Electronic Supplementary Material (ESI) for ChemComm.

Supporting information

for

Ruthenium Catalyzed Remote C4-Selective C-H Functionalization of Carbazoles via σ-Activation

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Contents

1. General

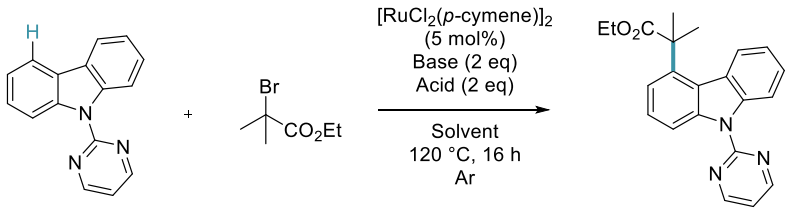
Proton, carbon and fluorine NMR spectra were recorded on Bruker 300 MHz, or Agilent Technologies 500 MHz, spectrometer (^{1}H NMR at 500 MHz, or 300 MHz, ^{13}C NMR at 126 MHz, or 75 MHz, and ^{19}F NMR at 470 MHz. Chemical shifts for protons are reported in parts per million downfield from $Si(CH_3)_4$ and are referenced to residual protium in the deuterated solvent ($CHCl_3$ at 7.26 ppm, or CH_3OH at 3.31 & 4.87 depending on solvent used). Chemical shifts for fluorines are reported in parts per million downfield from $CFCl_3$. NMR data are presented in the following format: chemical shift (number of equivalent nuclei by integration, multiplicity [app = apparent, br = broad, d = doublet, t = triplet, q = quartet, dd = doublet of doublets), dt = doublet of triplets), dq = doublet of quartets), ddd = doublet of doublet of doublets), m = multiplet], coupling constant [in Hz], assignment). Electrospray ionisation ultrahigh resolution time-of-flight mass spectrometry (ESI–UHR–TOF–MS) was performed on a Bruker maXis mass spectrometer. Electrospray ionisation high resolution time-of-flight mass spectrometry (ESI–HR–TOF–MS) was performed on a Bruker micrOTOF spectrometer. Infrared (IR) spectra were recorded on a Perkin–Elmer 1600 FT (Fourier transform), IR spectrophotometer, with absorbencies quoted as wavelength (v [in cm−1]). Melting points were obtained on a Bibby Sterilin SMP10 melting point machine and are uncorrected.

Analytical thin-layer chromatography (TLC) was performed on aluminium-backed plates coated with Alugram® SIL G/UV254 purchased from Macherey–Nagel and visualised with UV light (254 or 365 nm), and/or KMnO4, 2,4-DNPH or I_2/Silica staining. Silica gel column chromatography was performed using 60 Å, 200–400 mesh particle size silica gel purchased from Sigma–Aldrich. Samples were loaded as saturated solutions in an appropriate solvent system.

All reactions were performed using reagents obtained from Sigma-Aldrich, Acros Organics, Alfa Aesar, Fluorochem chemicals without further purification unless stated. $[RuCl_2(p\text{-cymene})]_2$ was purchased from STREM chemicals or Acros Organics. All water used was purified through a Merck Millipore reverse osmosis purification system prior to use. Anhydrous solvents were dried and degassed by passing through anhydrous alumina columns using an Innovative Technology Inc. PS–400–7 solvent purification system (SPS) and stored under an atmosphere of N_2 prior to use.

Reactions were performed in oven-dried glassware and under a blanket of N_2 if not stated. Temperatures quoted are external. Solvents were removed under reduced pressure using Bü chi-Rotorvapor apparatus.

2. Optimization



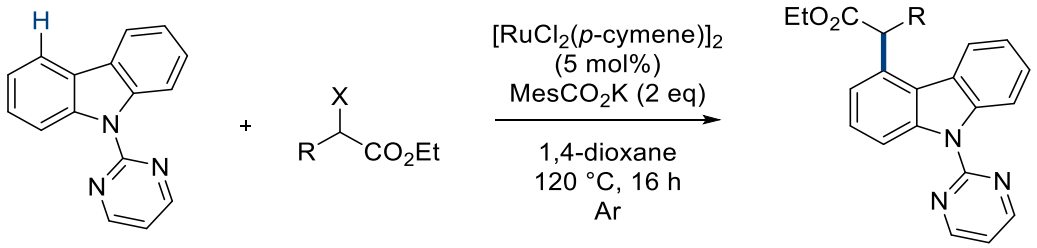
Entry	Base	Acid	Acid eq	Solvent	C4 % (IY)
1	KOAc	-	-	1,4-dioxane	53
2	KOAc	AcOH	2	1,4-dioxane	68 (48)
3	K_2CO_3 (+ $MesCO_2H$ 30%)	-	-	1,4-dioxane	7
4	K_2CO_3 (+ Piv-Val-OH 30%)	-	-	1,4-dioxane	7
5	K_2CO_3	AcOH	2	1,4-dioxane	-
6	K_3Citrate	AcOH	2	1.4-dioxane	45
7	K_2Oxalate	AcOH	2	1,4-dioxane	-
8	K_2Tartrate	AcOH	2	1,4-dioxane	56
9	KO_2CH	AcOH	2	1,4-dioxane	25
10	-	Piv-Val-OH	2	1,4-dioxane	Trace
11	$AdCO_2Na$	AcOH	2	1,4-dioxane	58
12	$MesCO_2K$	AcOH	2	1,4-dioxane	80 (61)
13	$MesCO_2K$	$MesCO_2H$	2	1,4-dioxane	64
14	$MesCO_2K$	$AdCO_2H$	2	1,4-dioxane	66
15	$MesCO_2K$	TFA	2	1,4-dioxane	15
16	$MesCO_2K$	HO_2CH	2	1,4-dioxane	34
17	$MesCO_2K$	conc. $HCl_{(aq)}$	2	1,4-dioxane	17
18	$MesCO_2K$	AcOH	2	2-MeTHF	55
19	$MesCO_2K$	AcOH	2	PhMe	-
20	$MesCO_2K$	AcOH	2	MeCN	72
21	$MesCO_2K$	AcOH	2	C_6H_6	39
22	$MesCO_2K$	AcOH	2	2-butanone	55
23	$MesCO_2K$	AcOH	2	AcOH	31
24	$MesCO_2K$	AcOH	2	DCE	38
25	$MesCO_2K$	AcOH	2	DME	49
26	$MesCO_2K$	AcOH	0.5	1,4-dioxane	80
27	**$MesCO_2K$**	**AcOH**	**1**	**1,4-dioxane**	**84 (68)**
28	$MesCO_2K$	AcOH	4	1,4-dioxane	68
29[a]	$MesCO_2K$	AcOH	1	1,4-dioxane	61
30[b]	$MesCO_2K$	AcOH	1	1,4-dioxane	76
31[c]	$MesCO_2K$	AcOH	1	1,4-dioxane	-
32[d]	**$MesCO_2K$**	**AcOH**	**1**	**1,4-dioxane**	**90 (76)**

General Conditions: 5CP-A (0.25-0.5 mmol), methyl α-bromoisobutyrate (0.75-1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 0.0125-0.025 mmol), solvent (1-2 mL), 120 °C, 16 h. [a] : Reaction carried out at 100 °C. [b] : Reaction carried out under air. [c] : Without $[RuCl_2(p\text{-cymene})]_2$. [d] : $[Ru(O_2CMes)_2(p\text{-cymene})]$ (10 mol%)

Further Experiments

We carried out further experiments to elucidate whether secondary and primary alkyl esters were amenable to the reaction methodology. Unfortunately, on using both the chloro and bromo ester coupling partners, no conversion to any product was observed.

Scheme S1: Ruthenium Catalysed C4-Alkylation using Primary and Secondary Alkyl Halides

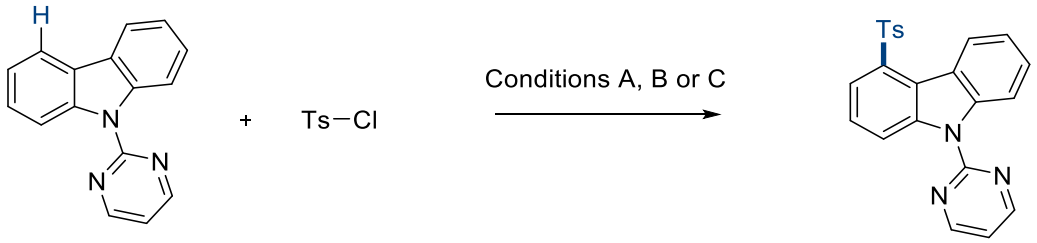


a: X = Br, R = Me
b: X = Cl, R = Me
c: X = Br, R = H
d: X = Cl, R = H

a-d: 0%

We were intrigued to investigate whether carbazole templates could be applied to other σ-activation protocols. To that end, we identified *meta*-sulfonation and *meta*-bromination methodologies as potentially the most amenable to this template. Unfortunately using the original conditions, the carbazole conditions from this report, and amalgamations, no C4-functionalised products were observed.

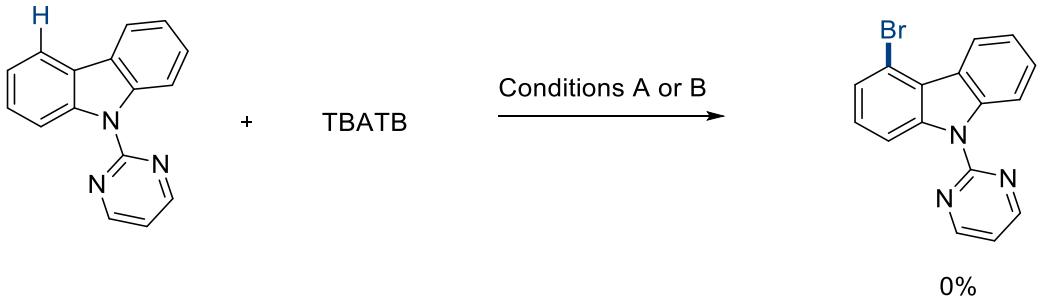
Scheme S2: Proposed Ruthenium-Catalysed C4-Sulfonation of *N*-pyrimidinylcarbazole



0%

A: $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $MesCO_2K$ (2 eq), 1,4-dioxane, 120 °C, 16 h
B: $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $MesCO_2K$ (2 eq), MeCN, 120 °C, 16 h
C: $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), K_2CO_3 (2 eq), MeCN, 120 °C, 16 h

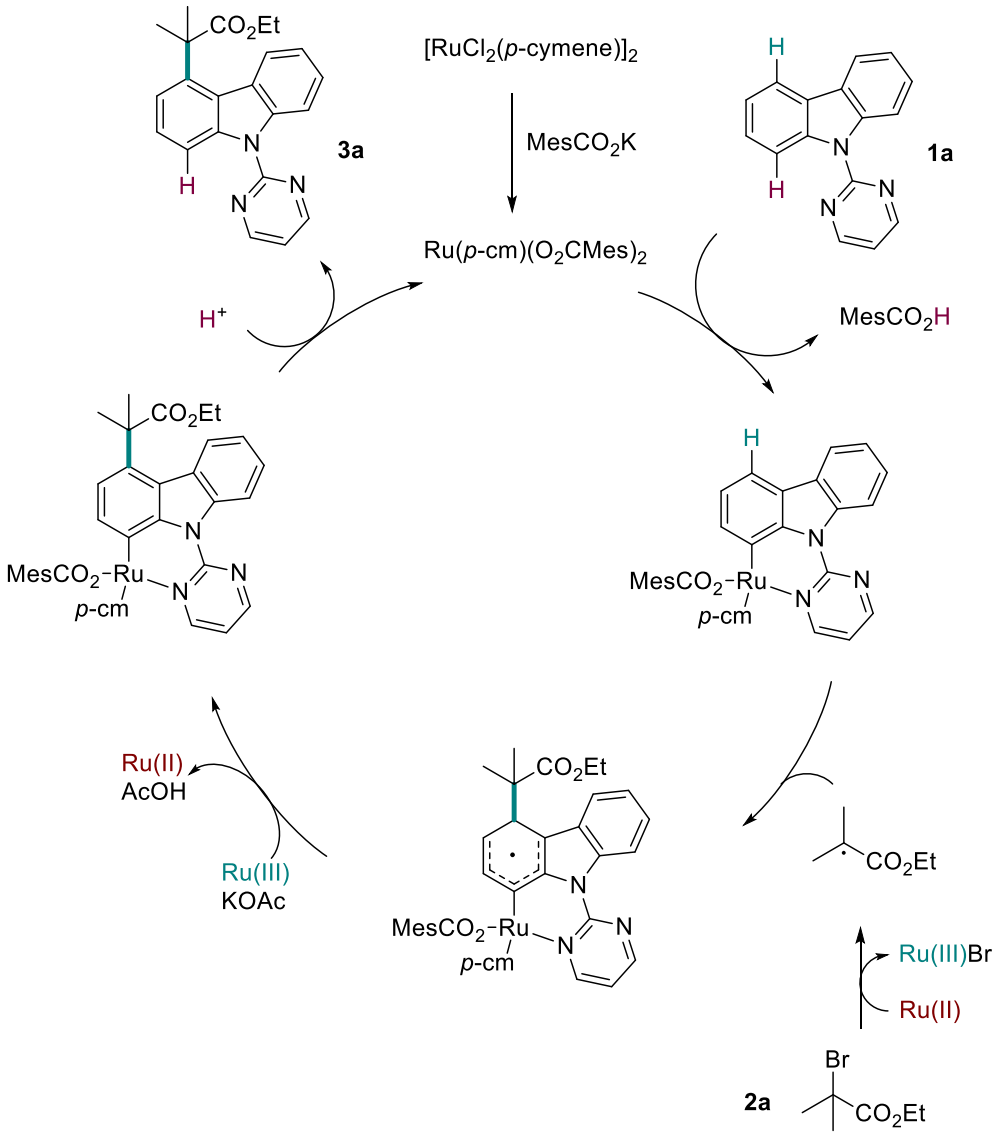
Scheme S3: Proposed Ruthenium-Catalysed C4-Bromination of *N*-pyrimidinylcarbazole



0%

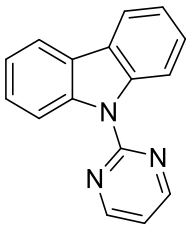
TBATB = tetrabutylammonium tribromide
A: $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $MesCO_2H$ (30 mol%), K_2CO_3 (2 eq), 1,4-dioxane, 120 °C, 16 h
B: $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $MesCO_2K$ (2 eq), AcOH (2 eq), 1,4-dioxane, 120 °C, 16 h

Scheme S4: Plausible Mechanism for the Remote C4-Selective C-H Alkylation of Carbazole Derivatives



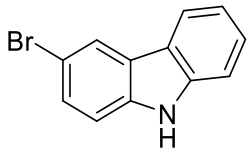
3. Synthesis of Starting Materials

Synthesis of 9-(pyrimidin-2-yl)-9*H*-carbazole (**1a**)



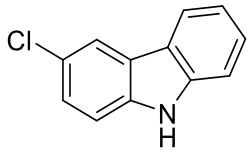
To a stirred solution of 9*H*-carbazole (1.67 g, 10 mmol) in DMF (10 mL) was added sodium hydride (60% wt. in mineral oil, 0.43 g, 11 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 1 hour. The reaction mixture was allowed to return to room temperature and 2-chloropyrimidine (1.38 g, 12 mmol) was added. The reaction mixture was heated to 150 °C overnight. After returning to room temperature the solution was poured into a separating funnel containing brine (150 mL). EtOAc (150 mL) was added and the organics were extracted. The resulting aqueous mixture was reextracted with EtOAc (2 x 150 mL). The combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified *via* silica gel column chromatography (EtOAc:Petroleum Spirit 40-60 °C, 10:90 v:v) to give a white powdery solid, **1a**, 32% (790 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.93–8.80 (4H, m, Ar*H*), 8.21–7.76 (2H, m, Ar*H*), 7.51 (2H, ddd, *J* = 8.5, 7.2, 1.3 Hz, Ar*H*), 7.38 (2H, ddd, *J* = 8.1, 7.2, 1.0 Hz, Ar*H*), 7.13 (1H, t, *J* = 4.7 Hz, Ar*H*). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.3 (Ar*C*), 158.0 (Ar*C*), 139.3 (Ar*C*), 126.7 (Ar*C*), 125.9 (Ar*C*), 122.4 (Ar*C*), 119.7 (Ar*C*), 116.4 (Ar*C*), 116.1 (Ar*C*). Data is in line with literature precedent.[1]

Synthesis of 3-bromo-9*H*-carbazole



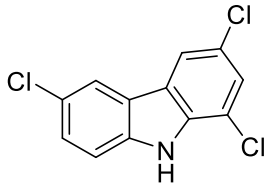
To a solution of 9*H*-carbazole (4 g, 24 mmol) in CH_2Cl_2 (75 mL) was added *N*-bromosuccinimide (4.25 g, 24 mmol) in DMF (8 mL) dropwise at room temperature. The reaction mixture was stirred for 4 hours before H_2O (100 mL) was added. The organic phase extracted, dried over $MgSO_4$, and concentrated *in vacuo*. The crude residue was purified *via* recrystallization from EtOH to give a crystalline white solid, 55% (3.26 g). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.43 (1H, s, N*H*), 8.35 (1H, dd, *J* = 2.0, 0.6 Hz, Ar*H*), 8.16 (1H, dt, *J* = 7.9, 1.1 Hz, Ar*H*), 7.53–7.45 (3H, m, Ar*H*), 7.42 (1H, ddd, *J* = 8.2, 7.1, 1.2 Hz, Ar*H*), 7.17 (1H,ddd, *J* = 8.0, 7.1, 1.0 Hz, Ar*H*). **^{13}C NMR** (126 MHz, DMSO-d_6) δ 140.1 (Ar*C*), 138.4 (Ar*C*), 127.8 (Ar*C*), 126.3 (Ar*C*), 124.4 (Ar*C*), 122.7 (Ar*C*), 121.4 (Ar*C*), 120.7 (Ar*C*), 118.9 (Ar*C*), 112.9 (Ar*C*), 111.2 (Ar*C*), 110.5 (Ar*C*). Data is in line with literature precedent.[2]

Synthesis of 3-chloro-9*H*-carbazole



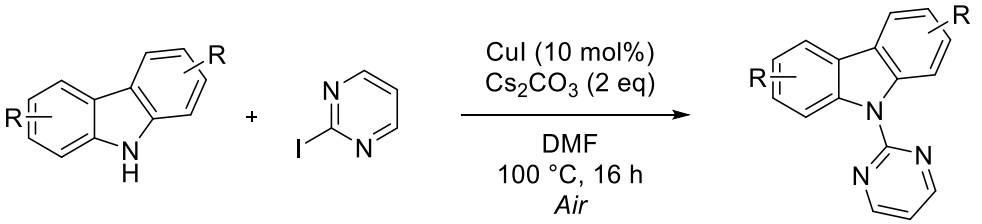
To a solution of 9*H*-carbazole (2 g, 12 mmol) in CH_2Cl_2 (20 mL) was added SO_2Cl_2 (1.0 mL, 800 mg, 12 mmol) dropwise at 0 °C. After addition was complete the reaction mixture was allowed to return to room temperature and stir overnight. The mixture was then diluted in CH_2Cl_2 (80 mL) and sat. $NaHCO_3$ solution (100 mL). The organic layer was separated and washed with aq. $NaHSO_3$ solution (100 mL), and brine (100 mL). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified *via* silica gel column chromatography (EtOAc:Petroleum Spirit 40-60 °C, 10:90 v:v) to give mono-chlorinated product as a powdery white solid, 37% (900 mg). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.41 (1H, s, N*H*), 8.22 (1H, d, *J* = 2.1 Hz, Ar*H*), 8.16 (1H, d, *J* = 7.8 Hz, Ar*H*), 7.50 (2H, dd, *J* = 8.4, 2.2 Hz, Ar*H*), 7.44–7.37 (2H, m, Ar*H*), 7.21–7.11 (1H, m, Ar*H*). **^{13}C NMR** (126 MHz, DMSO-d_6) δ 140.3 (Ar*C*), 138.1 (Ar*C*), 126.3 (Ar*C*), 125.2 (Ar*C*), 123.7 (Ar*C*), 122.8 (Ar*C*), 121.5 (Ar*C*), 120.7 (Ar*C*), 119.7 (Ar*C*), 118.8 (Ar*C*), 112.4 (Ar*C*), 111.2 (Ar*C*). Data is in line with literature precedent.[3]

