Supporting Information

Catalytic Dehydrogenative Synthesis of α, β-Unsaturated Secondary Amides without External Oxidants

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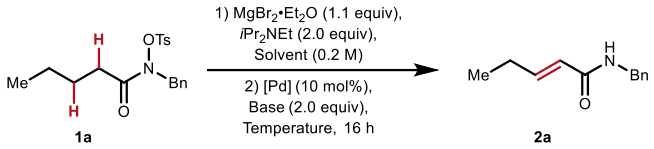
1. General information

Commercial reagents were purchased from Biomedical, TCI, J&K, Accela, Macklin, Bidepharm or Adamas and used without further purification. The anhydrous solvents used in the experiments were all purchased and used directly. All reactions were carried out with oven-dried glassware. Analytical thin layer chromatography (TLC) was performed on 0.20 mm silica gel HSGF-254 plates (Huanghai, China). Column chromatography was performed on 200-300 mesh silica gel or 300-400 mesh silica gel (General-Reagent, China).

^{1}H NMR (400 MHz or 600 MHz), ^{13}C NMR (101 MHz or 150 MHz) and ^{19}F NMR (376 MHz or 565 MHz) were recorded on an NMR spectrometer (Bruker Ascend 400 M/600 M or Qone AS 400) with $CDCl_3$ as the solvent. Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm). The residual solvent signals were used as references and the chemical shifts were converted to the TMS scale ($CDCl_3$: δ H = 7.26 ppm, δ C = 77.16 ppm). All coupling constants (*J* values) were reported in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet doublet, dt = doublet triplet, td = triplet doublet, m = multiplet, br = broad. High resolution mass spectrometer data of new compounds were recorded on an LTQ Orbitrap Elite LC/MS (ESI or APCI) or an MAT 95XP (Thermo, EI).

2. Reaction optimization for the synthesis of α, β - unsaturated secondary amides

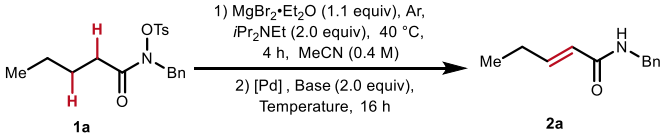
Table S1. General screening for the one-step synthesis of α, β - unsaturated secondary amides[a]



Entry	Pd	Base	Solvent	Temperature	Ligand	^{1}H-NMR Yield[b]
1	$Pd(PPh_3)_4$	Cs_2CO_3	MeCN	100 °C	none	9%
2	$Pd(OAc)_2$	Cs_2CO_3	MeCN	100 °C	40 mol% PPh_3	3%
3	$Pd(PPh_3)_4$	Cs_2CO_3	DCE	100 °C	none	4%
4	$Pd(PPh_3)_4$	Cs_2CO_3	DMF	100 °C	none	N.R.
5	$Pd(PPh_3)_4$	Cs_2CO_3	Dioxane	100 °C	none	N.D.
6	$Pd(PPh_3)_4$	Cs_2CO_3	DMSO	100 °C	none	N.D.
7	$Pd(PPh_3)_4$	Cs_2CO_3	PhMe	100 °C	none	2%
8	$Pd(PPh_3)_4$	Cs_2CO_3	PhH	100 °C	none	3%
9	$Pd(PPh_3)_4$	Cs_2CO_3	PhCl	100 °C	none	7%
10	$Pd(PPh_3)_4$	*i*Pr_2NEt	MeCN	100 °C	none	12 %
11	$Pd(PPh_3)_4$	*i*Pr_2NEt	MeCN	100 °C	40 mol% $P(^tBu)_3$•BF_4	N.D.
12	$Pd(PPh_3)_4$	*i*Pr_2NEt	MeCN	100 °C	40 mol% $P(Cy)_3$•BF_4	N.D.
13[c]	$Pd(PPh_3)_4$	Cs_2CO_3	MeCN	100 °C	none	N.D.
14[d]	$Pd(PPh_3)_4$	Cs_2CO_3	MeCN	100 °C	none	N.D.

[a] Reaction conditions: **1a** (1.0 equiv, 0.20 mmol), $MgBr_2 \cdot Et_2O$ (1.1 equiv, 0.22 mmol), *i*Pr_2NEt (2.0 equiv, 0.40 mmol), solvent (1.00 mL), [Pd] (0.1 equiv, 0.02 mmol), base (2.0 equiv, 0.40 mmol), 100 °C, 16 h. [b] The yields were determined by ^{1}H NMR (1,3,5-trimethoxybenzene as the internal standard). [c] 1.1 equiv LiBr instead of $MgBr_2 \cdot Et_2O$. [d] 1.1 equiv $CuBr_2$ instead of $MgBr_2 \cdot Et_2O$.

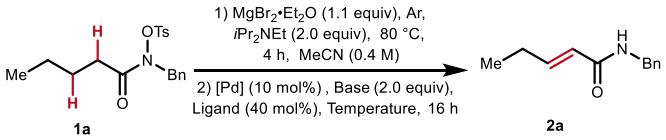
Table S2. Base and ligand screening for the one-pot two-step synthesis of α, β-unsaturated secondary amides[a]



Entry	Pd	Base	Temperature	Ligand	^{1}H-NMR Yield[b]
1	$Pd(PPh_3)_4$	Cs_2CO_3	100 °C	none	22%
2	$Pd(PPh_3)_4$	Ag_2CO_3	100 °C	none	7%
3	$Pd(PPh_3)_4$	K_2CO_3	100 °C	none	16%
4	$Pd(PPh_3)_4$	Li_2CO_3	100 °C	none	14%
5	$Pd(PPh_3)_4$	Cs_2CO_3	100 °C	40 mol% $P(o\text{-}Me\text{-}Ph)_3$	26%
6	$Pd(PPh_3)_4$	Cs_2CO_3	100 °C	40 mol% X-Phos	20%
7	$Pd(PPh_3)_4$	Cs_2CO_3	100 °C	40 mol% $P(p\text{-}Cl\text{-}Ph)_3$	10%
8	$Pd_2(dba)_3$	Cs_2CO_3	100 °C	none	< 1%
9	$Pd(PPh_3)_4$	Cs_2CO_3	80 °C	none	30%
10[c]	$Pd(PPh_3)_4$	Cs_2CO_3	100 °C	none	17 %
11[c]	$Pd(OAc)_2$	Cs_2CO_3	100 °C	40 mol% PPh_3	45 %

[a] Reaction conditions: **1a** (1.0 equiv, 0.20 mmol), $MgBr_2 \cdot Et_2O$ (1.1 equiv, 0.22 mmol), *i*Pr_2NEt (2.0 equiv, 0.40 mmol), MeCN (0.50 mL), 40 °C, 4 h; then [Pd] (0.1 equiv, 0.02 mmol), base (2.0 equiv, 0.40 mmol), ligand (0.4 equiv, 0.08 mmol), temperature, 16 h. [b] The yields were determined by ^{1}H NMR (1,3,5-trimethoxybenzene as the internal standard). [c] Dioxane (1.0 mL) was added into the mixture as co-solvent. $Pd_2(dba)_3$ = Tris(dibenzylideneacetone)dipalladium. X-Phos = 2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl.

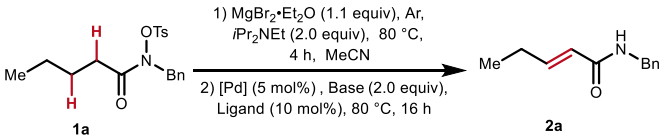
Table S3. Co-solvent and ligand screening for the one-pot two-step synthesis of α, β -unsaturated secondary amides[a]



Entry	Pd	Base	Temperature	Ligand	Co-solvent	^{1}H-NMR Yield[b]
1	$Pd_2(dba)_3$	Cs_2CO_3	100 °C	PPh_3	dioxane	27%
2	$Pd(OAc)_2$	Cs_2CO_3	100 °C	PPh_3	dioxane	42%
3	$Pd(OAc)_2$	K_2CO_3	100 °C	PPh_3	dioxane	46%
4	$Pd(OAc)_2$	K_2CO_3	100 °C	PPh_3	DME	35%
5	$Pd(OAc)_2$	K_2CO_3	100 °C	PPh_3	EtOAc	39%
6	$Pd(OAc)_2$	K_2CO_3	100 °C	PPh_3	EtOH	34%
7	$Pd(OAc)_2$	K_2CO_3	100 °C	PPh_3	THF	28%
8	$Pd(OAc)_2$	K_2CO_3	100 °C	20 mol% PPh_3	dioxane	39%
9	$Pd(OAc)_2$	K_2CO_3	100 °C	60 mol% PPh_3	dioxane	31 %
10	$Pd(OAc)_2$	K_2CO_3	100 °C	Binap	dioxane	25%
11	$Pd(OAc)_2$	K_2CO_3	100 °C	dppb	dioxane	13 %
12	$Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% DPEphos	dioxane	69%
13	$Pd(OAc)_2$	K_2CO_3	80 °C	20 mol% DPEphos	dioxane	57%
14	$Pd(OAc)_2$	K_2CO_3	80 °C	30 mol% DPEphos	dioxane	62%
15	$Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% DPEphos	2.5 mL dioxane	44%
16	$Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% DPEphos	3.5 mL dioxane	75%
17	$Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% DPEphos	3.5 mL dioxane	75%
18	5 mol% $Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% DPEphos	3.5 mL dioxane	74%
19	15 mol% $Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% DPEphos	3.5 mL dioxane	41%
20	5 mol% $Pd(OAc)_2$	K_2CO_3	60 °C	10 mol% DPEphos	3.5 mL dioxane	49%
21	5 mol% $Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% DPEphos	none	75%
22	5 mol% $Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% XantPhos	none	82%
23	5 mol% $Pd(OAc)_2$	K_2CO_3	80 °C	10 mol% dppf	none	70%

[a] Reaction conditions: **1a** (1.0 equiv, 0.20 mmol), $MgBr_2 \cdot Et_2O$ (1.1 equiv, 0.22 mmol), iPr$_2$NEt (2.0 equiv, 0.40 mmol), MeCN (0.50 mL), 80 °C, 4 h; then [Pd] (0.1 equiv, 0.02 mmol), base (2.0 equiv, 0.40 mmol), ligand (0.4 equiv, 0.08 mmol), co-solvent (1.0 mL), temperature, 16 h. [b] The yields were determined by ^{1}H NMR (1,3,5-trimethoxybenzene as the internal standard). dppb = 1,4-Bis(diphenylphosphino)butane. DPEPhos = 1-(Diphenylphosphino)-2-(2-(diphenylphosphino)phenoxy)benzene. XantPhos = 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene. dppf = 1,1'-Bis(diphenylphosphino)ferrocene.

Table S4. General screening of different parameters for the one-pot two-step synthesis of α, β - unsaturated secondary amides[a]



Entry	Pd	Base	Temperature	Ligand	^{1}H-NMR Yield[b]
1	none	K_2CO_3	80 °C	XantPhos	0%
2	$Pd(OAc)_2$	K_2CO_3	80 °C	none	15%
3	$Pd(OAc)_2$	none	80 °C	XantPhos	11%
4	$Pd(OAc)_2$	K_2CO_3	80 °C	XantPhos	82%
5	$Pd(OAc)_2$	K_2CO_3	80 °C	X-Phos	15%
6	$Pd(OAc)_2$	K_2CO_3	80 °C	S-Phos	11%
7	$Pd(OAc)_2$	K_2CO_3	80 °C	dppb	12%
8	$Pd(OAc)_2$	K_2CO_3	80 °C	dppp	9%
9	$Pd(OAc)_2$	K_2CO_3	80 °C	P(^{t}Bu)$_3$•BF_4	41%
10	$Pd(OAc)_2$	K_2CO_3	80 °C	P(cy)$_3$•BF_4	7 %
11	$Pd(OAc)_2$	K_2CO_3	80 °C	BINAP	29 %
12	$Pd(OAc)_2$	K_2CO_3	80 °C	PPh_3	21%
13	$Pd(OAc)_2$	K_2CO_3	80 °C	DPEphos	63%
14	$Pd(OAc)_2$	K_2CO_3	80 °C	dppf	45%
15	$Pd(OAc)_2$	K_2CO_3	80 °C	P(o-Me-Ph)$_3$	36%
16	$Pd(OAc)_2$	K_2CO_3	80 °C	P(p-Cl-Ph)$_3$	21%
17	$Pd(PPh_3)_4$	K_2CO_3	80 °C	XantPhos	26%
18	$Pd_2(dba)_3$	K_2CO_3	80 °C	XantPhos	67%
19	$Pd(OAc)_2$	Na_2CO_3	80 °C	XantPhos	21%
20	$Pd(OAc)_2$	Cs_2CO_3	80 °C	XantPhos	7%
21[c]	$Pd(OAc)_2$	K_2CO_3	80 °C	XantPhos	61%
22[d]	$Pd(OAc)_2$	K_2CO_3	80 °C	XantPhos	51%

[a] Reaction conditions: **1a** (1.0 equiv, 0.20 mmol), $MgBr_2$·Et_2O (1.1 equiv, 0.22 mmol), iPr$_2$NEt (2.0 equiv, 0.40 mmol), MeCN (0.50 mL), 80 °C, 4 h; then [Pd] (0.05 equiv, 0.01 mmol), base (2.0 equiv, 0.40 mmol), ligand (0.10 equiv, 0.02 mmol), temperature, 16 h. [b] The yields were determined by ^{1}H NMR (1,3,5-trimethoxybenzene as the internal standard). [c] 1.0 mL MeCN instead of 0.5 mL MeCN. [d] 2.0 mL MeCN instead of 0.5 mL MeCN. XantPhos = 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene. X-Phos = 2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl. S-Phos = 2-Dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl. dppb = 1,4-Bis(diphenylphosphino)butane. dppp = 1,3-Bis(diphenylphosphino)propane. BINAP= 1.1'-Binaphthyl-2.2'-diphemyl phosphine. DPEPhos = 1-(Diphenylphosphino)-2-(2-(diphenylphosphino)phenoxy)benzene. dppf = 1,1'-Bis(diphenylphosphino)ferrocene.

3. Preparation and characterization of starting materials

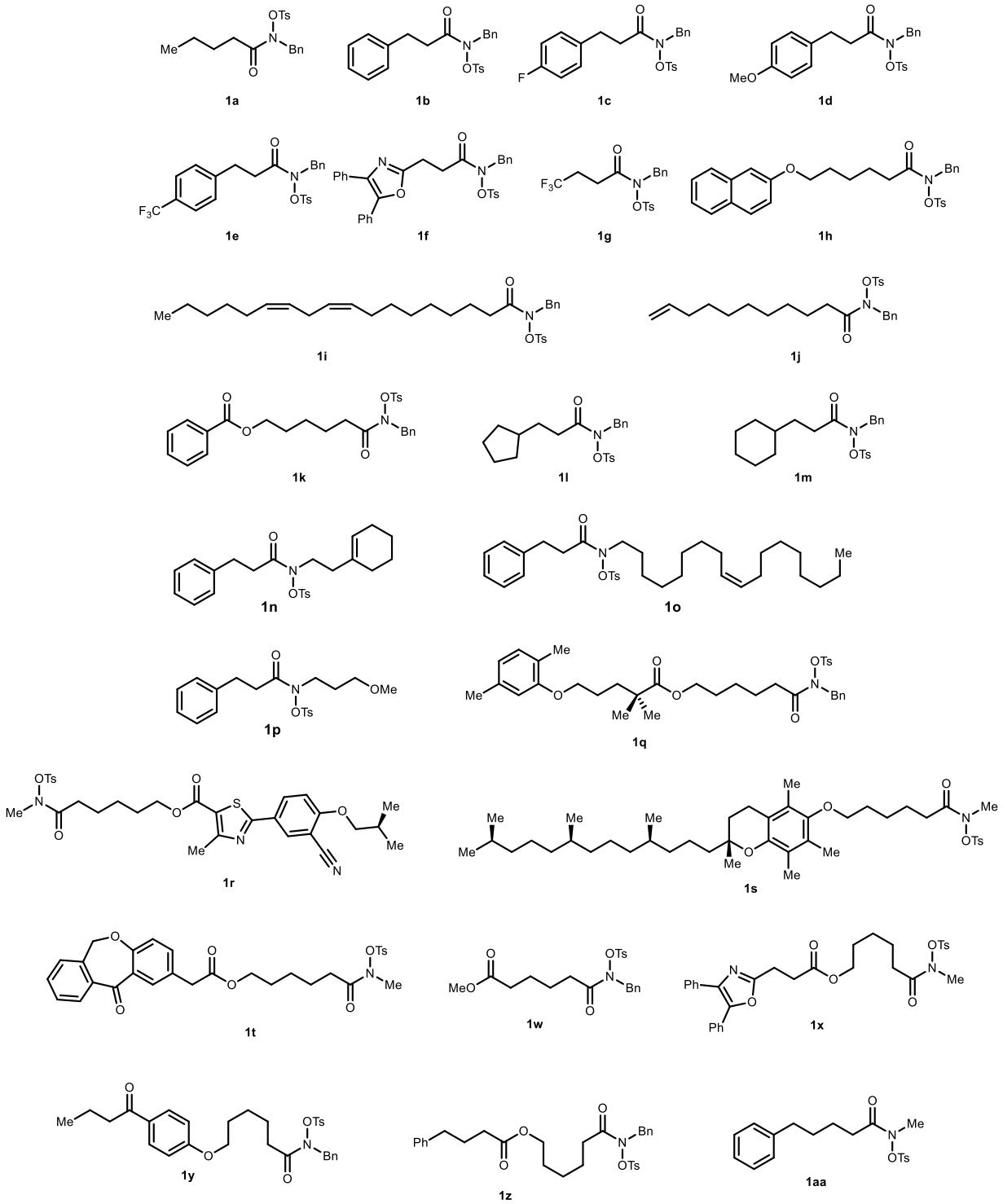
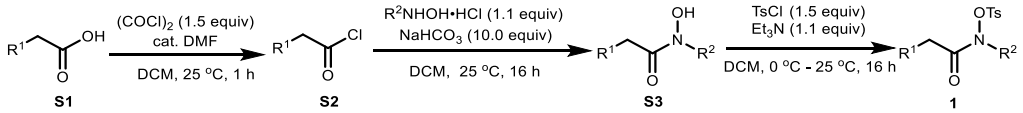


Figure S1. List of starting materials **1a-1t, 1w-1aa**

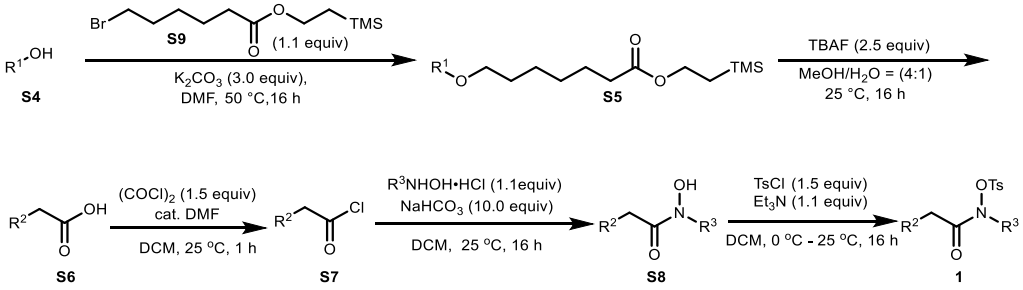
General Procedure A for the preparation of *O*-tosyl hydroxamate substrates **1a-1g, 1i, 1j, 1l, 1m, 1w, 1aa**[1]



To a stirred solution of acid **S1** (1.0 mmol, 1.0 equiv) in dichloromethane (2.0 mL), was added 1 drop *N*,*N*-dimethylformamide. Then oxalyl chloride (127.0 μL, 1.5 mmol, 1.5 equiv) was added slowly into the mixture. The reaction was stirred at 25 °C for 1 h before being concentrated. $NaHCO_3$ (864 mg, 10.0 mmol, 10.0 equiv) was charged slowly (note: bubble was generated) into the acyl chloride **S2** and *N*-R^2-hydroxylamine hydrochloride (1.1 mmol, 1.1 equiv) solution in dichloromethane (5.0 mL). The reaction was stirred at 25 °C for 16 h before being washed with H_2O (5.0 mL). The aqueous phase was extracted with dichloromethane (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to obtain crude hydroxylamide **S3**.

To a stirred solution of hydroxylamide **S3** in dichloromethane (5.0 mL), was added *p*-toluenesulfonyl chloride (285.9 mg, 1.5 mmol, 1.5 equiv). A solution of Et_3N (152.0 μL, 1.5 mmol, 1.5 equiv) in dichloromethane (1.0 mL) was charged slowly into reaction at 0 °C. The reaction was stirred at 25 °C for 16 h before being washed with H_2O (5.0 mL). The aqueous phase was extracted with dichloromethane (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced. The residual was purified by column chromatography on silica gel to afford *O*-tosyl hydroxamate **1**.

General Procedure B for the preparation of *O*-tosyl hydroxamate substrates **1h, 1k, 1q-1t, 1x-1z**



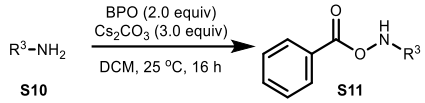
To a stirred solution of acid **S4** (2.0 mmol, 1.0 equiv) in DMF (4.0 mL), was added **S9** (2.2 mmol, 1.1 equiv) and K_2CO_3 (6.0 mmol, 3.0 equiv). Then the reaction was stirred for 16 h at 50 °C before being washed with H_2O (3 × 5.0 mL). The aqueous phase was extracted with EtOAc (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residual was directly used for the next step without any further purification to afford crude **S5**.

To a stirred solution of **S5** in MeOH and H_2O (4.0 mL and 1.0 mL), was added tetrabutylammonium fluoride (1 mol/L in THF, 2.5 mmol, 2.5 equiv). The reaction was stirred at 25 °C for 16 h before being washed with 1 M HCl (5.0 mL). The aqueous phase was extracted with dichloromethane (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced. The residual was directly used for the next step without any further purification to afford

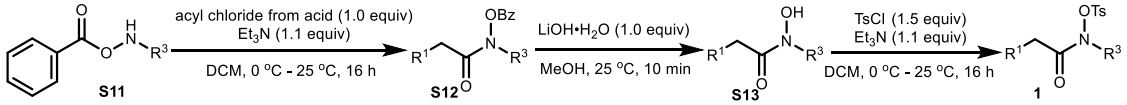
crude **S6**.

The following steps could follow the **General Procedure A** to afford *O*-tosyl hydroxamate **1**.

General Procedure C for the preparation of *O*-tosyl hydroxamate substrates **1n-1p**

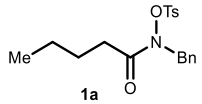


According to the synthesis method reported in literature[2], benzoyl peroxide (75%, 1.93 g, 6.0 mmol, 2.0 equiv) and Cs_2CO_3 (2.93 g, 9.0 mmol, 3.0 equiv) were taken in a tube equipped with a magnetic stir bar. Dichloromethane (20.0 mL) was added to it and the reaction was stirred vigorously for 2 h at 25 °C. After that a solution of amine **S10** (3 mmol, 1.0 equiv,) in dichloromethane (10.0 mL) was then added slowly and the mixture was further stirred for 16 h. The reaction was washed with water (10.0 mL) and extracted with dichloromethane (3 × 10.0 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residual was purified by column chromatography on silica gel to obtain *O*-benzoylhydroxylamine **S11**.



To a solution of *O*-benzoylhydroxylamine **S11** (2 mmol, 1.0 equiv) and acyl chloride (from corresponding acid, 2 mmol, 1.0 equiv) in dichloromethane (4.0 mL), was added slowly a solution of Et_3N (305.2 μL, 2.2 mmol, 1.1 equiv) in dichloromethane (1.0 mL) at 0 °C. Then the reaction was stirred for 16 h at 25 °C before being washed with H_2O (5.0 mL). The aqueous phase was extracted with dichloromethane (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residual was purified by column chromatography on silica gel to afford *O*-benzoyl hydroxamate **S12**. To a solution of *O*-benzoyl hydroxamate **S12** (1.0 equiv) in MeOH (2.0 mL), was added slowly a solution of $LiOH{\cdot}H_2O$ (83.9 mg, 2.0 mmol, 1.0 equiv) in MeOH (2.0 mL) at 25 °C. Then the reaction was stirred for 10 min at 25 °C before being concentrated under reduced pressure to obtain crude hydroxylamide **S13**. To a solution of crude hydroxylamide **S13** and *p*-toluenesulfonyl chloride (571.9 mg, 3.0 mmol, 1.5 equiv) in dichloromethane (5.0 mL), was added slowly a solution of Et_3N (305.2 μL, 2.2 mmol, 1.1 equiv) in dichloromethane (2.0 mL) at 0 °C. Then the reaction was stirred for 16 h at 25 °C before being washed with H_2O (5.0 mL). The aqueous phase was extracted with dichloromethane (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residual was purified by column chromatography on silica gel to afford *O*-tosyl hydroxamate **1**.

***N*-Benzyl-*N*-(tosyloxy)pentanamide (1a)**



1a

Prepared following **General Procedure A** using valeric acid (164.2 mg, 1.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (175.6 mg, 1.1 mmol, 1.1 equiv) and Et_3N (152.0 μL, 1.1 mmol, 1.1 equiv) as starting materials to afford **1a** as a white solid.

Yield 307.3 mg (85%).

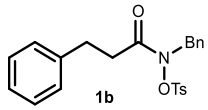
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 – 7.83 (m, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.26 (m, 3H), 7.19 – 7.14 (m, 2H), 4.74 (s, 2H), 2.48 (s, 3H), 2.15 (t, *J* = 7.5 Hz, 2H), 1.43 – 1.36 (m, 2H), 1.19 – 1.10 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.2, 146.8, 135.1, 131.2, 130.3, 129.5, 129.0, 128.6, 128.1, 54.0, 32.8, 25.9, 22.2, 21.9, 13.8

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{19}H_{24}NO_4S^+$: 362.1421, found: 362.1417.

***N*-Benzyl-3-phenyl-*N*-(tosyloxy)propanamide (1b)**



1b

Prepared following **General Procedure A** using 3-phenylpropionic acid (300.4 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.0 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1b** as a white solid.

Yield 496.7 mg (61%).

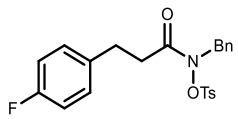
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.19 – 7.13 (m, 5H), 7.11 (d, *J* = 7.2 Hz, 1H), 7.03 (dd, *J* = 6.6, 2.8 Hz, 2H), 6.99 – 6.94 (m, 2H), 4.67 (s, 2H), 2.70 (t, *J* = 7.7 Hz, 2H), 2.43– 2.40 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.2, 146.9, 140.6, 134.9, 131.1, 130.4, 129.5, 128.9, 128.7, 128.5, 128.4, 128.1, 126.3, 53.9, 34.7, 29.8, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{24}NO_4S^+$: 410.1421, found: 410.1419

***N*-Benzyl-3-(4-fluorophenyl)-*N*-(tosyloxy)propenamide (1c)**



1c

Prepared following **General Procedure A** using 3-(4-fluorophenyl)propanoic acid (336.3 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1c** as a white solid.

Yield 355.7 mg (41%).

NMR Spectroscopy:

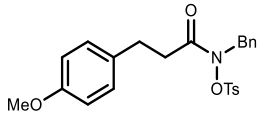
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.74 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.19 – 7.17 (m, 3H), 7.02 – 6.97 (m, 2H), 6.94 – 6.91 (m, 2H), 6.87 – 6.81 (m, 2H), 4.62 (s, 2H), 2.69 (t, *J* = 7.5 Hz, 2H), 2.44 – 2.41 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.0, 161.5 (d, *J* = 244.4 Hz), 147.0, 136.2 (d, *J* = 3.0 Hz), 134.8, 131.1, 130.4, 129.9 (d, *J* = 8.1 Hz), 129.5, 128.9, 128.6, 128.2, 115.2 (d, *J* = 21.2 Hz), 53.8, 34.7, 29.0, 22.0.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -117.24.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{23}FNO_4S^+$: 428.1327, found: 428.1325

***N*-Benzyl-3-(4-methoxyphenyl)-*N*-(tosyloxy)propenamide (1d)**



1d

Prepared following **General Procedure A** using 3-(4-methoxyphenyl)propanoic acid (360.4 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1d** as a colourless oil.

Yield 628.7 mg (72%).

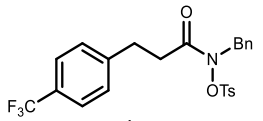
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.23 – 7.17 (m, 3H), 7.02 – 7.00 (m, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.70 (d, *J* = 8.3 Hz, 2H), 4.65 (s, 2H), 3.71 (s, 3H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.40 – 2.36 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.2, 158.1, 146.9, 134.9, 132.6, 131.1, 130.4, 129.5, 129.4, 128.9, 128.6, 128.1, 113.9, 55.4, 53.9, 34.9, 29.0, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{26}NO_5S^+$: 440.1526, found: 440.1525.

***N*-Benzyl-*N*-(tosyloxy)-3-(4-(trifluoromethyl)phenyl)propenamide (1e)**



1e

Prepared following **General Procedure A** using 3-(4-trifluoromethyl)propanoic acid (445.2 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1e** as a white solid.

Yield 663.5 mg (69%).

NMR Spectroscopy:

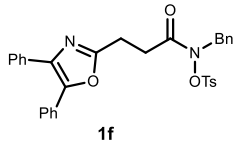
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.29 – 7.25 (m, 3H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.10 – 7.05 (m, 2H), 4.69 (s, 2H), 2.88 (t, *J* = 7.4 Hz, 2H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.50 (s, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 176.7, 147.1, 144.7, 134.7, 131.0, 130.4, 129.4, 128.9, 128.8, 128.6, 128.4, 128.2, 125.4 (q, *J* = 4.5 Hz), 124.4 (q, *J* = 271.8 Hz), 53.8, 34.1, 29.6, 21.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.34.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{23}F_3NO_4S^+$: 478.1294, found: 478.1292.

***N*-Benzyl-3-(4,5-diphenyloxazol-2-yl)-*N*-(tosyloxy)propenamide (1f)**



1f

Prepared following **General Procedure A** using oxaprozin (586.6 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1f** as a yellow oil.

Yield 578.9 mg (52%).

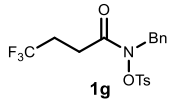
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.62 (d, *J* = 7.0 Hz, 2H), 7.56 (dd, *J* = 7.8, 1.8 Hz, 2H), 7.39 – 7.31 (m, 8H), 7.22 – 7.13 (m, 5H), 4.75 (s, 2H), 3.05 (t, *J* = 7.3 Hz, 2H), 2.86 (t, *J* = 7.3 Hz, 2H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.2, 161.9, 147.1, 145.5, 135.1, 134.7, 132.6, 131.0, 130.4, 129.5, 129.1, 128.8, 128.7, 128.67, 128.65, 128.18, 128.15, 128.1, 126.7, 54.0, 30.3, 22.8, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{32}H_{29}N_2O_5S^+$: 553.1792, found: 553.1788.

***N*-Benzyl-4,4,4-trifluoro-*N*-(tosyloxy)butanamide (1g)**



1g

Prepared following **General Procedure A** using 4,4,4-trifluorobutanoic acid (284.2 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1g** as a colorless oil.

Yield 505.8 mg (63%).

NMR Spectroscopy:

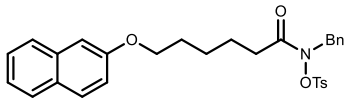
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 – 7.86 (m, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.33 – 7.29 (m, 3H), 7.19 (dd, *J* = 6.6, 3.0 Hz, 2H), 4.80 (s, 2H), 2.51 (s, 3H), 2.45 – 2.36 (m, 2H), 2.36 – 2.25 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.9, 147.4, 134.6, 130.7, 130.5, 129.4, 129.0, 128.8, 128.4, 126.6 (q, *J* = 277.8 Hz), 54.1, 28.6 (q, *J* = 30.3 Hz), 26.3 (q, *J* = 3.1 Hz), 21.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -66.79.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}F_3NO_4S^+$: 402.0982, found: 402.0978.

***N*-Benzyl-6-(naphthalen-2-yloxy)-*N*-(tosyloxy)hexanamide (1h)**



1h

Prepared following **General Procedure B** using naphthalen-2-ol (288.3 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1h** as a colourless oil.

Yield 732.4 mg (71%).

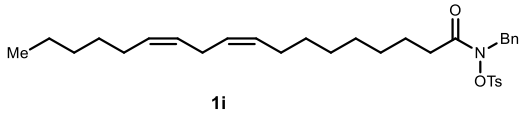
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 – 7.83 (m, 2H), 7.79 – 7.70 (m, 3H), 7.47 – 7.41 (m, 1H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.35 – 7.30 (m, 1H), 7.27 (d, *J* = 1.8 Hz, 1H), 7.26 (s, 2H), 7.20 – 7.08 (m, 4H), 4.74 (s, 2H), 4.00 (t, *J* = 6.5 Hz, 2H), 2.46 (s, 3H), 2.23 (t, *J* = 7.4 Hz, 2H), 1.80 – 1.70 (m, 2H), 1.53 (d, *J* = 7.7 Hz, 2H), 1.40 – 1.31 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.0, 157.1, 146.9, 135.0, 134.7, 131.0, 130.4, 129.49, 129.47, 129.0, 128.7, 128.2, 127.8, 126.8, 126.5, 123.6, 119.1, 106.6, 67.7, 53.9, 32.9, 29.0, 25.6, 23.6, 22.0.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{30}H_{31}NO_5SNa^+$: 540.1815, found: 540.1811.

(9*Z*,12*Z*)-*N*-Benzyl-*N*-(tosyloxy)octadeca-9,12-dienamide (1i)



1i

Prepared following **General Procedure A** using linoleic acid (622.0 μL, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1i** as a colourless oil.

Yield 736.2 mg (68%).

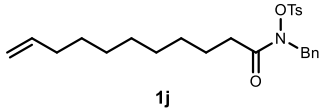
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 2.5 Hz, 3H), 7.09 (dd, *J* = 6.7, 2.9 Hz, 2H), 5.37 – 5.21 (m, 4H), 4.66 (s, 2H), 2.70 (t, *J* = 6.3 Hz, 2H), 2.41 (s, 3H), 2.08 (t, *J* = 7.4 Hz, 2H), 2.03 – 1.91 (m, 4H), 1.39 – 1.05 (m, 16H), 0.82 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.2, 146.8, 135.0, 131.1, 130.4, 130.3, 130.2, 129.5, 129.0, 128.6, 128.2, 128.1, 128.0, 53.9, 53.6, 33.0, 31.7, 29.7, 29.5, 29.3, 29.2, 29.0, 27.3, 25.8, 23.8, 22.7, 22.0, 14.2.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{32}H_{45}NO_4SNa^+$: 562.2961, found: 562.2956.

***N*-Benzyl-*N*-(tosyloxy)undec-10-enamide (1j)**



1j

Prepared following **General Procedure A** using undecenoic acid (404.1 μL, 2.0 mmol,

1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1j** as a colourless oil.

Yield 441.5 mg (50%).

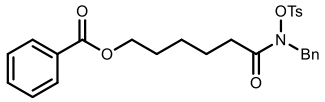
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.85 (m, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.32 – 7.28 (m, 3H), 7.18 (dd, *J* = 6.7, 3.0 Hz, 2H), 5.89 – 5.78 (m, 1H), 5.06 – 4.94 (m, 2H), 4.75 (s, 2H), 2.51 (s, 3H), 2.16 (t, *J* = 7.4 Hz, 2H), 2.08 – 2.02 (m, 2H), 1.48 – 1.35 (m, 4H), 1.32 – 1.11 (m, 8H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.2, 146.8, 139.3, 135.1, 131.2, 130.3, 129.5, 129.0, 128.6, 128.1, 114.3, 53.9, 33.9, 33.1, 29.4, 29.3, 29.2, 29.1, 29.0, 23.9, 22.0.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{25}H_{33}NO_4SNa^+$: 466.2022, found: 466.2020.

6-(Benzyl(tosyloxy)amino)-6-oxohexyl benzoate (1k)



1k

Prepared following **General Procedure B** using benzoic acid (244.2 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1k** as a colourless oil.

Yield 226.6 mg (23%).

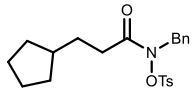
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 – 8.05 (m, 2H), 7.92 – 7.87 (m, 2H), 7.63 – 7.57 (m, 1H), 7.52 – 7.46 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 3.1 Hz, 3H), 7.24 – 7.17 (m, 2H), 4.75 (s, 2H), 4.28 (t, *J* = 6.6 Hz, 2H), 2.50 (s, 3H), 2.26 (t, *J* = 7.3 Hz, 2H), 1.74 – 1.65 (m, 2H), 1.61 – 1.53 (m, 2H), 1.34 – 1.30 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.9, 166.8, 146.9, 135.0, 133.0, 131.1, 130.6, 130.3, 129.7, 129.5, 129.0, 128.6, 128.5, 128.2, 64.9, 53.9, 32.9, 28.6, 25.6, 23.6, 22.0.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{27}H_{29}NO_6SNa^+$: 518.1608, found: 518.1606.

***N*-Benzyl-3-cyclopentyl-*N*-(tosyloxy)propenamide (1l)**



1l

Prepared following **General Procedure A** using 3-cyclopentylpropanoic acid (290.0 μL, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1l** as a white solid.

Yield 567.8 mg (71%).

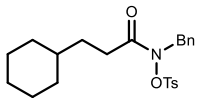
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.30 (dd, *J* = 4.8, 1.9 Hz, 3H), 7.20 (dd, *J* = 6.7, 2.9 Hz, 2H), 4.78 (s, 2H), 2.51 (s, 3H), 2.14 (t, *J* = 7.7 Hz, 2H), 1.67 – 1.54 (m, 6H), 1.48 – 1.40 (m, 3H), 1.02 – 0.88 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.3, 146.9, 135.0, 131.1, 130.3, 129.5, 129.1, 128.6, 128.1, 54.0, 39.5, 32.5, 32.3, 29.9, 25.2, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{22}H_{28}NO_4S^+$: 402.1734, found: 402.1731.

***N*-Benzyl-3-cyclohexyl-*N*-(tosyloxy)propenamide (1m)**



1m

Prepared following **General Procedure A** using 3-cyclohexylpropanoic acid (312.4 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1m** as a white solid.

Yield 574.1 mg (69%).

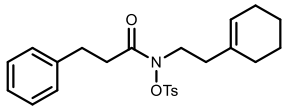
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 – 7.77 (m, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.22 – 7.19 (m, 3H), 7.14 – 7.08 (m, 2H), 4.68 (s, 2H), 2.41 (s, 3H), 2.04 (t, *J* = 7.7 Hz, 2H), 1.61 – 1.52 (m, 3H), 1.46 – 1.39 (m, 2H), 1.25 – 1.18 (m, 2H), 1.08 – 0.88 (m, 4H), 0.72 – 0.62 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.5, 146.9, 135.0, 131.2, 130.3, 129.5, 129.1, 128.6, 128.1, 54.0, 37.1, 33.0, 31.1, 30.6, 26.6, 26.3, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{30}NO_4S^+$: 416.1890, found: 416.1886.

***N*-(2-(Cyclohex-1-en-1-yl)ethyl)-3-phenyl-*N*-(tosyloxy)propenamide (1n)**



1n

Prepared following **General Procedure C** using 2-(cyclohex-1-en-1-yl)ethan-1-amine (418.3 μL, 3.0 mmol, 1.0 equiv), 3-phenylpropionic acid (300.4 mg, 2.0 mmol) and Et_3N (304.2 μL, 2.2 mmol) as starting materials to afford **1n** as a colourless oil.

Yield 673.3 mg (52%).

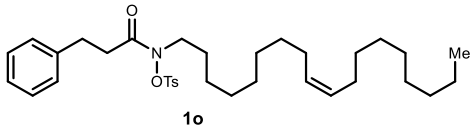
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 – 7.84 (m, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.28 (s, 2H), 7.24 – 7.18 (m, 1H), 7.09 – 7.06 (m, 2H), 5.39 (s, 1H), 3.69 (s, 2H), 2.80 – 2.74 (m, 2H), 2.49 – 2.44 (m, 5H), 2.14 (t, *J* = 6.9 Hz, 2H), 1.97 – 1.90 (m, 2H), 1.88 – 1.84 (m, 2H), 1.59 – 1.48 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.1, 146.8, 140.8, 134.1, 131.2, 130.3, 129.5, 128.5, 128.4, 126.3, 124.7, 49.3, 34.7, 34.6, 30.1, 27.9, 25.5, 22.9, 22.3, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{30}NO_4S^+$: 428.1890, found: 428.1882.

(*Z*)-*N*-(Octadec-9-en-1-yl)-3-phenyl-*N*-(tosyloxy)propenamide (1o)



1o

Prepared following **General Procedure C** using oleylamine (987.0 µL, 3.0 mmol, 1.0 equiv), 3-phenylpropionic acid (300.4 mg, 2.0 mmol) and Et_3N (304.2 µL, 2.2 mmol) as starting materials to afford **1o** as a colourless oil.

Yield 931.8 mg (55%).

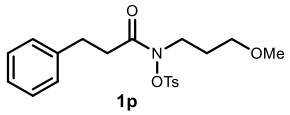
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 7.9 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 3.0 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 2H), 5.41 – 5.36 (m, 2H), 3.57 (t, *J* = 7.5 Hz, 2H), 2.81 (t, *J* = 7.8 Hz, 2H), 2.51 – 2.47 (m, 5H), 2.04 (d, *J* = 6.5 Hz, 2H), 1.50 (q, *J* = 7.5 Hz, 2H), 1.42 – 1.09 (m, 24H), 0.91 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.9, 146.8, 140.7, 131.2, 130.3, 130.1, 129.9, 129.4, 128.5, 128.4, 126.3, 50.9, 34.6, 32.0, 30.1, 29.92, 29.87, 29.8, 29.7, 29.48, 29.45, 29.3, 29.2, 27.4, 27.3, 26.7, 26.2, 22.8, 22.0, 14.2.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{34}H_{51}NO_4SNa^+$: 592.3431, found: 592.3419.

***N*-(3-Methoxypropyl)-3-phenyl-*N*-(tosyloxy)propenamide (1p)**



1p

Prepared following **General Procedure C** using 3-methoxypropan-1-amine (306.0 µL, 3.0 mmol, 1.0 equiv), 3-phenylpropionic acid (300.4 mg, 2.0 mmol) and Et_3N (304.2 µL, 2.2 mmol) as starting materials to afford **1p** as a colourless oil.

Yield 349.3 mg (30%).

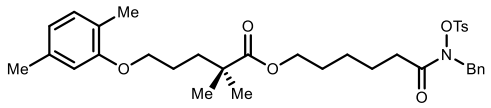
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 7.9 Hz, 2H), 7.28 (d, *J* = 2.2 Hz, 2H), 7.21 (d, *J* = 7.0 Hz, 1H), 7.13 – 7.06 (m, 2H), 3.70 (t, *J* = 7.2 Hz, 2H), 3.30 – 3.26 (m, 5H), 2.81 (t, *J* = 7.8 Hz, 2H), 2.53 – 2.49 (m, 5H), 1.83 – 1.77 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.0, 146.8, 140.7, 131.1, 130.3, 129.5, 128.5, 128.4, 126.3, 69.9, 58.6, 48.4, 34.6, 30.1, 26.5, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{26}NO_5S^+$: 392.1526, found: 392.1517.

6-(Benzyl(tosyloxy)amino)-6-oxohexyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (1q)



1q

Prepared following **General Procedure B** using gemfibrozil (500.6 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1q** as a colourless oil.

Yield 900.8 mg (72%).

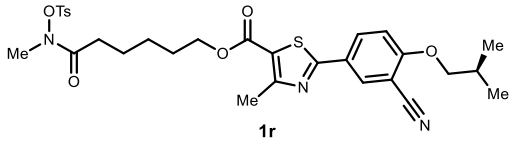
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 – 7.74 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 4.6 Hz, 3H), 7.09 – 7.03 (m, 2H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.59 – 6.55 (m, 1H), 6.52 (d, *J* = 1.6 Hz, 1H), 4.60 (s, 2H), 3.90 (t, *J* = 6.7 Hz, 2H), 3.85 – 3.80 (m, 2H), 2.39 (s, 3H), 2.21 (s, 3H), 2.13 (t, *J* = 7.3 Hz, 2H), 2.08 (s, 3H), 1.72 – 1.60 (m, 6H), 1.48 – 1.36 (m, 4H), 1.12 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.9, 157.1, 146.9, 136.6, 135.0, 131.1, 130.4, 130.3, 129.5, 129.0, 128.6, 128.2, 123.7, 120.8, 112.1, 68.1, 64.3, 53.9, 42.2, 37.2, 32.9, 28.5, 25.5, 25.3, 23.5, 22.0, 21.5, 15.9.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{35}H_{46}NO_7S^+$: 624.2990, found: 624.2982.

6-(Methyl(tosyloxy)amino)-6-oxohexyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (1r)



1r

Prepared following **General Procedure B** using febuxostat (958.1 mg, 3.0 mmol, 1.0 equiv), *N*-methylhydroxylamine hydrochloride (200.0 mg, 2.2 mmol) and Et_3N (304.2 μL, 2.2 mmol) as starting materials to afford **1r** as a colourless oil.

Yield 1177.5 mg (64%).

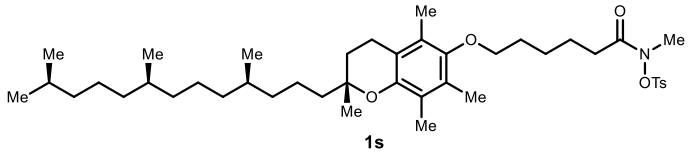
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 2.4 Hz, 1H), 8.10 (d, *J* = 8.7 Hz, 1H), 7.90 – 7.85 (m, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 1H), 4.26 (t, *J* = 6.5 Hz, 2H), 3.89 (d, *J* = 6.5 Hz, 2H), 3.08 (d, *J* = 1.1 Hz, 3H), 2.76 (d, *J* = 1.1 Hz, 3H), 2.48 (s, 3H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.20 (dt, *J* = 13.3, 6.6 Hz, 1H), 1.76 – 1.67 (m, 2H), 1.60 – 1.52 (m, 2H), 1.36 (q, *J* = 8.2 Hz, 2H), 1.08 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.5, 167.4, 162.6, 162.2, 161.3, 146.9, 132.7, 132.2, 131.0, 130.4, 129.5, 126.1, 121.9, 115.5, 112.7, 103.1, 75.8, 65.3, 38.2, 32.5, 28.5, 28.3, 25.6, 23.6, 22.0, 19.2, 17.6.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{36}N_3O_7S_2^+$: 614.1989, found: 614.1982.

***N*-Methyl-6-(((*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)-*N*-(tosyloxy)hexanamide (1s)**



1s

Prepared following **General Procedure B** using vitamin E (861.4 mg, 2.0 mmol, 1.0 equiv), *N*-methylhydroxylamine hydrochloride (200.0 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1s** as a colourless oil.

Yield 1049.1 mg (72%).

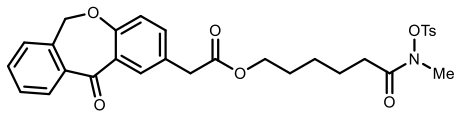
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 3.15 (s, 3H), 2.57 (t, *J* = 6.8 Hz, 2H), 2.48 (s, 3H), 2.22 (t, *J* = 7.4 Hz, 2H), 2.16 (s, 2H), 2.10 (d, *J* = 11.9 Hz, 6H), 1.86 – 1.69 (m, 4H), 1.59 – 1.49 (m, 6H), 1.45 – 1.35 (m, 6H), 1.31 – 1.22 (m, 11H), 1.17 – 1.05 (m, 6H), 0.89 – 0.84 (m, 12H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.5, 148.4, 147.8, 146.9, 131.0, 130.3, 129.5, 127.9, 125.9, 122.9, 117.6, 72.8, 40.3, 39.5, 38.4, 37.7, 37.6, 37.5, 37.4, 32.9, 32.8, 32.6, 31.4, 30.2, 28.1, 25.8, 24.9, 24.6, 24.0, 23.9, 22.9, 22.8, 22.0, 21.2, 20.8, 19.9, 19.8, 12.9, 12.0, 11.9.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{43}H_{70}NO_6S^+$: 728.4919, found: 728.4900.

6-(Methyl(tosyloxy)amino)-6-oxohexyl 2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl)acetate (1t)



1t

Prepared following **General Procedure B** using isoxepac (536.5 mg, 2.0 mmol, 1.0 equiv), *N*-methylhydroxylamine hydrochloride (200.0 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1t** as a yellow oil.

Yield 662.2 mg (58%).

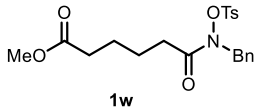
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 2.4 Hz, 1H), 7.95 – 7.83 (m, 3H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.48 – 7.35 (m, 5H), 7.03 (d, *J* = 8.4 Hz, 1H), 5.19 (s, 2H), 4.06 (t, *J* = 6.7 Hz, 2H), 3.63 (s, 2H), 3.10 (s, 3H), 2.47 (s, 3H), 2.20 (t, *J* = 7.4 Hz, 2H), 1.60 – 1.44 (m, 5H), 1.26 – 1.17 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 190.9, 178.3, 171.6, 160.6, 146.9, 140.6, 136.5, 135.7, 132.9, 132.6, 131.0, 130.3, 129.6, 129.5, 129.4, 128.1, 127.9, 125.3, 121.2, 73.8, 64.9, 40.4, 38.3, 32.4, 28.4, 25.5, 23.5, 21.9.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{32}NO_8S^+$: 566.1843, found: 566.1838.

Methyl 6-(benzyl(tosyloxy)amino)-6-oxohexanoate (1w)



1w

Prepared following **General Procedure A** using 6-methoxy-6-oxohexanoic acid (296.0 μL, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.1 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1w** as a colourless oil.

Yield 450.6 mg (54%).

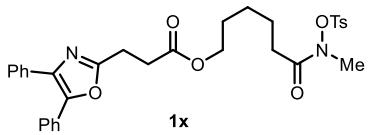
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.76 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.23 – 7.19 (m, 3H), 7.09 –7.07(m, 2H), 4.84 – 4.56 (m, 2H), 3.58 (s, 3H), 2.42 (s, 3H), 2.16 – 2.10 (m, 4H), 1.41 – 1.37 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.6, 173.8, 147.0, 135.0, 131.0, 130.4, 129.5, 129.0, 128.7, 128.2, 53.9, 51.7, 33.8, 32.7, 24.3, 23.3, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{21}H_{26}NO_6S^+$: 420.1746, found: 420.1472.

6-(Methyl(tosyloxy)amino)-6-oxohexyl 3-(4,5-diphenyloxazol-2-yl)propanoate (1x)



1x

Prepared following **General Procedure B** using oxaprozin (440.0 mg, 1.5 mmol, 1.0 equiv), *N*-methylhydroxylamine hydrochloride (100.0 mg, 1.1 mmol) and Et_3N (152.1 μL, 1.1 mmol) as starting materials to afford **1x** as a colourless oil.

Yield 502.4 mg (57%).

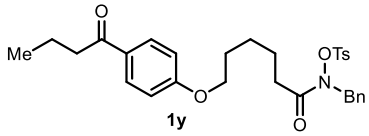
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 – 7.84 (m, 2H), 7.66 – 7.60 (m, 2H), 7.59 – 7.55 (m, 2H), 7.43 – 7.29 (m, 8H), 4.08 (t, *J* = 6.6 Hz, 2H), 3.19 (d, *J* = 8.3 Hz, 2H), 3.09 (s, 3H), 2.91 (d, *J* = 8.4 Hz, 2H), 2.47 (s, 3H), 2.20 (t, *J* = 7.4 Hz, 2H), 1.59 – 1.44 (m, 4H), 1.26 – 1.20 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.4, 172.2, 162.0, 146.9, 145.6, 135.2, 132.5, 131.0, 130.3, 129.5, 129.1, 128.8, 128.7, 128.6, 128.2, 128.0, 126.6, 64.8, 38.3, 32.4, 31.3, 28.4, 25.5, 23.7, 23.5, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{32}H_{35}N_2O_7S^+$: 591.2159, found: 591.2141.

***N*-Benzyl-6-(4-butyrylphenoxy)-*N*-(tosyloxy)hexanamide (1y)**



1y

Prepared following **General Procedure B** using 1-(4-hydroxyphenyl)butan-1-one (335.1 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1y** as a colourless oil.

Yield 912.0 mg (85%).

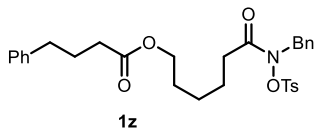
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.20 – 7.15 (m, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 4.72 (s, 2H), 3.97 (t, *J* = 6.4 Hz, 2H), 2.92 (t, *J* = 7.3 Hz, 2H), 2.50 (s, 3H), 2.27 (t, *J* = 7.3 Hz, 2H), 1.81 – 1.69 (m, 4H), 1.53 (d, *J* = 7.8 Hz, 2H), 1.33 (dd, *J* = 14.6, 6.8 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.2, 178.0, 162.9, 146.9, 135.0, 131.1, 130.4, 130.4, 130.2, 129.5, 129.0, 128.6, 128.2, 114.2, 68.0, 53.9, 40.3, 32.9, 28.9, 25.5, 23.6, 22.0, 18.2, 14.1.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{36}NO_6S^+$: 538.2258, found: 538.2253.

6-(Benzyl(tosyloxy)amino)-6-oxohexyl 4-phenylbutanoate (1z)



1z

Prepared following **General Procedure B** using 4-phenylbutyric acid (328.4 mg, 2.0 mmol, 1.0 equiv), *N*-benzylhydroxylamine hydrochloride (351.2 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1z** as a colourless oil.

Yield 342.5 mg (32%).

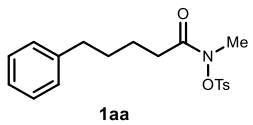
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 7.9 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 5H), 7.25 – 7.15 (m, 5H), 4.72 (s, 2H), 4.02 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.51 (s, 3H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.24 (t, *J* = 7.3 Hz, 2H), 1.99 (q, *J* = 7.6 Hz, 2H), 1.57 – 1.48 (m, 4H), 1.22 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 177.9, 173.7, 146.9, 141.6, 135.0, 131.1, 130.4, 129.5, 129.0, 128.6, 128.5, 128.2, 126.1, 64.3, 53.9, 35.3, 33.8, 32.9, 28.5, 26.7, 25.4, 23.5, 22.0.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{30}H_{35}NO_6SNa^+$: 560.2077, found: 560.2076.

N-Methyl-5-phenyl-*N*-(tosyloxy)pentanamide (1aa)



1aa

Prepared following **General Procedure A** using 5-phenylvaleric acid (356.5 mg, 2.0 mmol, 1.0 equiv), *N*-methylhydroxylamine hydrochloride (200.0 mg, 2.2 mmol, 1.1 equiv) and Et_3N (304.2 μL, 2.2 mmol, 1.1 equiv) as starting materials to afford **1aa** as a colourless oil.

Yield 602.4 mg (83%).

NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 – 7.87 (m, 2H), 7.41 (d, *J* = 8.1 Hz,

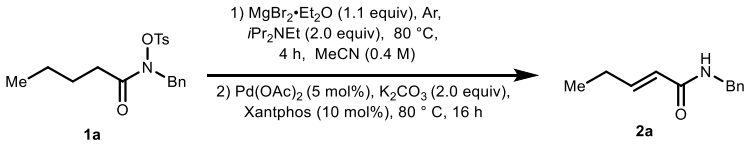
2H), 7.32 – 7.28 (m, 2H), 7.23 – 7.15 (m, 3H), 3.15 (s, 3H), 2.56 (t, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 2.23 (t, *J* = 6.8 Hz, 2H), 1.56 – 1.47 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.4, 146.9, 142.3, 130.9, 130.3, 129.5, 128.5, 128.4, 125.9, 38.4, 35.7, 32.4, 30.9, 23.6, 21.9.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{23}NO_4SNa^+$: 384.1240, found: 384.1229.

4. General procedures for the synthesis of α, β - unsaturated secondary amides

(*E*)-*N*-Benzylpent-2-enamide (2a)



Under argon atmosphere, *N*-benzyl-*N*-(tosyloxy)pentanamide **1a** (72.3 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =3:1) to afford (*E*)-*N*-benzylpent-2-enamide **2a** as a white solid.

R_f = 0.4 (Eluent: petroleum ether/ethyl acetate = 3:1).

Yield 28.5 mg (75%).

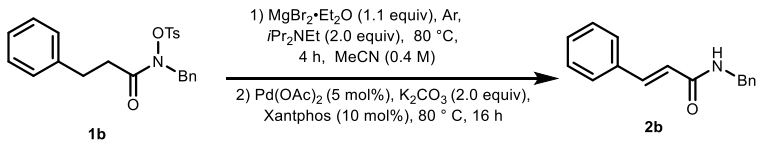
NMR Spectroscopy:

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.36 – 7.22 (m, 5H), 6.87 (dt, *J* = 15.3, 6.4 Hz, 1H), 6.34 (br, 1H), 5.81 (d, *J* = 15.3 Hz, 1H), 4.44 (d, *J* = 5.8 Hz, 2H), 2.20 – 2.13 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.3, 146.4, 138.5, 128.7, 127.8, 127.4, 122.6, 43.6, 25.1, 12.5.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{15}NONa^+$: 212.1046, found: 212.1047.

N-Benzylcinnamamide (2b)



Under argon atmosphere, *N*-benzyl-3-phenyl-*N*-(tosyloxy)propanamide **1b** (81.9 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford *N*-benzylcinnamamide **2b** as a white solid.

