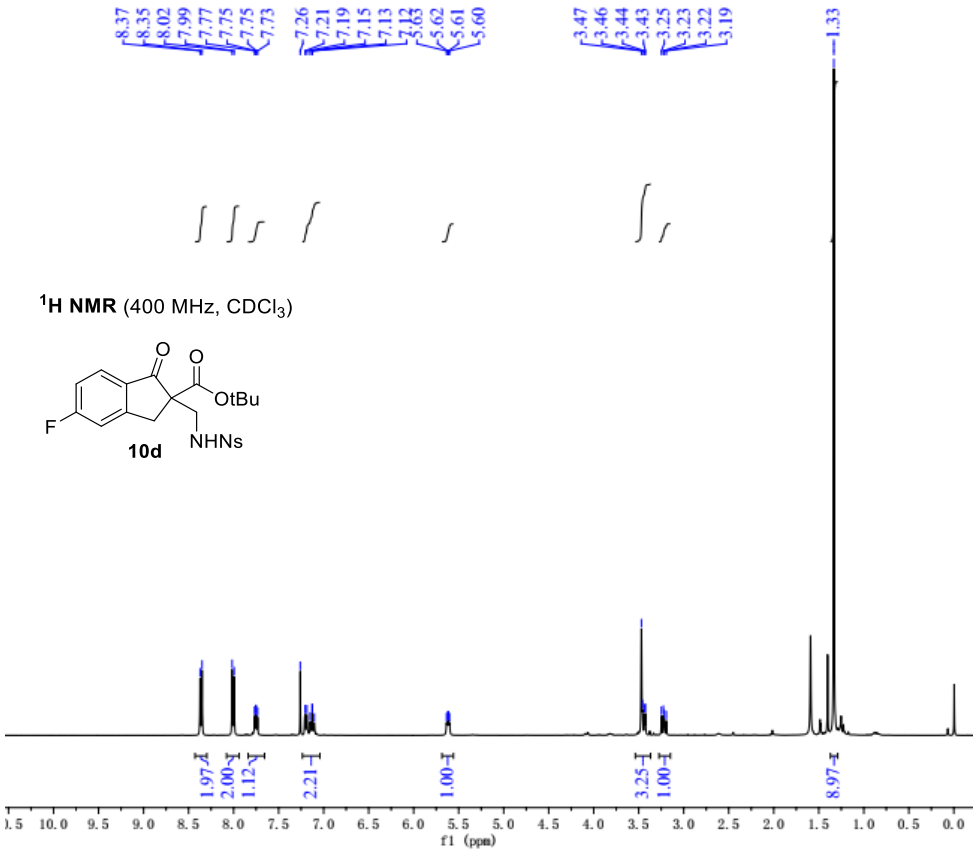


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	13.187	1024541	47243497	50.224
2	17.280	726191	46821786	49.776

Enantioselective:

