Electronic Supplementary Material (ESI) for Chemical Science.

Pd(II)-Catalyzed β– and γ– C-(Sp3)-H Dienylation with Allenyl Acetates

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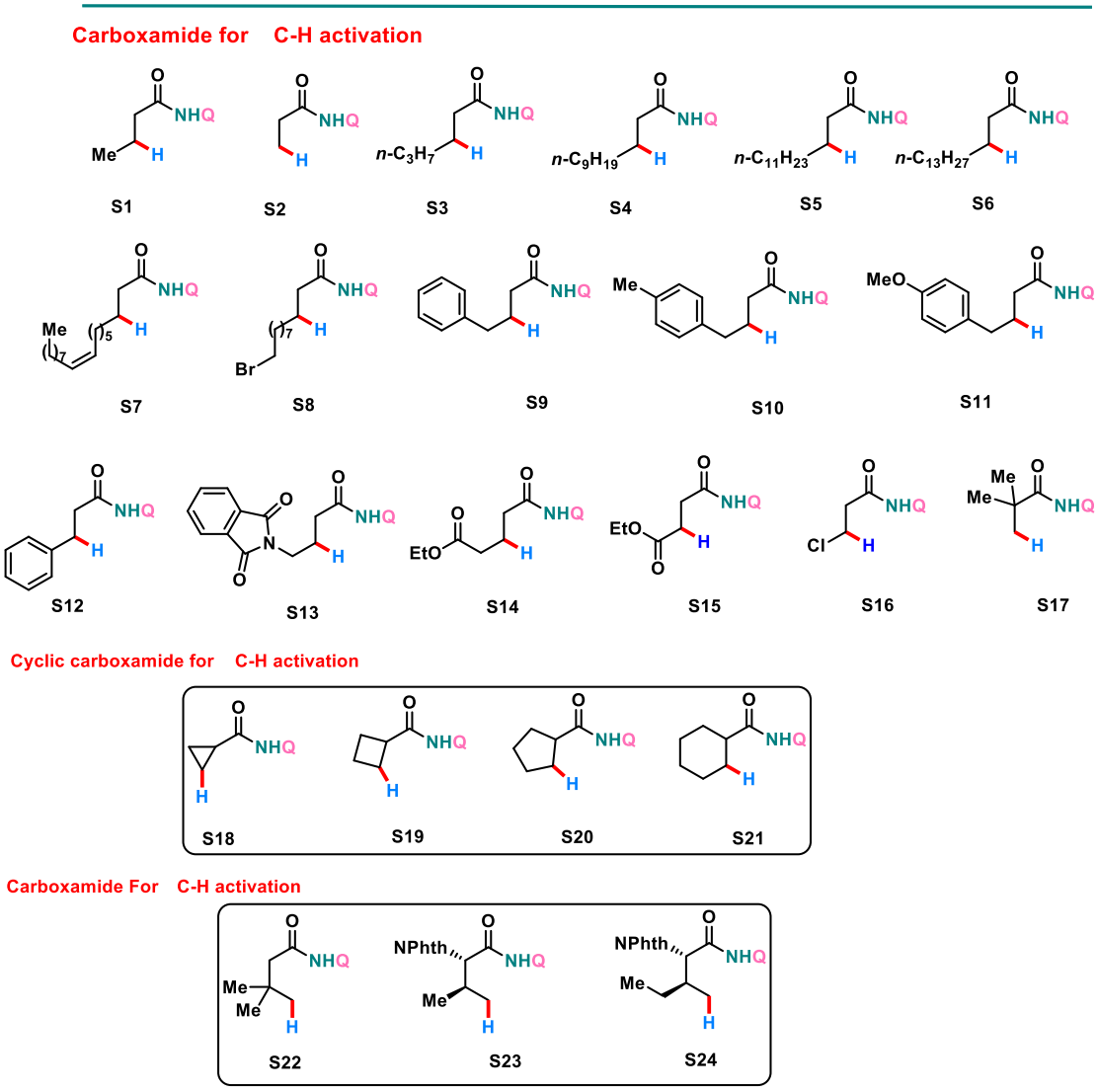
1. General considerations and reagent information

Unless otherwise stated, all reactions were carried out under air atmosphere in screw cap reaction tubes. All the solvents were bought from Aldrich in sure-seal bottle and were used as received. $Pd(OAc)_2$ and other reagents were bought from Aldrich. The reactions were performed using IKA RCT basic stirrer equipped with oil bath for heating. For column chromatography, silica gel (100–200 mesh) from Finar Co. was used. A gradient elution using petroleum ether and ethyl acetate was performed based on Merck aluminum TLC sheets (silica gel 60F254). All directing groups attached to the aliphatic acids and allenes were prepared according to the reported procedures in the literatures and the analytical data are in accord with the literature. Analytical information of All new isolated compounds are characterized by ^1H NMR, ^{13}C NMR spectroscopy. In addition, all the compounds are further characterized by HRMS. Copies of ^1H NMR and ^{13}C NMR can be found in the supporting information. Nuclear magnetic resonance spectra were recorded either on a Bruker 500 or a 400 MHz instrument. All ^1H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All ^{13}C NMR spectra were reported in ppm relative to deuteron chloroform (77.16 ppm), unless otherwise stated, and all were obtained with ^1H decoupling.

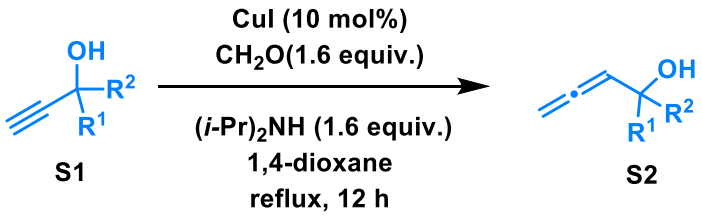
2. General procedure for the preparation of 8-aminoquinolinyl amides Synthesis of Amides from Carboxylic Acids[1]

To a stirred solution of carboxylic acid (15 mmol) in CH_2Cl_2 (10 mL), $(COCl)_2$, (1.5 mL, 18 mmol) was added dropwise. The solution was magnetically stirred at room temperature for 2 h. The solvent was then eliminated under reduced pressure, and the resulting residue was dissolved in CH_2Cl_2 (15 mL). After cooling the reaction mixture to 0 °C, a solution of 8-Aminoquinoline (15 mmol) and triethylamine (36 mmol) in 10 mL of the same solvent were added dropwise. The resulting mixture was allowed to warm to rt and stirred overnight. The crude product was washed with saturated aqueous $NaHCO_3$ (20 mL), and CH_2Cl_2 (3x20 mL). The organic phase was washed with 1 M HCl aq. (20 mL). The organic phase was dried over anhydrous Na_2SO_4 and the solvent removed by evaporation of the solvent. The resulting crude amide was purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 9/1).



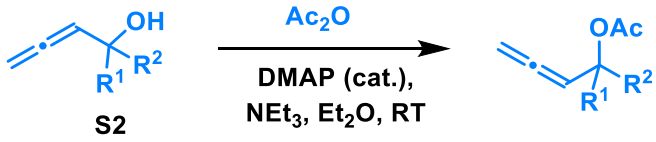
3. General Procedure for the preparation of allenyl Alcohols and Allenyl Acetates[2,3]:

Step 1: To a two-necked round bottom-flask equipped with a magnetic stir bar were added under nitrogen CuI (10 mol%), paraformaldehyde (1.6 equiv.) and 1,4-dioxane followed by propargylic alcohol (**S1**, 1 equiv.) and *N,N*-Di-isopropyl-amine (1.4 equiv.). The reaction mixture was refluxed for 6 hours and then cooled to room temperature. Then the mixture was filtered through a Celite plug and diluted with water followed by diethyl ether and acidified with 6 *N* HCl to pH 2. The organic layer was separated and the aqueous phase was extracted with diethyl ether for two additional times. The organic phase was then washed with saturated $NaHCO_3$, brine and dried over $MgSO_4$. After filtration and evaporation under reduced pressure, the residue was directly used for the next step.

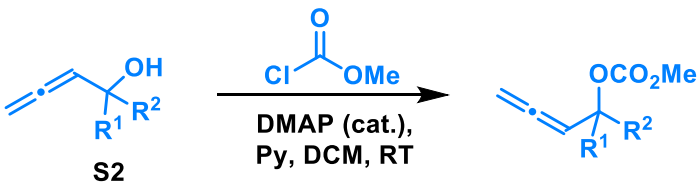


Step 2:

(a) Preparation of allenyl acetate: To a solution of **S2** (16.5 mmol) in Et_2O (50 mL) were added Ac_2O (2.4 mL, d = 1.08 g/mL, 2.53 g, 25 mmol, 1.5 equiv.), Et_3N (3.6 mL, d = 0.70 g/mL, 2.52 g, 25 mmol, 1.5 equiv.), and DMAP (0.7001 g, 5.7 mmol, 35 mol %). The resulting mixture was stirred at room temperature until complete conversion of **S2** as monitored by TLC. The reaction mixture was then quenched with water (10 mL), extracted with Et_2O (3 × 40 mL), sequentially washed with 5% HCl, sat. $NaHCO_3$(aq.), brine, and dried over anhydrous Na_2SO_4. After filtration and evaporation, flash chromatography on silica gel (eluent: petroleum ether/diethyl ether = 100/1)

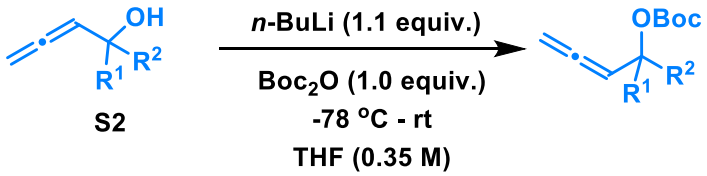


(b) Preparation of allenyl carbinol carbonates: To a round bottom flask equipped with a magnetic stir bar were added under argon allenol **S2** (1equiv.), DMAP (122 mg, 1.0 mmol, 0.2 equiv.), pyridine (790 mg, 10 mmol, 2.0 equiv.) and dichloromethane (0.3 M). The mixture was cooled to 0 °C and then methyl chloroformate (708.8 mg, 7.5 mmol, 1.5 equiv.) was slowly added. The reaction was allowed to stir at room temperature until completion). The mixture was diluted with dichloromethane and washed successively with 1N HCl, saturated $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography to yield the desired product.



(c) Boc protection of allenylic alcohols: A dried 100 mL RBF containing a magnetic

stir-bar was charged with allenylic alcohol derivative (**S2**, 1.0 equiv.). The flask was fitted with a rubber septum and **S2** was dissolved in Dry THF (0.35 M). The resulting homogeneous solution was cooled to -78 °C. *n*-BuLi (1.1 equiv., 1.6 M in hexanes) was added drop-wise over 5 minutes, which resulted in a darkly colored solution once the addition was >90% complete. The resulting solution was stirred at this temperature for 30 minutes before a freshly prepared 1 M THF solution of Boc_2O (1.00 equiv.) was added over 5 minutes. The solution was allowed to stir for 30 minutes at this temperature before all excess CO_2(s) were removed from the cold bath. Then the reaction was allowed to slowly warm to room temperature and stirred for 12 hours. After which, the dark reddish/purple solution was cooled to 0 °C and quenched by the addition of water (50 mL). After stirring the biphasic mixture for 10 minutes, it was warmed to room temperature, diluted with EtOAc (50 mL) and transferred to a separatory funnel. The layers were separated, and the aqueous phase was extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated. This crude residue was typically of high purity (^{1}H NMR) and could be used without further purification.



4. Optimization for the Dienylation of Unactivated sp3 C-H bond.

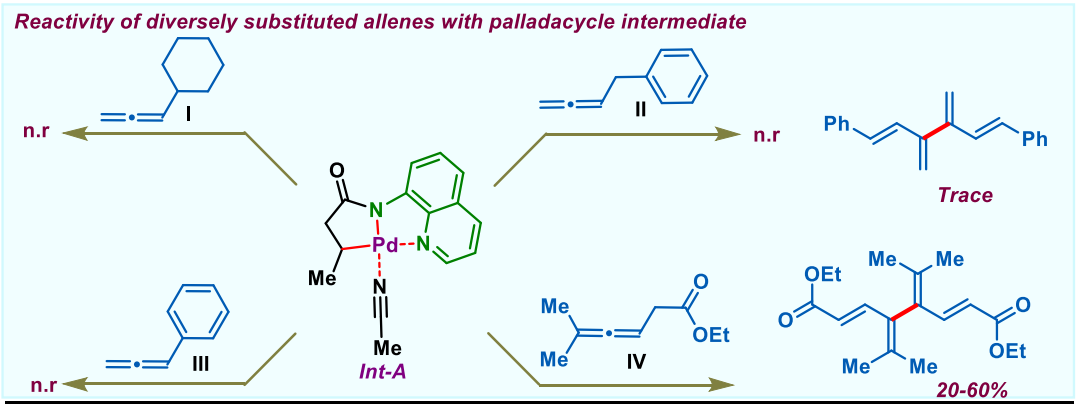
4a) Isolation of Int-A:- The Int-A was synthesize by following the previously known reported procedure. [4]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.04 (d, J = 7.8, 1 H), 8.37 (d, J = 4.7 Hz, 1 H), 8.19 (d, J = 8.4, Hz, 1 H), 7.51 (d, J = 8.0 Hz, 1 H), 7.36 – 7.27 (m, 2 H), 2.96 – 2.90 (m, 1 H), 2.58 – 2.51 (m, 2 H), 2.42 (s, 3 H), 1.13 (d, J = 6.7 Hz, 3 H).

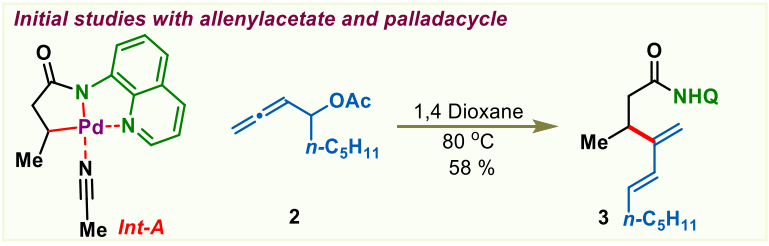
4b) Stochiometric trial of Int-A with various Allenes for dienylation of sp3 C-H bond.

Entry	Allene	Solvent	Temperature	Result
1.	**I**	1, 4-Dioxane	60-100 °C	*n.r*
2.	**II**	1, 4-Dioxane	60-100 °C	*Dimerization of allene II in trace amount*
3.	**III**	1, 4-Dioxane	60-100 °C	*n.r*
4.	**IV**	1, 4-Dioxane	60-100 °C	*Dimerization of IV in 20-40% was observed*

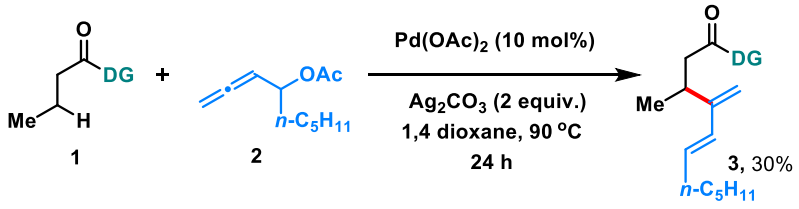
5.	**IV**	Toluene	60-100 °C	*Dimerization of IV in 30-60% was observed*



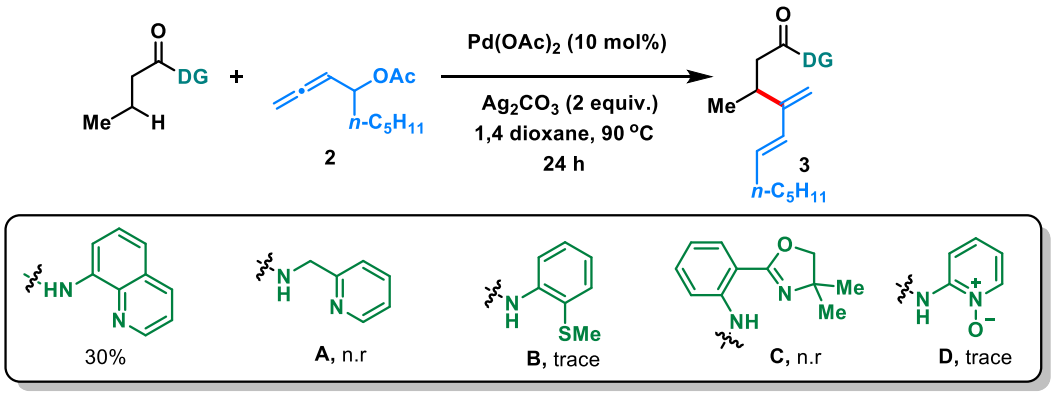
4c) Stochiometric trial of Int-A with various Allenes for dienylation of sp^3 C-H bond



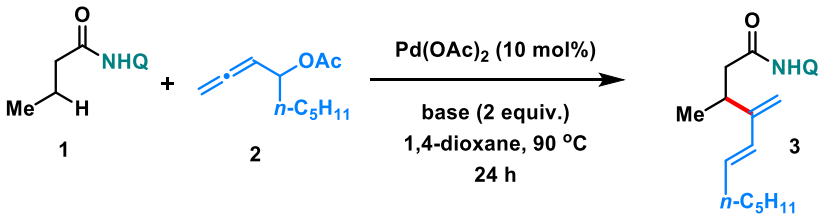
4d) Catalytic Pd(II) catalyzed dienylation of β-sp^3 C-H bond of 1 with allenyl acetate



4e) Screening of other directing group.



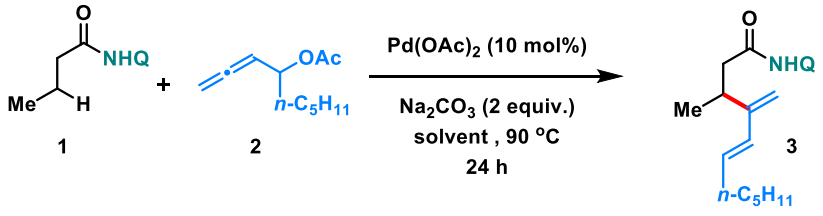
4f) Optimization for Base



Entry	Base	Yield[1]
1	Ag_2CO_3	30
2	$Cu(OAc)_2$	10
3	Na_2CO_3	65 (60)[2]
4	$NaHCO_3$	60
5	NaOPiv	15
6	NaOAc	29
7	K_2CO_3	55
8	KOAc	35
9	K_3PO_4	59
10	Cs_2CO_3	40
11	CsOAc	18
12	LiCl	<5
13	NaOH	-
14	DABCO	-

Conditions: **1** (0.1mmol), **2** (0.15 mmol), [1]NMR yield (using 1,3,5-trimethoxybenzene as internal standard) [2](Isolated Yield.)

4g) Optimization for solvent.

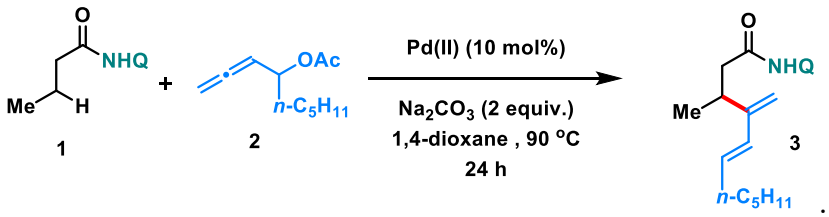


S.N	solvents	Yield[1]
1	1,4-dioxane	65 (60)[2]
2	Toluene	64

3	DCE	40
4	Acetonitrile	20
5	t-Amyl-OH	49
6	TFE	10
7	HFIP	5
8	DMF	30
9	Acetone	10
10	Xylene	49
11	NMP	20
12	DCM	23
13	Chlorobenzene	35
14	Benzene	25
15	chloroform	12
16	t-BuOH	10
17	EtOH	15

[1](NMR yields.) [2](Isolated Yield.)

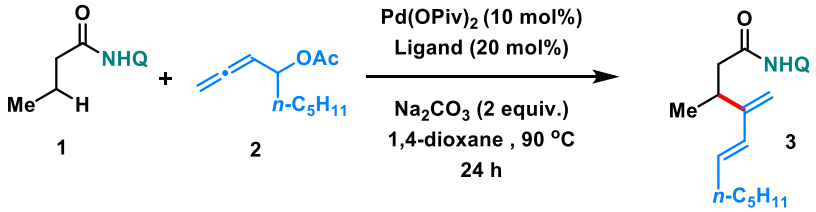
4h) Optimization with respect to Palladium Catalyst.



Entry	Palladium Catalyst (10mol%)	Yield[1]
2	$Pd(OAc)_2$	65
1	$Pd(OTf)_2$	15 %
2	$Pd(TPP)_2Cl_2$	30%
3	$Pd(acac)_2$	45%
4	$Pd(TFA)_2$	60%
5	$Pd(CH_3CN)_2Cl_2$	55%
6	$PdSO_4$	Trace
7	$Pd(DMSO)_2Cl_2$	35%
8	$PdCl_2$	53
9	$Pd(PivO)_2$	69(65)[2]

Conditions: **1** (0.1mmol), **2** (0.15 mmol), [1]NMR yield (using 1,3,5-trimethoxybenzene as internal standard) [2](Isolated Yield.)

4i) Ligand Optimization: mono-protected amino acids (MPAA).



Entry	Ligand	Yield[1]
1	-	69
2	Ac-Gly-OH	70
3	Fmoc-Gly-OH	62
4	Ac-Ala-OH	57
5	Ac-DL-Val-OH	25
6	Ac-Phe-OH	37
7	Ac-L-Leu-OH	47
8	*N*-α-Ac-L-Lys-OH	<5
9	Ac-4-hydroxy-L-Proline	10
10	Boc-Gly-OH	80 (78)[2]
11	Boc-Ala-OH	65
12	Boc-*L*-iso-Leu-OH	62

Conditions: **1** (0.1mmol), **2** (0.15 mmol), [1]NMR yield (using 1,3,5-trimethoxybenzene as internal standard) [2](Isolated Yield.)

Ligand Optimization: Nitrogen containing ligands.

Entry	Ligand	Yield %[1]
1	L1	15
2	L2	25
3	L3	17
4	L4	16

5	L5	40
6	L6	29
7	L7	60
8	L8	55
9	L9	70
10	L10	38
11	L11	44
12	L12	49
13	L13	57
14	L14	62
15	L15	59

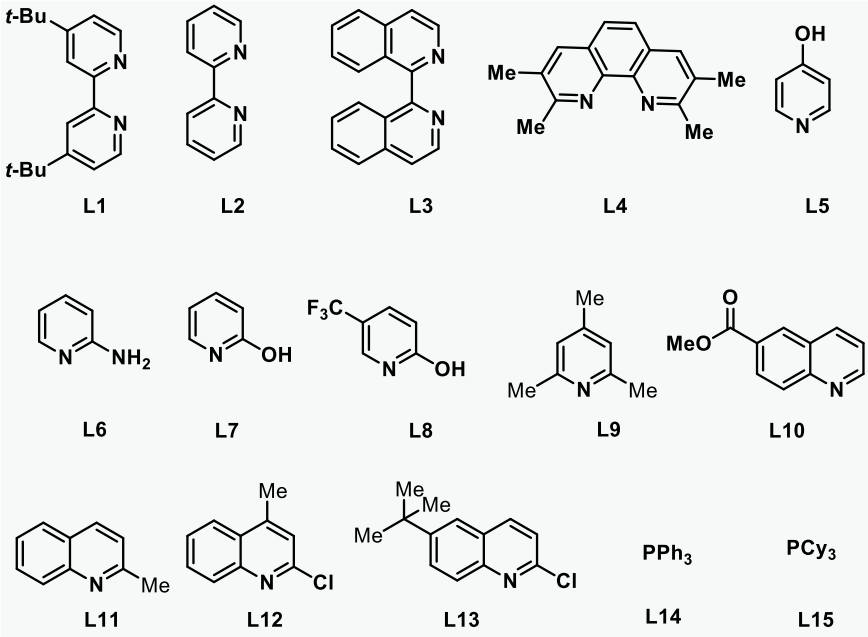
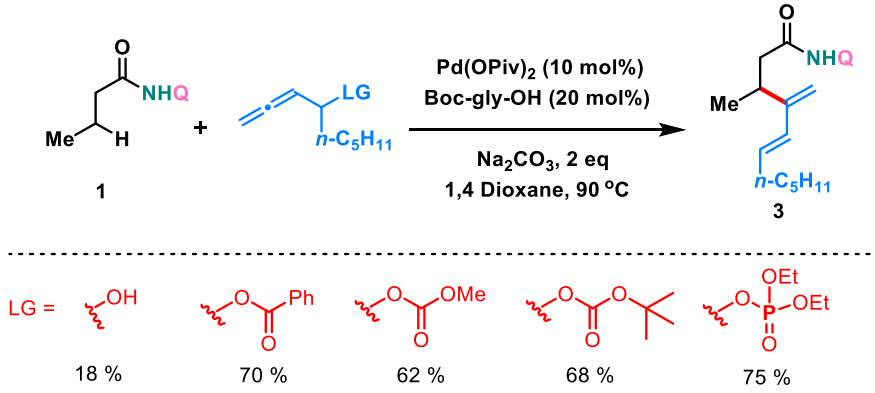


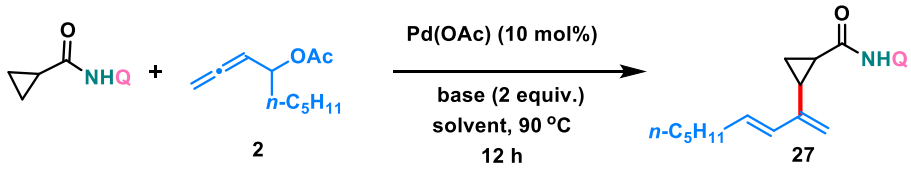
Figure 1 Ligands screened for the reaction

[1](NMR yields.)

4j) Leaving group Optimization.



5. Optimization for the cyclic carboxamide



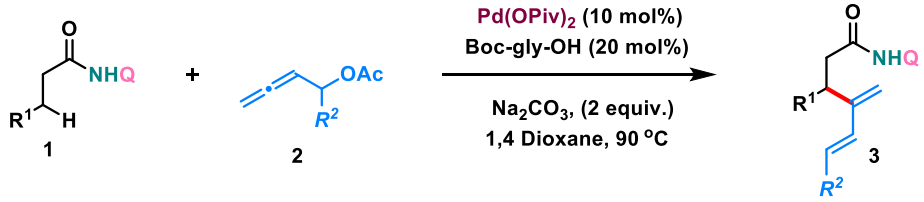
entry	solvent	base	ligand	yield[1]
1	1,4-dioxane	Na_2CO_3	Boc-gly-OH	70
2	1,4-dioxane	Na_2CO_3	L12	50
3	1,4-dioxane	Na_2CO_3	-	78
4	1,4-dioxane	$NaHCO_3$	-	80
5	1,4-dioxane	K_2CO_3	-	65
6	1,4-dioxane	$KHCO_3$	-	72
7	Toluene	$NaHCO_3$	-	88(83)[2]
8	Toluene	$NaHCO_3$	-	82[3]
9	DMF	$NaHCO_3$	-	40
10	1,2-DCE	$NaHCO_3$	-	63
11	MeOH	$NaHCO_3$	-	20
12	HFIP	$NaHCO_3$	-	25
13	NMP	$NaHCO_3$	-	47

Conditions: **1** (0.1mmol), **2** (0.15 mmol), [1]NMR yield (using 1,3,5-trimethoxybenzene as internal standard) [2](Isolated Yield.) [3](1 equiv. $NaHCO_3$)

6. General Procedure for the Pd(II)-Catalyzed sp3 C-H dienylation with allenyl acetates:

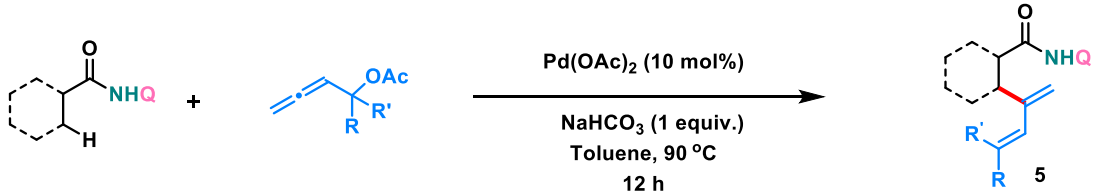
a. General Procedure for the β C-H dienylation of Acyclic carboxamide

To an oven-dried screw-cap reaction tube equipped with a stir bar, were added amide (0.2 mmol), freshly prepared allenyl acetate (0.3 mmol), $Pd(OPiv)_2$ (10 mol%), Boc-gly-OH (20 mol%) and Na_2CO_3 (0.4 mmol) followed by dry 1,4 Dioxane (2.0 mL). The reaction mixture was heated for 24 h at 90 °C. Upon completion as detected by TLC. The organic phase was evaporated under reduced pressure and the product was separated by using silica-gel column chromatography.



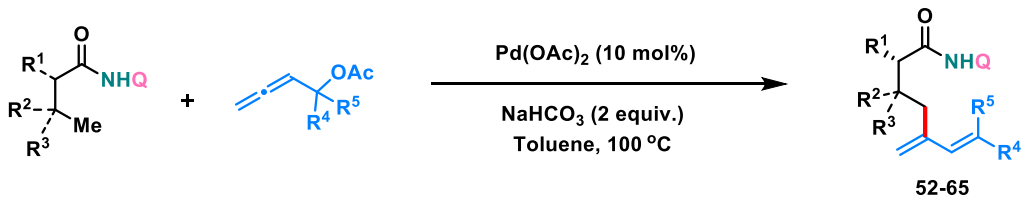
b. General Procedure for the β-sp^3(C-H) dienylation of cyclic carboxamide

To an oven dried screw-cap reaction tube equipped with stir bar, were added amide (0.2 mmol), freshly prepared allenyl acetate (0.3 mmol), $Pd(OAc)_2$ (10 mol%) and $NaHCO_3$ (0.2 mmol) followed by dry Toluene (2.0 mL). The reaction mixture was heated for 24 h at 90 °C. Upon completion as detected by TLC. The organic phase was evaporated under reduced pressure and the product was separated by using silica-gel column chromatography.

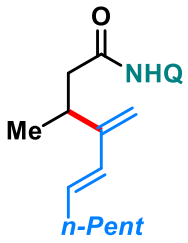


c. General Procedure for the γC-H dienylation of Acyclic carboxamide

To an oven dried screw-cap reaction tube equipped with stir bar, were added amide (0.2 mmol), allenyl acetate (0.3 mmol), $Pd(OAc)_2$ (10 mol%) and $NaHCO_3$ (0.4 mmol) followed by dry Toluene (2.0 mL). The reaction mixture was heated for 24 h at 100 °C. After completion of the reaction (detected by TLC) the organic phase was evaporated under reduced pressure and the product was separated by using silica-gel column chromatography.



7. Spectroscopic data for new compounds.



3, 78%

(*E*)-3-methyl-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (3)

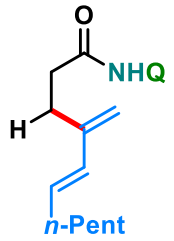
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)butyramide **S1** (0.20 mmol 43 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a **3** Yellow liq**.** (52.5 mg, 78%).

***R*$_f$:** 0.25 (hexane/ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, CDCl$_3$) δ 9.85 (s, 1H), 8.88 – 8.77 (m, 2H), 8.18 (d, *J* = 7.6 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.07 (d, *J* = 15.9 Hz, 1H), 6.00 – 5.85 (m, 1H), 5.01 (s, 1H), 4.98 (s, 1H), 3.29 – 3.14 (m, 1H), 2.86 (dd, *J* = 14.5, 5.3 Hz, 1H), 2.52 (dd, *J* = 14.5, 8.9 Hz, 1H), 2.12 (dd, *J* = 14.3, 7.1 Hz, 2H), 1.41 (dt, *J* = 14.4, 7.3 Hz, 2H), 1.33 – 1.28 (m, 4H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, CDCl$_3$) δ= 171.01, 150.57, 148.09, 138.32, 136.63, 134.60, 131.05, 130.89, 128.08, 127.61, 121.66, 121.52, 116.73, 111.41, 45.18, 33.10, 32.31, 31.59, 29.16, 22.64, 20.07, 14.16.

HRMS (ESI) calculated for $[C_{22}H_{29}N_2O]^+$ $(M+H)^+$ m/z: 337.2274, found 337.2275.



4, 65%

(*E*)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (4)

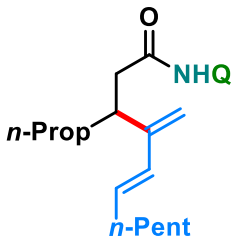
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)propionamide **S2** (0.20 mmol 40 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a **4** light-Yellow liq**.** (42.0 mg, 65%).

***R*$_f$:** 0.26 (hexane/ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.85 (s, 1H), 8.82 – 8.77 (m, 2H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.10 (d, *J* = 15.9 Hz, 1H), 5.84 (dd, *J* = 14.8, 7.9 Hz, 1H), 4.96 (s, 2H), 2.81 – 2.70 (m, 4H), 2.11 (td, *J* = 7.9, 1.0 Hz, 2H), 1.45 – 1.37 (m, 2H), 1.33 – 1.26 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.44, 148.13, 144.98, 136.65, 134.62, 131.55, 131.12, 128.12, 127.65, 121.69, 121.55, 116.76, 113.75, 37.05, 32.99, 31.60, 29.19, 28.02, 22.67, 14.18.

HRMS (ESI) calculated for $[C_{21}H_{27}N_2O]^+$ $(M+H)^+$ m/z: 323.2118; Found 323.2120.



5, 68%

(*E*)-4-methylene-3-propyl-*N*-(quinolin-8-yl)undec-5-enamide (5)

According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)hexanamide **S3** (0.20 mmol 48.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a **5** yellow liq**.** (49.6 mg, 68%).

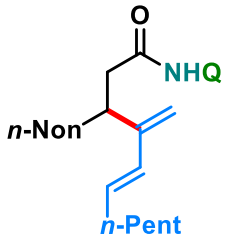
***R*$_f$:** 0.25 (hexane/ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ= 9.70 (s, 1H), 8.74 – 8.67 (m, 2H), 8.03 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.33 (dd, *J* = 8.2, 4.2 Hz, 1H), 5.95 (d, *J* = 16.0 Hz, 1H), 5.85 (dt, *J*

= 15.7, 6.6 Hz, 1H), 4.96 (s, 1H), 4.85 (s, 1H), 3.00 (dd, *J* = 14.2, 7.1 Hz, 1H), 2.63 (dd, *J* = 14.5, 7.1 Hz, 1H), 2.53 (dd, *J* = 14.5, 7.3 Hz, 1H), 1.98 (dt, *J* = 13.9, 6.8 Hz, 2H), 1.49 (dd, *J* = 14.9, 7.7 Hz, 2H), 1.31 – 1.24 (m, 3H), 1.21 – 1.15 (m, 5H), 0.88 – 0.64 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 170.89, 148.78, 148.08, 138.42, 136.33, 134.67, 131.02, 130.99, 127.97, 127.46, 121.57, 121.35, 116.47, 112.20, 44.13, 38.18, 36.59, 33.05, 31.51, 29.07, 22.58, 20.39, 14.27, 14.12.

HRMS (ESI): calculated for $[C_{24}H_{33}N_2O]^+$ $[M+H]^+$ m/z: 365.2587, found 365.2585.



6, 75%

(*E*)-3-(nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)dodecanamide (6)

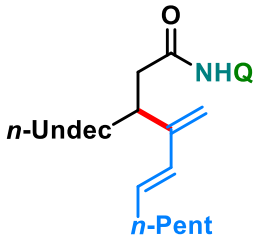
The title compound was prepared according to the general procedure as mentioned from N-(quinolin-8-yl)dodecanamide **S4** (0.10 mmol 32.6 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a Yellow oily liq. **6** (33.6 mg, 75%).

***R*$_f$:** 0.27 (hexane/ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.81 (s, 1H), 8.88 – 8.74 (m, 2H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.06 (d, *J* = 15.9 Hz, 1H), 5.96 (dt, *J* = 15.7, 6.7 Hz, 1H), 5.06 (s, 1H), 4.96 (s, 1H), 3.16 – 3.02 (m, 1H), 2.73 (dd, *J* = 14.5, 7.1 Hz, 1H), 2.64 (dd, *J* = 14.5, 7.3 Hz, 1H), 2.09 (ddd, *J* = 12.8, 7.9, 5.0 Hz, 2H), 2.05 (ddd, *J* = 12.2, 9.6, 5.6 Hz, 1H), 1.61 (dd, *J* = 14.6, 7.0 Hz, 2H), 1.32 – 1.23 (m, 20H), 0.91 – 0.86 (m, 7H).

^{13}C NMR (126 MHz, $CDCl_3$) δ= 170.98, 148.88, 148.13, 138.50, 136.41, 134.73, 131.10, 131.06, 128.05, 127.55, 121.63, 121.39, 116.55, 112.25, 44.19, 38.47, 34.39, 33.11, 32.01, 31.57, 29.86, 29.83, 29.70, 29.44, 29.14, 27.26, 22.79, 22.64, 14.23, 14.17.

HRMS (ESI): calculated for $[C_{30}H_{45}N_2O]^+$ $[M+H]^+$ m/z: 449.3526 and found: 449.3532.



7, 70%

(*E*)-3-(nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)tetradecanamide (7)

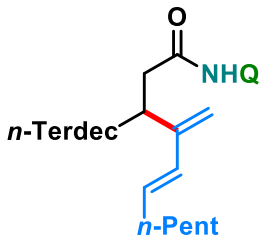
According to the general procedure, the title compound was prepared as mentioned from N-(quinolin-8-yl)tetradecanamide **S5** (0.1 mmol 35.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-Yellow oily liq**. 7** (33.4 mg, 70%).

***R_f*:** 0.27 (hexane/ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 9.70 (s, 1H), 8.78 – 8.66 (m, 2H), 8.05 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.35 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.96 (d, *J* = 15.8 Hz, 1H), 5.85 (dt, *J* = 15.7, 6.6 Hz, 1H), 4.96 (s, 1H), 4.85 (s, 1H), 3.07 – 2.90 (m, 1H), 2.63 (dd, *J* = 14.5, 7.1 Hz, 1H), 2.53 (dd, *J* = 14.5, 7.3 Hz, 1H), 2.00 (dd, *J* = 14.4, 7.2 Hz, 2H), 1.51 (dd, *J* = 14.3, 7.1 Hz, 2H), 1.33 – 1.25 (m, 3H), 1.21 – 1.13 (m, 21H), 0.82 – 0.76 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 169.95, 147.85, 147.11, 137.47, 135.38, 133.71, 130.07, 127.02, 126.52, 120.60, 120.37, 115.52, 111.24, 43.17, 37.43, 33.38, 32.10, 31.02, 30.55, 28.84, 28.77, 28.73, 28.68, 28.46, 28.13, 26.24, 21.80, 21.63, 13.23, 13.15.

HRMS (ESI): calculated for $[C_{32}H_{49}N_2O]^+$[M+H]$^+$ m/z: 477.3839 and found: 477.3834.



8, 60%

(*E*)-3-(nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)hexadecanamide (8)

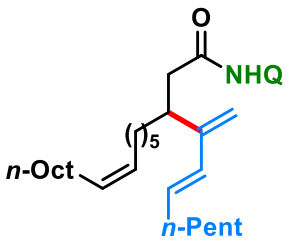
According to the general procedure, the title compound was prepared as mentioned from N-(quinolin-8-yl)palmitamide **S6** (0.1 mmol 38 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a sticky liq. **8** (30.3 mg, 60%).

***R_f*:** 0.27 (hexane/ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.82 – 8.72 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55 – 7.47 (m, , 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.01 (d, 1H), 5.95 (dt, 1H), 5.04 (s, 1H), 4.93 (s, 1H), 3.14 – 2.96 (m, 1H), 2.69 (dd, *J* = 7.1 Hz, 1H), 2.63 (dd, *J* = 7.3 Hz, 1H), 2.11 – 2.05 (m, 2H), 2.03 – 1.99 (m, 1H), 1.62 – 1.56 (m, 4H), 1.27 – 1.22 (m, 22H), 0.89 – 0.85 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.02, 148.93, 148.16, 138.55, 136.45, 134.78, 131.15, 131.07, 128.09, 127.60, 121.65, 121.42, 116.60, 112.26, 44.22, 38.56, 34.43, 33.13, 32.07, 31.60, 29.88, 29.84, 29.80, 29.77, 29.72, 29.50, 29.17, 27.29, 22.84, 22.66, 14.26, 14.18

HRMS (ESI): calculated for $[C_{34}H_{53}N_2O]^+[M+H]^+$ m/z: 505.4152; Found: 505.4156.



9, 50%

(*Z*)-3-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)heptadec-9-enamide (9)

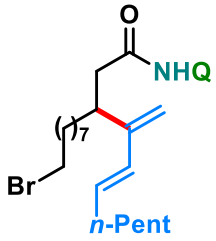
The title compound was prepared according to the general procedure as mentioned from (*Z*)-*N*-(quinolin-8-yl)octadec-9-enamide **S7** (0.1 mmol 40.8 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a Yellow oily liq. **9** (26.5 mg, 50%).

***R_f*:** 0.24 (hexane/ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.84 – 8.69 (m, 2H), 8.15 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.45 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.03 (d, *J* = 15.8 Hz, 1H), 5.95 (s, 1H), 5.32 (td, *J* = 5.8, 3.5 Hz, 2H), 5.04 (s, 1H), 4.93 (s, 1H), 3.13 – 3.00 (m, 1H), 2.70 (dd, *J* = 7.1 Hz, 1H), 2.63 (dd, *J* = 7.3 Hz, 1H), 2.11 – 2.05 (m, 2H), 2.02 – 1.95 (m, 4H), 1.59 (d, *J* = 6.0 Hz, 2H), 1.32 – 1.24 (m, 26H), 0.89 – 0.86 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.98, 148.85, 148.12, 138.46, 136.50, 134.71, 131.14, 131.05, 130.06, 129.91, 128.07, 127.60, 121.64, 121.43, 116.64, 112.28, 44.18, 38.49, 34.38, 33.12, 32.03, 31.58, 29.90, 29.83, 29.80, 29.65, 29.53, 29.45, 29.15, 27.34, 27.30, 27.19, 22.81, 22.64, 14.24, 14.17.

HRMS (ESI): calculated for $[C_{36}H_{55}N_2O]^+$ $(M+H)^+$ m/z: 531.4309 found: 531.4315.



10, 70%

(*E*)-3-(7-bromoheptyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (10)

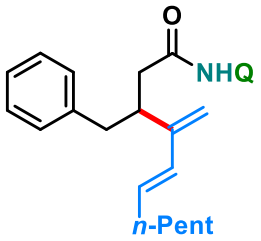
According to the general procedure, the title compound was prepared as mentioned from 11-bromo-N-(quinolin-8-yl)undecanamide **S8** (0.10 mmol 39.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a Yellow sticky liq**. 10** (35.8 mg, 70%).

***R*$_f$:** 0.27 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.84 – 8.78 (m, 2H), 8.17 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.06 (d, *J* = 15.8 Hz, 1H), 5.95 (dt, *J* = 15.7, 6.7 Hz, 1H), 5.06 (s, 1H), 4.95 (s, 1H), 3.40 (t, 2H), 3.13 – 3.04 (m, 1H), 2.74 (dd, *J* = 14.5, 7.0 Hz, 1H), 2.63 (dd, *J* = 14.5, 7.4 Hz, 1H), 2.10 (dd, *J* = 14.2, 7.0 Hz, 2H), 1.87 – 1.79 (m, 2H), 1.64 – 1.57 (m, 2H), 1.41 – 1.36 (m, 4H), 1.33 – 1.25 (m, 11H), 0.89 (t, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 170.96, 148.81, 148.15, 138.48, 136.43, 134.70, 131.12, 131.02, 128.04, 127.55, 121.65, 121.43, 116.54, 112.29, 44.18, 38.40, 34.28, 34.14, 33.10, 32.92, 31.56, 29.68, 29.42, 29.14, 28.80, 28.25, 27.16, 22.64, 14.18.

HRMS (ESI):: $C_{29}H_{41}BrN_2NaO$,$[M+Na]^+$, Calculated= 535.2294;Found=535.2286



11, 64%

(*E*)-3-benzyl-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide(11)

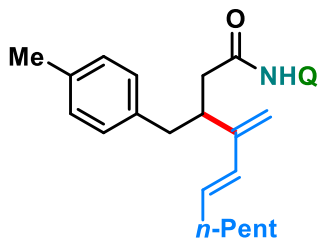
The title compound was prepared according to the general procedure as mentioned from 4-phenyl-*N*-(quinolin-8-yl)butanamide **S9** (0.10 mmol 29 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow sticky solid **11** (26.4 mg, 64%).

***R*$_f$:** 0.23 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.77 (s, 1H), 8.80 (dd, *J*=4.2, 1.7, 1H), 8.75 (dd, *J*=7.1, 1.8, 1H), 8.15 (dd, *J*=8.3, 1.7, 1H), 7.55 – 7.47 (m, 2H), 7.44 (dd, *J*=8.3, 4.2, 1H), 7.28 – 7.21 (m, 4H), 7.20 – 7.13 (m, 1H), 6.06 (d, *J*=16.2, 1H), 5.96 (dt, *J*=15.8, 6.6, 1H), 5.04 (s, 1H), 4.91 (s, *J*=14.1, 1H), 3.45 (p, *J*=7.1, 1H), 2.97 (dd, *J*=13.7, 6.9, 1H), 2.86 (dd, *J*=13.7, 7.3, 1H), 2.78 – 2.64 (m, 2H), 2.14 – 2.05 (m, 2H), 1.43 – 1.33 (m, 2H), 1.32 – 1.25 (m, 4H), 0.88 (t, *J*=6.9, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.56, 148.11, 148.08, 139.92, 138.42, 136.45, 134.62, 131.15, 131.07, 129.47, 128.23, 128.02, 127.53, 126.16, 121.63, 121.43, 116.60, 112.94, 42.34, 40.57, 39.46, 33.10, 31.57, 29.12, 22.64, 14.17.

HRMS (ESI): calculated for $[C_{28}H_{32}N_2NaO]^+$ $(M+Na)^+$ m/z: 435.2407, found: 435.2422.



12, 68%

(*E*)-3-(4-methylbenzyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (12)

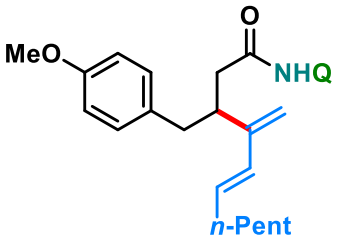
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)-4-(p-tolyl)butanamide **S10** (0.10 mmol 30.4 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-Yellow sticky liq. of **12** (29.0 mg, 68%).

***R*$_f$:** 0.24 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.77 (s, 1H), 8.82 (d, *J*=3.7, 1H), 8.75 (m, 1H), 8.17 (d, *J*=8.2, 1H), 7.57 – 7.43 (m, 3H), 7.14 (d, *J*=7.7, 2H), 7.07 (d, *J*=7.7, 2H), 6.08 (d, *J*=15.9, 1H), 6.03 – 5.95 (m, 1H), 5.06 (s, 1H), 4.93 (s, 1H), 3.49 – 3.38 (m, 1H), 2.96 (dd, *J*=13.7, 6.8, 1H), 2.83 (dd, *J*=13.7, 7.4, 1H), 2.78 – 2.67 (m, 2H), 2.40 – 2.34 (m, 1H), 2.28 (s, 3H), 2.14 – 2.09 (m, 2H), 1.42 – 1.38 (m, 2H), 1.36 – 1.24 (m, 3H), 0.90 (t, *J*=6.8, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 170.67, 148.22, 148.10, 138.43, 136.78, 136.44, 135.58, 134.65, 131.11, 129.34, 128.94, 128.03, 127.53, 121.62, 121.40, 116.59, 112.85, 42.38, 40.17, 39.52, 33.12, 31.59, 29.14, 22.65, 21.09, 14.17.

HRMS (ESI): calculated for $[C_{29}H_{35}N_2O]^+$ $(M+H)^+$ m/z: 427.2744, found: 427.2740.



13, 70%

(*E*)-3-(4-methoxybenzyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (13)

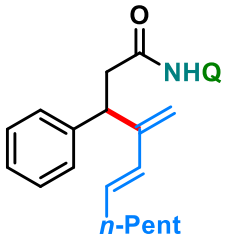
The title compound was prepared according to the general procedure as mentioned from 4-(4-methoxyphenyl)-*N*-(quinolin-8-yl)butanamide **S11** (0.10 mmol 32.0 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a Yellow oily liq. **13** (31.0 mg, 70%).

***R*$_f$:** 0.22 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.75 (s, 1H), 8.79 (dd, *J*=4.2, 1.6, 1H), 8.74 (dd, *J*=7.0, 1.9, 1H), 8.16 (d, *J*=8.2, 1H), 7.50 (dd, *J*=12.8, 5.3, 2H), 7.45 (dd, *J*=8.2, 4.2, 1H), 7.15 – 7.11 (m, 2H), 6.80 – 6.74 (m, 2H), 6.08 – 5.89 (m, 2H), 5.03 (s, 1H), 4.89 (s, 1H), 3.72 (s, 3H), 3.43 – 3.35 (m, 1H), 2.91 (dd, *J*=13.8, 6.8, 1H), 2.78 (dd, *J*=13.8, 7.3, 1H), 2.11 – 2.02 (m, 4H), 1.30 – 1.26 (m, 6H), 0.87 (t, *J*=6.9, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.71, 158.04, 148.21, 148.03, 134.60, 131.97, 131.13, 130.41, 128.07, 127.60, 121.63, 121.43, 113.65, 112.91, 55.27, 42.34, 39.68, 33.13, 31.60, 29.15, 22.65, 14.18.

HRMS (ESI): calculated for $[C_{29}H_{35}N_2O_2]^+$ $(M+H)^+$ m/z: 443.2693, found: 443.2687.



14, 64%

(*E*)-4-methylene-3-phenyl-*N*-(quinolin-8-yl)undec-5-enamide(14)

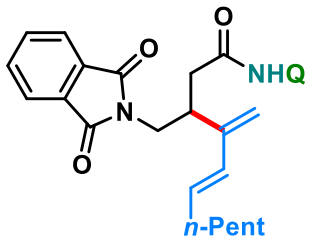
The title compound was prepared according to the general procedure as mentioned from 3-phenyl-*N*-(quinolin-8-yl)propanamide **S12** (0.10 mmol 27.6 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow liq. **14** (25.5 mg, 64%).

***R*$_f$:** 0.26 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.77 (s, 1H), 8.79 – 8.71 (m, 2H), 8.15 (d, *J*=8.3, 1H), 7.54 – 7.46 (m, 2H), 7.44 (dd, *J*=8.2, 4.3, 1H), 7.35 (d, *J*=7.3, 2H), 7.26 (t, *J*=7.6, 2H), 7.15 (dd, *J*=11.5, 4.3, 1H), 6.01 (d, *J*=15.9, 1H), 5.83 (dt, *J*=15.7, 6.8, 1H), 5.14 (d, *J*=28.2, 2H), 4.43 (t, *J*=7.6, 1H), 3.15 (dd, *J*=14.9, 7.3, 1H), 3.01 (dd, *J*=14.9, 7.9, 1H), 2.10 – 1.98 (m, 2H), 1.31 – 1.20 (m, 4H), 1.14 (ddd, *J*=13.7, 7.6, 4.4, 2H), 0.83 (t, *J*=7.2, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 170.11, 147.90, 147.82, 142.86, 134.41, 132.36, 131.05, 128.59, 128.53, 128.08, 127.98, 127.86, 127.66, 126.60, 121.60, 121.57, 117.01, 113.15, 44.05, 43.86, 32.99, 31.39, 28.99, 22.60, 14.13.

HRMS (ESI): calculated for $[C_{27}H_{31}N_2O]^+$ $(M+H)^+$ m/z: 399.2431, found: 399.2437.



15, 55%

(*E*)-3-((1,3-dioxoisoindolin-2-yl)methyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (15)

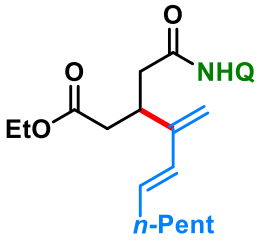
The title compound was prepared according to the general procedure as mentioned from 4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide **S13** (0.1 mmol 35.9 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a sticky solid **15** (26.4 mg, 55%).

***R*$_f$:** 0.15 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 9.75 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.41 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.60 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.50 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.39 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.32 (d, *J* = 7.9 Hz, 1H), 6.23 – 6.12 (m, 1H), 6.09 (d, 1H), 5.10 (s, 1H), 5.07 (s, 1H), 3.89 – 3.80 (m, 2H), 2.78 (dd, *J* = 7.0 Hz, 2H), 2.13 – 2.06 (m, 2H), 1.29 – 1.25 (m, 5H), 0.87 – 0.85 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 169.75, 168.64, 148.23, 146.55, 138.38, 136.29, 134.43, 133.74, 132.08, 132.00, 130.72, 127.89, 127.37, 123.11, 121.66, 121.31, 116.31, 113.46, 42.49, 41.09, 36.18, 33.18, 31.64, 29.07, 22.64, 14.24.

HRMS (ESI): calculated for $[C_{30}H_{32}N_3O_3]^+$ $(M+H)^+$ m/z: 482.2438, found: 482.2434.



16, 72%

ethyl (*E*)-4-methylene-3-(2-oxo-2-(quinolin-8-ylamino)ethyl)undec-5-enoate (16)

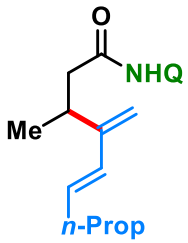
According to the general procedure, the title compound was prepared as mentioned from ethyl 5-oxo-5-(quinolin-8-ylamino)pentanoate **S14** (0.1 mmol 28.6 mg). The crude product was purified *via* flash column chromatography (Hex/EtOAc) to afford a light-yellow liq. **16** (29.4 mg, 72%).

***R*$_f$:** 0.20 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 9.82 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.76 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.04 (d, *J* = 16.0 Hz, 1H), 5.98 (dt, *J* = 6.3 Hz, 1H), 5.04 (s, 1H), 4.97 (s, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.64 – 3.53 (m, 1H), 2.81 (dd, *J* = 14.7, 6.5 Hz, 1H), 2.74 (dd, *J* = 13.9, 6.8 Hz, 1H), 2.71 – 2.63 (m, 2H), 2.13 – 2.05 (m, 2H), 1.42 – 1.34 (m, 2H), 1.29 – 1.24 (m, 4H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 8.9, 5.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 172.16, 170.02, 148.22, 147.72, 138.49, 136.44, 134.61, 131.46, 130.63, 128.05, 127.52, 121.69, 121.56, 116.60, 112.66, 60.53, 42.70, 38.87, 34.47, 33.09, 31.59, 29.07, 22.63, 14.31, 14.15.

HRMS (ESI): calculated for $[C_{25}H_{33}N_2O_3]^+$ $(M+H)^+$ m/z: 409.2486, found: 409.2492.



17, 70%

(*E*)-3-methyl-4-methylene-*N*-(quinolin-8-yl)non-5-enamide (18)

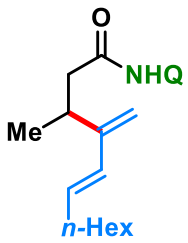
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)butyramide **S1** (0.10 mmol 21.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily liq. **17** (21.6 mg, 70%).

***R*$_f$:** 0.27 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 9.81 (s, 1H), 8.82 – 8.76 (m, 2H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.06 (d, *J* = 16.0 Hz, 1H), 5.93 (dt, *J* = 15.8, 6.7 Hz, 1H), 4.99 (s, 1H), 4.95 (s, 1H), 3.20 (dd, *J* = 14.9, 6.4 Hz, 1H), 2.83 (dd, *J* = 14.5, 5.3 Hz, 1H), 2.49 (dd, *J* = 14.5, 8.9 Hz, 1H), 2.13 – 2.05 (m, 2H), 1.49 – 1.37 (m, 2H), 1.25 (d, *J* = 6.8 Hz, 4H), 0.90 (t, *J* = 7.4 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 170.98, 150.56, 148.21, 138.49, 136.46, 134.68, 131.27, 130.63, 128.06, 127.55, 121.68, 121.50, 116.57, 111.45, 45.20, 35.18, 32.37, 22.63, 20.05, 13.86.

HRMS (ESI): calculated for $[C_{20}H_{25}N_2O]^+$ $(M+H)^+$ m/z: 309.1961, found: 309.1962.



18, 74%

(*E*)-3-methyl-4-methylene-*N*-(quinolin-8-yl)dodec-5-enamide (18)

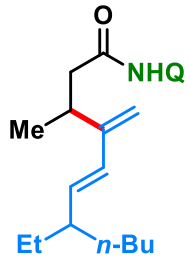
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)butyramide **S2** (0.20 mmol 43 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily liq**.** of **18** (51.8 mg, 74%).

***R_f*:** 0.28 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.84 (s, 1H), 8.82 (dd, *J* = 4.5, 1.3 Hz, 2H), 8.18 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.60 – 7.50 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.08 (d, *J* = 15.9 Hz, 1H), 6.01 – 5.90 (m, 1H), 3.23 (dd, *J* = 14.3, 6.7 Hz, 1H), 2.86 (dd, *J* = 14.5, 5.3 Hz, 1H), 2.52 (dd, *J* = 14.5, 8.9 Hz, 1H), 2.16 – 2.09 (m, 2H), 1.45 – 1.37 (m, 2H), 1.32 – 1.26 (m, 9H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ= 171.00, 150.58, 148.16, 138.42, 136.53, 134.65, 131.05, 130.91, 128.07, 127.58, 121.67, 121.51, 116.63, 111.39, 45.20, 33.14, 32.33, 31.84, 29.45, 29.05, 22.71, 20.07, 14.21.

HRMS (ESI): calculated for $[C_{23}H_{31}N_2O]^+$ $(M+H)^+$ m/z: 351.2431, found: 351.2437.



19, 54% dr 1:1

(*E*)-7-ethyl-3-methyl-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (19, dr 1:1)

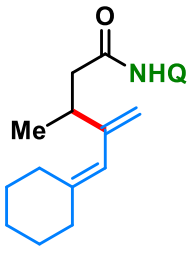
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)butyramide **S1** (0.20 mmol 43 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a oily liq. **19 (dr 1:1)** (39.4 mg, 54%).

***R*$_f$:** 0.28 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (500 MHz, CDCl$_3$) δ 9.84 (s, 1H), 8.82 (d, *J* = 7.6 Hz, 2H), 8.18 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.64 – 7.40 (m, 2H), 6.03 (d, *J* = 15.9 Hz, 1H), 5.67 (dd, *J* = 15.8, 9.0 Hz, 1H), 5.02 (s, 1H), 4.98 (s, 1H) 3.32 – 3.11 (m, 1H), 2.87 (dd, *J* = 14.4, 5.1 Hz, 1H), 2.51 (ddd, *J* = 14.3, 9.2, 3.1 Hz, 1H), 1.92 (dt, *J* = 12.5, 4.0 Hz, 1H), 1.75 – 1.69 (m, 1H), 1.50 – 1.41 (m, 2H), 1.29 – 1.25 (m, 6H), 1.14 – 1.04 (m, 2H), 0.90 – 0.82 (m, 6H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 170.90, 150.49, 150.45, 148.09, 138.36, 136.34, 135.18, 134.56, 130.85, 127.94, 127.44, 121.57, 121.39, 116.44, 111.24, 45.17, 45.15, 45.09, 45.05, 42.40, 34.80, 32.24, 29.65, 28.18, 28.15, 22.83, 22.80, 19.96, 19.88, 14.10, 14.08, 11.91, 11.89.

HRMS (ESI): calculated for $[C_{24}H_{32}N_2ONa]^+$ $(M+Na)^+$ m/z: 387.2407, found: 387.2401.



20, 48%

4-(cyclohexylidenemethyl)-3-methyl-*N*-(quinolin-8-yl)pent-4-enamide (20)

The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)butyramide **S1** (0.20 mmol 43 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow liq. **20** (32.1 mg, 48%).

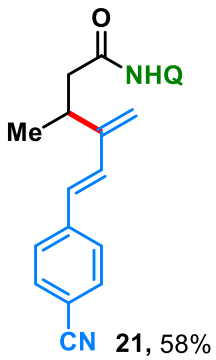
Physical appearance = Yellow oily liq**.**

***R*$_f$:** 0.27 (ethyl acetate /hexane, 1: 9 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.81 (s, 1H), 8.80 (dd, *J*=4.3, 2.7, 2H), 8.17 (d, *J*=8.2, 1H), 7.56 – 7.48 (m, 2H), 7.46 (dd, *J*=8.2, 4.2, 1H), 5.67 (s, 1H), 5.09 (s, 1H), 4.76 (s, 1H), 2.97 – 2.88 (m, 1H), 2.72 (dd, *J*=14.5, 6.6, 1H), 2.46 (dd, *J*=14.5, 8.1, 1H), 2.26 (dtd, *J*=19.3, 13.1, 6.4, 2H), 2.15 (t, *J*=5.7, 4H), 1.54 (ddd, *J*=16.7, 10.1, 4.9, 4H), 1.42 (dd, *J*=11.6, 5.4, 2H), 1.18 (d, *J*=6.9, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ= 171.07, 149.12, 148.05, 144.43, 136.72, 134.64, 128.12, 127.68, 121.65, 121.50, 121.00, 116.83, 112.04, 44.55, 38.05, 37.75, 29.92, 28.89, 28.25, 26.92, 19.64.

HRMS (ESI): calculated for $[C_{22}H_{27}N_2O]^+$ $(M+H)^+$ m/z: 335.2118, found: 335.2114.



21, 58%

(*E*)-6-(4-cyanophenyl)-3-methyl-4-methylene-*N*-(quinolin-8-yl)hex-5-enamide (21)

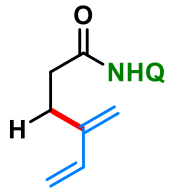
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)butyramide **S1** (0.20 mmol 43 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow sticky solid **21** (42.6 mg, 58%).

***R*$_f$:** 0.19 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.86 (s, 1H), 8.84 – 8.77 (m, 2H), 8.18 (dd, *J*=8.2, 1.3, 1H), 7.59 (d, *J*=8.2, 2H), 7.56 – 7.51 (m, 2H), 7.50 (d, *J*=8.3, 2H), 7.48 – 7.46 (m, 1H), 6.92 (d, *J*=16.4, 1H), 6.84 – 6.80 (m, 1H), 5.36 (s, 1H), 5.32 (s, 1H), 3.40 (dq, *J*=13.4, 6.7, 1H), 2.90 (dd, *J*=14.6, 5.6, 1H), 2.66 – 2.59 (m, 1H), 1.34 (d, *J*=6.8, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 170.50, 150.00, 148.25, 142.01, 138.40, 136.53, 134.47, 133.98, 132.46, 128.05, 127.52, 127.01, 126.57, 121.75, 121.70, 119.18, 116.77, 116.60, 110.53, 45.09, 31.80, 20.23.

HRMS (ESI): calculated for $[C_{24}H_{22}N_3O]^+$ $(M+H)^+$ m/z: 368.1757, found: 368.1755.



22, 52%

4-methylene-*N*-(quinolin-8-yl)hex-5-enamide (22)

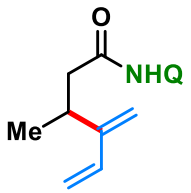
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)propionamide **S2** (0.20 mmol 40 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow liq. **22** (54.0 mg, 52%).

***R*$_f$:** 0.25 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.84 (s, 1H), 8.83 – 8.76 (m, 2H), 8.16 (dd, *J*=8.3, 1.6, 1H), 7.57 – 7.48 (m, 2H), 7.46 (dd, *J*=8.3, 4.2, 1H), 6.42 (dd, *J*=17.6, 10.9, 1H), 5.36 (d, *J*=17.7, 1H), 5.12 (t, *J*=11.5, 3H), 2.81 – 2.73 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 171.23, 148.19, 145.02, 138.53, 136.61, 134.59, 128.10, 127.61, 121.71, 121.58, 116.70, 116.47, 113.87, 36.77, 27.10.

HRMS (ESI): calculated for $[C_{16}H_{17}N_2O]^+$ $(M+H)^+$ m/z: 253.1335, found: 253.1331.



23, 58%

4-methylene-3-propyl-*N*-(quinolin-8-yl)hex-5-enamide (23)

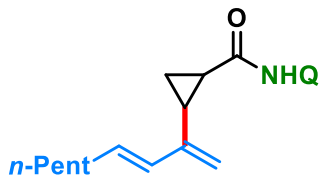
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)hexanamide **S1** (0.20 mmol 48.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow liq. of **23** (34.1 mg, 58%).

***R*$_f$:** 0.27 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.81 (s, 1H), 8.85 – 8.74 (m, 2H), 8.16 (dd, *J*=8.3, 1.5, 1H), 7.56 – 7.48 (m, 2H), 7.45 (dd, *J*=8.2, 4.2, 1H), 6.51 – 6.25 (m, 1H), 5.47 (d, *J*=17.7, 1H), 5.12 (t, *J*=9.5, 3H), 3.34 – 3.18 (m, 1H), 2.85 (dd, *J*=14.6, 5.3, 1H), 2.51 (dd, *J*=14.6, 8.9, 1H), 1.26 (d, *J*=6.8, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 170.79, 150.70, 148.25, 138.51, 138.14, 136.49, 134.67, 128.09, 127.59, 121.71, 121.55, 116.61, 113.98, 113.85, 45.02, 31.56, 20.01.

HRMS (ESI): calculated for $[C_{17}H_{19}N_2O]^+$ $(M+H)^+$ m/z: 267.1492, found: 267.1482.



27, 83%

2-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (27)

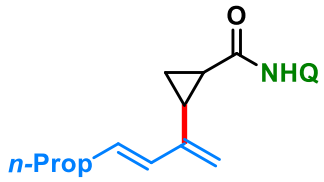
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow semi solid of **27** (27.8 mg, 83%).

***R*$_f$:** 0.24 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.90 (s, 1H), 8.81 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.71 (dd, *J* = 7.3, 1.4 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.51 – 7.42 (m, 3H), 6.12 (d, *J* = 15.8 Hz, 1H), 6.07 – 5.97 (m, 1H), 5.17 (d, *J*=4.2, 2H), 2.29 – 2.20 (m, 1H), 2.14 (q, *J* = 8.5 Hz, 1H), 1.96 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.87 (dt, *J* = 14.6, 7.5 Hz, 1H), 1.68 (dt, *J* = 7.3, 5.2 Hz, 1H), 1.28 (td, *J* = 8.2, 4.9 Hz, 1H), 1.16 – 1.08 (m, 1H), 1.07 – 0.93 (m, 3H), 0.93 – 0.79 (m, 2H), 0.59 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ= 168.71, 147.97, 141.39, 138.33, 136.40, 134.92, 132.03, 131.52, 128.03, 127.62, 121.53, 120.98, 116.52, 116.44, 32.91, 31.35, 28.99, 23.73, 23.57, 22.32, 13.90, 10.16.

HRMS (ESI): calculated for $[C_{22}H_{27}N_2O]^+$ $(M+H)^+$ m/z: 335.2118, found: 335.2122.



28, 58%

(*E*)-2-(hepta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropanecarboxamide (28)

The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was

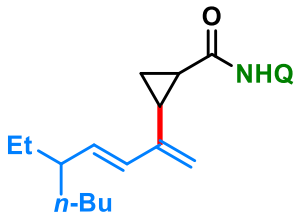
purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow liq. of **28** (23.9 mg, 78%).

***R*$_f$:** 0.24 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.89 (s, 1H), 8.81 (s, 1H), 8.71 (d, *J* = 6.8 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.35 (m, 3H), 6.12 (d, *J* = 15.7 Hz, 1H), 6.08 – 5.98 (m, 1H), 5.17 (s, 2H), 2.24 (dd, *J* = 5.3 Hz, 1H), 2.14 (dd, *J* = 7.8 Hz, 1H), 1.96 (dd, *J* = 13.2, 6.5 Hz, 1H), 1.85 (dd, *J* = 13.7, 6.8 Hz, 1H), 1.68 (d, *J* = 4.9 Hz, 1H), 1.27 (d, *J* = 6.7 Hz, 1H), 1.23 – 1.06 (m, 2H), 0.58 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ= 168.64, 147.91, 141.27, 138.31, 136.33, 134.90, 132.26, 131.15, 127.92, 127.54, 121.49, 120.93, 116.44, 116.40, 34.82, 23.65, 23.58, 22.31, 13.48, 10.09.

HRMS (ESI): calculated for $[C_{20}H_{23}N_2O]^+$ $(M+H)^+$ m/z: 307.1805, found: 307.1806.



29, 69%, dr= 1:1

(*E*)-2-(5-ethylnona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropanecarboxamide (29, dr 1:1)

According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily liq. **29** (25.0 mg, 69%).

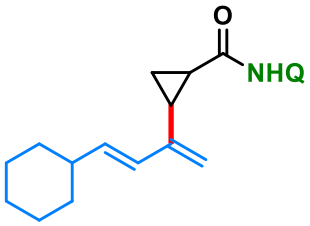
***R*$_f$:** 0.26 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.84 – 8.73 (m, 1H), 8.70 (td, *J* = 7.3, 2.0 Hz, 1H), 8.19 – 8.02 (m, 1H), 7.49 – 7.33 (m, 3H), 6.06 (dd, *J* = 15.7, 8.1 Hz, 1H), 5.70 (ddd, *J* = 15.7, 9.1, 3.1 Hz, 1H), 5.25 – 5.07 (m, 2H), 2.26 – 2.18 (m, 1H), 2.17 – 2.08 (m, 1H), 1.75 – 1.64 (m, 2H), 1.27 (m, 3H), 1.18 – 1.11 (m, 2H), 1.09 – 0.96 (m, 2H), 0.85 – 0.66 (m, 5H), 0.29 – 0.15 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.64, 147.94, 147.92, 141.29, 141.27, 138.35, 136.37, 135.83, 135.81, 134.95, 132.08, 128.05, 127.94, 127.66, 127.61, 121.53, 120.94, 120.92,

116.58, 116.56, 116.49, 116.46, 45.15, 45.09, 35.09, 34.82, 29.70, 29.48, 28.31, 28.09, 23.99, 23.92, 23.59, 23.55, 22.90, 22.34, 14.16, 13.71, 11.90, 11.48, 10.17, 10.15.

HRMS (ESI): calculated for $[C_{24}H_{31}N_2O]^+$ $(M+H)^+$ m/z: 363.2431, found: 363.2423.



30, 85%

2-((E)-4-cyclohexylbuta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (30)

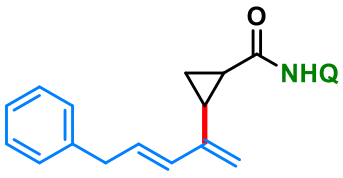
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily liq. **30** (29.4 mg, 85%).

***R*$_f$:** 0.25 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.80 (m, 1H), 8.70 (dd, *J* = 7.4, 1.3 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.51 – 7.40 (m, 3H), 6.08 (d, *J* = 15.9 Hz, 1H), 5.95 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.17 (s, 1H), 5.16 (s, 1H), 2.24 (td, *J* = 8.4, 5.5 Hz, 1H), 2.13 (dd, *J* = 16.6, 8.4 Hz, 1H), 1.84 – 1.78 (m, 1H), 1.68 (dt, *J* = 7.3, 5.1 Hz, 1H), 1.55 – 1.47 (m, 2H), 1.32 – 1.25 (m, 3H), 1.10 – 1.03 (m, 1H), 1.01 – 0.96 (m, 1H), 0.94 – 0.90 (m, 1H), 0.88 – 0.85 (m, 1H), 0.77 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.65, 147.86, 141.57, 138.24, 137.07, 136.34, 134.90, 129.45, 127.92, 127.56, 121.45, 120.91, 116.62, 116.36, 40.73, 32.83, 32.49, 26.06, 25.89, 25.81, 23.68, 23.52, 10.16.

HRMS (ESI): calculated for $[C_{23}H_{27}N_2O]^+$ $(M+H)^+$ m/z: 347.2118, found: 347.2126.



31, 87%

2-((*E*)-5-phenylpenta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (31)

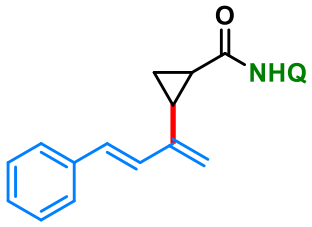
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a white sticky solid of **31** (30.9 mg, 87%).

***R*$_f$:** 0.25 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.83 (s, 1H), 8.72 (m, 2H), 8.17 (d, *J* = 7.4 Hz, 1H), 7.52 – 7.43 (m, 3H), 6.92 (dd, *J* = 6.8, 2.6 Hz, 2H), 6.85 – 6.70 (m, 3H), 6.26 – 6.07 (m, 2H), 5.21 (d, *J* = 6.2 Hz, 2H), 3.31 – 3.19 (m, 2H), 2.22 – 2.14 (m, 1H), 2.14 – 2.06 (m, 1H), 1.68 – 1.64 (m, 2H), 1.25 (td, *J* = 8.3, 4.9 Hz, 2H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 168.56, 147.88, 141.03, 140.09, 138.25, 136.29, 134.82, 133.49, 129.32, 128.31, 127.97, 127.94, 127.54, 125.63, 121.48, 120.98, 117.55, 116.40, 39.05, 23.65, 23.32, 10.21.

HRMS (ESI): calculated for $[C_{24}H_{22}N_2NaO]^+$ $(M+Na)^+$ m/z: 377.1624, found: 377.1632.



32, 80%

2-((*E*)-4-phenylbuta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (32)

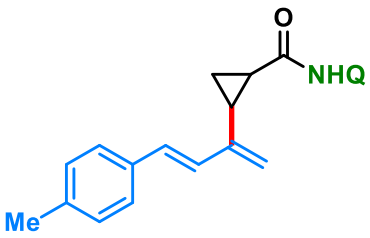
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow viscous compound of **32** (27.3 mg, 80%).

