

Palladium Catalyzed Direct Aliphatic γ C(sp³)-H Alkenylation with Alkenes and Alkenyl Iodides

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Supporting Information

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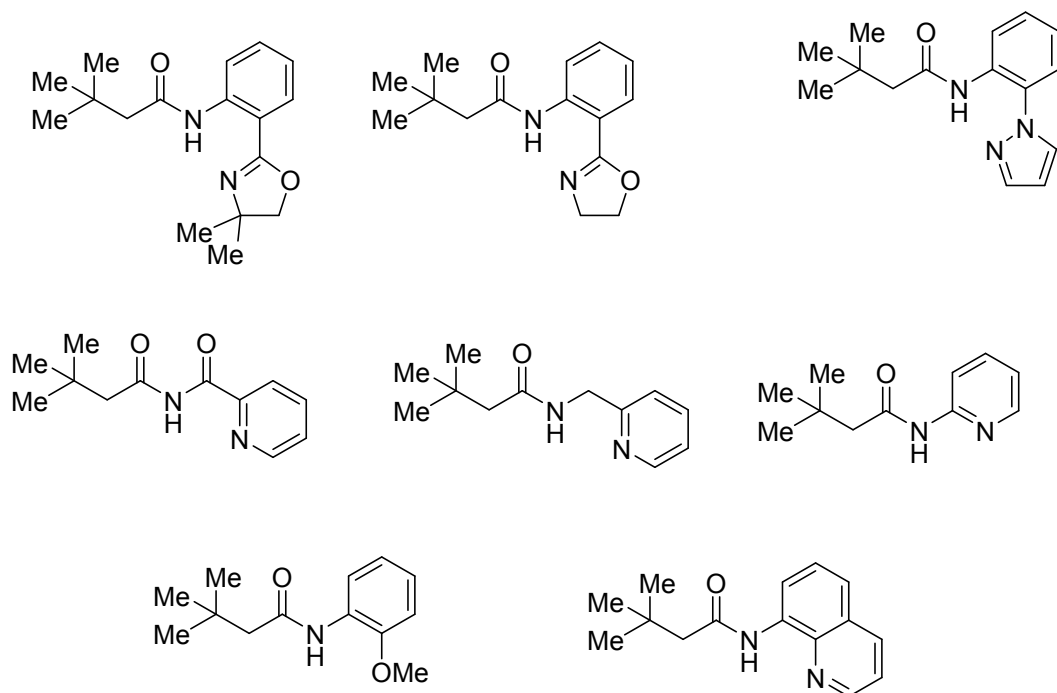
General considerations:

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 4,4'-Di-tert-butyl-2,2'-bipyridine, were bought from Aldrich. Oxidants like AgOAc and Ag₂CO₃ were also bought from Aldrich. For column chromatography, silica gel (100–200 mesh) from SRL Co. was used. A gradient elution using petroleum ether and ethyl acetate was performed based on Merck aluminium TLC sheets (silica gel 60F₂₅₄).

Analytical Information. All isolated compounds are characterized by ¹H NMR, ¹³C NMR spectroscopy, gas chromatography mass spectra (GC-MS). In addition, all the compounds are further characterized by HRMS. Copies of ¹H NMR and ¹³C 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 ¹³C NMR spectra are reported in ppm relative to deuterium chloroform (77.16 ppm), unless otherwise stated, and all were obtained with ¹H decoupling. All GCMS analysis were done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector).

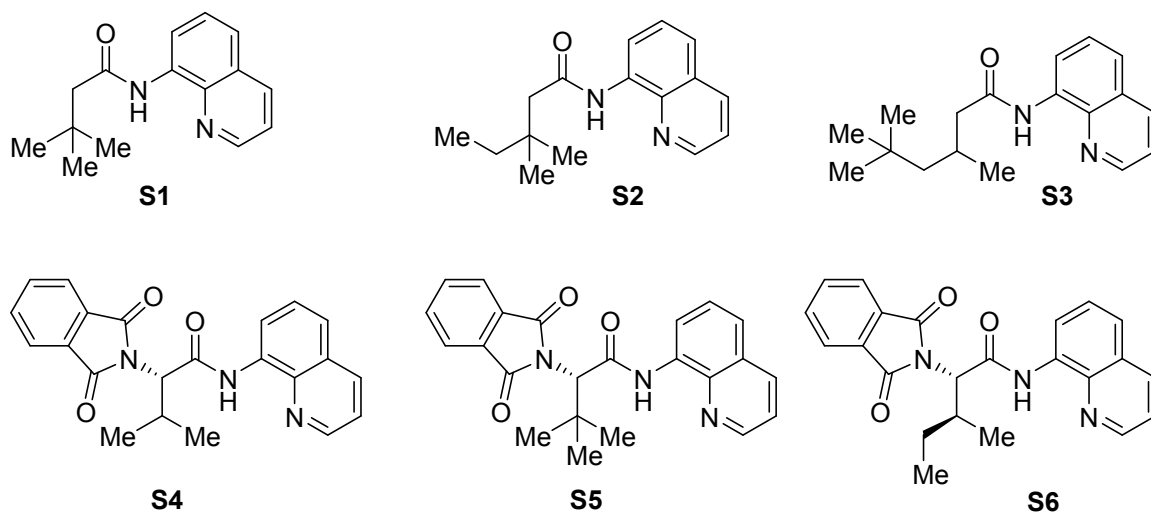


Different bidentate directing group's preparation:



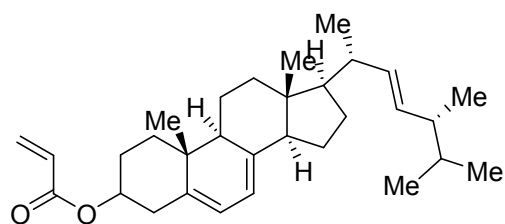
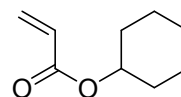
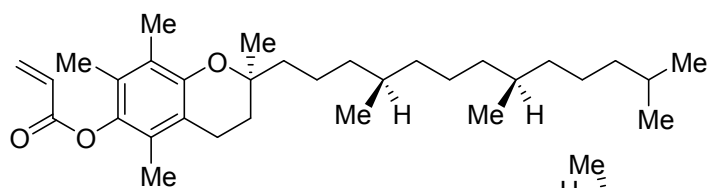
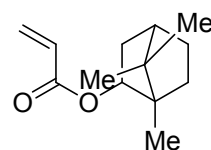
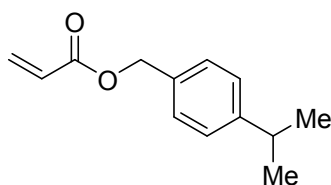
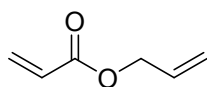
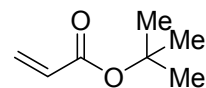
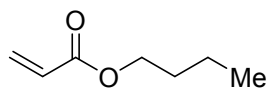
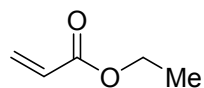
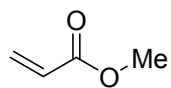
Preparation of different amides.

Preparation of 8-aminoquinolinyl amides

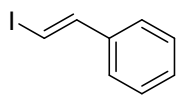


The carboxylic acid derivatives were prepared according to the literature procedure¹⁻⁵.

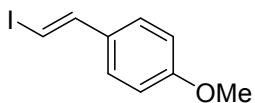
Available alkenes and prepared alkenes:



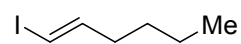
Preparation of Alkenyliodides: Vinyl iodides **13**,⁶ **14**,⁶ **15**,⁶ **11**,⁷ **10**,⁸ **7**,⁹ **9**,⁹ **16**,¹⁰ **8**,¹¹ **12**¹² were prepared as reported in the literature.



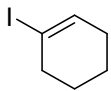
S7



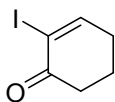
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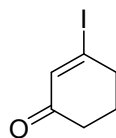
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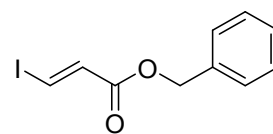
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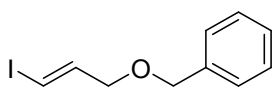
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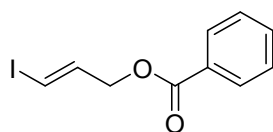
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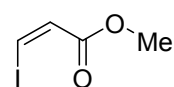
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S14

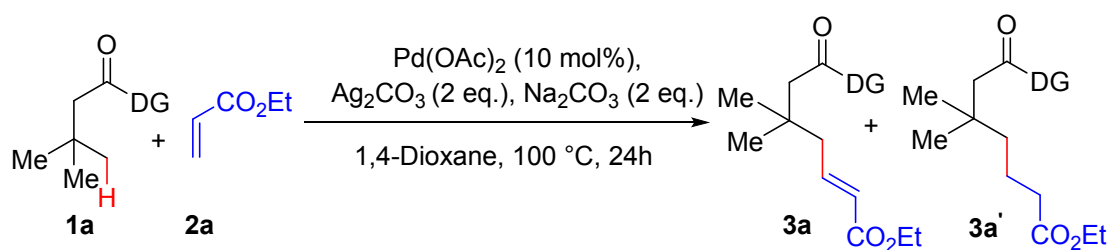


S15



S16

Solvent Optimization Details



Entry	Solvent	Ratio (3a : 3a')	NMR Yield ¹
1	1,2-DCE	4:1	25
2	TCP	4:1	10%
3	1,4-dioxane	5:1	22
4	Toluene	5:1	20
5	Xylene	2:1	18
6	THF	-	-
7	TFT	4:1	32
8	DMF	-	-
9	NMP	-	-
10	1,4-dioxane/140 °C	>10:1	22
11	HFIP	-	-

¹ The ratios of products were determined by the ¹H NMR analysis of crude reaction mixture

Oxidant optimization:

Entry	Oxidant/additive	NMR Yield ¹
1	Ag ₂ CO ₃ (2 eq)	22
2	Ag ₂ CO ₃ (3 eq)	29
3	Ag ₂ CO ₃ (5 eq)	45
4	Ag ₂ CO ₃ (5 eq)/p-TsOH.H ₂ O	traces

5	Ag ₂ CO ₃ (5 eq)/TBAI	traces
6	Ag ₂ CO ₃ (5 eq)/ adamantyl acid	48
7	Ag ₂ CO ₃ (5 eq)/CuSO ₄	traces
8	Ag ₂ CO ₃ (5 eq)/H ₂ O	--
9	Ag ₂ CO ₃ (5 eq)/pyridine	traces

Palladium catalyst Optimization details:

Entry	Palladium Catalyst (10mol %)	NMR Yield ¹
1	Pd(OTf) ₂	40
2	Pd(PPh ₃) ₂ Cl ₂	45% ²
3	Pd(acac) ₂	31%
4	Pd(COD) ₂ Cl ₂	14%
5	Pd(CH ₃ CN) ₂ Cl ₂	26%
6	Pd ₂ (dba) ₃	trace
7	Pd ₂ SO ₄	trace

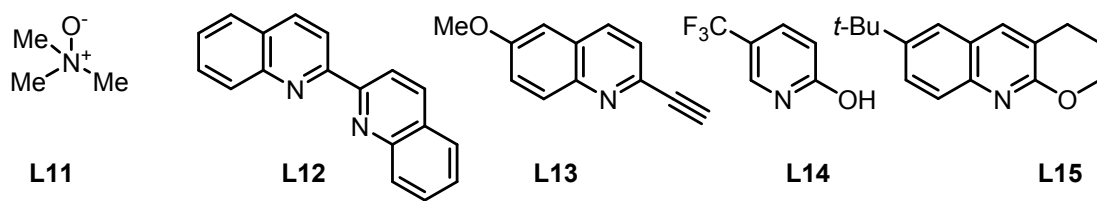
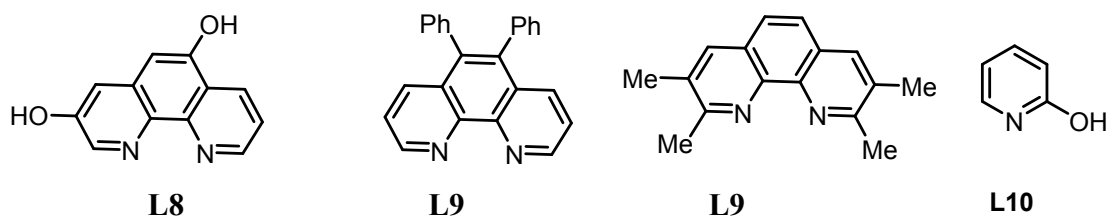
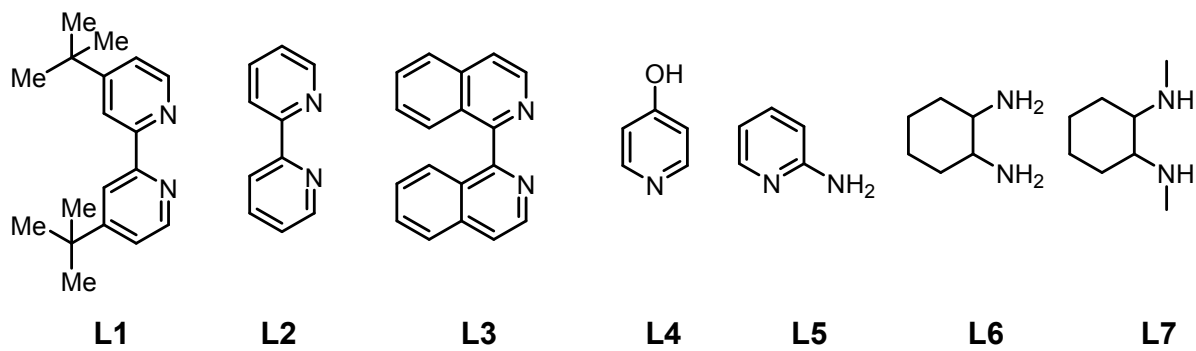
Ligand Optimization: mono protected amino acids (MPAA).

Entry	Ligand	Yield%
1	Ac-Gly-OH	21
2	Form-Gly-OH	29
3	Ac-Ala-OH	24
4	Ac-DL-Val-OH	5
5	Ac-Phe-OH	30
6	Ac-L-Leu-OH	trace
7	Na-Ac-L-Lys-OH	<5

8	Ac-4-hydroxy-L-Proline	-
9	DL-Proline	-
10	Boc-Ala-OH	trace
11	Boc-L-iso-Leu-OH	24
12	N-acetyl-Ala-OH	trace

Ligand Optimization: Nitrogen containing ligands.

Entry	Ligand	NMR Yield%
1	L1	64
2	L2	25
3	L3	24
4	L4	5
5	L5	30
6	L6	trace
7	L7	<5
8	L8	-
9	L9	-
10	L10	trace
11	L11	24
12	L12	trace
13	L13	trace
14	L14	-
15	L15	35%



(A). General Procedure for γ -Sp³ C–H Activation with Alkenes:

In an oven dried reaction tube, charged with magnetic stir-bar, Pd(OAc)₂ (10 mol%; 4.6 mg), Ag₂CO₃ (1.0 mmol; 53.6 mg), Na₂CO₃ (0.4 mmol; 49.66 mg), 4,4'-di-tert-butyl-2,2'-dipyridyl (20 mol% DTBD), and aliphatic amide substrate (**1**) (0.2 mmol) were added. Freshly prepared or available alkene (**2**) was added to the reaction mixture followed by 1,4-dioxane (2 mL). The reaction tube was capped and stirred at 140 °C temperature for 6h hours, then cooled to room temperature again olefin (0.2 mmol) was added. Upon completion, the reaction mixture was evaporated under reduced pressure and passed through the column for purification. Petroleum ether and ethyl acetate mixture was used as an eluent.

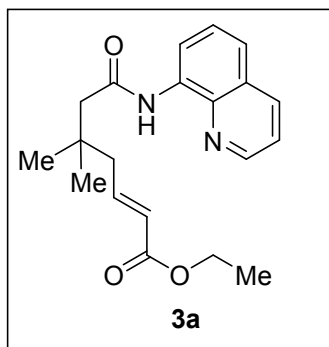
Note: The ratios of products were determined by the ¹H NMR analysis of crude reaction mixture. Minor product as in none of the cases was not characterized. Calculated yield is combined products.

(B). General Procedure for γ -Sp³ C–H Activation with Alkenyliodides:

In an oven dried reaction tube, charged with magnetic stir-bar, Pd(OAc)₂ (10 mol%; 4.6 mg), AgOAc (0.2 mmol; 53.6 mg), and aliphatic amide substrate (**1**) (0.2 mmol) were added. Freshly prepared alkenyliodides (**4**) was added to the reaction mixture followed by dry toluene (2 mL). The reaction tube was capped and stirred at 80 °C temperature for 24h hours. Upon completion, the reaction mixture was evaporated under reduced pressure and passed through the column for purification. Petroleum ether and ethyl acetate mixture was used as an eluent.

Note: The ratios of products were determined by the ¹H NMR analysis of crude reaction mixture. Minor product as in none of the cases was not characterized. Calculated yield is combined products.

Characterization of substrate:



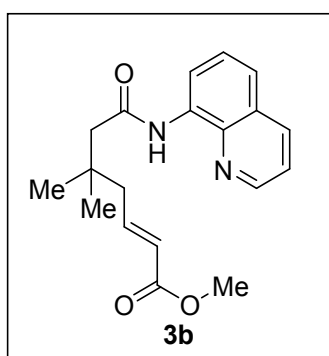
Ethyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3a) was synthesized by general procedure **A** with acrylate (0.8 mmol, 80 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3a** was obtained as liquid in 61% (42 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate:Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ 9.81 (s, 1H), 8.82 (ddd, *J* = 8.8, 5.7, 1.6, 2H), 8.20 (d, *J* = 8.2, 1H), 7.64 – 7.43 (m, 3H), 7.16 – 7.01 (m, 1H), 6.02 – 5.90 (m, 1H), 4.21 (q, *J* = 7.1, 2H), 2.50 (d, *J* = 16.4, 2H), 2.44 – 2.35 (m, 2H), 1.31 (t, *J* = 7.1, 3H), 1.20 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 170.97, 170.23, 166.62, 148.21, 145.79, 134.46, 128.15, 127.70, 124.59, 121.72, 121.69, 121.66, 121.50, 60.38, 52.27, 49.82, 44.73, 34.73, 27.75, 14.42.

IR (thin film) 3353, 2967, 2931, 1711, 1686, 1526, 1154, 756. cm⁻¹.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₂₀H₂₄N₂O₃Na 363.2146, found 363.2149.



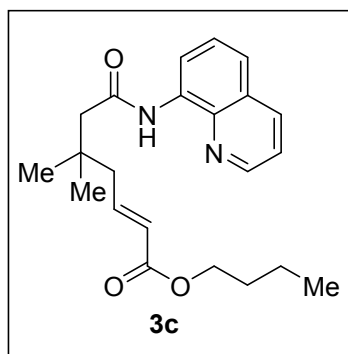
Methyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3b) was synthesized by general procedure **A** with methyl acrylate (0.8 mmol, 69 mg) and amide (0.2 mmol, 48

mg) as the substrates. Compound **3b** and **3b**¹ (4:1) was obtained as liquid in 62 % (40 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ = 9.77 (s, 1H), 8.79 (ddt, *J*=18.0, 10.9, 5.3, 2H), 8.23 – 8.15 (m, 1H), 7.61 – 7.40 (m, 3H), 7.08 (dt, *J*=15.6, 7.9, 1H), 5.94 (ddd, *J*=13.0, 7.1, 1.3, 1H), 3.73 (s, 2H), 2.45 (s, 2H), 2.40 (dd, *J*=7.9, 1.3, 2H), 1.18 (s, 5H).

¹³C NMR (101 MHz, CDCl₃) δ 170.03, 166.98, 148.27, 146.03, 138.41, 136.60, 134.50, 128.10, 127.56, 124.07, 121.73, 121.65, 116.65, 51.57, 49.82, 44.69, 34.65, 27.76, 27.43.

IR (thin film) 3353, 3016, 2968, 1721, 1693, 1593, 1526, 1216, 1152, 758 cm⁻¹



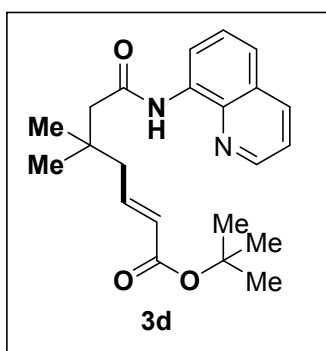
Butyl-(E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3c) was synthesized by general procedure **A** with acrylate (0.8 mmol, 102 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3c** was obtained as liquid in 58% (43 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). Ratio 5:1

R_f: 0.4 (10:90 ethyl acetate:Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ = 9.78 (s, 1H), 8.84 – 8.76 (m, 2H), 8.17 (d, *J*=7.7, 1H), 7.50 (ddt, *J*=12.4, 8.2, 6.2, 4H), 7.07 (dt, *J*=15.6, 7.9, 1H), 5.96 (d, *J*=15.5, 1H), 4.17 – 4.11 (m, 3H), 2.47 (d, *J*=16.6, 2H), 2.43 – 2.35 (m, 2H), 1.69 – 1.60 (m, 3H), 1.45 – 1.35 (m, 3H), 1.18 (s, 6H), 0.93 (t, *J*=5.6, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 170.12, 166.71, 149.90, 148.19, 145.64, 134.40, 131.17, 129.07, 128.14, 127.64, 124.52, 121.73, 121.68, 64.33, 49.84, 44.73, 34.67, 30.86, 29.85, 27.75, 19.33, 13.89.

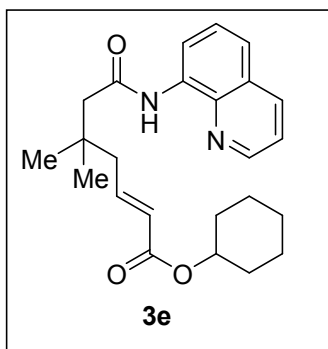
HRMS (ESI, M+Na⁺) m/z calcd. for C₂₂H₂₈N₂NaO₃ 391.1992, found 391.1991.



tert-butyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3d) was synthesized by general procedure **A** with acrylate (0.8 mmol, 102 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3d** was obtained as liquid in 66% (major isomer) (49 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). ratio 10:1, **R_f**: 0.4 (10:90 ethyl acetate:Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.77 (s, 1H), 8.83 – 8.75 (m, 2H), 8.17 (dd, *J* = 8.3, 1.6, 1H), 7.57 – 7.42 (m, 3H), 6.96 (dt, *J* = 15.6, 7.9, 1H), 5.88 (dt, *J* = 15.5, 1.3, 1H), 2.45 (s, 2H), 2.35 (dt, *J* = 18.6, 9.3, 2H), 1.48 (s, 9H), 1.16 (s, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 170.15, 166.02, 148.25, 144.32, 136.62, 134.53, 128.10, 127.58, 126.19, 121.71, 121.61, 116.66, 80.30, 49.87, 44.67, 34.63, 28.31, 27.70.



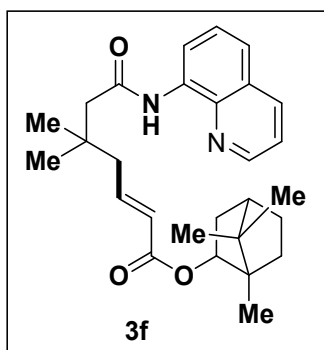
cyclohexyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3e) was synthesized by general procedure A with acrylate (0.8 mmol, 123 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3e** was obtained as liquid in 61% (48 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.77 (s, 1H), 8.80 (dd, *J* = 13.6, 5.5, 2H), 8.16 (d, *J* = 8.2, 1H), 7.64 – 7.42 (m, 3H), 7.05 (dt, *J* = 15.6, 7.8, 1H), 5.95 (d, *J* = 15.5, 1H), 4.89 – 4.72 (m, 1H), 2.45 (s, 2H), 2.39 (d, *J* = 7.8, 2H), 1.87 (d, *J* = 10.8, 2H), 1.77 – 1.69 (m, 3H), 1.55 (d, *J* = 11.5, 1H), 1.39 (dt, *J* = 23.0, 9.8, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 170.09, 166.05, 148.31, 145.23, 138.46, 136.53, 134.54, 128.08, 127.54, 125.06, 121.73, 116.57, 72.82, 49.87, 44.74, 34.66, 31.83, 27.73, 25.56, 23.93.

IR (thin film) 3356, 3016, 2938, 2860, 1711, 1687, 1596, 1578, 1196, 756 cm⁻¹.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₂₄H₃₀N₂NaO₃ 417.2144, found 417.2149.



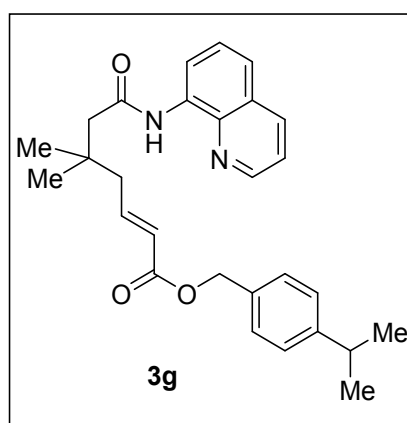
(E)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3f) was synthesized by general procedure A with acrylate (0.8 mmol, 167 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3f** was obtained as liquid in 59% (53 mg) yield after column chromatography of the crude reaction mixture (silica gel,

mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate:Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ 9.76 (s, 1H), 8.87 – 8.72 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6, 1H), 7.57 – 7.41 (m, 3H), 7.10 – 6.96 (m, 1H), 5.98 – 5.88 (m, 1H), 4.76 (dd, *J* = 7.7, 3.7, 1H), 2.44 (s, 2H), 2.39 (dd, *J* = 7.9, 1.2, 2H), 1.84 – 1.72 (m, 6H), 1.00 – 0.97 (m, 3H), 0.83 (t, *J* = 6.1, 13H).

¹³C NMR (126 MHz, CDCl₃) δ 170.05, 166.07, 148.36, 145.23, 138.54, 136.50, 128.11, 127.55, 124.97, 121.75, 121.63, 116.58, 80.92, 49.96, 48.97, 47.09, 45.23, 44.66, 38.98, 34.62, 33.88, 27.69, 27.21, 20.26, 20.05, 11.61.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₂₈H₃₆N₂NaO₃ 471.2618, found 471.2618.

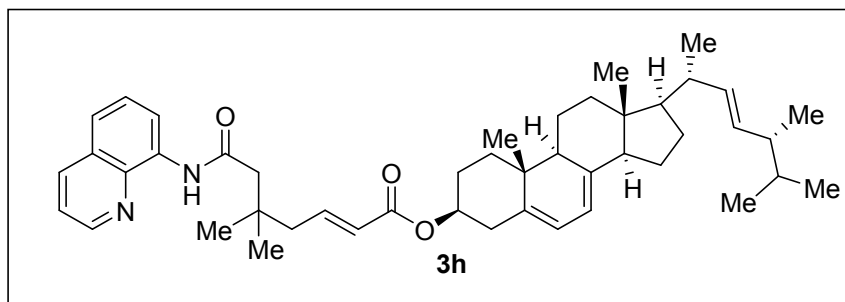


4-isopropylbenzyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3g) was synthesized by general procedure A with acrylate (0.8 mmol, 163 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3g** was obtained as liquid in 56% (50 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ 9.76 (s, 1H), 8.80 – 8.75 (m, 2H), 8.17 – 8.14 (m, 1H), 7.55 – 7.48 (m, 3H), 7.42 (dd, *J* = 8.2, 4.2, 1H), 7.31 (d, *J* = 8.1, 2H), 7.25 – 7.19 (m, 4H), 7.17 – 7.06 (m, 2H), 6.04 – 5.98 (m, 1H), 5.15 (s, 2H), 2.95 – 2.87 (m, 1H), 2.45 (s, 2H), 2.40 (dd, *J* = 7.9, 1.2, 2H), 1.25 (d, *J* = 6.9, 6H), 1.18 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 169.75, 166.18, 148.88, 148.11, 146.01, 138.23, 136.21, 134.28, 133.31, 128.34, 127.81, 127.27, 126.51, 124.02, 121.48, 121.37, 116.29, 65.96, 49.59, 44.49, 34.43, 33.78, 27.52, 23.84.

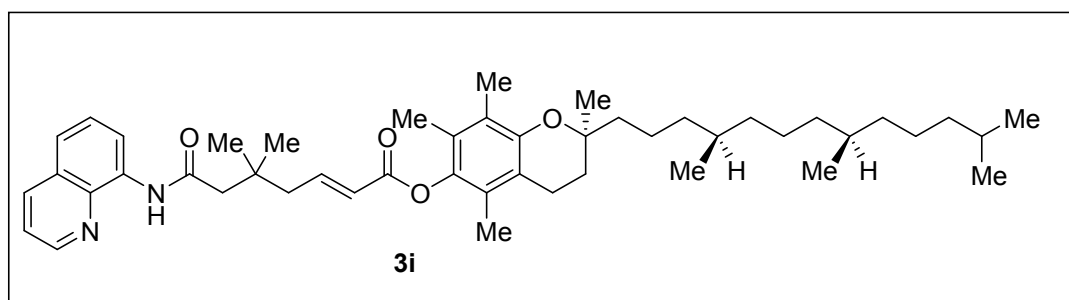
HRMS (ESI, M+Na⁺) *m/z* calcd. for C₂₈H₃₂N₂NaO₃ 467.2305, found 467.2307.



(3S,9S,10R,13R,14R,17R)-17-((*2R,5R,E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl (*E*)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (**3h**) was synthesized by general procedure A with acrylate (0.8 mmol, 360 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3h** was obtained as liquid in 40 % (55 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). Ratio 4:1. **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.80 (s, 1H), 8.81 (ddd, *J* = 8.9, 5.7, 1.7, 2H), 8.19 (d, *J* = 7.4, 1H), 7.59 – 7.44 (m, 4H), 7.17 – 6.84 (m, 2H), 6.03 – 5.86 (m, 1H), 5.25 – 5.15 (m, 3H), 4.14 – 3.91 (m, 1H), 2.46 (s, 2H), 2.42 – 2.37 (m, 3H), 2.14 – 1.54 (m, 21H), 1.52 – 1.23 (m, 14H), 1.06 (dd, *J* = 15.9, 4.6, 4H), 0.98 – 0.90 (m, 7H), 0.86 – 0.78 (m, 11H).

¹³C NMR (126 MHz, CDCl₃) δ 169.92, 165.84, 148.16, 145.38, 141.49, 138.70, 138.34, 136.43, 135.58, 134.41, 132.00, 129.53, 127.98, 127.43, 126.60, 124.73, 123.85, 121.59, 121.49, 121.15, 120.16, 116.53, 116.33, 114.60, 72.67, 69.11, 61.52, 55.76, 54.55, 51.79, 49.71, 46.09, 44.62, 42.83, 41.74, 40.39, 39.06, 37.96, 37.14, 36.74, 34.53, 33.10, 30.88, 29.69, 29.32, 28.26, 28.18, 27.63, 25.03, 24.18, 23.00, 22.67, 21.10, 21.05, 19.94, 19.64, 17.59, 16.22, 12.06, 11.34.



(S)-2,5,7,8-tetramethyl-2-((*4R,8R*)-4,8,12-trimethyltridecyl)chroman-6-yl (*E*)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (**3i**) was synthesized by general procedure A with acrylate (0.8 mmol, 388 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3i** was obtained as liquid in 52 % (major isomer) (75 mg) yield after column chromatography of

the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

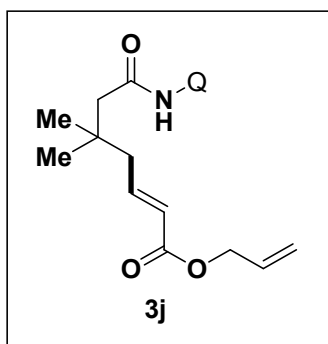
¹H NMR (400 MHz, CDCl₃) δ = 9.84 (s, 1H), 8.89 – 8.75 (m, 2H), 8.28 – 8.11 (m, 1H), 7.61 – 7.44 (m, 3H), 7.40 – 7.28 (m, 1H), 6.24 (d, *J* = 15.5, 1H), 2.59 (t, *J* = 6.7, 2H), 2.51 (d, *J* = 5.4, 4H), 2.10 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H), 1.87 – 1.72 (m, 3H), 1.53 (ddd, *J* = 19.8, 13.3, 6.7, 4H), 1.44 – 1.19 (m, 26H), 1.17 – 1.05 (m, 7H), 0.86 (dd, *J* = 9.2, 5.5, 16H).

¹³C NMR (101 MHz, CDCl₃) δ 170.06, 165.02, 149.49, 148.28, 147.63, 140.53, 134.40, 128.14, 127.64, 126.98, 125.20, 123.66, 123.12, 121.73, 117.49, 75.16, 49.84, 44.83, 39.50, 37.52, 37.42, 34.71, 32.91, 28.11, 27.81, 24.95, 24.58, 22.86, 22.77, 21.17, 20.74, 19.89, 19.83, 13.13, 12.29, 11.97.

HRMS (ESI, M+H⁺) m/z

calcd. for C₄₇H₆₉N₂O₄

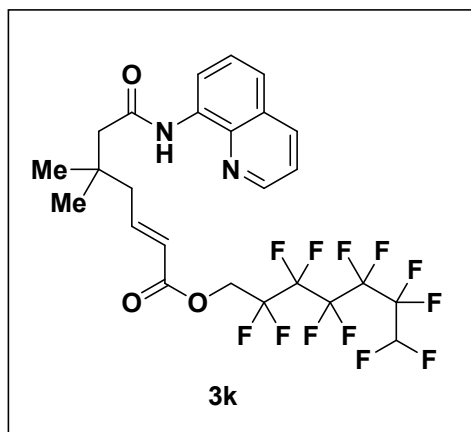
725.5255, found 725.5252.



allyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3j) was synthesized by general procedure A with acrylate (0.8 mmol, 90 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **3j** was obtained as liquid in 41% (29 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate:Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ 9.79 (s, 1H), 8.86 – 8.78 (m, 2H), 8.19 (dt, *J* = 8.2, 1.9, 1H), 7.60 – 7.43 (m, 4H), 7.14 (dt, *J* = 15.6, 7.9, 1H), 6.04 – 5.91 (m, 2H), 5.36 (ddd, *J* = 17.2, 3.0, 1.5, 1H), 5.26 (dt, *J* = 6.1, 3.1, 1H), 4.67 (dt, *J* = 5.7, 1.3, 2H), 2.49 – 2.39 (m, 4H), 1.41 (s, 3H), 1.19 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 169.89, 149.04, 148.23, 146.15, 136.38, 134.46, 132.33, 128.02, 127.40, 127.06, 124.02, 121.63, 121.52, 121.31, 118.14, 116.42, 65.00, 49.73, 44.59, 34.55, 30.63, 27.64.

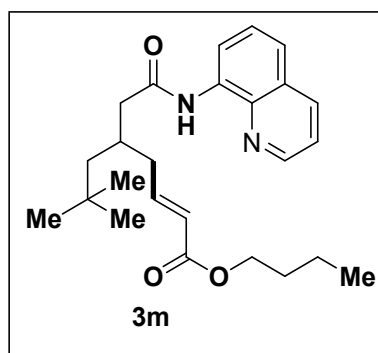


2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl (*E*)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (**3**) was synthesized by general procedure A with acrylate (0.8 mmol, 80 mg) and amide (0.2 mmol, 51 mg) as the substrates. Compound **3k** and **3k^l** (4:1) was obtained as liquid in 12% (8 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). R_f : 0.4 (10:90 ethyl acetate: Petroleum ether).

^1H NMR (400 MHz, CDCl_3) δ = 9.78 (s, 1H), 8.79 (ddd, $J=8.8, 5.5, 1.7$, 2H), 8.17 (dd, $J=8.3, 1.5$, 1H), 7.57 – 7.44 (m, 3H), 7.21 (dt, $J=15.7, 7.9$, 1H), 6.21 – 5.90 (m, 2H), 4.64 (t, $J=13.6, 2\text{H}$), 2.46 (d, $J=4.8, 4\text{H}$), 1.19 (s, 6H).

^{13}C NMR (101 MHz, CDCl_3) δ 169.88, 164.61, 149.15, 148.36, 138.47, 136.54, 134.46, 128.09, 127.52, 122.35, 121.78, 121.72, 116.56, 59.58, 49.81, 44.65, 34.73, 30.75, 27.78.

HRMS (ESI, $\text{M}+\text{H}^+$) m/z calcd. for $\text{C}_{47}\text{H}_{69}\text{N}_2\text{O}_4$ 627.1510, found 627.1512.

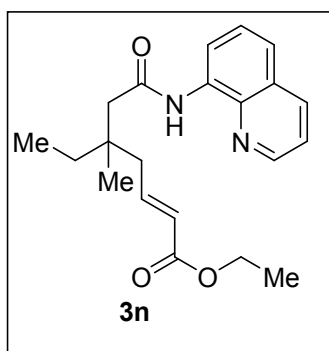


allyl (*E*)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (**3k**) was synthesized by general procedure A with acrylate (0.8 mmol, 102 mg) and amide (0.2 mmol, 57 mg) as the substrates. Pure **3k** was obtained as liquid in 37 % (major isomer) (30 mg) yield after column

chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). R_f : 0.4 (10:90 ethyl acetate:Petroleum ether).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.78 (s, 1H), 8.78 (ddd, $J = 8.9, 5.6, 1.7$, 2H), 8.17 (dd, $J = 8.3, 1.5$, 1H), 7.58 – 7.42 (m, 3H), 7.05 – 6.93 (m, 1H), 5.90 (d, $J = 15.5$, 1H), 4.08 (t, $J = 5.4$, 2H), 2.62 – 2.45 (m, 2H), 2.37 (d, $J = 6.3$, 3H), 1.60 (dt, $J = 14.6, 6.9$, 1H), 1.40 – 1.33 (m, 2H), 0.95 (s, 9H), 0.92 (t, $J = 3.5$, 3H).

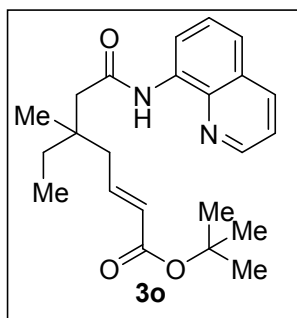
$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.78, 166.65, 148.28, 146.99, 136.59, 134.58, 128.09, 127.58, 123.74, 121.74, 121.63, 116.93, 64.27, 47.35, 44.72, 38.96, 31.45, 31.38, 30.82, 30.00, 19.29, 13.87.



ethyl (E)-5-ethyl-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3l) was synthesized by general procedure A with acrylate (0.8 mmol, 80 mg) and amide (0.2 mmol, 51 mg) as the substrates. Pure **3l** was obtained as liquid in 56% (40 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). R_f : 0.4 (10:90 ethyl acetate: Petroleum ether).

