Palladium(II)-catalysed intramolecular hydroamination of 3-alkynyltetrahydroquinolines to methanobenzo[b]azepines

Supporting Information

Chi Bong Eric Chao,[a] Lloyd R. Kellermann,[a] Christopher Richardson,[a] Andrew J. Tague,*[a] Stephen G. Pyne,*[a] Christopher J. T. Hyland*[a]

School of Science, Molecular Horizons Research Institute, University of Wollongong, Wollongong, 2522, New South Wales.

Table of Contents

1. General experimental information

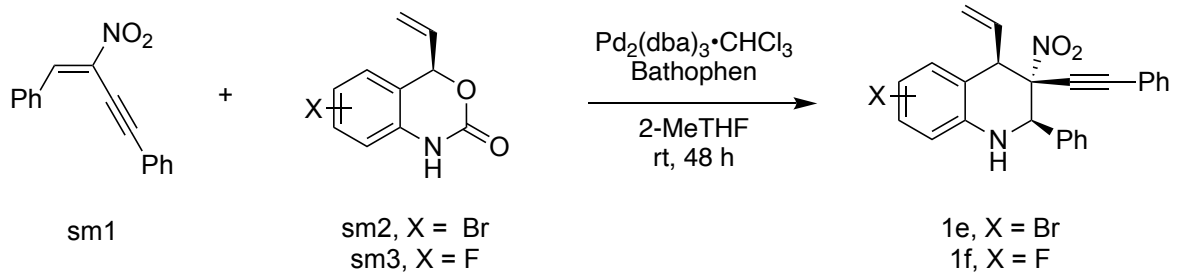
Chemicals and solvents were purchased from commercial sources (Sigma Aldrich, AK Scientific, Ambeed, Thermofisher and ChemSupply) and were used without further purification. All reactions were performed under an atmosphere of nitrogen unless otherwise indicated. Anhydrous THF was prepared by passing the solvent through a column packed with activated alumina followed by degassing and storage under nitrogen over 3Å molecular sieves (>10% m/v). Heating of reactions was performed with a paraffin oil bath. Cold reaction temperatures were obtained by using an ice bath (0 °C). All filtrations were gravity filtrations through filter paper in a glass funnel. Solvent removal via concentration was performed on a rotary evaporator under reduced pressure. All final compounds were dried under high vacuum before determination of chemical yields and spectroscopic analysis. Flash column chromatography was performed using silica gel 60 (230–400 mesh) purchased from ChemSupply. Thin-layer chromatography (TLC) was performed using Merck TLC Silica Gel 60 F254 aluminium-backed sheets. TLC spots were visualized under a UV lamp (wavelength 254 or 279 nm). ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded with either a Bruker Avance III HD 400 spectrometer (400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR) or a Bruker Avance Neo 500 spectrometer (500 MHz for ^{1}H NMR, 126 MHz for ^{13}C NMR, and 470 MHz for ^{19}F, NMR). Abbreviations used in the descriptions of NMR resonances include: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd), doublet of triplet (dt), doublet of doublet of doublets (ddd). Melting points (MP) were obtained using a Buchi Melting point M-560 apparatus with temperatures increasing by 2 °C/min. Values are reported in degree Celsius (°C). X-ray crystallography data was collected using a XtaLAB Mini II diffractometer outfitted with a Hybrid Pixel Array Detector (HyPix Bantam HPC-3000). Data collection, reduction, cell refinement and scaling as implemented in the SCALE3 ABSPACK scaling algorithm were performed using CrysAlis PRO version 1.171.40.48a.

2. Preparation of tetrahydroquinoline adducts (compounds **1a–d**, **1g–h**)

Known tetrahydroquinoline adducts were prepared accordingly to previously reported literature methods.[1]

3. Preparation of novel tetrahydroquinoline adducts (**1e–f**)

General procedure A:



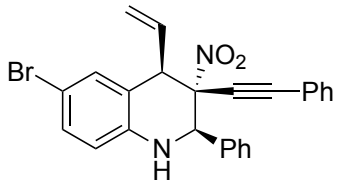
sm1 | sm2, X = Br; sm3, X = F | 1e, X = Br; 1f, X = F

Scheme S1: Synthesis of tetrahydroquinoline adducts

Novel tetrahydroquinoline adducts **1e** and **1f** were prepared according to the following procedure: An oven-dried reaction vessel was charged with the nitroenyne (1.25 eq.), 4-vinylbenzoxazinanone (1.0 eq.), $Pd_2(dba)_3 \cdot CHCl_3$ (5 mol%), bathophenanthroline

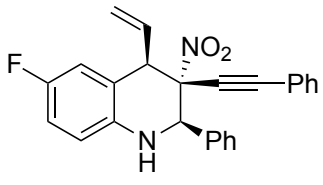
(10 mol%) and a stir bar under N_2 atmosphere before anhydrous 2-MeTHF (25.0 mL/mmol) was added via syringe. The reaction mixture was stirred at rt. Upon completion, indicated by TLC, the reaction mixture was concentrated under reduced pressure. The isolated residue was then purified by automated flash column chromatography using silica gel (CH_2Cl_2/hexane – 10:90 to 40:60 v/v) to obtain the tetrahydroquinoline cycloadduct **1** as an enriched mixture of diastereomers. The major diastereomer could be readily obtained in pure form by recrystallisation of the diastereomeric mixture with CH_2Cl_2/hexane.

(±)-(2*R*,3*R*,4*R*)-6-Bromo-3-nitro-2-phenyl-3-(phenylethynyl)-4-vinyl-1,2,3,4-tetrahydroquinoline (1e)



The titled compound was prepared following ***General Procedure A*** using nitroenyne, **sm1** (39.9 mg, 0.160 mmol), vinyl benzoxazinanone, **sm2** (32.7 mg, 0.128 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (6.9 mg, 0.007 mmol), and bathophenanthroline (4.8 mg, 0.010 mmol) to give cycloadduct **1e** as a yellow solid (6.7:1 *dr*, 45.5 mg, 77%) after purification by automated flash column chromatography on silica gel (CH_2Cl_2/hexane – 10:90 to 40:60 v/v). Recrystallisation from CH_2Cl_2/hexane gave the pure major diastereomer as a yellow solid (22.2 mg, 38%). MP 177–178 °C TLC: (CH_2Cl_2/hexane – 20:80), R_f = 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.7, 1.9 Hz, 2H, ArH,), 7.43 – 7.23 (m, 9H, ArH), 7.25 – 7.17 (m, 1H, ArH), 6.54 (d, *J* = 8.5 Hz, 1H, ArH), 5.99 (dt, *J* = 16.9, 9.7 Hz, 1H, CH_2=C*H*), 5.48 (dd, *J* = 10.0, 1.5 Hz, 1H, CH_EH_Z=CH), 5.40 (dd, *J* = 17.0, 1.5 Hz, 1H, CH_EH_Z=CH), 5.07 (d, *J* = 1.3 Hz, 1H, Ph-C*H*), 4.51 (d, *J* = 9.3 Hz, 1H, vinyl-C*H*), 4.35 (s, 1H, N*H*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3 (ArC), 135.1 (ArC), 133.1 (CH_2=*C*H), 132.0 (ArCH, C × 2), 131.3 (ArCH), 131.1 (ArCH), 130.0 (ArCH), 129.4 (ArCH), 128.8 (ArCH, C × 2), 128.4 (ArCH C × 2), 128.2 (ArCH C × 2), 123.2 (*C*H_2=CH), 121.7 (C≡C-*C*Ar), 121.4 (ArCH), 115.8 (ArCH), 110.2 (Ar*C*-Br), 95.1 (C≡*C*-Ph), 92.3 (C-NO_2), 77.9 (*C*≡C-Ph), 63.8 (Ph-*C*), 54.0 (vinyl-*C*H) ppm. HRMS (ESI) m/z: $[M - H]^-$: Calcd for $C_{25}H_{18}BrN_2O_2$ 457.0552; Found 457.0562. IR ν_{max} (neat): 3404, 1599, 1549, 1488, 1308, 1266, 1137, 1105, 1009, 714, 701 cm^{-1}.

(±)-(2*R*,3*R*,4*R*)-6-Fluoro-3-nitro-2-phenyl-3-(phenylethynyl)-4-vinyl-1,2,3,4-tetrahydroquinoline (1f)



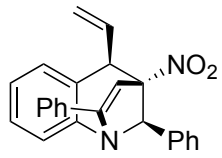
The titled compound was prepared following ***General Procedure A*** using nitroenyne **sm1** (67.5 mg, 0.27 mmol), vinyl benzoxazinanone, **sm3** (39.8 mg, 0.21 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (10.3 mg, 0.01 mmol) and bathophenanthroline (6.4 mg, 0.02 mmol) to give cycloadduct **1f** as a (4:1 *dr*, 62.3 mg, 76%) after purification by automated flash column chromatography on silica gel (CH_2Cl_2/hexane – 10:90 – 40:60 v/v). Precipitation from CH_2Cl_2/hexane gave the pure major diastereomer as an orange gum (26.0 mg, 32%). TLC: (CH_2Cl_2/hexane – 20:80), R_f = 0.14. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.7, 2.2 Hz, 2H, ArH), 7.44 – 7.22 (m, 8H, ArH), 7.00 – 6.81 (m,

2H, ArH), 6.60 (dd, *J* = 8.8, 4.7 Hz, 1H, ArH), 6.00 (dt, *J* = 17.4, 9.7 Hz, 1H, CH_2=C*H*), 5.47 (d, *J* = 10.0 Hz, 1H, CH_E*H*$_Z$=CH), 5.40 (d, *J* = 17.1 Hz, 1H, C*H*$_E$H$_Z$=CH), 5.05 (S, 1H, Ph-C*H*), 4.54 (d, *J* = 9.3 Hz, 1H, vinyl-C*H*), 4.24 (s, 1H, N*H*) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2 (d, ^1J(C, F) = 236.5 Hz, F-Ar*C*) 138.4, (d, ^4J(C, F) = 2.1 Hz, ArC) 135.2 (ArC), 133.2 (CH_2=*C*H), 131.9 (ArCH, C × 2), 129.8 (ArCH), 129.3 (ArCH), 128.6 (ArCH, C × 2), 128.3 (ArCH, C × 2), 128.2 (ArCH, C × 2), 122.9 (*C*H_2=CH), 121.4 (C≡C-*C*Ar), 121.1, (d, ^3J(C, F) = 7.1Hz, ArC), 115.3 (d, ^3J(C, F) = 7.8 Hz, ArCH) 115.2 (d, ^2J(C, F) = 23.9 Hz), 115.1 (d, ^2J(C, F) = 23.9 Hz) , 94.9 (C≡*C*-Ph), 92.5 (C-NO_2), 78.0 (*C*≡C-Ph), 64.0 (Ph-*C*), 54.1 (vinyl-*C*H) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.68. HRMS (ESI) m/z: $[M - H]^-$: Calcd for $C_{25}H_{18}FN_2O_2$ 397.1352; Found 397.1354. IR ν_{max} (neat): 3418 2923, 1621, 1546, 1498, 1455, 1318, 1260, 1222, 928, 811, 787, 754, 688 cm^{-1}.

4. *General Procedure B*: Synthesis of methanobenzo[*b*]azepines (Compounds 2a–2i)

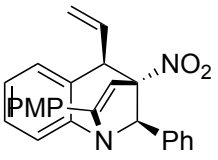
An oven dried vial was equipped with a dry stir bar and cooled under nitrogen. Tetrahydroquinoline **1** (1 equiv.), $Pd(TFA)_2$ (10 mol%), THF (0.1M wrt **1**) and $HBF_{4(aq)}$ (30 mol%). The reaction mixture was then stirred at rt – 40 ºC for 48 –144 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with saturated $NaHCO_3$ and extracted with ethyl acetate (3 × 5 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was then concentrated under reduced pressure and the residue purified by FCC over silica gel (2–5% Et_2O in hexane) to yield hydroamination product **2**.

(±)-(1*R*,4*R*,5*R*,10*R*)-4-Nitro-2,10-diphenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2a)



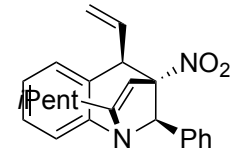
The titled compound was prepared following ***General Procedure A*** using tetrahydroquinoline **1a** (38.6 mg 0.101 mmol), $Pd(TFA)_2$ (3.3 mg 0.010 mmol) and aqueous HBF_4 (3.9 μL, 0.0300 mmol). Purification by FCC (Et_2O/hexane – 2:98 v/v) afforded the desired product as a white solid (23.5 mg, 62% yield). MP 185–186 °C. TLC: (Et_2O/hexane – 10:90) R_f = 0.51. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 7.9, 1.7 Hz, 2H, ArH), 7.47 – 7.37 (m, 3H, ArH), 7.34 – 7.23 (m, 7H, ArH), 7.19 (td, *J* = 7.5, 1.2 Hz, 1H, ArH), 7.13 – 7.04 (m, 1H, ArH), 6.18 (s, 1H, N-C(Ph)=C*H*), 5.81 (dt, *J* = 17.0, 9.7 Hz, 1H, CH_2=C*H*), 5.45 (dd, *J* = 17.0, 1.3 Hz, 1H, C*H*$_E$H$_Z$=CH), 5.37 (dd, *J* = 10.0, 1.3 Hz, 1H, CH_E*H*$_Z$=CH), 4.92 (s, 1H, Ph-C*H*), 4.84 (d, *J* = 9.4 Hz, 1H, vinyl-C*H*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.4 (HC=*C*–N), 148.6 (ArC), 134.6 (ArC), 133.9 (ArC), 132.5 (CH_2=*C*H), 131.0 (ArCH), 130.5 (ArC), 130.0 (ArCH), 128.8 (ArCH, C × 2), 128.4 (ArCH, C × 2), 128.4 (ArCH), 127.6 (ArCH, C × 2), 127.3 (ArCH), 127.2 (ArCH), 127.0 (ArCH, C × 2), 125.6 (ArCH), 121.5 (*C*H_2=CH), 110.0 (N-C(Ph)=*C*H), 102.9 (*C*-NO_2), 78.3 (Ph-*C*H), 53.0 (vinyl-*C*H) ppm. HRMS–ASAP $[M + H]^+$: Calcd for $C_{25}H_{21}N_2O_2$ 381.1603; Found 381.1598. IR ν_{max} (neat): 2950, 2921, 2853, 1623, 1531, 1470, 1450, 1353, 1269, 1174, 1023, 935 cm^{-1}.

(±)-(1*R*,4*R*,5*R*,10*R*)-2-(4-Methoxyphenyl)-4-nitro-10-phenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2b)



The titled compound was prepared following ***General Procedure A*** using tetrahydroquinoline **1b** (21.7 mg 0.052 mmol), $Pd(TFA)_2$ (1.6 mg 0.005 mmol) and aqueous HBF_4 (2.0 μL, 0.015 mmol). Purification by FCC (Et_2O/hexane – 5:95 v/v) afforded the desired product as a yellow gum (21.1 mg, 55% yield). TLC: (Et_2O/hexane – 10:90), R_f = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.8 Hz, 2H, ArH), 7.35 – 7.21 (m, 7H, ArH), 7.19 (td, *J* = 7.5, 1.4 Hz, 1H, ArH), 7.08 (td, *J* = 7.6, 1.6 Hz, 1H, ArH), 6.94 (d, *J* = 8.8 Hz, 2H, ArH), 6.01 (s, 1H, N-C(Ph)=C*H*), 5.80 (dt, *J* = 17.0, 9.7 Hz, 1H, CH_2=C*H*), 5.44 (dd, *J* = 17.0, 1.5 Hz, 1H, CH_EH$_Z$=CH), 5.36 (dd, *J* = 10.0, 1.5 Hz, 1H, CH$_E$$H_Z$=CH), 4.88 (s, 1H, Ph-C*H*), 4.81 (d, *J* = 9.4 Hz, 1H, vinyl-C*H*), 3.83 (s, 3H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (Ar*C*-OMe), 159.2 (HC=*C*–N), 148.8 (ArC), 134.8 (ArC), 134.0 (ArC), 132.7 (CH_2=*C*H), 131.0 (ArCH), 128.5 (ArCH, C × 2), 128.4 (ArCH, C × 3), 127.7 (ArCH, C × 2), 127.2 (ArCH), 127.1 (ArCH), 125.6 (ArCH), 123.2 (ArC), 121.4 (*C*H_2=CH), 114.2 (ArCH, C × 2), 107.5 (N-C(PMP)=*C*H), 103.0 (*C*-NO_2), 78.0 (Ph-*C*H), 55.4 (O*C*H_3), 53.0 (vinyl-*C*H) ppm. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{26}H_{23}N_2O_3$ 411.1709; Found 411.1726. IR ν_{max} (neat): 2931, 1623, 1604, 1536, 1507, 1301, 1250, 1169, 1026, 743 cm^{-1}.

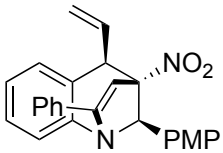
(±)-(1*S*,4*R*,5*R*,10*R*)-2-Isopentyl-4-nitro-10-phenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2c)



The titled compound was prepared following ***General Procedure A*** using tetrahydroquinoline **1c** (14.2 mg 0.038 mmol), $Pd(TFA)_2$ (1.40 mg 0.004 mmol) and aqueous HBF_4 (1.5 μL, 0.011 mmol). Purification by FCC (Et_2O/hexane – 2:98 v/v) afforded the desired product as a yellow oil (8.8 mg, 62% yield). TLC: (Et_2O/hexane – 10:90, R_f = 0.26. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (s, 6H, ArH), 7.26 (td, *J* = 7.6, 7.1, 2.1 Hz, 1H, ArH), 7.21 (dd, *J* = 7.7, 1.8 Hz, 1H, ArH), 7.19 (d, *J* = 1.9 Hz, 1H, ArH), 5.68 (dt, *J* = 17.0, 9.8 Hz, 1H, CH_2=C*H*), 5.52 (s, 1H, N-C(Ph)=C*H*), 5.41 (dd, *J* = 17.1, 1.6 Hz, 1H, CH_EH$_Z$=CH), 5.32 (dd, *J* = 10.0, 1.6 Hz, 1H, CH$_E$$H_Z$=CH), 4.75 (s, 1H, Ph-C*H*), 4.69 (d, *J* = 9.5 Hz, 1H, vinyl-C*H*), 2.47 – 2.30 (m, 1H, CH$_a$$H_b$), 2.22 – 2.07 (m, 1H, C$H_aH_b$), 1.62 – 1.45 (m, 2H, C*H*(CH$_3$)$_2$, CH_CH$_D$-C=C), 1.40 – 1.19 (m, 1H, CH$_C$$H_D$-C=C), 0.86 (dd, *J* = 9.1, 6.3 Hz, 6H, (CH_3)$_2$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4 (HC=*C*–N), 148.8 (ArC), 135.1 (ArC), 134.4 (ArC), 132.7 (CH_2=*C*H), 131.3 (ArCH), 128.6 (ArCH), 128.6 (ArCH, C × 2), 127.9 (ArCH, C × 2), 127.4 (ArCH), 127.4 (ArCH), 125.6 (ArCH), 121.6 (*C*H_2=CH), 110.2 (N-C(*i*-pentyl)=*C*H), 102.5 (*C*-NO_2), 78.1 (Ph-*C*H), 53.0 (vinyl-*C*H), 35.0 (*C*H$_C$H$_D$-C=C), 27.9 *C*H(CH$_3$)$_2$, 27.3 (*C*H$_a$H$_b$), 22.7 (*C*H$_3$), 22.4 (*C*H$_3$) ppm. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{24}H_{27}N_2O_2$ 375.2073; Found 375.2082. IR ν_{max} (neat): 2945, 1532, 1498, 738 cm^{-1}.

