Tridentate Directing Groups Stabilize 6-Membered Palladacycles in Catalytic Alkene Hydrofunctionalization

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Contents

General Information

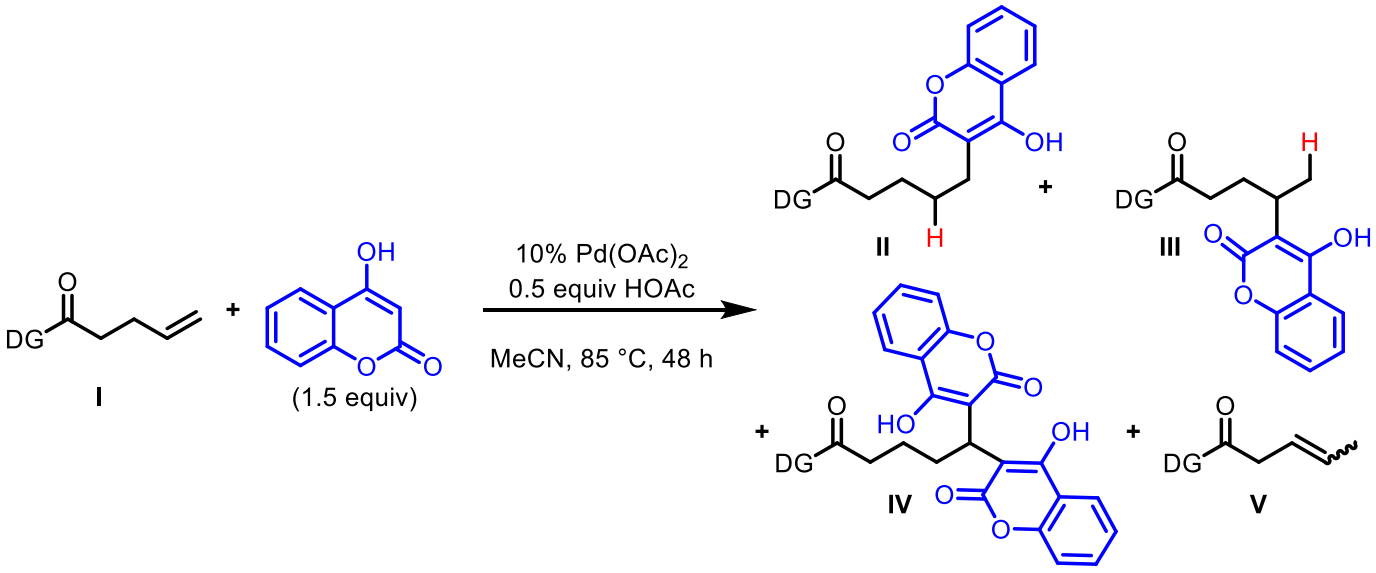
Unless otherwise stated, all materials were used as received from commercial sources without further purification. 1 Dram reaction vials and caps were purchased from ChemGlass (Cat#: CG-4904-05) with TFE septa. Ambient temperature refers to 21–24 °C. Elevated temperatures were maintained by an Ika heating 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, 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 Bruker DRX-500 and AV-600 instruments. Spectra were internally referenced to Me_4Si or residual solvent signals. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer.

Chemicals and Suppliers

The following chemicals were purchased from: **Acros**: 3-butenylamine, 2-chloroquinoline, *cis*-4-hexen-1-ol, *trans*-4-hexen-1-ol; **Alfa Aesar**: but-3-enoic acid, 2,2'-bipyridine, 2-methyl-4-pentenoic acid, 2-(tributylstannyl)thiophene, vinyl acetic acid; **Ark Pharm**: XPhos; **Chem-Impex**: DL-2-allylglycine; **Combi-Blocks**: L-2-allylglycine, 3-cyclopentenecarboxylic acid, 4-hydroxycoumarin; **Frontier**: tributyl(pyridin-2-yl)stannane, 2-(tributylstannyl)pyrimidine; **Johnson Matthey**: $Pd(OAc)_2$; **Oakwood**: 8-aminoquinoline, 3-cyclohexene-1-carboxylic acid, EDC, HATU, $Pd(PPh_3)_4$, pent-4-enoic acid; **Sigma Aldrich**: 6-methyl-2,2'-bipy, 3-methyl-4-pentenoic acid, palladium on carbon (10% weight loading, matrix activated carbon support), TMSCN.
All other chemicals were purchased from Fisher or VWR and used as obtained.

Optimization of Directing Groups

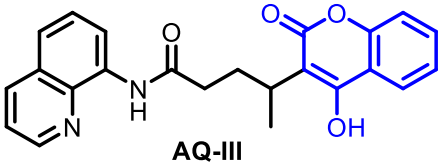
Optimization of Directing Groups for Carboxylic Acid Substrates



Data for **I**: see substrates **1**, **S25–S29**, and **3a** below.

Data for **II**: see product **4a** below.

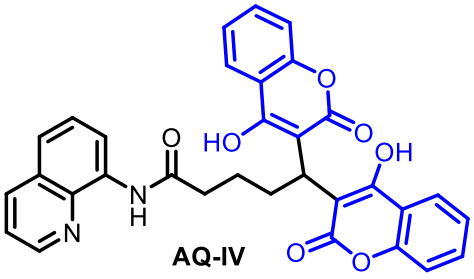
Data for **III**: **4-(4-Hydroxy-2-oxochroman-3-yl)-*N*-(quinolin-8-yl)pentanamide**[1]



^{1}H NMR (600 MHz, $CDCl_3$) δ 11.58 (s, 1H), 10.16 (s, 1H), 8.84 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.81 (dd, *J* = 6.6, 2.3 Hz, 1H), 8.21 (dd, *J* = 8.2, 1.7 Hz, 1H), 8.02–7.97 (m, 1H), 7.63–7.58 (m, 2H), 7.53–7.47 (m, 2H), 7.32–7.25 (m, 2H), 3.45 (dtd, *J* = 13.7, 6.9, 3.9 Hz, 1H), 2.70 (ddd, *J* = 13.9, 5.8, 2.4 Hz, 1H), 2.51 (dddd, *J* = 14.5, 11.8, 5.8, 3.1 Hz, 1H), 2.37 (td, *J* = 13.6, 3.1 Hz, 1H), 1.90 (tt, *J* = 13.7, 2.9 Hz, 1H), 1.45 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (150 MHz, CDCl3) δ 174.9, 162.5, 162.0, 153.1,

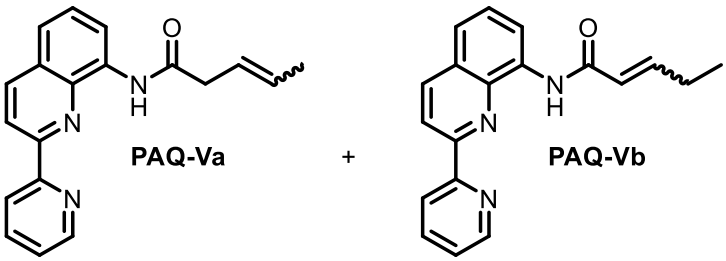
148.8, 138.6, 136.7, 133.7, 131.5, 128.2, 127.4, 124.2, 123.8, 123.1, 122.2, 117.7, 116.3, 117.4, 106.9, 36.2, 30.8, 29.5, 18.7; **HRMS** calcd. for $C_{23}H_{21}N_2O_4^+$ $[M+H]^+$ 389.14958, found: 389.1495.

Data for **IV**: **5,5-Bis(4-hydroxy-2-oxo-2*H*-chromen-3-yl)-*N*-(quinolin-8-yl)pentanamide**[1]



^{1}H NMR (600 MHz, CD_3OD) δ 8.73 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.54 (dd, *J* = 7.6, 1.3 Hz, 1H), 8.24 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.93 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.56 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.51–7.43 (m, 4H), 7.25–7.17 (m, 4H), 5.10 (t, *J* = 8.3 Hz, 1H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.39 (q, *J* = 8.2 Hz, 2H), 1.84–1.75 (m, 2H); **^{13}C NMR** (150 MHz, CD_3OD) δ 174.6, 170.3, 168.5, 154.0, 149.8, 140.0, 137.5, 135.5, 132.0, 129.5, 127.9, 125.2, 124.4, 123.3, 122.9, 121.3, 118.3, 116.7, 105.7, 38.6, 33.2, 30.8, 25.9; **HRMS** calcd. for $C_{32}H_{25}N_2O_7^+$ $[M+H]^+$ 549.16563, found: 549.1655.

Data for **V**: ***N*-(2-(Pyridin-2-yl)quinolin-8-yl)pent-3-enamide and -pent-2-enamide**



The major product observed in unsuccessful or low-yielding reactions is isomerized starting material **V**, which was isolated from a representative reaction in a 3:1 **Va** (*E*/*Z* = 5.3) : **Vb** (*E*/*Z* = 3.8) mixture. The NMR sample also contains a trace (11%) of unreacted starting material.

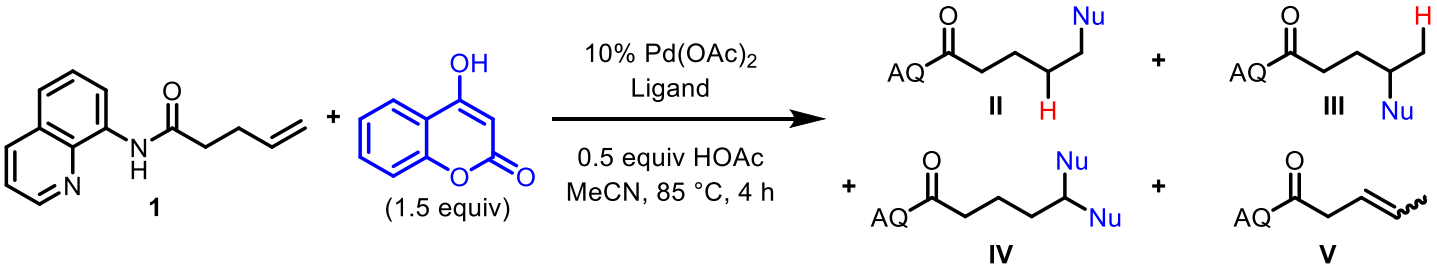
***N*-(2-(Pyridin-2-yl)quinolin-8-yl)pent-3-enamide (Va): ^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.28 (s, 1H, *Z*), 10.14 (s, 1H, *E*), 8.83–8.77 (m, 1H, *E*+*Z*), 8.76–8.74 (m, 1H, *E*+*Z*), 8.62 (d, *J* = 8.6 Hz, 1H, *E*+*Z*), 8.53 (dt, *J* = 7.9, 1.1 Hz, 1H, *E*+*Z*), 6.14–6.06 (m, 1H, *Z*), 5.99–5.91 (m, 1H, *E*+*Z*), 5.91–5.84 (m, 1H, *E*), 3.41 (dt, *J* = 7.8, 1.0 Hz, 2H, *Z*), 3.33 (d, *J* = 7.1 Hz, 2H, *E*), 1.92 (dq, *J* = 6.3, 1.2 Hz, 3H, *E*), 1.85–1.82 (m, 3H, *Z*).

***N*-(2-(Pyridin-2-yl)quinolin-8-yl)pent-2-enamide (Vb): ^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.99 (s, 1H, *Z*), 9.92 (s, 1H, *E*), 8.90–8.84 (m, 1H, *E*+*Z*), 8.77–8.76 (m, 1H, *E*+*Z*), 8.61–8.63 (m, 2H, *E*+*Z*), 8.30–8.27 (m, 1H, *E*+*Z*), 7.94–7.90 (m, 1H, *E*+*Z*), 7.59–7.54 (m, 1H, *E*+*Z*), 7.41–7.39 (m, 2H, *E*+*Z*), 7.14 (dt, *J* = 15.2, 6.5 Hz, 1H, *E*), 6.66–6.57 (m, 1H, *Z*), 6.35–6.29 (m, 1H, *Z*), 6.19 (dt, *J* = 15.2, 1.7 Hz, 1H, *E*), 2.45–2.31 (m, 2H, *E*+*Z*), 1.18 (t, *J* = 7.5 Hz, 3H, *E*+*Z*).

HRMS calc. for $C_{19}H_{18}N_3O^+$ $[M+H]^+$ 304.1450, found 304.1451.

Control Reactions: Effect of External Ligand

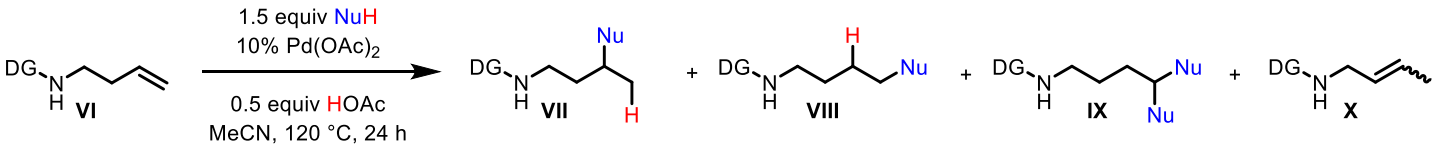
To determine if the tridentate directing group is necessary to suppress *beta*-hydride elimination and stabilize a six-membered palladacycle in substrates **I**, or if the same effect could be obtained by combining bidentate directing groups with external ligands, the following control reactions were carried out (Table S1): Addition of external ligand (pyridine, quinoline or PPh_3) in varying amounts (from 10 mol% to 1.0 equiv) to the hydrofunctionalization reaction of substrate **1**, bearing the bidentate 8-aminoquinoline directing group, gave mainly products of *beta*-hydride elimination (**IV**) and isomerization (**III** and **V**) under otherwise standard conditions. The desired product **II**, which is formed by proceeding through a six-membered palladacycle, was only observed in trace amounts. This suggests that the tridentate directing group is indeed necessary to stabilize the six-membered palladacycle intermediate.

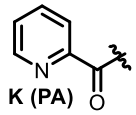
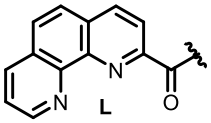
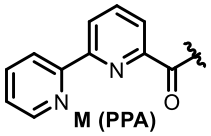


Entry	Ligand (amount)	II : III : IV : V : 1[a]
1	-	11 : 34 : 30 : 0 : 0[b]
2	pyridine (10 mol%)	11 : 23 : 36 : 3 : 4
3	pyridine (20 mol%)	9 : 30 : 38 : 4 : 5
4	pyridine (50 mol%)	6 : 18 : 30 : 33 : 0
5	pyridine (1.0 equiv)	2 : 3 : 19 : 57 : 0
6	quinoline (10 mol%)	2 : 6 : 11 : 80 : 0
7	PPh_3 (10 mol%)	13 : 22 : 10 : 9 : 20

Table S1. Effect of adding external ligand to hydrofunctionalization reactions with bidentate AQ directing group. AQ = 8-aminoquinoline. [a] ^{1}H NMR ratios determined by integrating the product peak(s) relative to 0.33 equiv 1,3,5-triisopropylbenzene. [b]Reaction time = 24 hours; see reference [1].

Optimization of Directing Groups for Amine Substrates



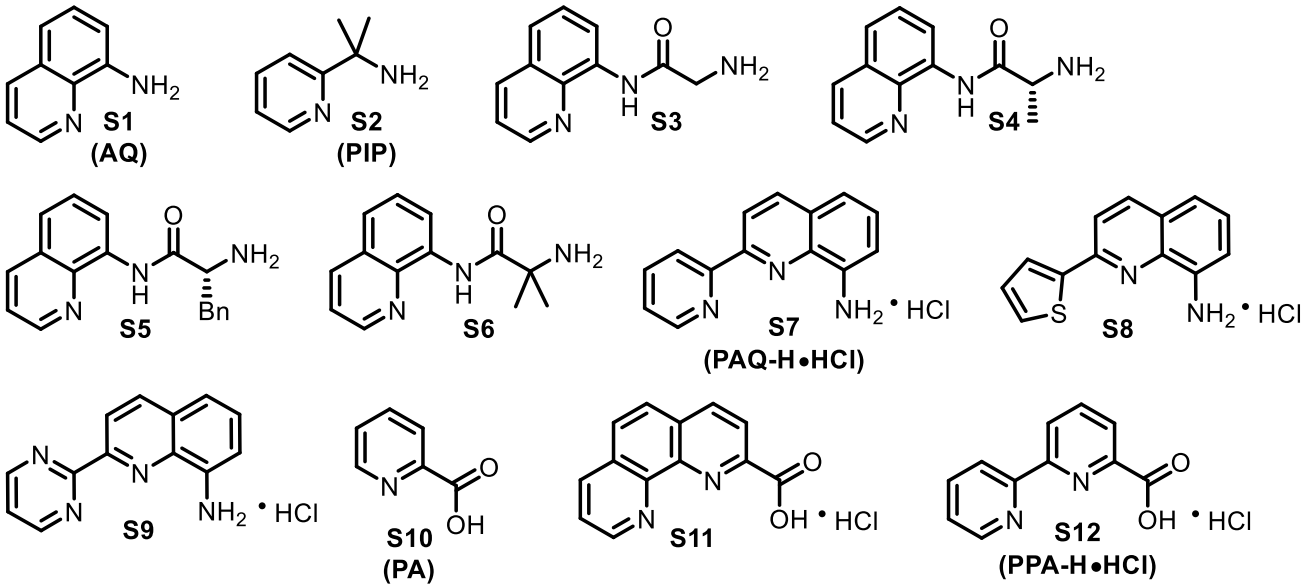
DG		Yield VII [%][a]	VI : VII : VIII : IX : X[b]
 K (PA)		4	20 : 4 : 0 : 7 : 16
 L		34	no data available[c]
 M (PPA)	24 h	82	0 : 82 : 0 : 0 : 0
	12 h	76	5 : 76 : 0 : 0 : 0
	85 °C, 12 h	68	0 : 68 : 0 : 0 : 0
	85 °C, 4 h	67	24 : 67 : 0 : 0 : 0
	no Pd	0	85 : 0 : 0 : 0 : 4

PA = picolinamide. PPA = 2,2'-bipyridylamide. [a]Yields are of isolated products. [b] ^{1}H NMR ratios obtained from crude reaction mixture. [c]Reaction mixture too insoluble to provide meaningful crude ratios.

Data for **VI**: see substrate **6** below.

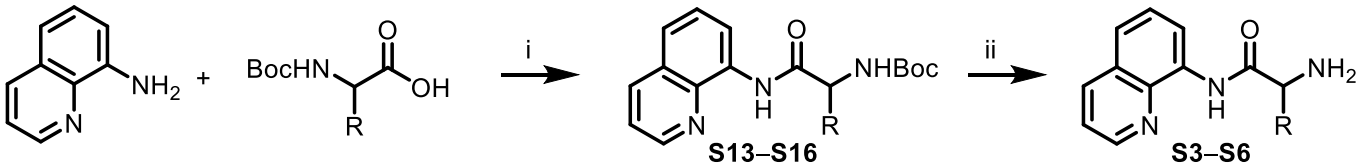
Data for **VII**: see product **7a** below.

Directing Group Synthesis



S1 and **S10** were obtained from commercial suppliers, **S2** was synthesized as previously reported.[2]

Synthesis of Amino Acid AQ Derivatives S3–S6



(i) NEt_3, ethyl chloroformate, THF, –15 °C to rt, 16 h; (ii) TFA, DCM, 0 °C to rt, 16 h

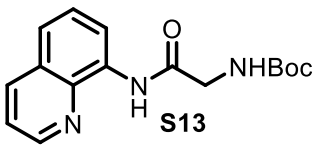
General Procedure A (GP A) for Amide Coupling with Ethyl Chloroformate

N-Boc-amino acid (1.0 equiv) was charged into a 25 mL RB flask containing THF (0.2 M) under N_2 and cooled in a −15 °C ice and brine bath. Triethylamine (1.0 equiv) and ethyl chloroformate (1.0 equiv) were added dropwise, and the reaction was stirred at −15 °C for 1 h. A cold solution of 8-aminoquinoline (1.0 equiv) dissolved in a minimal amount of THF was added to the reaction. After 1 h of stirring at −15 °C, the reaction was allowed to warm to room temperature and ran overnight. The reaction was then filtered, and the filtrate was concentrated. The crude mixture was purified by silica flash column chromatography to afford the pure product.

General Procedure B (GP B) for Boc Deprotection

S13–S16 (0.75 mmol) were dissolved in DCM (0.75 mL, 1 M) in a 25 mL RB flask. The solution was cooled to 0 °C, and trifluoroacetic acid (0.75 mL) was added dropwise. The reaction was allowed to warm to room temperature and was stirred overnight. Once complete, the reaction was washed with sat. $NaHCO_3$, and the organic layer was concentrated to give the crude amines **S3–S6**, which were taken through to the next step without further purification.

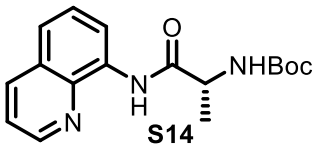
***tert*-Butyl (2-oxo-2-(quinolin-8-ylamino)ethyl)carbamate (S13)**



Synthesized from *N*-(*tert*-butoxycarbonyl)glycine following GP A (1.5 mmol scale). Purification by silica flash column chromatography (eluent: 100% EtOAc) afforded **S13** (449 mg, 99%) as a yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.79 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.75 (dd, *J* = 6.8, 2.3 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59–7.50 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.32 (s, 1H), 4.13 (d, *J* = 5.8 Hz, 2H), 1.52 (s, 9H);

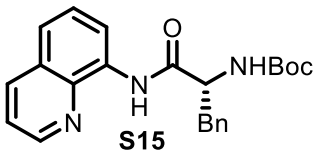
^{13}C NMR (150 MHz, $CDCl_3$) δ 167.97, 156.07, 148.44, 138.64, 136.44, 134.09, 128.08, 127.45, 122.04, 121.82, 116.74, 80.46, 45.47, 28.52 (×3); **HRMS** calcd. for $C_{16}H_{20}N_3O_3^+$ $[M+H]^+$ 302.1499, found 302.1496.

***tert*-butyl (*R*)-(1-oxo-1-(quinolin-8-ylamino)propan-2-yl)carbamate (S14)**



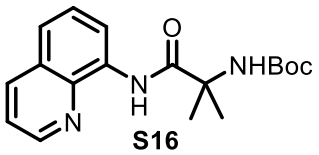
Synthesized from *N*-(*tert*-butoxycarbonyl)alanine following GP A (1.5 mmol scale). Purification by silica flash column chromatography (eulent: 100% EtOAc) afforded **S14** (389 mg, 82%) as a yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.33 (s, 1H), 8.80 (dd, J = 4.2, 1.7 Hz, 1H), 8.75 (dd, J = 7.0, 2.0 Hz, 1H), 8.16 (dd, J = 8.2, 1.7 Hz, 1H), 7.58–7.49 (m, 2H), 7.45 (dd, J = 8.2, 4.2 Hz, 1H), 5.23 (s, 1H), 4.53 (s, 1H), 1.55 (d, J = 7.1 Hz, 3H), 1.49 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.37, 155.48, 148.43, 138.75, 136.40, 134.31, 128.07, 127.44, 121.96, 121.79, 116.71, 80.28, 51.47, 28.52 (×3), 19.03; **HRMS** calcd. for $C_{17}H_{22}N_3O_3^+$ $[M+H]^+$ 316.1656, found 316.1655.

***tert*-butyl (*R*)-(1-oxo-3-phenyl-1-(quinolin-8-ylamino)propan-2-yl)carbamate (S15)**



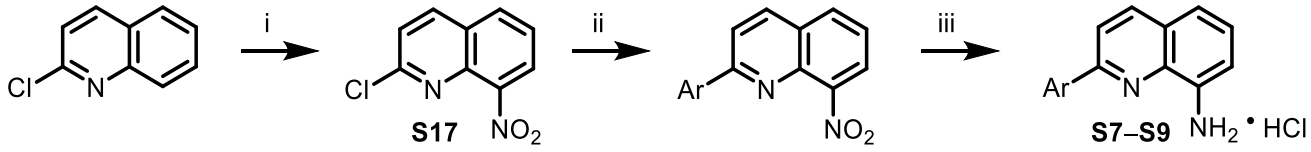
Synthesized from *N*-(*tert*-butoxycarbonyl)phenylalanine following GP A (1.5 mmol scale). Purification by silica flash column chromatography (eluent: 100% EtOAc) afforded **S15** (513 mg, 87%) as a yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.18 (s, 1H), 8.75 (d, J = 6.9 Hz, 1H), 8.71 (d, J = 2.1 Hz, 1H), 8.13 (dd, J = 8.3, 1.7 Hz, 1H), 7.58–7.47 (m, 2H), 7.42 (dd, J = 8.2, 4.2 Hz, 1H), 7.28–7.26 (m, 4H), 7.23–7.16 (m, 1H), 5.22 (s, 1H), 4.72 (s, 1H), 3.26 (d, J = 6.7 Hz, 2H), 1.45 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 169.95, 155.47, 148.33, 138.68, 136.62, 136.29, 134.07, 129.49 (×2), 128.85 (×2), 128.00, 127.39, 127.06, 122.02, 121.75, 116.66, 80.32, 56.86, 38.87, 28.48 (×3); **HRMS** calcd. for $C_{23}H_{26}N_3O_3^+$ $[M+H]^+$ 392.1969, found 392.1967.

***tert*-Butyl (2-methyl-1-oxo-1-(quinolin-8-ylamino)propan-2-yl)carbamate (S16)**



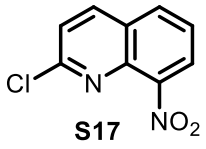
8-Aminoquinoline (721 mg, 5.00 mmol) was charged into a 100 mL RB flask containing 25 mL of DCM. 2-((*tert*-butoxycarbonyl)amino)-2-methylpropanoic acid (1.22 g, 6.00 mmol), pyridine (0.81 mL, 10.0 mmol), and HATU (2.28 g, 6.00 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 16 h. The deep brown solution was diluted with 100 mL EtOAc, washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), and purified by column chromatography (20–40% EtOAc in Hexanes) to afford **S16** (478 mg, 29%) as a tan solid. Note: 310 mg (27%) of crude 2-amino-2-methyl-*N*-(quinolin-8-yl)propenamide **S6** was also isolated as a brown oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.63 (s, 1H), 8.82–8.75 (m, 2H), 8.15 (dd, J = 8.2, 1.7 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H), 7.50 (dd, J = 8.2, 1.5 Hz, 1H), 7.44 (dd, J = 8.3, 4.2 Hz, 1H), 5.24 (s, 1H), 1.67 (s, 6H), 1.43 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.32, 154.50, 148.28, 138.94, 136.34, 134.72, 128.07, 127.52, 121.66, 121.51, 116.38, 80.16, 57.97, 28.43 (×3), 25.96 (×2); **HRMS** calcd. for $C_{18}H_{24}N_3O_3^+$ $[M+H]^+$ 330.1812, found 330.1812.

Synthesis of 2-Heteroaromatic AQ Derivatives S7–S9



(i) HNO_3/H_2SO_4, rt, 1 h; (ii) $ArSnBu_3$, $Pd(PPh_3)_4$, dioxane, 100 °C, 16 h; (iii) 1. H_2, Pd/C, EtOAc, rt, 16 h; 2. HCl

2-Chloro-8-nitroquinoline (S17)



S17 was synthesized following a literature procedure:[3] To 2-chloroquinoline (1.64 g, 10 mmol) in a RB flask at 0 °C was added conc. H_2SO_4 (4 mL). Conc. HNO_3 (2 mL) was then added dropwise and the reaction was allowed to warm to room temperature while stirring for 12 h. The crude mixture was carefully poured into ice water, slowly neutralized with conc. $NaOH_{(aq)}$ (in an ice bath) and extracted with DCM. The combined organic layers were washed with water, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by silica flash column chromatography (eluent: 20%-40% EtOAc/Hexanes) afforded **S17** (814 mg, 39%) as an off-white solid. **Note**: When the reaction is performed on a larger scale (>10 g),

the product becomes difficult to separate from the 2-chloro-5-nitroquinoline isomer formed as a by-product. In this case, the mixture of 5- and 8-nitro isomers obtained from column chromatography was taken through to the next step without further purification. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.6 Hz, 1H), 8.10 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.04 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.69–7.61 (m, 1H), 7.55 (d, *J* = 8.7 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 153.5, 147.0, 138.9, 138.8, 131.9, 127.6, 125.8, 124.9, 124.5. NMR analysis matched that reported in the literature.[3]

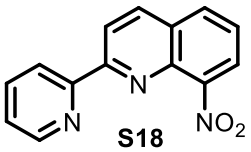
General Procedure C (GP C) for Stille Coupling with 2-chloro-8-nitroquinoline

GP C was adapted from a literature procedure:[4] To a round bottom flask equipped with a magnetic stir bar and a reflux condenser were added 2-chloro-8-nitroquinoline (1 equiv), $Pd(PPh_3)_4$ (5 mol%), anhydrous 1,4-dioxane (0.08 M), and aryl tributylstannane (1.2 equiv). The flask was evacuated and back-filled with N_2 three times, before stirring at 100 °C for 16 h. After cooling to room temperature, the reaction was diluted with EtOAc, washed once each with 20% aqueous NaOH, water, and then brine. The organic layer was dried over Mg_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by silica flash column chromatography to afford the pure product. **Note**: the yield of this reaction drops significantly when wet 1,4-dioxane is used and when the reaction is not performed under air-free conditions.

General Procedure D (GP D) for Nitro Reduction

To a round bottom flask equipped with a magnetic stir bar were added 8-nitro-2-(aryl)quinoline (1 equiv), palladium on carbon (20 mol%), and EtOAc (0.16 M). The flask was flushed thoroughly with N_2, a H_2 balloon was affixed and the reaction was stirred overnight. The crude reaction mixture was filtered over Celite, reduced *in vacuo* to *ca.* 5 mL of EtOAc and then added dropwise to a solution of acetyl chloride in anhydrous methanol (1:4.3 v/v ratio), which was pre-stirred for an hour before addition. The amine HCl salt precipitated out of solution as a white solid, which was filtered, collected and dried to afford the pure product.

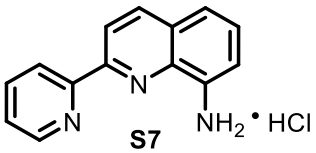
8-Nitro-2-(pyridin-2-yl)quinoline (S18)



S18

Synthesized following GP C, from **S17** (085 mg, 4.72 mmol) and tributyl(pyridin-2-yl)stannane (1.84 mL, 5.68 mmol). Purification by flash column chromatography (eluent: 20–40% EtOAc/Hexane) afforded **S18** (1.19 g, >99%) as a pale-yellow, fluffy solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.7 Hz, 1H), 8.72 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.69 (dt, *J* = 7.9, 1.1 Hz, 1H), 8.36 (d, *J* = 8.7 Hz, 1H), 8.07–8.03 (m, 2H), 7.88 (ddd, *J* = 8.0, 7.5, 1.8 Hz, 1H), 7.60 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.39 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 158.0, 155.0, 149.1, 148.4, 139.1, 137.2, 136.8, 131.7, 129.0, 125.2, 124.9, 123.8, 122.6, 120.5; **HRMS** calcd. for $C_{14}H_{10}N_3O_2^+$ $[M+H]^+$ 252.0768, found 252.0766.

2-(Pyridin-2-yl)quinolin-8-amine hydrochloride (S7)



S7
(PAQ-H HCl)

Synthesized from **S18** (1.69 g, 6.7 mmol), following GP D, to give **S7** (1.71 g, 99%) as a red-brown/beige solid. **^{1}H NMR** (500 MHz, $(CD_3)_2SO$) δ 9.02 (d, *J* = 8.1 Hz, 1H), 8.98 (d, *J* = 5.4 Hz, 1H), 8.64–8.51 (m, 3H), 7.96 (t, *J* = 6.5 Hz, 1H), 7.56 (dt, *J* = 15.6, 8.0 Hz, 2H), 7.36 (d, *J* = 7.2 Hz, 1H).

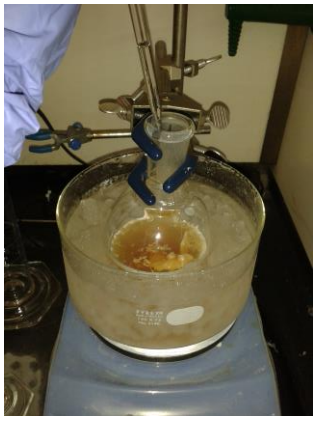
The HCl salt **S7** was too insoluble in DMSO-d_6 to provide a good ^{13}C NMR. Recorded below are the spectra of the free amine: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 3.1 Hz, 1H), 8.58 (d, *J* = 8.0 Hz, 1H), 8.52 (d, *J* = 8.6 Hz, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 7.75 (td, *J* = 7.7, 1.8 Hz, 1H), 7.35–7.19 (m, 2H), 7.13 (d, *J* = 8.2 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 5.09 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 156.3, 153.0, 149.0, 144.2, 137.6, 136.7, 136.6, 128.7, 127.7, 123.7, 121.4, 118.9, 115.8, 110.2; **HRMS** calcd. for $C_{14}H_{12}N_3^+$ $[M+H]^+$ 222.1026, found 222.1026.

Large-Scale Synthesis of S7

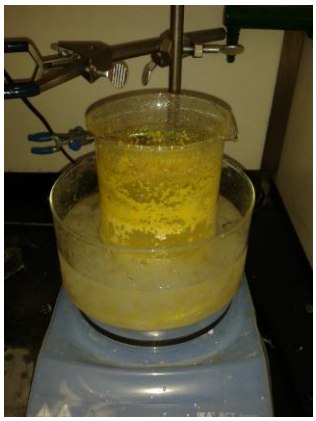
S17 was synthesized on a 10 g scale and taken through to the Stille Coupling (GP C) as a mixture of 5-nitro and 8-nitro isomers. Purification of **S18** by silica flash column chromatography (eluent: 10-40% EtOAc/Hexanes), followed by recrystallization afforded pure **S18** (5.2 g, 31% yield over two steps). (Recrystallization: **S18** was dissolved in hot EtOAc, cooled to room temperature and the minimum amount of Hexanes necessary to initiate crystallization was added; recrystallization was only successful if **S18** obtained from column chromatography was of *ca.* 80% or higher purity.) **S18** was then submitted to GP D to afford **S7** (5.4 g, >99%).

Photo Reel for Large-Scale Synthesis of S7

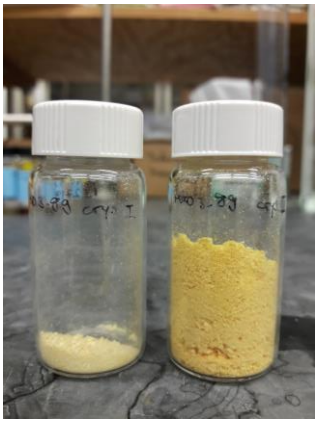
Weighing out 2-chloroquinoline



Nitration: dropwise addition of HNO_3

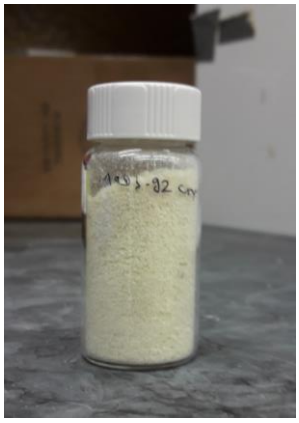


Nitration: quenching with NaOH



S17: >90% pure (left) and 75% pure (right)

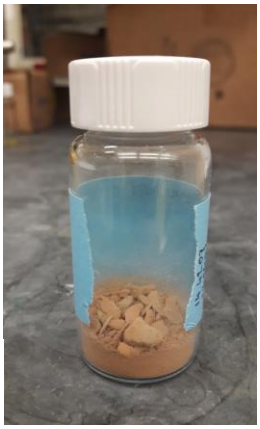
Stille reaction: rxn set-up (l), t = 0 (r, top), t = 16 h (r, bottom)



Stille product **S18**

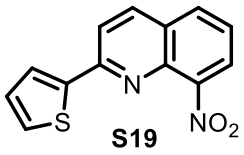
H_2, Pd/C reduction of **S18**

Addition of crude amine to HCl/MeOH



PAQ-H·HCl directing group **S7**

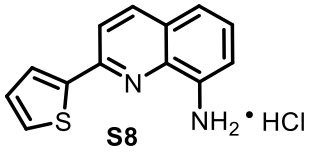
8-Nitro-2-(thiophen-2-yl)quinoline (S19)



S19

Synthesized following GP C (3.72 mmol scale), from **S17** and 2-(tributylstannyl)thiophene (1.42 mL, 4.46 mmol). Purification by silica flash column chromatography (20–40% EtOAc/hexanes) afforded **S19** (0.753 g, 79%) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.7 Hz, 1H), 8.00 (d, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.77 (d, *J* = 3.7 Hz, 1H), 7.49 (dd, *J* = 9.3, 6.4 Hz, 2H), 7.14 (t, *J* = 4.4 Hz, 1H); **^{13}C NMR** (500 MHz, $CDCl_3$) δ 154.3, 147.7, 144.3, 139.4, 136.6, 131.6, 130.4, 128.3, 127.9, 127.3, 124.4, 124.2, 119.1; **HRMS** calcd. for $C_{13}H_9N_2O_2S^+$ $[M+H]^+$ 257.0379, found 257.0378.

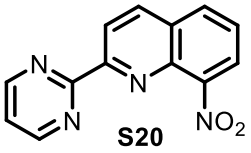
2-(Thiophen-2-yl)quinolin-8-amine hydrochloride (S8)



S8

Synthesized from **S19**, following GP D (2.81 mmol scale), to afford **S8** (501 mg, 79 %) as a yellow solid. **^{1}H NMR** (500 MHz, CD_3OD) δ 8.42 (d, *J* = 8.7 Hz, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 7.99 (t, *J* = 6.6 Hz, 2H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.67 (d, *J* = 5.0 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 4.4 Hz, 1H); **^{13}C NMR** (500 MHz, CD_3OD) δ 154.5, 145.3, 142.2, 138.5, 131.1, 130.3, 129.5, 129.4, 129.2, 128.8, 126.8, 124.1, 120.5; **HRMS** calcd. for $C_{13}H_{11}N_2S^+$ $[M+H]^+$ 227.0637, found 227.0636.

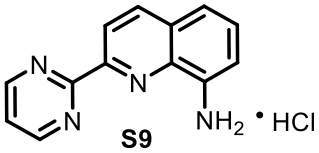
8-Nitro-2-(pyrimidin-2-yl)quinoline (S20)



S20

To a RB flask equipped with a magnetic stir bar and a reflux condenser were added 2-chloro-8-nitroquinoline **S17** (0.109g, 0.5 mmol), 2-(tributylstannyl)pyrimidine (0.173 mL, 0.55 mmol), $Pd(OAc)_2$, (11mg, 5 mol%), XPhos (48 mg, 0.1 mmol), and THF (2.8 mL). The flask was evacuated and back-filled with N_2 three times, before stirring at 60 °C for 24 h. After cooling to room temperature, the reaction was diluted with EtOAc, washed once each with 20% aqueous NaOH, water, and then brine. The organic layer was dried over Mg_2SO_4 and concentrated *in vacuo*. Purification by silica flash column chromatography (40% EtOAc/hexanes) afforded **S20** (80 mg, 63%) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.01 (d, *J* = 4.8 Hz, 2H), 8.75 (d, *J* = 8.7 Hz, 1H), 8.44 (d, *J* = 8.7 Hz, 1H), 8.20 (d, *J* = 7.5 Hz, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.68 (t, *J* = 7.9 Hz, 1H), 7.40 (t, *J* = 4.8 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 163.1, 157.9, 157.2, 148.3, 139.8, 137.2, 132.2, 129.3, 126.1, 125.2, 122.6, 121.0; **HRMS** calcd. for $C_{13}H_9N_4O_2^+$ $[M+H]^+$ 253.0720, found 253.0720.

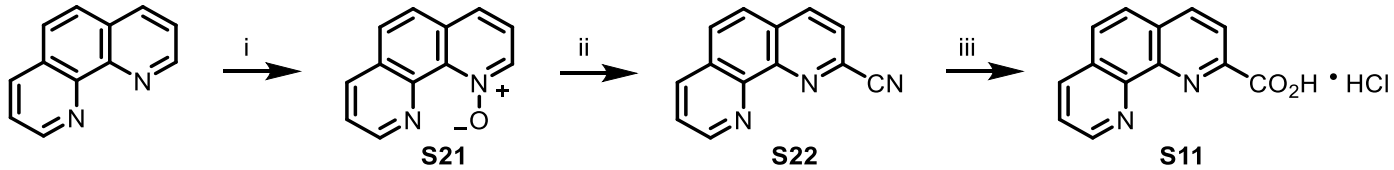
2-(Pyrimidin-2-yl)quinoline-8-amine (S9)



S9

Synthesized from **S20**, following GP D (0.69 mmol scale), to afford **S9** (120 mg, 78 %) as a yellow solid. **^{1}H NMR** (500 MHz, CD_3OD) δ 8.88 (d, *J* = 4.9 Hz, 2H), 8.46 (d, *J* = 8.6 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.43 (t, *J* = 4.9 Hz, 1H), 7.26 (t, *J* = 7.9 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.7 Hz, 1H); **^{13}C NMR** (150 MHz, CD_3OD) δ 155.6, 150.1, 142.8, 138.7, 130.4, 129.1, 122.1, 121.3, 113.2, 112.3, 106.7, 102.6; **HRMS** calcd. for $C_{13}H_{11}N_4^+$ $[M+H]^+$ 223.0978, found 223.0978.

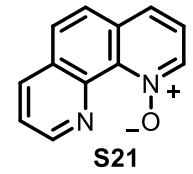
Synthesis of Directing Groups S11–S12



S21 **S22** **S11**

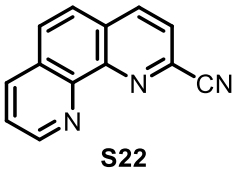
(i) HOAc, H_2O_2, 70 °C, 3 h; (ii) KCN, H_2O, benzoyl chloride, rt, 45 min; (iii) 1. NaOH, EtOH, H_2O, 92 °C, 30 min; 2. HCl

1-Oxo-1λ⁵-1,10-phenanthroline (S21)



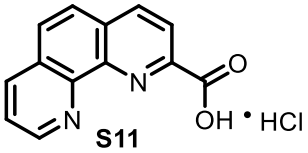
S21 was synthesized following a literature procedure:[5] To a round-bottom flask equipped with a magnetic stir bar was added 1,10-phenanthroline (1.51 g, 8.4 mmol), water (0.67 mL), conc. acetic acid (10 mL), and H_2O_2 (30% wt in H_2O, 1 mL). The reaction was stirred at 70 °C. After 2 h, another equivalent of H_2O_2 was added. After another hour, 0.7 mL of H_2O_2 was added to the reaction, and it was cooled to room temperature. The mixture was then diluted with water, neutralized with K_2CO_3 and Na_2CO_3, and extracted with chloroform four times. The organic layer was dried over Mg_2SO_4, filtered and concentrated *in vacuo* to afford **S21** (1.65 g, >99%) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.31 (d, *J* = 2.5 Hz, 1H), 8.74 (d, *J* = 6.3 Hz, 1H), 8.22 (d, *J* = 6.7 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.73 (d, *J* = 10.0 Hz, 2H), 7.66 (dd, *J* = 8.1, 4.3 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$)δ 150.0, 142.6, 140.8, 138.3, 135.9, 133.3, 129.1, 128.9, 126.5, 124.6, 123.2, 122.9. NMR analysis matched that reported in the literature.[5]

1,10-Phenanthroline-2-carbonitrile (S22)



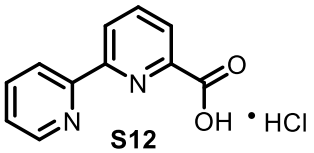
S22 was synthesized following a literature procedure:[5] To a round-bottom flask equipped with a magnetic stir bar was added **S21** (1.65 g, 8.4 mmol), KCN (1.67 g, 25.2 mmol) and water (14.5 mL). The reaction was stirred at room temperature for 15 min, then benzoyl chloride (1.47 mL, 12.62 mmol) was added dropwise. After another 30 min, the precipitate was collected, washed with water and recrystallized from hot ethanol to afford **S18** (914 mg, 53%) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.29 (dd, *J* = 4.4, 1.7 Hz, 1H), 8.41 (d, *J* = 8.2 Hz, 1H), 8.32 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.98 (dd, *J* = 8.5, 5.7 Hz, 2H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.75 (dd, *J* = 8.1, 4.3 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 151.3, 146.8, 145.4, 137.3, 136.3, 133.5, 129.9, 129.8, 129.3, 126.3, 125.8, 124.2, 117.5. NMR analysis matched that reported in the literature.[5]

1,10-Phenanthroline-2-carboxylic acid hydrochloride (S11)



S11 was synthesized following a literature procedure:[5] To a round-bottom flask equipped with a magnetic stir bar was added **S22** (0.723 g, 3.5 mmol), NaOH (0.60 g, 15 mmol), ethanol (7.2 mL) and water (7.2 mL). The reaction was refluxed at 92 °C for 30 min. The ethanol was evaporated off, and conc. HCl was added dropwise until solid crashed out. The precipitate was collected, washed with water and concentrated *in vacuo* to afford **S11** (714 mg, 78%) as a white solid. **^{1}H NMR** (500 MHz, $(CD_3)_2SO$) δ 9.41 (d, *J* = 5.2 Hz, 1H), 9.27 (d, *J* = 8.7 Hz, 1H), 8.91 (d, *J* = 8.4 Hz, 1H), 8.55 (d, *J* = 8.3 Hz, 1H), 8.40 (d, *J* = 2.0 Hz, 2H), 8.34 (dd, *J* = 8.2, 5.2 Hz, 1H); **^{13}C NMR** (150 MHz, $(CD_3)_2SO$) δ 165.2, 147.7, 145.7, 144.6, 139.2, 139.0, 138.3, 130.8, 129.7, 128. NMR analysis matched that reported in the literature.[5]

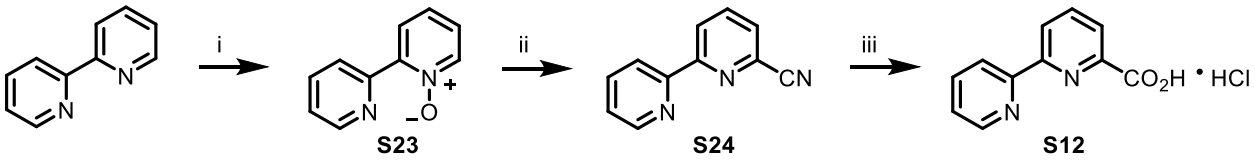
[2,2'-Bipyridine]-6-carboxylic acid hydrochloride (S12)



S12 was synthesized following a literature procedure:[6] To a round-bottom flask equipped with a magnetic stir bar was added 6-methyl-2,2'-bipyridine (0.449 mL, 2.87 mmol), $KMnO_4$ (1.59 g, 10.05 mmol), and water (34 mL). The solution was stirred for 3 days at 90 °C, after which it was cooled to room temperature and washed with ether three times. The aqueous layer was then acidified with 2 M HCl and concentrated *in vacuo* to afford **S12** (649 mg, 83%) as a white solid. **^{1}H NMR** (500 MHz, $(CD_3)_2SO$) δ 8.73 (d, *J* = 4.9 Hz, 1H), 8.58 (dd, *J* = 15.5, 7.8 Hz, 2H), 8.13 (dt, *J* = 15.5, 7.6 Hz, 2H), 8.04 (t, *J* = 7.7 Hz, 1H), 7.59–7.48 (m, 1H); **^{13}C NMR** (150 MHz, $(CD_3)_2SO$) δ 165.9, 154.7, 153.9, 149.0, 148.0, 138.9, 138.0, 124.9, 124.8, 123.7, 121.3. NMR analysis matched that reported in the literature.[6]

Large-Scale Synthesis of S12

Due to the price of 6-methyl-2,2'-bipyridine, the large-scale (10 g) synthesis of **S12** was achieved from cheaper, more readily available 2,2'-bipyridine, following a similar procedure as outlined for **S11** above:

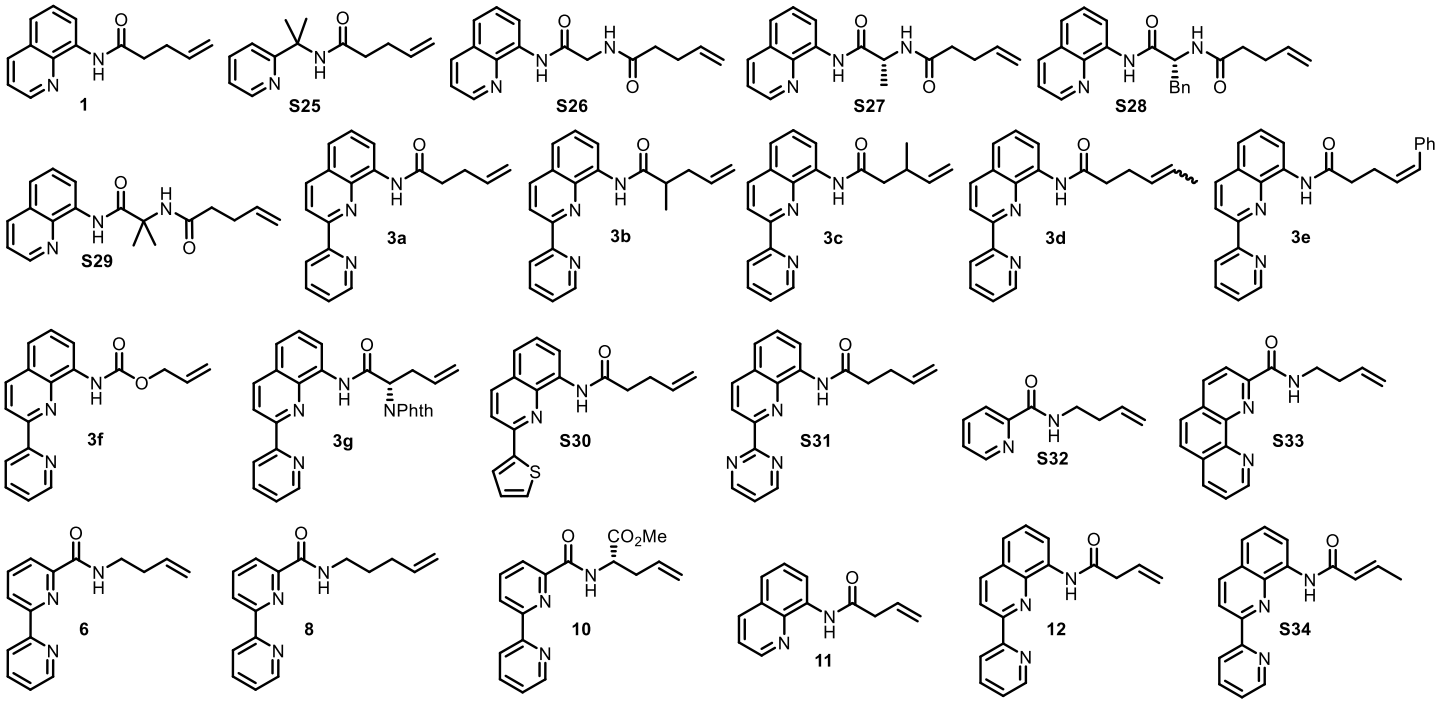


(i) TFA, H_2O_2, rt, 2.5 h; (ii) TMSCN, DCM, 4 d; (iii) 1. NaOH, EtOH/H_2O, 92 °C, 30 min; 2. HCl

S23 (16.0 g, 93%) and **S24** (11.6 g, 69%) were synthesized following a literature procedure.[7] **S12** was synthesized following a literature procedure.[8] After the reaction was complete, the cooled solution was acidified to pH = 3.8 with conc. HCl. The pure product crashed out of solution as a white solid, which was filtered and washed with cold water, followed by cold acetone. The mother liquor was concentrated *in vacuo* to one-third of its previous volume and a second batch of product crashed out of solution. Both batches were dried under high-vacuum to provide pure **S12** (9.9 g, 79%) as a white solid.

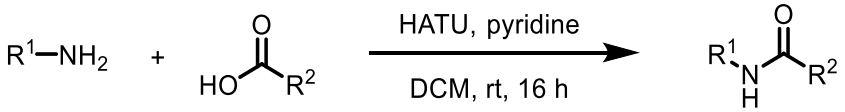
Substrate Synthesis

(Yields are unoptimized)



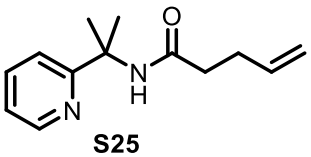
Alkene **1** was synthesized following a literature procedure.[1]

General Procedure E (GP E) for the Amide Coupling used for Substrate Synthesis



To a round bottom flask equipped with a magnetic stir bar were added directing group (1.0 equiv), carboxylic acid or amine coupling partner (1.5 equiv), HATU (1.5 equiv), pyridine (4–5 equiv), and DCM (0.4 M). The reaction was stirred at room temperature overnight. The crude reaction mixture was diluted with EtOAc, washed with $NaHCO_3$(aq) and brine, dried over Mg_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by silica flash column chromatography to afford the pure product.

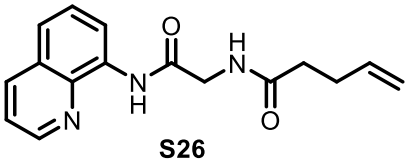
***N*-(2-(Pyridin-2-yl)propan-2-yl)pent-4-enamide (S25)**



S25

S2 (545 mg, 4.00 mmol) was charged into a 100 mL RB flask containing 10.0 mL of DCM. 4-Pentenoic acid (601 mg, 6.00 mmol), collidine (1.07 mL, 8.00 mmol), and HATU (1.83 mg, 4.80 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 5 days. The deep brown solution was diluted with 50 mL EtOAc, washed with sat. $NaHCO_3$ (50 mL, ×2) and brine (50 mL, ×1), and purified by column chromatography (20–50% EtOAc in Hexanes) to afford **S25** (459 mg, 53%) as a brown liquid. Note: Trace amounts of collidine and tetramethylurea were removed by heating at 80 °C under reduced pressure. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.51 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.81–7.64 (m, 2H), 7.40 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.19 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H), 5.86 (ddt, *J* = 16.7, 10.1, 6.3 Hz, 1H), 5.08 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.99 (ddd, *J* = 10.2, 1.9, 1.0 Hz, 1H), 2.45–2.39 (m, 2H), 2.35 (ddd, *J* = 8.0, 6.6, 1.2 Hz, 2H), 1.75 (s, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.6, 164.7, 147.7, 137.5, 137.2, 122.0, 119.7, 115.4, 56.6, 37.0, 29.9, 27.7 (×2); **HRMS** calcd. for $C_{13}H_{19}N_2O^+$ $[M+H]^+$ 219.1492, found 219.1491.

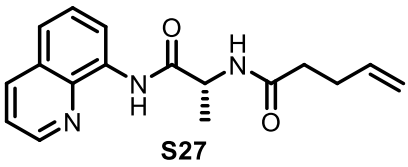
***N*-(2-Oxo-2-(quinolin-8-ylamino)ethyl)pent-4-enamide (S26)**



S26

S13 (226 mg, 0.75 mmol) was deprotected following GP B to afford crude **S3** (150 mg, 99%) as a yellow solid, which was submitted to GP E. Purification by silica flash column chromatography (33–40% EtOAc in Hexanes) afforded **S26** (187 mg, 88%) as a yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.79 (d, *J* = 4.3 Hz, 1H), 8.70 (t, *J* = 4.5 Hz, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 7.57–7.49 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.44 (s, 1H), 5.89 (ddt, *J* = 16.8, 10.2, 6.3 Hz, 1H), 5.12 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.03 (dd, *J* = 10.2, 1.6 Hz, 1H), 4.30 (d, *J* = 5.1 Hz, 2H), 2.52–2.47 (m, 2H), 2.47–2.42 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.2, 166.6, 147.9, 137.9, 136.5, 135.9, 133.3, 127.5, 126.8, 121.6, 121.3, 116.1, 115.3, 43.5, 35.2, 29.1; **HRMS** calcd. for $C_{16}H_{18}N_3O_2^+$ $[M+H]^+$ 284.1394, found 284.1395.

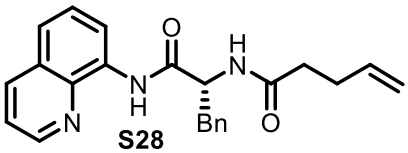
(R)-*N*-(1-Oxo-1-(quinolin-8-ylamino)propan-2-yl)pent-4-enamide (S27)



S27

S14 (237 mg, 0.75 mmol) was deprotected following GP B to afford crude **S4** (154 mg, 96%) as a yellow solid, which was submitted to GP E. Purification by silica flash column chromatography (33–40% EtOAc in Hexanes) afforded **S27** (118 mg, 55%) as an off-white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.81 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.71 (dd, *J* = 5.4, 3.5 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.55–7.50 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.40 (d, *J* = 7.8 Hz, 1H), 5.86 (ddt, *J* = 16.8, 10.3, 6.4 Hz, 1H), 5.09 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.01 (dq, *J* = 10.2, 1.4 Hz, 1H), 4.87 (p, *J* = 7.1 Hz, 1H), 2.46 (dtd, *J* = 8.3, 6.7, 1.3 Hz, 2H), 2.43–2.36 (m, 2H), 1.57 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.1, 170.9, 148.6, 138.6, 137.0, 136.4, 134.1, 128.0, 127.3, 122.2, 121.9, 116.7, 115.8, 50.1, 35.9, 29.7, 19.3; **HRMS** calcd. for $C_{17}H_{20}N_3O_2^+$ $[M+H]^+$ 298.1550, found 298.1549.

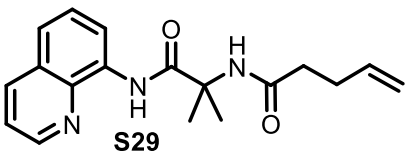
(R)-*N*-(1-Oxo-3-phenyl-1-(quinolin-8-ylamino)propan-2-yl)pent-4-enamide (S28)



S28

S15 (294 mg, 0.75 mmol) was deprotected following GP B to afford crude **S5** (180 mg, 82%) as a yellow solid, which was submitted to GP E. Purification by silica flash column chromatography (33% EtOAc in Hexanes) afforded **S28** (148 mg, 64%) as an off-white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.71 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.69 (dd, *J* = 6.0, 2.9 Hz, 1H), 8.13 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.55–7.50 (m, 2H), 7.43 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.26–7.22 (m, 4H), 7.21–7.16 (m, 1H), 6.29 (d, *J* = 7.7 Hz, 1H), 5.81 (ddt, *J* = 16.8, 10.2, 6.2 Hz, 1H), 5.10–5.02 (m, 2H), 4.98 (dq, *J* = 10.2, 1.4 Hz, 1H), 3.25 (h, *J* = 7.3 Hz, 2H), 2.44–2.38 (m, 2H), 2.38–2.31 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.3, 169.4, 148.4, 138.6, 137.0, 136.4, 136.3, 133.9, 129.5 (×2), 128.8 (×2), 128.0, 127.3, 127.1, 122.2, 121.8, 116.7, 115.9, 55.4, 38.9, 35.9, 29.6; **HRMS** calcd. for $C_{23}H_{24}N_3O_2^+$ $[M+H]^+$ 374.1863, found 374.1862.

***N*-(2-Methyl-1-oxo-1-(quinolin-8-ylamino)propan-2-yl)pent-4-enamide (S29)**

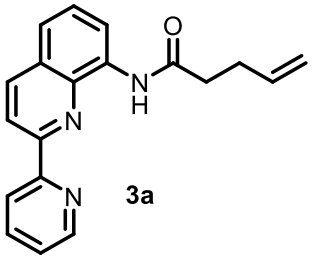


S29

S16 (250 mg, 0.76 mmol) was deprotected following GP B to afford crude **S6** (160 mg, 92%) as a brown oil, which was submitted to GP E. Purification by silica flash column chromatography (33–40% EtOAc in Hexanes) afforded **S29** (294 mg, 70%) as a yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.45 (s, 1H), 8.78 (dd, *J* = 4.2,

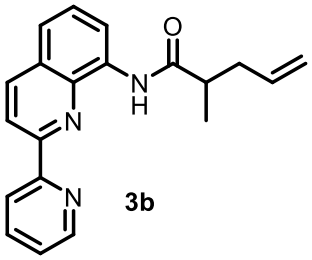
1.5 Hz, 1H), 8.74 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.15 (dt, *J* = 8.3, 1.4 Hz, 1H), 7.57–7.47 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.48 (d, *J* = 4.6 Hz, 1H), 5.87 (ddt, *J* = 16.8, 10.1, 6.4 Hz, 1H), 5.10 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.00 (dt, *J* = 10.3, 1.5 Hz, 1H), 2.48–2.41 (m, 2H), 2.40–2.35 (m, 2H), 1.76 (d, *J* = 1.4 Hz, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.98, 171.99, 148.34, 138.86, 137.25, 136.45, 134.40, 128.07, 127.48, 121.73 (×2), 116.46, 115.73, 58.15, 36.44, 29.70, 25.44 (×2); **HRMS** calcd. for $C_{18}H_{22}N_3O_2^+$ $[M+H]^+$ 312.1707, found 312.1708.

_N_-[2-(Pyridin-2-yl)quinolin-8-yl]pent-4-enamide (3a)



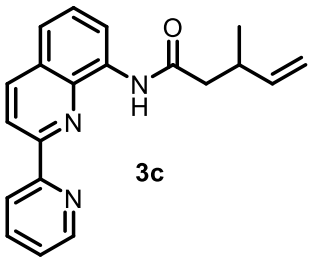
Synthesized from **S7** (2.21 g, 10 mmol) and pent-4-enoic acid (1.53 mL, 15 mmol) following GP E. Purification by silica flash column chromatography (10–20% EtOAc/hexanes) afforded **3a** (2.75 g, 91%) as a pale-yellow solid. **Note**: If desired, the product can be recrystallized from hot DCM or hot EtOAc, provided that the purity after column chromatography is >80%. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.79 (dd, *J* = 6.7, 2.3 Hz, 1H), 8.75 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.61 (d, *J* = 8.6 Hz, 1H), 8.51 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 7.93–7.87 (m, 1H), 7.55–7.51 (m, 2H), 7.39 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 5.99 (ddt, *J* = 16.8, 10.2, 6.4 Hz, 1H), 5.20 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.08 (dq, *J* = 10.2, 1.3 Hz, 1H), 2.74–2.71 (m, 2H), 2.65–2.61 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.6, 155.7, 154.1, 149.4, 137.6, 137.3, 136.9, 136.9, 134.5, 127.9, 127.7, 124.2, 121.4, 121.3, 119.5, 116.7, 115.9, 37.5, 29.5; **HRMS** calcd. for $C_{19}H_{18}N_3O^+$ $[M+H]^+$ 304.1444, found 304.1444.

2-Methyl-_N_-[2-(pyridin-2-yl)quinolin-8-yl]pent-4-enamide (3b)



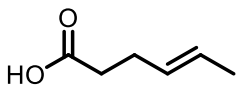
Synthesized from **S7** and 2-methyl-4-pentenoic acid (1.5 equiv) following GP E (1 mmol scale). Purification by silica flash column chromatography (5% acetone/hexanes) afforded **3b** (210 mg, 66%) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.80 (dd, *J* = 5.7, 3.3 Hz, 1H), 8.77 (d, *J* = 4.0 Hz, 1H), 8.64 (d, *J* = 8.6 Hz, 1H), 8.54 (d, *J* = 7.9 Hz, 1H), 8.30 (d, *J* = 8.6 Hz, 1H), 7.91 (td, *J* = 7.7, 1.8 Hz, 1H), 7.59–7.51 (m, 2H), 7.43–7.36 (m, 1H), 5.93 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.18 (d, *J* = 17.1 Hz, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 2.75 (h, *J* = 6.9 Hz, 1H), 2.66 (dt, *J* = 14.0, 7.0 Hz, 1H), 2.40 (dt, *J* = 14.1, 7.1 Hz, 1H), 1.42 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 174.2, 155.8, 154.1, 149.4, 137.8, 137.4, 136.9, 135.6, 134.5, 128.0, 127.8, 124.2, 121.4, 121.2, 119.5, 117.3, 116.8, 42.8, 38.6, 17.5; **HRMS** calcd. for $C_{20}H_{20}N_3O^+$ $[M+H]^+$ 318.1601, found 318.1601.

3-Methyl-_N_-[2-(pyridin-2-yl)quinolin-8-yl]pent-4-enamide (3c)



Synthesized from **S7** and 3-methyl-4-pentenoic acid (1.5 equiv) following GP E (1 mmol scale). Purification by silica flash column chromatography (5% acetone/hexanes) afforded **3c** (75 mg, 56% yield) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.80 (dd, *J* = 5.9, 3.0 Hz, 1H), 8.76 (d, *J* = 4.8 Hz, 1H), 8.62 (d, *J* = 8.6 Hz, 1H), 8.53 (d, *J* = 7.9 Hz, 1H), 8.28 (d, *J* = 8.7 Hz, 1H), 7.91 (t, *J* = 7.7 Hz, 1H), 7.58–7.49 (m, 2H), 7.40 (dd, *J* = 7.5, 4.9 Hz, 1H), 5.96 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.16 (d, *J* = 17.2 Hz, 1H), 5.03 (d, *J* = 10.3 Hz, 1H), 2.95 (sept, *J* = 6.9 Hz, 1H), 2.67 (dd, *J* = 14.3, 7.0 Hz, 1H), 2.55 (dd, *J* = 14.3, 7.3 Hz, 1H), 1.22 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.2, 155.8, 154.1, 149.4, 142.6, 137.6, 137.3, 136.9, 134.5, 127.9, 127.7, 124.2, 121.4, 121.3, 119.5, 116.8, 113.7, 45.4, 34.9, 19.8; **HRMS** calcd. for $C_{20}H_{20}N_3O^+$ $[M+H]^+$ 318.1601, found 318.1601.

(4_E_)-Hex-4-enoic acid ((_E_)-S36)



***(E)*-S36**

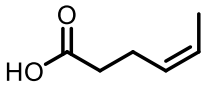
(*E*)-S36 was synthesized following a literature procedure:[11]

Preparation of Jones reagent: To a vial equipped with a magnetic stir bar was added CrO_3 (1 g, 10 mmol) and 2 mL of water. The vial was cooled to 0 °C, and 1 mL of conc. H_2SO_4 was added. The mixture was then diluted to 5 mL.

To a round-bottom flask equipped with a magnetic stir bar was added *trans*-4-hexen-1-ol (0.588 mL, 5 mmol) and 12.5 mL acetone. The flask was cooled to 0 °C, and freshly prepared Jones reagent (10 mmol) was added dropwise over 20 mins. The mixture was then stirred for 3 h at 0 °C, quenched with 5 mL ethanol and extracted with DCM twice. The organic layer was then basified with aqueous K_2CO_3 and washed with Et_2O. The aqueous layer was acidified with aqueous HCl and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and

concentrated *in vacuo* to afford crude **(*E*)-S36** (322 mg, 56%), which was taken through to the next step without further purification. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.81 (s, 1H), 5.54–5.46 (m, 1H), 5.46–5.39 (m, 1H), 2.46–2.36 (m, 2H), 2.30 (q, *J* = 7.3 Hz, 2H), 1.64 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (500 MHz, $CDCl_3$) δ 179.3, 128.3, 125.8, 33.6, 27.0, 17.3. NMR analysis matched that reported in the literature.[11]

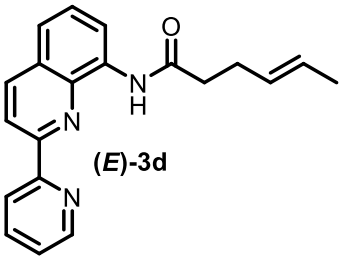
(4*Z*)-Hex-4-enoic acid ((*Z*)-S36)



(*Z*)-S36

Synthesized as **(*E*)-S36** above,[11] from *cis*-4-hexen-1-ol (1.2 mL, 10 mmol). Crude **(*Z*)-S34** (510 mg, 50%) was taken through to the next step without further purification. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.50 (dt, *J* = 13.6, 6.6 Hz, 1H), 5.37 (dq, *J* = 11.5, 6.0 Hz, 1H), 2.40 (m, 4H), 1.63 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 179.7, 127.8, 125.4, 33.8, 22.0, 12.4. NMR analysis matched that reported in the literature.[11]

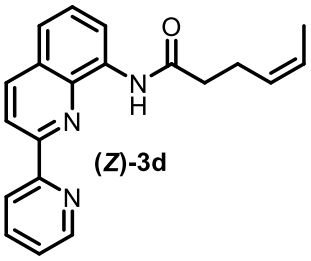
(4*E*)-*N*-[2-(pyridin-2-yl)quinolin-8-yl]hex-4-enamide ((*E*)-3d)



(*E*)-3d

Synthesized from **S7** and **(*E*)-S36**, following GP E (1 mmol scale). Purification by silica flash column chromatography (eluent: 30% EtOAc/Hex) afforded ***E*-3d** (218 mg, 69%) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.73 (d, *J* = 7.6 Hz, 1H), 8.68 (d, *J* = 4.8 Hz, 1H), 8.48 (d, *J* = 8.6 Hz, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 8.08 (d, *J* = 8.6 Hz, 1H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.29 (t, *J* = 6.2 Hz, 1H), 5.66–5.50 (m, 2H), 2.63 (t, *J* = 7.4 Hz, 2H), 2.57–2.45 (m, 2H), 1.63 (d, *J* = 4.2 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.7, 155.4, 153.7, 149.2, 137.4, 137.0, 136.7, 134.4, 129.3, 127.7, 127.5, 126.4, 124.1, 121.2, 121.1, 119.2, 116.5, 38.0, 28.4, 17.9; **HRMS** calcd. for $C_{20}H_{20}N_3O^+$ $[M+H]^+$ 318.1601, found 318.1603.

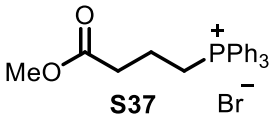
(4*Z*)-*N*-[2-(Pyridin-2-yl)quinolin-8-yl]hex-4-enamide ((*Z*)-3d)



(*Z*)-3d

Synthesized from **S7** and **(*Z*)-S36**, following GP E (1 mmol scale). Purification by silica flash column chromatography (eluent: 2:1:7 acetone:DCM:hexanes) afforded **(*Z*)-3d** (137 mg, 62%) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.78 (d, *J* = 7.1 Hz, 1H), 8.73 (d, *J* = 4.9 Hz, 1H), 8.58 (d, *J* = 8.6 Hz, 1H), 8.48 (d, *J* = 7.9 Hz, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 7.85 (td, *J* = 7.7, 1.8 Hz, 1H), 7.55–7.44 (m, 2H), 7.36 (dd, *J* = 7.5, 4.8 Hz, 1H), 5.63–5.49 (m, 2H), 2.70–2.57 (m, 4H), 1.69 (d, *J* = 5.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.9, 155.6, 153.9, 149.3, 137.5, 137.2, 136.8, 134.5, 128.4, 127.9, 127.7, 125.8, 124.2, 121.3, 121.2, 119.4, 116.6, 38.1, 23.1, 12.8; **HRMS** calcd. for $C_{20}H_{20}N_3O^+$ $[M+H]^+$ 318.1601, found 318.1601.

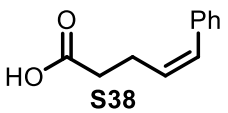
(4-Methoxy-4-oxobutyl)triphenylphosphonium bromide (S37)



S37

Synthesized following a published procedure:[21] To a solution of 4-bromobutyric acid (1.0 eq, 100 mmol) in MeOH at 0 °C was added thionyl chloride (1.5 eq) dropwise and the reaction was stirred at room temperature for 16 h. The reaction was quenched with $NaHCO_3$ and extracted with Et_2O. The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude methyl 4-bromobutanoate was taken through to the next step without further purification: Methyl 4-bromobutanoate (1.0 eq) and triphenyl phosphine (1.0 eq) was refluxed in MeCN for 6 h, after which the crude phosphonium bromide was recrystallized from MeCN/Et_2O to afford 3.3 g **S37** (75% yield over two steps) as a white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.83 (ddd, *J* = 12.7, 8.4, 1.3 Hz, 6H), 7.78–7.71 (m, 3H), 7.66 (td, *J* = 7.9, 3.5 Hz, 6H), 3.96 (dddd, *J* = 13.3, 9.1, 4.9, 2.7 Hz, 2H), 3.60 (s, 3H), 2.85 (td, *J* = 6.6, 1.4 Hz, 2H), 1.95–1.82 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.6, 135.1, 135.1, 133.7, 130.5, 51.8, 33.0, 21.6, 18.1.

(*Z*)-5-Phenylpent-4-enoic acid (S38)

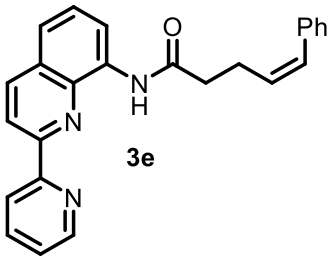


S38

Synthesized following a published procedure:[21] To a solution of Wittig salt **S37** (1.33 g, 3.0 mmol) in THF (10 mL) at −20 °C was added NaHMDS (1.9 mL, 3.6 mmol) dropwise. The reaction was then cooled to −78 °C and benzaldehyde (0.31 mL, 3.0 mmol) was added dropwise. The mixture was allowed to warm to room temperature and stirred overnight, after which it was quenched with NH_4Cl, extracted with Et2O, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica flash column chromatography (eluent: 5–10% EtOAc/Hex) afforded a 1:1 mixture of methyl (*Z*)-5-phenylpent-

4-enoate and benzaldehyde, which was taken through to the next step without further purification: the mixture was dissolved in THF/H_2O (1:1, 2mL). LiOH (200 mg) was added and the reaction was stirred at room temperature overnight. The reaction was diluted with water and extracted with DCM. The organic layer was discarded and the aqueous phase was acidified with 1M HCl and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford crude (*Z*)-5-phenylpent-4-enoic acid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37–7.32 (m, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 7.24 (dd, *J* = 8.2, 6.5 Hz, 1H), 6.49 (dd, *J* = 11.7, 1.9 Hz, 1H), 5.64 (dt, *J* = 11.6, 7.2 Hz, 1H), 2.71–2.63 (m, 2H), 2.50 (dd, *J* = 8.0, 6.9 Hz, 2H). Analytical data matched published values.[22]

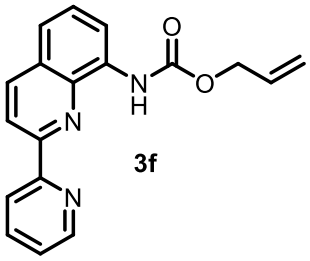
(*Z*)-5-Phenyl-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pent-4-enamide (3e)



3e

Synthesized from **S7** and **S38**, following GP E (0.6 mmol scale). Purification by silica flash column chromatography (eluent: 20% EtOAc/Hex) afforded **3e** (200 mg, 88%) as a pale-yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.80 (dd, *J* = 6.4, 2.5 Hz, 1H), 8.75 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.61 (d, *J* = 8.6 Hz, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 7.80 (td, *J* = 7.7, 1.8 Hz, 1H), 7.55–7.51 (m, 2H), 7.37 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.34–7.29 (m, 4H), 7.20 (ddt, *J* = 8.7, 6.7, 2.0 Hz, 1H), 6.53 (dt, *J* = 11.6, 1.8 Hz, 1H), 5.81 (dt, *J* = 11.6, 7.2 Hz, 1H), 2.93 (dtd, *J* = 7.9, 6.7, 6.2, 1.8 Hz, 2H), 2.81–2.72 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.7, 155.8, 154.2, 149.5, 137.7, 137.4, 137.3, 137.0, 134.6, 130.6, 130.5, 128.9, 128.4, 128.1, 127.8, 127.0, 124.3, 121.6, 121.4, 119.6, 116.9, 38.4, 24.8; **HRMS** calcd. for $C_{25}H_{22}N_3O^+$ $[M+H]^+$ 380.1763, found 380.1766.

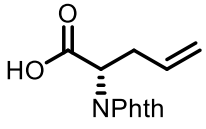
Allyl (2-(pyridin-2-yl)quinolin-8-yl)carbamate (3f)



3f

To a solution of **S7** (258 mg, 1.0 mmol) in DCM (13 mL, 0.08 M) at 0 °C was added pyridine (0.18 mL, 2.2 mmol), followed by dropwise addition of allyl chloroformate (0.11 mL, 1.1 mmol). The reaction was stirred for 3 h while warming to room temperature, after which the crude mixture was washed with 1M HCl, sodium bicarbonate and brine, and the organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica flash column chromatography (eluent: 10–20% EtOAc/hexanes) afforded **3f** (133 mg, 44%) as a white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.71 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.57 (d, *J* = 8.5 Hz, 1H), 8.54 (d, *J* = 7.9 Hz, 1H), 8.43 (brs, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 7.86 (td, *J* = 7.7, 1.8 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.45 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.34 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 6.08 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H), 5.45 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.32 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.79 (dt, *J* = 5.8, 1.4 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 155.7, 154.1, 153.3, 149.3, 137.5, 137.2, 137.0, 134.7, 132.8, 128.1, 127.6, 124.2, 121.6, 120.7, 119.5, 118.5, 115.0, 66.1; **HRMS** calcd. for $C_{18}H_{16}N_3O_2^+$ $[M+H]^+$ 306.1243, found 306.1243.

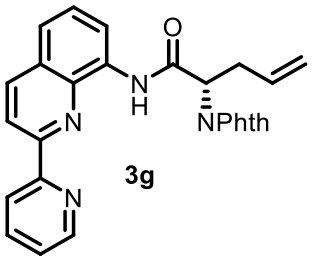
(*S*)-2-(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)pent-4-enoic acid (S35)



S35

S35 was synthesized following a literature procedure:[9] To a RB flask fitted with a magnetic stir bar was added L-allylglycine (518 mg, 4.5 mmol), sodium carbonate (477 mg, 4.5 mmol), and water (11.25 mL, 0.4 M). After mixing thoroughly, *N*-carboethoxyphthalimide (986 mg, 4.5 mmol) was added slowly, and the reaction was stirred at room temperature for 3 h. The reaction was then washed with EtOAc three times, the aqueous layer was acidified with conc. HCl and extracted twice with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford pure **L-S35** (1.1 g, 99% yield) as an off-white solid. **Synthesis of the racemic standard:** To a round-bottom flask equipped with a magnetic stir bar was added DL-2-allylglycine (576 mg, 5 mmol). The flask was evacuated and back-filled with N_2 three times, and triethylamine (1.39 mL, 10 mmol), toluene (33.3 mL, 0.15 M), and phthalic anhydride (1.481g, 10 mmol) were added. The flask was then fitted with a Dean–Stark apparatus and refluxed at 140 °C for 16 h. The crude reaction mixture was then concentrated in vacuo, acidified with water and HCl, then extracted into EtOAc and washed with water. After concentrating in vacuo, the crude solid was dissolved in aqueous K_2CO_3, washed with ether. The aqueous layer was acidified with HCl and extracted with EtOAc. The organic layers were dried over $MgSO_4$ and concentrated in vacuo to afford crude racemic **S35** (779 mg, 51% yield, 80% purity by ^{1}H NMR), which was taken through to the next step without further purification. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 (dd, J = 5.5, 3.1 Hz, 2H), 7.73 (dd, J = 5.5, 3.1 Hz, 2H), 5.71 (ddd, J = 25.3, 9.2, 5.6 Hz, 1H), 5.07 (d, J = 17.0 Hz, 1H), 5.00 (d, J = 9.4 Hz, 2H), 3.09–2.90 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 174.4, 167.5, 134.2, 133.0, 131.6, 123.6, 118.9, 51.4, 33.0. NMR analysis matched that reported in the literature.[9]

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pent-4-enamide (3g)



3g

The synthesis of **3g** was adapted from a literature procedure:[10] To a RB flask fitted with a magnetic stir bar was added **L-S35** (319 mg, 1.3 mmol), thionyl chloride (285 mL, 3.9 mmol), toluene (2.6 mL, 0.5 M) and a drop of DMF. The flask was then fitted with a reflux condenser and the reaction was stirred at 80 °C for 2 h. The reaction was then concentrated *in vacuo*, and the resulting acid chloride was dissolved in DCM (0.65 mL, 2 M) and taken through to the next step without further purification. To another RB flask fitted with a magnetic stir bar was added **S7** (125 mg, 0.5 mmol), 2,6-lutidine (0.075 mL, 0.65 mmol), and DCM (1 mL, 0.5 M). The acid chloride in DCM solution was then added dropwise, and the reaction was stirred overnight at room temperature. The reaction was diluted with DCM, washed with 1 M HCl twice, once with brine, then dried and concentrated *in vacuo*. Purification by column chromatography (hexanes : DCM : EtOAc = 50 : 40 : 10) afforded **3g** (78 mg, 52% yield, 99% *ee*) as an off-white solid. The racemic standard was synthesized from **S7** and **S35** following GP E (1 mmol, 74 mg, 24% yield). The enantiomeric excess of **3f** was determined by chiral SFC on a Daicel Chiralpak AS-H column (0.46 cm × 25 cm), Hexanes / IPA = 80 / 20, 1.0 mL/min, λ = 250 nm, t (major) = 14.060 min, t (minor) = 30.520 min. The enantiomers were detected by UV absorption (Fig. S1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.37 (s, 1H), 8.78 (p, *J* = 4.4 Hz, 1H), 8.66 (d, *J* = 4.5 Hz, 1H), 8.55 (d, *J* = 8.6 Hz, 1H), 8.29 (d, *J* = 7.9 Hz, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 7.88 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.58 (td, *J* = 7.7, 1.8 Hz, 1H), 7.51 (d, *J* = 4.5 Hz, 2H), 7.29 (dd, *J* = 8.3, 5.6 Hz, 1H), 5.85 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.33–5.22 (m, 1H), 5.17 (d, *J* = 17.1 Hz, 1H), 5.05 (d, *J* = 10.2 Hz, 1H), 3.26 (t, *J* = 8.5 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.8, 166.3, 155.5, 154.1, 149.2, 137.7, 137.2, 136.6, 134.4, 134.0, 133.4, 131.6, 127.9, 127.5, 124.0, 123.7, 121.9, 121.1, 119.5, 119.2, 117.0, 54.6, 33.0; **HRMS** calcd. for $C_{27}H_{21}N_4O_3^+$ [M+H]$^+$ 449.1608, found 449.1608.

Area % Report

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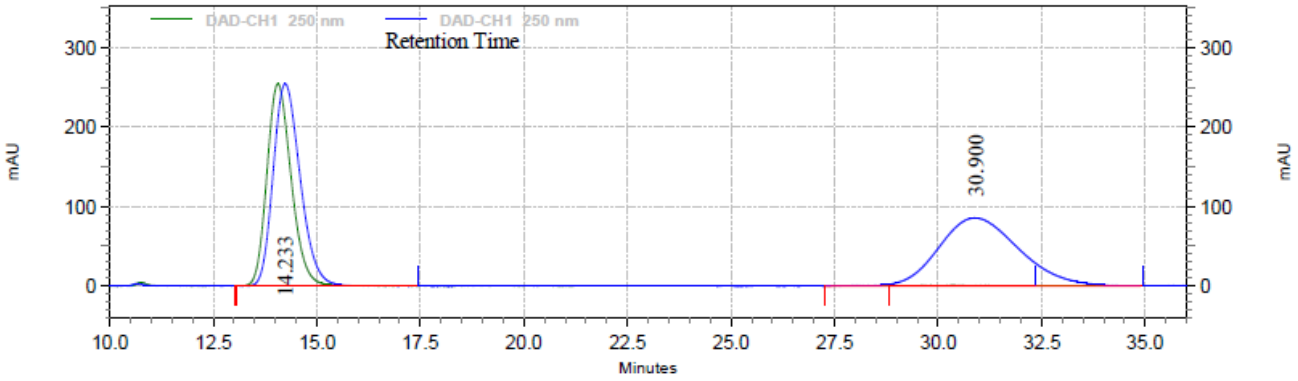
Printed: 6/5/2017 4:16:34 PM

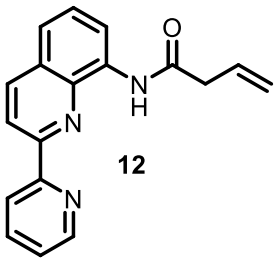


DAD-CH1 250 nm Results

Retention Time	Area	Area %	Height	Height %
14.060	41730151	99.50	1020380	99.81
30.520	209112	0.50	1986	0.19
Totals	41939263	100.00	1022366	100.00

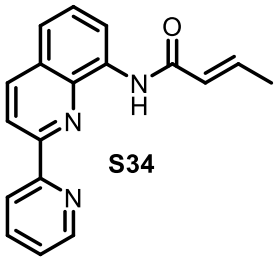
Figure S1. HPLC trace and report for *ee* determination of **3g**.

***N*-[2-(Pyridin-2-yl)quinolin-8-yl]but-3-enamide (12)**



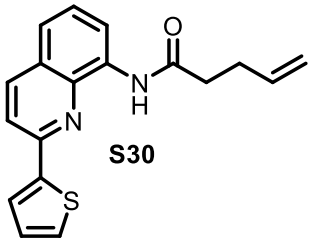
Synthesized from **S7** and but-3-enoic acid, following GP E (0.4 mmol scale). Purification by silica flash column chromatography (20–40% EtOAc/hexanes) afforded **12** (97 mg, 84%) as a pale-yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.81–8.71 (m, 2H), 8.63 (d, *J* = 8.6 Hz, 1H), 8.57 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 8.6 Hz, 1H), 7.88 (td, *J* = 7.7, 1.8 Hz, 1H), 7.55 (d, *J* = 1.2 Hz, 1H), 7.54 (s, 1H), 7.39 (ddd, *J* = 7.4, 4.8, 1.2 Hz, 1H), 6.26 (ddt, *J* = 17.1, 9.6, 7.3 Hz, 1H), 5.58–5.52 (m, 2H), 3.42 (d, *J* = 7.3 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.8, 155.7, 154.0, 149.4, 137.8, 137.3, 136.7, 134.4, 131.5, 128.0, 127.7, 124.2, 121.6, 121.3, 120.9, 119.4, 116.6, 43.5; **HRMS** calcd. for $C_{18}H_{16}N_3O^+$ $[M+H]^+$ 290.1288, found 290.1287.

(2*E*)-*N*-[2-(pyridin-2-yl)quinolin-8-yl]but-2-enamide (S34)



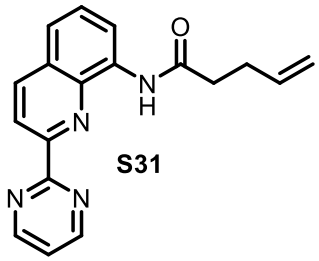
To a RB flask equipped with a magnetic stir bar was added **S7** (0.129g, 0.5 mmol), crotonic acid (0.215g, 2.5 mmol), HATU (0.950 g, 2.5 mmol), triethylamine (0.35 mL, 2.5 mmol), and THF (0.08 M). The reaction was stirred at room temperature overnight. The crude reaction mixture was diluted with EtOAc, washed with $NaHCO_{3(aq)}$ and brine, dried over Mg_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by silica flash column chromatography (20% EtOAc/hexanes) to afford **S34** (54 mg, 37%) as a pale-yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.84 (d, *J* = 7.2 Hz, 1H), 8.75 (d, *J* = 4.7 Hz, 1H), 8.59 (d, *J* = 8.6 Hz, 1H), 8.52 (d, *J* = 7.9 Hz, 1H), 8.25 (d, *J* = 8.6 Hz, 1H), 7.90 (t, *J* = 7.8 Hz, 1H), 7.62–7.45 (m, 2H), 7.42–7.31 (m, 1H), 7.10 (dq, *J* = 13.9, 6.8 Hz, 1H), 6.22 (d, *J* = 15.0 Hz, 1H), 2.00 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 164.0, 155.7, 154.0, 149.3, 141.4, 137.7, 137.3, 136.9, 134.7, 127.9, 127.7, 126.1, 124.2, 121.4, 121.3, 119.4, 116.9, 17.9; **HRMS** calcd. for $C_{18}H_{16}N_3O^+$ $[M+H]^+$ 290.1288, found 290.1289.

***N*-[2-(Thiophen-2-yl)quinolin-8-yl]pent-4-enamide (S30)**



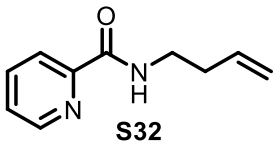
Synthesized from **S8** and pent-4-enoic acid, following GP E (0.86 mmol scale). Purification by silica flash column chromatography (60% ether/hexanes) afforded **S30** (201 mg, 79%) as a brown solid. **^{1}H NMR** (500 MHz, $(CD_3)_2CO$) δ 9.83 (s, 1H), 8.73 (d, *J* = 7.6 Hz, 1H), 8.37 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 8.6 Hz, 1H), 7.99 (d, *J* = 3.7 Hz, 1H), 7.70 (d, *J* = 5.0 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.24 (t, *J* = 4.4 Hz, 1H), 6.00 (ddt, *J* = 16.9, 10.3, 6.5 Hz, 1H), 5.18 (d, *J* = 17.2 Hz, 1H), 5.02 (d, *J* = 11.0 Hz, 1H), 2.74 (t, *J* = 7.4 Hz, 2H), 2.59 (q, *J* = 7.2 Hz, 2H); **^{13}C NMR** (150 MHz, $(CD_3)_2CO$) δ 171.0, 151.5, 145.6, 138.4, 138.4, 138.2, 135.4, 130.1, 129.4, 127.9, 127.7, 127.6, 122.1, 119.0, 117.4, 115.9, 37.8, 30.3; **HRMS** calcd. for $C_{18}H_{17}N_2OS^+$ $[M+H]^+$ 309.1056, found 309.1055.

***N*-[2-(Pyrimidin-2-yl)quinolin-8-yl]pent-4-enamide (S31)**



Synthesized from **S9** and 4-pentenoic acid following GP E (0.45 mmol scale). Purification by silica flash column chromatography (20% acetone/DCM) afforded **S31** (76 mg, 55 %) as a brown solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.44 (s, 1H), 8.89 (d, *J* = 4.6 Hz, 2H), 8.86 (d, *J* = 7.7 Hz, 1H), 8.56 (d, *J* = 8.5 Hz, 1H), 8.26 (d, *J* = 8.5 Hz, 1H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.31 (t, *J* = 4.8 Hz, 1H), 5.93 (ddt, *J* = 16.9, 10.4, 6.5 Hz, 1H), 5.14 (d, *J* = 17.1 Hz, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 2.84–2.76 (m, 2H), 2.56 (q, *J* = 7.7 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 171.8, 163.1, 157.5, 152.1, 138.4, 137.3, 137.3, 135.7, 128.6, 128.5, 121.2, 121.0, 120.7, 117.5, 115.4, 36.8, 29.4; **HRMS** calcd. for $C_{18}H_{17}N_4O^+$ $[M+H]^+$ 305.1397, found 305.1397.

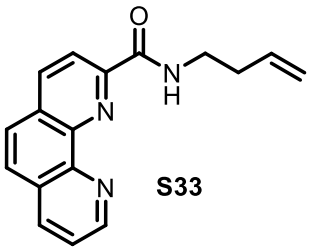
***N*-(But-3-en-1-yl)picolinamide (S32)**



The synthesis of **S32** was adapted from a literature procedure:[13] 3-Buten-1-amine hydrochloride (430 mg, 4.00 mmol) and 2-pyridinecarbonyl chloride hydrochloride (854 mg, 4.80 mmol) were charged into a 100 mL RB flask containing 20.0 mL of DCM. The suspension was cooled to 0 °C, and triethylamine was added dropwise. The reaction was allowed to warm to room temperature and was stirred at ambient temperature for 20 h. The reaction was quenched with water, and the solution was extracted with DCM (25 mL, ×3). The combined organic layers were washed with brine (50 mL, ×1) and purified by column chromatography (33–66% Et_2O in Hexanes) to

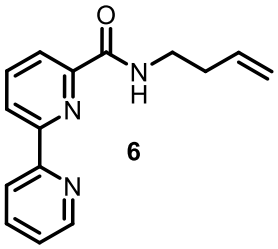
afford **S32** (535 mg, 76%) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.54 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.20 (dt, *J* = 7.8, 1.1 Hz, 1H), 8.11 (s, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 5.86 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.16 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.11 (dq, *J* = 10.2, 1.3 Hz, 1H), 3.56 (td, *J* = 6.9, 6.0 Hz, 2H), 2.40 (qt, *J* = 6.8, 1.4 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 164.4, 150.1, 148.2, 137.5, 135.4, 126.2, 122.3, 117.3, 38.7, 34.0; **HRMS** calcd. for $C_{10}H_{13}N_2O^+$ $[M+H]^+$ 177.10224, found 177.1023.

N-(But-3-en-1-yl)-1,10-phenanthroline-2-carboxamide (S33)



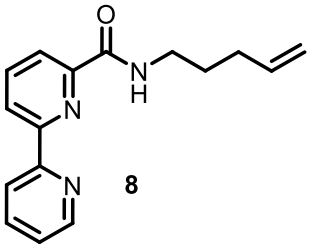
Synthesized from **S11** and but-3-en-1-amine hydrochloride, following GP E (1 mmol scale). Purification by silica flash column chromatography (80% EtOAc/hexanes to 5% MeOH/DCM) afforded **S33** (114 mg, 41%) as a pale-yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 9.15 (d, *J* = 4.4 Hz, 1H), 8.58 (d, *J* = 8.3 Hz, 1H), 8.40 (d, *J* = 8.3 Hz, 1H), 8.31 (d, *J* = 8.1 Hz, 1H), 7.86 (s, 2H), 7.69 (dd, *J* = 8.1, 4.4 Hz, 1H), 5.92 (ddt, *J* = 17.4, 10.2, 7.0 Hz, 1H), 5.17 (d, *J* = 17.1 Hz, 1H), 5.08 (d, *J* = 10.3 Hz, 1H), 3.66 (q, *J* = 6.9 Hz, 2H), 2.52 (q, *J* = 7.0, 6.6 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 164.7, 150.2, 149.6, 145.5, 144.1, 137.2, 136.7, 135.7, 129.9, 129.0, 127.6, 126.5, 123.4, 121.4, 116.4, 39.2, 33.8; **HRMS** calcd. for $C_{17}H_{16}N_3O^+$ $[M+H]^+$ 278.1288, found 278.1287.

N-(But-3-en-1-yl)[2,2'-bipyridine]-6-carboxamide (6)



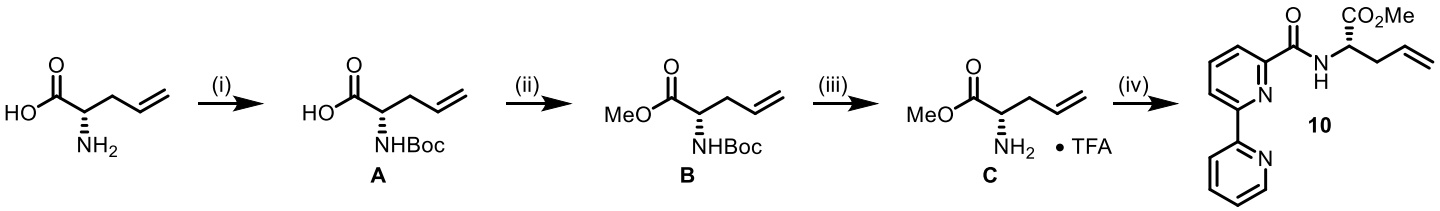
Synthesized from **S11** and but-3-en-1-amine, following GP E (1 mmol scale). Purification by silica flash column chromatography (20% EtOAc/hexanes) afforded **6** (269 mg, 81%) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.71 (ddt, *J* = 4.8, 1.7, 0.8 Hz, 1H), 8.56 (dt, *J* = 7.9, 0.9 Hz, 1H), 8.36 (dq, *J* = 7.9, 0.9 Hz, 1H), 8.23 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.98 (td, *J* = 7.8, 0.7 Hz, 1H), 7.89–7.81 (m, 1H), 7.36 (ddt, *J* = 7.4, 4.7, 0.9 Hz, 1H), 5.97–5.86 (m, 1H), 5.23 (ddd, *J* = 17.1, 1.9, 0.7 Hz, 1H), 5.18 (ddd, *J* = 10.2, 1.9, 0.9 Hz, 1H), 3.61 (q, *J* = 6.3 Hz, 2H), 2.46 (q, *J* = 6.8 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 164.2, 155.2, 154.6, 149.4, 149.3, 138.4, 136.9, 135.5, 124.1, 123.5, 122.2, 120.8, 117.3, 38.3, 33.9; **HRMS** calcd. for $C_{15}H_{16}N_3O^+$ $[M+H]^+$ 254.1288, found 254.1286.

N-(Pent-4-en-1-yl)[2,2'-bipyridine]-6-carboxamide (8)



Synthesized from **S12** and pent-4-en-1-amine, following GP E (1 mmol scale). Purification by silica flash column chromatography (40% acetone/hexanes) afforded **8** (220 mg, 82%) as an off-white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 5.0 Hz, 1H), 8.54 (d, *J* = 7.6 Hz, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 8.28 (t, *J* = 6.2 Hz, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 7.93 (t, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.8, 1.8 Hz, 1H), 7.31 (dd, *J* = 7.3, 5.0 Hz, 1H), 5.86 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.08 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.01 (d, *J* = 10.1 Hz, 1H), 3.54 (q, *J* = 6.9 Hz, 2H), 2.19 (q, *J* = 7.2 Hz, 2H), 1.79 (p, *J* = 7.3 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 164.2, 155.0, 154.6, 149.4, 149.3, 138.3, 137.8, 136.9, 124.1, 123.5, 122.2, 120.9, 115.2, 39.0, 31.2, 28.9; **HRMS** calcd. for $C_{16}H_{18}N_3O^+$ $[M+H]^+$ 268.1444, found 268.1443.

Synthesis of (*S*)-2-([2,2'-bipyridine]-6-carboxamido)pent-4-enoate (10)



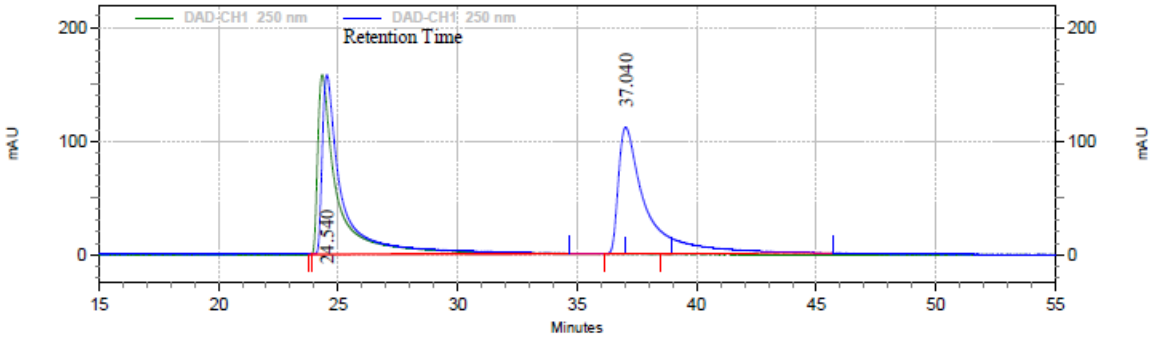
(i) Boc_2O, Na_2CO_3, H_2O/THF, 0 °C to rt, 16 h; (ii) MeI, K_2CO_3, DMF, rt, 16 h; (iii) TFA, DCM, rt, 30 min; (iv) **S12**, HATU, py, DCM, rt, 16 h.

Compound **10** was synthesized following a modified literature procedure:[12] To a solution of L-allylglycine (576 mg, 5 mmol) in THF/H_2O (10:1, 11 mL) at 0 °C were added Boc_2O (1.20 g, 5.5 mmol) and Na_2CO_3 (1.06 g, 10 mmol). The reaction was allowed to warm to room temperature and stirred for 16 h, after which the reaction mixture was acidified to pH 2 with 2M HCl and extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed *in vacuo* to afford crude (*S*)-2-((*tert*-butoxycarbonyl)amino)pent-4-enoic acid **A** (1.07 g, 99%) as a colourless oil. Crude **A** (1.07 g, 4.79 mmol) was re-dissolved in DMF (7.3 mL), to

which MeI (0.46 mL, 7.46 mmol) and K_2CO_3 (756 mg, 5.47 mmol) were added. The reaction mixture was stirred at room temperature for 16 h. The reaction was diluted with H_2O and extracted with EtOAc. The combined organic layers were washed with H_2O, brine, dried over $MgSO_4$ and evaporated *in vacuo* to give crude methyl (*S*)-2-((*tert*-butoxycarbonyl)amino)pent-4-enoate **B** (900 mg, 79%) as a pale-yellow oil which was re-dissolved in DCM (2 mL). TFA (2 mL) was added to the reaction mixture, which was then stirred at room temperature for 30 minutes. The solvent was removed *in vacuo* (TFA was removed by co-evaporation with toluene) to yield crude methyl (*S*)-2-aminopent-4-enoate as its trifluoroacetate salt **C** (158 mg, 17%) as a yellow oil. Crude **C** (158 mg, 0.65 mmol) was subjected to GP E for amide coupling with **S12** (156 mg, 0.78 mmol). Purification by preparative TLC (2× 2% MeOH/DCM) afforded **10** (82 mg, 5% yield over 4 steps, >99% *ee*) as a pale-yellow oil. The racemic standard was synthesized following the same procedure (55 mg, 5% yield over 4 steps). The enantiomeric excess of **10** was determined by chiral SFC on a Daicel Chiralpak IC column (0.46 cm × 25 cm), Hexanes / IPA = 85 / 15, 1.0 mL/min, λ = 250 nm, t (major) = 24.340 min, t (minor) = 38.673 min. The enantiomers were detected by UV absorption (Fig. S2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.67 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 8.65 (brs, 1H), 8.58 (dd, *J* = 7.9, 1.1 Hz, 1H), 8.39 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.18 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.96 (t, *J* = 7.8 Hz, 1H), 7.84 (td, *J* = 7.7, 1.8 Hz, 1H), 7.33 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 5.82 (ddt, *J* = 17.3, 10.1, 7.2 Hz, 1H), 5.24–5.15 (m, 2H), 4.89 (dt, *J* = 8.0, 5.8 Hz, 1H), 3.79 (s, 3H), 2.88–2.60 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.2, 164.0, 155.1, 154.9, 149.4, 148.8, 138.5, 137.1, 132.5, 124.3, 123.9, 122.4, 121.0, 119.4, 52.6, 51.8, 36.8; **HRMS** calc. for $C_{17}H_{18}N_3O_3$ $[M+H]^+$ 312.1348, found 312.1348.

Area % Report

Data File: C:\ENGLE LAB DATA\dwgao\4\MOD-4-56-chiral-IC-0.15-1.0.dat
Method: C:\ENGLE LAB DATA\dwgao\METHOD\15% 1.0 70 min.met
Acquired: 6/16/2017 5:59:09 PM
Printed: 6/16/2017 9:00:25 PM



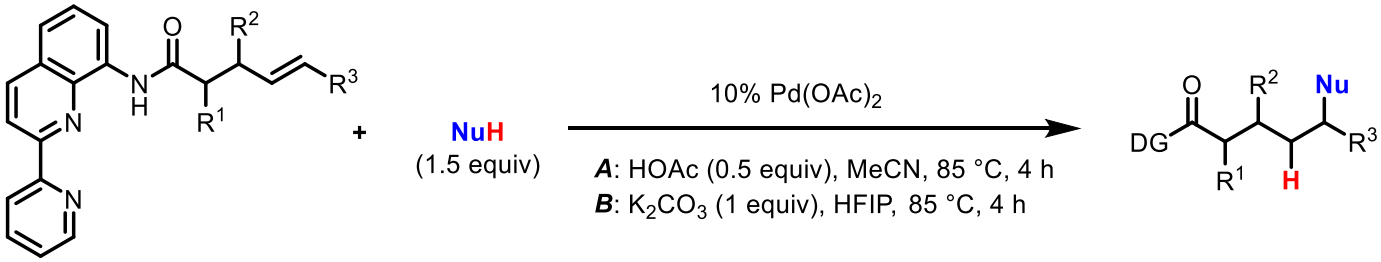
DAD-CH1 250 nm Results

Retention Time	Area	Area %	Height	Height %
24.340	37858431	99.99	632385	99.93
38.673	5422	0.01	422	0.07
Totals	37863853	100.00	632807	100.00

Figure S2. HPLC trace and report for *ee* determination of **10**.

Hydrofunctionalization of Alkenes

General Procedure for the Hydrofunctionalization of Alkenes

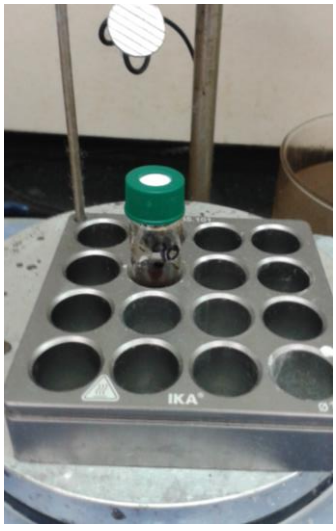


Conditions A: To a 1 dram (4 mL) vial equipped with a magnetic stir bar were added $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), alkene (0.1 mmol), acetic acid (3.0 µL, 0.05 mmol), carbon nucleophile (0.15 mmol) and MeCN (0.05 mL, 2M). The vial was sealed with an unpunctured TFE septum-covered screw cap, and placed in a heating block that was pre-heated to 85 °C. After 4 h, the reaction was purified by silica flash column chromatography directly (without aqueous workup) to afford pure product. ^{1}H NMR yields were determined by adding 1,3,5-triisopropylbenzene (8 µL, 0.33 equiv) to the crude sample and integrating the product peak(s) relative to this internal standard before isolation. **Note**: The reactions work best at high concentration (2M) with a large headspace in the reaction vessel (see photo below). This should be considered especially when scaling up (see page S31 for scale-up procedure of **4a**). Solubility profile and reaction color vary widely depending on the nucleophile (and reaction solvent) used. **Conditions B:** As conditions **A**, but using K_2CO_3 (13.8 mg, 0.1 mmol) and HFIP (0.05 mL) with a reaction time of 24 h. **Conditions C:** As conditions **A**, but at 120 °C for 24 h. **Conditions D:** As conditions **B**, but at 120 °C for 24 h. **Note:** For substrates that gave only moderate yields, the major by-product observed was usually isomerized starting material **V**.