Synthesis of 1,3,6-trichloro-9*H*-carbazole



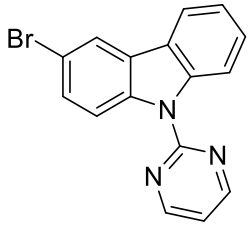
To a solution of 9*H*-carbazole (4 g, 24 mmol) in CH_2Cl_2 (40 mL) was added SO_2Cl_2 (4.0 mL, 6.4 g, 48 mmol) dropwise at 0 °C. After addition was complete the reaction mixture was allowed to return to room temperature and stir overnight. A further portion of SO_2Cl_2 (2.0 mL, 3.2 g, 24 mmol) was added at room temperature and allowed to stir for a further 4 hours. The mixture was then diluted in CH_2Cl_2 (80 mL) and sat. $NaHCO_3$ solution (200 mL). The organic layer was separated and washed with aq. $NaHSO_3$ solution (200 mL), and brine (200 mL). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified *via* silica gel column chromatography (EtOAc:Petroleum Spirit 40-60 °C, 10:90 v:v) to give di-chlorinated product as a powdery white solid, 42% (2.7 g). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.91 (1H, s, N*H*), 8.32 (2H, dd, *J* = 8.1, 2.0 Hz, Ar*H*), 7.61 (1H, d, *J* = 1.9 Hz, Ar*H*), 7.56 (1H, d, *J* = 8.6 Hz, Ar*H*), 7.48 (1H, dd, *J* = 8.7, 2.1 Hz, Ar*H*). **^{13}C NMR** (126 MHz, DMSO-d_6) δ 138.9 (Ar*C*), 135.9 (Ar*C*), 127.0 (Ar*C*), 125.0 (Ar*C*), 124.1 (Ar*C*), 124.0 (Ar*C*), 123.3 (Ar*C*), 123.0 (Ar*C*), 120.8 (Ar*C*), 119.5 (Ar*C*), 116.1 (Ar*C*), 113.3 (Ar*C*). Data is in line with literature precedent.[4]

General Procedure **A** for N-Arylation of Substituted Carbazoles



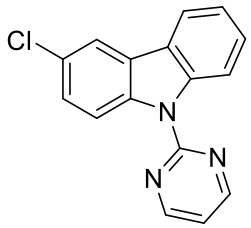
To an oven-dried carousel tube was charged relevant carbazole derivative (2 mmol), copper iodide (38 mg, 0.2 mmol, 20 mol%), caesium carbonate (1.3 g, 4 mmol) and 2-iodopyrimidine (824 mg, 4 mmol). The tube was sealed with a Teflon cap and anhydrous DMF (6 mL) was added *via* syringe. The reaction mixture was heated to 100 °C for 16 h. After this time the reaction mixture was allowed to return to room temperature. The mixture was diluted in EtOAc and filtered through a plug of celite, eluting with EtOAc. The filtrate was then concentrated *in vacuo*. The resulting crude residue was purified *via* silica gel column chromatography (EtOAc:Petroleum Spirit 40-60 °C, 10:90 v:v) to give desired arylated carbazole derivative. Note: The efficiency of this Ullmann reaction is directly affected by the quality of the 2-iodopyrimidine.

Synthesis of **1b**



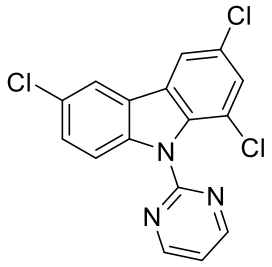
General Procedure **A** was followed using 3-bromo-9*H*-carbazole (492 mg, 2 mmol). Silica gel column chromatography gave a powdery white solid, 34% (220 mg). **mp** (from $CHCl_3$): 167-170 °C. **FT-IR** (thin film): ν_{max} (cm^{-1}) = 1581.7, 1558.2. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.96 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.77 (1H, d, *J* = 8.5 Hz, Ar*H*), 8.70 (1H, d, *J* = 8.9 Hz, Ar*H*), 8.45 (1H, d, *J* = 2.1 Hz, Ar*H*), 8.25 (1H, d, *J* = 7.7 Hz, Ar*H*), 7.62 (1H, dd, *J* = 8.9, 2.1 Hz, Ar*H*), 7.53 (1H, ddd, *J* = 8.4, 7.2, 1.3 Hz, Ar*H*), 7.43–7.34 (2H, m, Ar*H*). **^{13}C NMR** (126 MHz, DMSO-d_6) δ 158.6 (Ar*C*), 157.9 (Ar*C*), 138.7 (Ar*C*), 137.1 (Ar*C*), 129.0 (Ar*C*), 127.4 (Ar*C*), 127.0 (Ar*C*), 123.7 (Ar*C*), 122.5 (Ar*C*), 122.5 (Ar*C*), 120.4 (Ar*C*), 117.9 (Ar*C*), 117.2 (Ar*C*), 116.1 (Ar*C*), 114.60 (Ar*C*). **HRMS** (ESI): m/z calculated for $C_{16}H_{10}Br_1N_3$ requires 345.9950 for $[M+Na]^+$, found 345.9968.

Synthesis of **1c**



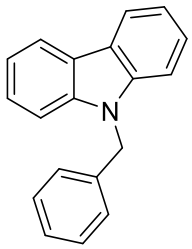
General Procedure **A** was followed using 3-chloro-9*H*-carbazole (403 mg, 2 mmol). Silica gel column chromatography gave a powdery white solid, 88% (492 mg). **mp** (from $CHCl_3$): 156-159 °C. **FT-IR** (thin film): ν_{max} (cm^{-1}) = 2980.9, 1582.9, 1558.1. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.98 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.78 (2H, dd, *J* = 8.7, 7.4 Hz, Ar*H*), 8.34 (1H, d, *J* = 2.2 Hz, Ar*H*), 8.30–8.25 (1H, m, Ar*H*), 7.61–7.49 (2H, m, Ar*H*), 7.47–7.33 (2H, m, Ar*H*). **^{13}C NMR** (126 MHz, DMSO-d_6) δ 158.7 (Ar*C*), 157.9 (Ar*C*), 138.8 (Ar*C*), 136.8 (Ar*C*), 127.5 (Ar*C*), 126.7 (Ar*C*), 126.5 (Ar*C*), 126.3 (Ar*C*), 123.9 (Ar*C*), 122.6 (Ar*C*), 120.4 (Ar*C*), 119.6 (Ar*C*), 117.5 (Ar*C*), 117.3 (Ar*C*), 116.2 (Ar*C*). **HRMS** (ESI): m/z calculated for $C_{16}H_{10}N_3Cl_1$ requires 280.0636 for $[M+H]^+$, found 280.0652.

Synthesis of **1d**



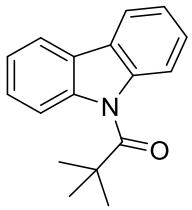
General Procedure **A** was followed using 1,3,6-trichloro-9*H*-carbazole (540 mg, 2 mmol). Silica gel column chromatography gave a powdery white solid, 41% (289 mg). **mp** (from $CHCl_3$): 175-179 °C. **FT-IR** (thin film): ν_{max} (cm^{-1}) = 2981.1, 1565.3. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.90 (2H, d, *J* = 4.8 Hz, Ar*H*), 7.94 (1H, dd, *J* = 19.7, 2.0 Hz, Ar*H*), 7.88 (1H, d, *J* = 8.8 Hz, Ar*H*), 7.48 (1H,d, *J* = 1.9 Hz, Ar*H*), 7.42 (1H, dd, *J* = 8.8, 2.1 Hz, Ar*H*), 7.33 (1H, t, *J* = 4.8 Hz, Ar*H*). **^{13}C NMR** (126 MHz,$CDCl_3$) δ 158.7 (Ar*C*), 157.3 (Ar*C*), 140.4 (Ar*C*), 135.7 (Ar*C*), 128.5 (Ar*C*), 128.3 (Ar*C*), 128.12 (Ar*C*), 128.08 (Ar*C*), 127.9 (Ar*C*), 124.9 (Ar*C*), 120.3 (Ar*C*), 120.2 (Ar*C*), 119.1 (Ar*C*), 118.9 (Ar*C*), 113.8 (Ar*C*). **HRMS** (ESI): m/z calculated for $C_{16}H_8N_3Cl_3$ requires 369.9684 for $[M+Na]^+$, found 369.9666.

Synthesis of 9-benzyl-9*H*-carbazole (**1e**)



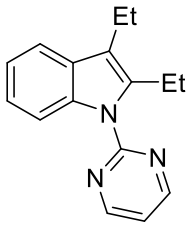
To a solution of 9*H*-carbazole (3 g, 18 mmol) in toluene (20 mL) was added sodium hydroxide (12 M in H_2O, 23 mL) and the reaction mixture allowed to stir at room temperature for 10 mins. After this time, tetebutylammonium iodide (650 mg, cat.) and subsequently benzyl bromide (2.6 mL, 3.69 g, 21.6 mmol) were added in one portion. The reaction mixture was left to stir overnight. The organic and aqueous phases were then separated and aqueous layer re-extracted with CH_2Cl_2 (2 x 50 mL). The combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified *via* recrystallization from EtOH to give a crystalline white solid, 81% (3.76 g). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (2H, dt, *J* = 7.8, 1.0 Hz, Ar*H*), 7.44 (2H, ddd, *J* = 8.3, 7.1, 1.2 Hz, Ar*H*), 7.38 (2H, dt, *J* = 8.2, 0.9 Hz, Ar*H*), 7.31–7.23 (4H, m, Ar*H*), 7.16 (2H, ddd, *J* = 7.6, 2.0, 1.0 Hz, Ar*H*), 5.52 (2H, s, C*H*$_2$Ph). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.8 (Ar*C*), 137.3 (Ar*C*), 128.9 (Ar*C*), 127.6 (Ar*C*), 126.5 (Ar*C*), 126.0 (Ar*C*), 123.2 (Ar*C*), 120.5 (Ar*C*), 119.3 (Ar*C*), 109.0 (Ar*C*), 46.68 (*C*H_2Ph). Data is in line with literature precedent.[5]

Synthesis of 1-(9*H*-carbazol-9-yl)-2,2-dimethylpropan-1-one (**1f**)



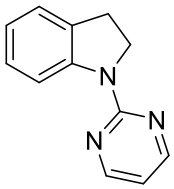
To a stirred solution of 9*H*-carbazole (1.67 g, 10 mmol), triethylamine (2.1 mL, 1.52 g, 15 mmol), and *N',N'*-dimethylaminopyridine (DMAP, 122 mg, 1 mmol) in anhydrous CH_2Cl_2 (30 mL) was added trimethylacetyl chloride (pivaloyl chloride, 1.5 mL, 1.45 g, 12 mmol) dropwise at 0 °C. After addition was complete, the reaction mixture was allowed to return to room temperature and stirred overnight. The reaction mixture was concentrate *in vacuo*, and the resulting residue was partitioned between EtOAc (100 mL) and brine (100 mL). The organic layer was extracted and the aqueous phase was re-extracted with EtOAc (2 x 100 mL). The combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. The resulting residue was purified *via* silica gel column chromatography (EtOAc:Petroleum Spirit, 5:95 v:v) to give (on standing at 4 °C overnight) a crystalline white solid, 65% (1.62 g). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (2H, dd, *J* = 7.6, 1.4 Hz, Ar*H*), 7.75–7.63 (2H, m, Ar*H*), 7.45 (2H, ddq, *J* = 8.3, 7.1, 1.3 Hz, Ar*H*), 7.37–7.29 (2H, m, Ar*H*), 1.54 (6H, app d, Piv*H*). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 184.2 (C*O*t*B*u), 139.4 (Ar*C*), 126.5 (Ar*C*), 124.9 (Ar*C*), 122.0 (Ar*C*), 120.2 (Ar*C*), 113.9 (Ar*C*), 43.9 (*C*(CH_3)$_3$), 28.5 (C(*C*H_3)$_3$). Data is in line with literature precedent.[6]

Synthesis of 2,3-diethyl-1-(pyrimidin-2-yl)-1*H*-indole (**4a**)



To an oven dried carousel tube was charged *N*-(2-bromophenyl)pyrimidin-2-amine (62.5 mg, 0.25 mmol), palladium(II) acetate (5.6 mg, 0.025 mmol), lithium chloride (1.1 mg, 0.025 mmol) and sodium carbonate (132 mg, 1.25 mmol). The reactor tube was evacuated and refilled with argon three times. Dimethylformamide (1 mL) and hex-3-yne (0.085 mL, 0.75 mmol) were then added *via* septum. The vessel was heated to 100 ^{o}C for 16 hours. Then the reaction mixture was cooled to room temperature, and EtOAc and 5 % LiCl solution (100 mL) were added. The organic layer was separated and the aqueous was washed with further EtOAc (3 × 100 mL). The organic layer was dried over $MgSO_4$ and the solvents were removed under vacuum. The resulting residue was purified by silica gel column chromatography (EtOAc:Petroleum Ether 40-60 °C, 5:95 v:v) to give as an orange oil in 56 % yield (35 mg). **FT-IR:** (thin film): vmax (cm^{-1}) = 3044, 2963, 2929, 2871, 2160, 2008, 1694, 1560, 1455, 1422. **^{1}H NMR:** (500 MHz, $CDCl_3$) δ 8.79 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.22 (1H, d, *J* = 7.1 Hz, Ar*H*), 7.54 (1H, d, *J* = 6.7 Hz, Ar*H*), 7.24–7.16 (2H, m, Ar*H*), 7.12 (1H, t, *J* = 4.8 Hz, Ar*H*), 3.19 (2H, q, *J* = 7.4 Hz, CH_2CH$_3$), 2.78 (2H, q, *J* = 7.6 Hz, CH_2CH$_3$), 1.28 (3H, t, *J* = 7.5 Hz, CH$_2$CH_3), 1.11 (3H, t, *J* = 7.4 Hz, CH$_2$CH_3). **^{13}C NMR:** (126 MHz, $CDCl_3$) δ 165.8 (Ar*C*), 158.1 (Ar*C*), 138.3 (Ar*C*), 136.4 (Ar*C*), 129.6 (Ar*C*), 122.5 (Ar*C*), 121.3 (Ar*C*), 118.8 (Ar*C*), 118.0 (Ar*C*), 116.7 (Ar*C*), 113.5 (Ar*C*), 19.3 (*C*H$_2$CH$_3$) , 17.4 (*C*H$_2$CH$_3$), 15.4 (CH$_2$*C*H$_3$), 15.0 (CH$_2$*C*H$_3$). **HRMS:** (ESI): m/z calculated for $C_{16}H_{17}N_4$ required 274.1315 for $[M+Na]^+$ and found 274.1302.

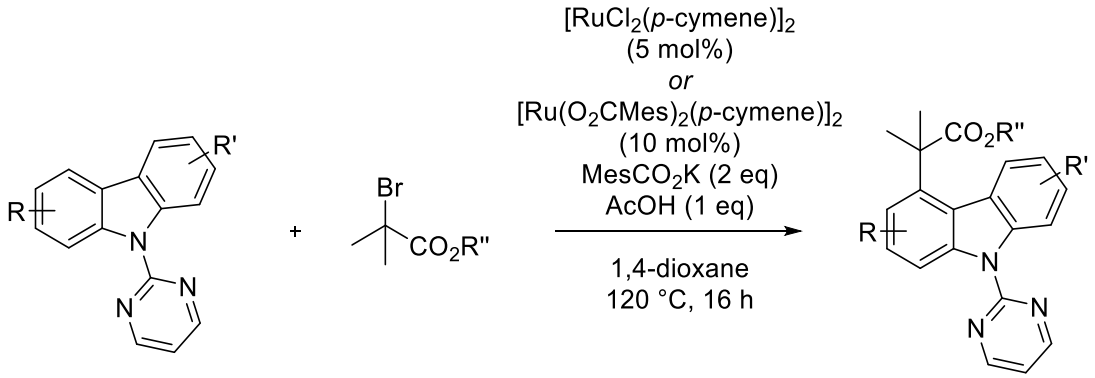
Synthesis of 1-(pyrimidin-2-yl)indoline (**4b**)



To a solution of indoline (0.56 mL, 5 mmol) and 2-chloropyrimidine (0.69 g, 5 mmol) in EtOH (40 mL) and water (20 mL) was added conc. HCl (1 mL). The reaction mixture was then refluxed overnight. The EtOH and water were then removed *in vacuo*. The crude residue was partitioned between water (100 mL) and CH_2Cl_2 (100 mL) and the organic layer extracted. The aqueous layer was re-extracted with CH_2Cl_2 (2 x 100 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified *via* silica gel column chromatography to give a bronze oil, 65% (0.632 g). **FT-IR** (thin film): ν_{max} (cm^{-1}) = 3041.9, 2955.9, 1557.0, 1548.0. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.49 (2H, d, *J* = 4.7 Hz, Ar*H*), 8.40 (1H, d, *J* = 8.1 Hz, Ar*H*), 7.25–7.18 (2H, m, Ar*H*), 6.94 (1H, td, *J* = 7.4, 1.1 Hz, Ar*H*), 6.68 (1H, t, *J* = 4.8 Hz, Ar*H*), 4.24 (2H, dd, *J* = 9.2, 8.2 Hz, C*H*$_2$), 3.31–3.13 (2H, m, C*H*$_2$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.57 (Ar*C*), 143.74 (Ar*C*), 132.31 (Ar*C*), 127.38 (Ar*C*), 124.74 (Ar*C*), 121.63 (Ar*C*), 115.46 (Ar*C*), 111.52 (Ar*C*), 48.87 (*C*H$_2$), 27.41 (*C*H$_2$). **HRMS** (ESI): m/z calculated for $C_{12}H_{11}N_3$ requires 220.0853 for $[M+Na]^+$, found 220.0891.

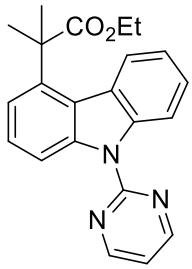
4. Synthesis of C4-Functionalized Carbazoles

General Procedure **B** for the Remote C4-Alkylation of Carbazole Derivatives



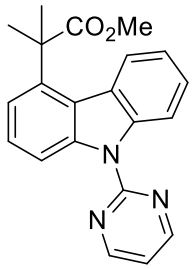
To an oven dried carousel tube was charged with relevant carbazole derivative (0.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (8 mg, 0.0125 mmol, 5 mol%) or $[Ru(O_2CMes)_2(p\text{-cymene})]$ (14 mg, 0.025 mmol, 10 mol%), and potassium 2,4,6-trimethylbenzoate ($MesCO_2K$, 102 mg, 0.5 mmol). The reaction vessel was then sealed with a Teflon cap, and then evacuated and refilled with Argon three times. 1,4-dioxane (1 mL), acetic acid (0.015 mL, 15 mg, 0.25 mmol) and relevant coupling partner (0.75 mmol) were added *via* syringe. The flask was then heated at 120 °C for 16 h. The reaction mixture was allowed to return to room temperature and was then diluted in EtOAc (20 mL) and sat. $NaHCO_3$ solution (20 mL). The organic layer was extracted and the aqueous layer was re-extracted with EtOAc (2 x 20 mL). The combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was then purified *via* silica gel column chromatography (EtOAc:Petroleum Spirit 40-60 °C, 10:90-20:80 v:v), to give pure C4-alkylated structures.