***R*$_f$:** 0.22 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ = 9.95 (s, 1H), 8.67 (dd, *J*=4.2, 1.7, 1H), 8.62 (dd, *J*=7.1, 1.9, 1H), 8.07 (dd, *J*=8.3, 1.6, 1H), 7.45 – 7.34 (m, 3H), 7.31 – 7.27 (m, 2H), 7.17 – 7.12 (m, 2H), 7.11 – 7.06 (m, 1H), 6.93 (d, *J*=16.2, 1H), 6.82 (d, *J*=16.2, 1H), 5.38 (s, 1H), 5.33 (s, 1H), 2.39 – 2.33 (m, 1H), 2.24 (dt, *J*=19.1, 9.5, 1H), 1.73 (dt, *J*=7.4, 5.2, 1H), 1.34 (td, *J*=8.2, 5.0, 1H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 168.53, 147.96, 141.15, 138.32, 137.44, 136.34, 134.78, 131.25, 129.02, 128.39, 127.96, 127.50, 127.31, 126.62, 121.49, 121.10, 119.33, 116.49, 23.85, 23.29, 10.04.

HRMS (ESI): calculated for $[C_{23}H_{21}N_2O]^+$ $(M+H)^+$ m/z: 341.1648, found: 341.1652.



33, 85%

<u>*N*-(quinolin-8-yl)-2-((*E*)-4-(p-tolyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxamide (33)</u>

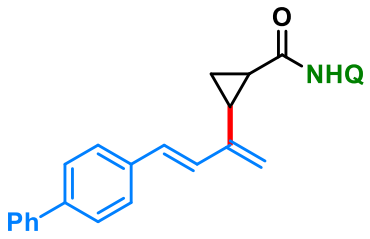
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily of **33** (30.1 mg, 85%).

***R*$_f$:** 0.25 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.95 (s, 1H), 8.69 (dd, *J*=4.2, 1.7, 1H), 8.63 (dd, *J*=7.1, 1.9, 1H), 8.07 (dd, *J*=8.3, 1.7, 1H), 7.45 – 7.33 (m, 3H), 7.19 (d, *J*=8.1, 2H), 6.96 (d, *J*=8.0, 2H), 6.93 – 6.75 (m, 2H), 5.36 (s, 1H), 5.30 (s, 1H), 2.35 (ddd, *J*=13.4, 8.7, 4.7, 1H), 2.30 – 2.19 (m, 4H), 1.73 (dt, *J*=7.4, 5.2, 1H), 1.33 (td, *J*=8.2, 4.9, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.58, 147.93, 141.22, 138.31, 137.12, 136.33, 134.79, 134.66, 130.32, 129.11, 128.94, 127.95, 127.50, 126.54, 121.46, 121.07, 118.78, 116.49, 23.84, 23.36, 21.25, 10.08.

HRMS (ESI): calculated for $[C_{24}H_{22}N_2NaO]^+$ $(M+Na)^+$ m/z: 377.1624, found: 377.1620.



34, 69%

<u>2-((*E*)-4-([1,1'-biphenyl]-4-yl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide(34)</u>

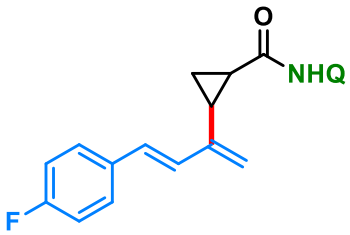
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow sticky solid of **34** (28.7 mg, 69%).

***R*$_f$:** 0.21 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.98 (s, 1H), 8.70 (dd, *J*=4.2, 1.4, 1H), 8.65 (dd, *J*=7.4, 1.1, 1H), 8.05 (dd, *J*=8.3, 1.4, 1H), 7.52 (d, *J*=7.4, 2H), 7.42 – 7.33 (m, 10H), 6.98 (d, *J*=16.2, 1H), 6.88 (d, *J*=16.2, 1H), 5.42 (s, 1H), 5.37 (s, 1H), 2.42 – 2.35 (m, 1H), 2.28 (dd, *J*=17.4, 9.1, 1H), 1.80 – 1.72 (m, 1H), 1.38 – 1.32 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.49, 147.91, 141.19, 140.76, 139.92, 138.25, 136.46, 136.29, 134.73, 131.26, 128.82, 128.53, 127.90, 127.44, 127.29, 127.01, 126.90, 121.45, 121.08, 119.45, 116.44, 23.80, 23.27, 10.03.

HRMS (ESI): calculated for $[C_{29}H_{25}N_2O]^+$ $(M+H)^+$ m/z: 417.1961, found: 417.1967.



35, 80%

2-((*E*)-4-(4-fluorophenyl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (35)

According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light brown semi-solid of **35** (28.7 mg, 80%).

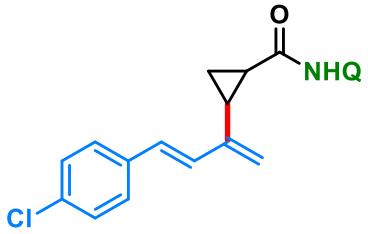
***R*$_f$:** 0.22 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.94 (s, 1H), 8.68 (dd, *J*=4.2, 1.6, 1H), 8.61 (dd, *J*=6.9, 2.1, 1H), 8.09 (dd, *J*=8.3, 1.6, 1H), 7.45 – 7.35 (m, 3H), 7.26 – 7.20 (m, 2H), 6.93 – 6.68 (m, 4H), 5.37 (s, 1H), 5.32 (s, 1H), 2.40 – 2.30 (m, 1H), 2.24 (dd, *J*=16.1, 7.4, 1H), 1.75 – 1.71 (m, 1H), 1.37 – 1.31 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.51, 163.39, 160.93, 147.95, 141.11, 138.30, 136.42, 134.75, 133.58, 131.03, 128.09, 128.01, 127.98, 127.84, 127.54, 121.53, 121.15, 119.46, 116.50, 115.37, 115.16, 23.81, 23.28, 10.11.

^{19}F NMR (376 MHz, $CDCl_3$) δ -114.94.

HRMS (ESI): calculated for $[C_{23}H_{20}FN_2O]^+$ $(M+H)^+$ m/z: 359.1554, found: 359.1555.



36, 95%

2-((*E*)-4-(4-chlorophenyl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (36)

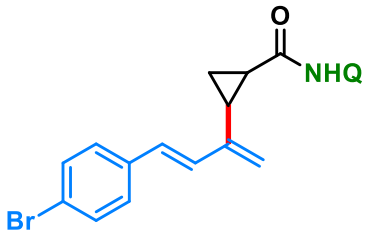
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a white solid of **36** (35.6 mg, 95%).

***R*$_f$:** 0.24 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.93 (s, 1H), 8.75 – 8.56 (m, 2H), 8.13 – 8.01 (m, 1H), 7.46 – 7.35 (m, 3H), 7.17 (d, *J*=8.5, 2H), 7.06 (d, *J*=8.5, 2H), 6.88 – 6.74 (m, 2H), 5.37 (d, *J*=14.3, 2H), 2.34 (td, *J*=8.3, 5.6, 1H), 2.22 (q, *J*=8.5, 1H), 1.76 – 1.69 (m, 1H), 1.36 – 1.30 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.41, 147.91, 141.03, 138.22, 136.37, 135.89, 134.66, 132.76, 131.76, 128.44, 127.92, 127.70, 127.45, 121.50, 121.14, 119.96, 116.43, 23.73, 23.20, 10.08.

HRMS (ESI): calculated for $[C_{23}H_{20}ClN_2O]^+$ $(M+H)^+$ m/z: 375.1259, found: 375.1261.



37, 89%

2-((*E*)-4-(4-bromophenyl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (37)

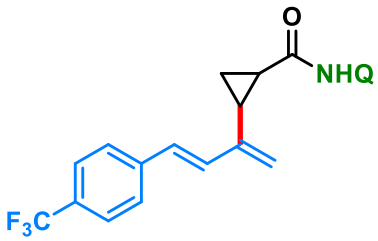
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light brown solid of **37** (37.3 mg, 89%).

***R*$_f$:** 0.25 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.93 (s, 1H), 8.67 (dd, *J*=4.2, 1.6, 1H), 8.62 (dd, *J*=7.3, 1.7, 1H), 8.05 (dd, *J*=8.3, 1.6, 1H), 7.42 – 7.34 (m, 3H), 7.21 (d, *J*=8.5, 2H), 7.09 (d, *J*=8.5, 2H), 6.81 (m, 2H), 5.39 (s, 1H), 5.36 (s, 1H), 2.39 – 2.29 (m, 1H), 2.26 – 2.16 (m, 1H), 1.72 (dt, *J*=7.3, 5.2, 1H), 1.36 – 1.29 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.35, 147.86, 140.99, 138.14, 136.33, 136.27, 134.61, 131.81, 131.33, 127.98, 127.86, 127.72, 127.40, 121.47, 121.11, 120.89, 120.05, 116.36, 23.67, 23.15, 10.04.

HRMS (ESI): calculated for $[C_{23}H_{20}BrN_2O]^+$ $(M+H)^+$ m/z: 419.0754, found: 419.0755.



38, 87%

(*N*-(quinolin-8-yl)-2-((*E*)-4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxamide (38)

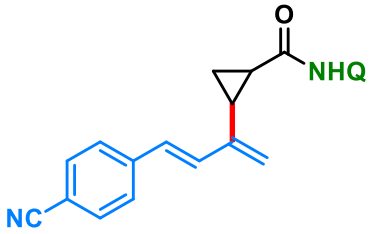
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light brown solid of **38** (35.5 mg, 87%).

***R_f*:** 0.22 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.94 (s, 1H), 8.66 (dd, *J*=4.2, 1.6, 1H), 8.60 (dd, *J*=7.2, 1.7, 1H), 8.06 (dd, *J*=8.3, 1.5, 1H), 7.46 – 7.27 (m, 7H), 6.92 (d, *J*=16.2, 1H), 6.86 (d, *J*=16.3, 1H), 5.45 (s, 1H), 5.41 (s, 1H), 2.42 – 2.31 (m, 1H), 2.24 (q, *J*=8.5, 1H), 1.74 (dt, *J*=7.3, 5.2, 1H), 1.35 (td, *J*=8.2, 5.0, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.34, 147.91, 140.98, 140.84, 138.18, 136.40, 134.62, 133.52, 128.65, 127.91, 127.54, 127.44, 126.59, 125.61, 125.22, 125.18, 122.91, 121.52, 121.18, 121.11, 116.40, 23.68, 23.12, 10.12.

HRMS (ESI): calculated for $[C_{24}H_{20}F_3N_2O]^+$ $(M+H)^+$ m/z: 409.1522., found: 409.1520.



39, 89%

2-((*E*)-4-(4-cyanophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (39)

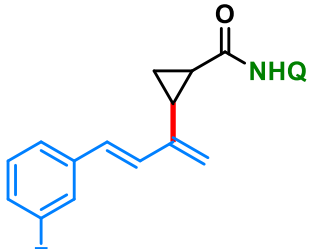
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow sticky liq. **39** (32.5 mg, 89%).

***R*$_f$:** 0.18 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.93 (s, 1H), 8.68 (dd, *J*=4.2, 1.6, 1H), 8.63 – 8.51 (m, 1H), 8.08 (d, *J*=8.3, 1H), 7.43 – 7.36 (m, 3H), 7.34 (d, *J*=8.4, 2H), 7.30 – 7.24 (m, 2H), 6.88 (s, 2H), 5.46 (s, 1H), 5.44 (d, *J*=1.3, 1H), 2.41 – 2.29 (m, 1H), 2.22 (q, *J*=8.6, 1H), 1.72 (dt, *J*=7.3, 5.2, 1H), 1.35 (td, *J*=8.2, 5.0, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.25, 147.91, 141.87, 140.88, 138.15, 136.46, 134.66, 134.55, 132.05, 127.90, 127.46, 127.16, 126.86, 122.02, 121.55, 121.22, 119.10, 116.42, 110.13, 23.61, 23.02, 10.18.

HRMS (ESI): calculated for $[C_{24}H_{20}N_3O]^+$ $(M+H)^+$ m/z: 366.1601., found: 366.1604.



40, 80%

2-((*E*)-4-(3-fluorophenyl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (40)

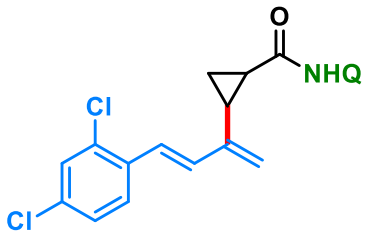
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow liq. **40** (28.7 mg, 80%).

***R*$_f$:** 0.23 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.95 (s, 1H), 8.70 (d, *J* = 3.6 Hz, 1H), 8.62 (d, *J* = 7.2 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H), 7.44 – 7.33 (m, 3H), 7.11 – 7.00 (m, 2H), 6.96 (d, *J* = 10.5 Hz, 1H), 6.91 – 6.72 (m, 3H), 5.41 (s, 1H), 5.37 (s, 1H), 2.35 (td, *J* = 8.4, 5.5 Hz, 1H), 2.22 (q, *J* = 8.4 Hz, 1H), 1.74 (dd, *J* = 12.4, 5.2 Hz, 1H), 1.33 (td, *J* = 8.2, 5.0 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 168.34, 164.13, 161.69, 147.99, 140.88, 139.76, 139.68, 138.17, 136.31, 134.63, 132.39, 129.70, 129.62, 127.88, 127.84, 127.81, 127.39, 122.20, 122.18, 121.51, 121.13, 120.32, 116.38, 114.06, 113.85, 113.21, 112.99, 23.70, 23.16, 9.97.

HRMS (ESI): calculated for $[C_{23}H_{20}FN_2O]^+$ $(M+H)^+$ m/z: 359.1554., found: 359.1560.



41, 75%

2-((*E*)-4-(2,4-dichlorophenyl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (41)

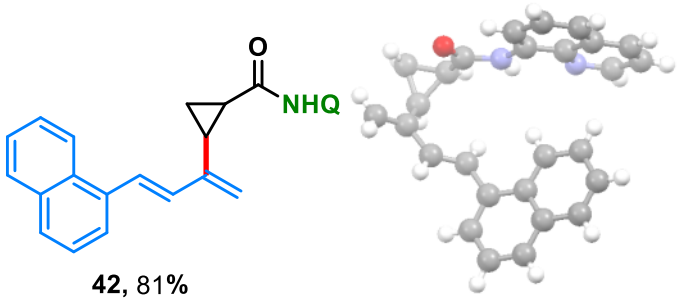
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow sticky solid. **41** (30.7 mg, 75%).

***R*$_f$:** 0.22 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.01 (s, 1H), 8.70 – 8.65 (m, 1H), 8.62 (d, *J* = 7.3 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.50 – 7.28 (m, 4H), 7.20 – 7.11 (m, 2H), 6.89 (t, *J* = 7.9 Hz, 1H), 6.76 (d, *J* = 16.1 Hz, 1H), 5.45 (s, 1H), 5.42 (s, 1H), 2.38 (td, *J* = 8.3, 5.6 Hz, 1H), 2.27 (q, *J* = 8.3 Hz, 1H), 1.74 (dd, *J* = 12.3, 5.2 Hz, 1H), 1.35 (td, *J* = 8.1, 5.0 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 168.36, 148.00, 141.11, 138.15, 137.78, 136.15, 134.73, 134.61, 133.02, 131.43, 128.73, 127.83, 127.33, 126.84, 125.24, 124.67, 121.51, 121.26, 121.09, 116.27, 23.46, 23.28, 10.18.

HRMS (ESI): calculated for $[C_{23}H_{19}Cl_2N_2O]^+$ $(M+H)^+$ m/z: 409.0869., found: 409.0868.



42, 81%

CCDC 2095999

2-((*E*)-4-(naphthalen-1-yl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (42)

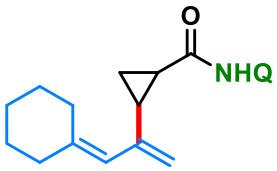
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow solid of **42** (31.6 mg, 81%).

***R*$_f$:** 0.24 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, CDCl$_3$) δ = 10.12 (s, 1H), 8.71 (d, *J*=7.4, 1H), 8.53 (dd, *J*=4.2, 1.5, 1H), 8.08 (d, *J*=8.2, 1H), 8.04 (d, *J*=8.5, 1H), 7.74 (d, *J*=8.2, 1H), 7.65 (m, 2H), 7.47 – 7.40 (m, 3H), 7.36 – 7.31 (m, 2H), 7.30 – 7.24 (m, 1H), 6.98 – 6.93 (m, 1H), 6.89 (d, *J*=15.9, 1H), 5.48 (s, *J*=12.8, 1H), 5.44 (s, 1H), 2.46 (td, *J*=8.3, 5.5, 1H), 2.38 (dd, *J*=16.5, 8.3, 1H), 1.82 (dt, *J*=7.2, 5.2, 1H), 1.42 (td, *J*=8.1, 4.9, 1H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 168.59, 147.96, 141.59, 138.27, 136.24, 135.34, 134.79, 134.36, 133.56, 131.36, 128.38, 127.91, 127.67, 127.54, 126.24, 125.63, 125.61, 125.54, 124.02, 123.88, 121.44, 121.12, 119.93, 116.52, 23.73, 23.59, 10.35.

HRMS (ESI): calculated for $[C_{27}H_{23}N_2O]^+$ $(M+H)^+$ m/z: 391.1805., found: 391.1809.



43, 65%

2-(3-cyclohexylideneprop-1-en-2-yl)-*N*-(quinolin-8-yl)cyclopropanecarboxamide (43)

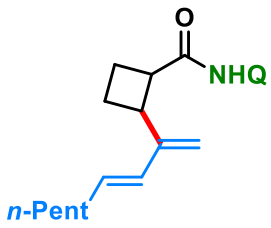
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow liq. of **43a** (21.6 mg, 65%).

***R*$_f$:** 0.25 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.91 (s, 1H), 8.81 (d, 1H), 8.75 (d, *J* = 7.3 Hz, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.54 – 7.38 (m, 3H), 5.63 (s, 1H), 5.22 (s, 1H), 5.02 (s, 1H), 2.26 (s, 2H), 2.13 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.07 (dd, *J* = 16.3, 8.1 Hz, 1H), 1.94 (s, 2H), 1.68 (d, *J* = 5.2 Hz, 1H), 1.41 – 1.20 (m, 7H).

^{13}C NMR (125 MHz, $CDCl_3$) δ= 168.54, 147.97, 142.97, 140.30, 138.30, 136.32, 134.91, 127.94, 127.49, 122.83, 121.51, 120.98, 116.42, 115.84, 37.60, 29.78, 28.40, 27.78, 27.43, 26.64, 24.23, 10.64.

HRMS (ESI): calculated for $[C_{22}H_{25}N_2O]^+$ $(M+H)^+$ m/z: 333.1961., found: 333.1973.



44, 69%

2-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclobutane-1-carboxamide (44)

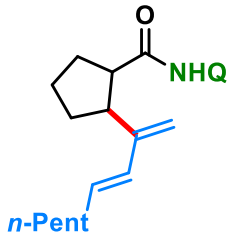
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclobutanecarboxamide **S19** (0.10 mmol 22.6 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow sticky solid of **44** (24.0 mg, 69%).

***R*$_f$:** 0.24 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 9.59 (s, 1H), 8.79 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.73 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.12 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.52 – 7.43 (m, 2H), 7.43 – 7.39 (m, 1H), 5.97 (d, *J* = 16.0 Hz, 1H), 5.83 (dt, *J* = 15.9, 6.6 Hz, 1H), 5.00 (s, 2H), 3.75 (dd, *J* = 18.0, 9.0 Hz, 1H), 3.67 – 3.56 (m, 1H), 2.63 (dd, *J* = 19.9, 9.9 Hz, 1H), 2.41 (tt, *J* = 9.4, 2.8 Hz, 1H), 2.30 – 2.19 (m, 1H), 2.14 – 2.05 (m, 2H), 2.01 – 1.94 (m, 1H), 1.34 – 1.28 (m, 3H), 1.20 – 1.16 (m, 3H), 0.79 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 171.61, 147.59, 144.48, 138.27, 136.39, 134.80, 131.66, 130.56, 127.96, 127.55, 121.36, 120.98, 116.41, 114.35, 47.41, 40.02, 32.95, 31.59, 28.88, 23.33, 22.49, 20.91, 14.02.

HRMS (ESI): calculated for $[C_{23}H_{29}N_2O]^+$ $(M+H)^+$ m/z: 349.2274, found: 349.2271.



45, 25%

(*E*)-2-(deca-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopentanecarboxamide (45)

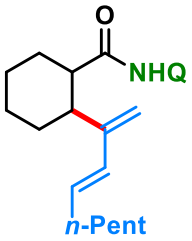
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopentanecarboxamide **S20** (0.20 mmol 48.1 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow oily liq. of **45** (18.1 mg, 25%).

***R*$_f$:** 0.26 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.66 (s, 1H), 8.76 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.73 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.15 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.54 – 7.37 (m, 3H), 6.08 (d, *J* = 15.9 Hz, 1H), 5.98 – 5.88 (m, 1H), 5.00 (s, 1H), 4.87 (s, 1H), 3.41 – 3.30 (m, 1H), 3.21 – 3.09 (m, 1H), 2.39 – 2.32 (m, 1H), 2.24 – 2.17 (m, 1H), 2.13 – 2.09 (m, 2H), 2.06 – 2.02 (m, 2H), 1.83 – 1.78 (m, 1H), 1.73 – 1.68 (m, 1H), 1.47 – 1.42 (m, 2H), 1.32 – 1.30 (m, 4H), 0.90 (t, *J* = 5.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ= 173.47, 147.84, 144.95, 138.64, 136.29, 134.91, 133.30, 130.16, 128.05, 127.59, 121.51, 121.03, 116.24, 114.05, 50.02, 46.43, 33.18, 31.82, 29.83, 29.22, 28.20, 23.98, 22.72, 14.20.

HRMS (ESI): calculated for $[C_{24}H_{31}N_2O]^+$ $(M+H)^+$ m/z: 363.2431, found: 363.2422.



46, 58%

2-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclohexane-1-carboxamide (46)

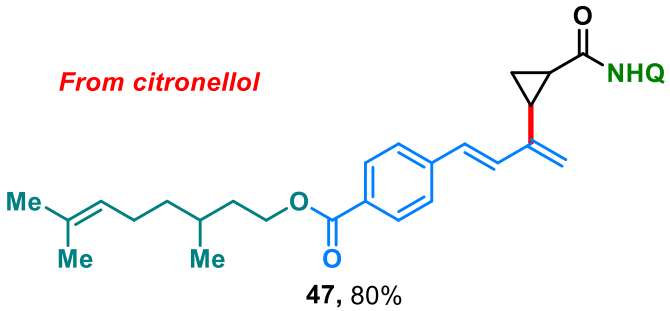
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclohexanecarboxamide **S21** (0.20 mmol 50.9 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily liq. of **46** (43.7 mg, 58%).

***R*$_f$:** 0.26 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.76 (m, 2H), 8.11 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.49 – 7.39 (m, 3H), 5.96 (d, *J* = 16.3 Hz, 1H), 5.87 (dt, *J* = 15.7, 6.4 Hz, 1H), 4.97 (s, 1H), 4.92 (s, 1H), 2.73 (td, *J* = 11.3, 3.2 Hz, 1H), 2.61 (td, *J* = 11.5, 3.5 Hz, 1H), 2.13 (dd, *J* = 12.6, 2.3 Hz, 1H), 2.03 – 1.94 (m, 3H), 1.47 – 1.38 (m, 3H), 1.35 – 1.20 (m, 8H), 0.84 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.94, 149.97, 147.98, 138.49, 136.29, 134.73, 130.92, 130.71, 127.93, 127.45, 121.47, 121.12, 116.49, 111.56, 52.03, 42.62, 33.41, 32.96, 31.53, 30.91, 28.98, 26.32, 25.79, 22.54, 14.07.

HRMS (ESI): calculated for $[C_{25}H_{33}N_2O]^+$ $(M+H)^+$ m/z: 377.2587, found: 377.2592.



47, 80%

3,7-dimethyloct-6-en-1-yl (*E*)-4-(3-(2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate (47)

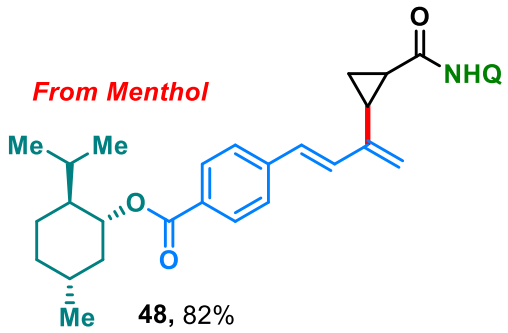
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow semi solid **47** (41.7 mg, 80%).

***R*$_f$:** 0.18 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.71 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.66 – 8.60 (m, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.45 – 7.37 (m, 3H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.01 – 6.88 (m, 2H), 5.45 (d, *J* = 21.8 Hz, 2H), 5.11 (t, *J* = 7.0 Hz, 1H), 4.37 – 4.27 (m, 2H), 2.40 (dd, *J* = 13.9, 8.3 Hz, 1H), 2.27 (q, *J* = 8.3 Hz, 1H), 2.07 – 1.95 (m, 2H), 1.82 – 1.75 (m, 2H), 1.68 (s, *J* = 9.3 Hz, 3H), 1.65 (dd, *J* = 12.7, 5.9 Hz, 1H), 1.62 (s, 3H), 1.59 – 1.53 (m, 1H), 1.44 – 1.34 (m, 2H), 1.28 – 1.21 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.40, 166.55, 147.86, 141.84, 141.03, 136.56, 134.57, 133.56, 131.50, 129.65, 128.93, 128.02, 127.95, 127.52, 126.36, 124.66, 121.52, 121.20, 120.98, 116.61, 63.49, 37.08, 35.59, 29.65, 25.83, 25.50, 23.72, 23.16, 19.61, 17.78, 10.09.

HRMS (ESI): calculated for $[C_{34}H_{39}N_2O_3]^+$ $(M+H)^+$ m/z: 523.2955, found: 523.2961.



48, 82%

(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl 4-((*E*)-3-(2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate (48)

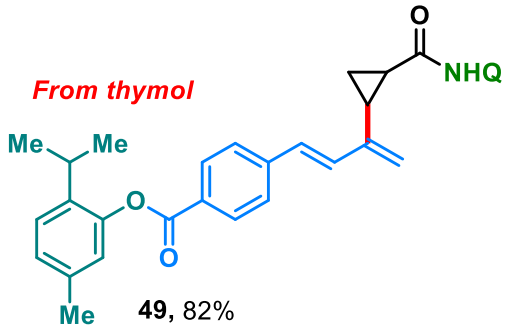
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow sticky solid **48** (42.9 mg, 82%).

***R_f*:** 0.19 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.68 (ddd, *J* = 7.2, 4.2, 1.1 Hz, 1H), 8.60 (d, *J* = 7.1 Hz, 1H), 8.05 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.79 (dd, *J* = 8.2, 3.2 Hz, 2H), 7.43 – 7.33 (m, 3H), 7.30 (d, *J* = 8.3 Hz, 2H), 6.99 – 6.84 (m, 2H), 5.44 (s, 1H), 5.40 (s, 1H), 4.93 – 4.80 (m, 1H), 2.36 (dd, *J* = 13.9, 8.3 Hz, 1H), 2.24 (q, *J* = 8.3 Hz, 1H), 2.11 – 2.04 (m, 1H), 1.94 – 1.84 (m, 1H), 1.79 – 1.68 (m, 3H), 1.56 – 1.42 (m, 2H), 1.37 – 1.31 (m, 1H), 1.16 – 1.01 (m, 2H), 0.92 – 0.86 (m, 6H), 0.77 (dd, *J* = 6.8, 1.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.36, 165.94, 147.96, 141.74, 141.70, 141.05, 141.02, 138.19, 136.33, 134.63, 133.47, 133.44, 129.66, 129.64, 129.24, 128.04, 127.90, 127.43, 126.31, 121.52, 121.49, 121.15, 120.92, 116.40, 74.74, 47.33, 41.06, 34.40, 31.51, 26.60, 26.55, 23.70, 23.14, 22.15, 20.85, 16.67, 16.62, 10.12, 10.07.

HRMS (ESI): calculated for $[C_{34}H_{39}N_2O_3]^+$ $(M+H)^+$ m/z: 523.2955, found: 523.2957.



49, 82%

5-isopropyl-2-methylphenyl 4-((E)-3-2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate (49)

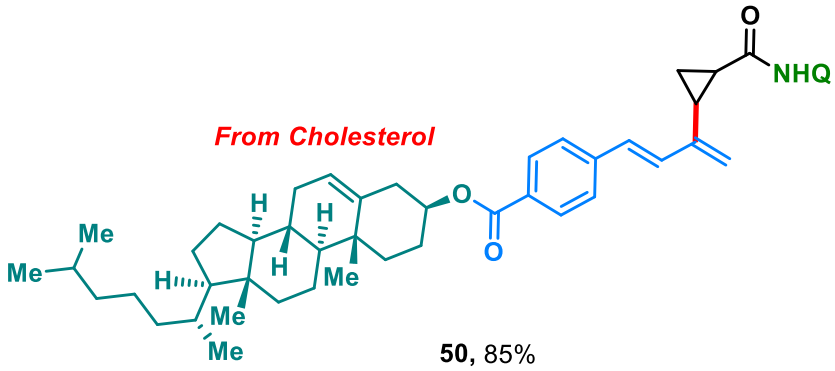
According to the general procedure, the title compound was prepared as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow semi solid **49** (40.3 mg, 78%).

***R*$_f$:** 0.21 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.00 (s, 1H), 8.72 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.64 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.07 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.00 – 7.91 (m, 2H), 7.47 – 7.34 (m, 5H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.06 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.98 (d, *J* = 2.7 Hz, 2H), 6.91 (d, *J* = 0.9 Hz, 1H), 5.49 (s, 1H), 5.45 (s, 1H), 3.02 (hept, *J* = 6.9 Hz, 1H), 2.42 – 2.36 (m, 1H), 2.34 (s, 3H), 2.27 (dd, *J* = 16.3, 8.6 Hz, 1H), 1.76 (dt, *J* = 7.3, 5.2 Hz, 1H), 1.37 (td, *J* = 8.2, 4.9 Hz, 1H), 1.21 (s, 3H), 1.20 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 168.34, 165.17, 148.21, 147.94, 142.58, 141.01, 138.17, 137.21, 136.68, 136.38, 134.62, 134.01, 130.23, 127.91, 127.85, 127.44, 127.19, 126.56, 126.53, 122.94, 121.52, 121.32, 121.16, 116.44, 27.34, 23.66, 23.11, 20.93, 10.11.

HRMS (ESI): calculated for $[C_{34}H_{33}N_2O_3]^+$ $(M+H)^+$ m/z: 517.2486, found: 517.2480.



50, 85%

(*3S,8S,9S,10R,13R,14S,17R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-((*E*)-3-(2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate (50)

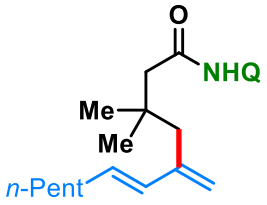
The title compound was prepared according to the general procedure as mentioned from *N*-(quinolin-8-yl)cyclopropanecarboxamide **S18** (0.10 mmol 21.2 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow semi solid **50** (64.0 mg, 85%).

***R*$_f$:** 0.20 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.95 (s, 1H), 8.68 (dd, *J* = 4.1, 1.1 Hz, 1H), 8.60 (dd, *J* = 7.0, 1.6 Hz, 1H), 8.06 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.46 – 7.34 (m, 3H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.00 – 6.86 (m, 2H), 5.44 (s, 1H), 5.40 (s, 2H), 4.85 – 4.71 (m, 1H), 2.41 (t, *J* = 7.6 Hz, 2H), 2.38 – 2.32 (m, 1H), 2.24 (q, *J* = 8.3 Hz, 1H), 2.04 – 1.92 (m, 3H), 1.89 – 1.80 (m, 2H), 1.77 – 1.69 (m, 2H), 1.60 – 1.43 (m, 6H), 1.40 – 1.29 (m, 4H), 1.28 – 1.23 (m, 1H), 1.22 – 1.07 (m, 7H), 1.05 (s, 3H), 1.04 – 0.95 (m, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 1.3 Hz, 3H), 0.86 (d, *J* = 1.3 Hz, 3H), 0.68 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 168.34, 165.85, 147.97, 141.73, 141.00, 139.75, 138.20, 136.36, 134.63, 133.48, 129.65, 129.24, 128.04, 127.91, 127.45, 126.30, 122.85, 121.55, 121.17, 120.92, 116.41, 74.53, 56.78, 56.23, 50.12, 42.41, 39.83, 39.62, 38.32, 37.12, 36.73, 36.29, 35.91, 32.03, 31.96, 28.35, 28.13, 27.98, 24.40, 23.95, 23.72, 23.14, 22.95, 22.69, 21.14, 19.48, 18.83, 11.97, 10.07.

HRMS (ESI): calculated for $[C_{51}H_{65}N_2O_3]^+$ $(M+H)^+$ m/z: 753.4990, found: 753.4976.



52, 67%

(*E*)-3,3-dimethyl-5-methylene-*N*-(quinolin-8-yl)dodec-6-enamide (52)

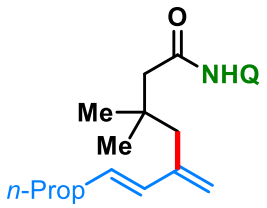
According to the general procedure, the title compound was prepared as mentioned from 3,3-dimethyl-*N*-(quinolin-8-yl)butanamide **S22** (0.20 mmol 48.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow liq. of **52** (48.8 mg, 67%).

***R*$_f$:** 0.24 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.77 (s, 1H), 8.83 – 8.78 (m, 2H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.45 (dd, *J* = 8.1, 4.2 Hz, 1H), 6.08 (d, *J* = 15.7 Hz, 1H), 5.84 – 5.73 (m, 1H), 5.11 (s, 1H), 4.89 (s, 1H), 2.49 (s, 2H), 2.41 (s, 2H), 2.09 – 2.04 (m, 2H), 1.38 – 1.35 (m, 2H), 1.27 – 1.24 (m, 4H), 1.16 – 1.11 (m, 6H), 0.85 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ= 170.87, 148.80, 148.15, 143.47, 136.66, 134.67, 133.54, 131.43, 131.23, 128.12, 127.64, 121.66, 121.45, 116.96, 50.68, 43.82, 34.72, 32.98, 31.58, 29.21, 28.08, 22.63, 14.17.

HRMS (ESI): calculated for $[C_{24}H_{33}N_2O]^+$ $(M+H)^+$ m/z: 365.2587, found: 365.2585



53, 50%

(*E*)-3,3-dimethyl-5-methylene-*N*-(quinolin-8-yl)dec-6-enamide (53)

The title compound was prepared according to the general procedure as mentioned from 3,3-dimethyl-*N*-(quinolin-8-yl)butanamide **S22** (0.20 mmol 48.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow liq. of **53** (33.6 mg, 50%).

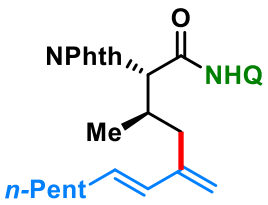
***R*$_f$:** 0.27 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 9.75 (s, 1H), 8.84 – 8.77 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57 – 7.42 (m, 4H), 6.09 (d, *J* = 15.7 Hz, 1H), 5.78 (d, *J* = 15.7 Hz, 1H), 5.12 (d, *J* =

2.0 Hz, 1H), 4.90 (d, *J* = 1.9 Hz, 1H), 2.48 (s, 2H), 2.41 (s, 2H), 2.08 – 2.04 (m, 2H), 1.43 – 1.37 (m, 3H), 1.14 (s, 6H), 0.88 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 170.83, 148.27, 143.47, 138.55, 136.48, 134.73, 133.77, 130.95, 128.09, 127.57, 121.68, 121.43, 117.00, 116.50, 50.73, 43.87, 35.08, 34.72, 28.07, 22.70, 13.86.

HRMS (ESI): calculated for $[C_{22}H_{29}N_2O]^+$, $(M+H)^+$ m/z: 337.2274;Found=337.2277



54, 64%

(*S*)-(*E*)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-5-methylene-*N*-(quinolin-8-yl)dodec-6-enamide (54)

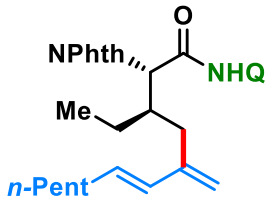
The title compound was prepared according to the general procedure as mentioned from (S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)butanamide **S23** (0.20 mmol 74.7 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow sticky solid of **54** (63.4 mg, 64%).

***R_f*:** 0.14 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 10.78 (s, 1H), 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.79 (dd, *J* = 5.7, 3.4 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.52 (d, *J* = 2.3 Hz, 1H), 7.51 (s, 1H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.99 (d, *J* = 15.9 Hz, 1H), 5.79 (dt, *J* = 15.8, 6.8 Hz, 1H), 4.96 (s, 1H), 4.92 (s, 1H), 4.79 (d, *J* = 10.8 Hz, 1H), 3.31 (dd, *J* = 6.7, 3.5 Hz, 1H), 2.80 (dd, *J* = 13.5, 2.9 Hz, 1H), 2.02 (dd, *J* = 13.5, 10.8 Hz, 1H), 1.95 – 1.85 (m, 2H), 1.19 – 1.04 (m, 6H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.80 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 168.24, 166.90, 148.65, 143.65, 138.90, 136.26, 134.44, 131.71, 131.22, 128.06, 127.39, 123.83, 122.14, 121.73, 117.22, 115.62, 62.66, 37.60, 33.03, 31.53, 31.10, 28.92, 22.57, 16.10, 14.13.

HRMS (ESI): calculated for $[C_{31}H_{34}N_3O_3]^+$ $(M+H)^+$ m/z: 496.2595, found: 496.2592.



55, 66%

(*2S,3R,E*)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-*N*-(quinolin-8-yl)dodec-6-enamide (55)

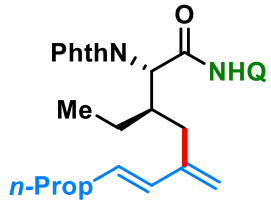
The title compound was prepared according to the general procedure as mentioned from (2S,3S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)pentanamide **S24** (0.20 mmol 77.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily liq. of **55** (67.3 mg, 66%).

***R*$_f$:** 0.15 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 10.80 (s, 1H), 8.88 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.82 – 8.73 (m, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.52 – 7.49 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.95 (d, *J* = 15.9 Hz, 1H), 5.80 (m, 1H), 4.95 (m, 4H), 3.50 – 3.29 (m, 1H), 2.54 (d, *J* = 3.9 Hz, 1H), 2.37 – 2.26 (m, 1H), 1.93 – 1.82 (m, 2H), 1.64 – 1.53 (m, 2H), 1.36 – 1.26 (m, 3H), 1.20 – 1.02 (m, 7H), 0.88 – 0.77 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 168.30, 167.23, 148.65, 143.63, 138.91, 136.25, 134.51, 134.42, 131.75, 131.65, 131.18, 128.06, 127.38, 123.82, 122.13, 121.73, 117.23, 115.44, 60.10, 35.27, 33.18, 33.04, 31.53, 28.92, 22.59, 21.36, 14.15, 8.50.

HRMS (ESI): calculated for $[C_{32}H_{36}N_3O_3]^+$ $(M+H)^+$ m/z: 510.2751, found: 510.2755.



56, 60%

(*3R,E*)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)dec-6-enamide (56)

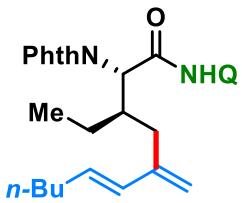
The title compound was prepared according to the general procedure as mentioned from (2S,3S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)pentanamide **S23** (0.20 mmol 77.5 mg). The crude product was purified *via* flash column chromatography (Hex/EtOAc) to afford a light yellow thick oily of **56** (57.8 mg, 60%).

***R*$_f$:** 0.13 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 10.77 (s, 1H), 8.88 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.80 – 8.75 (m, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.50 (dd, *J* = 6.4, 2.2 Hz, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.96 (d, *J* = 15.9 Hz, 1H), 5.83 – 5.73 (m, 1H), 4.96 (t, *J* = 5.5 Hz, 3H), 3.45 – 3.32 (m, , 1H), 2.57 (dd, *J* = 13.9, 4.0 Hz, 1H), 2.32 (dd, *J* = 13.9, 10.4 Hz, 1H), 1.94 – 1.83 (m, 2H), 1.61 (ddd, *J* = 14.6, 7.5, 3.5 Hz, 1H), 1.36 – 1.27 (m, 1H), 1.20 – 1.06 (m, 2H), 0.84 (t, *J* = 7.5 Hz, 3H), 0.74 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 168.29, 167.20, 148.63, 143.63, 138.89, 136.25, 134.49, 134.40, 131.75, 131.39, 128.04, 127.36, 123.80, 122.12, 121.72, 117.21, 115.44, 60.05, 35.27, 35.08, 33.24, 22.39, 21.39, 13.75, 8.54.

HRMS (ESI): calculated for $[C_{30}H_{32}N_3O_3]^+$ $(M+H)^+$ m/z: 482.2438, found: 482.2434.



57, 58%

(*3R*,*E*)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-*N*-(quinolin-8-yl)undec-6-enamide (57)

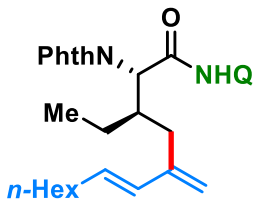
The title compound was prepared according to the general procedure as mentioned from (2S,3S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)pentanamide **S23** (0.20 mmol 77.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow thick oily of **57** (57.5 mg, 58%).

***R*$_f$:** 0.14 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 10.80 (s, 1H), 8.88 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.83 – 8.69 (m, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.88 (dd, *J* = 6.6, 3.3 Hz, 2H), 7.73 (dd, 4H), 7.54 – 7.49 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.96 (d, *J* = 15.9 Hz, 1H), 5.79 (dd, *J* = 14.8, 7.9 Hz, 1H), 4.95 (m, 3H), 3.47 – 3.32 (m, 1H), 2.56 (dd, *J* = 13.9, 4.0 Hz, 1H), 2.32 (dd, *J* = 13.9, 10.4 Hz, 1H), 1.93 – 1.83 (m, 2H), 1.64 – 1.52 (m, 1H), 1.37 – 1.23 (m, 2H), 1.18 – 1.01 (m, 4H), 0.84 (t, *J* = 7.5 Hz, 3H), 0.76 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 168.30, 167.23, 148.65, 143.63, 138.91, 136.25, 134.52, 134.41, 131.76, 131.59, 131.19, 128.06, 127.38, 123.81, 122.12, 121.73, 117.23, 115.43, 60.09, 35.29, 33.19, 32.74, 31.35, 22.35, 21.37, 13.98, 8.51.

HRMS (ESI): calculated for $[C_{31}H_{34}N_3O_3]^+$ $(M+H)^+$ m/z: 496.2595, found: 496.2589.



58, 70%

(*2S,3R,E*)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-*N*-(quinolin-8-yl)tridec-6-enamide (58)

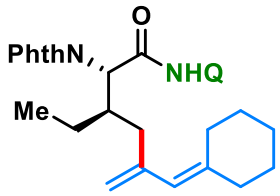
The title compound was prepared according to the general procedure as mentioned from (2S,3S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)pentanamide **23** (0.20 mmol 77.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a sticky solid **58** (77.31 mg, 70%).

***R_f*:** 0.16 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ= 10.80 (s, 1H), 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.83 – 8.72 (m, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.53 – 7.48 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.95 (d, *J* = 15.9 Hz, 1H), 5.78 (d, *J* = 15.8 Hz, 1H), 4.95 (t, *J* = 5.6 Hz, 3H), 3.44 – 3.33 (m, 1H), 2.54 (dd, *J* = 4.0 Hz, 1H), 2.37 – 2.27 (m, 1H), 1.94 – 1.83 (m, 2H), 1.64 – 1.57 (m, 1H), 1.32 – 1.21 (m, 5H), 1.13 – 1.08 (m, 4H), 0.84 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 168.17, 167.10, 148.52, 143.51, 138.79, 136.12, 134.38, 134.29, 131.63, 131.53, 131.05, 127.93, 127.25, 123.69, 122.00, 121.60, 117.11, 115.30, 59.97, 35.16, 33.06, 32.95, 31.66, 29.07, 28.87, 22.56, 21.23, 14.10, 8.37.

HRMS (ESI): calculated for $[C_{33}H_{37}N_3NaO_3]^+$ $(M+Na)^+$ m/z: 546.2727, found: 546.2725.



59, 68%

(*2S,3R*)-5-(cyclohexylidenemethyl)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-*N*-(quinolin-8-yl)hex-5-enamide (59)

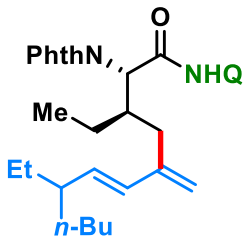
The title compound was prepared according to the general procedure as mentioned from (2S,3S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)pentanamide **23** (0.20 mmol 77.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a light-yellow liq. of **59** (69.0 mg, 68%).

***R*$_f$:** 0.17 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.63 (s, 1H), 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.80 – 8.67 (m, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.87 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.50 (d, *J* = 4.5 Hz, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.58 (s, 1H), 5.03 (s, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 4.80 (s, 1H), 3.21 (d, *J* = 4.5 Hz, 1H), 2.40 (dd, *J* = 4.1 Hz, 1H), 2.32 (dd, *J* = 9.9, 4.7 Hz, 2H), 2.29 – 2.24 (m, 1H), 2.10 – 2.05 (m, 2H), 1.58 – 1.47 (m, 6H), 1.37 – 1.26 (m, 2H), 0.87 (t, *J* = 9.7, 5.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.28, 167.02, 148.60, 143.74, 143.17, 138.90, 136.26, 134.43, 134.35, 131.80, 128.03, 127.35, 123.76, 122.75, 122.08, 121.74, 117.14, 115.02, 59.53, 37.95, 37.72, 36.10, 29.96, 28.75, 28.12, 26.90, 21.51, 9.08.

HRMS (ESI): calculated for $[C_{32}H_{34}N_3O_3]^+$ $(M+H)^+$ m/z: 508.2595, found: 508.2584.



60, 66%, dr= 1:1

(*2S,3R,E*)-2-(1,3-dioxoisoindolin-2-yl)-3,8-diethyl-5-methylene-*N*-(quinolin-8-yl)dodec-6-enamide(60 dr 1:1)

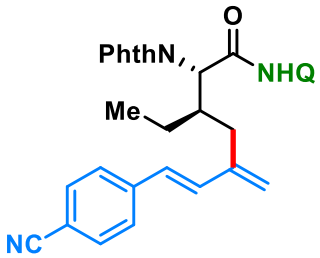
The title compound was prepared according to the general procedure as mentioned from (2S,3S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)pentanamide **S23** (0.20 mmol 77.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a yellow oily liq. of **60** in **dr 1:1** (71.0 mg, 66%).

***R*$_f$: 0.15** (hexane /ethyl acetate, 9:1 v/v).

H NMR (400 MHz, $CDCl_3$) δ 10.72 (s, 1H), 8.86 (td, *J* = 4.2, 1.7 Hz, 1H), 8.78 (dd, *J* = 9.0, 4.3 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.89 (ddd, *J* = 5.4, 3.0, 1.3 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.53 – 7.47 (m, 2H), 7.44 (ddd, *J* = 8.3, 4.2, 0.7 Hz, 1H), 5.94 (d, *J* = 15.9 Hz, 1H), 5.63 – 5.42 (m, 1H), 4.98 (dt, *J* = 7.9, 3.8 Hz, 3H), 3.42 – 3.29 (m, 1H), 2.63 – 2.51 (m, 1H), 2.41 – 2.24 (m, 1H), 1.83 – 1.73 (m, 1H), 1.66 – 1.59 (m, 1H), 1.33 – 1.21 (m, 6H), 1.19 – 1.04 (m, 5H), 0.89 – 0.81 (m, 7H), 0.76 (t, *J* = 5.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.30, 168.28, 167.28, 167.24, 148.64, 143.76, 138.90, 136.25, 136.01, 135.94, 134.55, 134.54, 134.38, 131.81, 131.79, 131.20, 131.18, 128.04, 127.36, 123.81, 123.79, 122.09, 121.71, 117.21, 115.29, 115.24, 60.00, 59.94, 45.08, 44.94, 35.75, 35.62, 34.61, 33.25, 29.68, 29.55, 28.03, 27.93, 22.91, 21.65, 21.49, 14.24, 14.14, 11.96, 11.83, 8.99, 8.82.

HRMS (ESI): calculated for $[C_{34}H_{40}N_3O_3]^+$ $(M+H)^+$ m/z: 538.3064, found: 538.3061.



61, 65 %

(*2S,3R,E*)-7-(4-cyanophenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-*N*-(quinolin-8-yl)hept-6-enamide (61)

The title compound was prepared according to the general procedure as mentioned (2S,3S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)pentanamide **S23** (0.20 mmol 77.5 mg). The crude product was purified via flash column chromatography (Hex/EtOAc) to afford a sticky solid of **61** (70.3 mg, 65%).

***R*$_f$: 0.10** (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.78 (s, 1H), 8.82 (dd, *J*=5.5, 3.4, 1H), 8.72 (d, *J*=2.9, 1H), 8.13 (d, *J*=7.3, 1H), 7.88 (dd, *J*=5.3, 3.0, 2H), 7.73 (dd, *J*=5.3, 3.0, 2H), 7.56 – 7.50 (m,

2H), 7.44 – 7.31 (m, 3H), 7.10 (d, *J*=8.2, 2H), 6.81 – 6.63 (m, 2H), 5.29 (s, 1H), 5.26 (s, 1H), 4.95 (t, *J*=14.8, 1H), 3.46 (m, 1H), 2.72 (dd, *J*=13.9, 3.2, 1H), 2.46 (dd, *J*=13.8, 10.5, 1H), 1.33 – 1.18 (m, 2H), 0.87 (t, *J*=7.4, 3H).

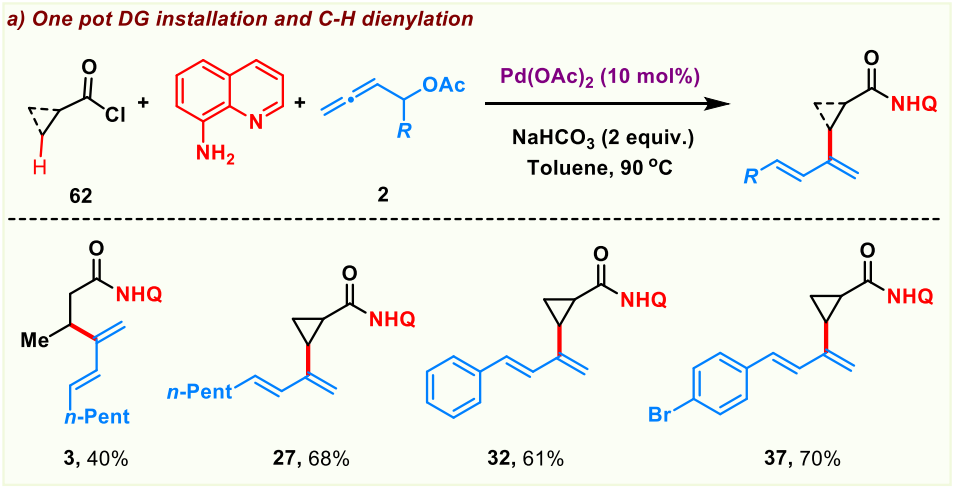
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.23, 167.12, 148.69, 143.05, 141.95, 138.72, 136.24, 134.53, 134.42, 133.76, 132.13, 131.63, 128.06, 127.60, 127.40, 126.82, 123.87, 122.29, 121.79, 120.99, 119.26, 117.23, 110.11, 59.72, 35.00, 32.71, 21.18, 8.28.

HRMS (ESI): calculated for $[C_{34}H_{29}N_4O_3]^+$ $(M+H)^+$ m/z: 541.2234, found: 541.2226.

8. One pot synthesis.

(i) Typical Procedure for the All-in-One-Pot Synthesis of 3, 27, 32 and 37.

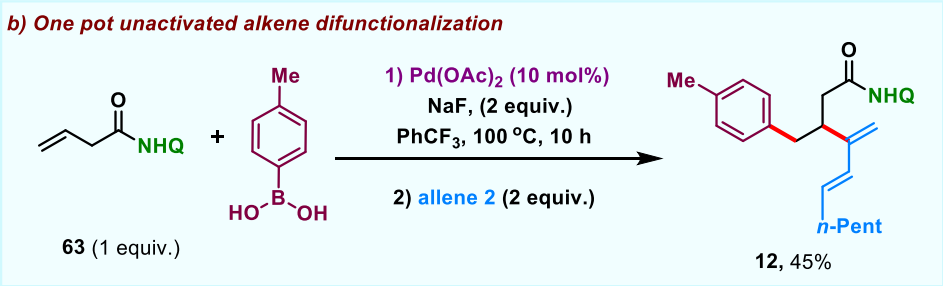
Corresponding acid Chloride (0.1 mmol 1 equiv.), 8-aminoquinoline (0.1 mmol 1 equiv.), $NaHCO_3$ (2 equiv.), allenyl acetate (0.15 mmol 1.5 equiv.), $Pd(OAc)_2$ (10 mol %) and Toluene (2 mL) were added to an oven-dried reaction tube equipped with a stir bar. The reaction mixture was stirred at 90 °C for 12 h. After completing reaction, the resulting mixture was cooled to room temperature, filtered through cotton wool, washed with ethyl acetate and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, mesh 100-200; hexane: ethyl acetate; 80:20) to give desire the product.



(ii) Typical Procedure for the All-in-One-Pot Synthesis of 3j.

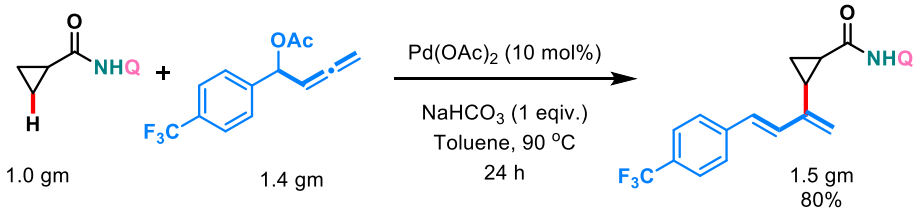
To an oven dried screw-cap reaction tube equipped with a magnetic stir bar were added $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), alkene (21.2 mg, 0.1 mmol), phenyl boronic acid (0.2 mmol), NaF (8.4 mg, 0.2 mmol), and benzotrifluoride (1.0 mL). The vial was sealed with screw cap and placed in a pre-heated oil bath at100 °C. After 10 h, the reaction was brought to room temperature, and added allenyl acetate (0.15 mmol) followed by continue the reaction at the

same temperature for 10-12 h. Later completing reaction, the resulting mixture was cooled to room temperature, filtered through cotton wool, washed with ethyl acetate and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, mesh 100-200; hexane: ethyl acetate; 80:20) to give the desire product.



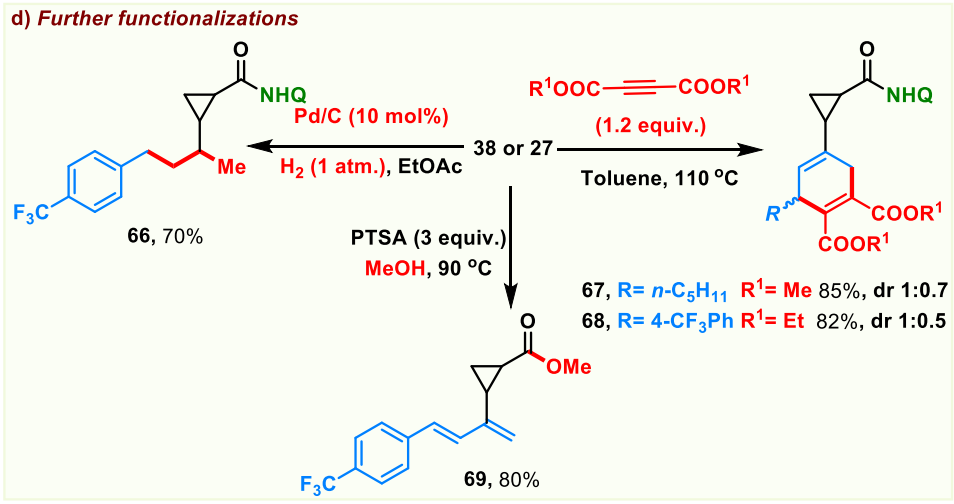
9. Gram scale reaction and further functionalization's.

(i) Gram scale reaction.



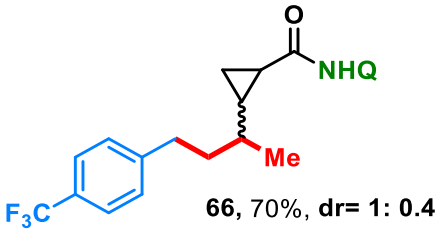
An oven dried Schlenk was charged with Teflon coated magnetic stir bar under argon atmosphere added **4a** *N*-(quinolin-8-yl)cyclopropanecarboxamide (1.0 g, 4.7 mmol, 1.0 eq), $Pd(OAc)_2$ (10 mol%), and followed by toluene (30 mL). Subsequently added sodium bicarbonate (1.0 equiv.) and **2x** 1-(4-(trifluoromethyl)phenyl)buta-2,3-dien-1-yl acetate (1.2 eq, 5.6 mmol, 1.45 g). The closed Schlenk tube containing reaction mixture were placed in preheated oil bath at 90°C for 24 hours. The reaction mixture was allowed to cool to room temperature after above mentioned time. Removal of solvent followed by column chromatography on silica gel afforded dienylated product **7a** with 80% (1.5 g)

(ii) Functionalization:



a. <u>Hydrogenation of (*N*-(quinolin-8-yl)-2-((*E*)-4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxamide (38)</u>

To a solution of **38** (*E*)-*N*-(quinolin-8-yl)-2-(4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxamide (0.10 mmol 40.8 mg) in EtOAc (3 mL) was added Pd/C (10 wt.%, 0.0267mmol) and H_2 gas was bubbled from a balloon at room temperature. After 2 h, mixture was filtered through a pad of celite and washed with EtOAc (10 mL) and diethyl ether (10 mL). The combined organic phase was dried with Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (silica gel mesh100-200; hexane: ethyl acetate; (95:05) to give the desire product yellow liq. (28.9 mg, 70%yield).



***N*-(quinolin-8-yl)-2-(4-(4-(trifluoromethyl)phenyl)butan-2-yl)cyclopropane-1-carboxamide (66)**

Yield= 70%, 28.9 mg

***R*$_f$:** 0.3 (hexane /ethyl acetate, 9:1 v/v).

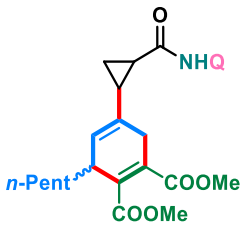
^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.08 (s, 1H), 8.85 (dd, *J*=4.2, 1.6, 1H), 8.79 (d, *J*=8.3, 1H), 8.19 (dd, *J*=8.2, 1.3, 1H), 7.57 – 7.52 (m, 4H), 7.51 – 7.48 (m, 2H), 7.34 (d, *J*=7.9, 2H),

2.79 (dd, *J*=10.1, 5.0, 1H), 1.96 (td, *J*=8.2, 5.4, 1H), 1.86 – 1.82 (m, 1H), 1.71 – 1.65 (m, 2H), 1.32 – 1.28 (m, 2H), 1.19 – 1.15 (m, 2H), 1.01 (d, *J*=6.3, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.48, 148.22, 148.05, 147.48, 138.39, 136.53, 134.97, 128.71, 128.55, 128.15, 127.64, 127.50, 127.42, 126.35, 125.38, 125.35, 124.89, 121.71, 121.61, 121.40, 121.27, 116.38, 39.58, 33.90, 31.74, 29.41, 21.24, 20.69, 12.97.

HRMS (ESI): calculated for $[C_{24}H_{24}F_3N_2O]^+$, $(M+H)^+$ m/z: 413.1835;Found=413.1846

b. Diels-alder reaction. To a solution of the synthesized **27** (0.1 mmol) in toluene (1 mL) was added the dienophile dimethyl but-2-ynedioate or diethyl but-2-ynedioate (0.15 mmol, 1.5 equiv). The reaction was stirred at 120 °C for 12 h. The reaction mixture was subjected to flash column chromatography to afford the titled product **67** and **68**.



67, 85% **(dr 1:0.7)**

dimethyl 3-pentyl-5-(2-(quinolin-8-ylcarbamoyl)cyclopropyl)cyclohexa-1,4-diene-1,2-dicarboxylate(67)

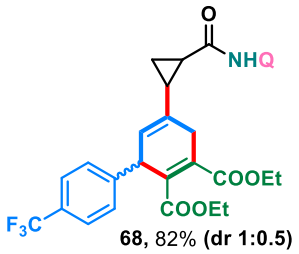
Yield= 85%, 40.5 mg

***R*$_f$:** 0.3 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (s, *J* = 6.9 Hz, 1H), 8.83 (s, *J* = 45.0 Hz, 1H), 8.71 (dd, *J* = 7.3, 4.3 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 7.60 – 7.41 (m, 3H), 5.71 – 5.53 (m, 1H), 3.82 – 3.59 (m, 6H), 3.21 – 2.82 (m, 2H), 2.17 (ddd, *J* = 16.7, 14.1, 8.2 Hz, 1H), 2.07 – 1.85 (m, 1H), 1.71 – 1.62 (m, 2H), 1.48 – 1.39 (m, 1H), 1.38 – 1.31 (m, 1H), 1.25 – 1.11 (m, 4H), 1.10 – 1.03 (m, 2H), 0.85 – 0.71 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.60, 168.68, 168.03, 167.90, 167.48, 167.46, 148.19, 140.37, 140.04, 138.37, 136.49, 134.79, 129.84, 129.72, 129.02, 128.84, 128.09, 127.62, 127.56, 125.60, 124.51, 121.66, 121.23, 116.61, 116.48, 52.17, 52.12, 39.10, 38.82, 34.13, 33.98, 32.08, 32.01, 31.55, 31.30, 26.13, 25.13, 24.77, 24.06, 23.79, 22.55, 22.48, 14.28, 14.14, 10.13, 9.16.

HRMS (ESI): calculated for $[C_{28}H_{33}N_2O_5]^+$, $(M+H)^+$ m/z: 477.2384;Found=477.2390



68, 82% **(dr 1:0.5)**

diethyl 5-(2-(quinolin-8-ylcarbamoyl)cyclopropyl)-4'-(trifluoromethyl)-1,4-dihydro-[1,1'-biphenyl]-2,3-dicarboxylate (68)

Yield= 82%, 47.4 mg

***R_f*:** 0.3 (hexane /ethyl acetate, 9:1 v/v).

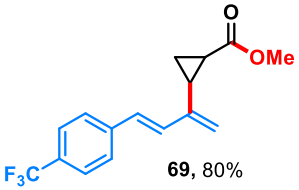
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 – 9.82 (m, 1H), 8.80 – 8.59 (m, 2H), 8.20 – 8.08 (m, 1H), 7.59 – 7.47 (m, 2H), 7.45 – 7.39 (m, 1H), 7.30 – 7.19 (m, 4H), 5.78 – 5.53 (m, 1H), 4.51 – 4.36 (m, 1H), 4.20 – 4.07 (m, 2H), 3.99 – 3.86 (m, 2H), 3.44 – 2.91 (m, 2H), 2.23 – 2.13 (m, 1H), 2.09 – 1.93 (m, 1H), 1.68 – 1.57 (m, 1H), 1.23 – 1.16 (m, 4H), 0.96 – 0.90 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.50, 167.93, 167.67, 167.43, 167.35, 167.09, 148.22, 148.15, 145.72, 145.20, 138.32, 138.29, 136.53, 135.45, 134.66, 134.56, 131.87, 130.74, 129.32, 129.17, 129.02, 128.96, 128.09, 128.06, 127.53, 127.46, 125.27, 125.24, 125.01, 123.27, 121.69, 121.62, 121.54, 121.49, 116.58, 116.46, 61.32, 60.97, 60.90, 45.40, 45.19, 31.75, 31.49, 29.80, 25.77, 25.62, 23.90, 23.84, 22.79, 14.21, 14.02, 13.69, 9.98, 9.49.

HRMS (ESI): calculated for $[C_{32}H_{30}F_3N_2O_5]^+$, $(M+H)^+$ m/z: 579.2109;Found=579.2115.

c. Removal of DG

In an oven dried reaction tube 0.10 mmol 40.8 mg of **5n** (*E*)-*N*-(quinolin-8-yl)-2-(4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxamide was taken. Then 3 equiv. *p*-toluenesulphonic acid and 3 mL methanol was added to it. The mixture was stirred in a preheated oil bath at 90 °C for 12 hours. After completion reaction was cooled to room temperature, filtered through celite and evaporated under vacuum. Pure product was isolated by column chromatography through a silica gel column (mesh 100- 200). Eluent: ethyl acetate / petroleum ether (2:98 v/v); light yellow liquid; isolated yield (24.0 mg, 80%).



69, 80%

methyl-2-((*E*)-4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxylate (69)

***R_f*:** 0.30 (hexane /ethyl acetate, 9:1 v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.55 (dd, *J*=10.4, 5.5, 2H), 7.52 (dd, *J*=11.8, 5.3, 2H), 6.92 (d, *J*=16.2, 1H), 6.79 (d, *J*=16.3, 1H), 5.43 (s, 1H), 5.33 (s, 1H), 3.51 (s, 3H), 2.14 (dd, *J*=7.9, 6.6, 2H), 1.55 – 1.46 (m, 1H), 1.33 – 1.28 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.71, 140.98, 140.88 (q, *J* = 6.3 Hz), 133.22, 130.94 (q, *J* = 290 Hz), 129.06 (q, *J* = 22 Hz), 127.52, 126.69, 125.68 (q, *J* = 3.7 Hz), 121.40, 51.73, 23.07, 20.08, 11.07.

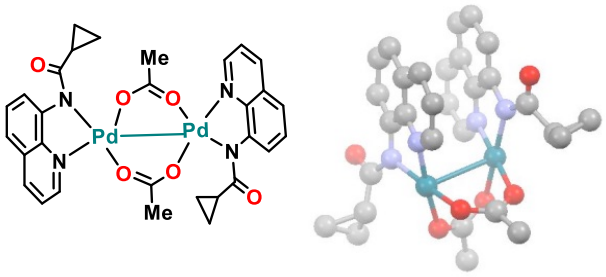
HRMS (ESI): calculated for $[C_{16}H_{16}F_3O_2]^+$, $(M+H)^+$ m/z: 297.1097;Found=297.1098.

10. Mechanistic studies

1. Isolation of palladium complexes.

a. General Procedure for synthesis of Pd(II) Complex 70.

To a 15 mL sealed-tube were added amide **S18** (1.0 equiv.), $Pd(OAc)_2$ (1.0 equiv.), and CH_3CN (2 mL). The tube was sealed and kept at r.t for 1h. The reaction mixture concentrated on rotavapor under reduced pressure. Then the palladium complex **70** were purified by washing with mixture of 1:1 ethyl acetate and hexane or recrystallization in DCM.



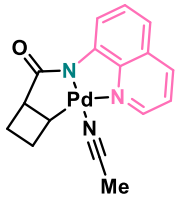
CCDC 2096002

^{1}H NMR (500 MHz, CD_3CN) δ 8.80 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.52 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.35 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.36 (dd, *J* = 8.1, 1.2 Hz, 1H), 2.00 (s, 6H), 1.97 (m, 1H), 1.71 (ddd, *J* = 9.0, 6.1, 3.2 Hz, 1H), 0.96 (td, *J* = 4.5, 3.1 Hz, 1H), 0.87 (ddd, *J* = 8.7, 7.5, 4.4 Hz, 1H), 0.79 (ddd, *J* = 7.6, 6.1, 4.8 Hz, 1H).

^{13}C NMR (100 MHz, CD_3CN) δ 171.93, 146.95, 144.61, 138.26, 129.93, 128.55, 121.26, 119.24, 118.39, 26.53, 19.79, 18.03.

b. General Procedure for synthesis of Pd(II) Complex 71.[5]

To a 15 mL sealed-tube were added amide **S19** (1.0 equiv.), $Pd(OAc)_2$ (1.0 equiv.), and CH_3CN (2 mL). The tube was sealed and heated at 60 °C for 12h. The reaction mixture was cooled to RT and concentrated on rotavapor under reduced pressure. Then the palladium complex **71** were purified by washing twice with mixture of 1:1 ethyl acetate and hexane or recrystallization in DCM.

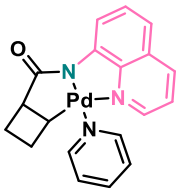


^{1}H NMR (500 MHz, CD_3CN) δ 8.94 (dd, *J* = 7.8, 1.0 Hz, 1H), 8.54 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.36 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.39 (dd, *J* = 8.0, 0.9 Hz, 1H), 3.14 (dd, *J* = 14.8, 7.4 Hz, 1H), 2.94 (ddd, *J* = 10.4, 5.0, 2.6 Hz, 1H), 2.53 – 2.37 (m, 4H), 1.99 (s, *J* = 1.7 Hz, 3H).

^{13}C NMR (125 MHz, CD_3CN) δ 188.57, 171.77, 147.21, 144.86, 138.15, 129.86, 128.44, 121.29, 119.62, 118.60, 53.63, 28.26, 27.52, 24.91, 19.79.

c. General Procedure for synthesis of Pd(II) Complex 72.[5]

To a 15 mL sealed-tube were added amide **S19** (1.0 equiv.), $Pd(OAc)_2$ (1.0 equiv.), pyridine (2.0 equiv.) and CH_3CN (2 mL). The tube was sealed and heated at 60 °C for 8 hrs. The reaction mixture was cooled to RT and concentrated on rotavapor under reduced pressure. Then the palladium complex **72** were purified by washing twice with mixture of 1:1 ethyl acetate and hexane or recrystallization in DCM.

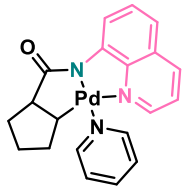


^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (d, *J* = 7.3 Hz, 1H), 8.82 (m, 2H), 8.10 (d, *J* = 7.7 Hz, 1H), 7.90 (d, *J* = 6.6 Hz, 1H), 7.80 (s, 1H), 7.47 (m, 3H), 7.22 (d, *J* = 6.9 Hz, 2H), 3.40 (d, *J* = 6.8 Hz, 1H), 2.77 (s, 1H), 2.57 (d, *J* = 7.3 Hz, 2H), 1.98 – 1.76 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 189.24, 151.69, 146.11, 145.49, 145.38, 137.82, 137.57, 129.71, 128.84, 125.72, 120.98, 120.59, 118.57, 54.04, 27.81, 27.38, 26.68.

d. General Procedure for synthesis of Pd(II) Complex 73.[5]

To a 15 mL sealed-tube were added amide **S20** (1.0 equiv.), $Pd(OAc)_2$ (1.0 equiv.), pyridine (2.0 equiv.) and CH_3CN (2 mL). The tube was sealed and heated at 60 °C for 12h. The reaction mixture was cooled to RT and concentrated on rotavapor under reduced pressure. Then the palladium complex **73** were purified by washing twice with mixture of 1:1 ethyl acetate and hexane or recrystallization in DCM.

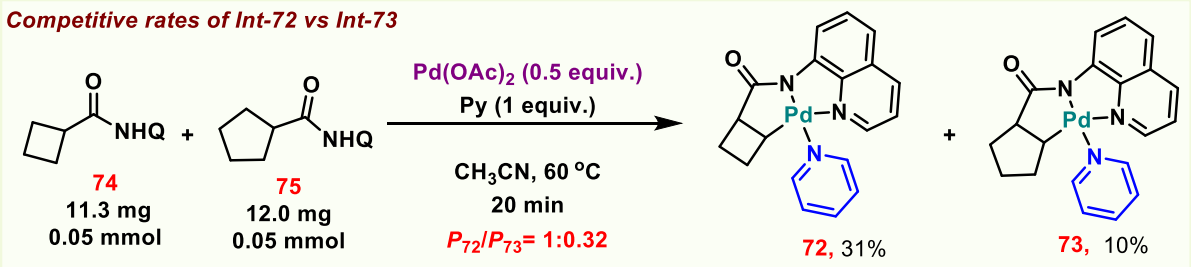


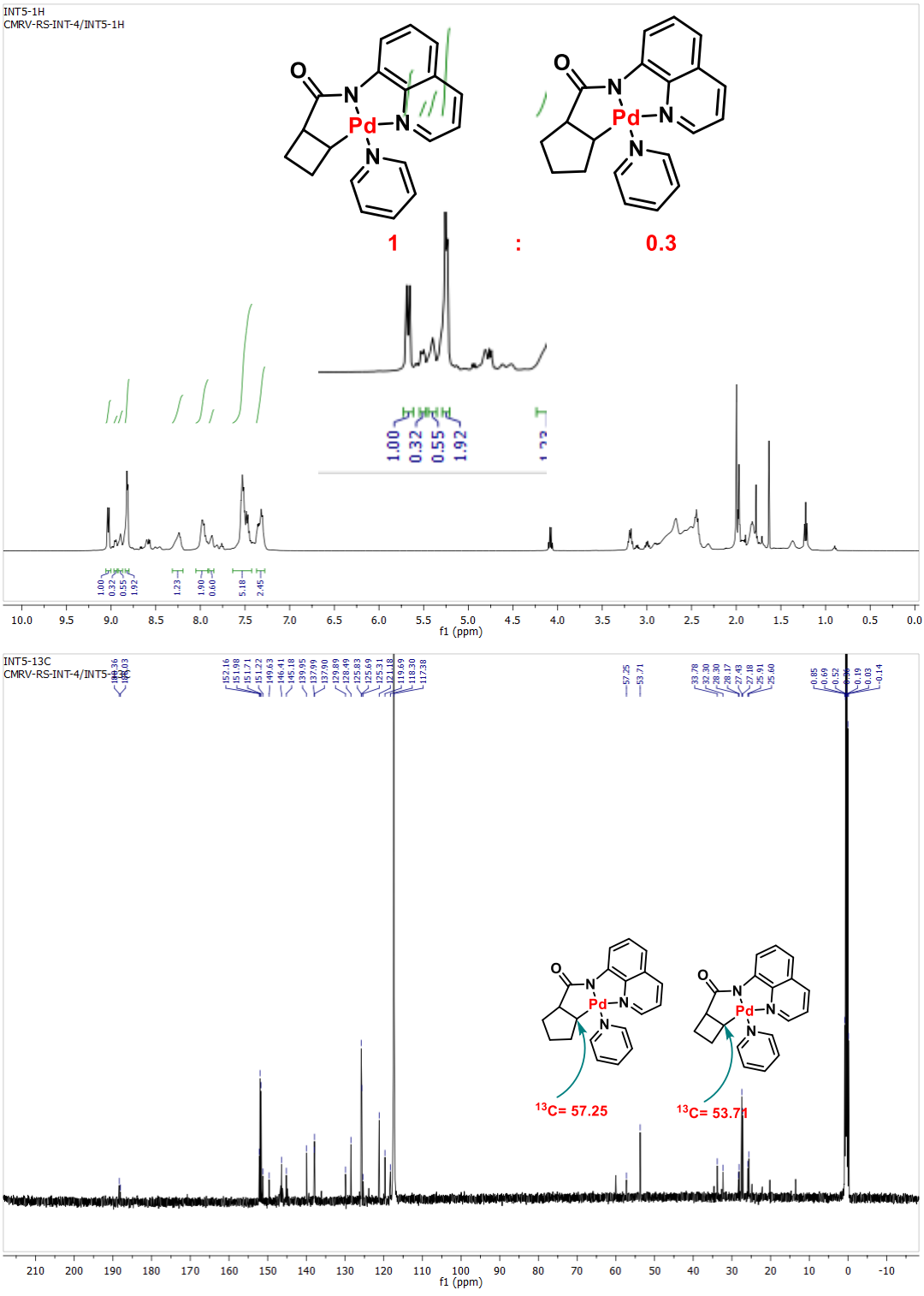
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (d, *J* = 7.9 Hz, 1H), 8.89 (d, *J* = 4.9 Hz, 2H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 4.1 Hz, 1H), 7.45 (dd, *J* = 12.9, 6.8 Hz, 3H), 7.21 – 7.13 (m, 2H), 3.13 (dd, *J* = 15.9, 8.5 Hz, 1H), 2.35 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.09 – 1.96 (m, 1H), 1.97 – 1.88 (m, 1H), 1.79 – 1.66 (m, 1H), 1.37 (td, *J* = 14.1, 6.8 Hz, 2H), 1.23 (dt, *J* = 12.6, 6.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 188.83, 152.10, 146.73, 145.34, 145.05, 137.83, 137.52, 129.85, 129.18, 125.70, 121.04, 120.51, 118.23, 57.62, 34.07, 32.55, 29.31, 26.22.

d. General Procedure for The Competitive Rate Determination Of Pd(II) Complex 72 and 73.