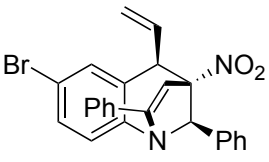
(±)-(1*R*,4*R*,5*R*,10*R*)-10-(4-Methoxyphenyl)-4-nitro-2-phenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2d)

The titled compound was prepared following modified ***General Procedure A*** using tetrahydroquinoline **1d** (24.2 mg 0.058 mmol), $Pd(TFA)_2$ (1.9 mg 0.006 mmol) and aqueous HBF_4 (2.3 μL, 0.017 mmol) for 48 h. This was followed by a re-subjection of



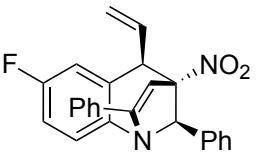
crude reaction mixture for an additional 48 h using $Pd(TFA)_2$ (1.70 mg 0.005 mmol) aqueous HBF_4 (2.3 μL, 0.017 mmol). Purification by FCC (Et_2O/hexane – 2:98 v/v) afforded the desired product as a yellow solid (13.7 mg, 57% yield). MP 158–160 °C. TLC: (Et_2O/hexane – 10:90), R_f = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.8, 1.8 Hz, 2H, ArH), 7.51 – 7.36 (m, 2H, ArH), 7.32 – 7.14 (m, 6H, ArH), 7.08 (td, *J* = 7.3, 1.5 Hz, 1H, ArH), 6.79 (d, *J* = 8.9 Hz, 2H, ArH), 6.19 (s, 1H, N-C(Ph)=C*H*), 5.80 (dt, *J* = 17.0, 9.7 Hz, 1H, CH_2=C*H*), 5.44 (dd, *J* = 17.0, 1.6 Hz, 1H, CH_EH$_Z$=CH), 5.36 (dd, *J* = 10.0, 1.5 Hz, 1H, CH_EH$_Z$=CH), 4.88 (s, 1H, PMP-C*H*), 4.81 (d, *J* = 9.4 Hz, 1H, vinyl-C*H*), 3.74 (s, 3H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6 (Ar*C*-OMe), 159.5 (HC=*C*–N), 148.8 (ArC), 133.9 (ArC), 132.6 (CH_2=*C*H), 131.0 (ArCH), 130.6 (ArC), 130.0 (ArC), 128.8 (ArCH), 128.8 (ArCH, C × 2), 127.2 (ArCH), 127.1 (ArCH), 127.0 (ArCH, C × 2), 126.7 (ArC), 125.6 (ArCH), 121.4 (*C*H_2=CH), 113.9 (ArCH), 110.0 (N-C(Ph)=*C*H), 102.9 (*C*-NO_2), 78.0 (PMP-*C*H), 55.2 (ArC-O*C*H_3), 53.0 (vinyl-*C*H) ppm. HRMS (ESI) m/z: [M + H]$^+$: Calcd for $C_{26}H_{23}N_2O_3$ 411.1709; Found 411.1725. IR ν_{max} (neat): 2931, 1605, 1537, 1471, 1451, 1419. 1364 1300, 1251, 746 cm^{-1}.

(±)-(1*R*,4*R*,5*R*,10*R*)-7-Bromo-4-nitro-2,10-diphenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2e)



The titled compound was prepared following modified ***General Procedure A*** using tetrahydroquinoline **1e** (21.3 mg 0.046mmol), $Pd(TFA)_2$ (1.7 mg 0.005 mmol) and aqueous HBF_4 (2.0 μL, 0.016 mmol) for 48 h. This was followed by a re-subjection of crude reaction mixture for an additional 96 h using $Pd(TFA)_2$ (3.70 mg 0.011 mmol) aqueous HBF_4 (4.0 μL, 0.033 mmol) at 40 ºC. Purification by FCC (Et_2O/hexane – 3:97 v/v) afforded the desired product as a pale-yellow powder (7.9 mg, 37% yield). MP 220–221. °C TLC: (Et_2O/hexane – 20:80), R_f = 0.60. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.74 (m, 2H, ArH), 7.47 – 7.39 (m, 4H, ArH), 7.28 (s, 5H, ArH), 7.21 (ddd, *J* = 8.3, 2.3, 0.7 Hz, 1H, ArH), 7.13 (d, *J* = 8.4 Hz, 1H, ArH), 6.17 (s, 1H, N-C(Ph)=C*H*), 5.79 (dt, *J* = 17.0, 9.7 Hz, 1H, CH_2=C*H*), 5.47 (d, *J* = 16.8 Hz, 1H, CH_EH$_Z$=CH), 5.41 (dd, *J* = 9.9, 1.4 Hz, 1H, CH_EH$_Z$=CH), 4.87 (s, 1H, Ph-C*H*), 4.81 (d, *J* = 9.4 Hz, 1H, vinyl-C*H*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (HC=*C*–N), 147.8 (ArC), 136.3 (ArC),134.2 (ArC), 133.9 (ArCH), 131.8 (CH_2=*C*H), 130.4 (ArCH), 130.3 (ArCH), 130.2 (ArC), 128.9 (ArCH, C × 2), 128.6 (ArCH), 128.5 (ArCH, C × 2), 127.6 (ArCH, C × 2), 127.2 (ArCH), 127.0 (ArCH, C × 2), 122.4 (*C*H_2=CH), 120.5 (ArC), 110.0 (N-C(Ph)=*C*H), 102.5 (*C*-NO_2), 78.1 (Ph-*C*H), 52.9 (vinyl-*C*H) ppm. HRMS (ESI) m/z: [M + H]$^+$: Calcd for $C_{25}H_{20}BrN_2O_2$ 459.0708; Found 459.0725. IR ν_{max} (neat): 3067, 2920, 2851, 1735, 1622, 1576, 1531, 1491, 1468, 1171, 1074, 745 cm^{-1}.

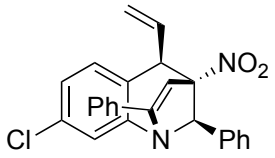
(±)-(1*R*,4*R*,5*R*,10*R*)-7-Fluoro-4-nitro-2,10-diphenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2f)



The titled compound was prepared following modified ***General Procedure A*** using tetrahydroquinoline **1f** (26.4 mg 0.066mmol), $Pd(TFA)_2$ (2.4 mg 0.007 mmol) and aqueous HBF_4 (2.9 μL, 0.198 mmol) for 48 h. Purification by short silica plug in Et_2O afforded the desired product as a yellow solid (23.0 mg, 87% yield). MP 139–140 °C. TLC:

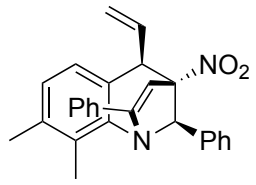
(Et_2O/hexane – 10:90), R_f = 0.22. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H, ArH), 7.45 – 7.38 (m, 3H, ArH), 7.31 – 7.25 (m, 5H, ArH), 7.24 – 7.20 (m, 1H, ArH), 6.99 (ddd, *J* = 9.1, 2.9, 1.0 Hz, 1H, ArH), 6.76 (td, *J* = 8.4, 2.9 Hz, 1H, ArH), 6.17 (s, 1H, N-C(Ph)=C*H*), 5.79 (dt, *J* = 17.0, 9.7 Hz, 1H, CH_2=C*H*), 5.47 (dd, *J* = 17.0, 1.3 Hz, 1H, CH_EH$_Z$=CH), 5.40 (dd, *J* = 10.0, 1.4 Hz, 1H, CH$_E$H$_Z$=CH), 4.88 (s, 1H, Ph-C*H*), 4.81 (d, *J* = 9.4 Hz, 1H, vinyl-C*H*) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.5 (d, ^1J (C, F) = 245.9 Hz, F-ArC) 159.8 (HC=*C*–N), 144.7 (d, ^4J (C, F) = 2.9 Hz, ArC), 136.3 (d, ^3J (C, F) = 7.9 Hz, ArC) 134.6 (ArC), 132.1 (CH_2=*C*H), 130.5 (ArCH), 130.4 (ArCH), 129.1 (ArCH, C × 2), 128.7 (ArCH, C × 2), 128.7 (ArCH), 127.7 (ArCH, C × 2), 127.2 (ArC), 127.2 (ArCH, C × 2), 122.4 (*C*H$_2$=CH), 118.0 (d, ^2J (C, F) = 23.8 Hz, ArCH), 114.1 (d, ^2J (C, F) = 22.4 Hz, ArCH) 110.0 (N-C(Ph)=*C*H), 102.7 (*C*-NO_2), 78.6 (Ph-*C*H), 53.3 (d, ^4J (C, F) = 1.8 Hz, vinyl-*C*H) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ -114.15. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{25}H_{20}FN_2O_2$ 399.1509; Found 399.1526. IR ν_{max} (neat): 2967 1540, 1479, 1173, 751 cm^{-1}.

(±)-(1*S*,4*R*,5*R*,10*R*)-8-Chloro-4-nitro-2,10-diphenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2g)



The titled compound was prepared following modified ***General Procedure A*** using tetrahydroquinoline **1g** (15.4 mg 0.037mmol), $Pd(TFA)_2$ (1.0 mg 0.003 mmol) and aqueous HBF_4 (1.5 μL, 0.111 mmol) for 48 h. Purification by FCC (Et_2O/hexane – 3:97 v/v) afforded the desired product as a yellow solid (9.5 mg, 62% yield). MP 200–201 °C. TLC: (Et_2O/hexane – 20:80) R_f = 0.46. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 7.6, 1.6 Hz, 2H, ArH), 7.52 – 7.39 (m, 3H, ArH), 7.27 (d, *J* = 4.7 Hz, 6H, ArH), 7.23 – 7.20 (m, 1H, ArH), 7.20 – 7.16 (m, 1H, ArH), 6.19 (s, 1H, N-C(Ph)=C*H*), 5.77 (dt, *J* = 17.0, 9.7 Hz, 1H, CH_2=C*H*), 5.45 (ddd, *J* = 17.0, 1.4, 0.7 Hz, 1H, CH_EH$_Z$=CH), 5.38 (dd, *J* = 10.0, 1.4 Hz, 1H, CH$_E$H$_Z$=CH), 4.86 (s, 1H, Ph-C*H*), 4.79 (d, *J* = 9.3 Hz, 1H, vinyl-C*H*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1 (HC=*C*–N), 149.7 (ArC), 134.2 (ArC), 132.5 (ArC), 132.5 (ArC), 132.1 (ArCH), 132.0 (CH_2=*C*H), 130.3 (ArCH), 130.2 (ArC), 129.0 (ArCH, C × 2), 128.6 (ArCH), 128.5 (ArCH, C × 2), 127.5 (ArCH, C × 2), 127.4 (ArCH), 126.9 (ArCH, C × 2), 125.9 (ArCH), 122.0 (*C*H$_2$=CH), 110.3 (N-C(Ph)=*C*H), 102.5 (*C*-NO_2), 78.2 (Ph-*C*H), 52.6 (vinyl-*C*H) ppm. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{25}H_{20}ClN_2O_2$ 415.1213; Found 415.1223. IR ν_{max} (neat): 2922,1626, 1595, 1538, 1467, 1450, 1351, 921, 747 cm^{-1}.

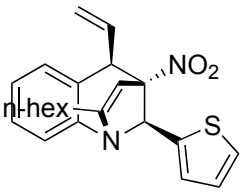
(±)-(1*S*,4*R*,5*R*,10*R*)-8,9-Dimethyl-4-nitro-2,10-diphenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2h)



The titled compound was prepared following modified ***General Procedure A*** using tetrahydroquinoline **1h** (26.8 mg 0.066mmol), $Pd(TFA)_2$ (2.3 mg 0.007 mmol) and aqueous HBF_4 (2.6 μL, 0.021 mmol) for 48 h Purification by short silica plug in Et_2O afforded the desired product as a brown solid (26.5 mg, 99% yield). MP 157–158°C. TLC: (Et_2O/hexane – 10:90), R_f = 0.24. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.69 (m, 2H, ArH), 7.44 – 7.38 (m, 2H, ArH), 7.38 – 7.28 (m, 6H, ArH), 7.00 (q, *J* = 7.9 Hz, 2H, ArH), 6.10 (s, 1H, N-C(Ph)=C*H*), 5.88 (dt, *J* = 17.0, 9.7 Hz, 1H, CH_2=C*H*), 5.42 (d, *J* = 17.2 Hz, 1H, CH_EH$_Z$=CH), 5.36 (dd, *J* = 10.0, 1.5 Hz, 1H, CH$_E$H$_Z$=CH), 4.83 (s, 1H, Ph-C*H*), 4.71 (d, *J* = 9.3 Hz, 1H, vinyl-C*H*), 2.27 (s, 3H, (C8)

C<u>*H*₃</u>), 2.12 (s, 3H, (C7) C<u>*H*₃</u>). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1 (HC=<u>*C*</u>–N), 146.9 (ArC), 136.6 (ArC), 135.4 (ArC), 133.1 (CH_2=<u>*C*</u>H), 132.9 (ArC), 131.6 (ArC), 129.9 (ArCH), 128.4 (ArCH), 128.4 (ArCH, C × 4), 128.1 (ArCH), 127.9 (ArCH, C × 2), 127.8 (ArCH), 127.8 (ArC), 127.7 (ArCH, C × 2), 121.1 (<u>*C*</u>H_2=CH), 112.3 (N-C(Ph)=<u>*C*</u>H), 102.7 (<u>*C*</u>-NO_2), 79.0 (Ph-<u>*C*</u>H), 52.9 (vinyl-<u>*C*</u>H), 20.3 (C8, <u>*C*</u>H_3), 15.2 (C7, <u>*C*</u>H_3) ppm. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{27}H_{25}N_2O_2$ 409.1916; Found 409.1936. IR ν_{max} (neat): 2923, 1628, 1602,1533, 1445, 1351, 1265, 1074, 937, 738 cm^{-1}.

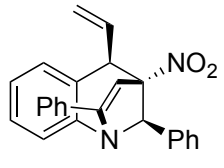
(±)-(1*S*,4*R*,5*R*,10*S*)-2-Hexyl-4-nitro-10-(thiophen-2-yl)-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2i)



The titled compound was prepared following modified ***General Procedure A*** using tetrahydroquinoline **1i** (10.1 mg 0.026mmol), $Pd(TFA)_2$ (1.6 mg 0.005 mmol) and aqueous HBF_4 (1.1 μL, 0.015 mmol) for 48 h. Purification by FCC (Et_2O/hexane – 3:97 v/v) afforded the desired product as a light yellow oil (4.2 mg, 42% yield). TLC: (Et_2O/hexane – 10:90), R_f = 0.39. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 1.5 Hz, 2H, ArH), 7.26 – 7.15 (m, 3H, ArH), 6.99 (d, *J* = 3.1 Hz, 1H, ArH), 6.92 (dd, *J* = 5.1, 3.5 Hz, 1H, ArH), 5.76 – 5.61 (m, 2H, CH_2=C<u>*H*</u>, N-C(n-hex)=C<u>*H*</u>), 5.39 (dd, *J* = 16.8, 0.9 Hz, 1H, C<u>*H*_{*E*}</u>H_Z=CH), 5.33 (dd, *J* = 9.9, 1.5 Hz, 1H, CH_E<u>*H*_{*Z*}</u>=CH), 5.01 (s, 1H, thiophene-C<u>*H*</u>), 4.55 (d, *J* = 9.5 Hz, 1H, vinyl-C<u>*H*</u>), 2.42 – 2.25 (m, 1H, C=C-C<u>*H*_{*A*}</u>H_B), 2.17 – 2.04 (m, 1H, C=C-CH_A<u>*H*_{*B*}</u>), 1.70 – 1.56 (m, 1H, C=C-CH_2-C<u>*H*_{*C*}</u>H_D), 1.51 – 1.39 (m, 1H, C=C-CH_2-CH_C<u>*H*_{*D*}</u>), 1.33 – 1.18 (m, 6H, ((C<u>*H*₂</u>)$_3$), 0.86 (t, *J* = 7.1 Hz, 3H, C<u>*H*₃</u>) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7 (HC=<u>*C*</u>–N), 148.0 (ArC), 136.8 (ArC), 133.4 (ArC), 132.4 (CH_2=<u>*C*</u>H), 131.0 (ArCH), 128.2 (ArCH), 127.3 (ArCH), 127.3 (ArCH), 126.4 (ArCH), 125.7 (ArCH), 125.5 (ArCH), 121.4 (<u>*C*</u>H_2=CH), 110.7 (N-C(Ph)=<u>*C*</u>H), 101.9 (<u>*C*</u>-NO_2), 74.7 (thiophene-<u>*C*</u>H), 52.6 (vinyl-<u>*C*</u>H), 31.5 $(CH_2)_n$, 29.5 (C=C-<u>*C*</u>$H_A$$H_B$), 28.9 $(CH_2)_n$, 25.9 (<u>*C*</u>$H_C$$H_D$), 22.5 $(CH_2)_n$, 14.0 (<u>*C*</u>H_3). HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{23}H_{27}N_2O_2S$ 395.1793; Found 395.1812. IR ν_{max} (neat): 2929, 2857, 1604, 1540, 1250, 1169, 933, 698 cm^{-1}.

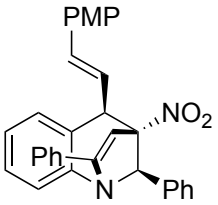
5. Post Synthetic modifications:

1 mmol scale synthesis of (±)-(1*R*,4*R*,5*R*,10*R*)-4-Nitro-2,10-diphenyl-5-vinyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (2a)



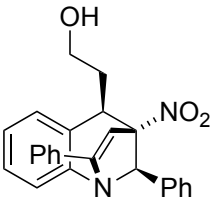
The titled compound was prepared following ***General Procedure A*** using tetrahydroquinoline **1a** (380.4 mg 1,00 mmol), $Pd(TFA)_2$ (29.9 mg 0.100 mmol) and aqueous HBF_4 (39 μL, 0.300 mmol). Purification by FCC (Et_2O/hexane – 2:98 v/v) afforded the desired product as a white solid (303.6 mg, 80% yield).