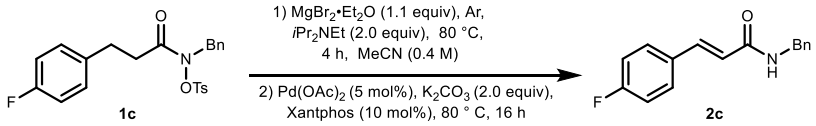
R_f = 0.5 (Eluent: petroleum ether/ethyl acetate = 2:1).
Yield 30.8 mg (65%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 15.6 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.36 – 7.25 (m, 8H), 6.51 – 6.38 (m, 2H), 4.52 (d, *J* = 5.8 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0, 141.4, 138.3, 134.9, 129.8, 128.9, 128.8, 127.9, 127.9, 127.6, 120.7, 43.9.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}NO^+$: 238.1227, found: 238.1224.

(*E*)-*N*-Benzyl-3-(4-fluorophenyl)acrylamide (2c)



Under argon atmosphere, *N*-benzyl-3-(4-fluorophenyl)-*N*-(tosyloxy)propanamide **1c** (85.5 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.
Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-*N*-benzyl-3-(4-fluorophenyl)acrylamide **2c** as a white solid.

R_f = 0.5 (Eluent: petroleum ether/ethyl acetate = 2:1).
Yield 29.0 mg (57%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 15.5 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.38 – 7.26 (m, 5H), 7.07 – 6.97 (m, 2H), 6.35 (d, *J* = 15.6 Hz, 1H), 6.11 (s, 1H), 4.55 (d, *J* = 5.7 Hz, 2H).

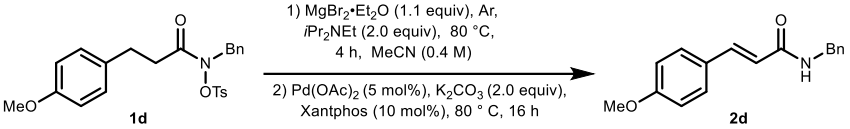
^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.8, 163.7 (d, *J* = 251.5 Hz), 140.3, 138.3, 131.1 (d, *J* = 3.0 Hz), 129.7 (d, *J* = 6.1 Hz), 128.9, 128.0, 127.7, 120.4, 116.1 (d, *J*

= 14.1 Hz), 44.0.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -110.57.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{15}FNO^+$: 256.1132, found: 256.1129.

(*E*)-*N*-Benzyl-3-(4-methoxyphenyl)acrylamide (2d)



Under argon atmosphere, *N*-benzyl-3-(4-methoxyphenyl)-*N*-(tosyloxy)propenamide **1d** (87.8 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-*N*-benzyl-3-(4-methoxyphenyl)acrylamide **2d** as a yellow solid.

R_f = 0.1 (Eluent: petroleum ether/ethyl acetate = 2:1).

Yield 22.5 mg (42%).

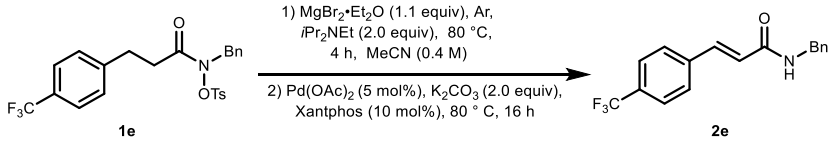
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 15.6 Hz, 1H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.39 – 7.27 (m, 5H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.28 (d, *J* = 15.5 Hz, 1H), 5.86 (s, 1H), 4.57 (d, *J* = 5.6 Hz, 2H), 3.83 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.2, 161.1, 141.2, 138.5, 129.5, 128.9, 128.1, 127.7, 127.6, 118.1, 114.4, 55.5, 44.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{18}NO_2^+$: 268.1332, found: 268.1331.

(*E*)-*N*-Benzyl-3-(4-(trifluoromethyl)phenyl)acrylamide (2e)



Under argon atmosphere, *N*-benzyl-*N*-(tosyloxy)-3-(4-(trifluoromethyl)phenyl)propanamide **1e** (92.5 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: DCM/MeOH = 100:1) to afford (*E*)-*N*-benzyl-3-(4-(trifluoromethyl)phenyl)acrylamide **2e** as a yellow solid.

R_f = 0.5 (Eluent: DCM/MeOH = 100:1).
Yield 43.4 mg (71%).
NMR Spectroscopy:

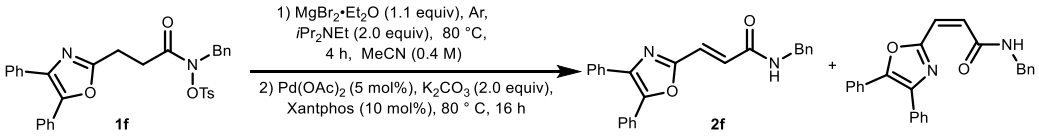
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 – 7.57 (m, 5H), 7.33 (q, *J* = 7.5 Hz, 5H), 6.48 (d, *J* = 15.6 Hz, 1H), 5.99 (br, 1H), 4.59 (d, *J* = 5.6 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 139.7, 138.3, 138.1, 131.4 (q, *J* = 33.3 Hz), 128.9, 128.01, 127.97, 127.8, 125.9 (q, *J* = 4.0 Hz), 124.0 (q, *J* = 272.7 Hz), 123.2, 44.0.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.78.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{15}F_3NO^+$: 306.1100, found: 306.1097.

***N*-Benzyl-3-(4,5-diphenyloxazol-2-yl)acrylamide (2f)**



Under argon atmosphere, *N*-benzyl-3-(4,5-diphenyloxazol-2-yl)-*N*-(tosyloxy)propanamide **1f** (110.5 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.
Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford *N*-benzyl-3-(4,5-diphenyloxazol-2-yl)acrylamide **2f** as a yellow solid.

R_f = 0.3 (Eluent: petroleum ether/ethyl acetate = 2:1).
Yield 67.1 mg (88%). (E/Z = 1:1)
NMR Spectroscopy:(E/Z mixture)

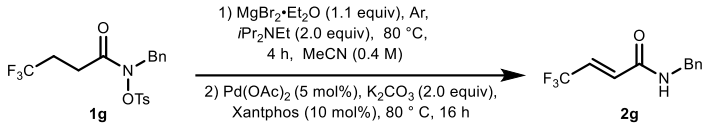
^{1}H NMR (600 MHz, Chloroform-*d*) δ 11.17 (br, 1H), 7.65 – 7.62 (m, 2H), 7.60 – 7.55 (m, 4H), 7.51 (d, *J* = 15.5 Hz, 1H), 7.39 – 7.30 (m, 16H), 7.29 – 7.24 (m, 8H), 6.93 (d, *J* = 15.5 Hz, 1H), 6.64 (d, *J* = 13.8 Hz, 1H), 6.46 (br, 1H), 6.31 (d, *J* = 13.8

Hz, 1H), 4.60 (d, J = 5.3 Hz, 2H), 4.57 (d, J = 5.7 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.6, 164.5, 158.2, 157.6, 146.6, 146.3, 138.2, 137.9, 137.6, 136.2, 132.0, 131.8, 131.0, 129.6, 129.2, 128.94, 128.86, 128.82, 128.75, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.51 127.45, 127.0, 126.8, 125.7, 118.3, 44.2, 44.1.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{25}H_{20}N_2O_2Na^+$: 403.1417, found: 403.1413.

(*E*)-*N*-Benzyl-4,4,4-trifluorobut-2-enamide (2g)



Under argon atmosphere, *N*-benzyl-4,4,4-trifluoro-*N*-(tosyloxy)butanamide **1g** (80.3 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =5:1) to afford (*E*)-*N*-benzyl-4,4,4-trifluorobut-2-enamide **2g** as a white solid.

R_f = 0.6 (Eluent: petroleum ether/ ethyl acetate =5:1).

Yield 22.8 mg (50%).

NMR Spectroscopy:

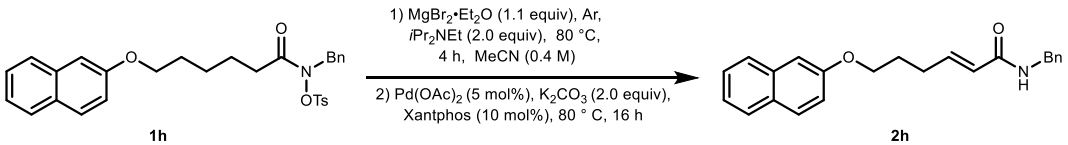
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.24 (m, 5H), 6.83 – 6.69 (m, 1H), 6.49 (dq, J = 15.4, 2.0 Hz, 1H), 6.26 (br, 1H), 4.51 (d, J = 5.7 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.6, 137.2, 130.7 (q, J = 6.1 Hz), 129.0, 128.9 (q, J = 35.4 Hz), 128.09, 128.07, 122.6 (q, J = 270.7 Hz), 44.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -65.06.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{11}FNO^+$: 230.0787, found: 230.0786.

(*E*)-*N*-Benzyl-6-(naphthalen-2-yloxy)hex-2-enamide (2h)



Under argon atmosphere, *N*-benzyl-6-(naphthalen-2-yloxy)-*N*-(tosyloxy)hexanamide **1h** (103.5 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40

mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.
Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-*N*-benzyl-6-(naphthalen-2-yloxy)hex-2-enamide **2h** as a yellow solid.

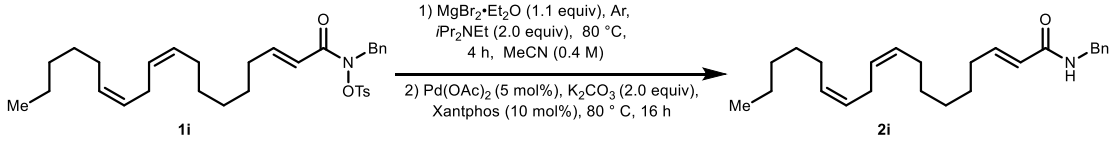
R_f = 0.5 (Eluent: petroleum ether/ethyl acetate = 2:1).
Yield 62.2 mg (90%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 – 7.67 (m, 3H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.34 – 7.25 (m, 6H), 7.16 – 7.08 (m, 2H), 6.94 (dt, *J* = 14.5, 6.9 Hz, 1H), 5.83 (d, *J* = 15.1 Hz, 1H), 5.71 (br, 1H), 4.49 (d, *J* = 5.3 Hz, 2H), 4.09 (t, *J* = 6.1 Hz, 2H), 2.43 (q, *J* = 7.2 Hz, 2H), 2.08 – 1.97 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.8, 157.0, 144.2, 138.4, 134.7, 129.5, 129.1, 128.9, 128.0, 127.8, 127.7, 126.9, 126.5, 124.3, 123.7, 119.0, 106.8, 66.9, 43.8, 28.7, 28.0.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{23}NO_2Na^+$: 368.1621, found: 368.1619.

(2*E*,9*Z*,12*Z*)-*N*-Benzyloctadeca-2,9,12-trienamide (2i)



Under argon atmosphere, (2*E*,9*Z*,12*Z*)-*N*-benzyl-*N*-(tosyloxy)octadeca-2,9,12-trienamide **1i** (108.0 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.
Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (2*E*,9*Z*,12*Z*)-*N*-benzyloctadeca-2,9,12-trienamide **2i** as a coloursless oil.

R_f = 0.1 (Eluent: petroleum ether/ethyl acetate = 2:1).
Yield 29.8 mg (41%).

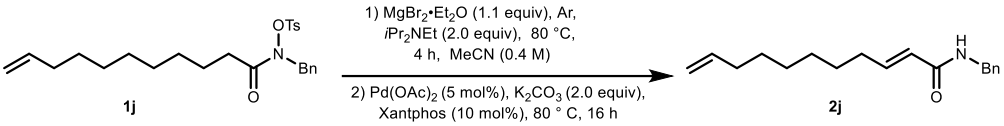
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.25 (m, 5H), 6.87 (dt, *J* = 14.5, 6.9 Hz, 1H), 5.90 – 5.74 (m, 2H), 5.41 – 5.29 (m, 4H), 4.49 (d, *J* = 5.7 Hz, 2H), 2.77 (t, *J* = 6.3 Hz, 2H), 2.17 (q, *J* = 7.3 Hz, 2H), 2.05 (q, *J* = 7.2 Hz, 4H), 1.49 – 1.42 (m, 2H), 1.37 – 1.26 (m, 10H), 0.89 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0, 145.4, 138.5, 130.4, 130.0, 128.8, 128.3, 128.00, 127.96, 127.6, 123.4, 43.7, 32.2, 31.6, 29.55, 29.45, 28.9, 28.3, 27.3, 27.2, 25.7, 22.7, 14.2.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{25}H_{37}NONa^+$: 390.2767, found: 390.2762.

(*E*)-*N*-Benzylundeca-2,10-dienamide (2j)



Under argon atmosphere, (*E*)-*N*-benzylundeca-2,10-dienamide **1j** (88.7 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-*N*-benzylundeca-2,10-dienamide **2j** as a white solid.

R_f = 0.6 (Eluent: petroleum ether/ethyl acetate = 2:1).

Yield 34.6 mg (64%).

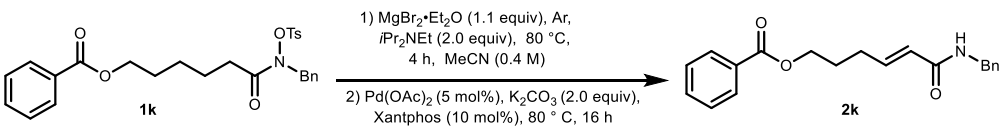
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.26 (m, 5H), 6.88 (dt, *J* = 14.6, 7.0 Hz, 1H), 5.78 (d, *J* = 14.4 Hz, 2H), 5.51 – 5.28 (m, 1H), 5.02 – 4.92 (m, 1H), 4.50 (d, *J* = 5.5 Hz, 2H), 2.17 (q, *J* = 7.4 Hz, 2H), 2.04 (q, *J* = 7.1 Hz, 2H), 1.79 (s, 1H), 1.64 – 1.59 (m, 1H), 1.47 – 1.29 (m, 7H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.1, 145.5, 139.2, 138.5, 128.8, 128.0, 127.7, 123.4, 114.4, 43.8, 33.9, 32.2, 29.1, 29.0, 28.9, 28.3.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{26}NO^+$: 272.2009, found: 272.2003.

(*E*)-6-(Benzylamino)-6-oxohex-4-en-1-yl benzoate (2k)



Under argon atmosphere, 6-(benzyl(tosyloxy)amino)-6-oxohexyl benzoate **1k** (99.1 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-6-(benzylamino)-6-oxohex-4-en-1-yl benzoate **2k** as a yellow solid.

R_f = 0.4 (Eluent: petroleum ether/ ethyl acetate =2:1).

Yield 34.4 mg (53%).

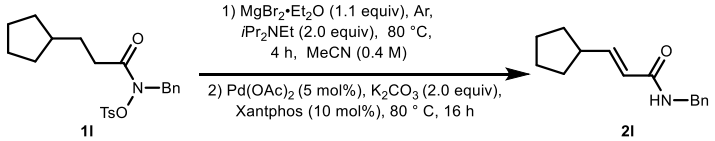
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.35 – 7.24 (m, 5H), 6.90 (dt, *J* = 14.6, 6.9 Hz, 1H), 6.00 (br, 1H), 5.85 (d, *J* = 15.3 Hz, 1H), 4.48 (d, *J* = 5.6 Hz, 2H), 4.32 (t, *J* = 6.4 Hz, 2H), 2.34 (q, *J* = 7.2 Hz, 2H), 1.95 – 1.88 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.7, 165.7, 143.6, 138.3, 133.1, 130.3, 129.6, 128.8, 128.5, 127.9, 127.6, 124.3, 64.2, 43.7, 28.7, 27.5.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{20}H_{21}NO_3Na^+$: 346.1413, found: 346.1413.

(*E*)-*N*-Benzyl-3-cyclopentylacrylamide (2l)



1l 2l

Under argon atmosphere, *N*-benzyl-3-cyclopentyl-*N*-(tosyloxy)propanamide **1l** (80.3 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-*N*-benzyl-3-cyclopentylacrylamide **2l** as a yellow solid.

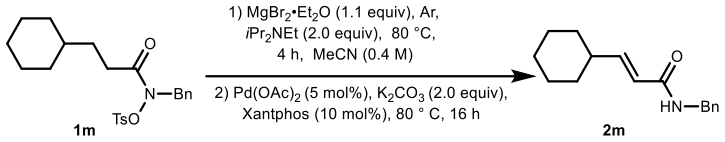
R_f = 0.5 (Eluent: petroleum ether/ ethyl acetate =2:1).
Yield 27.0 mg (58%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.26 (m, 5H), 6.85 (dd, *J* = 15.2, 8.0 Hz, 1H), 5.93 (br, 1H), 5.77 (d, *J* = 15.2 Hz, 1H), 4.48 (d, *J* = 5.7 Hz, 2H), 2.60 – 2.50 (m, 1H), 1.85 – 1.79 (m, 2H), 1.73 – 1.55 (m, 4H), 1.42 – 1.33 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.3, 149.5, 138.5, 128.8, 128.0, 127.9, 127.6, 121.6, 43.7, 42.8, 32.6, 25.3.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{20}NO^+$: 230.1540, found: 230.1538.

(*E*)-*N*-Benzyl-3-cyclohexylacrylamide (2m)



Under argon atmosphere, *N*-benzyl-3-cyclohexyl-*N*-(tosyloxy)propanamide **1m** (83.1 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-*N*-benzyl-3-cyclohexylacrylamide **2m** as a white solid.

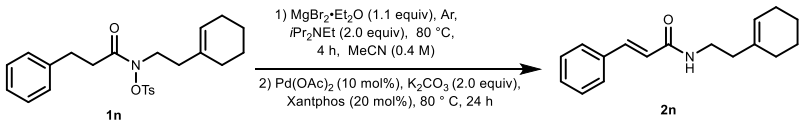
R_f = 0.6 (Eluent: petroleum ether/ ethyl acetate =2:1).
Yield 27.2 mg (56%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 5H), 6.83 (dd, *J* = 15.4, 6.8 Hz, 1H), 5.77 – 5.71 (m, 2H), 4.51 (d, *J* = 5.6 Hz, 2H), 2.14 – 2.06 (m, 1H), 1.80 – 1.67 (m, 5H), 1.31 – 1.11 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.4, 150.5, 138.5, 128.8, 128.1, 127.7, 121.0, 43.8, 40.4, 32.1, 26.1, 25.9.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{22}NO^+$: 244.1696, found: 244.1694.

N-(2-(Cyclohex-1-en-1-yl)ethyl)cinnamamide (2n)



Under argon atmosphere, *N*-(2-(cyclohex-1-en-1-yl)ethyl)-3-phenyl-*N*-(tosyloxy)propanamide **1n** (85.5 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.
Then palladium (II) acetate (4.6 mg, 0.02 mmol, 0.10 equiv), Xantphos (23.2 mg, 0.04 mmol, 0.20 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 24 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =5:1) to afford *N*-(2-(cyclohex-1-en-1-yl)ethyl)cinnamamide **2n** as a white solid.

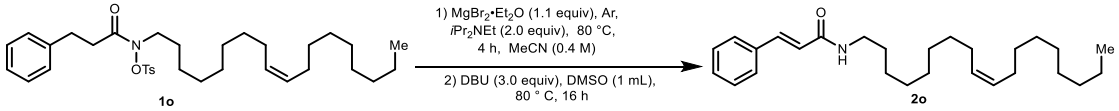
R_f = 0.3 (Eluent: petroleum ether/ethyl acetate = 5:1).
Yield 31.3 mg (61%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 15.6 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.35 (q, *J* = 3.3, 2.0 Hz, 3H), 6.43 (d, *J* = 15.6 Hz, 1H), 5.89 (br, 1H), 5.52 (d, *J* = 3.9 Hz, 1H), 3.48 (q, *J* = 6.5 Hz, 2H), 2.22 (t, *J* = 7.0 Hz, 2H), 2.06 – 2.00 (m, 2H), 1.95 (d, *J* = 6.3 Hz, 2H), 1.68 – 1.61 (m, 2H), 1.61 – 1.54 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.9, 140.8, 135.1, 134.8, 129.6, 128.9, 127.8, 123.6, 121.1, 37.7, 37.6, 28.1, 25.3, 22.9, 22.5.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{22}NO^+$: 256.1696, found: 256.1692.

***N*-((*Z*)-Octadec-9-en-1-yl)cinnamamide (2o)**

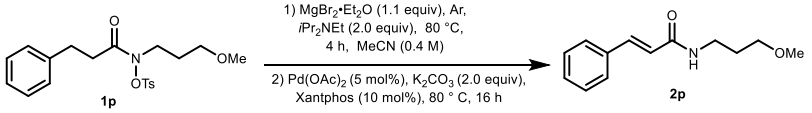


1o 2o

Under argon atmosphere, (*Z*)-*N*-(octadec-9-en-1-yl)-3-phenyl-*N*-(tosyloxy)propanamide **1o** (114.0 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.
Then DBU (90.0 μL, 0.60 mmol, 3.0 equiv) and dry DMSO (1.0 mL) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h before being washed with H_2O (5.0 mL). The aqueous phase was extracted with ethyl acetate (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =5:1) to afford *N*-((*Z*)-octadec-9-en-1-yl)cinnamamide **2o** as a white solid.

R_f = 0.5 (Eluent: petroleum ether/ethyl acetate = 5:1).
Yield 38.6 mg (49%).
NMR Spectroscopy:
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 15.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.33 (d, *J* = 5.2 Hz, 3H), 6.42 (d, *J* = 15.6 Hz, 1H), 5.86 (br, 1H), 5.43 – 5.28 (m, 2H), 3.37 (q, *J* = 6.7 Hz, 2H), 2.03 – 1.95 (m, 4H), 1.57 (q, *J* = 7.1 Hz, 2H), 1.36 – 1.25 (m, 22H), 0.88 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0, 140.8, 135.1, 130.1, 129.9, 129.7, 128.9, 127.9, 121.1, 40.0, 32.7, 32.0, 29.89, 29.86, 29.82, 29.77, 29.64, 29.57, 29.43, 29.35, 27.34, 27.32, 27.1, 22.8, 14.2.
HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{27}H_{44}NO^+$: 398.3417, found: 398.3411.

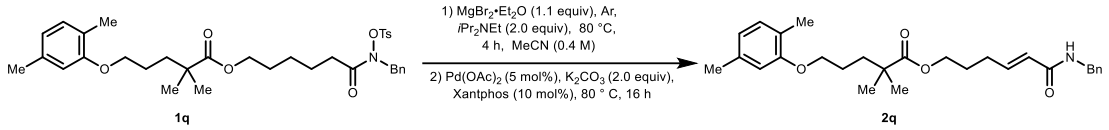
***N*-(3-Methoxypropyl)cinnamamide (2p)**



Under argon atmosphere, *N*-(3-methoxypropyl)-3-phenyl-*N*-(tosyloxy)propenamide **1p** (78.2 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.
Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford *N*-(3-methoxypropyl)cinnamamide **2p** as a colourless oil.

R_f = 0.1 (Eluent: petroleum ether/ethyl acetate = 2:1).
Yield 28.2 mg (64%).
NMR Spectroscopy:
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 15.6 Hz, 1H), 7.51 (dd, *J* = 7.3, 2.4 Hz, 2H), 7.40 – 7.34 (m, 3H), 6.41 (d, *J* = 15.7 Hz, 2H), 3.54 – 3.51 (m, 4H), 3.38 (s, 3H), 1.87 (q, *J* = 6.1 Hz, 2H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0, 140.7, 135.1, 129.6, 128.9, 127.9, 121.2, 71.9, 58.9, 38.5, 29.2.
HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_{18}NO_2^+$: 220.1332, found: 230.1329.

(*E*)-6-(Benzylamino)-6-oxohex-4-en-1-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (2q)



Under argon atmosphere, 6-(benzyl(tosyloxy)amino)-6-oxohexyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate **1q** (124.8 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely. Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =3:1) to afford (*E*)-6-(benzylamino)-6-oxohex-4-en-1-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate **2q** as a yellow oil.

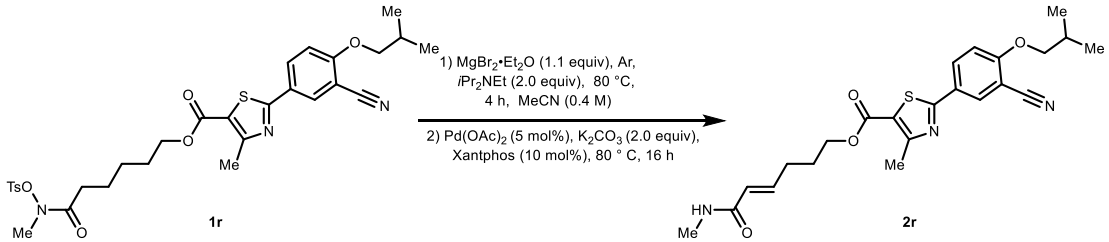
R_f = 0.2 (Eluent: petroleum ether/ ethyl acetate =3:1).
Yield 37.3mg (41%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.28 (m, 5H), 7.00 (d, *J* = 7.4 Hz, 1H), 6.88 (dt, *J* = 14.6, 6.9 Hz, 1H), 6.69 – 6.61 (m, 2H), 5.86 – 5.75 (m, 2H), 4.48 (d, *J* = 5.8 Hz, 2H), 4.10 (t, *J* = 6.4 Hz, 2H), 3.93 (d, *J* = 5.6 Hz, 2H), 2.30 (d, *J* = 6.7 Hz, 5H), 2.19 (s, 3H), 1.85 – 1.74 (m, 6H), 1.23 (d, *J* = 6.2 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.8, 165.6, 157.0, 143.6, 138.4, 136.6, 130.4, 128.7, 127.9, 127.5, 124.2, 123.6, 120.9, 112.1, 68.1, 63.6, 43.7, 42.2, 37.2, 28.6, 27.4, 25.32, 25.27, 21.5, 15.9.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{28}H_{37}NO_4Na^+$: 474.2615, found: 474.2611.

(*E*)-6-(Methylamino)-6-oxohex-4-en-1-yl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (2r)



Under argon atmosphere, 6-(methyl(tosyloxy)amino)-6-oxohexyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate **1r** (162.7 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added

successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely. Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =1:2) to afford (*E*)-6-(methylamino)-6-oxohex-4-en-1-yl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate **2r** as a yellow solid.

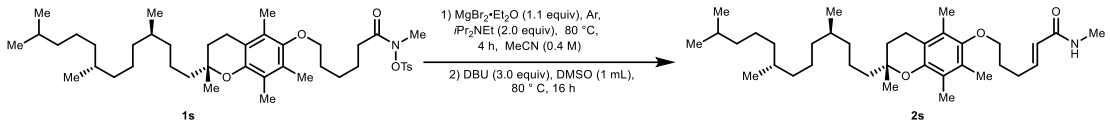
R_f = 0.2 (Eluent: petroleum ether/ ethyl acetate =1:2).
Yield 52.4 mg (59%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (s, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.02 (d, *J* = 8.9 Hz, 1H), 6.86 (dt, *J* = 14.5, 6.9 Hz, 1H), 5.89 – 5.77 (m, 2H), 4.31 (t, *J* = 6.5 Hz, 2H), 3.90 (d, *J* = 6.4 Hz, 2H), 2.87 (d, *J* = 4.8 Hz, 3H), 2.75 (s, 3H), 2.34 (q, *J* = 7.3 Hz, 2H), 2.27 – 2.16 (m, 1H), 1.95 – 1.88 m, 2H), 1.09 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.4, 166.5, 162.6, 162.0, 161.4, 142.7, 132.7, 132.2, 126.0, 124.5, 121.7, 115.5, 112.7, 103.0, 75.8, 64.5, 28.6, 28.2, 27.5, 26.4, 19.1, 17.6.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{28}N_3O_4S^+$: 442.1795, found: 442.1791.

(*E*)-*N*-Methyl-6-(((*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)hex-2-enamide (2s)



Under argon atmosphere, *N*-methyl-6-(((*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)-*N*-(tosyloxy)hexanamide **1s** (145.6 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then DBU (90.0 μL, 0.60 mmol, 3.0 equiv) and dry DMSO (1.0 mL) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h before being washed with H_2O (5.0 mL). The aqueous phase was extracted with ethyl acetate (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 1:1)

to afford (*E*)-*N*-methyl-6-(((*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)hex-2-enamide **2s** as a white solid.

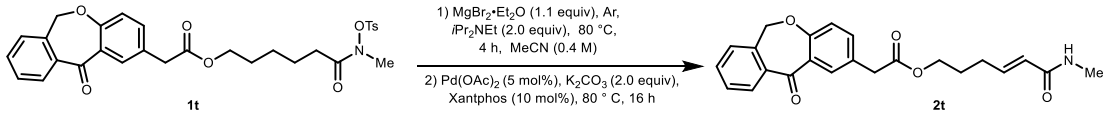
R_f = 0.5 (Eluent: petroleum ether/ethyl acetate = 1:1).
Yield 53.1 mg (48%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.88 (dt, *J* = 14.5, 6.9 Hz, 1H), 5.83 (d, *J* = 15.3 Hz, 1H), 5.75 (br, 1H), 3.65 (d, *J* = 6.6 Hz, 2H), 2.86 (d, *J* = 4.8 Hz, 3H), 2.56 (t, *J* = 6.8 Hz, 2H), 2.42 (q, *J* = 7.4 Hz, 2H), 2.15 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H), 1.92 (t, *J* = 7.2 Hz, 2H), 1.84 – 1.70 (m, 3H), 1.56 – 1.43 (m, 3H), 1.41 – 1.36 (m, 3H), 1.29 – 1.22 (m, 8H), 1.17 – 1.12 (m, 3H), 1.11 – 1.04 (m, 4H), 0.87 (s, 4H), 0.86 – 0.83 (m, 10H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.8, 148.2, 147.9, 143.7, 127.8, 125.8, 124.1, 122.9, 117.6, 74.9, 72.1, 40.2, 39.5, 37.7, 37.6, 37.5, 37.4, 32.9, 32.8, 31.4, 29.1, 28.9, 28.1, 26.4, 24.9, 24.5, 24.0, 22.8, 22.7, 21.1, 20.8, 19.9, 19.8, 19.7, 12.9, 12.0, 11.9.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{36}H_{61}NO_3Na^+$: 578.4543, found: 578.4539.

(*E*)-6-(Methylamino)-6-oxohex-4-en-1-yl 2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl)acetate (2t)



Under argon atmosphere, 6-(methyl(tosyloxy)amino)-6-oxohexyl 2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl)acetate **1t** (113.1 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely. Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =3:2) to afford (*E*)-6-(methylamino)-6-oxohex-4-en-1-yl 2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl)acetate **2t** as a yellow oil.

R_f = 0.2 (Eluent: petroleum ether/ ethyl acetate =3:2).
Yield 39.0 mg (49%).
NMR Spectroscopy:

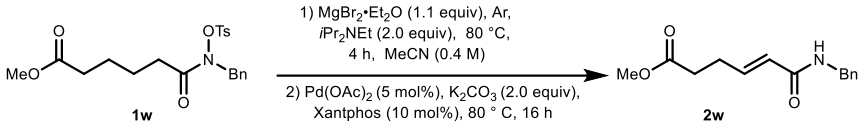
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 2.4 Hz, 1H), 7.88 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.51 – 7.45 (m, 1H), 7.42 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.37 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.77 (dt, *J* = 15.3, 7.0

Hz, 1H), 5.86 (br, 1H), 5.79 (dt, *J* = 15.3, 1.5 Hz, 1H), 5.19 (s, 2H), 4.11 (t, *J* = 6.4 Hz, 2H), 3.64 (s, 2H), 2.84 (d, *J* = 4.9 Hz, 3H), 2.22 –2.16(m, 2H), 1.81 – 1.75 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 191.1, 171.4, 166.6, 160.6, 142.6, 140.4, 136.6, 135.7, 133.0, 132.4, 129.5, 129.4, 128.1, 128.0, 125.3, 124.6, 121.2, 73.8, 64.0, 40.4, 28.3, 27.2, 26.4.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{24}NO_5^+$: 394.1649, found: 394.1645.

Methyl (*E*)-6-(benzylamino)-6-oxohex-4-enoate (2w)



Under argon atmosphere, methyl 6-(benzyl(tosyloxy)amino)-6-oxohexanoate **1w** (83.9 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford methyl (*E*)-6-(benzylamino)-6-oxohex-4-enoate **2w** as a yellow solid.

R_f = 0.2 (Eluent: petroleum ether/ethyl acetate = 2:1).

Yield 30.0 mg (61%).

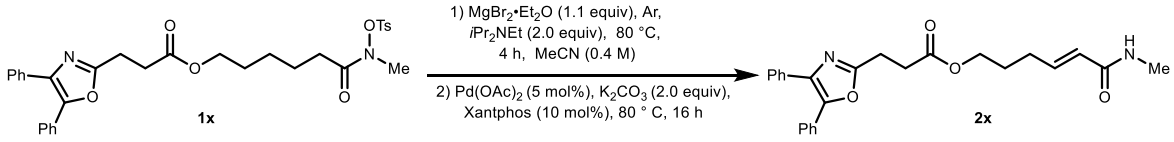
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.24 (m, 5H), 6.84 (dt, *J* = 15.3, 6.2 Hz, 1H), 5.89 – 5.74 (m, 2H), 4.50 (d, *J* = 5.7 Hz, 2H), 3.67 (s, 3H), 2.56 – 2.43 (m, 4H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 173.0, 165.6, 142.7, 138.3, 128.9, 128.0, 127.7, 124.5, 51.9, 43.8, 32.6, 27.2.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{18}NO_3^+$: 248.1281, found: 248.1279.

(*E*)-6-(Methylamino)-6-oxohex-4-en-1-yl 3-(4,5-diphenyloxazol-2-yl)propanoate (2x)



Under argon atmosphere, 6-(methyl(tosyloxy)amino)-6-oxohexyl 3-(4,5-diphenyloxazol-2-yl)propanoate **1x** (118.1 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =1:1) to afford (*E*)-6-(methylamino)-6-oxohex-4-en-1-yl 3-(4,5-diphenyloxazol-2-yl)propanoate **2x** as a colourless oil.

R_f = 0.1 (Eluent: petroleum ether/ ethyl acetate =1:1).

Yield 38.2 mg (46%).

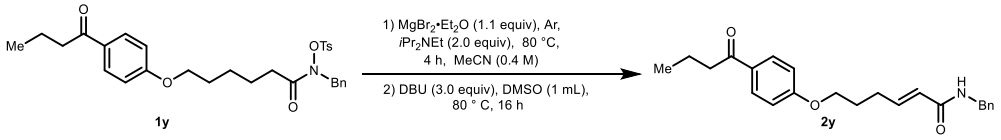
NMR Spectroscopy:

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.58 – 7.54 (m, 2H), 7.52 – 7.48 (m, 2H), 7.32 – 7.23 (m, 6H), 6.68 (dt, *J* = 15.2, 7.0 Hz, 1H), 5.61 (d, *J* = 15.3 Hz, 1H), 5.36 (br, 1H), 4.06 (t, *J* = 6.4 Hz, 2H), 3.11 (t, *J* = 7.3 Hz, 2H), 2.85 (t, *J* = 7.3 Hz, 2H), 2.74 (d, *J* = 4.9 Hz, 3H), 2.16 – 2.12 (m, 2H), 1.73 – 1.70 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.0, 166.5, 161.9, 145.6, 142.8, 135.1, 132.4, 129.0, 128.8, 128.72, 128.65, 128.2, 128.0, 126.6, 124.4, 64.0, 31.2, 28.4, 27.3, 26.3, 23.6.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{25}H_{26}N_2O_4Na^+$: 441.1785, found: 441.1769.

(*E*)-*N*-Benzyl-6-(4-butyrylphenoxy)hex-2-enamide (2y)



Under argon atmosphere, *N*-benzyl-6-(4-butyrylphenoxy)-*N*-(tosyloxy)hexanamide **1y** (107.5 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then DBU (90.0 μL, 0.60 mmol, 3.0 equiv) and dry DMSO (1.0 mL) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h before being washed with H_2O (5.0 mL). The aqueous phase was extracted with ethyl acetate (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residual was purified

by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2:1) to afford (*E*)-*N*-benzyl-6-(4-butyrylphenoxy)hex-2-enamide **2y** as a white solid.

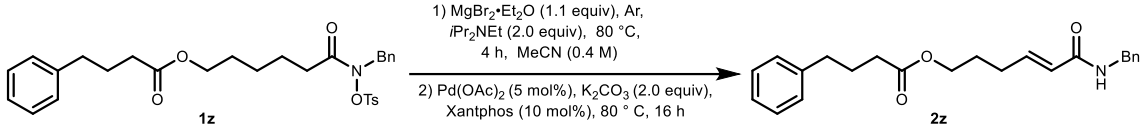
R_f = 0.3 (Eluent: petroleum ether/ethyl acetate = 2:1).
Yield 29.9 mg (41%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.6 Hz, 2H), 7.26 – 7.15 (m, 5H), 6.85 – 6.79 (m, 2H), 5.85 – 5.61 (m, 2H), 4.47 – 4.32 (m, 2H), 3.94 (t, *J* = 6.1 Hz, 2H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.31 (q, *J* = 7.3 Hz, 2H), 1.88 (t, *J* = 6.9 Hz, 2H), 1.71 – 1.64 (m, 3H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.3, 165.7, 162.7, 143.8, 138.3, 130.4, 130.3, 128.8, 128.0, 127.7, 124.4, 114.2, 67.1, 43.8, 40.3, 28.6, 27.9, 18.1, 14.1.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{28}NO_3^+$: 366.2064, found: 366.2062.

(*E*)-6-(Benzylamino)-6-oxohex-4-en-1-yl 4-phenylbutanoate (2z)



Under argon atmosphere, 6-(benzyl(tosyloxy)amino)-6-oxohexyl 4-phenylbutanoate **1z** (107.5 mg, 0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =2:1) to afford (*E*)-6-(benzylamino)-6-oxohex-4-en-1-yl 4-phenylbutanoate **2z** as a yellow oil.

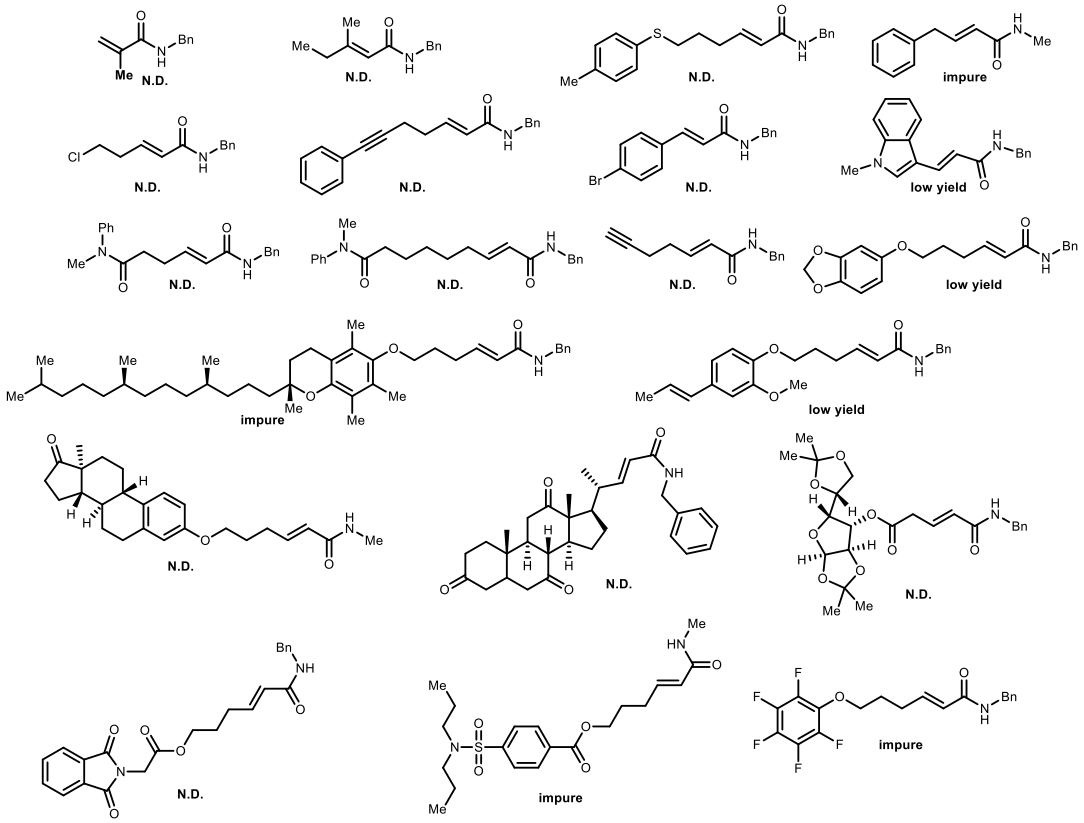
R_f = 0.4 (Eluent: petroleum ether/ ethyl acetate =2:1).
Yield 33.6 mg (46%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.23 (m, 7H), 7.22 – 7.13 (m, 3H), 6.97 – 6.78 (m, 1H), 5.93 (br, 1H), 5.80 (d, *J* = 15.2 Hz, 1H), 4.48 (d, *J* = 2.4 Hz, 2H), 4.06 (t, *J* = 6.5, 2H), 2.67 – 2.61 (m, 2H), 2.34 – 2.29 (m, 2H), 2.23 (q, *J* = 7.8 Hz, 2H), 1.98 – 1.90 (m, 2H), 1.82 – 1.72 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.6, 165.7, 143.6, 141.4, 138.3, 128.8, 128.6, 128.5, 127.9, 127.6, 126.1, 124.2, 63.5, 43.7, 35.2, 33.7, 28.6, 27.4, 26.6.

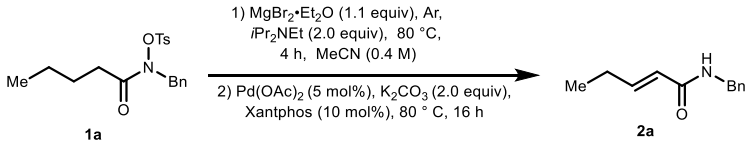
HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{28}NO_3^+$: 366.2064, found: 366.2061.

Failed substrates



5. Scaled-up reaction

(*E*)-*N*-Benzylpent-2-enamide (2a)

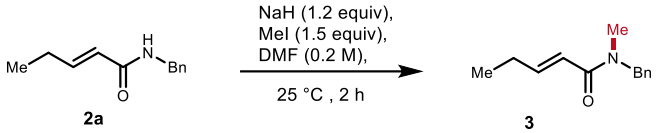


Under argon atmosphere, *N*-benzyl-*N*-(tosyloxy)pentanamide **1a** (2.17 g, 6.0 mmol, 1.0 equiv), magnesium bromide ethyl etherate (1.72 g, 6.6 mmol, 1.1 equiv), dry acetonitrile (15.0 mL) and *N*-ethyldiisopropylamine (2.09 mL, 12.0 mmol, 2.0 equiv) were added successively to a 100 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 ^{o}C for 16 h.

Then palladium (II) acetate (69.0 mg, 0.30 mmol, 0.05 equiv), Xantphos (347.2 mg, 0.60 mmol, 0.10 equiv) and K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 ^{o}C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =3:1) to afford (*E*)-*N*-benzylpent-2-enamide **2a** as a white solid in 68% yield (0.77 g).

6. Derivatization to other compounds

(*E*)-*N*-Benzyl-*N*-methylpent-2-enamide (3)



Under argon atmosphere, (*E*)-*N*-benzylpent-2-enamide **2a** (37.9 mg, 0.20 mmol, 1.0 equiv), dry *N*,*N*-dimethylformamide (1.0 mL) and NaH (60%, dispersion in Paraffin Liquid) (9.6 mg, 0.24 mmol, 1.2 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar at 0 °C. The sealed tube was then stirred at 25 °C for 0.5 h. Then the MeI (19.6 μL, 0.30 mmol, 1.5 equiv) was added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 25 °C for 2 h. Then the mixture was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5:1) to afford (*E*)-*N*-benzyl-*N*-methylpent-2-enamide **3** as a colorless oil.

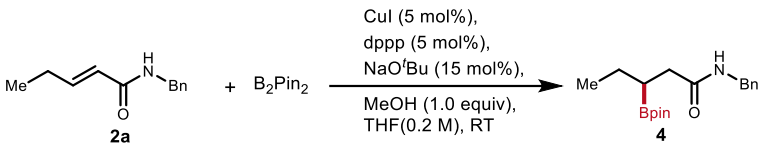
R_f = 0.9 (Eluent: petroleum ether/ ethyl acetate =5:1).
Yield 30.5 mg (75%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.27 (m, 3H), 7.27 – 7.15 (m, 2H), 7.08 – 6.95 (m, 1H), 6.30 – 6.22 (m, 1H), 4.65 (s, 1H), 4.59 (s, 1H), 2.98 (s, 3H), 2.29 – 2.18 (m, 2H), 1.11 – 1.01 (m, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.6, 167.1, 148.6, 148.4, 137.5, 137.0, 129.0, 128.7, 128.1, 127.7, 127.4, 126.6, 119.3, 53.5, 51.2, 35.0, 34.2, 25.7, 25.7, 12.7.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{17}NONa^+$: 226.1202, found: 226.1200.

N-Benzyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanamide (4)



To a flame-dried 10 mL Schlenk tube was added CuCl (1 mg, 0.01 mmol, 0.05 equiv), NaO^{t}Bu (2.8 mg, 0.03 mmol, 0.15 equiv), dppp ligand (4.1 mg, 0.01 mmol, 0.05 equiv), dry THF (0.40 mL) was added under nitrogen[3]. The reaction mixture was stirred at room temperature for 0.5 h, after which time bis(pinacolato)diboron (141.0 mg, 0.22mmol, 1.1 equiv.) in THF (0.30 mL) was added. The reaction mixture was stirred for 10 min and then (*E*)-*N*-benzylpent-2-enamide **2a** (37.9 mg, 0.2 mmol, 1.0 equiv) in THF (0.30 mL) were added, followed by MeOH (16.0 μL, 0.4 mmol, 2.0 equiv). The resulting mixture was stirred until complete consumption of starting material as indicated by TLC. The resulting mixture was diluted with acetone (10 mL), filtered (Celite), and concentrated under a reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3:1) to

afford *N*-benzyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanamide **4** as a white solid.

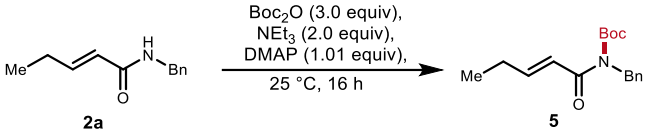
R_f = 0.7 (Eluent: petroleum ether/ ethyl acetate =3:1).
Yield 58.6 mg (92%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.23 (m, 5H), 6.04 (d, *J* = 7.9 Hz, 1H), 4.41 (dd, *J* = 5.7, 3.6 Hz, 2H), 2.42 – 2.25 (m, 2H), 1.53 – 1.39 (m, 2H), 1.37 – 1.28 (m, 1H), 1.20 (d, *J* = 4.8 Hz, 12H), 0.93 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.3, 138.6, 128.7, 128.0, 127.5, 83.3, 43.7, 37.9, 24.9, 24.8, 24.0, 13.4.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{29}BNO_3^+$: 318.2235, found: 318.2233.

tert-butyl (*E*)-Benzyl(pent-2-enoyl)carbamate (5)



To a flame-dried 25 mL flask was added (*E*)-*N*-benzylpent-2-enamide **2a** (94.6 mg, 0.50 mmol, 1.0 equiv), di-*tert*-butyl decarbonate (345.0 μL, 1.50 mmol, 3.0 equiv), triethylamine (138.7 μL, 1.00 mmol, 2.0 equiv), 4-dimethylaminopyridine (61.7 mg, 0.51 mmol, 1.01 equiv) and DCM (1.0 mL) was added. The resulting mixture was stirred 25 °C until complete consumption of starting material as indicated by TLC. Then the mixture was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5:1) to afford *tert*-butyl (*E*)-benzyl(pent-2-enoyl)carbamate **5** as a colorless oil.

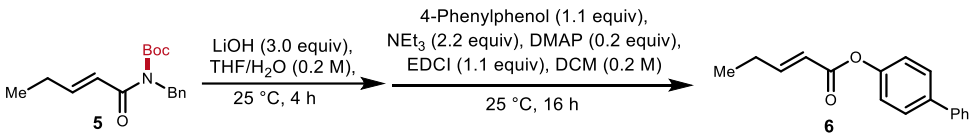
R_f = 0.9 (Eluent: petroleum ether/ ethyl acetate =5:1).
Yield 116.5 mg (81%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.21 (m, 5H), 7.05 (dt, *J* = 15.2, 6.4 Hz, 1H), 6.82 (d, *J* = 15.1 Hz, 1H), 4.90 (s, 2H), 2.33 – 2.22 (m, 2H), 1.40 (s, 9H), 1.09 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.0, 153.4, 149.5, 138.5, 128.4, 127.6, 127.1, 123.4, 83.3, 47.8, 28.0, 25.7, 12.5.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{23}NO_3Na^+$: 312.1570, found: 312.1570.

[1,1'-Biphenyl]-4-yl (*E*)-pent-2-enoate (6)



To a solution of *tert*-butyl (*E*)-benzyl(pent-2-enoyl)carbamate **5** (57.9 mg, 0.20 mmol, 1.0 equiv) in THF (0.5 mL) and H_2O (0.5 mL) was added $LiOH·H_2O$ (25.2 mg, 0.60

mmol, 3.0 equiv). The reaction mixture was allowed to stir for 2.5 h at 25 °C. The reaction was washed by DCM (3 × 2 mL), the aqueous layer was acidified with hydrochloric acid and extracted with DCM (3 × 2 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product (*E*)-pent-2-enoic acid was used directly for next step reaction without purification.

To a solution of (*E*)-pent-2-enoic acid in DCM (1.5 mL) was added *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (42.2 mg, 0.22 mmol, 1.1 equiv), 4-dimethylaminopyridine (4.9 mg, 0.04 mmol, 0.20 equiv) and triethylamine (45.8 μL, 0.44 mmol, 2.2 equiv). The reaction mixture was allowed to stir for 16 h at 25 °C. The reaction was concentrated and the residue was purified by flash chromatography (eluent: petroleum ether/ethyl acetate = 10:1) to afford [1,1'-biphenyl]-4-yl (*E*)-pent-2-enoate **6** as a white solid.

R_f = 0.8 (Eluent: petroleum ether/ ethyl acetate =10:1).

Yield 44.1 mg (87%).

NMR Spectroscopy:

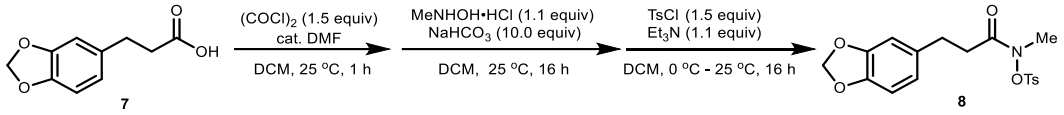
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.55 (m, 4H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.29 (m, 1H), 7.28 – 7.21 (m, 1H), 7.21 – 7.16 (m, 2H), 6.04 (d, *J* = 15.7 Hz, 1H), 2.36 – 2.09 (m, 2H), 1.14 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 153.3, 150.4, 140.6, 139.0, 128.9, 128.3, 127.4, 127.3, 122.0, 119.8, 25.7, 12.2.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{17}NO_2^+$: 253.1223, found: 253.1220.

7. Synthesis of llepcimide

3-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-methyl-*N*-(tosyloxy)propenamide (8)



Prepared following **General Procedure A** using 3-(benzo[*d*][1,3]dioxol-5-yl)propanoic acid **7** (500.0 mg, 2.5 mmol, 1.0 equiv), *N*-methylhydroxylamine hydrochloride (250.0 mg, 2.8 mmol, 1.1 equiv) and Et_3N (381.5 μL, 2.8 mmol, 1.1 equiv) as starting materials to afford **8** as a colourless oil.

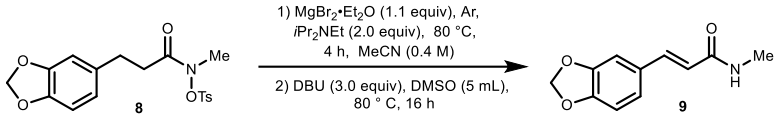
R_f = 0.4 (Eluent: petroleum ether/ ethyl acetate =5:1).
Yield 909.4 mg (96%).
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.43 – 7.36 (m, 2H), 6.69 (d, *J* = 8.3 Hz, 1H), 6.52 – 6.50 (m, 2H), 5.92 (s, 2H), 3.13 (d, *J* = 1.9 Hz, 3H), 2.69 (t, *J* = 7.7 Hz, 2H), 2.48 (s, 3H), 2.44 – 2.41 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.7, 147.7, 147.0, 146.0, 134.4, 130.9, 130.4, 129.5, 121.2, 108.9, 108.3, 100.9, 38.4, 34.6, 29.7, 22.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{20}NO_6S^+$: 378.1006, found: 378.1001.

(*E*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-methylacrylamide (9)



Under argon atmosphere, 3-(benzo[*d*][1,3]dioxol-5-yl)-*N*-methyl-*N*-(tosyloxy)propenamide (566.1 mg, 1.50 mmol, 1.0 equiv), magnesium bromide ethyl etherate (426.0 mg, 1.65 mmol, 1.1 equiv), dry acetonitrile (5.0 mL) and *N*-ethyldiisopropylamine (517.5 μL, 3.00 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 4 h or more until the starting materials were consumed completely.

Then DBU (90.0 μL, 0.60 mmol, 3.0 equiv) and dry DMSO (5.0 mL) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 °C for 16 h before being washed with H_2O (10.0 mL). The aqueous phase was extracted with ethyl acetate (3 × 20.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 1:1) to afford (*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)-*N*-methylacrylamide **9** as a white solid

R_f = 0.1 (Eluent: petroleum ether/ethyl acetate = 1:1).
Yield 190.9 mg (80%).
NMR Spectroscopy:

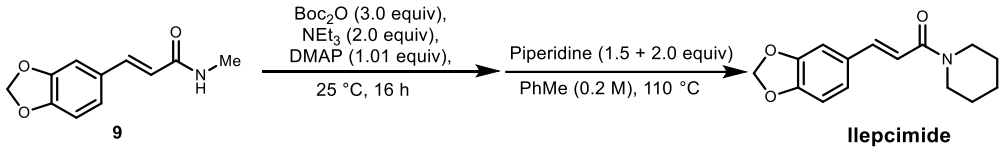
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (dd, *J* = 15.6, 3.7 Hz, 1H), 6.93 (d, *J* =

14.6 Hz, 2H), 6.80 – 6.68 (m, 1H), 6.43 – 6.18 (m, 2H), 5.95 (d, *J* = 3.9 Hz, 2H), 2.91 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.1, 149.0, 148.3, 140.4, 129.4, 123.8, 118.9, 108.5, 106.4, 101.5, 26.6.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{12}NO_3$: 206.0812, found: 206.0806.

(*E*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-1-(piperidin-1-yl)prop-2-en-1-one (llepcimide)



To a flame-dried 10 mL flask was added (*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)-*N*-methylacrylamide **9** (184.6 mg, 0.90 mmol, 1.0 equiv), di-*tert*-butyl decarbonate (620.3 μL, 2.70 mmol, 3.0 equiv), triethylamine (249.7 μL, 1.80 mmol, 2.0 equiv), 4-dimethylaminopyridine (111.1 mg, 0.91 mmol, 1.01 equiv) and DCM (5 mL) was added. The resulting mixture was stirred 25 °C until complete consumption of starting material as indicated by TLC. The mixture was filtered through a pad of silica gel (eluent: petroleum ether/ethyl acetate = 3:1) and the filtrate was concentrated under reduced pressure. to afford crude *tert*-butyl (*E*)-(3-(benzo[*d*][1,3]dioxol-5-yl)acryloyl)(methyl)carbamate as a white solid, which can be used for the next step without further purification (259.4 mg, 94%).

To a solution of crude *tert*-butyl (*E*)-(3-(benzo[*d*][1,3]dioxol-5-yl)acryloyl)(methyl)carbamate (54.9 mg, 0.18 mmol, 1.0 equiv) in PhMe (1.0 mL) was added piperidine (29.6 μL, 0.30 mmol, 1.5 equiv)[4]. The reaction mixture was allowed to stir for 12 h at 110 °C. Then the additional piperidine (39.5 μL, 0.40 mmol, 2.0 equiv) was added to the mixture. The sealed tube was then vigorously stirred at 110 °C for 12 h. The reaction was concentrated and the residue was purified by flash chromatography (eluent: petroleum ether/ethyl acetate = 1:1) to afford **llepcimide** as a yellow oil.

R_f = 0.1 (Eluent: petroleum ether/ethyl acetate = 1:1).

Yield 29.1 mg (62%).

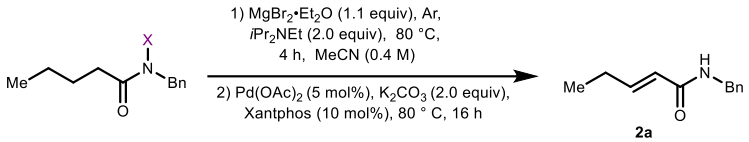
NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 15.3 Hz, 1H), 7.02 (d, *J* = 1.7 Hz, 1H), 6.98 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 15.3 Hz, 1H), 5.98 (s, 2H), 3.60 (d, *J* = 31.3 Hz, 4H), 1.69 – 1.64 (m, 2H), 1.62 – 1.56 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.6, 148.9, 148.3, 142.1, 130.0, 123.7, 115.8, 108.6, 106.4, 101.5, 47.1, 43.5, 26.9, 25.7, 24.8.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{18}NO_3^+$: 260.1281, found: 260.1274.

8. Reactivity of different leaving groups



Under argon atmosphere, starting materials containing different leaving groups (0.20 mmol, 1.0 equiv), magnesium bromide ethyl etherate (56.8 mg, 0.22 mmol, 1.1 equiv), dry acetonitrile (0.5 mL) and *N*-ethyldiisopropylamine (69.0 μL, 0.40 mmol, 2.0 equiv) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 ^{o}C for 4 h.

