Activation of Diverse Carbon–Heteroatom and Carbon–Carbon Bonds *via* Palladium(II)-Catalyzed β-X Elimination

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General Information

Unless stated otherwise, all materials were used as received from commercial sources without further purification. All glassware and stirring bars were dried in an oven at 100 °C overnight unless otherwise stated. DCM, MeCN, and DMF were purchased from Aldrich and used as received without additional drying. 1-Dram reaction vials and caps were purchased from ChemGlass (Cat#: CG-4904-05) with TFE septa. Ambient temperature refers to 21–24 °C. Elevated temperatures were maintained by an Ika heating block for 1-Dram vials or a silicon oil bath for larger vessels. Thin-layer chromatography (TLC) was performed using EMD Millipore 250 mm silica gel F-254 plates (250 μm) with F-254 fluorescent indicator and visualized by UV fluorescence quenching, iodine, Seebach's stain, or potassium permanganate stain. SiliCycle SiliaFlash P60 silica gel (particle size 40–63 μm) was used for flash chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX equipped with a 5mm DCH cryoprobe (600 MHz and 150 MHz, respectively). ^{19}F spectra were recorded on a Bruker DPX with a 5 mm QNP probe (376 MHz). ^{1}H spectra were reported relative to Me_4Si (δ 0.0) or residual solvent signals unless otherwise stated. ^{13}C NMR spectra were calibrated to residual solvent signals ($CDCl_3$ at 77.16 ppm, DMSO at 39.52 ppm, $(CD_3)_2CO$ at 29.84, and CD_3OD at 49.00). High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization (Positive mode) time of flight experiments.

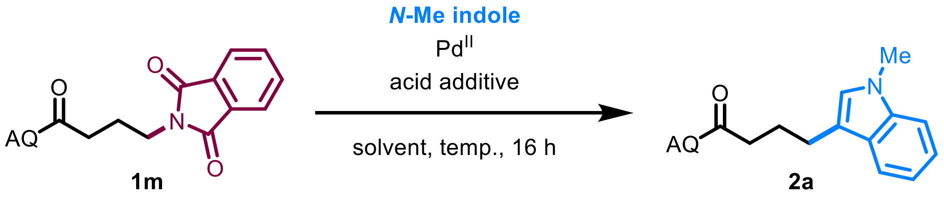
Chemical and Supplier:

The following chemicals were purchased from:
Alfa Aesar: vinyl acetic acid
Oakwood: 8-Aminoquinoline, EDC, HATU
Fisher: pyridine and acetic acid

All other chemicals were purchased from Aldrich and used as received.

Optimization Data

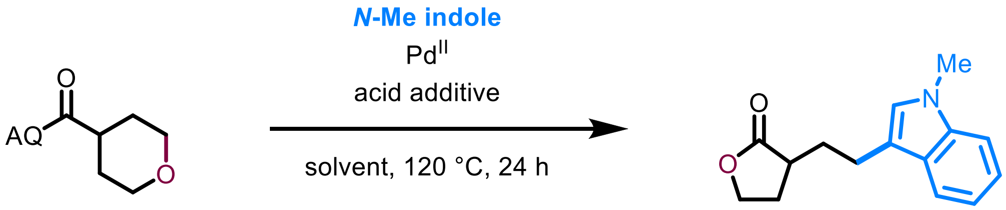
Table S1. Optimization of C–N activation of phthalimide[a]



Entry	Pd Source	Solvent	Acid Additive	*N*-Me indole (equiv)	Temperature (ºC)	% Yield[b]
1	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	2	120	64
2	5% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	2	120	35
3	10% $Pd(OAc)_2$	MeCN (1M)	none	2	120	41
4	10% $Pd(OAc)_2$	MeCN (0.5M)	50% AcOH	2	120	32
5	10% $Pd(OAc)_2$	MeCN (1M)	50% 4-anisic acid	2	120	64
6	10% $Pd(OAc)_2$	MeCN (1M)	50% pivalic acid	2	120	70
7	10% $Pd(OAc)_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	120	76
8	10% $Pd(OAc)_2$	MeCN (2M)	50% 1-Ada-CO_2H	2	120	49
9	10% $Pd(OAc)_2$	toluene (1M)	50% 1-Ada-CO_2H	2	120	53
10	10% $Pd(OAc)_2$	*t*-BuOH (1M)	50% 1-Ada-CO_2H	2	120	60
11	10% $Pd(OAc)_2$	DCE (1M)	50% 1-Ada-CO_2H	2	120	57
12	10% $Pd(OAc)_2$	HFIP (1M)	50% 1-Ada-CO_2H	2	120	50
13	10% $Pd(OAc)_2$	dioxane (1M)	50% 1-Ada-CO_2H	2	120	48
14	10% $Pd(OAc)_2$	DMF (1M)	50% 1-Ada-CO_2H	2	120	63
15	10% $Pd(OAc)_2$	$MeNO_2$ (1M)	50% 1-Ada-CO_2H	2	120	64
16	10% $Pd(OAc)_2$	benzonitrile (1M)	50% 1-Ada-CO_2H	2	120	64
17	10% $Pd(OAc)_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	100	63
18	10% $Pd(OAc)_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	80	19
19	10% $Pd(OAc)_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	140	58
20	10% $Pd(OAc)_2$	MeCN (1M)	25% 1-Ada-CO_2H	2	120	73
21	10% $Pd(OAc)_2$	MeCN (1M)	100% 1-Ada-CO_2H	2	120	72
22	20% $Pd(OAc)_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	120	75
23	10% $Pd(OAc)_2$	MeCN (1M)	100% 1-Ada-CO_2H	1	120	51
24	10% $Pd(OAc)_2$	MeCN (1M)	100% 1-Ada-CO_2H	4	120	72
25	10% $Pd(TFA)_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	120	38
26	10% $PdCl_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	120	0
27	10% $Pd(acac)_2$	MeCN (1M)	50% 1-Ada-CO_2H	2	120	66

[a] Reaction conditions: **1m** (36 mg, 0.1 mmol), Pd^{II} catalyst, 1-methylindole, acid additive, and solvent were charged into a 1-Dram reaction vial with a magnetic stir bar. The vial was capped and placed in a heating block that was pre-heated to the indicated temperature. The reaction was allowed to stir at the indicated temperature for 16 h. [b] Yields determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard.

Table S2. Optimization of ring-opening *via* C–O activation[a]

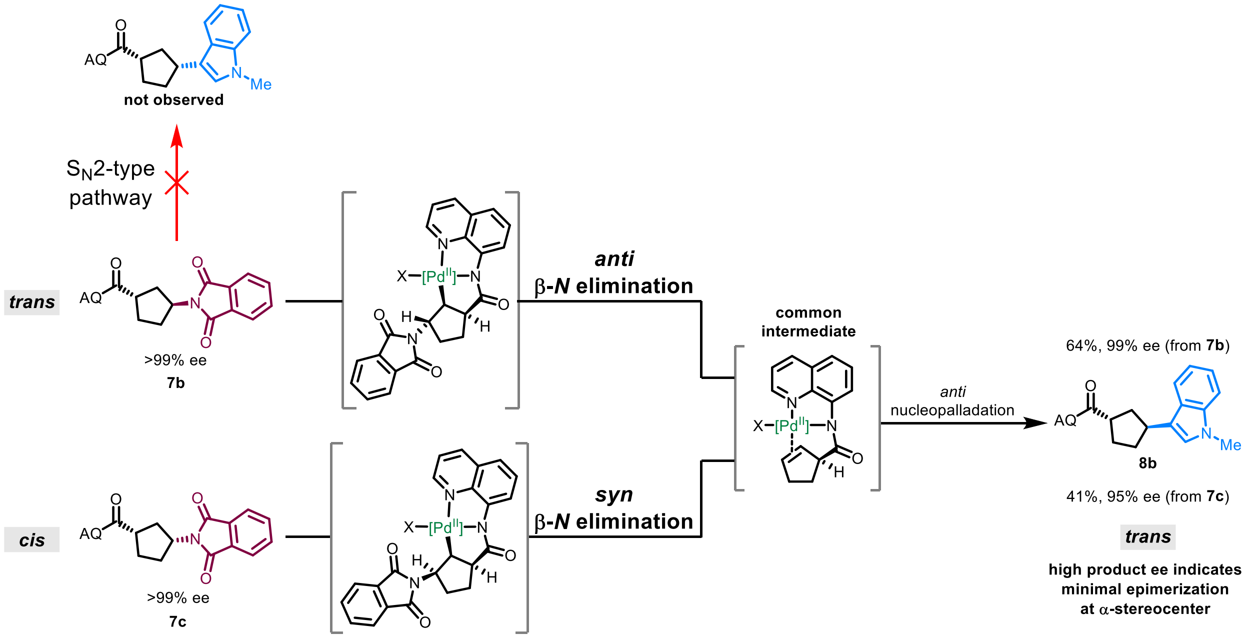


5a **6a**

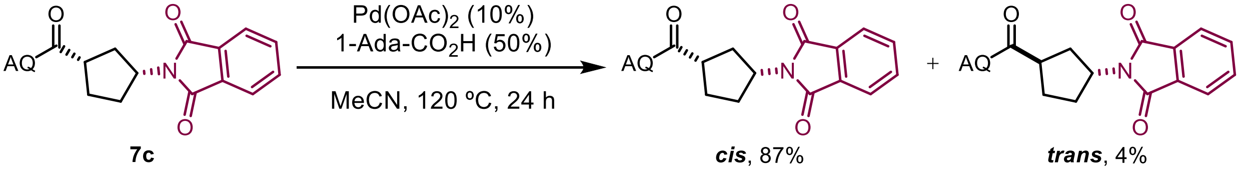
Entry	Pd Source	Solvent	Acid Additive	Other Additive	% Yield[b]
1	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	-	12
2	none	MeCN (1M)	50% AcOH	-	0
3	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	10% 8-AQ	3
4	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $CuBr_2$	0
5	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $Cu(OTf)_2$	0
6	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $Cu(NO_3)_2$•$3H_2O$	0
7	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $Cu(ClO_4)_2$•$6H_2O$	0
8	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $CuCO_3$•$Cu(OH)_2$	5
9	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $Cu(OAc)_2$	32
10	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $Cu(OBz)_2$•H_2O	38
11	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $CuSO_4$•$5H_2O$	55
12	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	1 equiv $CuSO_4$•$5H_2O$	42
13	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	0.5 equiv $CuSO_4$•$5H_2O$	40
14	10% $Pd(OAc)_2$	MeCN (1M)	50% AcOH	2 equiv $CuSO_4$•$5H_2O$	38
15	10% $Pd(OAc)_2$	HFIP (1M)	50% AcOH	1 equiv $CuSO_4$•$5H_2O$	34
16	10% $Pd(OAc)_2$	AcOH (1M)	-	1 equiv $CuSO_4$•$5H_2O$	64
17	none	AcOH (1M)	-	1 equiv $CuSO_4$•$5H_2O$	0
18	10% $Pd(OAc)_2$	HFIP (1M)	50% AcOH	1 equiv $CuSO_4$•$5H_2O$	34
19	10% $Pd(OAc)_2$	AcOH/H_2O (1:1, 1M)	-	1 equiv $CuSO_4$•$5H_2O$	84

[a] Reaction conditions: **5a** (26 mg, 0.1 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), 1-methylindole (26.2 mg, 0.2 mmol), indicated additives, and solvent(s) (0.1 mL, 1M) were charged into a 1-Dram reaction vial with a magnetic stir bar. The vial was capped and placed in a heating block that was pre-heated to 120 °C. The reaction was allowed to stir at 120 °C for 24 h. [b] Yields determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard.

Mechanistic Studies

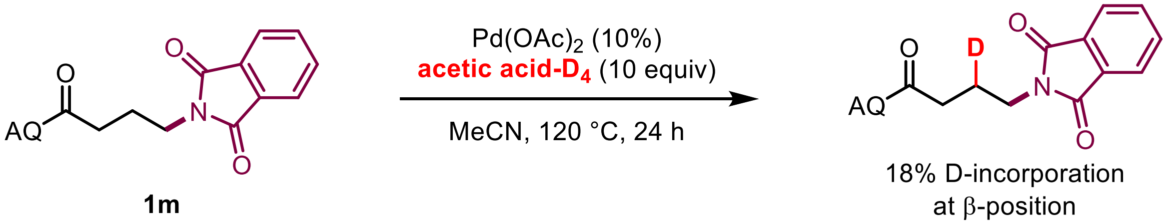


Epimerization Control Experiment

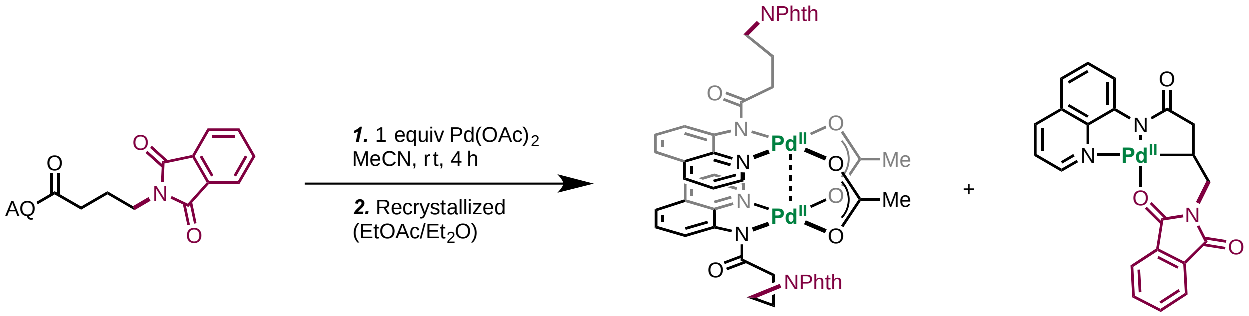


7c (38.5 mg, 0.1 mmol), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol), and 1-Adamantane-carboxylic acid (9.0 mg, 0.05 mmol) were charged into a 1-Dram reaction vial containing MeCN (0.1 mL). The vial was capped and placed in a heating block that was pre-heated to 120 °C. The reaction was allowed to run for 24 h, and yields were determined by ^{1}H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard.

Deuterium Exchange Experiment



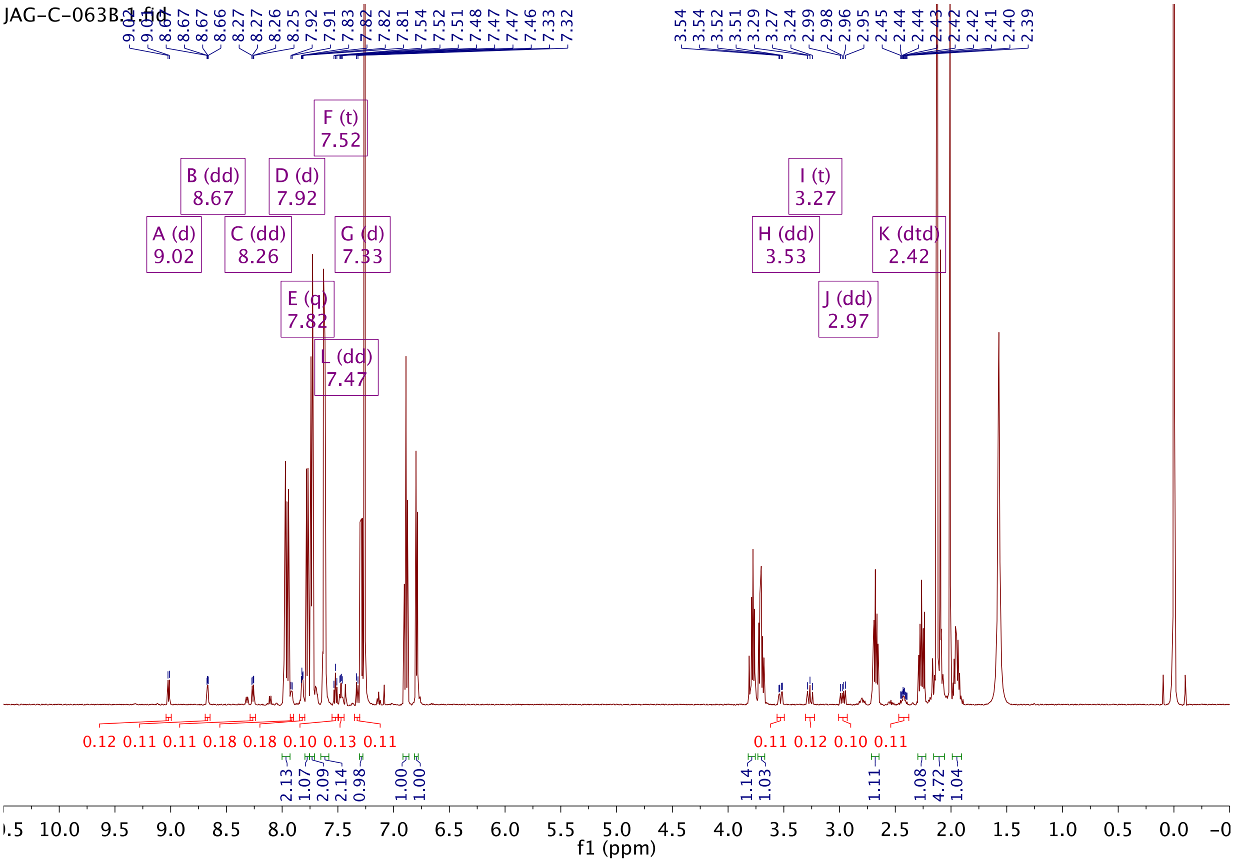
1m (36 mg, 0.1 mmol), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol), and acetic acid-D$_4$ (64 mg, 1 mmol) were charged into a 1-Dram reaction vial containing MeCN (0.1 mL). The vial was capped and placed in a heating block that was pre-heated to 120 °C. The reaction was allowed to run for 24 h, and percent deuterium incorporation was determined by ^{1}H NMR analysis of the crude reaction mixture.



[X-ray]
S1

[X-ray]
1m'

Palladium complexes: A 1-Dram vial containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (22.5 mg, 0.100 mmol), substrate **1m** (35.9 mg, 0.100 mmol), and MeCN (1.0 mL). The resulting mixture was stirred at ambient temperature for 4 h, during which, a yellow precipitate was formed. The reaction mixture was filtered, and the filter cake was rinsed with MeCN (1 mL) and diethyl ether (1 mL), collected, and dried *in vacuo* to afford 36.3 mg (69%) of a yellow powder. Crystals were grown by vapor diffusion of diethyl ether into a saturated solution of the yellow powder dissolved in ethyl acetate. Two palladium complexes crystallized out with distinguishable crystal forms: **S1** as blocks and **1m'** as needles. The dimeric structure of **S1** in the solid state was established by X-ray crystallography and was in accordance with previous reports on related complexes.[1–3] Note: The yellow precipitate is a mixture of two palladium complexes by ^1H NMR (below). The major complex (integrals in blue) appears to be **S1**, while the identity of the minor complex (integrals in red) is unknown, although it could be **1m'**.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B (dd) 8.67
C (dd) 8.26
D (d) 7.92
E (q) 7.82
F (t) 7.52
G (d) 7.33
L (dd) 7.47
H (dd) 3.53
I (t) 3.27
J (dd) 2.97
K (dtd) 2.42
0.12 0.11 0.11 0.18 0.18 0.10 0.13 0.11
2.13 1.07 2.09 2.14 0.98 1.00 1.00
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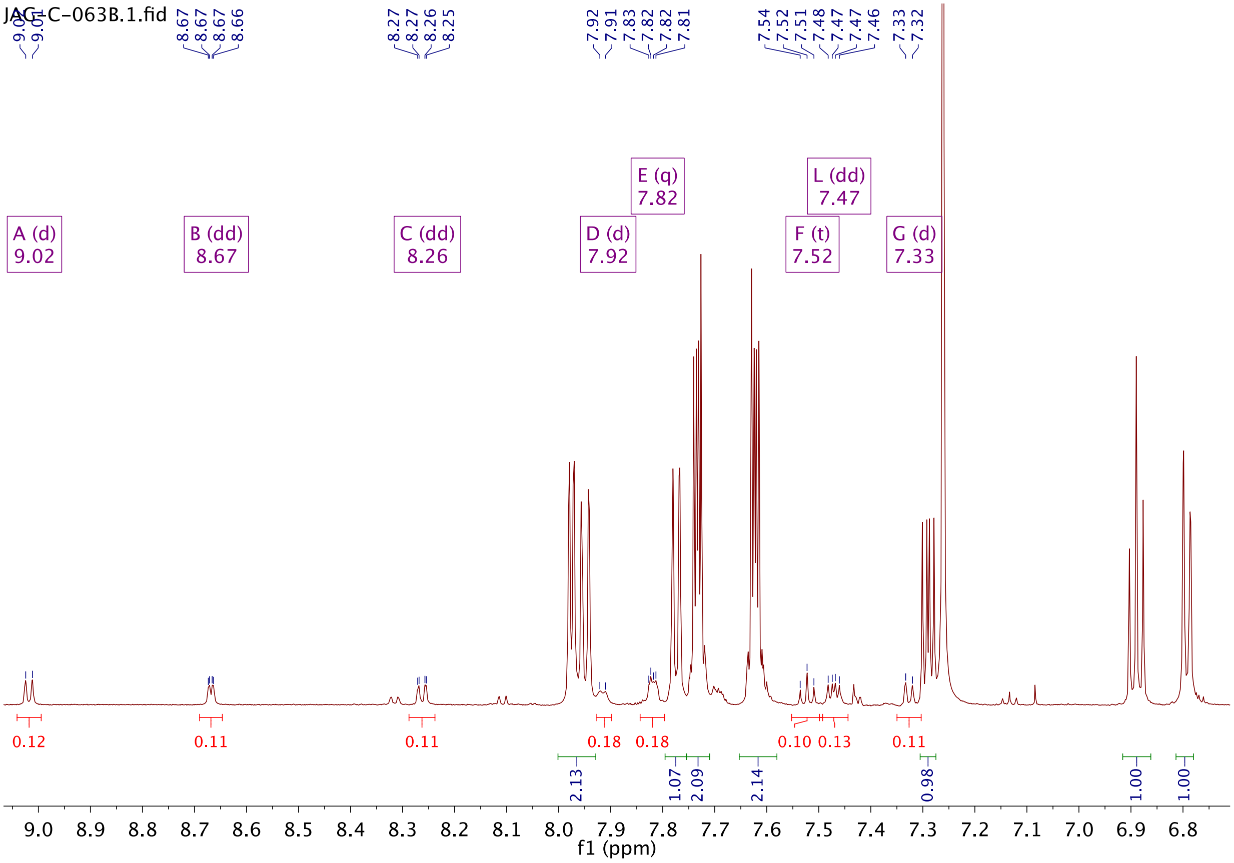
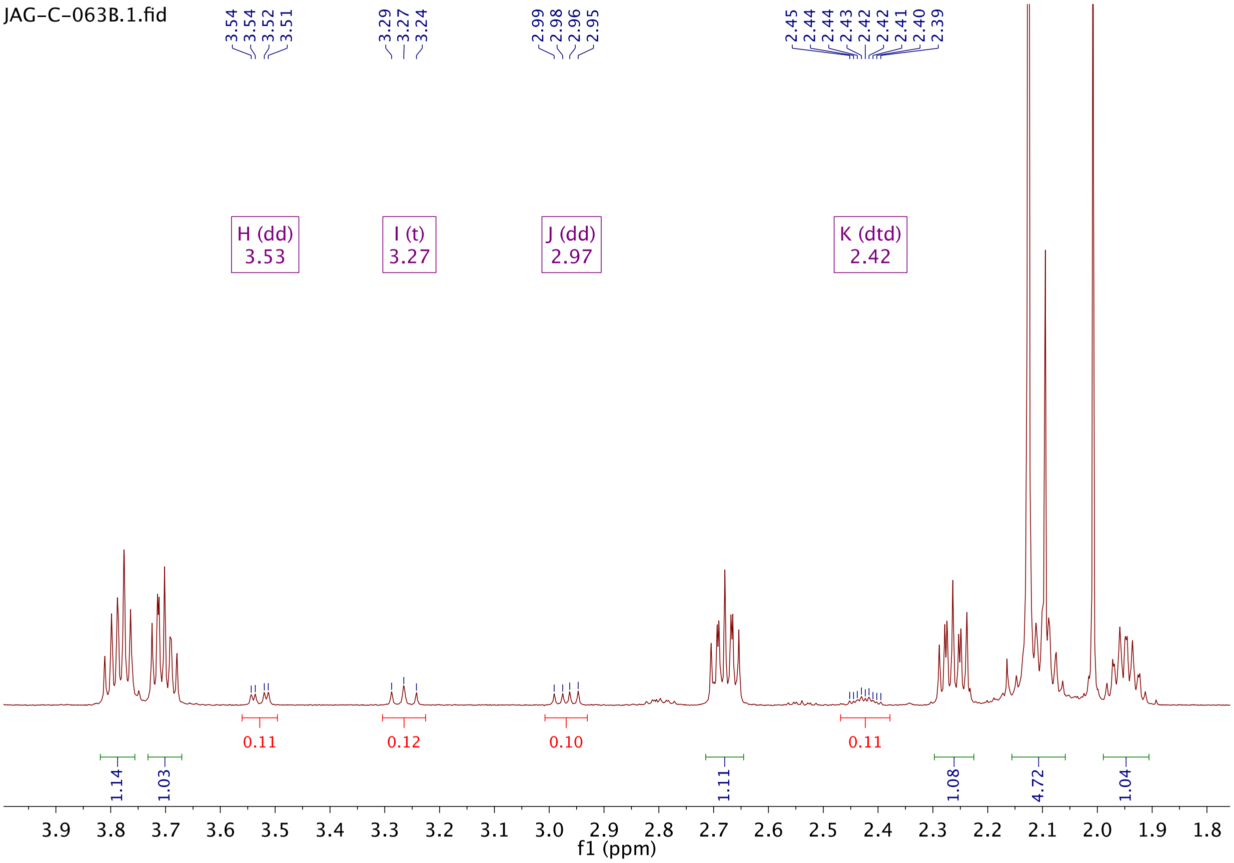
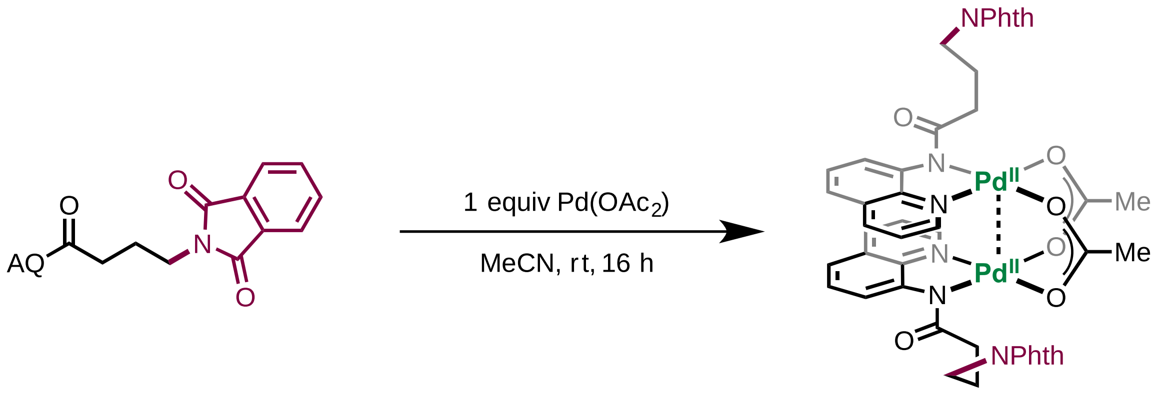
1.14 1.03 1.11 1.08 4.72 1.04
f1 (ppm)


JAG-C-063B.1.fid
A (d) 9.02
B (dd) 8.67
C (dd) 8.26
D (d) 7.92
E (q) 7.82
F (t) 7.52
L (dd) 7.47
G (d) 7.33
0.12 0.11 0.11 0.18 0.18 0.10 0.13 0.11
2.13 1.07 2.09 2.14 0.98 1.00 1.00
f1 (ppm)

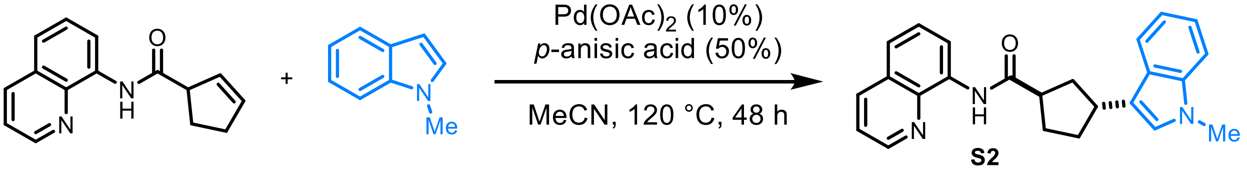




S1

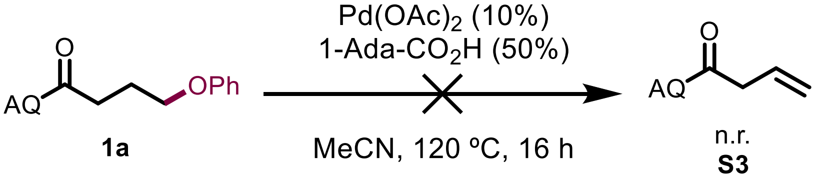
When following the same procedure as above but for longer time (16 h), **S1** (27.1 mg, 52%) was isolated as a yellow powder. ^{1}**H NMR** (600 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 5.3, 1.4 Hz, 1H), 7.95 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.77 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.73 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.62 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.29 (dd, *J* = 8.2, 5.2 Hz, 1H), 6.89 (t, *J* = 7.9 Hz, 1H), 6.79 (dd, *J* = 8.1, 1.1 Hz, 1H), 3.82 – 3.76 (m, 1H), 3.70 (ddd, *J* = 13.6, 7.7, 6.0 Hz, 1H), 2.68 (ddd, *J* = 15.2, 8.6, 6.6 Hz, 1H), 2.26 (ddd, *J* = 15.2, 8.7, 6.2 Hz, 1H), 2.15 – 2.07 (m, 4H), 1.95 (dtt, *J* = 14.0, 7.9, 6.1 Hz, 1H). ^{13}**C NMR** (150 MHz, $CDCl_3$) δ 184.61, 178.31, 167.89, 148.81, 146.59, 144.40, 138.51, 133.17, 131.73, 128.57, 128.13, 122.48, 121.53, 120.00, 118.69, 37.57, 35.33, 25.41, 23.53.

Relative Stereochemistry of Nucleopalladation



(*trans*)-(±)-3-(1-methyl-1*H*-indol-3-yl)-*N*-(quinolin-8-yl)cyclopentane-1-carboxamide (S2): The title compound was prepared using a procedure adapted from an earlier report from our laboratory.[4] *N*-(Quinolin-8-yl)cyclopent-2-ene-1-carboxamide was prepared according to a previous report from our laboratory.[4] *N*-(Quinolin-8-yl)cyclopent-2-ene-1-carboxamide (23.8 mg, 0.100 mmol), 1-methylindole (19.7 mg, 0.150 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol), and *p*-anisic acid (7.6 mg, 0.050 mmol) were charged into a 1-Dram vial containing MeCN (0.05 mL). The vial was sealed with an unpunctured TFE septum-covered screw cap and placed in a heating block that was pre-heated to 120 °C. The reaction was run for 48 h, and the product was purified by preparative TLC (30% EtOAc in Hexanes) to afford **S2** (18.2 mg, 49% yield) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.83 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.70 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.50 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.30 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.23 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 2H), 7.11 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 6.88 (s, 1H), 3.76 (s, 3H), 3.67 (p, *J* = 8.1 Hz, 1H), 3.25 (qd, *J* = 8.4, 6.0 Hz, 1H), 2.62 (ddd, *J* = 13.6, 8.1, 6.0 Hz, 1H), 2.41–2.27 (m, 2H), 2.27–2.16 (m, 2H), 1.98–1.88 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 174.68, 147.64, 137.98, 136.90, 135.91, 134.29, 127.51, 127.02, 126.94, 124.28, 121.12, 121.10, 120.81, 119.24, 118.26, 118.12, 115.94, 108.75, 45.94, 36.89, 36.21, 33.10, 32.17, 29.95. **HRMS** calcd. for $C_{24}H_{24}N_3O$+ [M+H]$^+$: 370.19139, Found: 370.19140.

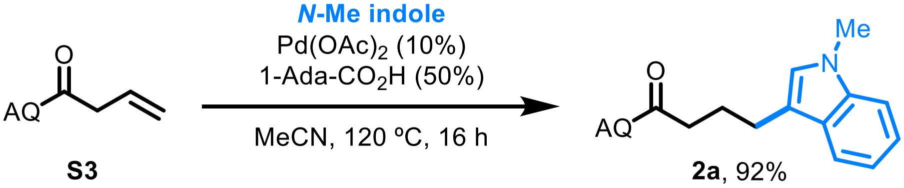
Attempt to Observe Alkene



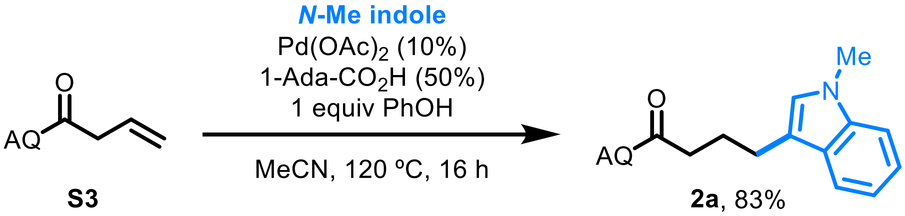
1a (30.6 mg, 0.1 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), and 1-Adamantane-carboxylic acid (9.0 mg, 0.05 mmol) were charged into a 1-Dram reaction vial containing MeCN (0.1 mL). The vial was capped and placed in a heating block that was pre-heated to 120 °C. The reaction was allowed to run for 16 h, and the yield was determined by ^{1}H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard.

Alkene Intermediacy Control Experiments

These experiments demonstrate the plausibility of an intermediate alkene under the reaction conditions.



S3 (21.2 mg, 0.1 mmol), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol), 1-methylindole (26.2 mg. 0.2 mmol), and 1-Adamantane-carboxylic acid (9.0 mg, 0.05 mmol) were charged into a 1-Dram reaction vial containing MeCN (0.1 mL). The vial was capped and placed in a heating block that was pre-heated to 120 °C. The reaction was allowed to run for 16 h, and the yield was determined by ^{1}H NMR analysis of the crude reaction mixture using CH$_2$Br$_2$ as internal standard.



S3

2a, 83%

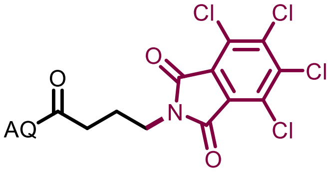
S3 (21.2 mg, 0.1 mmol), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol), 1-methylindole (26.2 mg. 0.2 mmol), phenol (9.4 mg, 0.1 mmol), and 1-Adamantane-carboxylic acid (9.0 mg, 0.05 mmol) were charged into a 1-Dram reaction vial containing MeCN (0.1 mL). The vial was capped and placed in a heating block that was pre-heated to 120 °C. The reaction was allowed to run for 16 h, and the yield was determined by ^{1}H NMR analysis of the crude reaction mixture using CH$_2$Br$_2$ as internal standard.

Substrate Synthesis

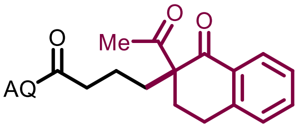
(Yields are unoptimized)

The following compounds were prepared according to previous reports from our laboratory:[5,6]

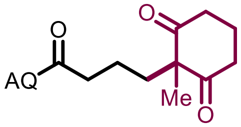
Table S3. Previously characterized substrates



1p



1s



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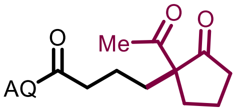

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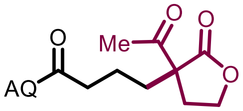
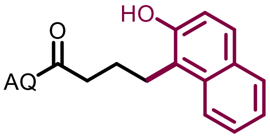
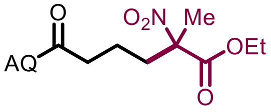


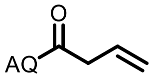
1v



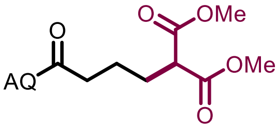
2e



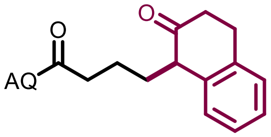
2i



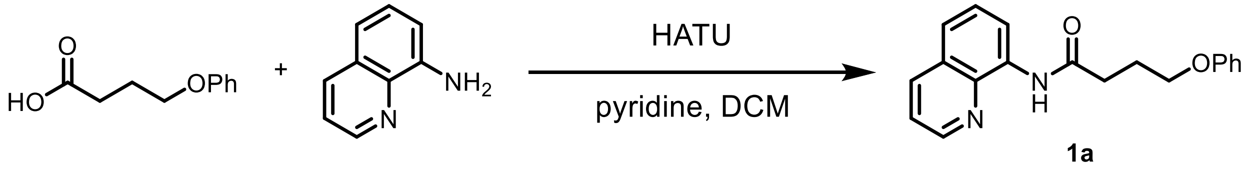
S3



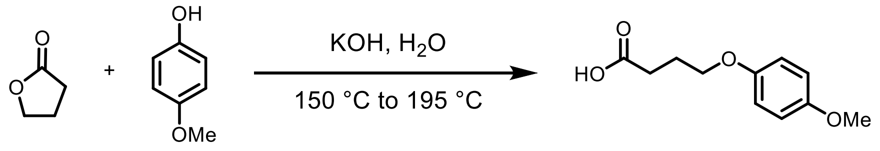
S4

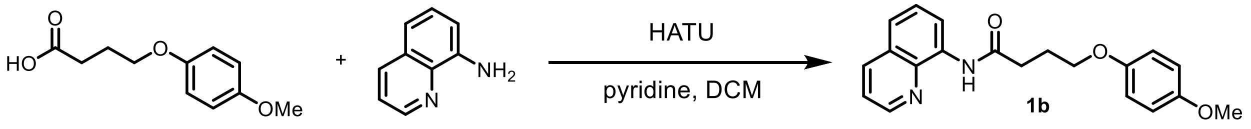


S5

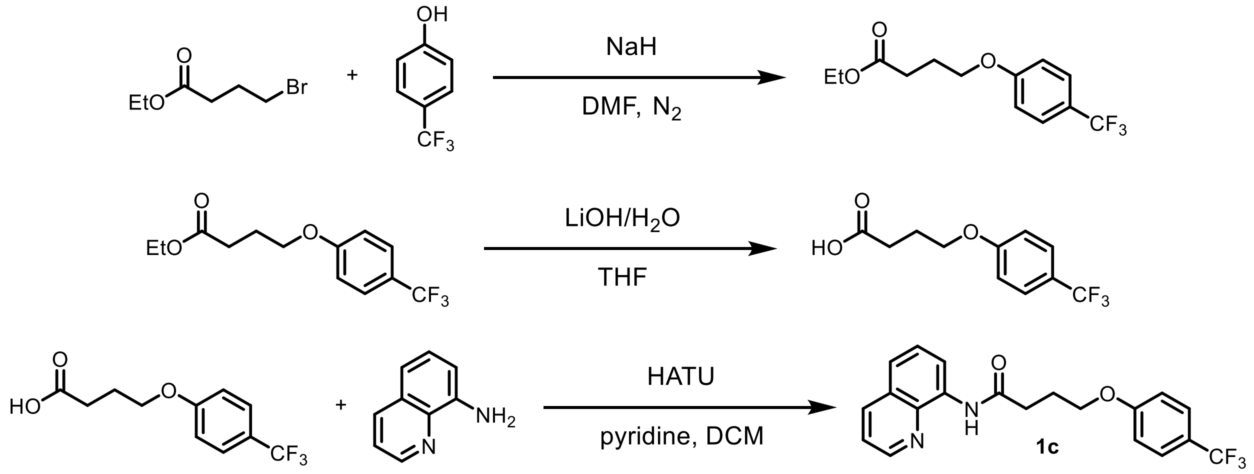


4-phenoxy-*N*-(quinolin-8-yl)butanamide (1a): 4-Phenoxybutanoic acid (3.60 g, 20.0 mmol) was charged into a 250-mL RB flask containing DCM (45 mL). 8-Aminoquinoline (2.22 g, 15.4 mmol), pyridine (2.5 mL, 30.8 mmol), and HATU (7.61 g, 20.0 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (200 mL), washed with sat. $NaHCO_3$ (200 mL, ×2) and brine (200 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (15% DCM/15% Ether/70% Hexanes) to afford **1a** (4.20 g, 89% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.78 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.56–7.52 (m, 1H), 7.50 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.29–7.24 (m, 3H), 6.96–6.90 (m, 3H), 4.12 (t, *J* = 6.0 Hz, 2H), 2.80 (t, *J* = 7.3 Hz, 2H), 2.35–2.27 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.21, 159.01, 148.26, 138.45, 136.47, 134.62, 129.56, 128.07, 127.54, 121.73, 121.59, 120.83, 116.58, 114.68, 66.88, 34.56, 25.31. **HRMS** calcd. for $C_{19}H_{19}N_2O_2$+ [M+H]$^+$: 307.14410, Found: 307.14405.

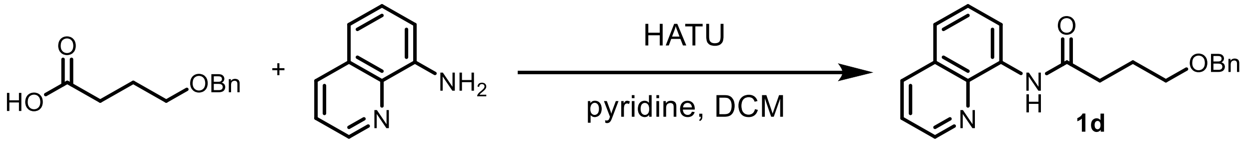




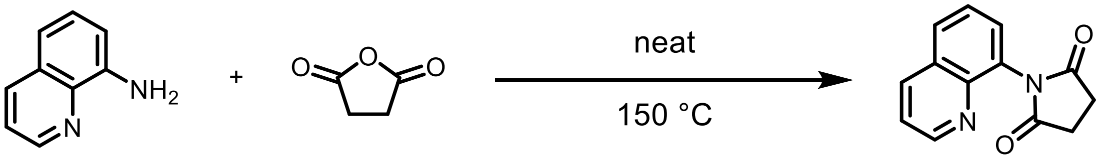
4-(4-methoxyphenoxy)-*N*-(quinolin-8-yl)butanamide (1b): 4-(4-Methoxyphenoxy)butanoic acid[7] (347 mg, 1.65 mmol) was charged into a 25-mL RB flask containing DCM (4 mL). 8-Aminoquinoline (216 mg, 1.50 mmol), pyridine (0.24 mL, 3.00 mmol), and HATU (627 mg, 1.65 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (20% EtOAc in Hexanes) to afford **1b** (387 mg, 77% yield) as a white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.78 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57–7.52 (m, 1H), 7.50 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.89–6.84 (m, 2H), 6.84–6.79 (m, 2H), 4.06 (t, *J* = 6.0 Hz, 2H), 3.75 (s, 3H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.32–2.24 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.26, 153.95, 153.19, 148.25, 138.45, 136.47, 134.64, 128.07, 127.54, 121.73, 121.57, 116.56, 115.64, 114.76, 67.67, 55.87, 34.60, 25.41. **HRMS** calcd. for $C_{20}H_{21}N_2O_3^+$ [M+H]$^+$: 337.15467, Found: 337.15455.

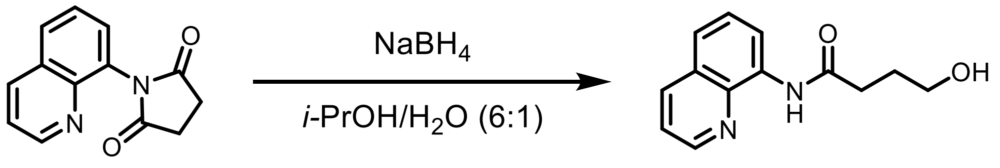


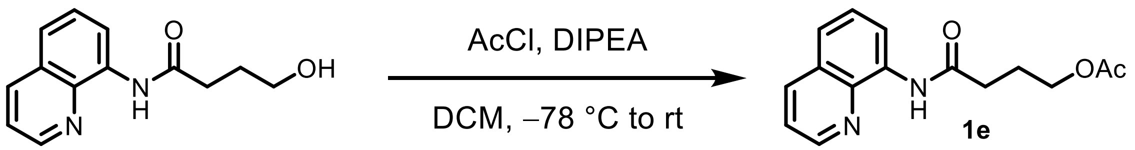
***N*-(quinolin-8-yl)-4-(4-(trifluoromethyl)phenoxy)butanamide (1c):** Ethyl 4-(4-(trifluoromethyl)phenoxy)butanoate was prepared using a procedure adapted from MacMillan.[8] Crude ethyl 4-(4-(trifluoromethyl)phenoxy)butanoate (332 mg, 1.20 mmol) was charged into a 100-mL RB flask containing THF (13 mL) and water (3.5 mL). Lithium hydroxide monohydrate (439 mg, 10.5 mmol) was added, and the reaction was stirred at ambient temperature for 16 h. The organic layer was acidified with conc. HCl, and extracted with EtOAc (50 mL, ×3). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Crude 4-(4-(trifluoromethyl)phenoxy)butanoic acid (458 mg, 1.80 mmol) was charged into a 100-mL RB flask containing DCM (4 mL). 8-Aminoquinoline (236 mg, 1.64 mmol), pyridine (0.26 mL, 3.27 mmol), and HATU (684 mg, 1.80 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (15% EtOAc in Hexanes) to afford **1c** (423 mg, 69% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.77 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57–7.49 (m, 4H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 2H), 4.16 (t, *J* = 6.0 Hz, 2H), 2.80 (t, *J* = 7.2 Hz, 2H), 2.37–2.29 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.92, 161.46, 148.26, 138.41, 136.51, 134.53, 128.08, 127.53, 126.97 (q, J_{C-F} = 3.7 Hz), 124.58 (q, J_{C-F} = 271 Hz), 122.97 (q, J_{C-F} = 32.7 Hz) 121.77, 121.69, 116.59, 114.61, 67.23, 34.32, 25.08. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.77. **HRMS** calcd. for $C_{20}H_{18}F_3N_2O_2^+$ $[M+H]^+$: 375.13149, Found: 375.13151.



4-(benzyloxy)-*N*-(quinolin-8-yl)butanamide (1d): 4-(Benzyloxy)butanoic acid (0.58 mL, 3.3 mmol) was charged into a 50-mL RB flask containing DCM (7 mL). 8-Aminoquinoline (433 mg, 3.0 mmol), pyridine (0.48 mL, 6.0 mmol), and HATU (1.26 g, 3.3 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (20% EtOAc in Hexanes) to afford **1d** (699 mg, 73% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.78 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.56–7.52 (m, 1H), 7.50 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.38–7.33 (m, 2H), 7.33–7.28 (m, 2H), 7.28–7.23 (m, 1H), 4.54 (s, 2H), 3.62 (t, *J* = 6.1 Hz, 2H), 2.70 (t, *J* = 7.4 Hz, 2H), 2.20–2.09 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.61, 148.23, 138.56, 138.50, 136.46, 134.72, 128.49, 128.07, 127.80, 127.68, 127.56, 121.71, 121.50, 116.56, 73.16, 69.40, 34.99, 25.85. **HRMS** calcd. for $C_{20}H_{21}N_2O_2^+$ [M+H]$^+$: 321.15975, Found: 321.15977.

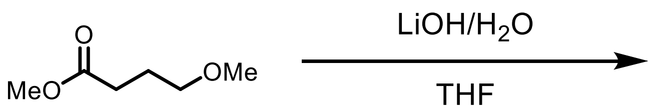


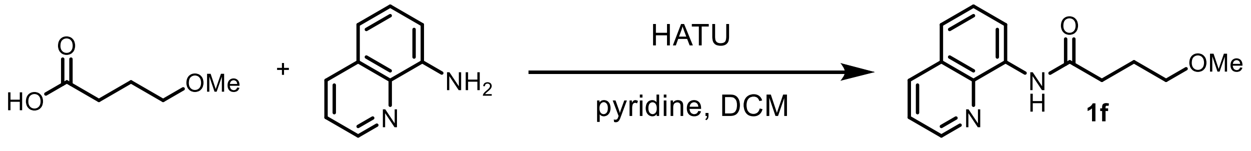




1e

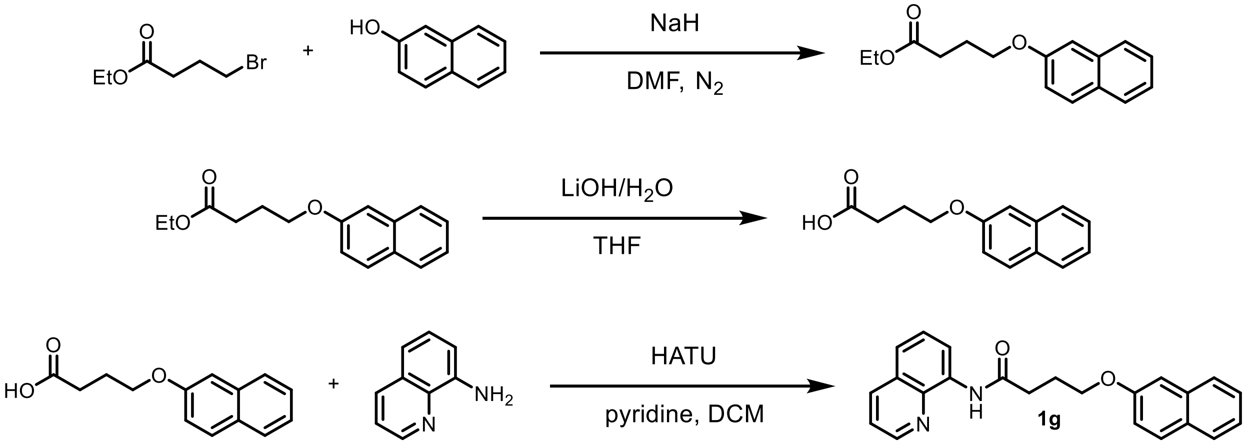
4-oxo-4-(quinolin-8-ylamino)butyl acetate (1e): The title compound was prepared using a procedure adapted from Yamamoto.[9] 4-Hydroxy-*N*-(quinolin-8-yl)butanamide[10,11] (230 mg, 1.0 mmol) was charged into a 25-mL RB flask containing DCM (4 mL) and DIPEA (0.35 mL, 2.0 mmol) at –78 °C. Acetyl chloride (70 µL, 1.0 mmol) was added dropwise, and the reaction was stirred at –78 °C for 3 h followed by ambient temperature for 1 h. 1M HCl (50 mL) was added, and the aqueous layer was extracted with EtOAc (50 mL, ×3). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and purified by column chromatography (30% EtOAc in Hexanes) to afford **1e** (267 mg, 98% yield) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.77 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.57–7.49 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.21 (t, *J* = 6.3 Hz, 2H), 2.67 (t, *J* = 7.4 Hz, 2H), 2.21–2.13 (m, 2H), 2.05 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.21, 170.74, 148.26, 138.40, 136.53, 134.50, 128.06, 127.53, 121.75, 121.65, 116.59, 63.80, 34.56, 24.64, 21.07. **HRMS** calcd. for $C_{15}H_{17}N_2O_3^+$ [M+H]$^+$: 273.12337, Found: 273.12338.



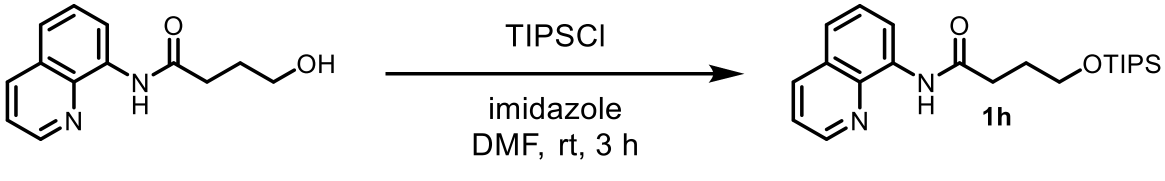


1f

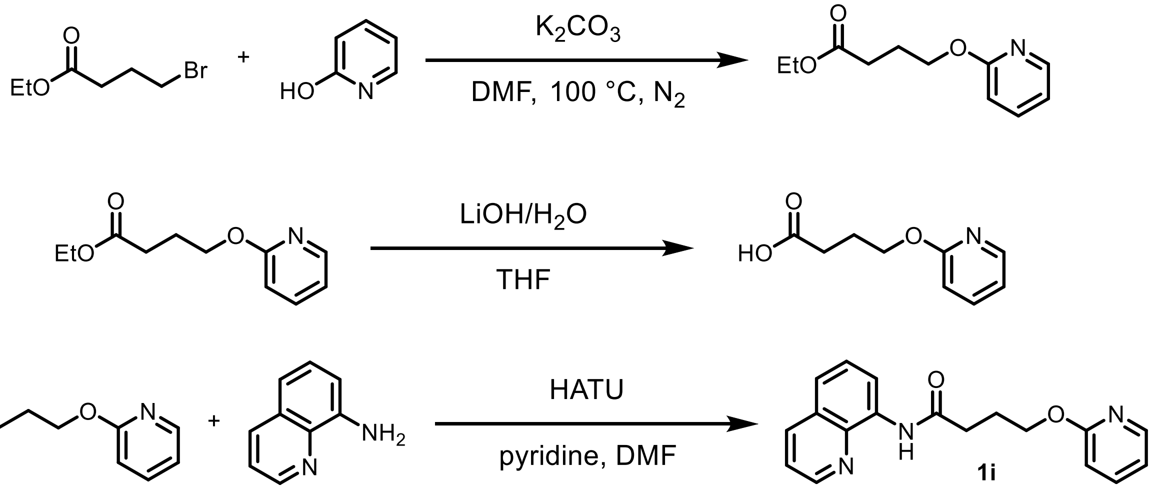
4-methoxy-*N*-(quinolin-8-yl)butanamide (1f): 4-Methoxybutanoic acid[12] (521 mg, 4.40 mmol) was charged into a 100-mL RB flask containing DCM (11 mL). 8-Aminoquinoline (529 mg, 3.67 mmol), pyridine (0.60 mL, 7.30 mmol), and HATU (1.67 g, 4.40 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (30% EtOAc in Hexanes) to afford **1f** (703 mg, 78% yield) as a brown oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.85–8.75 (m, 2H), 8.15 (dt, *J* = 8.3, 1.5 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.51–7.47 (m, 1H), 7.44 (ddt, *J* = 8.3, 4.1, 1.3 Hz, 1H), 3.52 (t, *J* = 6.2 Hz, 2H), 3.37 (s, 3H), 2.67 (t, *J* = 7.4 Hz, 2H), 2.13–2.05 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.57, 148.23, 138.48, 136.44, 134.70, 128.06, 127.53, 121.69, 121.49, 116.53, 71.76, 58.79, 34.81, 25.67. **HRMS** calcd. for $C_{14}H_{17}N_2O_2^+$ [M+H]$^+$: 245.12900, Found: 245.12897.



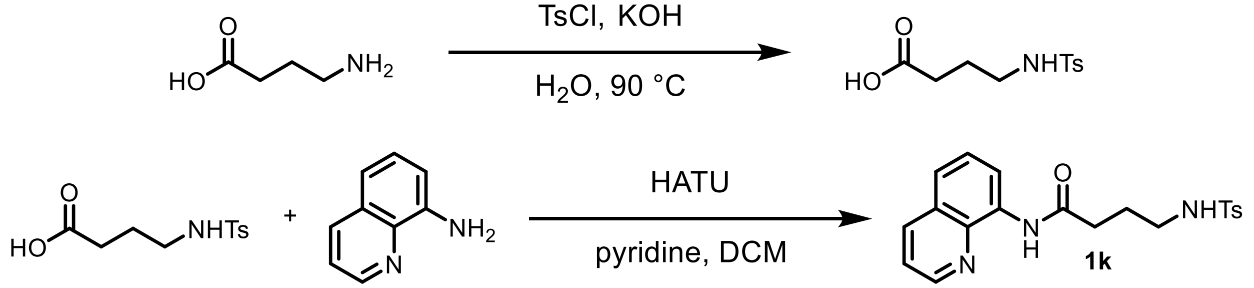
4-(naphthalen-2-yloxy)-*N*-(quinolin-8-yl)butanamide (1g): Crude ethyl 4-(naphthalen-2-yloxy)butanoate[8] (1.58 g, 6.1 mmol) was charged into a 100-mL RB flask containing THF (15 mL) and water (4 mL). Lithium hydroxide monohydrate (512 mg, 12.2 mmol) was added, and the reaction was stirred at ambient temperature for 16 h. The organic layer was acidified with conc. HCl, and extracted with EtOAc (50 mL, × 3). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Crude 4-(naphthalen-2-yloxy)butanoic acid (760 mg, 3.30 mmol) was charged into a 100-mL RB flask containing DCM (7.7 mL). 8-Aminoquinoline (433 mg, 3.00 mmol), pyridine (0.48 mL, 6.00 mmol), and HATU (1.26 mg, 3.30 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (20% EtOAc in Hexanes) to afford **1g** (374 mg, 35% yield) as a light brown solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.79 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.73 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.72 (td, *J* = 17.2, 16.8, 8.2 Hz, 3H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.50 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.44–7.39 (m, 2H), 7.32 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.19–7.13 (m, 2H), 4.24 (t, *J* = 6.0 Hz, 2H), 2.85 (t, *J* = 7.3 Hz, 2H), 2.41–2.34 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.20, 156.98, 148.25, 138.45, 136.47, 134.69, 134.63, 129.46, 129.10, 128.08, 127.74, 127.55, 126.88, 126.44, 123.69, 121.73, 121.61, 119.05, 116.59, 106.88, 67.05, 34.64, 25.30. **HRMS** calcd. for $C_{23}H_{21}N_2O_2^+$ [M+H]$^+$: 357.16030, Found: 357.16031.



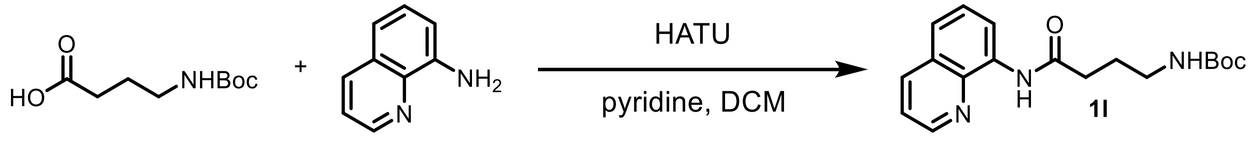
N-(quinolin-8-yl)-4-((triisopropylsilyl)oxy)butanamide (1h): The title compound was prepared using a procedure adapted from Stoltz.[13] 4-Hydroxy-*N*-(quinolin-8-yl)butanamide (104 mg, 0.45 mmol) was charged into a 25-mL RB flask containing DMF (1.5 mL). TIPSCl (0.14 mL, 0.68 mmol) and imidazole (67.4 mg, 0.99 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 3 h. Water (10 mL) was added, and the solution was extracted with diethyl ether (10 mL, ×3). The combined organic layers were washed with brine (10 mL, ×1), dried over $MgSO_4$, and concentrated *in vacuo* to afford **1h** (177 mg, 46% yield) as clear oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.84–8.76 (m, 2H), 8.16 (dd, J = 8.3, 1.7 Hz, 1H), 7.56–7.51 (m, 1H), 7.49 (dd, J = 8.2, 1.4 Hz, 1H), 7.45 (dd, J = 8.2, 4.2 Hz, 1H), 3.83 (t, J = 6.0 Hz, 2H), 2.70 (t, J = 7.3 Hz, 2H), 2.10–2.02 (m, 2H), 1.06 (d, J = 6.7 Hz, 21H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.94, 148.20, 138.50, 136.45, 134.76, 128.06, 127.57, 121.68, 121.43, 116.53, 62.47, 34.67, 28.98, 18.18, 12.13. **HRMS** calcd. for $C_{22}H_{35}N_2O_2Si^+$ [M+H]$^+$: 387.24678, Found: 387.24681.



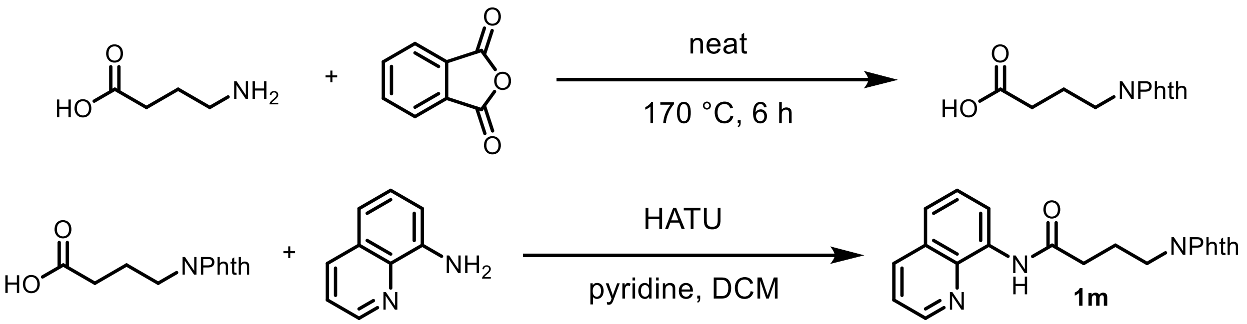
4-(pyridin-2-yloxy)-*N*-(quinolin-8-yl)butanamide (1i): Ethyl 4-(pyridin-2-yloxy)butanoate was prepared using a procedure adapted from Hagmann.[14] Ethyl-4-bromobutyrate (1.97 mL, 13.8 mmol), 2-hydroxypyridine (656 mg, 6.90 mmol), and potassium carbonate (2.86 g, 20.7 mmol) were dissolved in DMF (20 mL) under a nitrogen atmosphere, and the solution was heated to 110 °C for 16 h. The reaction was cooled to ambient temperature, diluted with water (200 mL), and extracted with EtOAc (200 mL, ×2). The combined organic layers were washed with brine (200 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (10% EtOAc in Hexanes) to afford ethyl 4-(pyridin-2-yloxy)butanoate (567 mg, 39% crude yield) as a clear oil. Crude ethyl 4-(pyridin-2-yloxy)butanoate (567 mg, 2.71 mmol) was charged into a 100-mL RB flask containing THF (7 mL) and water (2 mL). Lithium hydroxide monohydrate (228 mg, 5.42 mmol) was added, and the reaction was stirred at ambient temperature for 16 h. The organic layer was acidified with conc. HCl, and extracted with EtOAc (50 mL, ×3). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to afford 491 mg of 4-(pyridin-2-yloxy)butanoic acid, which was used in the next step without further purification. Crude 4-(pyridin-2-yloxy)butanoic acid (491 mg, 2.71 mmol) was charged into a 50-mL RB flask containing DMF (7 mL). 8-Aminoquinoline (301 mg, 2.08 mmol), pyridine (0.34 mL, 4.17 mmol), and HATU (1.03 g, 2.71 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (10% EtOAc in Hexanes) to afford **1i** (530 mg, 83% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.79 (dd, J = 7.5, 1.4 Hz, 1H), 8.76 (dd, J = 4.2, 1.7 Hz, 1H), 8.15 (dd, J = 8.3, 1.7 Hz, 1H), 8.13 (ddd, J = 5.1, 2.0, 0.9 Hz, 1H), 7.54 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 2H), 7.50 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.83 (ddd, *J* = 7.1, 5.0, 1.0 Hz, 1H), 6.74 (dt, *J* = 8.3, 0.9 Hz, 1H), 4.44 (t, *J* = 6.2 Hz, 2H), 2.77 (t, *J* = 7.2 Hz, 2H), 2.36–2.27 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.27, 163.94, 148.21, 147.02, 138.63, 138.46, 136.47, 134.67, 128.06, 127.56, 121.70, 121.52, 116.81, 116.59, 111.17, 65.05, 34.89, 25.25. **HRMS** calcd. for $C_{18}H_{18}N_3O_2^+$ [M+H]$^+$: 308.13935, Found: 308.13955.



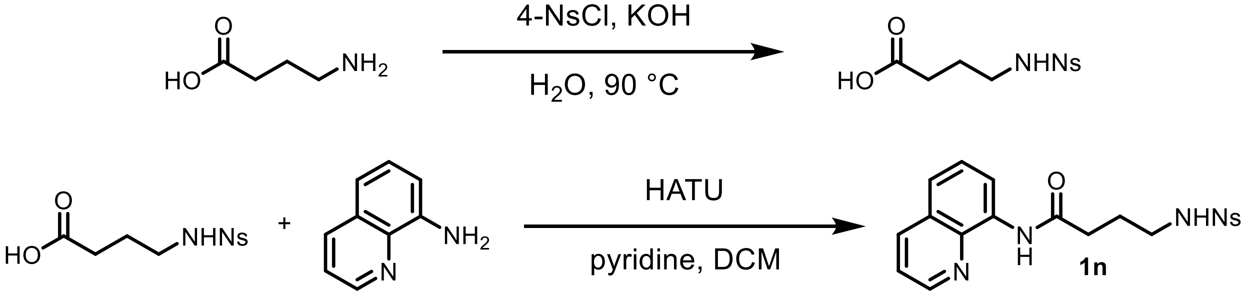
4-((4-methylphenyl)sulfonamido)-*N*-(quinolin-8-yl)butanamide (1k): To a solution of γ-aminobutyric acid (1.03 g, 10.0 mmol) in water (15 mL) in a 100-mL RB flask was added KOH (1.29 g, 23.0 mmol). The solution was heated to 90 °C, and TsCl (2.00 g, 10.5 mmol) was added portionwise over 15 min. The reaction was stirred at 90 °C for 3 h, and then cooled to room temperature. 6N HCl was added dropwise until the solution had reached pH = 2–3, and the solution was placed in the fridge overnight. The resulting white solid was collected by filtration, and used without further purification in the next step. 4-((4-Methylphenyl)sulfonamido)butanoic acid (890 mg, 3.46 mmol) was charged into a 100-mL RB flask containing DCM (8 mL). 8-Aminoquinoline (453 mg, 3.14 mmol), pyridine (0.51 mL, 6.28 mmol), and HATU (1.32 g, 3.46 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% EtOAc in Hexanes) to afford **1k** (283 mg, 24% yield) as a yellow solid. Characterization data were consistent with previously reported data.[6]



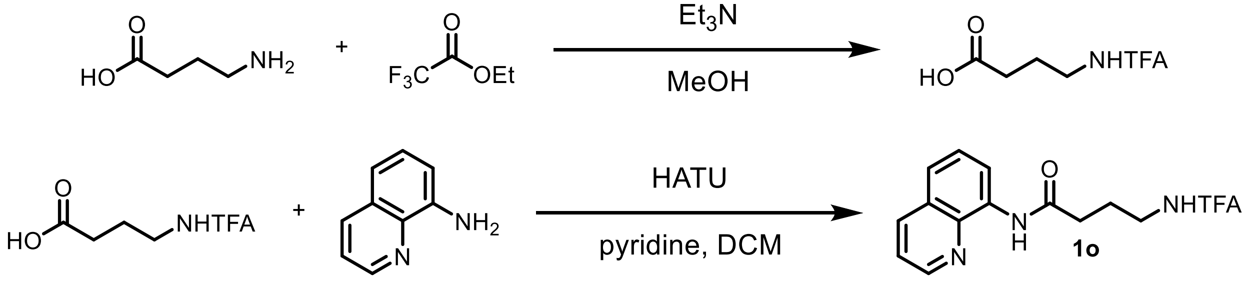
***tert*-butyl (4-oxo-4-(quinolin-8-ylamino)butyl)carbamate (1l):** 4-((*tert*-butoxycarbonyl)amino)butanoic acid (1.12 g, 5.50 mmol) was charged into a 100-mL RB flask containing DCM (13 mL). 8-Aminoquinoline (721 mg, 5.00 mmol), pyridine (0.80 mL, 10.0 mmol), and HATU (2.09 g, 5.50 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (30% EtOAc in Hexanes) to afford **1l** (1.10 g, 67% yield) as a white solid. Characterization data were consistent with previously reported data.[6]



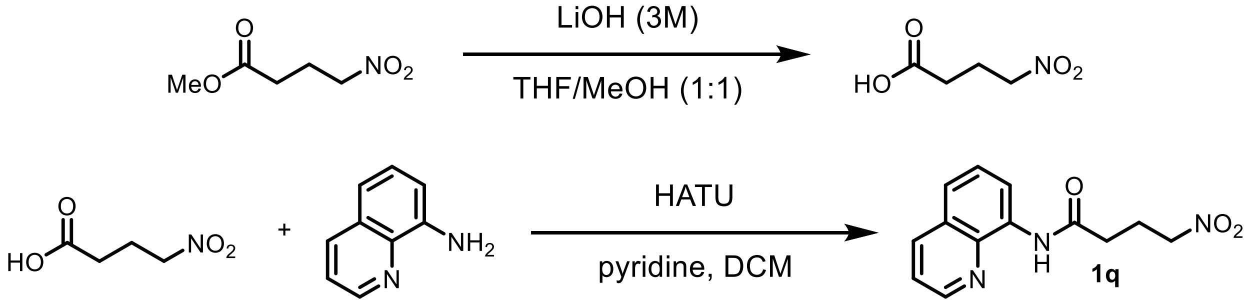
4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (1m): γ-Aminobutyric acid (6.19 g, 60.0 mmol) and phthalic anhydride (8.89 g, 60.0 mmol) were added to a 100-mL RB flask and heated to 170 °C for 6 h. The reaction was allowed to cool to room temperature, diluted with EtOAc, and washed with 2M HCl. The organic layer was dried over Na_2SO_4 and concentrated to give a brown solid. Crude 4-(1,3-Dioxoisoindolin-2-yl)butanoic acid (10.3 g, 44.0 mmol) was charged into a 250-mL RB flask containing DCM (100 mL). 8-Aminoquinoline (5.77 g, 40.0 mmol), pyridine (6.44 mL, 80.0 mmol), and HATU (16.7 g, 44.0 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (300 mL), washed with sat. $NaHCO_3$ (300 mL, ×2) and brine (300 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% EtOAc in Hexanes) to afford **1m** (10.2 g, 71% yield) as a yellow solid. Characterization data were consistent with previously reported data.[6]



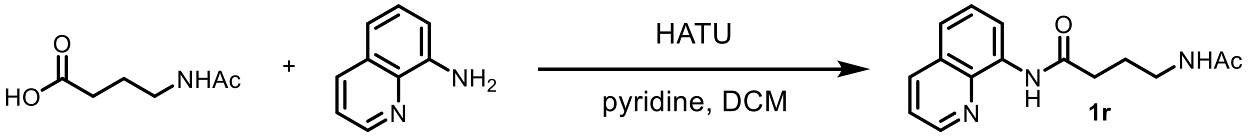
4-((4-nitrophenyl)sulfonamido)-*N*-(quinolin-8-yl)butanamide (1n): To a solution of γ-aminobutyric acid (516 mg, 5.00 mmol) in water (7.5 mL) in a 100-mL RB flask was added KOH (645 mg, 11.5 mmol). The solution was heated to 90 °C, and 4-NsCl (1.16 g, 5.25 mmol) was added portionwise over 15 min. The reaction was stirred at 90 °C for 3 h, and then cooled to room temperature. 6N HCl was added dropwise until the solution had reached pH = 2–3, and the solution was placed in the fridge overnight. The resulting white solid was collected by filtration, and used without further purification in the next step. Crude 4-((4-Nitrophenyl)sulfonamido)butanoic acid (846 mg, 2.93 mmol) was charged into a 100-mL RB flask containing DCM (8 mL). 8-Aminoquinoline (385 mg, 2.66 mmol), pyridine (0.43 mL, 5.32 mmol), and HATU (1.12 g, 2.93 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography twice (40% EtOAc in Hexanes and 30% Acetone in DCM) to afford **1n** (433 mg, 36% yield) as an orange solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.70 (p, *J* = 4.5 Hz, 1H), 8.22–8.16 (m, 3H), 8.06–8.00 (m, 2H), 7.59–7.54 (m, 2H), 7.49 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.85 (t, *J* = 5.6 Hz, 1H), 3.25–3.18 (m, 2H), 2.67–2.61 (m, 2H), 1.99 (p, *J* = 6.3 Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.24, 149.95, 148.51, 146.27, 138.31, 136.70, 134.03, 128.36, 128.13, 127.48, 124.39, 122.26, 121.99, 116.84, 43.47, 35.34, 24.48. **HRMS** calcd. for $C_{19}H_{19}N_4O_5S+$ $[M+H]^+$: 415.10762, Found: 415.10759.



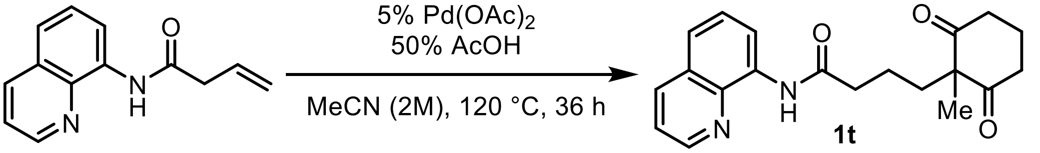
***N*-(quinolin-8-yl)-4-(2,2,2-trifluoroacetamido)butanamide (1o):** Crude 4-(2,2,2-trifluoroacetamido)butanoic acid[15] (797 mg, 4.00 mmol) was charged into a 50-mL RB flask containing DCM (9 mL). 8-Aminoquinoline (524 mg, 3.64 mmol), pyridine (0.59 mL, 7.27 mmol), and HATU (1.52 g, 4.00 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (50% EtOAc in Hexanes) to afford **1o** (687 mg, 58% yield) as an off-white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.81 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.72 (dd, *J* = 6.7, 2.2 Hz, 1H), 8.18 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.90 (s, 1H), 7.59–7.51 (m, 2H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 3.52 (q, *J* = 5.9 Hz, 2H), 2.75 (t, *J* = 6.3 Hz, 2H), 2.10 (p, *J* = 6.5 Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.97, 157.00 (q, J_{C-F} = 36.9 Hz), 147.83, 137.82, 135.99, 133.50, 127.48, 126.88, 121.54, 121.29, 116.26, 115.50 (q, J_{C-F} = 287.6 Hz), 39.67, 35.10, 23.13. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -76.24. **HRMS** calcd. for $C_{15}H_{15}F_3N_3O_2^+$ $[M+H]^+$: 326.11109, Found: 326.11108.



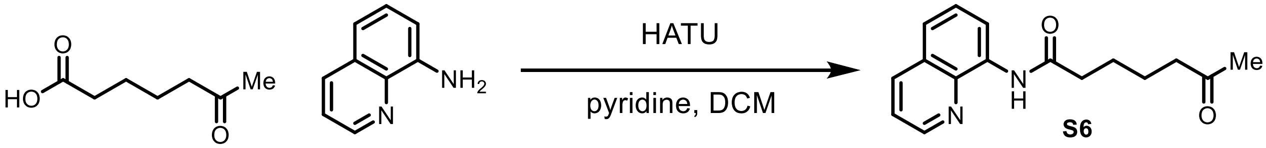
4-nitro-*N*-(quinolin-8-yl)butanamide (1q): 4-Nitrobutanoic acid[16] (1.73 g, 13.0 mmol) was charged into a 250-mL RB flask containing DCM (30 mL). 8-Aminoquinoline (1.44 g, 10.0 mmol), pyridine (1.61 mL, 20.0 mmol), and HATU (4.94 g, 13.0 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (30% Acetone in Hexanes) to afford **1q** (636 mg, 25% yield) as a brown oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.73 (dd, *J* = 6.9, 2.2 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.57–7.50 (m, 2H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.60 (t, *J* = 6.6 Hz, 2H), 2.75 (t, *J* = 7.0 Hz, 2H), 2.50 (p, *J* = 6.8 Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 169.41, 148.40, 138.36, 136.54, 134.25, 128.07, 127.46, 121.95, 121.87, 116.64, 74.80, 33.78, 22.92. **HRMS** calcd. for $C_{13}H_{14}N_3O_3^+$ $[M+H]^+$: 260.10297, Found: 260.10297.



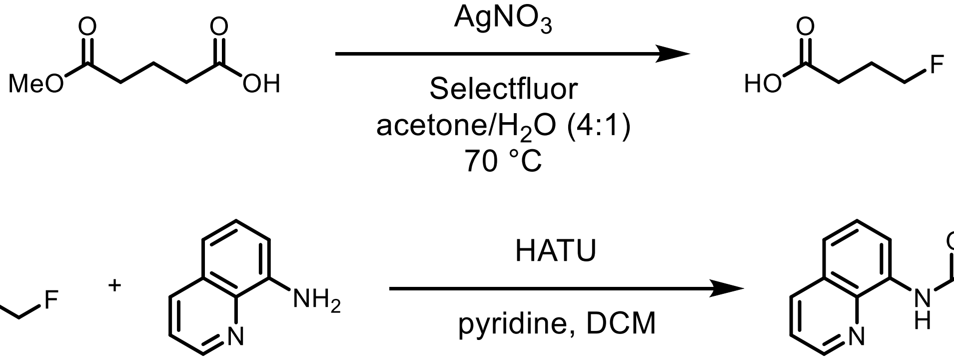
4-acetamido-*N*-(quinolin-8-yl)butanamide (1r): 4-Acetamidobutanoic acid (479 mg, 3.30 mmol) was charged into a 50-mL RB flask containing DCM (7 mL). 8-Aminoquinoline (433 mg, 3.00 mmol), pyridine (0.48 mL, 6.00 mmol), and HATU (1.26 g, 3.30 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (50% Acetone in Hexanes). The fractions containing product were concentrated and purified by a short plug of silica (100% acetone) to afford **1r** (543 mg, 67% yield) as a brown oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.74 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.58–7.49 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.20 (s, 1H), 3.40 (q, *J* = 6.6 Hz, 2H), 2.65 (t, *J* = 7.0 Hz, 2H), 2.03 (p, *J* = 6.9 Hz, 2H), 1.96 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.62, 170.56, 148.38, 138.41, 136.52, 134.40, 128.07, 127.43, 121.83, 121.82, 116.61, 39.46, 35.64, 25.08, 23.42. **HRMS** calcd. for $C_{15}H_{18}N_3O_2^+$ $[M+H]^+$: 272.13935, Found: 272.13951.



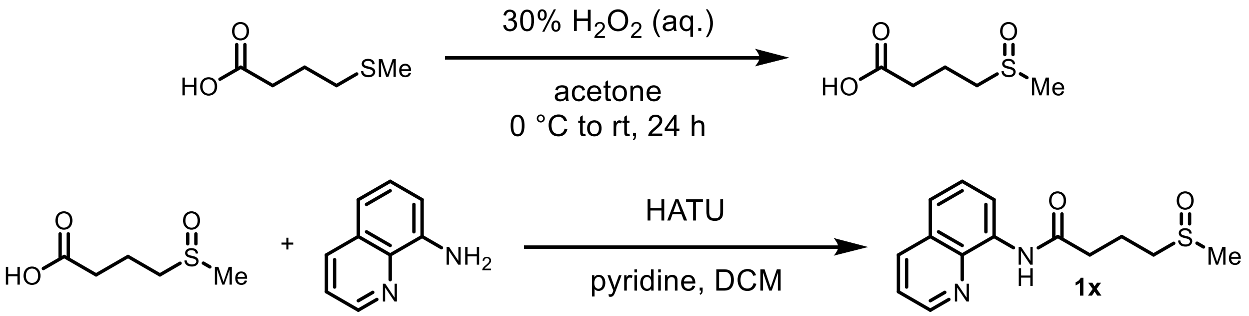
4-(1-methyl-2,6-dioxocyclohexyl)-*N*-(quinolin-8-yl)butanamide (1t): The title compound was prepared using a procedure adapted from a previous report from our group.[5] *N*-(quinolin-8-yl)but-3-enamide (637 mg, 3.00 mmol), 2-methyl-1,3-cyclohexanedione (568 mg, 4.5 mmol), $Pd(OAc)_2$ (34 mg, 0.15 mmol), and acetic acid (90 mg, 1.5 mmol) were charged into a 48-mL bomb flask containing MeCN (1.5 mL). The resulting mixture was sealed and heated to 120 °C in a silicon oil bath. The reaction was run for 36 h, cooled to room temperature, and diluted with EtOAc (100 mL). The resulting solution was washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1). The organic layer was dried over Na_2SO_4 and concentrated. The crude mixture was purified by column chromatography (40% EtOAc in Hexanes) to afford **1t** (365 mg, 36% yield) as a white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.74 (dd, *J* = 7.3, 1.6 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55–7.49 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 2.77 (ddd, *J* = 15.7, 10.0, 5.7 Hz, 2H), 2.63 (ddd, *J* = 16.0, 6.7, 5.0 Hz, 2H), 2.55 (t, *J* = 7.2 Hz, 2H), 2.03 (dtt, *J* = 13.9, 6.7, 5.6 Hz, 1H), 1.98–1.91 (m, 2H), 1.86 (dtt, *J* = 14.0, 10.0, 5.0 Hz, 1H), 1.69–1.62 (m, 2H), 1.28 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 210.27, 170.82, 148.29, 138.43, 136.52, 134.51, 128.08, 127.53, 121.77, 121.63, 116.59, 65.82, 38.06, 37.72, 36.70, 20.78, 19.29, 17.88. **HRMS** calcd. for $C_{20}H_{23}N_2O_3^+$ $[M+H]^+$: 339.17032, Found: 339.17035.



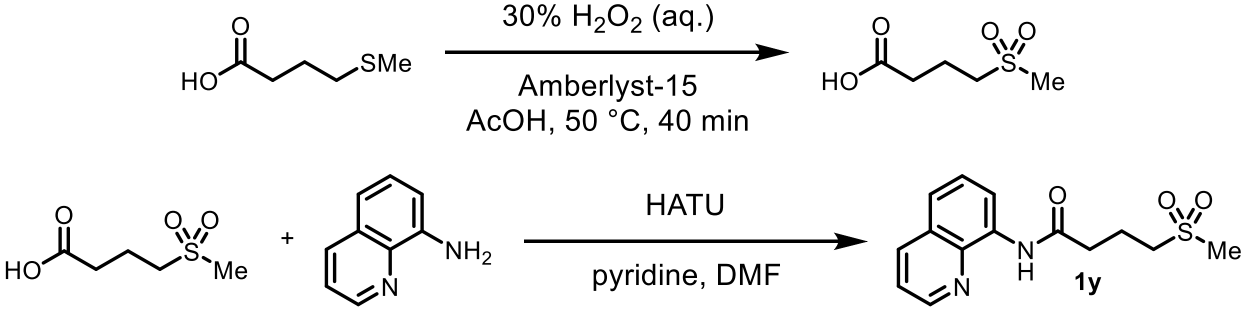
6-oxo-*N*-(quinolin-8-yl)heptanamide (S6): 6-Oxoheptanoic acid (281 mg, 1.95 mmol) was charged into a 50-mL RB flask containing DCM (4.5 mL). 8-Aminoquinoline (216 mg, 1.5 mmol), pyridine (0.24 mL, 3.00 mmol), and HATU (741 mg, 1.95 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% EtOAc in Hexanes) to afford **S6** (321 mg, 79% yield) as an off-white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81 (dt, *J* = 4.2, 1.6 Hz, 1H), 8.77 (d, *J* = 7.4 Hz, 1H), 8.16 (dq, *J* = 8.3, 1.7 Hz, 1H), 7.57–7.48 (m, 2H), 7.48–7.42 (m, 1H), 2.61–2.56 (m, 2H), 2.54–2.49 (m, 2H), 2.15 (s, 3H), 1.86–1.79 (m, 2H), 1.76–1.69 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 208.78, 171.43, 148.27, 138.44, 136.50, 134.60, 128.06, 127.54, 121.73, 121.55, 116.54, 43.55, 38.00, 30.08, 25.17, 23.49. **HRMS** calcd. for $C_{16}H_{19}N_2O_2^+$ [M+H]$^+$: 271.14410, Found: 271.14422.



4-fluoro-*N*-(quinolin-8-yl)butanamide (1w): 4-Fluorobutanoic acid was prepared using a procedure adapted from Li.[17] Monomethyl glutarate (0.38 mL, 3.00 mmol), silver(I) nitrate (102 mg, 0.60 mmol), and Selectfluor (4.25 g, 12.0 mmol) were charged into a 100-mL Schlenk flask, and the vessel was purged with nitrogen gas. Acetone (48 mL) and water (12 mL) were added into the flask, and the reaction was heated at 70 °C for 10 h. The reaction was allowed to cool to ambient temperature, and acetone was removed *in vacuo*. The resulting mixture was diluted with 1M HCl (100 mL), and was extracted with DCM (100 mL, ×3). The combined organic layers were washed with brine (100 mL, ×1), dried over Na_2SO_4, and concentrated to afford crude 4-fluorobutanoic acid, which was used in the next step without further purification. Crude 4-fluorobutanoic acid (371 mg, 3.50 mmol) was charged into a 50-mL RB flask containing DCM (8 mL). 8-Aminoquinoline (420 mg, 2.91 mmol), pyridine (0.47 mL, 5.83 mmol), and HATU (1.33 g, 3.50 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (15% DCM/15% Ether/70% Hexanes) to afford **1w** (130 mg, 19% yield) as a light yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.76 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55–7.47 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.63 (t, *J* = 5.8 Hz, 1H), 4.54 (t, *J* = 5.8 Hz, 1H), 2.72 (t, *J* = 7.4 Hz, 2H), 2.28–2.14 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.66, 148.27, 138.38, 136.45, 134.49, 128.02, 127.45, 121.72, 121.64, 116.53, 83.29 (d, J_{C-F} = 165.1 Hz), 33.51 (d, J_{C-F} = 4.7 Hz), 26.32 (d, J_{C-F} = 20.1 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -172.18. **HRMS** calcd. for $C_{13}H_{14}FN_2O^+$ [M+H]$^+$: 233.10847, Found: 233.10851.