(±)-(1*R*,4*R*,5*R*,10*R*)-5-((*E*)-4-Methoxystyryl)-4-nitro-2,10-diphenyl-4,5-dihydro-1,4-methanobenzo[*b*]azepine (3)



The titled compound was prepared following a literature procedure on a base-free Heck reaction[2] using **2a**, (38.4 mg 0.100 mmol), Pd_2dba_3•$CHCl_3$, (3.0 mg, 0.003 mmol) and *para*-methoxyphenyl diazonium salt (34.3 mg, 0.155 mmol) in DMA (1.00 mL, 0.1 M) at rt for 21 h that produced compound **3** (35.5 mg, 75% yield) as a light, tan powder via automated flash column chromatography (Et_2O/*n*-hexane – 4% → 8%) of the crude reaction isolate. MP: 109–111 °C. TLC (Et_2O/*n*-hexane – 10:90), R_f = 0.30. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 8.0, 1.6 Hz, 2H, ArH), 7.48 – 7.38 (m, 3H, ArH), 7.36 – 7.24 (m, 9H, ArH), 7.19 (td, *J* = 7.5, 1.4 Hz, 1H, ArH), 7.13 – 7.06 (m, 1H, ArH), 6.86 (d, *J* = 8.8 Hz, 2H, ArH), 6.70 (d, *J* = 15.7 Hz, 1H, (PMP-C*H*=CH), 6.23 (s, 1H, N-C(Ph)=C*H*), 6.01 (ddd, *J* = 15.7, 9.5 Hz, 1H, (PMP-CH=C*H*), 5.00 (d, *J* = 9.5 Hz, 1H, CH=CH-C*H*), 4.96 (s, 1H, Ph-C*H*), 3.81 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.7 (Ar*C*-OMe), 159.5 (HC=*C*–N), 148.7 (ArC), 135.5 (PMP-*C*H=CH), 134.7 (ArC), 134.6 (ArC), 131.2 (ArCH), 130.6 (ArC), 130.0 (ArCH), 128.9 (ArC), 128.8 (ArCH, C × 2), 128.4 (ArCH, C × 3), 128.0 (ArCH, C × 2), 127.6 (ArCH, C × 2), 127.2 (ArCH), 127.2 (ArCH), 127.0 (ArCH, C × 2), 125.6 (ArCH), 121.2 (PMP-CH=*C*H), 114.0 (ArCH, C × 2), 110.2 (N-C(Ph)=*C*H), 103.1 (*C*-NO_2), 78.5 (Ph-*C*H), 55.4 (O*C*H_3), 52.3 (PMP-CH=CH-*C*H). HRMS–ASAP $[M + H]^+$: Calcd for $C_{32}H_{27}N_2O_3$ 487.2022; Found 487.2033. IR ν_{max} (neat): 3030, 2952, 2922, 2853, 1605, 1536, 1510, 1450, 1356, 1297, 1250, 1174, 1027, 965, 818, 744, 694, 513 cm^{-1}.

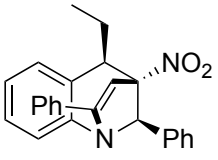
(±)-2-((1*R*,4*S*,5*R*,10*R*)-4-Nitro-2,10-diphenyl-4,5-dihydro-1,4-methanobenzo[*b*]azepin-5-yl)ethan-1-ol (4)



The title compound was prepared by dissolving **2a** (38.0 mg, 0.100 mmol) in THF (1 mL) at 0 ºC for 5 minutes. This was followed by dropwise addition of DMS•BH_3 (2M in THF, 0.6 mL, overall molarity was 0.0625 M). The reaction mixture was left to stir for 21 h at rt. Upon reaction completion indicated by TLC, the reaction mixture was cooled to 0 ºC for an oxidative workup by dropwise addition of NaOH (3.75 M, 0.15 mL, 0.500 mmol) followed by H_2O_2 (35 % wt in H_2O, 0.1 mL, 1 mmol). The reaction mixture was left to stir at 0 ºC for 10 min, then 1 h at rt. The reaction mixture was diluted with H_2O and extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, then concentrated *in vacuo*. The crude reaction mixture was then purified by FCC over silica gel (EtOAc/hexane – 20:80 – 50:50 v/v) as an orange oil (11.0 mg, 28% yield). TLC: (EtOAc/hexane – 20:80) R_f = 0.05. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 6.8, 1.0 Hz, 2H, ArH), 7.47 – 7.36 (m, 5H, ArH), 7.27 – 7.19 (m, 6H, ArH), 7.07 (t, *J* = 7.6 Hz, 1H, ArH), 6.25 (s, 1H, N-C(Ph)=C*H*), 4.83 (s, 1H, Ph-C*H*), 4.53 (dd, *J* = 8.2, 4.7 Hz, 1H, C*H*-$(CH_2)_2$OH), 3.84 – 3.70 (m, 2H, CH-CH_2), 2.27 – 2.06 (m, 2H, CH_2-OH), 1.63 (s, 1H, OH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6 (HC=*C*–N), 148.5 (ArC), 136.5 (ArC), 134.7 (ArC), 130.6 (ArC), 130.1 (ArCH, C × 2), 128.8 (ArCH, C × 2), 128.5 (ArCH), 128.4 (ArCH, C × 2),

127.5 (ArCH, C × 2), 127.3 (ArCH), 127.1 (ArCH, C × 2), 126.9 (ArCH), 125.8 (ArCH), 110.8 (N-C(Ph)=<u>C</u>H), 103.1 (<u>C</u>-NO_2), 79.6 (Ph-<u>C</u>H), 60.5 (<u>C</u>H-$(CH_2)_2$OH), 44.0 (CH-<u>C</u>H_2), 34.6 (<u>C</u>H_2-OH) ppm. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{25}H_{23}N_2O_3$ 399.1709; Found 399.1721. IR ν_{max} (neat): 3348, 3063, 2968, 1603, 1537, 1492, 1473, 1359 1269, 1027, 757, 696 cm^{-1}.

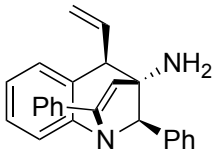
(±)-(1*R*,4*R*,5*R*,10*R*)-5-Ethyl-4-nitro-2,10-diphenyl-4,5-dihydro-1,4-methanobenzo[b]azepine (5)



The titled compound was prepared by dissolving **2a** (38.4 mg, 0.100 mmol) and $[C_8H_{12}IrP(C_6H_{11})_3C_5H_5N]$ PF_6 (8.5 mg, 0.010 mmol) in CH_2Cl_2 (0.5 mL, 0.2 M). The reaction was stirred at rt under 1 atmospheric pressure of H_2 for 21 h. Upon addition of H_2, an instant colour change of reaction mixture was observed from orange to brown. The reaction mixture was diluted in EtOAc, and passed through a pad of silica gel. The filtrate was concentrated to afford **5** as a brown powder (42.3 mg, quant. yield). TLC: (Et_2O/hexane – 10:90) R_f = 0.48. MP 98–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.0, 1.6 Hz, 2H, ArH), 7.55 – 7.32 (m, 5H, ArH), 7.31 – 7.21 (m, 5H, ArH), 7.20 (td, *J* = 7.6, 1.4 Hz, 1H, ArH), 7.05 (td, *J* = 7.6, 1.5 Hz, 1H, ArH), 6.26 (s, 1H, N-C(Ph)=C<u>H</u>), 4.81 (s, 1H, Ph-C<u>H</u>), 4.31 (dd, *J* = 8.8, 4.6 Hz, 1H, C<u>H</u>-CH_2-CH_3), 2.02 – 1.86 (m, 2H, CH-C<u>H_2</u>-CH_3), 1.05 (t, *J* = 7.6 Hz, 3H, CH-CH_2-C<u>H_3</u>). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0 (HC=<u>C</u>–N), 148.4 (ArC), 136.7 (ArC), 134.8 (ArC), 130.7 (ArC), 129.9 (ArCH), 129.8 (ArCH), 128.8 (ArCH, C × 2), 128.4 (ArCH), 128.4 (ArCH, C × 2), 127.6 (ArCH, C × 2), 127.1 (ArCH), 127.0 (ArCH, C × 2), 126.7 (ArCH), 125.8 (ArCH), 110.9 (N-C(Ph)=<u>C</u>H), 103.0 (<u>C</u>-NO_2), 79.6 (Ph-<u>C</u>H), 48.2 (<u>C</u>H-CH_2CH_3), 25.0 (CH-<u>C</u>H_2CH_3), 12.0 (CH-CH_2<u>C</u>H_3) ppm. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{25}H_{23}N_2O_2$ 383.1760; Found 383.1770. IR ν_{max} (neat): 2932, 1574, 1535, 1449. 1357, 1184. 1026 964, 841 cm^{-1}.

(±)-(1*R*,4*R*,5*R*,10*R*)-2,10-Diphenyl-5-vinyl-1,4-methanobenzo[*b*]azepin-4(5*H*)-amine (6)

Following a literature procedure,[3] a solution of **2a** (38.4 mg, 0.100 mmol) in MeOH/THF (1.2:0.6 mL 0.055 M) was cooled to 0 ºC (ice bath). Concentrated aq HCl solution (32% w/w – 0.2 mL) was added to the solution followed by careful small addition of Zn dust (196.2 mg, 3 mmol) over 5 min. The reaction mixture was stirred at 0 ºC for 30 min and rt for 1 h. The resulting reaction mixture was treated with sat aq. $NaHCO_3$ solution followed by the addition of MeOH (1.5 mL) and was left to stir for 10 min at rt and then filtered over a plug of Celite. The filtrate was concentrated *in vacuo* to remove organic solvents. The aqueous solution was treated with sat. aq $NaHCO_3$ solution again and the aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine, dried over anhydrous K_2CO_3, filtered, then concentrated *in vacuo*. The final product was purified by FCC on silica gel (EtOAc/Hex – 20:80 v/v) to give amine product **6** as dark yellow solid (30.4 mg, 86 yield). MP 164–166 °C. TLC: (EtOAc/hexane – 20:80), R_f = 0.20. ^{1}H NMR (400 MHz,



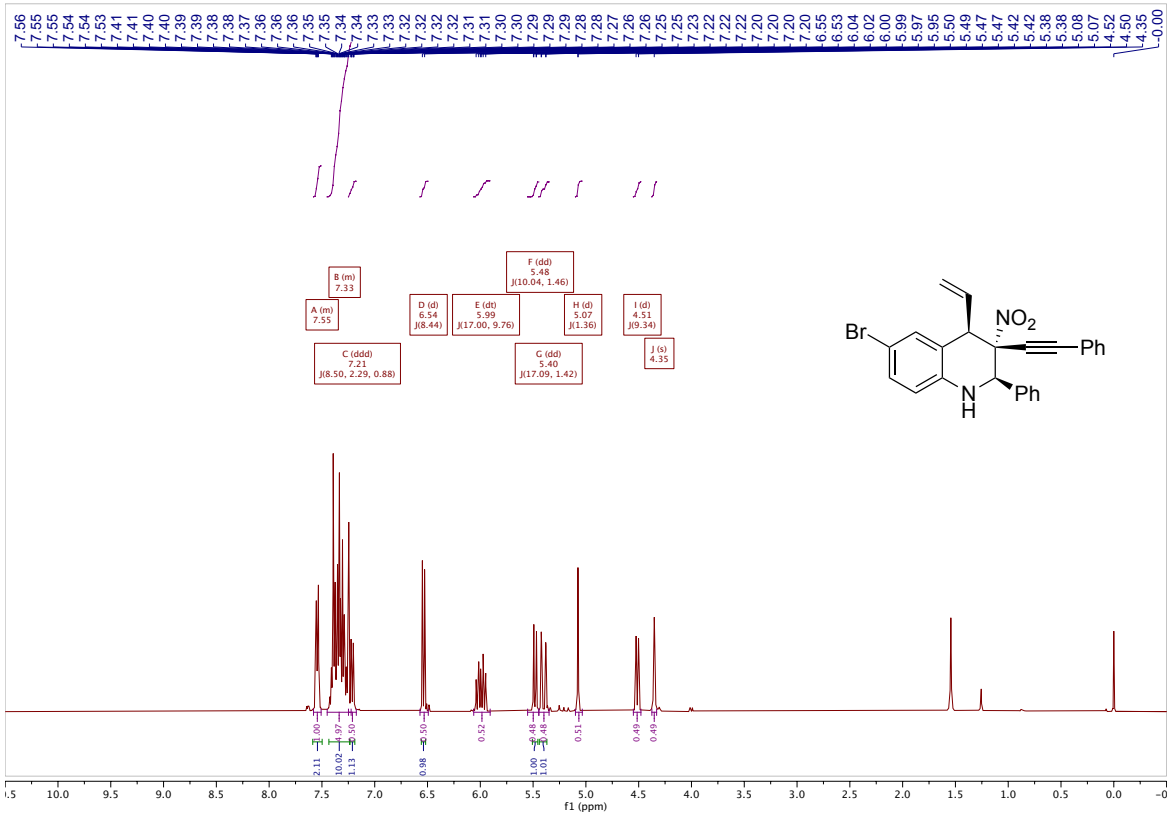
$CDCl_3$) δ 7.90 (dd, *J* = 8.1, 1.3 Hz, 2H, ArH), 7.42 – 7.35 (m, 4H, ArH), 7.32 (dd, *J* = 7.8, 1.9 Hz, 1H, ArH), 7.31 – 7.26 (m, 3H, ArH), 7.26 – 7.20 (m, 2H, ArH), 7.13 (td, *J* = 7.5, 1.4 Hz, 1H, ArH), 7.05 – 7.00 (m, 1H, ArH), 5.84 (dt, *J* = 17.0, 9.9 Hz, 1H, CH_2=C*H*), 5.55 (s, 1H, N-C(Ph)=C*H*), 5.49 (dd, *J* = 17.0, 2.0 Hz, 1H, CH_EH$_Z$=CH), 5.38 (dd, *J* = 9.9, 2.0 Hz, 1H, CH_EH$_Z$=CH), 4.41 (s, 1H, Ph-C*H*), 3.76 (d, *J* = 9.8 Hz, 1H, vinyl-C*H*) ppm, NH_2 not observed. ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7 (HC=*C*–N), 150.4 (ArC), 137.4 (ArC), 136.0 (ArC and CH_2=*C*H)*, 131.9 (ArC), 131.3 (ArCH), 128.8 (ArCH, C × 2), 128.5 (ArCH, C × 2), 128.4 (ArCH), 128.0 (ArCH, C × 2), 127.3 (ArCH), 126.7 (ArCH, C × 2), 126.5 (ArCH), 126.4 (ArCH), 125.4 (ArCH), 119.7 (*C*H_2=CH), 119.5 (N-C(Ph)=*C*H), 78.9 (Ph-*C*H), 67.1 (*C*-NH_2) , 56.4 (vinyl-*C*H) ppm. * This carbon resonance represents both ArC and CH_2=*C*H as they overlap. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{25}H_{23}N_2$ 351.1861; Found 351.1870. IR ν_{max} (neat): 3068, 2926, 1600, 1574, 1490, 1471, 1447, 1321, 1247 1105 1082, 1002, 863, 743, 694 cm^{-1}.

6. References

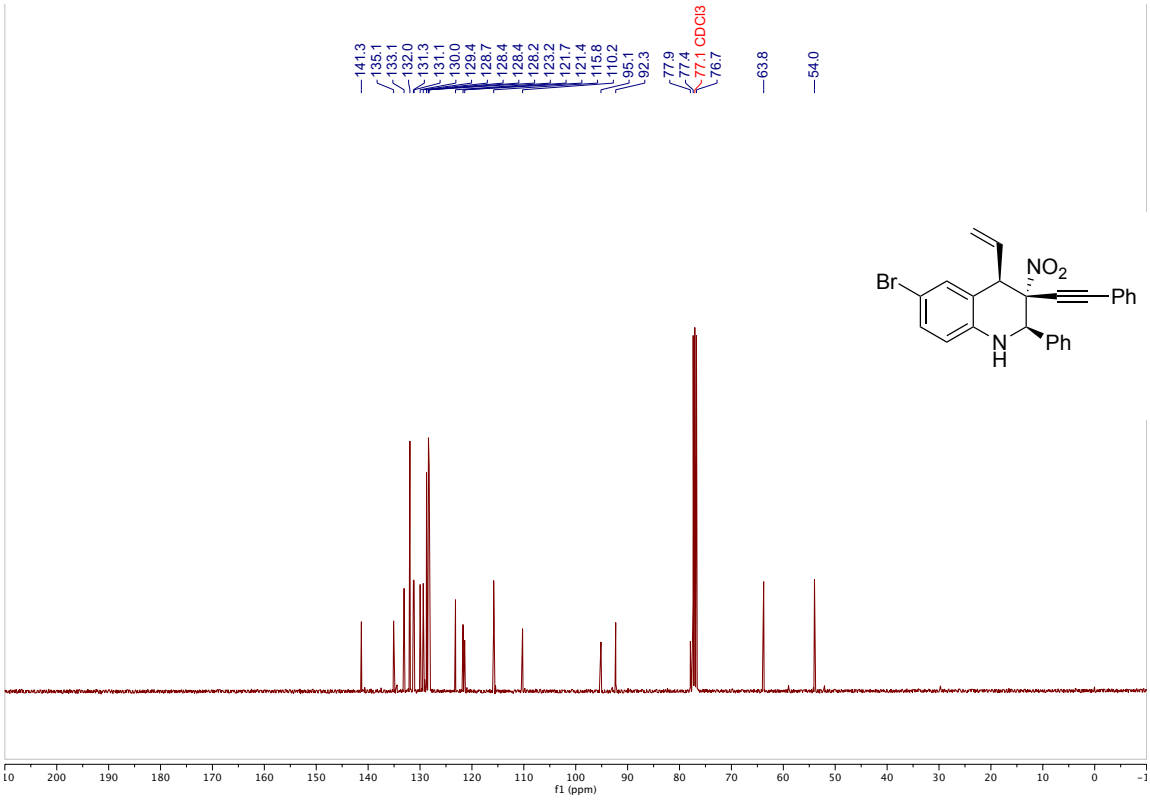
1. A. J. Tague, Q. Hoang Pham, C. Richardson, S. G. Pyne and C. J. T. Hyland, *Chem. – Eur. J.*, 2023, **29**, e202302406.
2. E. W. Werner and M. S. Sigman, *J. Am. Chem. Soc.*, 2011, **133**, 9692–9695.
3. B. M. Trost, V. Ehmke, B. M. O'Keefe and D. A. Bringley, *J. Am. Chem. Soc.*, 2014, **136**, 8213–8216.