Synthesis of **3a**



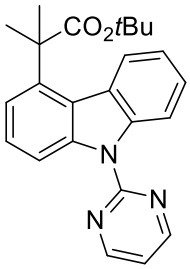
General Procedure **B** was followed using **1a** (61 mg, 0.25 mmol) and ethyl α-bromoisobutyrate (0.12 mL, 146 mg, 0.75 mmol). Silica gel column chromatography gave a white solid. $[RuCl_2(p\text{-cymene})]_2$ as catalyst: 68% (61 mg). $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalyst: 76% (68 mg). **mp** (from $CHCl_3$): 127-129 ^oC. **mp** (from $CHCl_3$): 130-133 °C. **FT-IR:** (thin film): vmax (cm^{-1}) = 3040, 2983, 2874, 2164, 1725, 1580, 1564, 1427. **^{1}H NMR:** (500 MHz, $CDCl_3$) δ 8.87 (2H, d, *J* = 4.78 Hz, Ar*H*), 8.69 (2H, d, *J* = 8.37 Hz, Ar*H*), 8.02 (1H, d, *J* = 8.11 Hz, Ar*H*), 7.46 (3H, m, Ar*H*), 7.32 (1H, t, *J* = 7.63 Hz, Ar*H*), 7.17 (1H, t, *J* = 4.77 Hz, Ar*H*), 4.04 (2H, q, *J* = 7.10 Hz, $CO_2CH_2CH_3$), 1.88 (6H, s, $C(CH_3)_2$), 0.95 (3H, t, *J* = 7.11 Hz, $CO_2CH_2CH_3$). **^{13}C NMR:** (126 MHz, $CDCl_3$) δ 178.3 (CO_2Et), 158.7 (Ar*C*), 158.0 (Ar*C*), 140.0 (Ar*C*), 139.5 (Ar*C*), 139.0 (Ar*C*), 126.0 (Ar*C*), 125.7 (Ar*C*), 124.5 (Ar*C*), 123.5 (Ar*C*), 123.2 (Ar*C*), 121.8 (Ar*C*), 119.5 (Ar*C*), 116.7 (Ar*C*), 114.4 (Ar*C*), 113.7 (Ar*C*), 61.1 ($CO_2CH_2CH_3$), 47.0 ($C(CH_3)_2$), 27.0 ($C(CH_3)_2$), 13.9 ($CO_2CH_2CH_3$). **HRMS:** (ESI): found m/z calculated for $C_{22}H_{21}N_3O_2$ required 360.1707 for $[M+H]^+$, found 360.1715.

Synthesis of **3aa**



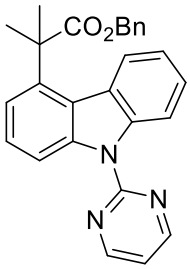
General Procedure **B** was followed using **1a** (61 mg, 0.25 mmol) and methyl α-bromoisobutyrate (0.10 mL, 136 mg, 0.75 mmol). Silica gel column chromatography gave a white solid, $[RuCl_2(p\text{-cymene})]_2$ as catalyst: 70% (60 mg). $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalyst: 65% (56 mg). **FT-IR** (thin film): ν_{max} (cm^{-1}) = 2981.1, 1726.1, 1561.3. **mp** (from $CHCl_3$): 162-165 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.85 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.74–8.66 (2H, m, Ar*H*), 7.54–7.45 (1H, m, Ar*H*), 7.45–7.41 (2H, m, Ar*H*), 7.38–7.32 (1H, m, Ar*H*), 7.14 (1H, t, *J* = 4.8 Hz, Ar*H*), 3.53 (3H, s, CO_2CH_3), 1.91 (6H, s, $C(CH_3)_2$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.1 (CO_2Me), 158.8 (Ar*C*), 158.2 (Ar*C*), 140.1 (Ar*C*), 139.5 (Ar*C*), 139.1 (Ar*C*), 126.1 (Ar*C*), 125.9 (Ar*C*), 124.6 (Ar*C*), 123.3 (Ar*C*), 123.2 (Ar*C*), 122.1 (Ar*C*), 119.5 (Ar*C*), 116.9 (Ar*C*), 114.6 (Ar*C*), 114.0 (Ar*C*), 52.65 (CO_2CH_3), 47.1 ($C(CH_3)_2$), 27.2 ($C(CH_3)_2$). **HRMS** (ESI): m/z calculated for $C_{21}H_{19}N_3O_2$ requires 346.1550 for $[M+H]^+$, found 346.1583.

Synthesis of **3ab**



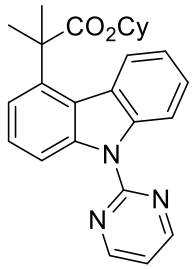
General Procedure **B** was followed using **1a** (61 mg, 0.25 mmol) and *tert*-butyl α-bromoisobutyrate (0.14 mL, 167 mg, 0.75 mmol). Silica gel column chromatography gave a white solid, $[RuCl_2(p\text{-cymene})]_2$ as catalyst: 72% (69 mg). $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalyst: 92% (89 mg). **mp** (from $CHCl_3$): 180-183 °C. **FT-IR** (thin film): ν_{max} (cm^{-1}) = 2980.8, 1717.2, 1561.2 **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.84 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.72–8.63 (2H, m, Ar*H*), 8.18–8.15 (1H, m, Ar*H*), 7.50–7.43 (1H, m, Ar*H*), 7.40 (1H, dd, *J* = 7.7, 1.0 Hz, Ar*H*), 7.36–7.31 (1H, m, Ar*H*), 7.13 (1H, t, *J* = 4.8 Hz, Ar*H*), 1.86 (6H, s, $C(CH_3)_2$), 1.27 (9H, s, $C(CH_3)_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.2 (CO_2R), 158.8 (Ar*C*), 158.1 (Ar*C*), 140.1 (Ar*C*), 140.1 (Ar*C*), 139.1 (Ar*C*), 126.0 (Ar*C*), 125.8 (Ar*C*), 124.6 (Ar*C*), 124.5 (Ar*C*), 123.3 (Ar*C*), 121.7 (Ar*C*), 119.7 (Ar*C*), 116.7 (Ar*C*), 114.4 (Ar*C*), 113.6 (Ar*C*), 80.9 (Alk*C*), 47.8 (Alk*C*) , 27.8 (Alk*C*), 26.9 (Alk*C*). **HRMS** (ESI): m/z calculated for $C_{24}H_{25}N_3O_2$ requires 388.1947 for $[M+H]^+$, found 388.2069.

Synthesis of **3ac**



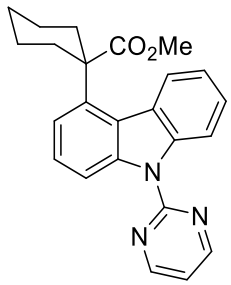
General Procedure **B** was followed using **1a** (61 mg, 0.25 mmol) and benzyl α-bromoisobutyrate (0.13 mL, 178 mg, 0.75 mmol). Silica gel column chromatography gave a white solid, $[RuCl_2(p\text{-cymene})]_2$ as catalyst: 51% (54 mg). $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalyst: 74% (78 mg). **mp** (from $CHCl_3$): 112-116 °C. **FTIR** (thin film): ν_{max} = 2968, 1718, 1583, 1563. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.88 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.69 (2H, dd, *J* = 8.3, 1.1 Hz, Ar*H*), 7.96 (1H, ddd, *J* = 8.2, 1.2, 0.6 Hz, Ar*H*), 7.48 (1H, dd, *J* = 8.4, 7.6 Hz, Ar*H*), 7.43-7.40 (2H, m, Ar*H*), 7.22-7.15 (5H, m, Ar*H*), 7.02-6.99 (2H, m, Ar*H*), 5.02 (2H, s, CH_2Ph), 1.90 (6H, s, $C(CH_3)_2$). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* 178.4 (CO_2Bn), 163.5 (Ar*C*), 158.4 (Ar*C*), 139.6 (Ar*C*), 139.1 (Ar*C*), 128.6 (Ar*C*), 128.2 (Ar*C*), 126.4 (Ar*C*), 126.0 (Ar*C*), 125.9 (Ar*C*), 124.8 (Ar*C*), 123.6 (Ar*C*), 123.5 (Ar*C*), 122.3 (Ar*C*), 119.9 (Ar*C*), 117.1 (Ar*C*), 114.8 (Ar*C*), 114.2 (Ar*C*), 67.2 CO_2CH_2Ph), 47.4 ($C(CH_3)_2$), 27.4 ($C(CH_3)_2$). **HRMS** (ESI): m/z calculated for $C_{27}H_{23}N_3O_2$ requires 422.1870 for $[M+H]^+$ found 422.1943.

Synthesis of **3ad**



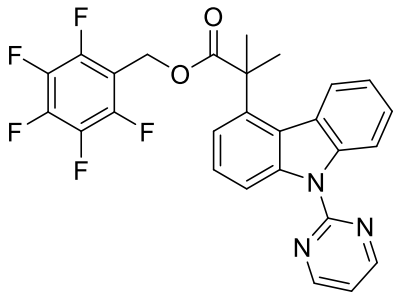
General Procedure **B** was followed using **1a** (61 mg, 0.25 mmol) and cyclohexyl α-bromoisobutyrate (147 mg, 0.75 mmol). Silica gel column chromatography gave an amorphous solid, $[RuCl_2(p\text{-cymene})]_2$ as catalyst: 54% (56 mg). $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalyst: 74% (76 mg). **FTIR** (thin film): ν_{max} = 2929, 2855, 1718, 1570. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.88 (2H, d, *J* = 4.8 Hz,Ar*H*), 8.68 (2H, ddd, *J* = 8.4, 3.4, 1.0 Hz, Ar*H*), 8.05 (1H, dd, *J* = 8.2, 1.1 Hz, Ar*H*), 7.49-7.44 (2H, m, Ar*H*), 7.43-7.39 (1H, m, Ar*H*), 7.30 (1H, ddd, *J* = 8.2, 7.2, 1.1 Hz, Ar*H*), 7.14 (1H, m, Ar*H*), 4.81-4.73 (1H, m, CO_2CH), 1.87 (6H, s, $C(CH_3)_2$), 1.56 (3H, broad s, Cy*H*), 1.45-1.32 (3H, m, Cy*H*), 1.22-1.00 (4H, m, Cy*H*). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 178.2 (CO_2Cy), 163.3 (Ar*C*), 158.2 (Ar*C*), 139.4 (Ar*C*), 135.9 (Ar*C*), 128.4 (Ar*C*), 128.0 (Ar*C*), 126.2 (Ar*C*), 125.8 (Ar*C*), 124.6 (Ar*C*), 123.4 (Ar*C*), 122.1 (Ar*C*), 119.7 (Ar*C*), 116.9 (Ar*C*), 114.6 (Ar*C*), 114.0 (Ar*C*), 67.0 (CO_2CH), 47.2 ($C(CH_3)_2$), 27.2 ($C(CH_3)_2$), 27.1 (Cy*C*), 25.3 (Cy*C*), 24.6 (Cy*C*). **HRMS** (ESI): m/z calculated for $C_{26}H_{27}N_3O_2$ requires 436.1995 for $[M+Na]^+$ found 436.2027.

Synthesis of **3af**



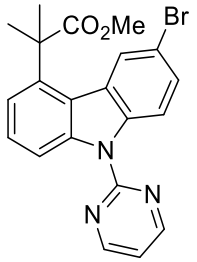
General Procedure **B** was followed using **1a** (61 mg, 0.25 mmol) and methyl 1-bromocyclohexane-1-carboxylate (0.12 mL, 166 mg, 0.75 mmol). Silica gel column chromatography gave a white solid, $[RuCl_2(p\text{-cymene})]_2$ as catalyst: 35% (34 mg). $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalyst: 42% (40 mg). **mp** (from $CHCl_3$): 182-185 °C. **FTIR** (thin film): ν_{max} = 2955, 2932, 2362, 2165, 2034, 1718, 1560. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.89 (d, *J* = 4.8 Hz, 2H), 8.66–8.61 (2H, m, Ar*H*), 8.10–8.06 (1H, m, Ar*H*), 7.52–7.46 (2H, m, Ar*H*), 7.45 (1H, ddd, *J* = 8.4, 7.1, 1.2 Hz, Ar*H*), 7.45 (1H, ddd, *J* = 8.3, 7.1, 1.2 Hz, Ar*H*), 7.20 (1H, t, *J* = 4.8 Hz, Ar*H*), 3.49 (3H, s, CO_2CH_3), 2.48 (5H, s, Cy*H*), 1.81 (3H, s, Cy*H*), 1.26 (2H, s, Cy*H*). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.6 (CO_2Me), 158.3 (Ar*C*), 140.5 (Ar*C*), 139.1 (Ar*C*), 138.5 (Ar*C*), 125.9 (Ar*C*), 125.8 (Ar*C*), 124.7 (Ar*C*), 124.2 (Ar*C*), 123.4 (Ar*C*), 122.0 (Ar*C*), 121.9 (Ar*C*), 117.0 (Ar*C*), 114.3 (Ar*C*), 113.5 (Ar*C*), 52.5 (CO_2CH_3), 50.9 (*C*(Cy)), 34.0 (Cy*C*), 25.9 (Cy*C*), 22.8 (Cy*C*). **HRMS** (ESI): m/z calculated for $C_{24}H_{23}N_3O_2$ requires 386.1870 for $[M+H]^+$ found 386.1922.

Synthesis of **3ah**



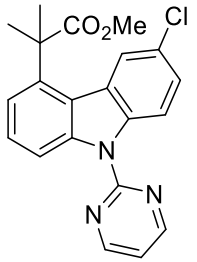
General Procedure **B** was followed using **1a** (61 mg, 0.25 mmol) and (perfluorophenyl)methyl-2-bromo-2-methylpropanoate (260 mg, 0.75 mmol),. Silica gel column chromatography gave a white solid, $[RuCl_2(p\text{-cymene})]_2$ as catalyst: 41% (52 mg). $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalyst: 39% (50 mg). **mp** (from $CHCl_3$): 165-168 ^oC. **FTIR** (thin film): ν_{max} = 2959, 1742, 1661, 1570, 1509. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.88 (2H, d, J = 4.8 Hz, Ar*H*), 8.69 (2H, dd, J = 10.8, 8.4 Hz, Ar*H*), 7.78 (1H, d, J = 8.1 Hz, Ar*H*), 7.49 (1H, t, J = 8.0 Hz, Ar*H*), 7.43-7.38 (2H, m, Ar*H*), 7.18 (1H, t, J = 4.8 Hz, Ar*H*), 7.12 (1H, t, J = 7.6 Hz, Ar*H*), 5.06 (2H, s, CH_2Ar), 1.89 (6H, s, (C(CH_3)$_2$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.8 (*C*O_2R), 158.8 (Ar*C*), 158.2 (Ar*C*), 145.5 (dddd, J = 251.3, 11.3, 7.7, 4.0 Hz, Ar_FC), 143.0–140.2 (m, Ar_FC), 140.1 (Ar*C*), 139.0 (Ar*C*), 138.8 (Ar*C*), 138.4–135.7 (Ar_FC), 126.3 (Ar*C*), 125.6 (Ar*C*), 124.1 (Ar*C*), 123.0 (Ar*C*), 122.9 (Ar*C*), 121.5 (Ar*C*), 119.5 (Ar*C*), 116.9 (Ar*C*), 114.7 (Ar*C*), 114.2 (Ar*C*), 109.2 (td, J = 17.5, 3.7 Hz, Ar_FC), 53.9 (*C*H_2R), 47.1 (*C*(CH_3)$_2$), 29.8 (C(*C*H_3)$_2$). **^{19}F NMR** (470 MHz, $CDCl_3$): δ -141.85 (2F, dd, J = 22.4, 8.3 Hz, o-*F*), -153.06 (1F, s, *p*-F), -161.99 (2F, m, *m*-F). **HRMS** (ESI): m/z calculated for $C_{27}H_{18}F_5N_3O_2$ requires 512.1392 for $[M+H]^+$ found 512.1426.

Synthesis of **3b**



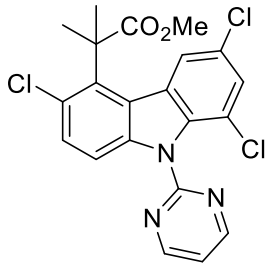
General Procedure **B** was followed using **1b** (81 mg, 0.25 mmol) and methyl α-bromoisobutyrate (0.1 mL, 136 mg, 0.75 mmol). Silica gel column chromatography gave a white solid, 54% (57 mg). **FT-IR** (thin film): ν_{max} (cm^{-1}) = 2981.2, 1727.8, 1567.3. **mp** (from $CHCl_3$): 183-185 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.81 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.71 (1H, dd, *J* = 8.4, 1.0 Hz, Ar*H*), 8.62 (1H, d, *J* = 8.9 Hz, Ar*H*), 8.09 (1H, d, *J* = 1.9 Hz, Ar*H*), 7.55 (1H, dd, *J* = 9.0, 1.9 Hz, Ar*H*), 7.52 (1H, dd, *J* = 8.5, 7.6 Hz, Ar*H*), 7.43 (1H, dd, *J* = 7.7, 1.0 Hz, Ar*H*), 7.14 (1H, t, *J* = 4.8 Hz, Ar*H*), 3.68 (3H, s, CO_2CH_3), 1.89 (6H, s, $C(CH_3)_2$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.3 (CO_2Me), 158.5 (Ar*C*), 158.2 (Ar*C*), 140.5 (Ar*C*), 139.8 (Ar*C*), 137.8 (Ar*C*), 128.4 (Ar*C*), 126.9 (Ar*C*), 126.4 (Ar*C*), 125.7 (Ar*C*), 122.1 (Ar*C*), 119.8 (Ar*C*), 117.0 (Ar*C*), 116.4 (Ar*C*), 115.0 (Ar*C*), 114.4 (Ar*C*), 52.6 (CO_2CH_3), 47.1 ($C(CH_3)_2$), 27.1 ($C(CH_3)_2$). **HRMS** (ESI): m/z calculated for $C_{21}H_{18}N_3O_2Br_1$ requires 446.0482 for $[M+Na]^+$, found 446.0554.

Synthesis of **3c**



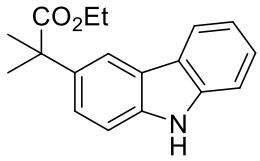
General Procedure **B** was followed using **1c** (70 mg, 0.25 mmol) and methyl α-bromoisobutyrate (0.1 mL, 136 mg, 0.75 mmol). Silica gel column chromatography gave a white solid, 60% (57 mg). **mp** (from $CHCl_3$): 200-203 °C. **FT-IR** (thin film): ν_{max} (cm^{-1}) = 2981.2, 1727.8, 1567.3. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.82 (2H, d, *J* = 4.8 Hz, Ar*H*), 8.69 (2H, dd, *J* = 23.7, 8.9 Hz, Ar*H*), 7.95 (1H, s, Ar*H*), 7.51 (1H, d, *J* = 8.3 Hz, Ar*H*), 7.47–7.37 (2H, m, Ar*H*), 7.14 (1H, d, *J* = 4.9 Hz, Ar*H*), 3.66 (3H, s, CO_2CH_3), 1.89 (6H, s, $C(CH_3)_2$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.3 (CO_2Me), 158.5 (Ar*C*), 158.2 (Ar*C*), 140.6 (Ar*C*), 139.7 (Ar*C*), 137.5 (Ar*C*), 127.4 (Ar*C*), 126.9 (Ar*C*), 125.8 (Ar*C*), 125.7 (Ar*C*), 122.7 (Ar*C*), 122.3 (Ar*C*), 119.8 (Ar*C*), 117.0 (Ar*C*), 116.0 (Ar*C*), 114.4 (Ar*C*), 52.6 (CO_2CH_3), 47.1 ($C(CH_3)_2$), 27.1 ($C(CH_3)_2$). **HRMS** (ESI): m/z calculated for $C_{21}H_{18}N_3O_2Cl_1$ requires 402.0988 for $[M+Na]^+$, found 402.0918.