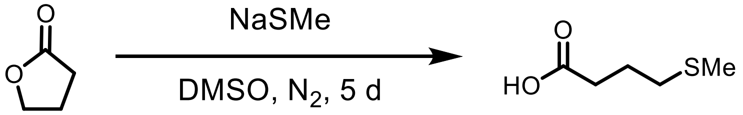


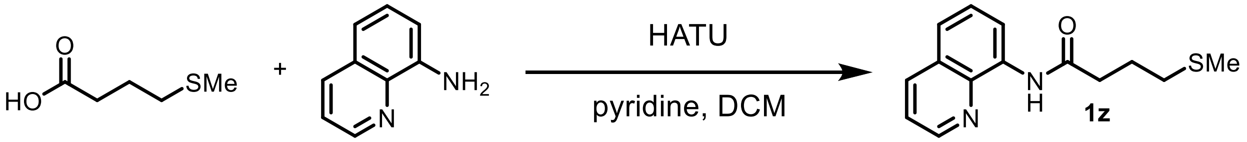
4-(methylsulfinyl)-*N*-(quinolin-8-yl)butanamide (1x): 4-(Methylthio)butanoic acid was prepared using a procedure adapted from Griesbeck.[18] 4-(Methylthio)butanoic acid (1.48 g, 11.0 mmol) was charged into a 100-mL RB flask containing acetone (11 mL). The solution was cooled to 0 °C, and 30 wt. % H_2O_2 in water (1.33 mL, 11.8 mmol) was added dropwise. The reaction was allowed to warm to ambient temperature, and then was stirred at ambient temperature for 24 h. The reaction was concentrated *in vacuo* to afford crude 4-(methylsulfinyl)butanoic acid (1.63 g, 99% crude yield) as a white solid, which was used in the next step without further purification. Crude 4-(methylsulfinyl)butanoic acid (508 mg, 3.38 mmol) was charged into a 50-mL RB flask containing DCM (7 mL). 8-Aminoquinoline (375 mg, 2.60 mmol), pyridine (0.42 mL, 5.20 mmol), and HATU (1.29 g, 3.38 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% Acetone in DCM to 100% Acetone) to afford **1x** (188 mg, 68% yield) as a white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.74 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.58–7.50 (m, 2H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 2.96–2.84 (m, 2H), 2.84–2.76 (m, 2H), 2.61 (s, 3H), 2.36–2.27 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.20, 148.38, 138.40, 136.52, 134.36, 128.07, 127.46, 121.84 (×2), 116.61, 53.80, 38.78, 36.18, 18.79. **HRMS** calcd. for $C_{14}H_{17}N_2O_2S^+$ [M+H]$^+$: 277.10052, Found: 277.10057.



4-(methylsulfonyl)-*N*-(quinolin-8-yl)butanamide (1y): 4-(Methylsulfonyl)butanoic acid was prepared using a procedure adapted from Tumula.[19] 4-(Methylthio)butanoic acid (1.48 g, 11.0 mmol) and Amberlyst-15 (616 mg) were charged into a 250-mL RB flask containing AcOH (60 mL). The solution was heated to 50 °C, and 30 wt. % H_2O_2 in water (4.24 mL, 37.4 mmol) was added with vigorous stirring. The reaction was stirred at 50 °C for 40 min and then filtered. The filtrate was extracted with DCM (50 mL, ×3), dried over Na_2SO_4, and concentrated to afford crude 4-(methylsulfonyl)butanoic acid (392 mg, 21% crude yield) as an off-white solid, which was used in the next step without further purification. Crude 4-(methylsulfonyl)butanoic acid (392 mg, 2.36

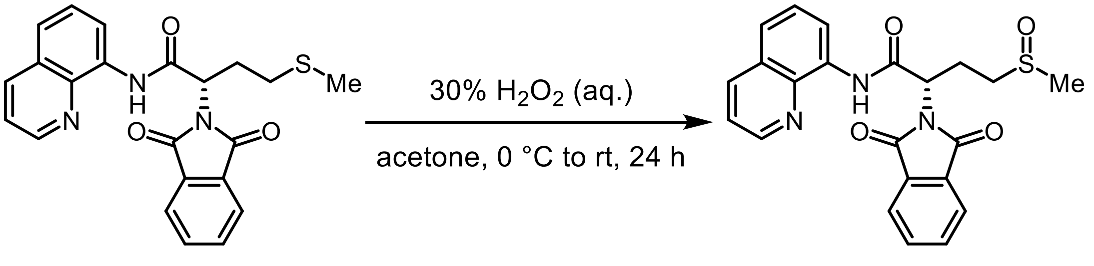
mmol) was charged into a 50-mL RB flask containing DMF (5.5 mL). 8-Aminoquinoline (283 mg, 1.96 mmol), pyridine (0.32 mL, 3.93 mmol), and HATU (896 mg, 2.36 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (3% MeOH in DCM) to afford **1y** (166 mg, 29% yield) as a brown solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.72 (dd, *J* = 6.7, 2.3 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.57–7.51 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 3.26–3.21 (m, 2H), 2.96 (s, 3H), 2.83 (t, *J* = 6.9 Hz, 2H), 2.40–2.33 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 169.81, 148.39, 138.36, 136.51, 134.26, 128.06, 127.41, 121.91, 121.85, 116.59, 53.87, 40.75, 35.42, 18.56. **HRMS** calcd. for $C_{14}H_{17}N_2O_3S^+$ $[M+H]^+$: 293.09544, Found: 293.09537.





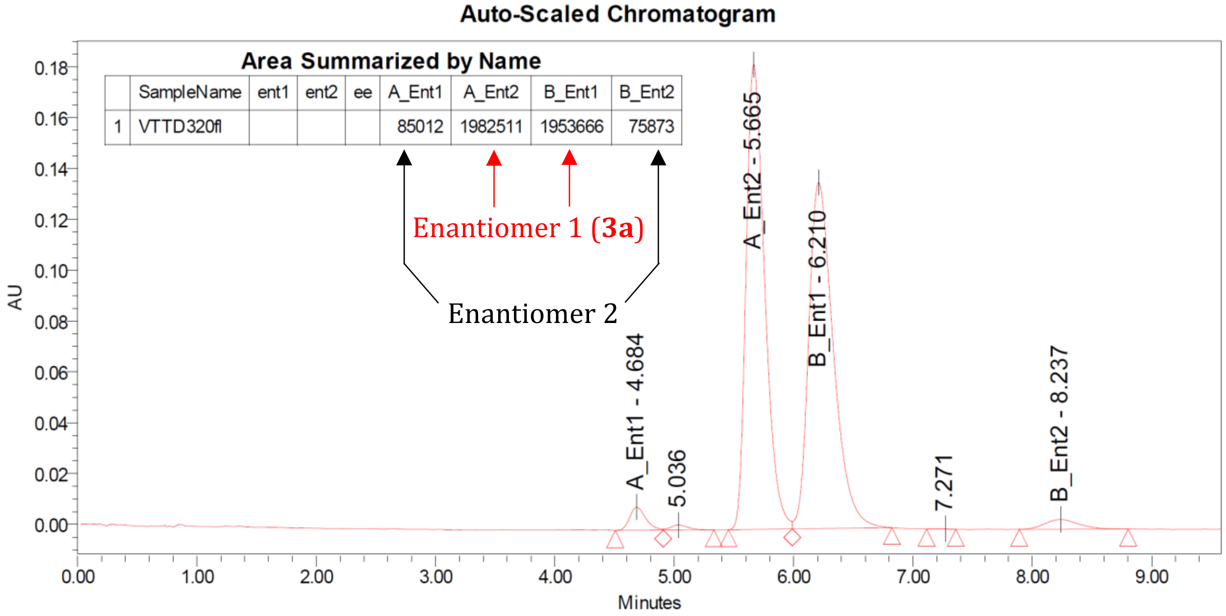
1z

4-(methylthio)-*N*-(quinolin-8-yl)butanamide (1z): Dihydrofuran-2(3*H*)-one (7.69 mL, 100 mmol) and sodium thiomethoxide (9.35 g, 133 mmol) were charged into a 250-mL RB flask containing DMSO (83 mL, dried over 3 Å molecular sieves) under a nitrogen atmosphere, and the reaction was stirred at ambient temperature for 5 d. Upon completion, 1M HCl (250 mL) was added, and the solution was extracted with diethyl ether (200 mL, ×4), dried over $MgSO_4$, and concentrated to afford crude 4-(methylthio)butanoic acid[20] (11.20 g, 83% crude yield) as a yellow oil, which was used in the next step without further purification. Crude 4-(methylthio)butanoic acid (628 mg, 4.68 mmol) was charged into a 100-mL RB flask containing DCM (11 mL). 8-Aminoquinoline (519 mg, 3.60 mmol), pyridine (0.58 mL, 7.20 mmol), and HATU (1.78 g, 4.68 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (30% EtOAc in Hexanes) to afford **1z** (775 mg, 83% yield) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.81 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.77 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.56–7.48 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 2.72 (t, *J* = 7.3 Hz, 2H), 2.66 (t, *J* = 7.1 Hz, 2H), 2.16–2.09 (m, 5H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.12, 148.29, 138.46, 136.50, 134.61, 128.08, 127.55, 121.75, 121.59, 116.57, 36.65, 33.73, 24.69, 15.47. **HRMS** calcd. for $C_{14}H_{17}N_2OS^+$ $[M+H]^+$: 261.10561, Found: 261.10566.



3a

(2*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylsulfinyl)-*N*-(quinolin-8-yl)butanamide (3a): The title compound was prepared using a procedure adapted from Griesbeck.[18] (*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylthio)butanoic acid (890 mg, 2.19 mmol) and acetone (2 mL) were charged into a 25-mL RB flask. The resulting solution was allowed to cool to 0 °C in an ice bath, and 30 wt. % H_2O_2 in water (0.27 mL, 2.34 mmol) was added dropwise with vigorous stirring. The reaction was allowed to warm to ambient temperature and stir for 24 h. Solvent was removed *in vacuo*, and the crude mixture was purified by column chromatography (30% acetone in DCM) to afford **3a** (787 mg, 85% yield, 92% ee) as a white solid. Compound **3a** was analyzed by chiral SFC on a Daicel IA column (3 mm, 4.6 × 250 mm) under isocratic conditions [40% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (238 nm). Note: The NMR spectra show an approximate 1:1 mixture of two diastereomers due to non-defined stereochemistry at sulfur. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.29 (d, *J* = 9.3 Hz, 1H), 8.70–8.65 (m, 1H), 8.63 (dt, *J* = 4.3, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.93 (dt, *J* = 5.4, 3.1 Hz, 2H), 7.83–7.76 (m, 2H), 7.55–7.49 (m, 2H), 7.40 (dd, *J* = 8.2, 4.2 Hz, 1H), 5.26 (td, *J* = 9.0, 5.7 Hz, 1H), 3.04–2.93 (m, 2H), 2.93–2.81 (m, 2H), 2.62 (d, *J* = 3.3 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.00, 165.86, 165.82, 148.58, 138.58, 138.55, 136.42, 134.70, 133.75, 133.72, 131.81, 127.98, 127.35, 123.99, 122.36, 121.85, 116.96, 116.94, 54.19, 53.97, 51.68, 51.43, 38.87, 38.71, 22.69, 22.53. **HRMS** calcd. for $C_{22}H_{20}N_3O_4S^+$ [M+H]$^+$: 422.11690, Found: 422.11708.



Area Summarized by Name

	SampleName	ent1	ent2	ee	A_Ent1	A_Ent2	B_Ent1	B_Ent2
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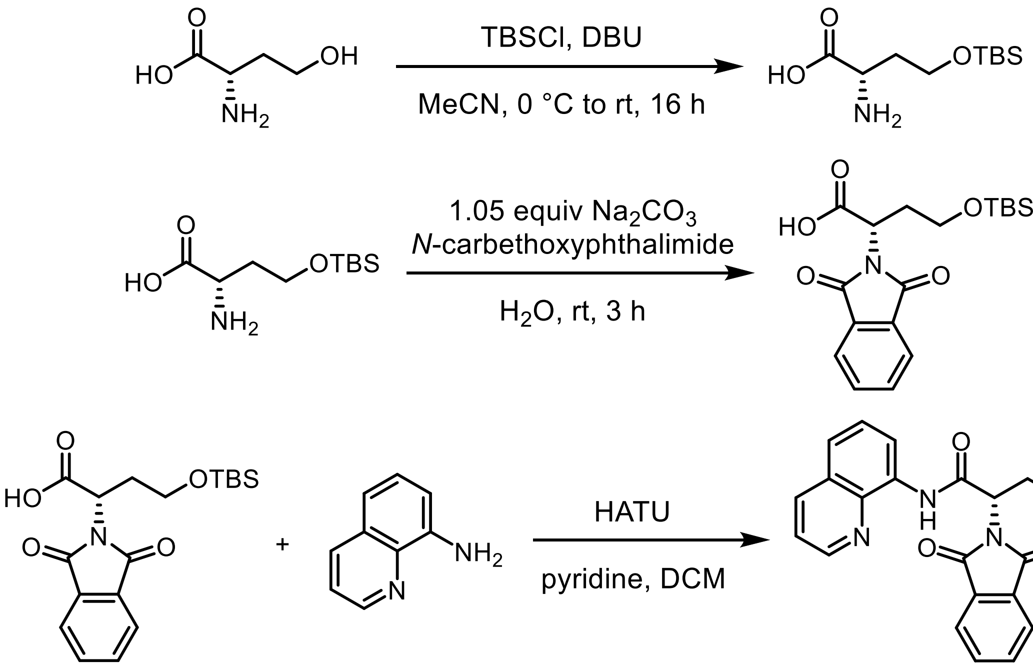
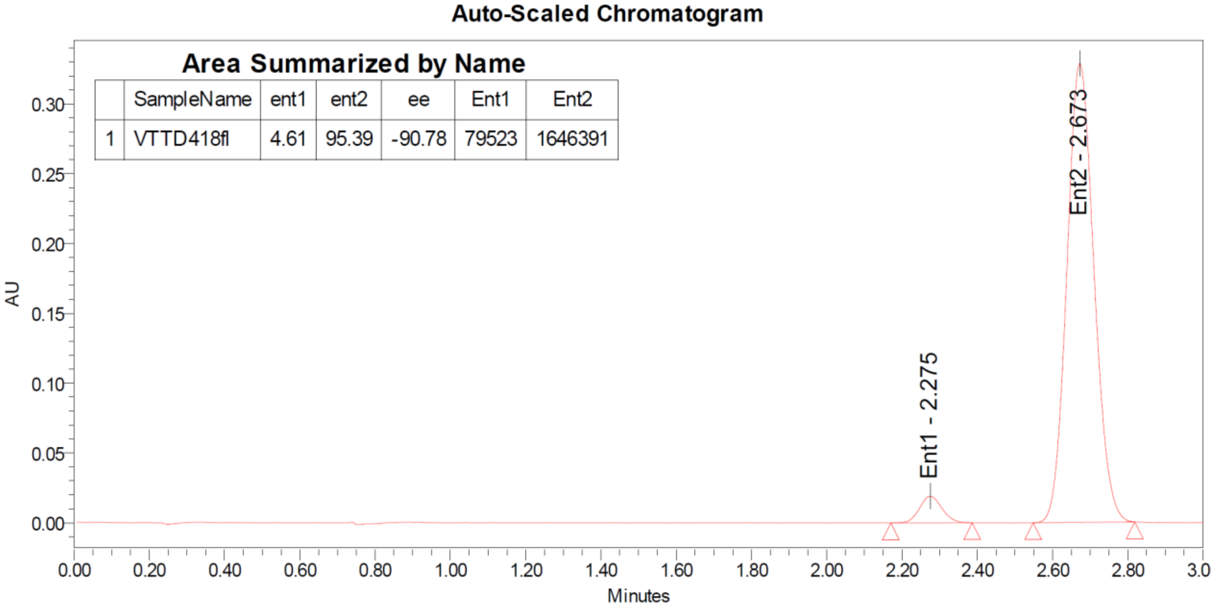


3b

(*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (3b): L-Homoserine (2.38 g, 20.0 mmol) was dissolved in MeCN (45 mL) in a 250-mL RB flask, and the solution was cooled to 0 °C with stirring. 1,8-Diazabicyclo[5.4.0]undec-7-ene (3.14 mL, 21.0 mmol) was added slowly, and the solution allowed to stir for 1 min. A solution of TBSCl (3.17 g, 21.0 mmol) in MeCN (45 mL) was added dropwise and the reaction was allowed to warm to ambient temperature and stir for 16 h. The resulting precipitate was isolated by vacuum filtration, washed with MeCN (50 mL, ×3), and allowed to dry under vacuum, affording crude *O*-(*tert*-butyldimethylsilyl)-L-homoserine[21] (4.10 g, 88% yield) as a white powder, which was used in the next step without further purification. Na_2CO_3 (1.11 g, 10.5 mmol) and water (26 mL) were charged into a 100-mL RB flask. To this solution was added crude *O*-(*tert*-butyldimethylsilyl)-L-homoserine (2.33 g, 10.0 mmol). *N*-Carbethoxyphthalimide (2.19 g, 10.0 mmol) was added, and the reaction allowed to stir at ambient temperature for 3 h. The reaction was then diluted with sat. $NaHCO_3$ (50 mL). The aqueous layer was washed with EtOAc (150 mL, ×3) then acidified with conc. HCl to pH = 1 and extracted with EtOAc (100 mL, ×3). The organic layers were combined, dried over Na_2SO_4, and concentrated to give crude (*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2-(1,3-dioxoisoindolin-2-yl)butanoic acid as a white solid (quantitative yield of crude material), which was used in the next step without further purification. Crude (*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2-(1,3-dioxoisoindolin-2-yl)butanoic acid (3.63 g, 10.0 mmol) was charged into a 100-mL RB flask containing DCM (23 mL). 8-Aminoquinoline (1.11 g, 7.69 mmol), pyridine (1.24 mL, 15.4 mmol), and HATU (3.80 g, 10.0 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (15% DCM/15% Ether/70% Hexanes) to afford **3b** (1.64 g, 44% yield, 91% ee) as a white solid. Compound **3b** was analyzed by chiral SFC on a Daicel IC column (3 mm, 4.6 × 250 mm) under isocratic conditions [30% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (238 nm). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.72 (dd, *J* = 6.1, 2.9 Hz, 1H), 8.67 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.90 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.54–7.47 (m, 2H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.41 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.88 (ddd, *J* =

10.6, 6.0, 4.5 Hz, 1H), 3.73 (ddd, *J* = 10.6, 7.9, 4.0 Hz, 1H), 2.76 (dddd, *J* = 14.1, 10.0, 6.0, 4.0 Hz, 1H), 2.67 (ddt, *J* = 14.3, 7.8, 4.8 Hz, 1H), 0.86 (s, 9H), –0.02 (d, *J* = 8.3 Hz, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.24, 167.45, 148.43, 138.68, 136.35, 134.25, 134.14, 132.21, 127.98, 127.42, 123.68, 121.97, 121.72, 116.83, 60.24, 52.63, 31.82, 26.01, 18.44, -5.41. **HRMS** calcd. for $C_{27}H_{32}N_3O_4Si^+$ [M+H]$^+$: 490.21566, Found: 490.21565.



Area Summarized by Name

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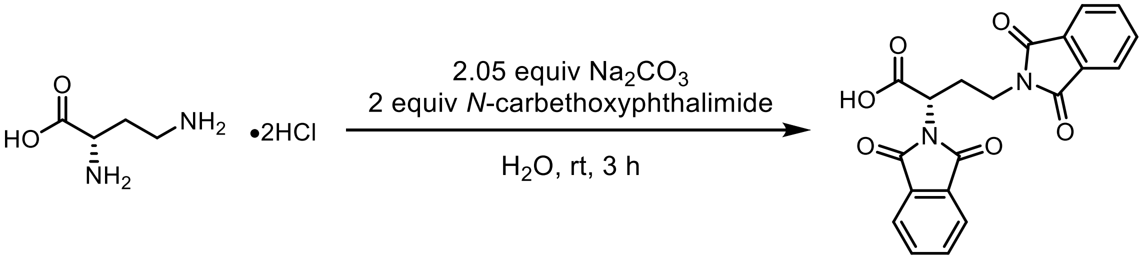
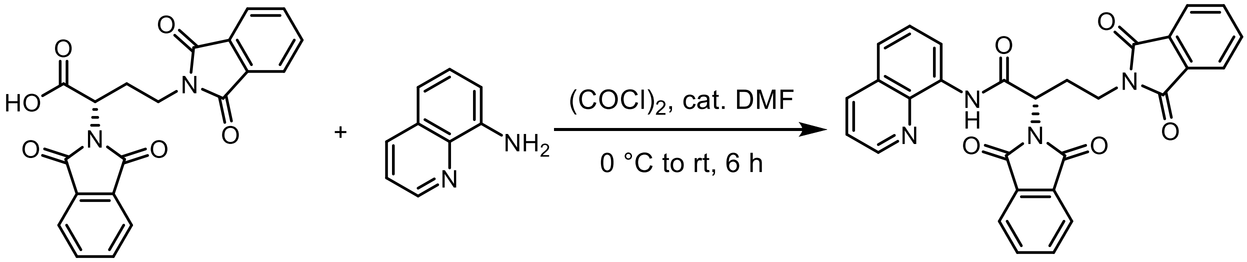
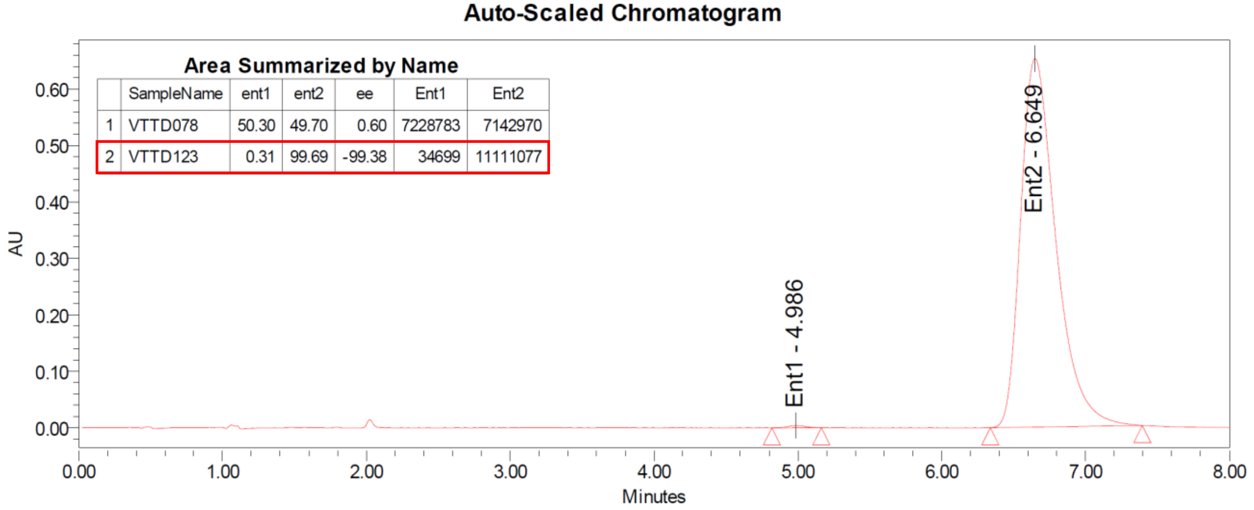




3c

(*S*)-2,4-bis(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (3c): (*S*)-2,4-Bis(1,3-dioxoisoindolin-2-yl)butanoic acid was prepared using a procedure adapted from Watson.[22] Na_2CO_3 (1.30 g, 12.3 mmol) and water (16 mL) were charged into a 50-mL RB flask. To this solution was added L-2,4-diaminobutyric acid dihydrochloride (1.15 g, 6.00 mmol). Once all solids were dissolved, *N*-carbethoxyphthalimide (2.63 g, 12.0 mmol) was added, and the reaction was allowed to stir at ambient temperature for 3 h. The reaction was then diluted with sat. $NaHCO_3$ (50 mL). The aqueous layer was washed with EtOAc (150 mL, ×3) then acidified with conc. HCl to pH = 1 and extracted with EtOAc (100 mL, ×3). The organic layers were combined, dried over Na_2SO_4, and concentrated to give crude (*S*)-2,4-bis(1,3-dioxoisoindolin-2-yl)butanoic acid as a white viscous oil (quantitative yield of crude material), which was used in the next step without further purification. Crude (*S*)-2,4-bis(1,3-dioxoisoindolin-2-yl)butanoic acid (757 mg, 2.00 mmol) was charged into a 50-mL RB flask containing DCM (12.5 mL) and cooled to 0 °C. Oxalyl chloride (0.16 mL, 1.90 mmol) was added dropwise to the solution followed by 2–3 drops of *N,N*-dimethylformamide. The reaction was allowed to warm to ambient temperature stir for 3 h. The reaction was then cooled to 0 °C, and 8-aminoquinoline (260 mg, 1.80 mmol) was added. The reaction was allowed to warm to room temperature and stir for 3 h. The resulting solution was diluted with DCM (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2), brine (50 mL, ×1), dried over Na_2SO_4, and concentrated. The crude mixture was purified by column chromatography (40% EtOAc in Hexanes) to afford **3c** (391 mg, 39% yield, 99% ee) as a white solid. Compound **3c** was analyzed by chiral SFC on a Daicel IA column (3 mm, 4.6 × 250 mm) under isocratic conditions [60% MeOH / CO_2 (3 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (220 nm). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.67 (dd, *J* = 5.0, 4.0 Hz, 1H), 8.64 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.90 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.80 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.52–7.46 (m, 2H), 7.39 (dd, *J* = 8.3, 4.3 Hz, 1H), 5.14 (t, *J* = 8.1 Hz, 1H), 3.94 (dt, *J* = 14.6, 7.4 Hz, 1H), 3.86 (dt, *J* = 14.1, 6.0 Hz, 1H), 3.00 (td, *J* = 7.6, 5.9 Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.33, 168.15, 166.24, 148.50, 138.58, 136.35, 134.41, 134.14, 133.91, 132.11, 132.02, 127.93, 127.37, 123.80, 123.46, 122.13, 121.75, 116.91, 52.72, 35.37, 27.34. **HRMS** calcd. for $C_{29}H_{21}N_4O_5^+$ [M+H]$^+$: 505.15065, Found: 505.15073.



Area Summarized by Name

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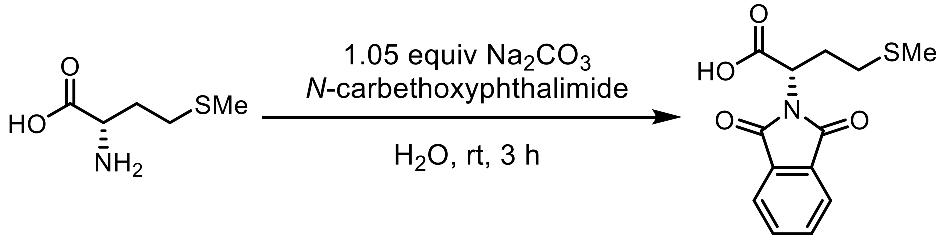
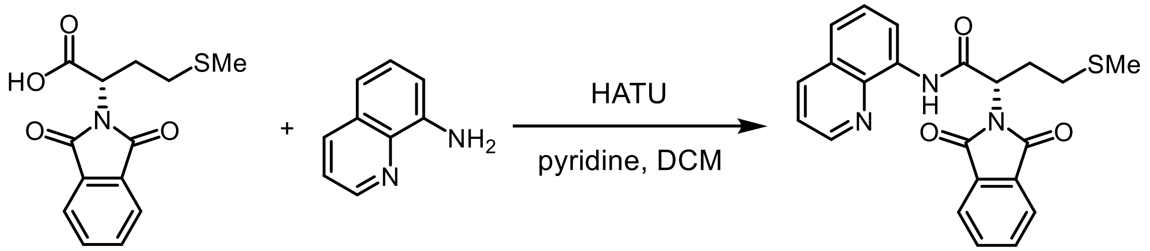
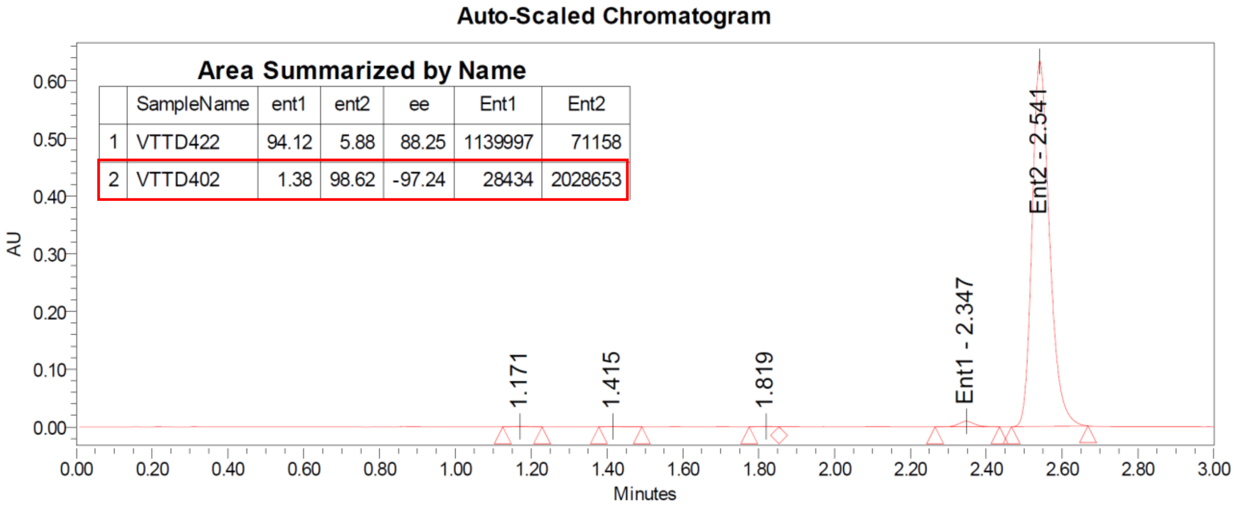




3d

(*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylthio)-*N*-(quinolin-8-yl)butanamide (3d): (*S*)-2-(1,3-Dioxoisoindolin-2-yl)-4-(methylthio)butanoic acid was prepared using a procedure adapted from Watson.[22] Na_2CO_3 (3.34 g, 31.5 mmol) and water (80 mL) were charged into a 250-mL RB flask. To this solution was added L-methionine (4.48 g, 30.0 mmol). Once all solids were dissolved, *N*-carbethoxyphthalimide (6.58 g, 30.0 mmol) was added, and the reaction was allowed to stir at ambient temperature for 3 h. The reaction was then diluted with sat. $NaHCO_3$ (50 mL). The aqueous layer was washed with EtOAc (150 mL, ×3) then acidified with conc. HCl to pH = 1 and extracted with EtOAc (100 mL, ×3). The organic layers were combined, dried over Na_2SO_4, and concentrated to give crude (*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylthio)butanoic acid as a white solid (quantitative yield of crude material), which was used in the next step without further purification. Crude (*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylthio)butanoic acid (1.44 g, 10.8 mmol) was charged into a 100-mL RB flask containing DCM (25 mL). 8-Aminoquinoline (1.30 g, 9.00 mmol), pyridine (1.45 mL, 18.0 mmol), and HATU (4.11 g, 10.8 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (30% EtOAc in Hexanes) to afford **3d** (2.08 g, 83% yield, 97% ee) as a yellow oil. Compound **3d** was analyzed by chiral SFC on a Daicel IB column (3 mm, 4.6 × 250 mm) under isocratic conditions [40% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (238 nm). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.30 (s, 1H), 8.70 (dd, *J* = 5.5, 3.5 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.92 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.77 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.54–7.48 (m, 2H), 7.40 (dd, *J* = 8.3, 4.3 Hz, 1H), 5.36 (dd, *J* = 10.2, 5.2 Hz, 1H), 2.85 (dddd, *J* = 13.8, 10.0, 7.5, 5.5 Hz, 1H), 2.77–2.59 (m, 3H), 2.16 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.16, 166.68, 148.47, 138.58, 136.40, 134.46, 133.93, 131.95, 127.97, 127.41, 123.83, 122.11, 121.77, 116.83, 54.10, 31.31, 28.13, 15.62. **HRMS** calcd. for $C_{22}H_{20}N_3O_3S^+$ $[M+H]^+$: 406.12199, Found: 406.12222.



Area Summarized by Name

	SampleName	ent1	ent2	ee	Ent1	Ent2
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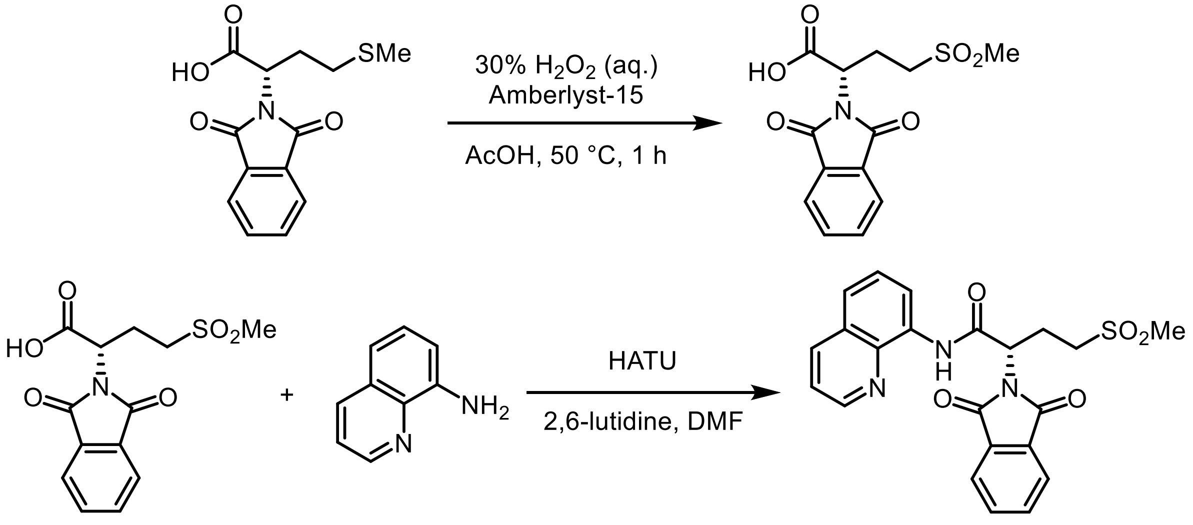
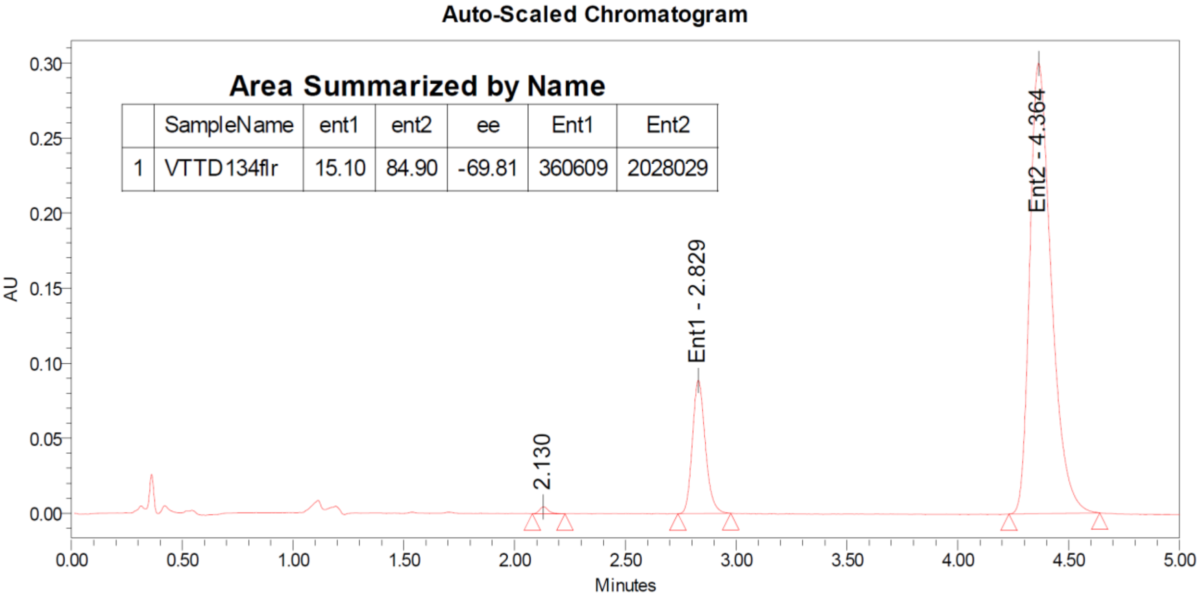


S7

(*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylsulfonyl)-*N*-(quinolin-8-yl)butanamide (S7): (*S*)-2-(1,3-Dioxoisoindolin-2-yl)-4-(methylsulfonyl)butanoic acid was prepared using a procedure adapted from Tumula.[19] Crude (*S*)-2-(1,3-Dioxoisoindolin-2-yl)-4-(methylthio)butanoic acid (838 mg, 3 mmol) was charged into a 50-mL RB flask containing AcOH (17 mL) and Amberlyst-15 (168 mg). The resulting mixture was heated to 50 °C with stirring in an oil bath. Next, 30 wt. % H_2O_2 in water (1.16 mL, 10.2 mmol) was added slowly and the reaction was allowed to stir at 50 °C for 1 h. The resulting mixture was filtered to remove Amberlyst-15 and diluted with water (50 mL). The aqueous solution was extracted with DCM (50 mL, ×2), and the organic layers were dried over Na_2SO_4 and concentrated to give crude (*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylsulfonyl)butanoic acid (803 mg, 86% crude yield) as a white solid, which was used in the next step without further purification. Crude (*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(methylsulfonyl)butanoic acid (255 mg, 0.82 mmol) was charged into a 10-mL RB flask containing DMF (2 mL). 8-Aminoquinoline (98.4 mg, 0.68 mmol), 2,6-lutidine (0.16 mL, 1.36 mmol), and HATU (311 mg, 0.82 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (20 mL), washed with sat. $NaHCO_3$ (20 mL, ×2) and brine (20 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (5% acetone in DCM) to afford **S7** (172 mg, 58% yield, 70% ee) as a brown solid. Compound **S7** was analyzed by chiral SFC on a Daicel IB column (3 mm, 4.6 × 250 mm) under isocratic conditions [60% MeOH / CO_2 (3 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (238 nm). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.28 (s, 1H), 8.67 (p, *J* = 4.5 Hz, 1H), 8.61 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.93 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.85–7.78 (m, 2H), 7.53 (d, *J* = 4.5 Hz, 2H), 7.41 (dd, *J* = 8.2, 4.2 Hz, 1H), 5.33–5.24 (m, 1H), 3.35 (ddd, *J* = 14.2, 10.4, 5.5 Hz, 1H), 3.21 (ddd, *J* = 14.2, 10.3, 5.3 Hz, 1H), 3.07–3.01 (m, 1H), 2.99 (s, 3H), 2.91 (dddd, *J* = 14.1, 10.5, 8.7, 5.4 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.28, 165.03, 147.77, 137.65, 136.18, 134.18, 132.89, 131.13, 127.45, 126.88, 123.46, 121.90, 121.24, 116.73, 52.67, 51.59, 40.11, 22.53. **HRMS** calcd. for $C_{22}H_{20}N_3O_5S^+$ [M+H]$^+$: 438.11182, Found: 438.11196.



	SampleName	ent1	ent2	ee	Ent1	Ent2
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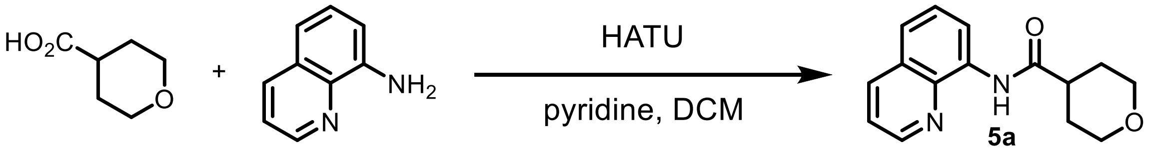
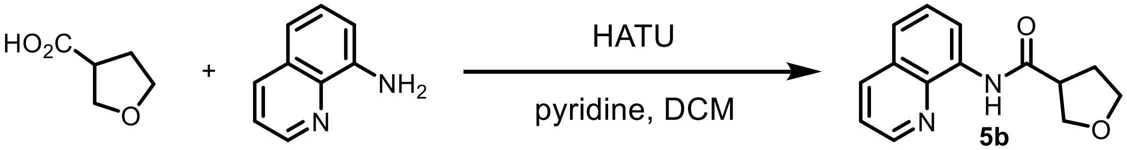
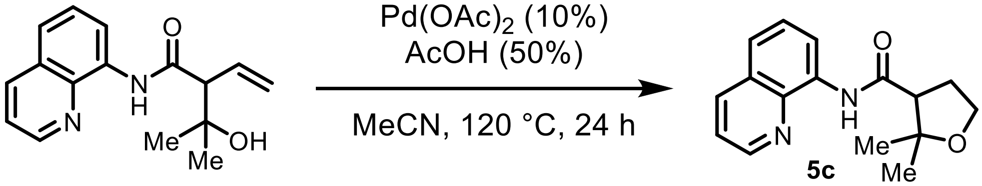


***N*-(quinolin-8-yl)tetrahydro-2*H*-pyran-4-carboxamide (5a):** Tetrahydro-2*H*-pyran-4-carboxylic acid (2.96 g, 11.0 mmol) was charged into a 100-mL RB flask containing DCM (25 mL). 8-Aminoquinoline (1.44 g, 10.0 mmol), pyridine (1.61 mL, 20.0 mmol), and HATU (4.18 g, 11.0 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% EtOAc in Hexanes) to afford **5a** (2.15 g, 84% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.78 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57–7.49 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.11 (ddd, *J* = 11.5, 4.0, 2.3 Hz, 2H), 3.54 (td, *J* = 11.4, 3.0 Hz, 2H), 2.74 (tt, *J* = 10.9, 4.6 Hz, 1H), 2.08–1.95 (m, 4H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.01, 148.33, 138.61, 136.56, 134.49, 128.09, 127.58, 121.78, 121.69, 116.65, 67.46, 43.79, 29.48. **HRMS** calcd. for $C_{15}H_{17}N_2O_2^+$ [M+H]$^+$: 257.12845, Found: 257.12849.



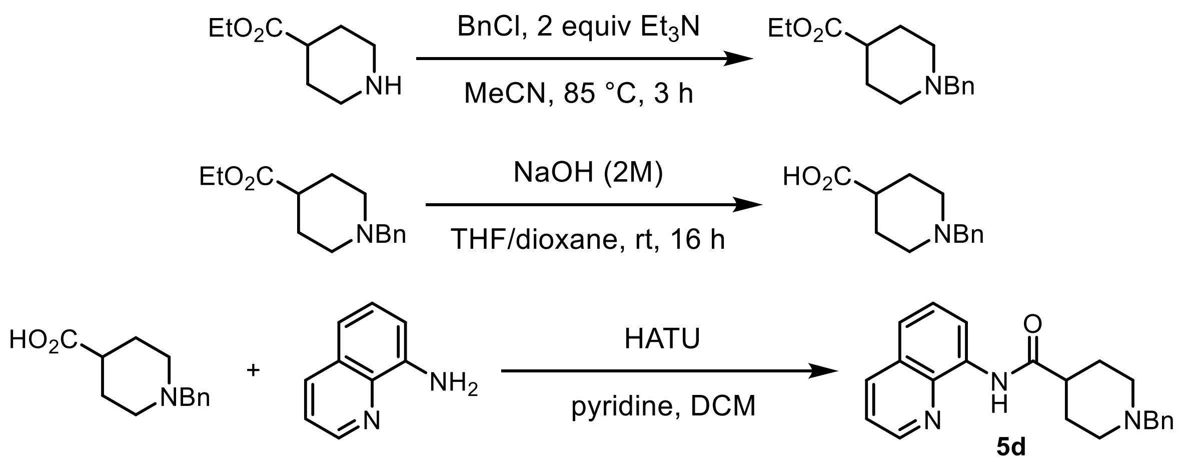
5b

N-(quinolin-8-yl)tetrahydrofuran-3-carboxamide (5b): Tetrahydrofuran-3-carboxylic acid (2.49 mL, 26.0 mmol) was charged into a 250-mL RB flask containing DCM (60 mL). 8-Aminoquinoline (2.88 g, 20.0 mmol), pyridine (3.22 mL, 40.0 mmol), and HATU (9.89 g, 26.0 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 36 h. The deep brown solution was diluted with EtOAc (200 mL), washed with sat. $NaHCO_3$ (200 mL, ×2) and brine (200 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (30% EtOAc in Hexanes) to afford **5b** (4.02 g, 83% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.77 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.57–7.49 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.16–4.04 (m, 3H), 3.93 (ddd, *J* = 8.5, 7.6, 6.5 Hz, 1H), 3.30 (ddt, *J* = 9.0, 7.6, 6.2 Hz, 1H), 2.39 (ddt, *J* = 12.6, 7.9, 6.3 Hz, 1H), 2.32 (dddd, *J* = 12.5, 9.1, 7.6, 5.9 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.09, 148.39, 138.50, 136.52, 134.49, 128.06, 127.51, 121.82, 121.79, 116.73, 71.19, 68.61, 47.16, 30.85. **HRMS** calcd. for $C_{14}H_{15}N_2O_2^+$ [M+H]$^+$: 243.11280, Found: 243.11279.



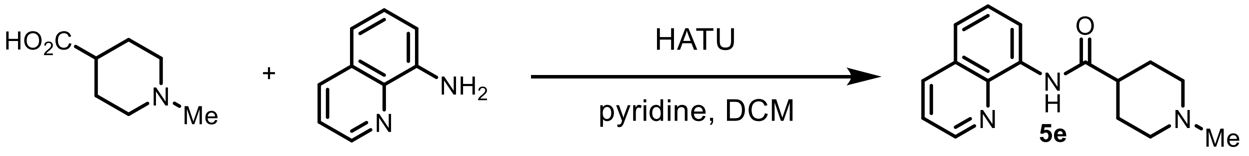
5c

2,2-dimethyl-N-(quinolin-8-yl)tetrahydrofuran-3-carboxamide (5c): 2-(2-Hydroxypropan-2-yl)-*N*-(quinolin-8-yl)but-3-enamide was prepared according to a previous report from our laboratory.[6] To a 48-mL bomb flask equipped with a magnetic stir bar were added $Pd(OAc)_2$ (12.2 mg., 0.054 mmol), 2-(2-hydroxypropan-2-yl)-*N*-(quinolin-8-yl)but-3-enamide (147 mg, 0.54 mmol), acetic acid (16.3 mg., 0.27 mmol), and MeCN (0.54 mL). The flask was sealed and heated to 120 °C for 24 h. The reaction was allowed to cool to ambient temperature, and the crude mixture was directly purified by column chromatography (20–30% EtOAc in Hexanes) to afford **5c** (118 mg, 81% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.77 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.59–7.50 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.14 (td, *J* = 8.6, 4.5 Hz, 1H), 3.96 (q, *J* = 7.8 Hz, 1H), 2.97 (t, *J* = 8.3 Hz, 1H), 2.63 (dtd, *J* = 12.7, 8.6, 7.5 Hz, 1H), 2.31 (dtd, *J* = 12.7, 8.1, 4.5 Hz, 1H), 1.56 (s, 3H), 1.26 (s, 4H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.44, 148.49, 138.60, 136.51, 134.51, 128.09, 127.54, 121.80, 121.74, 116.64, 82.24, 65.60, 56.79, 29.34, 28.62, 23.34. **HRMS** calcd. for $C_{16}H_{19}N_2O_2^+$ [M+H]$^+$: 271.14410, Found: 271.14406.



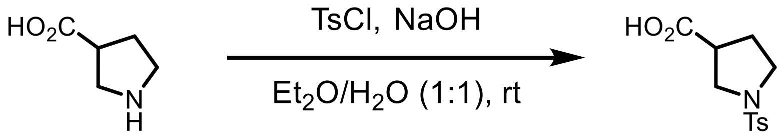
5d

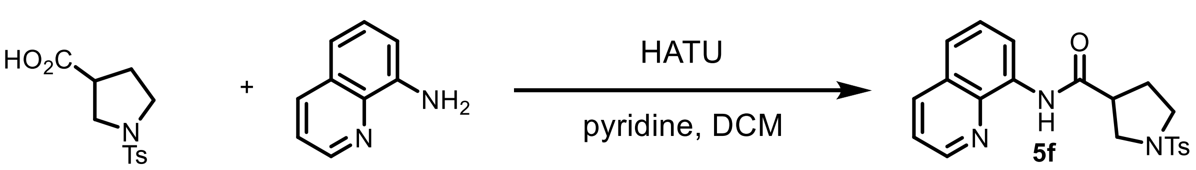
1-benzyl-*N*-(quinolin-8-yl)piperidine-4-carboxamide (5d): To a 48-mL bomb flask equipped with a magnetic stir bar were added MeCN (4 mL) and triethylamine (0.84 mL, 6.00 mmol). The solution was stirred for 30 sec., and ethyl piperidine-4-carboxylate (0.46 mL, 3.00 mmol) was added. After stirring for an additional 30 sec., benzylchloride (0.35 mL, 3.00 mmol) was added dropwise. The flask was sealed and heated to 85 °C for 3 h. After cooling to ambient temperature, the solvent was removed *in vacuo*. The resulting crude material was suspended in 2M NaOH (3 mL) and extracted with DCM (10 mL, ×3). The organic layers were combined, dried over Na_2SO_4, and concentrated to give crude ethyl 1-benzylpiperidine-4-carboxylate as a dark yellow liquid (quantitative yield of crude material), which was used in the next step without further purification. To a 25-mL RB flask was added crude ethyl 1-benzylpiperidine-4-carboxylate (742 mg, 3.00 mmol) followed by THF (3 mL), dioxane (3 mL), and 2M NaOH solution (3.2 mL, 6.40 mmol). The reaction was allowed to stir at ambient temperature for 16 h. The reaction mixture was then neutralized to pH = 7 with 2M HCl, and the solvent was removed *in vacuo*. Ethanol (5 mL) was added, and the resulting suspension was filtered. The filtrate was concentrated to give crude 1-benzylpiperidine-4-carboxylic acid (621 mg, 94% crude yield) as a light orange solid, which was used in the next step without further purification. Crude 1-benzylpiperidine-4-carboxylic acid (621 mg, 2.83 mmol) was charged into a 25-mL RB flask containing DCM (6.6 mL). 8-Aminoquinoline (314 mg, 2.18 mmol), pyridine (0.35 mL, 4.36 mmol), and HATU (1.08 g, 2.83 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 48 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (20% EtOAc in Pentane) to afford **5d** (562 mg, 75% yield) as a light yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.80 (t, *J* = 1.5 Hz, 1H), 8.79 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.49 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.45 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.37–7.31 (m, 4H), 7.28–7.24 (m, 1H), 3.55 (s, 2H), 3.06–2.98 (m, 2H), 2.48 (tt, *J* = 11.4, 4.1 Hz, 1H), 2.11 (td, *J* = 11.5, 2.7 Hz, 2H), 2.07–1.94 (m, 4H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.90, 148.26, 138.63, 138.52, 136.50, 134.63, 129.27, 128.35, 128.07, 127.57, 127.14, 121.71, 121.51, 116.61, 63.41, 53.30, 45.08, 29.22. **HRMS** calcd. for $C_{22}H_{24}N_3O^+$ [M+H]$^+$: 346.19139, Found: 346.19142.



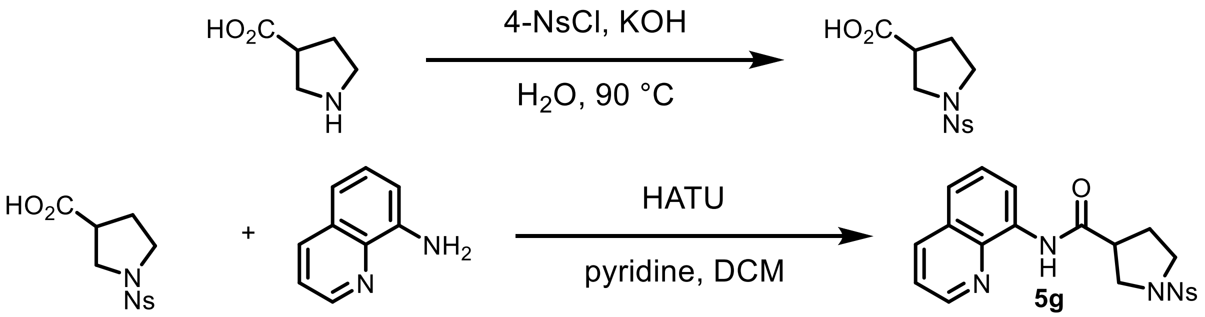
5e

1-methyl-*N*-(quinolin-8-yl)piperidine-4-carboxamide (5e): 1-Methylpiperidine-4-carboxylic acid (687 mg, 4.80 mmol) was charged into a 50-mL RB flask containing DCM (11 mL). 8-Aminoquinoline (577 mg, 4.00 mmol), pyridine (0.64 mL, 8.00 mmol), and HATU (1.83 g, 4.80 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (10% MeOH in DCM) to afford **5e** (576 mg, 54% yield) as a tan solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.79 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57–7.48 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 3.00 (dt, *J* = 11.7, 3.6 Hz, 2H), 2.47 (tt, *J* = 11.3, 3.9 Hz, 1H), 2.34 (s, 3H), 2.16–2.06 (m, 4H), 2.06–1.96 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.72, 148.30, 138.63, 136.53, 134.60, 128.09, 127.58, 121.74, 121.58, 116.62, 55.35, 46.54, 29.18, 25.71. **HRMS** calcd. for $C_{16}H_{20}N_3O^+$ [M+H]$^+$: 270.16009, Found: 270.16005.

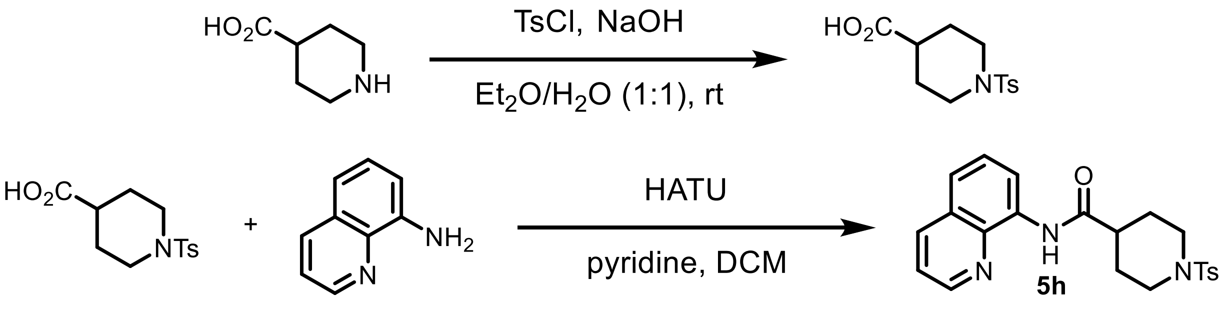




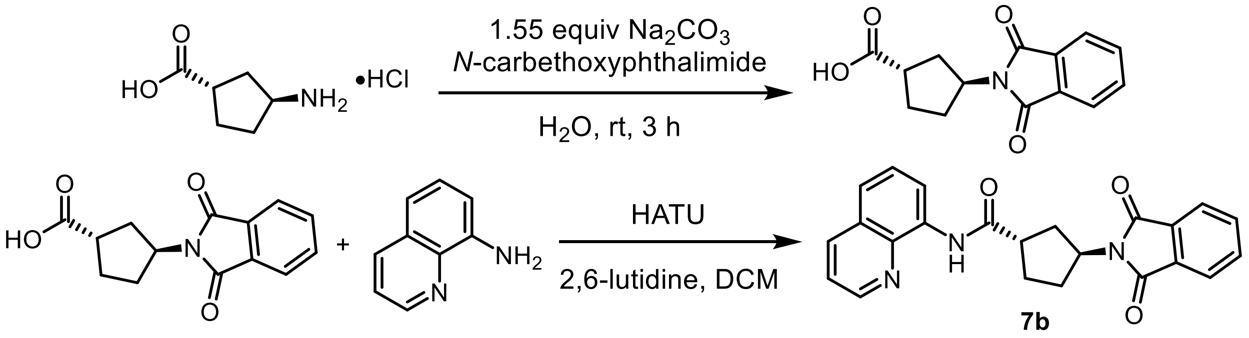
***N*-(quinolin-8-yl)-1-tosylpyrrolidine-3-carboxamide (5f):** To a solution of pyrrolidin-3-yl formate (2.30 g, 20.0 mmol) in diethyl ether (20 mL) and water (20 mL) in a 200-mL RB flask was added NaOH (1.60 g, 40.0 mmol). To the vigorously stirring solution was added TsCl (3.81 g, 20.0 mmol) portionwise over 15 min. The reaction was stirred at ambient temperature for 6 h, and then was diluted with equal portions of diethyl ether and water until all precipitates were redissolved. The aqueous layer was collected and acidified to pH = 2–3 with dropwise addition of 6N HCl. The precipitate was collected by filtration and used without further purification in the next step. 1-Tosylpyrrolidin-3-carboxylic acid (2.96 g, 11.0 mmol) was charged into a 100-mL RB flask containing DCM (25 mL). 8-Aminoquinoline (1.44 g, 10.0 mmol), pyridine (1.61 mL, 20.0 mmol), and HATU (4.18 g, 11.0 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% EtOAc in Hexanes) to afford **5f** (2.07 g, 52% yield) as a yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.63 (dd, *J* = 6.4, 2.6 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.54–7.49 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 3.79 (dd, *J* = 10.1, 7.8 Hz, 1H), 3.53–3.44 (m, 2H), 3.41 (ddd, *J* = 9.8, 8.2, 5.3 Hz, 1H), 3.21 (p, *J* = 7.9 Hz, 1H), 2.41 (s, 3H), 2.29–2.16 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.07, 148.47, 143.79, 138.38, 136.56, 134.11, 133.47, 129.89, 128.03, 127.82, 127.40, 122.07, 121.92, 116.71, 50.97, 47.74, 45.88, 29.31, 21.68. **HRMS** calcd. for $C_{21}H_{22}N_3O_3S^+$ [M+H]$^+$: 396.13764, Found: 396.13762.



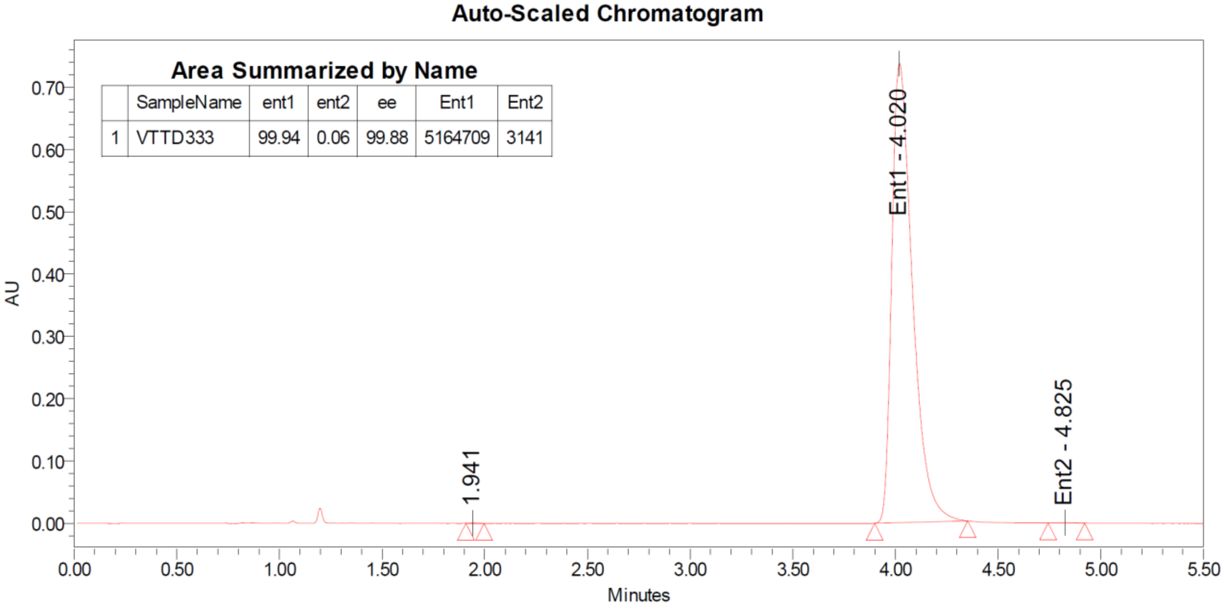
1-((4-nitrophenyl)sulfonyl)-*N*-(quinolin-8-yl)pyrrolidine-3-carboxamide (5g): To a solution of pyrrolidin-3-carboxylic acid (1.51 g, 10.0 mmol) in water (15 mL) in a 100-mL RB flask was added KOH (1.29 g, 23.0 mmol). The solution was heated to 90 °C, and 4-NsCl (2.33 g, 10.5 mmol) was added portionwise over 15 min. The reaction was stirred at 90 °C for 3 h, and then cooled to room temperature. The solution was washed with diethyl ether, and 6N HCl was added dropwise until the solution reached pH = 2–3. The solution was then extracted with diethyl ether (50 mL, ×3), and the organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo* to afford the product, which was used without further purification in the next step. 1-((4-Nitrophenyl)sulfonyl)pyrrolidin-3-carboxylic acid (976 mg, 3.25 mmol) was charged into a 50-mL RB flask containing DCM (7 mL). 8-Aminoquinoline (360 mg, 2.50 mmol), pyridine (0.40 mL, 5.00 mmol), and HATU (1.24 g, 3.25 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% EtOAc in Hexanes) to afford **5g** (564 mg, 53% yield) as a bright yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.51 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.32–8.27 (m, 2H), 8.18 (dd, *J* = 8.2, 1.7 Hz, 1H), 8.06–8.01 (m, 2H), 7.53 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.51–7.47 (m, 2H), 3.84 (dd, *J* = 10.4, 7.6 Hz, 1H), 3.64 (dd, *J* = 10.4, 6.3 Hz, 1H), 3.59 (ddd, *J* = 9.8, 7.5, 6.2 Hz, 1H), 3.46 (ddd, *J* = 9.8, 7.7, 6.5 Hz, 1H), 3.27 (p, *J* = 7.0 Hz, 1H), 2.34–2.24 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 169.86, 150.22, 148.50, 142.87, 138.31, 136.70, 133.85, 128.81, 128.06, 127.42, 124.46, 122.33, 121.98, 116.72, 51.09, 47.86, 45.70, 29.59. **HRMS** calcd. for $C_{20}H_{19}N_4O_5S^+$ $[M+H]^+$: 427.10707, Found: 427.10705.



***N*-(quinolin-8-yl)-1-tosylpiperidine-4-carboxamide (5h):** To a solution of piperidine-4-carboxylic acid (1.29 g, 10.0 mmol) in diethyl ether (10 mL) and water (10 mL) in a 100-mL RB flask was added NaOH (800 mg, 20.0 mmol). To the vigorously stirring solution was added TsCl (1.91 g, 10.0 mmol) portionwise over 15 min. The reaction was stirred at ambient temperature for 6 h, and then was diluted with equal portions of diethyl ether and water until all precipitates were redissolved. The aqueous layer was collected and acidified to pH = 2–3 with dropwise addition of 6N HCl. The precipitate was collected by filtration and used without further purification in the next step. 1-Tosylpiperidine-4-carboxylic acid (2.03 g, 7.15 mmol) was charged into a 50-mL RB flask containing DCM (16 mL). 8-Aminoquinoline (793 mg, 5.50 mmol), pyridine (0.89 mL, 11.0 mmol), and HATU (2.72 g, 7.15 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (40% EtOAc in Hexanes) to afford 2.00 g (89%) yield of **5h** as a yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.71 (dd, *J* = 6.8, 2.2 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.72–7.66 (m, 2H), 7.55–7.48 (m, 2H), 7.45 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.37–7.32 (m, 2H), 3.86 (dt, *J* = 11.5, 2.9 Hz, 2H), 2.49 (td, *J* = 11.7, 2.8 Hz, 2H), 2.46–2.40 (m, 4H), 2.16–2.08 (m, 2H), 2.03 (dtd, *J* = 13.3, 11.3, 4.0 Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.33, 148.35, 143.76, 138.50, 136.57, 134.25, 133.26, 129.83, 128.05, 127.87, 127.51, 121.82, 121.82, 116.62, 45.78, 43.75, 28.40, 21.69. **HRMS** calcd. for $C_{22}H_{24}N_3O_3S^+$ [M+H]$^+$: 410.15329, Found: 410.15332.



(1*S*,3*S*)-3-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)cyclopentane-1-carboxamide (7b): Na_2CO_3 (124 mg, 1.17 mmol) and water (2 mL) were charged into a 10-mL RB flask. To this solution was added (1*S*,3*S*)-3-aminocyclopentane-1-carboxylic acid hydrochloride (125 mg, 0.75 mmol). *N*-Carbethoxyphthalimide (165 mg, 0.75 mmol) was added and the reaction allowed to stir at ambient temperature for 3 h. The reaction was then diluted with sat. $NaHCO_3$ (10 mL). The aqueous layer was washed with EtOAc (20 mL, ×3) then acidified with conc. HCl to pH = 1 and extracted with EtOAc (20 mL, ×3). The organic layers were combined, dried over Na_2SO_4, and concentrated to give crude (1*S*,3*S*)-3-(1,3-dioxoisoindolin-2-yl)cyclopentane-1-carboxylic acid as a white viscous oil (quantitative yield of crude material), which was used in the next step without further purification. Crude (1*S*,3*S*)-3-(1,3-dioxoisoindolin-2-yl)cyclopentane-1-carboxylic acid (194 mg, 0.75 mmol) was charged into a 10-mL RB flask containing DCM (1.75 mL). 8-Aminoquinoline (90.1 mg, 0.63 mmol), 2,6-lutidine (0.15 mL, 1.25 mmol), and HATU (285.2 mg, 0.75 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (25 mL), washed with sat. $NaHCO_3$ (25 mL, ×2) and brine (25 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (35% EtOAc in Hexanes) to afford **7b** (112 mg, 46%, >99% ee) as a white solid. Compound **7b** was analyzed by chiral SFC on a Daicel IA column (3 mm, 4.6 × 250 mm) under isocratic conditions [40% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (241 nm). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.80 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.84 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.58–7.52 (m, 1H), 7.50 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.99 (dtd, *J* = 10.1, 8.4, 5.9 Hz, 1H), 3.56 (tt, *J* = 9.1, 7.5 Hz, 1H), 2.51 (ddd, *J* = 13.6, 10.1, 7.8 Hz, 1H), 2.47–2.38 (m, 2H), 2.30–2.19 (m, 2H), 2.12–2.02 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.86, 168.47, 148.30, 138.52, 136.46, 134.71, 134.06, 132.17, 128.06, 127.54, 123.25, 121.74, 121.56, 116.59, 50.13, 46.97, 33.87, 30.96, 30.85. **HRMS** calcd. for $C_{23}H_{20}N_3O_3^+$ [M+H]+: 386.14992, Found: 386.14987.



Area Summarized by Name

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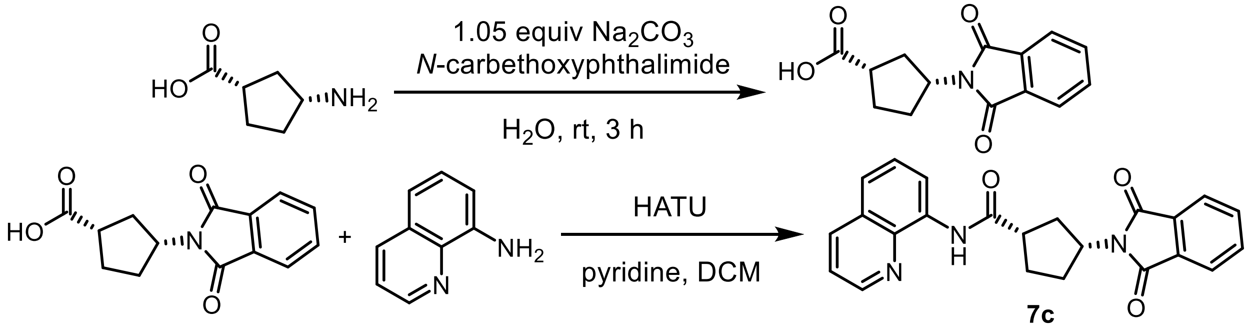
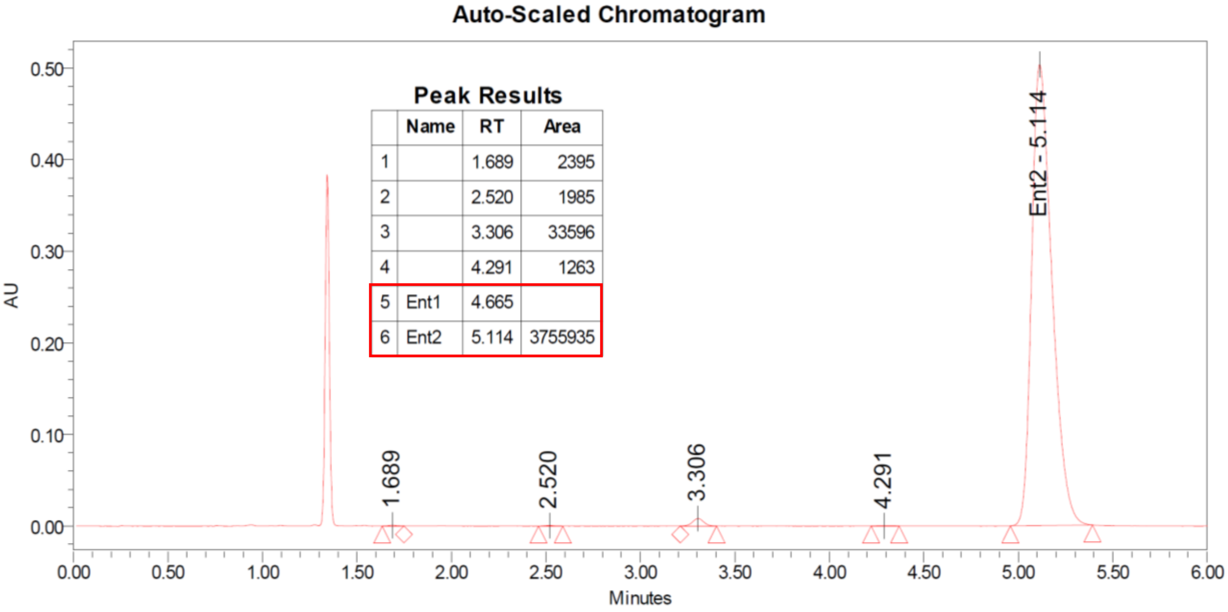
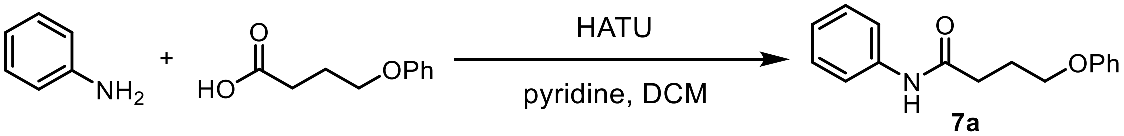


(1*S*,3*R*)-3-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)cyclopentane-1-carboxamide (7c): Na_2CO_3 (334 mg, 3.15 mmol) and water (7.9 mL) were charged into a 25-mL RB flask. To this solution was added (1*S*,3*R*)-3-aminocyclopentane-1-carboxylic acid (387 mg, 3.00 mmol). *N*-Carbethoxyphthalimide (658 mg, 3.00 mmol) was added, and the reaction was allowed to stir at ambient temperature for 3 h. The reaction was then diluted with sat. $NaHCO_3$ (20 mL). The aqueous layer was washed with EtOAc (50 mL, ×3) then acidified with conc. HCl to pH = 1 and extracted with EtOAc (50 mL, ×3). The organic layers were combined, dried over Na_2SO_4, and concentrated to give crude (1*S*,3*R*)-3-(1,3-dioxoisoindolin-2-yl)cyclopentane-1-carboxylic acid as a white viscous oil (quantitative yield of crude material), which was used in the next step without further purification. Crude (1*S*,3*R*)-3-(1,3-dioxoisoindolin-2-yl)cyclopentane-1-carboxylic acid (778 mg, 3.00 mmol) was charged into a 25-mL RB flask containing DCM (7 mL). 8-Aminoquinoline (360 mg, 2.50 mmol), pyridine (0.4 mL, 5.00 mmol), and HATU (1.14 g, 3.00 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The deep brown solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (35% EtOAc in Hexanes) to afford **7c** (510 mg, 53% yield, >99% ee) as a light yellow solid. Compound **7c** was analyzed by chiral SFC on a Daicel IBN column (3 mm, 4.6 × 250 mm) under isocratic conditions [40% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (241 nm). **^{1}H NMR** (600 MHz,

$CDCl_3$) δ 9.93 (s, 1H), 8.84–8.80 (m, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.84 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.73–7.68 (m, 2H), 7.56–7.53 (m, 1H), 7.50 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.45 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.78 (ddt, *J* = 10.7, 9.2, 7.6 Hz, 1H), 3.09 (dtd, *J* = 11.3, 8.6, 7.1 Hz, 1H), 2.77–2.70 (m, 1H), 2.52 (dtd, *J* = 12.2, 9.3, 8.9, 6.6 Hz, 1H), 2.44 (dddd, *J* = 12.9, 10.0, 7.8, 5.0 Hz, 1H), 2.40–2.36 (m, 1H), 2.22–2.16 (m, 1H), 2.13–2.06 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.76, 168.37, 148.29, 138.57, 136.50, 134.71, 134.04, 132.20, 128.07, 127.62, 123.30, 121.71, 121.51, 116.67, 50.69, 46.48, 33.72, 28.66, 28.33. **HRMS** calcd. for $C_{23}H_{20}N_3O_3^+$ [M+H]$^+$: 386.14992, Found: 386.14987.



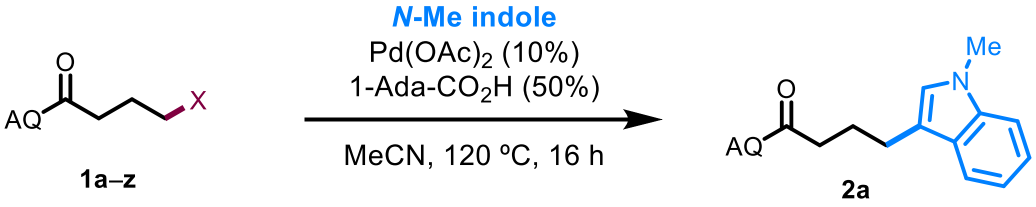
	Name	RT	Area
1		1.689	2395
2		2.520	1985
3		3.306	33596
4		4.291	1263
5	Ent1	4.665	
6	Ent2	5.114	3755935



7a

4-phenoxy-*N*-phenylbutanamide (7a): 4-Phenoxybutanoic acid (703 mg, 3.90 mmol) was charged into a 25-mL RB flask containing DCM (8 mL). Aniline (0.27 mL, 3.00 mmol), pyridine (0.48 mL, 6.00 mmol), and HATU (1.48 g, 3.90 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 24 h. The light yellow solution was diluted with EtOAc (100 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), dried over Na_2SO_4, and purified by column chromatography (20% EtOAc in Hexanes) to afford **7a** (651 mg, 85% yield) as a light orange solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.35 (s, 1H), 7.32–7.26 (m, 4H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.98–6.93 (m, 1H), 6.93–6.86 (m, 2H), 4.06 (t, *J* = 5.8 Hz, 2H), 2.58 (t, *J* = 7.2 Hz, 2H), 2.21 (p, *J* = 6.6 Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.78, 158.85, 137.96, 129.67, 129.13, 124.39, 121.04, 119.93, 114.62, 66.85, 34.28, 25.25. **HRMS** calcd. for $C_{16}H_{18}NO_2^+$ [M+H]$^+$: 256.13321, Found: 256.13342.

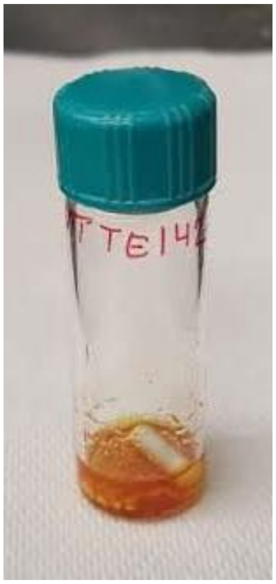
General Procedure for Evaluating Leaving Group Scope



Unless otherwise stated, the procedure was as follows. To a 1-Dram (4 mL) vial equipped with a magnetic stir bar were added $Pd(OAc)_2$ (4.5 mg., 0.02 mmol), substrate (0.2 mmol), 1-Adamantanecarboxylic acid (18.0 mg., 0.1 mmol), 1-methylindole (52.5 mg., 0.4 mmol), and MeCN (0.2 mL). The vial was sealed with a solid screw cap and placed in a heating block that was pre-heated to 120 °C. After the designated reaction time, the dark brown/black reaction mixture was purified either by flash column chromatography directly or an aqueous workup followed by flash column chromatography to produce **2a** (characterization data as previously reported[5]).

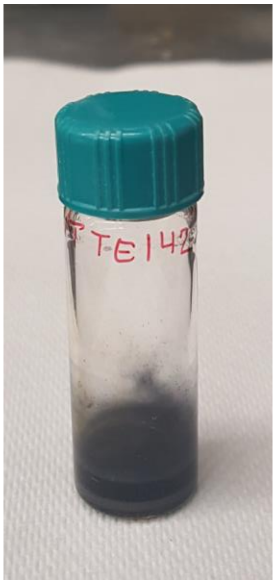
Photo Reel of General Reaction Set-Up

All reagents in 1-Dram vial

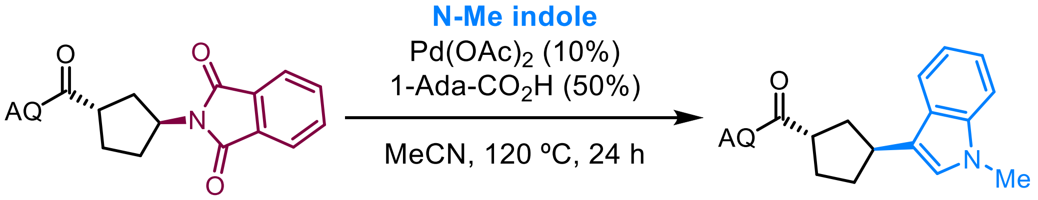


Addition of solvent, stir bar, and cap

Reaction in 120 °C heating block

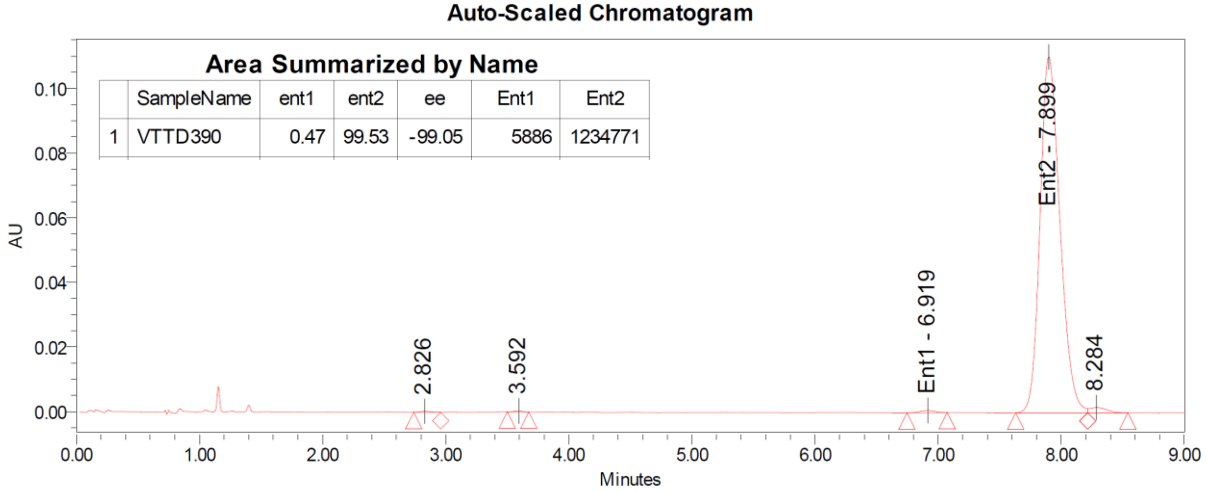


Crude reaction after 16 h



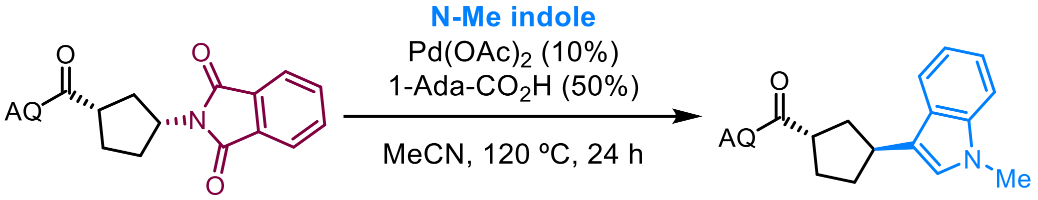
8b

(1*S*,3*S*)-3-(1-methyl-1H-indol-3-yl)-*N*-(quinolin-8-yl)cyclopentane-1-carboxamide (8b): The reaction was carried out according to the general procedure using **7b** (38.5 mg, 0.1 mmol), 1-methylindole (26.2 mg, 0.2 mmol), 1-Adamantane carboxylic acid (9.0 mg, 0.05 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), and MeCN (0.1 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (30% EtOAc in Hexanes) to afford 23.5 mg (64%, 99% ee) of **8b** as a yellow oil. Characterization data the same as **S2**. Compound **8b** was analyzed by chiral SFC on a Daicel IBN column (3 mm, 4.6 × 250 mm) under isocratic conditions [40% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (241 nm).



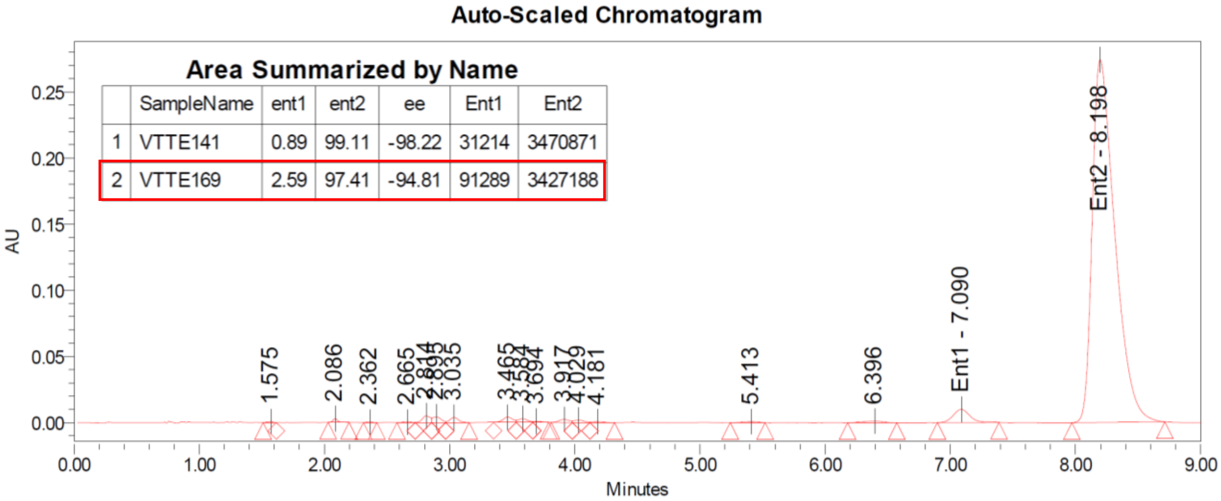
Area Summarized by Name

	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTD390	0.47	99.53	-99.05	5886	1234771



8b

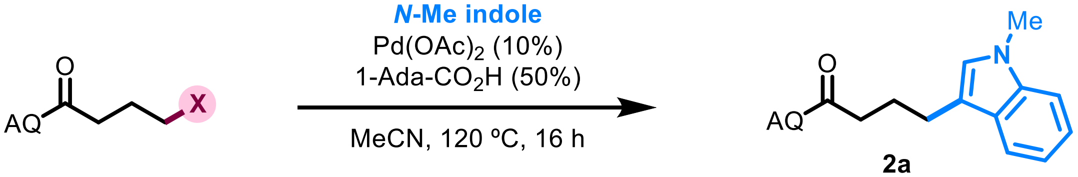
(1*S*,3*S*)-3-(1-methyl-1H-indol-3-yl)-*N*-(quinolin-8-yl)cyclopentane-1-carboxamide (8b): The reaction was carried out according to the general procedure using **7c** (77.1 mg, 0.2 mmol), 1-methylindole (52.5 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (30% EtOAc in Hexanes) to afford 31.4 mg (41%, 95% ee) of **8b** as a yellow oil. Characterization data the same as **S2**.



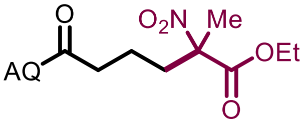
Area Summarized by Name

	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTE141	0.89	99.11	-98.22	31214	3470871
2	VTTE169	2.59	97.41	-94.81	91289	3427188

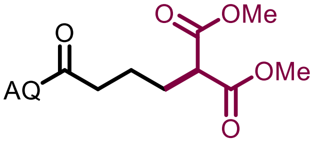
Unsuccessful Carbon Leaving Groups



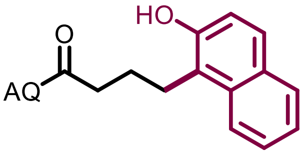
2a



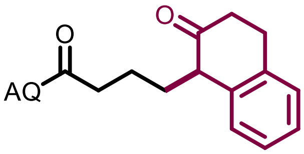
2i, 6%*



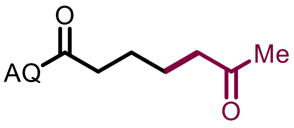
S4, n.r.