In an oven dried reaction tube, charged with magnetic stir-bar, **S19** (0.05 mmol), **S20** (0.05 mmol), and $Pd(OAc)_2$ (1.0 mmol, 1.0 equiv.), were added under air. Then CH_3CN (1 mL) was added into the reaction tube. The reaction tube was capped and the reaction mixture was allowed to stir at 60 °C for 20 min. After completion of the reaction, reaction mixture was cooled to room temperature and evaporated under reduced pressure. The ^{1}H NMR of crude reaction mixture was recorded which suggesting that the intermediate **72** formation rate is faster than **73**. Integration of highest de-shielded proton of both intermediate provided the ratio of the intermediate **72**:**73** is 1:0.3.

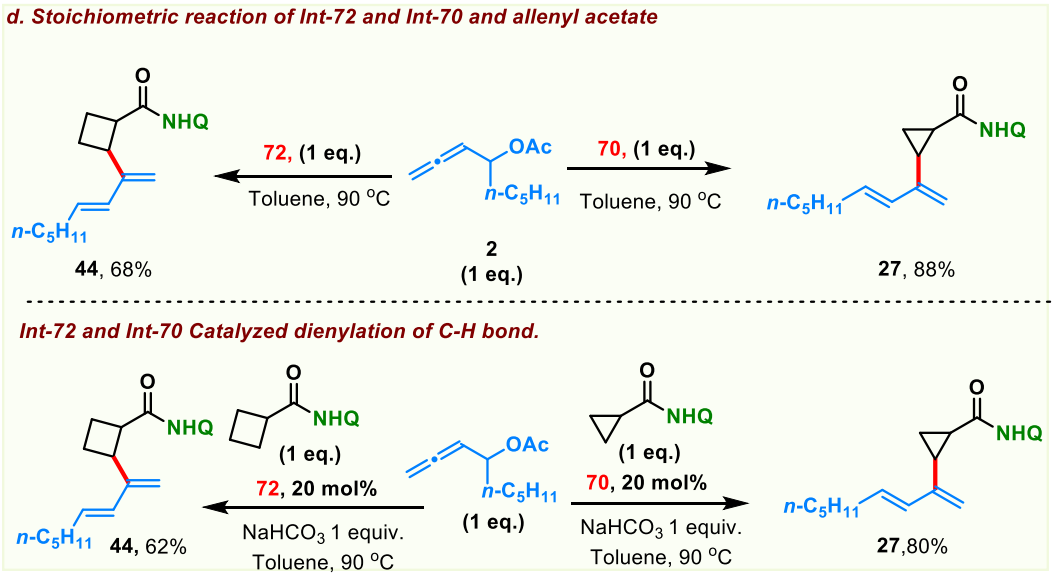




b. Dienylation of sp^3 C-H bond by using isolated intermediates.

An oven dried Schlenk was charged with Teflon coated magnetic stir bar under argon atmosphere added the dimeric intermediate **70** (1.0 equiv.), and followed by allenyl acetate **2** in toluene (1 mL). The closed Schlenk tube containing reaction mixture were placed in preheated oil bath at 90°C for 24 hours. The reaction mixture was allowed to cool to room temperature after above mentioned time. Removal of solvent followed by column

chromatography on silica gel afforded dienylated product **27** with 88% yield. Same procedure used for the dienylation of intermediate **72** and afforded the desired product in 68%.

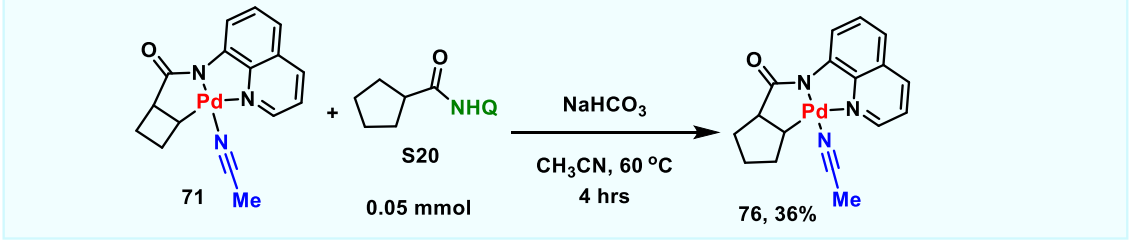


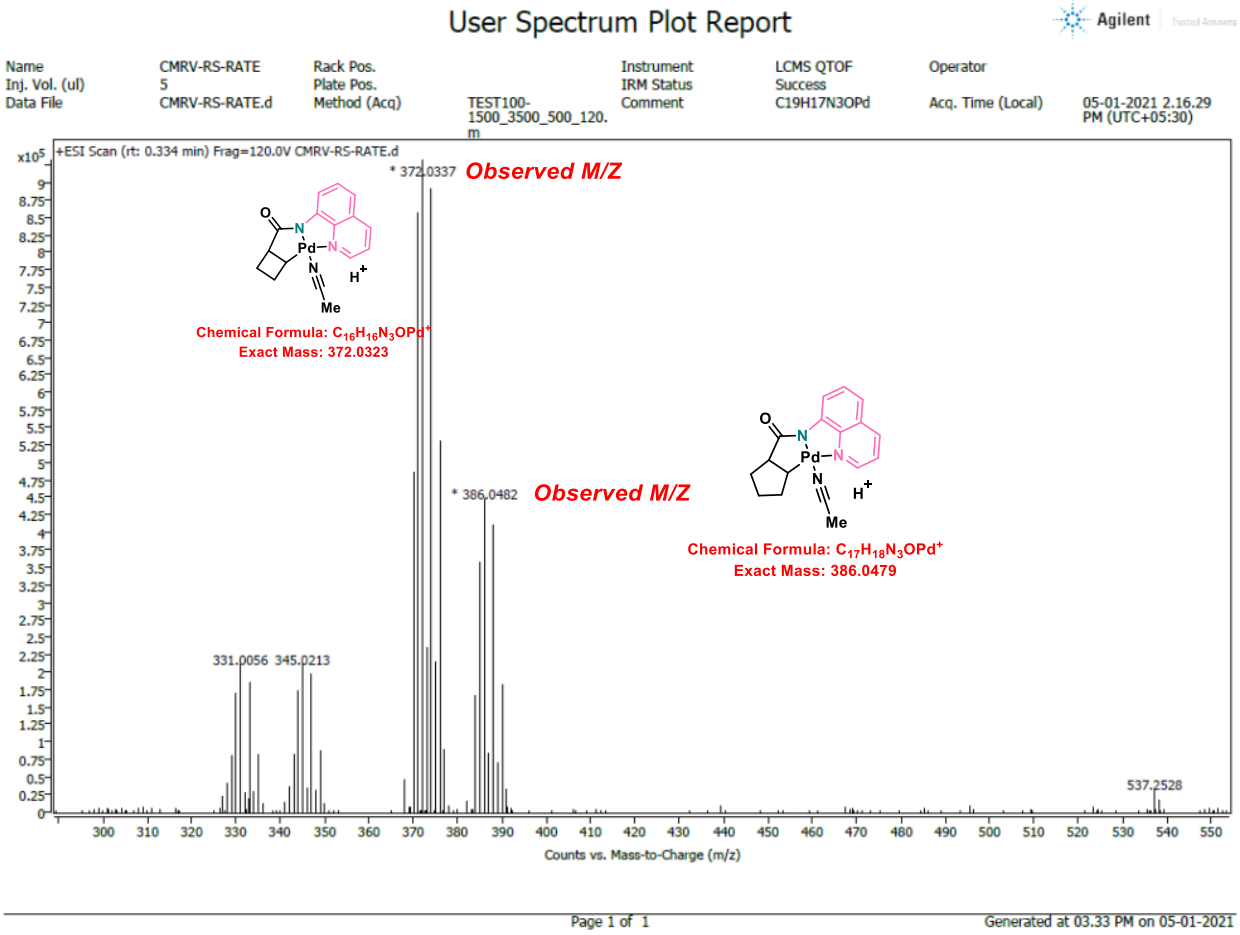
Further we used these intermediate in catalytic amount for the C-H dienylation to check its chemically and kinetically compatible with the reaction. The procedure is given here, To an oven dried screw-cap reaction tube equipped with stir bar, were added amide (0.1 mmol), freshly prepared allenyl acetate **2** (0.12 mmol), Intermediate **70** or **72** (20 mol%) and $NaHCO_3$ (0.1 mmol) followed by dry Toluene (1.0 mL). The reaction mixture was heated for 24 h at 90 °C. Upon completion as detected by TLC. The organic phase was evaporated under reduced pressure and the product was separated by using silica-gel column chromatography afforded dienylated product in 80% and 62% yield.

c. Probing the impact of base in reaction condition.

Study on the role of base: In screw cap reaction tubes with previously placed stir bars were charged with *N*-(quinolin-8-yl)cyclopentanecarboxamide **S20** (0.05 mmol 12 mg), palladium complex **71** (20.5 mg, 0.05 mmol) and sodium bicarbonate (4.2 mg, 0.05 mmol). The caps were fitted with a rubber septum and acetonitrile (1 mL) was added to this mixture by syringe under nitrogen atmosphere. The reaction mixture was vigorously stirred (600 rpm on Heidolph MR Hei-Standard stirrer) in a preheated oil bath of 60 °C for 4 h. Mass was taken from the reaction mixture and found 372.0337 along with 386.0482 peak in mass spectrometer. Following the same procedure in absence of sodium bicarbonate, the mass peak at 386.0482 was not observed.

c. Probing Base-Assisted Reversible C-H Activation

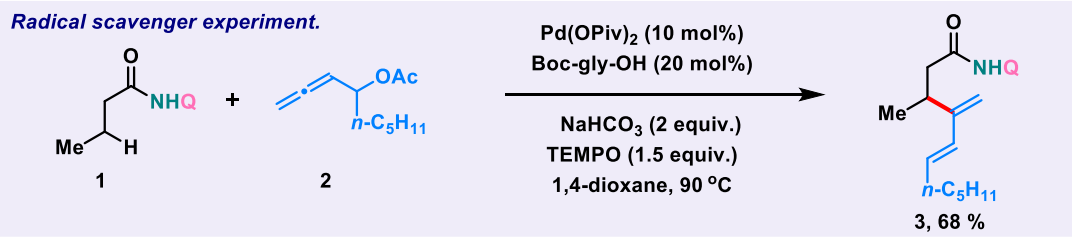




e. Radical Scavenger Experiment

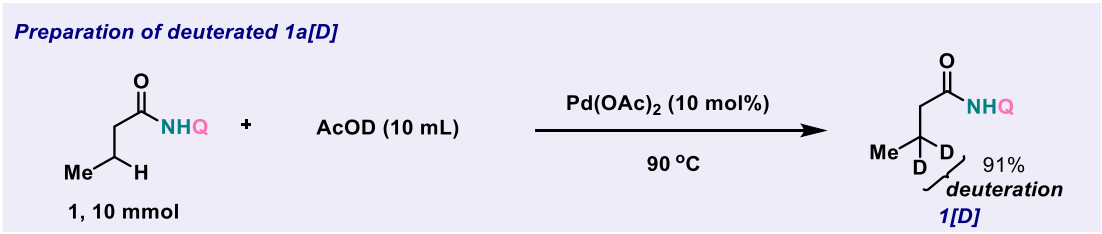
To an oven dried screw-cap reaction tube equipped with stir bar, were added amide (1 equiv.), TEMPO (equiv.), allenyl acetate (1.5 equiv.), $Pd(OAc)_2$ (10 mol%) and Na_2CO_3 (2 equiv.) followed by dry 1,4-dixane (1 mL). The reaction mixture was heated overnight at 90 ^oC. Upon completion as detected by TLC, the work up of the reaction mixture was done in ethyl acetate- water solvent mixture system. The organic phase was evaporated under reduced pressure and then the product was purified on flash silica gel chromatography afforded 68%

yield. This experiment clearly suggesting that reaction is not proceeding with any radical step.



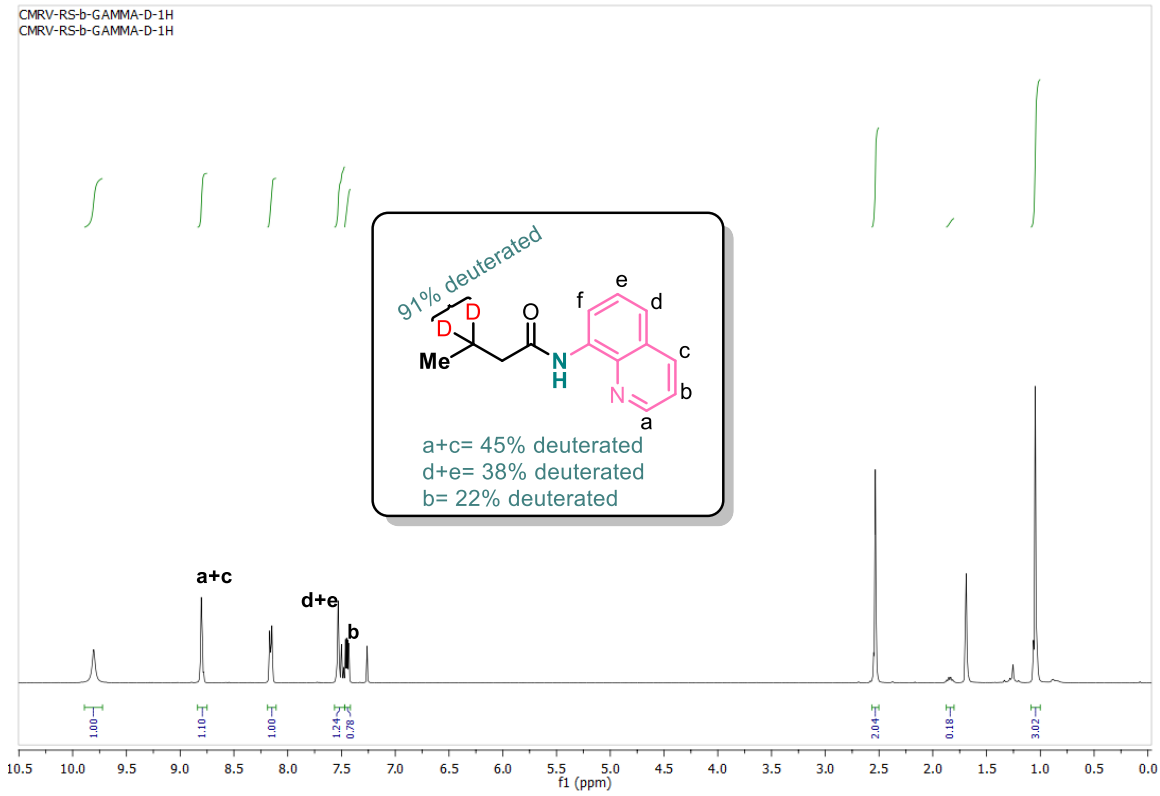
f. Preparation of deuterated substrate 1[D]

The solution of **1** (2.14 g, 10 mmol, 1 equiv.) and $Pd(OAc)_2$ (224.5 mg, 1 mmol, 0.1 equiv.) in deuterated acetic acid (10 mL) was heated at 90 °C for 24 hours. After completion the reaction was filtrated and concentrated, then the product was purified on flash silica gel chromatography (PE : EtOAc = 20:1). This procedure was repeated twice, giving 1.52 g of deuterated substrate **1[D]** in 70% yield.



^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.80 (m, 1.1 H), 8.19 – 8.11 (m, 1H), 7.56 – 7.47 (m, 1.24H), 7.45 (dd, *J* = 8.2, 4.2 Hz, 0.78H), 2.53 (s, 2H), 1.84 (0.18H), 1.05 (s, 2H).

^{13}C NMR (CDCl3, 100 MHz, ppm) δ 171.8, 148.1, 138.3, 136.4, 134.6, 127.9, 127.5, 121.6, 121.3, 116.4, 40.0, 18.6, 13.6

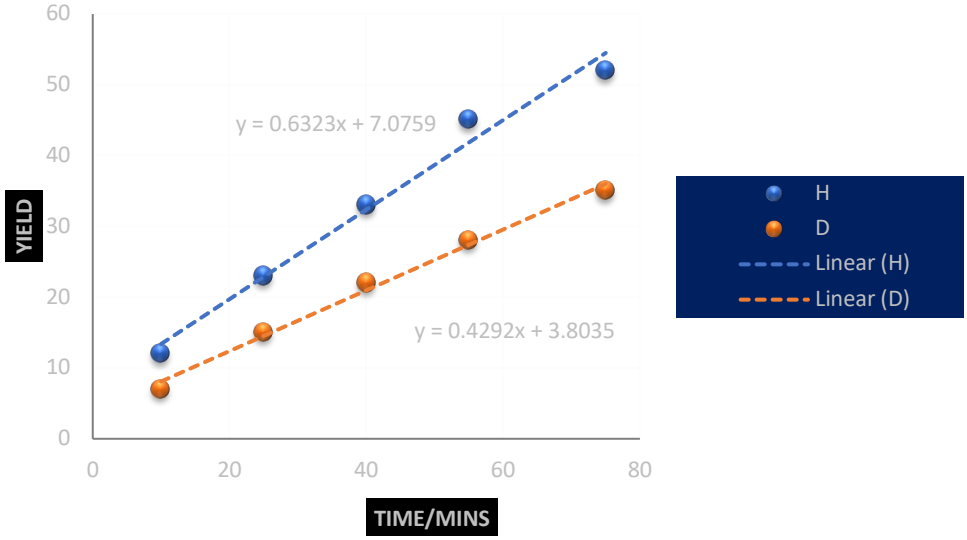


g. Parallel KIE

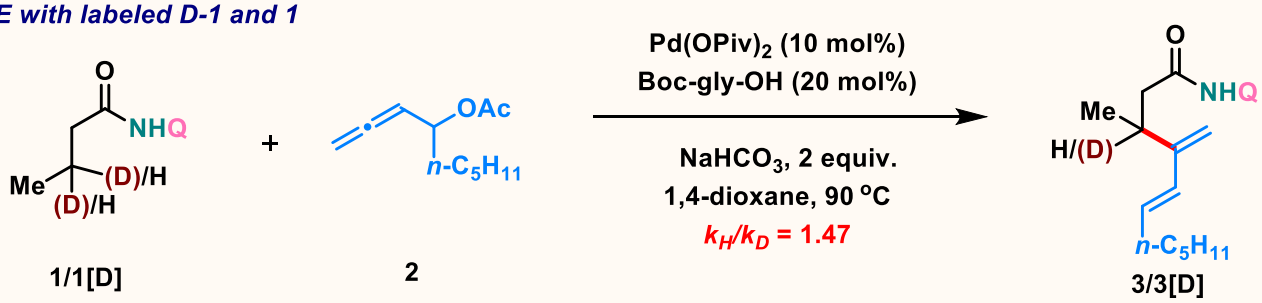
Kinetic isotope effect (KIE) of the dienylation of substrate **1** and deuterated **1-(D)** with **2** under standard condition **A**. Substrate **1-H** or **1-D** was subjected to the dienylation reaction with allenyl acetate under the general reaction condition **A** for 10, 25, 40, 55, and 75 min in different reaction tubes. Data was collected at 10, 25, 40, 55, and 75 min, Data collecting method: at specified reaction time, the reaction vial was quenched and isolated by silica gel flash chromatography. Average data of repeating experiments were used. K_H/K_D (~1.47) was estimated based on the ratio of dienylation yield.

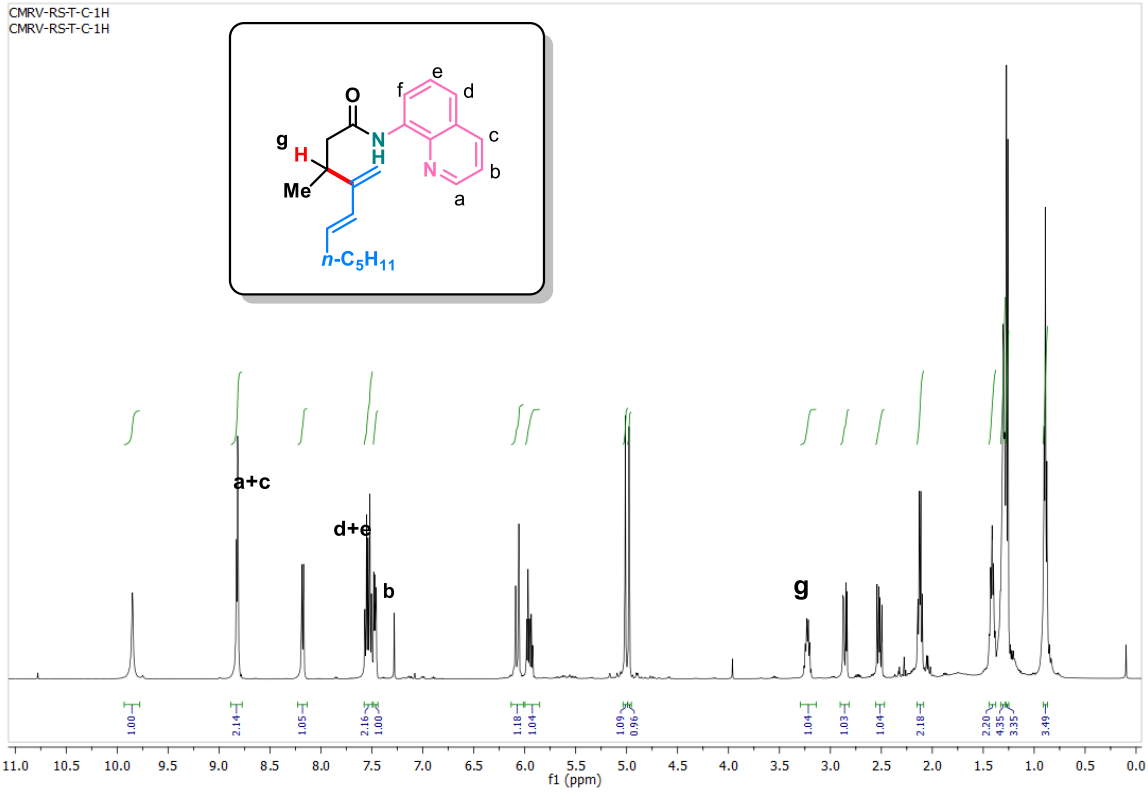
Time/Mins	*1-H Yield*	*1-D yield*
10	*12*	*7*
25	*23*	*15*
40	*33*	*22*
55	*45*	*28*
75	*52*	*35*

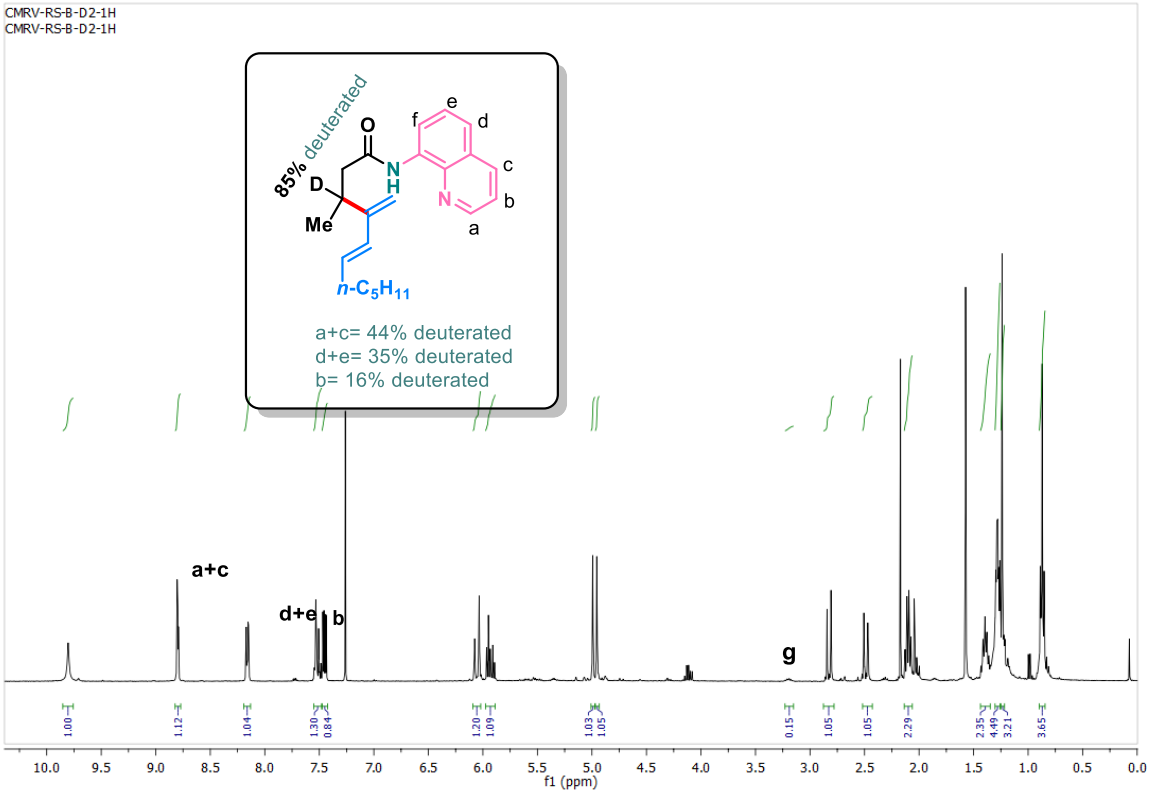
Kinetic Isotopic Effect



KIE with labeled D-1 and 1







12. References.

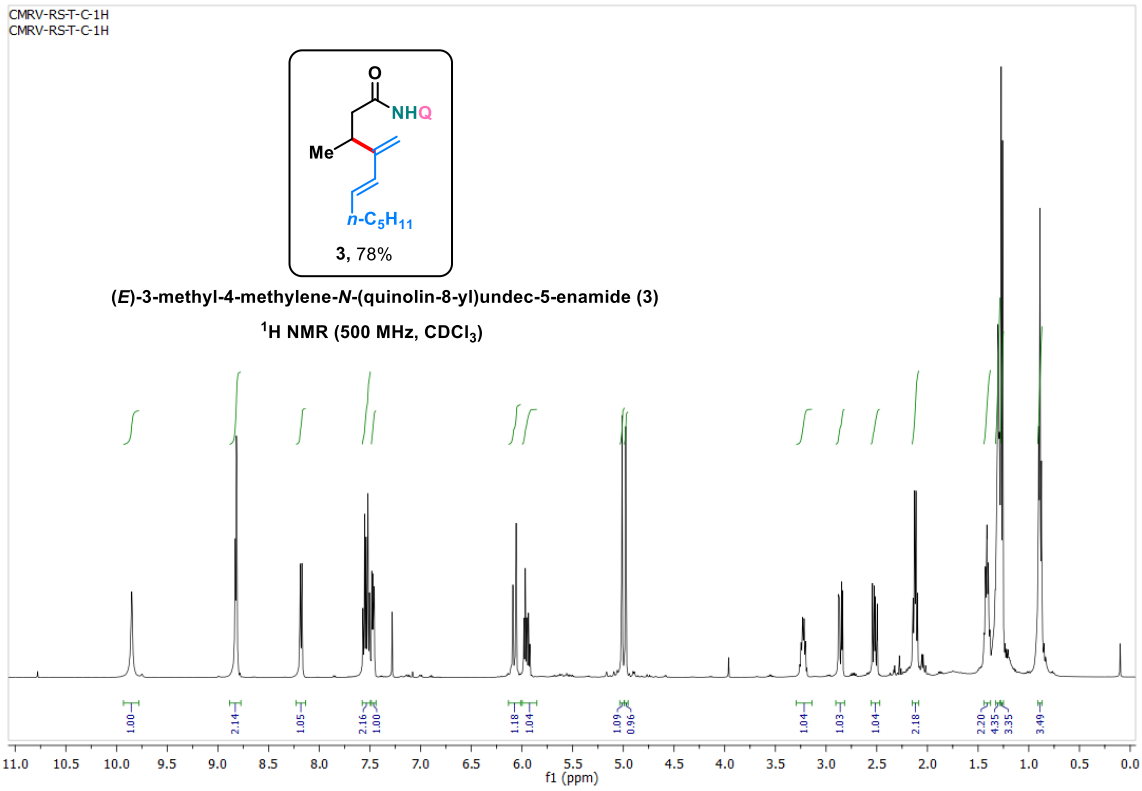
1. a) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc*. **2005**, *127*, 13154. b) Ano, Y.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc*. **2011**, *133*, 12984.

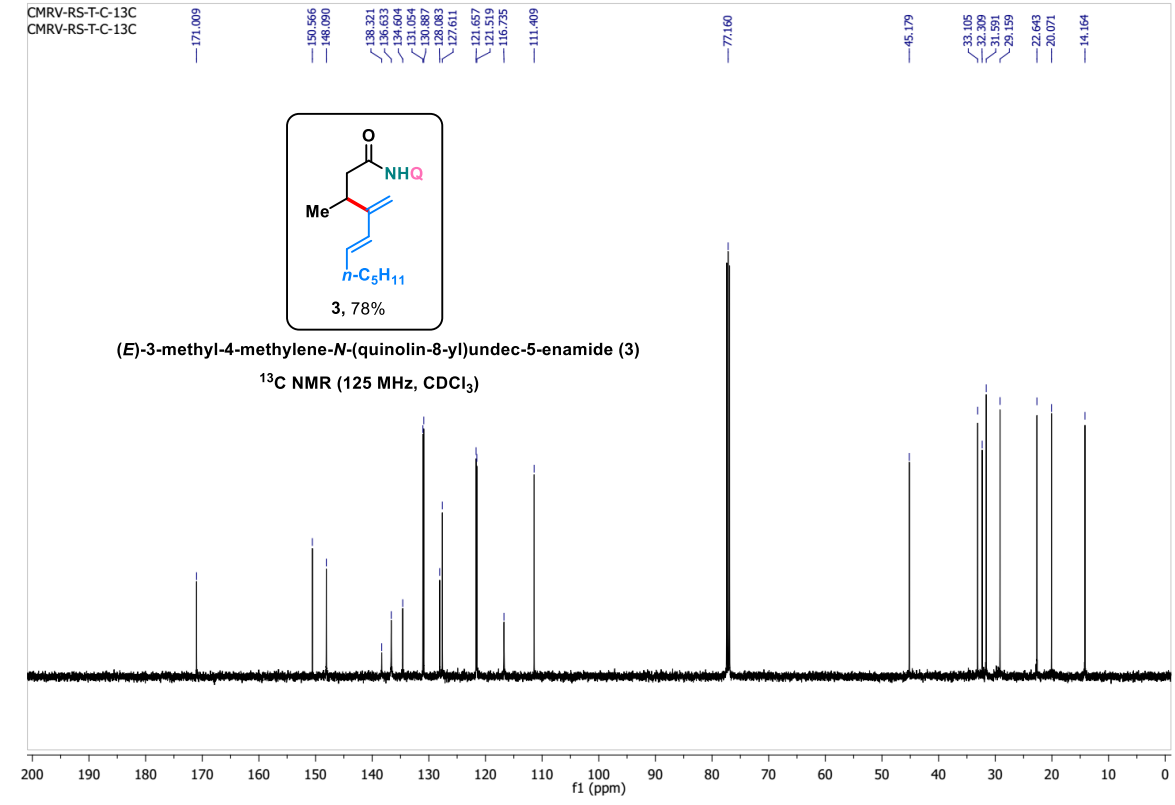
2. Li, Q.; Fu, C.; Ma, S. *Angew. Chem., Int. Ed*. **2012**, *51*, 11783−11786.

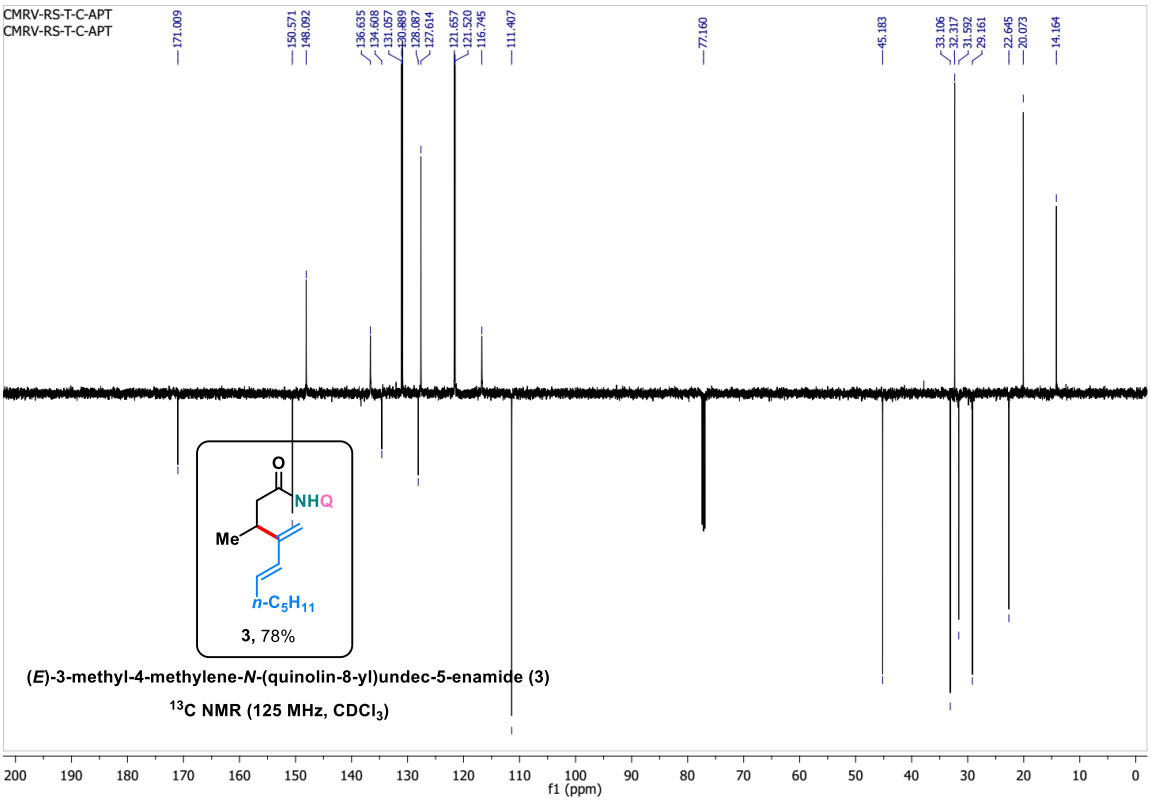
3. a) Wang, H.; Beiring, B.; Yu, D.; Collins, K.; Glorius, F. *Angew. Chem. Int. Ed*. **2013**, *52*, 47, 12430. b) Petrone, D. A.; Isomura, M.; Franzoni, I.; Rossler, S. L.; Carreira, E. M. *J. Am. Chem. Soc*. **2018**, *140*, 4697. c) Handa, S.; Lippincott, D. J.; Aue, D. H.; Lipshutz, B. H. *Angew. Chem., Int. Ed*. **2014**, 53, 10658.

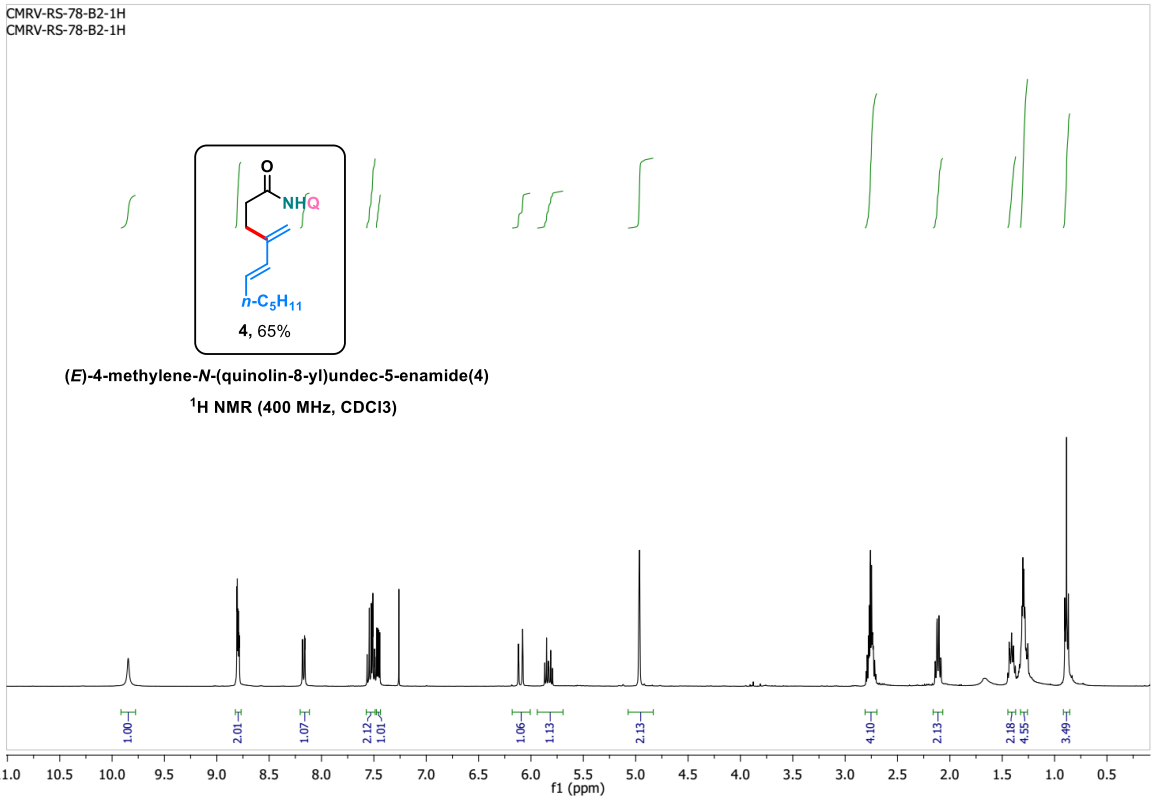
4. Pérez-Gómez, M.; Azizollahi, H.; Franzoni, I.; Larin, E. M.; Lautens, M.; García-López, J. A. *Organometallics* **2019**, 38, 973−980.

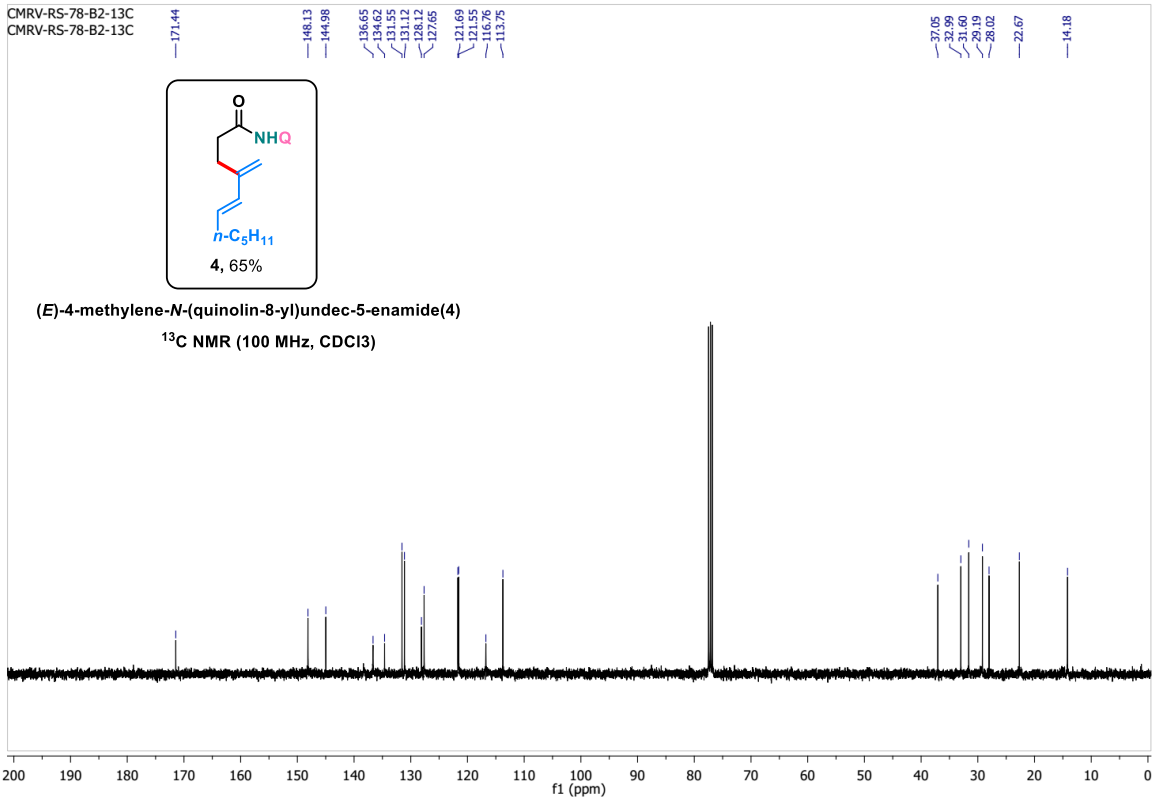
5. Yang, X.; Sun, T.- Y.; Rao, Y. *Chem. - Eur. J.* **2016**, *22*, 3273.

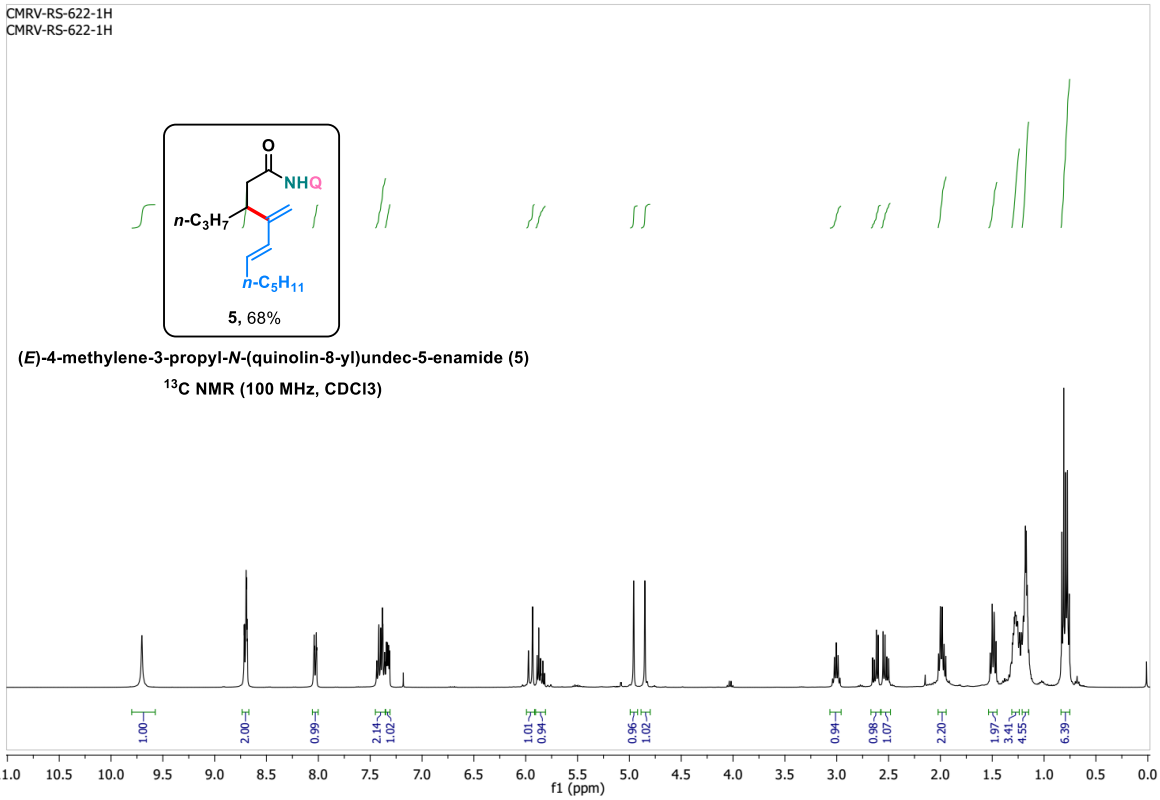

CMRV-RS-T-C-1H
CMRV-RS-T-C-1H
O
NHQ
Me
n-C5H11
3, 78%
(E)-3-methyl-4-methylene-N-(quinolin-8-yl)undec-5-enamide (3)
1H NMR (500 MHz, CDCl3)
f1 (ppm)

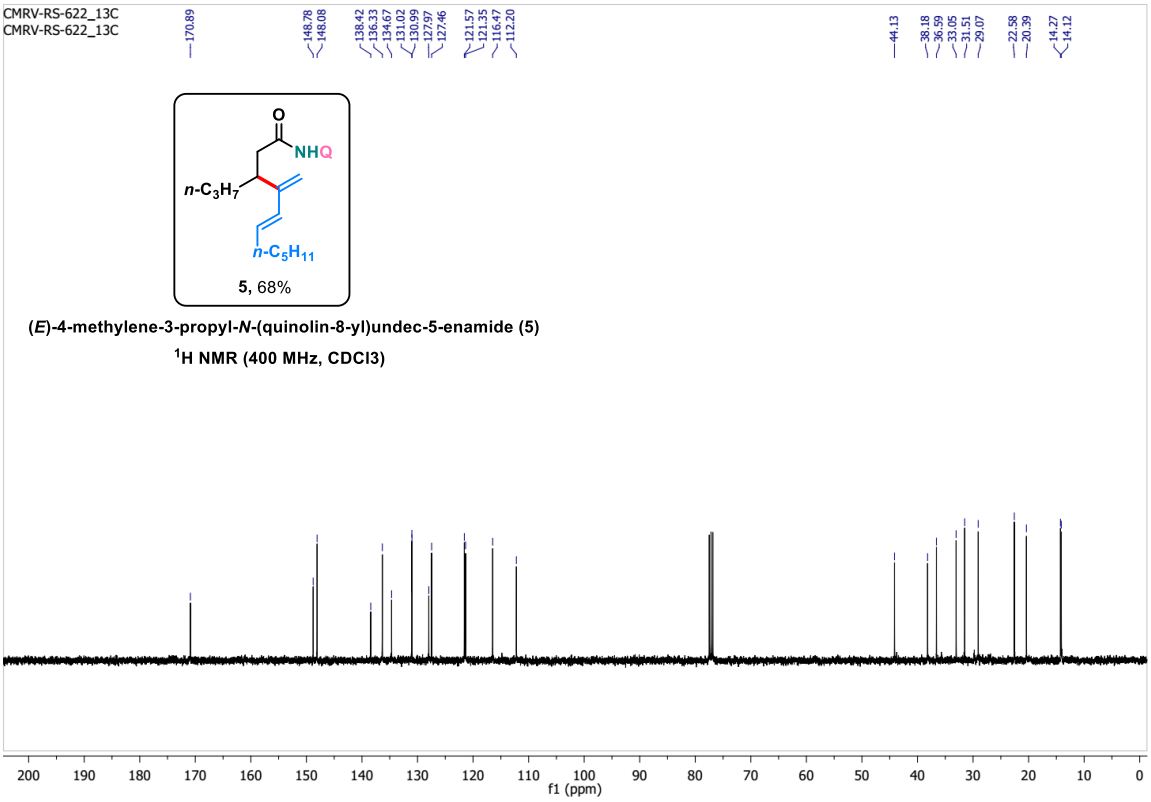

CMRV-RS-T-C-13C
CMRV-RS-T-C-13C
O
NHQ
Me
n-C5H11
3, 78%
(E)-3-methyl-4-methylene-N-(quinolin-8-yl)undec-5-enamide (3)
13C NMR (125 MHz, CDCl3)
f1 (ppm)

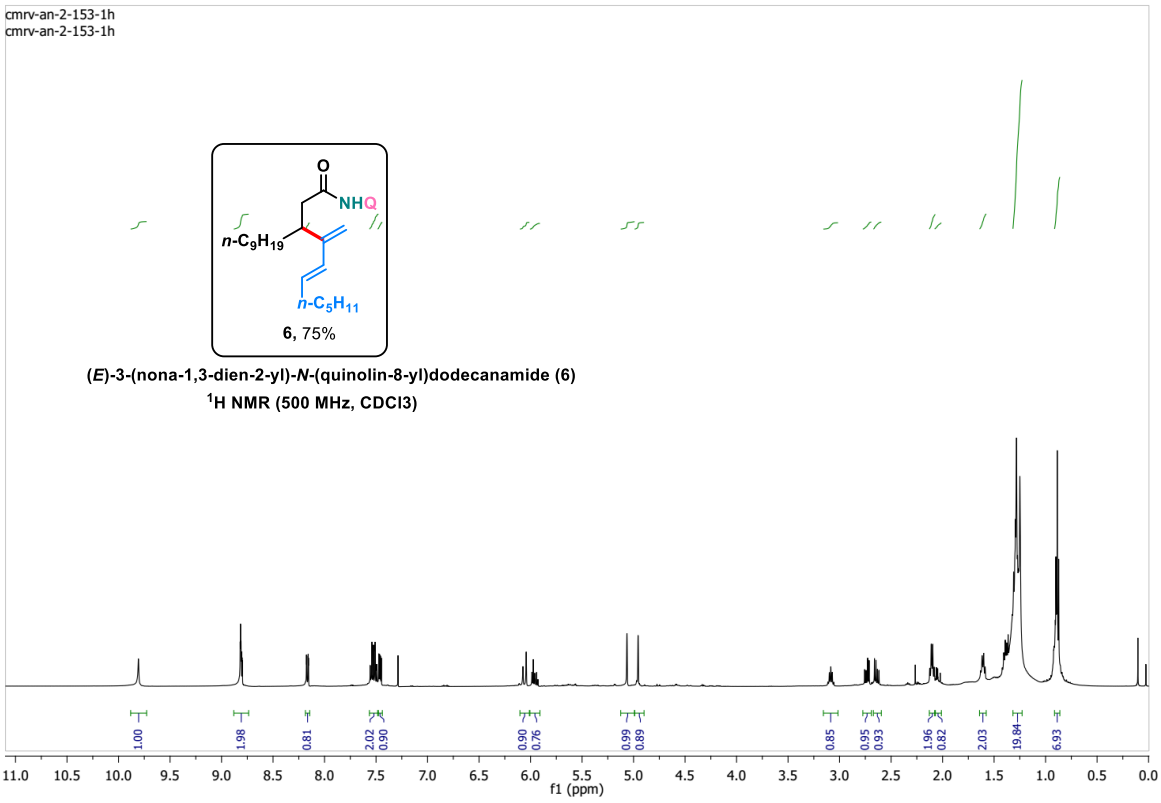

CMRV-RS-T-C-APT
CMRV-RS-T-C-APT
171.009
150.571
148.092
136.635
134.608
131.057
130.889
128.087
127.614
121.657
121.520
116.745
111.407
77.160
45.183
33.106
32.317
31.592
29.161
22.645
20.073
14.164
O
NHQ
Me
n-C5H11
3, 78%
(E)-3-methyl-4-methylene-N-(quinolin-8-yl)undec-5-enamide (3)
13C NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


CMRV-RS-78-B2-1H
CMRV-RS-78-B2-1H
O
NHQ
n-C5H11
4, 65%
(E)-4-methylene-N-(quinolin-8-yl)undec-5-enamide(4)
1H NMR (400 MHz, CDCl3)
1.00
2.01
1.07
2.12
1.01
1.06
1.13
2.13
4.10
2.13
2.18
4.55
3.49
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


CMRV-RS-78-B2-13C
CMRV-RS-78-B2-13C
171.44
148.13
144.98
136.65
134.62
131.55
131.12
128.12
127.65
121.69
121.55
116.76
113.75
37.05
32.99
31.60
29.19
28.02
22.67
14.18
O
NHQ
n-C5H11
4, 65%
(E)-4-methylene-N-(quinolin-8-yl)undec-5-enamide(4)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

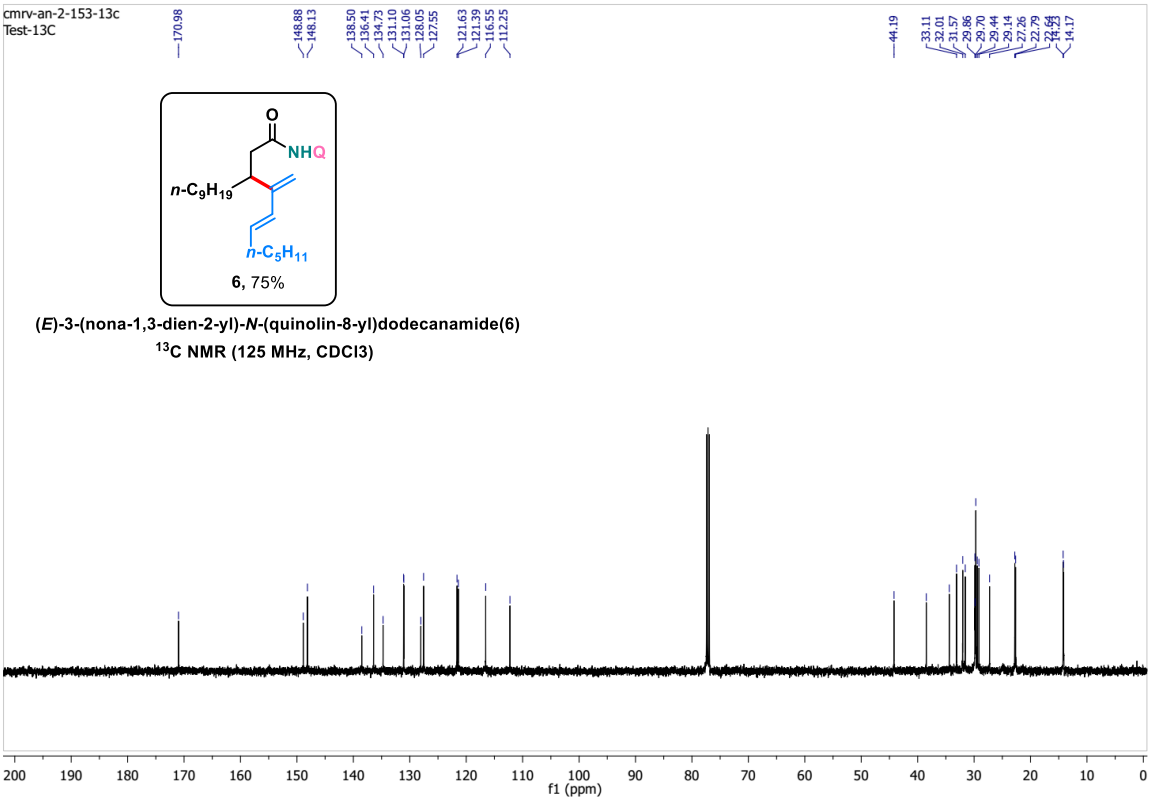

CMRV-RS-622-1H
CMRV-RS-622-1H
O
NHQ
n-C3H7
n-C5H11
5, 68%
(E)-4-methylene-3-propyl-N-(quinolin-8-yl)undec-5-enamide (5)
13C NMR (100 MHz, CDCl3)
1.00
2.00
0.99
2.14
1.02
1.01
0.94
0.96
1.02
0.94
0.98
1.07
2.20
1.97
3.41
4.55
6.39
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-622_13C
CMRV-RS-622_13C
170.89
148.78
148.08
138.42
136.33
134.67
131.02
130.99
127.97
127.46
121.57
121.35
116.47
112.20
44.13
38.18
36.59
33.05
31.51
29.07
22.58
20.39
14.27
14.12
O
NHQ
n-C3H7
n-C5H11
5, 68%
(E)-4-methylene-3-propyl-N-(quinolin-8-yl)undec-5-enamide (5)
1H NMR (400 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



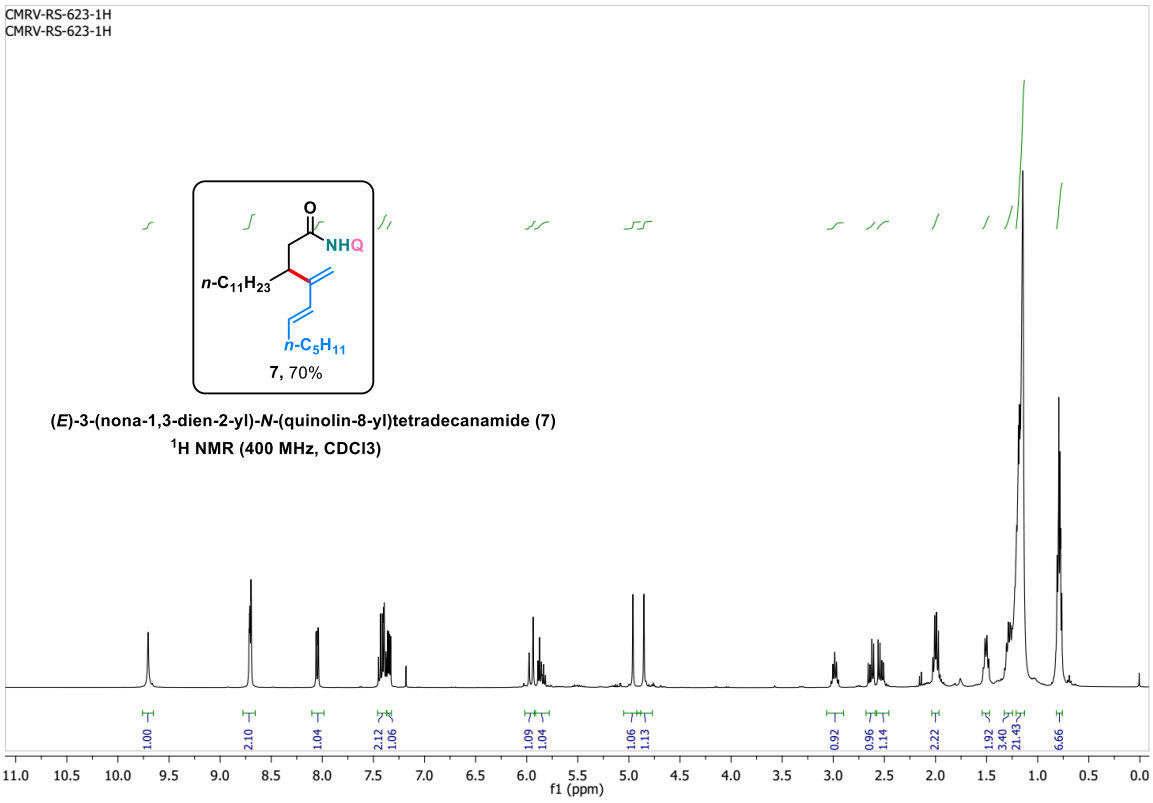
(*E*)-3-(nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)dodecanamide (6)

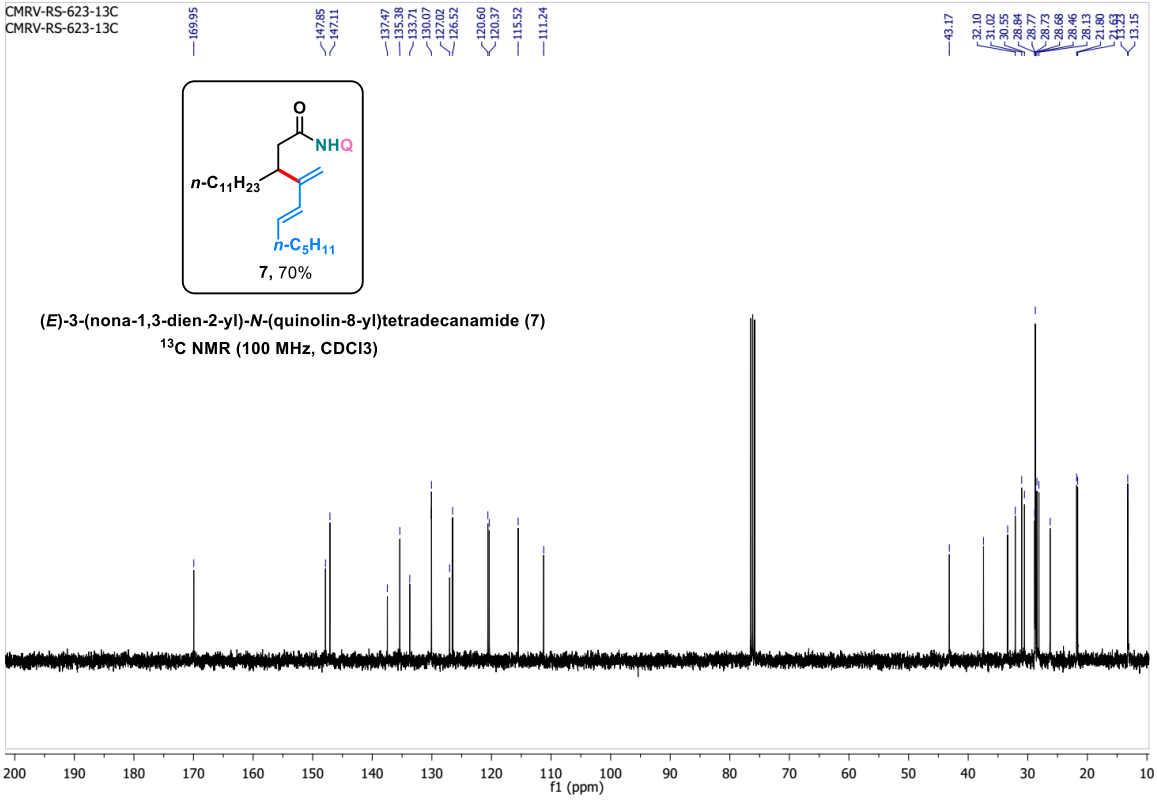
^{1}H NMR (500 MHz, CDCl3)

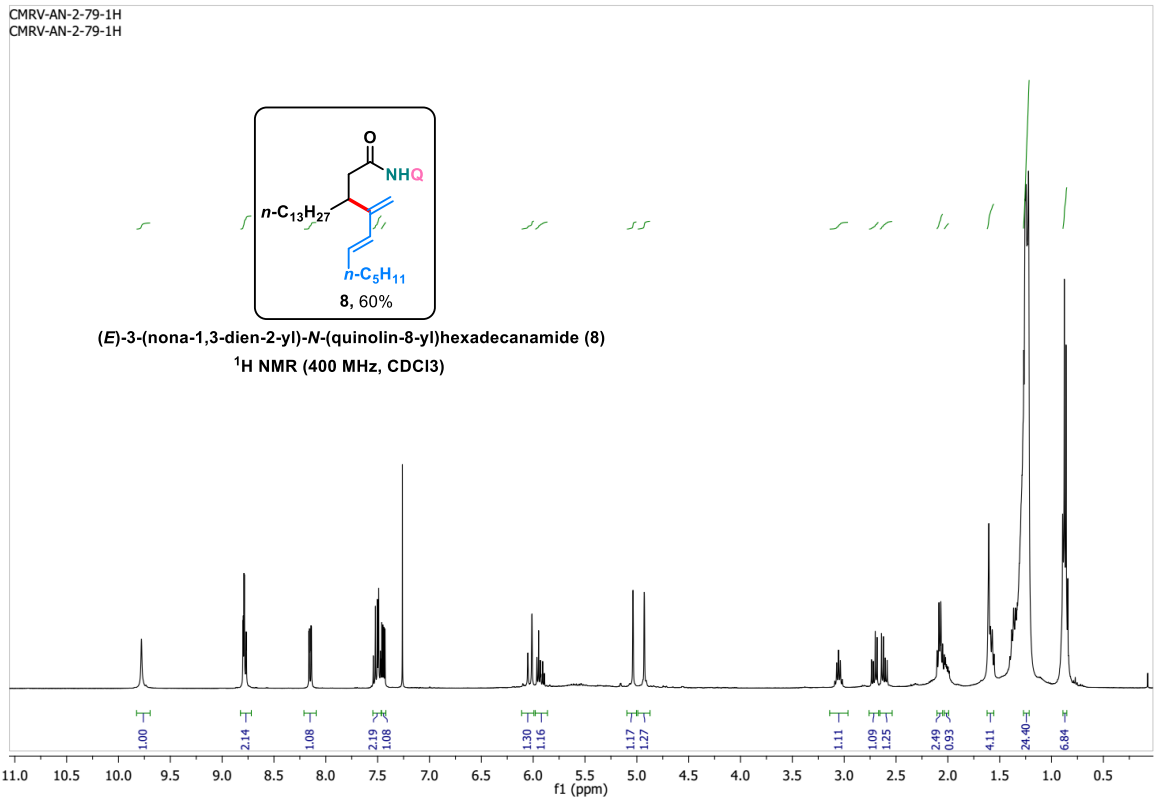


(*E*)-3-(nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)dodecanamide(6)

^{13}C NMR (125 MHz, CDCl3)

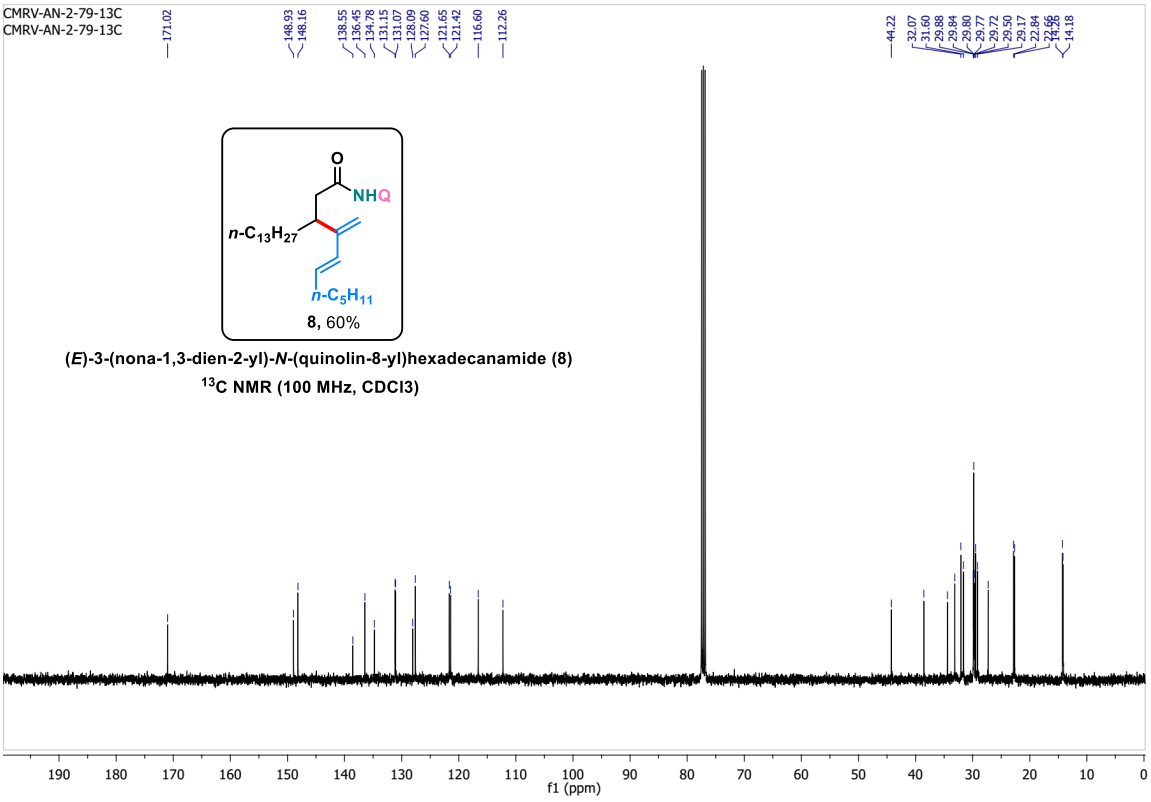

CMRV-RS-623-1H
CMRV-RS-623-1H
O
NHQ
n-C11H23
n-C5H11
7, 70%
(E)-3-(nona-1,3-dien-2-yl)-N-(quinolin-8-yl)tetradecanamide (7)
1H NMR (400 MHz, CDCl3)
1.00
2.10
1.04
2.12
1.06
1.09
1.04
1.06
1.13
0.92
0.96
1.14
2.22
1.92
3.40
21.43
6.66
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-623-13C
CMRV-RS-623-13C
169.95
147.85
147.11
137.47
135.38
133.71
130.07
127.02
126.52
120.60
120.37
115.52
111.24
43.17
32.10
31.02
30.55
28.84
28.77
28.73
28.68
28.46
28.13
21.80
13.93
13.83
13.15
O
NHQ
n-C11H23
n-C5H11
7, 70%
(E)-3-(nona-1,3-dien-2-yl)-N-(quinolin-8-yl)tetradecanamide (7)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



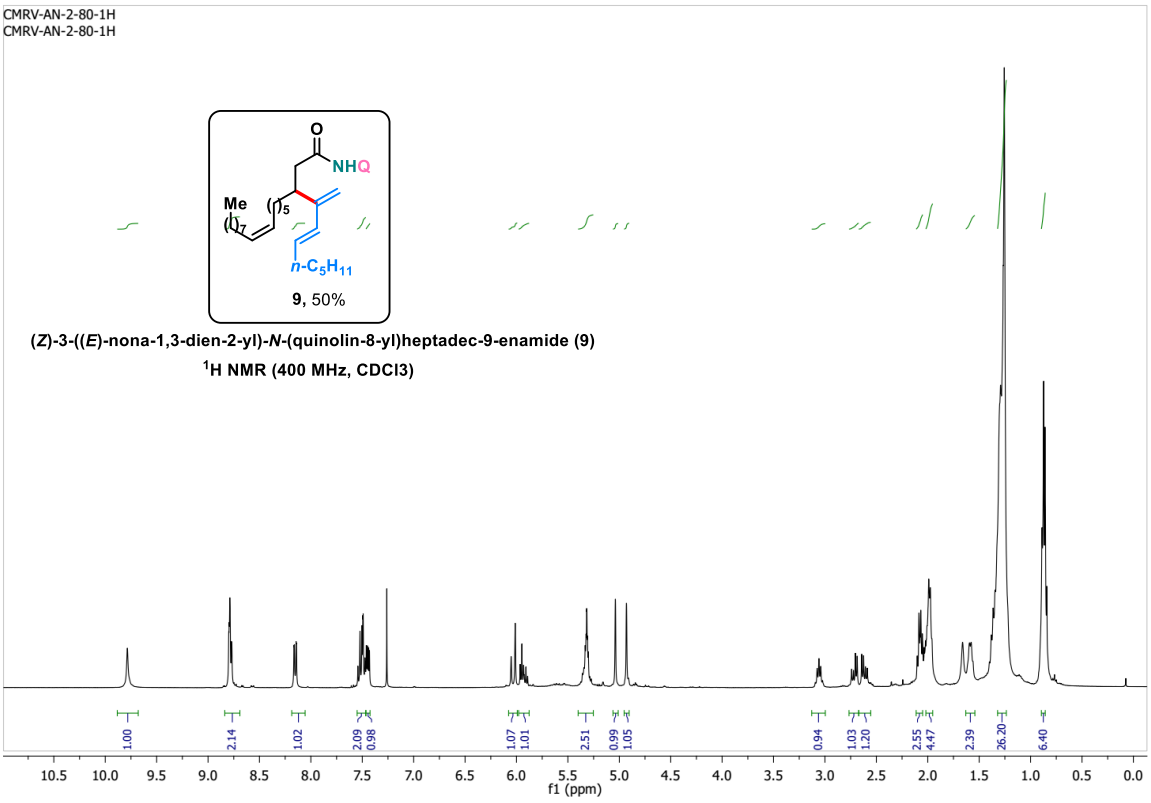
(*E*)-3-(nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)hexadecanamide (8)

^{1}H NMR (400 MHz, CDCl3)