Photo Reel of Reaction Set-Up

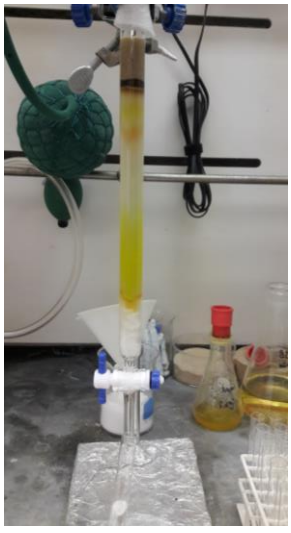
Solid reagents in 1 dram vial

Addition of HOAc and MeCN



Reaction in 85 °C heating block

Crude reaction after 4 h

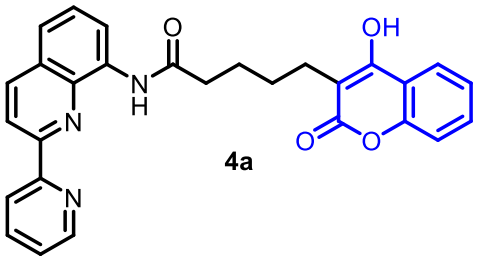


Purification

Hydrofunctionalization of Carboxylic Acid Substrates

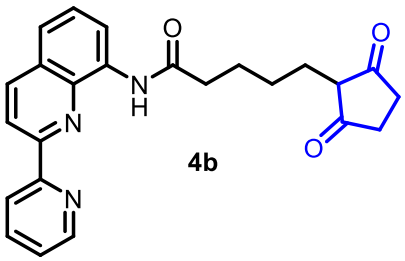
Investigation of Nucleophile Scope

5-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4a)



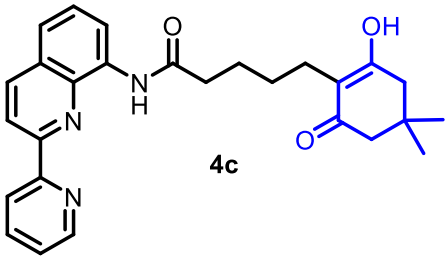
Synthesized following conditions A, from alkene **3a** (30.3 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4a** (44.2 mg, 95% yield) as a pale-yellow solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 11.29 (brs, 1H, –O*H*), 10.08 (s, 1H, –N*H*), 8.88 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.74 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.67–8.58 (m, 2H), 8.51 (d, *J* = 8.6 Hz, 1H), 8.00 (td, *J* = 7.7, 1.8 Hz, 1H), 7.89 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.69 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.63–7.55 (m, 2H), 7.50 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 7.37–7.28 (m, 2H), 2.70 (t, *J* = 7.4 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 1.77 (p, *J* = 7.5 Hz, 2H), 1.68–1.56 (m, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.8, 163.0, 159.9, 154.8, 154.0, 151.9, 149.3, 137.8, 137.8, 137.5, 134.8, 131.6, 128.0, 127.5, 124.9, 123.9, 123.2, 122.0, 121.8, 119.1, 117.5, 116.4, 116.2, 105.0, 37.0, 27.8, 25.3, 23.6; **HRMS** calc. for $C_{28}H_{24}N_3O_4^+$ [M+H]$^+$ 466.1767, found 466.1766; **X-ray** (single-crystal) colorless blocks of X-ray diffraction quality crashed out of a saturated solution of **4a** in DMSO-d_6 (CCDC 1567386).[14]

5-(2,5-Dioxocyclopentyl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4b)



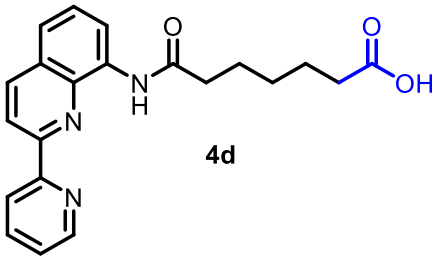
Synthesized following conditions A, from alkene **3a** (30.3 mg) and 1,3-cyclopentanedione (14.7 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4b-keto** (19.8 mg, 49% yield) and **4b-enol** (10.5 mg, 26% yield) as off-white solids (combined yield: 75%, keto/enol = 1.88). **Keto**: **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.99 (s, 1H), 9.00 (d, *J* = 7.9 Hz, 1H), 8.76 (dt, *J* = 4.5, 1.4 Hz, 1H), 8.70–8.60 (m, 2H), 8.52 (d, *J* = 8.6 Hz, 1H), 8.11 (td, *J* = 7.7, 1.8 Hz, 1H), 7.68 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.62–7.49 (m, 2H), 3.67 (t, *J* = 8.0 Hz, 1H), 3.17 (d, *J* = 3.3 Hz, 2H), 2.55 (t, *J* = 7.6 Hz, 2H), 2.10 (s, 4H), 1.57 (q, *J* = 7.8 Hz, 2H), 1.46 (q, *J* = 7.7 Hz, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 172.0, 154.7, 153.9, 149.2, 137.7, 137.6, 137.5, 134.7, 127.8, 127.4, 124.8, 122.2, 121.5, 118.9, 117.3, 117.0, 48.6, 40.1, 37.1, 31.6, 24.3, 24.2; **HRMS** calc. for $C_{24}H_{24}N_3O_3^+$ [M+H]$^+$ 402.1818, found 402.1820. **Enol**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.20 (s, 1H), 8.98 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.82–8.74 (m, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 8.6 Hz, 1H), 8.06 (td, *J* = 7.8, 1.7 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.56 (ddd, *J* = 8.1, 4.1, 1.0 Hz, 2H), 2.76–2.65 (m, 2H), 2.46–2.43 (m, 2H), 2.41 (t, *J* = 6.3 Hz, 2H), 2.38–2.30 (m, 2H), 1.75 (td, *J* = 10.8, 6.6 Hz, 2H), 1.72–1.66 (m, 2H).

5-(2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4c)



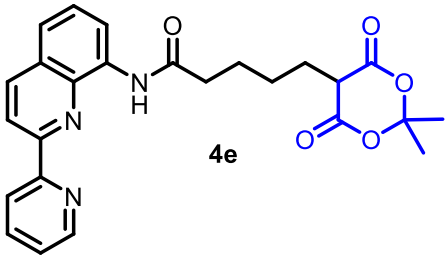
Synthesized following conditions A, from alkene **3a** (30.3 mg) and 5,5-dimethyl-1,3-cyclohexanedione (21.0 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4c-enol** (29.2 mg, 66% yield) and **4c-keto** (10.2 mg, 23% yield) as off-white solids (combined yield: 89%, enol/keto = 2.9). **Enol**: **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.90 (d, *J* = 7.9 Hz, 1H), 8.76 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.67–8.61 (m, 2H), 8.51 (d, *J* = 8.6 Hz, 1H), 8.06 (td, *J* = 7.7, 1.8 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.55 (dd, *J* = 7.5, 4.8 Hz, 1H), 3.07 (d, *J* = 13.7 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.22 (d, *J* = 13.6 Hz, 2H), 2.02–1.87 (m, 2H), 1.67 (p, *J* = 7.6 Hz, 2H), 1.39–1.24 (m, 2H), 1.07 (s, 3H), 0.68 (s, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 207.3, 171.5, 154.7, 153.9, 149.3, 137.7, 137.6, 137.5, 134.7, 127.8, 127.4, 124.8, 122.0, 121.7, 119.0, 117.3, 109.5, 89.1, 50.8, 37.7, 36.6, 30.8, 29.3, 26.1, 25.0, 22.5; **HRMS** calc. for $C_{27}H_{30}N_3O_3^+$ [M+H]$^+$ 444.2287, found 444.2287. **Keto**: **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.91 (d, *J* = 7.9 Hz, 1H), 8.76 (dd, *J* = 4.9, 1.9 Hz, 1H), 8.66–8.61 (m, 2H), 8.52 (d, *J* = 8.6 Hz, 1H), 8.05 (td, *J* = 7.7, 1.8 Hz, 1H), 7.69 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.55 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 2.64 (t, *J* = 7.4 Hz, 2H), 2.28–2.19 (m, 2H), 2.19–2.12 (m, 4H), 1.65 (p, *J* = 7.5 Hz, 2H), 1.45–1.37 (m, 2H), 0.93 (s, 6H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 207.3, 171.8, 154.7, 153.8, 149.3, 149.3, 137.7, 137.6, 137.5, 127.8, 127.4, 124.8, 122.0, 121.6, 119.0, 117.2, 112.9, 89.1, 50.8, 37.0, 31.5, 30.7, 28.1, 28.0, 25.4, 21.2.

2-(5-Oxo-5-((2-(pyridin-2-yl)quinolin-8-yl)amino)pentyl)malonic acid (4d)



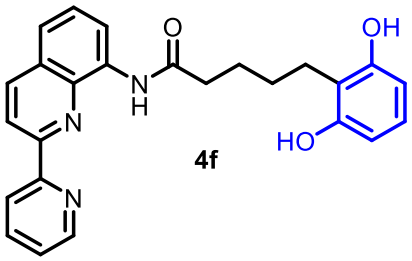
Synthesized following conditions A, from alkene **3a** (30.3 mg) and Meldrum's acid (21.6 mg). *In situ* hydrolysis/decarboxylation affords **4d** (24.3 mg, 67% yield) as a brown solid after purification by silica flash column chromatography (eluent: 5% MeOH/DCM to 10% MeOH/DCM). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.08 (s, 1H), 8.89 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.76 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.67–8.57 (m, 2H), 8.51 (d, *J* = 8.6 Hz, 1H), 8.06 (td, *J* = 7.7, 1.8 Hz, 1H), 7.69 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.54 (ddd, *J* = 7.4, 4.7, 1.2 Hz, 1H), 2.67 (t, *J* = 7.4 Hz, 2H), 2.23 (t, *J* = 7.4 Hz, 2H), 1.72 (p, *J* = 7.6 Hz, 2H), 1.59 (p, *J* = 7.5 Hz, 2H), 1.46–1.36 (m, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 174.5, 172.5, 171.6, 171.4, 154.7, 153.8, 149.3, 137.6, 137.4, 134.7, 127.8, 127.4, 124.8, 121.9, 121.6, 118.9, 117.3, 36.6, 33.6, 28.2, 24.9, 24.4; **HRMS** calc. for $C_{21}H_{22}N_3O_3^+$ $[M+H]^+$ 364.1661, found: 364.1663.

5-(6-Hydroxy-2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-5-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4e)



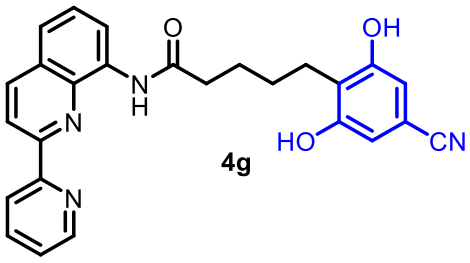
Synthesized following conditions B, from alkene **3a** (30.3 mg) and Meldrum's acid (21.6 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM to 5% MeOH/DCM) afforded **4e** (17.8 mg, 40% yield) as a brown solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.04 (s, 1H, –N*H*), 8.84 (d, *J* = 8.0 Hz, 1H), 8.73 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.61–8.56 (m, 2H), 8.47 (d, *J* = 8.6 Hz, 1H), 8.06 (td, *J* = 7.7, 1.8 Hz, 1H), 7.65 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.51 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.02 (t, *J* = 7.5 Hz, 2H), 1.66–1.72 (m, 7H), 1.55 (p, *J* = 7.5 Hz, 2H), 1.37 (tt, *J* = 9.9, 6.4 Hz, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 176.5, 171.6, 154.7, 153.8, 149.2, 137.6, 137.5, 137.5, 134.6, 127.8, 127.3, 124.8, 121.8, 121.6, 118.9, 117.2, 37.1, 36.9, 28.9, 26.0, 25.8, 25.3, 24.4; **HRMS** calc. for $C_{25}H_{26}N_3O_5^+$ $[M+H]^+$ 448.1872, not found; hydrolyzed/decarboxylated product (**4d**): calc. for $C_{21}H_{22}N_3O_3^+$ $[M+H]^+$ 364.1661, found: 364.1662.

5-(2,6-Dihydroxyphenyl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4f)



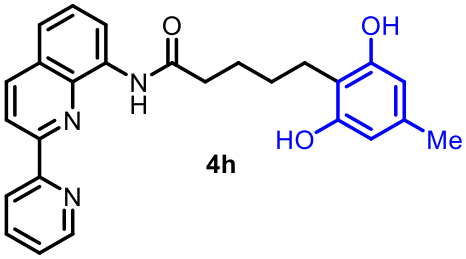
Synthesized following conditions B, from alkene **3a** (30.3 mg) and resorcinol (16.5 mg). Purification by silica flash column chromatography (eluent: 60% EtOAc/Hex) afforded **4f** (26.3 mg, 64% yield) as a pale-yellow solid. Conditions A afforded 6.5 mg (16% yield) of the desired product. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.08 (s, 1H), 9.02 (s, 1H), 8.92–8.86 (m, 2H), 8.77 (ddd, J = 4.7, 1.8, 0.9 Hz, 1H), 8.64–8.62 (m, 2H), 8.52 (d, J = 8.7 Hz, 1H), 8.04 (d, J = 8.7 Hz, 1H), 7.70 (dd, J = 8.3, 1.3 Hz, 1H), 7.59 (t, J = 7.9 Hz, 1H), 7.54 (ddd, J = 7.4, 4.7, 1.1 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 6.24 (d, J = 2.4 Hz, 1H), 6.08 (dd, J = 8.1, 2.4 Hz, 1H), 2.68 (t, J = 7.5 Hz, 2H), 2.48 (t, J = 7.5 Hz, 2H), 1.72 (p, J = 7.5 Hz, 2H), 1.61 (p, J = 7.5, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.7, 156.1, 155.7, 154.7, 153.9, 149.3, 137.7, 137.6, 137.4, 134.7, 129.9, 127.8, 127.4, 124.8, 121.9, 121.6, 119.0, 118.6, 117.3, 105.8, 102.4, 36.8, 29.4, 28.8, 25.1; **HRMS** calc. for $C_{25}H_{24}N_3O_3^+$ $[M+H]^+$ 414.1818, found 414.1820.

5-(4-Cyano-2,6-dihydroxyphenyl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4g)



Synthesized following conditions B, from alkene **3a** (30.3 mg) and 4-cyanoresorcinol (20.3 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4g** (22.1 mg, 50% yield) as an off-white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.05 (s, 1H), 9.68 (s, 1H), 8.85 (d, *J* = 8.0 Hz, 1H), 8.73 (dt, *J* = 4.6, 1.5 Hz, 1H), 8.65–8.57 (m, 2H), 8.48 (d, *J* = 8.6 Hz, 1H), 7.99 (td, *J* = 7.7, 1.8 Hz, 1H), 7.66 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.51 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 2.77–2.61 (m, 4H), 1.74 (p, *J* = 7.5 Hz, 2H), 1.64 (dt, *J* = 10.8, 6.7 Hz, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.5, 154.7, 154.1, 153.8, 149.2, 137.6, 137.6, 137.3, 134.7, 127.8, 127.4, 124.7, 122.5, 121.9, 121.6, 118.9, 117.6, 117.3, 112.9, 107.1, 36.8, 29.3, 27.8, 25.1; **HRMS** calc. for $C_{26}H_{23}N_4O_3^+$ $[M+H]^+$ 439.1770, found 439.1771.

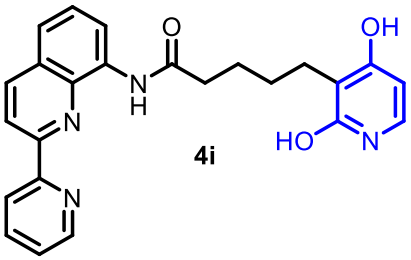
5-(2,6-Dihydroxy-4-methylphenyl)-N-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4h)



4h

Synthesized following conditions B, from alkene **3a** (30.3 mg) and 3,5-dihydroxytoluene (18.6 mg). Purification by silica flash column chromatography (eluent: 2% MeOH/DCM) afforded **4h** (19.7 mg, 46% yield) as an off-white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.86 (d, *J* = 10.4 Hz, 3H), 8.76 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.67–8.58 (m, 2H), 8.51 (d, *J* = 8.6 Hz, 1H), 8.02 (td, *J* = 7.7, 1.8 Hz, 1H), 7.68 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.54 (ddd, *J* = 7.6, 4.7, 1.1 Hz, 1H), 3.34 (s, 3H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.54 (t, *J* = 7.4 Hz, 2H), 2.05 (s, 3H), 1.72 (p, *J* = 7.6 Hz, 2H), 1.63–1.50 (m, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.8, 156.0, 154.7, 153.8, 149.2, 137.6, 137.6, 137.5, 135.0, 134.7, 127.8, 127.4, 124.8, 121.9, 121.6, 119.0, 117.2, 111.8, 107.0, 37.1, 28.6, 25.4, 22.4, 21.0; **HRMS** calc. for $C_{26}H_{25}N_3O_3^+$ $[M+H]^+$ 427.1896, found 427.1899.

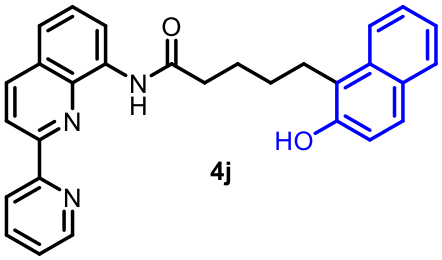
5-(2,4-Dihydroxypyridin-3-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4i)



4i

Synthesized following conditions B, from alkene **3a** (30.3 mg) and pyridine-2,4-diol (21.0 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4i** (18.2 mg, 44% yield) as an off-white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.86 (s, 1H), 10.08 (s, 1H), 10.04 (s, 1H), 8.90 (d, *J* = 8.0 Hz, 1H), 8.76 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.67–8.58 (m, 2H), 8.52 (d, *J* = 8.6 Hz, 1H), 8.05 (td, *J* = 7.7, 1.8 Hz, 1H), 7.69 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.54 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 5.87 (d, *J* = 7.2 Hz, 1H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.42 (t, *J* = 7.5 Hz, 2H), 1.71 (p, *J* = 7.6 Hz, 2H), 1.60–1.49 (m, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.8, 164.1, 162.6, 154.7, 153.8, 149.2, 137.6, 137.6, 137.5, 134.7, 132.2, 127.8, 127.4, 124.8, 121.9, 121.6, 118.9, 117.3, 111.0, 99.0, 37.0, 27.5, 25.4, 22.5; **HRMS** calc. for $C_{24}H_{23}N_4O_3^+$ $[M+H]^+$ 415.1770, found 415.1771.

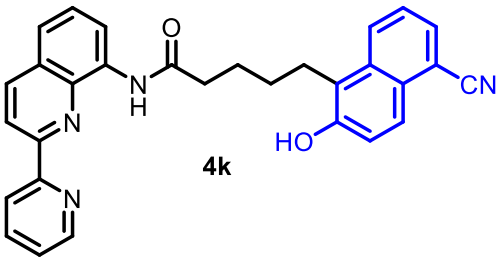
5-(2-Hydroxynaphthalen-1-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4j)



4j

Synthesized following conditions B, from alkene **3a** (30.3 mg) and 2-naphthol (21.6 mg). Purification by silica flash column chromatography (eluent: 40% EtOAc/Hex) afforded **4j** (41.8 mg, 93% yield) as an off-white solid. Conditions A afforded 3% of the desired product by ^{1}H NMR. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.91 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.74–8.62 (m, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 8.18 (d, *J* = 8.1 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 8.06–7.87 (m, 2H), 7.68 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.62–7.51 (m, 2H), 7.49–7.35 (m, 3H), 7.30–7.20 (m, 1H), 7.03 (d, *J* = 8.8 Hz, 1H), 3.38 (t, *J* = 6.5 Hz, 2H), 3.04–2.63 (m, 2H), 2.07–1.89 (m, 2H), 1.85–1.68 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 174.2, 155.2, 153.3, 152.6, 149.5, 138.9, 138.4, 137.9, 136.1, 133.5, 129.0, 128.6, 128.5, 127.9, 127.3, 126.1, 124.6, 123.1, 123.0, 122.5, 121.1, 120.0, 119.3, 118.3, 117.8, 37.9, 28.4, 25.5, 22.1; **HRMS** calc. for $C_{29}H_{26}N_3O_2^+$ $[M+H]^+$ 448.2025, found 448.2024.

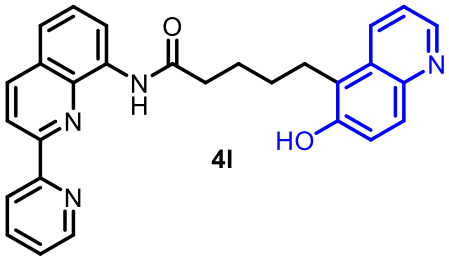
5-(5-Cyano-2-hydroxynaphthalen-1-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4k)



4k

Synthesized following conditions B, from alkene **3a** (30.3 mg) and 6-hydroxynaphthalene-1-carbonitrile (25.4 mg). Purification by silica flash column chromatography (eluent: 40% EtOAc/Hex to 60% EtOAc/Hex) afforded **4k** (35.0 mg, 74% yield) as a white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.08 (s, 1H), 8.84 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.75 (dt, *J* = 4.8, 1.2 Hz, 1H), 8.65–8.56 (m, 2H), 8.50 (d, *J* = 8.6 Hz, 1H), 8.34 (d, *J* = 1.8 Hz, 1H), 8.01 (d, *J* = 8.9 Hz, 1H), 7.96 (td, *J* = 7.7, 1.8 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.68 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.55–7.47 (m, 2H), 7.28 (d, *J* = 8.8 Hz, 1H), 3.05 (t, *J* = 7.7 Hz, 2H), 2.72 (t, *J* = 7.4 Hz, 2H), 1.85 (p, *J* = 7.5 Hz, 2H), 1.76–1.61 (m, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.7, 155.3, 154.7, 153.8, 149.2, 137.6, 137.4, 134.7, 134.7, 134.7, 128.2, 127.8, 127.4, 127.0, 126.2, 124.8, 124.0, 121.9, 121.7, 120.2, 119.7, 119.6, 119.0, 117.4, 104.1, 36.8, 29.0, 25.5, 24.1; **HRMS** calc. for $C_{30}H_{25}N_4O_2^+$ $[M+H]^+$473.1978, found 473.1980.

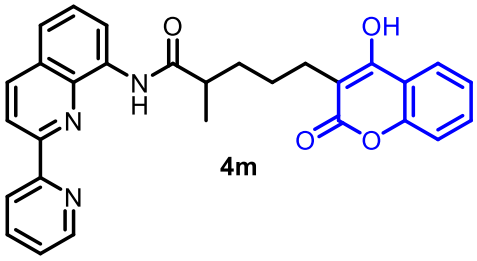
5-(6-Hydroxyquinolin-5-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4l)



Synthesized following conditions B, from alkene **3a** (30.3 mg) and 5-hydroxyquinoline (21.8 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4l** (36.7 mg, 82% yield) as a brown solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.10 (s, 1H), 8.87 (d, *J* = 8.0 Hz, 1H), 8.74 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.66–8.58 (m, 3H), 8.51 (d, *J* = 8.6 Hz, 1H), 8.30 (ddd, *J* = 8.6, 1.6, 0.8 Hz, 1H), 7.98 (td, *J* = 7.7, 1.8 Hz, 1H), 7.73–7.65 (m, 2H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.51 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 7.44 (d, *J* = 9.1 Hz, 1H), 7.29 (dd, *J* = 8.6, 4.1 Hz, 1H), 3.09–2.98 (m, 2H), 2.73 (t, *J* = 7.4 Hz, 2H), 1.85 (p, *J* = 7.5 Hz, 2H), 1.75–1.62 (m, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.7, 154.7, 153.8, 152.7, 149.2, 146.2, 143.3, 137.6, 137.6, 137.4, 134.7, 130.8, 127.9, 127.9, 127.8, 127.4, 124.8, 121.9, 121.7, 121.4, 120.8, 119.4, 119.0, 117.3, 36.8, 29.2, 25.4, 24.0; **HRMS** calc. for $C_{28}H_{25}N_4O_2^+$ $[M+H]^+$ 449.1978, found 449.1977.

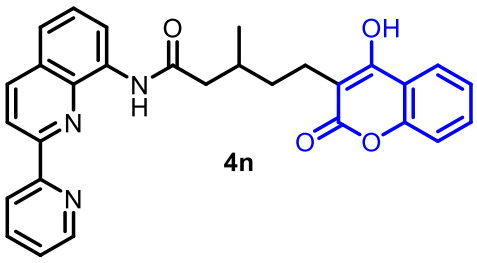
Investigation of Alkene Scope

5-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-methyl-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4m)



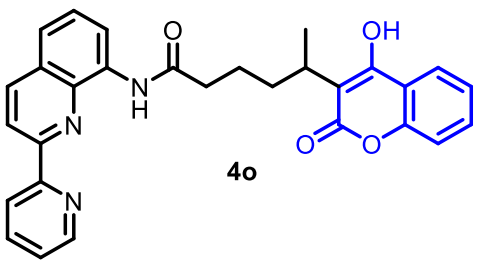
Synthesised following conditions A, from alkene **3b** (31.7 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4m** (43.5 mg, 91% yield) as a pale-yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.43 (s, 1H), 8.84 (t, *J* = 4.5 Hz, 1H), 8.72–8.58 (m, 1H), 8.45 (d, *J* = 8.6 Hz, 1H), 8.37 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 7.97 (td, *J* = 7.7, 1.8 Hz, 1H), 7.74 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.61–7.53 (m, 2H), 7.49–7.35 (m, 2H), 7.30–7.17 (m, 1H), 7.04 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1H), 3.08–2.99 (m, 1H), 2.94–2.84 (m, 1H), 2.71 (ddd, *J* = 13.7, 6.8, 5.3 Hz, 1H), 1.92–1.80 (m, 2H), 1.80–1.69 (m, 2H), 1.42 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.8, 164.3, 161.5, 155.3, 153.6, 152.6, 149.3, 138.4, 138.0, 137.9, 134.7, 131.1, 128.2, 128.0, 124.7, 123.5, 123.5, 122.2, 122.0, 119.7, 117.7, 116.8, 116.5, 105.9, 41.3, 32.7, 25.1, 22.4, 17.6; **HRMS** calc. for $C_{29}H_{26}N_3O_4^+$ $[M+H]^+$ 480.1923, found 480.1923.

5-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-3-methyl-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4n)



Synthesized following conditions A, from alkene **3c** (31.7 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4n** (42.6 mg, 89% yield) as a pale-yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.25 (s, 1H), 8.82 (t, *J* = 4.5 Hz, 1H), 8.67 (d, *J* = 6.5 Hz, 1H), 8.50 (d, *J* = 8.5 Hz, 1H), 8.40 (d, *J* = 7.9 Hz, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 7.95 (td, *J* = 7.7, 1.8 Hz, 1H), 7.84 (d, *J* = 6.4 Hz, 1H), 7.58 (d, *J* = 4.6 Hz, 2H), 7.50–7.35 (m, 2H), 7.30–7.20 (m, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 2.92–2.77 (m, 3H), 2.69 (dd, *J* = 13.4, 6.6 Hz, 1H), 2.22–2.09 (m, 1H), 1.89–1.78 (m, 1H), 1.66–1.52 (m, 1H), 1.19 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.5, 164.3, 161.3, 155.4, 153.9, 152.6, 149.3, 138.2, 137.8, 137.7, 134.4, 131.2, 128.1, 128.0, 124.6, 123.6, 123.6, 122.2, 122.0, 119.8, 117.9, 116.8, 116.5, 105.9, 43.9, 34.4, 30.9, 21.8, 21.4; **HRMS** calc. for $C_{29}H_{26}N_3O_4^+$ $[M+H]^+$ 480.1923, found 480.1925.

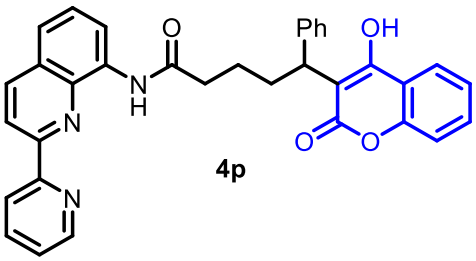
5-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)hexanamide (4o)



Synthesized following conditions A, from alkene **3d** (31.8 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 0.5% MeOH/DCM) afforded **4o** (30.1 mg, 63% yield from ***E*-3d**; 30.0 mg, 63% yield from ***Z*-3d**) as a pale-yellow solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.05 (s, 1H), 8.86 (d, *J* = 8.0 Hz, 1H), 8.75 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.62 (d, *J* = 8.6 Hz, 1H), 8.60 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.50 (d, *J* = 8.7 Hz, 1H), 8.02 (td, *J* = 7.7, 1.8 Hz, 1H), 7.93 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.68 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.62–7.47 (m, 3H), 7.40–7.09 (m, 2H),

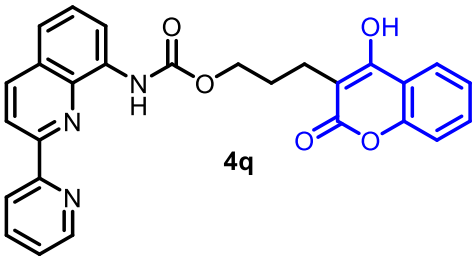
3.35–3.26 (m, 2H), 2.70–2.56 (m, 2H), 2.03–1.94 (m, 1H), 1.76–1.65 (m, 2H), 1.25 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.6, 161.4, 159.9, 154.7, 153.8, 152.0, 149.2, 137.6, 137.6, 137.4, 134.6, 131.5, 127.8, 127.4, 124.8, 123.6, 123.2, 121.8, 121.6, 118.9, 117.3, 116.2, 115.9, 108.6, 37.0, 33.0, 29.5, 24.0, 18.3; **HRMS** calc. for $C_{29}H_{26}N_3O_4^+$ $[M+H]^+$ 480.1923, found 480.1924.

5-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-5-phenyl-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4p)



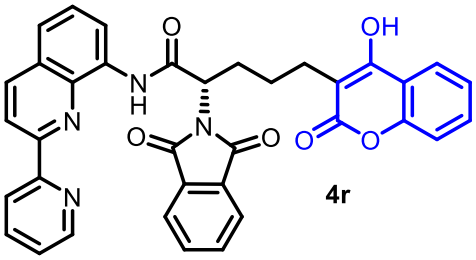
Synthesized following conditions A, from alkene **3e** (37.9 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **4p** (17.0 mg, 31% yield) as a white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.87 (dt, *J* = 8.0, 1.0 Hz, 1H), 8.76 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.67 – 8.56 (m, 2H), 8.50 (d, *J* = 8.7 Hz, 1H), 8.01 (td, *J* = 7.7, 1.8 Hz, 1H), 7.99 (dd, *J* = 8.0, 1.3 Hz, 2H), 7.68 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.55 – 7.50 (m, 1H), 7.42 – 7.37 (m, 2H), 7.32 (ddd, *J* = 8.3, 7.3, 1.1 Hz, 1H), 7.30 – 7.28 (m, 1H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.15 – 7.08 (m, 1H), 4.53 (dd, *J* = 9.3, 6.3 Hz, 1H), 2.74 (td, *J* = 7.5, 3.5 Hz, 2H), 2.44 (dtd, *J* = 13.1, 10.0, 5.2 Hz, 1H), 2.29 – 2.21 (m, 1H), 1.80 – 1.65 (m, 2H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 171.6, 171.5, 161.5, 160.5, 154.7, 153.8, 152.1, 149.2, 143.4, 137.6, 137.4, 134.5, 131.8, 127.9, 127.8, 127.7, 127.4, 125.8, 124.8, 123.7, 123.3, 121.9, 121.6, 118.9, 117.2, 116.1, 116.0, 107.7, 36.9, 30.7, 30.0, 24.1; **HRMS** calcd for $C_{34}H_{28}N_3O_4^+$ $[M+H]^+$ 542.2080, found 542.2080.

3-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)propyl (2-(pyridin-2-yl)quinolin-8-yl)carbamate (4q)



Synthesized following conditions A, from alkene **3f** (30.5 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (0.5-1% MeOH/DCM) afforded **4q** (27.4 mg, 37%) as an off-white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.37 (s, 1H), 8.82–8.70 (m, 2H), 8.61 (d, *J* = 8.6 Hz, 1H), 8.52 (d, *J* = 8.6 Hz, 1H), 8.37–8.25 (m, 1H), 8.06 (td, *J* = 7.7, 1.8 Hz, 1H), 7.95–7.88 (m, 1H), 7.66 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.57–7.48 (m, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 4.26 (t, *J* = 6.7 Hz, 2H), 2.70 (dd, *J* = 8.3, 6.5 Hz, 2H), 1.94 (p, *J* = 7.0 Hz, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 163.0, 160.3, 154.9, 154.0, 153.3, 152.0, 149.5, 137.8, 137.6, 137.4, 134.7, 131.7, 128.0, 127.6, 124.9, 123.9, 123.3, 121.8, 121.2, 119.3, 116.4, 116.2, 115.6, 104.3, 64.8, 27.3, 20.5; **HRMS** calcd. for $C_{27}H_{22}N_3O_5^+$ $[M+H]^+$ 468.1559, found 468.1558.

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-5-(4-hydroxy-2-oxo-2H-chromen-3-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)pentanamide (4r)



Synthesized following conditions A, from alkene **3g** (44.8 mg, 99% *ee*) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 1–2% MeOH/DCM) afforded **L-4r** (36.6 mg, 60% yield, 98% *ee*) as a yellow solid. The racemic standard was synthesized following the same conditions (39.3 mg, 64%). The enantiomeric excess of **L-4r** was determined by chiral SFC on a Daicel Chiralpak AD-H column (0.46 cm x 25 cm), Hexanes / IPA = 80 / 20, 1.0 mL/min, λ = 250 nm, t (minor) = 27.513 min, t (major) = 34.493 min. The enantiomers were detected by UV absorption (Fig. S3). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.65 (dd, *J* = 5.9, 3.1 Hz, 1H), 8.47 (dt, *J* = 4.6, 1.3 Hz, 1H), 8.37–8.28 (m, 2H), 8.23 (d, *J* = 8.6 Hz, 1H), 7.89 (td, *J* = 7.8, 1.8 Hz, 1H), 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.59 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.51–7.43 (m, 2H), 7.37–7.31 (m, 2H), 7.22 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.98–6.87 (m, 1H), 5.51 (dd, *J* = 11.0, 4.6 Hz, 1H), 3.01 (ddd, *J* = 13.5, 9.5, 6.6 Hz, 1H), 2.90–2.74 (m, 2H), 2.40–2.25 (m, 1H), 1.90–1.80 (m, 1H), 1.73–1.64 (m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.5, 168.5, 164.3, 161.7, 154.6, 152.9, 152.6, 148.7, 138.5, 138.3, 137.8, 134.5, 134.4, 131.8, 131.2, 128.1, 128.0, 124.7, 123.7, 123.6, 123.4, 122.7, 122.2, 119.4, 118.5, 116.7, 116.6, 106.6, 54.7, 27.4, 24.6, 22.3; **HRMS** calc. for $C_{36}H_{27}N_4O_6^+$ $[M+H]^+$ 611.1931, found 611.1932.

Area % Report

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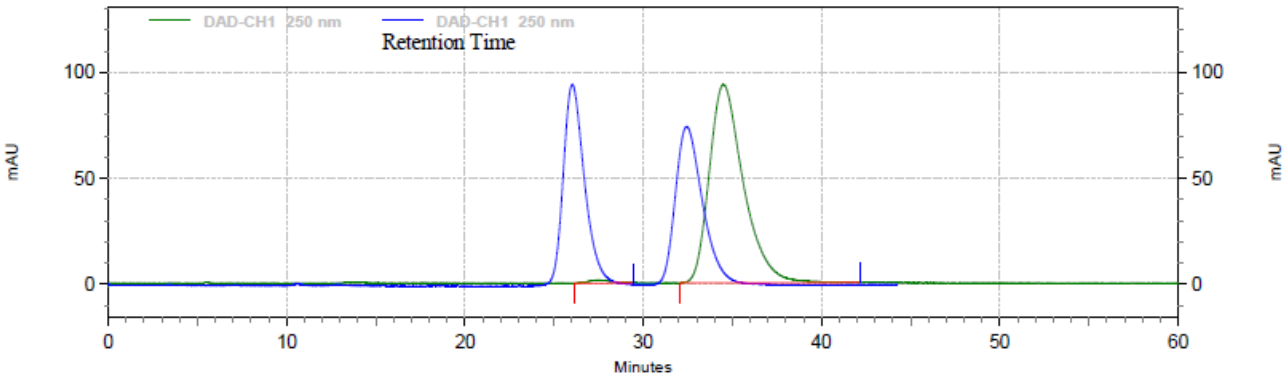


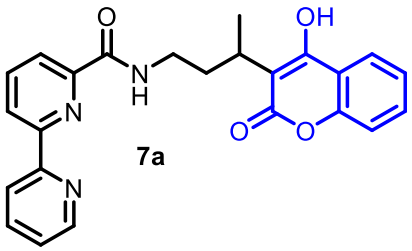
DAD-CH1 250 nm Results

Retention Time	Area	Area %	Height	Height %
27.513	523363	1.04	5802	1.52
34.493	49933692	98.96	375132	98.48
Totals	50457055	100.00	380934	100.00

Figure S3. HPLC trace and report for *ee* determination of **4r**.

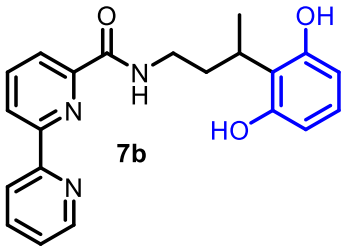
Hydrofunctionalization of Amine Substrates

***N*-(3-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)butyl)-[2,2'-bipyridine]-6-carboxamide (7a)**



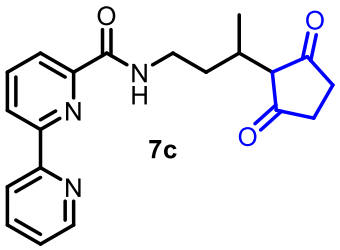
Synthesized following conditions C, from alkene **6** (25.3 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **7a** (29.0 mg, 70% yield) as a white solid. Conditions A afforded 27.7 mg (67% yield) of product **7a**. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.93 (t, *J* = 6.1 Hz, 1H), 8.82–8.76 (m, 1H), 8.72–8.68 (m, 1H), 8.53 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.08 (t, *J* = 7.7 Hz, 1H), 8.01 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.00–7.93 (m, 2H), 7.55 (ddd, *J* = 8.5, 7.3, 1.5 Hz, 1H), 7.49 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 7.32 (ddd, *J* = 8.2, 7.4, 1.1 Hz, 1H), 7.29 (dd, *J* = 8.2, 1.0 Hz, 1H), 3.39–3.20 (m, 3H, overlaps with H_2O peak), 2.17 (dtd, *J* = 13.1, 8.5, 6.4 Hz, 1H), 1.94 (ddd, *J* = 13.5, 8.0, 6.2 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 163.5, 161.6, 160.1, 154.3, 154.2, 152.0, 149.7, 149.2, 138.8, 137.3, 131.5, 124.6, 123.7, 123.3, 122.7, 121.9, 121.4, 116.4, 116.0, 108.4, 38.0, 33.5, 27.7, 18.3; **HRMS** calc. for $C_{24}H_{22}N_3O_4^+$ $[M+H]^+$ 416.1610, found 416.1611.

***N*-(3-(2,6-Dihydroxyphenyl)butyl)-[2,2'-bipyridine]-6-carboxamide (7b)**



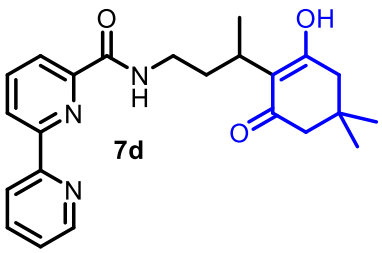
Synthesized following conditions C, from alkene **6** (25.3 mg) and resorcinol (16.5 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **7b** (19.2 mg, 53% yield) as an off-white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.99–8.92 (m, 2H), 8.79 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.71 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.55 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.11 (t, *J* = 7.7 Hz, 1H), 8.06 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.99 (td, *J* = 7.7, 1.8 Hz, 1H), 7.50 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 6.29 (d, *J* = 2.4 Hz, 1H), 6.20 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.35–3.28 (m, 1H), 3.25–3.18 (m, 1H), 3.08 (h, *J* = 7.1 Hz, 1H), 1.86–1.73 (m, 2H), 1.16 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 163.4, 154.2, 149.8, 149.2, 138.8, 137.4, 127.0, 124.6, 123.0, 122.7, 122.0, 121.4, 106.3, 102.4, 37.7, 37.0, 30.7, 28.8, 21.1; **HRMS** calc. for $C_{21}H_{22}N_3O_3^+$ $[M+H]^+$ 364.1661, found 364.1661.

***N*-(3-(2,5-Dioxocyclopentyl)butyl)-[2,2'-bipyridine]-6-carboxamide (7c)**



Synthesized following conditions C, from alkene **6** (25.3 mg) and 1,3-cyclopentanedione (14.7 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **7c** (27.9 mg, 79% yield) as a yellow solid (keto:enol 89:13). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.82 (t, *J* = 6.1 Hz, 1H), 8.72 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 8.40–8.28 (m, 2H), 8.22 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.99 (t, *J* = 7.8 Hz, 1H), 7.93 (td, *J* = 7.7, 1.8 Hz, 1H), 7.43 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1H), 3.53–3.42 (m, 1H), 3.37 (dtd, *J* = 13.9, 6.3, 3.8 Hz, 1H), 2.80 (dqd, *J* = 10.7, 7.1, 3.6 Hz, 1H), 2.38 (s, 4H), 2.17–2.08 (m, 1H), 1.77 (ddt, *J* = 14.1, 9.2, 3.7 Hz, 1H), 1.24 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 164.5, 154.4, 153.8, 149.5, 148.9, 138.6, 137.9, 124.5, 123.7, 122.5, 121.7, 120.4, 84.7, 38.6, 34.9, 27.2, 18.9; **HRMS** calc. for $C_{20}H_{22}N_3O_3^+$ $[M+H]^+$ 352.1661, found 352.1660.

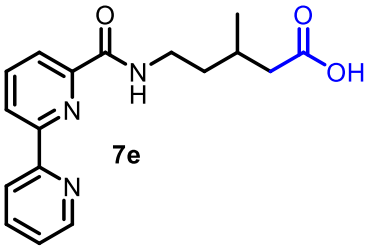
***N*-(3-(2,5-Dioxocyclopentyl)butyl)-[2,2'-bipyridine]-6-carboxamide (7d)**



Synthesized following conditions C, from alkene **6** (25.3 mg) and 5,5-dimethyl-1,3-dihexaneone (21.0 mg). Purification by silica flash column chromatography (eluent: 1–5% MeOH/DCM) afforded **7d** (37.3 mg, 95% yield) as a yellow oil (enol:keto 78:22). **Enol: ^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.72–8.68 (m, 1H), 8.55 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.38–8.34 (m, 1H), 8.20 (dd, *J* = 7.6, 1.1 Hz, 1H), 8.13 (t, *J* = 6.1 Hz, 1H), 7.98 (t, *J* = 7.8 Hz, 1H), 7.87 (td, *J* = 7.7, 1.9 Hz, 1H), 7.36 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 3.64 (tdd, *J* = 16.6, 13.6, 7.5 Hz, 1H), 3.51–3.36 (m, 1H), 2.87 (dd, *J* = 26.0, 13.8 Hz, 2H), 2.52–2.47 (m, 1H), 2.43 (dd, *J* = 13.8, 2.9 Hz, 1H), 2.37 (dd, *J* = 13.9, 2.8 Hz, 1H), 1.79–1.51 (m, 2H), 1.07 (s, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.74 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 206.4, 206.1, 164.9, 155.3, 155.2, 149.7, 149.4, 138.8, 137.4, 124.6, 124.2, 122.6, 121.4, 93.27, 51.6, 51.2, 39.7, 37.5, 31.7, 31.1, 30.8, 26.7, 13.4; **HRMS** calc. for $C_{23}H_{28}N_3O_3^+$ $[M+H]^+$ 294.2131, found 394.2131. **Keto: ^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.79 (d, *J* = 6.3 Hz, 1H), 8.75 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.57–8.51 (m, 1H), 8.28 (ddd, *J* = 8.0, 3.4, 1.0 Hz, 2H), 8.24 (dd, *J* = 7.7, 1.0 Hz,

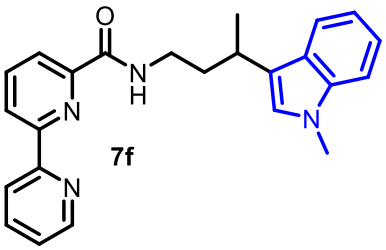
1H), 7.98–7.93 (m, 1H), 7.46 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 3.42–3.34 (m, 1H), 3.19 (ddd, *J* = 11.3, 7.2, 4.3 Hz, 1H), 2.44 (dd, *J* = 14.0, 2.9 Hz, 1H), 2.38 (dd, *J* = 13.9, 2.8 Hz, 1H), 2.33 (s, 2H), 2.19–2.15 (m, 2H), 1.86–1.73 (m, 2H), 1.24 (d, *J* = 7.1 Hz, 3H), 0.93 (s, 6H).

***N*-(3-(4,4-Dimethyl-2,6-dioxocyclohexyl)butyl)-[2,2'-bipyridine]-6-carboxamide (7e)**



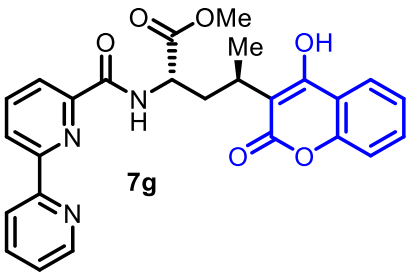
Synthesized following conditions C, from alkene **6** (25.3 mg) and Meldrum's acid (21.6 mg). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM to 5% MeOH/DCM) afforded **7e** (22.1 mg, 74% yield) as a white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.08 (t, *J* = 6.1 Hz, 1H), 8.85 (d, *J* = 8.0 Hz, 1H), 8.71 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.56 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.12 (t, *J* = 7.7 Hz, 1H), 8.07 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.00 (td, *J* = 7.7, 1.8 Hz, 1H), 7.50 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 3.40 (dtd, *J* = 8.1, 6.4, 4.4 Hz, 2H), 2.45–2.33 (m, 1H), 1.93 (ddt, *J* = 13.8, 8.2, 7.0 Hz, 1H), 1.64 (ddt, *J* = 13.1, 8.0, 6.4 Hz, 1H), 1.13 (d, *J* = 7.0 Hz, 3H), one CH_2 peak obstructed by solvent signal; **^{13}C NMR** (150 MHz, DMSO-d_6) δ 177.3, 163.6, 154.3, 154.2, 149.7, 149.2, 138.8, 137.3, 124.6, 122.7, 122.0, 121.5, 37.1, 36.8, 33.2 17.0; HRMS calcd. for $H_{17}H_{20}N_3O_3^+$ [M + H]$^+$ 314.1505, found 314.1507.

***N*-(3-(1-Methyl-1*H*-indol-3-yl)butyl)-[2,2'-bipyridine]-6-carboxamide (7f)**



Synthesized following conditions D, from alkene **6** (25.3 mg) and *N*-methyl indole (19 µL). Purification by silica flash column chromatography (eluent: 1% MeOH/DCM) afforded **7f** (18.4 mg, 48% yield) as a white solid. Conditions C afforded 5% of the desired product by ^{1}H NMR. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.70 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.53 (dd, *J* = 7.9, 1.1 Hz, 1H), 8.26 (dt, *J* = 7.9, 1.1 Hz, 1H), 8.21 (dd, *J* = 7.6, 1.1 Hz, 1H), 8.14–8.04 (m, 1H), 7.96 (t, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.7, 1.8 Hz, 1H), 7.67 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.34 (ddd, *J* = 7.4, 4.8, 1.2 Hz, 1H), 7.24 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.18 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.06 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 6.89 (s, 1H), 3.69 (s, 3H), 3.62–3.55 (m, 1H), 3.55–3.46 (m, 1H), 3.26–3.18 (m, 1H), 2.19–2.04 (m, 2H), 1.44 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 164.3, 155.3, 154.8, 149.6, 149.4, 138.4, 137.3, 137.1, 127.1, 125.3, 124.2, 123.6, 122.3, 121.6, 121.1, 119.9, 119.3, 118.7, 109.5, 38.3, 37.4, 32.7, 29.1, 22.0; **HRMS** calc. for $C_{24}H_{25}N_4O^+$ [M+H]$^+$ 385.2028, found 385.2029.

Methyl (2*S*,4*R*)-2-([2,2'-bipyridine]-6-carboxamido)-4-(4-hydroxy-2-oxo-2*H*-chromen-3-yl)pentanoate (7g)



Synthesized following conditions C, from alkene **10** (31.1 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 1–2% MeOH/DCM) afforded **7g** (41.5 mg, 88% yield, 93:7 dr, 98% *ee* major diastereoisomer, 39% *ee* minor diastereoisomer) as a yellow oil. (Determination of *dr* is demonstrated in Fig. S4). A small amount was subjected to purification by preparative TLC (3× 2% MeOH/DCM) to afford analytical samples of both diastereoisomers. The major diastereoisomer was assigned by analogy to previously observed stereocontrol in the nucleopalladation step: due to *gauche* interactions between the two substituents, a transition state with both substituents *anti* to each other is energetically preferred.[15] The racemic standard was synthesized following the same procedure (38.1 mg, 80% yield). The enantiomeric excess of **7g–major diastereoisomer** was determined by chiral SFC on a Daicel IA column (3 mm, 4.6x250 mm) under isocratic conditions (30% MeOH / CO2 (4 mL/min), 1600 psi backpressure) at 30 °C. The enantiomers were detected by UV light (281 nm) (Fig. S5); the enantiomeric excess of **7g–minor diastereoisomer** was determined by chiral SFC on a Daicel Chiralpak AD-H column (0.46 cm x 25 cm), Hexanes / IPA = 90 / 10, 1.0 mL/min, λ = 250 nm, t (major) = 5.100 min, t (minor) = 43.827 min. The enantiomers were detected by UV light (Fig. S6). **Major Diastereoisomer: ^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.77 (brs, 1H), 8.71 (d, *J* = 4.8 Hz, 1H), 8.36 (dd, *J* = 26.1, 7.8 Hz, 2H), 7.95 (brs, 1H), 7.92 (t, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.78 (s, 1H), 7.39 (t, *J* = 6.3 Hz, 1H), 7.29 (t, *J* = 8.3 Hz, 1H), 7.06 (s, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 4.82 (brs, 1H), 3.64 (s, 3H), 3.56 (brs, 1H), 2.85 (brs, 1H), 2.14 (brs, 1H), 1.39 (d, *J* = 6.8 Hz, 3H); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.14 (brs, 1H), 8.94 (brs, 1H), 8.72 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 8.54 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.06 (t, *J* = 7.8 Hz, 1H), 8.00 (td, *J* = 7.7, 1.8 Hz, 1H), 7.97 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.82 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.52 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 7.38 (ddd, *J* = 8.5, 7.2, 1.6 Hz, 1H), 7.21–7.11 (m, 1H), 7.02 (dd, *J* = 8.2, 1.1 Hz, 1H), 4.68

(td, *J* = 8.1, 5.1 Hz, 1H), 3.49 (s, 3H), 3.43 (dp, *J* = 9.3, 6.9 Hz, 1H), 2.55 (ddd, *J* = 13.7, 9.2, 7.8 Hz, 1H), 2.25–2.14 (m, 1H), 1.26 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 185.1, 172.3, 163.4, 162.1, 154.4, 154.2, 152.3, 149.1, 148.9, 138.7, 137.4, 130.7, 124.6, 123.5, 123.0, 122.8, 122.1, 121.7, 115.5, 51.8, 51.2, 34.8, 26.6, 18.5; **HRMS** calc. for $C_{26}H_{24}N_3O_6$ $[M+H]^+$ 474.1665, found 474.1665. **Minor Diastereoisomer: ^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.88 (d, *J* = 7.9 Hz, 1H), 8.73 (dt, *J* = 4.8, 1.3 Hz, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 8.36 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.0 Hz, 1H), 8.00 (td, *J* = 7.7, 1.7 Hz, 1H), 7.92 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.46 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.38 (ddd, *J* = 8.5, 7.3, 1.6 Hz, 1H), 7.16 (ddd, *J* = 8.2, 7.3, 1.1 Hz, 1H), 7.07 (dd, *J* = 8.3, 1.1 Hz, 1H), 4.73 (q, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 3.53 (ddd, *J* = 11.3, 7.1, 4.8 Hz, 1H), 2.82 (ddd, *J* = 13.9, 10.7, 6.5 Hz, 1H), 2.26 (ddd, *J* = 13.9, 7.3, 4.7 Hz, 1H), 1.45 (d, *J* = 6.8 Hz, 3H).

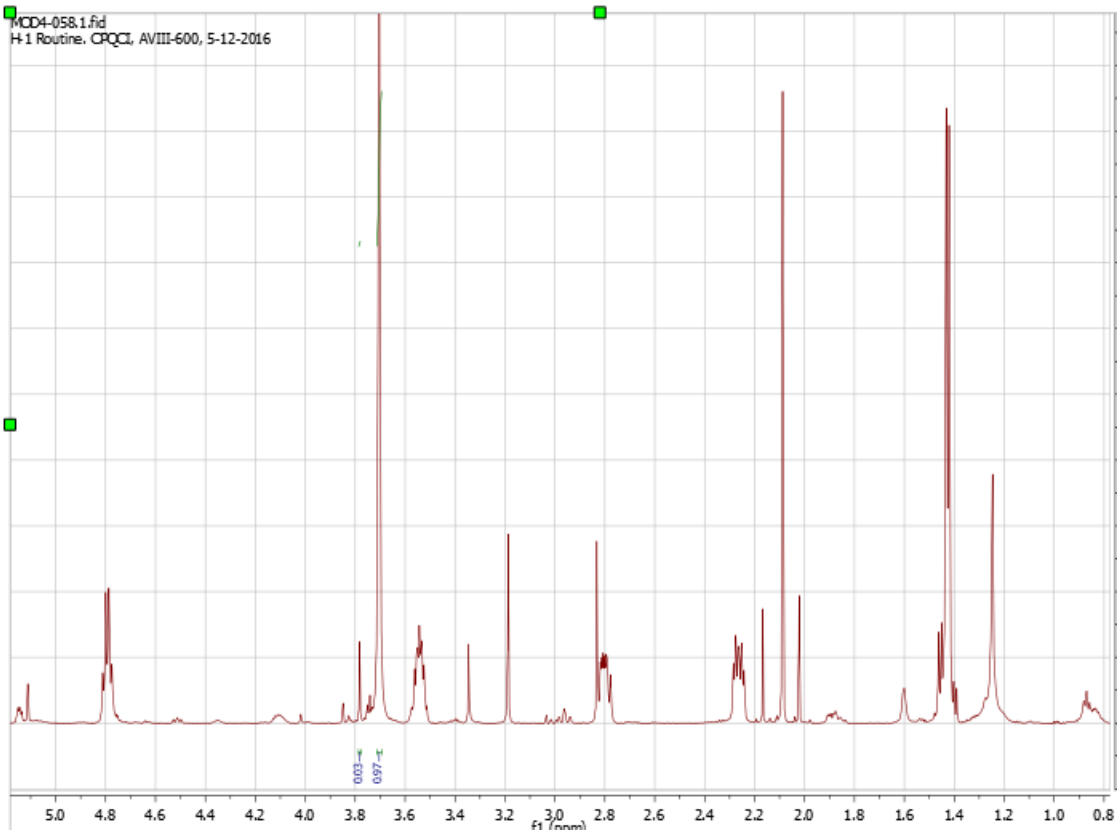
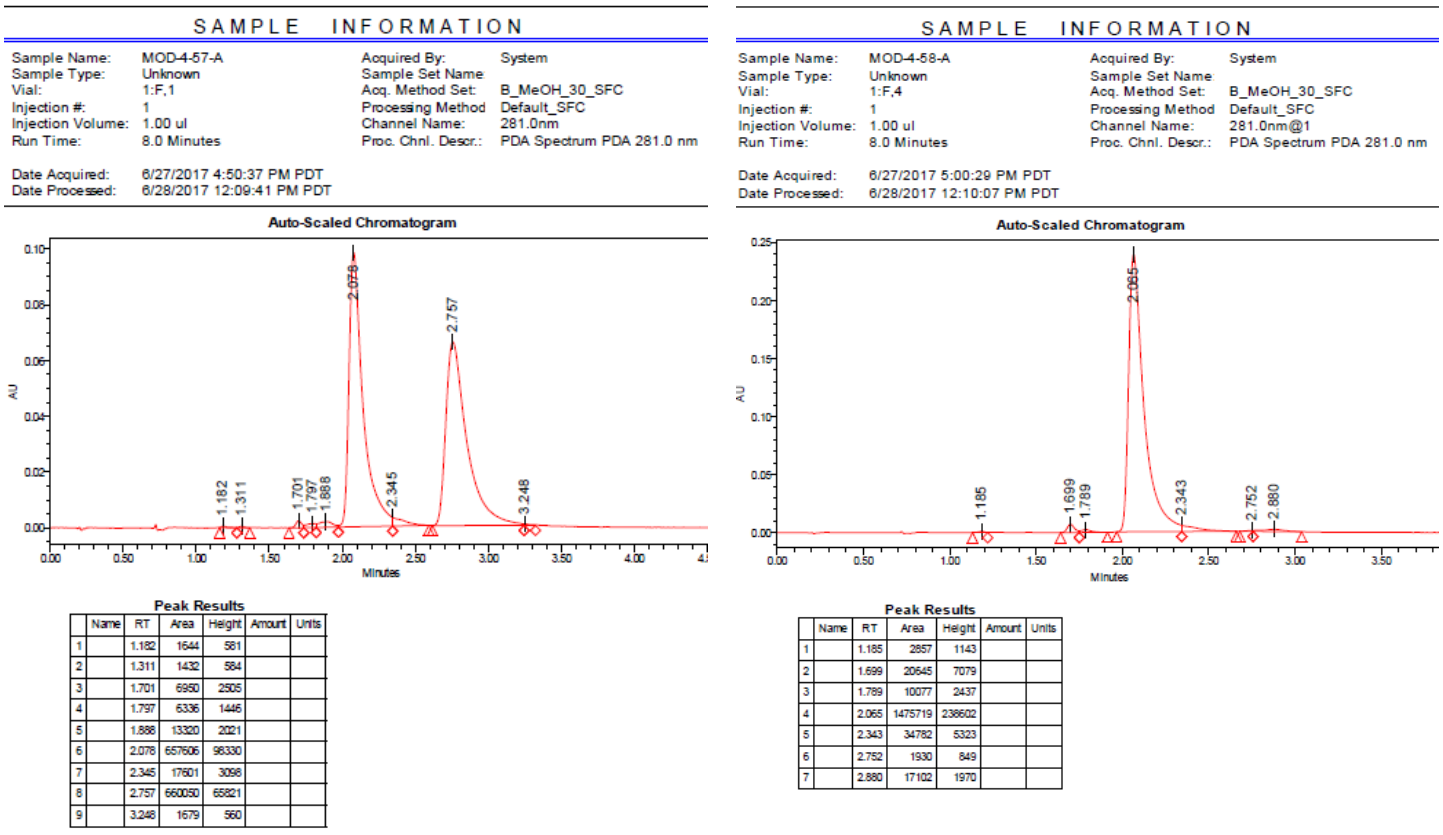


Figure S4. ^{1}H NMR of **7g** after column chromatography, but before preparative TLC: mixture of major and minor diastereoisomers. Integration of the $-CH_3$ peak shows a diastereomeric ratio of 97:3.



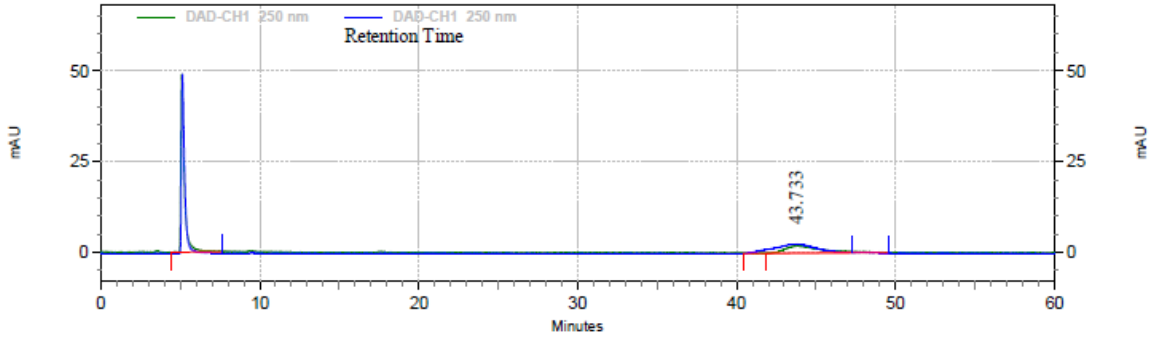
	Name	RT	Area	Height	Amount	Units
1		1.182	1644	581		
2		1.311	1432	564		
3		1.701	6950	2505		
4		1.797	6336	1446		
5		1.888	13320	2021		
6		2.078	657606	98330		
7		2.345	17601	3098		
8		2.757	660050	65821		
9		3.248	1679	560		

	Name	RT	Area	Height	Amount	Units
1		1.185	2857	1143		
2		1.699	20645	7079		
3		1.789	10077	2437		
4		2.065	1475719	238602		
5		2.343	34782	5323		
6		2.752	1930	849		
7		2.880	17102	1970		

Figure S5. HPLC trace and report for *ee* determination of **7g**–major diastereoisomer: left – racemic standard, right – chiral sample.

Area % Report

Data File: C:\ENGLE LAB DATA\dwgao\4\mod-4-58-chiral-AD-0.10-1.0.dat
Method: C:\ENGLE LAB DATA\dwgao\METHOD\10% 1.0 90 min.met
Acquired: 6/17/2017 2:10:22 PM
Printed: 6/18/2017 5:31:19 PM

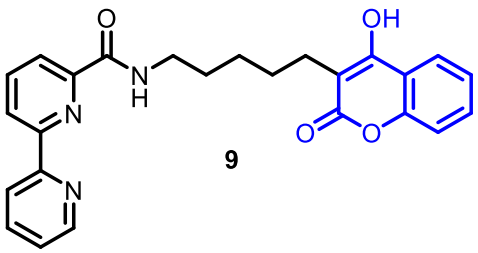


DAD-CH1 250 nm Results

Retention Time	Area	Area %	Height	Height %
5.100	3010002	69.31	195943	96.06
43.827	1332762	30.69	8038	3.94
Totals	4342764	100.00	203981	100.00

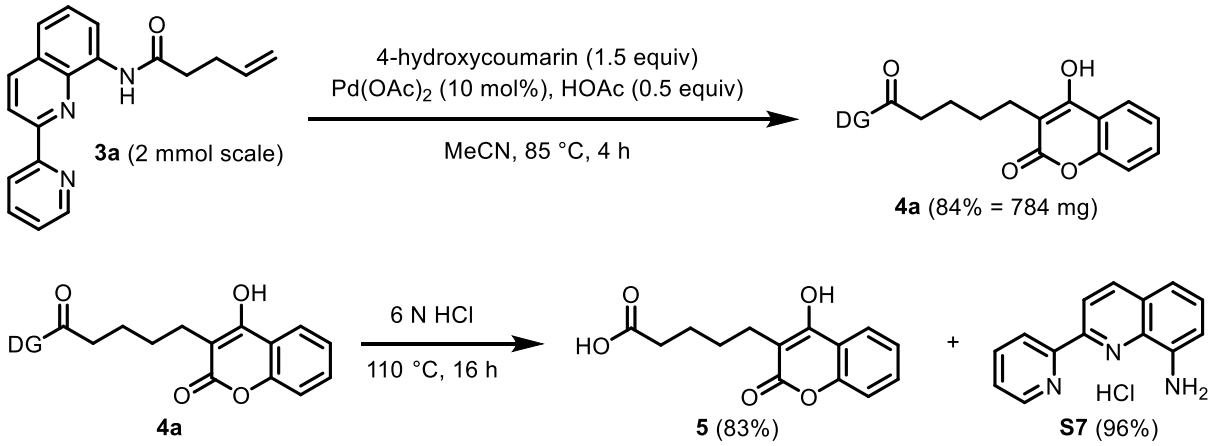
Figure S6. HPLC trace and report for ee determination of **7g**–minor diastereoisomer.

_N_-(5-(4-hydroxy-2-oxo-2_H_-chromen-3-yl)pentyl)-[2,2'-bipyridine]-6-carboxamide (9)



Synthesized following conditions C, from alkene **8** (26.7 mg) and 4-hydroxycoumarin (24.3 mg). Purification by silica flash column chromatography (eluent: 60% EtOAc/Hes) afforded **9** (28.5 mg, 66% yield) as an off-white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.00 (t, *J* = 6.2 Hz, 1H), 8.82 (d, *J* = 7.9 Hz, 1H), 8.71 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.55 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.11 (t, *J* = 7.7 Hz, 1H), 8.05 (d, *J* = 7.7 Hz, 1H), 7.99 (td, *J* = 7.8, 1.8 Hz, 1H), 7.87 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.56–7.47 (m, 2H), 7.28 (dt, *J* = 7.5, 3.3 Hz, 2H), 3.38–3.34 (m, 4H), 1.63 (p, *J* = 7.5 Hz, 2H), 1.53–1.45 (m, 2H), 1.38 (p, *J* = 7.7 Hz, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 185.1, 163.5, 163.1, 154.3, 154.22, 152.0, 149.8, 149.2, 138.8, 137.3, 131.1, 124.6, 123.4, 123.3, 122.6, 122.0, 121.4, 115.9, 29.6, 29.4, 27.9, 26.5, 23.6; **HRMS** calc. for $C_{25}H_{24}N_3O_4^+$ $[M+H]^+$ 430.1767, found 430.1769.

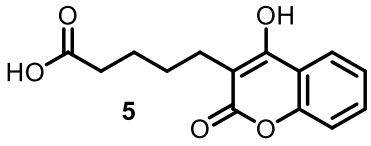
Scale-Up and Deprotection of 4a



Large-Scale Synthesis of 4a

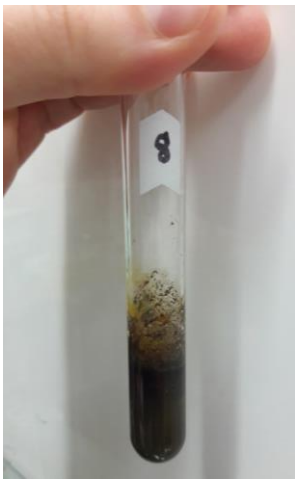
To an 8 mL culture tube equipped with a magnetic stir bar were added alkene **3a** (606 mg, 2 mmol), 4-hydroxycoumarin (486 mg, 3 mmol), $Pd(OAc)_2$ (45 mg, 0.2 mmol), acetic acid (57 µL, 1 mmol), and MeCN (1 mL). The tube was sealed with an unpunctured TFE septum-covered screw cap, and placed in an oil-bath that was pre-heated to 85 °C. After 4 h, the reaction was purified by silica flash column chromatography directly (without aqueous workup; eluent: 1% MeOH/DCM) to afford **4a** (784 mg, 84% yield) as a pale-yellow solid. Analytical data as above.

5-(4-Hydroxy-2-oxo-2_H_-chromen-3-yl)pentanoic acid (5)

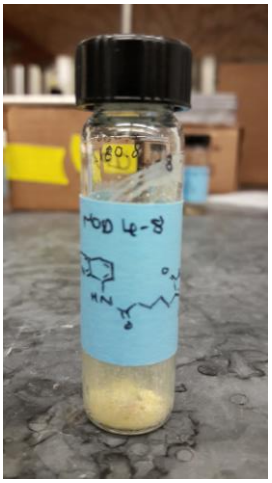


4a (233 mg, 0.5 mmol) and 6 N HCl (2.5 mL) were stirred at 110 °C in a sealed tube for 16 h. The reaction was cooled to rt, diluted with water and extracted with EtOAc. The organic layers were washed with H_2O, dried over $MgSO_4$ and the solvent was removed *in vacuo*. Trituration of the dried solid with ice-cold EtOAc and subsequent drying afforded the free acid **5** (109 mg, 83% yield) as an off-white solid. The directing group **S7** (124 mg, 96% yield) was recovered by evaporation of H_2O from the combined aqueous layers and trituration of the resulting solid with ice-cold MeOH. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 7.94–7.90 (m, 1H), 7.61–7.55 (m, 1H), 7.34 (dd, *J* = 8.2, 7.3 Hz, 2H), 2.54–2.50 (m, 2H), 2.23 (t, *J* = 7.3 Hz, 2H), 1.58–1.50 (m, 2H), 1.46 (tdd, *J* = 8.5, 6.1, 3.7 Hz, 2H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 174.4, 162.8, 159.7, 151.8, 131.5, 123.8, 123.1, 116.3, 116.1, 104.9, 33.6, 27.4, 24.2, 23.2; **HRMS** calc. for $C_{14}H_{15}O_5^+$ $[M + H]^+$ 263.0919, found 263.0919.

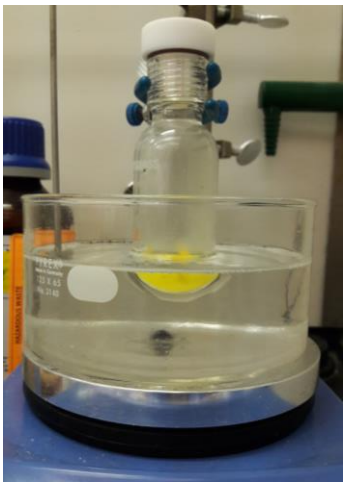
Photo Reel for Scale-Up and Deprotection Procedure



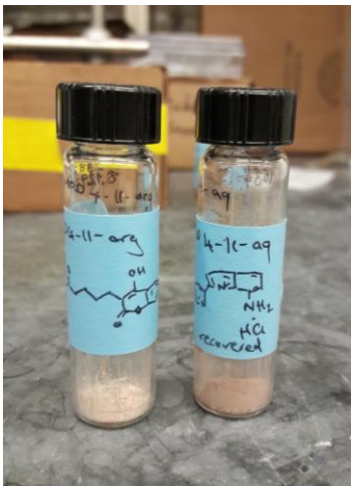
Large-scale synthesis of **4a**: crude reaction mixture



Purified Product **4a**

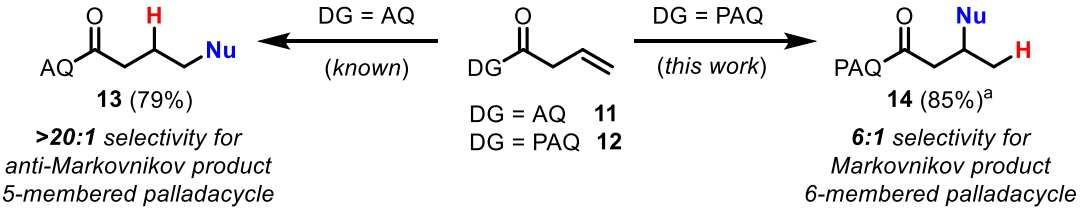


Hydrolysis of the directing group



Free acid **5** (left) and recovered DG **S7** (right)

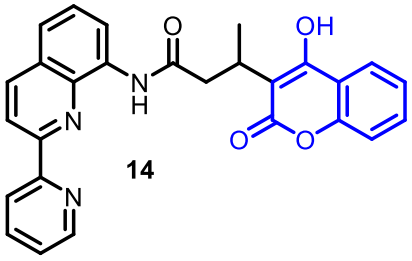
Directing-Group Controlled Regioselectivity of Alkene Hydrofunctionalization



Reaction conditions: 4-hydroxycoumarin (1.5 equiv), $Pd(OAc)_2$ (10 mol%), HOAc (0.5 equiv.), MeCN, 120 °C, 4 h. Yields are of isolated products. [a] 15% linear, anti-Markovnikov product was observed.

Alkene **11** was synthesized and hydrofunctionalized as previously reported.[1,14]

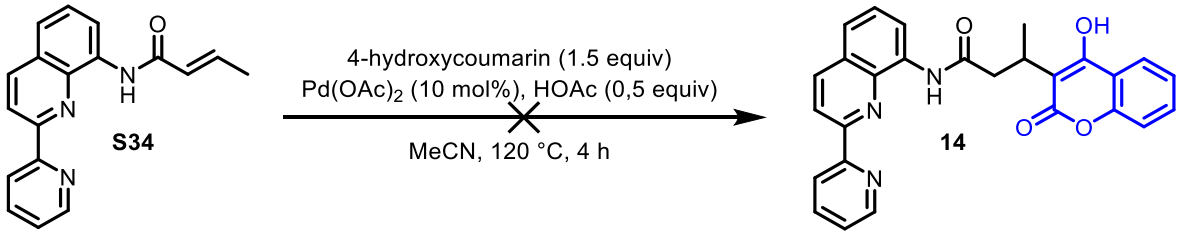
3-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-*N*-(2-(pyridin-2-yl)quinolin-8-yl)butanamide (14)



14

To a 1 dram (4 mL) vial equipped with a magnetic stir bar were added alkene **12** (28.9 mg, 0.1 mmol), 4-hydroxycoumarin (24.3 mg, 0.15 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), acetic acid (3.0 µL, 0.05 mmol) and 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. After 4 h, the reaction was purified by silica flash column chromatography directly (without aqueous workup; eluent: 1% MeOH/DCM) to afford **14** (45.2 mg, >99% yield, 85% purity; inseparable from 15% linear, anti-Markovnikov addition product) as an off-white solid. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.13 (s, 1H), 9.02 (d, *J* = 7.9 Hz, 1H), 8.77 (dt, *J* = 4.6, 1.4 Hz, 1H), 8.66–8.56 (m, 2H), 8.48 (d, *J* = 8.6 Hz, 1H), 8.10 (td, *J* = 7.7, 1.8 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.64 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.60–7.49 (m, 2H), 7.44 (ddd, *J* = 8.5, 7.3, 1.6 Hz, 1H), 7.23–7.18 (m, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 3.85 (dt, *J* = 8.5, 6.7 Hz, 1H), 3.31 (dd, *J* = 14.3, 8.5 Hz, 1H), 2.93 (dd, *J* = 14.2, 6.8 Hz, 1H), 1.34 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.4, 162.3, 154.8, 153.9, 152.3, 152.1, 149.2, 137.6, 137.6, 137.5, 134.7, 131.0, 127.8, 127.4, 124.8, 123.6, 123.1, 122.1, 121.5, 119.0, 117.0, 116.0, 115.7, 41.9, 27.4, 18.6; **HRMS** calcd. for $C_{27}H_{22}N_3O_4^+$ $[M+H]^+$ 452.1610, found 452.1609.

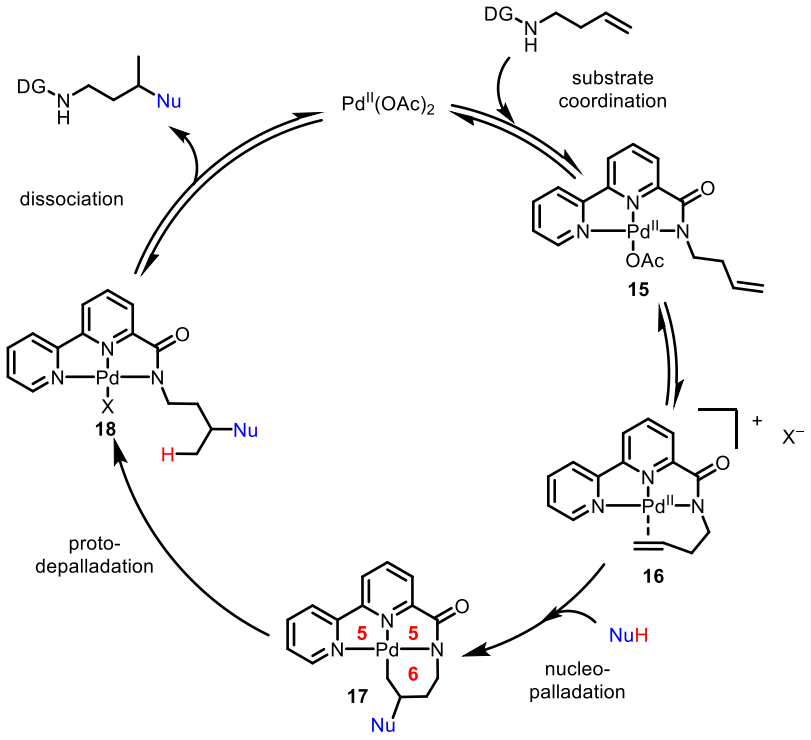
***Control Reaction*:** In order to show conclusively that **14** is formed *via* the 6-membered palladacycle from alkene **12** and not through isomerization to the internal alkene **S34** which then reacts *via* catalytic Michael-addition, **S34** was submitted to the same reaction conditions as **12**. Only unreacted starting material (no evidence of formation of product **14**) was observed by ^{1}H NMR, ruling out an isomerization/Michael-addition mechanism.



Preliminary Mechanistic Studies

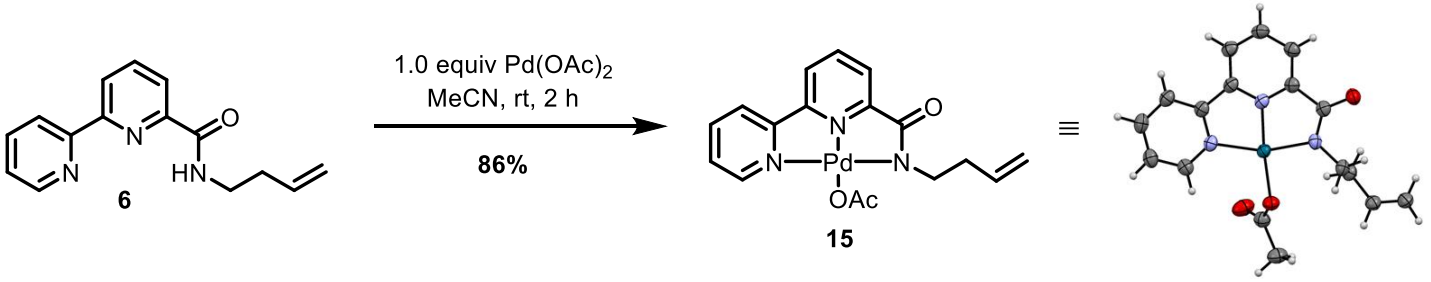
Efforts to obtain mechanistic data for substrates bearing the PAQ directing group proved challenging due to solubility issues; mechanistic considerations therefore focused on amine-derived substrates bearing the PPA group.

Proposed Mechanism



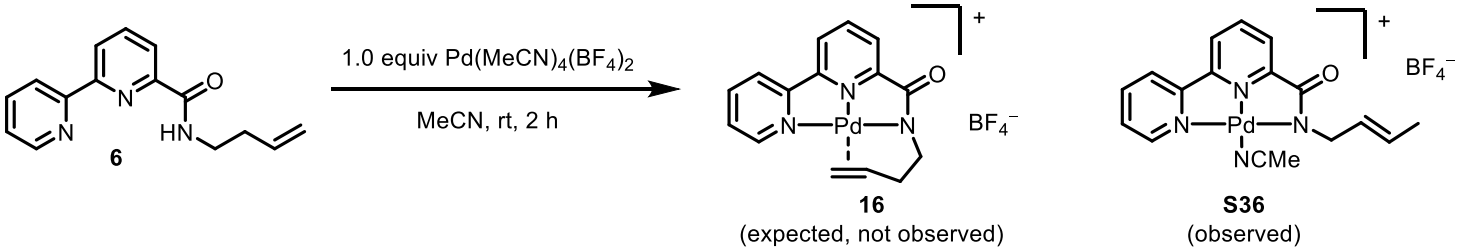
Mechanistic Experiments and Data

Formation of Complex 15



A 1 dram vial containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), alkene **6** (25.3 mg, 0.1 mmol) and MeCN (1 mL). The resulting yellow solution was stirred at room temperature for 1.5 h, during which a precipitate crashed out. The reaction mixture was filtered, and the filter cake was collected and dried *in vacuo* to afford 31 mg (86%) of complex **15** as a greenish-yellow powder. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.49 (ddd, *J* = 5.4, 1.7, 0.8 Hz, 1H), 8.14–8.07 (m, 2H), 8.01 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.86 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.81 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.58 (ddd, *J* = 7.7, 5.4, 1.3 Hz, 1H), 5.92 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.12 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.00 (ddt, *J* = 10.1, 2.1, 1.1 Hz, 1H), 3.32–3.11 (m, 2H), 2.46–2.34 (m, 2H), 2.16 (s, 3H); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.56 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.46 (dd, *J* = 8.1, 1.1 Hz, 1H), 8.41–8.32 (m, 2H), 8.29 (ddd, *J* = 5.4, 1.6, 0.7 Hz, 1H), 7.81 (ddd, *J* = 7.7, 5.4, 1.3 Hz, 1H), 7.70 (dd, *J* = 7.7, 1.0 Hz, 1H), 5.81 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.03 (dq, *J* = 17.2, 1.6 Hz, 1H), 4.95 (ddt, *J* = 10.2, 2.3, 1.2 Hz, 1H), 3.13–2.93 (m, 2H), 2.26–2.14 (m, 2H), 1.94 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 178.4, 170.4, 155.4, 154.8, 153.2, 151.6, 140.8, 140.3, 137.1, 127.5, 125.3, 122.9, 122.3, 115.7, 45.5, 34.9, 23.8; HRMS calcd. for $C_{15}H_{14}N_3OPd^+$ $[M–OAc^-]^+$ 358.9172, found 358.0174; **X-ray** (single-crystal) yellow needles of X-ray diffraction quality were obtained by vapor diffusion of pentane into a saturated solution of **15** in DCM (CCDC 1567384).[14]

Attempts to synthesize π-alkene complex 16 from Pd(II) precursor with weakly coordinating counteranions



We hypothesized that use of a palladium source with a less strongly coordinating counteranion would enable the alkene to coordinate, allowing for isolation and characterization of putative intermediate **16**. A 1 dram vial containing a magnetic stirring bar was charged with $Pd(MeCN)_4(BF_4)_2$ (44.4 mg, 0.1 mmol), alkene **6** (25.3 mg, 0.1 mmol) and MeCN (1 mL). The resulting yellow solution was stirred at room temperature for 2 h. As no precipitate crashed out of solution, acetonitrile was removed in vacuo to afford 62.7 mg of a yellow solid. Unfortunately, this was not π-complex **16**. Instead, the yellow solid was determined to be a 4:1 mixture of **S36** and **6**. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.60 (d, *J* = 7.9 Hz, 1H), 8.50 (d, *J* = 8.1 Hz, 1H), 8.45–8.35 (m, 3H), 7.87 (ddd, *J* = 7.8, 5.4, 1.3 Hz, 1H), 7.75 (dt, *J* = 7.7, 0.9 Hz, 1H), 5.72–5.63 (m, 1H), 5.59–5.52 (m, 1H), 3.67 (d, *J* = 5.3 Hz, 2H), 1.67 (dd, *J* = 6.4, 1.6 Hz, 3H), MeCN signal obstructed by solvent peak; **^{13}C NMR** (150 MHz, DMSO-d_6) δ 170.4, 154.7, 152.9, 149.6, 149.4, 142.6, 141.9, 136.5, 129.0, 128.4, 124.9, 124.2, 124.1, 118.1, 46.2, 17.6, 1.2; HRMS calc. for $C_{15}H_{14}ON_3Pd^+$ $[M]^+$ 358.0172, found 358.0172.

Attempts to observe π-alkene complex 16: observation of complex 15 under elevated temperatures

A ^{1}H NMR sample of complex **15** in DMSO-d_6 was monitored during a temperature increase from 25 °C to 70 °C in 5 °C increments. We had speculated that **15** might partially transform to the corresponding π-alkene complex **16** at elevated temperatures, however no chemical shift change in the alkene region—which would be indicative of this transformation—was observed (Fig. S7).

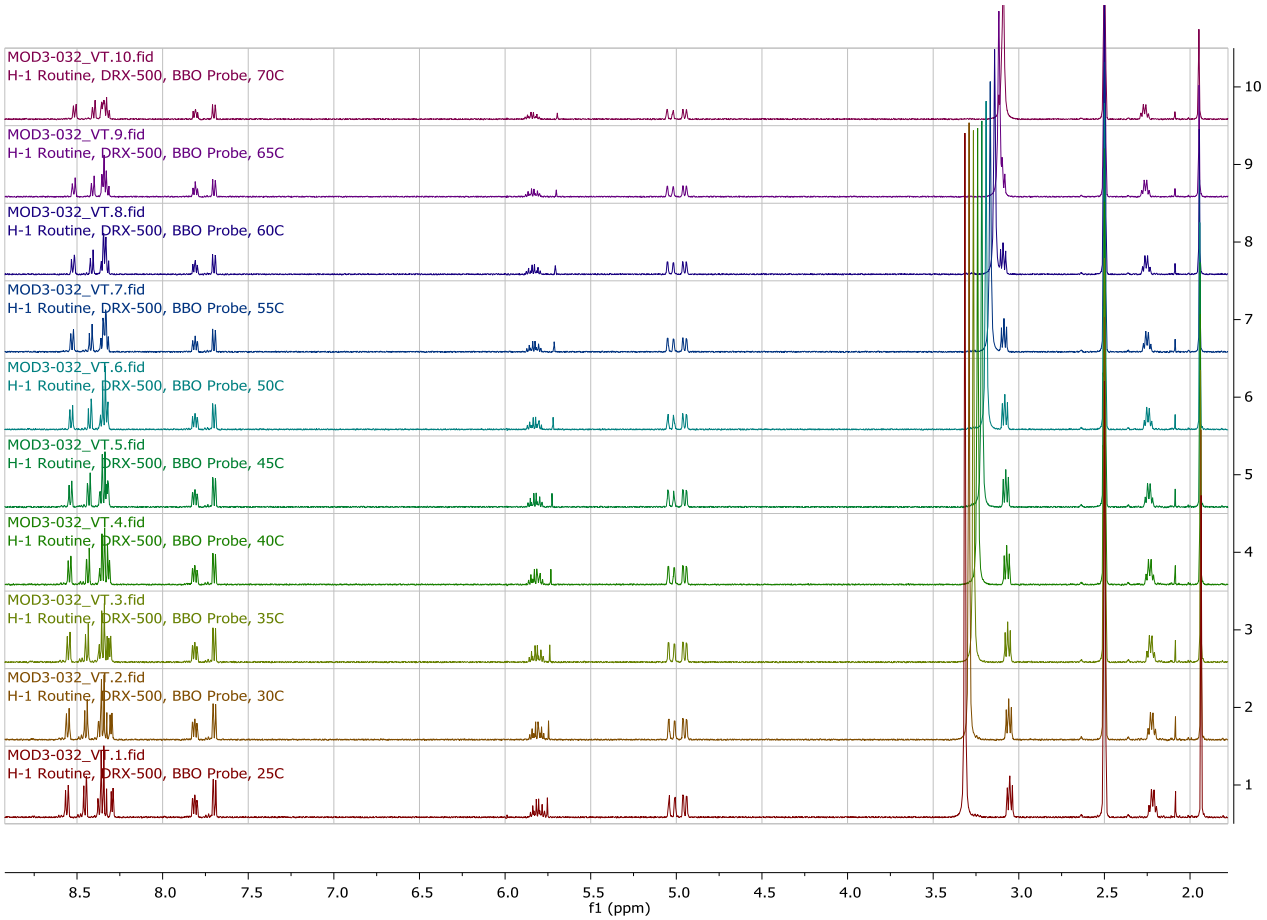
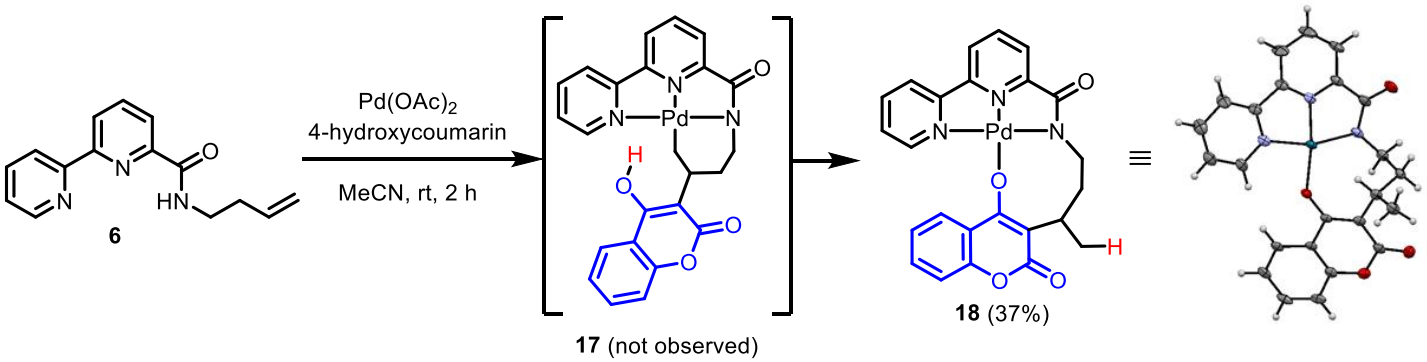


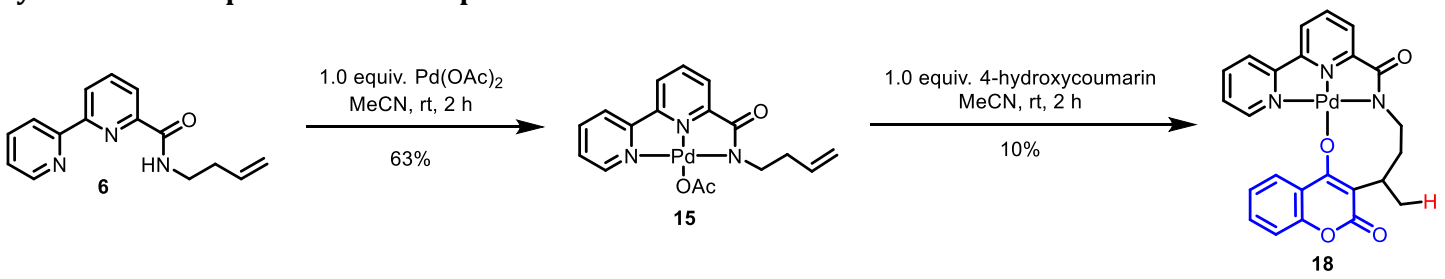
Figure S7. Variable temperature ^{1}H NMR (500 MHz, DMSO-d_6) of **15** from 25 °C (bottom) to 70 °C (top) in 5 °C steps.

Formation of complex 18



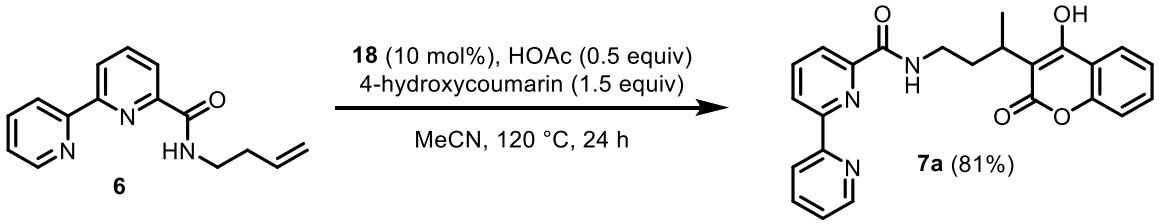
A 1 dram vial containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), alkene **6** (25.3 mg, 0.1 mmol), 4-hydroxycoumarin (16.2 mg, 0.1 mmol) and MeCN (1 mL). The resulting yellow solution was stirred at room temperature for 2 h, during which a greenish-yellow precipitate crashed out. The reaction mixture was filtered, and the filter cake was collected and dried *in vacuo* to afford 19 mg (37%) of complex **18** as a greenish-yellow powder. **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.66–8.58 (m, 2H), 8.49 (dd, *J* = 8.2, 1.1 Hz, 1H), 8.43 (td, *J* = 7.8, 1.6 Hz, 1H), 8.36 (t, *J* = 7.9 Hz, 1H), 7.98 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.95 (ddd, *J* = 7.7, 5.4, 1.3 Hz, 1H), 7.74 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.49 (ddd, *J* = 8.2, 7.2, 1.7 Hz, 1H), 7.28 (ddd, *J* = 8.0, 7.2, 1.1 Hz, 1H), 7.22 (dd, *J* = 8.2, 1.1 Hz, 1H), 4.66 (dtd, *J* = 13.8, 6.9, 3.3 Hz, 1H), 3.86 (dt, *J* = 13.1, 3.3 Hz, 1H), 2.14 (td, *J* = 12.9, 2.1 Hz, 1H), 1.86 (tt, *J* = 12.9, 2.6 Hz, 1H), 1.41 (tt, *J* = 12.9, 3.4 Hz, 1H), 1.32 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 170.2, 169.3, 162.1, 155.0, 154.5, 152.9, 152.3, 148.2, 142.0, 141.8, 130.4, 128.5, 124.8, 124.7, 124.2, 123.9, 123.0, 120.7, 115.6, 103.1, 41.9, 35.4, 25.1, 18.9; **HRMS** calcd. for $C_{24}H_{20}N_3O_4Pd^+$ $[M]^+$ 520.0489, found 520.0489; **X-ray** (single-crystal) needles of X-ray diffraction quality were obtained by leaving a saturated solution of **18** in DMSO-d_6 stand at room temperature for several weeks (CCDC 1567385).[14]

Synthesis of complex 18 from complex 15

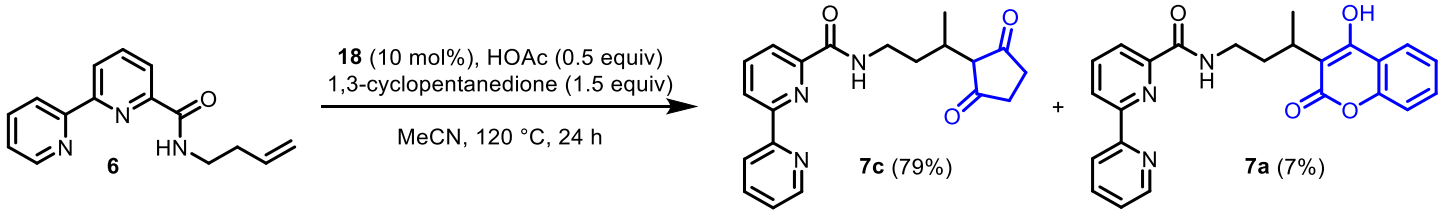


A 1 dram vial containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), alkene **10** (25.3 mg, 0.1 mmol) and MeCN (1 mL). The resulting yellow solution was stirred at room temperature for 2 h, during which a precipitate crashed out. The reaction mixture was filtered and the filter cake was collected and dried *in vacuo* to afford 29.7 mg (63%, 0.06 mmol) of complex **15** as a yellow powder. Complex **15** was re-suspended in MeCN (1 mL) and sonicated for 1 min. 4-Hydroxycoumarin (9.7 mg, 0.06 mmol) was added and the reaction was stirred at rt for 2 h, after which the yellow solid was filtered and the filter cake was dried *in vacuo* to afford a mixture of 23% **15** and 10% **18**.

Complex 18 as a competent reaction intermediate: use as pre-catalyst

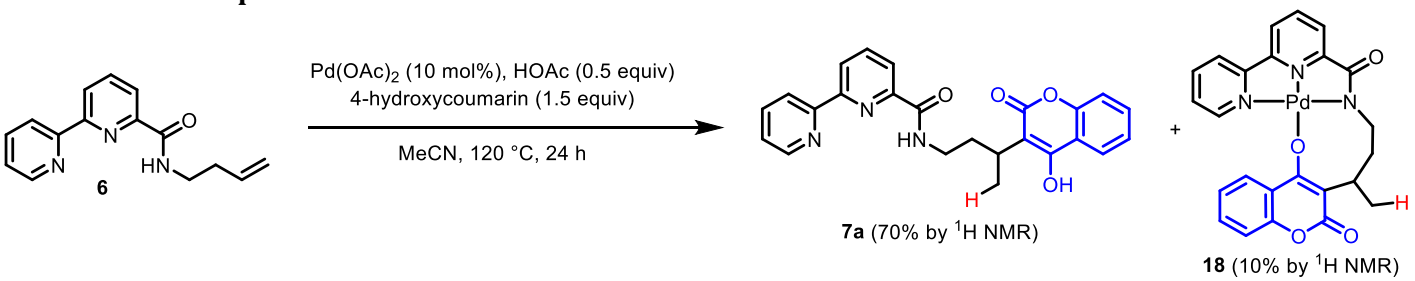


To a 1 dram vial equipped with a magnetic stir bar were added complex **18** (5.2 mg, 0.01 mmol), alkene **6** (25.3 mg, 0.1 mmol), 4-hydroxycoumarin (24.3 mg, 0.15 mmol), acetic acid (3.0 µL, 0.05 mmol) and MeCN (0.05 mL, 2M). The vial was sealed with an unpunctured TFE septum-covered screw cap, and placed in a heating block that was pre-heated to 120 °C. After 24 h, the reaction was purified by silica flash column chromatography (eluent: 1% MeOH/DCM) directly (without aqueous workup) to afford **7a** (33.8 mg, 81%) as a white solid, proving that complex **18** is a catalytically active species.



To a 1 dram vial equipped with a magnetic stir bar were added complex **18** (5.2 mg, 0.01 mmol), alkene **6** (25.3 mg, 0.1 mmol), 1,3-cyclopentanedione (14.7 mg, 0.15 mmol), acetic acid (3.0 µL, 0.05 mmol) and MeCN (0.05 mL, 2M). 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. After 24 h, the reaction was purified by silica flash column chromatography (eluent: 1% MeOH/DCM) directly (without aqueous workup) to afford **7c** (27.7 mg, 79%) and **7a** (3.1 mg, 7%) as yellow solids, suggesting that ligand exchange (dissociation of the directing group from the metal catalyst) takes place under these conditions.

Formation of complex 18 under standard reaction conditions



^{1}H NMR of the crude reaction mixture of substrate **6** under conditions A shows that *ca.* 10% of complex **18** is present before purification, along with *ca.* 70% of the desired product **7a** (Fig. S8). Due to the polarity of the PAQ and PPA directing groups, aqueous workup of our reactions resulted in a substantial loss of product (*ca.* 20–50%). We thus decided against an aqueous workup employing strong chelating reagents (such as dithiocarbamates) which are known to remove transition metals from organic reaction media.[16] Direct purification of the crude reaction mixture may therefore have resulted in lower yields in some cases.

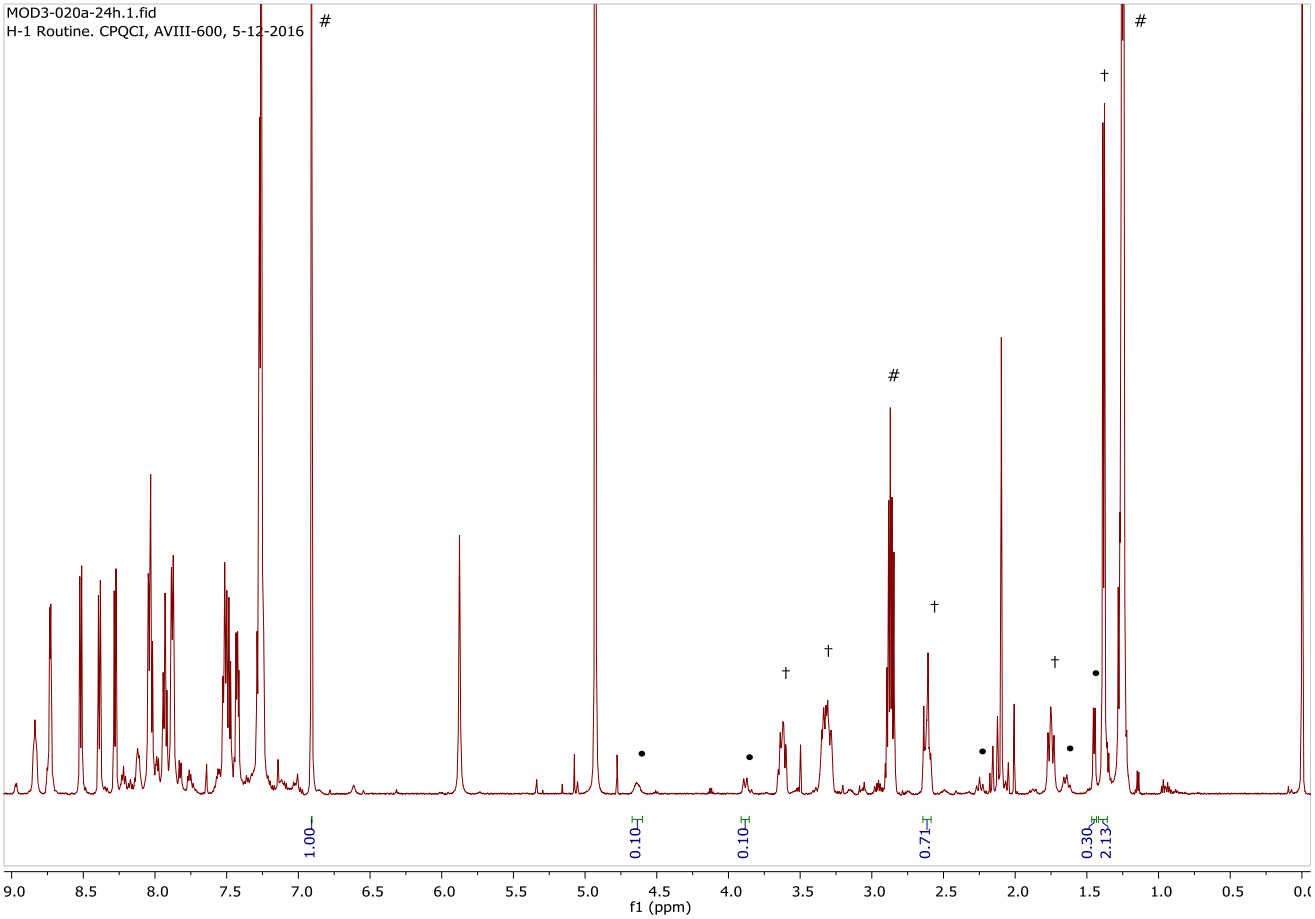
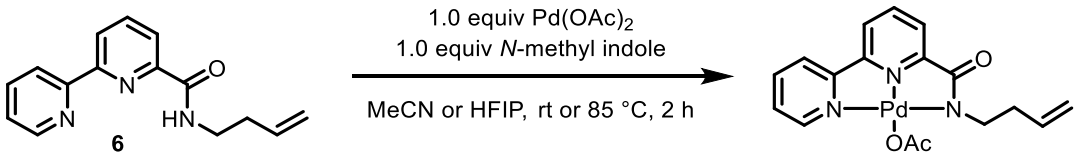
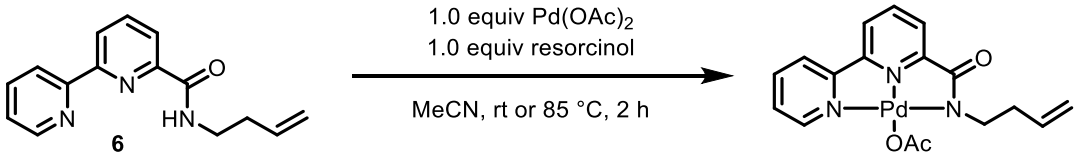


Figure S8. Crude ^{1}H NMR of the reaction of **6** with 4-hydroxycoumarin under conditions A. The spectrum shows: internal standard 1,3,5-triisopropylbenzene (#), 70% product **7a** (†), 10% complex **18** (•).

Attempts to synthesize complex 17 with less reactive nucleophiles



A 1 dram vial containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), alkene **6** (25.3 mg, 0.1 mmol), *N*-methyl indole (12.5 mg, 0.1 mmol) and MeCN (1 mL). The resulting yellow solution was stirred at room temperature for 2 h, during which a yellow solid crashed out of solution. The reaction mixture was filtered, and the filter cake was collected and dried *in vacuo* to afford 18.3 mg (44%) of complex **15** as a yellow powder. The reaction was repeated in HFIP at rt (no solid crashes out–solvent is removed *in vacuo* to isolate product) as well as in MeCN at 85 °C. In all three cases, complex **15** was the only product observed and none of the cyclopalladated complex **17** was observed.



A 1 dram vial containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), alkene **6** (25.3 mg, 0.1 mmol), resorcinol (11.0 mg, 0.1 mmol) and MeCN (1 mL). The resulting yellow solution was stirred at room temperature for 2 h, during which a yellow solid crashed out of solution. The reaction mixture was filtered, and the filter cake was collected and dried *in vacuo* to afford 32.3 mg (77%) of complex **15** as a yellow powder. Repeating the reaction at 85 °C (0.078 mmol scale) afforded 17.5 mg (54%) of complex **15**. In both cases, cyclopalladated complex **17** was not observed.

Computational Details

All calculations were performed with Gaussian 09.[17] The M06[18] density functional and a mixed basis set of SDD for Pd and 6-31G(d) for other atoms were used in geometry optimizations. Single-point energies were calculated with M06 and a mixed basis set of SDD for Pd and 6-311+G(d,p) for other atoms. Solvation energy corrections were calculated using the SMD model.[19] In accordance with the experimental conditions, CH_3CN (ε = 35.7) was used as solvent in the calculations.