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 9.78 (s, 1H), 8.86 – 8.73 (m, 2H), 8.16 (dd, $J = 8.3, 1.6$, 1H), 7.58 – 7.41 (m, 3H), 7.11 – 6.98 (m, 1H), 6.05 – 5.90 (m, 1H), 4.18 (dt, $J = 11.0, 5.2$, 1H), 2.45 (s, 1H), 2.43 – 2.39 (m, 1H), 1.57 – 1.52 (m, 1H), 1.30 – 1.27 (m, 1H), 1.14 (s, 3H), 0.96 (dd, $J = 9.9, 5.1$, 6H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.16, 166.63, 148.34, 145.71, 138.51, 136.50, 134.57, 128.09, 127.54, 124.47, 121.74, 121.61, 116.54, 60.36, 47.33, 41.80, 37.44, 32.43, 24.78, 14.41, 8.35.



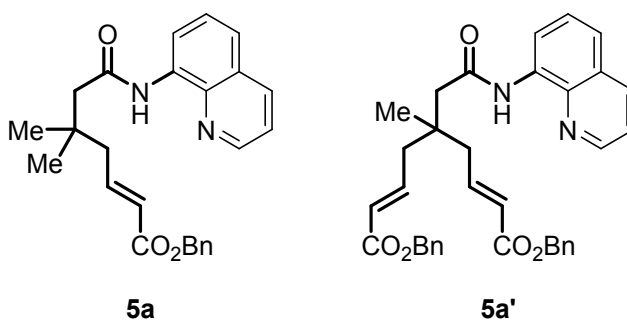
tert-butyl (E)-5-ethyl-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (3m) was synthesized by general procedure A with acrylate (0.8 mmol, 102 mg) and amide (0.2 mmol, 51 mg) as the substrates. Pure **3m** was obtained as liquid in 60% (46 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.78 (s, 1H), 8.80 (ddd, *J* = 8.7, 5.6, 1.5, 2H), 8.16 (dd, *J* = 8.2, 1.3, 1H), 7.57 – 7.41 (m, 3H), 6.96 (ddd, *J* = 20.1, 10.1, 5.6, 1H), 5.89 (dd, *J* = 15.5, 6.2, 1H), 2.44 (s, 2H), 2.38 (d, *J* = 7.8, 2H), 1.55 – 1.51 (m, 2H), 1.48 (s, 9H), 1.14 (s, 3H), 0.96 (t, *J* = 7.5, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 170.22, 166.06, 148.34, 144.38, 138.53, 136.49, 134.62, 128.09, 127.55, 126.15, 121.73, 121.57, 116.54, 80.28, 47.50, 41.67, 37.45, 32.36, 30.76, 28.32, 24.76, 8.37.

IR (thin film) 3353, 3018, 2970, 1724, 1693, 1593, 1526, 1216, 1152, 758 cm⁻¹.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₂₃H₃₀N₂O₄Na 405.2148, found 405.2149.



benzyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (5a) was synthesized by general procedure B with acrylate (0.8 mmol, 130 mg) and amide (0.2 mmol, 48 mg) as the substrates. Pure **5a** was obtained as liquid in 60% (major isomer) (45 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.76 (s, 1H), 8.80 – 8.73 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7, 1H), 7.57 – 7.48 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2, 1H), 7.38 – 7.36 (m, 4H), 7.35 – 7.32 (m, 1H), 7.19 – 7.08 (m, 1H), 6.02 (dt, *J* = 15.5, 1.3, 1H), 5.18 (s, 2H), 2.45 (s, 1H), 2.40 (dd, *J* = 7.9, 1.3, 2H), 1.19 (s, 6H).

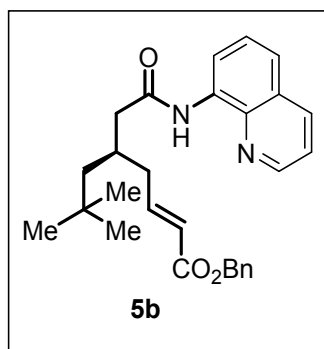
¹³C NMR (126 MHz, CDCl₃) δ 170.01, 166.38, 148.37, 146.44, 138.49, 136.48, 136.23, 134.53, 128.69, 128.07, 127.53, 124.17, 121.74, 121.64, 116.55, 66.26, 49.84, 44.73, 34.70, 27.80.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₂₅H₂₆N₂NaO₃ 425.1834, found 425.1836.

(2*E*,7*E*)-dibenzyl-5-methyl-5-(2-oxo-2-(quinolin-8-ylamino)ethyl)nona-2,7-dienedioate (5a')

¹H NMR (400 MHz, CDCl₃) δ 9.78 (s, 1H), 8.73 (ddd, *J* = 5.9, 5.3, 2.1, 2H), 8.14 (dd, *J* = 8.3, 1.6, 1H), 7.56 – 7.47 (m, 2H), 7.45 – 7.29 (m, 13H), 7.11 (dt, *J* = 15.6, 7.8, 3H), 6.03 (d, *J* = 15.5, 2H), 5.17 (s, 4H), 2.54 – 2.38 (m, 6H), 1.20 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 169.29, 166.16, 148.42, 145.23, 138.43, 136.11, 134.34, 128.69, 128.04, 127.45, 124.83, 121.82, 121.78, 116.61, 66.33, 46.95, 42.47, 37.89, 25.26.



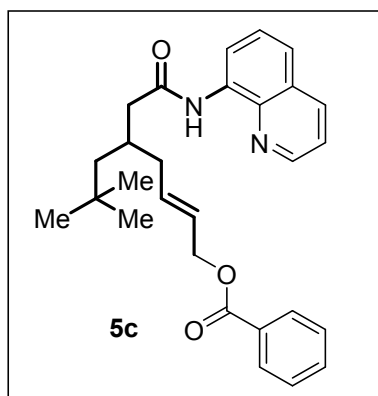
Benzyl (S,E)-7,7-dimethyl-5-(2-oxo-2-(quinolin-8-ylamino)ethyl)oct-2-enoate (5b) was synthesized by general procedure **B** with vinyl iodides (0.4 mmol, 114 mg) and amide (0.2 mmol, 57 mg) as the substrates. Pure **5b** was obtained as liquid in 76 % (68 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.78 (s, 1H), 8.79 – 8.73 (m, 2H), 8.15 (dd, *J* = 8.3, 1.6, 1H), 7.57 – 7.47 (m, 2H), 7.42 (dd, *J* = 8.3, 4.2, 1H), 7.39 – 7.30 (m, 6H), 7.12 – 7.01 (m, 1H), 5.96 (d, *J* = 15.6, 1H), 5.14 (s, 2H), 2.63 – 2.42 (m, 3H), 2.37 (t, *J* = 6.8, 2H), 1.37 – 1.32 (m, 2H), 0.95 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ 170.69, 166.29, 148.34, 147.75, 138.43, 136.45, 134.49, 128.66, 128.05, 127.52, 123.41, 121.73, 121.61, 116.59, 66.19, 47.35, 44.68, 38.97, 31.45, 31.38, 29.99.

IR (thin film) 3022, 1722, 1647, 1527, 1442, 1375, 1220, 1038, 918, 759, 668 cm^{-1} .

HRMS (ESI, $\text{M}+\text{H}^+$) m/z calcd. for $\text{C}_{35}\text{H}_{35}\text{N}_2\text{O}_5$ 563.2538, found 563.2540.

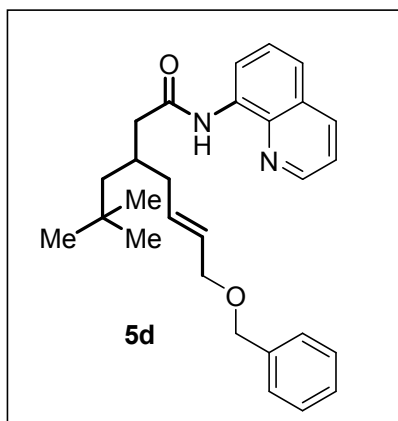


(E)-7,7-dimethyl-5-(2-oxo-2-(quinolin-8-ylamino)ethyl)oct-2-en-1-yl benzoate (**5c**) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 114 mg) and amide (0.2 mmol, 57 mg) as the substrates. Pure **5c** was obtained as liquid in 71% (63 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). R_f : 0.4 (10:90 ethyl acetate: petroleum ether).

^1H NMR (500 MHz, CDCl_3) δ 9.78 (s, 1H), 8.78 (dd, $J = 4.5, 1.5$, 1H), 8.22 – 8.10 (m, 1H), 8.08 – 7.95 (m, 2H), 7.58 – 7.34 (m, 6H), 5.90 (dt, $J = 13.8, 6.8$, 1H), 5.80 – 5.68 (m, 1H), 4.76 (d, $J = 6.1$, 2H), 2.53 (ddd, $J = 21.7, 14.5, 6.3$, 2H), 2.25 (dt, $J = 14.3, 7.5$, 3H), 1.40 – 1.28 (m, 3H), 0.95 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.20, 166.51, 148.28, 138.48, 136.48, 134.64, 132.94, 130.49, 129.73, 128.53, 128.42, 128.09, 127.58, 126.64, 121.71, 121.51, 116.58, 65.57, 47.44, 44.90, 39.25, 31.82, 31.35, 30.06. IR (thin film) 2927, 1719, 1684, 1526, 1486, 1385, 1273, 1217, 762, 713 cm^{-1} .

HRMS (ESI, $\text{M}+\text{Na}^+$) m/z calcd. for $\text{C}_{28}\text{H}_{32}\text{N}_2\text{NaO}_3$ 467.2305, found 467.2305.



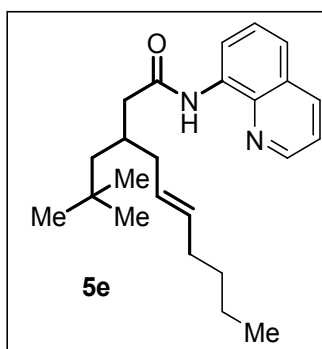
(E)-7-(benzyloxy)-3-neopentyl-*N*-(quinolin-8-yl)hept-5-enamide (**5d**) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 120 mg) and amide (0.2 mmol, 57 mg) as the substrates. Pure **5d** was obtained as liquid in 68% (64 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). R_f : 0.4 (10:90 ethyl acetate:Petroleum ether).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 9.79 (s, 1H), 8.88 – 8.73 (m, 2H), 8.15 (dd, J = 8.3, 1.6, 1H), 7.58 – 7.48 (m, 2H), 7.44 (dd, J = 8.3, 4.2, 1H), 7.38 – 7.32 (m, 4H), 7.30 – 7.24 (m, 3H), 5.82 – 5.72 (m, 1H), 5.67 (dt, J = 15.3, 5.9, 1H), 4.47 (s, 2H), 3.98 (dd, J = 5.8, 1.5, 2H), 2.52 (dd, J = 6.2, 2.7, 2H), 2.30 – 2.22 (m, 1H), 1.34 (dddd, J = 25.5, 21.0, 10.4, 4.6, 2H), 0.95 (s, 9H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 171.31, 148.25, 138.55, 138.44, 136.46, 135.04, 134.65, 132.24, 129.16, 128.52, 128.02, 127.87, 124.10, 121.70, 121.47, 116.52, 71.98, 70.91, 47.43, 44.88, 39.29, 31.85, 31.34, 30.06.

IR (thin film) 3022, 1720, 1530, 1374, 1038, 757 cm^{-1} .

HRMS (ESI, $\text{M}+\text{Na}^+$) m/z calcd. for $\text{C}_{28}\text{H}_{34}\text{N}_2\text{NaO}_2$ 453.2518, found 453.2512.



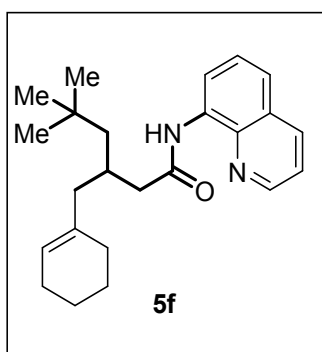
(E)-3-neopentyl-*N*-(quinolin-8-yl)dec-5-enamide (**5e**) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 84 mg) and amide (0.2 mmol, 57 mg) as the substrates. Pure **5e** was obtained as liquid in 66% (48 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.77 (s, 1H), 8.83 – 8.76 (m, 2H), 8.16 (dd, *J* = 8.3, 1.5, 1H), 7.59 – 7.38 (m, 3H), 5.51 – 5.37 (m, 2H), 2.50 (d, *J* = 6.6, 2H), 2.27 – 2.06 (m, 5H), 1.97 (dd, *J* = 12.4, 6.2, 2H), 1.31 (ddt, *J* = 4.6, 7.5, 4.9, 7H), 0.94 (s, 3H), 0.84 (t, *J* = 7.0, 4H).

¹³C NMR (101 MHz, CDCl₃) δ 171.65, 148.20, 138.50, 136.47, 134.75, 133.41, 128.08, 127.74, 127.61, 121.67, 121.39, 116.52, 47.36, 44.97, 39.58, 32.46, 32.18, 31.80, 31.34, 30.09, 22.38, 14.06.

IR (thin film) 2944, 2633, 1655, 1420, 1375, 1039, 921, 770 cm⁻¹.

HRMS (ESI, M+K⁺) *m/z* calcd. for C₂₄H₃₄KN₂O 405.2309, found 405.2303.

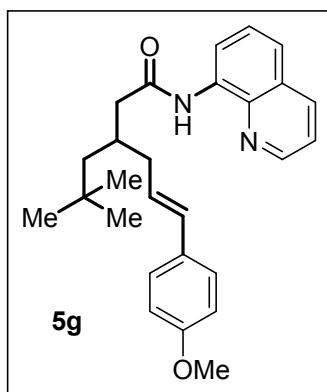


3-(cyclohex-1-en-1-ylmethyl)-5,5-dimethyl-*N*-(quinolin-8-yl)hexanamide (**5f**) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 83 mg) and amide (0.2 mmol, 57 mg) as the substrates. Pure **5f** was obtained as liquid in 70% (51 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ 9.78 (s, 1H), 8.90 – 8.73 (m, 2H), 8.18 (dd, *J* = 8.3, 1.7, 1H), 7.64 – 7.40 (m, 3H), 5.49 (s, 1H), 2.55 – 2.46 (m, 2H), 2.35 – 2.26 (m, 1H), 2.11 (dd, *J* = 13.4, 6.0, 2H), 2.02 – 1.90 (m, 4H), 1.66 – 1.57 (m, 2H), 1.55 – 1.49 (m, 2H), 1.33 (tdd, *J* = 14.1, 9.5, 4.9, 3H), 0.96 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 171.74, 148.19, 138.45, 136.47, 136.38, 134.79, 128.05, 127.60, 123.93, 121.66, 121.29, 116.42, 48.15, 46.45, 45.22, 31.29, 30.14, 29.90, 28.26, 25.43, 23.06, 22.57. **IR** (thin film) 2925, 2861, 1690, 1525, 1485, 1386, 793 cm⁻¹.

HRMS (ESI, M+Na⁺) m/z calcd. for C₂₄H₃₂N₂NaO 387.2405, found 387.2407.

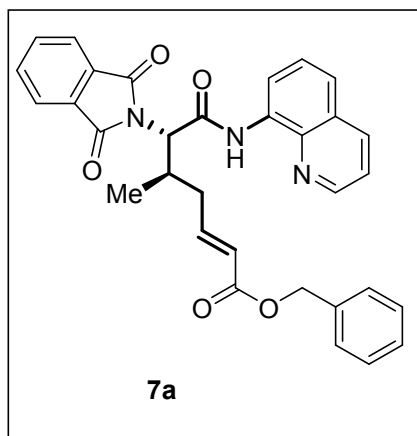


(E)-6-(4-methoxyphenyl)-3-neopentyl-N-(quinolin-8-yl)hex-5-enamide (5g) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 104 mg) and amide (0.2 mmol, 57 mg) as the substrates. Pure **5g** was obtained as liquid in 76 % (63 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 9.79 (s, 1H), 8.85 – 8.73 (m, 2H), 8.14 (dd, *J* = 8.3, 1.6, 1H), 7.58 – 7.38 (m, 3H), 7.23 – 7.16 (m, 3H), 6.79 – 6.71 (m, 1H), 6.37 (d, *J* = 15.8, 1H), 6.11 (dt, *J* = 15.7, 7.0, 1H), 3.78 (s, 3H), 2.60 – 2.51 (m, 2H), 2.41 – 2.29 (m, 2H), 1.48 – 1.29 (m, 3H), 0.97 (s, 9H).

¹³C NMR (101 MHz, CDCl₃) δ 171.47, 158.80, 148.18, 138.46, 136.45, 134.70, 131.68, 130.63, 128.07, 127.59, 127.23, 126.35, 121.65, 121.42, 116.56, 113.91, 55.41, 47.60, 45.07, 40.06, 32.35, 31.45, 30.10.

IR (thin film) 3390, 1677, 1526, 1279, 1216, 757, 668. cm⁻¹.

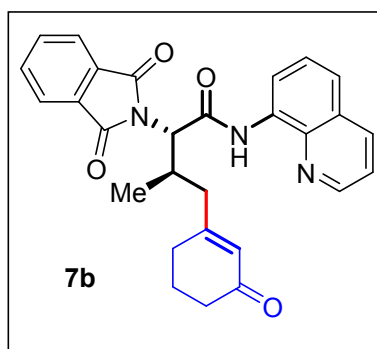


Benzyl (5*R*,6*S*,*E*)-6-(1,3-dioxisoindolin-2-yl)-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (7a) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 114 mg) and amide (0.2 mmol, 73 mg) as the substrates. Pure **7a** was obtained as liquid in 76% (79 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). **R_f**: 0.4 (20:80 ethyl acetate: Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ 10.51 (s, 1H), 8.76 (dd, *J* = 4.2, 1.6, 1H), 8.71 (dt, *J* = 8.4, 4.2, 1H), 8.12 (dd, *J* = 8.3, 1.6, 1H), 7.92 – 7.86 (m, 2H), 7.77 – 7.71 (m, 2H), 7.53 – 7.49 (m, 2H), 7.40 (dt, *J* = 8.5, 4.2, 1H), 7.37 – 7.30 (m, 5H), 7.15 – 7.02 (m, 1H), 5.98 (d, *J* = 15.6, 1H), 5.14 (s, 2H), 4.81 (d, *J* = 10.5, 1H), 3.35 – 3.23 (m, 1H), 2.78 – 2.67 (m, 1H), 2.24 (dt, *J* = 4.5, 8.7, 1H), 0.99 (d, *J* = 6.7, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 168.12, 166.29, 166.12, 148.72, 146.54, 138.76, 136.32, 136.15, 134.54, 134.08, 131.64, 128.67, 128.30, 128.00, 127.33, 123.91, 123.63, 122.30, 121.81, 117.18, 66.23, 60.96, 37.12, 31.81, 16.48. **IR** (thin film) 3019, 2969, 1720, 1678, 1593, 1526, 1485, 1216, 844, 758, 668 cm⁻¹.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₃₂H₂₇N₃NaO₅ 556.1845, found 556.1843.



(2*S*,3*R*)-2-(1,3-dioxisoindolin-2-yl)-3-methyl-4-(3-oxocyclohex-1-en-1-yl)-*N*-(quinolin-8-yl)butanamide (7b) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol,

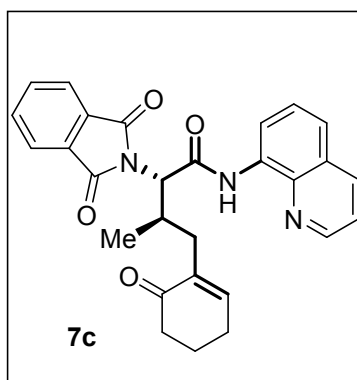
93mg) and amide (0.2 mmol, 73 mg) as the substrates. Pure **7b** was obtained as liquid in 58% (53 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). **R_f**: 0.4 (20:80 ethyl acetate: Petroleum ether). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 10.48 (s, 1H), 8.77 (dd, *J* = 4.2, 1.6, 1H), 8.75 – 8.68 (m, 1H), 8.13 (dd, *J* = 8.3, 1.6, 1H), 7.93 – 7.86 (m, 2H), 7.78 – 7.71 (m, 2H), 7.53 – 7.49 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2, 1H), 5.94 (s, 1H), 4.80 (d, *J* = 10.5, 1H), 3.46 – 3.27 (m, 1H), 2.76 (dd, *J* = 13.4, 2.5, 1H), 2.49 (dt, *J* = 17.9, 5.9, 1H), 2.40 – 2.29 (m, 3H), 2.12 (dd, *J* = 13.4, 10.5, 1H), 2.01 – 1.92 (m, 2H), 0.91 (d, *J* = 6.6, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 199.82, 168.05, 166.18, 163.76, 148.68, 138.71, 136.40, 134.61, 133.99, 131.58, 128.02, 127.96, 127.32, 123.94, 122.38, 121.86, 117.20, 60.99, 43.47, 37.45, 30.18, 29.39, 22.84, 16.26.

IR (thin film) 3332, 2926, 1769, 1718, 1672, 1530, 1487, 1381, 1326, 1071, 883, 722, 331 cm⁻¹.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₂₈H₂₅N₃NaO₄ 490.1741, found 490.1737.

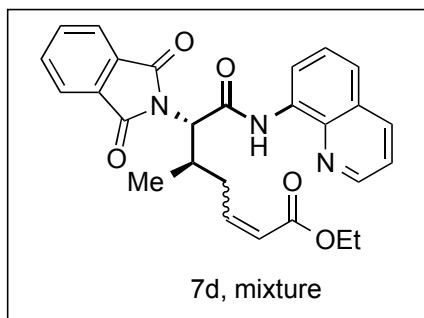


(2*S*,3*R*)-2-(1,3-dioxisoindolin-2-yl)-3-methyl-4-(6-oxocyclohex-1-en-1-yl)-*N*-(quinolin-8-yl)butanamide (7c) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 93mg) and amide (0.2 mmol, 73 mg) as the substrates. Pure **7c** was obtained as liquid in 32 % (major isomer, dr 10:1) (29 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). **R_f**: 0.4 (20:80 ethyl acetate: Petroleum ether). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 10.58 (s, 1H), 8.83 (dd, *J* = 4.2, 1.5, 1H), 8.79 – 8.70 (m, 1H), 8.12 (dt, *J* = 6.9, 3.4, 1H), 7.92 – 7.85 (m, 2H), 7.72 (dd, *J* = 5.4, 3.0, 2H), 7.53 – 7.47 (m, 3H), 7.42 (dt, *J* = 13.6, 6.8, 1H), 6.92 (t, *J* = 4.0, 1H), 4.83 (d, *J* = 10.2, 1H), 3.32 – 3.16 (m, 1H), 2.61 – 2.19 (m, 4H), 1.86 (qd, *J* = 13.0, 6.7, 2H), 1.69 (s, 2H), 0.91 (d, *J* = 6.7, 3H).

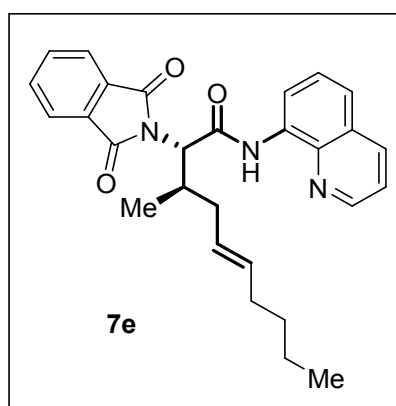
^{13}C NMR (126 MHz, CDCl_3) δ 199.20, 168.20, 166.74, 148.69, 147.50, 138.87, 137.40, 136.24, 134.39, 131.78, 128.04, 127.32, 123.80, 122.11, 121.78, 117.14, 61.54, 38.44, 33.89, 32.28, 26.23, 23.02, 16.72.

IR (thin film) 3021, 1720, 1663, 1532, 1487, 1218, 756, 668, 531 cm^{-1} .



Methyl (6S)-6-(1,3-dioxisoindolin-2-yl)-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (7d) was synthesized by general procedure A with vinyl iodide (0.4 mmol, 93mg) and amide (0.2 mmol, 73 mg) as the substrates. Compound **7d** was obtained as liquid in 24% (mixture of isomers) (21 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). R_f : 0.4 (10:90 ethyl acetate: Petroleum ether).

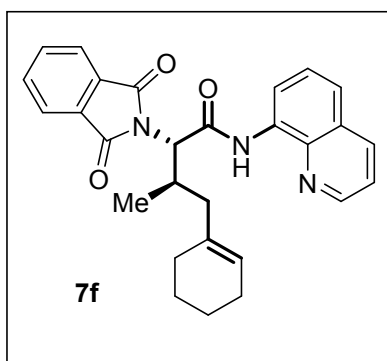
^1H NMR (500 MHz, CDCl_3) δ = 10.54 (s, 1H), 8.81 (d, $J=29.2$, 3H), 8.21 (d, $J=8.0$, 2H), 8.03 – 7.77 (m, 2H), 7.77 (s, 3H), 7.65 – 7.40 (m, 3H), 6.37 (s, 1H), 5.87 (d, $J=12.8$, 1H), 5.15 – 4.81 (m, 1H), 4.07 (d, $J=7.1$, 2H), 3.30 (s, 1H), 3.04 (s, 1H), 2.92 (s, 1H), 1.03 (d, $J=6.5$, 3H).



(2S,3R,E)-2-(1,3-dioxisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)dec-5-enamide (7e) was synthesized by general procedure A with vinyl iodide (0.4 mmol, 84 mg) and amide (0.2 mmol, 73 mg) as the substrates. Pure **7e** was obtained as liquid in 52 % (major isomer) (46 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). R_f : 0.4 (20:80 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 10.54 (s, 1H), 8.88 – 8.82 (m, 1H), 8.79 – 8.71 (m, 1H), 8.13 (dd, *J* = 8.3, 1.7, 1H), 7.92 – 7.80 (m, 2H), 7.76 – 7.71 (m, 2H), 7.52 – 7.48 (m, 2H), 7.48 – 7.40 (m, 1H), 5.52 – 5.47 (m, 2H), 4.80 (d, *J* = 10.7, 1H), 3.26 – 3.05 (m, 1H), 2.43 (dt, *J* = 5.9, 3.6, 1H), 2.11 – 1.91 (m, 4H), 0.95 (d, *J* = 6.7, 4H), 0.87 (dd, *J* = 8.6, 4.3, 5H).

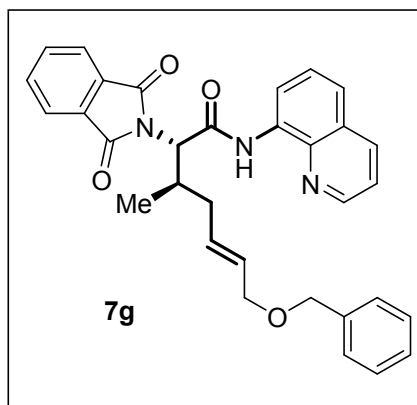
¹³C NMR (101 MHz, CDCl₃) δ 168.28, 168.26, 166.84, 148.62, 138.87, 136.30, 134.38, 134.01, 131.79, 128.05, 127.39, 126.38, 123.78, 122.08, 121.73, 117.15, 61.36, 37.34, 32.35, 31.70, 29.50, 22.83, 16.26, 14.24.



(2*S*,3*R*)-4-(cyclohex-1-en-1-yl)-2-(1,3-dioxoisindolin-2-yl)-3-methyl-*N*-(quinolin-8-yl)butanamide (7f) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 83 mg) and amide (0.2 mmol, 73 mg) as the substrates. Pure **7f** was obtained as liquid in 61% (54 mg, dr 10:1) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). **R_f**: 0.4 (20:80 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 10.58 (s, 1H), 8.82 (dt, *J* = 14.6, 7.3, 1H), 8.74 (dd, *J* = 9.0, 4.4, 1H), 8.14 (dd, *J* = 8.3, 1.6, 1H), 7.92 – 7.85 (m, 1H), 7.77 – 7.69 (m, 3H), 7.50 (t, *J* = 3.7, 2H), 7.44 (dd, *J* = 8.2, 4.2, 2H), 5.47 (s, 1H), 4.74 (t, *J* = 9.2, 1H), 3.35 – 3.17 (m, 1H), 2.41 (d, *J* = 12.2, 1H), 2.17 – 2.02 (m, 2H), 2.02 – 1.79 (m, 3H), 1.71 – 1.46 (m, 5H), 0.94 – 0.88 (m, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 168.26, 166.88, 148.53, 138.75, 136.36, 135.18, 134.39, 131.82, 128.07, 127.44, 124.03, 123.80, 122.08, 121.75, 117.28, 62.20, 43.50, 30.27, 28.26, 25.44, 23.08, 22.55, 16.31.



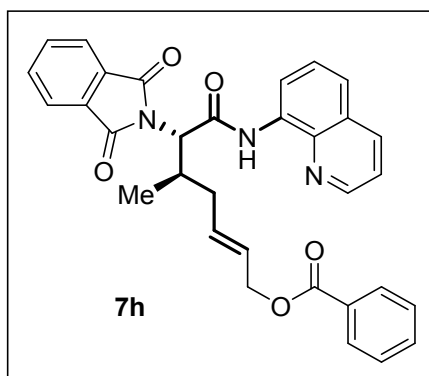
(2*S*,3*R*,*E*)-7-(benzyloxy)-2-(1,3-dioxisoindolin-2-yl)-3-methyl-*N*-(quinolin-8-yl)hept-5-enamide (7g) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 93mg) and amide (0.2 mmol, 73 mg) as the substrates. Pure **7g** was obtained as liquid in 63% (63 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). **R_f**: 0.4 (20:80 ethyl acetate:Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 8.79 (dd, *J* = 4.2, 1.6, 1H), 8.77 – 8.72 (m, 1H), 8.13 (dd, *J* = 8.3, 1.6, 1H), 7.92 – 7.86 (m, 2H), 7.76 – 7.71 (m, 2H), 7.51 (dd, *J* = 8.5, 4.5, 2H), 7.42 (dd, *J* = 8.3, 4.2, 1H), 7.35 – 7.30 (m, 4H), 7.29 – 7.20 (m, 2H), 5.91 – 5.77 (m, 1H), 5.70 (dt, *J* = 15.4, 5.9, 1H), 4.82 (d, *J* = 10.7, 1H), 4.47 (s, 2H), 3.97 (d, *J* = 5.9, 2H), 3.31 – 3.14 (m, 1H), 2.54 (dt, *J* = 13.9, 4.4, 1H), 2.15 (dt, *J* = 14.3, 8.3, 1H), 0.99 (d, *J* = 6.7, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 168.22, 166.66, 148.66, 138.78, 138.50, 136.30, 134.43, 134.25, 131.71, 130.88, 129.68, 128.47, 128.01, 127.90, 127.63, 127.35, 123.82, 122.17, 121.77, 117.13, 71.95, 70.71, 61.24, 37.14, 32.10, 16.35.

IR (thin film) 3337, 3018, 2931, 1772, 1720, 1529, 1487, 1378, 1328, 1216, 1099, 826, 791, 756, 721, 531 cm⁻¹.

HRMS (ESI, M+Na⁺) *m/z* calcd. for C₃₂H₂₉N₃NaO₄ 542.2053, found 542.2050.



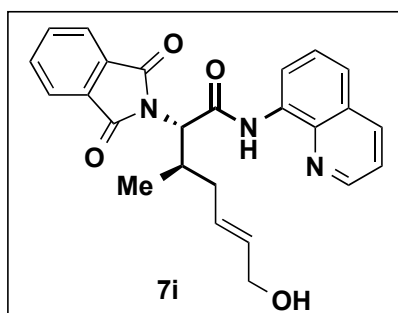
(5*R*,6*S*,*E*)-6-(1,3-dioxisoindolin-2-yl)-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-en-1-yl benzoate (**7h**) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 120 mg) and amide (0.2 mmol, 73 mg) as the substrates. Pure **7h** was obtained as liquid in 71% (74 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). **R_f**: 0.4 (20:80 ethyl acetate: Petroleum ether).

¹H NMR (500 MHz, CDCl₃) δ 10.54 (s, 1H), 8.79 (dd, *J* = 4.2, 1.6, 1H), 8.77 – 8.71 (m, 1H), 8.12 (dt, *J* = 8.3, 4.1, 1H), 8.04 – 7.99 (m, 1H), 7.91 – 7.86 (m, 1H), 7.76 – 7.69 (m, 1H), 7.56 – 7.51 (m, 1H), 7.50 (t, *J* = 4.2, 1H), 7.45 – 7.37 (m, 1H), 6.00 – 5.90 (m, 1H), 5.79 (dt, *J* = 15.3, 6.1, 1H), 4.82 (d, *J* = 10.6, 1H), 4.74 (t, *J* = 6.6, 1H), 3.30 – 3.15 (m, 1H), 2.62 – 2.51 (m, 1H), 2.16 (dt, *J* = 14.4, 8.3, 1H), 0.99 (d, *J* = 6.7, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 168.19, 166.60, 166.46, 148.65, 138.81, 136.31, 134.44, 134.25, 132.96, 132.52, 131.73, 130.44, 129.75, 128.43, 128.03, 127.36, 127.06, 123.83, 122.19, 121.76, 117.17, 65.36, 61.25, 37.20, 32.11, 16.38.

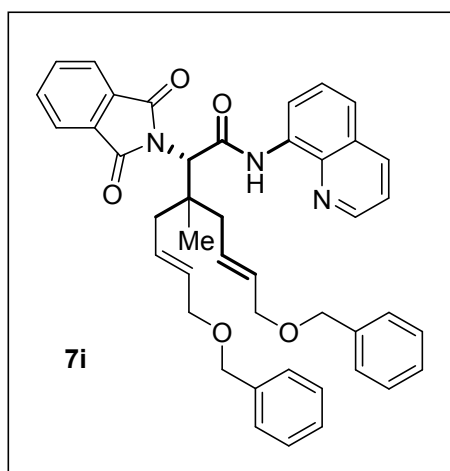
IR (thin film) 3354, 3025, 2958, 1716, 1682, 1526, 1486, 1424, 791, 756, 697 cm⁻¹.

HRMS (ESI, M+H⁺) *m/z* calcd. for C₃₂H₂₈N₃O₅ 534.2020, found 534.2023.



(2*S*,3*R*,*E*)-2-(1,3-dioxisoindolin-2-yl)-7-hydroxy-3-methyl-N-(quinolin-8-yl)hept-5-enamide, was synthesized by general procedure **A** with acrylate (0.8 mmol, 80 mg) and amide (0.2 mmol, 51 mg) as the substrates. compound **7i** was obtained as liquid in 10% (12 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (10:90 ethyl acetate: Petroleum ether).

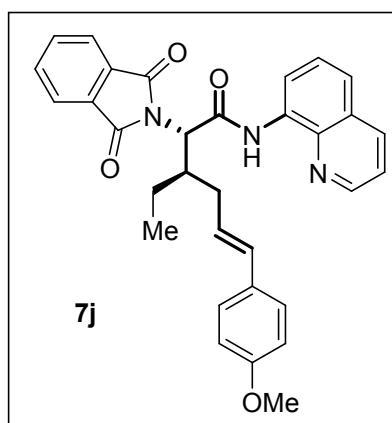
¹H NMR (400 MHz, CDCl₃) δ = 10.53 (s, 1H), 8.94 – 8.59 (m, 2H), 8.15 (dd, *J*=8.3, 1.6, 1H), 7.95 – 7.85 (m, 2H), 7.82 – 7.68 (m, 2H), 7.58 – 7.35 (m, 4H), 5.91 – 5.69 (m, 2H), 4.78 (dd, *J*=30.6, 17.2, 1H), 4.15 – 4.00 (m, 2H), 3.95 (s, 1H), 3.41 – 3.15 (m, 1H), 2.48 (dt, *J*=9.7, 4.7, 1H), 2.29 – 2.02 (m, 2H), 1.09 – 0.95 (m, 3H).



(S,E)-7-(benzyloxy)-3-((*E*)-4-(benzyloxy)but-2-en-1-yl)-2-(1,3-dioxoisindolin-2-yl)-3-methyl-*N*-(quinolin-8-yl)hept-5-enamide (**7i**) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 93mg) and amide (0.2 mmol, 75 mg) as the substrates. Pure **7i** was obtained as liquid in 78% (103 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 10:1). **R_f**: 0.4 (20:80 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 10.27 (s, 1H), 8.71 (dd, *J* = 6.7, 2.3, 1H), 8.58 (dd, *J* = 4.2, 1.6, 1H), 8.10 (dd, *J* = 8.3, 1.6, 1H), 7.89 (dd, *J* = 5.5, 3.0, 2H), 7.74 (dd, *J* = 5.5, 3.1, 2H), 7.54 – 7.47 (m, 2H), 7.36 (dd, *J* = 8.3, 4.2, 1H), 7.33 – 7.23 (m, 10H), 5.89 – 5.67 (m, 4H), 5.25 (s, 1H), 4.47 (d, *J* = 9.9, 4H), 3.98 (d, *J* = 5.4, 2H), 3.92 (d, *J* = 5.7, 2H), 2.81 (dd, *J* = 14.1, 7.7, 1H), 2.58 – 2.45 (m, 2H), 2.39 (dd, *J* = 13.9, 6.5, 1H), 1.35 (s, 3H).

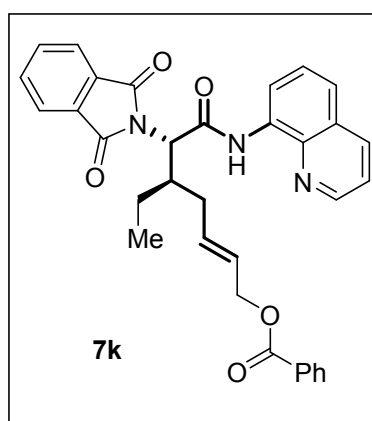
¹³C NMR (126 MHz, CDCl₃) δ 168.67, 166.00, 148.38, 138.77, 138.61, 138.57, 136.30, 134.44, 131.82, 130.86, 129.46, 129.40, 128.01, 127.89, 127.61, 127.43, 123.81, 121.97, 121.67, 117.10, 71.90, 71.89, 70.80, 70.70, 61.00, 41.75, 41.12, 40.44, 23.17.