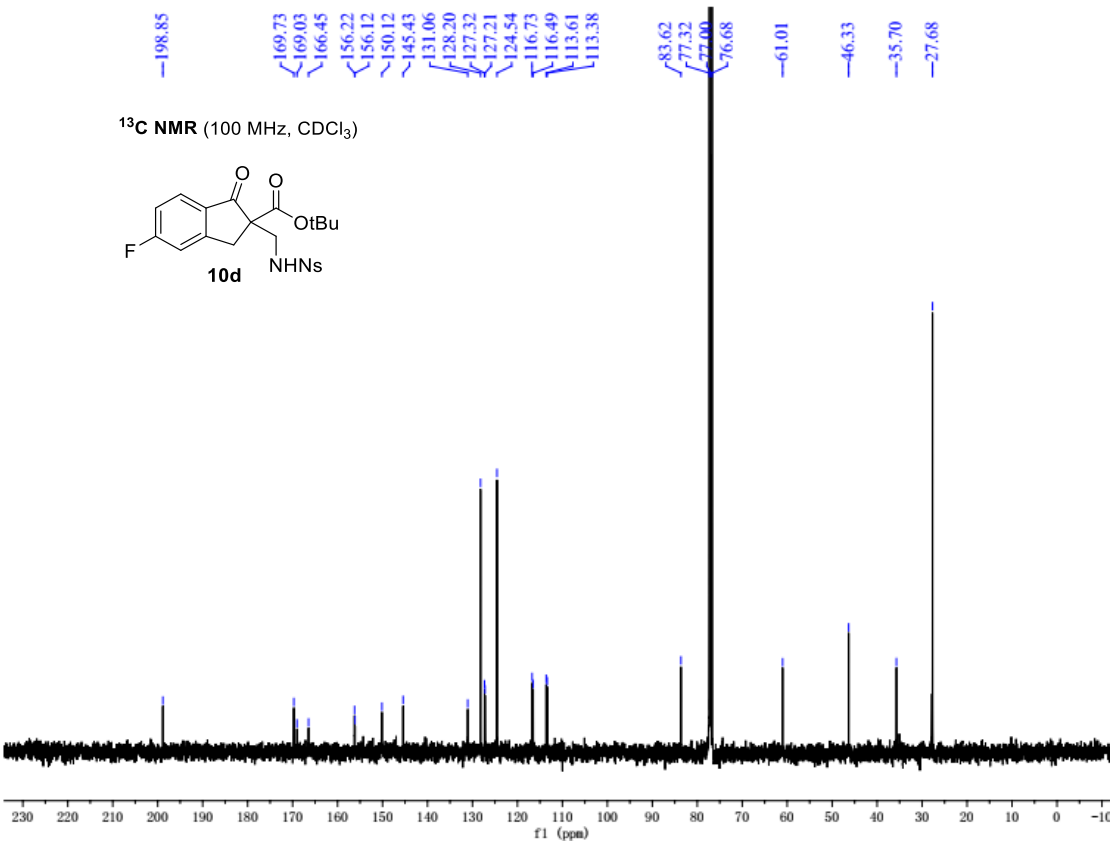


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	11.673	203746	10282570	73.747
2	15.843	57456	3660435	26.253



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

10d

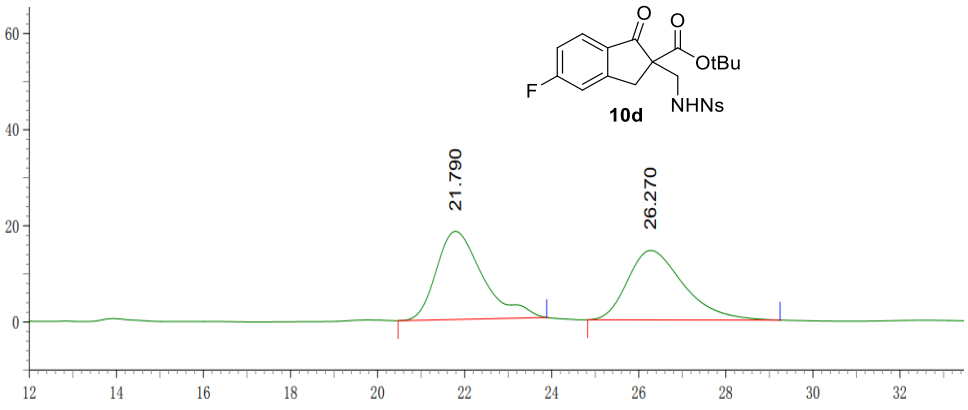


^{13}C NMR (100 MHz, $CDCl_3$)

