Electronic Supplementary Material (ESI) for ChemComm.

Stereodefined Synthesis of Cyclic Amidines by Domino 1,7–H Shift and 6π-Electrocyclization

Supporting Information

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CAUTION

NITROGEN-RICH COMPOUNDS, SUCH AS AZIDES, DIAZOCOMPOUNDS AND TRIAZOLES, CAN DECOMPOSE VIOLENTLY WITH THE LOSS OF NITROGEN GAS.

Although no problems were encountered in the course of this study, appropriate precautions should be taken.

General Experimental Considerations

- Melting points were recorded using a Barnstead Electrothermal 9100 melting point apparatus. Where no solvent is indicated, the solids obtained from the described procedure were melted directly without recrystallization.

- NMR spectra were recorded using dilute solutions in deuterated chloroform on a Bruker Avance^{III} 400 MHz or 500 MHz spectrometers using the deuterated solvent as the internal deuterium lock. Spectra were processed using MestreNova. ^{1}H chemical shift data are given in units δ relative to the residual protic solvent where $\delta(CDCl_3)$ = 7.26 ppm, s. ^{13}C chemical shift data were recorded with broadband proton decoupling and are given in units δ relative to the solvent where $\delta(CDCl_3)$ = 77.0 ppm, t.

- IR spectra were recorded as thin films using an ATR accessory, selected frequencies (ν_{max}) are reported.

- High resolution mass spectra were recorded using a Bruker microTOFq High Resolution Mass Spectrometer (ESI) at the University of Glasgow.

- Single-crystal structure data for **9a** were collected on a Bruker D8 VENTURE diffractometer equipped with a Photon II CPAD detector, with an Oxford Cryosystems Cryostream device mounted on an IμS 3.0 (dual Cu and Mo) microfocus sealed tube generator. Data were collected at 150 K using Mo-Kα radiation (λ = 0.71073 Å). The structure was solved using SHELXT[1] and refined using SHELXL[2] within Olex2.[3] All non-hydrogen atoms were refined freely with anisotropic atom displacement parameters (adps) apart from N1, C2-3, C6, C8-9 and C10-11 which were disordered over two orientations and were modelled over two partially occupied sites with occupancies 0.8 and 0.2, distance restraints were applied to the C-C distances and the minor component was refined with isotropic adps. Hydrogen atoms were included in geometrically calculated positions as part of a riding model, except the Me hydrogens which were included as a rigid rotor.

- Experiments were conducted under an argon atmosphere with glassware flame dried *in vacuo* where appropriate.

- Purification was performed using Fluorochem LC60A (40–63 μm) silica gel; or by TeledyneISCO CombiFlash R*f*+ automated purification machine using RediSep and RediSep Gold silica cartridges.

Abbreviations

NMO	*N*-methyl-morpholine *N*-oxide
Ns	4-nitrosulfonyl
Ts	*p*-toluenesulfonyl

Reagents

Reagents were used as received except as described below.

Solvents

Tetrahydrofuran (THF), diethyl ether and dichloromethane were passed through a column of activated alumina under nitrogen in an Innovative Technology PureSolv Solvent Purification System before use.

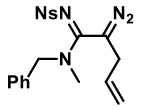
General Procedures

General Procedure: Cyclic amidine synthesis

Trimethylsilyl triflate (6.0 equiv.) was added to a solution of boron trifluoride diethyl etherate (3.0 equiv.) in acetonitrile (0.3 M with respect to $BF_3{\cdot}OEt_2$) and the mixture was stirred for 10 min at ambient temperature under an argon atmosphere. The diene (1.0 equiv.) was added as a solution in acetonitrile (total reaction concentration of 0.03 M with respect to diene) and the mixture was heated for the time indicated. The reaction mixture was cooled to ambient temperature and saturated aqueous NH_4Cl was added to the solution and stirred for 1 h. Saturated aqueous Na_2CO_3 and then water was added to the mixture and the aqueous phase was extracted with ethyl acetate (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purified by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 60%) gave the cyclic amidine.

Substrate Synthesis

Substrates were synthesised using the method developed previously within the research group.[4]

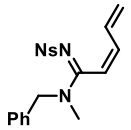


5`h

Trichloroacetyl chloride (5.3 mL, 47.5 mmol, 1.2 equiv.) was added dropwise, under an argon atmosphere, to a stirred solution of *N*-benzylmethanamine (5.0 mL, 38.7 mmol, 1.0 equiv.) and triethylamine (5.4 mL, 38.7 mmol, 1.0 equiv.) in CH_2Cl_2 (8 mL) at 0 °C. The solution was allowed to reach ambient temperature and stirred until the starting amine was consumed (TLC, approx. 0.5 h). Water was added and the aqueous phase was extracted with ethyl acetate (3 ×). The combined organic layers were then washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give ***N*-benzyl-*N*-methyl-2,2,2-trichloroacetamide** (9.6 g, 93%) as a colourless oil that existed as two rotamers in 50:50 ratio.
^{1}H NMR (400 MHz, 25.5 °C, $CDCl_3$) δ = 7.40–7.29 (3 H, m, Ph), 7.28–7.24 (2 H, m, Ph), 4.97 (0.6 H, br s, Bn CH_2′), 4.69 (1.4 H, br s, Bn CH_2), 3.29 (2.1 H, br s, NCH_3) and 2.97 (0.9 H, br s, NCH_3); ^{13}C{^{1}H} NMR (101 MHz, 25.4 °C, $CDCl_3$) δ = 160.9 (C=O), 135.7 (Ph), 128.9 (2 × Ph), 127.9 (3 × Ph), 93.2 (CCl_3), 55.0 (Bn CH_2) and 37.8 (NCH_3).

Tri-*n*-butyl phosphine (3.80 mL, 15.2 mmol, 1.3 equiv.) was added dropwise, under an argon atmosphere, to a solution of *N*-benzyl-*N*-methyl-2,2,2-trichloroacetamide (3.11 g, 11.7 mmol, 1.0 equiv.) in 1,2-dichloroethane (15 mL). The solution was heated to 80 °C and stirred for 1 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The crude mixture was purified by filtration through a short pad a silica using a 20% ethyl acetate in petroleum ether eluent to give ***N*-benzyl-*N*-methyl-1,2,2-trichloroethenamine** (2.87 g, >98%) that was very unstable to hydrolysis and therefore used directly in the following procedure.

A solution of ***N*-benzyl-*N*-methyl-1,2,2-trichloroethenamine** (2.87 g, 11.5 mmol, 1.1 equiv.) in tetrahydrofuran (0.7 M) was cooled to −10 °C under an argon atmosphere and *n*BuLi (2.5 M in hexanes, 9.2 mL, 23.0 mmol, 2.2 equiv.) was added dropwise. The solution was allowed to reach room temperature and stirred for 1 h, during which time the colour changed from pale yellow to dark orange. DMPU (2.1 mL, 17.4 mmol, 1.7 equiv.) followed by allyl bromide (1.50 mL, 17.3 mmol, 1.7 equiv.) were added and the mixture was heated under reflux for 1 h. The solution was cooled to −10 °C and a solution of 4-nitrobenzenesulfonyl azide in tetrahydrofuran (2.40 g, 10.3 mmol, 2.0 M, 1.0 equiv.) was added in one portion, then the reaction mixture was stirred for 10 min at −10 °C. The solution was allowed to reach room temperature and stirred for a further 30 min. The reaction mixture was then concentrated in vacuo and purified by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 60%) to give ***N*^{1}-benzyl,*N*^{1}-methyl,*N*^{2}-(4-nitrobenzenesulfonyl)-2-diazopent-4-enamidine 6'h** (2.22 g, 52%) as a yellow oil.
IR (film) 3105, 3065, 2932, 2872, 2137, 2075, 2075, 1526, 1348, 1292, 1148 and 1088 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{19}H_{19}N_5NaO_4S^+$ 436.1050; Found 436.1044; ^{1}H NMR (400 MHz, 25.6 °C, $CDCl_3$) δ = 8.24 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.05 (2 H, d, *J* = 8.9 Hz, Ns Ar), 7.35–7.29 (3 H, m, Ph), 7.14–7.09 (2 H, m, Ph), 5.87 (1 H, ddt, *J* = 17.2, 9.8, 6.8 Hz, 4–H), 5.24 (1 H, ddt, *J* = 17.2, 1.4, 1.3 Hz, 5–H_Z), 5.23 (1 H, ddt, *J* = 9.8, 1.4, 1.3 Hz, 5–H_E), 4.51 (2 H, s, benzyl CH_2), 3.33 (2 H, dt, *J* = 6.8, 1.3 Hz, 3–H_2) and 2.94 (3 H, s, NCH_3); ^{13}C{^{1}H} NMR (101 MHz, 25.5 °C, $CDCl_3$) δ = 162.7 (C1), 150.1 (Ns Ar), 149.2 (Ns Ar), 135.0 (Ph), 131.4 (C4), 129.0 (2 × Ph), 128.2 (Ph), 127.4 (2 × Ph), 127.2 (2 × Ns Ar), 123.9 (2 × Ns Ar), 119.4 (C5), 57.1 (C2), 55.7 (benzyl CH_2), 38.4 (NCH_3) and 31.2 (C3).

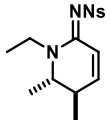


8`h

N^1-Benzyl,N^1-methyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine

Rhodium(II) tetrakis(triphenylacetate) (27.0 mg, 0.019 mmol, 5 mol %) was added to a solution of N^1-benzyl,N^1-methyl,N^2-(4-nitrobenzenesulfonyl)-2-diazopent-4-enamidine **6'h** (153 mg, 0.370 mmol, 1.0 equiv.) in 1,2-dichloroethene (2 mL) and the mixture was stirred under an argon atmosphere at 60 °C for 1 h. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 60%) to give the title compound (126 mg, 88%) as a brown oil that existed as a 40:60 mixture of rotamers.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{19}N_3NaO_4S^+$ 408.0988; Found 408.0989; IR (film) 3103, 3063, 3036, 2934, 1524, 1476, 1414, 1346, 1292, 1150 and 1088 cm^{-1}; ^1H NMR (400 MHz, 25.6 °C, $CDCl_3$) δ = 8.26 (0.8 H, d, *J* = 8.9 Hz, Ns Ar'), 8.22 (1.2 H, d, *J* = 8.9 Hz, Ns Ar), 8.08 (0.8 H, d, *J* = 8.9 Hz, Ns Ar'), 7.99 (1.2 H, d, *J* = 8.9 Hz, Ns Ar), 7.39–7.31 (3 H, m, Ar and Ar'), 7.28–7.24 (1.2 H, m, Ar), 7.12–7.09 (0.8 H, m, Ar'), 6.43–6.25 (2 H, m, 2–H and 3–H), 6.07 (0.4 H, dddd, *J* = 16.8, 11.0, 10.0, 0.8 Hz, 4–H'), 5.92 (0.6 H, ddd, *J* = 16.8, 10.5, 10.4 Hz, 4–H), 5.37 (0.4 H, d, *J* = 16.8 Hz, 5–H_{Z}'), 5.35 (0.6 H, d, *J* = 16.8 Hz, 5–H_{Z}), 5.25 (0.4 H, d, *J* = 10.0 Hz, 5–H_{E}'), 5.21 (0.6 H, d, *J* = 10.5 Hz, 5–H_{E}), 4.79 (1.2 H, s, Bn CH_2), 4.58 (0.8 H, s, Bn CH_2'), 3.06 (1.2 H, s, NCH_3') and 3.00 (1.8 H, s, NCH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 25.5 °C, $CDCl_3$) δ = 164.8 (0.4 × C1'), 164.7 (0.6 × C1), 149.3 (Ns Ar), 149.0 (Ns Ar), 135.6 (0.4 × C3'), 135.2 (0.6 × C3), 135.0 (0.6 × Ar), 134.5 (0.4 × Ar'), 131.3 (0.4 × C4'), 130.9 (0.6 × C4), 129.1 (0.8 × Ar'), 128.9 (1.2 × Ar), 128.4 (0.8 × Ar'), 128.3 (1.2 × Ns Ar), 128.1 (1.2 × Ar), 128.0 (0.8 × Ns Ar'), 127.3 (Ar), 124.1 (0.6 × C5), 123.9 (0.4 × C5'), 123.7 (0.8 × Ns Ar'), 123.7 (1.2 × Ns Ar), 120.8 (0.6 × C2), 120.7 (0.4 × C2'), 55.4 (0.4 × Bn C'), 53.5 (0.6 × Bn C), 37.4 (0.6 × NCH_3) and 36.0 (0.4 × NCH_3').

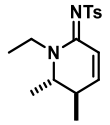


9a

N-(4-Nitrobenzenesulfonyl)-*trans*-1-ethyl-5,6-dimethyl-5,6-dihydropyridin-2-imine

N^1,N^1-Diethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (31 mg, 0.092 mmol, 1.0 equiv.) was treated according to the General Procedure at 100 °C for 18 h to give the title compound (19 mg, 61%) as a white solid. m.pt. 134–139 °C; ^{1}H NMR (400 MHz, 27.0 °C, $CDCl_3$) δ = 8.30 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.11 (2 H, d, *J* = 8.9 Hz, Ns Ar), 7.04 (1 H, d, *J* = 10.0 Hz, 3–H), 6.57 (1 H, ddd, *J* = 10.0, 6.9, 1.4 Hz, 4–H), 4.05 (1 H, dq, *J* = 13.7, 7.2 Hz, NEt CH_A), 3.36 (1 H, qdd, *J* = 6.7, 1.4, 1.3 Hz, 6–H), 2.91 (1 H, dq, *J* = 13.7, 7.2 Hz, NEt CH_B), 2.32 (1 H, qdd, *J* = 7.1, 6.9, 1.3 Hz, 5–H), 1.24 (3 H, d, *J* = 6.7 Hz, 6–CH_3), 1.14 (3 H, t, *J* = 7.2 Hz, NEt CH_3) and 1.09 (3 H, d, *J* = 7.1 Hz, 5–CH_3); ^{13}C{^{1}H} NMR (101 MHz, 27.0 °C, $CDCl_3$) δ = 155.8 (C2), 150.0 (Ns Ar), 149.3 (Ns Ar), 143.9 (C4), 127.4 (2 × Ns Ar), 123.8 (2 × Ns Ar), 118.6 (C3), 57.8 (C6), 43.6 (NEt CH_2), 34.4 (C5), 18.1 (5–CH_3), 18.1 (6–CH_3) and 11.9 (NEt CH_3); HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{19}N_3NaO_4S^+$ 360.0988; Found 360.0977; IR (film) 2972, 2934, 1641, 1528, 1478, 1348, 1281, 1142 and 1092 cm^{-1}.