Synthesis of **3d**



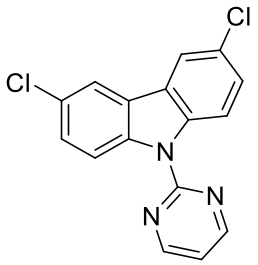
General Procedure **B** was followed using **1d** (87 mg, 0.25 mmol) and methyl α-bromoisobutyrate (0.1 mL, 136 mg, 0.75 mmol). Silica gel column chromatography gave a white solid, 10% (11 mg). **FT-IR** (thin film): ν_{max} (cm^{-1}) = 2950.9, 1731.1, 1566.7. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.92 (2H, d, *J* = 4.9 Hz, Ar*H*), 8.03 (1H, d, *J* = 1.8 Hz, Ar*H*), 7.59 (1H, d, *J* = 8.9 Hz, Ar*H*), 7.45–7.41 (2H, m, Ar*H*), 7.38 (1H, t, *J* = 4.9 Hz, Ar*H*), 3.63 (3H, s, CO_2CH_3), 2.08 (6H, s, $C(CH_3)_2$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.2 (*C*O_2Me), 158.9 (Ar*C*), 137.0 (Ar*C*), 131.7 (Ar*C*), 127.7 (Ar*C*), 127.4 (Ar*C*), 126.8 (Ar*C*), 123.9 (Ar*C*), 122.8 (Ar*C*), 119.8 (Ar*C*), 119.2 (Ar*C*), 111.8 (Ar*C*), 52.69 (CO_2CH_3), 50.0 ($C(CH_3)_2$), 27.8 ($C(CH_3)_2$). **HRMS** (ESI): m/z calculated for $C_{21}H_{16}N_3O_2Cl_3$ requires 470.0200 for $[M+Na]^+$, found 470.0162.

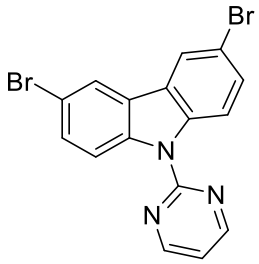
Synthesis of **3g**



General Procedure **B** was followed using 9*H*-carbazole, **16** (87 mg, 0.25 mmol) and ethyl α-bromoisobutyrate (0.11 mL, 146 mg, 0.75 mmol). Silica gel column chromatography gave an amorphous solid, 14% (10 mg). **FT-IR** (thin film): ν_{max} (cm^{-1}) = 3419.2, 2928.7, 1715.5. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.11–8.05 (2H, m, Ar*H*), 8.03 (1H, s, N*H*), 7.45–7.33 (4H, m, Ar*H*), 7.23 (1H, ddd, *J* = 8.0, 4.8, 3.4 Hz, Ar*H*), 4.14 (2H, q, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 1.70 (6H, s, $C(CH_3)_2$), 1.18 (3H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.5 (*C*O_2Et), 140.1 (Ar*C*), 138.4 (Ar*C*), 136.3 (Ar*C*), 126.0 (Ar*C*), 124.1 (Ar*C*), 123.6 (Ar*C*), 123.4 (Ar*C*), 120.4 (Ar*C*), 119.6 (Ar*C*), 117.2 (Ar*C*), 110.78 (Ar*C*), 110.5 (Ar*C*), 60.9 ($CO_2CH_2CH_3$), 46.5 ($C(CH_3)_2$), 27.2 ($C(CH_3)_2$), 14.2 ($CO_2CH_2CH_3$). **HRMS** (ESI) m/z calculated for $C_{18}H_{19}N_1O_2$ requires 304.1316 for $[M+Na]^+$, found 304.1340.

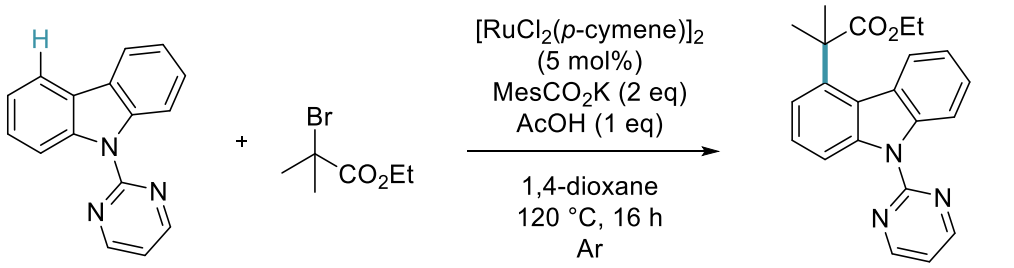
Bromo and chloro disubstituted compounds were not amenable to the Ullmann coupling proceeding in low yields, due to perceived lack of solubility under the conditions. The small amounts brought through from these reactions were also not amenable to the C4-alkylation methodology, again due to lack of solubility.





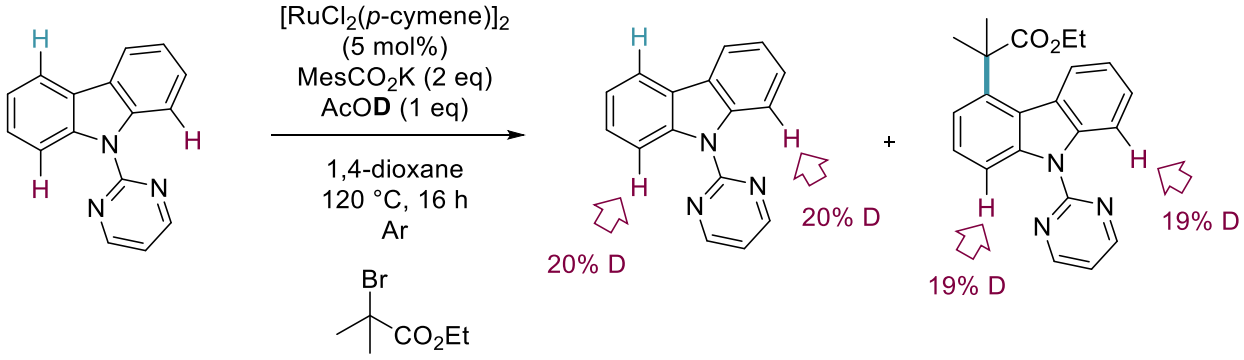
5. Mechanistic Studies

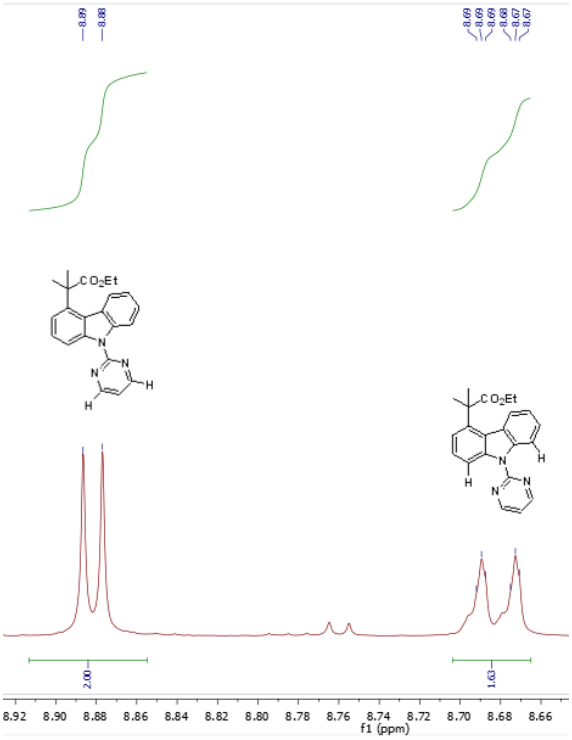
TEMPO Studies



TEMPO (30 mol%) - 66%
TEMPO (100 mol%) - 15%

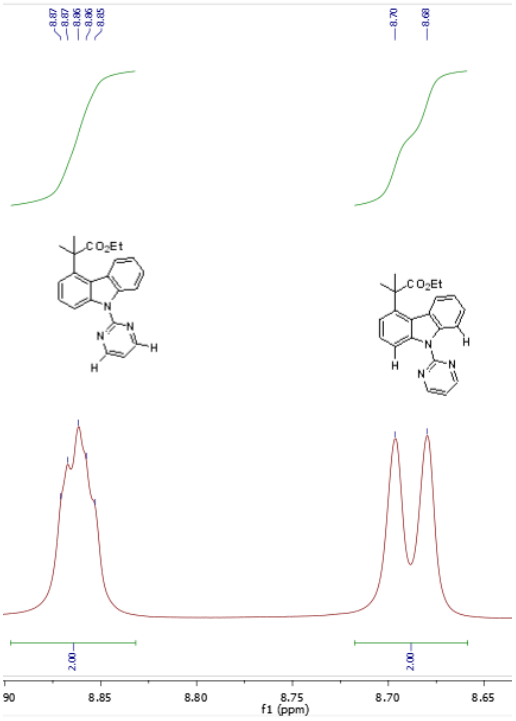
Deuterium Experiments



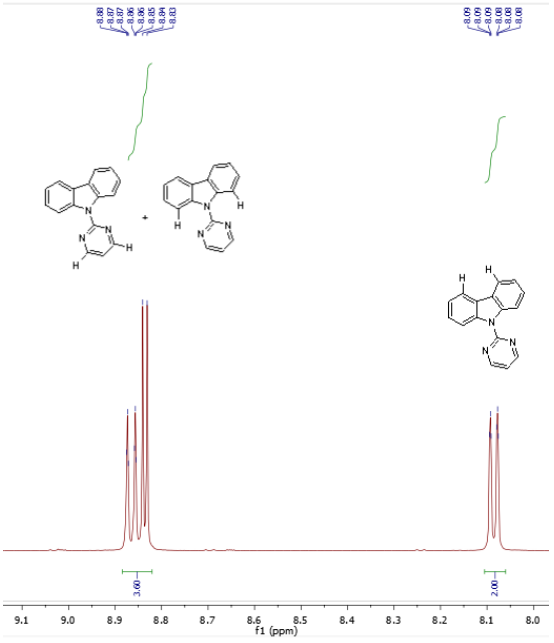


Product from D-Experiment

D incorporation = 18.5%

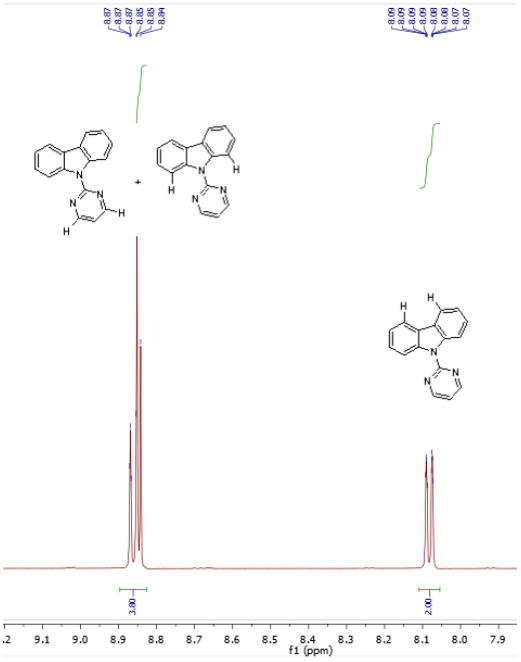


NMR 3a



Product from D-Experiment

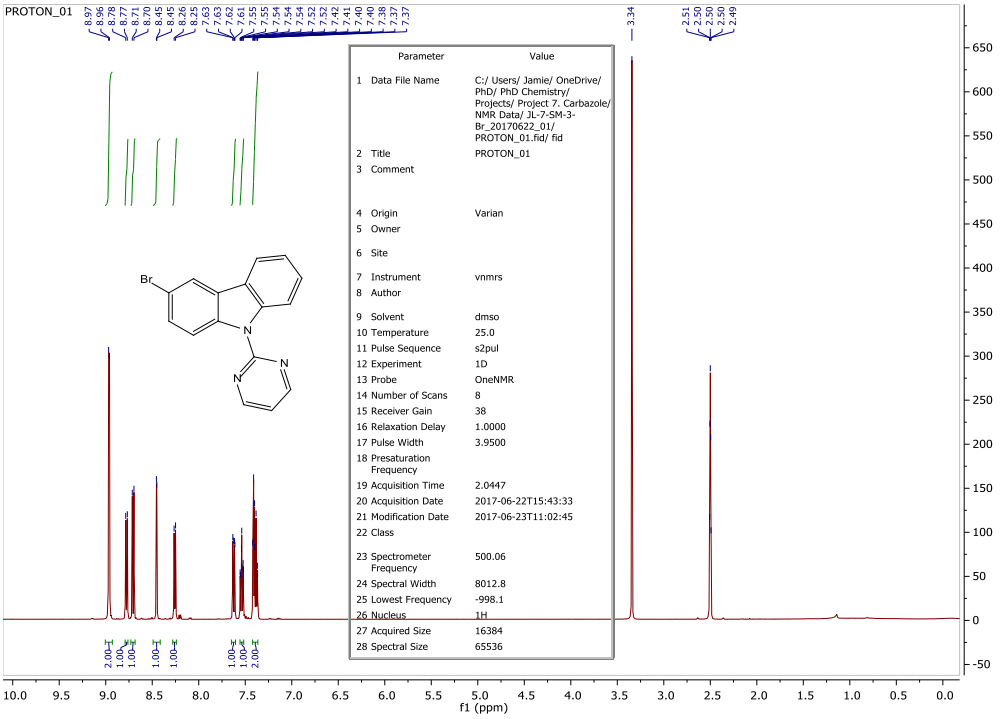
D incorporation = 10%



NMR 1a

6. NMR Data

1b – ^{1}H NMR (500 MHz, DMSO-d_6)



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3	Comment	
4	Origin	Varian
5	Owner	
6	Site	
7	Instrument	vnmrs
8	Author	
9	Solvent	dmso
10	Temperature	25.0
11	Pulse Sequence	s2pul
12	Experiment	1D
13	Probe	OneNMR
14	Number of Scans	8
15	Receiver Gain	38
16	Relaxation Delay	1.0000
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22	Class	
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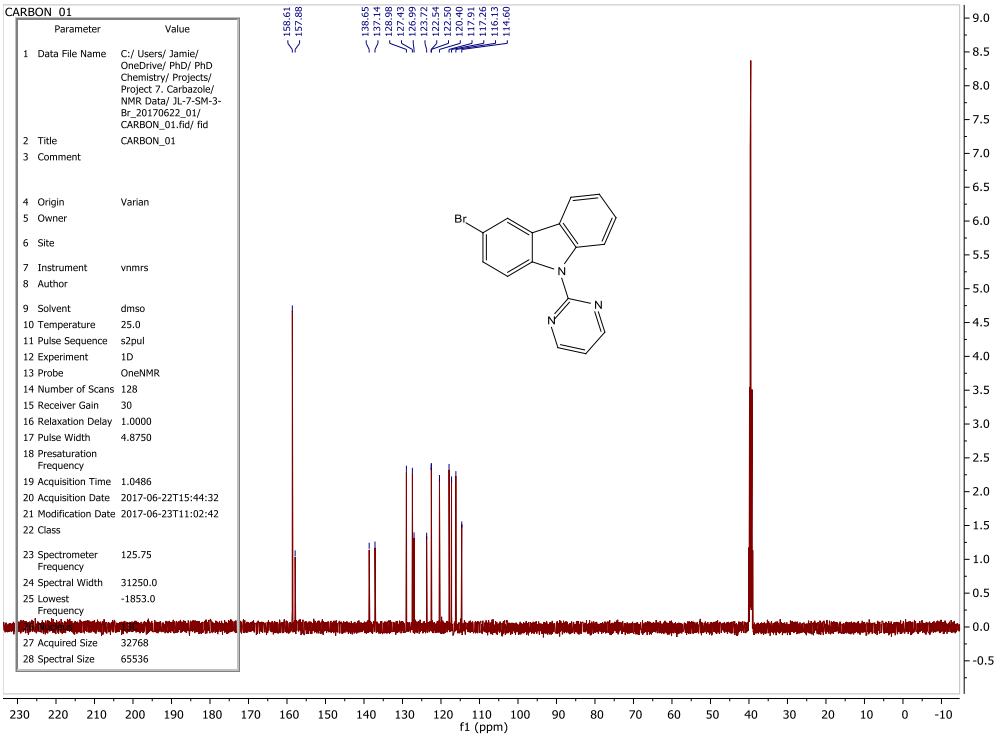
1b – ^{13}C NMR (126 MHz, DMSO-d_6)