7. NMR spectra of novel compounds

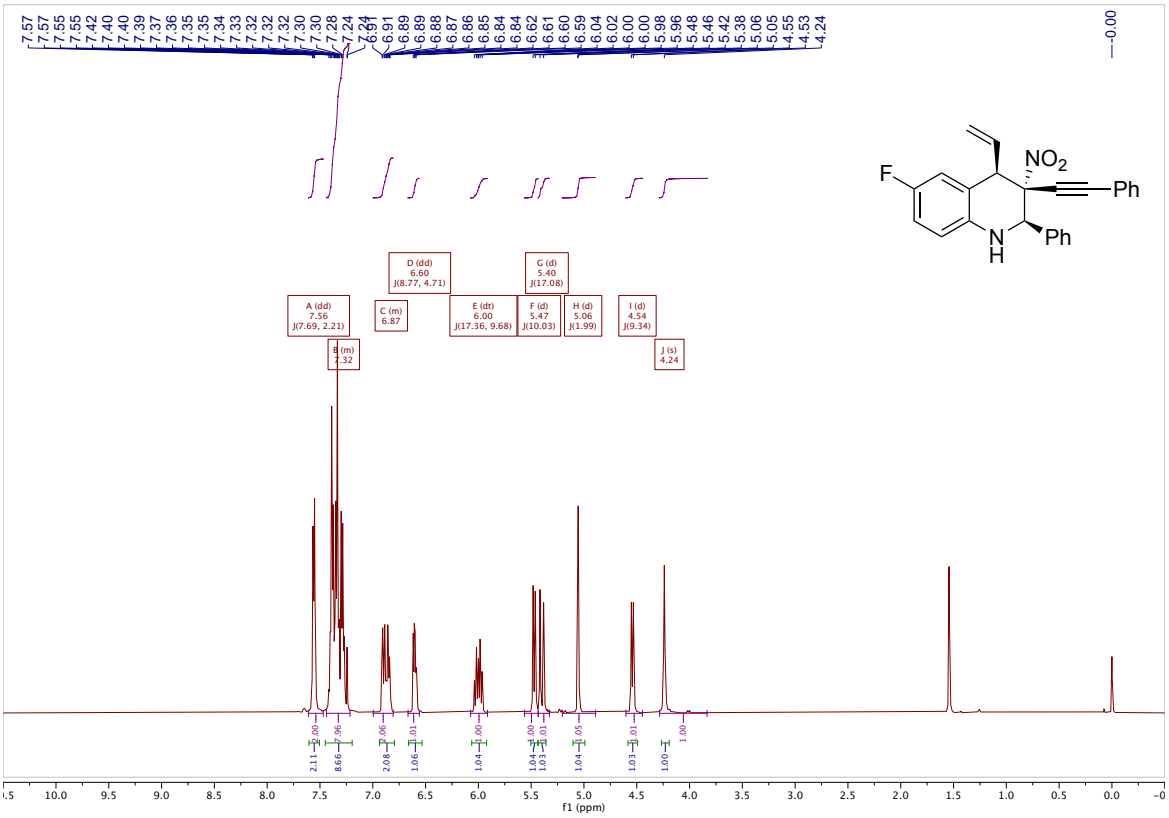
^{1}H NMR (400 MHz, $CDCl_3$) Compound **1e**



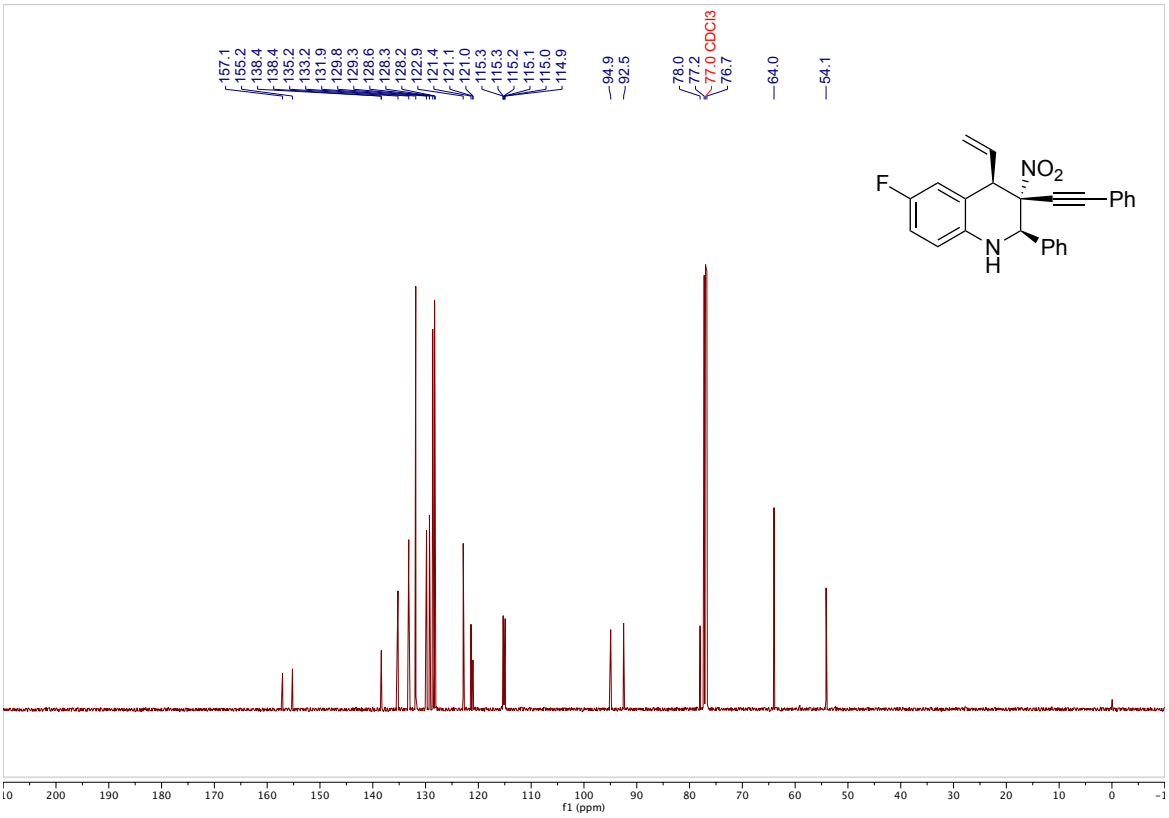
^{13}C NMR (101 MHz, $CDCl_3$): Compound **1e**



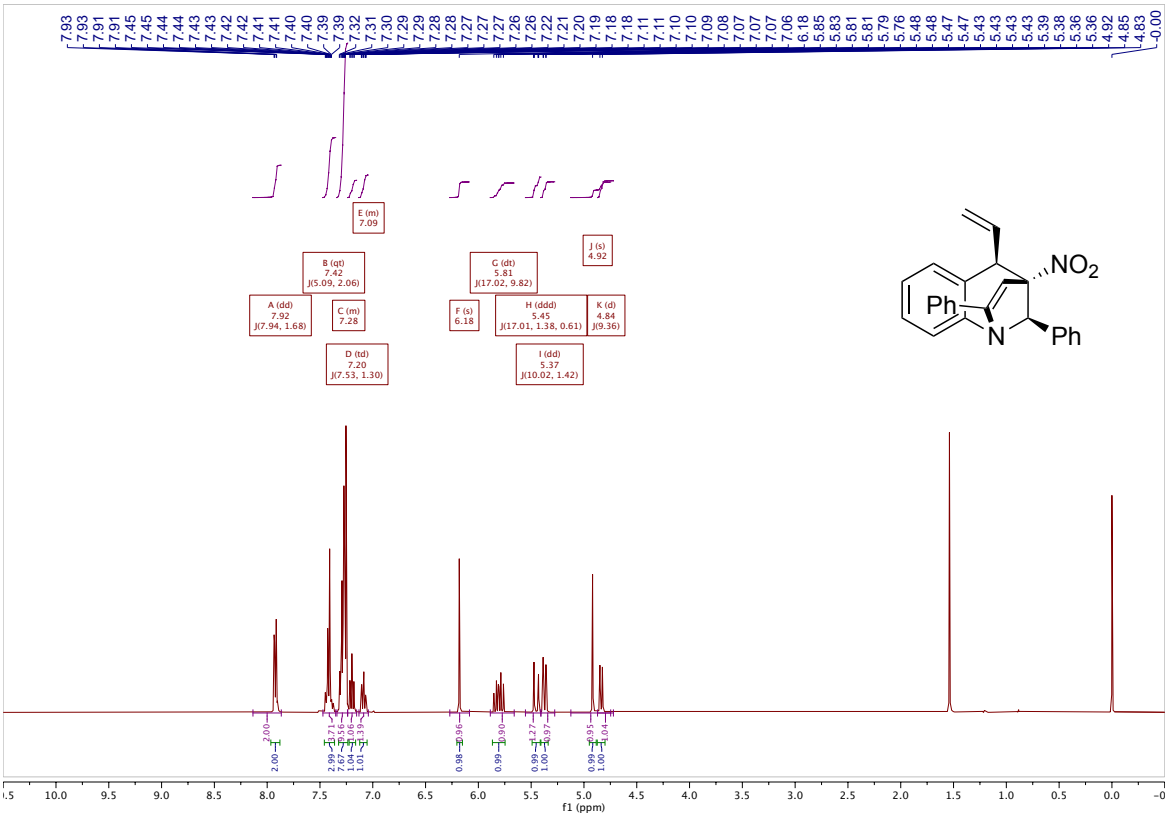
^{1}H NMR (400 MHz, $CDCl_3$) Compound **1f**



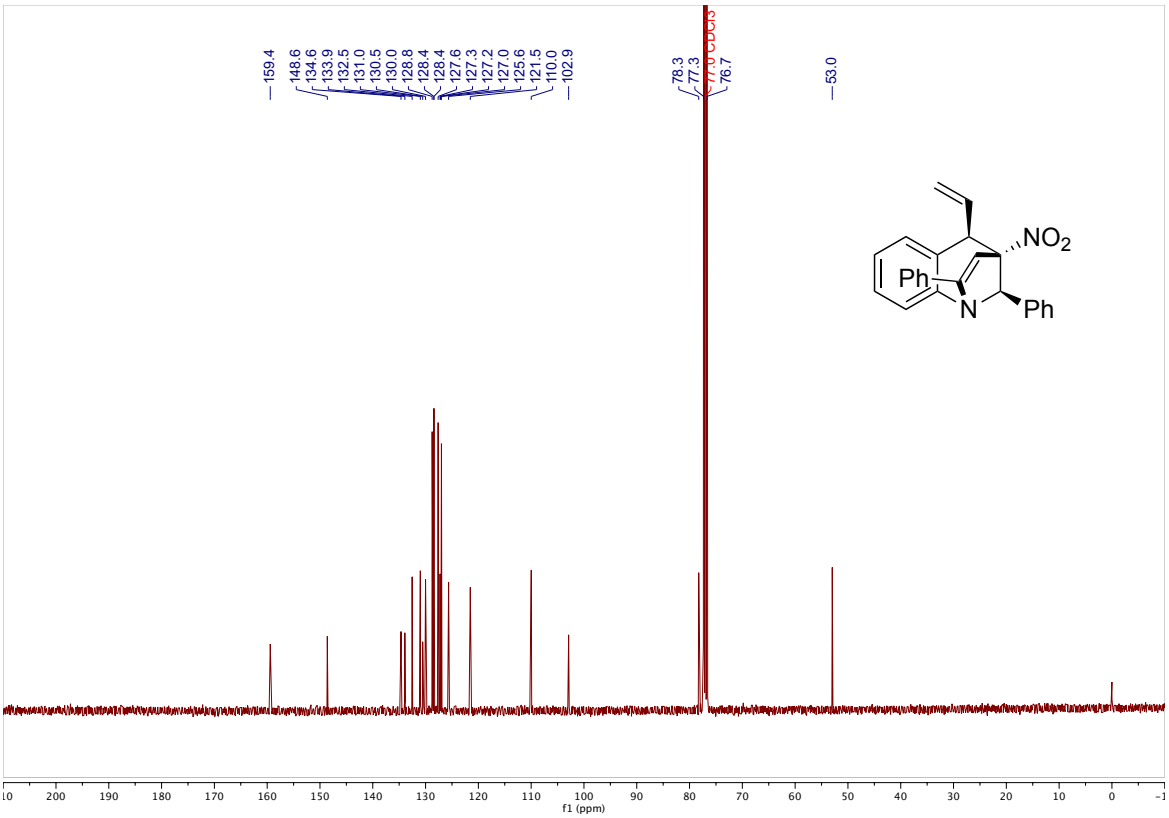
^{13}C NMR (101 MHz, $CDCl_3$): Compound **1f**



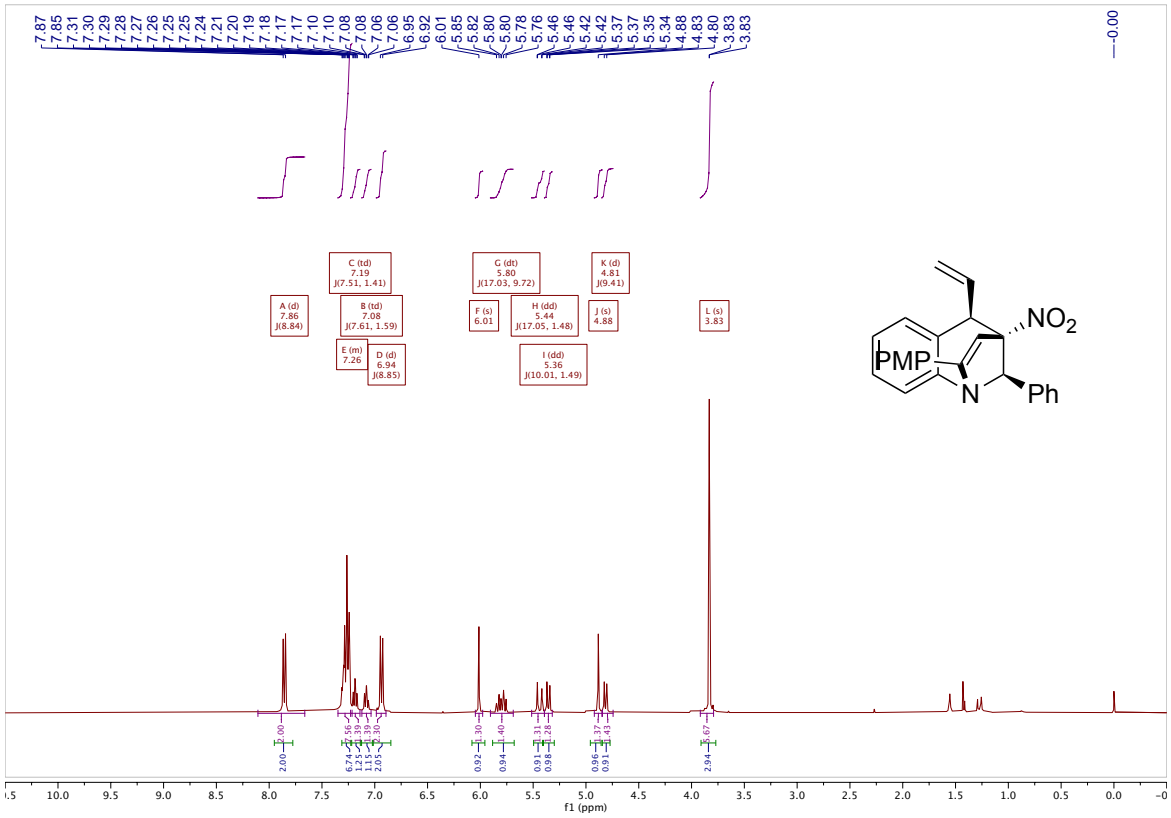
^{1}H NMR (400 MHz, $CDCl_3$) Compound **2a**



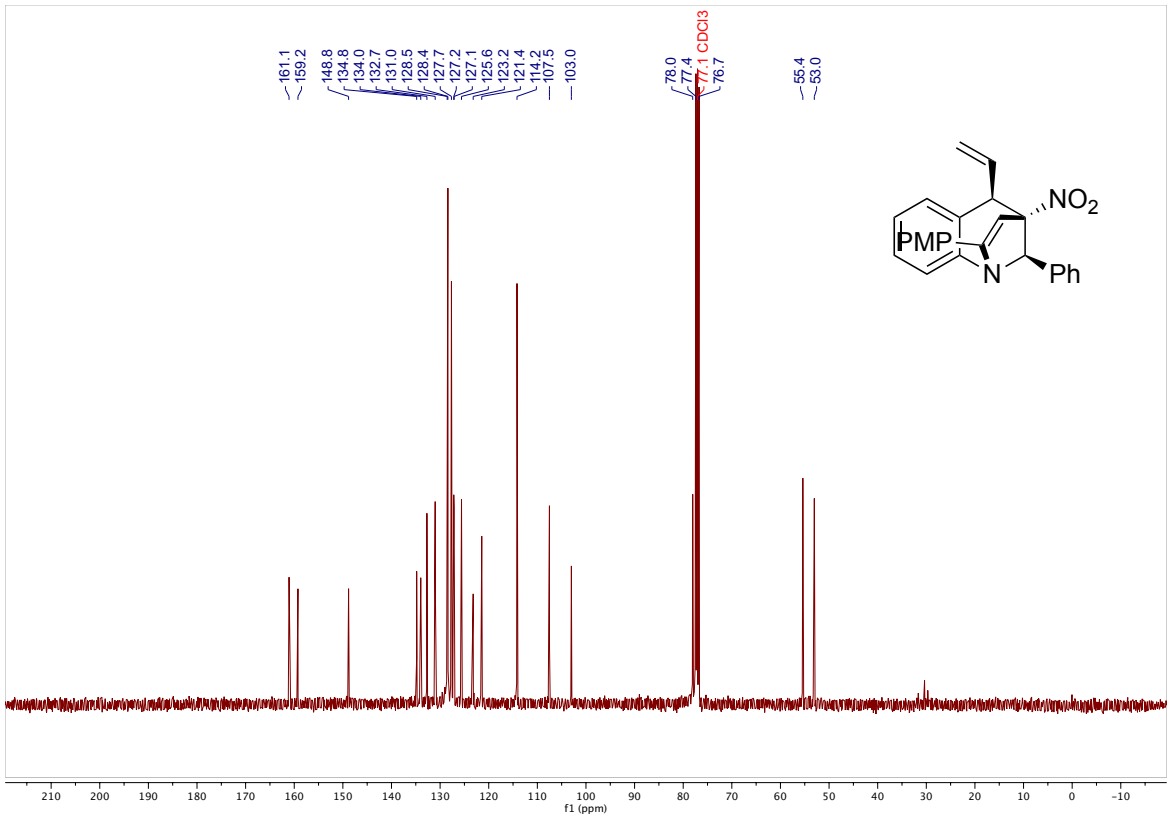
^{13}C NMR (101 MHz, $CDCl_3$): Compound **2a**