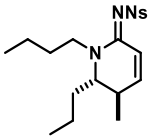
The product was crystallised by vapour diffusion (CH_2Cl_2 and pentane) to give crystals that were suitable for single crystal x-ray structure determination.
There was a 0.8 : 0.2 occupancy split between two confomers. Deposition number 2118194 contains the supplementary crystallographic data for this paper. These data are provided free of charge by the Cambridge Crystallographic Data Centre.



9aTS

N-(4-Toluenesulfonyl)-*trans*-1-ethyl-5,6-dimethyl-5,6-dihydropyridin-2-imine

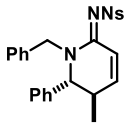
N^1,N^1-Diethyl,N^2-(4-toluenesulfonyl)-(*Z*)-pentadienamidine (54 mg, 0.178 mmol, 1.0 equiv.) was treated according to the General Procedure at 100 °C for 18 h to give the title compound (10 mg, 18%) as a white solid. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{22}N_2NaO_2S^+$ 329.1294; Found 329.1293; ^{1}H NMR (400 MHz, 17.3 °C, $CDCl_3$) δ = 7.80 (2 H, d, *J* = 8.2 Hz, Ts Ar), 7.24 (2 H, d, *J* = 8.2 Hz, Ts Ar), 7.06 (1 H, d, *J* = 10.0 Hz, 3–H), 6.49 (1 H, ddd, *J* = 10.0, 6.4, 1.5 Hz, 4–H), 4.11 (1 H, dq, *J* = 14.1, 7.1 Hz, NEt CH_A), 3.32 (1 H, qdd, *J* = 7.0, 1.5, 1.4 Hz, 6–H), 2.86 (1 H, dq, *J* = 14.1, 7.1 Hz, NEt CH_B), 2.39 (3 H, s, Ts CH_3), 2.26 (1 H, qdd, *J* = 6.7, 6.4, 1.4 Hz, 5–H), 1.21 (3 H, d, *J* = 6.7 Hz, 5–CH_3), 1.14 (3 H, t, *J* = 7.1 Hz, NEt CH_3) and 1.06 (3 H, d, *J* = 7.1 Hz, 6–CH_3); ^{13}C{^{1}H} NMR (101 MHz, 17.9 °C, $CDCl_3$) δ = 155.6 (C2), 142.8 (C4), 141.6 (Ts Ar), 141.6 (Ts Ar), 129.0 (2 × Ts Ar), 126.1 (2 × Ts Ar), 118.6 (C3), 57.6 (C6), 43.2 (NEt CH_2), 34.4 (Ts CH_3), 21.4 (C5), 18.2 (5–CH_3), 18.1 (6–CH_3) and 11.9 (NEt CH_3); IR (film) 2971, 2930, 2872, 1641, 1534, 1474, 1456, 1366, 1272 and 1140 cm^{-1}.



9b

N-(4-Nitrobenzenesulfonyl)-*trans*-1-butyl-5-methyl-6-propyl-5,6-dihydropyridin-2-imine

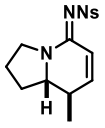
N^1,N^1-Di-*n*-butyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (31 mg, 0.078 mmol, 1.0 equiv.) was treated according to the General Procedure at 80 °C for 18 h to give the title compound (11 mg, 36%) as a colourless oil. IR (film) 2959, 2930, 2872, 1639, 1528, 1477, 1468, 1348, 1281, 1142 and 1092 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{19}H_{27}N_3NaO_4S^+$ 416.1614; Found 416.1625; ^1H NMR (500 MHz, 25.0 °C, $CDCl_3$) δ = 8.30 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.10 (2 H, d, *J* = 8.9 Hz, Ns Ar), 7.03 (1 H, d, *J* = 9.9 Hz, 3–H), 6.54 (1 H, ddd, *J* = 9.9, 6.5, 1.5 Hz, 4–H), 4.07 (1 H, ddd, *J* = 13.2, 9.5, 6.3 Hz, NBu 1–H_A), 3.15 (1 H, dddd, *J* = 9.0, 4.9, 1.5, 1.3 Hz, 6–H), 2.71 (1 H, ddd, *J* = 13.2, 9.5, 5.5 Hz, NBu 1–H_B), 2.45 (1 H, qdd, *J* = 7.0, 6.5, 1.3 Hz, 5–H), 1.66–1.42 (8 H, m, NBu CH_2 & 6–Pr), 1.09 (3 H, d, *J* = 7.0 Hz, 5–CH_3), 0.92 (3 H, t, *J* = 7.3 Hz, CH_3) and 0.85 (3 H, t, *J* = 7.3 Hz, CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 27.0 °C, $CDCl_3$) δ = 156.2 (C2), 150.0 (Ns Ar), 149.2 (Ns Ar), 143.9 (C4), 127.4 (2 × Ns Ar), 123.8 (2 × Ns Ar), 118.8 (C3), 62.6 (C6), 48.9 (NBu C1), 33.9 (6–Pr C1), 31.5 (C5), 28.9 (NBu C2), 20.1 (6–Pr C2), 19.7 (NBu C3), 18.3 (5–CH_3), 13.9 (CH_3) and 13.7 (CH_3).



9c

N-(4-Nitrobenzenesulfonyl)-*trans*-1-benzyl-5-methyl-6-phenyl-5,6-dihydropyridin-2-imine

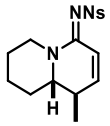
N^1,N^1-Dibenzyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (83 mg, 0.180 mmol, 1.0 equiv.) was treated according to the General Procedure at 80 °C for 18 h to give the title compound (11 mg, 14%) as a colourless oil. HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{25}H_{23}N_3NaO_4S^+$ 484.1301; Found 484.1304; IR (film) 3105, 3032, 2967, 2928, 1641, 1526, 1348, 1287, 1142 and 1086 cm^{-1}; ^1H NMR (400 MHz, 24.7 °C, $CDCl_3$) δ = 8.29 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.10 (2 H, d, *J* = 8.9 Hz, Ns Ar), 7.38–7.32 (4 H, m, Ph), 7.31–7.27 (2 H, m, Ph), 7.25 (1 H, d, *J* = 10.0 Hz, 3–H), 7.16–7.09 (4 H, m, Ph), 6.49 (1 H, ddd, *J* = 10.0, 6.1, 1.0 Hz, 4–H), 5.58 (1 H, d, *J* = 14.7 Hz, Bn CH_2), 4.36 (1 H, br s, 6–H), 3.62 (1 H, d, *J* = 14.7 Hz, 6–Bn), 2.63 (1 H, qd, *J* = 7.1, 6.1 Hz, 5–H) and 1.03 (3 H, d, *J* = 7.1 Hz, 5–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 25.4 °C, $CDCl_3$) δ = 158.0 (C2), 149.5 (Ns Ar), 148.7 (Ns Ar), 143.9 (C4), 138.1 (Ph), 135.3 (Ph), 129.1 (2 × Ph), 128.8 (2 × Ph), 128.4 (Ph), 128.3 (2 × Ph), 128.1 (Ph), 127.6 (2 × Ns Ar), 126.2 (2 × Ph), 123.9 (2 × Ns Ar), 119.0 (C3), 64.5 (C6), 51.4 (Bn CH_2), 36.9 (C5) and 19.7 (5–CH_3).



9d

N-(4-Nitrobenzenesulfonyl)-*cis*-8-methyl-1,2,3,8-tetrahydroindolizin-5-imine

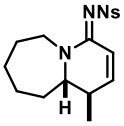
N-(4-Nitrobenzenesulfonyl)-(*Z*)-1-(pyrrolidin-1-yl)penta-2,4-dien-1-imine (640 mg, 1.908 mmol, 1.0 equiv.) was treated according to the General Procedure at 80 °C for 18 h to give the title compound (620 mg, 97%) as a pale yellow solid. *N*-(4-Nitrobenzenesulfonyl)-(*Z*)-1-(pyrrolidin-1-yl)penta-2,4-dien-1-imine (33 mg, 0.099 mmol, 1.0 equiv.) was treated according to the General Procedure at 80 °C for 18 h to give the title compound (31 mg, 93%) as a pale yellow solid. HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{15}H_{17}N_3NaO_4S^+$ 358.0832; Found 358.0821; IR (film) 3103, 2968, 2880, 1632, 1526, 1472, 1348, 1319, 1281, 1140 and 1088 cm^{-1}; ^1H NMR (400 MHz, 24.8 °C, $CDCl_3$) δ = 8.29 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.13 (2 H, d, *J* = 8.9 Hz, Ns Ar), 7.05 (1 H, dd, *J* = 9.9, 2.9 Hz, 7–H), 6.38 (1 H, dd, *J* = 9.9, 1.9 Hz, 6–H), 3.72 (1 H, dd, *J* = 13.2, 9.1 Hz, 3–H_A), 3.46 (1 H, ddd, *J* = 13.2, 10.2, 7.5 Hz, 3–H_B), 3.31 (1 H, ddd, *J* = 10.7, 7.2, 5.9 Hz, 8a–H), 2.41 (1 H, qdddd, *J* = 7.2, 7.2, 2.9, 1.9 Hz, 8–H), 2.33 (1 H, ddd, *J* = 12.2, 6.3, 5.9 Hz, 1–H_A), 2.08 (1 H, dtdt, *J* = 12.8, 7.5, 6.9, 1.6 Hz, 2–H_A), 1.80 (1 H, ddddd, *J* = 12.8, 12.7, 10.2, 9.1, 6.3 Hz, 2–H_B), 1.62 (1 H, dddd, *J* = 12.7, 12.2, 10.7, 6.9 Hz, 1–H_B) and 1.18 (3 H, d, *J* = 7.2 Hz, 8–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 24.8 °C, $CDCl_3$) δ = 156.7 (C5), 149.7 (Ns Ar), 149.3 (Ns Ar), 146.7 (C6), 127.6 (2 × Ns Ar), 123.8 (2 × Ns Ar), 120.0 (C7), 62.7 (C8a), 47.3 (C3), 35.6 (C8), 32.2 (C1), 22.4 (C2) and 16.6 (5–CH_3); m.pt. 133–136 °C.



9e

N-(4-Nitrobenzenesulfonyl)-*cis*-1-methyl-1,6,7,8,9,9a-hexahydroquinolizin-4-imine

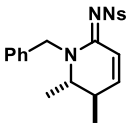
N-(4-Nitrobenzenesulfonyl)-(*Z*)-1-(piperidin-1-yl)penta-2,4-dien-1-imine (36 mg, 0.102 mmol, 1.0 equiv.) was treated according to the General Procedure at 80 °C for 18 h to give the title compound (8 mg, 23%) as a pale yellow solid. HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{16}H_{19}N_3NaO_4S^+$ 372.0988; Found 372.0976; IR (film) 2926, 2857, 1645, 1524, 1477, 1447, 1348, 1348, 1277, 1152 and 1092 cm^{-1}; $^{13}C\{^1H\}$ NMR (101 MHz, 24.9 °C, $CDCl_3$) δ = 157.4 (C4), 149.8 (Ns Ar), 149.3 (Ns Ar), 145.2 (C2), 127.5 (2 × Ns Ar), 123.9 (2 × Ns Ar), 117.5 (C3), 62.9 (C9a), 47.2 (C6), 34.4 (C1), 32.6 (C9), 25.2 (C8), 24.0 (C7) and 19.3 (1–CH_3); ^1H NMR (400 MHz, 24.8 °C, $CDCl_3$) δ = 8.30 (2 H, d, *J* = 8.8 Hz, Ns Ar), 8.12 (2 H, d, *J* = 8.8 Hz, Ns Ar), 7.01 (1 H, dd, *J* = 10.1, 1.7 Hz, 3–H), 6.48 (1 H, dd, *J* = 10.1, 4.5 Hz, 2–H), 4.61 (1 H, ddd, *J* = 13.0, 3.4, 2.1 Hz, 6–H_A), 3.21 (1 H, ddd, *J* = 11.1, 5.7, 2.3 Hz, 9a–H), 2.67 (1 H, dt, *J* = 13.0, 3.5 Hz, 6–H_B), 2.34 (1 H, qdd, *J* = 7.2, 4.5, 2.3 Hz, 1–H), 1.92–1.85 (1 H, m, 7–H_A), 1.81–1.74 (1 H, m, 9–H_A), 1.73–1.65 (1 H, m, 8–H_A), 1.61–1.49 (3 H, m, 9–H_B, 8–H_B & 7–H_B) and 1.17 (3 H, d, *J* = 7.2 Hz, 1–CH_3); m.pt. 131–134 °C.



9f

N-(4-Nitrobenzenesulfonyl)-*cis*-1-methyl-1,6,7,8,9,10-hexahydropyrido[1,2-*a*]azepin-4-imine

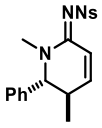
N-(4-Nitrobenzenesulfonyl)-(*Z*)-1-(azepan-1-yl)penta-2,4-dien-1-imine (44 mg, 0.120 mmol, 1.0 equiv.) was treated according to the General Procedure at 80 °C for 18 h to give the title compound (35 mg, 81%) as a pale yellow solid. IR (film) 2928, 2859, 1638, 1524, 1477, 1441, 1346, 1277, 1140 and 1090 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{17}H_{21}N_3NaO_4S^+$ 386.1145; Found 386.1137; ^1H NMR (400 MHz, 24.9 °C, $CDCl_3$) δ = 8.30 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.11 (2 H, d, *J* = 8.9 Hz, Ns Ar), 7.02 (1 H, d, *J* = 10.0 Hz, 3–H), 6.57 (1 H, ddd, *J* = 10.0, 6.1, 1.4 Hz, 2–H), 4.48 (1 H, ddd, *J* = 13.6, 6.7, 3.6 Hz, 6–H_A), 3.33 (1 H, ddd, *J* = 11.2, 4.0, 2.2 Hz, 10a–H), 2.83 (1 H, ddd, *J* = 13.6, 8.4, 5.6 Hz, 6–H_B), 2.37 (1 H, qd, *J* = 7.1, 6.1 Hz, 1–H), 1.94 (1 H, dddt, *J* = 13.7, 8.4, 6.7, 4.0 Hz, 7–H_A), 1.86–1.73 (1 H, m, 10–H_A), 1.70–1.46 (5 H, m, 10–H_B, 9–H, 8–H_A, 7–H_B), 1.44–1.35 (1 H, m, 8–H_B) and 1.11 (3 H, d, *J* = 7.1 Hz, 1–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 25.0 °C, $CDCl_3$) δ = 156.5 (C4), 150.0 (Ns Ar), 149.2 (Ns Ar), 144.8 (C2), 127.4 (2 × Ns Ar), 123.8 (2 × Ns Ar), 118.0 (C3), 64.8 (C10a), 50.4 (C6), 34.3 (C1), 33.2 (C10), 26.1 (C7), 25.8 (C9), 25.3 (C8) and 18.1 (1–CH_3); m.pt. 153–155 °C.