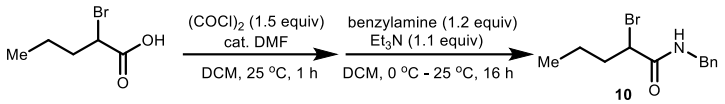
Then palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv) and K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) were added to the mixture under argon atmosphere. The sealed tube was then vigorously stirred at 80 ^{o}C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The yield was determined by ^{1}H NMR analysis with 1,3,5-trimethoxybenzene as an internal standard. The results were shown in the **Table S5** below.

Table S5. ^{1}H NMR yield of different leaving groups

X	OTs	Cl	OAc	OMe
^{1}H NMR yield	82%	0%	0%	0%

9. Potential intermediate for the dehydrogenation

N-Benzyl-2-bromopentanamide (10)



To a stirred solution of 2-bromopentanoic acid (262 μL, 2.0 mmol, 1.0 equiv) in dichloromethane (2.0 mL), was added 2 drops *N*,*N*-dimethylformamide. Then oxalyl chloride (200.0 μL, 2.2 mmol, 1.1 equiv) was added slowly into the mixture. The reaction was stirred at 25 °C for 1 h before being concentrated.

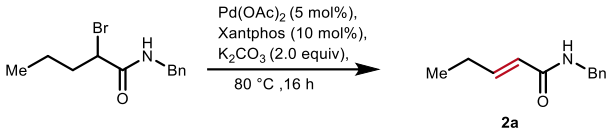
To a stirred solution of mixture was added benzylamine (262 μL, 2.4 mmol, 1.2 equiv). A solution of Et_3N (305.0 μL, 2.2 mmol, 1.1 equiv) in dichloromethane (1.0 mL) was charged slowly into reaction at 0 °C. The reaction was stirred at 25 °C for 16 h before being washed with H_2O (5.0 mL). The aqueous phase was extracted with dichloromethane (3 × 5.0 mL). After that, the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced. The residual was purified by column chromatography on silica gel to afford *N*-benzyl-2-bromopentanamide **10** as a white solid. All analytical data were in good accordance with data reported in the literature.[5]

NMR Spectroscopy:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.26 (m, 5H), 6.68 (br, 1H), 4.47 (d, *J* = 5.8 Hz, 2H), 4.37 (dd, *J* = 8.4, 5.1 Hz, 1H), 2.22 – 2.09 (m, 1H), 2.08 – 1.95 (m, 1H), 1.58 – 1.44 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.9, 137.7, 128.9, 127.84, 127.79, 52.0, 44.3, 38.1, 20.7, 13.4.

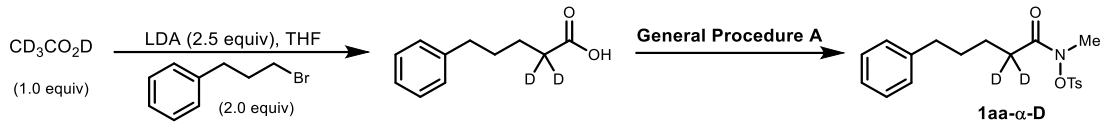
(*E*)-*N*-Benzylpent-2-enamide (2a)



Under argon atmosphere, *N*-benzyl-2-bromopentanamide **10** (54.0 mg, 0.20 mmol, 1.0 equiv), palladium (II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), Xantphos (11.6 mg, 0.02 mmol, 0.10 equiv), K_2CO_3 (55.5 mg, 0.40 mmol, 2.0 equiv) and dry acetonitrile (0.5 mL) were added successively to a 10 mL Schlenk tube with a magnetic bar. The sealed tube was then stirred at 80 °C for 16 h. The mixture was filtered through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residual was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate =3:1) to afford (*E*)-*N*-benzylpent-2-enamide **2a** as a white solid in 79% yield. (29.9 mg)

10. Kinetic Isotope Effect Studies

N-Methyl-5-phenyl-*N*-(tosyloxy)pentanamide-2,2-d$_2$ (1aa-α-D)



To a solution of lithium diisopropylamide (2.5 mL, 5.0 mmol, 2.5 equiv) in THF (2 M) was added the acetic acid-d$_4$ (112.4 μL, 2.0 mmol, 1.0 equiv) via syringe dropwise at 0 °C.[6] The resulting mixture was stirred at 0 °C for 5 minutes. Then it was heated at reflux for 3 hours. After cooling down to room temperature, 1-bromo-3-phenylpropane (607.9 μL, 4.0 mmol, 2.0 equiv) was added dropwise, then the mixture was heated at reflux overnight. The resulting solution was quenched with water and extracted with EtOAc. The aqueous layer was acidified with 1M HCl and extracted with EtOAc. The combined organic layer was washed with brine and dried over Na_2SO_4. After filtration and concentration, the obtained crude acid was used in next step without further purification. The next step follows the **General Procedure A** to afford *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide-2,2-d$_2$ as a colourless oil.

Yield 261.2 mg (36%).

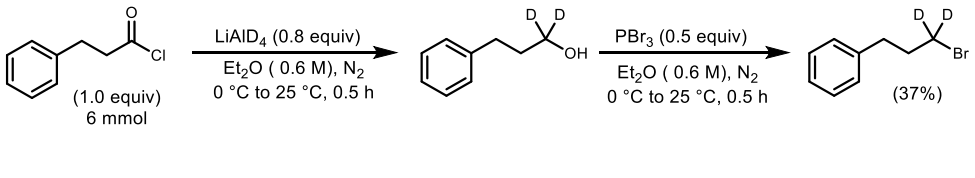
NMR Spectroscopy:

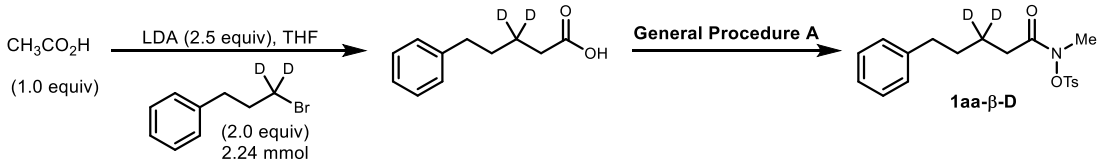
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 – 7.86 (m, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.32 – 7.28 (m, 2H), 7.23 – 7.15 (m, 3H), 3.15 (s, 3H), 2.56 (t, *J* = 7.0 Hz, 2H), 2.47 (s, 3H), 1.55 – 1.47 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.5, 146.9, 142.3, 130.9, 130.3, 129.5, 128.5, 128.4, 125.9, 38.3, 35.7, 30.9, 23.5, 23.4, 21.9.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{21}D_2NO_4SNa^+$: 386.1366, found: 386.1351.

N-Methyl-5-phenyl-*N*-(tosyloxy)pentanamide-3,3-d$_2$ (1aa-β-D)





Lithium aluminum deuteride (901.2 mg, 4.8 mmol, 0.8 equiv) was suspended in anhydrous Et_2O (10.0 mL) and cooled to 0 °C.[7] A solution of hydrocinnamoyl chloride (891.4 μL, 6.0 mmol, 1.0 equiv) in Et_2O (5.0 mL) was added dropwise at 0 °C. The resulting mixture was then allowed to warm up to room temperature and stirred for 2 hours. The resulting solution was quenched with water. The resulting precipitate was

removed by filtration, washed thoroughly with Et_2O. The filtrate was washed with brine and dried over Na_2SO_4. After filtration and concentration, the obtained crude alcohol was used in next step without further purification.

To a solution of the above crude alcohol in anhydrous Et_2O (20.0 mL) was added PBr_3 (282 μL, 3.0 mmol, 0.5 equiv) via a syringe at 0 °C. The mixture was stirred for 30 minutes at 0°C and for additional 30 minutes at room temperature. Ice was added to quench the reaction. The organic layer was washed with brine and dried over Na_2SO_4. After filtration and concentration, the obtained crude (3-bromopropyl-3,3-d_2)benzene was used in next step without further purification.

To a solution of lithium diisopropylamide (1.9 mL, 3.8 mmol, 2.5 equiv) in THF (2M) was added the acetic acid (85.9 μL, 1.5 mmol, 1.0 equiv) via syringe dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 5 minutes. Then it was heated at reflux for 3 hours. After cooling down to room temperature, crude (3-bromopropyl-3,3-d_2)benzene was added dropwise, then the mixture was heated at reflux overnight. The resulting solution was quenched with water and extracted with EtOAc. The aqueous layer was acidified with 1 M HCl and extracted with EtOAc. The combined organic layer was washed with brine and dried over Na_2SO_4. After filtration and concentration, the obtained crude acid was used in next step without further purification. The next step follows the **General Procedure A** to afford *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide-3,3-d_2 as a colourless oil.

Yield 90.0 mg (17%).

NMR Spectroscopy:

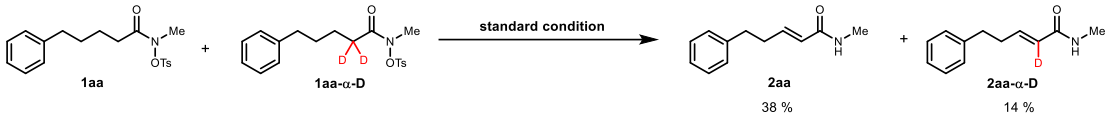
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.31 – 7.28 (m, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.16 (d, *J* = 7.1 Hz, 2H), 3.15 (s, 3H), 2.57 – 2.54 (m, 2H), 2.47 (s, 3H), 2.21 (s, 2H), 1.49 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.5, 146.9, 142.3, 131.0, 130.3, 129.5, 128.5, 128.4, 125.9, 38.4, 35.7, 32.3, 30.8, 21.9.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{21}D_2NO_4SNa^+$: 386.1366, found: 386.1364.

Intermolecular competitive KIE experiments with *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide **1aa**, *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide-2,2-d_2 **1aa-α-D** and *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide-3,3-d_2 **1aa-β-D**

A) Reactions were performed with *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide **1aa** (36.1 mg, 0.1 mmol), *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide-2,2-d_2 **1aa-α-D** (36.3 mg, 0.1 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol) and Xantphos (11.6 mg, 0.02 mmol) and K_2CO_3 (55.2 mg, 0.40 mmol), 0.5 mL dry acetonitrile, following the general procedure of the desaturation reaction. After the reaction proceeded for 1+14 hours, the reaction solution was filtered through silica gel and the crude ^{1}H NMR was taken using CH_2Br_2 as the internal standard.



P_H / P_D = 0.27/(0.37-0.27) = 2.7

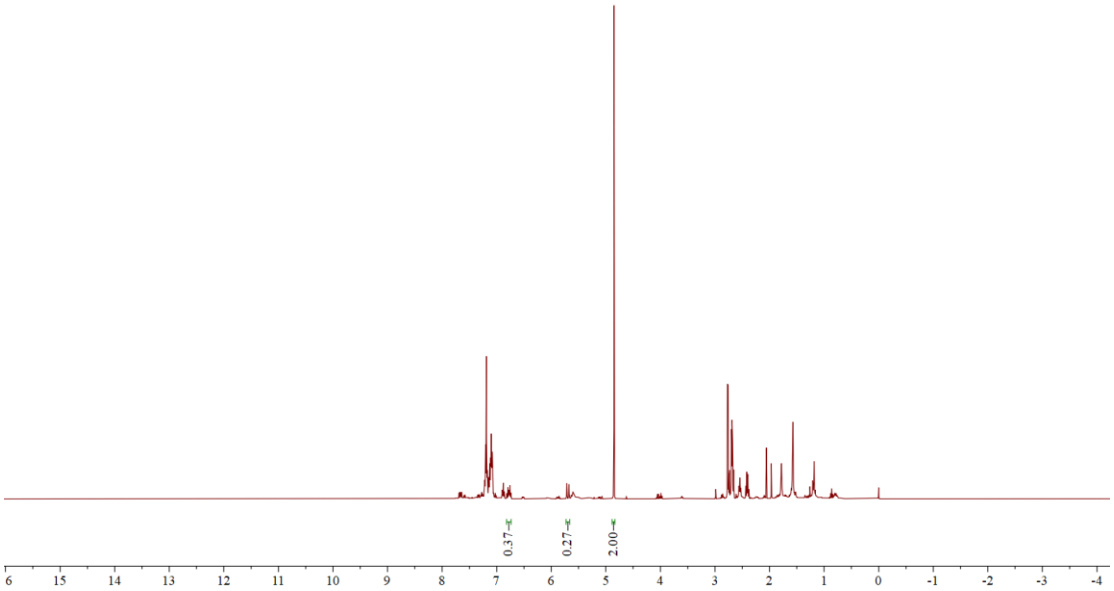
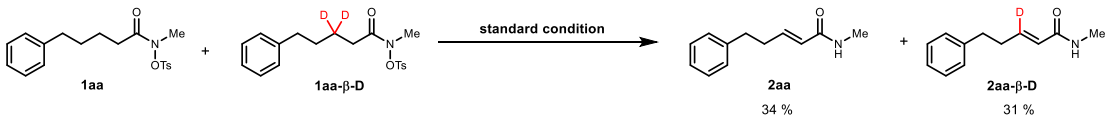


Figure S2. KIE experiments between **1aa** and **1aa-α-D** (CH_2Br_2 as the internal standard) ($CDCl_3$, 400 MHz)

B) Reactions were performed with *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide **1aa** (36.1 mg, 0.1 mmol), *N*-methyl-5-phenyl-*N*-(tosyloxy)pentanamide-3,3-d_2 **1aa-β-D** (36.3 mg, 0.1 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol) and Xantphos (11.6 mg, 0.02 mmol) and K_2CO_3 (55.2 mg, 0.40 mmol), 0.5 mL dry acetonitrile, following the general procedure of the desaturation reaction. After the reaction proceeded for 4+6 hours, the reaction solution was filtered through silica gel and the crude ^1H NMR was taken using CH_2Br_2 as the internal standard.



P_H / P_D = 0.12*2/(0.34-0.12) = 1.1

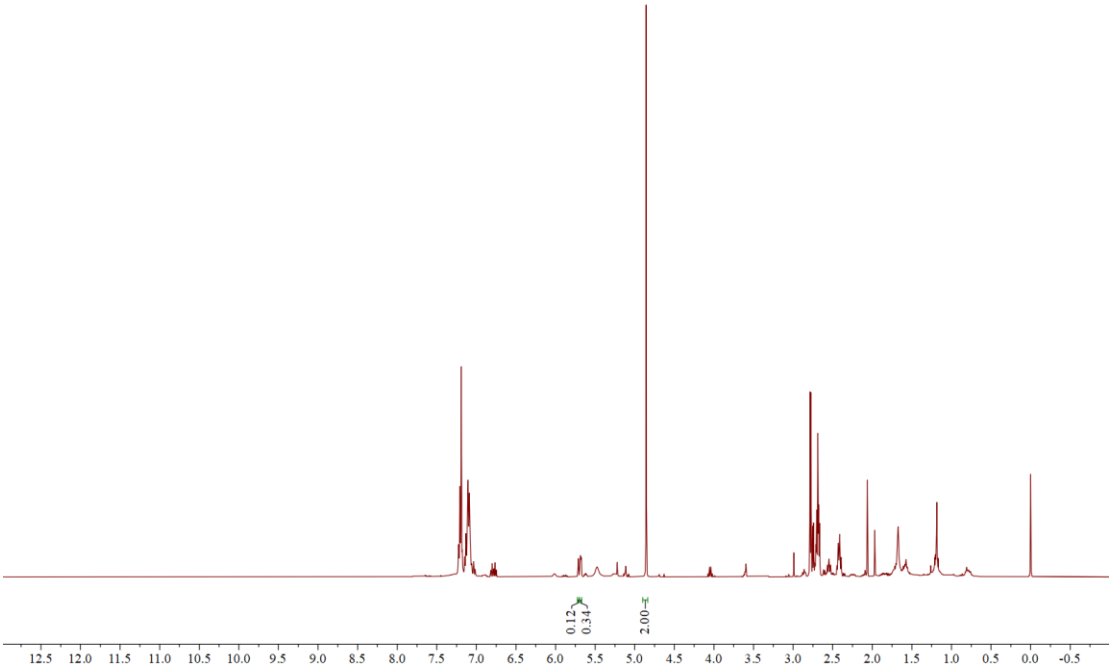


Figure S3. KIE experiments between **1aa** and **1aa-β-D** (CH_2Br_2 as the internal standard) ($CDCl_3$, 400 MHz)

11. Copies of NMR spectra

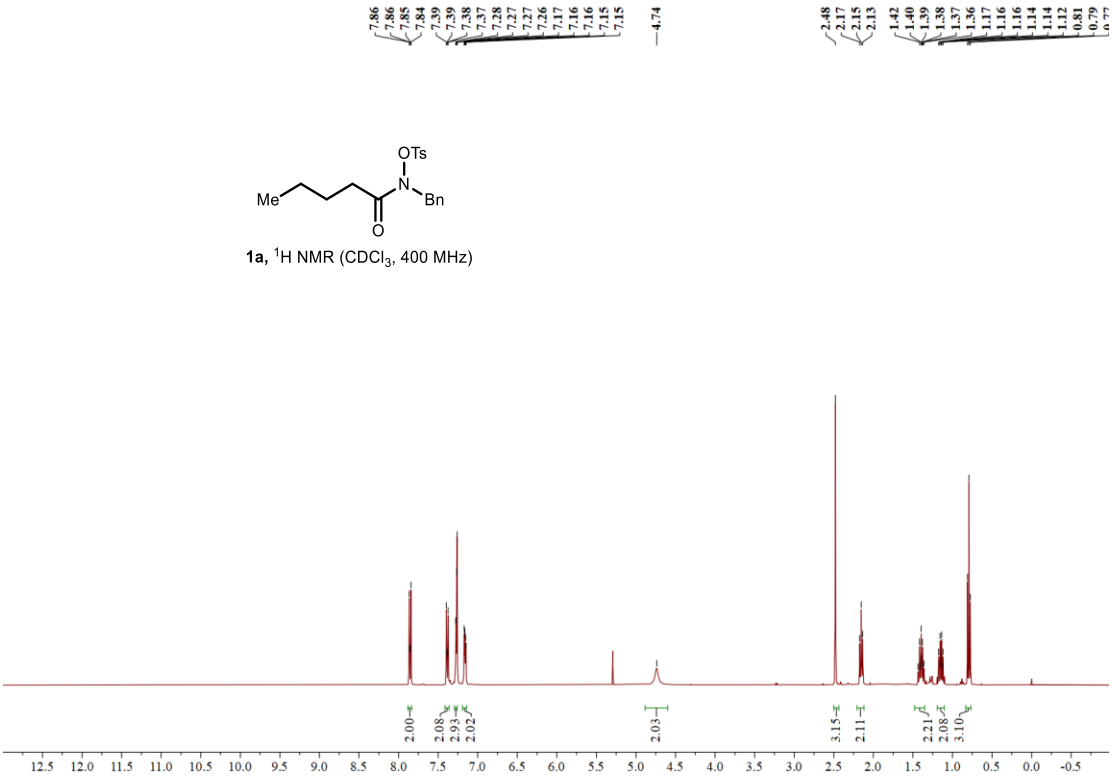


Figure S4. ^{1}H NMR of **1a** ($CDCl_3$, 400 MHz)

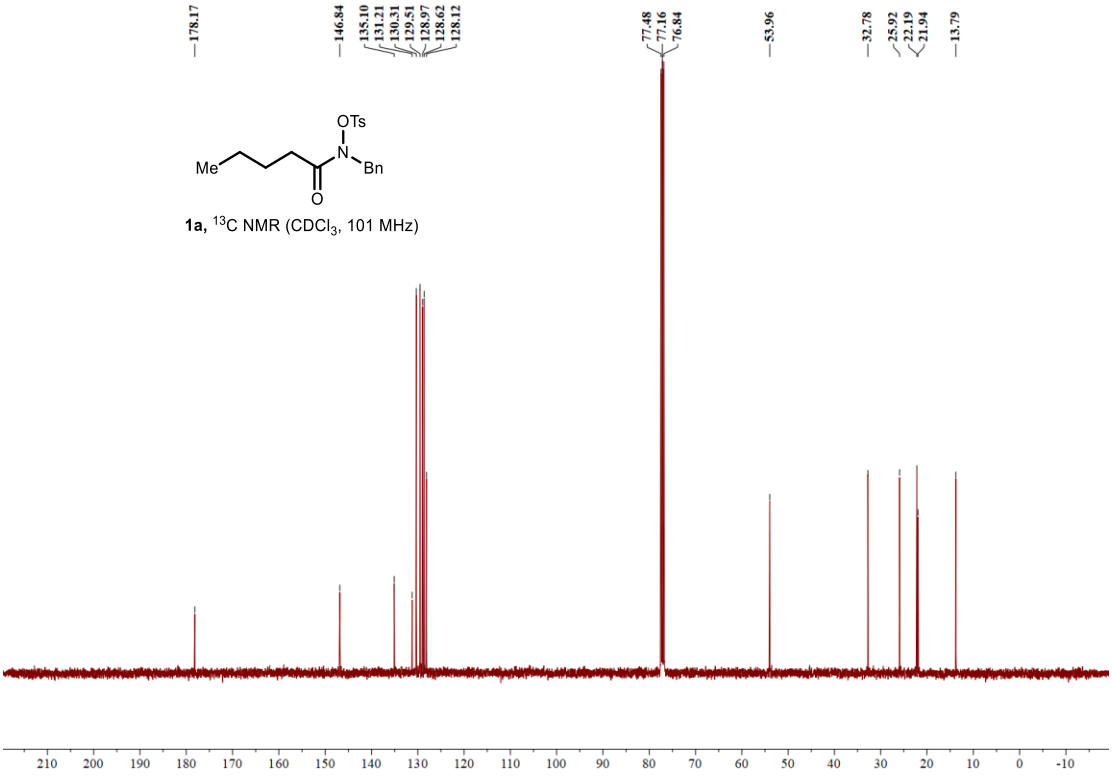


Figure S5. ^{13}C NMR of **1a** ($CDCl_3$, 101 MHz)

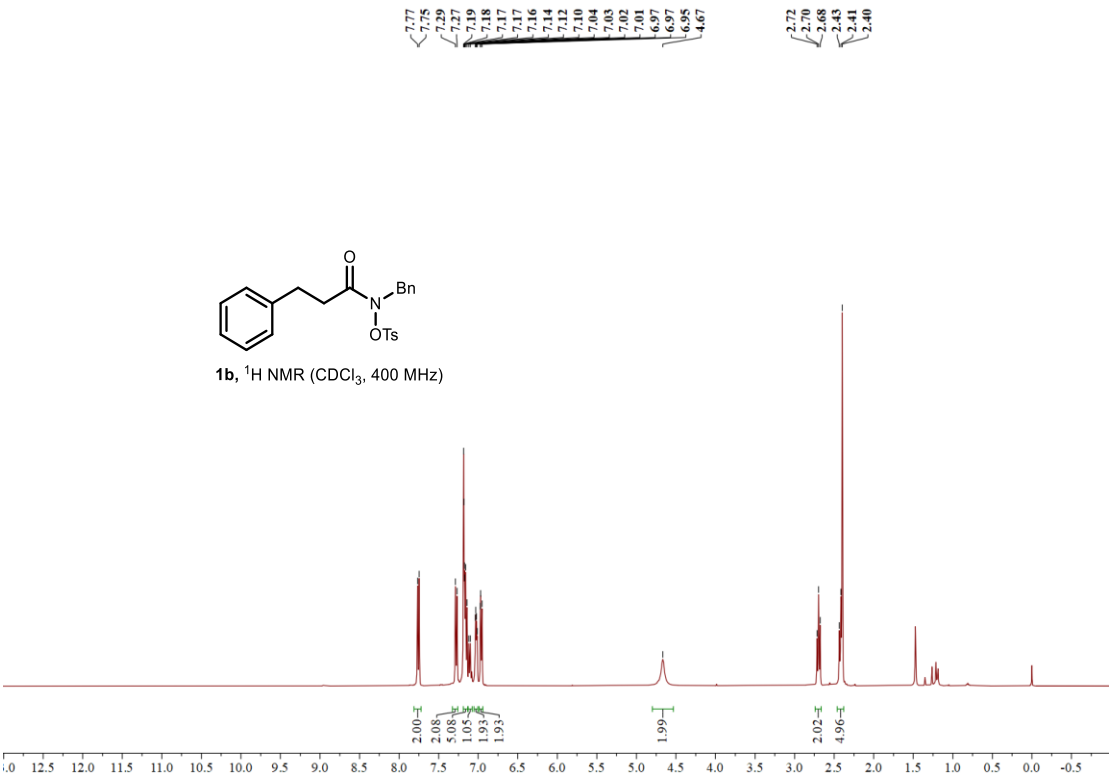


Figure S6. ^{1}H NMR of **1b** ($CDCl_3$, 400 MHz)

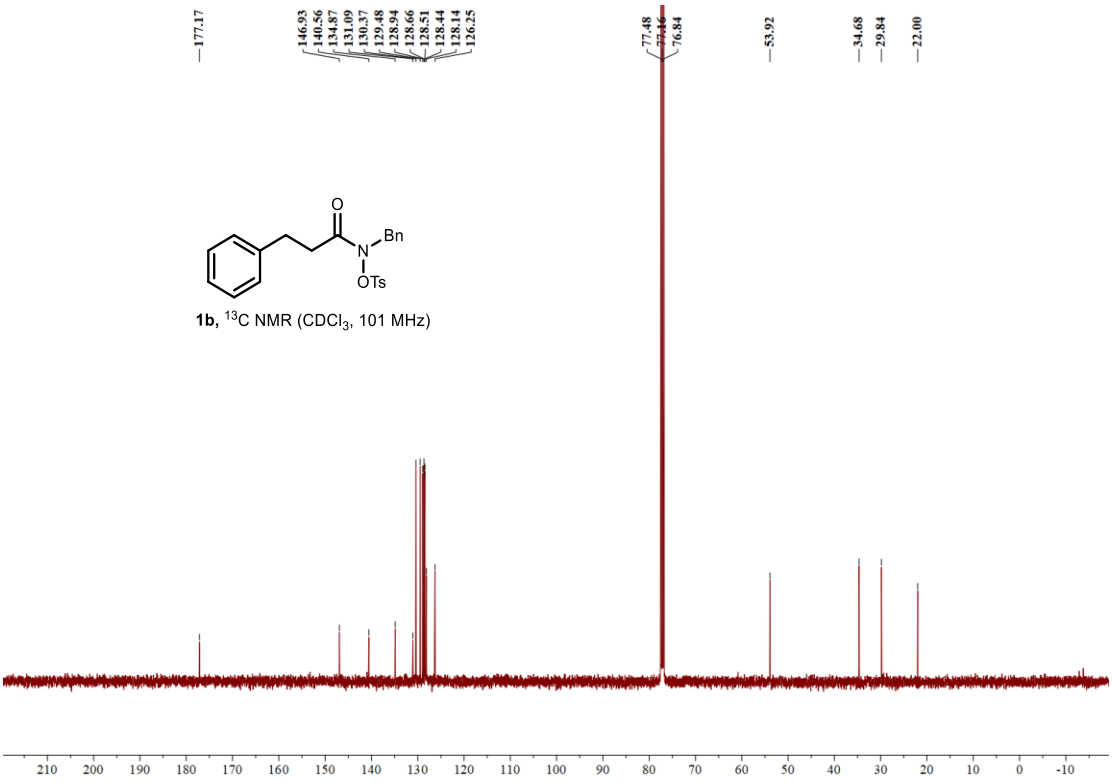


Figure S7. ^{13}C NMR of **1b** ($CDCl_3$, 101 MHz)

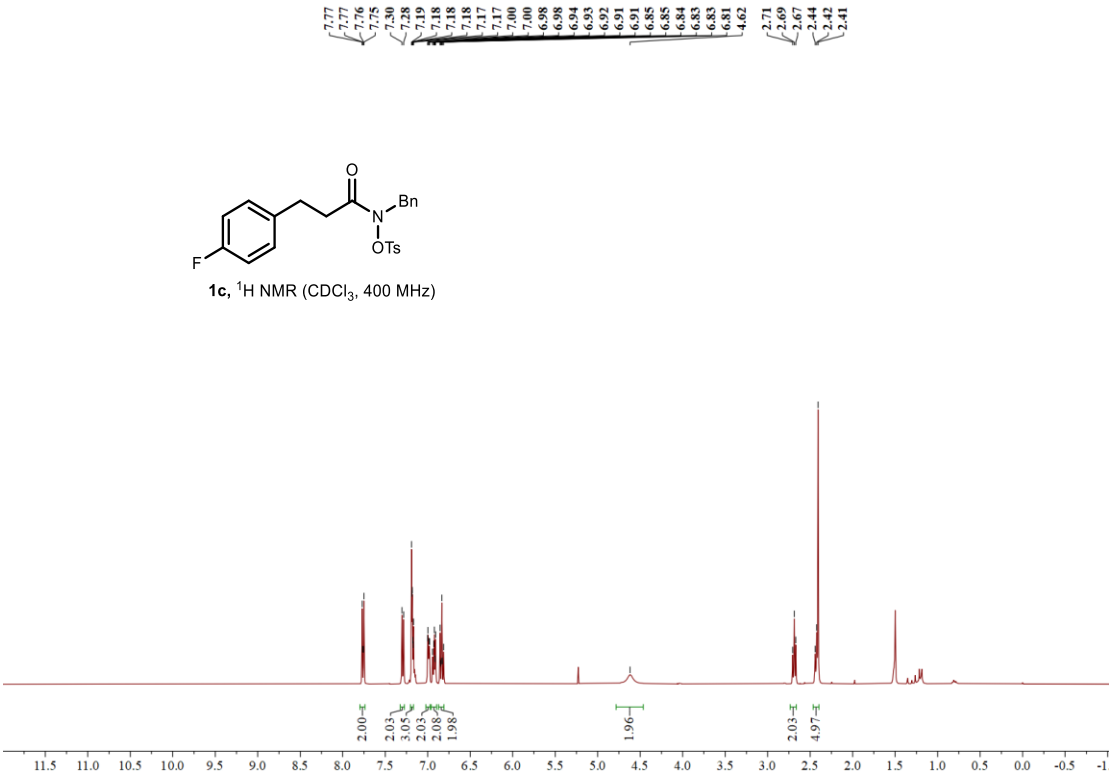


Figure S8. ^{1}H NMR of **1c** ($CDCl_3$, 400 MHz)

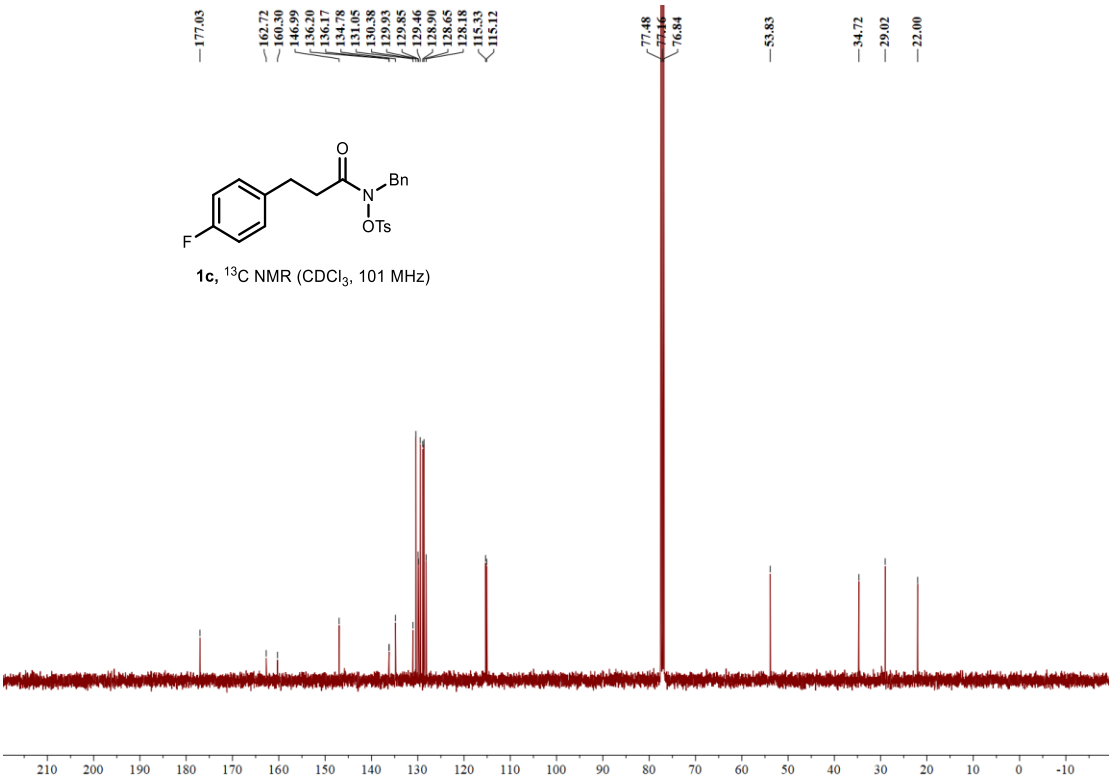


Figure S9. ^{13}C NMR of **1c** ($CDCl_3$, 101 MHz)

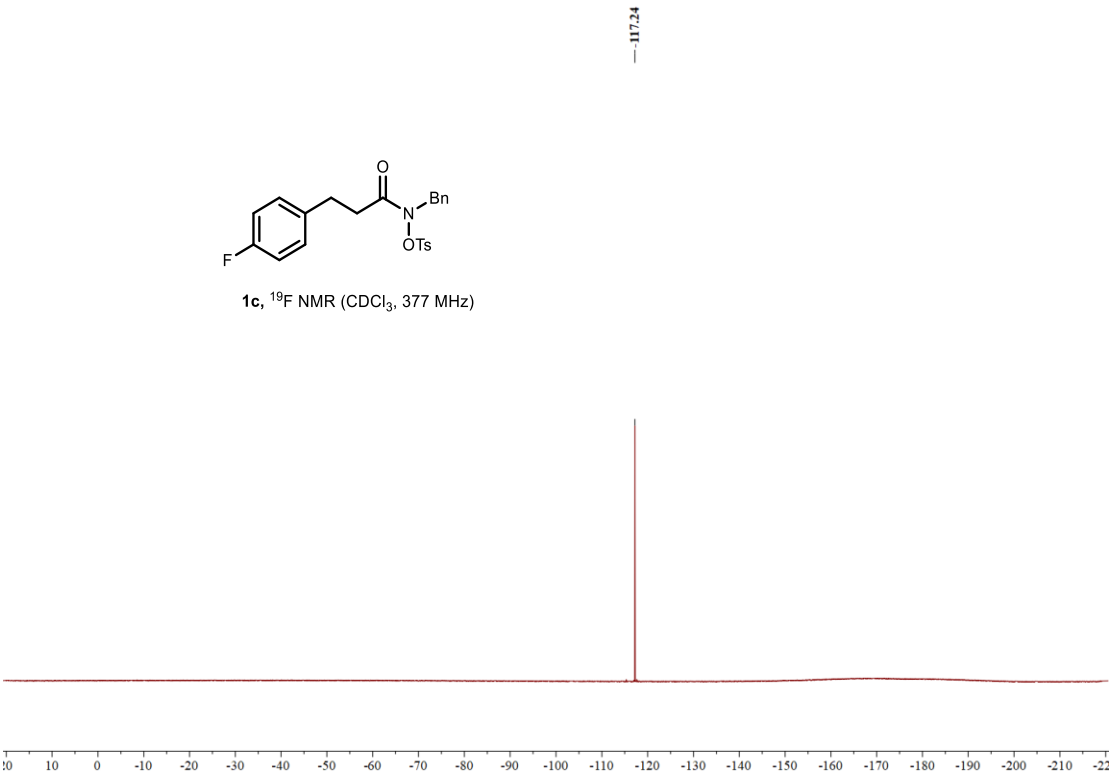


Figure S10. ^{19}F NMR of **1c** ($CDCl_3$, 377 MHz)

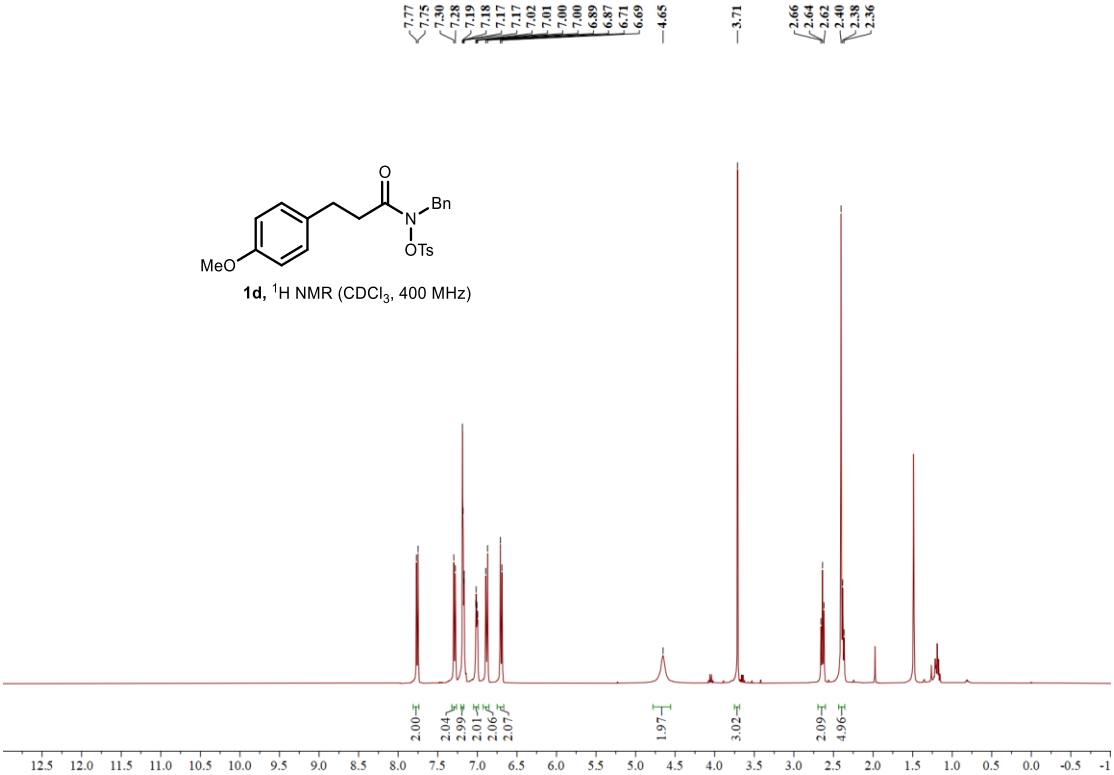


Figure S11. ^{1}H NMR of **1d** ($CDCl_3$, 400 MHz)

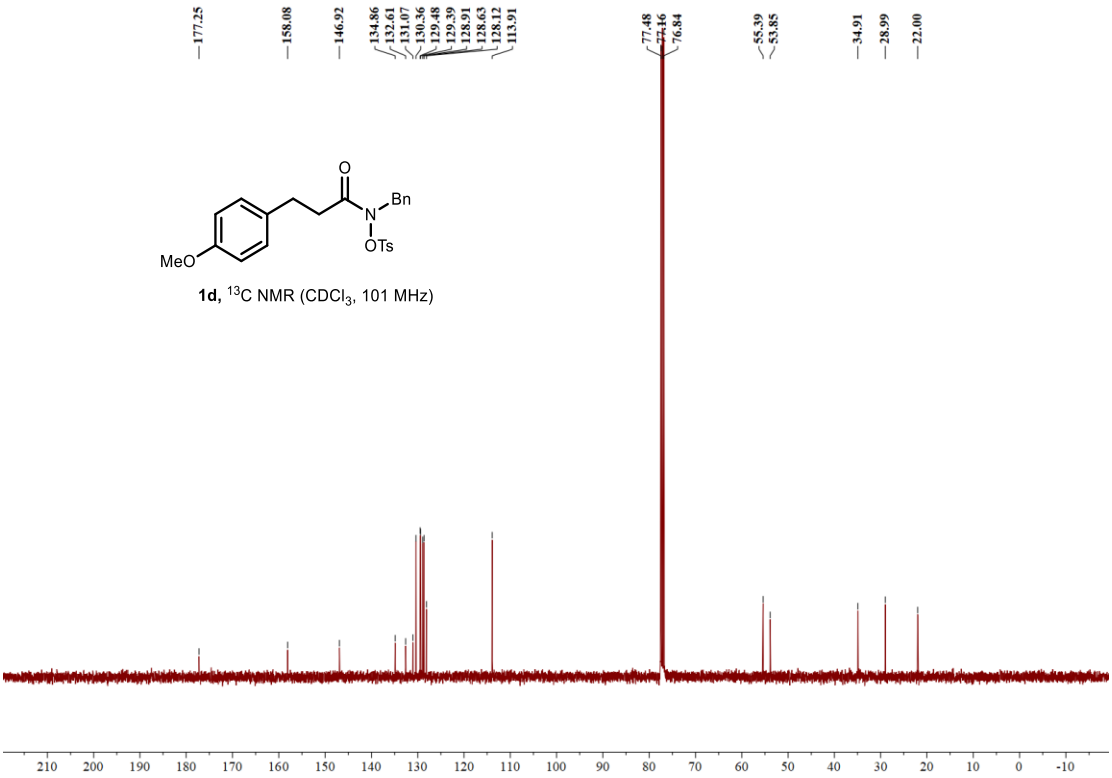


Figure S12. ^{13}C NMR of **1d** ($CDCl_3$, 101 MHz)

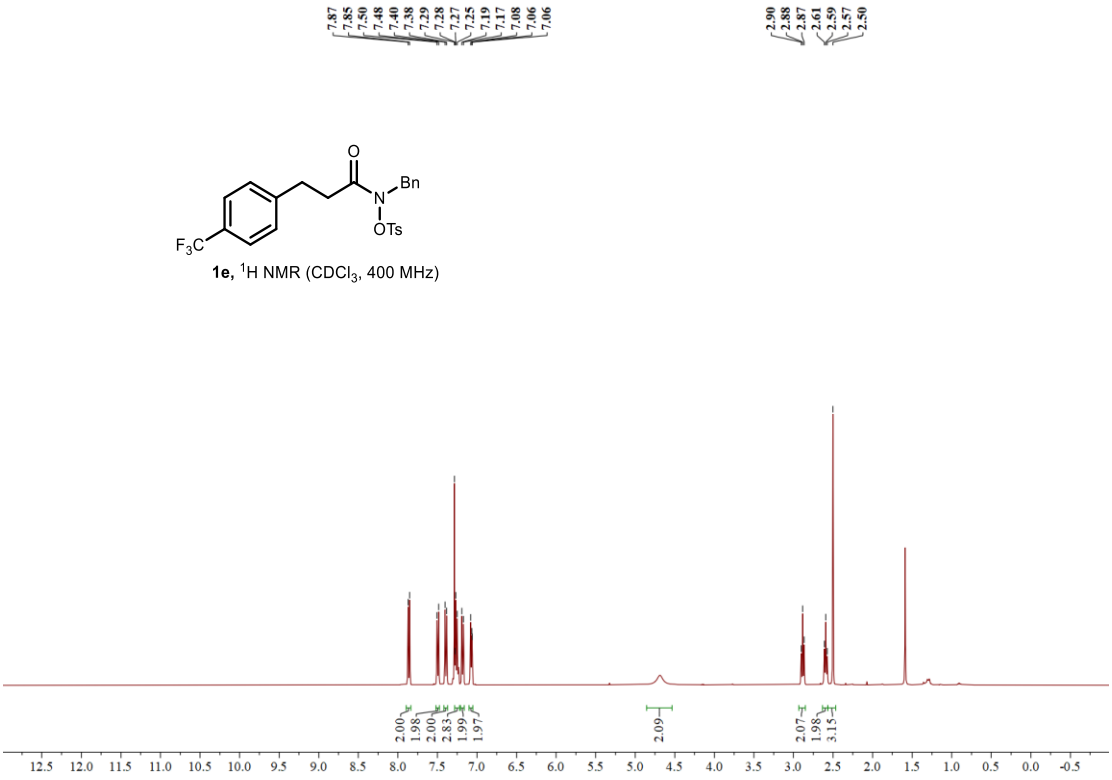


Figure S13. ^{1}H NMR of **1e** ($CDCl_3$, 400 MHz)

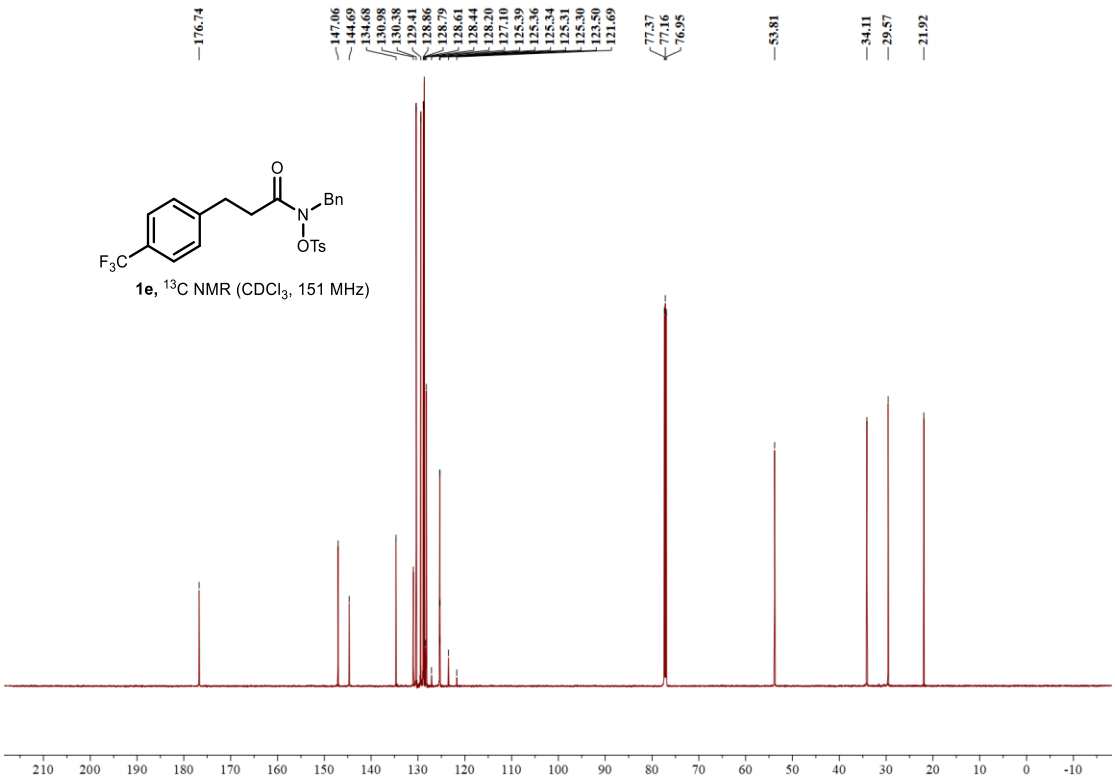


Figure S14. ^{13}C NMR of **1e** ($CDCl_3$, 151 MHz)

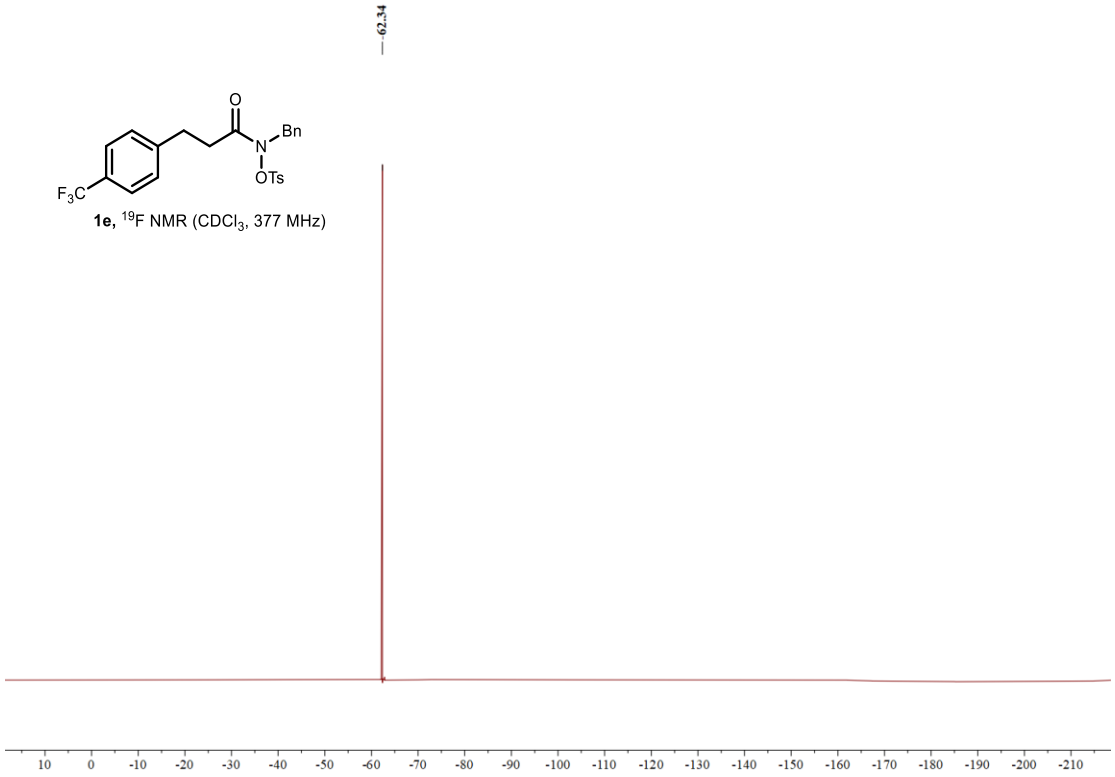


Figure S15. ^{19}F NMR of **1e** ($CDCl_3$, 377 MHz)

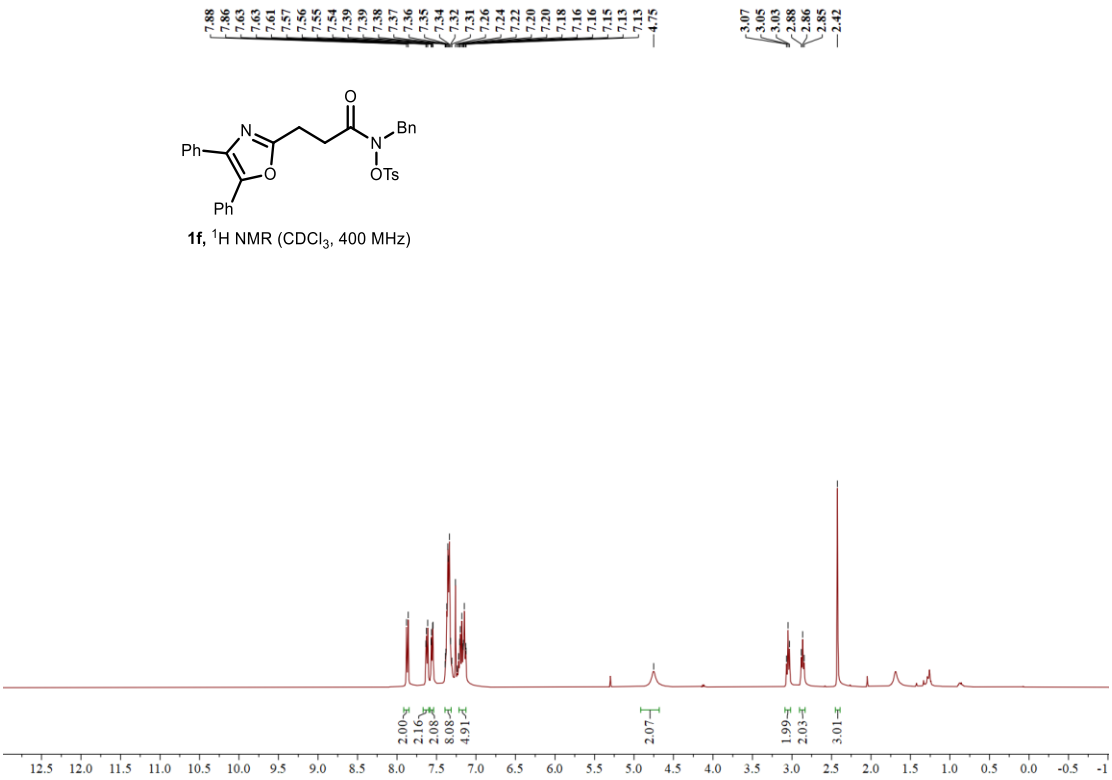


Figure S16. ^{1}H NMR of **1f** ($CDCl_3$, 400 MHz)

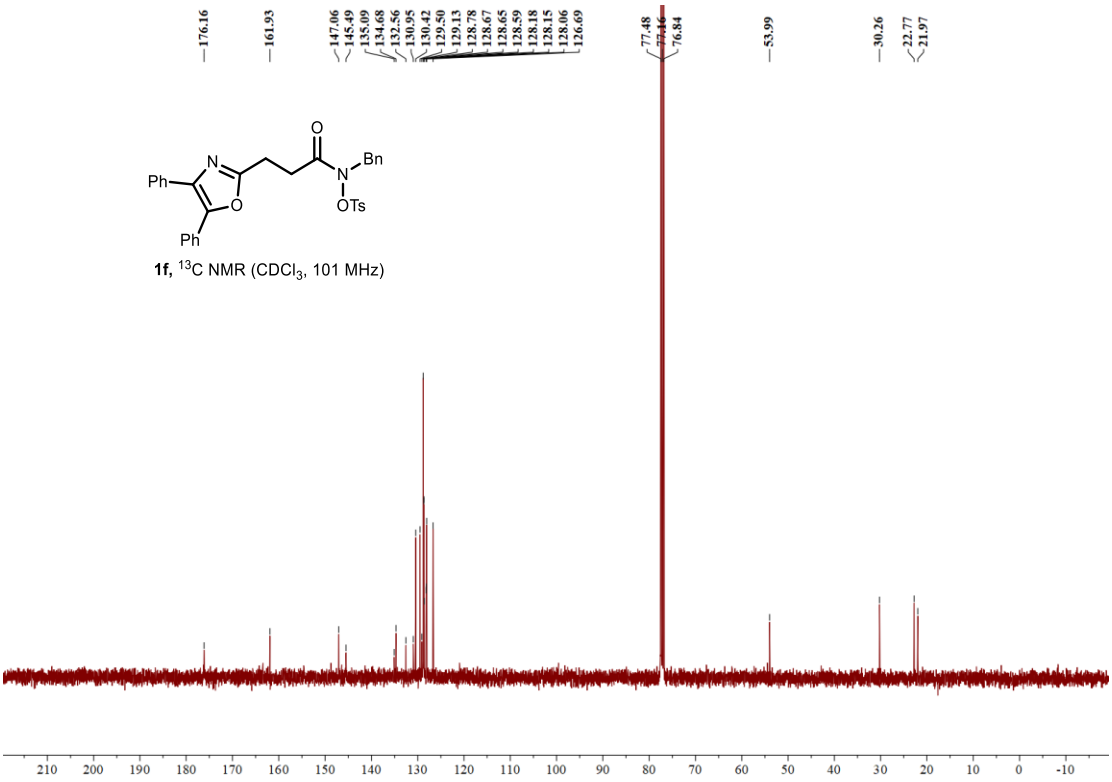


Figure S17. ^{13}C NMR of **1f** ($CDCl_3$, 101 MHz)

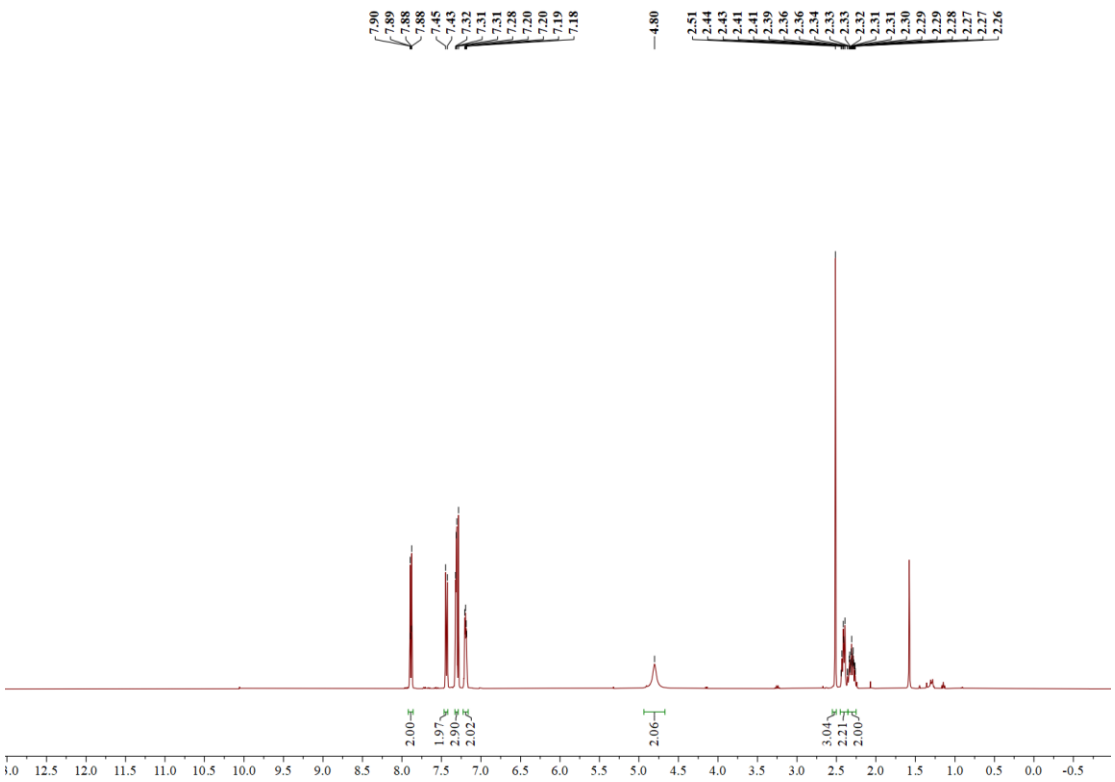


Figure S18. ^{1}H NMR of **1g** ($CDCl_3$, 400 MHz)