To confirm the nature of the stationary points, vibrational frequency calculations were performed for all optimized structures. All optimized transition state structures have only one imaginary (negative) frequency, and all minima (reactants, products, and intermediates) have no imaginary frequencies. The imaginary frequencies of all transition states are provided in the "Cartesian Coordinates and Energies of the Optimized Structures" section below. The reported Gibbs free energies and enthalpies include zero-point vibrational energies and thermal corrections at 298 K.

The conjugate base of 4-hydroxycoumarin was used as the active nucleophile in the calculations. Due to the strong acidity of 4-hydroxycoumarin (pK_a = 4.2)[20] a considerable amount of the conjugate base of 4-hydroxycoumarin is expected under the reaction conditions. A detailed computational investigation of the possible nucleopalladation pathways and the origin of regioselectivity will be published in a separate manuscript in due course.

Intermolecular Protodepalladation in the Reaction of Alkene 6 with 4-Hydroxycoumarin

The intermolecular protodepalladation *via* the association of an HOAc molecule followed by a retro-CMD mechanism is strongly disfavored because the tridentate directing group blocks the binding site for HOAc (Fig. S9). The activation free energy of this process is 25.8 kcal/mol higher than that of the intramolecular protodepalladation (Fig. 3 in the main text).

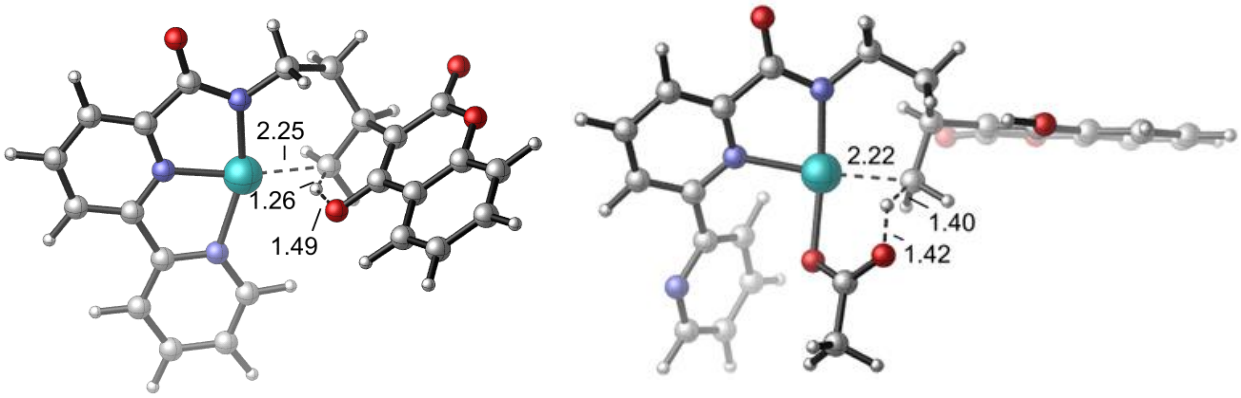


Figure S9. Optimized geometries and relative activation free energies of the intra and intermolecular protodepalladation transition states. The energy of **TS2$_{inter}$** was calculated with respect to **TS2** and a separate HOAc molecule.

The Role of the Tridentate Directing Group in Suppressing *beta*-Hydride Elimination

Experimental results in Table 1 (main text) demonstrated that in the hydrocarbofunctionalization of 4-pentenoic acid derivatives, the use of the tridentate PAQ directing group completely prevents the formation of side products from β-H elimination. (In the reaction of PPA-bearing substrate **6**, no β-H elimination product was observed either – see "Optimization of Directing Groups for Amine Substrates", page S4. This is due to the unfavorable endocyclic β-H elimination from palladacycle **17**. We choose **3a** as a model substrate to investigate the effects of directing group on the rate of β-H elimination because palladacycle intermediate **19** bearing the PAQ directing group (Fig. 10A) is more susceptible to elimination of the exocyclic β-H in this reaction.) We calculated the activation free energies of the competing intramolecular protodepalladation (**TS3**) and β-H elimination (**TS4**) pathways from palladacycle intermediate **19** in the reaction of **3a** (Fig. S10A). **TS3**, which eventually leads to the experimentally observed hydrocarbofunctionalization product, is 7.1 kcal/mol more stable than the β-H elimination transition state **TS4**. **TS4** is destabilized due to the dissociation of the pyridine group to accommodate the hydride that is being transferred to the square planar Pd. In contrast, intramolecular protodepalladation (**TS3**) does not require the partial dissociation of the tridentate directing group. In addition, the electron-donating, strongly coordinating PAQ directing group stabilizes the partial positive charge on the Pd center in the protodepalladation transition state. (The NPA charge on Pd in **19**, **TS3**, and **TS4** is 0.395, 0.527, and 0.206, respectively.) In the reaction of alkene **1**, bearing the bidentate AQ directing group, the selectivity is completely switched to favor β-H elimination from the six-membered palladacycle **22a** (Fig. S10B). These computational results highlight the important role of the tridentate directing group in suppressing β-H elimination and promoting protodepalladation.

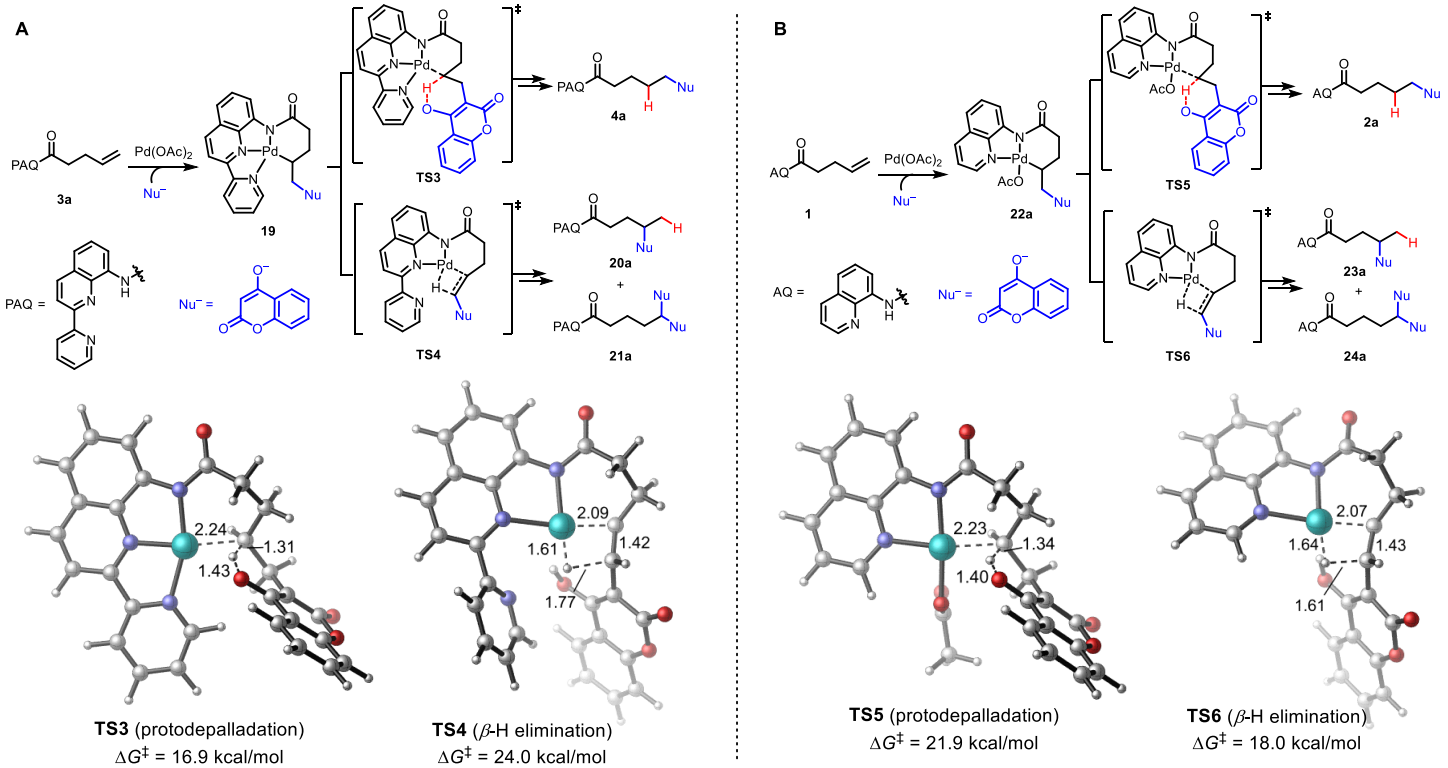


Figure S10. Activation free energies and optimized transition state structures of the intramolecular protodepalladation and β-H elimination in the reactions with (A) **3a** and (B) **1**. The calculated energies are with respect to the six-membered palladacycle intermediates **19** and **22a**, respectively.

The Effect of the Tridentate Directing Group on Regioselectivity

We performed DFT calculations to investigate the catalytic cycle of the hydrocarbofunctionalization of alkene **3a** with the PAQ directing group using 4-hydroxycoumarin as the nucleophile. The computed reaction energy profile is shown in Figure S11. Similar to the high substrate binding energy in the reaction of **6** with the PPA directing group, coordination of the PAQ directing group to the Pd and the acetate-assisted N–H deprotonation to form the reactant complex **S11_1** is highly exergonic by 13.9 kcal/mol. The dissociation of the acetate anion from **S11_1** to form the cationic π-alkene complex **S11_2** is endergonic by 2.0 kcal/mol. Subsequently, anti-Markovnikov and Markovnikov nucleopalladation can take place via the *anti*-attack of the deprotonated 4-hydroxycoumarin (**S11_TS1** and **S11_TS2**). This step requires Gibbs free energy barriers of 14.0 kcal/mol and 17.9 kcal/mol, respectively, with respect to **S11_1**. Upon tautomerization, tricyclic palladacycle intermediates **19** and **S11_3** are formed. The six-membered palladacycle **19** is significantly more stable than the seven-membered palladacycle **S11_3** by 9.4 kcal/mol. This indicates the experimentally observed regioselectivity for the anti-Markovnikov product **4a** in the reaction with **3a** is due to the more favorable formation of the six-membered palladacycle compared to the seven-membered palladacycle. From **19**, an intramolecular protodepalladation takes place via a six-membered cyclic transition state (**TS3**) that protonates the α-C and cleaves the Pd–C bond in a concerted fashion. The dissociation of the strongly coordinating tridentate directing group from **S11_4** to regenerate the active catalyst $Pd(OAc)_2$ and liberate the product **4a** is endergonic by 9.8 kcal/mol.

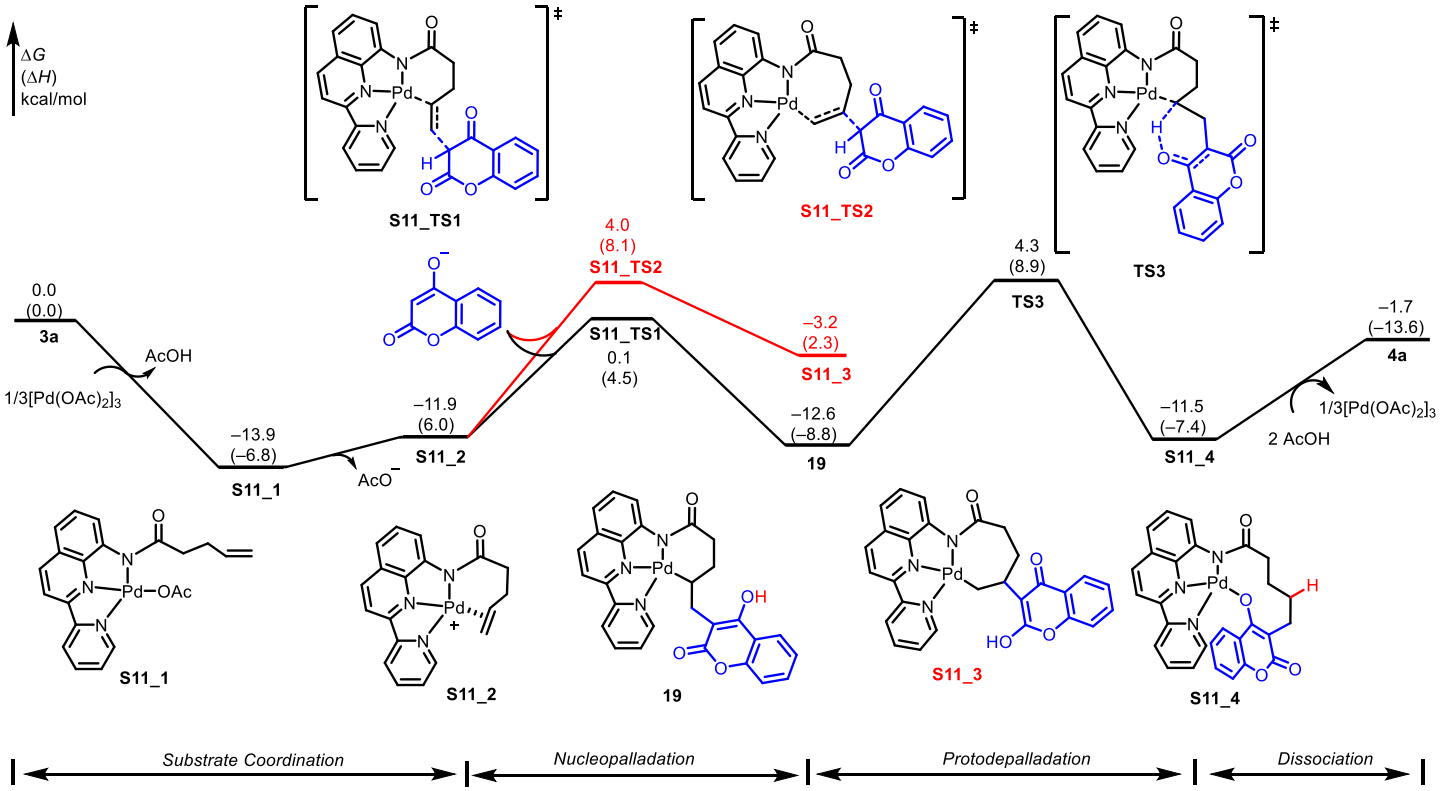


Figure S11. Computed energy profile of the reaction of **3a** with 4-hydroxycoumarin.

We also performed DFT calculations to investigate the two regioisomeric pathways of the hydrocarbofunctionalization of alkene **6** with 4-hydroxycoumarin. The computed reaction energy profile is shown in Figure S12. Markovnikov and *anti*-Markovnikov nucleopalladation of the cationic π-alkene complex **16** take place via the *anti*-attack of the deprotonated 4-hydroxycoumarin to the internal and terminal positions of the double bond, respectively (**TS1** and **TS1'**). Although **TS1'** requires slightly lower kinetic barrier than **TS1** (20.3 and 22.5 kcal/mol, respectively, with respect to **15**), the five-membered palladacycle intermediate **17'** is 2.7 kcal/mol less stable than the six-membered metallacycle **17**. The five-membered metallacycle **17'** is destabilized by the steric repulsion between the secondary alkyl group and the pyridine ligand on the Pd. Subsequent protodepalladation of the more

sterically congested five-membered palladacycle **17'** (via **TS2'**) requires a much higher barrier than the protodepalladation of **17** (via **TS2**). The overall barrier of the *anti*-Markovnikov pathway (from **15** to **TS2'**, shown in red in Figure S12) is higher than that of the Markovnikov pathway (from **15** to **TS1**, shown in black), because of the high barrier to protodepalladation via **TS2'**. Although computations underestimated the energy difference between the two pathways, the calculation results are consistent with the experiment that the Markovnikov product **7a** is preferred in the reaction of **6** with 4-hydroxycoumarin.

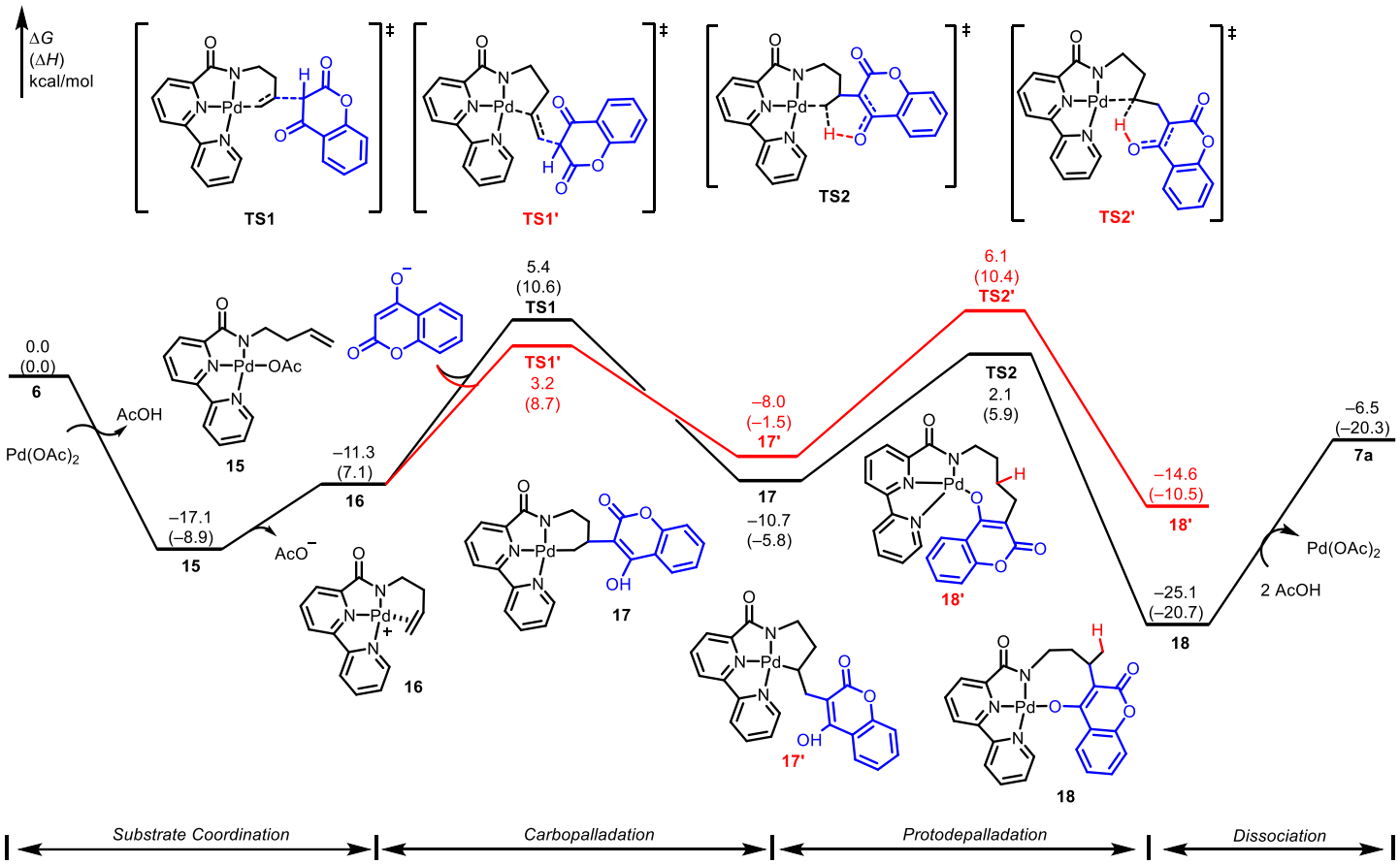


Figure S12. Computed energy profile of the reaction of **6** with 4-hydroxycoumarin.

Cartesian Coordinates and Energies of the Optimized Structures

6

M06 SCF energy:	−819.50245354 a.u.
M06 enthalpy:	−819.209790 a.u.
M06 free energy:	−819.274393 a.u.
M06 SCF energy in solution:	−819.75197392 a.u.
M06 enthalpy in solution:	−819.459310 a.u.
M06 free energy in solution:	−819.523913 a.u.

Cartesian coordinates

ATOM	X	Y	Z	C	−1.712733	1.298725	−0.338383
C	−3.322958	−0.467675	−0.832962	O	−2.555843	2.186185	−0.307795
H	−3.289834	−1.346452	−1.490393	N	−1.974529	−0.000510	−0.609336
H	−3.863638	0.326493	−1.365789	C	−0.259253	1.584058	−0.069443

C	0.125535	2.888227	0.228064	H	−6.995506	−2.698429	0.255823
C	1.881844	0.778287	0.122052	H	−5.357014	−3.199322	0.964230
C	1.468160	3.118552	0.491616	N	0.588054	0.558014	−0.123240
H	−0.630043	3.669146	0.252561	C	2.788409	−0.396566	0.050048
C	2.359378	2.054399	0.442389	C	4.143861	−0.242177	−0.257086
H	1.820564	4.116826	0.745382	C	4.954830	−1.367844	−0.309733
H	3.410666	2.207910	0.677621	H	4.554199	0.741320	−0.478123
H	−1.188517	−0.640512	−0.552441	C	3.028602	−2.663239	0.225819
C	−4.059770	−0.806176	0.463847	C	4.391059	−2.611715	−0.059566
H	−4.044530	0.092126	1.100952	H	6.011897	−1.273063	−0.552553
H	−3.517629	−1.597277	1.003928	H	2.547640	−3.624043	0.422168
C	−5.466425	−1.232078	0.197547	H	4.985563	−3.522089	−0.088888
C	−5.964561	−2.432322	0.481745	N	2.239777	−1.595863	0.281112
H	−6.106060	−0.488338	−0.287588				

7a

M06 SCF energy: −1391.43247544 a.u.
M06 enthalpy: −1390.993014 a.u.
M06 free energy: −1391.079377 a.u.
M06 SCF energy in solution: −1391.84985792 a.u.
M06 enthalpy in solution: −1391.410396 a.u.
M06 free energy in solution: −1391.496759 a.u.

Cartesian coordinates

ATOM	X	Y	Z				
C	0.191128	−1.883622	1.394933	C	4.353467	3.411983	0.181941
H	−0.023017	−2.918434	1.092107	C	6.720394	3.133520	0.185620
C	2.199229	−2.442373	0.100587	H	7.348181	1.107322	−0.197266
O	1.861770	−3.594153	−0.142163	C	5.621302	3.969612	0.329194
N	1.481209	−1.559845	0.833342	H	3.464419	4.036116	0.293113
C	3.498052	−1.882173	−0.417090	H	7.731886	3.517420	0.307598
C	4.332827	−2.707049	−1.165595	H	5.737534	5.027044	0.556044
C	4.922541	−0.090662	−0.580051	N	4.133342	2.131281	−0.097117
C	5.520252	−2.165691	−1.637583	N	3.779322	−0.612633	−0.129183
H	4.029224	−3.732432	−1.358403	H	−2.438740	−2.388739	0.784836
C	5.821415	−0.842002	−1.345718	C	−7.038368	2.075025	−1.602380
H	6.202388	−2.764548	−2.238644	C	−6.155229	2.377240	−0.578922
H	6.730416	−0.385192	−1.732066	C	−5.229622	1.417348	−0.177687
C	−0.895249	−0.934669	0.908417	C	−5.183311	0.161965	−0.789595
H	−0.816335	−0.843831	−0.185894	C	−6.083560	−0.125217	−1.824242
H	−0.736006	0.069965	1.325913	C	−7.004828	0.824164	−2.228263
C	−2.311020	−1.400664	1.269911	H	−7.763355	2.821490	−1.921590
C	−2.499242	−1.651912	2.768035	H	−6.157602	3.341400	−0.076057
H	−3.548098	−1.884198	2.993083	C	−4.197796	−0.775715	−0.306114
H	−1.892610	−2.502463	3.103229	H	−6.040087	−1.103101	−2.297666
C	5.196037	1.331453	−0.249474	H	−7.702214	0.598090	−3.031938
C	6.507869	1.793247	−0.107085	C	−3.351039	−0.452633	0.716089
				C	−3.414009	0.877589	1.301524

O	−4.213915	−1.955770	−0.946980	H	0.251536	−1.871106	2.493884
O	−2.696225	1.300129	2.177858	H	−3.520719	−2.533070	−0.590947
O	−4.377295	1.747464	0.820135	H	1.879930	−0.630070	0.933842
H	−2.215973	−0.767220	3.348016				

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M06 SCF energy: −1175.22078332 a.u.
M06 enthalpy: −1174.880406 a.u.
M06 free energy: −1174.959147 a.u.
M06 SCF energy in solution: −1175.54484235 a.u.
M06 enthalpy in solution: −1175.204465 a.u.
M06 free energy in solution: −1175.283206 a.u.

Cartesian coordinates

ATOM	X	Y	Z	H	−5.225790	1.746979	2.838168
C	−2.959744	0.128594	−0.698428	C	2.840789	0.196403	0.307610
H	−2.863470	−0.694397	−1.422397	C	4.211143	0.054063	0.488653
H	−3.583593	0.911034	−1.152828	C	2.520152	−2.096312	0.611691
C	−1.426619	2.005351	−0.618967	C	4.734893	−1.210138	0.735426
O	−2.238633	2.886003	−0.887548	H	4.865564	0.921001	0.433477
N	−1.636759	0.676530	−0.467793	C	3.881700	−2.303850	0.798354
C	0.028880	2.378046	−0.433350	H	1.790025	−2.903650	0.649570
C	0.547783	3.659803	−0.551628	H	5.806271	−1.336618	0.875457
C	2.169309	1.480014	0.023267	H	4.257600	−3.305771	0.986480
C	1.917388	3.831304	−0.372656	N	2.017807	−0.885115	0.375333
H	−0.132402	4.476196	−0.782169	Pd	0.006673	−0.409872	−0.009218
C	2.743110	2.743603	−0.084544	N	0.842669	1.361377	−0.153528
H	2.356666	4.822983	−0.460636	H	−3.033319	1.325833	1.844374
H	3.812462	2.887245	0.051628	C	−1.096112	−2.841800	−0.861478
C	−3.608750	−0.388155	0.586380	O	−0.733368	−2.451464	−1.965202
H	−2.929460	−1.138967	1.022737	O	−0.836756	−2.240967	0.267377
H	−4.544973	−0.908748	0.330475	C	−1.955096	−4.074361	−0.686852
C	−3.886637	0.696395	1.574268	H	−1.616109	−4.678032	0.162302
C	−5.073829	0.940643	2.122846	H	−2.981769	−3.753427	−0.462721
H	−5.949361	0.338417	1.874300	H	−1.961399	−4.671694	−1.602855

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M06 SCF energy: −946.65781333 a.u.
M06 enthalpy: −946.373759 a.u.
M06 free energy: −946.435224 a.u.
M06 SCF energy in solution: −946.95368585 a.u.
M06 enthalpy in solution: −946.669632 a.u.
M06 free energy in solution: −946.731097 a.u.

Cartesian coordinates

ATOM	X	Y	Z	C	3.474086	−0.625476	−0.056790

H	4.235063	−0.180115	0.596978
H	3.864968	−0.583227	−1.086671
C	2.255776	1.487517	−0.002497
O	3.256408	2.179052	−0.048104
N	2.226977	0.126143	0.038860
C	0.872196	2.083730	0.018271
C	0.588595	3.439273	0.029002
C	−1.418115	1.515354	0.003844
C	−0.749959	3.822326	0.030200
H	1.413886	4.147762	0.033176
C	−1.763518	2.864376	0.018134
H	−1.014064	4.877347	0.039467
H	−2.805559	3.173821	0.019826
C	3.133821	−2.048609	0.338582
H	2.955744	−2.113619	1.421212
H	3.957614	−2.734312	0.092872
C	1.902726	−2.469380	−0.406866
C	0.758164	−2.952113	0.172074
H	0.709119	−3.138006	1.246918
H	−0.005539	−3.421308	−0.447838
C	−2.327343	0.357542	−0.004222
C	−3.710435	0.480392	0.007690
C	−2.499140	−1.959873	−0.004475
C	−4.501537	−0.662530	0.013164
H	−4.170035	1.465535	0.015070
C	−3.886854	−1.905997	0.009625
H	−1.983826	−2.916996	−0.004368
H	−5.585434	−0.577416	0.022728
H	−4.463019	−2.826857	0.017793
N	−1.729259	−0.868481	−0.014932
Pd	0.422192	−0.735272	−0.027751
N	−0.116120	1.189582	0.004487
H	1.977016	−2.472387	−1.499120

17

M06 SCF energy: −1518.16691947 a.u.
M06 enthalpy: −1517.749785 a.u.
M06 free energy: −1517.832922 a.u.
M06 SCF energy in solution: −1518.57799729 a.u.
M06 enthalpy in solution: −1518.160863 a.u.
M06 free energy in solution: −1518.244000 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	−0.118587	−2.851733	0.126946
H	−0.264575	−3.783717	−0.439903
H	0.071998	−3.152782	1.173034
C	−2.502641	−2.701546	0.080891
O	−2.685894	−3.914833	0.168676
N	−1.316925	−2.048396	0.043226
C	−3.707319	−1.779951	0.003171
C	−5.033855	−2.194454	0.002470
C	−4.339691	0.490572	−0.103183
C	−6.020881	−1.212506	−0.059402
H	−5.257080	−3.257518	0.050910
C	−5.690168	0.143205	−0.111088
H	−7.070287	−1.501325	−0.064257
H	−6.474062	0.896172	−0.155610
C	1.092204	−2.098870	−0.403049
H	0.860911	−1.853051	−1.458973
H	1.952729	−2.785401	−0.401827
C	1.418944	−0.831395	0.407744
C	0.564428	0.368999	0.005626
H	0.847390	0.727364	−1.002909
H	0.725473	1.193892	0.720471
C	−3.741269	1.846600	−0.138649
C	−4.502421	3.009777	−0.181788
C	−1.778292	3.097799	−0.141179
C	−3.868415	4.245926	−0.204755
H	−5.588180	2.947346	−0.194981
C	2.481348	4.294868	−0.184432
H	−0.689411	3.075155	−0.120194
H	−4.456281	5.160817	−0.235708
H	−1.944404	5.239556	−0.199228
N	−2.378477	1.906180	−0.118742
Pd	−1.436081	−0.020337	−0.032103
N	−3.429370	−0.482659	−0.052072
H	1.183702	−1.060691	1.457916
C	7.702047	0.863012	−0.266736
C	6.841600	0.869007	0.819307
C	5.527115	0.444107	0.645161
C	5.067128	0.014041	−0.602744
C	5.951877	0.016373	−1.689662

C	7.259602	0.436600	−1.523013	C	2.883068	−0.438416	0.408633
H	8.730830	1.194209	−0.136595	C	3.387009	0.075592	1.674328
H	7.156841	1.195893	1.807478	O	3.305407	−0.771131	−1.928137
C	3.690399	−0.411674	−0.690460	O	2.745417	0.193322	2.691028
H	5.588929	−0.319766	−2.658061	O	4.714586	0.471972	1.726419
H	7.942802	0.434979	−2.369782	H	2.376486	−1.051749	−1.910655

17'

M06 SCF energy: −1518.15760661 a.u.
M06 enthalpy: −1517.741114 a.u.
M06 free energy: −1517.826914 a.u.
M06 SCF energy in solution: −1518.57043257 a.u.
M06 enthalpy in solution: −1518.153940 a.u.
M06 free energy in solution: −1518.239740 a.u.

Cartesian coordinates

ATOM	X	Y	Z				
C	0.205953	−2.856225	−0.274031	C	2.317188	4.233772	0.224970
H	0.268940	−3.818649	0.253810	H	0.577646	2.950995	0.119435
H	−0.071941	−3.077105	−1.320570	H	4.255854	5.176177	0.309598
C	2.686970	−2.778799	−0.261920	H	1.741406	5.152988	0.292455
O	2.924863	−3.982166	−0.325912	N	2.306119	1.843341	0.037655
N	1.484217	−2.168568	−0.241008	Pd	1.450398	−0.195121	−0.143096
C	3.837491	−1.779290	−0.181520	N	3.487218	−0.495436	−0.113890
C	5.185042	−2.116231	−0.170032	H	−0.829144	−0.489361	−1.289571
C	4.340123	0.521963	−0.025303	C	−7.825822	−0.067485	−0.412259
C	6.115302	−1.081388	−0.080928	C	−7.018137	−0.323436	0.683998
H	5.468873	−3.164486	−0.225888	C	−5.648522	−0.091175	0.586978
C	5.708880	0.251291	−0.005772	C	−5.084200	0.391738	−0.599014
H	7.178934	−1.312239	−0.066681	C	−5.916026	0.641408	−1.698170
H	6.449678	1.044546	0.070226	C	−7.277901	0.415647	−1.605203
C	−0.799261	−1.897633	0.350006	H	−8.897129	−0.246411	−0.340431
H	−0.651925	−1.875241	1.441463	H	−7.416548	−0.701187	1.622787
H	−1.831837	−2.253816	0.181352	C	−3.658158	0.600310	−0.604795
C	−0.592094	−0.479393	−0.205248	H	−5.469669	1.013453	−2.617590
C	−1.409413	0.584733	0.520728	H	−7.921463	0.612652	−2.459960
H	−1.093443	0.628603	1.571812	C	−2.900174	0.363040	0.501525
H	−1.187537	1.580081	0.088296	C	−3.519811	−0.155646	1.707820
C	3.669480	1.843606	0.055280	O	−3.153006	1.058494	−1.764899
C	4.384826	3.033245	0.151738	O	−2.947758	−0.425540	2.736059
C	1.665346	3.010654	0.125930	O	−4.892933	−0.352996	1.679187
C	3.704865	4.241014	0.235052	H	−2.184958	1.070028	−1.704463
H	5.472092	3.012519	0.162576				

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M06 SCF energy: −1518.19391972 a.u.
M06 enthalpy: −1517.776837 a.u.
M06 free energy: −1517.859291 a.u.
M06 SCF energy in solution: −1518.60168614 a.u.
M06 enthalpy in solution: −1518.184603 a.u.

M06 free energy in solution: −1518.267057 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.549707	2.647691	0.813670
H	0.366537	3.544920	1.419104
C	−1.859413	2.569056	0.911949
O	−2.025623	3.747273	1.212606
N	−0.694983	1.904016	0.720216
C	−3.065668	1.680663	0.717173
C	−4.385598	2.073027	0.890359
C	−3.725422	−0.500772	0.083471
C	−5.385007	1.134064	0.655591
H	−4.585786	3.096291	1.199165
C	−5.064840	−0.162129	0.248635
H	−6.430011	1.407598	0.785717
H	−5.850580	−0.890766	0.063298
C	1.096300	3.032806	−0.554148
H	1.990415	3.659771	−0.425048
H	0.339930	3.644074	−1.074139
C	1.464377	1.826204	−1.425014
C	1.888609	2.269533	−2.824080
H	2.153454	1.404318	−3.446912
H	1.063447	2.802580	−3.317188
C	−3.165847	−1.796055	−0.346925
C	−3.923605	−2.917545	−0.661196
C	−1.185319	−2.951050	−0.804871
C	−3.274822	−4.082074	−1.058319
H	−5.008739	−2.884735	−0.597631
C	−1.888054	−4.104907	−1.132681
H	−0.097016	−2.877759	−0.834405
H	−3.855012	−4.967453	−1.309407
H	−1.351279	−4.998713	−1.438707
N	−1.809782	−1.837385	−0.426608
Pd	−0.896287	−0.018579	0.102470
N	−2.790931	0.435987	0.330376
H	0.552201	1.220112	−1.554256
C	5.316678	−2.600063	1.459489
C	5.571005	−1.348432	0.923265
C	4.516082	−0.603105	0.397744
C	3.209933	−1.097408	0.398197
C	2.975243	−2.361649	0.952992
C	4.014968	−3.110022	1.477744
H	6.137362	−3.184338	1.872560
H	6.570356	−0.919262	0.900580
C	2.148566	−0.277499	−0.184916
H	1.952939	−2.734387	0.964897
H	3.820232	−4.090997	1.907725
C	2.483654	0.939390	−0.747929
C	3.832976	1.452507	−0.637924
O	0.955742	−0.809740	−0.150129
O	4.215028	2.551374	−0.977735
O	4.807861	0.619610	−0.094936
H	2.756438	2.935738	−2.780331
H	1.283096	2.027784	1.351378

18'

M06 SCF energy: −1518.17678208 a.u.
M06 enthalpy: −1517.759369 a.u.
M06 free energy: −1517.841392 a.u.
M06 SCF energy in solution: −1518.58567552 a.u.
M06 enthalpy in solution: −1518.168262 a.u.
M06 free energy in solution: −1518.250285 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	-1.461007	-3.335524	-0.800159
H	-1.588209	-3.662510	-1.844421
H	-2.100975	-3.995317	-0.191310
C	-3.312987	-1.851099	-0.567599
O	-4.159706	-2.728784	-0.713629
N	-1.969089	-1.975162	-0.647149
C	-3.753637	-0.453817	-0.214689
C	-5.074878	-0.048834	-0.085115
C	-2.964765	1.692610	0.369714
C	-5.324025	1.269608	0.279372
H	-5.858206	-0.779952	-0.270965
C	-4.269992	2.153502	0.509897
H	-6.347784	1.621904	0.387000
H	-4.470844	3.184781	0.789883
C	-0.008915	-3.480346	-0.378601
H	0.627169	-2.929234	-1.079059
H	0.264554	-4.543446	-0.466156
C	0.251947	-3.006060	1.046260
C	1.716052	-2.783718	1.384845
H	1.823766	-2.697692	2.476091
H	2.285598	-3.698566	1.140855

C	-1.720147	2.454768	0.564068
C	-1.686717	3.775695	0.991838
C	0.604995	2.377144	0.480462
C	-0.458856	4.404810	1.163439
H	-2.612343	4.308424	1.196725
C	0.705855	3.696811	0.907127
H	1.487654	1.779761	0.258515
H	-0.418205	5.438731	1.498952
H	1.687452	4.146019	1.030336
N	-0.571287	1.771897	0.307066
Pd	-0.935460	-0.240995	-0.290481
N	-2.766215	0.410408	0.017086
H	-0.150897	-3.753135	1.749717
C	4.949001	2.077736	-1.609324
C	5.245956	1.243001	-0.544325
C	4.300370	0.308203	-0.122978
C	3.054064	0.204632	-0.745158
C	2.780720	1.052020	-1.829066
C	3.713693	1.981804	-2.258106
H	5.686822	2.804868	-1.944868
H	6.200334	1.285277	-0.023743
C	2.070884	-0.770848	-0.248468
H	1.813902	0.951654	-2.320056
H	3.489108	2.628434	-3.104547
C	2.461234	-1.617724	0.773576
C	3.783997	-1.489483	1.368905
O	0.936608	-0.783651	-0.896268
O	4.219689	-2.187567	2.255510
O	4.635085	-0.487535	0.913308
H	-0.312072	-2.083302	1.253305

AcOH

M06 SCF energy:	−228.95407560 a.u.
M06 enthalpy:	−228.886331 a.u.
M06 free energy:	−228.918565 a.u.
M06 SCF energy in solution:	−229.04077022 a.u.
M06 enthalpy in solution:	−228.973026 a.u.
M06 free energy in solution:	−229.005260 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	−0.092767	0.124743	0.000268
O	−0.655047	1.191561	−0.000115
O	−0.761058	−1.047747	0.000034
H	−1.706369	−0.814602	−0.000062
C	1.387849	−0.097926	−0.000082
H	1.680081	−0.679899	0.881722
H	1.679636	−0.680800	−0.881443
H	1.905008	0.863881	−0.000685

Nu$^-$

M06 SCF energy:	−571.34630582 a.u.
M06 enthalpy:	−571.217909 a.u.
M06 free energy:	−571.261273 a.u.
M06 SCF energy in solution:	−571.59895136 a.u.
M06 enthalpy in solution:	−571.470555 a.u.
M06 free energy in solution:	−571.513919 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	−2.706167	−1.111066	0.000015
C	−1.429633	−1.653928	0.000002
C	−0.311838	−0.811866	−0.000003
C	−0.477560	0.577711	0.000007
C	−1.769769	1.102032	0.000020
C	−2.884320	0.275415	0.000024
H	−3.572486	−1.774308	0.000018
H	−1.263108	−2.730588	−0.000006
C	0.713969	1.474343	0.000011
H	−1.848097	2.189301	0.000029
H	−3.888851	0.699736	0.000035
C	1.944453	0.780624	−0.000012
C	2.101546	−0.620050	−0.000034

O	0.898348	−1.399204	−0.000019	O	0.557843	2.710154	0.000008
O	3.121521	−1.288700	−0.000019	H	2.866760	1.358561	−0.000019

OAc^-

M06 SCF energy: −228.37236236 a.u.
M06 enthalpy: −228.318451 a.u.
M06 free energy: −228.352017 a.u.
M06 SCF energy in solution: −228.56318926 a.u.
M06 enthalpy in solution: −228.509278 a.u.
M06 free energy in solution: −228.542844 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.219188	0.000843	−0.011265
O	0.771825	−1.120555	0.002599
O	0.722122	1.146074	0.002461
C	−1.344379	−0.024362	−0.004282
H	−1.738353	−0.987146	−0.359567
H	−1.707335	0.128763	1.024258
H	−1.754743	0.795353	−0.611890

$[Pd(OAc)_2]_3$

M06 SCF energy: −1754.06796388 a.u.
M06 enthalpy: −1753.716170 a.u.
M06 free energy: −1753.815922 a.u.
M06 SCF energy in solution: −1754.46384745 a.u.
M06 enthalpy in solution: −1754.112054 a.u.
M06 free energy in solution: −1754.211806 a.u.

Cartesian coordinates

ATOM	X	Y	Z	C	−0.787234	−2.457778	−1.875672
Pd	−1.776456	−0.423092	−0.006144	O	−1.654621	−1.556378	−1.691284
C	−0.692421	−2.483051	1.867212	O	0.287566	−2.628936	−1.239829
O	−1.685794	−2.061046	1.213272	C	−1.095465	−3.453428	−2.959620
O	0.525230	−2.207311	1.676506	H	−1.578631	−2.950885	−3.803026
C	−1.807243	1.826829	1.882172	H	−0.188343	−3.969383	−3.283703
O	−0.933417	2.474294	1.244482	H	−1.804344	−4.191321	−2.564399
O	−2.174804	0.633866	1.684950	C	−1.731130	1.918804	−1.867941
C	−2.517282	2.568820	2.980338	O	−0.519640	2.221389	−1.672197
H	−3.360283	3.116009	2.540532	O	−2.424666	1.081692	−1.229189
H	−2.914071	1.868891	3.720671	Pd	1.252736	−1.317694	−0.003661
H	−1.845333	3.293647	3.447822	C	2.504521	0.645832	1.875096
C	−1.004853	−3.411818	3.007695	O	2.623044	−0.430521	1.226989
H	−0.093590	−3.864695	3.405389	O	1.660524	1.566540	1.686371
H	−1.511114	−2.845541	3.798128	C	2.523896	0.565019	−1.868663
H	−1.699145	−4.187336	2.667690	O	2.146764	1.581277	−1.224487

O	2.174828	−0.635523	−1.683277	H	3.414522	0.045883	−3.747232
C	3.470564	0.837759	3.011136	H	3.428924	1.806897	−3.370058
H	3.498040	1.882846	3.328868	Pd	0.525478	1.754154	0.007636
H	3.152313	0.211905	3.853466	C	−2.409885	2.629465	−3.005947
H	4.466983	0.499837	2.709645	H	−2.162699	3.695285	−2.984789
C	3.529710	0.798006	−2.961635	H	−2.031106	2.219579	−3.950075
H	4.535729	0.691472	−2.537346	H	−3.491685	2.481298	−2.964524

TS1

M06 SCF energy: −1518.12119939 a.u.
M06 enthalpy: −1517.707410 a.u.
M06 free energy: −1517.791096 a.u.
M06 SCF energy in solution: −1518.54848958 a.u.
M06 enthalpy in solution: −1518.134700 a.u.
M06 free energy in solution: −1518.218386 a.u.
Imaginary frequency: −69.7080 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z	H	−5.068358	3.015252	−0.241036
C	−0.010054	−2.952065	0.583669	C	−1.925525	4.131337	0.352357
H	0.055588	−3.960822	0.153700	H	−0.207073	2.814109	0.452223
H	−0.185121	−3.078052	1.665538	H	−3.830602	5.127140	0.204405
C	−2.359536	−2.814311	−0.033380	H	−1.350487	5.022050	0.589188
O	−2.613049	−3.996226	0.158072	N	−1.936385	1.774824	−0.020917
N	−1.136169	−2.223307	−0.004356	Pd	−1.155826	−0.211275	−0.077257
C	−3.483087	−1.826969	−0.294048	N	−3.125871	−0.547494	−0.196150
C	−4.809842	−2.145827	−0.545828	H	0.890647	−0.396082	1.670250
C	−3.952377	0.493674	−0.356162	C	5.805380	0.716816	−2.361936
C	−5.709153	−1.095606	−0.720148	C	4.949175	1.509579	−1.612407
H	−5.101445	−3.192151	−0.596477	C	4.394886	0.998111	−0.438648
C	−5.292854	0.233956	−0.631058	C	4.697169	−0.297376	−0.012434
H	−6.754992	−1.309847	−0.930868	C	5.558814	−1.079729	−0.783361
H	−6.006057	1.041840	−0.777577	C	6.113634	−0.583692	−1.951796
C	1.266306	−2.158349	0.340004	H	6.237672	1.115831	−3.278834
H	1.570246	−2.258731	−0.712740	H	4.693961	2.524511	−1.911688
H	2.097310	−2.540722	0.956088	C	4.104649	−0.820991	1.239908
C	1.062922	−0.702976	0.639313	H	5.769613	−2.084601	−0.420025
C	0.923679	0.232453	−0.380875	H	6.785358	−1.198987	−2.548010
H	1.208158	−0.065754	−1.393824	C	3.247532	0.101094	1.904263
H	1.017051	1.294539	−0.156518	C	2.906976	1.385023	1.414039
C	−3.291118	1.805285	−0.179969	H	2.814329	−0.187929	2.859952
C	−3.988272	3.003848	−0.114285	O	4.300527	−1.990307	1.605454
C	−1.278911	2.902399	0.262996	O	2.038790	2.140506	1.837573
C	−3.295516	4.181950	0.144705	O	3.537721	1.808913	0.240215

TS1'

M06 SCF energy: −1518.12269338 a.u.
M06 enthalpy: −1517.708988 a.u.
M06 free energy: −1517.794146 a.u.
M06 SCF energy in solution: −1518.54279768 a.u.
M06 enthalpy in solution: −1518.129092 a.u.
M06 free energy in solution: −1518.214250 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.425359	-3.270154	-0.607289
H	0.404810	-4.117321	0.092333
H	0.626861	-3.683933	-1.610139
C	2.694486	-2.734990	0.211859
O	3.078764	-3.885001	0.383286
N	1.483915	-2.334765	-0.240225
C	3.606319	-1.558832	0.516387
C	4.916571	-1.662335	0.958447
C	3.710748	0.802364	0.510905
C	5.624213	-0.481725	1.175616
H	5.343893	-2.650058	1.114783
C	5.032232	0.761310	0.954400
H	6.655308	-0.524105	1.520713
H	5.597692	1.673988	1.127156
C	-0.866719	-2.468007	-0.610908
H	-1.180842	-2.254273	0.422870
H	-1.690795	-3.014111	-1.091139
C	-0.627538	-1.163772	-1.340403
C	-1.098114	0.076346	-0.920753
H	-1.425247	0.228575	0.109351
H	-0.900368	0.961231	-1.518334
C	2.888383	2.001289	0.233751
C	3.364982	3.289342	0.438939
C	0.813623	2.828688	-0.413013
C	2.528893	4.375440	0.203724
H	4.382200	3.444776	0.790768
C	1.230606	4.142685	-0.219060
H	-0.214251	2.633405	-0.732372
H	2.892144	5.388660	0.361559
H	0.527984	4.951236	-0.400540
N	1.617435	1.781126	-0.209988
Pd	1.189057	-0.378979	-0.425043
N	3.069807	-0.353891	0.319895
H	-0.375926	-1.262348	-2.402278
C	-5.601690	-0.139606	2.683558
C	-4.941908	0.933335	2.104077
C	-4.374694	0.784325	0.839055
C	-4.470085	-0.428739	0.151265
C	-5.136479	-1.497717	0.755129
C	-5.700835	-1.362320	2.012377
H	-6.045101	-0.023379	3.671626
H	-4.849413	1.893643	2.607502
C	-3.885237	-0.560597	-1.202546
H	-5.191544	-2.427170	0.190135
H	-6.219952	-2.198719	2.476956
C	-3.229635	0.625988	-1.666760
C	-3.125595	1.835216	-0.924961
H	-2.901764	0.661034	-2.703249
O	-3.909971	-1.627996	-1.823462
O	-2.457547	2.815865	-1.225952
O	-3.710961	1.864556	0.337841

TS2

M06 SCF energy: −1518.13220451 a.u.
M06 enthalpy: −1517.720876 a.u.
M06 free energy: −1517.802416 a.u.
M06 SCF energy in solution: −1518.55346252 a.u.
M06 enthalpy in solution: −1518.142134 a.u.
M06 free energy in solution: −1518.223674 a.u.
Imaginary frequency: −973.6372 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z
C	0.673391	−2.569981	−0.114167
H	1.351984	−2.118799	0.630089
C	−1.563483	−2.657721	0.828060
O	−1.454131	−3.751404	1.370115
N	−0.658059	−2.012353	0.050607
C	−2.835169	−1.861069	1.025177
C	−3.949215	−2.289325	1.734460

C	−3.829622	0.241302	0.596938
C	−5.022343	−1.411697	1.857545
H	−3.940220	−3.285899	2.169017
C	−4.975019	−0.136218	1.291866
H	−5.911445	−1.715931	2.406070
H	−5.817694	0.543062	1.397435
C	1.249772	−2.382582	−1.509496
C	1.687244	−0.957912	−1.888719
C	0.504937	0.003675	−2.001802
H	−0.284091	−0.441098	−2.630282
H	0.785334	0.952383	−2.485625
C	−3.545082	1.536027	−0.052240
C	−4.409475	2.622613	−0.005149
C	−1.982540	2.781899	−1.248302
C	−4.033444	3.819637	−0.602820
H	−5.366403	2.537917	0.504624
C	−2.798006	3.907282	−1.228925
H	−1.000360	2.796917	−1.717862
H	−4.699309	4.679042	−0.569761
H	−2.459696	4.828546	−1.694860
N	−2.344740	1.626286	−0.689045
Pd	−1.201873	−0.169265	−0.540180
N	−2.823692	−0.639372	0.498570
C	5.936102	1.762854	2.249573
C	6.068484	0.799722	1.262327
C	4.948062	0.416816	0.524973
C	3.697817	0.990756	0.771010
C	3.586259	1.961870	1.771540
C	4.692945	2.348939	2.508044
H	6.810021	2.061458	2.827065
H	7.022711	0.326560	0.040139
C	2.546282	0.553827	−0.021928
H	2.603009	2.394808	1.946145
H	4.596707	3.104829	3.285699
C	2.777682	−0.419173	−0.993720
C	4.075381	−0.984924	−1.215668
O	1.400044	1.090855	0.212409
O	4.355744	−1.837297	−2.036021
O	5.130187	−0.526343	−0.426135
H	0.530111	0.504255	−0.845850
H	0.609635	−3.641803	0.115140
H	0.520777	−2.753884	−2.250112
H	2.142845	−3.016435	−1.594113
H	2.117176	−1.057876	−2.900003

TS2'

M06 SCF energy:	−1518.13124321 a.u.
M06 enthalpy:	−1517.720159 a.u.
M06 free energy:	−1517.802327 a.u.
M06 SCF energy in solution:	−1518.54614772 a.u.
M06 enthalpy in solution:	−1518.135064 a.u.
M06 free energy in solution:	−1518.217232 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.596347	-3.294048	0.080713
H	0.536681	-3.959312	0.953187
H	0.913669	-3.912225	-0.777571
C	2.786541	-2.474847	0.874704
O	3.227512	-3.530591	1.311342
N	1.575268	-2.249581	0.317907
C	3.630140	-1.211535	0.910331
C	4.916196	-1.118285	1.421518
C	3.645016	1.066503	0.262552
C	5.562861	0.113247	1.340104
H	5.372654	-2.002805	1.859645
C	4.938215	1.216974	0.758756
H	6.571987	0.221360	1.732657
H	5.457488	2.170569	0.697994
C	-0.735150	-2.619129	-0.220275
H	-1.162660	-2.224295	0.713703
H	-1.459857	-3.353218	-0.609474
C	-0.560759	-1.481031	-1.232096
C	-1.854490	-1.124419	-1.992612
H	-1.608042	-0.349738	-2.741957
H	-2.184253	-2.012268	-2.551944
C	2.786101	2.088561	-0.373537
C	3.170718	3.412174	-0.542627
C	0.690383	2.533306	-1.295210
C	2.276741	4.311745	-1.114110
H	4.156045	3.743108	-0.222391
C	1.015770	3.872134	-1.488908
H	-0.294408	2.127058	-1.523552
H	2.564596	5.351676	-1.252503
H	0.283358	4.549148	-1.919850
N	1.554781	1.663876	-0.770228
Pd	1.235281	-0.421066	-0.376110
N	3.060559	-0.133188	0.368920
H	0.171025	-1.765462	-2.007018
C	-5.822932	1.568452	2.358941

C	-6.041599	0.607234	1.384776
C	-4.982102	0.200622	0.574068
C	-3.707143	0.756374	0.736206
C	-3.506380	1.723308	1.726387
C	-4.554222	2.130239	2.534636
H	-6.650253	1.884556	2.992674
H	-7.017824	0.152224	1.230935
C	-2.649159	0.291441	-0.147851
H	-2.506019	2.138099	1.837854
H	-4.393210	2.882610	3.304746
C	-2.956813	-0.663128	-1.096611
C	-4.263055	-1.235928	-1.225084
O	-1.440836	0.750738	-0.032600
O	-4.611453	-2.096017	-2.004303
O	-5.243628	-0.747251	-0.354990
H	-0.648276	-0.274614	-0.596490

3a

M06 SCF energy: −973.02754324 a.u.
M06 enthalpy: −972.685676 a.u.
M06 free energy: −972.756309 a.u.
M06 SCF energy in solution: −973.31595703 a.u.
M06 enthalpy in solution: −972.974090 a.u.
M06 free energy in solution: −973.044723 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	−3.307788	−0.915317	−0.149732
H	−2.814269	−1.500311	0.642052
H	−2.936718	−1.336350	−1.099232
C	−2.857969	0.531068	−0.064548
O	−3.635464	1.468807	−0.038375
N	−1.491795	0.664663	−0.030441
C	−0.739350	1.834492	0.001314
C	0.680467	1.636740	−0.002790
C	−1.245181	3.118266	0.031204
C	1.544403	2.763898	0.011112
C	−0.366240	4.222069	0.051378
H	−2.319772	3.263263	0.036260
C	2.430154	0.136244	−0.027642
C	2.929659	2.490144	−0.013721
C	0.997501	4.066115	0.039097
H	−0.795844	5.222270	0.075494
C	3.375361	1.195242	−0.035067
H	3.633773	3.322588	−0.026010
H	1.665701	4.926694	0.050375
H	4.440726	0.981514	−0.085779
N	1.132069	0.364585	−0.018923
H	−0.908189	−0.171585	−0.060374
C	−4.819569	−1.066695	−0.058809
H	−5.278696	−0.416329	−0.818356
H	−5.173279	−0.692166	0.912243
C	−5.241212	−2.486447	−0.254184
C	−5.899660	−3.217201	0.641035
H	−4.960326	−2.940739	−1.210116
H	−6.177599	−4.251950	0.449496
H	−6.194634	−2.802480	1.605871
C	2.869936	−1.282669	−0.029647
C	4.121369	−1.647645	0.476970
C	2.375184	−3.460143	−0.522815
C	4.489948	−2.986294	0.465302
H	4.788551	−0.899329	0.900114
C	3.601624	−3.920620	−0.049017
H	1.648698	−4.165733	−0.932172
H	5.456300	−3.294344	0.861050
H	3.845226	−4.980194	−0.080269
N	2.007189	−2.183929	−0.517819

19

M06 SCF energy: −1671.70579771 a.u.
M06 enthalpy: −1671.238715 a.u.
M06 free energy: −1671.326167 a.u.
M06 SCF energy in solution: −1672.14752242 a.u.
M06 enthalpy in solution: −1671.680440 a.u.

M06 free energy in solution: −1671.767892 a.u.

Cartesian coordinates

ATOM	X	Y	Z	C	5.764527	0.596867	−0.108368
C	1.598487	0.017057	0.737190	C	7.097385	0.878773	−0.393916
C	0.777464	−0.277614	−0.521908	C	8.041837	−0.126145	−0.259717
H	1.407914	−0.745740	1.510926	H	8.414898	−2.189249	0.257101
C	0.426434	−2.804575	−0.214120	H	6.024903	−2.671893	0.758027
H	1.050074	0.468051	−1.290556	H	7.361124	1.883551	−0.715482
H	0.873759	−3.766091	−0.494499	H	9.085812	0.087898	−0.481277
Pd	−1.203549	0.054197	−0.174507	C	3.523536	1.440869	0.000753
C	−1.080007	−3.041202	−0.232705	C	3.073212	0.145136	0.465973
O	−1.492096	−4.197586	−0.247036	O	3.649190	−2.122053	0.975053
N	−1.857327	−1.916806	−0.178161	C	3.968152	−0.877674	0.586150
C	−3.248220	−1.992319	−0.063539	O	4.868541	1.604593	−0.255919
C	−3.951774	−0.745468	0.071031	O	2.812818	2.408448	−0.178065
C	−4.054684	−3.129134	−0.060718	C	−2.627121	2.639876	0.081524
C	−5.362343	−0.638719	0.193482	C	−2.905211	3.999034	0.158602
C	−5.455201	−3.024763	0.069661	C	−0.348760	3.086514	−0.147875
H	−3.586187	−4.100736	−0.160726	C	−1.865293	4.919368	0.078313
C	−3.676925	1.598570	0.152469	H	−3.931635	4.337179	0.281203
C	−5.884126	0.675513	0.301198	C	−0.567192	4.459732	−0.075179
C	−6.121607	−1.824643	0.194339	H	0.661470	2.686804	−0.261164
H	−6.030410	−3.950093	0.066718	H	−2.074990	5.985553	0.137311
C	−5.071280	1.787533	0.278413	H	0.278790	5.138575	−0.138869
H	−6.963060	0.797687	0.398446	N	−1.343057	2.198607	−0.074020
H	−7.205523	−1.780237	0.288754	C	0.979364	−1.675469	−1.082315
H	−5.502687	2.783464	0.353965	H	0.685156	−2.641106	0.849475
N	−3.204734	0.369612	0.070774	H	1.263194	0.962024	1.187629
C	7.664978	−1.407789	0.154892	H	2.057285	−1.866003	−1.252702
C	6.338497	−1.681847	0.435667	H	0.513512	−1.736591	−2.077235
C	5.369325	−0.677755	0.308272	H	2.687309	−2.201562	1.082428

TS3

M06 SCF energy: −1671.66121342 a.u.
M06 enthalpy: −1671.200519 a.u.
M06 free energy: −1671.289261 a.u.
M06 SCF energy in solution: −1672.11285605 a.u.
M06 enthalpy in solution: −1671.652162 a.u.
M06 free energy in solution: −1671.740904 a.u.
Imaginary frequency: 1432.4943 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z	H	1.461893	0.048181	−2.541185
C	1.766664	−0.863908	−1.993734	C	−0.231045	−3.213148	0.420752
C	0.540603	−1.416287	−1.254136	H	−0.292259	−1.374248	−1.975702
H	2.048911	−1.575300	−2.787568	Pd	−1.006946	−0.132948	−0.270222

C	−1.732498	−3.059328	0.247930	H	3.146368	−0.013193	2.893352
O	−2.481189	−4.023019	0.332948	H	7.432122	0.083445	0.387530
N	−2.180594	−1.761998	0.082540	H	7.435288	0.415540	2.864039
C	−3.514929	−1.395461	0.257237	C	4.229971	−0.546318	−1.820127
C	−3.764661	0.012370	0.301134	C	2.970052	−0.596881	−1.134779
C	−4.632842	−2.209125	0.418145	O	1.732668	−0.394126	0.861834
C	−5.047103	0.589030	0.485310	C	2.862166	−0.395985	0.234780
C	−5.908630	−1.641088	0.616989	O	5.370696	−0.313873	−1.050444
H	−4.508840	−3.284653	0.390649	O	4.400968	−0.675339	−3.013516
C	−2.739123	2.139205	0.095136	C	−1.430047	2.766743	−0.163674
C	−5.107173	2.004344	0.468775	C	−1.219047	4.138528	−0.152472
C	−6.141190	−0.282490	0.652469	C	0.823310	2.382327	−0.633922
H	−6.748015	−2.323913	0.740041	C	0.058296	4.633881	−0.395741
C	−3.984312	2.778026	0.271186	H	−2.043918	4.815976	0.055292
H	−6.076075	2.484608	0.604175	C	1.095886	3.747285	−0.637195
H	−7.141825	0.121131	0.796279	H	1.608568	1.644782	−0.803808
H	−4.062836	3.862146	0.240192	H	0.236899	5.706929	−0.388635
N	−2.692465	0.815433	0.141299	H	2.109283	4.091347	−0.823391
C	5.291623	0.226362	3.048262	N	−0.402341	1.904674	−0.415181
C	4.101596	0.016440	2.372504	C	0.670987	−2.856025	−0.759621
C	4.094213	−0.171528	0.986456	H	1.710679	−3.027019	−0.444144
C	5.307253	−0.142868	0.290225	H	−0.074412	−4.262813	0.695590
C	6.509514	0.070159	0.963875	H	0.074274	−2.596479	1.281304
C	6.495961	0.252502	2.337584	H	0.486785	−3.542894	−1.600327
H	5.291573	0.367584	4.127503	H	0.774755	−0.782019	−0.128235

TS4

M06 SCF energy: −1671.65880305 a.u.
M06 enthalpy: −1671.197541 a.u.
M06 free energy: −1671.286905 a.u.
M06 SCF energy in solution: −1672.10156593 a.u.
M06 enthalpy in solution: −1671.640304 a.u.
M06 free energy in solution: −1671.729668 a.u.
Imaginary frequency: −395.3858 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z				
C	−1.067049	−1.615502	−0.930811	N	2.636077	−1.558412	0.209352
C	−0.185320	−2.430895	−0.172386	C	3.593854	−0.684649	0.683908
H	−0.395162	0.001097	−1.170336	C	3.333122	0.709027	0.461116
H	−1.116550	−1.833405	−2.000761	C	4.795184	−1.023042	1.302482
C	1.989959	−3.502642	−1.103006	C	4.300970	1.690628	0.820620
H	−0.364699	−2.458998	0.908362	C	5.732631	−0.039806	1.662392
H	2.404281	−4.491297	−1.333842	H	4.999277	−2.071664	1.482648
Pd	0.882085	−0.649381	−0.447476	C	1.863806	2.349083	−0.323033
C	2.920194	−2.871295	−0.070190	C	3.995106	3.037069	0.540610
O	3.877867	−3.506937	0.356215	C	5.510668	1.295520	1.428769
				H	6.658117	−0.358435	2.140143

C	2.794085	3.368366	−0.028273	C	−2.571908	−0.398837	0.734414
H	4.721880	3.807795	0.797796	O	−4.767334	−1.227597	−0.767837
H	6.239779	2.055584	1.705959	O	−3.426590	−2.179053	−2.246631
H	2.522872	4.404401	−0.219750	C	0.521100	2.745688	−0.812548
N	2.140707	1.067606	−0.113032	C	0.385602	3.591387	−1.913486
C	−5.507264	0.898078	2.693745	C	−1.744508	2.690702	−0.485085
C	−4.197147	0.633878	2.336311	C	−0.891457	3.971604	−2.308234
C	−3.916887	−0.096687	1.172567	H	1.267426	3.922456	−2.459733
C	−4.979411	−0.541016	0.380419	C	−1.983018	3.518673	−1.578408
C	−6.299883	−0.278426	0.734205	H	−2.572368	2.320398	0.124859
C	−6.557002	0.439206	1.891218	H	−1.030740	4.615017	−3.174969
H	−5.720842	1.462423	3.598894	H	−2.999449	3.797805	−1.845388
H	−3.365548	0.981102	2.945006	N	−0.527518	2.302677	−0.108262
H	−7.094948	−0.642887	0.088037	C	0.514603	−3.653064	−0.727823
H	−7.587401	0.648357	2.172639	H	2.058387	−2.894397	−2.018885
C	−3.503763	−1.555206	−1.215190	H	−0.772692	0.225978	1.022279
C	−2.368840	−1.124728	−0.408125	H	−0.028878	−4.002837	−1.618166
O	−1.612367	0.090128	1.521207	H	0.419316	−4.451095	0.021986

TS2$_{inter}$

M06 SCF energy:	−1747.09538261 a.u.
M06 enthalpy:	−1746.614036 a.u.
M06 free energy:	−1746.709930 a.u.
M06 SCF energy in solution:	−1747.57328108 a.u.
M06 enthalpy in solution:	−1747.091934 a.u.
M06 free energy in solution:	−1747.187828 a.u.
Imaginary frequency:	−1423.4575 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z	C	1.724032	0.825871	−0.194867
C	0.425479	2.988862	−0.148960	C	0.945111	−0.247646	0.566182
H	0.305163	3.950732	0.369761	H	1.557789	−0.551293	1.434218
H	0.676308	3.233772	−1.196329	H	0.829536	−1.164327	−0.029552
C	−1.937944	3.032658	−0.267259	C	−4.026164	−1.316779	−0.729632
O	−1.970224	4.252493	−0.416164	C	−2.995178	−1.785900	−1.545870
N	−0.833762	2.271878	−0.109895	C	−4.835795	−3.421420	−0.393876
C	−3.212459	2.241033	−0.303264	C	−2.894594	−3.152844	−1.758805
C	−4.440791	2.874661	−0.383578	H	−2.285554	−1.091003	−1.992553
C	−4.188693	0.133228	−0.489667	C	−3.824750	−3.994183	−1.160509
C	−5.585389	2.090632	−0.459941	H	−5.596225	−4.050365	0.072448
H	−4.452216	3.961613	−0.379430	H	−2.100234	−3.554024	−2.385452
C	−5.458339	0.710655	−0.529458	H	−3.780882	−5.072596	−1.295282
H	−6.570534	2.551837	−0.497153	N	−4.951933	−2.112093	−0.184909
H	−6.317054	0.052797	−0.635227	Pd	−1.186008	0.326515	0.330563
C	1.578510	2.210559	0.453375	N	−3.097950	0.901227	−0.315230
H	1.402688	2.121332	1.543039	H	1.298241	0.894635	−1.205291
H	2.488556	2.811618	0.308464	C	7.966418	−1.080253	−0.492925

C	6.902716	−1.211784	−1.370543	O	4.044459	1.048473	1.706415
C	5.660048	−0.698505	−1.009430	O	2.513720	−0.657036	−2.454791
C	5.475697	−0.052683	0.217094	O	4.641616	−0.856776	−1.887838
C	6.562842	0.067277	1.093451	H	3.147871	1.398575	1.827310
C	7.799474	−0.442733	0.740923	C	−1.307053	−1.691999	2.290139
H	8.940458	−1.479126	−0.770146	O	−1.797783	−1.524003	1.130903
H	7.003536	−1.703927	−2.335012	O	−0.398958	−0.961506	2.772406
C	4.157832	0.462804	0.501856	C	−1.859004	−2.810774	3.123932
H	6.412914	0.567015	2.047465	H	−1.048051	−3.322755	3.651081
H	8.641219	−0.347250	1.423324	H	−2.528282	−2.385708	3.881834
C	3.144017	0.347035	−0.403629	H	−2.427311	−3.514019	2.509273
C	3.362547	−0.399652	−1.633515	H	0.049861	−0.236185	1.642738

1

M06 SCF energy: −726.11882503 a.u.
M06 enthalpy: −725.851124 a.u.
M06 free energy: −725.908098 a.u.
M06 SCF energy in solution: −726.33729418 a.u.
M06 enthalpy in solution: −726.069593 a.u.
M06 free energy in solution: −726.126567 a.u.
Imaginary frequency: −22.8808 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z				
C	−2.836696	−0.385369	0.256243	H	2.498185	3.531710	−0.149952
H	−2.760399	−0.894223	1.231931	C	3.989660	−2.069934	−0.035596
H	−2.708212	−1.175687	−0.499864	H	5.301390	−0.371986	−0.146408
C	−1.696855	0.610482	0.150206	H	4.446095	1.996265	−0.185296
O	−1.868455	1.816173	0.126319	H	4.778694	−2.818356	−0.048507
N	−0.463568	0.008208	0.095402	N	1.629206	−1.629599	0.056760
C	0.791474	0.608072	0.023219	H	−0.407790	−1.008203	0.120192
C	1.898398	−0.299960	0.003383	C	−4.203562	0.268351	0.108120
C	1.025200	1.967154	−0.032402	H	−4.276785	0.754845	−0.874910
C	3.220538	0.213558	−0.072192	H	−4.286886	1.074349	0.852286
C	2.346822	2.454400	−0.107026	C	−5.307081	−0.724517	0.278009
H	0.182248	2.648758	−0.019235	C	−6.206790	−1.027125	−0.653594
C	2.638515	−2.470470	0.037070	H	−5.346118	−1.238198	1.244269
C	4.272781	−0.729387	−0.089464	H	−6.988935	−1.764815	−0.484544
C	3.428543	1.611019	−0.127027	H	−6.198508	−0.538825	−1.629001
				H	2.389518	−3.532922	0.079665

22a

M06 SCF energy: −1653.25031081 a.u.
M06 enthalpy: −1652.801302 a.u.
M06 free energy: −1652.892184 a.u.
M06 SCF energy in solution: −1653.75338504 a.u.
M06 enthalpy in solution: −1653.304376 a.u.

M06 free energy in solution: −1653.395258 a.u.

Cartesian coordinates

ATOM	X	Y	Z	H	−0.627318	−2.770963	0.865027
C	1.242672	2.339197	−0.551084	C	−0.693113	3.195894	0.831289
C	0.280376	2.057718	0.612088	H	−1.288047	3.000934	1.736881
H	0.710765	2.301187	−1.515932	H	−0.123332	4.125913	1.030047
H	1.624505	3.370551	−0.447993	H	−1.035133	3.540347	−1.273614
C	−1.620668	3.465227	−0.341994	C	4.642444	−2.771169	−1.651211
H	−2.109998	4.442098	−0.232193	C	3.520085	−1.965240	−1.743194
Pd	−0.790013	0.327895	0.416493	C	3.524282	−0.677589	−1.194028
C	−2.761881	2.497094	−0.616007	C	4.673453	−0.227943	−0.536646
O	−3.765815	2.965930	−1.158509	C	5.806131	−1.033720	−0.439717
N	−2.576053	1.186390	−0.264948	C	5.787095	−2.301515	−0.999735
C	−3.600772	0.257175	−0.422119	H	4.630129	−3.772515	−2.078562
C	−3.293707	−1.117386	−0.120598	H	2.610727	−2.311473	−2.228553
C	−4.917955	0.511922	−0.818509	H	6.676080	−0.644489	0.085170
C	−4.271659	−2.147051	−0.215511	H	6.669869	−2.935240	−0.923913
C	−5.875267	−0.513128	−0.905352	C	3.626213	1.851462	0.073907
H	−5.189405	1.529176	−1.067239	C	2.424602	1.421200	−0.609571
C	−1.668115	−2.644201	0.563789	O	1.304715	−0.271137	−1.863420
C	−3.863902	−3.462196	0.104680	C	2.378450	0.201062	−1.216363
C	−5.584576	−1.824835	−0.616496	O	4.725867	0.990735	0.045100
H	−6.884787	−0.242274	−1.216865	O	3.786511	2.899768	0.654858
C	−2.573177	−3.719380	0.492357	C	2.599741	−1.371080	2.447580
H	−4.599737	−4.265273	0.036478	H	3.346678	−0.592759	2.233200
H	−6.334200	−2.612892	−0.691754	H	2.719616	−1.685625	3.489668
H	−2.243500	−4.724844	0.745362	H	2.803004	−2.206903	1.766415
N	−2.024797	−1.412956	0.267024	O	0.537710	−0.371981	3.152156
O	0.894970	−0.760354	0.960882	H	0.870557	1.890795	1.527338
C	1.213202	−0.786252	2.215174	H	0.484700	0.031740	−1.397068

TS5

M06 SCF energy: −1653.21420043 a.u.
M06 enthalpy: −1652.770880 a.u.
M06 free energy: −1652.862865 a.u.
M06 SCF energy in solution: −1653.71750906 a.u.
M06 enthalpy in solution: −1653.274189 a.u.
M06 free energy in solution: −1653.366174 a.u.
Imaginary frequency: −1581.8602 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z	C	0.199601	−2.914285	−0.404906
C	−1.773840	0.045746	−1.962683	H	0.295761	−0.355416	−2.116171
C	−0.519285	−0.673045	−1.444699	Pd	1.013177	0.214243	−0.097398
H	−2.029532	−0.381589	−2.948129	C	1.706094	−2.744744	−0.477472
H	−1.515638	1.096398	−2.172356	O	2.419734	−3.719419	−0.709636

N	2.172140	−1.478802	−0.210037	H	−3.141356	−0.899588	2.898333
C	3.513018	−1.217188	0.023636	H	−7.442702	0.059246	0.617904
C	3.811084	0.094016	0.521366	H	−7.433226	−0.488795	3.058343
C	4.596233	−2.081790	−0.139850	C	−4.240161	0.244382	−1.689083
C	5.131811	0.491822	0.857045	C	−2.982390	−0.038133	−1.073140
C	5.902254	−1.676602	0.187541	O	−1.755892	−0.611366	0.860883
H	4.407149	−3.077023	−0.520991	C	−2.869715	−0.347622	0.277699
C	2.953703	2.181993	1.131726	O	−5.391287	0.178138	−0.880681
C	5.305666	1.803169	1.354394	O	−4.438600	0.536710	−2.851540
C	6.189738	−0.425136	0.680097	C	−0.620797	−2.199674	−1.475794
H	6.710258	−2.393283	0.039074	H	−1.674295	−2.483676	−1.329747
C	4.230656	2.644484	1.496602	H	0.024092	−3.995777	−0.464639
H	6.311271	2.131817	1.620353	H	−0.154251	−2.566803	0.577943
H	7.207390	−0.125333	0.929319	H	−0.338007	−2.569654	−2.475138
H	4.346341	3.656921	1.876188	H	−0.787191	−0.485182	−0.144887
N	2.768008	0.961177	0.671462	H	2.059616	2.799796	1.204142
C	−5.288226	−0.734317	3.148115	C	0.085359	2.783487	−0.896954
C	−4.103424	−0.697845	2.430426	O	−0.026386	1.967912	0.107180
C	−4.102630	−0.393382	1.066215	O	0.850976	2.659785	−1.848783
C	−5.319232	−0.122899	0.432176	C	−0.888538	3.943480	−0.806419
C	−6.517018	−0.157123	1.148211	H	−0.670064	4.693058	−1.572997
C	−6.497273	−0.462520	2.500382	H	−1.905614	3.556555	−0.955308
H	−5.278580	−0.973080	4.210857	H	−0.863110	4.397886	0.191063

TS6

M06 SCF energy: −1424.74641694 a.u.
M06 enthalpy: −1424.358769 a.u.
M06 free energy: −1424.438082 a.u.
M06 SCF energy in solution: −1425.12431338 a.u.
M06 enthalpy in solution: −1424.736665 a.u.
M06 free energy in solution: −1424.815978 a.u.
Imaginary frequency: −565.5555 cm^{-1}

Cartesian coordinates

ATOM	X	Y	Z				
C	−1.256444	1.519128	−0.742415	C	4.307382	−0.068958	1.637663
C	−0.373820	2.014183	0.270695	C	4.015033	−2.197428	−0.171285
H	−0.532118	0.366380	−1.630032	C	5.178581	−1.173496	1.662900
C	1.819515	3.398145	0.265977	H	4.436465	0.755681	2.329451
H	−0.537152	1.624229	1.282575	C	1.945236	−2.017984	−1.991828
H	2.163717	4.357696	0.668247	C	3.815545	−3.222565	−1.120946
Pd	0.778569	0.579170	−0.674584	C	5.052838	−2.223641	0.785742
C	2.586783	2.310454	1.023075	H	5.974514	−1.185871	2.406174
O	3.394763	2.618194	1.890837	C	2.793287	−3.136764	−2.033035
N	2.379779	1.044784	0.537615	H	4.488879	−4.079998	−1.117447
C	3.269818	0.001711	0.714052	H	5.731632	−3.074946	0.811448
C	3.119013	−1.094097	−0.199152	H	2.625175	−3.911387	−2.776800
				N	2.098515	−1.040805	−1.114238

C	−5.206435	−2.648174	1.725608	O	−1.491042	−0.983212	0.917360
C	−3.953870	−2.115699	1.481515	C	−2.543465	−0.369367	0.371564
C	−3.816255	−0.983804	0.665890	O	−4.888301	0.679695	−0.700161
C	−4.960709	−0.407682	0.105578	O	−3.737268	2.257567	−1.740886
C	−6.224230	−0.938315	0.348501	C	0.280010	3.373628	0.240231
C	−6.340051	−2.056445	1.158095	H	2.176860	3.337227	−0.773771
H	−5.309440	−3.525831	2.359735	H	1.117408	−1.914011	−2.691201
H	−3.060192	−2.558727	1.914419	H	−1.404347	2.169826	−1.608477
H	−7.087324	−0.459384	−0.107714	H	−0.060438	3.922967	−0.649562
H	−7.325360	−2.476865	1.350544	H	−0.101395	3.933057	1.107322
C	−3.695965	1.300209	−1.005447	H	−0.644117	−0.609428	0.580271
C	−2.485164	0.750584	−0.413840				

S11_1

M06 SCF energy: −1328.74871970 a.u.
M06 enthalpy: −1328.358981 a.u.
M06 free energy: −1328.441962 a.u.
M06 SCF energy in solution: −1329.10566113 a.u.
M06 enthalpy in solution: −1328.715922 a.u.
M06 free energy in solution: −1328.798903 a.u.

Cartesian coordinates

ATOM	X	Y	Z				
C	3.041185	0.750536	0.065402	H	4.794042	1.773752	−0.684580
H	2.967082	0.061757	−0.787804	C	5.396569	0.119229	0.534698
H	2.741055	0.151496	0.940899	C	6.416730	−0.269747	−0.227288
C	2.043807	1.869004	−0.109254	H	5.180329	−0.434239	1.455724
O	2.413866	3.035673	−0.160526	H	7.051690	−1.111726	0.043608
N	0.716041	1.478226	−0.169491	H	6.662270	0.249526	−1.154880
C	−0.299232	2.429908	−0.103370	C	−2.758915	−1.546862	0.042070
C	−1.625932	1.911293	0.027911	C	−3.812237	−2.442750	0.174253
C	−0.212636	3.824096	−0.123874	C	−1.255153	−3.300027	−0.301855
C	−2.793988	2.712026	0.152213	C	−3.560805	−3.806047	0.064137
C	−1.366945	4.621753	−0.001663	H	−4.819133	−2.079684	0.365951
H	0.758980	4.288398	−0.230341	C	−2.267683	−4.245948	−0.180416
C	−2.893907	−0.085615	0.122530	H	−0.219433	−3.566562	−0.502450
C	−4.025037	2.024222	0.271171	H	−4.375122	−4.519683	0.169860
C	−2.639511	4.109709	0.138033	H	−2.035017	−5.302942	−0.274499
H	−1.232567	5.702565	−0.022265	N	−1.495327	−1.995995	−0.190376
C	−4.087633	0.649678	0.257636	Pd	−0.086187	−0.452213	−0.241598
H	−4.940133	2.607947	0.367758	C	2.020851	−2.253348	0.314697
H	−3.510681	4.756218	0.226965	O	1.599840	−2.173294	1.464711
H	−5.044822	0.139894	0.339326	O	1.482034	−1.666465	−0.718194
N	−1.738542	0.568106	0.025047	C	3.270661	−3.027516	−0.033504
C	4.470879	1.250422	0.226420	H	3.147905	−3.580583	−0.971424
H	4.498805	1.998124	1.033655	H	4.091057	−2.310531	−0.187093
				H	3.540731	−3.705668	0.781210

S11_2

M06 SCF energy: −1100.18607989 a.u.
M06 enthalpy: −1099.852508 a.u.

M06 free energy: −1099.919077 a.u.
M06 SCF energy in solution: −1100.51979534 a.u.
M06 enthalpy in solution: −1100.186223 a.u.
M06 free energy in solution: −1100.252792 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	2.348751	−3.058383	0.194257
C	2.767820	−1.611834	−0.016662
O	3.957016	−1.373807	−0.146140
N	1.794778	−0.629845	−0.044233
C	2.152503	0.739342	−0.056469
C	1.066961	1.653514	0.019887
C	3.416211	1.314116	−0.106016
C	1.210101	3.066363	0.059652
C	3.572571	2.719730	−0.060839
H	4.289826	0.679943	−0.176769
C	−1.299434	1.818294	0.081214
C	0.018331	3.821790	0.116593
C	2.516160	3.595578	0.021575
H	4.587036	3.111553	−0.099033
C	−1.225083	3.220675	0.124412
H	0.090785	4.908262	0.145295
H	2.668381	4.672518	0.047370
H	−2.127274	3.826144	0.152236
N	−0.170263	1.116176	0.042517
C	1.106673	−3.345025	1.016124
C	−0.196554	−3.060796	0.342691
C	−0.367808	−2.870601	−1.007987
H	−1.086169	−3.202060	0.964354
H	−1.357780	−2.902216	−1.463284
H	0.467470	−2.914759	−1.706374
Pd	−0.236111	−0.850085	−0.110525
H	1.092481	−4.413483	1.289587
H	3.217492	−3.519446	0.677228
H	2.289940	−3.544474	−0.791767
H	1.143218	−2.807340	1.975251
C	−2.513429	0.988437	0.054997
C	−3.799808	1.502588	0.142181
C	−3.356185	−1.178843	−0.096210
C	−4.888740	0.638302	0.106379
H	−3.950455	2.574507	0.242081
C	−4.666886	−0.725817	−0.015138
H	−3.142191	−2.242284	−0.190584
H	−5.900095	1.031889	0.174982
H	−5.487590	−1.436596	−0.047378
N	−2.304947	−0.356669	−0.064536

S11_3

M06 SCF energy: −1671.68030128 a.u.
M06 enthalpy: −1671.214215 a.u.
M06 free energy: −1671.304417 a.u.
M06 SCF energy in solution: −1672.12876808 a.u.
M06 enthalpy in solution: −1671.662682 a.u.
M06 free energy in solution: −1671.752884 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	−0.736885	0.255820	−0.754539
C	−1.629608	−0.209459	0.386077
H	−1.016315	1.282495	−1.051556
H	−0.840435	−0.379446	−1.640380
C	−0.754916	−2.614295	0.014536
H	−1.511385	0.570839	1.165777
Pd	1.242182	0.254338	−0.261983
C	0.728142	−2.872963	−0.202267
O	1.071287	−4.016616	−0.479918
N	1.603172	−1.813619	−0.047491
C	2.969963	−2.062632	0.091295
C	3.835529	−0.918566	0.199462
C	3.623483	−3.294639	0.195311
C	5.243660	−0.995239	0.394185
C	5.013242	−3.369782	0.406608
H	3.045471	−4.204719	0.099123
C	3.896328	1.438962	0.128593
C	5.941569	0.236697	0.449959
C	5.833748	−2.265685	0.504866
H	5.453927	−4.363194	0.486213
C	5.295713	1.444470	0.316154
H	7.021712	0.212887	0.594659
H	6.908203	−2.361282	0.653045
H	5.858936	2.374650	0.348100
N	3.253335	0.285079	0.094512
C	−7.756640	0.652582	1.235721
C	−6.426328	0.601080	1.612109
C	−5.451583	0.187233	0.694230
C	−5.843310	−0.177559	−0.595659

C	−7.181029	−0.129349	−0.980765
C	−8.130552	0.287866	−0.062262
H	−8.511491	0.976295	1.949229
H	−6.114047	0.879770	2.615897
H	−7.442988	−0.423978	−1.994285
H	−9.177957	0.326786	−0.355974
C	−3.582604	−0.713158	−1.242102
C	−3.115889	−0.239515	0.052600
O	−3.734751	0.480604	2.251694
C	−4.041771	0.128755	0.989595
O	−4.942062	−0.601846	−1.508402
O	−2.913752	−1.200145	−2.122580
C	3.019913	2.610543	−0.060487
C	3.487307	3.920174	−0.009441
C	0.862432	3.371681	−0.480278
C	2.605018	4.975430	−0.200697
H	4.540301	4.110942	0.183446
C	1.266513	4.701097	−0.441241
H	−0.176401	3.103690	−0.669500
H	2.963601	6.001890	−0.161212
H	0.539108	5.493100	−0.597484
N	1.700620	2.351245	−0.297909
C	−1.147238	−1.529637	1.017284
H	−1.141153	−3.590240	0.331561
H	−1.221082	−2.428263	−0.964313
H	−1.942152	−1.915258	1.676311
H	−0.285465	−1.310743	1.665853
H	−2.781678	0.369835	2.393496

S11_4

M06 SCF energy:	-1671.69724158 a.u.
M06 enthalpy:	-1671.230564 a.u.
M06 free energy:	-1671.318589 a.u.
M06 SCF energy in solution:	-1672.14482117 a.u.
M06 enthalpy in solution:	-1671.678144 a.u.
M06 free energy in solution:	-1671.766169 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	3.886978	-1.650999	-1.584624
C	2.657917	-2.325559	-2.175442
H	4.581402	-2.415824	-1.206381
H	4.452711	-1.150914	-2.389020
C	0.322569	-3.113755	-1.604497
H	2.992215	-3.072822	-2.912169
Pd	-0.560601	-0.061786	-0.597785
C	-0.655454	-3.198090	-0.462139
O	-1.021936	-4.272794	-0.009706
N	-1.130982	-1.972860	-0.002272
C	-2.356701	-1.926178	0.657543
C	-3.069105	-0.694328	0.534838
C	-3.010111	-2.928493	1.372454
C	-4.360800	-0.460869	1.077258
C	-4.293924	-2.704639	1.908959
H	-2.524737	-3.887882	1.498946
C	-2.937399	1.510596	-0.318552
C	-4.910412	0.826077	0.868133
C	-4.976907	-1.512975	1.779696
H	-4.759661	-3.522015	2.457760
C	-4.218925	1.803900	0.188428
H	-5.899039	1.042698	1.271975
H	-5.964457	-1.371903	2.215332
H	-4.647063	2.795473	0.061526
N	-2.440956	0.285395	-0.148229
C	1.380348	2.270742	2.691042
C	1.335848	1.495024	1.543925
C	2.469103	0.829523	1.051766
C	3.656908	0.987182	1.780158
C	3.718581	1.773689	2.930108
C	2.581582	2.415659	3.386640
H	0.476238	2.760979	3.048354
H	0.386526	1.380582	1.024548
H	4.675298	1.853780	3.441599
H	2.626494	3.025175	4.287507
C	4.877116	-0.458602	0.319807
C	3.667732	-0.681807	-0.450006
O	1.470701	-0.041932	-0.981934
C	2.496451	-0.001683	-0.164569
O	4.810678	0.397071	1.408787
O	5.959297	-0.949379	0.091853
C	-2.011731	2.442374	-0.979761
C	-2.327522	3.741420	-1.358694
C	0.183165	2.706545	-1.745740
C	-1.346384	4.530468	-1.951103
H	-3.329953	4.131478	-1.198968
C	-0.073247	4.013057	-2.148247
H	1.154489	2.222571	-1.854778
H	-1.580543	5.548448	-2.255258
H	0.715787	4.604231	-2.604539
N	-0.759586	1.952520	-1.186050
C	1.769328	-2.988308	-1.127379
H	1.787223	-2.391000	-0.205715
H	0.074508	-2.247509	-2.234643

H	0.186586	-4.019715	-2.209466	H	2.067010	-1.583792	-2.726643
H	2.157320	-3.978828	-0.848004				

S11_TS1

M06 SCF energy:	-1671.65709771 a.u.
M06 enthalpy:	-1671.194195 a.u.
M06 free energy:	-1671.282840 a.u.
M06 SCF energy in solution:	-1672.12214796 a.u.
M06 enthalpy in solution:	-1671.659245 a.u.
M06 free energy in solution:	-1671.747890 a.u.

Cartesian coordinates

ATOM	X	Y	Z				
C	1.058644	-1.277238	0.366764	C	4.425074	0.087417	0.908236
C	0.709426	-1.425959	-0.965525	C	4.917147	1.366965	1.182409
H	1.635921	-0.425055	0.717696	C	5.209908	2.227995	0.134554
H	0.792695	-2.000953	1.134927	H	5.241354	2.512393	-2.010161
C	-0.749530	-3.493173	-0.591500	H	4.338950	0.202111	-2.469078
H	1.229705	-0.796447	-1.695774	H	5.069305	1.652222	2.221550
Pd	-0.872990	-0.152940	-0.244797	H	5.611840	3.217565	0.352220
C	-2.156044	-2.971397	-0.339337	C	3.604866	-2.004900	1.802332
O	-3.074489	-3.776391	-0.259147	C	3.399499	-2.443113	0.463814
N	-2.321683	-1.608597	-0.187051	O	3.399499	-2.013053	-1.859090
C	-3.583218	-1.048412	0.071946	C	3.675571	-1.676892	-0.694166
C	-3.624936	0.376041	0.199164	O	4.133466	-0.699040	1.966628
C	-4.812537	-1.688090	0.212138	O	3.330786	-2.586312	2.829146
C	-4.805723	1.125954	0.442067	C	-0.897156	2.776850	-0.034902
C	-5.990319	-0.948966	0.457419	C	-0.498703	4.106235	0.000671
H	-4.858734	-2.765710	0.128225	C	1.293705	2.099794	-0.469914
C	-2.292476	2.337325	0.153895	C	0.839503	4.427723	-0.206259
C	-4.651859	2.530144	0.535553	H	-1.231170	4.888308	0.185788
C	-6.018607	0.422785	0.573905	C	1.751754	3.413472	-0.450003
H	-6.919675	-1.507647	0.557431	H	1.987026	1.277551	-0.662699
C	-3.424595	3.141862	0.393627	H	1.159573	5.466979	-0.178923
H	-5.536913	3.136680	0.726007	H	2.808051	3.605199	-0.620806
H	-6.945032	0.961200	0.765286	N	0.013796	1.784739	-0.265854
H	-3.337240	4.223080	0.469558	C	0.155529	-2.703115	-1.523308
N	-2.451740	1.024070	0.077160	H	3.015347	-3.454651	0.344794
C	5.000514	1.834325	-1.192316	H	-0.898278	-4.502547	-0.990879
C	4.508178	0.563052	-1.454824	H	-0.264260	-3.639872	0.387030
C	4.223339	-0.325107	-0.414501	H	1.030344	-3.316527	-1.796918
				H	-0.369702	-2.491243	-2.466339

S11_TS2

M06 SCF energy:	-1671.65548689 a.u.
M06 enthalpy:	-1671.192442 a.u.
M06 free energy:	-1671.280463 a.u.
M06 SCF energy in solution:	-1672.11644689 a.u.
M06 enthalpy in solution:	-1671.653402 a.u.
M06 free energy in solution:	-1671.741423 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.771287	-1.092743	1.231391
C	1.102118	-1.476955	-0.073435
H	1.377693	-0.333050	1.729685
H	0.366784	-1.836390	1.919982
C	-0.477567	-3.480659	0.025525
H	1.630706	-0.756629	-0.701233
Pd	-0.859784	-0.088937	0.329536
C	-1.922981	-3.014967	0.171727
O	-2.792905	-3.872103	0.257162
N	-2.187507	-1.658996	0.172913
C	-3.498771	-1.179051	0.034962
C	-3.634202	0.235886	-0.145058
C	-4.695464	-1.892570	0.024768
C	-4.874304	0.905871	-0.314508
C	-5.929447	-1.233063	-0.162313
H	-4.668645	-2.965868	0.164213
C	-2.431556	2.276805	-0.210549
C	-4.818556	2.315581	-0.432878
C	-6.048320	0.129168	-0.328370
H	-6.829404	-1.846377	-0.162795
C	-3.627135	3.006186	-0.375036
H	-5.753299	2.861915	-0.557089
H	-7.018444	0.606666	-0.454477
H	-3.617795	4.091320	-0.442431
N	-2.497399	0.956151	-0.130053
C	4.893572	2.240471	0.673070
C	4.475750	1.070079	1.289778
C	4.219400	-0.081435	0.540199
C	4.388312	-0.043953	-0.848221
C	4.799588	1.133219	-1.479335
C	5.051914	2.264669	-0.717747
H	5.116165	3.127684	1.265220
H	4.340848	0.993148	2.368554
H	4.922055	1.128225	-2.560503
H	5.386410	3.176410	-1.211960
C	3.669460	-2.331380	-1.111691
C	3.405865	-2.364991	0.285893
O	3.535248	-1.353515	2.416436
C	3.735159	-1.320772	1.195527
O	4.148058	-1.114208	-1.641007
O	3.437870	-3.201950	-1.926875
H	3.080332	-3.322037	0.690983
C	-1.059741	2.806797	-0.090883
C	-0.736495	4.143986	-0.277545
C	1.178750	2.289244	0.317224
C	0.588168	4.552922	-0.159492
H	-1.515495	4.860902	-0.525790
C	1.563340	3.614159	0.138751
H	1.925207	1.526358	0.550521
H	0.850538	5.598091	-0.308462
H	2.614881	3.873241	0.232347
N	-0.090844	1.892266	0.215637
C	0.492512	-2.640246	-0.790344
H	-0.572878	-4.471772	-0.432528
H	-0.069992	-3.676056	1.029779
H	1.310263	-3.270479	-1.179854
H	-0.005713	-2.259465	-1.696485

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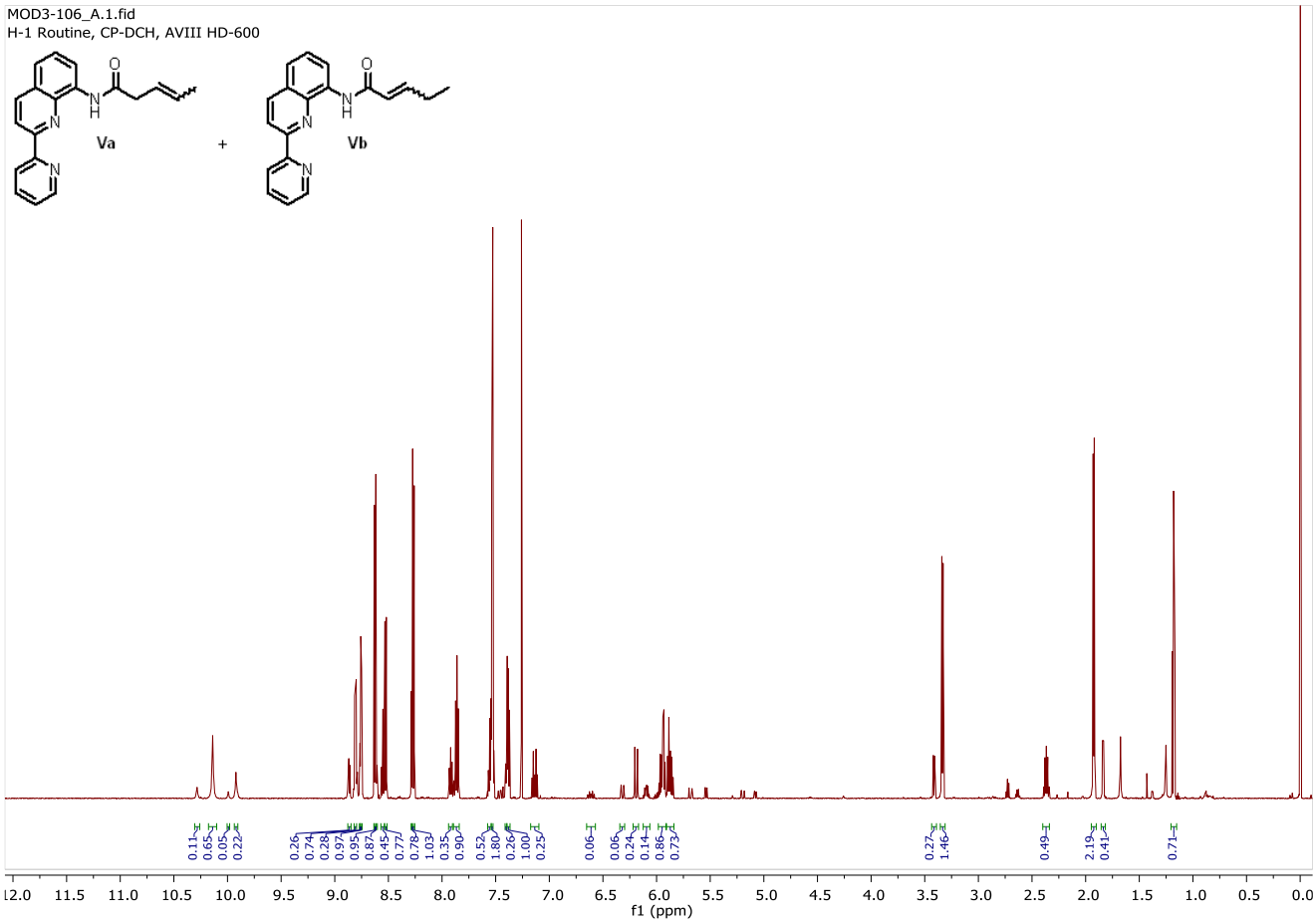
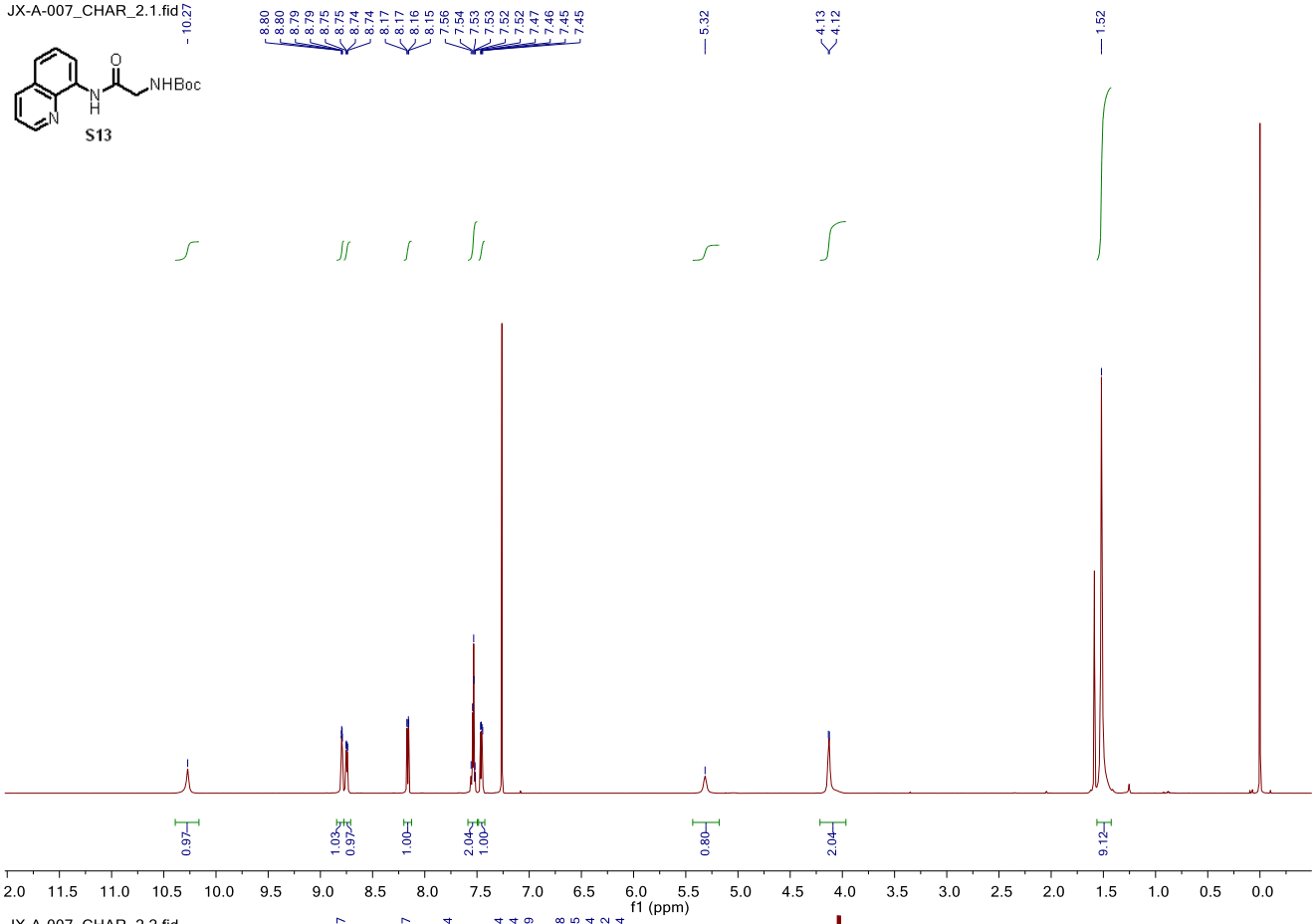
^{1}H and ^{13}C NMR Spectra