9g

N-(4-Nitrobenzenesulfonyl)-*trans*-1-benzyl-5,6-dimethyl-5,6-dihydropyridin-2-imine

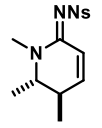
N^1-Benzyl,N^1-ethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (36 mg, 0.090 mmol, 1.0 equiv.) was treated according to the General Procedure at 80 °C for 18 h to give the title compound (25 mg, 68%) as a colourless oil. IR (film) 3103, 2972, 2930, 2872, 1639, 1524, 1479, 1454, 1387, 1348, 1281, 1142, 1086 and 1011 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{20}H_{21}N_3NaO_4S^+$ 422.1145; Found 422.1142; ^1H NMR (400 MHz, 24.8 °C, $CDCl_3$) δ = 8.26 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.05 (2 H, d, *J* = 8.9 Hz, Ns Ar), 7.30–7.26 (3 H, m, Ph), 7.22–7.17 (2 H, m, Ph), 7.12 (1 H, d, *J* = 10.0 Hz, 3–H), 6.60 (1 H, ddd, *J* = 10.0, 6.4, 1.4 Hz, 4–H), 5.35 (1 H, d, *J* = 14.5 Hz, Bn CH_2), 3.93 (1 H, d, *J* = 14.5 Hz, Bn CH_2), 3.37 (1 H, qdd, *J* = 6.8, 1.4, 1.3 Hz, 6–H), 2.27 (1 H, qdd, *J* = 7.1, 6.4, 1.3 Hz, 5–H), 1.24 (3 H, d, *J* = 6.8 Hz, 6–CH_3) and 0.84 (3 H, d, *J* = 7.1 Hz, 5–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 24.8 °C, $CDCl_3$) δ = 156.5 (C2), 149.6 (Ns Ar), 149.3 (Ns Ar), 144.5 (C4), 135.5 (Ph), 128.7 (2 × Ph), 128.4 (2 × Ph), 128.1 (Ph), 127.5 (2 × Ns Ar), 123.8 (2 × Ns Ar), 118.3 (C3), 57.1 (C6), 51.3 (Bn CH_2), 34.6 (C5), 18.1 (5–CH_3) and 17.8 (6–CH_3).



9h

N-(4-Nitrobenzenesulfonyl)-*trans*-1,5-dimethyl-6-phenyl-5,6-dihydropyridin-2-imine

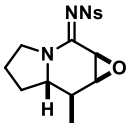
N^1-Benzyl,N^1-methyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (44 mg, 0.114 mmol, 1.0 equiv.) was treated according to the General Procedure at 100 °C for 96 h to give the title compound (26 mg, 59%) as a white solid. IR (film) 3105, 2968, 2928, 2872, 1641, 1524, 1476, 1346, 1279, 1144 and 1088 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{19}H_{19}N_3NaO_4S^+$ 408.0988; Found 408.0990; ^1H NMR (400 MHz, 20.8 °C, $CDCl_3$) δ = 8.33 (2 H, d, *J* = 9.0 Hz, Ns Ar), 8.18 (2 H, d, *J* = 9.0 Hz, Ns Ar), 7.39–7.29 (3 H, m, Ph), 7.16 (1 H, dd, *J* = 10.0, 1.0 Hz, 3–H), 7.11–7.07 (2 H, m, Ph), 6.49 (1 H, ddd, *J* = 10.0, 5.8, 0.9 Hz, 4–H), 4.36 (1 H, dd, *J* = 2.5, 0.9 Hz, 6–H), 3.03 (3 H, s, NCH_3), 2.69 (1 H, qddd, *J* = 7.3, 5.8, 2.5, 1.0 Hz, 5–H) and 1.28 (3 H, d, *J* = 7.3 Hz, 5–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 21.7 °C, $CDCl_3$) δ = 158.2 (C2), 149.6 (Ns Ar), 149.3 (Ns Ar), 143.8 (C4), 138.2 (Ph), 129.1 (2 × Ph), 128.4 (Ph), 127.6 (2 × Ns Ar), 126.0 (2 × Ph), 123.9 (2 × Ns Ar), 118.7 (C3), 68.4 (C6), 37.6 (NCH_3), 37.0 (C5) and 19.7 (5–CH_3); m.pt. 139–141 °C.



9i

N-(4-Nitrobenzenesulfonyl)-*trans*-1,5,6-trimethyl-5,6-dihydropyridin-2-imine

N^1-Ethyl,N^1-methyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (20 mg, 0.062 mmol, 1.0 equiv.) was treated according to the General Procedure at 100 °C for 18 h to give the title compound (7 mg, 35%) as a colourless oil. HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{14}H_{17}N_3NaO_4S^+$ 346.0832; Found 346.0826; ^1H NMR (400 MHz, 25.2 °C, $CDCl_3$) δ = 8.30 (2 H, d, *J* = 9.0 Hz, Ns Ar), 8.13 (2 H, d, *J* = 9.0 Hz, Ns Ar), 7.04 (1 H, d, *J* = 10.0 Hz, 3–H), 6.59 (1 H, ddd, *J* = 10.0, 6.3, 1.5 Hz, 4–H), 3.34 (1 H, qdd, *J* = 6.8, 1.5, 1.4 Hz, 6–H), 3.08 (3 H, s, NCH_3), 2.33 (1 H, qdd, *J* = 7.1, 6.3, 1.4 Hz, 5–H), 1.24 (3 H, d, *J* = 6.8 Hz, 6–CH_3) and 1.12 (3 H, d, *J* = 7.1 Hz, 5–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 24.6 °C, $CDCl_3$) δ = 156.7 (C2), 149.8 (Ns Ar), 149.3 (Ns Ar), 144.1 (C4), 127.5 (2 × Ns Ar), 123.8 (2 × Ns Ar), 118.1 (C3), 60.8 (C6), 37.1 (NCH_3), 34.7 (C5), 18.4 (6–CH_3) and 17.7 (5–CH_3); IR (film) 3105, 2973, 2877, 1640, 1527, 1480, 1349, 1280, 1142 and 1089 cm^{-1}.



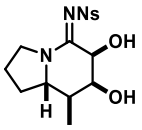
10d

(6*R,7*S**,8*S**,8a*S**)-*N*-(4-Nitrobenzenesulfonyl)-6,7-epoxy-8-methylhexahydroindolizin-5-imine**

Hydrogen peroxide (0.02 mL, 30% in H_2O, 0.17 mmol) was added dropwise to a solution of *N*-(4-nitrobenzenesulfonyl)-*cis*-8-methyl-2,3,8,8a-tetrahydroindolizin-5-imine **9d** (50.4 mg, 0.150 mmol) in methanol (1.0 mL) and dichloromethane (1.0 mL) and the mixture was stirred at 0 °C under an atmosphere of argon for 5 min. An aqueous solution of sodium hydroxide (0.07 mL, 1.0 M, 0.5 equiv.) was added dropwise to the solution at 0 °C and the resulting mixture was slowly warmed to ambient temperature over 2.5 h. The mixture was neutralised by the addition of hydrochloric acid (1.0 M) and the aqueous phase was extracted with dichloromethane (3 ×). The combined organic layers were then washed with brine, dried ($MgSO_4$), concentrated *in vacuo*. Purification by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 100%) gave the title compound (34.1 mg, 65%) as a white solid.

IR (film) 3103, 2972, 2882, 1564, 1524, 1489, 1346, 1279, 1142 and 1088 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{15}H_{17}N_3NaO_5S^+$ 374.0781; Found 374.0778; ^1H NMR (400 MHz, 27.0 °C, $CDCl_3$) δ = 8.31 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.15 (2 H, d, *J* = 8.8 Hz, Ns Ar), 4.81 (1 H, d, *J* = 3.9 Hz, 6–H), 3.60–3.38 (2 H, m, 3–H), 3.48 (1 H, d, *J* = 3.9 Hz, 7–H), 3.28 (1 H, dt, *J* = 10.7, 5.5 Hz, 8a–H), 2.27 (1 H, dt, *J* = 12.1, 6.9 Hz, 1–H_A), 1.99 (1 H, dt, *J* = 12.8, 6.9 Hz, 2–H_A), 1.90 (1 H, dq, *J* = 10.7, 6.9 Hz, 8–H), 1.83–1.70 (1 H, m, 2–H_B), 1.51 (1 H, dq, *J* = 12.1, 6.9 Hz, 1–H_B) and 1.29 (3 H, d, *J* = 6.9 Hz, 8–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 27.0 °C, $CDCl_3$) δ = 160.1 (C5), 149.4 (Ns Ar), 149.4 (Ns Ar), 127.6 (2 × Ns Ar), 123.9 (2 × Ns Ar), 59.4 (C8a), 58.8 (C7), 49.0 (C3), 47.3 (C6), 35.3 (C8), 31.9 (C1), 22.1 (C2) and 15.5 (8–CH_3); m.pt. 172–178 °C.

Stereochemistry was assigned by analogy with the dihydroxylation (see below).



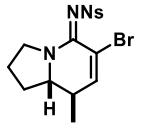
11d

(6*R**,7*S**,8*R**,8a*R**)-*N*-(4-Nitrobenzenesulfonyl)-6,7-dihydroxy-8-methylhexahydroindolizin-5-imine

OsO_4 (0.031 mL, 4% in H_2O, 0.005 mmol) and NMO (24 mg, 0.178 mmol) were added to a solution of *N*-(4-nitrobenzenesulfonyl)-*cis*-8-methyl-2,3,8,8a-tetrahydroindolizin-5-imine **9d** (32.7 mg, 0.088 mmol) in acetone and H_2O (0.6 mL, 2:1) and the reaction mixture was stirred at ambient temperature for 24 h. Dichloromethane (5 mL) was added and the organic layer was washed with saturated aqueous $NaHCO_3$ (2 mL) and brine then dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 100%) gave the title compound (29.4 mg, 82%) as a white solid.

HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{15}H_{19}N_3NaO_6S^+$ 392.0887; Found 392.0892; IR (film) 3452, 2968, 2883, 1557, 1525, 1471, 1349, 1277, 1139 and 1086 cm^{-1}; ^1H NMR (500 MHz, 25.0 °C, $CDCl_3$) δ = 8.31 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.14 (2 H, d, *J* = 8.9 Hz, Ns Ar), 5.60 (1 H, d, *J* = 4.8 Hz, 6–OH), 4.73 (1 H, dd, *J* = 4.8, 4.5 Hz, 6–H), 4.09 (1 H, dd, *J* = 4.5, 1.5 Hz, 7–H), 3.73 (1 H, ddd, *J* = 12.0, 10.7, 5.6 Hz, 8a–H), 3.62–3.49 (2 H, m, 3–H), 3.04 (1 H, s, 7–OH), 2.22 (1 H, ddd, *J* = 12.1, 5.7, 5.6 Hz, 1–H_A), 2.07–2.00 (1 H, m, 2–H_A), 1.92–1.80 (1 H, m, 2–H_B), 1.66 (1 H, dqd, *J* = 10.7, 6.7, 1.5 Hz, 8–H), 1.44 (1 H, dddd, *J* = 12.5, 12.1, 12.0, 7.3 Hz, 1–H_B) and 1.20 (3 H, d, *J* = 6.7 Hz, 8–CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 27.0 °C, $CDCl_3$) δ = 163.4 (C5), 149.4 (Ns Ar), 149.3 (Ns Ar), 127.4 (2 × Ns Ar), 123.9 (2 × Ns Ar), 70.0 (C7), 68.5 (C6), 59.8 (C8a), 49.1 (C3), 38.1 (C8), 31.2 (C1), 22.1 (C2) and 14.3 (8–CH_3); m.pt. 167–170 °C.

The reaction was selective for the *exo* face. Stereochemistry was assigned by comparison with 10.1002/ejoc.200200412;[5] and 10.1016/j.tetlet.2004.04.121.[6]

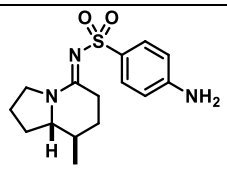


12d

N-(4-Nitrobenzenesulfonyl)-*cis*-6-bromo-8-methyl-2,3,8,8a-tetrahydroindolizin-5-imine

A solution of bromine (0.6 mL, 0.31 M, 3 equiv.) was added dropwise to a stirred solution of *N*-(4-nitrobenzenesulfonyl)-*cis*-8-methyl-2,3,8,8a-tetrahydroindolizin-5-imine **9d** (20 mg, 0.060 mmol) in dichloromethane (0.3 mL) at −10 °C under an argon atmosphere. The mixture was slowly warmed to ambient temperature and stirred for 3 h. Saturated aqueous sodium thiosulfate solution (1 mL) was added dropwise and the aqueous phase was extracted with dichloromethane (3 ×) and the combined organic layers were concentrated *in vacuo*. Dichloromethane (0.6 mL) and triethylamine (0.040 mL, 0.3 mmol) were added. The mixture was heated at 45 °C for 3 hours and then cooled to ambient temperature. Saturated aqueous NH_4Cl (1.0 mL) was added to the solution and the aqueous phase was extracted with dichloromethane (3 ×). The combined organic layers were then washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* and purified by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 100%) to give the title compound (10 mg, 40%) as a colourless foam.

HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{15}H_{16}BrN_3NaO_4S^+$ 435.9937; Found 435.9936; ^1H NMR (500 MHz, 25.0 °C, $CDCl_3$) δ = 8.31 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.25 (2 H, d, *J* = 8.9 Hz, Ns Ar), 6.74 (1 H, d, *J* = 2.1 Hz, 7–H), 4.47 (1 H, ddd, *J* = 12.5, 8.4, 3.4 Hz, 3–H_A), 4.20 (1 H, dt, *J* = 12.5, 8.4 Hz, 3–H_B), 3.57 (1 H, ddd, *J* = 14.5, 9.5, 6.3 Hz, 8a–H), 2.51 (1 H, dqd, *J* = 14.5, 7.2, 2.1 Hz, 8–H), 2.28 (1 H, dddd, *J* = 12.5, 6.4, 6.3, 3.4 Hz, 1–H_A), 2.14 (1 H, dddd, *J* = 16.7, 8.4, 6.9, 3.4 Hz, 2–H_A), 2.02–1.91 (1 H, m, 2–H_B), 1.73 (1 H, dddd, *J* = 12.5, 10.7, 9.5, 6.9 Hz, 1–H_B) and 1.20 (3 H, d, *J* = 7.2 Hz, 8–CH_3); $^{13}C\{^1H\}$ NMR (126 MHz, 25.0 °C, $CDCl_3$) δ = 150.7 (C5), 150.1 (2 × Ns Ar), 146.5 (C7), 127.5 (2 × Ns Ar), 123.7 (2 × Ns Ar), 119.1 (C6), 65.9 (C8a), 52.5 (C3), 37.2 (C8), 30.6 (C1), 23.7 (C2) and 16.9 (8–CH_3); IR (film) 3104, 2968, 1570, 1519, 1457, 1422, 1399, 1350, 1271, 1134, 1108 and 1086 cm^{-1}.



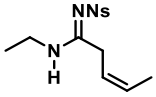
13d

N-(4-Aminobenzenesulfonyl)-*cis*-8-methylhexahydroindolizin-5-imine

10% Palladium on carbon (1.0 mg) was added to a solution of *N*-(4-nitrobenzenesulfonyl)-*cis*-8-methyl-2,3,8,8a-tetrahydroindolizin-5-imine **9d** (23.8 mg, 0.071 mmol) in methanol (0.7 mL) and the mixture was stirred at ambient temperature under an atmosphere of hydrogen for 2 days. The mixture was diluted with ethyl acetate (4 mL), filtered through celite, concentrated *in vacuo*. Purification by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 100%) gave the title compound (16.8 mg, 77%) as a colourless gum.

IR (film) 3453, 3354, 3242, 2963, 2880, 1630, 1597, 1547, 1504, 1458, 1132 and 1086 cm^{-1}; ^{1}H NMR (400 MHz, 25.5 °C, $CDCl_3$) δ = 7.72 (2 H, d, *J* = 8.7 Hz, Ar), 6.64 (2 H, d, *J* = 8.7 Hz, Ar), 3.97 (2 H, br s, NH_2), 3.64–3.49 (2 H, m, 6–H), 3.24 (1 H, dd, *J* = 18.9, 6.1 Hz, 3–H_A), 2.98 (1 H, td, *J* = 10.5, 5.0 Hz, 8a–H), 2.86 (1 H, dddd, *J* = 18.9, 11.4, 7.4, 1.2 Hz, 3–H_B), 2.19 (1 H, app p, *J* = 5.8 Hz, 1–H_A), 2.01–1.92 (1 H, m, 7–H_A), 1.87–1.80 (1 H, m, 2–H), 1.79–1.66 (1 H, m, 7–H_B), 1.47–1.28 (3 H, m, 8–H, 1–H_B & 2–H_B) and 1.01 (3 H, d, *J* = 6.2 Hz, 8–CH_3); $^{13}C\{^{1}H\}$ NMR (101 MHz, 25.3 °C, $CDCl_3$) δ = 163.8 (C5), 149.2 (Ar), 133.5 (Ar), 128.2 (2 × Ar), 113.8 (2 × Ar), 65.7 (C8a), 48.2 (C6), 34.2 (C8), 31.9 (C1), 28.7 (C2), 27.8 (C3), 21.9 (C7) and 18.1 (8–CH_3); HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{15}H_{21}N_3NaO_2S^+$ 330.1247; Found 330.1246.

Mechanism Studies

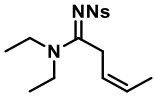


16a

N^1-Ethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pent-3-enamidine

N^1,N^1-Diethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (14 mg, 0.042 mmol, 1.0 equiv.) was treated according to the General Procedure at 65 °C for 18 h. Analysis of the crude reaction mixture showed the presence of the title compound (37% by ^{1}H NMR) as well as unreacted diene **8a** and cyclic amidine **9a**. The title compound could not be separated from the other products.

^{1}H NMR (400 MHz, 25.2 °C, $CDCl_3$) δ = 8.32 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.14 (2 H, d, *J* = 8.9 Hz, Ns Ar), 6.05–5.94 (1 H, m, 4–H), 5.48 (1 H, dtq, *J* = 8.9, 7.5, 1.8 Hz, 3–H), 3.74 (2 H, d, *J* = 7.5 Hz, 2–H_2), 3.35–3.28 (2 H, m, NEt CH_2), 1.67 (3 H, dd, *J* = 6.9, 1.8 Hz, 5–H_3) and 1.14 (3 H, t, *J* = 7.2 Hz, NEt CH_3); ^{13}C{^{1}H} NMR (101 MHz, 25.0 °C, $CDCl_3$) δ = 166.3 (C1), 149.4 (Ns Ar), 149.3 (Ns Ar), 133.6 (C4), 127.6 (2 × Ns Ar), 123.9 (2 × Ns Ar), 120.5 (C3), 37.1 (NEt CH_2), 31.6 (C2), 13.6 (NEt CH_3) and 13.0 (C5).

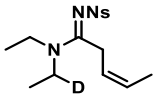


15a

N^1,N^1-Diethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pent-3-enamidine

N^1,N^1-Diethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (27.5 mg, 0.082 mmol, 1.0 equiv.) was treated according to the General Procedure at 65 °C for 18 h. Then, the reaction mixture was cooled to 0 °C and sodium borohydride (4.6 mg, 0.121 mmol, 1.5 equiv.) and methanol (0.5 mL) were added and the reaction mixture was stirred for 1 h. The mixture was warmed to ambient temperature and the reaction was quenched by the addition of saturated aqueous NH_4Cl, followed by stirring for 1 h. Saturated aqueous Na_2CO_3 and water were added and the aqueous phase was extracted with ethyl acetate (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 60%) gave the title compound (14.8 mg, 53%) as a colourless oil.

IR (film) 3103, 3028, 2976, 2936, 2859, 1549, 1528, 1477, 1458, 1437, 1348, 1285, 1144, 1092 and 1080 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{21}N_3NaO_4S^+$ 362.1145; Found 362.1131; ^{1}H NMR (400 MHz, 25.0 °C, $CDCl_3$) δ = 8.30 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.11 (2 H, d, *J* = 8.9 Hz, Ns Ar), 5.70 (1 H, dqt, *J* = 10.6, 6.9, 2.1 Hz, 4–H), 5.39 (1 H, dtq, *J* = 10.6, 6.4, 1.8 Hz, 3–H), 3.74 (2 H, br dd, *J* = 6.4, 2.1 Hz, 2–H_2), 3.44 (2 H, q, *J* = 7.1 Hz, NEt CH_2), 3.35 (2 H, q, *J* = 7.2 Hz, NEt CH_2'), 1.70 (3 H, br dd, *J* = 6.9, 1.8 Hz, 5–H_3), 1.25 (3 H, t, *J* = 7.2 Hz, NEt CH_3') and 1.10 (3 H, t, *J* = 7.1 Hz, NEt CH_3); ^{13}C{^{1}H} NMR (101 MHz, 24.9 °C, $CDCl_3$) δ = 166.3 (C1), 150.0 (Ns Ar), 149.2 (Ns Ar), 128.1 (C4), 127.4 (2 × Ns Ar), 123.8 (2 × Ns Ar), 122.2 (C3), 43.7 (NEt CH_2'), 43.4 (NEt CH_2), 30.4 (C2), 13.8 (NEt CH_3), 13.1 (C5) and 12.0 (NEt CH_3').



***d*-15a**

N^1-(1-Deuteroeth-1-yl)-N^1-ethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pent-3-enamidine

N^1,N^1-Diethyl,N^2-(4-nitrobenzenesulfonyl)-(*Z*)-pentadienamidine (31.0 mg, 0.093 mmol, 1.0 equiv.) was treated according to the General Procedure at 65 °C for 18 h. Then, the reaction mixture was cooled to 0 °C and sodium borodeuteride (10.0 mg, 0.239 mmol, 2.6 equiv.) and methanol (0.5 mL) were added and the reaction mixture was stirred for 1 h. The mixture was warmed to ambient temperature and the reaction was quenched by the addition of saturated aqueous NH_4Cl, followed by stirring for 1 h. Saturated aqueous Na_2CO_3 and water were added and the aqueous phase was extracted with ethyl acetate (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (ethyl acetate in petroleum ether, gradient from 5 to 60%) gave the title compound (8.8 mg, 28%) as a colourless oil.

HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $C_{15}H_{20}[^2H]N_3NaO_4S^+$ 363.1208; Found 363.1224; IR (film) 3104, 2978, 2934, 2854, 1545, 1527, 1472, 1349, 1284, 1145 and 1086 cm^{-1}; ^1H NMR (400 MHz, 25.0 °C, $CDCl_3$) δ = 8.30 (2 H, d, *J* = 8.9 Hz, Ns Ar), 8.11 (2 H, d, *J* = 8.9 Hz, Ns Ar), 5.70 (1 H, dqt, *J* = 10.6, 6.9, 2.1 Hz, 4–H), 5.39 (1 H, dtq, *J* = 10.6, 6.4, 1.7 Hz, 3–H), 3.73 (2 H, d, *J* = 6.4 Hz, 2–H_2), 3.44 (1.5 H, q, *J* = 7.1 Hz, NEt CDH), 3.35 (1.5 H, q, *J* = 7.1 Hz, NEt CDH), 1.70 (3 H, dd, *J* = 6.9, 1.7 Hz, 5–H_3) and 1.27–1.22 (6 H, m, NEt CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, 25.0 °C, $CDCl_3$) δ = 166.3 (C1), 149.9 (Ns Ar), 149.2 (Ns Ar), 128.1 (C4), 127.4 (2 × Ns Ar), 123.8 (2 × Ns Ar), 122.2 (C3), 43.7 (NEt CDH), 43.4 (NEt CDH), 30.4 (C2), 13.8 (d, *J* = 11.8 Hz, NEt CH_3), 13.1 (C5) and 11.9 (d, *J* = 11.9 Hz, NEt CH_3).

References

[1] G. M. Sheldrick, *Acta Crystallogr. A*, 2015, **A71**, 3-8.

[2] G. M. Sheldrick, *Acta Crystallogr. C*, 2015, **C71**, 3-8.

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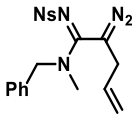
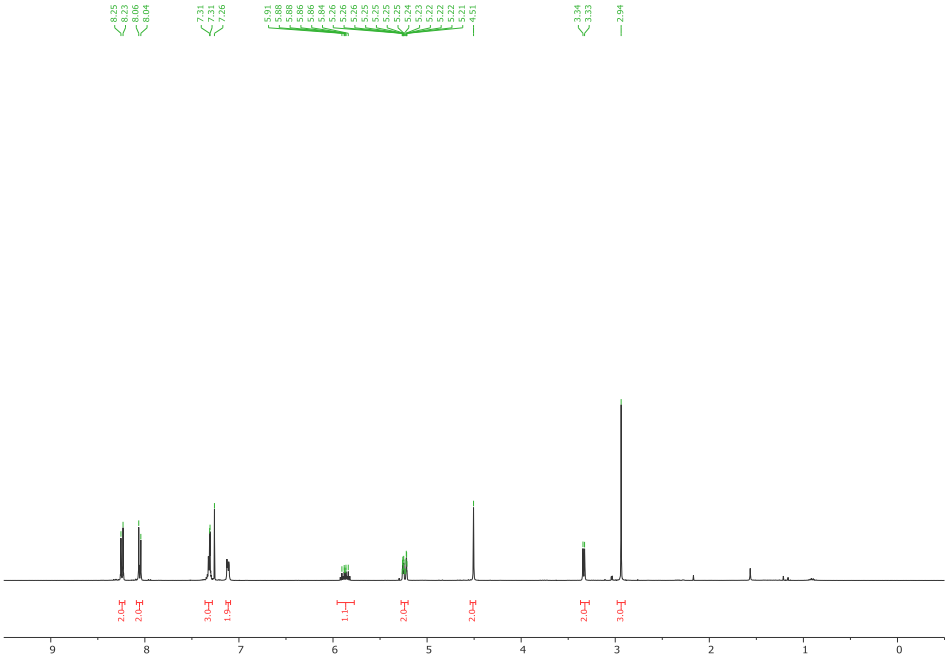
NMR Spectra