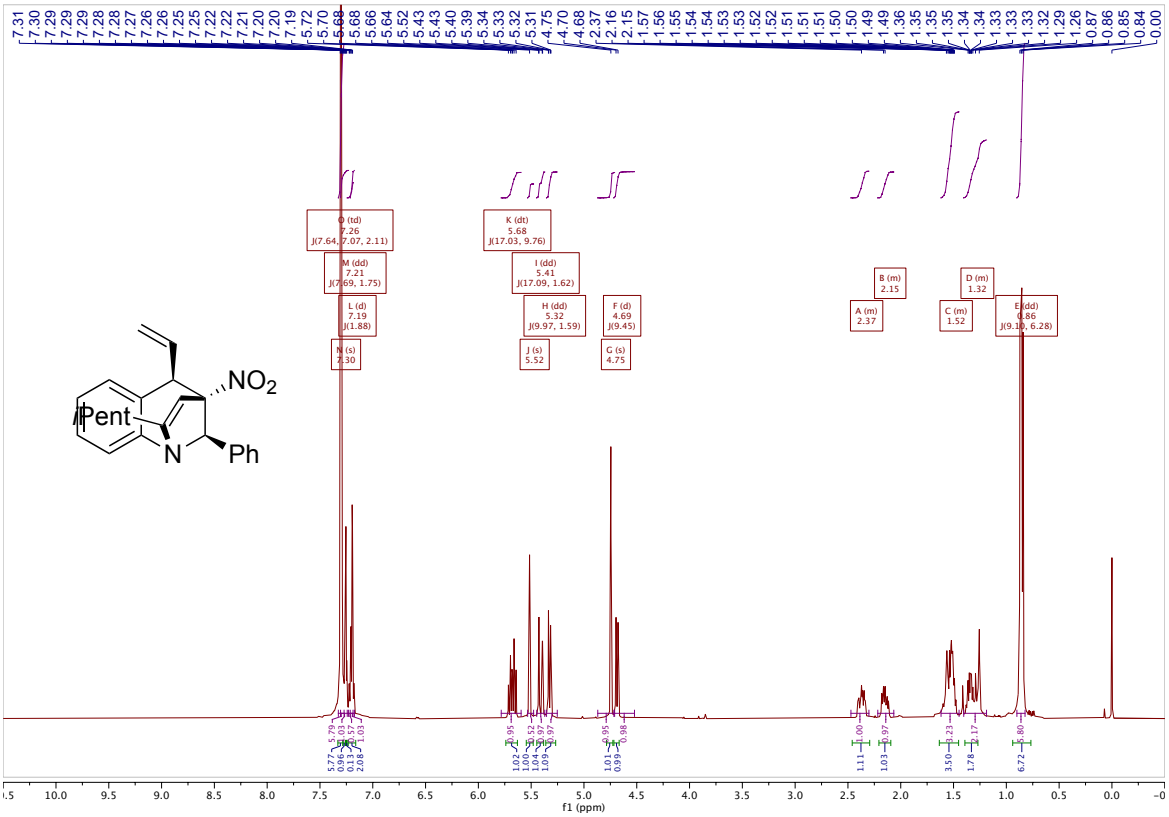
^{1}H NMR (400 MHz, $CDCl_3$) Compound **2b**



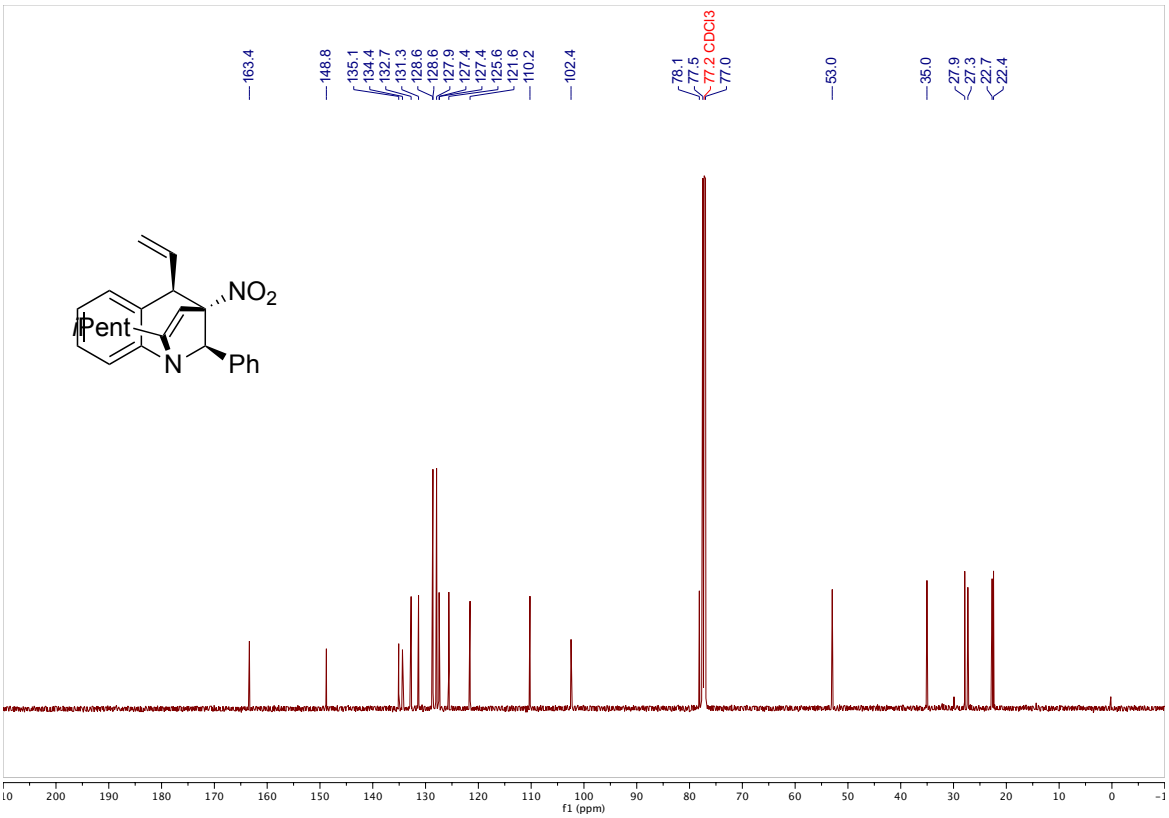
^{13}C NMR (101 MHz, $CDCl_3$): Compound **2b**



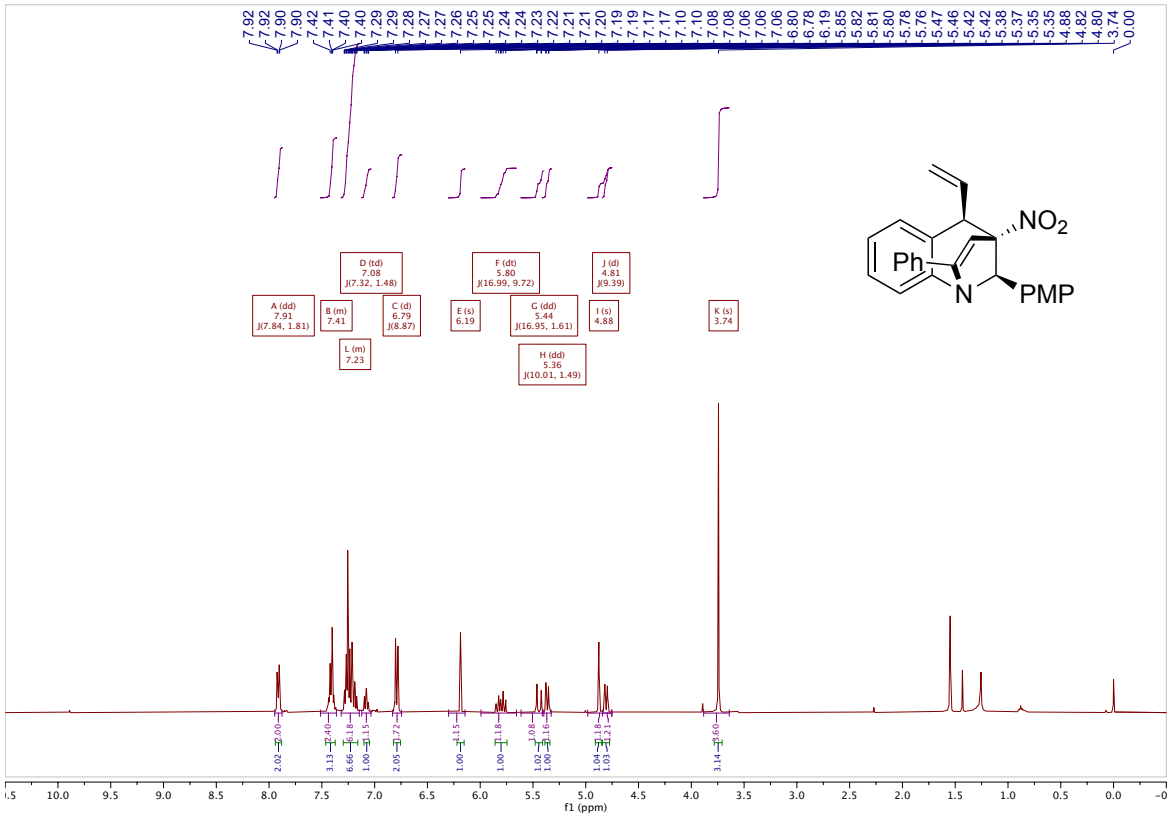
^{1}H NMR (500 MHz, $CDCl_3$) Compound **2c**



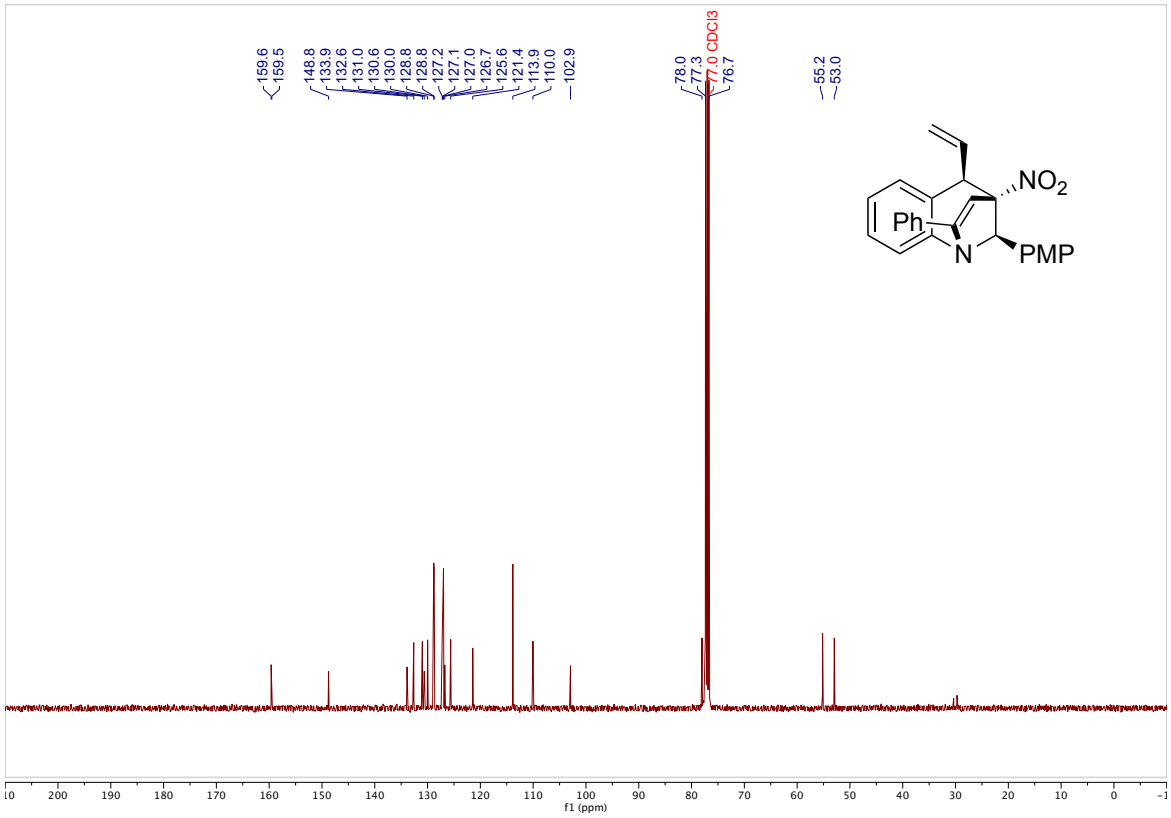
^{13}C NMR (126 MHz, $CDCl_3$): Compound **2c**



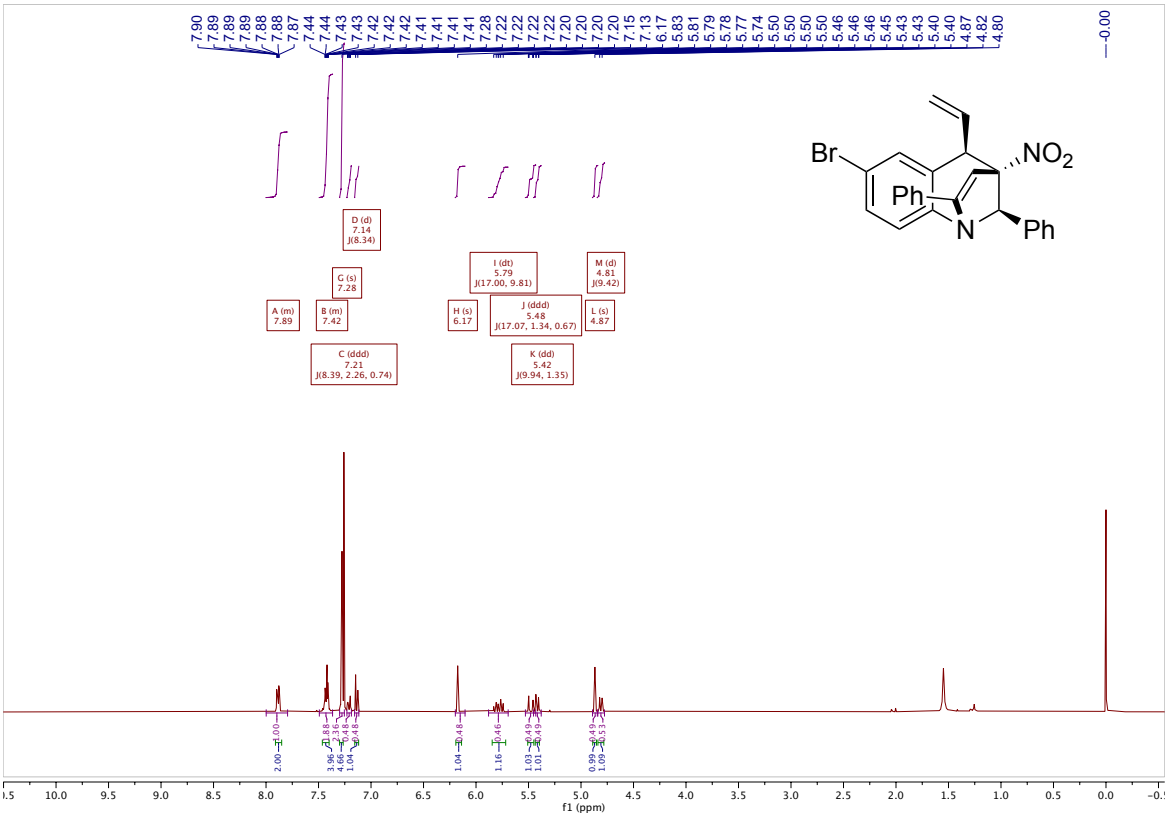
^{1}H NMR (400 MHz, $CDCl_3$) Compound **2d**



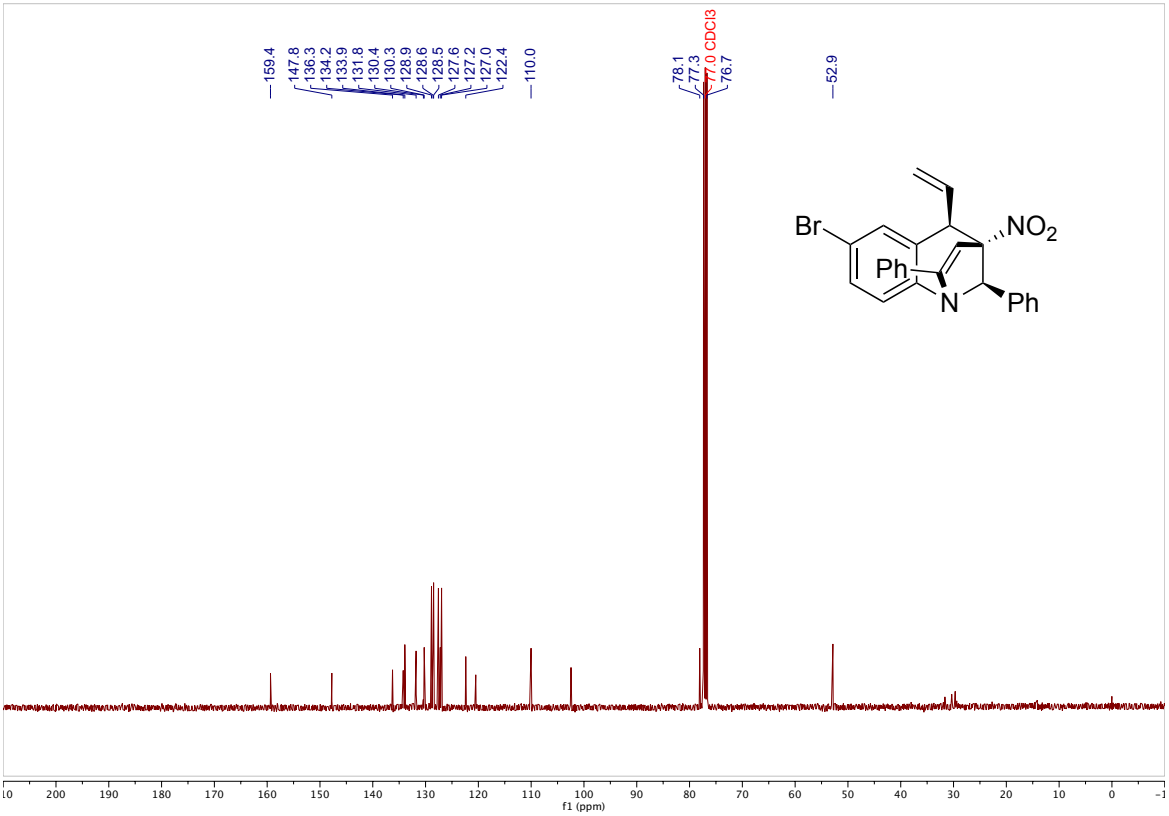
^{13}C NMR (101 MHz, $CDCl_3$): Compound **2d**