Parameter		Value
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3	Comment	
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6	Site	
7	Instrument	vnmrs
8	Author	
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12	Experiment	1D
13	Probe	OneNMR
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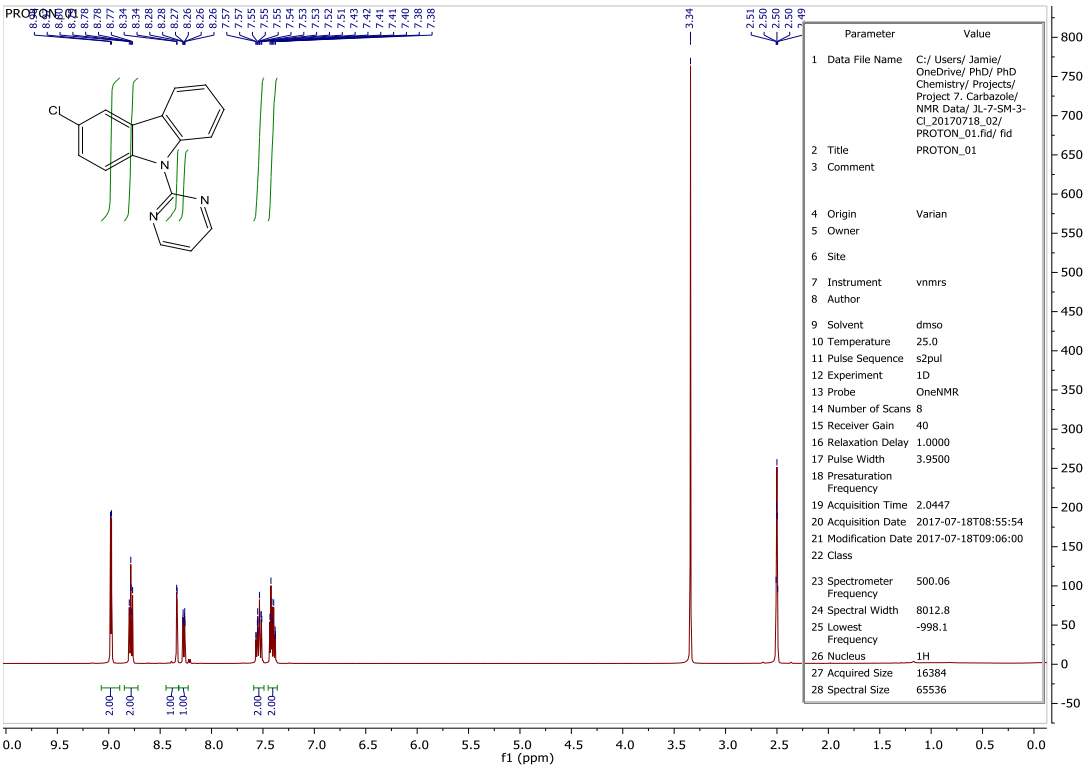
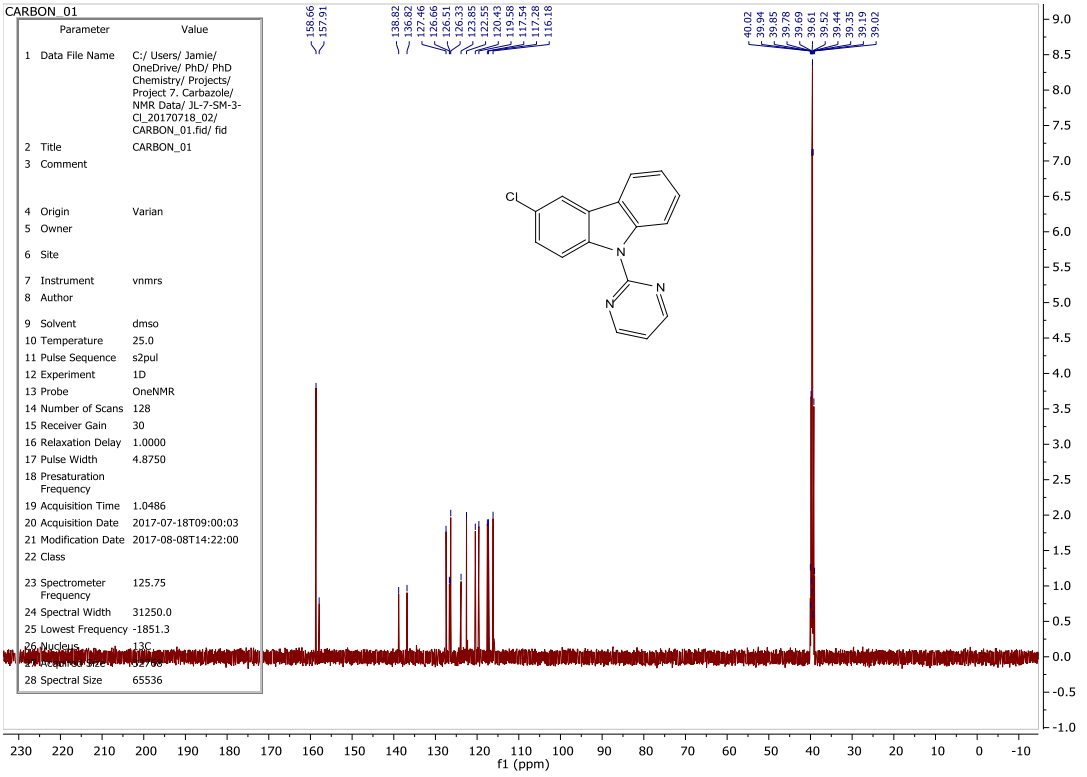
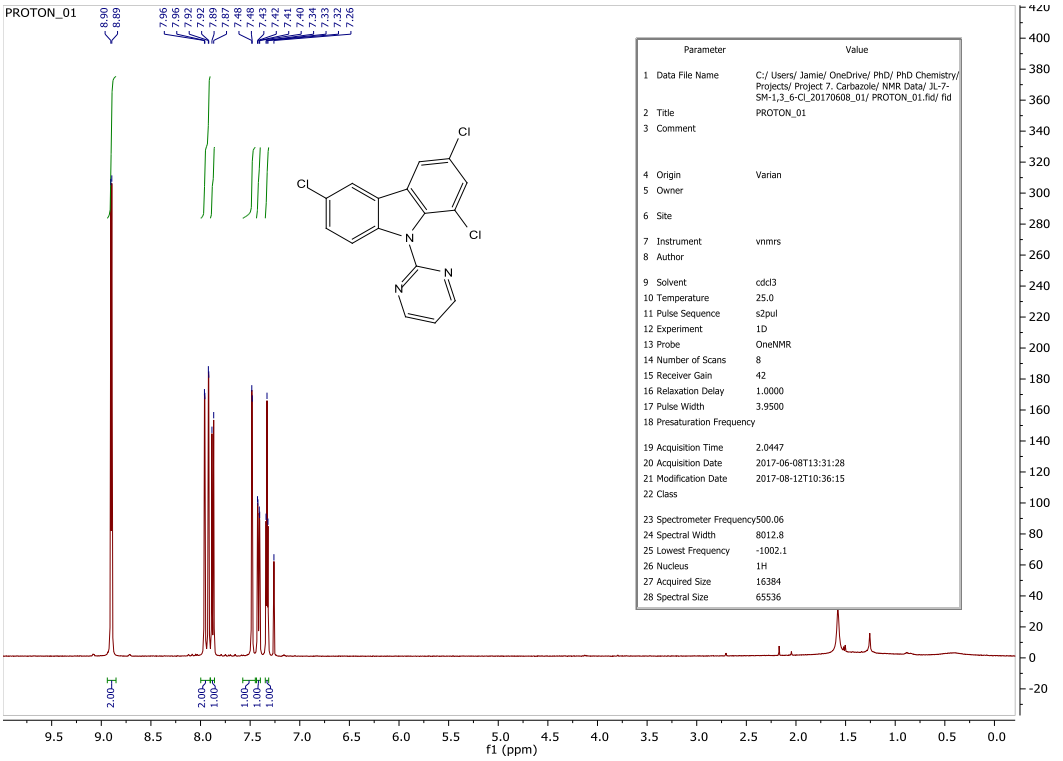
1c – ^{1}H NMR (500 MHz, DMSO-d_6)



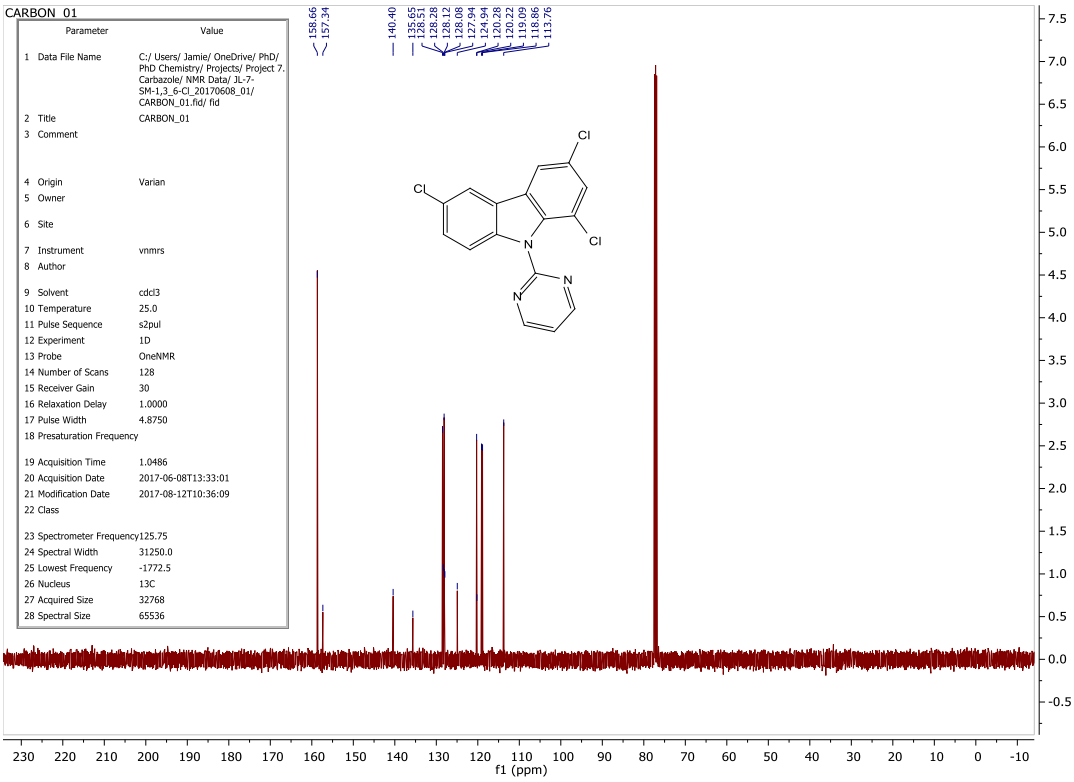
1c – ^{13}C NMR (126 MHz, DMSO-d_6)



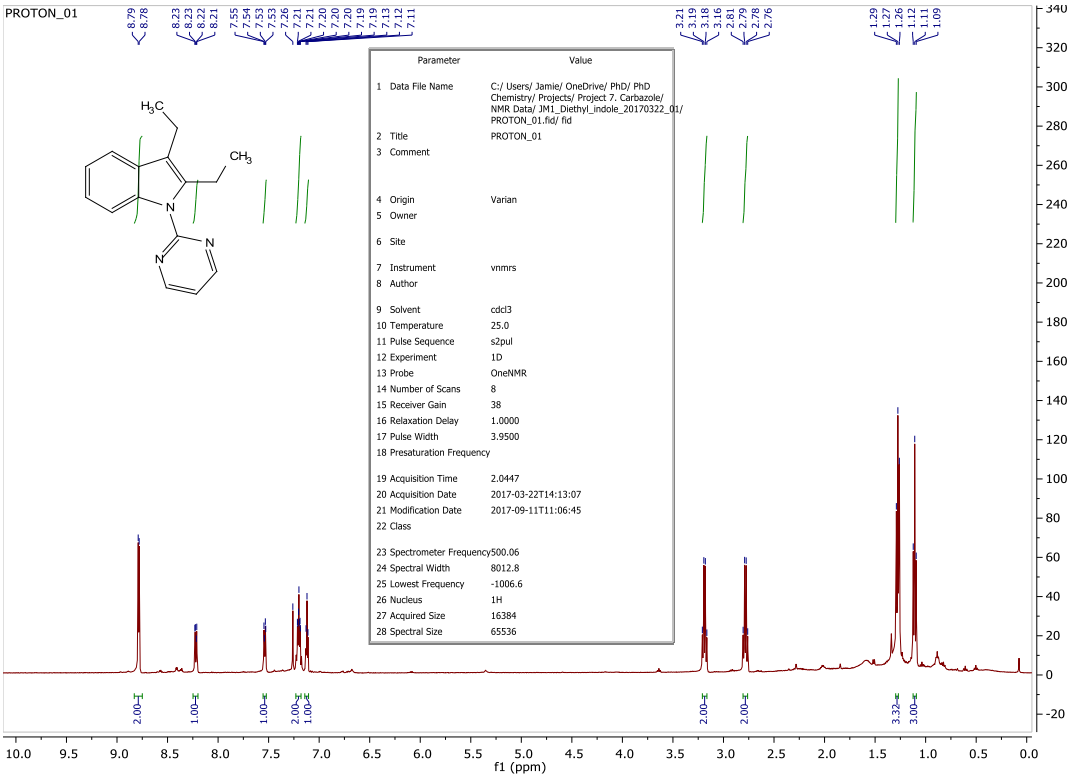
1d – ^{1}H NMR (500 MHz, $CDCl_3$)



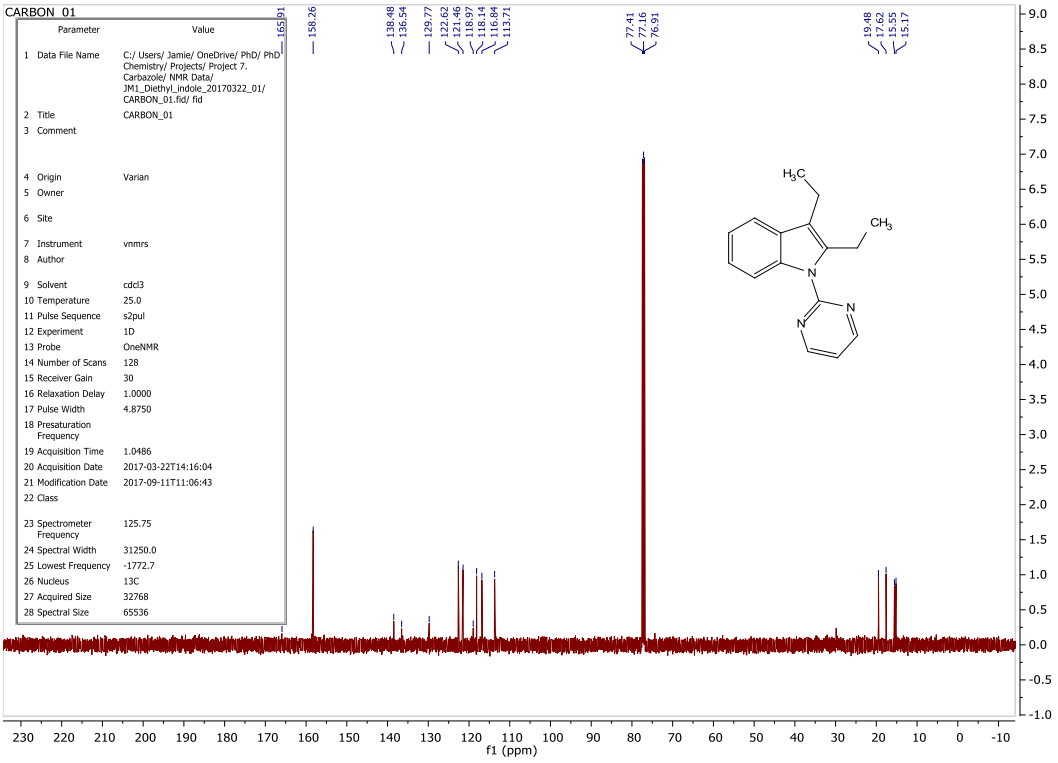
1d – ^{13}C NMR (126 MHz, $CDCl_3$)



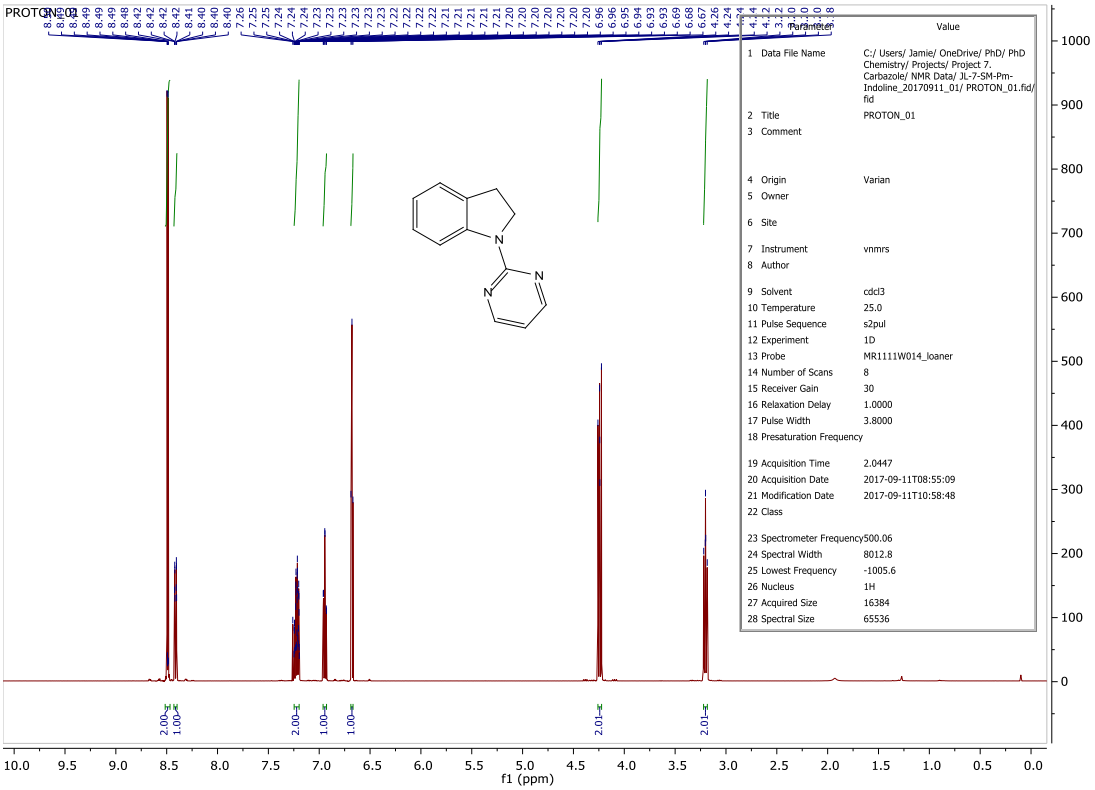
4a – ^{1}H NMR (500 MHz, $CDCl_3$)



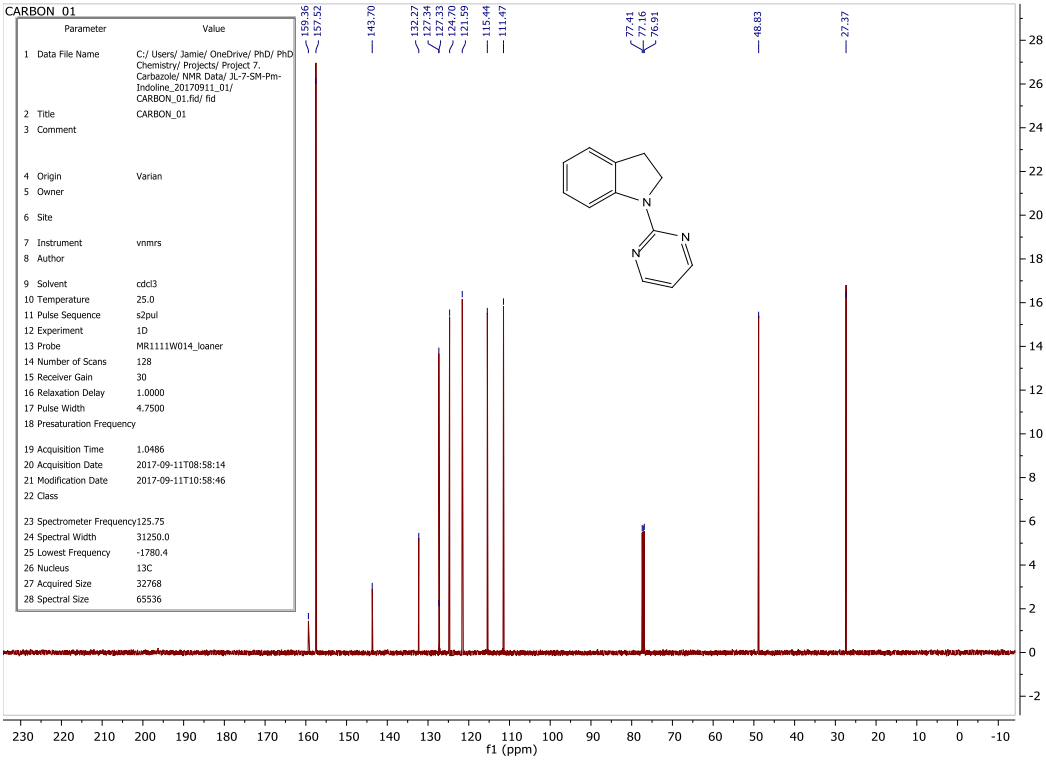
4a – ^{13}C NMR (126 MHz, $CDCl_3$)



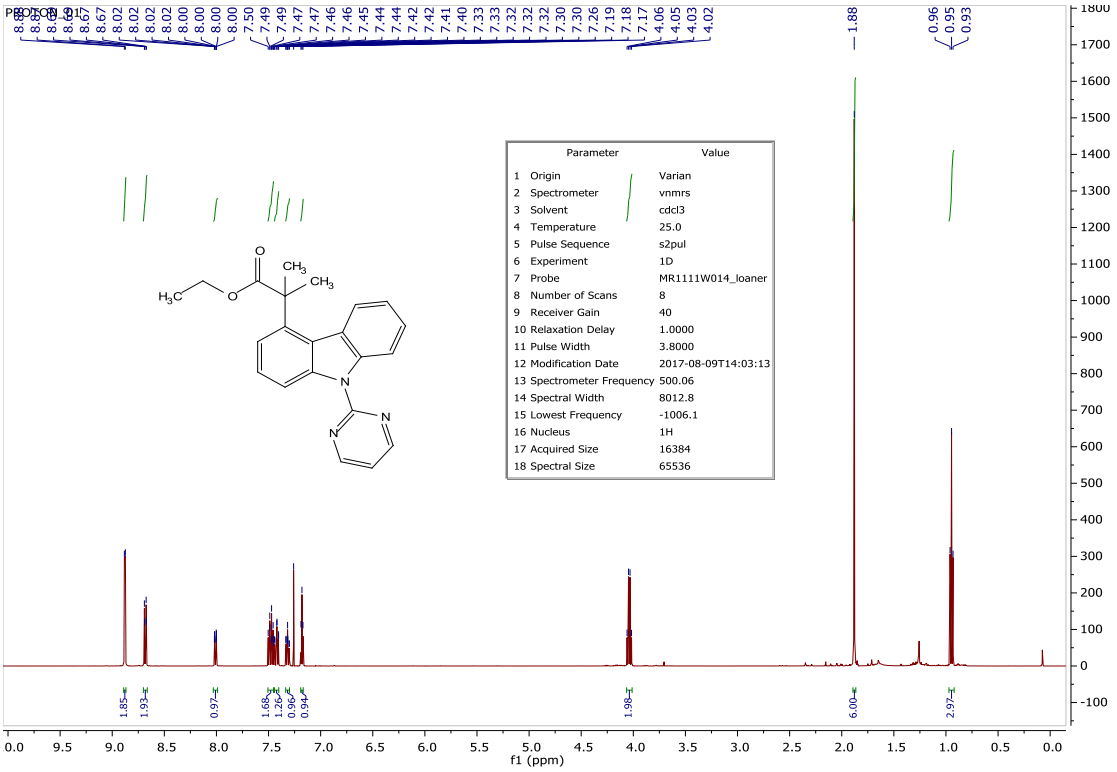
4b – ^{1}H NMR (500 MHz, $CDCl_3$)