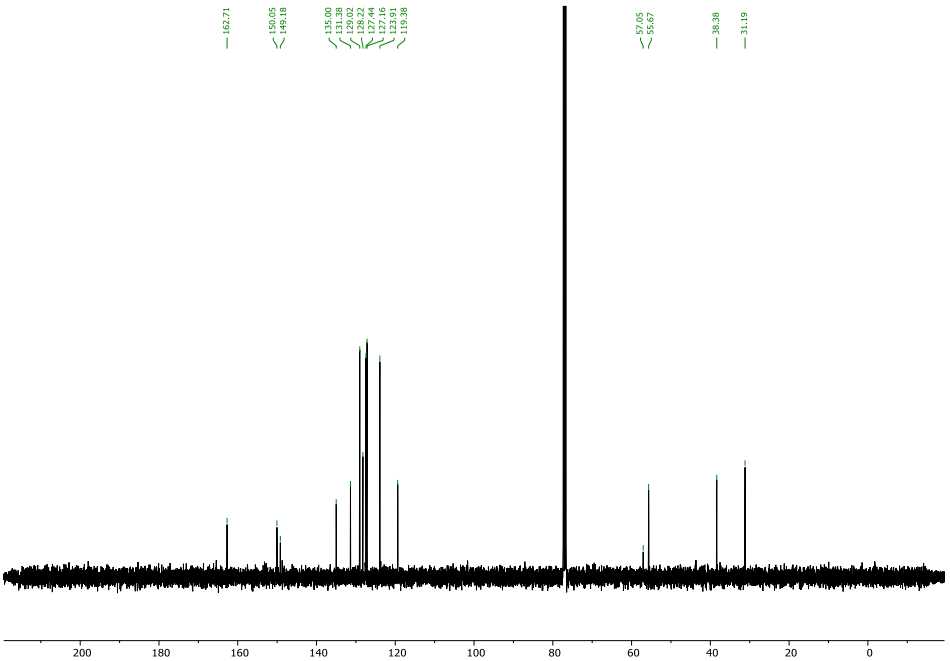


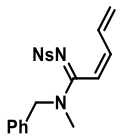
5`h

^{1}H NMR, $CDCl_3$, 400 MHz



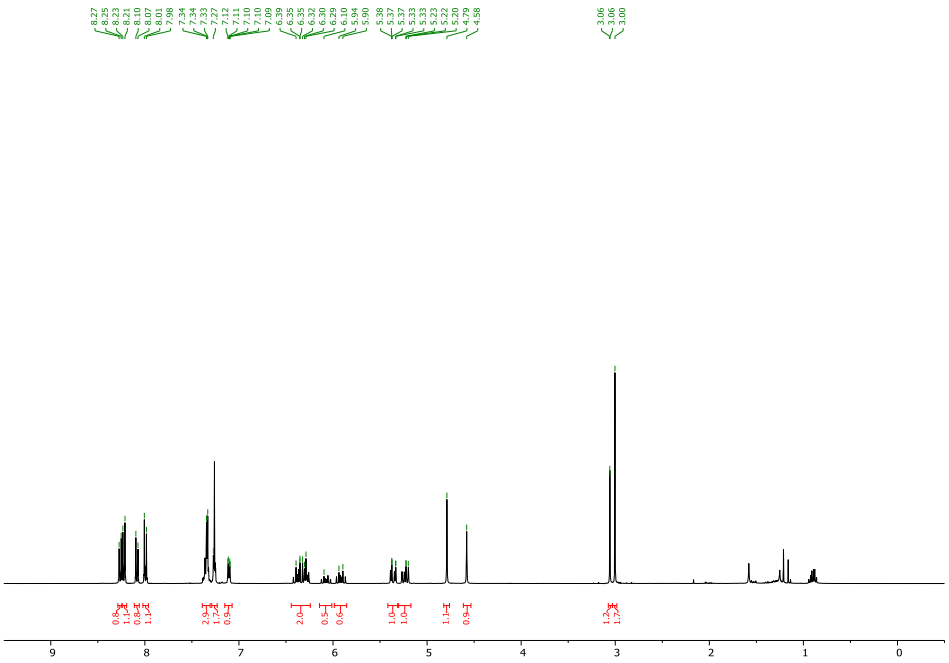
^{13}C NMR, $CDCl_3$, 101 MHz



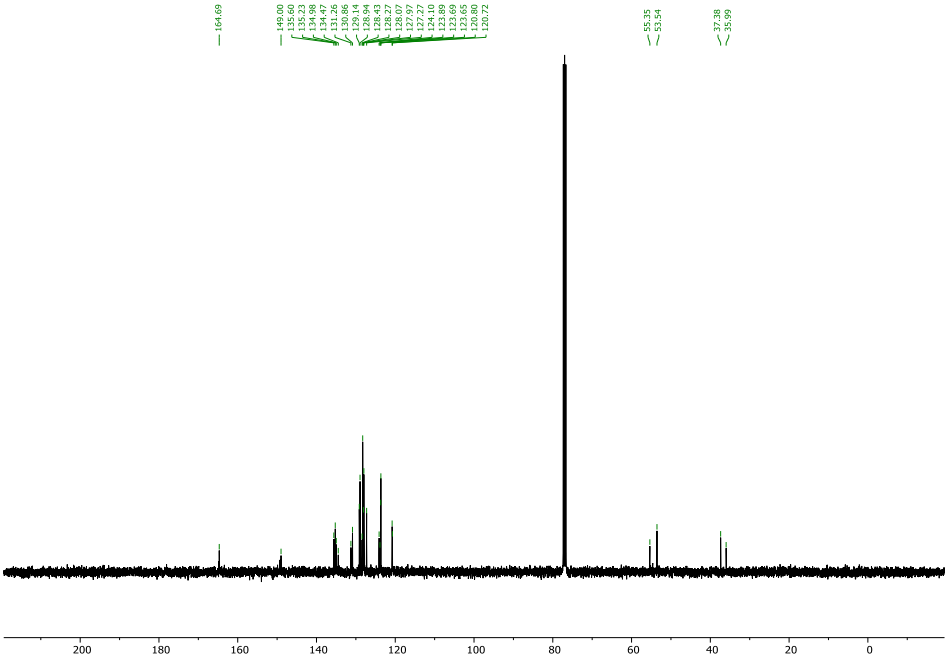


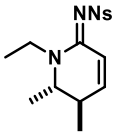
8`h

^{1}H NMR, $CDCl_3$, 400 MHz



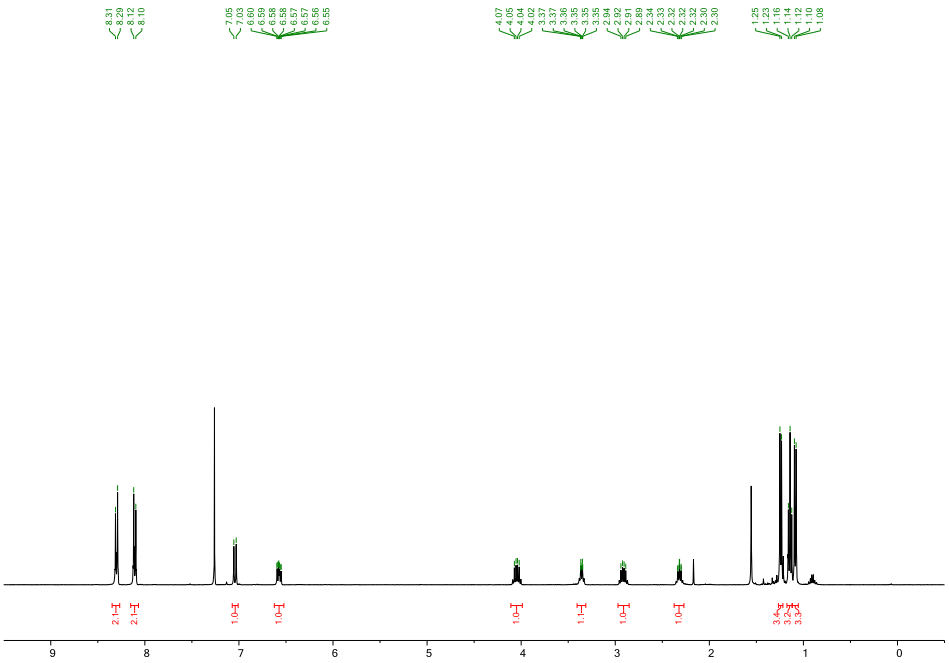
^{13}C NMR, $CDCl_3$, 101 MHz



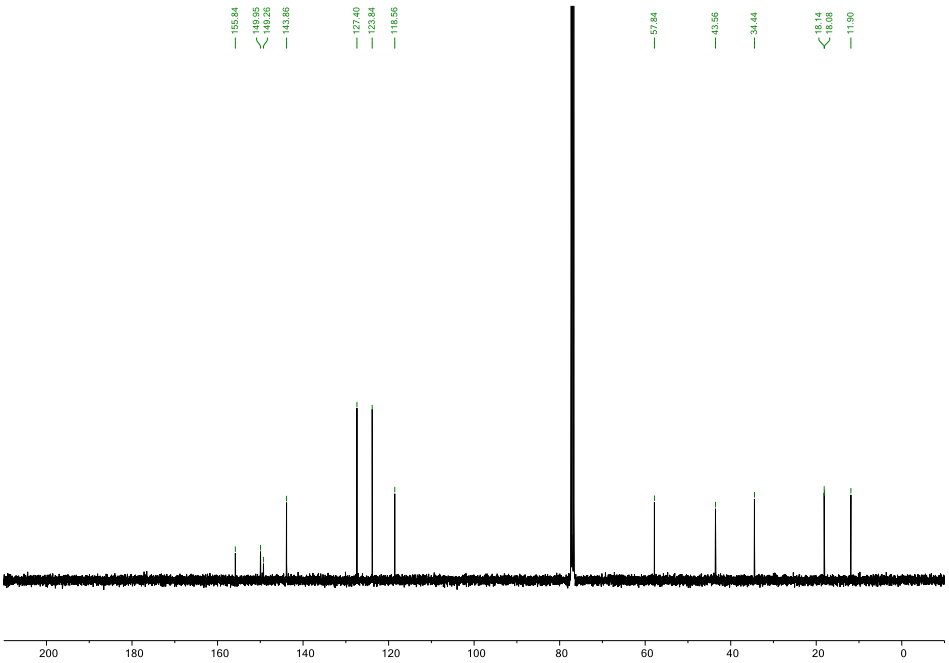


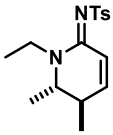
9a

^{1}H NMR, $CDCl_3$, 400 MHz



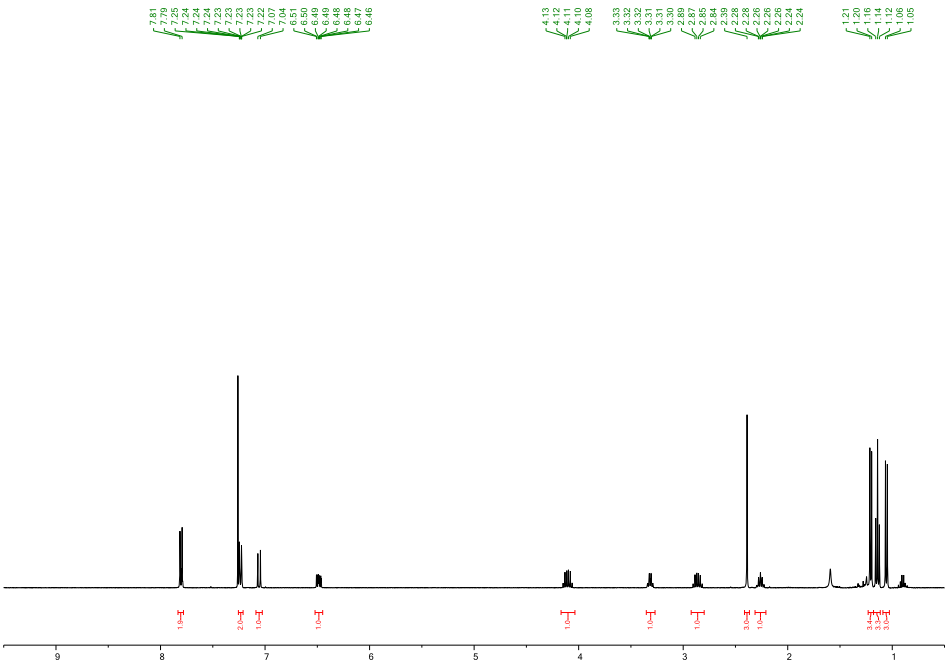
^{13}C NMR, $CDCl_3$, 101 MHz



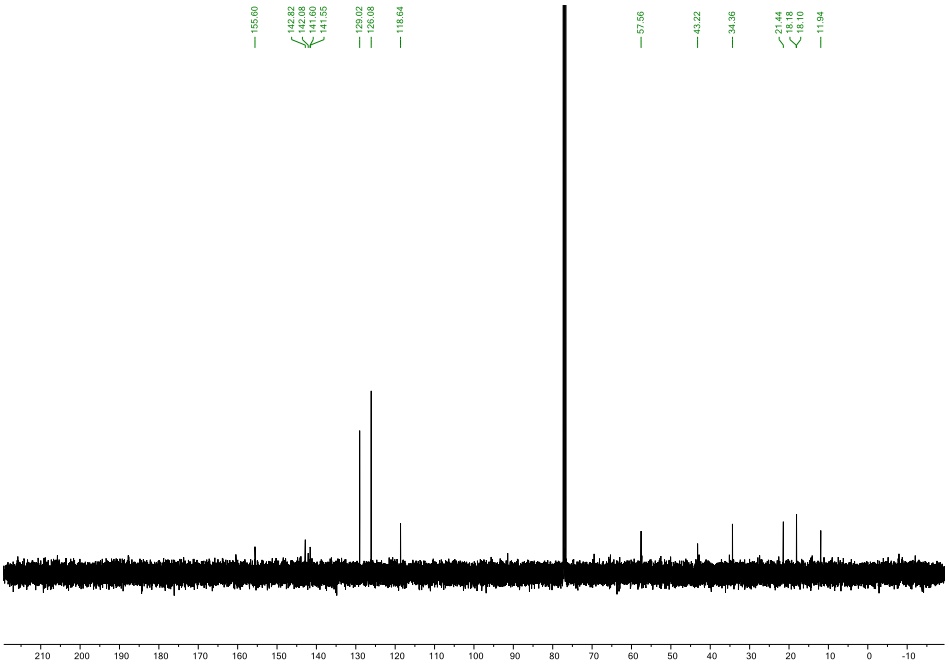


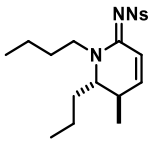
9aTS

^{1}H NMR, $CDCl_3$, 400 MHz