2e, n.r.



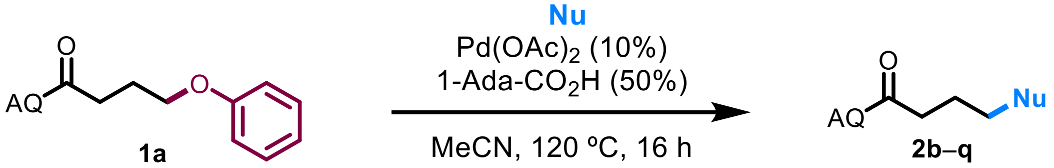
S5, n.r.



S6, n.r.

All yields determined by ^{1}H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard (n.r. = no reaction).

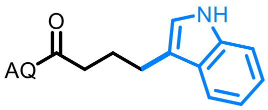
General Procedure for Evaluating Nucleophile Scope



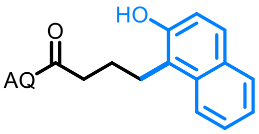
Unless otherwise stated, the procedure was as follows. To a 1-Dram (4 mL) vial equipped with a magnetic stir bar were added $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), substrate (61.3 mg, 0.2 mmol), 1-Adamantanecarboxylic acid (18.0 mg., 0.1 mmol), nucleophile (0.4 mmol), and MeCN (0.2 mL). The vial was sealed with a solid screw cap and placed in a heating block that was pre-heated to 120 °C. After the designated reaction time, the dark brown/black reaction was purified either by flash column chromatography directly or an aqueous workup followed by flash column chromatography to produce the desired product.

Characterization data for the following products match as previously reported by our group:[5,6,23]

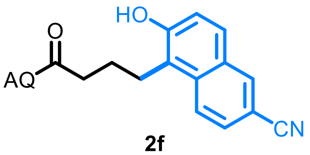
Table S4. Previously characterized products



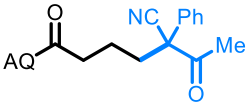
2d



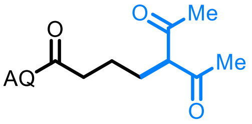
2e



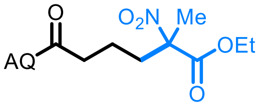
2f



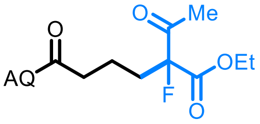
2g



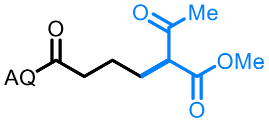
2h



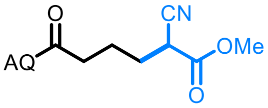
2i



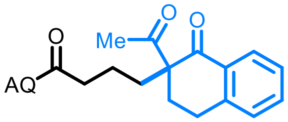
2j



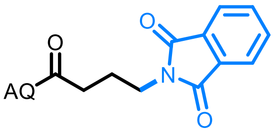
2k



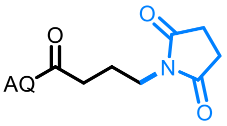
2l



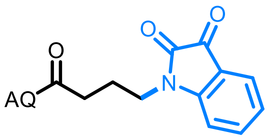
1s



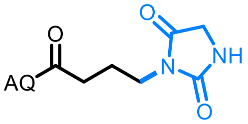
1m



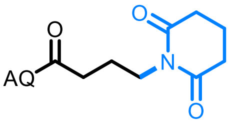
2m



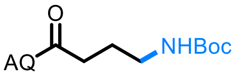
2n



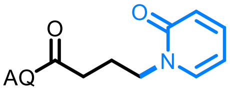
2o



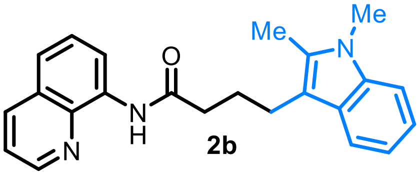
2q



1l

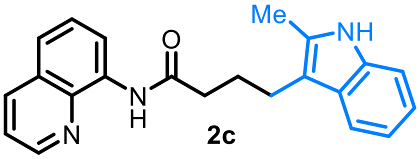


1j



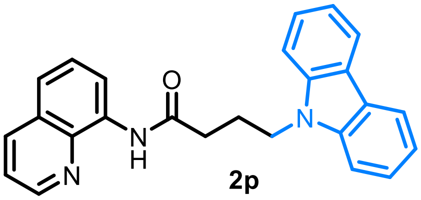
2b

4-(1,2-dimethyl-1*H*-indol-3-yl)-*N*-(quinolin-8-yl)butanamide (2b): The reaction was carried out according to the general procedure using **1a** (61.3 mg, 0.2 mmol), 1,2-dimethyl-1*H*-indole (58.1 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 16 h, and the product was purified by flash column chromatography (30% EtOAc in Hexanes) to afford **2b** (65.6 mg, 92% yield) as a yellow oil. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 9.72 (s, 1H), 8.78 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.45 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.40 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.24 – 7.17 (m, 1H), 7.12 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.05 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 3.59 (s, 3H), 2.87 (t, *J* = 7.3 Hz, 2H), 2.56 (t, *J* = 7.4 Hz, 2H), 2.33 (s, 3H), 2.16 (p, *J* = 7.3 Hz, 2H). **^{13}C NMR** (125 MHz, CDCl$_3$) δ 171.90, 148.14, 138.40, 136.65, 136.41, 134.65, 133.24, 128.01, 127.87, 127.50, 121.61, 121.40, 120.54, 118.78, 118.15, 116.54, 110.33, 108.56, 37.53, 29.53, 26.62, 23.83, 10.39. **HRMS** calcd. for $C_{23}H_{24}N_3O^+$ [M+H]$^+$: 358.19139, Found: 358.19123.



2c

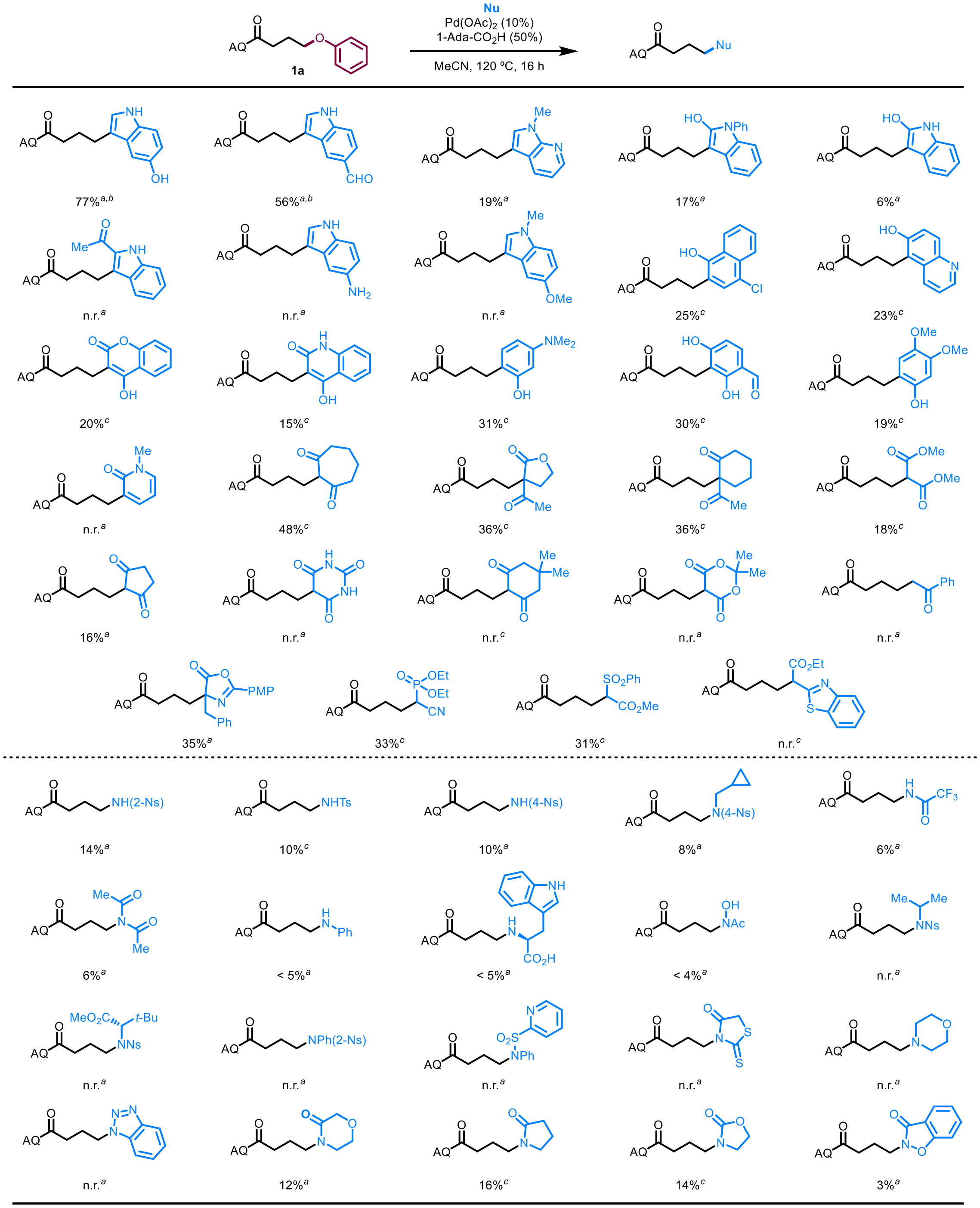
4-(2-methyl-1*H*-indol-3-yl)-*N*-(quinolin-8-yl)butanamide (2c): The reaction was carried out according to the general procedure using **1a** (61.3 mg, 0.2 mmol), 2-methyl-1*H*-indole (52.5 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 16 h, and the product was purified by flash column chromatography (20% EtOAc in Hexanes) to afford **2c** (61.7 mg. 90% yield) as a yellow oil. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 9.75 (s, 1H), 8.80 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.89 (s, 1H), 7.54 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.45 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.06 (dtd, *J* = 17.0, 7.1, 1.3 Hz, 2H), 2.83 (t, *J* = 7.3 Hz, 2H), 2.56 (t, *J* = 7.4 Hz, 2H), 2.31 (s, 3H), 2.16 (p, *J* = 7.4 Hz, 2H). **^{13}C NMR** (125 MHz, CDCl$_3$) δ 171.95, 148.17, 138.41, 136.42, 135.41, 134.62, 131.40, 128.83, 128.02, 127.49, 121.64, 121.46, 120.90, 119.15, 118.18, 116.56, 110.98, 110.28, 37.54, 26.38, 23.53, 11.74. **HRMS** calcd. for $C_{22}H_{22}N_3O^+$ [M+H]$^+$: 344.17574, Found: 344.17567.



2p

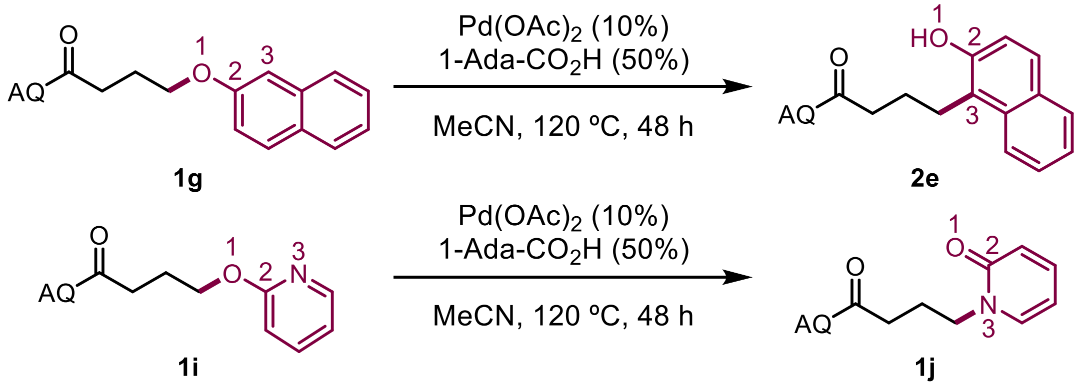
4-(9*H*-carbazol-9-yl)-*N*-(quinolin-8-yl)butanamide (2p): The reaction was carried out according to the general procedure using **1a** (61.3 mg, 0.2 mmol), carbazole (66.9 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 16 h, and the product was purified by flash column chromatography (40% EtOAc in Hexanes) to afford **2p** (40.2 mg, 53% yield) as a yellow oil. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 9.68 (s, 1H), 8.80 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.72 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.09 (dt, *J* = 7.7, 0.9 Hz, 2H), 7.59 – 7.52 (m, 1H), 7.52 – 7.46 (m, 3H), 7.41 (ddd, *J* = 8.2, 5.5, 1.5 Hz, 3H), 7.21 (ddd, *J* = 7.9, 7.1, 1.0 Hz, 2H), 4.48 (t, *J* = 7.0 Hz, 2H), 2.58 (t, *J* = 7.0 Hz, 2H), 2.40 (p, *J* = 7.0 Hz, 2H). **^{13}C NMR** (150 MHz, CDCl$_3$) δ 170.67, 148.22, 140.55, 138.38, 136.45, 134.47, 128.04, 127.50, 125.88, 123.01, 121.73, 121.68, 120.45, 119.02, 116.62, 108.86, 42.22, 34.57, 24.51. **HRMS** calcd. for $C_{25}H_{22}N_3O^+$ [M+H]$^+$: 380.17574, Found: 380.17565.

Unsuccessful Nucleophiles



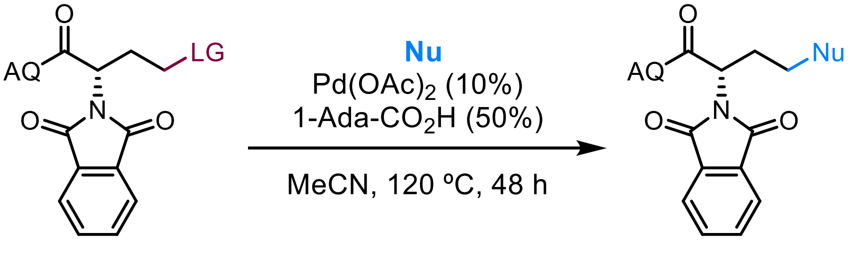
All yields determined by ^{1}H NMR analysis of the crude reaction mixture using CH$_2$Br$_2$ as internal standard (n.r. = no reaction). [a]Tentatively assigned based on ^{1}H NMR of crude reaction mixture. [b]Attempts at isolation lead to product decomposition upon concentration of eluent following column chromatography (30% EtOAc in Hexanes). [c]Previously characterized by our group.[5,14,23]

General Procedure for Formal [1,3]-Rearrangement



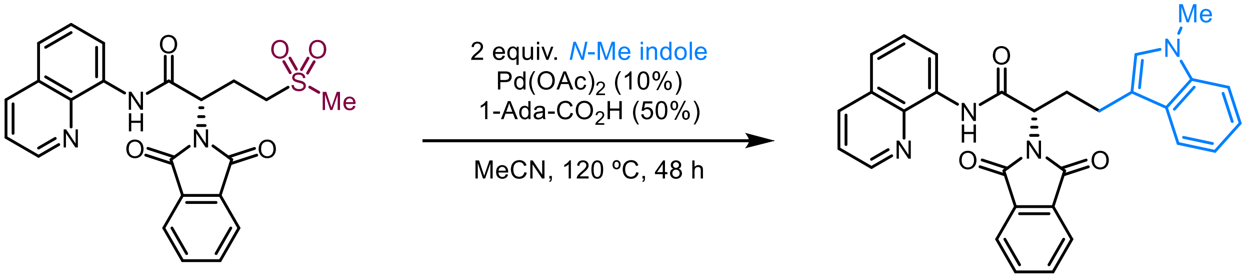
Unless otherwise stated, the procedure was as follows. To a 1-Dram (4 mL) vial equipped with a magnetic stir bar were added Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), substrate (0.2 mmol), 1-Adamantanecarboxylic acid (18.0 mg, 0.1 mmol), and MeCN (0.2 mL). The vial was sealed with a solid screw cap and placed in a heating block that was pre-heated to 120 °C. After the designated reaction time, the dark brown/black reaction was purified either by flash column chromatography directly or an aqueous workup followed by flash column chromatography to produce **2e** or **1j** (characterization data as previously reported[5,23]).

General Procedure for Amino Acid Upconversion



3a–d **4a–d**

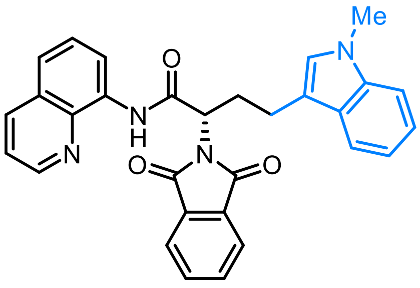
Unless otherwise stated, the procedure was as follows. To a 1-Dram (4 mL) vial equipped with a magnetic stir bar were added $Pd(OAc)_2$ (4.5 mg., 0.02 mmol), substrate (0.2 mmol), 1-Adamantanecarboxylic acid (18.0 mg, 0.1 mmol), nucleophile (0.4 mmol), and MeCN (0.2 mL). The vial was sealed with a solid screw cap and placed in a heating block that was pre-heated to 120 °C. After heating for 48 h, the dark brown/black reaction was filtered through a plug of silica (100% EtOAc) and purified by preparative TLC.



S7 **4a**, 8%

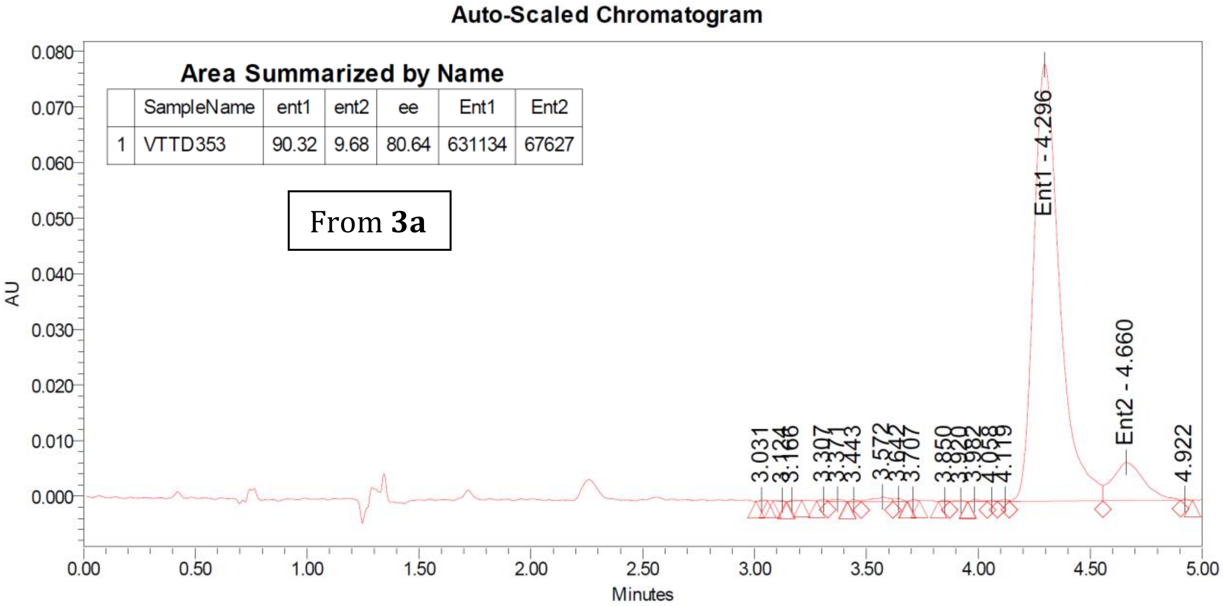
The reaction was carried out according to the general procedure using **S7** (43.7 mg, 0.1 mmol), 1-methylindole (26.2 mg, 0.2 mmol), 1-Adamantane carboxylic acid (9.0 mg, 0.05 mmol), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol), and MeCN (0.1 mL). The reaction was run for 48 h, and the yield was determined by ^{1}H NMR analysis of the crude reaction mixture using CH$_2$Br$_2$ as internal standard.

(*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(1-methyl-1H-indol-3-yl)-*N*-(quinolin-8-yl)butanamide



4a

(4a): The reaction was carried out according to the general procedure using **3a** (84.3 mg, 0.2 mmol) or **3c** (100.9 mg, 0.2 mmol) or **3d** (81.1 mg, 0.2 mmol), 1-methylindole (52.5 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 48 h, and the product was purified by preparative TLC (40% EtOAc in Hexanes) to afford **4a** (from **3a**: 79.7 mg, 82% yield, 81% ee; from **3c**: 49.8 mg, 51% yield, 96% ee; from **3d**: 18.6 mg 19% yield, 88% ee) as a yellow oil. For substrate **3b**, the reaction was performed on 0.1 mmol scale. The reaction was carried out according to the general procedure using **3b** (49.0 mg, 0.1 mmol), 1-methylindole (26.2 mg, 0.2 mmol), 1-Adamantane carboxylic acid (9.0 mg, 0.05 mmol), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol), and MeCN (0.1 mL). The reaction was run for 48 h, and the product was purified by preparative TLC (40% EtOAc in Hexanes) to afford 39.1 mg (80%, 78% ee) of **4a** as a yellow oil. Compound **4a** was analyzed by chiral SFC on a Daicel IA column (3 mm, 4.6 × 250 mm) under isocratic conditions [70% MeOH / CO$_2$ (2.5 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (295 nm). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 10.29 (s, 1H), 8.70 (dd, *J* = 6.3, 2.7 Hz, 1H), 8.64 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.83 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.62 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.53–7.45 (m, 2H), 7.39 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.20–7.13 (m, 2H), 7.12–7.05 (m, 1H), 6.90 (s, 1H), 5.21 (dd, *J* = 10.8, 4.7 Hz, 1H), 3.68 (s, 3H), 3.07 (dddd, *J* = 13.9, 10.8, 7.7, 6.4 Hz, 1H), 3.01–2.89 (m, 2H), 2.86–2.76 (m, 1H). **^{13}C NMR** (150 MHz, CDCl$_3$) δ 168.26, 167.23, 148.44, 138.63, 137.17, 136.34, 134.19, 134.08, 131.86, 127.95, 127.60, 127.41, 127.02, 123.52, 121.97, 121.71, 121.67, 119.24, 118.88, 116.79, 112.77, 109.17, 55.31, 32.67, 29.05, 22.63. **HRMS** calcd. for C$_{30}$H$_{25}$N$_4$O$_3^+$ [M+H]$^+$: 489.19212, Found: 489.19207.



Area Summarized by Name

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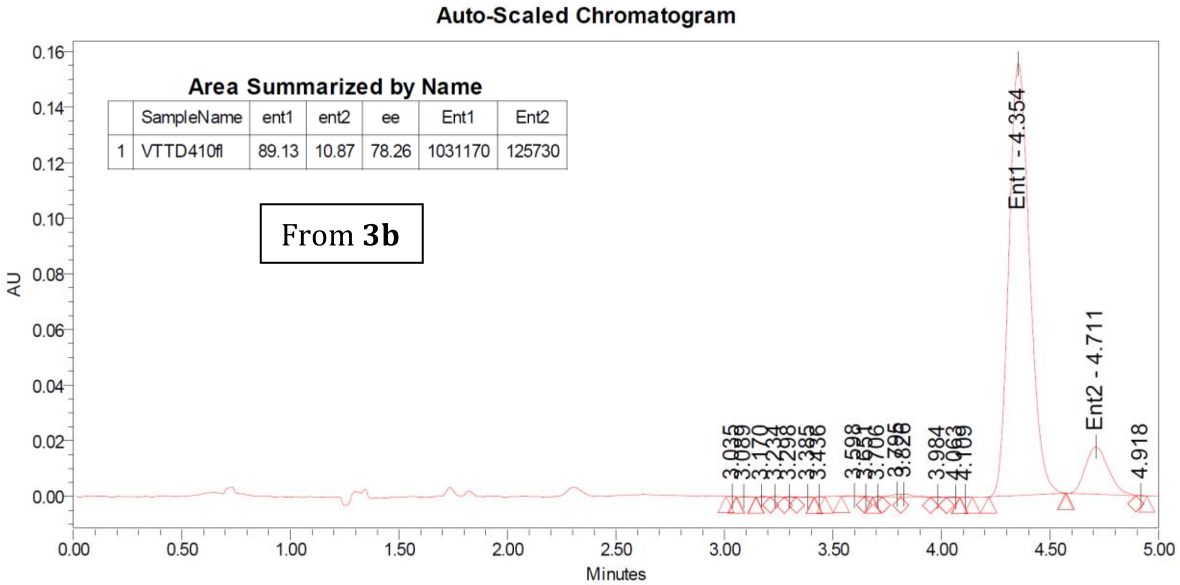
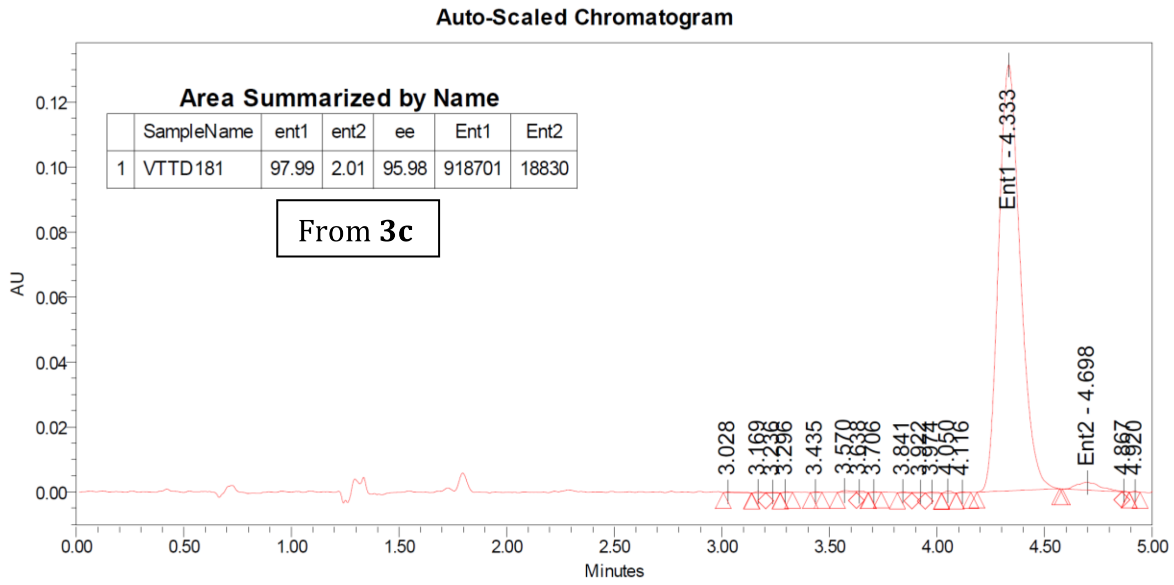
1	VTTD353	90.32	9.68	80.64	631134	67627



Area Summarized by Name

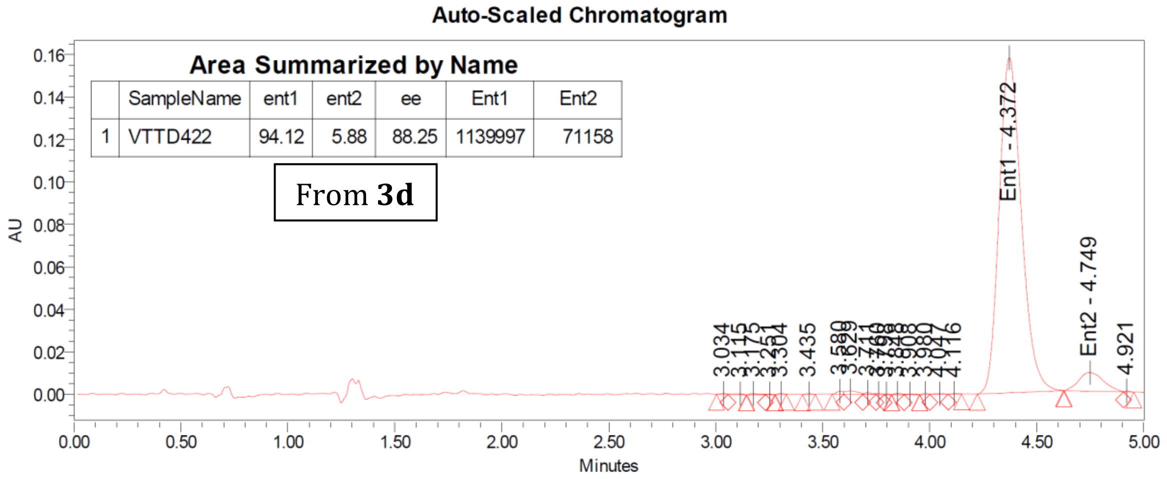
	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTD410fl	89.13	10.87	78.26	1031170	125730



Area Summarized by Name

	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTD181	97.99	2.01	95.98	918701	18830

From **3c**

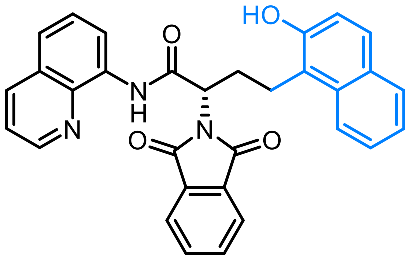


Area Summarized by Name

	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTD422	94.12	5.88	88.25	1139997	71158

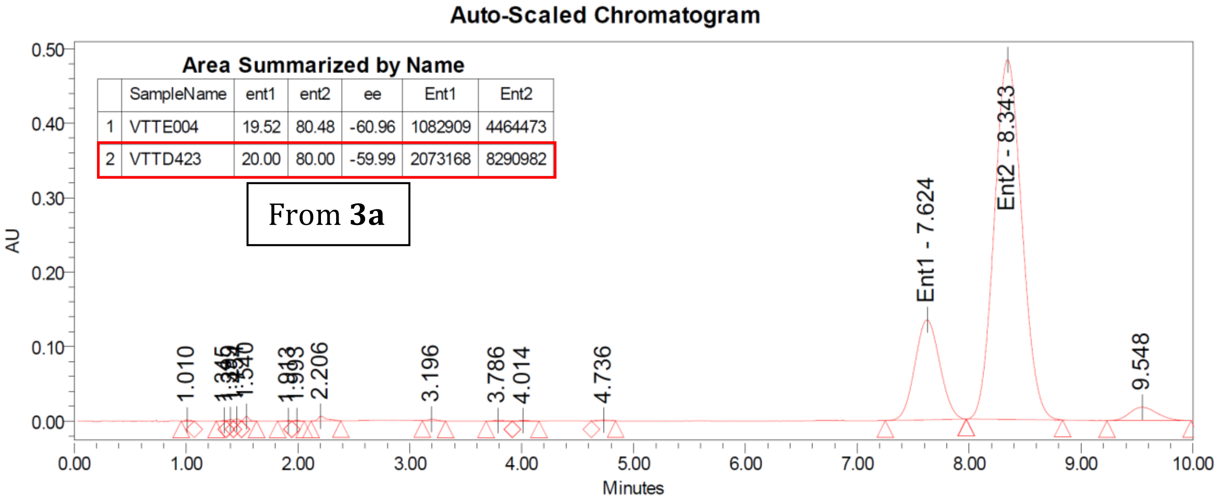
From **3d**

(*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-(2-hydroxynaphthalen-1-yl)-*N*-(quinolin-8-yl)butanamide (4b): The reaction was carried out according to the general procedure using **3a** (84.3 mg, 0.2 mmol) or **3b** (97.9 mg, 0.2 mmol), 2-naphthol (57.7 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 48 h, and the product was purified by preparative TLC (40% EtOAc in Hexanes) to afford **4b** (from **3a**: 40.2 mg, 40%, 60% ee; from **3b**: 54.0 mg, 54% yield, 61% ee) as an orange solid. Compound **4b** was analyzed by chiral SFC on a Daicel IA column (3 mm, 4.6 × 250 mm) under isocratic conditions [30% MeOH / CO$_2$ (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (224 nm). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 10.34 (s, 1H), 8.74 (dd, *J* = 6.9, 2.0 Hz, 1H), 8.55 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.07 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.73–7.68 (m, 3H), 7.61–7.53 (m, 2H), 7.51–7.46 (m, 2H), 7.42 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.33 (dd, *J* = 8.2, 4.3 Hz, 1H), 7.27 (ddd, *J* = 7.9, 6.8, 1.1 Hz, 1H), 7.17 (d, *J* = 8.8 Hz, 1H), 5.26 (dd, *J* = 8.1, 6.8 Hz, 1H), 3.37–3.24 (m, 2H), 2.88 (dddd, *J* = 14.4, 9.5, 8.0, 5.0 Hz, 1H), 2.69–2.59 (m, 1H). **^{13}C NMR** (150 MHz,



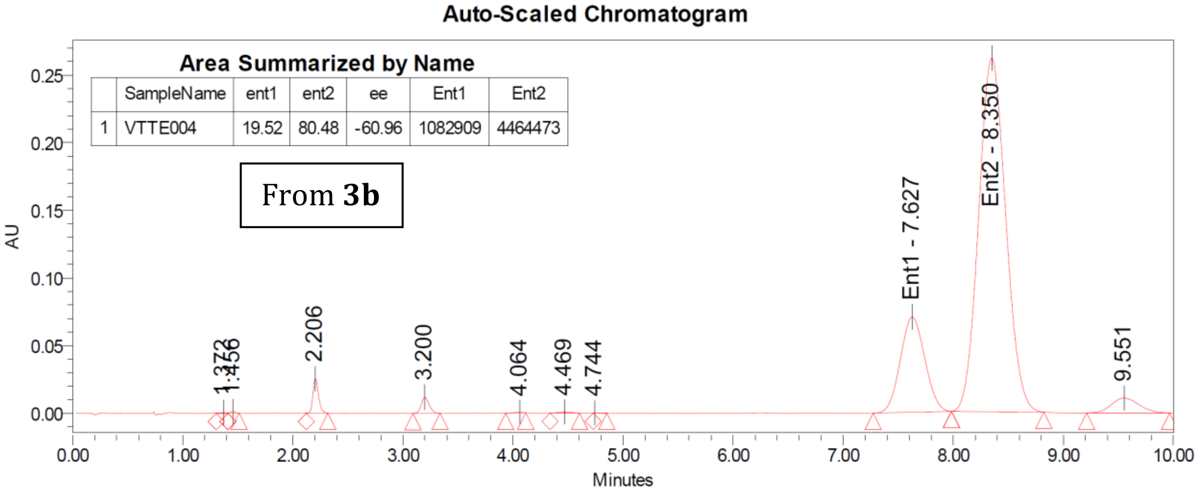
4b

CDCl$_3$) δ 168.15, 167.94, 152.23, 148.51, 138.53, 136.37, 134.46, 133.60, 133.10, 131.82, 129.27, 128.74, 128.29, 127.91, 127.34, 126.49, 123.79, 122.87, 122.53, 122.43, 121.73, 118.81, 117.84, 117.31, 54.46, 29.54, 22.69. **HRMS** calcd. for $C_{31}H_{24}N_3O_4^+$ [M+H]$^+$: 502.17613, Found: 502.17612.



Area Summarized by Name

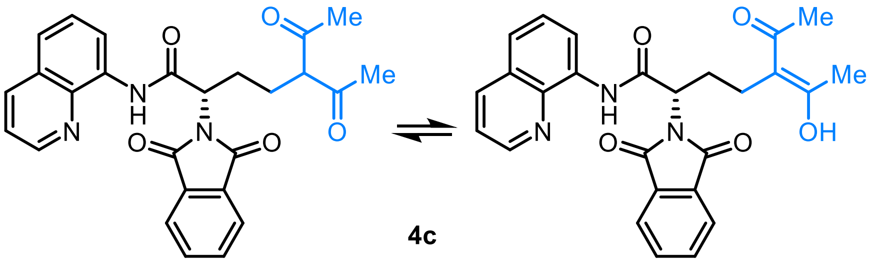
	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTE004	19.52	80.48	-60.96	1082909	4464473
2	VTTD423	20.00	80.00	-59.99	2073168	8290982



Area Summarized by Name

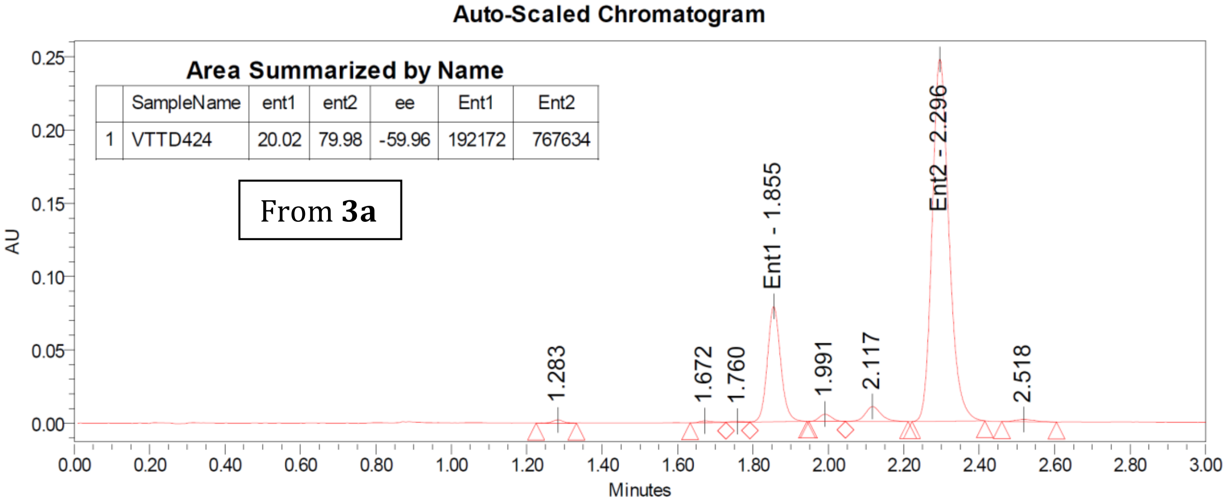
	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTE004	19.52	80.48	-60.96	1082909	4464473

(*S*)-5-acetyl-2-(1,3-dioxoisoindolin-2-yl)-6-oxo-*N*-(quinolin-8-yl)heptanamide (4c): The reaction was carried out according to the general procedure using **3a** (84.3 mg, 0.2 mmol) or **3b** (97.9 mg, 0.2 mmol), 2,4-pentanedione (40.0 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 48 h, and the product was purified by preparative TLC (50% EtOAc in Hexanes) to afford **4c** (from **3a**: 22.7 mg, 25% yield, 60% ee; from **3b**: 52.8 mg, 58% yield, 82% ee) as a yellow oil. Note: The NMR spectra show an approximate 3:2 mixture of two tautomers. Compound **4c** was analyzed by chiral SFC on a Daicel IB column (3 mm,



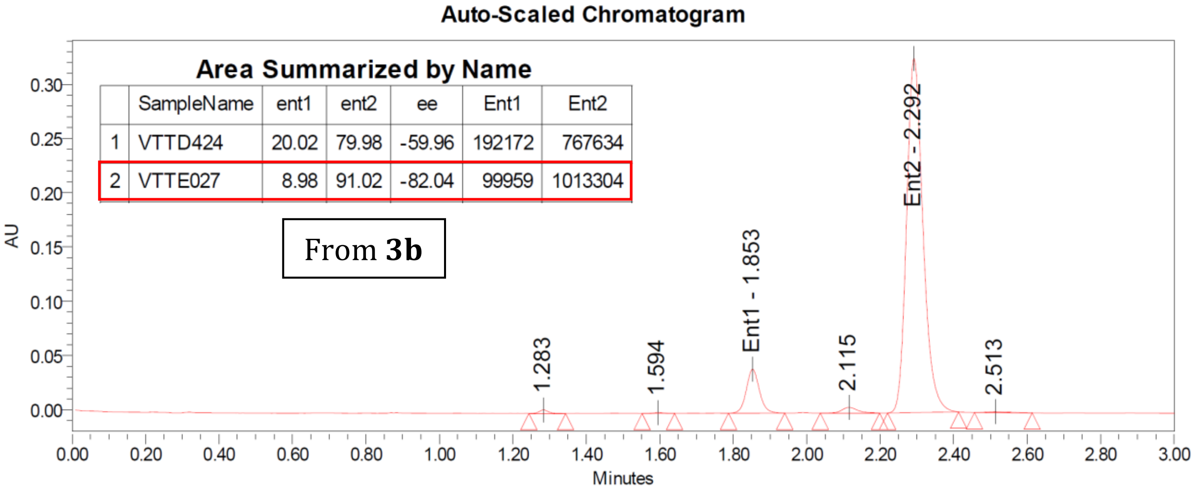
4c

4.6 × 250 mm) under isocratic conditions [40% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (238 nm). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.34–10.22 (m, 1H), 8.73–8.61 (m, 2H), 8.16–8.10 (m, 1H), 7.96–7.89 (m, 2H), 7.83–7.74 (m, 2H), 7.55–7.47 (m, 2H), 7.43–7.37 (m, 1H), 5.18–5.08 (m, 1H), 3.78 (t, *J* = 7.1 Hz, 0.6H), 2.63–2.24 (m, 2.8H), 2.24–2.15 (m, 6H), 2.06–1.91 (m, 1.2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 203.76, 203.64, 191.45, 168.20, 168.10, 166.42, 166.36, 148.53, 148.49, 138.56, 138.55, 136.45, 136.39, 134.63, 134.56, 133.83, 131.83, 131.80, 127.98, 127.95, 127.39, 127.36, 123.90, 123.89, 122.22, 122.18, 121.82, 121.78, 116.88, 116.84, 109.00, 68.10, 55.17, 54.86, 29.71, 29.47, 29.24, 26.79, 25.38, 25.17, 23.09. **HRMS** calcd. for $C_{26}H_{24}N_3O_5^+$ [M+H]$^+$: 458.17105, Found: 458.17113.



Area Summarized by Name

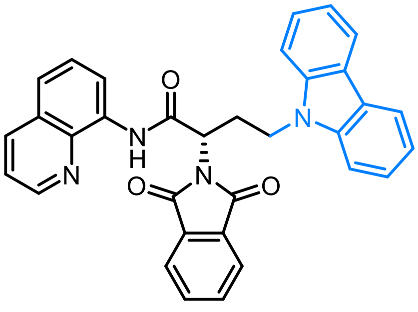
	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTD424	20.02	79.98	-59.96	192172	767634



Area Summarized by Name

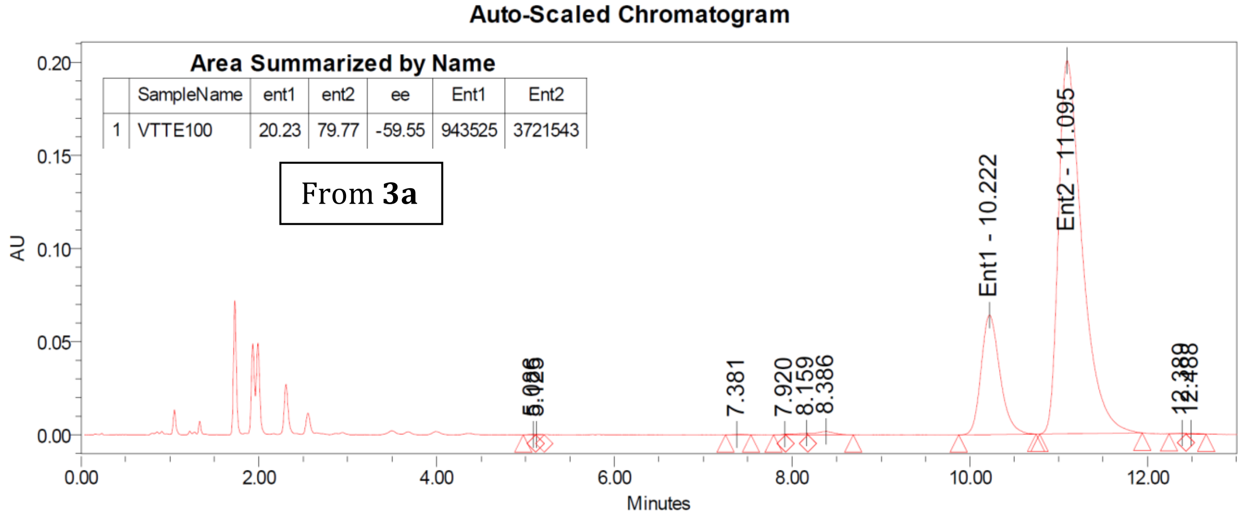
	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTD424	20.02	79.98	-59.96	192172	767634
2	VTTE027	8.98	91.02	-82.04	99959	1013304

(*S*)-4-(9H-carbazol-9-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (4d): The reaction was carried out according to the general procedure using **3a** (84.3 mg, 0.2 mmol) or **3b** (97.9 mg, 0.2 mmol), carbazole (66.9 mg, 0.4 mmol), 1-Adamantane carboxylic acid (18.0 mg, 0.1 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), and MeCN (0.2 mL). The reaction was run for 48 h, and the product was purified by preparative TLC (40% EtOAc in Hexanes) to afford **4d** (from **3a**: 54.3 mg, 52% yield, 60% ee; from **3b**: 50.0 mg 48% yield, 74% ee) as a yellow oil. Compound **4d** was analyzed



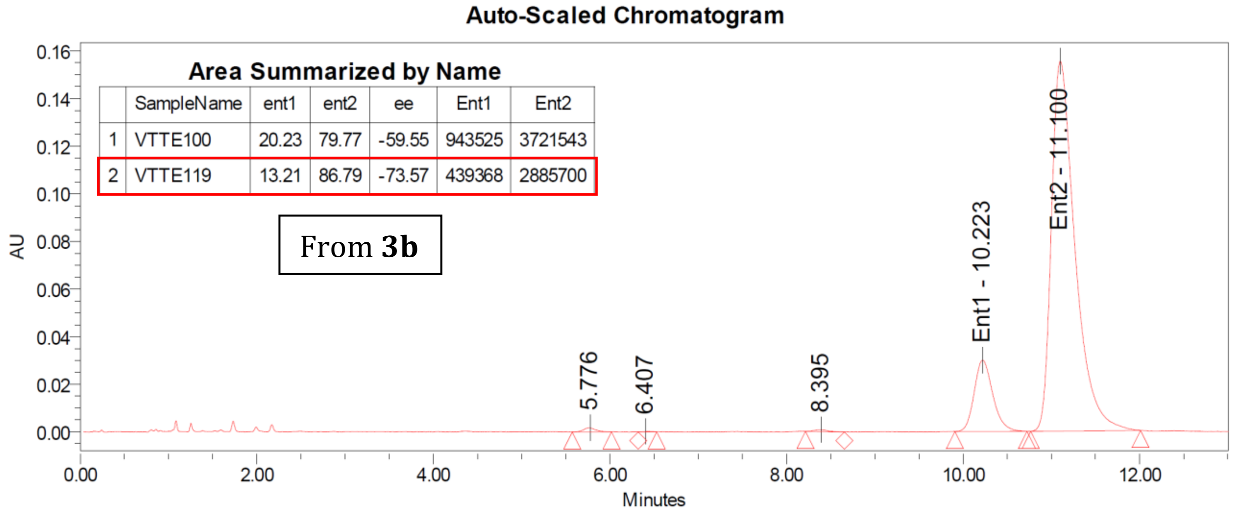
4d

by chiral SFC on a Daicel IB column (3 mm, 4.6 × 250 mm) under isocratic conditions [40% MeOH / CO_2 (4 mL/min), 1600 psi backpressure] at 30 °C. The enantiomers were detected by UV light (220 nm). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.21 (s, 1H), 8.69 (dd, *J* = 6.8, 2.3 Hz, 1H), 8.55 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.02 (dt, *J* = 7.7, 0.9 Hz, 2H), 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.53–7.47 (m, 2H), 7.45 (dt, *J* = 8.3, 0.9 Hz, 2H), 7.41 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 2H), 7.36 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.19 (ddd, *J* = 7.9, 7.0, 1.1 Hz, 2H), 5.21 (dd, *J* = 9.1, 6.3 Hz, 1H), 4.63 (ddd, *J* = 14.8, 9.0, 5.8 Hz, 1H), 4.52 (ddd, *J* = 15.0, 8.8, 6.4 Hz, 1H), 3.18–3.08 (m, 1H), 3.04 (ddt, *J* = 14.6, 8.8, 6.0 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.91, 166.30, 148.48, 140.23, 138.53, 136.36, 134.46, 133.79, 131.80, 127.93, 127.36, 125.97, 123.77, 123.15, 122.23, 121.76, 120.46, 119.25, 116.88, 108.84, 53.19, 40.86, 27.96. **HRMS** calcd. for $C_{33}H_{25}N_4O_3^+$ [M+H]$^+$: 525.19212, Found: 525.19256.



Area Summarized by Name

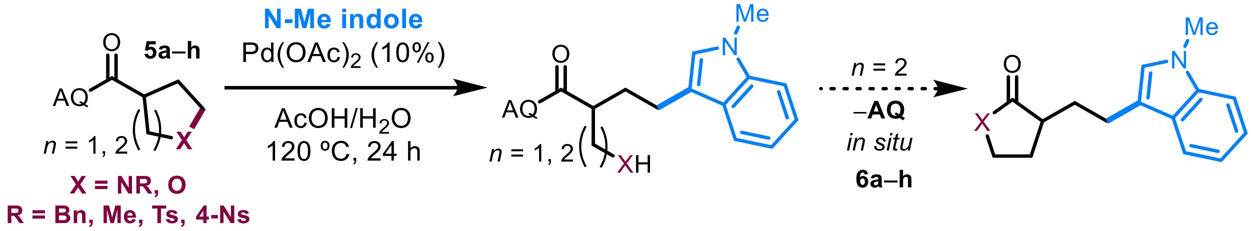
	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTE100	20.23	79.77	-59.55	943525	3721543



Area Summarized by Name

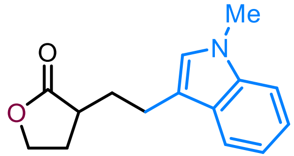
	SampleName	ent1	ent2	ee	Ent1	Ent2
1	VTTE100	20.23	79.77	-59.55	943525	3721543
2	VTTE119	13.21	86.79	-73.57	439368	2885700

General Procedure for Nucleophilic Opening of Unstrained Rings

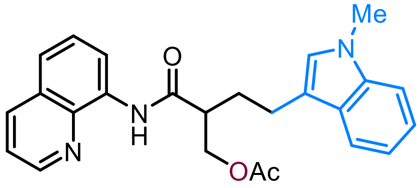


Unless otherwise stated, the procedure was as follows. To a 1-Dram (4 mL) vial equipped with a magnetic stir bar were added $Pd(OAc)_2$ (4.5 mg., 0.02 mmol), substrate (0.2 mmol), 1-Adamantanecarboxylic acid (18.0 mg, 0.1 mmol), 1-methylindole (52.5 mg., 0.4 mmol), and $AcOH/H_2O$ (1:1, 0.2 mL). The vial was sealed with a covered screw cap and placed in a heating block that was pre-heated to 120 °C. After heating for 24 h, the dark brown/black reaction was filtered through a plug of silica (100% EtOAc) and purified by preparative TLC.

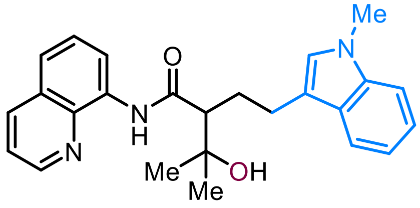
3-(2-(1-methyl-1H-indol-3-yl)ethyl)dihydrofuran-2(3H)-one (6a): The reaction was carried out according to a slightly modified procedure using **5a** (51.3 mg, 0.2 mmol), $CuSO_4•5H_2O$ (49.9 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), 1-methylindole (52.5 mg, 0.4 mmol), AcOH (0.1 mL), and water (0.1 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (30% EtOAc in Hexanes) to afford **6a** (41.9 mg, 86% yield) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.28 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.22 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.10 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.87 (s, 1H), 4.32 (td, *J* = 8.8, 2.9 Hz, 1H), 4.13 (td, *J* = 9.4, 6.8 Hz, 1H), 3.73 (s, 3H), 2.94 (dddd, *J* = 14.5, 8.5, 6.0, 0.9 Hz, 1H), 2.85 (dddd, *J* = 14.6, 8.2, 7.3, 0.8 Hz, 1H), 2.57 (dtd, *J* = 10.2, 8.9, 5.2 Hz, 1H), 2.38 (dddd, *J* = 12.6, 8.7, 6.8, 2.9 Hz, 1H), 2.31 (dddd, *J* = 13.8, 8.6, 7.3, 5.3 Hz, 1H), 1.96 (dtd, *J* = 12.6, 9.9, 8.5 Hz, 1H), 1.83 (dtd, *J* = 13.8, 8.6, 6.0 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 179.73, 137.15, 127.88, 126.48, 121.71, 118.93, 118.85, 113.50, 109.33, 66.58, 38.59, 32.72, 31.16, 28.93, 22.73. **HRMS** calcd. for $C_{15}H_{18}NO_2^+$ [M+H]$^+$: 244.13321, Found: 244.13317.

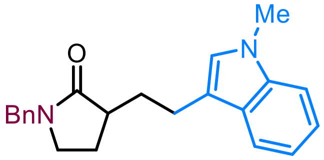

6a

4-(1-methyl-1H-indol-3-yl)-2-(quinolin-8-ylcarbamoyl)butyl acetate (6b): The reaction was carried out according to a slightly modified procedure using **5b** (48.5 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), 1-methylindole (52.5 mg, 0.4 mmol), and AcOH (0.1 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (40% EtOAc in Hexanes) to afford **6b** (62.7 mg, 75% yield) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.84 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.57–7.50 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.24 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.18 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.05 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.90 (s, 1H), 4.41–4.30 (m, 2H), 3.69 (s, 3H), 3.01–2.83 (m, 3H), 2.27 (dddd, *J* = 13.7, 9.4, 8.1, 5.7 Hz, 1H), 2.07–1.97 (m, 4H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.88, 170.93, 148.22, 138.52, 137.22, 136.48, 134.44, 128.06, 127.74, 127.53, 126.81, 121.80, 121.73, 121.64, 119.10, 118.78, 116.80, 113.55, 109.24, 65.45, 47.21, 32.66, 29.70, 22.82, 20.99. **HRMS** calcd. for $C_{25}H_{26}N_3O_3^+$ [M+H]$^+$: 416.19687, Found: 416.19693.

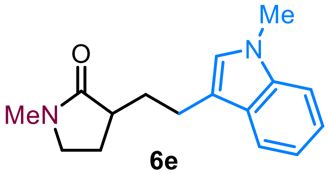

6b

3-hydroxy-3-methyl-2-(2-(1-methyl-1H-indol-3-yl)ethyl)-*N*-(quinolin-8-yl)butanamide (6c): The reaction was carried out according to a slightly modified procedure using **5c** (27.0 mg, 0.1 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), 1-methylindole (26.2 mg, 0.2 mmol), AcOH (0.05 mL), and water (0.05 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (40% EtOAc in Hexanes) to afford **6c** (15.9 mg, 40% yield) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.84 (dd, *J* = 6.9, 2.1 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.61–7.53 (m, 3H), 7.48 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.25–7.22 (m, 1H), 7.17 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.02 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.89 (s, 1H), 3.69 (s, 1H), 3.68 (s, 3H), 2.98 (dddd, *J* = 14.2, 8.0, 4.7, 1.1 Hz, 1H), 2.77 (dt, *J* = 14.7, 8.1 Hz, 1H), 2.47 (dd, *J* = 11.4, 2.8 Hz, 1H), 2.41 (tdd, *J* = 11.3, 7.5, 4.7 Hz, 1H), 2.25 (dtd, *J* = 13.5, 8.4, 2.8 Hz, 1H), 1.32 (s, 3H), 1.26 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.08, 148.39, 138.63, 137.28, 136.56, 134.07, 128.16, 127.85, 127.55, 126.91, 122.12, 121.80, 121.60, 119.26, 118.75, 117.09, 113.92, 109.20, 71.70, 57.10, 32.69, 29.85, 28.00, 27.18, 23.60. **HRMS** calcd. for $C_{25}H_{28}N_3O_2$+ [M+H]$^+$: 402.21760, Found: 402.21796.

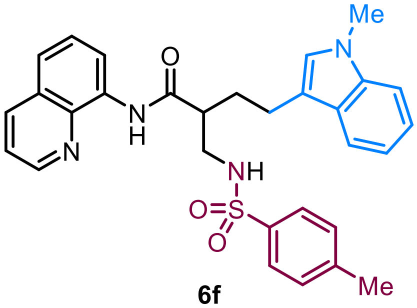

6c


6d

1-benzyl-3-(2-(1-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (6d): The reaction was carried out according to a slightly modified procedure using **5d** (69.1 mg, 0.2 mmol), CuSO$_4$•5H$_2$O (49.9 mg, 0.2 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), 1-methylindole (52.5 mg, 0.4 mmol), and AcOH (0.2 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (30% EtOAc in Hexanes) to afford **6d** (29.9 mg, 45% yield) as a yellow oil. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.60 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.35–7.29 (m, 2H), 7.29–7.25 (m, 2H), 7.24–7.19 (m, 3H), 7.09 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.89 (s, 1H), 4.46 (q, *J* = 14.7 Hz, 2H), 3.74 (s, 3H), 3.23–3.12 (m, 2H), 2.91 (dddd, *J* = 14.8, 9.4, 5.6, 0.9 Hz, 1H), 2.83 (dddd, *J* = 14.7, 8.9, 7.1, 0.9 Hz, 1H), 2.55 (qd, *J* = 8.8, 4.0 Hz, 1H), 2.34 (dddd, *J* = 13.9, 9.4, 7.1, 4.6 Hz, 1H), 2.20 (dddd, *J* = 12.5, 8.8, 7.6, 3.5 Hz, 1H), 1.82–1.75 (m, 1H), 1.72 (dtd, *J* = 12.7, 8.8, 7.9 Hz, 1H). **^{13}C NMR** (150 MHz, CDCl$_3$) δ 176.95, 137.12, 136.81, 128.78, 128.22, 128.06, 127.61, 126.39, 121.58, 119.08, 118.71, 114.37, 109.24, 46.84, 45.02, 41.55, 32.72, 32.21, 25.13, 22.68. **HRMS** calcd. for C$_{22}$H$_{25}$N$_2$O$^+$ [M+H]$^+$: 333.19614, Found: 333.19607.

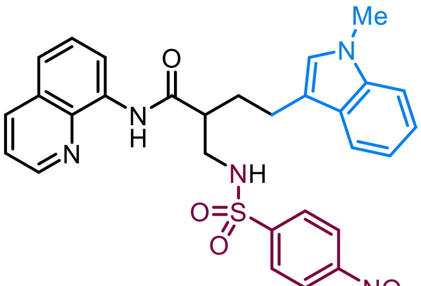

6e

1-methyl-3-(2-(1-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (6e): The reaction was carried out according to a slightly modified procedure using **5e** (53.9 mg, 0.2 mmol), CuSO$_4$•5H$_2$O (49.9 mg, 0.2 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), 1-methylindole (52.5 mg, 0.4 mmol), and AcOH (0.2 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (30% EtOAc in Hexanes) to afford **6e** (11.3 mg, 22% yield) as a yellow oil. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.60 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.20 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.09 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.88 (s, 1H), 3.73 (s, 3H), 3.34–3.24 (m, 2H), 2.93–2.78 (m, 5H), 2.47 (qd, *J* = 8.9, 4.5 Hz, 1H), 2.34–2.18 (m, 2H), 1.80–1.69 (m, 2H). **^{13}C NMR** (150 MHz, CDCl$_3$) δ 176.98, 137.12, 128.08, 126.37, 121.56, 119.08, 118.68, 114.44, 109.22, 47.81, 41.33, 32.71, 32.23, 29.85, 25.17, 22.70. **HRMS** calcd. for C$_{16}$H$_{21}$N$_2$O+ [M+H]$^+$: 257.16484, Found: 257.16474.


6f

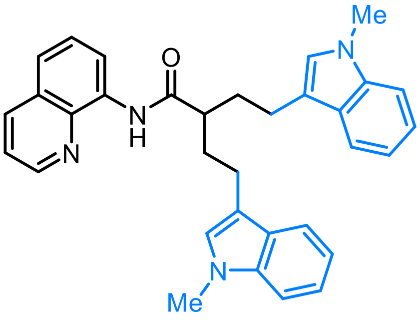
4-(1-methyl-1H-indol-3-yl)-2-(((4-methylphenyl)sulfonamido)methyl)-*N*-(quinolin-8-yl)butanamide (6f): The reaction was carried out according to the general procedure using **5f** (79.1 mg, 0.2 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), 1-methylindole (52.5 mg, 0.4 mmol), AcOH (0.1 mL), and water (0.1 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (50% EtOAc in Hexanes) to afford **6f** (58.6 mg, 56% yield) of as a yellow oil. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 9.74 (s, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.65 (dd, *J* = 5.4, 3.5 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.71–7.65 (m, 2H), 7.56 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.54–7.50 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.25 (s, 1H), 7.20 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.06 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 6.91 (s, 1H), 5.35 (t, *J* = 6.5 Hz, 1H), 3.71 (s, 3H), 3.28 (ddd, *J* = 12.9, 8.2, 6.2 Hz, 1H), 3.22 (ddd, *J* = 13.0, 6.7, 4.1 Hz, 1H), 2.93–2.82 (m, 2H), 2.78 (tdd, *J* = 8.1, 6.0, 4.2 Hz, 1H), 2.30 (s, 3H), 2.23–2.15 (m, 1H), 2.07–1.97 (m, 1H). **^{13}C NMR** (150 MHz, CDCl$_3$) δ 172.92, 148.42, 143.36, 138.52, 137.29, 137.14, 136.49, 134.04, 129.80, 128.06, 127.72, 127.37, 127.10, 126.85, 122.18, 121.84, 121.72, 119.12, 118.87, 117.00, 113.29, 109.30, 47.06, 44.78, 32.73, 30.90, 22.73, 21.56. **HRMS** calcd. for C$_{30}$H$_{31}$N$_4$O$_3$S$^+$ [M+H]$^+$: 527.21114, Found: 527.21113.

4-(1-methyl-1H-indol-3-yl)-2-(((4-nitrophenyl)sulfonamido)methyl)-*N*-(quinolin-8-yl)butanamide (6g): The reaction was carried out according to a slightly modified procedure using **5g** (85.3 mg, 0.2 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), 1-methylindole (52.5 mg, 0.4 mmol), AcOH (6.0 mg, 0.1 mmol), and HFIP (0.2 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (50% EtOAc in Hexanes) to afford **6g** (46.8 mg, 42% yield) as a yellow oil. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 9.58 (s, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.59 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 8.03–7.96 (m, 2H), 7.87–7.81 (m, 2H), 7.55 (dt, *J* = 8.0, 0.9 Hz, 1H), 7.54–7.46 (m, 3H), 7.29 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.24 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.08 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 6.89 (s, 1H), 5.71 (t, *J* = 6.3 Hz, 1H), 3.72 (s, 3H), 3.41 (ddd, *J* = 13.3, 8.5, 6.3 Hz, 1H), 3.31 (ddd, *J* = 13.3, 6.3, 3.9 Hz, 1H), 2.90 (dt, *J* = 14.3, 7.0 Hz, 1H), 2.83 (dt, *J* = 14.9, 7.5 Hz, 1H), 2.64 (tdd, *J* = 8.3, 6.0, 3.9 Hz, 1H), 2.24–2.13 (m, 1H), 2.04–1.94 (m, 1H). **^{13}C NMR** (150 MHz, CDCl$_3$) δ 172.58, 149.70, 148.50, 146.36, 138.28, 137.33, 136.64, 133.69, 128.13, 128.06, 127.63, 127.30, 126.98, 124.28, 122.47, 121.99, 121.91, 119.06, 119.05, 116.91, 112.84, 109.46, 46.64, 44.94, 32.73, 30.74, 22.71. **HRMS** calcd. for $C_{29}H_{28}N_5O_5S^+$ [M+H]$^+$: 558.18057, Found: 558.18035.



6g

4-(1-methyl-1H-indol-3-yl)-2-(2-(1-methyl-1H-indol-3-yl)ethyl)-*N*-(quinolin-8-yl)butanamide (6h): The reaction was carried out according to the general procedure using **5h** (81.9 mg, 0.2 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol), 1-methylindole (78.7 mg, 0.6 mmol), AcOH (0.1 mL), and water (0.1 mL). The reaction was run for 24 h, and the product was purified by preparative TLC (30% EtOAc in Hexanes) to afford **6h** (49.4 mg, 49% yield) as a yellow oil. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 9.84 (s, 1H), 8.90 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.78 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62–7.55 (m, 3H), 7.52 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.23 (dt, *J* = 8.1, 0.9 Hz, 2H), 7.17 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 2H), 7.03 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 2H), 6.80 (s, 2H), 3.66 (s, 6H), 2.89 (ddd, *J* = 14.5, 8.7, 5.7 Hz, 2H), 2.80 (dt, *J* = 15.0, 7.9 Hz, 2H), 2.62 (tt, *J* = 9.5, 4.9 Hz, 1H), 2.26 (dtd, *J* = 14.5, 8.9, 5.6 Hz, 2H), 2.07–1.98 (m, 2H). **^{13}C NMR** (150 MHz, CDCl$_3$) δ 174.85, 148.17, 138.62, 137.20, 136.50, 134.67, 128.14, 127.92, 127.67, 126.69, 121.68, 121.52, 119.27, 118.67, 116.71, 114.36, 109.16, 48.07, 33.83, 32.64, 23.18. **HRMS** calcd. for $C_{33}H_{33}N_4O^+$ [M+H]$^+$: 501.26489, Found: 501.26490.



6h

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For prior examples of β-elimination see:

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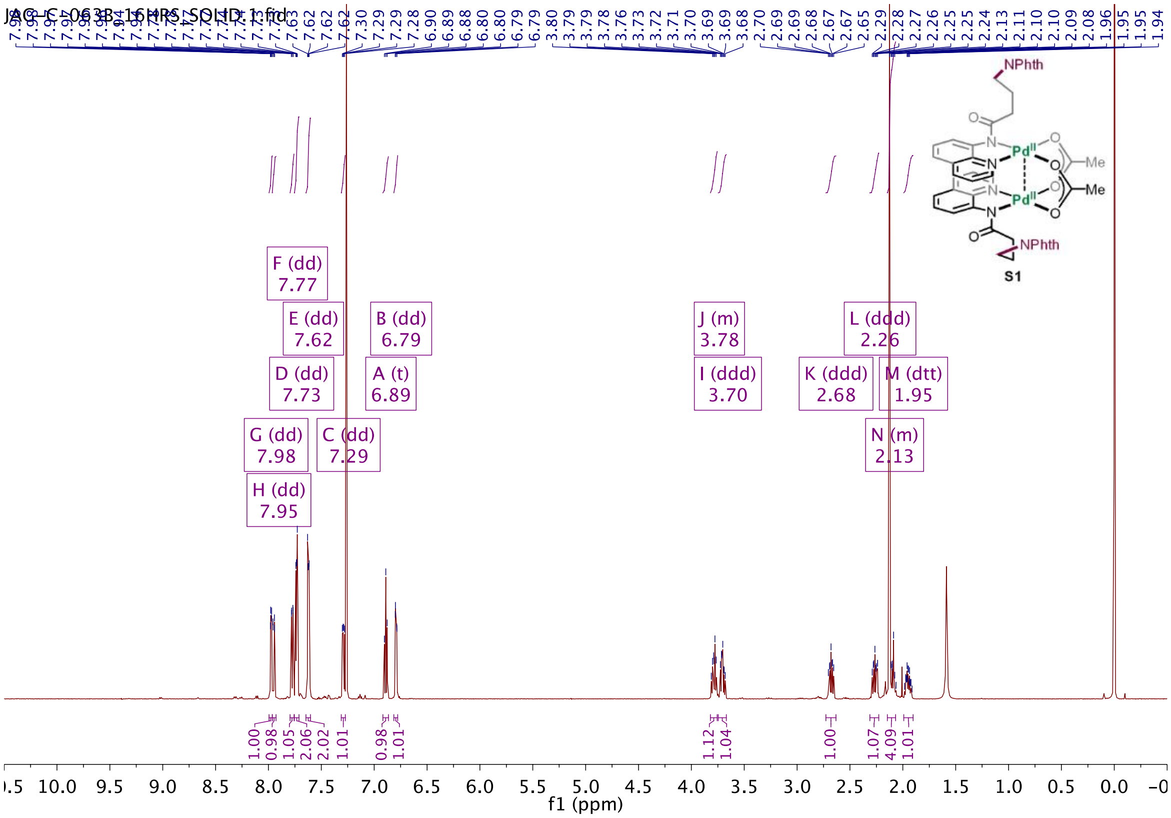
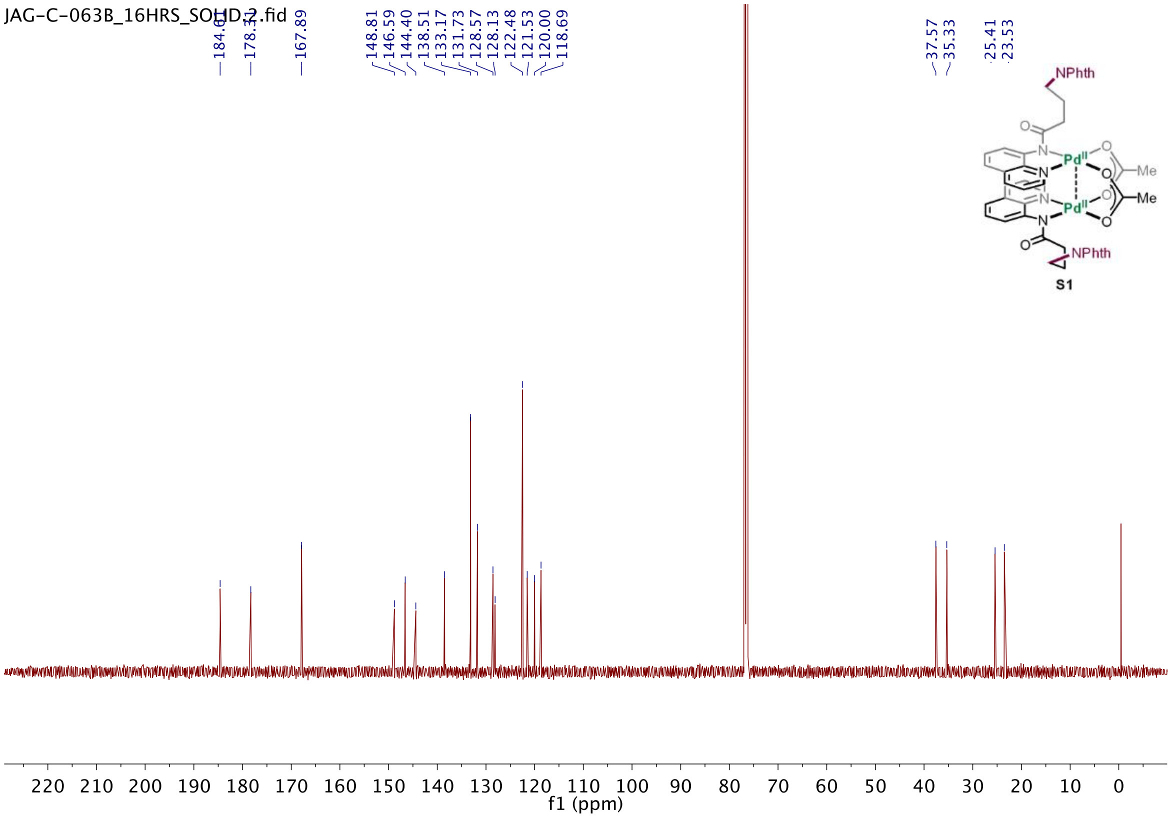
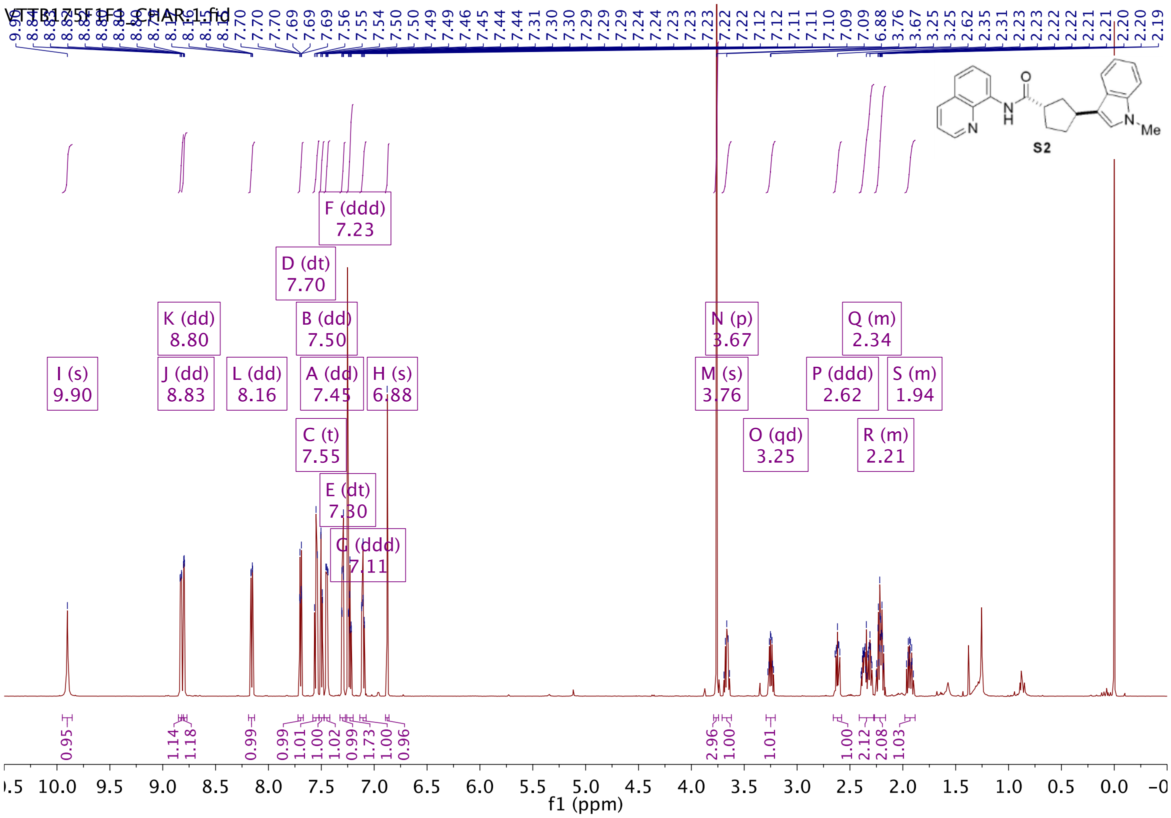
Selected ¹H and ¹³C NMR Spectra



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7.70
7.70
7.69
7.69
7.69
7.56
7.55
7.54
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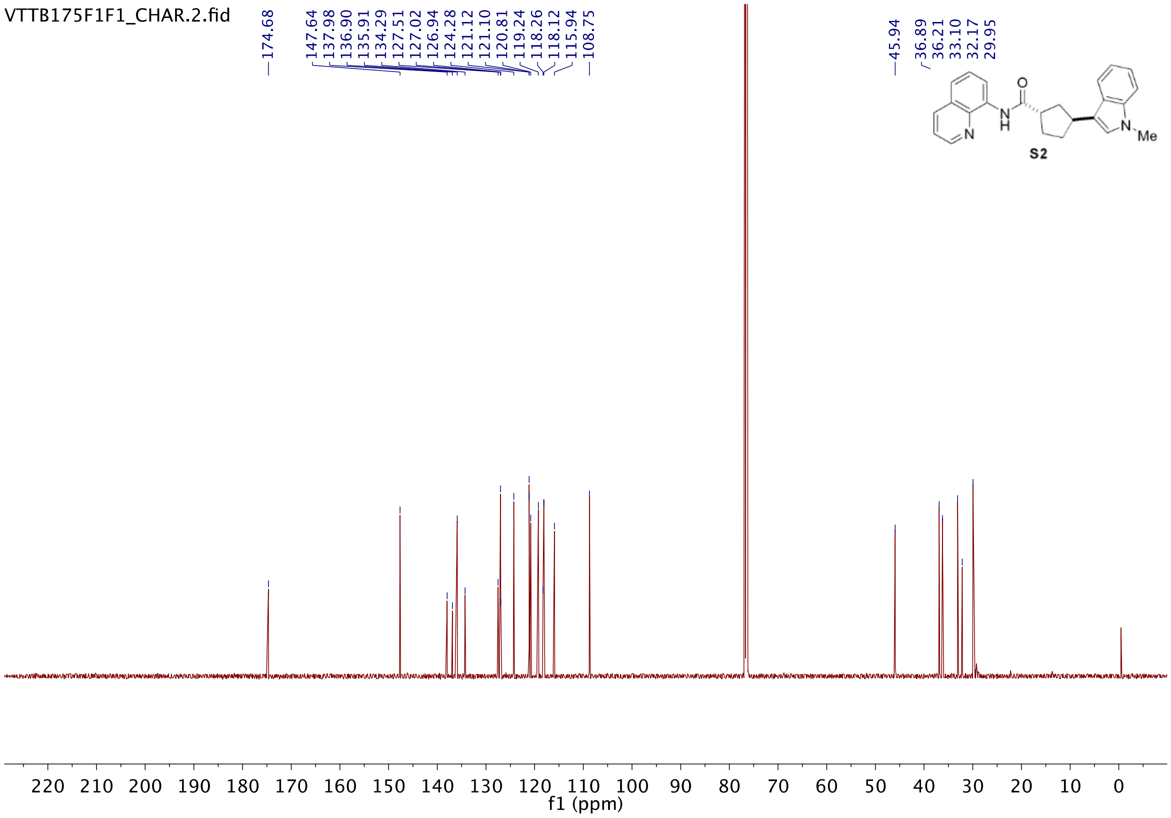
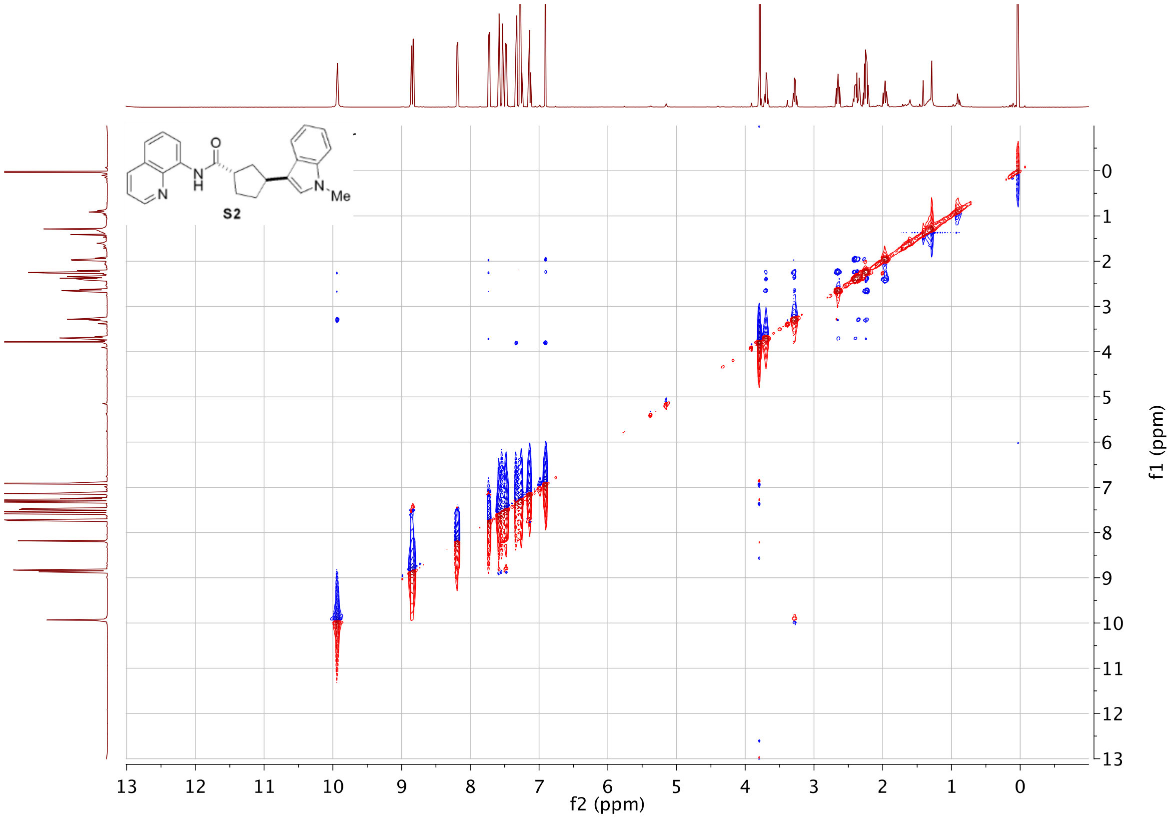
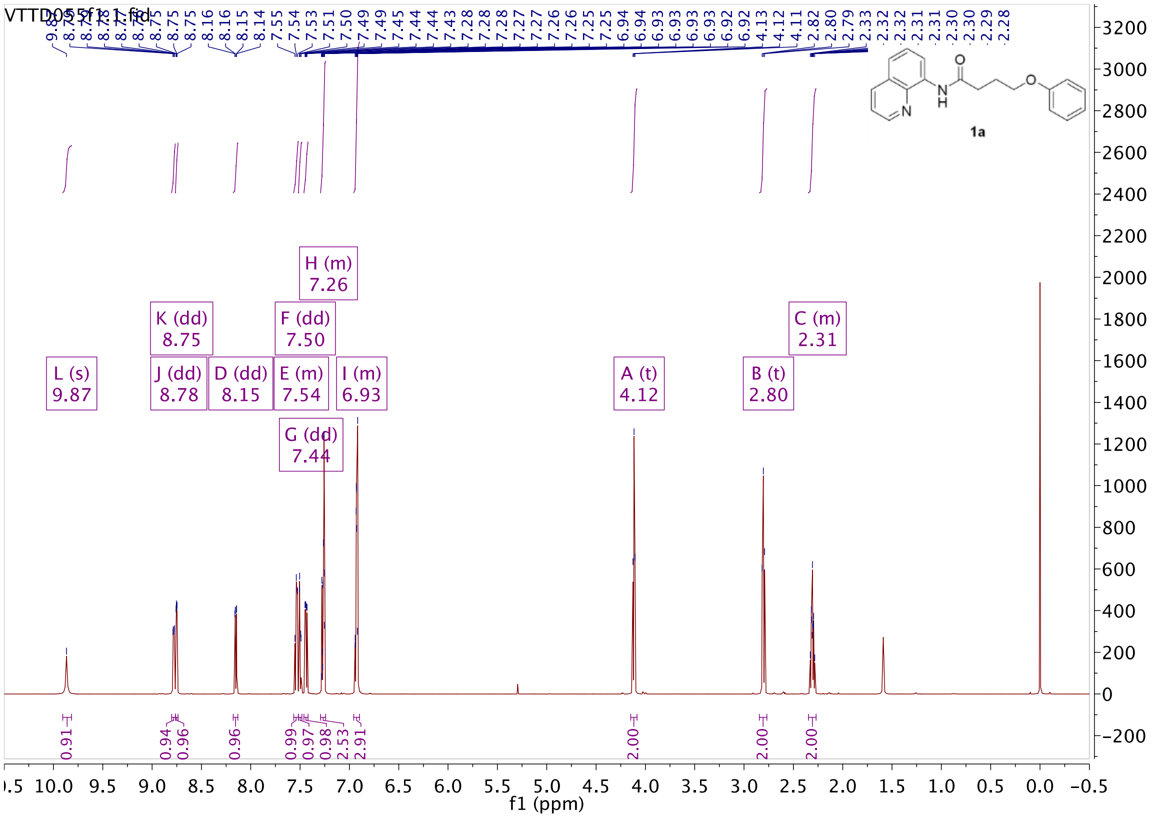
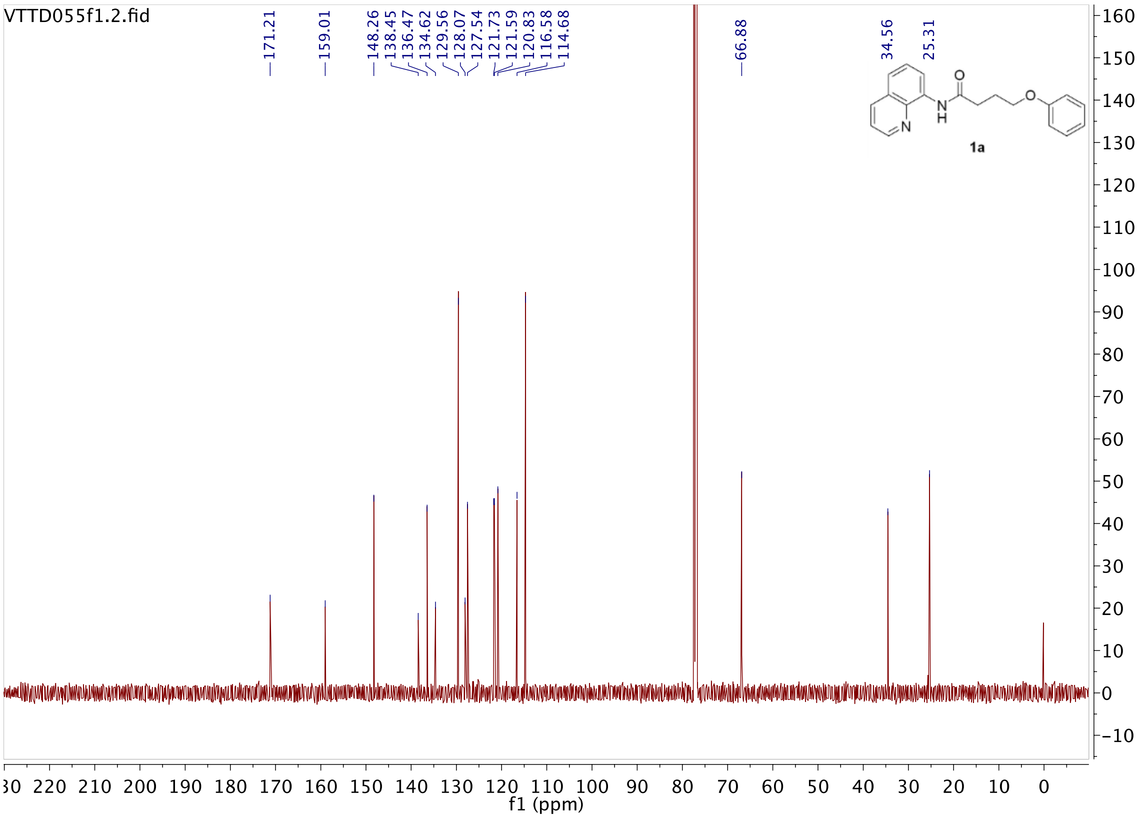
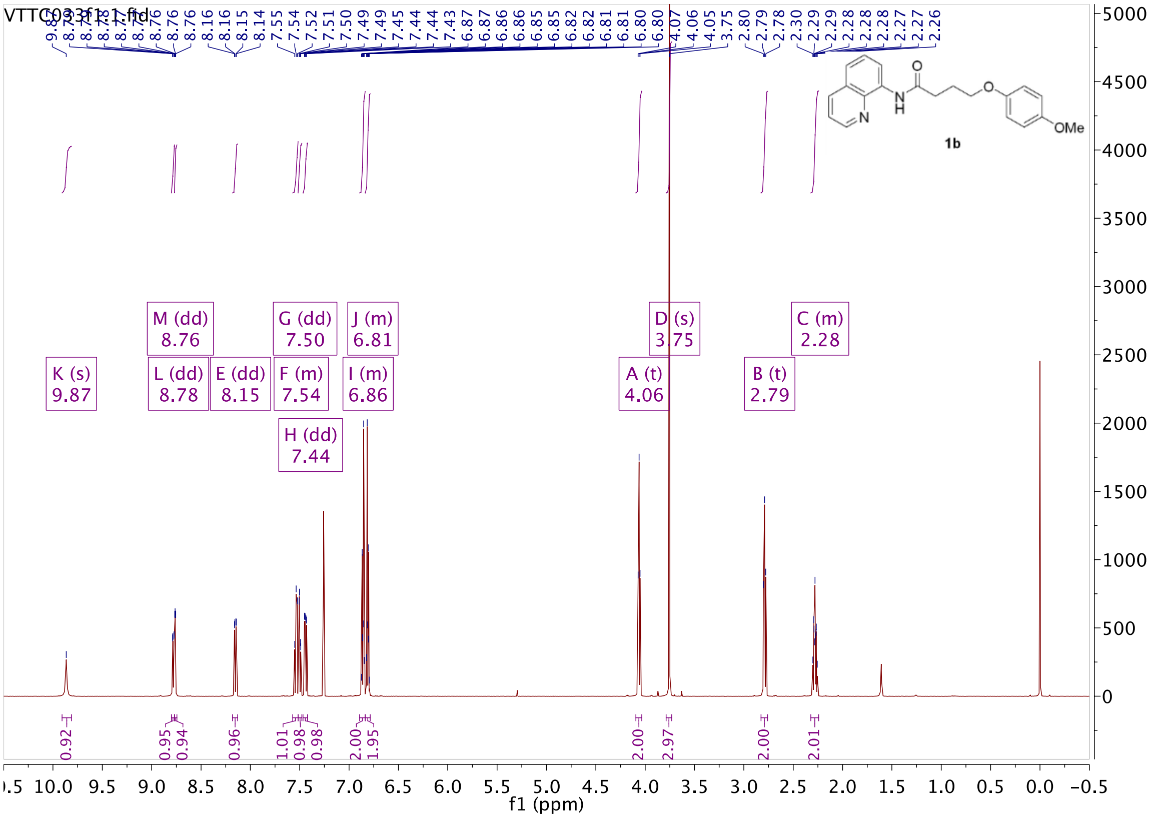
7.50
7.49
7.49
7.46
7.45
7.44
7.44
7.31
7.30
7.29
7.29
7.29
7.24
7.24
7.23
7.23
7.23
7.22
7.22
7.12
7.11
7.11
7.10
7.09
7.09
6.88
3.76
3.67
3.25
3.25
2.62
2.35
2.31
2.23
2.23
2.22
2.22
2.22
2.21
2.21
2.20
2.20
2.19
S2
N
N
H
O
N
Me
F (ddd)
7.23
D (dt)
7.70
K (dd)
8.80
B (dd)
7.50
N (p)
3.67
Q (m)
2.34
I (s)
9.90
J (dd)
8.83
L (dd)
8.16
A (dd)
7.45
H (s)
6.88
M (s)
3.76
P (ddd)
2.62
S (m)
1.94
C (t)
7.55
O (qd)
3.25
R (m)
2.21
E (dt)
7.30
G (ddd)
7.11
0.95
1.14
1.18
0.99
0.99
1.01
1.00
1.02
0.99
1.73
1.00
0.96
2.96
1.00
1.01
1.00
2.12
2.08
1.03
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)