10d

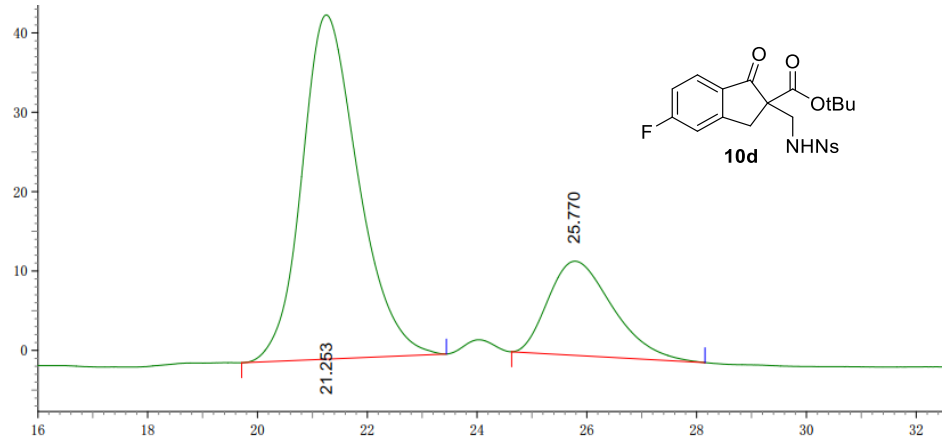
HPLC spectrum of compound **10d**:

Racemate:

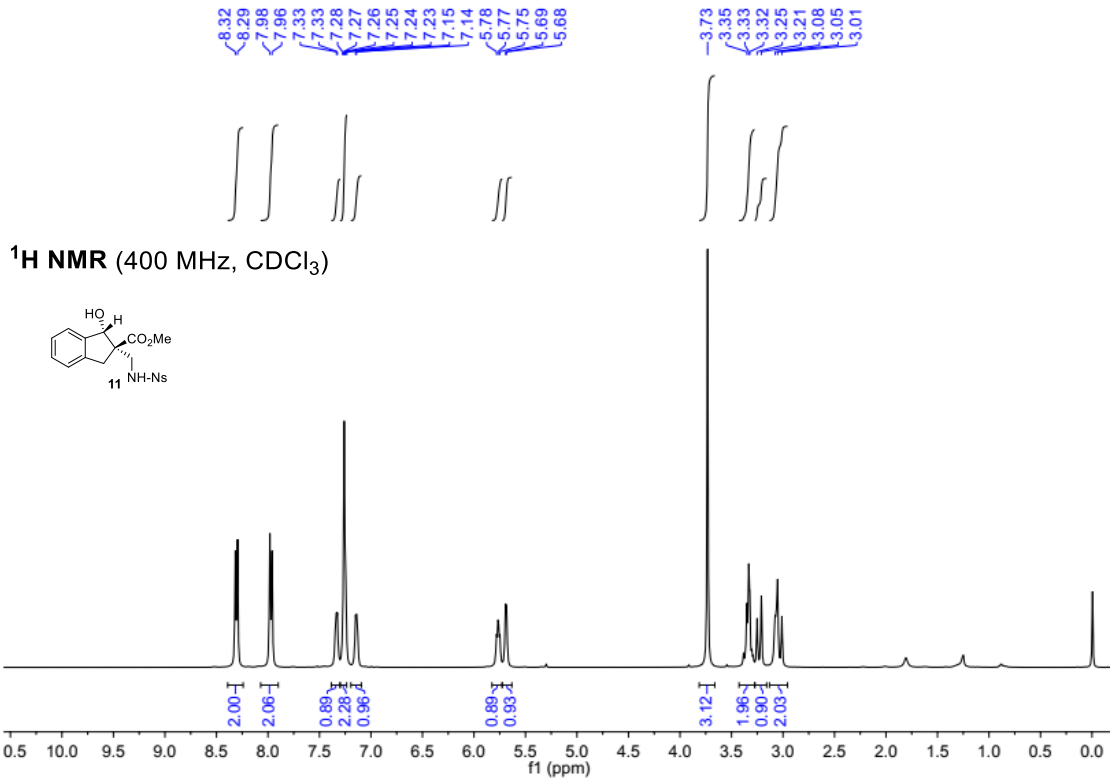


Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	21.790	73359	5416753	51.302
2	26.270	57765	5141784	48.698