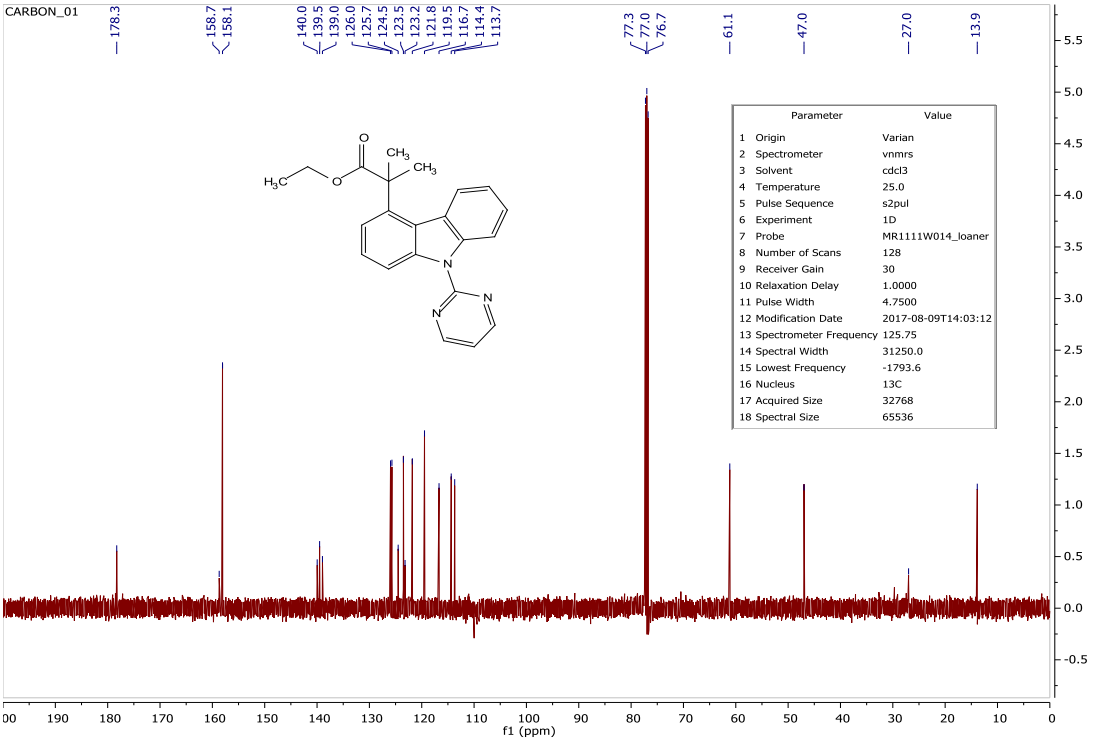
4b – ^{13}C NMR (126 MHz, $CDCl_3$)



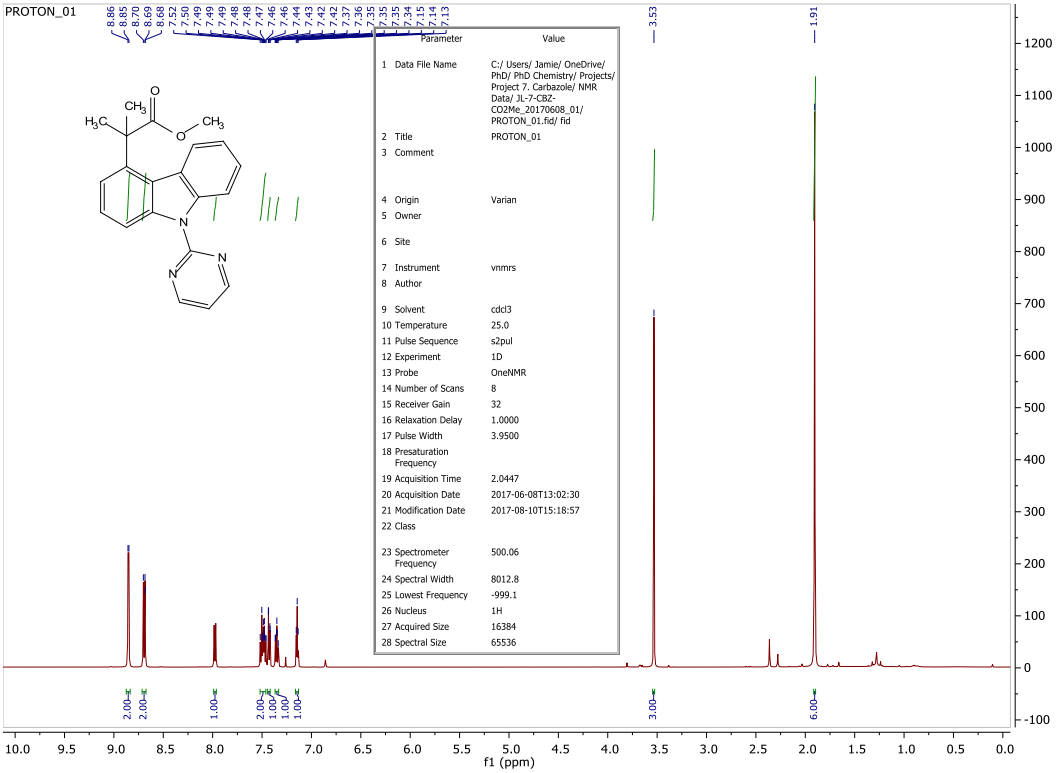
3a – ^{1}H NMR (500 MHz, $CDCl_3$)



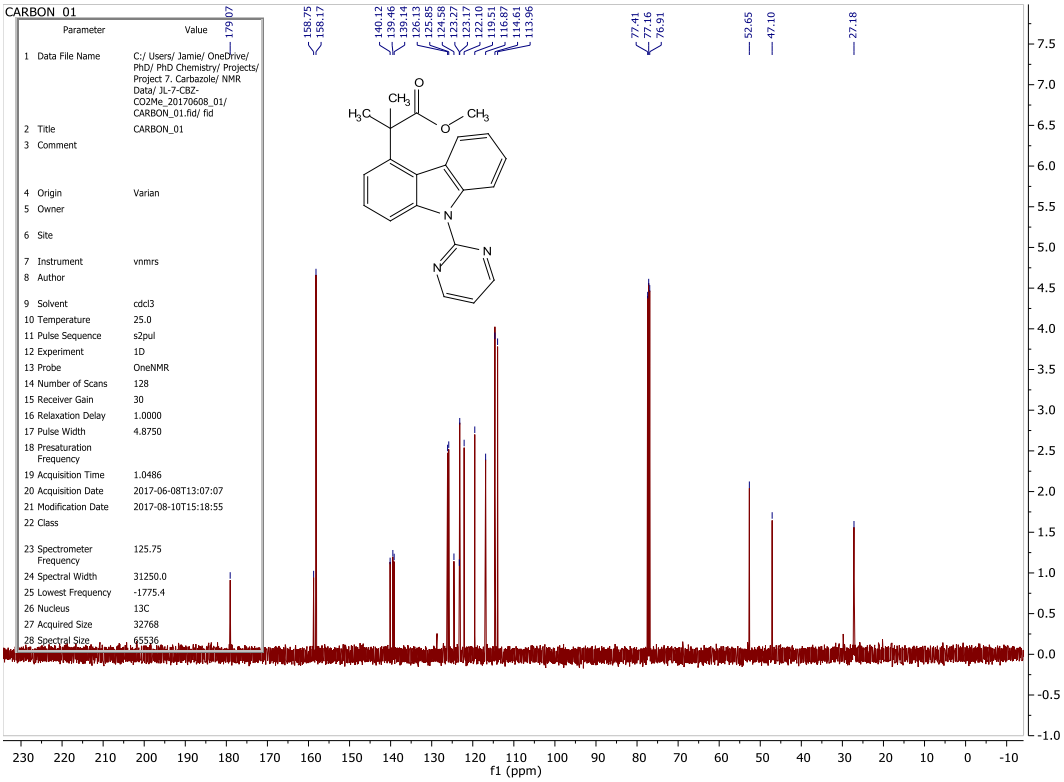
3a – ^{13}C NMR (126 MHz, $CDCl_3$)



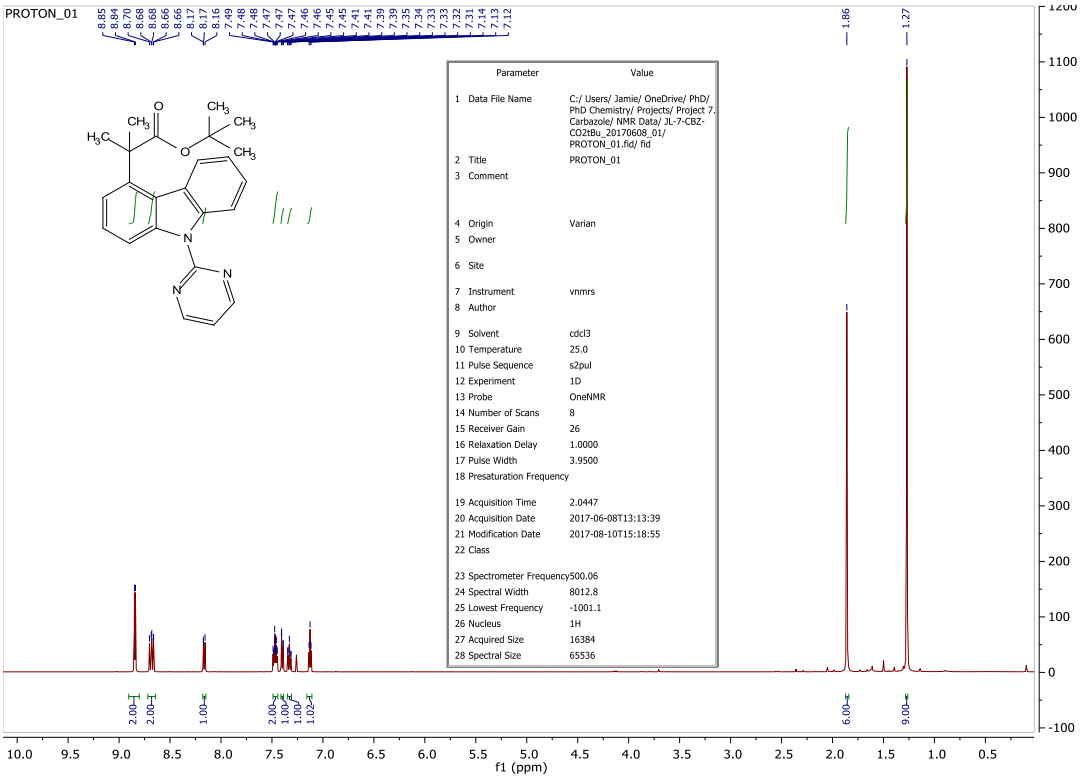
3aa – ^{1}H NMR (500 MHz, $CDCl_3$)



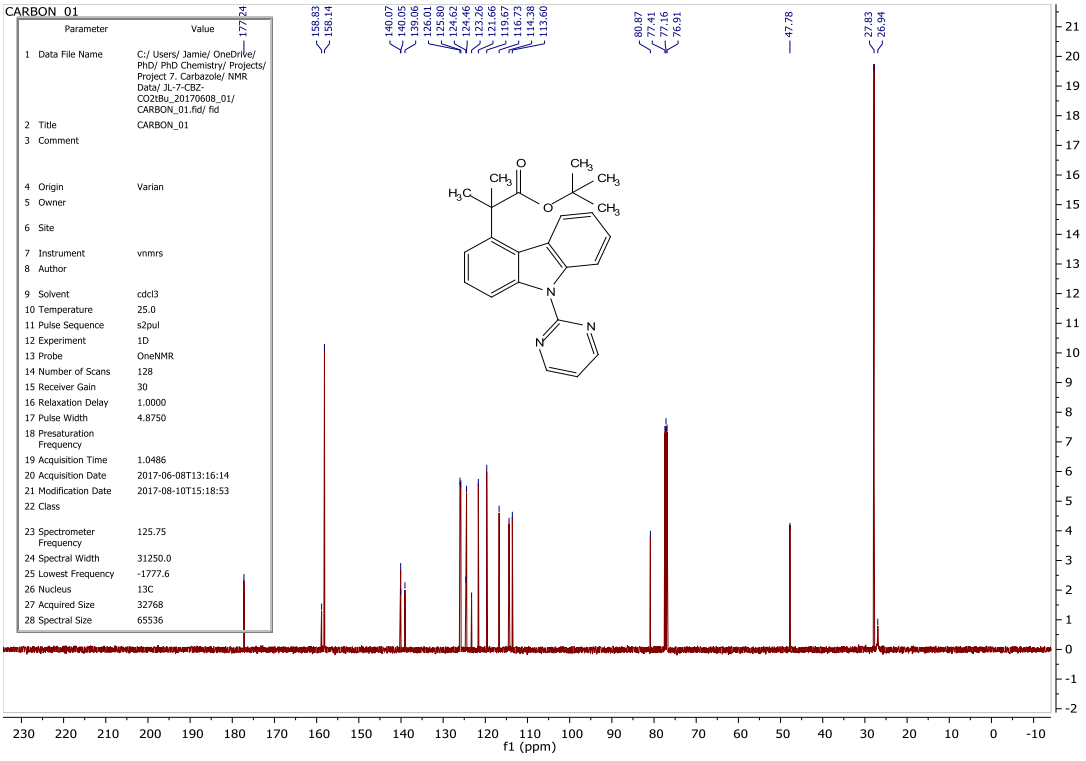
3aa – ^{13}C NMR (126 MHz, $CDCl_3$)



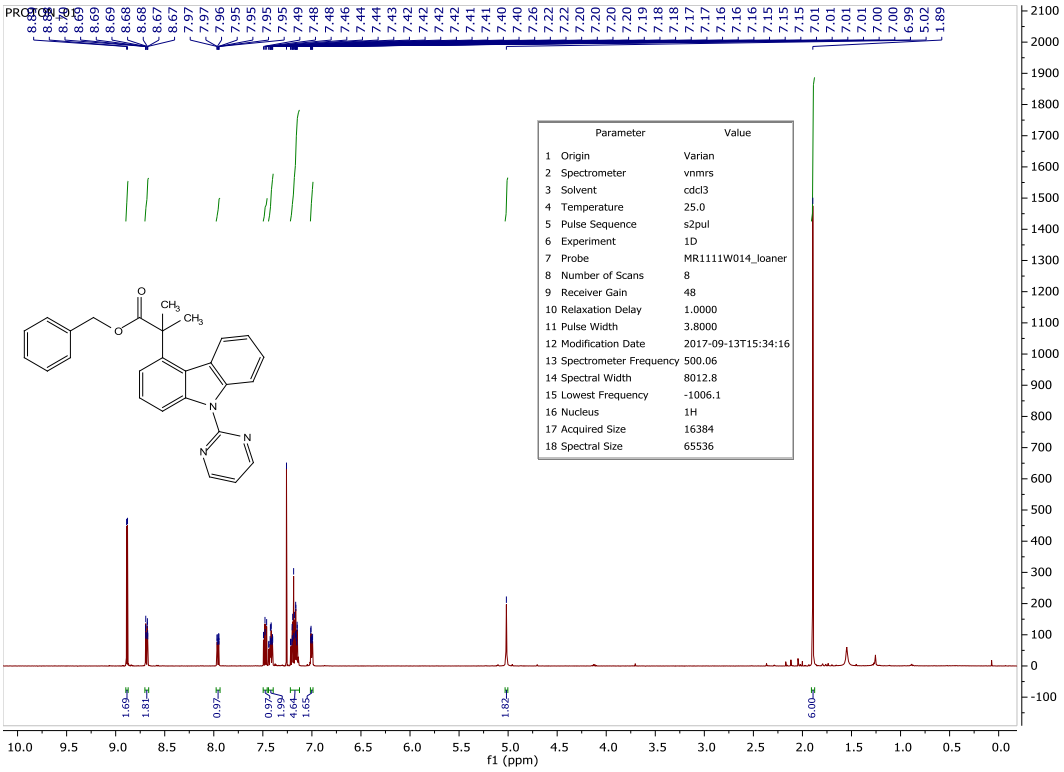
3ab – ^{1}H NMR (500 MHz, $CDCl_3$)



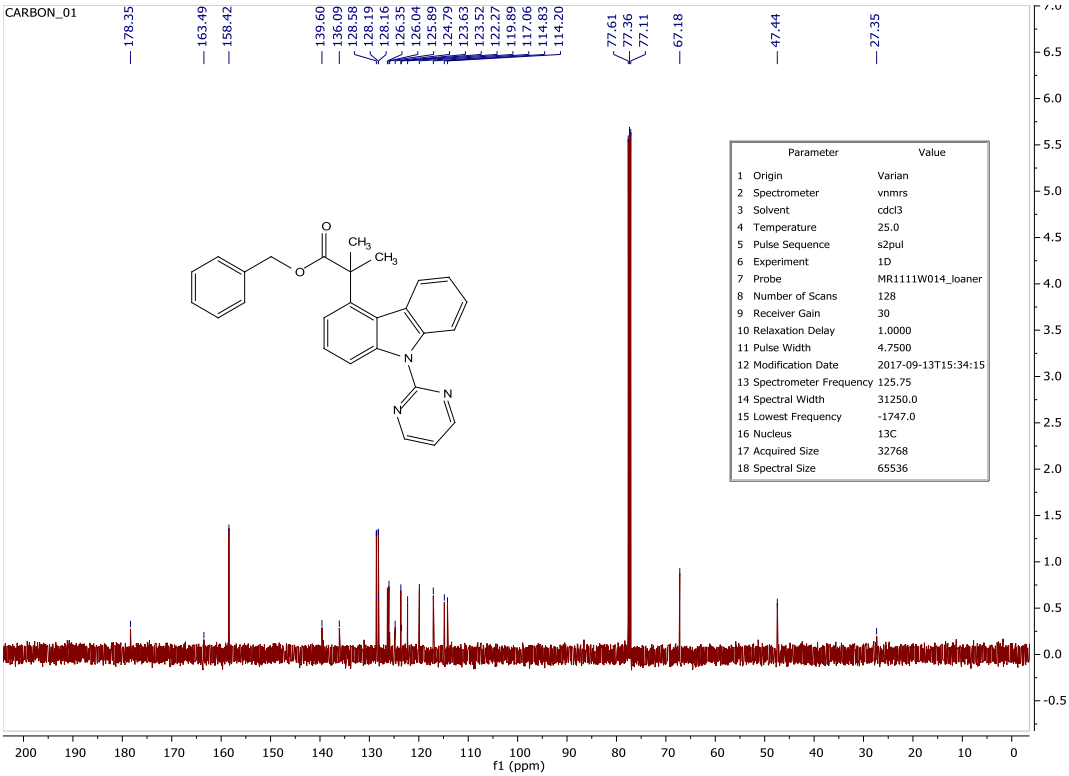
3ab – ^{13}C NMR (126 MHz, $CDCl_3$)