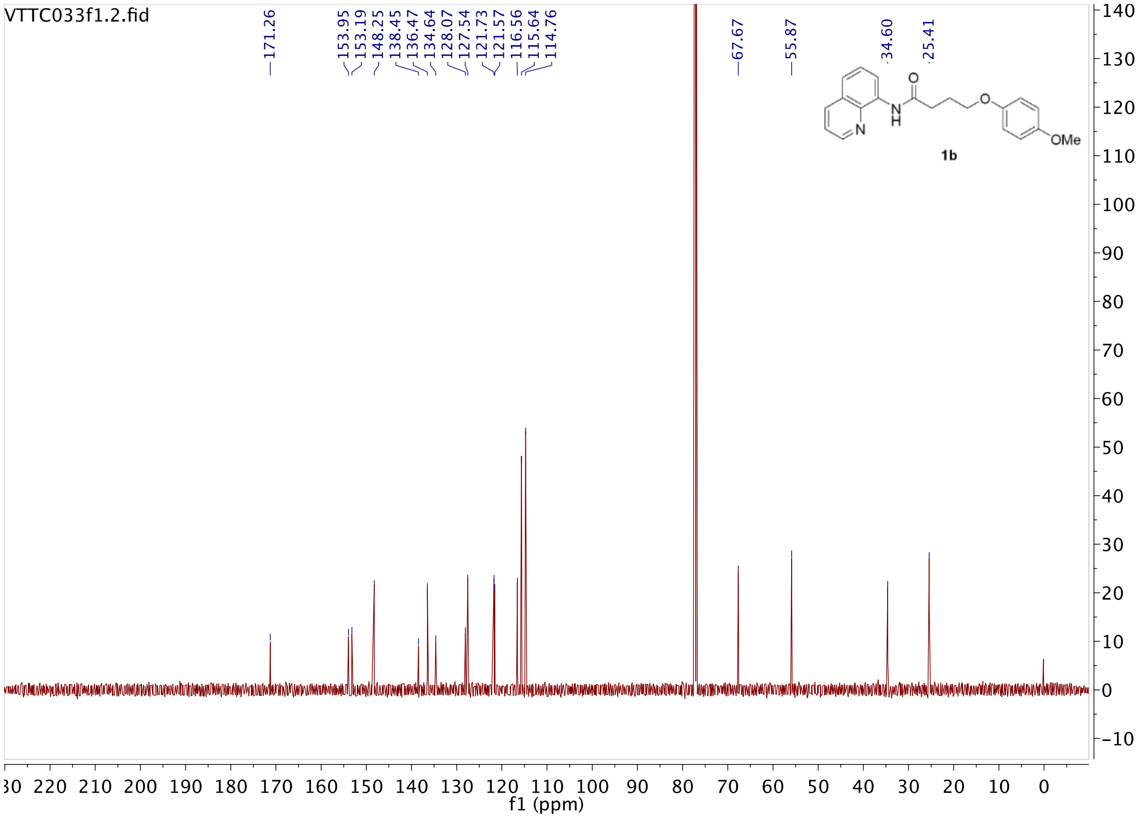

VTTB175F1F1_CHAR.2.fid
174.68
147.64
137.98
136.90
135.91
134.29
127.51
127.02
126.94
124.28
121.12
121.10
120.81
119.24
118.26
118.12
115.94
108.75
45.94
36.89
36.21
33.10
32.17
29.95
S2
N
N
H
O
N
Me
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

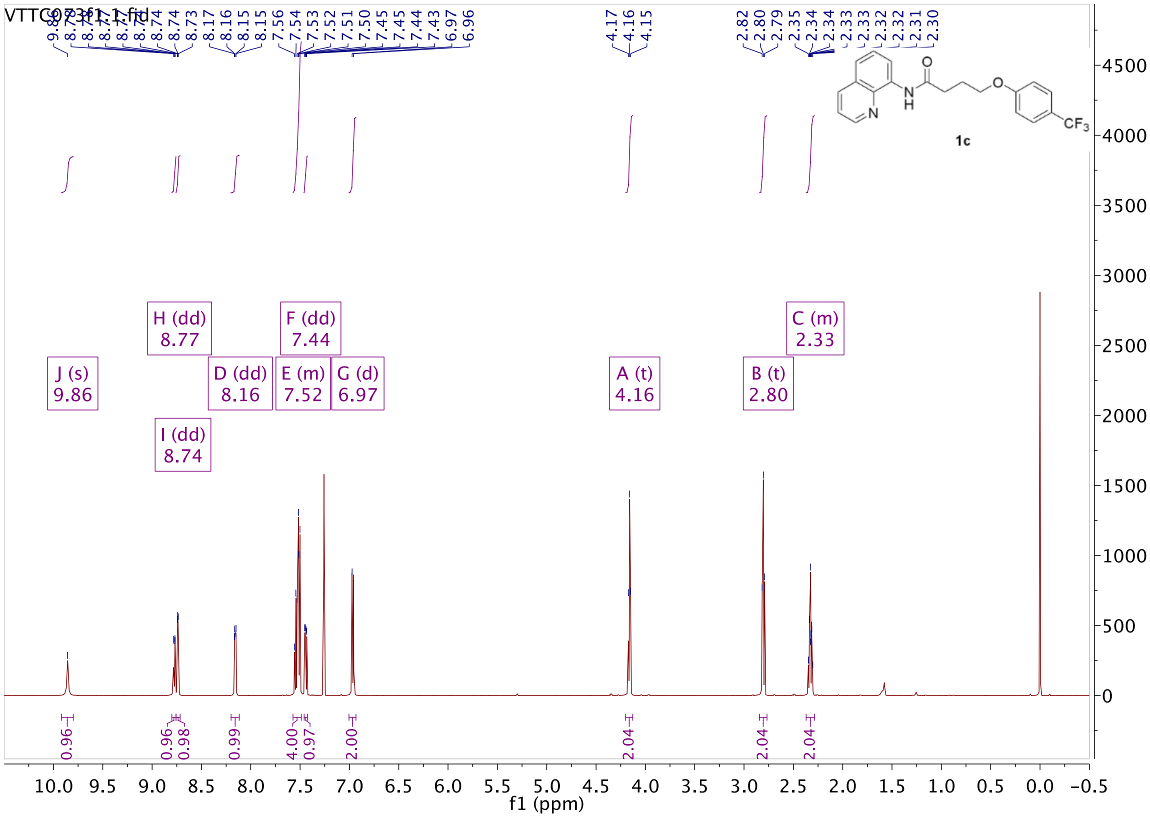

S2
N
H
O
N
Me
f2 (ppm)
f1 (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
0

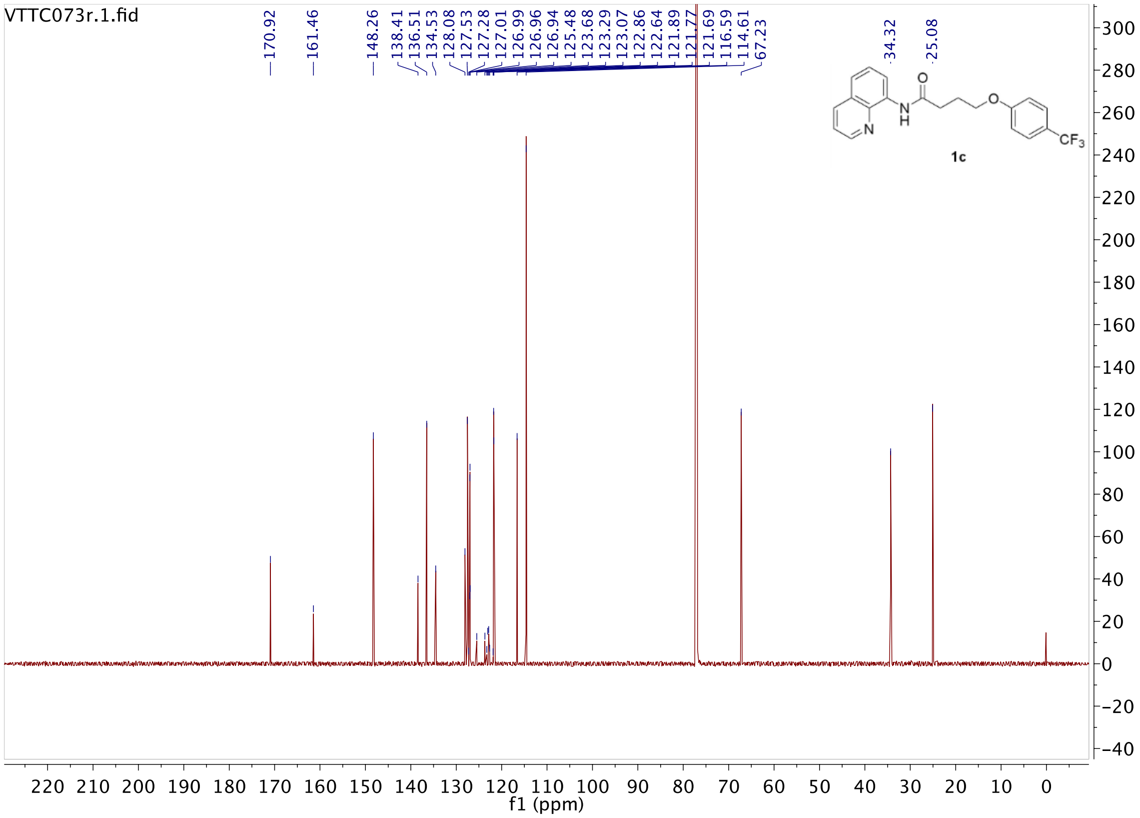

VTTD055f1.1.fid
8.16
8.16
8.15
8.14
7.55
7.54
7.53
7.51
7.50
7.49
7.49
7.45
7.44
7.44
7.43
7.28
7.28
7.27
7.26
7.25
7.25
6.94
6.94
6.93
6.93
6.93
6.93
6.92
4.13
4.12
4.11
2.82
2.80
2.79
2.33
2.32
2.32
2.31
2.31
2.30
2.30
2.29
2.28
1a
N
N
H
O
O
H (m)
7.26
K (dd)
8.75
F (dd)
7.50
C (m)
2.31
L (s)
9.87
J (dd)
8.78
D (dd)
8.15
E (m)
7.54
I (m)
6.93
A (t)
4.12
B (t)
2.80
G (dd)
7.44
0.91
0.94
0.96
0.96
0.99
0.97
0.98
2.53
2.91
2.00
2.00
2.00
f1 (ppm)
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200

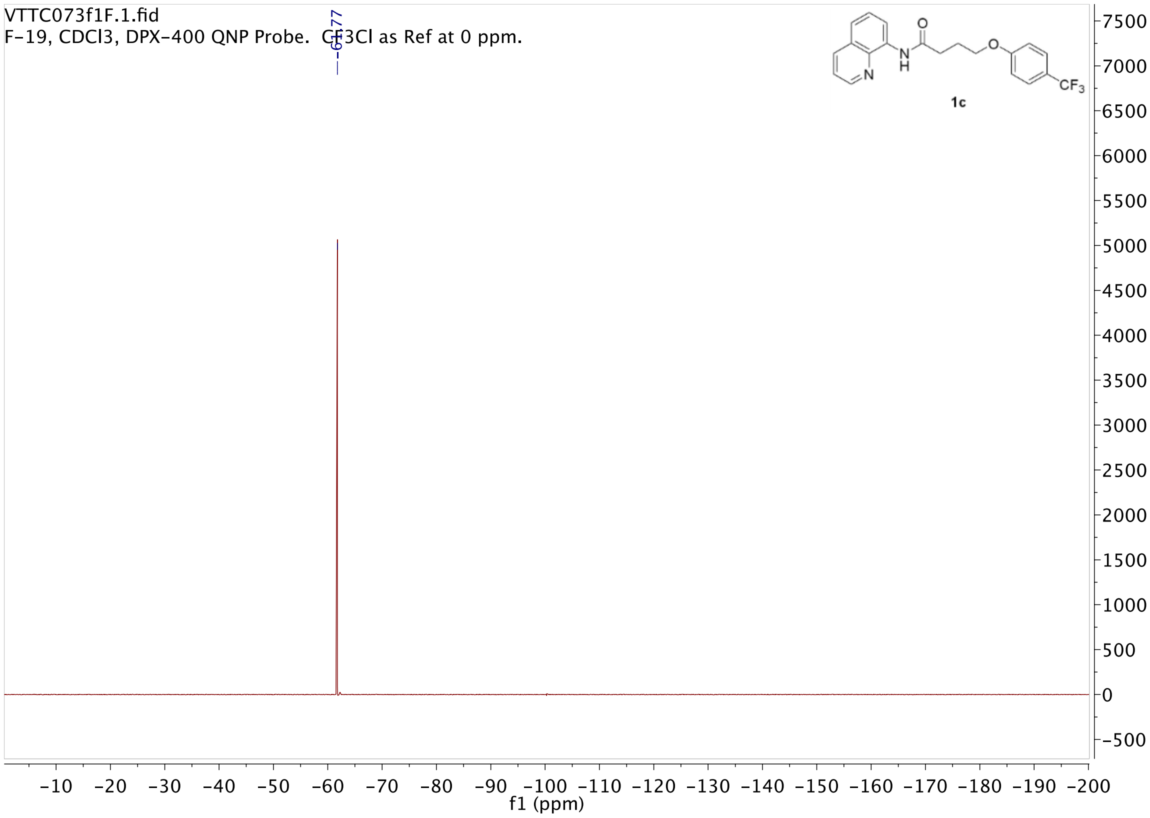

VTTD055f1.2.fid
171.21
159.01
148.26
138.45
136.47
134.62
129.56
128.07
127.54
121.73
121.59
120.83
116.58
114.68
66.88
34.56
25.31
1a
f1 (ppm)

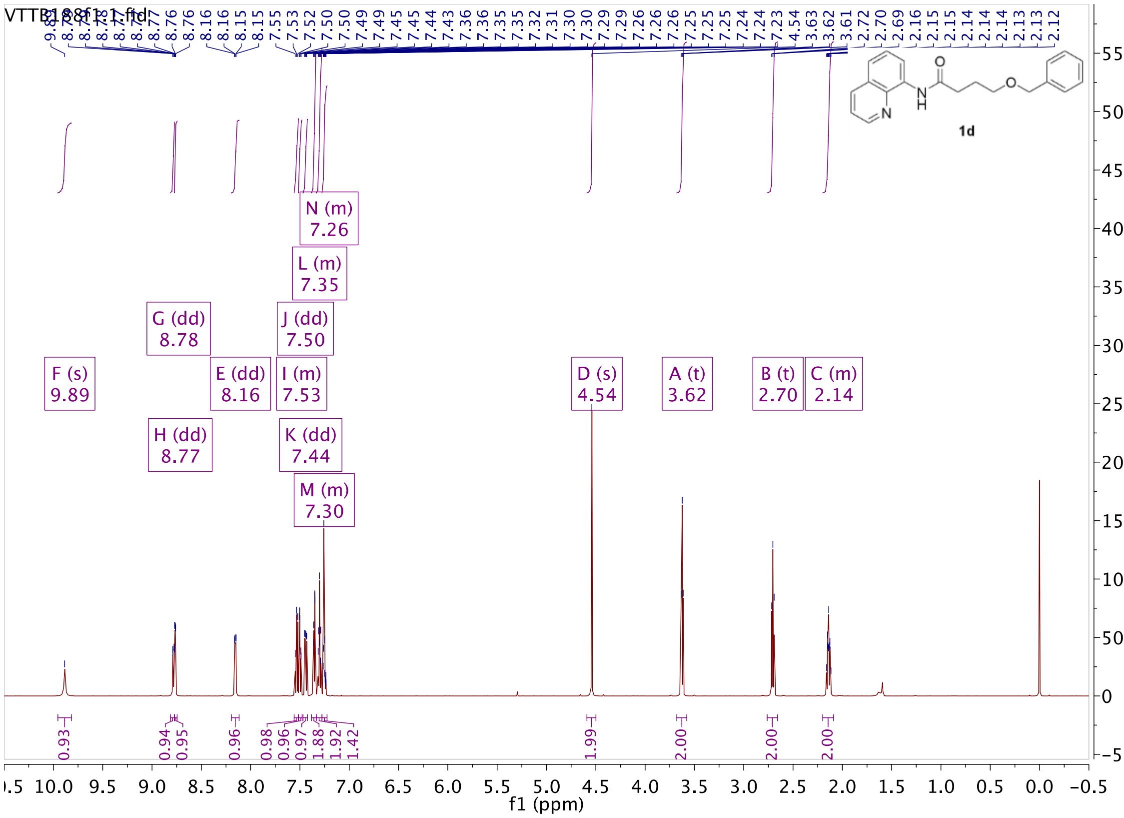

VTTC033f1.1.fid
K (s) 9.87
M (dd) 8.76
L (dd) 8.78
E (dd) 8.15
G (dd) 7.50
F (m) 7.54
H (dd) 7.44
J (m) 6.81
I (m) 6.86
A (t) 4.06
D (s) 3.75
B (t) 2.79
C (m) 2.28
1b
OMe
0.92
0.95
0.94
0.96
1.01
0.98
0.98
2.00
1.95
2.00
2.97
2.00
2.01
f1 (ppm)

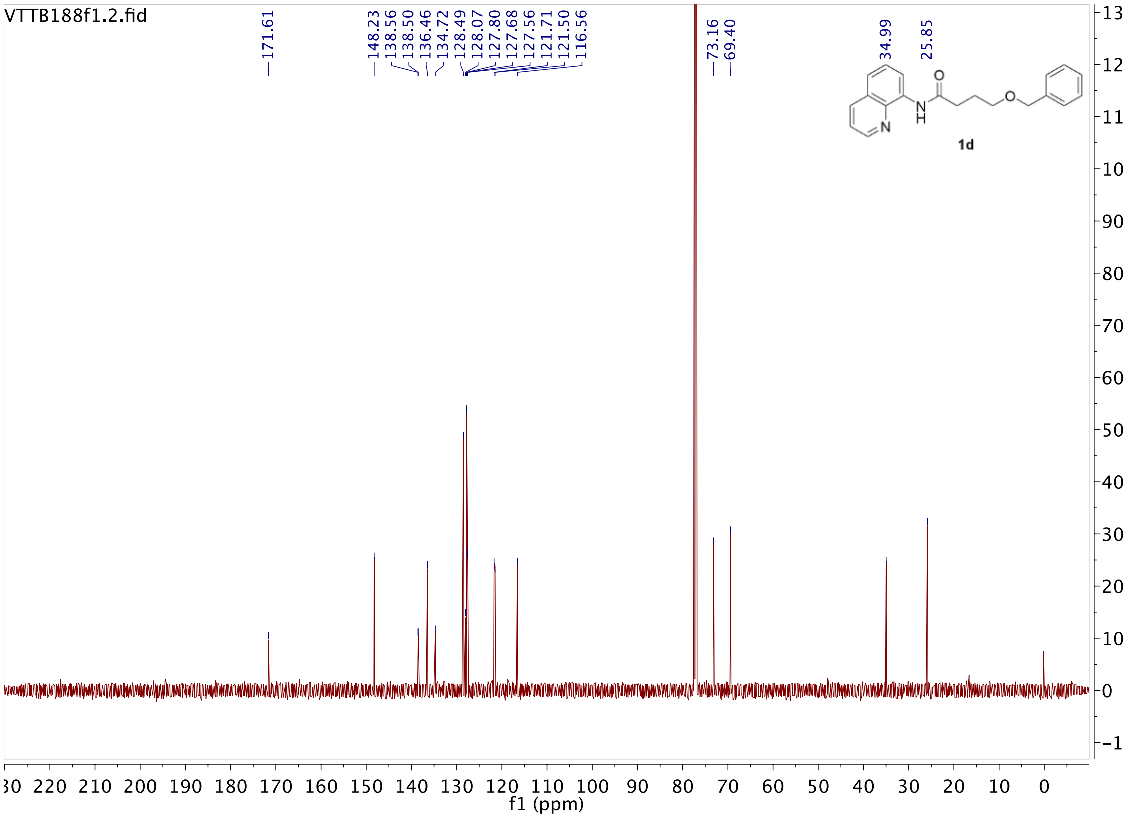

VTTC033f1.2.fid
171.26
153.95
153.19
148.25
138.45
136.47
134.64
128.07
127.54
121.73
121.57
116.56
115.64
114.76
67.67
55.87
34.60
25.41
OMe
O
N
H
1b
f1 (ppm)
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10


VTTC073f1.1.fid
9.86
8.78
8.77
8.77
8.76
8.74
8.74
8.73
8.17
8.16
8.15
8.15
7.56
7.54
7.53
7.52
7.51
7.50
7.45
7.45
7.44
7.43
6.97
6.96
4.17
4.16
4.15
2.82
2.80
2.79
2.35
2.34
2.34
2.33
2.33
2.32
2.32
2.31
2.30
CF3
O
N
H
1c
J (s) 9.86
H (dd) 8.77
I (dd) 8.74
D (dd) 8.16
F (dd) 7.44
E (m) 7.52
G (d) 6.97
A (t) 4.16
B (t) 2.80
C (m) 2.33
0.96
0.96
0.98
0.99
4.00
0.97
2.00
2.04
2.04
2.04
f1 (ppm)
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
4500 4000 3500 3000 2500 2000 1500 1000 500 0


VTTC073r.1.fid
170.92
161.46
148.26
138.41
136.51
134.53
128.08
127.53
127.28
127.01
126.99
126.96
126.94
125.48
123.68
123.29
123.07
122.86
122.64
121.89
121.77
121.69
116.59
114.61
67.23
34.32
25.08
O
N
H
N
O
CF3
1c
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


VTTC073f1F.1.fid
F-19, CDCl3, DPX-400 QNP Probe. CFl3Cl as Ref at 0 ppm.
-61.77
O
N
H
N
O
CF3
1c
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


VTTB188f1.1.fid
8.76
8.76
8.16
8.16
8.15
8.15
7.55
7.53
7.52
7.50
7.50
7.49
7.45
7.45
7.44
7.43
7.36
7.36
7.35
7.35
7.32
7.31
7.30
7.30
7.29
7.29
7.26
7.26
7.25
7.25
7.25
7.24
7.24
7.23
4.54
3.63
3.62
3.61
2.72
2.70
2.69
2.16
2.15
2.15
2.14
2.14
2.14
2.13
2.13
2.12
1d
N (m) 7.26
L (m) 7.35
G (dd) 8.78
J (dd) 7.50
F (s) 9.89
E (dd) 8.16
I (m) 7.53
D (s) 4.54
A (t) 3.62
B (t) 2.70
C (m) 2.14
H (dd) 8.77
K (dd) 7.44
M (m) 7.30
0.93
0.94
0.95
0.96
0.98
0.96
0.97
1.88
1.92
1.42
1.99
2.00
2.00
2.00
f1 (ppm)


VTTB188f1.2.fid
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148.23
138.56
138.50
136.46
134.72
128.49
128.07
127.80
127.68
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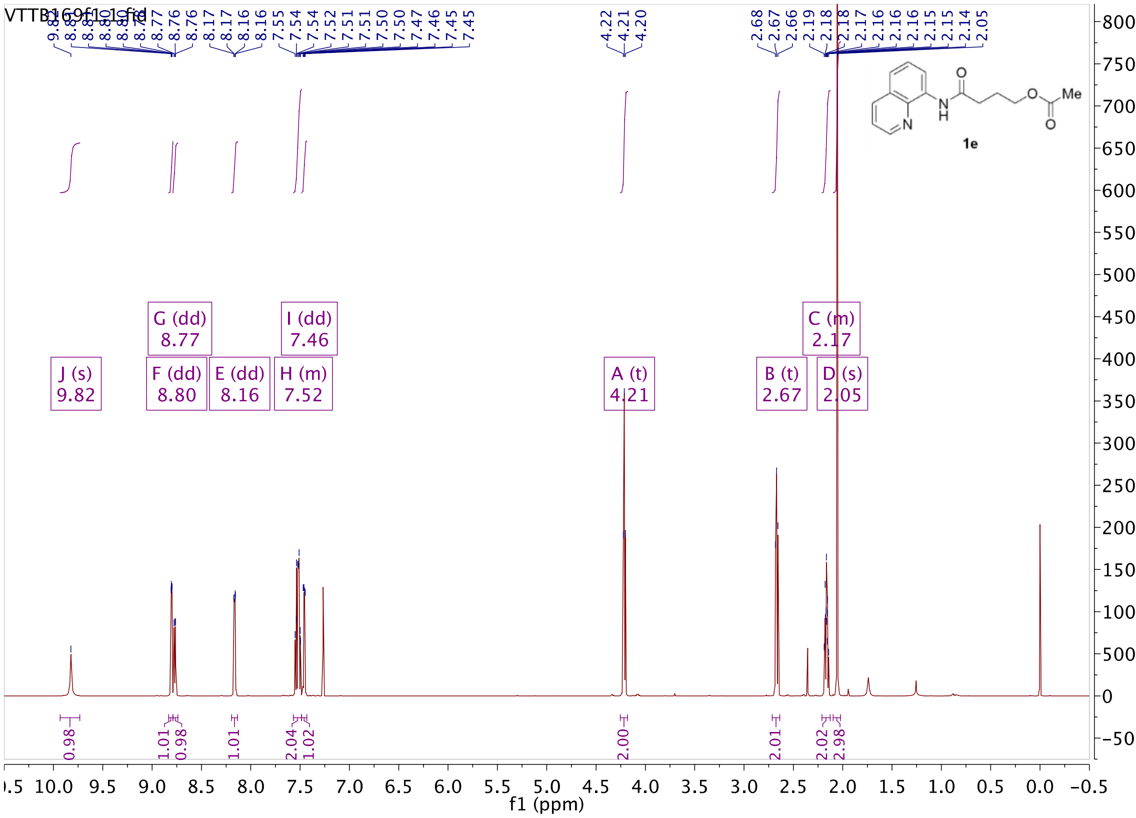
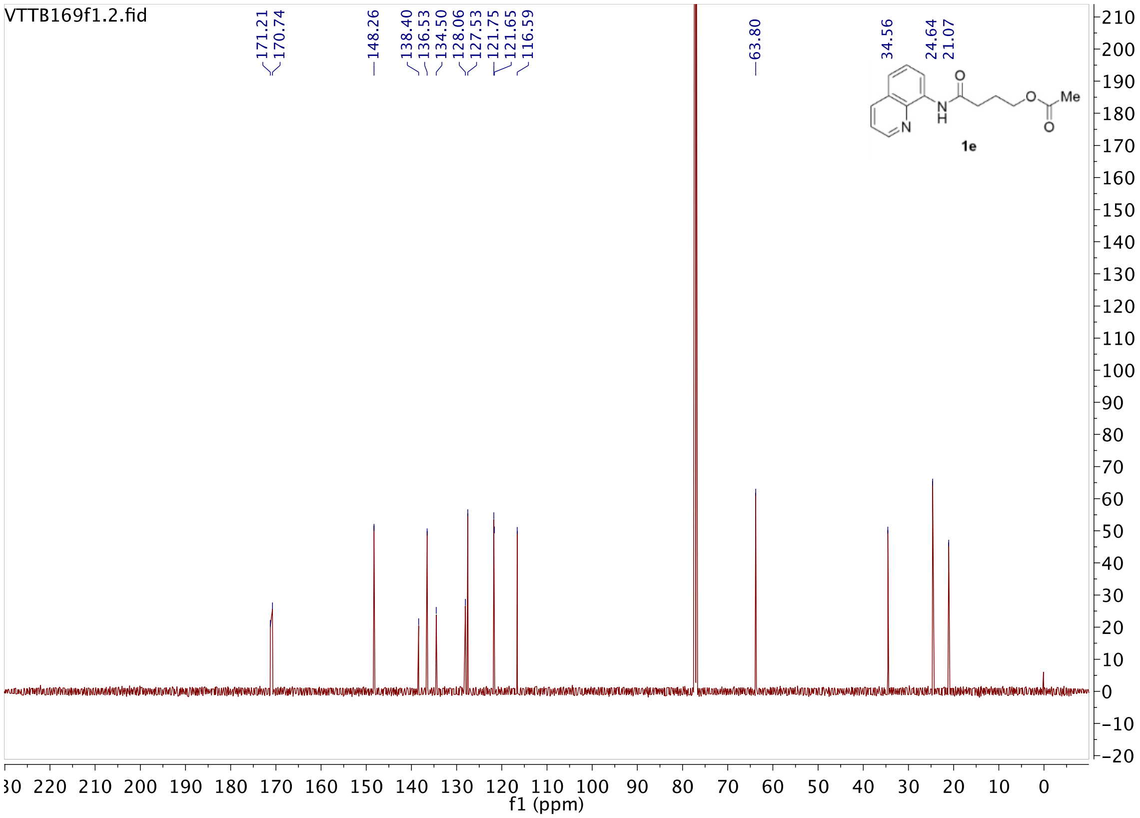
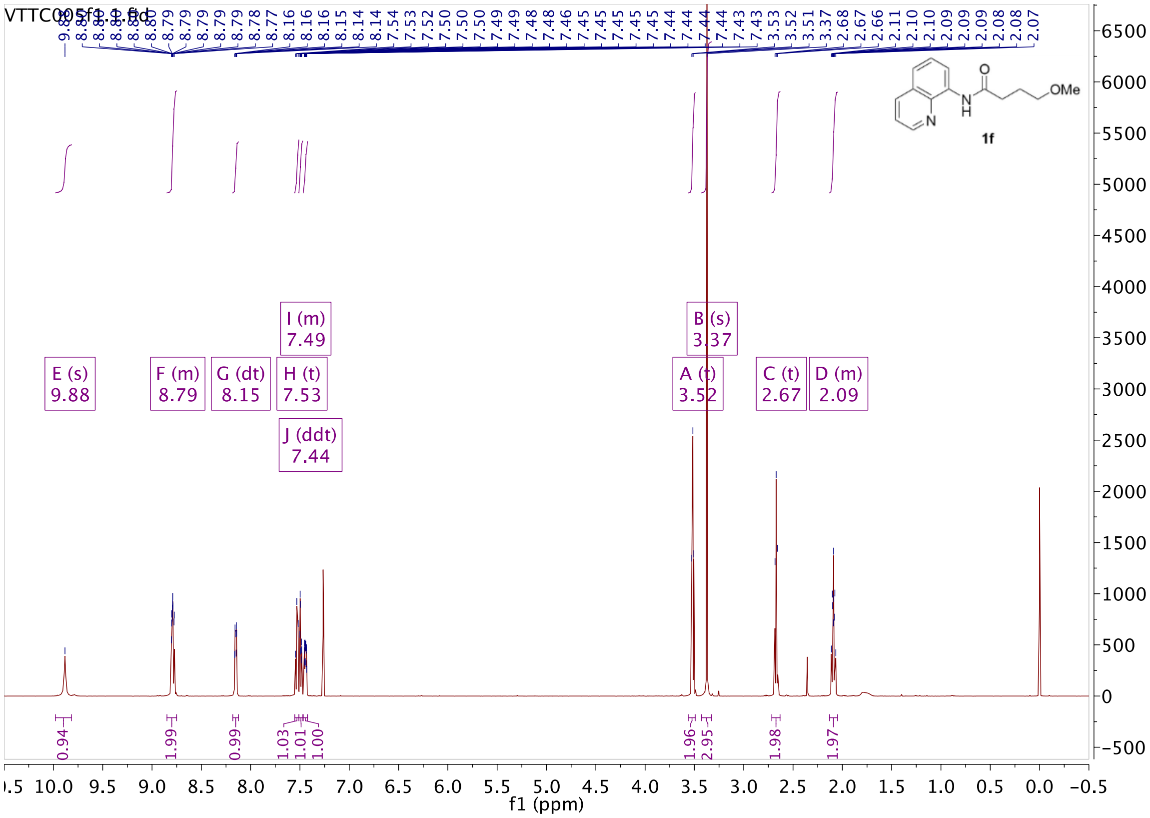
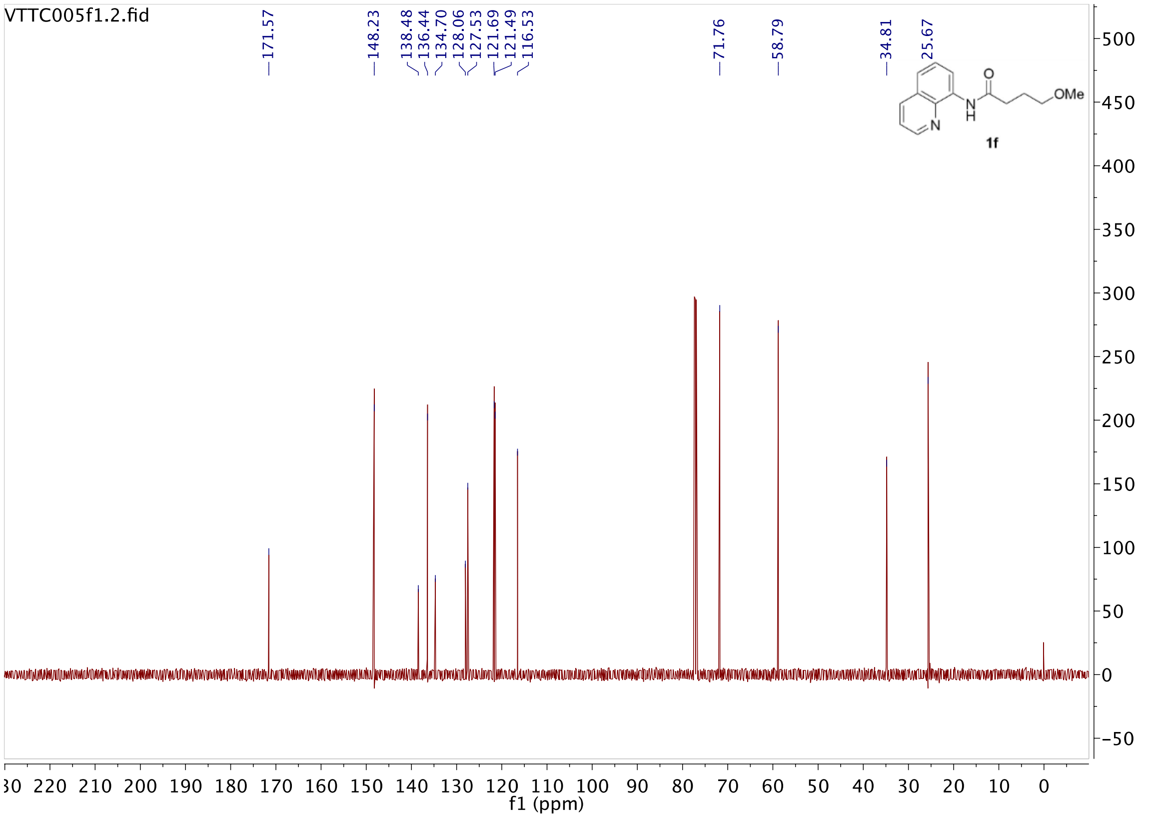
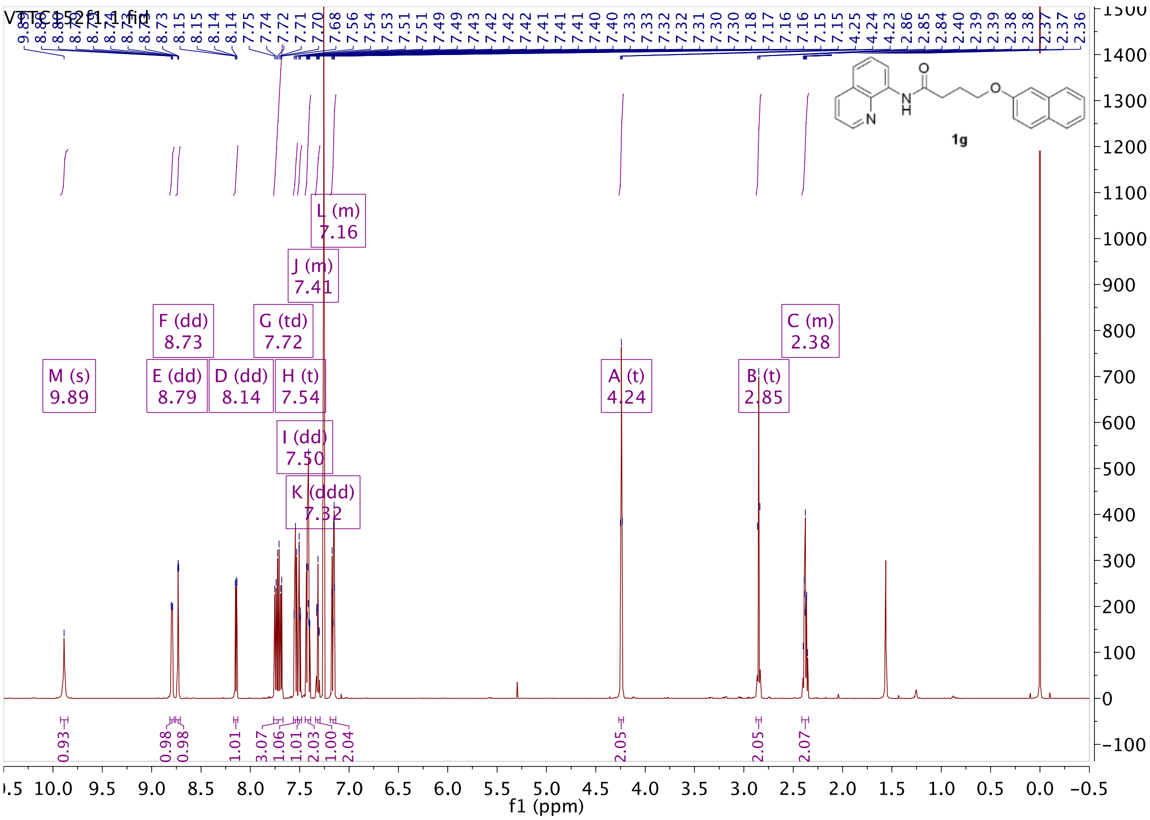
121.71
121.50
116.56
73.16
69.40
34.99
25.85
1d
f1 (ppm)

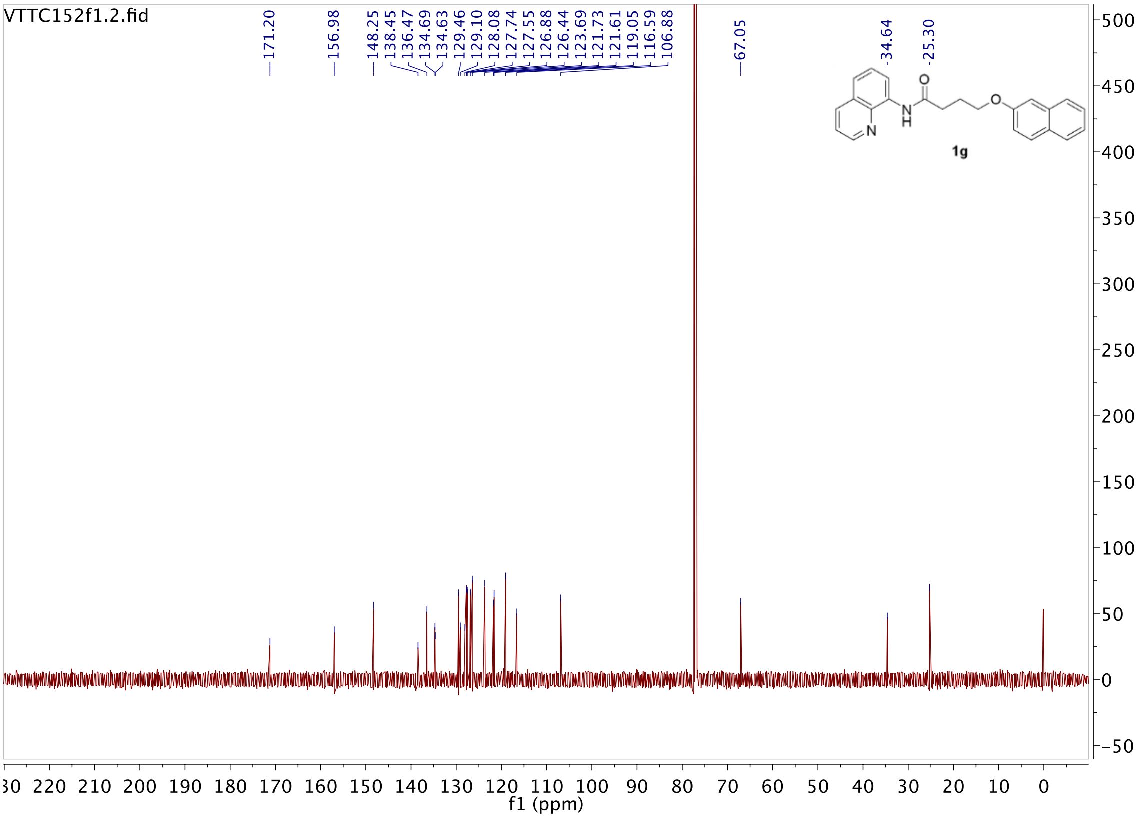

VTTB169f1.1.fid
8.77
8.76
8.76
8.17
8.17
8.16
8.16
7.55
7.54
7.54
7.52
7.51
7.51
7.50
7.47
7.46
7.45
7.45
4.22
4.21
4.20
2.68
2.67
2.66
2.19
2.18
2.18
2.17
2.16
2.16
2.15
2.15
2.14
2.05
N
H
O
O
Me
O
N
1e
G (dd) 8.77
I (dd) 7.46
C (m) 2.17
J (s) 9.82
F (dd) 8.80
E (dd) 8.16
H (m) 7.52
A (t) 4.21
B (t) 2.67
D (s) 2.05
0.98
1.01
0.98
1.01
2.04
1.02
2.00
2.01
2.02
2.98
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
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
f1 (ppm)

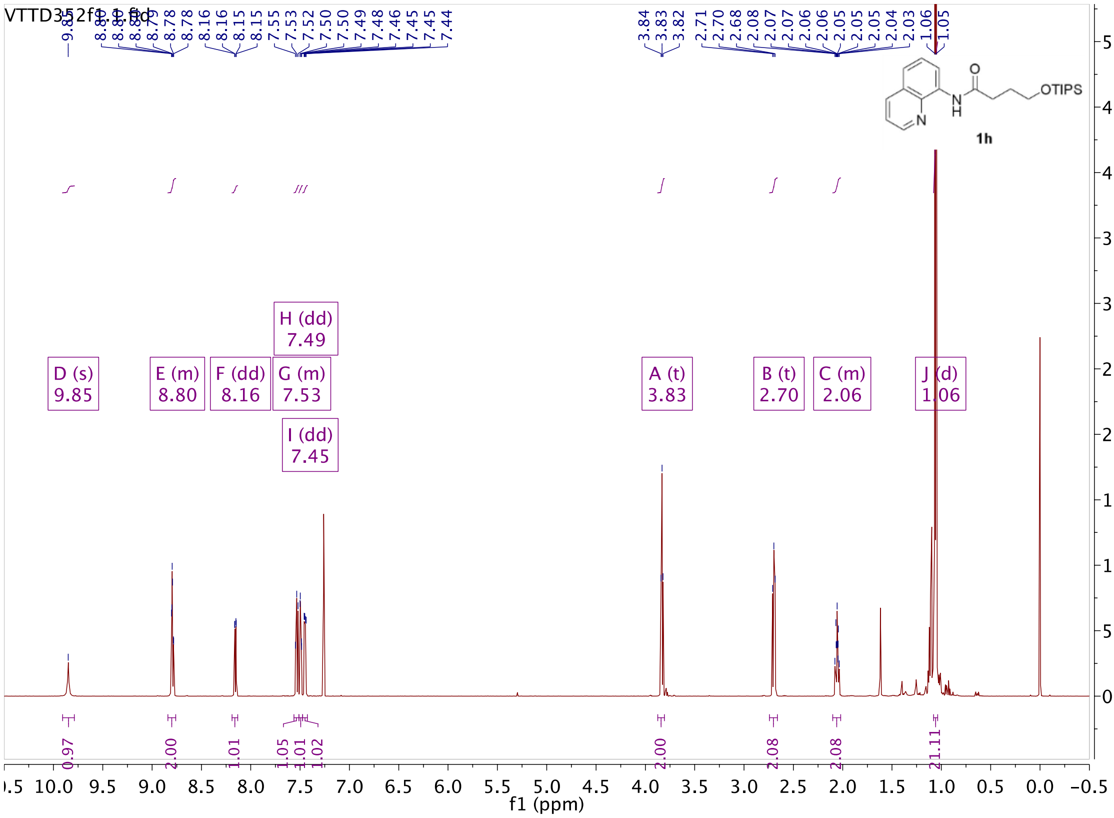

VTTB169f1.2.fid
171.21
170.74
148.26
138.40
136.53
134.50
128.06
127.53
121.75
121.65
116.59
63.80
34.56
24.64
21.07
N
H
O
O
Me
O
N
1e
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

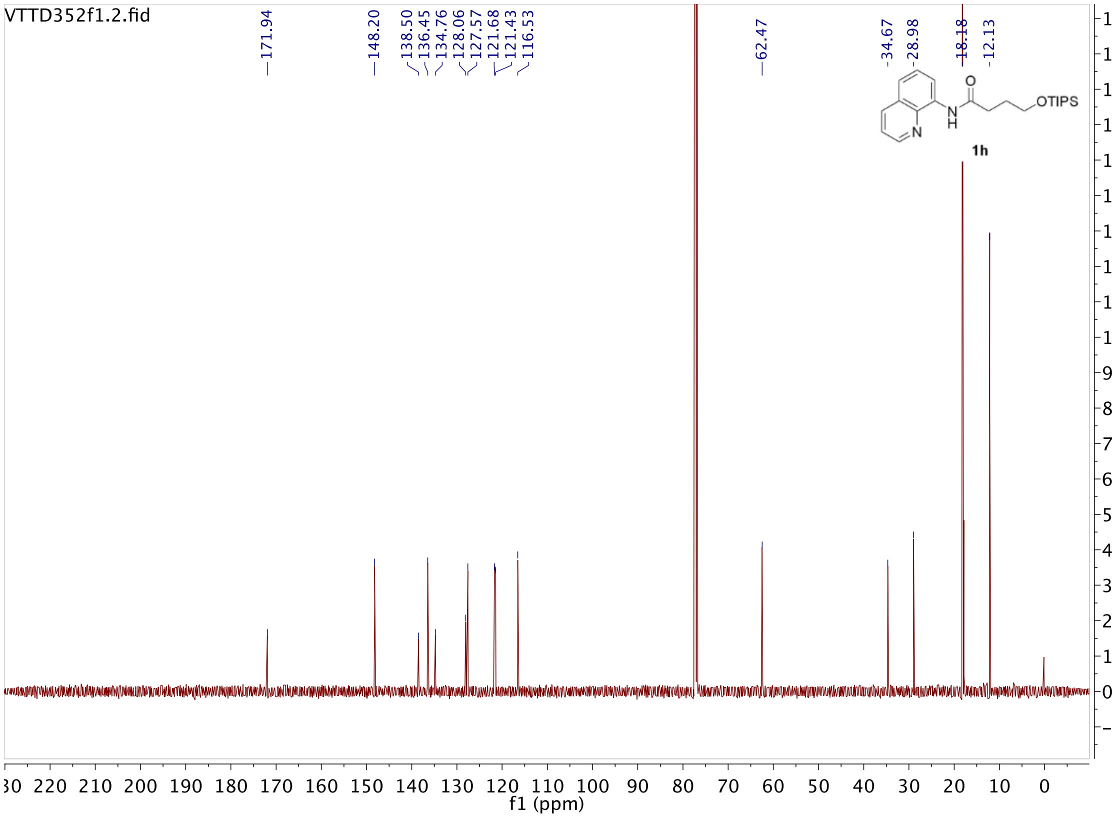

VTTC005f1.1.fid
9.88
8.81
8.80
8.80
8.80
8.80
8.79
8.79
8.79
8.79
8.78
8.77
8.16
8.16
8.16
8.15
8.14
8.14
7.54
7.53
7.52
7.50
7.50
7.49
7.49
7.48
7.48
7.46
7.45
7.45
7.45
7.45
7.45
7.44
7.44
7.44
7.44
7.43
7.43
3.53
3.52
3.51
3.37
2.68
2.67
2.66
2.11
2.10
2.09
2.09
2.09
2.08
2.08
2.07
O
N
H
N
OMe
1f
I (m)
7.49
B (s)
3.37
E (s)
9.88
F (m)
8.79
G (dt)
8.15
H (t)
7.53
A (t)
3.52
C (t)
2.67
D (m)
2.09
J (ddt)
7.44
0.94
1.99
0.99
1.03
1.01
1.00
1.96
2.95
1.98
1.97
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
f1 (ppm)
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

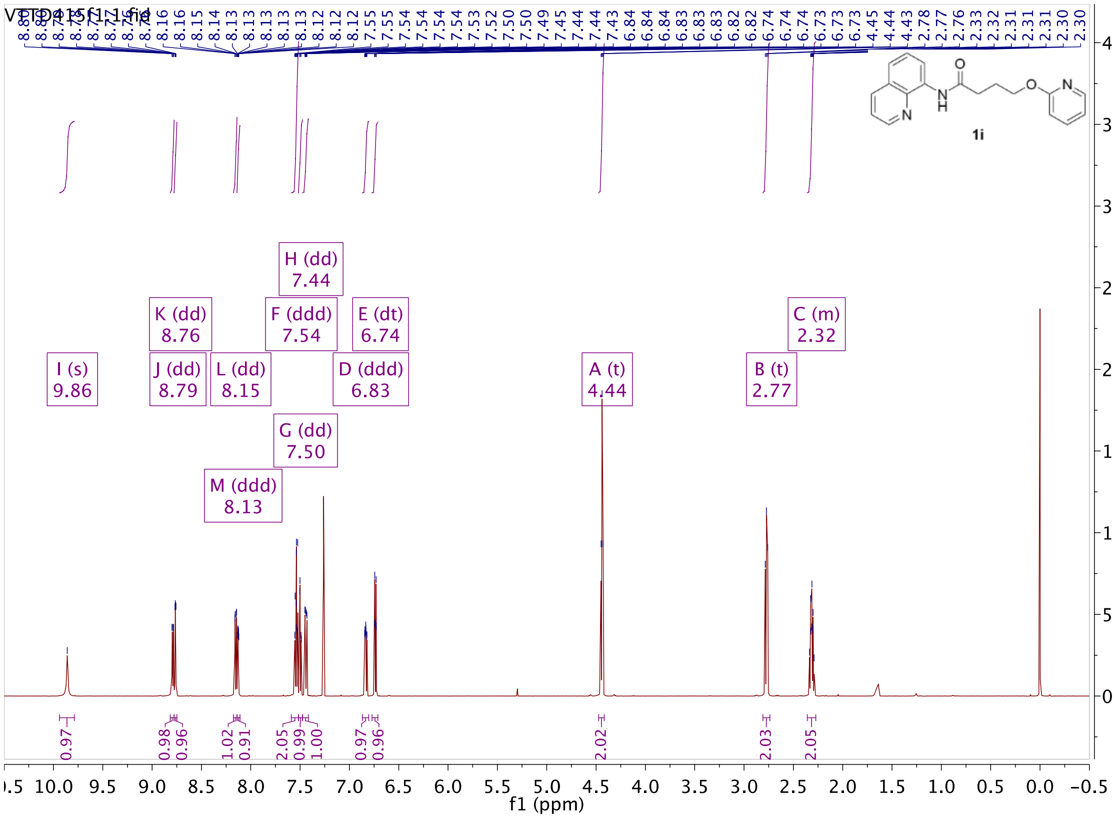

VTTC005f1.2.fid
171.57
148.23
138.48
136.44
134.70
128.06
127.53
121.69
121.49
116.53
71.76
58.79
34.81
25.67
O
N
H
N
OMe
1f
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
500
450
400
350
300
250
200
150
100
50
0
-50

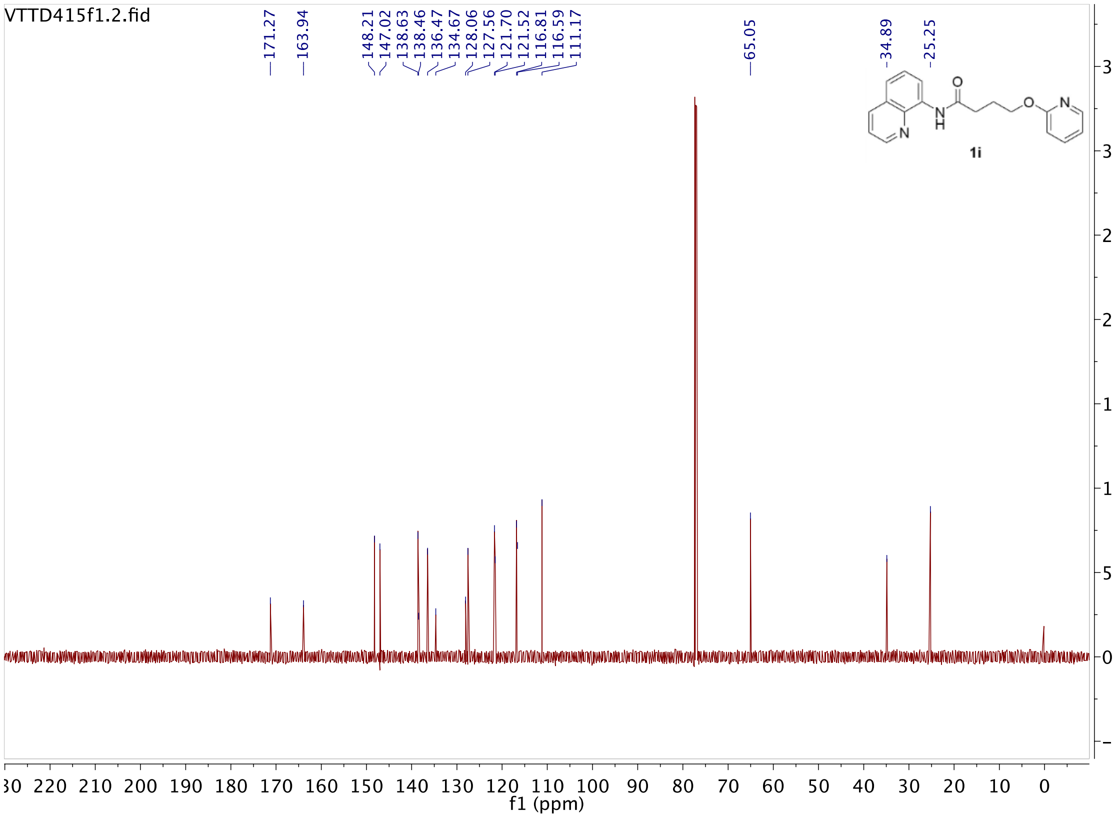

VTTC152f1.1.fid
9.89 8.80 8.80 8.79 8.79 8.74 8.74 8.73 8.73 8.15 8.15 8.14 8.14 7.75 7.74 7.72 7.71 7.70 7.68 7.56 7.54 7.53 7.51 7.51 7.49 7.49 7.43 7.42 7.42 7.42 7.41 7.41 7.41 7.40 7.40 7.33 7.33 7.32 7.32 7.31 7.30 7.30 7.18 7.17 7.16 7.16 7.15 7.15 4.25 4.24 4.23 2.86 2.85 2.84 2.40 2.39 2.39 2.38 2.38 2.37 2.37 2.36
O
N
H
N
O
1g
L (m) 7.16
J (m) 7.41
F (dd) 8.73
G (td) 7.72
C (m) 2.38
M (s) 9.89
E (dd) 8.79
D (dd) 8.14
H (t) 7.54
A (t) 4.24
B (t) 2.85
I (dd) 7.50
K (ddd) 7.32
0.93
0.98
0.98
1.01
3.07
1.06
1.01
2.03
1.00
2.04
2.05
2.05
2.07
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
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
f1 (ppm)

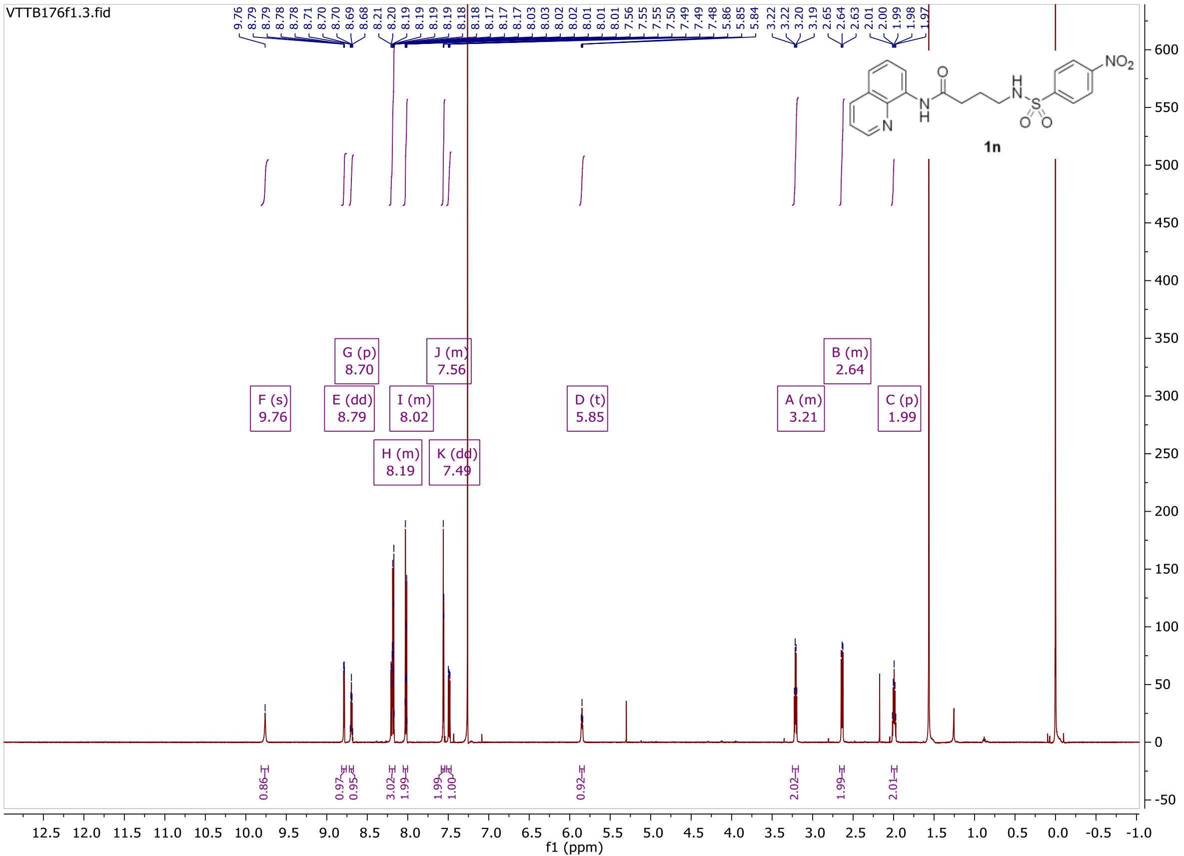

VTTC152f1.2.fid
171.20
156.98
148.25 138.45 136.47 134.69 134.63 129.46 129.10 128.08 127.74 127.55 126.88 126.44 123.69 121.73 121.61 119.05 116.59 106.88
67.05
34.64
25.30
O
N
H
N
O
1g
500
450
400
350
300
250
200
150
100
50
0
-50
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

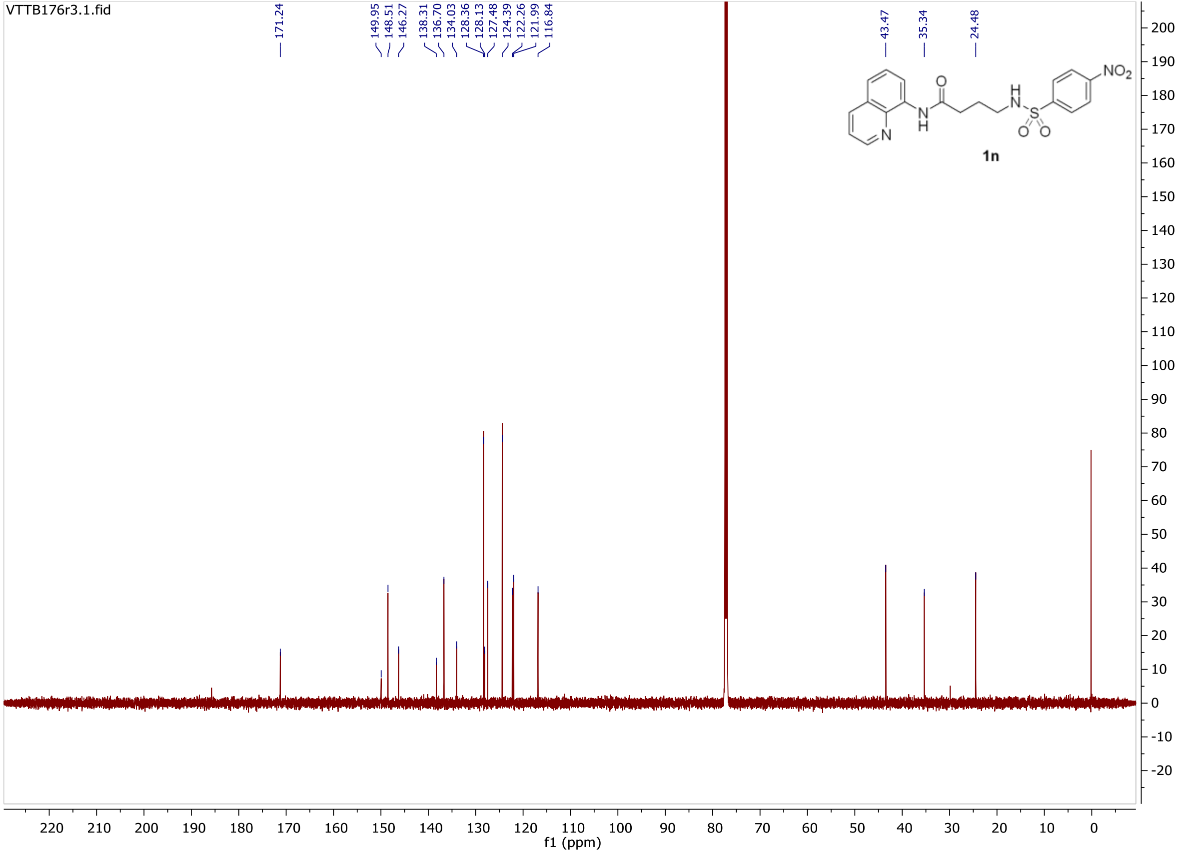

VTTD352f1.1.fid
9.85
8.78
8.78
8.16
8.16
8.15
8.15
7.55
7.53
7.52
7.50
7.49
7.48
7.46
7.45
7.44
3.84
3.83
3.82
2.71
2.70
2.68
2.08
2.07
2.07
2.06
2.06
2.05
2.05
2.05
2.04
2.03
1.06
1.05
OTIPS
O
N
H
N
1h
H (dd)
7.49
D (s)
9.85
E (m)
8.80
F (dd)
8.16
G (m)
7.53
A (t)
3.83
B (t)
2.70
C (m)
2.06
J (d)
1.06
I (dd)
7.45
0.97
2.00
1.01
1.05
1.01
1.02
2.00
2.08
2.08
21.11
f1 (ppm)

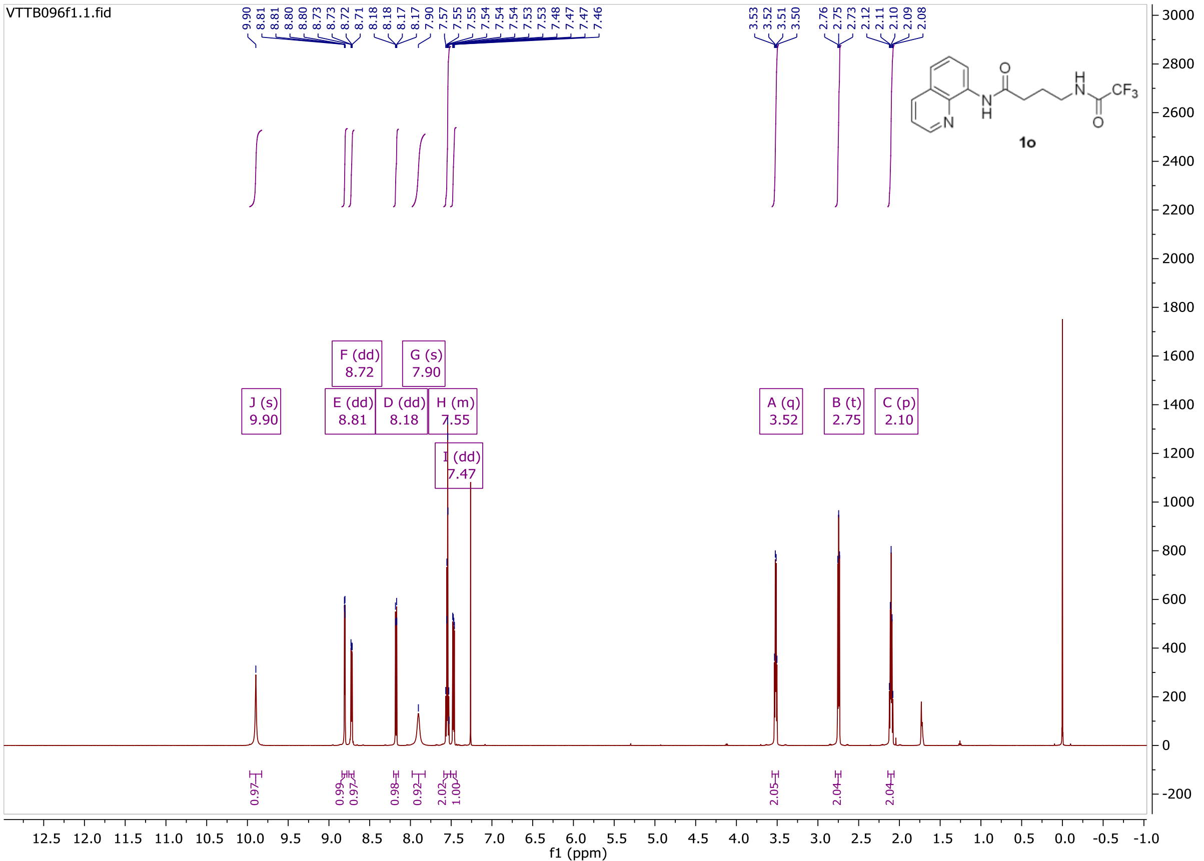

VTTD352f1.2.fid
171.94
148.20
138.50
136.45
134.76
128.06
127.57
121.68
121.43
116.53
62.47
34.67
28.98
18.18
12.13
OTIPS
O
N
H
N
1h
f1 (ppm)

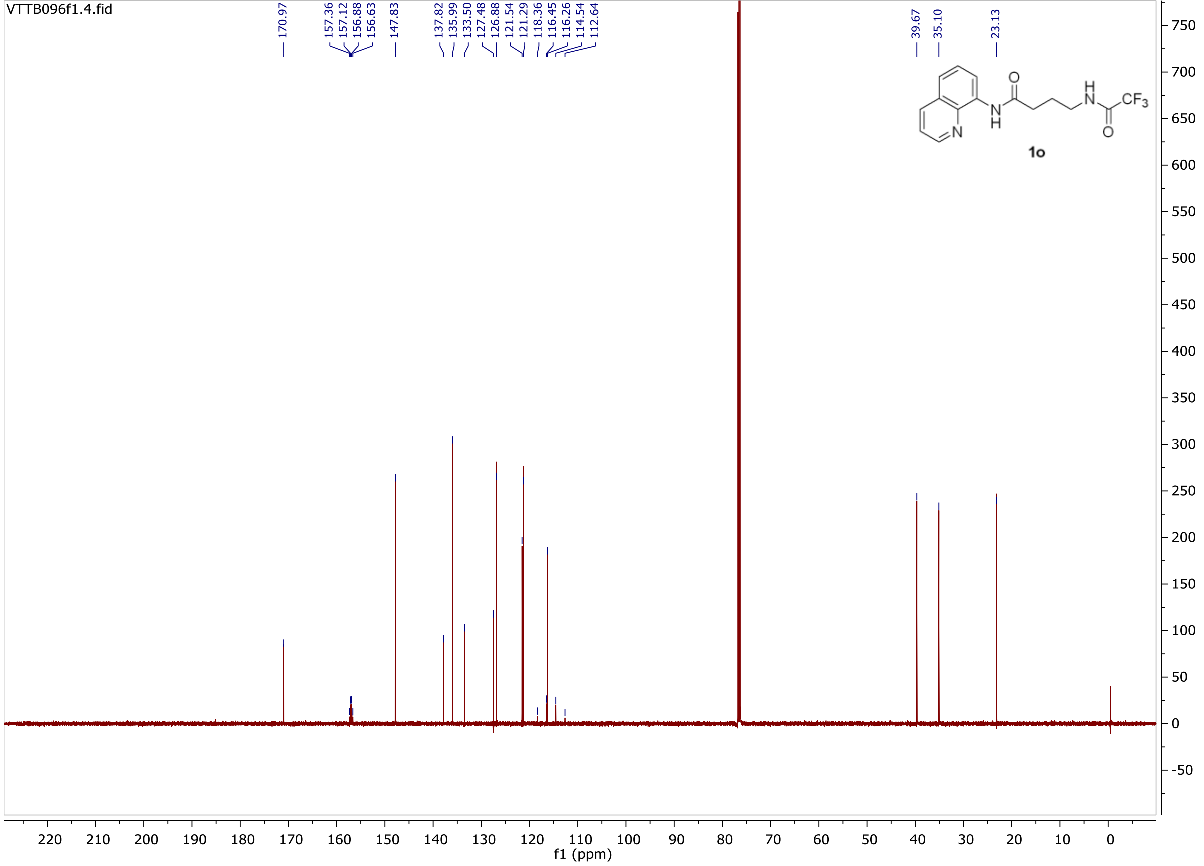

VTTD415f1.1.fid
8.16
8.16
8.15
8.14
8.13
8.13
8.13
8.13
8.13
8.12
8.12
7.55
7.55
7.54
7.54
7.54
7.53
7.52
7.50
7.49
7.45
7.44
7.44
7.43
6.84
6.84
6.84
6.83
6.83
6.83
6.82
6.74
6.74
6.74
6.73
6.73
6.73
4.45
4.44
4.43
2.78
2.77
2.76
2.33
2.32
2.31
2.31
2.31
2.30
1i
I (s) 9.86
K (dd) 8.76
J (dd) 8.79
L (dd) 8.15
M (ddd) 8.13
H (dd) 7.44
F (ddd) 7.54
G (dd) 7.50
E (dt) 6.74
D (ddd) 6.83
A (t) 4.44
B (t) 2.77
C (m) 2.32
0.97
0.98
0.96
1.02
0.91
2.05
0.99
1.00
0.97
0.96
2.02
2.03
2.05
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
f1 (ppm)
4000
3500
3000
2500
2000
1500
1000
500
0

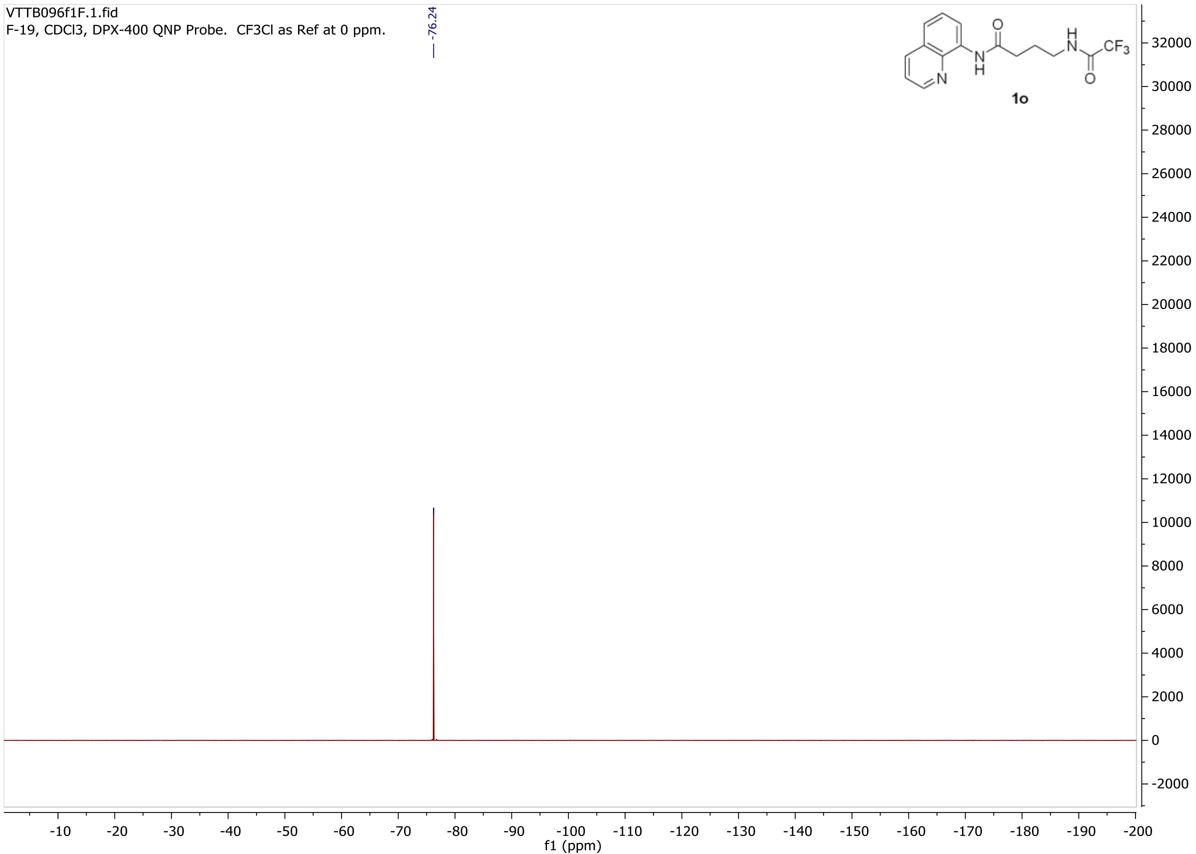

VTTD415f1.2.fid
171.27
163.94
148.21
147.02
138.63
138.46
136.47
134.67
128.06
127.56
121.70
121.52
116.81
116.59
111.17
65.05
34.89
25.25
1i
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
350
300
250
200
150
100
50
0
–50

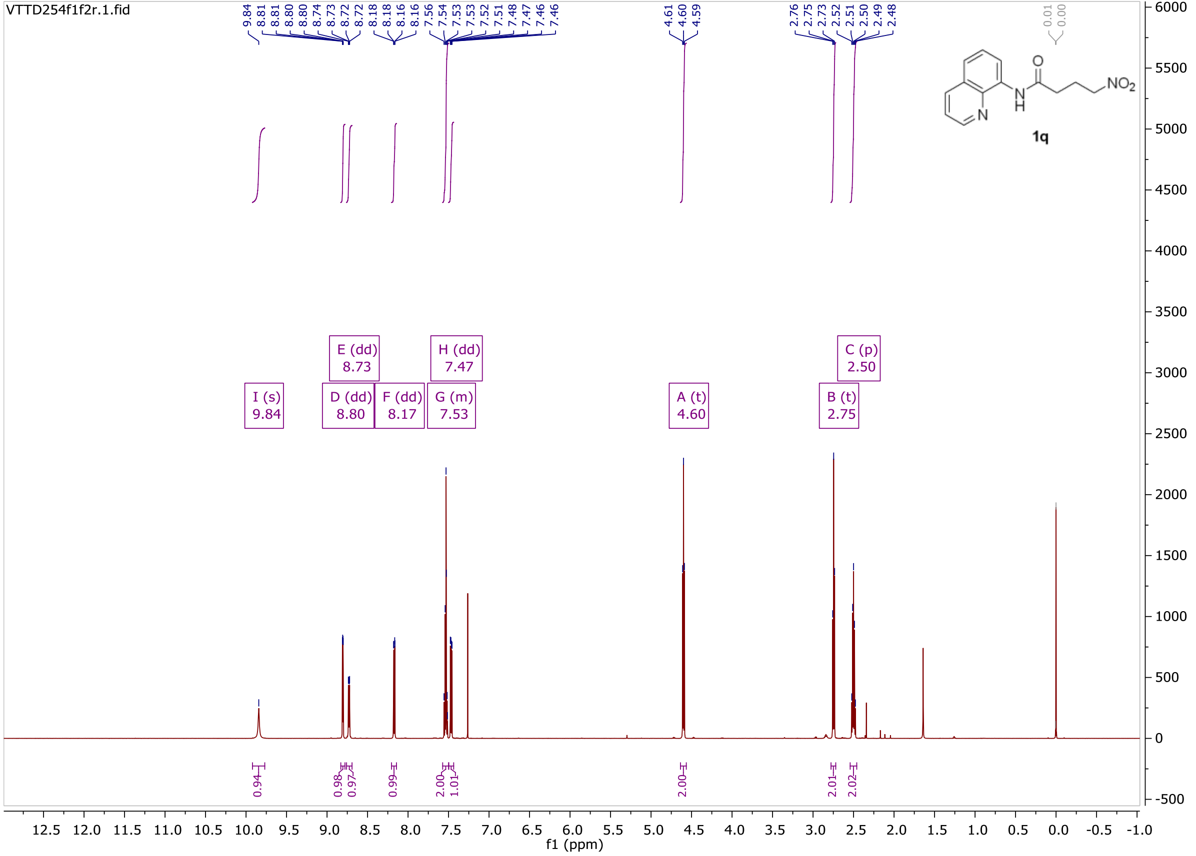

VTTB176f1.3.fid
9.76 8.79 8.79 8.78 8.78 8.71 8.70 8.70 8.69 8.68 8.21 8.20 8.19 8.19 8.19 8.19 8.18 8.18 8.17 8.17 8.17 8.03 8.03 8.02 8.02 8.01 8.01 7.56 7.55 7.55 7.50 7.49 7.48 5.86 5.85 5.84 3.22 3.22 3.20 3.19 2.65 2.64 2.63 2.01 2.00 1.99 1.98 1.97
NO2
N
H
N
O
H
N
S
O O
1n
G (p) 8.70
J (m) 7.56
B (m) 2.64
F (s) 9.76
E (dd) 8.79
I (m) 8.02
D (t) 5.85
A (m) 3.21
C (p) 1.99
H (m) 8.19
K (dd) 7.49
0.86
0.97
0.95
3.02
1.99
1.99
1.00
0.92
2.02
1.99
2.01
600 550 500 450 400 350 300 250 200 150 100 50 0 -50
12.5 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 -0.5 -1.0
f1 (ppm)

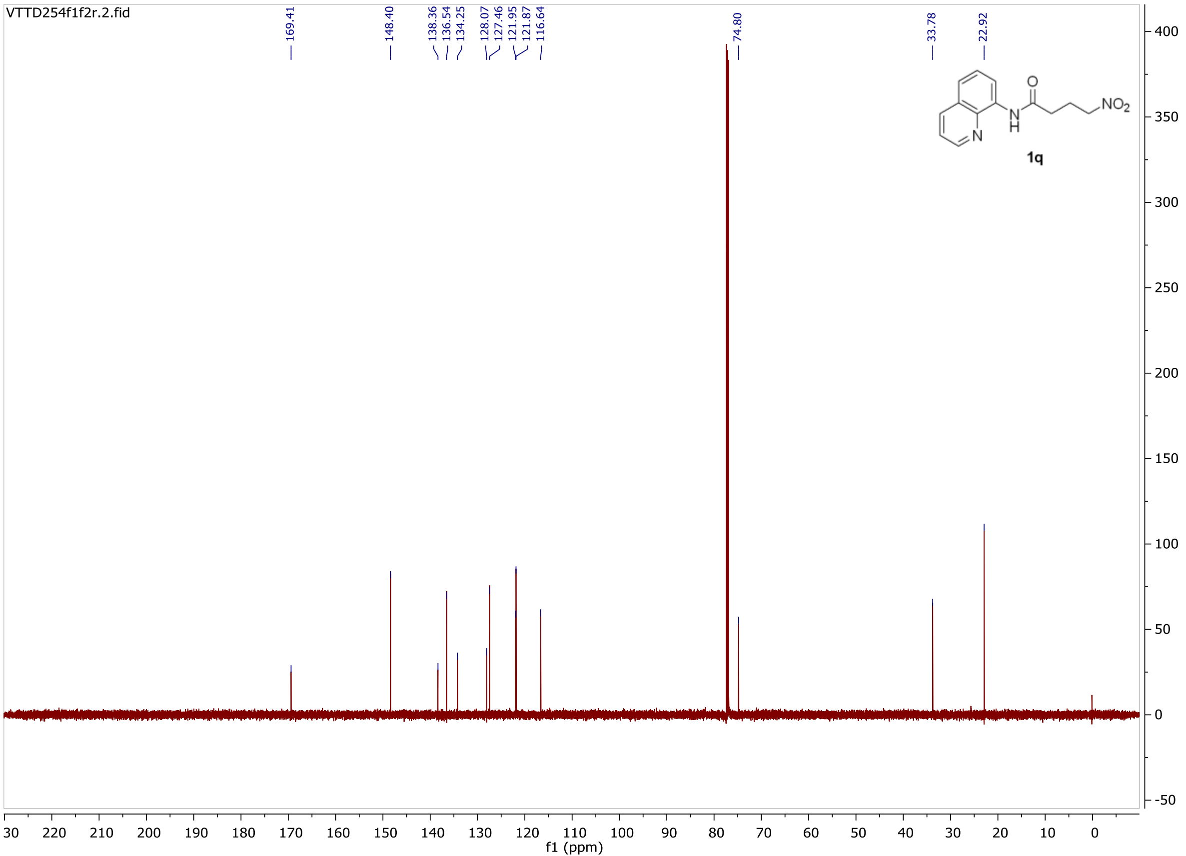

VTTB176r3.1.fid
171.24
149.95 148.51 146.27 138.31 136.70 134.03 128.36 128.13 127.48 124.39 122.26 121.99 116.84
43.47
35.34
24.48
NO2
N
H
N
O
H
N
S
O O
1n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