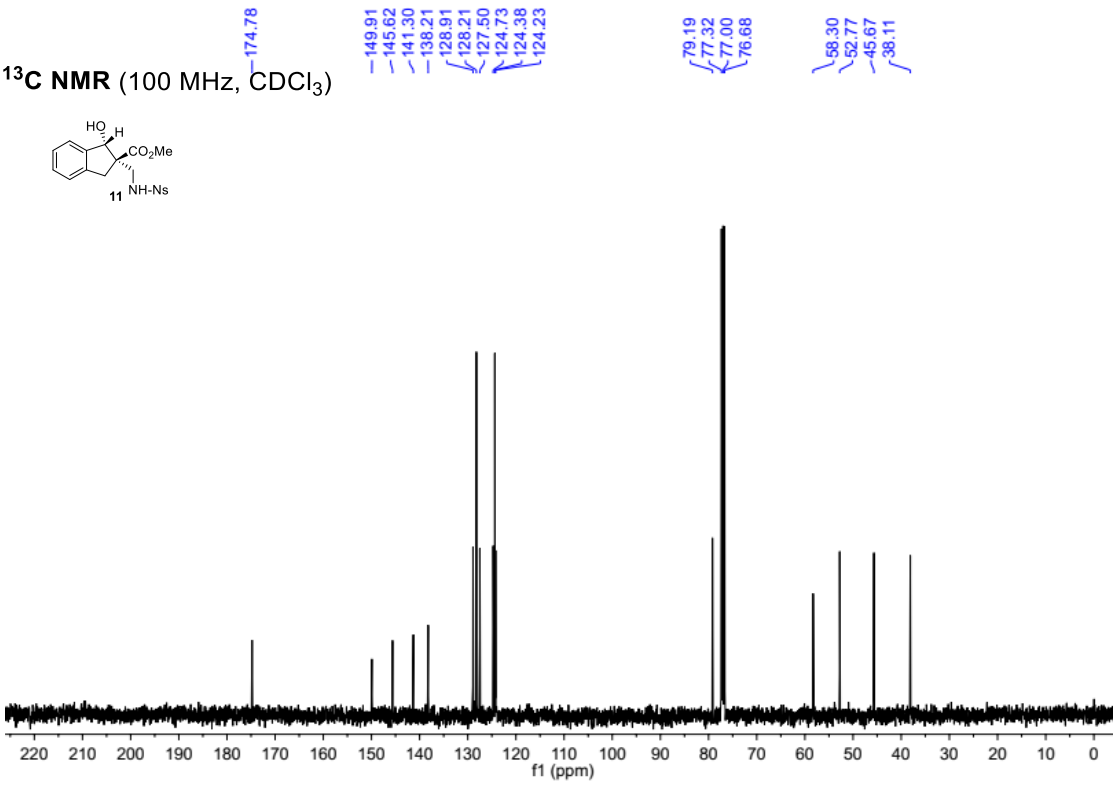
Enantioselective:



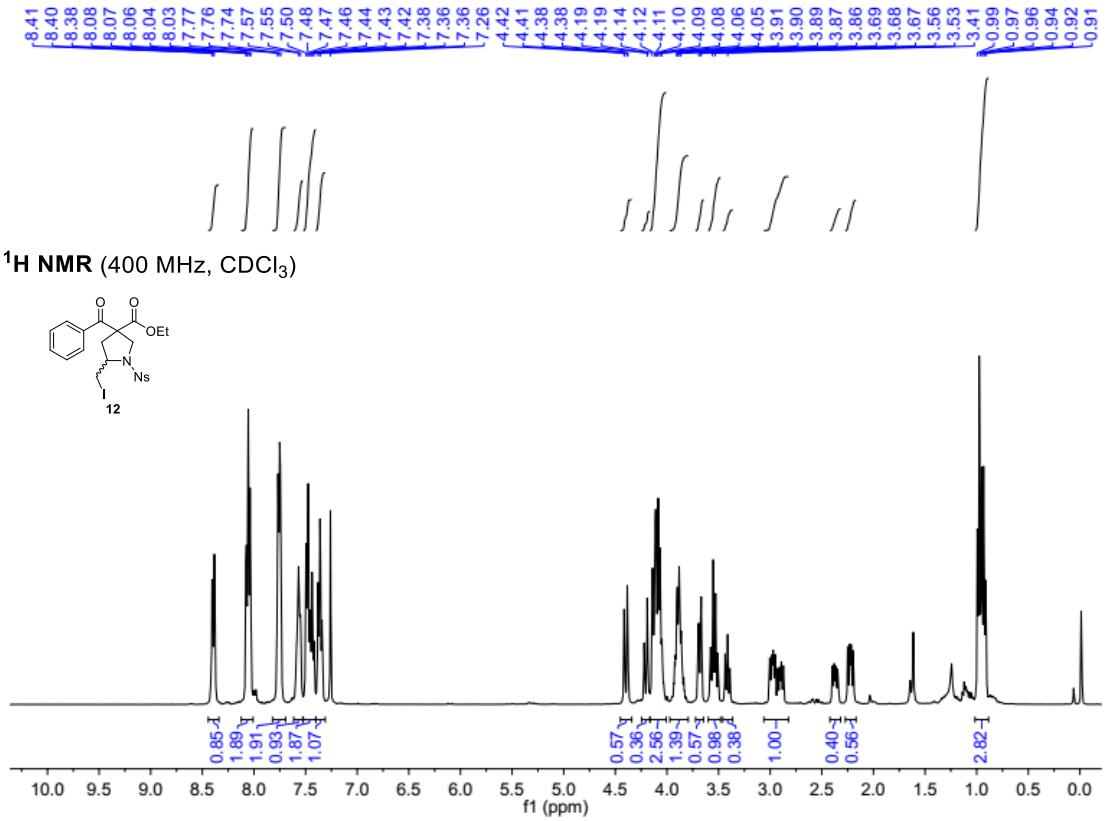
Peak #	RT(min)	Height(mAU)	Area(mAU*s)	Area(%)
1	21.253	173453	12407201	76.275
2	25.770	47379	3859122	23.725