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8.80
8.79
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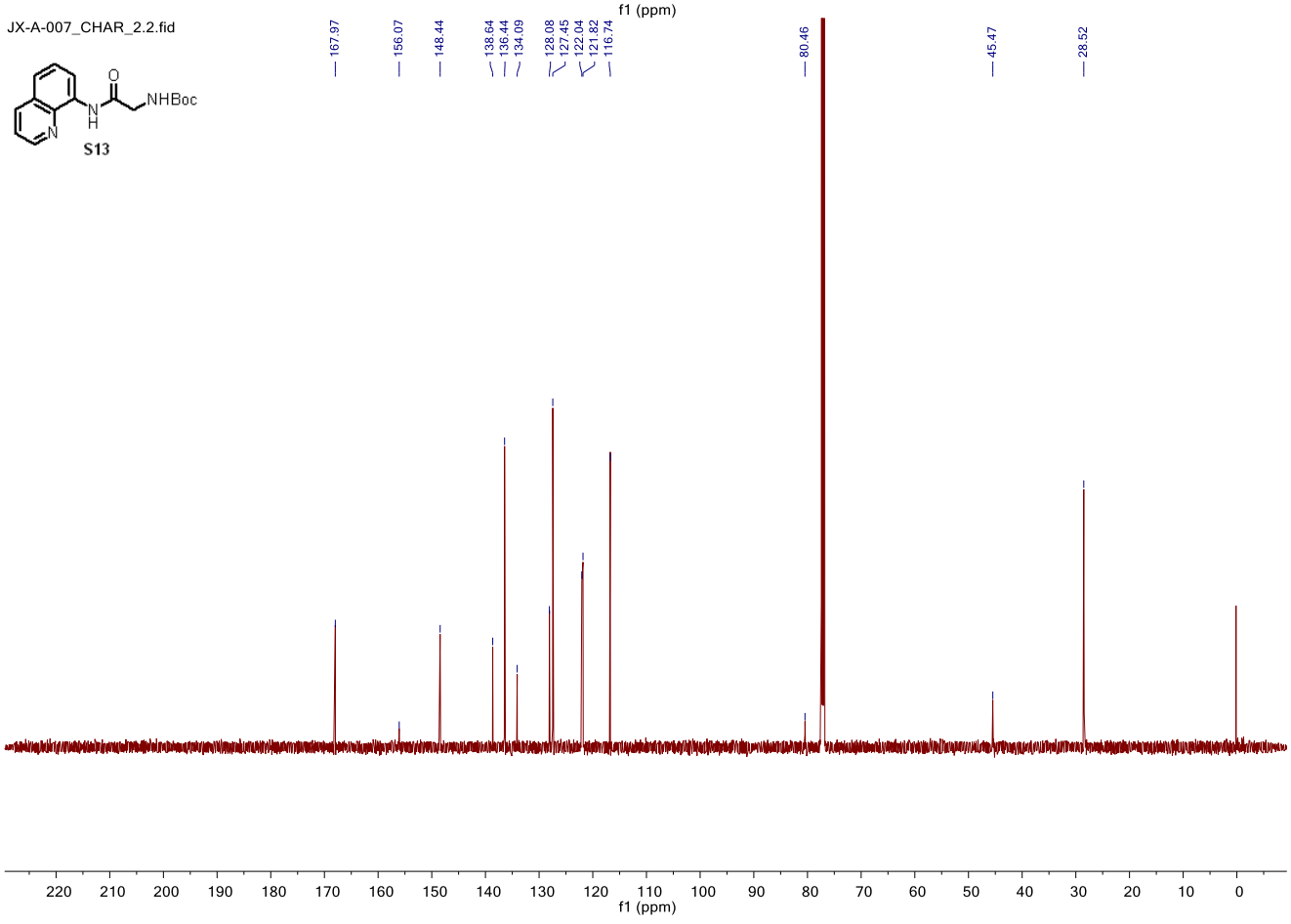
8.75
8.75
8.74
8.74
8.17
8.17
8.16
8.15
7.56
7.54
7.53
7.53
7.52
7.52
7.47
7.46
7.45
7.45
5.32
4.13
4.12
1.52
NHBoc
S13
0.97
1.03
0.97
1.00
2.04
1.00
0.80
2.04
9.12
f1 (ppm)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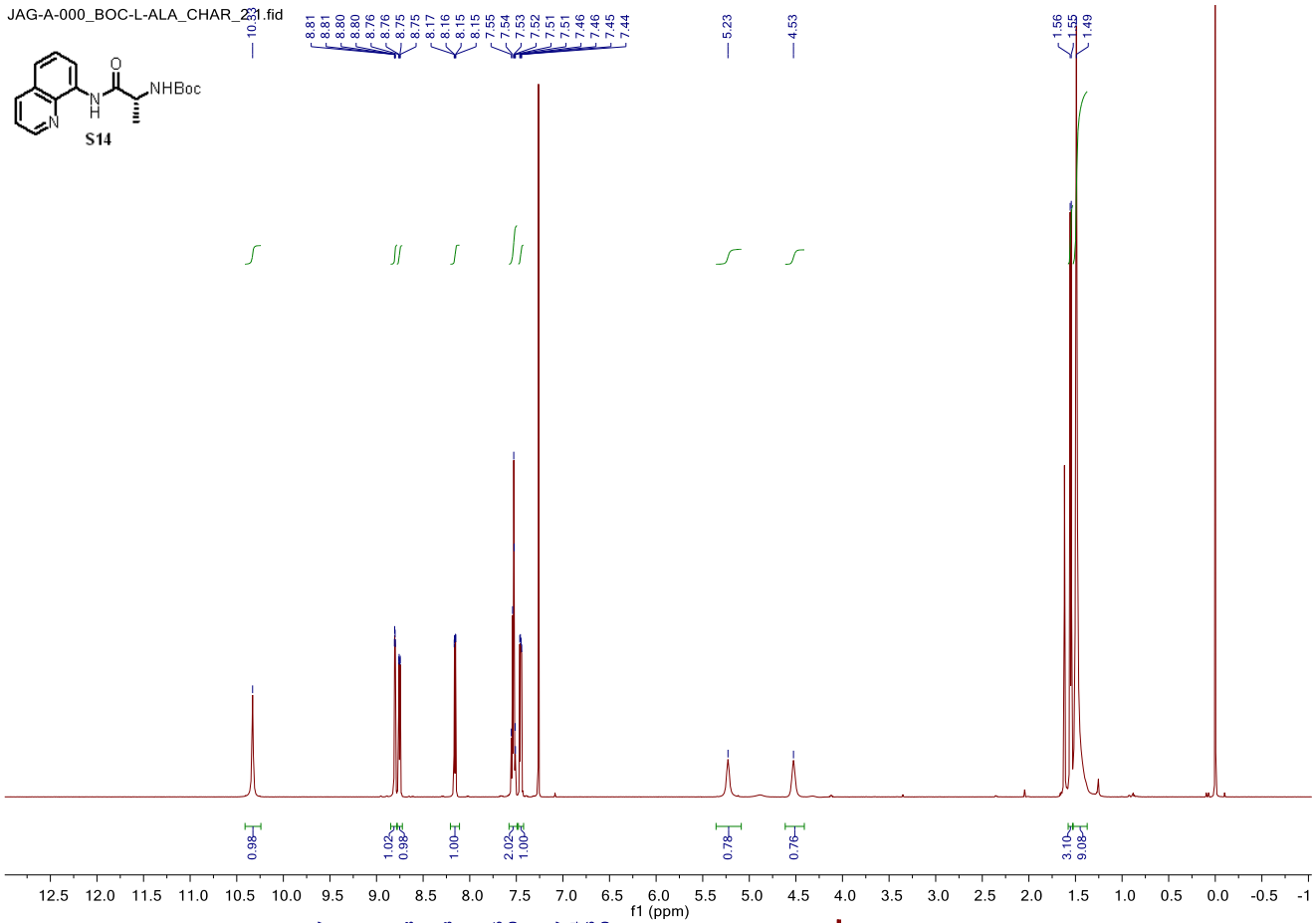
167.97
156.07
148.44
138.64
136.44
134.09
128.08
127.45
122.04
121.82
116.74
80.46
45.47
28.52
NHBoc
S13
f1 (ppm)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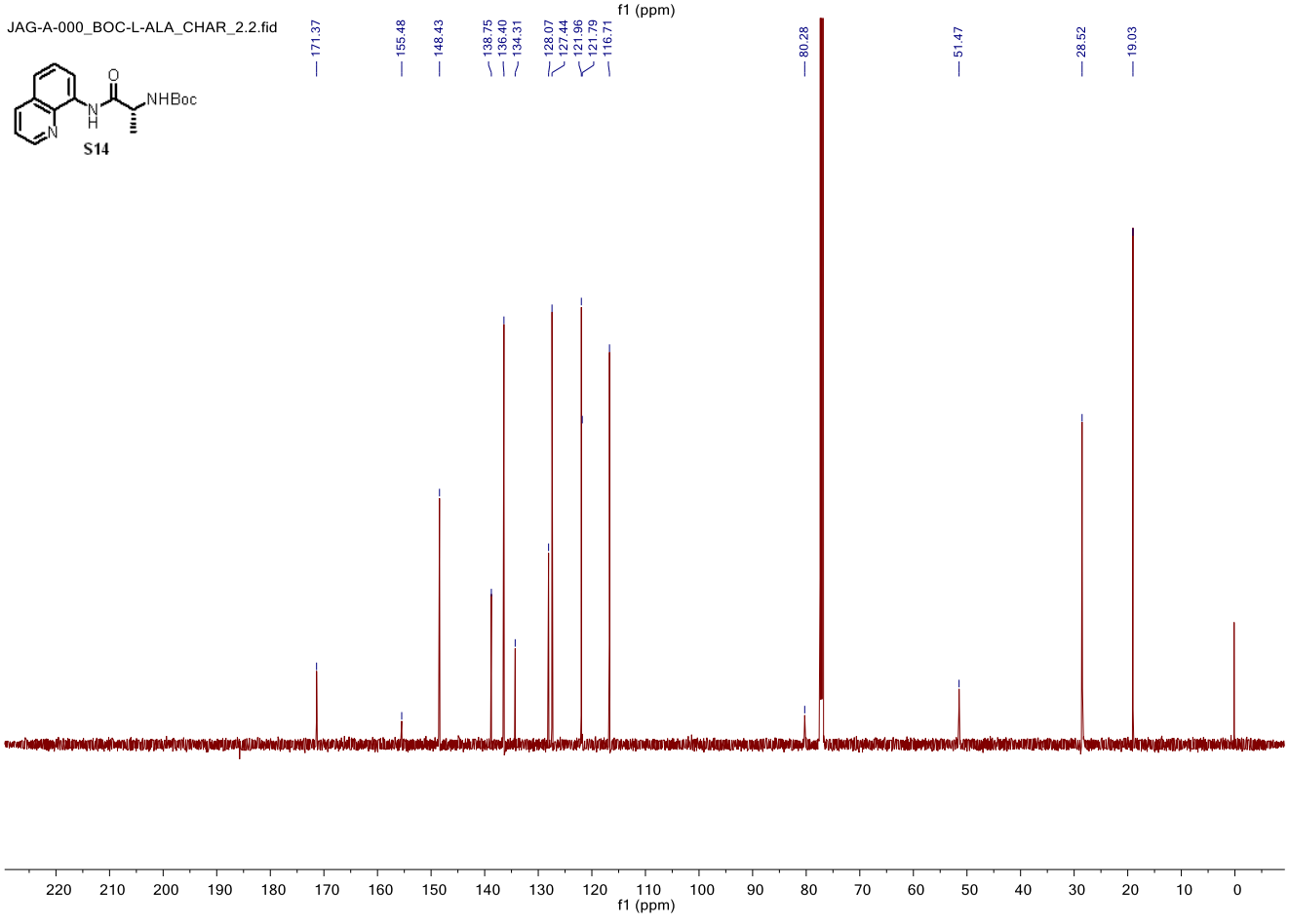
S14
10.53
8.81
8.81
8.80
8.80
8.76
8.76
8.75
8.75
8.17
8.16
8.15
8.15
7.55
7.54
7.53
7.52
7.51
7.51
7.46
7.46
7.45
7.44
5.23
4.53
1.56
1.55
1.49
0.98
1.02
0.98
1.00
2.02
1.00
0.78
0.76
3.10
9.08
f1 (ppm)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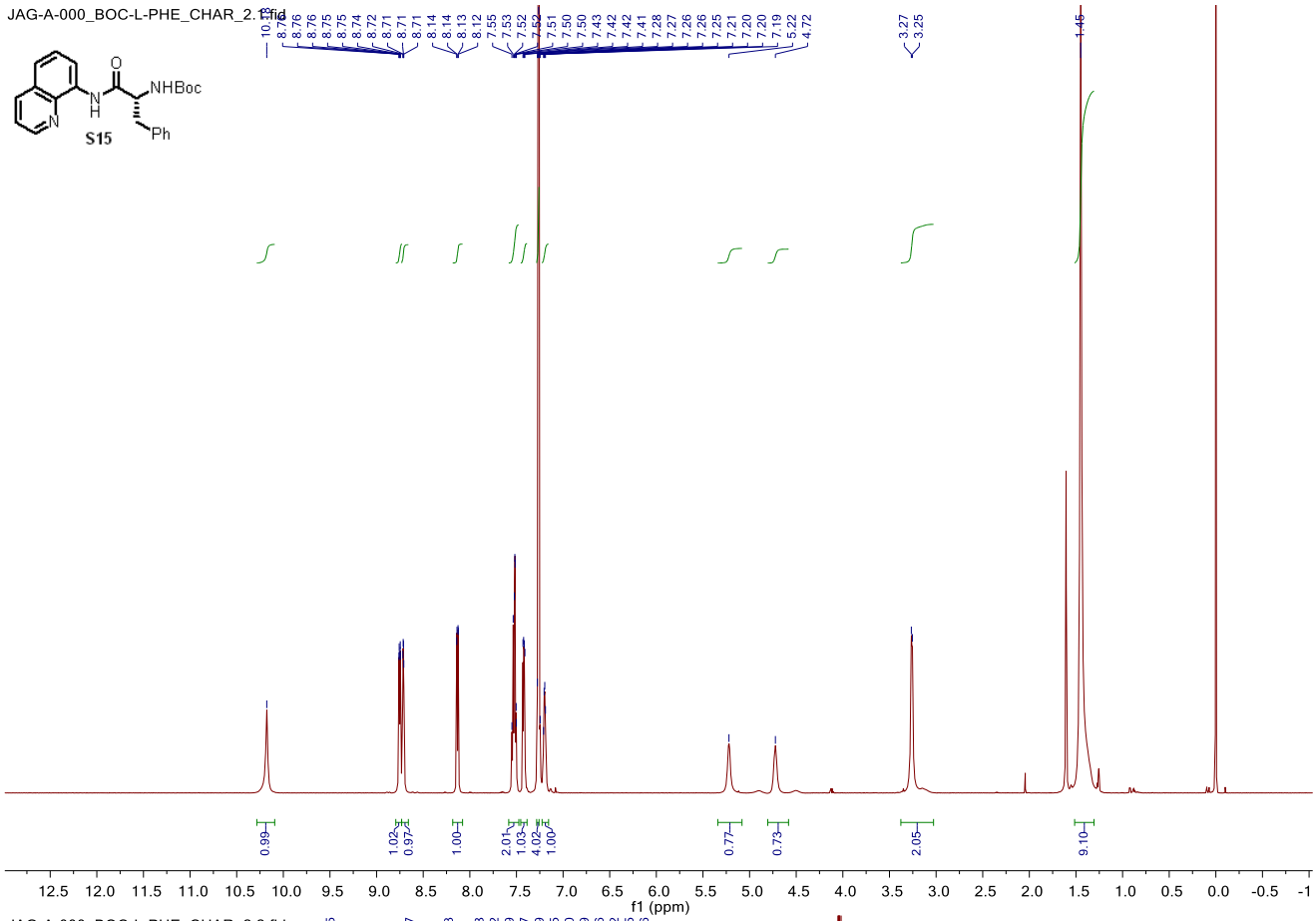
NHBoc
S14
171.37
155.48
148.43
138.75
136.40
134.31
128.07
127.44
121.96
121.79
116.71
80.28
51.47
28.52
19.03
f1 (ppm)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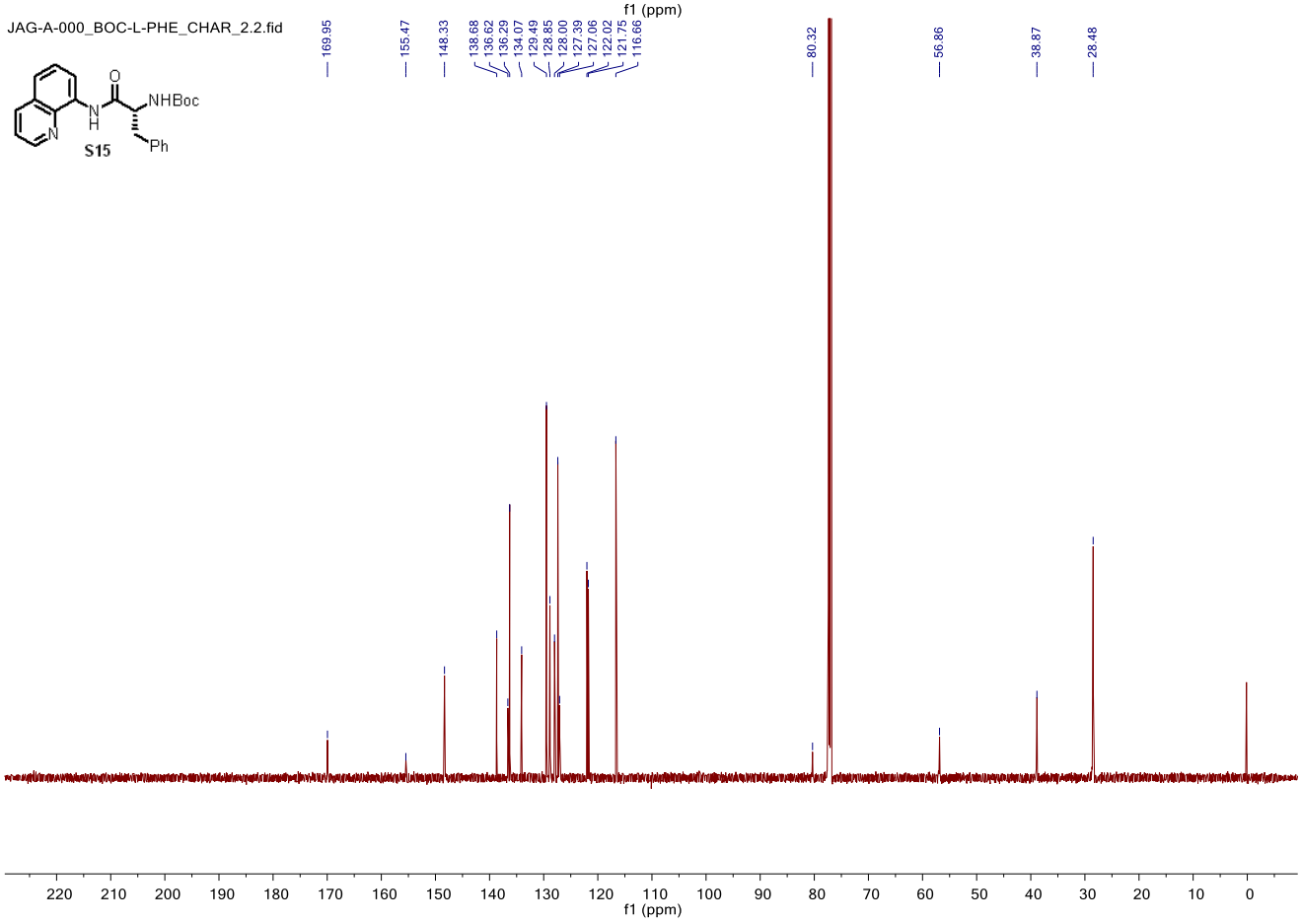
NHBoc
Ph
S15
f1 (ppm)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NHBoc
Ph
S15
f1 (ppm)

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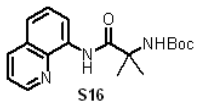

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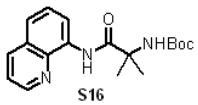
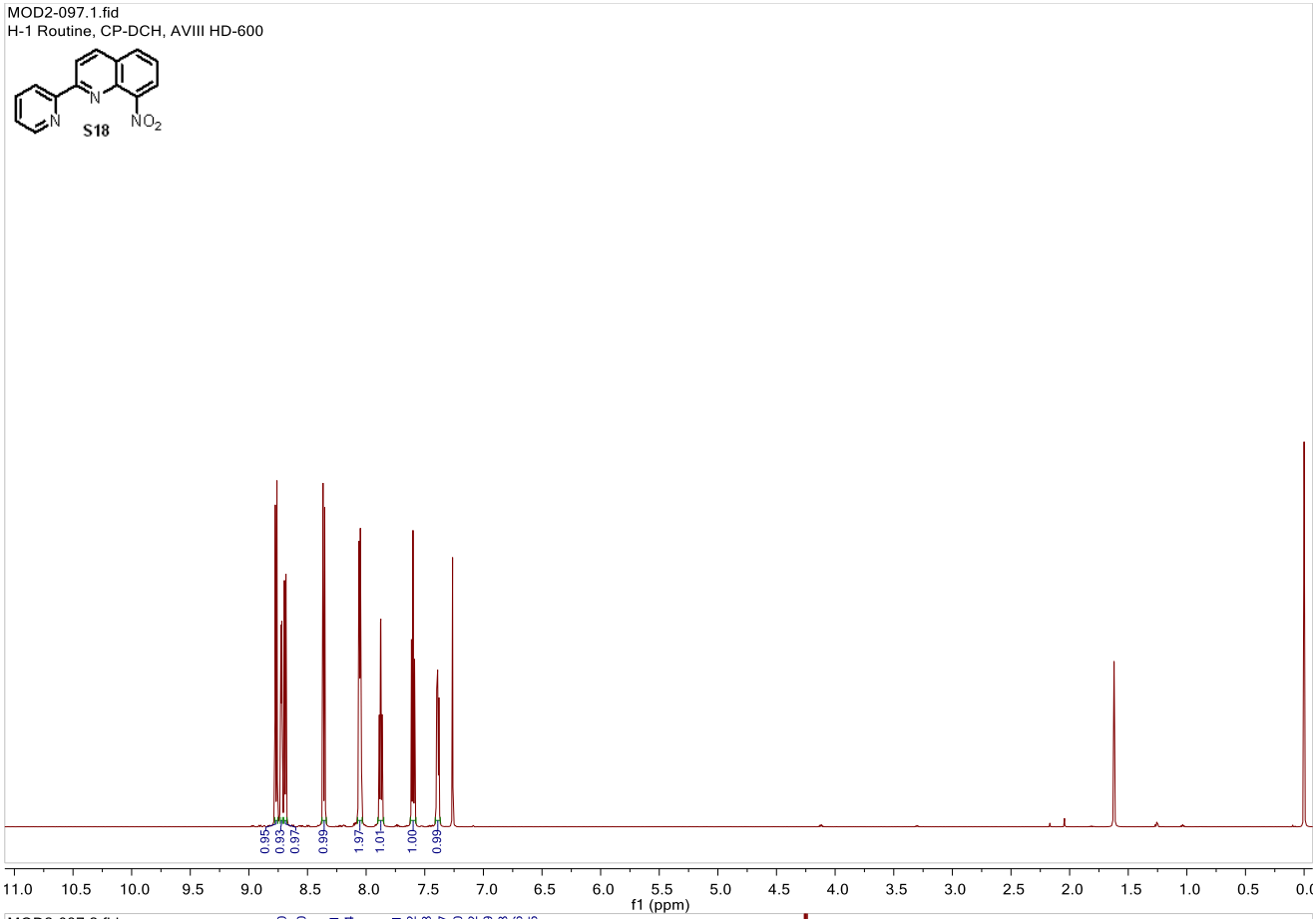
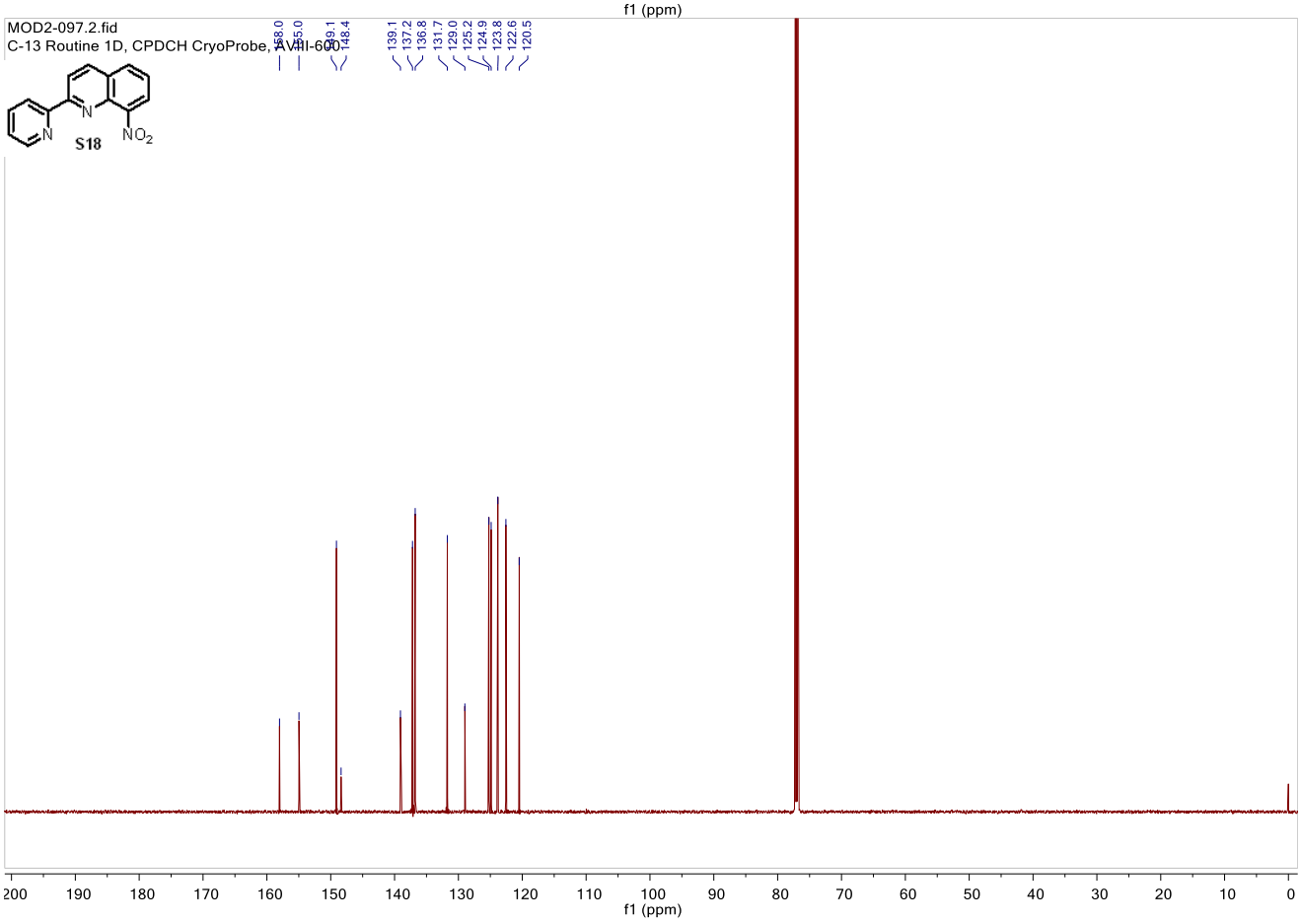
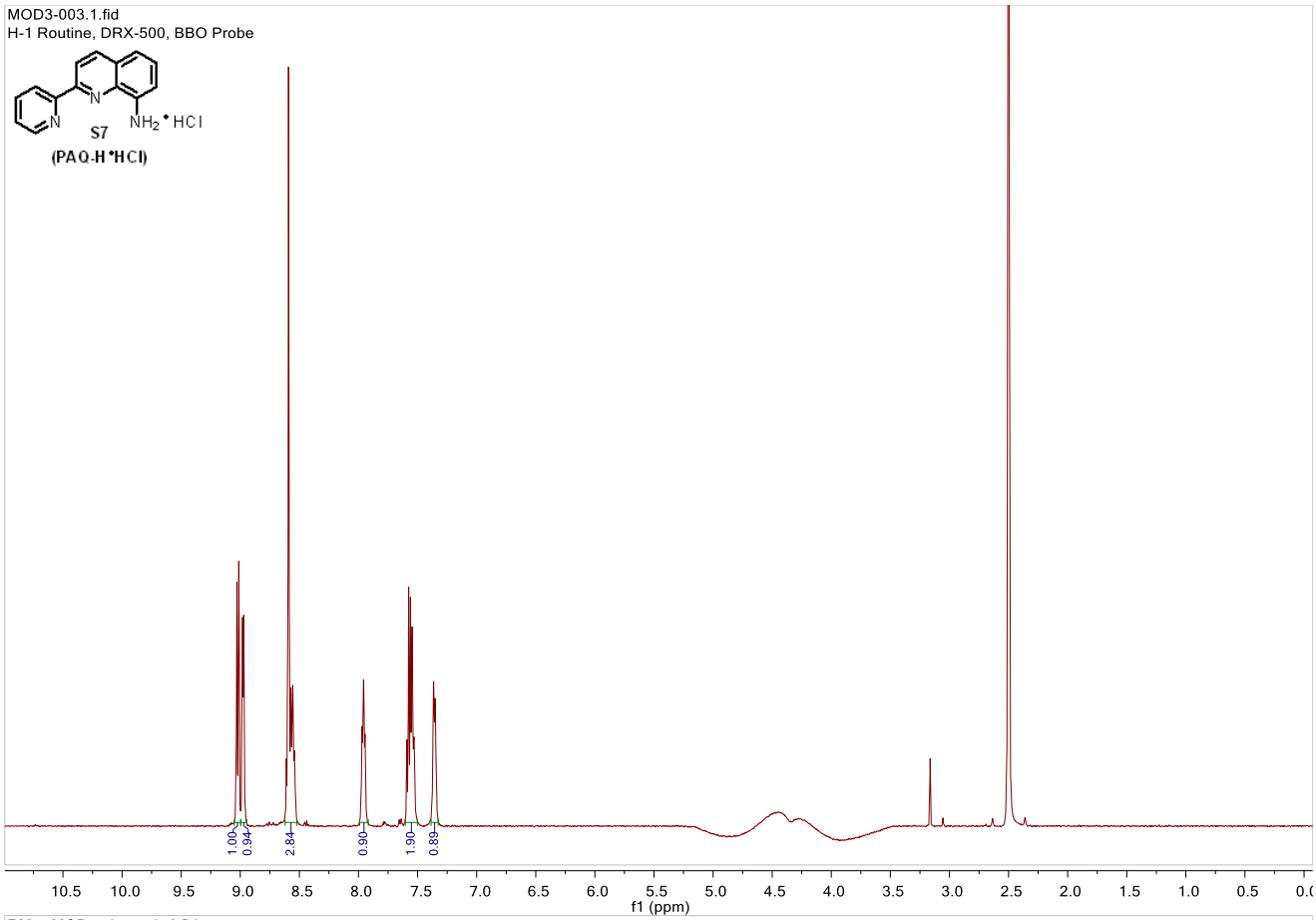



MOD2-097.1.fid
H-1 Routine, CP-DCH, AVIII HD-600
S18
0.95
0.93
0.97
0.99
1.97
1.01
1.00
0.99
f1 (ppm)


MOD2-097.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
S18
158.0
155.0
149.1
148.4
139.1
137.2
136.8
131.7
129.0
125.2
124.9
123.8
122.6
120.5
f1 (ppm)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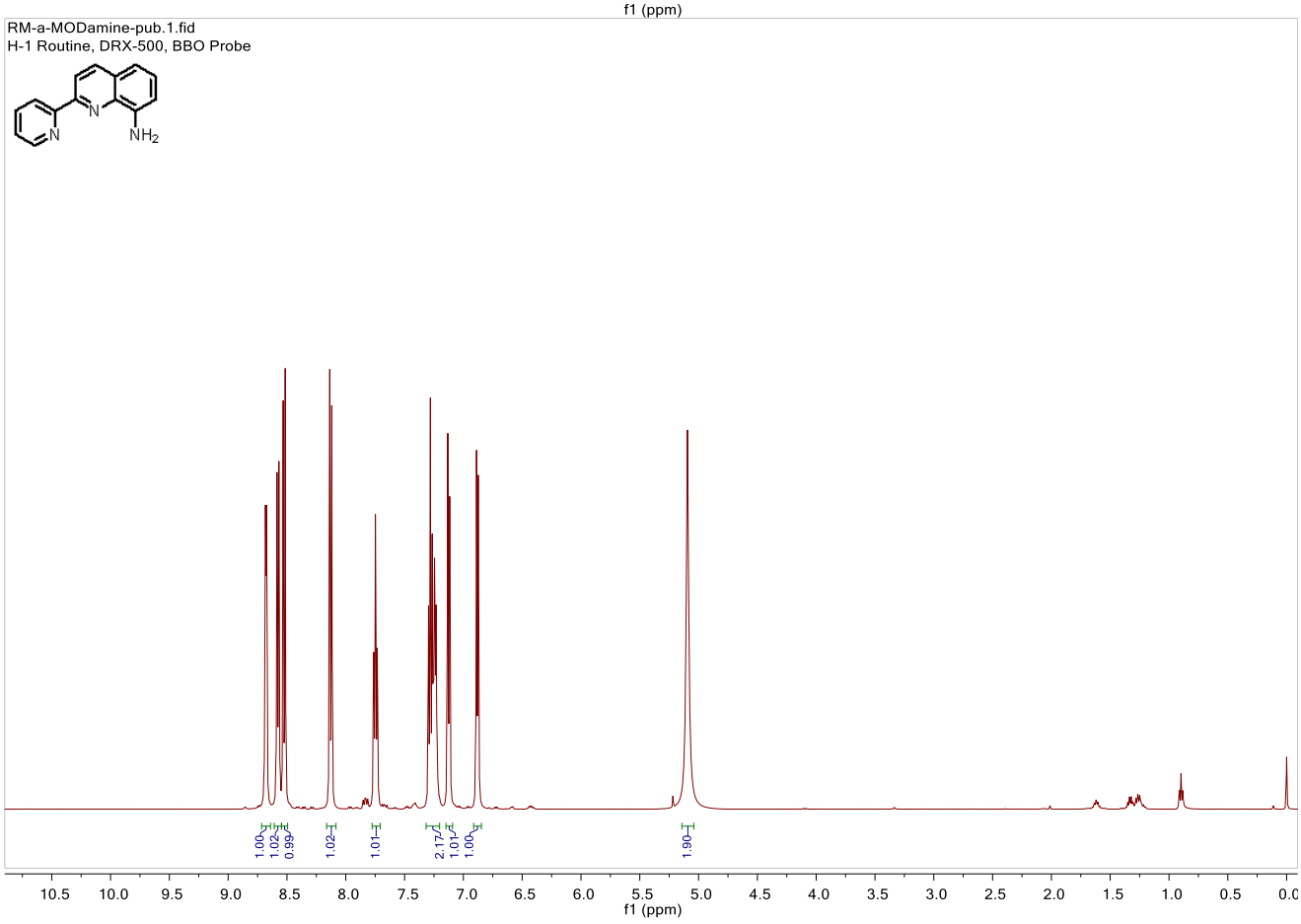
N
N
NH2 • HCl
S7
(PAQ-H •HCl)
1.00
0.94
2.84
0.90
1.90
0.89
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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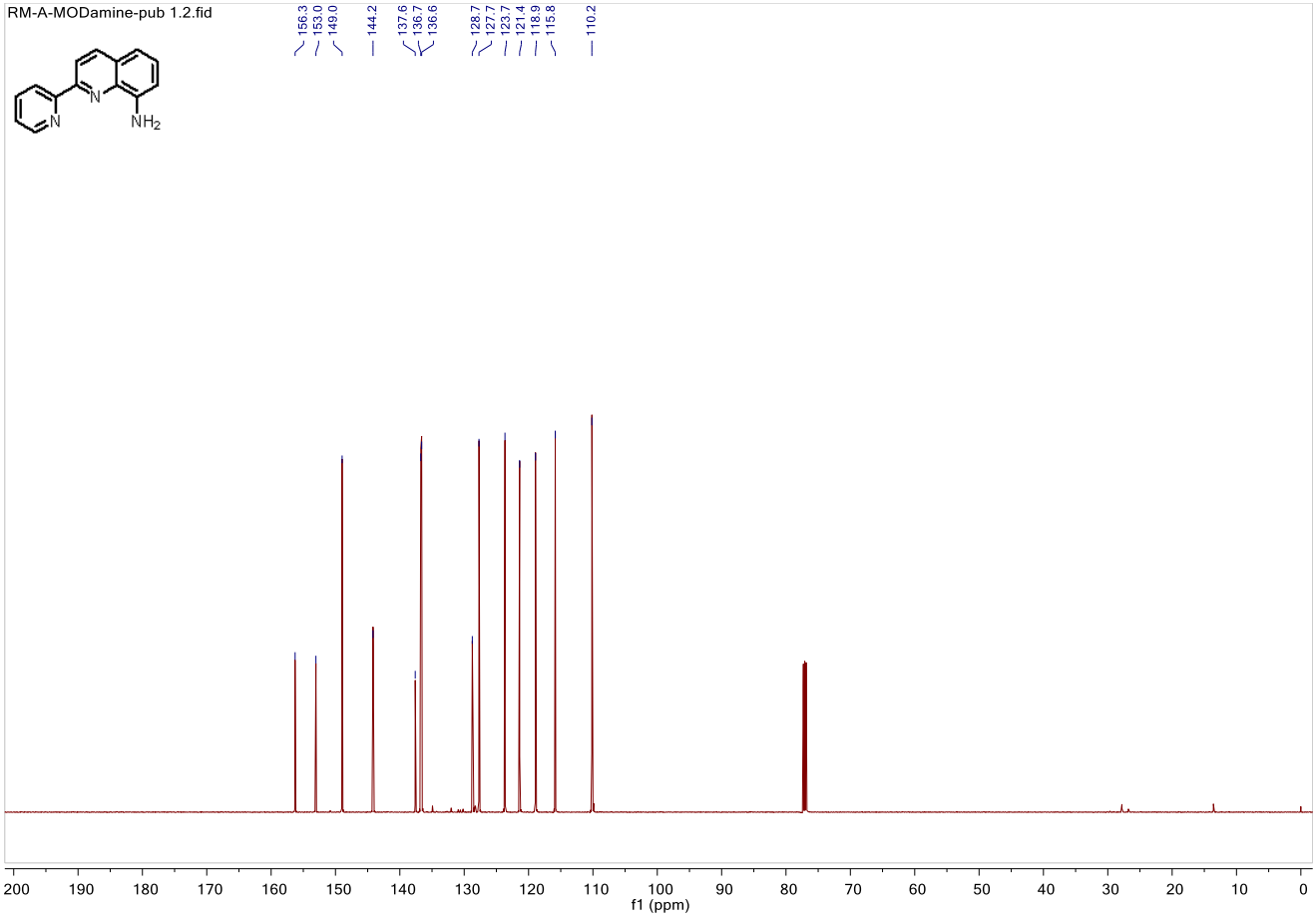
N
N
NH2
1.00
1.02
0.99
1.02
1.01
2.17
1.01
1.00
1.90
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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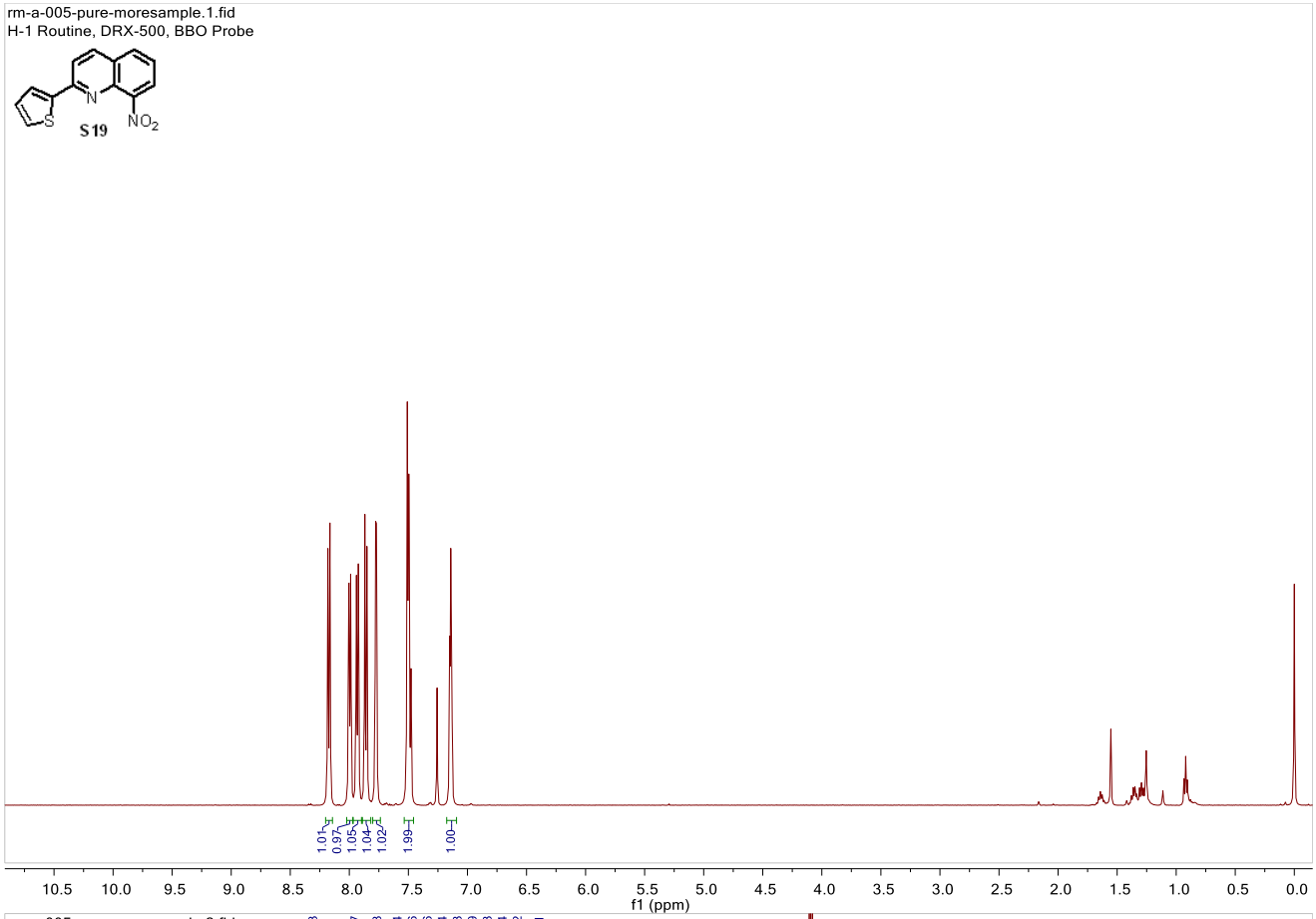
153.0
149.0
144.2
137.6
136.7
136.6
128.7
127.7
123.7
121.4
118.9
115.8
110.2
N
N
NH2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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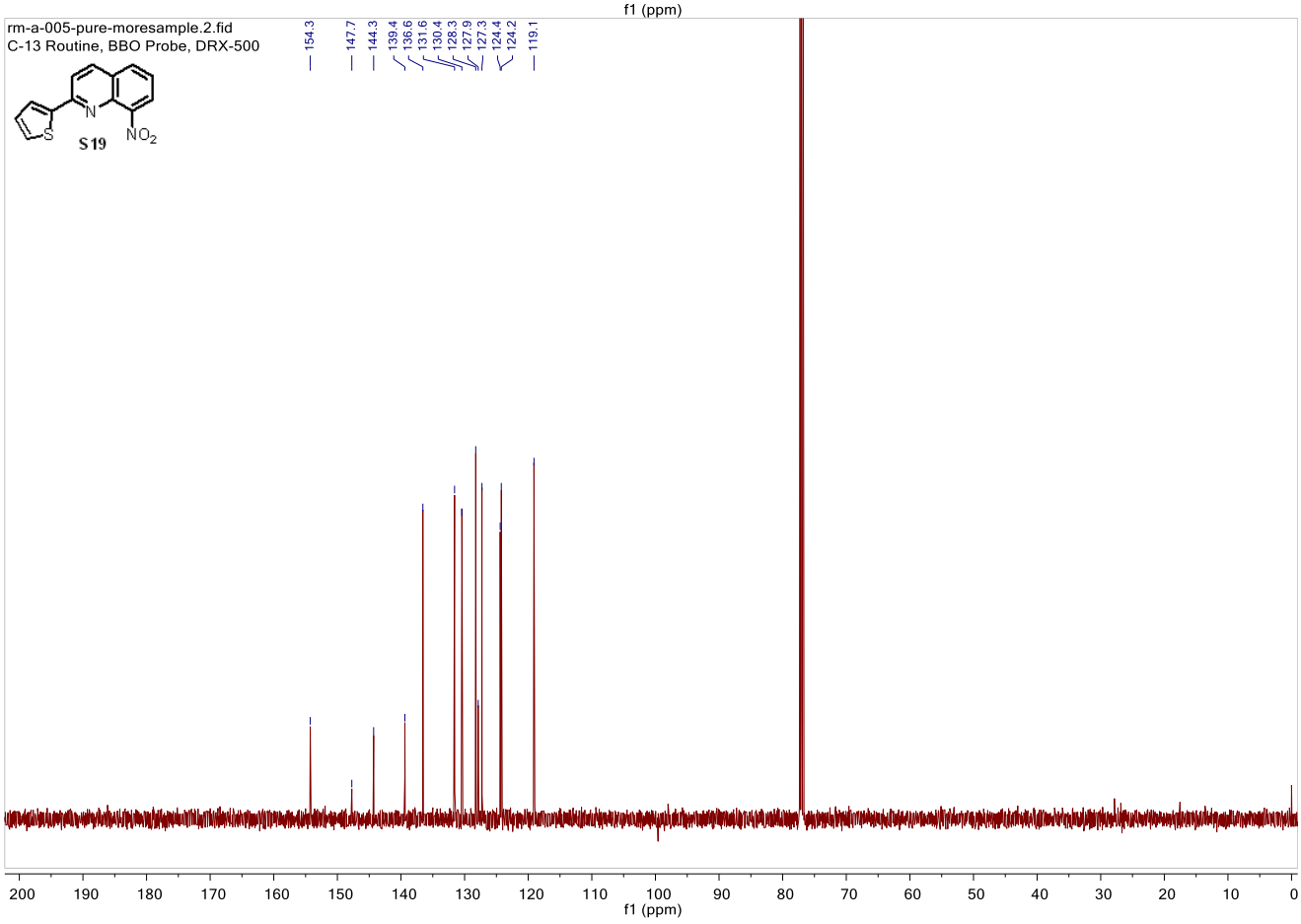
H-1 Routine, DRX-500, BBO Probe
S19
1.01
0.97
1.05
1.04
1.02
1.99
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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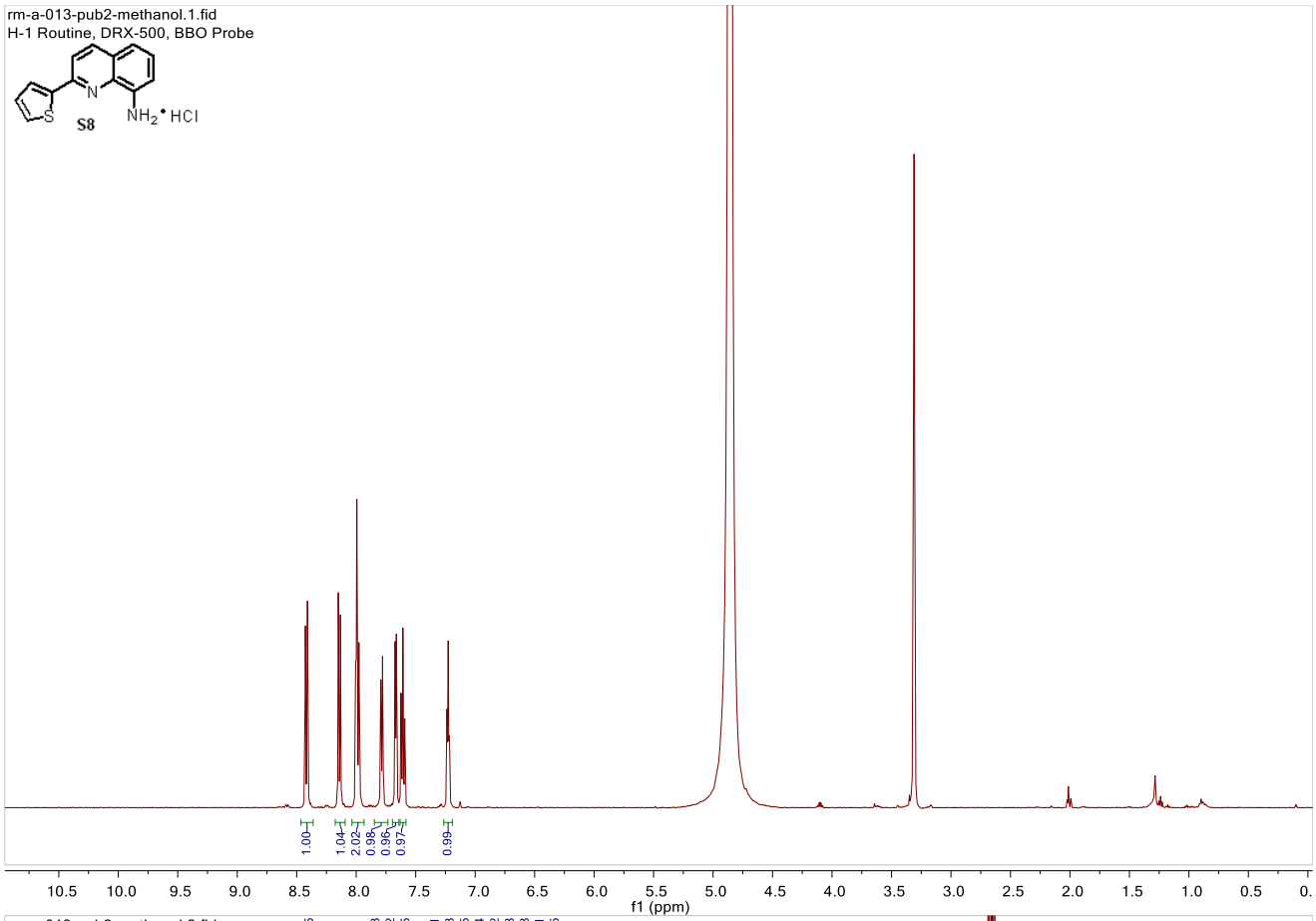
C-13 Routine, BBO Probe, DRX-500
S19
154.3
147.7
144.3
139.4
136.6
131.6
130.4
128.3
127.9
127.3
124.4
124.2
119.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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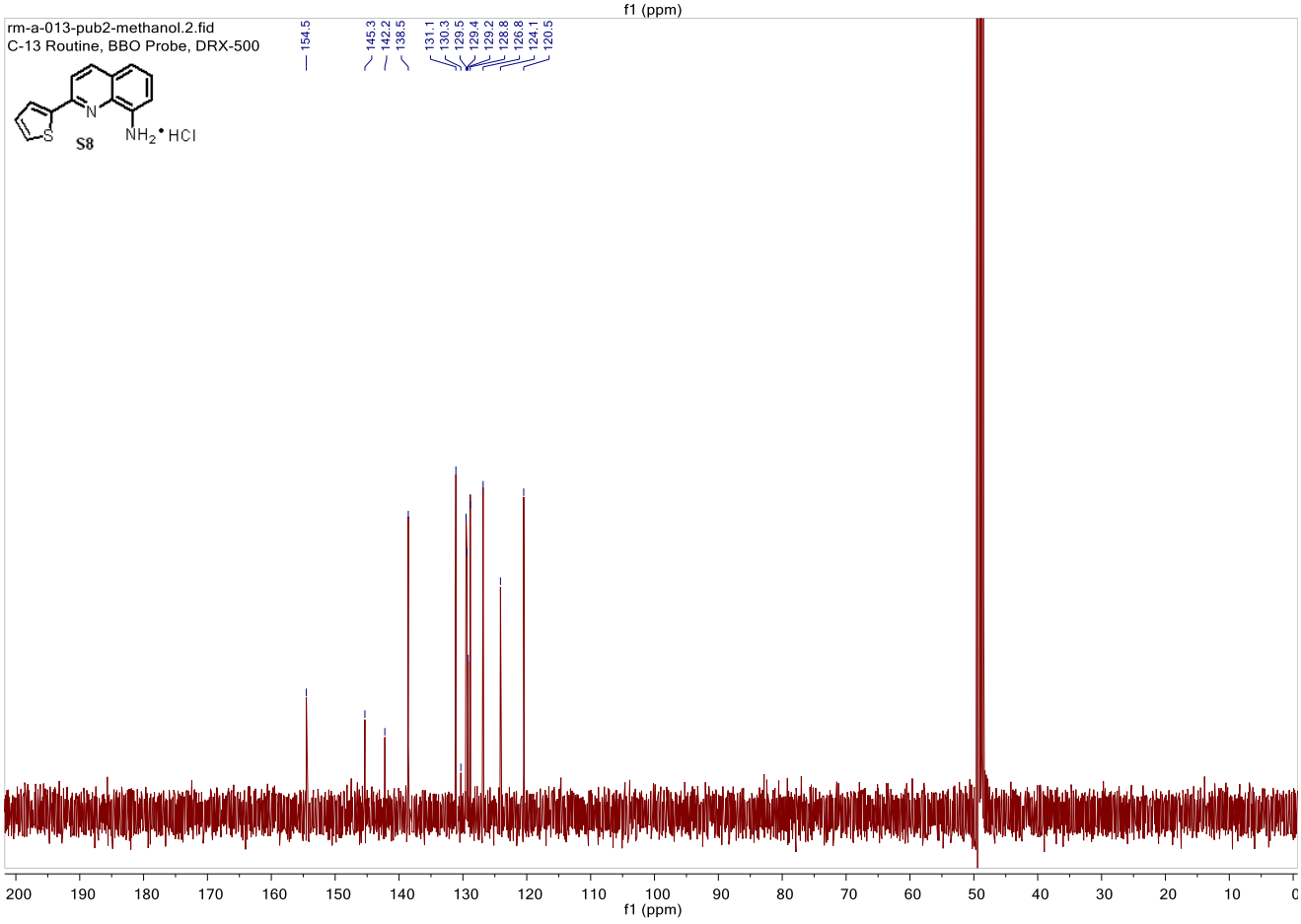
S8
NH2 • HCl
1.00
1.04
2.02
0.98
0.96
0.97
0.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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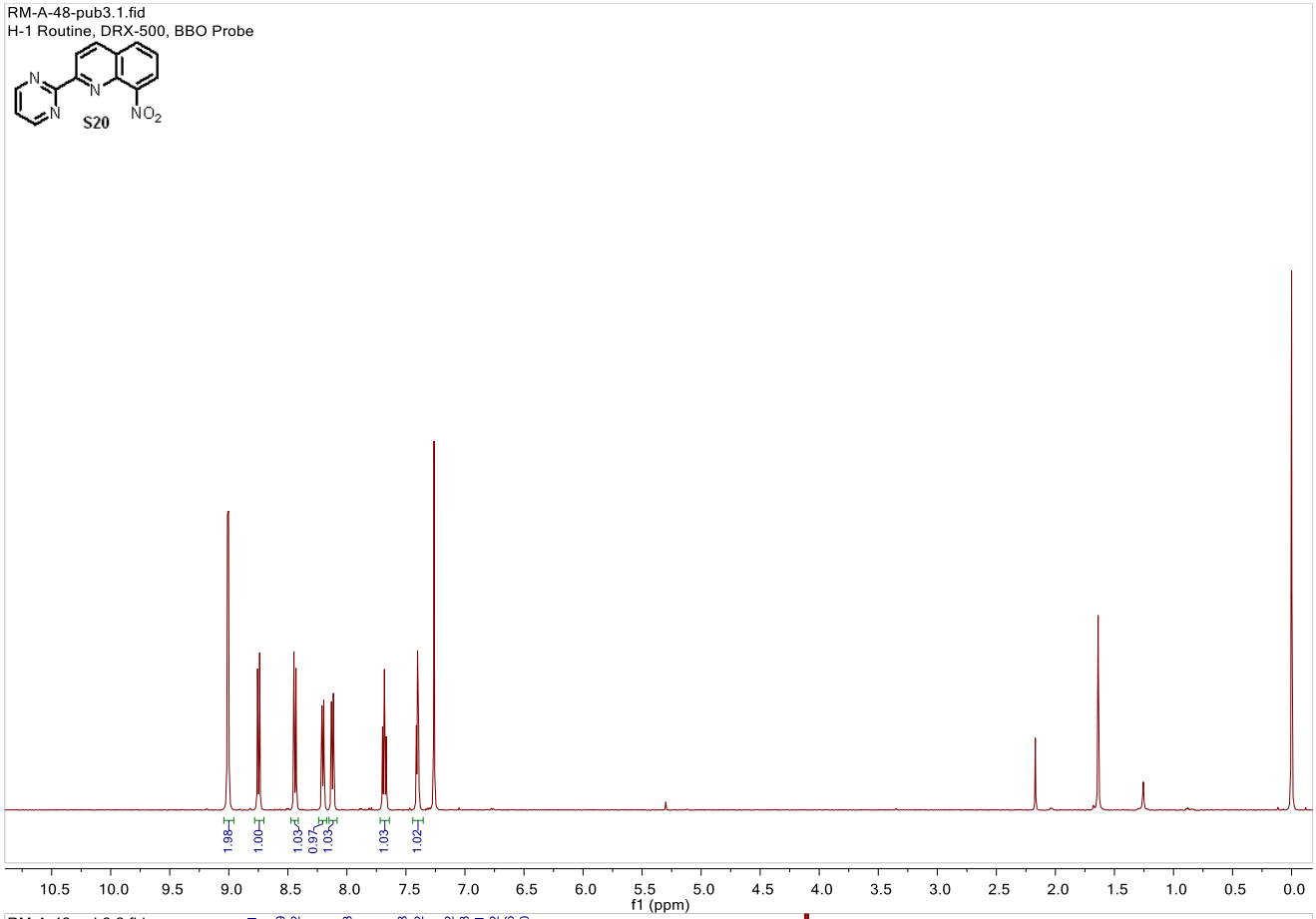
C-13 Routine, BBO Probe, DRX-500
S8
NH2 • HCl
154.5
145.3
142.2
138.5
131.1
130.3
129.5
129.4
129.2
128.8
126.8
124.1
120.5
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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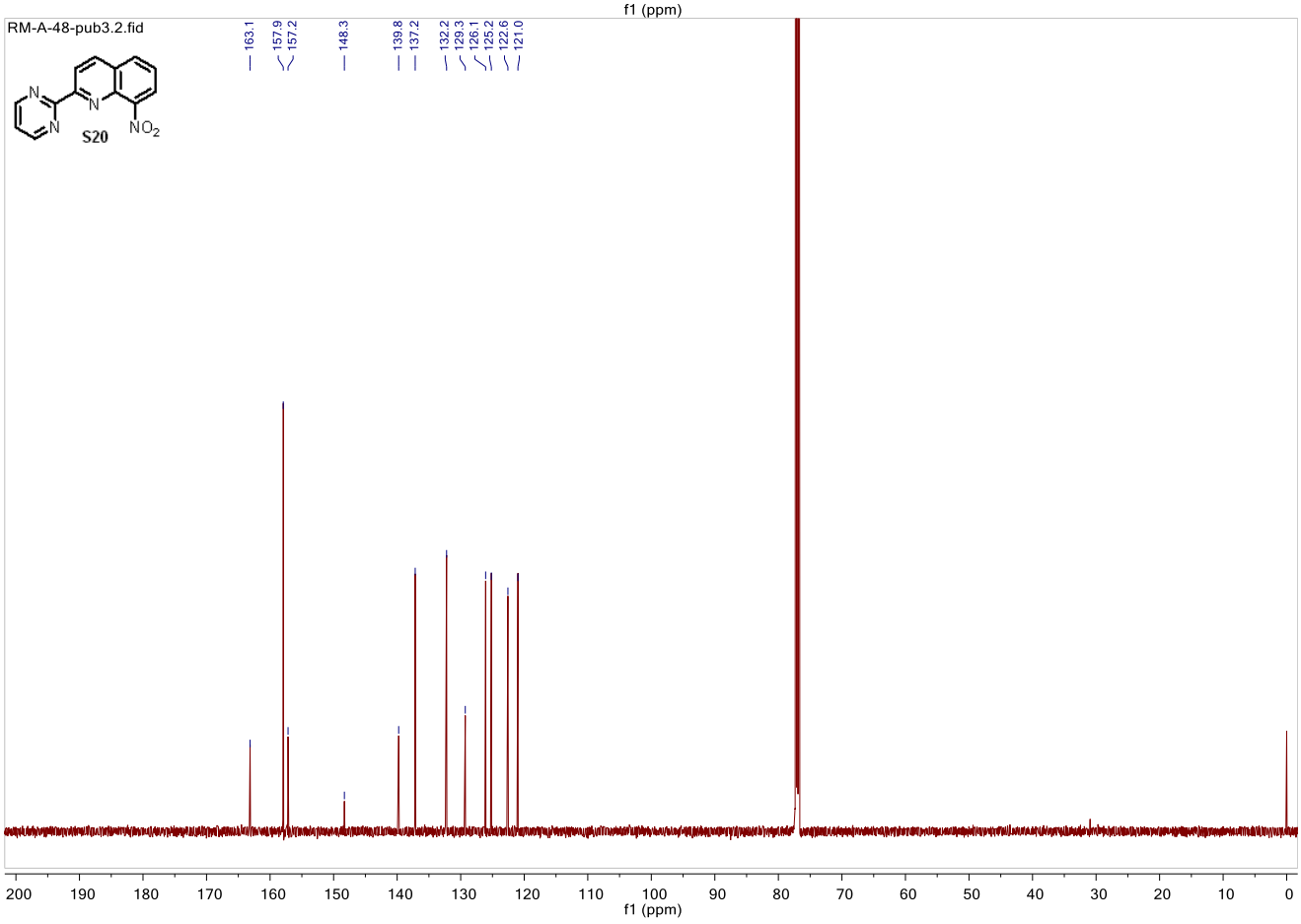
S20
1.98
1.00
1.03
0.97
1.03
1.03
1.02
f1 (ppm)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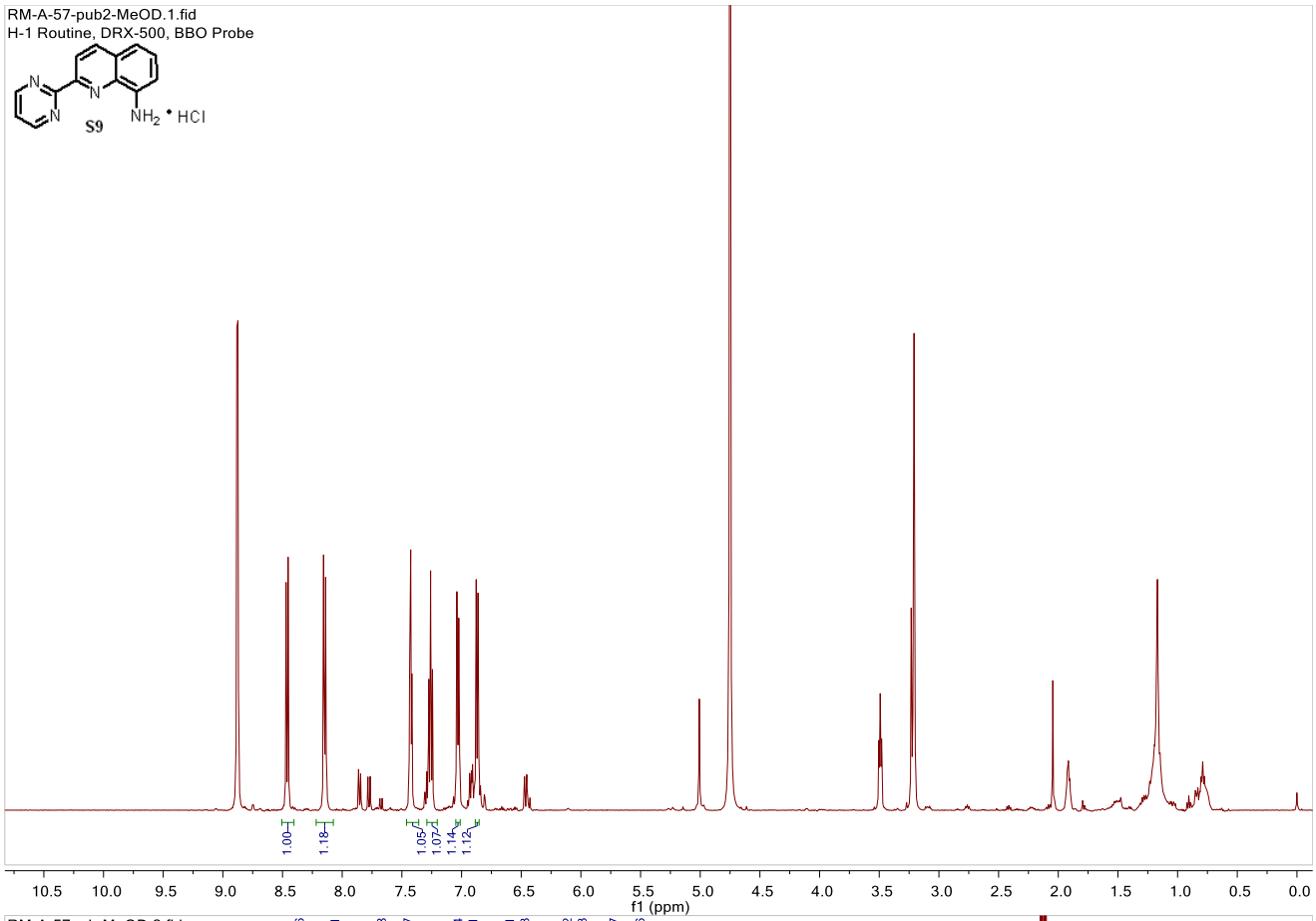
S20
163.1
157.9
157.2
148.3
139.8
137.2
132.2
129.3
126.1
125.2
122.6
121.0
f1 (ppm)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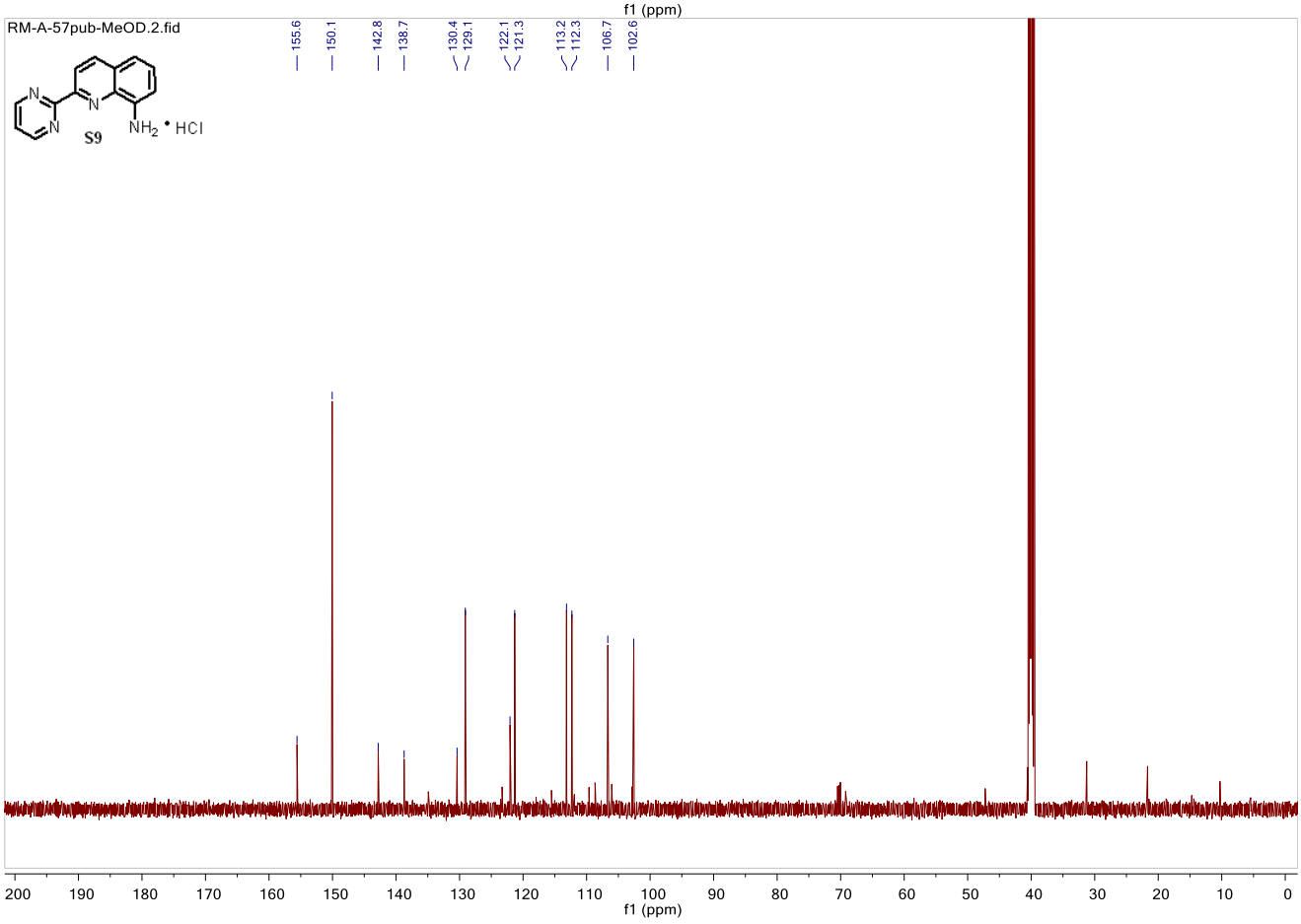
S9
NH2 • HCl
1.00
1.18
1.05
1.07
1.14
1.12
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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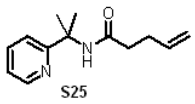
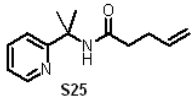
NH2 • HCl
155.6
150.1
142.8
138.7
130.4
129.1
122.1
121.3
113.2
112.3
106.7
102.6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

KME-A-078_CHAR 1.1.fid



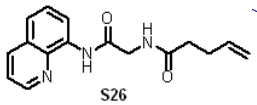
S25

KME-A-078_CHAR 1.2.fid



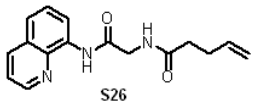
S25

JX-A-013_CHAR 1.1.fid



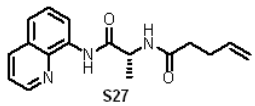
S26

JX-A-013_CHAR 1.2.fid

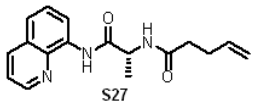


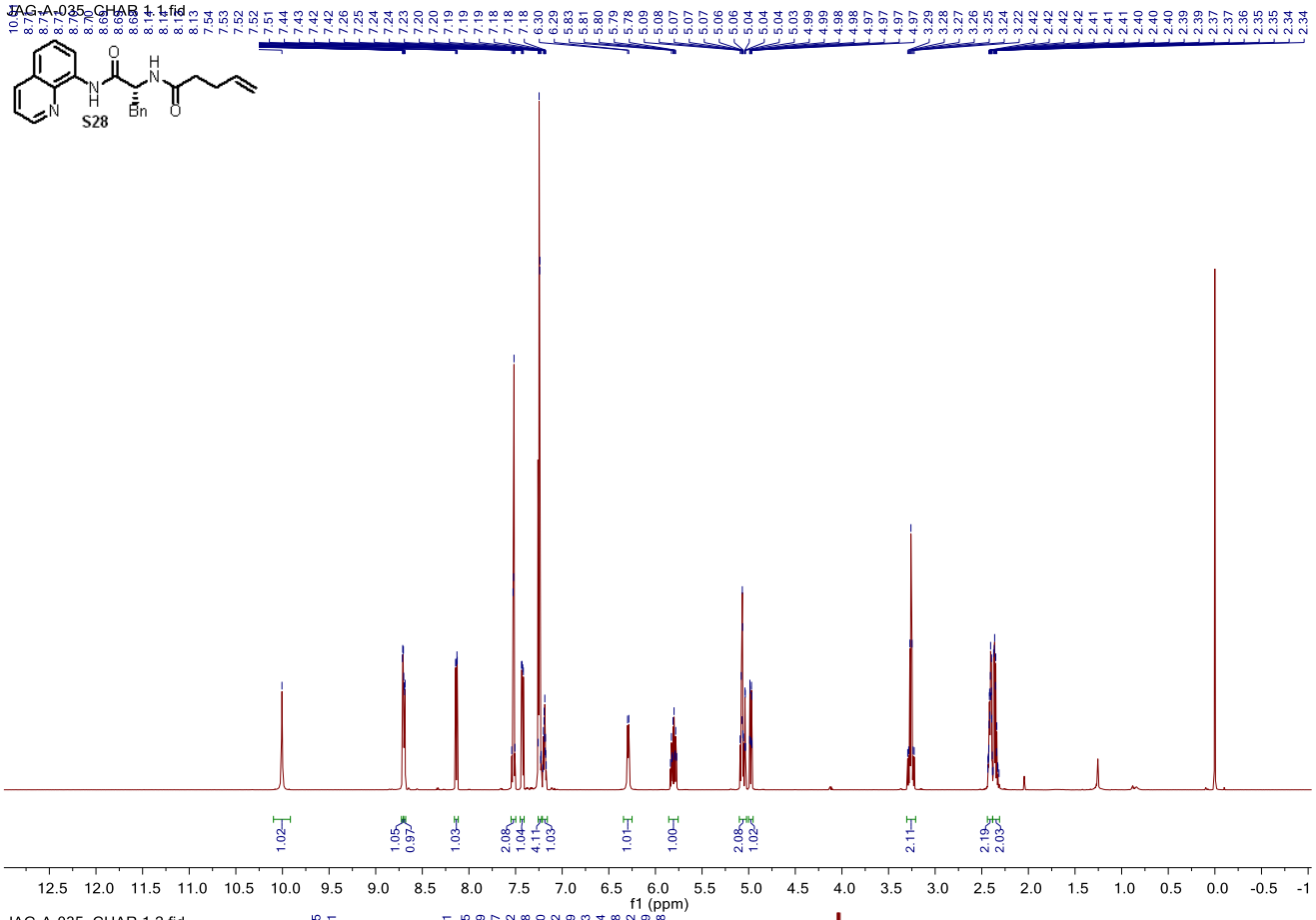
S26

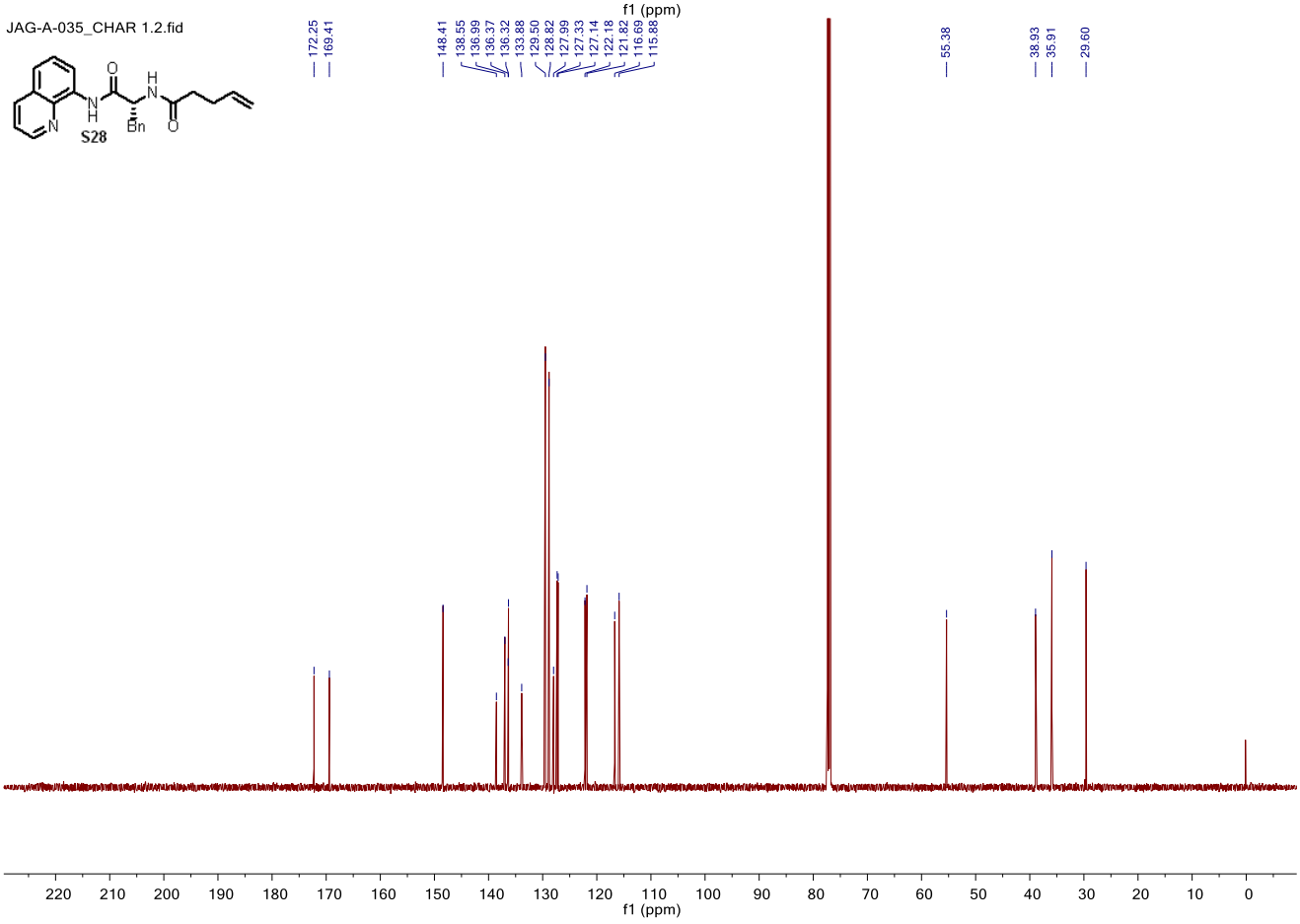
JAG-A-034_CHAR 1.1.fid

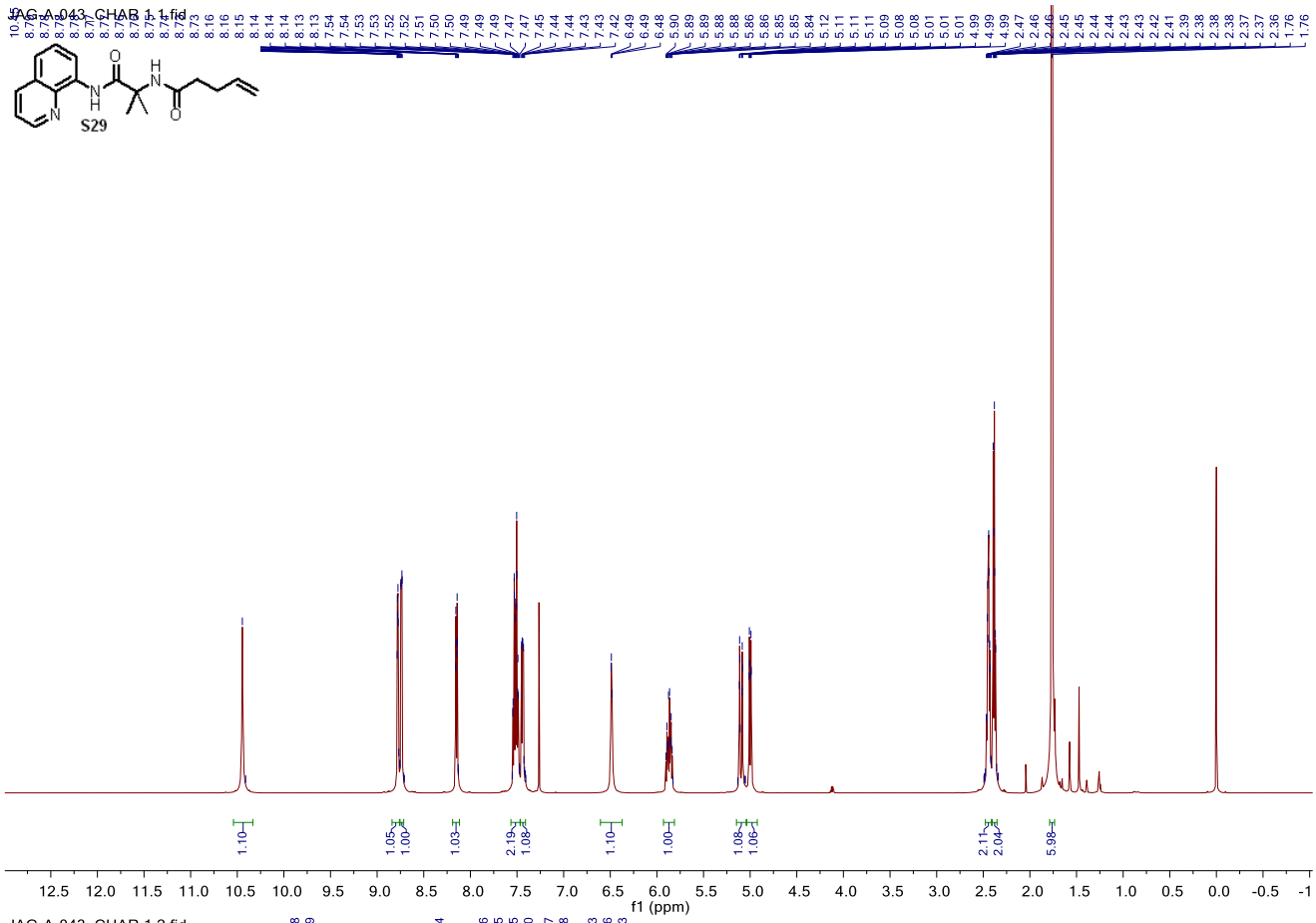


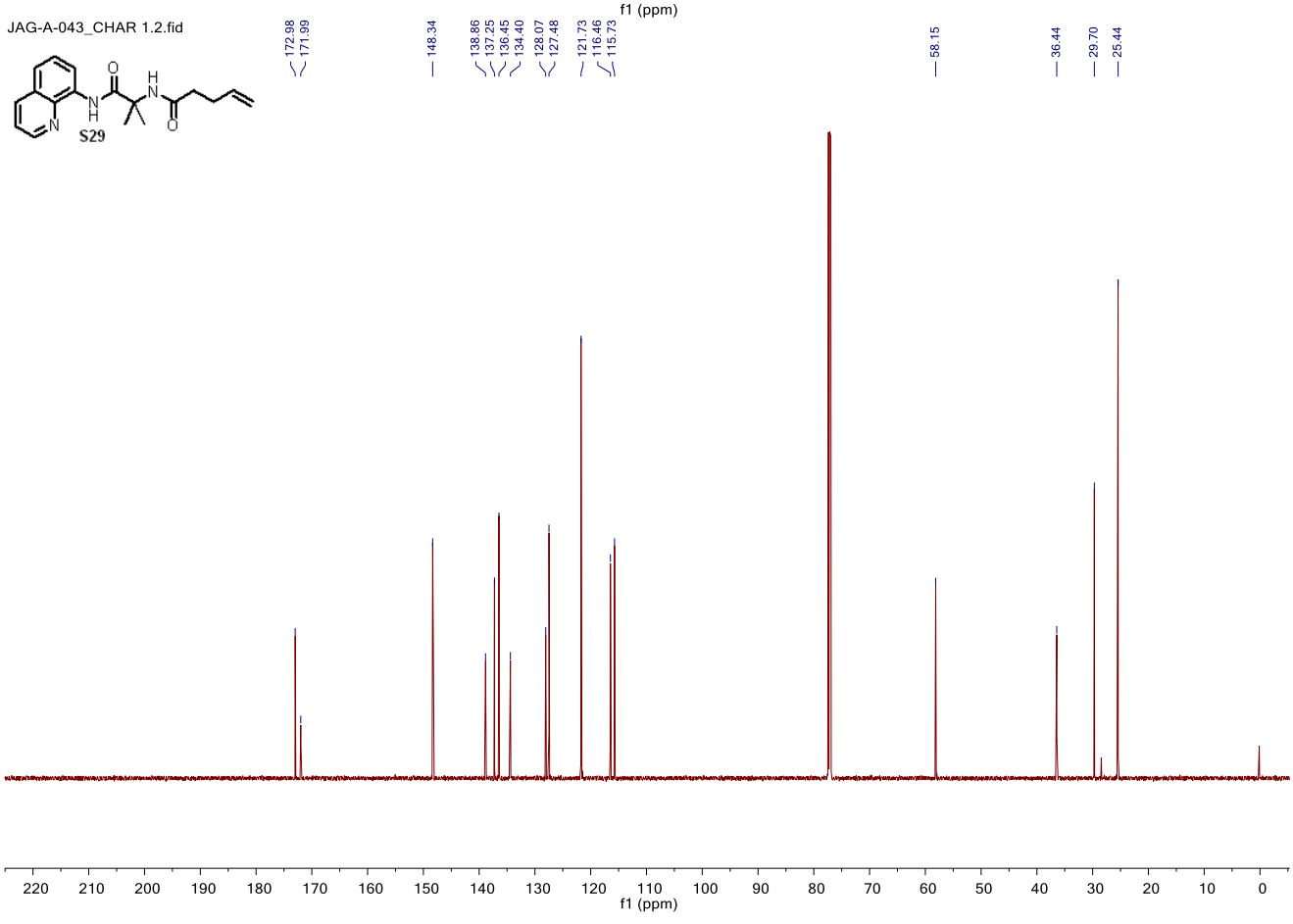
JAG-A-034_CHAR 1.2.fid

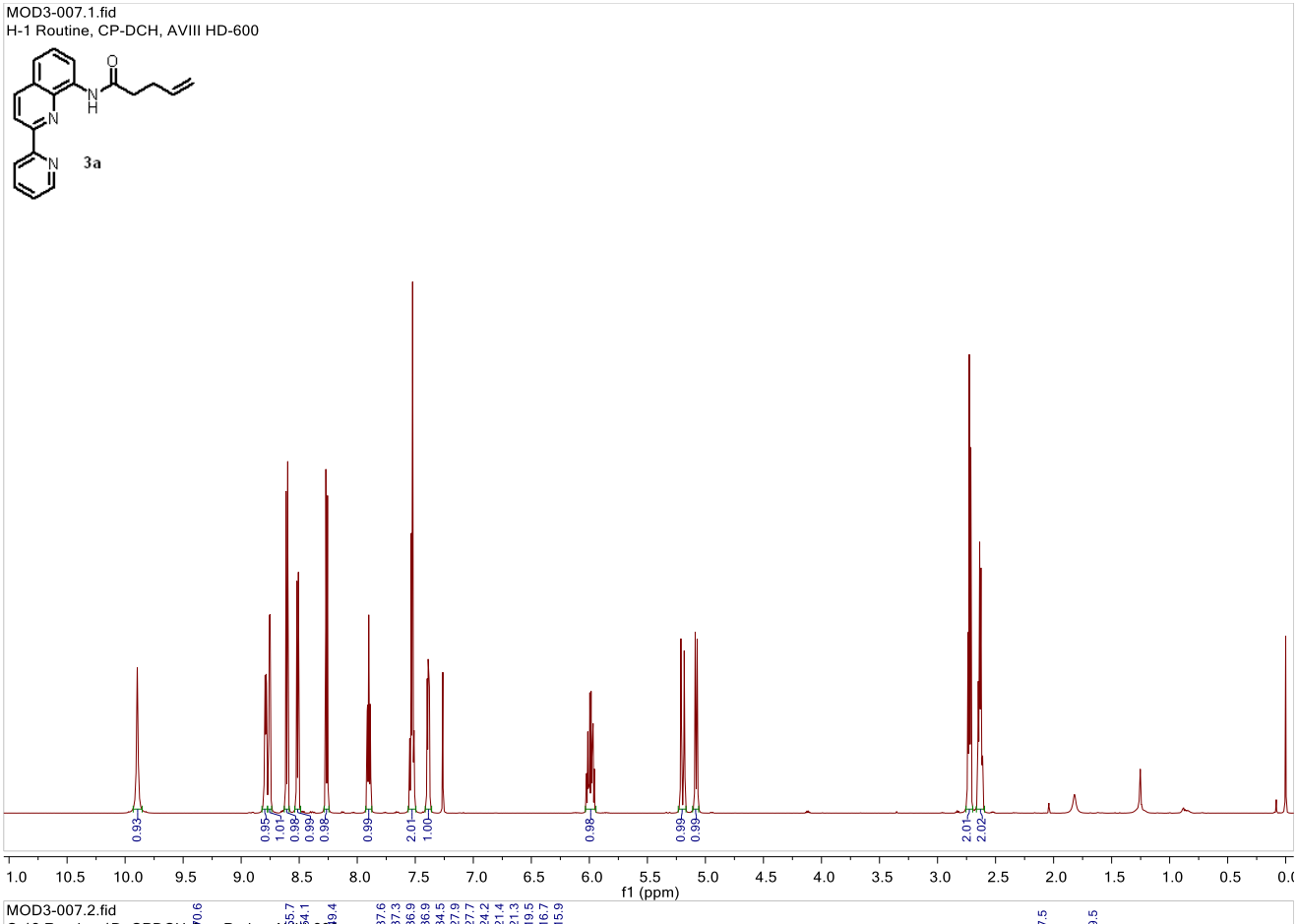


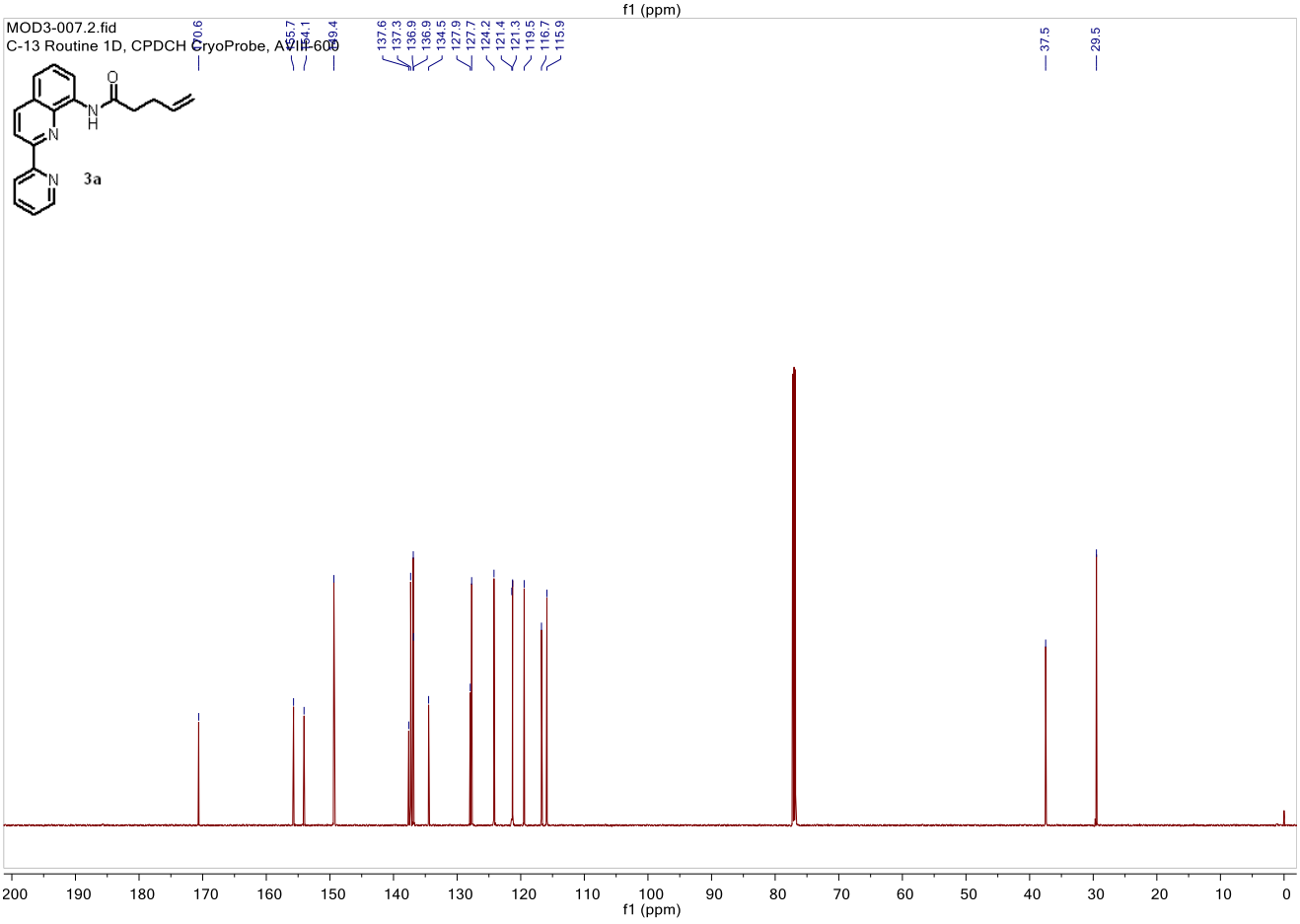

JAG-A-035_CHAR 1.1.fid
S28
f1 (ppm)

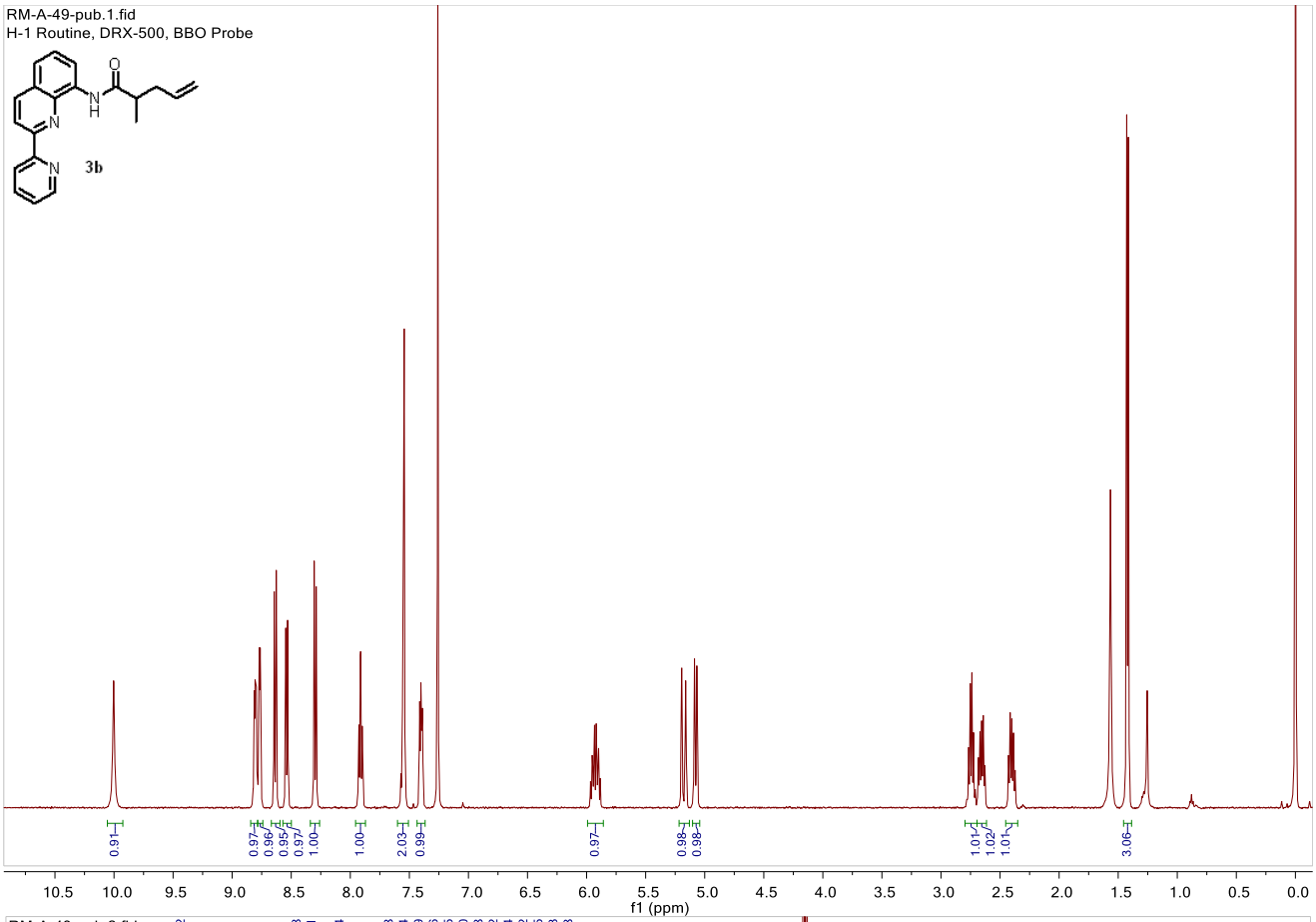

JAG-A-035_CHAR 1.2.fid
S28
f1 (ppm)

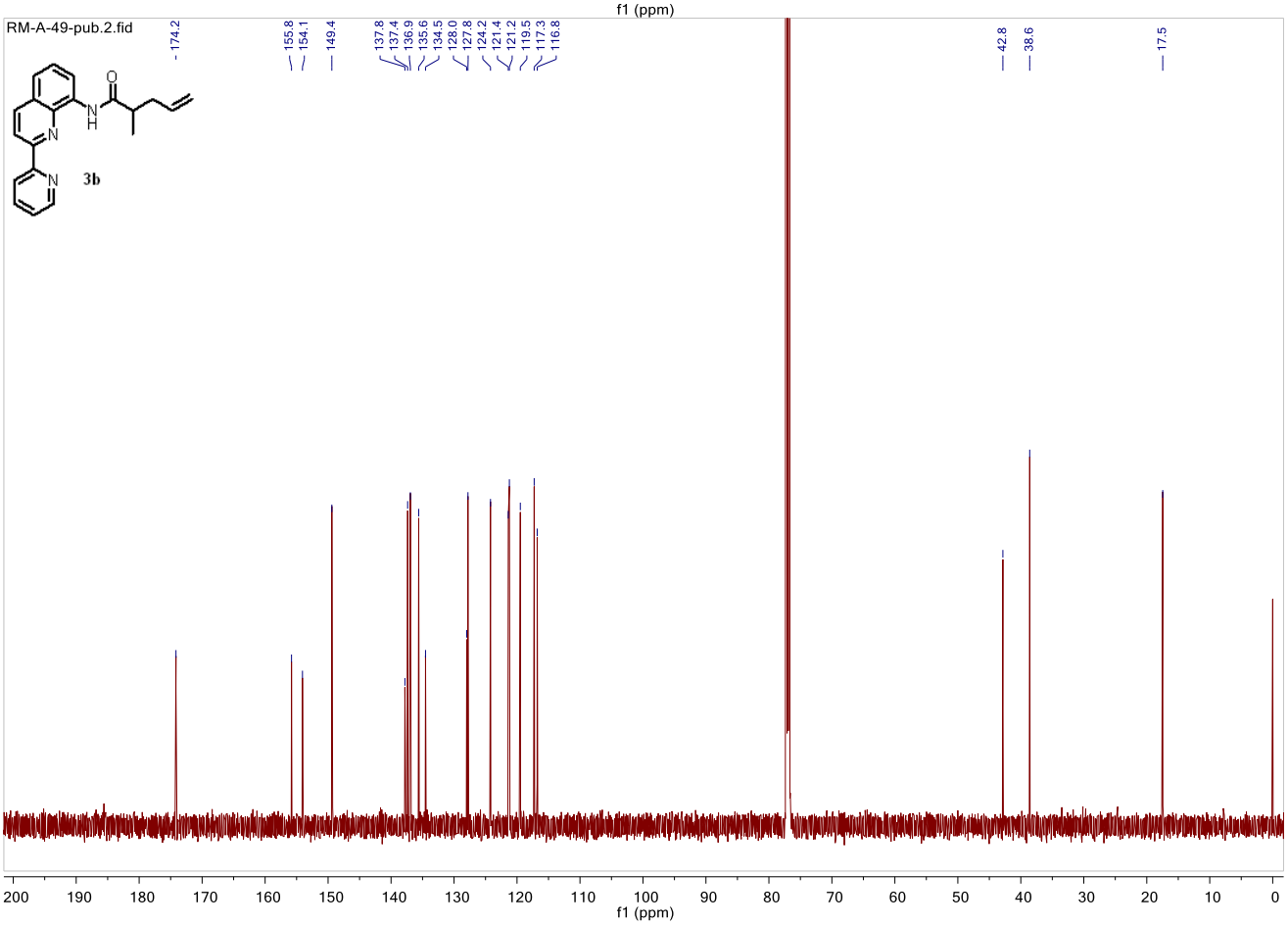

JAG-A-043_CHAR 1.1.fid
S29
1.10
1.05
1.00
1.03
2.19
1.08
1.10
1.00
1.08
1.06
2.11
2.04
5.98
f1 (ppm)

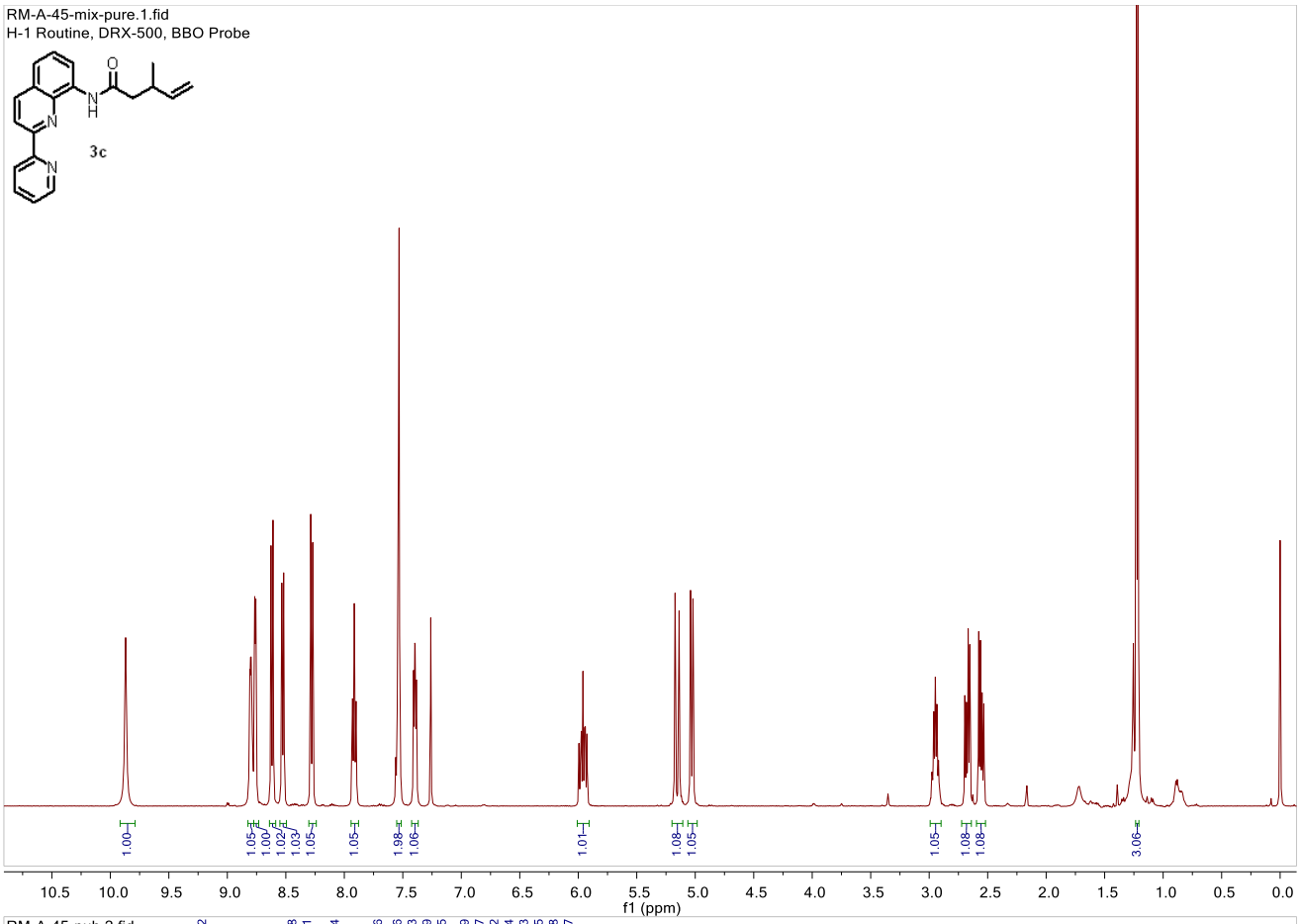

JAG-A-043_CHAR 1.2.fid
S29
172.98
171.99
148.34
138.86
137.25
136.45
134.40
128.07
127.48
121.73
116.46
115.73
58.15
36.44
29.70
25.44
f1 (ppm)

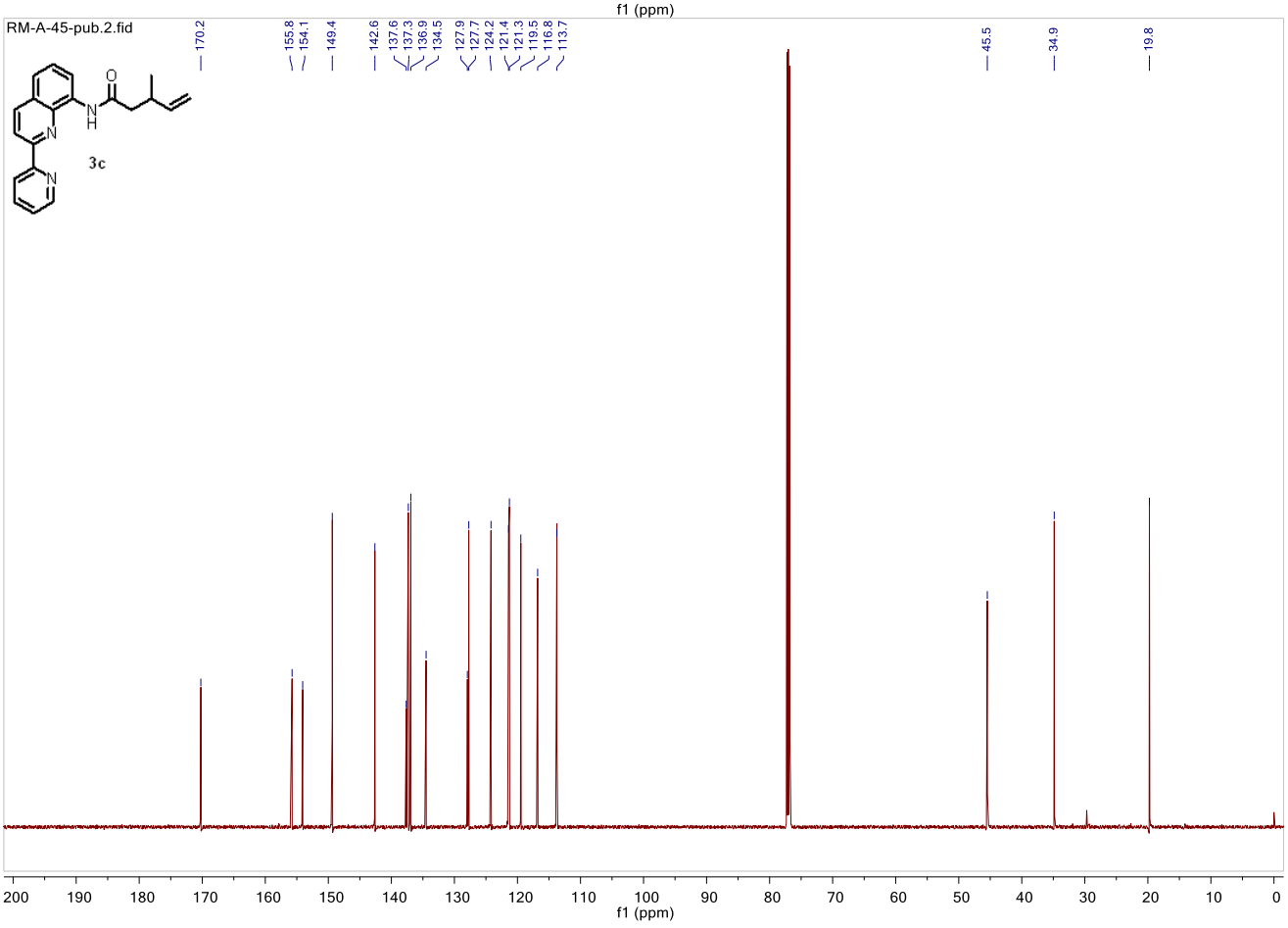

MOD3-007.1.fid
H-1 Routine, CP-DCH, AVIII HD-600
3a
f1 (ppm)