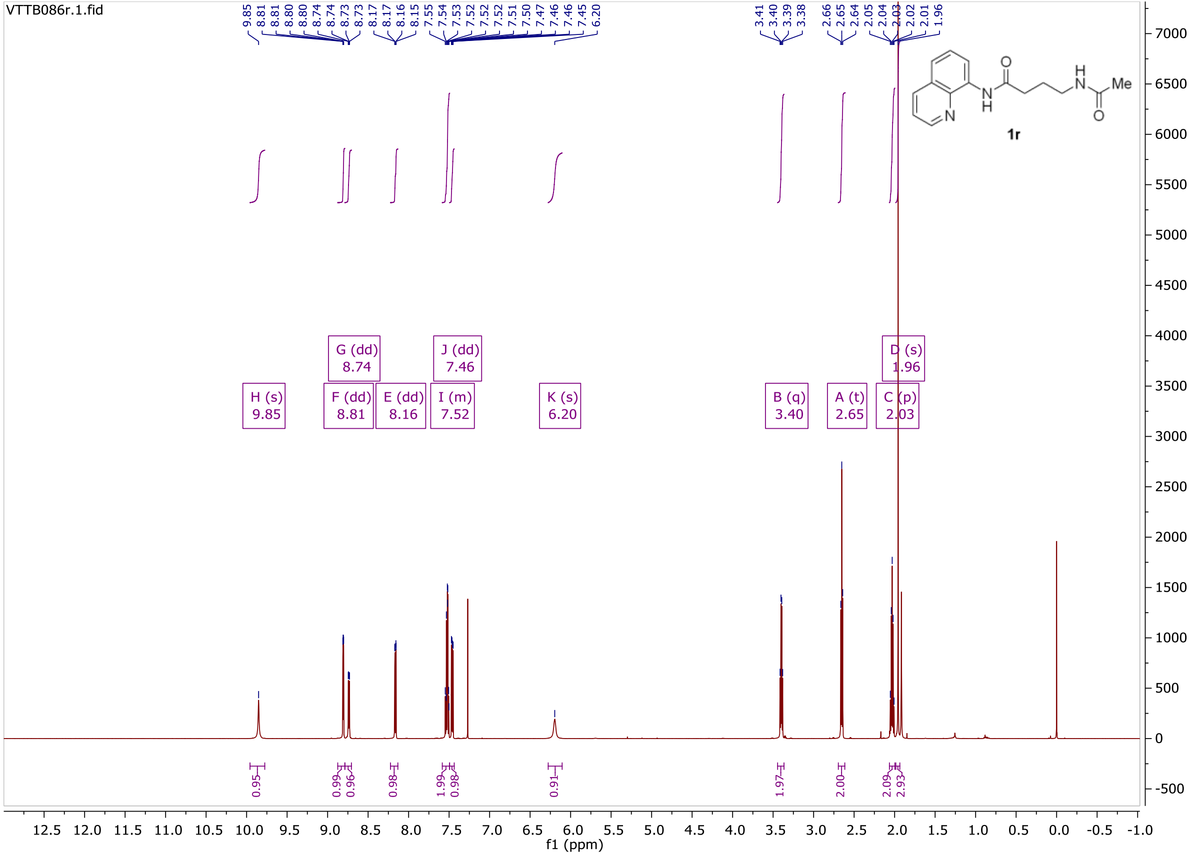

VTTB096f1.1.fid
9.90 8.81 8.81 8.80 8.80 8.73 8.73 8.72 8.71 8.18 8.18 8.17 8.17 7.90 7.57 7.55 7.55 7.54 7.54 7.54 7.53 7.53 7.48 7.47 7.47 7.46
3.53 3.52 3.51 3.50 2.76 2.75 2.73 2.12 2.11 2.10 2.09 2.08
1o
F (dd) 8.72
G (s) 7.90
J (s) 9.90
E (dd) 8.81
D (dd) 8.18
H (m) 7.55
I (dd) 7.47
A (q) 3.52
B (t) 2.75
C (p) 2.10
0.97 0.99 0.97 0.98 0.92 2.02 1.00 2.05 2.04 2.04
3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200
12.5 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 -0.5 -1.0
f1 (ppm)

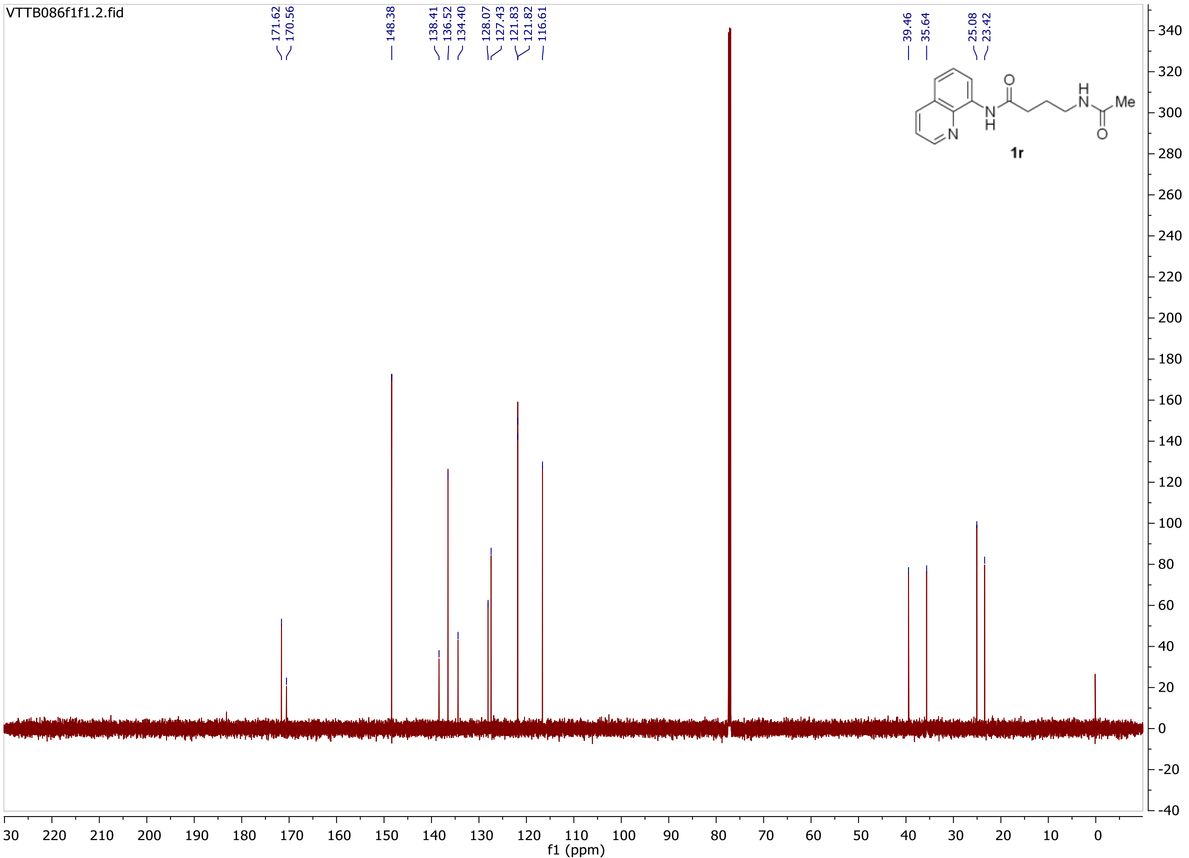

VTTB096f1.4.fid
170.97
157.36 157.12 156.88 156.63
147.83
137.82 135.99 133.50 127.48 126.88 121.54 121.29 118.36 116.45 116.26 114.54 112.64
39.67 35.10 23.13
1o
750 700 650 600 550 500 450 400 350 300 250 200 150 100 50 0 -50
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


VTTB096f1F.1.fid
F-19, CDCl3, DPX-400 QNP Probe. CF3Cl as Ref at 0 ppm.
-76.24
1o
N
H
O
CF3
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

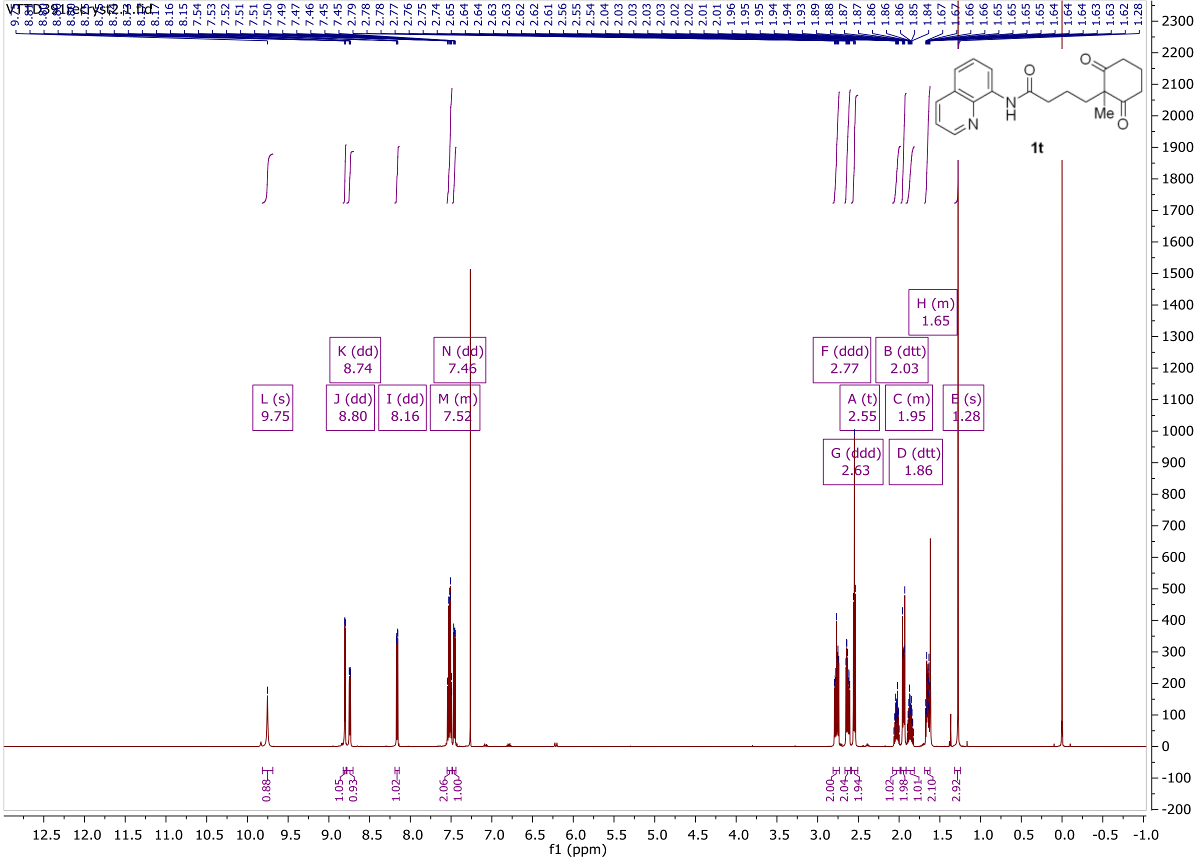

VTTD254f1f2r.1.fid
9.84 8.81 8.81 8.80 8.80 8.74 8.73 8.72 8.72 8.18 8.18 8.16 8.16 7.56 7.54 7.53 7.53 7.52 7.51 7.48 7.47 7.46 7.46
4.61 4.60 4.59
2.76 2.75 2.73 2.52 2.51 2.50 2.49 2.48
0.01 0.00
1q
NO2
I (s) 9.84
D (dd) 8.80
E (dd) 8.73
F (dd) 8.17
G (m) 7.53
H (dd) 7.47
A (t) 4.60
B (t) 2.75
C (p) 2.50
0.94 0.98 0.97 0.99 2.00 1.01 2.00 2.01 2.02
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.5 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 -0.5 -1.0
f1 (ppm)


VTTD254f1f2r.2.fid
169.41
148.40
138.36
136.54
134.25
128.07
127.46
121.95
121.87
116.64
74.80
33.78
22.92
NO2
N
H
O
1q
400
350
300
250
200
150
100
50
0
-50
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

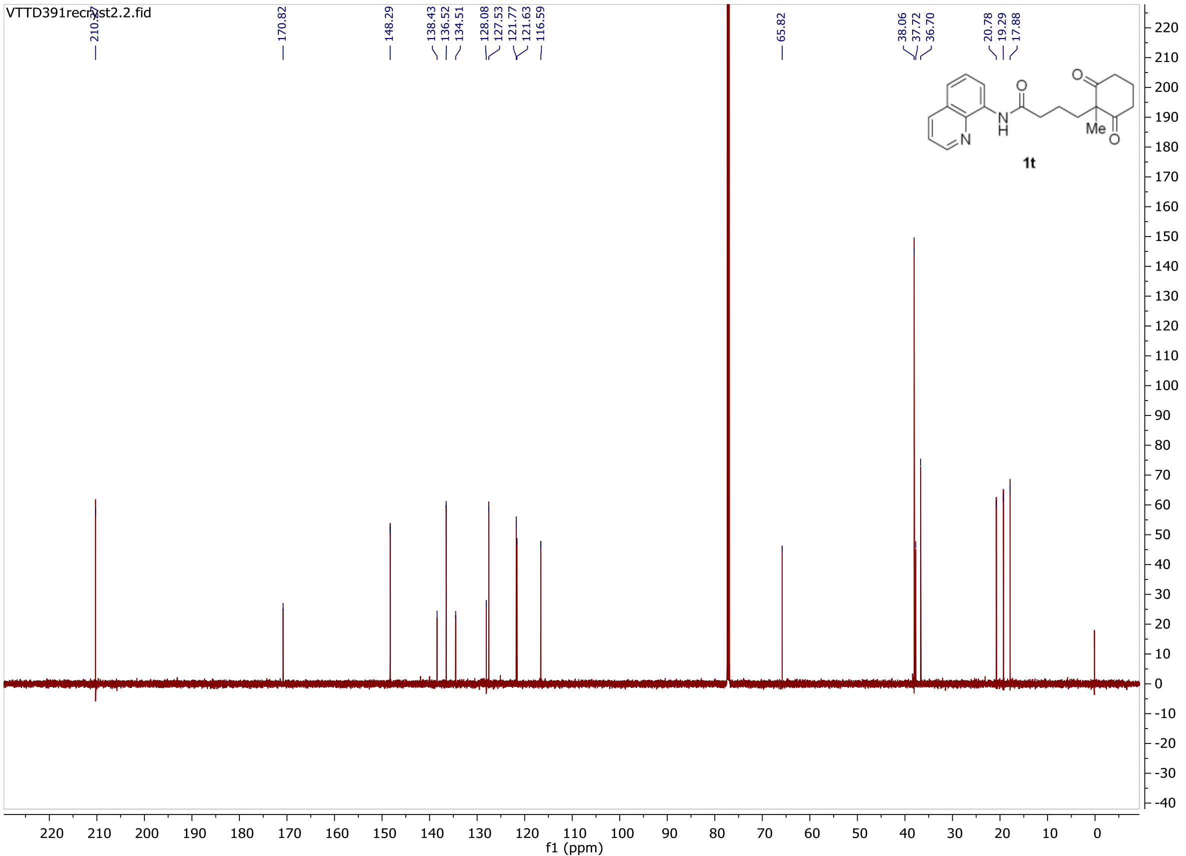

VTTB086r.1.fid
9.85
8.81
8.81
8.80
8.80
8.74
8.74
8.73
8.73
8.17
8.16
8.15
7.55
7.54
7.53
7.52
7.52
7.52
7.51
7.50
7.47
7.46
7.46
7.45
6.20
3.41
3.40
3.39
3.38
2.66
2.65
2.64
2.05
2.04
2.03
2.02
2.01
1.96
N
H
O
H
N
Me
O
1r
G (dd)
8.74
J (dd)
7.46
D (s)
1.96
H (s)
9.85
F (dd)
8.81
E (dd)
8.16
I (m)
7.52
K (s)
6.20
B (q)
3.40
A (t)
2.65
C (p)
2.03
0.95
0.99
0.96
0.98
1.99
0.98
0.91
1.97
2.00
2.09
2.93
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.5
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
-0.5
-1.0
f1 (ppm)

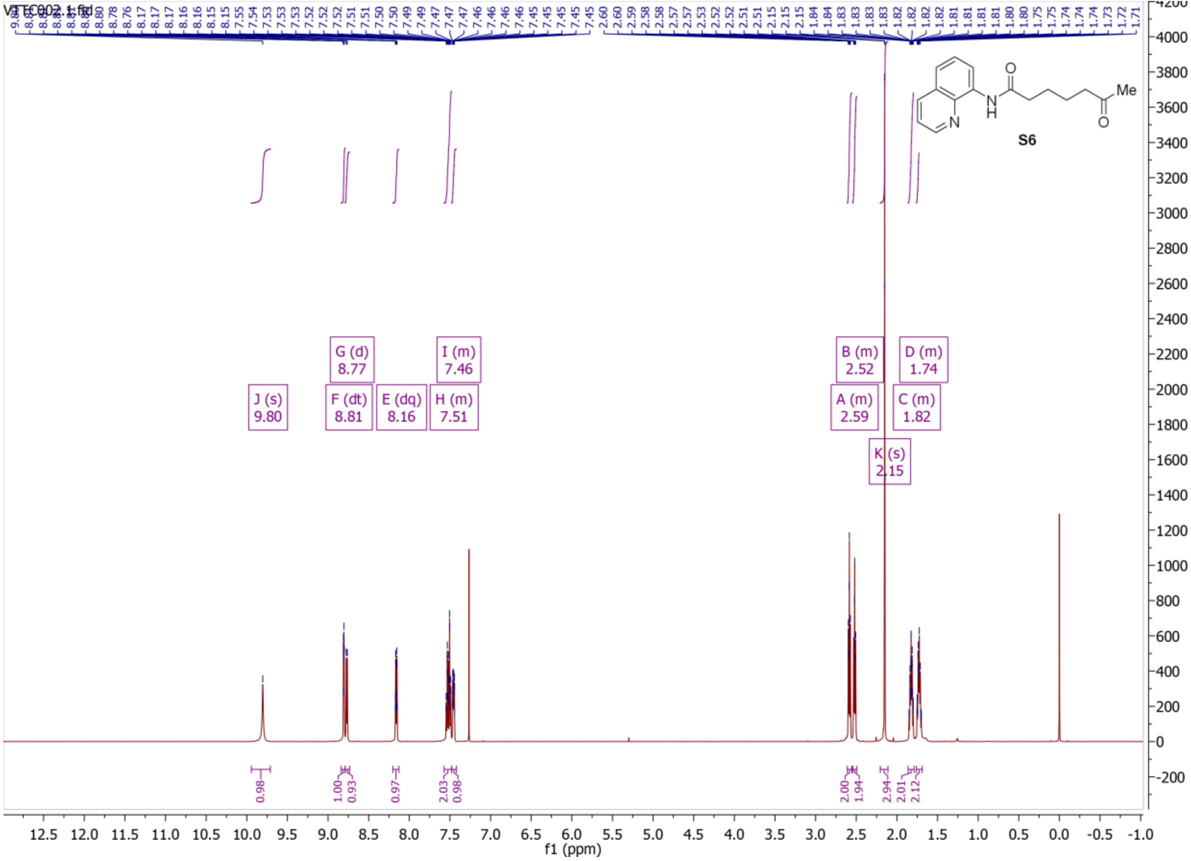

VTTB086f1f1.2.fid
171.62
170.56
148.38
138.41
136.52
134.40
128.07
127.43
121.83
121.82
116.61
39.46
35.64
25.08
23.42
O
N
H
N
H
N
Me
O
f1 (ppm)
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40

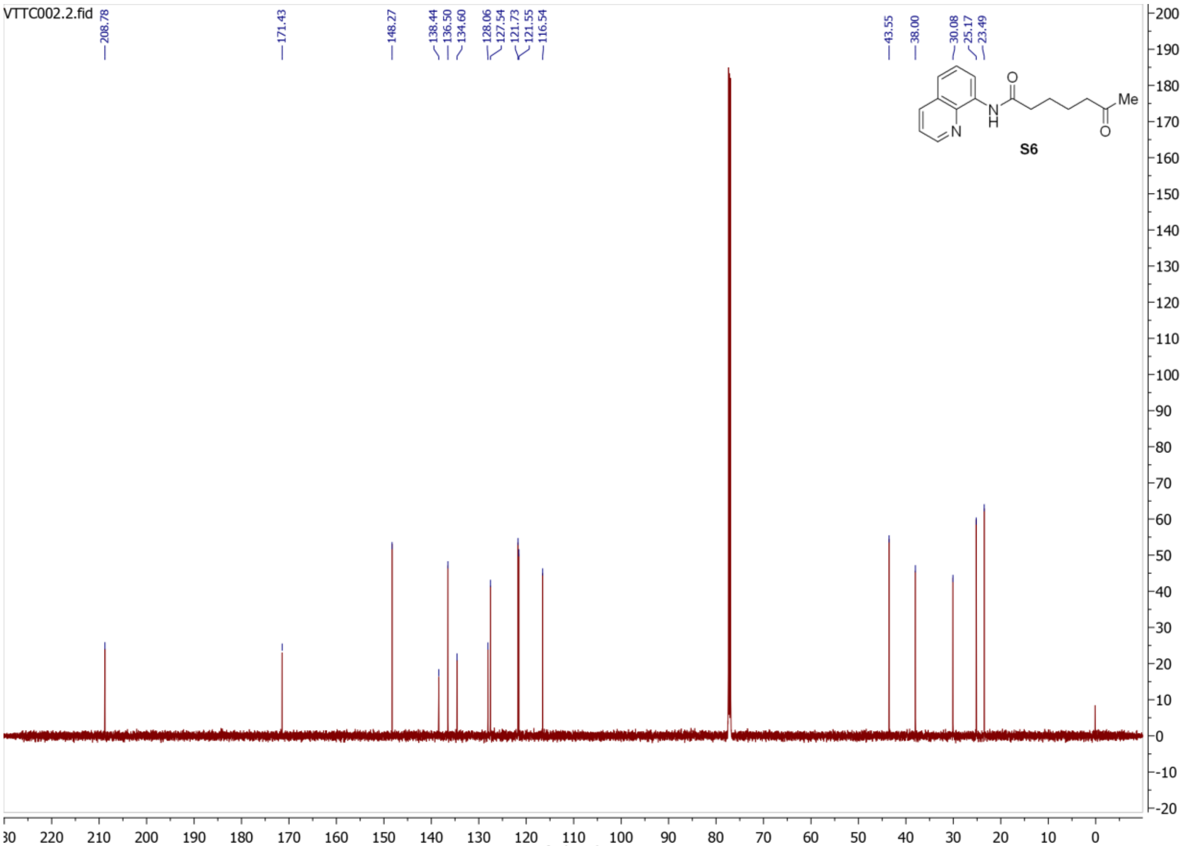
1r

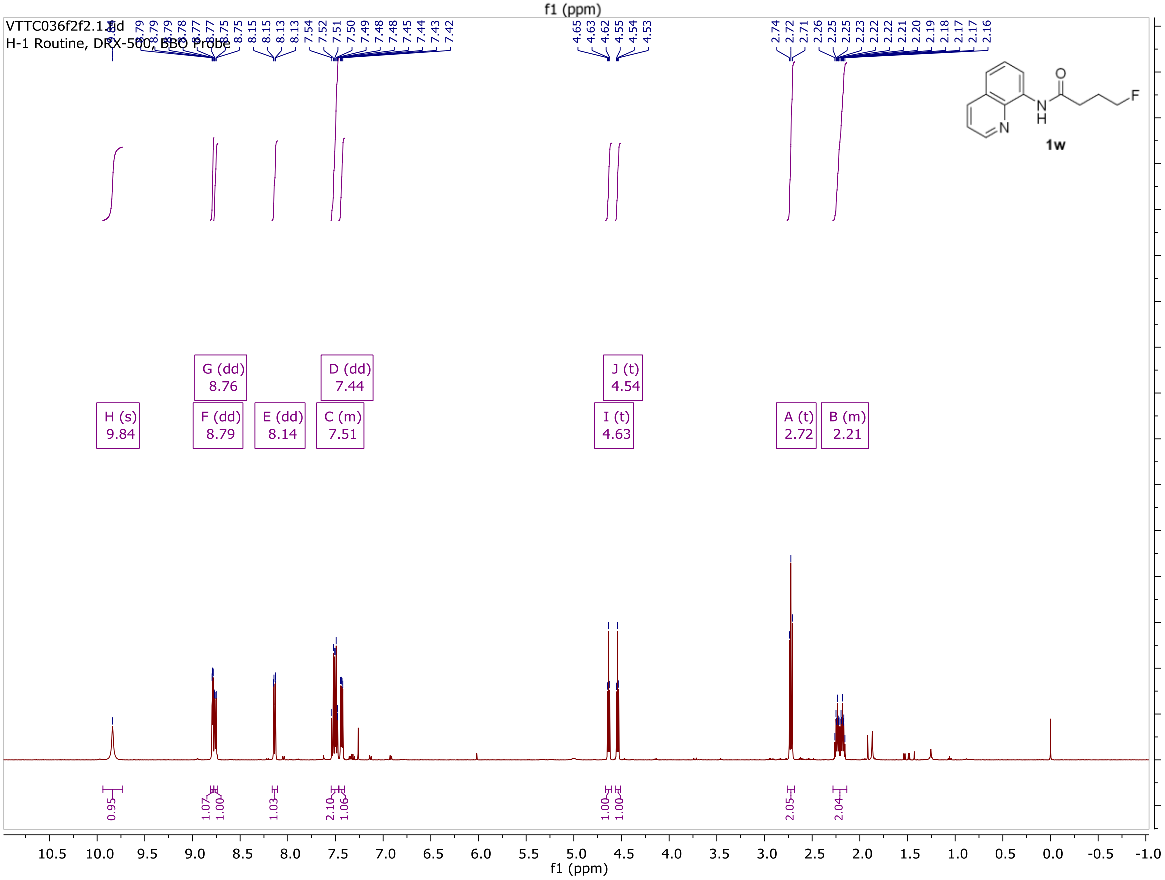

9.75
8.80
8.79
8.75
8.74
8.17
8.16
8.15
7.54
7.53
7.52
7.51
7.51
7.50
7.49
7.47
7.46
7.45
7.45
2.79
2.78
2.78
2.77
2.76
2.75
2.74
2.65
2.64
2.64
2.63
2.62
2.62
2.61
2.56
2.55
2.54
2.04
2.03
2.03
2.03
2.02
2.02
2.02
2.01
1.96
1.95
1.95
1.94
1.94
1.93
1.89
1.88
1.87
1.87
1.86
1.86
1.85
1.84
1.67
1.66
1.66
1.65
1.65
1.65
1.65
1.64
1.64
1.64
1.63
1.63
1.62
1.28
O
N
H
N
O
Me
O
L (s)
9.75
K (dd)
8.74
J (dd)
8.80
I (dd)
8.16
N (dd)
7.46
M (m)
7.52
F (ddd)
2.77
A (t)
2.55
G (ddd)
2.63
B (dtt)
2.03
C (m)
1.95
D (dtt)
1.86
H (m)
1.65
E (s)
1.28
0.88
1.05
0.93
1.02
2.06
1.00
2.00
2.04
1.94
1.02
1.98
1.01
2.10
2.92
12.5
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
-0.5
-1.0
f1 (ppm)
2300
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

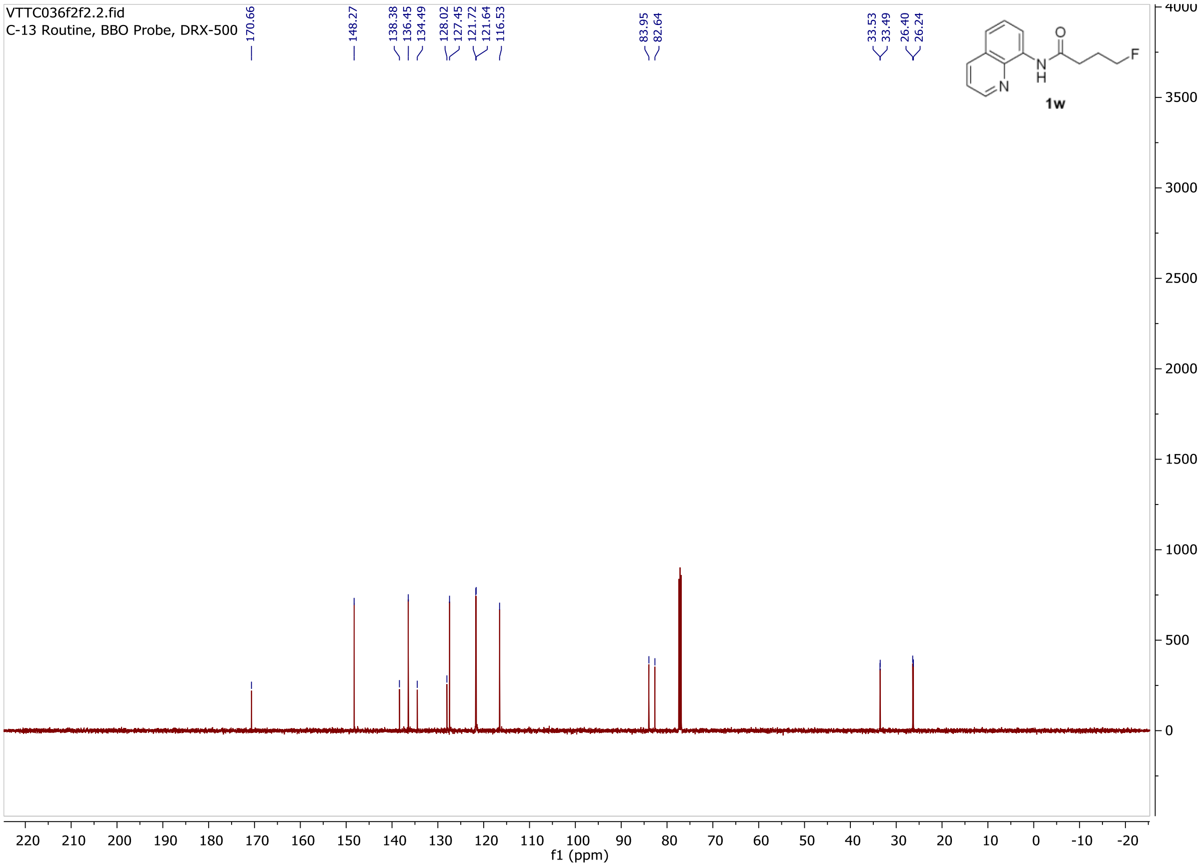
1t

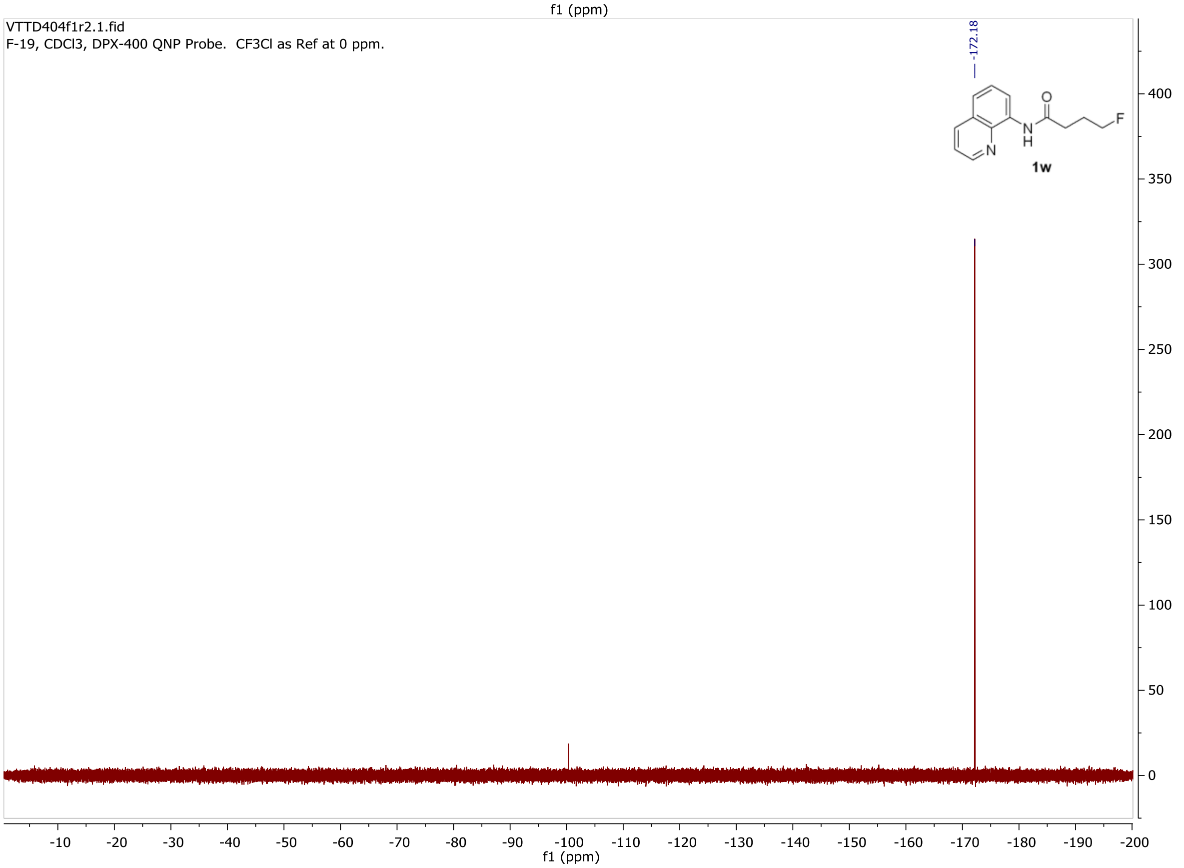

VTTD391recryst2.2.fid
210.2
170.82
148.29
138.43
136.52
134.51
128.08
127.53
121.77
121.63
116.59
65.82
38.06
37.72
36.70
20.78
19.29
17.88
1t
Me
N
H
O
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40

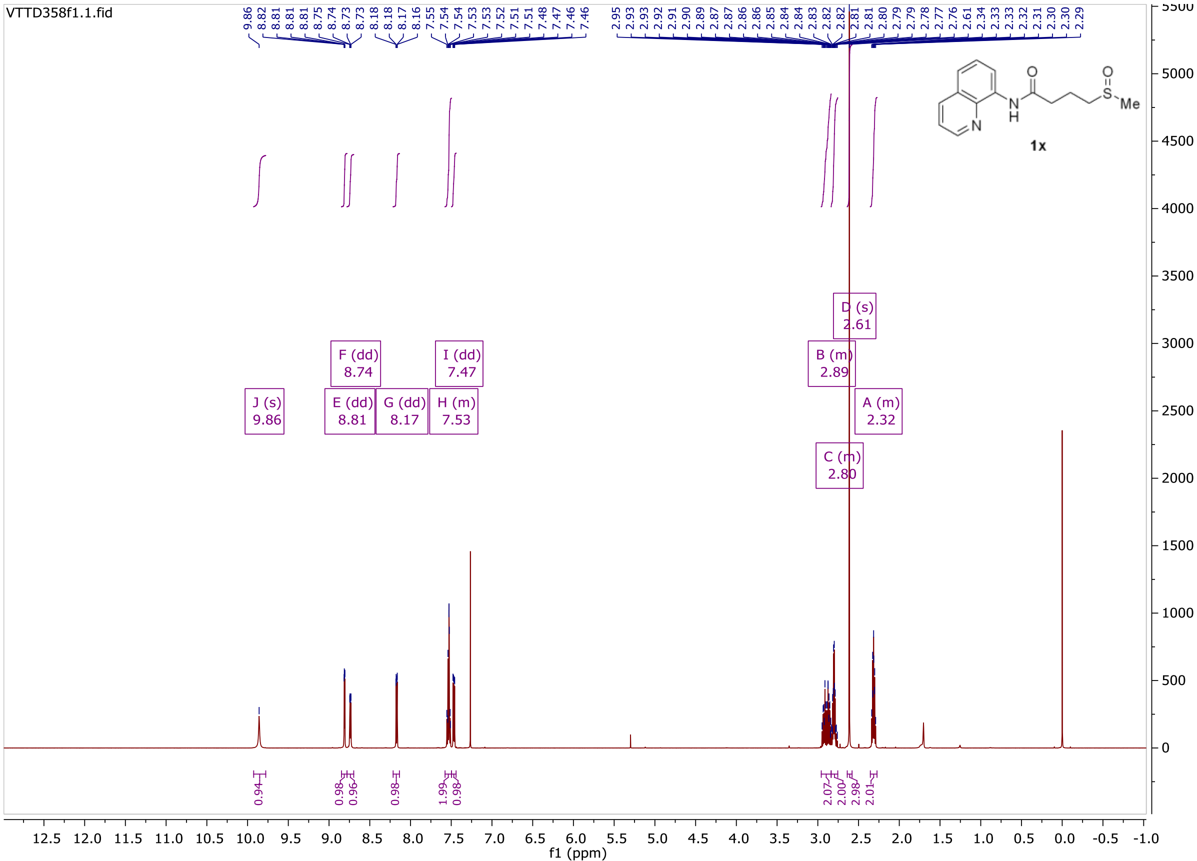

VTTC002.1.fid
8.80 8.78 8.76 8.17 8.17 8.17 8.16 8.16 8.15 8.15 7.55 7.54 7.53 7.53 7.52 7.52 7.51 7.51 7.50 7.49 7.49 7.47 7.47 7.46 7.46 7.46 7.45 7.45 7.45 7.45
2.60 2.59 2.58 2.58 2.57 2.53 2.52 2.52 2.51 2.15 2.15 2.15 1.84 1.84 1.83 1.83 1.83 1.83 1.82 1.82 1.82 1.81 1.81 1.81 1.80 1.80 1.75 1.74 1.74 1.74 1.72 1.71
S6
Me
N
H
O
J (s) 9.80
G (d) 8.77
F (dt) 8.81
E (dq) 8.16
I (m) 7.46
H (m) 7.51
B (m) 2.52
A (m) 2.59
K (s) 2.15
D (m) 1.74
C (m) 1.82
0.98
1.00
0.93
0.97
2.03
0.98
2.00
1.94
2.94
2.01
2.12
f1 (ppm)
12.5 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 -0.5 -1.0
4200 4000 3800 3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200

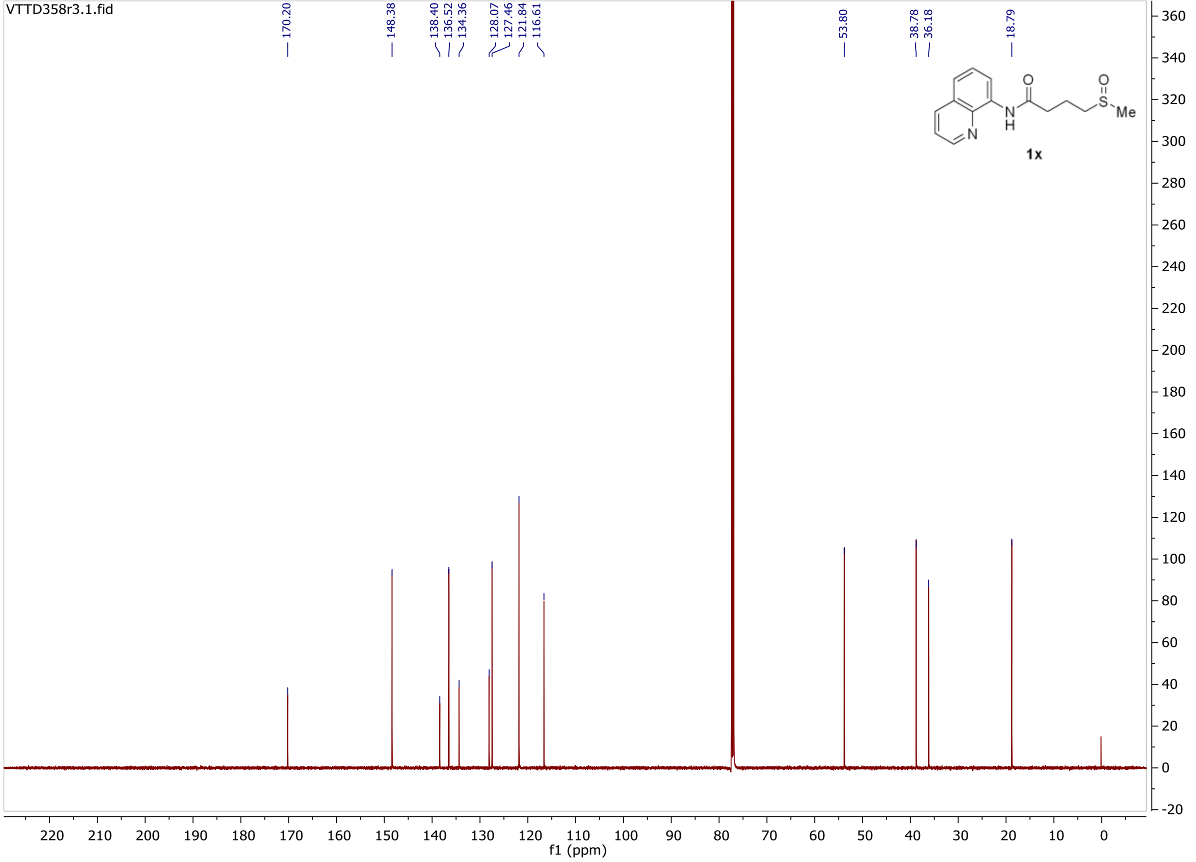

VTTC002.2.fid
208.78
171.43
148.27
138.44
136.50
134.60
128.06
127.54
121.73
121.55
116.54
43.55
38.00
30.08
25.17
23.49
Me
N
H
O
S6
f1 (ppm)

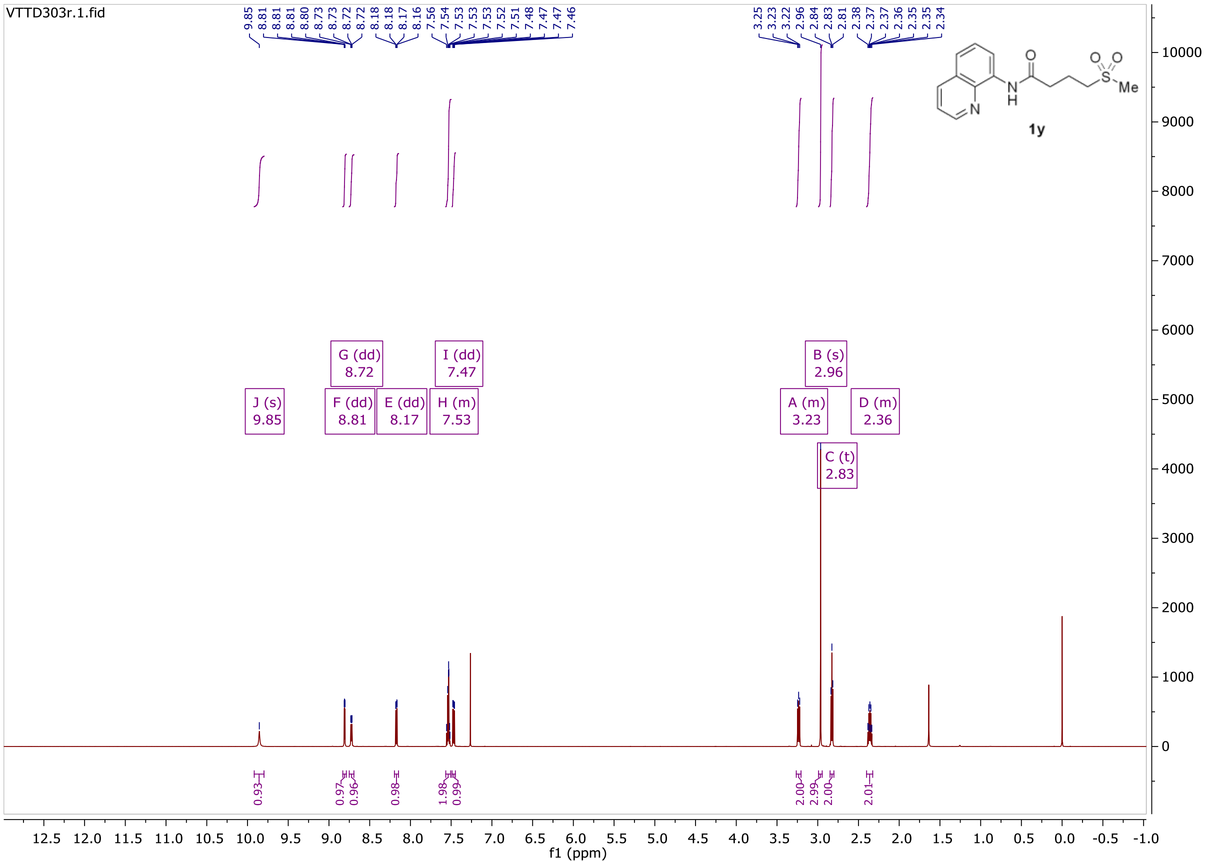

VTTC036f2f2.1.fid
H-1 Routine, DRX-500, BBO Probe
8.79
8.79
8.78
8.77
8.77
8.75
8.75
8.15
8.15
8.13
8.13
7.54
7.52
7.51
7.50
7.49
7.48
7.45
7.44
7.43
7.42
4.65
4.63
4.62
4.55
4.54
4.53
2.74
2.72
2.71
2.26
2.25
2.25
2.23
2.22
2.22
2.21
2.20
2.19
2.18
2.17
2.17
2.16
F
N
H
O
1w
G (dd) 8.76
D (dd) 7.44
J (t) 4.54
H (s) 9.84
F (dd) 8.79
E (dd) 8.14
C (m) 7.51
I (t) 4.63
A (t) 2.72
B (m) 2.21
0.95
1.07
1.00
1.03
2.10
1.06
1.00
1.00
2.05
2.04
f1 (ppm)

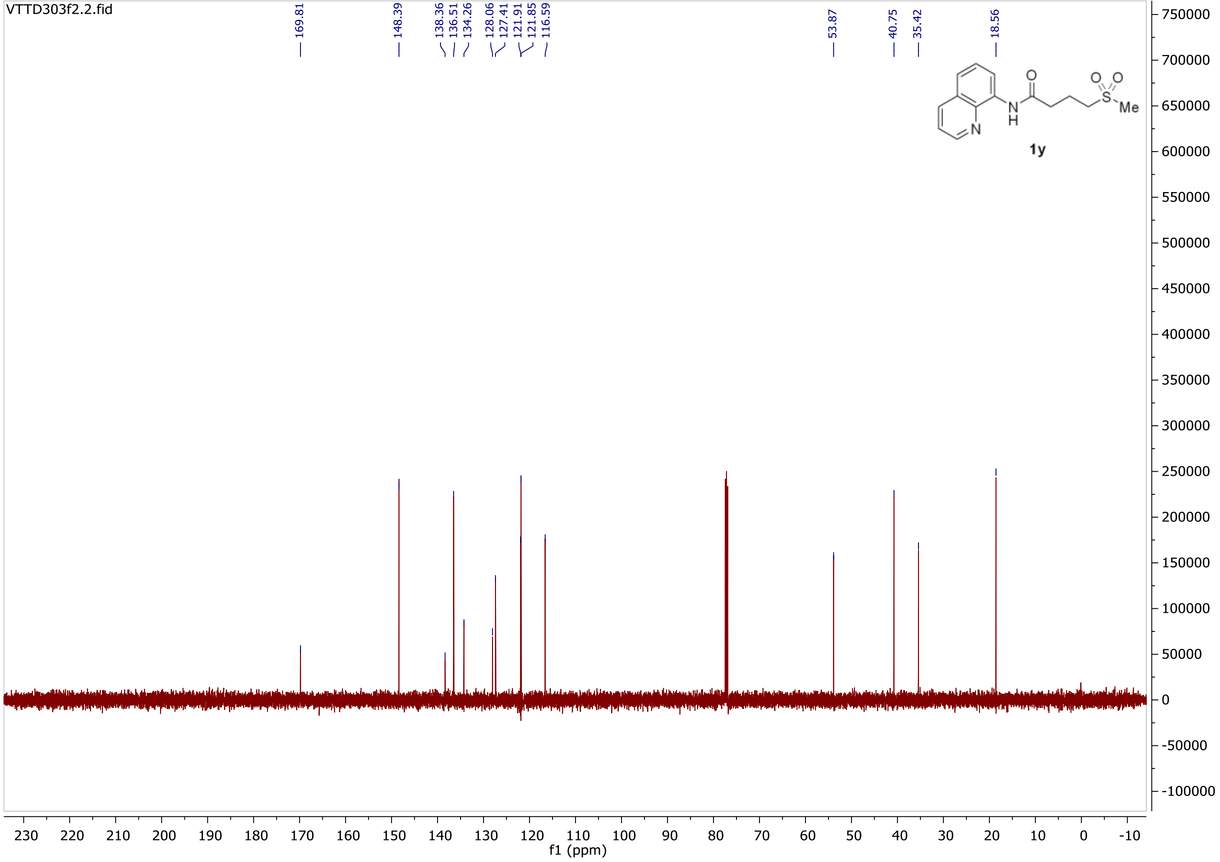

VTTC036f2f2.2.fid
C-13 Routine, BBO Probe, DRX-500
170.66
148.27
138.38
136.45
134.49
128.02
127.45
121.72
121.64
116.53
83.95
82.64
33.53
33.49
26.40
26.24
O
N
H
F
N
1w
4000
3500
3000
2500
2000
1500
1000
500
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

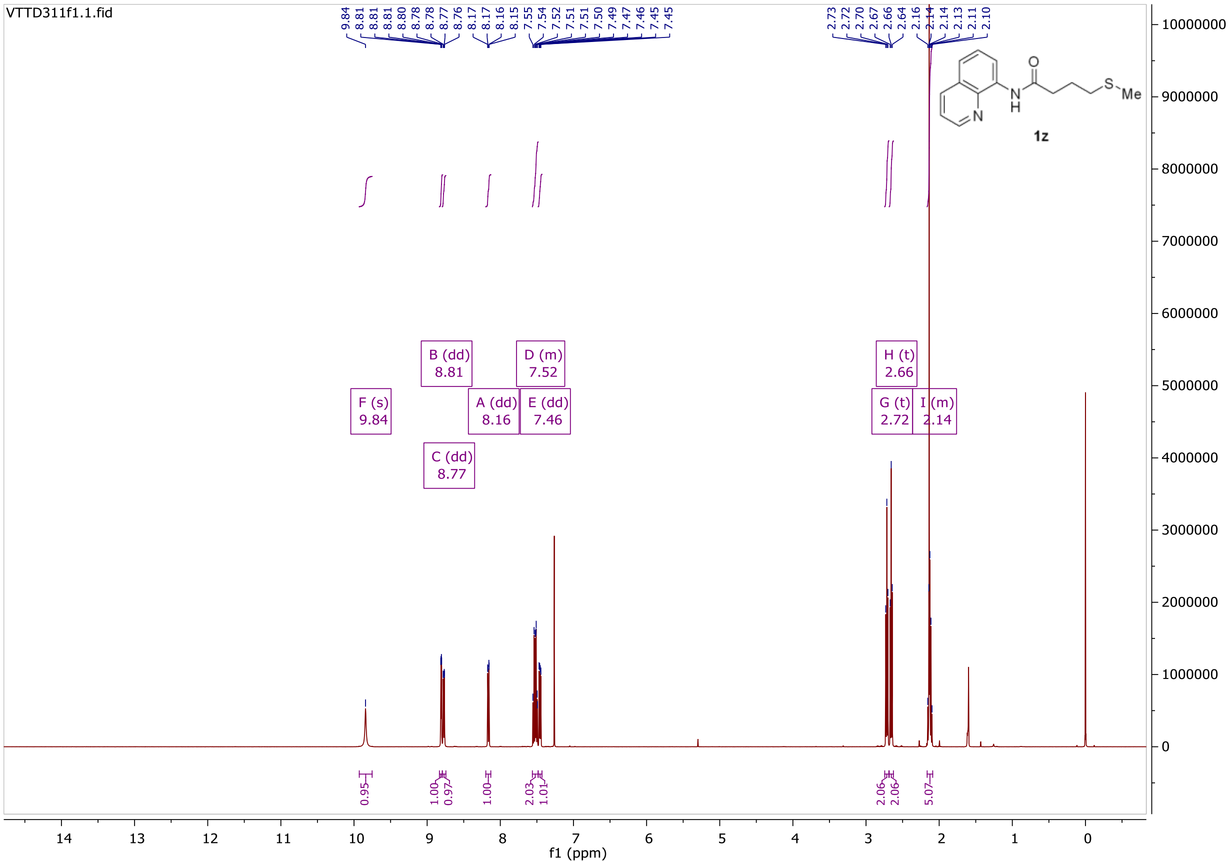

VTTD404f1r2.1.fid
F-19, CDCl3, DPX-400 QNP Probe. CF3Cl as Ref at 0 ppm.
-172.18
O
N
H
F
N
1w
400
350
300
250
200
150
100
50
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

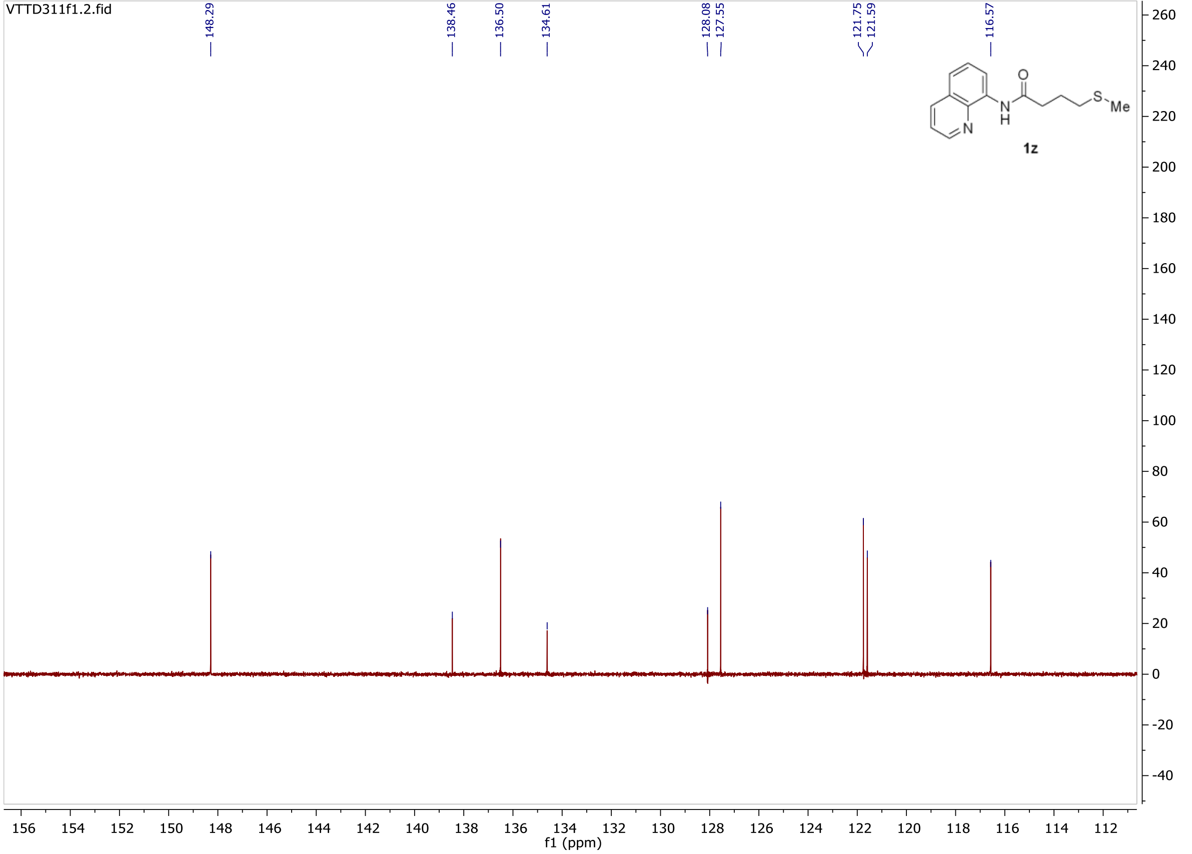

VTTD358f1.1.fid
9.86 8.82 8.81 8.81 8.81 8.75 8.74 8.73 8.73 8.18 8.18 8.17 8.16 7.55 7.54 7.54 7.53 7.53 7.52 7.51 7.51 7.48 7.47 7.46 7.46
2.95 2.93 2.93 2.92 2.91 2.90 2.89 2.87 2.87 2.86 2.86 2.85 2.84 2.84 2.83 2.82 2.82 2.81 2.81 2.80 2.79 2.79 2.78 2.77 2.76 2.61 2.34 2.33 2.33 2.32 2.31 2.30 2.29
O
N
H
N
O
S
Me
1x
J (s) 9.86
E (dd) 8.81
F (dd) 8.74
G (dd) 8.17
H (m) 7.53
I (dd) 7.47
B (m) 2.89
C (m) 2.80
D (s) 2.61
A (m) 2.32
0.94
0.98
0.96
0.98
1.99
0.98
2.07
2.00
2.98
2.01
12.5 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 -0.5 -1.0
f1 (ppm)
5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0

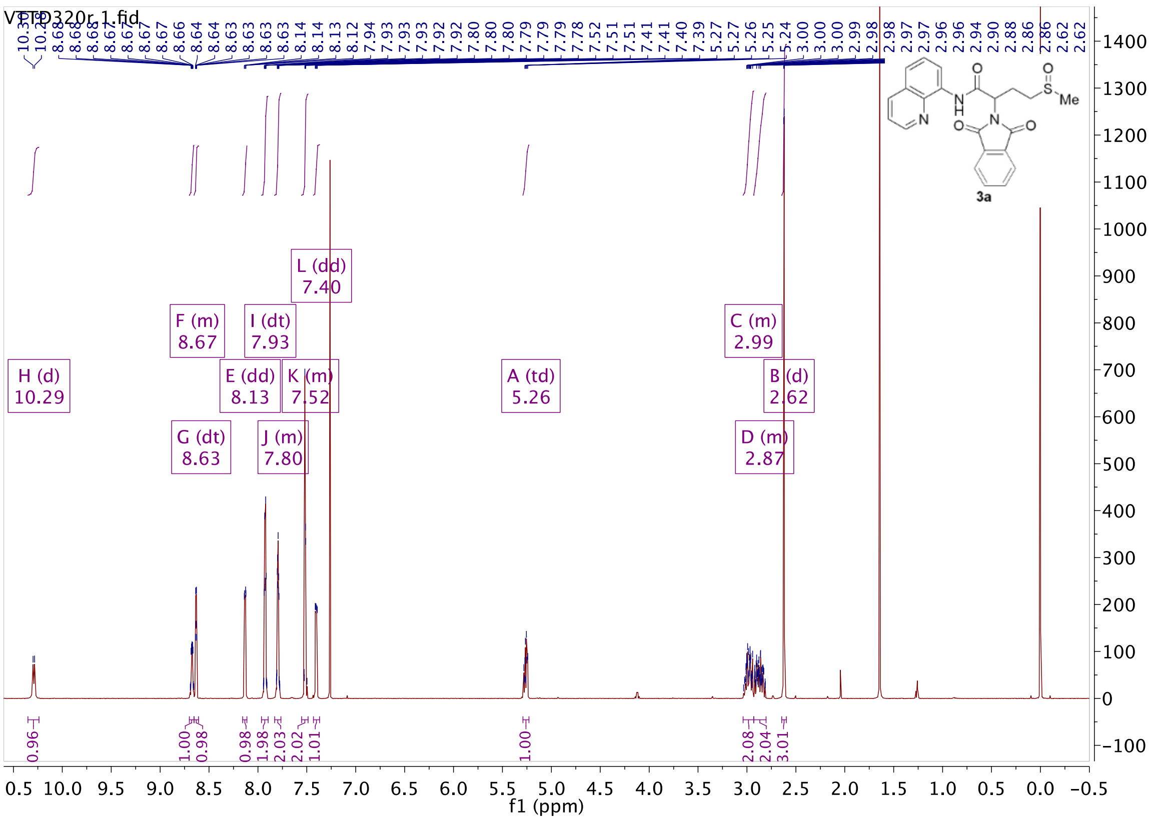

VTTD358r3.1.fid
170.20
148.38
138.40 136.52 134.36
128.07 127.46 121.84 116.61
53.80
38.78 36.18
18.79
O
N
H
N
O
S
Me
1x
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20 0 -20

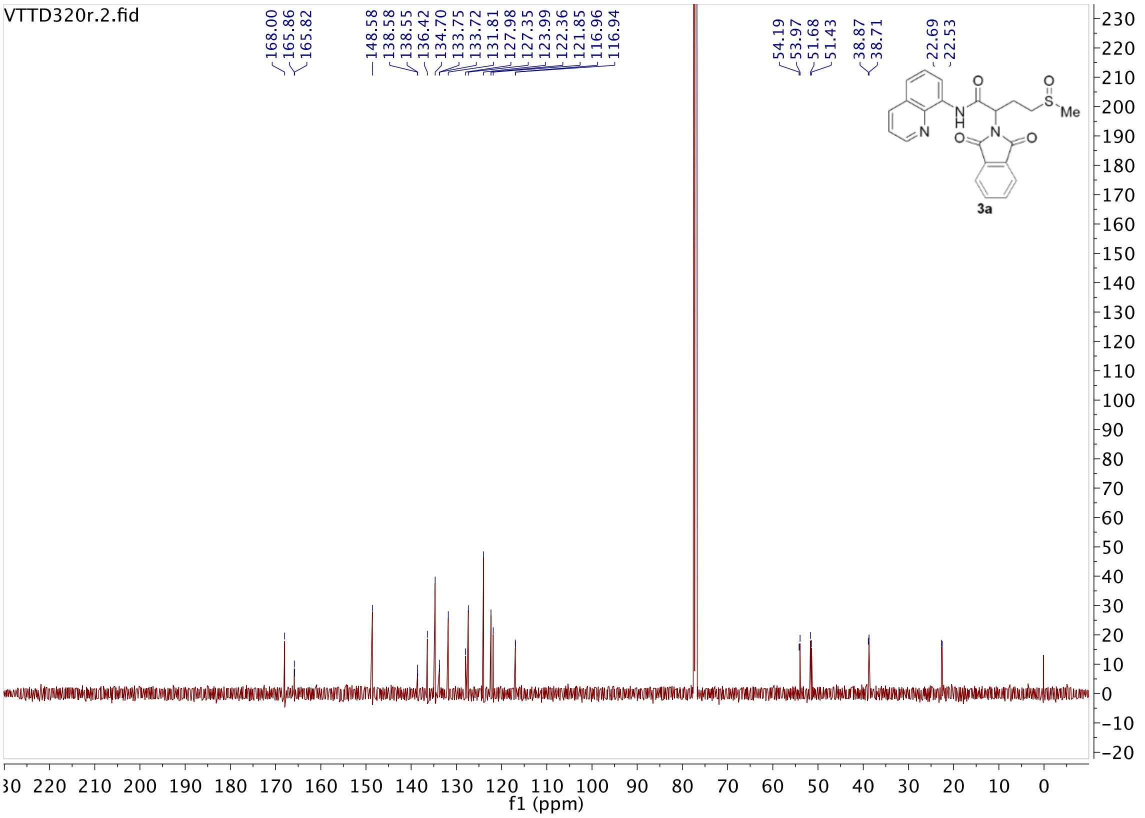

VTTD303r.1.fid
9.85
8.81
8.81
8.81
8.80
8.73
8.73
8.72
8.72
8.18
8.18
8.17
8.16
7.56
7.54
7.53
7.53
7.53
7.52
7.51
7.48
7.47
7.47
7.46
3.25
3.23
3.22
2.96
2.84
2.83
2.81
2.38
2.37
2.37
2.36
2.35
2.35
2.34
J (s) 9.85
G (dd) 8.72
F (dd) 8.81
E (dd) 8.17
I (dd) 7.47
H (m) 7.53
B (s) 2.96
A (m) 3.23
D (m) 2.36
C (t) 2.83
0.93
0.97
0.96
0.98
1.98
0.99
2.00
2.99
2.00
2.01
N
H
O
O
O
S
Me
N
1y
f1 (ppm)
12.5
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
-0.5
-1.0
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0

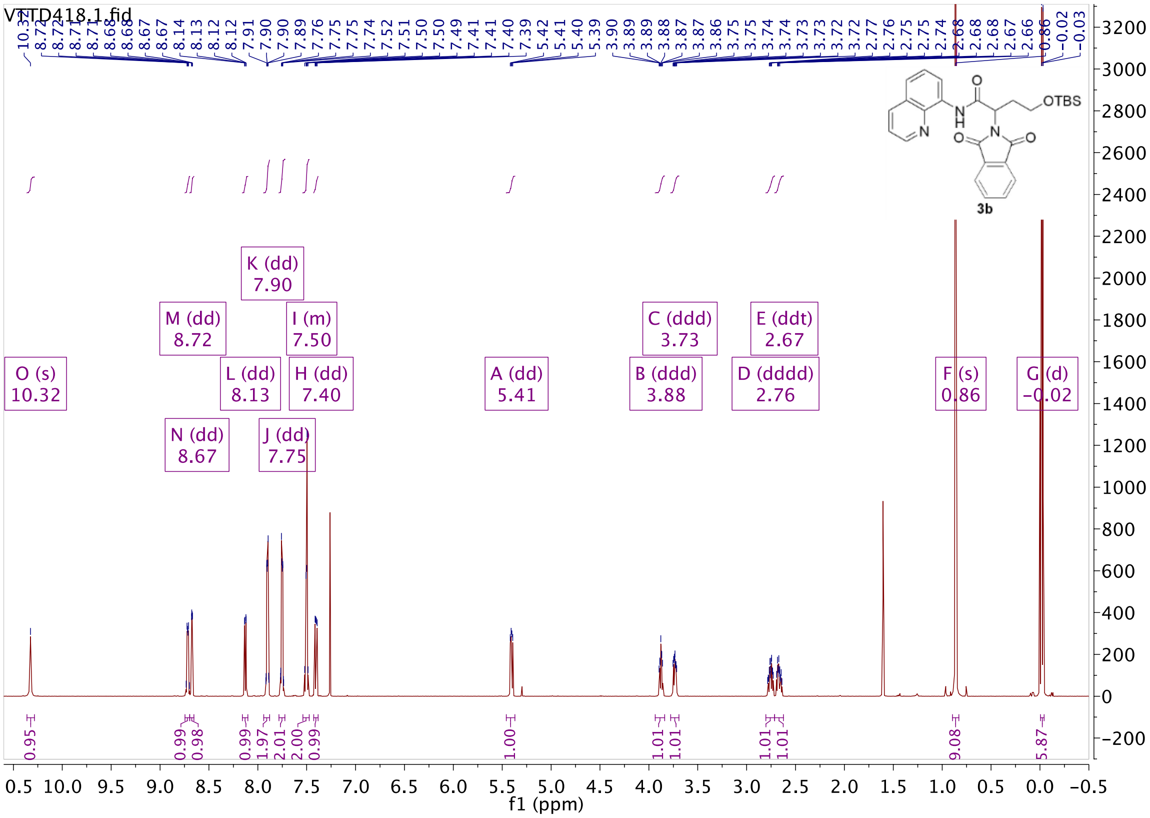

VTTD303f2.2.fid
169.81
148.39
138.36
136.51
134.26
128.06
127.41
121.91
121.85
116.59
53.87
40.75
35.42
18.56
N
H
O
O
O
S
Me
N
1y
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
750000
700000
650000
600000
550000
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
-50000
-100000

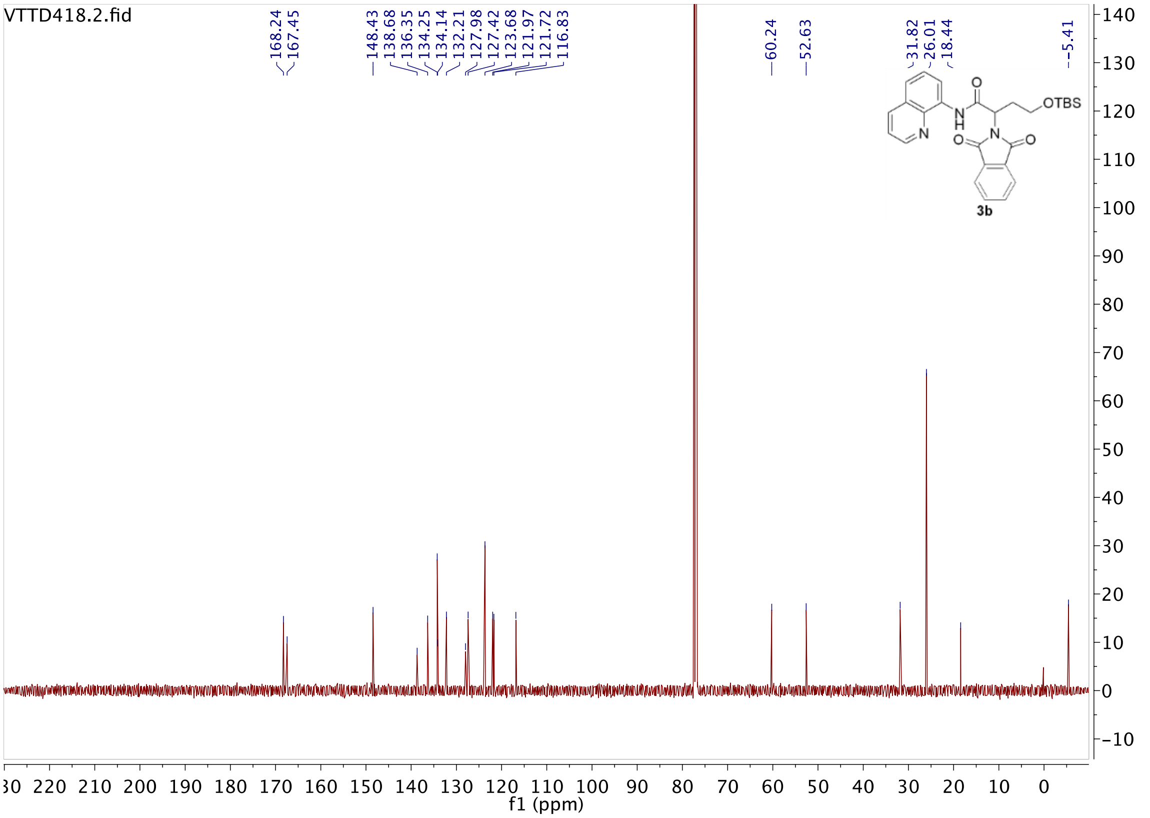

VTTD311f1.1.fid
9.84 8.81 8.81 8.81 8.80 8.78 8.77 8.76 8.17 8.17 8.16 8.15 7.55 7.54 7.52 7.51 7.51 7.50 7.49 7.47 7.46 7.45 7.45
2.73 2.72 2.70 2.67 2.66 2.64 2.16 2.14 2.14 2.13 2.11 2.10
F (s) 9.84
B (dd) 8.81
C (dd) 8.77
A (dd) 8.16
D (m) 7.52
E (dd) 7.46
H (t) 2.66
G (t) 2.72
I (m) 2.14
0.95 1.00 0.97 1.00 2.03 1.01 2.06 2.06 5.07
N
H
O
S
Me
N
1z
f1 (ppm)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
10000000 9000000 8000000 7000000 6000000 5000000 4000000 3000000 2000000 1000000 0

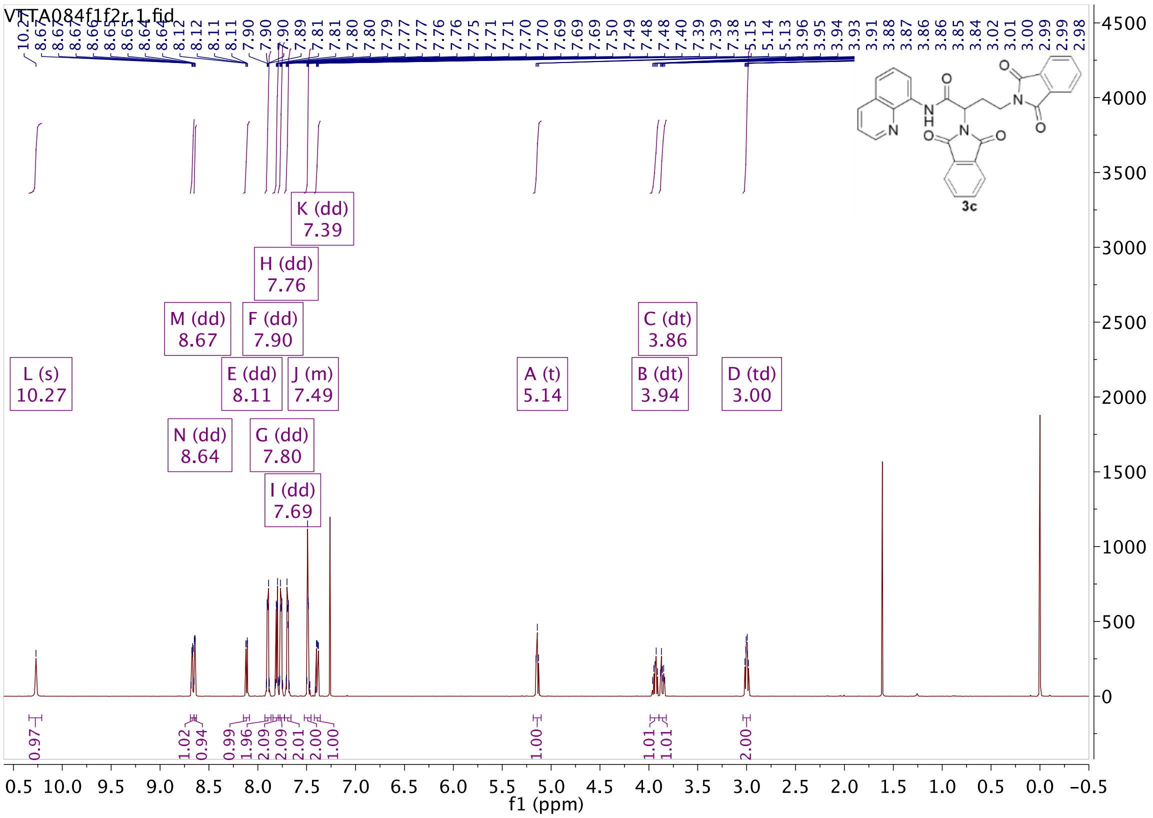

VTTD311f1.2.fid
148.29
138.46
136.50
134.61
128.08
127.55
121.75
121.59
116.57
N
H
O
S
Me
N
1z
f1 (ppm)
156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120 118 116 114 112
260 240 220 200 180 160 140 120 100 80 60 40 20 0 -20 -40

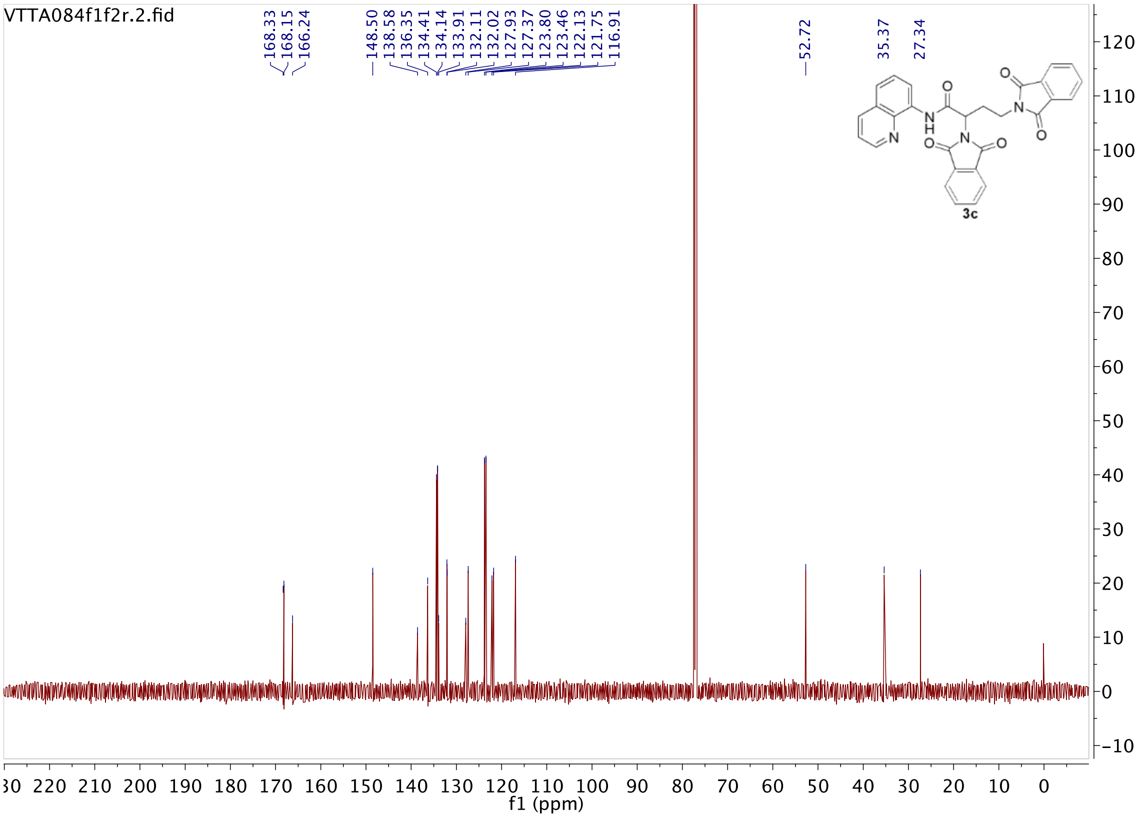

VTTD320r.1.fid
10.29
8.68
8.68
8.67
8.67
8.67
8.67
8.66
8.64
8.64
8.63
8.63
8.63
8.63
8.14
8.14
8.13
8.12
7.94
7.93
7.93
7.93
7.92
7.92
7.80
7.80
7.80
7.79
7.79
7.79
7.78
7.52
7.51
7.51
7.41
7.41
7.40
7.39
5.27
5.26
5.25
5.24
3.00
3.00
3.00
2.99
2.98
2.98
2.97
2.97
2.96
2.96
2.94
2.90
2.88
2.86
2.86
2.62
2.62
2.62
L (dd) 7.40
F (m) 8.67
I (dt) 7.93
C (m) 2.99
H (d) 10.29
E (dd) 8.13
K (m) 7.52
A (td) 5.26
B (d) 2.62
G (dt) 8.63
J (m) 7.80
D (m) 2.87
0.96
1.00
0.98
0.98
1.98
2.03
2.02
1.01
1.00
2.08
2.04
3.01
f1 (ppm)
N
H
N
O
O
O
N
O
S
Me
3a

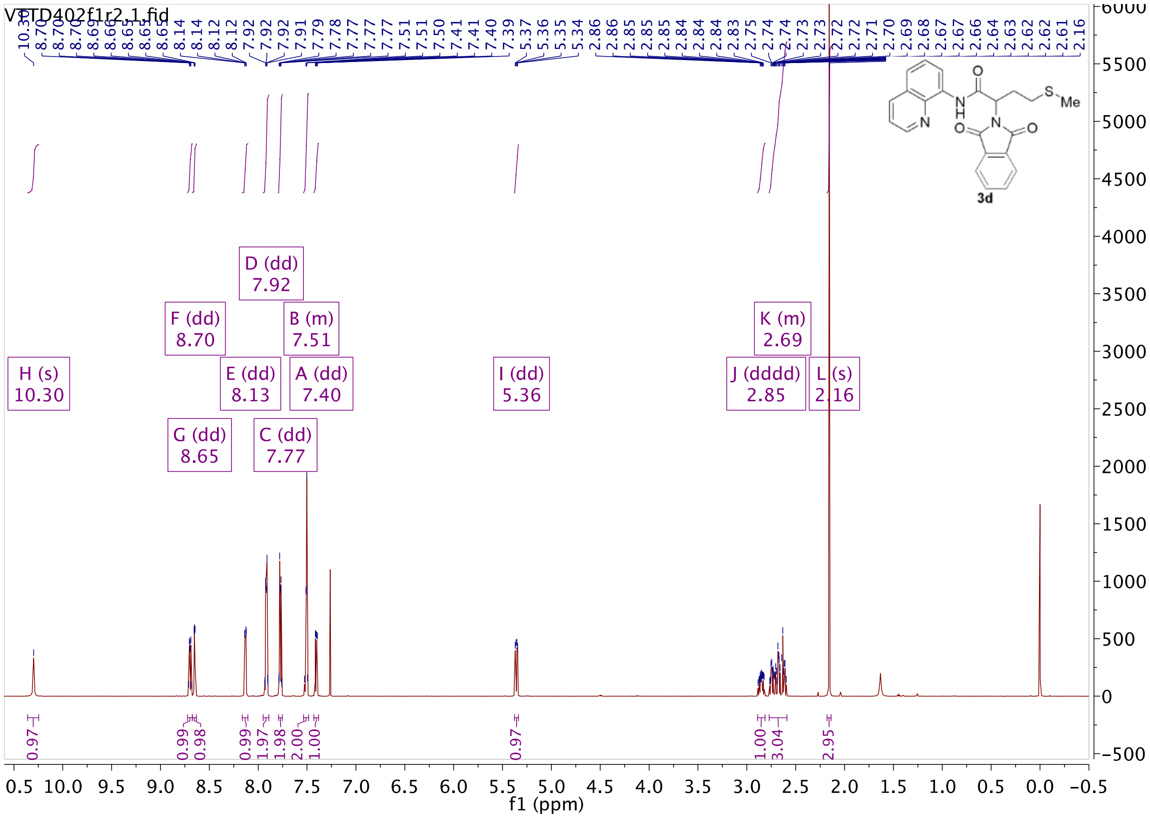

VTTD320r.2.fid
168.00
165.86
165.82
148.58
138.58
138.55
136.42
134.70
133.75
133.72
131.81
127.98
127.35
123.99
122.36
121.85
116.96
116.94
54.19
53.97
51.68
51.43
38.87
38.71
22.69
22.53
f1 (ppm)
N
H
N
O
O
O
N
O
S
Me
3a

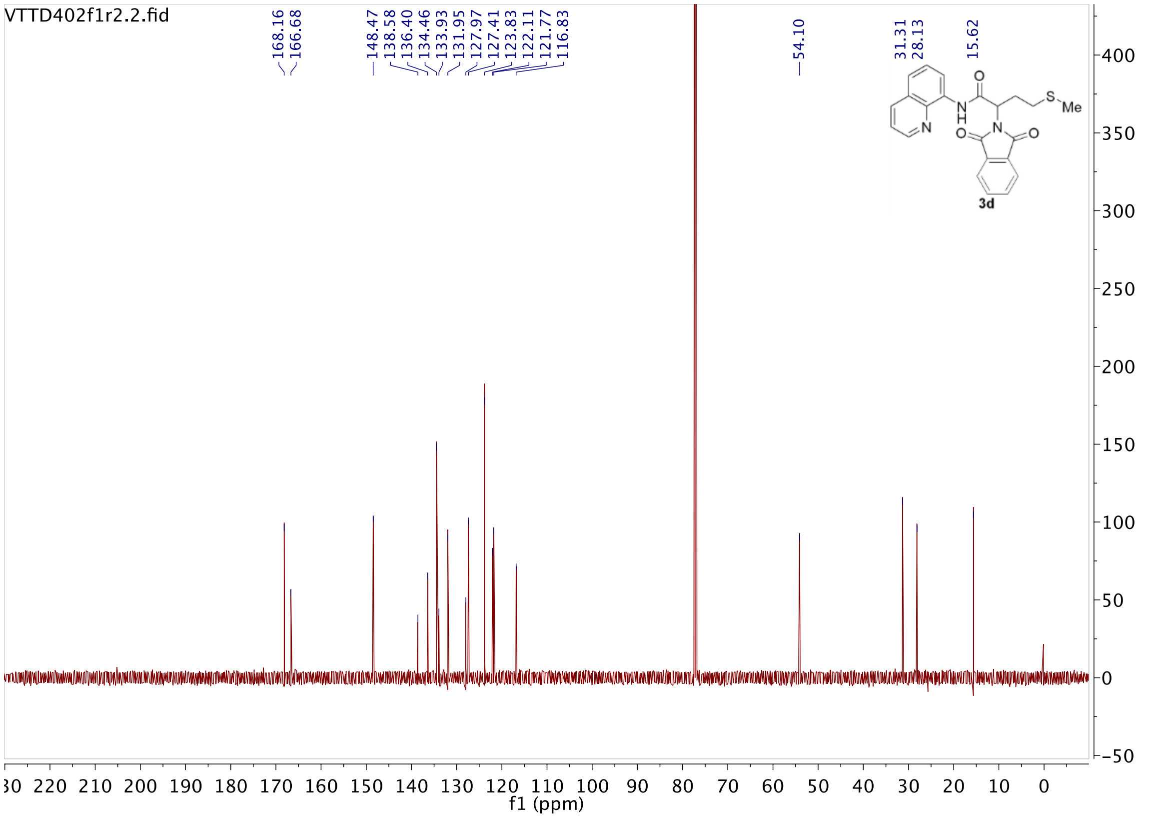

VTTD418.1.fid
10.32
8.72
8.72
8.71
8.71
8.68
8.68
8.67
8.67
8.14
8.13
8.13
8.12
7.91
7.90
7.90
7.89
7.76
7.75
7.75
7.74
7.52
7.51
7.50
7.50
7.49
7.41
7.40
7.39
5.42
5.41
5.40
5.39
3.90
3.89
3.89
3.88
3.87
3.87
3.86
3.75
3.75
3.74
3.74
3.73
3.73
3.72
3.72
2.77
2.76
2.75
2.75
2.74
2.68
2.68
2.68
2.67
2.66
0.86
-0.02
-0.03
O
N
H
N
O
O
N
OTBS
3b
K (dd) 7.90
M (dd) 8.72
I (m) 7.50
C (ddd) 3.73
E (ddt) 2.67
O (s) 10.32
L (dd) 8.13
H (dd) 7.40
A (dd) 5.41
B (ddd) 3.88
D (dddd) 2.76
F (s) 0.86
G (d) -0.02
N (dd) 8.67
J (dd) 7.75
0.95
0.99
0.98
0.99
1.97
2.01
2.00
0.99
1.00
1.01
1.01
1.01
1.01
9.08
5.87
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
0.5
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
f1 (ppm)