(2*S*,3*R*,*E*)-2-(1,3-dioxisoindolin-2-yl)-3-ethyl-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-enamide (7j) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 104 mg) and amide (0.2 mmol, 75 mg) as the substrates. Pure **7j** was obtained as liquid in 75% (86 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4 (20:80 ethyl acetate: Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 10.59 (s, 1H), 8.81 (dt, *J* = 7.5, 3.7, 1H), 8.77 – 8.70 (m, 1H), 8.16 – 8.10 (m, 1H), 7.91 – 7.85 (m, 2H), 7.77 – 7.71 (m, 2H), 7.50 – 7.45 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2, 1H), 7.18 – 7.12 (m, 2H), 6.77 – 6.69 (m, 2H), 6.38 (d, *J* = 15.8, 1H), 6.13 (dt, *J* = 7.7, 7.3, 1H), 4.98 (dd, *J* = 11.0, 4.5, 1H), 3.78 (s, 3H), 3.23 (qd, *J* = 10.9, 8.1, 1H), 2.62 – 2.41 (m, 2H), 1.59 (dtd, *J* = 18.5, 7.4, 3.7, 3H), 0.95 (t, *J* = 7.4, 3H).

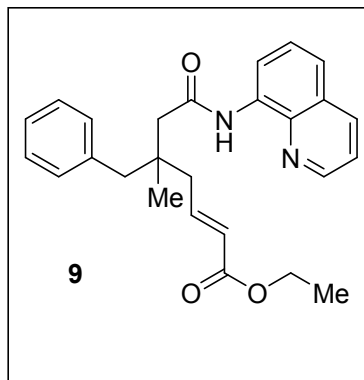
¹³C NMR (101 MHz, CDCl₃) δ 168.30, 167.02, 158.83, 148.57, 138.78, 136.33, 134.39, 131.98, 131.80, 130.43, 128.03, 127.36, 127.25, 124.72, 123.80, 122.13, 121.70, 117.32, 113.87, 59.83, 55.41, 37.68, 33.29, 22.30, 9.95.



(5*R*,6*S*,*E*)-6-(1,3-dioxisoindolin-2-yl)-5-ethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-en-1-yl benzoate (7k) was synthesized by general procedure **B** with vinyl iodide (0.4 mmol, 93mg) and amide (0.2 mmol, 75 mg) as the substrates. Pure **7k** was obtained as liquid in 66% (71 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.3 (20:80 ethyl acetate:Petroleum ether).

¹H NMR (400 MHz, CDCl₃) δ 10.59 (s, 1H), 8.85 – 8.80 (m, 1H), 8.77 – 8.71 (m, 1H), 8.13 (td, *J* = 8.0, 1.7, 1H), 8.02 – 7.97 (m, 1H), 7.91 – 7.85 (m, 1H), 7.78 – 7.70 (m, 1H), 7.56 – 7.47 (m, 1H), 7.45 – 7.36 (m, 1H), 5.94 (ddd, *J* = 14.4, 7.6, 6.7, 1H), 5.78 (dt, *J* = 15.4, 6.1, 1H), 4.95 (d, *J* = 11.0, 1H), 4.67 (d, *J* = 6.0, 1H), 3.18 (qd, *J* = 11.0, 8.0, 1H), 2.53 – 2.33 (m, 1H), 1.57 (ddd, *J* = 14.2, 7.5, 3.6, 1H), 1.34 (dt, *J* = 21.6, 7.4, 1H), 0.92 (t, *J* = 7.4, 3H).

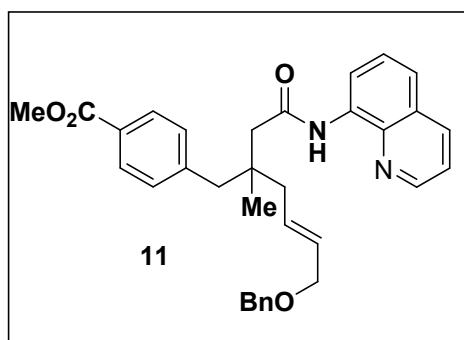
^{13}C NMR (101 MHz, CDCl_3) δ 168.24, 166.85, 166.41, 148.62, 138.71, 136.38, 134.42, 134.24, 132.93, 132.26, 131.72, 130.40, 129.72, 128.40, 128.02, 127.35, 126.97, 123.81, 122.22, 121.75, 117.28, 65.35, 59.60, 37.14, 32.62, 22.15, 9.79.



Ethyl (E)-5-benzyl-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate (9) was synthesized by general procedure A with acrylates (0.8 mmol, 40 mg) and amide (0.1 mmol, 31.8 mg) as the substrates. Compound **9** and **9¹** (4:1) was obtained as liquid in 44% (18.3 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). **R_f**: 0.4(10:90 ethyl acetate: Petroleum ether).

^1H NMR (500 MHz, CDCl_3) δ 9.81 (s, 1H), 8.87 – 8.81 (m, 3H), 8.20 (dd, J = 8.2, 1.3, 1H), 7.62 – 7.52 (m, 3H), 7.48 (dt, J = 13.2, 6.6, 2H), 7.33 – 7.24 (m, 8H), 7.18 (dt, J = 15.5, 7.8, 2H), 5.98 (d, J = 15.5, 1H), 4.23 – 4.18 (m, 2H), 3.01 – 2.82 (m, 2H), 2.59 – 2.39 (m, 4H), 1.31 – 1.26 (t, 3H), 1.16 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 170.12, 166.55, 148.21, 145.51, 137.95, 131.07, 128.13, 127.57, 126.45, 124.82, 121.73, 121.72, 60.37, 46.44, 45.92, 42.22, 38.24, 25.15, 14.38.



methyl (E)-4-(6-(benzyloxy)-2-methyl-2-(2-oxo-2-(quinolin-8-ylamino)ethyl)hex-4-en-1-yl)benzoate (11) was synthesized by general procedure B with vinyl iodide (0.23 mmol, 62

mg) and amide (0.11 mmol, 45 mg) as the substrates. Pure **11** was obtained as liquid in 62 % (38 mg) yield after column chromatography of the crude reaction mixture (silica gel, mesh 100-200; petroleum ether: ethyl acetate; 19:1). R_f : 0.3 (10:90 ethyl acetate: Petroleum ether).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.86 (s, 1H), 8.84 (d, $J = 7.2$, 1H), 8.77 (dd, $J = 4.2$, 1.5, 1H), 8.23 (d, $J = 6.8$, 1H), 7.95 (d, $J = 8.3$, 2H), 7.63 – 7.44 (m, 3H), 7.40 – 7.27 (m, 6H), 5.90 (dt, $J = 15.0$, 7.3, 1H), 5.77 – 5.67 (m, 1H), 4.50 (s, 2H), 4.03 (d, $J = 5.7$, 2H), 3.90 (s, 3H), 3.03 (d, $J = 13.0$, 1H), 2.87 (d, $J = 13.0$, 1H), 2.40 (ddd, $J = 21.6$, 18.8, 10.9, 3H), 2.23 (dd, $J = 13.9$, 7.1, 1H), 1.09 (s, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 176.92, 170.57, 167.36, 146.55, 138.53, 137.73, 131.18, 130.78, 129.87, 129.32, 128.33, 128.31, 128.29, 127.89, 127.74, 127.70, 123.92, 121.85, 121.67, 77.16, 72.11, 70.88, 52.14, 46.21, 45.62, 42.73, 38.13, 25.14.

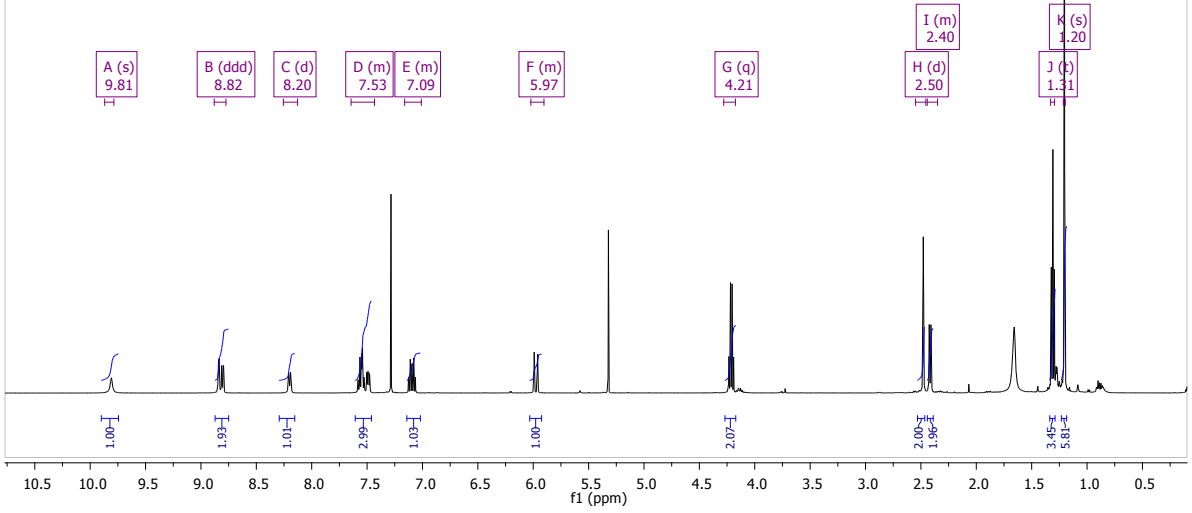
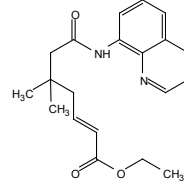
References:

1. Xie, Y.; Guo, S.; Wu, L.; Xia, C.; Huang, H. *Angew. Chem. Int. Ed.* **2015**, *54*, 5900.
2. Newman, S. M.; Gill, N. *J. Org. Chem.* **1966**, *31*, 3860.
3. Ravu, V. R.; Leung, G. Y. C.; Lim, C. S.; Ng, S. Y.; Sum, R. J.; Chen, D. K-Y. *Eur. J. Org. Chem.* **2011**, 463.
4. Zhang, H.; Cui, W-C.; Hu, Z-L.; Yu, S-Y.; Wang, S.; Yao, Z-J. *RSC Adv.* **2012**, *2*, 5101.
5. Wang, S.; Guo, R.; Wang, G.; Chen, Y, S.; Yu, Q, X. *Chem. Commun.*, **2014**, *50*, 12718.
6. Wang, B.; Lu, C.; Zhang, S.-Y.; He, G.; Nack, W. A.; Chen, G. *Org. Lett.* **2014**, *16*, 6260.
7. Wyler, B.; Brucelle, F.; Renaud, P. *Org. Lett.*, **2016**, *18*, 1370.
8. Kropp, P. J.; McNeely, S. A.; Davis, R. D. *J. Am. Chem. Soc.* **1983**, *105*, 6907.
9. Stille, J. K.; Simpson, J. H. *J. Am. Chem. Soc.* **1987**, *109*, 2138.
10. Faizi, D. J.; Issaian, A.; Davis, A. J.; Blum, S. A. *J. Am. Chem. Soc.* **2016**, *138*, 2126.
11. Xu, R.-S.; Yue, L.; Pan, Y.-J. *Tetrahedron*, **2012**, *68*, 5046.
12. Arai, S.; Koike, Y.; Hada, H.; Nishida, A. *J. Am. Chem. Soc.* **2010** *132*, 4522.

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DM-NT-49-P-1H

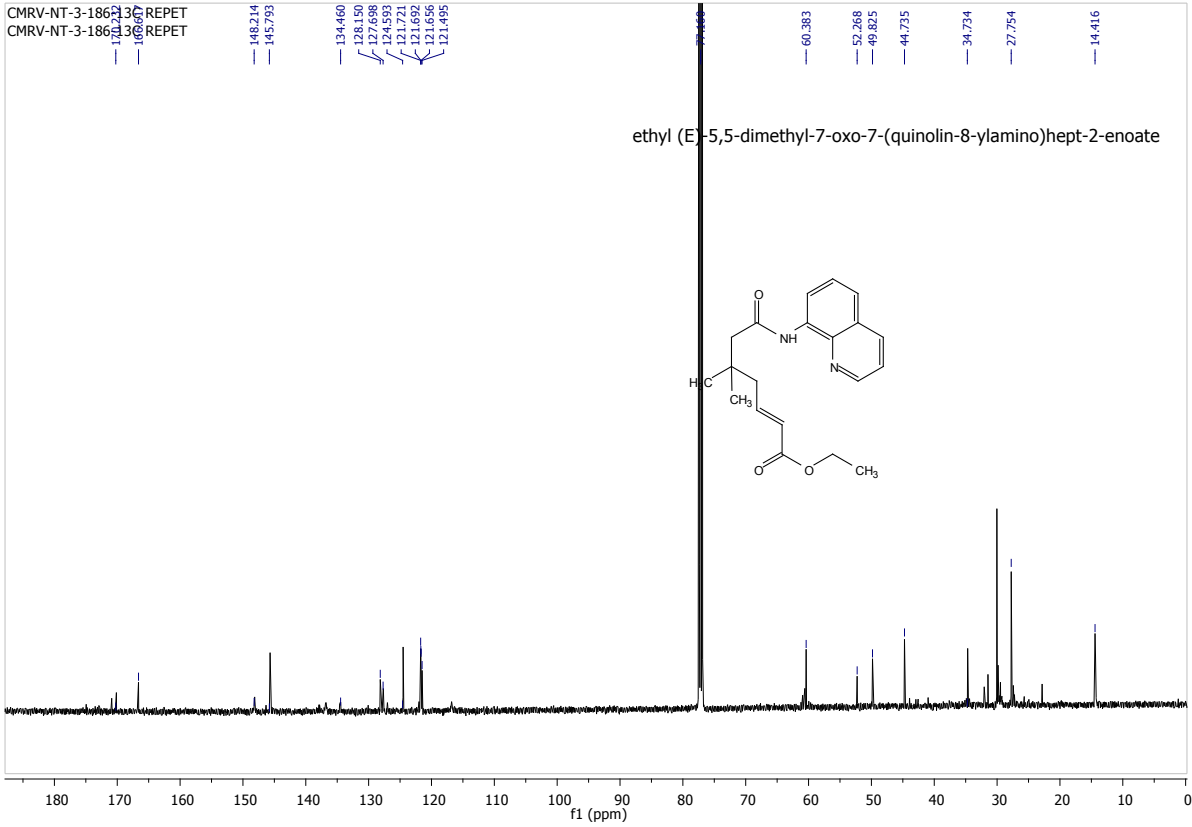
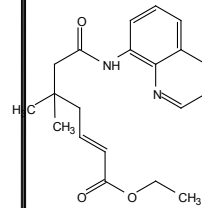
ethyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

¹H NMR (500 MHz, CDCl₃)



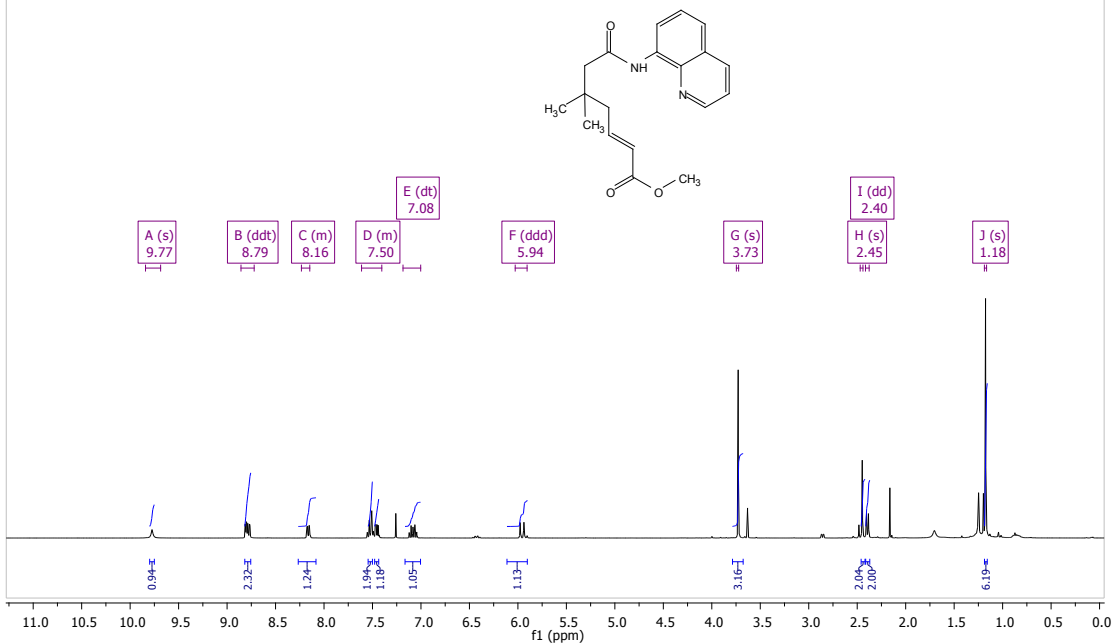
CMRV-NT-3-186
CMRV-NT-3-186

ethyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate



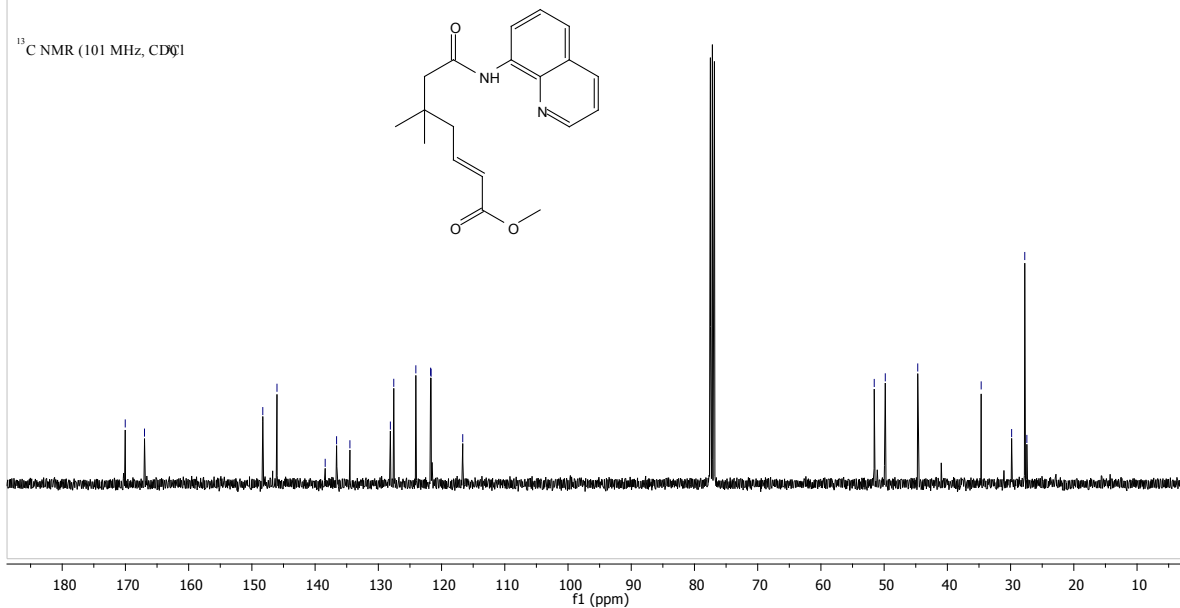
CRVM-SK-133-P-1H
CRVM-SK-133-P-1H

methyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate



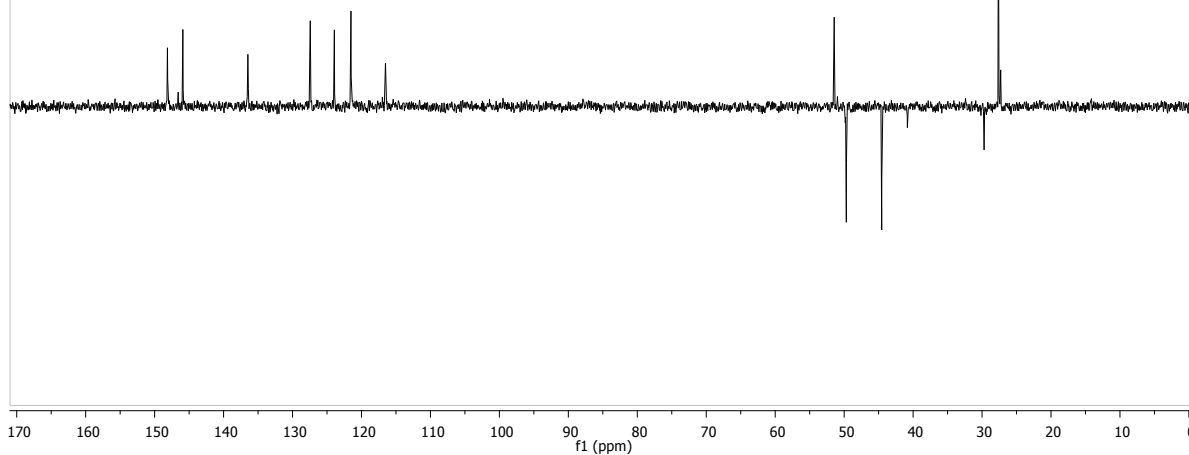
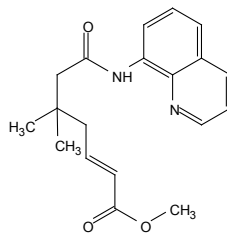
CRVM-SK-133-P-
CRVM-SK-133-P-

methyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate



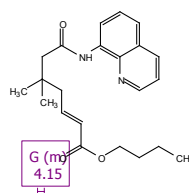
CRVM-SK-133-P-dept
CRVM-SK-133-P-dept

methyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

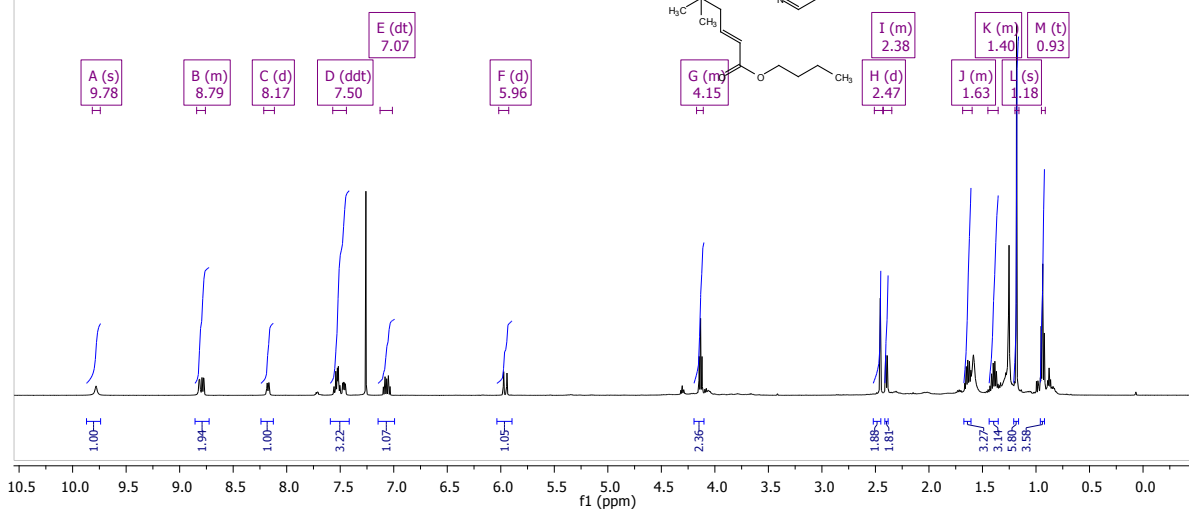


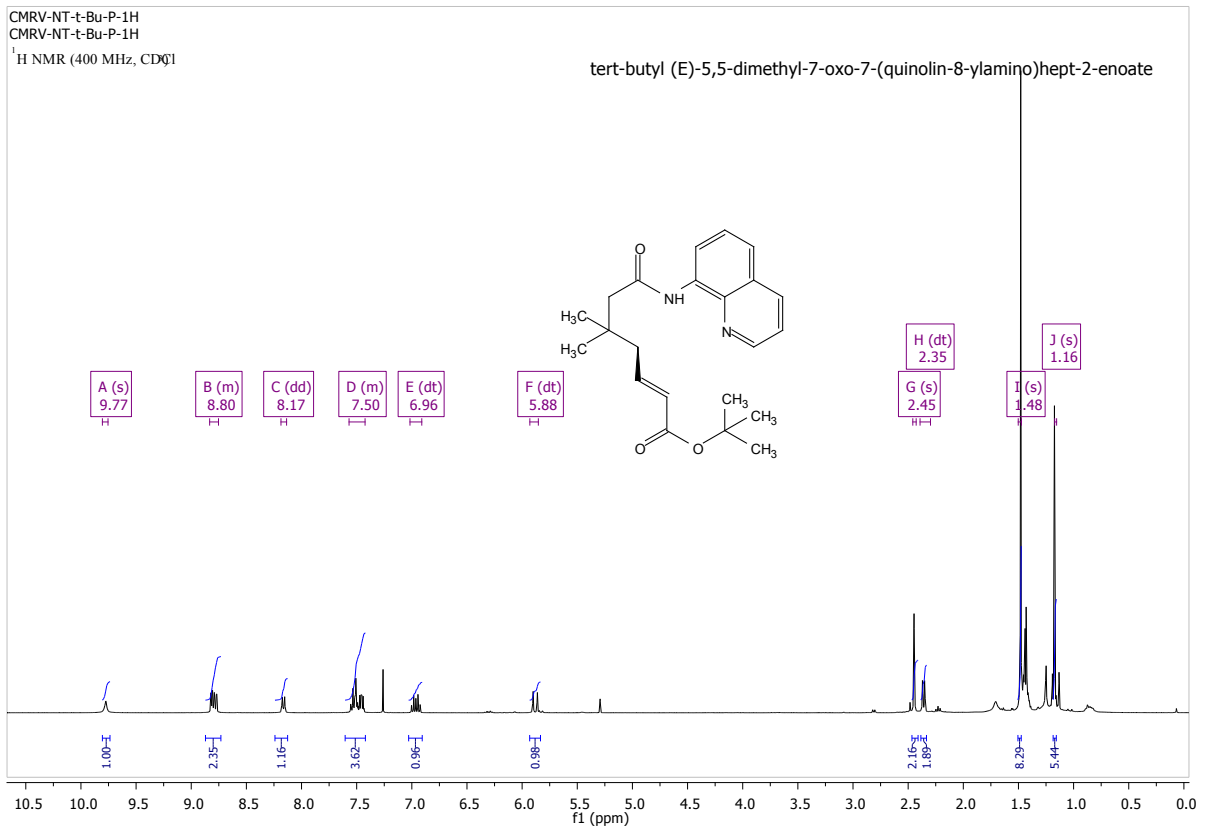
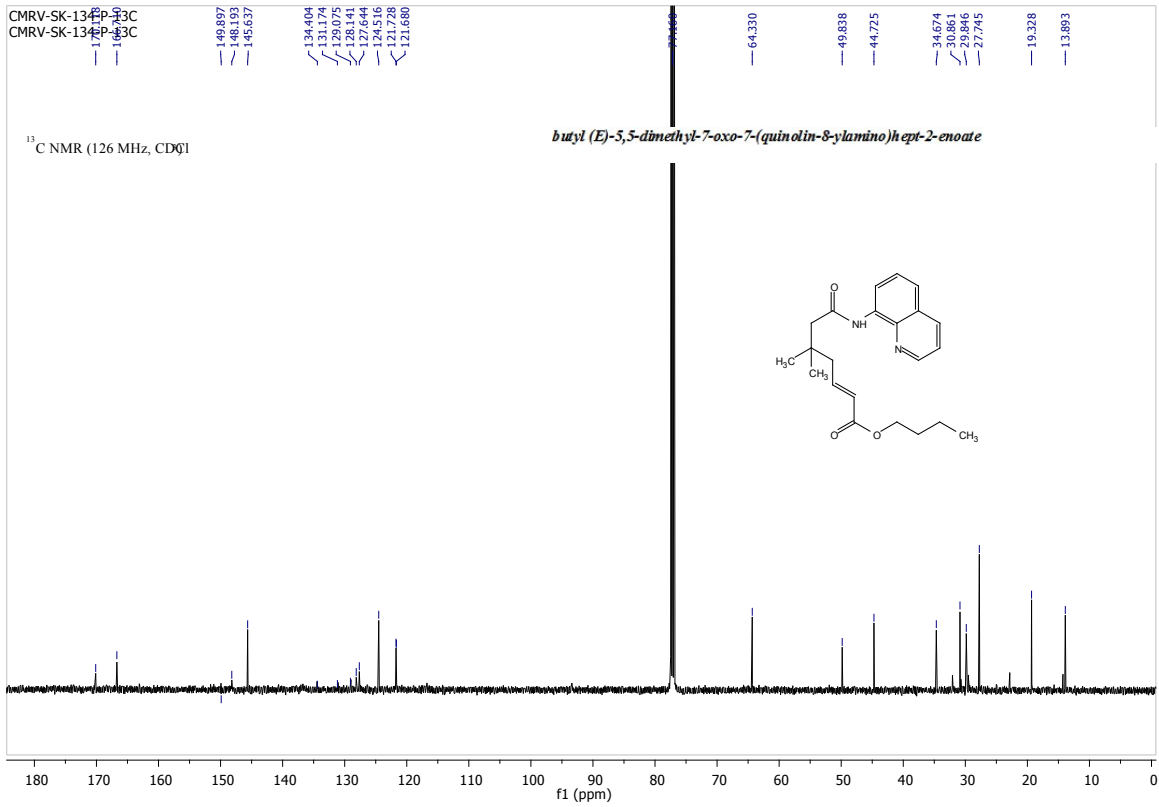
CMRV-SK-134-P-1H
CMRV-SK-134-P-1H

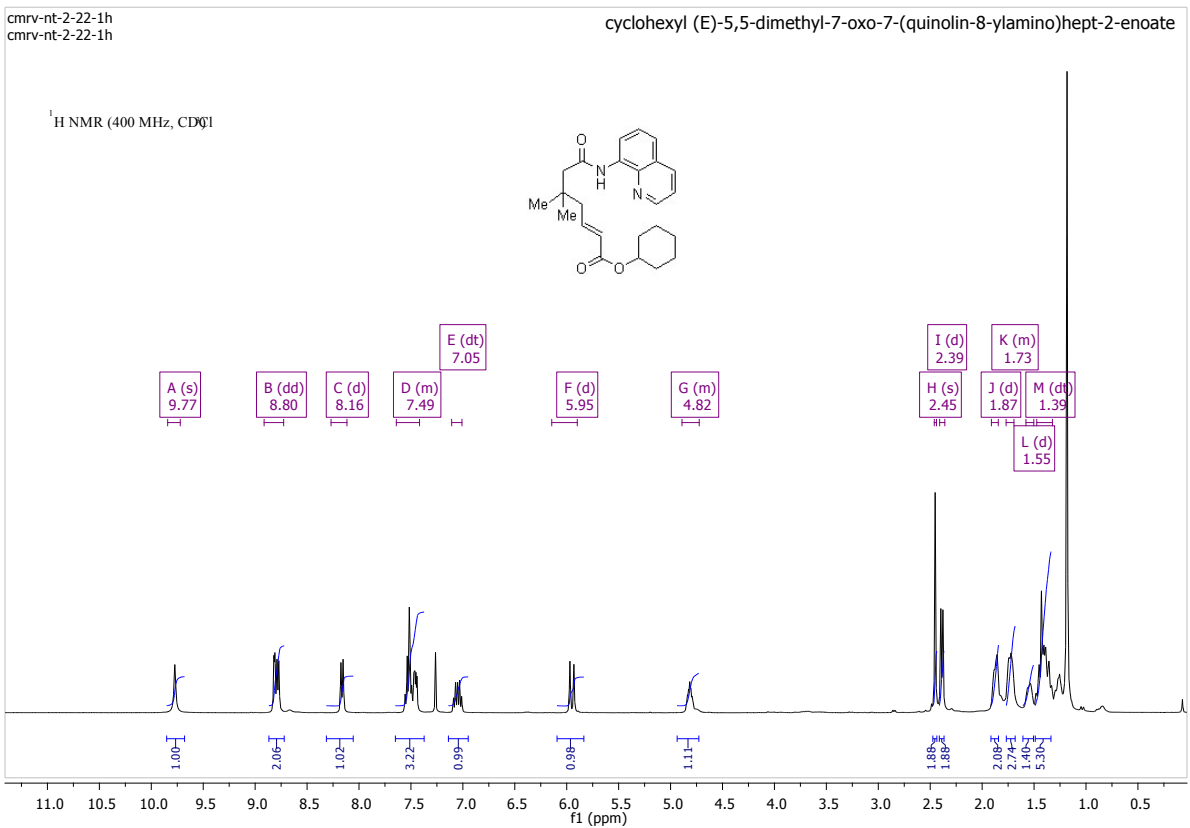
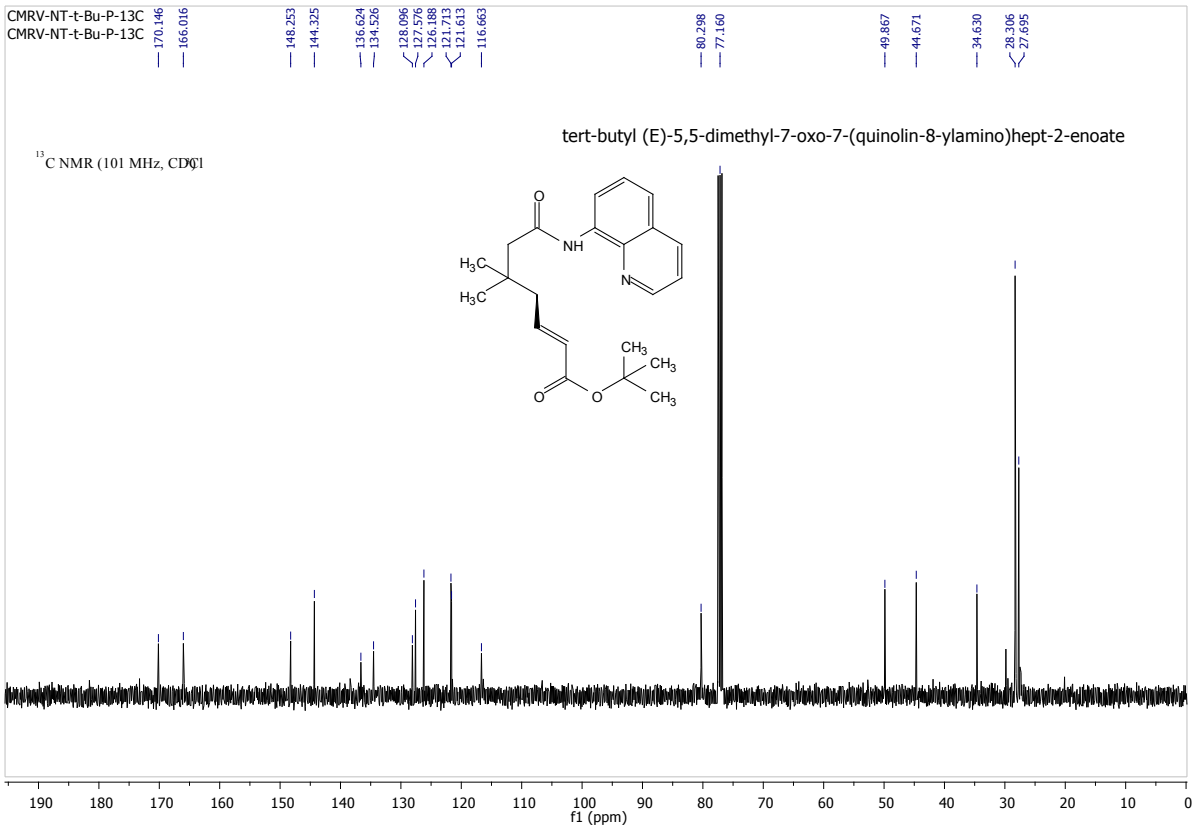
butyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

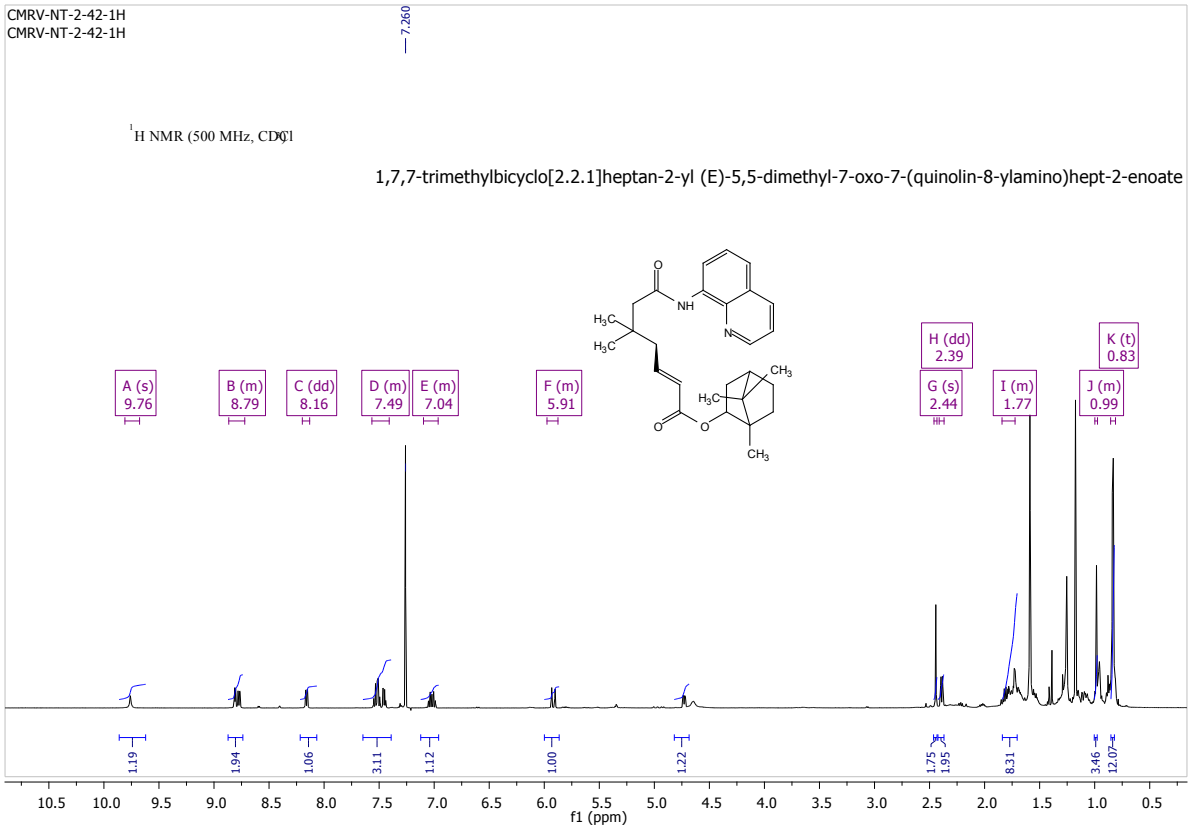
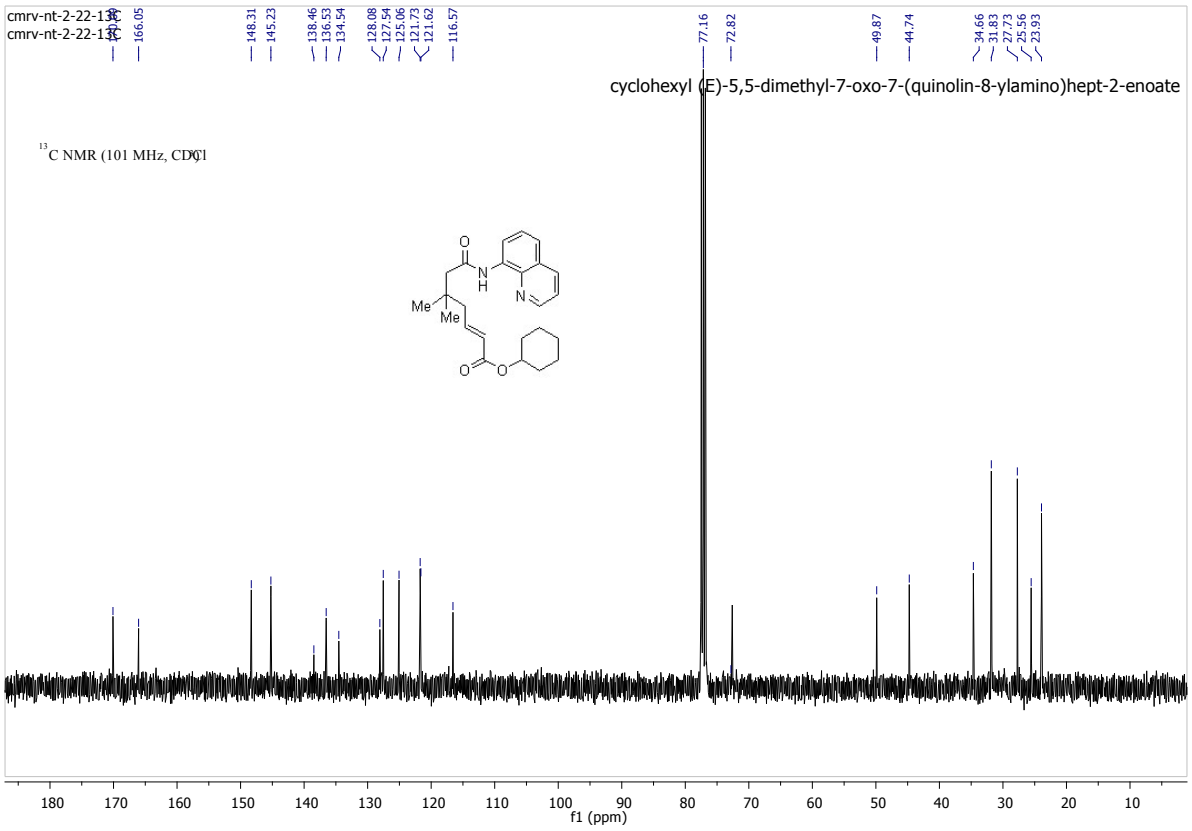