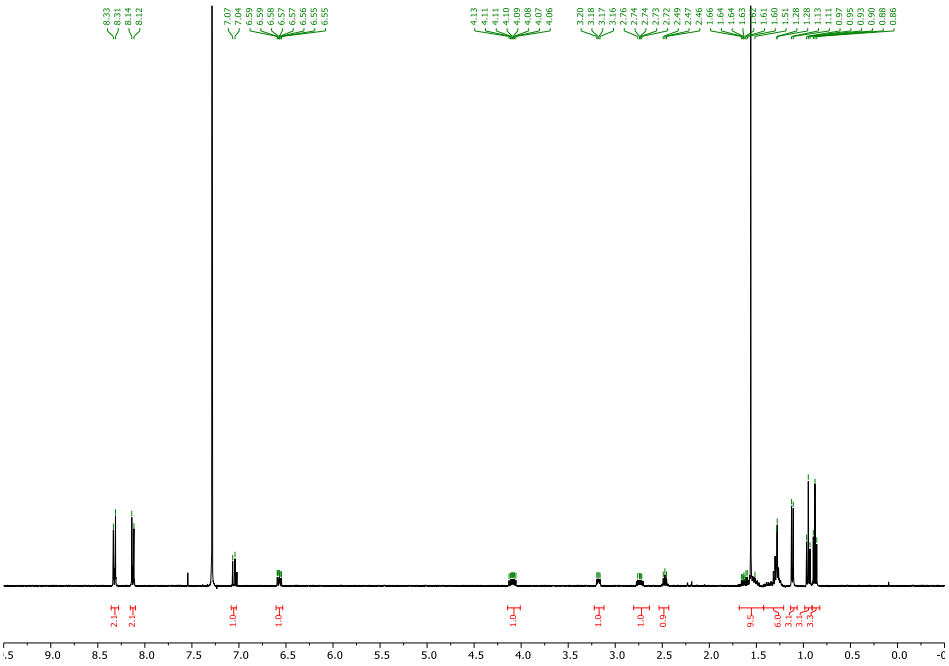
^{13}C NMR, $CDCl_3$, 101 MHz



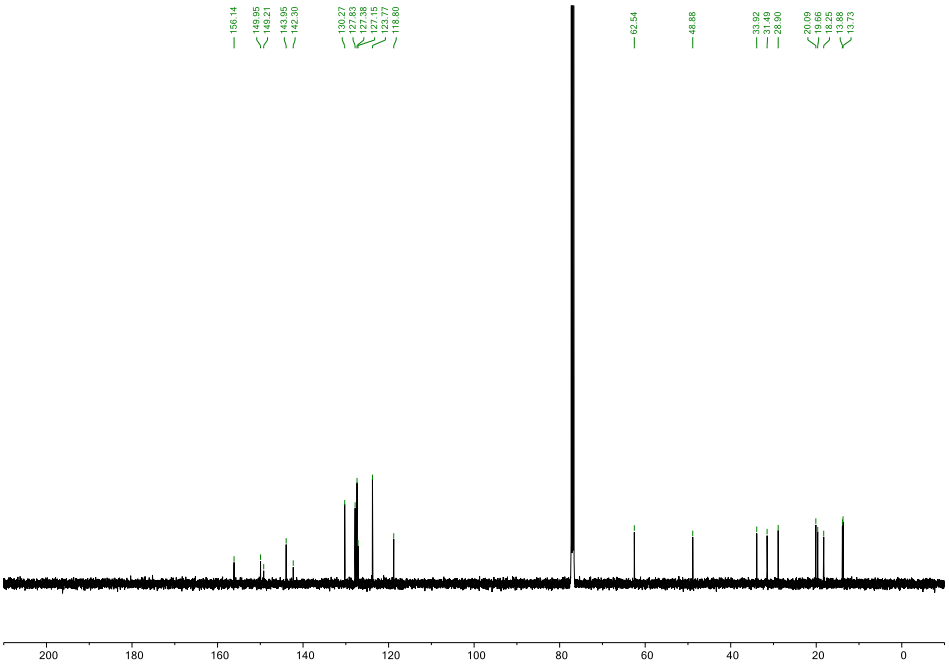


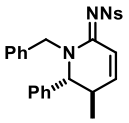
9b

^{1}H NMR, $CDCl_3$, 400 MHz



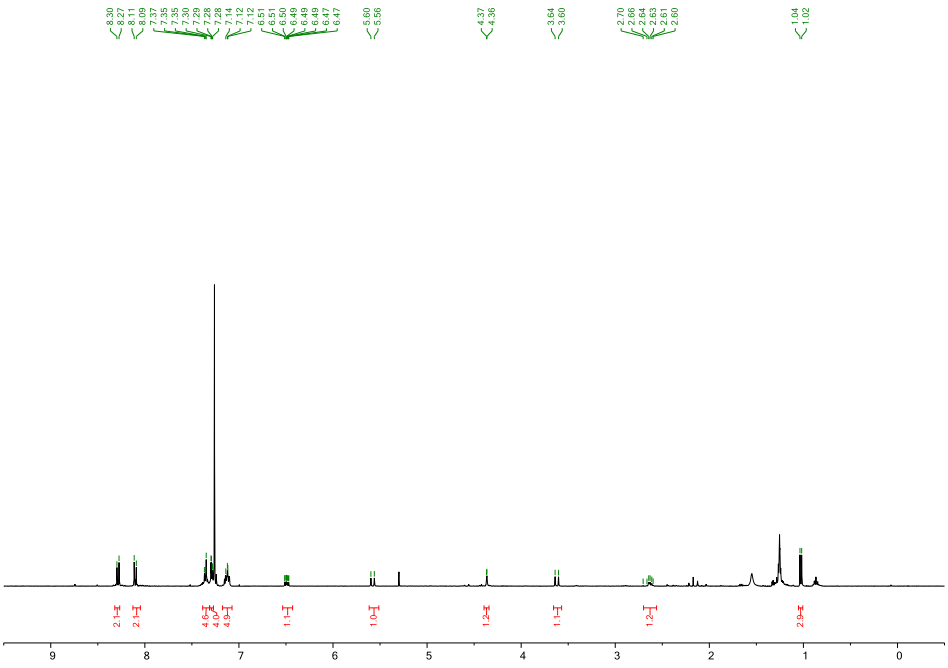
^{13}C NMR, $CDCl_3$, 126 MHz



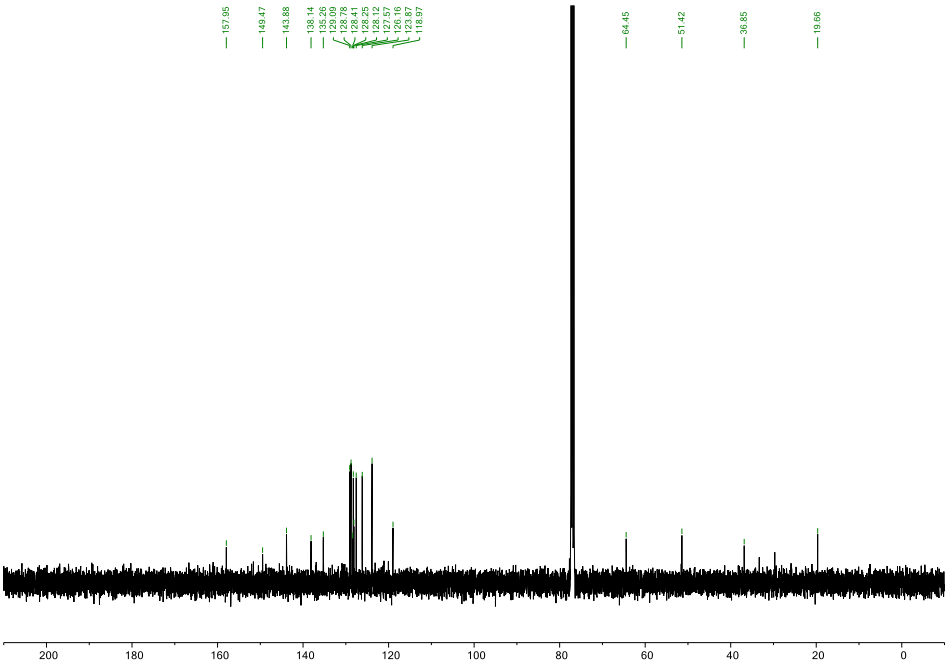


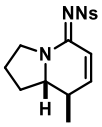
9c

^{1}H NMR, $CDCl_3$, 400 MHz



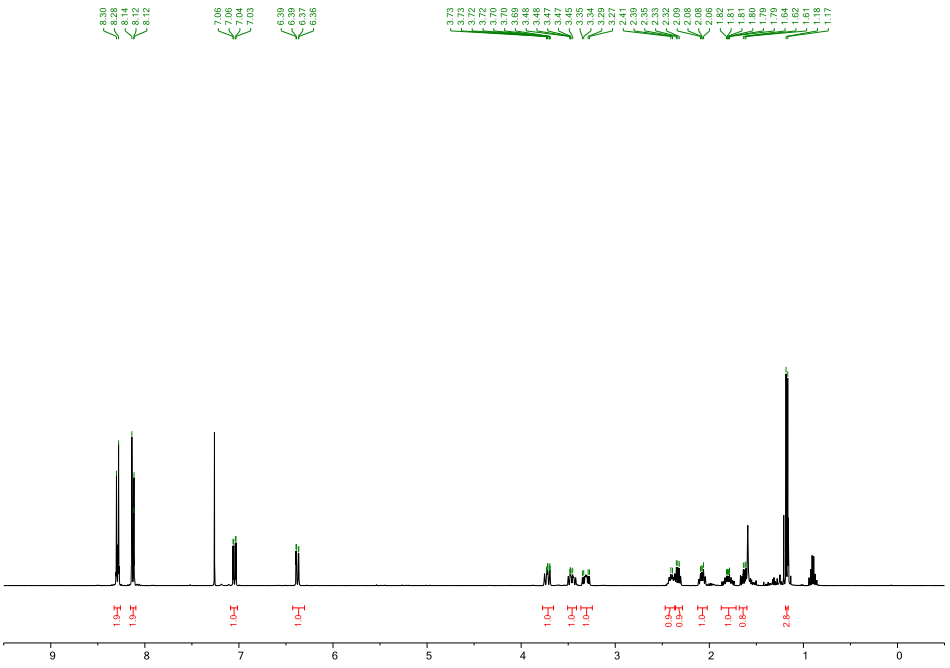
^{13}C NMR, $CDCl_3$, 101 MHz



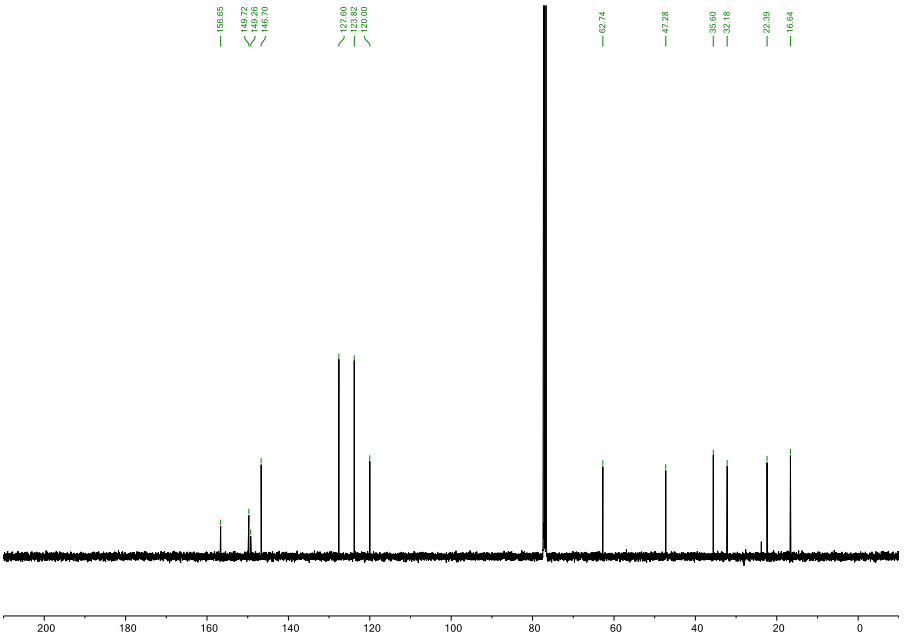


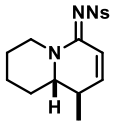
9d

^{1}H NMR, $CDCl_3$, 400 MHz



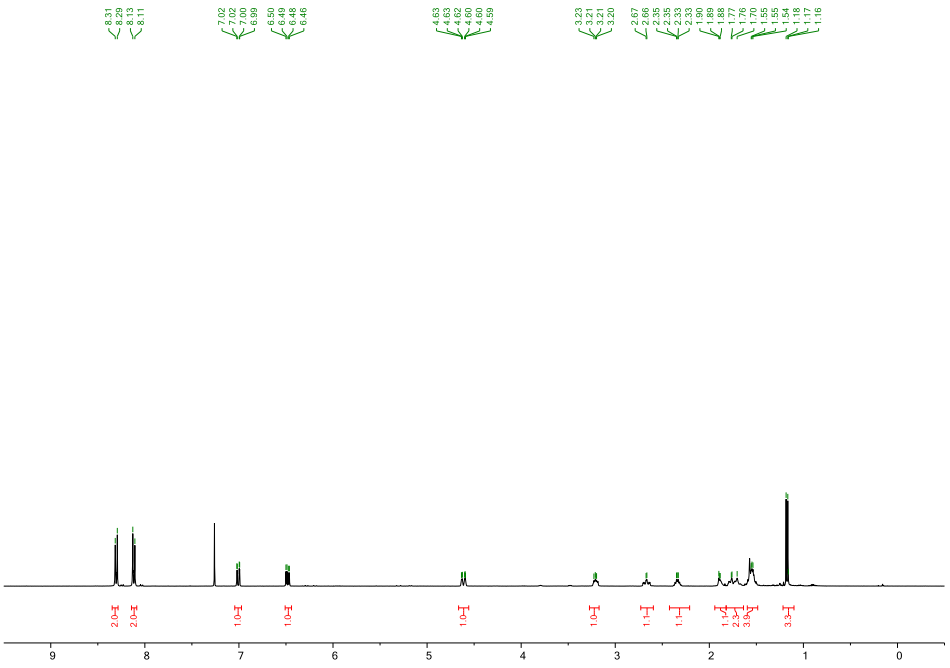
^{13}C NMR, $CDCl_3$, 101 MHz



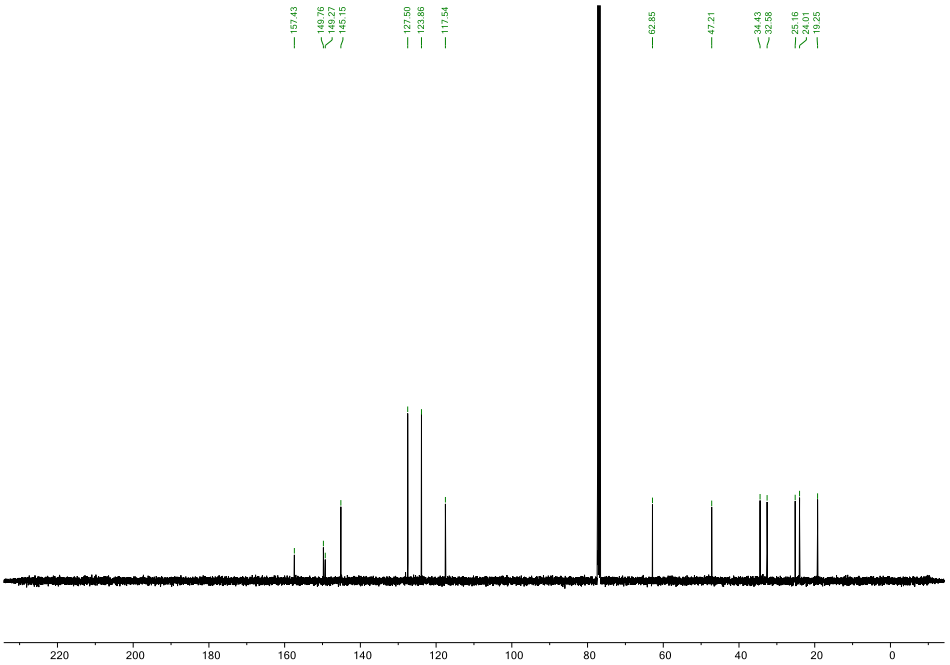