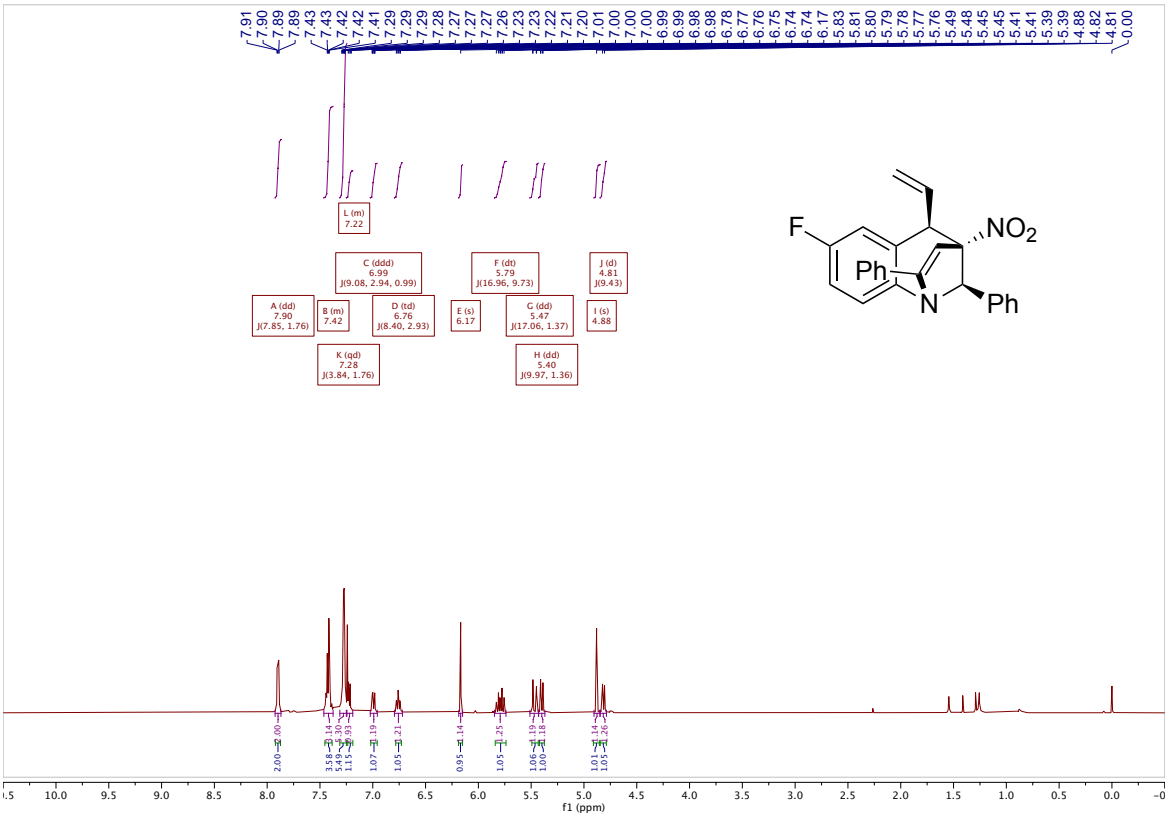
^{1}H NMR (400 MHz, $CDCl_3$) Compound **2e**



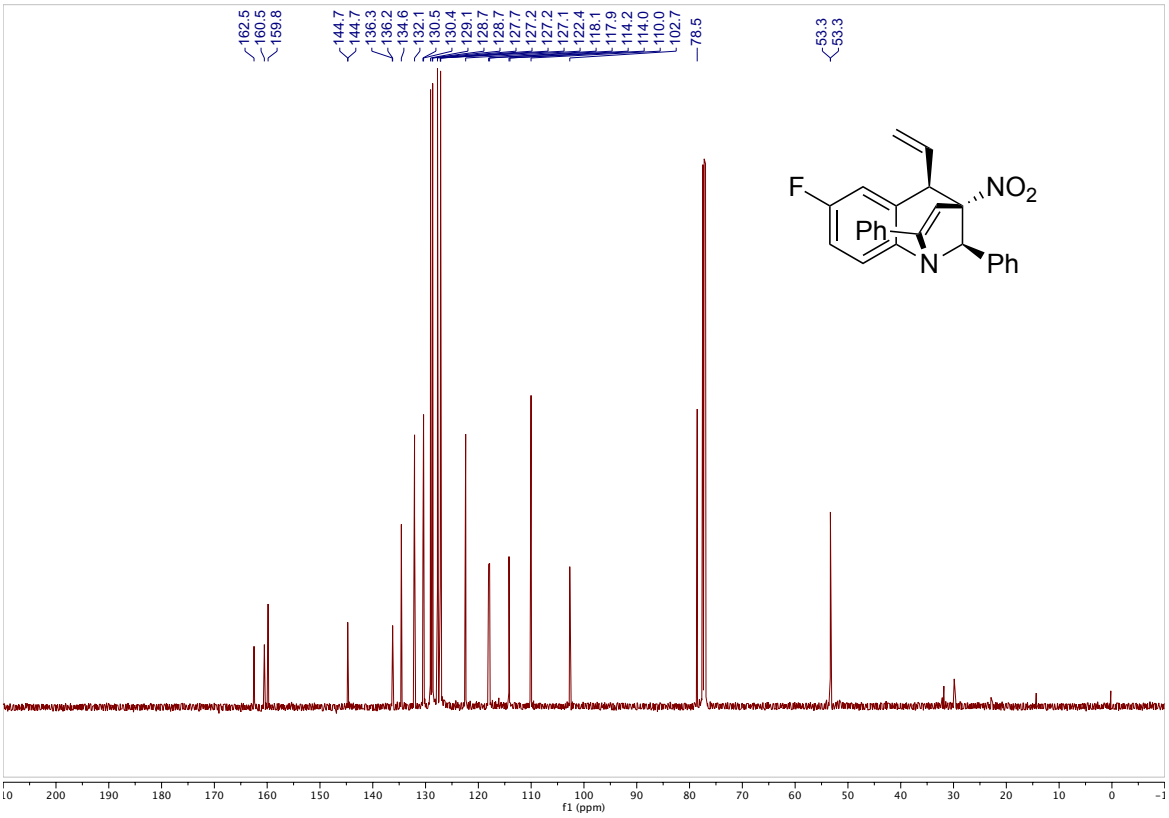
^{13}C NMR (101 MHz, $CDCl_3$): Compound **2e**



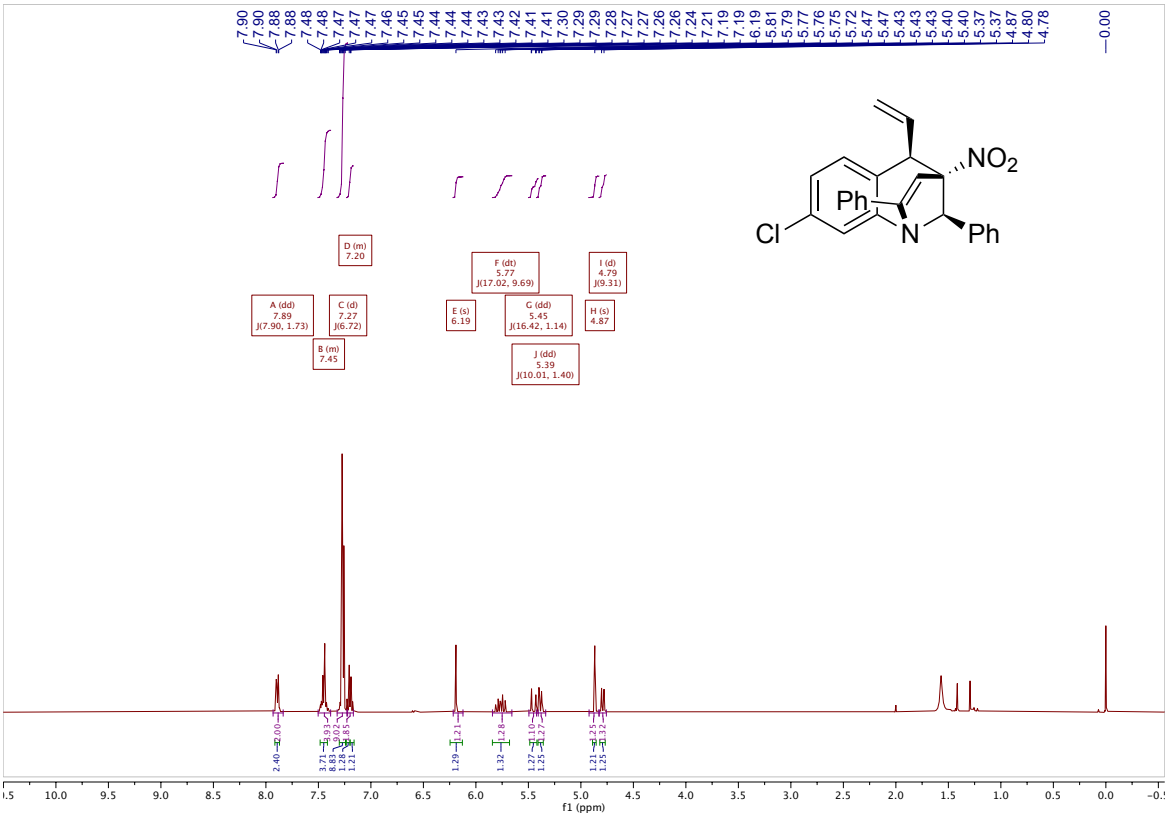
^{1}H NMR (500 MHz, $CDCl_3$) Compound **2f**



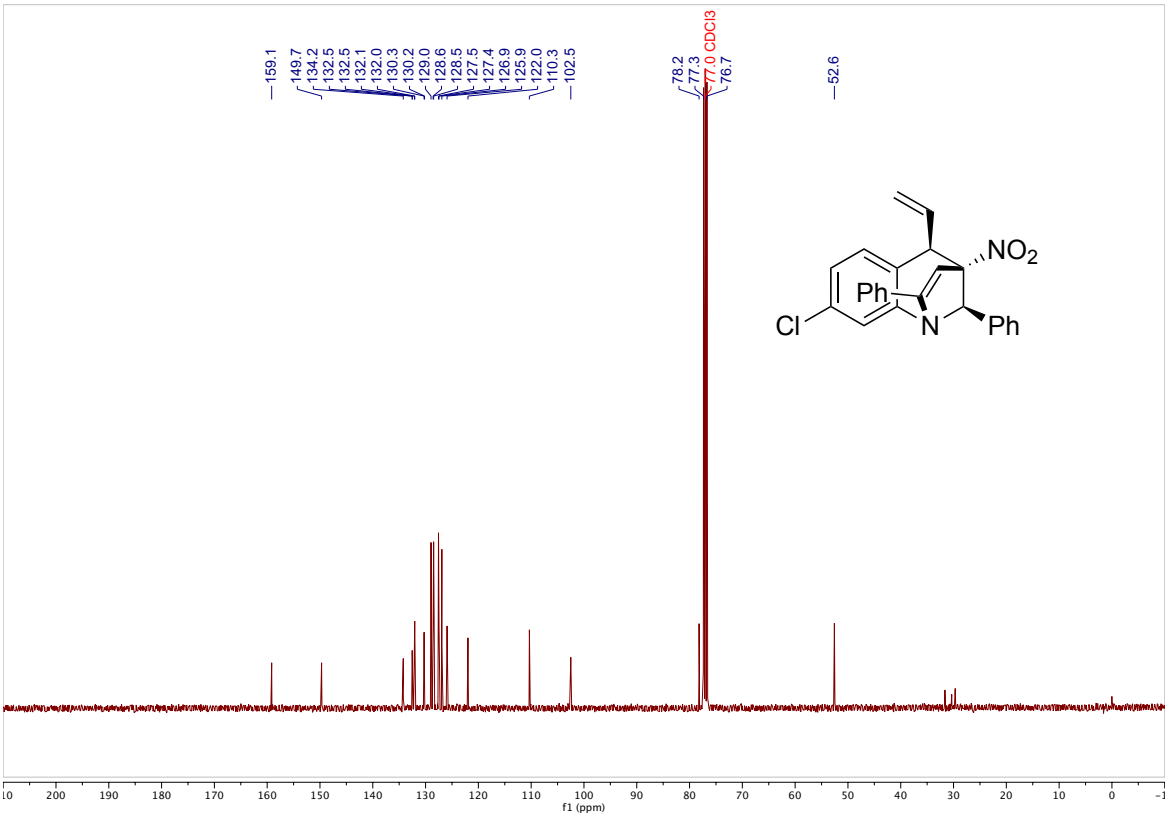
^{13}C NMR (126 MHz, $CDCl_3$): Compound **2f**



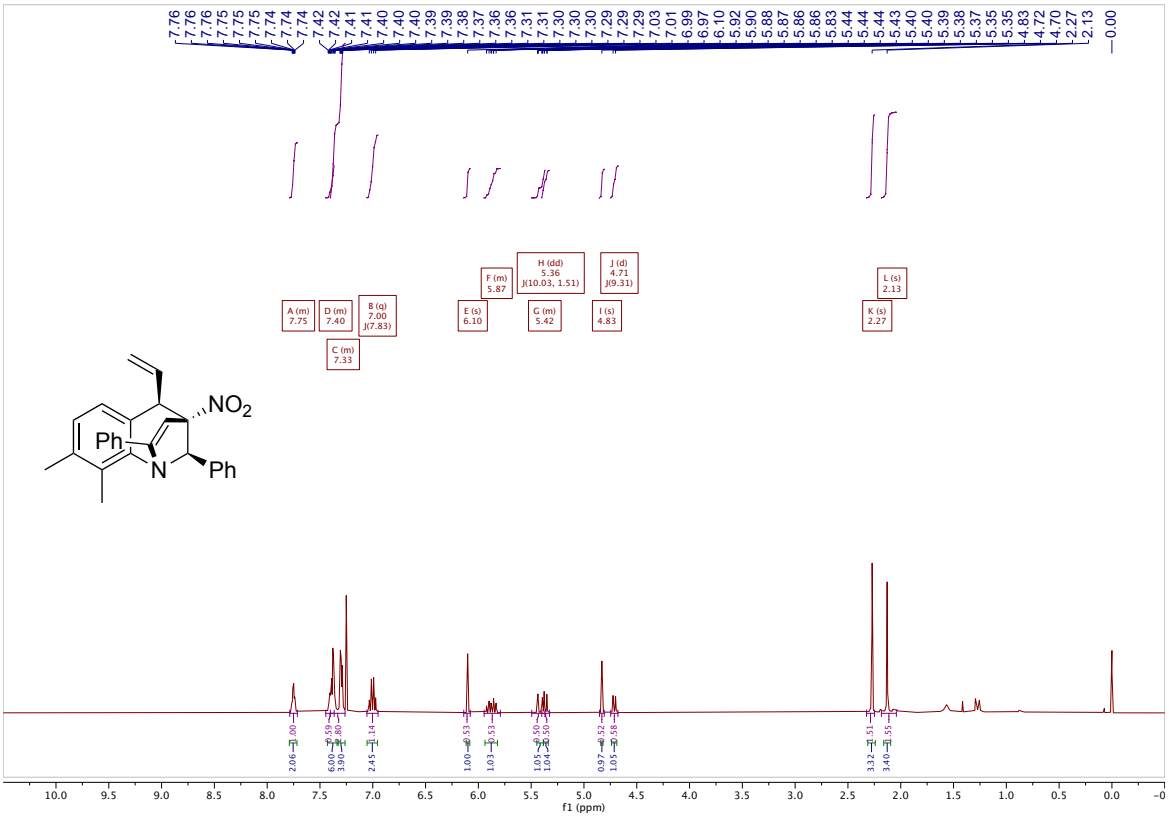
^{1}H NMR (400 MHz, $CDCl_3$) Compound **2g**



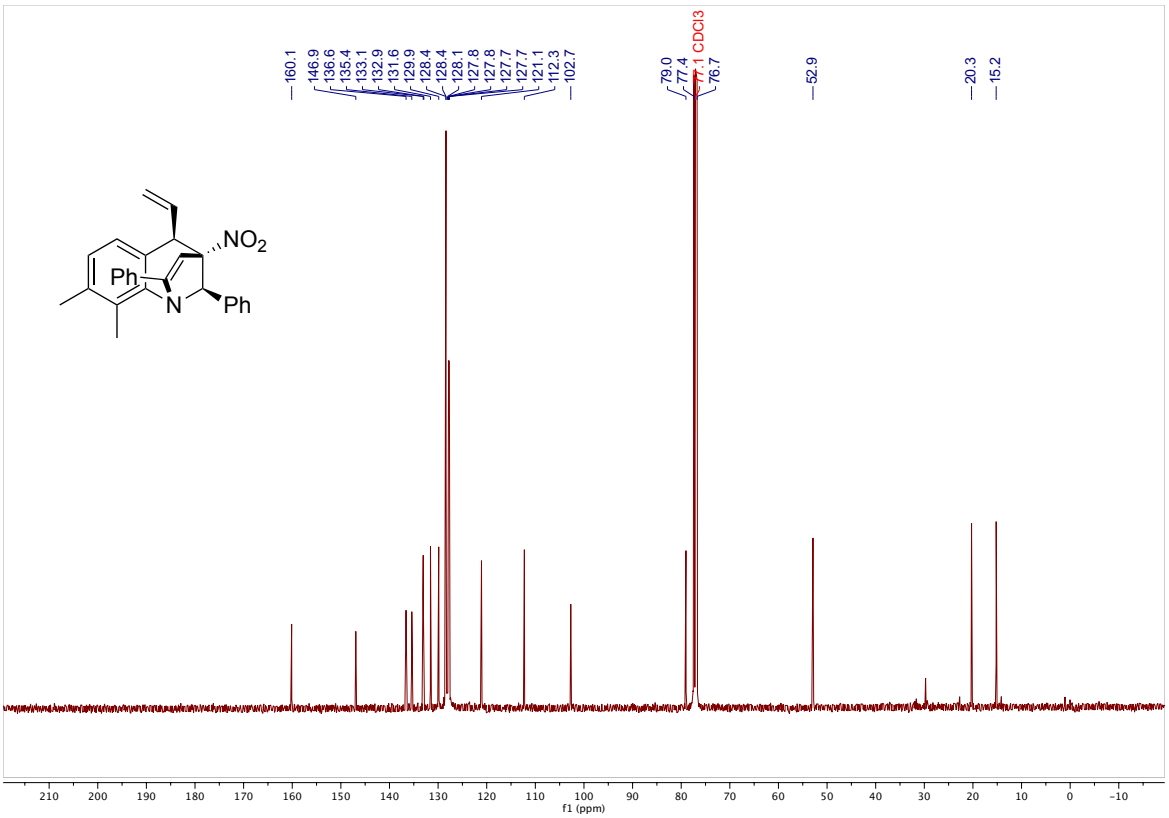
^{13}C NMR (126 MHz, $CDCl_3$): Compound **2g**