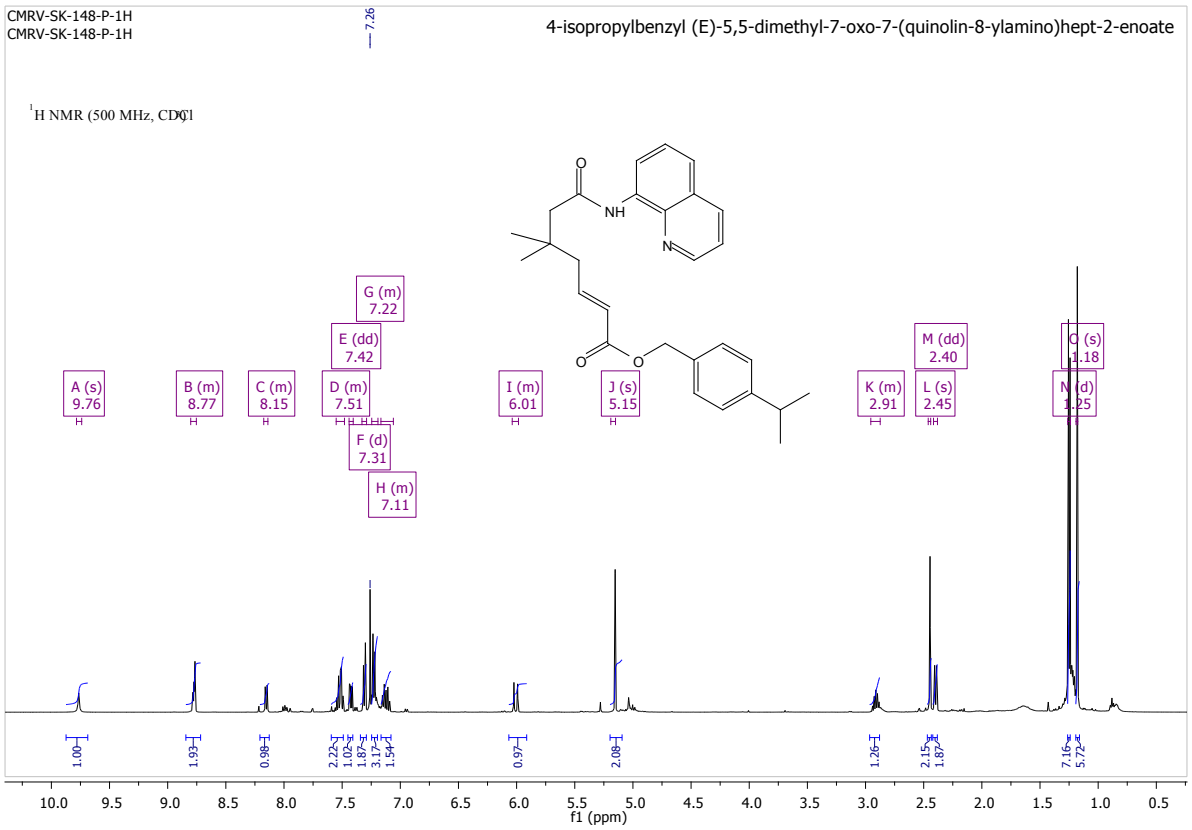
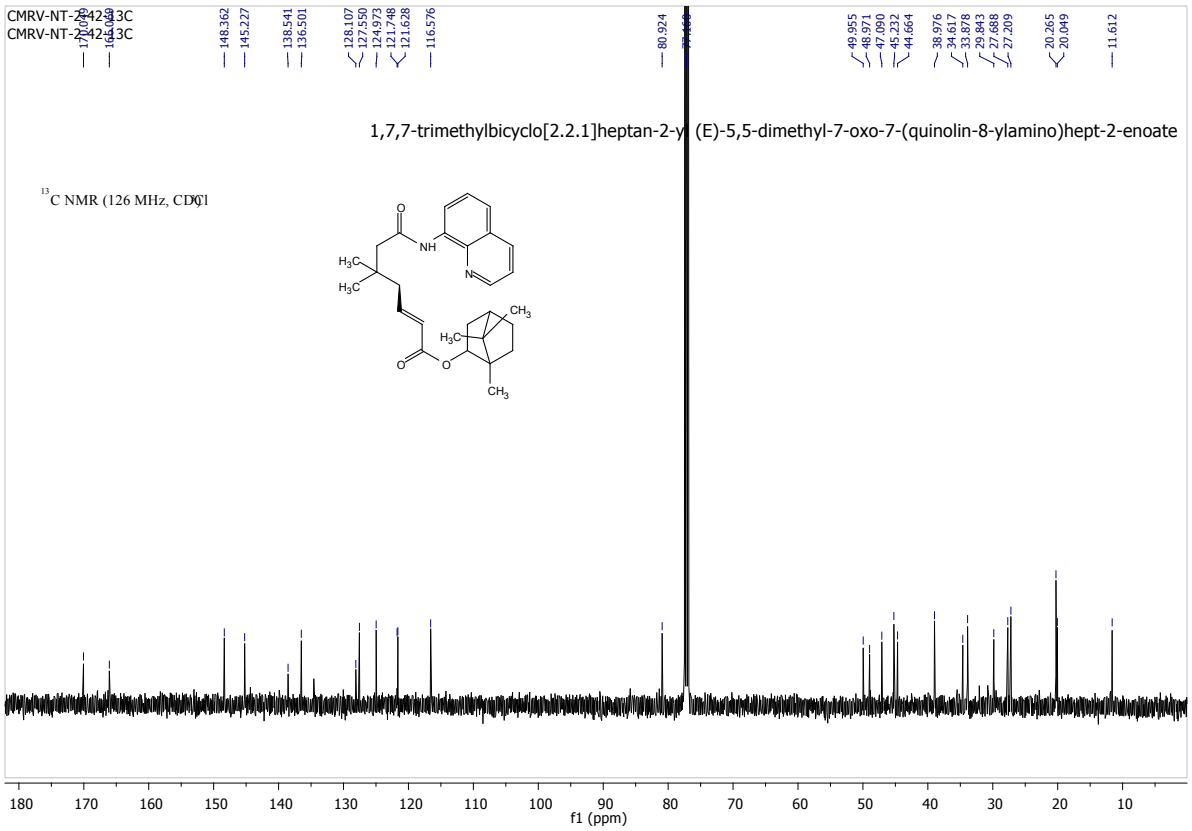
¹H NMR (500 MHz, CDCl₃)

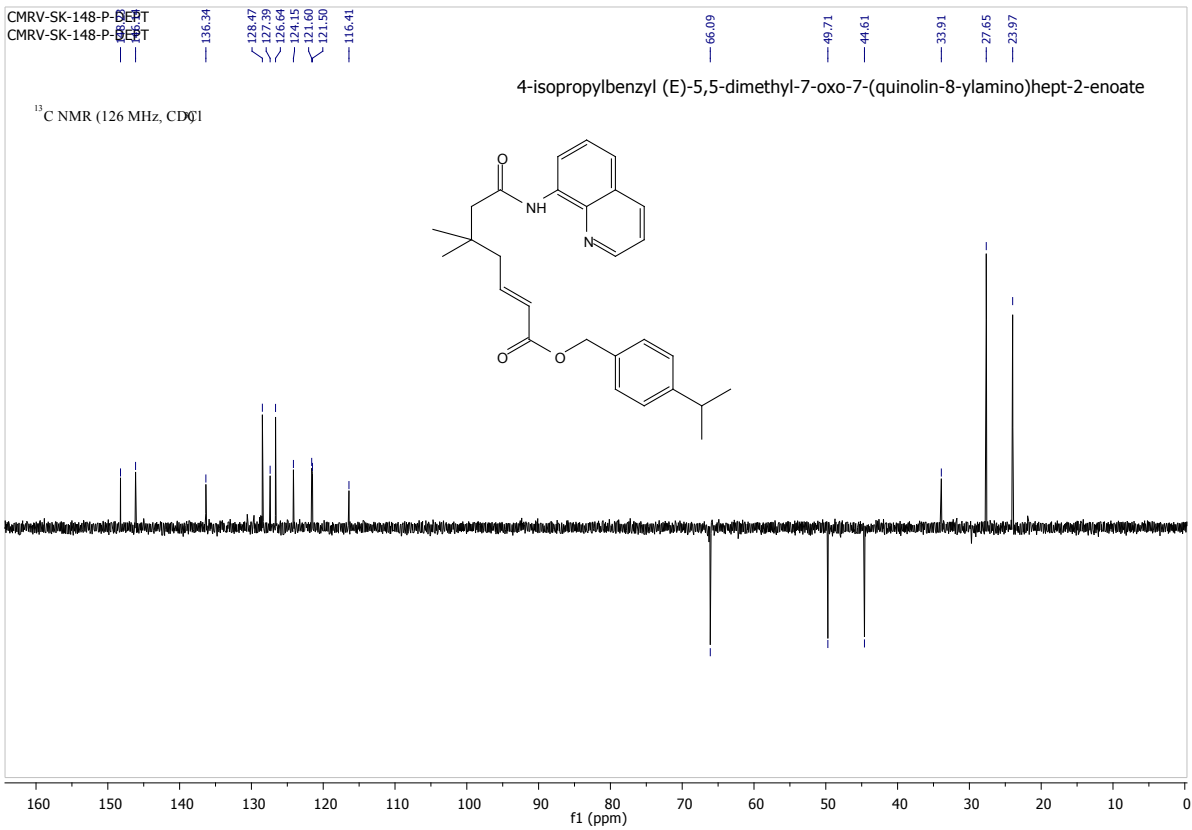
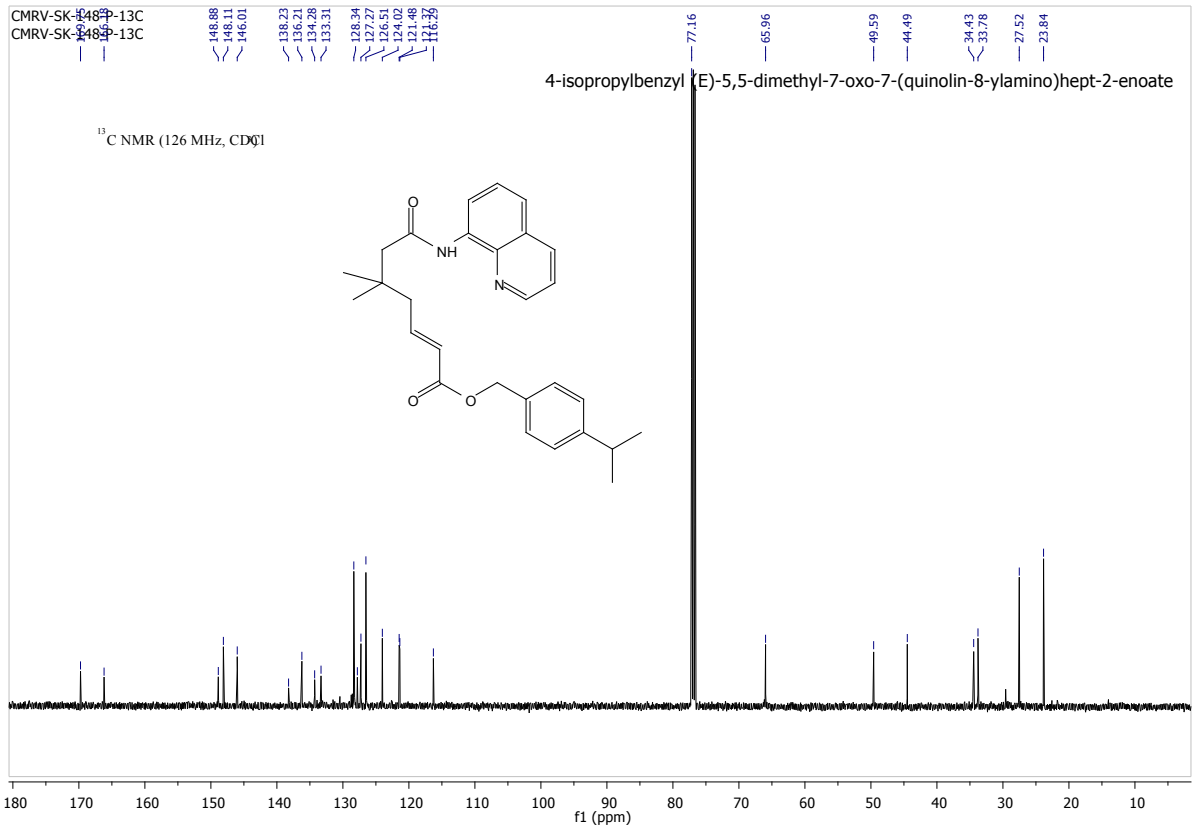


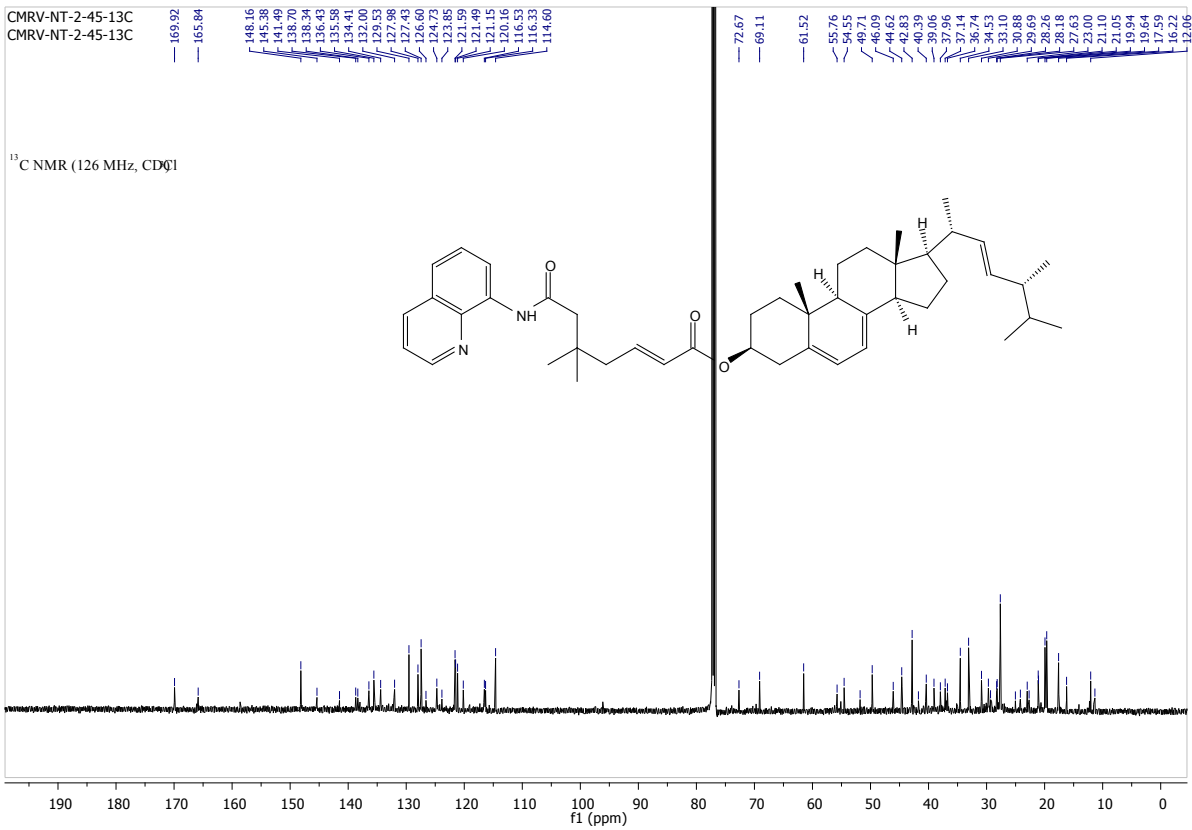
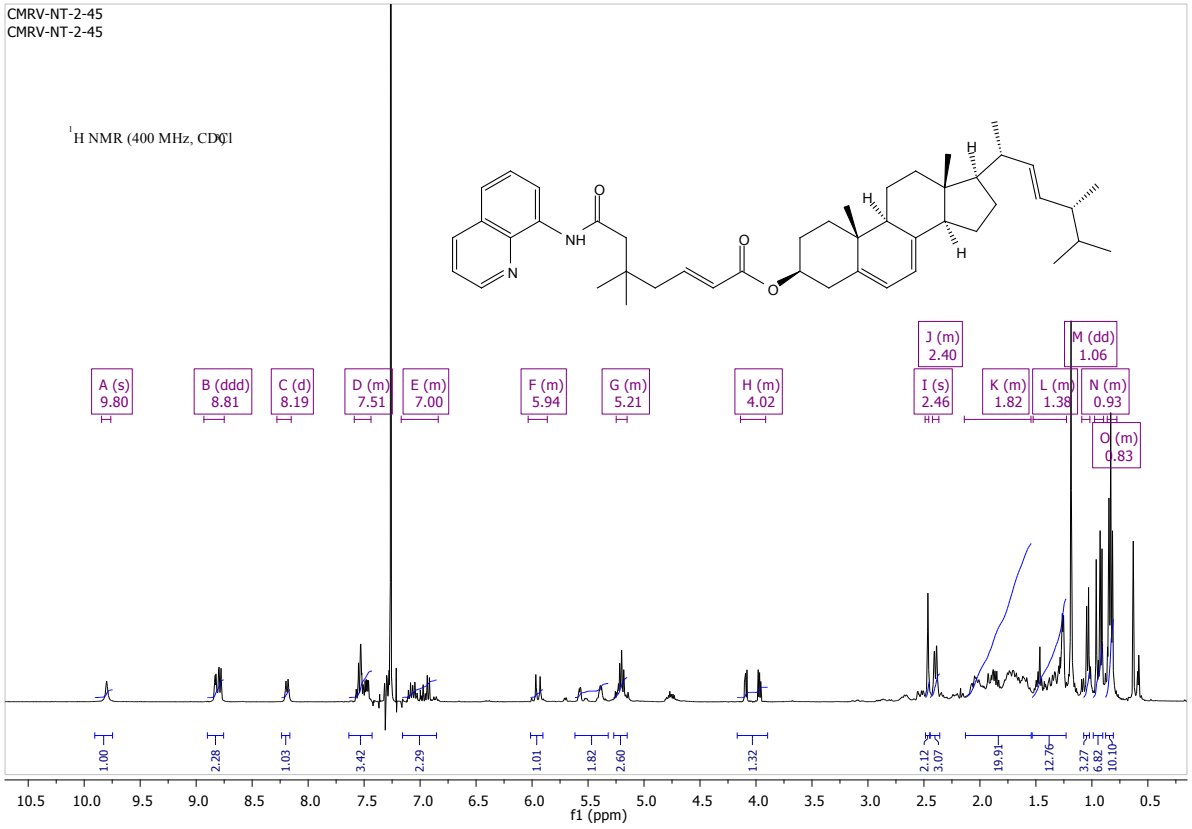






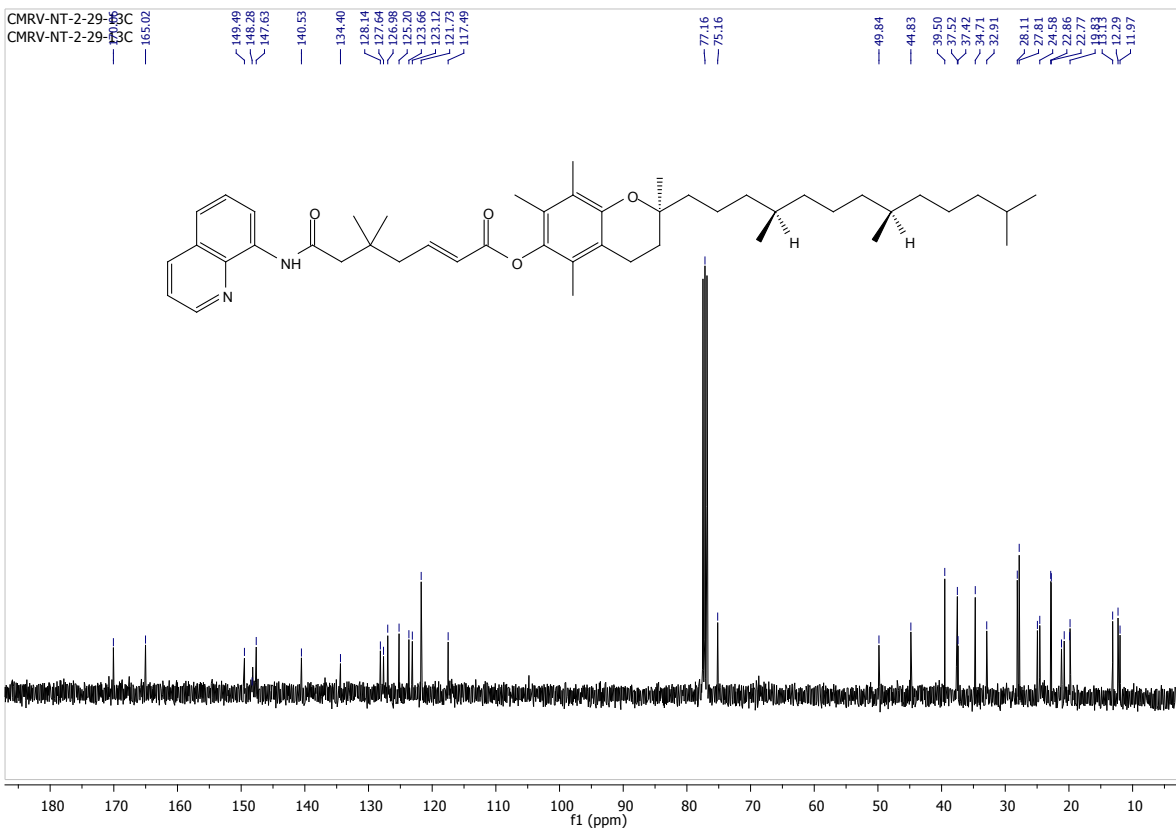
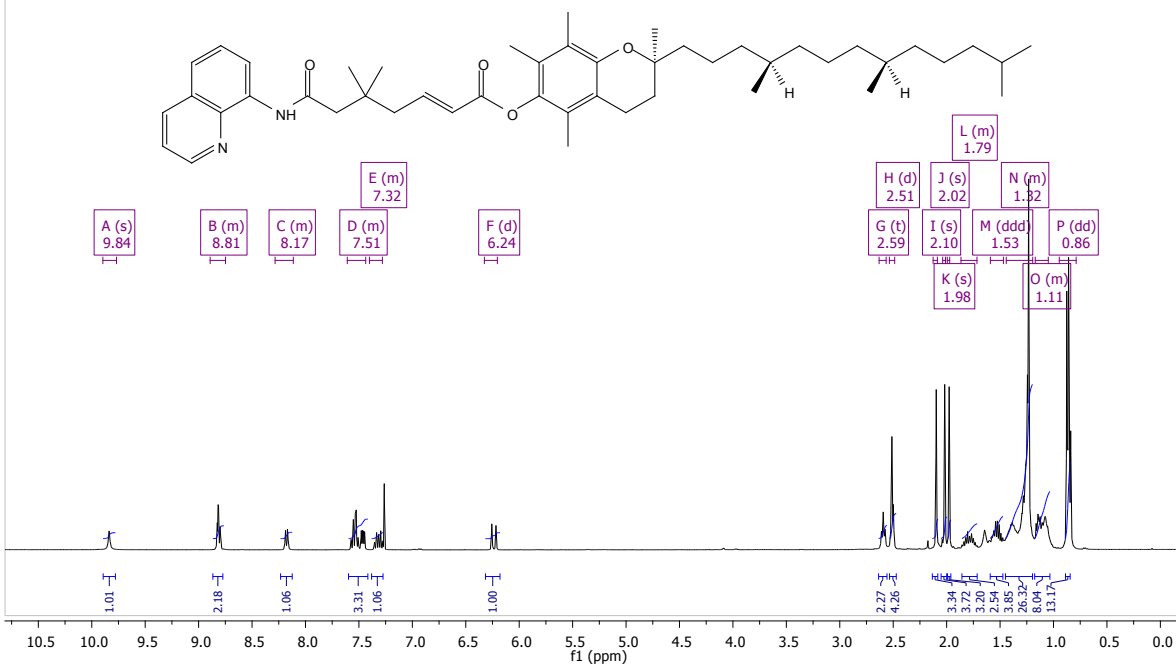






CMRV-NT-2-29-1H
CMRV-NT-2-29-1H

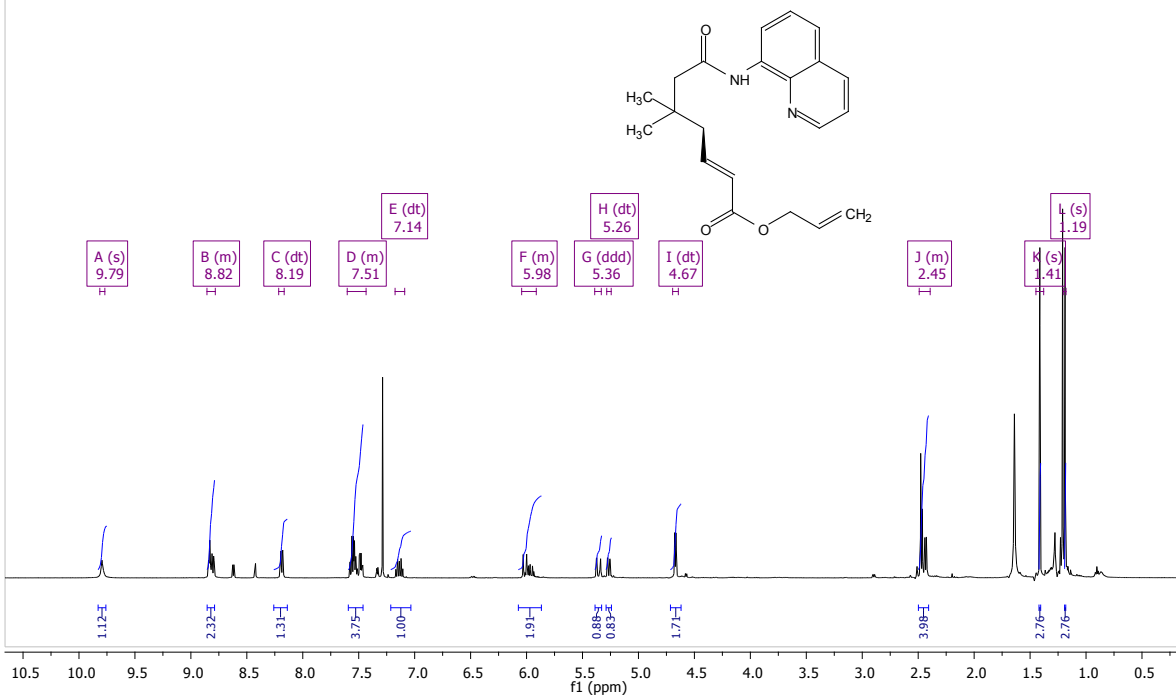
¹H NMR (400 MHz, CDCl₃)



CMRV-nt-2-91-1h
CMRV-nt-2-91-1h

allyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

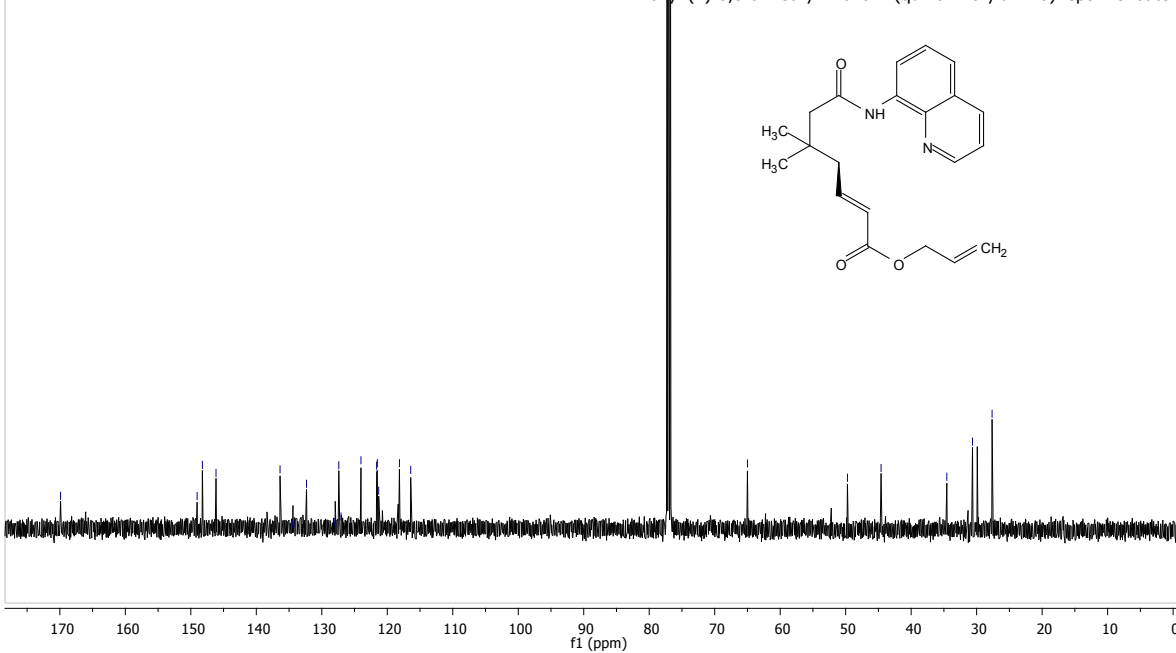
¹H NMR (500 MHz, CDCl₃)



CMRV-nt-2-91-13c
CMRV-nt-2-91-13c

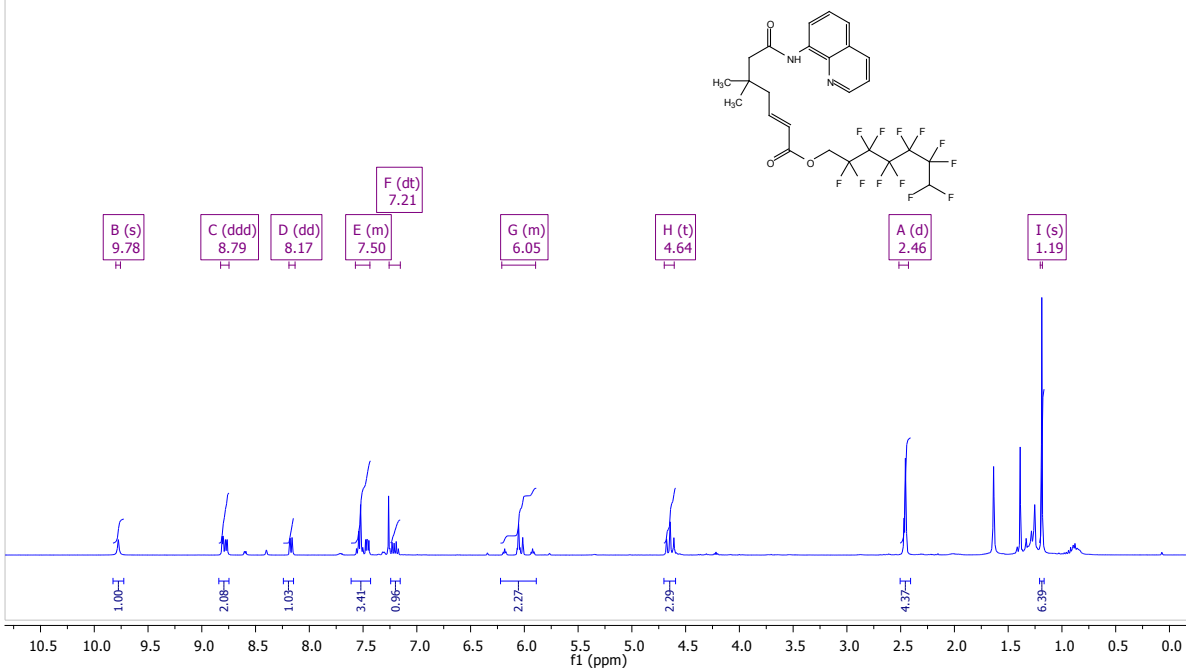
allyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

¹³C NMR (126 MHz, CDCl₃)



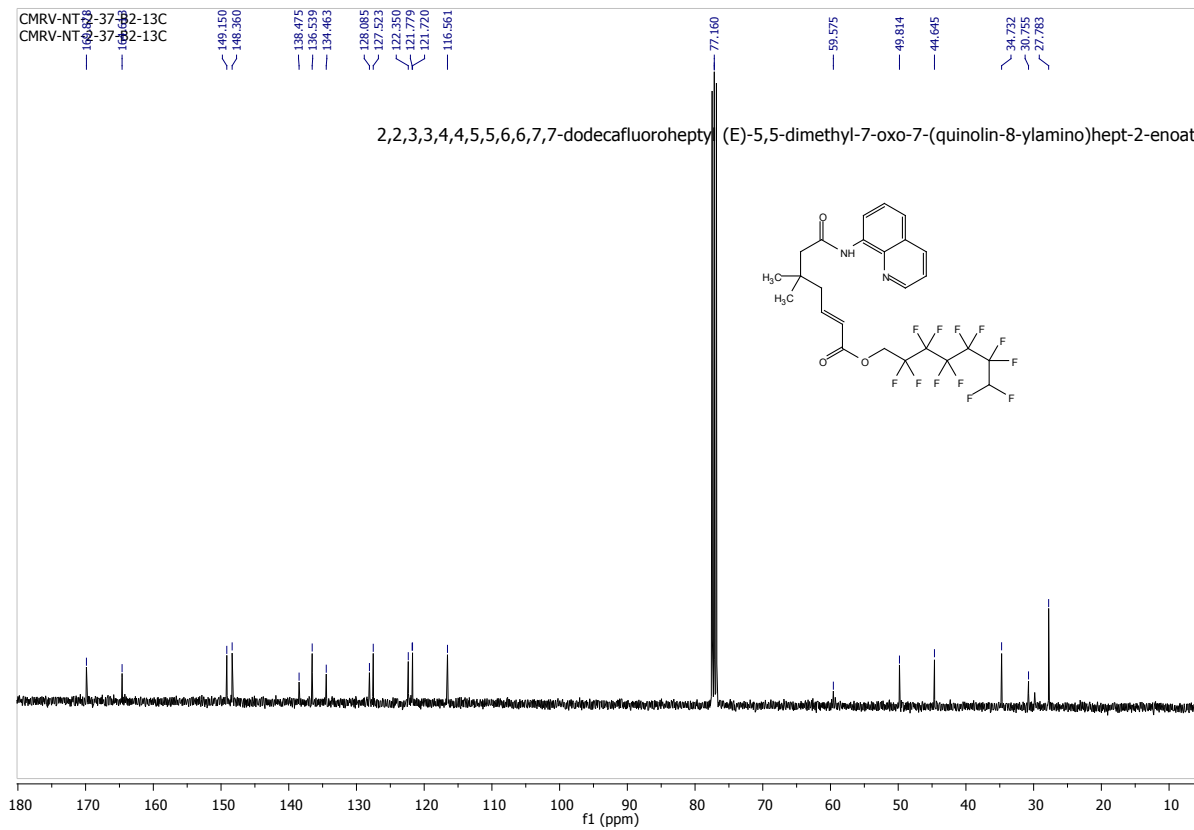
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CMRV-NT-2-37-B2-1H-