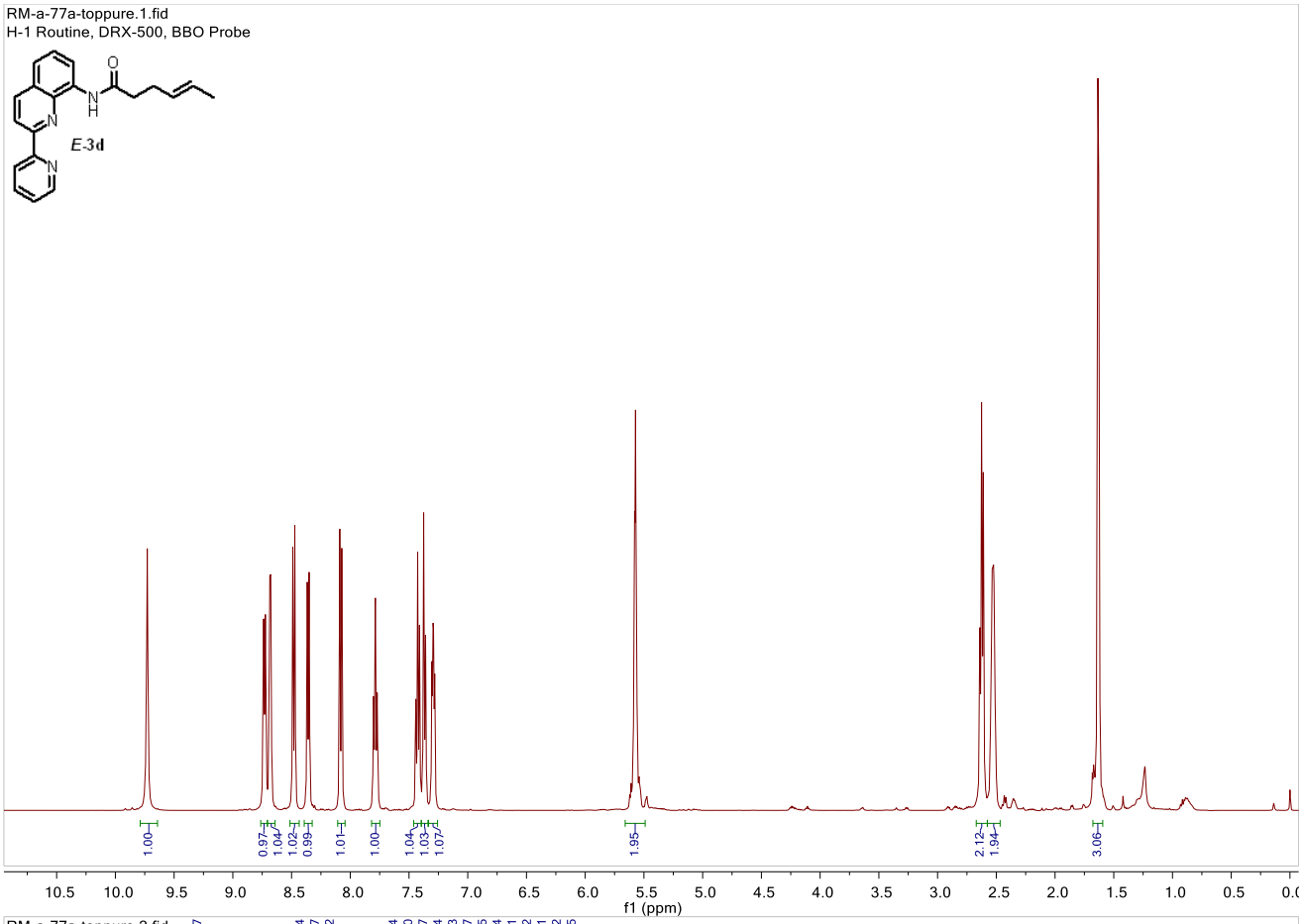

MOD3-007.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
3a
f1 (ppm)

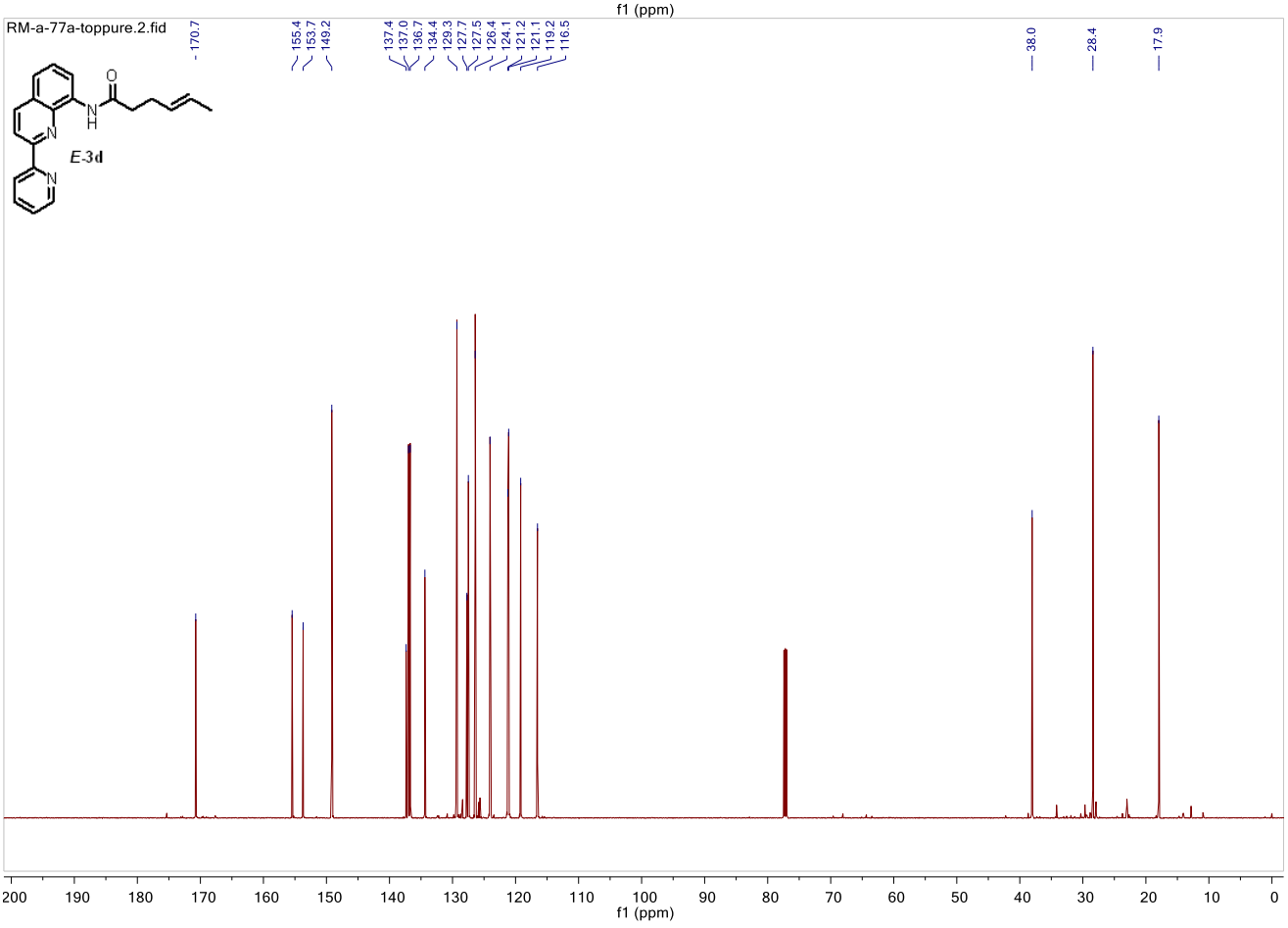

RM-A-49-pub.1.fid
H-1 Routine, DRX-500, BBO Probe
3b
f1 (ppm)

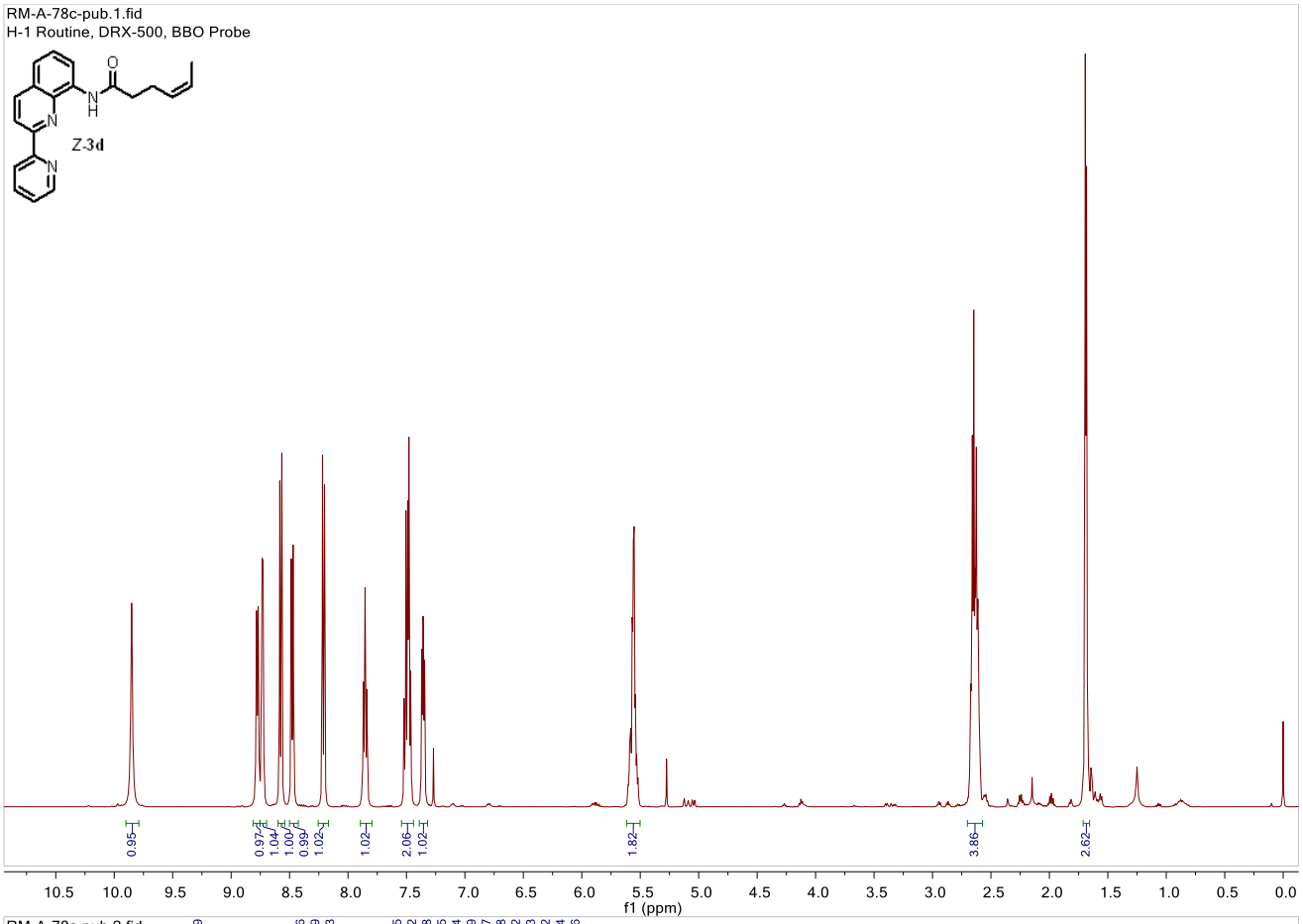

RM-A-49-pub.2.fid
3b
f1 (ppm)

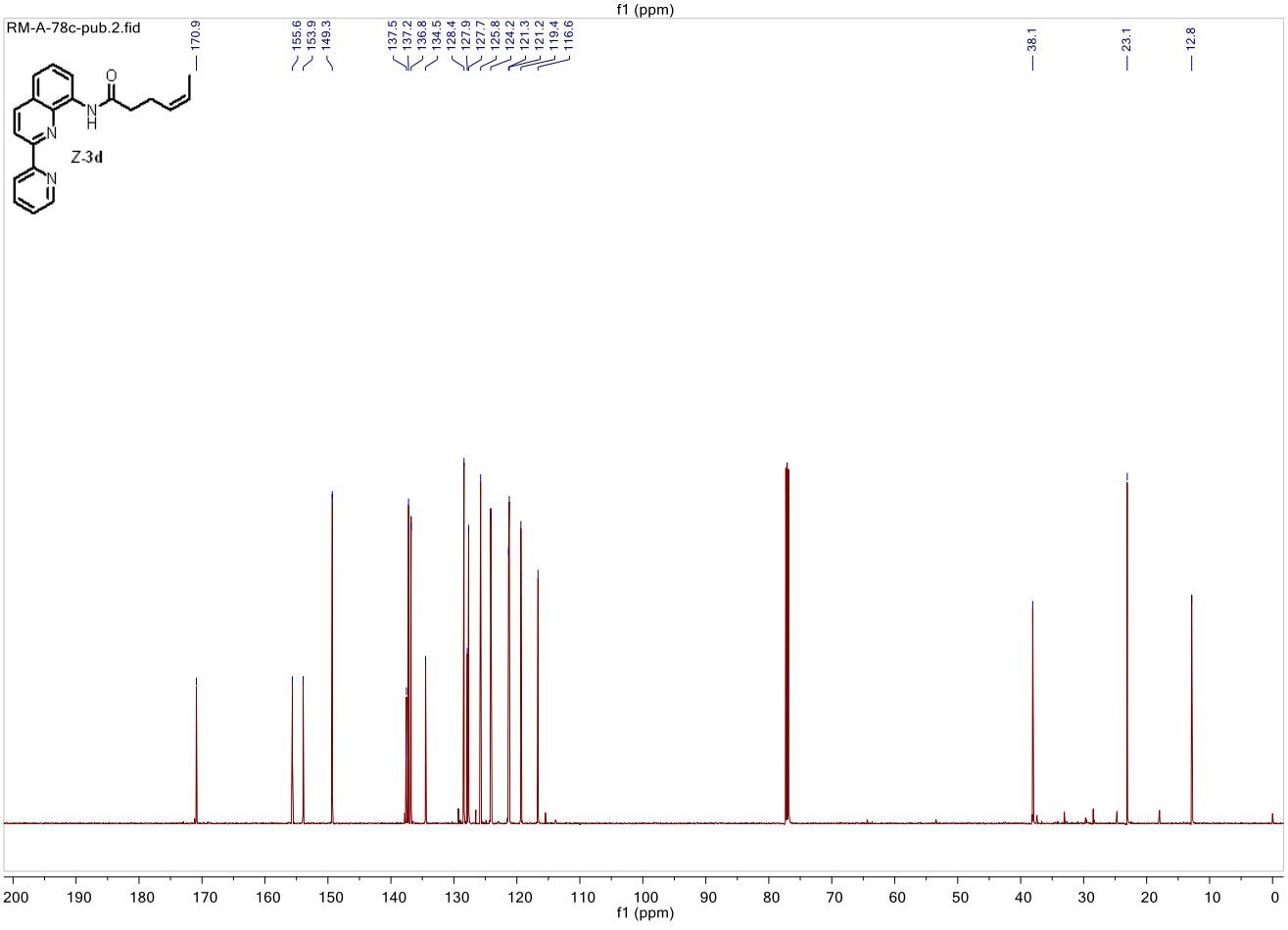

RM-A-45-mix-pure.1.fid
H-1 Routine, DRX-500, BBO Probe
3c
1.00
1.05
1.00
1.02
1.03
1.05
1.05
1.98
1.06
1.01
1.08
1.05
1.05
1.08
1.08
3.06
f1 (ppm)

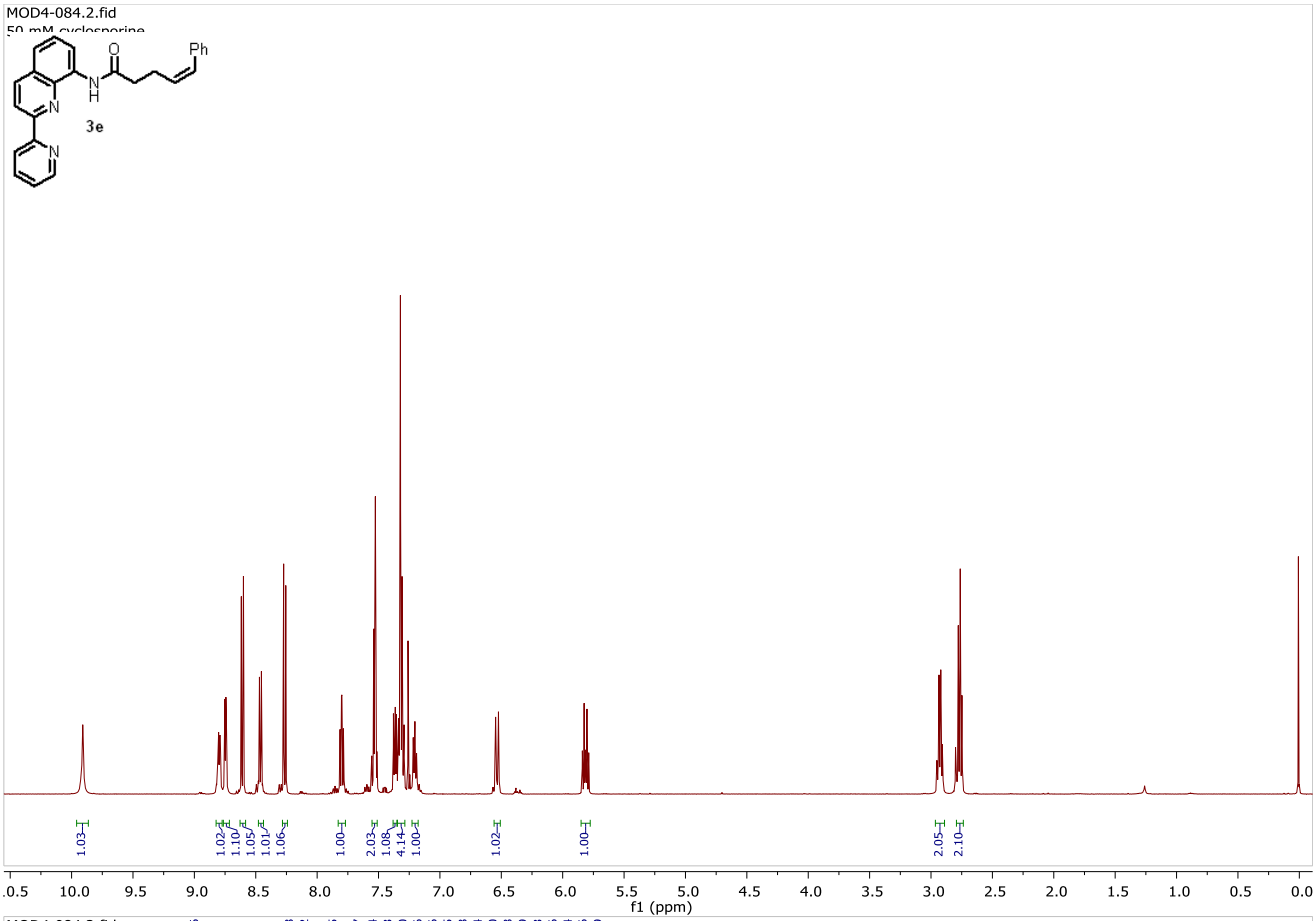

RM-A-45-pub.2.fid
3c
170.2
155.8
154.1
149.4
142.6
137.6
137.3
136.9
134.5
127.9
127.7
124.2
121.4
121.3
119.5
116.8
113.7
45.5
34.9
19.8
f1 (ppm)

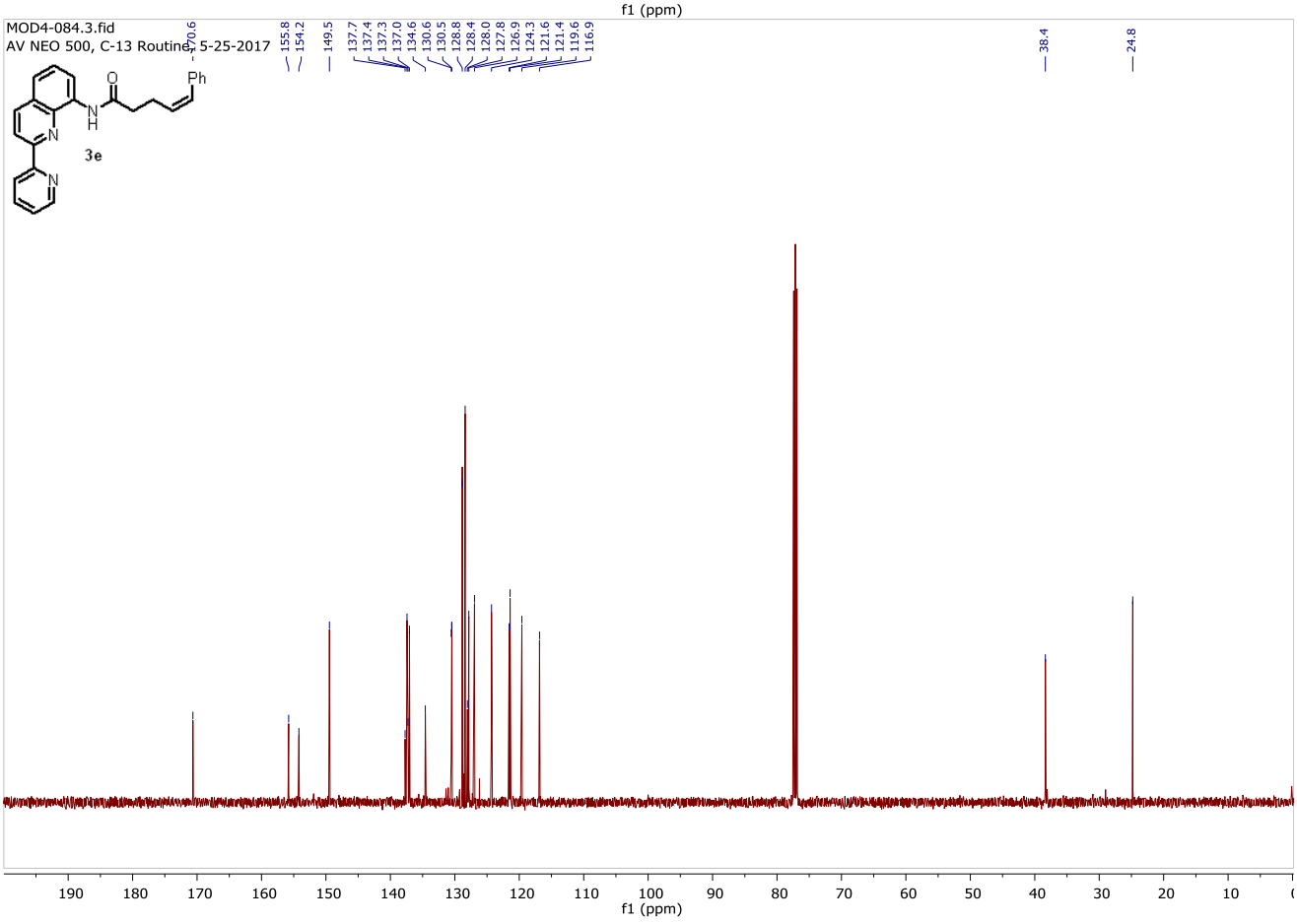

RM-a-77a-toppure.1.fid
H-1 Routine, DRX-500, BBO Probe
E-3d
1.00
0.97
1.04
1.02
0.99
1.01
1.00
1.04
1.03
1.07
1.95
2.12
1.94
3.06
f1 (ppm)

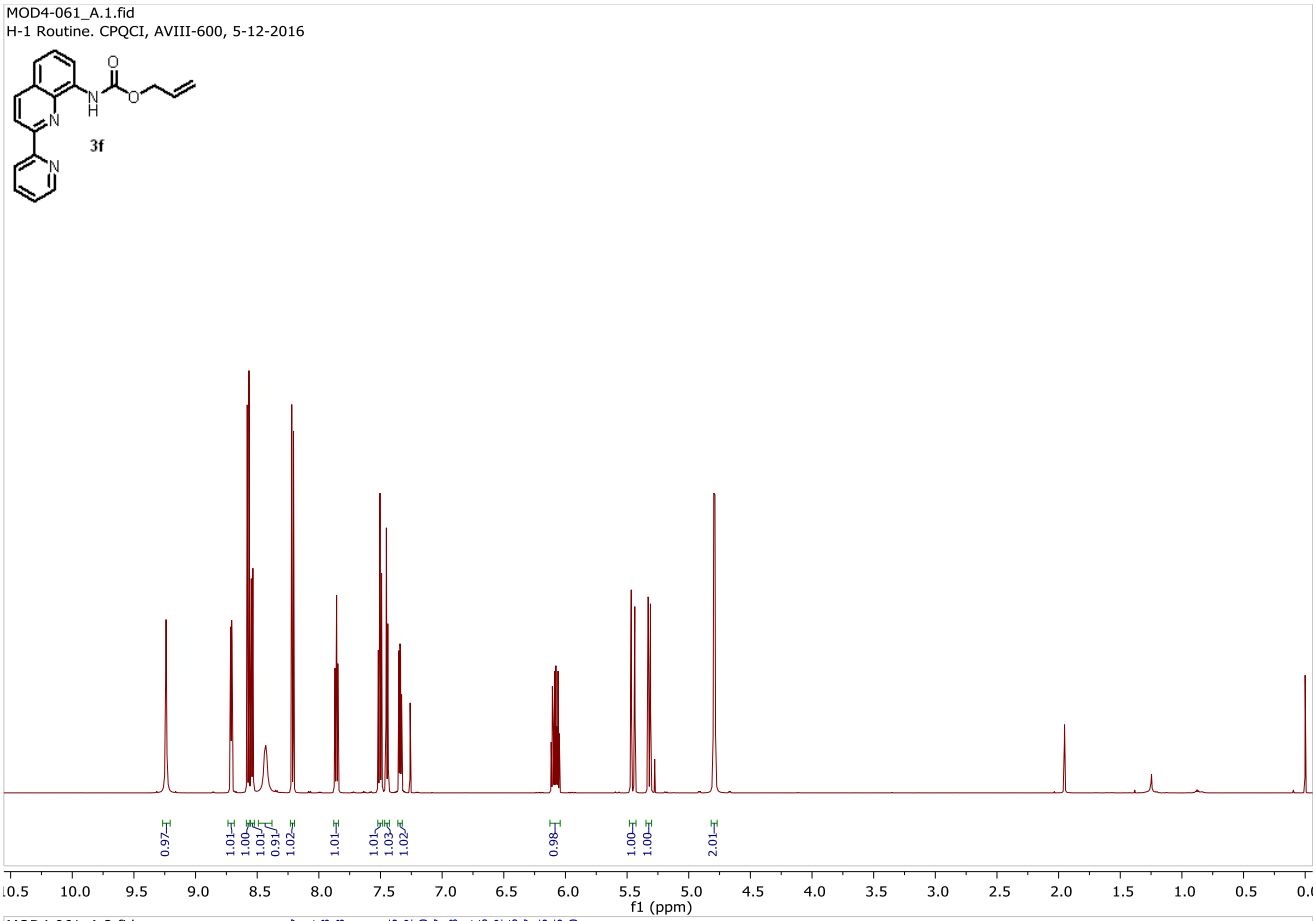

RM-a-77a-toppure.2.fid
E-3d
170.7
155.4
153.7
149.2
137.4
137.0
136.7
134.4
129.3
127.7
127.5
126.4
124.1
121.2
121.1
119.2
116.5
38.0
28.4
17.9
f1 (ppm)

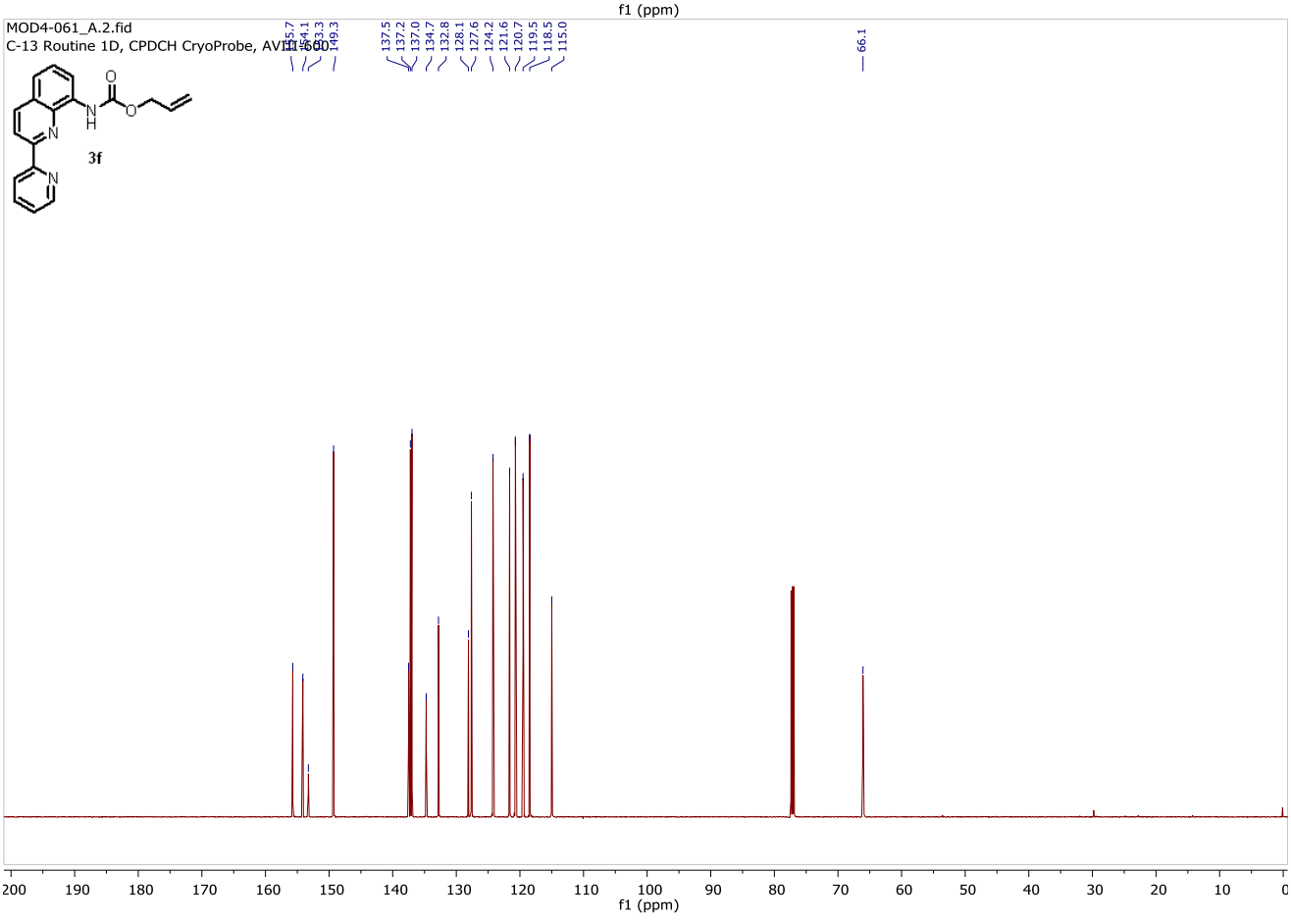

RM-A-78c-pub.1.fid
H-1 Routine, DRX-500, BBO Probe
Z-3d
0.95
0.97
1.04
1.00
0.99
1.02
1.02
2.06
1.02
1.82
3.86
2.62
f1 (ppm)

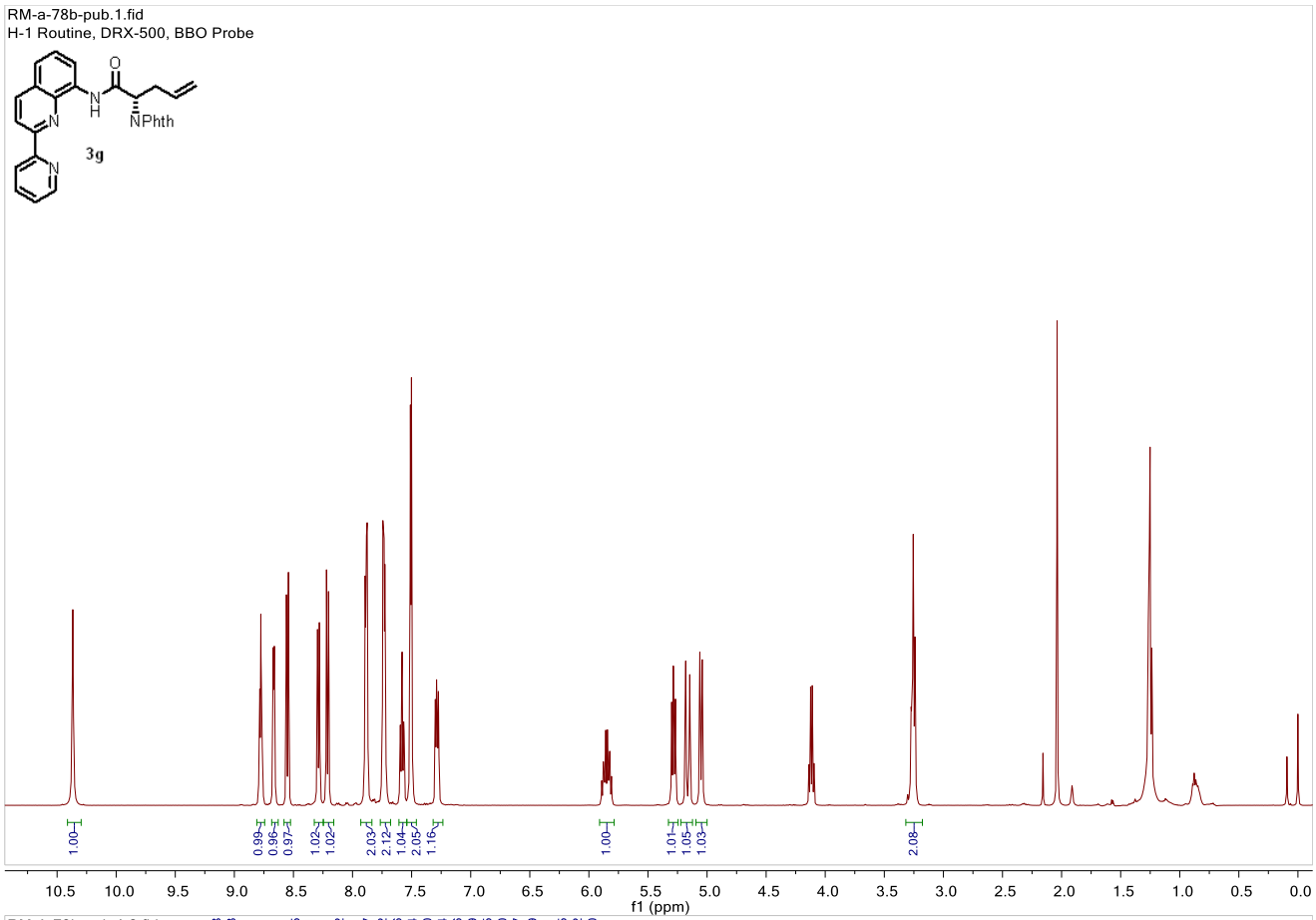

RM-A-78c-pub.2.fid
Z-3d
170.9
155.6
153.9
149.3
137.5
137.2
136.8
134.5
128.4
127.9
127.7
125.8
124.2
121.3
121.2
119.4
116.6
38.1
23.1
12.8
f1 (ppm)

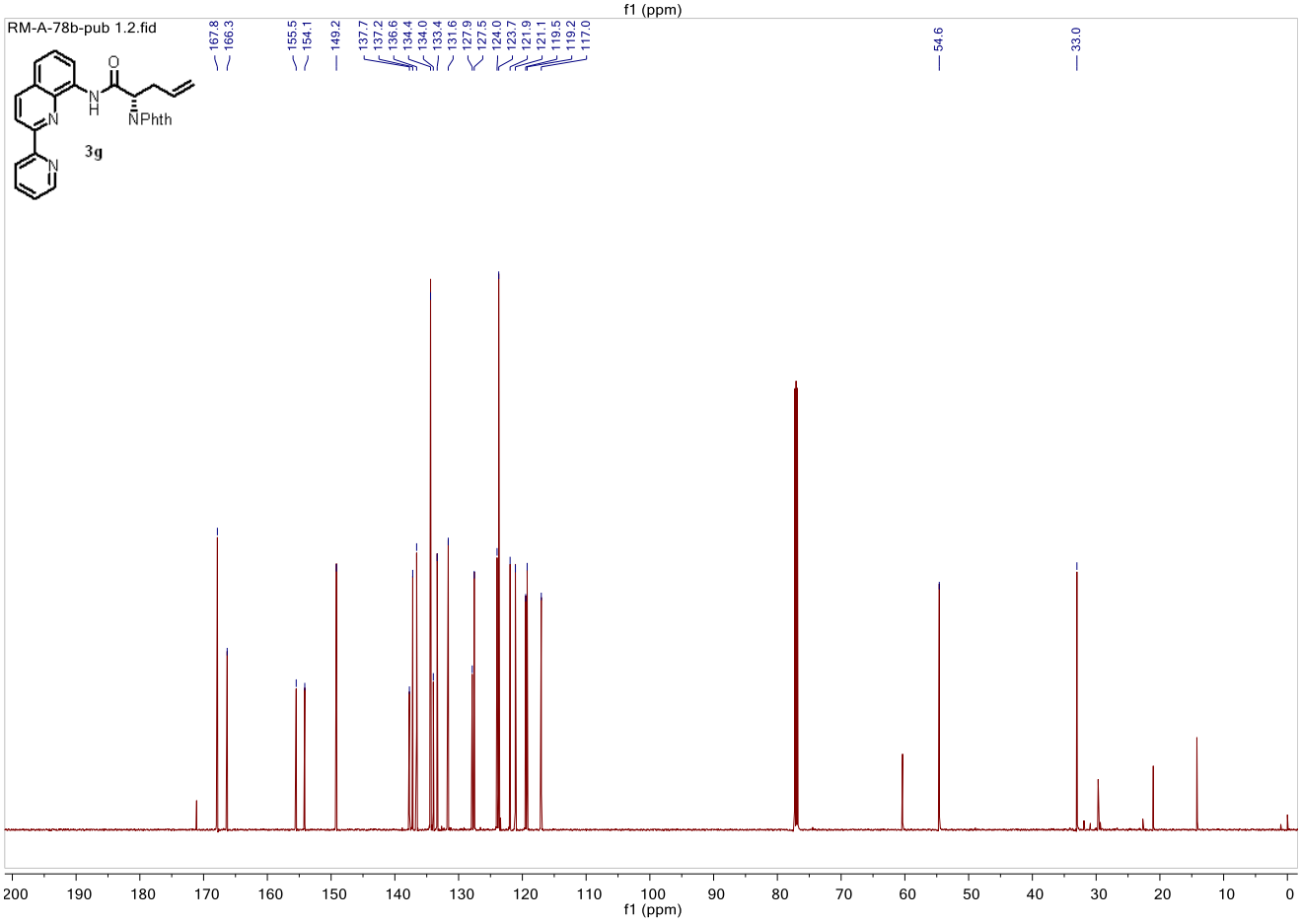

MOD4-084.2.fid
3e
f1 (ppm)

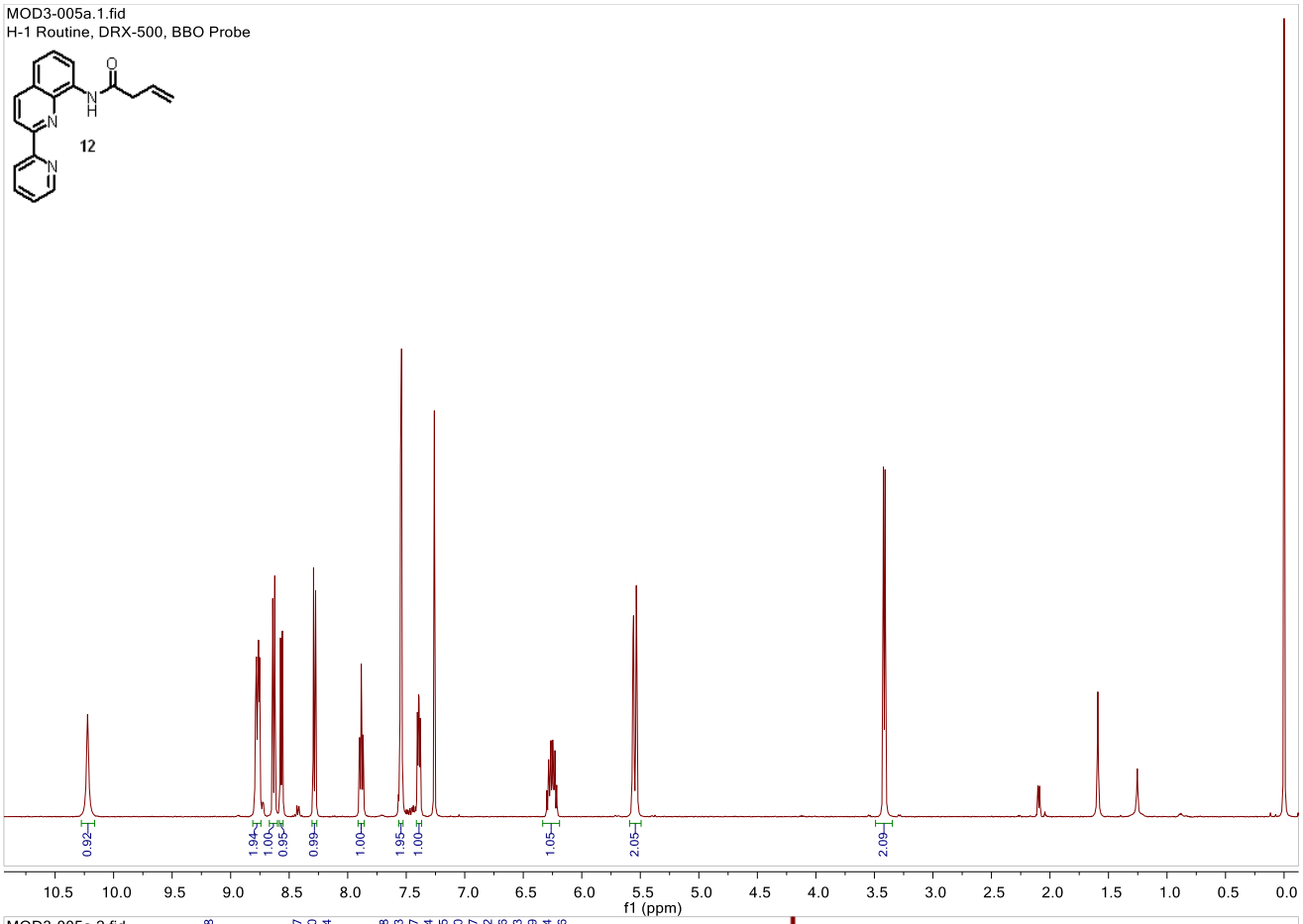

MOD4-084.3.fid
AV NEO 500, C-13 Routine, 5-25-2017
3e
f1 (ppm)

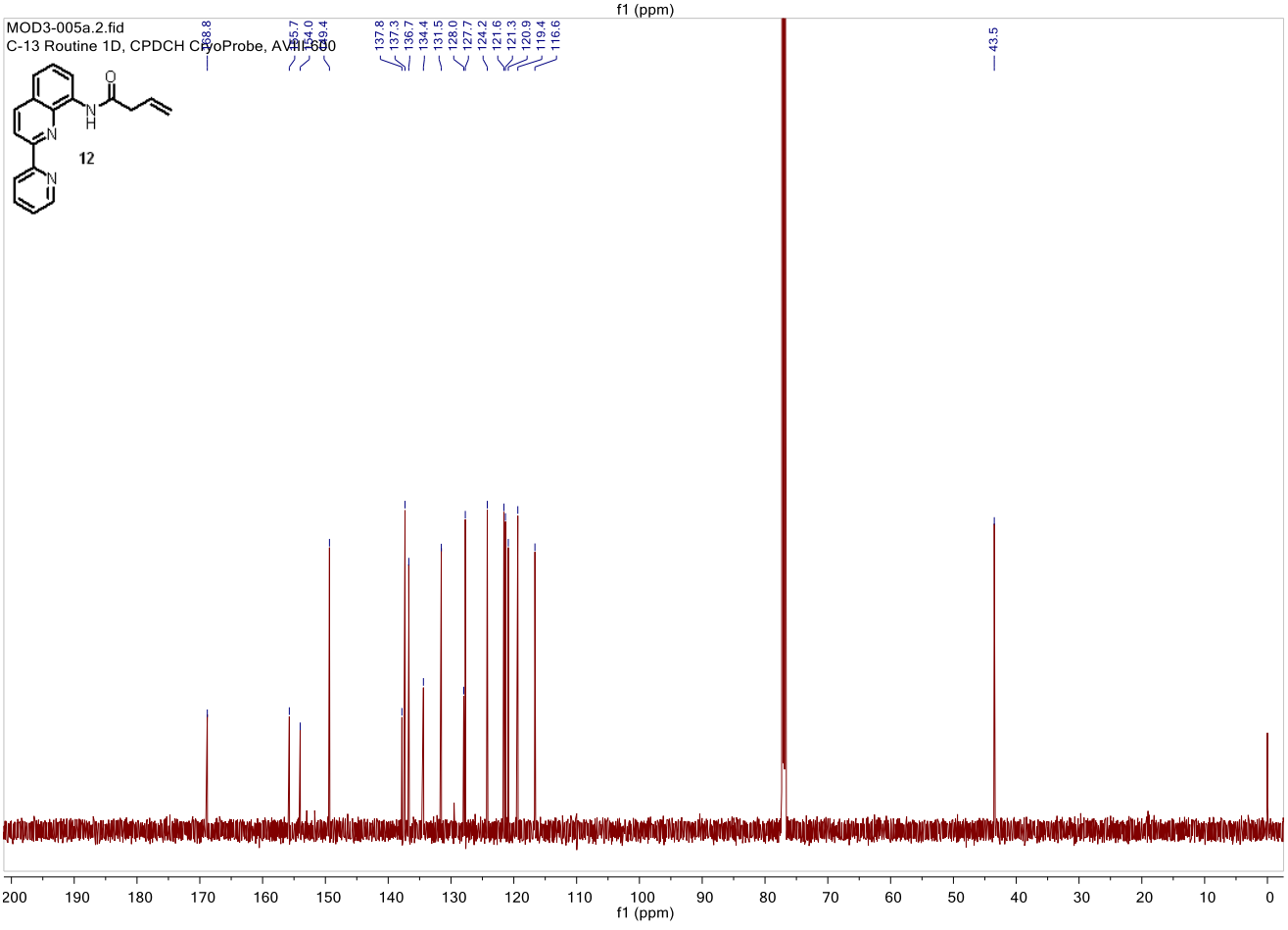

MOD4-061_A.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
3f
f1 (ppm)

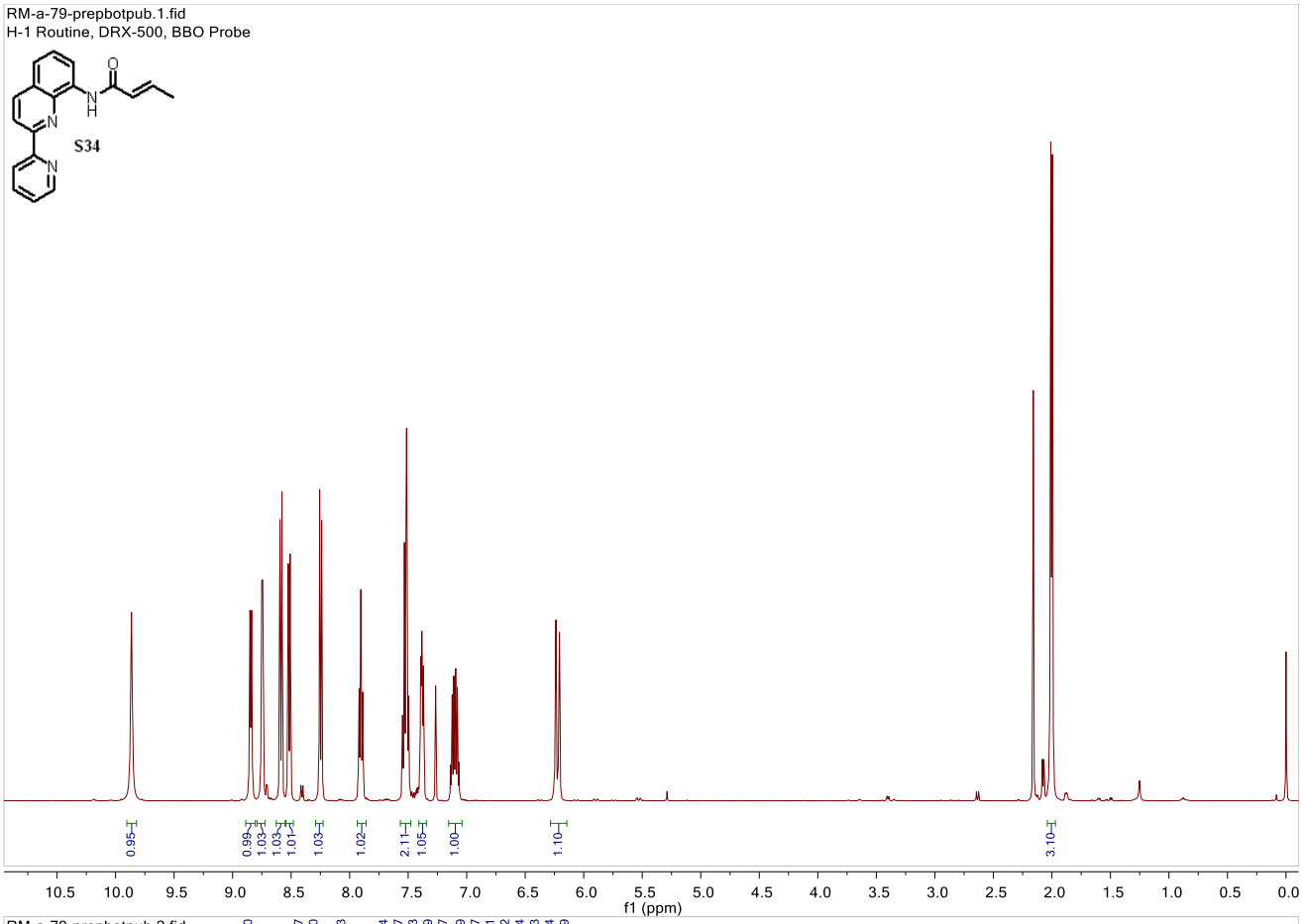

MOD4-061_A.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
3f
155.7
154.1
153.3
149.3
137.5
137.2
137.0
134.7
132.8
128.1
127.6
124.2
121.6
120.7
119.5
118.5
115.0
66.1
f1 (ppm)

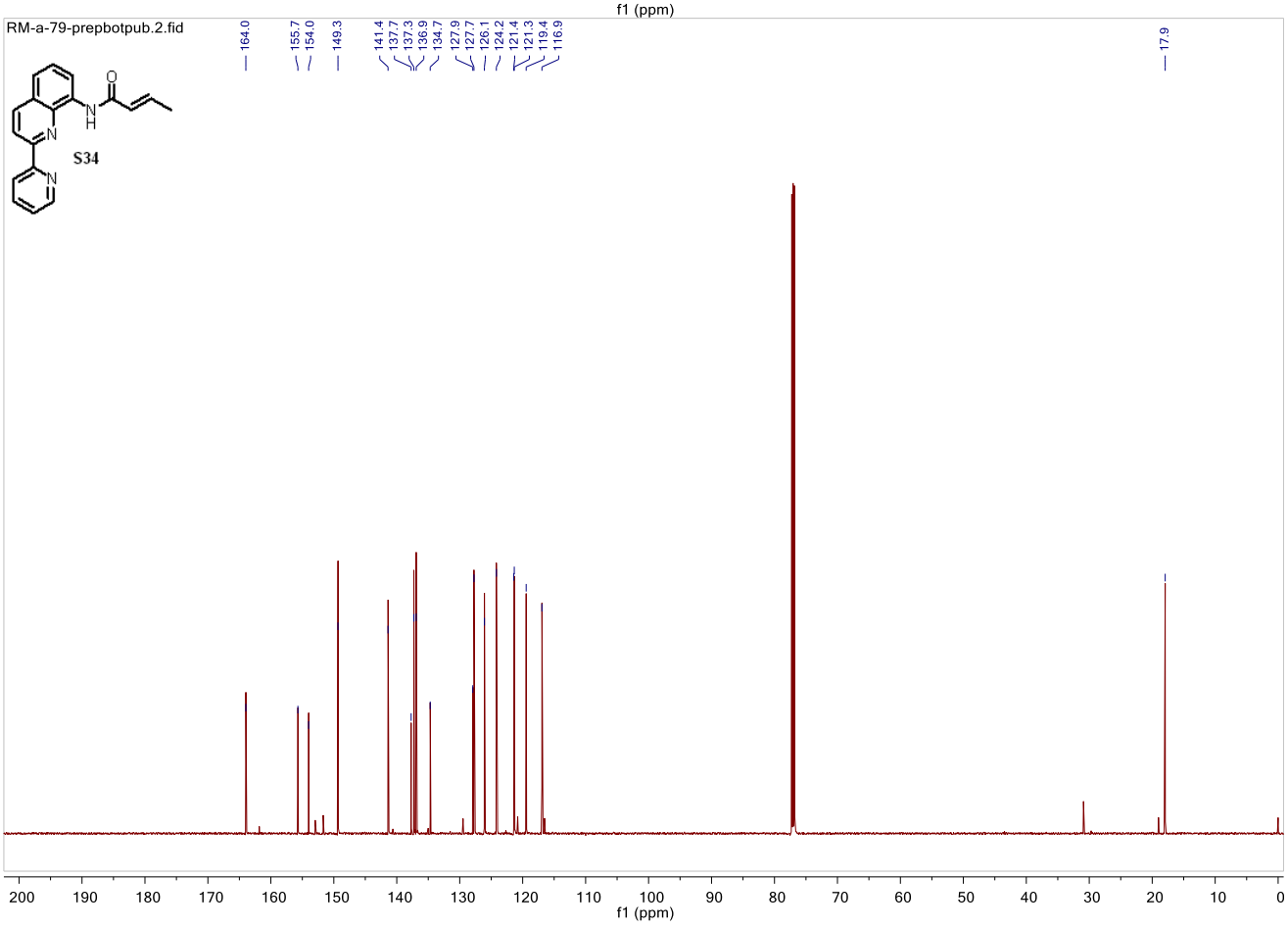

RM-a-78b-pub.1.fid
H-1 Routine, DRX-500, BBO Probe
O
N
H
NPhth
N
3g
1.00
0.99
0.96
0.97
1.02
1.02
2.03
2.12
1.04
2.05
1.16
1.00
1.01
1.05
1.03
2.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

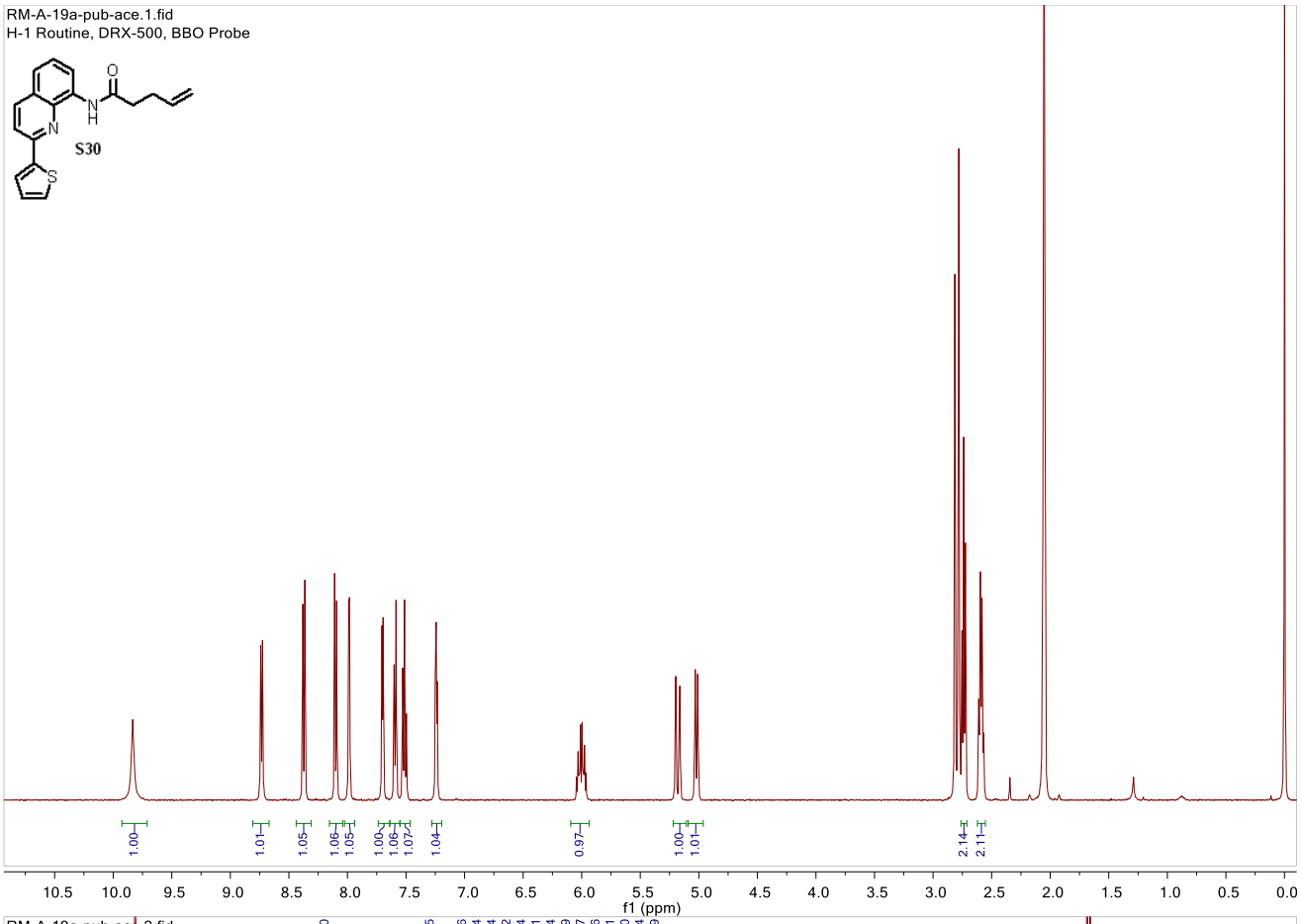

RM-A-78b-pub 1.2.fid
O
N
H
NPhth
N
3g
167.8
166.3
155.5
154.1
149.2
137.7
137.2
136.6
134.4
134.0
133.4
131.6
127.9
127.5
124.0
123.7
121.9
121.1
119.5
119.2
117.0
54.6
33.0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

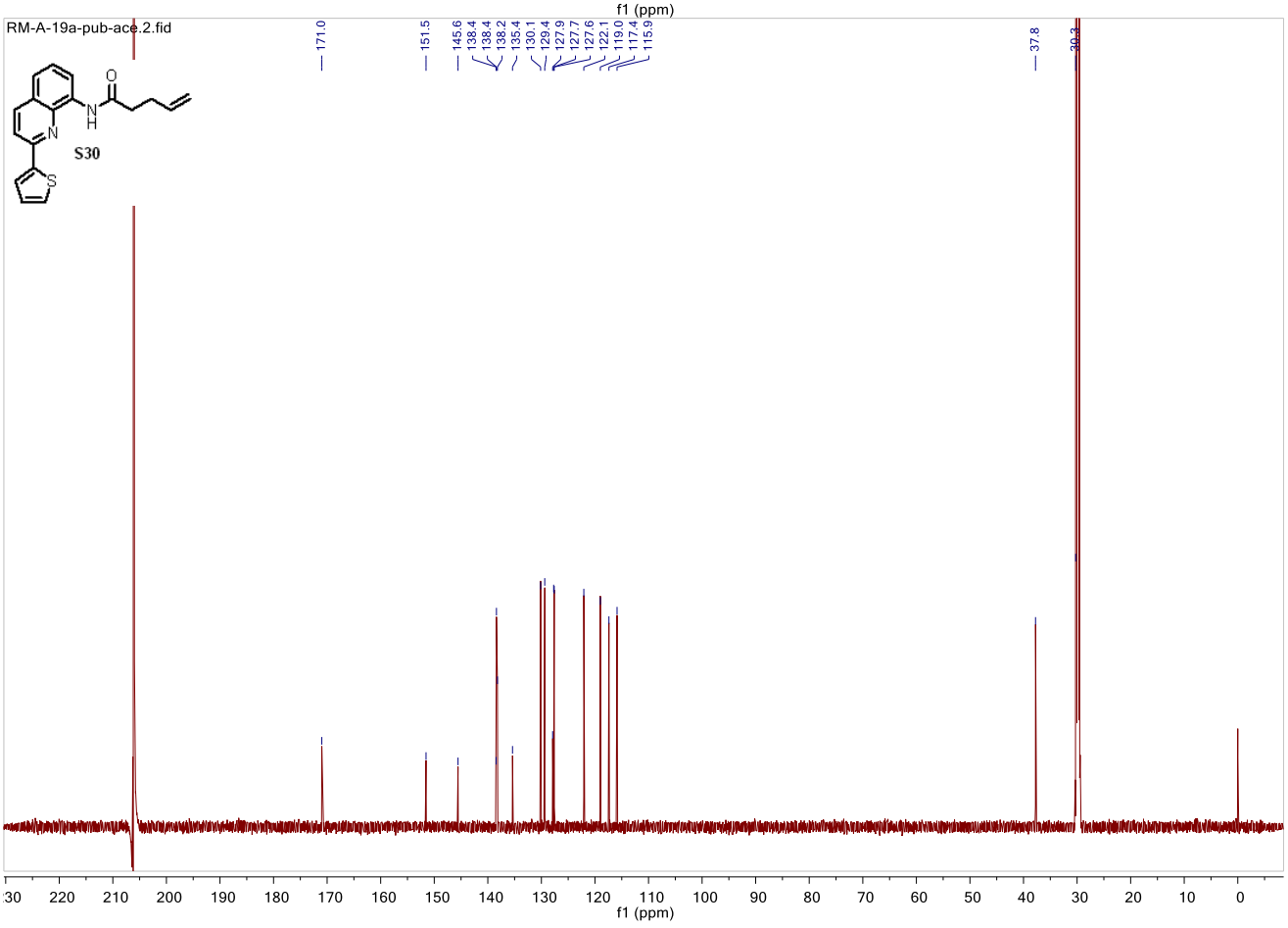

MOD3-005a.1.fid
H-1 Routine, DRX-500, BBO Probe
12
0.92
1.94
1.00
0.95
0.99
1.00
1.95
1.00
1.05
2.05
2.09
f1 (ppm)

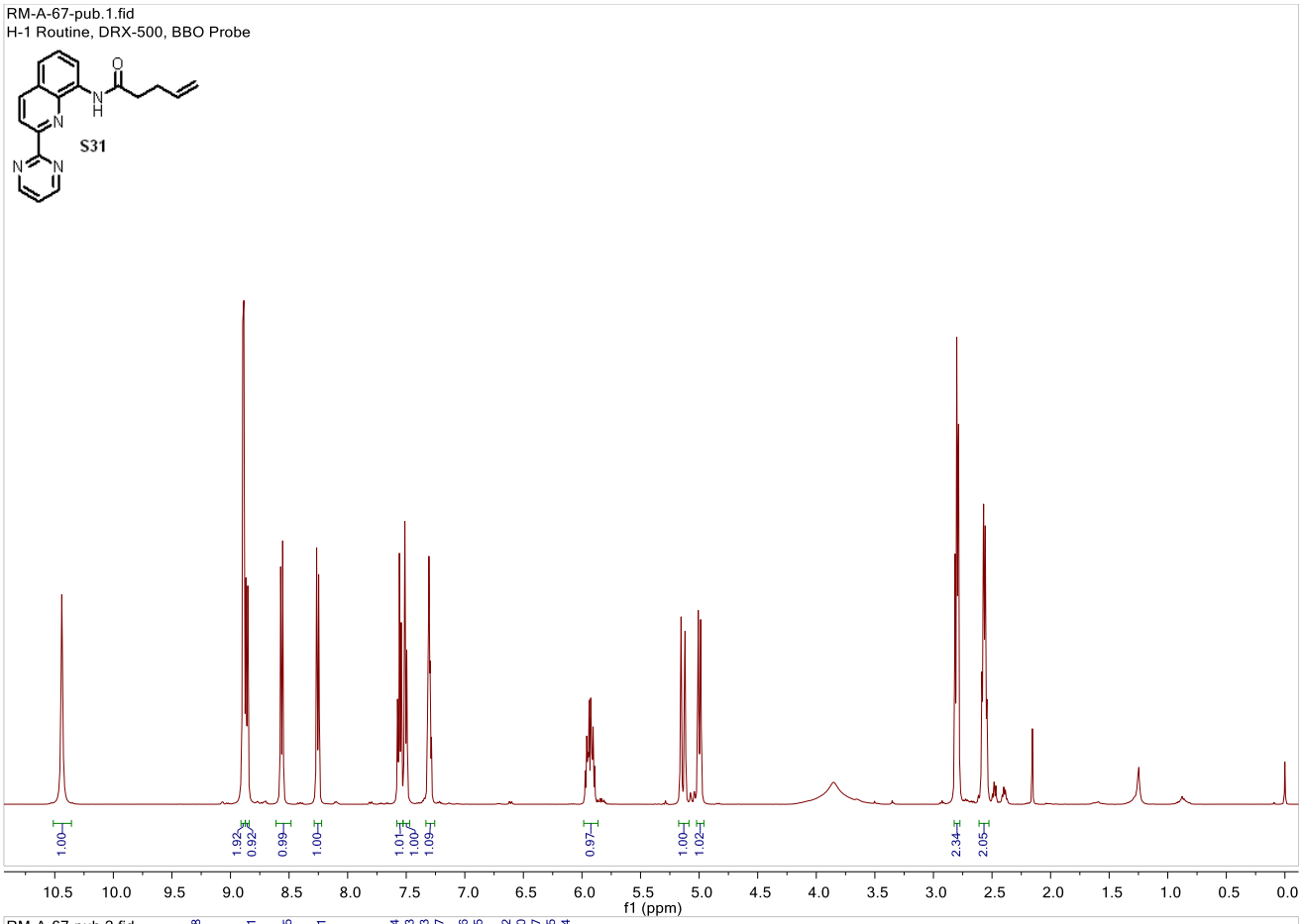

MOD3-005a.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
12
168.8
155.7
154.0
149.4
137.8
137.3
136.7
134.4
131.5
128.0
127.7
124.2
121.6
121.3
120.9
119.4
116.6
43.5
f1 (ppm)

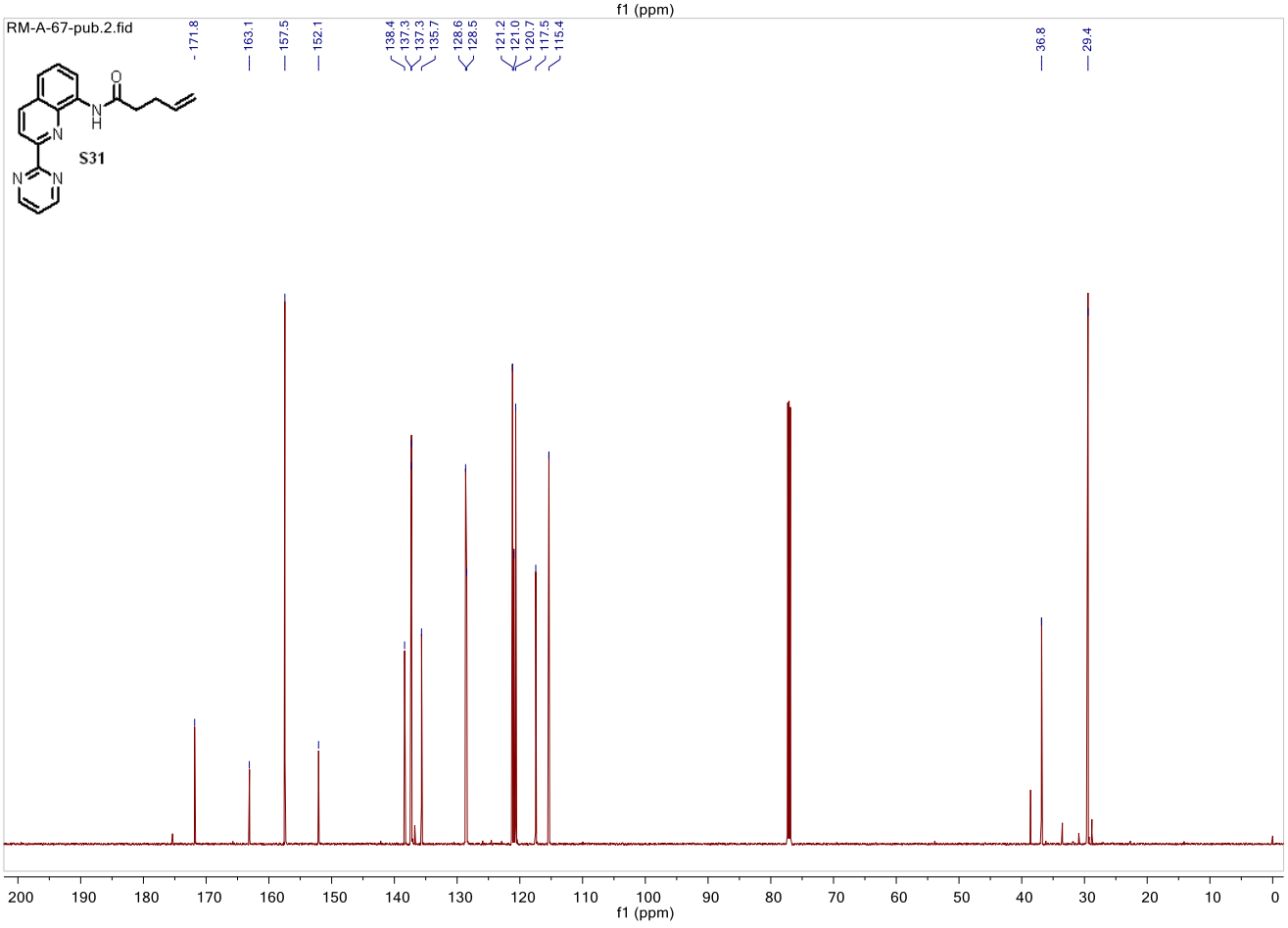

RM-a-79-prepbotpub.1.fid
H-1 Routine, DRX-500, BBO Probe
S34
0.95
0.99
1.03
1.03
1.01
1.03
1.02
2.11
1.05
1.00
1.10
3.10
f1 (ppm)


RM-a-79-prepbotpub.2.fid
S34
164.0
155.7
154.0
149.3
141.4
137.7
137.3
136.9
134.7
127.9
127.7
126.1
124.2
121.4
121.3
119.4
116.9
17.9
f1 (ppm)

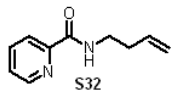

RM-A-19a-pub-ace.1.fid
H-1 Routine, DRX-500, BBO Probe
S30
1.00
1.01
1.05
1.06
1.05
1.00
1.06
1.07
1.04
0.97
1.00
1.01
2.14
2.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


RM-A-19a-pub-ace.2.fid
S30
171.0
151.5
145.6
138.4
138.4
138.2
135.4
130.1
129.4
127.9
127.7
127.6
122.1
119.0
117.4
115.9
37.8
30.3
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)

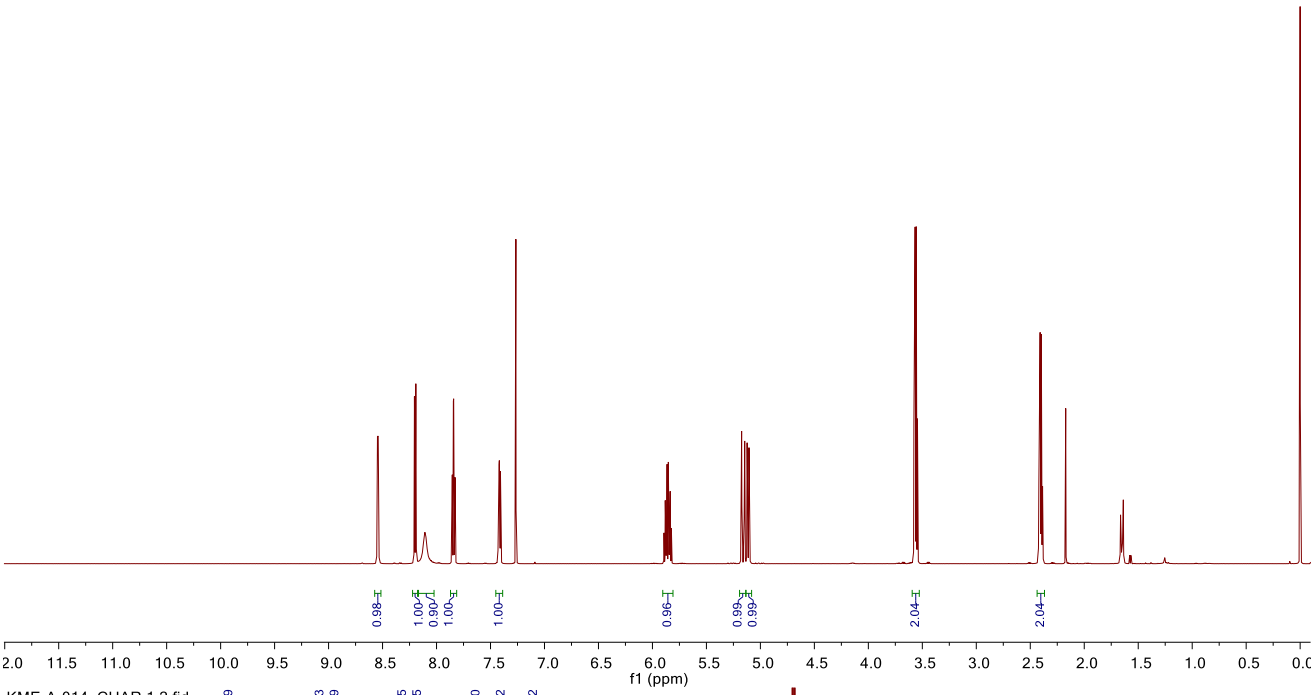

RM-A-67-pub.1.fid
H-1 Routine, DRX-500, BBO Probe
S31
1.00
1.92
0.92
0.99
1.00
1.01
1.00
1.09
0.97
1.00
1.02
2.34
2.05
f1 (ppm)


RM-A-67-pub.2.fid
171.8
163.1
157.5
152.1
138.4
137.3
137.3
135.7
128.6
128.5
121.2
121.0
120.7
117.5
115.4
36.8
29.4
S31
f1 (ppm)

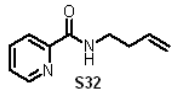
KME-A-014_CHAR 1.1.fid



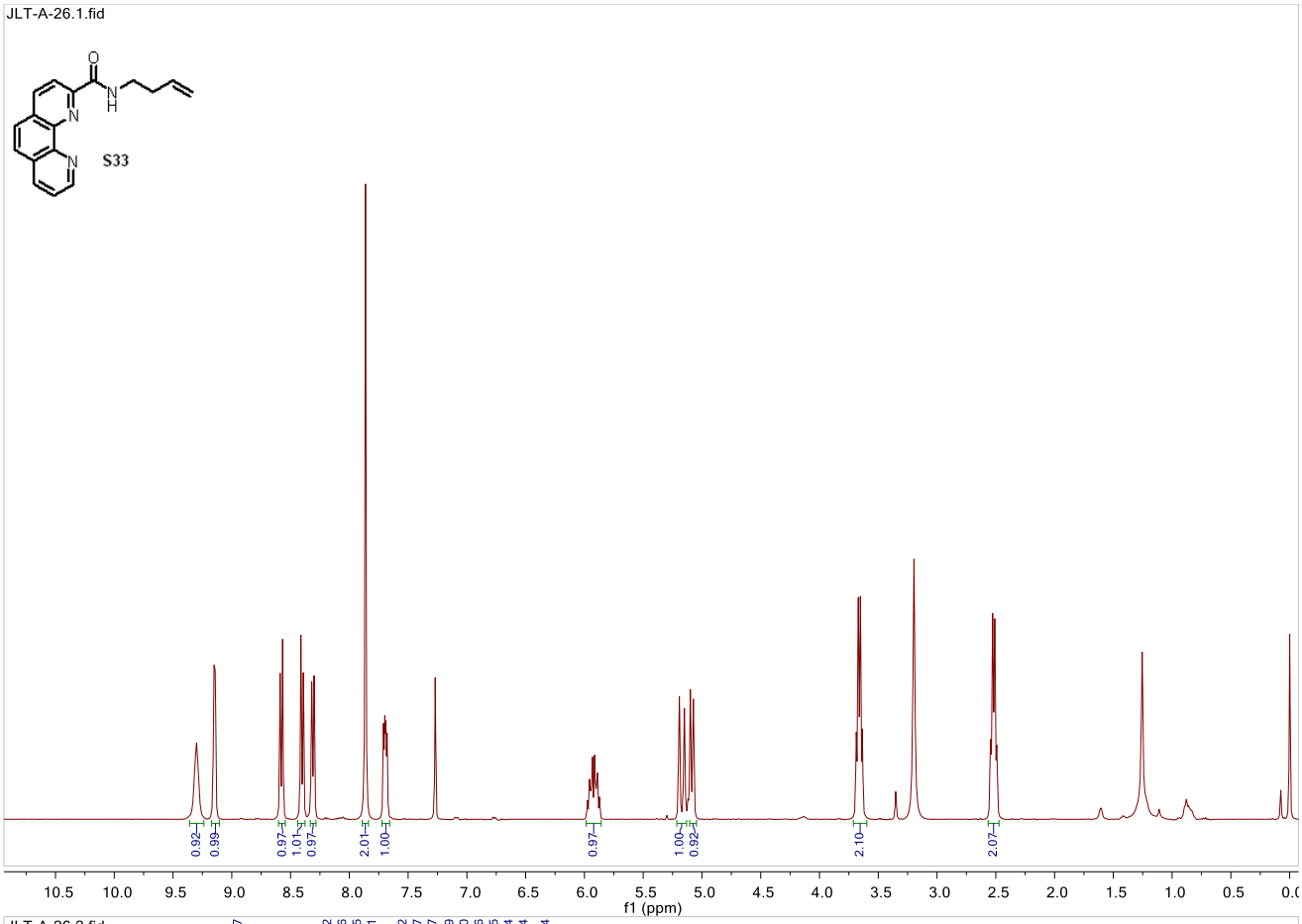
S32

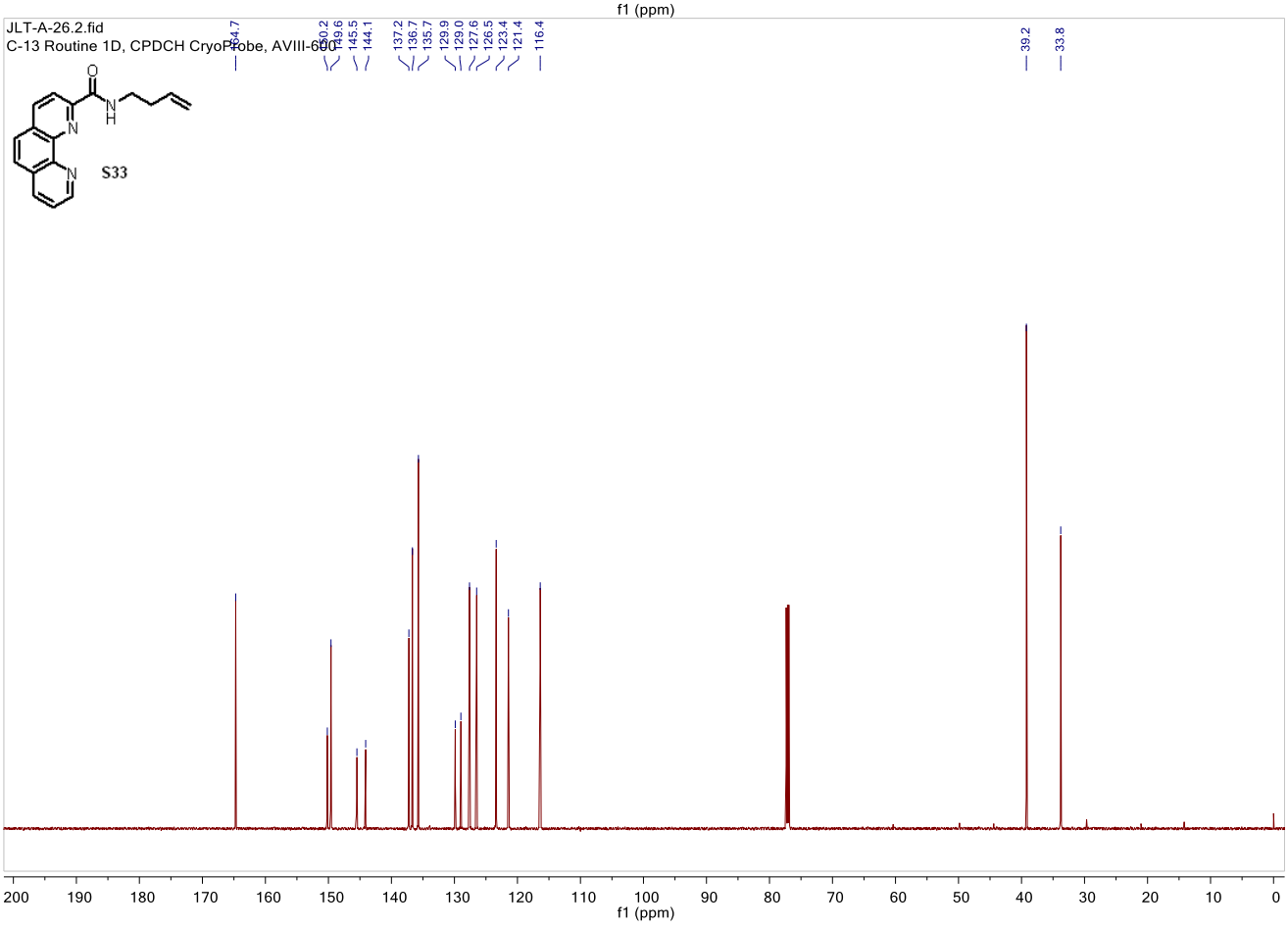


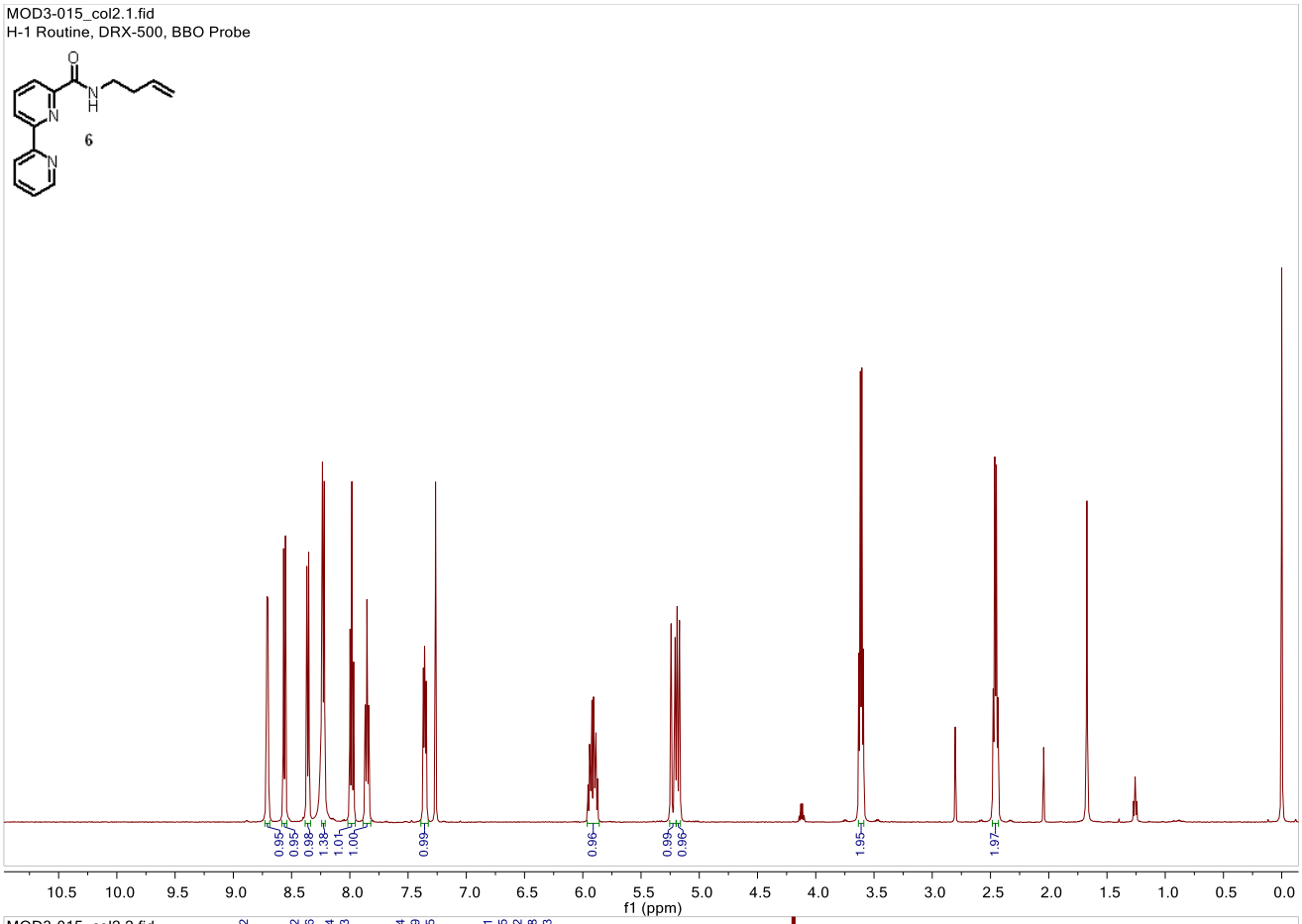
KME-A-014_CHAR 1.2.fid

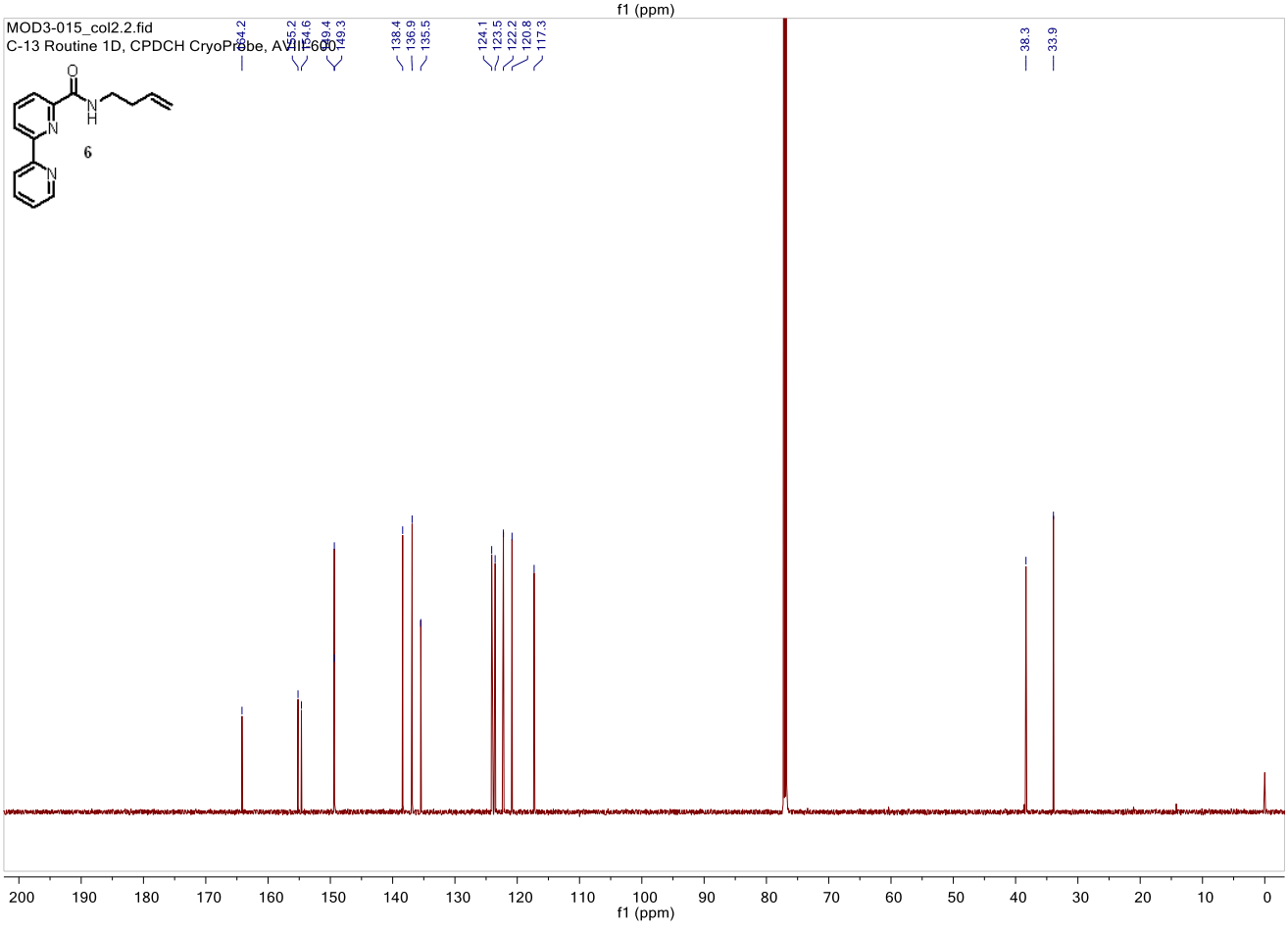


S32

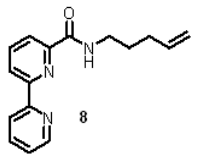

JLT-A-26.1.fid
S33
0.92
0.99
0.97
1.01
0.97
2.01
1.00
0.97
1.00
0.92
2.10
2.07
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


JLT-A-26.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
S33
174.7
150.2
149.6
145.5
144.1
137.2
136.7
135.7
129.9
129.0
127.6
126.5
123.4
121.4
116.4
39.2
33.8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

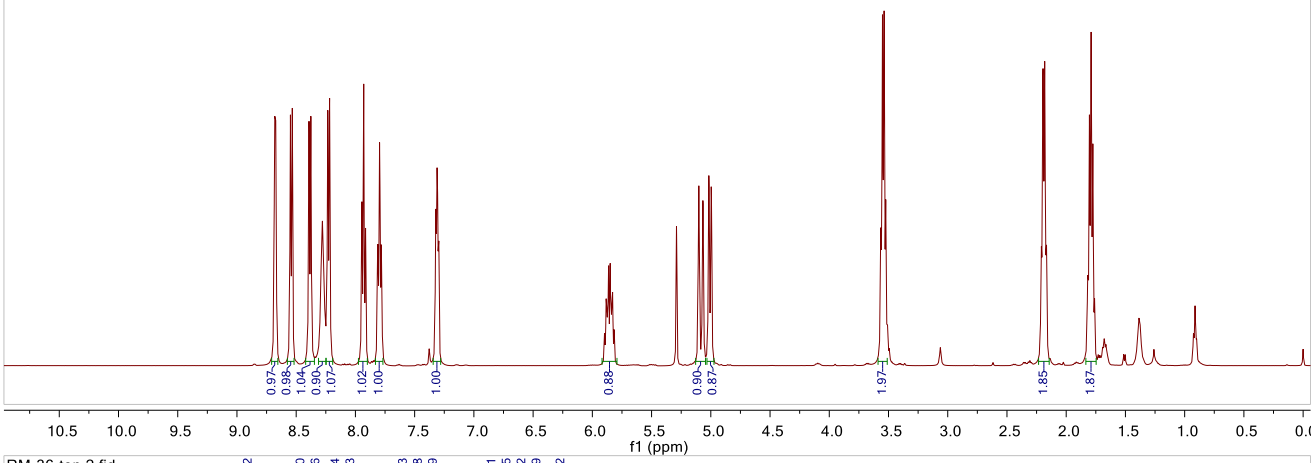

MOD3-015_col2.1.fid
H-1 Routine, DRX-500, BBO Probe
6
0.95
0.95
0.98
1.38
1.01
1.00
0.99
0.96
0.99
0.96
1.95
1.97
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


MOD3-015_col2.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
6
164.2
155.2
154.6
149.4
149.3
138.4
136.9
135.5
124.1
123.5
122.2
120.8
117.3
38.3
33.9
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

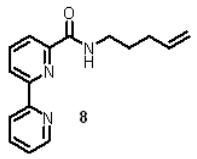
RM-36-top.1.fid
H-1 Routine, DRX-500, BBO Probe



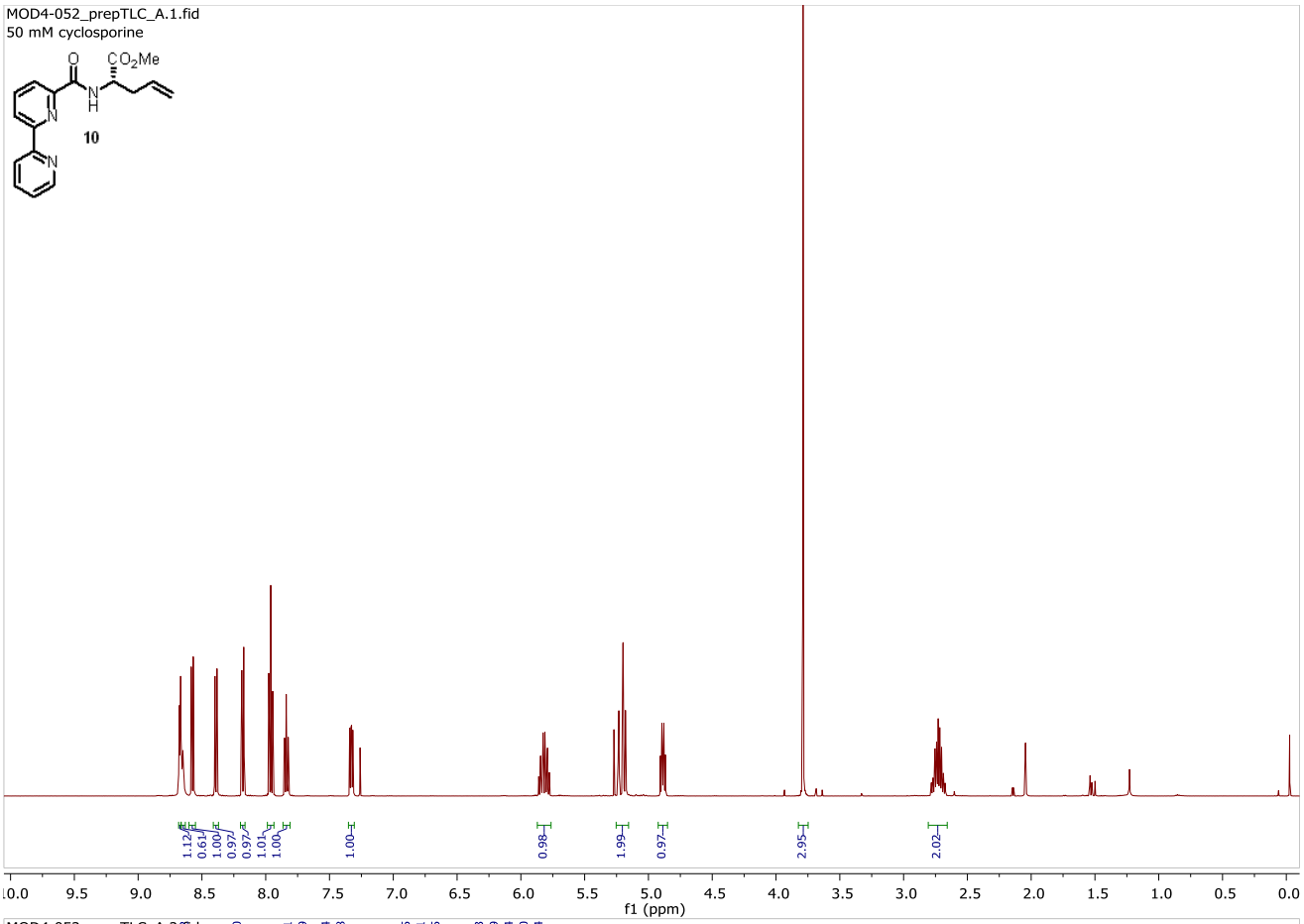
8

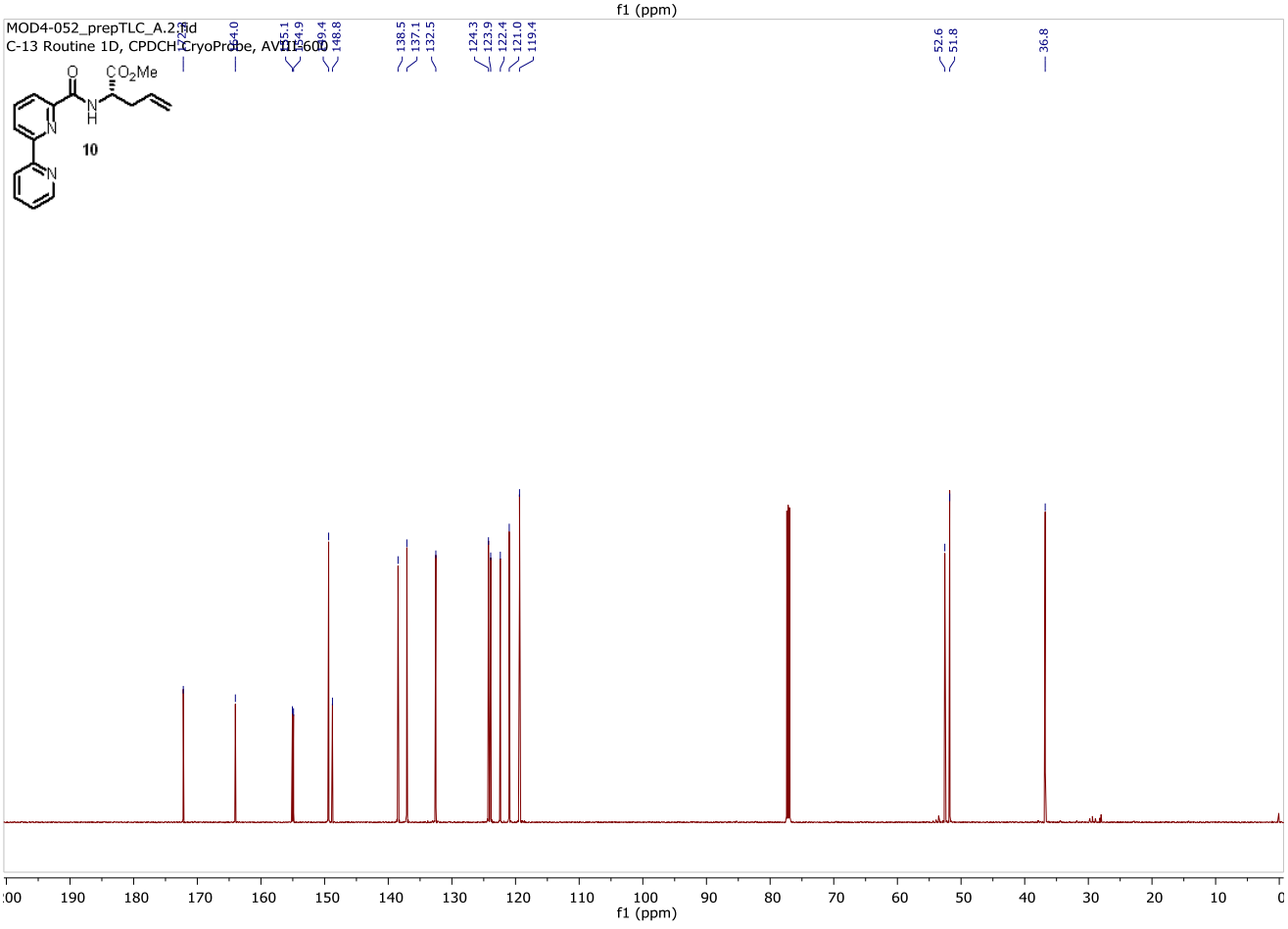


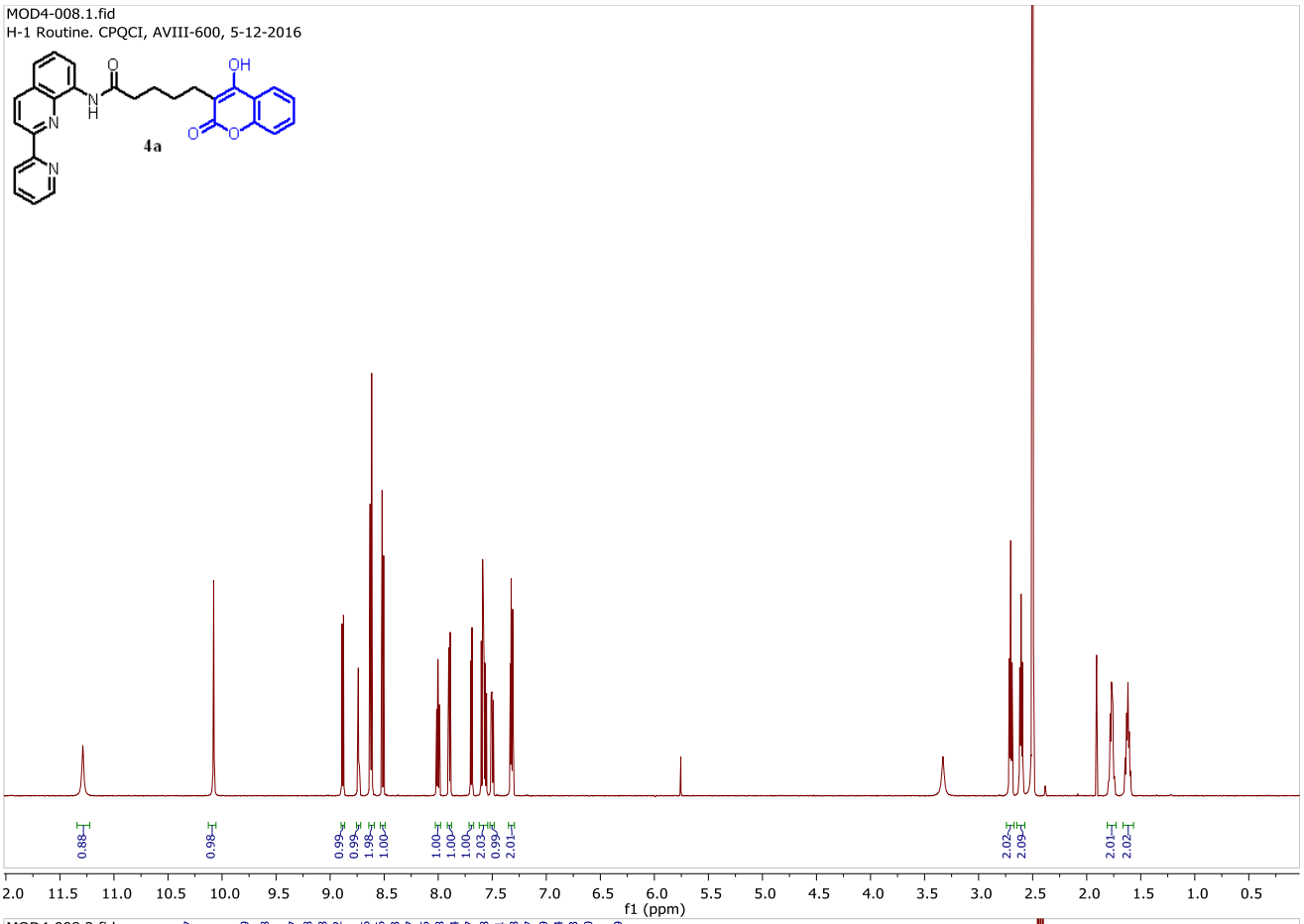
RM-36-top.2.fid

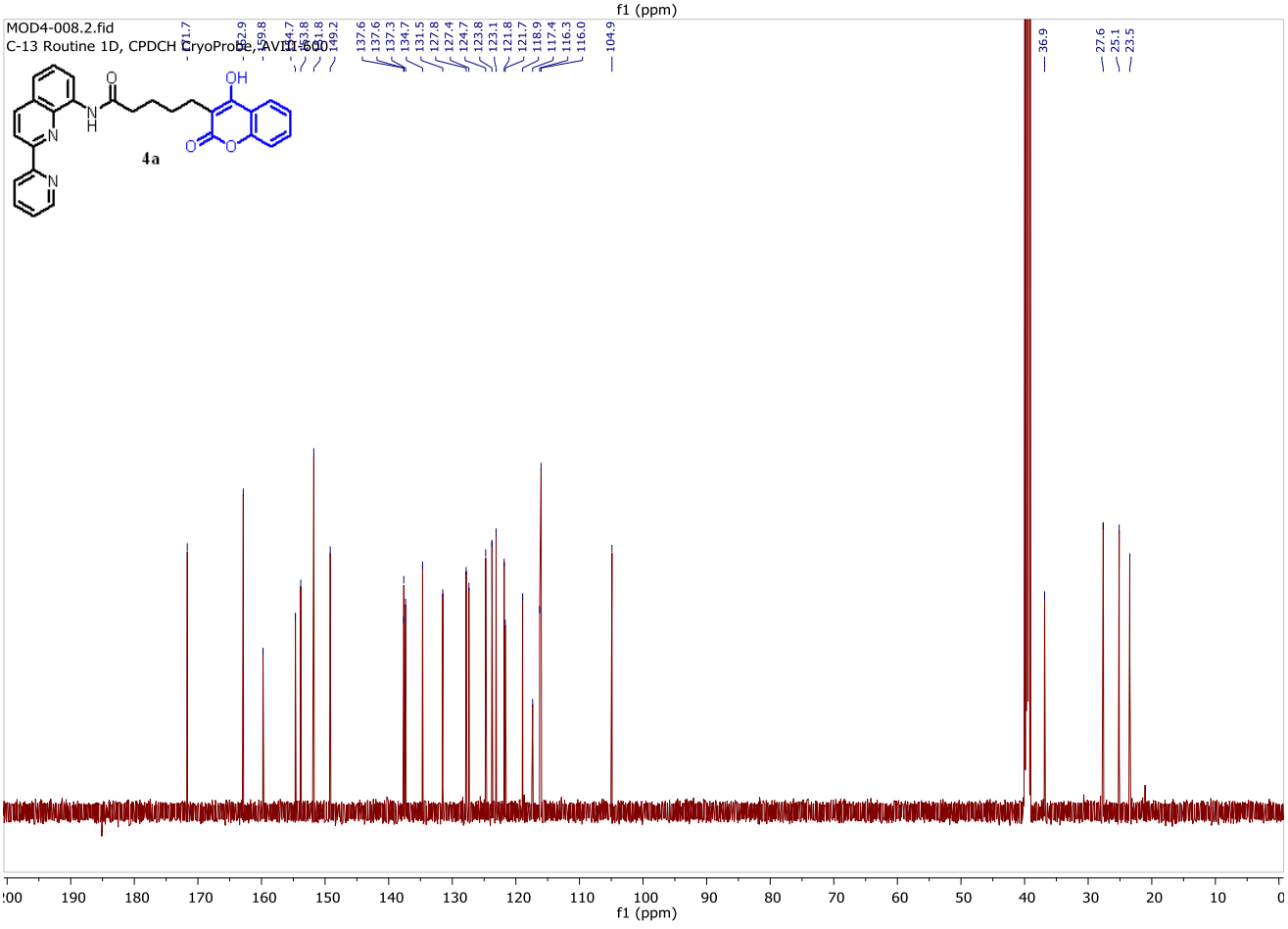


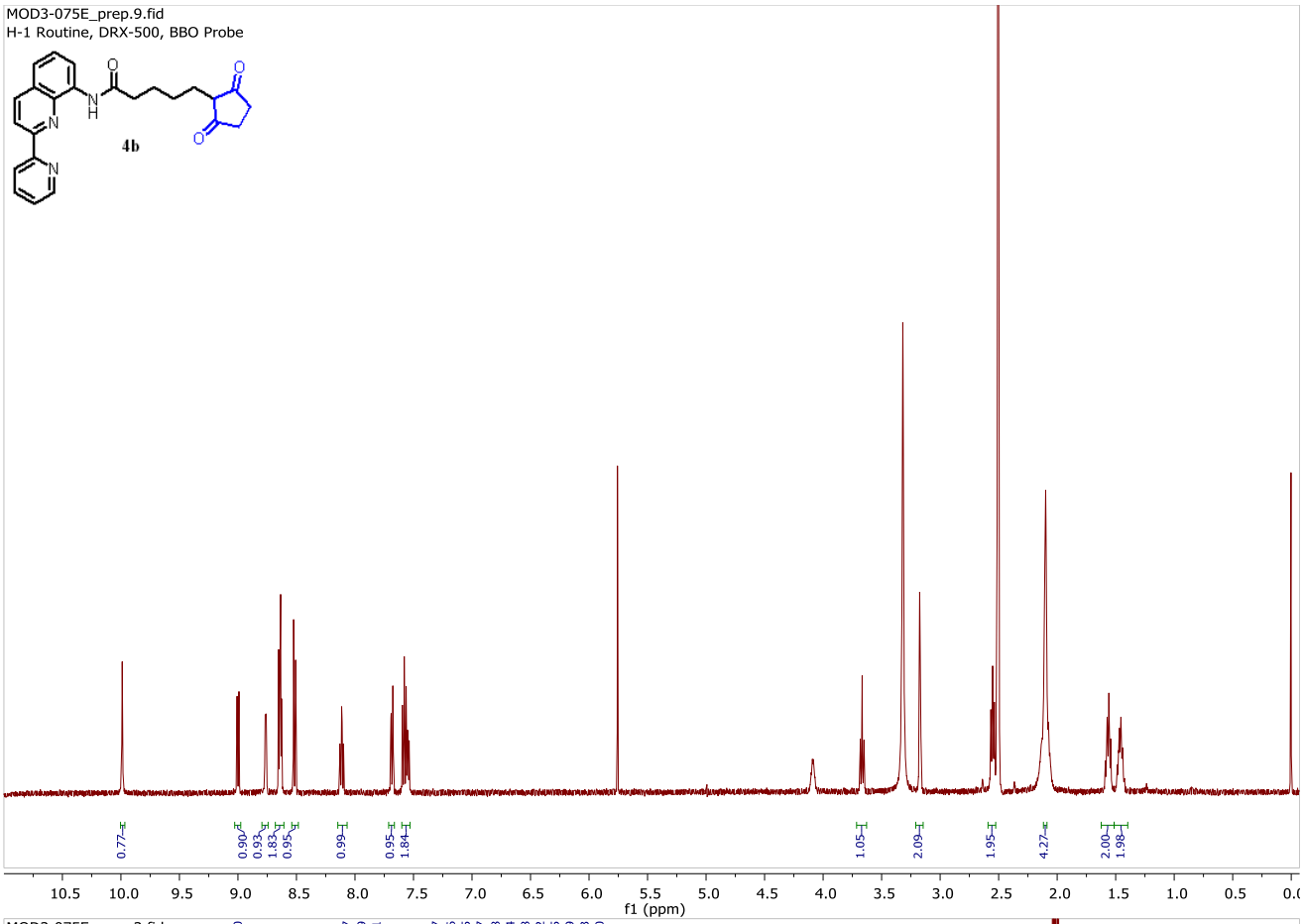
8

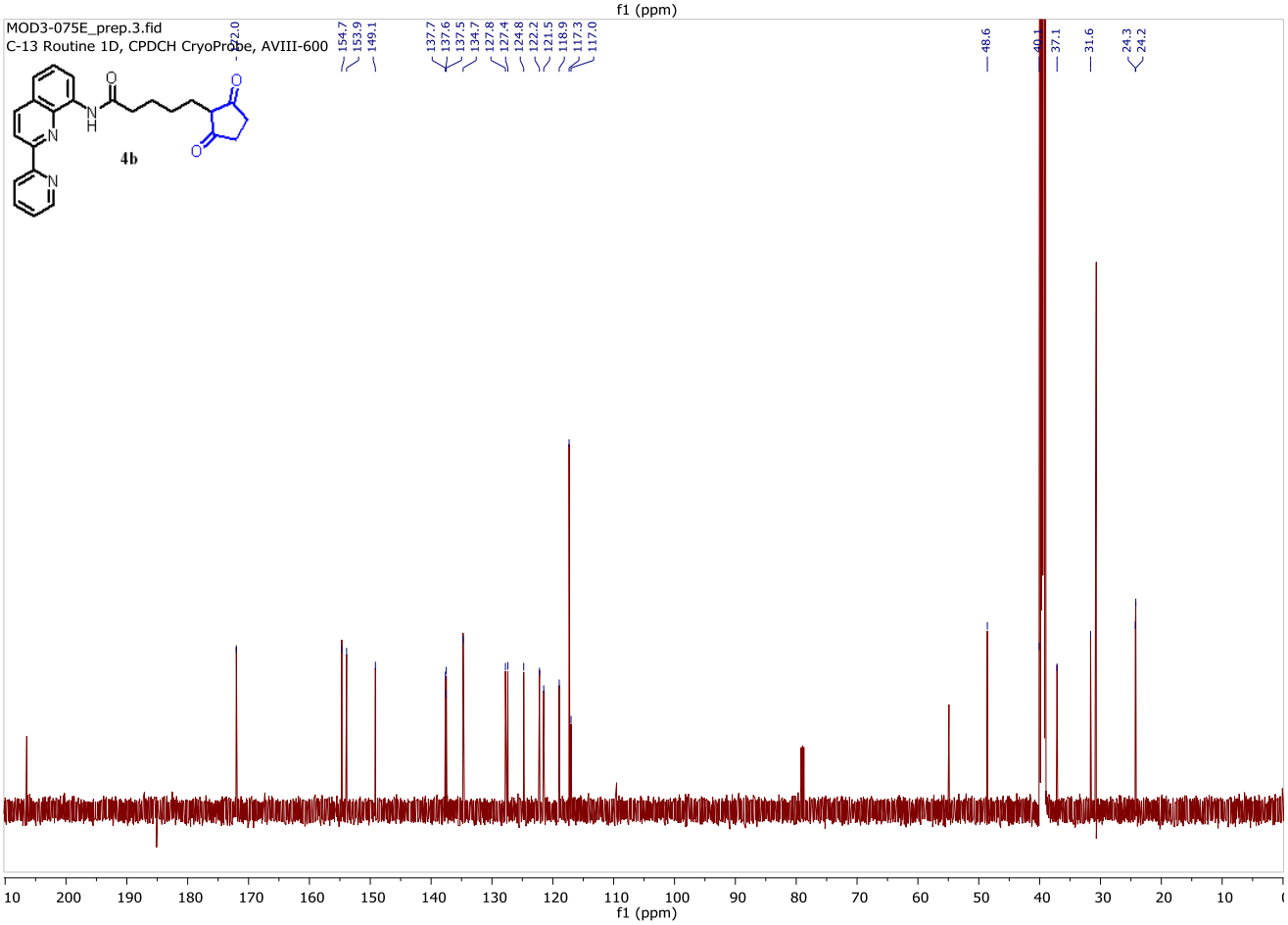

MOD4-052_prepTLC_A.1.fid
50 mM cyclosporine
10
f1 (ppm)