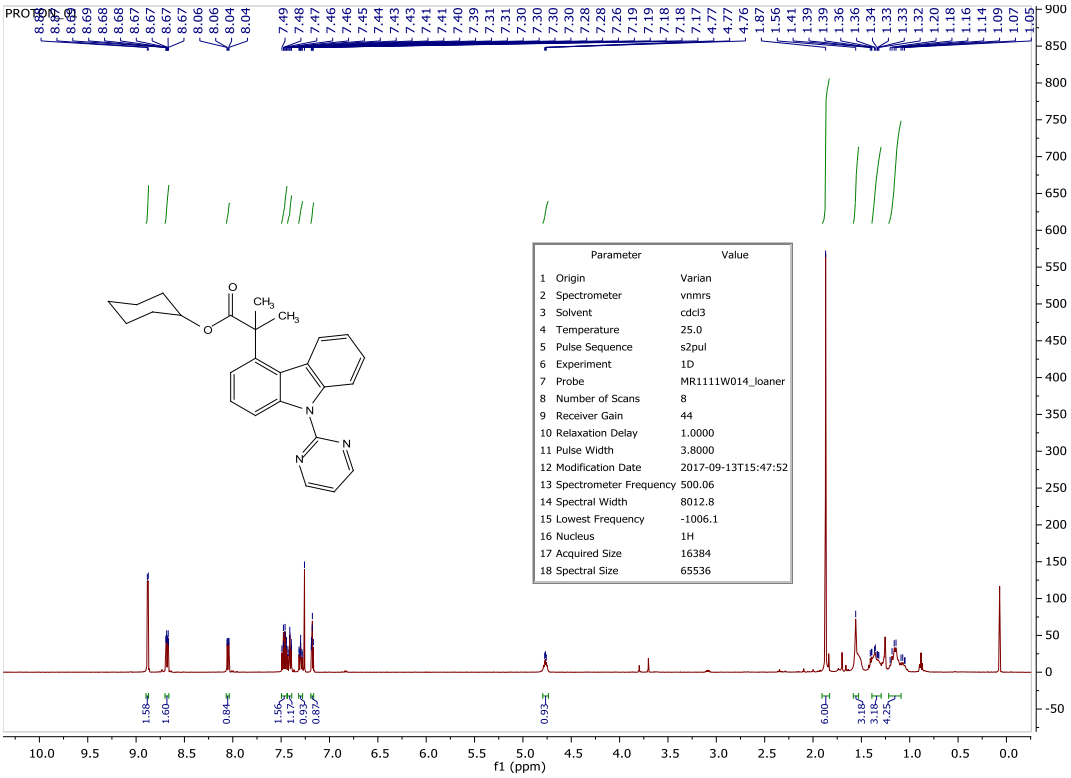
3ac – ^{1}H NMR (500 MHz, $CDCl_3$)



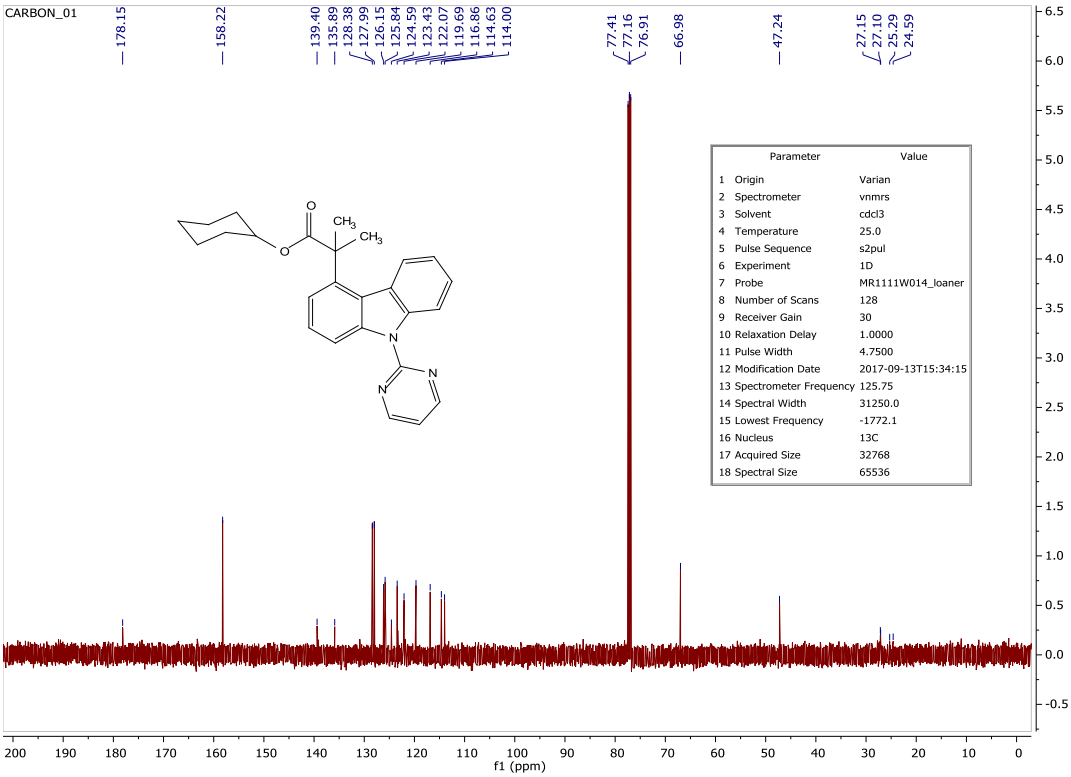
3ac – ^{13}C NMR (126 MHz, $CDCl_3$)



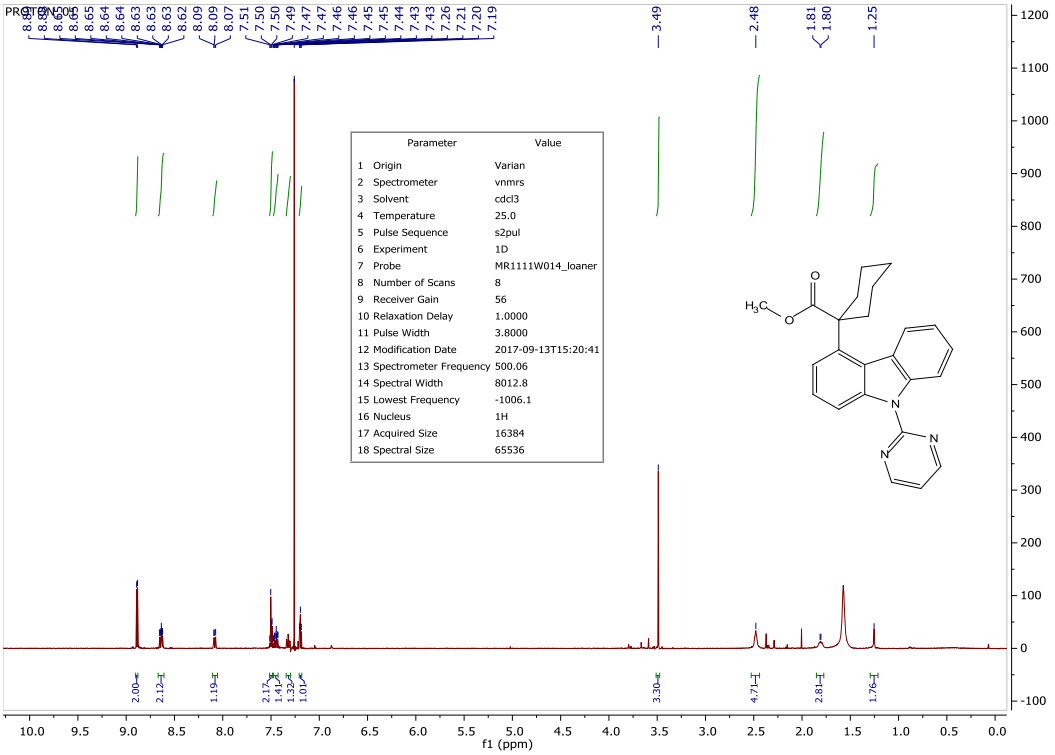
3ad – ^{1}H NMR (500 MHz, $CDCl_3$)



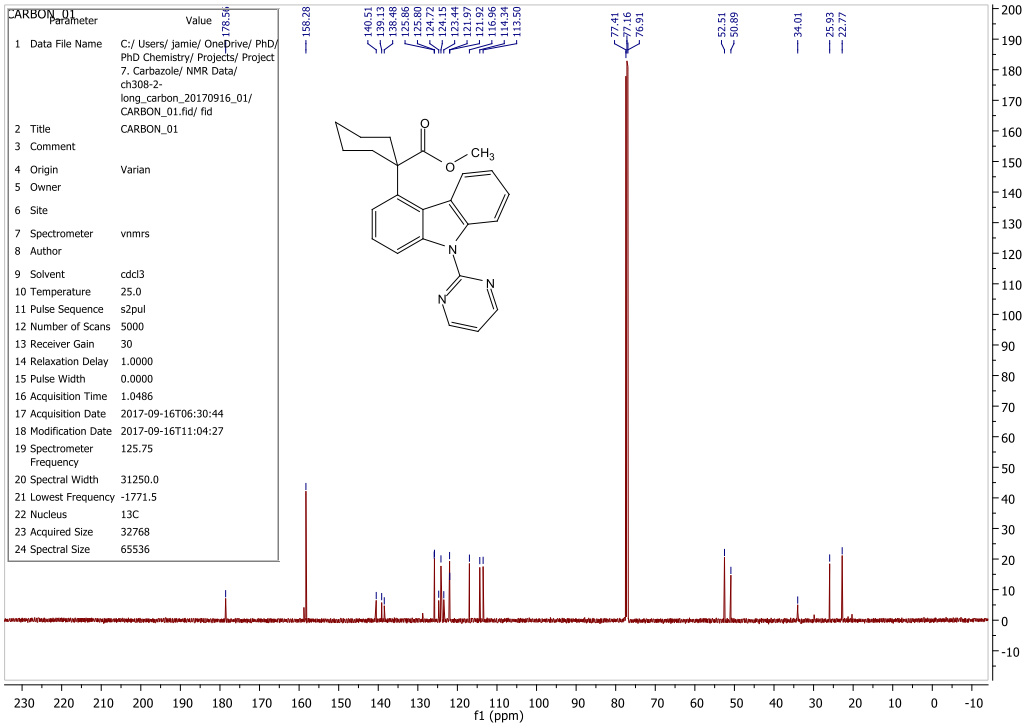
3ad – ^{13}C NMR (126 MHz, $CDCl_3$)



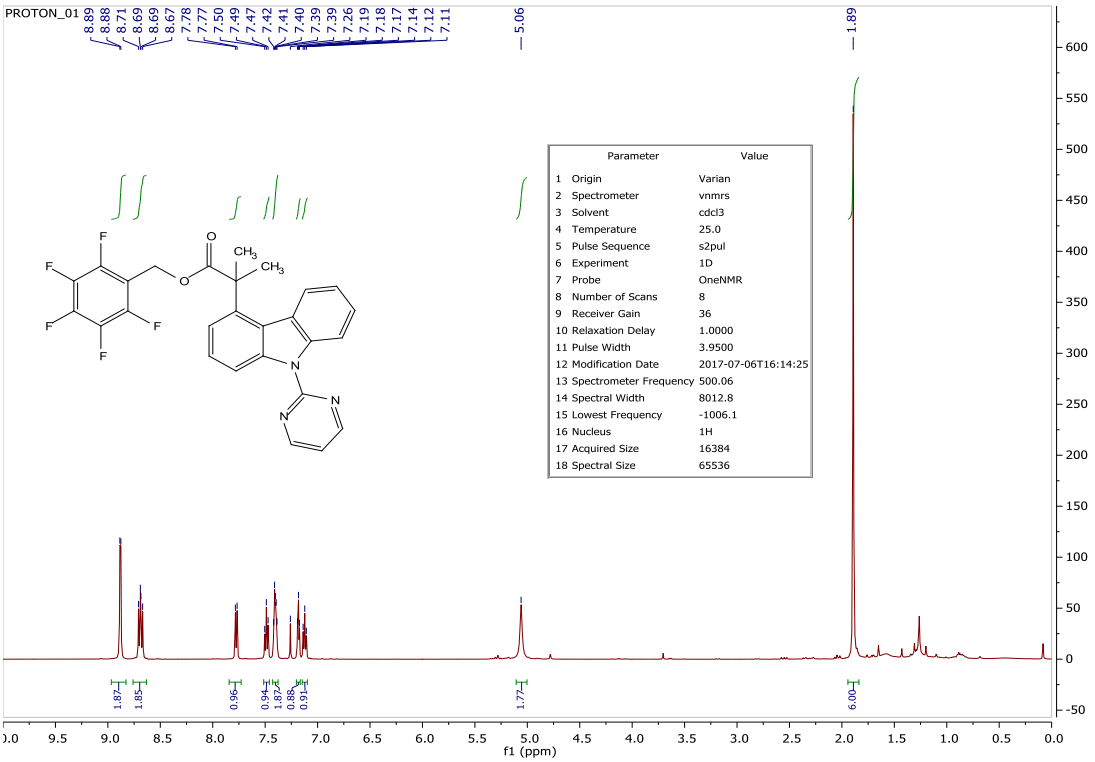
3af – ^{1}H NMR (500 MHz, $CDCl_3$)



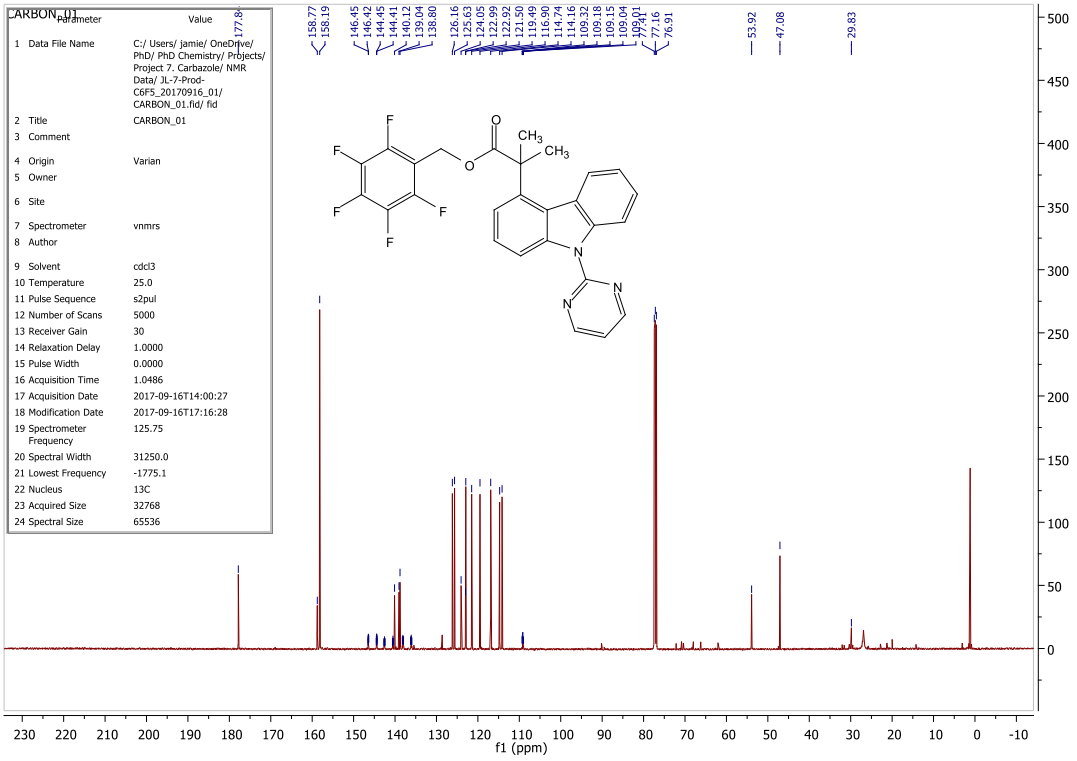
3af – ^{13}C NMR (126 MHz, $CDCl_3$)



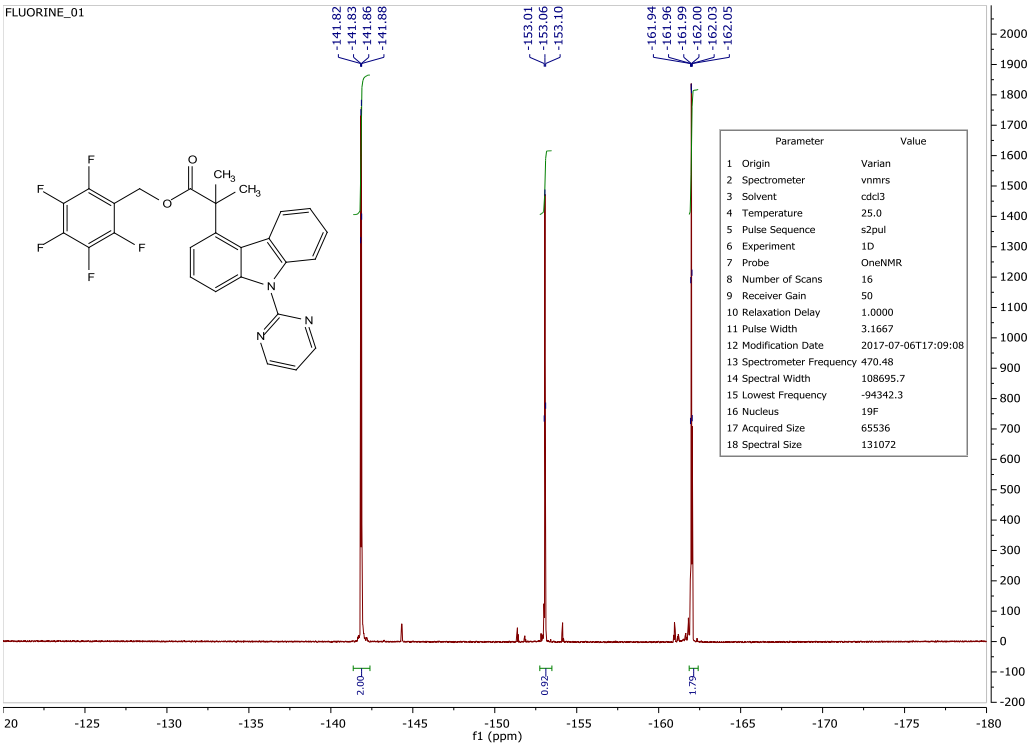
3ah – ^{1}H NMR (500 MHz, $CDCl_3$)



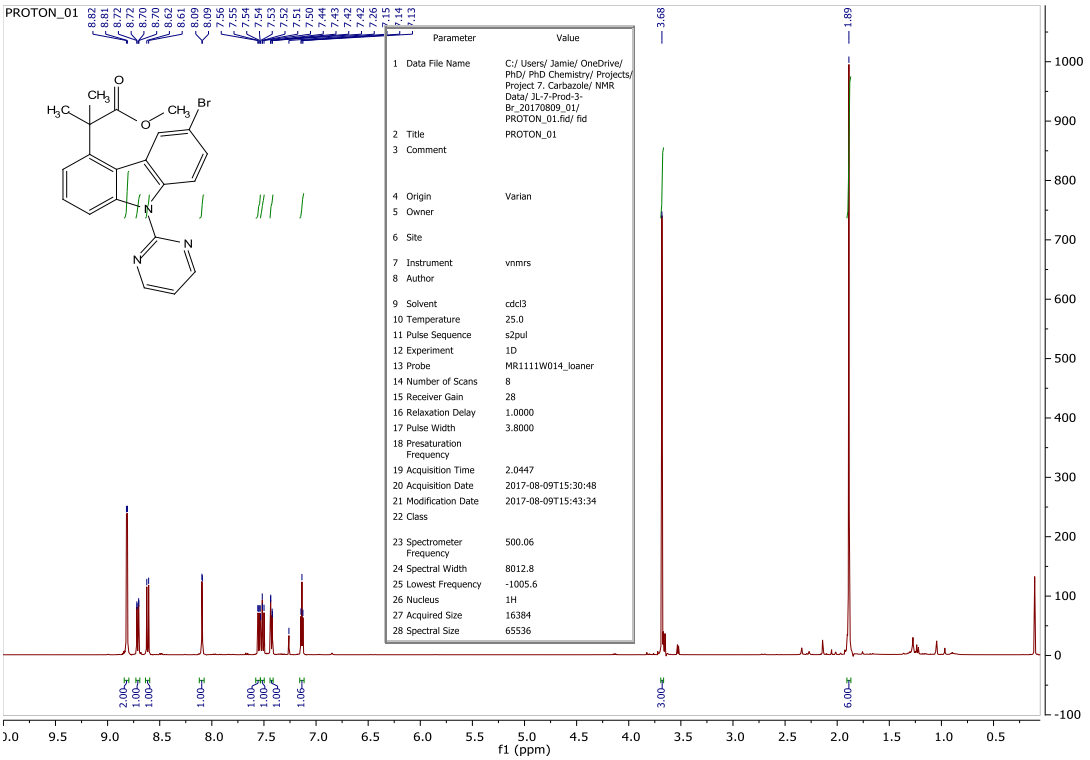
3ah – ^{13}C NMR (126 MHz, $CDCl_3$)