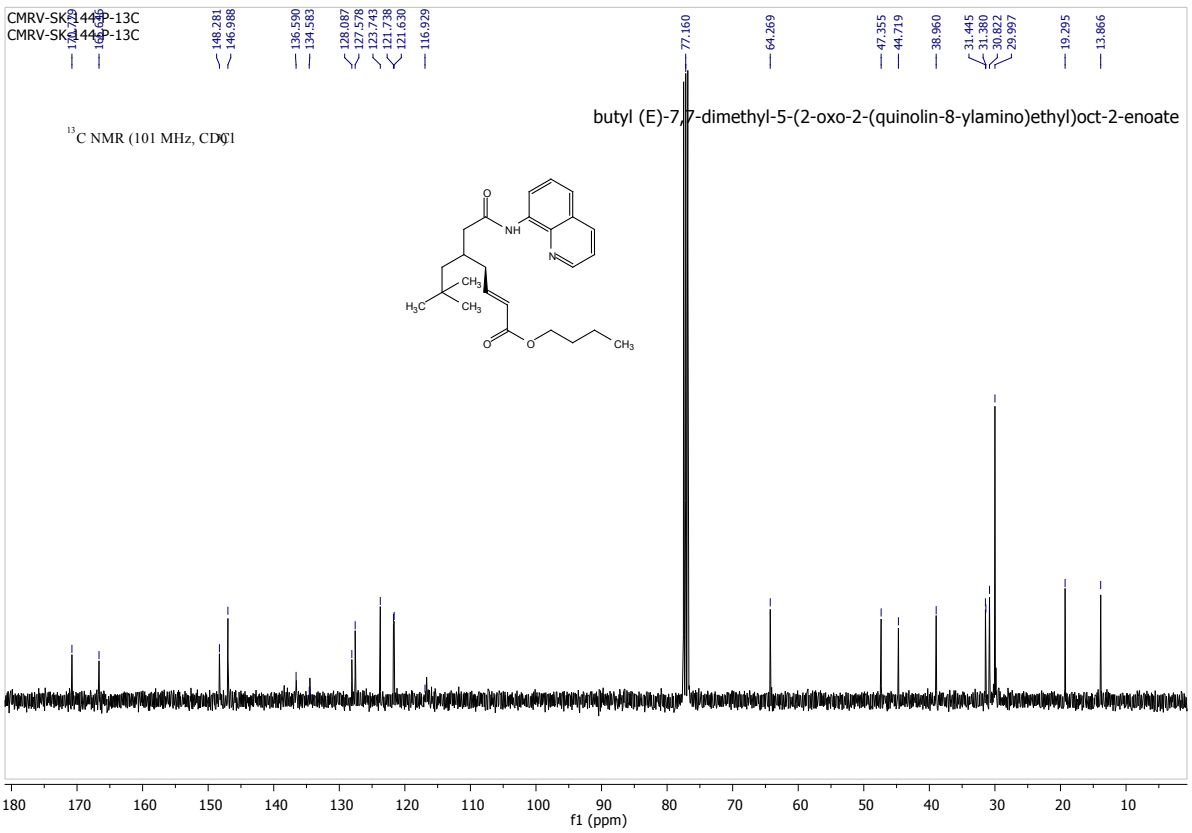
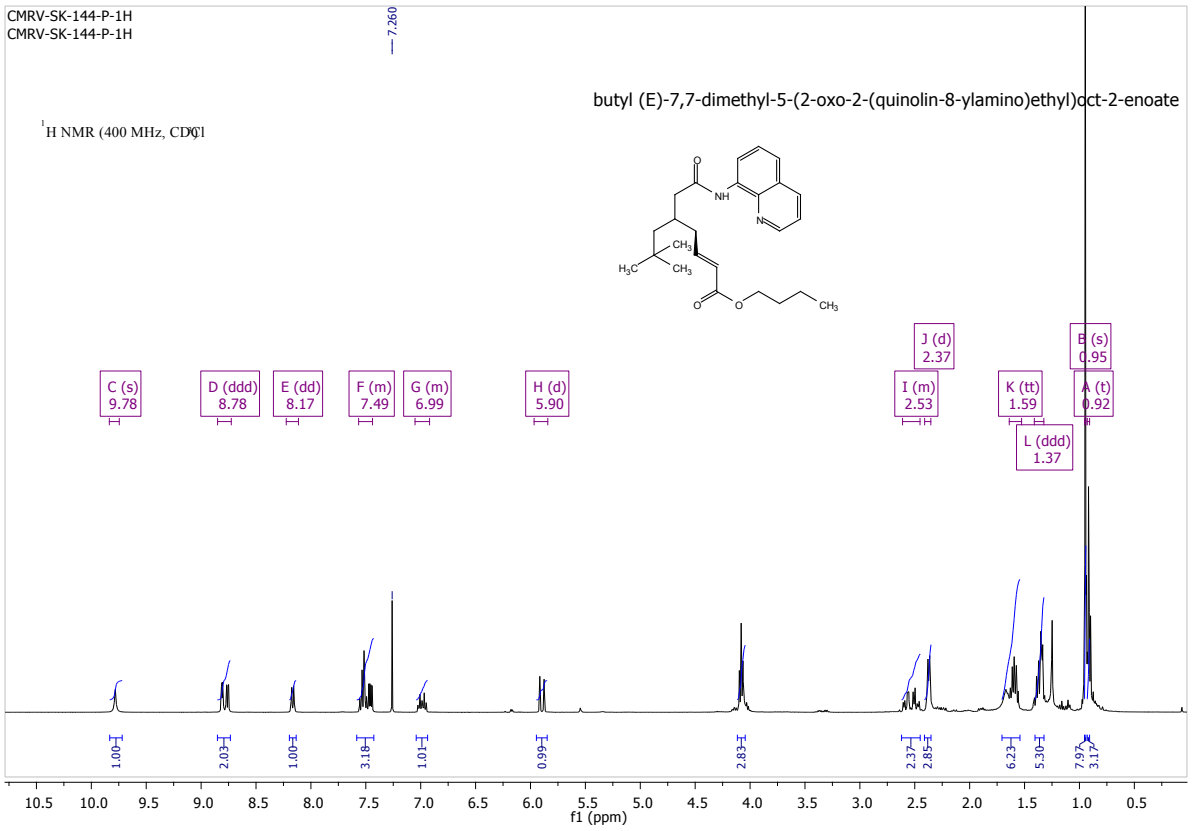
2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

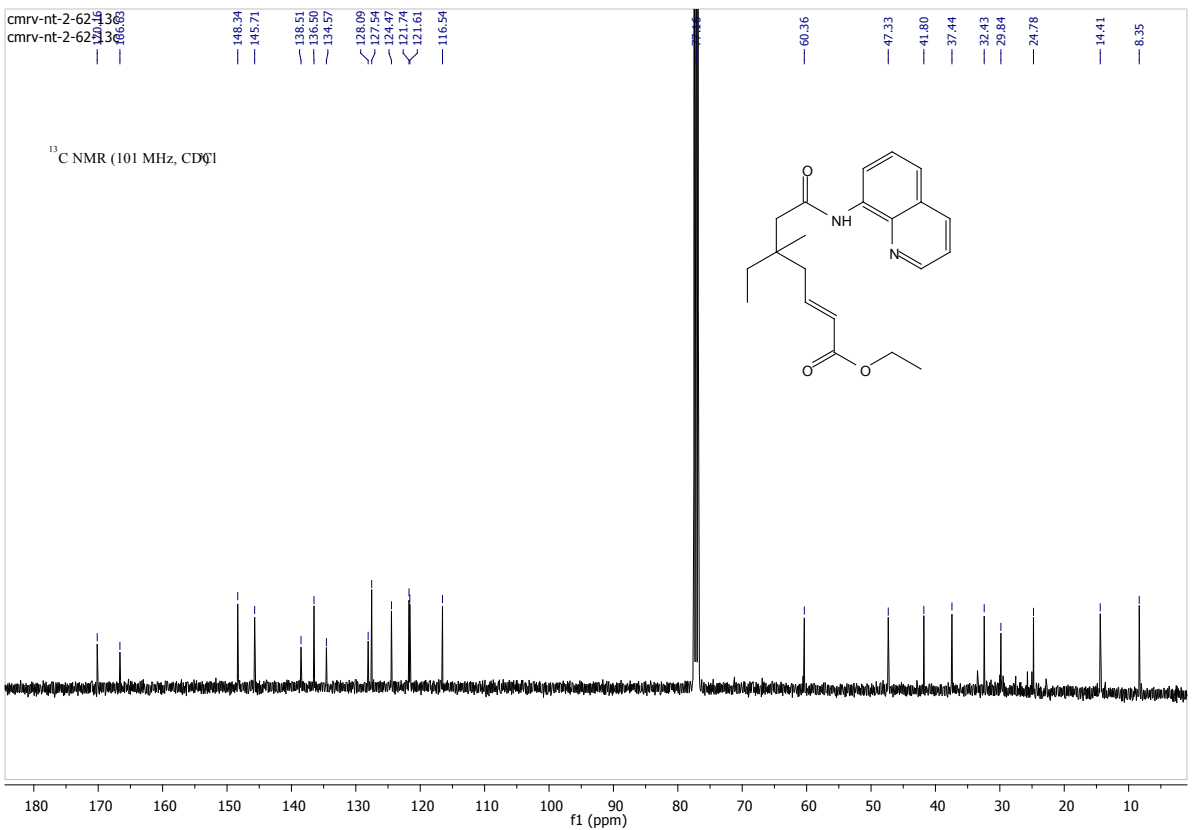
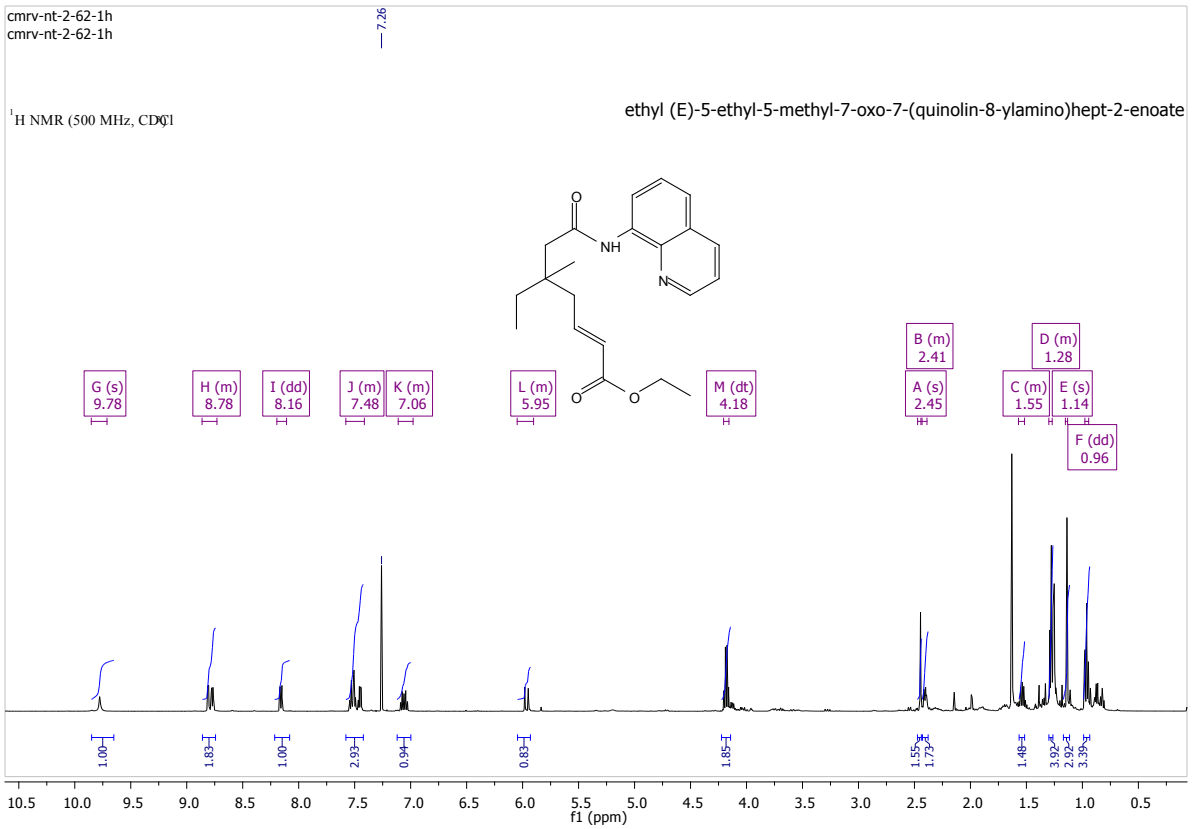


CMRV-NT-2-37-B2-13C
CMRV-NT-2-37-B2-13C

2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl (E)-5,5-dimethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate



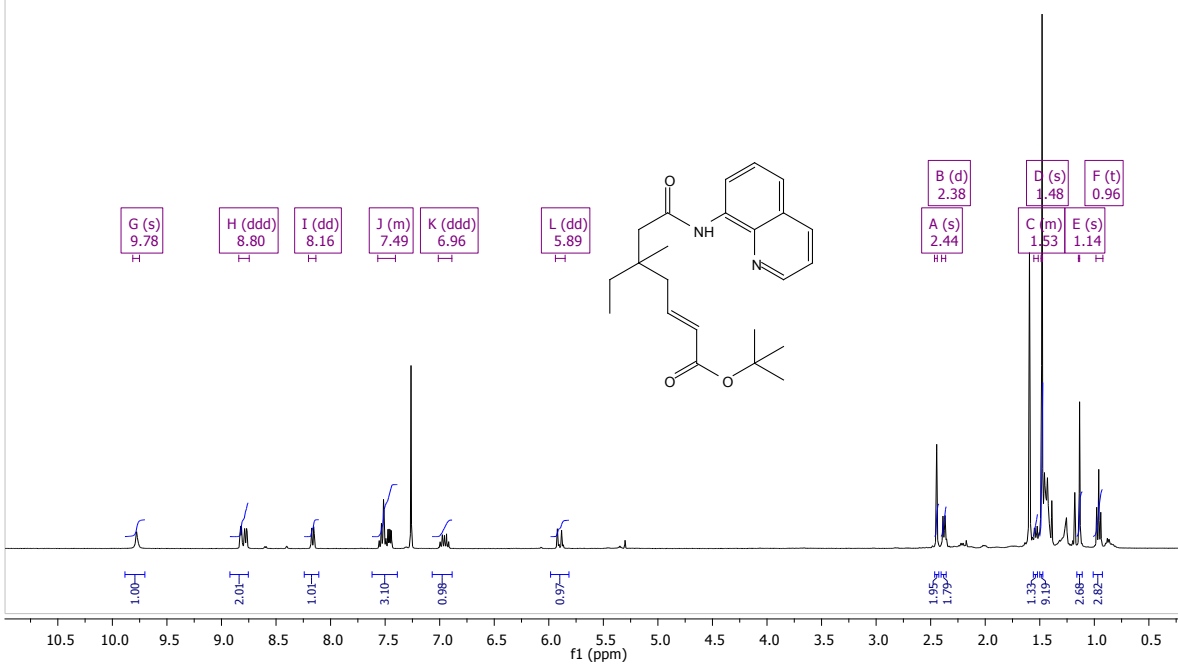




CMRV-NT-2-47-1H
CMRV-NT-2-47-1H

tert-butyl (E)-5-ethyl-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

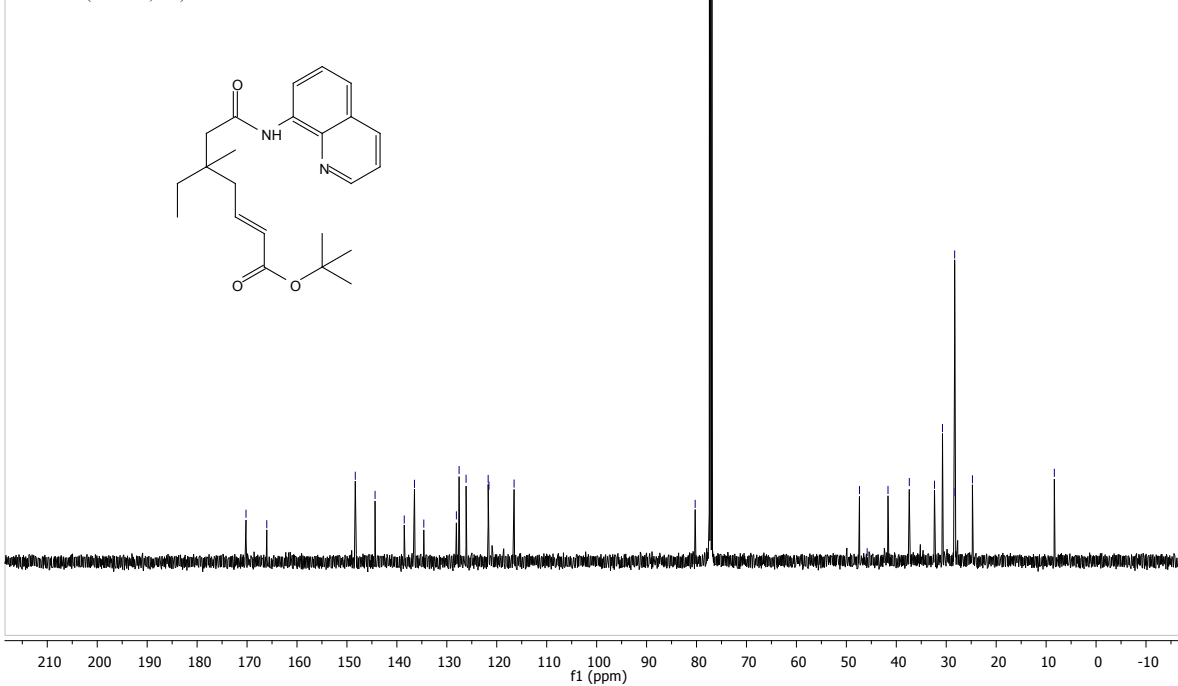
¹H NMR (400 MHz, CDCl₃)

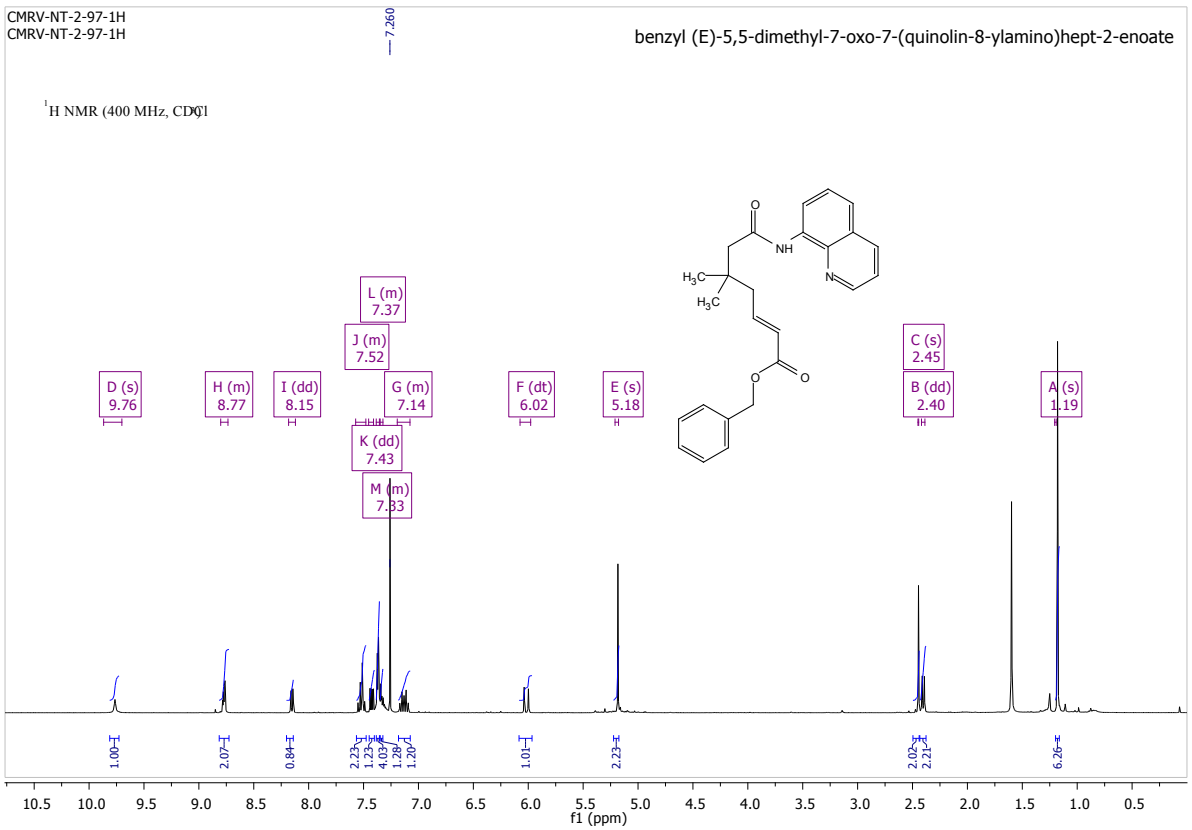
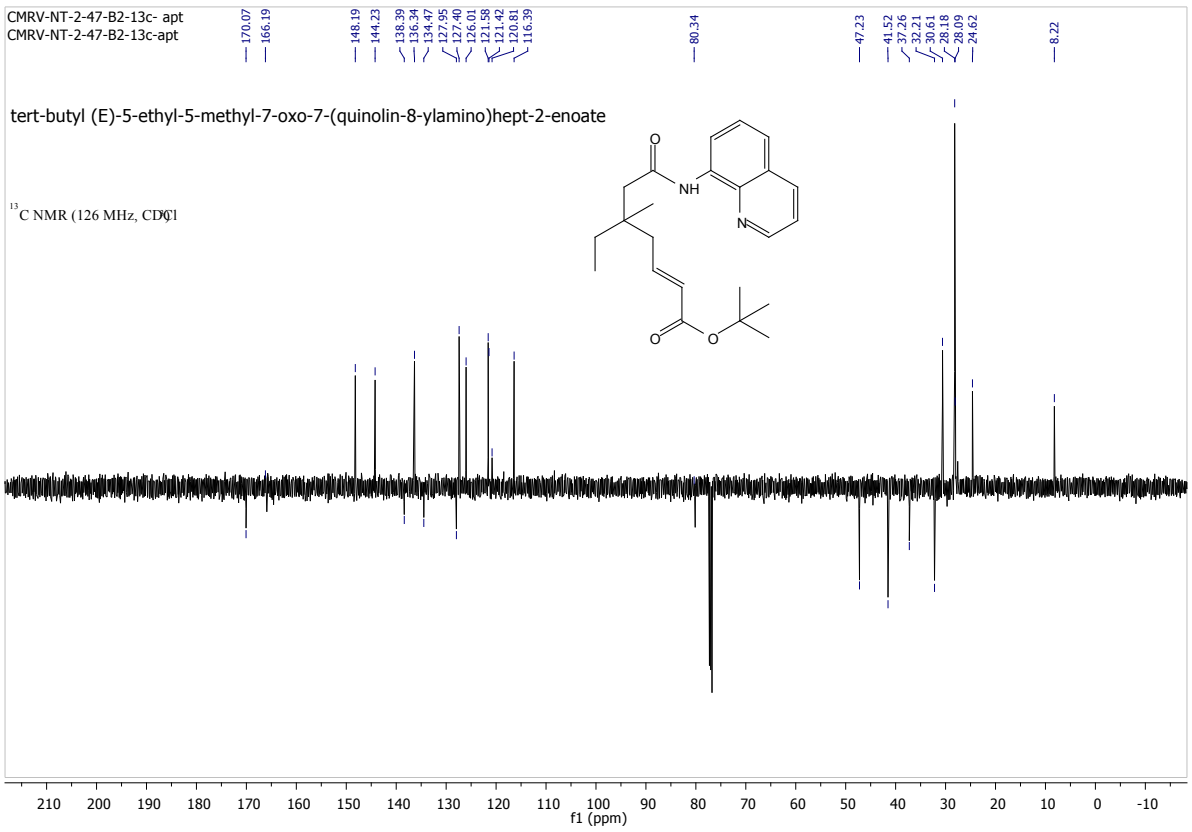


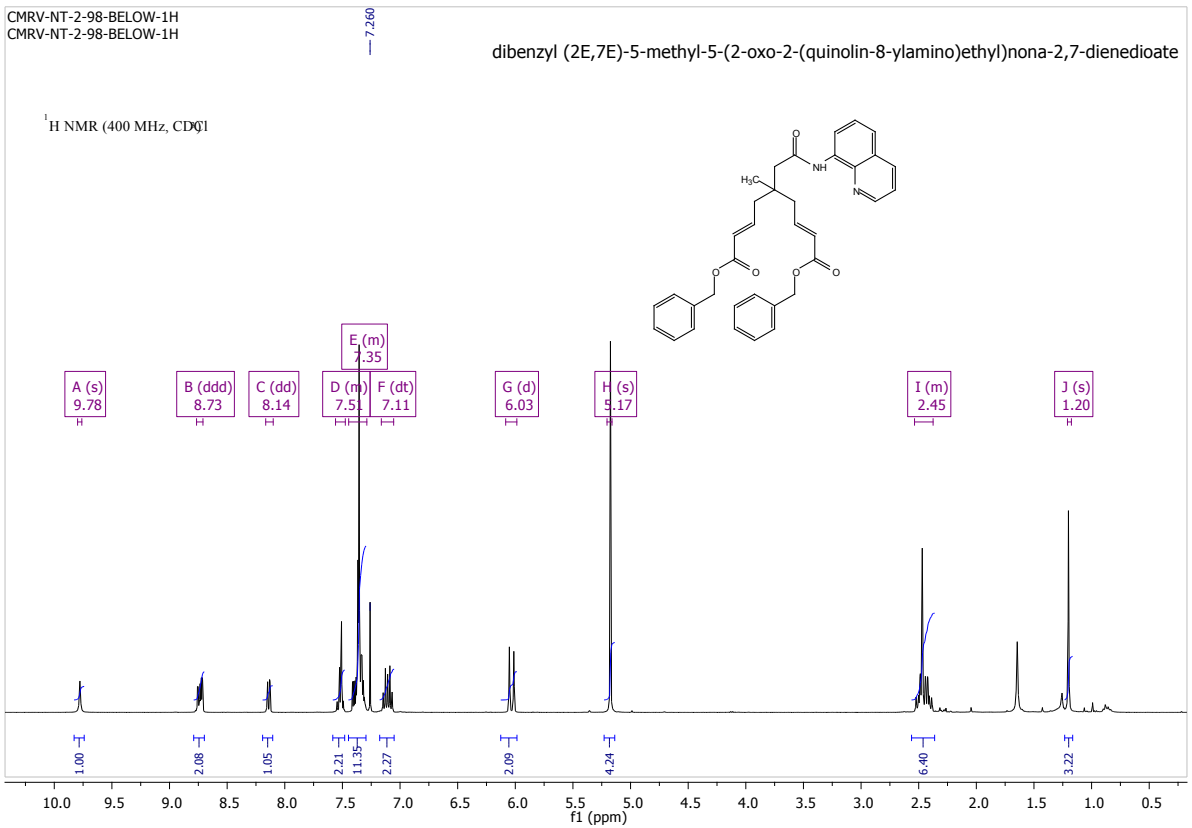
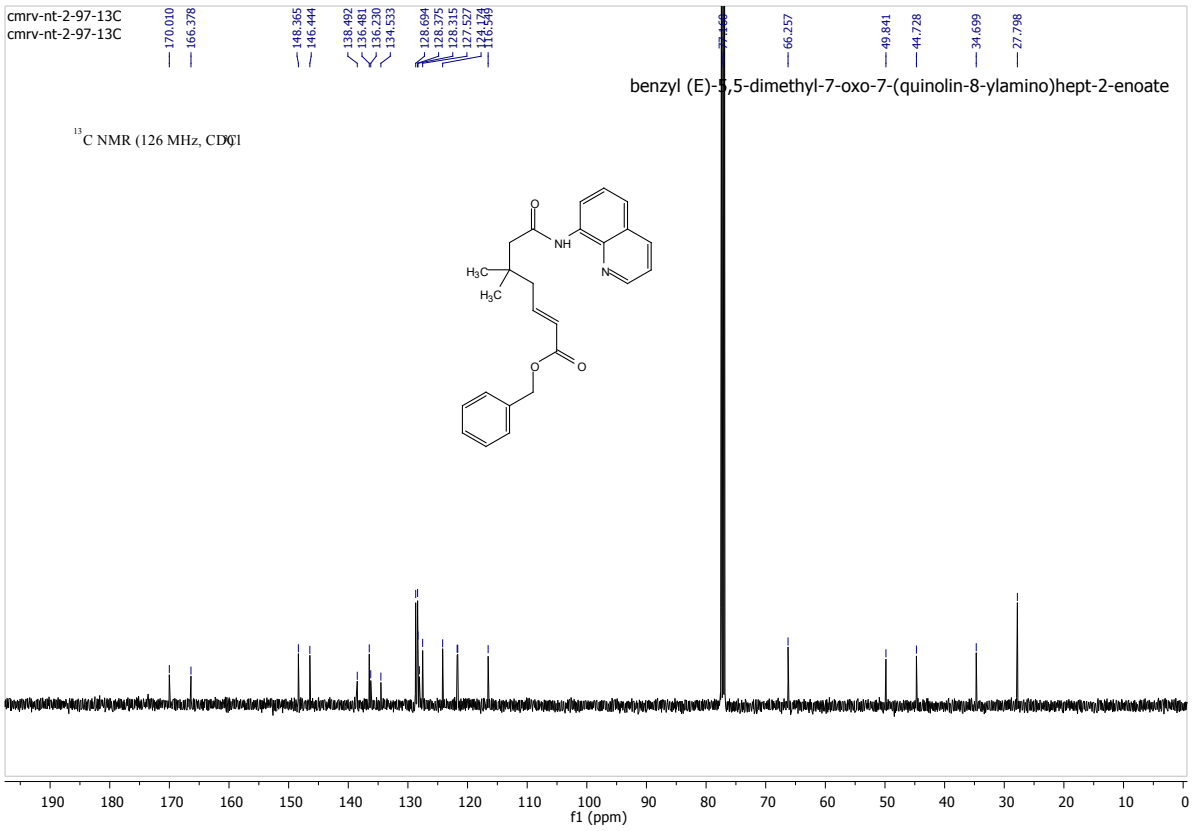
CMRV-NT-2-47-B2-13c
CMRV-NT-2-47-B2-13c

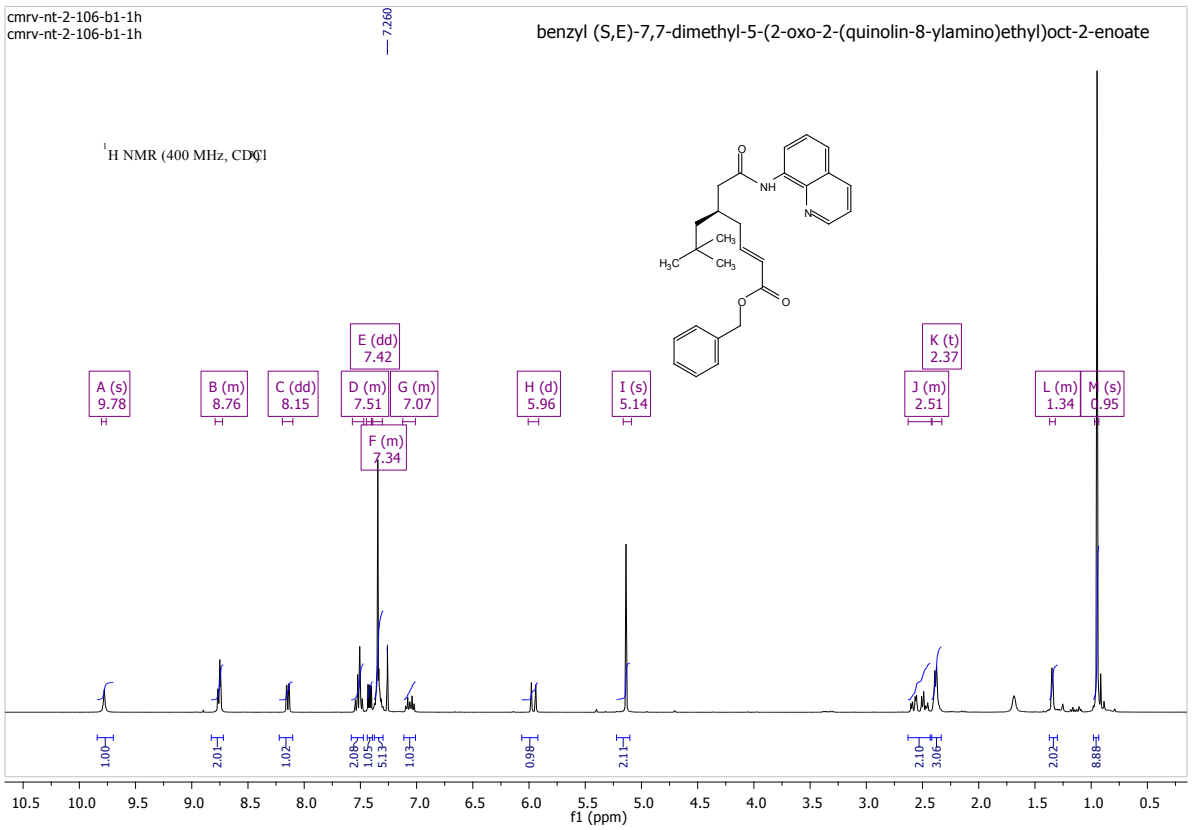
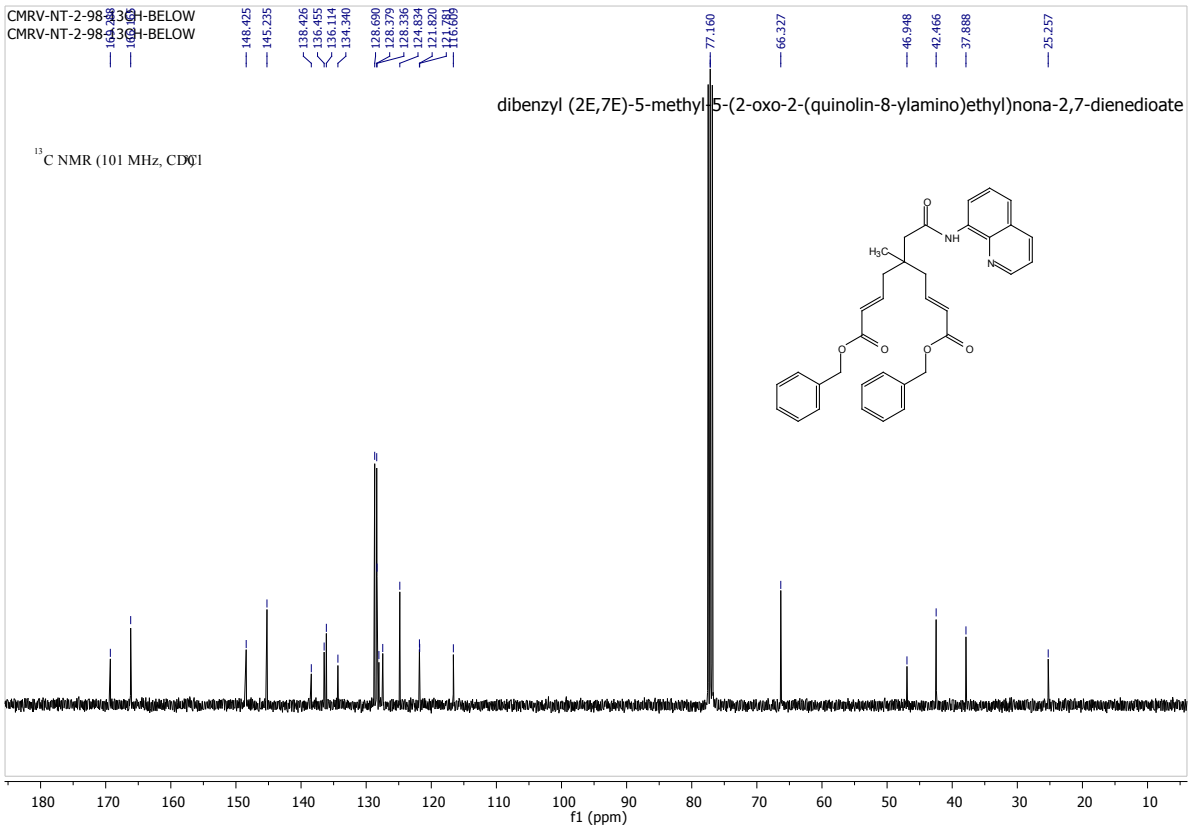
tert-butyl (E)-5-ethyl-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