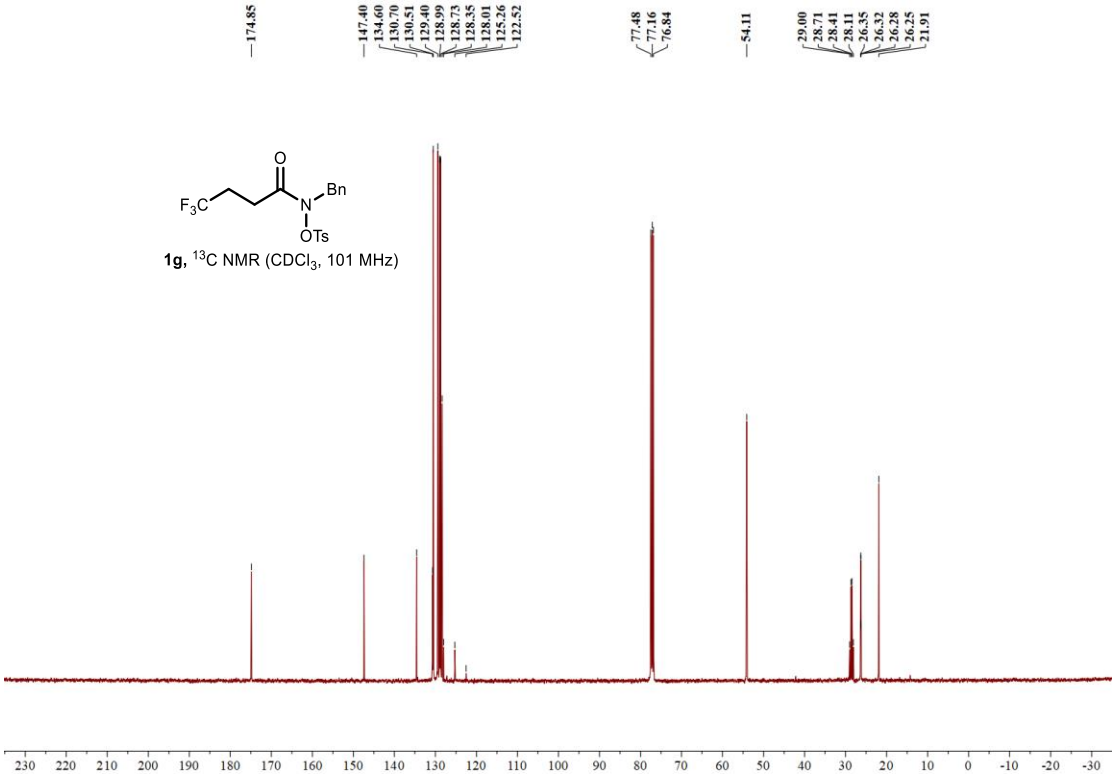


Figure S19. ^{13}C NMR of **1g** ($CDCl_3$, 101 MHz)

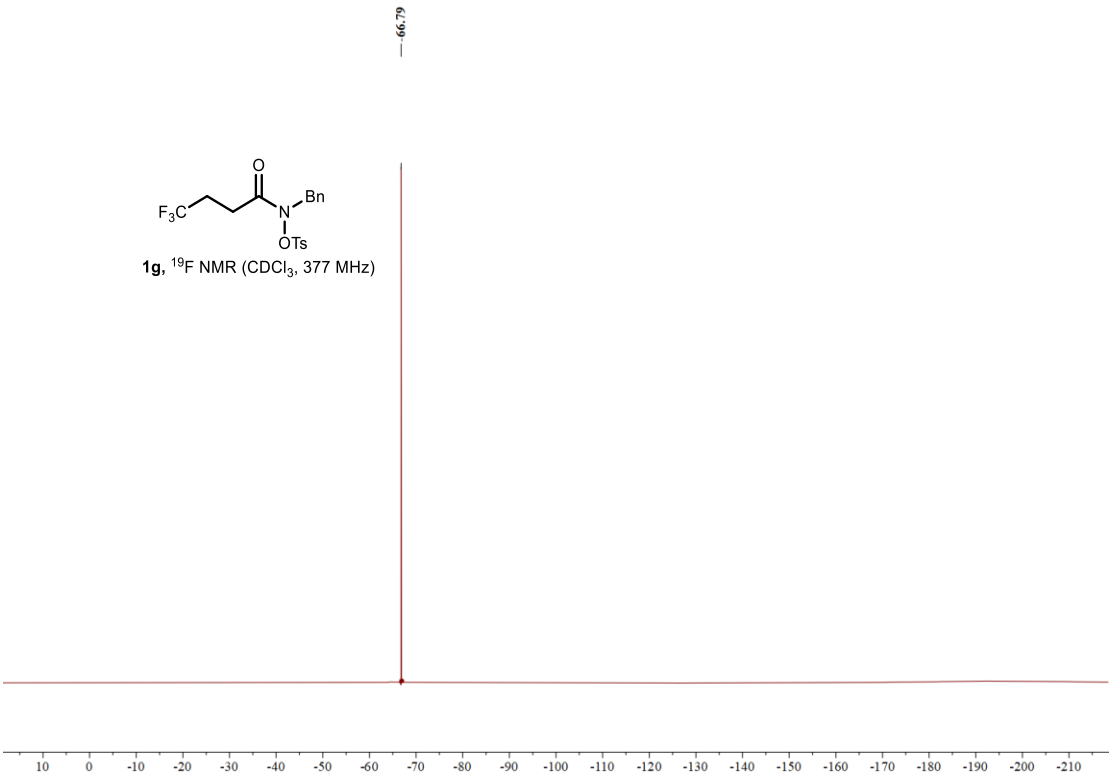


Figure S20. ^{19}F NMR of **1g** ($CDCl_3$, 377 MHz)

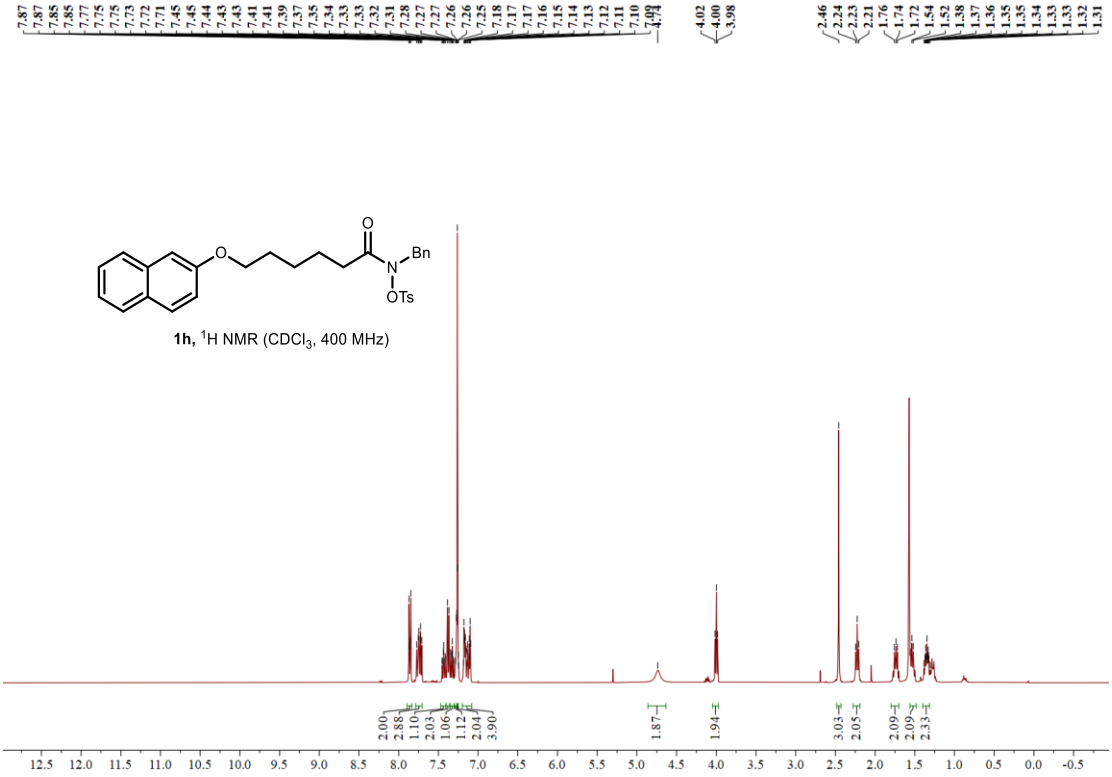


Figure S21. ^{1}H NMR of **1h** ($CDCl_3$, 400 MHz)

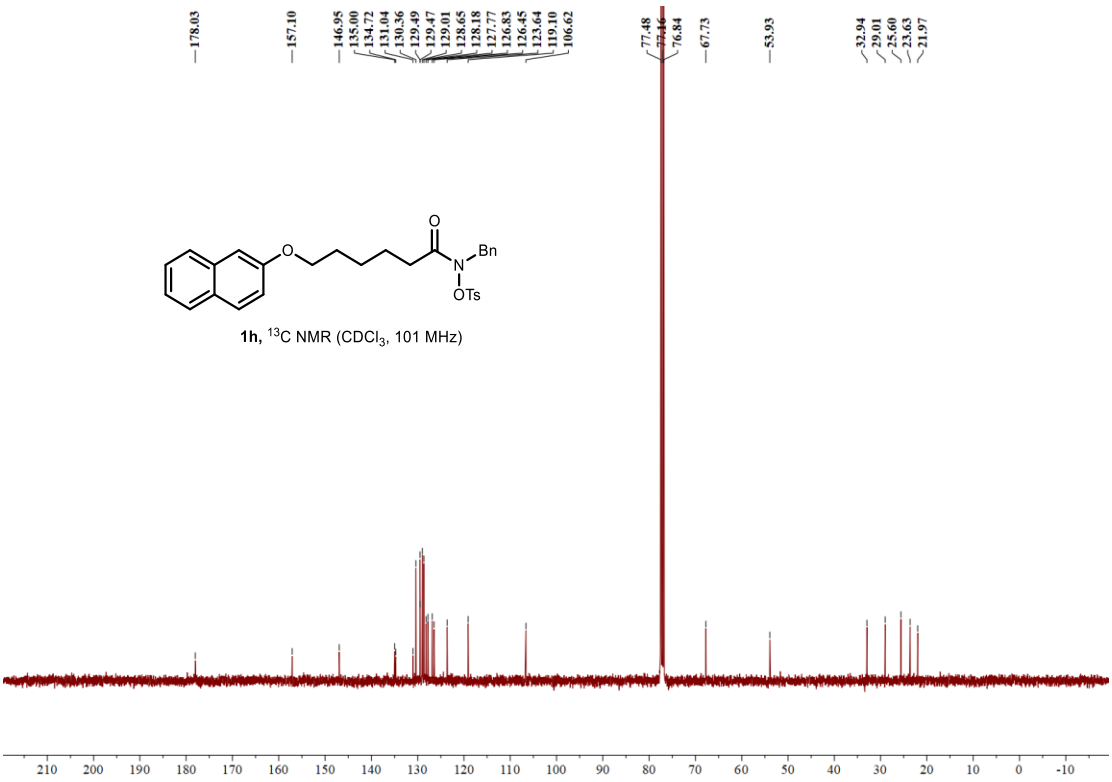


Figure S22. ^{13}C NMR of **1h** ($CDCl_3$, 101 MHz)

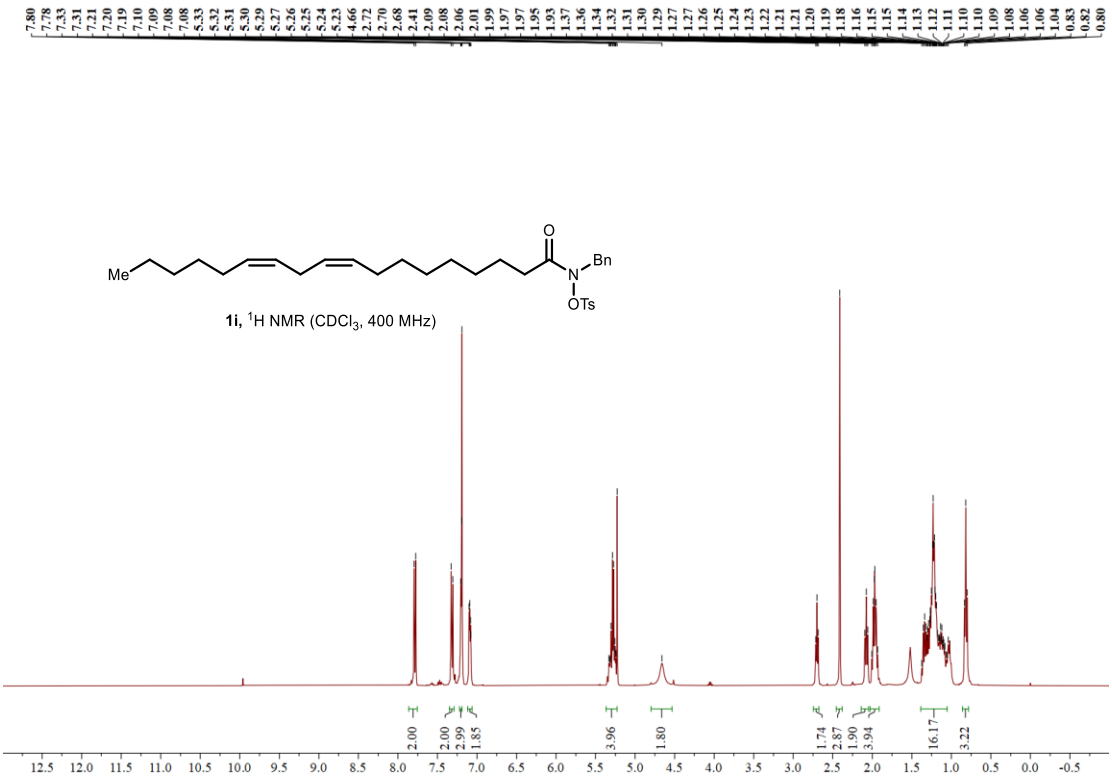


Figure S23. ^{1}H NMR of **1i** ($CDCl_3$, 400 MHz)

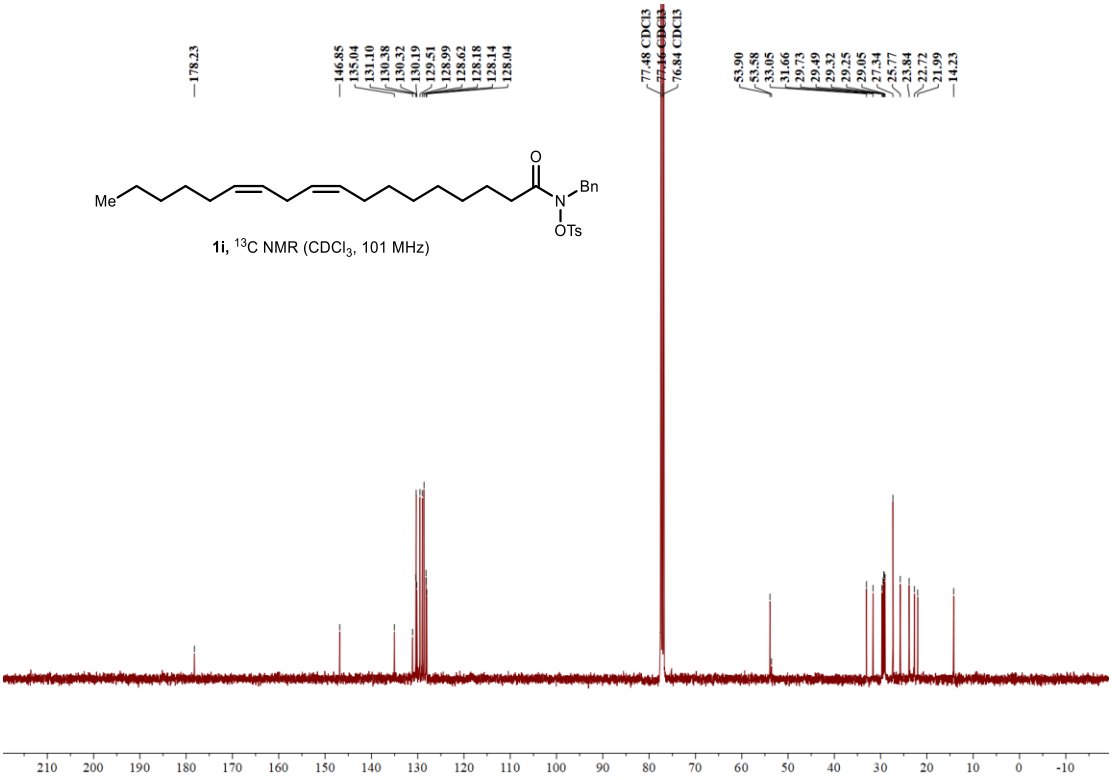


Figure S24. ^{13}C NMR of **1i** ($CDCl_3$, 101 MHz)

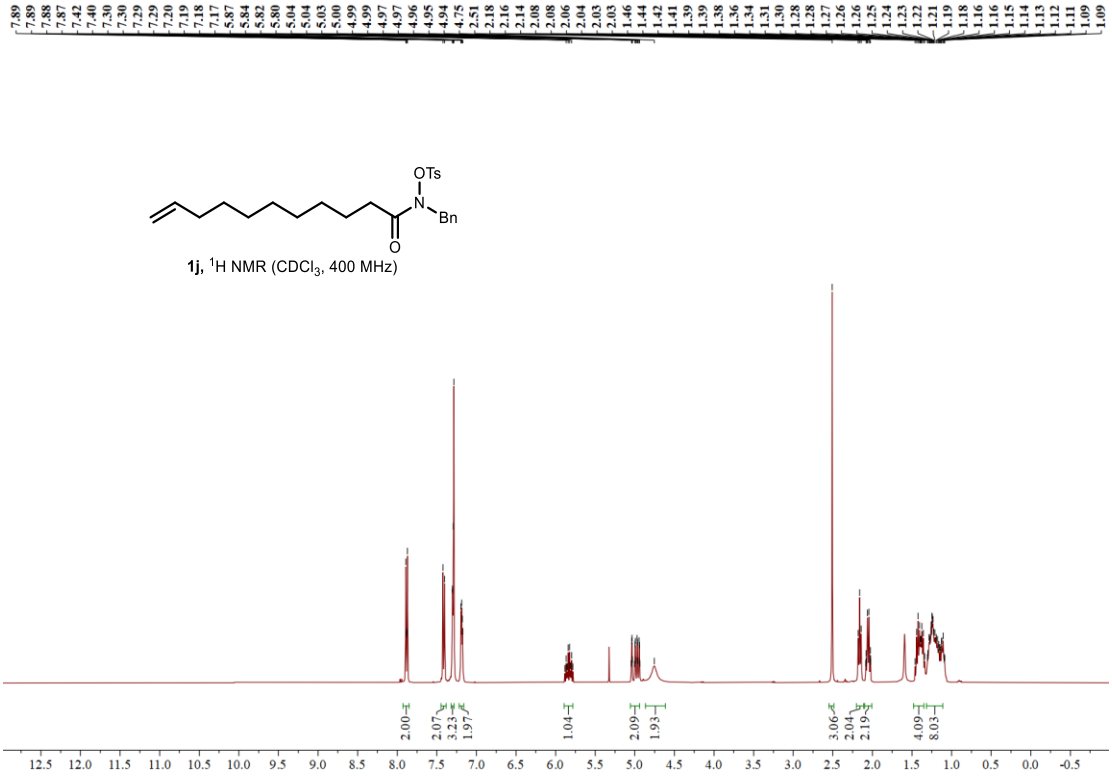


Figure S25. ^{1}H NMR of **1j** ($CDCl_3$, 400 MHz)

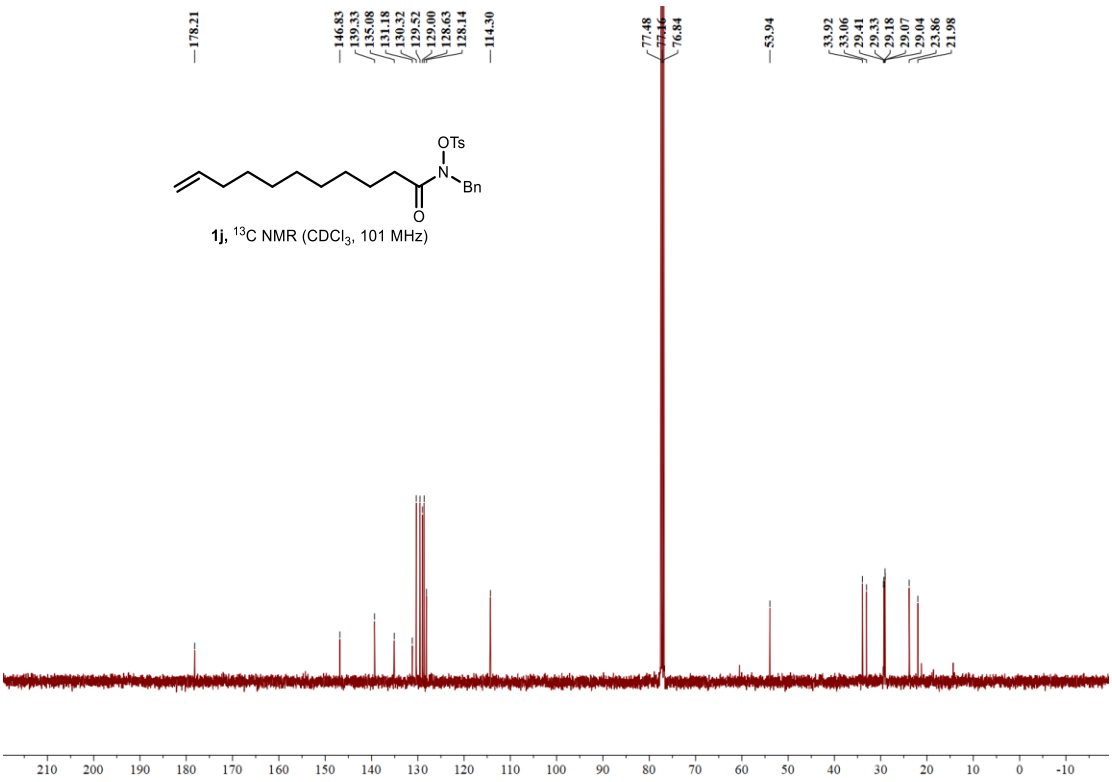


Figure S26. ^{13}C NMR of **1j** ($CDCl_3$, 101 MHz)

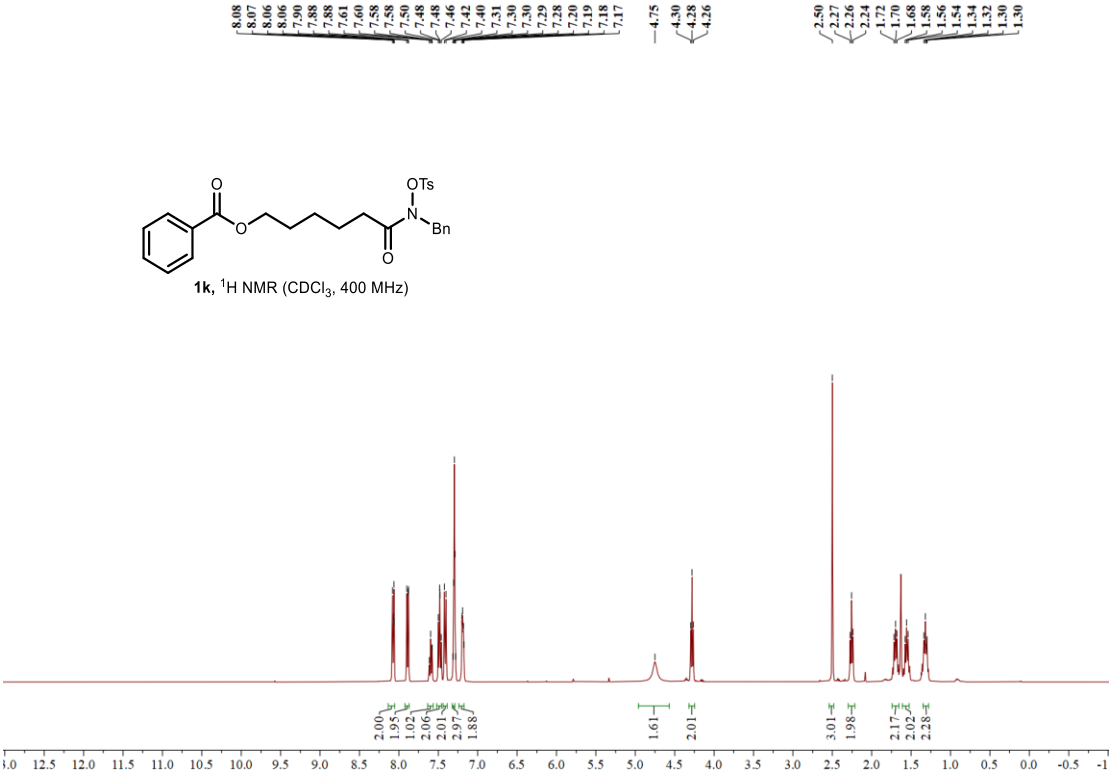


Figure S27. ^{1}H NMR of **1k** ($CDCl_3$, 400 MHz)

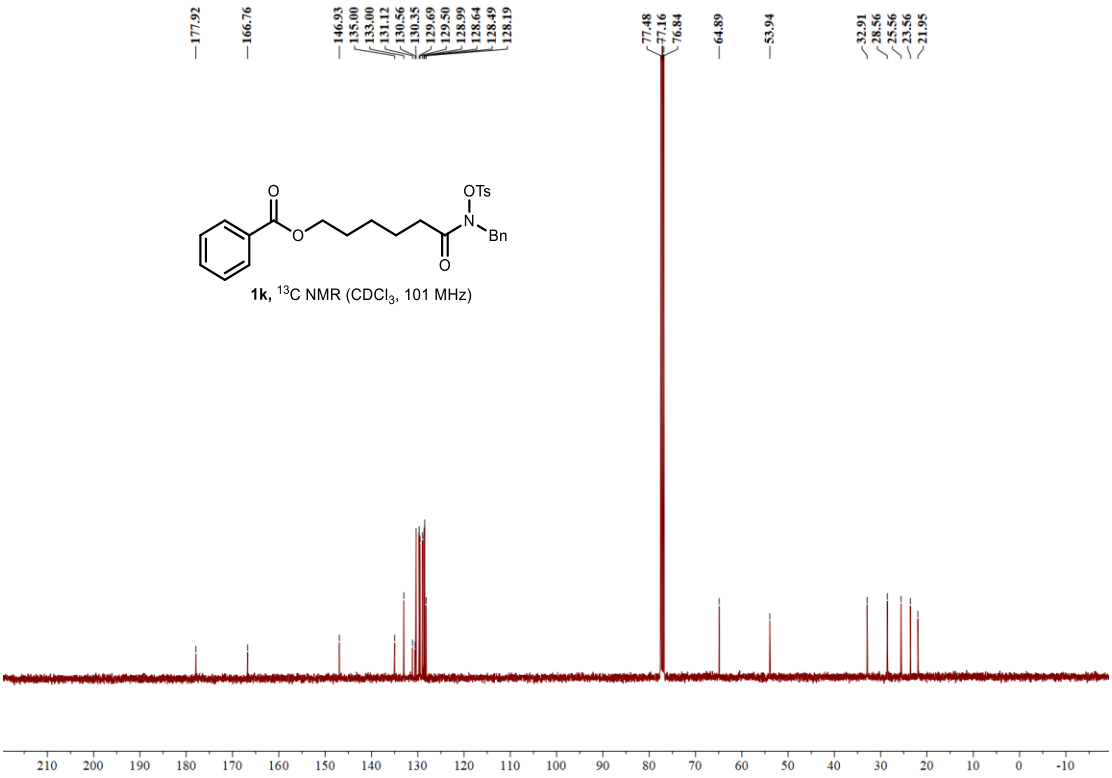


Figure S28. ^{13}C NMR of **1k** ($CDCl_3$, 101 MHz)

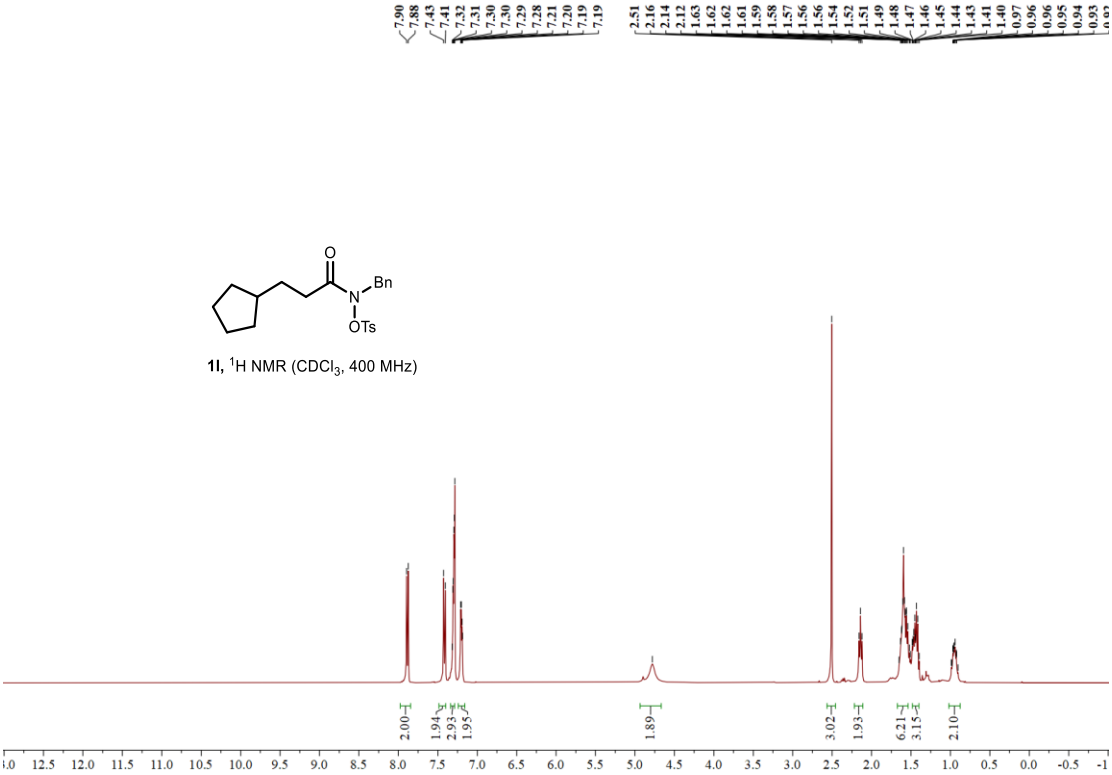


Figure S29. ^{1}H NMR of **1l** ($CDCl_3$, 400 MHz)

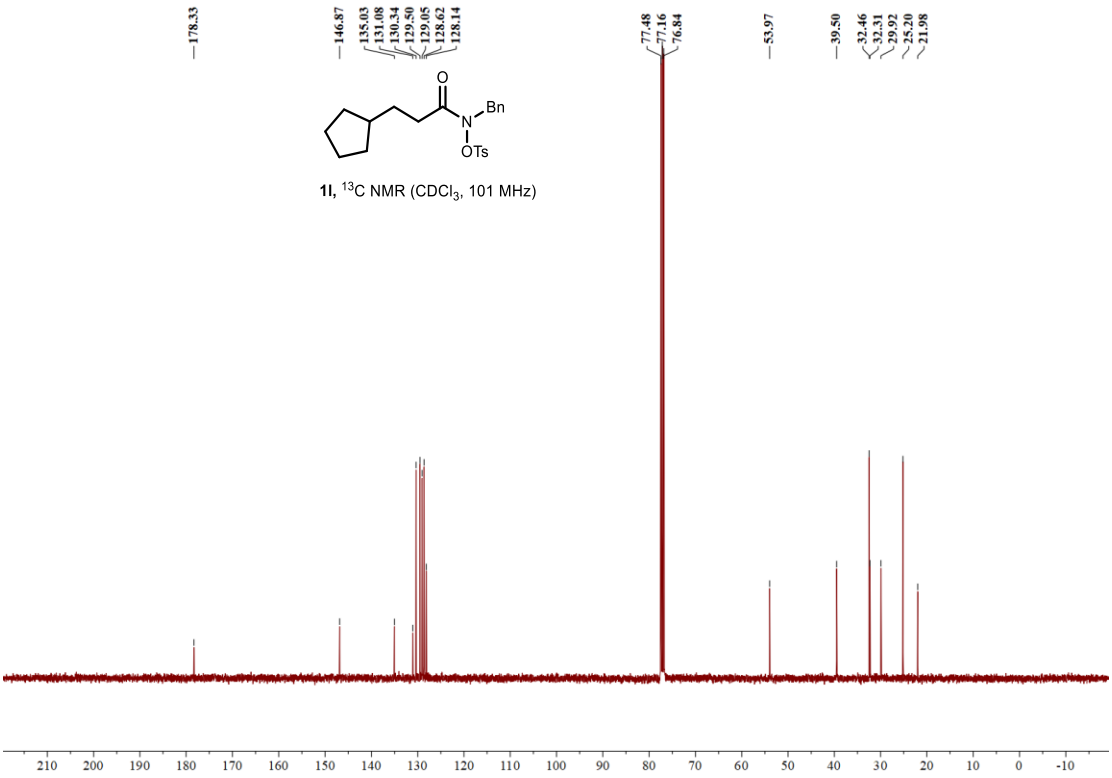


Figure S30. ^{13}C NMR of **1l** ($CDCl_3$, 101 MHz)

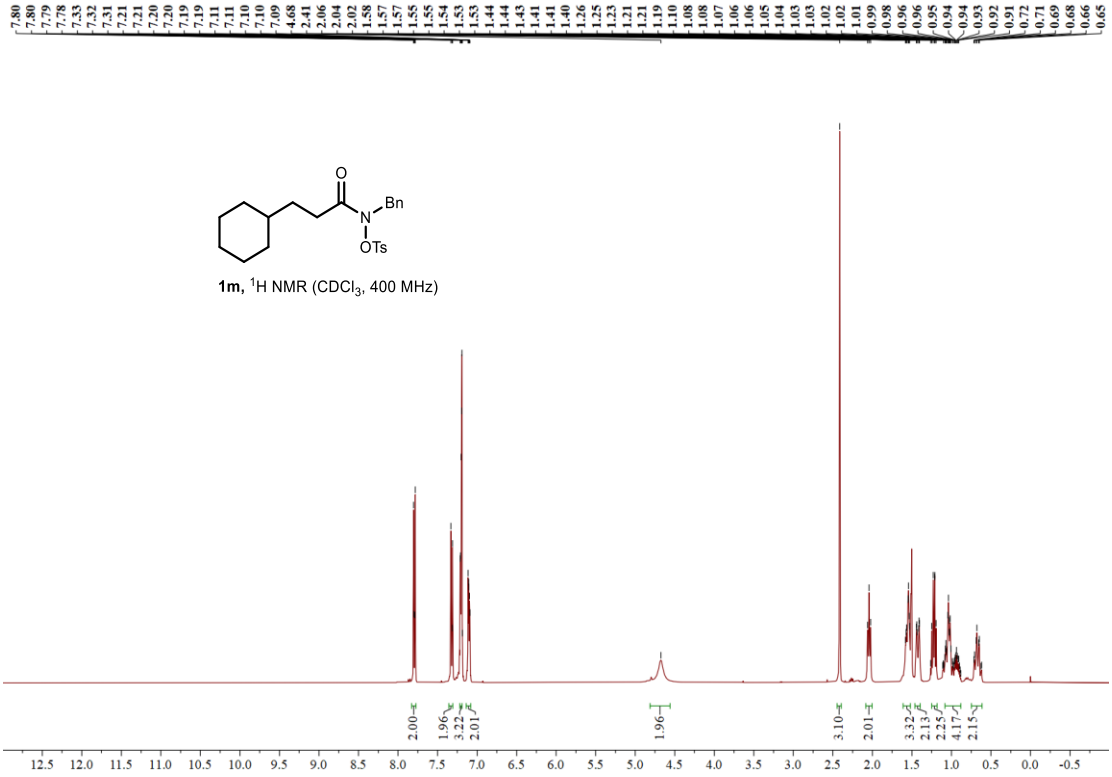


Figure S31. ^{1}H NMR of **1m** ($CDCl_3$, 400 MHz)

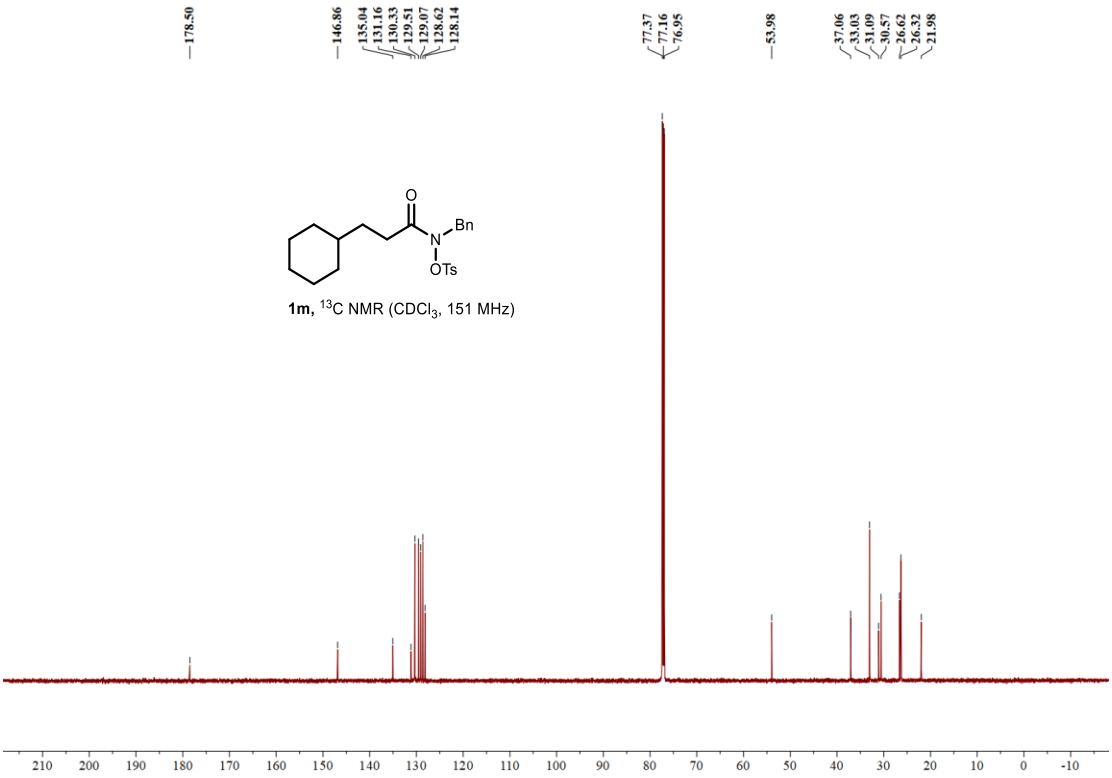


Figure S32. ^{13}C NMR of **1m** ($CDCl_3$, 151 MHz)

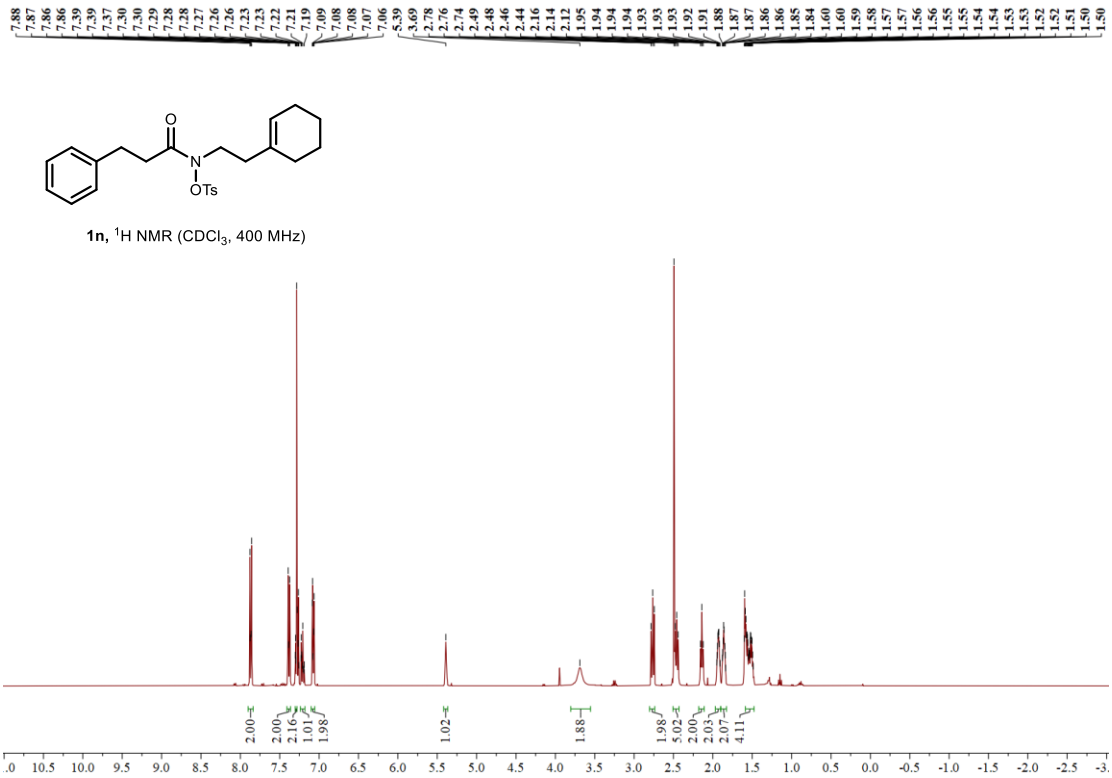


Figure S33. ^{1}H NMR of **1n** ($CDCl_3$, 400 MHz)

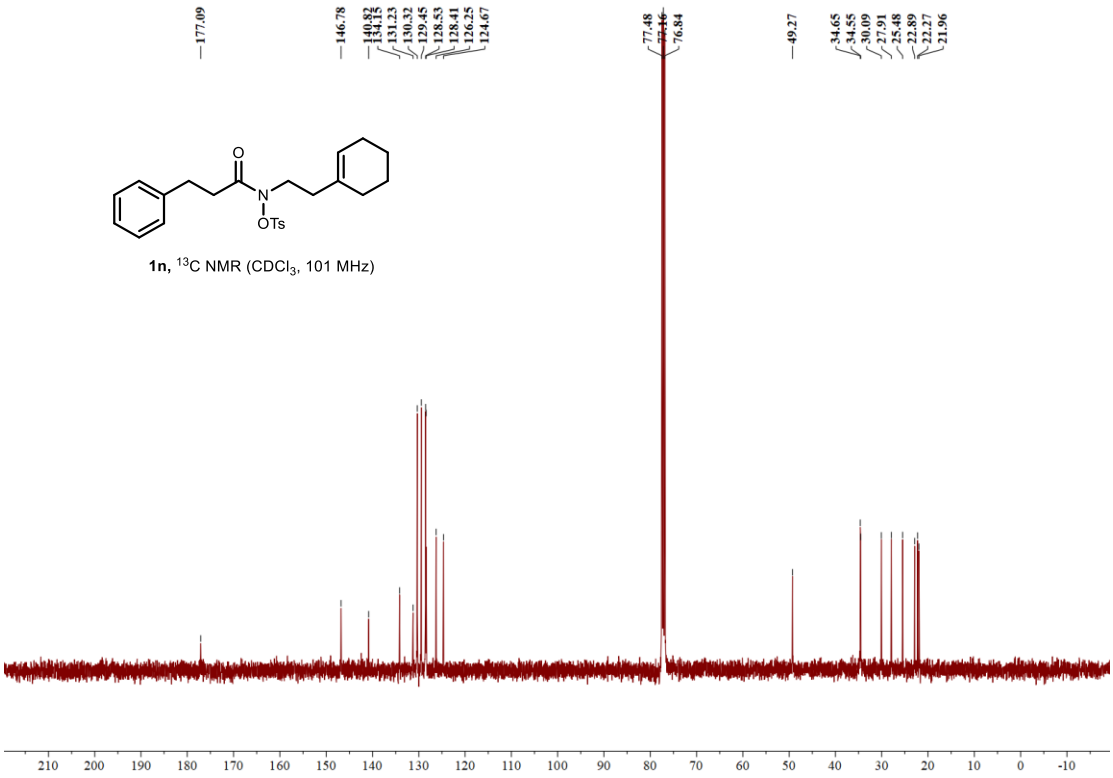


Figure S34. ^{13}C NMR of **1n** ($CDCl_3$, 101 MHz)

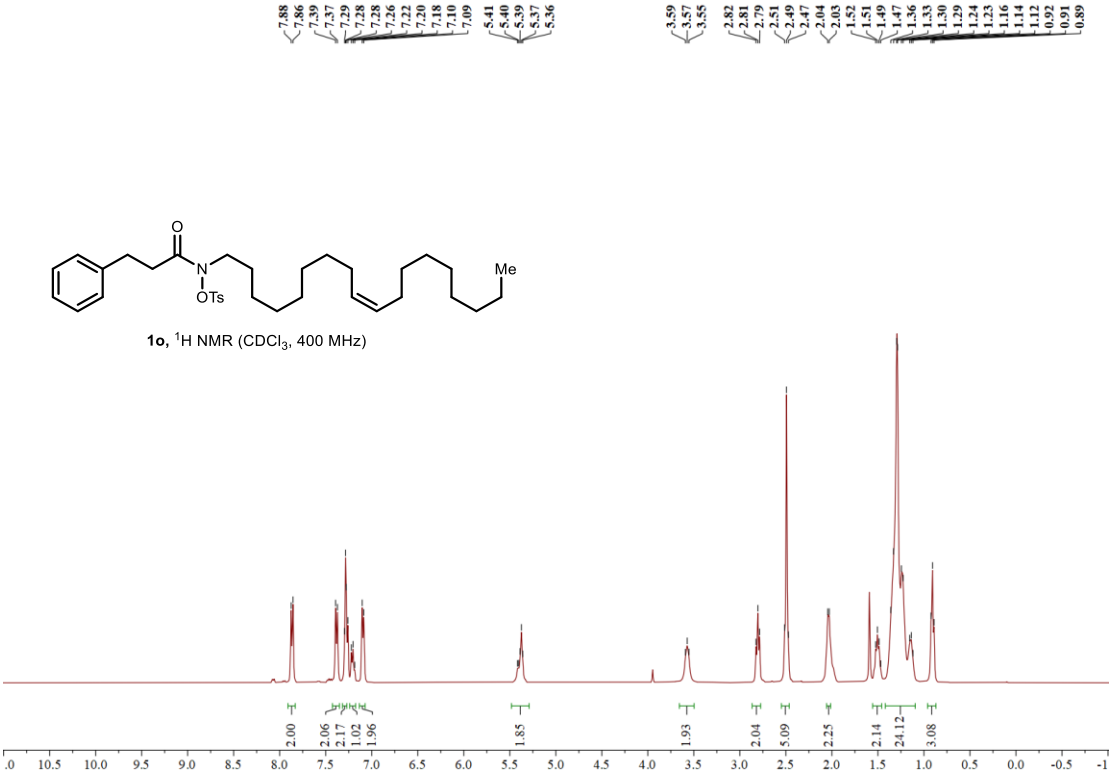


Figure S35. ^{1}H NMR of **1o** ($CDCl_3$, 400 MHz)

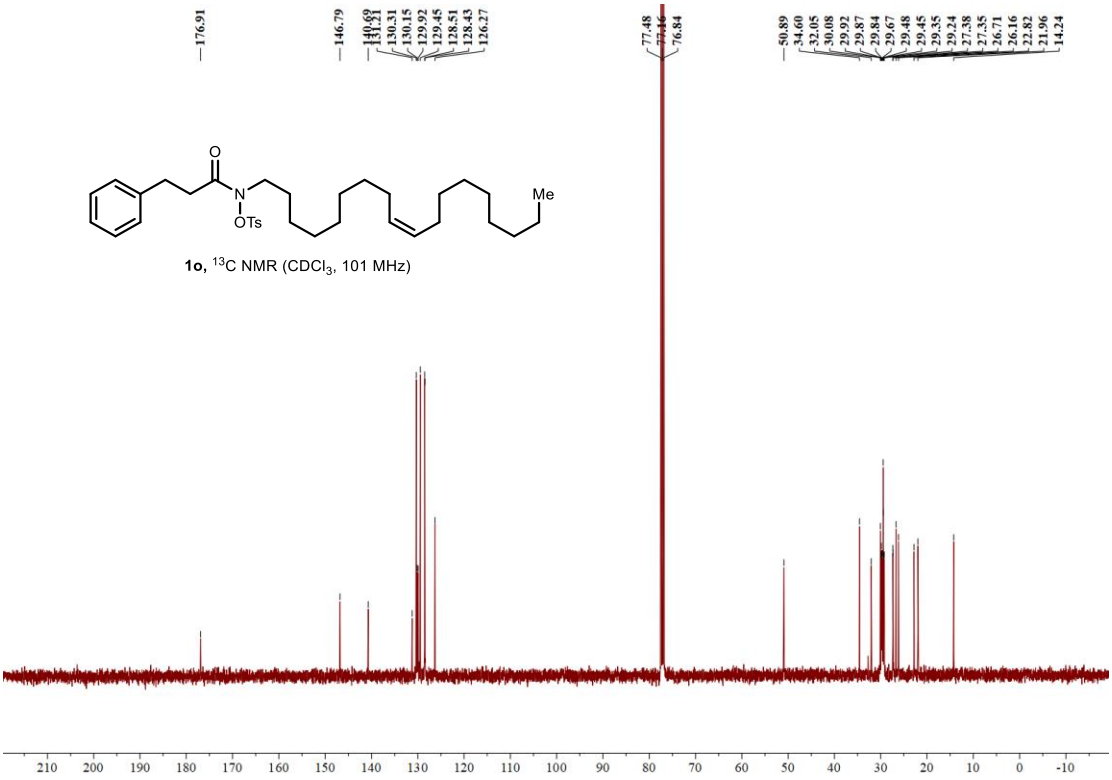


Figure S36. ^{13}C NMR of **1o** ($CDCl_3$, 101 MHz)

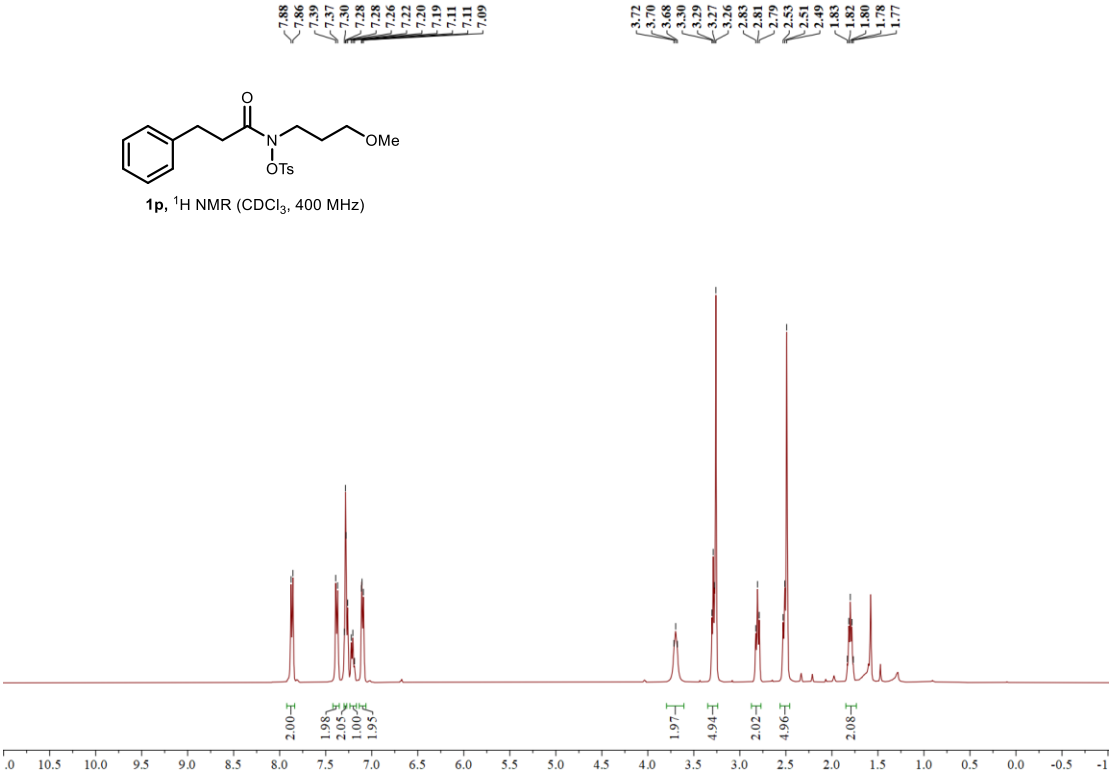


Figure S37. ^{1}H NMR of **1p** ($CDCl_3$, 400 MHz)

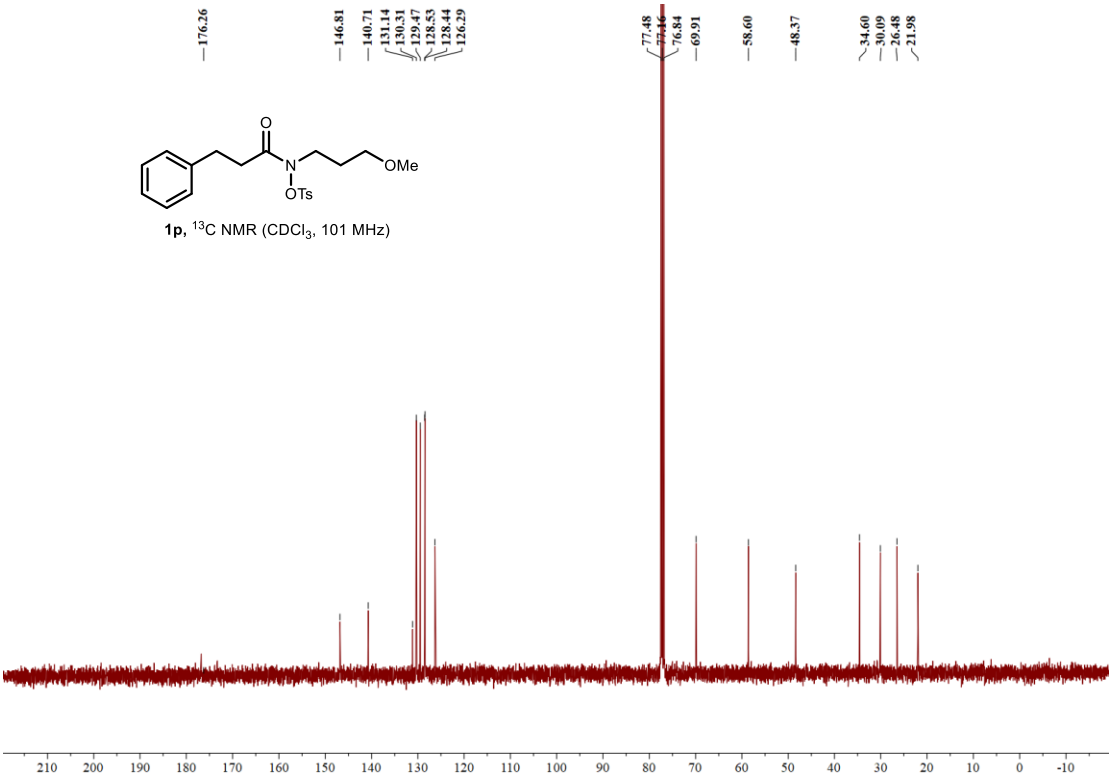


Figure S38. ^{13}C NMR of **1p** ($CDCl_3$, 101 MHz)

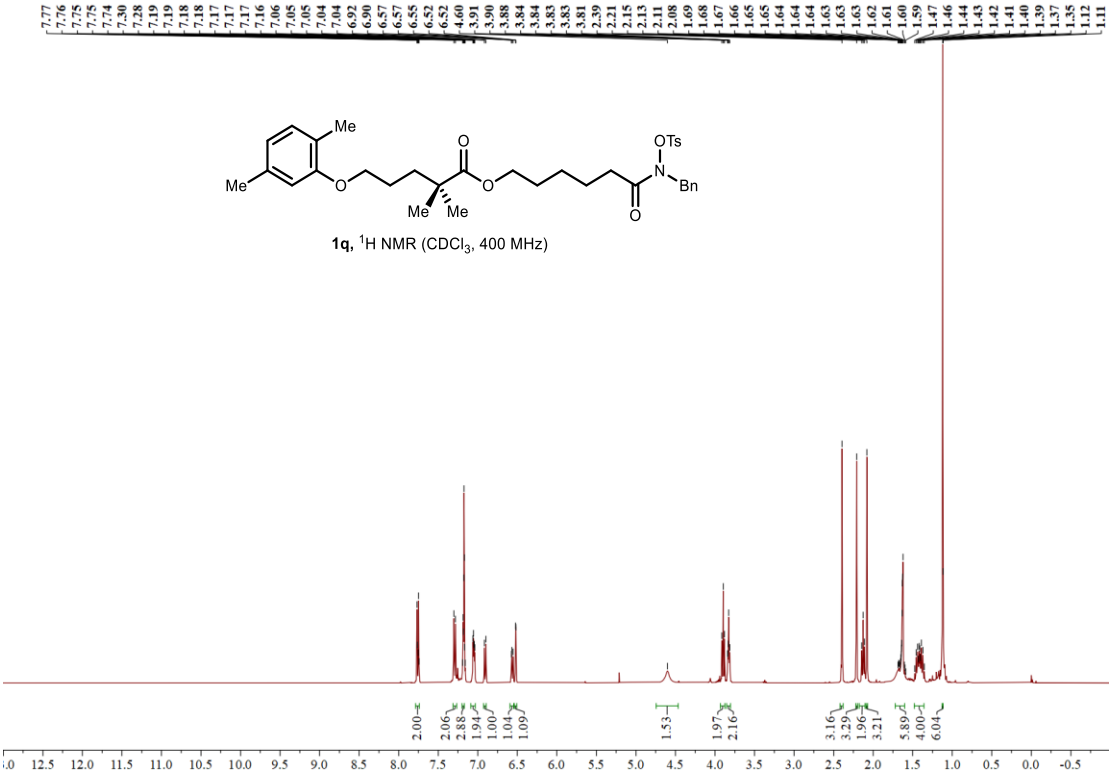


Figure S39. ^{1}H NMR of **1q** ($CDCl_3$, 400 MHz)