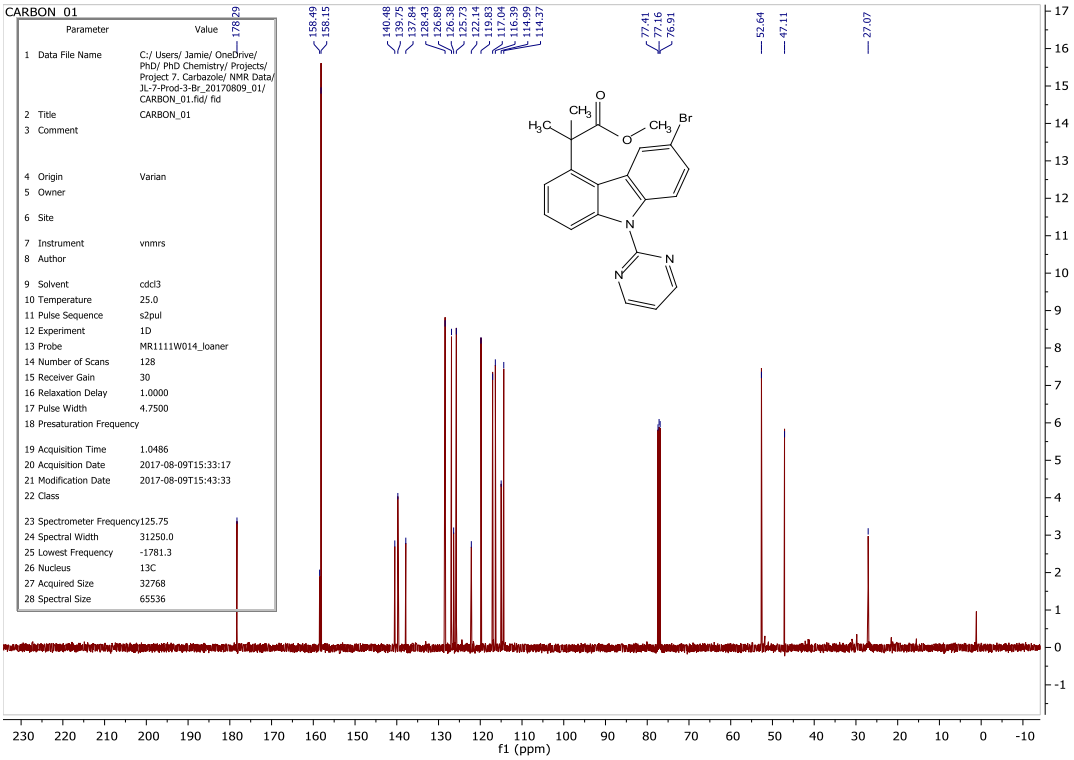
3ah – ^{19}F NMR (470 MHz, $CDCl_3$)



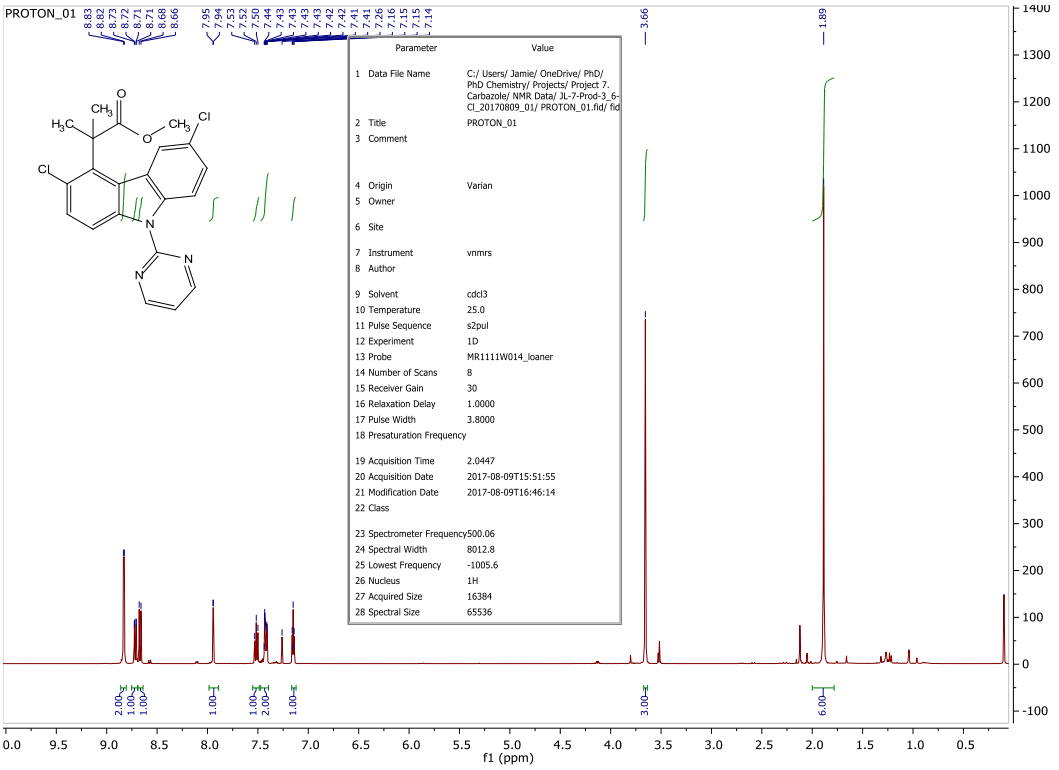
3b – ^{1}H NMR (500 MHz, $CDCl_3$)



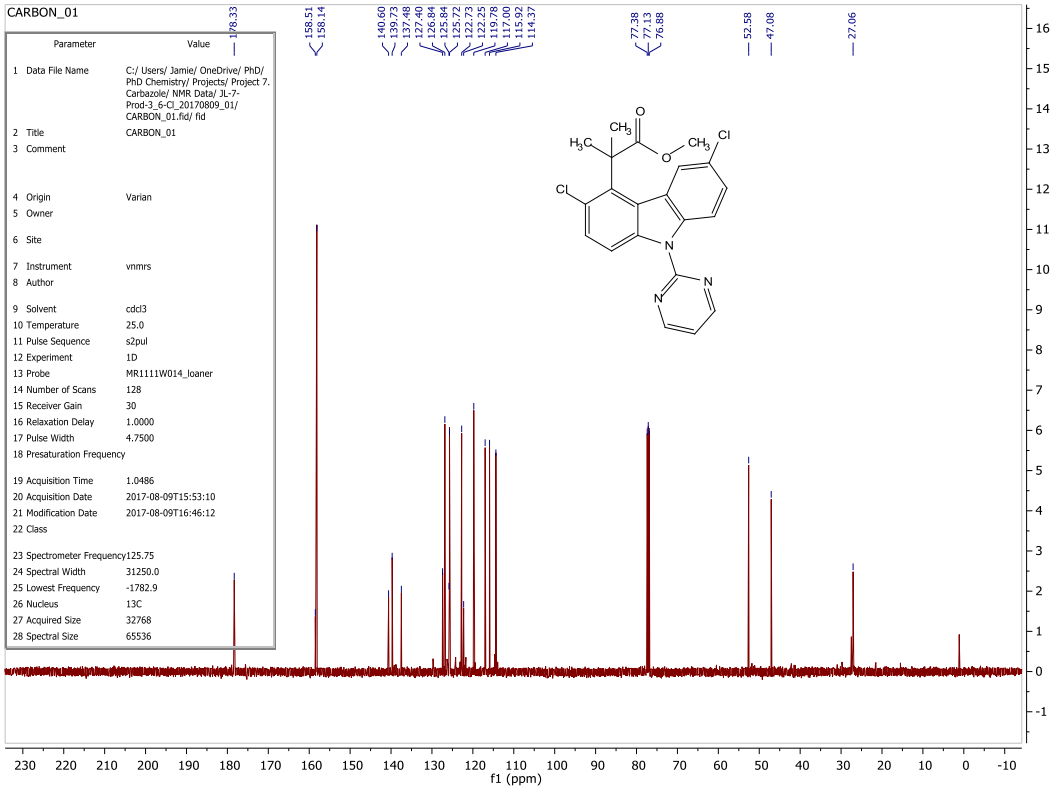
3b – ^{13}C NMR (126 MHz, $CDCl_3$)



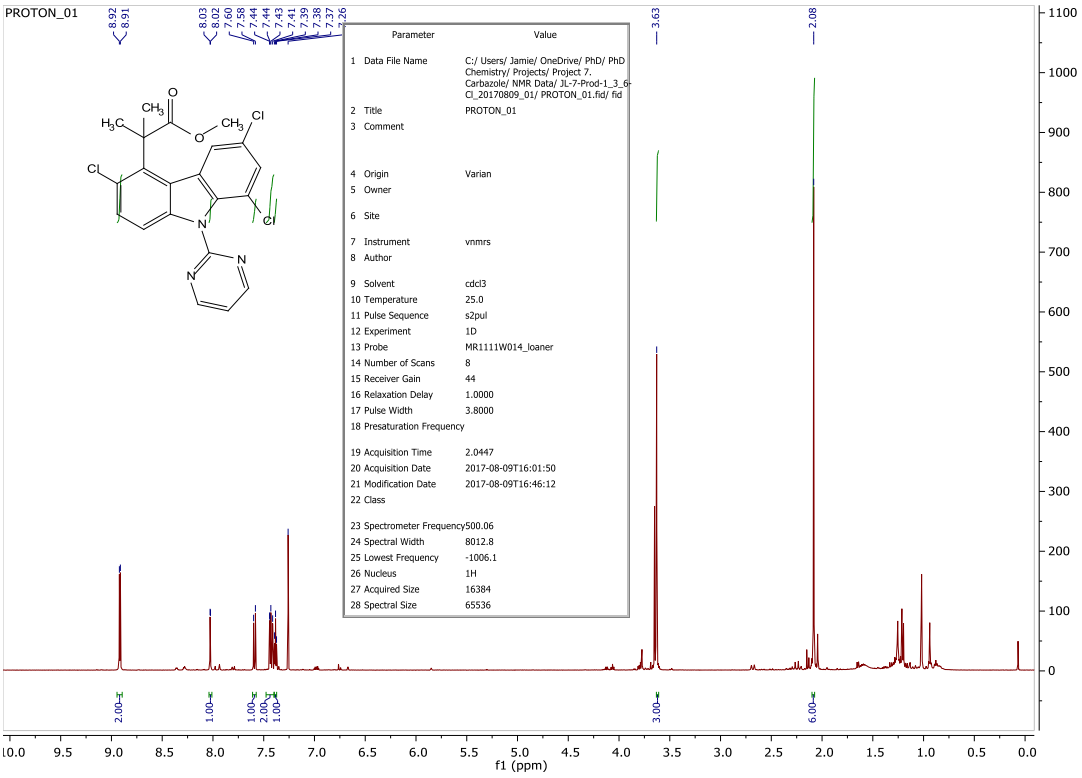
3c – ^{1}H NMR (500 MHz, $CDCl_3$)



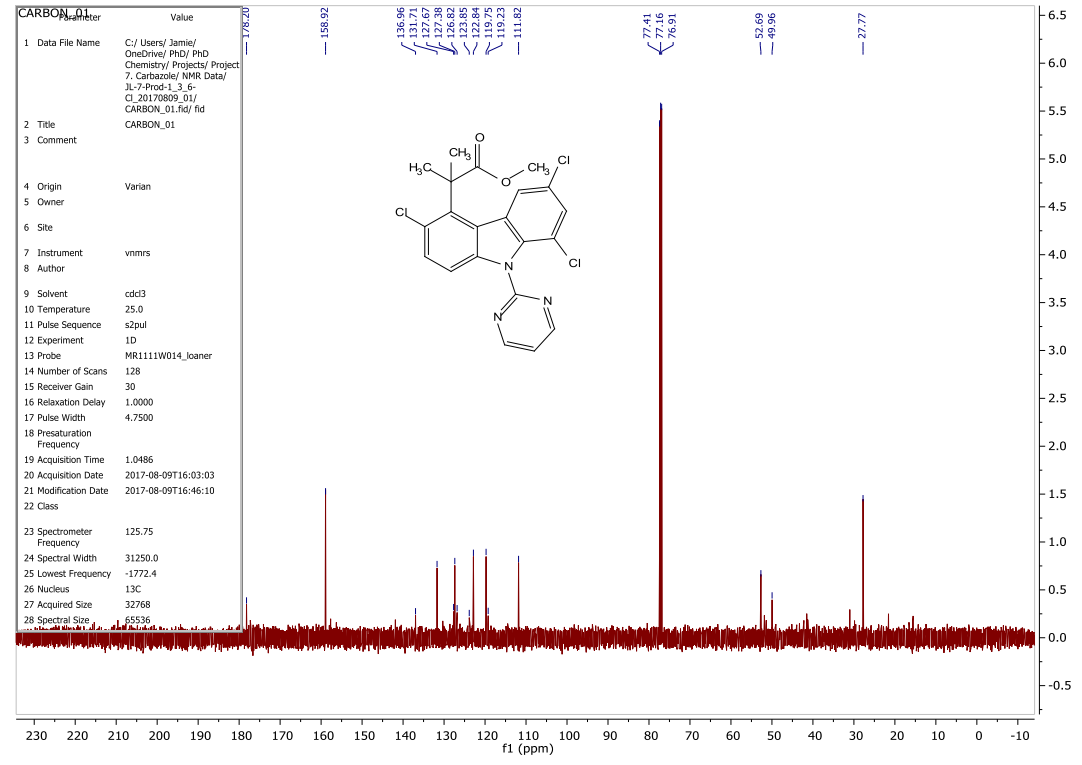
3c – ^{13}C NMR (126 MHz, $CDCl_3$)



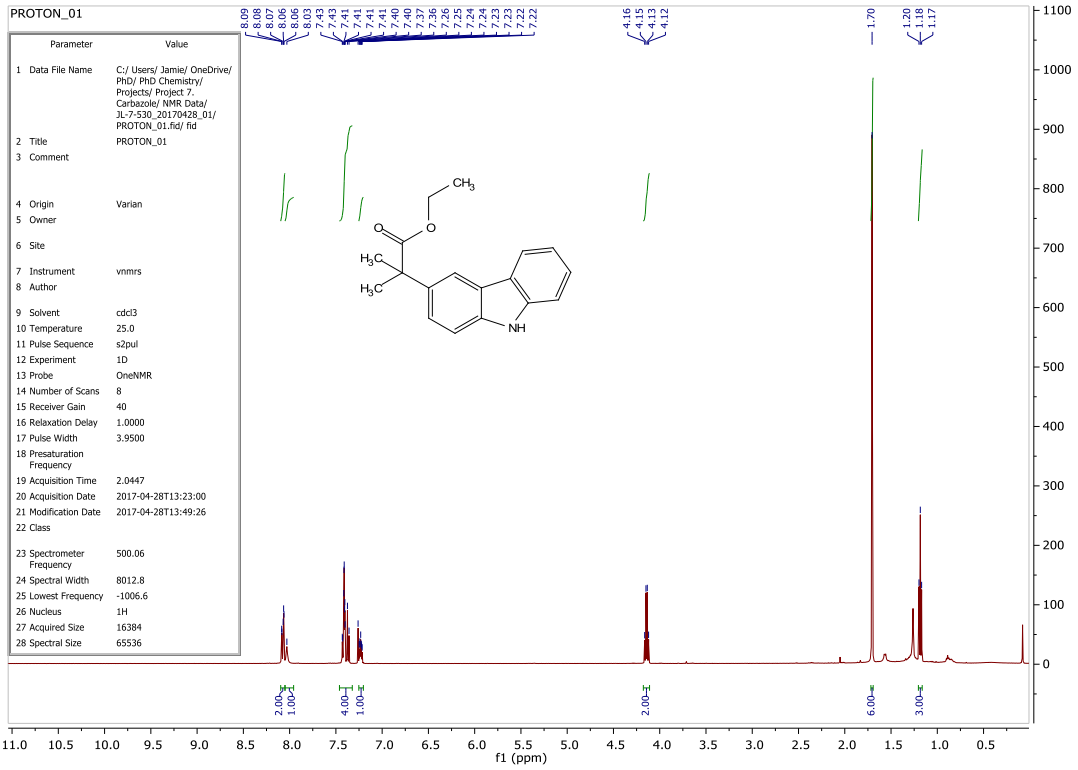
3d – ^{1}H NMR (500 MHz, $CDCl_3$)



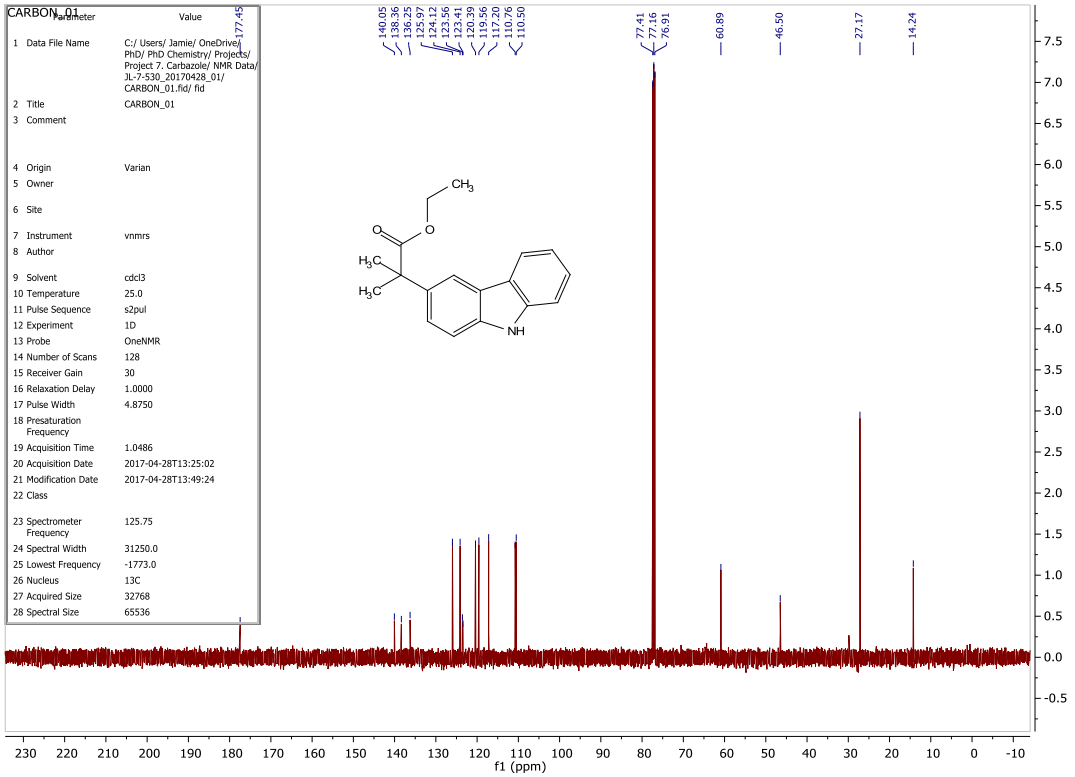
3d – ^{13}C NMR (126 MHz, $CDCl_3$)



3g – ^{1}H NMR (500 MHz, $CDCl_3$)



3g – ^{13}C NMR (126 MHz, $CDCl_3$)



7. References

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