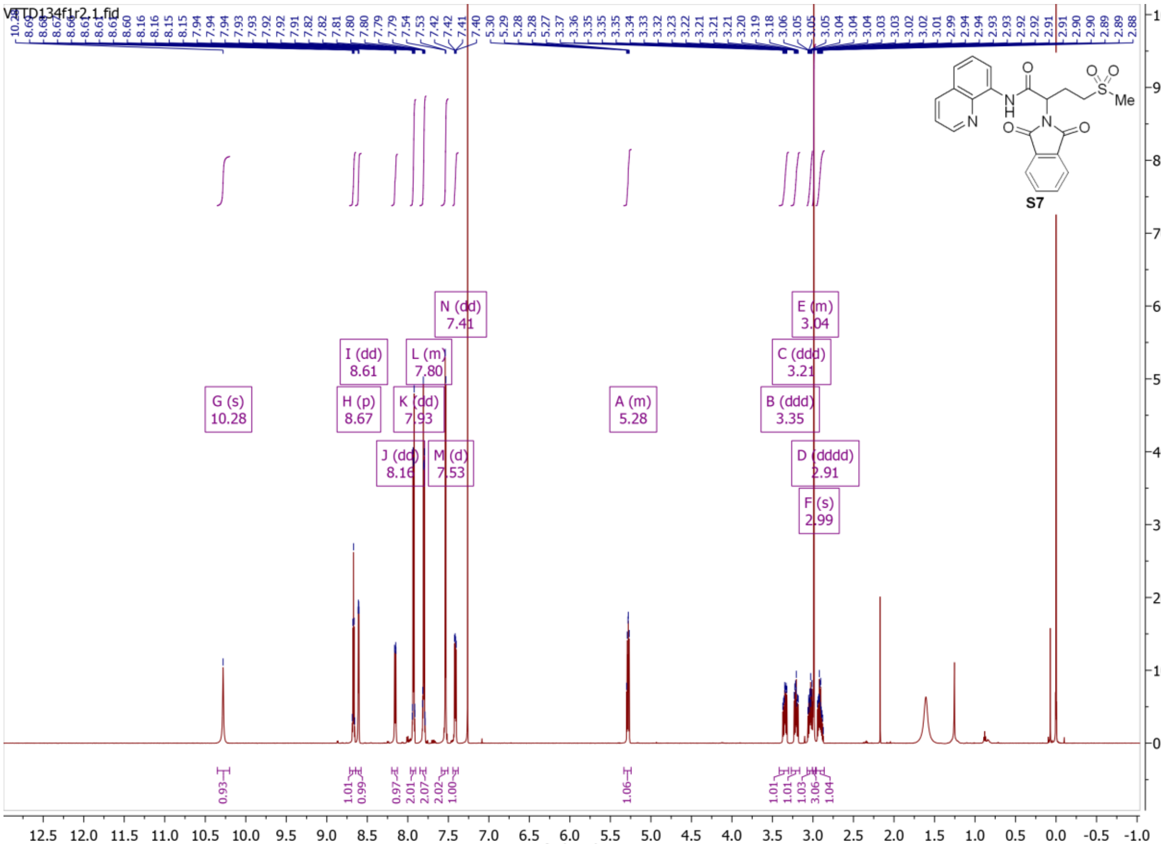

VTTD418.2.fid
168.24
167.45
148.43
138.68
136.35
134.25
134.14
132.21
127.98
127.42
123.68
121.97
121.72
116.83
60.24
52.63
31.82
26.01
18.44
-5.41
O
N
H
N
O
O
N
OTBS
3b
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

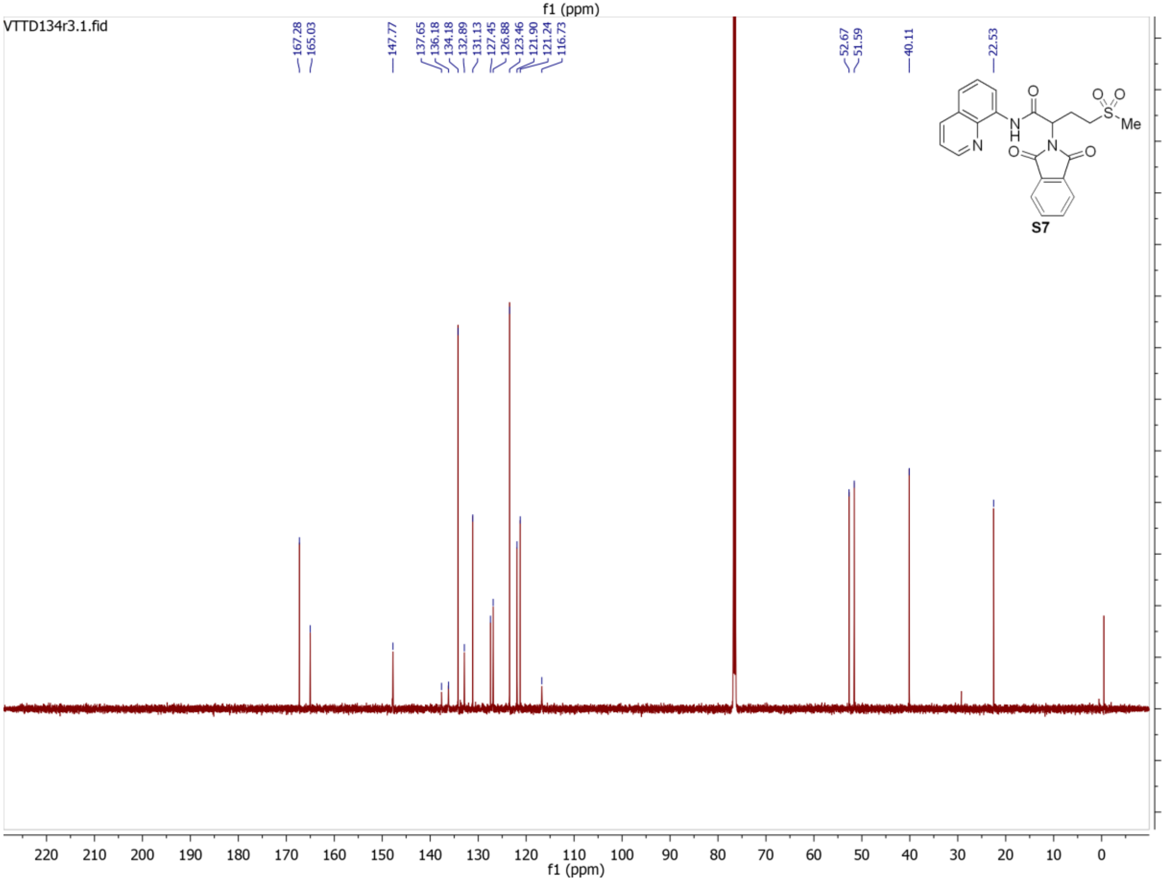

VTTA084f1f2r.1.fid
10.27
8.67
8.65
8.64
8.12
8.11
7.90
7.89
7.81
7.80
7.79
7.77
7.76
7.75
7.71
7.70
7.69
7.50
7.49
7.48
7.40
7.39
7.38
5.15
5.14
5.13
3.96
3.95
3.94
3.93
3.91
3.88
3.87
3.86
3.85
3.84
3.02
3.01
3.00
2.99
2.98
K (dd) 7.39
H (dd) 7.76
M (dd) 8.67
F (dd) 7.90
C (dt) 3.86
L (s) 10.27
E (dd) 8.11
J (m) 7.49
A (t) 5.14
B (dt) 3.94
D (td) 3.00
N (dd) 8.64
G (dd) 7.80
I (dd) 7.69
0.97
1.02
0.94
0.99
1.96
2.09
2.09
2.01
2.00
1.00
1.00
1.01
1.01
2.00
3c
f1 (ppm)

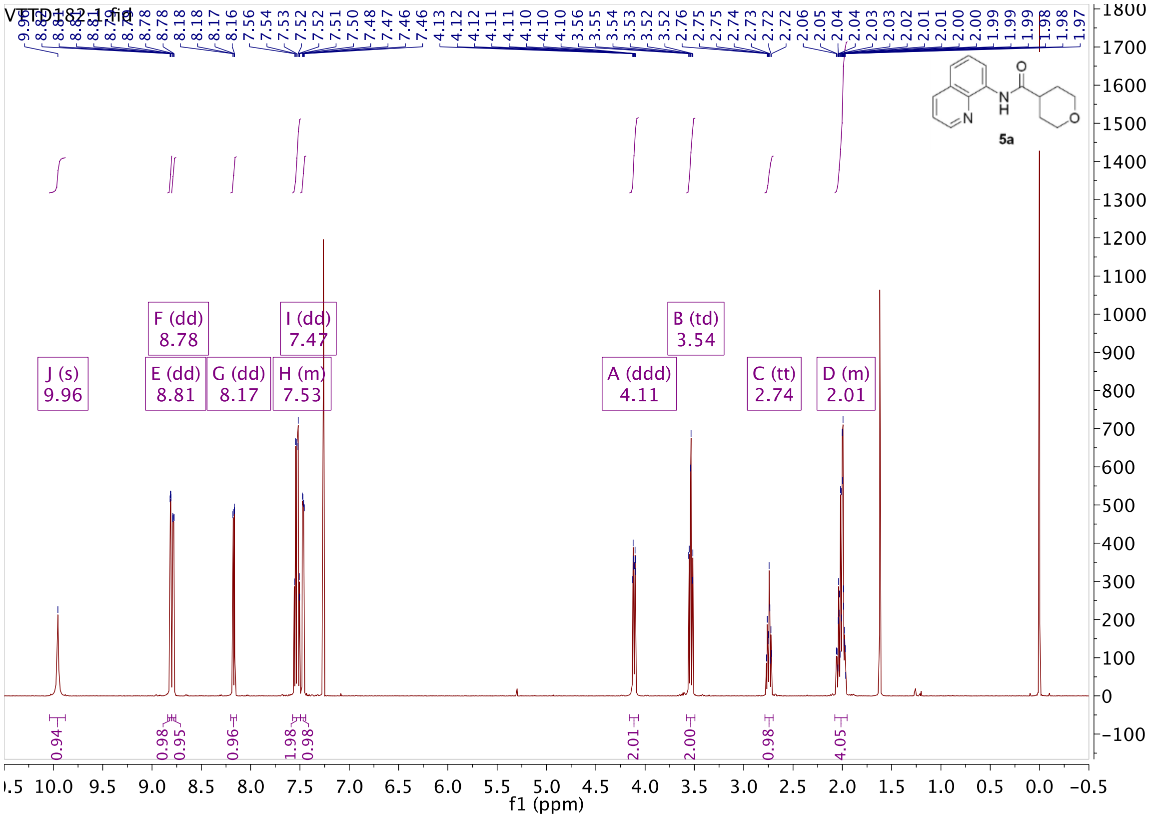

VTTA084f1f2r.2.fid
168.33
168.15
166.24
148.50
138.58
136.35
134.41
134.14
133.91
132.11
132.02
127.93
127.37
123.80
123.46
122.13
121.75
116.91
52.72
35.37
27.34
3c
f1 (ppm)

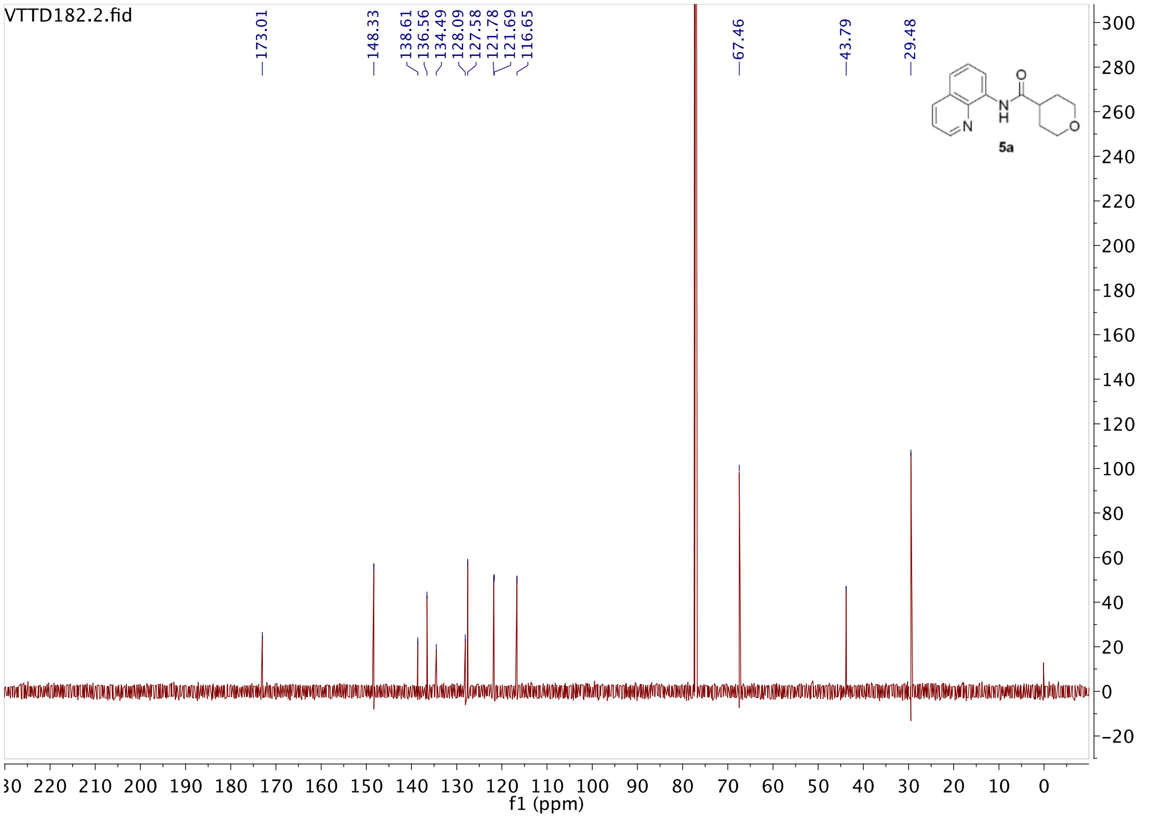

VTTD402f1r2.1.fid
10.30 8.70 8.70 8.70 8.69 8.66 8.65 8.65 8.65 8.14 8.14 8.12 8.12 7.92 7.92 7.92 7.91 7.79 7.78 7.77 7.77 7.77 7.51 7.51 7.50 7.41 7.41 7.40 7.39 5.37 5.36 5.35 5.34 2.86 2.86 2.85 2.85 2.85 2.84 2.84 2.84 2.83 2.75 2.74 2.74 2.73 2.73 2.72 2.72 2.71 2.70 2.69 2.68 2.67 2.67 2.66 2.64 2.63 2.62 2.62 2.61 2.16
O
N
H
S
Me
N
O
N
O
3d
D (dd)
7.92
F (dd)
8.70
B (m)
7.51
K (m)
2.69
H (s)
10.30
E (dd)
8.13
A (dd)
7.40
I (dd)
5.36
J (dddd)
2.85
L (s)
2.16
G (dd)
8.65
C (dd)
7.77
0.97
0.99
0.98
0.99
1.97
1.98
2.00
1.00
0.97
1.00
3.04
2.95
0.5 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
f1 (ppm)
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
−500

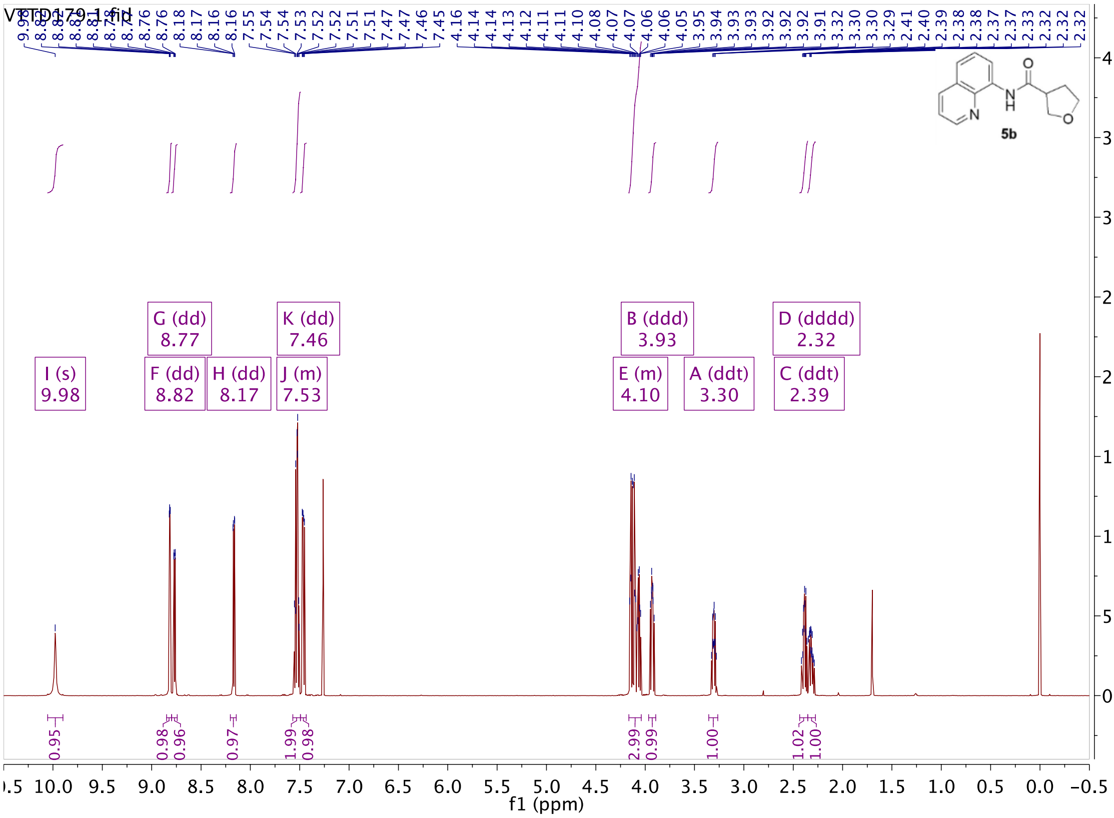

VTTD402f1r2.2.fid
168.16 166.68
148.47 138.58 136.40 134.46 133.93 131.95 127.97 127.41 123.83 122.11 121.77 116.83
54.10
31.31 28.13
15.62
O
N
H
S
Me
N
O
N
O
3d
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
400
350
300
250
200
150
100
50
0
−50

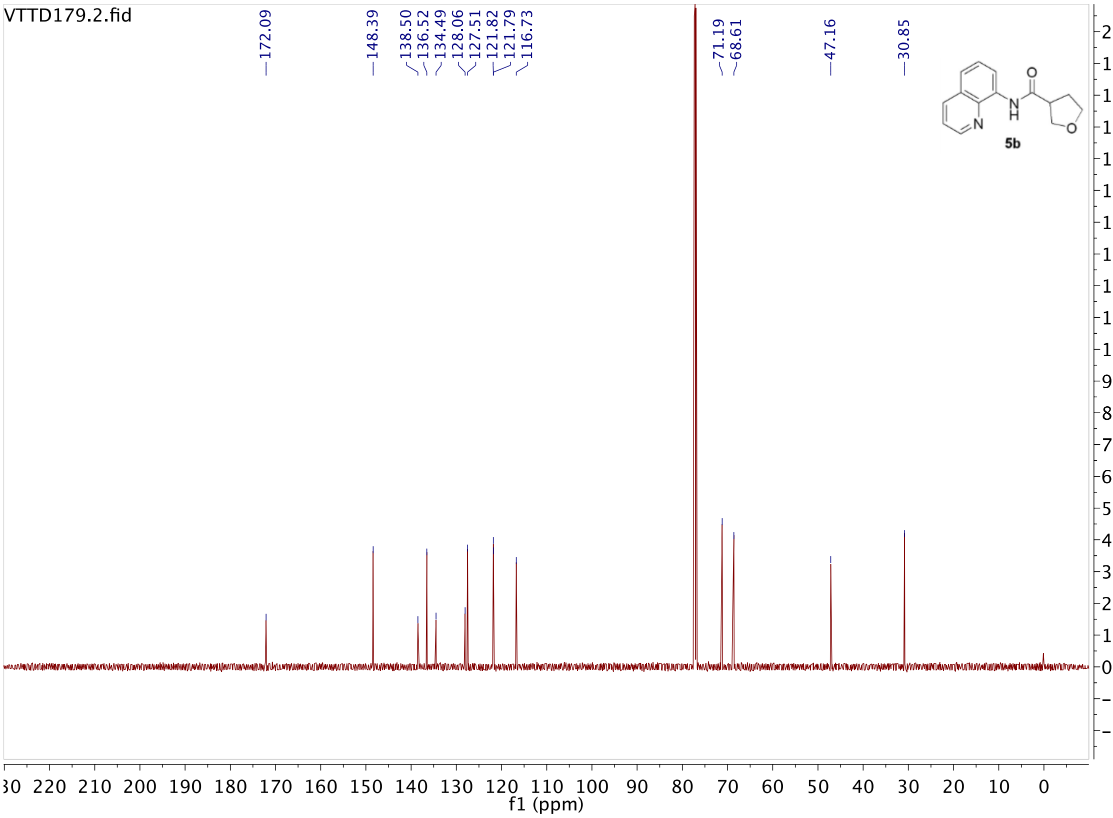

VTTD134f1r2.1.fid
G (s) 10.28
H (p) 8.67
I (dd) 8.61
J (dd) 8.16
K (dd) 7.93
L (m) 7.80
M (d) 7.53
N (dd) 7.41
A (m) 5.28
B (ddd) 3.35
C (ddd) 3.21
E (m) 3.04
F (s) 2.99
D (dddd) 2.91
0.93
1.01
0.99
0.97
2.01
2.07
2.02
1.00
1.06
1.01
1.01
1.03
3.06
1.04
f1 (ppm)
S7
Me

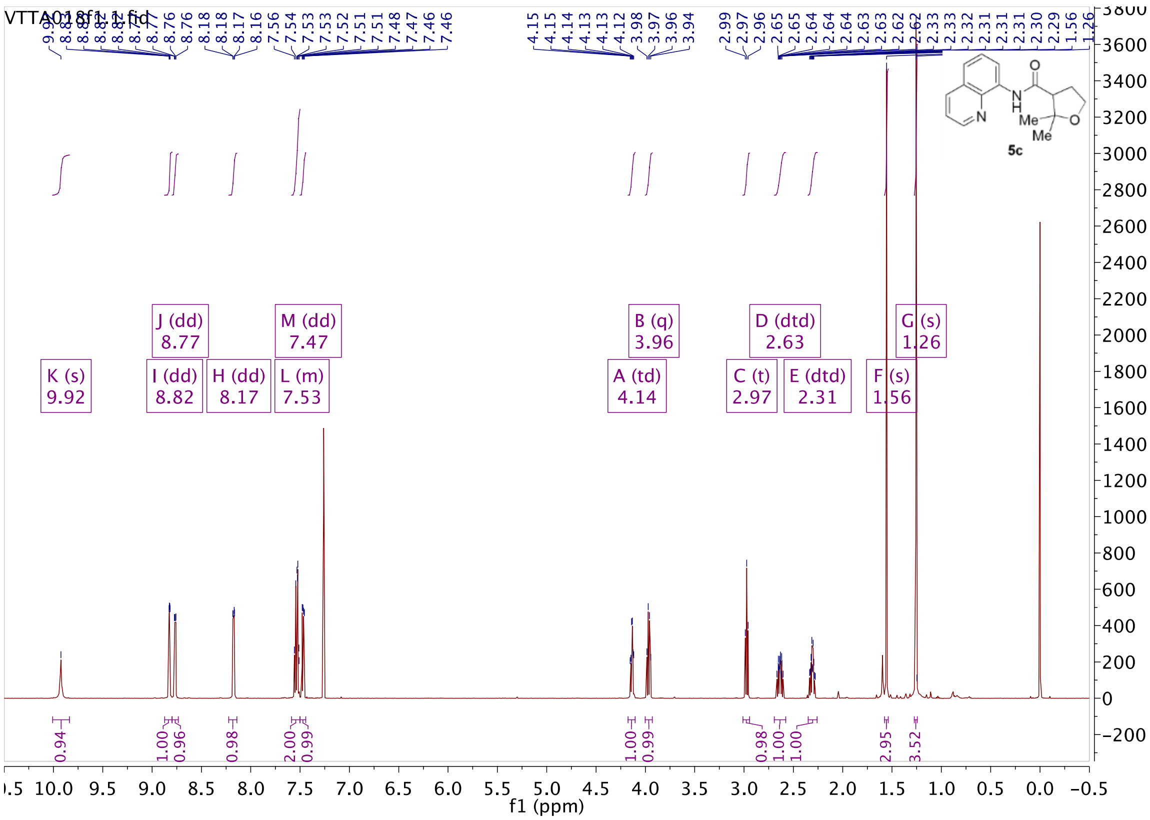

VTTD134r3.1.fid
167.28
165.03
147.77
137.65
136.18
134.18
132.89
131.13
127.45
126.88
123.46
121.90
121.24
116.73
52.67
51.59
40.11
22.53
f1 (ppm)
S7
Me

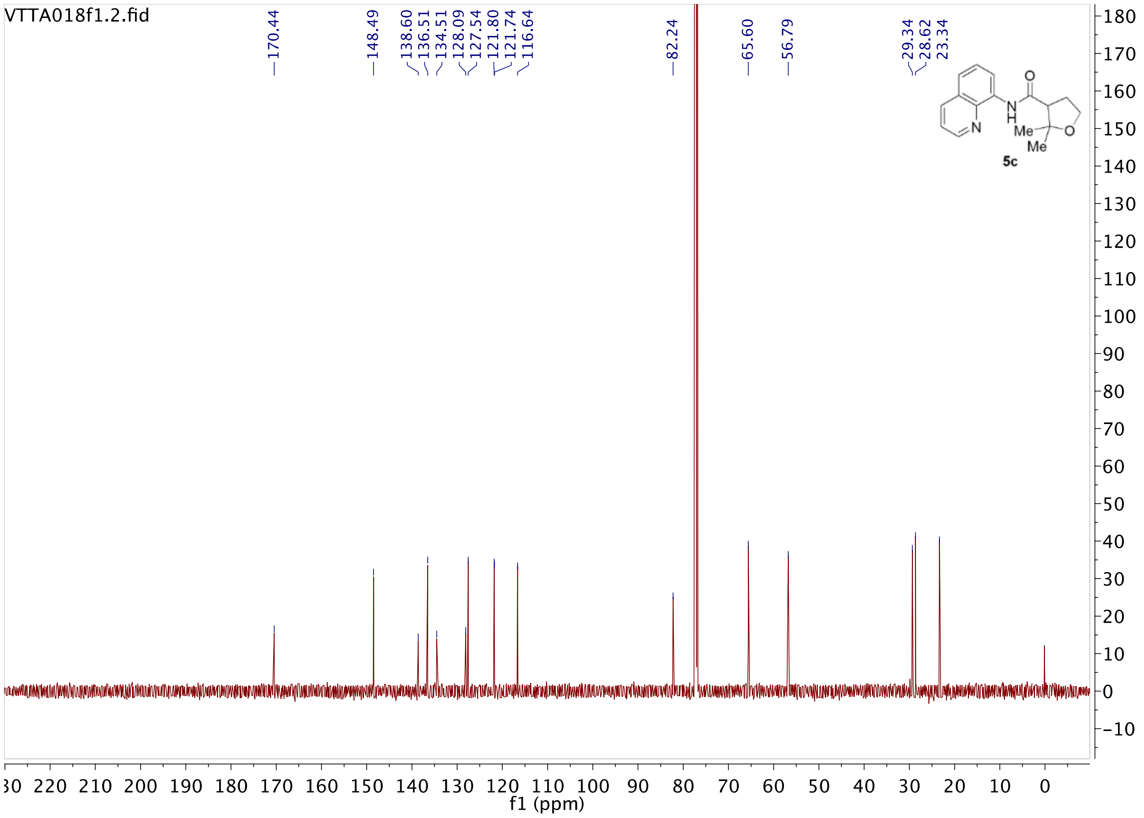

VTTD182.1.fid
7.56
7.54
7.53
7.52
7.52
7.51
7.50
7.48
7.47
7.46
4.13
4.12
4.12
4.11
4.11
4.10
4.10
3.56
3.55
3.54
3.53
3.52
2.76
2.75
2.75
2.74
2.73
2.72
2.06
2.05
2.04
2.04
2.03
2.03
2.02
2.01
2.01
2.00
2.00
1.99
1.99
1.99
1.98
1.98
1.97
J (s) 9.96
E (dd) 8.81
F (dd) 8.78
G (dd) 8.17
H (m) 7.53
I (dd) 7.47
A (ddd) 4.11
B (td) 3.54
C (tt) 2.74
D (m) 2.01
0.94
0.98
0.95
0.96
1.98
0.98
2.01
2.00
0.98
4.05
O
N
H
N
O
5a
f1 (ppm)

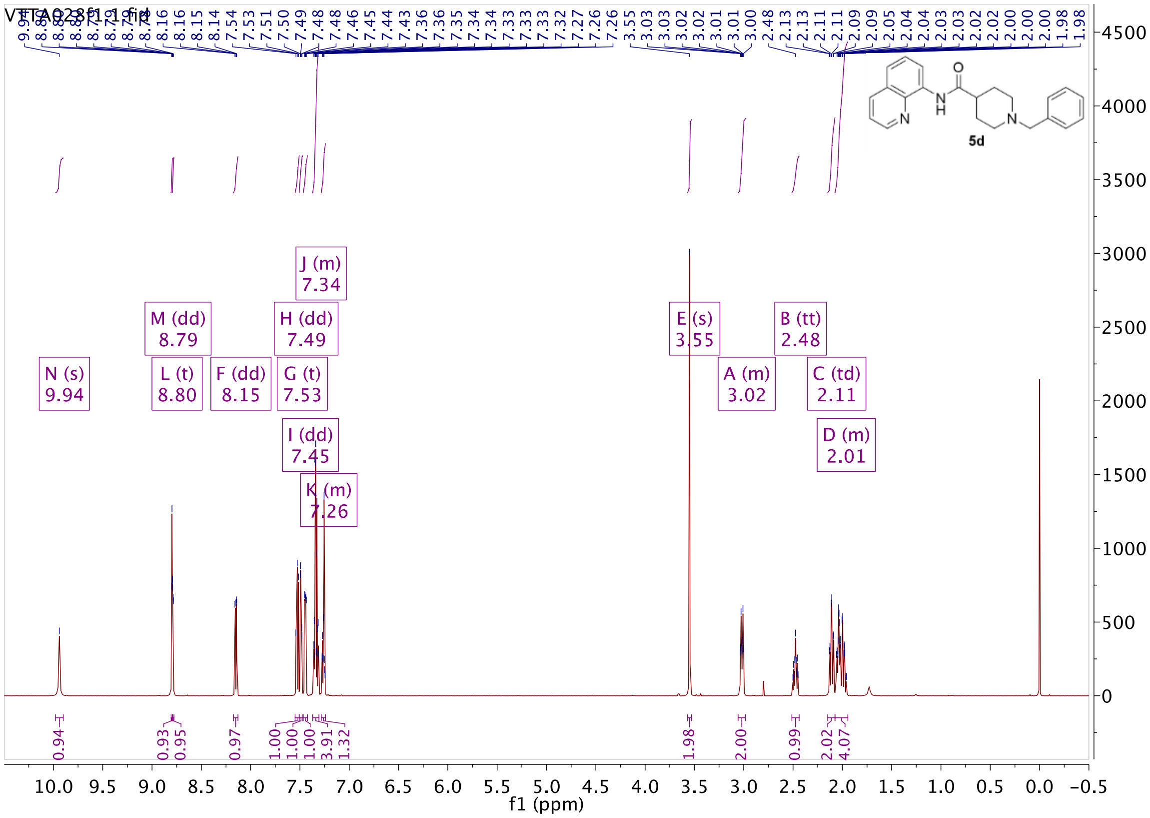

VTTD182.2.fid
173.01
148.33
138.61
136.56
134.49
128.09
127.58
121.78
121.69
116.65
67.46
43.79
29.48
O
N
H
N
O
5a
f1 (ppm)


VTTD179.1.fid
I (s) 9.98
F (dd) 8.82
G (dd) 8.77
H (dd) 8.17
J (m) 7.53
K (dd) 7.46
E (m) 4.10
B (ddd) 3.93
A (ddt) 3.30
C (ddt) 2.39
D (dddd) 2.32
5b
f1 (ppm)

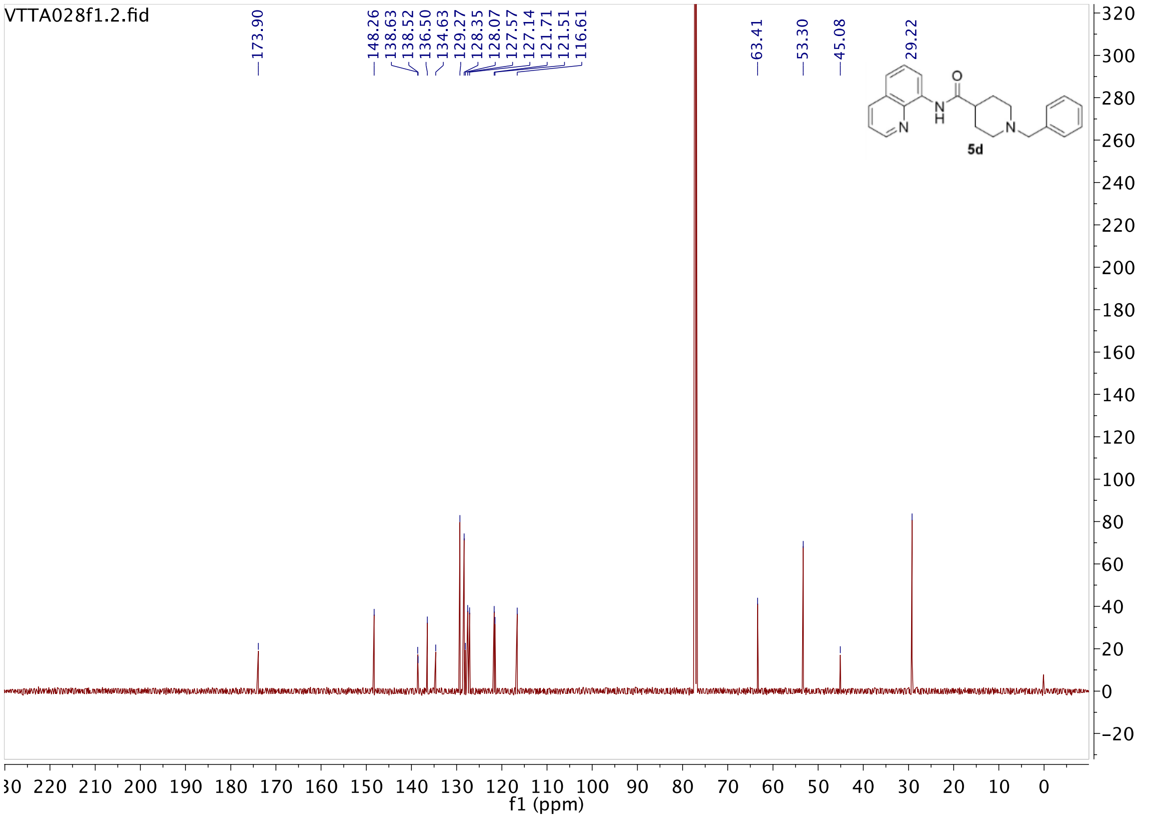

VTTD179.2.fid
172.09
148.39
138.50
136.52
134.49
128.06
127.51
121.82
121.79
116.73
71.19
68.61
47.16
30.85
5b
f1 (ppm)


VTTA018f1.1.fid
9.92
8.82
8.77
8.76
8.18
8.17
8.16
7.56
7.54
7.53
7.52
7.51
7.48
7.47
7.46
4.15
4.14
4.13
4.12
3.98
3.97
3.96
3.94
2.99
2.97
2.96
2.65
2.64
2.63
2.62
2.33
2.32
2.31
2.30
2.29
1.56
1.26
K (s) 9.92
I (dd) 8.82
J (dd) 8.77
H (dd) 8.17
L (m) 7.53
M (dd) 7.47
A (td) 4.14
B (q) 3.96
C (t) 2.97
D (dtd) 2.63
E (dtd) 2.31
F (s) 1.56
G (s) 1.26
0.94
1.00
0.96
0.98
2.00
0.99
1.00
0.99
0.98
1.00
1.00
2.95
3.52
O
N
H
N
Me
Me
O
5c
f1 (ppm)

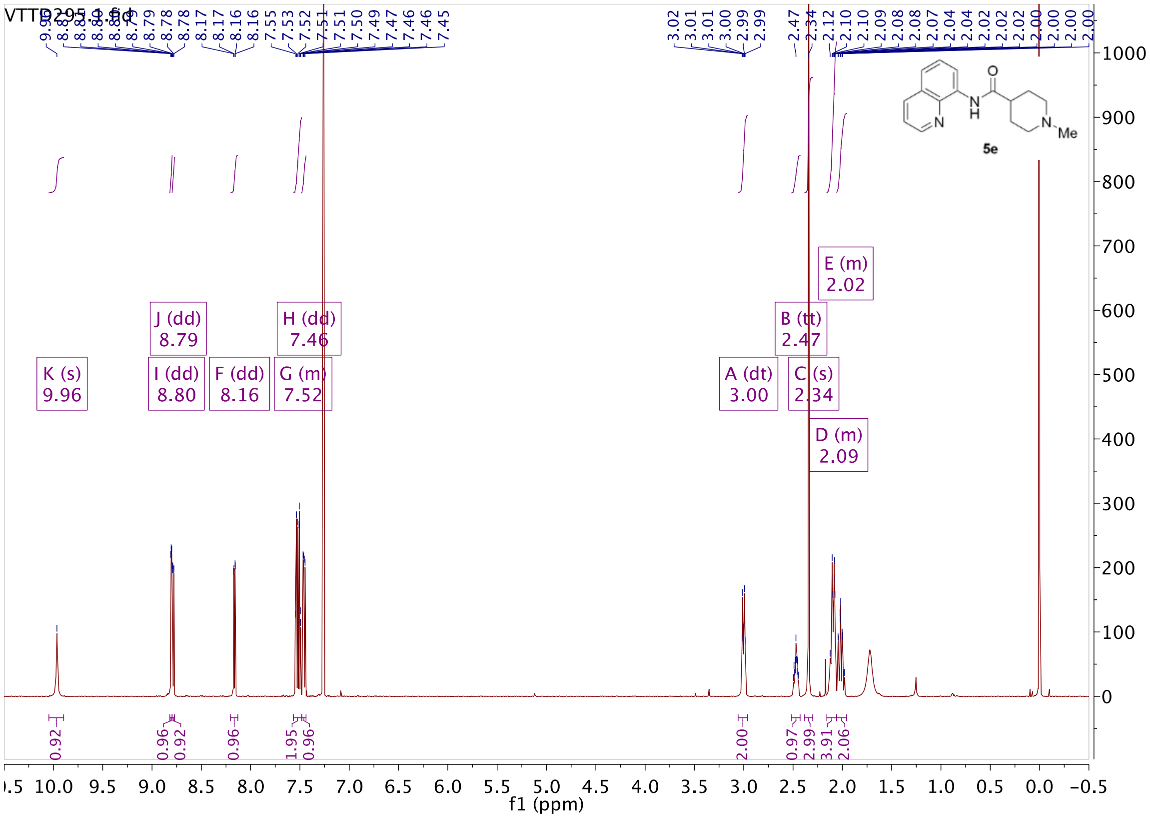

VTTA018f1.2.fid
170.44
148.49
138.60
136.51
134.51
128.09
127.54
121.80
121.74
116.64
82.24
65.60
56.79
29.34
28.62
23.34
O
N
H
N
Me
Me
O
5c
f1 (ppm)

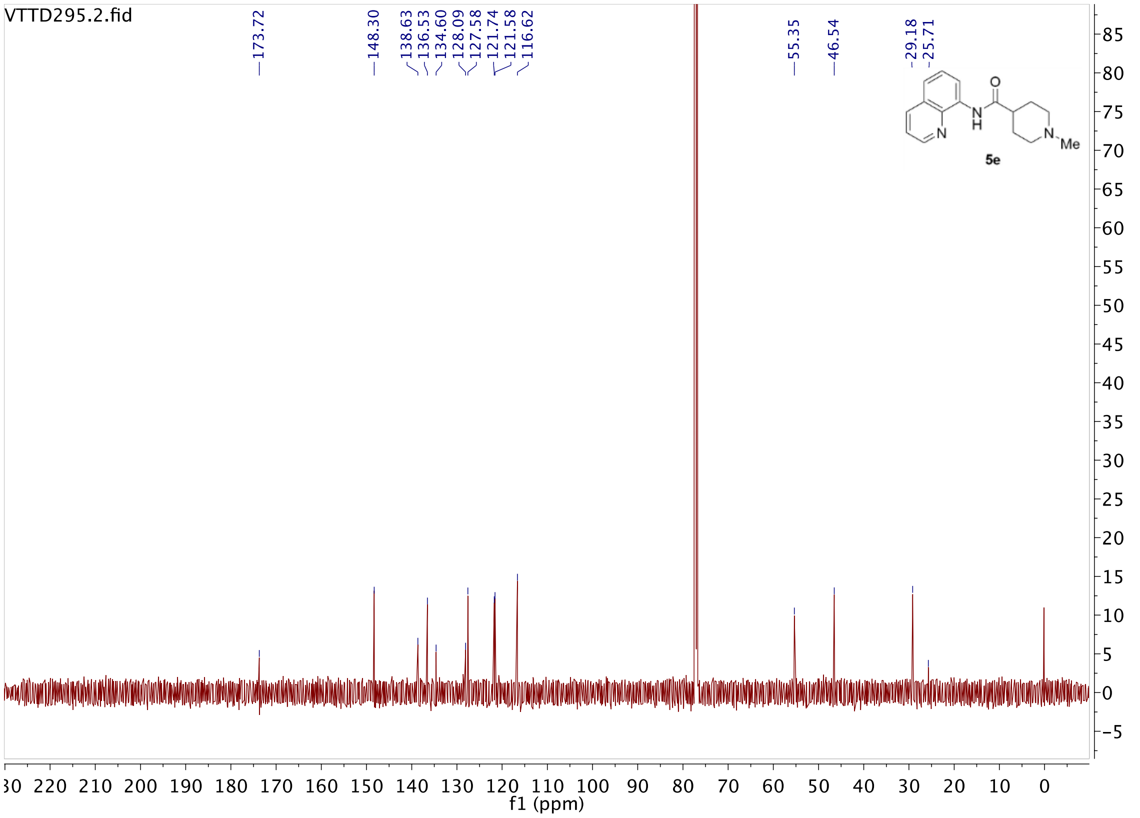


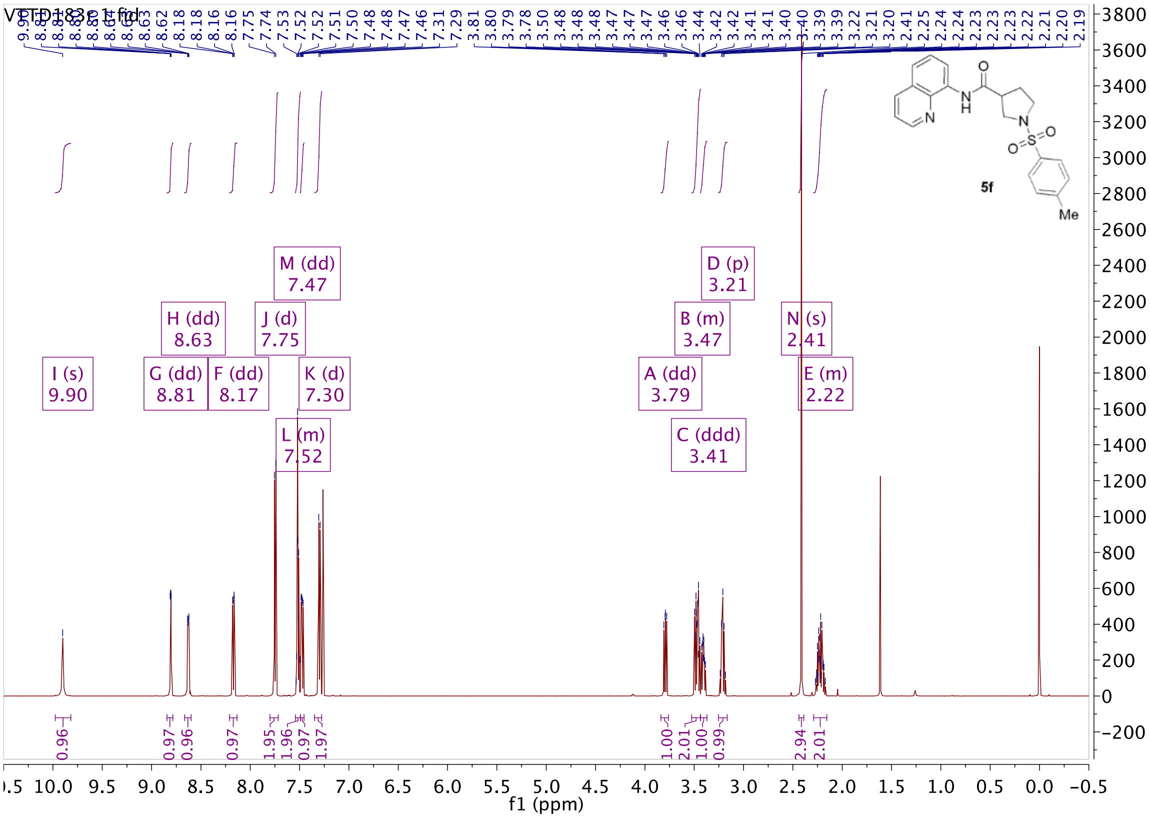
VTTA028f1.1.fid
8.16
8.16
8.15
8.14
7.54
7.53
7.51
7.50
7.49
7.48
7.48
7.46
7.45
7.44
7.43
7.36
7.36
7.35
7.34
7.34
7.33
7.33
7.33
7.32
7.27
7.26
7.26
3.55
3.03
3.03
3.02
3.02
3.01
3.01
3.00
2.48
2.13
2.13
2.11
2.11
2.09
2.09
2.05
2.04
2.04
2.03
2.03
2.02
2.02
2.00
2.00
2.00
1.98
1.98
O
N
H
N
N
5d
N (s) 9.94
M (dd) 8.79
L (t) 8.80
F (dd) 8.15
J (m) 7.34
H (dd) 7.49
G (t) 7.53
I (dd) 7.45
K (m) 7.26
E (s) 3.55
A (m) 3.02
B (tt) 2.48
C (td) 2.11
D (m) 2.01
0.94
0.93
0.95
0.97
1.00
1.00
1.00
3.91
1.32
1.98
2.00
0.99
2.02
4.07
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
f1 (ppm)
4500
4000
3500
3000
2500
2000
1500
1000
500
0

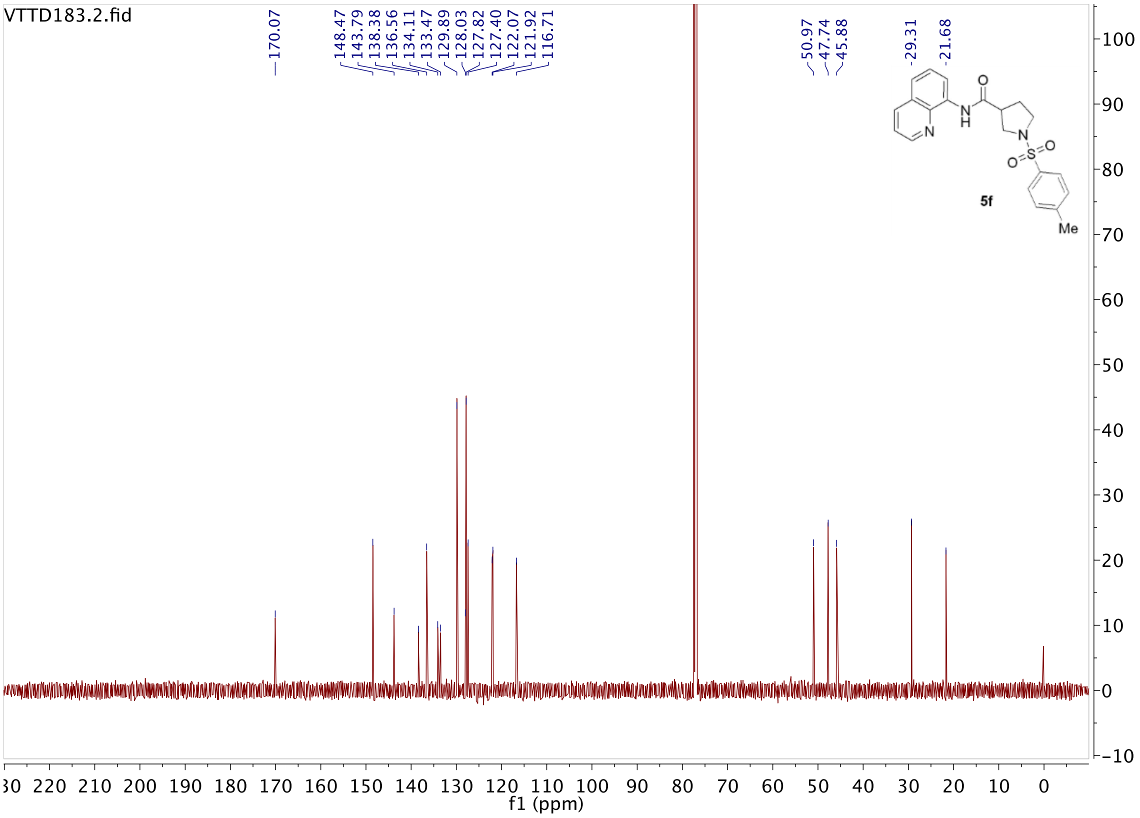


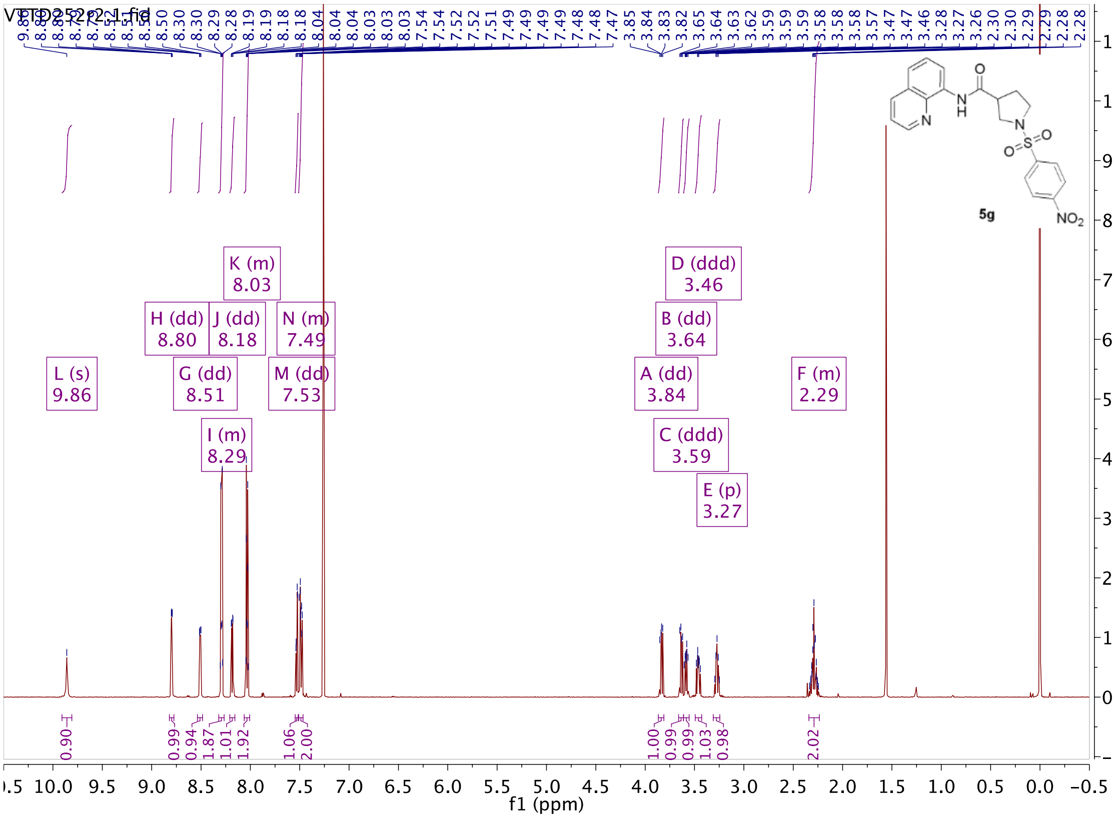
VTTA028f1.2.fid
173.90
148.26
138.63
138.52
136.50
134.63
129.27
128.35
128.07
127.57
127.14
121.71
121.51
116.61
63.41
53.30
45.08
29.22
O
N
H
N
N
5d
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
−20

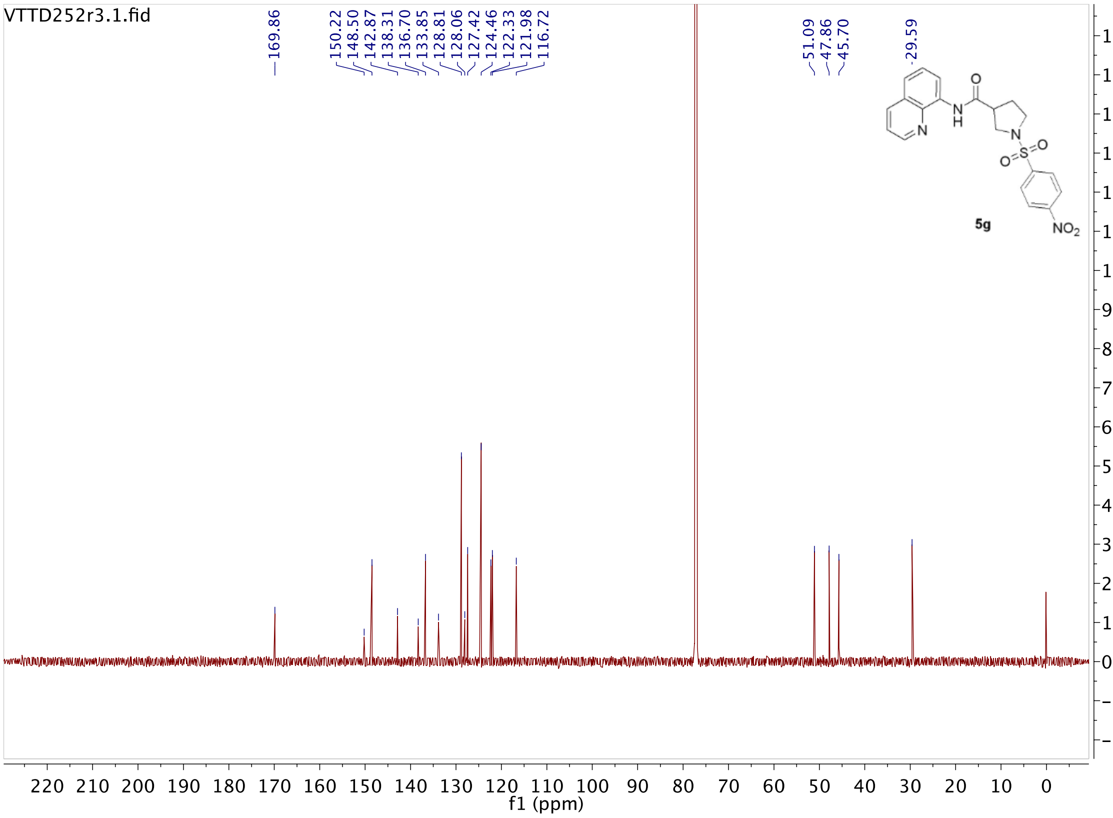

VTTD295.1.fid
8.80
8.80
8.79
8.79
8.78
8.17
8.17
8.16
8.16
7.55
7.53
7.52
7.51
7.51
7.50
7.49
7.47
7.46
7.46
7.45
3.02
3.01
3.01
3.00
2.99
2.99
2.47
2.34
2.12
2.10
2.09
2.08
2.07
2.04
2.04
2.02
2.02
2.02
2.00
2.00
2.00
2.00
K (s)
9.96
J (dd)
8.79
I (dd)
8.80
F (dd)
8.16
H (dd)
7.46
G (m)
7.52
A (dt)
3.00
B (tt)
2.47
C (s)
2.34
D (m)
2.09
E (m)
2.02
0.92
0.96
0.92
0.96
1.95
0.96
2.00
0.97
2.99
3.91
2.06
f1 (ppm)
O
N
H
N
N
Me
5e

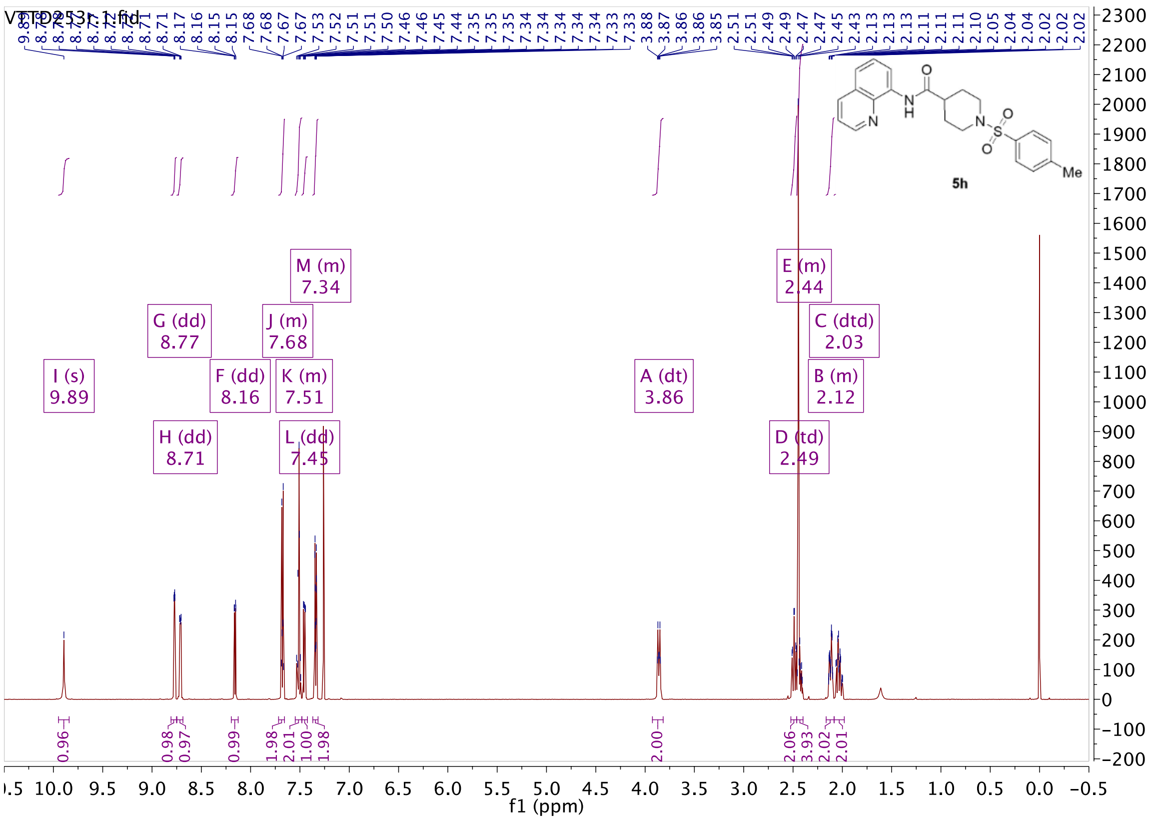

VTTD295.2.fid
173.72
148.30
138.63
136.53
134.60
128.09
127.58
121.74
121.58
116.62
55.35
46.54
29.18
25.71
f1 (ppm)
O
N
H
N
N
Me
5e

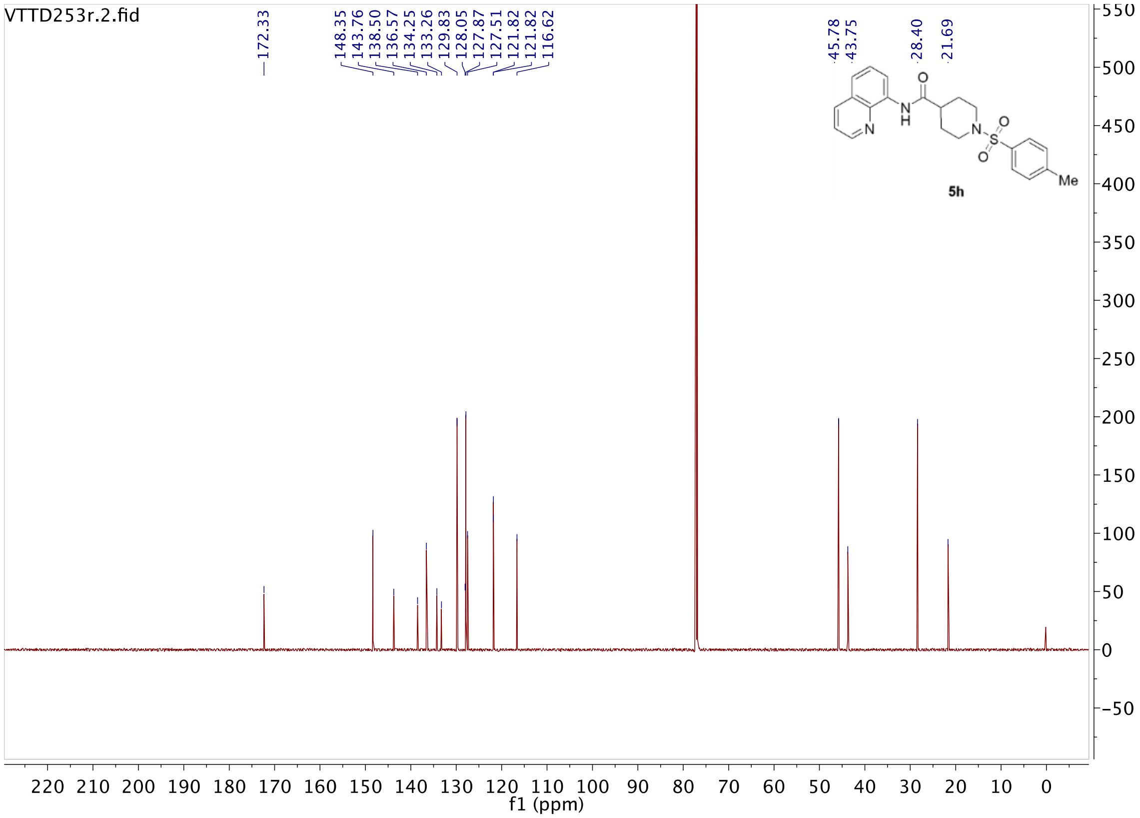

VTTD183c.1.fid
8.63
8.62
8.18
8.18
8.16
8.16
7.75
7.74
7.53
7.52
7.52
7.51
7.50
7.48
7.48
7.47
7.46
7.31
7.29
3.81
3.80
3.79
3.78
3.50
3.48
3.48
3.47
3.47
3.47
3.46
3.46
3.44
3.42
3.42
3.41
3.41
3.40
3.40
3.39
3.39
3.22
3.21
3.20
2.41
2.25
2.24
2.24
2.23
2.23
2.23
2.22
2.22
2.21
2.20
2.19
5f
Me
I (s) 9.90
G (dd) 8.81
H (dd) 8.63
F (dd) 8.17
J (d) 7.75
M (dd) 7.47
L (m) 7.52
K (d) 7.30
A (dd) 3.79
B (m) 3.47
C (ddd) 3.41
D (p) 3.21
N (s) 2.41
E (m) 2.22
0.96
0.97
0.96
0.97
1.95
1.96
0.97
1.97
1.00
2.01
1.00
0.99
2.94
2.01
f1 (ppm)

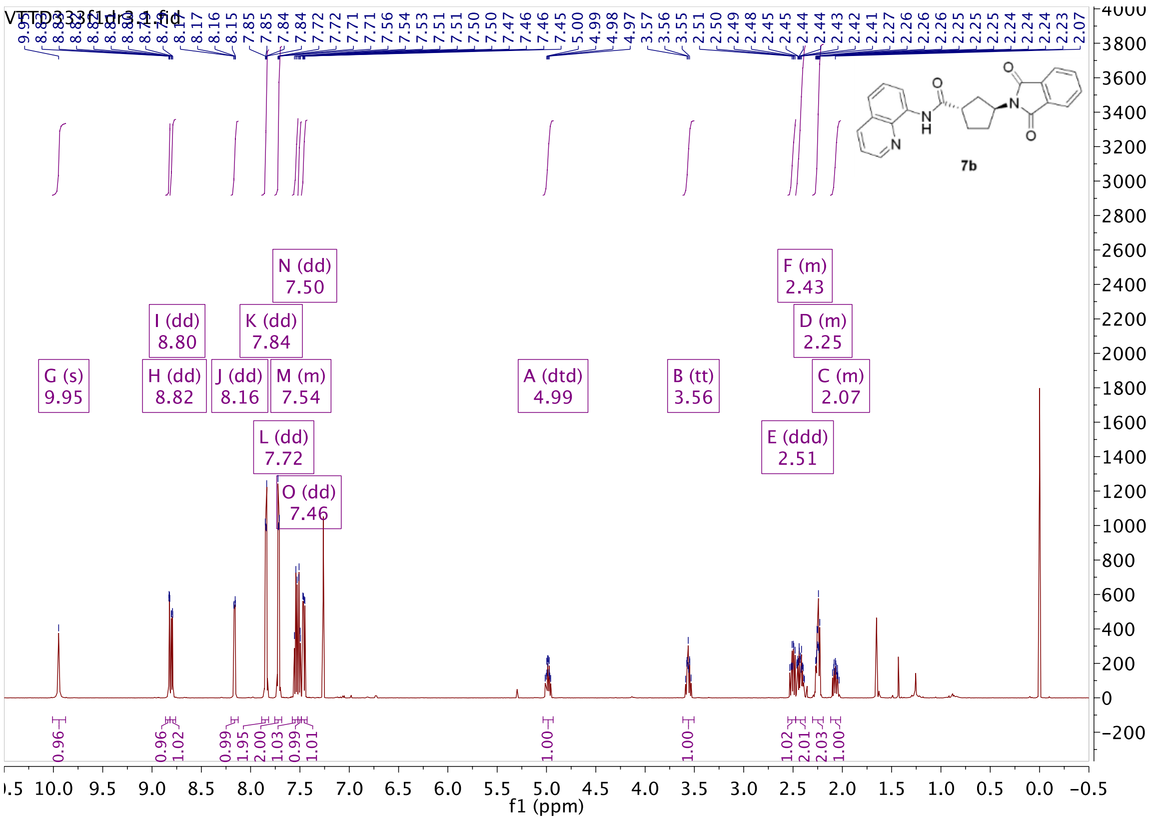

VTTD183.2.fid
170.07
148.47
143.79
138.38
136.56
134.11
133.47
129.89
128.03
127.82
127.40
122.07
121.92
116.71
50.97
47.74
45.88
29.31
21.68
5f
Me
f1 (ppm)

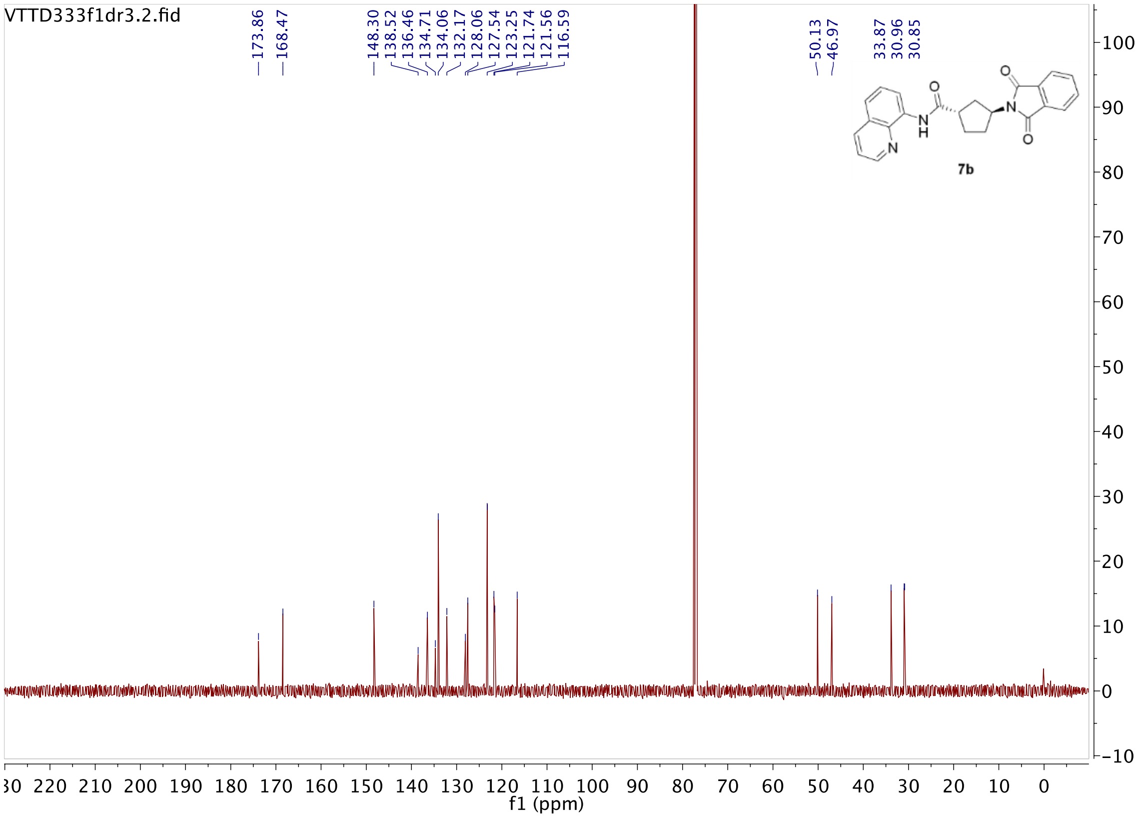

VTTD252r2.1.fid
8.50 8.30 8.30 8.29 8.28 8.19 8.19 8.18 8.18 8.04 8.04 8.03 8.03 8.03 7.54 7.54 7.52 7.52 7.51 7.49 7.49 7.49 7.49 7.48 7.47 3.85 3.84 3.83 3.82 3.65 3.64 3.63 3.62 3.59 3.59 3.59 3.58 3.58 3.58 3.57 3.47 3.46 3.28 3.27 3.26 2.30 2.30 2.29 2.29 2.28 2.28
K (m) 8.03
H (dd) 8.80
J (dd) 8.18
N (m) 7.49
L (s) 9.86
G (dd) 8.51
M (dd) 7.53
I (m) 8.29
D (ddd) 3.46
B (dd) 3.64
A (dd) 3.84
C (ddd) 3.59
E (p) 3.27
F (m) 2.29
0.90 0.99 0.94 1.87 1.01 1.92 1.06 2.00 1.00 0.99 0.99 1.03 0.98 2.02
5g
N
H
O
N
O
S
O
NO2
f1 (ppm)
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
1100 1000 900 800 700 600 500 400 300 200 100 0 −100

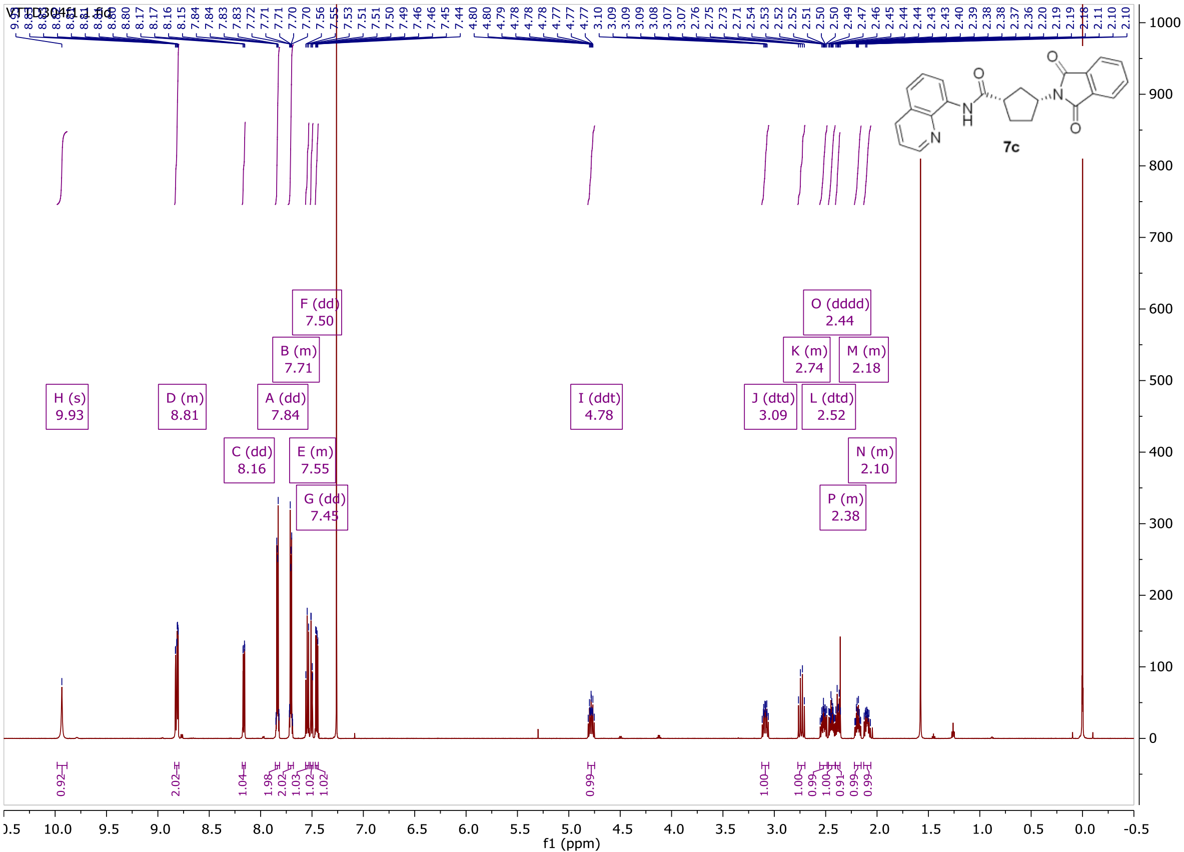

VTTD252r3.1.fid
169.86
150.22 148.50 142.87 138.31 136.70 133.85 128.81 128.06 127.42 124.46 122.33 121.98 116.72
51.09 47.86 45.70
29.59
5g
N
H
O
N
O
S
O
NO2
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20

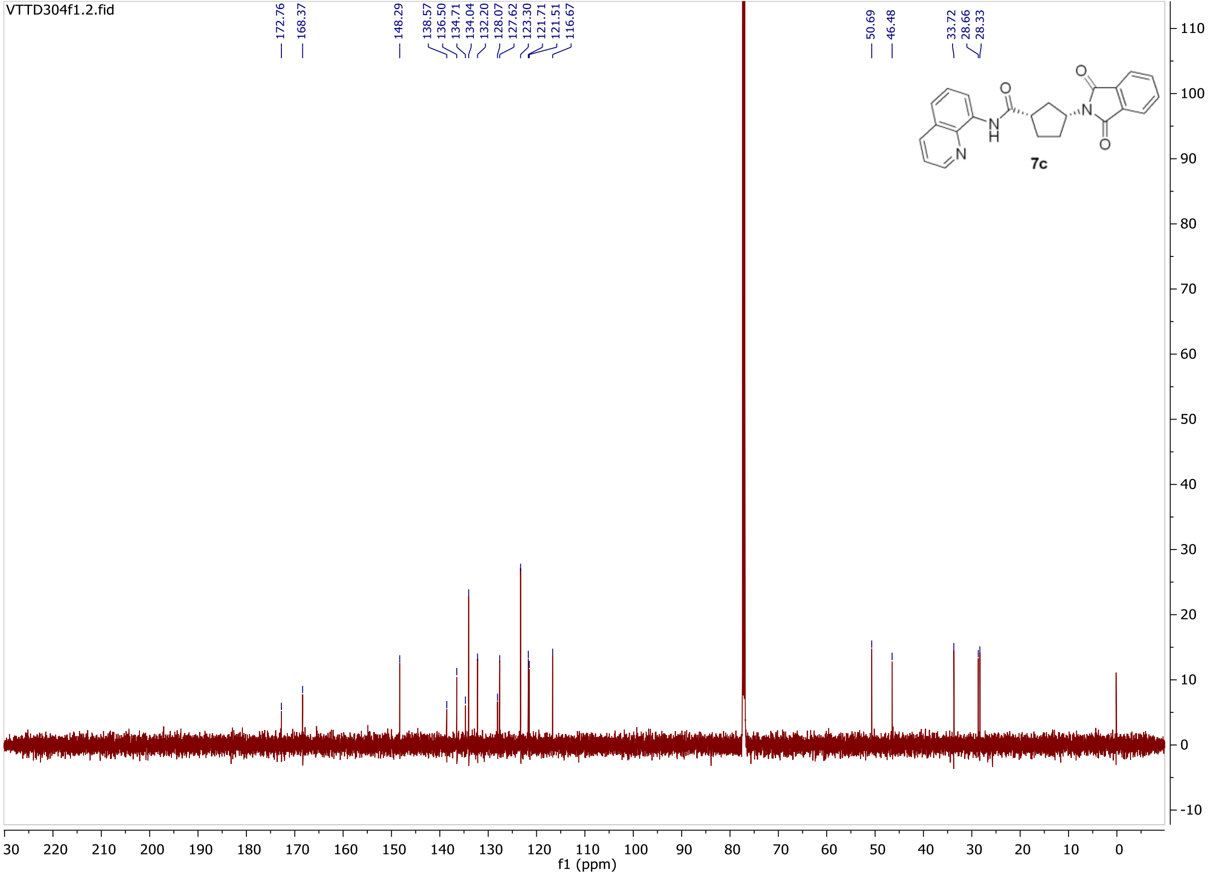

VTTD253r.1.fid
8.71
8.17
8.16
8.15
8.15
7.68
7.68
7.67
7.53
7.52
7.51
7.51
7.50
7.46
7.46
7.45
7.44
7.35
7.35
7.35
7.34
7.34
7.34
7.34
7.34
7.33
3.88
3.87
3.86
3.86
3.85
2.51
2.51
2.49
2.49
2.47
2.47
2.45
2.43
2.13
2.13
2.13
2.11
2.11
2.11
2.10
2.05
2.04
2.04
2.02
2.02
2.02
N
N
H
O
O
O
S
Me
5h
I (s)
9.89
G (dd)
8.77
H (dd)
8.71
F (dd)
8.16
J (m)
7.68
K (m)
7.51
L (dd)
7.45
M (m)
7.34
A (dt)
3.86
E (m)
2.44
D (td)
2.49
C (dtd)
2.03
B (m)
2.12
0.96
0.98
0.97
0.99
1.98
2.01
1.00
1.98
2.00
2.06
3.93
2.02
2.01
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
f1 (ppm)
2300
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

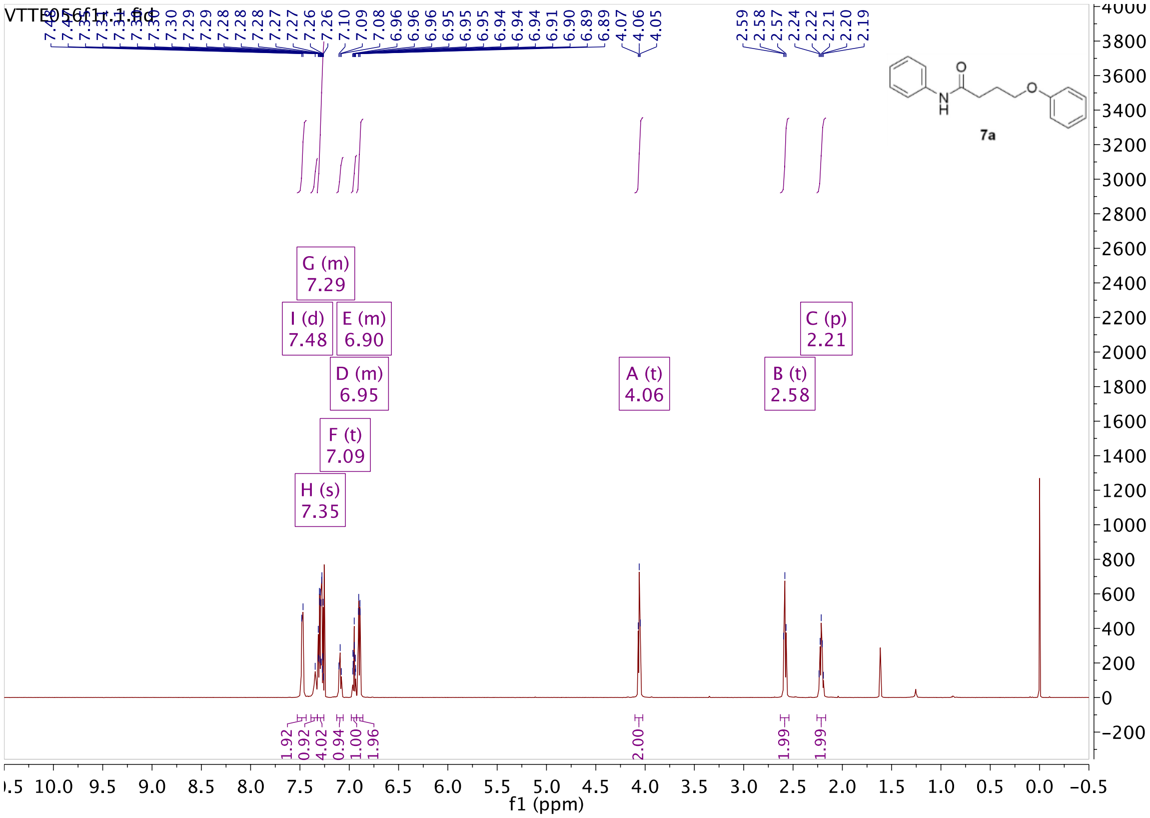

VTTD253r.2.fid
172.33
148.35
143.76
138.50
136.57
134.25
133.26
129.83
128.05
127.87
127.51
121.82
121.82
116.62
45.78
43.75
28.40
21.69
N
N
H
O
O
O
S
Me
5h
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
550
500
450
400
350
300
250
200
150
100
50
0
–50

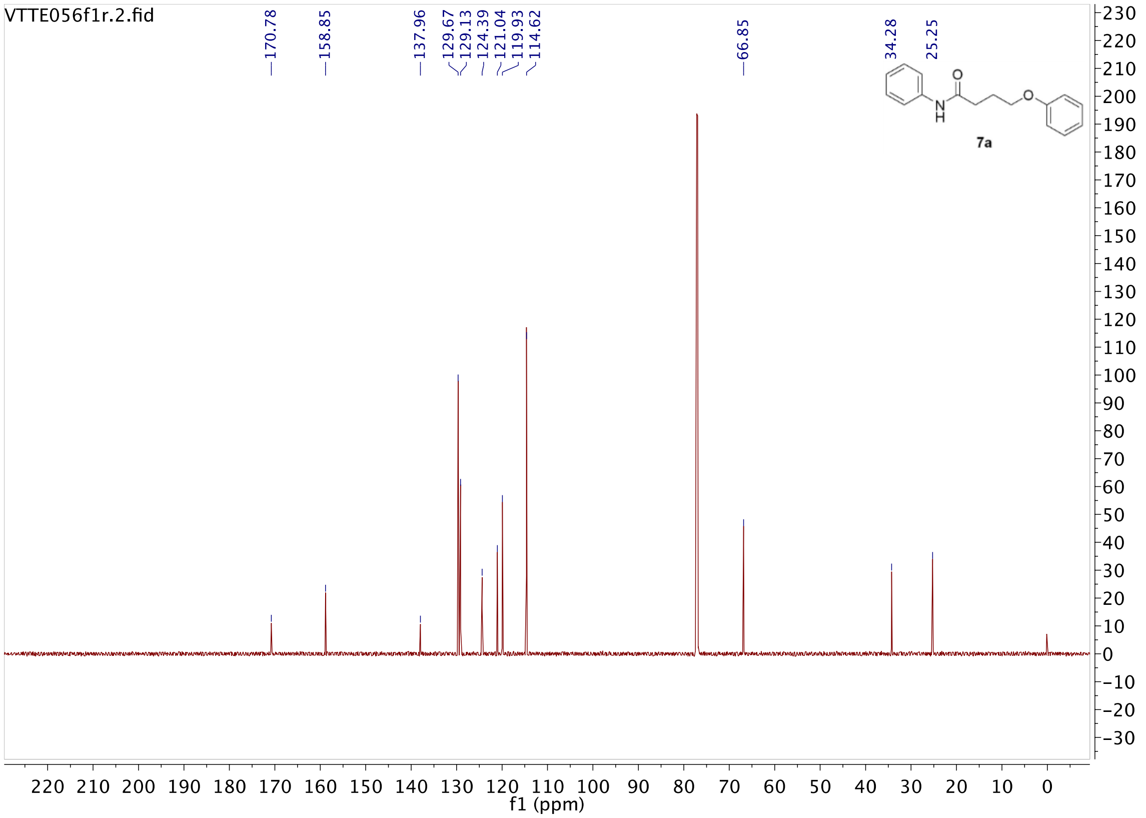

VTTD333f1dr3.1.fid
9.95
8.82
8.81
8.80
8.17
8.17
8.16
8.15
7.85
7.85
7.84
7.84
7.72
7.72
7.71
7.71
7.56
7.54
7.53
7.51
7.51
7.50
7.50
7.47
7.46
7.46
7.45
5.00
4.99
4.98
4.97
3.57
3.56
3.55
2.51
2.50
2.49
2.48
2.45
2.45
2.44
2.44
2.43
2.42
2.41
2.27
2.26
2.26
2.26
2.25
2.25
2.25
2.24
2.24
2.24
2.23
2.07
N
H
O
O
O
N
N
7b
N (dd)
7.50
I (dd)
8.80
K (dd)
7.84
G (s)
9.95
H (dd)
8.82
J (dd)
8.16
M (m)
7.54
L (dd)
7.72
O (dd)
7.46
A (dtd)
4.99
B (tt)
3.56
F (m)
2.43
D (m)
2.25
C (m)
2.07
E (ddd)
2.51
0.96
0.96
1.02
0.99
1.95
2.00
1.03
0.99
1.01
1.00
1.00
1.02
2.01
2.03
1.00
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200
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
f1 (ppm)