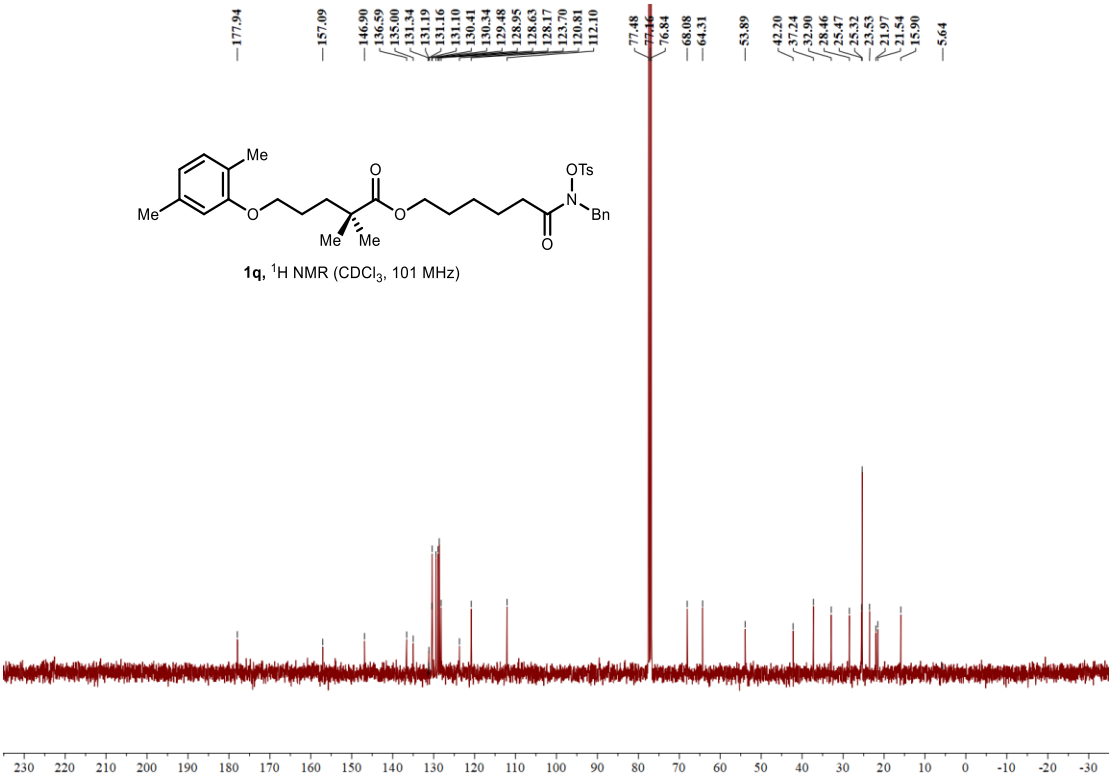


Figure S40. ^{13}C NMR of **1q** ($CDCl_3$, 101 MHz)

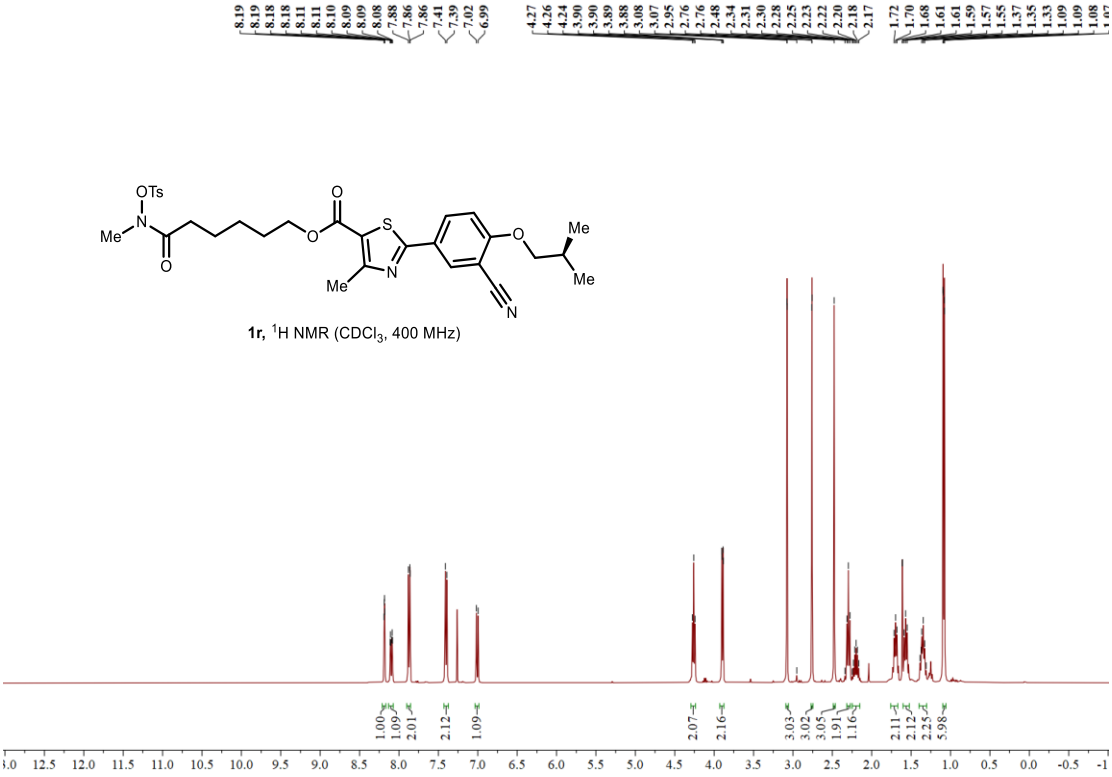


Figure S41. ^{1}H NMR of **1r** ($CDCl_3$, 400 MHz)

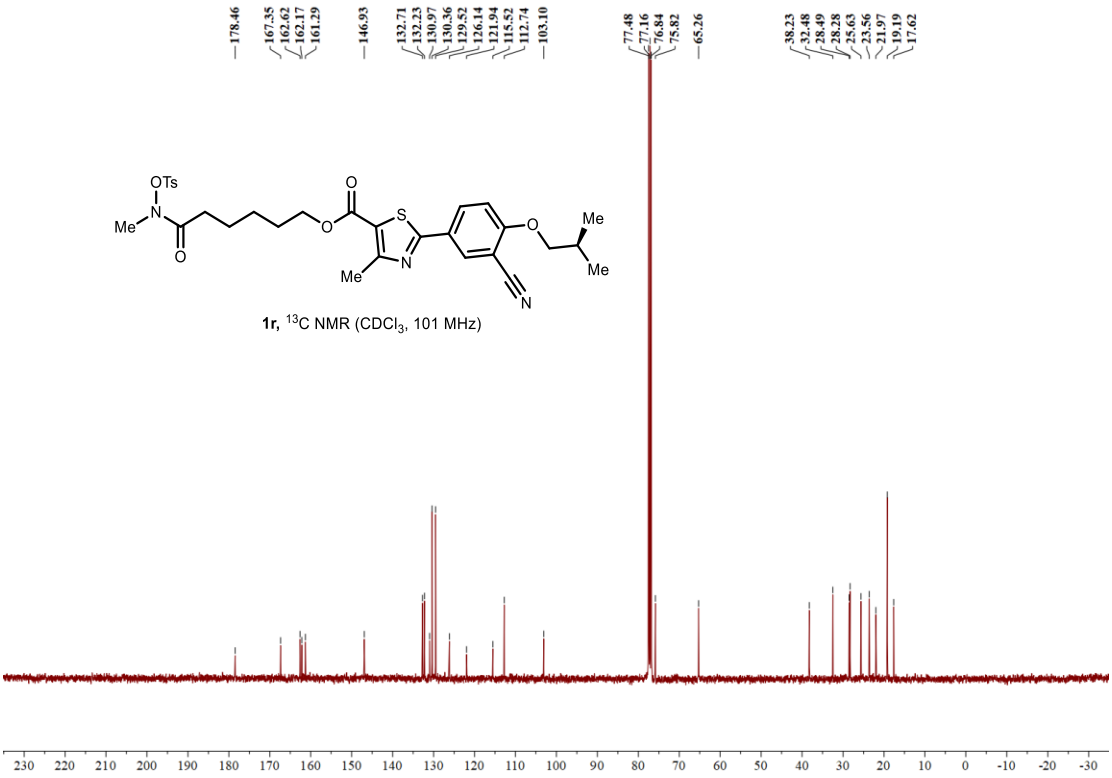


Figure S42. ^{13}C NMR of **1r** ($CDCl_3$, 101 MHz)

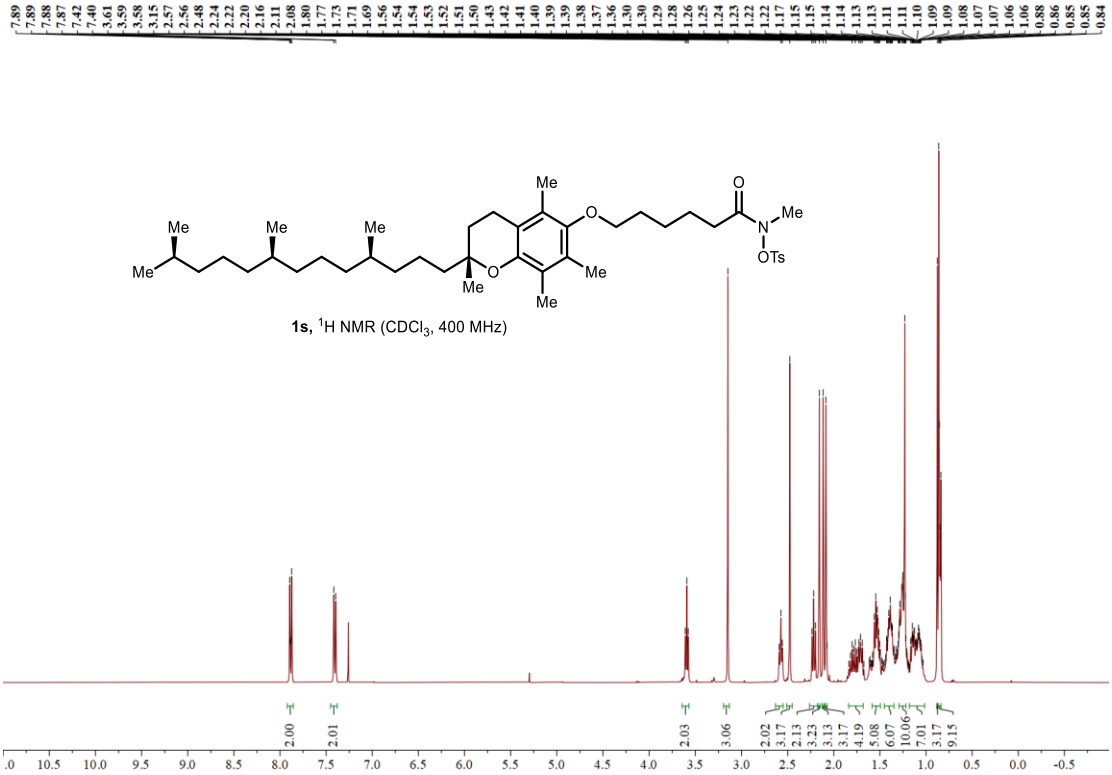


Figure S43. ^{1}H NMR of **1s** ($CDCl_3$, 400 MHz)

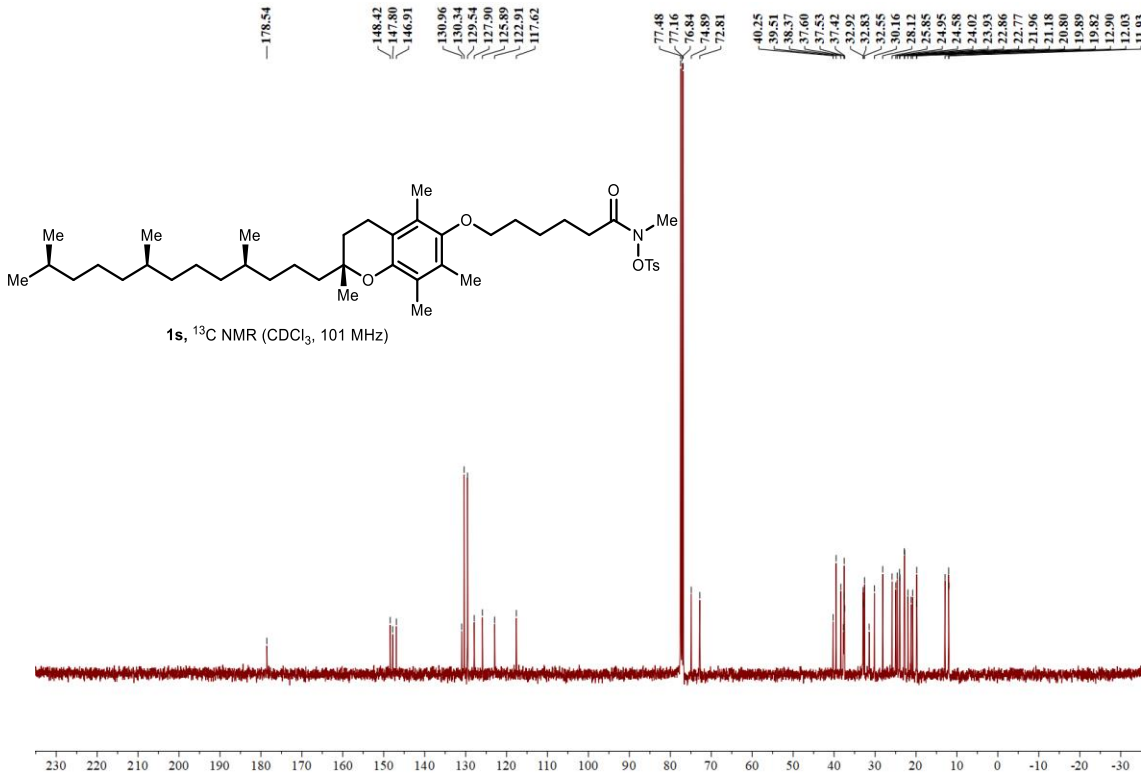


Figure S44. ^{13}C NMR of **1s** ($CDCl_3$, 101 MHz)

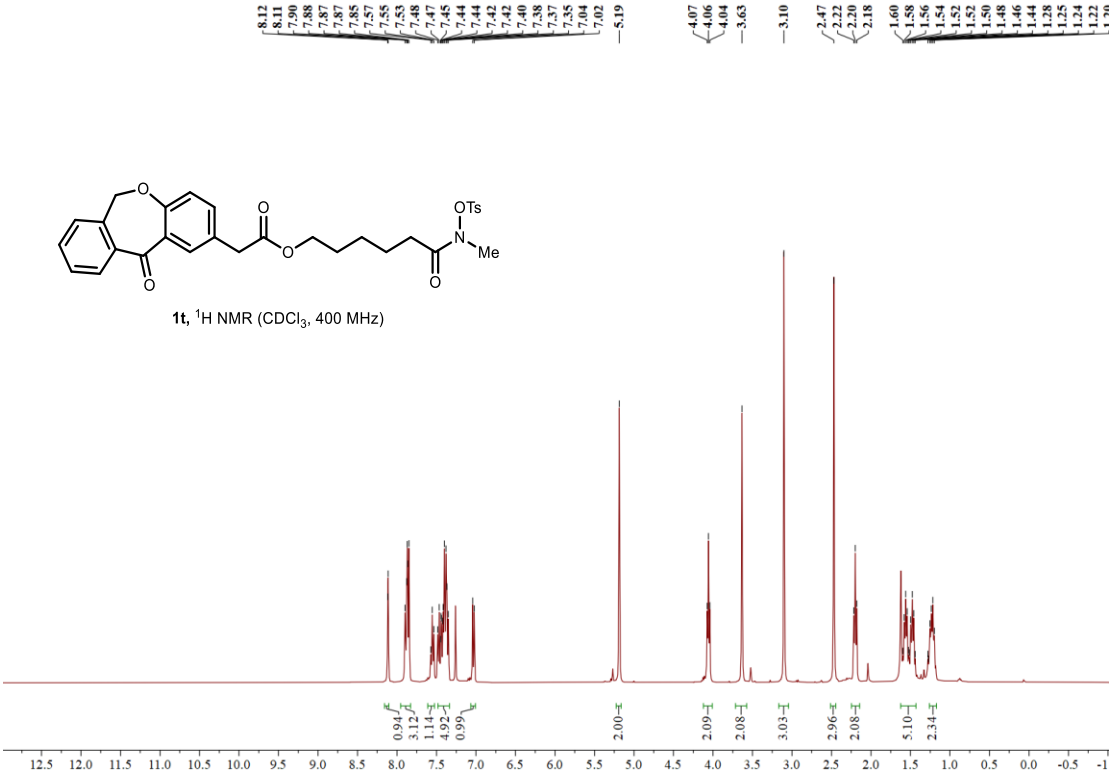


Figure S45. ^{1}H NMR of **1t** ($CDCl_3$, 400 MHz)

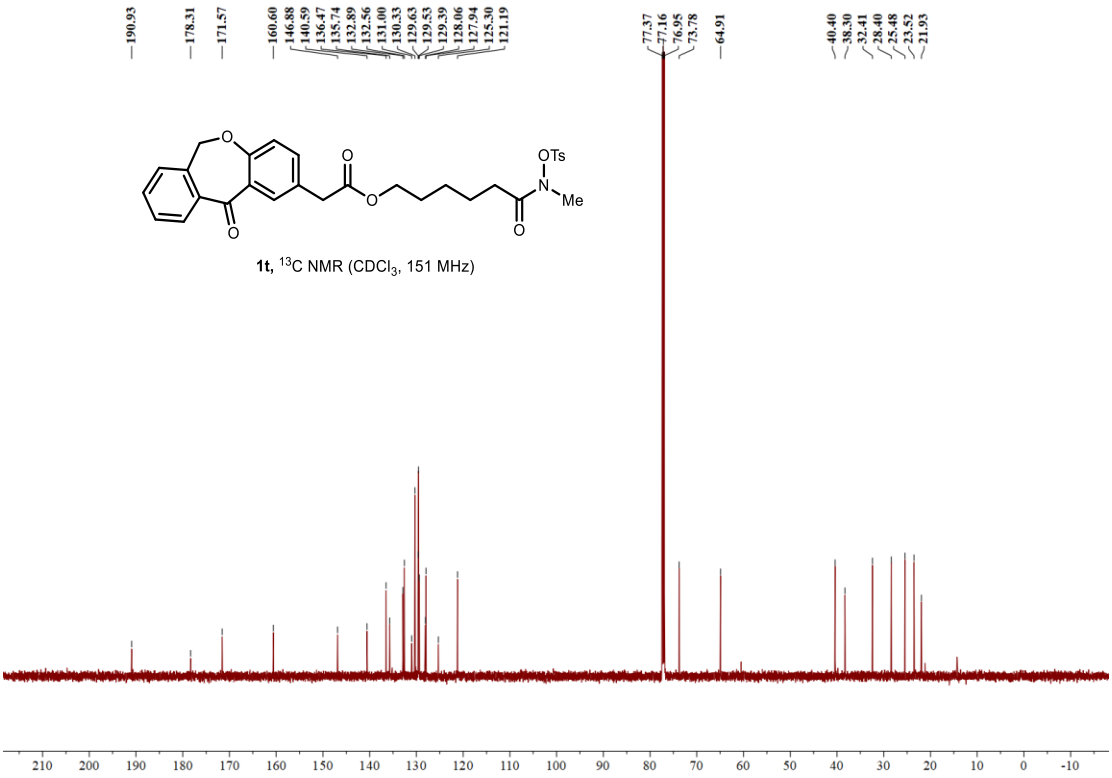


Figure S46. ^{13}C NMR of **1t** ($CDCl_3$, 151 MHz)

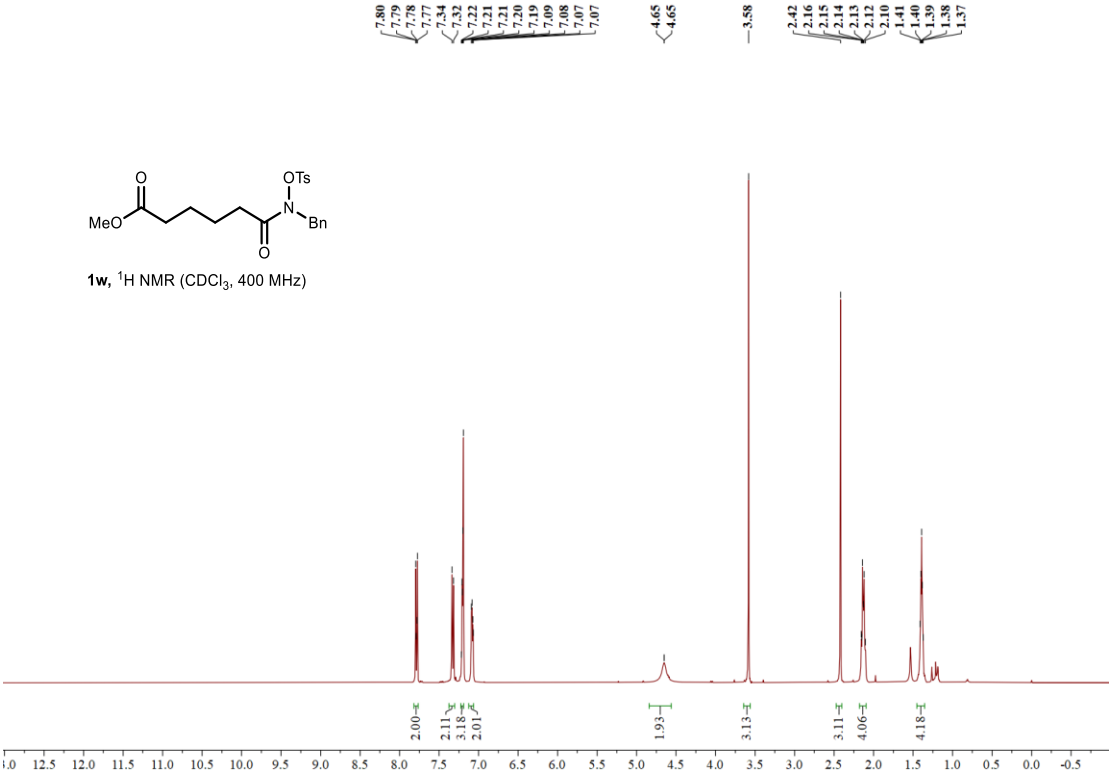


Figure S47. ^{1}H NMR of **1w** ($CDCl_3$, 400 MHz)

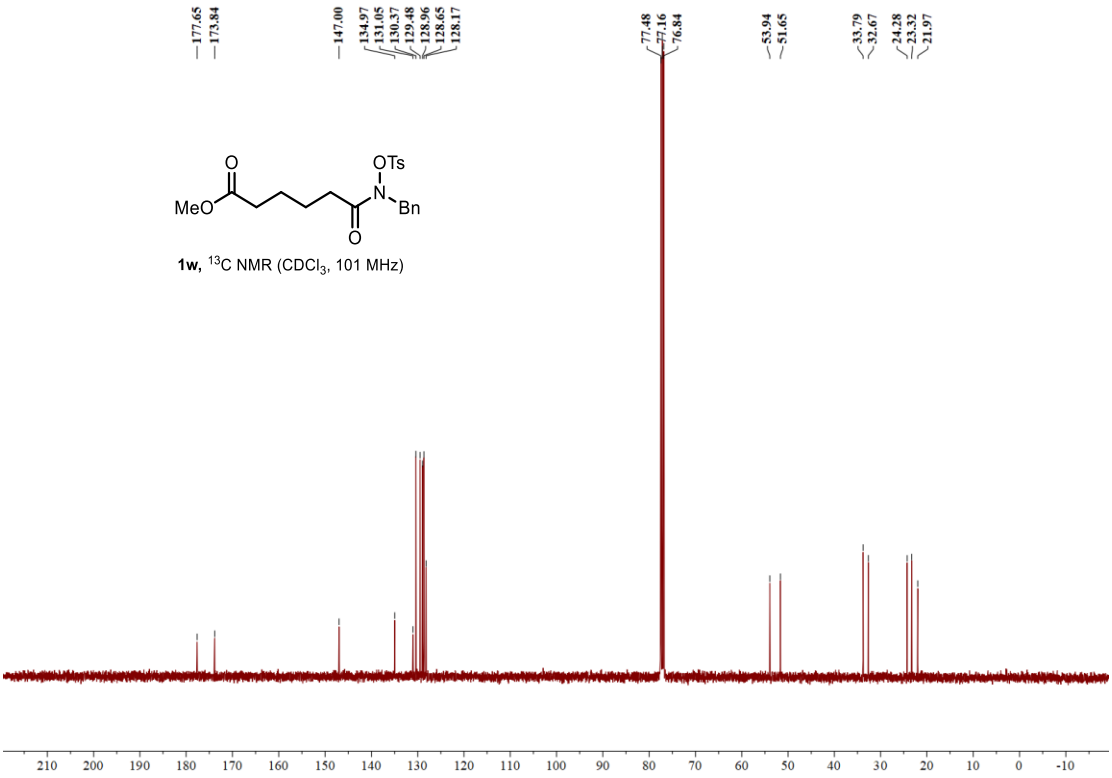


Figure S48. ^{13}C NMR of **1w** ($CDCl_3$, 101 MHz)

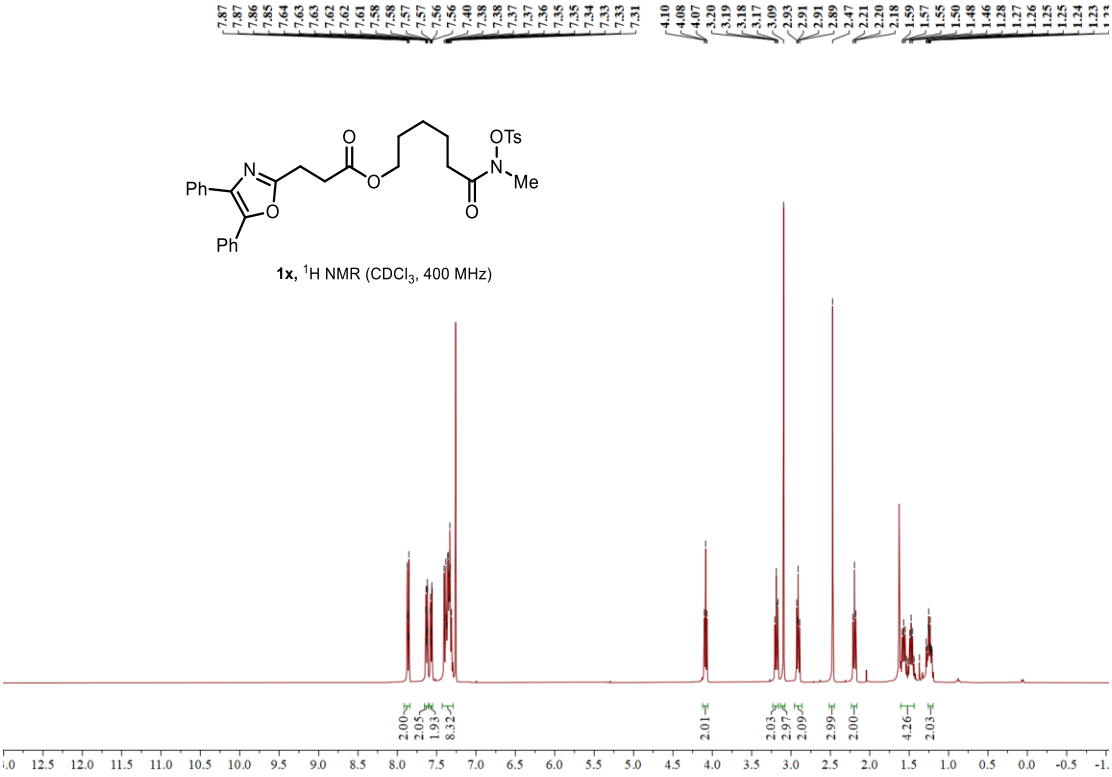


Figure S49. ^{1}H NMR of **1x** ($CDCl_3$, 400 MHz)

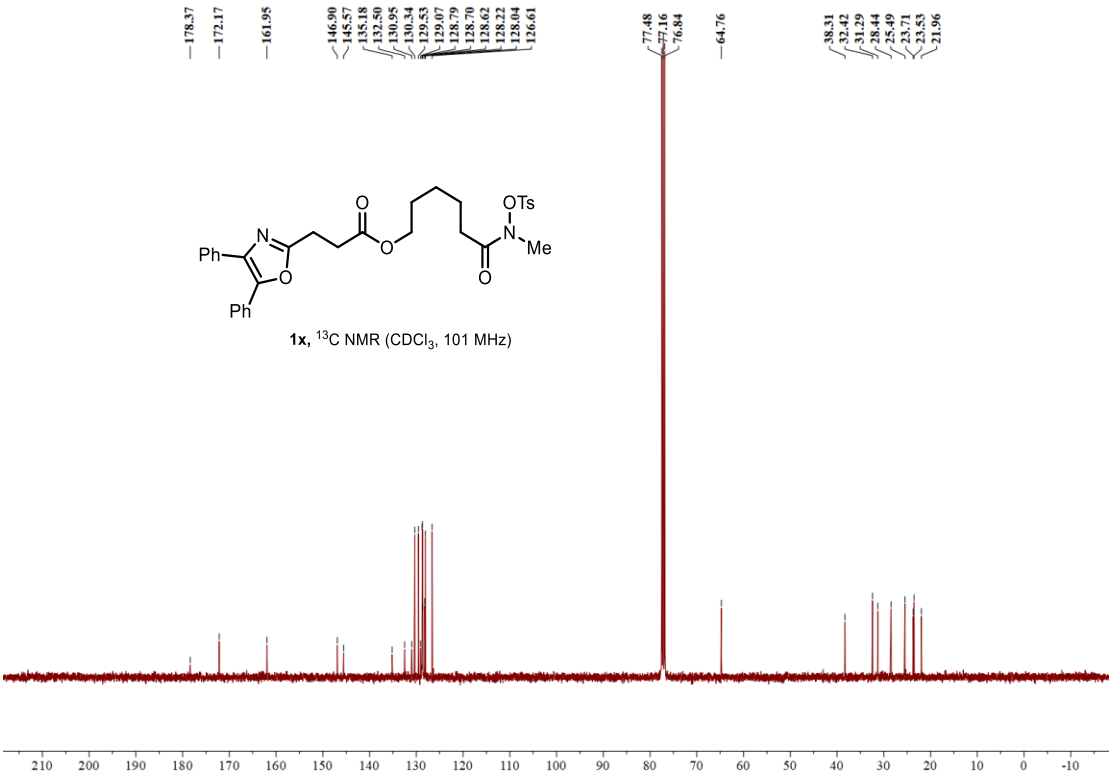


Figure S50. ^{13}C NMR of **1x** ($CDCl_3$, 101 MHz)

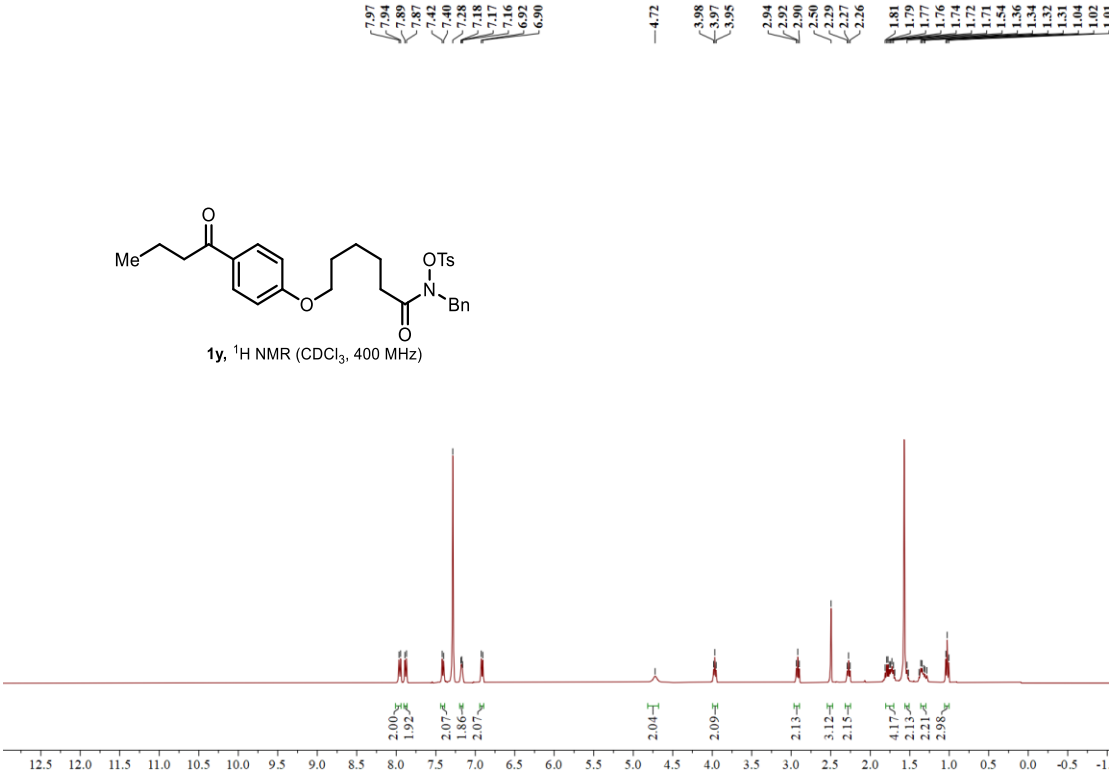


Figure S51. ^{1}H NMR of **1y** ($CDCl_3$, 400 MHz)

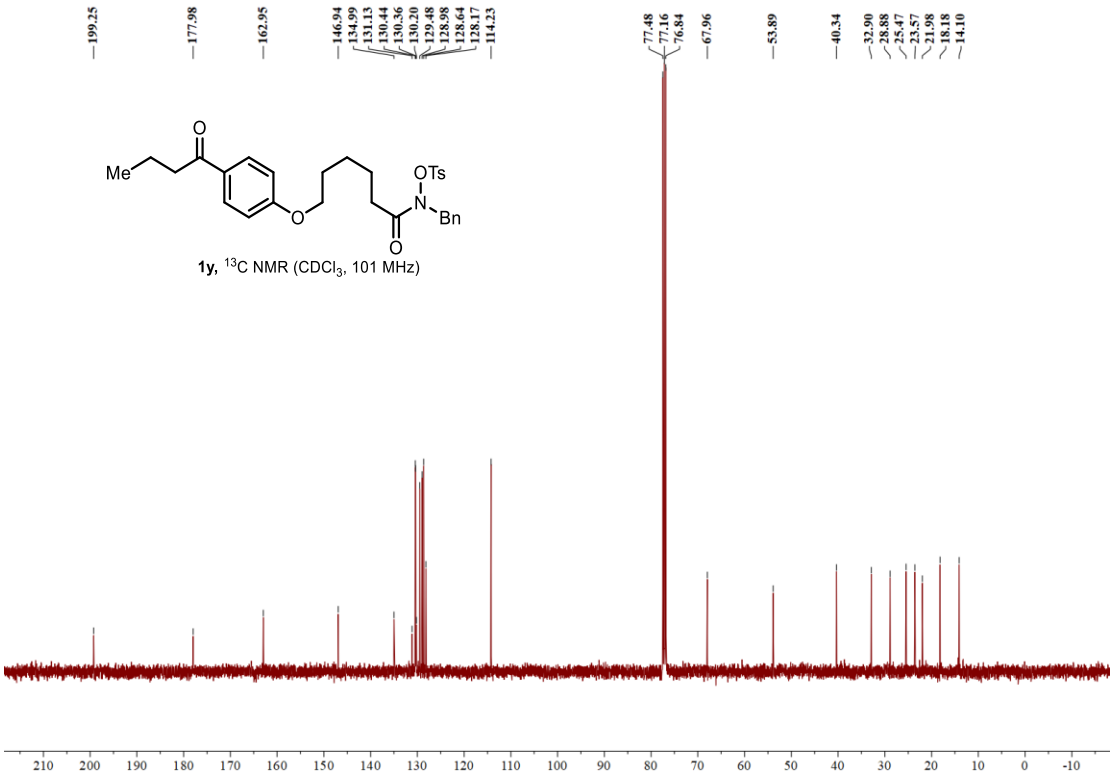


Figure S52. ^{13}C NMR of **1y** ($CDCl_3$, 101 MHz)

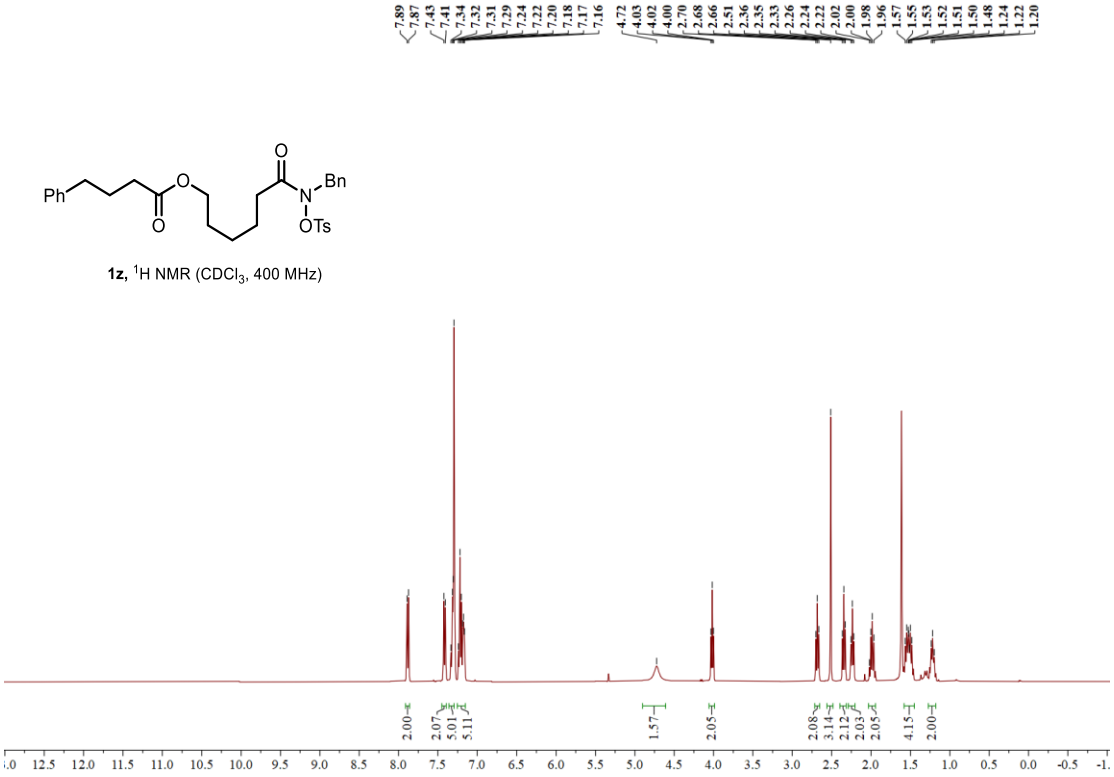
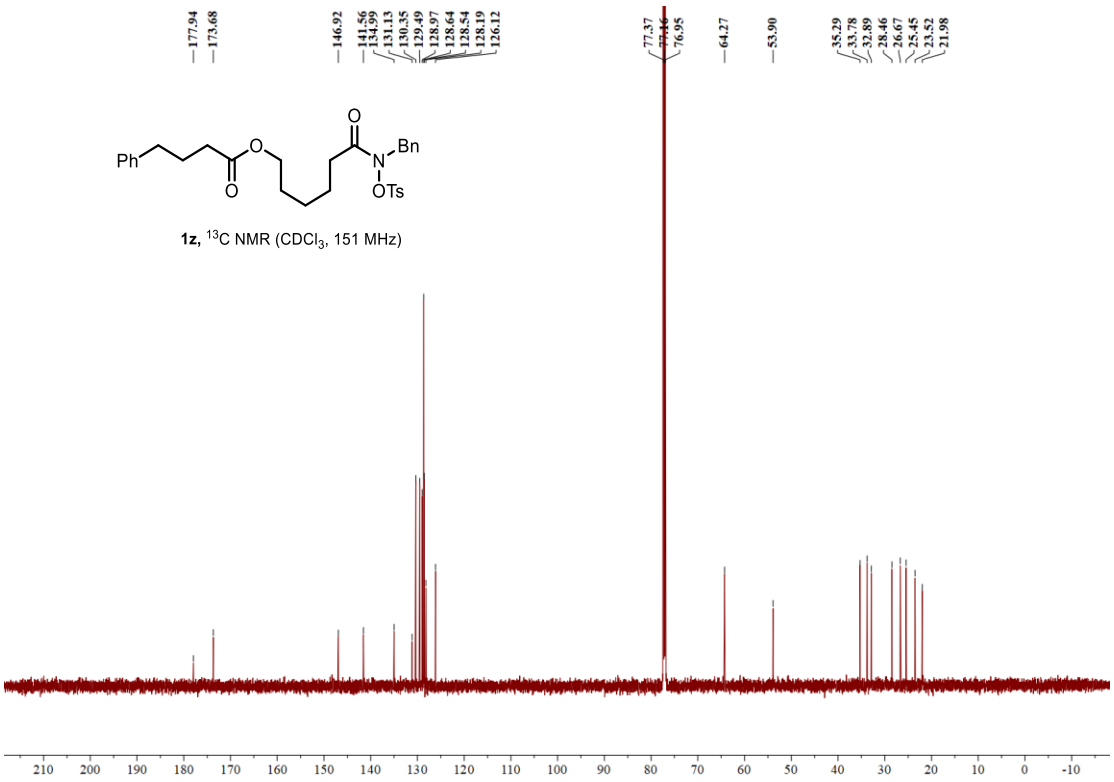
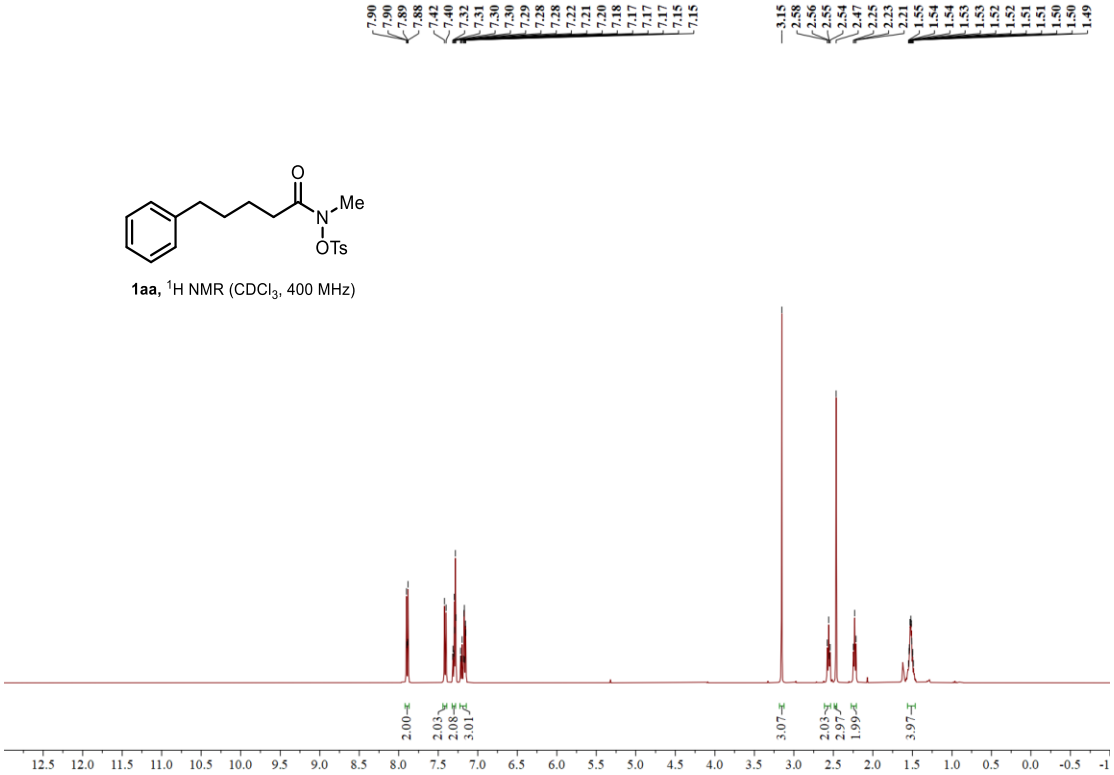


Figure S53. ^{1}H NMR of **1z** ($CDCl_3$, 400 MHz)



1z, ^{13}C NMR ($CDCl_3$, 151 MHz)

Figure S54. ^{13}C NMR of **1z** ($CDCl_3$, 151 MHz)



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

Figure S55. ^{1}H NMR of **1aa** ($CDCl_3$, 400 MHz)

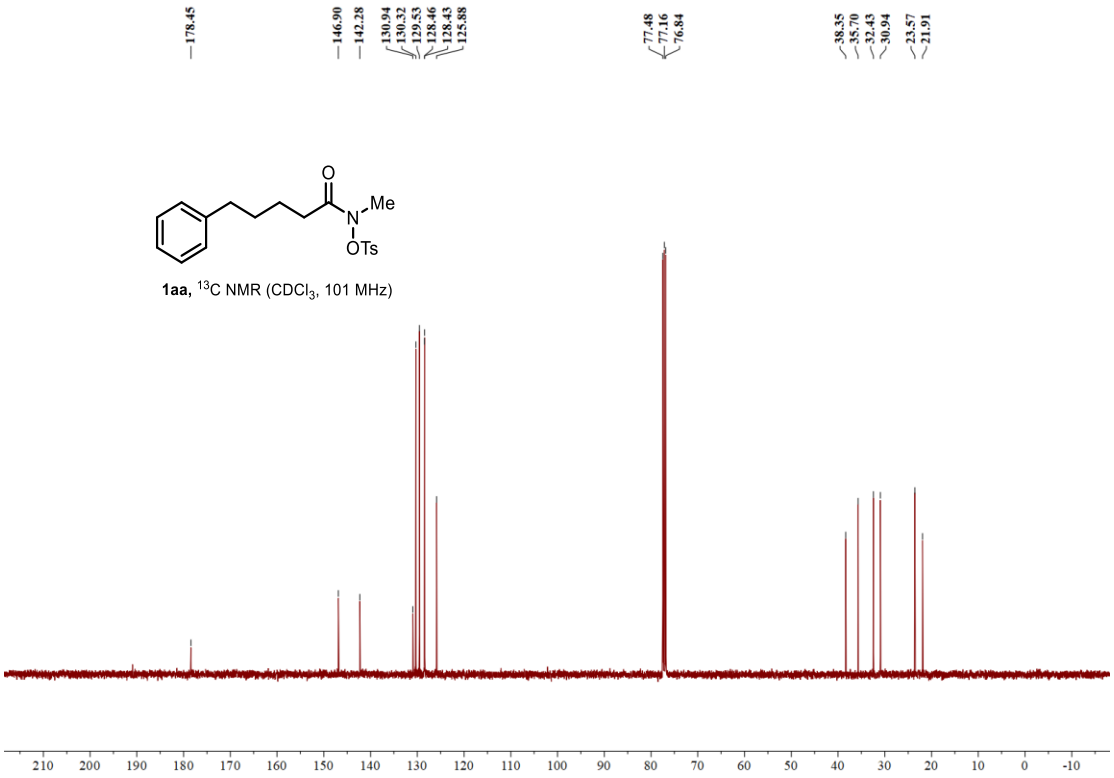


Figure S56. ^{13}C NMR of **1aa** ($CDCl_3$, 101 MHz)

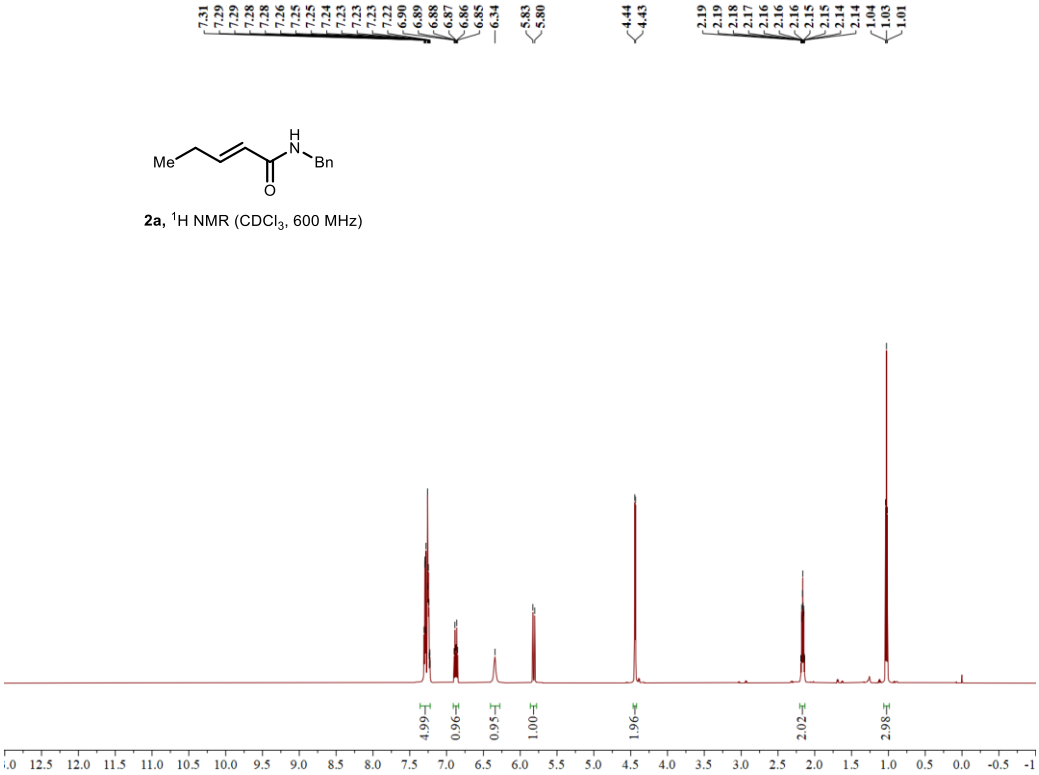


Figure S57. ^{1}H NMR of **2a** ($CDCl_3$, 600 MHz)

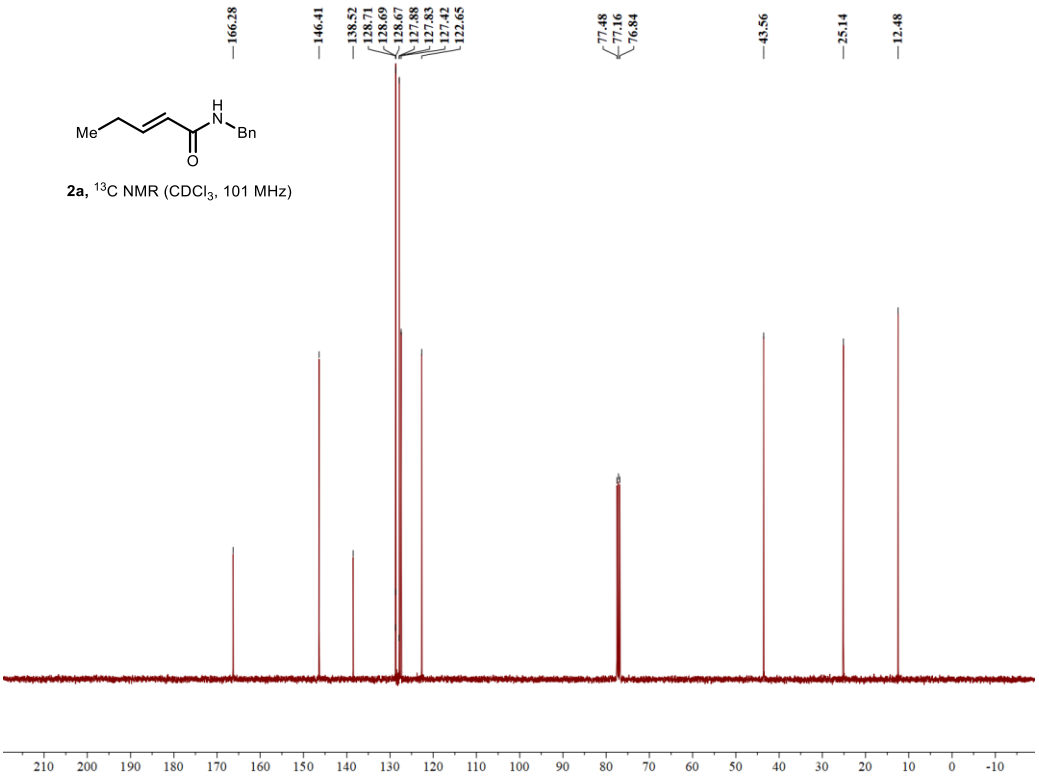


Figure S58. ^{13}C NMR of **2a** ($CDCl_3$, 101 MHz)

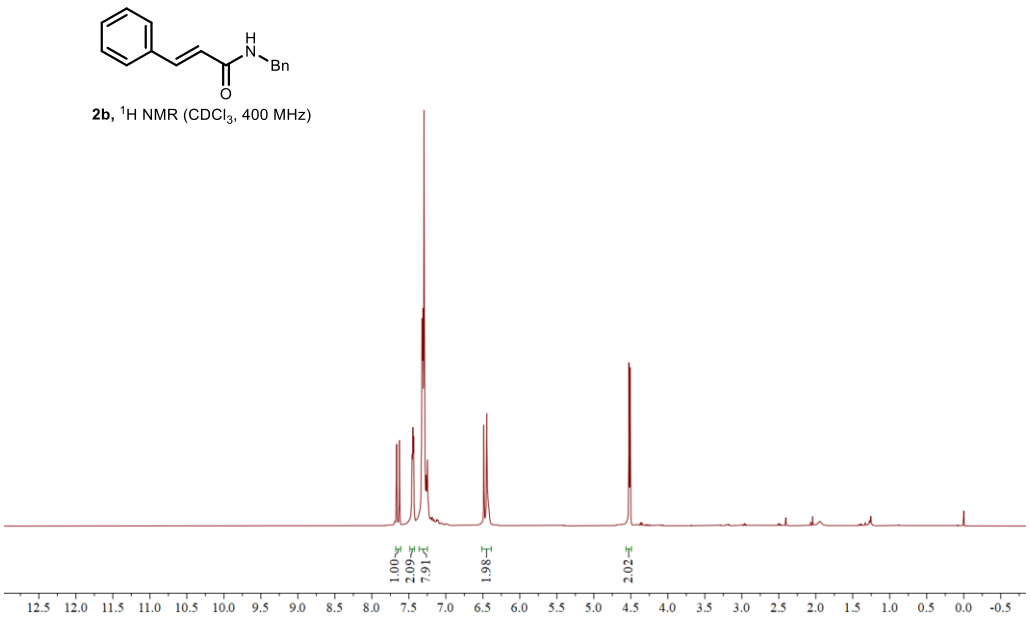


Figure S59. ^{1}H NMR of **2b** ($CDCl_3$, 400 MHz)

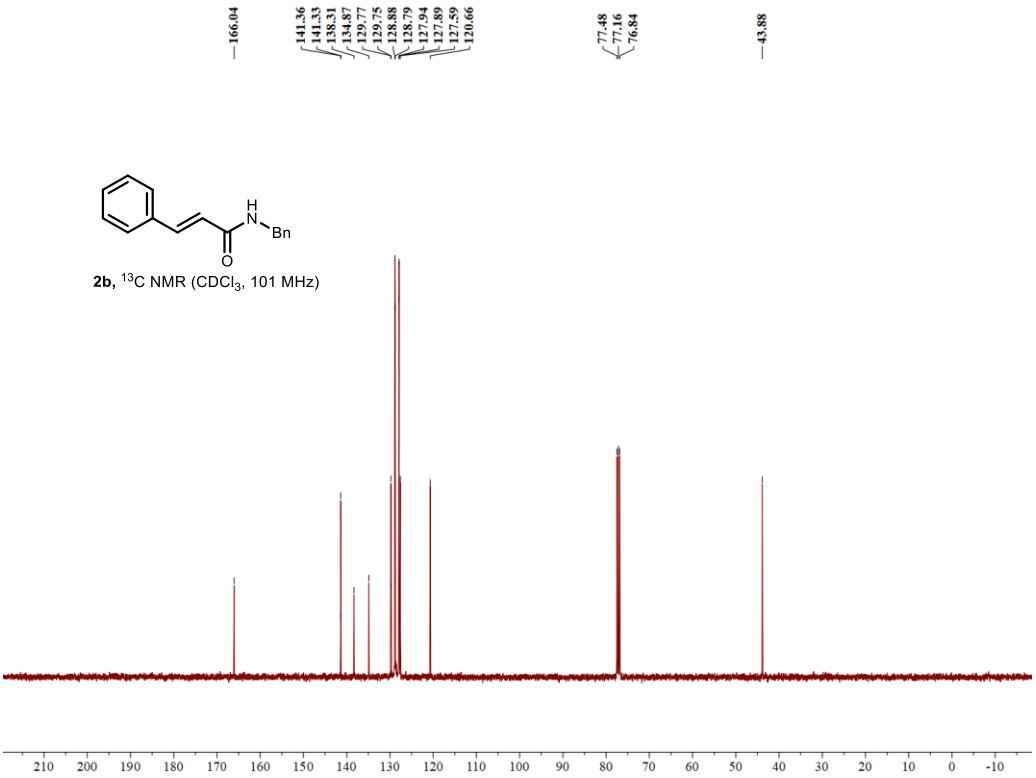


Figure S60. ^{13}C NMR of **2b** ($CDCl_3$, 101 MHz)