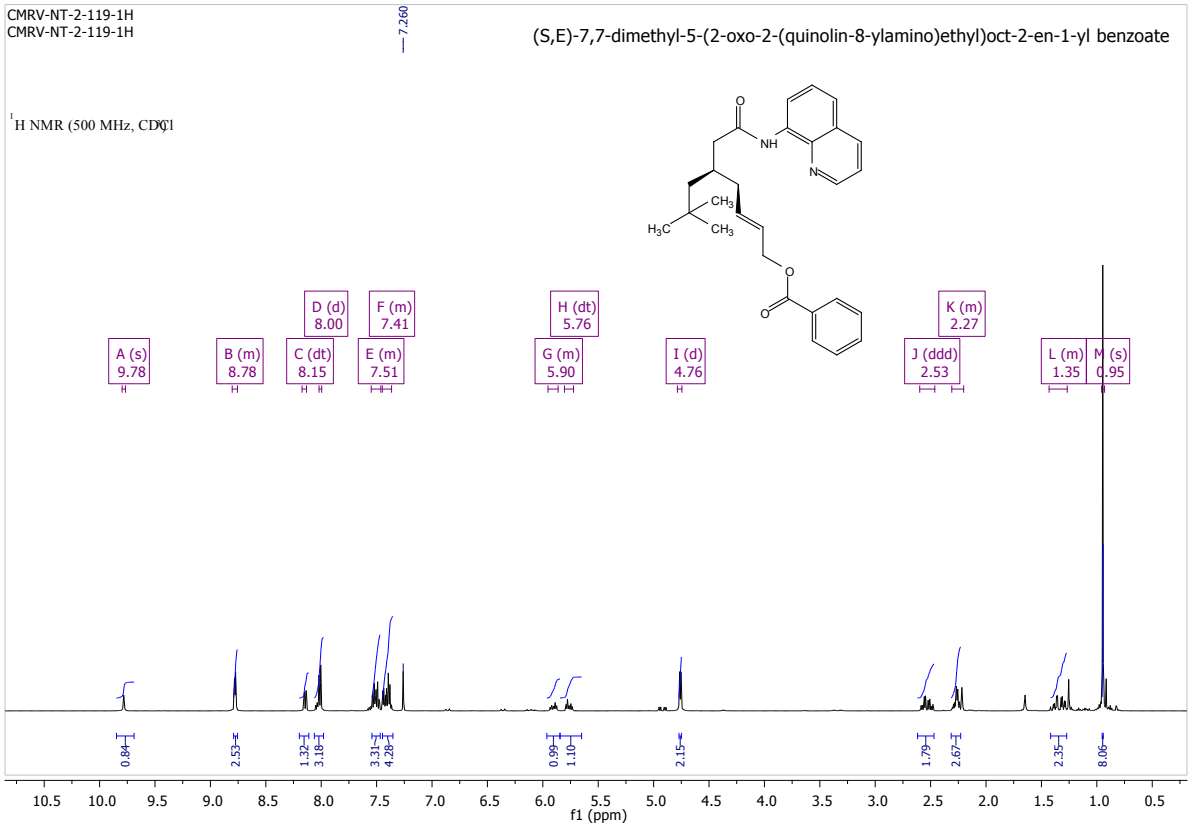
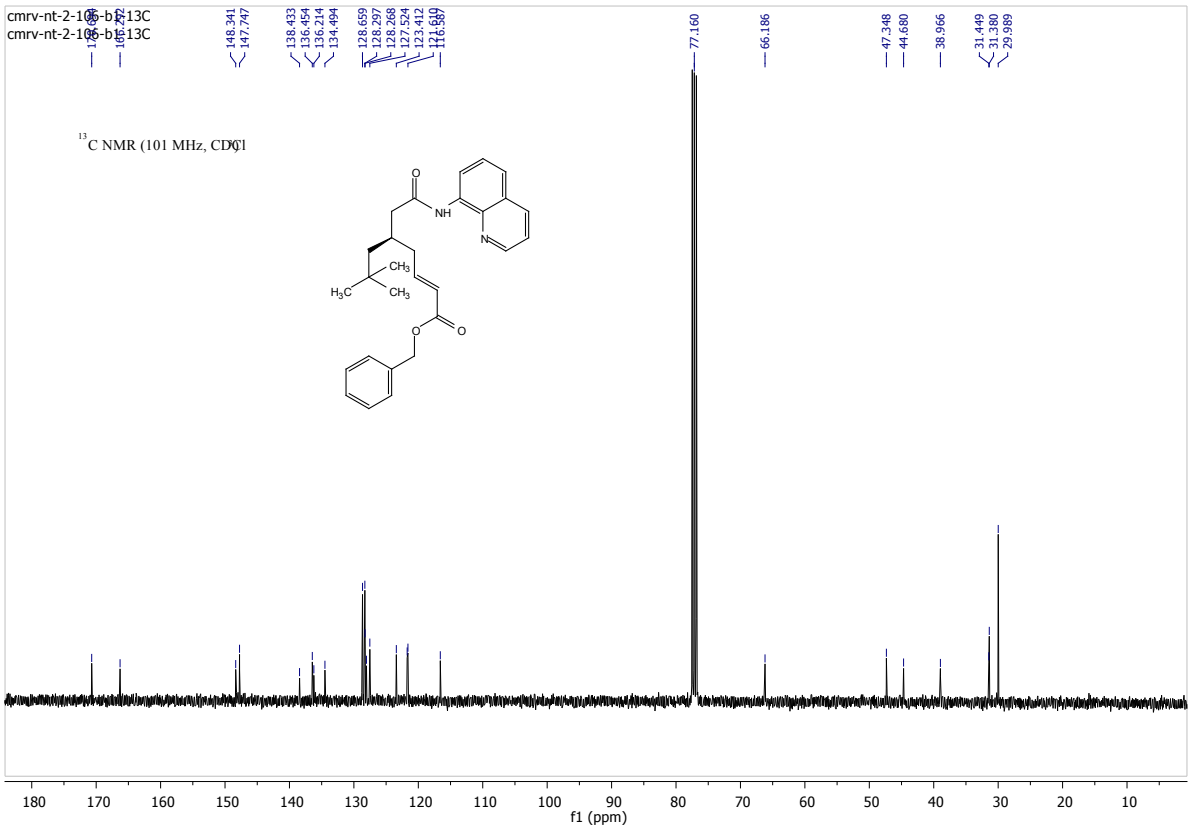
¹³C NMR (126 MHz, CDCl₃)

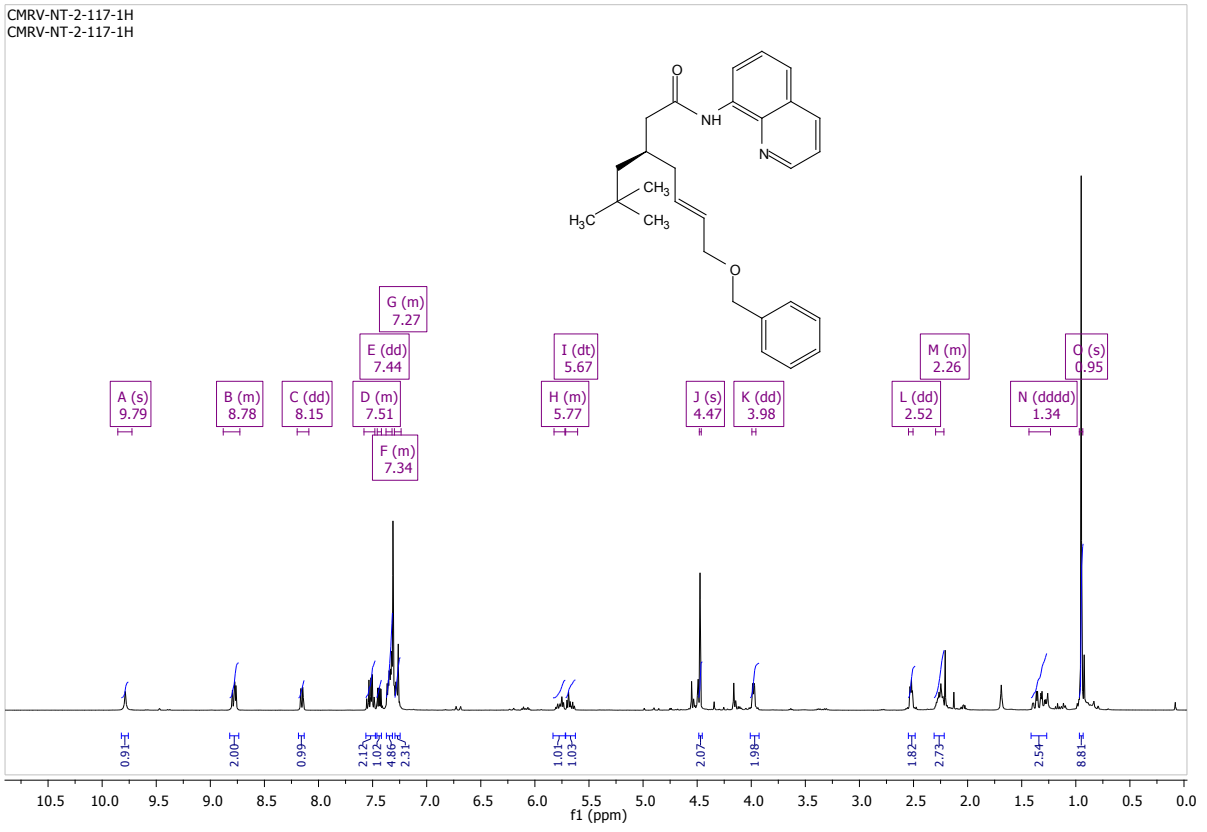
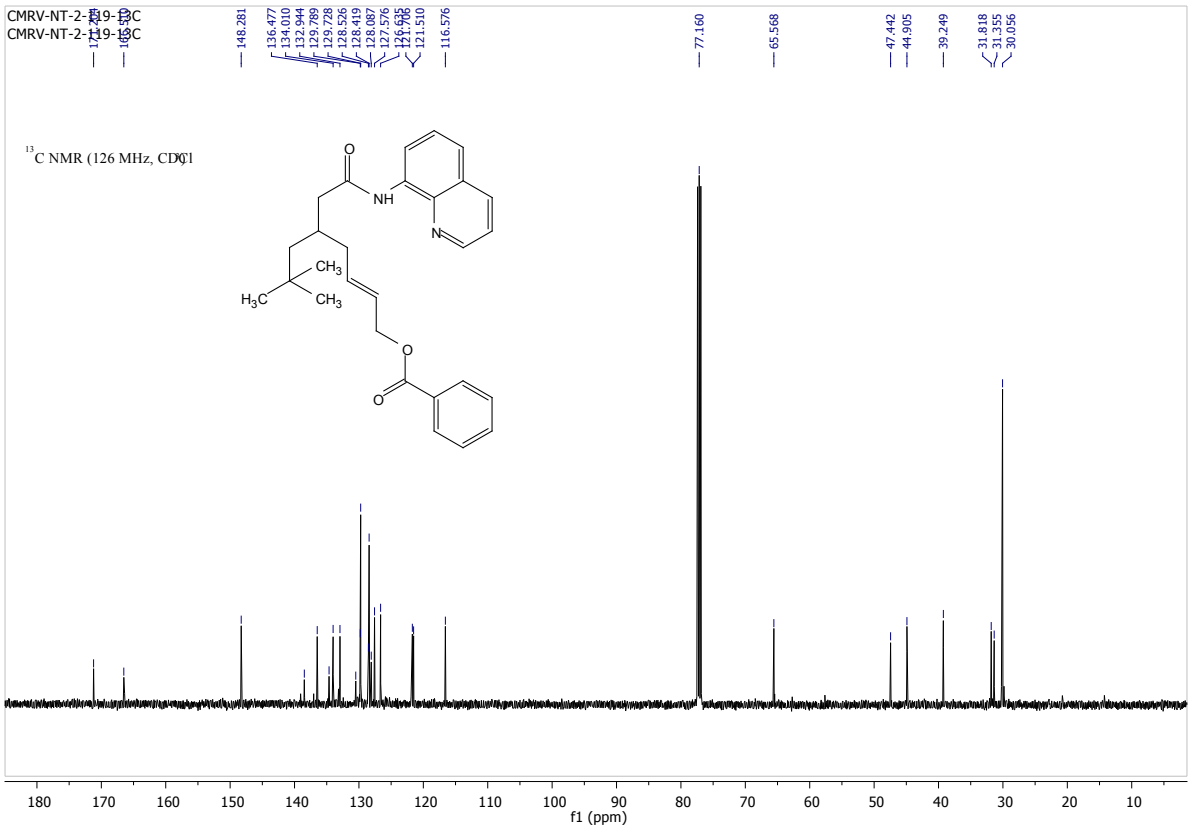


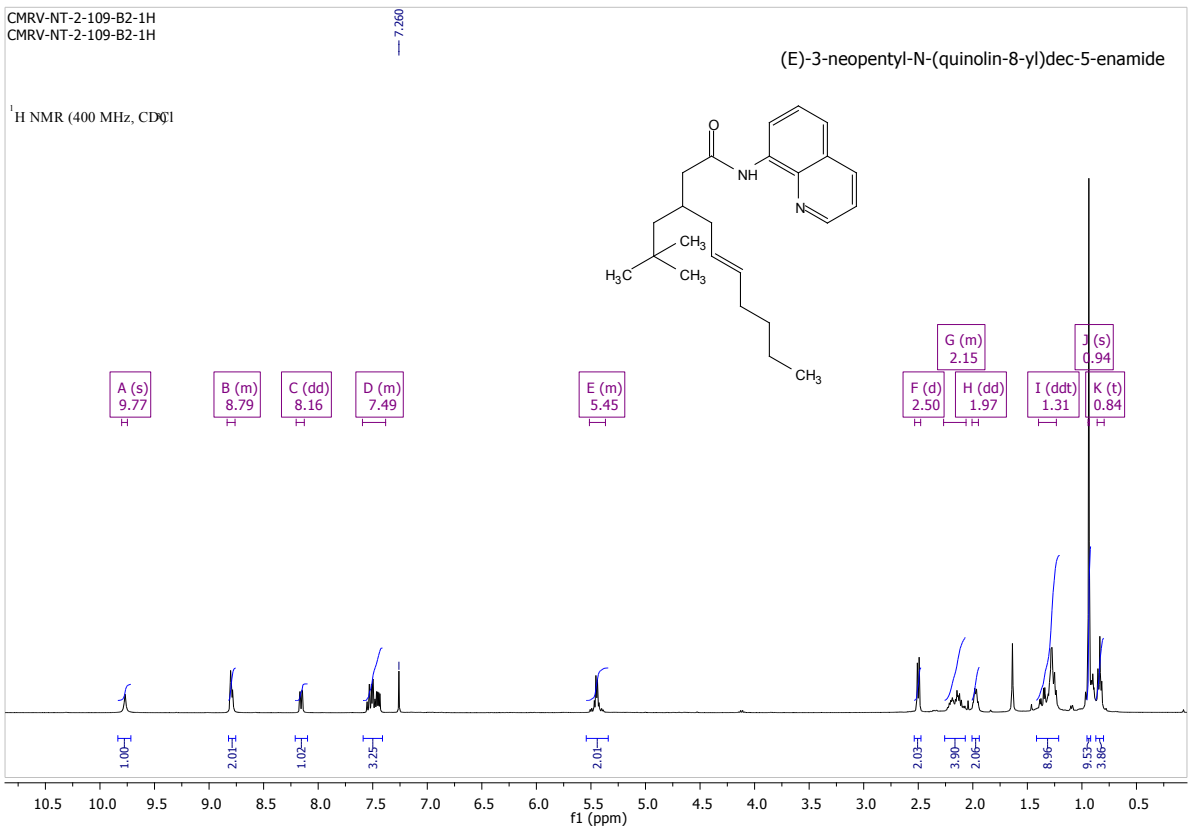
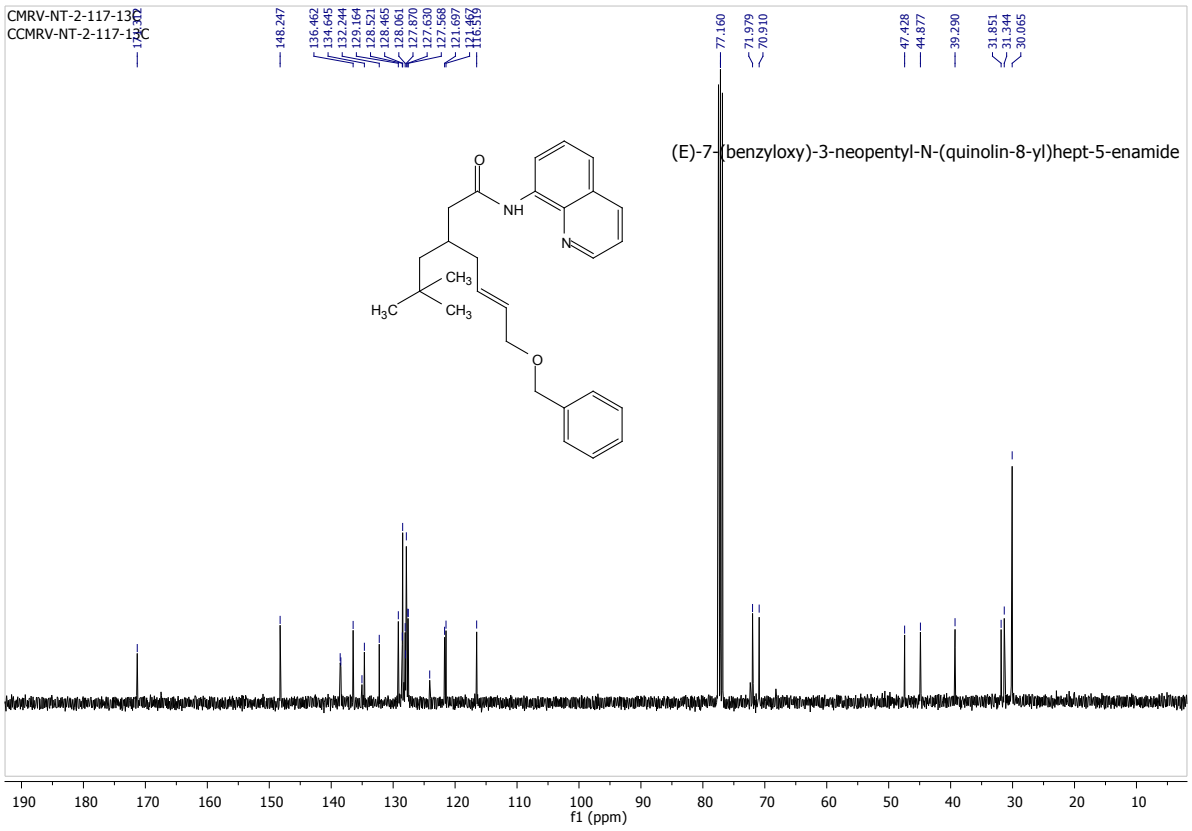


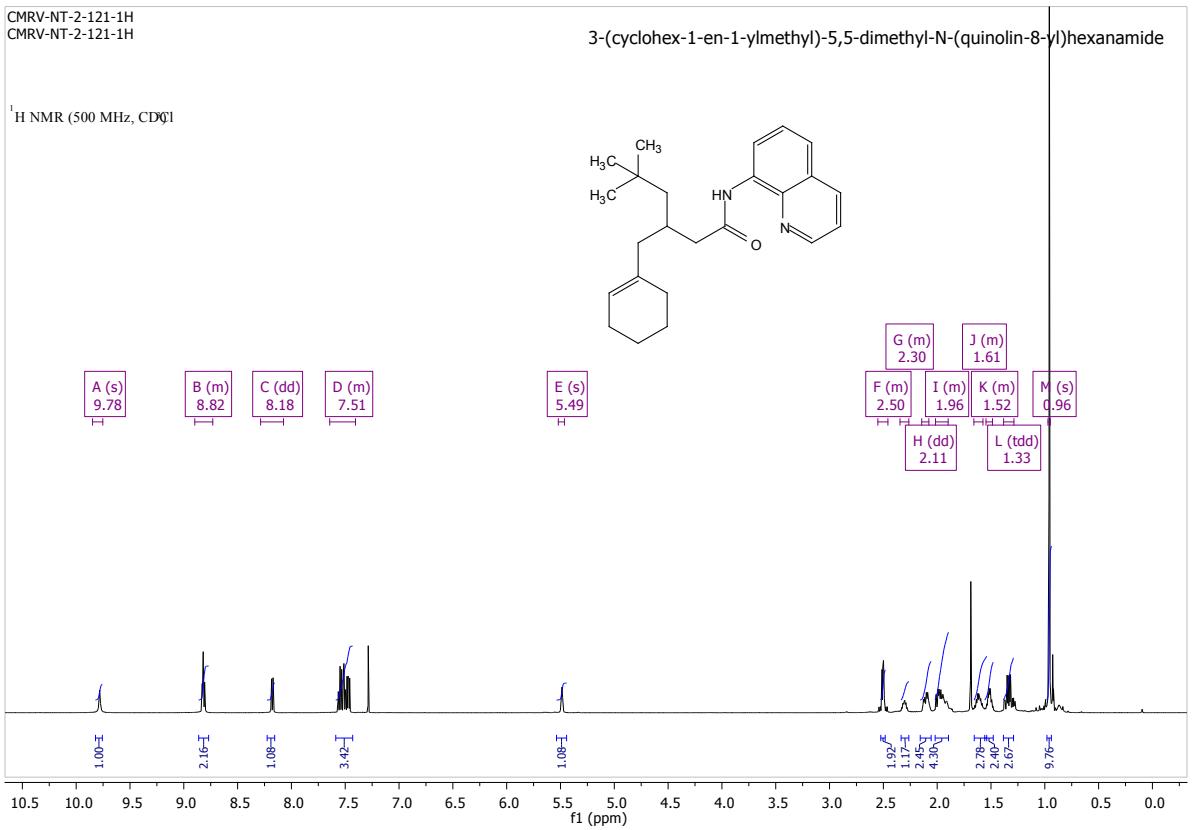
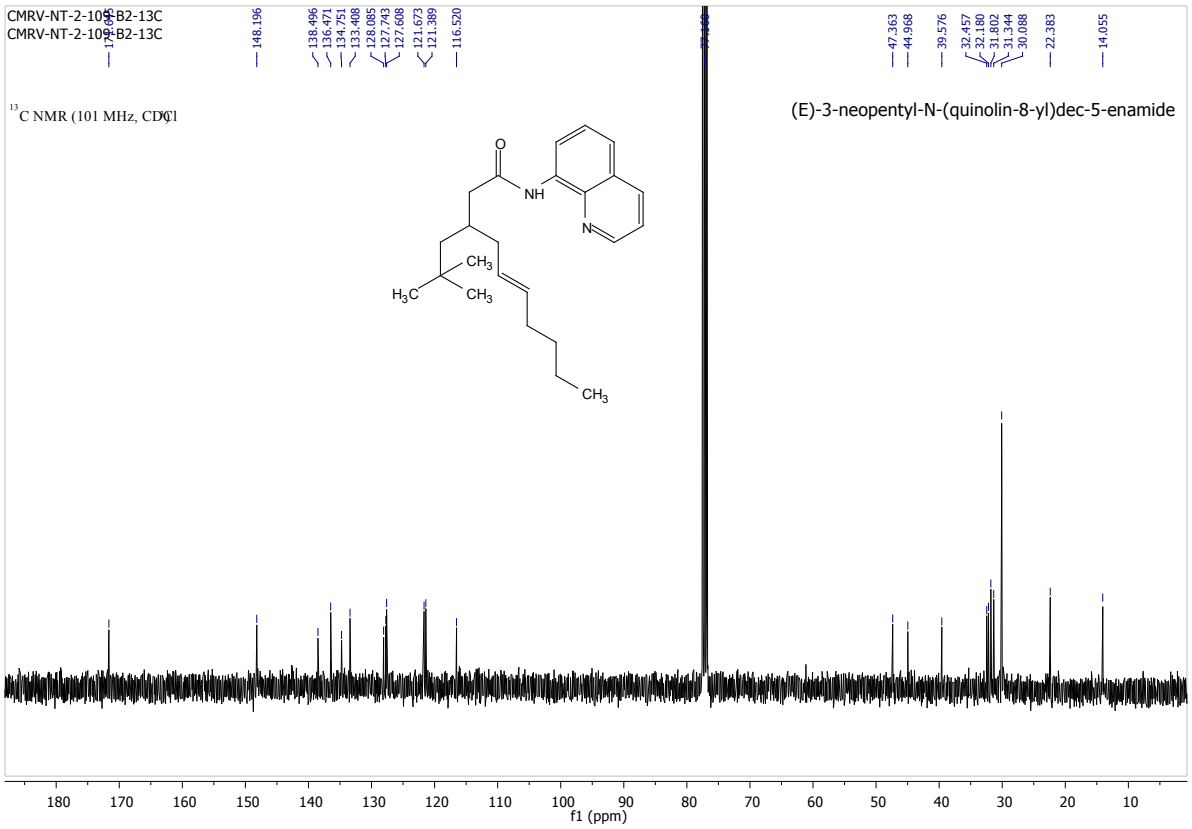


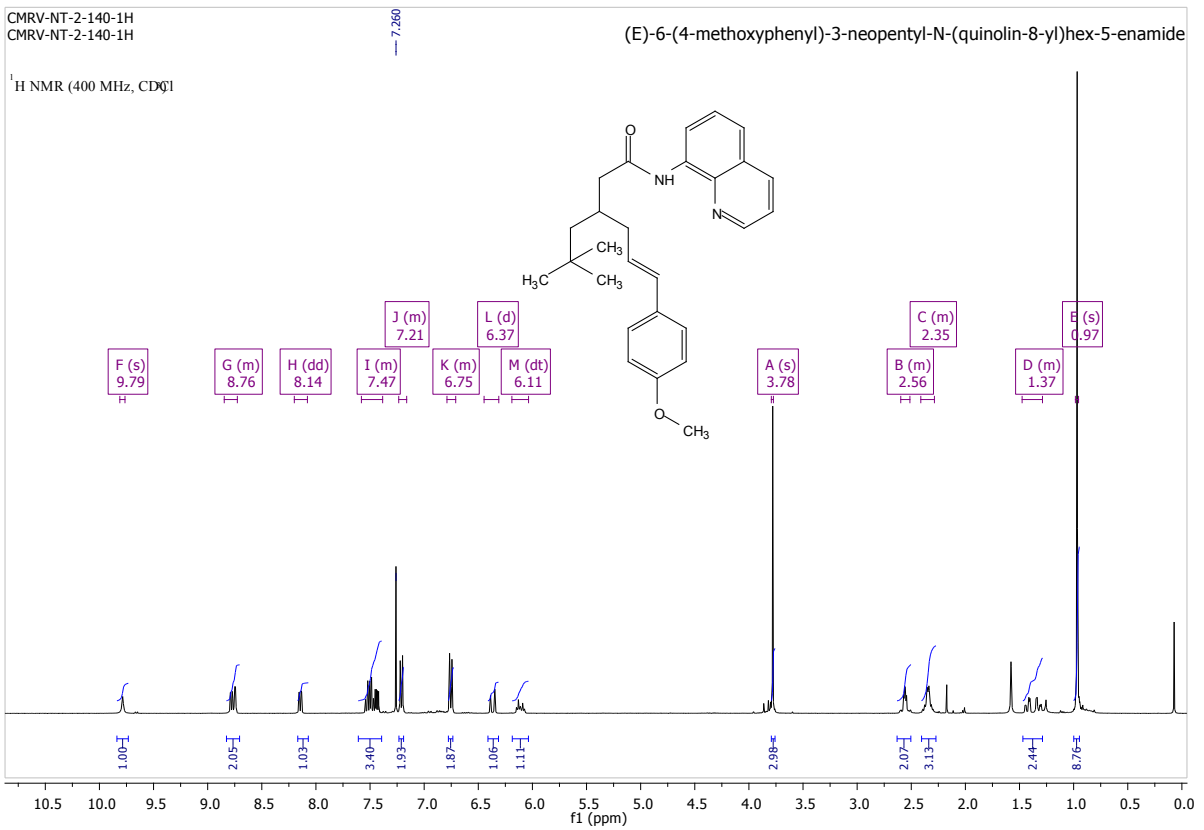
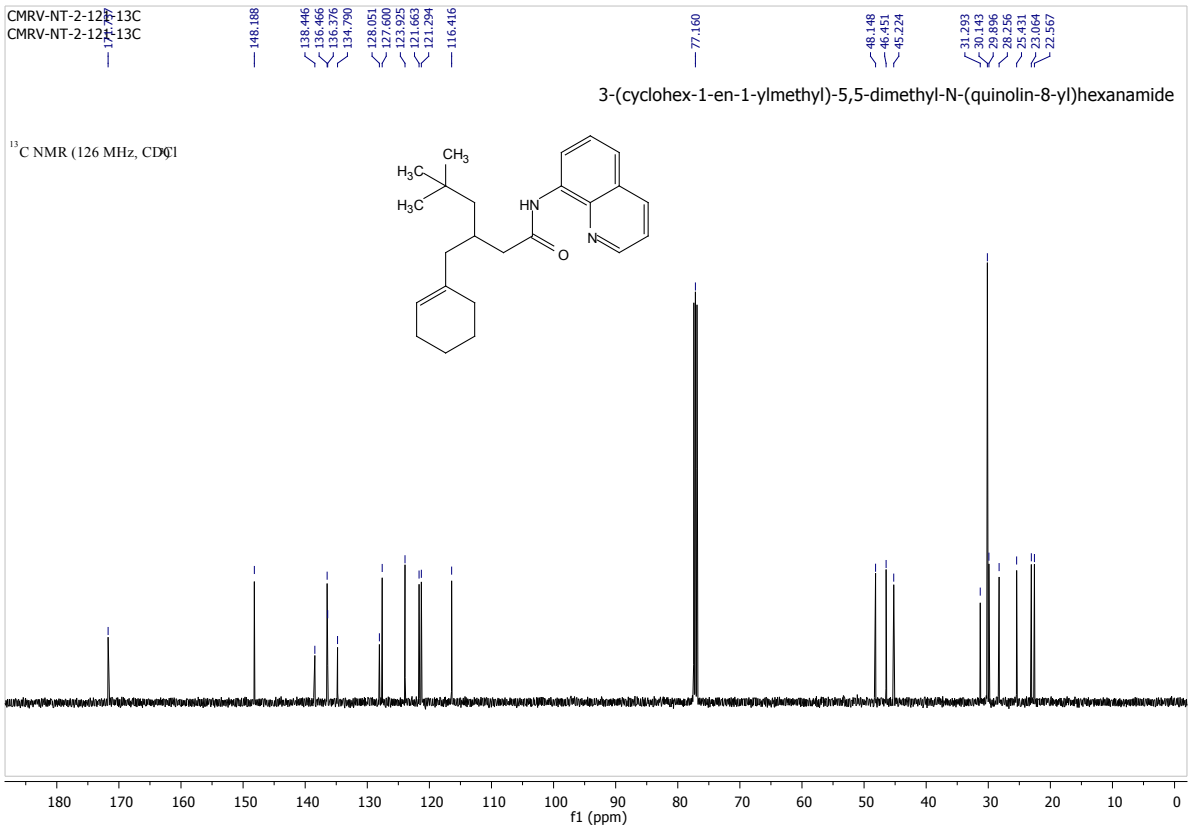


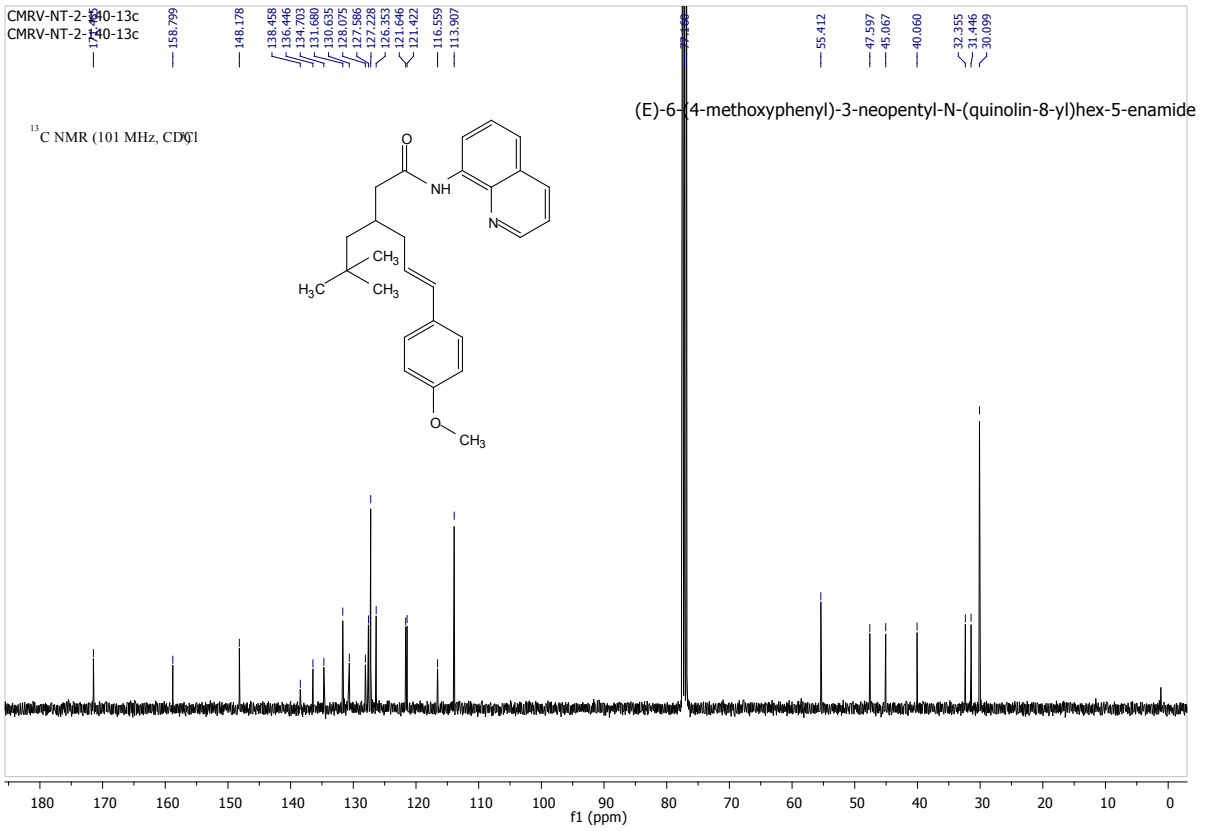


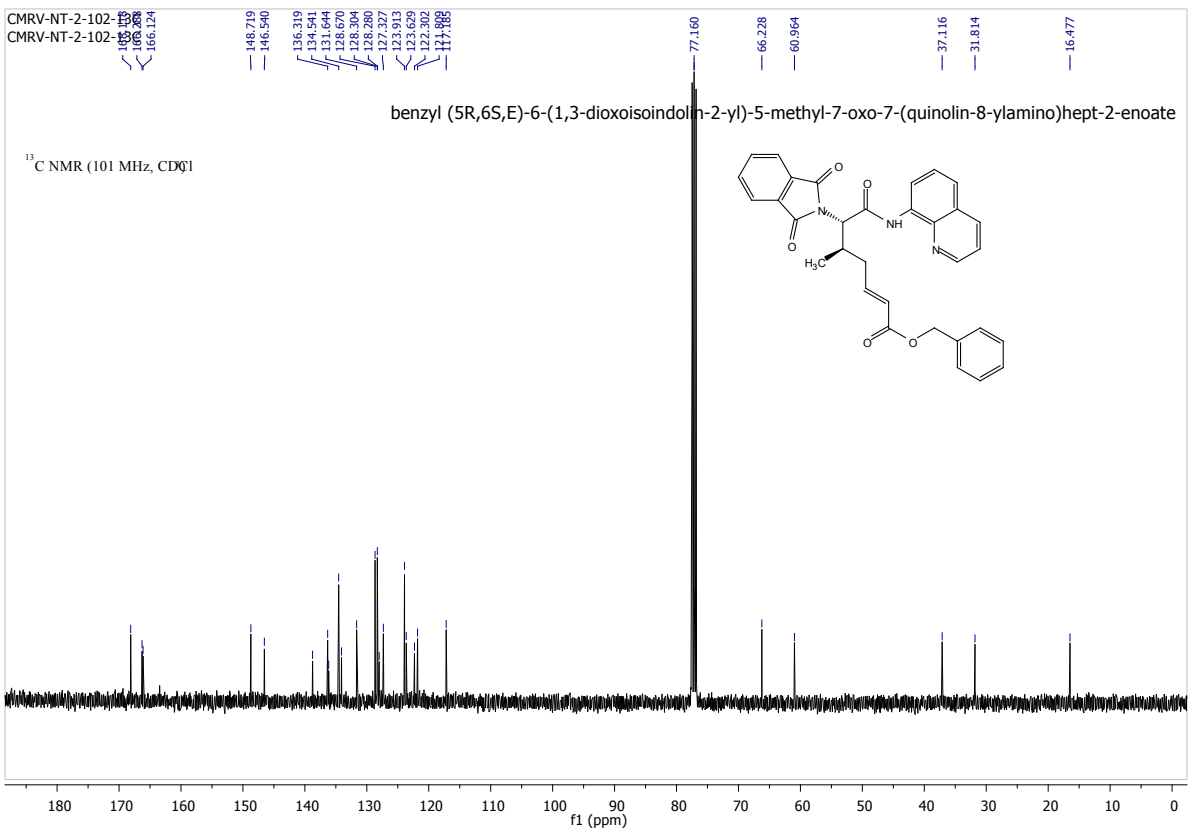
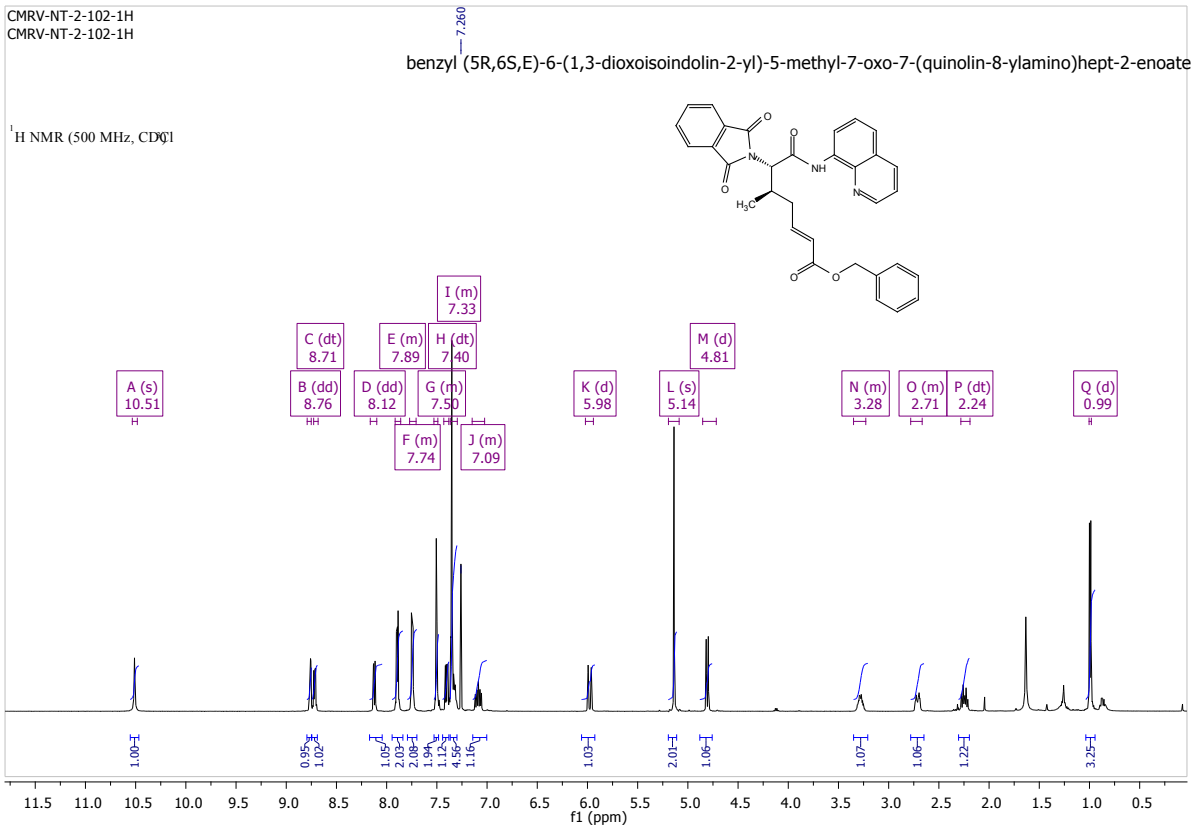