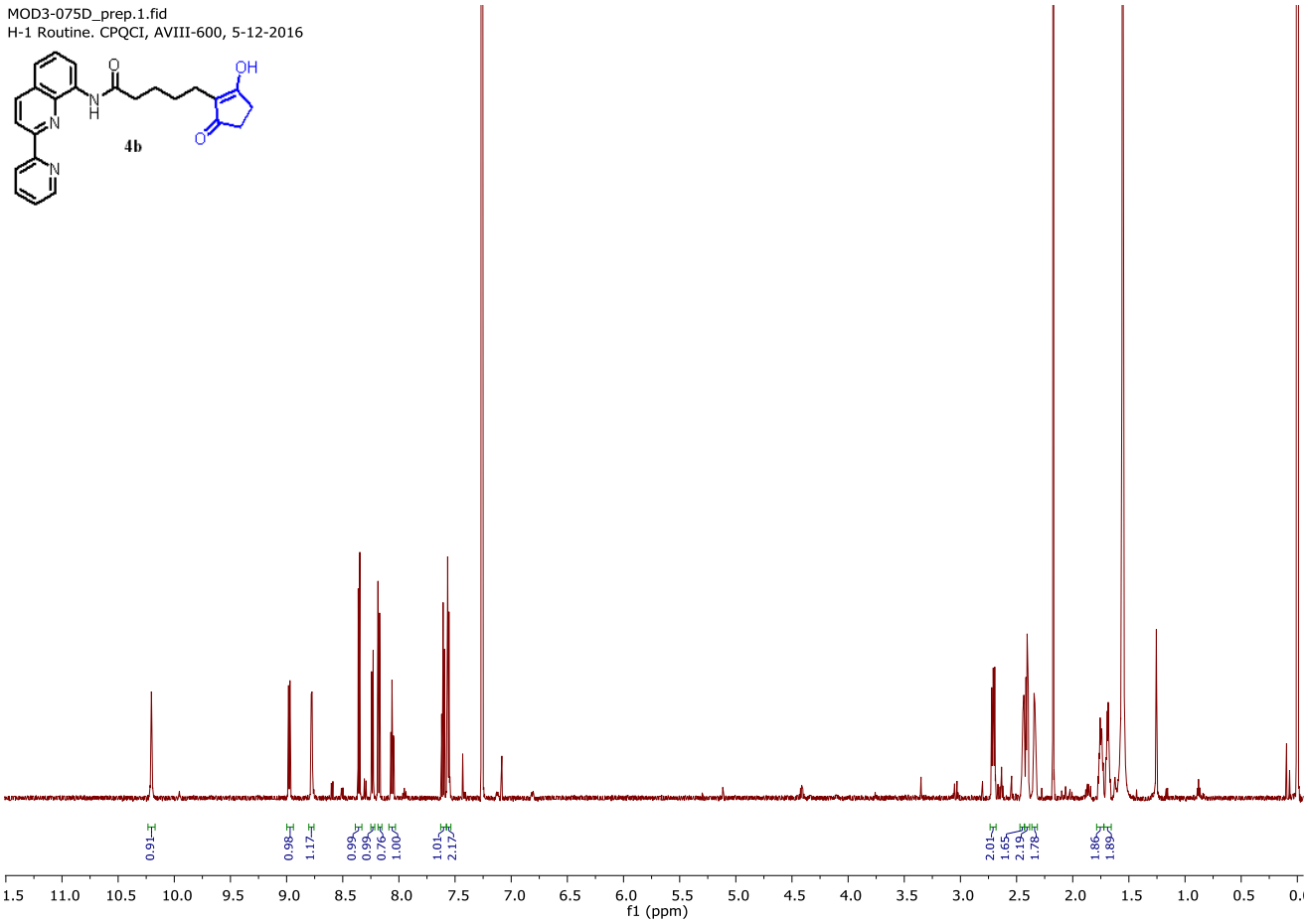

MOD4-052_prepTLC_A.2.fid
C-13 Routine 1D, CPDCH1 CryoProbe, AV111600
10
f1 (ppm)


MOD4-008.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4a
f1 (ppm)

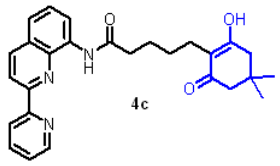

MOD4-008.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4a
f1 (ppm)


MOD3-075E_prep.9.fid
H-1 Routine, DRX-500, BBO Probe
4b
0.77
0.90
0.93
1.83
0.95
0.99
0.95
1.84
1.05
2.09
1.95
4.27
2.00
1.98
f1 (ppm)


MOD3-075E_prep.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4b
154.7
153.9
149.1
137.7
137.6
137.5
134.7
127.8
127.4
124.8
122.2
121.5
118.9
117.3
117.0
48.6
40.1
37.1
31.6
24.3
24.2
f1 (ppm)

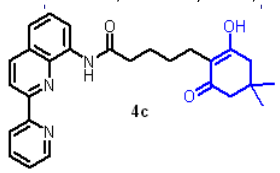

MOD3-075D_prep.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4b
f1 (ppm)

MOD3-159_prep-A.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016

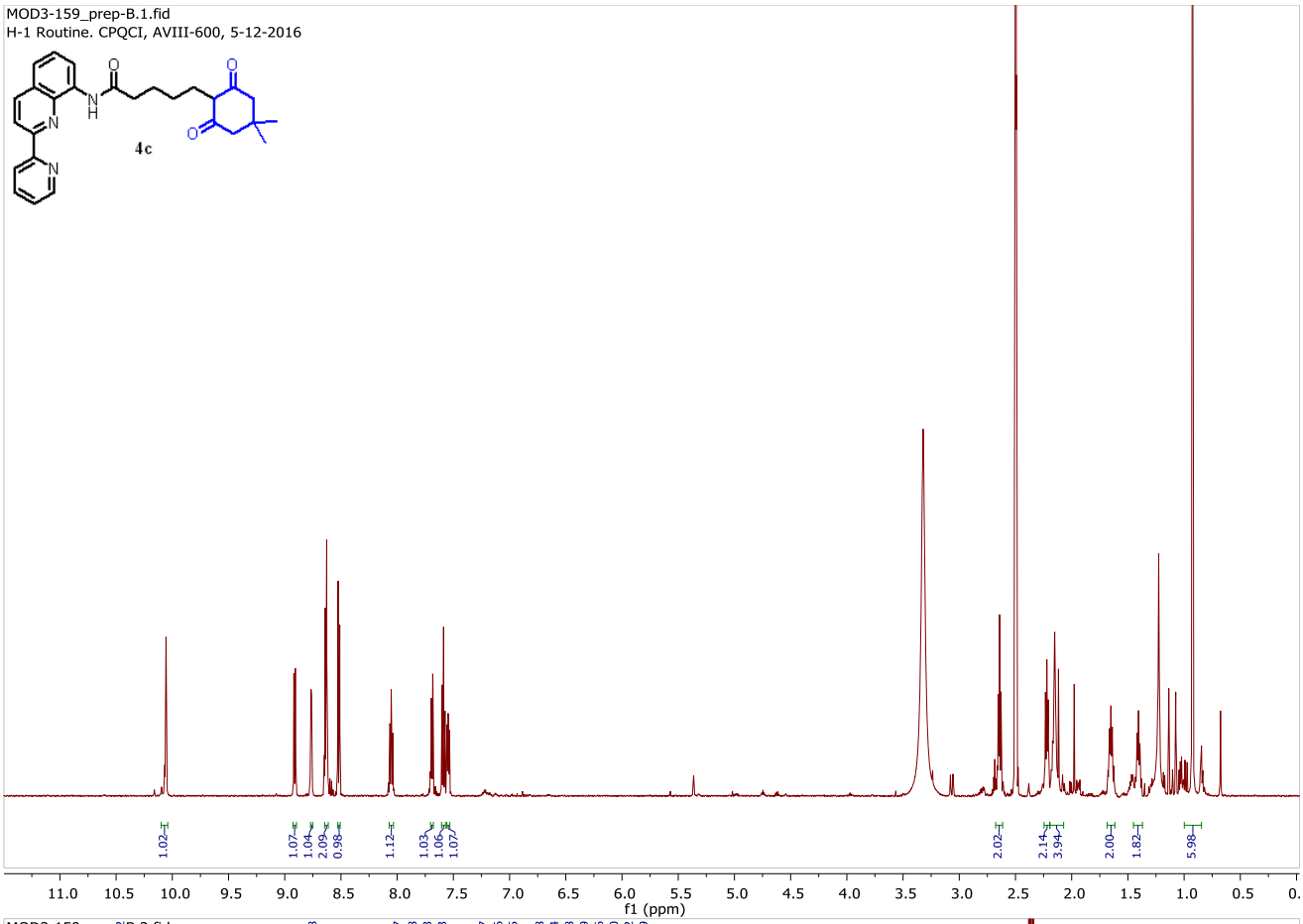


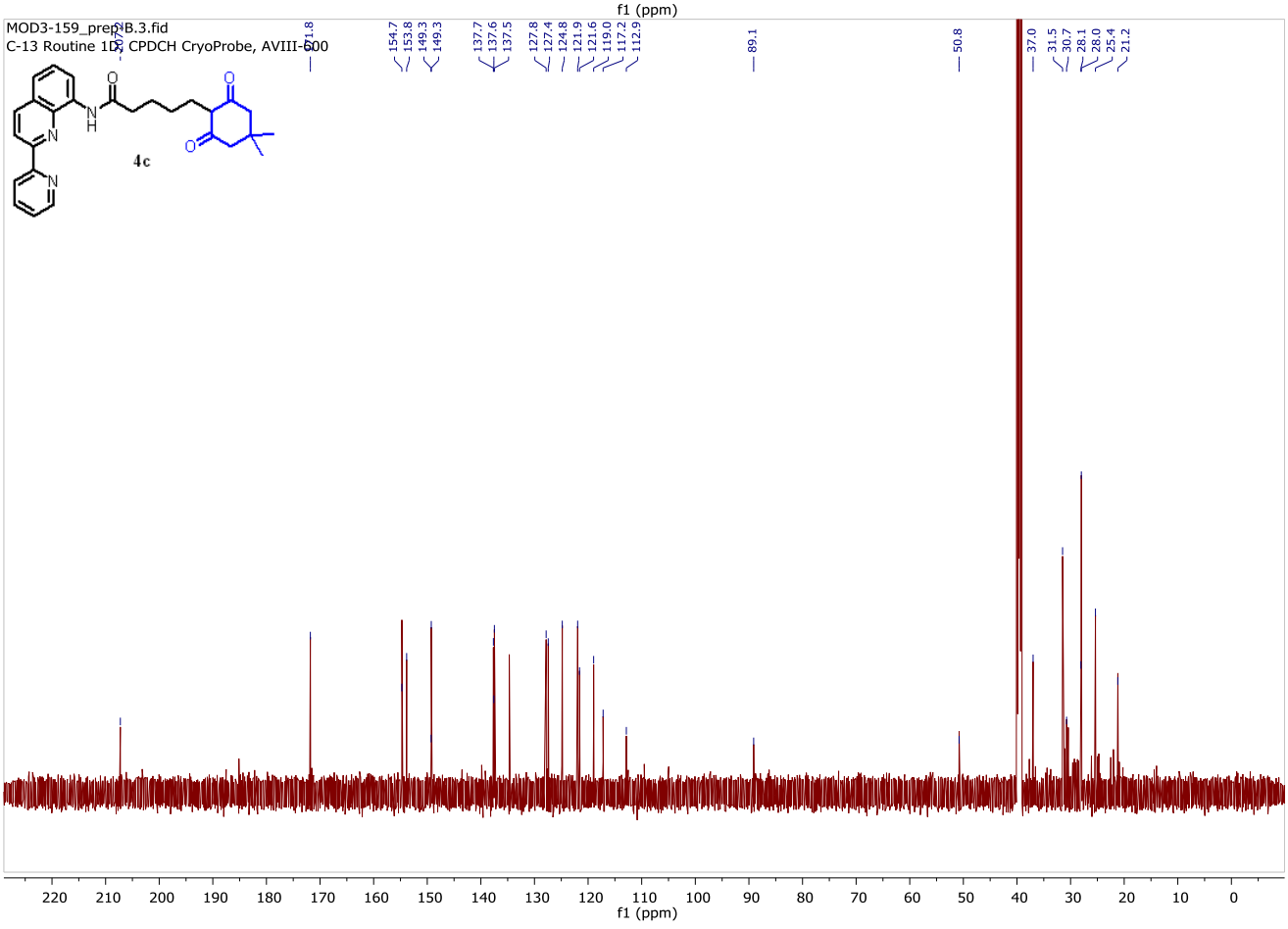
4c

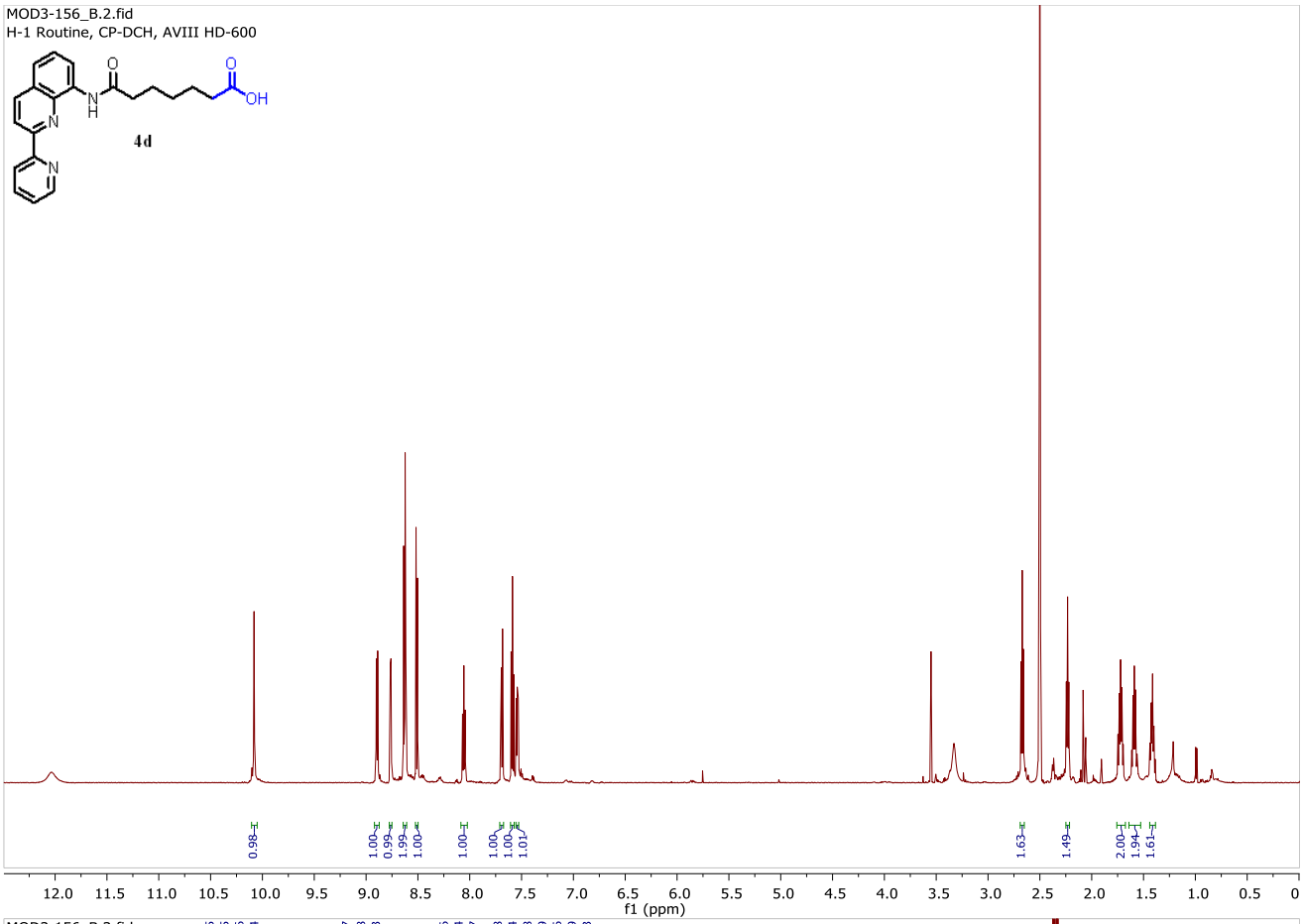
MOD3-159_prep-A.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600

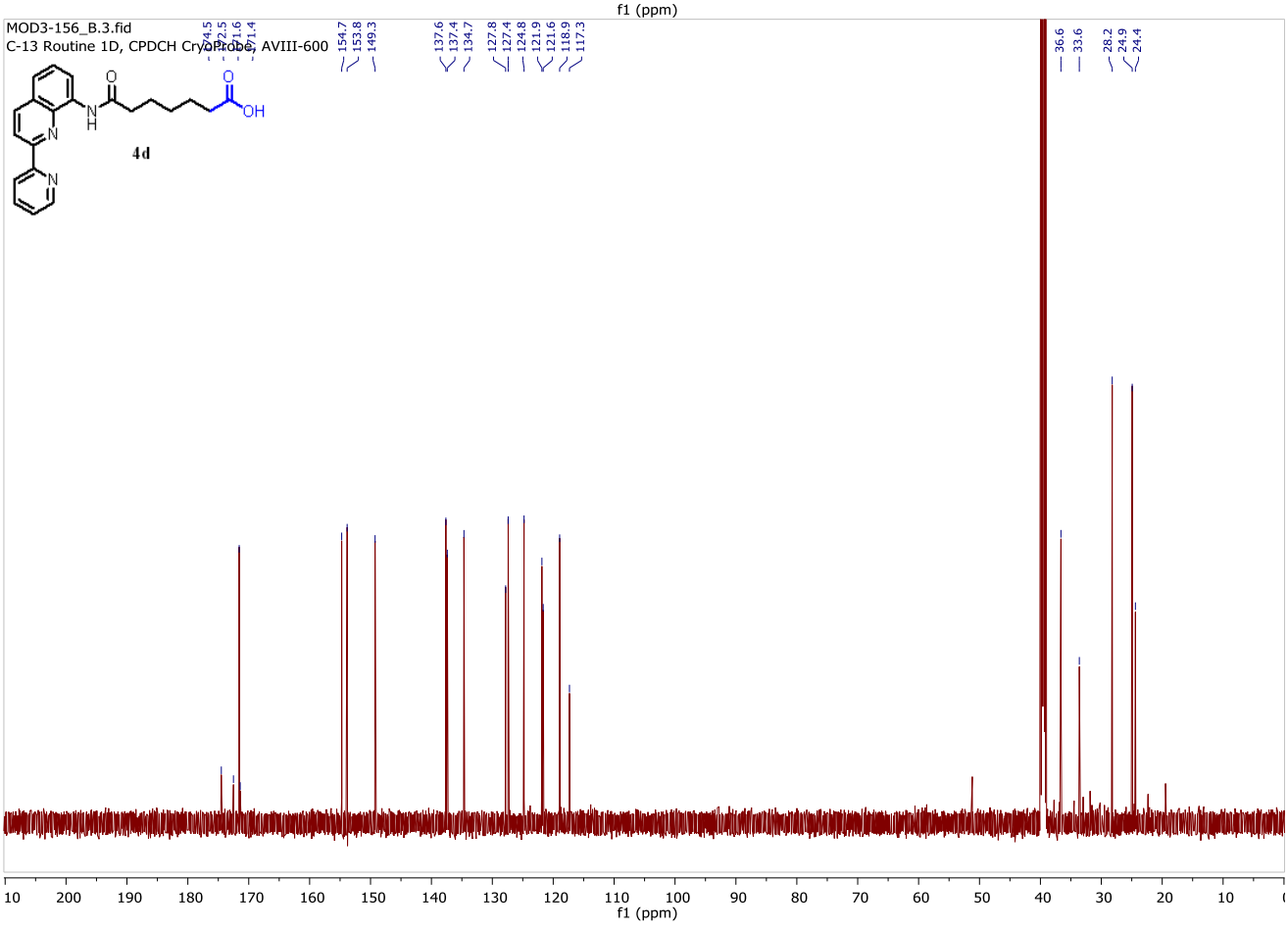


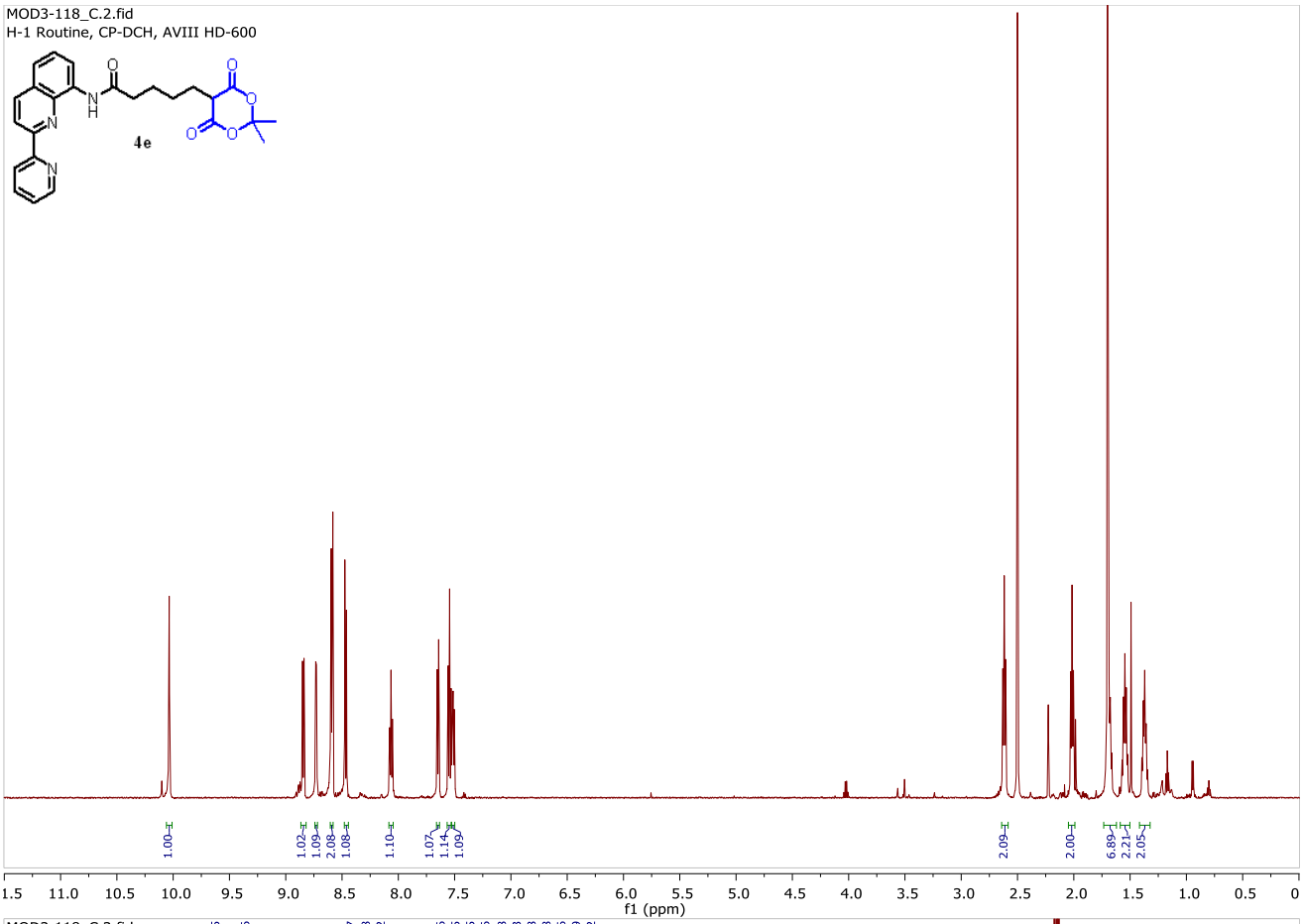
4c

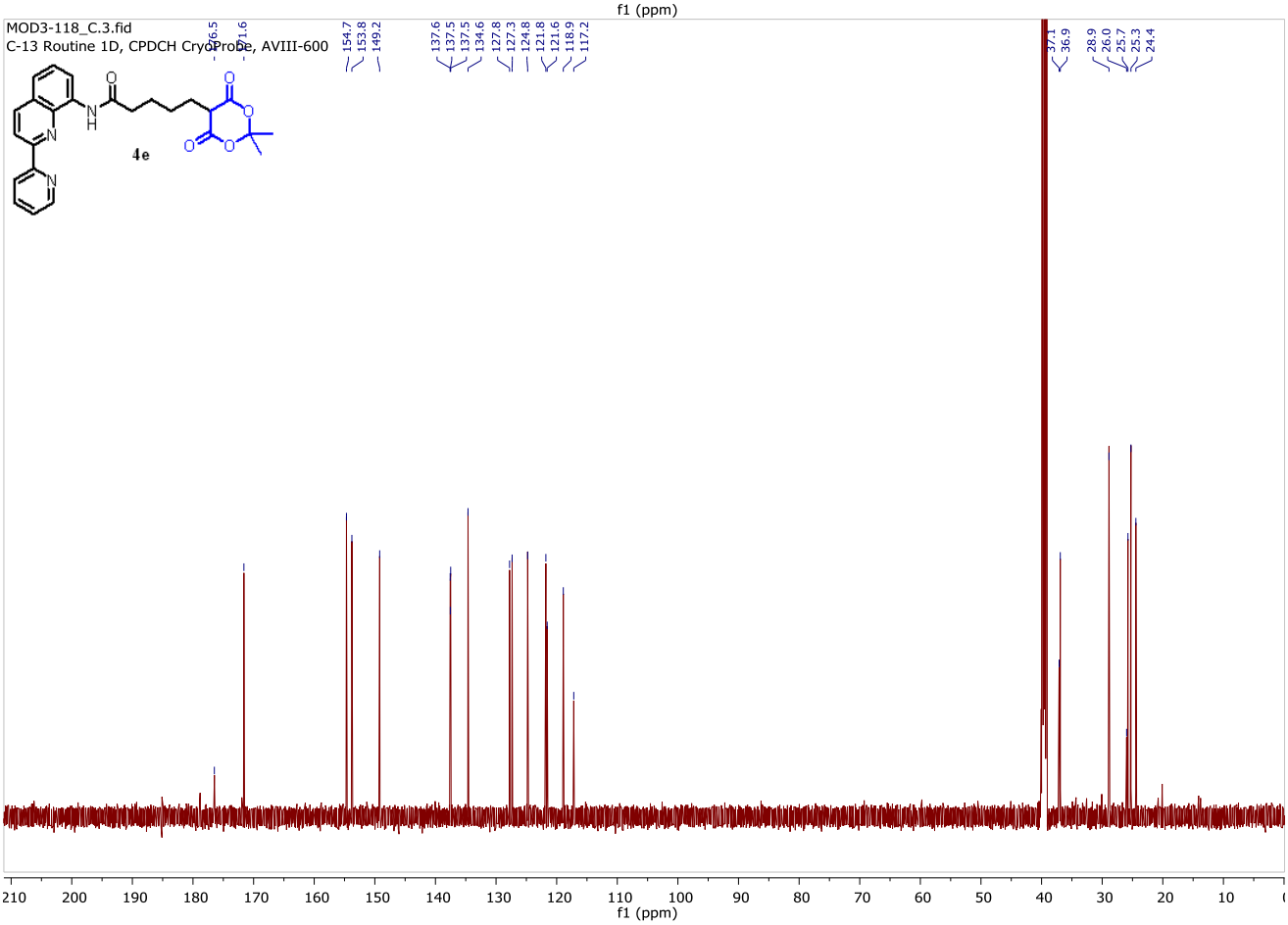

MOD3-159_prep-B.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4c
1.02
1.07
1.04
2.09
0.98
1.12
1.03
1.06
1.07
2.02
2.14
3.94
2.00
1.82
5.98
f1 (ppm)

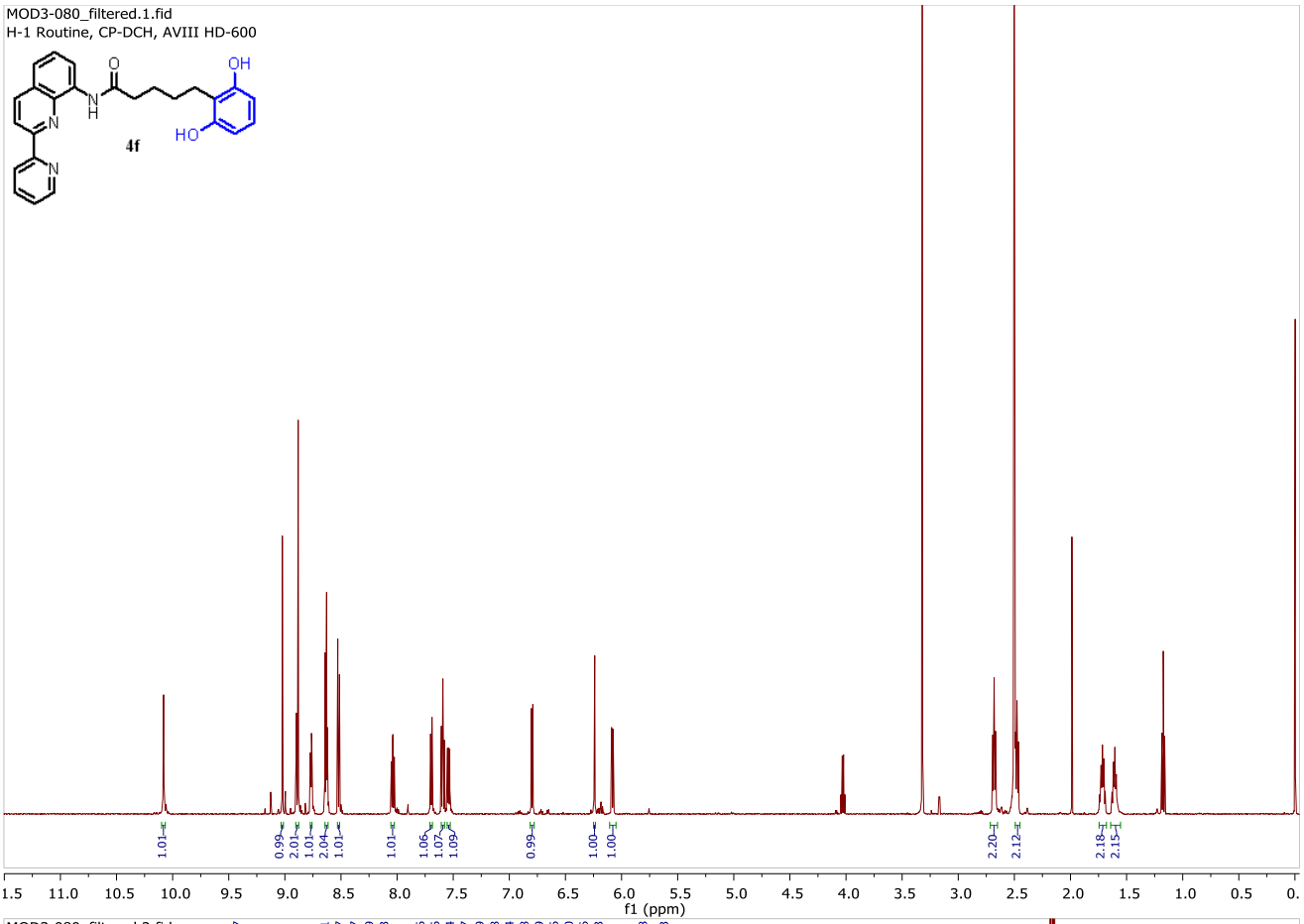

MOD3-159_prep-B.3.fid
C-13 Routine 1D CPDCH CryoProbe, AVIII-600
4c
154.7
153.8
149.3
149.3
137.7
137.6
137.5
127.8
127.4
124.8
121.9
121.6
119.0
117.2
112.9
89.1
50.8
37.0
31.5
30.7
28.1
28.0
25.4
21.2
f1 (ppm)

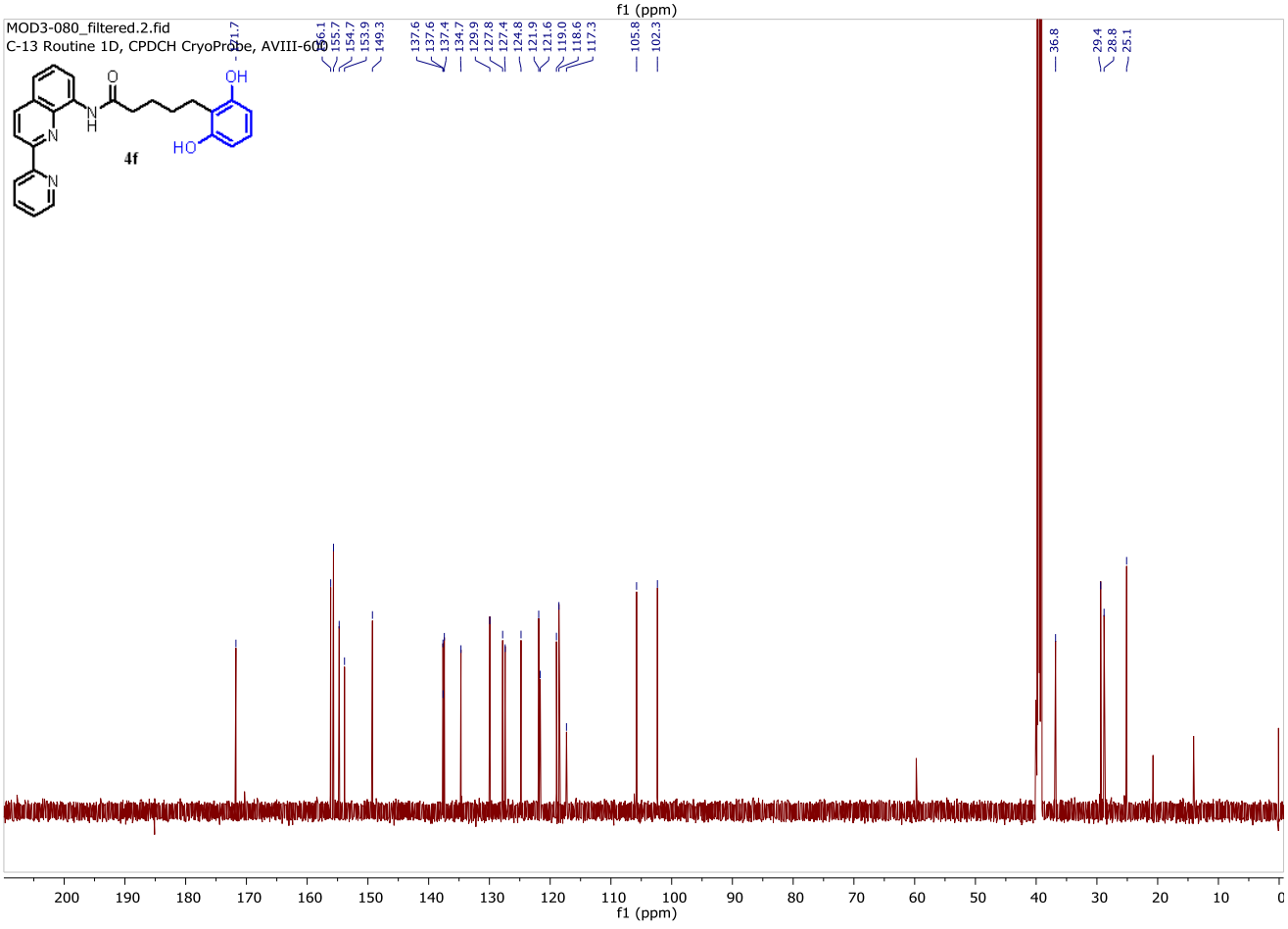

MOD3-156_B.2.fid
H-1 Routine, CP-DCH, AVIII HD-600
4d
f1 (ppm)

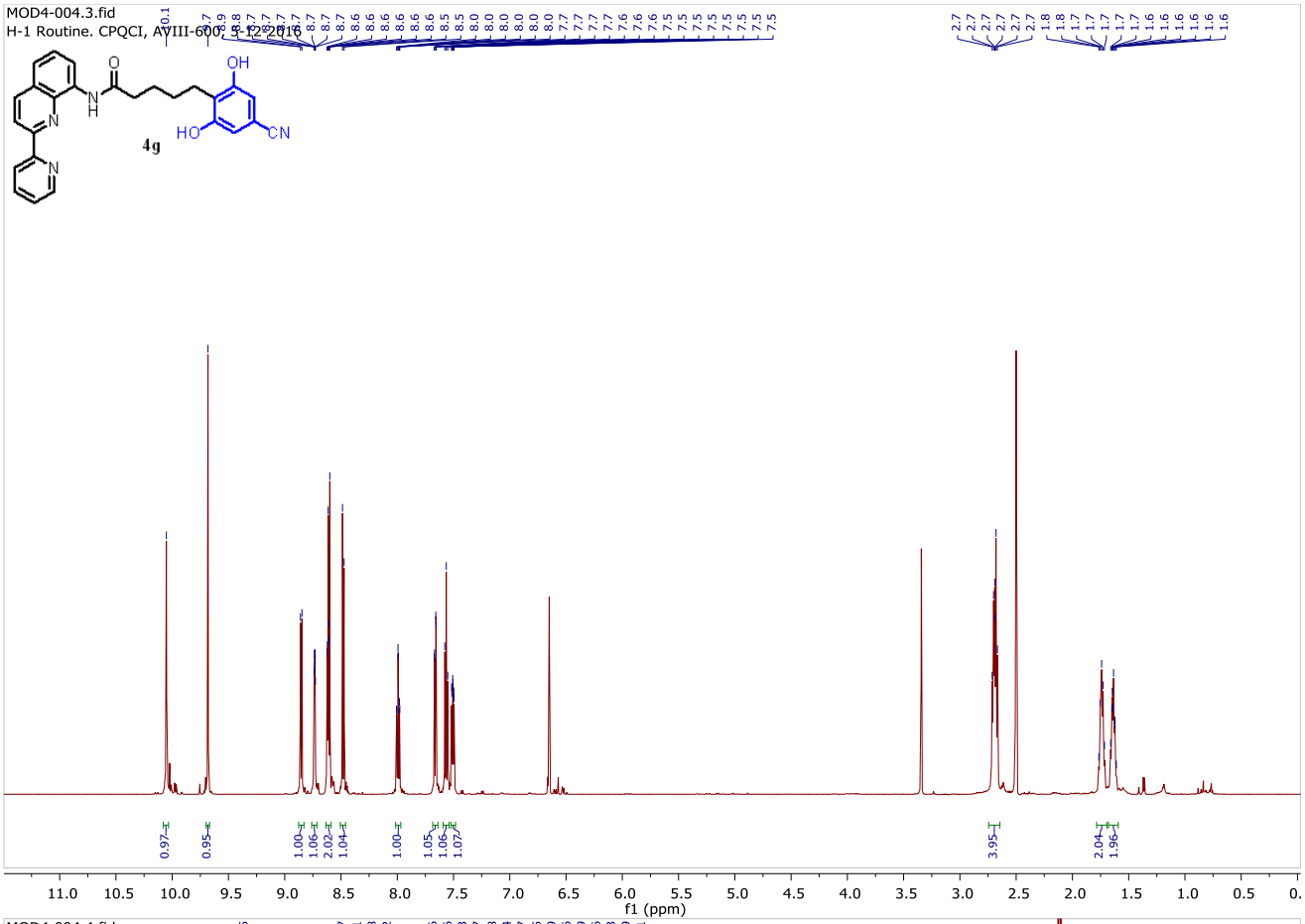

MOD3-156_B.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4d
f1 (ppm)

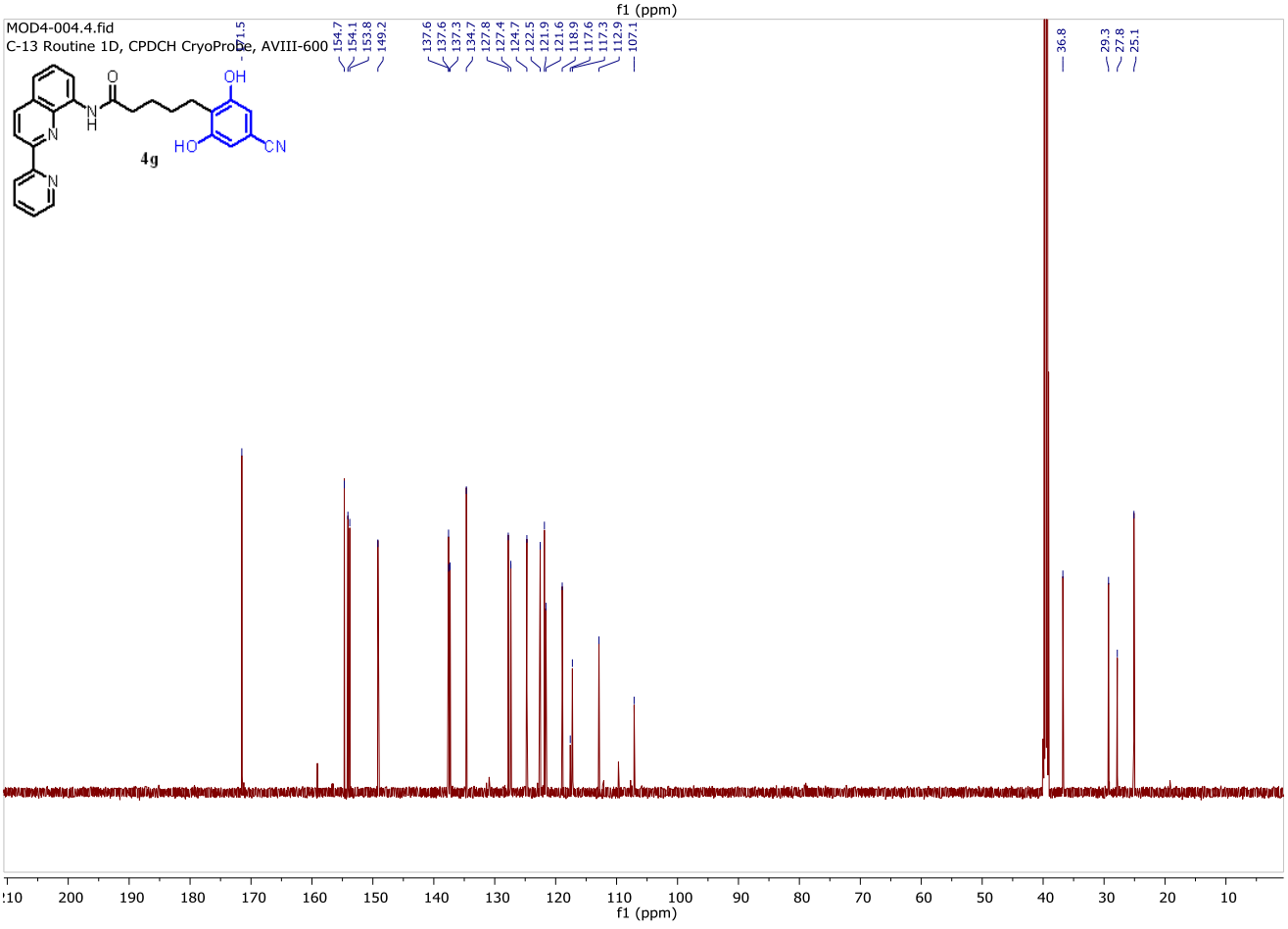

MOD3-118_C.2.fid
H-1 Routine, CP-DCH, AVIII HD-600
4e
1.00
1.02
1.09
2.08
1.08
1.10
1.07
1.14
1.09
2.09
2.00
6.89
2.21
2.05
f1 (ppm)

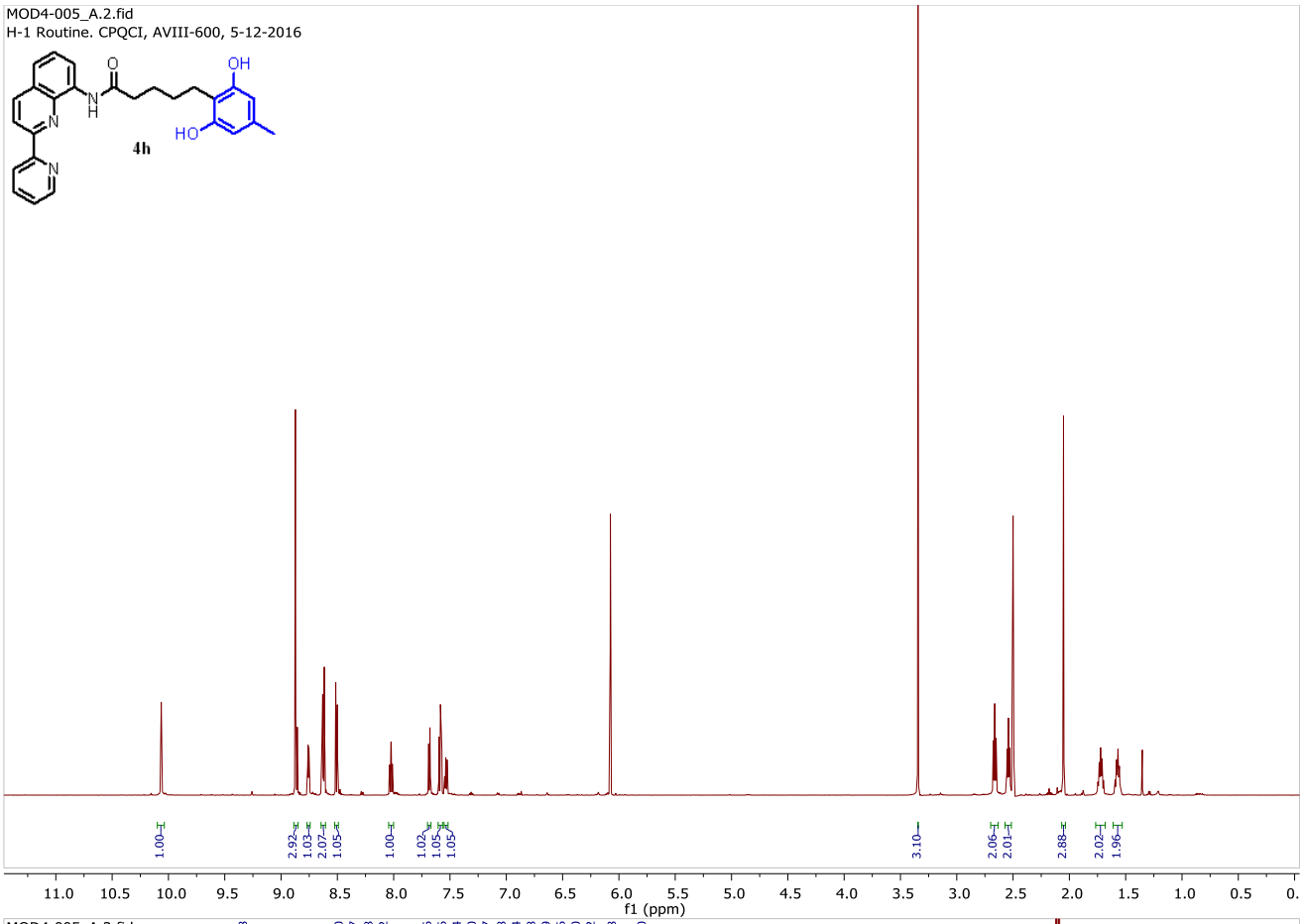

MOD3-118_C.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4e
166.5
161.6
154.7
153.8
149.2
137.6
137.5
137.5
134.6
127.8
127.3
124.8
121.8
121.6
118.9
117.2
37.1
36.9
28.9
26.0
25.7
25.3
24.4
f1 (ppm)

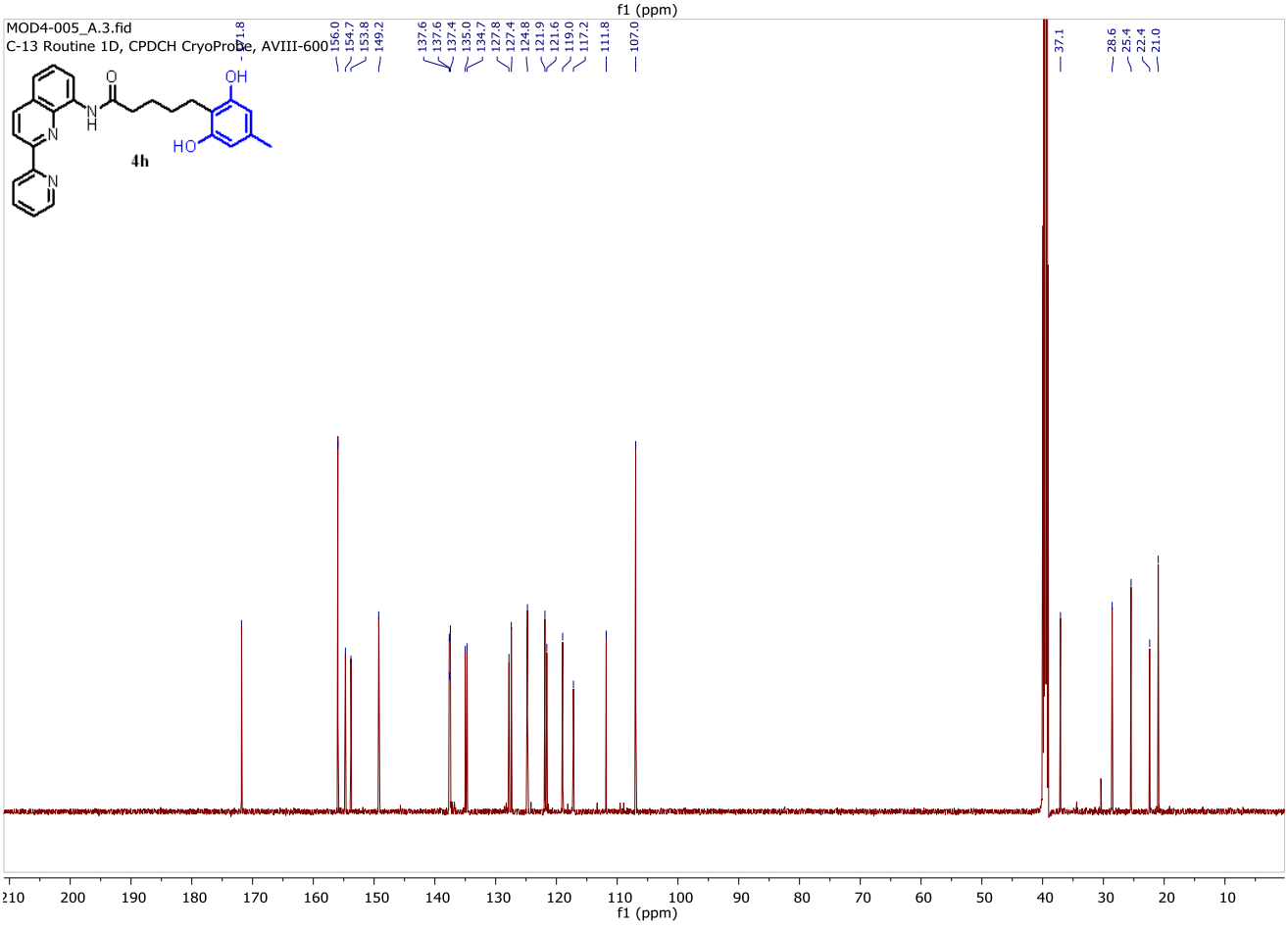

MOD3-080_filtered.1.fid
H-1 Routine, CP-DCH, AVIII HD-600
4f
f1 (ppm)

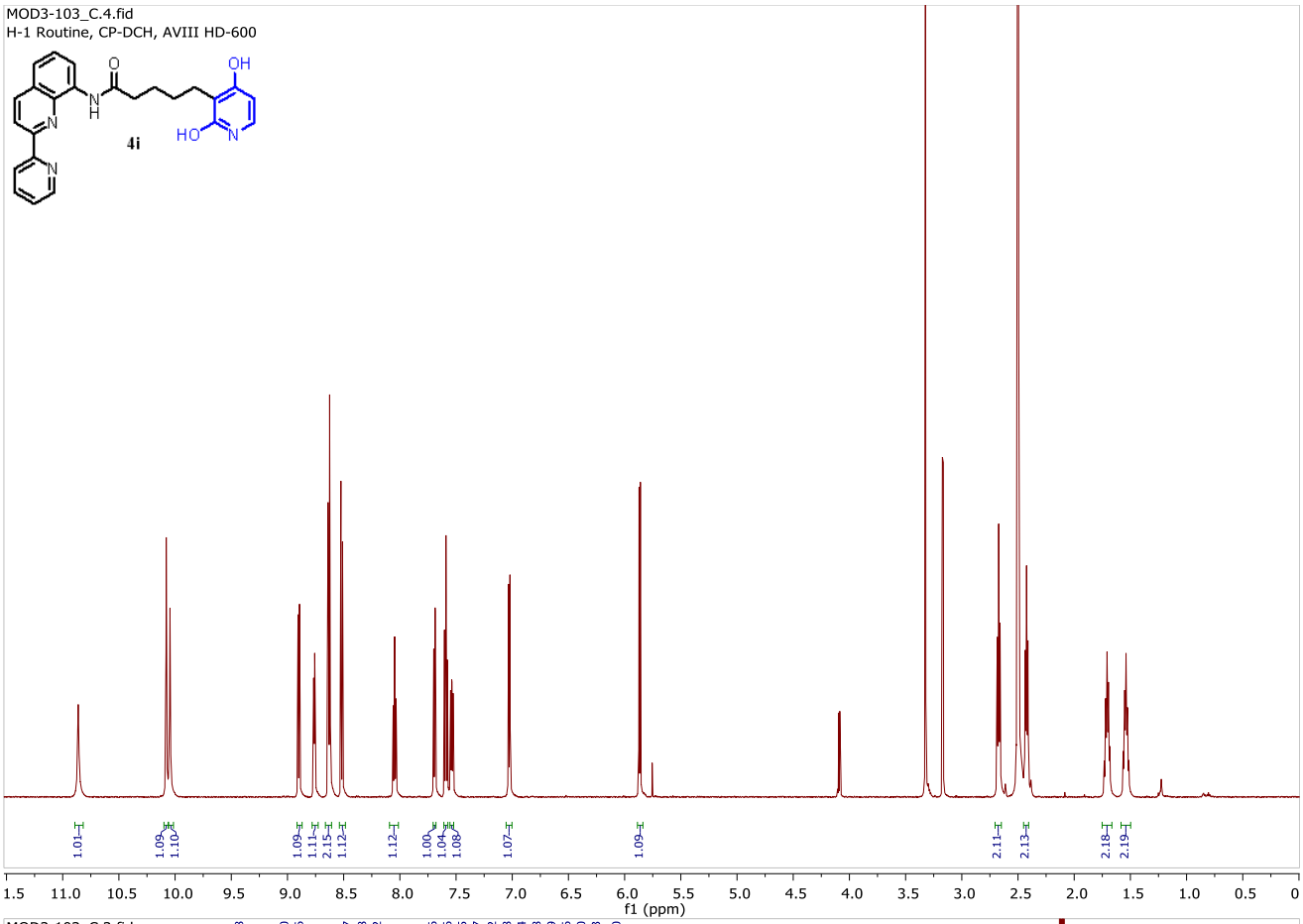

MOD3-080_filtered.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4f
f1 (ppm)

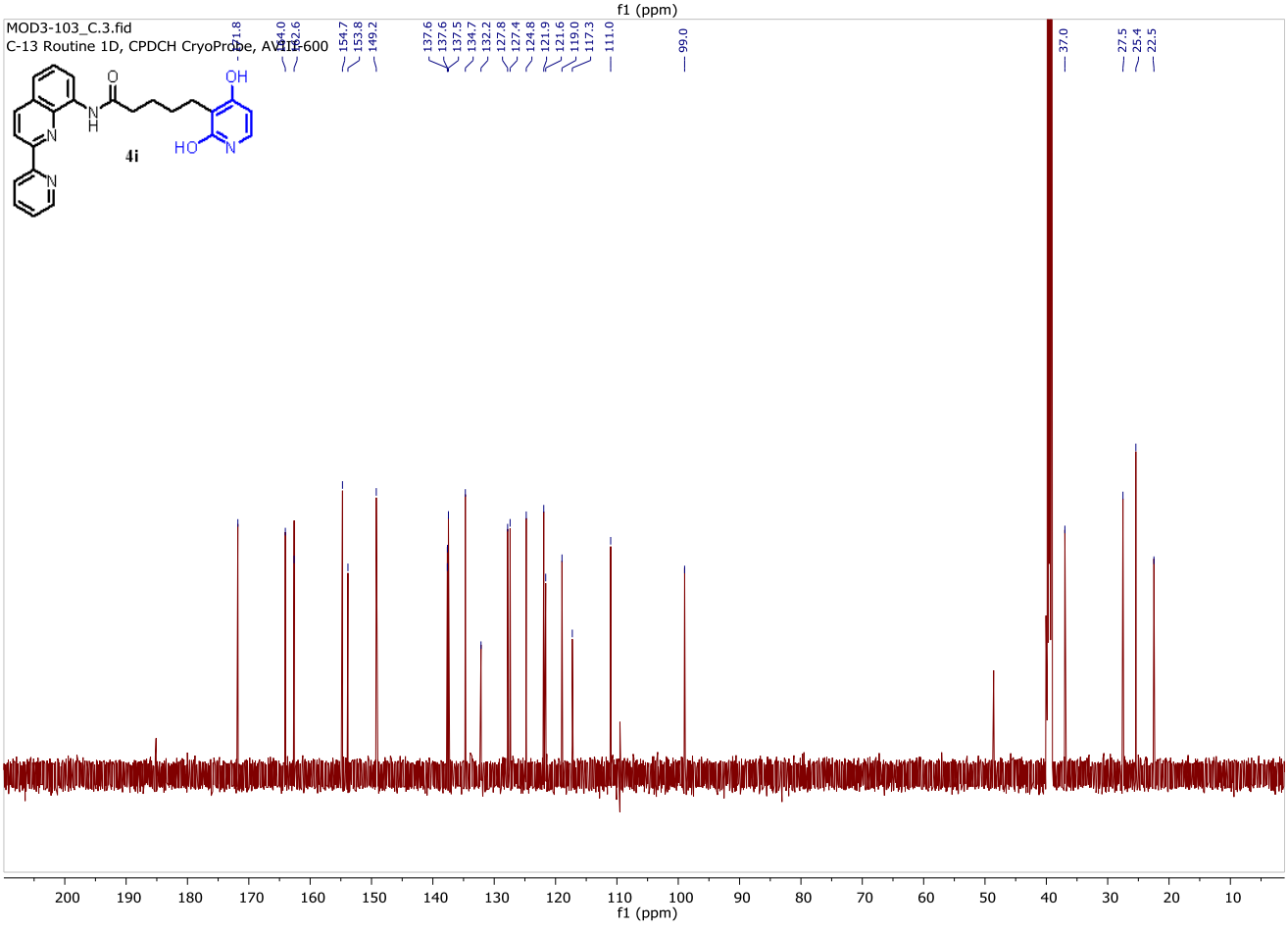

MOD4-004.3.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4g
f1 (ppm)

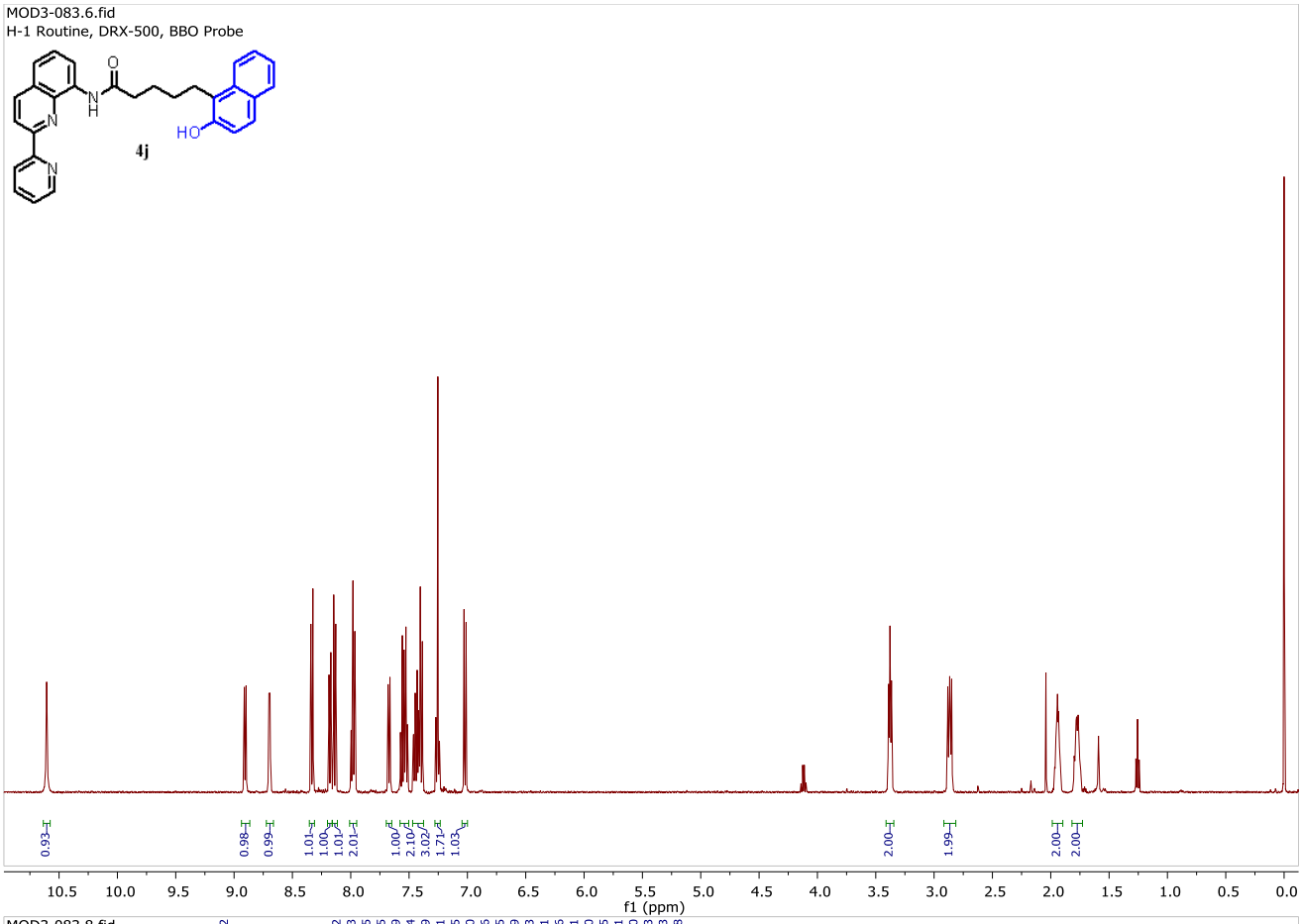

MOD4-004.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4g
f1 (ppm)

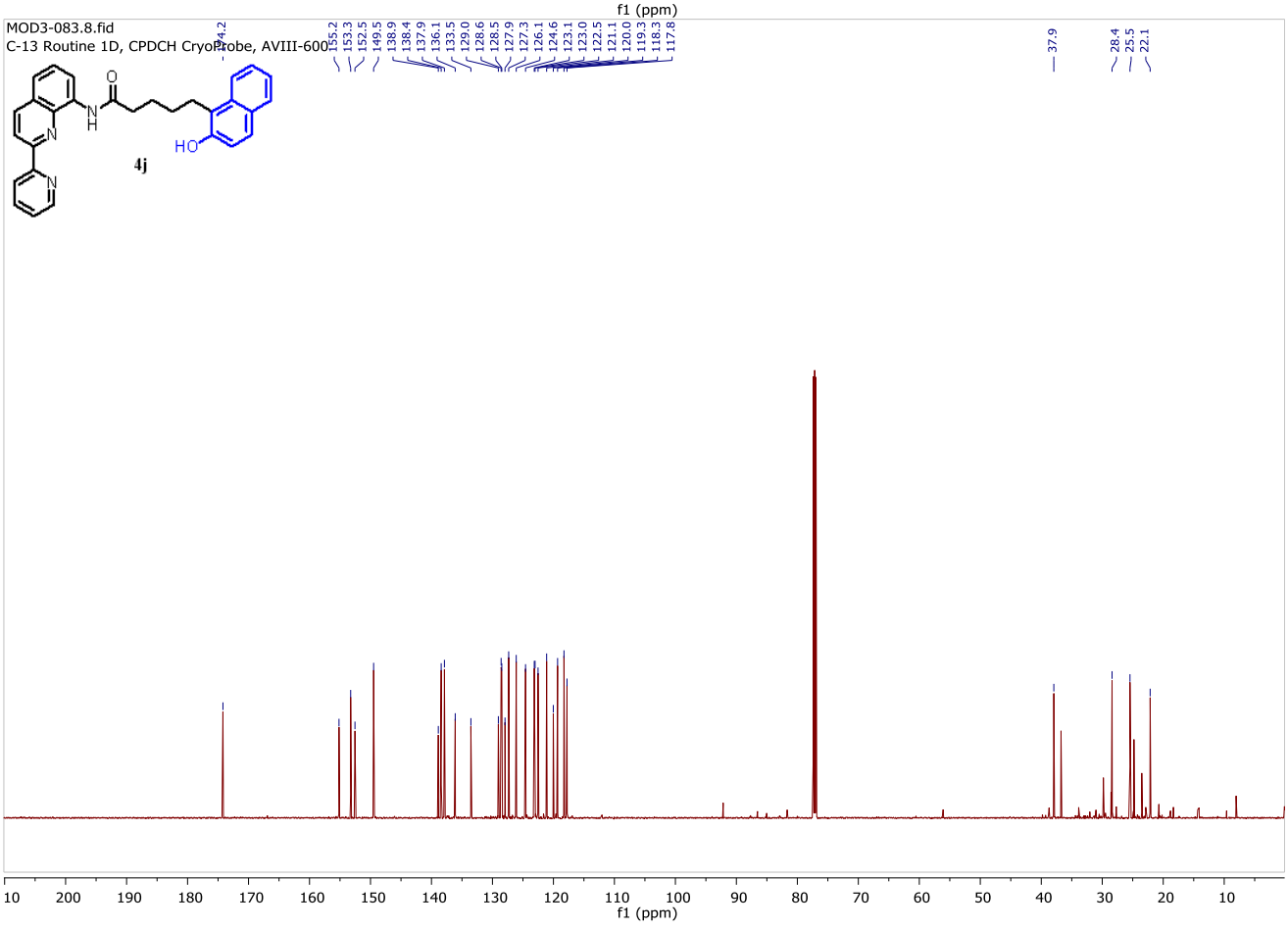

MOD4-005_A.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4h
1.00
2.92
1.03
2.07
1.05
1.00
1.02
1.05
1.05
3.10
2.06
2.01
2.88
2.02
1.96
f1 (ppm)

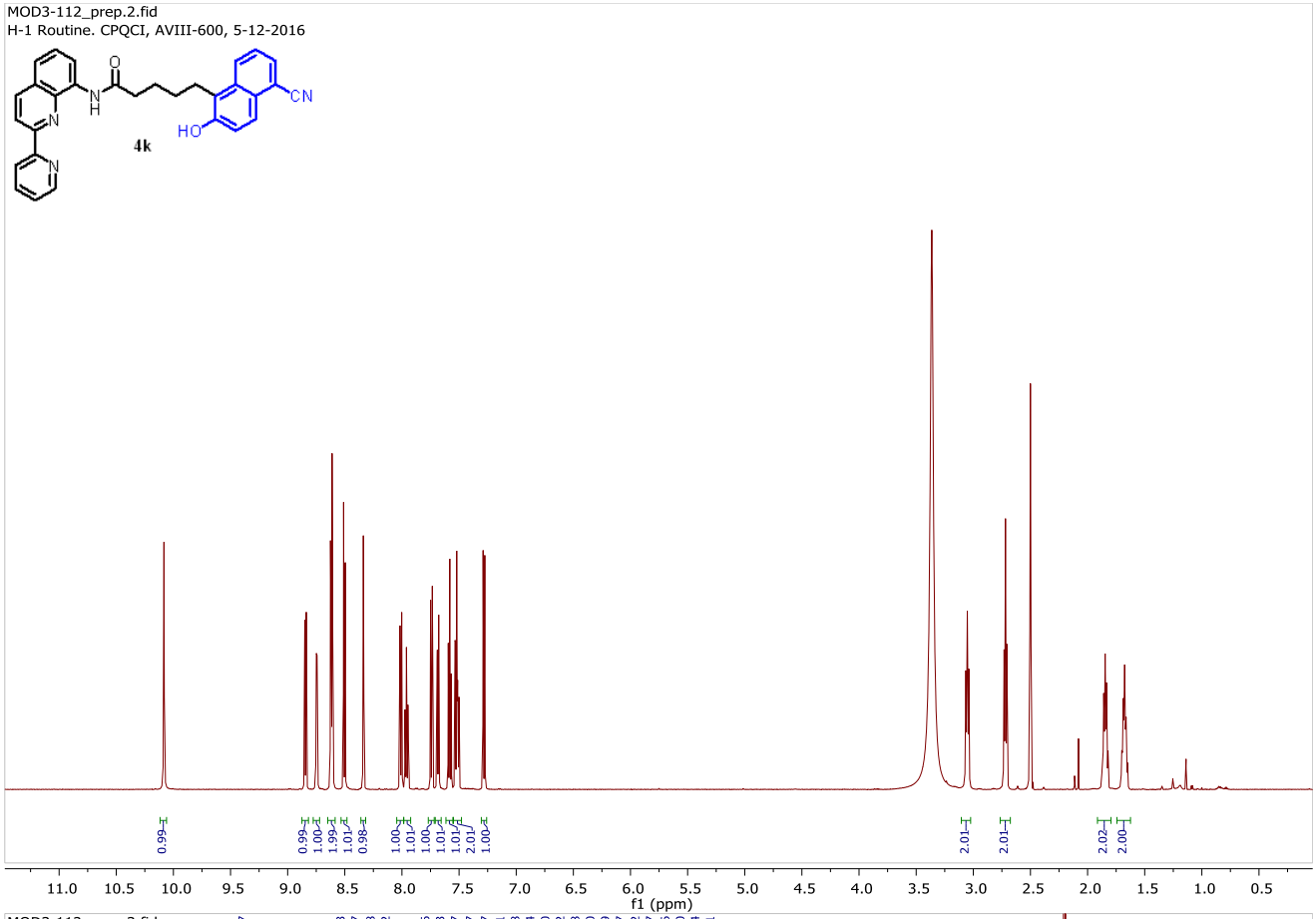

MOD4-005_A.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4h
156.0
154.7
153.8
149.2
137.6
137.6
137.4
135.0
134.7
127.8
127.4
124.8
121.9
121.6
119.0
117.2
111.8
107.0
37.1
28.6
25.4
22.4
21.0
f1 (ppm)

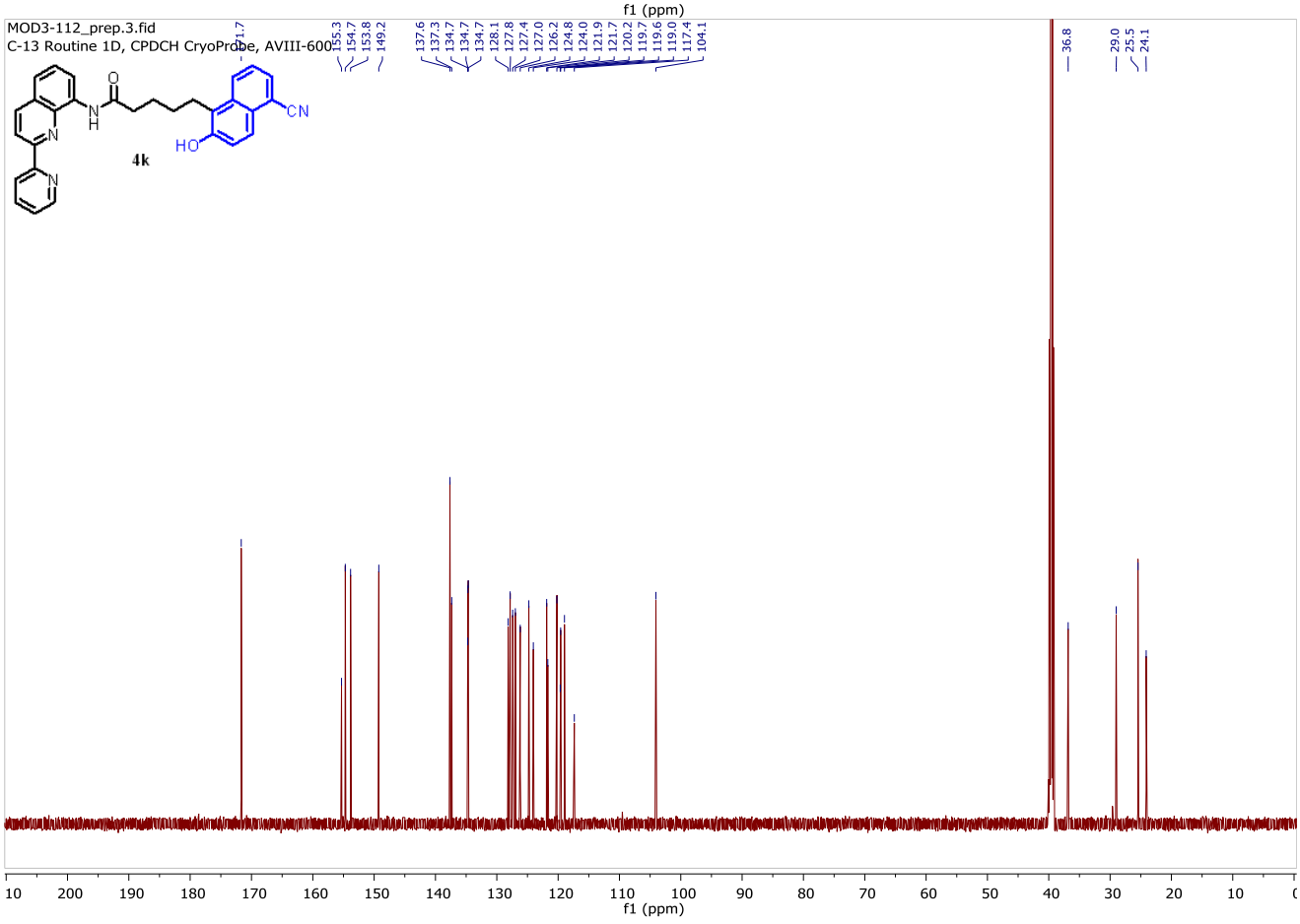

MOD3-103_C.4.fid
H-1 Routine, CP-DCH, AVIII HD-600
4i
f1 (ppm)

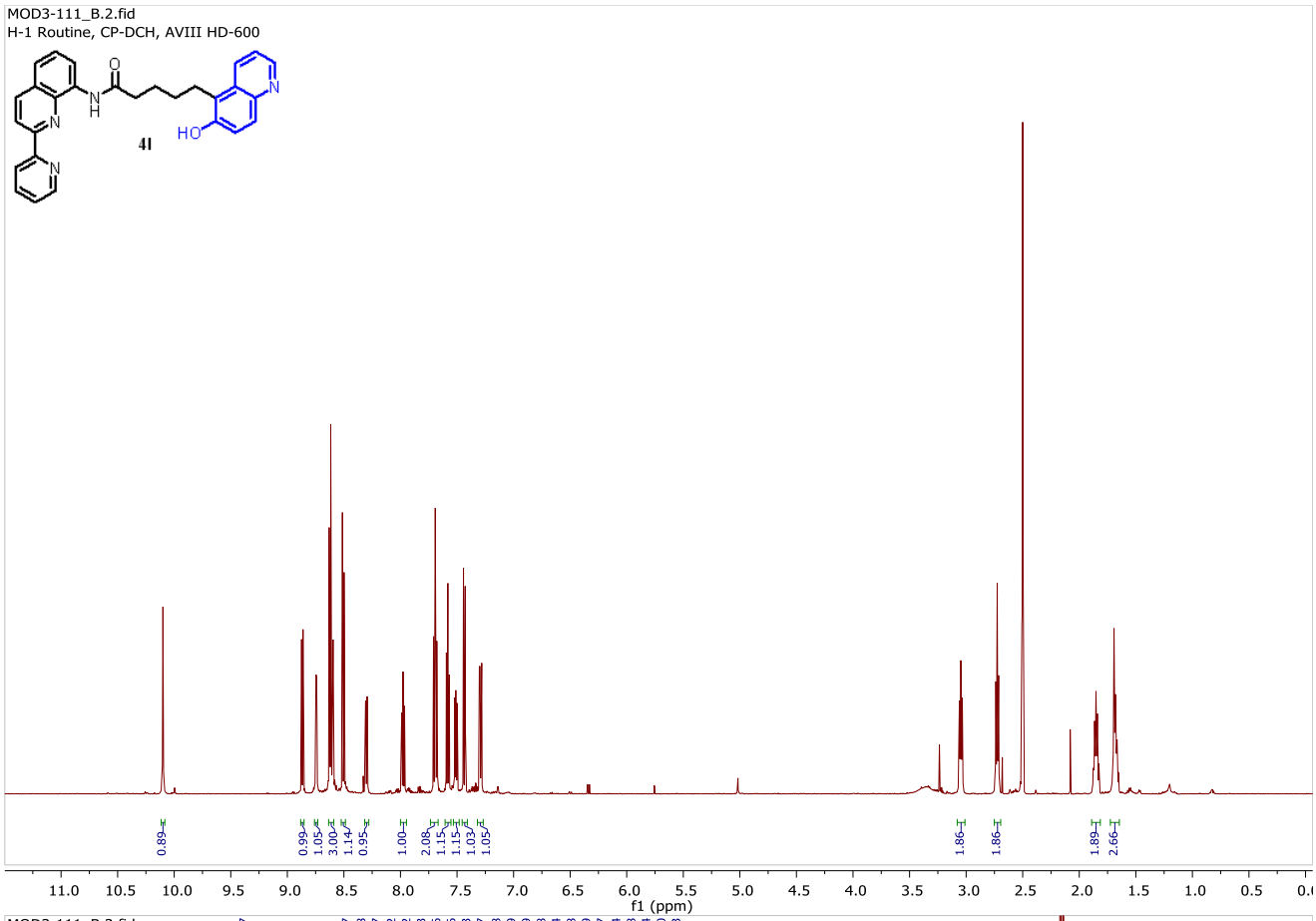

MOD3-103_C.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4i
f1 (ppm)

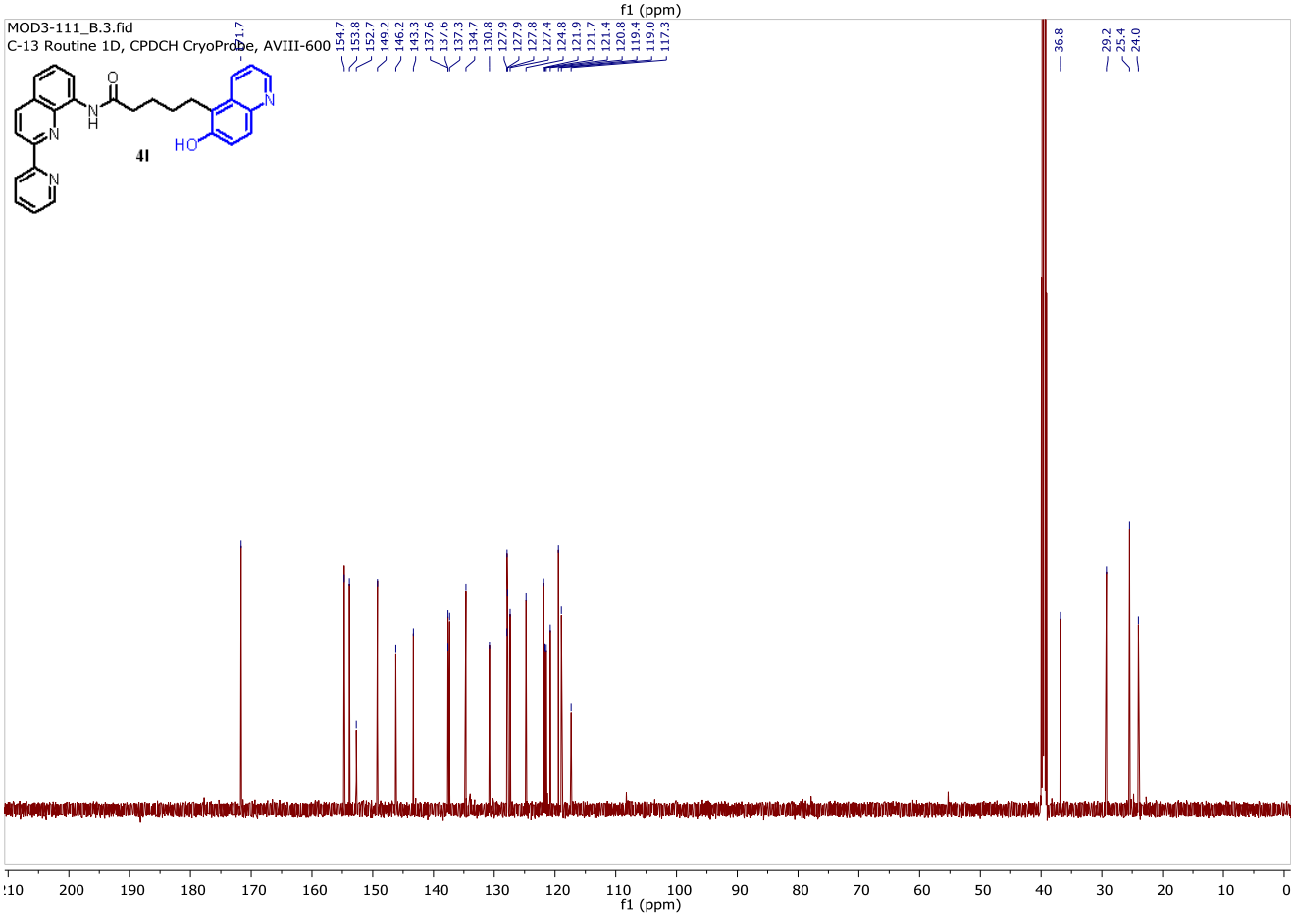

MOD3-083.6.fid
H-1 Routine, DRX-500, BBO Probe
4j
f1 (ppm)

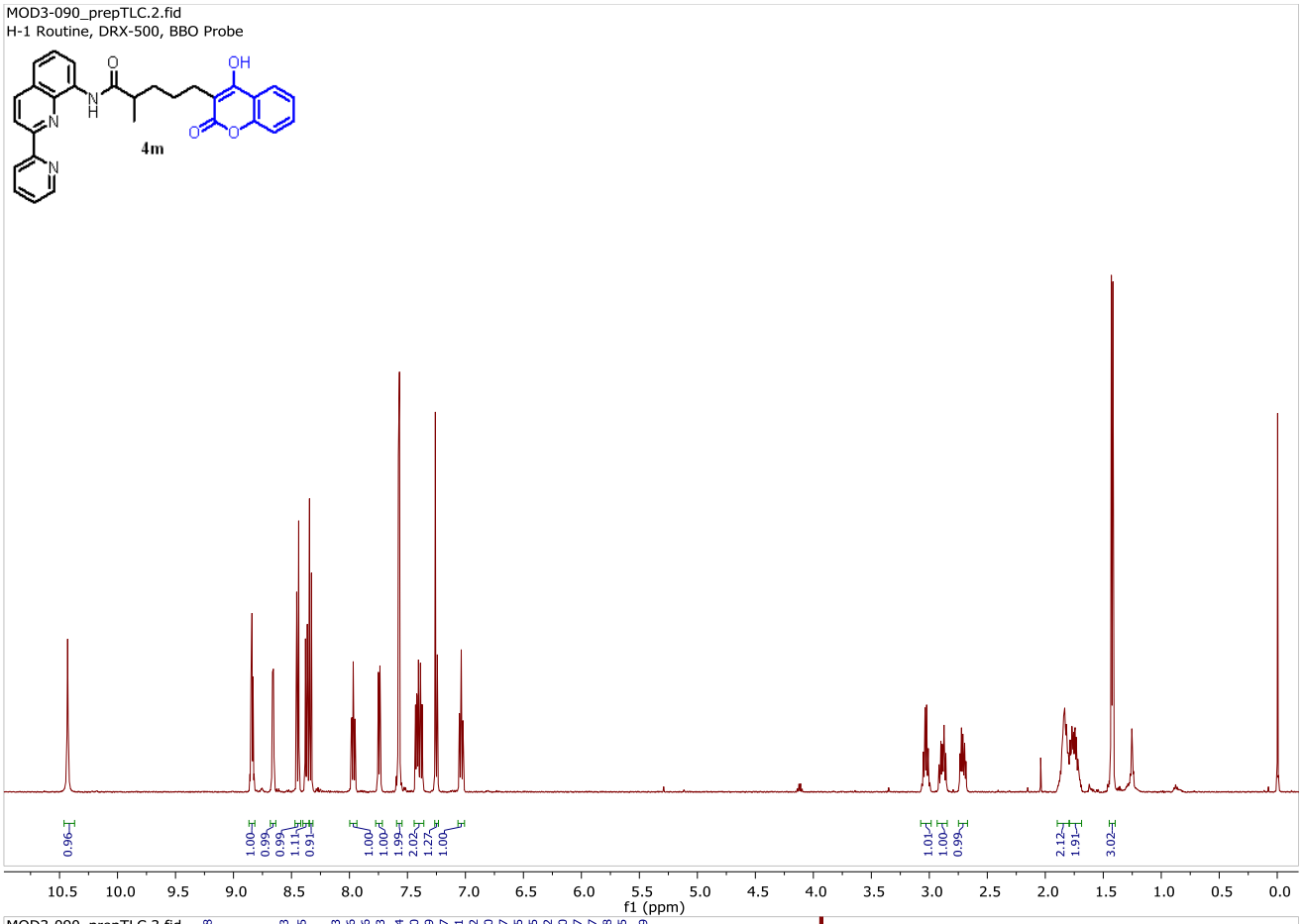

MOD3-083.8.fid
C-13 Routine 1D, CPDCH Cryoprobe, AVIII-600
4j
f1 (ppm)

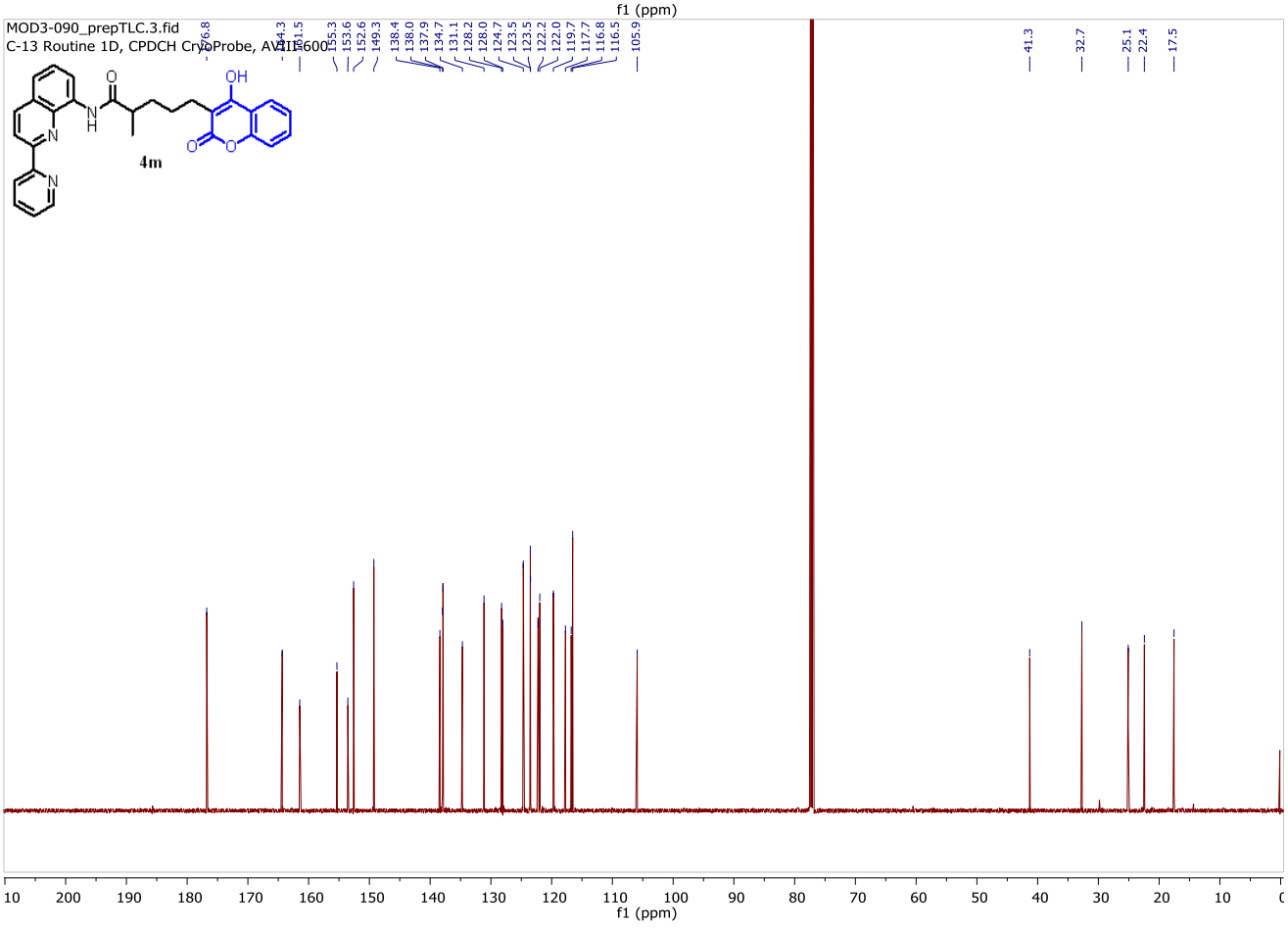

MOD3-112_prep.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4k
f1 (ppm)

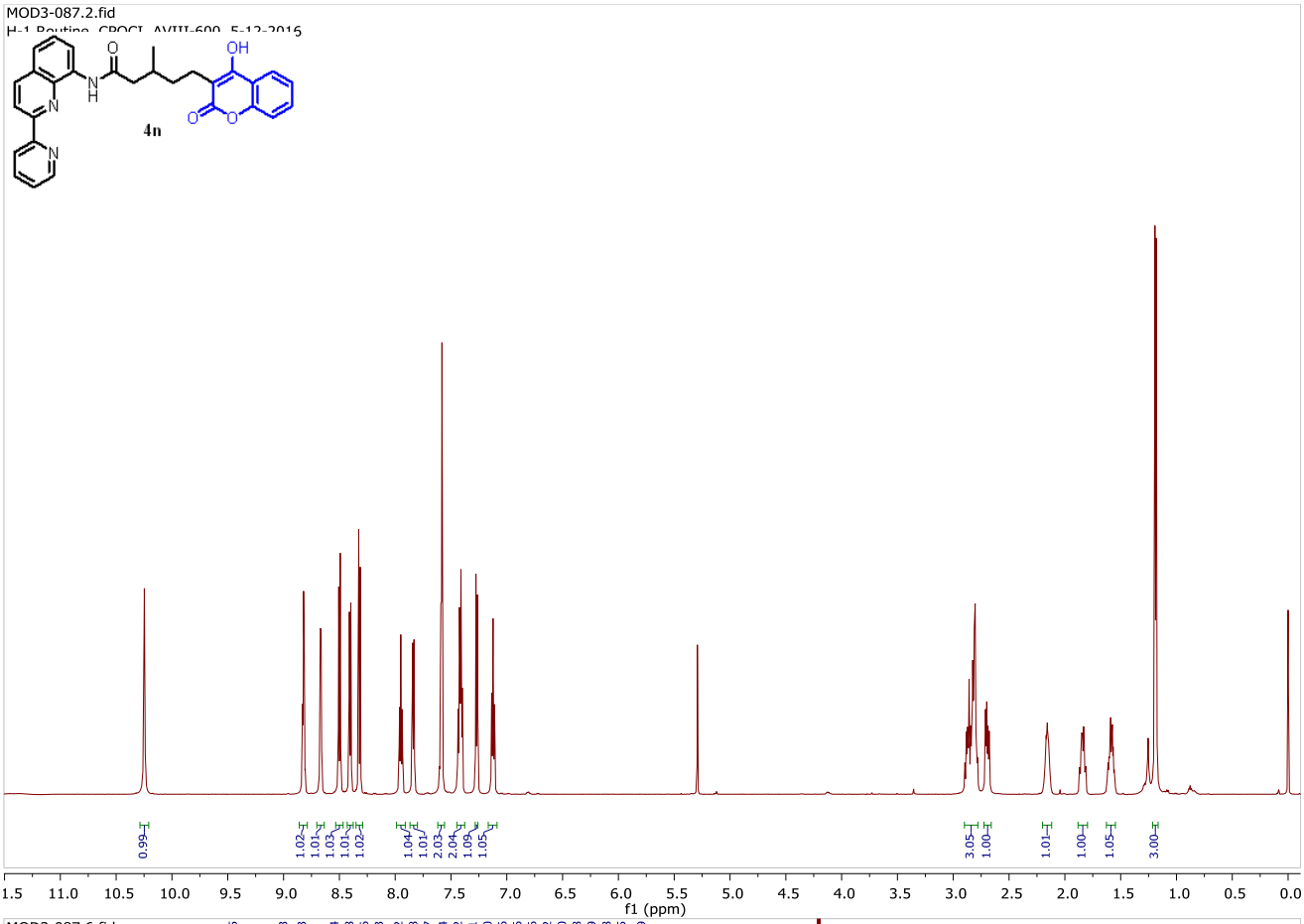

MOD3-112_prep.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4k
f1 (ppm)

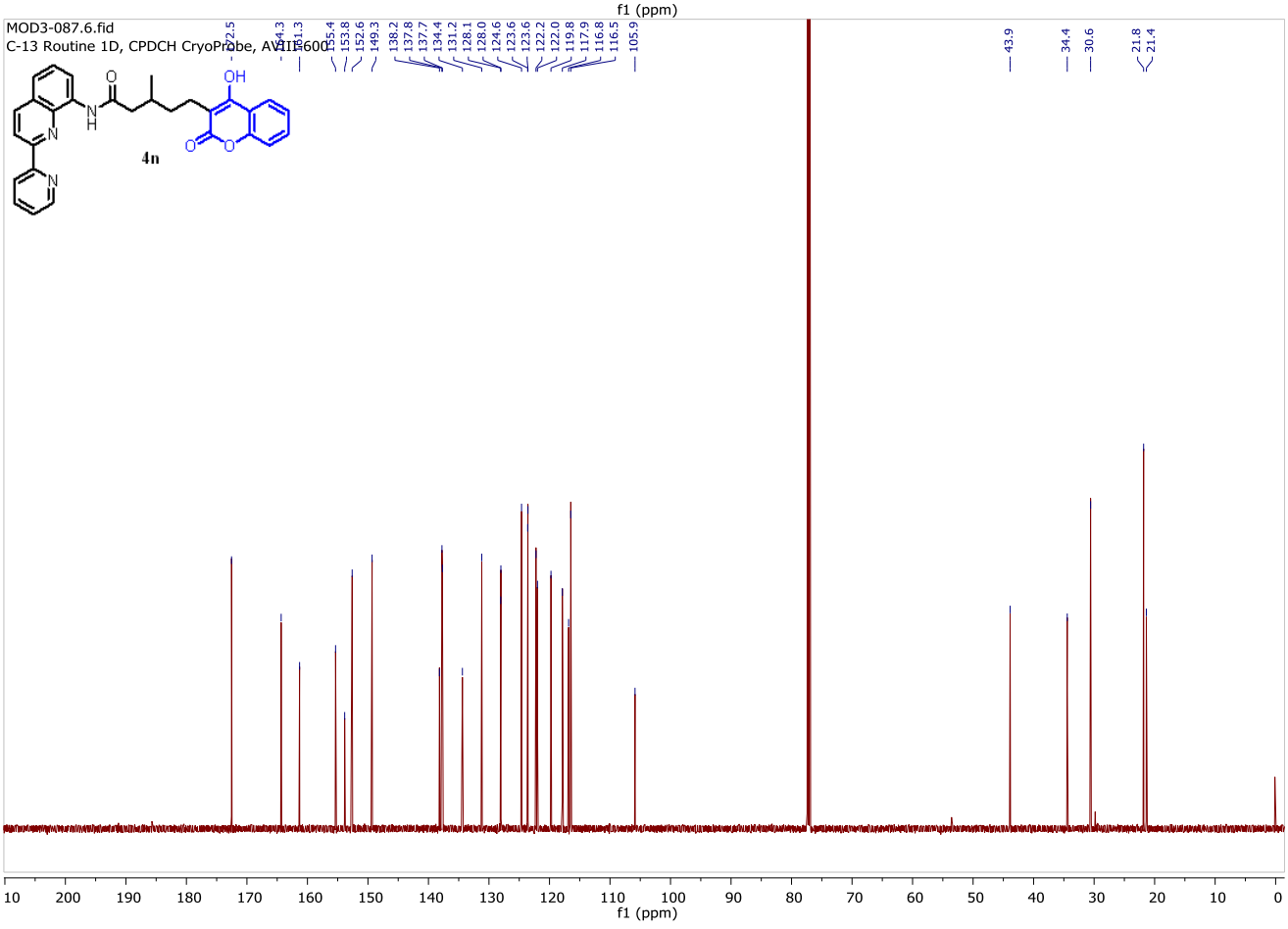

MOD3-111_B.2.fid
H-1 Routine, CP-DCH, AVIII HD-600
4l
0.89
0.99
1.05
3.00
1.14
0.95
1.00
2.08
1.15
1.15
1.03
1.05
1.86
1.86
1.89
2.66
f1 (ppm)