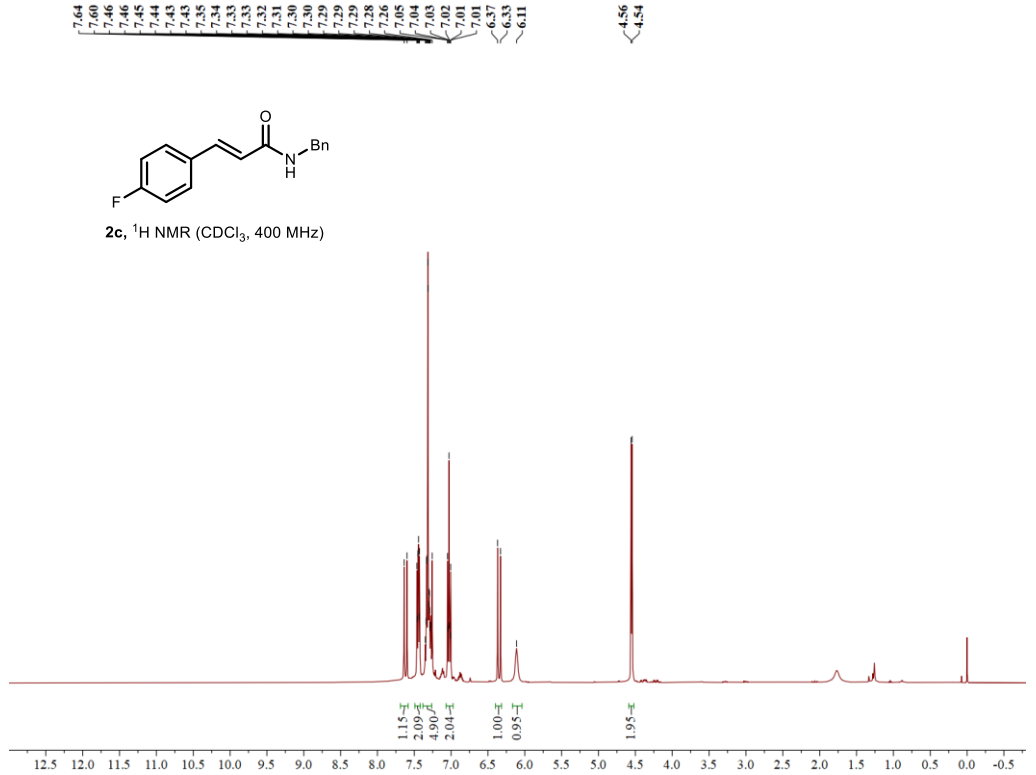


Figure S61. ^{1}H NMR of **2c** ($CDCl_3$, 400 MHz)

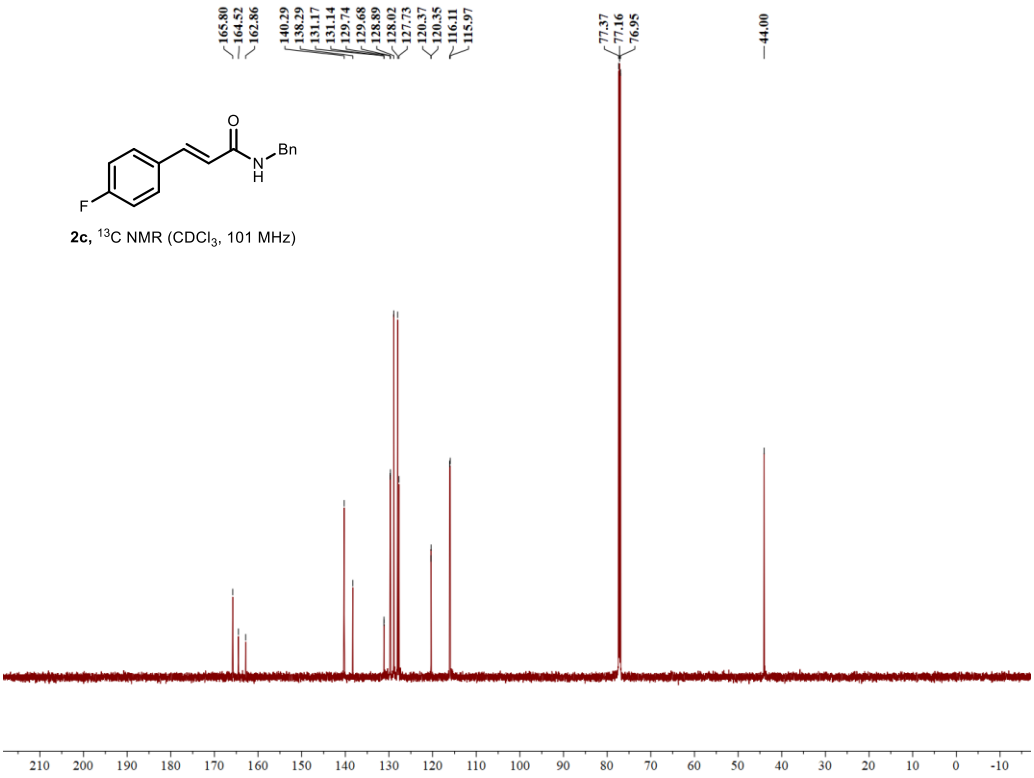


Figure S62. ^{13}C NMR of **2c** ($CDCl_3$, 101 MHz)

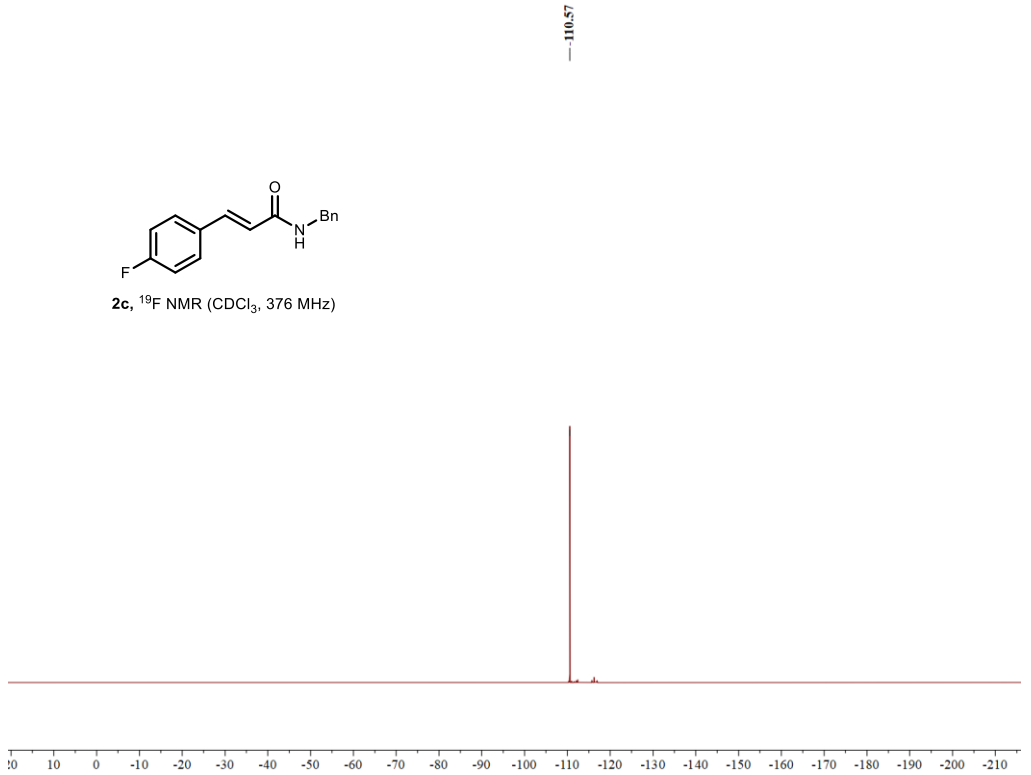


Figure S63. ^{19}F NMR of **2c** ($CDCl_3$, 376 MHz)

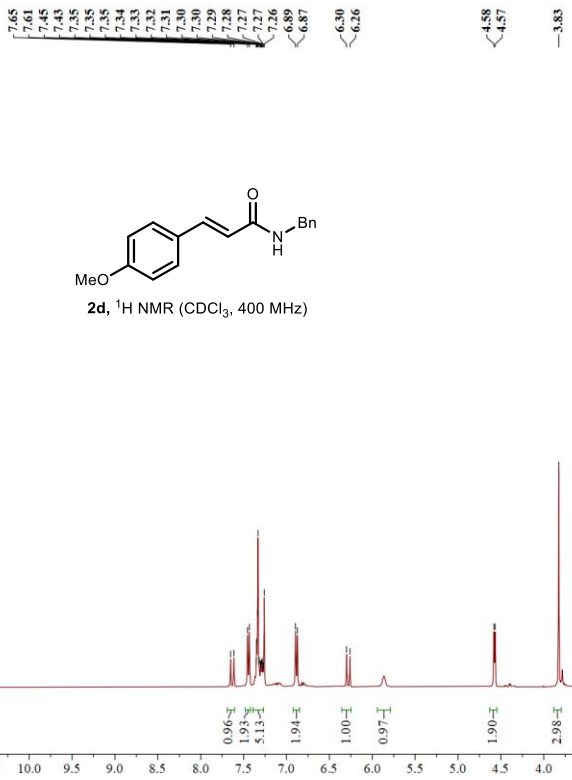


Figure S64. ^{1}H NMR of **2d** ($CDCl_3$, 400 MHz)

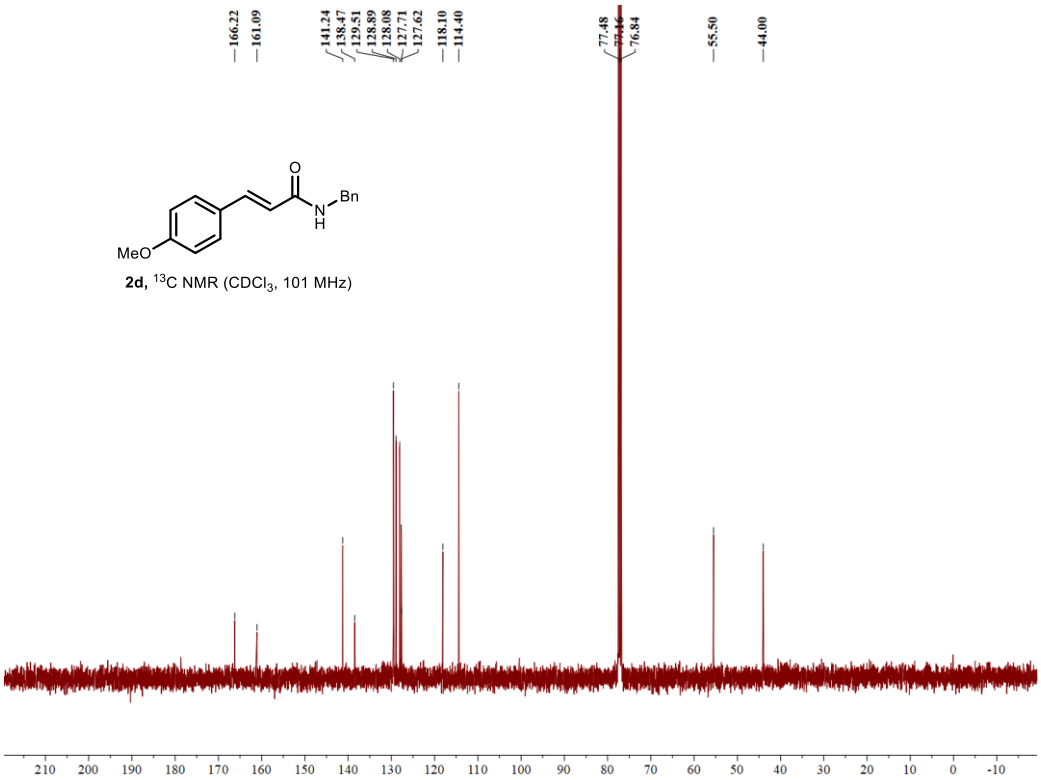
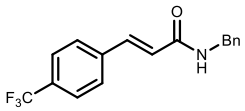


Figure S65. ^{13}C NMR of **2d** ($CDCl_3$, 101 MHz)



2e, ^{1}H NMR ($CDCl_3$, 400 MHz)

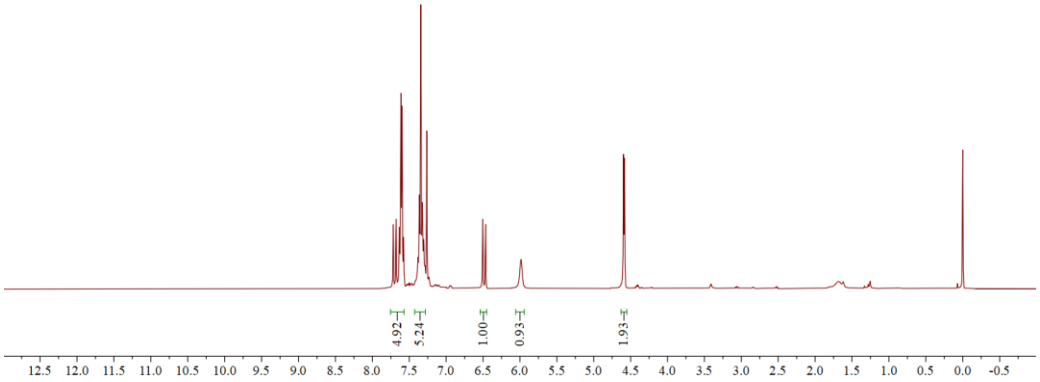
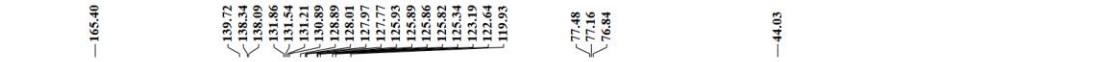
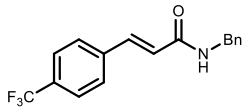


Figure S66. ^{1}H NMR of **2e** ($CDCl_3$, 400 MHz)





2e, ^{13}C NMR ($CDCl_3$, 151 MHz)

Figure S67. ^{13}C NMR of **2e** ($CDCl_3$, 151 MHz)

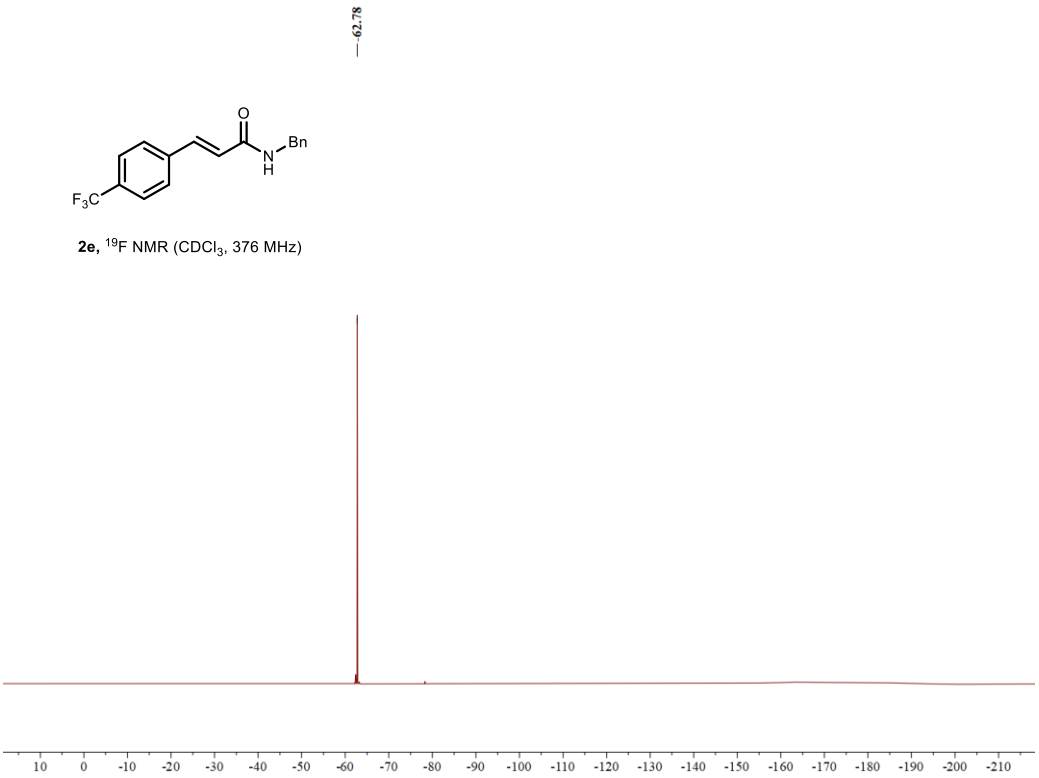


Figure S68. ^{19}F NMR of **2e** ($CDCl_3$, 376 MHz)

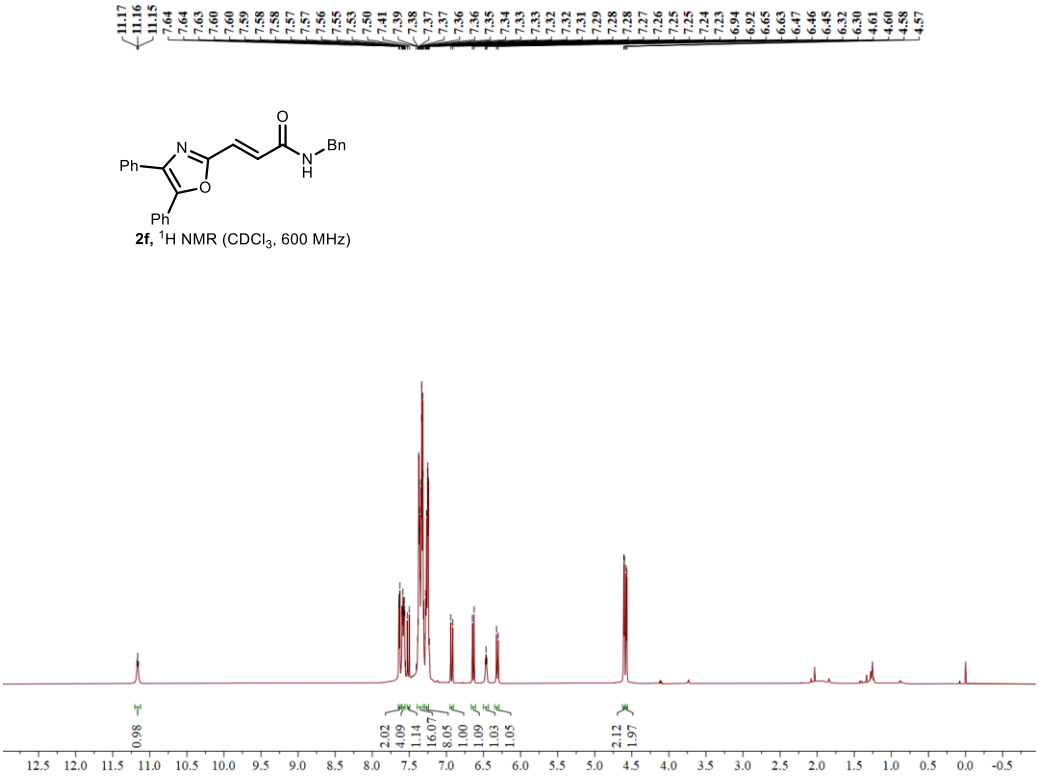


Figure S69. ^{1}H NMR of **2f** ($CDCl_3$, 600 MHz)

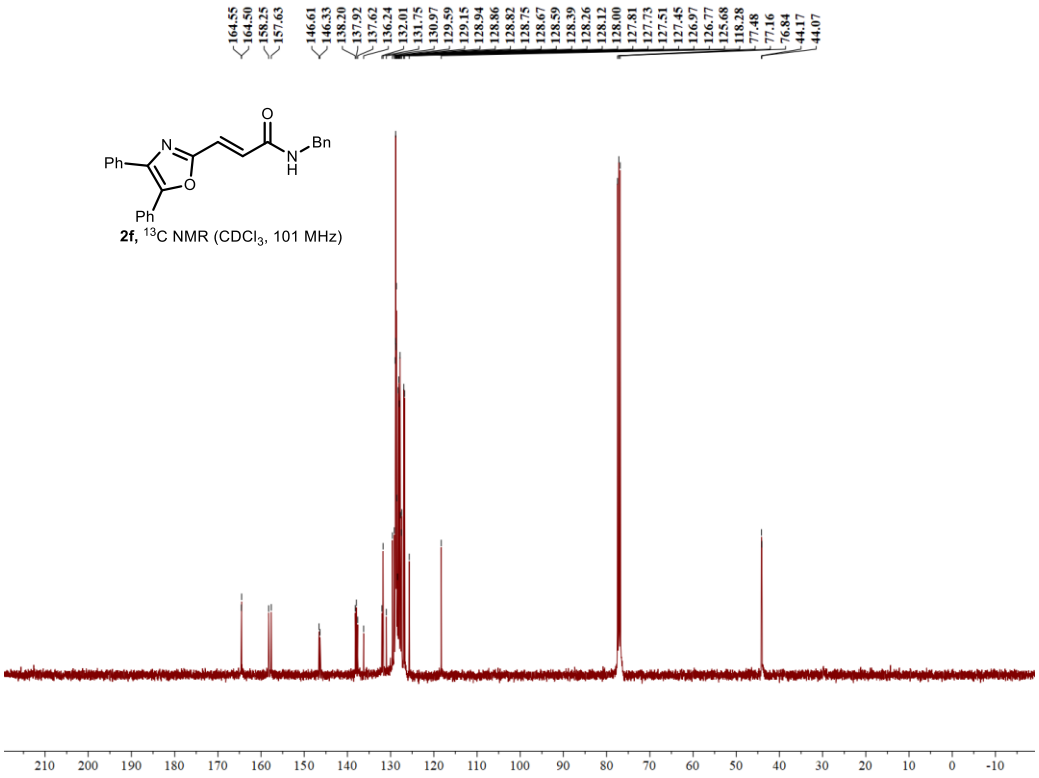
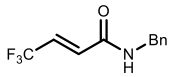


Figure S70. ^{13}C NMR of **2f** ($CDCl_3$, 101 MHz)



2g, ^{1}H NMR ($CDCl_3$, 400 MHz)

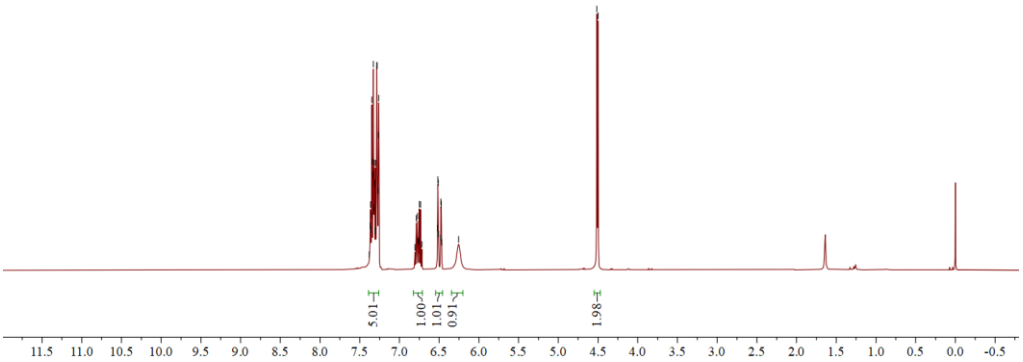


Figure S71. ^{1}H NMR of **2g** ($CDCl_3$, 400 MHz)

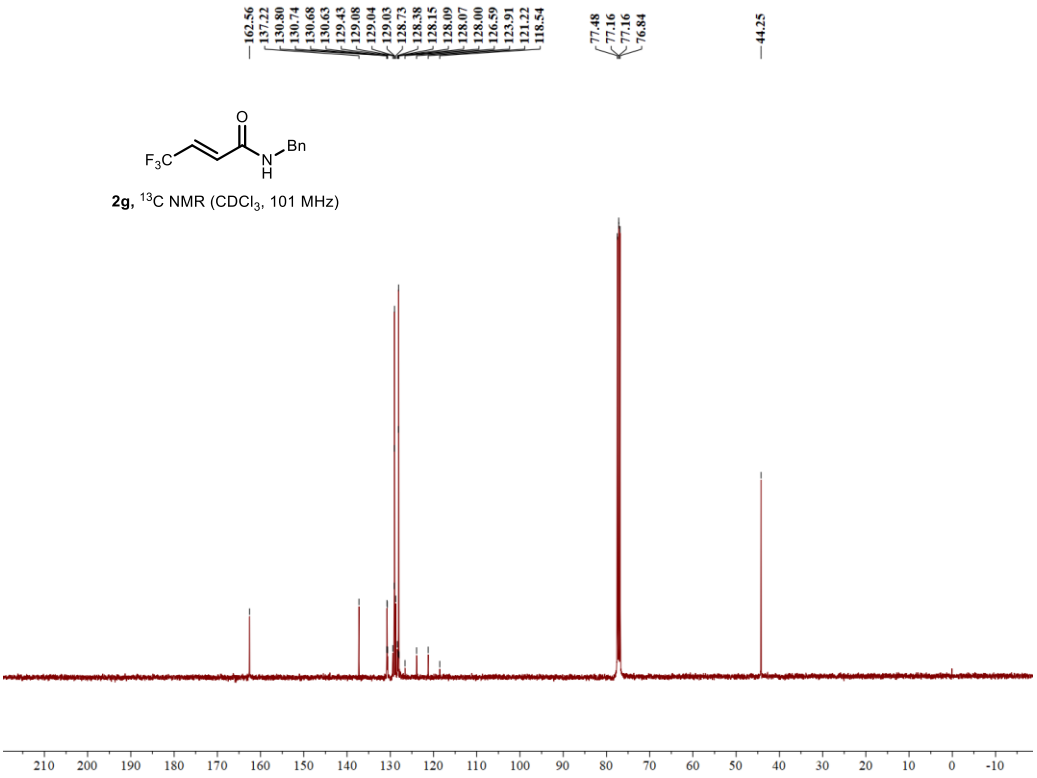


Figure S72. ^{13}C NMR of **2g** ($CDCl_3$, 101 MHz)

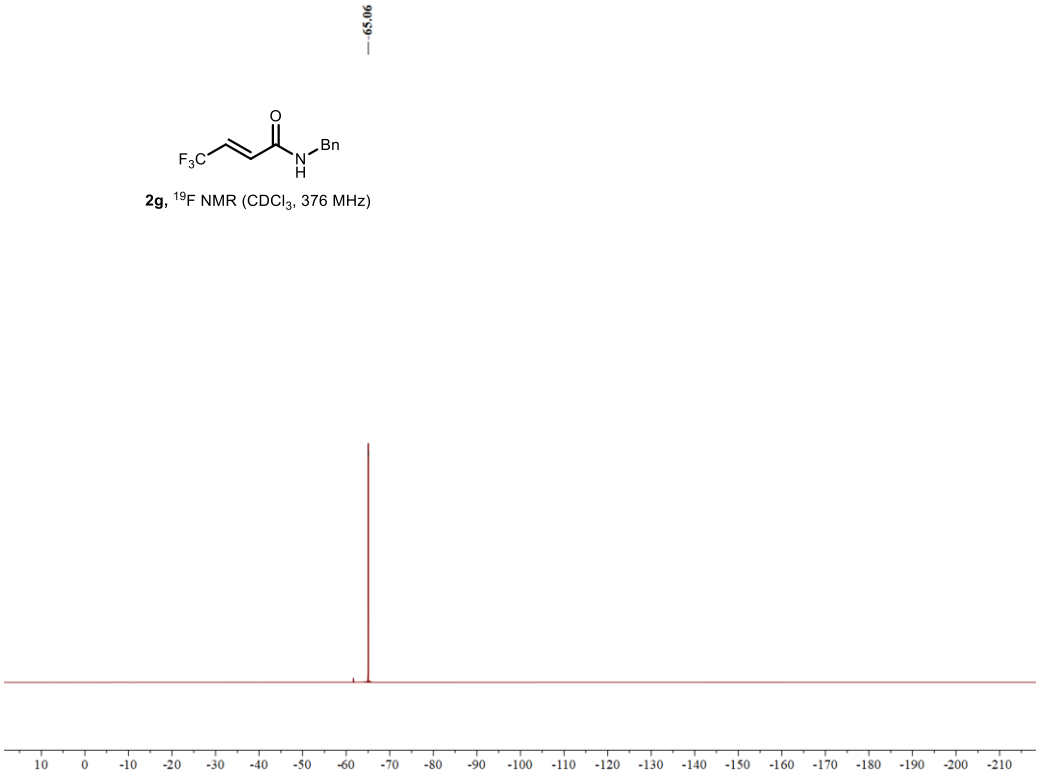


Figure S73 ^{19}F NMR of **2g** ($CDCl_3$, 376 MHz)

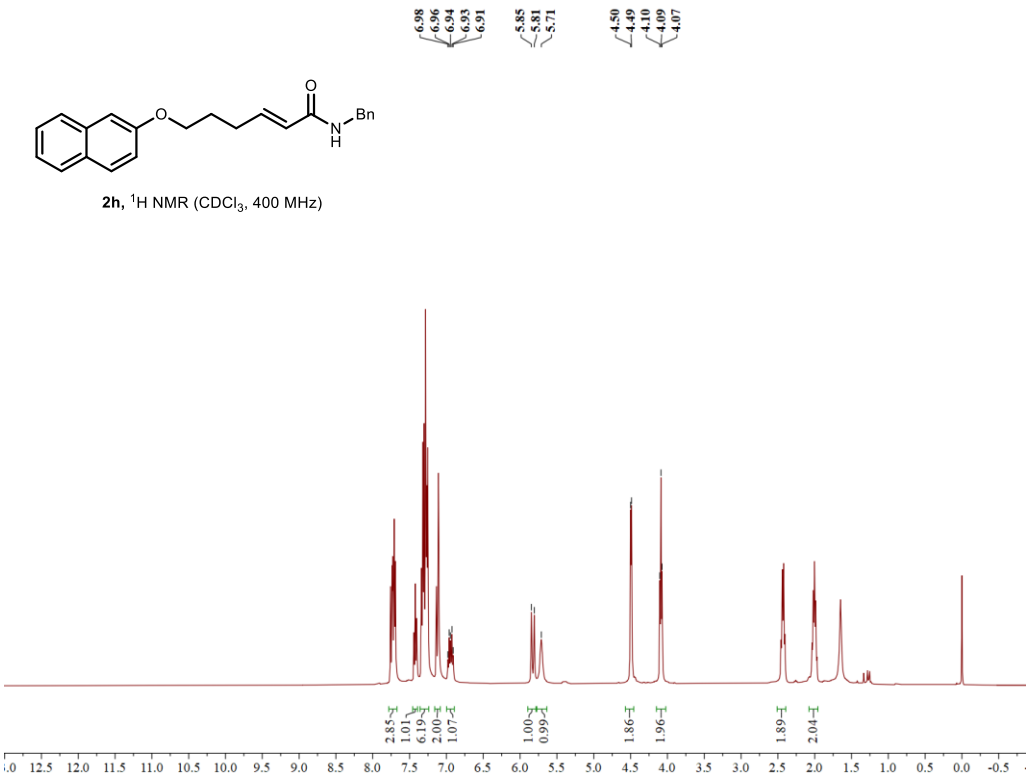


Figure S74. ^{1}H NMR of **2h** ($CDCl_3$, 400 MHz)

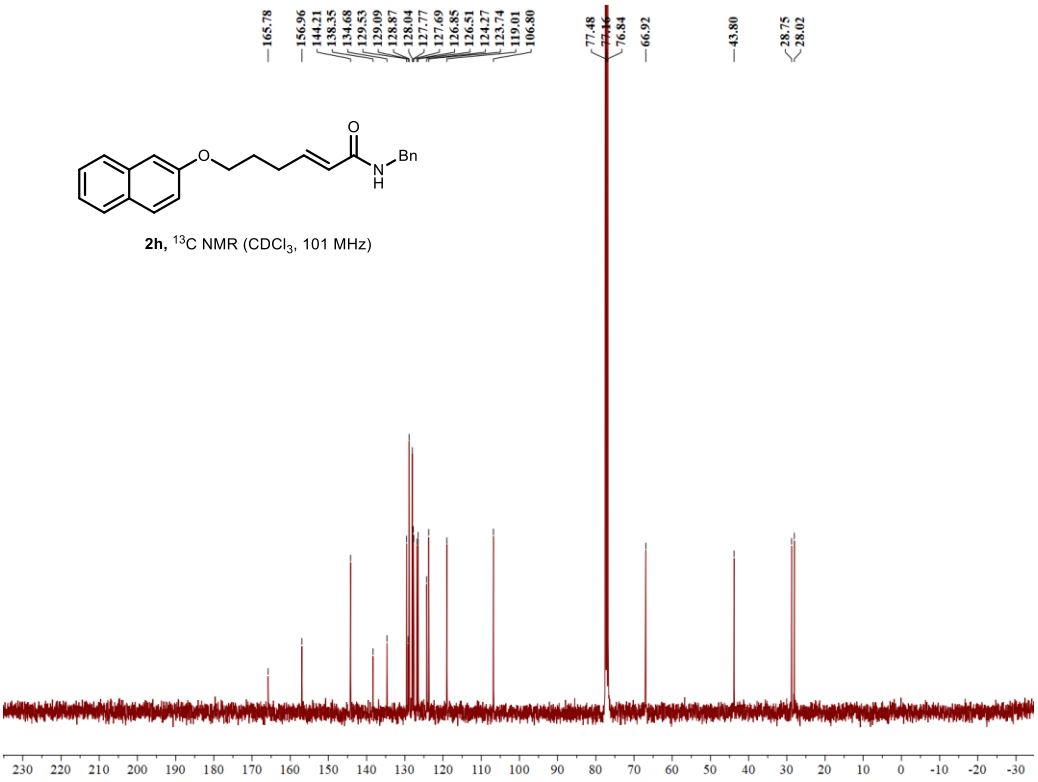


Figure S75. ^{13}C NMR of **2h** ($CDCl_3$, 101 MHz)

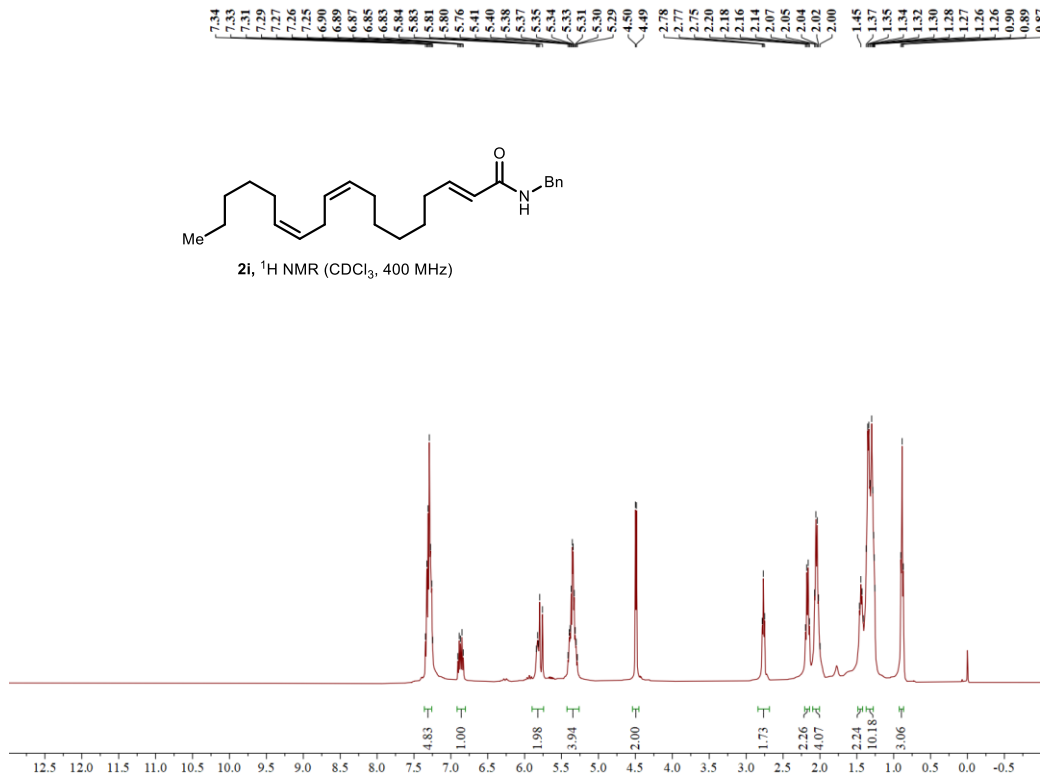


Figure S76. ^{1}H NMR of **2i** ($CDCl_3$, 400 MHz)

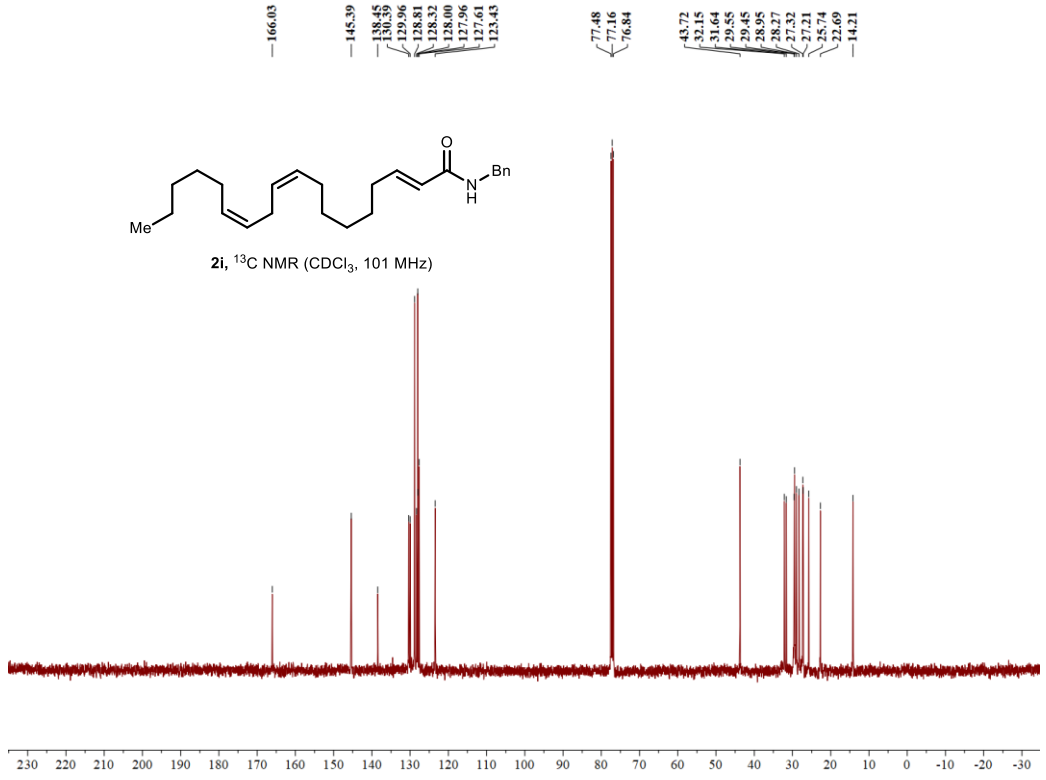
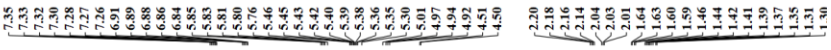
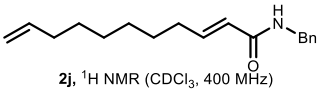


Figure S77. ^{13}C NMR of **2i** ($CDCl_3$, 101 MHz)





2j, ^{1}H NMR ($CDCl_3$, 400 MHz)

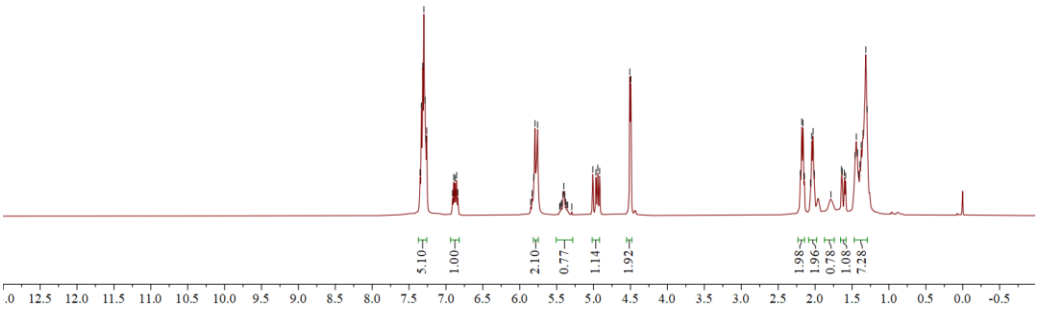
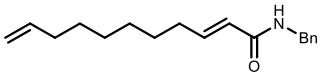


Figure S78. ^{1}H NMR of **2j** ($CDCl_3$, 400 MHz)



2j, ^{13}C NMR ($CDCl_3$, 101 MHz)

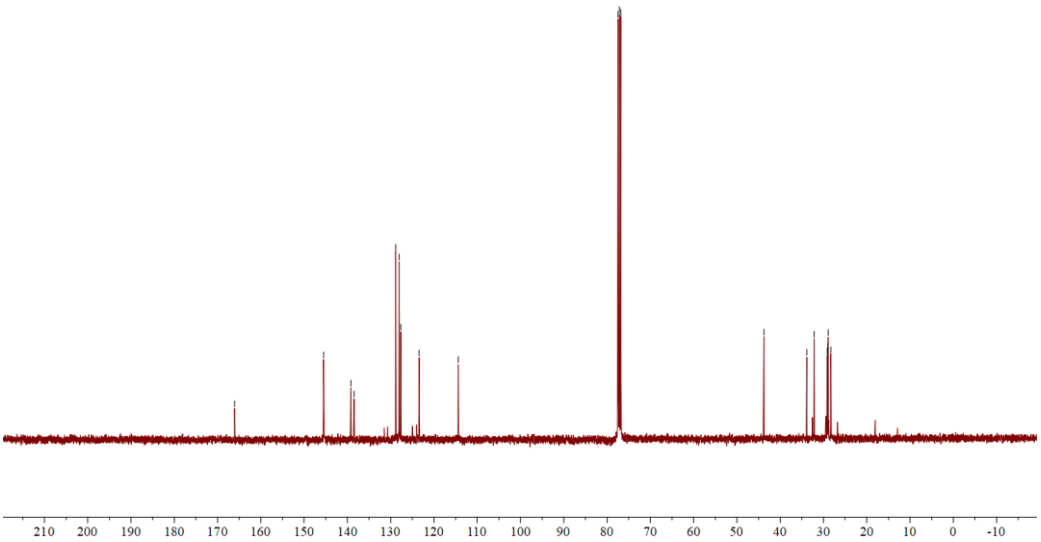


Figure S79. ^{13}C NMR of **2j** ($CDCl_3$, 101 MHz)

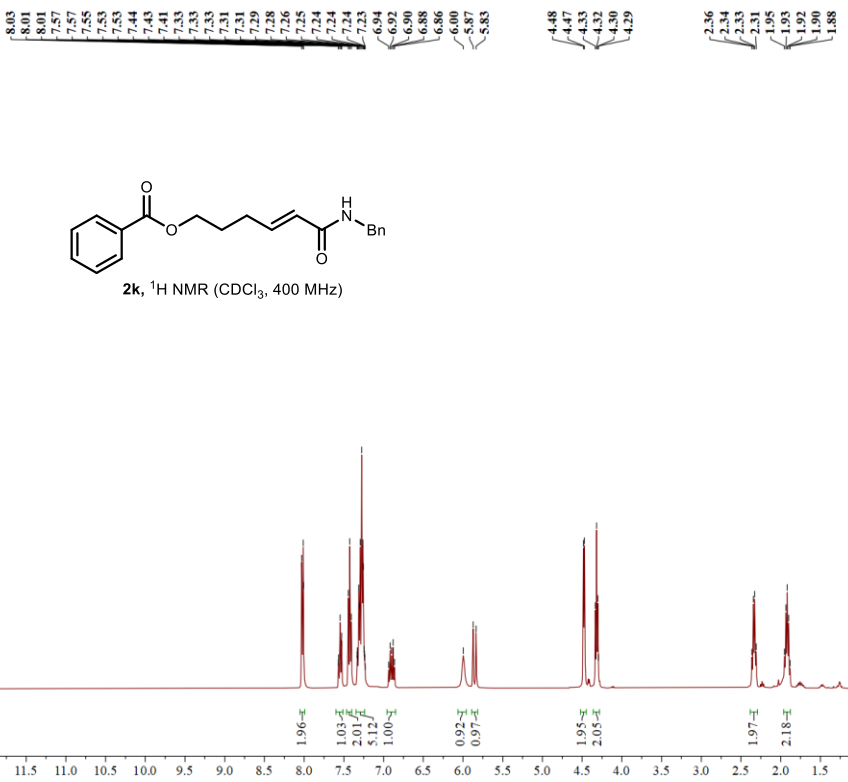


Figure S80. ^{1}H NMR of **2k** ($CDCl_3$, 400 MHz)

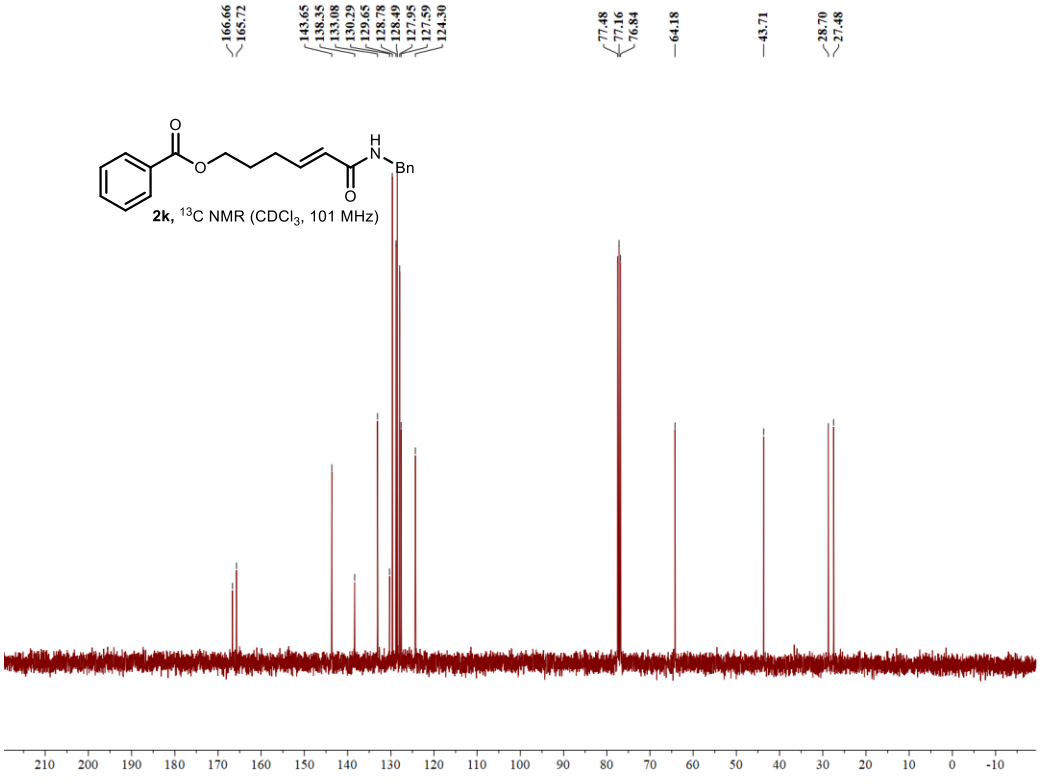


Figure S81. ^{13}C NMR of **2k** ($CDCl_3$, 101 MHz)

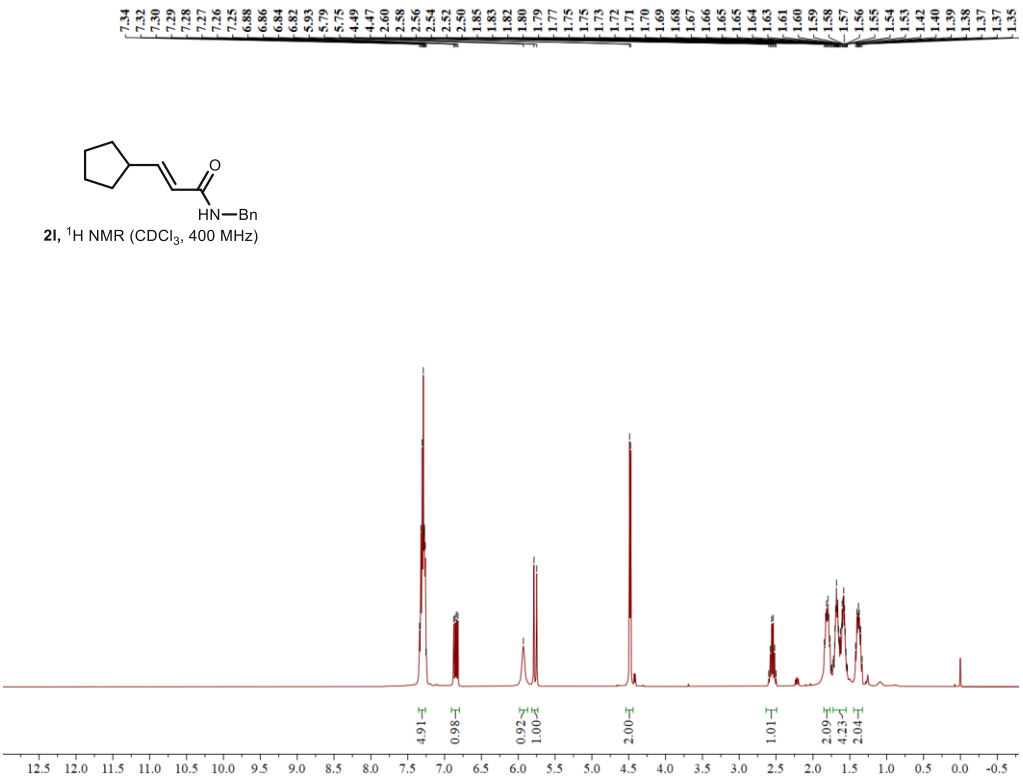


Figure S82. ^{1}H NMR of **2l** ($CDCl_3$, 400 MHz)

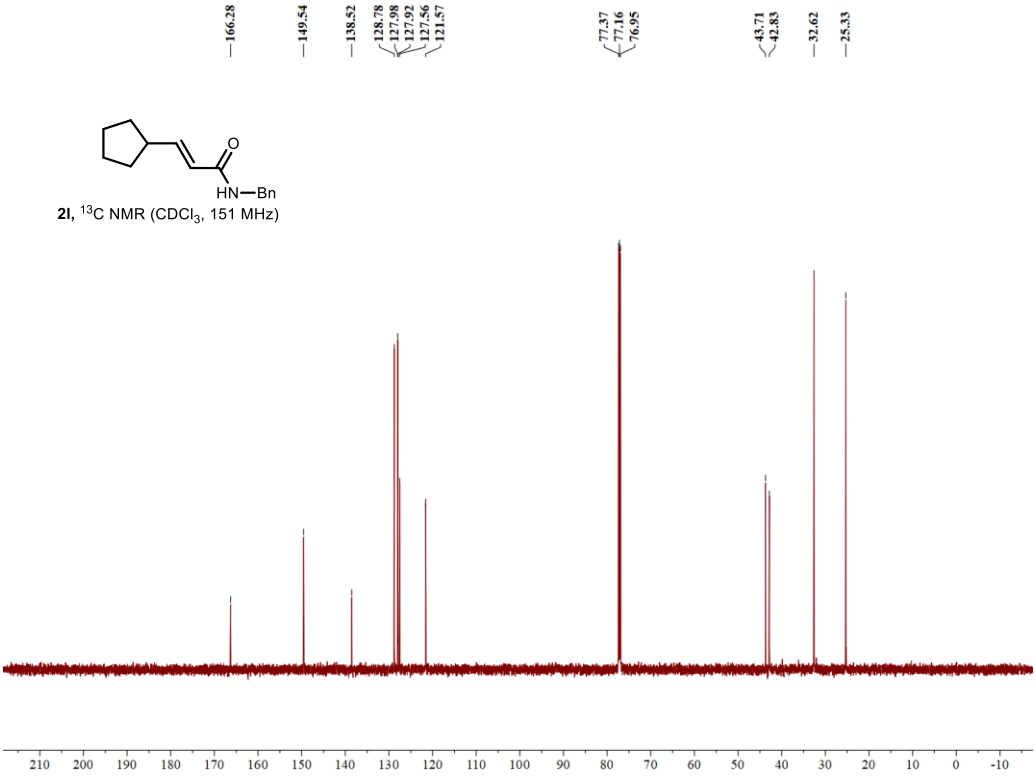


Figure S83. ^{13}C NMR of **2l** ($CDCl_3$, 151 MHz)

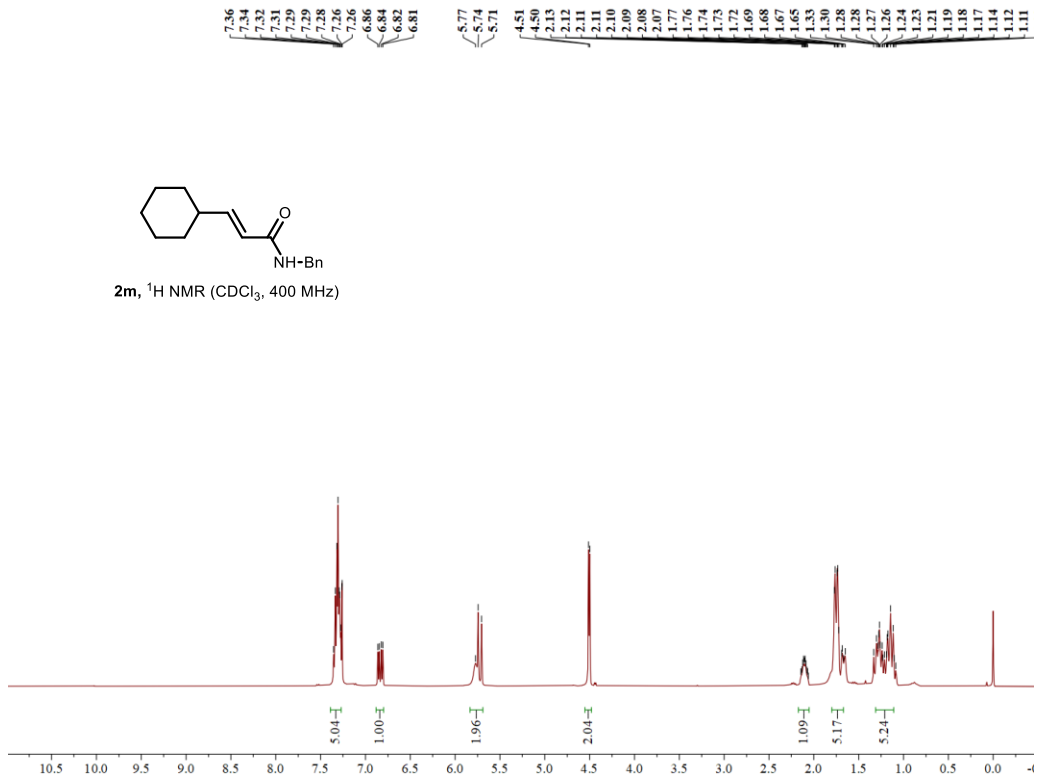


Figure S84. ^{1}H NMR of **2m** ($CDCl_3$, 400 MHz)

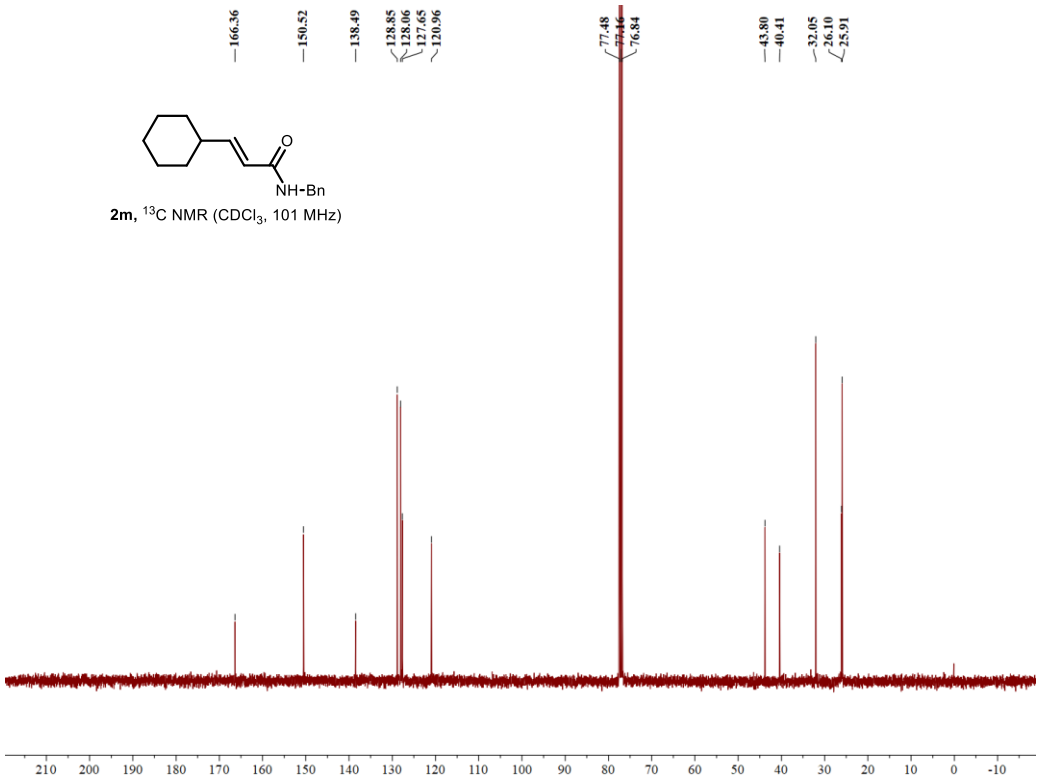


Figure S85. ^{13}C NMR of **2m** ($CDCl_3$, 101 MHz)