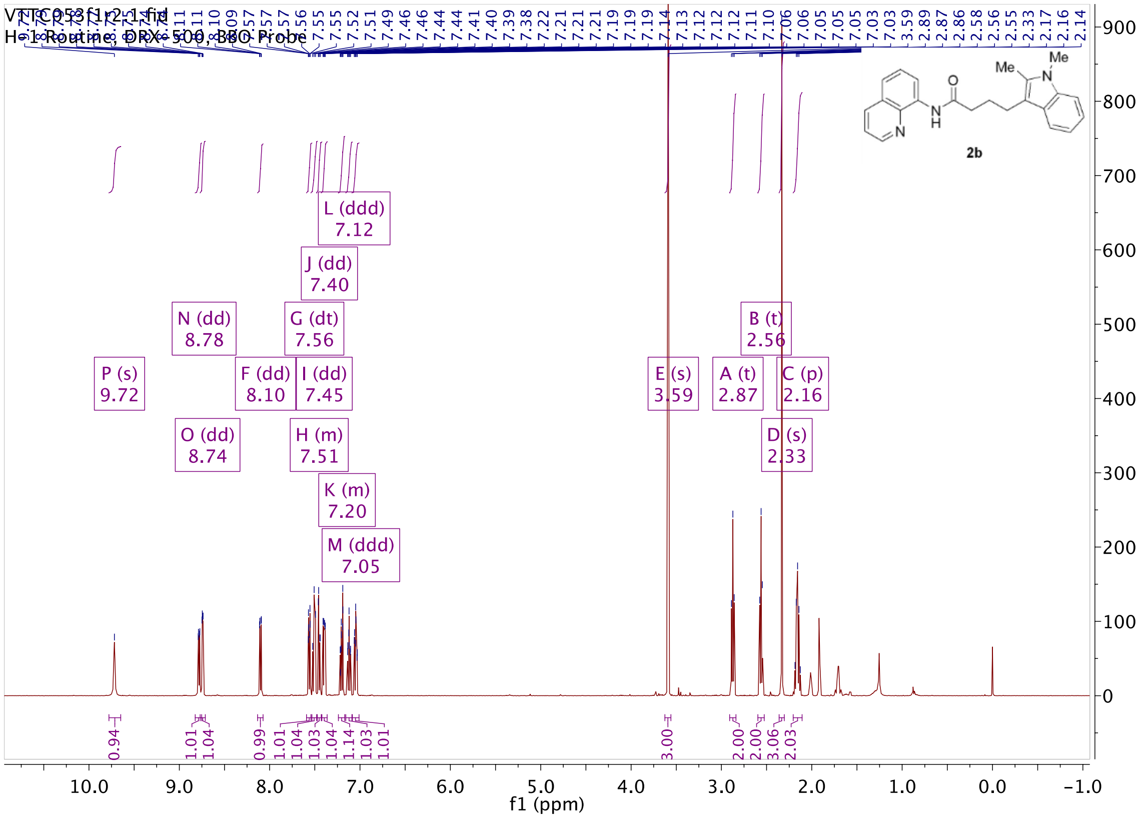

VTTD333f1dr3.2.fid
173.86
168.47
148.30
138.52
136.46
134.71
134.06
132.17
128.06
127.54
123.25
121.74
121.56
116.59
50.13
46.97
33.87
30.96
30.85
N
H
O
O
O
N
N
7b
100
90
80
70
60
50
40
30
20
10
0
−10
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

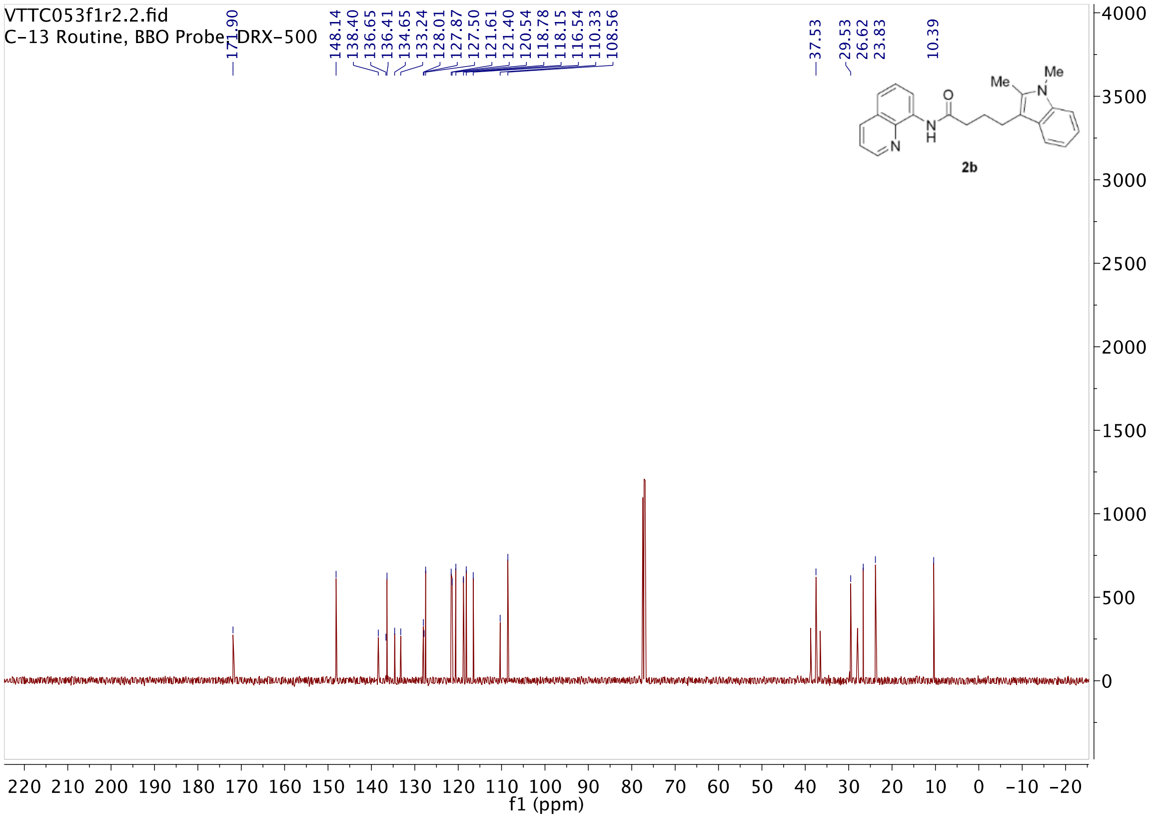

VTTD304f1.1.fid
8.81
8.80
8.80
8.80
8.17
8.16
8.15
7.84
7.84
7.83
7.72
7.71
7.71
7.70
7.56
7.55
7.53
7.51
7.51
7.50
7.49
7.46
7.46
7.45
7.44
4.80
4.79
4.78
4.78
4.78
4.77
4.77
3.10
3.09
3.09
3.09
3.08
3.07
3.07
2.76
2.75
2.73
2.71
2.54
2.53
2.52
2.52
2.51
2.50
2.50
2.49
2.47
2.46
2.45
2.44
2.44
2.43
2.43
2.40
2.39
2.38
2.38
2.37
2.36
2.20
2.19
2.19
2.18
2.11
2.10
2.10
7c
F (dd) 7.50
B (m) 7.71
H (s) 9.93
D (m) 8.81
A (dd) 7.84
C (dd) 8.16
E (m) 7.55
G (dd) 7.45
I (ddt) 4.78
J (dtd) 3.09
O (dddd) 2.44
K (m) 2.74
M (m) 2.18
L (dtd) 2.52
N (m) 2.10
P (m) 2.38
0.92
2.02
1.04
1.98
2.02
1.03
1.02
1.02
0.99
1.00
1.00
0.99
1.00
0.91
0.99
0.99
1000
900
800
700
600
500
400
300
200
100
0
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
f1 (ppm)

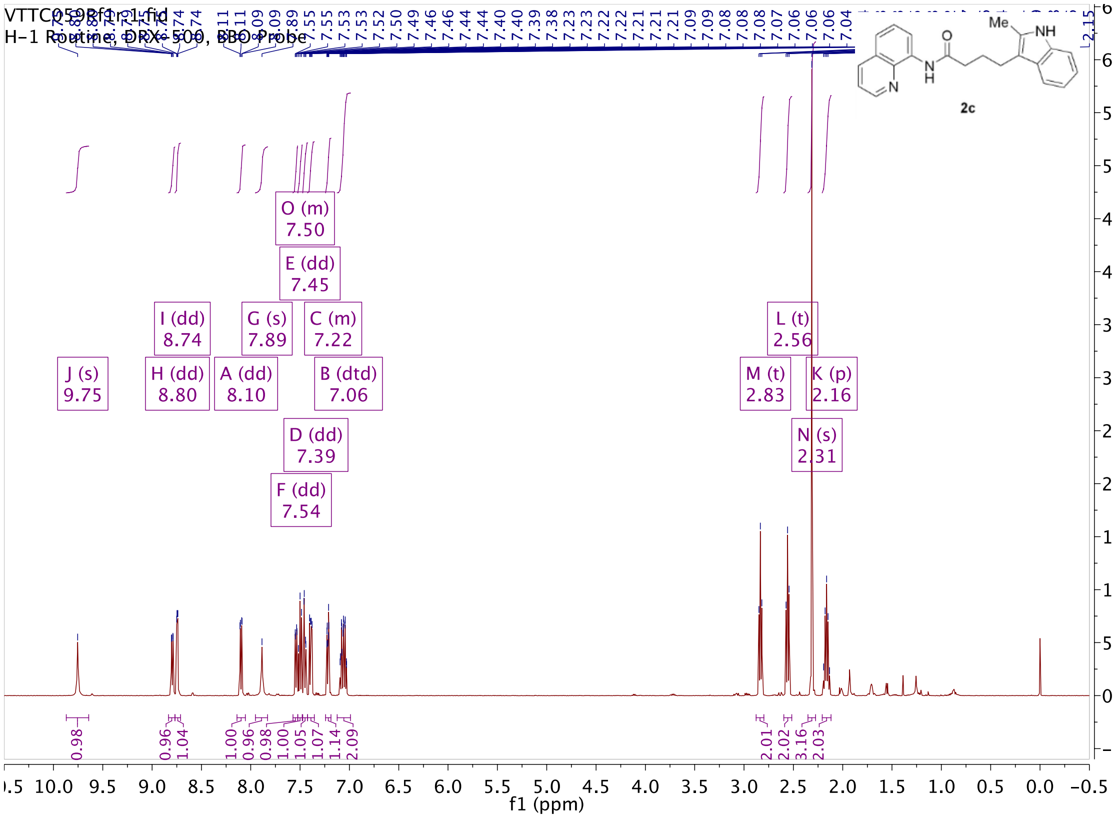

VTTD304f1.2.fid
172.76
168.37
148.29
138.57
136.50
134.71
134.04
132.20
128.07
127.62
123.30
121.71
121.51
116.67
50.69
46.48
33.72
28.66
28.33
7c
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


VTTE056f1r.1.fid
7.30
7.30
7.29
7.29
7.28
7.28
7.28
7.27
7.27
7.26
7.26
7.10
7.09
7.08
6.96
6.96
6.96
6.95
6.95
6.95
6.94
6.94
6.94
6.91
6.90
6.89
6.89
4.07
4.06
4.05
2.59
2.58
2.57
2.24
2.22
2.21
2.20
2.19
G (m) 7.29
I (d) 7.48
E (m) 6.90
D (m) 6.95
F (t) 7.09
H (s) 7.35
A (t) 4.06
B (t) 2.58
C (p) 2.21
1.92
0.92
4.02
0.94
1.00
1.96
2.00
1.99
1.99
7a
O
N
H
f1 (ppm)

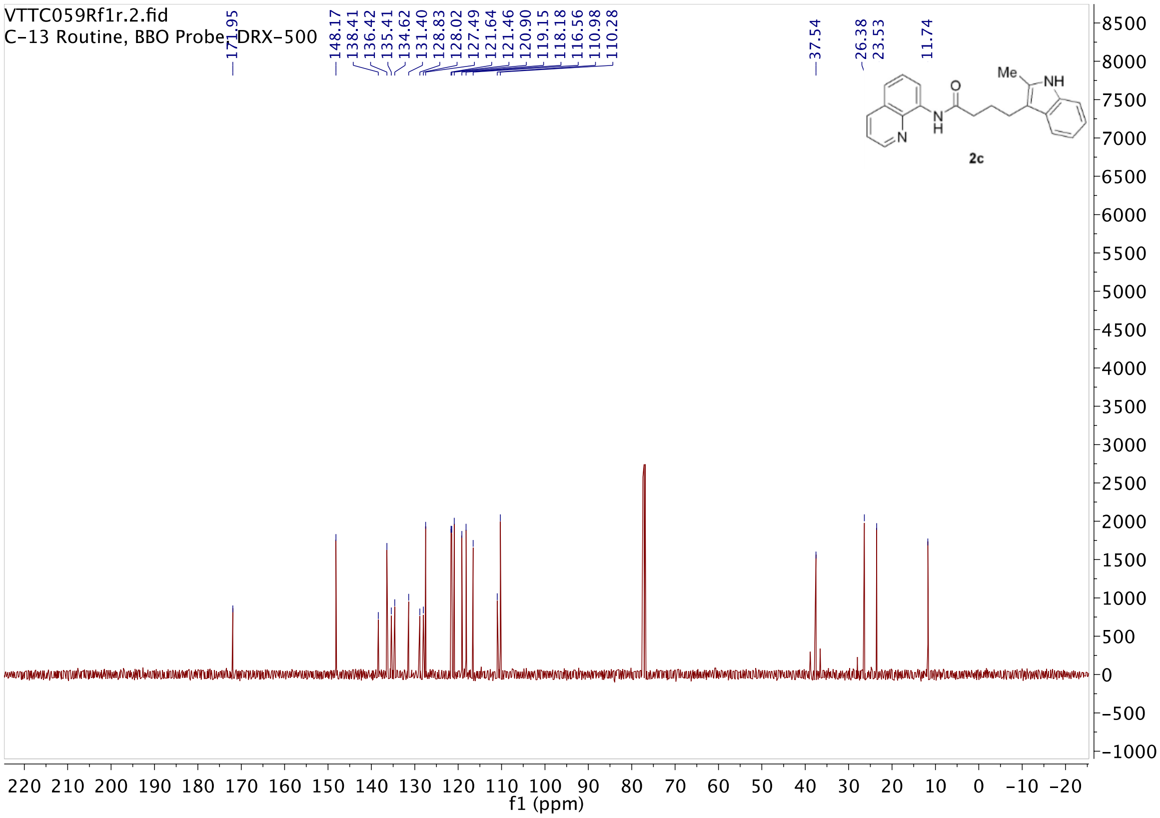

VTTE056f1r.2.fid
170.78
158.85
137.96
129.67
129.13
124.39
121.04
119.93
114.62
66.85
34.28
25.25
7a
O
N
H
f1 (ppm)


VTTC053f1r2.1.fid
H-1 Routine, DRX-500, BBO Probe
8.11
8.11
8.10
8.09
7.57
7.57
7.56
7.55
7.55
7.52
7.51
7.49
7.46
7.46
7.44
7.41
7.40
7.39
7.38
7.22
7.21
7.21
7.21
7.19
7.19
7.19
7.14
7.13
7.12
7.12
7.11
7.10
7.06
7.06
7.05
7.05
7.05
7.03
7.03
3.59
2.89
2.87
2.86
2.58
2.56
2.55
2.33
2.17
2.16
2.14
Me
Me
N
O
N
H
N
2b
L (ddd) 7.12
J (dd) 7.40
N (dd) 8.78
G (dt) 7.56
B (t) 2.56
P (s) 9.72
F (dd) 8.10
I (dd) 7.45
E (s) 3.59
A (t) 2.87
C (p) 2.16
O (dd) 8.74
H (m) 7.51
D (s) 2.33
K (m) 7.20
M (ddd) 7.05
0.94
1.01
1.04
0.99
1.01
1.04
1.03
1.04
1.14
1.03
1.01
3.00
2.00
2.00
3.06
2.03
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)
900
800
700
600
500
400
300
200
100
0

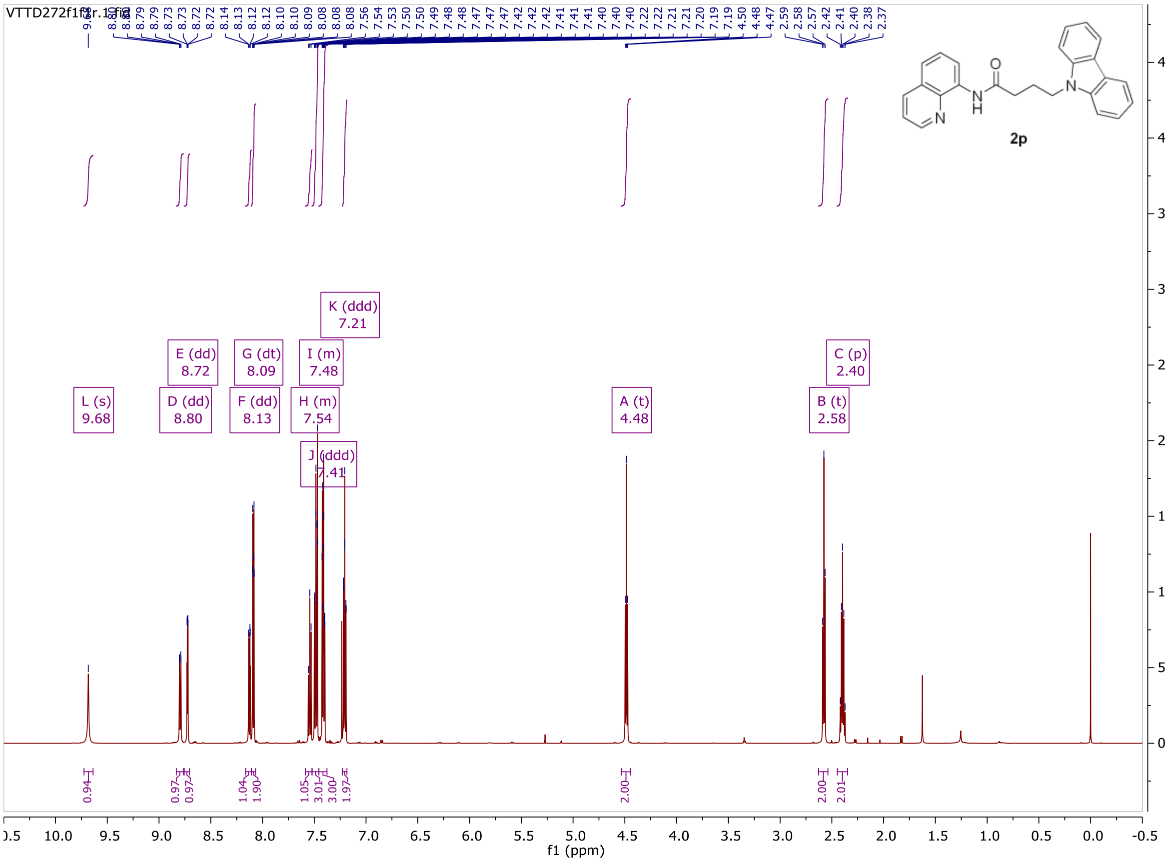

VTTC053f1r2.2.fid
C-13 Routine, BBO Probe, DRX-500
171.90
148.14
138.40
136.65
136.41
134.65
133.24
128.01
127.87
127.50
121.61
121.40
120.54
118.78
118.15
116.54
110.33
108.56
37.53
29.53
26.62
23.83
10.39
Me
Me
N
O
N
H
N
2b
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)
4000
3500
3000
2500
2000
1500
1000
500
0

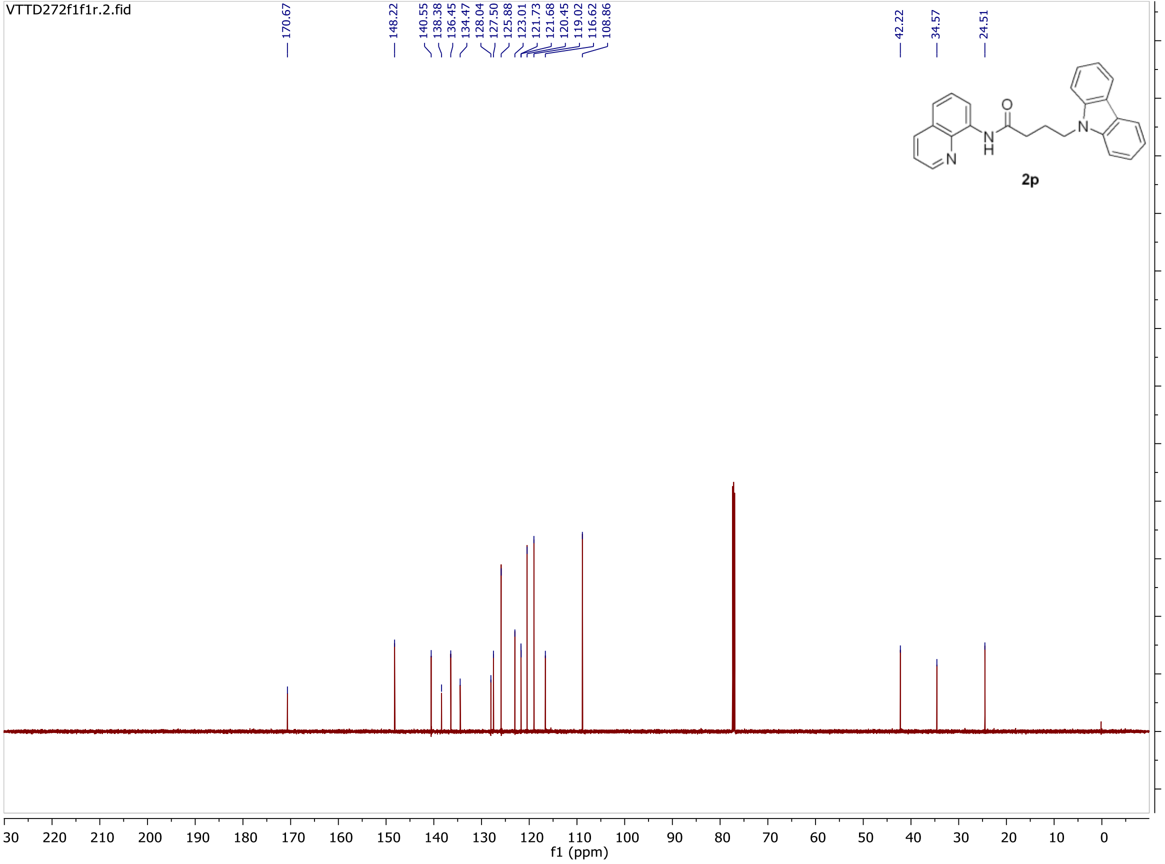


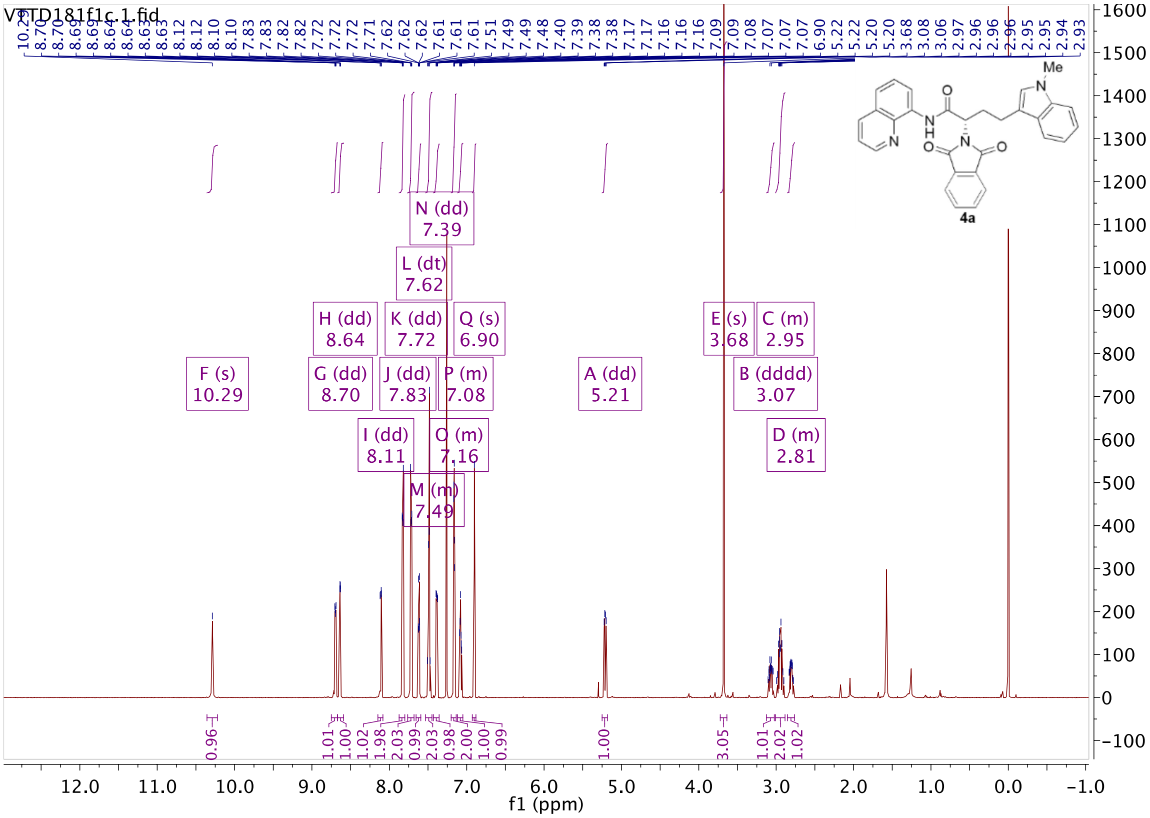
VTTC059Rf1r.1.fid
H-1 Routine, DRX-500, BBO Probe
9.11
9.09
8.89
7.55
7.55
7.53
7.53
7.52
7.50
7.49
7.46
7.46
7.44
7.44
7.40
7.40
7.39
7.38
7.33
7.23
7.22
7.22
7.21
7.21
7.21
7.09
7.09
7.08
7.08
7.07
7.06
7.06
7.06
7.04
2.15
Me
NH
O
N
H
N
2c
O (m)
7.50
E (dd)
7.45
I (dd)
8.74
G (s)
7.89
C (m)
7.22
L (t)
2.56
J (s)
9.75
H (dd)
8.80
A (dd)
8.10
B (dtd)
7.06
M (t)
2.83
K (p)
2.16
D (dd)
7.39
N (s)
2.31
F (dd)
7.54
0.98
0.96
1.04
1.00
0.96
0.98
1.00
1.05
1.07
1.14
2.09
2.01
2.02
3.16
2.03
f1 (ppm)

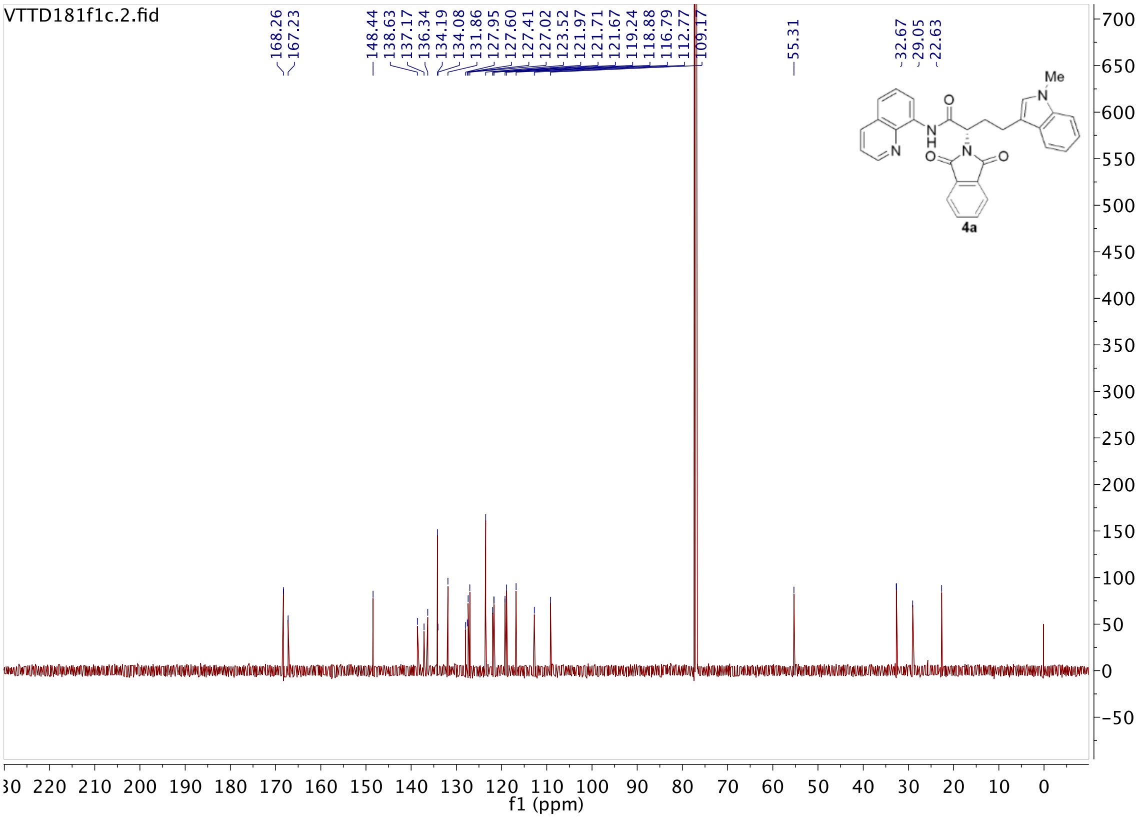


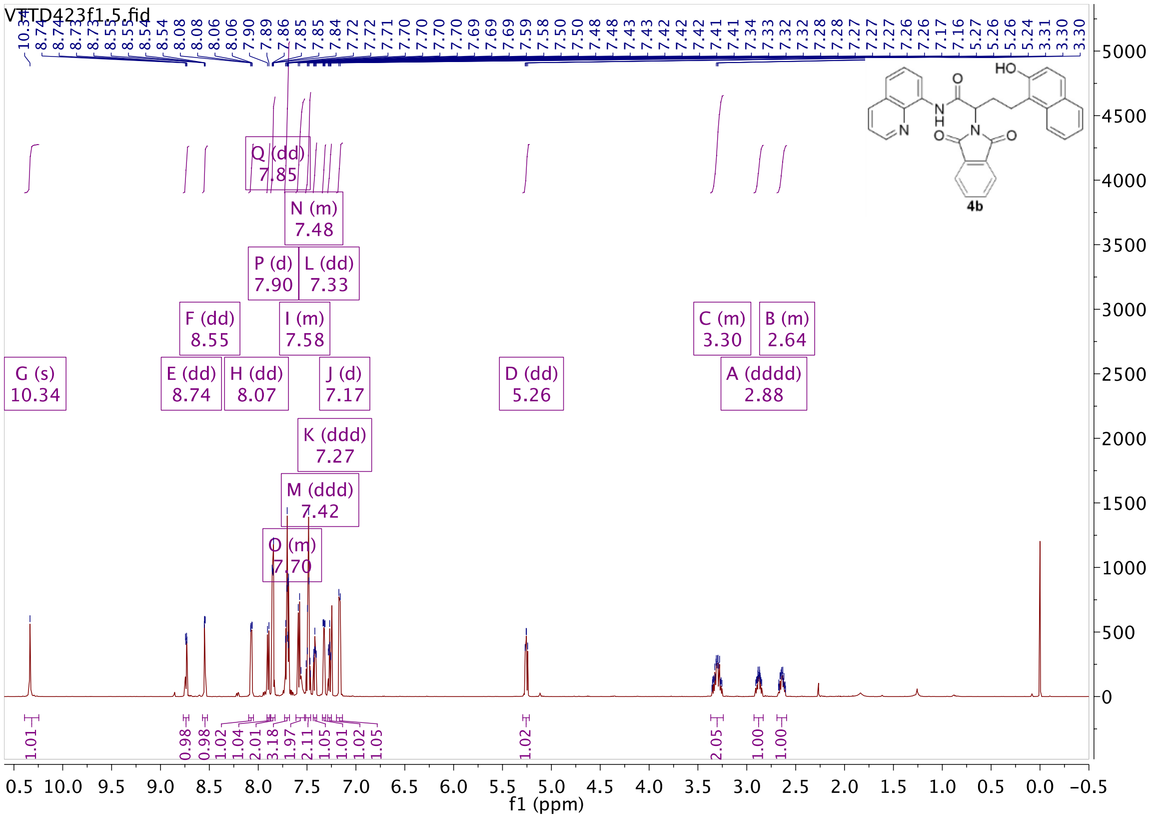
VTTC059Rf1r.2.fid
C-13 Routine, BBO Probe, DRX-500
171.95
148.17
138.41
136.42
135.41
134.62
131.40
128.83
128.02
127.49
121.64
121.46
120.90
119.15
118.18
116.56
110.98
110.28
37.54
26.38
23.53
11.74
Me
NH
O
N
H
N
2c
f1 (ppm)

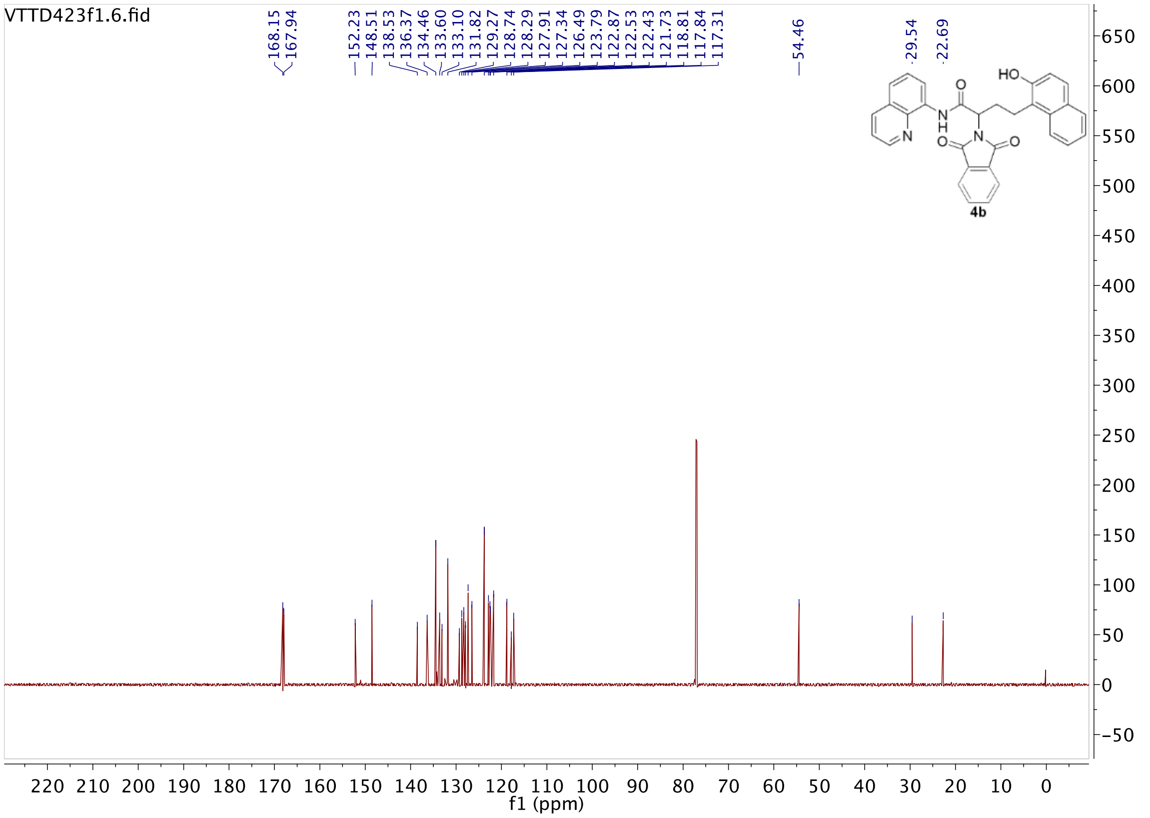

VTTD272f1f1r.1.fid
9.68 8.80 8.80 8.79 8.79 8.73 8.73 8.72 8.72 8.14 8.13 8.12 8.12 8.10 8.10 8.09 8.08 8.08 8.08 7.56 7.54 7.53 7.50 7.50 7.49 7.48 7.48 7.47 7.47 7.47 7.42 7.42 7.42 7.41 7.41 7.40 7.40 7.22 7.22 7.21 7.21 7.20 7.19 7.19 4.50 4.48 4.47 2.59 2.58 2.57 2.42 2.41 2.40 2.38 2.37
2p
L (s) 9.68
D (dd) 8.80
E (dd) 8.72
F (dd) 8.13
G (dt) 8.09
H (m) 7.54
I (m) 7.48
J (ddd) 7.41
K (ddd) 7.21
A (t) 4.48
B (t) 2.58
C (p) 2.40
0.94 0.97 0.97 1.04 1.90 1.05 3.01 3.00 1.97 2.00 2.00 2.01
f1 (ppm)

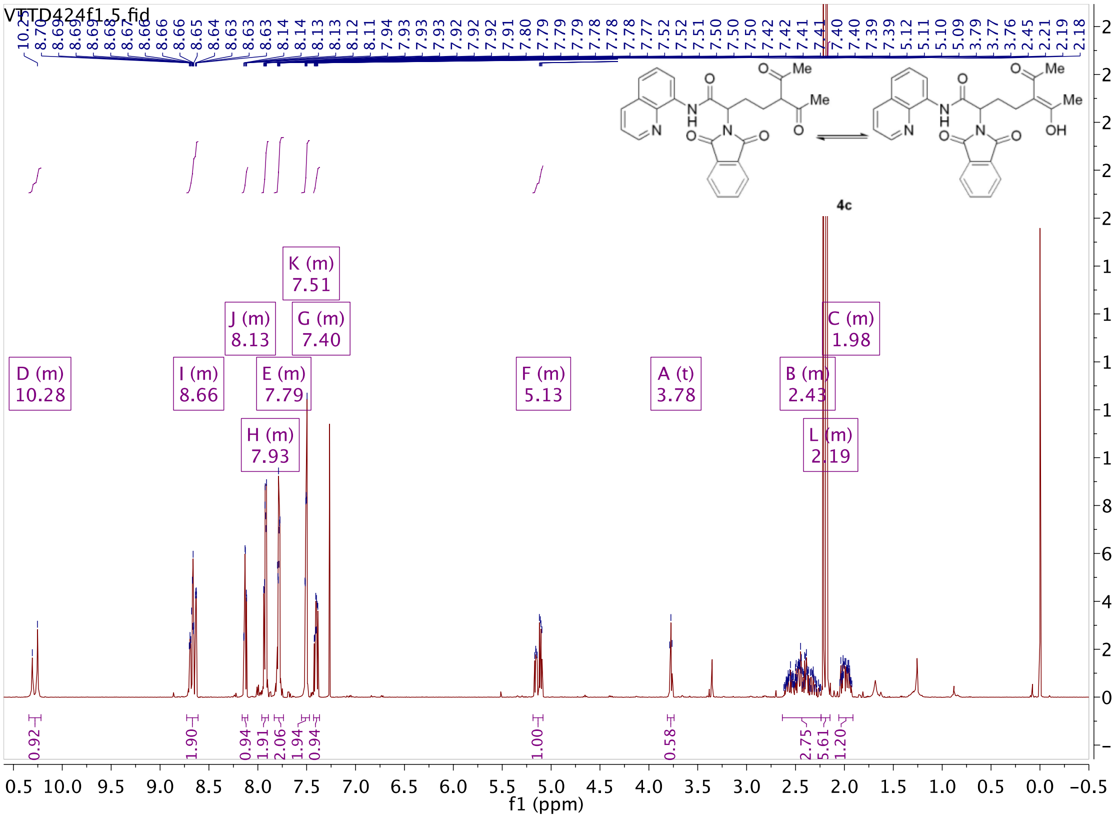

VTTD272f1f1r.2.fid
170.67 148.22 140.55 138.38 136.45 134.47 128.04 127.50 125.88 123.01 121.73 121.68 120.45 119.02 116.62 108.86 42.22 34.57 24.51
2p
f1 (ppm)


VTTD181f1c.1.fid
10.29
8.70
8.70
8.69
8.69
8.64
8.64
8.63
8.63
8.12
8.12
8.10
8.10
7.83
7.83
7.82
7.82
7.72
7.72
7.72
7.71
7.62
7.62
7.62
7.61
7.61
7.61
7.51
7.49
7.49
7.48
7.40
7.39
7.38
7.38
7.17
7.17
7.16
7.16
7.16
7.09
7.09
7.08
7.07
7.07
7.07
6.90
5.22
5.22
5.20
5.20
3.68
3.08
3.06
2.97
2.96
2.96
2.96
2.95
2.95
2.94
2.93
Me
N
O
N
H
N
N
O
O
4a
N (dd)
7.39
L (dt)
7.62
H (dd)
8.64
K (dd)
7.72
Q (s)
6.90
E (s)
3.68
C (m)
2.95
F (s)
10.29
G (dd)
8.70
J (dd)
7.83
P (m)
7.08
A (dd)
5.21
B (dddd)
3.07
I (dd)
8.11
O (m)
7.16
D (m)
2.81
M (m)
7.49
0.96
1.01
1.00
1.02
1.98
2.03
0.99
2.03
0.98
2.00
1.00
0.99
1.00
3.05
1.01
2.02
1.02
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

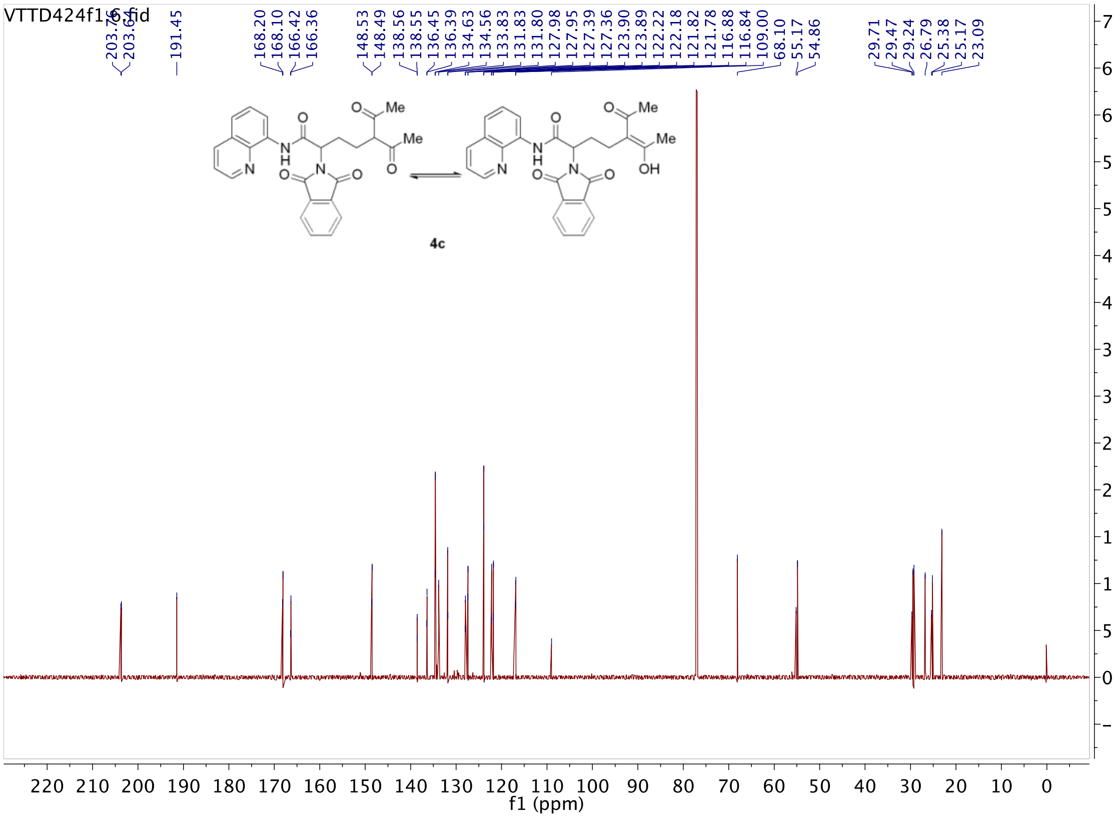

VTTD181f1c.2.fid
168.26
167.23
148.44
138.63
137.17
136.34
134.19
134.08
131.86
127.95
127.60
127.41
127.02
123.52
121.97
121.71
121.67
119.24
118.88
116.79
112.77
109.17
55.31
32.67
29.05
22.63
Me
N
O
N
H
N
N
O
O
4a
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50


VTTD423f1.5.fid
10.34
8.74
8.74
8.73
8.73
8.55
8.55
8.54
8.54
8.08
8.08
8.06
8.06
7.90
7.89
7.86
7.85
7.85
7.84
7.72
7.72
7.71
7.70
7.70
7.70
7.69
7.69
7.69
7.59
7.58
7.50
7.50
7.48
7.48
7.43
7.43
7.42
7.42
7.41
7.41
7.34
7.33
7.32
7.32
7.28
7.28
7.27
7.27
7.27
7.26
7.17
7.16
5.27
5.26
5.26
5.24
3.31
3.30
3.30
HO
O
N
H
N
O
N
O
4b
Q (dd) 7.85
N (m) 7.48
P (d) 7.90
L (dd) 7.33
F (dd) 8.55
I (m) 7.58
C (m) 3.30
B (m) 2.64
G (s) 10.34
E (dd) 8.74
H (dd) 8.07
J (d) 7.17
D (dd) 5.26
A (dddd) 2.88
K (ddd) 7.27
M (ddd) 7.42
O (m) 7.70
1.01
0.98
0.98
1.02
1.04
2.01
3.18
1.97
2.11
1.05
1.01
1.02
1.05
1.02
2.05
1.00
1.00
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
0.5
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
f1 (ppm)

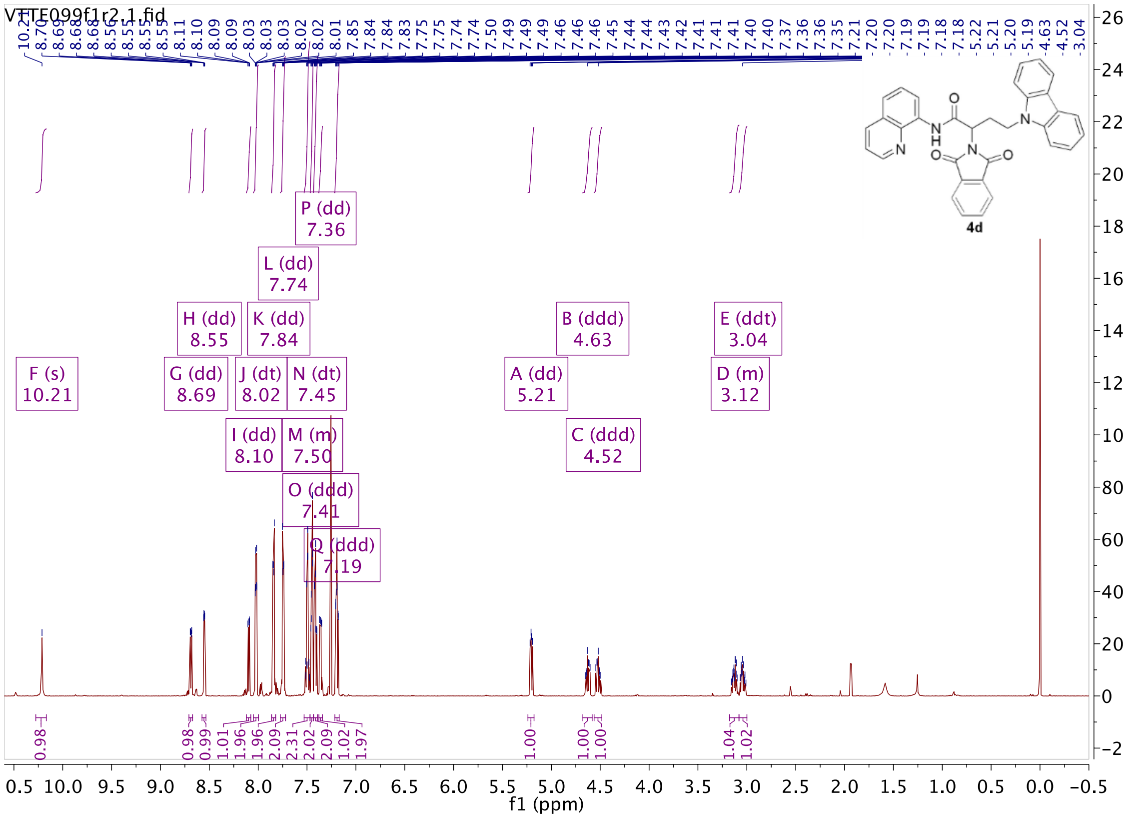

VTTD423f1.6.fid
168.15
167.94
152.23
148.51
138.53
136.37
134.46
133.60
133.10
131.82
129.27
128.74
128.29
127.91
127.34
126.49
123.79
122.87
122.53
122.43
121.73
118.81
117.84
117.31
54.46
29.54
22.69
HO
O
N
H
N
O
N
O
4b
650
600
550
500
450
400
350
300
250
200
150
100
50
0
–50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

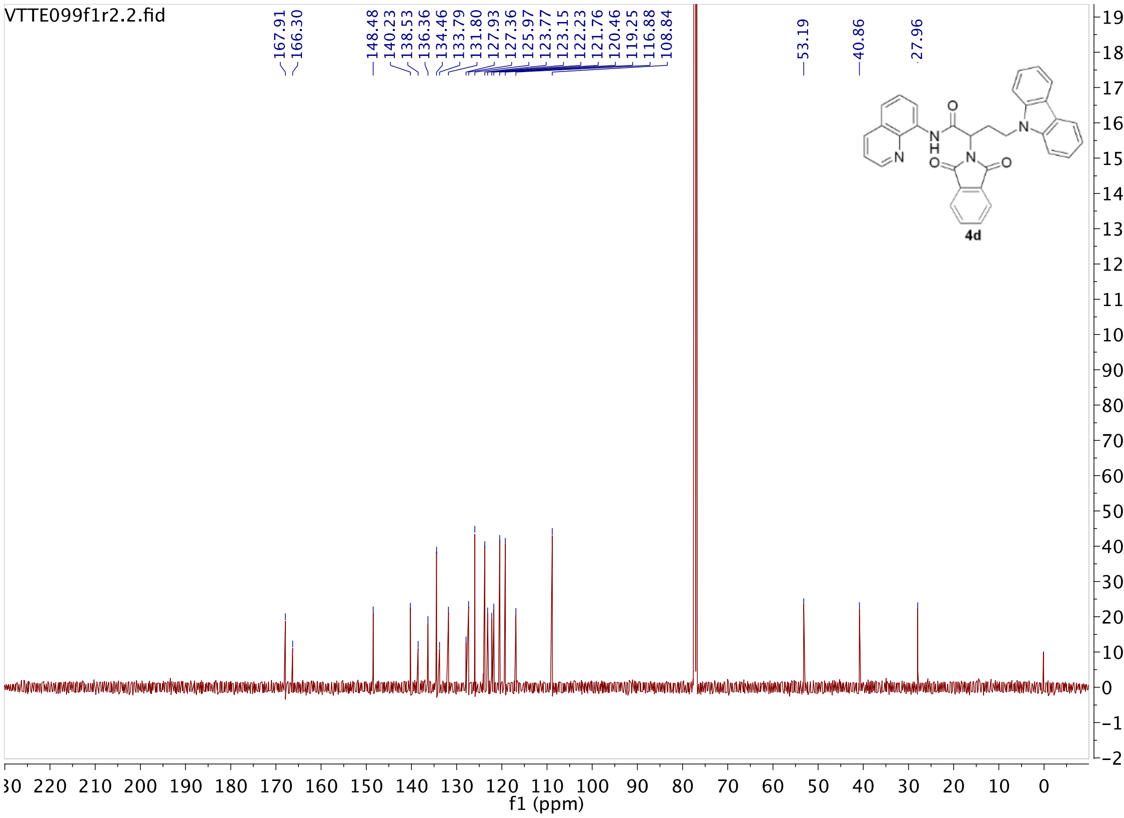

VTTD424f1.5.fid
10.25
8.70
8.69
8.69
8.69
8.68
8.67
8.66
8.66
8.66
8.65
8.64
8.63
8.63
8.63
8.14
8.14
8.13
8.13
8.12
8.11
7.94
7.93
7.93
7.93
7.92
7.92
7.92
7.91
7.80
7.79
7.79
7.79
7.78
7.78
7.78
7.77
7.52
7.52
7.51
7.50
7.50
7.50
7.42
7.42
7.41
7.41
7.40
7.40
7.39
7.39
5.12
5.11
5.10
5.09
3.79
3.77
3.76
2.45
2.21
2.19
2.18
O
Me
Me
N
H
N
O
N
O
O
OH
K (m)
7.51
J (m)
8.13
G (m)
7.40
C (m)
1.98
D (m)
10.28
I (m)
8.66
E (m)
7.79
F (m)
5.13
A (t)
3.78
B (m)
2.43
H (m)
7.93
L (m)
2.19
0.92
1.90
0.94
1.91
2.06
1.94
0.94
1.00
0.58
2.75
5.61
1.20
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200
0.5 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
f1 (ppm)

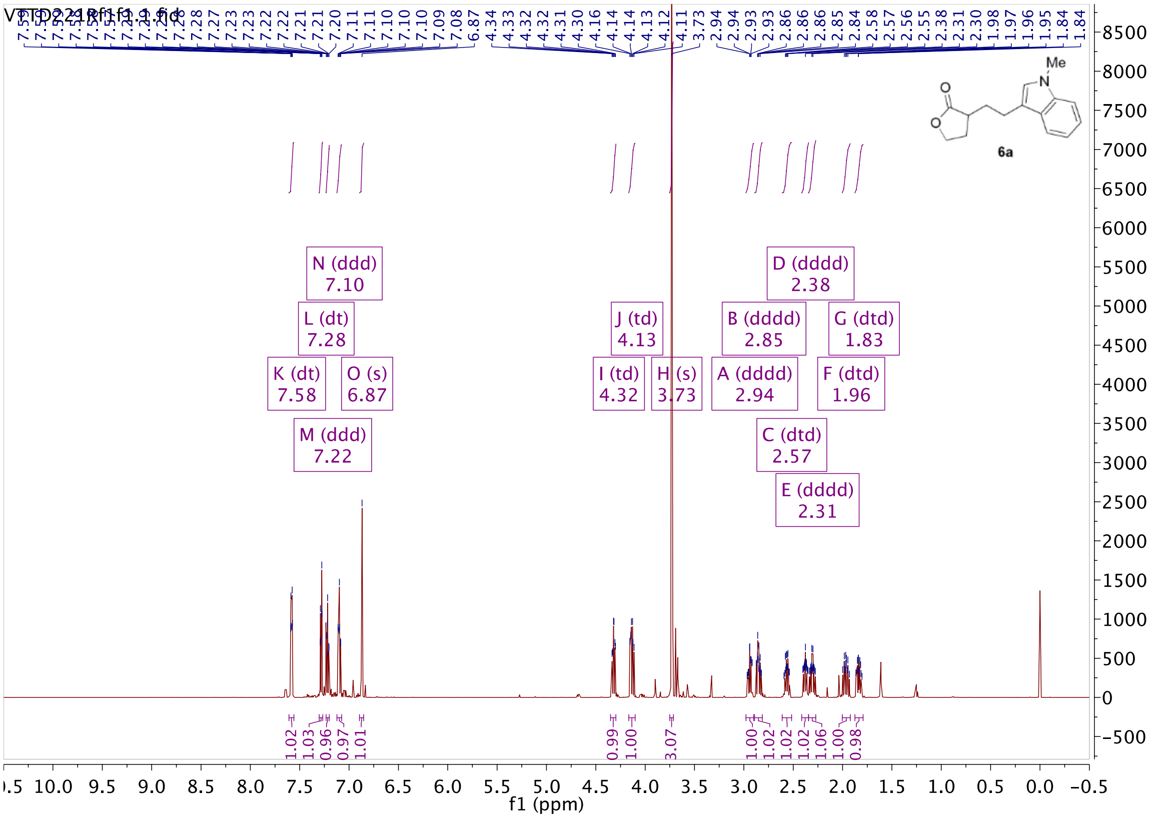
4c

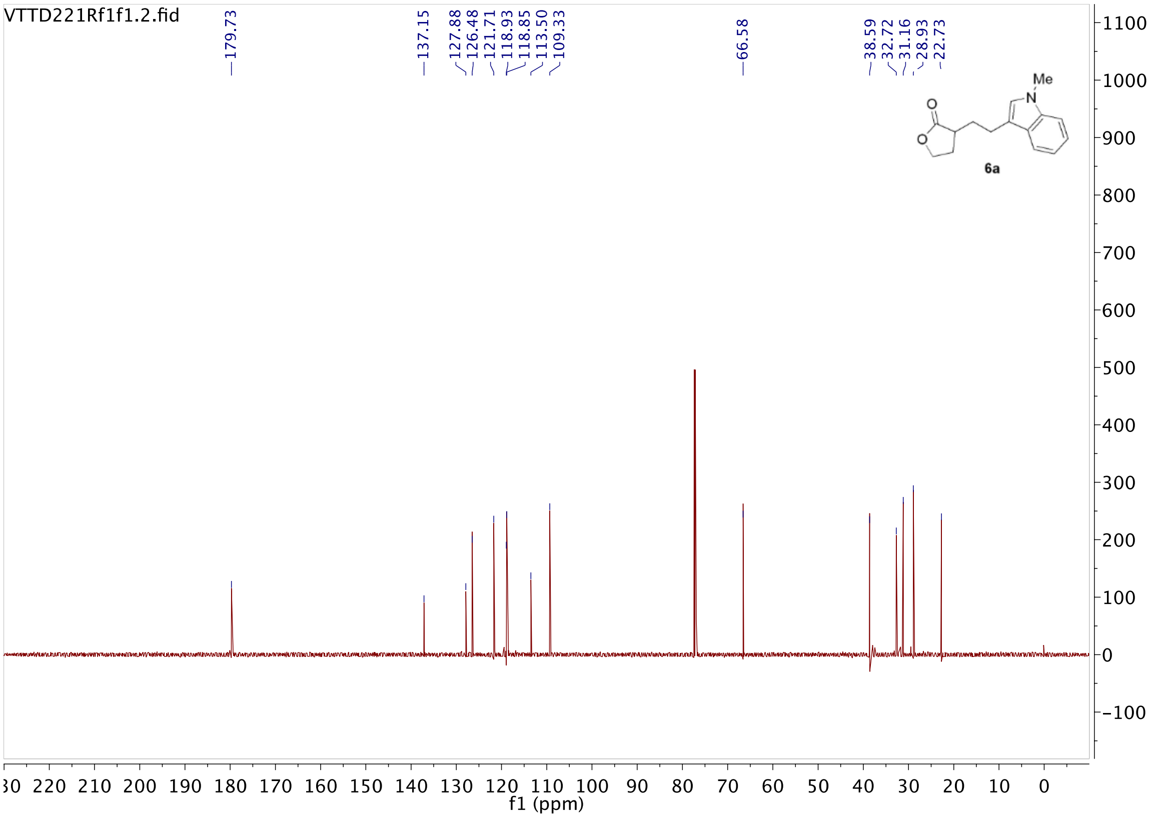

VTTD424f1.6.fid
203.76
203.64
191.45
168.20
168.10
166.42
166.36
148.53
148.49
138.56
138.55
136.45
136.39
134.63
134.56
133.83
131.83
131.80
127.98
127.95
127.39
127.36
123.90
123.89
122.22
122.18
121.82
121.78
116.88
116.84
109.00
68.10
55.17
54.86
29.71
29.47
29.24
26.79
25.38
25.17
23.09
O
Me
Me
N
H
N
O
N
O
O
OH
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
−50
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

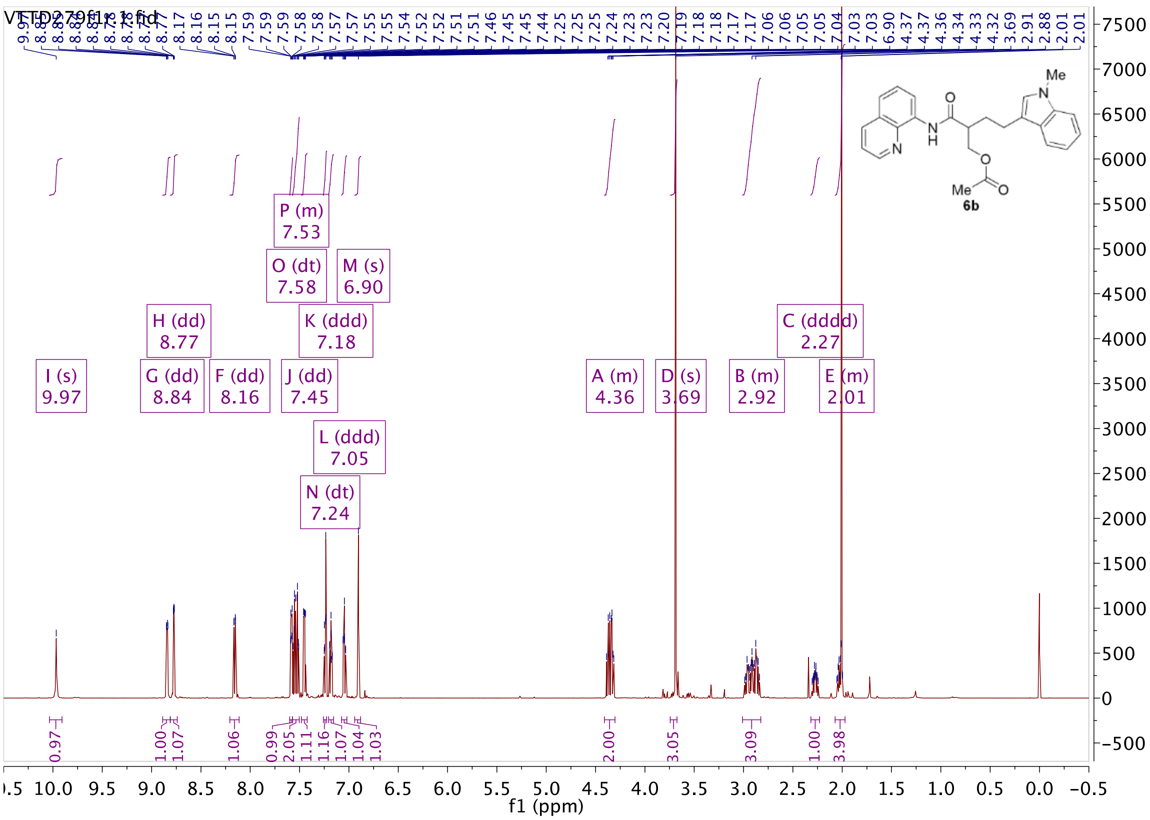
4c


VTTE099f1r2.1.fid
10.21
8.70
8.69
8.68
8.68
8.56
8.55
8.55
8.55
8.11
8.10
8.09
8.09
8.03
8.03
8.03
8.02
8.02
8.01
7.85
7.84
7.84
7.83
7.75
7.75
7.74
7.74
7.50
7.49
7.49
7.46
7.46
7.45
7.44
7.44
7.43
7.42
7.41
7.41
7.41
7.40
7.40
7.37
7.36
7.36
7.35
7.21
7.20
7.20
7.19
7.18
7.18
5.22
5.21
5.20
5.19
4.63
4.52
3.04
4d
P (dd) 7.36
L (dd) 7.74
H (dd) 8.55
K (dd) 7.84
B (ddd) 4.63
E (ddt) 3.04
F (s) 10.21
G (dd) 8.69
J (dt) 8.02
N (dt) 7.45
A (dd) 5.21
D (m) 3.12
I (dd) 8.10
M (m) 7.50
C (ddd) 4.52
O (ddd) 7.41
Q (ddd) 7.19
0.98
0.98
0.99
1.01
1.96
1.96
2.09
2.31
2.02
2.09
1.02
1.97
1.00
1.00
1.00
1.04
1.02
0.5 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
f1 (ppm)
2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 −200


VTTE099f1r2.2.fid
167.91
166.30
148.48
140.23
138.53
136.36
134.46
133.79
131.80
127.93
127.36
125.97
123.77
123.15
122.23
121.76
120.46
119.25
116.88
108.84
53.19
40.86
27.96
4d
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20


VTTD221Rf1f1.1.fid
7.28 7.27 7.23 7.23 7.22 7.22 7.21 7.21 7.20 7.11 7.11 7.10 7.10 7.09 7.08 6.87 4.34 4.33 4.32 4.32 4.31 4.30 4.16 4.14 4.14 4.13 4.12 4.11 3.73 2.94 2.94 2.93 2.93 2.86 2.86 2.86 2.85 2.84 2.58 2.57 2.56 2.55 2.38 2.31 2.30 1.98 1.97 1.96 1.95 1.84 1.84
Me
N
O
O
6a
N (ddd) 7.10
L (dt) 7.28
K (dt) 7.58
O (s) 6.87
M (ddd) 7.22
J (td) 4.13
I (td) 4.32
H (s) 3.73
D (dddd) 2.38
B (dddd) 2.85
G (dtd) 1.83
A (dddd) 2.94
F (dtd) 1.96
C (dtd) 2.57
E (dddd) 2.31
1.02 1.03 0.96 0.97 1.01 0.99 1.00 3.07 1.00 1.02 1.02 1.02 1.06 1.00 0.98
8500 8000 7500 7000 6500 6000 5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0 −500
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
f1 (ppm)


VTTD221Rf1f1.2.fid
179.73
137.15
127.88 126.48 121.71 118.93 118.85 113.50 109.33
66.58
38.59 32.72 31.16 28.93 22.73
Me
N
O
O
6a
1100 1000 900 800 700 600 500 400 300 200 100 0 −100
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


VTTD279f1r.1.fid
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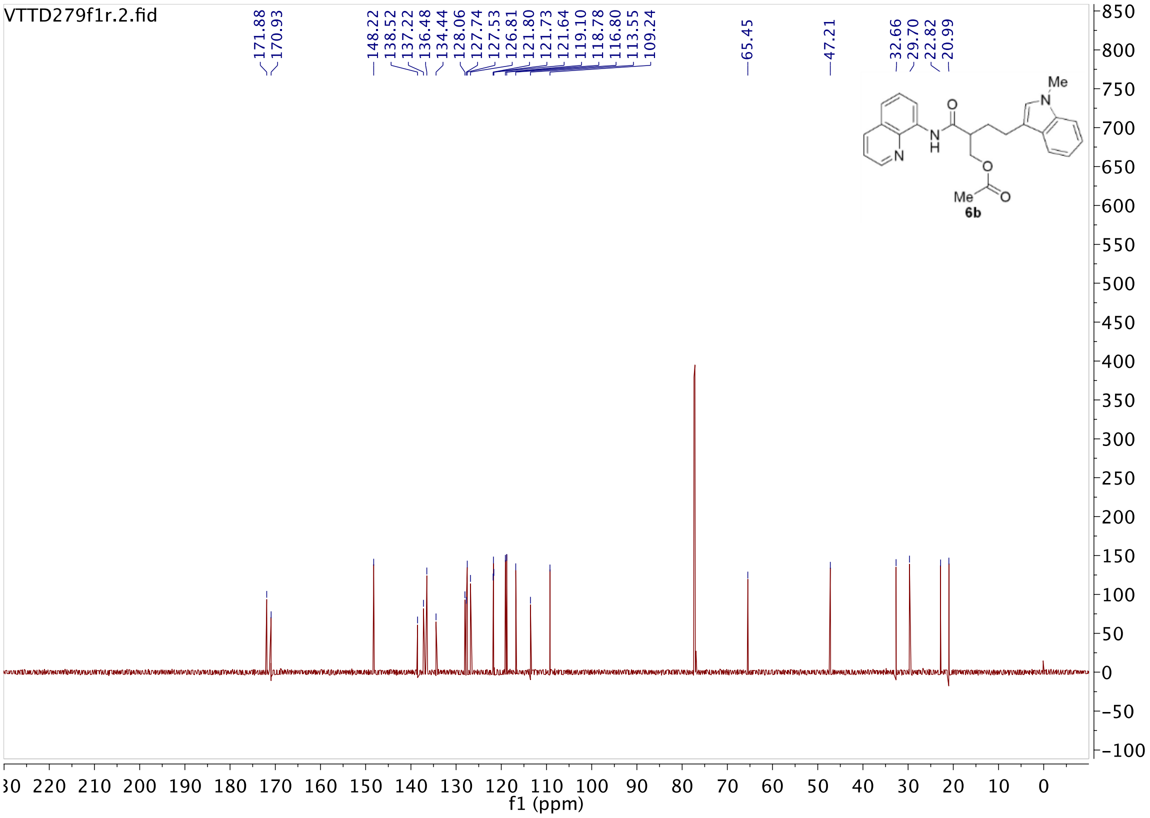
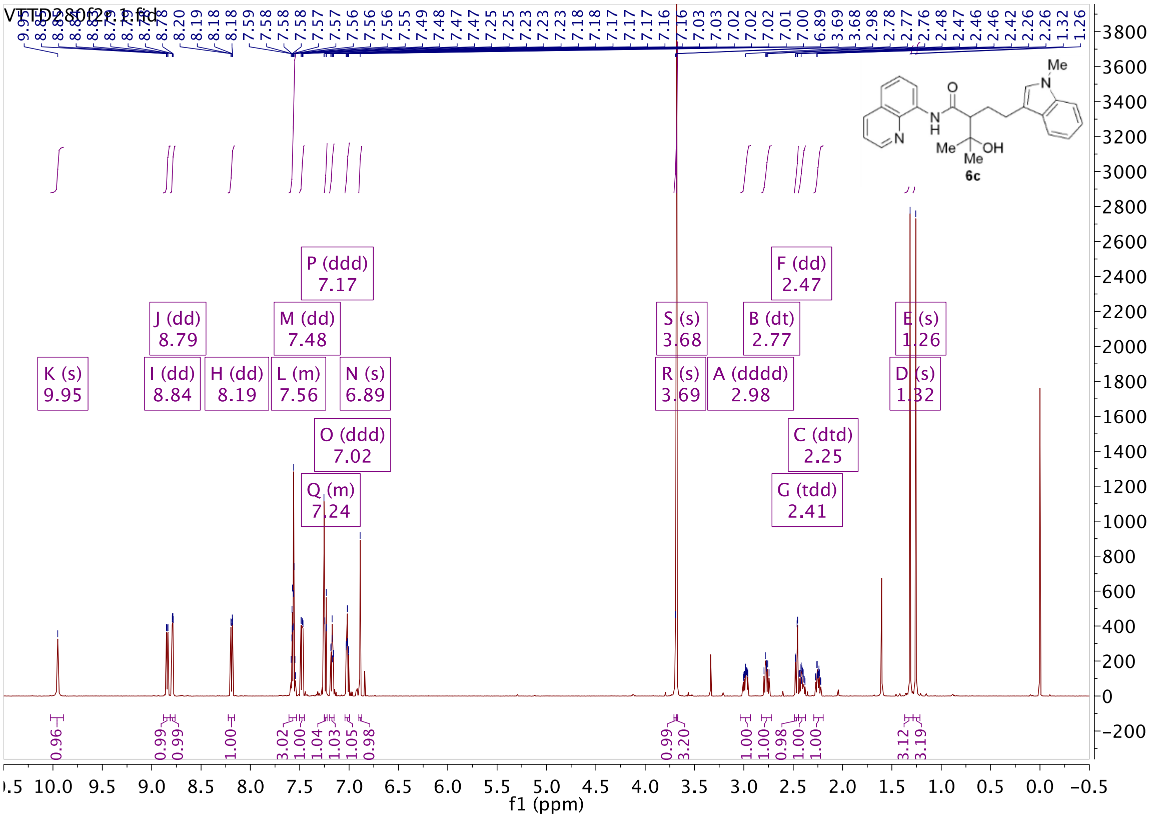
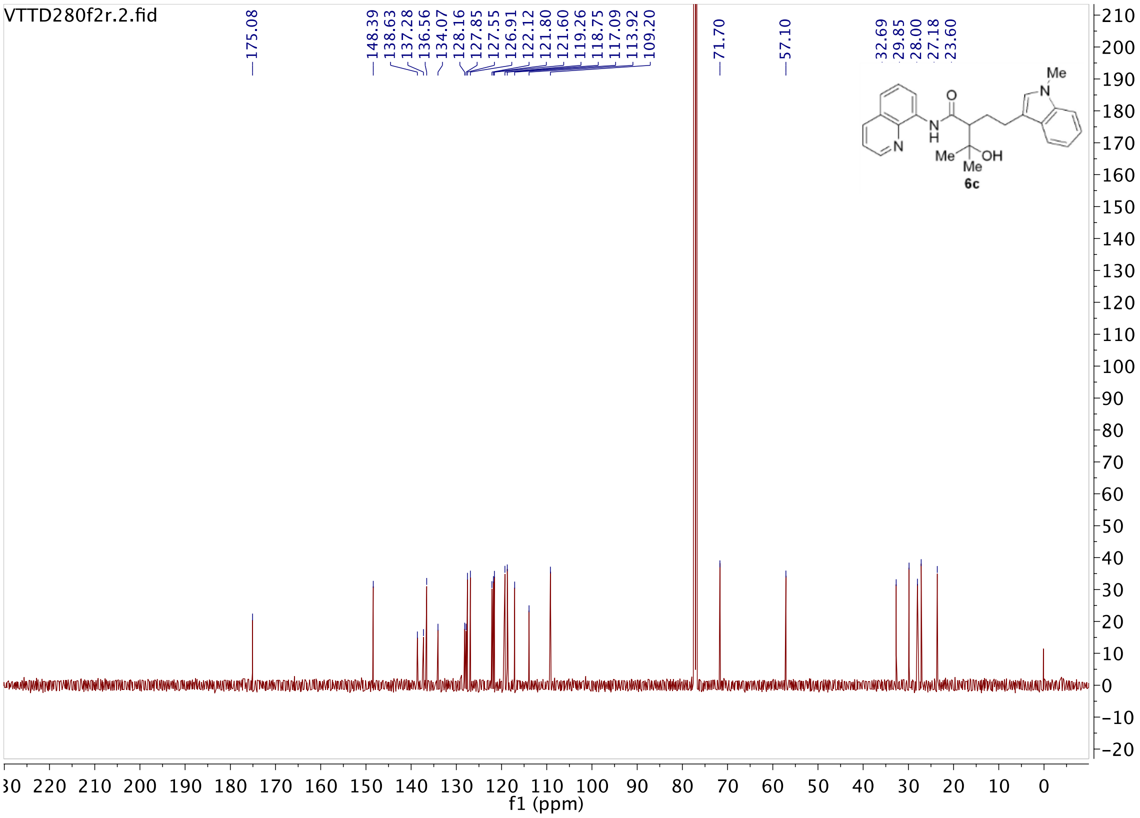
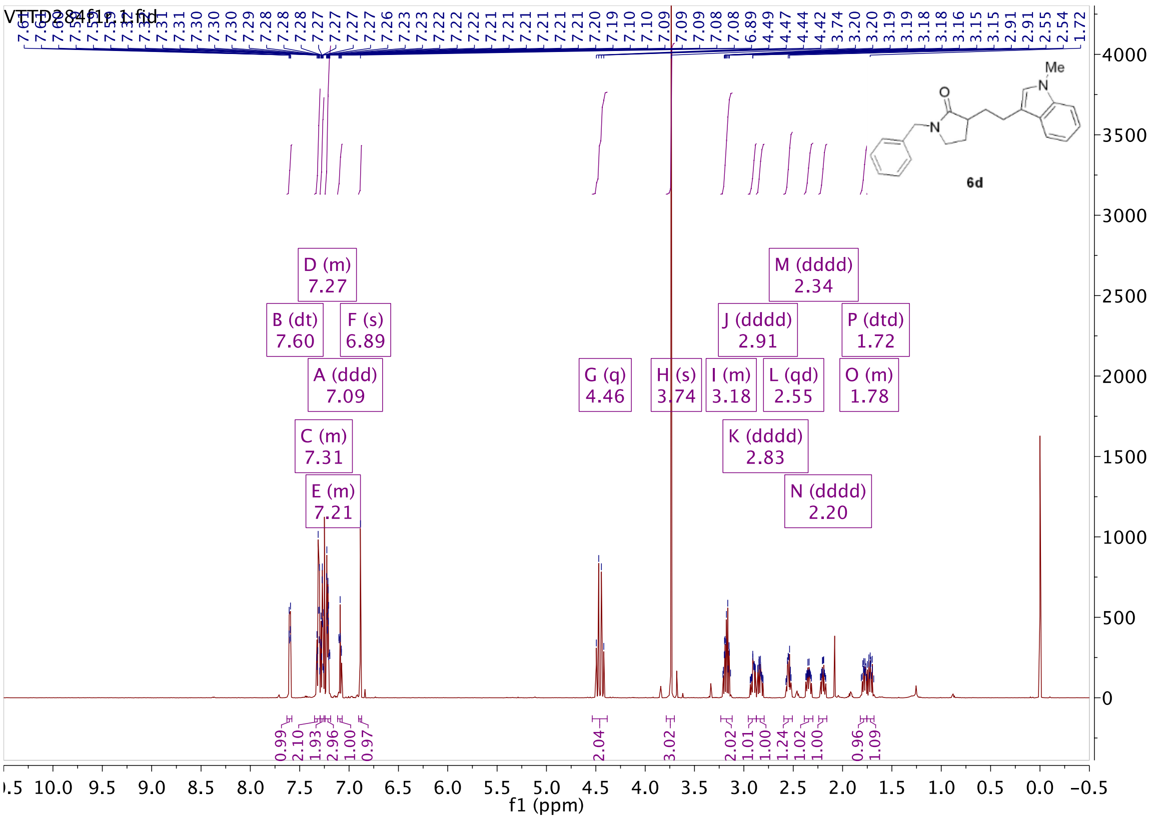
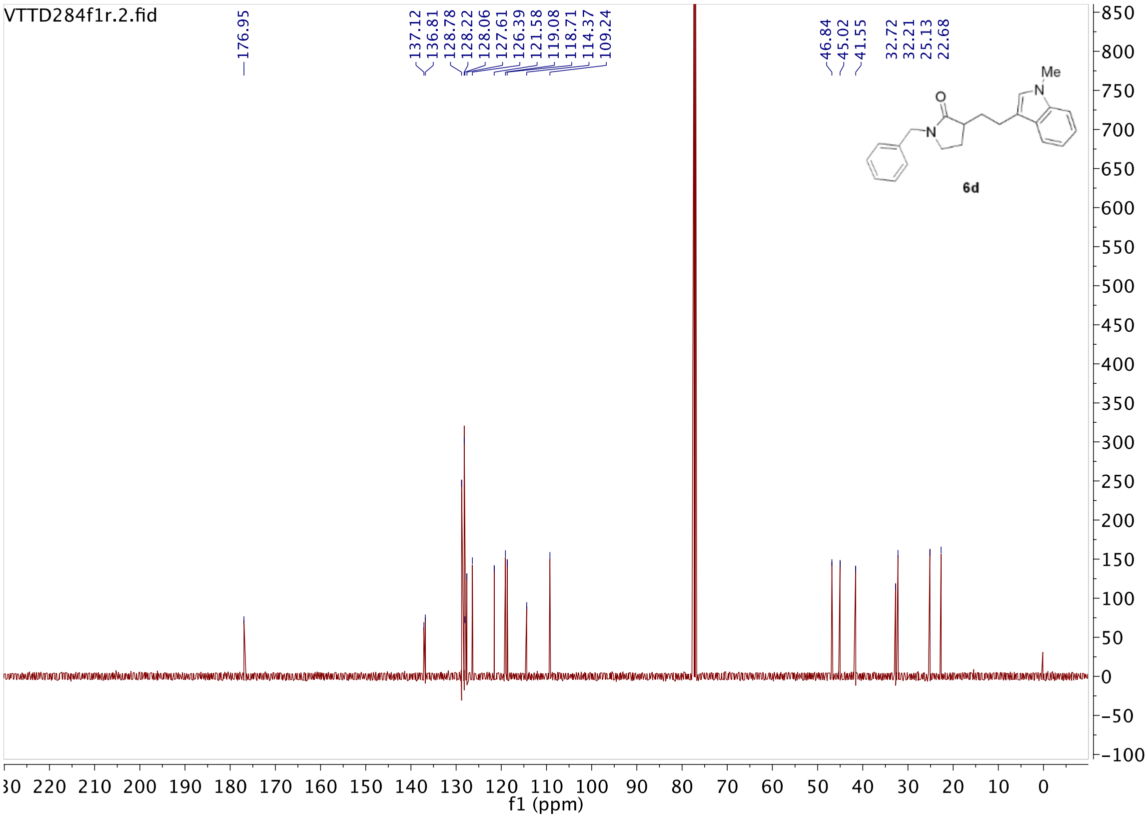
7.06
7.06
7.05
7.05
7.04
7.03
7.03
6.90
4.37
4.37
4.36
4.34
4.33
4.32
3.69
2.91
2.88
2.01
2.01
I (s) 9.97
G (dd) 8.84
H (dd) 8.77
F (dd) 8.16
J (dd) 7.45
P (m) 7.53
O (dt) 7.58
K (ddd) 7.18
L (ddd) 7.05
N (dt) 7.24
M (s) 6.90
A (m) 4.36
D (s) 3.69
B (m) 2.92
C (dddd) 2.27
E (m) 2.01
0.97
1.00
1.07
1.06
0.99
2.05
1.11
1.16
1.07
1.04
1.03
2.00
3.05
3.09
1.00
3.98
f1 (ppm)
Me
N
O
N
H
N
O
Me
O
6b

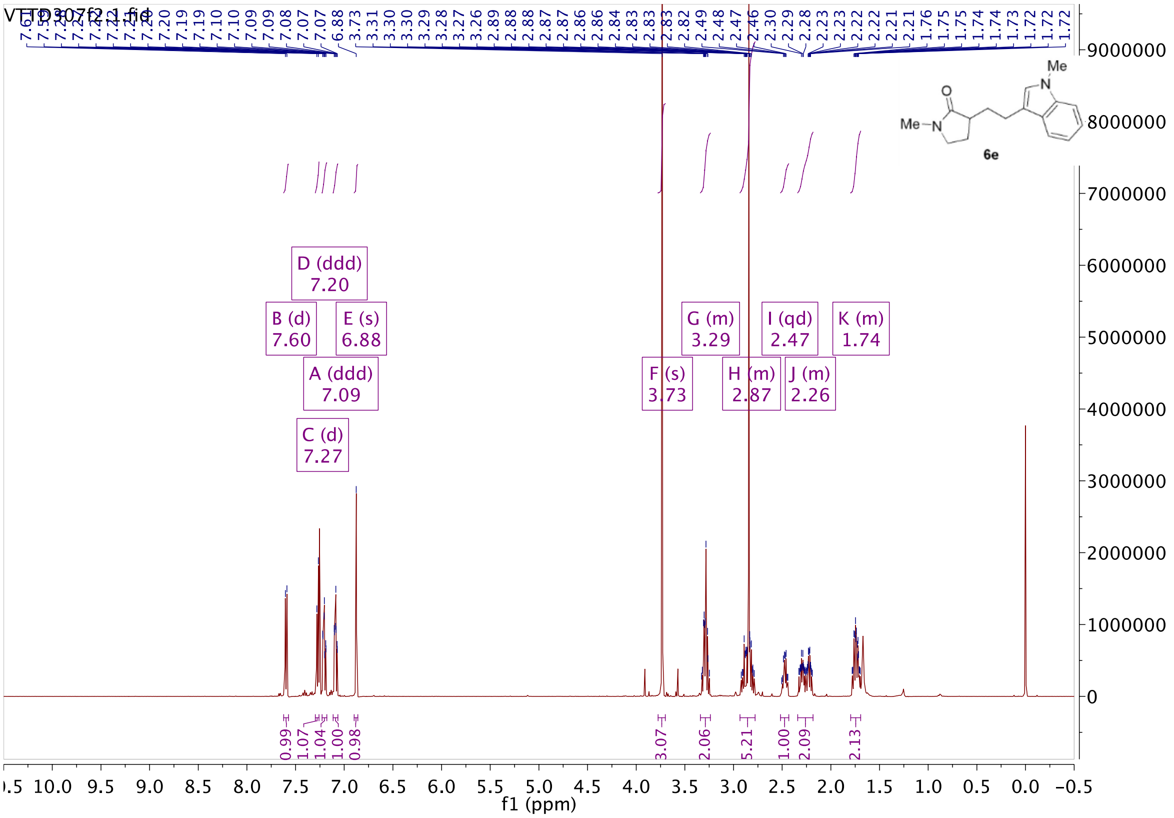

VTTD279f1r.2.fid
171.88
170.93
148.22
138.52
137.22
136.48
134.44
128.06
127.74
127.53
126.81
121.80
121.73
121.64
119.10
118.78
116.80
113.55
109.24
65.45
47.21
32.66
29.70
22.82
20.99
f1 (ppm)
Me
N
O
N
H
N
O
Me
O
6b