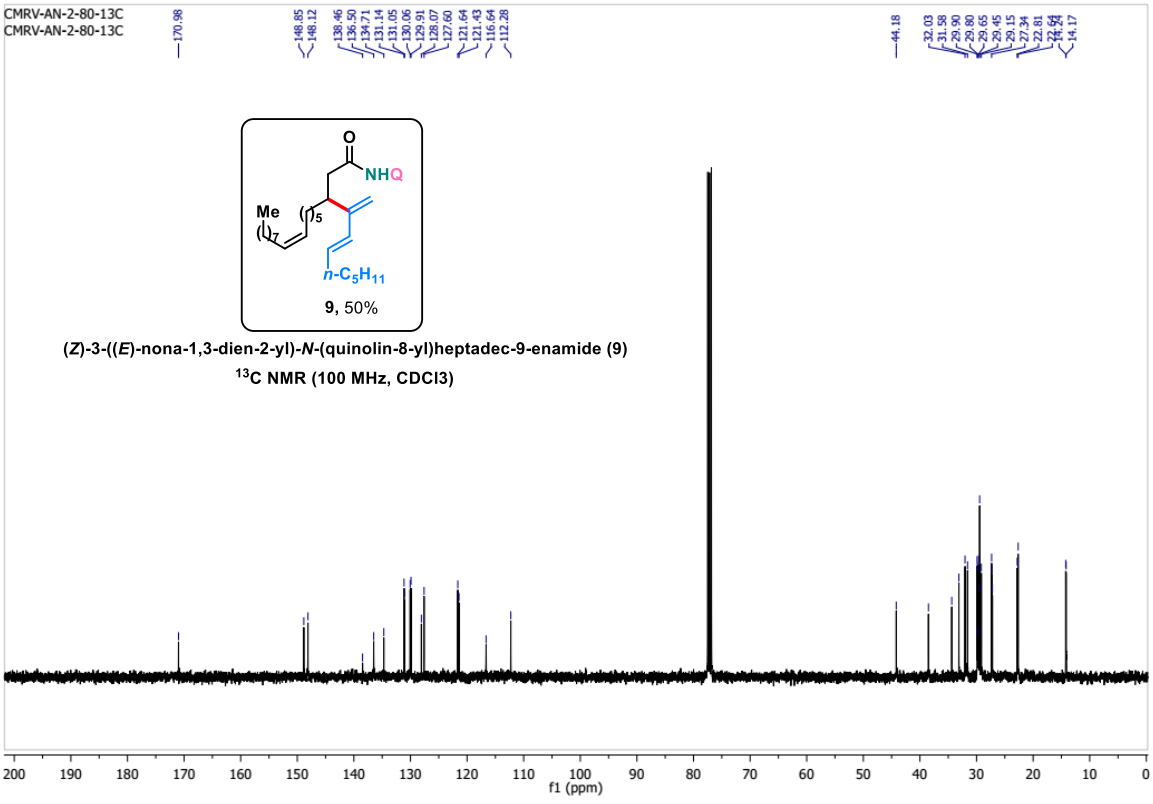
(*E*)-3-(nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)hexadecanamide (8)

^{13}C NMR (100 MHz, CDCl3)



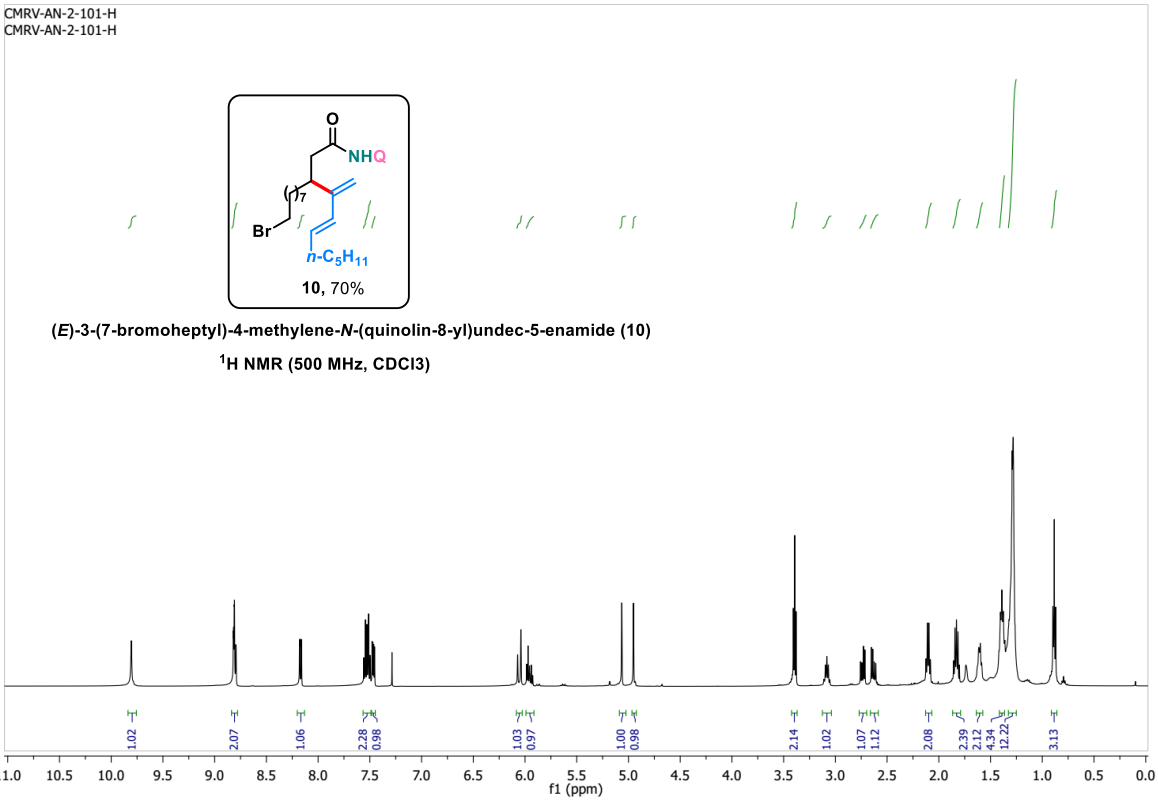
(*Z*)-3-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)heptadec-9-enamide (9)

^{1}H NMR (400 MHz, CDCl3)



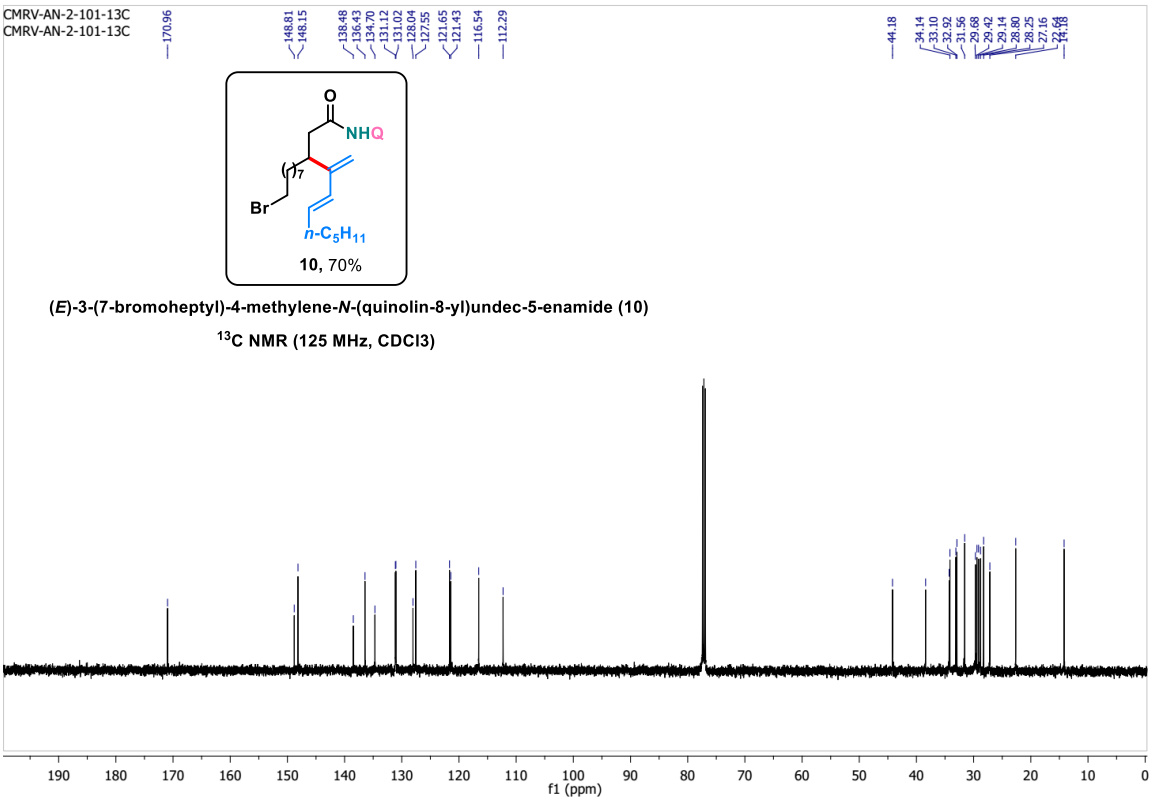
(*Z*)-3-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)heptadec-9-enamide (9)

^{13}C NMR (100 MHz, CDCl3)



(*E*)-3-(7-bromoheptyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (10)

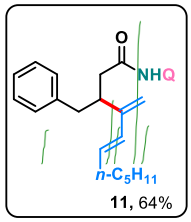
^{1}H NMR (500 MHz, CDCl3)



(*E*)-3-(7-bromoheptyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (10)

^{13}C NMR (125 MHz, CDCl3)

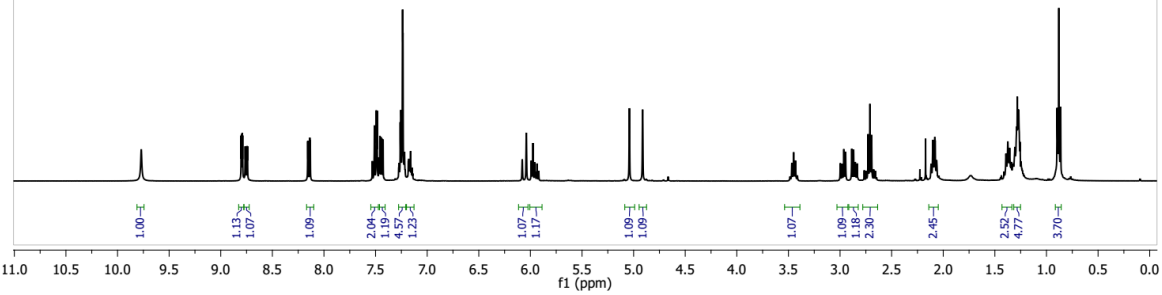
CMRV-RS-693-1H
CMRV-RS-693-1H



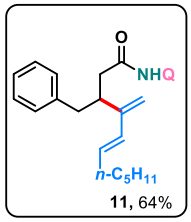
11, 64%

(*E*)-3-benzyl-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide(11)

^{1}H NMR (400 MHz, CDCl3)



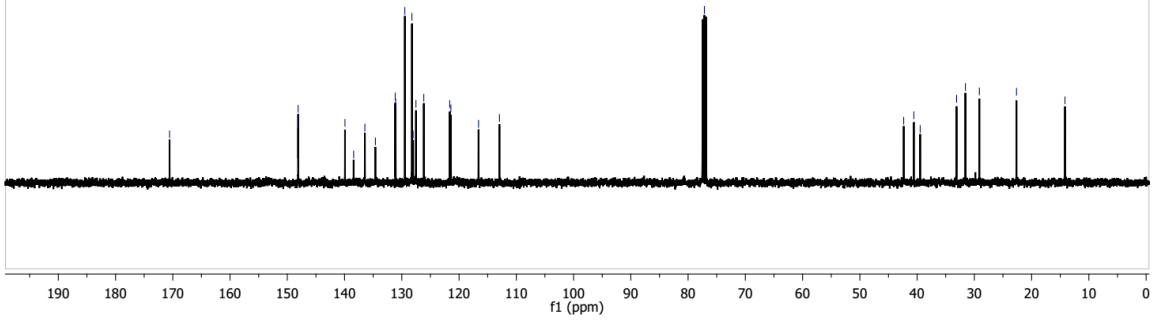
CMRV-RS-693-13C
CMRV-RS-693-13C



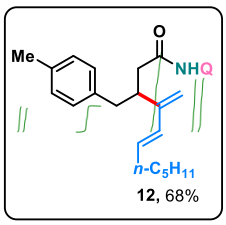
11, 64%

(*E*)-3-benzyl-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (11)

^{13}C NMR (100 MHz, CDCl3)

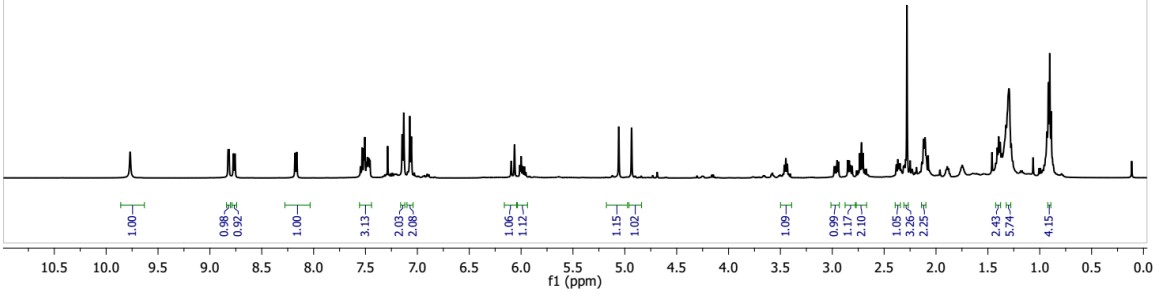


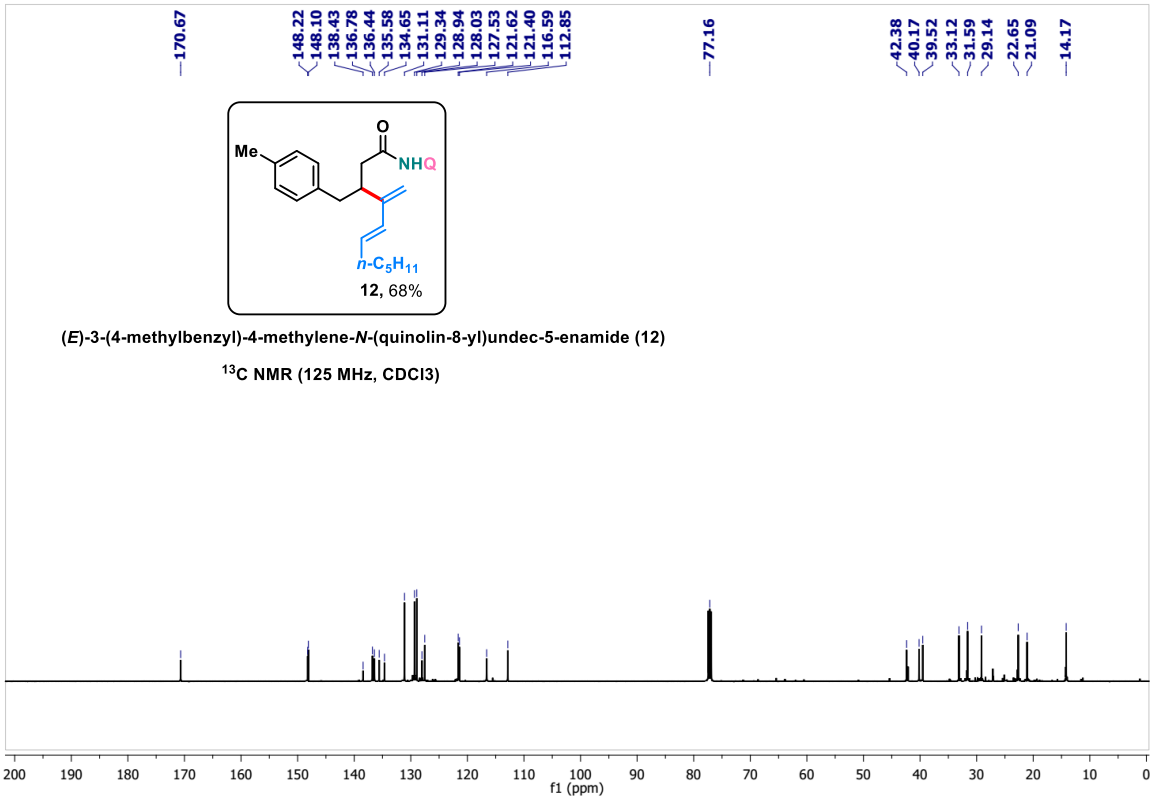
CMRV-RS-922-1H
CMRV-RS-922-1H



(*E*)-3-(4-methylbenzyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (12)

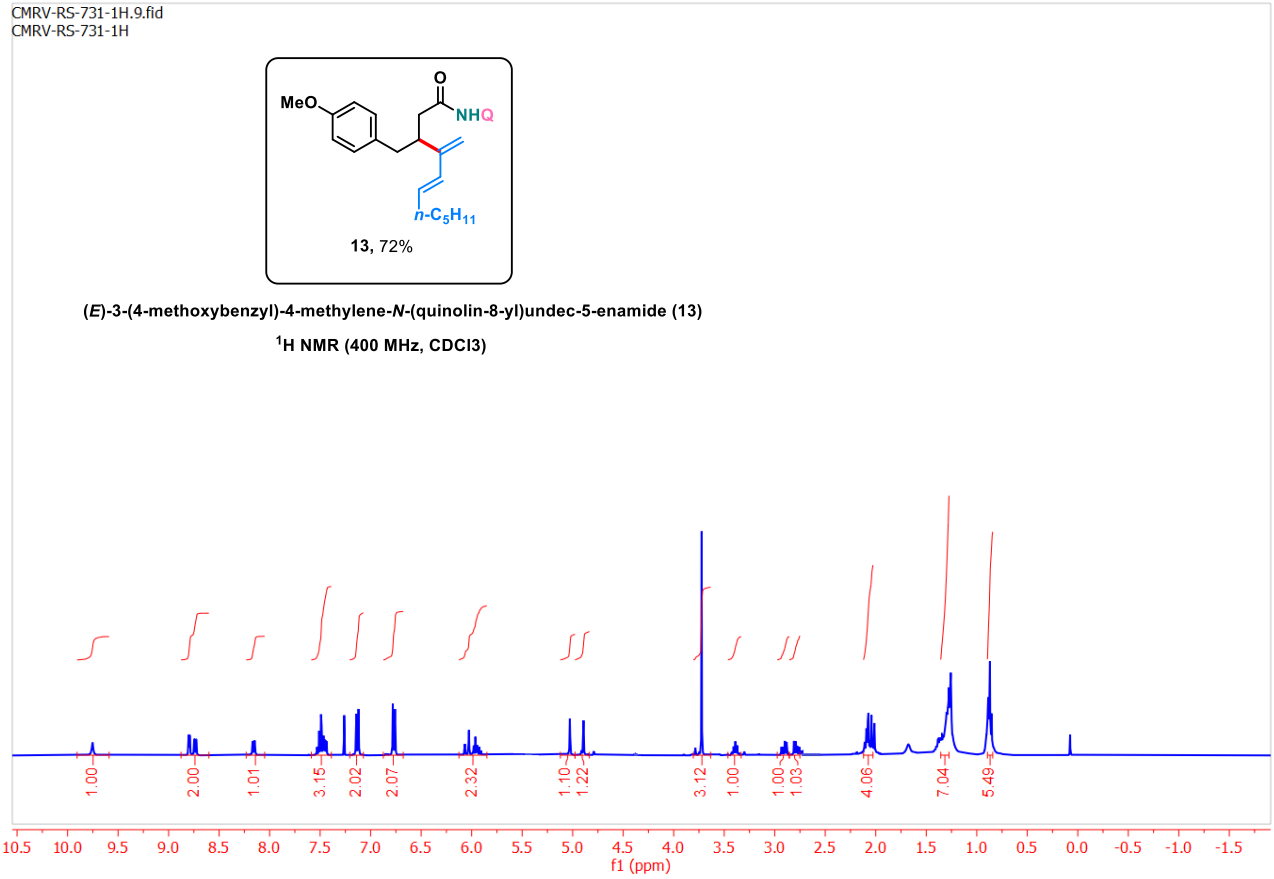
^{1}H NMR (500 MHz, CDCl3)

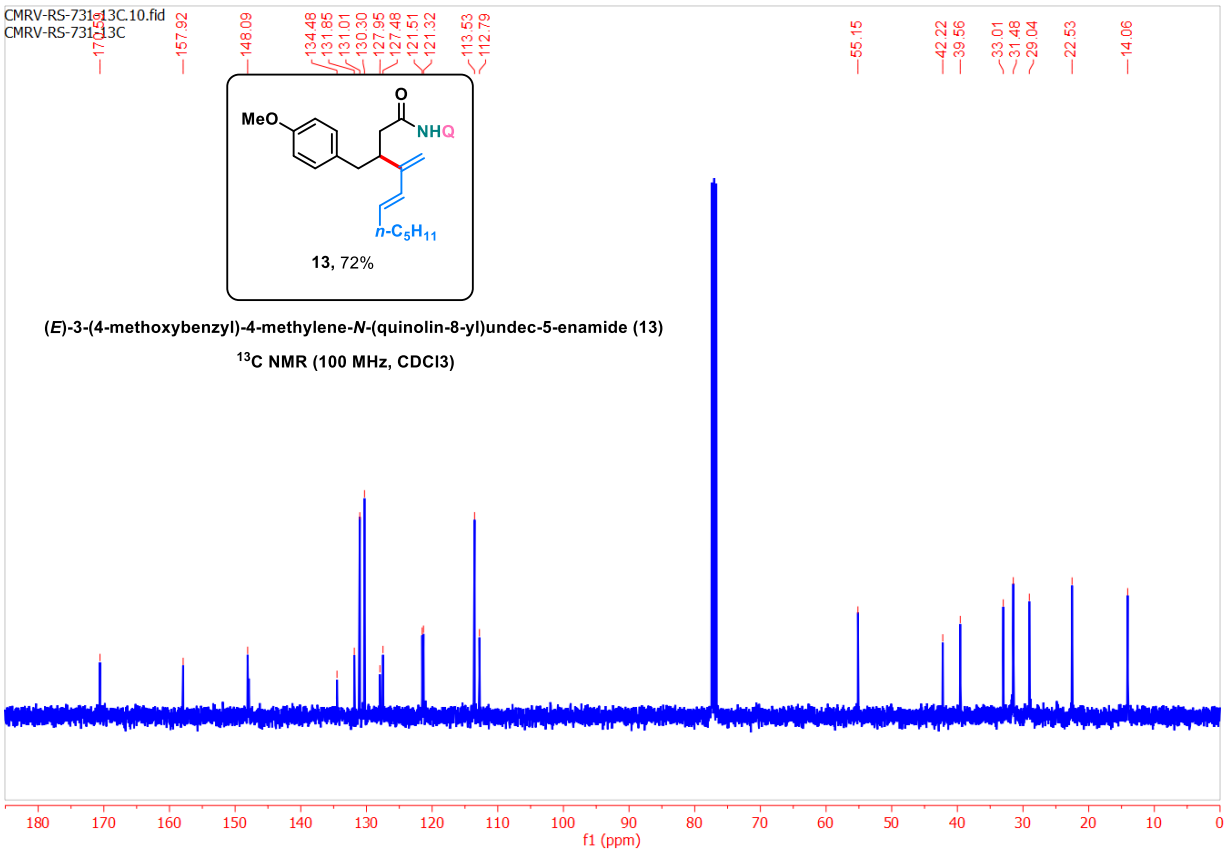


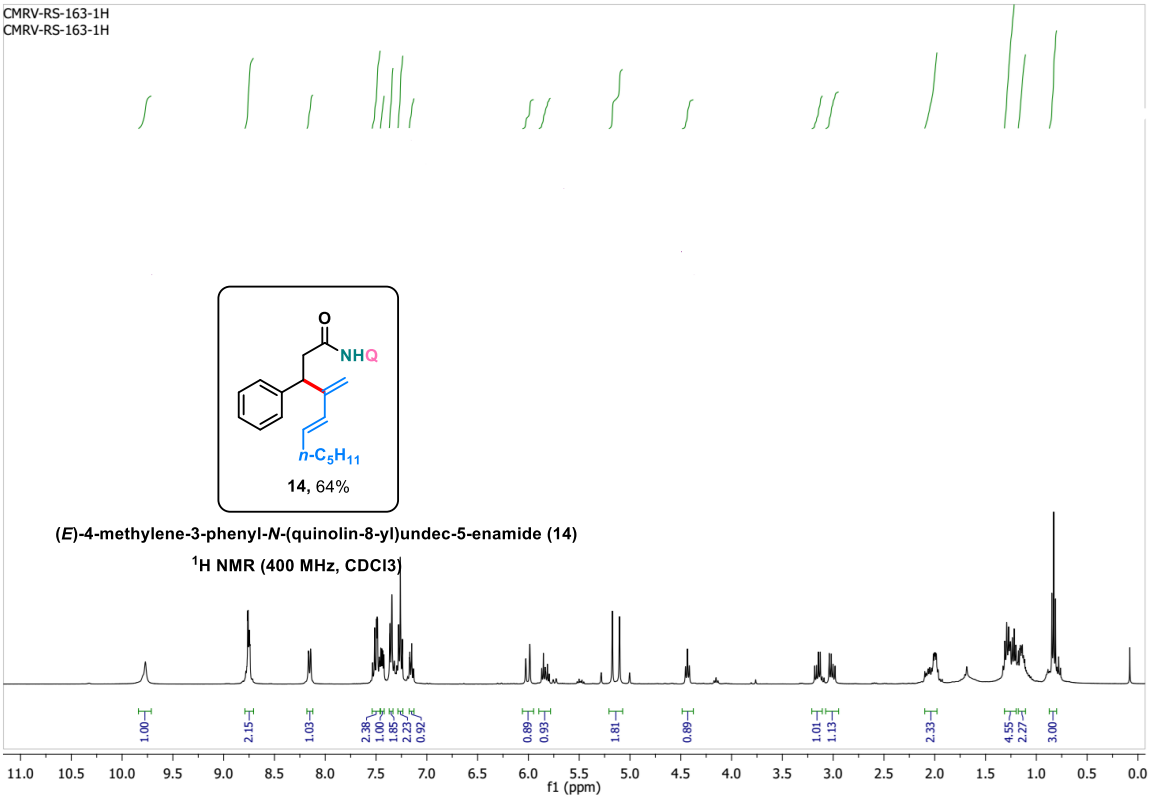


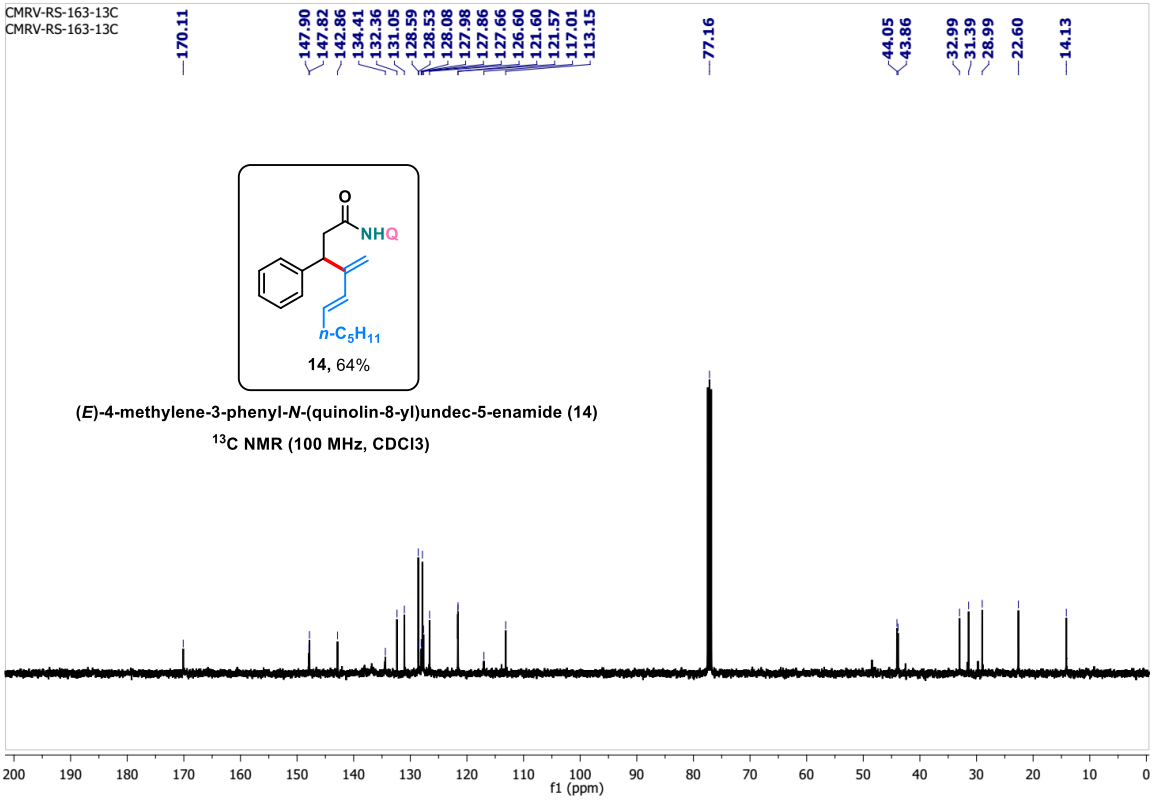
(*E*)-3-(4-methylbenzyl)-4-methylene-*N*-(quinolin-8-yl)undec-5-enamide (12)

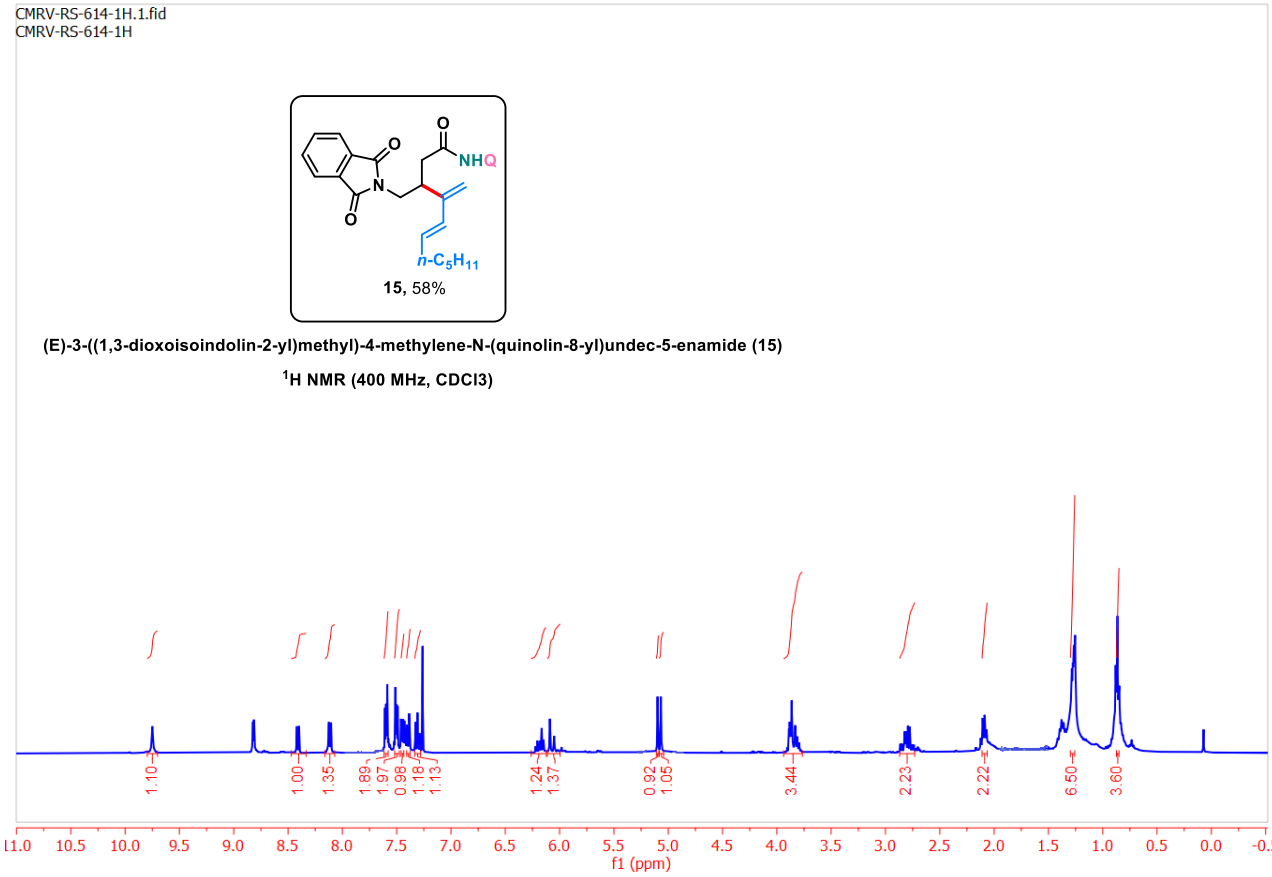
^{13}C NMR (125 MHz, CDCl3)

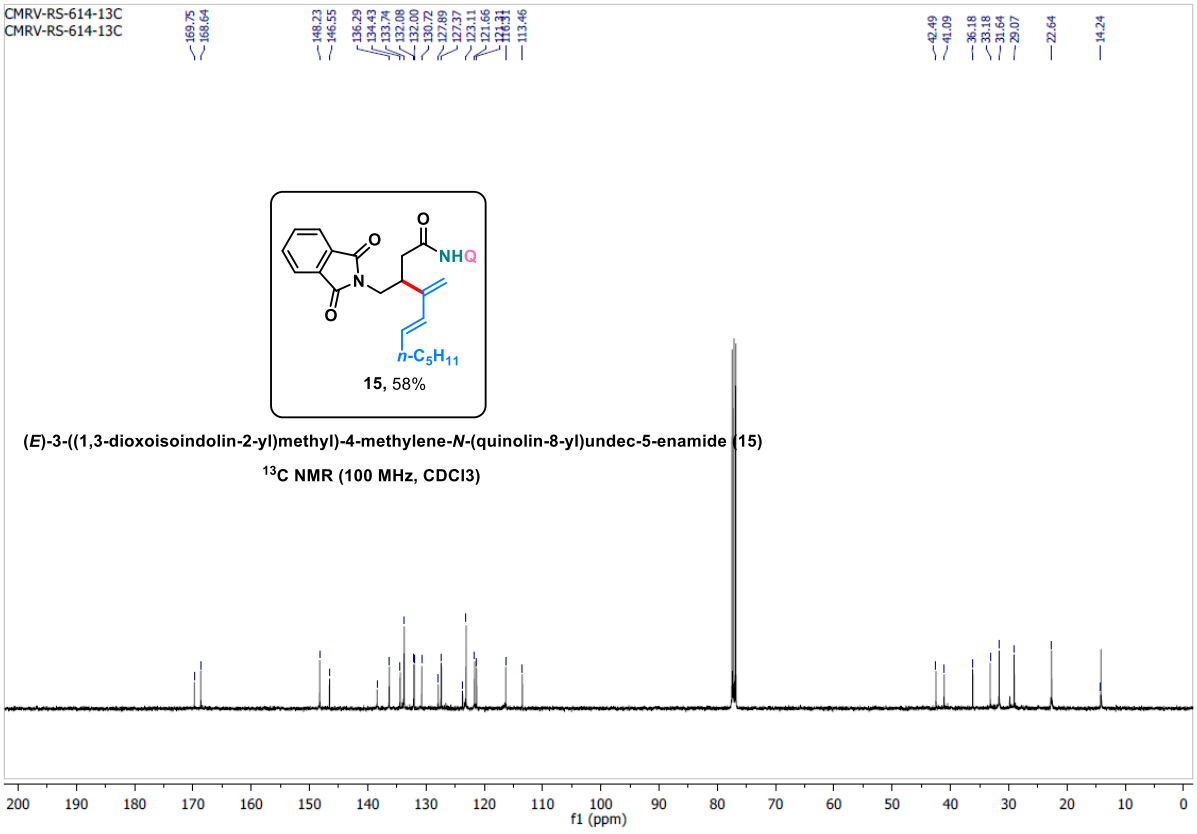

CMRV-RS-731-1H.9.fid
CMRV-RS-731-1H
MeO
O
NHQ
n-C5H11
13, 72%
(E)-3-(4-methoxybenzyl)-4-methylene-N-(quinolin-8-yl)undec-5-enamide (13)
1H NMR (400 MHz, CDCl3)
1.00
2.00
1.01
3.15
2.02
2.07
2.32
1.10
1.22
3.12
1.00
1.00
1.03
4.06
7.04
5.49
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

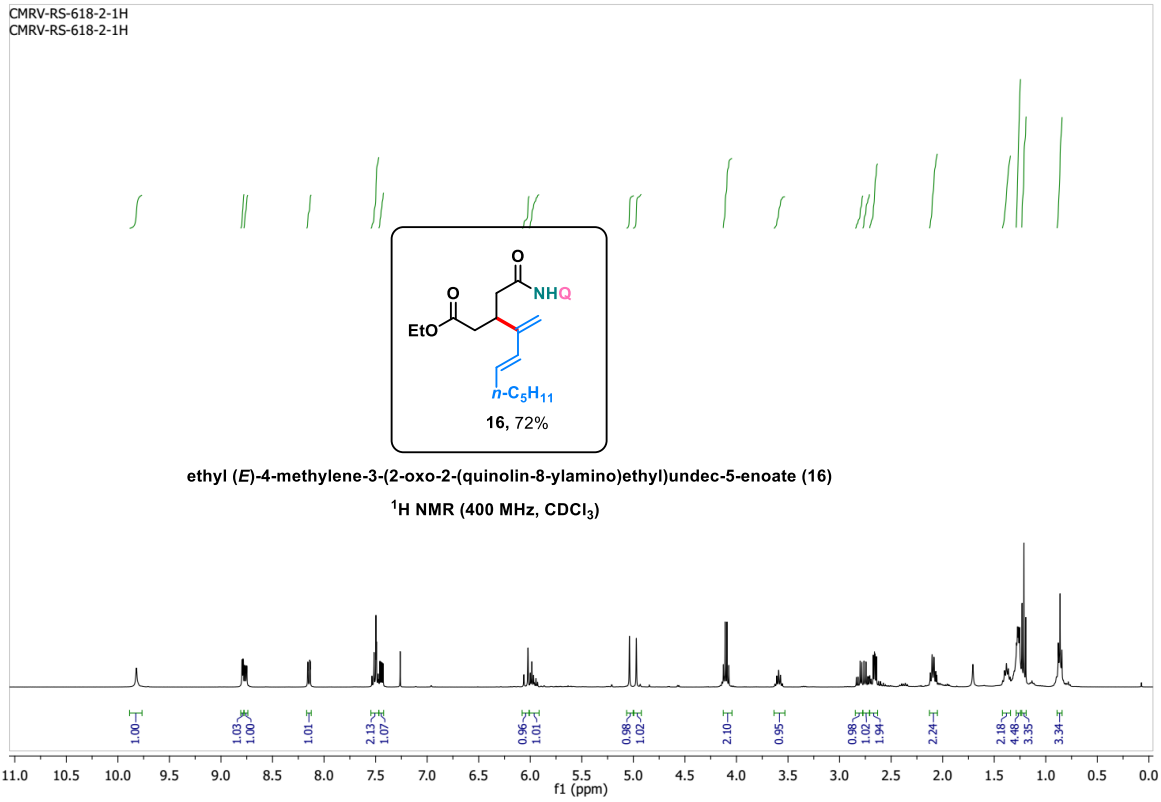

CMRV-RS-731-13C.10.fid
CMRV-RS-731-13C
157.92
148.09
134.48
131.85
131.01
130.30
127.95
127.48
121.51
121.32
113.53
112.79
55.15
42.22
39.56
33.01
31.48
29.04
22.53
14.06
MeO
O
NHQ
n-C5H11
13, 72%
(E)-3-(4-methoxybenzyl)-4-methylene-N-(quinolin-8-yl)undec-5-enamide (13)
13C NMR (100 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

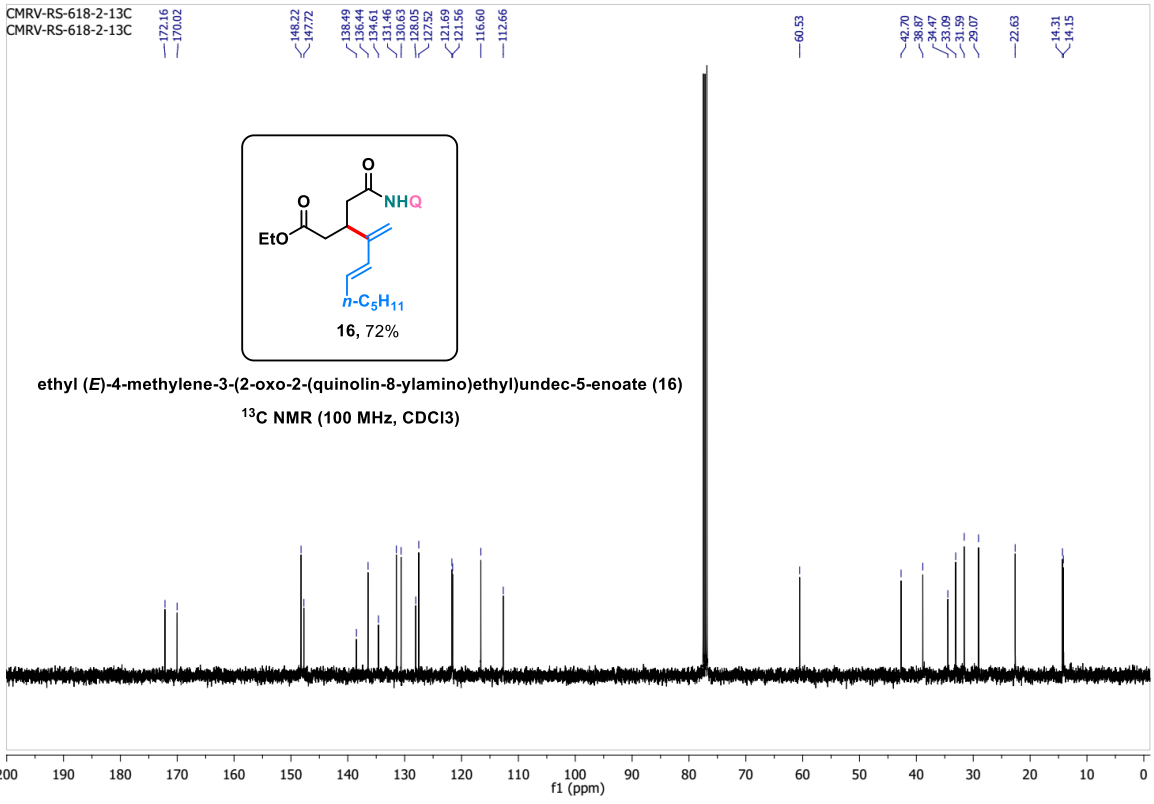

CMRV-RS-163-1H
CMRV-RS-163-1H
NHQ
n-C5H11
14, 64%
(E)-4-methylene-3-phenyl-N-(quinolin-8-yl)undec-5-enamide (14)
1H NMR (400 MHz, CDCl3)
1.00
2.15
1.03
2.38
1.00
1.85
2.23
0.92
0.89
0.93
1.81
0.89
1.01
1.13
2.33
4.55
2.27
3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

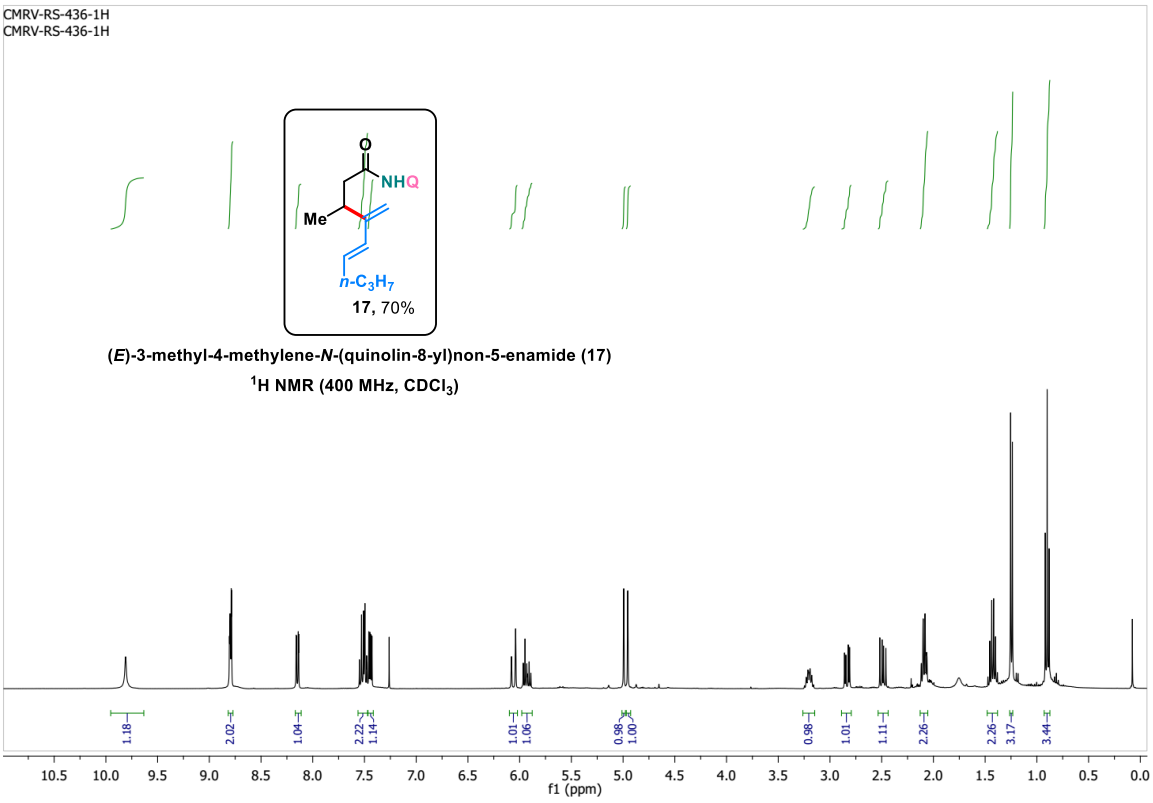

CMRV-RS-163-13C
CMRV-RS-163-13C
170.11
147.90
147.82
142.86
134.41
132.36
131.05
128.59
128.53
128.08
127.98
127.86
127.66
126.60
121.60
121.57
117.01
113.15
77.16
44.05
43.86
32.99
31.39
28.99
22.60
14.13
NHQ
n-C5H11
14, 64%
(E)-4-methylene-3-phenyl-N-(quinolin-8-yl)undec-5-enamide (14)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CMRV-RS-614-1H.1.fid
CMRV-RS-614-1H
NHQ
n-C5H11
15, 58%
(E)-3-((1,3-dioxoisoindolin-2-yl)methyl)-4-methylene-N-(quinolin-8-yl)undec-5-enamide (15)
1H NMR (400 MHz, CDCl3)
1.10
1.00
1.35
1.89
1.97
0.98
1.18
1.13
1.24
1.37
0.92
1.05
3.44
2.23
2.22
6.50
3.60
f1 (ppm)


CMRV-RS-614-13C
CMRV-RS-614-13C
169.75
168.64
148.23
146.55
136.29
134.43
133.74
132.08
132.00
130.72
127.89
127.37
123.11
121.66
113.46
42.49
41.09
36.18
33.18
31.64
29.07
22.64
14.24
NHQ
n-C5H11
15, 58%
(E)-3-((1,3-dioxoisoindolin-2-yl)methyl)-4-methylene-N-(quinolin-8-yl)undec-5-enamide (15)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

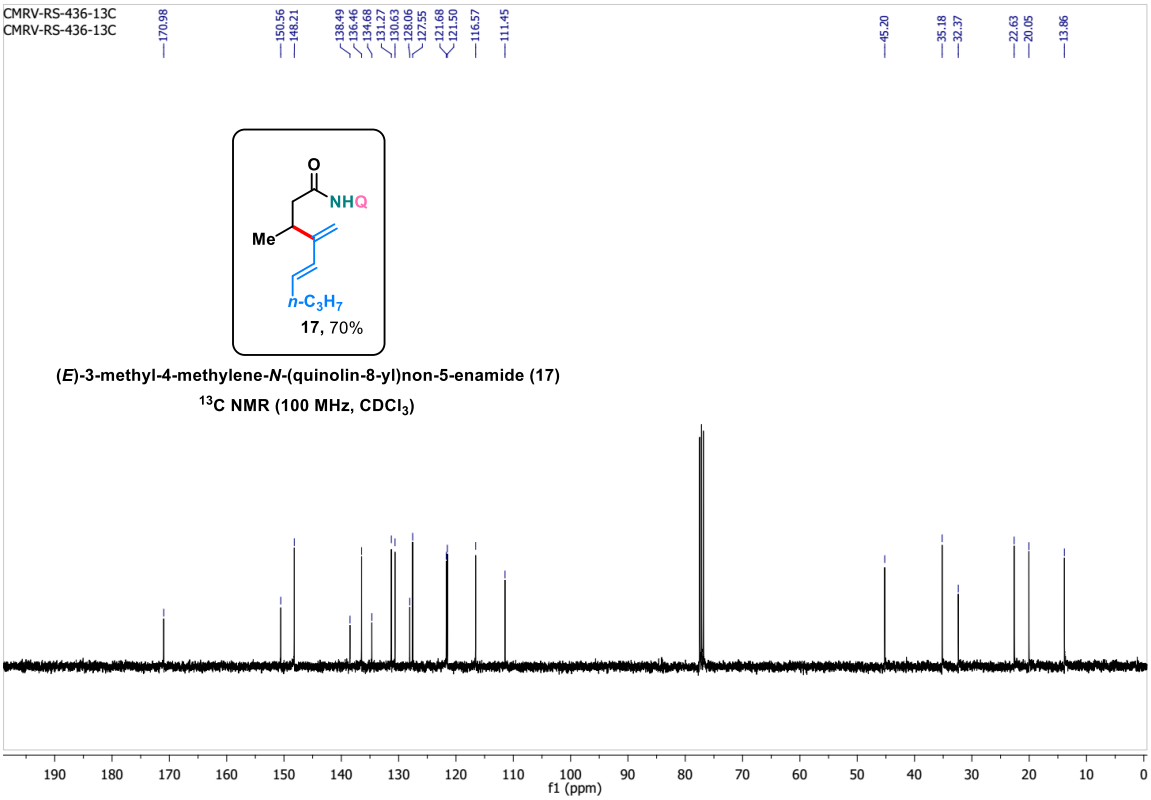

CMRV-RS-618-2-1H
CMRV-RS-618-2-1H
O
O
NHQ
EtO
n-C5H11
16, 72%
ethyl (E)-4-methylene-3-(2-oxo-2-(quinolin-8-ylamino)ethyl)undec-5-enoate (16)
1H NMR (400 MHz, CDCl3)
1.00
1.03
1.00
1.01
2.13
1.07
0.96
1.01
0.98
1.02
2.10
0.95
0.98
1.02
1.94
2.24
2.18
4.48
3.35
3.34
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-618-2-13C
CMRV-RS-618-2-13C
172.16
170.02
148.22
147.72
138.49
136.44
134.61
131.46
130.63
128.65
127.52
121.69
121.56
116.60
112.66
60.53
42.70
38.87
34.47
31.99
31.59
29.07
22.63
14.31
14.15
O
O
NHQ
EtO
n-C5H11
16, 72%
ethyl (E)-4-methylene-3-(2-oxo-2-(quinolin-8-ylamino)ethyl)undec-5-enoate (16)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



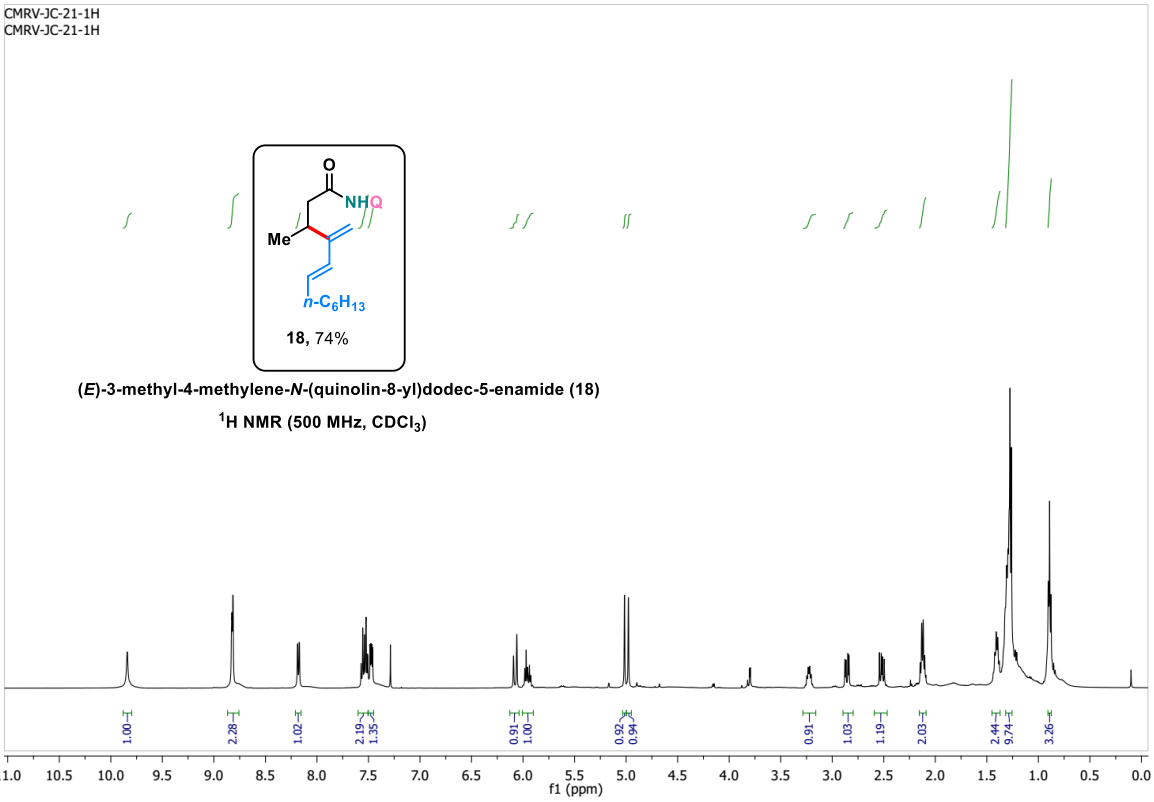
(*E*)-3-methyl-4-methylene-*N*-(quinolin-8-yl)non-5-enamide (17)

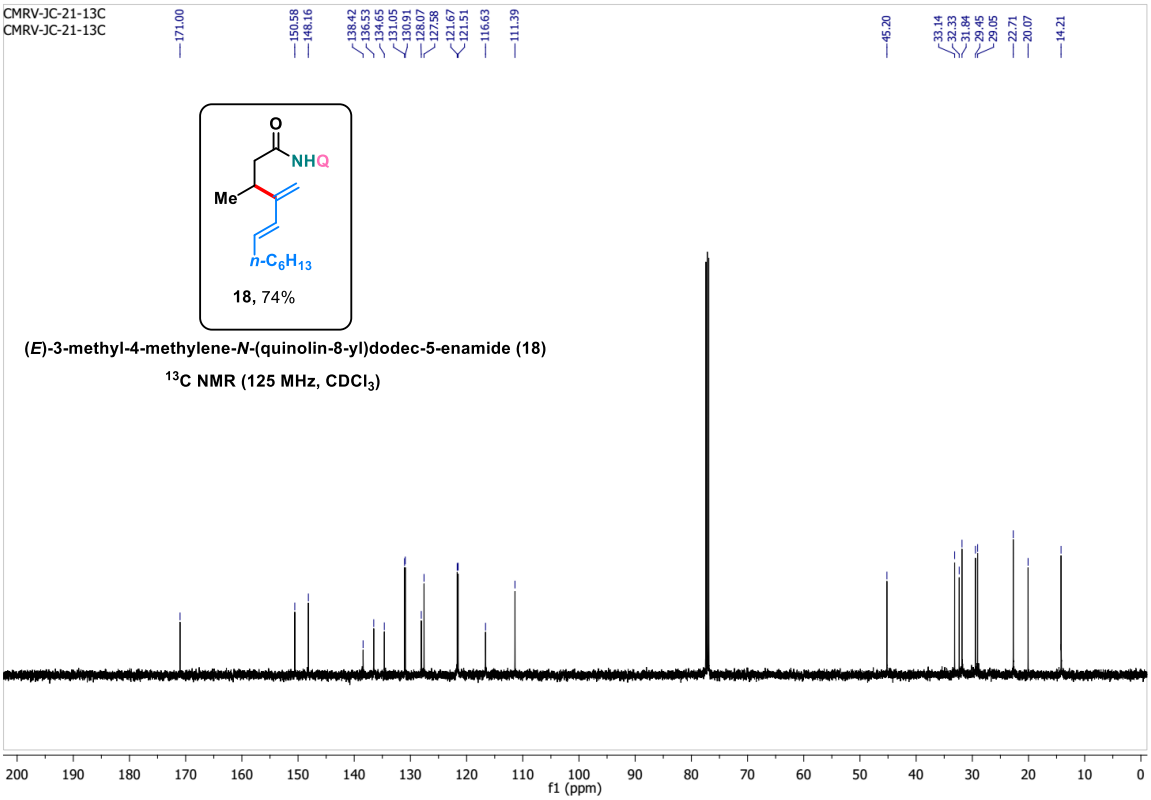
^{1}H NMR (400 MHz, $CDCl_3$)

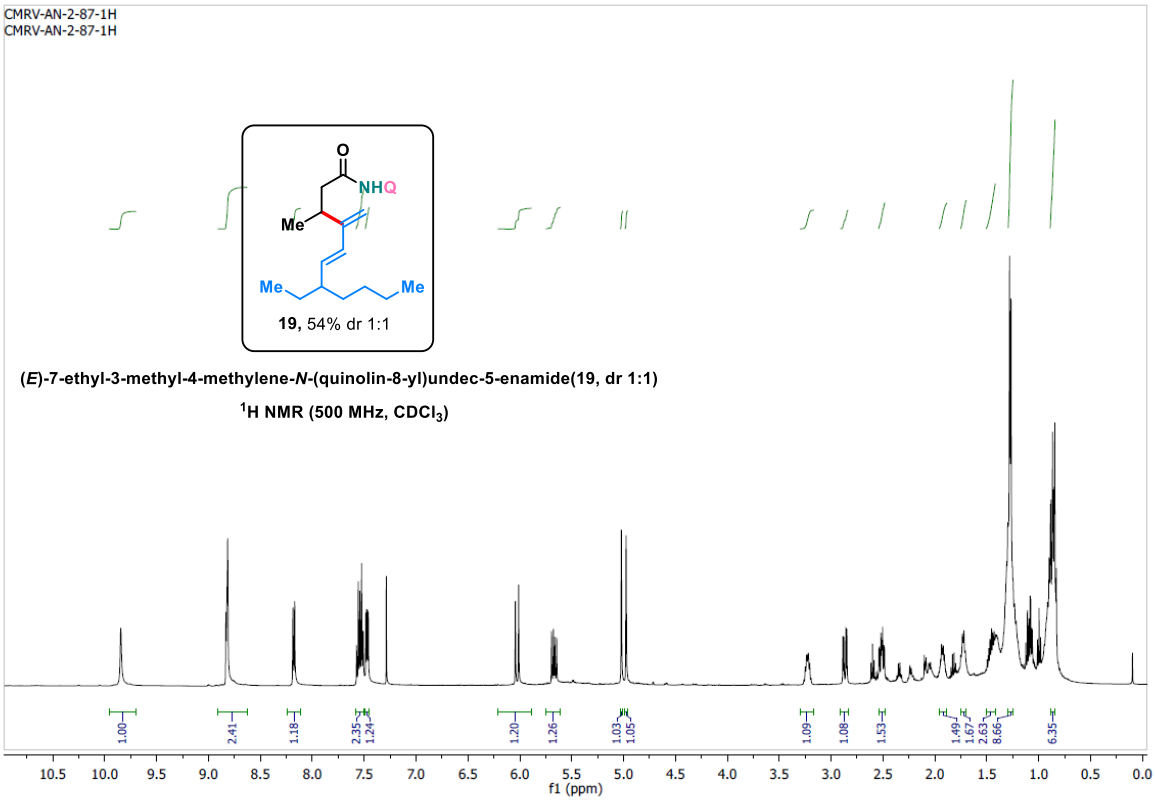


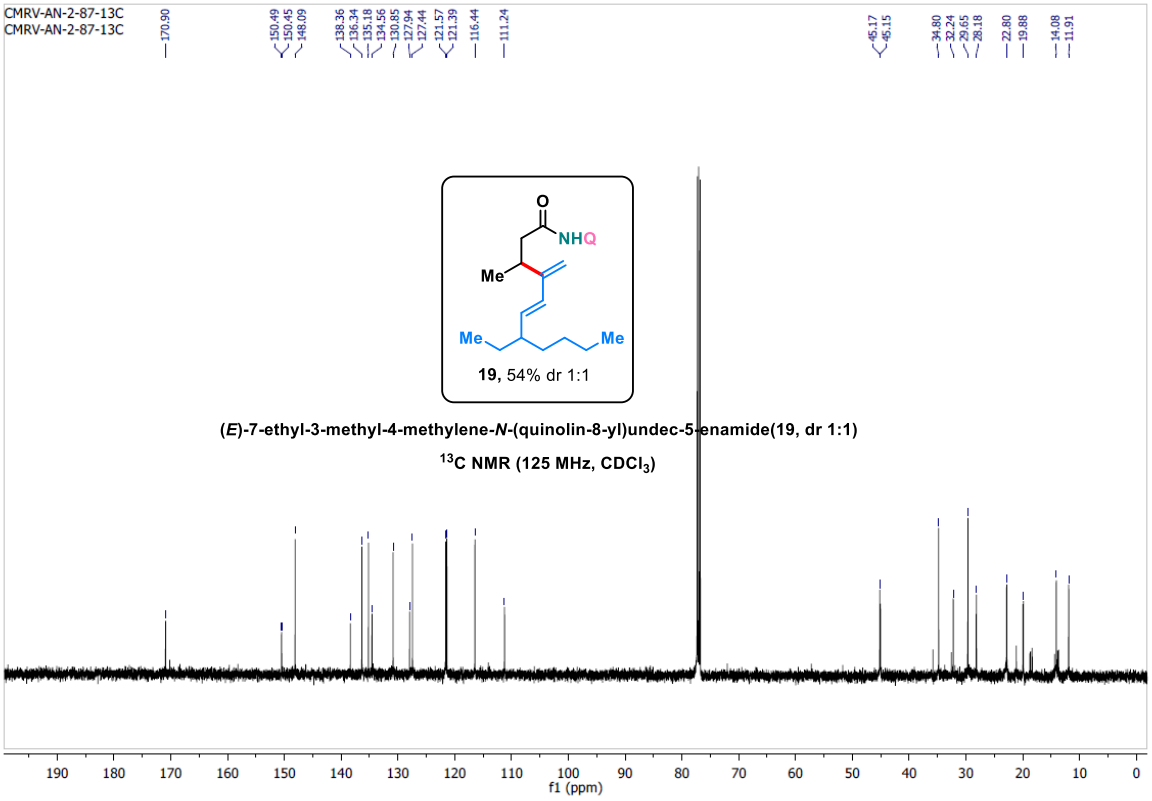
(*E*)-3-methyl-4-methylene-*N*-(quinolin-8-yl)non-5-enamide (17)

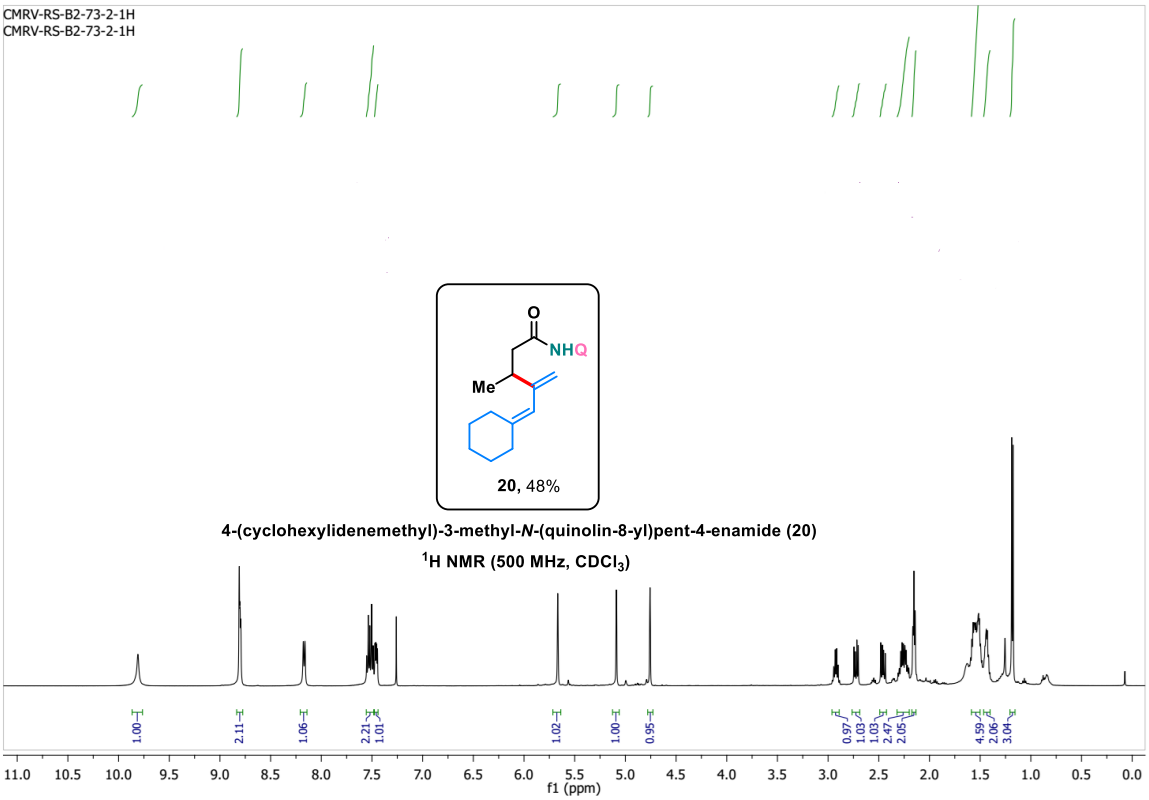
^{13}C NMR (100 MHz, $CDCl_3$)

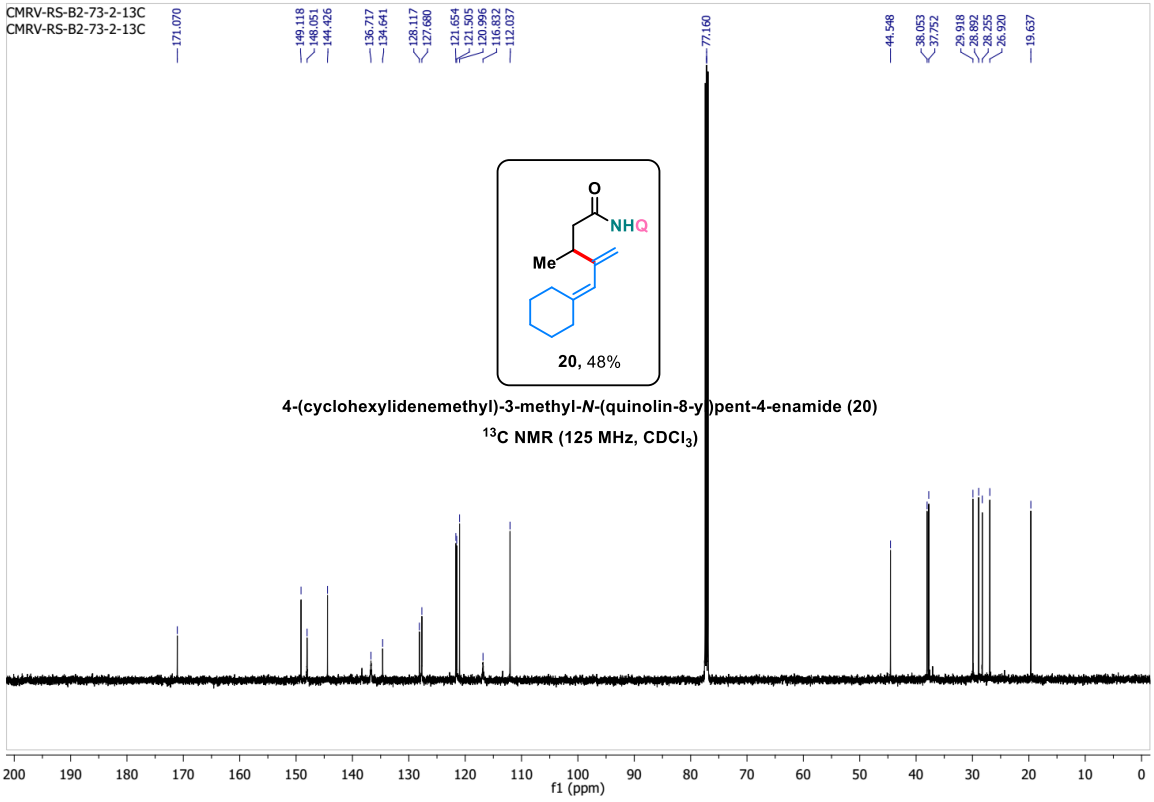

CMRV-JC-21-1H
CMRV-JC-21-1H
O
NHQ
Me
n-C6H13
18, 74%
(E)-3-methyl-4-methylene-N-(quinolin-8-yl)dodec-5-enamide (18)
1H NMR (500 MHz, CDCl3)
1.00
2.28
1.02
2.19
1.35
0.91
1.00
0.92
0.94
0.91
1.03
1.19
2.03
2.44
9.74
3.26
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

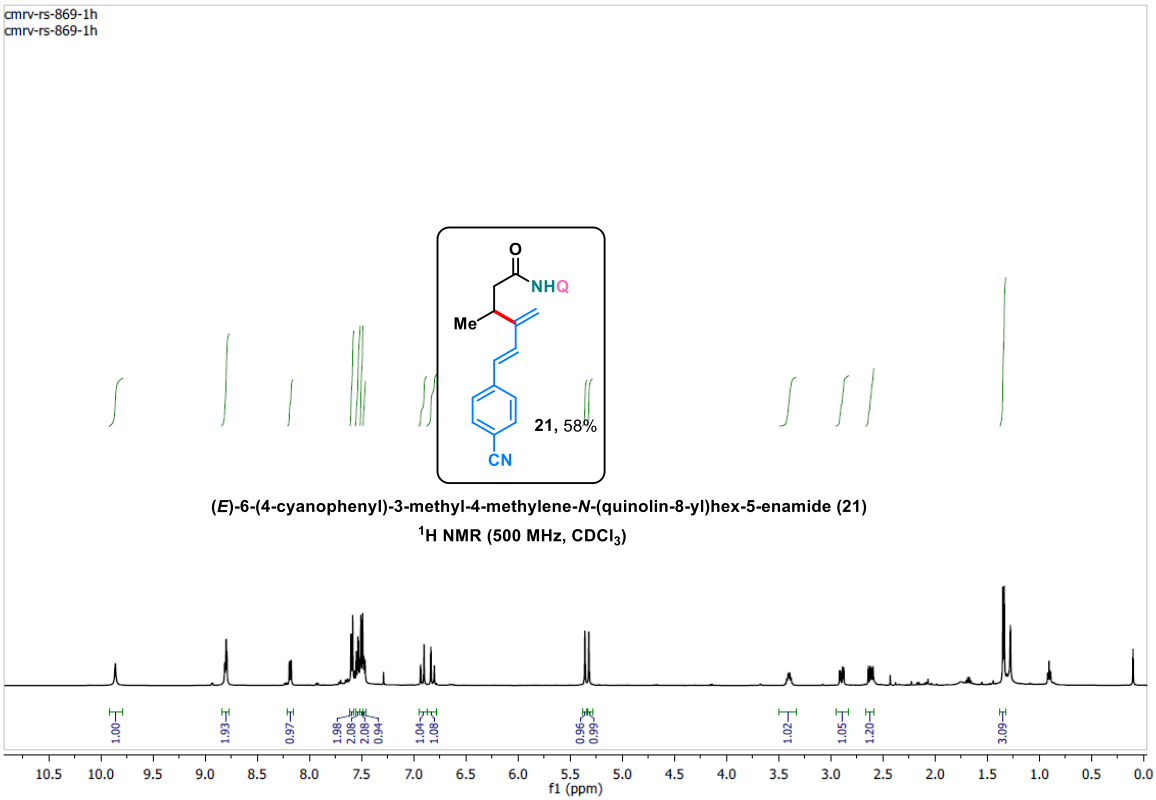

CMRV-JC-21-13C
CMRV-JC-21-13C
171.00
150.58
148.16
138.42
136.53
134.65
131.05
130.91
128.07
127.58
121.67
121.51
116.63
111.39
45.20
33.14
32.33
31.84
29.45
29.05
22.71
20.07
14.21
O
NHQ
Me
n-C6H13
18, 74%
(E)-3-methyl-4-methylene-N-(quinolin-8-yl)dodec-5-enamide (18)
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CMRV-AN-2-87-1H
CMRV-AN-2-87-1H
O
NHQ
Me
Me
Me
19, 54% dr 1:1
(E)-7-ethyl-3-methyl-4-methylene-N-(quinolin-8-yl)undec-5-enamide(19, dr 1:1)
1H NMR (500 MHz, CDCl3)
1.00
2.41
1.18
2.35
1.24
1.20
1.26
1.03
1.05
1.09
1.08
1.53
1.49
1.67
2.63
8.66
6.35
f1 (ppm)


CMRV-AN-2-87-13C
CMRV-AN-2-87-13C
170.90
150.49
150.45
148.09
138.36
136.34
135.18
134.56
130.85
127.94
127.44
121.57
121.39
116.44
111.24
45.17
45.15
34.80
32.24
29.65
28.18
22.80
19.88
14.08
11.91
O
NHQ
Me
Me
Me
19, 54% dr 1:1
(E)-7-ethyl-3-methyl-4-methylene-N-(quinolin-8-yl)undec-5-enamide(19, dr 1:1)
13C NMR (125 MHz, CDCl3)
f1 (ppm)