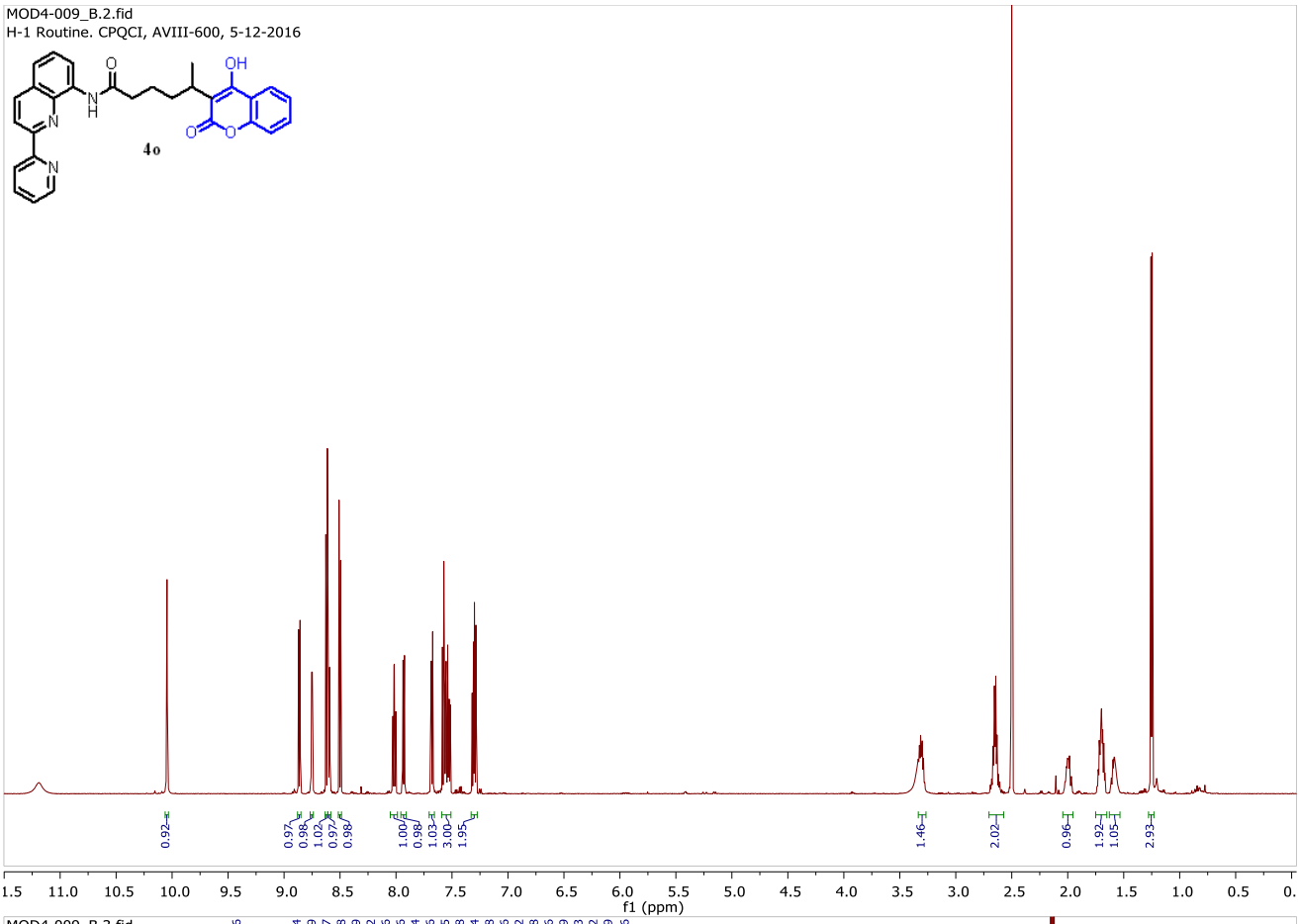

MOD3-111_B.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4l
154.7
153.8
152.7
149.2
146.2
143.3
137.6
137.6
137.3
134.7
130.8
127.9
127.9
127.8
127.4
124.8
121.9
121.7
121.4
120.8
119.4
119.0
117.3
36.8
29.2
25.4
24.0
f1 (ppm)

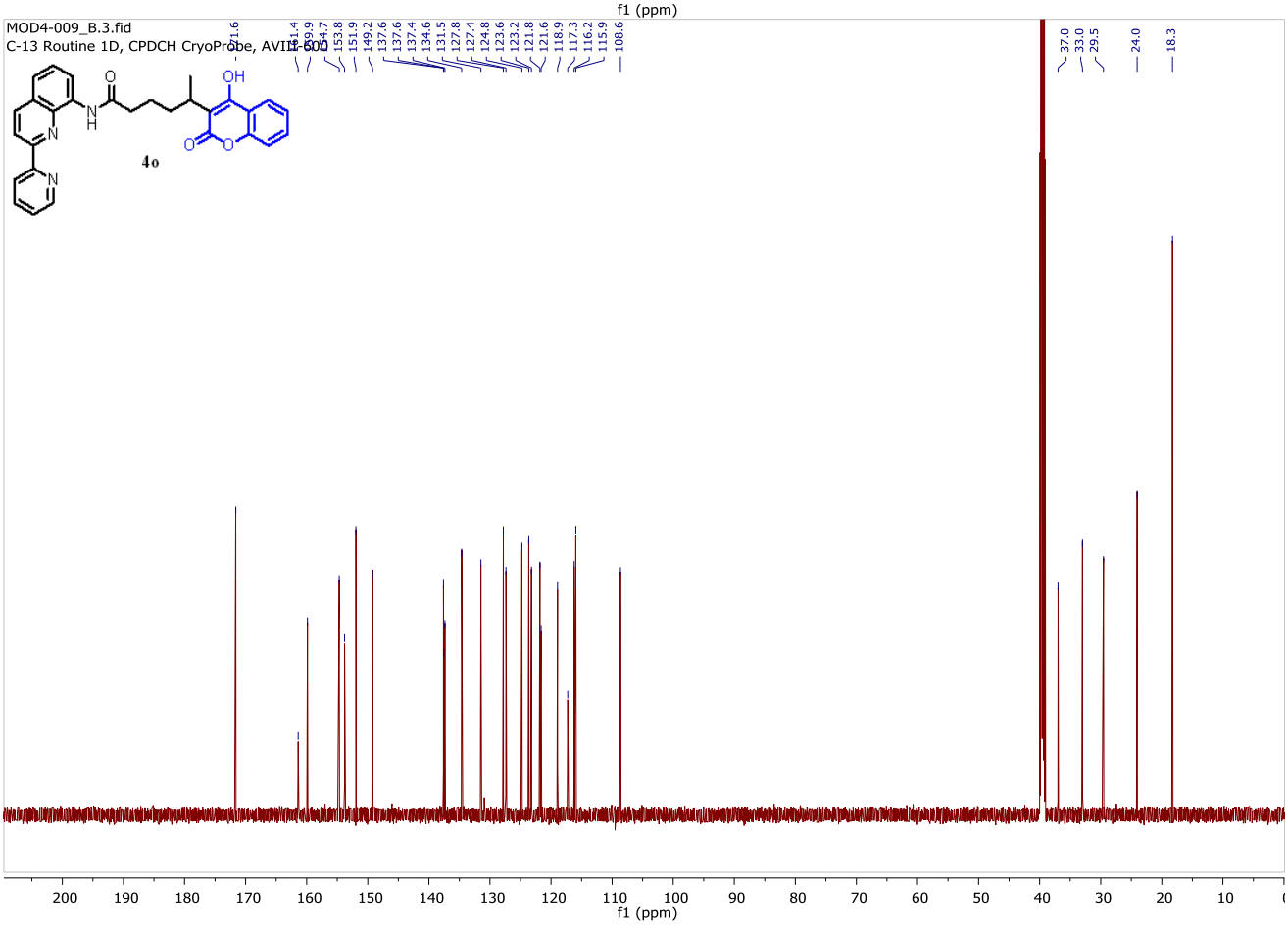

MOD3-090_prepTLC.2.fid
H-1 Routine, DRX-500, BBO Probe
4m
f1 (ppm)

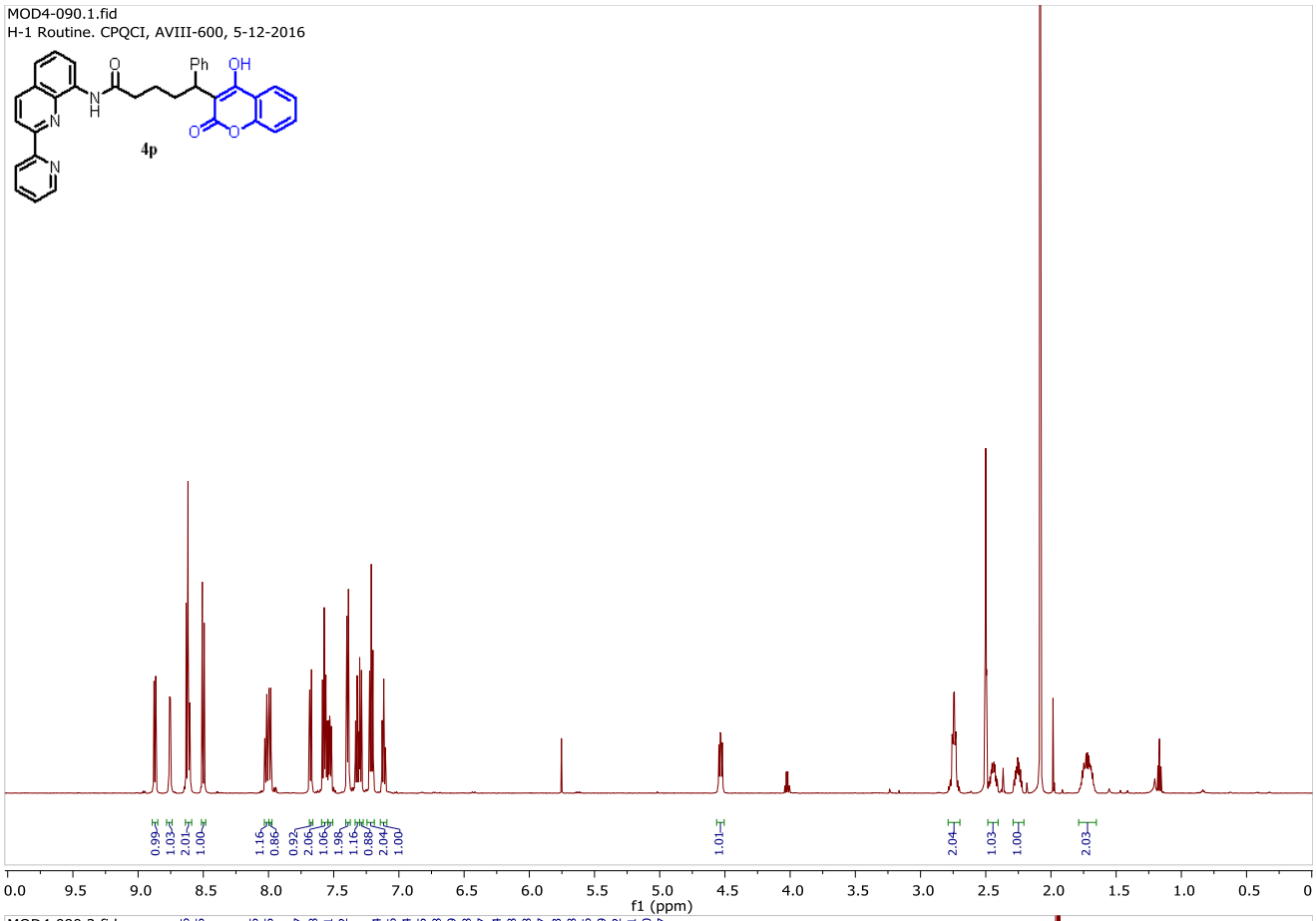

MOD3-090_prepTLC.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4m
f1 (ppm)

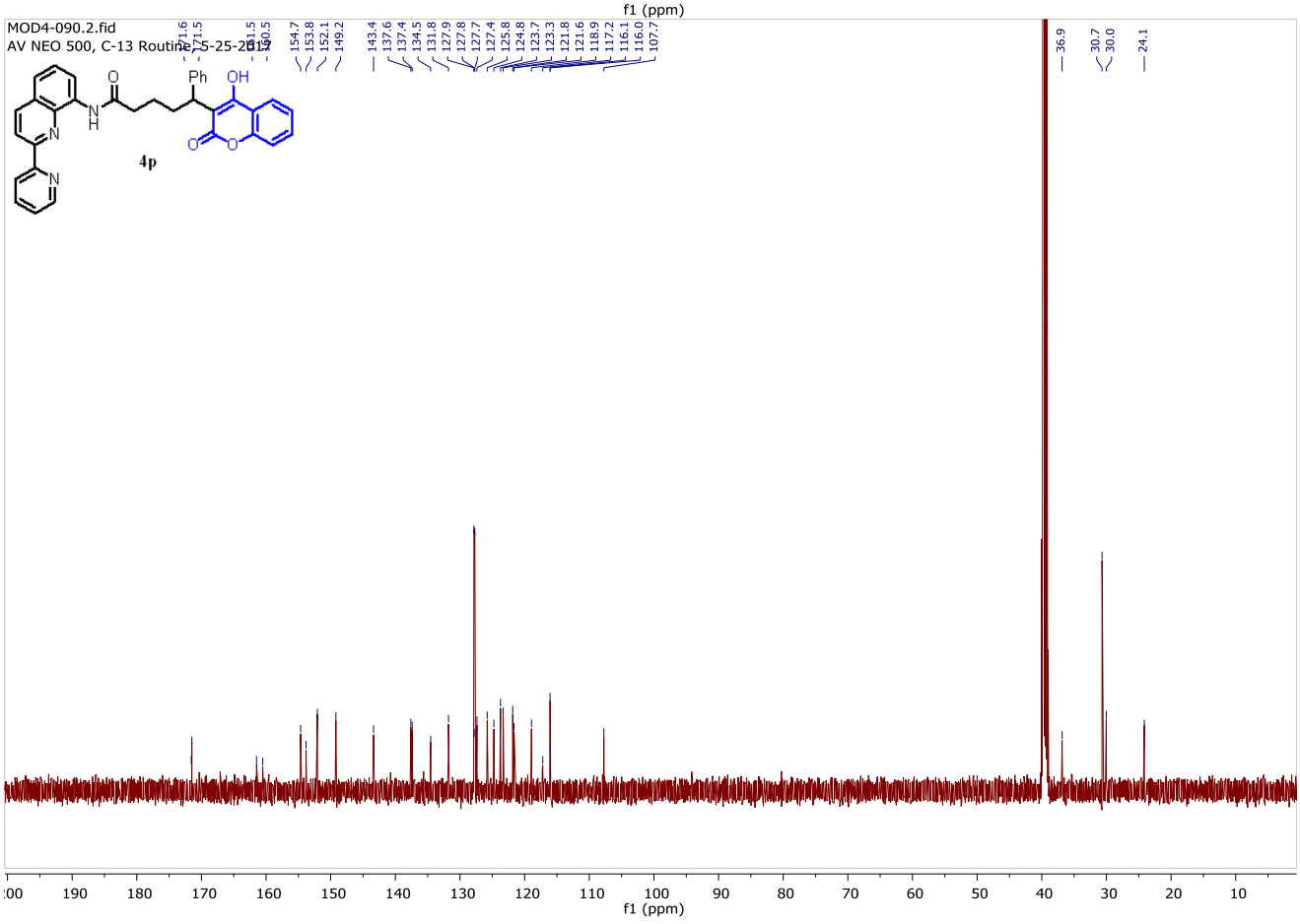

MOD3-087.2.fid
4n
f1 (ppm)

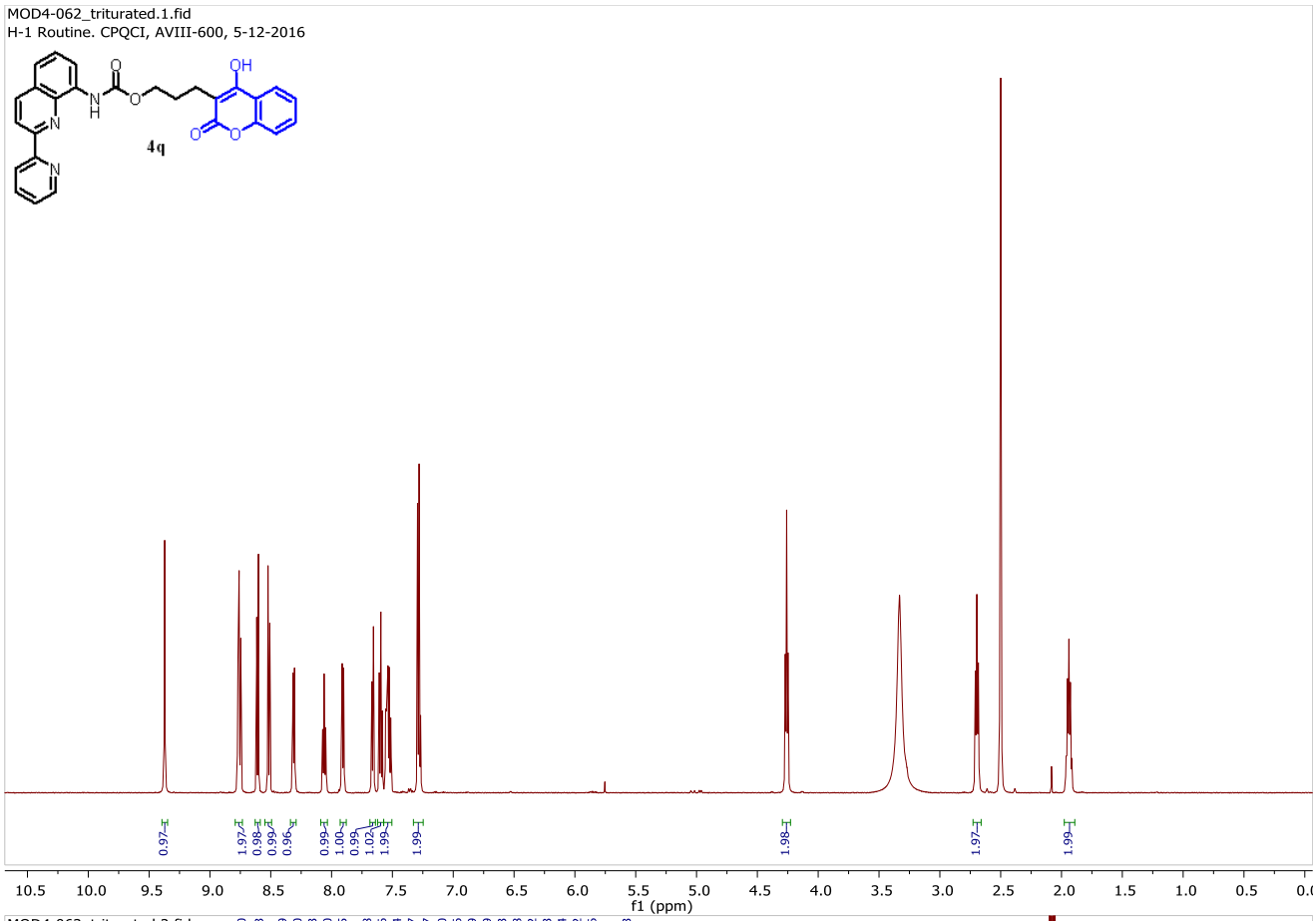

MOD3-087.6.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4n
f1 (ppm)

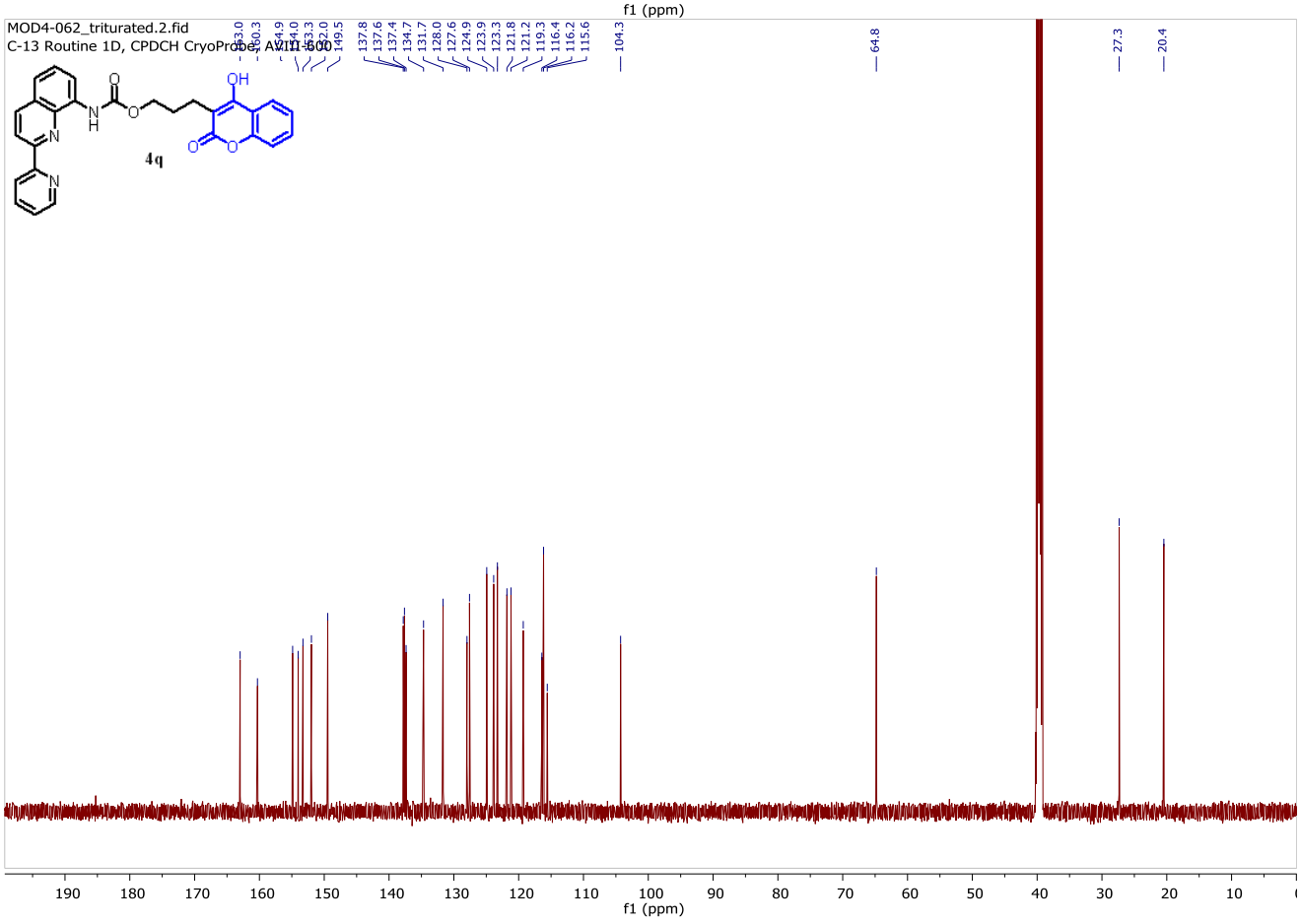

MOD4-009_B.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4o
f1 (ppm)

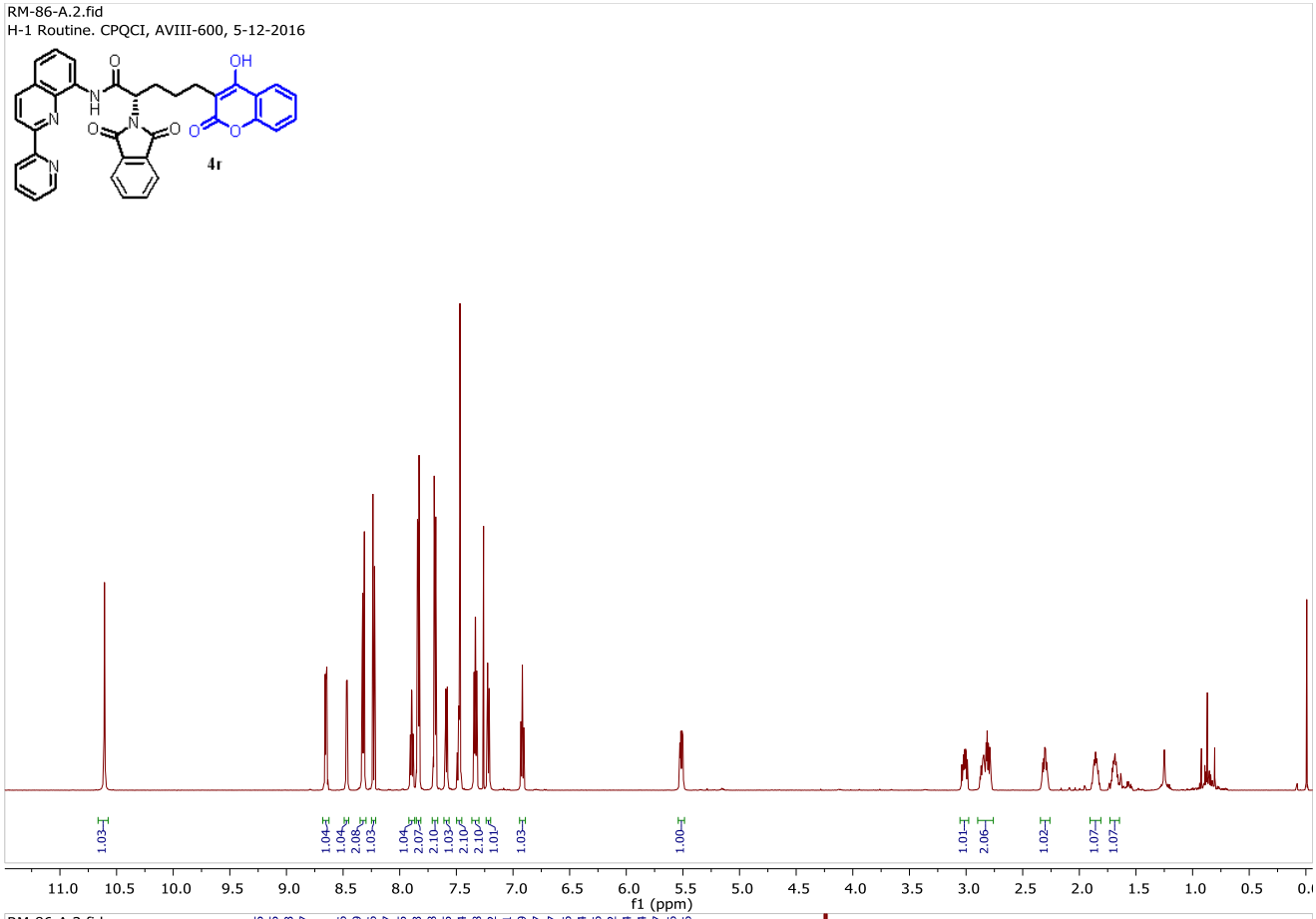

MOD4-009_B.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4o
f1 (ppm)

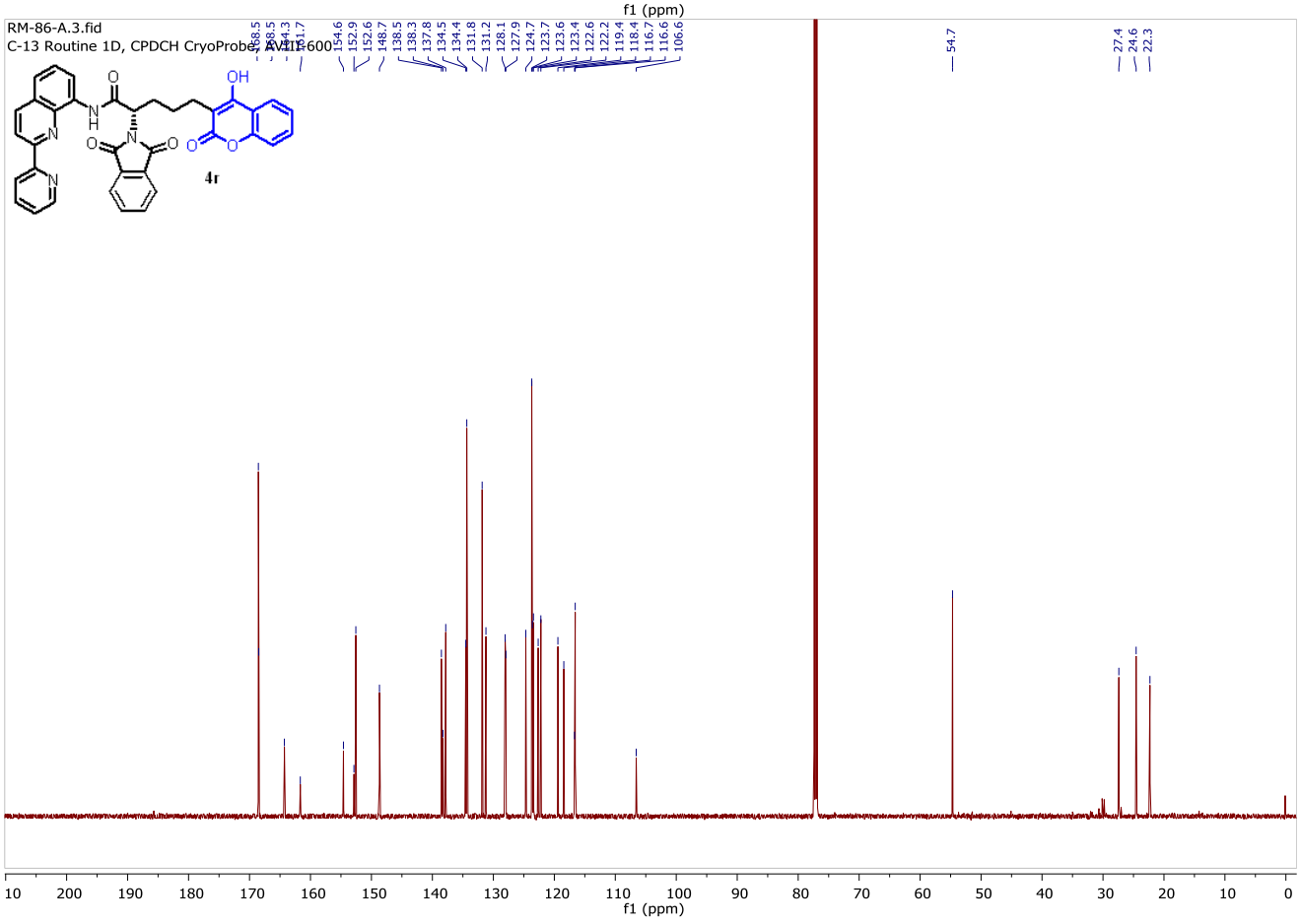

MOD4-090.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
Ph
OH
O
N
H
N
O
O
4p
0.99
1.03
2.01
1.00
1.16
0.86
0.92
2.06
1.06
1.98
1.16
0.88
2.04
1.00
1.01
2.04
1.03
1.00
2.03
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

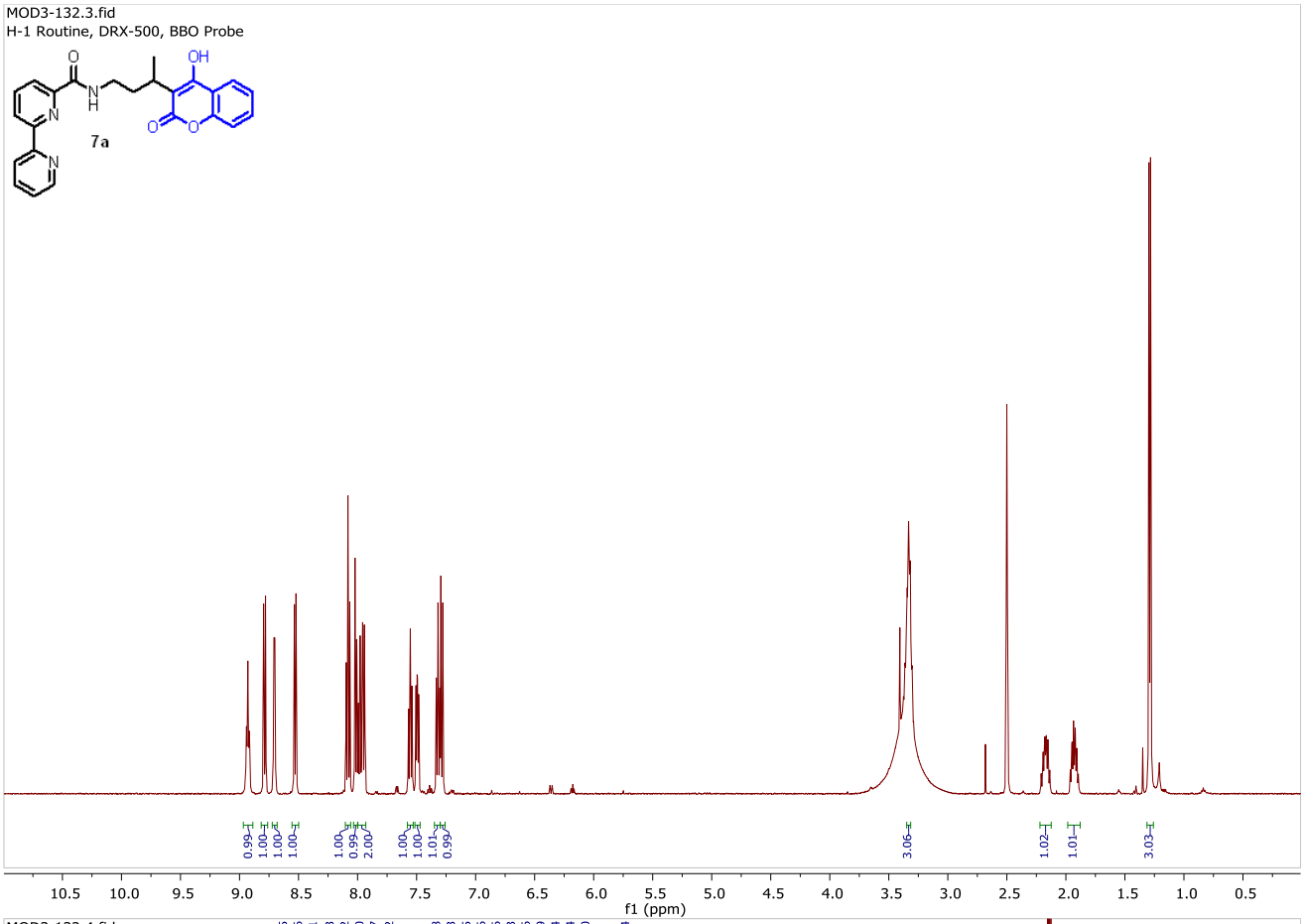

MOD4-090.2.fid
AV NEO 500, C-13 Routine, 5-25-2015
171.6
171.5
161.5
160.5
154.7
153.8
152.1
149.2
143.4
137.6
137.4
134.5
131.8
127.9
127.8
127.7
127.4
125.8
124.8
123.7
123.3
121.8
121.6
118.9
117.2
116.1
116.0
107.7
36.9
30.7
30.0
24.1
Ph
OH
O
N
H
N
O
O
4p
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

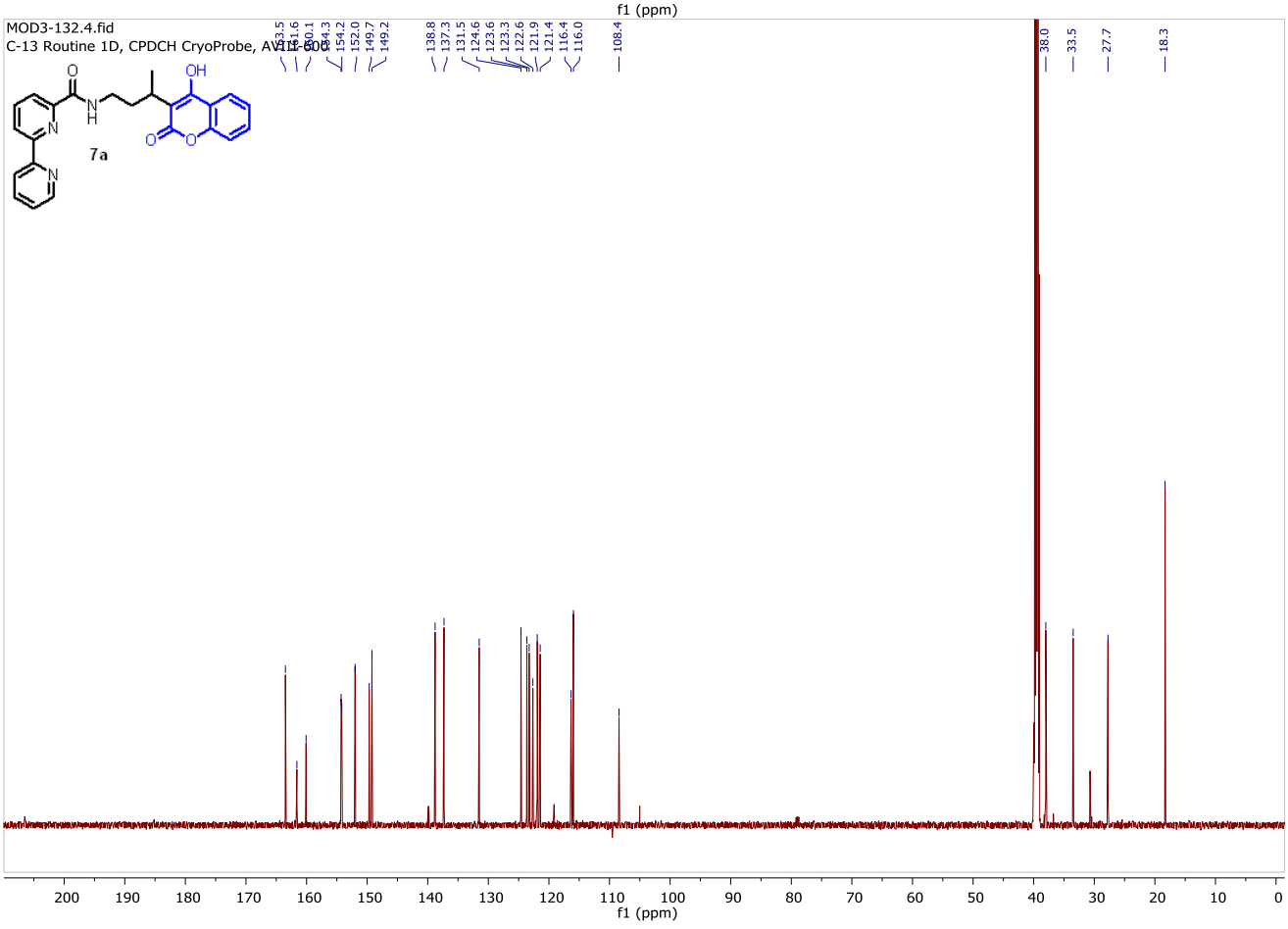

MOD4-062_triturated.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4q
f1 (ppm)

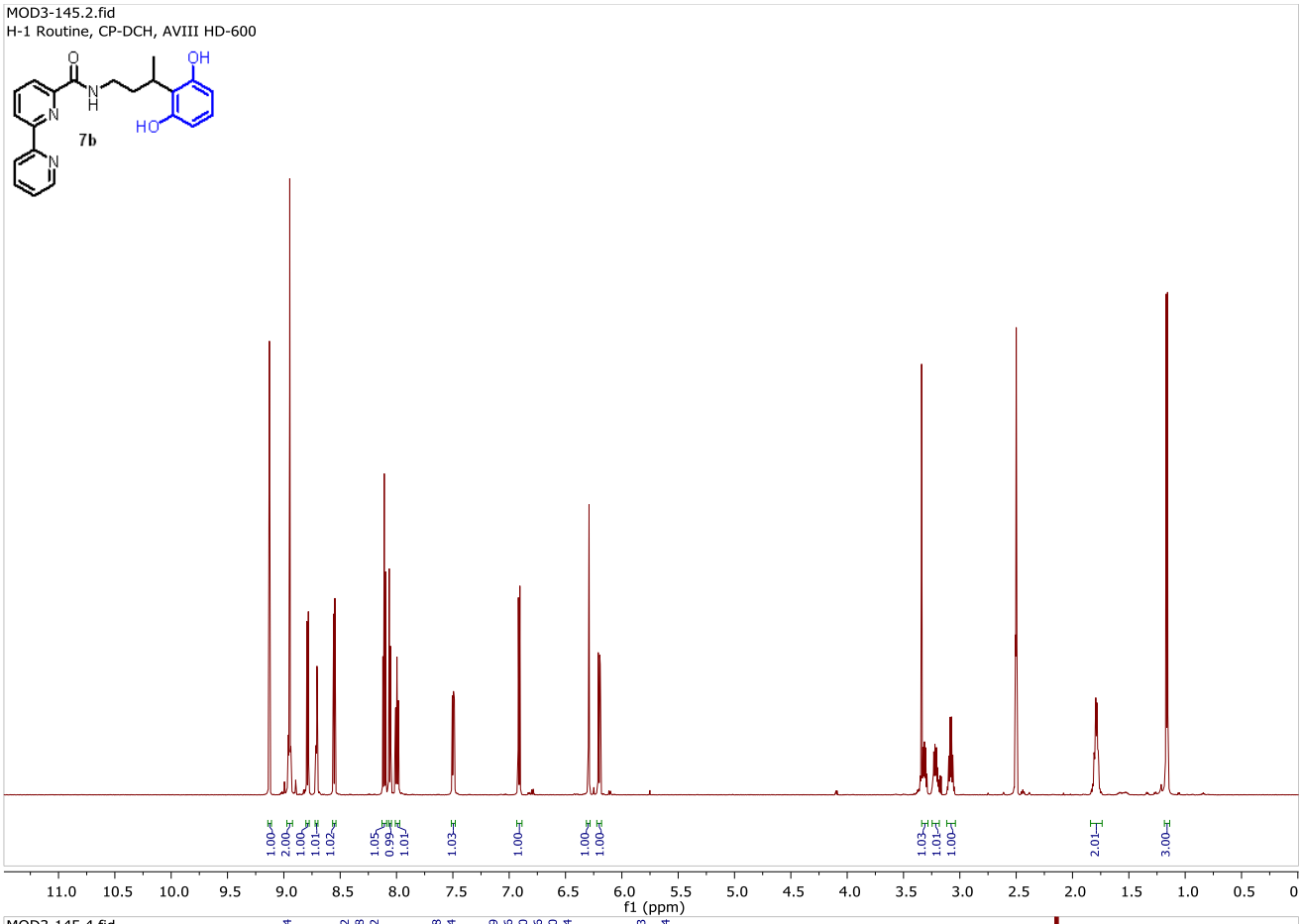

MOD4-062_triturated.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4q
f1 (ppm)

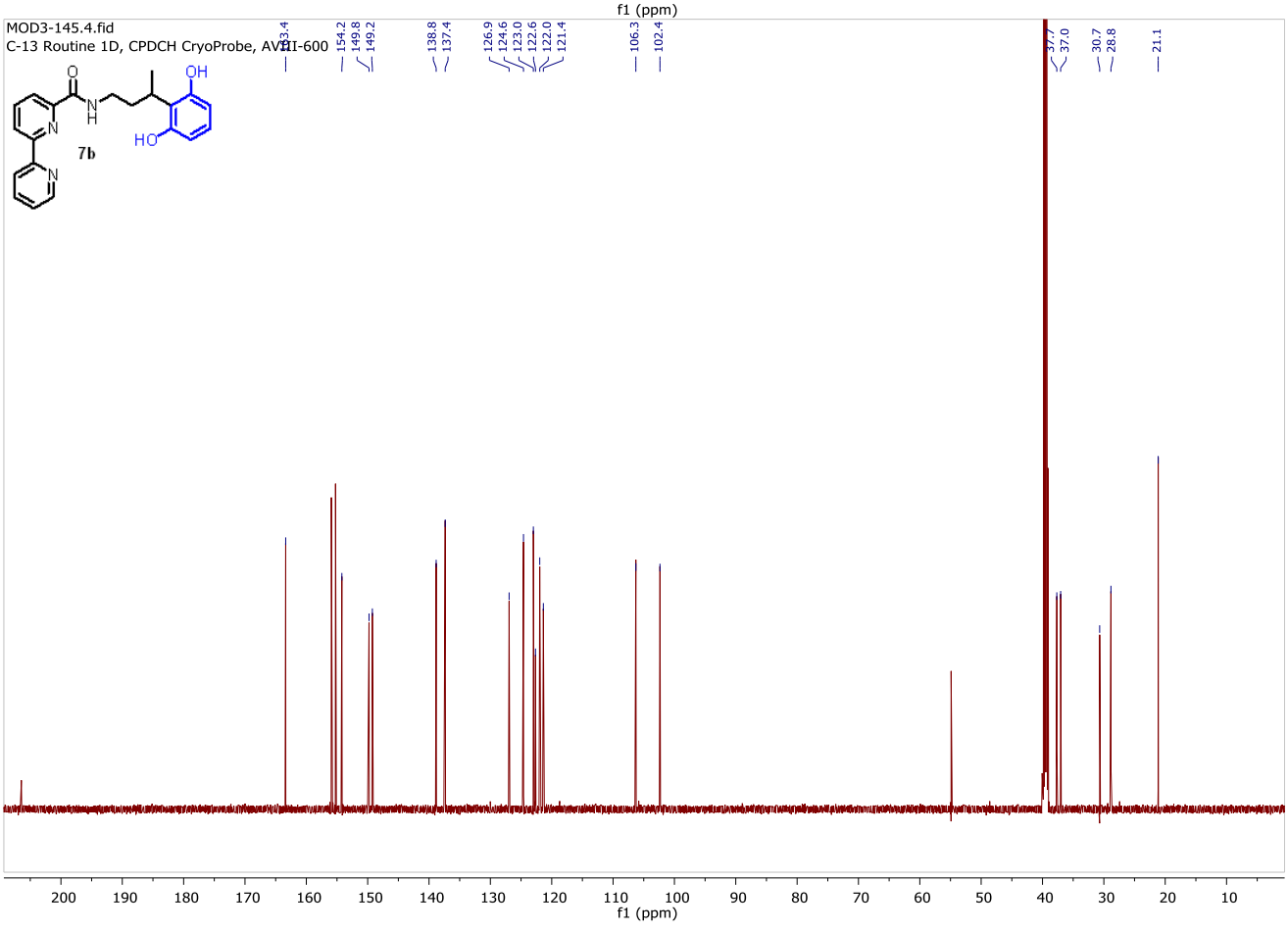

RM-86-A.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
4r
f1 (ppm)

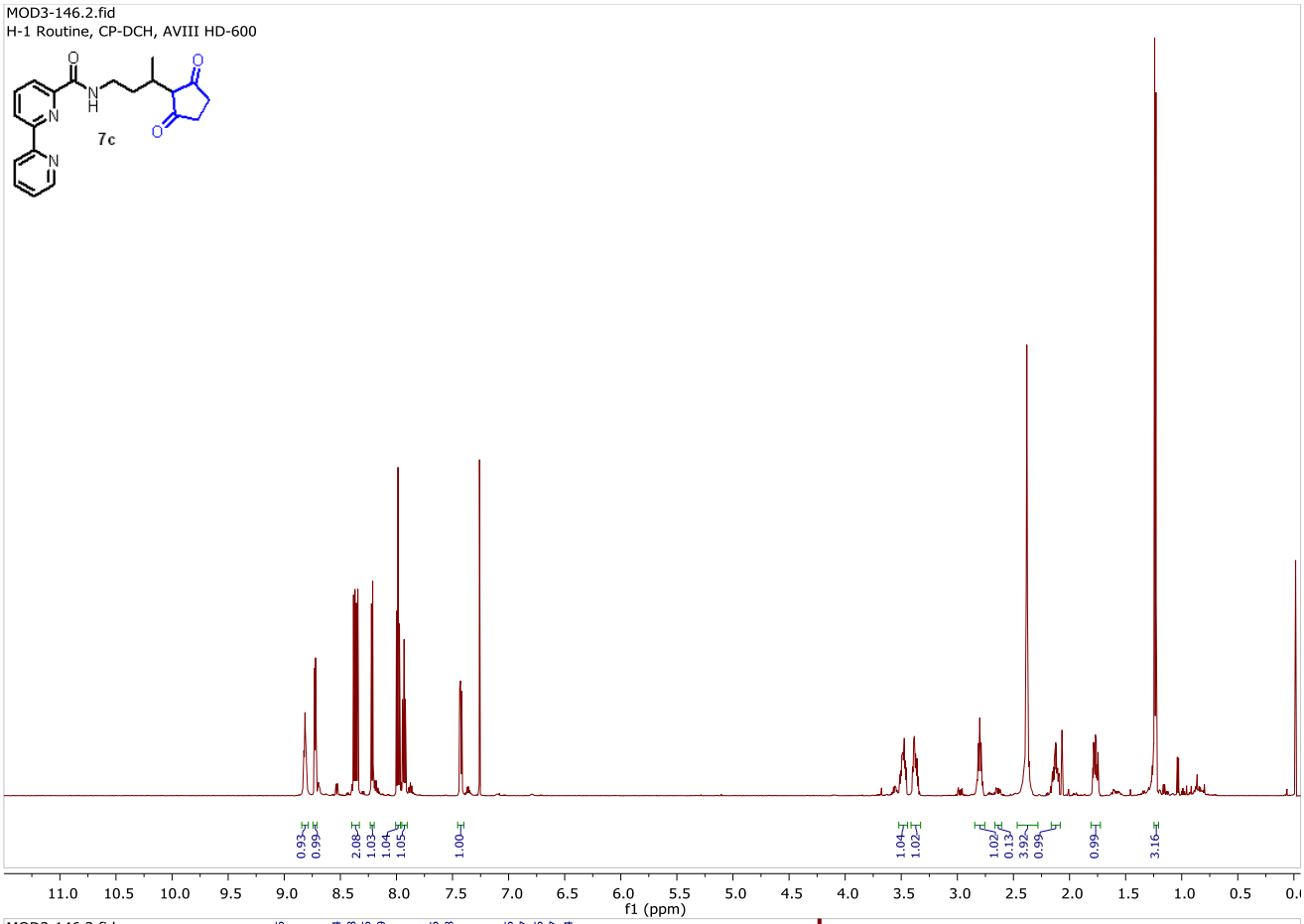

RM-86-A.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
4r
f1 (ppm)

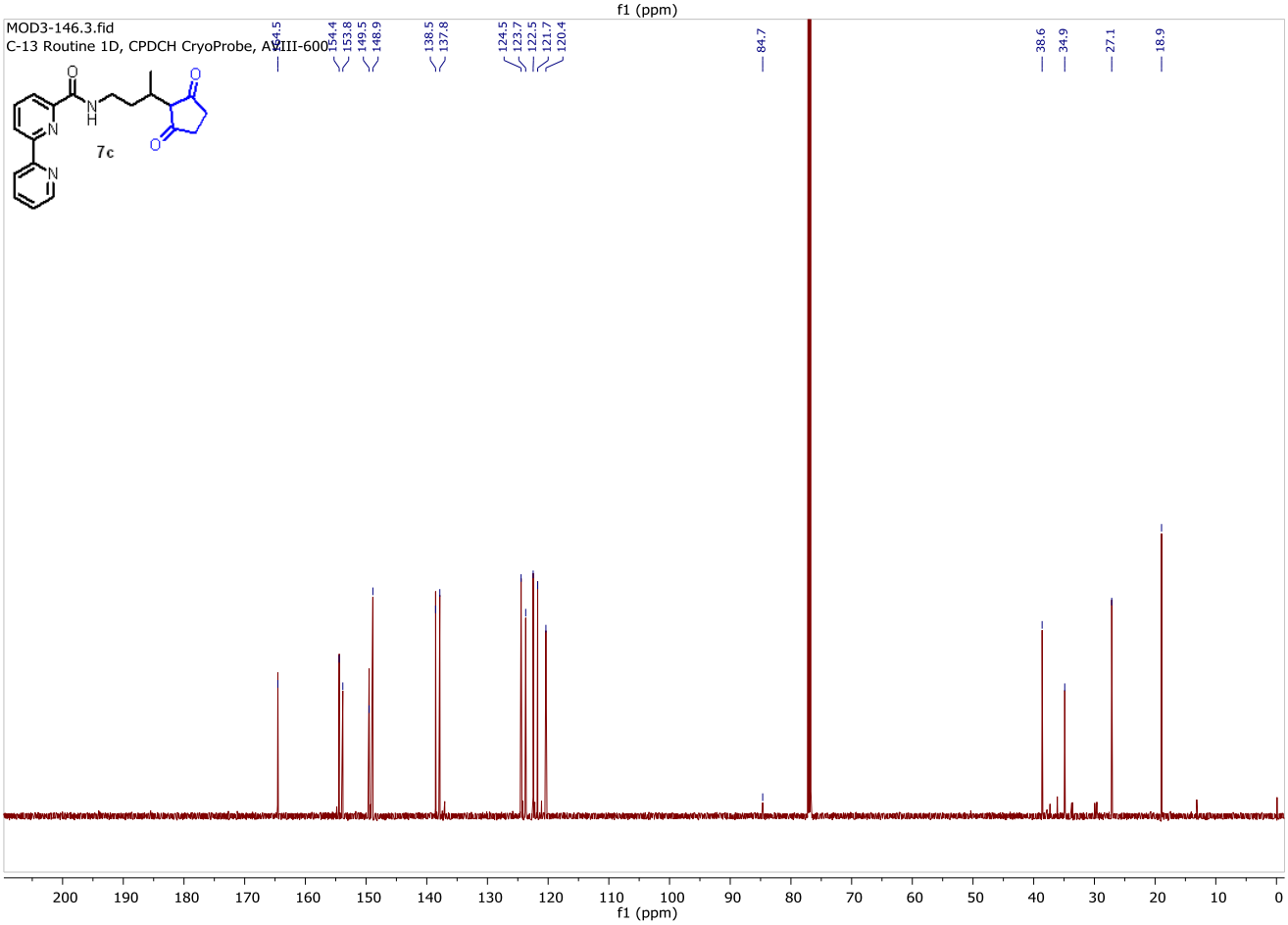

MOD3-132.3.fid
H-1 Routine, DRX-500, BBO Probe
7a
f1 (ppm)

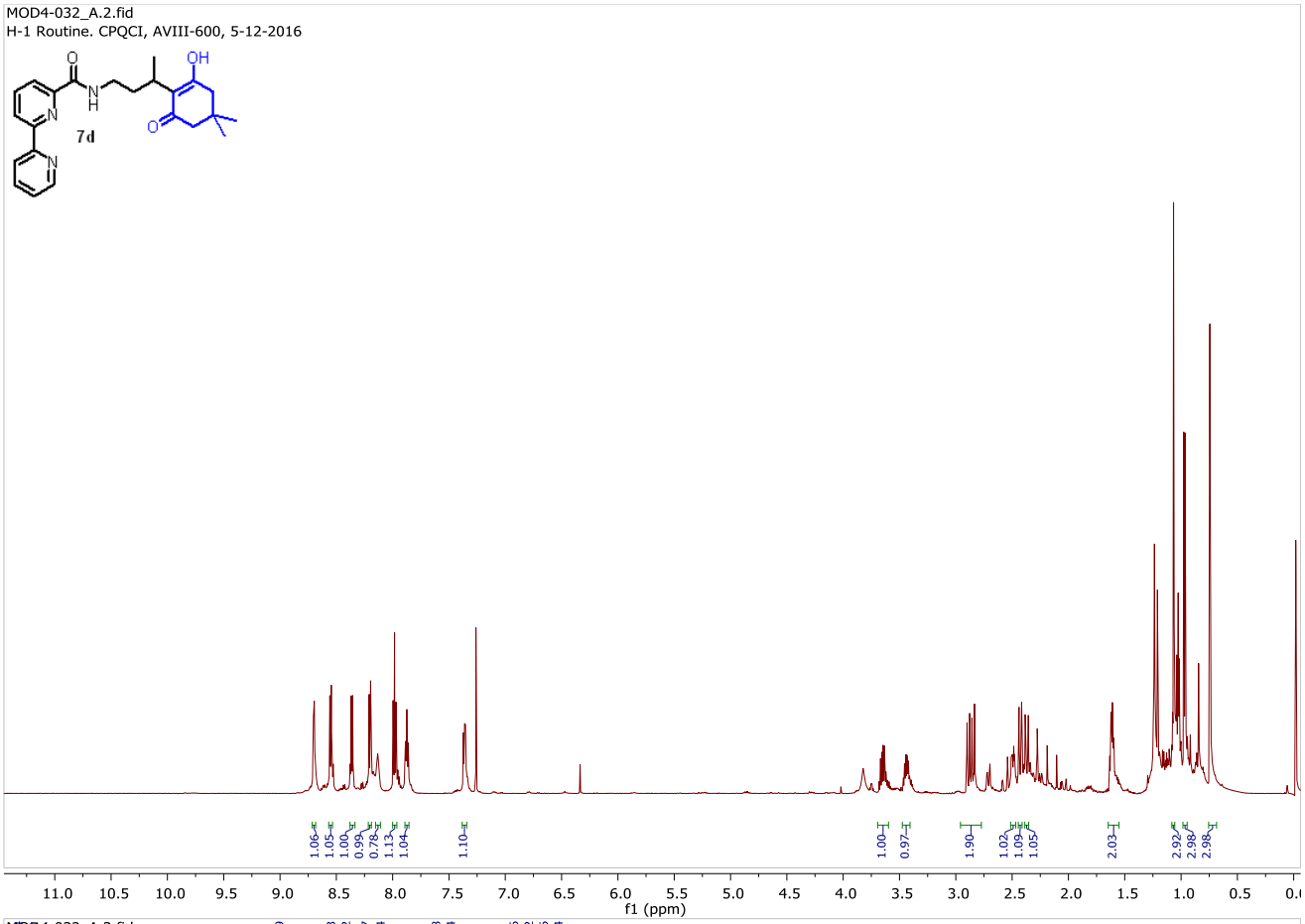

MOD3-132.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AV11-600
7a
f1 (ppm)

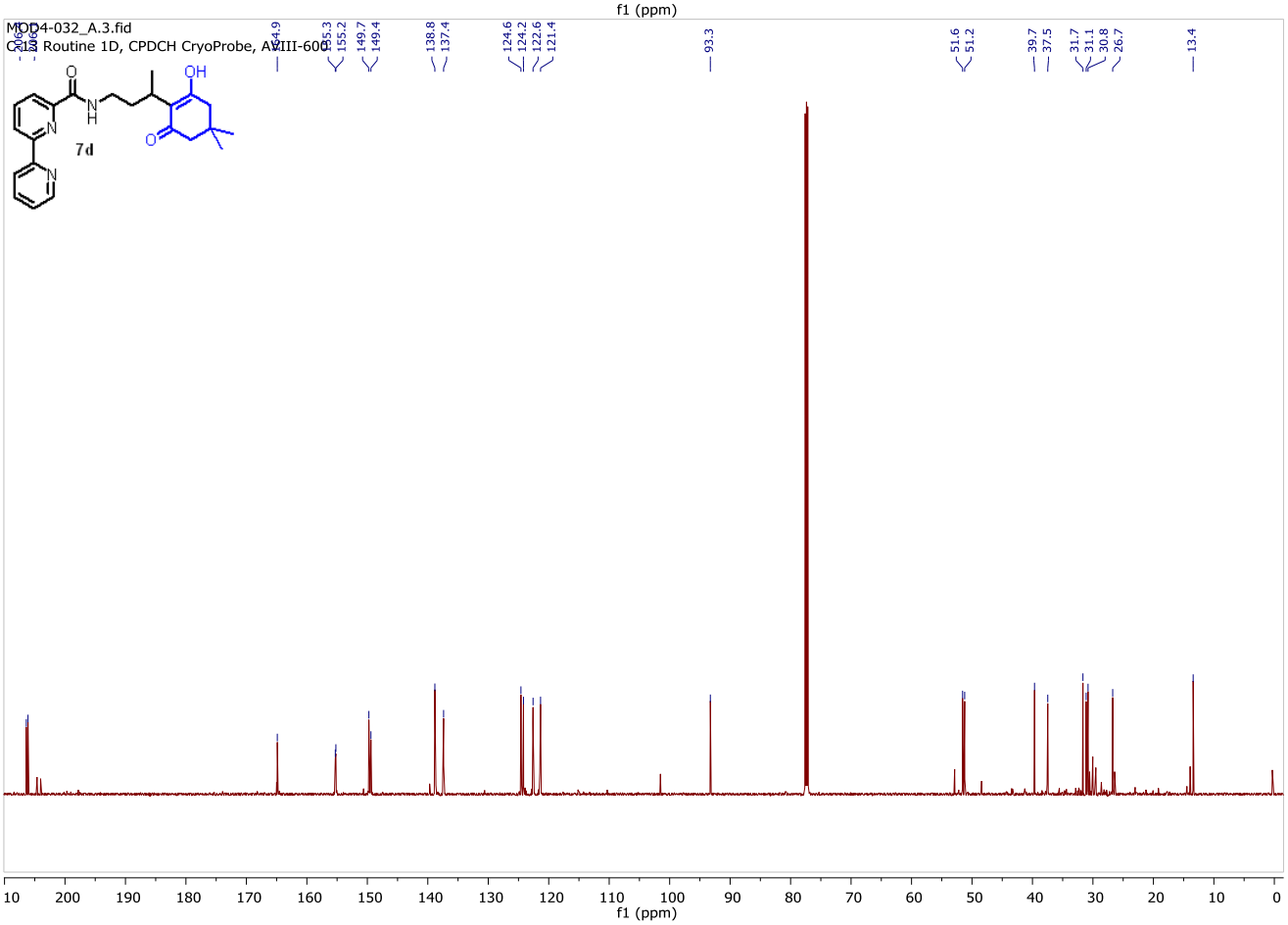

MOD3-145.2.fid
H-1 Routine, CP-DCH, AVIII HD-600
7b
f1 (ppm)

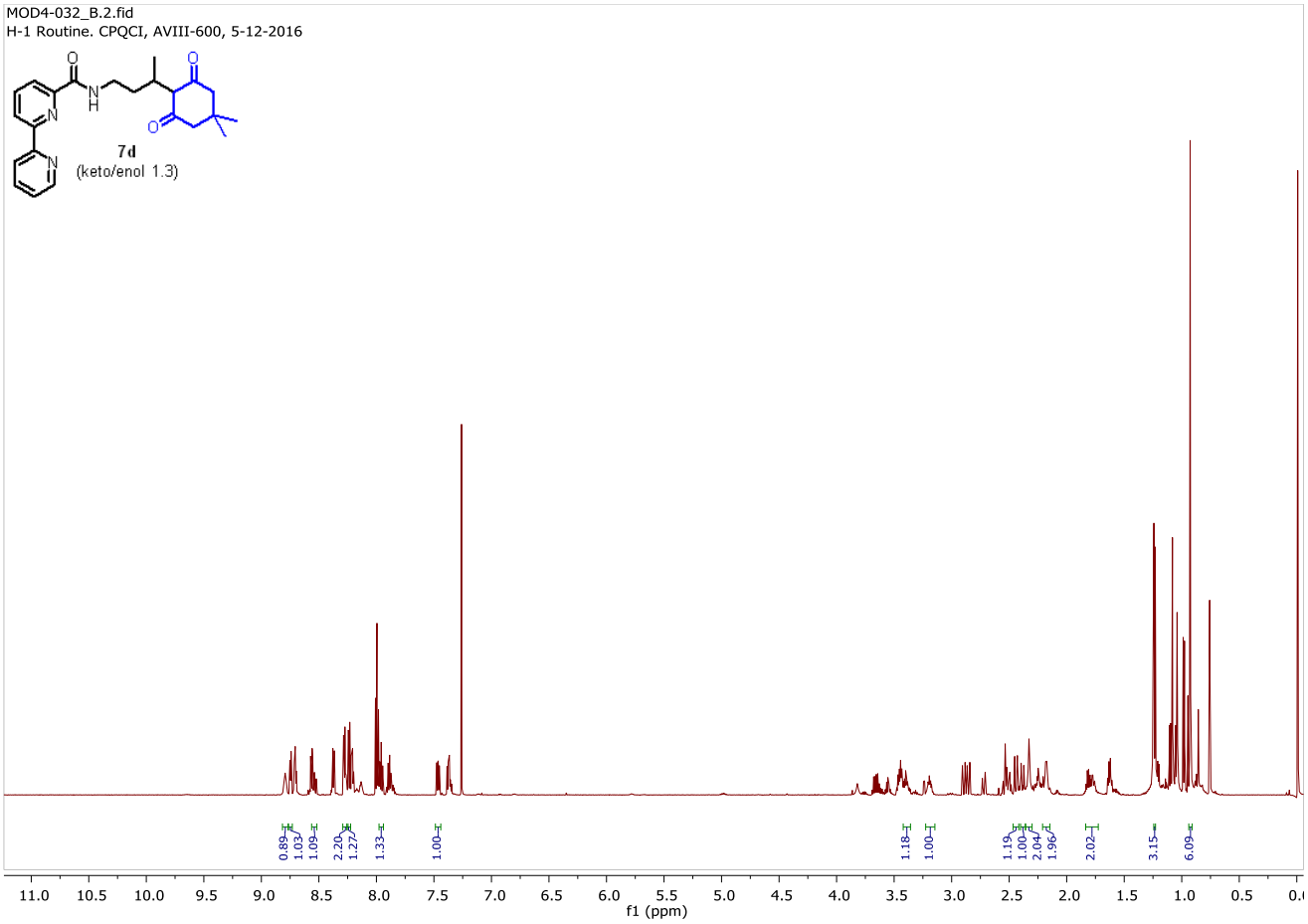

MOD3-145.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
7b
f1 (ppm)

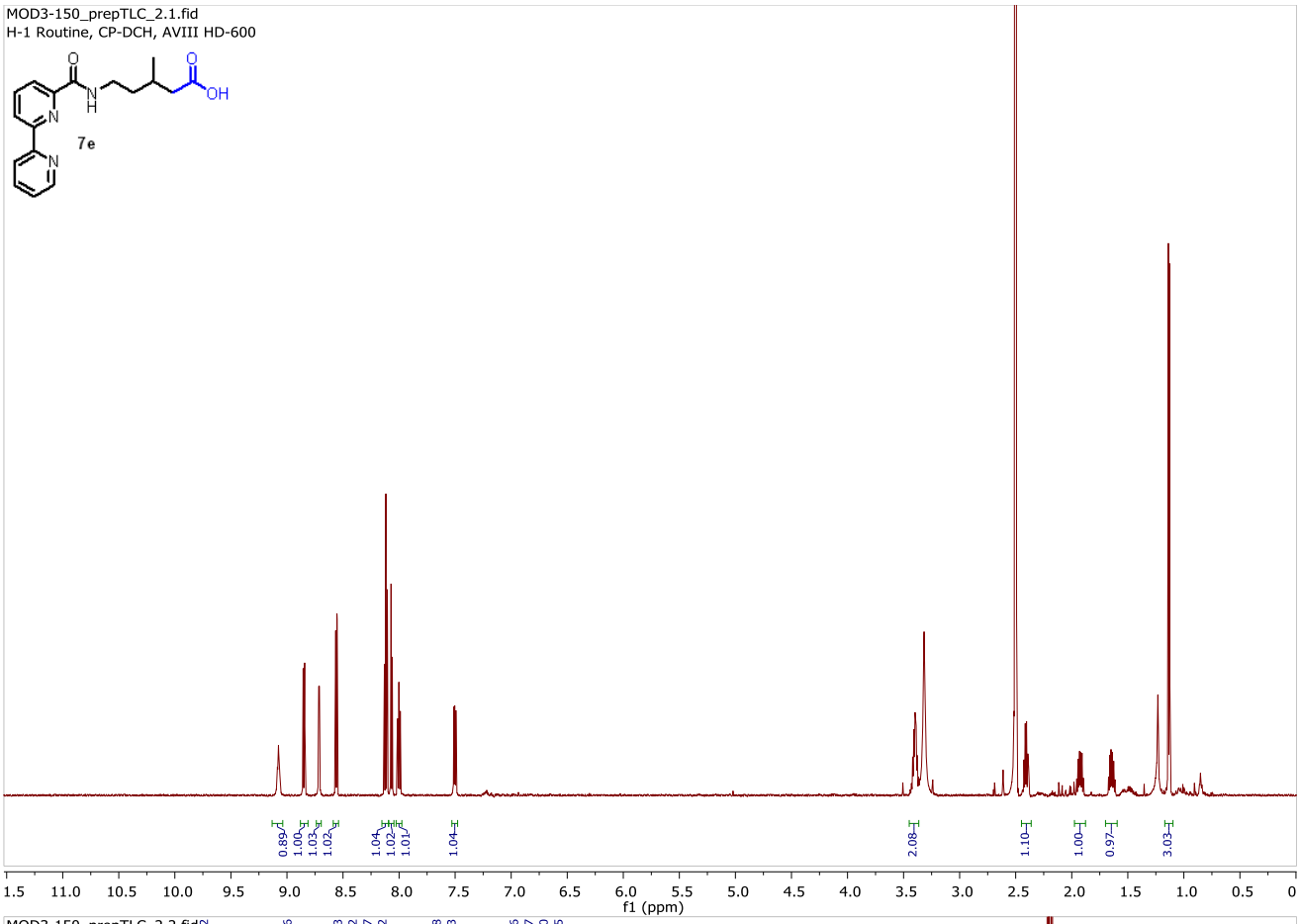

MOD3-146.2.fid
H-1 Routine, CP-DCH, AVIII HD-600
7c
0.93
0.99
2.08
1.03
1.04
1.05
1.00
1.04
1.02
1.02
0.13
3.92
0.99
0.99
3.16
f1 (ppm)

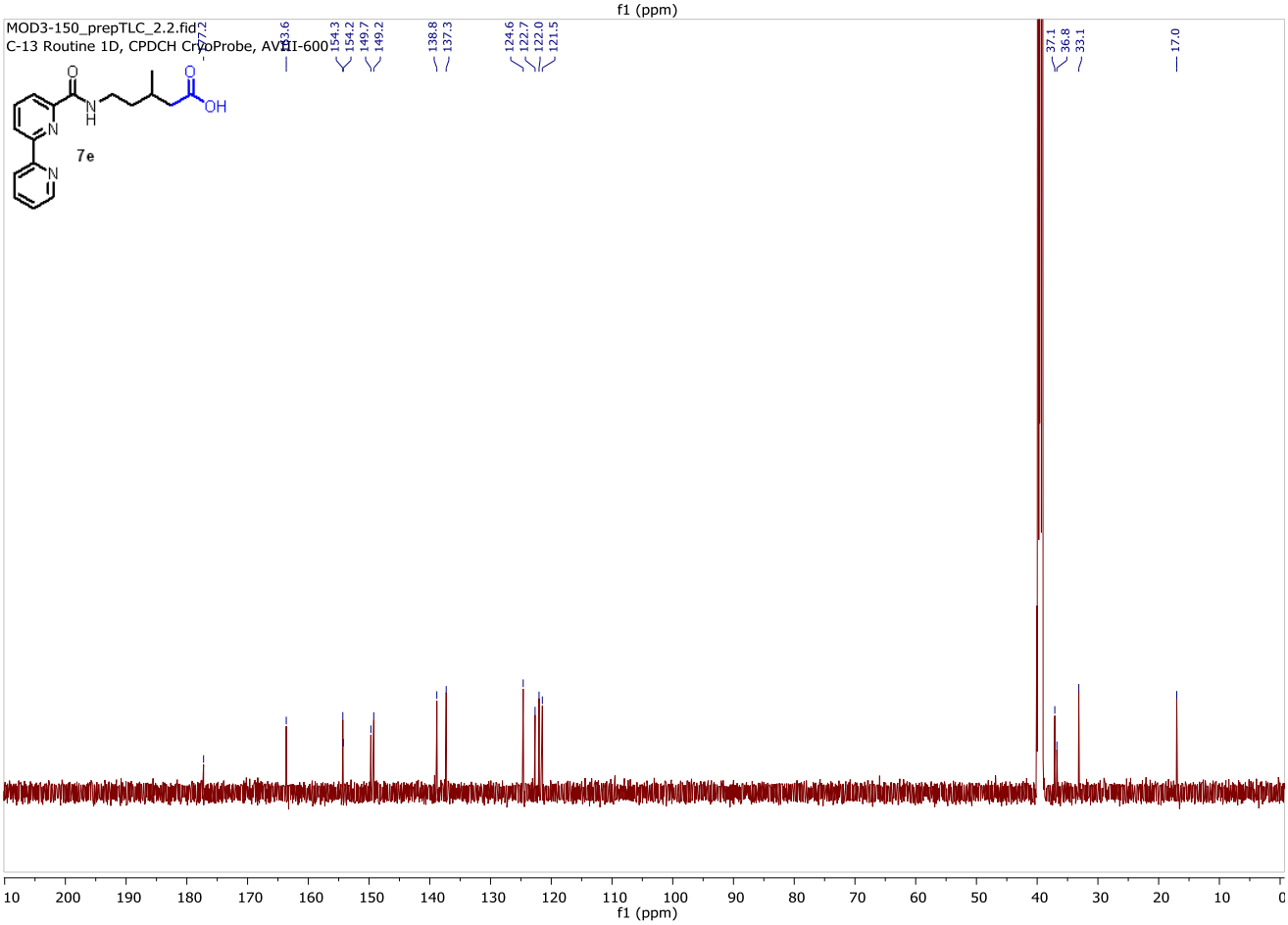

MOD3-146.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
7c
154.5
154.4
153.8
149.5
148.9
138.5
137.8
124.5
123.7
122.5
121.7
120.4
84.7
38.6
34.9
27.1
18.9
f1 (ppm)

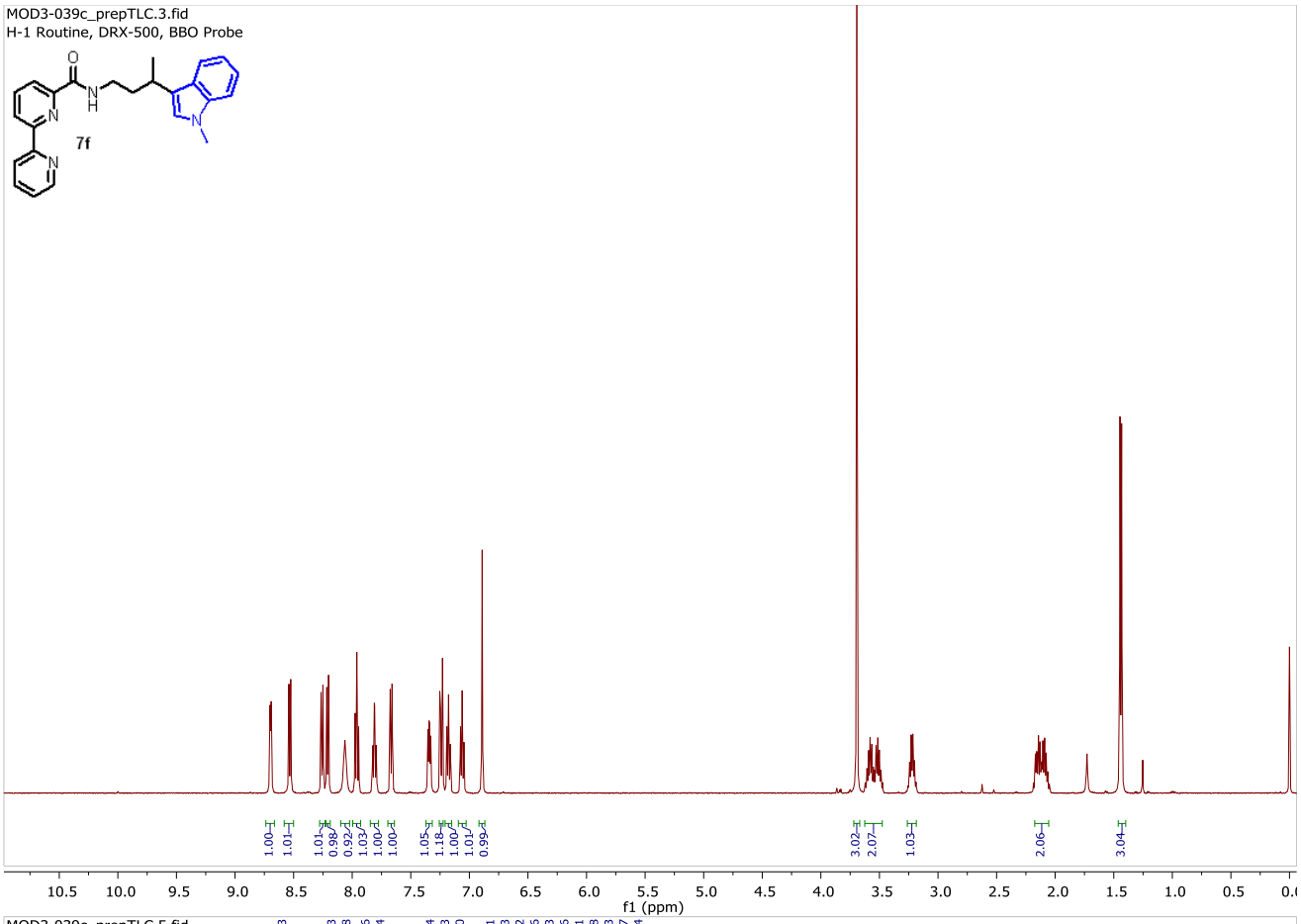

MOD4-032_A.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
7d
f1 (ppm)

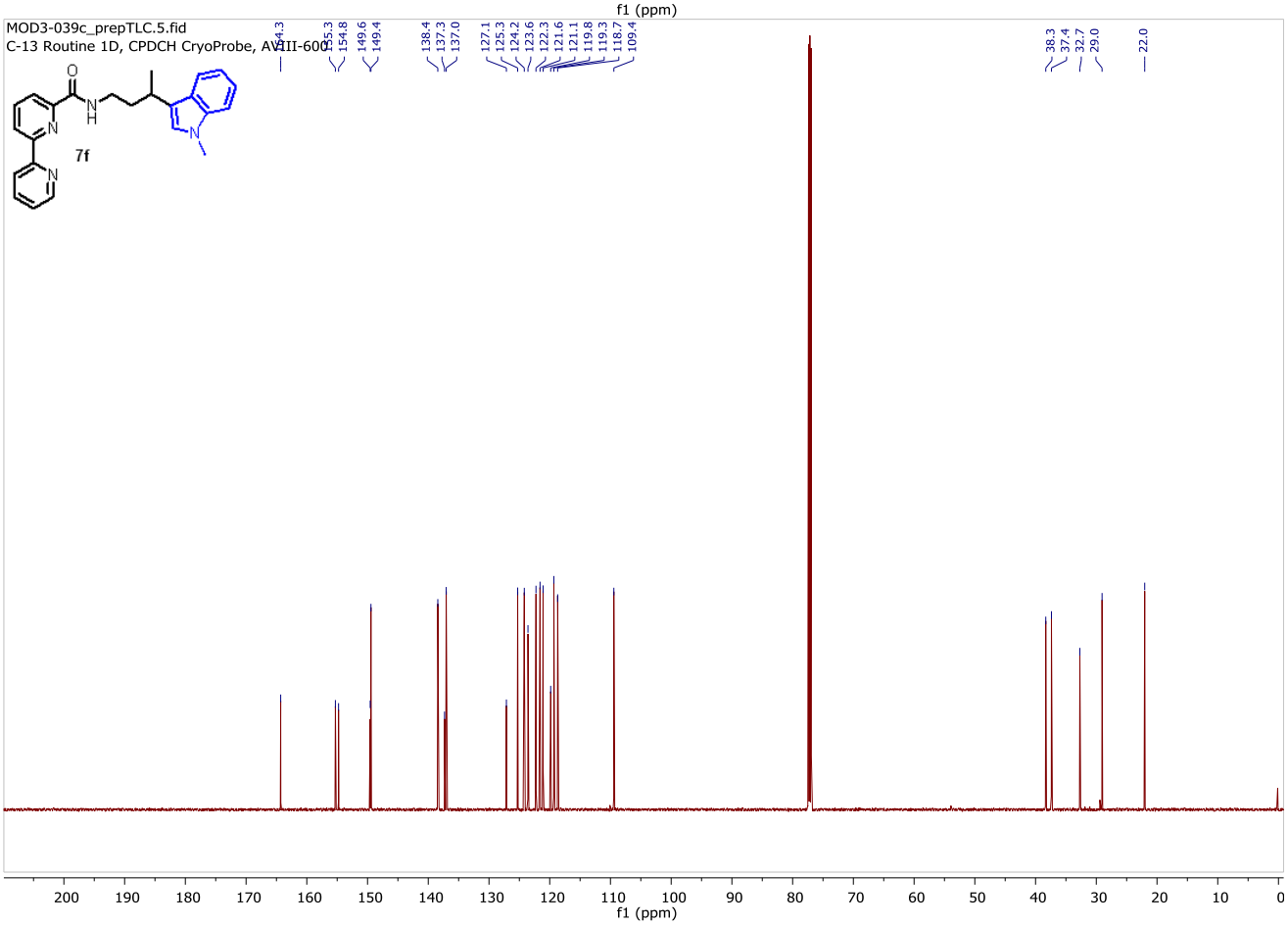

MOD4-032_A.3.fid
C13 Routine 1D, CPDCH CryoProbe, AVIII-600
7d
f1 (ppm)

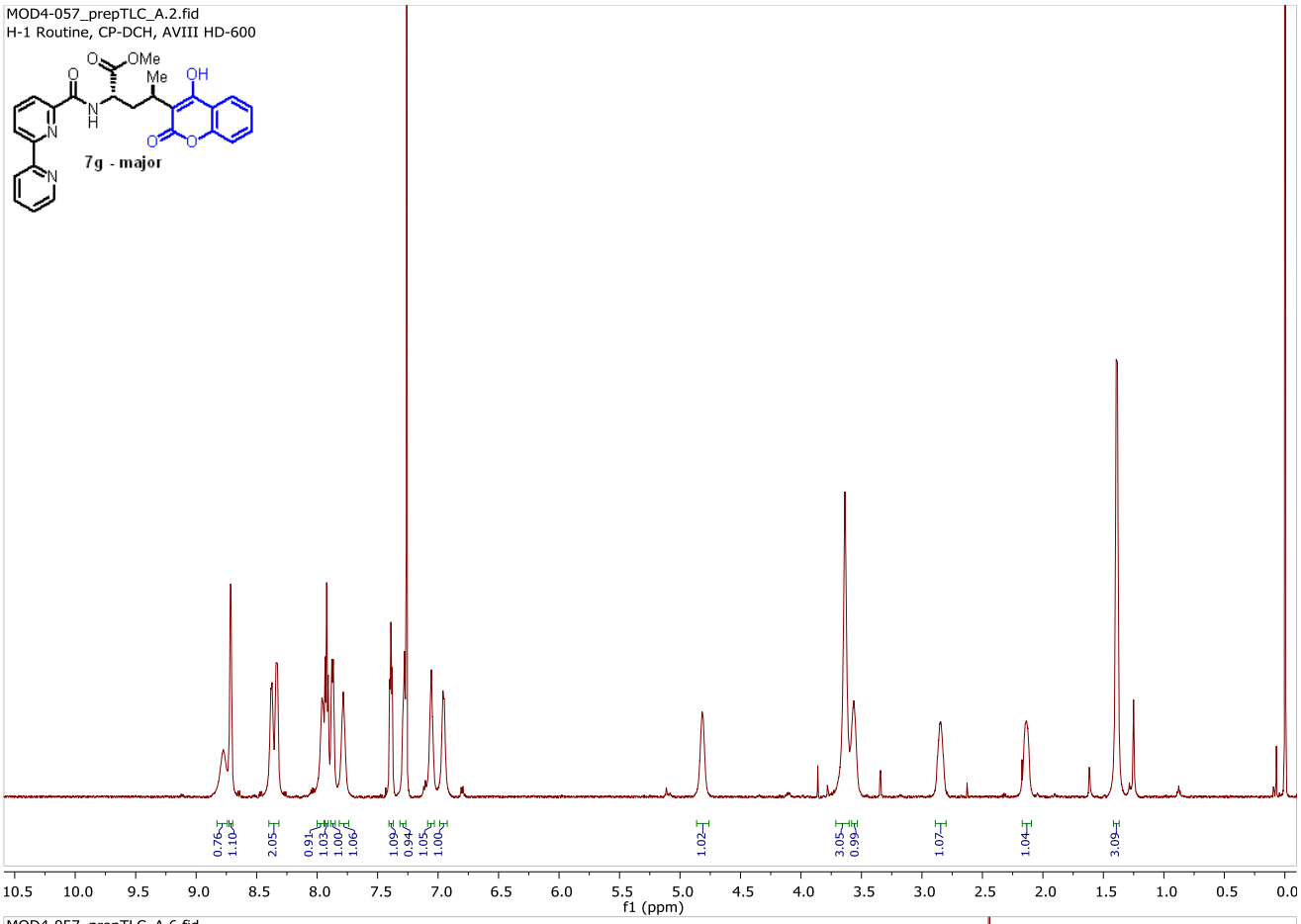

MOD4-032_B.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
7d
(keto/enol 1.3)
0.89
1.03
1.09
2.20
1.27
1.33
1.00
1.18
1.00
1.19
1.00
2.04
1.96
2.02
3.15
6.09
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

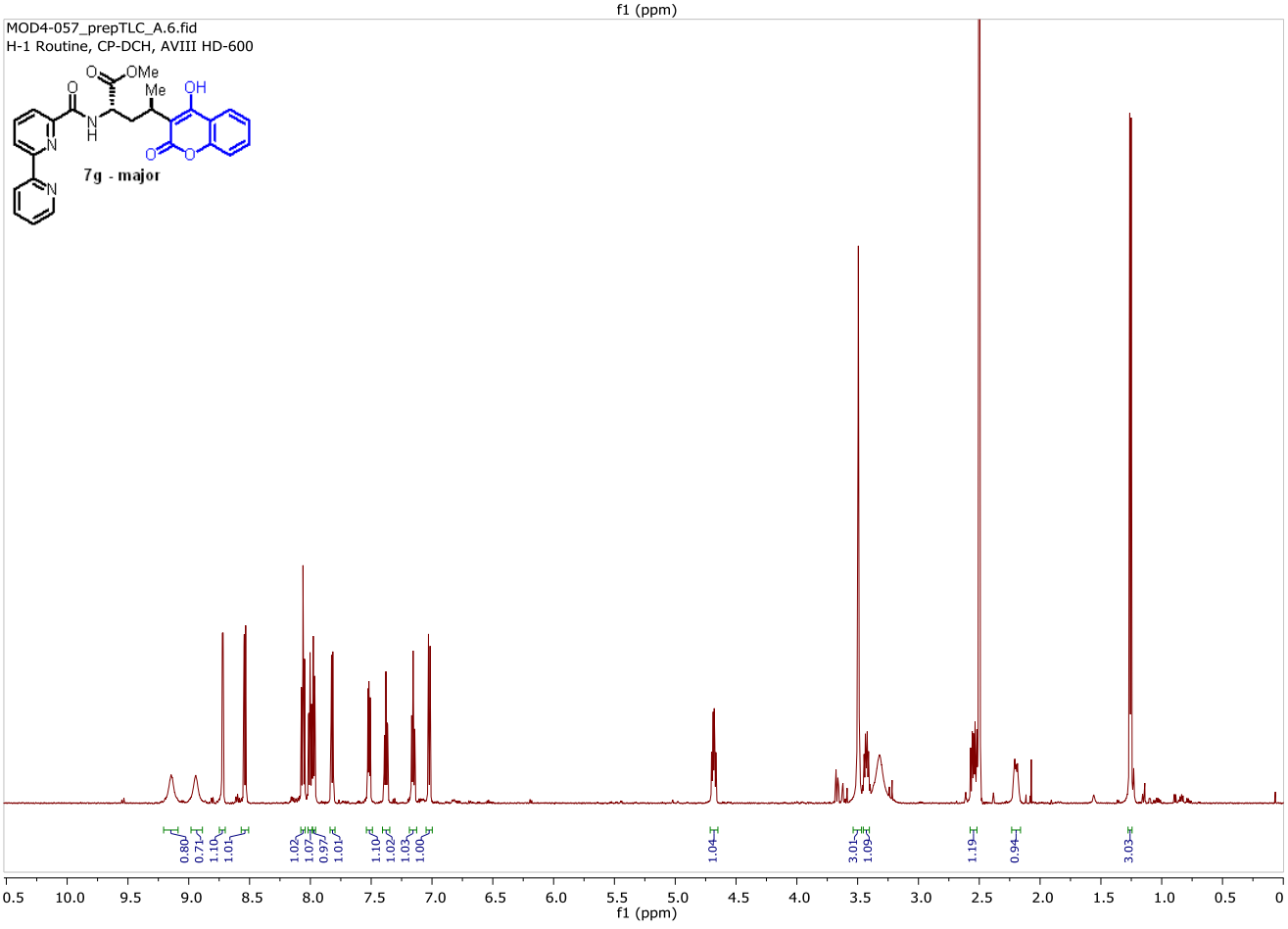

MOD3-150_prepTLC_2.1.fid
H-1 Routine, CP-DCH, AVIII HD-600
7e
0.89
1.00
1.03
1.02
1.04
1.02
1.01
1.04
2.08
1.10
1.00
0.97
3.03
f1 (ppm)

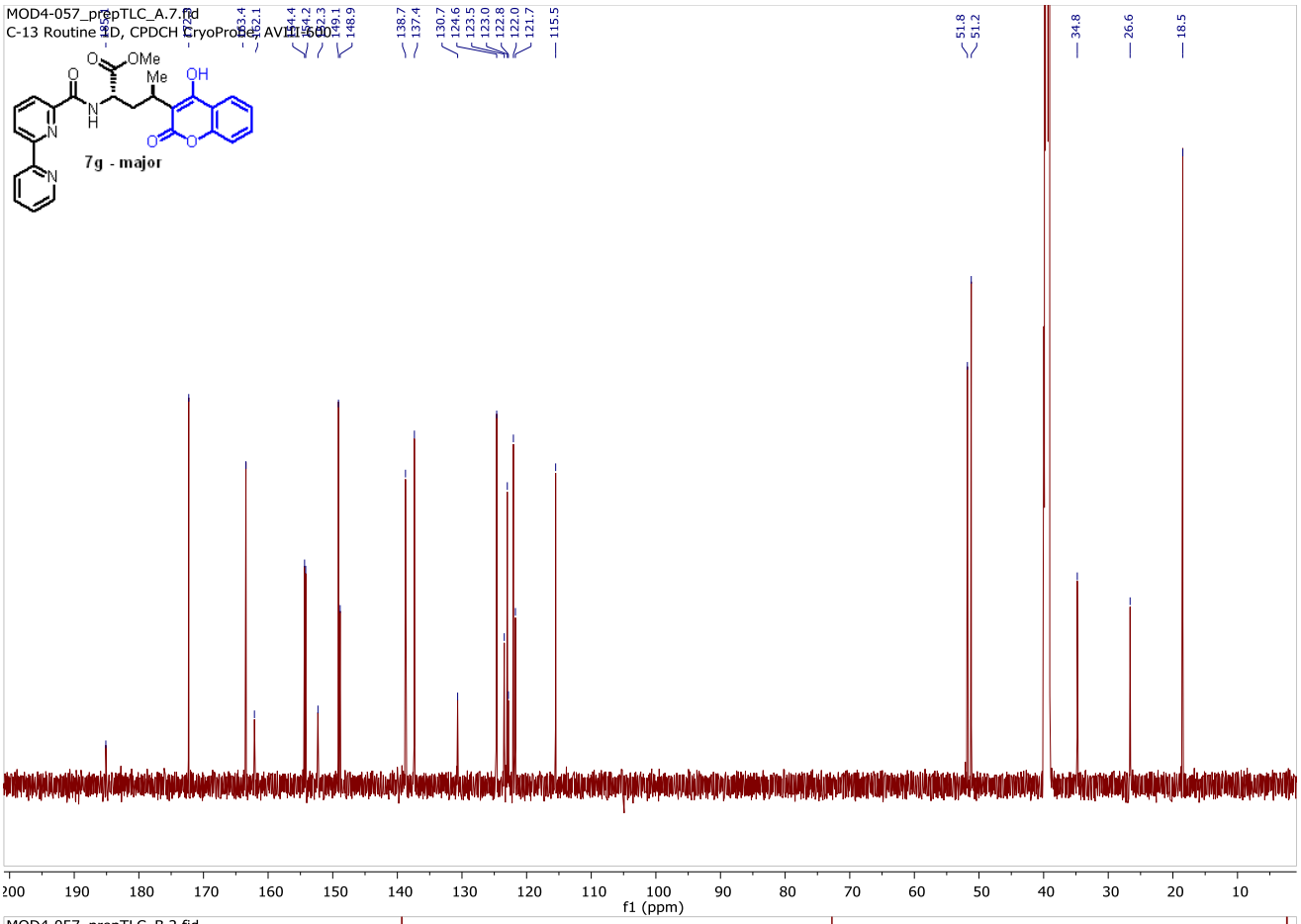

MOD3-150_prepTLC_2.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
7e
153.6
154.3
154.2
149.7
149.2
138.8
137.3
124.6
122.7
122.0
121.5
37.1
36.8
33.1
17.0
f1 (ppm)

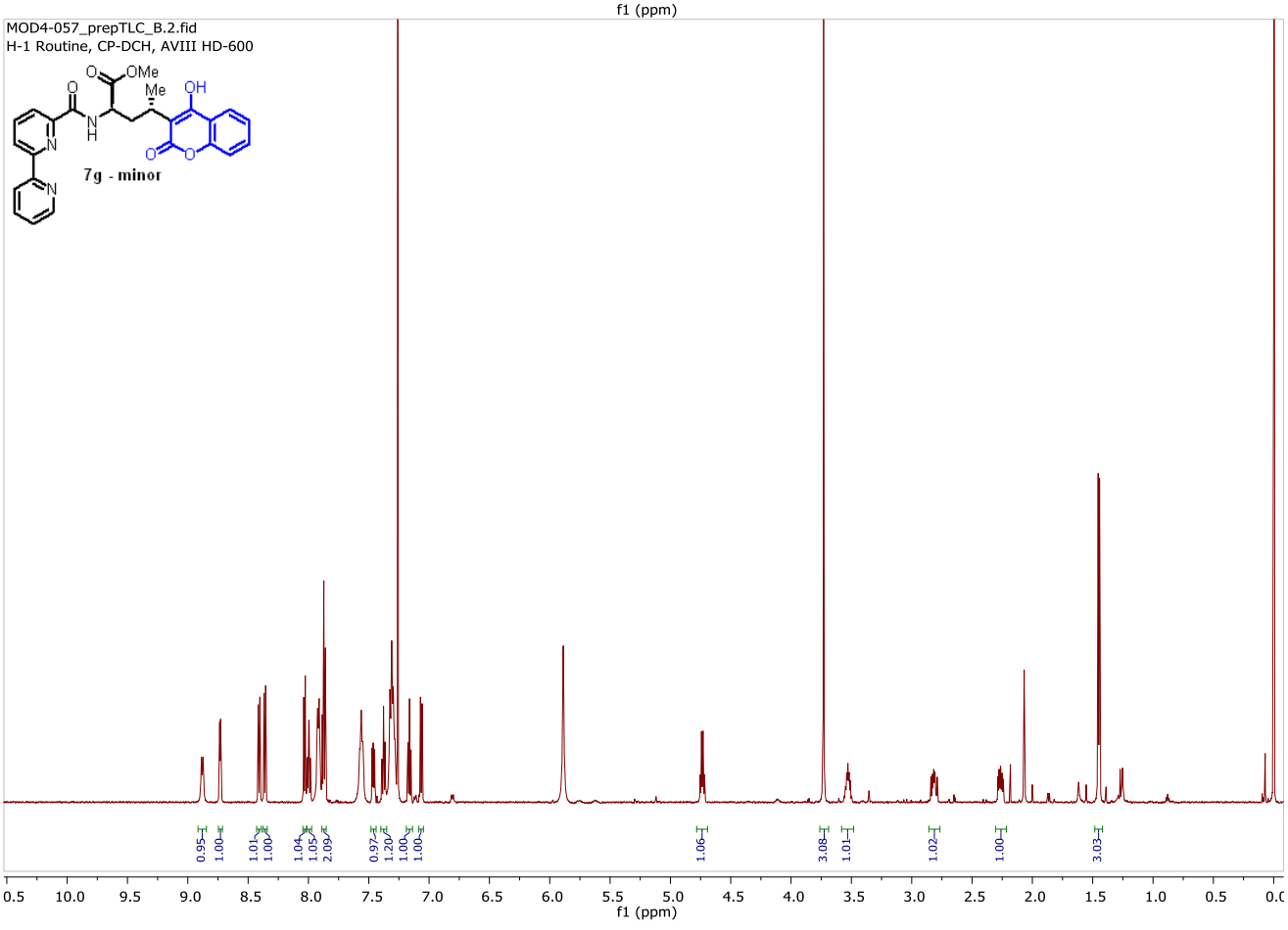

MOD3-039c_prepTLC.3.fid
H-1 Routine, DRX-500, BBO Probe
7f
1.00
1.01
1.01
0.98
0.92
1.03
1.00
1.00
1.05
1.18
1.00
1.01
0.99
3.02
2.07
1.03
2.06
3.04
f1 (ppm)

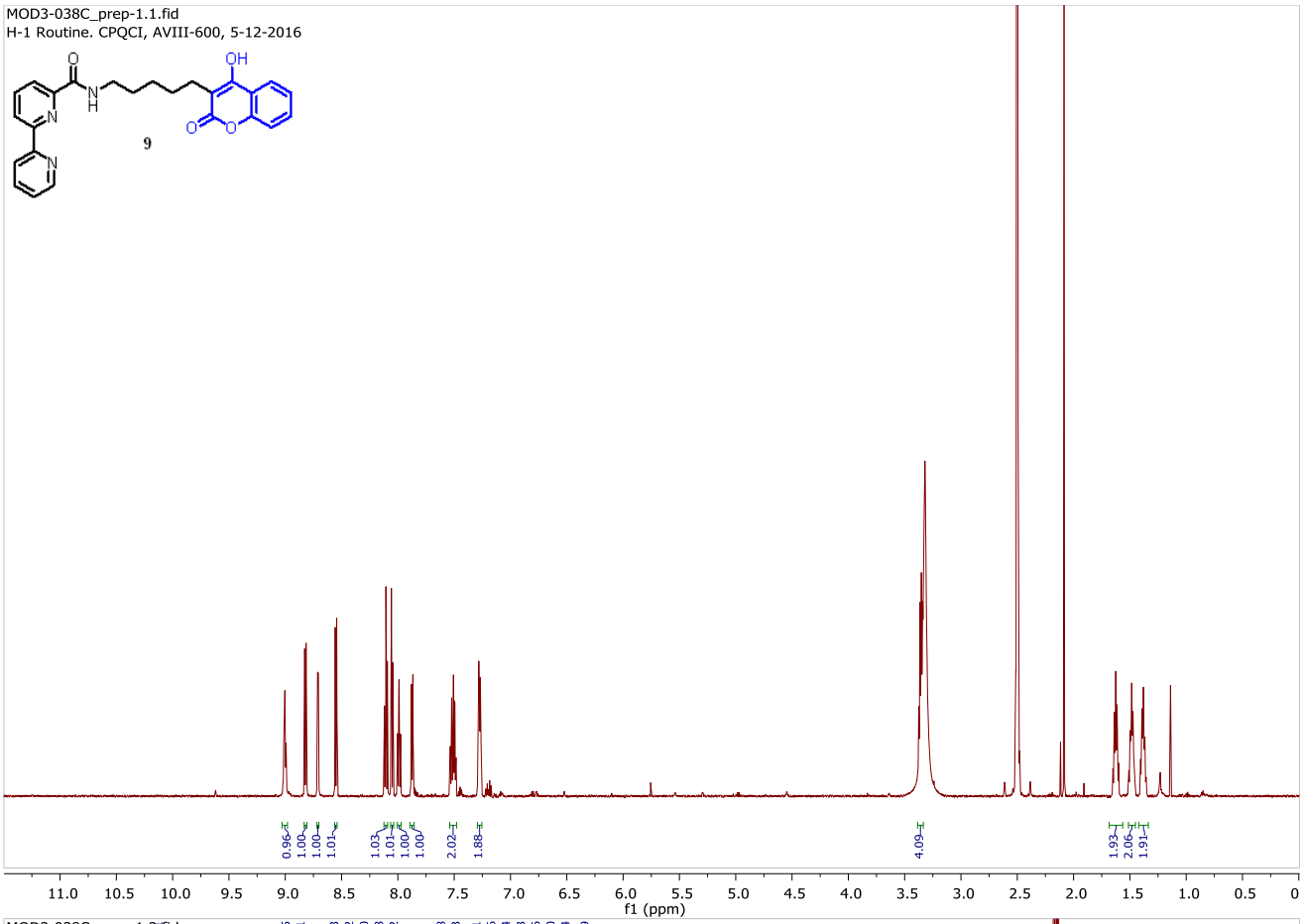

MOD3-039c_prepTLC.5.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
7f
164.3
155.3
154.8
149.6
149.4
138.4
137.3
137.0
127.1
125.3
124.2
123.6
122.3
121.6
121.1
119.8
119.3
118.7
109.4
38.3
37.4
32.7
29.0
22.0
f1 (ppm)

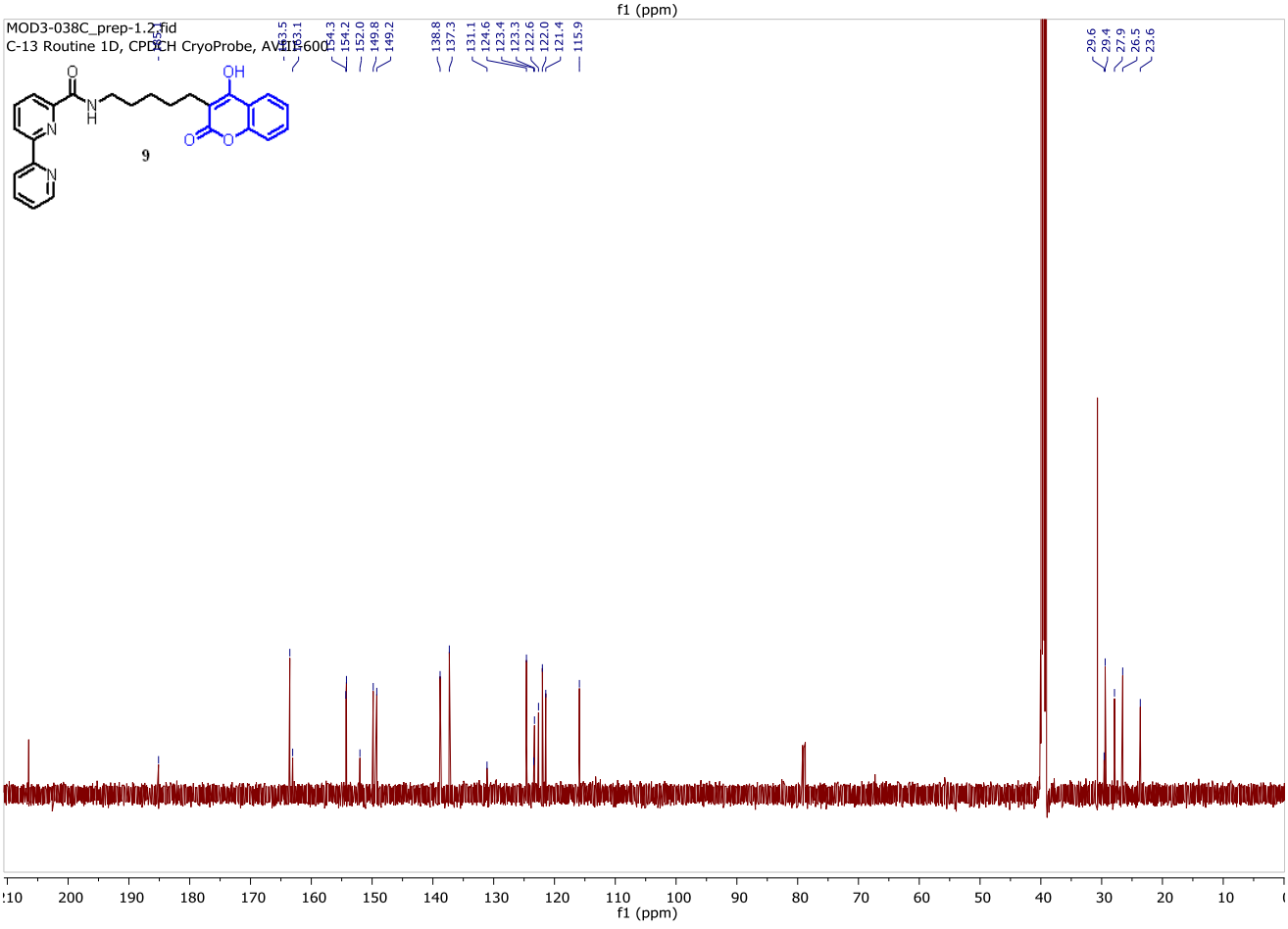

MOD4-057_prepTLC_A.2.fid
H-1 Routine, CP-DCH, AVIII HD-600
7g - major
f1 (ppm)