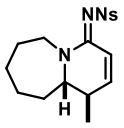
9e

^{1}H NMR, $CDCl_3$, 400 MHz



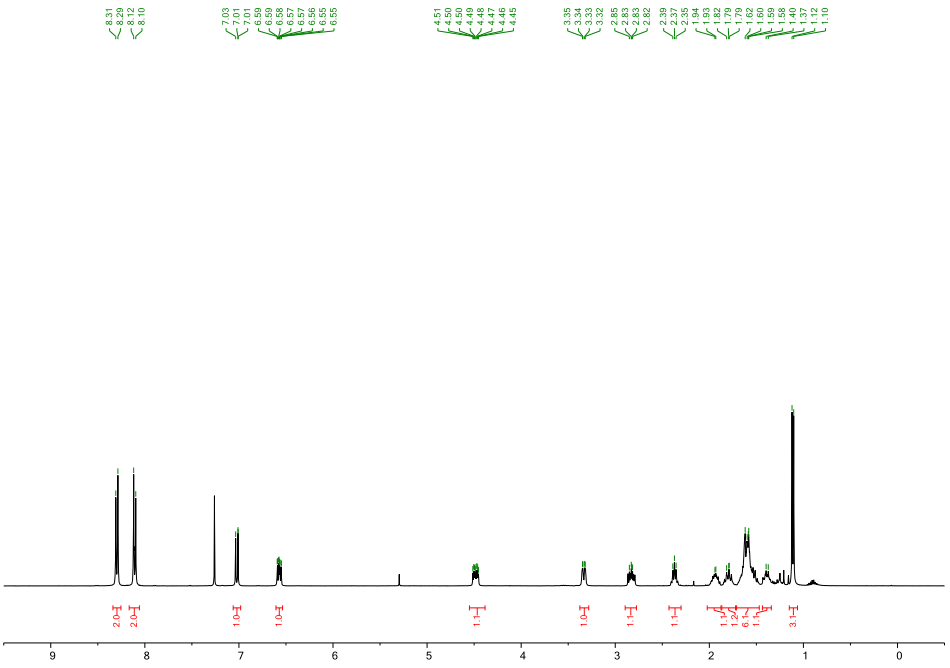
^{13}C NMR, $CDCl_3$, 101 MHz



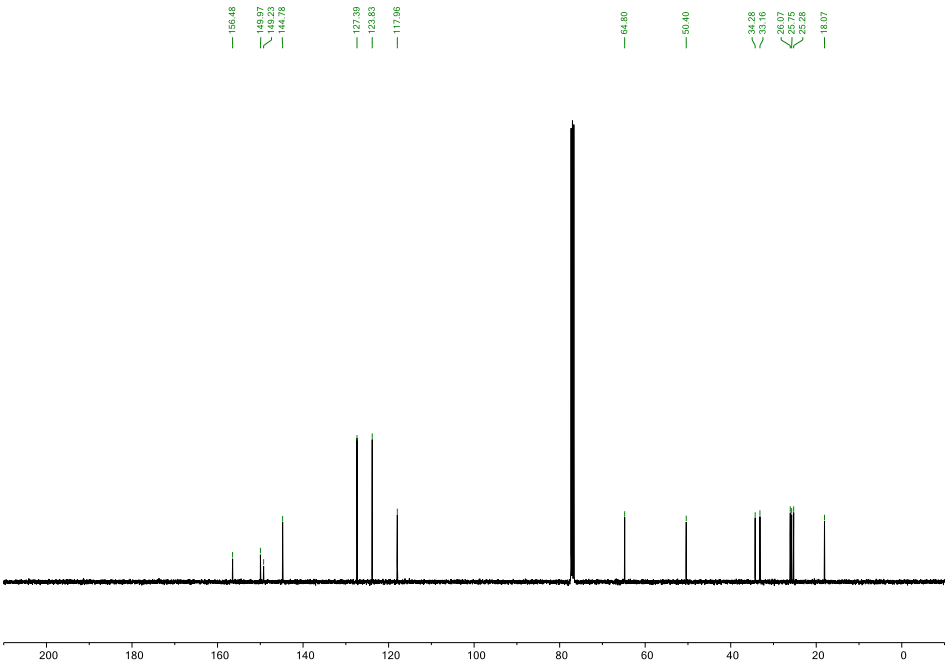


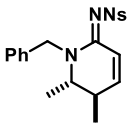
9f

^{1}H NMR, $CDCl_3$, 400 MHz



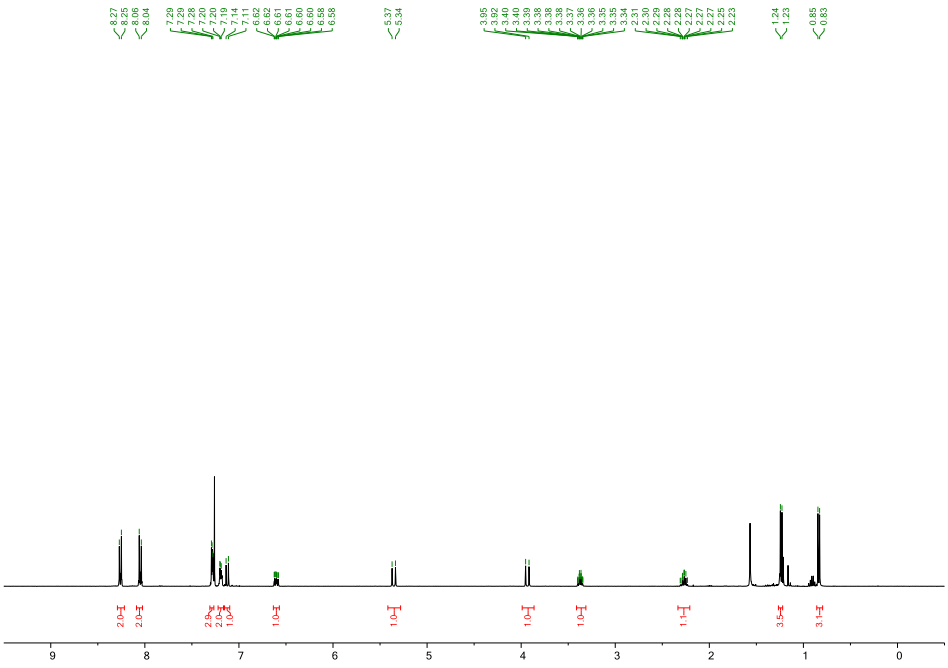
^{13}C NMR, $CDCl_3$, 101 MHz



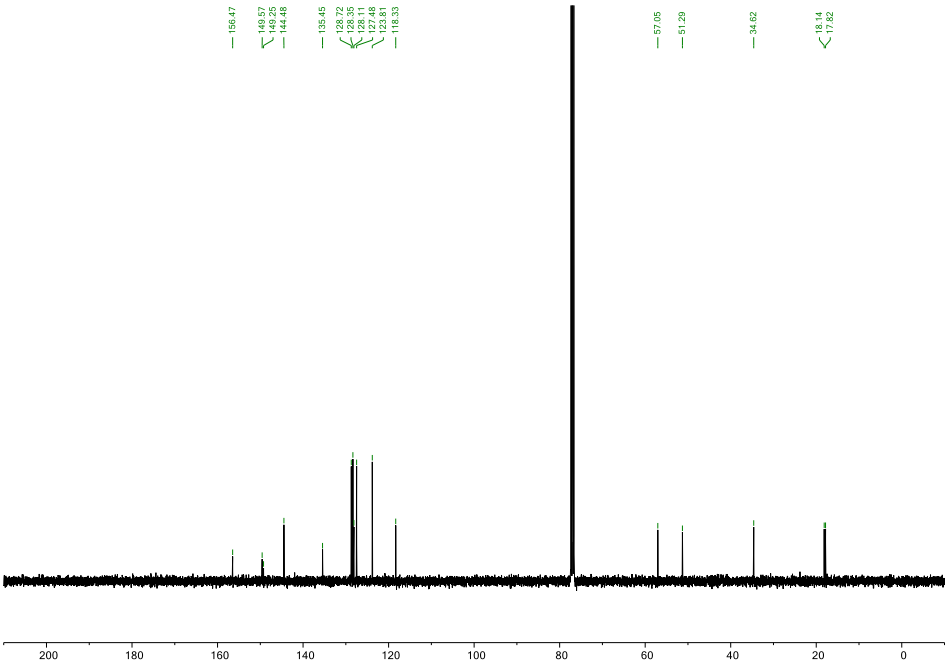


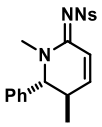
9g

^{1}H NMR, $CDCl_3$, 400 MHz



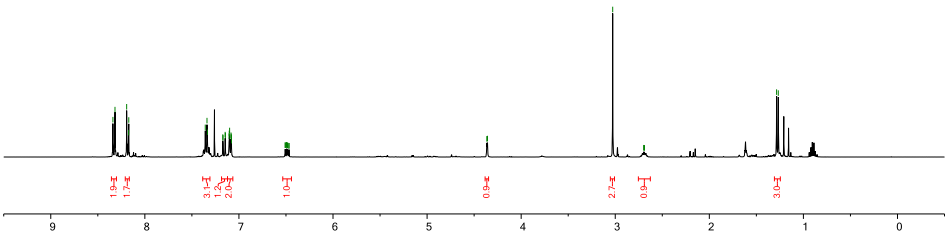
^{13}C NMR, $CDCl_3$, 101 MHz



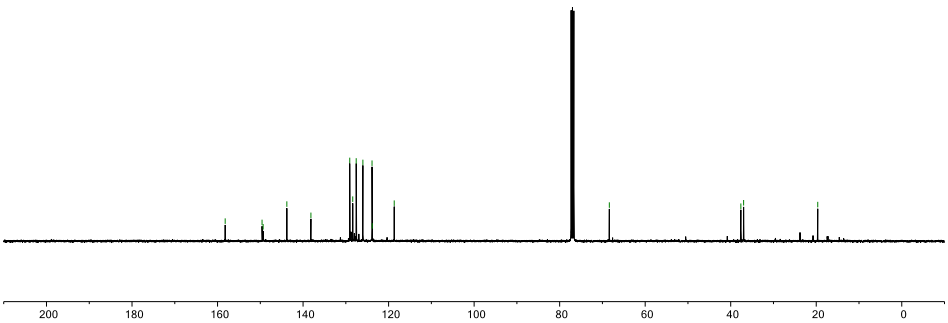


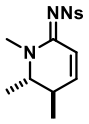
9h

^{1}H NMR, $CDCl_3$, 400 MHz



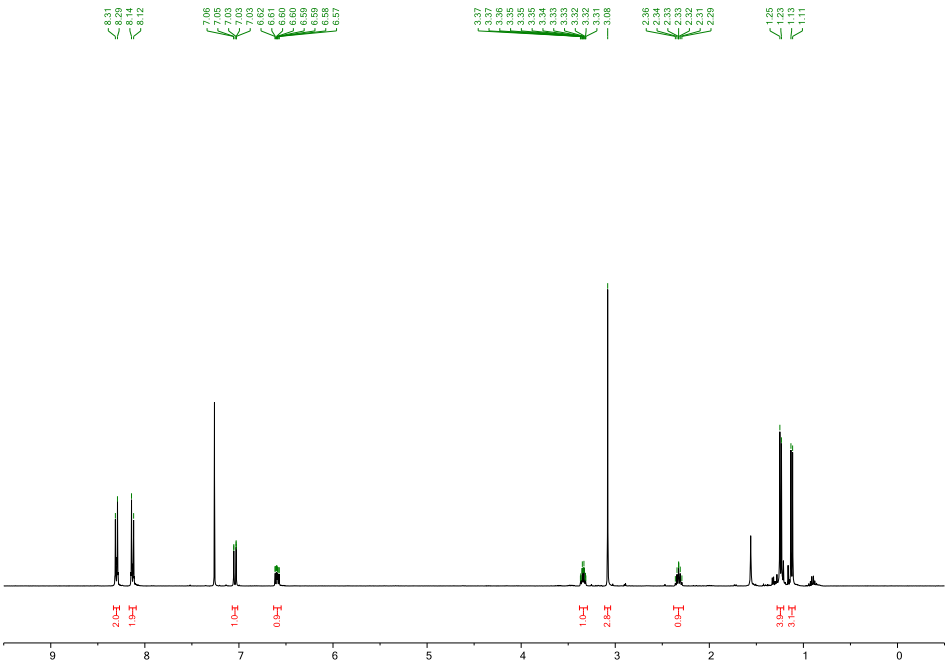
^{13}C NMR, $CDCl_3$, 101 MHz