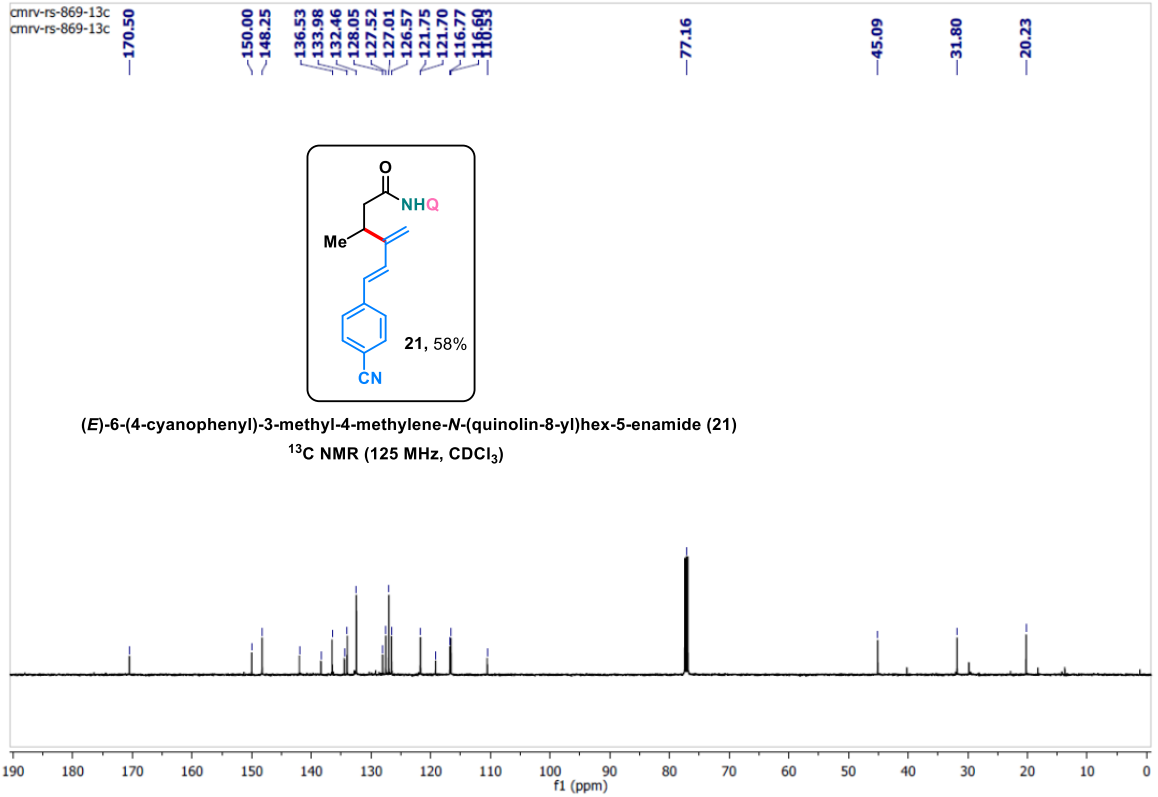

CMRV-RS-B2-73-2-1H
CMRV-RS-B2-73-2-1H
O
NHQ
Me
20, 48%
4-(cyclohexylidenemethyl)-3-methyl-N-(quinolin-8-yl)pent-4-enamide (20)
1H NMR (500 MHz, CDCl3)
1.00
2.11
1.06
2.21
1.01
1.02
1.00
0.95
0.97
1.03
1.03
2.47
2.05
4.59
2.06
3.04
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-B2-73-2-13C
CMRV-RS-B2-73-2-13C
171.070
149.118
148.051
144.426
136.717
134.641
128.117
127.680
121.654
121.505
120.996
116.832
112.037
77.160
44.548
38.053
37.752
29.918
28.892
28.255
26.920
19.637
O
NHQ
Me
20, 48%
4-(cyclohexylidenemethyl)-3-methyl-N-(quinolin-8-yl)pent-4-enamide (20)
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



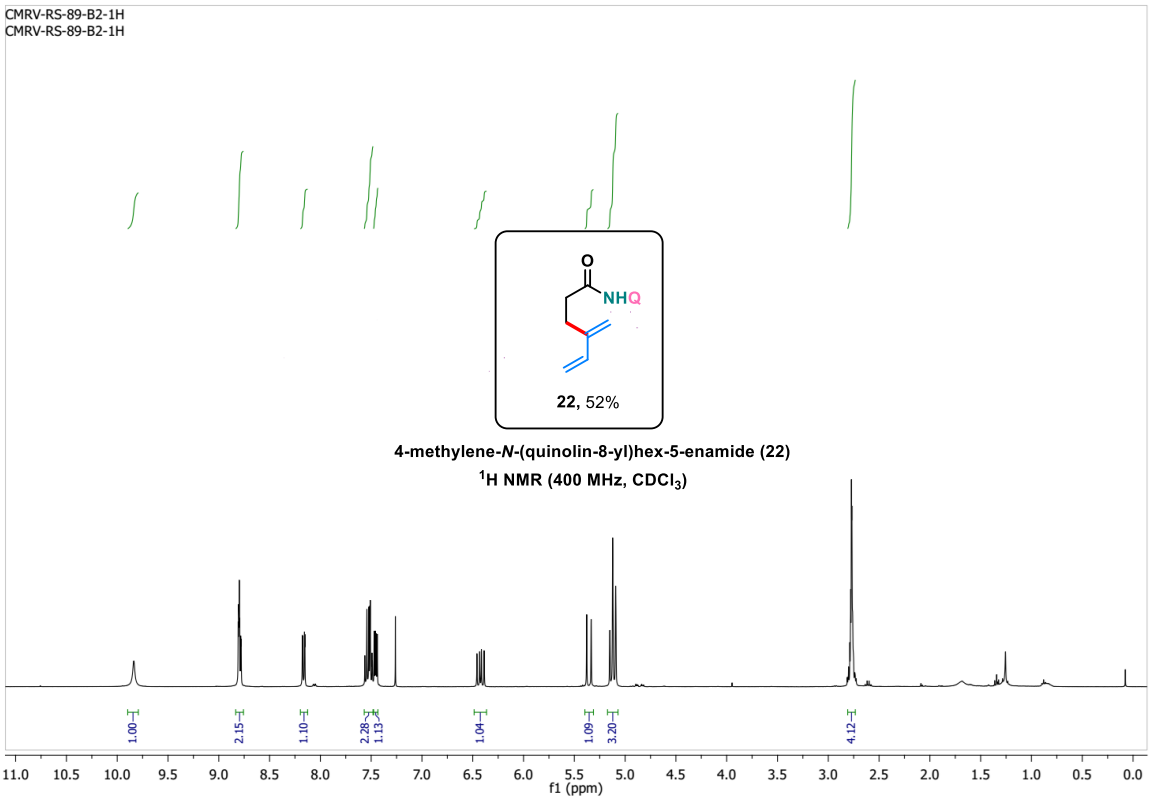
(*E*)-6-(4-cyanophenyl)-3-methyl-4-methylene-*N*-(quinolin-8-yl)hex-5-enamide (21)

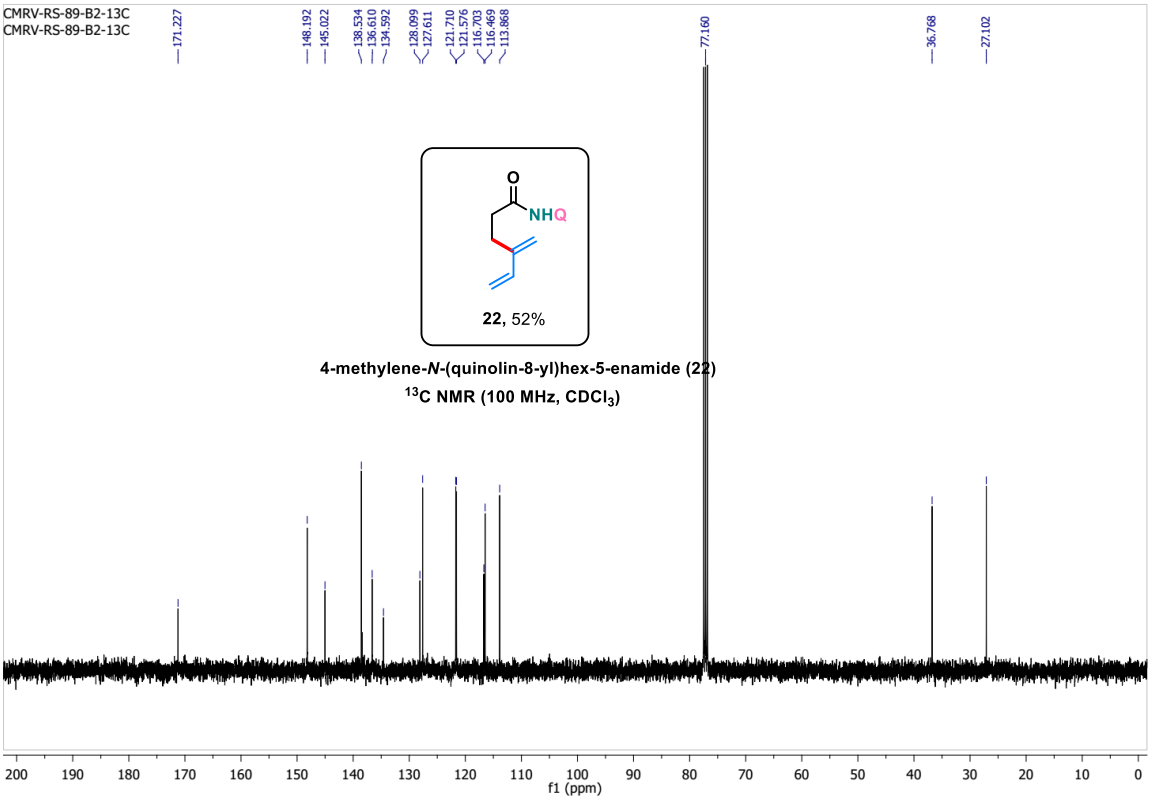
^{1}H NMR (500 MHz, $CDCl_3$)

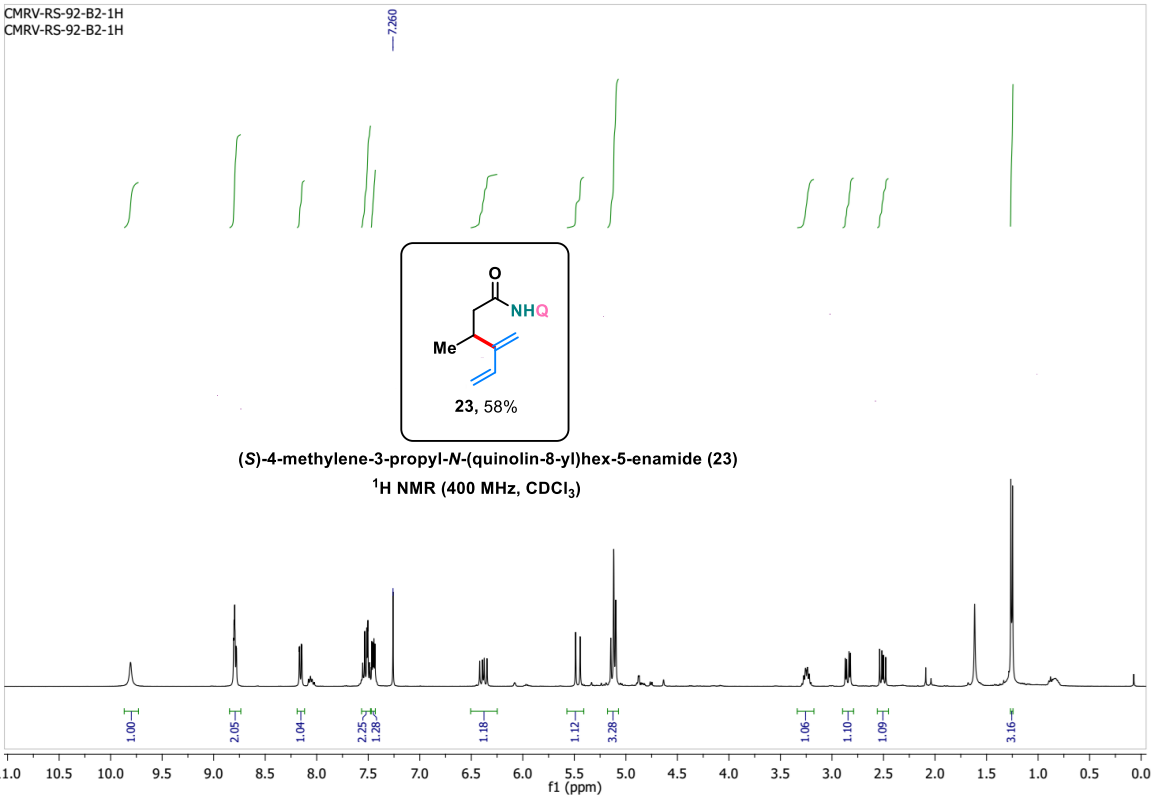


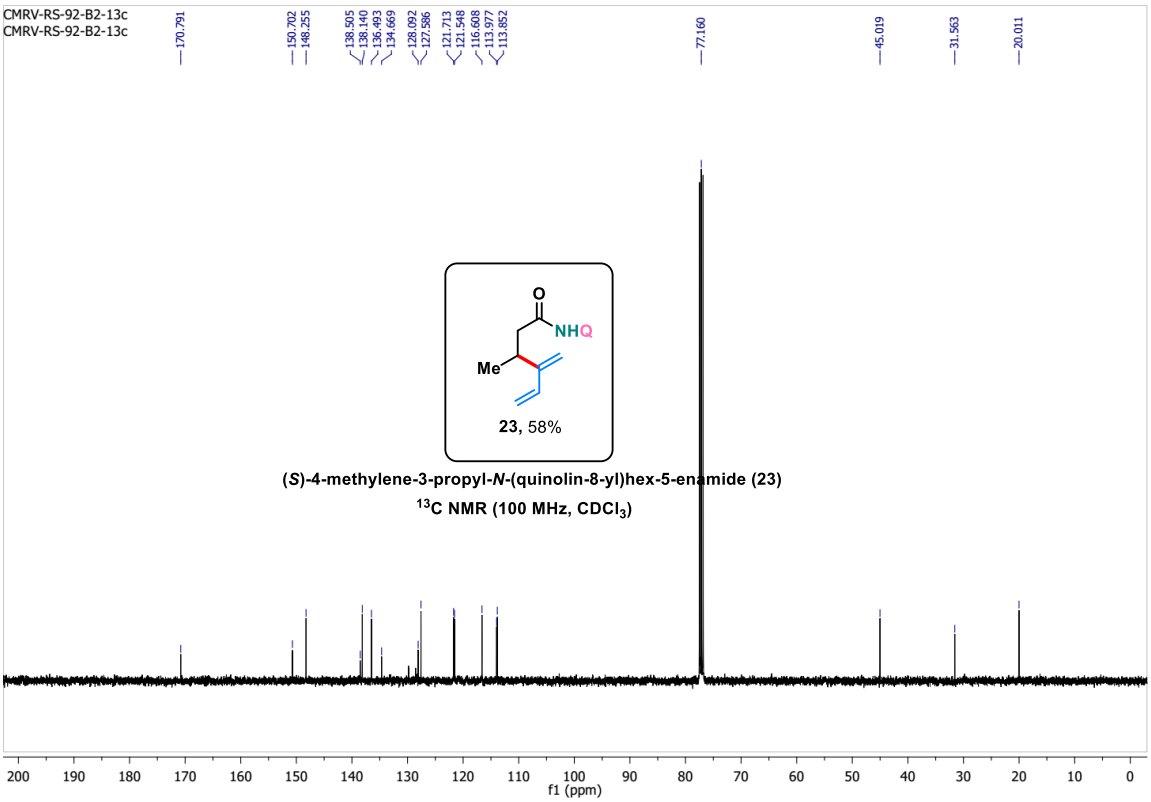
(*E*)-6-(4-cyanophenyl)-3-methyl-4-methylene-*N*-(quinolin-8-yl)hex-5-enamide (21)

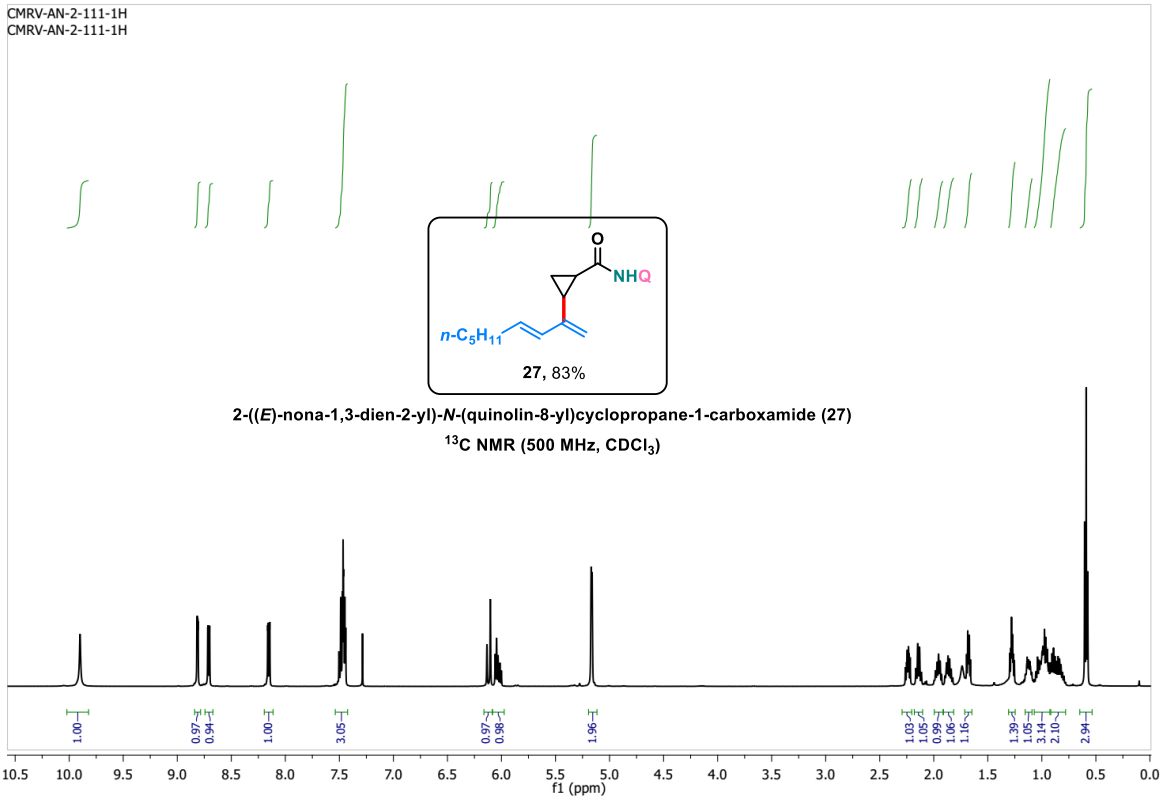
^{13}C NMR (125 MHz, $CDCl_3$)

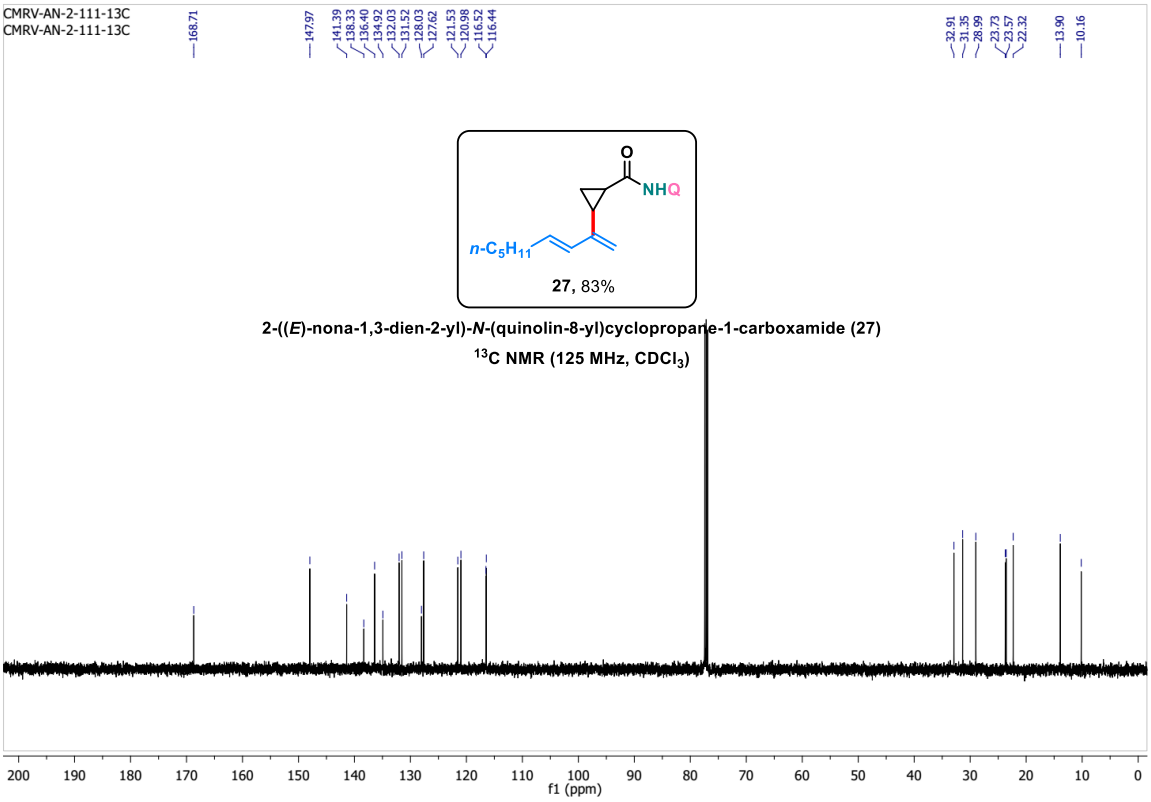

CMRV-RS-89-B2-1H
CMRV-RS-89-B2-1H
O
NHQ
22, 52%
4-methylene-N-(quinolin-8-yl)hex-5-enamide (22)
1H NMR (400 MHz, CDCl3)
1.00
2.15
1.10
2.28
1.13
1.04
1.09
3.20
4.12
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

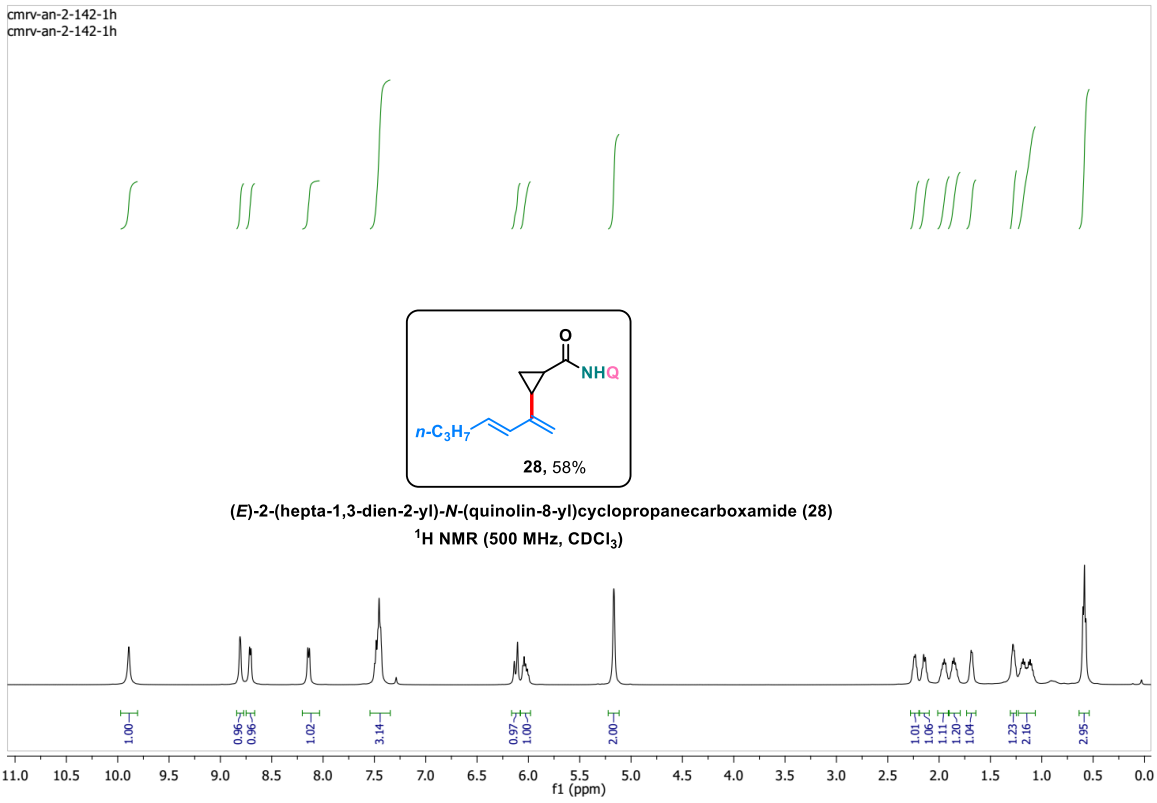

CMRV-RS-89-B2-13C
CMRV-RS-89-B2-13C
171.227
148.192
145.022
138.534
136.610
134.592
128.099
127.611
121.710
121.576
116.703
116.469
113.868
77.160
36.768
27.102
O
NHQ
22, 52%
4-methylene-N-(quinolin-8-yl)hex-5-enamide (22)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CMRV-RS-92-B2-1H
CMRV-RS-92-B2-1H
7.260
O
NHQ
Me
23, 58%
(S)-4-methylene-3-propyl-N-(quinolin-8-yl)hex-5-enamide (23)
1H NMR (400 MHz, CDCl3)
1.00
2.05
1.04
2.25
1.28
1.18
1.12
3.28
1.06
1.10
1.09
3.16
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-92-B2-13c
CMRV-RS-92-B2-13c
170.791
150.702
148.255
138.505
138.140
136.493
134.669
128.092
127.586
121.713
121.548
116.608
113.977
113.852
77.160
45.019
31.563
20.011
O
NHQ
Me
23, 58%
(S)-4-methylene-3-propyl-N-(quinolin-8-yl)hex-5-enamide (23)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

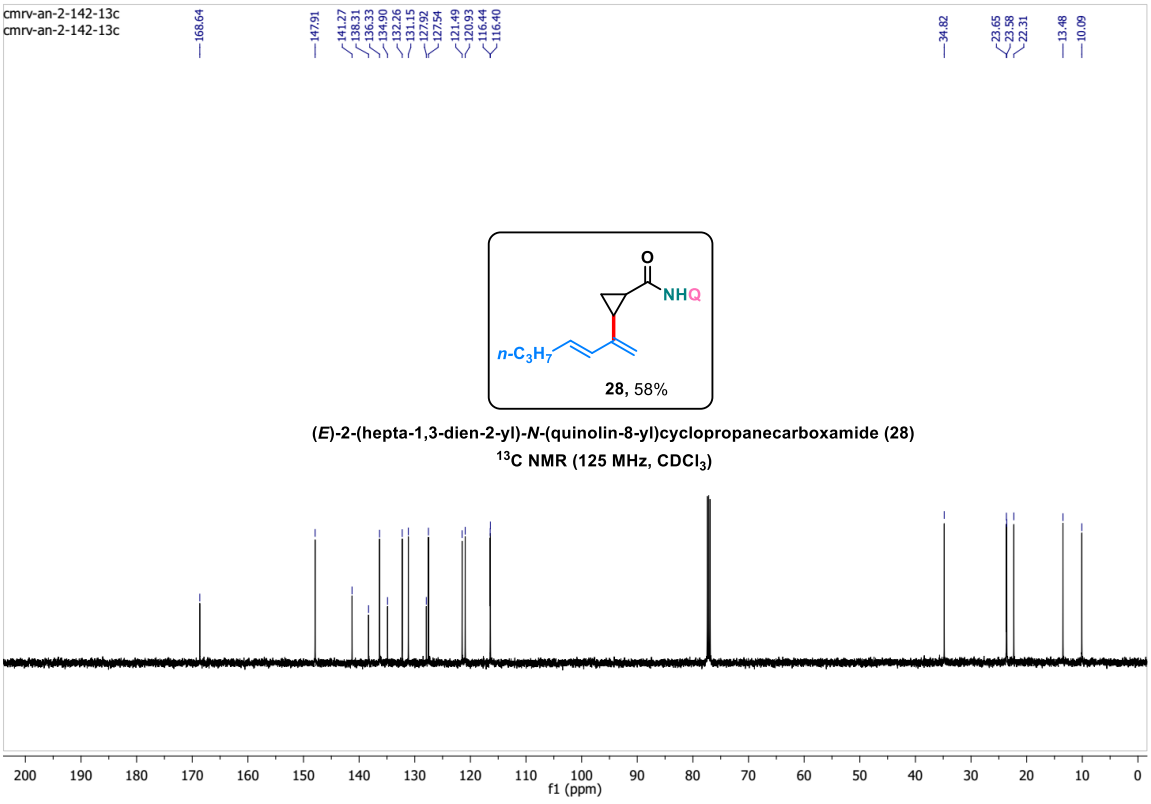

CMRV-AN-2-111-1H
CMRV-AN-2-111-1H
O
NHQ
n-C5H11
27, 83%
2-((E)-nona-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (27)
13C NMR (500 MHz, CDCl3)
1.00
0.97
0.94
1.00
3.05
0.97
0.98
1.96
1.03
1.05
0.99
1.06
1.16
1.39
1.05
3.14
2.10
2.94
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-AN-2-111-13C
CMRV-AN-2-111-13C
168.71
147.97
141.39
138.33
136.40
134.92
132.03
131.52
128.03
127.62
121.53
120.98
116.52
116.44
32.91
31.35
28.99
23.73
23.57
22.32
13.90
10.16
O
NHQ
n-C5H11
27, 83%
2-((E)-nona-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (27)
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



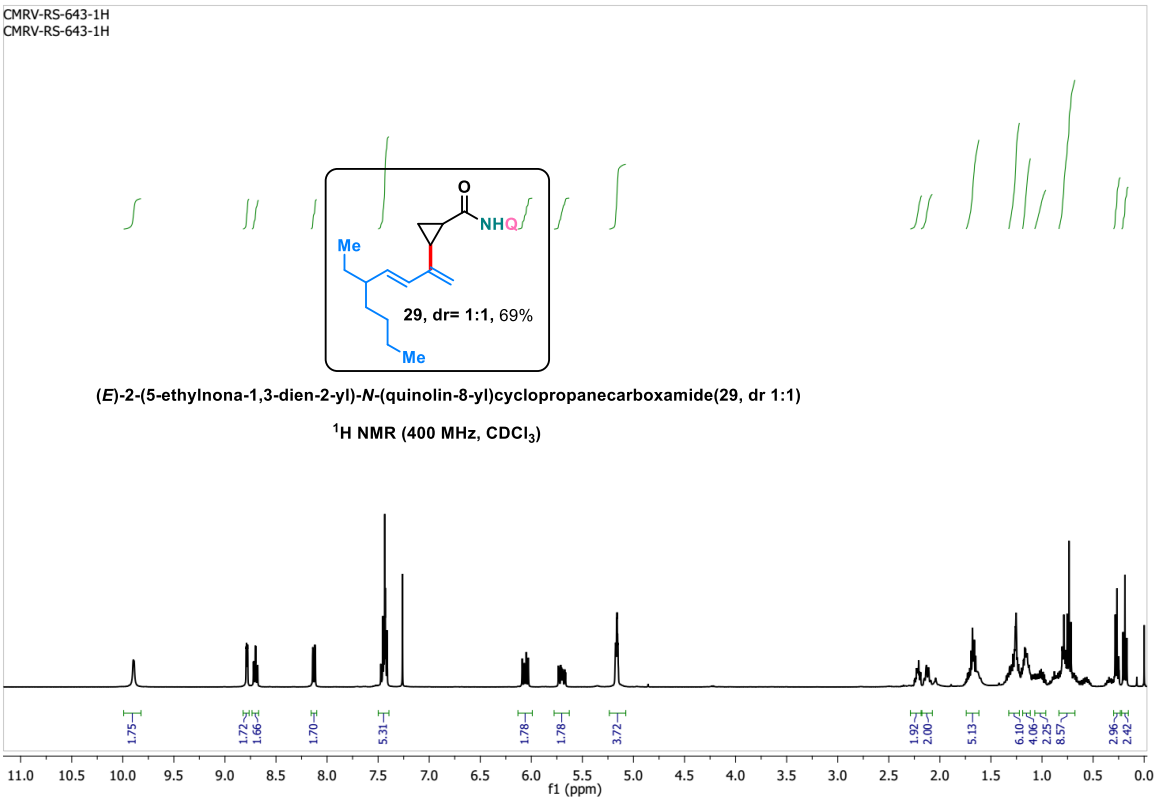
(*E*)-2-(hepta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropanecarboxamide (28)

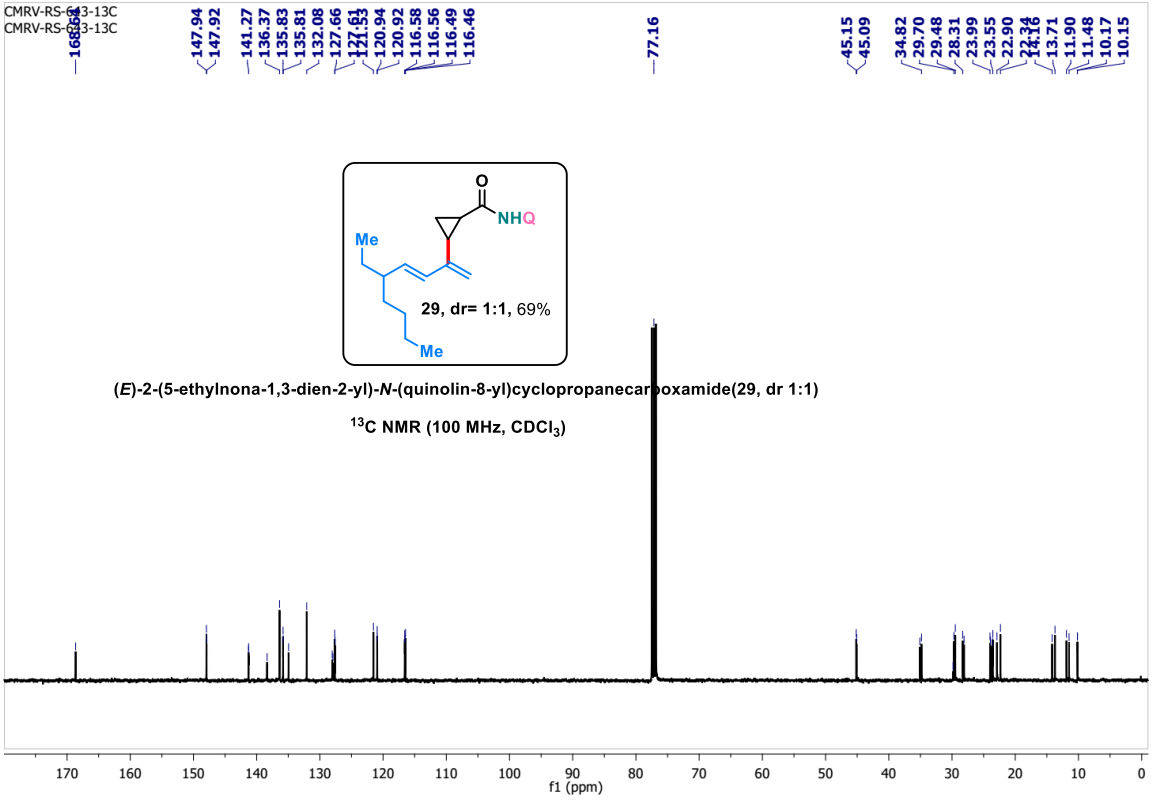
^{1}H NMR (500 MHz, $CDCl_3$)

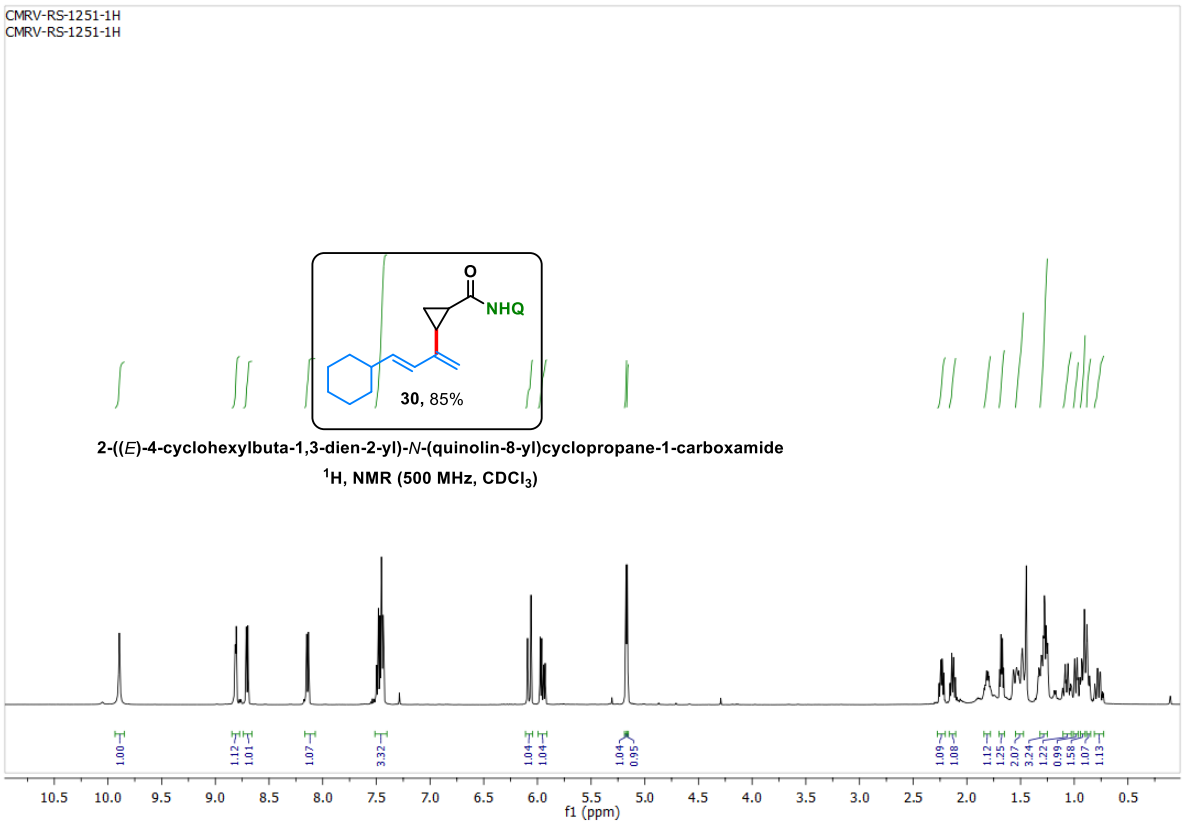


(*E*)-2-(hepta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropanecarboxamide (28)

^{13}C NMR (125 MHz, $CDCl_3$)

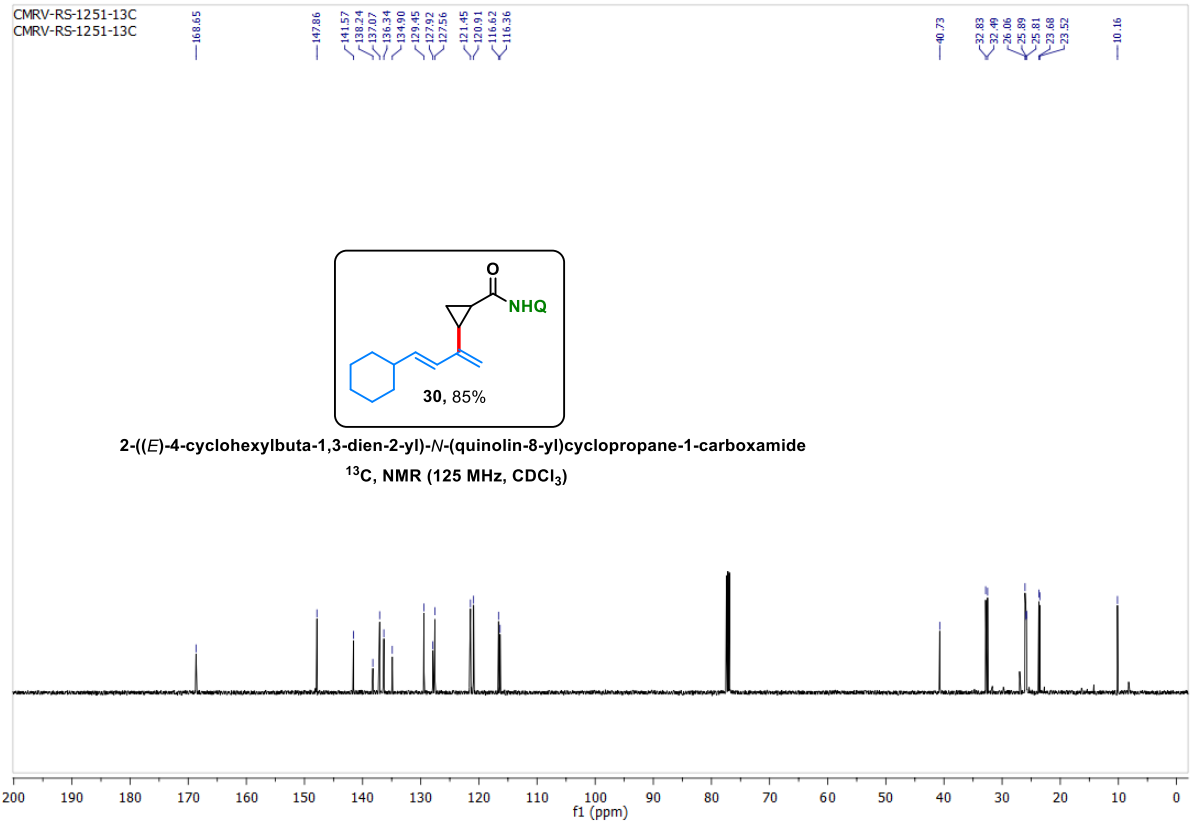

CMRV-RS-643-1H
CMRV-RS-643-1H
O
NHQ
Me
Me
29, dr= 1:1, 69%
(E)-2-(5-ethylnona-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropanecarboxamide(29, dr 1:1)
1H NMR (400 MHz, CDCl3)
1.75
1.72
1.66
1.70
5.31
1.78
1.78
3.72
1.92
2.00
5.13
6.10
4.06
2.25
8.57
2.96
2.42
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-643-13C
CMRV-RS-643-13C
147.94
147.92
141.27
136.37
135.83
135.81
132.08
127.66
120.94
120.92
116.58
116.56
116.49
116.46
77.16
45.15
45.09
34.82
29.70
29.48
28.31
23.99
23.55
22.90
13.71
11.90
11.48
10.17
10.15
O
NHQ
Me
Me
29, dr= 1:1, 69%
(E)-2-(5-ethylnona-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropanecarboxamide(29, dr 1:1)
13C NMR (100 MHz, CDCl3)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



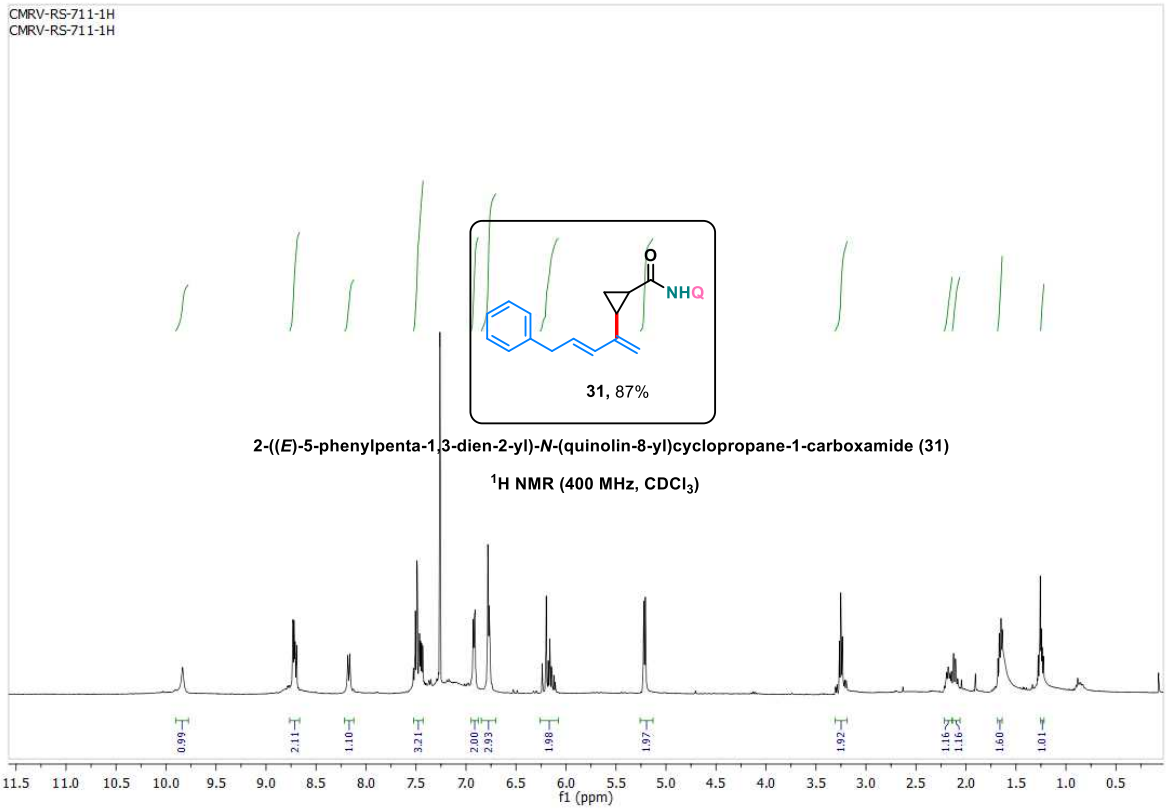
2-((*E*)-4-cyclohexylbuta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide

^{1}H, NMR (500 MHz, $CDCl_3$)



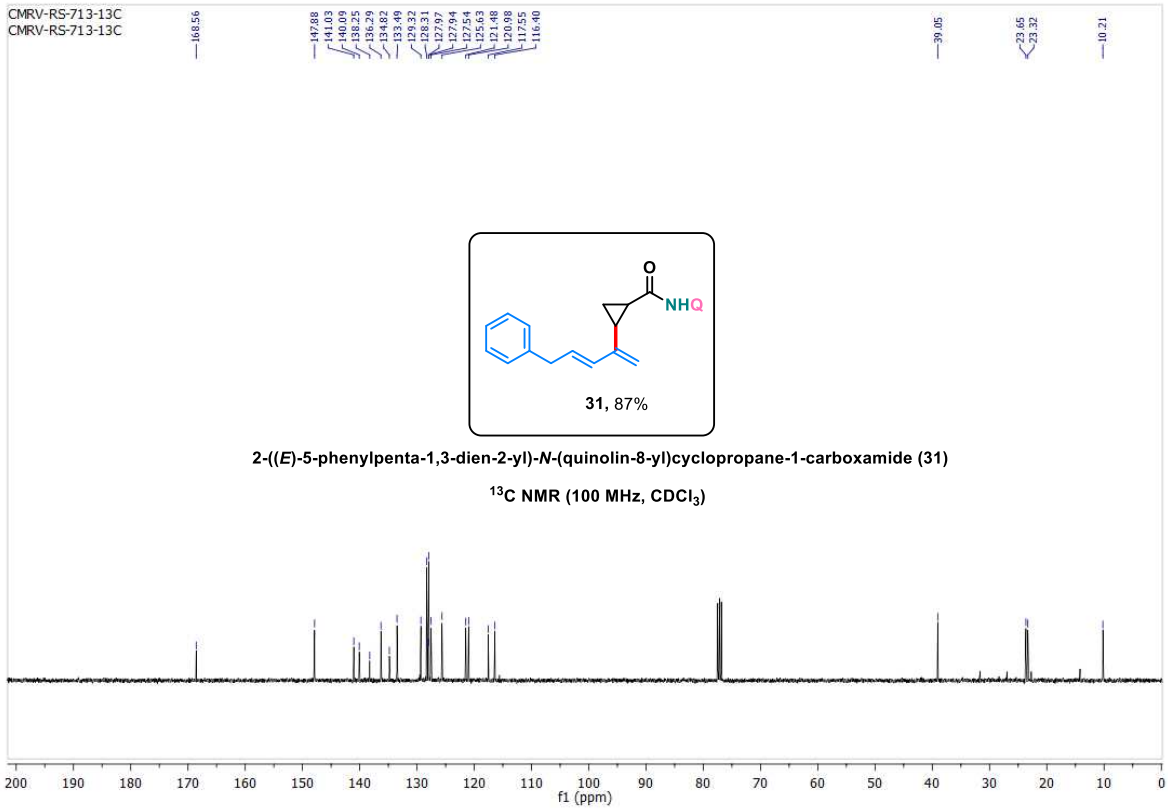
2-((*E*)-4-cyclohexylbuta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide

^{13}C, NMR (125 MHz, $CDCl_3$)



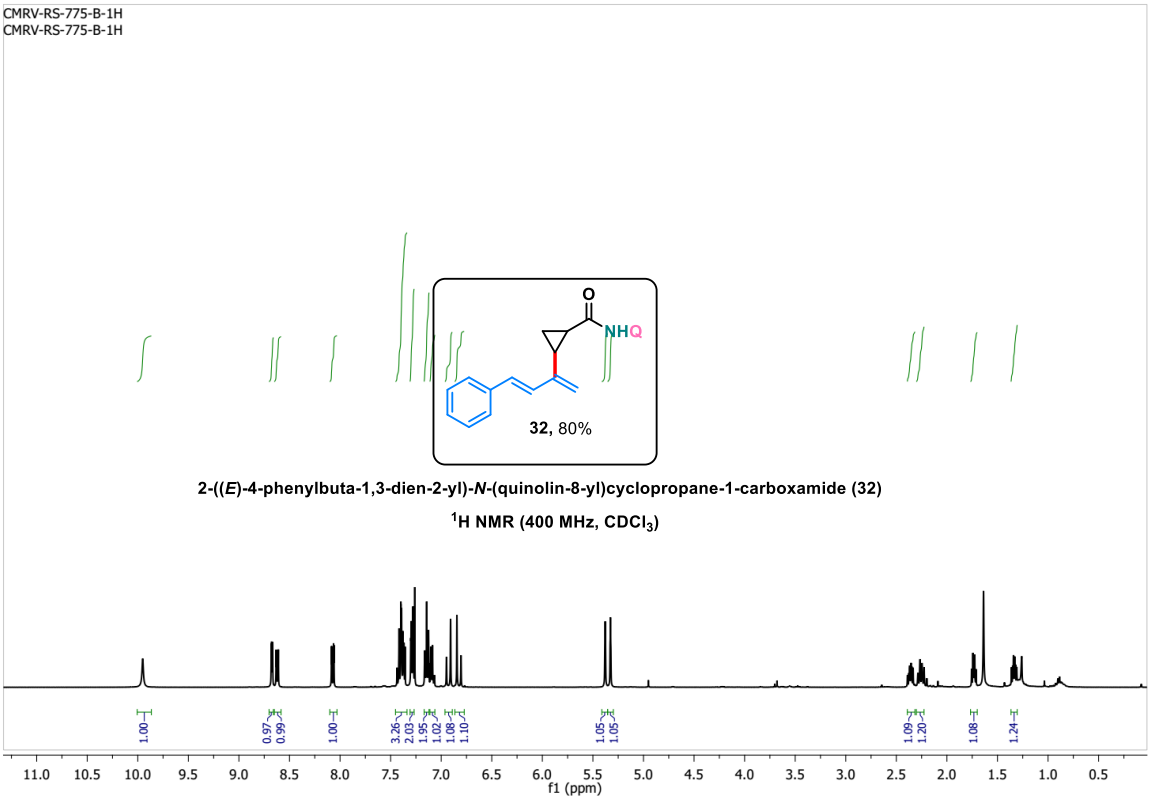
2-((*E*)-5-phenylpenta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (31)

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



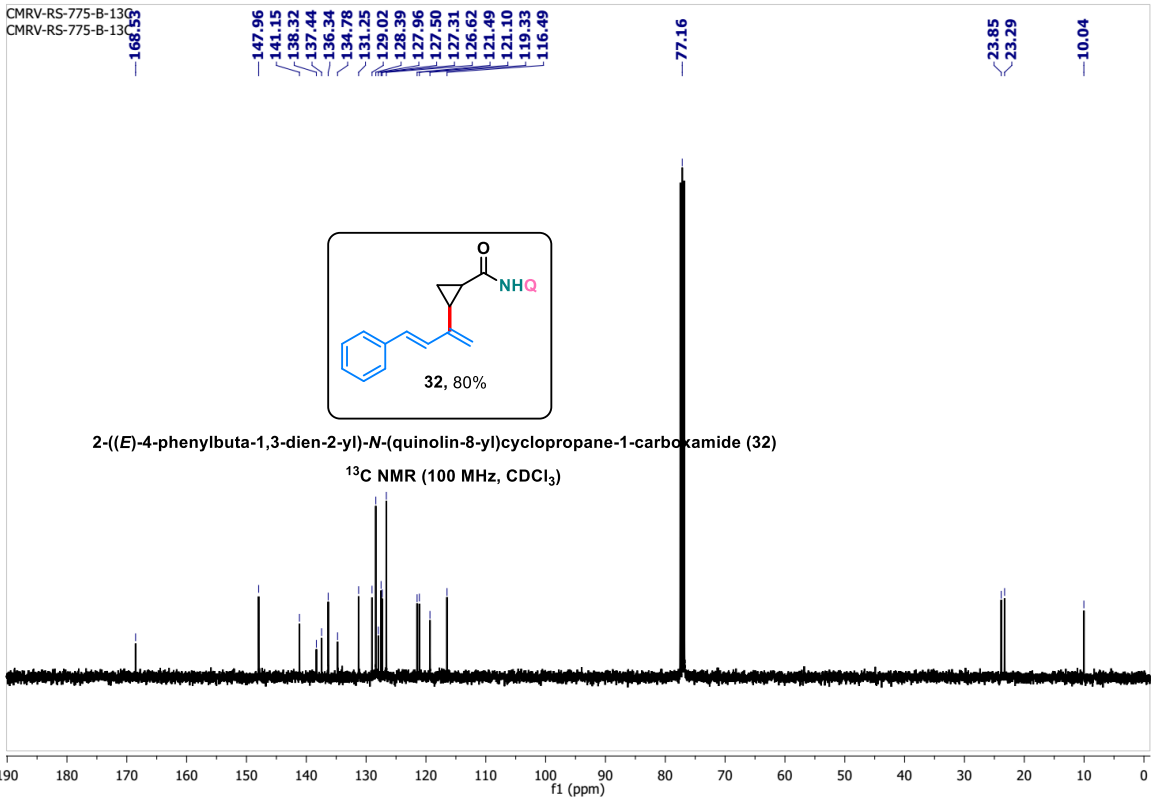
2-((*E*)-5-phenylpenta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (31)

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



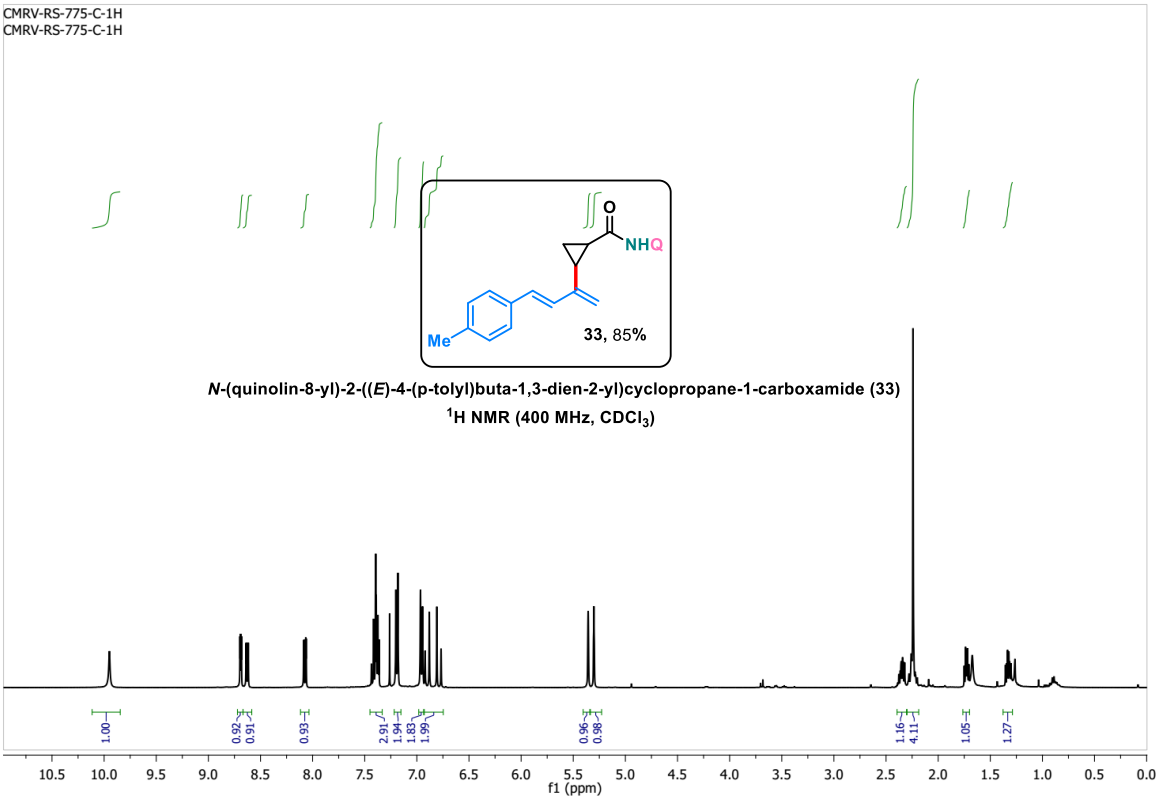
2-((*E*)-4-phenylbuta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (32)

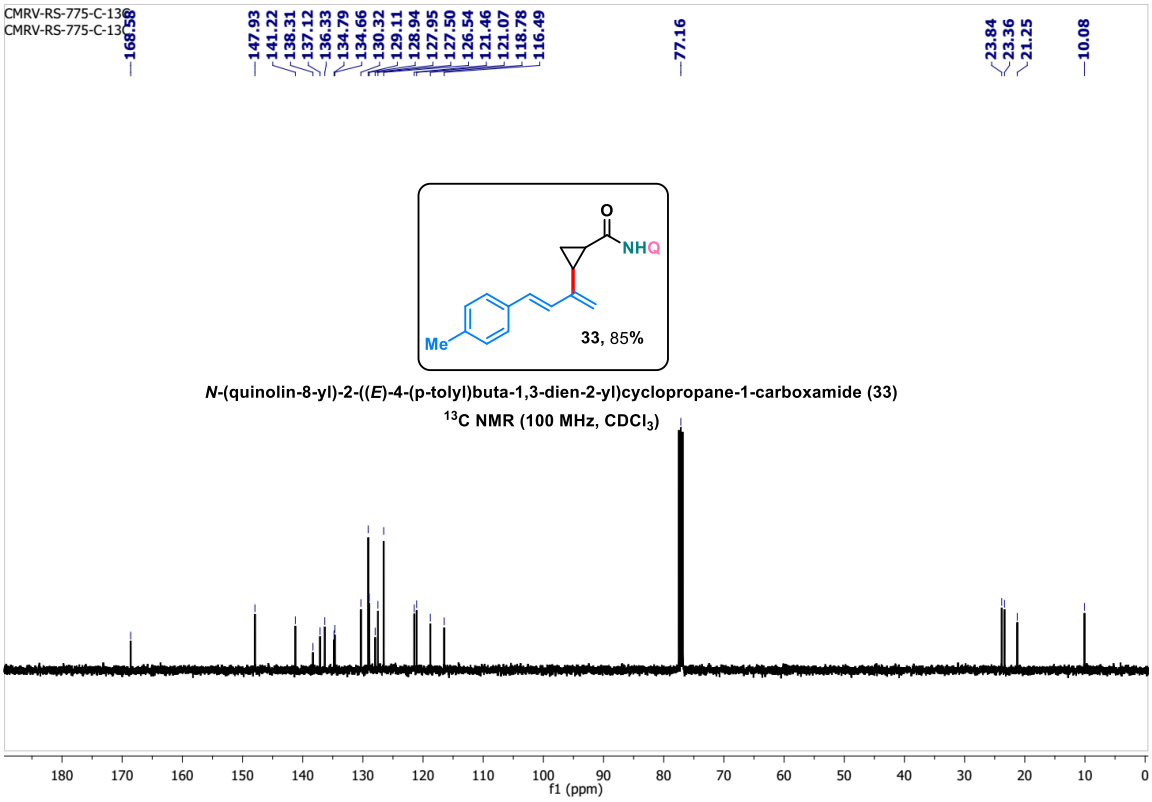
^{1}H NMR (400 MHz, $CDCl_3$)

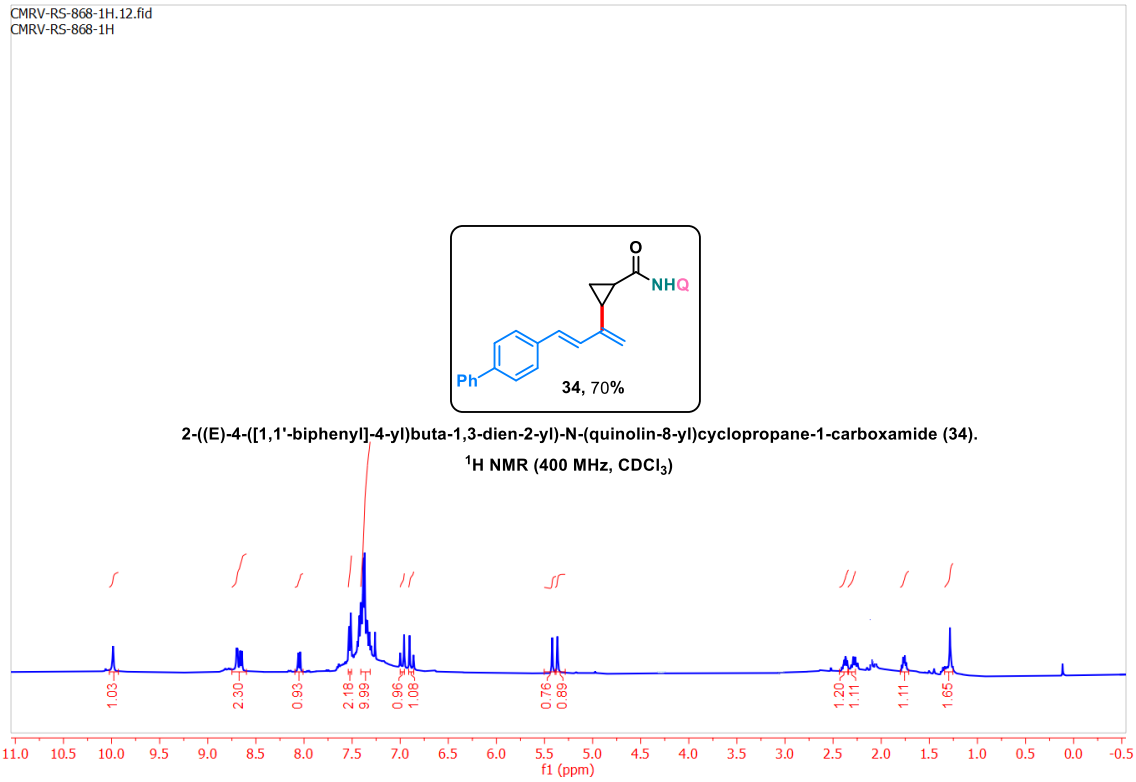


2-((*E*)-4-phenylbuta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (32)

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

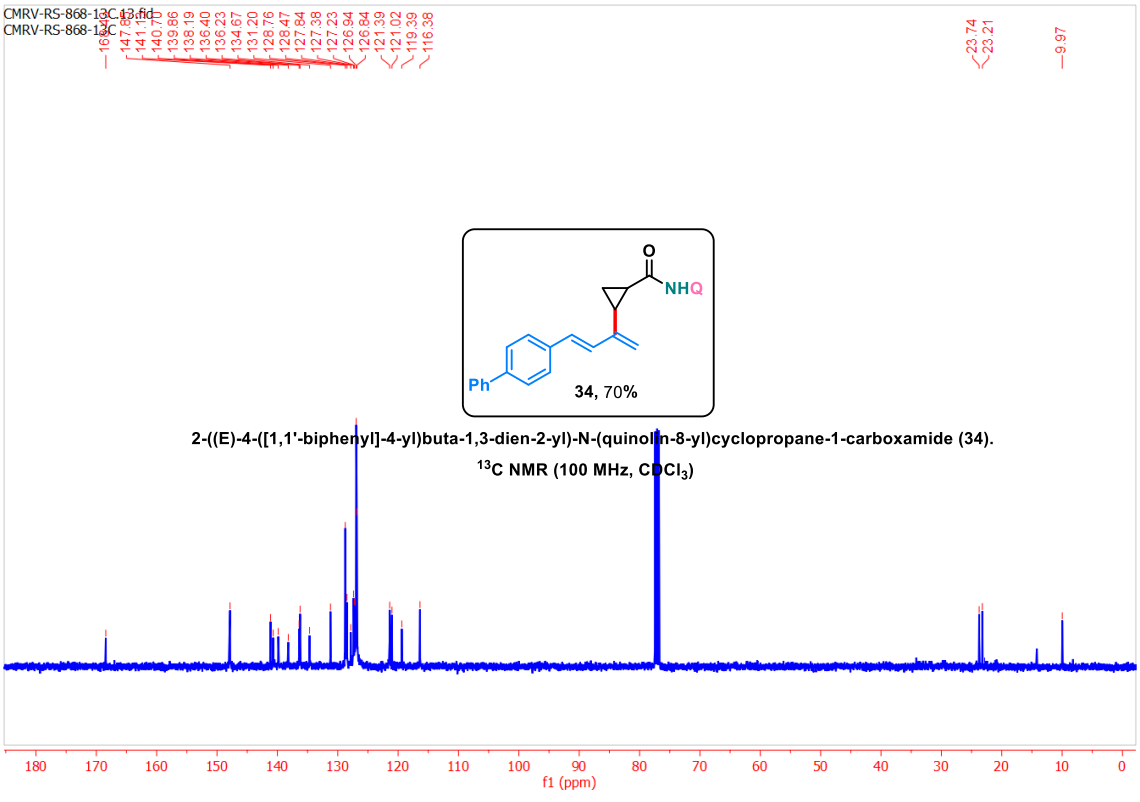

CMRV-RS-775-C-1H
CMRV-RS-775-C-1H
O
NHQ
Me
33, 85%
N-(quinolin-8-yl)-2-((E)-4-(p-tolyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxamide (33)
1H NMR (400 MHz, CDCl3)
1.00
0.92
0.91
0.93
2.91
1.94
1.83
1.99
0.96
0.98
1.16
4.11
1.05
1.27
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-775-C-13C
168.58
147.93
141.22
138.31
137.12
136.33
134.79
134.66
130.32
129.11
128.94
127.95
127.50
126.54
121.46
121.07
118.78
116.49
77.16
23.84
23.36
21.25
10.08
O
NHQ
Me
33, 85%
N-(quinolin-8-yl)-2-((E)-4-(p-tolyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxamide (33)
13C NMR (100 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



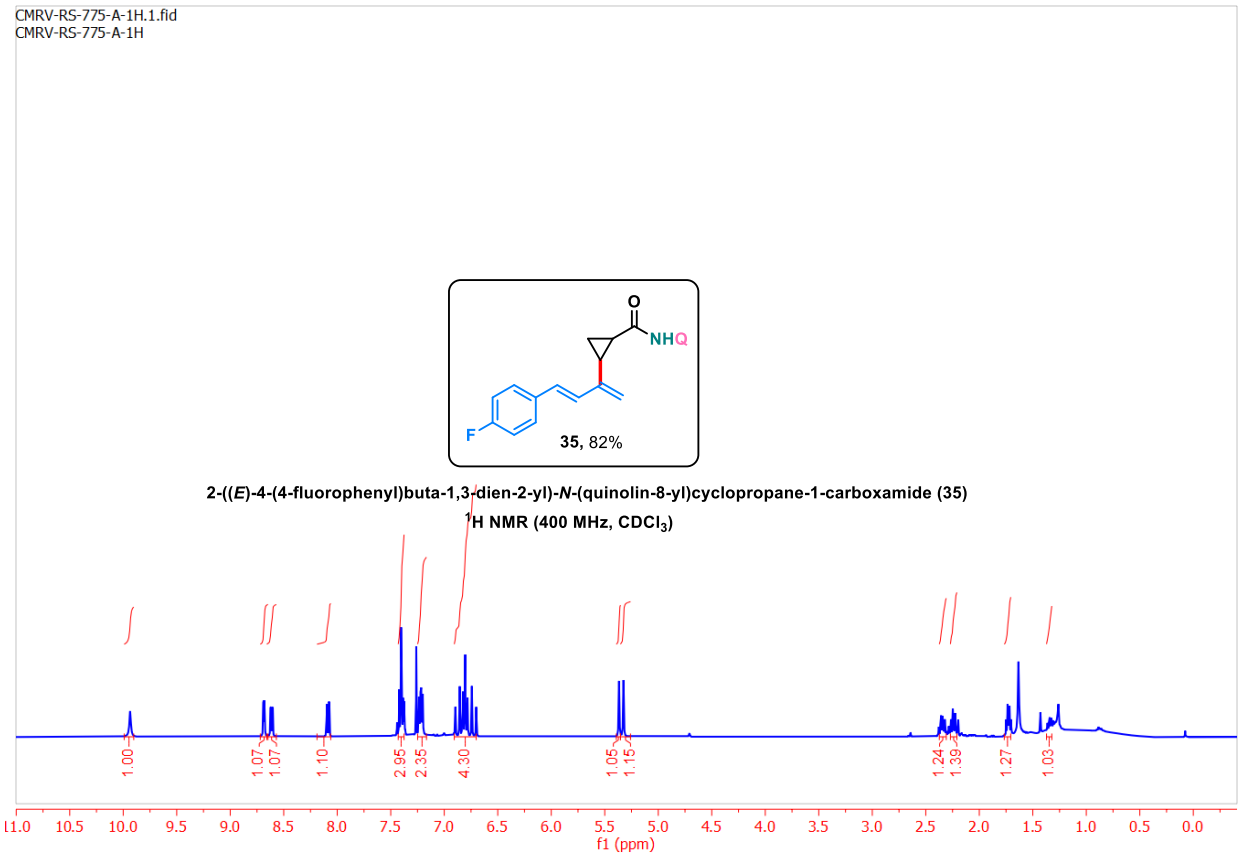
2-((E)-4-([1,1'-biphenyl]-4-yl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (34).