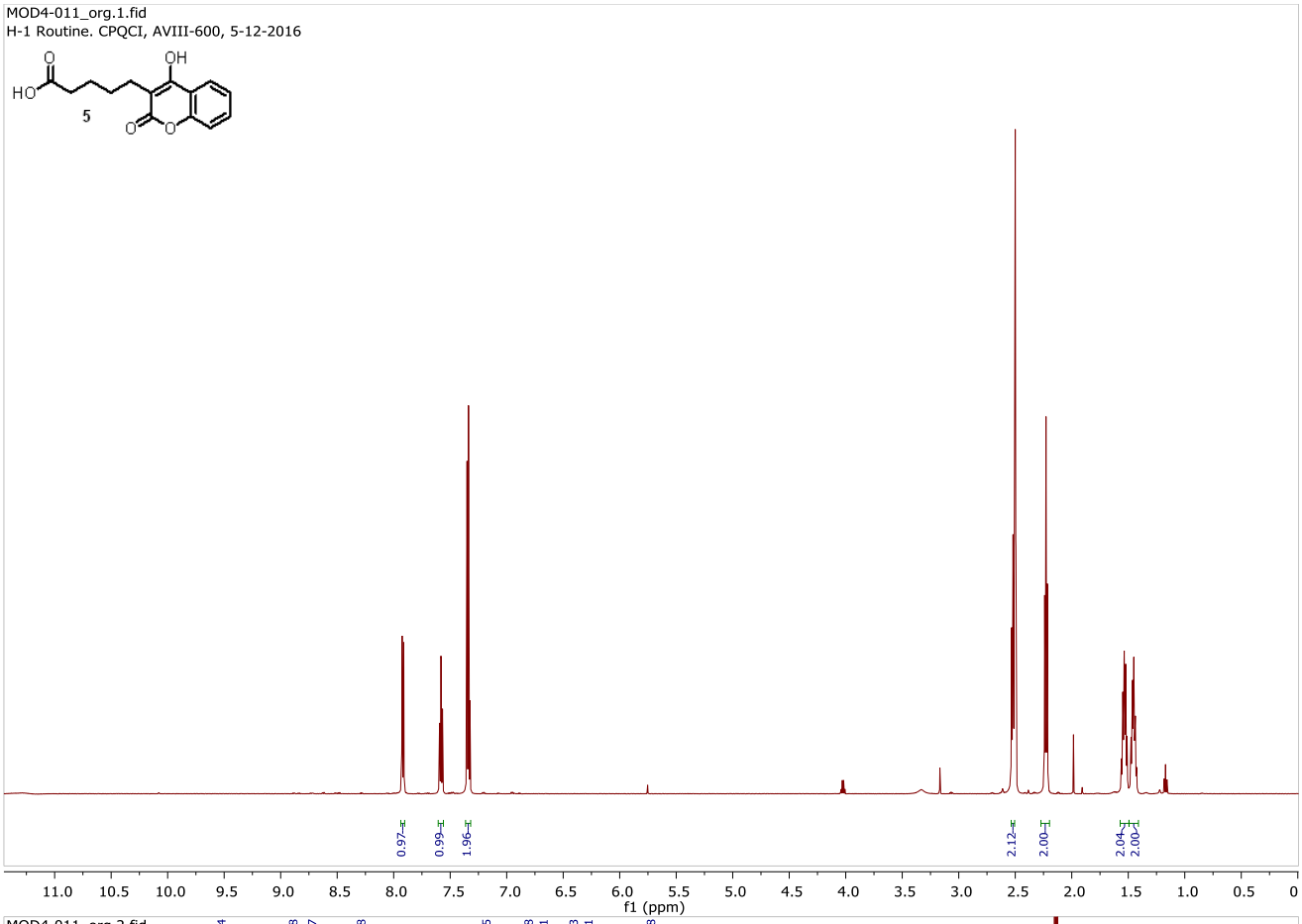

MOD4-057_prepTLC_A.6.fid
H-1 Routine, CP-DCH, AVIII HD-600
7g - major
f1 (ppm)

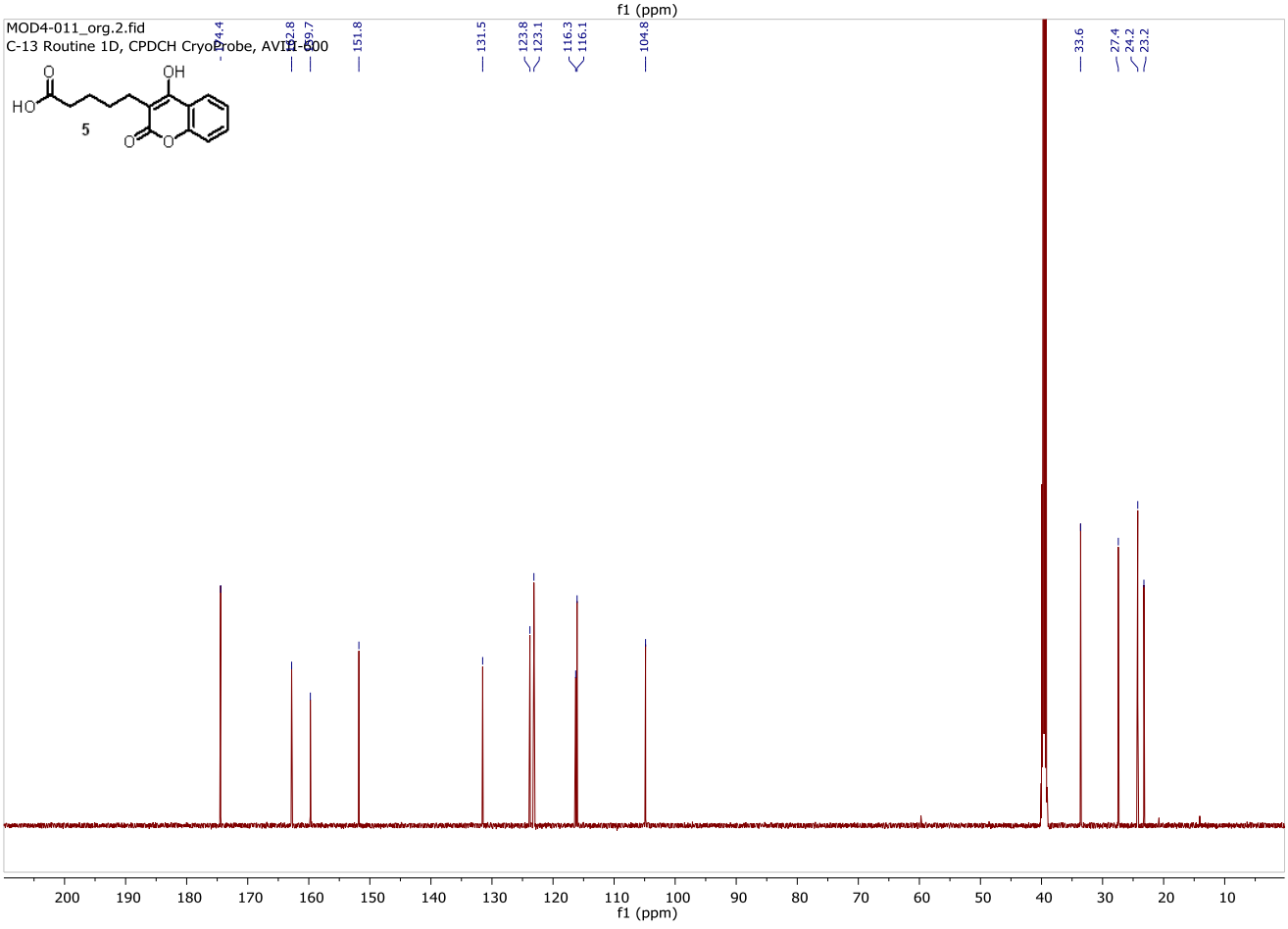

MOD4-057_prepTLC_A.7.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII HD-600
7g - major
163.4
152.1
144.4
144.2
142.3
149.1
148.9
138.7
137.4
130.7
124.6
123.5
123.0
122.8
122.0
121.7
115.5
51.8
51.2
34.8
26.6
18.5
f1 (ppm)

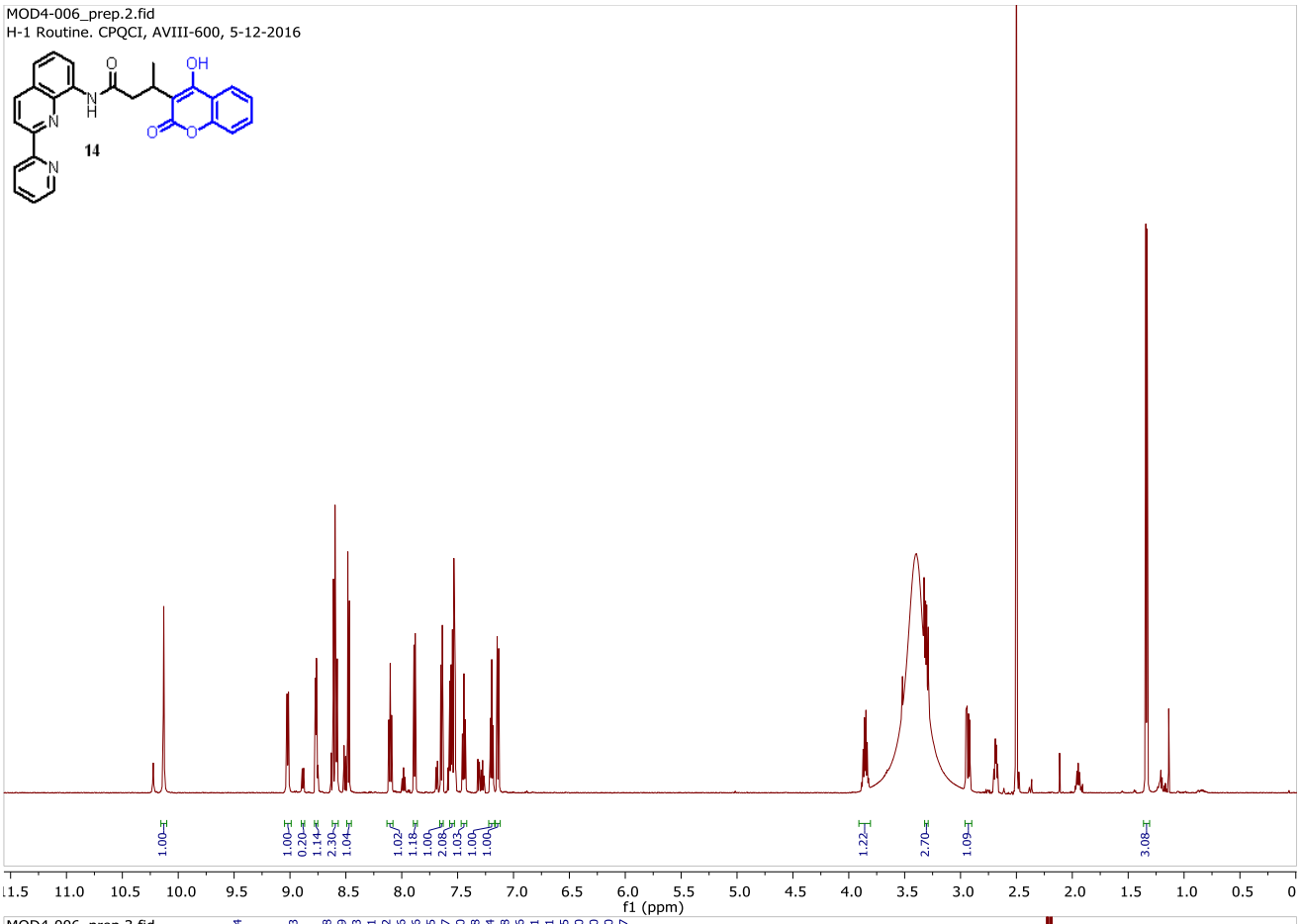

MOD4-057_prepTLC_B.2.fid
H-1 Routine, CP-DCH, AVIII HD-600
7g - minor
0.95
1.00
1.01
1.00
1.04
1.05
2.09
0.97
1.20
1.00
1.00
1.06
3.08
1.01
1.02
1.00
3.03
f1 (ppm)

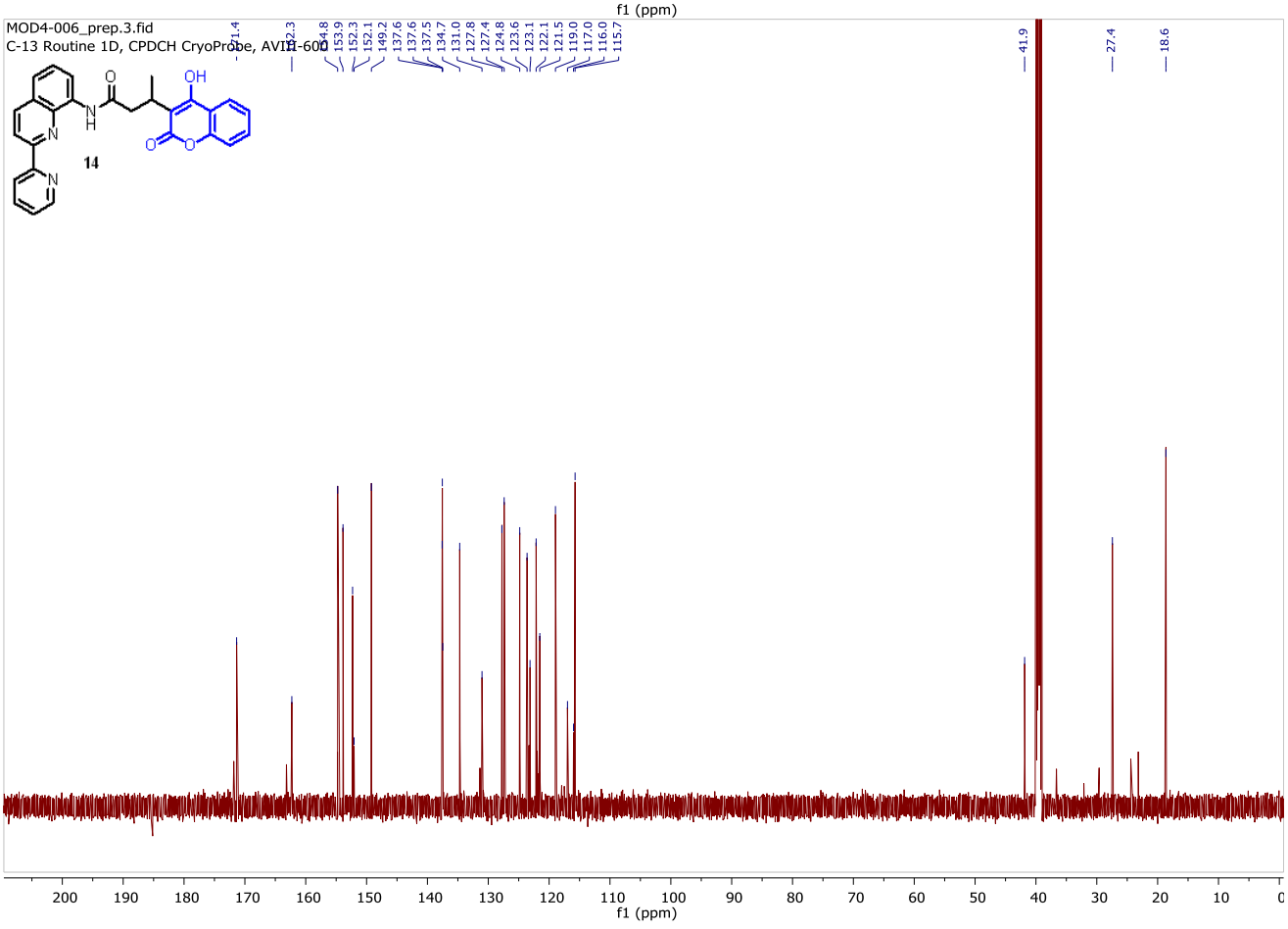

MOD3-038C_prep-1.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
9
0.96
1.00
1.00
1.01
1.03
1.01
1.00
1.00
2.02
1.88
4.09
1.93
2.06
1.91
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

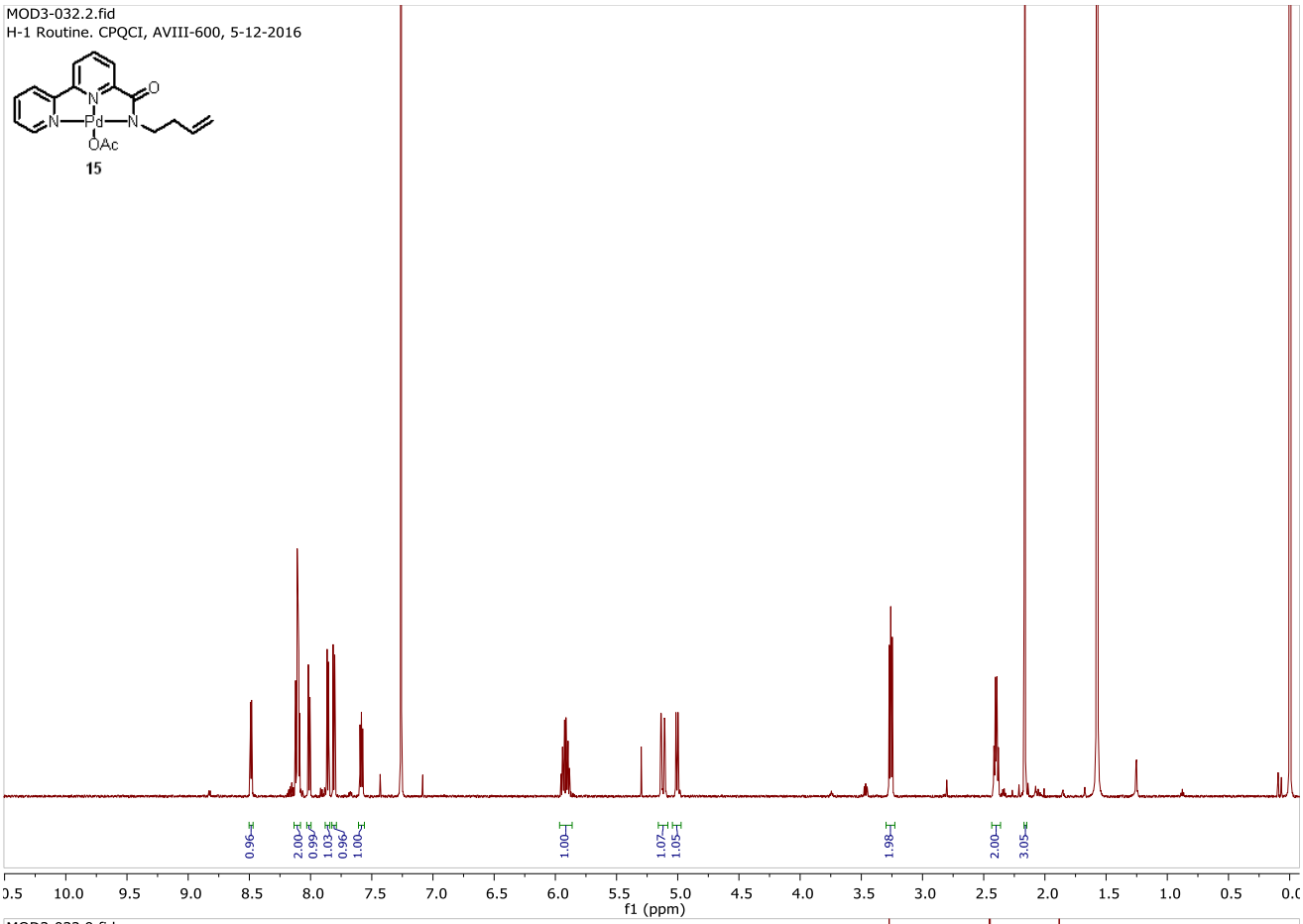

MOD3-038C_prep-1.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
9
163.5
163.1
154.3
154.2
152.0
149.8
149.2
138.8
137.3
131.1
124.6
123.4
123.3
122.6
122.0
121.4
115.9
29.6
29.4
27.9
26.5
23.6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

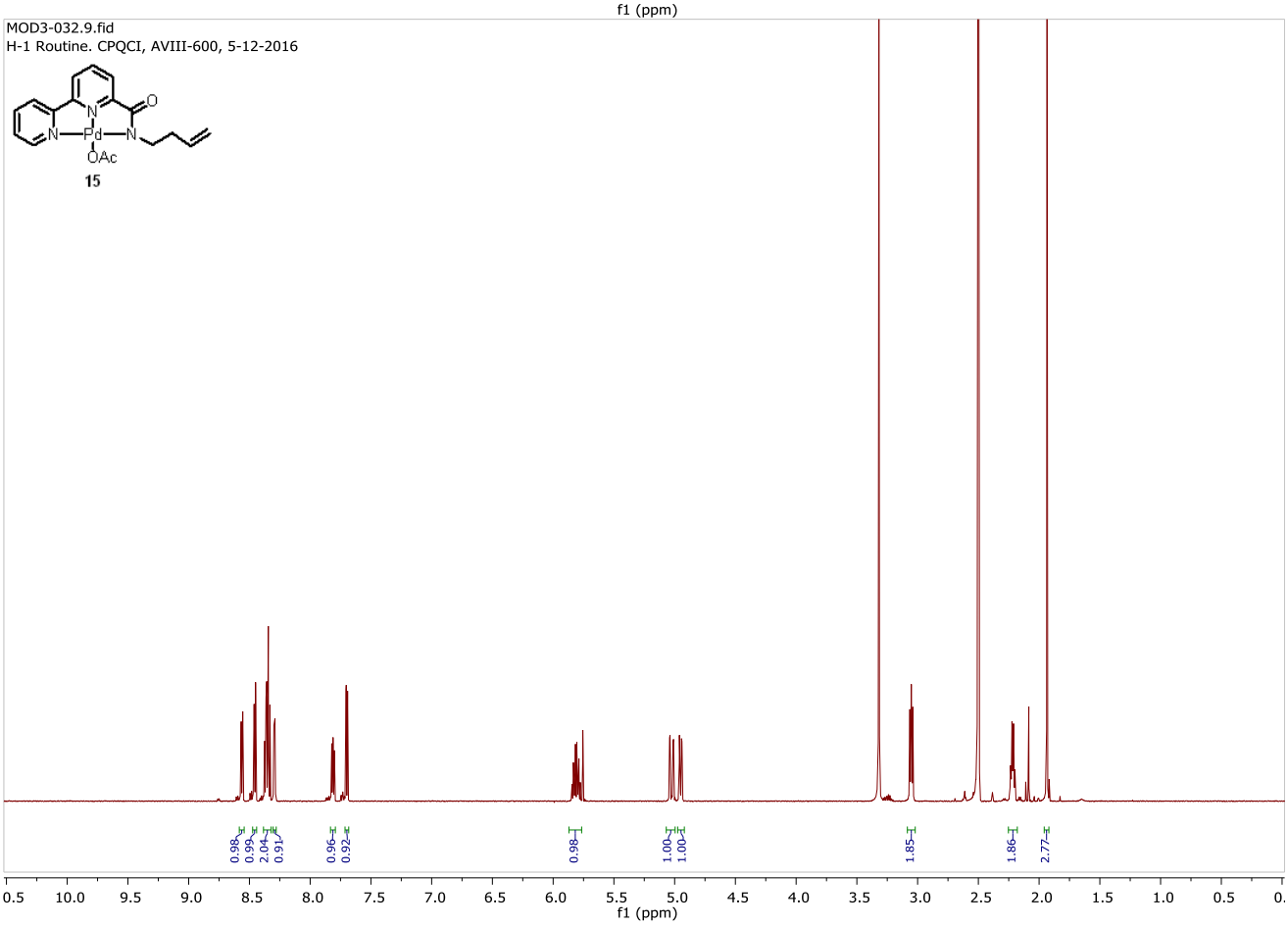

MOD4-011_org.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
HO
O
OH
O
O
5
0.97
0.99
1.96
2.12
2.00
2.04
2.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

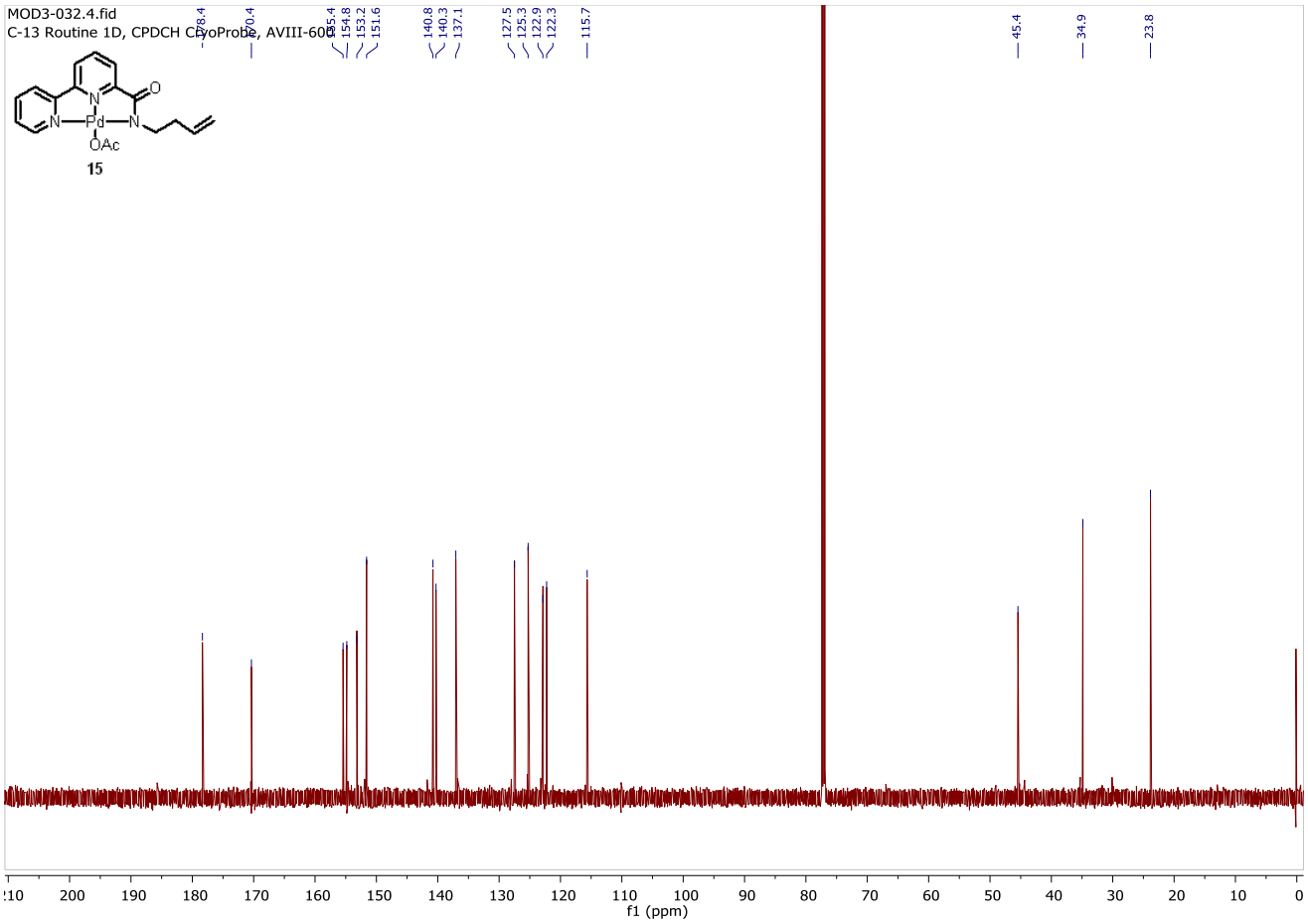

MOD4-011_org.2.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
HO
O
OH
O
O
5
164.4
152.8
149.7
151.8
131.5
123.8
123.1
116.3
116.1
104.8
33.6
27.4
24.2
23.2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

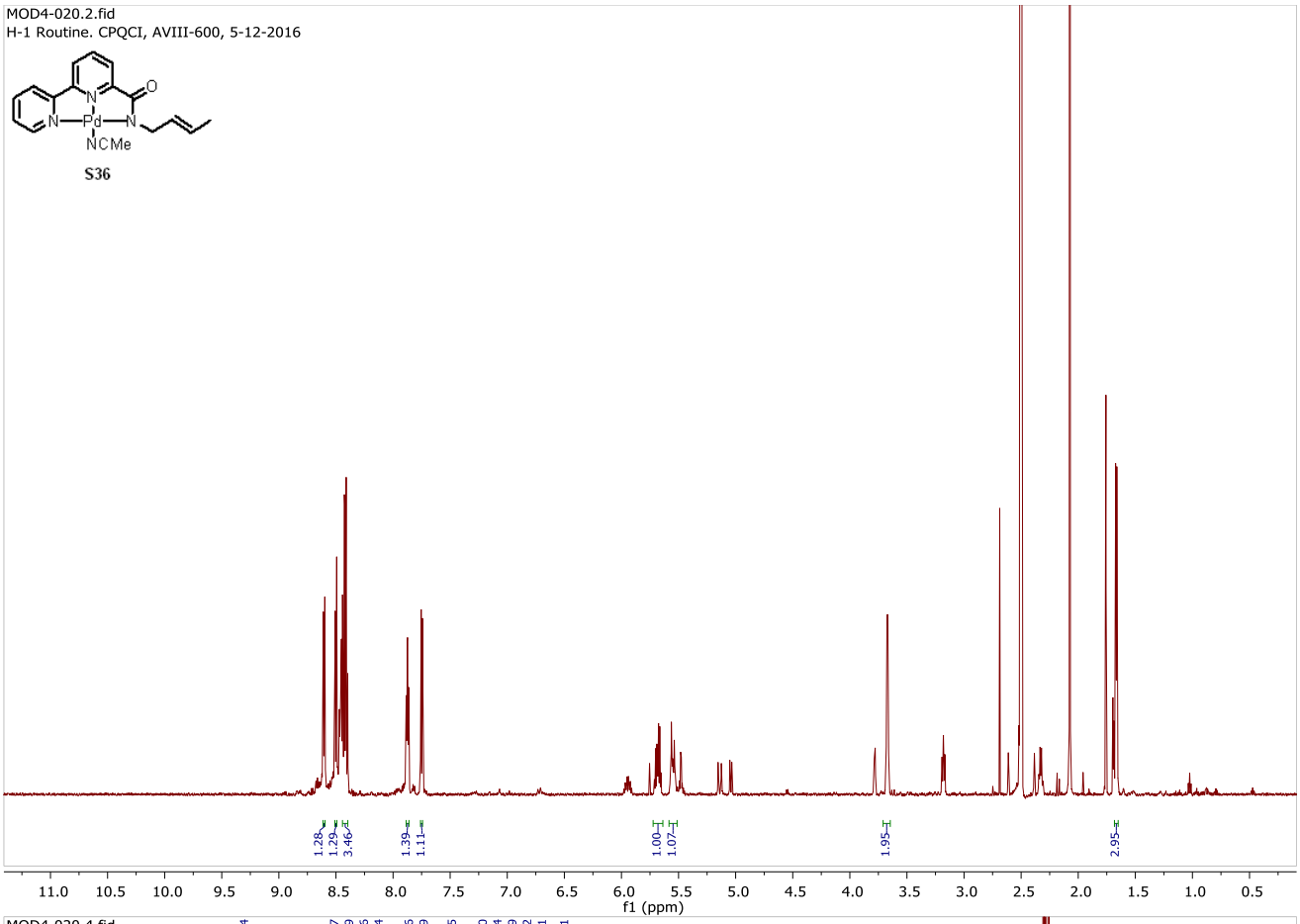

MOD4-006_prep.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
14
f1 (ppm)

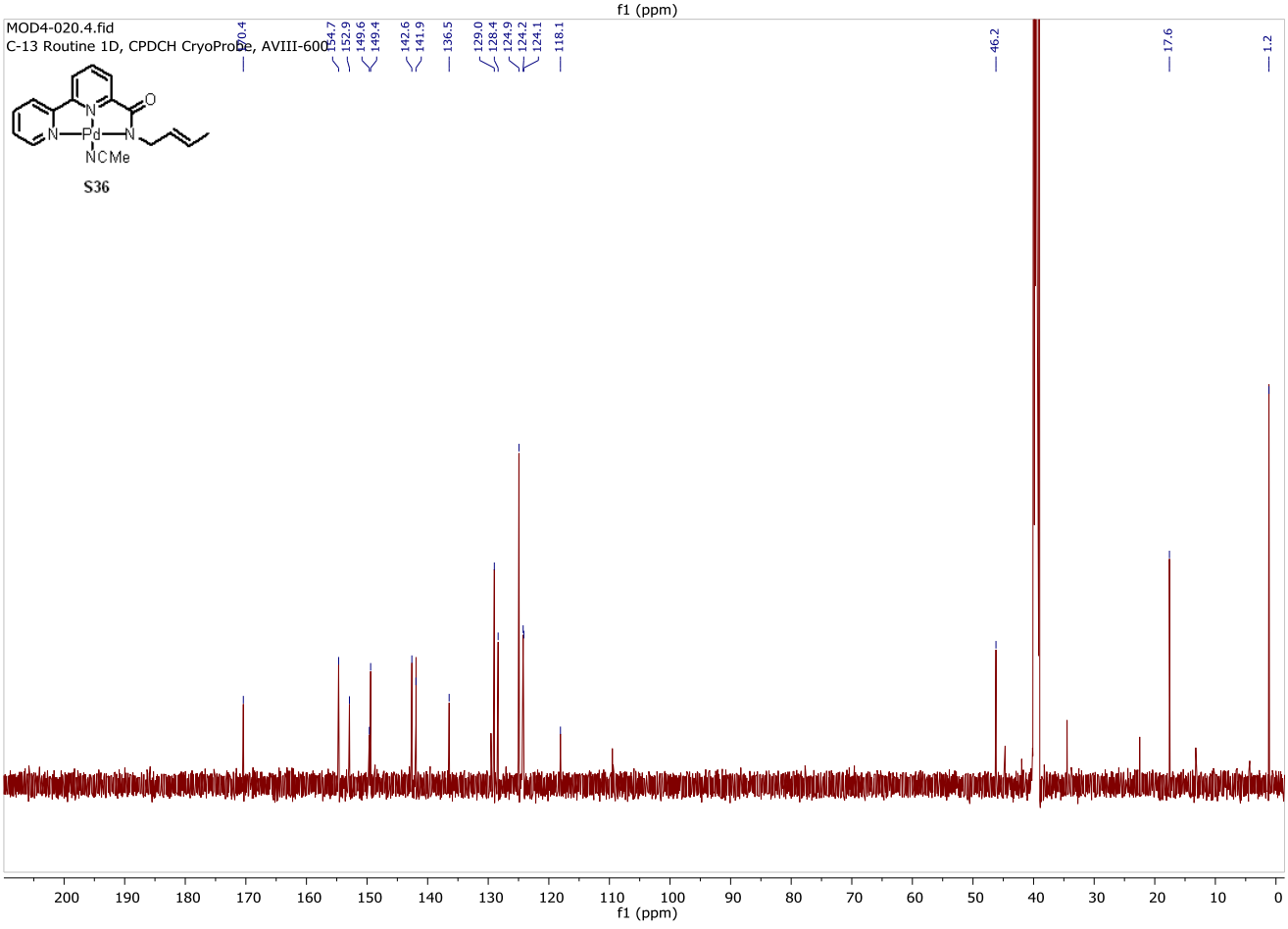

MOD4-006_prep.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
14
f1 (ppm)

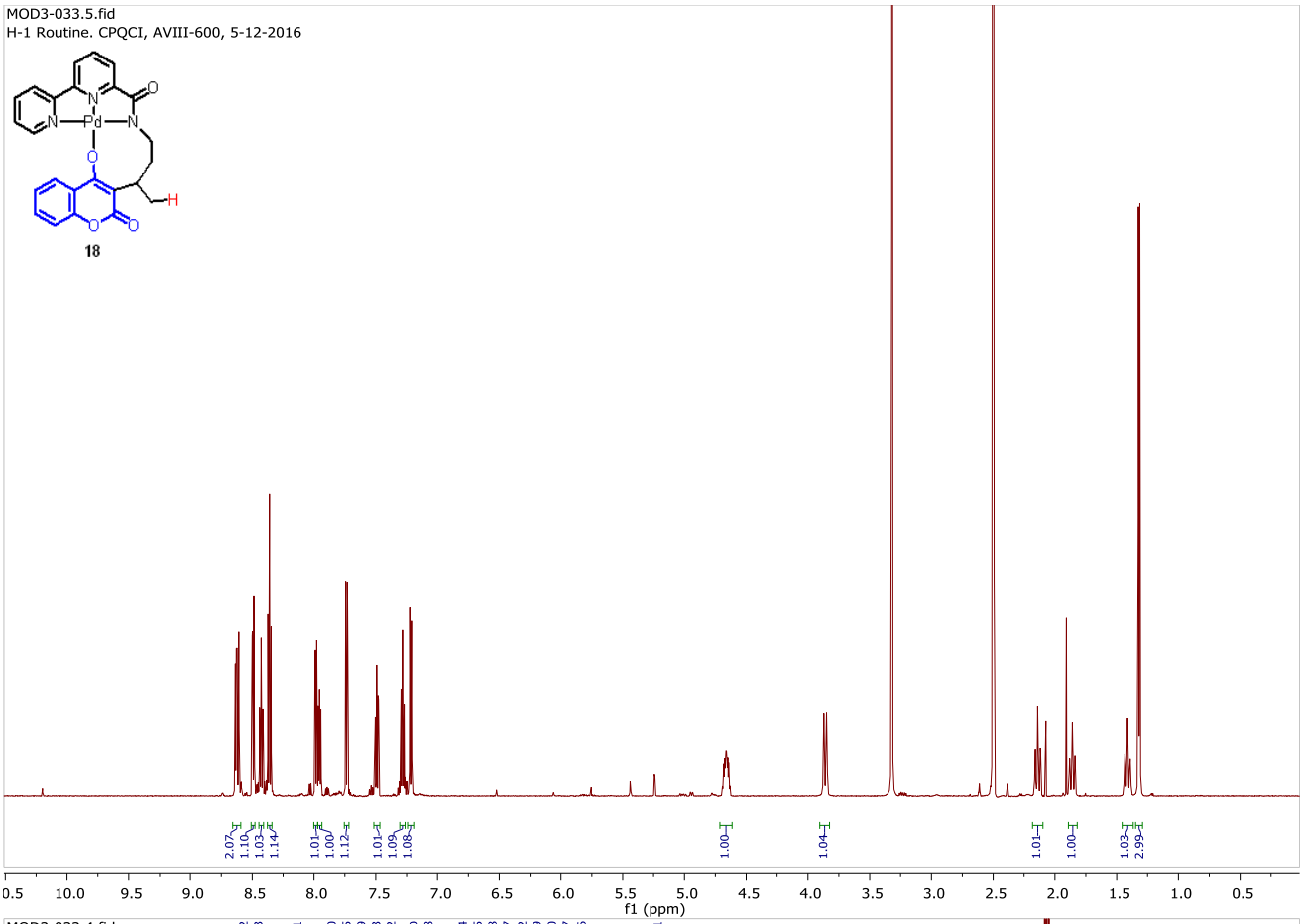

MOD3-032.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
15
f1 (ppm)

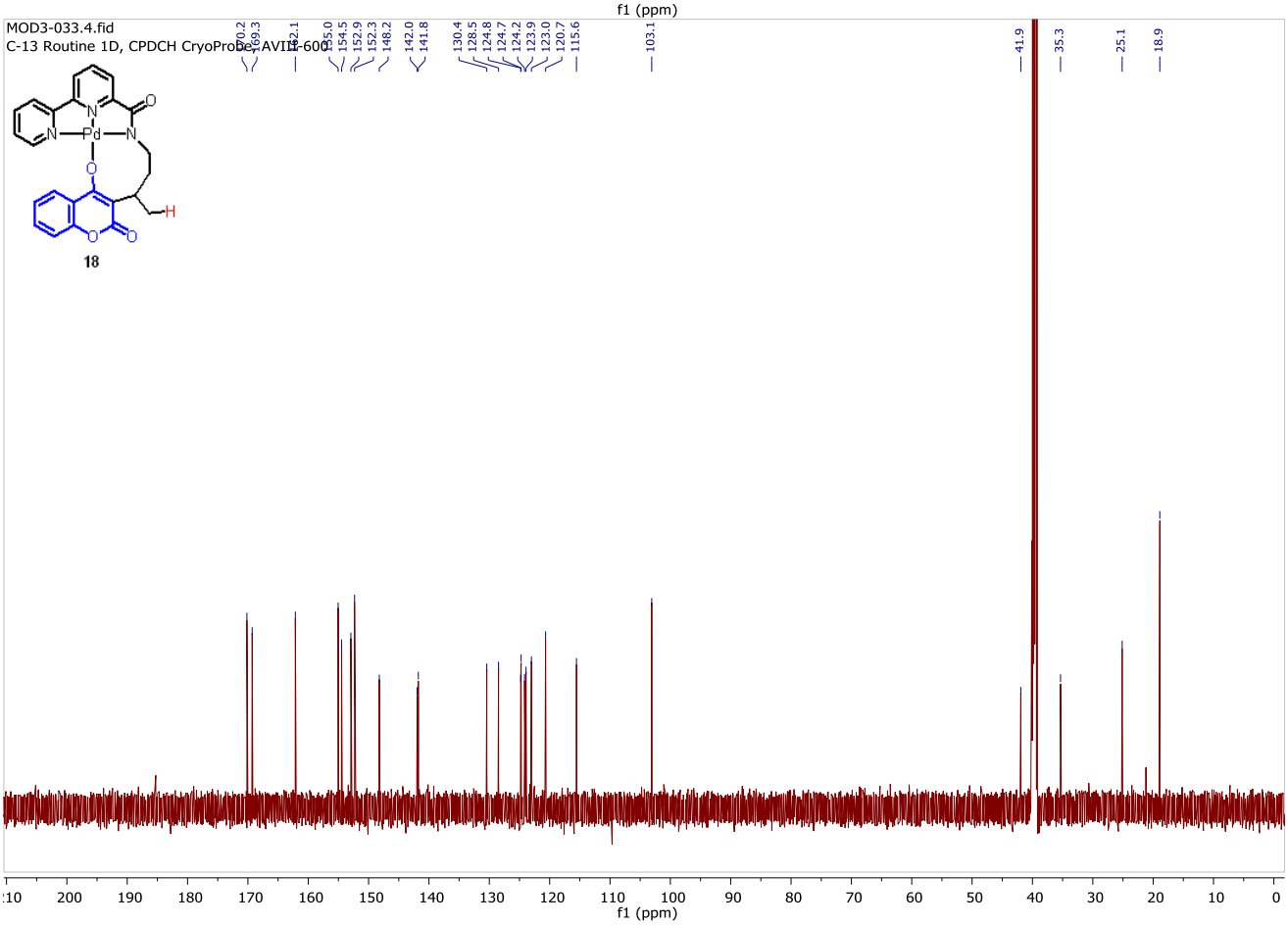

MOD3-032.9.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
15
f1 (ppm)


MOD3-032.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
178.4
170.4
155.4
154.8
153.2
151.6
140.8
140.3
137.1
127.5
125.3
122.9
122.3
115.7
45.4
34.9
23.8
N
Pd
N
O
OAc
15
f1 (ppm)


MOD4-020.2.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
S36
f1 (ppm)


MOD4-020.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
S36
f1 (ppm)


MOD3-033.5.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
18
f1 (ppm)


MOD3-033.4.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
18
f1 (ppm)

Crystal Data

Crystal Data for 4a

The single crystal X-ray diffraction studies were carried out on a Bruker Kappa APEX-II CCD diffractometer equipped with Mo K_α radiation (λ = 0.71073 Å). A 0.276 x 0.233 x 0.154 mm piece of a colorless block was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 40 mm and exposure time was 2 seconds per frame using a scan width of 2.0°. Data collection was 99.9% complete to 25.00° in θ. A total of 19220 reflections were collected covering the indices -10<=h<=10, -13<=k<=9, -21<=l<=16. 5313 reflections were found to be symmetry independent, with a Rint of 0.0599. Indexing and unit cell refinement indicated a primitive, triclinic lattice. The space group was found to be P-1. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure. All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. All other hydrogen atoms (H-bonding) were located in the difference map. Their relative positions were restrained using DFIX commands and their thermals freely refined. Crystallographic data are summarized in Table S1.

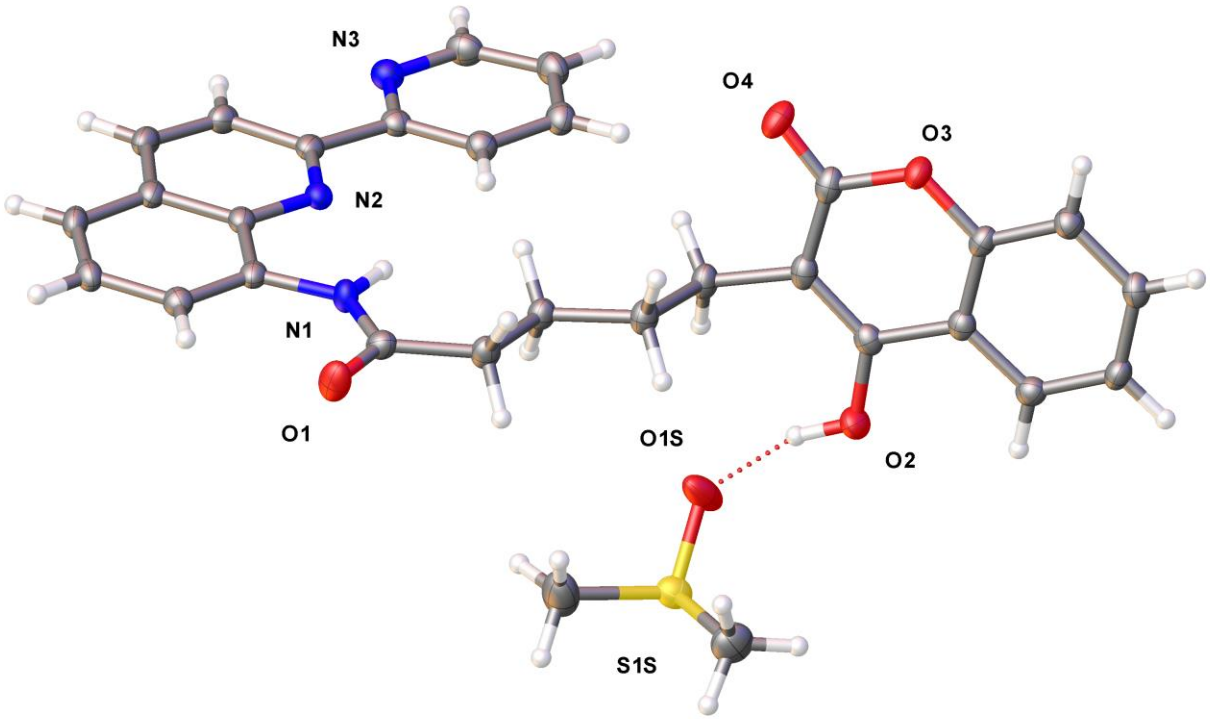


Table S1. Crystal data and structure refinement for 4a.

Report date	2017-03-15
Identification code	MOD3-35b
Empirical formula	C30 H29 N3 O5 S
Molecular formula	C28 H23 N3 O4, C2 H6 O S
Formula weight	543.62
Temperature	100.0 K

Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.1556(11) Å	a= 76.394(3)°.
	b = 10.4321(13) Å	b= 79.665(4)°.
	c = 16.817(2) Å	g = 71.200(3)°.
Volume	1308.1(3) $Å^3$	
Z	2	
Density (calculated)	1.380 Mg/m^3	
Absorption coefficient	0.171 mm^{-1}	
F(000)	572	
Crystal size	0.276 x 0.233 x 0.154 mm^3	
Crystal color, habit	Colorless Block	
Theta range for data collection	2.101 to 26.388°.	
Index ranges	-10<=h<=10, -13<=k<=9, -21<=l<=16	
Reflections collected	19220	
Independent reflections	5313 [R(int) = 0.0599, R(sigma) = 0.0635]	
Completeness to theta = 25.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.0909 and 0.0644	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5313 / 2 / 366	
Goodness-of-fit on F^2	1.039	
Final R indices [I>2sigma(I)]	R1 = 0.0450, wR2 = 0.1061	
R indices (all data)	R1 = 0.0578, wR2 = 0.1152	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.245 and -0.327 $e.Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 4a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	8701(2)	8205(1)	1573(1)	32(1)
O(2)	3355(2)	3222(1)	4688(1)	28(1)
O(3)	7997(2)	106(1)	4900(1)	23(1)
O(4)	9014(2)	767(1)	3618(1)	29(1)
N(1)	8161(2)	6797(2)	870(1)	21(1)
N(2)	7756(2)	5530(1)	-223(1)	19(1)
N(3)	6545(2)	2979(2)	-896(1)	24(1)
C(1)	8243(2)	7198(2)	1567(1)	22(1)
C(2)	7738(2)	6303(2)	2365(1)	24(1)
C(3)	7025(2)	5134(2)	2342(1)	21(1)
C(4)	6840(2)	4256(2)	3200(1)	24(1)
C(5)	6086(2)	3078(2)	3224(1)	23(1)
C(6)	6180(2)	2109(2)	4048(1)	22(1)
C(7)	4899(2)	2248(2)	4692(1)	21(1)
C(8)	5137(2)	1290(2)	5476(1)	20(1)
C(9)	6710(2)	254(2)	5550(1)	20(1)
C(10)	7784(2)	1002(2)	4149(1)	23(1)
C(11)	3874(2)	1370(2)	6157(1)	22(1)
C(12)	4199(2)	443(2)	6890(1)	22(1)
C(13)	5795(2)	-564(2)	6950(1)	23(1)
C(14)	7061(2)	-674(2)	6280(1)	23(1)
C(15)	8573(2)	7374(2)	45(1)	20(1)
C(16)	9133(2)	8523(2)	-231(1)	22(1)
C(17)	9494(2)	8985(2)	-1085(1)	24(1)
C(18)	9298(2)	8316(2)	-1653(1)	24(1)
C(19)	8702(2)	7130(2)	-1387(1)	21(1)
C(20)	8335(2)	6656(2)	-531(1)	19(1)
C(21)	8406(2)	6379(2)	-1918(1)	23(1)
C(22)	7788(2)	5273(2)	-1607(1)	22(1)
C(23)	7480(2)	4864(2)	-740(1)	20(1)
C(24)	6858(2)	3644(2)	-371(1)	20(1)
C(25)	6654(2)	3202(2)	479(1)	23(1)
C(26)	6145(2)	2025(2)	798(1)	25(1)

C(27)	5832(2)	1330(2)	267(1)	28(1)
C(28)	6042(2)	1851(2)	-570(1)	28(1)
S(1S)	1010(1)	6687(1)	3598(1)	26(1)
S(1SB)	2546(12)	6687(9)	3646(5)	26(1)
O(1S)	2195(2)	5282(1)	3499(1)	42(1)
C(1S)	2004(4)	7883(2)	2941(1)	47(1)
C(2S)	1292(3)	6959(2)	4562(1)	39(1)

Table S3. Bond lengths [Å] and angles [°] for 4a.

O(1)-C(1)	1.226(2)	C(5)-C(6)	1.510(2)
O(2)-H(2)	0.928(17)	C(6)-C(7)	1.362(2)
O(2)-C(7)	1.339(2)	C(6)-C(10)	1.445(3)
O(3)-C(9)	1.373(2)	C(7)-C(8)	1.456(2)
O(3)-C(10)	1.385(2)	C(8)-C(9)	1.389(2)
O(4)-C(10)	1.219(2)	C(8)-C(11)	1.396(2)
N(1)-H(1)	0.916(15)	C(9)-C(14)	1.384(2)
N(1)-C(1)	1.352(2)	C(11)-H(11)	0.9500
N(1)-C(15)	1.404(2)	C(11)-C(12)	1.385(2)
N(2)-C(20)	1.361(2)	C(12)-H(12)	0.9500
N(2)-C(23)	1.320(2)	C(12)-C(13)	1.388(3)
N(3)-C(24)	1.345(2)	C(13)-H(13)	0.9500
N(3)-C(28)	1.334(2)	C(13)-C(14)	1.384(2)
C(1)-C(2)	1.517(2)	C(14)-H(14)	0.9500
C(2)-H(2A)	0.9900	C(15)-C(16)	1.370(2)
C(2)-H(2B)	0.9900	C(15)-C(20)	1.428(2)
C(2)-C(3)	1.521(2)	C(16)-H(16)	0.9500
C(3)-H(3A)	0.9900	C(16)-C(17)	1.412(2)
C(3)-H(3B)	0.9900	C(17)-H(17)	0.9500
C(3)-C(4)	1.527(2)	C(17)-C(18)	1.366(3)
C(4)-H(4A)	0.9900	C(18)-H(18)	0.9500
C(4)-H(4B)	0.9900	C(18)-C(19)	1.419(2)
C(4)-C(5)	1.532(2)	C(19)-C(20)	1.418(2)
C(5)-H(5A)	0.9900	C(19)-C(21)	1.415(2)
C(5)-H(5B)	0.9900	C(21)-H(21)	0.9500

C(21)-C(22)	1.362(2)	O(1)-C(1)-N(1)	123.67(16)
C(22)-H(22)	0.9500	O(1)-C(1)-C(2)	120.85(15)
C(22)-C(23)	1.420(2)	N(1)-C(1)-C(2)	115.48(15)
C(23)-C(24)	1.482(2)	C(1)-C(2)-H(2A)	107.3
C(24)-C(25)	1.392(2)	C(1)-C(2)-H(2B)	107.3
C(25)-H(25)	0.9500	C(1)-C(2)-C(3)	119.91(14)
C(25)-C(26)	1.381(2)	H(2A)-C(2)-H(2B)	106.9
C(26)-H(26)	0.9500	C(3)-C(2)-H(2A)	107.3
C(26)-C(27)	1.376(3)	C(3)-C(2)-H(2B)	107.3
C(27)-H(27)	0.9500	C(2)-C(3)-H(3A)	109.5
C(27)-C(28)	1.386(3)	C(2)-C(3)-H(3B)	109.5
C(28)-H(28)	0.9500	C(2)-C(3)-C(4)	110.84(14)
S(1S)-O(1S)	1.5011(14)	H(3A)-C(3)-H(3B)	108.1
S(1S)-C(1S)	1.766(2)	C(4)-C(3)-H(3A)	109.5
S(1S)-C(2S)	1.775(2)	C(4)-C(3)-H(3B)	109.5
S(1SB)-O(1S)	1.660(9)	C(3)-C(4)-H(4A)	108.9
S(1SB)-C(1S)	1.515(9)	C(3)-C(4)-H(4B)	108.9
S(1SB)-C(2S)	1.719(9)	C(3)-C(4)-C(5)	113.42(14)
C(1S)-H(1SA)	0.9800	H(4A)-C(4)-H(4B)	107.7
C(1S)-H(1SB)	0.9800	C(5)-C(4)-H(4A)	108.9
C(1S)-H(1SC)	0.9800	C(5)-C(4)-H(4B)	108.9
C(1S)-H(1SD)	0.9800	C(4)-C(5)-H(5A)	109.3
C(1S)-H(1SE)	0.9800	C(4)-C(5)-H(5B)	109.3
C(1S)-H(1SF)	0.9800	H(5A)-C(5)-H(5B)	107.9
C(2S)-H(2SA)	0.9800	C(6)-C(5)-C(4)	111.74(14)
C(2S)-H(2SB)	0.9800	C(6)-C(5)-H(5A)	109.3
C(2S)-H(2SC)	0.9800	C(6)-C(5)-H(5B)	109.3
C(2S)-H(2SD)	0.9800	C(7)-C(6)-C(5)	124.46(16)
C(2S)-H(2SE)	0.9800	C(7)-C(6)-C(10)	119.46(15)
C(2S)-H(2SF)	0.9800	C(10)-C(6)-C(5)	116.03(15)
C(7)-O(2)-H(2)	116.2(17)	O(2)-C(7)-C(6)	125.91(15)
C(9)-O(3)-C(10)	121.04(14)	O(2)-C(7)-C(8)	113.63(15)
C(1)-N(1)-H(1)	121.1(13)	C(6)-C(7)-C(8)	120.46(16)
C(1)-N(1)-C(15)	129.59(15)	C(9)-C(8)-C(7)	118.22(16)
C(15)-N(1)-H(1)	109.3(13)	C(9)-C(8)-C(11)	118.44(15)
C(23)-N(2)-C(20)	119.02(15)	C(11)-C(8)-C(7)	123.33(16)
C(28)-N(3)-C(24)	117.17(16)	O(3)-C(9)-C(8)	121.39(15)

O(3)-C(9)-C(14)	116.76(15)	C(22)-C(21)-H(21)	119.7
C(14)-C(9)-C(8)	121.85(16)	C(21)-C(22)-H(22)	120.5
O(3)-C(10)-C(6)	119.42(15)	C(21)-C(22)-C(23)	119.08(16)
O(4)-C(10)-O(3)	115.11(16)	C(23)-C(22)-H(22)	120.5
O(4)-C(10)-C(6)	125.47(16)	N(2)-C(23)-C(22)	122.15(15)
C(8)-C(11)-H(11)	119.8	N(2)-C(23)-C(24)	116.67(15)
C(12)-C(11)-C(8)	120.44(17)	C(22)-C(23)-C(24)	121.17(16)
C(12)-C(11)-H(11)	119.8	N(3)-C(24)-C(23)	116.75(15)
C(11)-C(12)-H(12)	120.1	N(3)-C(24)-C(25)	122.38(16)
C(11)-C(12)-C(13)	119.79(17)	C(25)-C(24)-C(23)	120.86(16)
C(13)-C(12)-H(12)	120.1	C(24)-C(25)-H(25)	120.5
C(12)-C(13)-H(13)	119.6	C(26)-C(25)-C(24)	119.10(17)
C(14)-C(13)-C(12)	120.82(16)	C(26)-C(25)-H(25)	120.5
C(14)-C(13)-H(13)	119.6	C(25)-C(26)-H(26)	120.5
C(9)-C(14)-H(14)	120.7	C(27)-C(26)-C(25)	119.10(17)
C(13)-C(14)-C(9)	118.65(16)	C(27)-C(26)-H(26)	120.5
C(13)-C(14)-H(14)	120.7	C(26)-C(27)-H(27)	121.0
N(1)-C(15)-C(20)	113.73(14)	C(26)-C(27)-C(28)	118.09(17)
C(16)-C(15)-N(1)	126.32(16)	C(28)-C(27)-H(27)	121.0
C(16)-C(15)-C(20)	119.94(16)	N(3)-C(28)-C(27)	124.16(17)
C(15)-C(16)-H(16)	120.0	N(3)-C(28)-H(28)	117.9
C(15)-C(16)-C(17)	119.91(16)	C(27)-C(28)-H(28)	117.9
C(17)-C(16)-H(16)	120.0	O(1S)-S(1S)-C(1S)	106.20(11)
C(16)-C(17)-H(17)	119.1	O(1S)-S(1S)-C(2S)	107.06(9)
C(18)-C(17)-C(16)	121.72(16)	C(1S)-S(1S)-C(2S)	99.06(11)
C(18)-C(17)-H(17)	119.1	O(1S)-S(1SB)-C(2S)	102.7(5)
C(17)-C(18)-H(18)	120.1	C(1S)-S(1SB)-O(1S)	111.0(5)
C(17)-C(18)-C(19)	119.73(16)	C(1S)-S(1SB)-C(2S)	112.7(5)
C(19)-C(18)-H(18)	120.1	S(1S)-C(1S)-H(1SA)	109.5
C(20)-C(19)-C(18)	119.09(16)	S(1S)-C(1S)-H(1SB)	109.5
C(21)-C(19)-C(18)	124.67(16)	S(1S)-C(1S)-H(1SC)	109.5
C(21)-C(19)-C(20)	116.22(15)	S(1SB)-C(1S)-H(1SD)	109.5
N(2)-C(20)-C(15)	117.51(15)	S(1SB)-C(1S)-H(1SE)	109.5
N(2)-C(20)-C(19)	122.90(16)	S(1SB)-C(1S)-H(1SF)	109.5
C(19)-C(20)-C(15)	119.60(15)	H(1SA)-C(1S)-H(1SB)	109.5
C(19)-C(21)-H(21)	119.7	H(1SA)-C(1S)-H(1SC)	109.5
C(22)-C(21)-C(19)	120.60(16)	H(1SB)-C(1S)-H(1SC)	109.5

H(1SD)-C(1S)-H(1SE)	109.5	S(1SB)-C(2S)-H(2SF)	109.5
H(1SD)-C(1S)-H(1SF)	109.5	H(2SA)-C(2S)-H(2SB)	109.5
H(1SE)-C(1S)-H(1SF)	109.5	H(2SA)-C(2S)-H(2SC)	109.5
S(1S)-C(2S)-H(2SA)	109.5	H(2SB)-C(2S)-H(2SC)	109.5
S(1S)-C(2S)-H(2SB)	109.5	H(2SD)-C(2S)-H(2SE)	109.5
S(1S)-C(2S)-H(2SC)	109.5	H(2SD)-C(2S)-H(2SF)	109.5
S(1SB)-C(2S)-H(2SD)	109.5	H(2SE)-C(2S)-H(2SF)	109.5
S(1SB)-C(2S)-H(2SE)	109.5		

Table S4. Anisotropic displacement parameters ($Å^2$x 10^3) for 4a. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	49(1)	29(1)	27(1)	-9(1)	4(1)	-24(1)
O(2)	28(1)	25(1)	22(1)	1(1)	-3(1)	-2(1)
O(3)	21(1)	27(1)	18(1)	-2(1)	1(1)	-7(1)
O(4)	25(1)	41(1)	21(1)	-5(1)	3(1)	-12(1)
N(1)	25(1)	21(1)	18(1)	-1(1)	-1(1)	-11(1)
N(2)	18(1)	17(1)	20(1)	-2(1)	-2(1)	-3(1)
N(3)	25(1)	22(1)	26(1)	-5(1)	-3(1)	-6(1)
C(1)	22(1)	21(1)	23(1)	-6(1)	0(1)	-7(1)
C(2)	31(1)	23(1)	19(1)	-6(1)	0(1)	-11(1)
C(3)	24(1)	22(1)	18(1)	-4(1)	-1(1)	-9(1)
C(4)	30(1)	26(1)	18(1)	-3(1)	-2(1)	-12(1)
C(5)	29(1)	25(1)	17(1)	-2(1)	-2(1)	-12(1)
C(6)	28(1)	24(1)	18(1)	-3(1)	-3(1)	-14(1)
C(7)	24(1)	18(1)	21(1)	-3(1)	-5(1)	-8(1)
C(8)	23(1)	19(1)	20(1)	-4(1)	-2(1)	-9(1)
C(9)	21(1)	24(1)	17(1)	-6(1)	1(1)	-10(1)
C(10)	27(1)	29(1)	18(1)	-3(1)	-2(1)	-15(1)
C(11)	22(1)	21(1)	24(1)	-6(1)	-1(1)	-7(1)
C(12)	25(1)	24(1)	18(1)	-4(1)	2(1)	-10(1)
C(13)	27(1)	24(1)	19(1)	0(1)	-5(1)	-11(1)
C(14)	23(1)	23(1)	22(1)	-2(1)	-4(1)	-6(1)
C(15)	16(1)	20(1)	19(1)	-1(1)	-1(1)	-3(1)
C(16)	19(1)	21(1)	23(1)	-3(1)	-2(1)	-6(1)
C(17)	21(1)	20(1)	26(1)	2(1)	-1(1)	-6(1)

C(18)	22(1)	24(1)	20(1)	3(1)	0(1)	-5(1)
C(19)	18(1)	20(1)	20(1)	0(1)	-1(1)	-2(1)
C(20)	16(1)	18(1)	20(1)	-1(1)	-2(1)	-2(1)
C(21)	23(1)	24(1)	17(1)	-2(1)	-1(1)	-2(1)
C(22)	23(1)	23(1)	19(1)	-4(1)	-3(1)	-3(1)
C(23)	18(1)	19(1)	19(1)	-2(1)	-3(1)	-1(1)
C(24)	17(1)	19(1)	23(1)	-3(1)	-4(1)	-2(1)
C(25)	23(1)	22(1)	23(1)	-4(1)	-4(1)	-6(1)
C(26)	22(1)	25(1)	25(1)	-1(1)	-1(1)	-7(1)
C(27)	27(1)	22(1)	33(1)	-2(1)	-2(1)	-10(1)
C(28)	29(1)	24(1)	34(1)	-9(1)	-3(1)	-8(1)
S(1S)	28(1)	25(1)	26(1)	-7(1)	-7(1)	-5(1)
S(1SB)	28(1)	25(1)	26(1)	-7(1)	-7(1)	-5(1)
O(1S)	70(1)	22(1)	26(1)	-5(1)	-14(1)	3(1)
C(1S)	76(2)	32(1)	36(1)	-7(1)	1(1)	-22(1)
C(2S)	49(1)	41(1)	30(1)	-13(1)	-5(1)	-12(1)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 4a.

	x	y	z	U(eq)
H(2)	3170(40)	3870(20)	4206(13)	69(8)
H(1)	7810(30)	6038(18)	891(12)	34(6)
H(2A)	6856	6922	2700	29
H(2B)	8782	5895	2665	29
H(3A)	7820	4548	1963	25
H(3B)	5872	5522	2131	25
H(4A)	6075	4856	3579	29
H(4B)	8001	3862	3403	29
H(5A)	4855	3468	3108	28
H(5B)	6741	2556	2787	28
H(11)	2785	2064	6118	27
H(12)	3331	497	7351	27
H(13)	6023	-1187	7458	28
H(14)	8147	-1371	6321	27
H(16)	9279	9008	151	26
H(17)	9883	9783	-1269	28

H(18)	9560	8642	-2224	29
H(21)	8639	6648	-2497	28
H(22)	7566	4782	-1965	27
H(25)	6862	3704	835	27
H(26)	6012	1699	1376	30
H(27)	5482	516	469	33
H(28)	5815	1374	-935	33
H(1SA)	3200	7675	3066	71
H(1SB)	1341	8818	3024	71
H(1SC)	2021	7821	2367	71
H(1SD)	2126	8719	3063	71
H(1SE)	786	8031	2869	71
H(1SF)	2748	7674	2433	71
H(2SA)	813	6340	5008	59
H(2SB)	681	7919	4611	59
H(2SC)	2537	6768	4598	59
H(2SD)	1312	6069	4923	59
H(2SE)	90	7477	4457	59
H(2SF)	1760	7486	4828	59

Table S6. Hydrogen bonds for 4a [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2)...O(1S)	0.928(17)	1.723(18)	2.6187(18)	161(3)

Crystal Data for 15

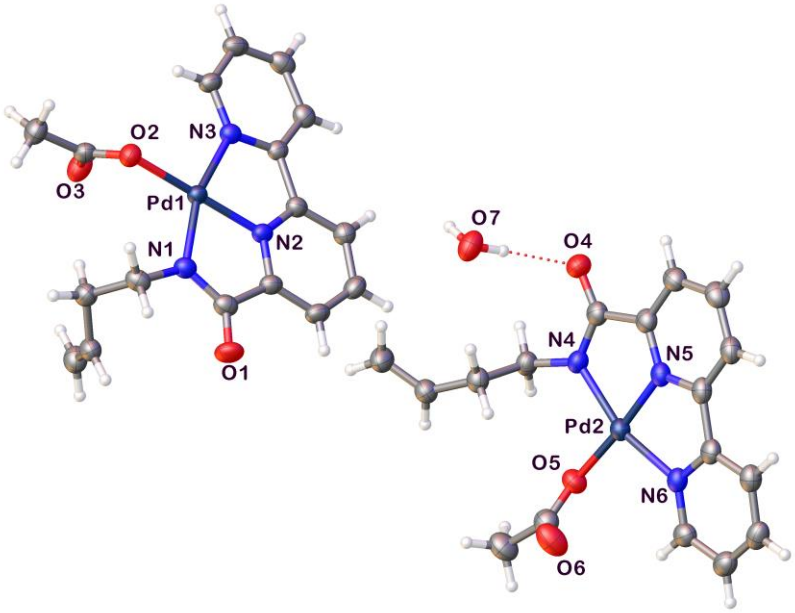


Table S7. Crystal data and structure refinement for 15.

Identification code	MOD3-32	
Empirical formula	C34 H36 N6 O7 Pd2	
Formula weight	853.49	
Temperature	100.15 K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.5111(5) Å	□= 81.916(3)°.
	b = 10.9386(6) Å	□= 86.459(2)°.
	c = 19.1791(10) Å	□ = 69.010(3)°.
Volume	1650.39(16) Å^3	
Z	2	
Density (calculated)	1.717 Mg/m^3	
Absorption coefficient	9.288 mm^{-1}	
F(000)	860	
Crystal size	0.29 x 0.1 x 0.07 mm^3	
Theta range for data collection	2.327 to 68.330°.	
Index ranges	-10<=h<=10, -13<=k<=13, -23<=l<=23	
Reflections collected	22119	
Independent reflections	5925 [R(int) = 0.0425]	
Completeness to theta = 67.679°	98.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.1665 and 0.0569	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5925 / 0 / 446	
Goodness-of-fit on F^2	1.052	
Final R indices [I>2sigma(I)]	R1 = 0.0311, wR2 = 0.0751	
R indices (all data)	R1 = 0.0346, wR2 = 0.0771	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.871 and -0.419 e.Å^{-3}	

Table S8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 15. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	3593(1)	9596(1)	5467(1)	27(1)
O(1)	6743(3)	5882(2)	5216(1)	44(1)
O(2)	4076(3)	10450(2)	6268(1)	36(1)
O(3)	1978(3)	10138(3)	6932(1)	44(1)
N(1)	5428(3)	7841(3)	5689(1)	32(1)
N(2)	3296(3)	8764(2)	4688(1)	27(1)
N(3)	1581(3)	11096(2)	4994(1)	29(1)
C(1)	4062(5)	5565(4)	7184(2)	44(1)
C(2)	5440(5)	5801(3)	6975(2)	37(1)
C(3)	5681(4)	7088(3)	6972(2)	37(1)
C(4)	6531(4)	7479(3)	6291(2)	35(1)
C(5)	5654(4)	6997(3)	5216(2)	33(1)
C(6)	4376(4)	7550(3)	4629(2)	31(1)
C(7)	4235(4)	6919(3)	4073(2)	35(1)
C(8)	2970(4)	7590(3)	3585(2)	37(1)
C(9)	1864(4)	8855(3)	3662(2)	34(1)
C(10)	2050(4)	9434(3)	4235(2)	29(1)
C(11)	1024(4)	10763(3)	4419(2)	28(1)
C(12)	-391(4)	11617(3)	4058(2)	34(1)
C(13)	-1227(4)	12849(3)	4281(2)	38(1)
C(14)	-627(4)	13189(3)	4848(2)	38(1)
C(15)	781(4)	12287(3)	5197(2)	33(1)
C(16)	3223(4)	10468(3)	6843(2)	35(1)
C(17)	3893(5)	10918(4)	7436(2)	42(1)
Pd(2)	1778(1)	4539(1)	393(1)	31(1)
O(4)	-361(3)	8378(2)	753(1)	42(1)
O(5)	902(3)	3273(2)	1033(1)	40(1)
O(6)	3415(4)	1841(3)	1365(2)	59(1)
N(4)	358(3)	6108(3)	862(1)	34(1)
N(5)	2402(3)	5884(3)	-183(1)	32(1)
N(6)	3462(3)	3390(3)	-285(1)	34(1)
C(18)	-638(5)	5949(4)	3340(2)	47(1)
C(19)	-251(5)	5246(3)	2816(2)	39(1)
C(20)	590(4)	5564(4)	2145(2)	37(1)

C(21)	-599(4)	6018(3)	1516(2)	36(1)
C(22)	420(4)	7270(3)	565(2)	35(1)
C(23)	1616(4)	7140(3)	-57(2)	34(1)
C(24)	1982(5)	8152(4)	-463(2)	38(1)
C(25)	3219(5)	7820(4)	-990(2)	42(1)
C(26)	4023(5)	6520(4)	-1107(2)	40(1)
C(27)	3578(4)	5532(4)	-693(2)	35(1)
C(28)	4203(4)	4100(3)	-743(2)	35(1)
C(29)	5426(4)	3495(4)	-1226(2)	39(1)
C(30)	5841(5)	2152(4)	-1256(2)	43(1)
C(31)	5031(5)	1452(4)	-808(2)	43(1)
C(32)	3867(4)	2101(3)	-324(2)	38(1)
C(33)	1888(5)	2275(4)	1426(2)	41(1)
C(34)	1005(5)	1651(4)	1998(2)	52(1)
O(7)	494(3)	8725(3)	2092(1)	49(1)

Table S9. Bond lengths [Å] and angles [°] for 15.

Pd(1)-Pd(1)#1	3.2048(4)	C(3)-C(4)	1.535(5)
Pd(1)-O(2)	2.039(2)	C(4)-H(4A)	0.9900
Pd(1)-N(1)	2.003(3)	C(4)-H(4B)	0.9900
Pd(1)-N(2)	1.928(3)	C(5)-C(6)	1.518(5)
Pd(1)-N(3)	2.052(3)	C(6)-C(7)	1.382(5)
O(1)-C(5)	1.240(4)	C(7)-H(7)	0.9500
O(2)-C(16)	1.280(4)	C(7)-C(8)	1.393(5)
O(3)-C(16)	1.232(4)	C(8)-H(8)	0.9500
N(1)-C(4)	1.453(4)	C(8)-C(9)	1.390(5)
N(1)-C(5)	1.341(4)	C(9)-H(9)	0.9500
N(2)-C(6)	1.332(4)	C(9)-C(10)	1.386(5)
N(2)-C(10)	1.341(4)	C(10)-C(11)	1.482(4)
N(3)-C(11)	1.368(4)	C(11)-C(12)	1.385(4)
N(3)-C(15)	1.337(4)	C(12)-H(12)	0.9500
C(1)-H(1A)	0.9500	C(12)-C(13)	1.394(5)
C(1)-H(1B)	0.9500	C(13)-H(13)	0.9500
C(1)-C(2)	1.316(5)	C(13)-C(14)	1.379(5)
C(2)-H(2)	0.9500	C(14)-H(14)	0.9500
C(2)-C(3)	1.493(5)	C(14)-C(15)	1.387(5)
C(3)-H(3A)	0.9900	C(15)-H(15)	0.9500
C(3)-H(3B)	0.9900	C(16)-C(17)	1.516(5)

C(17)-H(17A)	0.9800	C(30)-C(31)	1.386(6)
C(17)-H(17B)	0.9800	C(31)-H(31)	0.9500
C(17)-H(17C)	0.9800	C(31)-C(32)	1.383(5)
Pd(2)-Pd(2)#2	3.2253(5)	C(32)-H(32)	0.9500
Pd(2)-O(5)	2.032(2)	C(33)-C(34)	1.513(5)
Pd(2)-N(4)	2.007(3)	C(34)-H(34A)	0.9800
Pd(2)-N(5)	1.922(3)	C(34)-H(34B)	0.9800
Pd(2)-N(6)	2.064(3)	C(34)-H(34C)	0.9800
O(4)-C(22)	1.248(4)	O(7)-H(7A)	0.8696
O(5)-C(33)	1.286(4)	O(7)-H(7B)	0.8705
O(6)-C(33)	1.217(5)	O(2)-Pd(1)-Pd(1)#1	88.89(7)
N(4)-C(21)	1.465(4)	O(2)-Pd(1)-N(3)	101.71(10)
N(4)-C(22)	1.335(4)	N(1)-Pd(1)-Pd(1)#1	85.01(8)
N(5)-C(23)	1.346(5)	N(1)-Pd(1)-O(2)	96.43(10)
N(5)-C(27)	1.347(4)	N(1)-Pd(1)-N(3)	161.86(11)
N(6)-C(28)	1.365(4)	N(2)-Pd(1)-Pd(1)#1	87.61(7)
N(6)-C(32)	1.339(4)	N(2)-Pd(1)-O(2)	176.00(10)
C(18)-H(18A)	0.9500	N(2)-Pd(1)-N(1)	81.34(11)
C(18)-H(18B)	0.9500	N(2)-Pd(1)-N(3)	80.56(10)
C(18)-C(19)	1.307(5)	N(3)-Pd(1)-Pd(1)#1	95.49(7)
C(19)-H(19)	0.9500	C(16)-O(2)-Pd(1)	119.4(2)
C(19)-C(20)	1.492(5)	C(4)-N(1)-Pd(1)	124.6(2)
C(20)-H(20A)	0.9900	C(5)-N(1)-Pd(1)	115.2(2)
C(20)-H(20B)	0.9900	C(5)-N(1)-C(4)	120.2(3)
C(20)-C(21)	1.533(5)	C(6)-N(2)-Pd(1)	117.3(2)
C(21)-H(21A)	0.9900	C(6)-N(2)-C(10)	123.8(3)
C(21)-H(21B)	0.9900	C(10)-N(2)-Pd(1)	118.9(2)
C(22)-C(23)	1.508(5)	C(11)-N(3)-Pd(1)	112.9(2)
C(23)-C(24)	1.380(5)	C(15)-N(3)-Pd(1)	127.5(2)
C(24)-H(24)	0.9500	C(15)-N(3)-C(11)	119.5(3)
C(24)-C(25)	1.400(5)	H(1A)-C(1)-H(1B)	120.0
C(25)-H(25)	0.9500	C(2)-C(1)-H(1A)	120.0
C(25)-C(26)	1.383(5)	C(2)-C(1)-H(1B)	120.0
C(26)-H(26)	0.9500	C(1)-C(2)-H(2)	117.4
C(26)-C(27)	1.399(5)	C(1)-C(2)-C(3)	125.2(4)
C(27)-C(28)	1.478(5)	C(3)-C(2)-H(2)	117.4
C(28)-C(29)	1.393(5)	C(2)-C(3)-H(3A)	109.1
C(29)-H(29)	0.9500	C(2)-C(3)-H(3B)	109.1
C(29)-C(30)	1.392(5)	C(2)-C(3)-C(4)	112.6(3)
C(30)-H(30)	0.9500	H(3A)-C(3)-H(3B)	107.8

C(4)-C(3)-H(3A)	109.1	C(14)-C(15)-H(15)	119.2
C(4)-C(3)-H(3B)	109.1	O(2)-C(16)-C(17)	114.1(3)
N(1)-C(4)-C(3)	112.1(3)	O(3)-C(16)-O(2)	124.9(3)
N(1)-C(4)-H(4A)	109.2	O(3)-C(16)-C(17)	121.0(3)
N(1)-C(4)-H(4B)	109.2	C(16)-C(17)-H(17A)	109.5
C(3)-C(4)-H(4A)	109.2	C(16)-C(17)-H(17B)	109.5
C(3)-C(4)-H(4B)	109.2	C(16)-C(17)-H(17C)	109.5
H(4A)-C(4)-H(4B)	107.9	H(17A)-C(17)-H(17B)	109.5
O(1)-C(5)-N(1)	127.7(3)	H(17A)-C(17)-H(17C)	109.5
O(1)-C(5)-C(6)	120.0(3)	H(17B)-C(17)-H(17C)	109.5
N(1)-C(5)-C(6)	112.3(3)	O(5)-Pd(2)-Pd(2)#2	85.18(7)
N(2)-C(6)-C(5)	113.7(3)	O(5)-Pd(2)-N(6)	105.12(11)
N(2)-C(6)-C(7)	119.5(3)	N(4)-Pd(2)-Pd(2)#2	77.10(8)
C(7)-C(6)-C(5)	126.7(3)	N(4)-Pd(2)-O(5)	93.41(11)
C(6)-C(7)-H(7)	120.8	N(4)-Pd(2)-N(6)	161.47(11)
C(6)-C(7)-C(8)	118.4(3)	N(5)-Pd(2)-Pd(2)#2	91.59(8)
C(8)-C(7)-H(7)	120.8	N(5)-Pd(2)-O(5)	173.98(11)
C(7)-C(8)-H(8)	119.7	N(5)-Pd(2)-N(4)	80.90(11)
C(9)-C(8)-C(7)	120.6(3)	N(5)-Pd(2)-N(6)	80.57(11)
C(9)-C(8)-H(8)	119.7	N(6)-Pd(2)-Pd(2)#2	103.67(7)
C(8)-C(9)-H(9)	120.7	C(33)-O(5)-Pd(2)	121.9(2)
C(10)-C(9)-C(8)	118.5(3)	C(21)-N(4)-Pd(2)	123.8(2)
C(10)-C(9)-H(9)	120.7	C(22)-N(4)-Pd(2)	115.6(2)
N(2)-C(10)-C(9)	119.0(3)	C(22)-N(4)-C(21)	120.4(3)
N(2)-C(10)-C(11)	113.3(3)	C(23)-N(5)-Pd(2)	117.6(2)
C(9)-C(10)-C(11)	127.7(3)	C(23)-N(5)-C(27)	123.4(3)
N(3)-C(11)-C(10)	114.3(3)	C(27)-N(5)-Pd(2)	119.0(2)
N(3)-C(11)-C(12)	121.3(3)	C(28)-N(6)-Pd(2)	112.3(2)
C(12)-C(11)-C(10)	124.4(3)	C(32)-N(6)-Pd(2)	128.6(2)
C(11)-C(12)-H(12)	120.7	C(32)-N(6)-C(28)	119.1(3)
C(11)-C(12)-C(13)	118.6(3)	H(18A)-C(18)-H(18B)	120.0
C(13)-C(12)-H(12)	120.7	C(19)-C(18)-H(18A)	120.0
C(12)-C(13)-H(13)	120.2	C(19)-C(18)-H(18B)	120.0
C(14)-C(13)-C(12)	119.6(3)	C(18)-C(19)-H(19)	117.4
C(14)-C(13)-H(13)	120.2	C(18)-C(19)-C(20)	125.3(3)
C(13)-C(14)-H(14)	120.3	C(20)-C(19)-H(19)	117.4
C(13)-C(14)-C(15)	119.3(3)	C(19)-C(20)-H(20A)	109.1
C(15)-C(14)-H(14)	120.3	C(19)-C(20)-H(20B)	109.1
N(3)-C(15)-C(14)	121.6(3)	C(19)-C(20)-C(21)	112.6(3)
N(3)-C(15)-H(15)	119.2	H(20A)-C(20)-H(20B)	107.8

C(21)-C(20)-H(20A)	109.1	N(6)-C(28)-C(27)	114.9(3)
C(21)-C(20)-H(20B)	109.1	N(6)-C(28)-C(29)	121.2(3)
N(4)-C(21)-C(20)	109.8(3)	C(29)-C(28)-C(27)	123.8(3)
N(4)-C(21)-H(21A)	109.7	C(28)-C(29)-H(29)	120.6
N(4)-C(21)-H(21B)	109.7	C(30)-C(29)-C(28)	118.8(3)
C(20)-C(21)-H(21A)	109.7	C(30)-C(29)-H(29)	120.6
C(20)-C(21)-H(21B)	109.7	C(29)-C(30)-H(30)	120.3
H(21A)-C(21)-H(21B)	108.2	C(31)-C(30)-C(29)	119.5(3)
O(4)-C(22)-N(4)	127.5(3)	C(31)-C(30)-H(30)	120.3
O(4)-C(22)-C(23)	120.0(3)	C(30)-C(31)-H(31)	120.6
N(4)-C(22)-C(23)	112.5(3)	C(32)-C(31)-C(30)	118.9(3)
N(5)-C(23)-C(22)	113.2(3)	C(32)-C(31)-H(31)	120.6
N(5)-C(23)-C(24)	120.3(3)	N(6)-C(32)-C(31)	122.4(3)
C(24)-C(23)-C(22)	126.5(3)	N(6)-C(32)-H(32)	118.8
C(23)-C(24)-H(24)	121.1	C(31)-C(32)-H(32)	118.8
C(23)-C(24)-C(25)	117.9(3)	O(5)-C(33)-C(34)	114.6(3)
C(25)-C(24)-H(24)	121.1	O(6)-C(33)-O(5)	124.8(4)
C(24)-C(25)-H(25)	119.6	O(6)-C(33)-C(34)	120.6(3)
C(26)-C(25)-C(24)	120.9(3)	C(33)-C(34)-H(34A)	109.5
C(26)-C(25)-H(25)	119.6	C(33)-C(34)-H(34B)	109.5
C(25)-C(26)-H(26)	120.4	C(33)-C(34)-H(34C)	109.5
C(25)-C(26)-C(27)	119.1(3)	H(34A)-C(34)-H(34B)	109.5
C(27)-C(26)-H(26)	120.4	H(34A)-C(34)-H(34C)	109.5
N(5)-C(27)-C(26)	118.4(3)	H(34B)-C(34)-H(34C)	109.5
N(5)-C(27)-C(28)	113.0(3)	H(7A)-O(7)-H(7B)	109.5
C(26)-C(27)-C(28)	128.6(3)		

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+2,-z+1 #2 -x,-y+1,-z

Table S10. Anisotropic displacement parameters ($Å^2$x 10^3) for 15. 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)	28(1)	24(1)	26(1)	-4(1)	1(1)	-7(1)
O(1)	40(1)	28(1)	55(2)	-8(1)	-2(1)	0(1)
O(2)	41(1)	34(1)	32(1)	-6(1)	1(1)	-13(1)
O(3)	38(1)	56(2)	43(1)	-20(1)	7(1)	-21(1)
N(1)	30(1)	28(1)	33(1)	-2(1)	1(1)	-7(1)

N(2)	27(1)	24(1)	28(1)	-4(1)	5(1)	-6(1)
N(3)	29(1)	26(1)	30(1)	-3(1)	2(1)	-8(1)
C(1)	50(2)	49(2)	36(2)	-6(2)	-1(2)	-22(2)
C(2)	45(2)	34(2)	31(2)	-2(1)	-3(1)	-13(2)
C(3)	39(2)	34(2)	34(2)	-4(1)	-3(1)	-10(2)
C(4)	30(2)	32(2)	40(2)	2(1)	-4(1)	-9(1)
C(5)	29(2)	30(2)	38(2)	-1(1)	3(1)	-8(1)
C(6)	32(2)	25(2)	35(2)	-4(1)	4(1)	-8(1)
C(7)	37(2)	26(2)	40(2)	-8(1)	7(1)	-7(1)
C(8)	44(2)	36(2)	35(2)	-12(1)	3(1)	-16(2)
C(9)	36(2)	34(2)	32(2)	-4(1)	-1(1)	-12(1)
C(10)	29(2)	27(2)	30(2)	-2(1)	2(1)	-8(1)
C(11)	29(2)	26(1)	28(2)	-3(1)	5(1)	-11(1)
C(12)	32(2)	36(2)	32(2)	-1(1)	1(1)	-13(1)
C(13)	29(2)	34(2)	42(2)	5(1)	2(1)	-7(1)
C(14)	39(2)	26(2)	43(2)	-4(1)	9(1)	-7(1)
C(15)	37(2)	25(2)	36(2)	-7(1)	6(1)	-8(1)
C(16)	38(2)	26(2)	35(2)	-5(1)	-1(1)	-4(1)
C(17)	45(2)	45(2)	36(2)	-12(2)	0(2)	-15(2)
Pd(2)	34(1)	32(1)	26(1)	-3(1)	-1(1)	-11(1)
O(4)	50(1)	36(1)	39(1)	-8(1)	1(1)	-12(1)
O(5)	44(1)	37(1)	38(1)	2(1)	-1(1)	-16(1)
O(6)	45(2)	64(2)	59(2)	15(1)	-1(1)	-18(1)
N(4)	36(1)	34(1)	28(1)	-7(1)	0(1)	-8(1)
N(5)	32(1)	38(2)	26(1)	-3(1)	-3(1)	-14(1)
N(6)	33(1)	39(2)	27(1)	-5(1)	-3(1)	-10(1)
C(18)	63(2)	43(2)	37(2)	-6(2)	7(2)	-23(2)
C(19)	45(2)	37(2)	34(2)	-2(1)	-1(1)	-15(2)
C(20)	38(2)	42(2)	32(2)	-5(1)	-2(1)	-13(2)
C(21)	35(2)	38(2)	31(2)	-6(1)	1(1)	-9(2)
C(22)	37(2)	38(2)	30(2)	-4(1)	-5(1)	-13(2)
C(23)	37(2)	39(2)	30(2)	-5(1)	-6(1)	-15(2)
C(24)	44(2)	38(2)	36(2)	-3(1)	-6(1)	-18(2)
C(25)	47(2)	46(2)	39(2)	0(2)	-2(2)	-26(2)
C(26)	45(2)	50(2)	29(2)	-4(1)	-1(1)	-21(2)
C(27)	35(2)	46(2)	26(2)	-5(1)	-2(1)	-17(2)
C(28)	36(2)	42(2)	28(2)	-6(1)	-6(1)	-14(2)
C(29)	36(2)	49(2)	31(2)	-5(1)	-2(1)	-14(2)
C(30)	36(2)	51(2)	36(2)	-12(2)	-2(1)	-6(2)
C(31)	44(2)	41(2)	39(2)	-9(2)	-8(2)	-8(2)

C(32)	39(2)	36(2)	35(2)	-3(1)	-7(1)	-10(2)
C(33)	44(2)	42(2)	40(2)	-5(2)	-4(2)	-18(2)
C(34)	54(2)	51(2)	51(2)	7(2)	0(2)	-24(2)
O(7)	50(2)	61(2)	42(1)	-20(1)	8(1)	-24(1)

Table S11. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 15.

	x	y	z	U(eq)
H(1A)	3120	6244	7349	52
H(1B)	4009	4716	7169	52
H(2)	6354	5096	6814	44
H(3A)	6378	7028	7378	44
H(3B)	4572	7786	7028	44
H(4A)	6867	8234	6354	42
H(4B)	7563	6730	6199	42
H(7)	4982	6049	4025	42
H(8)	2863	7178	3195	44
H(9)	1000	9313	3330	41
H(12)	-783	11368	3666	40
H(13)	-2205	13450	4044	45
H(14)	-1174	14033	4999	45
H(15)	1187	12522	5590	40
H(17A)	4447	11538	7238	63
H(17B)	4707	10151	7708	63
H(17C)	2960	11355	7745	63
H(18A)	-382	6732	3312	56
H(18B)	-1174	5677	3750	56
H(19)	-528	4471	2865	46
H(20A)	1559	4771	2048	45
H(20B)	1029	6268	2201	45
H(21A)	-1176	5381	1498	43
H(21B)	-1466	6890	1570	43
H(24)	1413	9045	-388	46
H(25)	3510	8496	-1272	50
H(26)	4867	6301	-1463	48
H(29)	5968	3991	-1529	47
H(30)	6673	1718	-1581	51

H(31)	5270	541	-832	51
H(32)	3335	1615	-9	45
H(34A)	-213	2125	1968	78
H(34B)	1260	725	1936	78
H(34C)	1397	1699	2460	78
H(7A)	146	8648	1689	73
H(7B)	-361	9162	2340	73

Crystal Data for 18

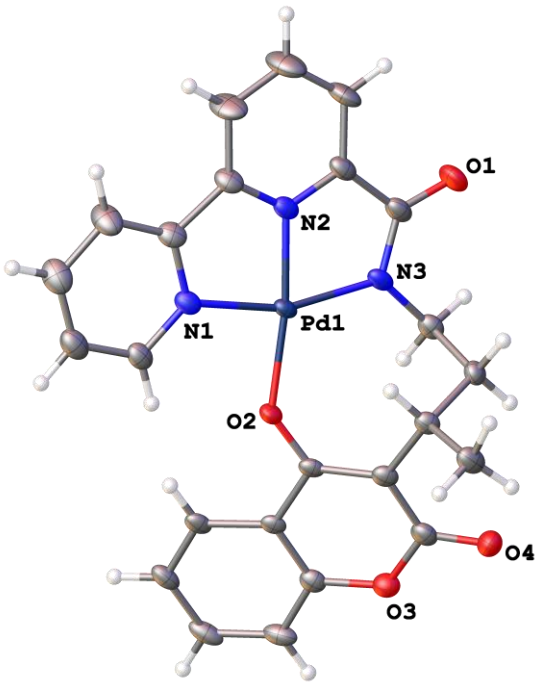


Table S12. Crystal data and structure refinement for 18.

Identification code	MOD 4-18	
Empirical formula	C24 H19 N3 O4 Pd	
Formula weight	519.82	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 30.5590(9) Å	□= 90°.
	b = 7.1819(2) Å	□= 103.310(2)°.
	c = 26.4061(9) Å	□ = 90°.
Volume	5639.7(3) $Å^3$	
Z	8	
Density (calculated)	1.224 Mg/m^3	
Absorption coefficient	0.686 mm^{-1}	
F(000)	2096	
Crystal size	0.28 x 0.14 x 0.08 mm^3	
Theta range for data collection	1.841 to 24.999°.	
Index ranges	-36<=h<=35, -7<=k<=8, -31<=l<=26	
Reflections collected	17836	
Independent reflections	4967 [R(int) = 0.0455]	
Completeness to theta = 24.999°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.2666 and 0.2214	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4967 / 0 / 290	
Goodness-of-fit on F^2	1.132	
Final R indices [I>2sigma(I)]	R1 = 0.0377, wR2 = 0.0901	
R indices (all data)	R1 = 0.0424, wR2 = 0.0929	
Largest diff. peak and hole	0.701 and -0.747 $e.Å^{-3}$	

SQUEEZE Found 1199 e/uc (approx. 4 DMSO/au)

Table S13. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 18. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	2451(1)	6653(1)	6485(1)	17(1)
O(2)	2657(1)	7319(4)	7243(1)	22(1)
O(3)	3836(1)	8078(4)	8344(1)	25(1)
O(4)	4202(1)	9005(4)	7759(1)	31(1)
O(1)	3205(1)	4532(4)	5532(1)	34(1)
N(3)	3002(1)	5728(4)	6263(1)	21(1)
N(2)	2177(1)	6021(4)	5777(1)	20(1)
N(1)	1797(1)	7283(4)	6476(1)	21(1)
C(19)	2668(1)	6719(5)	8280(1)	20(1)
C(17)	3039(1)	7695(5)	7566(1)	17(1)
C(16)	3421(1)	8417(5)	7440(1)	20(1)
C(18)	3049(1)	7307(5)	8113(1)	16(1)
C(11)	1634(1)	7927(5)	6872(2)	24(1)
C(20)	2699(1)	6336(5)	8798(1)	24(1)
C(14)	3427(1)	8998(5)	6889(1)	20(1)
C(6)	1732(1)	6220(5)	5608(1)	24(1)
C(23)	3451(1)	7505(5)	8481(1)	21(1)
C(2)	2444(1)	5342(5)	5486(1)	23(1)
C(22)	3486(1)	7095(5)	9004(1)	26(1)
C(12)	3464(1)	5663(5)	6578(1)	22(1)
C(7)	1510(1)	6938(5)	6009(1)	24(1)
C(13)	3680(1)	7586(5)	6625(1)	21(1)
C(24)	3833(1)	8553(5)	7829(1)	23(1)
C(21)	3108(1)	6497(5)	9162(1)	27(1)
C(15)	3602(1)	10993(5)	6856(2)	27(1)
C(10)	1180(1)	8229(6)	6821(2)	30(1)
C(1)	2928(1)	5167(5)	5765(1)	24(1)
C(9)	883(2)	7888(6)	6354(2)	35(1)
C(5)	1529(2)	5709(7)	5095(2)	39(1)
C(3)	2257(2)	4807(6)	4976(1)	32(1)
C(8)	1051(1)	7211(6)	5936(2)	35(1)
C(4)	1796(2)	4996(7)	4786(2)	44(1)

Table S14. Bond lengths [Å] and angles [°] for 18.

Pd(1)-O(2)	2.014(2)	C(12)-H(12A)	0.9900
Pd(1)-N(3)	2.020(3)	C(12)-H(12B)	0.9900
Pd(1)-N(2)	1.919(3)	C(12)-C(13)	1.524(5)
Pd(1)-N(1)	2.043(3)	C(7)-C(8)	1.386(6)
O(2)-C(17)	1.305(4)	C(13)-H(13A)	0.9900
O(3)-C(23)	1.369(4)	C(13)-H(13B)	0.9900
O(3)-C(24)	1.402(4)	C(21)-H(21)	0.9500
O(4)-C(24)	1.225(5)	C(15)-H(15A)	0.9800
O(1)-C(1)	1.244(4)	C(15)-H(15B)	0.9800
N(3)-C(12)	1.465(5)	C(15)-H(15C)	0.9800
N(3)-C(1)	1.342(5)	C(10)-H(10)	0.9500
N(2)-C(6)	1.337(5)	C(10)-C(9)	1.373(6)
N(2)-C(2)	1.336(5)	C(9)-H(9)	0.9500
N(1)-C(11)	1.339(5)	C(9)-C(8)	1.407(6)
N(1)-C(7)	1.362(5)	C(5)-H(5)	0.9500
C(19)-H(19)	0.9500	C(5)-C(4)	1.378(6)
C(19)-C(18)	1.404(5)	C(3)-H(3)	0.9500
C(19)-C(20)	1.376(5)	C(3)-C(4)	1.390(6)
C(17)-C(16)	1.388(5)	C(8)-H(8)	0.9500
C(17)-C(18)	1.465(5)	C(4)-H(4)	0.9500
C(16)-C(14)	1.518(5)		
C(16)-C(24)	1.433(5)	O(2)-Pd(1)-N(3)	106.03(11)
C(18)-C(23)	1.386(5)	O(2)-Pd(1)-N(1)	92.28(11)
C(11)-H(11)	0.9500	N(3)-Pd(1)-N(1)	161.51(12)
C(11)-C(10)	1.380(6)	N(2)-Pd(1)-O(2)	172.59(11)
C(20)-H(20)	0.9500	N(2)-Pd(1)-N(3)	81.08(12)
C(20)-C(21)	1.396(6)	N(2)-Pd(1)-N(1)	80.54(12)
C(14)-H(14)	1.0000	C(17)-O(2)-Pd(1)	136.6(2)
C(14)-C(13)	1.535(5)	C(23)-O(3)-C(24)	121.1(3)
C(14)-C(15)	1.538(5)	C(12)-N(3)-Pd(1)	127.1(2)
C(6)-C(7)	1.476(5)	C(1)-N(3)-Pd(1)	114.7(3)
C(6)-C(5)	1.402(5)	C(1)-N(3)-C(12)	118.2(3)
C(23)-C(22)	1.391(5)	C(6)-N(2)-Pd(1)	118.8(2)
C(2)-C(1)	1.497(6)	C(2)-N(2)-Pd(1)	117.4(3)
C(2)-C(3)	1.390(5)	C(2)-N(2)-C(6)	123.8(3)
C(22)-H(22)	0.9500	C(11)-N(1)-Pd(1)	127.3(3)
C(22)-C(21)	1.384(6)	C(11)-N(1)-C(7)	119.5(3)
		C(7)-N(1)-Pd(1)	113.2(2)

C(18)-C(19)-H(19)	120.0	C(13)-C(12)-H(12A)	109.4
C(20)-C(19)-H(19)	120.0	C(13)-C(12)-H(12B)	109.4
C(20)-C(19)-C(18)	120.0(4)	N(1)-C(7)-C(6)	114.0(3)
O(2)-C(17)-C(16)	126.7(3)	N(1)-C(7)-C(8)	121.4(3)
O(2)-C(17)-C(18)	114.7(3)	C(8)-C(7)-C(6)	124.6(4)
C(16)-C(17)-C(18)	118.6(3)	C(14)-C(13)-H(13A)	109.1
C(17)-C(16)-C(14)	121.9(3)	C(14)-C(13)-H(13B)	109.1
C(17)-C(16)-C(24)	120.2(3)	C(12)-C(13)-C(14)	112.4(3)
C(24)-C(16)-C(14)	117.8(3)	C(12)-C(13)-H(13A)	109.1
C(19)-C(18)-C(17)	122.4(3)	C(12)-C(13)-H(13B)	109.1
C(23)-C(18)-C(19)	118.5(3)	H(13A)-C(13)-H(13B)	107.9
C(23)-C(18)-C(17)	119.1(3)	O(3)-C(24)-C(16)	119.1(3)
N(1)-C(11)-H(11)	119.2	O(4)-C(24)-O(3)	114.2(3)
N(1)-C(11)-C(10)	121.6(4)	O(4)-C(24)-C(16)	126.6(3)
C(10)-C(11)-H(11)	119.2	C(20)-C(21)-H(21)	120.2
C(19)-C(20)-H(20)	119.5	C(22)-C(21)-C(20)	119.6(3)
C(19)-C(20)-C(21)	121.0(4)	C(22)-C(21)-H(21)	120.2
C(21)-C(20)-H(20)	119.5	C(14)-C(15)-H(15A)	109.5
C(16)-C(14)-H(14)	106.6	C(14)-C(15)-H(15B)	109.5
C(16)-C(14)-C(13)	111.8(3)	C(14)-C(15)-H(15C)	109.5
C(16)-C(14)-C(15)	113.0(3)	H(15A)-C(15)-H(15B)	109.5
C(13)-C(14)-H(14)	106.6	H(15A)-C(15)-H(15C)	109.5
C(13)-C(14)-C(15)	111.8(3)	H(15B)-C(15)-H(15C)	109.5
C(15)-C(14)-H(14)	106.6	C(11)-C(10)-H(10)	119.9
N(2)-C(6)-C(7)	113.5(3)	C(9)-C(10)-C(11)	120.1(4)
N(2)-C(6)-C(5)	118.9(4)	C(9)-C(10)-H(10)	119.9
C(5)-C(6)-C(7)	127.6(4)	O(1)-C(1)-N(3)	127.8(4)
O(3)-C(23)-C(18)	121.4(3)	O(1)-C(1)-C(2)	119.7(3)
O(3)-C(23)-C(22)	116.8(3)	N(3)-C(1)-C(2)	112.5(3)
C(18)-C(23)-C(22)	121.8(4)	C(10)-C(9)-H(9)	120.6
N(2)-C(2)-C(1)	114.3(3)	C(10)-C(9)-C(8)	118.7(4)
N(2)-C(2)-C(3)	119.2(4)	C(8)-C(9)-H(9)	120.6
C(3)-C(2)-C(1)	126.4(3)	C(6)-C(5)-H(5)	120.7
C(23)-C(22)-H(22)	120.4	C(4)-C(5)-C(6)	118.7(4)
C(21)-C(22)-C(23)	119.2(4)	C(4)-C(5)-H(5)	120.7
C(21)-C(22)-H(22)	120.4	C(2)-C(3)-H(3)	120.7
N(3)-C(12)-H(12A)	109.4	C(2)-C(3)-C(4)	118.7(4)
N(3)-C(12)-H(12B)	109.4	C(4)-C(3)-H(3)	120.7
N(3)-C(12)-C(13)	111.1(3)	C(7)-C(8)-C(9)	118.7(4)
H(12A)-C(12)-H(12B)	108.0	C(7)-C(8)-H(8)	120.6

C(9)-C(8)-H(8)	120.6	C(3)-C(4)-H(4)	119.6
C(5)-C(4)-C(3)	120.7(4)		
C(5)-C(4)-H(4)	119.6		

Symmetry transformations used to generate equivalent atoms:

Table S15. Anisotropic displacement parameters ($Å^2$x 10^3) for 18.

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)	26(1)	14(1)	13(1)	-1(1)	8(1)	-2(1)
O(2)	27(1)	27(1)	15(1)	-2(1)	9(1)	-6(1)
O(3)	28(1)	26(2)	22(1)	-1(1)	5(1)	-1(1)
O(4)	25(2)	40(2)	29(2)	-7(1)	8(1)	-7(1)
O(1)	39(2)	38(2)	30(2)	-11(1)	18(1)	1(1)
N(3)	34(2)	13(2)	19(2)	-3(1)	12(1)	-3(1)
N(2)	31(2)	14(2)	17(2)	2(1)	10(1)	-3(1)
N(1)	30(2)	15(2)	19(2)	3(1)	7(1)	2(1)
C(19)	33(2)	11(2)	18(2)	-3(2)	10(2)	-2(2)
C(17)	27(2)	10(2)	14(2)	-1(1)	5(2)	0(1)
C(16)	28(2)	12(2)	19(2)	-2(2)	6(2)	1(2)
C(18)	25(2)	9(2)	15(2)	-2(1)	5(1)	2(1)
C(11)	33(2)	17(2)	24(2)	3(2)	13(2)	-1(2)
C(20)	39(2)	17(2)	20(2)	0(2)	15(2)	3(2)
C(14)	28(2)	12(2)	20(2)	0(2)	7(2)	0(2)
C(6)	34(2)	22(2)	16(2)	6(2)	5(2)	5(2)
C(23)	28(2)	14(2)	21(2)	-1(2)	7(2)	3(2)
C(2)	36(2)	18(2)	19(2)	1(2)	13(2)	-2(2)
C(22)	37(2)	23(2)	16(2)	-2(2)	1(2)	11(2)
C(12)	30(2)	15(2)	23(2)	0(2)	10(2)	2(2)
C(7)	33(2)	21(2)	18(2)	6(2)	5(2)	4(2)
C(13)	23(2)	22(2)	20(2)	2(2)	9(2)	-1(2)
C(24)	31(2)	18(2)	22(2)	-4(2)	10(2)	1(2)
C(21)	49(2)	19(2)	15(2)	3(2)	11(2)	12(2)
C(15)	40(2)	18(2)	27(2)	0(2)	14(2)	-5(2)
C(10)	42(2)	23(2)	31(2)	4(2)	18(2)	1(2)
C(1)	36(2)	17(2)	23(2)	-3(2)	14(2)	-3(2)
C(9)	37(2)	34(2)	33(2)	14(2)	11(2)	13(2)
C(5)	42(3)	53(3)	16(2)	3(2)	-5(2)	14(2)
C(3)	48(3)	35(2)	15(2)	-1(2)	12(2)	9(2)

C(8)	35(2)	46(3)	22(2)	11(2)	5(2)	14(2)
C(4)	57(3)	56(3)	16(2)	-2(2)	2(2)	16(3)

Table S16. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 18.

	x	y	z	U(eq)
H(19)	2388	6586	8036	24
H(11)	1836	8182	7195	28
H(20)	2438	5957	8909	29
H(14)	3107	8990	6686	24
H(22)	3765	7222	9248	32
H(12A)	3643	4795	6417	26
H(12B)	3462	5188	6930	26
H(13A)	3687	8044	6273	25
H(13B)	3994	7486	6829	25
H(21)	3127	6199	9517	33
H(15A)	3446	11841	7046	41
H(15B)	3546	11377	6490	41
H(15C)	3926	11031	7010	41
H(10)	1072	8673	7109	36
H(9)	570	8106	6314	41
H(5)	1214	5852	4964	47
H(3)	2441	4321	4762	38
H(8)	853	6947	5610	42
H(4)	1662	4630	4439	52