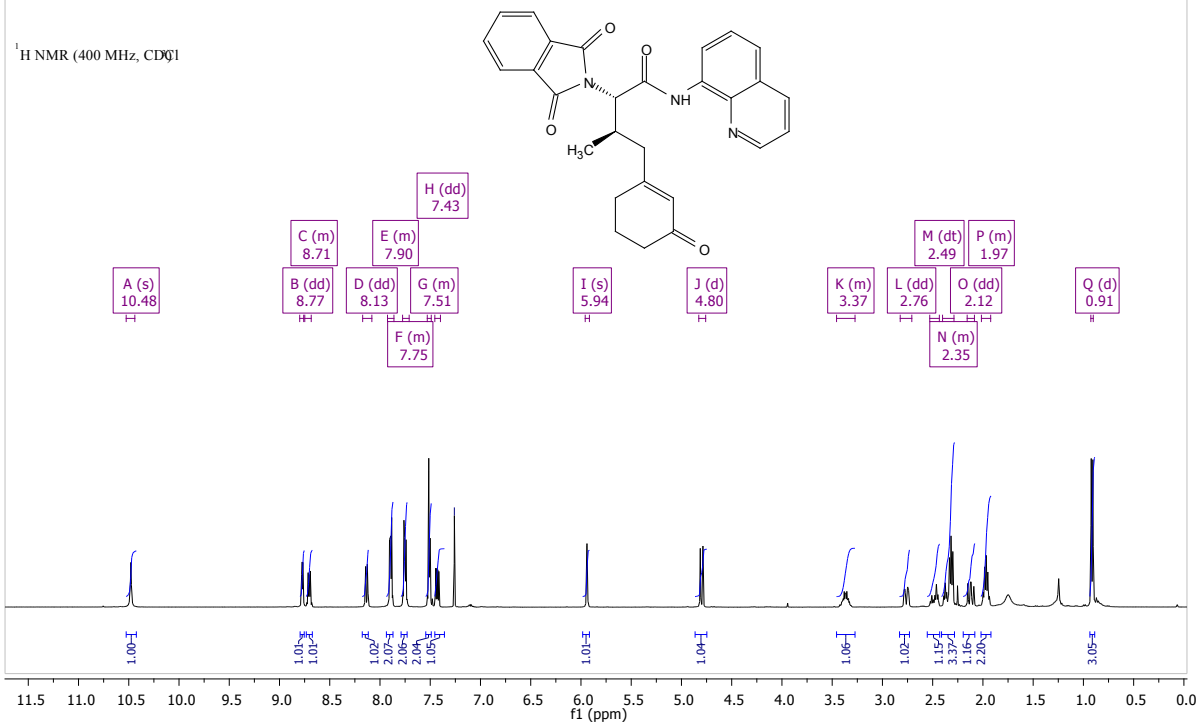




CMRV-NT-2-110-1H
CMRV-NT-2-110-1H

(2S,3R)-2-(1,3-dioxisoindolin-2-yl)-3-methyl-4-(3-oxocyclohex-1-en-1-yl)-N-(quinolin-8-yl)butanamide

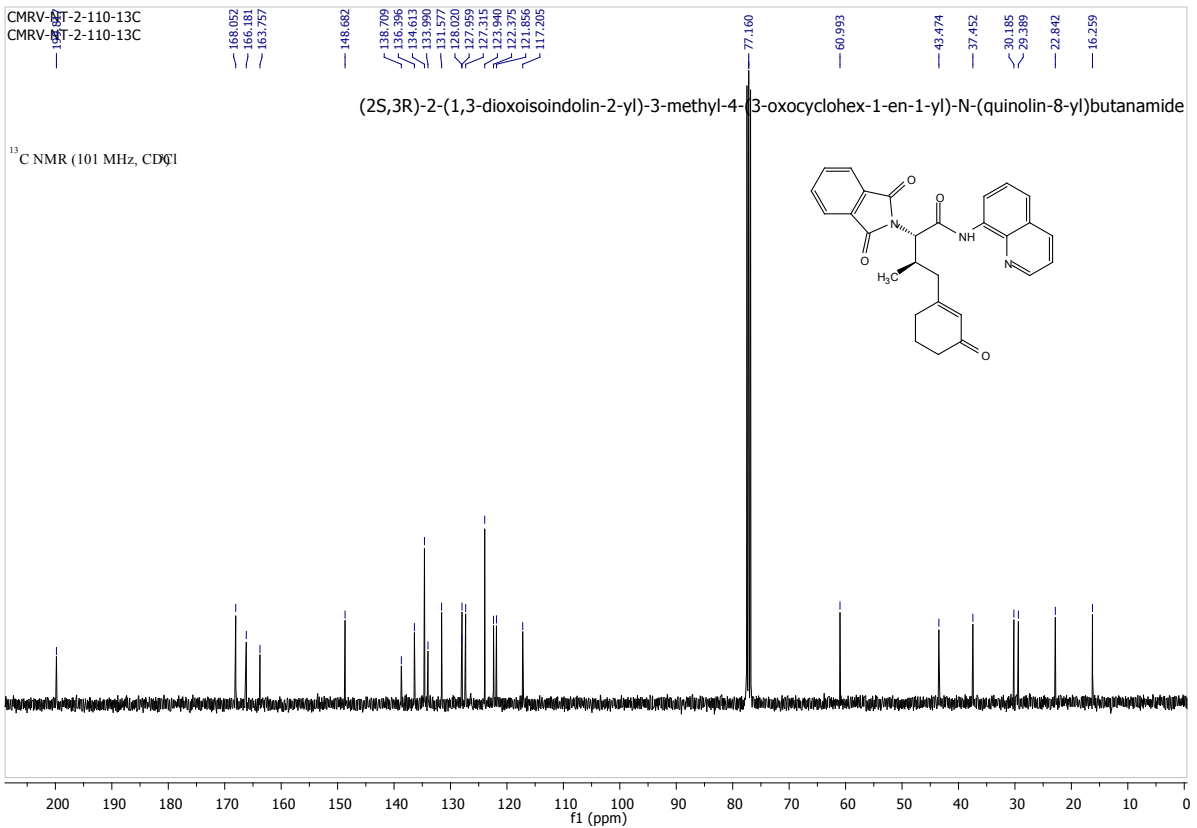
¹H NMR (400 MHz, CDCl₃)

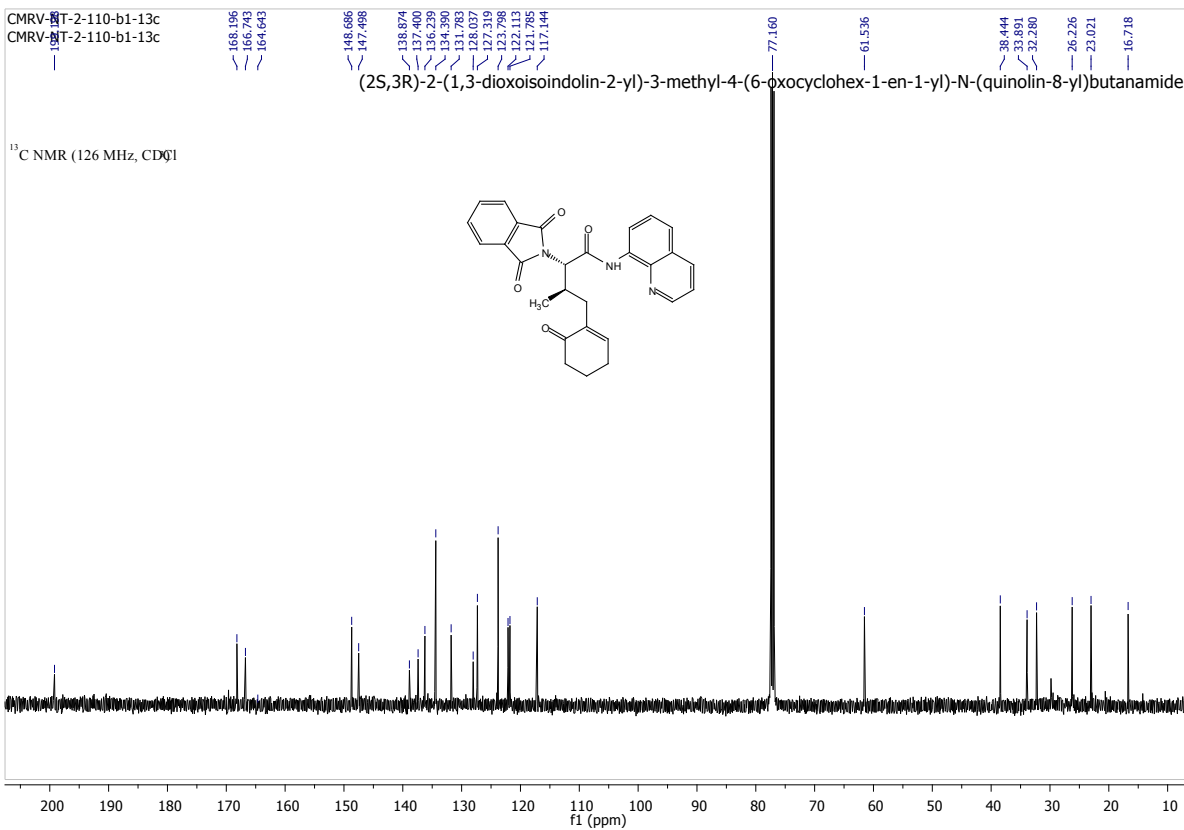
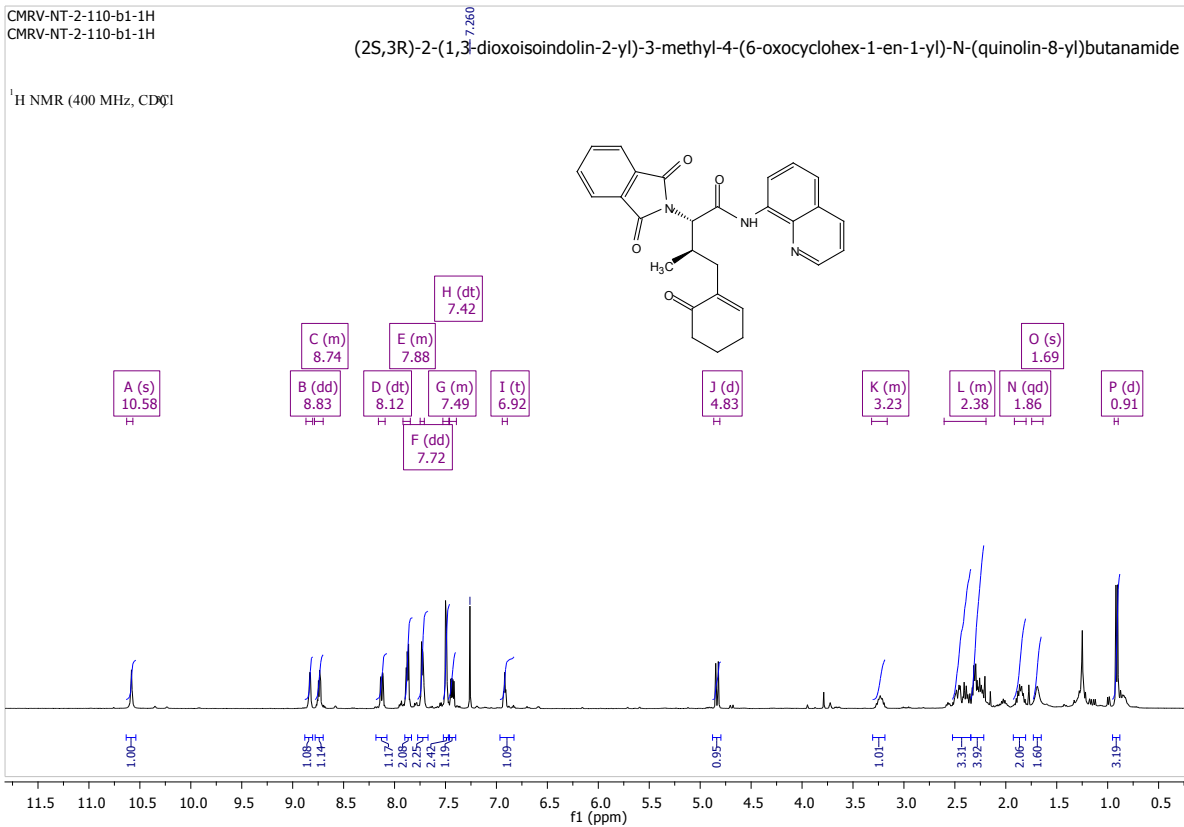


CMRV-NT-2-110-13C
CMRV-NT-2-110-13C

(2S,3R)-2-(1,3-dioxisoindolin-2-yl)-3-methyl-4-(3-oxocyclohex-1-en-1-yl)-N-(quinolin-8-yl)butanamide

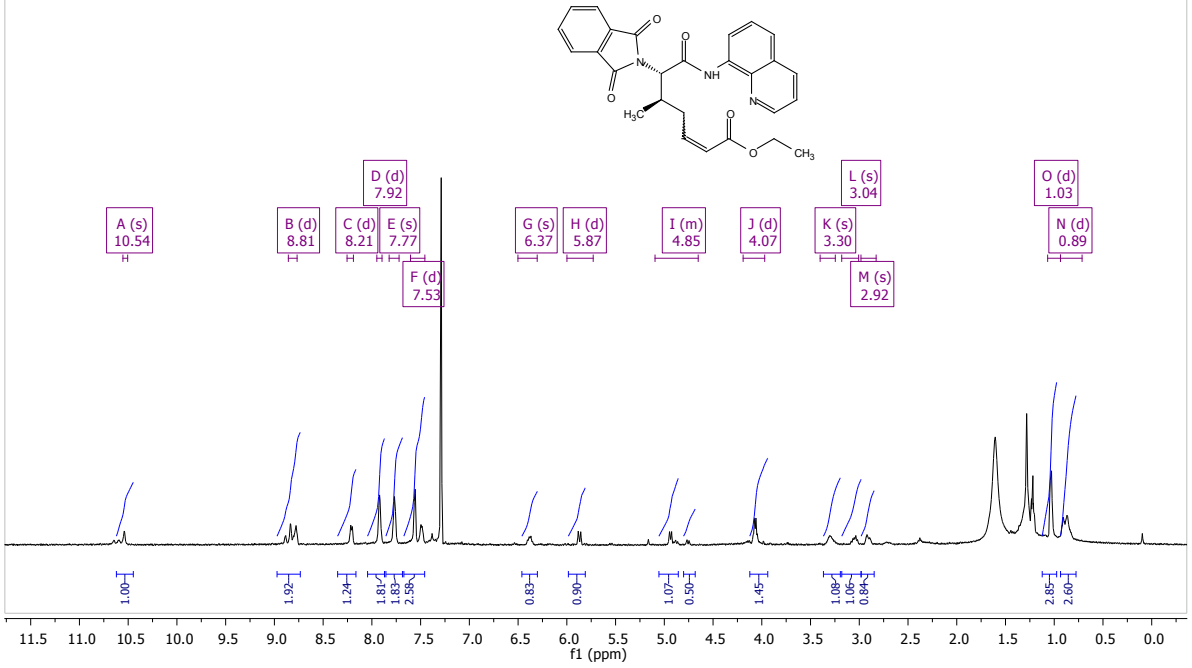
¹³C NMR (101 MHz, CDCl₃)





CMRV-NT-2-123-P1-1H
CMRV-NT-2-123-P1-1H

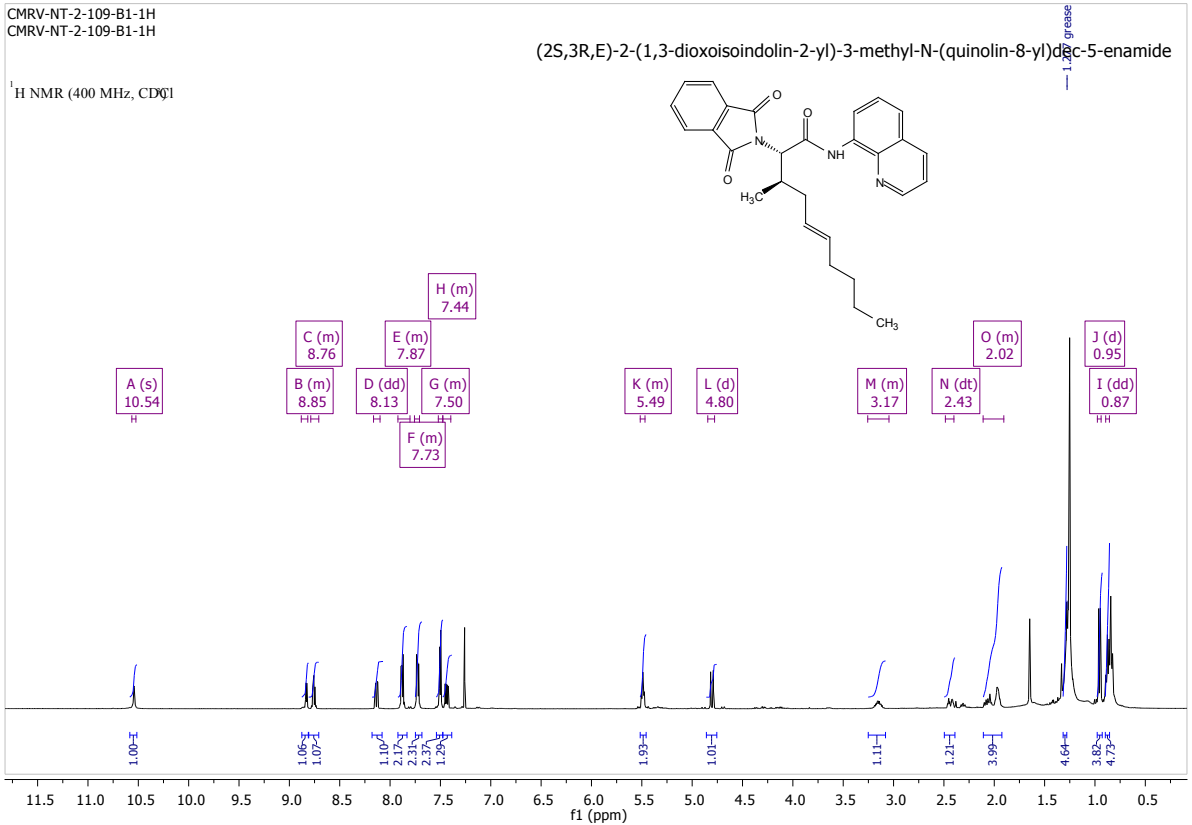
ethyl (5R,6S)-6-(1,3-dioxisoindolin-2-yl)-5-methyl-7-oxo-7-(quinolin-8-ylamino)hept-2-enoate

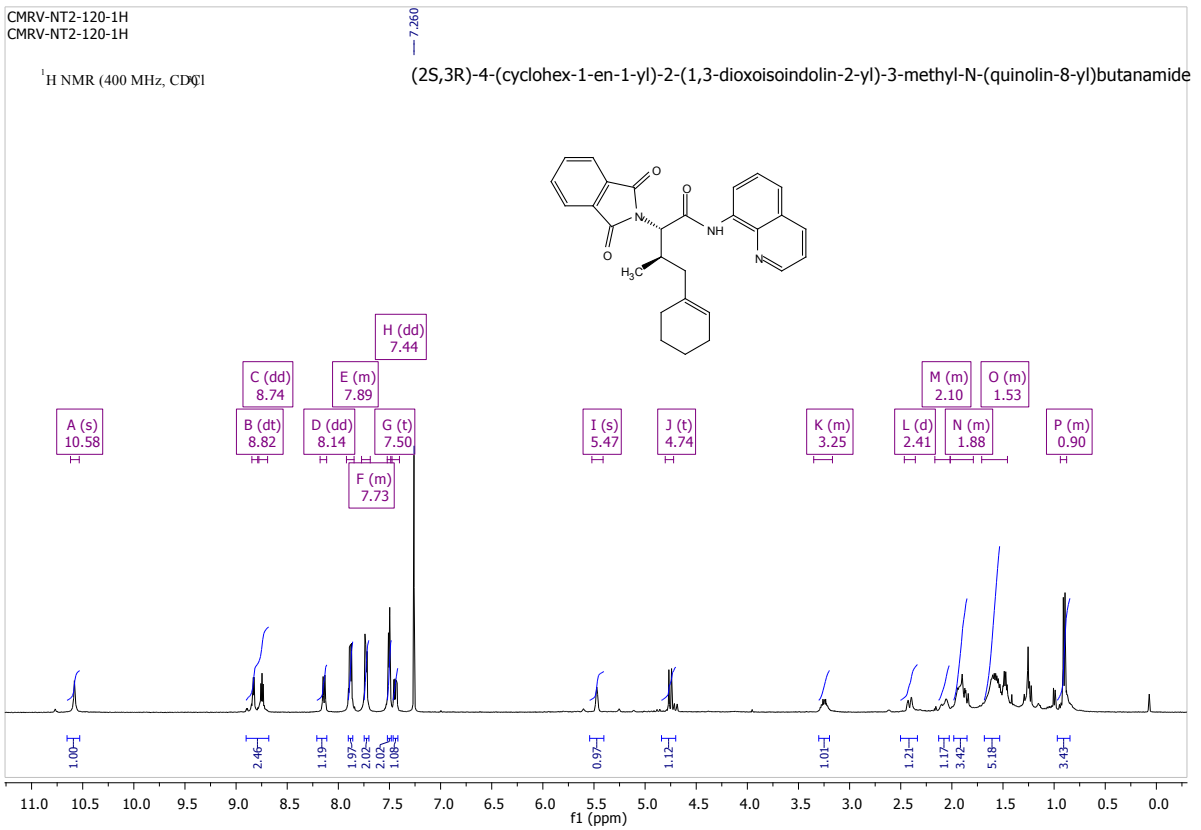
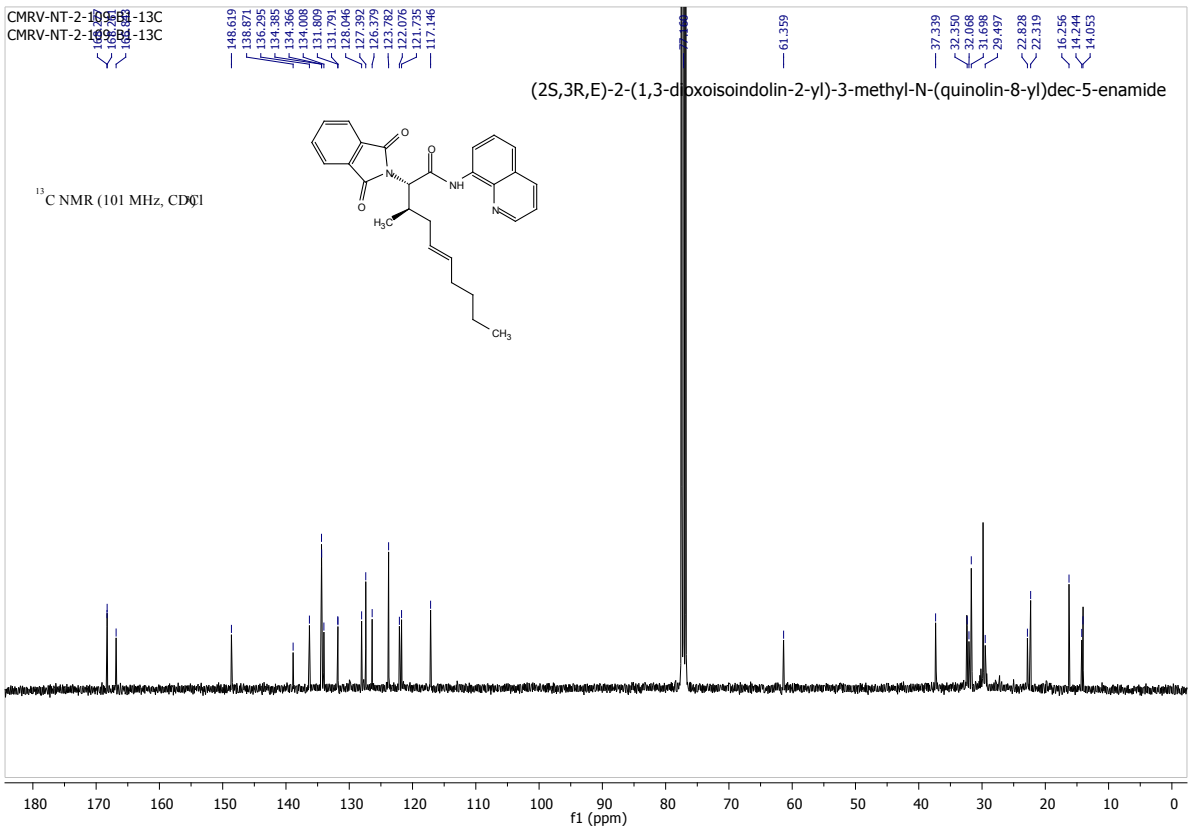


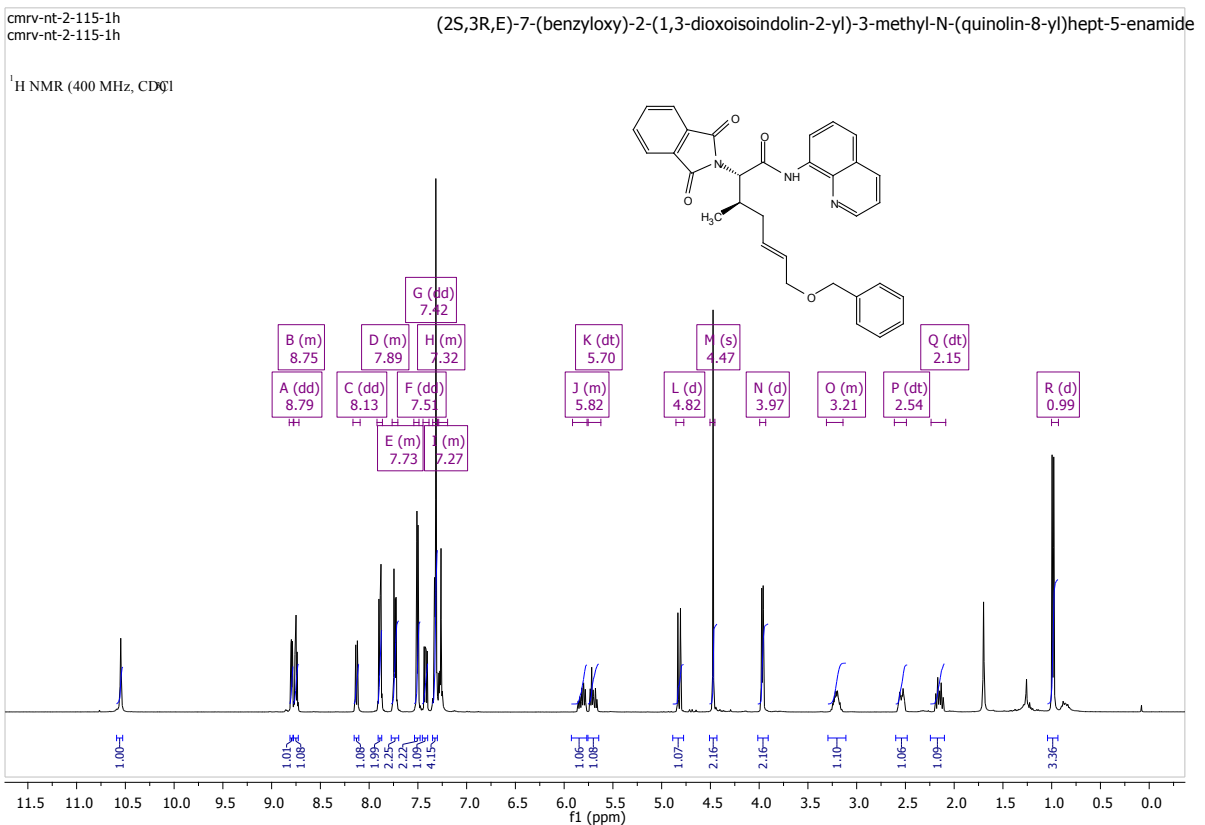
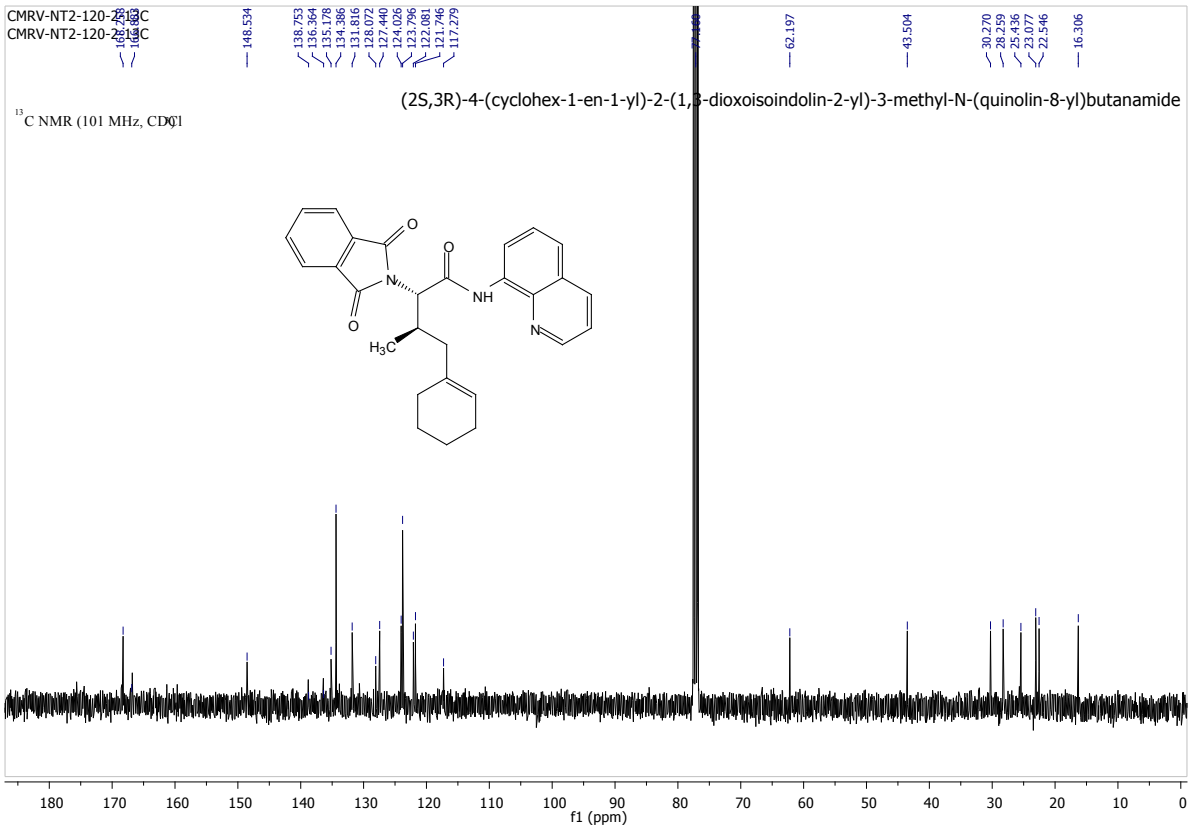
CMRV-NT-2-109-B1-1H
CMRV-NT-2-109-B1-1H

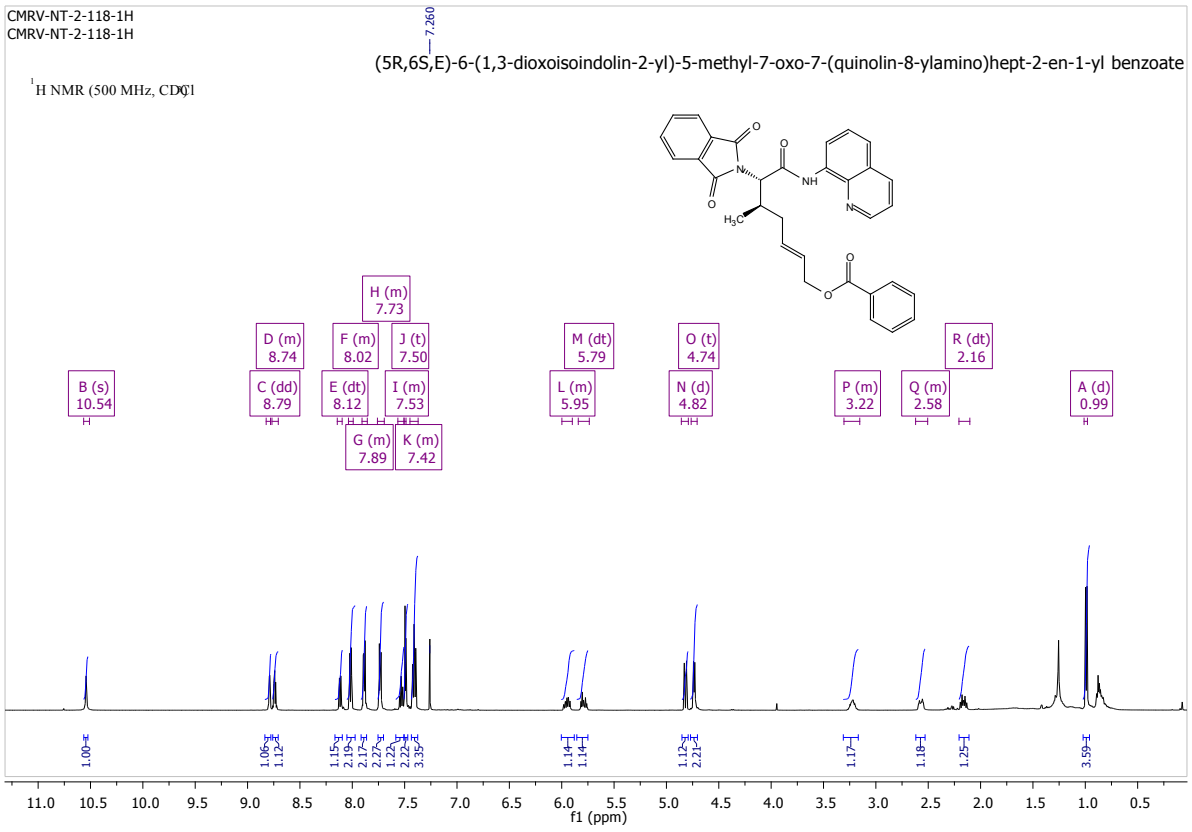
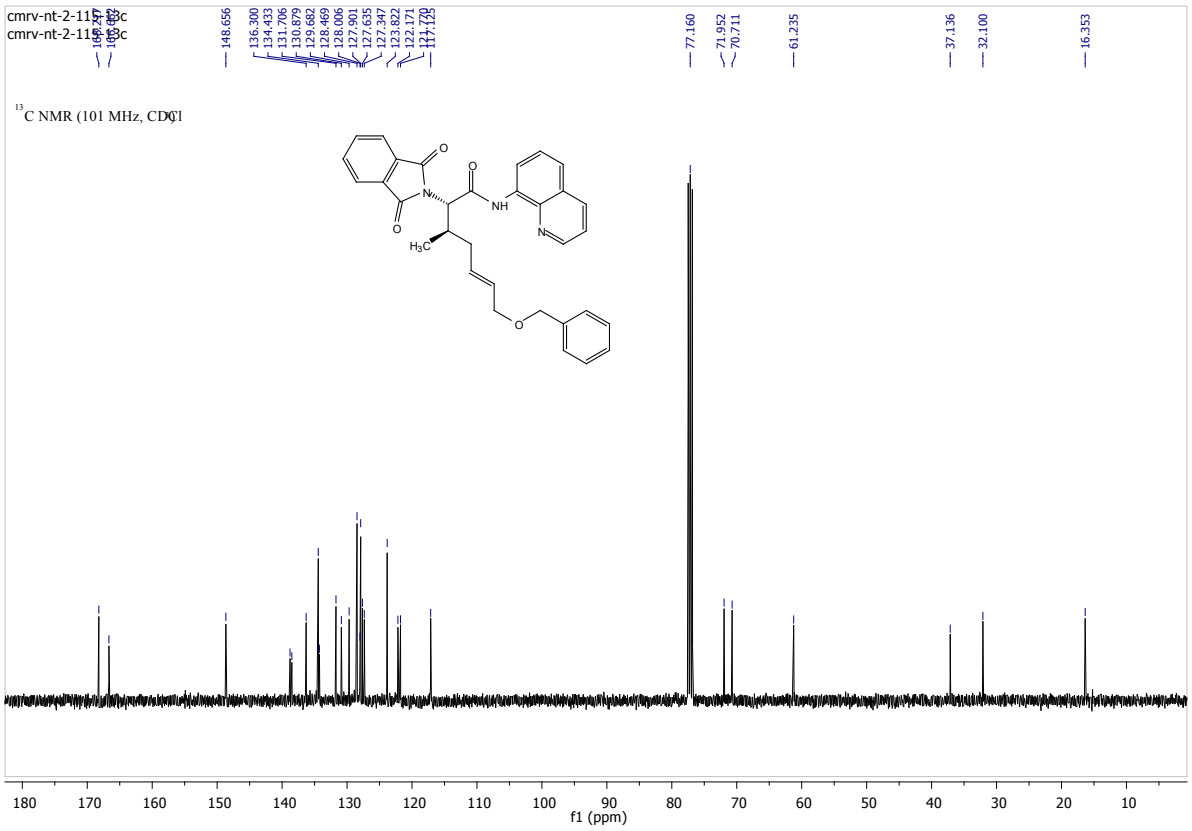
(2S,3R,E)-2-(1,3-dioxisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)dec-5-enamide