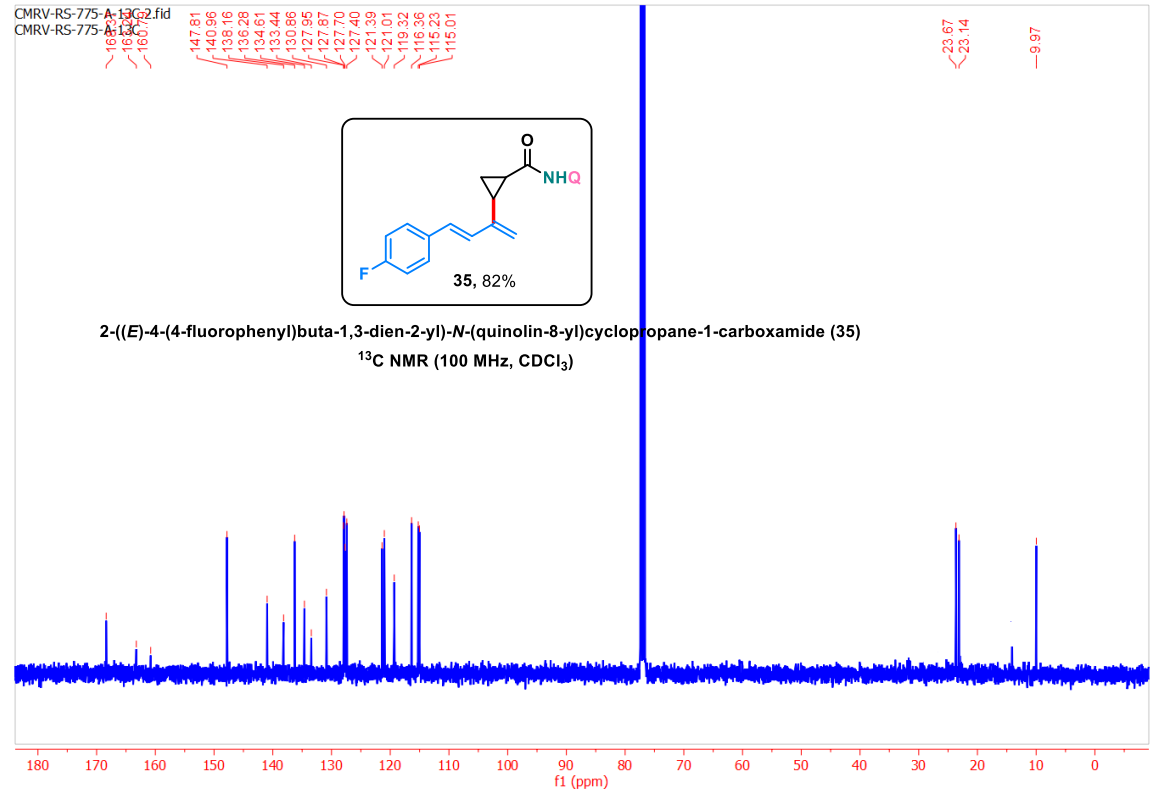
^{1}H NMR (400 MHz, $CDCl_3$)

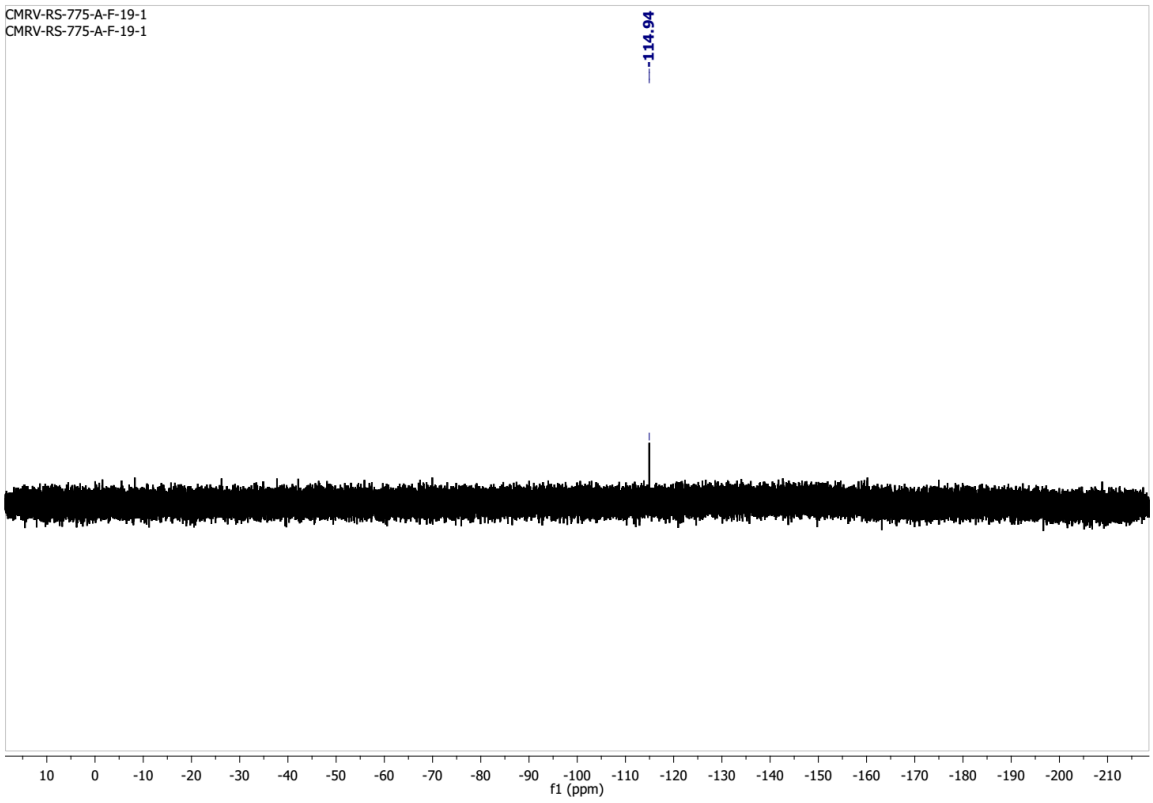


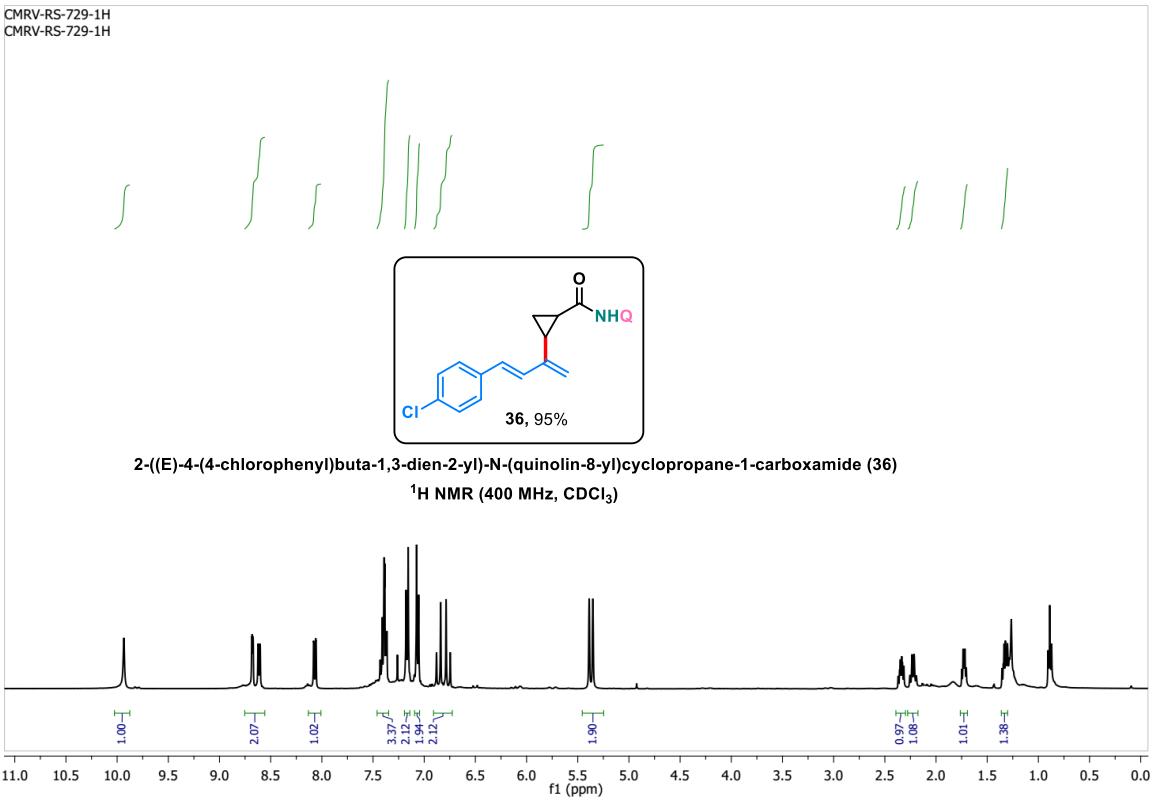
2-((E)-4-([1,1'-biphenyl]-4-yl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (34).

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


CMRV-RS-775-A-1H.1.fid
CMRV-RS-775-A-1H
O
NHQ
F
35, 82%
2-((E)-4-(4-fluorophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (35)
1H NMR (400 MHz, CDCl3)
1.00
1.07
1.07
1.10
2.95
2.35
4.30
1.05
1.15
1.24
1.39
1.27
1.03
f1 (ppm)

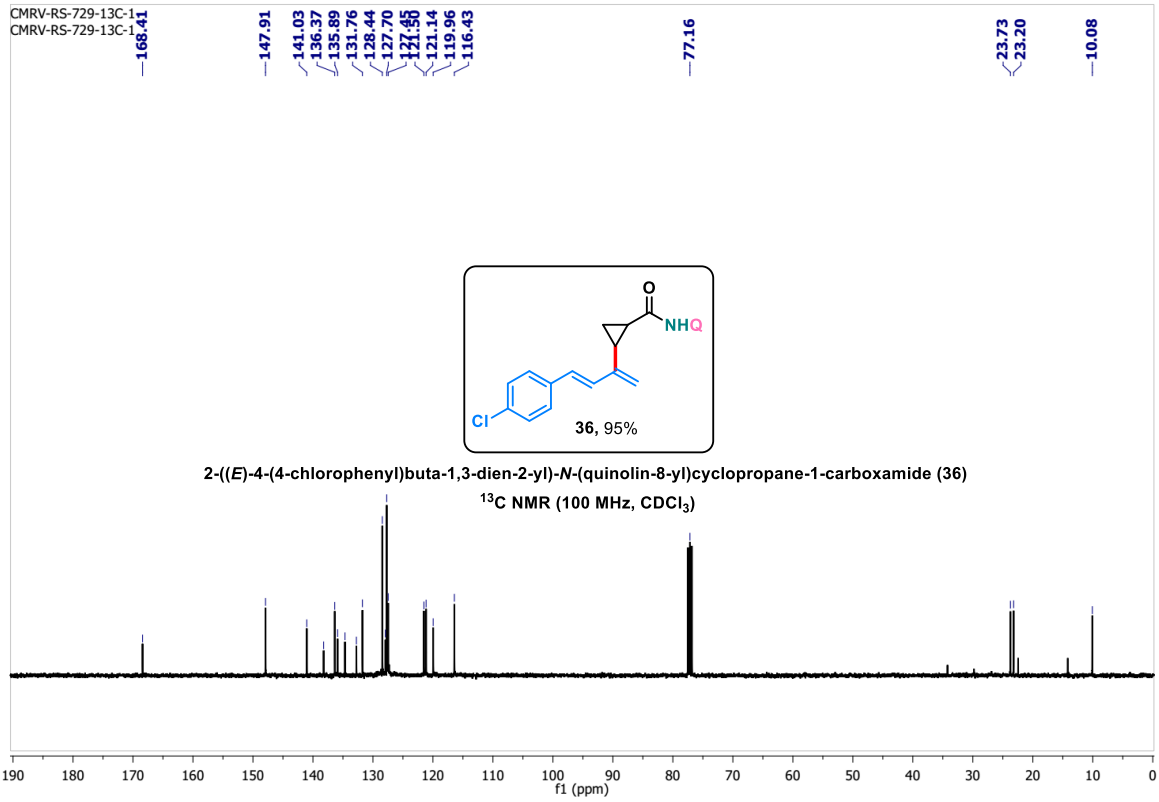

CMRV-RS-775-A-13C-2.fid
CMRV-RS-775-A-13C
147.81
140.96
138.16
136.28
134.61
133.44
130.86
127.95
127.87
127.70
127.40
121.39
121.01
119.32
116.36
115.23
115.01
23.67
23.14
9.97
O
NHQ
F
35, 82%
2-((E)-4-(4-fluorophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (35)
13C NMR (100 MHz, CDCl3)
f1 (ppm)


CMRV-RS-775-A-F-19-1
CMRV-RS-775-A-F-19-1
-114.94
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)



2-((E)-4-(4-chlorophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (36)

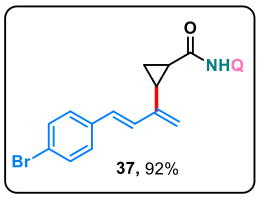
^{1}H NMR (400 MHz, $CDCl_3$)



2-((*E*)-4-(4-chlorophenyl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (36)

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

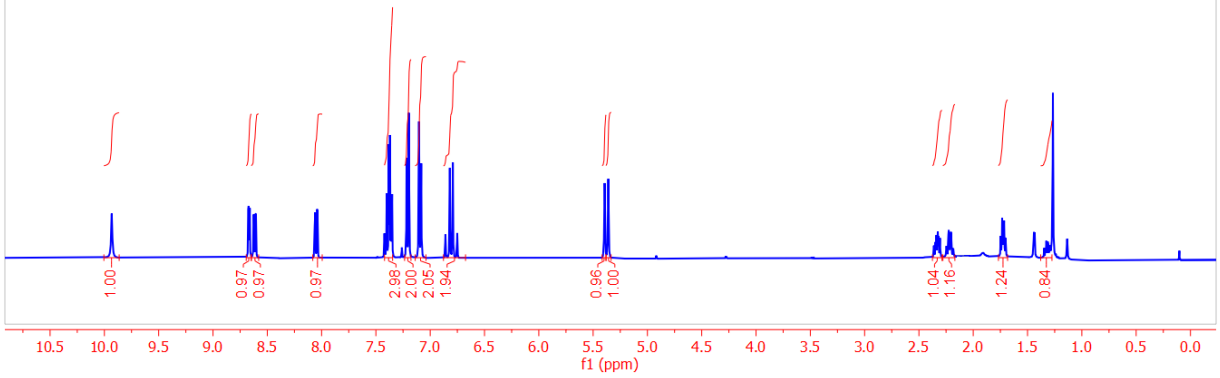
CMRV-RS-863-1H.1.fid
CMRV-RS-863-1H



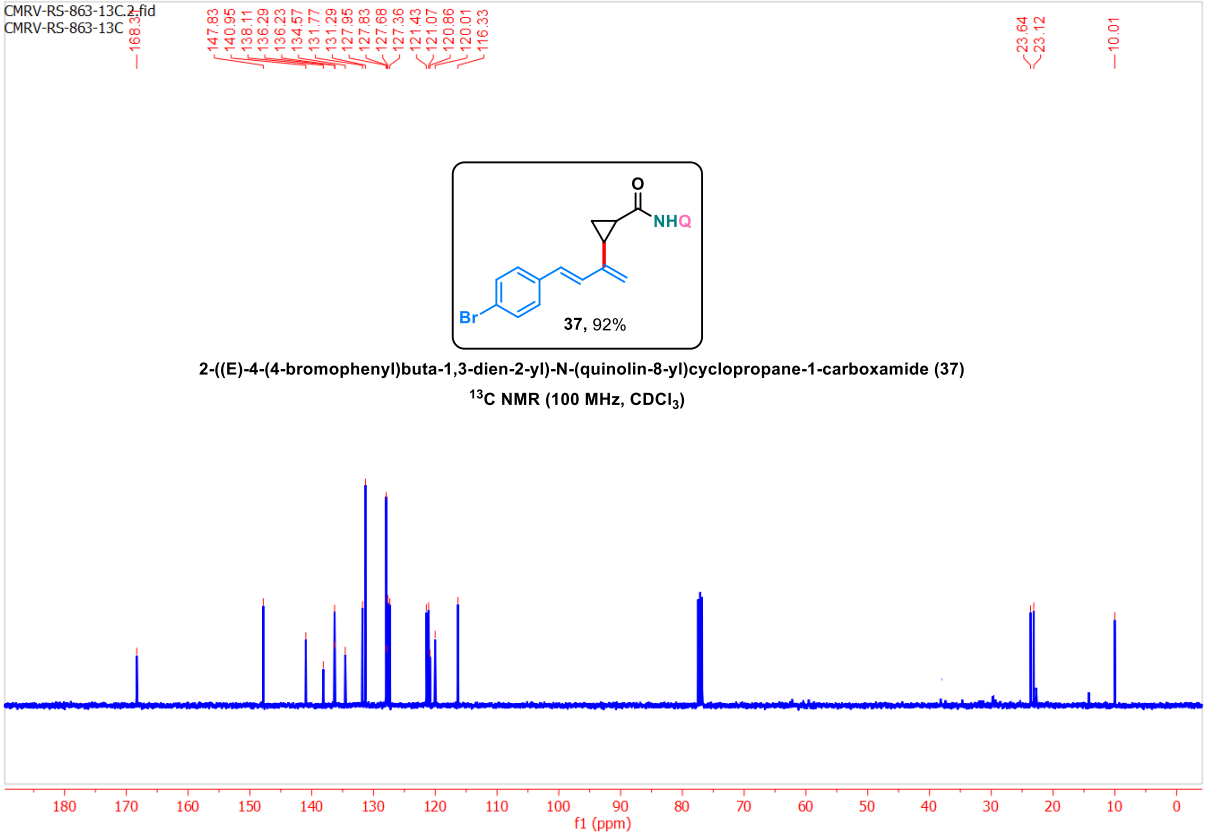
37, 92%

2-((*E*)-4-(4-bromophenyl)buta-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclopropane-1-carboxamide (37)

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



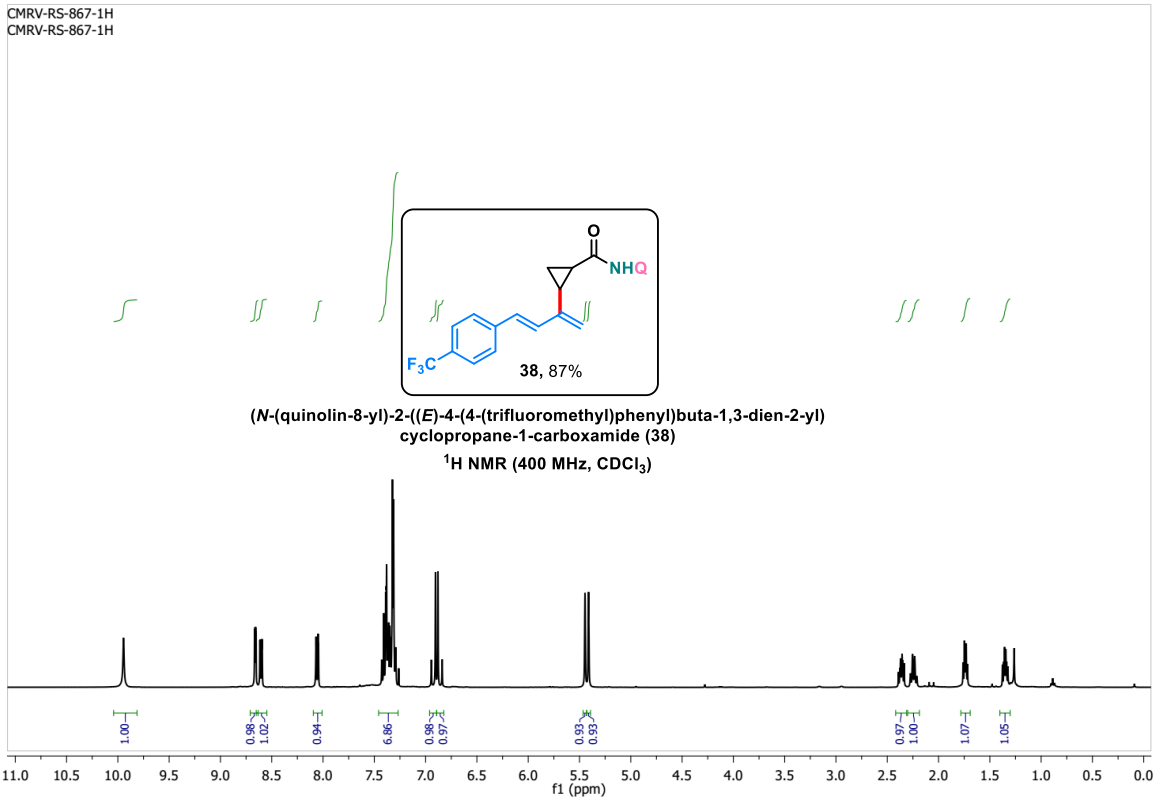
CMRV-RS-863-13C.2.fid
CMRV-RS-863-13C



37, 92%

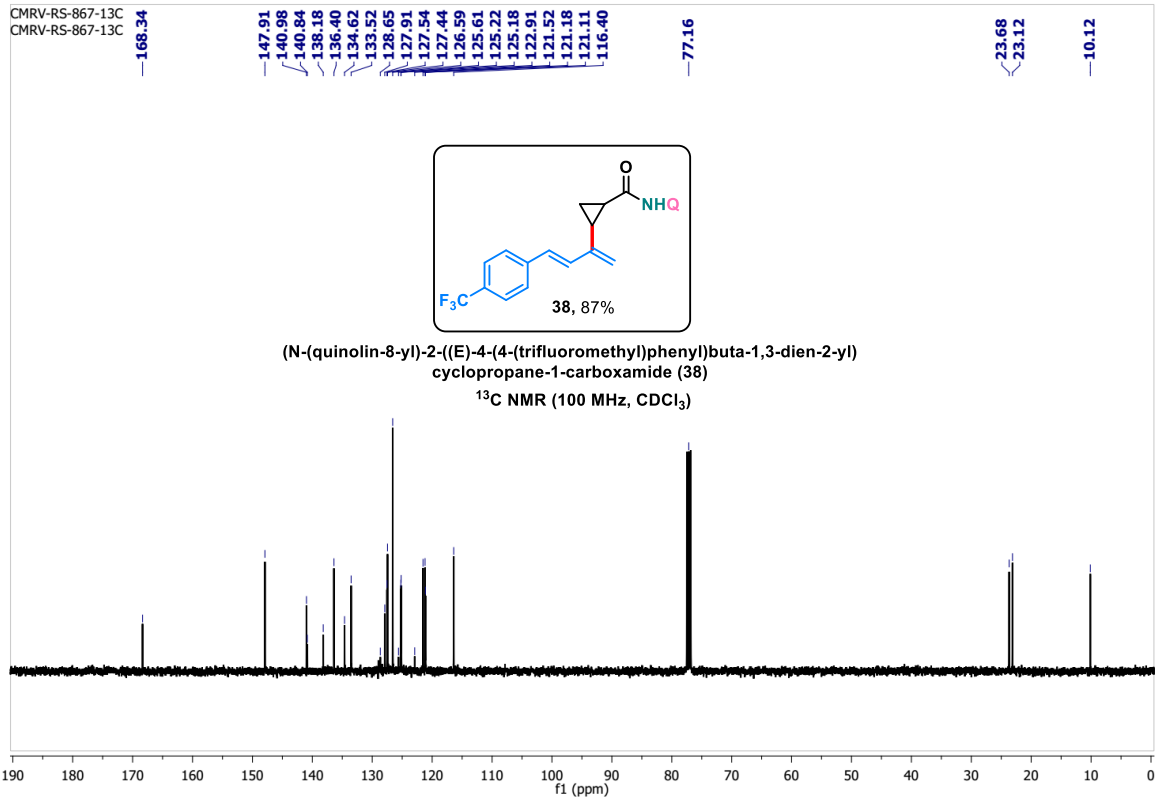
2-((E)-4-(4-bromophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopropane-1-carboxamide (37)

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



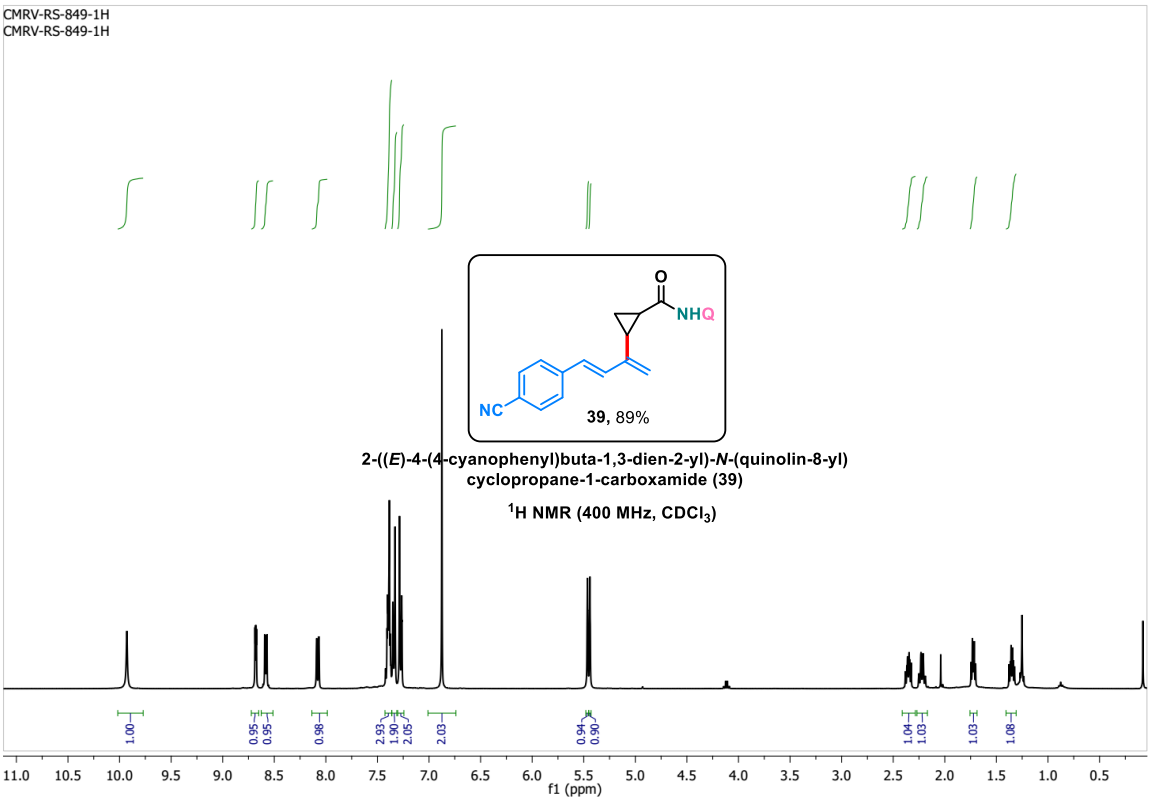
(*N*-(quinolin-8-yl)-2-((*E*)-4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl) cyclopropane-1-carboxamide (38)

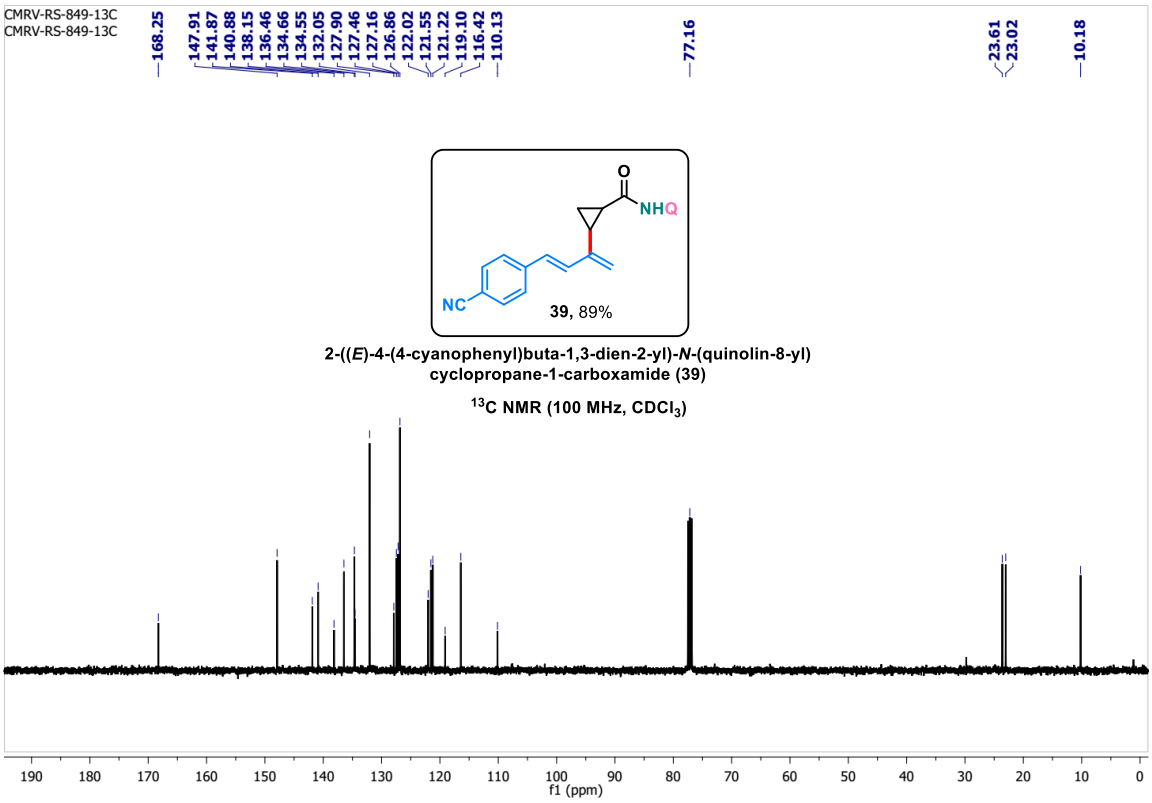
^{1}H NMR (400 MHz, $CDCl_3$)

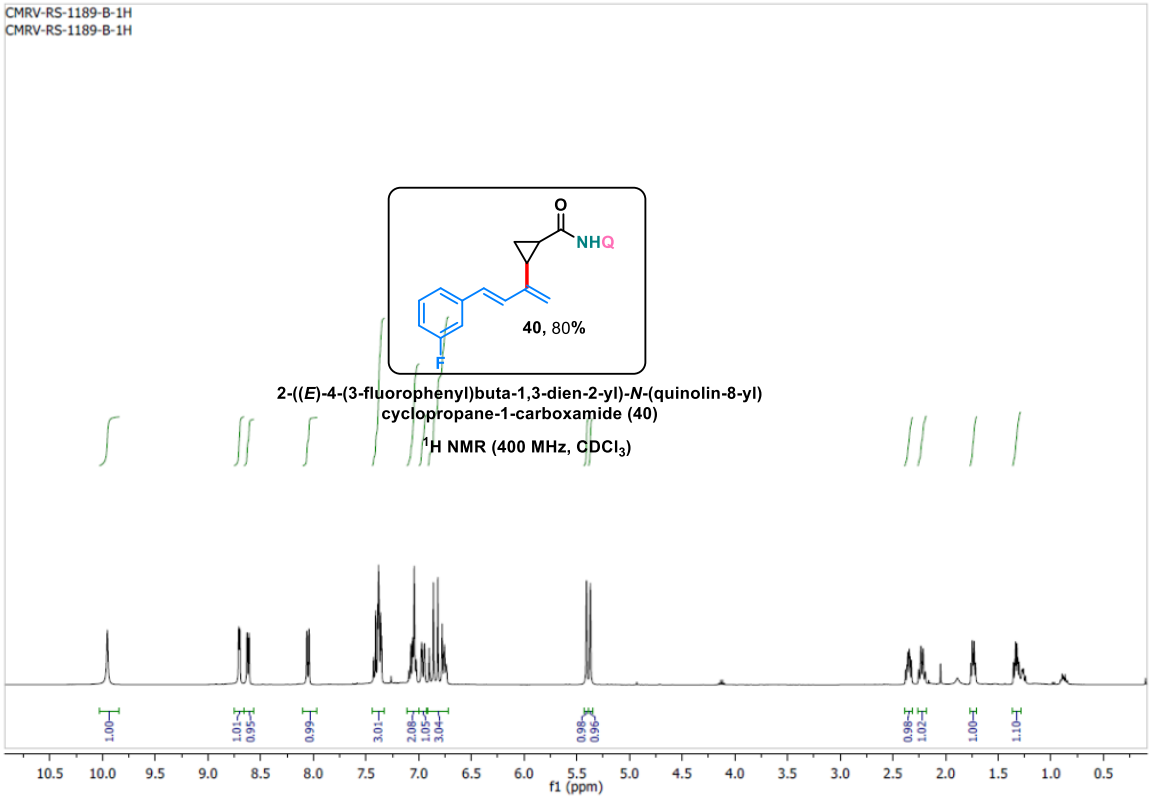


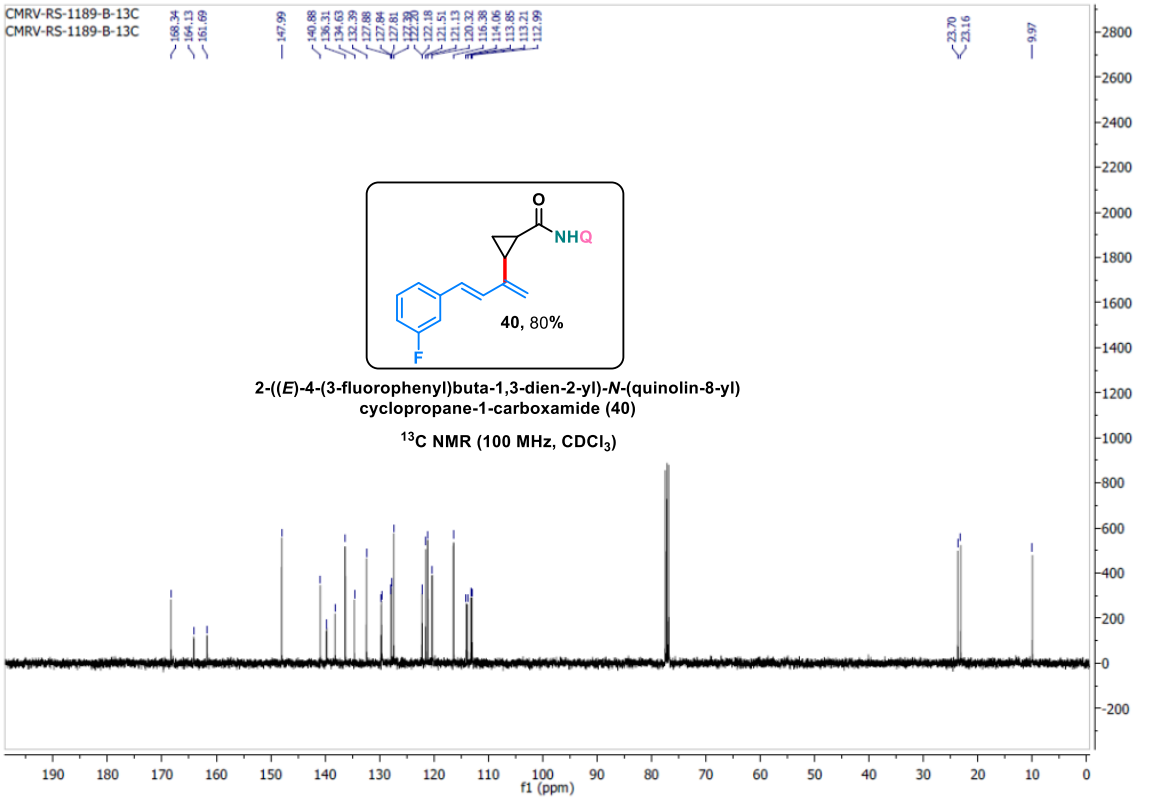
(N-(quinolin-8-yl)-2-((E)-4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl) cyclopropane-1-carboxamide (38)

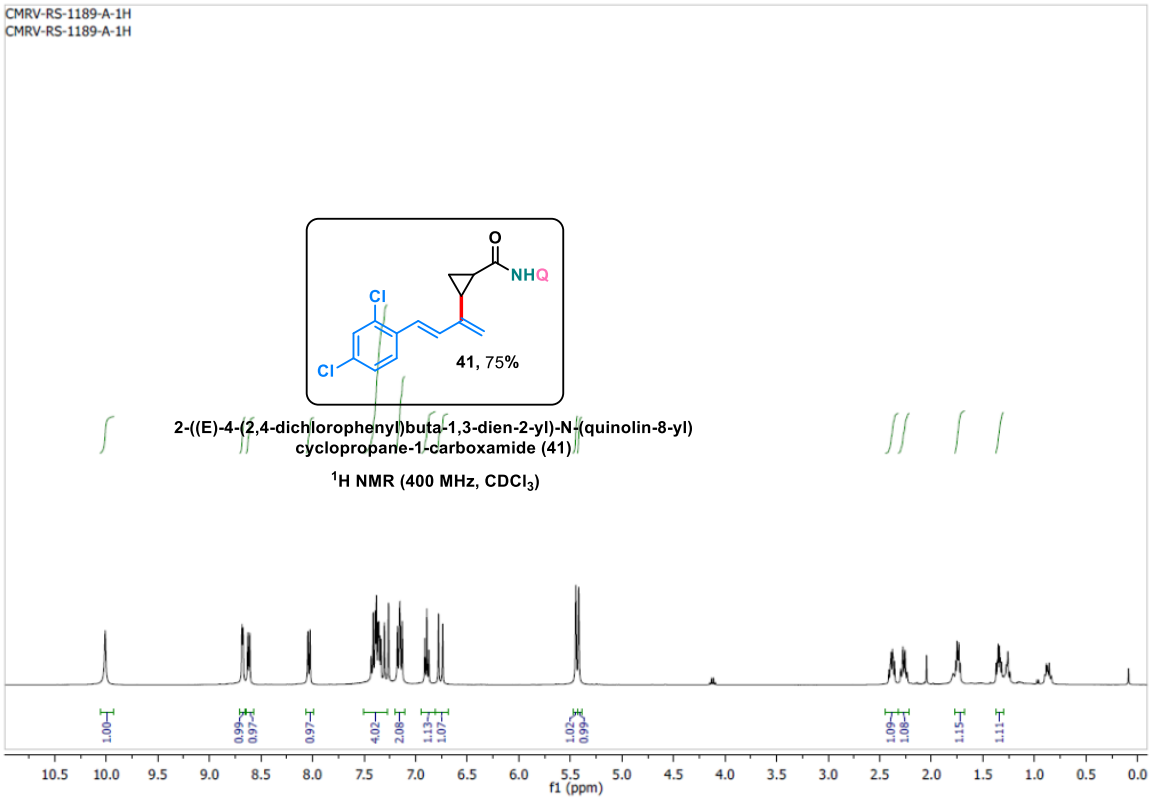
^{13}C NMR (100 MHz, $CDCl_3$)

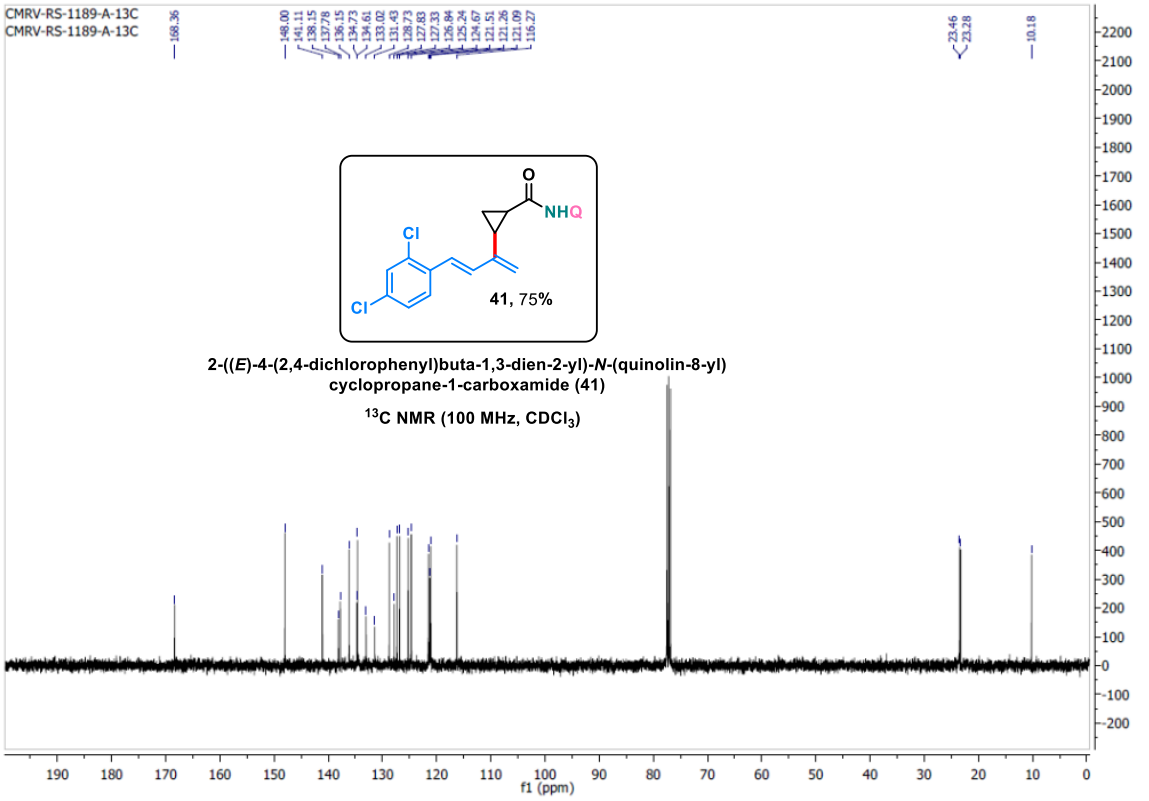

CMRV-RS-849-1H
CMRV-RS-849-1H
NHQ
NC
39, 89%
2-((E)-4-(4-cyanophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (39)
1H NMR (400 MHz, CDCl3)
f1 (ppm)

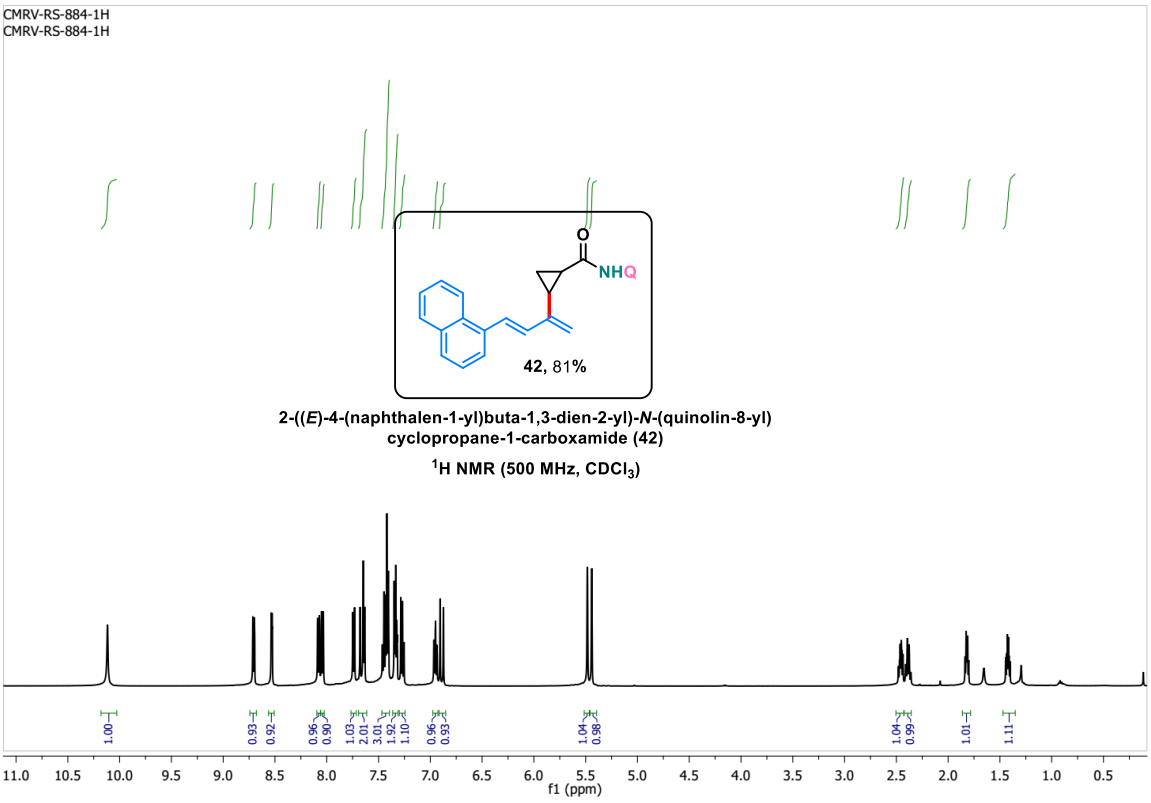

CMRV-RS-849-13C
CMRV-RS-849-13C
168.25
147.91
141.87
140.88
138.15
136.46
134.66
134.55
132.05
127.90
127.46
127.16
126.86
122.02
121.55
121.22
119.10
116.42
110.13
77.16
23.61
23.02
10.18
NHQ
NC
39, 89%
2-((E)-4-(4-cyanophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (39)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

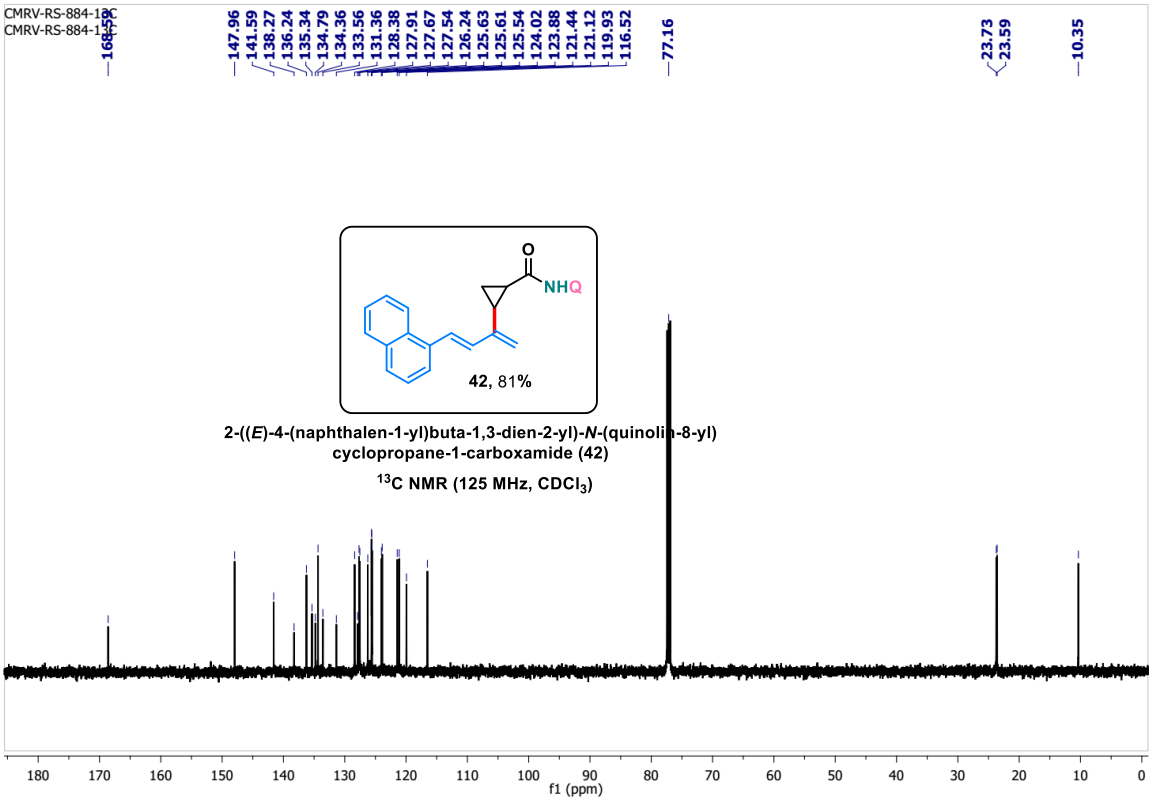

CMRV-RS-1189-B-1H
CMRV-RS-1189-B-1H
O
NHQ
F
40, 80%
2-((E)-4-(3-fluorophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (40)
1H NMR (400 MHz, CDCl3)
1.00
1.01
0.95
0.99
3.01
2.08
1.05
3.04
0.98
0.96
0.98
1.02
1.00
1.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

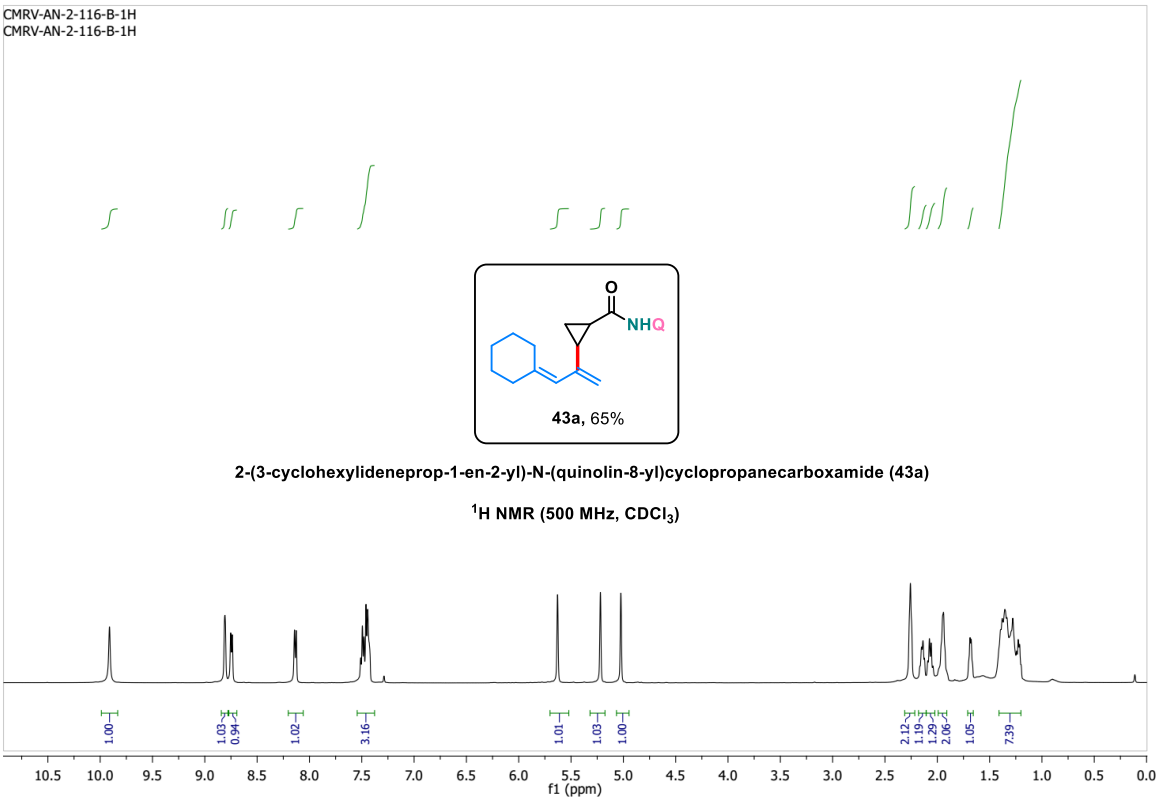

CMRV-RS-1189-B-13C
CMRV-RS-1189-B-13C
168.34
164.13
161.69
147.99
140.88
136.31
134.63
132.39
127.88
127.84
127.81
122.20
122.18
121.51
121.13
120.32
116.38
114.06
113.85
113.21
112.99
23.70
23.16
9.97
O
NHQ
F
40, 80%
2-((E)-4-(3-fluorophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (40)
13C NMR (100 MHz, CDCl3)
2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

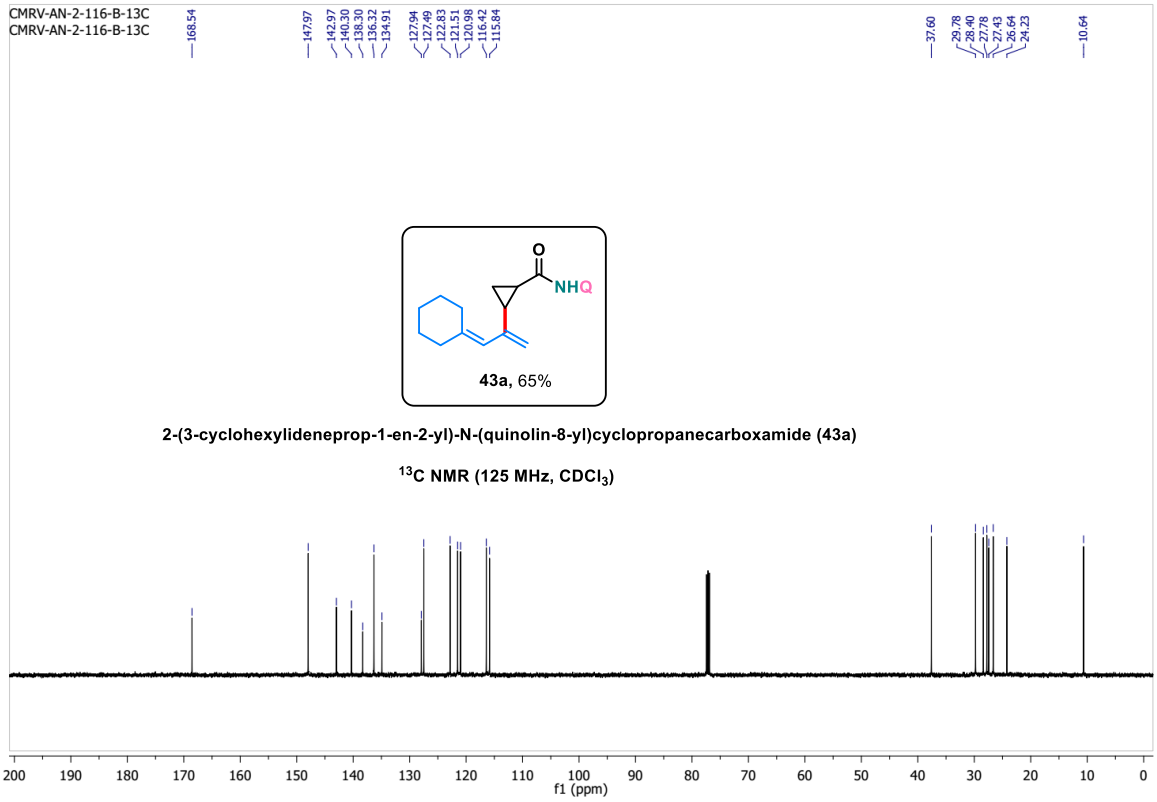

CMRV-RS-1189-A-1H
CMRV-RS-1189-A-1H
O
NHQ
Cl
Cl
41, 75%
2-((E)-4-(2,4-dichlorophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (41)
1H NMR (400 MHz, CDCl3)
1.00
0.99
0.97
0.97
4.02
2.08
1.13
1.07
1.02
0.99
1.09
1.08
1.15
1.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

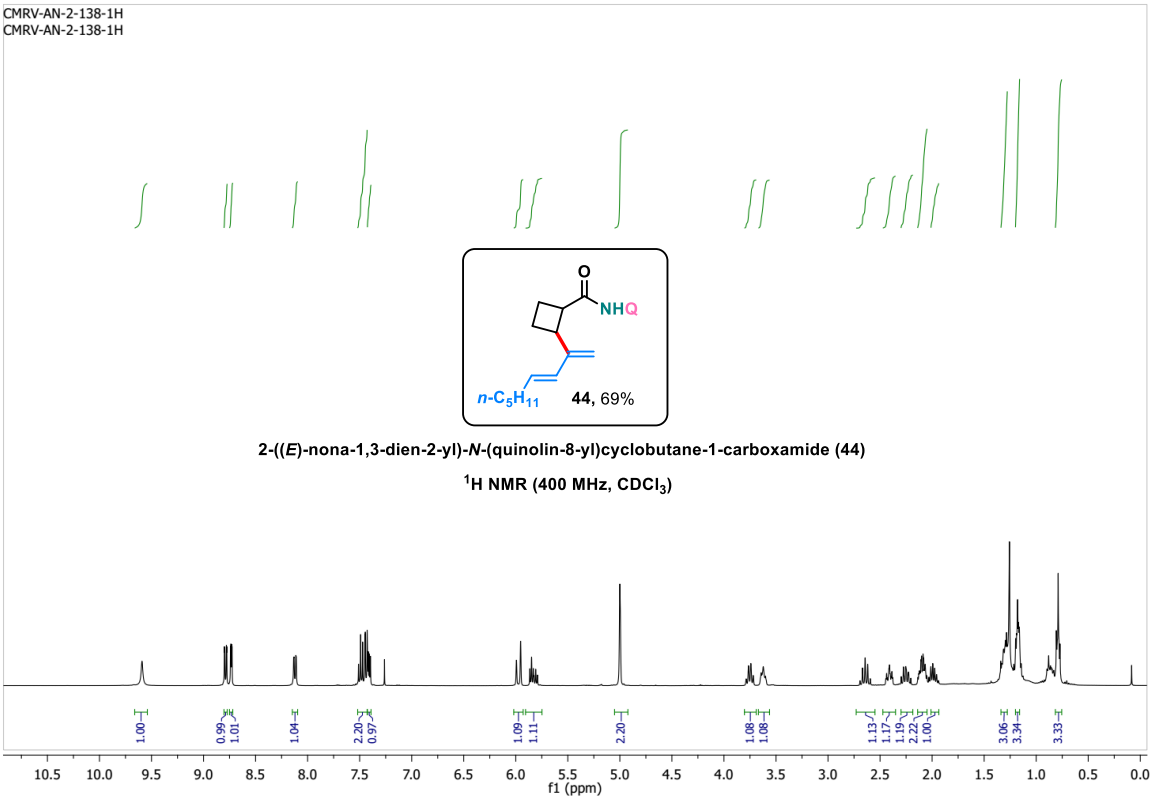

CMRV-RS-1189-A-13C
CMRV-RS-1189-A-13C
168.36
148.00
141.11
138.15
137.78
136.15
134.73
134.61
133.02
131.43
128.73
127.83
127.33
126.84
125.24
124.67
121.51
121.26
121.09
116.27
23.46
23.28
10.18
O
NHQ
Cl
Cl
41, 75%
2-((E)-4-(2,4-dichlorophenyl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (41)
13C NMR (100 MHz, CDCl3)
2200 2100 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100 -200
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CMRV-RS-884-1H
CMRV-RS-884-1H
NHQ
42, 81%
2-((E)-4-(naphthalen-1-yl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (42)
1H NMR (500 MHz, CDCl3)
1.00
0.93
0.92
0.96
0.90
1.03
2.01
3.01
1.92
1.10
0.96
0.93
1.04
0.98
1.04
0.99
1.01
1.11
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


CMRV-RS-884-13C
CMRV-RS-884-13C
168.58
147.96
141.59
138.27
136.24
135.34
134.79
134.36
133.56
131.36
128.38
127.91
127.67
127.54
126.24
125.63
125.61
125.54
124.02
123.88
121.44
121.12
119.93
116.52
77.16
23.73
23.59
10.35
NHQ
42, 81%
2-((E)-4-(naphthalen-1-yl)buta-1,3-dien-2-yl)-N-(quinolin-8-yl)
cyclopropane-1-carboxamide (42)
13C NMR (125 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

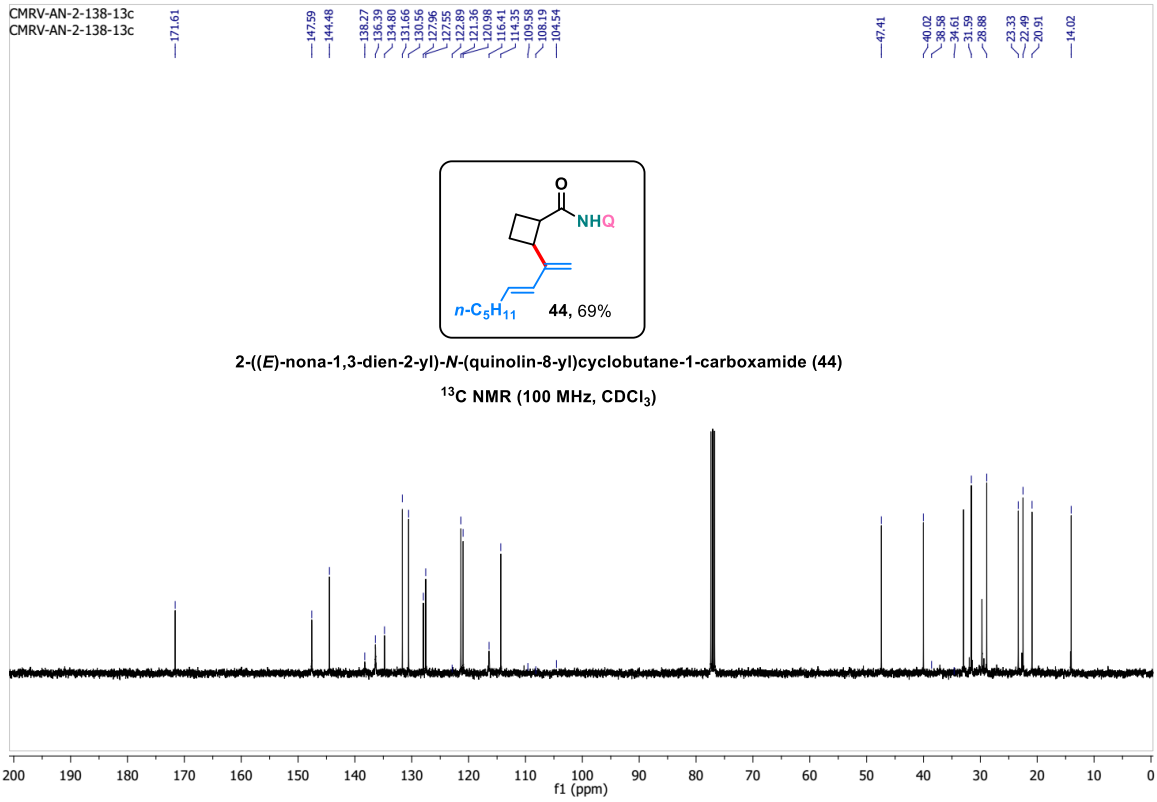

CMRV-AN-2-116-B-1H
CMRV-AN-2-116-B-1H
O
NHQ
43a, 65%
2-(3-cyclohexylideneprop-1-en-2-yl)-N-(quinolin-8-yl)cyclopropanecarboxamide (43a)
1H NMR (500 MHz, CDCl3)
1.00
1.03
0.94
1.02
3.16
1.01
1.03
1.00
2.12
1.19
1.29
2.06
1.05
7.39
f1 (ppm)


CMRV-AN-2-116-B-13C
CMRV-AN-2-116-B-13C
168.54
147.97
142.97
140.30
138.30
136.32
134.91
127.94
127.49
122.83
121.51
120.98
116.42
115.84
37.60
29.78
28.40
27.78
27.43
26.64
24.23
10.64
O
NHQ
43a, 65%
2-(3-cyclohexylideneprop-1-en-2-yl)-N-(quinolin-8-yl)cyclopropanecarboxamide (43a)
13C NMR (125 MHz, CDCl3)
f1 (ppm)



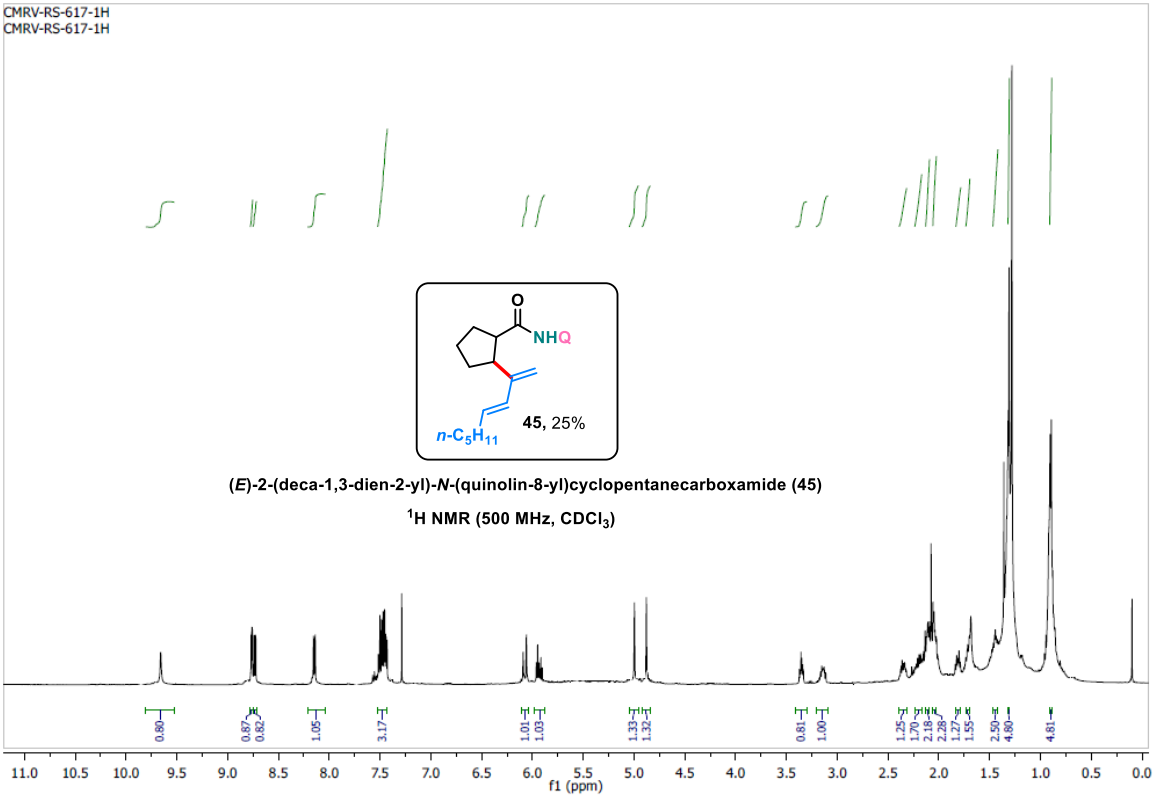
2-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclobutane-1-carboxamide (44)

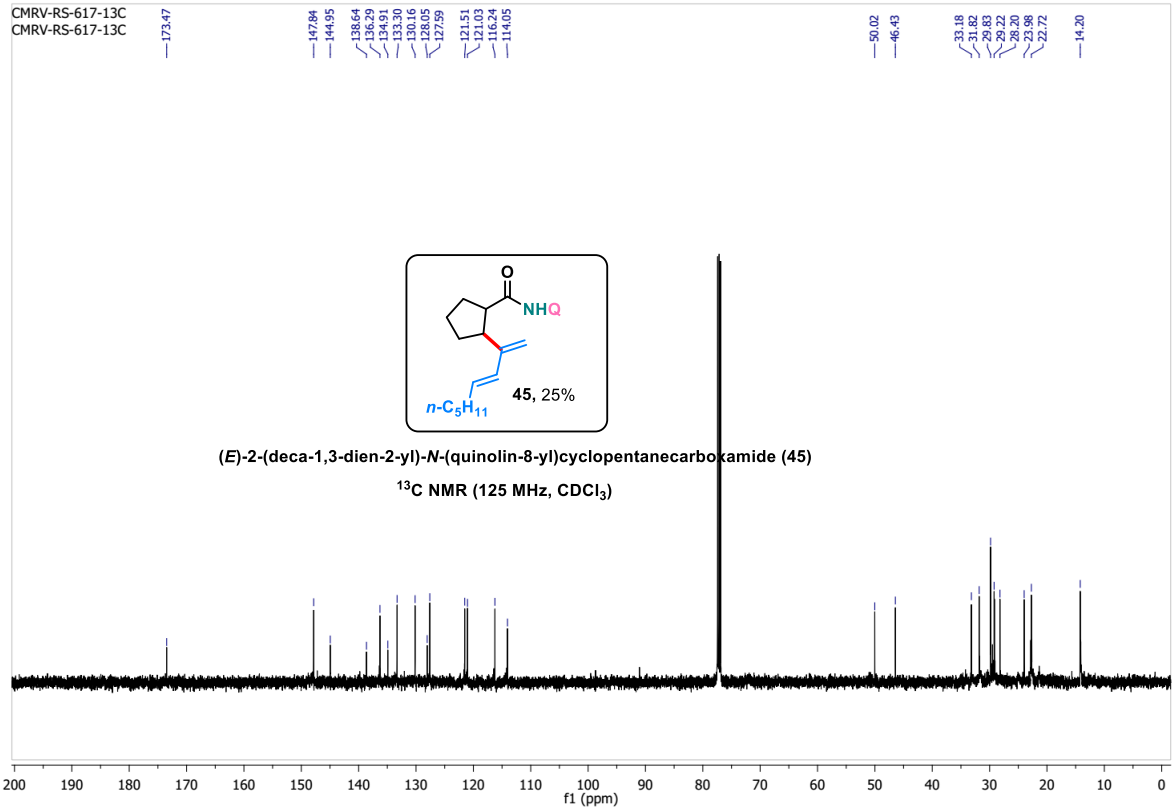
^{1}H NMR (400 MHz, $CDCl_3$)

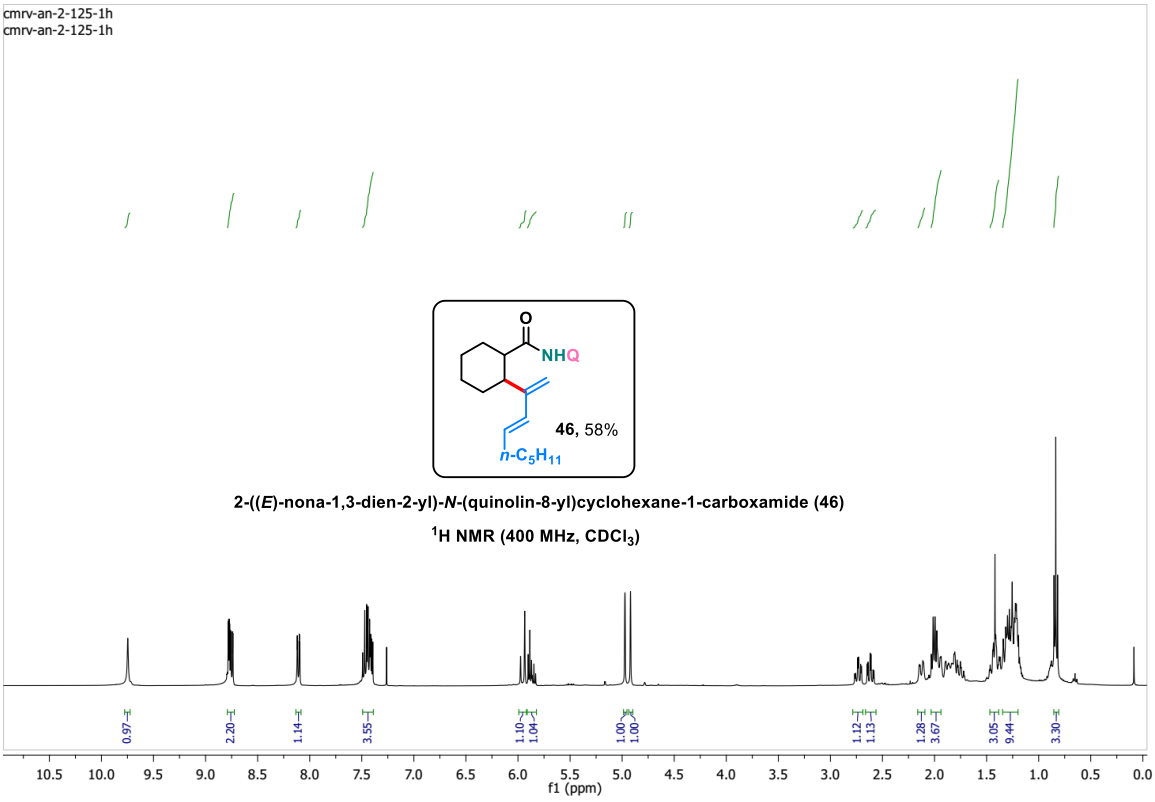


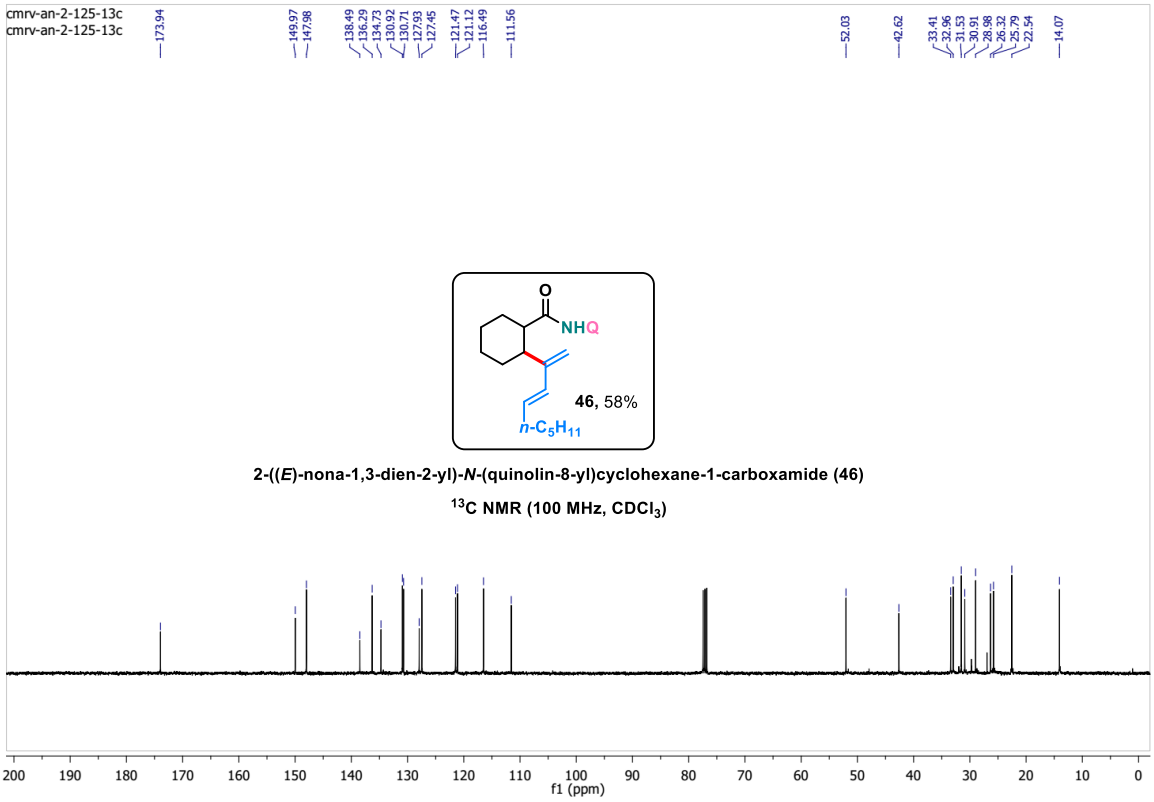
2-((*E*)-nona-1,3-dien-2-yl)-*N*-(quinolin-8-yl)cyclobutane-1-carboxamide (44)

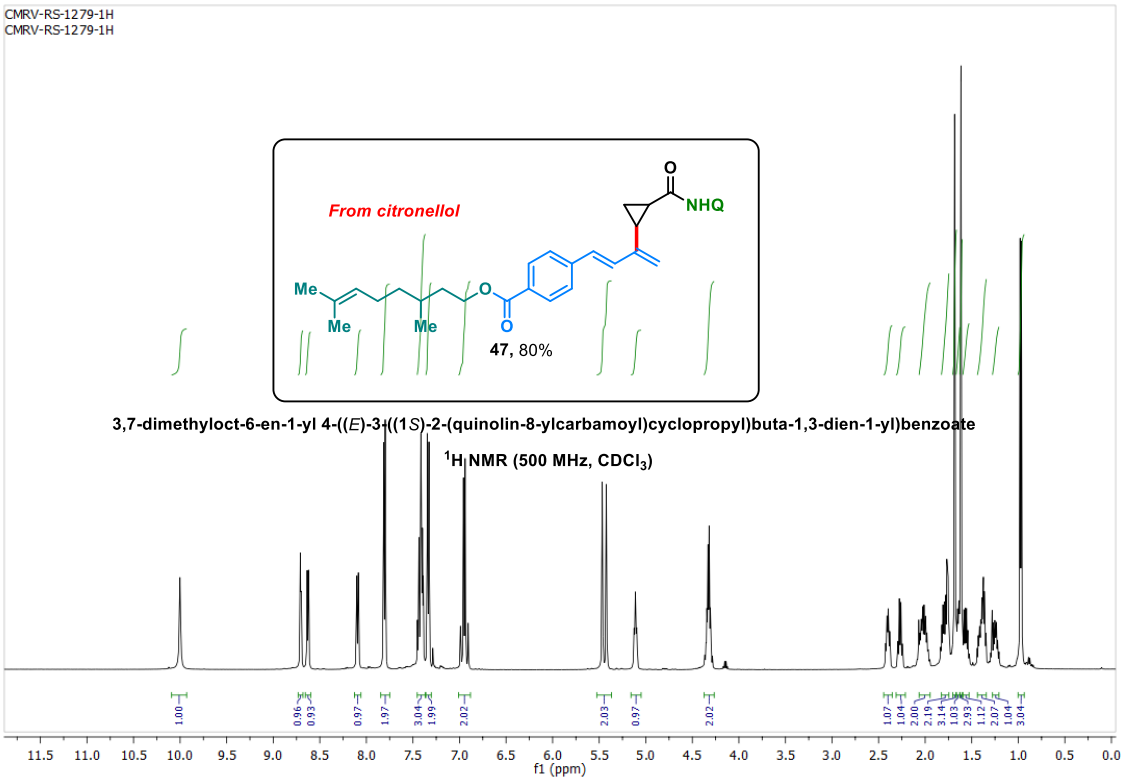
^{13}C NMR (100 MHz, $CDCl_3$)