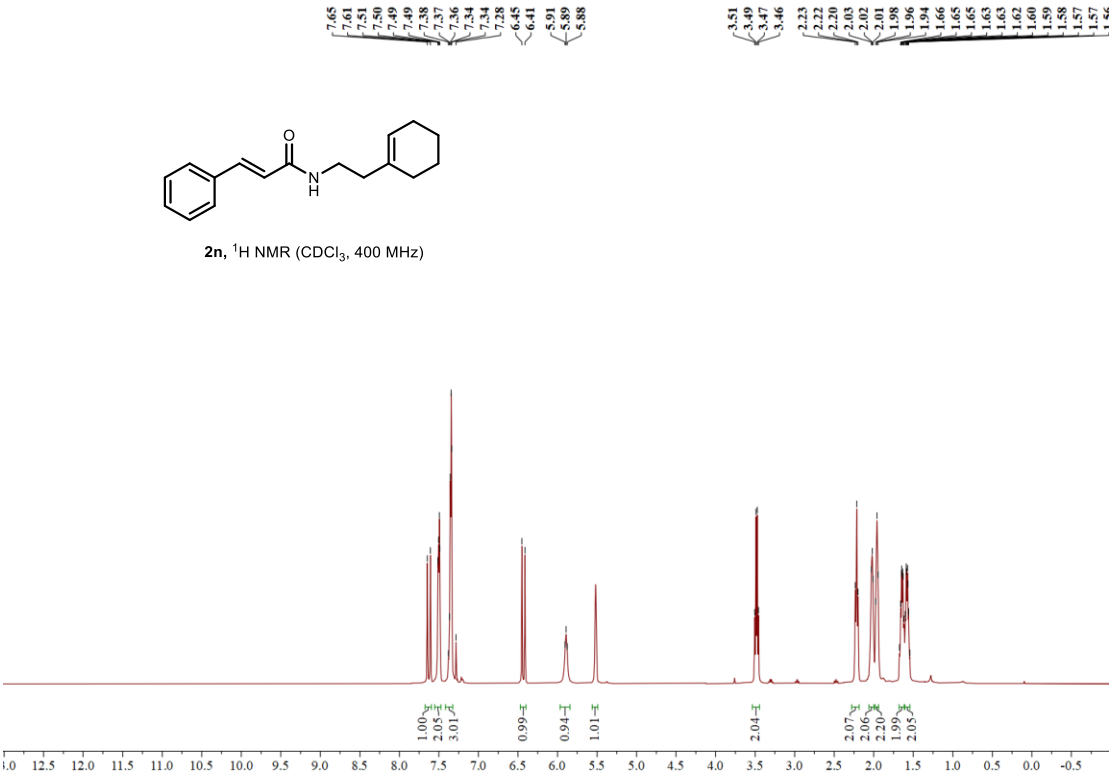


Figure S86. ^{1}H NMR of **2n** ($CDCl_3$, 400 MHz)

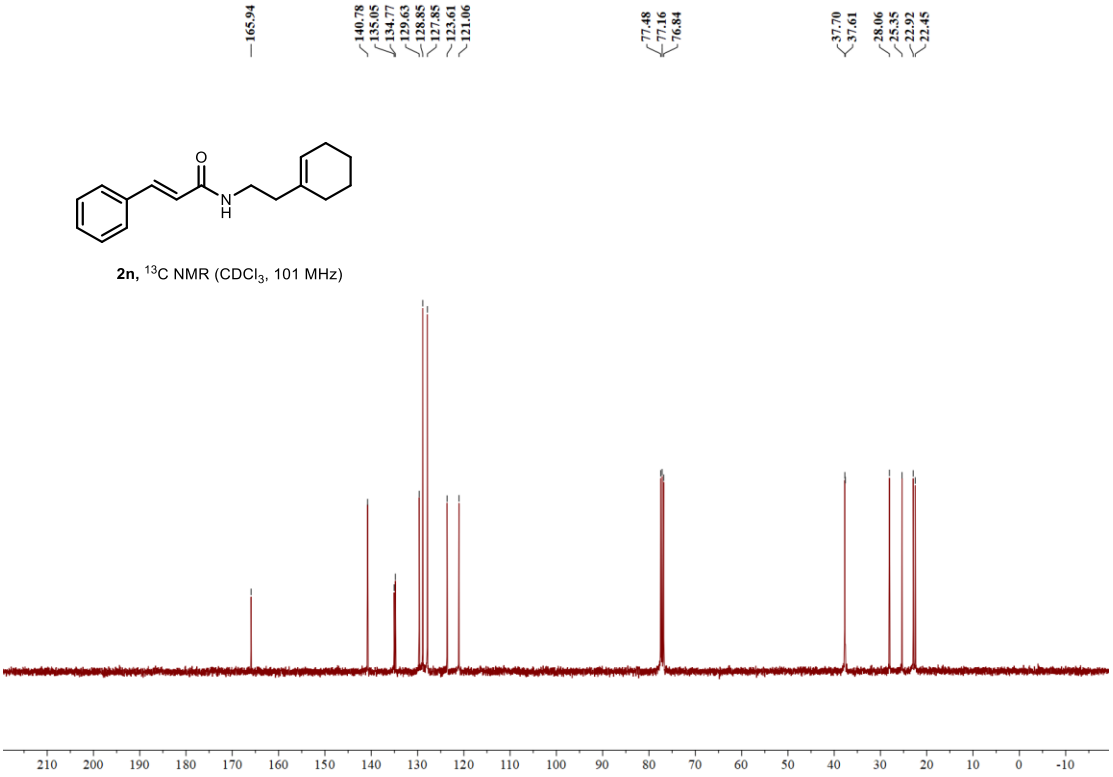


Figure S87. ^{13}C NMR of **2n** ($CDCl_3$, 101 MHz)

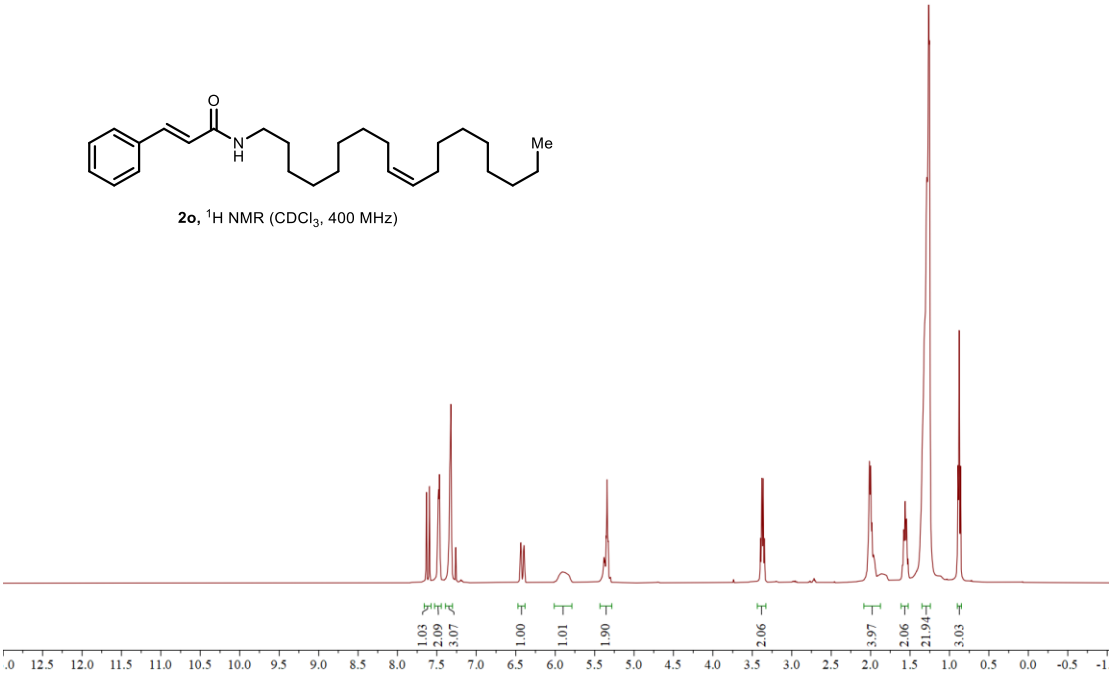


Figure S88. ^{1}H NMR of **2o** ($CDCl_3$, 400 MHz)

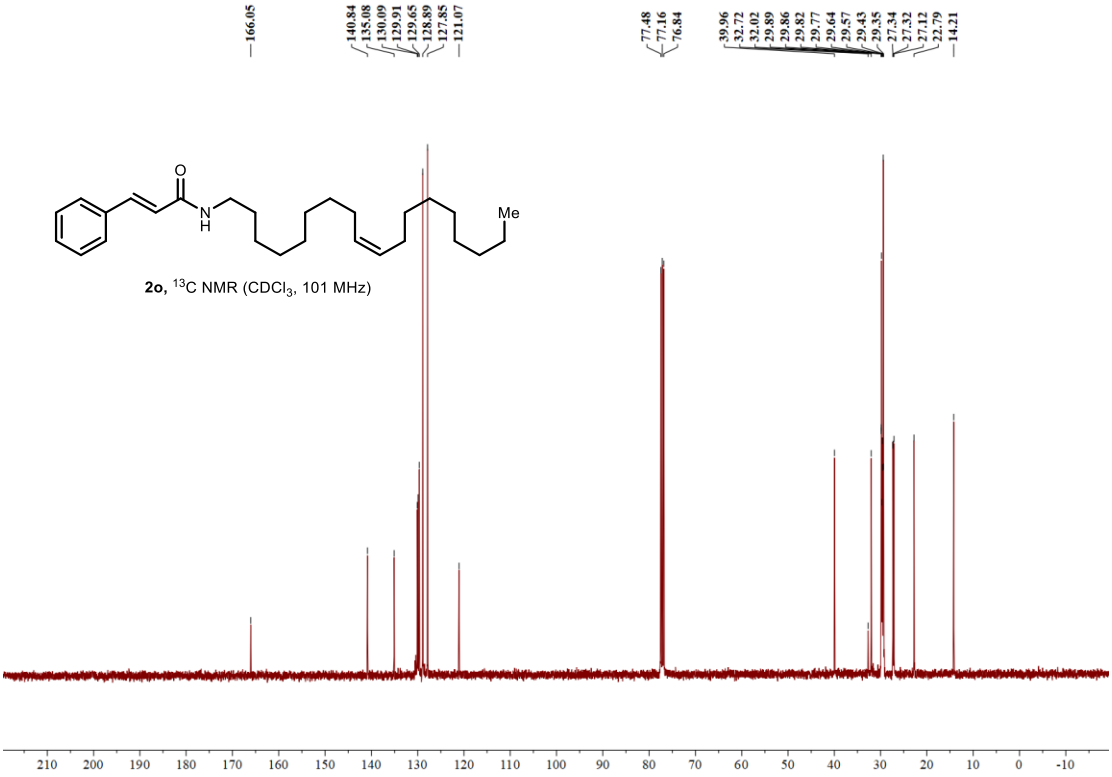


Figure S89. ^{13}C NMR of **2o** ($CDCl_3$, 101 MHz)

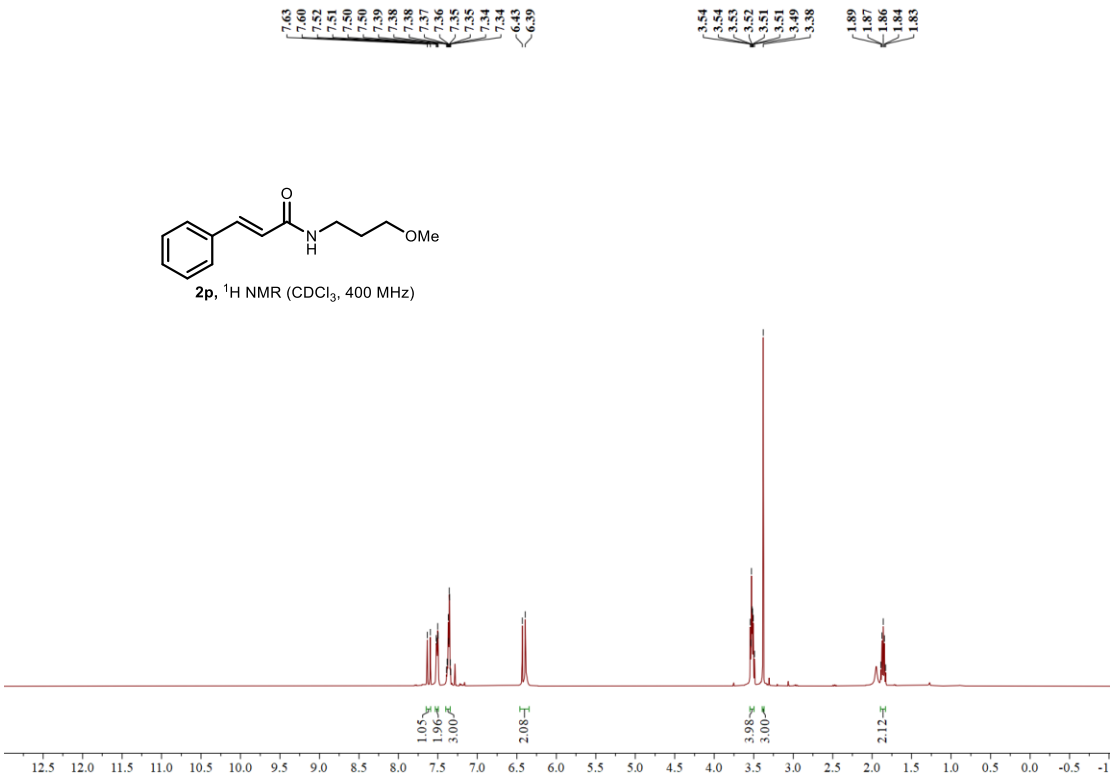


Figure S90. ^{1}H NMR of **2p** ($CDCl_3$, 400 MHz)

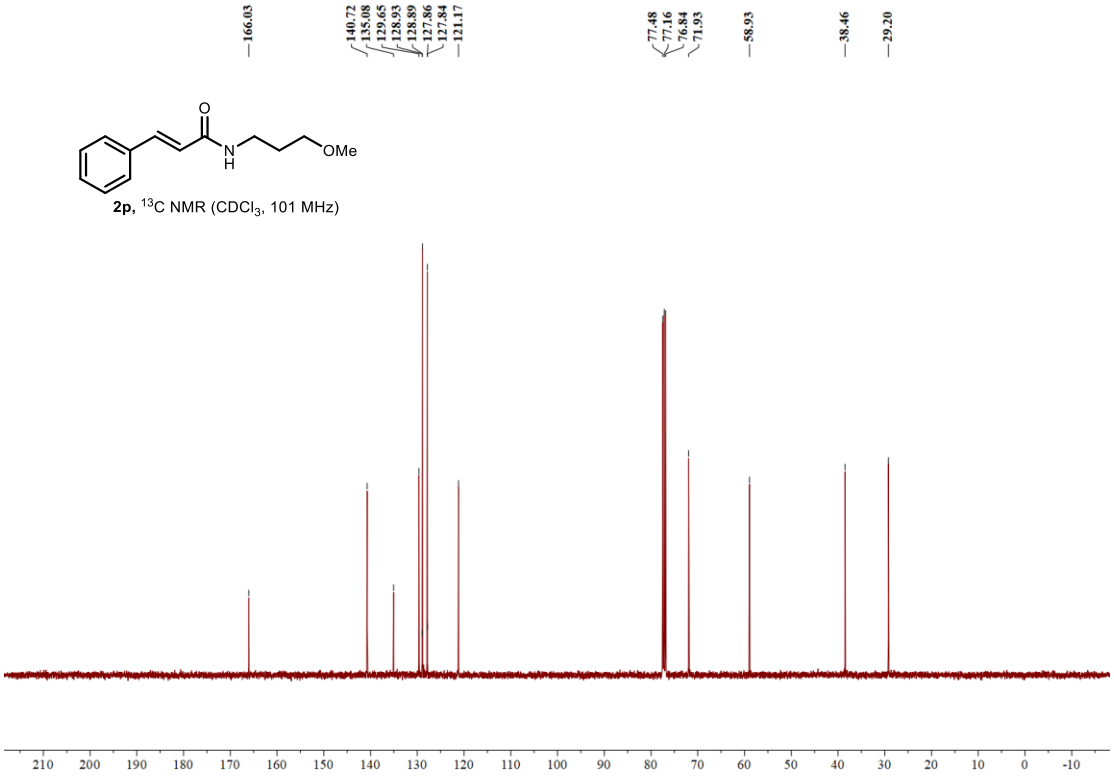


Figure S91. ^{13}C NMR of **2p** ($CDCl_3$, 101 MHz)

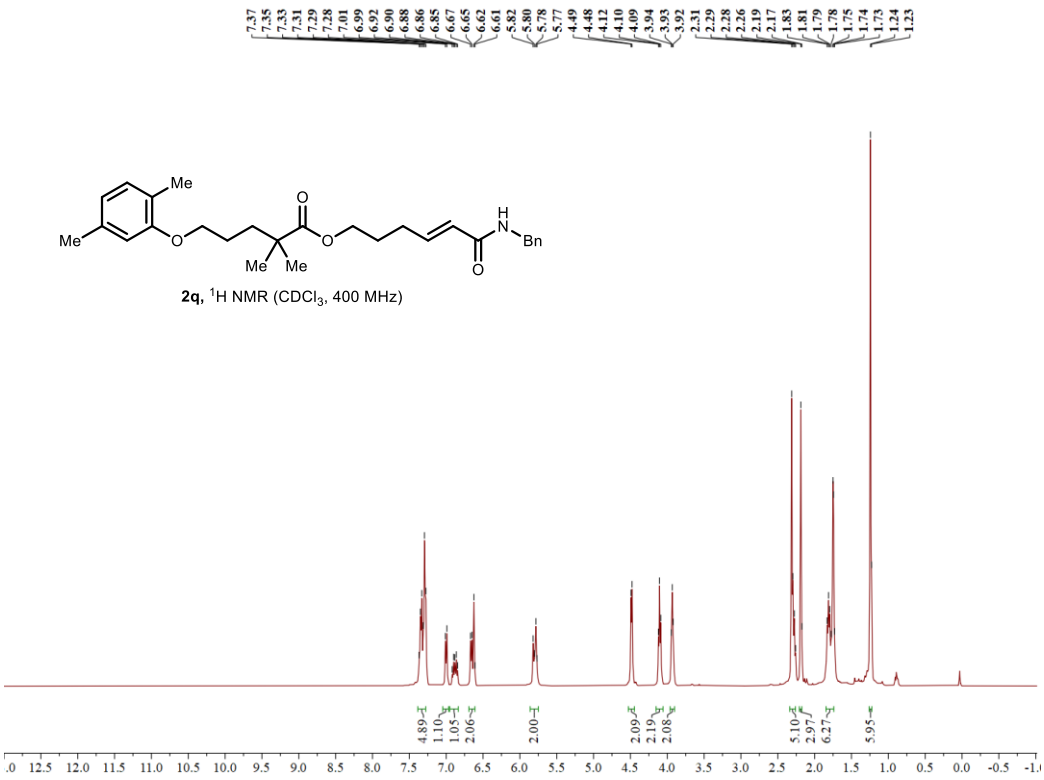


Figure S92. ^{1}H NMR of **2q** ($CDCl_3$, 400 MHz)

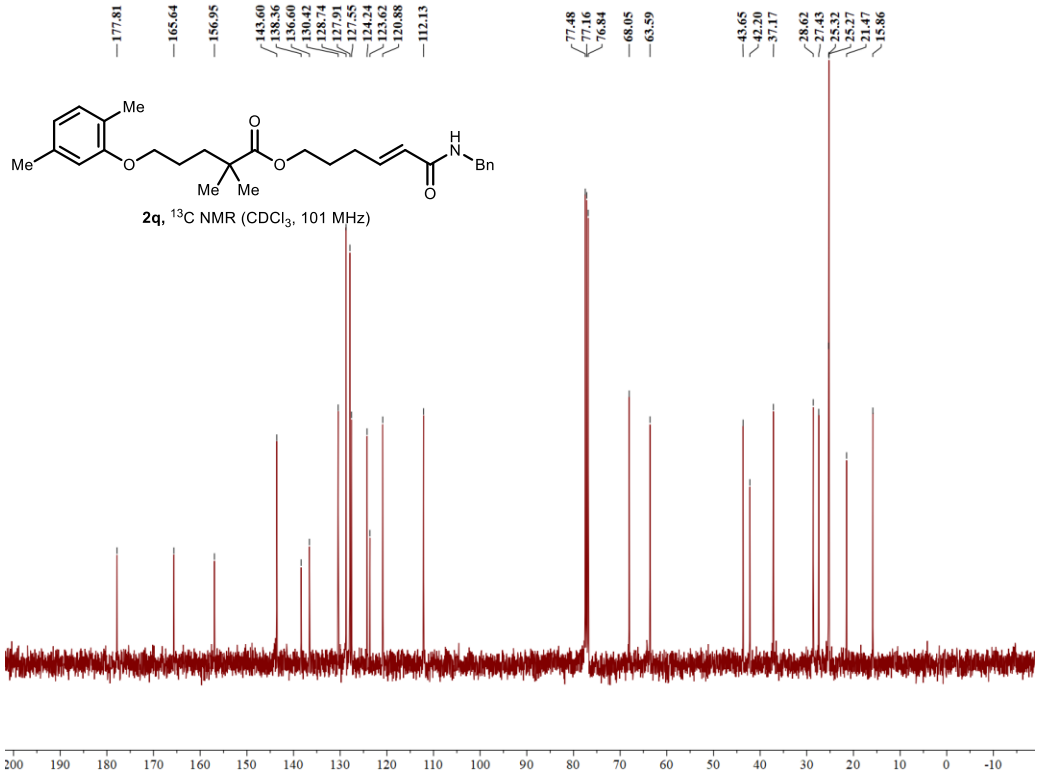


Figure S93. ^{13}C NMR of **2q** ($CDCl_3$, 101 MHz)

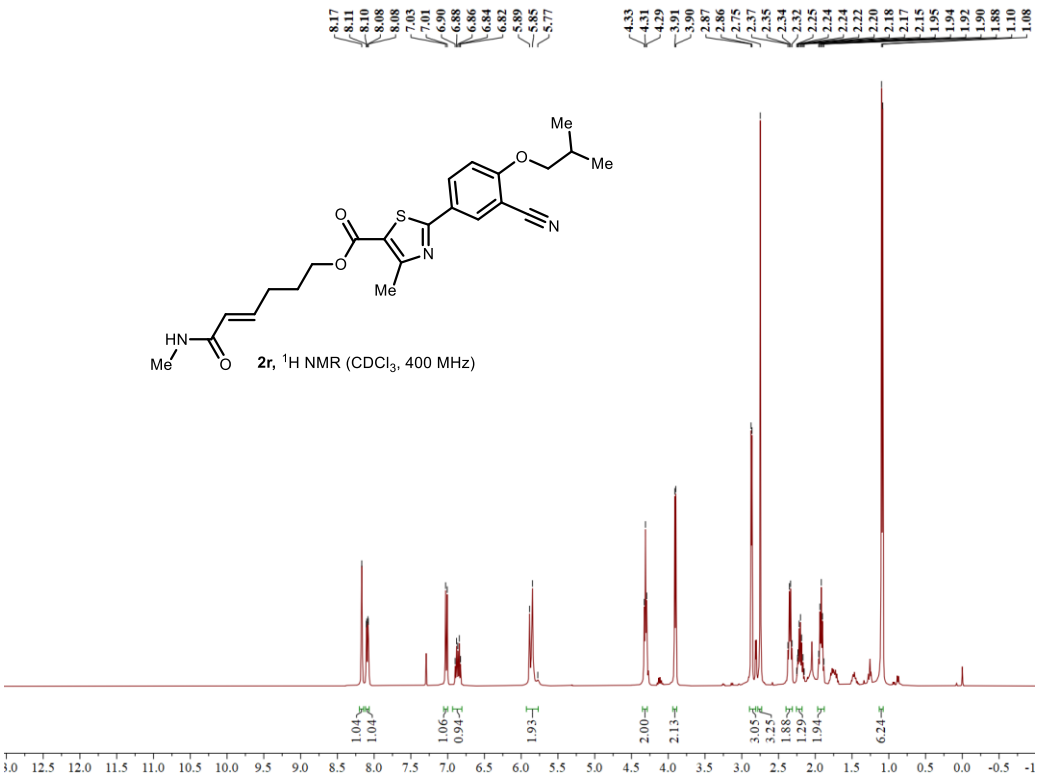


Figure S94. ^{1}H NMR of **2r** (CDCl$_3$, 400 MHz)

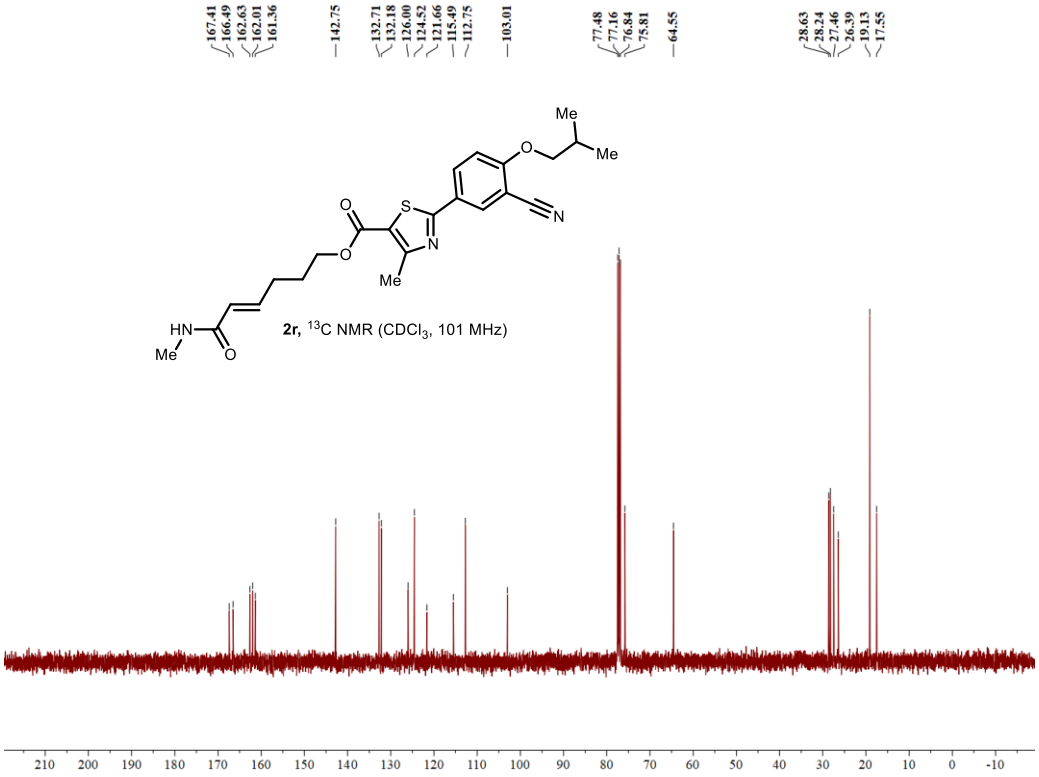


Figure S95. ^{13}C NMR of **2r** (CDCl$_3$, 101 MHz)

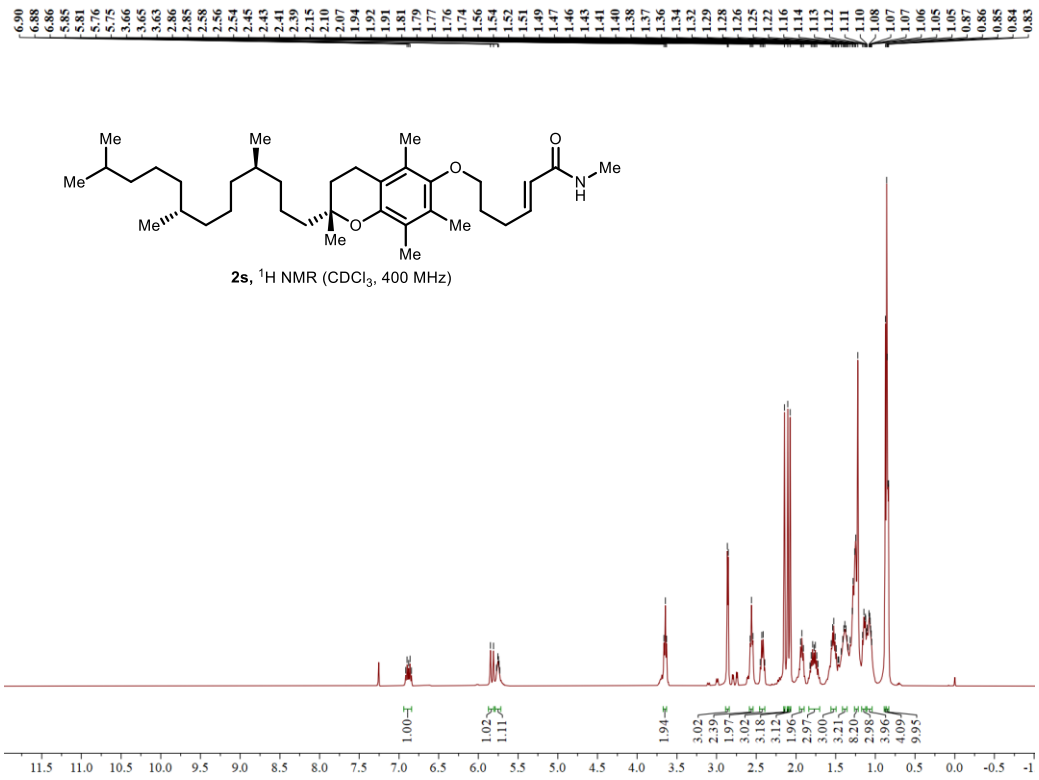


Figure S96. ^{1}H NMR of **2s** ($CDCl_3$, 400 MHz)

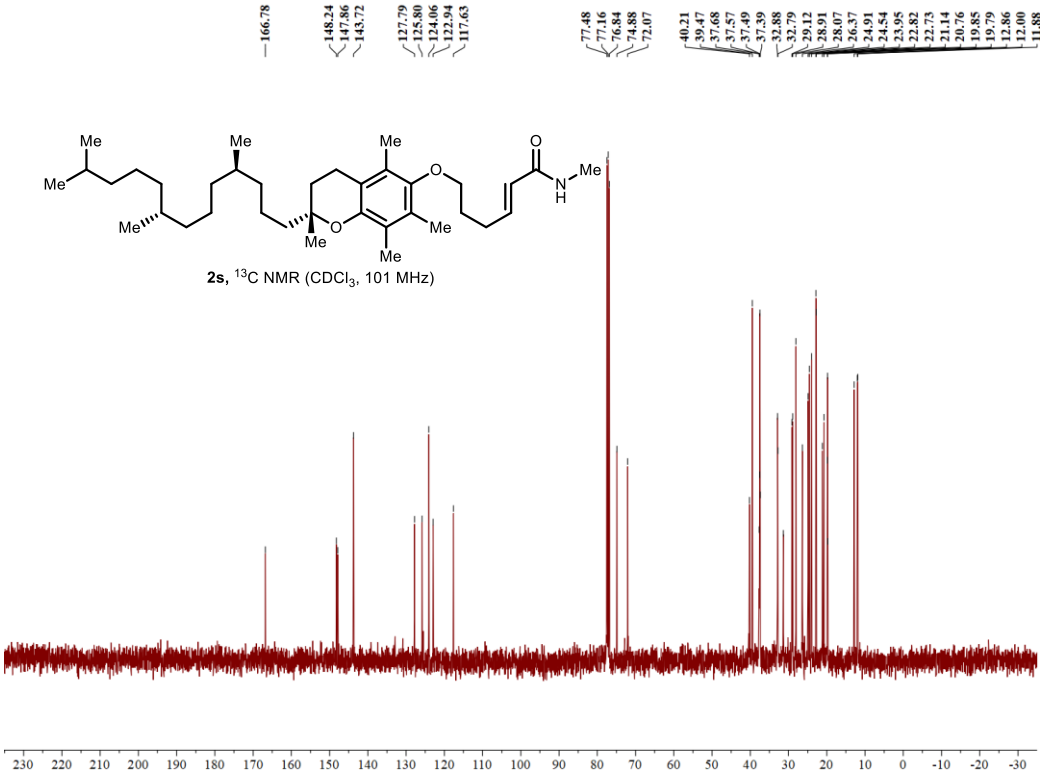


Figure S97. ^{13}C NMR of **2s** ($CDCl_3$, 101 MHz)

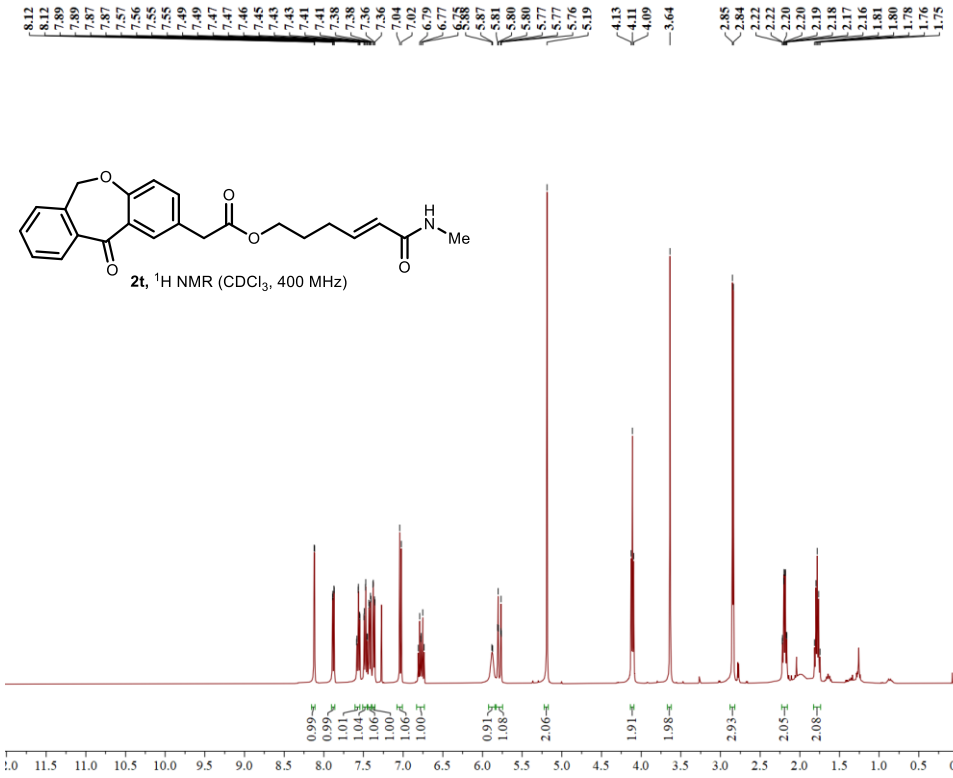


Figure S98. ^{1}H NMR of **2t** ($CDCl_3$, 400 MHz)

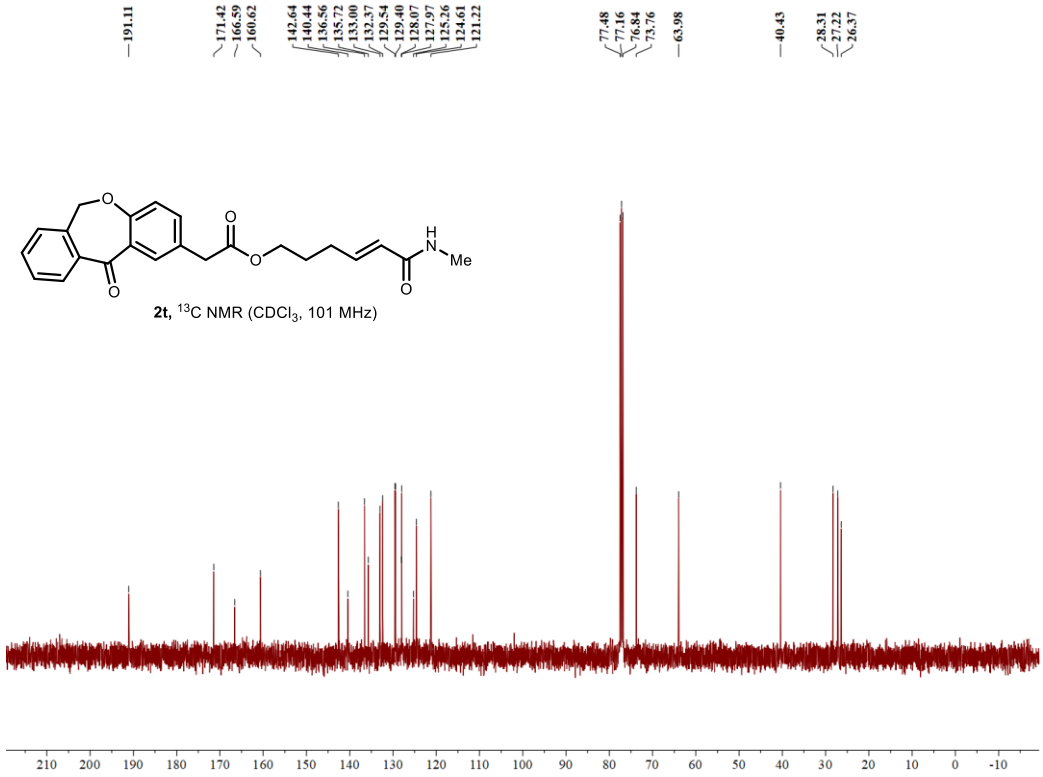
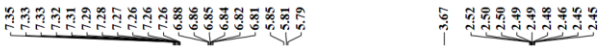
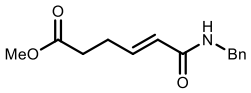


Figure S99. ^{13}C NMR of **2t** ($CDCl_3$, 101 MHz)





2w, ^{1}H NMR ($CDCl_3$, 400 MHz)

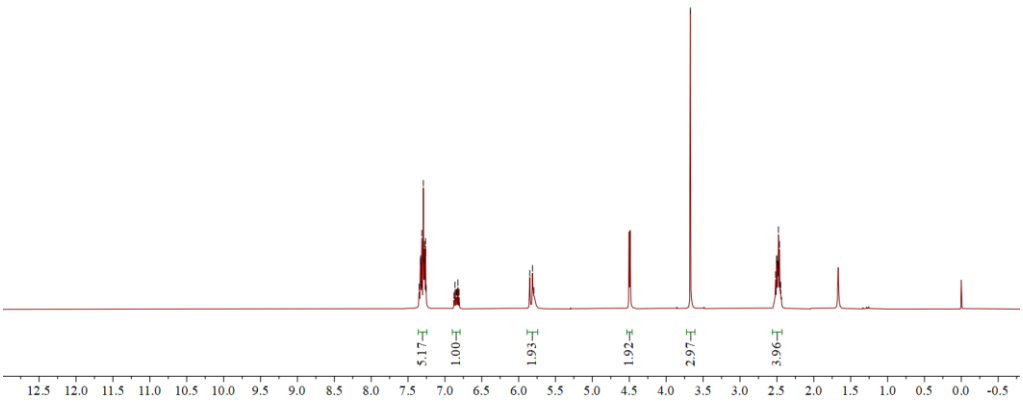
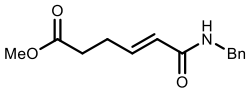


Figure S100. ^{1}H NMR of **2w** ($CDCl_3$, 400 MHz)



2w, ^{13}C NMR ($CDCl_3$, 101 MHz)

Figure S101. ^{13}C NMR of **2w** ($CDCl_3$, 101 MHz)

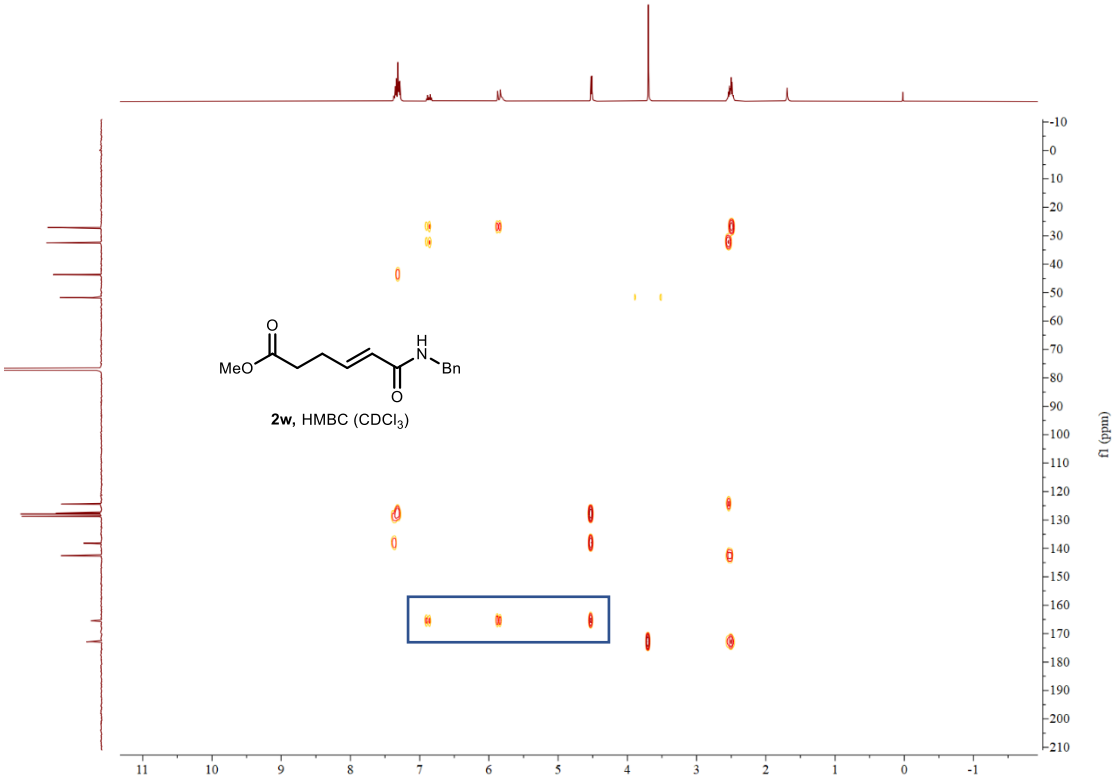
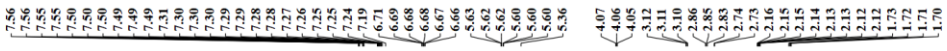
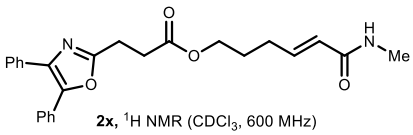


Figure S102 HMBC of **2w**





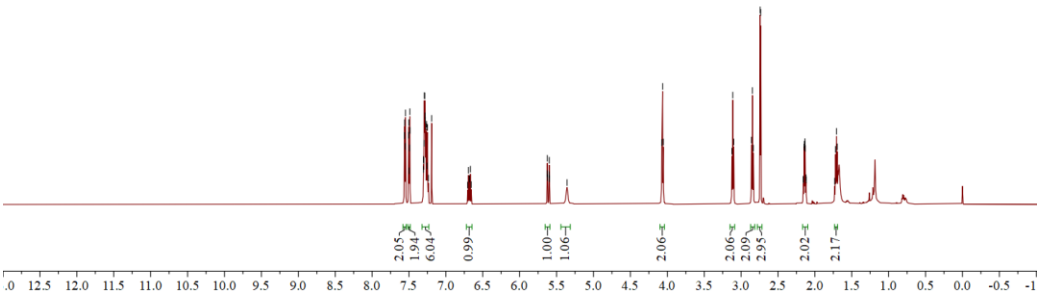


Figure S103. ^{1}H NMR of **2x** ($CDCl_3$, 600 MHz)

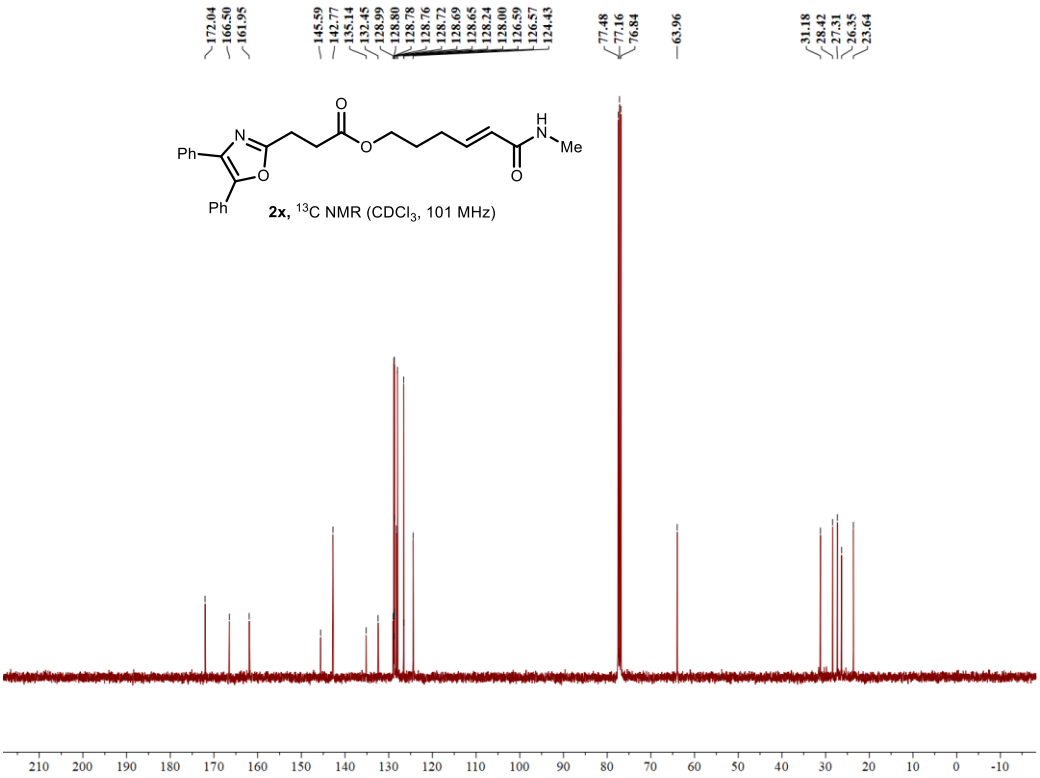


Figure S104. ^{13}C NMR of **2x** ($CDCl_3$, 101 MHz)

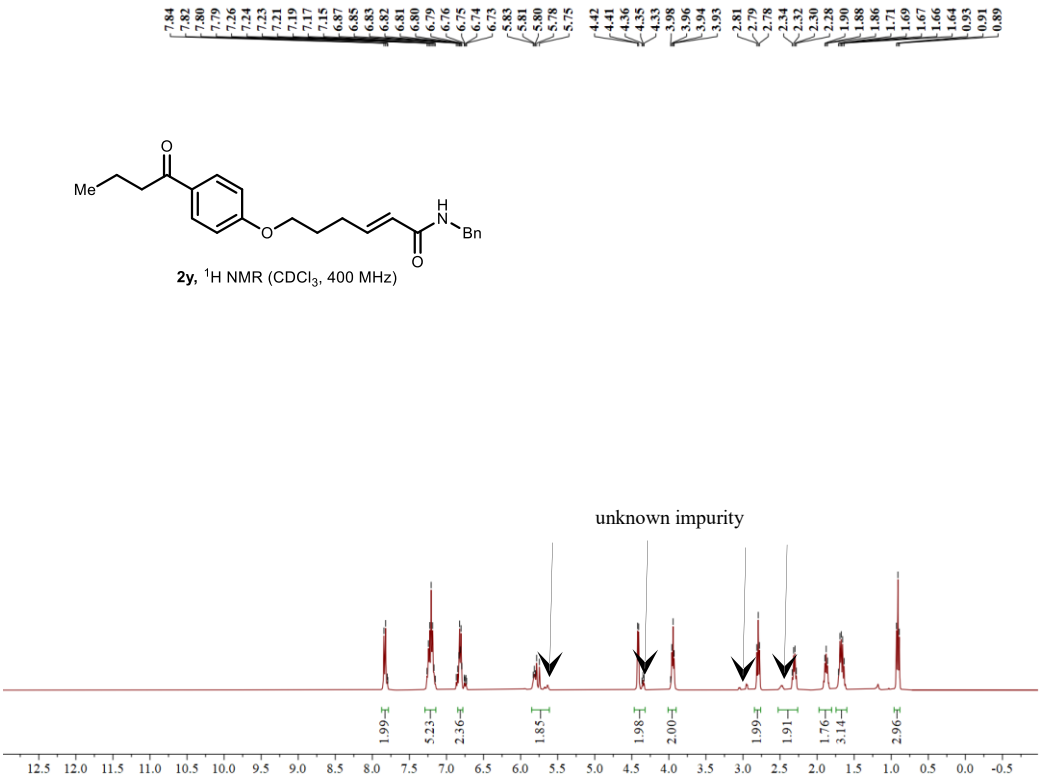


Figure S105. ^{1}H NMR of **2y** ($CDCl_3$, 400 MHz)

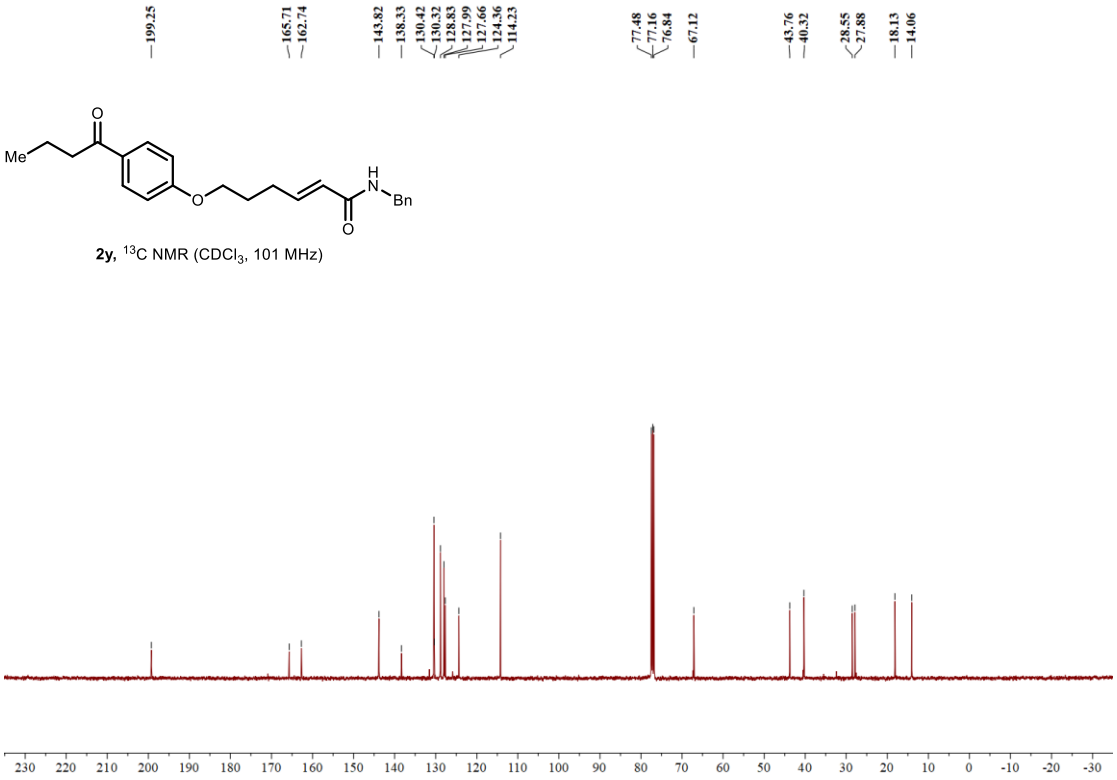


Figure S106. ^{13}C NMR of **2y** ($CDCl_3$, 101 MHz)

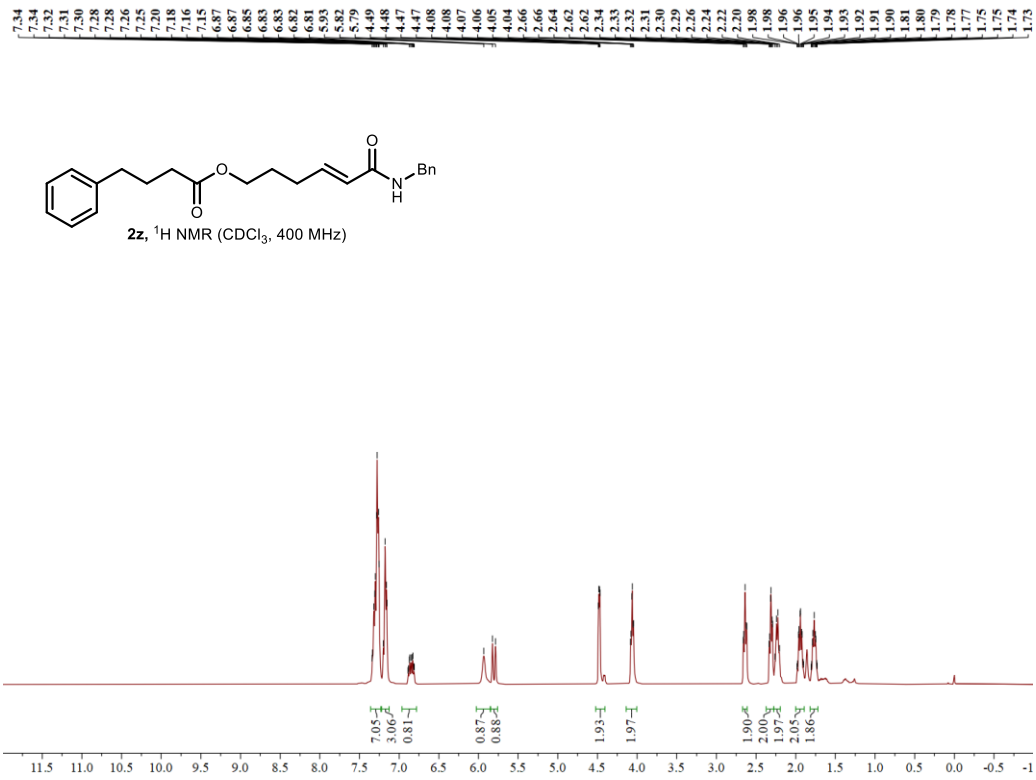


Figure S107. ^{1}H NMR of **2z** ($CDCl_3$, 400 MHz)

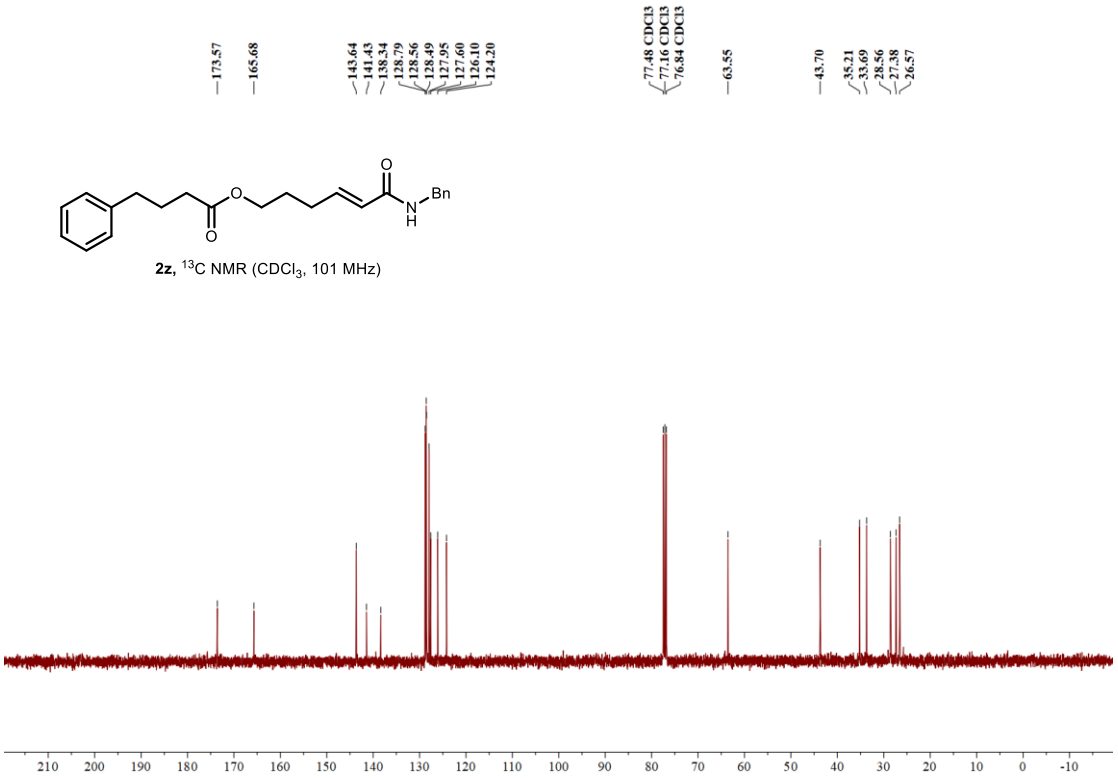


Figure S108. ^{13}C NMR of **2z** ($CDCl_3$, 101 MHz)