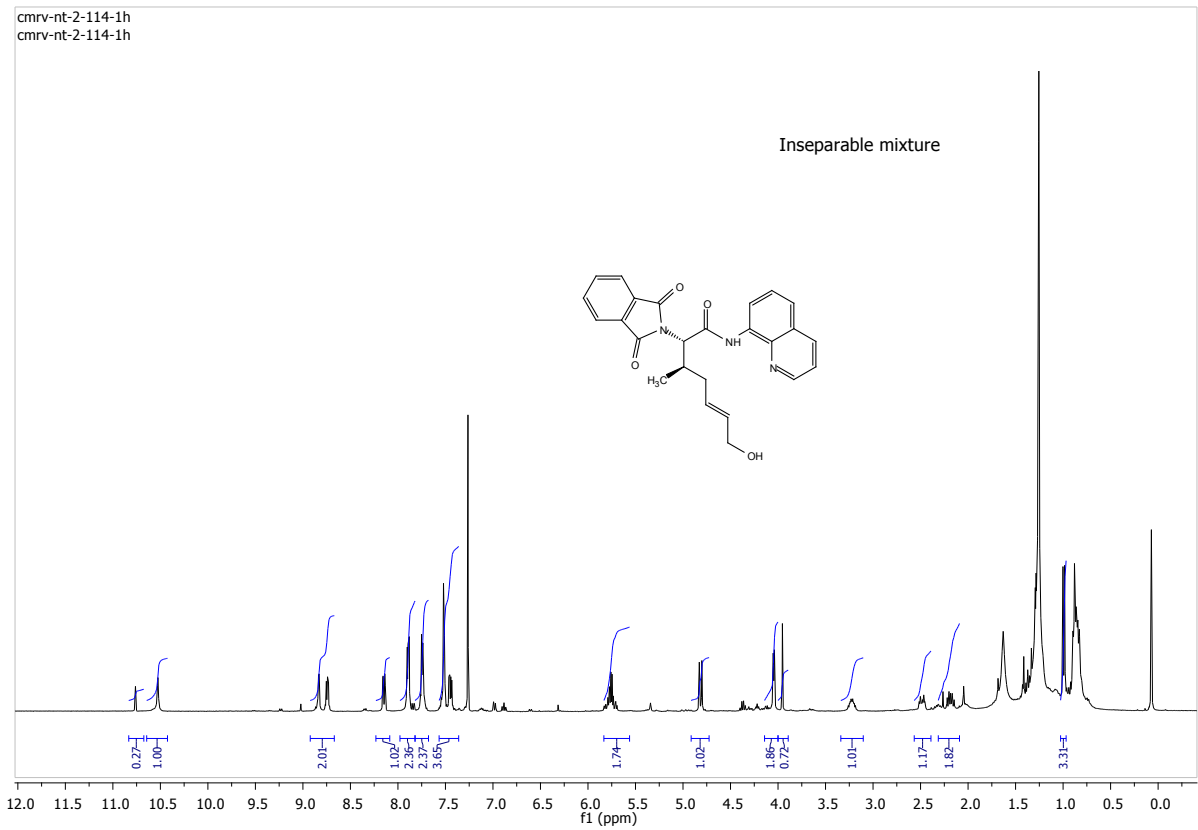
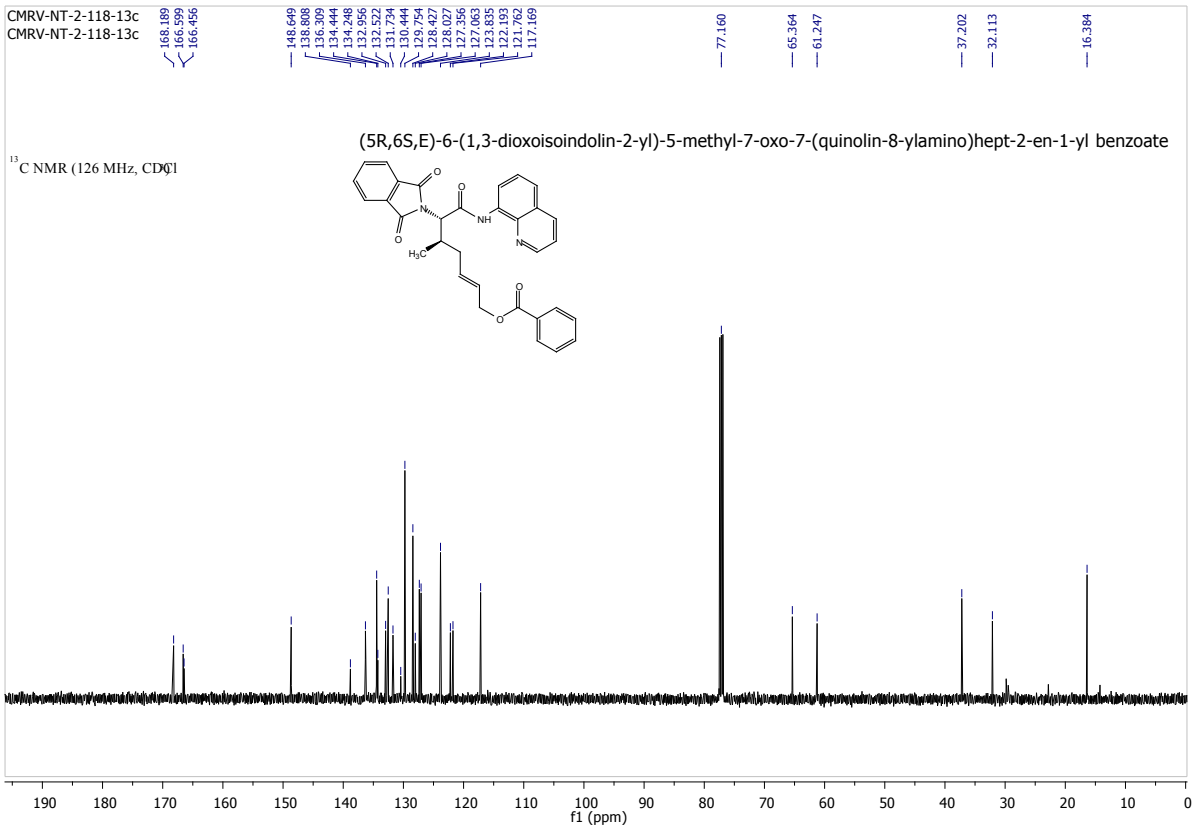
¹H NMR (400 MHz, CDCl₃)







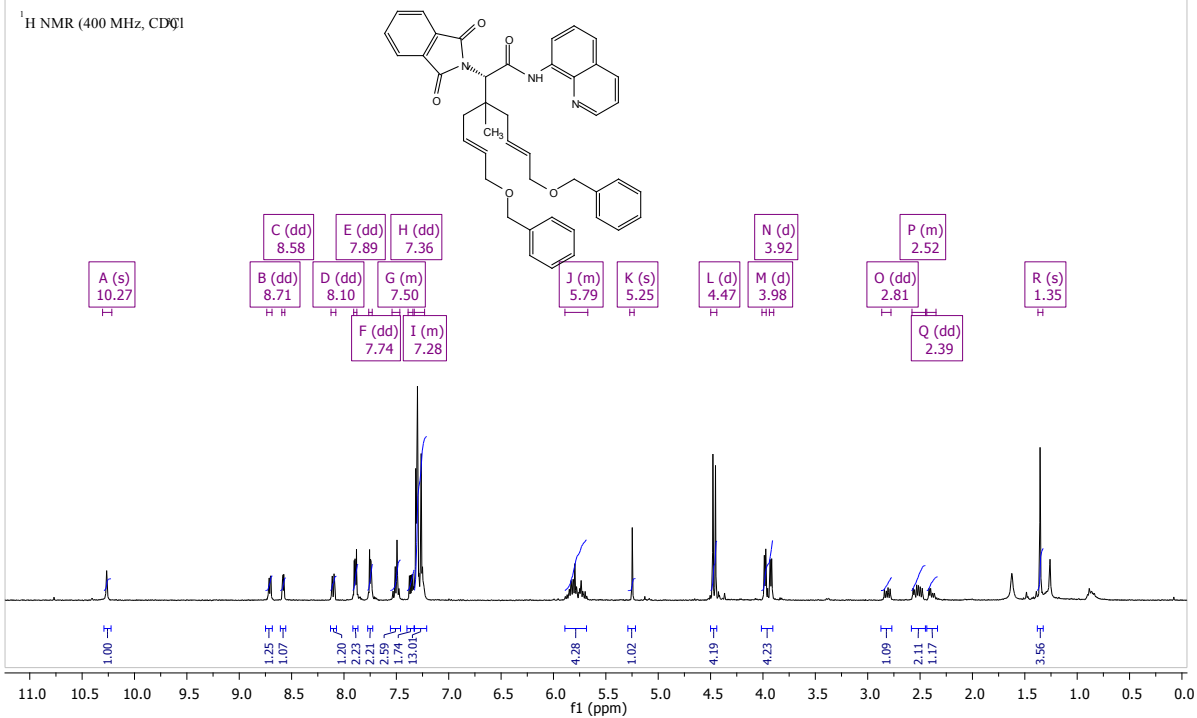




CMRV-NT-2-116-BELOW2-1H
CMRV-NT-2-116-BELOW2-1H

(S,E)-7-(benzyloxy)-3-((E)-4-(benzyloxy)but-2-en-1-yl)-2-(1,3-dioxoisindolin-2-yl)-3-methyl-N-(quinolin-8-yl)hept-5-enamide

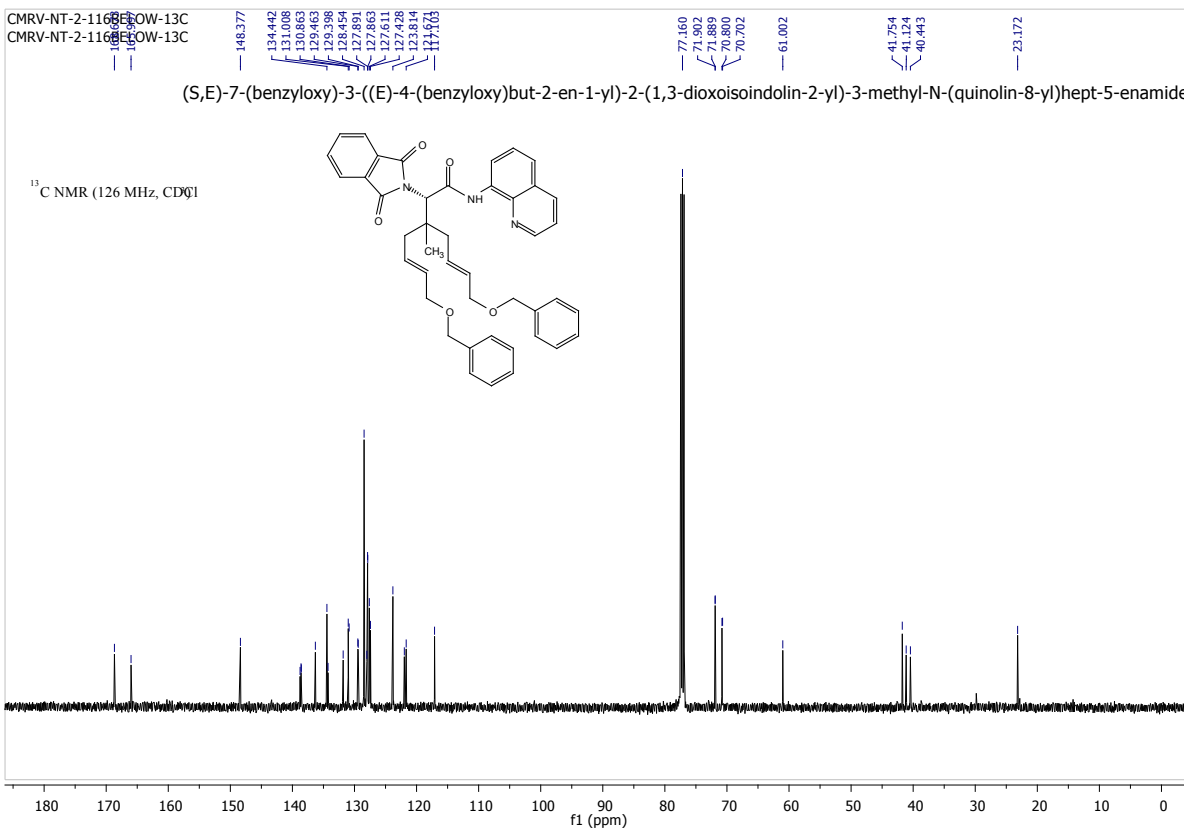
¹H NMR (400 MHz, CDCl₃)



CMRV-NT-2-116-BELOW-13C
CMRV-NT-2-116-BELOW-13C

(S,E)-7-(benzyloxy)-3-((E)-4-(benzyloxy)but-2-en-1-yl)-2-(1,3-dioxoisindolin-2-yl)-3-methyl-N-(quinolin-8-yl)hept-5-enamide

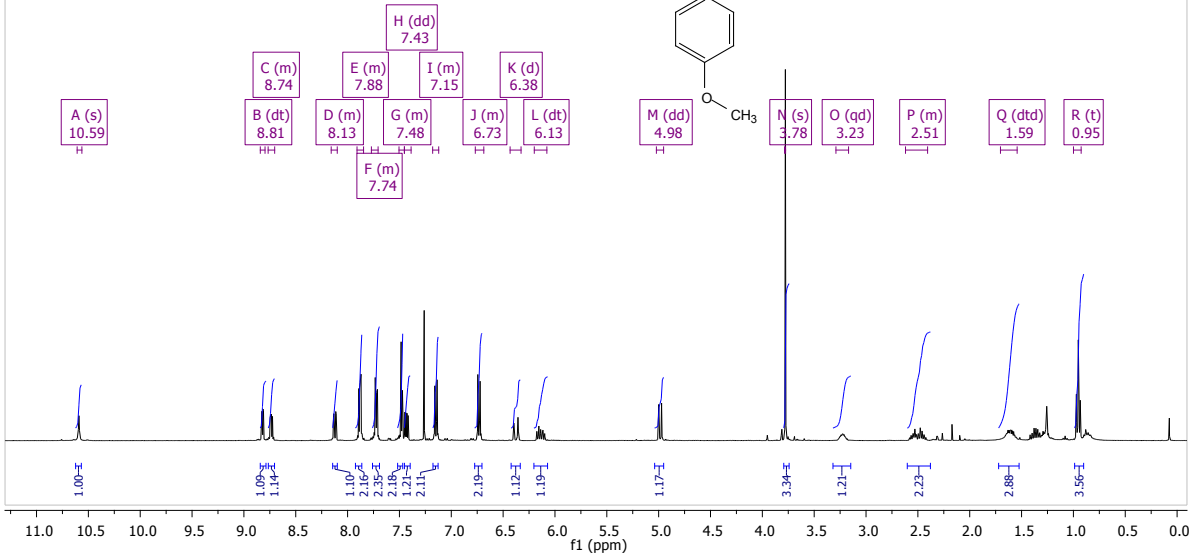
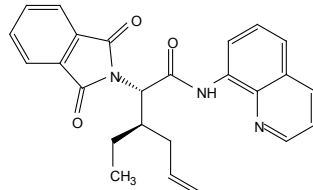
¹³C NMR (126 MHz, CDCl₃)



CMRV-NT-2-139-1H
CMRV-NT-2-139-1H

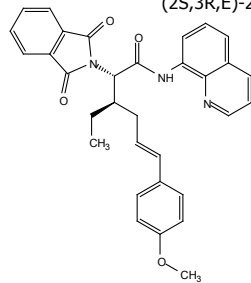
(2S,3R,E)-2-(1,3-dioxisoindolin-2-yl)-3-ethyl-6-(4-methoxyphenyl)-N-(quinolin-8-yl)hex-5-enamide

¹H NMR (400 MHz, CDCl₃)

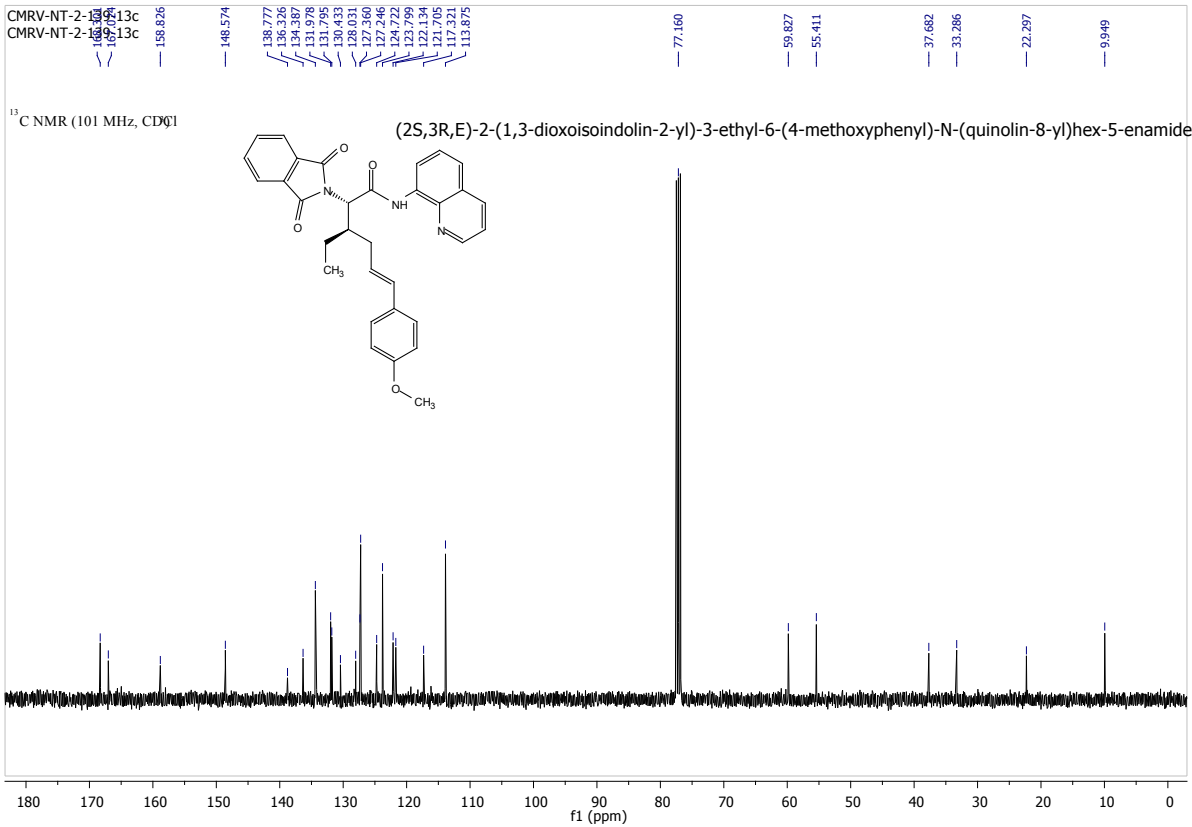


CMRV-NT-2-139-13C
CMRV-NT-2-139-13C

¹³C NMR (101 MHz, CDCl₃)



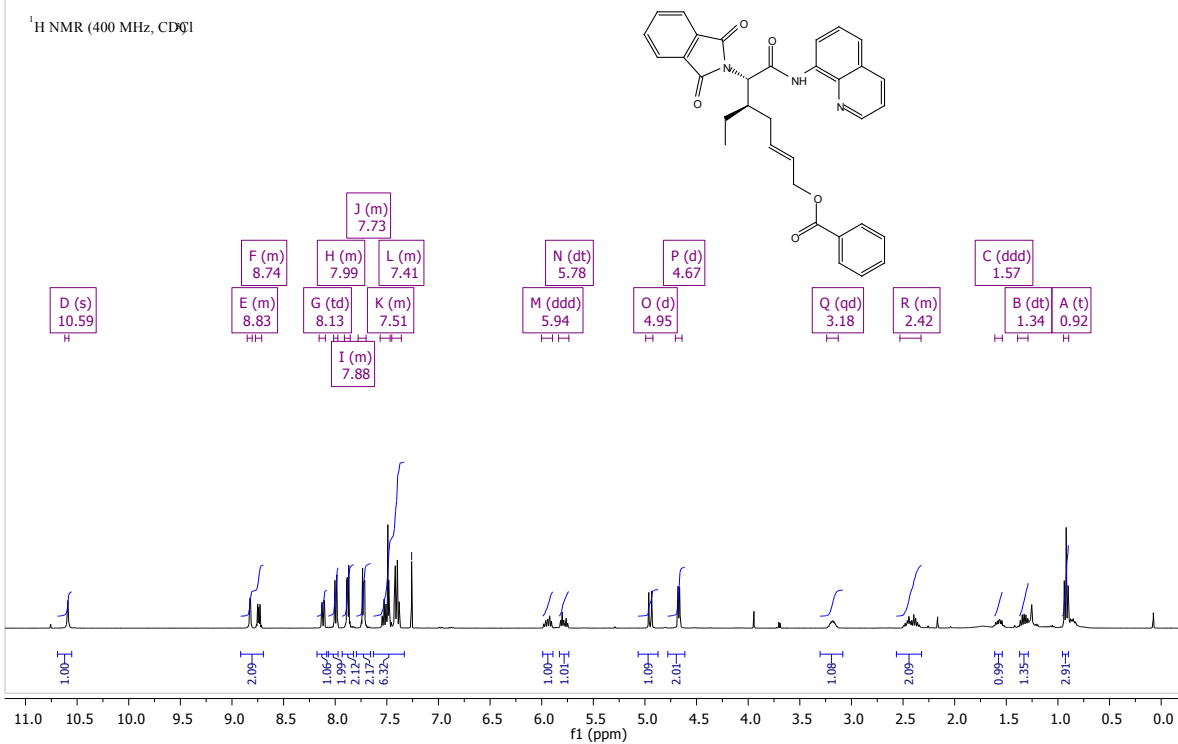
(2S,3R,E)-2-(1,3-dioxisoindolin-2-yl)-3-ethyl-6-(4-methoxyphenyl)-N-(quinolin-8-yl)hex-5-enamide



CMRV-NT-2-125-B1-1H
CMRV-NT-2-125-B1-1H

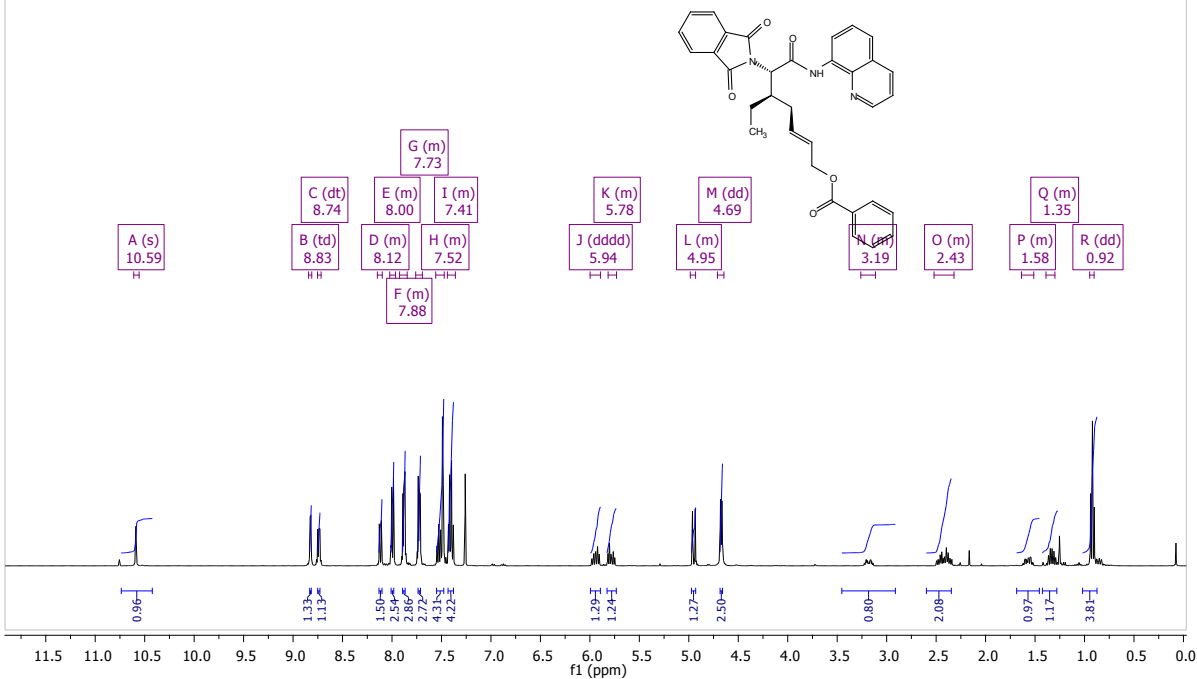
(5R,6S,E)-6-(1,3-dioxisoindolin-2-yl)-5-ethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-en-1-yl benzoate

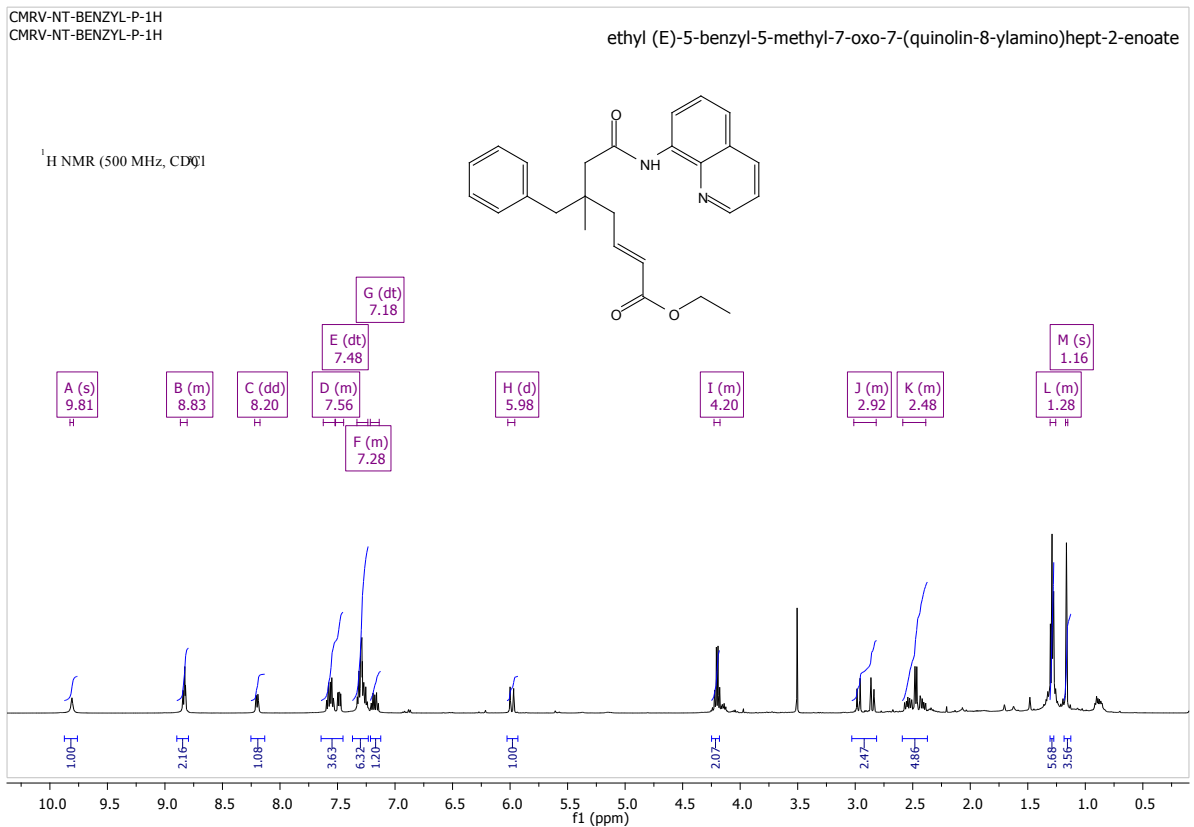
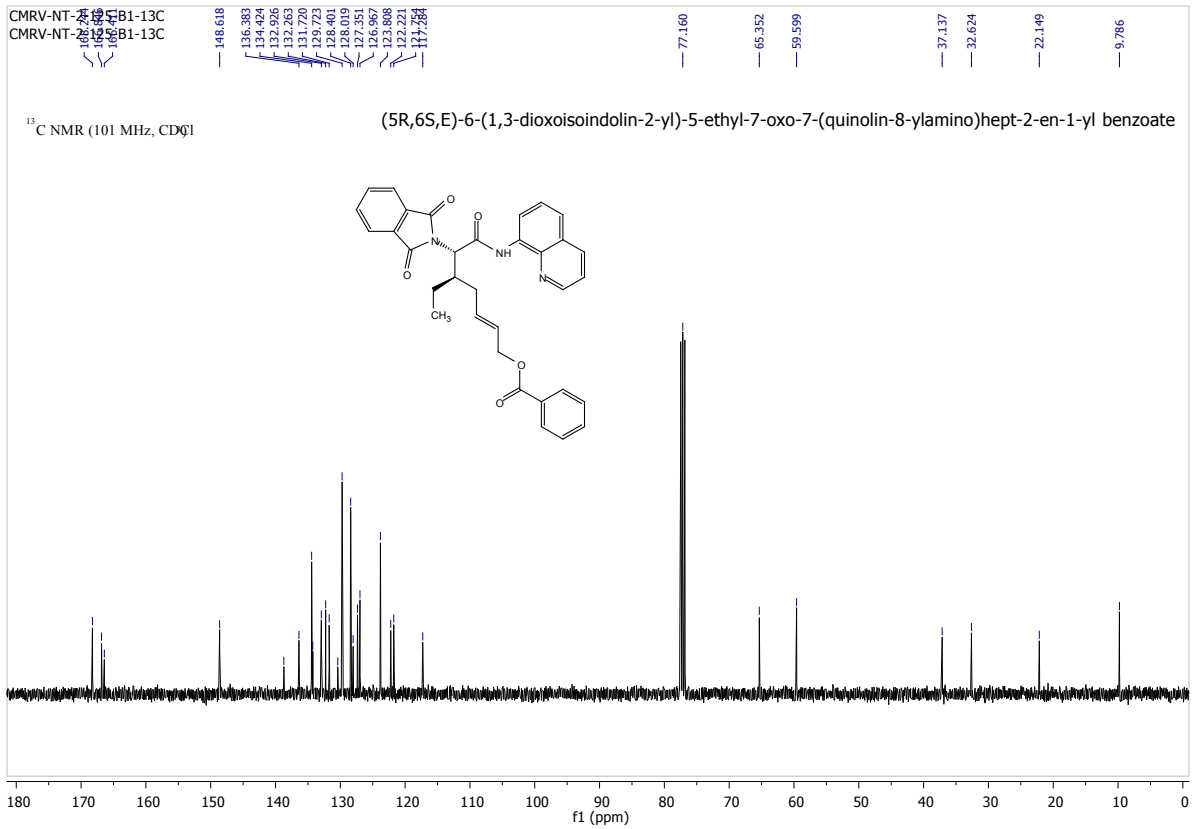
¹H NMR (400 MHz, CDCl₃)

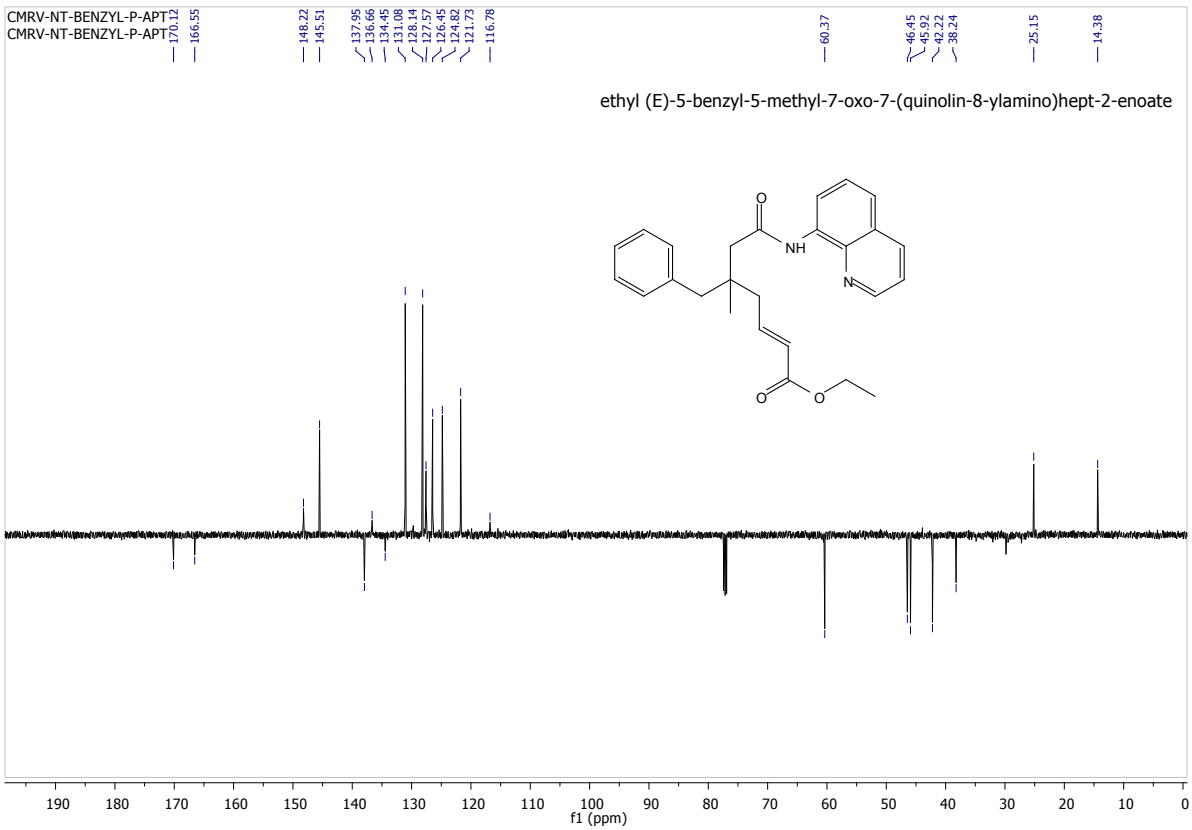
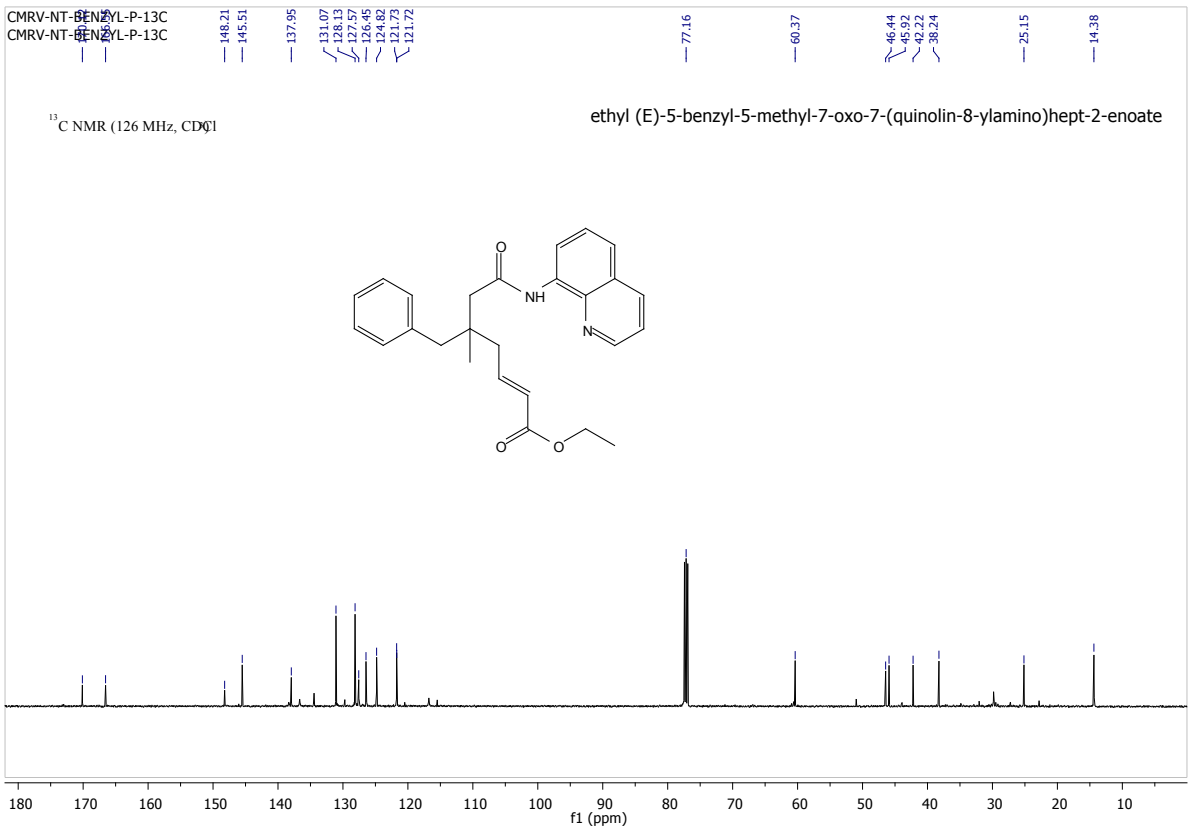


CMRV-NT-2-125-B1-1H
CMRV-NT-2-125-B1-1H

(5R,6S,E)-6-(1,3-dioxisoindolin-2-yl)-5-ethyl-7-oxo-7-(quinolin-8-ylamino)hept-2-en-1-yl benzoate



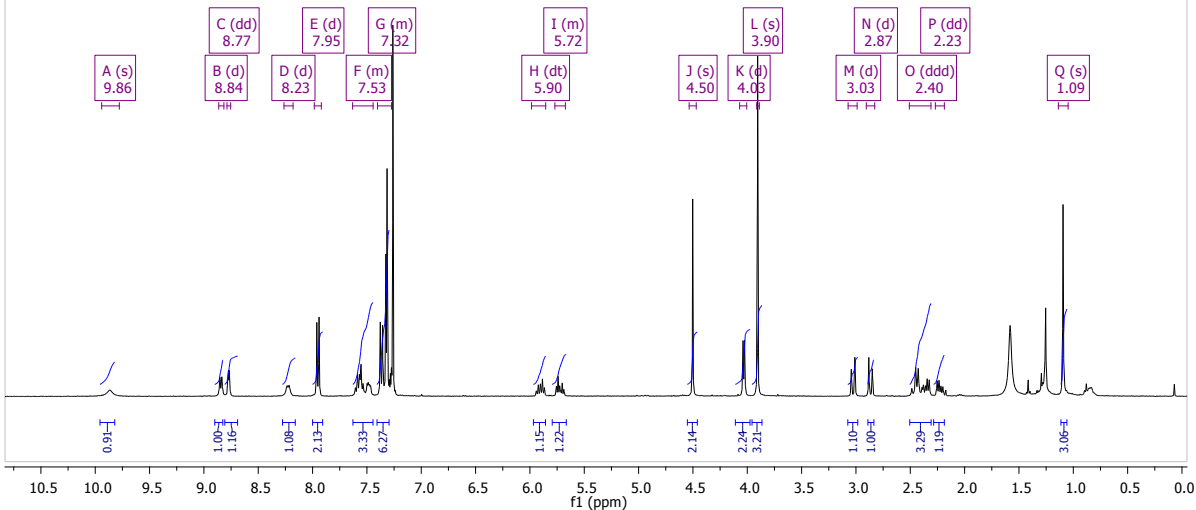
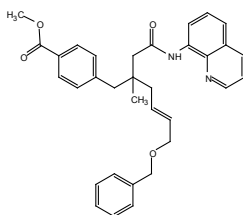




CMRV-NT-2-141-2-1H
CMRV-NT-2-141-2-1H

methyl (E)-4-(6-(benzyloxy)-2-methyl-2-(2-oxo-2-(quinolin-8-ylamino)ethyl)hex-4-en-1-yl)benzoate

¹H NMR (400 MHz, CDCl₃)



CMRV-NT-2-141-2-13C
CMRV-NT-2-141-2-13C

¹³C NMR (101 MHz, CDCl₃)