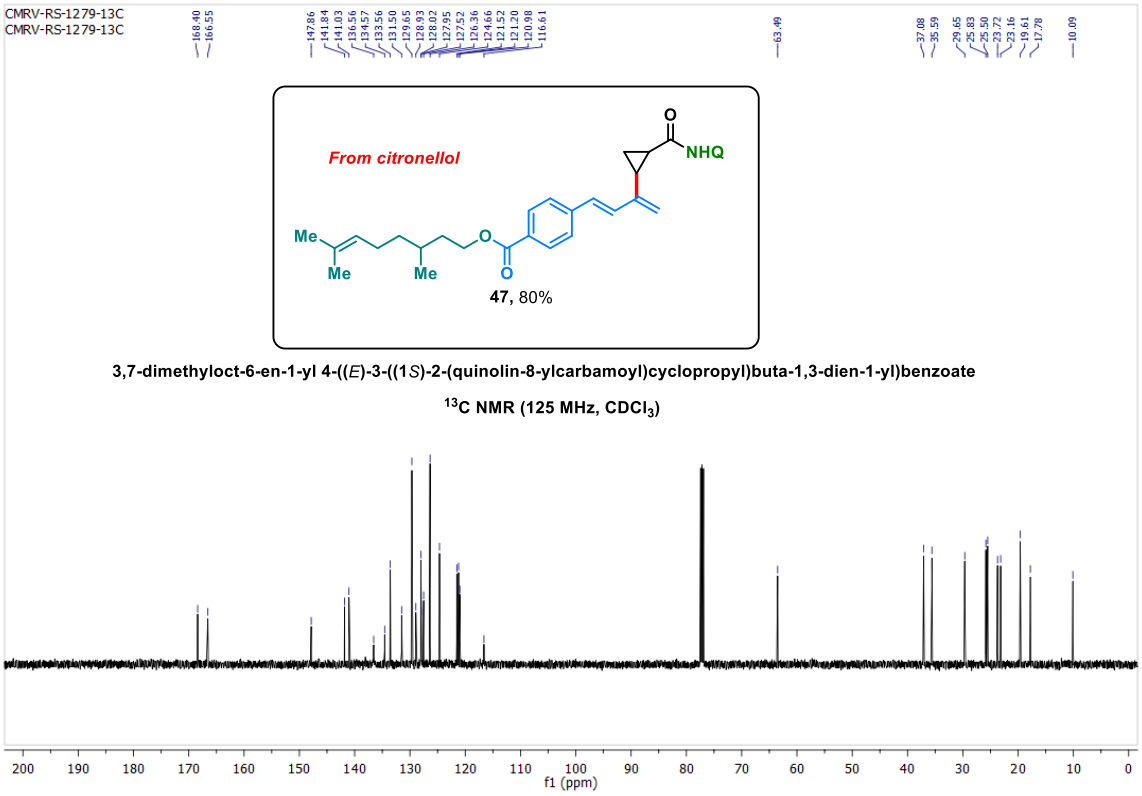

CMRV-RS-617-1H
CMRV-RS-617-1H
O
NHQ
n-C5H11
45, 25%
(E)-2-(deca-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopentanecarboxamide (45)
1H NMR (500 MHz, CDCl3)
f1 (ppm)

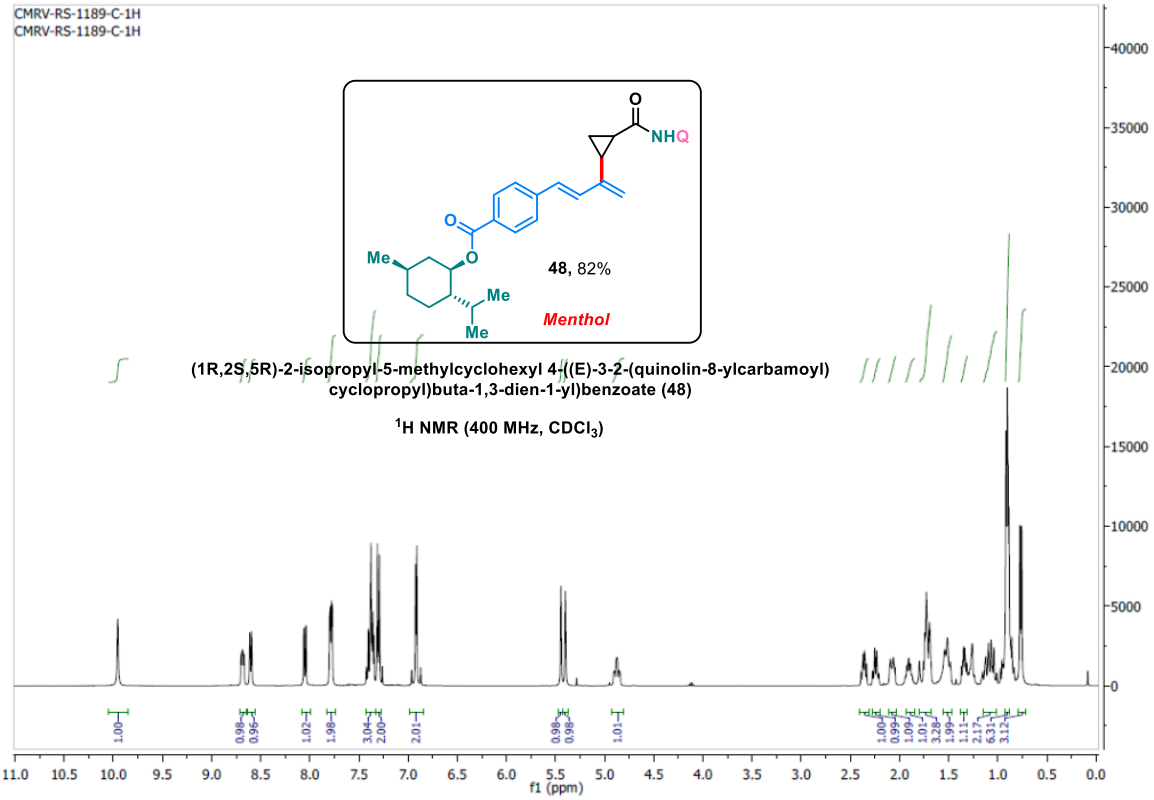

CMRV-RS-617-13C
CMRV-RS-617-13C
O
NHQ
n-C5H11
45, 25%
(E)-2-(deca-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclopentanecarboxamide (45)
13C NMR (125 MHz, CDCl3)
f1 (ppm)

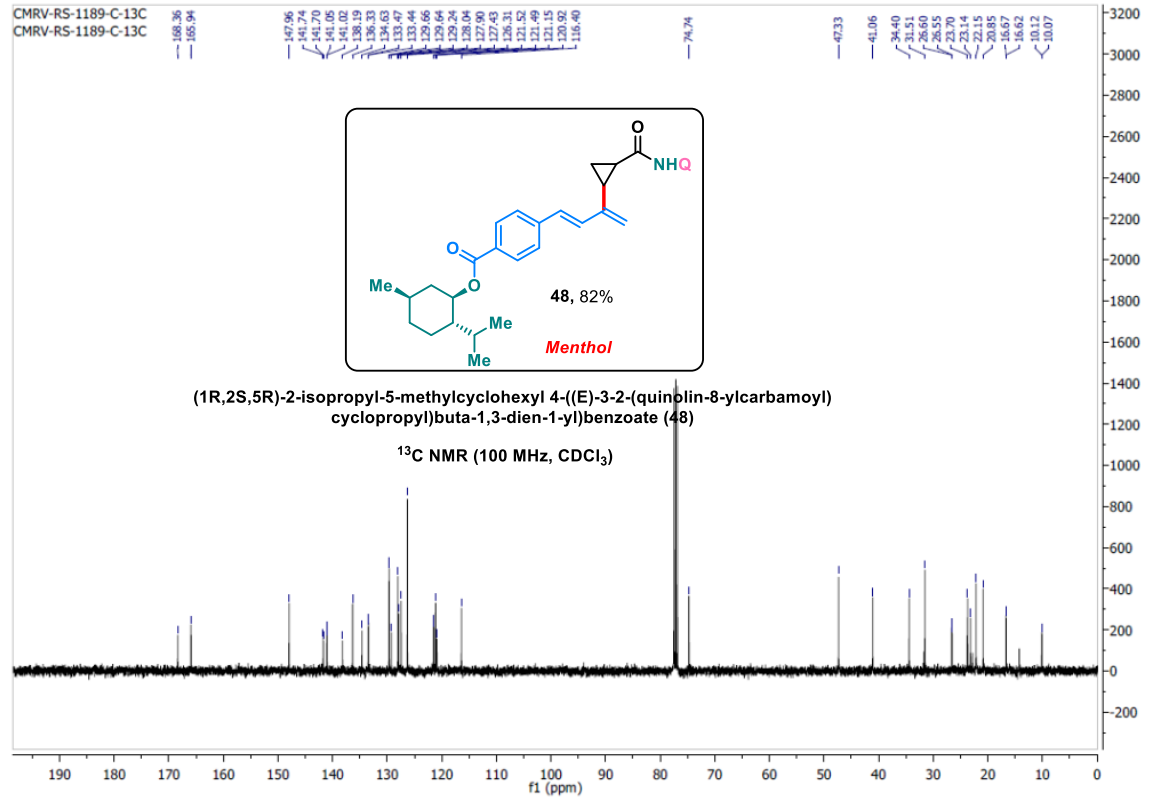

cmrv-an-2-125-1h
cmrv-an-2-125-1h
O
NHQ
46, 58%
n-C5H11
2-((E)-nona-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclohexane-1-carboxamide (46)
1H NMR (400 MHz, CDCl3)
0.97
2.20
1.14
3.55
1.10
1.04
1.00
1.00
1.12
1.13
1.28
3.67
3.05
9.44
3.30
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

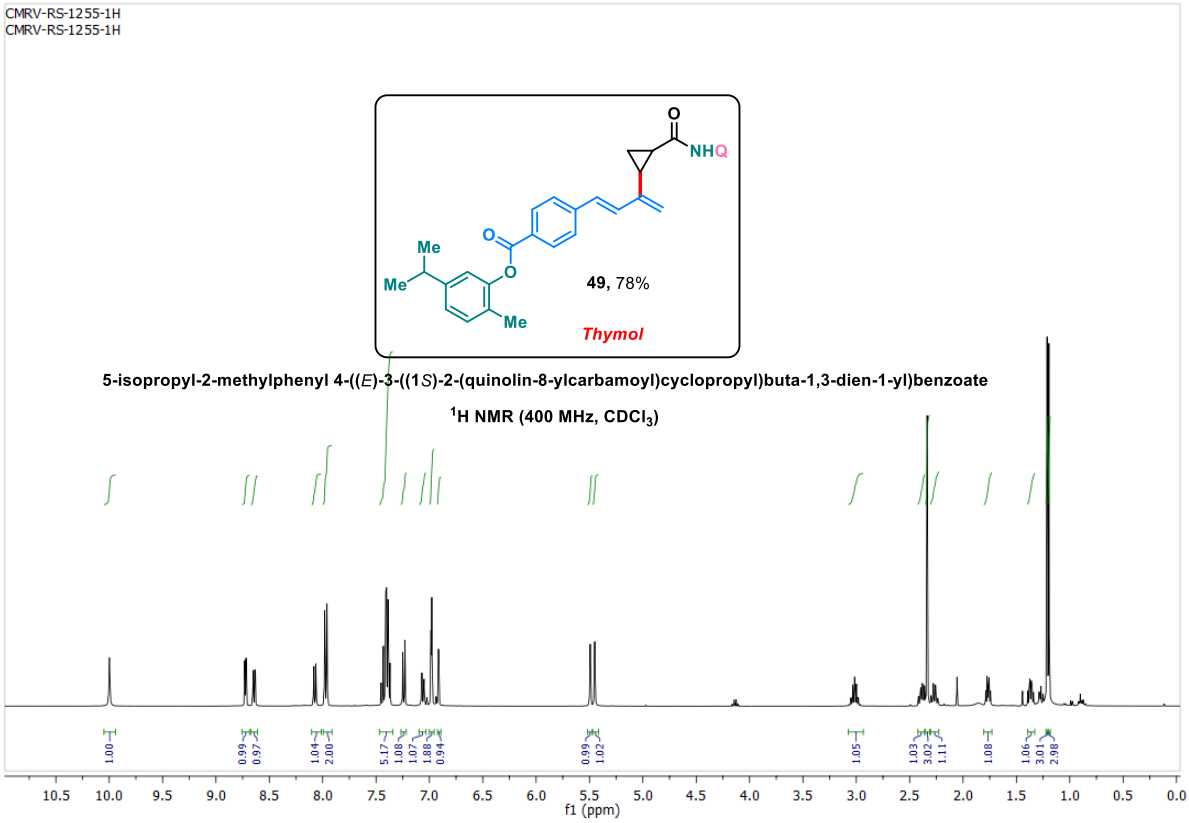

cmrv-an-2-125-13c
cmrv-an-2-125-13c
173.94
149.97
147.98
138.49
136.29
134.73
130.92
130.71
127.93
127.45
121.47
121.12
116.49
111.56
52.03
42.62
33.41
32.96
31.53
30.91
26.98
26.32
25.79
22.54
14.07
O
NHQ
46, 58%
n-C5H11
2-((E)-nona-1,3-dien-2-yl)-N-(quinolin-8-yl)cyclohexane-1-carboxamide (46)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

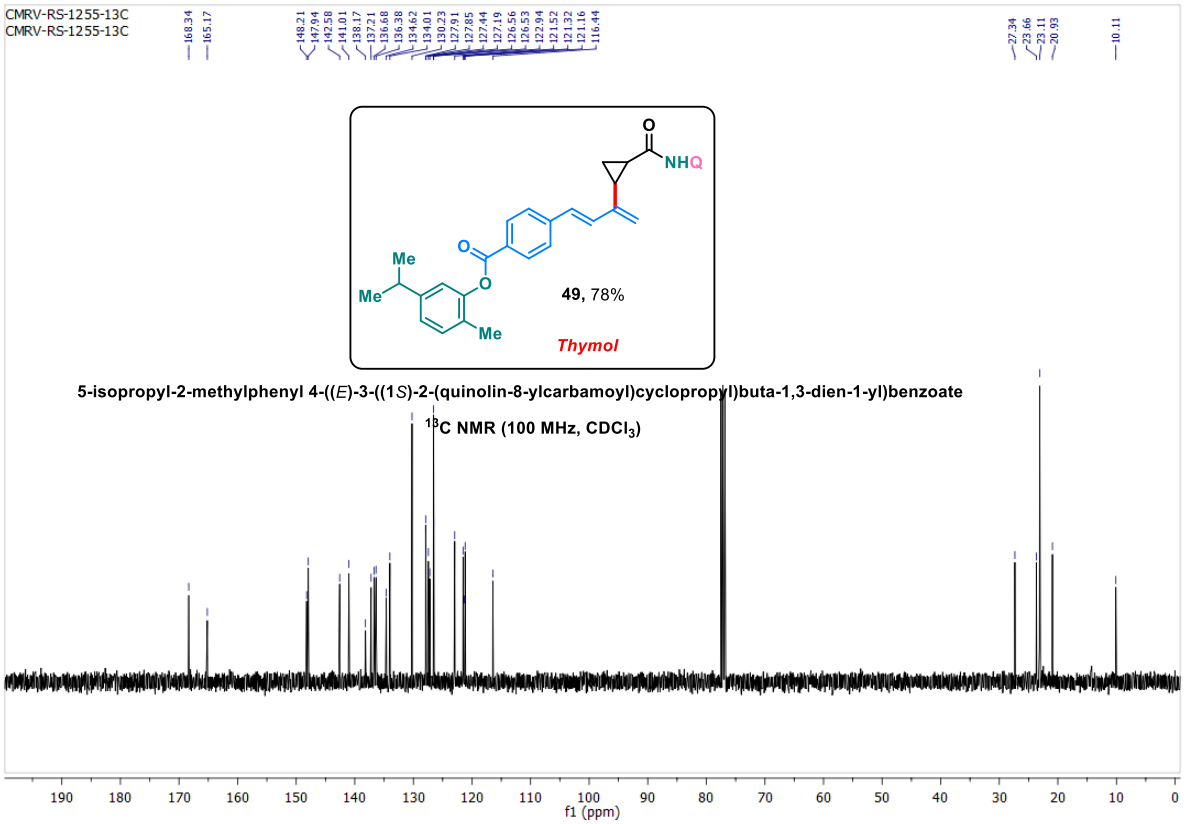

CMRV-RS-1279-1H
CMRV-RS-1279-1H
From citronellol
NHQ
Me
Me
Me
O
O
O
47, 80%
3,7-dimethyloct-6-en-1-yl 4-((E)-3-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate
^{1}H NMR (500 MHz, CDCl$_3$)
f1 (ppm)

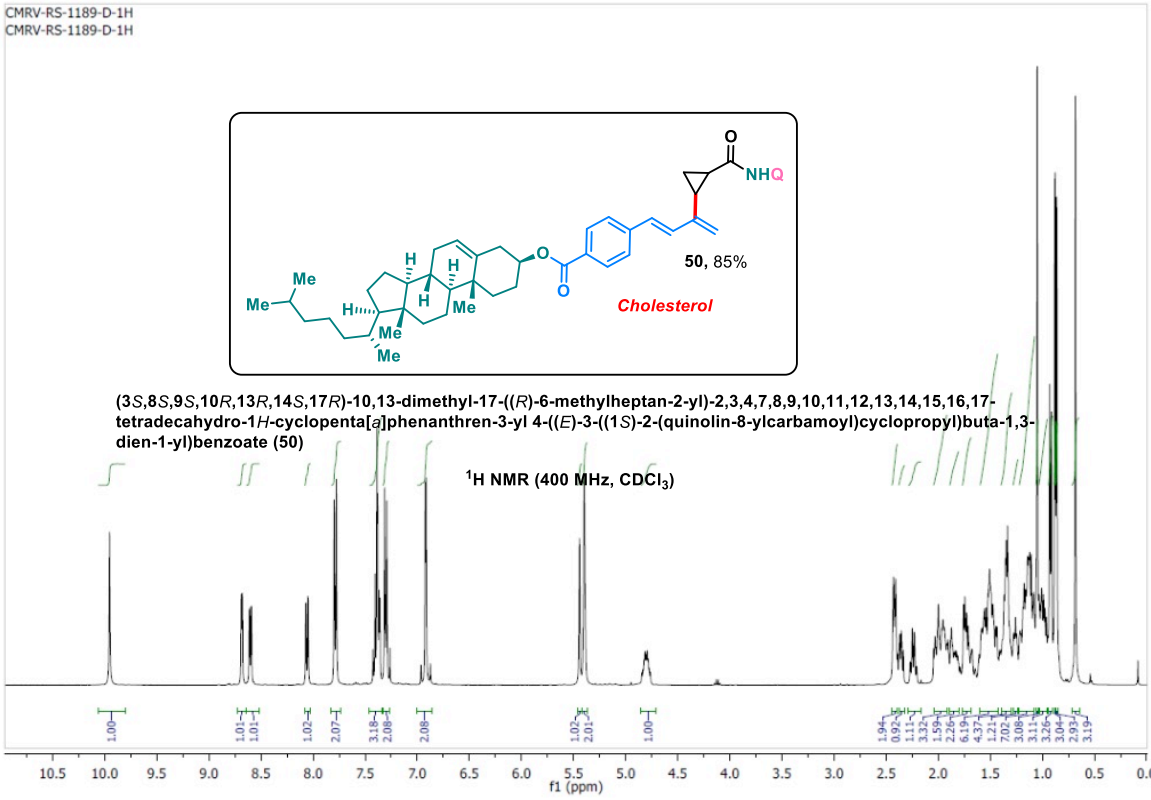

CMRV-RS-1279-13C
CMRV-RS-1279-13C
From citronellol
NHQ
Me
Me
Me
O
O
O
47, 80%
3,7-dimethyloct-6-en-1-yl 4-((E)-3-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate
^{13}C NMR (125 MHz, CDCl$_3$)
f1 (ppm)

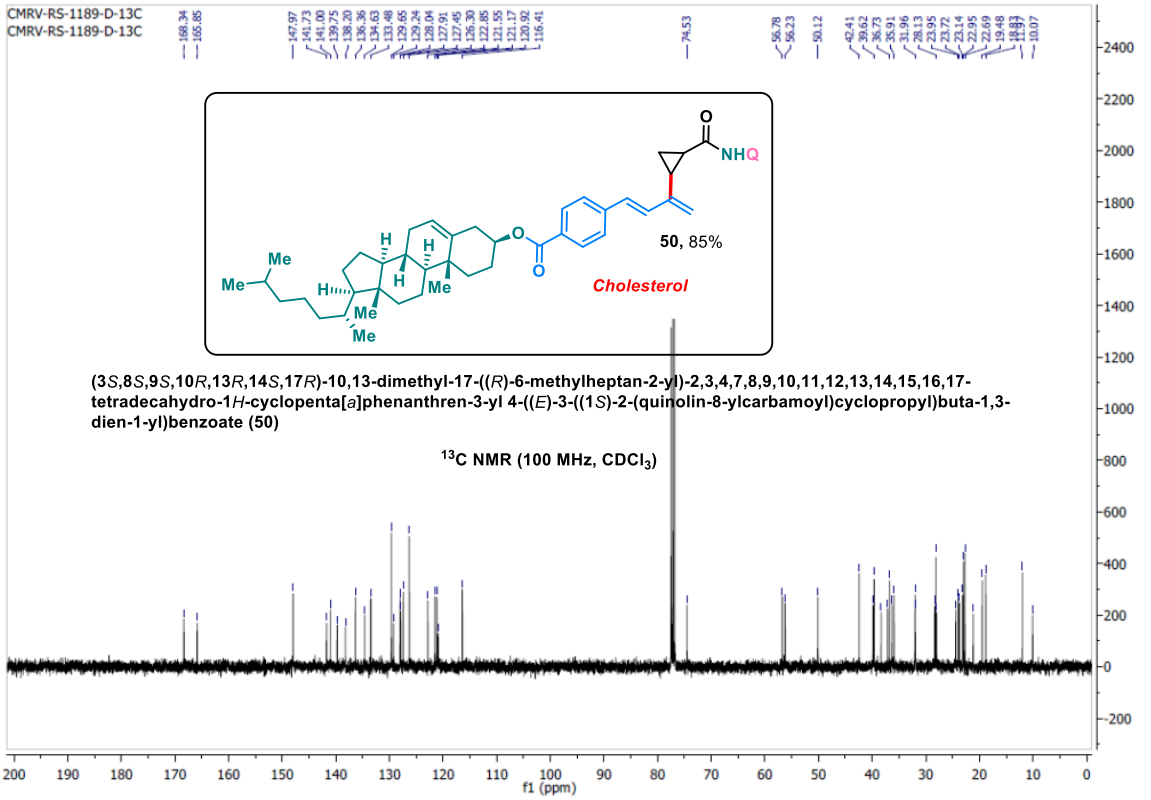

CMRV-RS-1189-C-1H
CMRV-RS-1189-C-1H
NHQ
O
Me
Me
Me
48, 82%
Menthol
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-((E)-3-2-(quinolin-8-ylcarbamoyl) cyclopropyl)buta-1,3-dien-1-yl)benzoate (48)
^{1}H NMR (400 MHz, CDCl$_3$)
f1 (ppm)

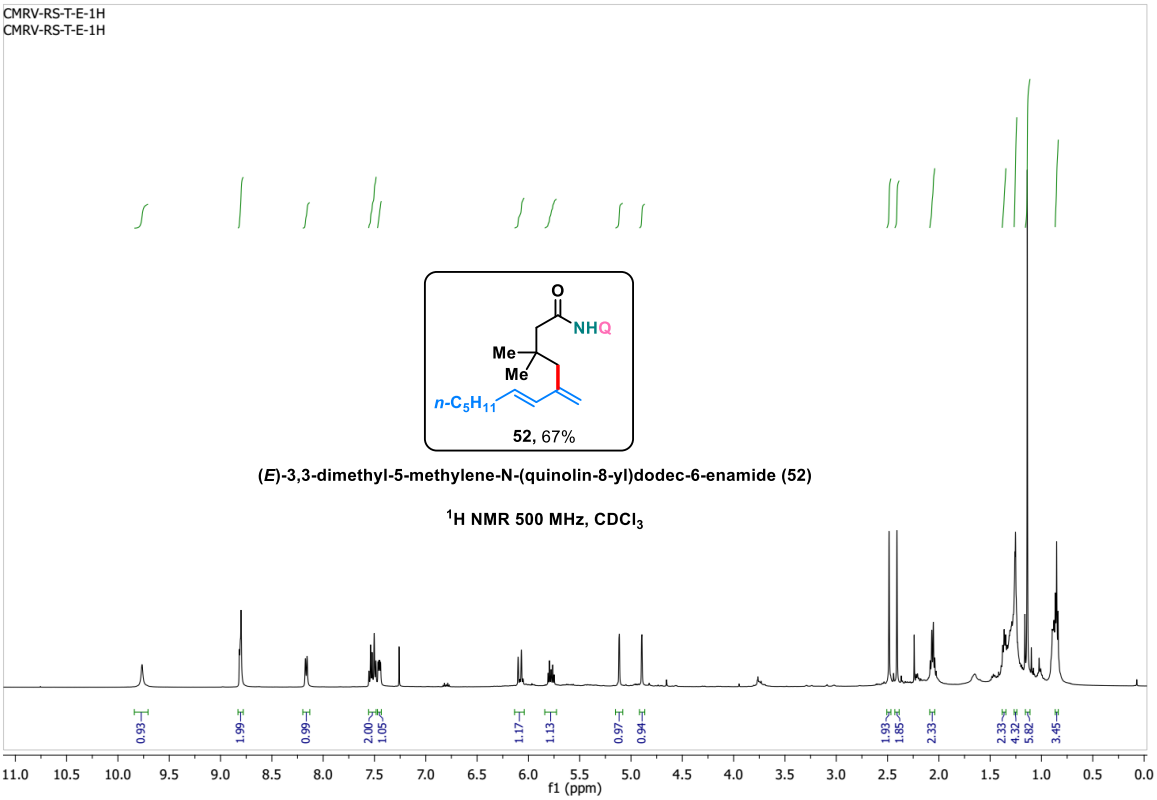

CMRV-RS-1189-C-13C
CMRV-RS-1189-C-13C
NHQ
O
Me
Me
Me
48, 82%
Menthol
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-((E)-3-2-(quinolin-8-ylcarbamoyl) cyclopropyl)buta-1,3-dien-1-yl)benzoate (48)
^{13}C NMR (100 MHz, CDCl$_3$)
f1 (ppm)

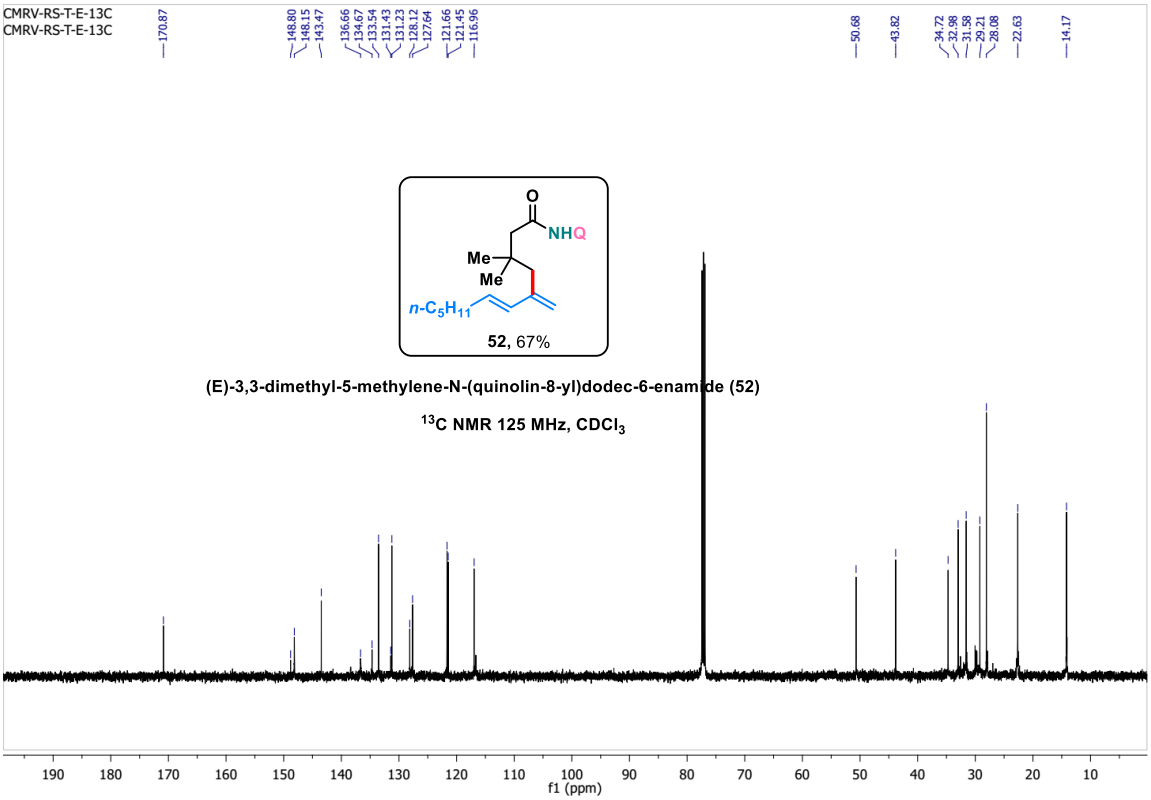

CMRV-RS-1255-1H
CMRV-RS-1255-1H
NHQ
Me
Me
Me
49, 78%
Thymol
5-isopropyl-2-methylphenyl 4-((E)-3-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate
1H NMR (400 MHz, CDCl3)
f1 (ppm)

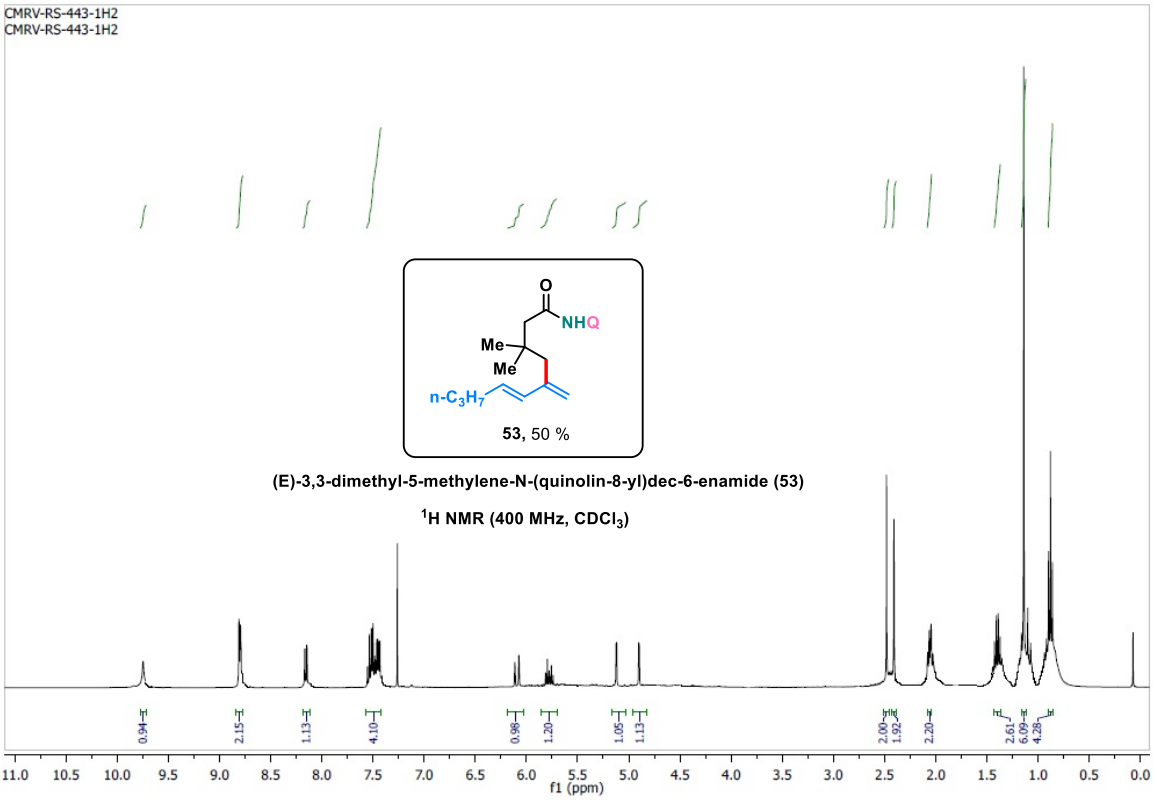

CMRV-RS-1255-13C
CMRV-RS-1255-13C
NHQ
Me
Me
Me
49, 78%
Thymol
5-isopropyl-2-methylphenyl 4-((E)-3-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate
13C NMR (100 MHz, CDCl3)
f1 (ppm)

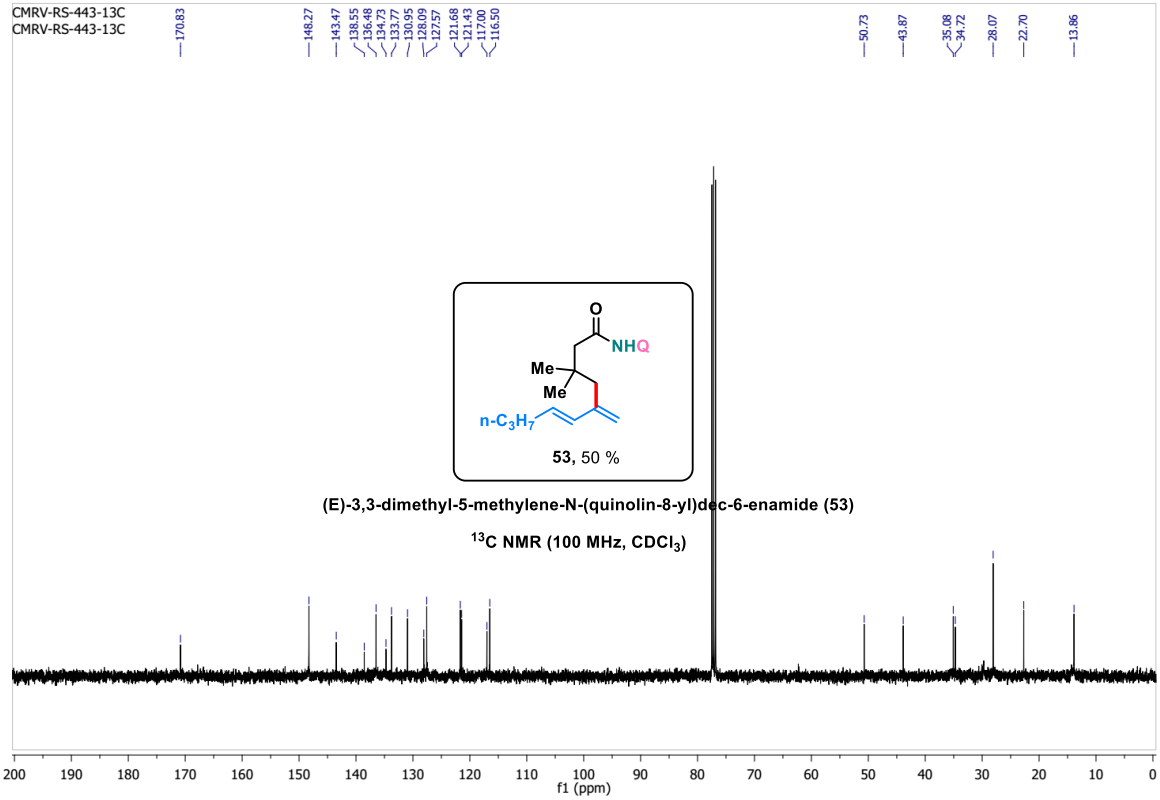

CMRV-RS-1189-D-1H
CMRV-RS-1189-D-1H
50, 85%
Cholesterol
(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-((E)-3-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate (50)
1H NMR (400 MHz, CDCl3)
f1 (ppm)

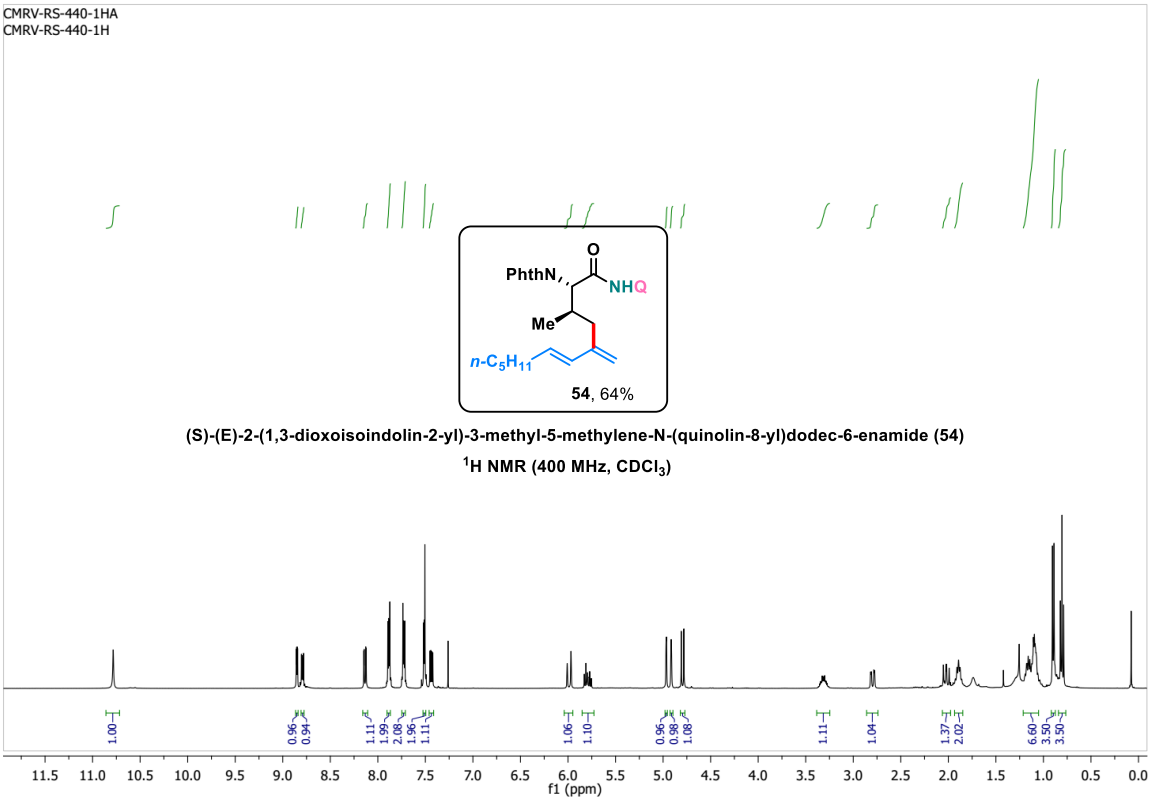

CMRV-RS-1189-D-13C
CMRV-RS-1189-D-13C
50, 85%
Cholesterol
(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-((E)-3-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)buta-1,3-dien-1-yl)benzoate (50)
13C NMR (100 MHz, CDCl3)
f1 (ppm)


CMRV-RS-T-E-1H
CMRV-RS-T-E-1H
O
NHQ
Me
Me
n-C5H11
52, 67%
(E)-3,3-dimethyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide (52)
1H NMR 500 MHz, CDCl3
0.93
1.99
0.99
2.00
1.05
1.17
1.13
0.97
0.94
1.93
1.85
2.33
2.33
4.32
5.82
3.45
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-T-E-13C
CMRV-RS-T-E-13C
170.87
148.80
148.15
143.47
136.66
134.67
133.54
131.43
131.23
128.12
127.64
121.66
121.45
116.96
50.68
43.82
34.72
32.98
31.58
29.21
28.08
22.63
14.17
O
NHQ
Me
Me
n-C5H11
52, 67%
(E)-3,3-dimethyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide (52)
13C NMR 125 MHz, CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

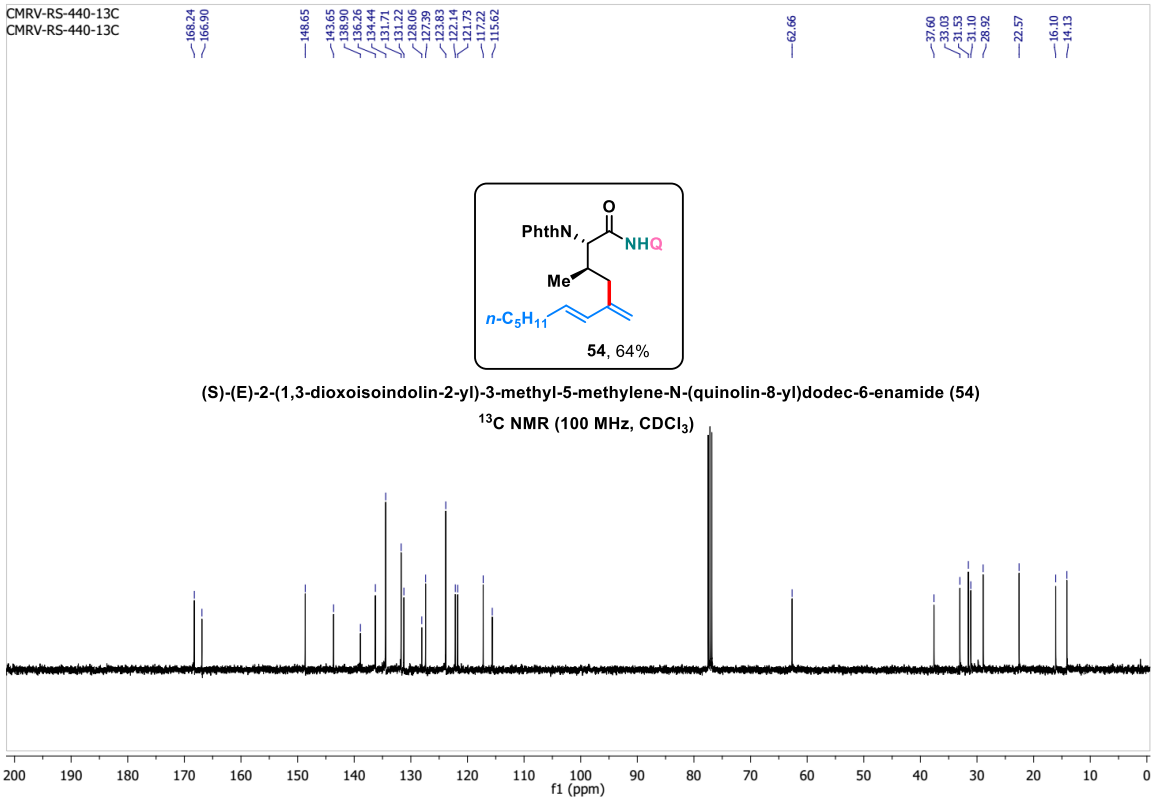

CMRV-RS-443-1H2
CMRV-RS-443-1H2
O
NHQ
Me
Me
n-C3H7
53, 50 %
(E)-3,3-dimethyl-5-methylene-N-(quinolin-8-yl)dec-6-enamide (53)
1H NMR (400 MHz, CDCl3)
0.94
2.15
1.13
4.10
0.98
1.20
1.05
1.13
2.00
1.92
2.20
2.61
6.09
4.28
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CMRV-RS-443-13C
CMRV-RS-443-13C
170.83
148.27
143.47
138.55
136.48
134.73
133.77
130.95
128.09
127.57
121.68
121.43
117.00
116.50
50.73
43.87
35.08
34.72
28.07
22.70
13.86
O
NHQ
Me
Me
n-C3H7
53, 50 %
(E)-3,3-dimethyl-5-methylene-N-(quinolin-8-yl)dec-6-enamide (53)
13C NMR (100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



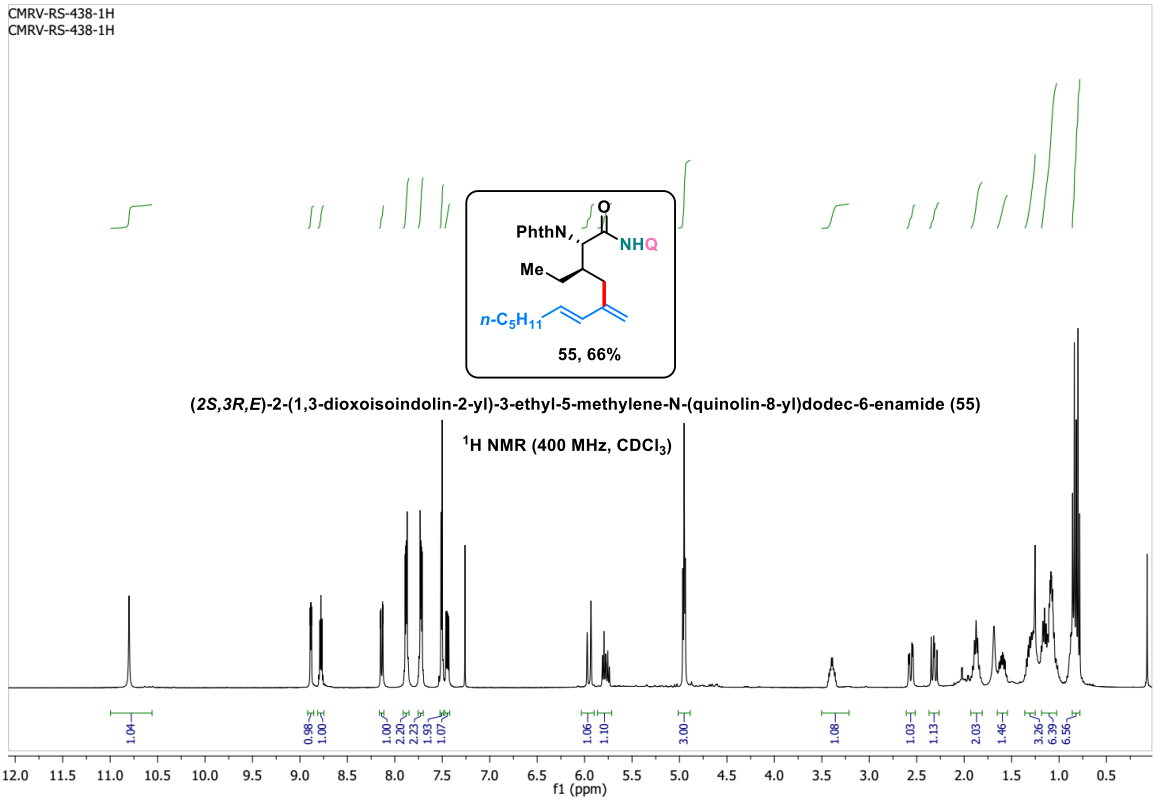
(S)-(E)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide (54)

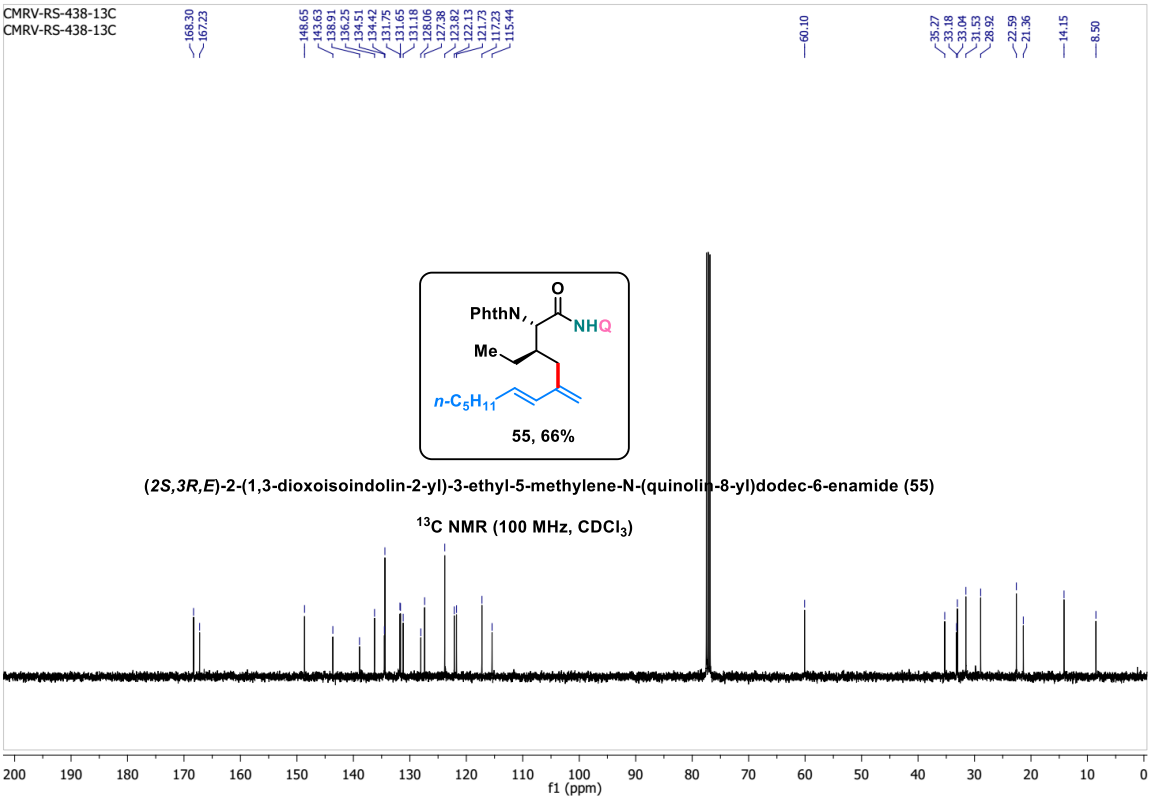
^{1}H NMR (400 MHz, $CDCl_3$)

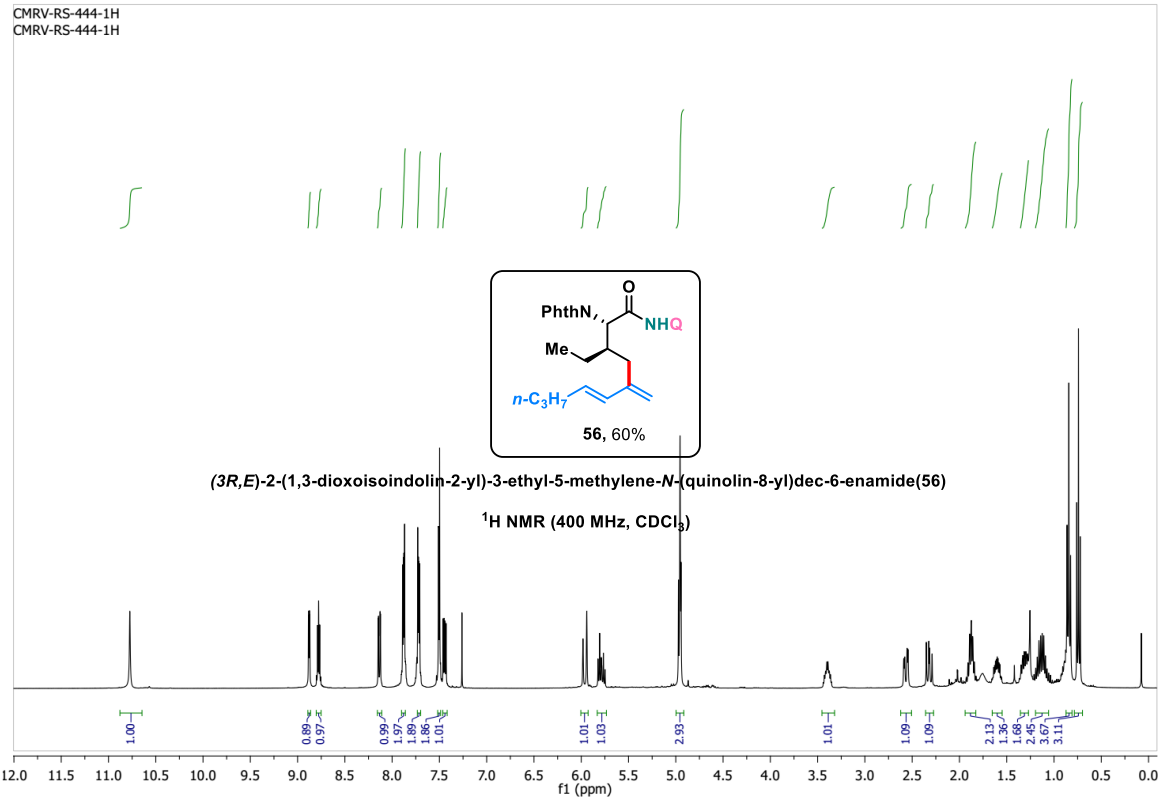


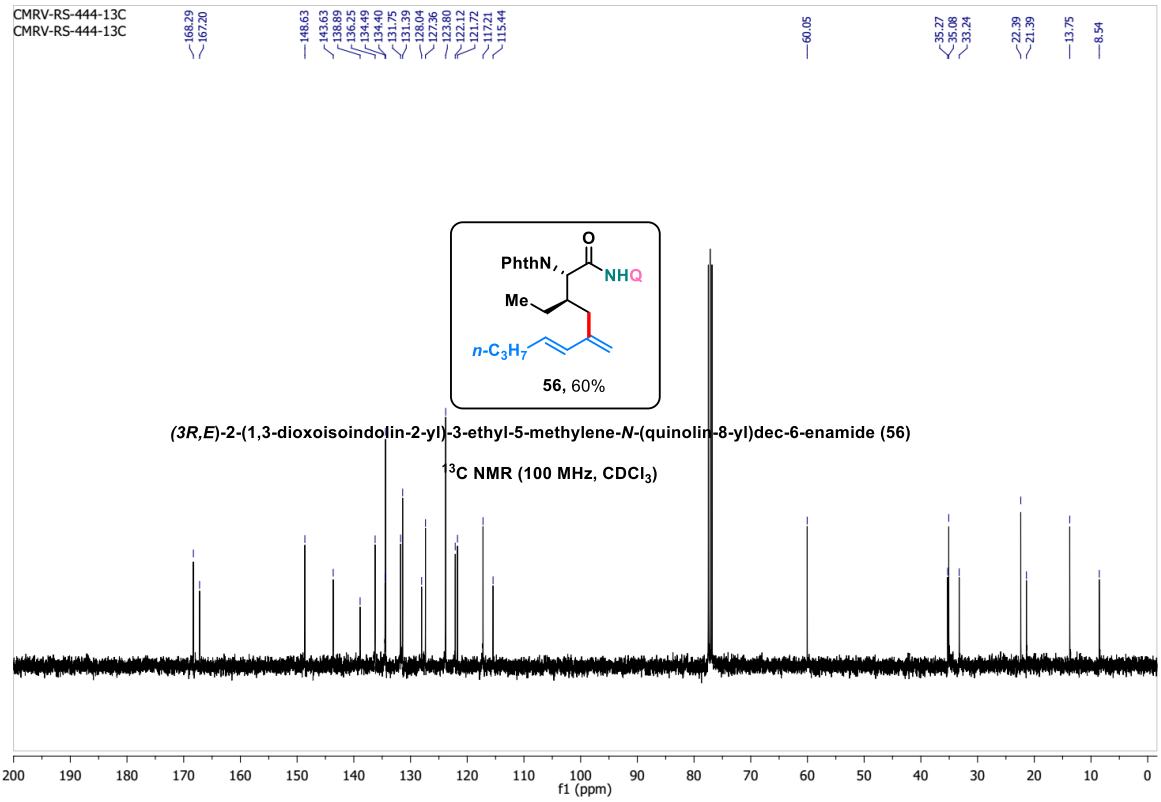
(S)-(E)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide (54)

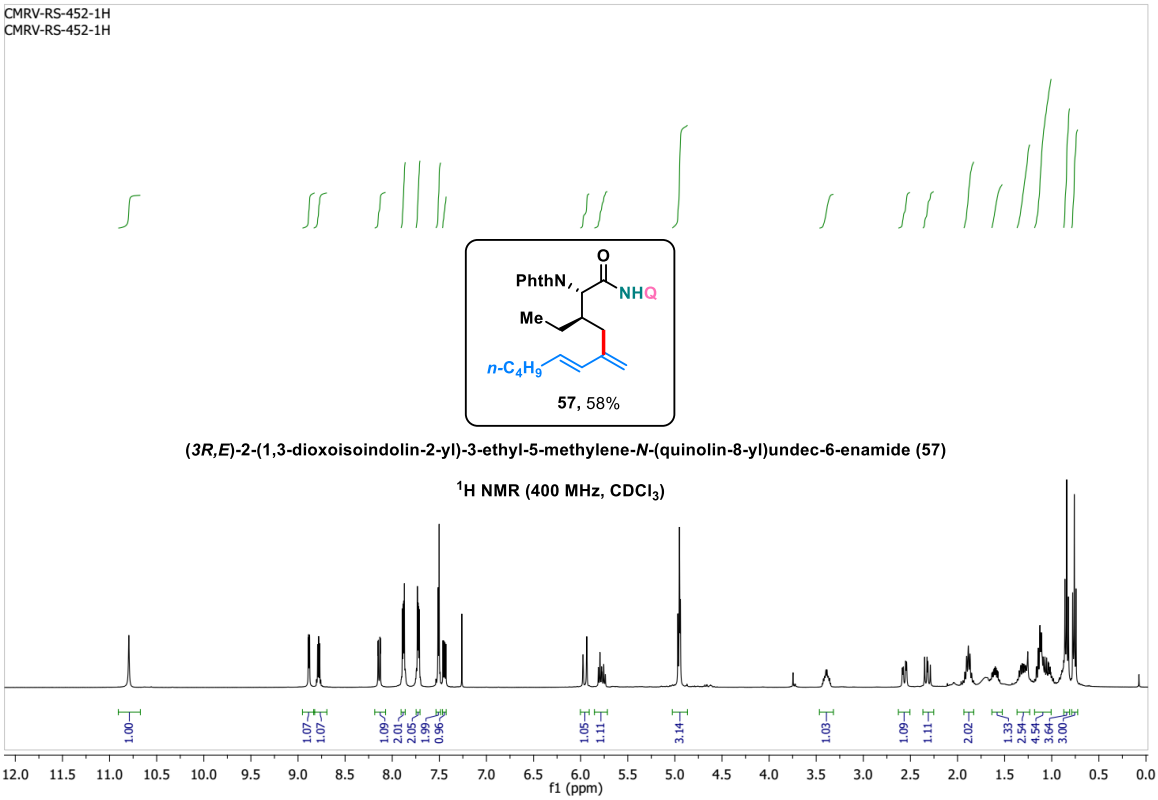
^{13}C NMR (100 MHz, $CDCl_3$)

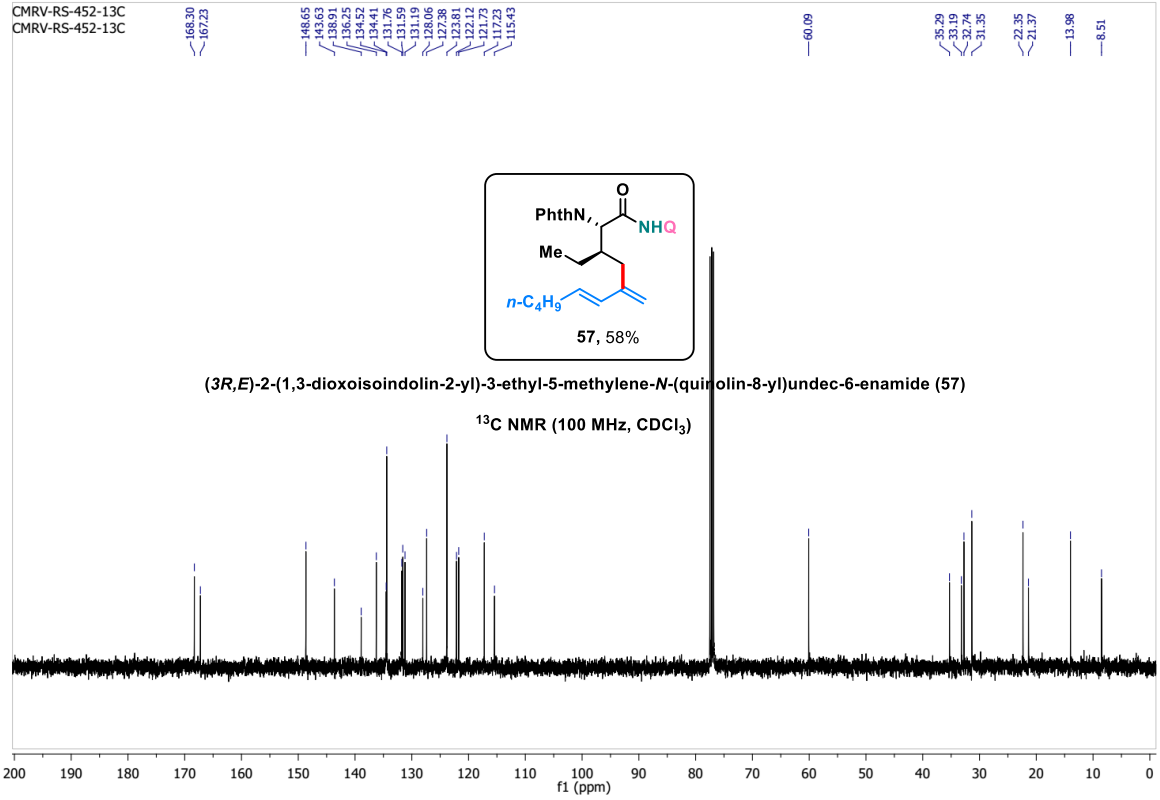

CMRV-RS-438-1H
CMRV-RS-438-1H
PhthN
O
NHQ
Me
n-C5H11
55, 66%
(2S,3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide (55)
1H NMR (400 MHz, CDCl3)
f1 (ppm)

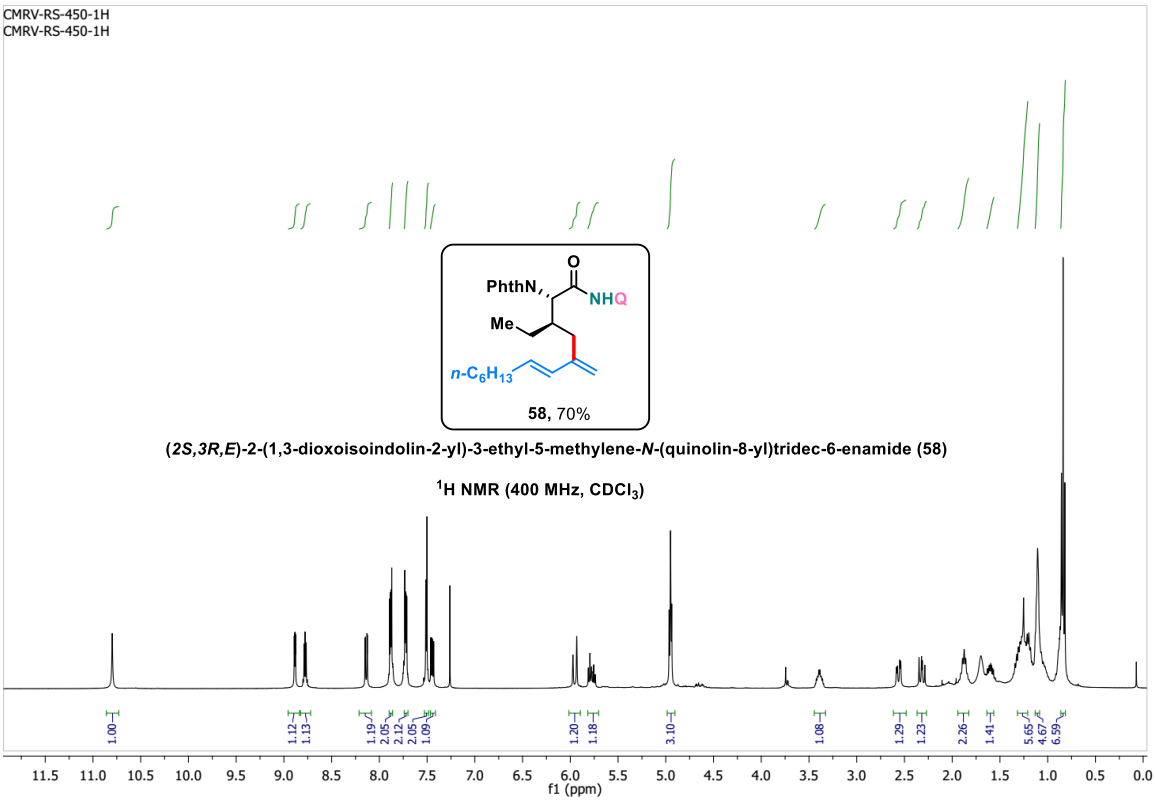

CMRV-RS-438-13C
CMRV-RS-438-13C
PhthN
O
NHQ
Me
n-C5H11
55, 66%
(2S,3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide (55)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

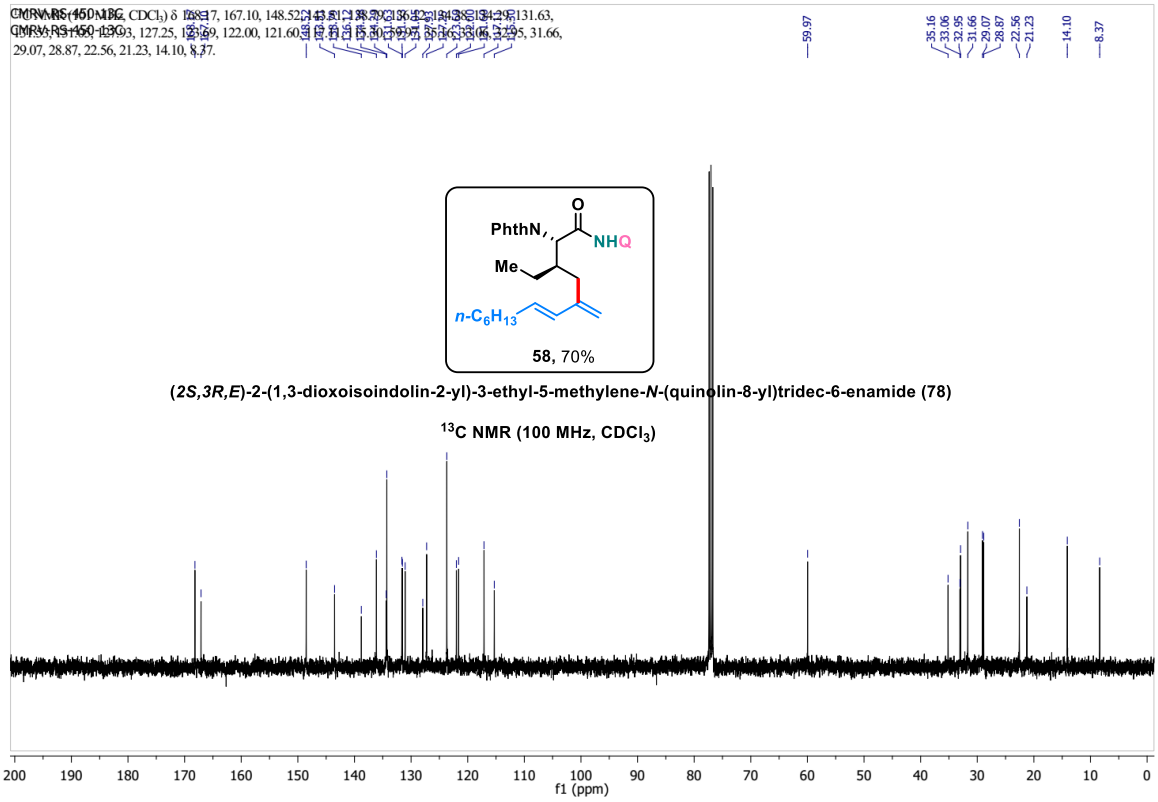

CMRV-RS-444-1H
CMRV-RS-444-1H
PhthN
NHQ
Me
n-C3H7
56, 60%
(3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)dec-6-enamide(56)
1H NMR (400 MHz, CDCl3)
f1 (ppm)

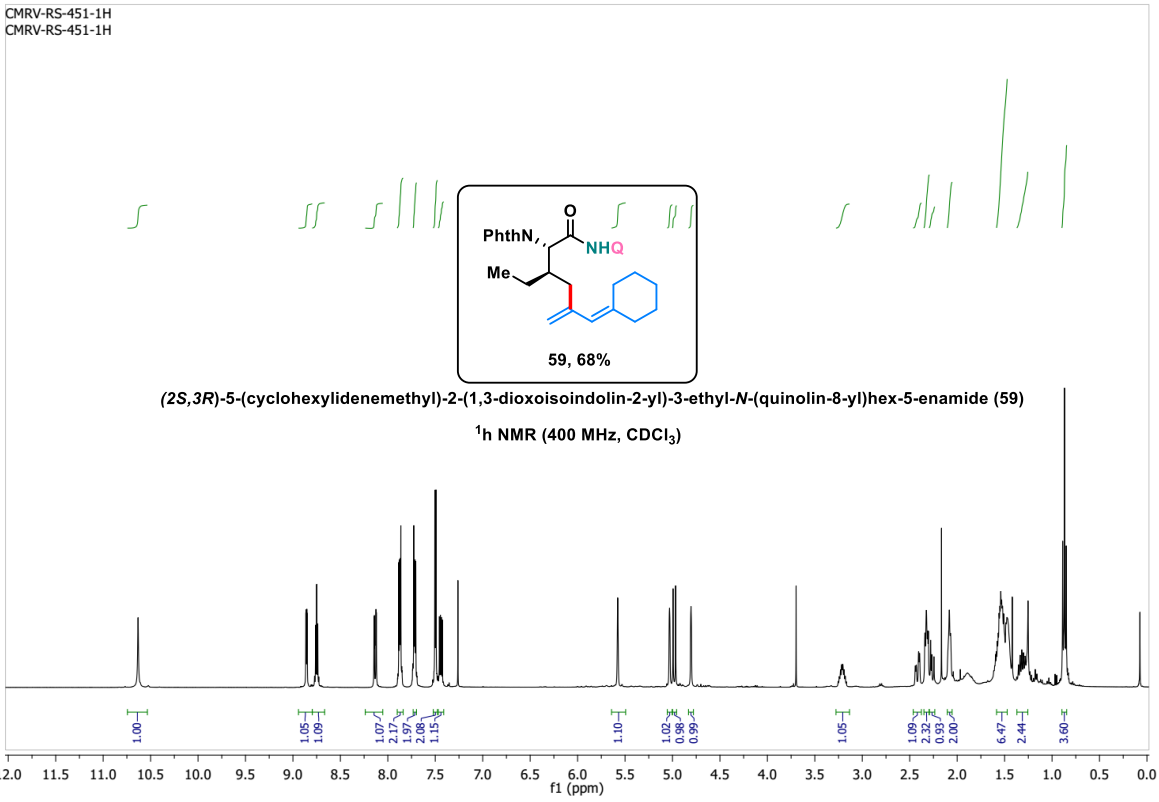

CMRV-RS-444-13C
CMRV-RS-444-13C
PhthN
NHQ
Me
n-C3H7
56, 60%
(3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)dec-6-enamide (56)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

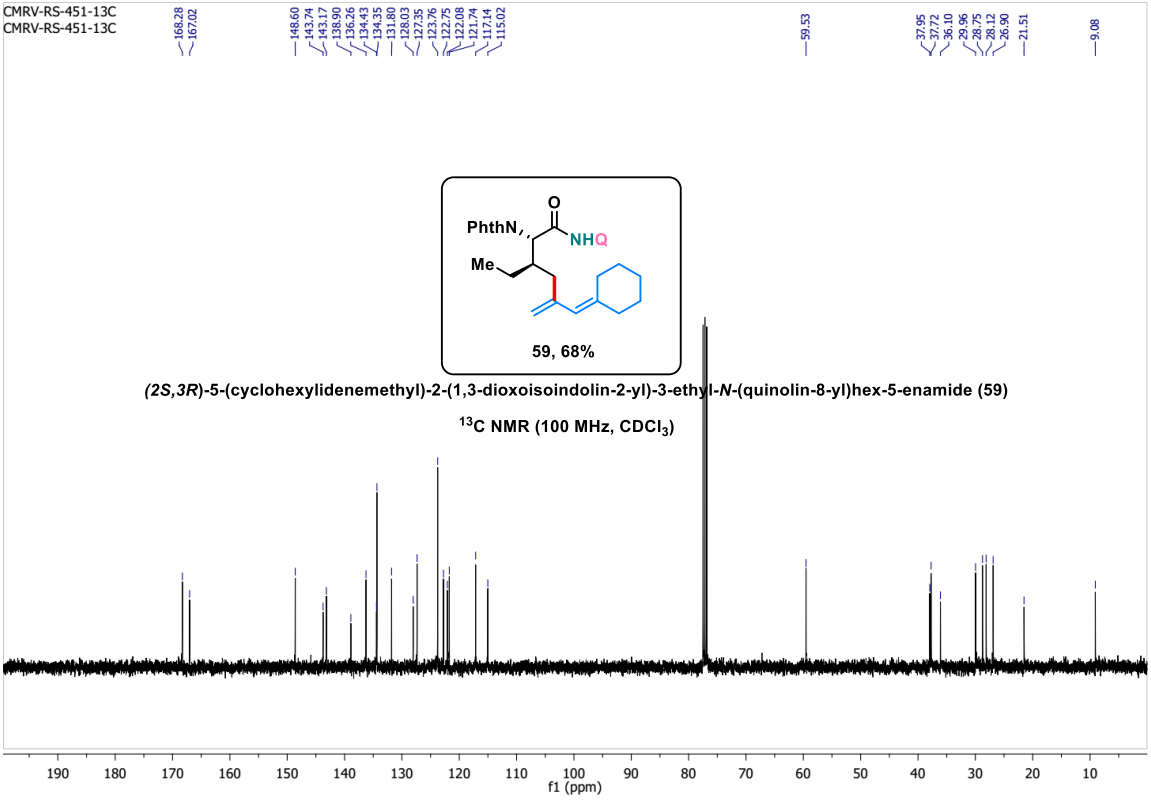

CMRV-RS-452-1H
CMRV-RS-452-1H
PhthN
O
NHQ
Me
n-C4H9
57, 58%
(3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)undec-6-enamide (57)
1H NMR (400 MHz, CDCl3)
f1 (ppm)