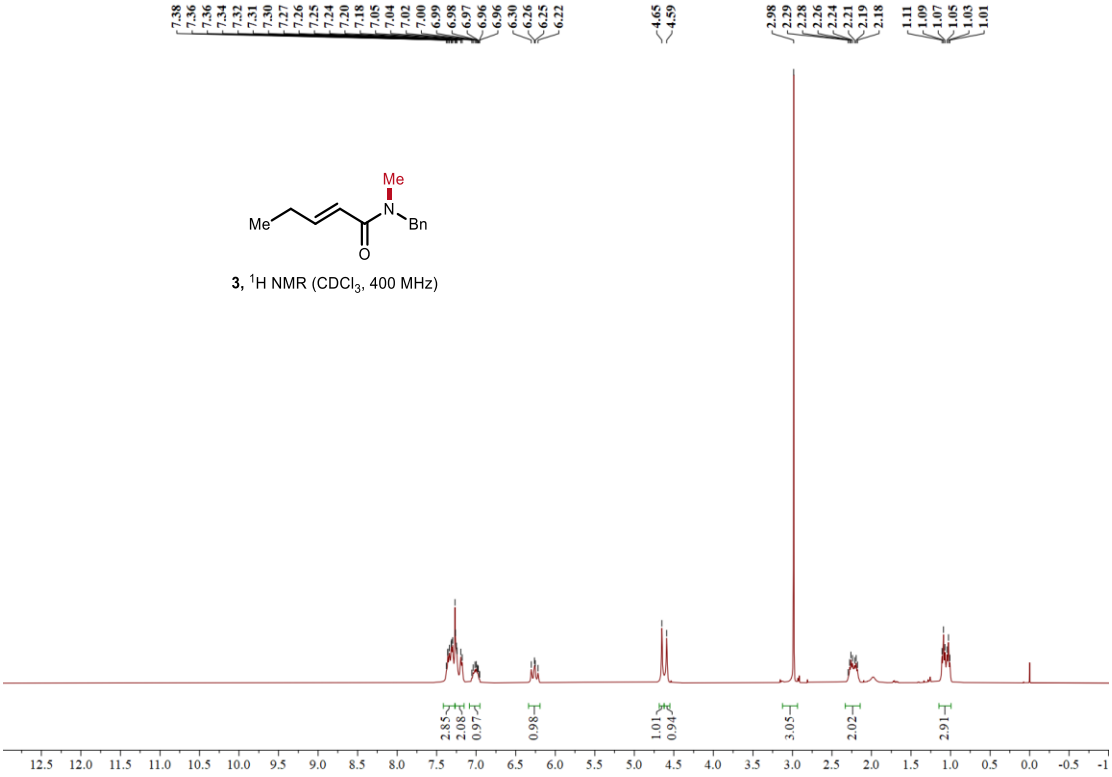


Figure S109. ^{1}H NMR of **3** ($CDCl_3$, 400 MHz)

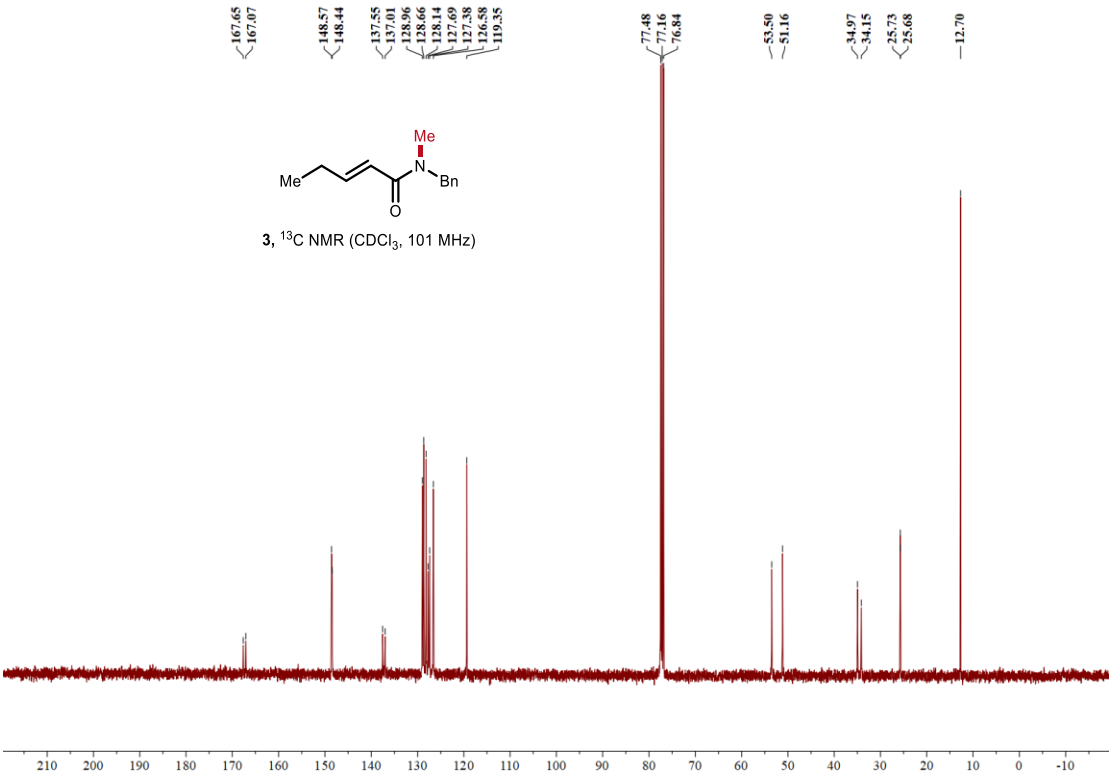


Figure S110. ^{13}C NMR of **3** ($CDCl_3$, 151 MHz)

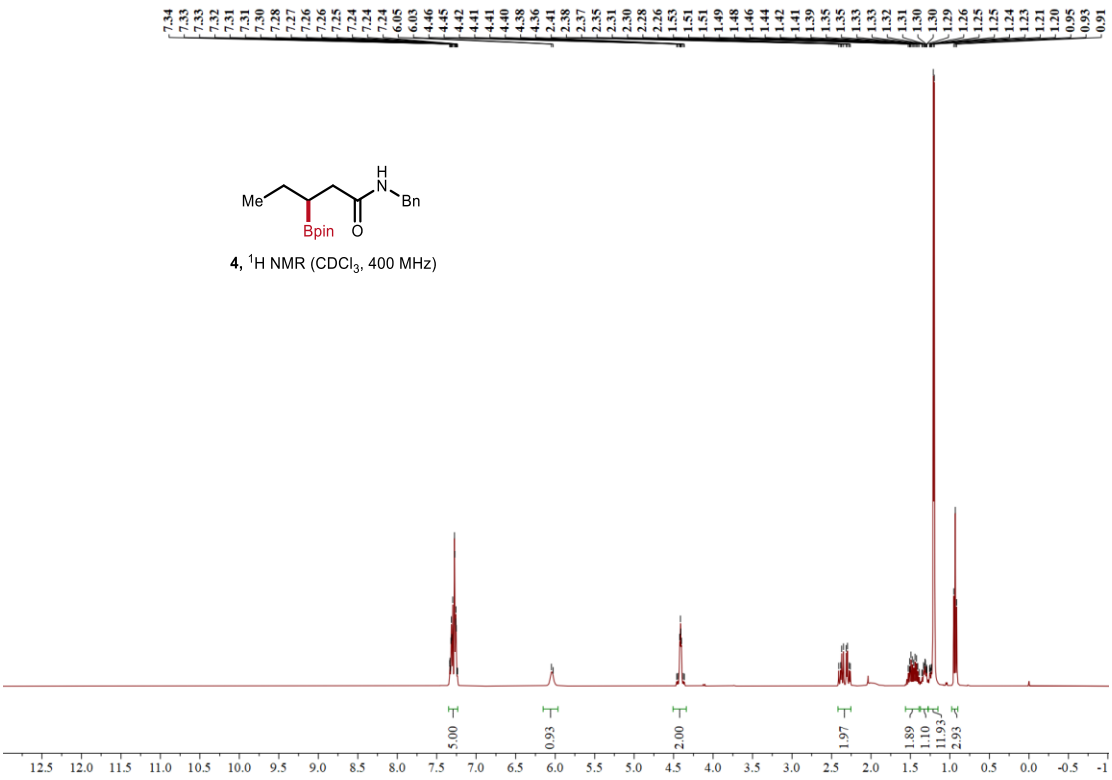


Figure S111. ^{1}H NMR of **4** ($CDCl_3$, 400 MHz)

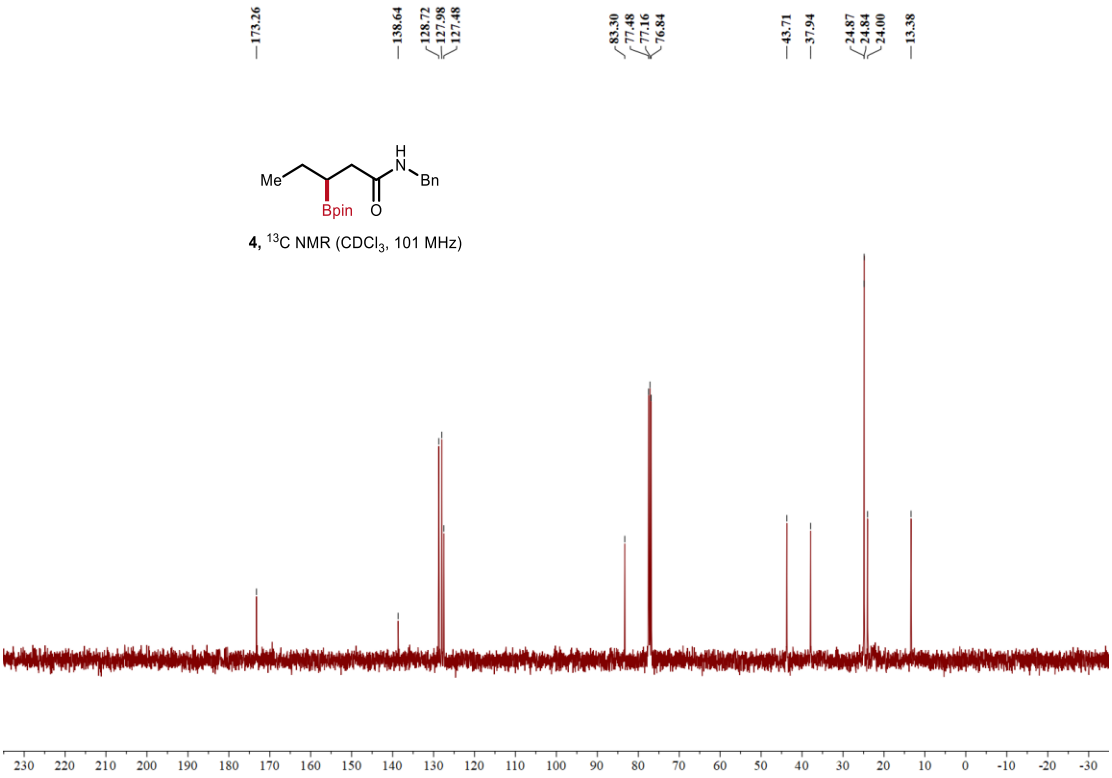


Figure S112. ^{13}C NMR of **4** ($CDCl_3$, 101 MHz)

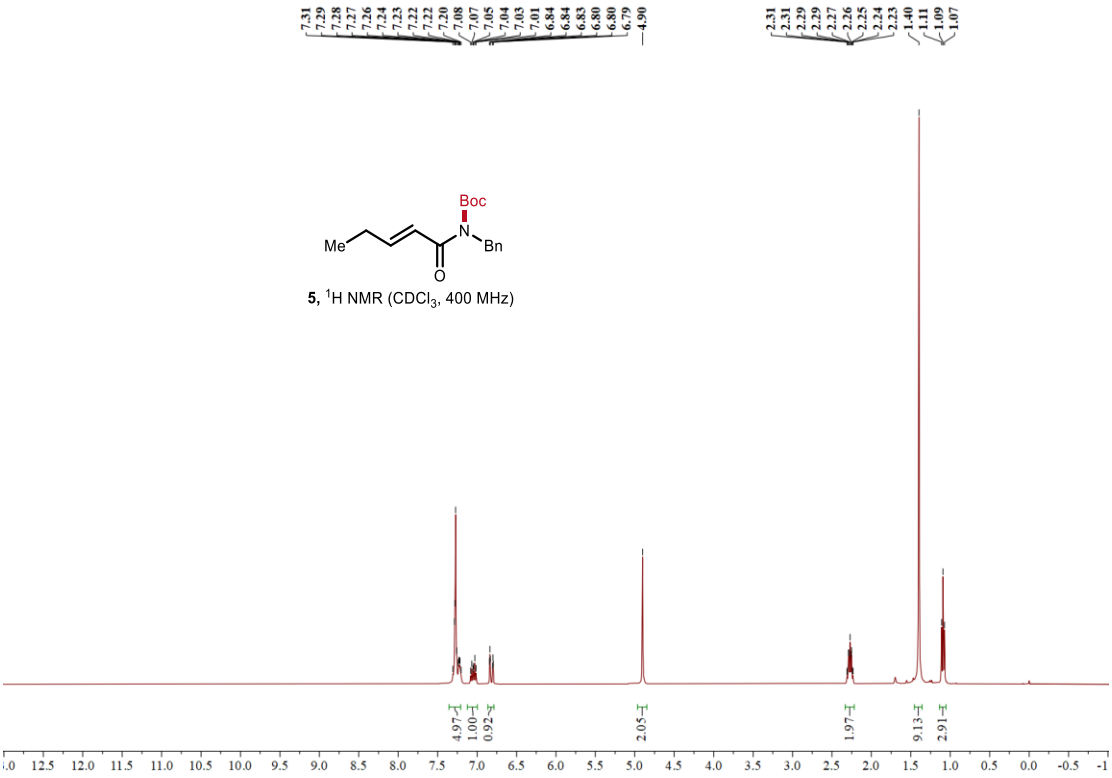


Figure S113. ^{1}H NMR of **5** ($CDCl_3$, 400 MHz)

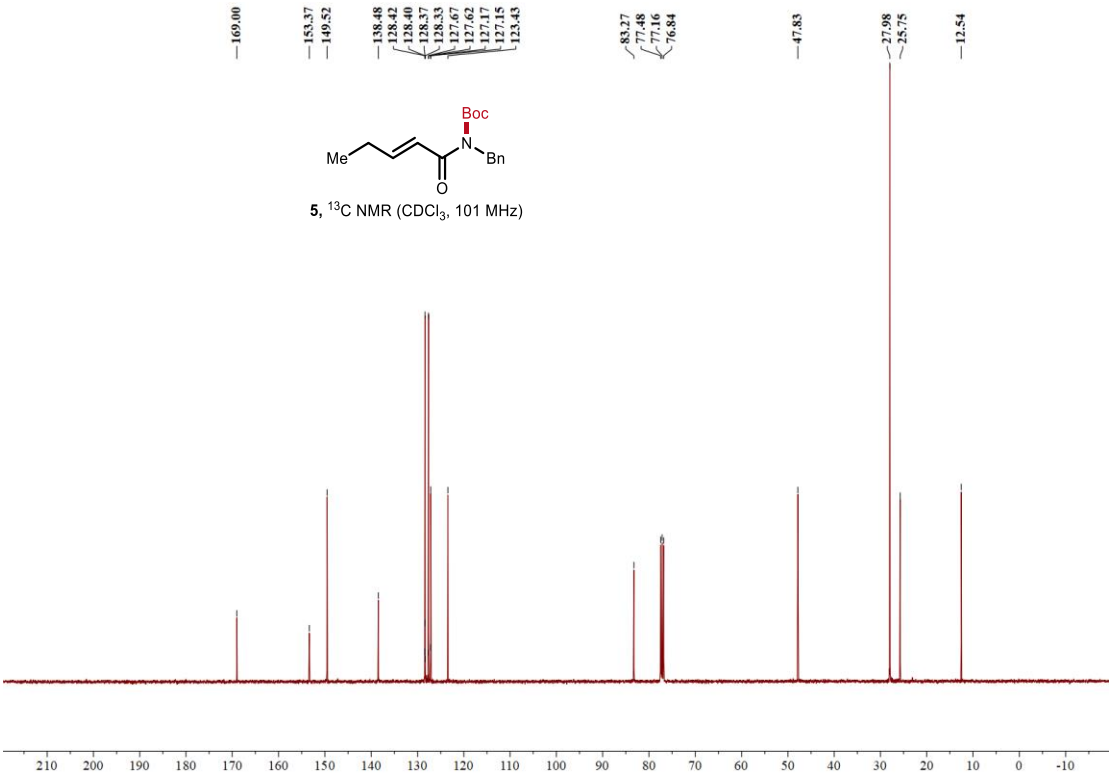


Figure S114. ^{13}C NMR of **5** ($CDCl_3$, 101 MHz)

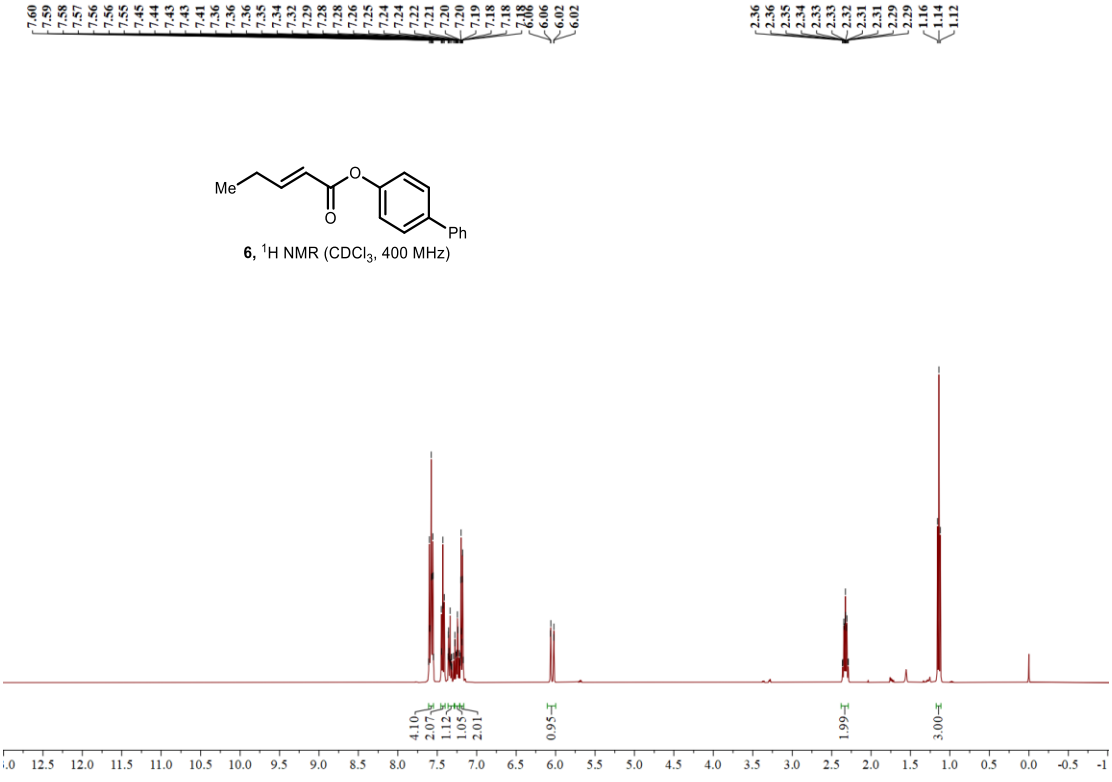


Figure S115. ^{1}H NMR of **6** ($CDCl_3$, 400 MHz)

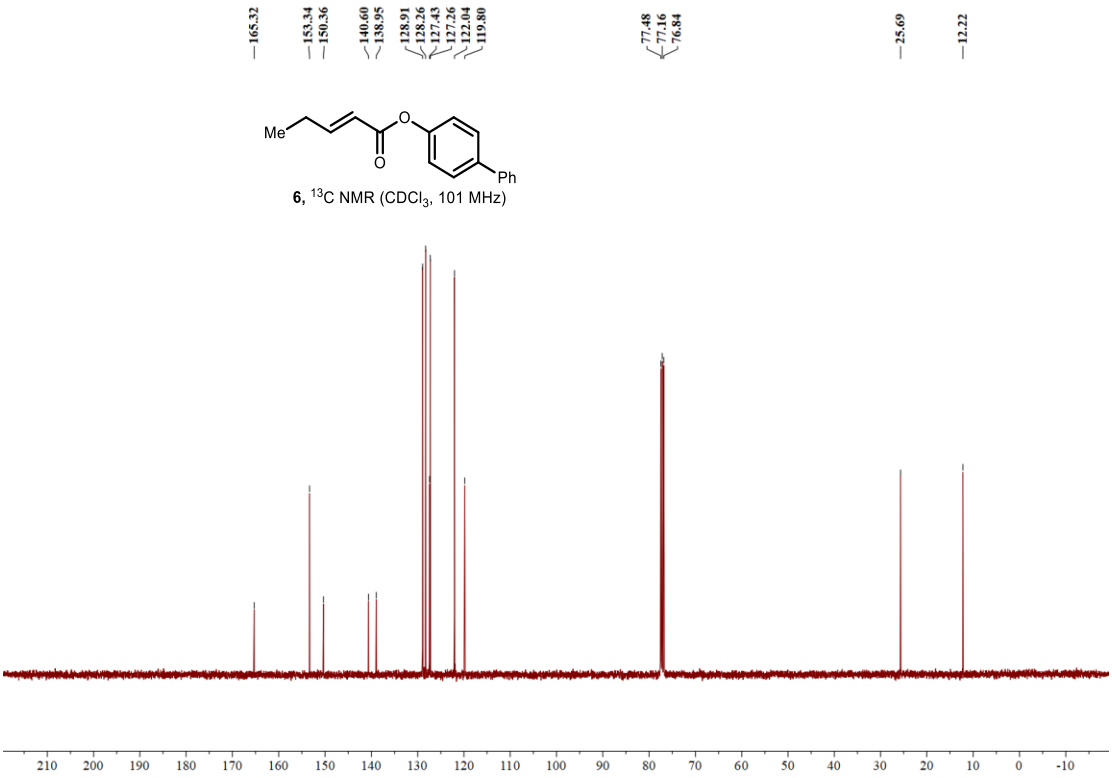


Figure S116. ^{13}C NMR of **6** ($CDCl_3$, 101 MHz)

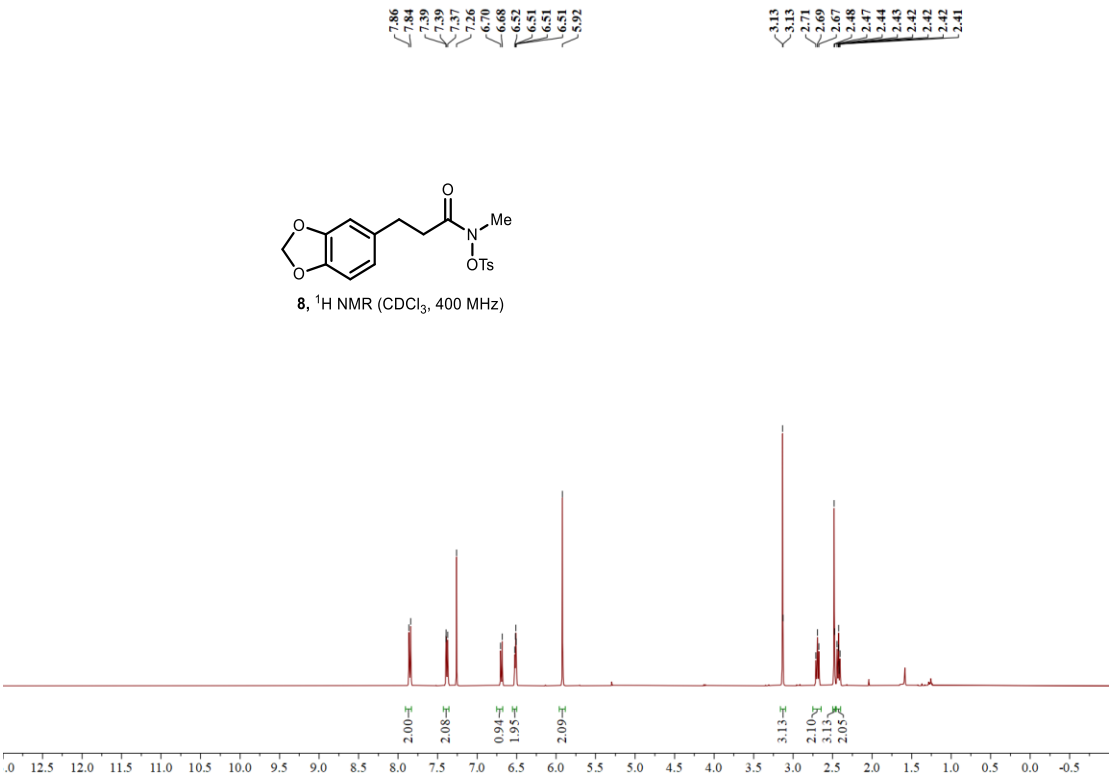


Figure S117. ^{1}H NMR of **8** ($CDCl_3$, 400 MHz)

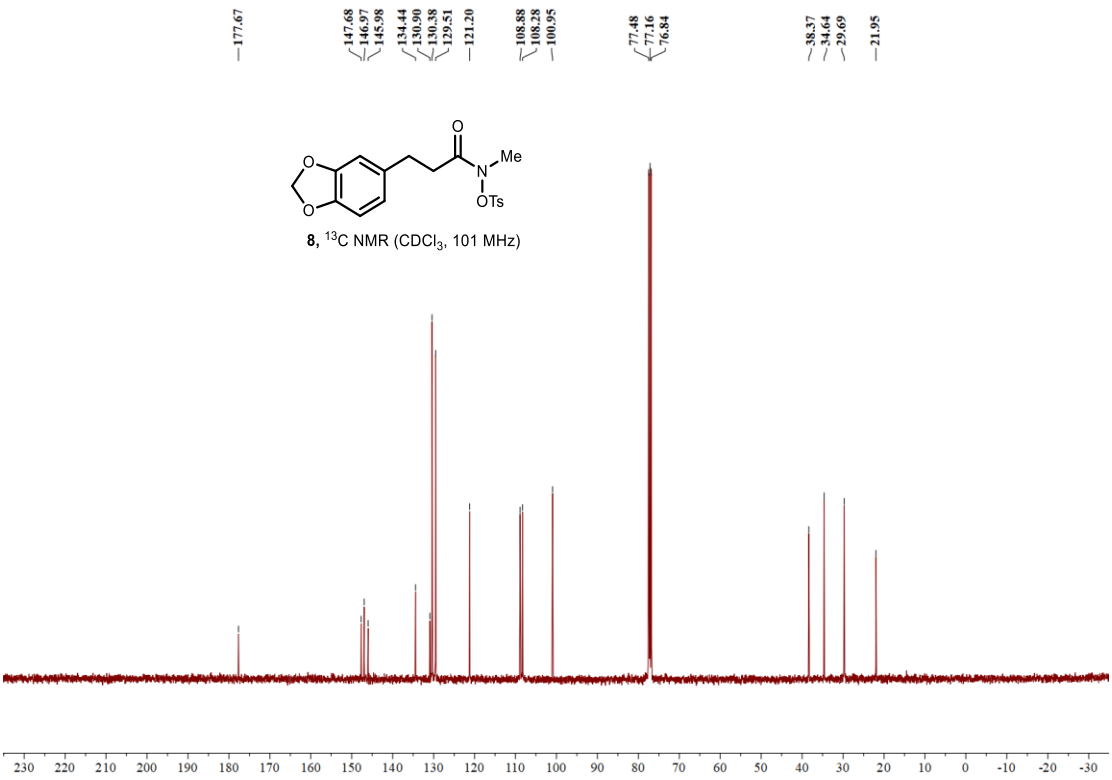


Figure S118. ^{13}C NMR of **8** ($CDCl_3$, 101 MHz)

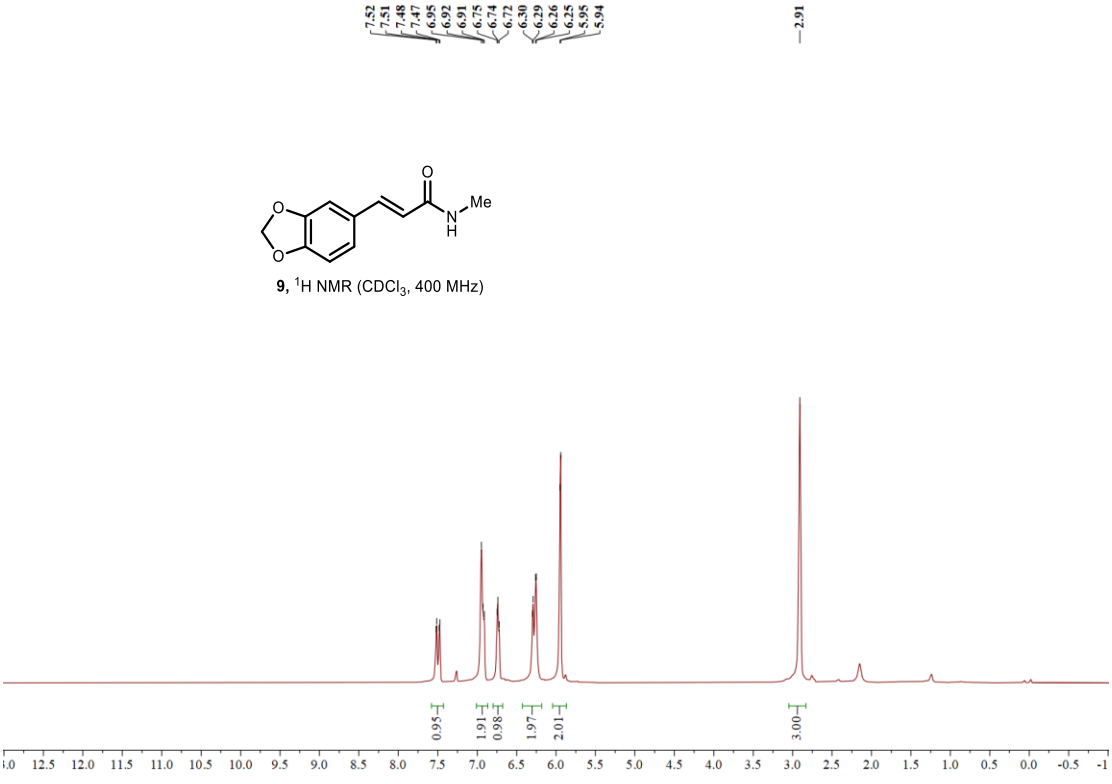


Figure S119. ^{1}H NMR of **9** ($CDCl_3$, 400 MHz)

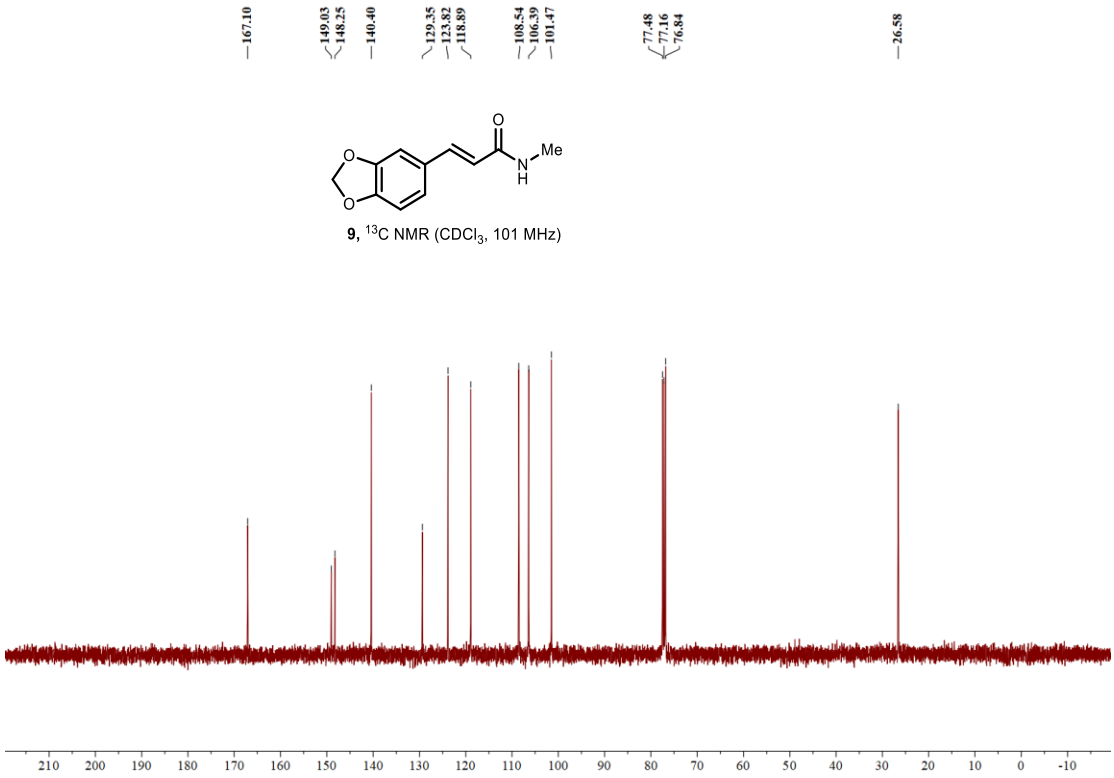


Figure S120. ^{13}C NMR of **9** ($CDCl_3$, 101 MHz)

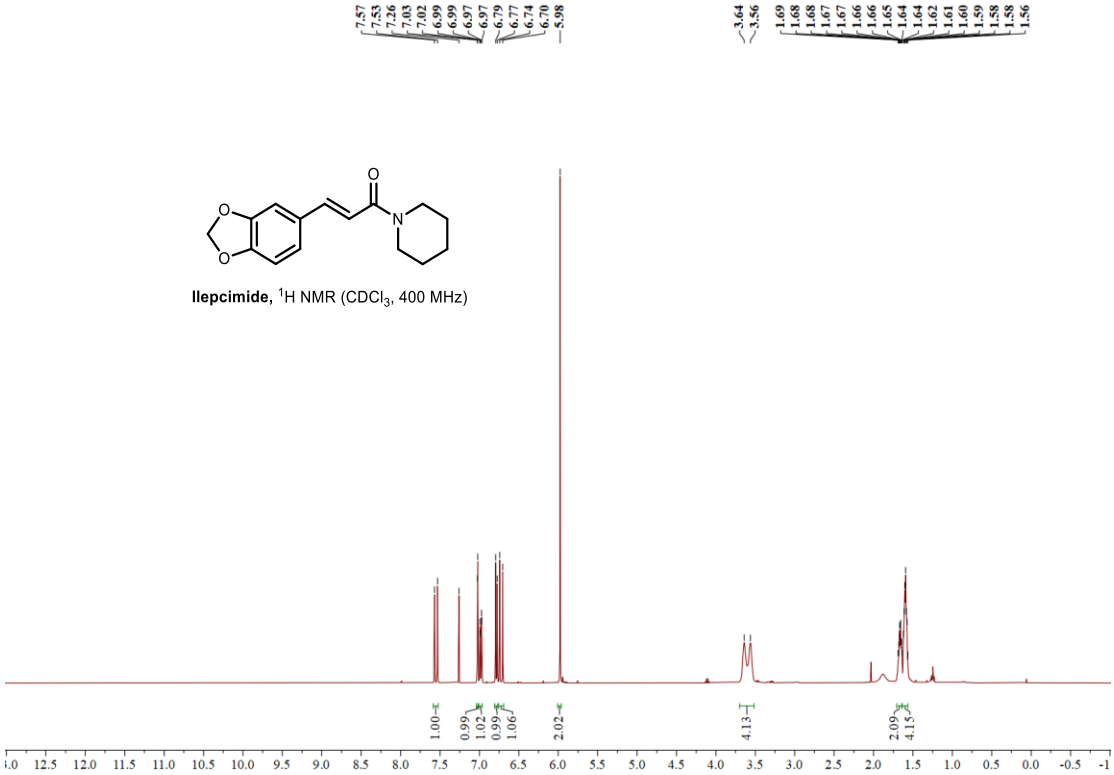


Figure S121. ^{1}H NMR of **Ilepcimide** ($CDCl_3$, 400 MHz)

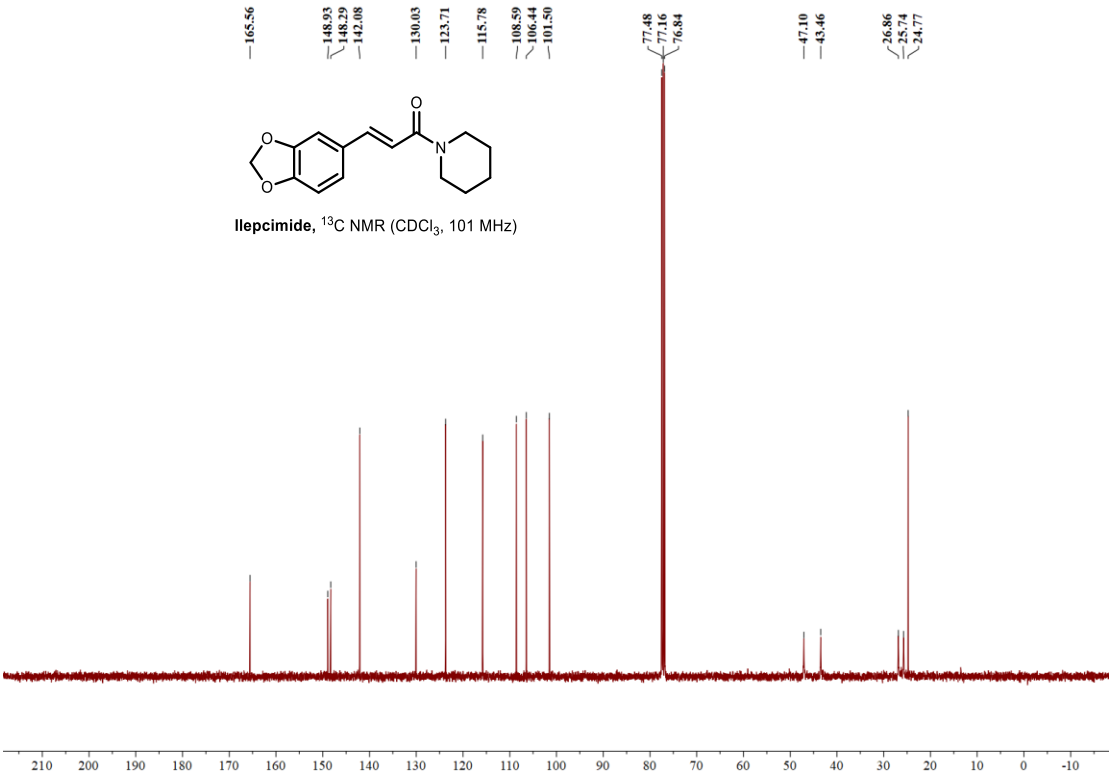


Figure S122. ^{13}C NMR of **Ilepcimide** ($CDCl_3$, 101 MHz)

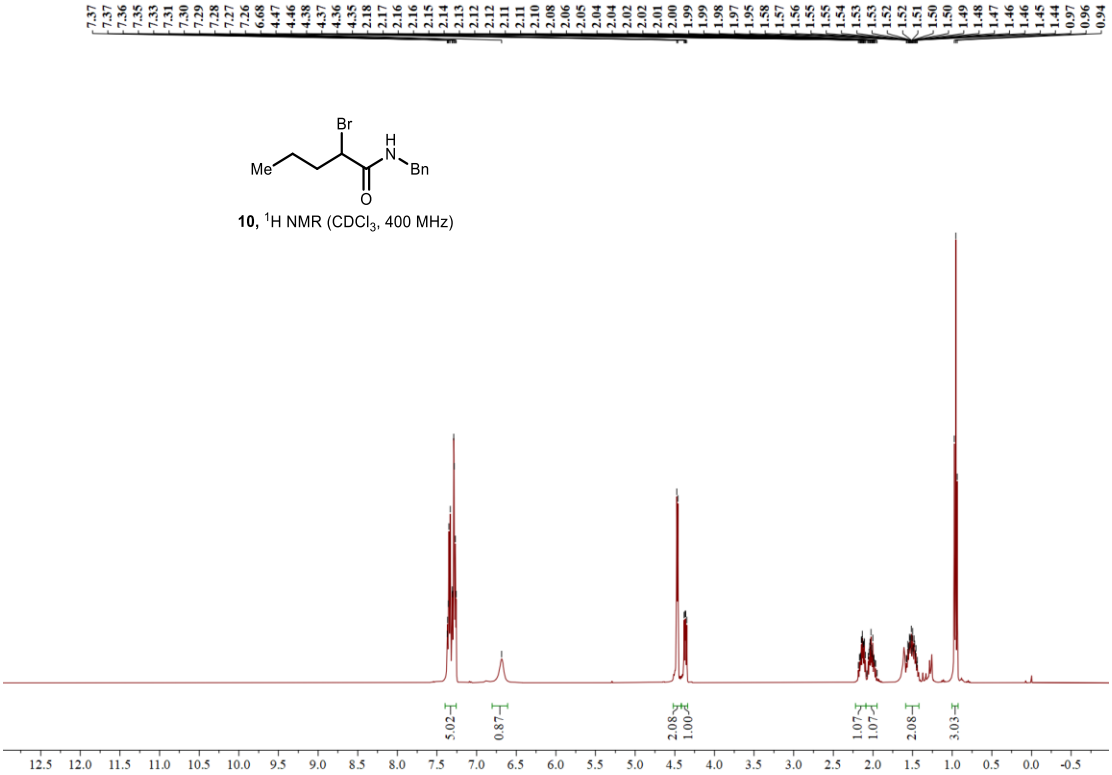


Figure S123. ^{1}H NMR of **10** ($CDCl_3$, 400 MHz)

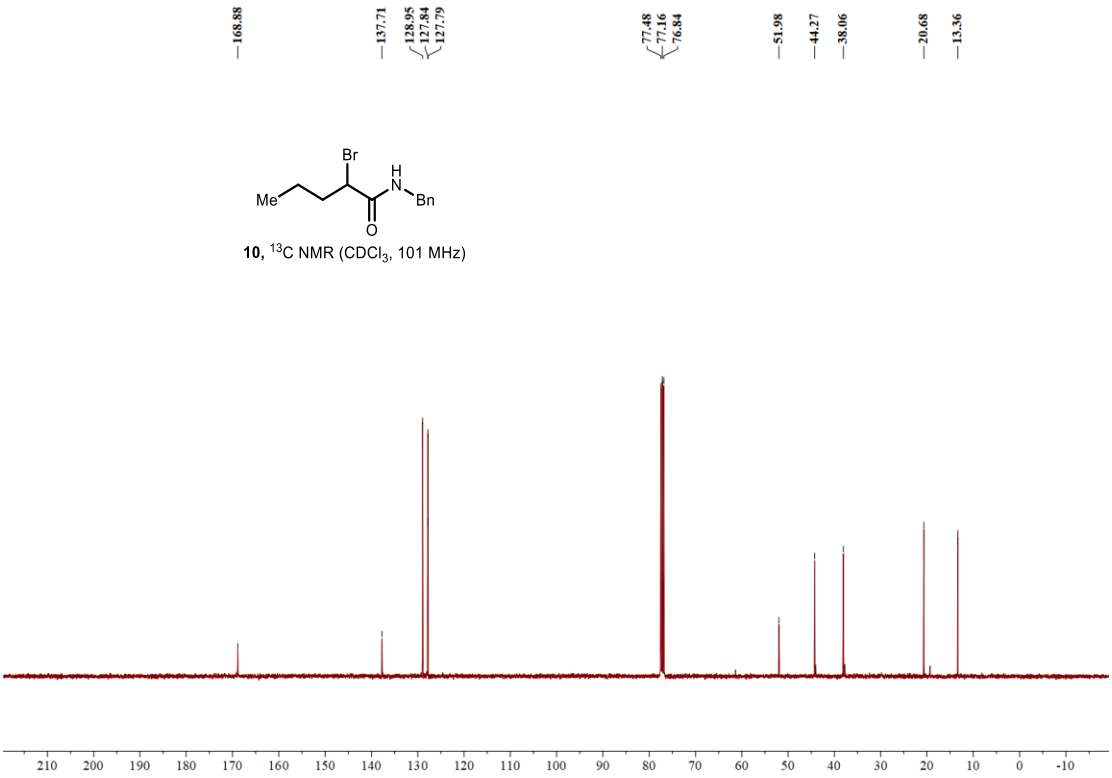


Figure S124. ^{13}C NMR of **10** ($CDCl_3$, 101 MHz)

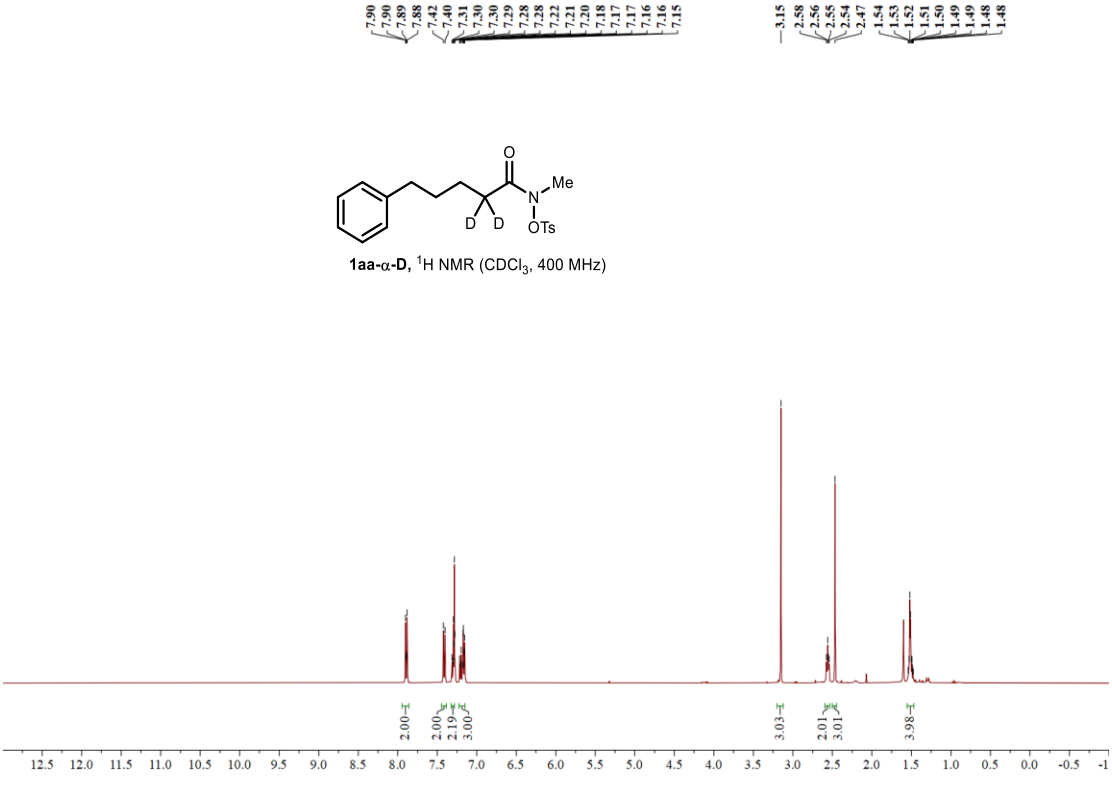


Figure S125. ^{1}H NMR of **1aa-α-D** ($CDCl_3$, 400 MHz)

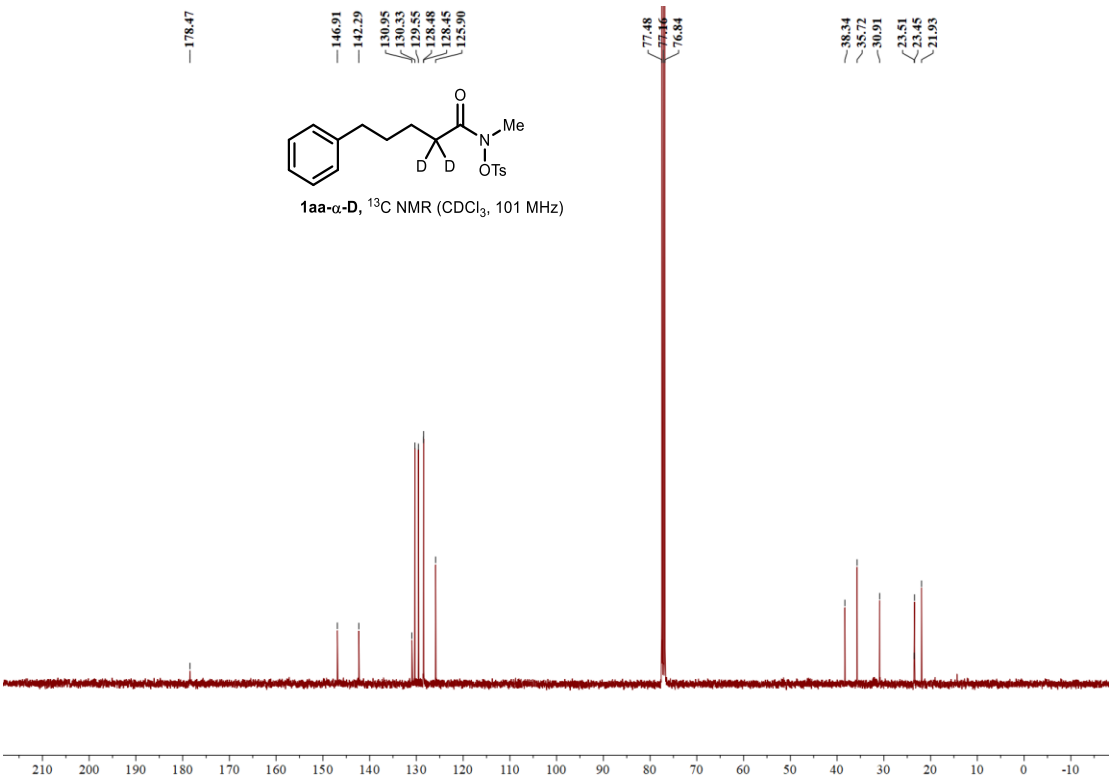


Figure S126. ^{13}C NMR of **1aa-α-D** ($CDCl_3$, 101 MHz)

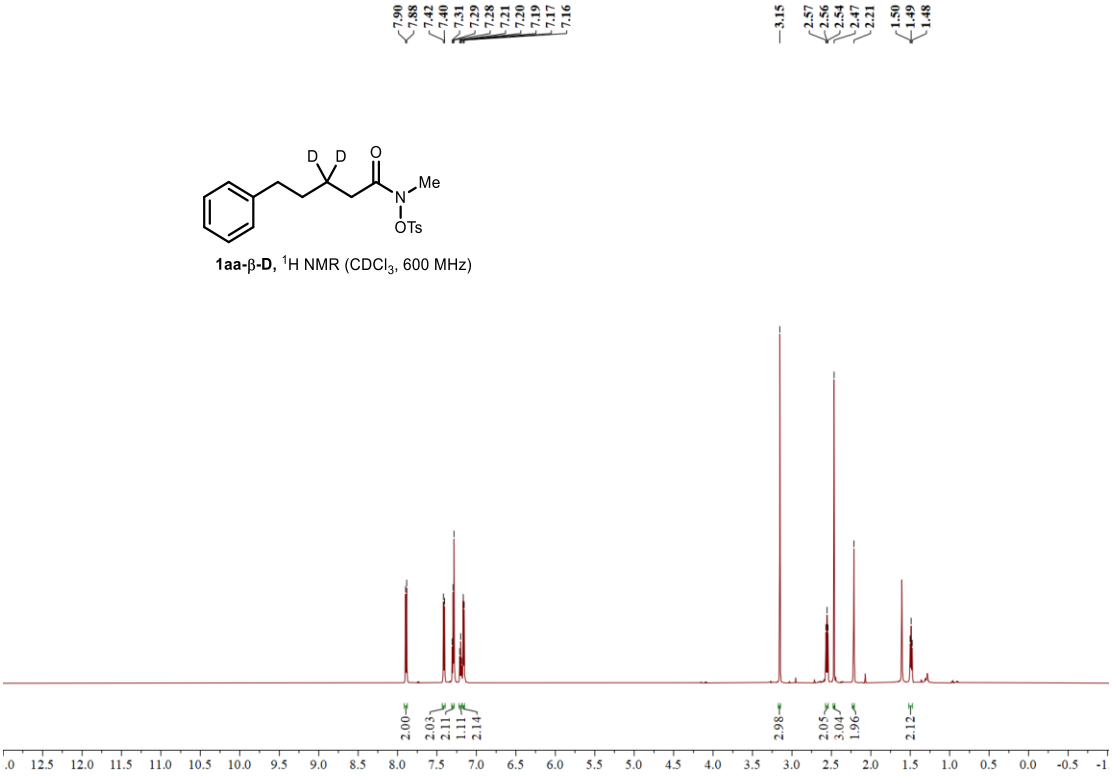


Figure S127. ^{1}H NMR of **1aa-β-D** ($CDCl_3$, 600 MHz)

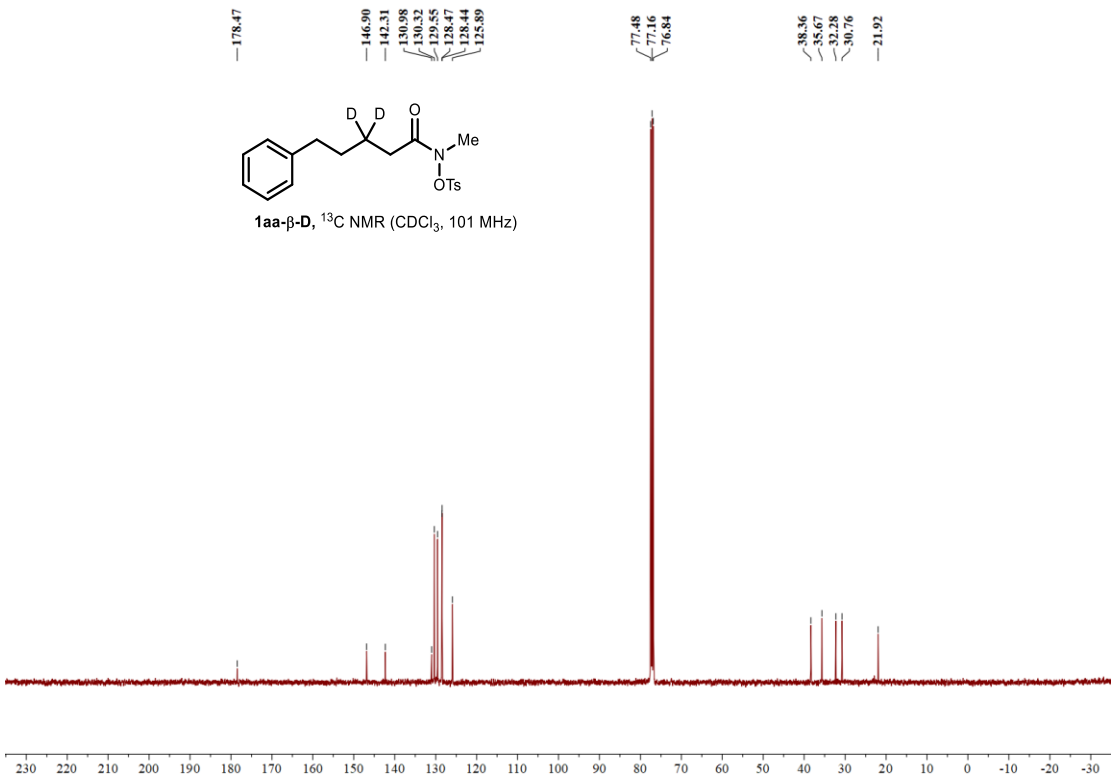


Figure S128. ^{13}C NMR of **1aa-β-D** ($CDCl_3$, 101 MHz)

12. References

1. Hoffman, R. V.; Nayyar, N. K.; Chen, W., .alpha.-Lactam intermediates in base-promoted reactions of O-sulfonylated hydroxamic acids with nucleophiles. *Journal of the American Chemical Society* **1993,** *115* (12), 5031-5034.
2. Banerjee, A.; Yamamoto, H., Direct N–O bond formation via oxidation of amines with benzoyl peroxide. *Chemical Science* **2019,** *10* (7), 2124-2129.
3. Chea, H.; Sim, H.-S.; Yun, J., Copper-Catalyzed Conjugate Addition of Diboron Reagents to α,β-Unsaturated Amides: Highly Reactive Copper-1,2- Bis(diphenylphosphino)benzene Catalyst System. *Advanced Synthesis & Catalysis* **2009,** *351* (6), 855-858.
4. Danfeng Ye, H. C., Zhiyuan Liu, Chuanhu Lei, Transamidation of N-Benzyl-N-Boc-amides under Transition Metal-Free and Base-Free Conditions. *Chinese Journal of Organic Chemistry*, **2021,** *41* (4), 1658-1669.
5. Barde, E.; Guérinot, A.; Cossy, J., Cobalt-Catalyzed Cross-Coupling of α-Bromo Amides with Grignard Reagents. *Organic Letters* **2017,** *19* (22), 6068-6071.
6. Yang, S.; Fan, H.; Xie, L.; Dong, G.; Chen, M., Photoinduced Desaturation of Amides by Palladium Catalysis. *Organic Letters* **2022,** *24* (35), 6460-6465.
7. Wang, Z.; He, Z.; Zhang, L.; Huang, Y., Iridium-Catalyzed Aerobic α,β-Dehydrogenation of γ,δ-Unsaturated Amides and Acids: Activation of Both α- and β-C–H bonds through an Allyl–Iridium Intermediate. *Journal of the American Chemical Society* **2018,** *140* (2), 735-740.