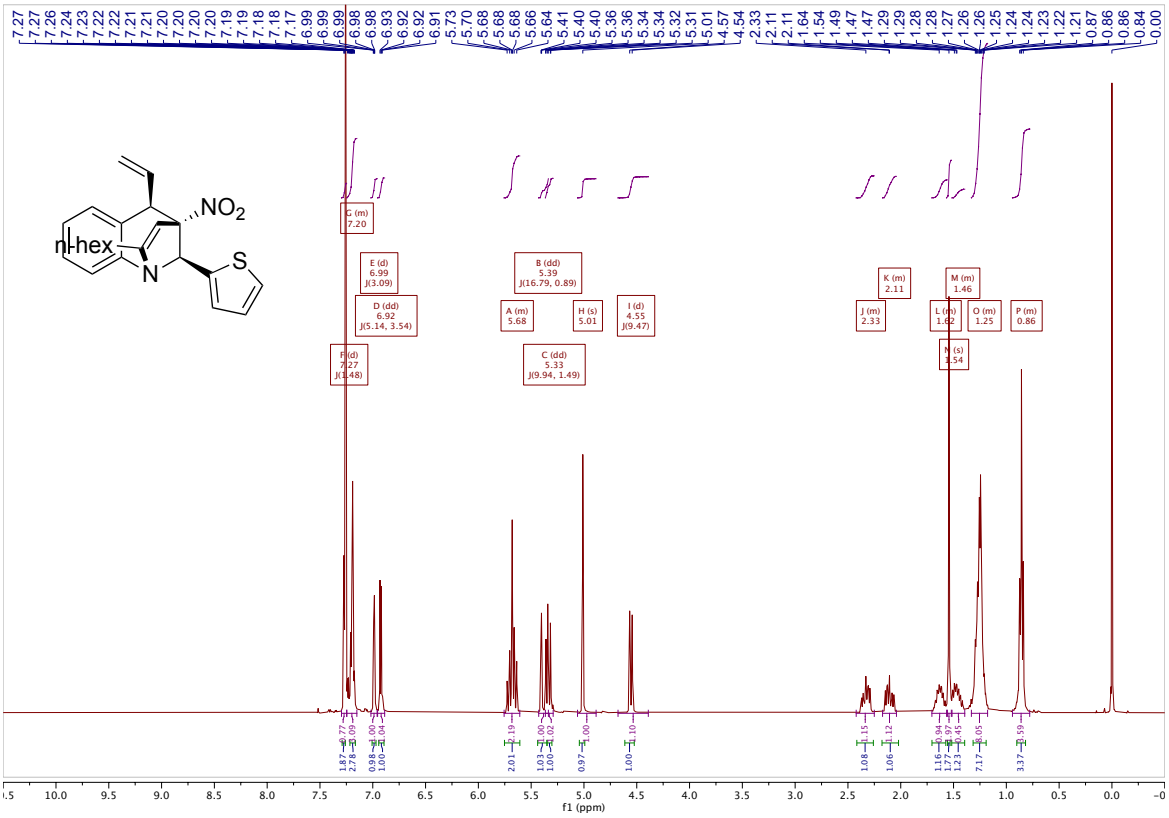
^{1}H NMR (500 MHz, $CDCl_3$) Compound **2h**



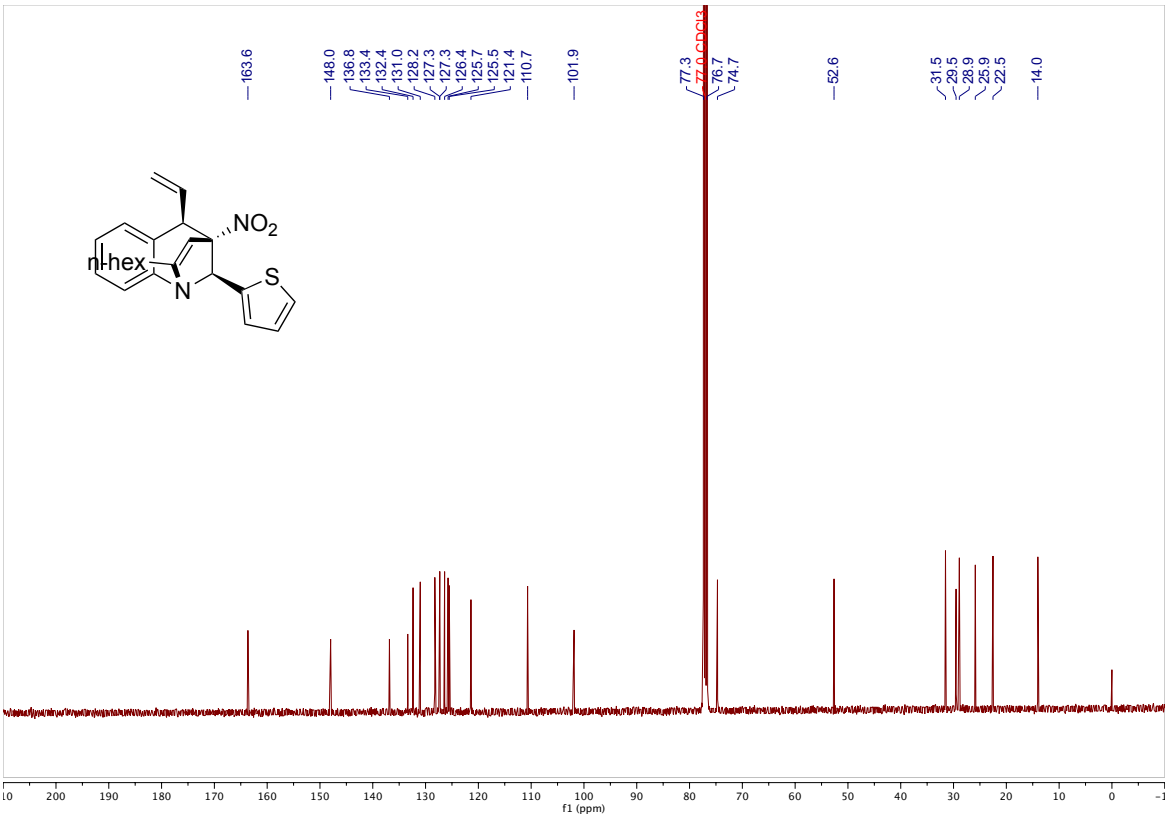
^{13}C NMR (101 MHz, $CDCl_3$): Compound **2h**



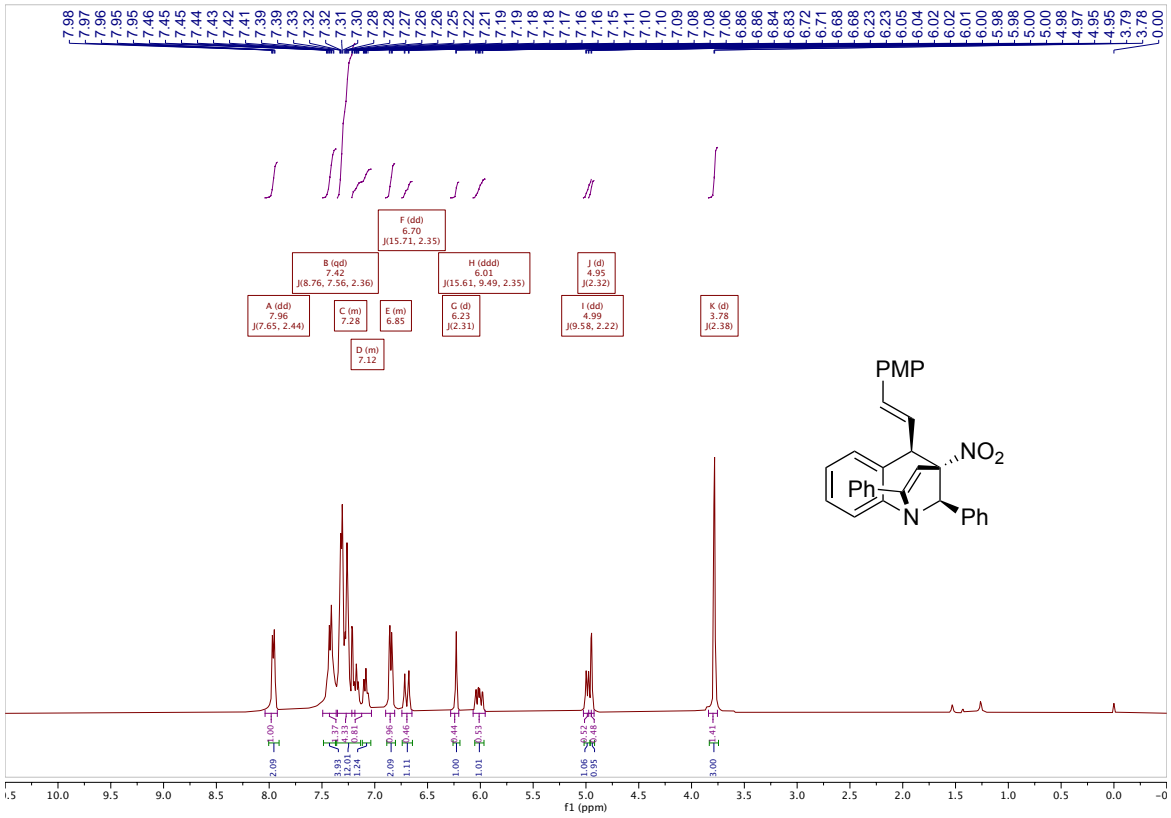
^{1}H NMR (400 MHz, $CDCl_3$) Compound **2i**



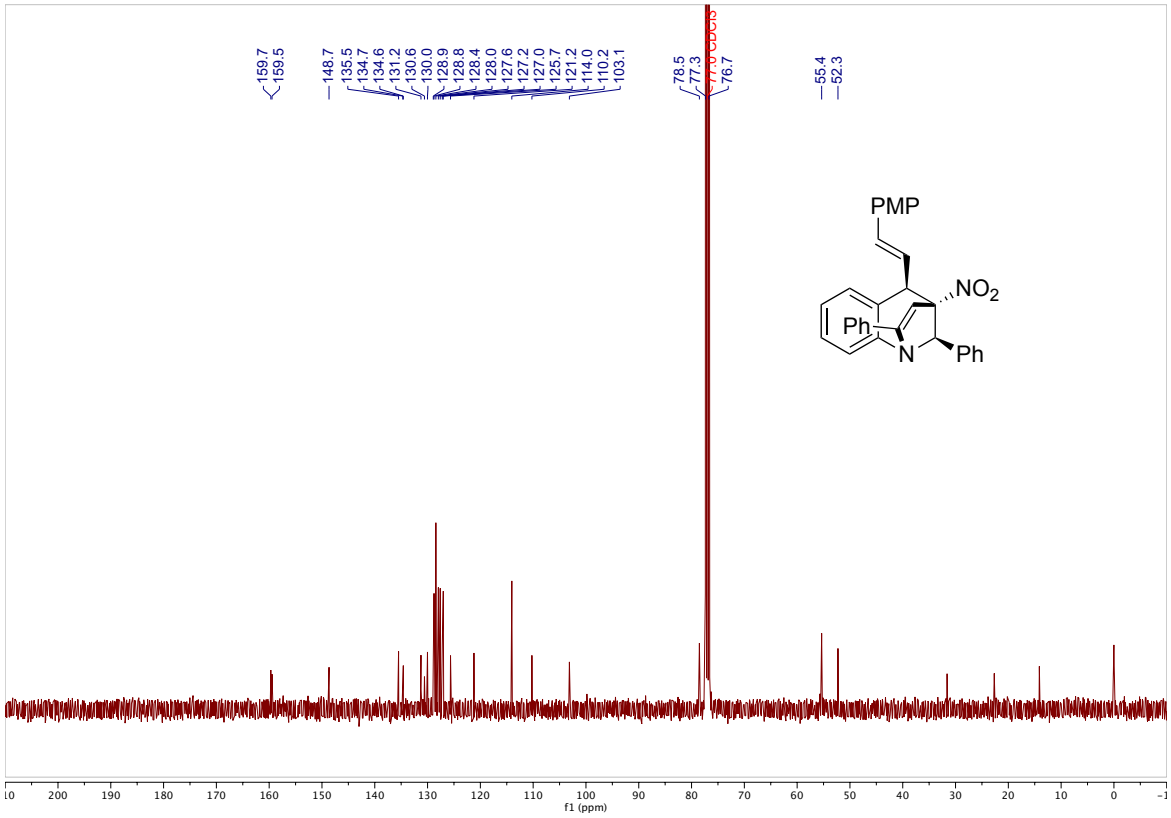
^{13}C NMR (101 MHz, $CDCl_3$): Compound **2i**



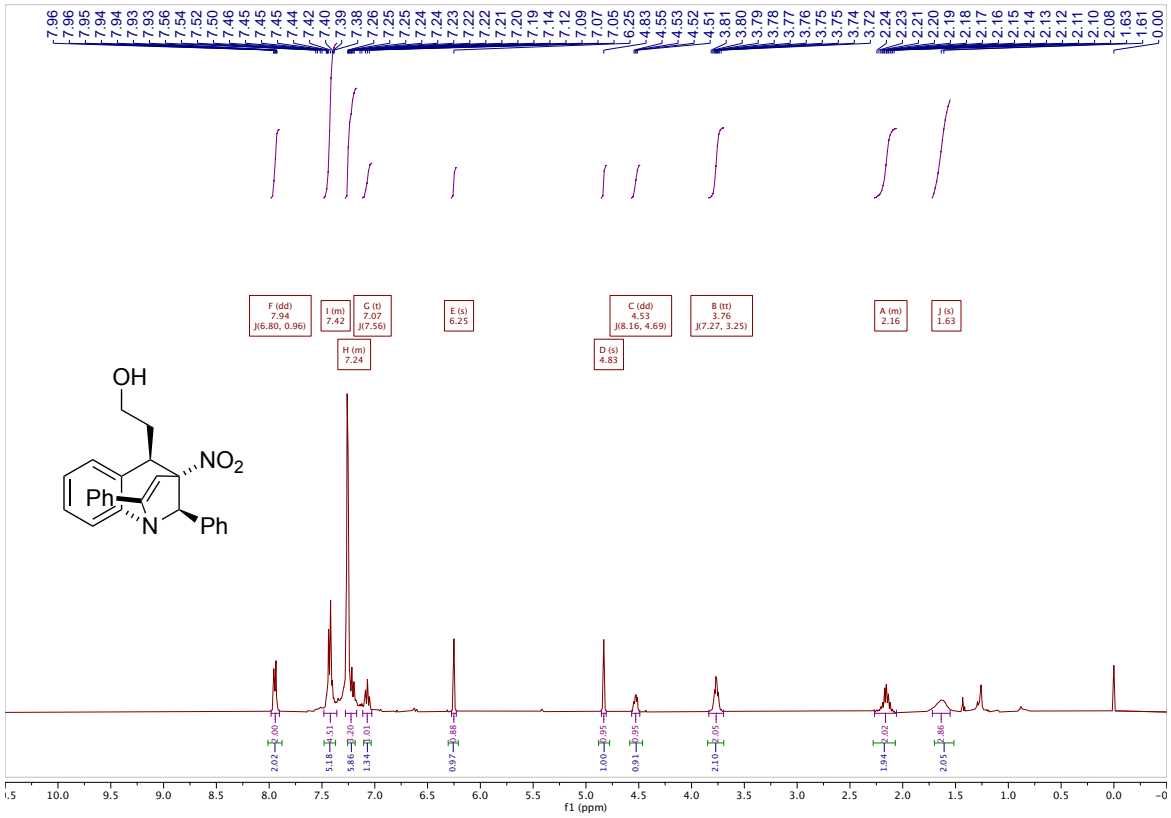
^{1}H NMR (400 MHz, $CDCl_3$) Compound **3**



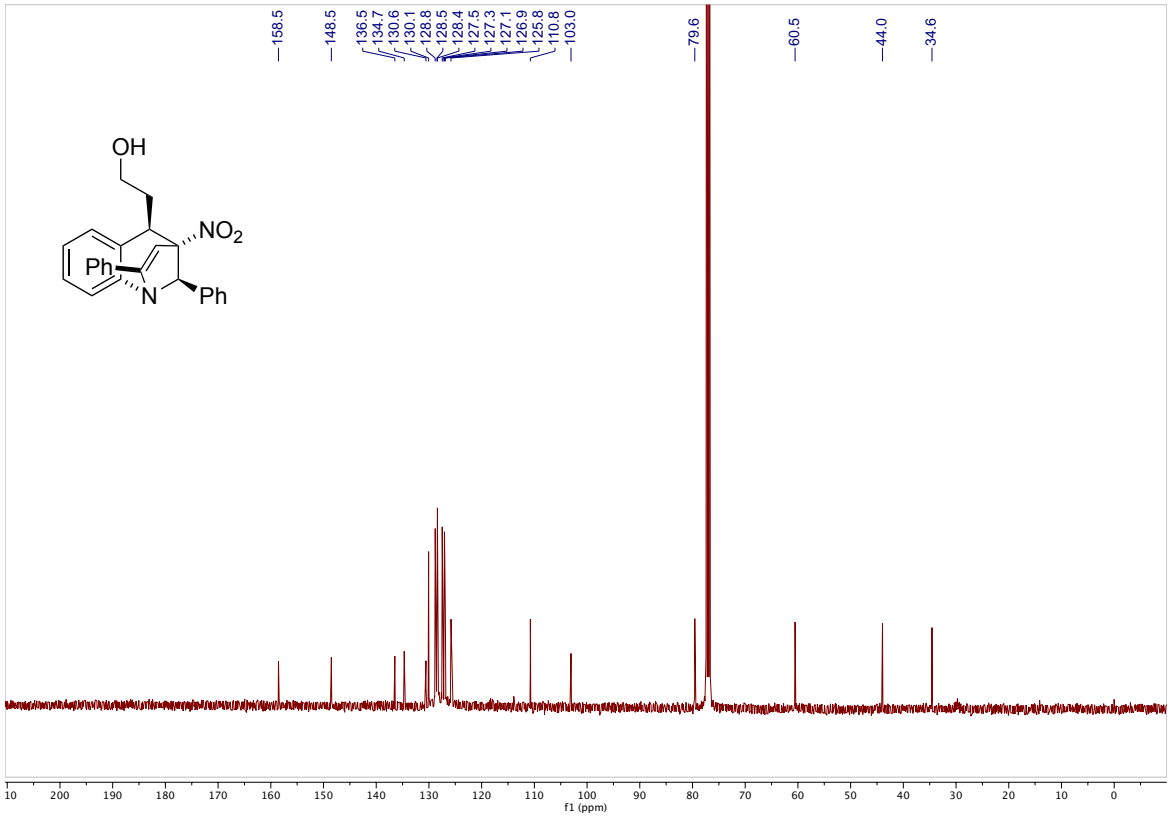
^{13}C NMR (101 MHz, $CDCl_3$): Compound **3**