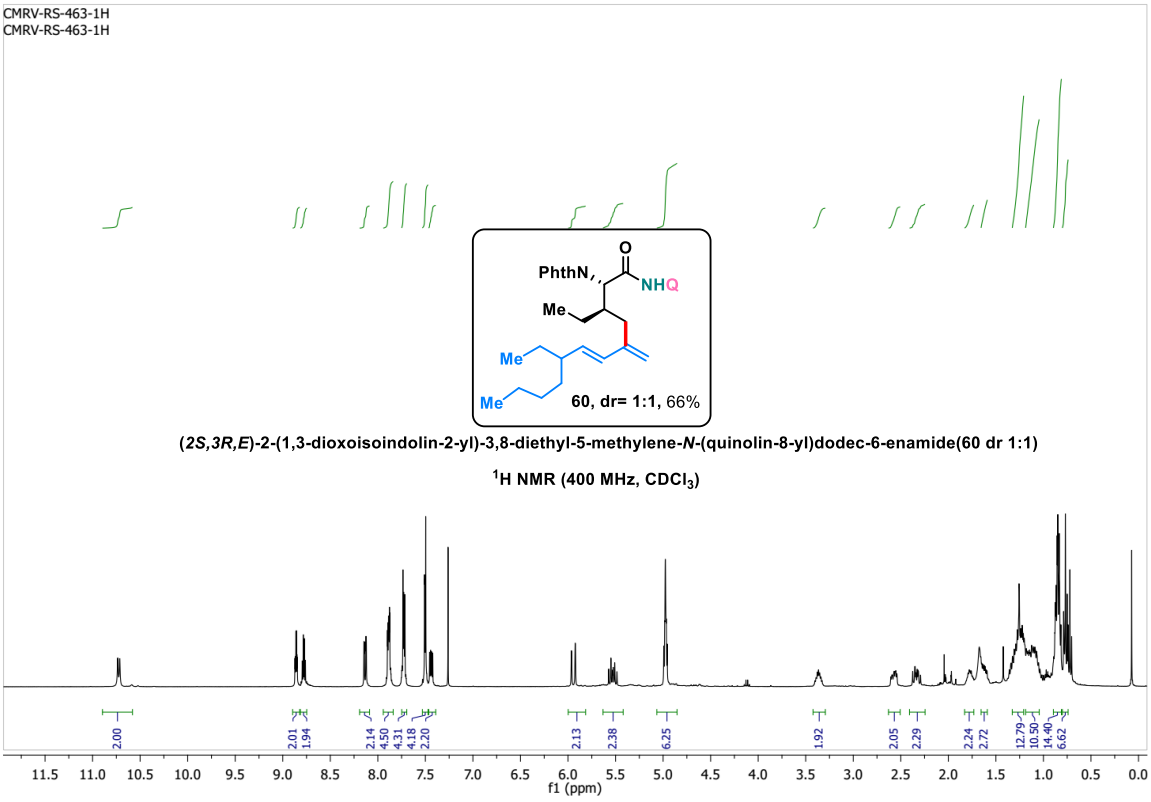

CMRV-RS-452-13C
CMRV-RS-452-13C
PhthN
O
NHQ
Me
n-C4H9
57, 58%
(3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)undec-6-enamide (57)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

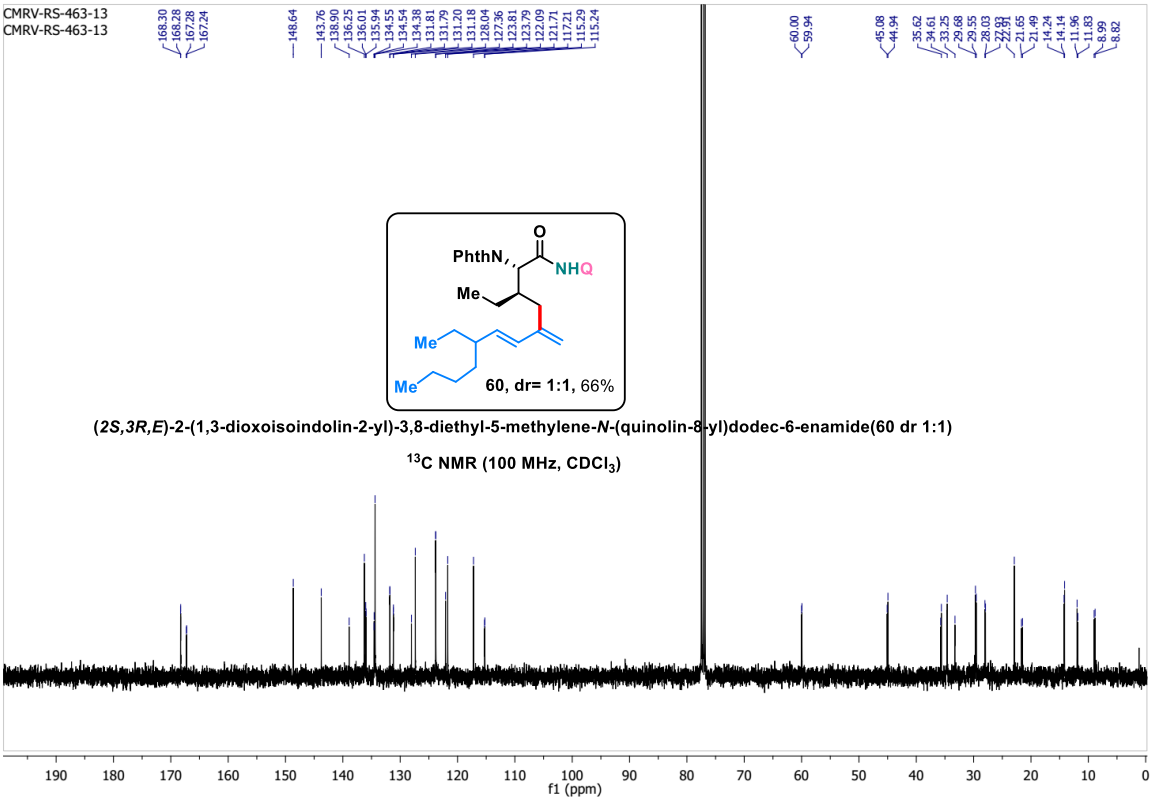

CMRV-RS-450-1H
CMRV-RS-450-1H
PhthN
O
NHQ
Me
n-C6H13
58, 70%
(2S,3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)tridec-6-enamide (58)
1H NMR (400 MHz, CDCl3)
1.00
1.12
1.13
1.19
2.05
2.12
2.05
1.09
1.20
1.18
3.10
1.08
1.29
1.23
2.26
1.41
5.65
4.67
6.59
f1 (ppm)

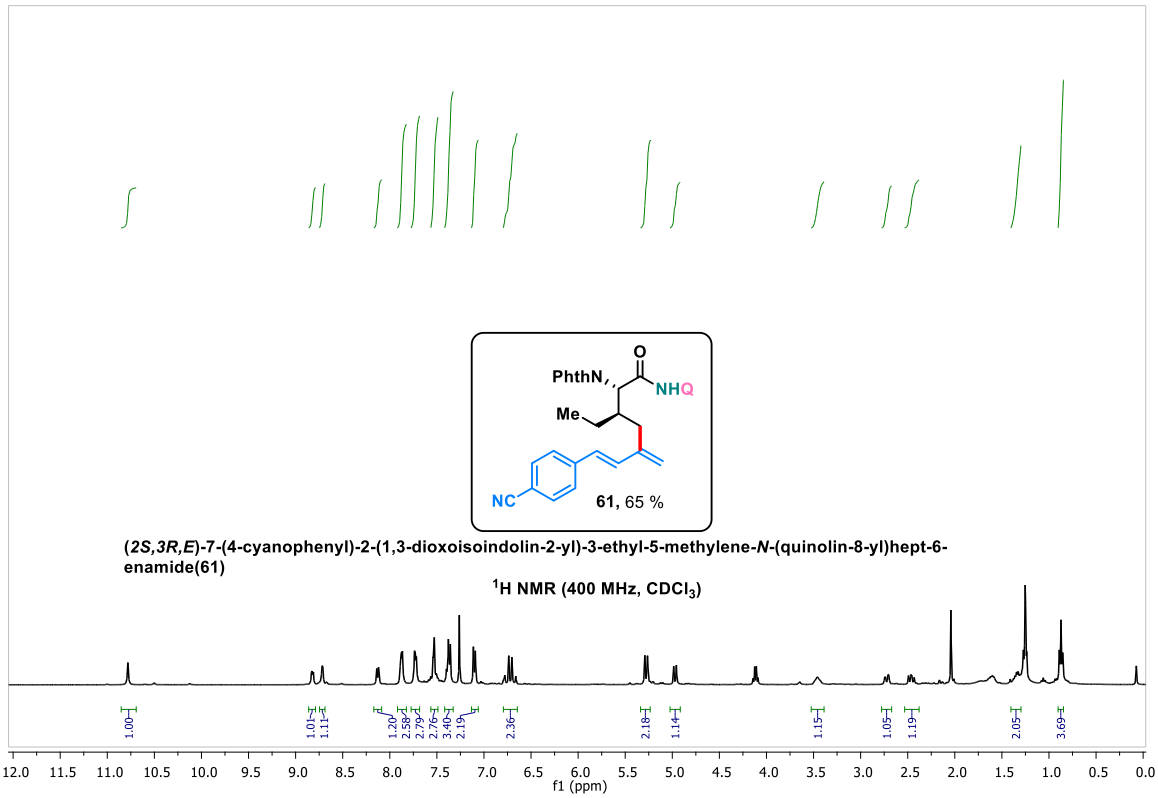

59.97
35.16
33.06
32.95
31.66
29.07
28.87
22.56
21.23
14.10
8.37
PhthN
O
NHQ
Me
n-C6H13
58, 70%
(2S,3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)tridec-6-enamide (78)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

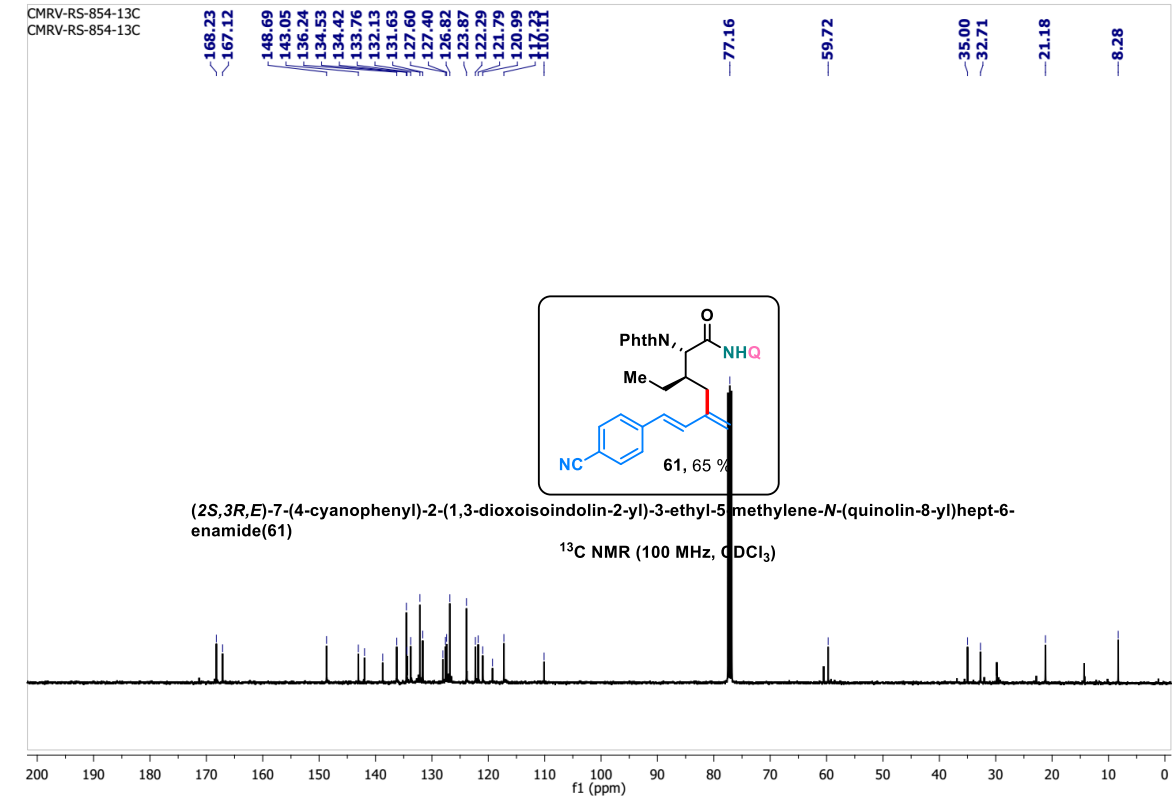

CMRV-RS-451-1H
CMRV-RS-451-1H
PhthN
O
NHQ
Me
59, 68%
(2S,3R)-5-(cyclohexylidenemethyl)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-N-(quinolin-8-yl)hex-5-enamide (59)
1h NMR (400 MHz, CDCl3)
f1 (ppm)

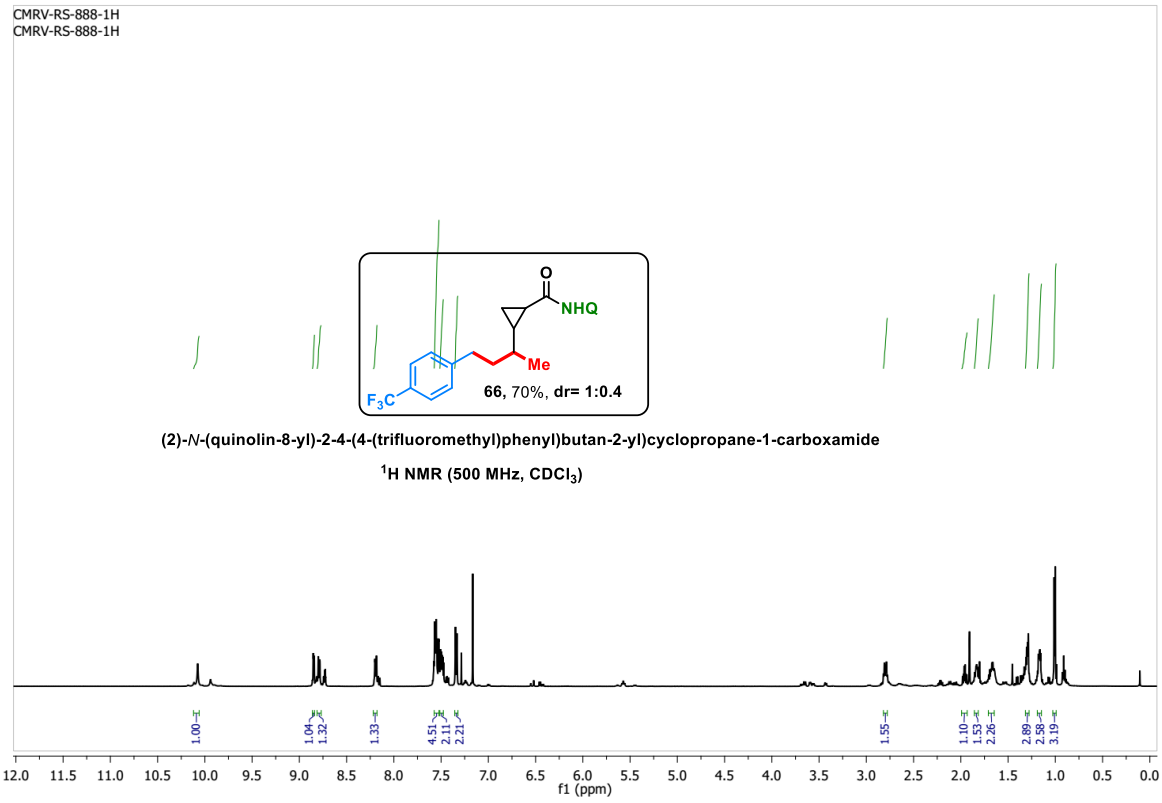

CMRV-RS-451-13C
CMRV-RS-451-13C
PhthN
O
NHQ
Me
59, 68%
(2S,3R)-5-(cyclohexylidenemethyl)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-N-(quinolin-8-yl)hex-5-enamide (59)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

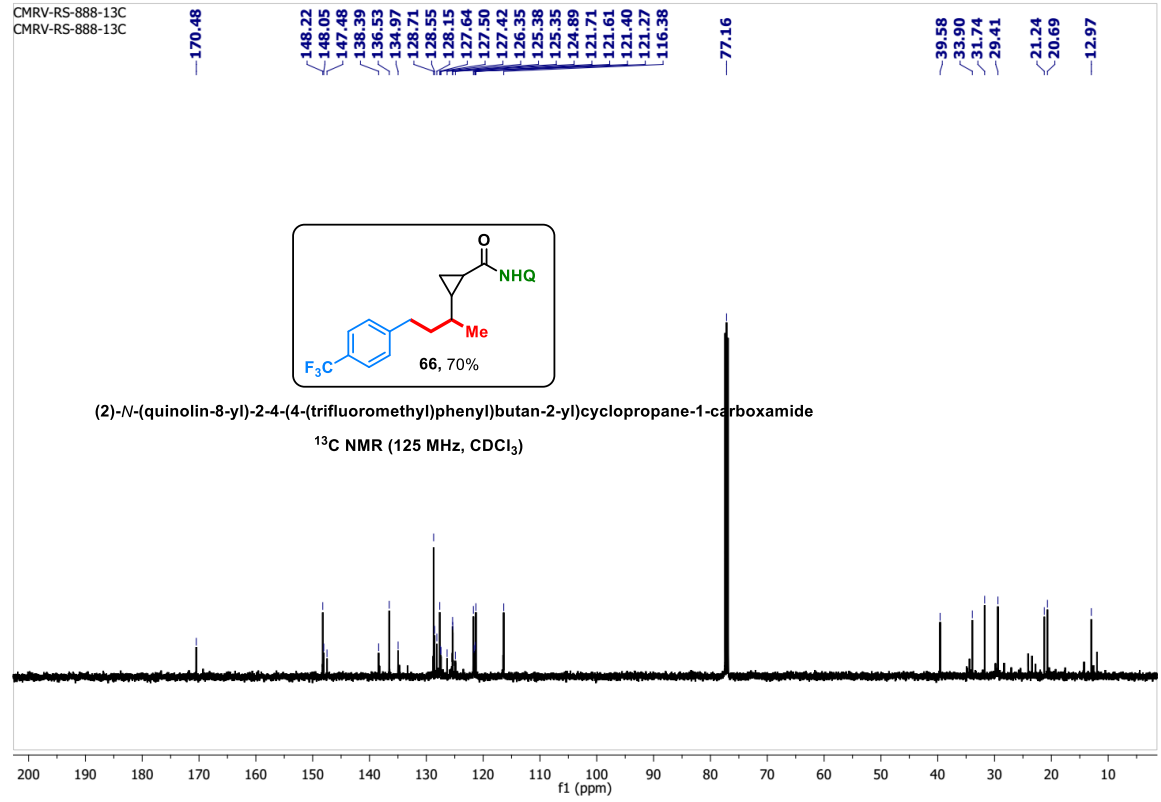

CMRV-RS-463-1H
CMRV-RS-463-1H
PhthN
O
NHQ
Me
Me
Me
60, dr= 1:1, 66%
(2S,3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3,8-diethyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide(60 dr 1:1)
1H NMR (400 MHz, CDCl3)
2.00
2.01
1.94
2.14
4.50
4.31
4.18
2.20
2.13
2.38
6.25
1.92
2.05
2.29
2.24
2.72
12.79
10.50
14.40
6.62
f1 (ppm)

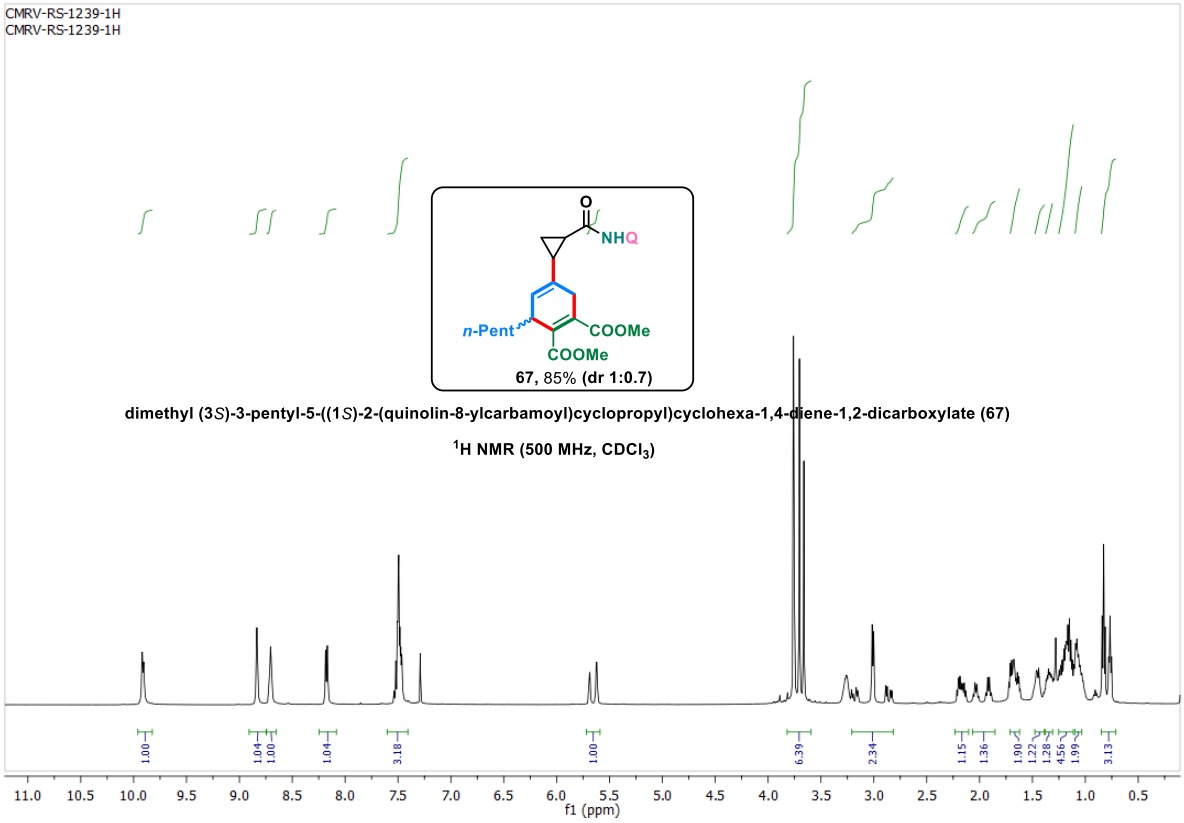

CMRV-RS-463-13
CMRV-RS-463-13
168.30
168.28
167.28
167.24
148.64
143.76
138.90
136.25
136.01
135.94
134.55
134.54
134.38
131.81
131.79
131.20
131.18
128.04
127.36
123.81
123.79
122.09
121.71
117.21
115.29
115.24
60.00
59.94
45.08
44.94
35.62
34.61
33.25
29.88
29.55
28.03
22.91
22.87
21.65
21.49
14.24
14.14
11.96
11.83
8.99
8.82
PhthN
O
NHQ
Me
Me
Me
60, dr= 1:1, 66%
(2S,3R,E)-2-(1,3-dioxoisoindolin-2-yl)-3,8-diethyl-5-methylene-N-(quinolin-8-yl)dodec-6-enamide(60 dr 1:1)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

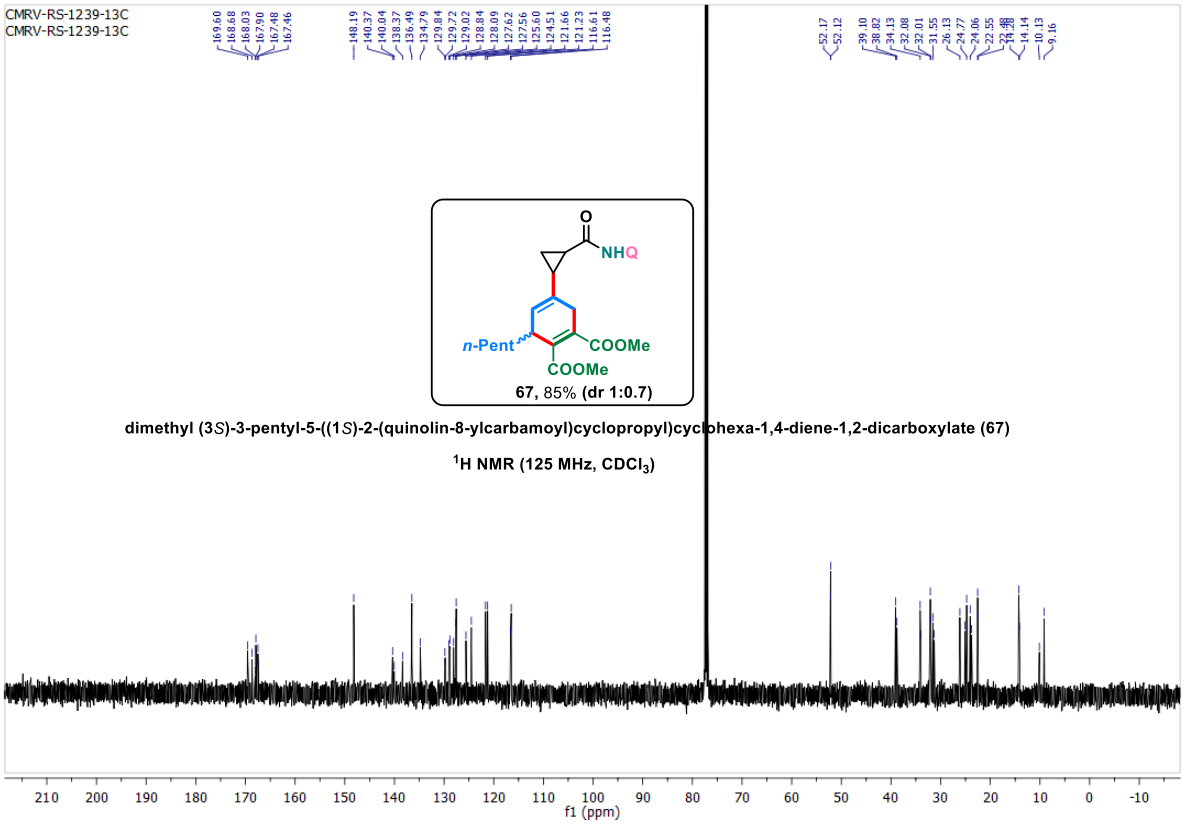

PhthN
O
NHQ
Me
NC
61, 65 %
(2S,3R,E)-7-(4-cyanophenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)hept-6-enamide(61)
1H NMR (400 MHz, CDCl3)
f1 (ppm)

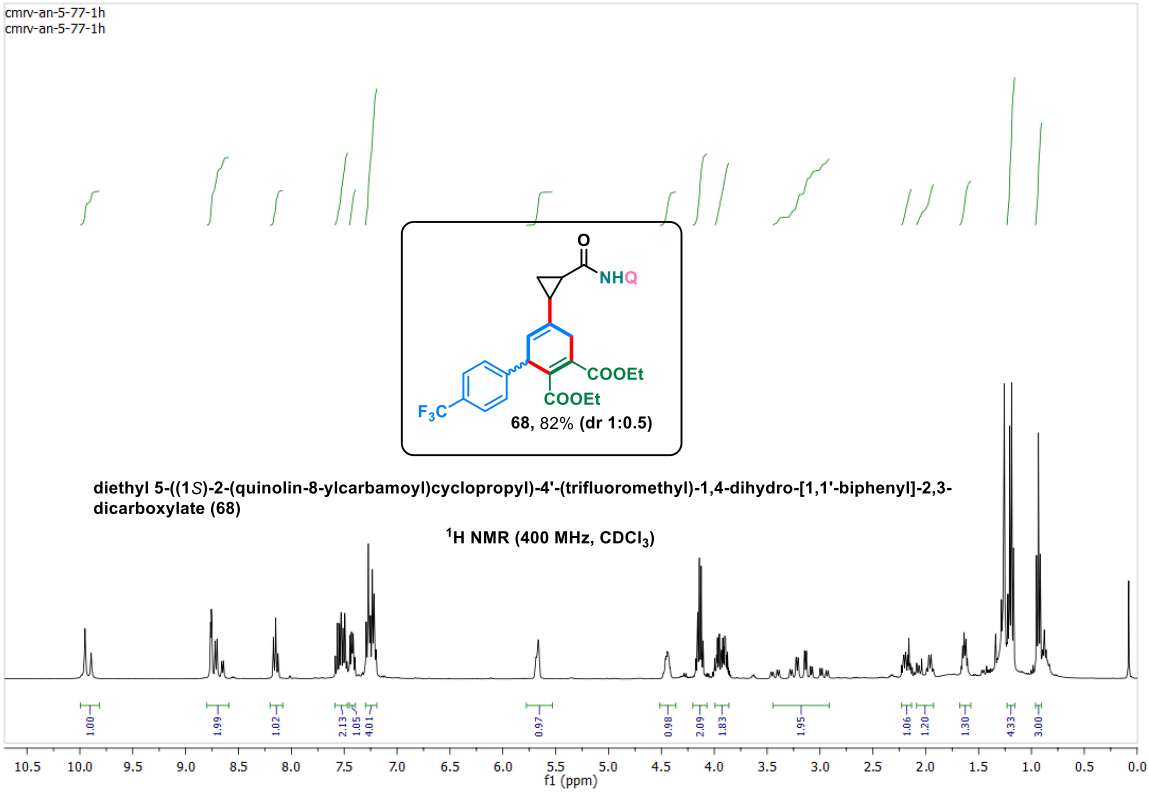

CMRV-RS-854-13C
CMRV-RS-854-13C
168.23
167.12
148.69
143.05
136.24
134.53
134.42
133.76
132.13
131.63
127.60
127.40
126.82
123.87
122.29
121.79
120.99
77.16
59.72
35.00
32.71
21.18
8.28
PhthN
O
NHQ
Me
NC
61, 65 %
(2S,3R,E)-7-(4-cyanophenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-ethyl-5-methylene-N-(quinolin-8-yl)hept-6-enamide(61)
13C NMR (100 MHz, CDCl3)
f1 (ppm)

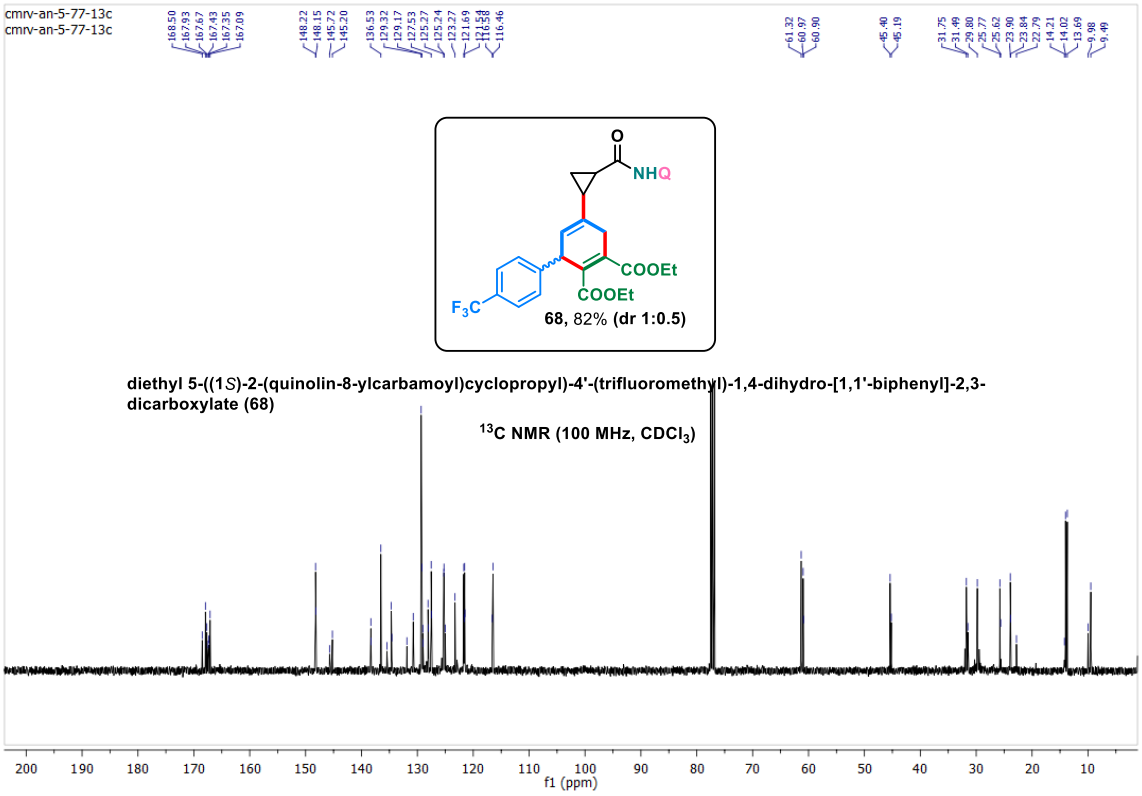

CMRV-RS-888-1H
CMRV-RS-888-1H
O
NHQ
Me
F3C
66, 70%, dr= 1:0.4
(2)-N-(quinolin-8-yl)-2-4-(4-(trifluoromethyl)phenyl)butan-2-yl)cyclopropane-1-carboxamide
1H NMR (500 MHz, CDCl3)
1.00
1.04
1.32
1.33
4.51
2.11
2.21
1.55
1.10
1.53
2.26
2.89
2.58
3.19
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

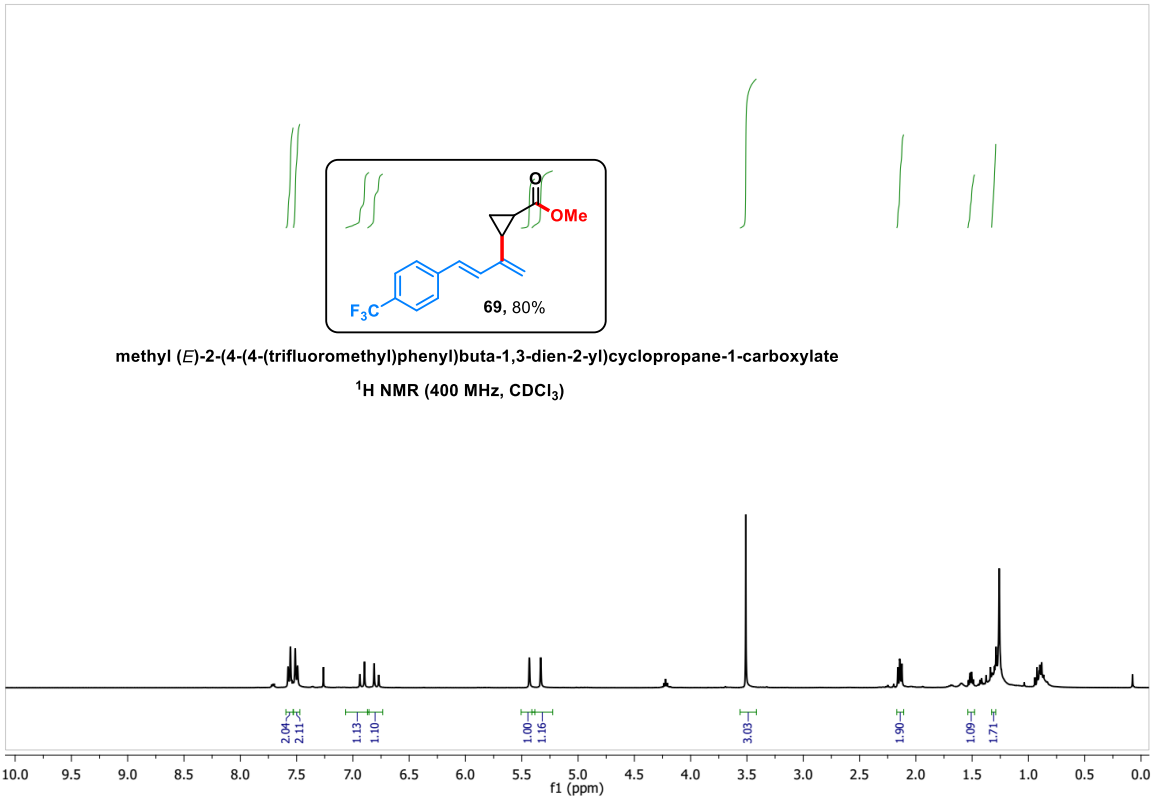

CMRV-RS-888-13C
CMRV-RS-888-13C
170.48
148.22
148.05
147.48
138.39
136.53
134.97
128.71
128.55
128.15
127.64
127.50
127.42
126.35
125.38
125.35
124.89
121.71
121.61
121.40
121.27
116.38
77.16
39.58
33.90
31.74
29.41
21.24
20.69
12.97
O
NHQ
Me
F3C
66, 70%
(2)-N-(quinolin-8-yl)-2-4-(4-(trifluoromethyl)phenyl)butan-2-yl)cyclopropane-1-carboxamide
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


CMRV-RS-1239-1H
CMRV-RS-1239-1H
O
NHQ
n-Pent
COOMe
COOMe
67, 85% (dr 1:0.7)
dimethyl (3S)-3-pentyl-5-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)cyclohexa-1,4-diene-1,2-dicarboxylate (67)
1H NMR (500 MHz, CDCl3)
1.00
1.04
1.00
1.04
3.18
1.00
6.39
2.34
1.15
1.36
1.90
1.22
1.28
4.56
1.99
3.13
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


CMRV-RS-1239-13C
CMRV-RS-1239-13C
169.60
168.68
168.03
167.90
167.48
167.46
148.19
140.37
140.04
138.37
136.49
134.79
129.84
129.72
129.02
128.84
128.09
127.62
127.56
125.60
124.51
121.66
121.23
116.61
116.48
52.17
52.12
39.10
38.82
34.13
32.08
32.01
31.55
26.13
24.77
24.06
22.55
14.14
10.13
9.16
O
NHQ
n-Pent
COOMe
COOMe
67, 85% (dr 1:0.7)
dimethyl (3S)-3-pentyl-5-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)cyclohexa-1,4-diene-1,2-dicarboxylate (67)
1H NMR (125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

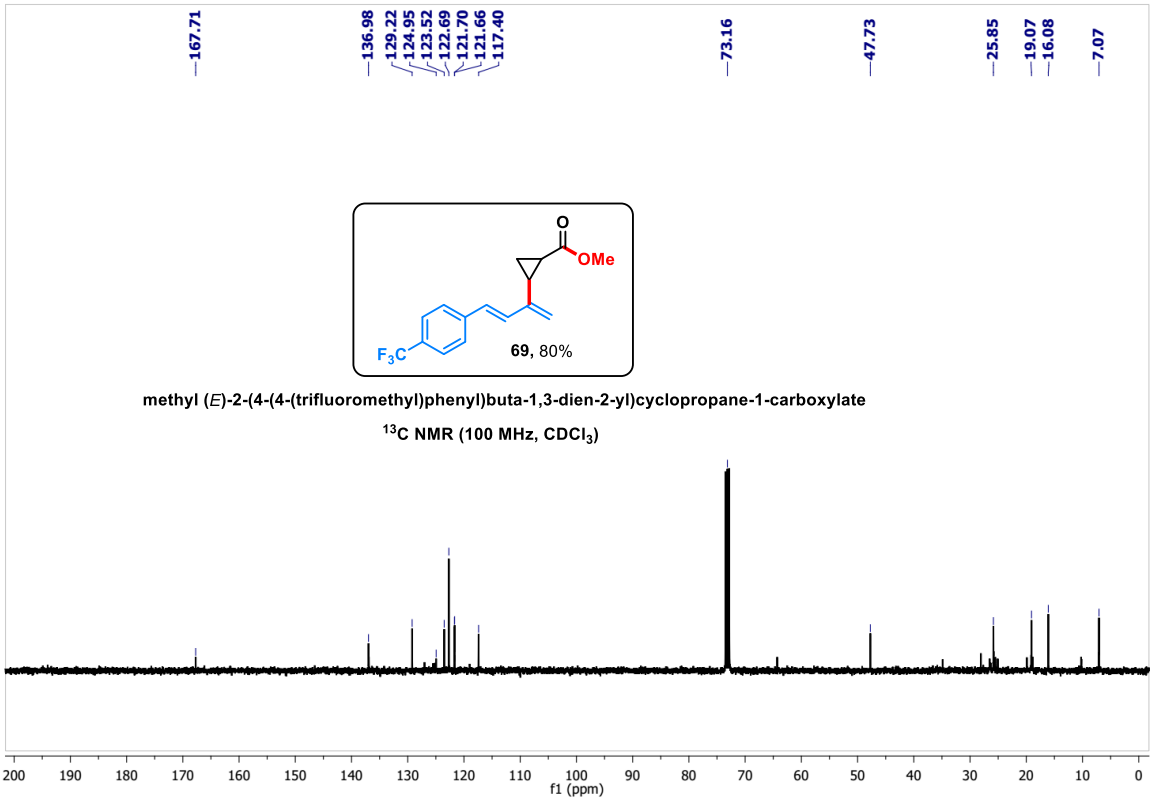

cmrv-an-5-77-1h
cmrv-an-5-77-1h
O
NHQ
COOEt
COOEt
F3C
68, 82% (dr 1:0.5)
diethyl 5-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)-4'-(trifluoromethyl)-1,4-dihydro-[1,1'-biphenyl]-2,3-dicarboxylate (68)
1H NMR (400 MHz, CDCl3)
f1 (ppm)


cmrv-an-5-77-13c
cmrv-an-5-77-13c
O
NHQ
COOEt
COOEt
F3C
68, 82% (dr 1:0.5)
diethyl 5-((1S)-2-(quinolin-8-ylcarbamoyl)cyclopropyl)-4'-(trifluoromethyl)-1,4-dihydro-[1,1'-biphenyl]-2,3-dicarboxylate (68)
13C NMR (100 MHz, CDCl3)
f1 (ppm)



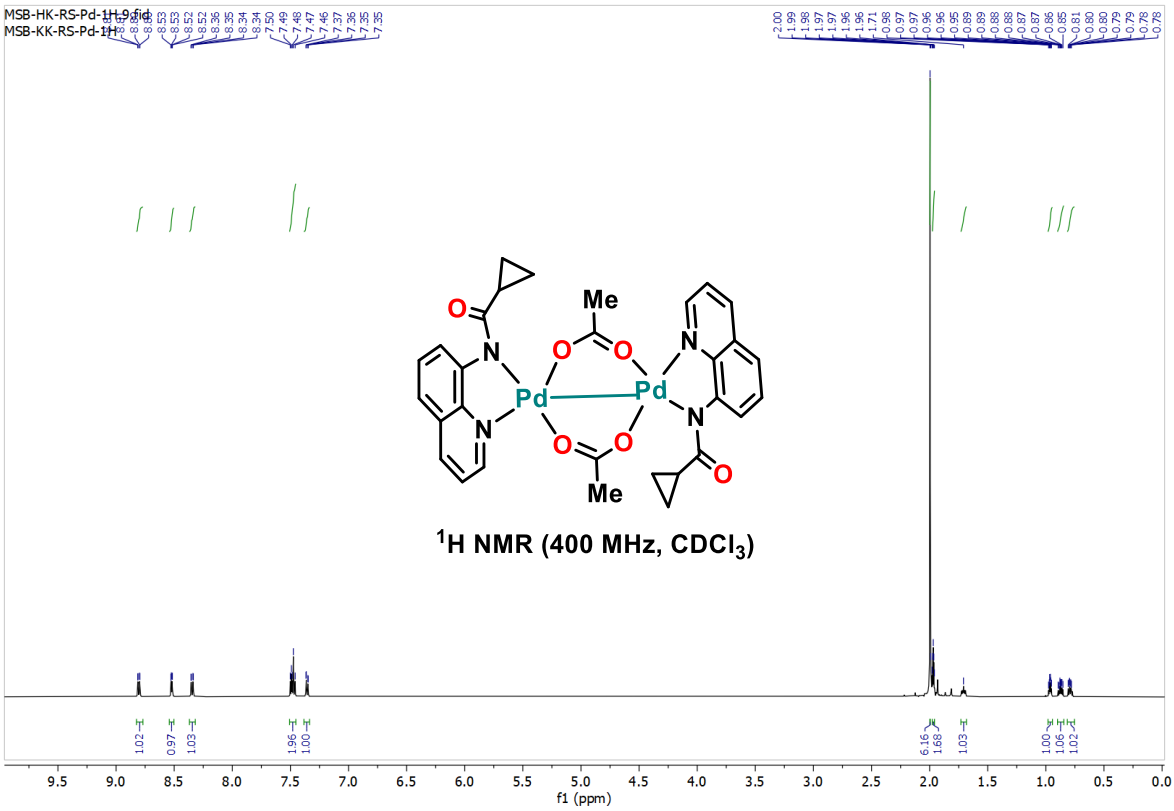
methyl (*E*)-2-(4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxylate

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

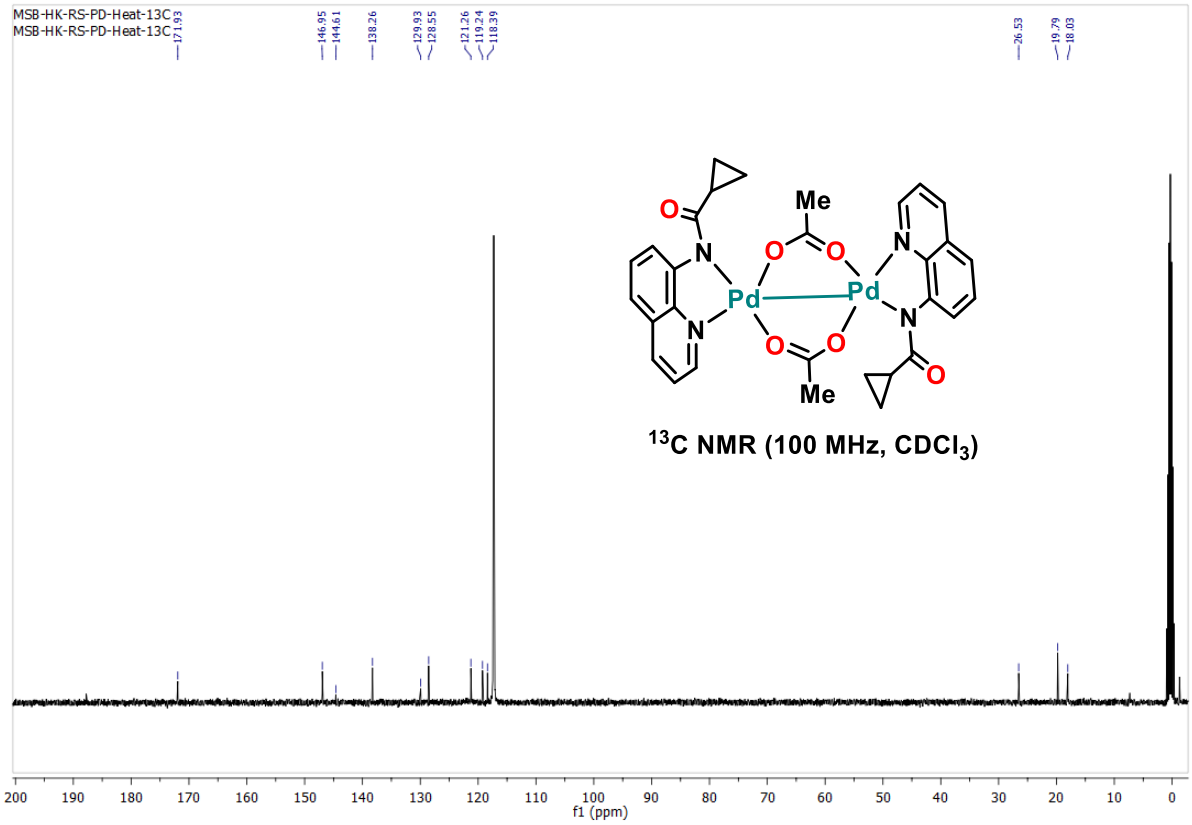


methyl (*E*)-2-(4-(4-(trifluoromethyl)phenyl)buta-1,3-dien-2-yl)cyclopropane-1-carboxylate

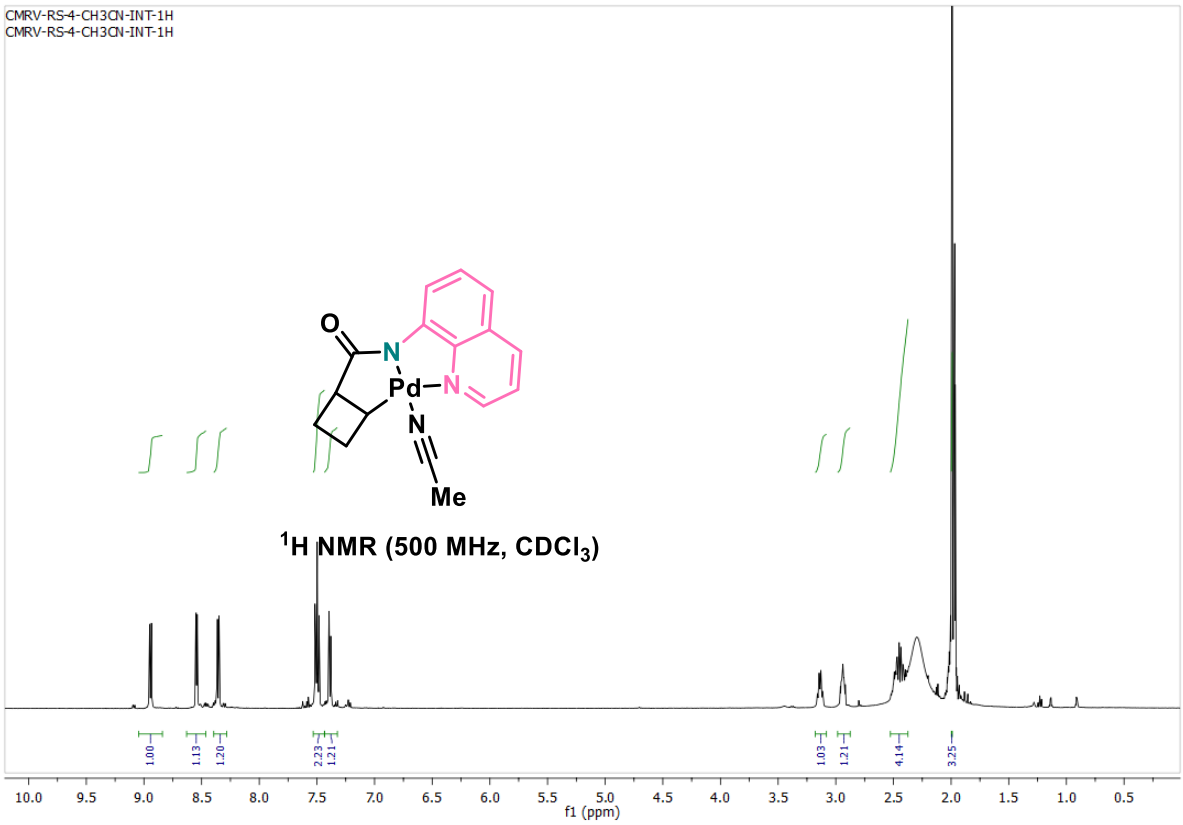
^{13}C NMR (100 MHz, $CDCl_3$)



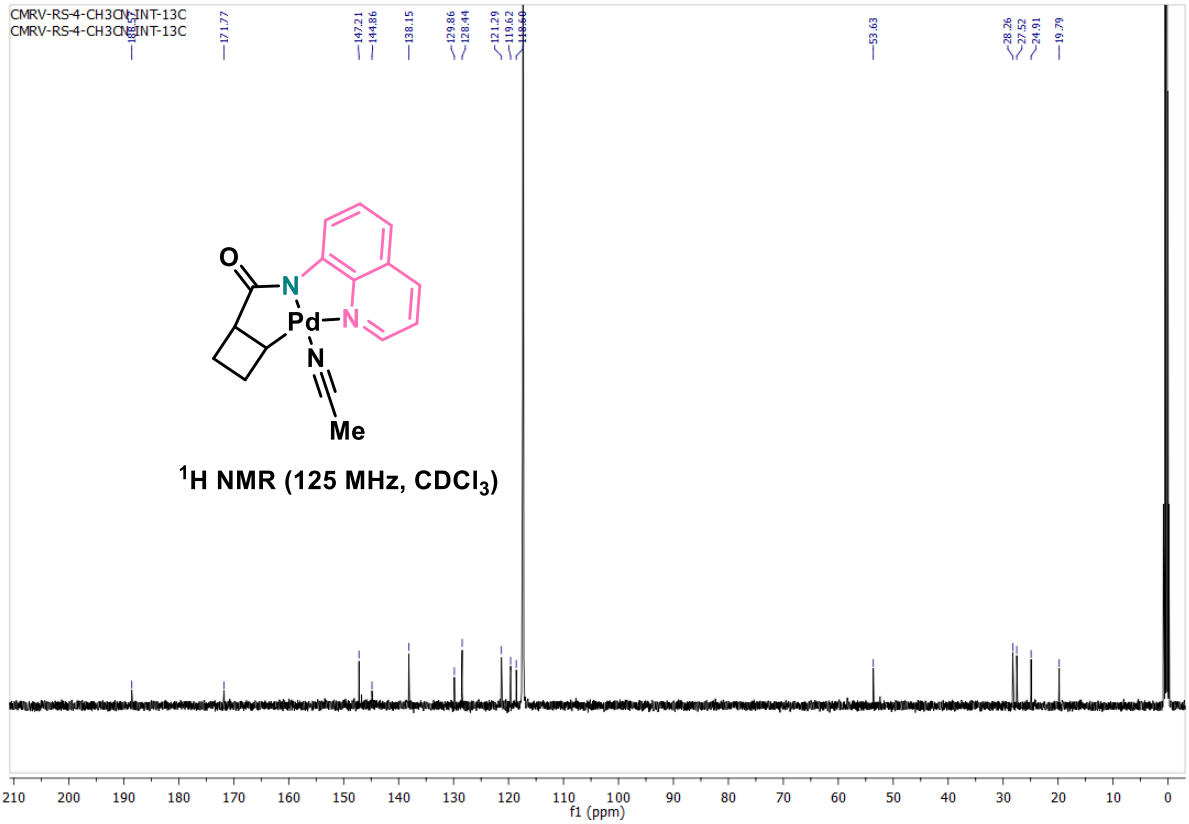
^{1}H NMR (400 MHz, $CDCl_3$)



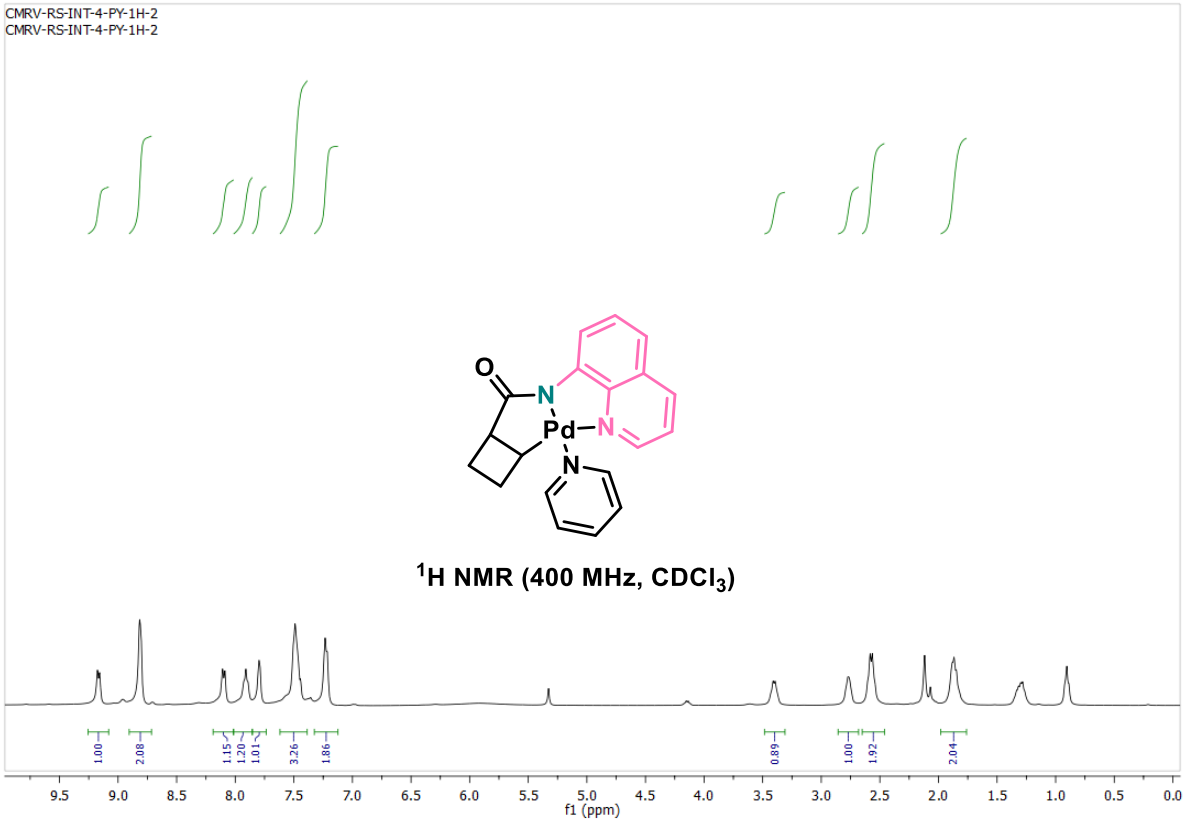
^{13}C NMR (100 MHz, $CDCl_3$)



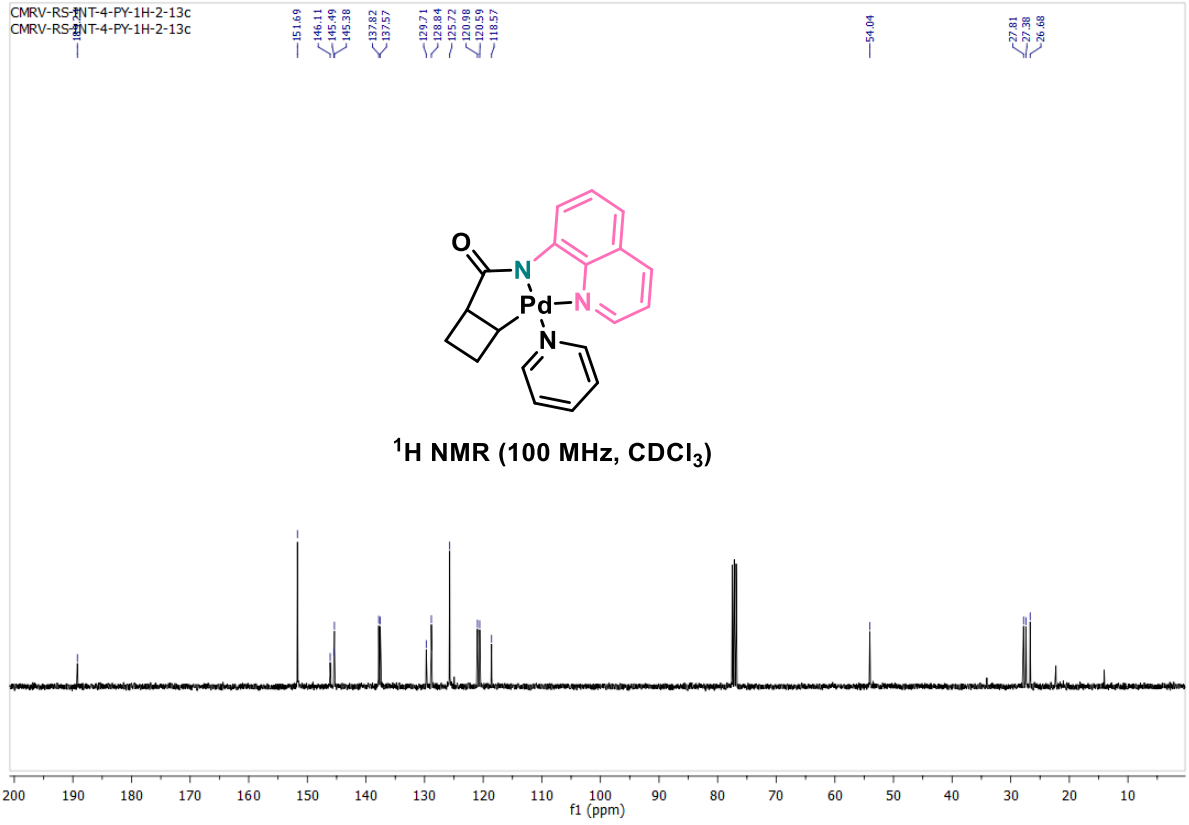
^{1}H NMR (500 MHz, $CDCl_3$)



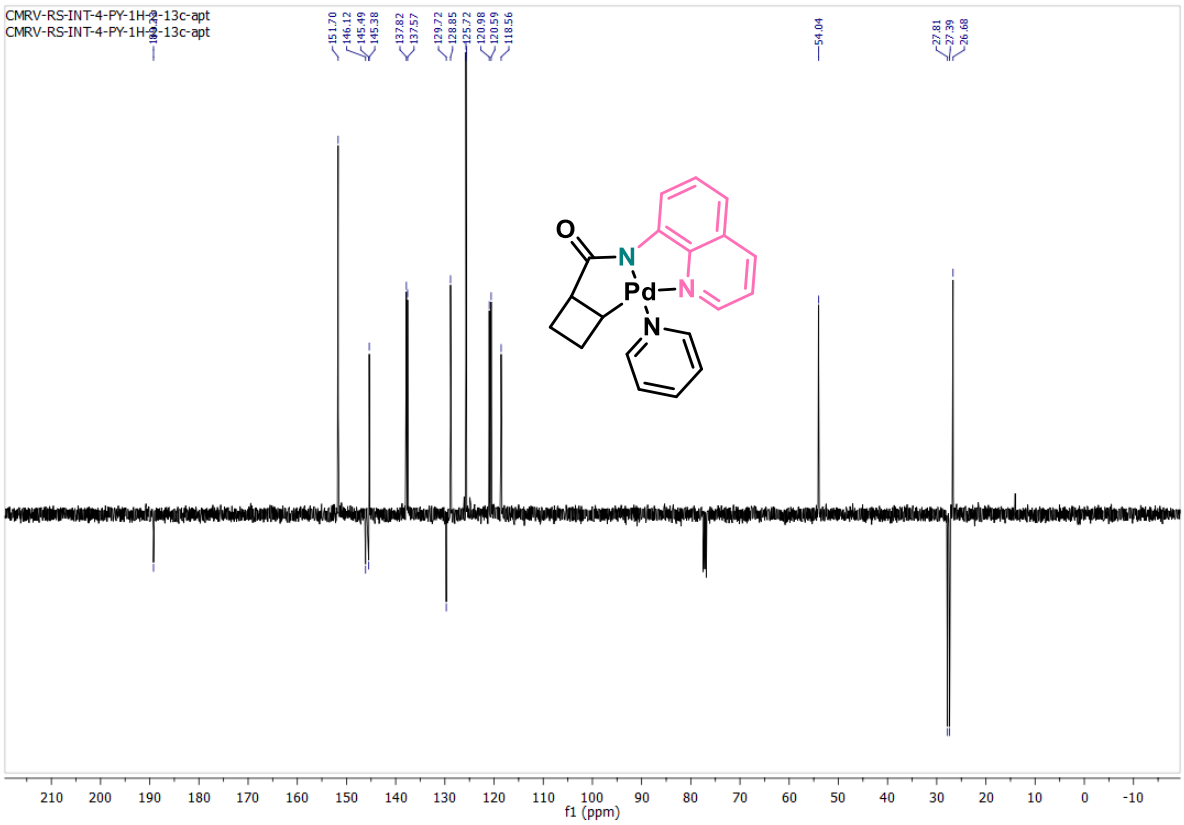
^{1}H NMR (125 MHz, $CDCl_3$)

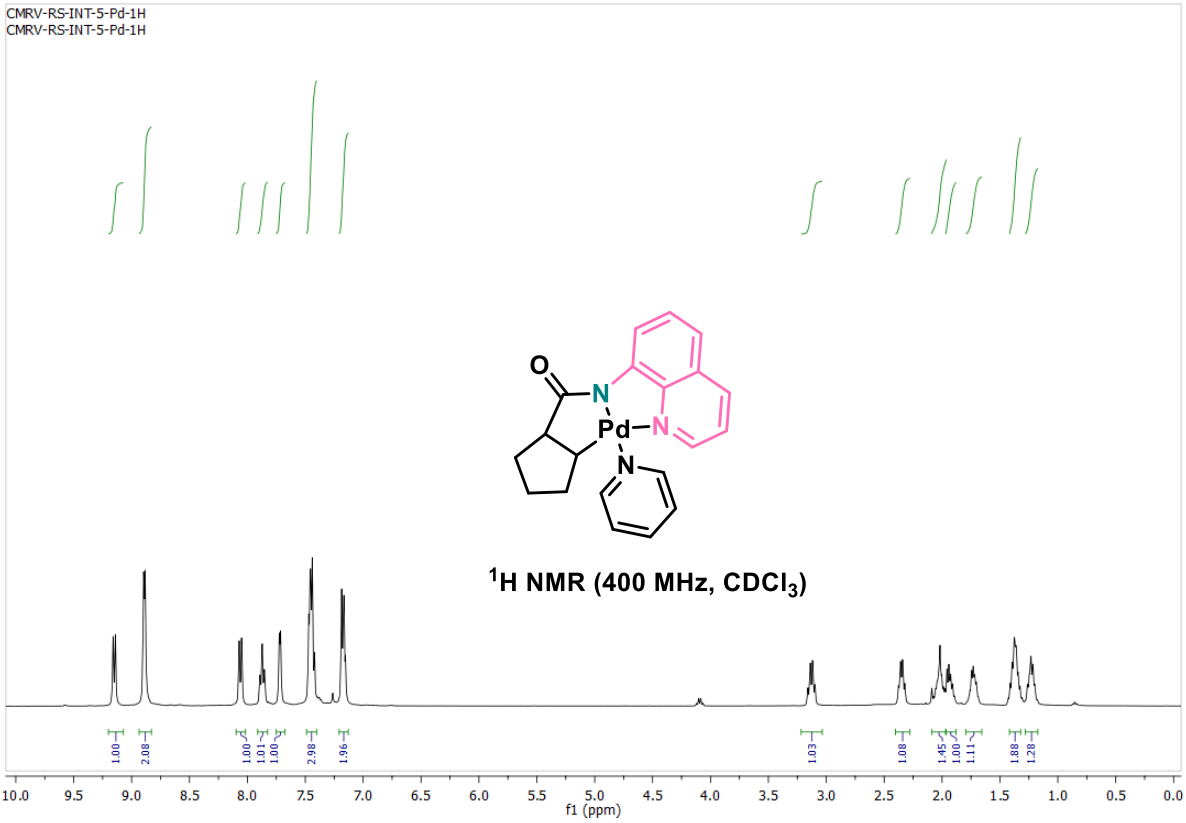


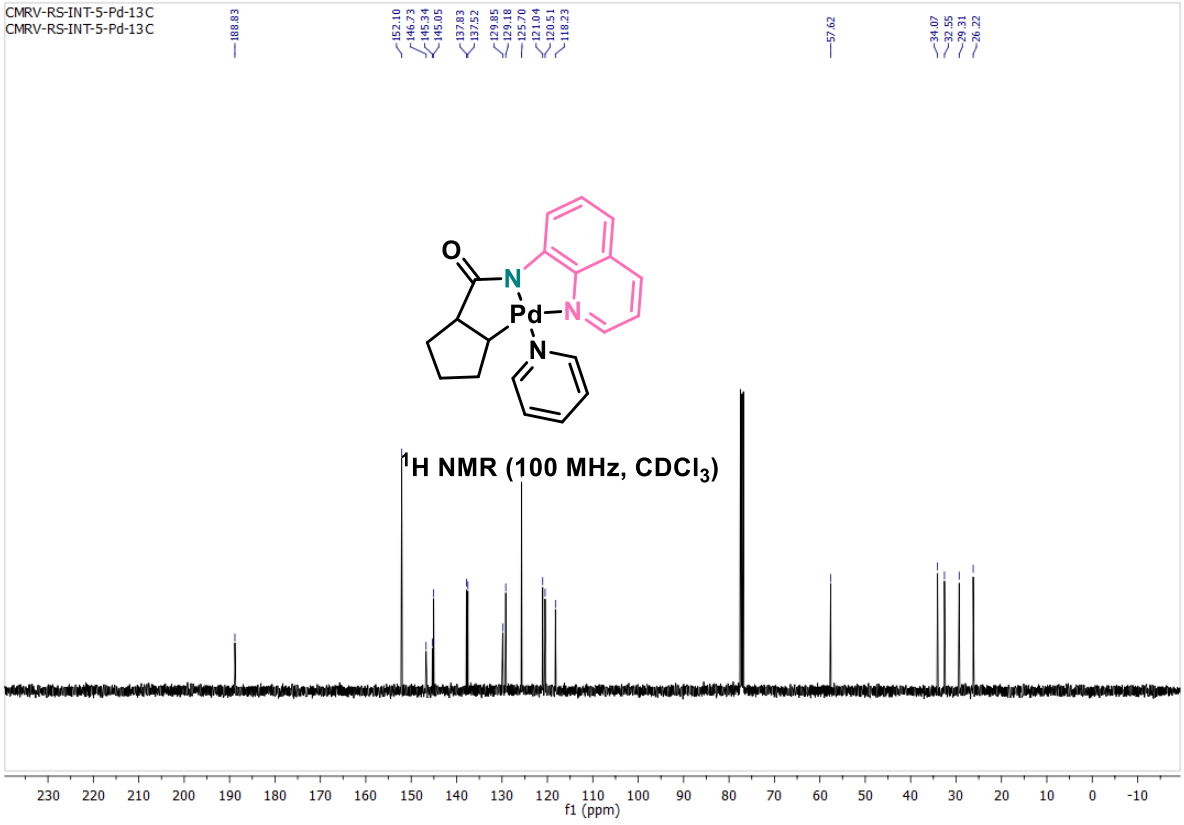
^{1}H NMR (400 MHz, $CDCl_3$)

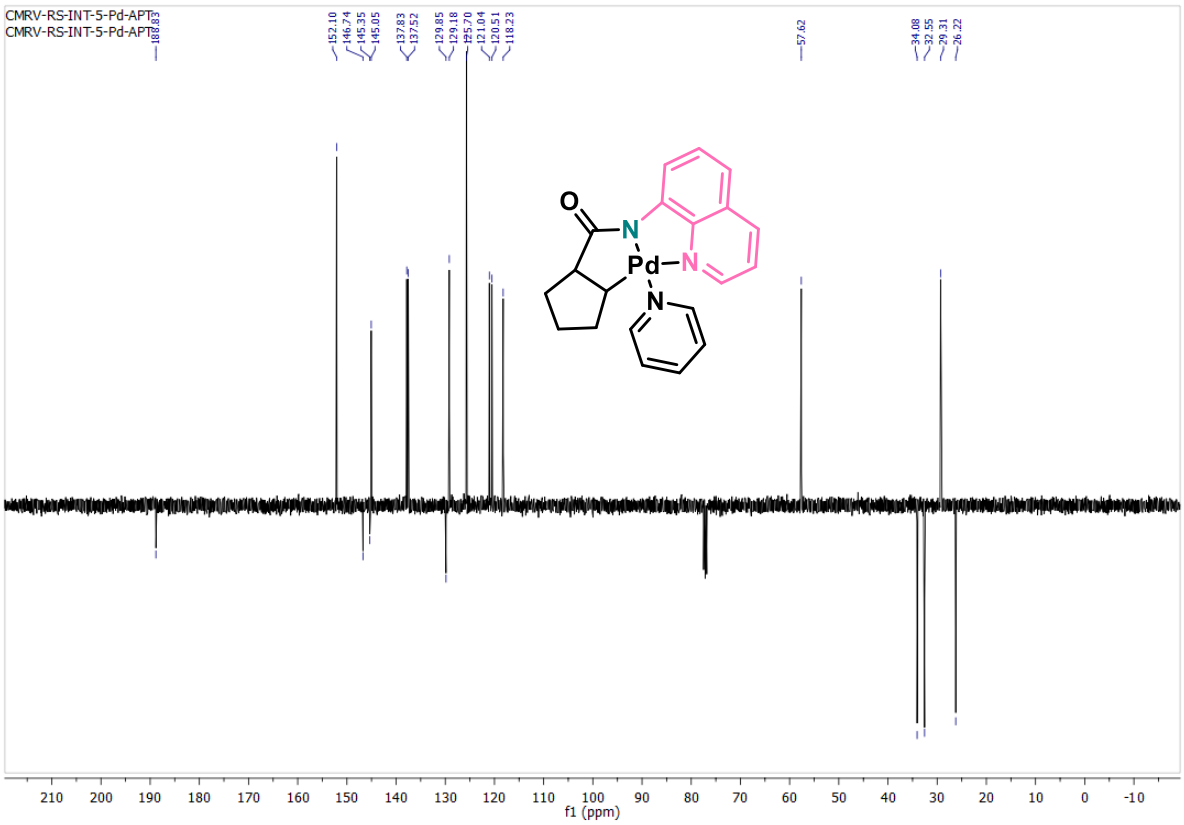


^{1}H NMR (100 MHz, $CDCl_3$)


CMRV-RS-INT-4-PY-1H-2-13c-apt
CMRV-RS-INT-4-PY-1H-2-13c-apt
151.70
146.12
145.49
145.38
137.82
137.57
129.72
128.85
125.72
120.98
120.59
118.56
54.04
27.81
27.39
26.68
O
N
Pd
N
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


CMRV-RS-INT-5-Pd-1H
CMRV-RS-INT-5-Pd-1H
O
N
Pd
N
N
1H NMR (400 MHz, CDCl3)
1.00
2.08
1.00
1.01
1.00
2.98
1.96
1.03
1.08
1.45
1.00
1.11
1.88
1.28
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


CMRV-RS-INT-5-Pd-13C
CMRV-RS-INT-5-Pd-13C
188.83
152.10
146.73
145.34
145.05
137.83
137.52
129.85
129.18
125.70
121.04
120.51
118.23
57.62
34.07
32.55
29.31
26.22
O
N
Pd
N
N
1H NMR (100 MHz, CDCl3)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


CMRV-RS-INT-5-Pd-APT
CMRV-RS-INT-5-Pd-APT
188.83
152.10
146.74
145.35
145.05
137.83
137.52
129.85
129.18
125.70
121.04
120.51
118.23
57.62
34.08
32.55
29.31
26.22
O
N
Pd
N
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)