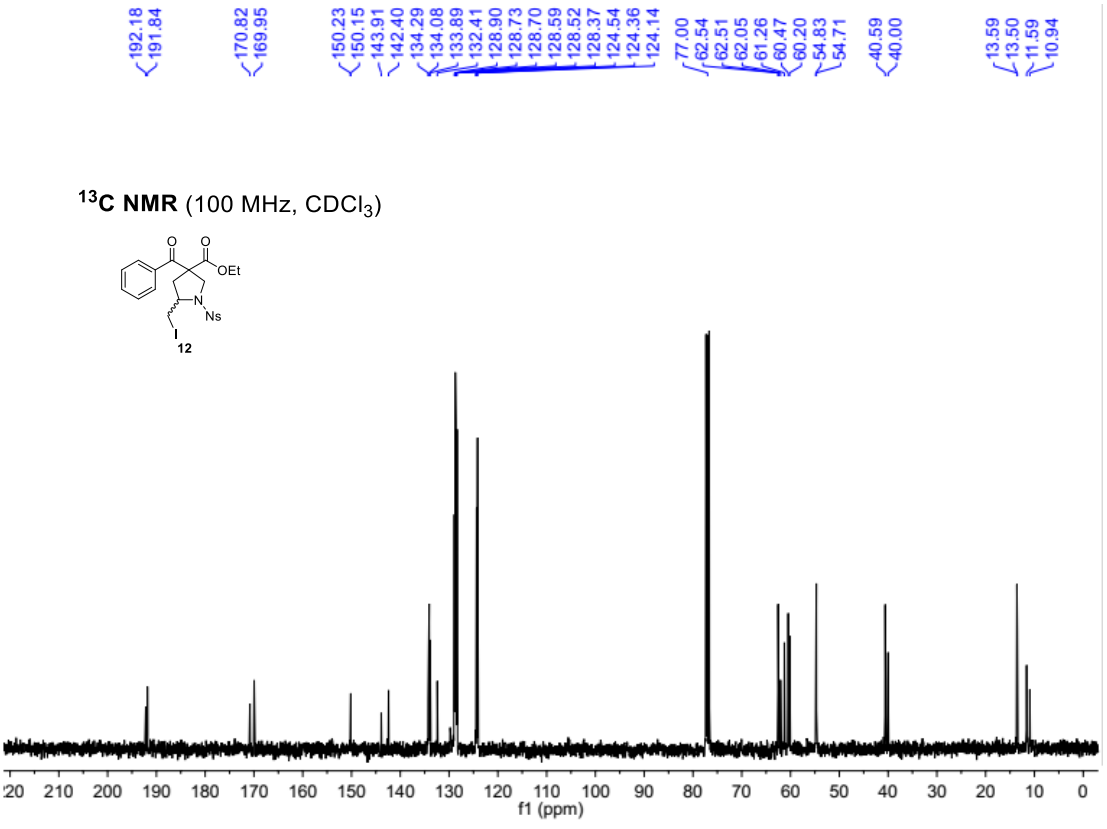
^{1}H NMR (400 MHz, $CDCl_3$)



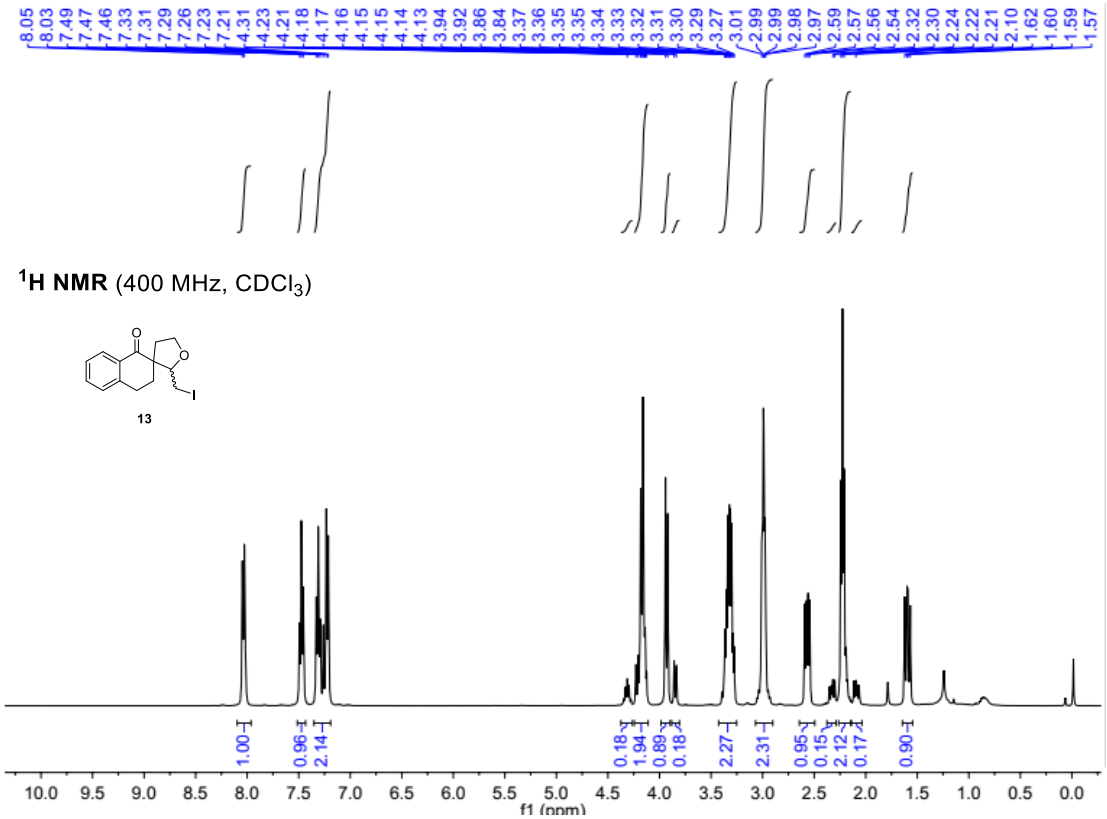
^{13}C NMR (100 MHz, $CDCl_3$)