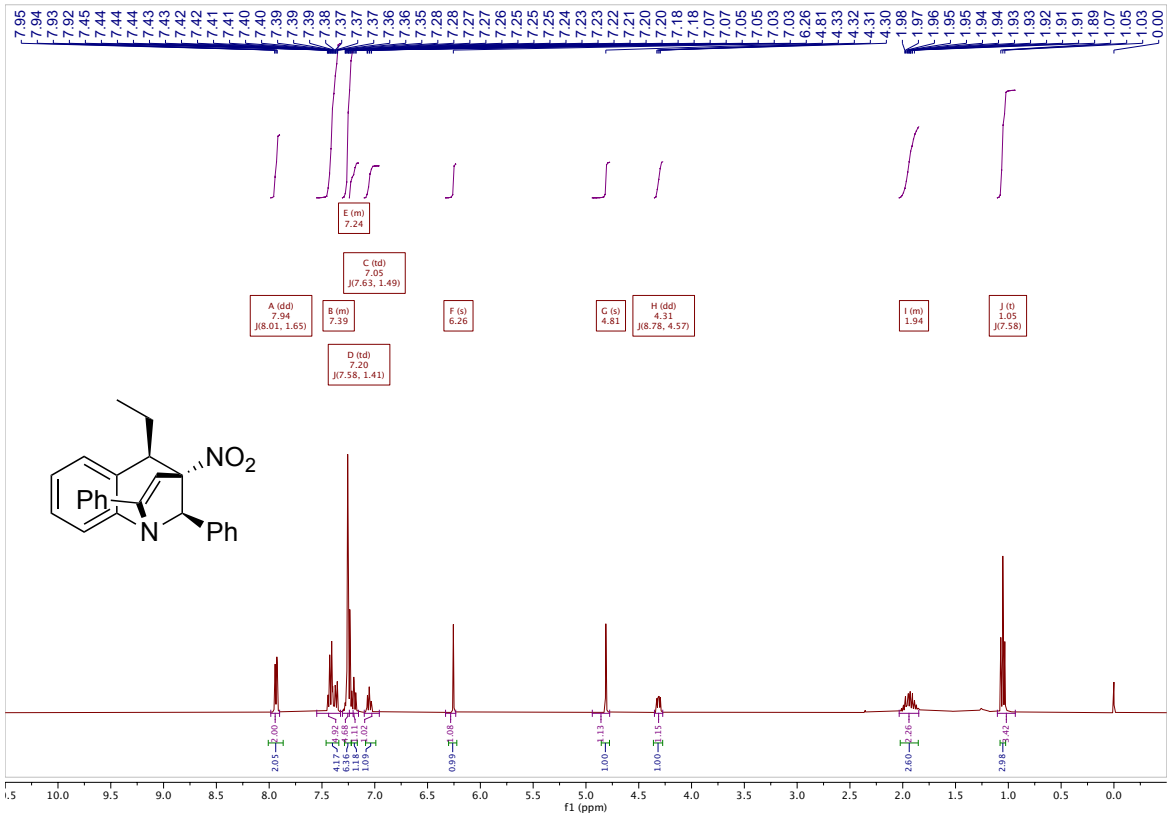
^{1}H NMR (400 MHz, $CDCl_3$) Compound **4**



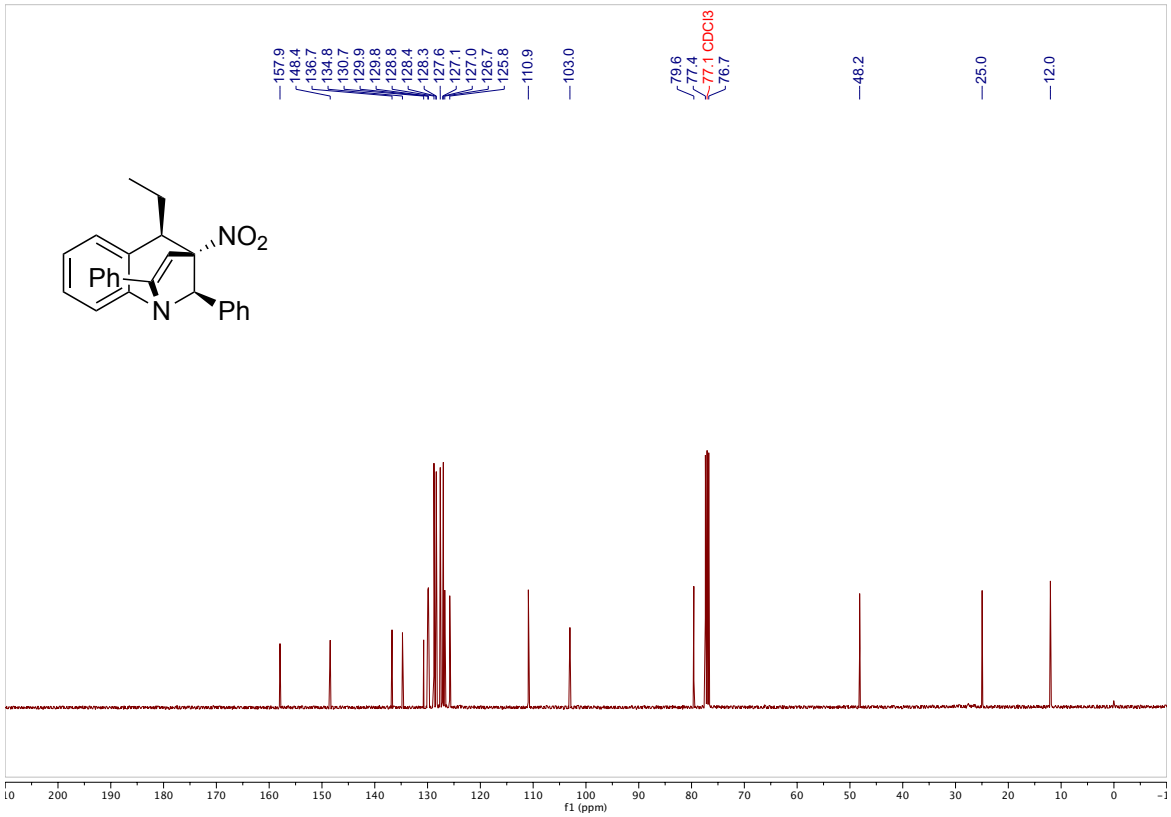
^{13}C NMR (101 MHz, $CDCl_3$): Compound **4**



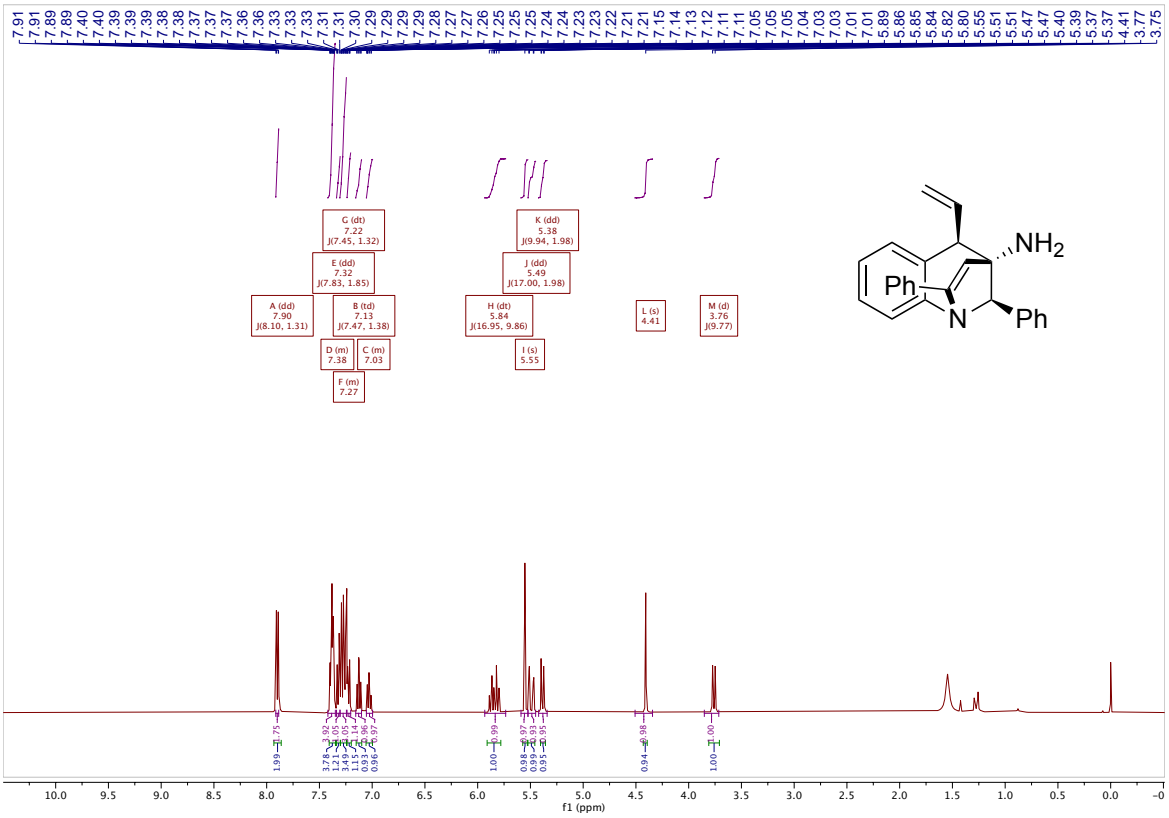
^{1}H NMR (400 MHz, $CDCl_3$) Compound **5**



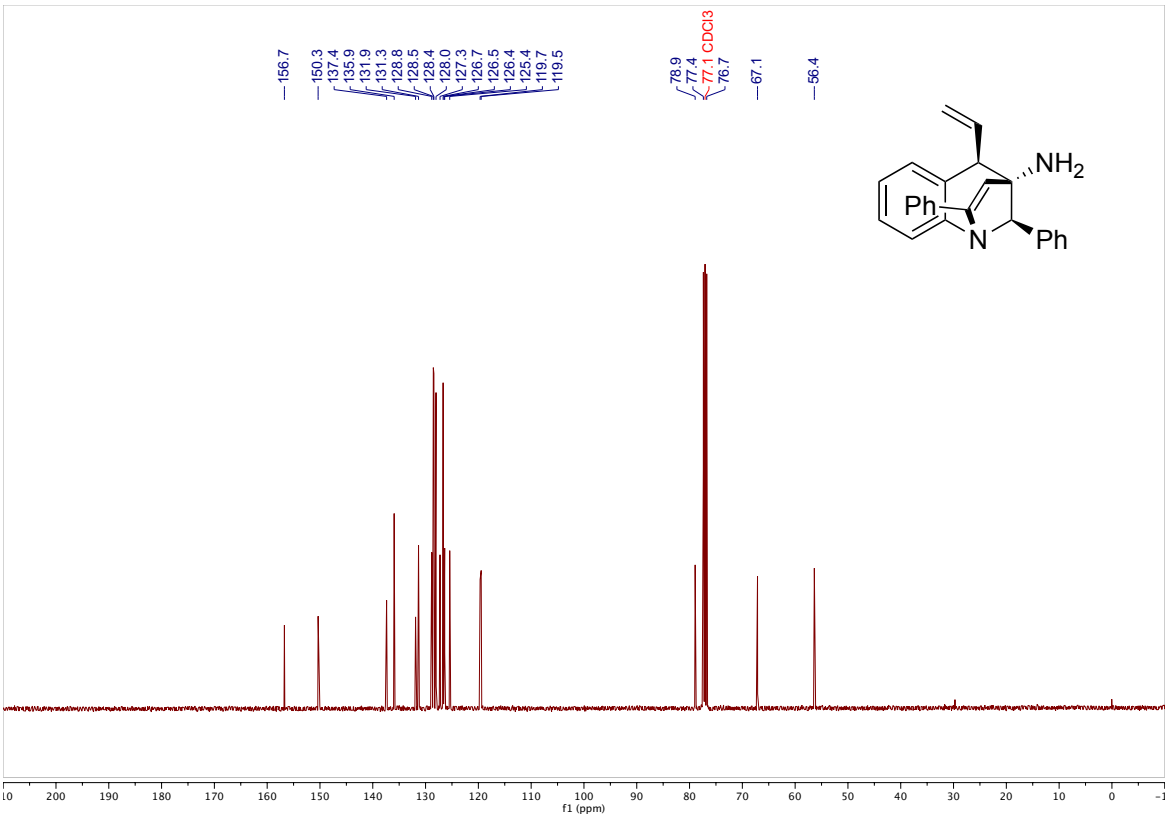
^{13}C NMR (101 MHz, $CDCl_3$): Compound **5**



^{1}H NMR (400 MHz, $CDCl_3$) Compound **6**



^{13}C NMR (101 MHz, $CDCl_3$): Compound **6**



8. X-ray Crystallography Data

Compound 2a

Sample Preparation: The isolated compound **2a** was recrystallized from CH_2Cl_2/*n*-hexane by liquid–liquid diffusion layering. Crystals were allowed to form at 5 °C (fridge) overnight and then at −20 °C (freezer) for another 48 h.

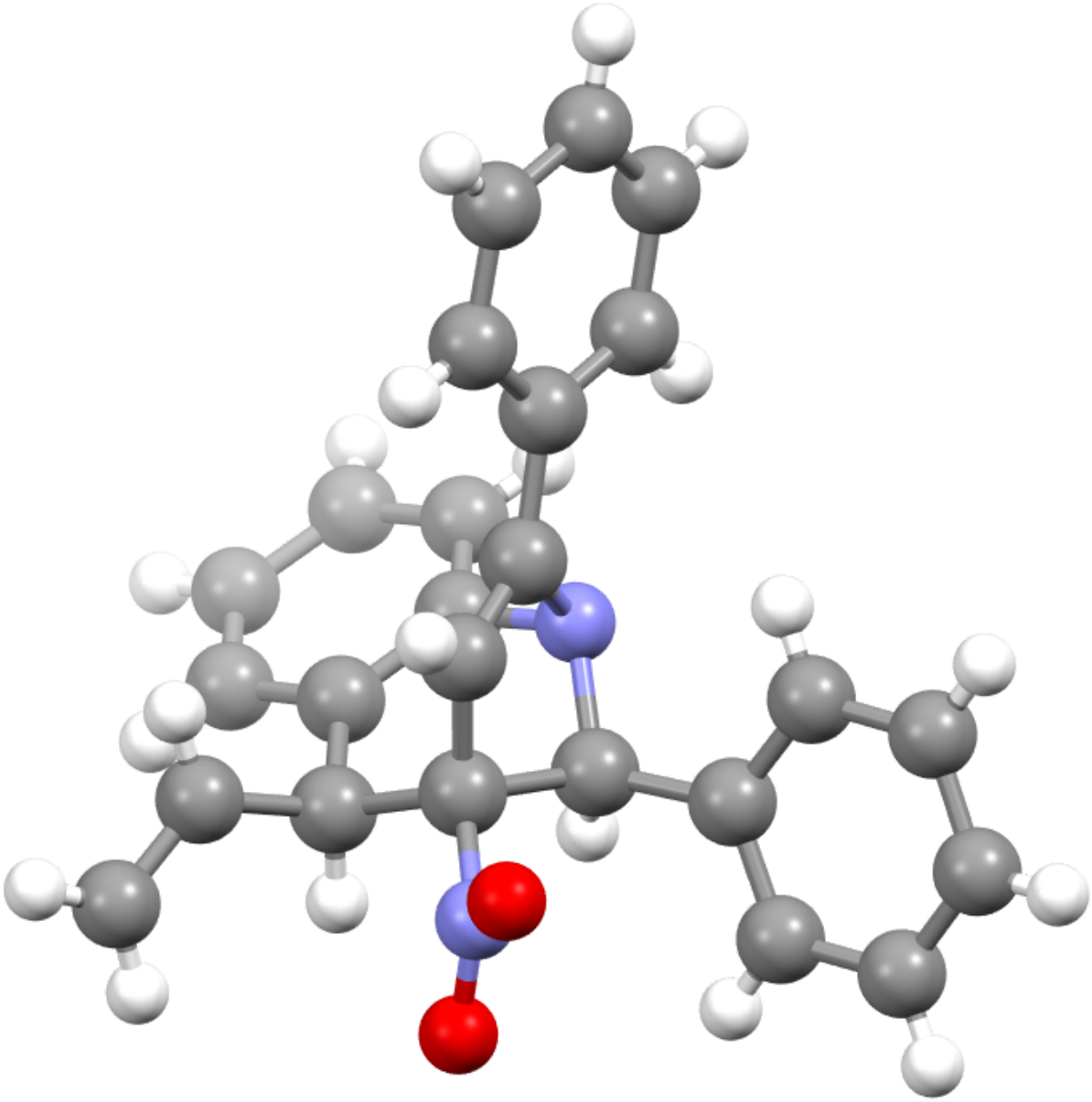


Figure S1 – X-ray crystallography structure for compound **2a**. Thermal ellipsoid plot of **5a** with ellipsoid contour probability 50%.

Crystal data and structure refinement for compound 2a

Identification code	Compound **2a**
Empirical formula	$C_{25}H_{20}N_2O_2$
Formula weight	380.43
Temperature/K	295(1)
Crystal system	monoclinic
Space group	C2/c
a/Å	14.3293(3)
b/Å	15.4688(4)
c/Å	18.2935(5)
α/°	90
β/°	96.135(2)
γ/°	90
Volume/Å^3	4031.66(17)
Z	8
ρ_{calc}g/cm^3	1.254
μ/mm^{-1}	0.080
F(000)	1600.0
Crystal size/mm^3	0.41 × 0.39 × 0.37
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	3.886 to 58.256
Index ranges	-19 ≤ h ≤ 19, -21 ≤ k ≤ 21, -25 ≤ l ≤ 25
Reflections collected	41975
Independent reflections	5428 [R_{int} = 0.0223, R_{sigma} = 0.0165]
Data/restraints/parameters	5428/0/262
Goodness-of-fit on F^2	1.054
Final R indexes [I>=2σ (I)]	R_1 = 0.0462, wR_2 = 0.1191
Final R indexes [all data]	R_1 = 0.0648, wR_2 = 0.1311
Largest diff. peak/hole / e Å^{-3}	0.20/-0.22