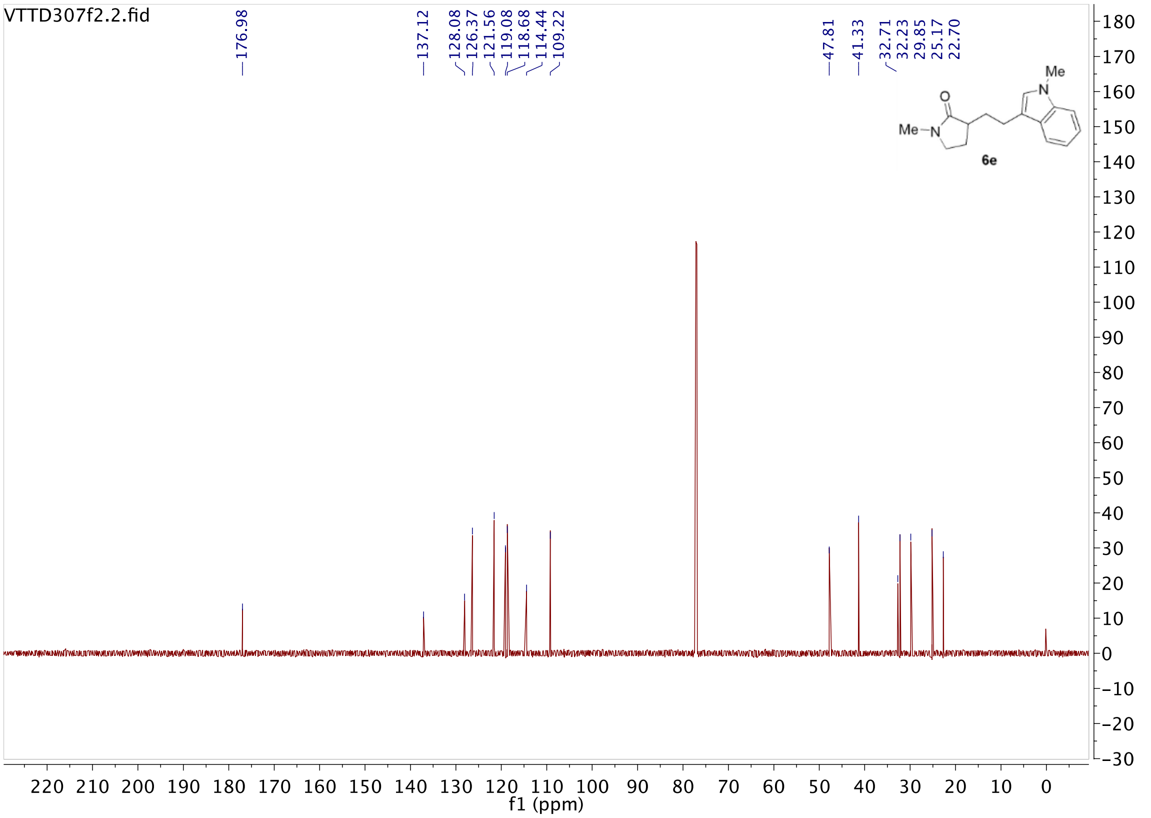

VTTD280f2r.1.fid
8.20
8.19
8.18
7.59
7.58
7.58
7.57
7.57
7.56
7.56
7.55
7.49
7.48
7.47
7.47
7.25
7.25
7.23
7.23
7.23
7.18
7.17
7.17
7.17
7.16
7.16
7.03
7.03
7.02
7.02
7.01
7.00
6.89
3.69
3.68
2.98
2.78
2.77
2.76
2.48
2.47
2.46
2.42
2.26
2.26
1.32
1.26
K (s) 9.95
J (dd) 8.79
I (dd) 8.84
H (dd) 8.19
M (dd) 7.48
P (ddd) 7.17
L (m) 7.56
N (s) 6.89
O (ddd) 7.02
Q (m) 7.24
S (s) 3.68
R (s) 3.69
A (dddd) 2.98
B (dt) 2.77
F (dd) 2.47
C (dtd) 2.25
G (tdd) 2.41
E (s) 1.26
D (s) 1.32
0.96
0.99
0.99
1.00
3.02
1.00
1.04
1.03
1.05
0.98
0.99
3.20
1.00
1.00
0.98
1.00
1.00
3.12
3.19
Me
N
O
N
H
N
Me
OH
Me
6c
f1 (ppm)

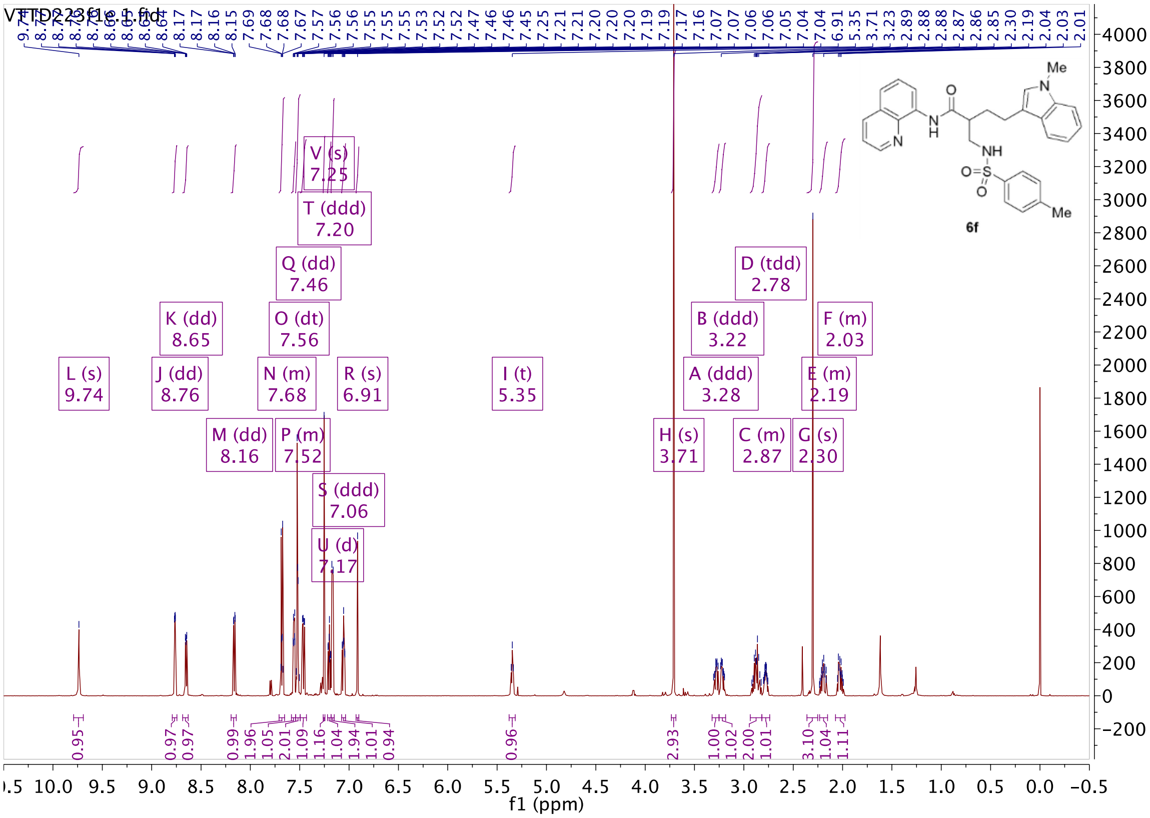

VTTD280f2r.2.fid
175.08
148.39
138.63
137.28
136.56
134.07
128.16
127.85
127.55
126.91
122.12
121.80
121.60
119.26
118.75
117.09
113.92
109.20
71.70
57.10
32.69
29.85
28.00
27.18
23.60
Me
N
O
N
H
N
Me
OH
Me
6c
f1 (ppm)

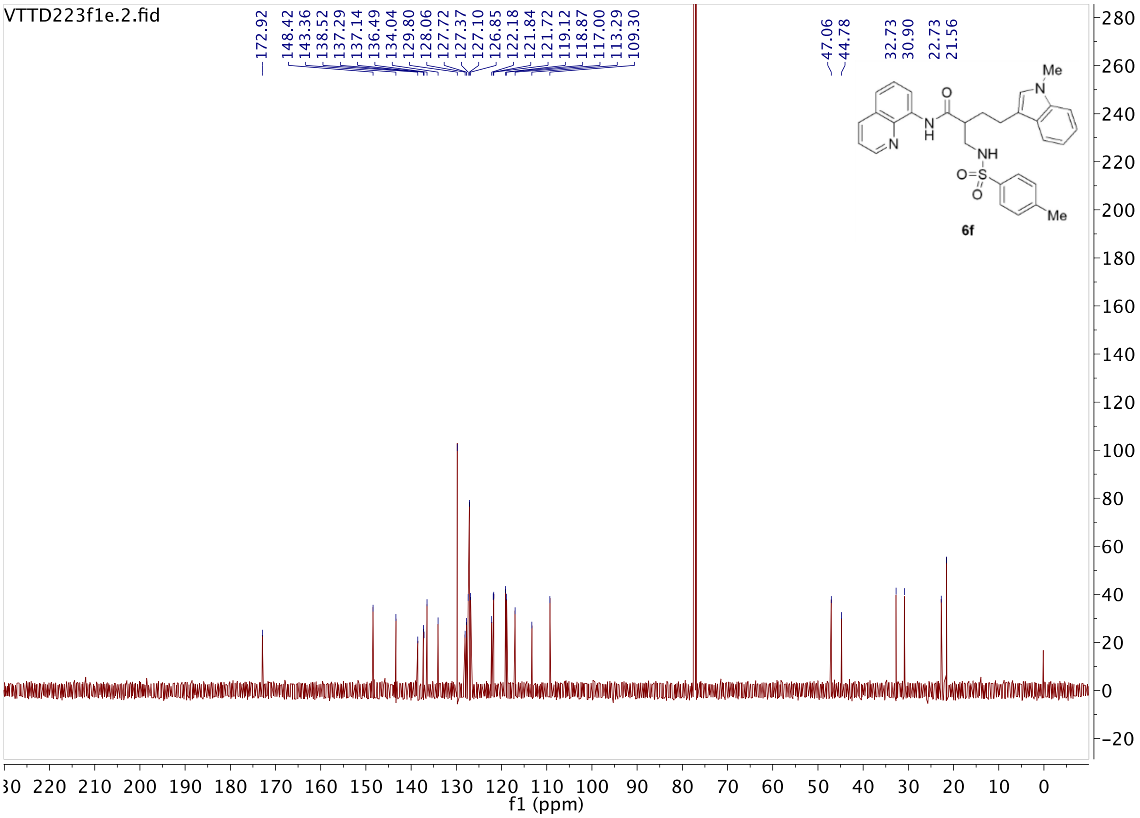

VTTD284f1r.1.fid
7.31 7.31 7.30 7.30 7.30 7.29 7.28 7.28 7.28 7.27 7.27 7.27 7.27 7.26 7.23 7.23 7.22 7.22 7.22 7.21 7.21 7.21 7.21 7.21 7.20 7.19 7.10 7.09 7.09 7.09 7.08 7.08 6.89 4.49 4.47 4.44 4.42 3.74 3.20 3.20 3.19 3.19 3.18 3.18 3.16 3.15 3.15 2.91 2.91 2.55 2.54 1.72
D (m) 7.27
B (dt) 7.60
F (s) 6.89
A (ddd) 7.09
C (m) 7.31
E (m) 7.21
G (q) 4.46
H (s) 3.74
I (m) 3.18
J (dddd) 2.91
K (dddd) 2.83
L (qd) 2.55
M (dddd) 2.34
N (dddd) 2.20
O (m) 1.78
P (dtd) 1.72
0.99 2.10 1.93 2.96 1.00 0.97 2.04 3.02 2.02 1.01 1.00 1.24 1.02 1.00 0.96 1.09
Me
N
O
6d
f1 (ppm)
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
4000 3500 3000 2500 2000 1500 1000 500 0

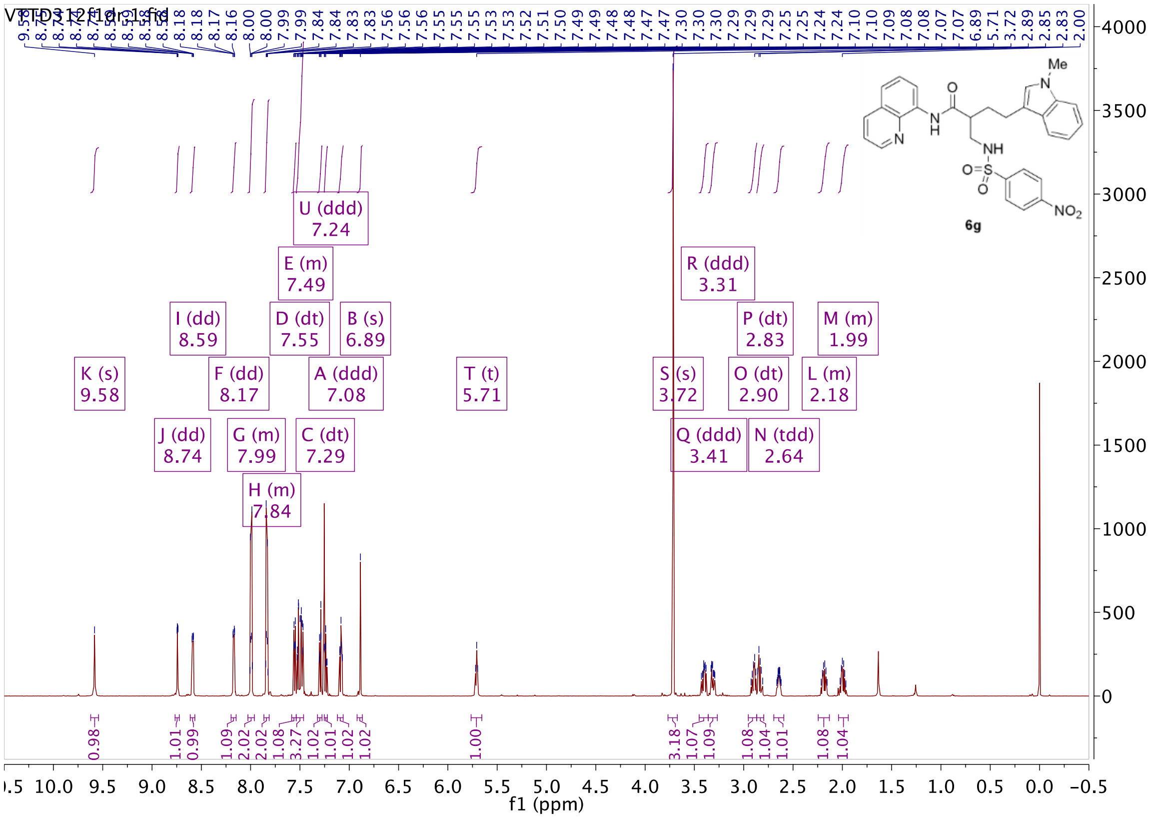

VTTD284f1r.2.fid
176.95
137.12 136.81 128.78 128.22 128.06 127.61 126.39 121.58 119.08 118.71 114.37 109.24
46.84 45.02 41.55
32.72 32.21 25.13 22.68
Me
N
O
6d
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
850 800 750 700 650 600 550 500 450 400 350 300 250 200 150 100 50 0 -50 -100

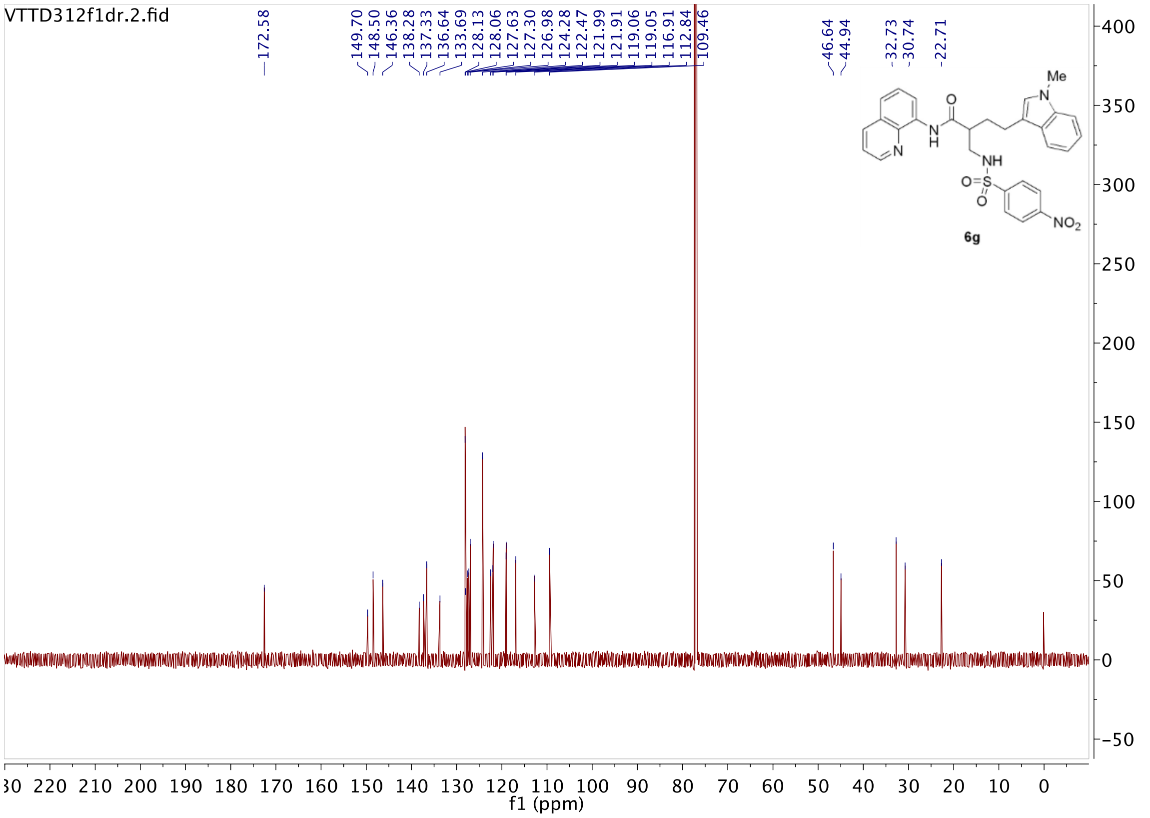

VTTD307f2.1.fid
7.20
7.19
7.19
7.10
7.10
7.09
7.09
7.08
7.07
7.07
6.88
3.73
3.31
3.30
3.30
3.29
3.28
3.27
3.26
2.89
2.88
2.88
2.87
2.87
2.86
2.86
2.84
2.83
2.83
2.83
2.82
2.49
2.48
2.47
2.46
2.30
2.29
2.28
2.23
2.23
2.22
2.22
2.21
2.21
1.76
1.75
1.75
1.74
1.74
1.73
1.72
1.72
1.72
Me
N
O
Me
N
6e
D (ddd)
7.20
B (d)
7.60
E (s)
6.88
A (ddd)
7.09
C (d)
7.27
F (s)
3.73
G (m)
3.29
H (m)
2.87
I (qd)
2.47
J (m)
2.26
K (m)
1.74
0.99
1.07
1.04
1.00
0.98
3.07
2.06
5.21
1.00
2.09
2.13
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
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
f1 (ppm)

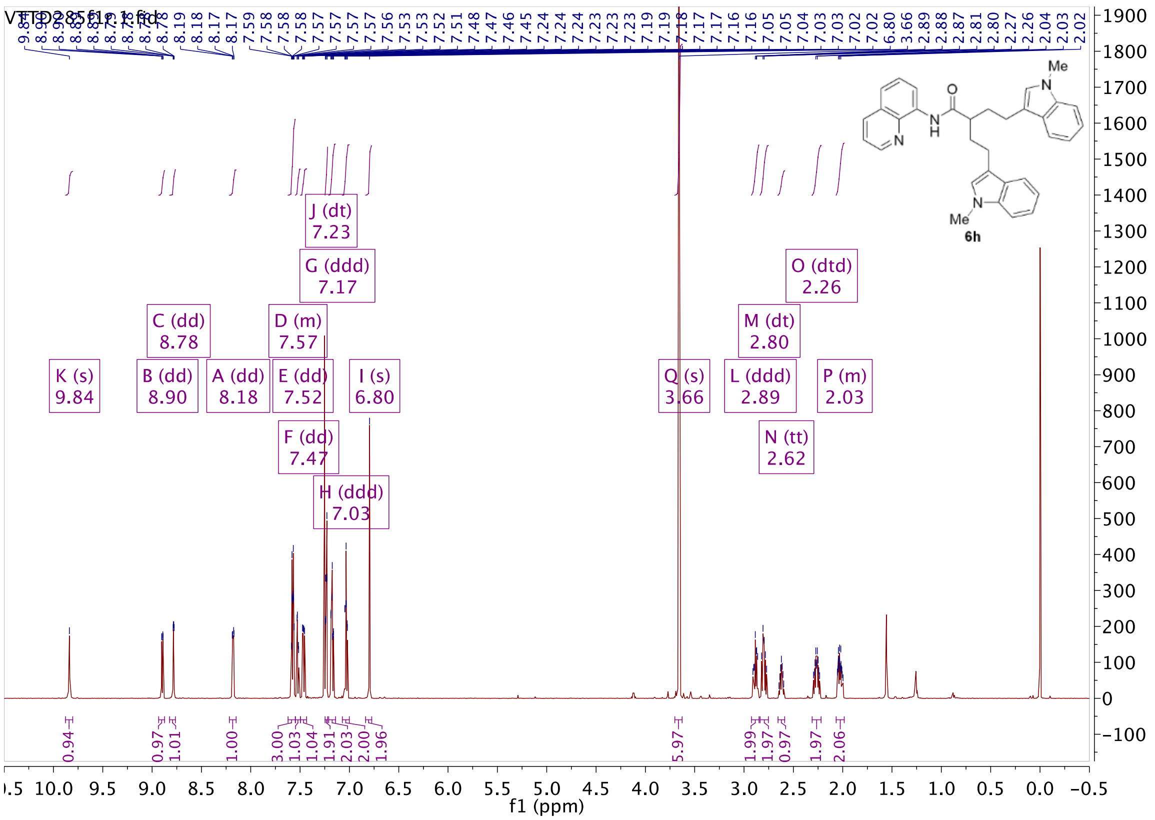

VTTD307f2.2.fid
176.98
137.12
128.08
126.37
121.56
119.08
118.68
114.44
109.22
47.81
41.33
32.71
32.23
29.85
25.17
22.70
Me
N
O
Me
N
6e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
–10
–20
–30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

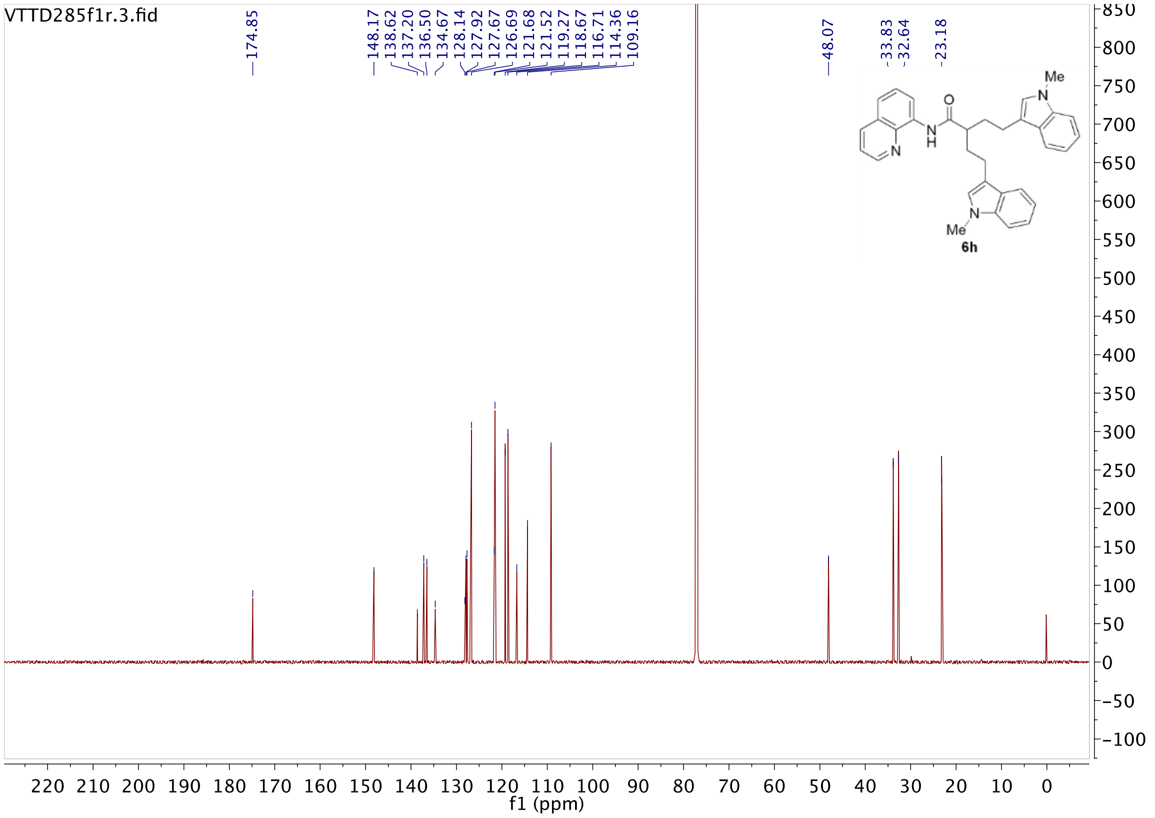

VTTD223f1e.1.fid
8.17 8.17 8.16 8.15 7.69 7.68 7.68 7.67 7.57 7.56 7.56 7.55 7.55 7.55 7.53 7.52 7.52 7.47 7.46 7.45 7.25 7.21 7.21 7.21 7.20 7.20 7.20 7.19 7.19 7.17 7.16 7.07 7.06 7.06 7.05 7.04 7.04 6.91 5.35 3.71 3.23 2.89 2.88 2.88 2.87 2.86 2.85 2.30 2.19 2.04 2.03 2.01
V (s) 7.25
T (ddd) 7.20
Q (dd) 7.46
D (tdd) 2.78
K (dd) 8.65
O (dt) 7.56
B (ddd) 3.22
F (m) 2.03
L (s) 9.74
J (dd) 8.76
N (m) 7.68
R (s) 6.91
I (t) 5.35
A (ddd) 3.28
E (m) 2.19
M (dd) 8.16
P (m) 7.52
H (s) 3.71
C (m) 2.87
G (s) 2.30
S (ddd) 7.06
U (d) 7.17
0.95 0.97 0.97 0.99 1.96 1.05 2.01 1.09 1.16 1.04 1.94 1.01 0.94 0.96 2.93 1.00 1.02 2.00 1.01 3.10 1.04 1.11
Me
N
O
N
H
N
NH
O=S
O
Me
6f
4000 3800 3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 −200
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
f1 (ppm)


VTTD223f1e.2.fid
172.92
148.42 143.36 138.52 137.29 137.14 136.49 134.04 129.80 128.06 127.72 127.37 127.10 126.85 122.18 121.84 121.72 119.12 118.87 117.00 113.29 109.30
47.06 44.78
32.73 30.90 22.73 21.56
Me
N
O
N
H
N
NH
O=S
O
Me
6f
280 260 240 220 200 180 160 140 120 100 80 60 40 20 0 −20
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


VTTD312f1dr.1.fid
9.58
8.75
8.74
8.74
8.74
8.59
8.59
8.58
8.58
8.18
8.18
8.17
8.16
8.00
8.00
7.99
7.99
7.84
7.84
7.83
7.83
7.56
7.56
7.56
7.55
7.55
7.55
7.53
7.53
7.52
7.51
7.50
7.49
7.49
7.48
7.48
7.47
7.47
7.30
7.30
7.30
7.29
7.29
7.29
7.25
7.25
7.24
7.24
7.10
7.10
7.09
7.08
7.08
7.07
7.07
6.89
5.71
3.72
2.89
2.85
2.83
2.00
U (ddd) 7.24
E (m) 7.49
I (dd) 8.59
D (dt) 7.55
B (s) 6.89
K (s) 9.58
F (dd) 8.17
A (ddd) 7.08
T (t) 5.71
J (dd) 8.74
G (m) 7.99
C (dt) 7.29
H (m) 7.84
R (ddd) 3.31
P (dt) 2.83
M (m) 1.99
S (s) 3.72
O (dt) 2.90
L (m) 2.18
Q (ddd) 3.41
N (tdd) 2.64
0.98
1.01
0.99
1.09
2.02
2.02
1.08
3.27
1.02
1.01
1.02
1.02
1.00
3.18
1.07
1.09
1.08
1.04
1.01
1.08
1.04
Me
N
O
N
H
N
NH
O=S
O
NO2
6g
4000
3500
3000
2500
2000
1500
1000
500
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
–0.5
f1 (ppm)


VTTD312f1dr.2.fid
172.58
149.70
148.50
146.36
138.28
137.33
136.64
133.69
128.13
128.06
127.63
127.30
126.98
124.28
122.47
121.99
121.91
119.06
119.05
116.91
112.84
109.46
46.64
44.94
32.73
30.74
22.71
Me
N
O
N
H
N
NH
O=S
O
NO2
6g
400
350
300
250
200
150
100
50
0
–50
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


VTTD285f1r.1.fid
8.19 8.18 8.17 8.17 7.59 7.58 7.58 7.57 7.57 7.57 7.57 7.56 7.53 7.53 7.52 7.51 7.48 7.47 7.46 7.45 7.24 7.24 7.24 7.23 7.23 7.23 7.19 7.19 7.18 7.17 7.17 7.16 7.05 7.05 7.04 7.03 7.03 7.02 7.02 6.80 3.66 2.89 2.88 2.87 2.81 2.80 2.27 2.26 2.04 2.03 2.02
K (s) 9.84
B (dd) 8.90
C (dd) 8.78
A (dd) 8.18
D (m) 7.57
E (dd) 7.52
F (dd) 7.47
J (dt) 7.23
G (ddd) 7.17
H (ddd) 7.03
I (s) 6.80
Q (s) 3.66
L (ddd) 2.89
M (dt) 2.80
N (tt) 2.62
O (dtd) 2.26
P (m) 2.03
0.94 0.97 1.01 1.00 3.00 1.03 1.04 1.91 2.03 2.00 1.96 5.97 1.99 1.97 0.97 1.97 2.06
Me
N
O
N
H
N
Me
N
6h
f1 (ppm)


VTTD285f1r.3.fid
174.85
148.17 138.62 137.20 136.50 134.67 128.14 127.92 127.67 126.69 121.68 121.52 119.27 118.67 116.71 114.36 109.16
48.07
33.83 32.64
23.18
Me
N
O
N
H
N
Me
N
6h
f1 (ppm)

Crystal Data

Experimental Summary for Crystal S1

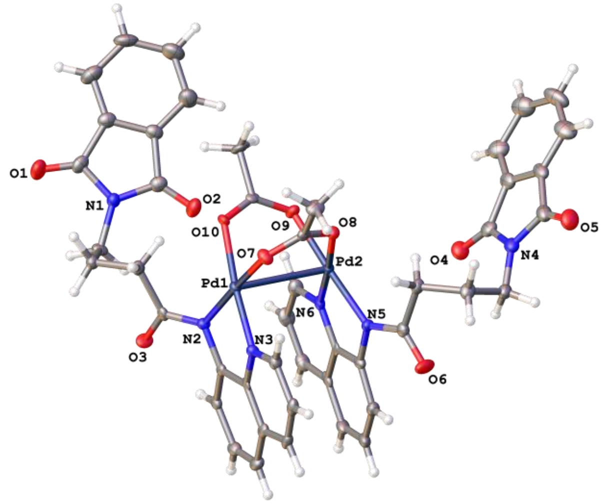


Table S5. Crystal data and structure refinement for engle55_0m_a.

Identification code	JAG-C-063B (Et2O → EtOAc)	
Empirical formula	C46 H38 N6 O10 Pd2	
Formula weight	1047.62	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.5489(15) Å	α= 76.628(4)°.
	b = 10.6184(15) Å	β= 84.772(5)°.
	c = 19.274(2) Å	γ = 81.899(5)°.
Volume	2075.6(5) Å^3	
Z	2	
Density (calculated)	1.676 Mg/m^3	
Absorption coefficient	0.936 mm^{-1}	
F(000)	1056	
Crystal size	0.28 x 0.24 x 0.2 mm^3	
Theta range for data collection	2.293 to 28.302°.	
Index ranges	-13<=h<=14, -14<=k<=13, -25<=l<=25	
Reflections collected	32347	
Independent reflections	10310 [R(int) = 0.0421]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.2627 and 0.2290	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10310 / 0 / 579	
Goodness-of-fit on F^2	1.025	
Final R indices [I>2sigma(I)]	R1 = 0.0307, wR2 = 0.0597	
R indices (all data)	R1 = 0.0472, wR2 = 0.0650	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.504 and -0.526 e.Å^{-3}	

Table S6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for engle55_0m_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(2)	2374(1)	7518(1)	2453(1)	15(1)
Pd(1)	4804(1)	8439(1)	1847(1)	14(1)
N(6)	2447(2)	6098(2)	1934(1)	18(1)
O(8)	2416(2)	8981(2)	2982(1)	20(1)
O(7)	4136(2)	9859(2)	2385(1)	22(1)
O(1)	10645(2)	3290(2)	2958(1)	36(1)
O(3)	7009(2)	5778(2)	776(1)	24(1)
O(10)	5419(2)	7345(2)	2807(1)	17(1)
N(2)	5491(2)	7204(2)	1215(1)	14(1)
O(5)	-3911(2)	10098(2)	3982(1)	36(1)
O(9)	3599(2)	6431(2)	3183(1)	20(1)
N(1)	8479(2)	3638(2)	2761(1)	21(1)
O(4)	-1101(2)	6952(2)	3184(1)	32(1)
O(6)	-665(2)	9844(2)	1317(1)	33(1)
O(2)	6274(2)	3691(2)	2929(1)	33(1)
C(25)	1893(2)	5619(2)	838(1)	21(1)
C(12)	6642(2)	6417(2)	1229(1)	16(1)
C(27)	3271(3)	4069(2)	1638(1)	27(1)
C(45)	3204(2)	9806(2)	2847(1)	18(1)
C(8)	9535(3)	3255(2)	3183(1)	24(1)
C(41)	3013(3)	10852(2)	3268(1)	26(1)
C(28)	3158(2)	4949(2)	2087(1)	22(1)
C(10)	8769(2)	5536(2)	1761(1)	19(1)
N(3)	4045(2)	9457(2)	955(1)	15(1)
C(15)	4086(2)	7190(2)	-515(1)	22(1)
N(5)	1054(2)	8389(2)	1744(1)	16(1)
C(9)	8623(2)	4090(2)	1985(1)	23(1)
C(24)	1259(2)	6064(3)	196(1)	25(1)
N(4)	-2461(2)	8749(2)	3418(1)	24(1)
C(13)	4805(2)	7482(2)	590(1)	14(1)
C(40)	1809(2)	6468(2)	1315(1)	17(1)

C(7)	9011(3)	2799(2)	3926(1)	25(1)
C(2)	7685(3)	2928(2)	3916(1)	24(1)
C(14)	4785(2)	6721(2)	100(1)	19(1)
C(38)	-1481(2)	10519(2)	2572(1)	24(1)
C(6)	9638(3)	2296(3)	4553(2)	34(1)
C(11)	7508(2)	6413(2)	1818(1)	19(1)
C(1)	7329(3)	3462(2)	3163(1)	24(1)
C(26)	2640(2)	4406(2)	1021(1)	25(1)
C(39)	-111(2)	9877(2)	2475(1)	20(1)
C(3)	6922(3)	2579(3)	4538(2)	34(1)
C(4)	7541(3)	2104(3)	5172(2)	39(1)
C(18)	2709(2)	10482(2)	-264(1)	21(1)
C(36)	-1774(3)	7499(2)	3597(1)	25(1)
C(5)	8864(3)	1961(3)	5176(2)	39(1)
C(30)	-2921(3)	7971(3)	4617(1)	27(1)
C(43)	4739(2)	6611(2)	3247(1)	16(1)
C(37)	-2487(2)	9588(2)	2703(1)	25(1)
C(20)	3393(2)	10645(2)	857(1)	18(1)
C(44)	83(2)	9369(2)	1792(1)	21(1)
C(17)	3396(2)	9219(2)	-177(1)	18(1)
C(29)	-3198(3)	9091(3)	4002(1)	29(1)
C(35)	-2073(3)	7017(3)	4376(1)	27(1)
C(32)	-3012(3)	6608(3)	5769(2)	46(1)
C(16)	3429(2)	8411(2)	-665(1)	23(1)
C(21)	1097(2)	7726(2)	1178(1)	16(1)
C(34)	-1682(3)	5841(3)	4820(2)	33(1)
C(31)	-3416(3)	7784(3)	5316(2)	37(1)
C(33)	-2166(3)	5646(3)	5534(2)	42(1)
C(22)	532(2)	8128(2)	533(1)	21(1)
C(19)	2714(2)	11181(2)	249(1)	22(1)
C(46)	4069(2)	8732(2)	448(1)	16(1)
C(23)	621(2)	7306(3)	50(1)	25(1)
C(42)	5324(2)	5879(2)	3933(1)	24(1)

Table S7. Bond lengths [Å] and angles [°] for engle55_0m_a.

Pd(2)-Pd(1)	2.9200(4)
Pd(2)-N(6)	1.9829(19)
Pd(2)-O(8)	2.0541(15)
Pd(2)-O(9)	2.0355(15)
Pd(2)-N(5)	2.0150(18)
Pd(1)-O(7)	2.0332(15)
Pd(1)-O(10)	2.0497(16)
Pd(1)-N(2)	2.0102(17)
Pd(1)-N(3)	1.9784(19)
N(6)-C(28)	1.325(3)
N(6)-C(40)	1.373(3)
O(8)-C(45)	1.260(3)
O(7)-C(45)	1.262(3)
O(1)-C(8)	1.213(3)
O(3)-C(12)	1.229(3)
O(10)-C(43)	1.258(3)
N(2)-C(12)	1.372(3)
N(2)-C(13)	1.413(3)
O(5)-C(29)	1.212(3)
O(9)-C(43)	1.265(3)
N(1)-C(8)	1.398(3)
N(1)-C(9)	1.462(3)
N(1)-C(1)	1.390(3)
O(4)-C(36)	1.211(3)
O(6)-C(44)	1.234(3)
O(2)-C(1)	1.211(3)
C(25)-C(24)	1.412(3)
C(25)-C(40)	1.418(3)
C(25)-C(26)	1.400(3)
C(12)-C(11)	1.519(3)
C(27)-H(27)	0.9500
C(27)-C(28)	1.399(3)
C(27)-C(26)	1.365(4)
C(45)-C(41)	1.502(3)

C(8)-C(7)	1.484(4)
C(41)-H(41A)	0.9800
C(41)-H(41B)	0.9800
C(41)-H(41C)	0.9800
C(28)-H(28)	0.9500
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(10)-C(9)	1.522(3)
C(10)-C(11)	1.523(3)
N(3)-C(20)	1.330(3)
N(3)-C(46)	1.373(3)
C(15)-H(15)	0.9500
C(15)-C(14)	1.408(3)
C(15)-C(16)	1.362(3)
N(5)-C(44)	1.367(3)
N(5)-C(21)	1.421(3)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(24)-H(24)	0.9500
C(24)-C(23)	1.373(4)
N(4)-C(36)	1.404(3)
N(4)-C(37)	1.458(3)
N(4)-C(29)	1.398(3)
C(13)-C(14)	1.380(3)
C(13)-C(46)	1.421(3)
C(40)-C(21)	1.417(3)
C(7)-C(2)	1.387(4)
C(7)-C(6)	1.390(3)
C(2)-C(1)	1.492(3)
C(2)-C(3)	1.387(4)
C(14)-H(14)	0.9500
C(38)-H(38A)	0.9900
C(38)-H(38B)	0.9900
C(38)-C(39)	1.523(3)
C(38)-C(37)	1.517(3)
C(6)-H(6)	0.9500

C(6)-C(5)	1.393(4)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(26)-H(26)	0.9500
C(39)-H(39A)	0.9900
C(39)-H(39B)	0.9900
C(39)-C(44)	1.521(3)
C(3)-H(3)	0.9500
C(3)-C(4)	1.395(4)
C(4)-H(4)	0.9500
C(4)-C(5)	1.383(4)
C(18)-H(18)	0.9500
C(18)-C(17)	1.412(3)
C(18)-C(19)	1.368(3)
C(36)-C(35)	1.490(4)
C(5)-H(5)	0.9500
C(30)-C(29)	1.489(4)
C(30)-C(35)	1.389(4)
C(30)-C(31)	1.381(4)
C(43)-C(42)	1.507(3)
C(37)-H(37A)	0.9900
C(37)-H(37B)	0.9900
C(20)-H(20)	0.9500
C(20)-C(19)	1.392(3)
C(17)-C(16)	1.408(3)
C(17)-C(46)	1.410(3)
C(35)-C(34)	1.374(4)
C(32)-H(32)	0.9500
C(32)-C(31)	1.384(4)
C(32)-C(33)	1.389(4)
C(16)-H(16)	0.9500
C(21)-C(22)	1.379(3)
C(34)-H(34)	0.9500
C(34)-C(33)	1.402(4)
C(31)-H(31)	0.9500
C(33)-H(33)	0.9500

C(22)-H(22)	0.9500
C(22)-C(23)	1.404(3)
C(19)-H(19)	0.9500
C(23)-H(23)	0.9500
C(42)-H(42A)	0.9800
C(42)-H(42B)	0.9800
C(42)-H(42C)	0.9800

N(6)-Pd(2)-Pd(1)	96.99(6)
N(6)-Pd(2)-O(8)	176.55(7)
N(6)-Pd(2)-O(9)	92.67(7)
N(6)-Pd(2)-N(5)	82.07(8)
O(8)-Pd(2)-Pd(1)	79.86(5)
O(9)-Pd(2)-Pd(1)	79.10(5)
O(9)-Pd(2)-O(8)	85.38(6)
N(5)-Pd(2)-Pd(1)	106.34(6)
N(5)-Pd(2)-O(8)	100.10(7)
N(5)-Pd(2)-O(9)	172.80(7)
O(7)-Pd(1)-Pd(2)	80.79(5)
O(7)-Pd(1)-O(10)	86.28(6)
O(10)-Pd(1)-Pd(2)	81.67(5)
N(2)-Pd(1)-Pd(2)	103.20(5)
N(2)-Pd(1)-O(7)	173.32(7)
N(2)-Pd(1)-O(10)	99.52(7)
N(3)-Pd(1)-Pd(2)	92.93(5)
N(3)-Pd(1)-O(7)	92.46(7)
N(3)-Pd(1)-O(10)	174.58(7)
N(3)-Pd(1)-N(2)	82.06(7)
C(28)-N(6)-Pd(2)	125.99(17)
C(28)-N(6)-C(40)	120.2(2)
C(40)-N(6)-Pd(2)	113.22(15)
C(45)-O(8)-Pd(2)	125.64(15)
C(45)-O(7)-Pd(1)	125.06(15)
C(43)-O(10)-Pd(1)	123.53(15)
C(12)-N(2)-Pd(1)	128.76(15)
C(12)-N(2)-C(13)	118.43(18)

C(13)-N(2)-Pd(1)	110.70(14)
C(43)-O(9)-Pd(2)	126.86(15)
C(8)-N(1)-C(9)	122.1(2)
C(1)-N(1)-C(8)	111.9(2)
C(1)-N(1)-C(9)	126.0(2)
C(24)-C(25)-C(40)	118.2(2)
C(26)-C(25)-C(24)	123.9(2)
C(26)-C(25)-C(40)	117.9(2)
O(3)-C(12)-N(2)	123.1(2)
O(3)-C(12)-C(11)	119.9(2)
N(2)-C(12)-C(11)	116.96(19)
C(28)-C(27)-H(27)	120.4
C(26)-C(27)-H(27)	120.4
C(26)-C(27)-C(28)	119.3(2)
O(8)-C(45)-O(7)	126.8(2)
O(8)-C(45)-C(41)	117.1(2)
O(7)-C(45)-C(41)	116.1(2)
O(1)-C(8)-N(1)	124.7(2)
O(1)-C(8)-C(7)	129.1(2)
N(1)-C(8)-C(7)	106.2(2)
C(45)-C(41)-H(41A)	109.5
C(45)-C(41)-H(41B)	109.5
C(45)-C(41)-H(41C)	109.5
H(41A)-C(41)-H(41B)	109.5
H(41A)-C(41)-H(41C)	109.5
H(41B)-C(41)-H(41C)	109.5
N(6)-C(28)-C(27)	121.9(2)
N(6)-C(28)-H(28)	119.1
C(27)-C(28)-H(28)	119.1
H(10A)-C(10)-H(10B)	107.8
C(9)-C(10)-H(10A)	109.0
C(9)-C(10)-H(10B)	109.0
C(9)-C(10)-C(11)	113.1(2)
C(11)-C(10)-H(10A)	109.0
C(11)-C(10)-H(10B)	109.0
C(20)-N(3)-Pd(1)	126.49(16)

C(20)-N(3)-C(46)	120.1(2)
C(46)-N(3)-Pd(1)	112.68(14)
C(14)-C(15)-H(15)	118.9
C(16)-C(15)-H(15)	118.9
C(16)-C(15)-C(14)	122.3(2)
C(44)-N(5)-Pd(2)	128.91(15)
C(44)-N(5)-C(21)	119.18(19)
C(21)-N(5)-Pd(2)	111.32(14)
N(1)-C(9)-C(10)	112.28(19)
N(1)-C(9)-H(9A)	109.1
N(1)-C(9)-H(9B)	109.1
C(10)-C(9)-H(9A)	109.1
C(10)-C(9)-H(9B)	109.1
H(9A)-C(9)-H(9B)	107.9
C(25)-C(24)-H(24)	120.5
C(23)-C(24)-C(25)	118.9(2)
C(23)-C(24)-H(24)	120.5
C(36)-N(4)-C(37)	125.2(2)
C(29)-N(4)-C(36)	112.2(2)
C(29)-N(4)-C(37)	122.5(2)
N(2)-C(13)-C(46)	114.39(19)
C(14)-C(13)-N(2)	128.7(2)
C(14)-C(13)-C(46)	116.8(2)
N(6)-C(40)-C(25)	120.4(2)
N(6)-C(40)-C(21)	116.9(2)
C(21)-C(40)-C(25)	122.7(2)
C(2)-C(7)-C(8)	107.8(2)
C(2)-C(7)-C(6)	121.9(3)
C(6)-C(7)-C(8)	130.3(3)
C(7)-C(2)-C(1)	108.3(2)
C(7)-C(2)-C(3)	121.2(2)
C(3)-C(2)-C(1)	130.5(3)
C(15)-C(14)-H(14)	119.6
C(13)-C(14)-C(15)	120.7(2)
C(13)-C(14)-H(14)	119.6
H(38A)-C(38)-H(38B)	107.6

C(39)-C(38)-H(38A)	108.7
C(39)-C(38)-H(38B)	108.7
C(37)-C(38)-H(38A)	108.7
C(37)-C(38)-H(38B)	108.7
C(37)-C(38)-C(39)	114.4(2)
C(7)-C(6)-H(6)	121.7
C(7)-C(6)-C(5)	116.6(3)
C(5)-C(6)-H(6)	121.7
C(12)-C(11)-C(10)	111.78(19)
C(12)-C(11)-H(11A)	109.3
C(12)-C(11)-H(11B)	109.3
C(10)-C(11)-H(11A)	109.3
C(10)-C(11)-H(11B)	109.3
H(11A)-C(11)-H(11B)	107.9
N(1)-C(1)-C(2)	105.8(2)
O(2)-C(1)-N(1)	125.5(2)
O(2)-C(1)-C(2)	128.7(3)
C(25)-C(26)-H(26)	119.8
C(27)-C(26)-C(25)	120.4(2)
C(27)-C(26)-H(26)	119.8
C(38)-C(39)-H(39A)	109.4
C(38)-C(39)-H(39B)	109.4
H(39A)-C(39)-H(39B)	108.0
C(44)-C(39)-C(38)	111.03(19)
C(44)-C(39)-H(39A)	109.4
C(44)-C(39)-H(39B)	109.4
C(2)-C(3)-H(3)	121.4
C(2)-C(3)-C(4)	117.3(3)
C(4)-C(3)-H(3)	121.4
C(3)-C(4)-H(4)	119.4
C(5)-C(4)-C(3)	121.1(3)
C(5)-C(4)-H(4)	119.4
C(17)-C(18)-H(18)	120.1
C(19)-C(18)-H(18)	120.1
C(19)-C(18)-C(17)	119.9(2)
O(4)-C(36)-N(4)	125.5(2)

O(4)-C(36)-C(35)	128.9(2)
N(4)-C(36)-C(35)	105.6(2)
C(6)-C(5)-H(5)	119.0
C(4)-C(5)-C(6)	121.9(3)
C(4)-C(5)-H(5)	119.0
C(35)-C(30)-C(29)	108.6(2)
C(31)-C(30)-C(29)	129.7(3)
C(31)-C(30)-C(35)	121.6(3)
O(10)-C(43)-O(9)	127.0(2)
O(10)-C(43)-C(42)	117.2(2)
O(9)-C(43)-C(42)	115.8(2)
N(4)-C(37)-C(38)	112.1(2)
N(4)-C(37)-H(37A)	109.2
N(4)-C(37)-H(37B)	109.2
C(38)-C(37)-H(37A)	109.2
C(38)-C(37)-H(37B)	109.2
H(37A)-C(37)-H(37B)	107.9
N(3)-C(20)-H(20)	119.2
N(3)-C(20)-C(19)	121.5(2)
C(19)-C(20)-H(20)	119.2
O(6)-C(44)-N(5)	123.4(2)
O(6)-C(44)-C(39)	118.2(2)
N(5)-C(44)-C(39)	118.4(2)
C(16)-C(17)-C(18)	124.3(2)
C(16)-C(17)-C(46)	118.1(2)
C(46)-C(17)-C(18)	117.5(2)
O(5)-C(29)-N(4)	125.0(3)
O(5)-C(29)-C(30)	129.5(3)
N(4)-C(29)-C(30)	105.5(2)
C(30)-C(35)-C(36)	108.1(2)
C(34)-C(35)-C(36)	130.0(3)
C(34)-C(35)-C(30)	121.8(3)
C(31)-C(32)-H(32)	119.0
C(31)-C(32)-C(33)	122.1(3)
C(33)-C(32)-H(32)	119.0
C(15)-C(16)-C(17)	119.4(2)

C(15)-C(16)-H(16)	120.3
C(17)-C(16)-H(16)	120.3
C(40)-C(21)-N(5)	114.16(19)
C(22)-C(21)-N(5)	129.2(2)
C(22)-C(21)-C(40)	116.6(2)
C(35)-C(34)-H(34)	121.5
C(35)-C(34)-C(33)	117.1(3)
C(33)-C(34)-H(34)	121.5
C(30)-C(31)-C(32)	116.8(3)
C(30)-C(31)-H(31)	121.6
C(32)-C(31)-H(31)	121.6
C(32)-C(33)-C(34)	120.6(3)
C(32)-C(33)-H(33)	119.7
C(34)-C(33)-H(33)	119.7
C(21)-C(22)-H(22)	119.3
C(21)-C(22)-C(23)	121.4(2)
C(23)-C(22)-H(22)	119.3
C(18)-C(19)-C(20)	120.0(2)
C(18)-C(19)-H(19)	120.0
C(20)-C(19)-H(19)	120.0
N(3)-C(46)-C(13)	116.4(2)
N(3)-C(46)-C(17)	121.0(2)
C(17)-C(46)-C(13)	122.6(2)
C(24)-C(23)-C(22)	122.1(2)
C(24)-C(23)-H(23)	119.0
C(22)-C(23)-H(23)	119.0
C(43)-C(42)-H(42A)	109.5
C(43)-C(42)-H(42B)	109.5
C(43)-C(42)-H(42C)	109.5
H(42A)-C(42)-H(42B)	109.5
H(42A)-C(42)-H(42C)	109.5
H(42B)-C(42)-H(42C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S8. Anisotropic displacement parameters ($Å^2$x 10^3) for engle55_0m_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Pd(2)	13(1)	18(1)	14(1)	-3(1)	-2(1)	-1(1)
Pd(1)	14(1)	14(1)	13(1)	-4(1)	1(1)	-1(1)
N(6)	16(1)	19(1)	18(1)	-3(1)	2(1)	-3(1)
O(8)	16(1)	28(1)	19(1)	-10(1)	-2(1)	-2(1)
O(7)	26(1)	18(1)	22(1)	-9(1)	2(1)	-2(1)
O(1)	24(1)	41(1)	36(1)	0(1)	-4(1)	6(1)
O(3)	25(1)	24(1)	23(1)	-13(1)	-4(1)	7(1)
O(10)	16(1)	22(1)	14(1)	-5(1)	0(1)	-2(1)
N(2)	14(1)	14(1)	14(1)	-4(1)	-1(1)	0(1)
O(5)	28(1)	43(1)	41(1)	-22(1)	-2(1)	3(1)
O(9)	17(1)	23(1)	18(1)	1(1)	-6(1)	-3(1)
N(1)	23(1)	20(1)	19(1)	-2(1)	-3(1)	2(1)
O(4)	30(1)	36(1)	30(1)	-15(1)	1(1)	1(1)
O(6)	31(1)	41(1)	26(1)	-12(1)	-13(1)	18(1)
O(2)	25(1)	38(1)	33(1)	-1(1)	-8(1)	-2(1)
C(25)	16(1)	26(1)	25(1)	-12(1)	6(1)	-8(1)
C(12)	17(1)	14(1)	16(1)	-2(1)	1(1)	-2(1)
C(27)	28(2)	18(1)	33(2)	-6(1)	4(1)	3(1)
C(45)	18(1)	20(1)	16(1)	-7(1)	-7(1)	6(1)
C(8)	22(1)	21(1)	30(2)	-6(1)	-5(1)	3(1)
C(41)	28(2)	27(1)	25(1)	-14(1)	-4(1)	2(1)
C(28)	22(1)	21(1)	23(1)	-2(1)	-1(1)	-2(1)
C(10)	16(1)	21(1)	18(1)	-4(1)	0(1)	1(1)
N(3)	13(1)	15(1)	16(1)	-2(1)	3(1)	-3(1)
C(15)	20(1)	31(1)	21(1)	-12(1)	-1(1)	-10(1)
N(5)	13(1)	19(1)	15(1)	-4(1)	-3(1)	-1(1)
C(9)	27(1)	23(1)	17(1)	-7(1)	-2(1)	5(1)
C(24)	19(1)	41(2)	20(1)	-16(1)	5(1)	-7(1)
N(4)	21(1)	32(1)	23(1)	-11(1)	-3(1)	-3(1)
C(13)	11(1)	16(1)	15(1)	-2(1)	2(1)	-4(1)
C(40)	11(1)	24(1)	16(1)	-4(1)	2(1)	-7(1)

C(7)	31(2)	18(1)	24(1)	-3(1)	-6(1)	2(1)
C(2)	32(2)	19(1)	20(1)	-2(1)	-3(1)	0(1)
C(14)	17(1)	19(1)	21(1)	-6(1)	0(1)	-5(1)
C(38)	22(1)	23(1)	28(1)	-13(1)	-4(1)	1(1)
C(6)	41(2)	30(2)	33(2)	-4(1)	-15(1)	-1(1)
C(11)	18(1)	18(1)	19(1)	-5(1)	-3(1)	1(1)
C(1)	26(2)	20(1)	26(1)	-5(1)	-3(1)	-1(1)
C(26)	26(2)	25(1)	29(1)	-14(1)	6(1)	-7(1)
C(39)	17(1)	18(1)	25(1)	-8(1)	-5(1)	1(1)
C(3)	34(2)	30(2)	32(2)	0(1)	2(1)	0(1)
C(4)	51(2)	36(2)	23(2)	2(1)	1(1)	-2(2)
C(18)	13(1)	24(1)	22(1)	3(1)	-3(1)	-3(1)
C(36)	22(1)	30(1)	28(1)	-10(1)	-4(1)	-7(1)
C(5)	57(2)	35(2)	21(2)	0(1)	-11(1)	-2(2)
C(30)	25(2)	36(2)	25(1)	-13(1)	0(1)	-14(1)
C(43)	19(1)	17(1)	14(1)	-8(1)	-2(1)	2(1)
C(37)	22(1)	30(1)	24(1)	-10(1)	-5(1)	3(1)
C(20)	18(1)	16(1)	20(1)	-4(1)	2(1)	-3(1)
C(44)	19(1)	22(1)	21(1)	-4(1)	-3(1)	-3(1)
C(17)	12(1)	22(1)	19(1)	-1(1)	1(1)	-7(1)
C(29)	23(2)	40(2)	30(2)	-20(1)	-1(1)	-10(1)
C(35)	25(2)	34(2)	25(1)	-9(1)	-1(1)	-15(1)
C(32)	66(2)	49(2)	29(2)	-13(2)	9(2)	-31(2)
C(16)	18(1)	33(1)	20(1)	-3(1)	-6(1)	-8(1)
C(21)	11(1)	23(1)	16(1)	-6(1)	2(1)	-7(1)
C(34)	38(2)	32(2)	35(2)	-9(1)	-5(1)	-14(1)
C(31)	44(2)	45(2)	31(2)	-21(1)	6(1)	-21(2)
C(33)	57(2)	38(2)	34(2)	1(1)	-5(2)	-24(2)
C(22)	14(1)	28(1)	19(1)	-3(1)	-1(1)	-2(1)
C(19)	16(1)	17(1)	29(1)	1(1)	-1(1)	-2(1)
C(46)	13(1)	18(1)	16(1)	-3(1)	3(1)	-6(1)
C(23)	17(1)	43(2)	16(1)	-8(1)	2(1)	-4(1)
C(42)	23(1)	29(1)	20(1)	-2(1)	-8(1)	-2(1)

Table S9. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for engle55_0m_a.

	x	y	z	U(eq)
H(27)	3780	3247	1761	33
H(41A)	2535	11639	2992	38
H(41B)	3849	11050	3365	38
H(41C)	2529	10547	3720	38
H(28)	3605	4715	2513	27
H(10A)	9130	5732	1261	23
H(10B)	9386	5737	2065	23
H(15)	4073	6637	-837	27
H(9A)	7863	3926	1769	27
H(9B)	9387	3584	1799	27
H(24)	1272	5513	-129	30
H(14)	5249	5871	180	22
H(38A)	-1536	10949	2979	28
H(38B)	-1679	11206	2138	28
H(6)	10547	2186	4556	41
H(11A)	7060	6106	2288	22
H(11B)	7689	7314	1789	22
H(26)	2709	3813	715	30
H(39A)	494	10520	2457	24
H(39B)	79	9146	2890	24
H(3)	6014	2661	4531	41
H(4)	7046	1874	5609	47
H(18)	2244	10845	-678	25
H(5)	9257	1624	5617	47
H(37A)	-3347	10096	2640	30
H(37B)	-2338	9039	2345	30
H(20)	3390	11140	1210	22
H(32)	-3323	6455	6256	55
H(16)	2996	8714	-1095	28
H(34)	-1108	5188	4651	40

H(31)	-4007	8432	5479	44
H(33)	-1912	4850	5860	51
H(22)	73	8977	413	25
H(19)	2255	12031	191	26
H(23)	228	7621	-392	30
H(42A)	6247	5651	3841	37
H(42B)	4922	5082	4121	37
H(42C)	5184	6430	4283	37

Experimental Summary for Crystal 1m’

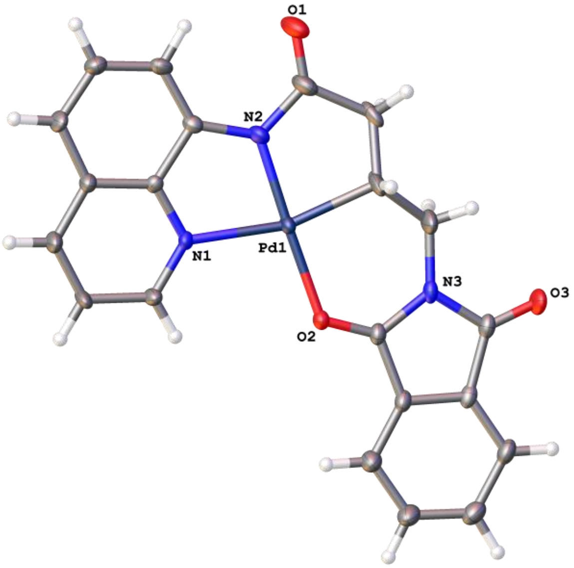


Table S10. Crystal data and structure refinement for engle55b_0m_b.

Identification code	JAG-C-063B (small vial)	
Empirical formula	C21 H15 N3 O3 Pd	
Formula weight	463.76	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P n	
Unit cell dimensions	a = 15.0023(14) Å	α= 90°.
	b = 6.9693(9) Å	β= 112.945(2)°.
	c = 17.7197(15) Å	γ = 90°.
Volume	1706.1(3) Å^3	
Z, Z’	4, 2	
Density (calculated)	1.805 Mg/m^3	
Absorption coefficient	1.118 mm^{-1}	
F(000)	928	
Crystal size	0.29 x 0.14 x 0.1 mm^3	
Theta range for data collection	2.496 to 28.348°.	
Index ranges	-19<=h<=20, -9<=k<=8, -23<=l<=16	
Reflections collected	15944	
Independent reflections	6919 [R(int) = 0.0334]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.1525 and 0.1201	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6919 / 536 / 506	
Goodness-of-fit on F^2	1.044	
Final R indices [I>2sigma(I)]	R1 = 0.0461, wR2 = 0.1074	
R indices (all data)	R1 = 0.0498, wR2 = 0.1095	
Absolute structure parameter	0.49(6)	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.795 and -0.941 e.Å^{-3}	

Table S11. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for engle55b_0m_b. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1')	5694(1)	416(1)	4934(1)	17(1)
Pd(1)	4237(1)	4916(1)	5031(1)	18(1)
O(2)	5704(6)	5543(10)	5476(5)	22(2)
O(3)	6560(6)	5309(11)	3267(5)	34(2)
N(3')	4146(7)	-240(11)	5791(6)	22(2)
N(2')	7098(5)	1042(12)	5397(5)	20(1)
N(1)	3991(6)	4800(9)	6133(6)	18(1)
C(13)	4901(9)	4846(17)	3650(9)	39(3)
O(2')	4231(6)	-121(9)	4509(6)	24(2)
C(14')	3784(7)	-297(11)	4959(6)	20(2)
O(1')	8413(4)	1627(10)	6596(4)	31(2)
C(9)	3029(7)	4529(11)	5972(6)	15(1)
C(8)	2393(6)	4206(12)	5127(5)	20(2)
N(1')	5945(6)	154(10)	3834(6)	17(1)
C(20)	7497(6)	5998(12)	4692(5)	20(2)
C(10')	7548(6)	1253(12)	6214(5)	20(2)
C(4)	2672(7)	4515(13)	6604(6)	23(2)
N(2)	2862(5)	4298(13)	4581(5)	25(2)
C(6)	1089(7)	3902(14)	5577(6)	28(2)
C(21')	3411(7)	-459(12)	6093(6)	22(2)
C(7')	8493(6)	1517(13)	4983(6)	24(2)
C(1)	4608(8)	5056(13)	6903(7)	24(2)
C(15)	7232(6)	6030(12)	5355(5)	21(2)
C(3')	6605(12)	-32(15)	2567(10)	32(2)
C(8')	7533(6)	1068(12)	4826(5)	19(1)
C(21)	6649(7)	5530(12)	3955(6)	23(2)
C(2')	5680(9)	-428(15)	2444(7)	33(2)
C(5)	1668(7)	4213(15)	6386(6)	29(2)
O(3')	3547(7)	-410(11)	6811(5)	38(2)
C(19)	8439(6)	6399(13)	4778(6)	27(2)
C(15')	2725(6)	-618(13)	4672(6)	23(2)

C(14)	6188(7)	5603(13)	5051(6)	20(2)
C(1')	5375(8)	-303(13)	3061(7)	26(2)
C(11')	6859(6)	960(13)	6648(5)	23(2)
C(5')	8261(7)	887(15)	3574(6)	29(2)
C(12)	4024(7)	5271(17)	3845(6)	38(2)
C(19')	1561(6)	-1120(12)	5289(6)	27(2)
C(11)	3123(7)	4332(16)	3327(6)	31(2)
C(12')	5749(6)	1034(16)	6068(5)	29(2)
O(1)	1534(5)	3854(13)	3360(4)	43(2)
C(16')	2028(7)	-784(17)	3888(6)	38(2)
C(7)	1430(6)	3866(13)	4961(6)	25(2)
C(9')	6909(7)	568(11)	4004(6)	16(1)
C(16)	7900(6)	6400(15)	6144(6)	32(2)
N(3)	5859(8)	5351(10)	4213(6)	18(2)
C(20')	2491(7)	-725(13)	5358(6)	22(2)
C(17)	8836(7)	6734(17)	6229(6)	37(2)
C(18')	870(7)	-1355(14)	4504(6)	33(2)
C(3)	3323(11)	4810(20)	7407(10)	33(3)
C(17')	1081(8)	-1180(20)	3827(7)	52(3)
C(4')	7272(7)	461(12)	3382(6)	22(2)
C(10)	2396(7)	4147(15)	3740(6)	32(2)
C(18)	9120(7)	6782(13)	5578(6)	30(2)
C(6')	8846(6)	1414(14)	4348(6)	28(2)
C(2)	4292(9)	5035(15)	7586(7)	32(2)
C(13')	5186(8)	-167(17)	6332(8)	39(3)

Table S12. Bond lengths [Å] and angles [°] for engle55b_0m_b.

Pd(1')-N(2')	1.988(7)
Pd(1')-O(2')	2.059(9)
Pd(1')-N(1')	2.133(10)
Pd(1')-C(12')	2.025(9)
Pd(1)-O(2)	2.075(8)
Pd(1)-N(1)	2.124(10)
Pd(1)-N(2)	1.948(8)
Pd(1)-C(12)	2.014(10)
O(2)-C(14)	1.235(13)
O(3)-C(21)	1.184(13)
N(3')-C(14')	1.358(15)
N(3')-C(21')	1.409(14)
N(3')-C(13')	1.480(15)
N(2')-C(10')	1.346(11)
N(2')-C(8')	1.400(11)
N(1)-C(9)	1.370(13)
N(1)-C(1)	1.330(15)
C(13)-H(13C)	0.9900
C(13)-H(13D)	0.9900
C(13)-C(12)	1.514(16)
C(13)-N(3)	1.438(16)
O(2')-C(14')	1.232(14)
C(14')-C(15')	1.485(13)
O(1')-C(10')	1.235(10)
C(9)-C(8)	1.446(12)
C(9)-C(4)	1.418(13)
C(8)-N(2)	1.402(12)
C(8)-C(7)	1.379(12)
N(1')-C(1')	1.339(15)
N(1')-C(9')	1.387(13)
C(20)-C(15)	1.379(12)
C(20)-C(21)	1.461(13)
C(20)-C(19)	1.390(12)
C(10')-C(11')	1.524(12)

C(4)-C(5)	1.417(13)
C(4)-C(3)	1.39(2)
N(2)-C(10)	1.381(12)
C(6)-H(6)	0.9500
C(6)-C(5)	1.372(14)
C(6)-C(7)	1.374(13)
C(21')-O(3')	1.208(13)
C(21')-C(20')	1.495(13)
C(7')-H(7')	0.9500
C(7')-C(8')	1.392(11)
C(7')-C(6')	1.421(12)
C(1)-H(1)	0.9500
C(1)-C(2)	1.462(16)
C(15)-C(14)	1.474(12)
C(15)-C(16)	1.390(12)
C(3')-H(3')	0.9500
C(3')-C(2')	1.35(2)
C(3')-C(4')	1.44(2)
C(8')-C(9')	1.435(12)
C(21)-N(3)	1.431(14)
C(2')-H(2')	0.9500
C(2')-C(1')	1.343(18)
C(5)-H(5)	0.9500
C(19)-H(19)	0.9500
C(19)-C(18)	1.412(13)
C(15')-C(16')	1.380(13)
C(15')-C(20')	1.392(12)
C(14)-N(3)	1.381(14)
C(1')-H(1')	0.9500
C(11')-H(11A)	0.9900
C(11')-H(11B)	0.9900
C(11')-C(12')	1.580(12)
C(5')-H(5')	0.9500
C(5')-C(4')	1.418(13)
C(5')-C(6')	1.359(13)
C(12)-H(12)	1.0000

C(12)-C(11)	1.459(14)
C(19')-H(19')	0.9500
C(19')-C(20')	1.380(12)
C(19')-C(18')	1.382(13)
C(11)-H(11C)	0.9900
C(11)-H(11D)	0.9900
C(11)-C(10)	1.537(14)
C(12')-H(12')	1.0000
C(12')-C(13')	1.394(15)
O(1)-C(10)	1.221(11)
C(16')-H(16')	0.9500
C(16')-C(17')	1.409(14)
C(7)-H(7)	0.9500
C(9')-C(4')	1.409(14)
C(16)-H(16)	0.9500
C(16)-C(17)	1.373(13)
C(17)-H(17)	0.9500
C(17)-C(18)	1.377(13)
C(18')-H(18')	0.9500
C(18')-C(17')	1.363(14)
C(3)-H(3)	0.9500
C(3)-C(2)	1.370(19)
C(17')-H(17')	0.9500
C(18)-H(18)	0.9500
C(6')-H(6')	0.9500
C(2)-H(2)	0.9500
C(13')-H(13A)	0.9900
C(13')-H(13B)	0.9900

N(2')-Pd(1')-O(2')	176.4(3)
N(2')-Pd(1')-N(1')	81.9(3)
N(2')-Pd(1')-C(12')	85.3(3)
O(2')-Pd(1')-N(1')	101.2(4)
C(12')-Pd(1')-O(2')	91.5(4)
C(12')-Pd(1')-N(1')	166.4(4)
O(2)-Pd(1)-N(1)	101.4(3)

N(2)-Pd(1)-O(2)	178.1(3)
N(2)-Pd(1)-N(1)	80.4(3)
N(2)-Pd(1)-C(12)	83.6(4)
C(12)-Pd(1)-O(2)	94.8(4)
C(12)-Pd(1)-N(1)	161.8(3)
C(14)-O(2)-Pd(1)	124.4(7)
C(14')-N(3')-C(21')	111.6(9)
C(14')-N(3')-C(13')	125.3(10)
C(21')-N(3')-C(13')	122.8(10)
C(10')-N(2')-Pd(1')	118.3(6)
C(10')-N(2')-C(8')	126.6(7)
C(8')-N(2')-Pd(1')	114.9(6)
C(9)-N(1)-Pd(1)	111.1(7)
C(1)-N(1)-Pd(1)	129.6(8)
C(1)-N(1)-C(9)	119.2(10)
H(13C)-C(13)-H(13D)	106.8
C(12)-C(13)-H(13C)	107.1
C(12)-C(13)-H(13D)	107.1
N(3)-C(13)-H(13C)	107.1
N(3)-C(13)-H(13D)	107.1
N(3)-C(13)-C(12)	121.1(11)
C(14')-O(2')-Pd(1')	123.6(8)
N(3')-C(14')-C(15')	107.3(9)
O(2')-C(14')-N(3')	127.7(11)
O(2')-C(14')-C(15')	125.0(10)
N(1)-C(9)-C(8)	117.0(8)
N(1)-C(9)-C(4)	121.9(9)
C(4)-C(9)-C(8)	121.1(8)
N(2)-C(8)-C(9)	113.7(7)
C(7)-C(8)-C(9)	117.5(8)
C(7)-C(8)-N(2)	128.9(8)
C(1')-N(1')-Pd(1')	133.2(8)
C(1')-N(1')-C(9')	117.9(10)
C(9')-N(1')-Pd(1')	108.9(6)
C(15)-C(20)-C(21)	109.0(7)
C(15)-C(20)-C(19)	121.4(8)

C(19)-C(20)-C(21)	129.6(8)
N(2')-C(10')-C(11')	112.0(7)
O(1')-C(10')-N(2')	126.3(8)
O(1')-C(10')-C(11')	121.7(7)
C(5)-C(4)-C(9)	118.4(9)
C(3)-C(4)-C(9)	118.4(9)
C(3)-C(4)-C(5)	123.3(10)
C(8)-N(2)-Pd(1)	117.6(6)
C(10)-N(2)-Pd(1)	117.9(7)
C(10)-N(2)-C(8)	124.2(8)
C(5)-C(6)-H(6)	118.3
C(5)-C(6)-C(7)	123.5(8)
C(7)-C(6)-H(6)	118.3
N(3')-C(21')-C(20')	106.0(9)
O(3')-C(21')-N(3')	124.2(10)
O(3')-C(21')-C(20')	129.8(10)
C(8')-C(7')-H(7')	119.8
C(8')-C(7')-C(6')	120.4(8)
C(6')-C(7')-H(7')	119.8
N(1)-C(1)-H(1)	119.1
N(1)-C(1)-C(2)	121.8(10)
C(2)-C(1)-H(1)	119.1
C(20)-C(15)-C(14)	107.7(8)
C(20)-C(15)-C(16)	121.8(8)
C(16)-C(15)-C(14)	130.6(8)
C(2')-C(3')-H(3')	120.7
C(2')-C(3')-C(4')	118.7(13)
C(4')-C(3')-H(3')	120.7
N(2')-C(8')-C(9')	115.3(7)
C(7')-C(8')-N(2')	126.5(8)
C(7')-C(8')-C(9')	118.2(8)
O(3)-C(21)-C(20)	131.1(9)
O(3)-C(21)-N(3)	122.9(10)
N(3)-C(21)-C(20)	106.0(8)
C(3')-C(2')-H(2')	119.6
C(1')-C(2')-C(3')	120.7(12)

C(1')-C(2')-H(2')	119.6
C(4)-C(5)-H(5)	120.6
C(6)-C(5)-C(4)	118.8(9)
C(6)-C(5)-H(5)	120.6
C(20)-C(19)-H(19)	121.5
C(20)-C(19)-C(18)	117.1(8)
C(18)-C(19)-H(19)	121.5
C(16')-C(15')-C(14')	130.3(9)
C(16')-C(15')-C(20')	121.7(8)
C(20')-C(15')-C(14')	108.0(8)
O(2)-C(14)-C(15)	125.3(9)
O(2)-C(14)-N(3)	127.1(10)
N(3)-C(14)-C(15)	107.6(8)
N(1')-C(1')-C(2')	124.3(12)
N(1')-C(1')-H(1')	117.8
C(2')-C(1')-H(1')	117.8
C(10')-C(11')-H(11A)	108.6
C(10')-C(11')-H(11B)	108.6
C(10')-C(11')-C(12')	114.7(7)
H(11A)-C(11')-H(11B)	107.6
C(12')-C(11')-H(11A)	108.6
C(12')-C(11')-H(11B)	108.6
C(4')-C(5')-H(5')	119.9
C(6')-C(5')-H(5')	119.9
C(6')-C(5')-C(4')	120.2(9)
Pd(1)-C(12)-H(12)	105.1
C(13)-C(12)-Pd(1)	114.6(8)
C(13)-C(12)-H(12)	105.1
C(11)-C(12)-Pd(1)	109.4(7)
C(11)-C(12)-C(13)	116.3(10)
C(11)-C(12)-H(12)	105.1
C(20')-C(19')-H(19')	121.7
C(20')-C(19')-C(18')	116.7(8)
C(18')-C(19')-H(19')	121.7
C(12)-C(11)-H(11C)	108.9
C(12)-C(11)-H(11D)	108.9

C(12)-C(11)-C(10)	113.2(8)
H(11C)-C(11)-H(11D)	107.8
C(10)-C(11)-H(11C)	108.9
C(10)-C(11)-H(11D)	108.9
Pd(1')-C(12')-H(12')	108.2
C(11')-C(12')-Pd(1')	105.3(5)
C(11')-C(12')-H(12')	108.2
C(13')-C(12')-Pd(1')	114.2(8)
C(13')-C(12')-C(11')	112.6(9)
C(13')-C(12')-H(12')	108.2
C(15')-C(16')-H(16')	122.0
C(15')-C(16')-C(17')	116.0(9)
C(17')-C(16')-H(16')	122.0
C(8)-C(7)-H(7)	119.6
C(6)-C(7)-C(8)	120.8(8)
C(6)-C(7)-H(7)	119.6
N(1')-C(9')-C(8')	118.9(8)
N(1')-C(9')-C(4')	120.4(8)
C(4')-C(9')-C(8')	120.6(8)
C(15)-C(16)-H(16)	121.7
C(17)-C(16)-C(15)	116.5(9)
C(17)-C(16)-H(16)	121.7
C(21)-N(3)-C(13)	121.9(10)
C(14)-N(3)-C(13)	128.2(10)
C(14)-N(3)-C(21)	109.8(9)
C(15')-C(20')-C(21')	107.0(8)
C(19')-C(20')-C(21')	131.3(9)
C(19')-C(20')-C(15')	121.6(8)
C(16)-C(17)-H(17)	118.3
C(16)-C(17)-C(18)	123.4(9)
C(18)-C(17)-H(17)	118.3
C(19')-C(18')-H(18')	118.8
C(17')-C(18')-C(19')	122.3(9)
C(17')-C(18')-H(18')	118.8
C(4)-C(3)-H(3)	119.6
C(2)-C(3)-C(4)	120.8(13)

C(2)-C(3)-H(3)	119.6
C(16')-C(17')-H(17')	119.2
C(18')-C(17')-C(16')	121.6(10)
C(18')-C(17')-H(17')	119.2
C(5')-C(4')-C(3')	122.9(10)
C(9')-C(4')-C(3')	117.9(10)
C(9')-C(4')-C(5')	119.2(9)
N(2)-C(10)-C(11)	110.6(8)
O(1)-C(10)-N(2)	126.1(9)
O(1)-C(10)-C(11)	123.2(9)
C(19)-C(18)-H(18)	120.1
C(17)-C(18)-C(19)	119.8(8)
C(17)-C(18)-H(18)	120.1
C(7')-C(6')-H(6')	119.4
C(5')-C(6')-C(7')	121.3(8)
C(5')-C(6')-H(6')	119.4
C(1)-C(2)-H(2)	121.1
C(3)-C(2)-C(1)	117.8(12)
C(3)-C(2)-H(2)	121.1
N(3')-C(13')-H(13A)	108.4
N(3')-C(13')-H(13B)	108.4
C(12')-C(13')-N(3')	115.3(10)
C(12')-C(13')-H(13A)	108.4
C(12')-C(13')-H(13B)	108.4
H(13A)-C(13')-H(13B)	107.5

Symmetry transformations used to generate equivalent atoms:

Table S13. Anisotropic displacement parameters ($Å^2$x 10^3) for engle55b_0m_b. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Pd(1')	14(1)	27(1)	10(1)	0(1)	4(1)	-3(1)
Pd(1)	16(1)	28(1)	12(1)	-1(1)	6(1)	1(1)
O(2)	19(3)	34(4)	14(3)	1(3)	10(2)	-2(3)
O(3)	30(4)	61(5)	21(3)	-7(3)	20(3)	-8(3)
N(3')	22(3)	30(4)	16(3)	-3(3)	10(3)	-3(3)
N(2')	13(3)	31(4)	13(2)	1(3)	3(2)	-2(3)
N(1)	13(3)	29(3)	14(3)	2(2)	7(2)	-2(2)
C(13)	25(4)	79(8)	17(5)	-2(4)	14(3)	-5(4)
O(2')	21(3)	36(4)	20(4)	-8(3)	11(3)	-11(3)
C(14')	19(3)	22(4)	17(3)	-1(3)	7(2)	0(3)
O(1')	17(3)	54(4)	17(3)	-3(3)	0(2)	-4(2)
C(9)	15(3)	17(3)	15(3)	-1(3)	8(2)	0(3)
C(8)	18(3)	25(4)	15(3)	-1(3)	4(2)	0(3)
N(1')	12(3)	24(3)	13(3)	-1(2)	4(2)	10(2)
C(20)	22(3)	23(4)	21(3)	4(3)	13(2)	6(3)
C(10')	17(3)	27(4)	13(3)	0(3)	3(2)	-3(3)
C(4)	18(3)	37(4)	16(3)	2(3)	9(3)	-2(3)
N(2)	20(3)	38(4)	14(3)	-7(3)	3(2)	-3(3)
C(6)	19(4)	35(5)	29(4)	-1(3)	7(3)	-5(3)
C(21')	20(3)	30(4)	19(3)	1(3)	10(3)	2(3)
C(7')	21(3)	33(4)	17(4)	-3(3)	6(3)	-7(3)
C(1)	13(4)	45(5)	16(3)	-3(3)	8(3)	-4(3)
C(15)	21(3)	28(4)	18(3)	5(3)	11(2)	0(3)
C(3')	24(4)	57(5)	13(4)	-7(4)	4(3)	1(3)
C(8')	17(3)	22(4)	16(3)	1(3)	6(2)	1(3)
C(21)	27(3)	27(4)	21(3)	0(3)	16(3)	-2(3)
C(2')	21(4)	56(6)	14(4)	-5(4)	-1(3)	3(4)
C(5)	19(3)	48(5)	25(4)	-4(4)	15(3)	-4(3)
O(3')	28(4)	70(5)	17(3)	0(3)	12(3)	-4(3)
C(19)	27(3)	28(4)	32(4)	2(3)	18(3)	-1(3)
C(15')	19(3)	33(4)	18(3)	-2(3)	7(2)	-6(3)

C(14)	22(3)	23(4)	16(3)	3(3)	11(3)	0(3)
C(1')	13(4)	43(5)	16(4)	-2(3)	-1(3)	6(3)
C(11')	19(3)	34(4)	12(3)	-1(3)	3(3)	-4(3)
C(5')	19(4)	50(5)	20(4)	-2(4)	9(3)	-4(3)
C(12)	27(4)	74(7)	14(3)	4(4)	10(3)	6(4)
C(19')	29(3)	28(4)	32(4)	-1(3)	20(3)	-2(3)
C(11)	30(4)	51(5)	10(4)	-3(4)	6(3)	10(4)
C(12')	18(3)	54(5)	15(3)	0(4)	6(3)	6(3)
O(1)	22(3)	81(5)	21(3)	-12(4)	3(2)	-1(3)
C(16')	24(4)	73(7)	17(3)	-3(4)	8(3)	-14(4)
C(7)	20(3)	29(4)	20(4)	-4(3)	0(3)	-4(3)
C(9')	14(3)	18(4)	13(3)	4(3)	2(2)	5(2)
C(16)	21(3)	56(6)	21(3)	4(4)	8(3)	-3(3)
N(3)	26(3)	19(4)	16(3)	2(2)	13(2)	2(3)
C(20')	24(3)	26(4)	20(3)	-5(3)	13(2)	-2(3)
C(17)	20(4)	61(6)	28(4)	9(4)	9(3)	-4(4)
C(18')	24(4)	43(5)	36(4)	3(4)	16(3)	-7(4)
C(3)	19(4)	68(8)	18(4)	-1(4)	12(3)	-4(4)
C(17')	24(4)	100(10)	28(4)	1(5)	6(4)	-18(5)
C(4')	16(3)	33(4)	15(3)	-1(3)	5(3)	0(3)
C(10)	24(3)	50(6)	16(3)	-7(4)	2(2)	2(3)
C(18)	23(4)	35(5)	35(4)	4(4)	14(3)	-3(3)
C(6')	15(4)	43(5)	26(4)	-5(3)	10(3)	-11(3)
C(2)	16(4)	71(7)	10(4)	0(4)	5(3)	-2(3)
C(13')	19(4)	84(7)	12(4)	0(4)	5(3)	-9(4)

Table S14. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10 ^{3}) for engle55b_0m_b.

	x	y	z	U(eq)
H(13C)	4902	3448	3552	47
H(13D)	4795	5486	3123	47
H(6)	416	3702	5436	34
H(7')	8915	1895	5519	29
H(1)	5274	5259	7013	29
H(3')	6814	-77	2125	39
H(2')	5237	-800	1914	40
H(5)	1401	4226	6792	34
H(19)	8618	6414	4320	32
H(1')	4712	-555	2943	31
H(11A)	6990	1960	7074	27
H(11B)	6999	-300	6928	27
H(5')	8515	804	3161	35
H(12)	3900	6674	3738	45
H(19')	1404	-1226	5757	32
H(11C)	3274	3035	3181	37
H(11D)	2820	5073	2814	37
H(12')	5517	2381	6063	35
H(16')	2179	-641	3417	46
H(7)	996	3603	4415	30
H(16)	7717	6419	6601	39
H(17)	9312	6944	6764	44
H(18')	224	-1650	4435	40
H(3)	3093	4865	7835	40
H(17')	578	-1322	3300	63
H(18)	9772	7072	5667	36
H(6')	9504	1720	4466	33
H(2)	4743	5170	8136	39
H(13A)	5246	260	6882	47
H(13B)	5453	-1483	6389	47