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

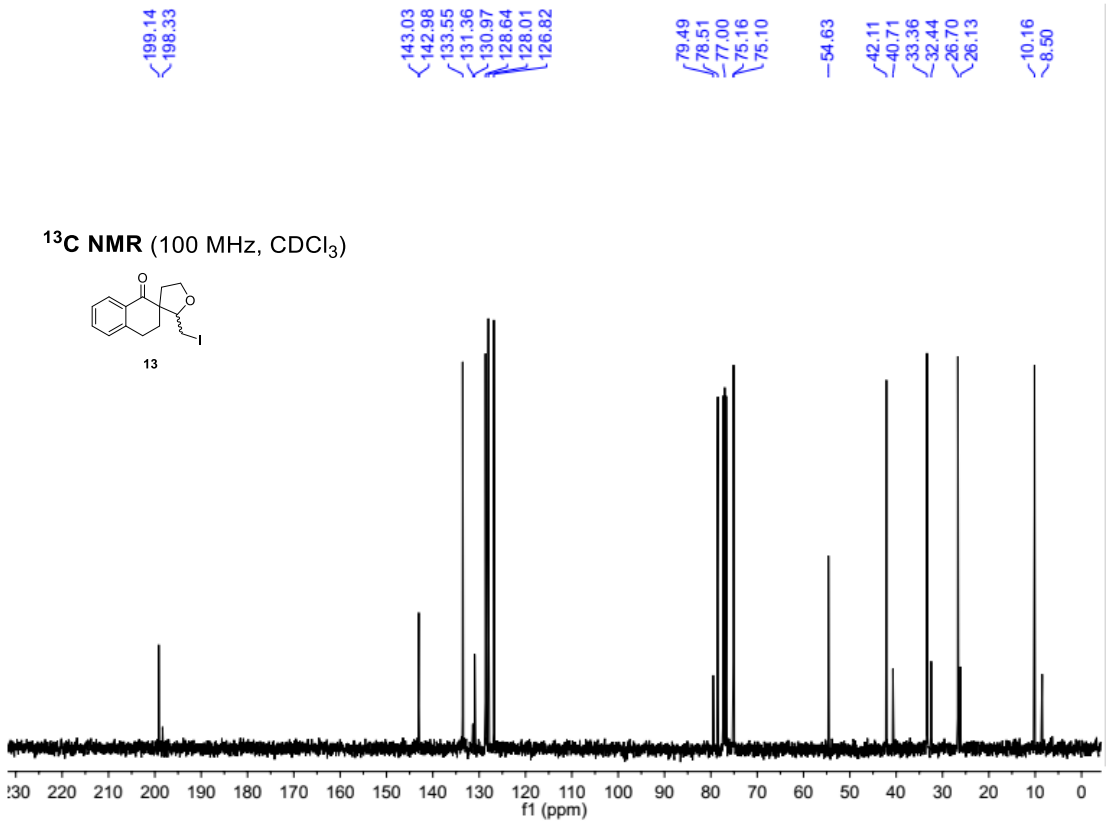


^{13}C NMR (100 MHz, $CDCl_3$)



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

13



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

13