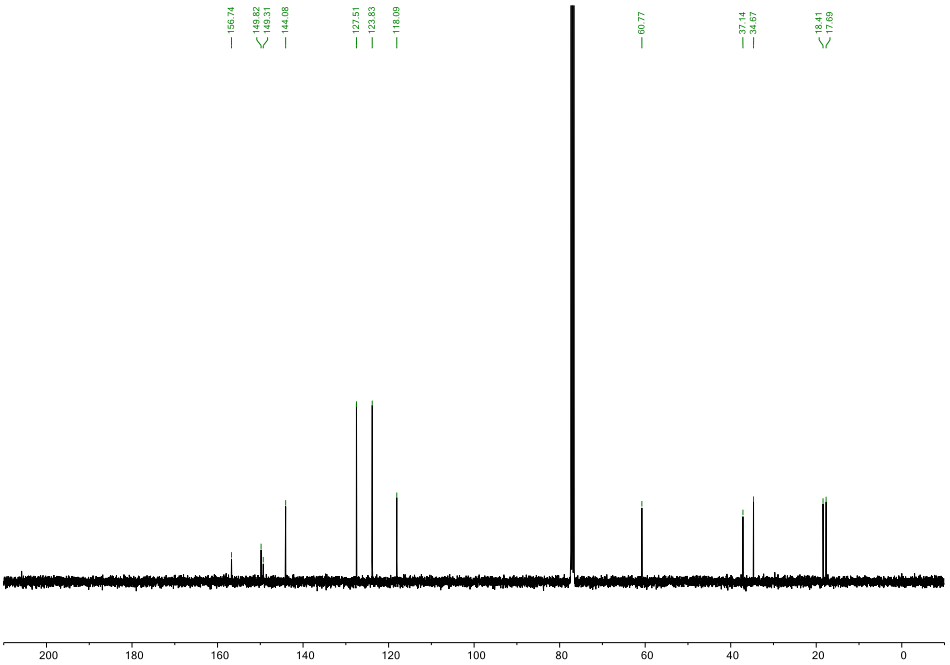


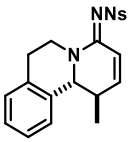
9i

^{1}H NMR, $CDCl_3$, 400 MHz



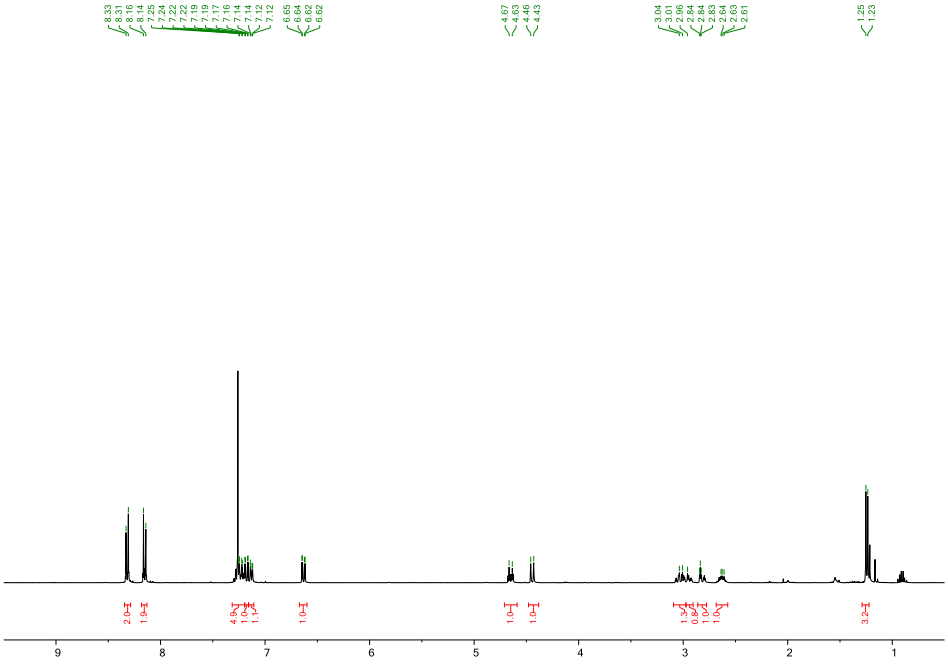
^{13}C NMR, $CDCl_3$, 101 MHz



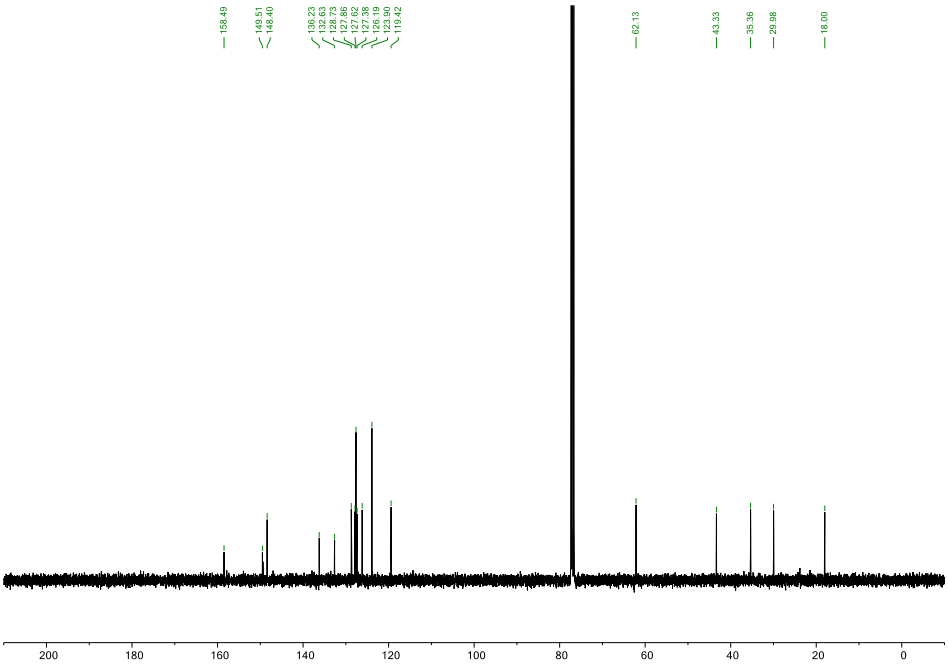


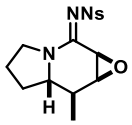
9j

^{1}H NMR, $CDCl_3$, 400 MHz



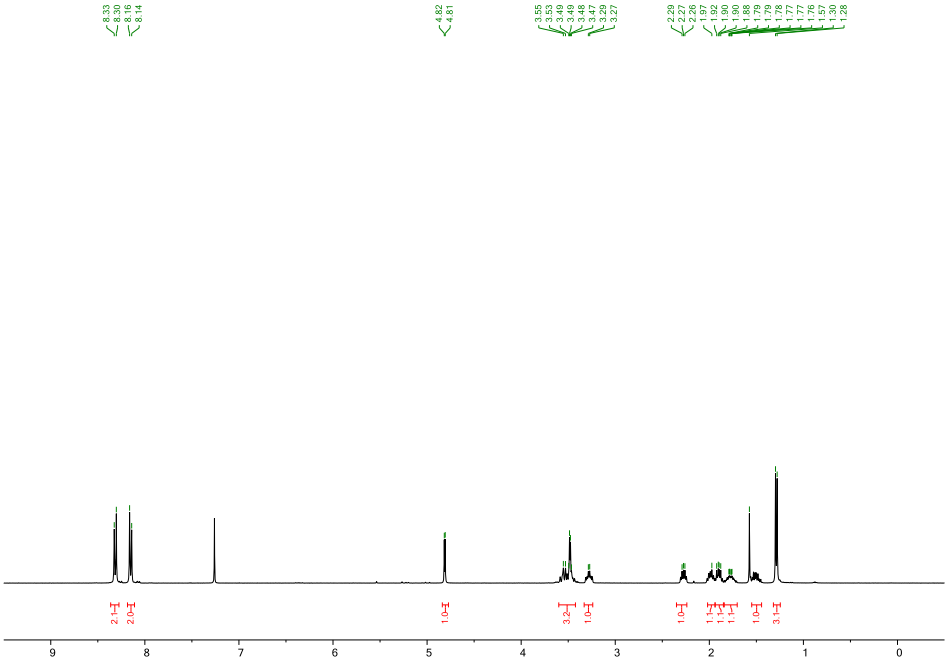
^{13}C NMR, $CDCl_3$, 101 MHz



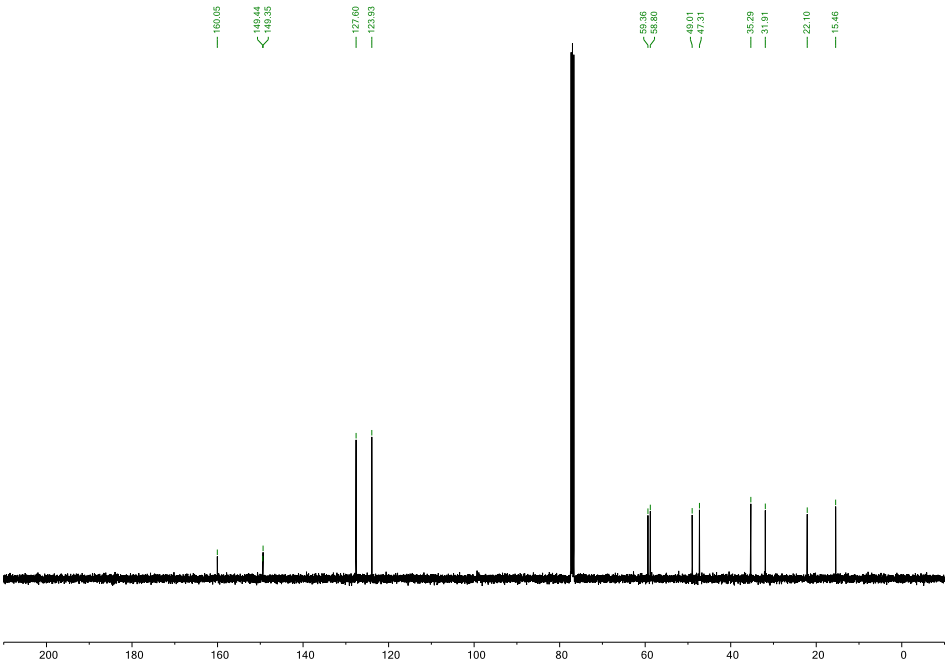


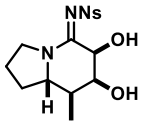
10d

^{1}H NMR, $CDCl_3$, 400 MHz



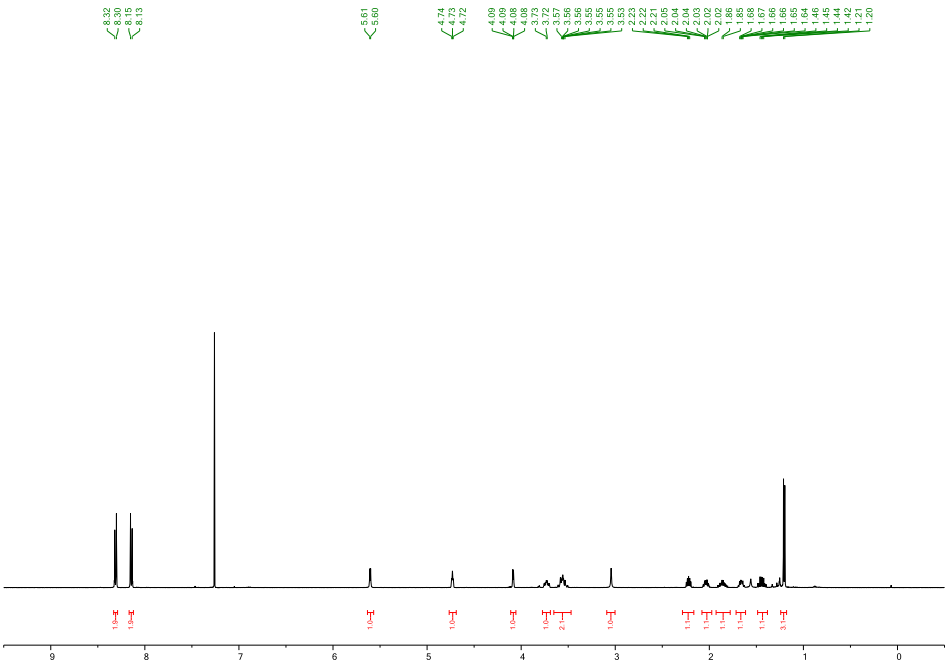
^{13}C NMR, $CDCl_3$, 101 MHz



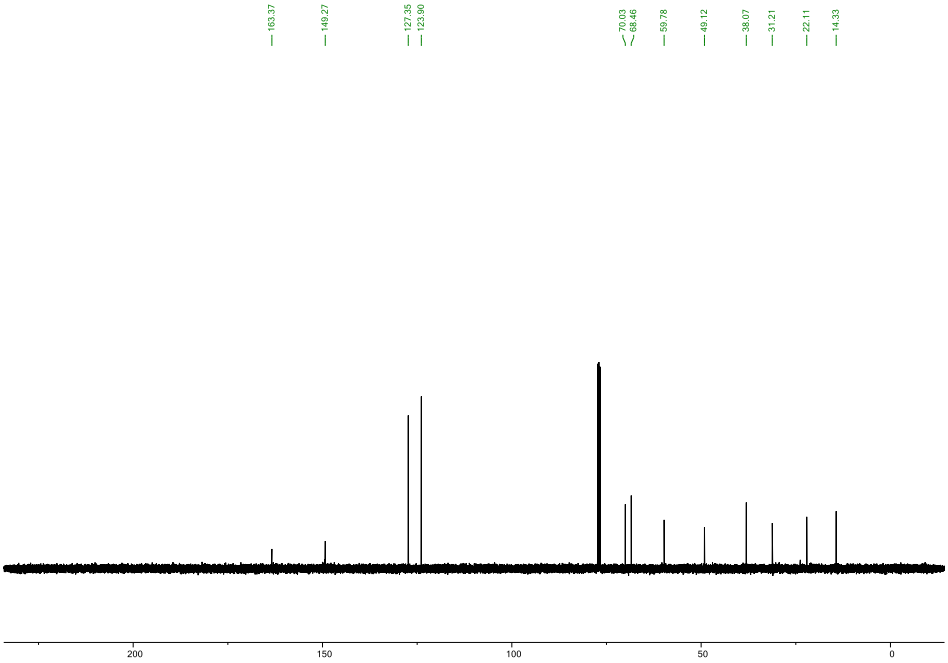


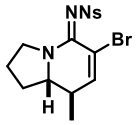
11d

^{1}H NMR, $CDCl_3$, 500 MHz



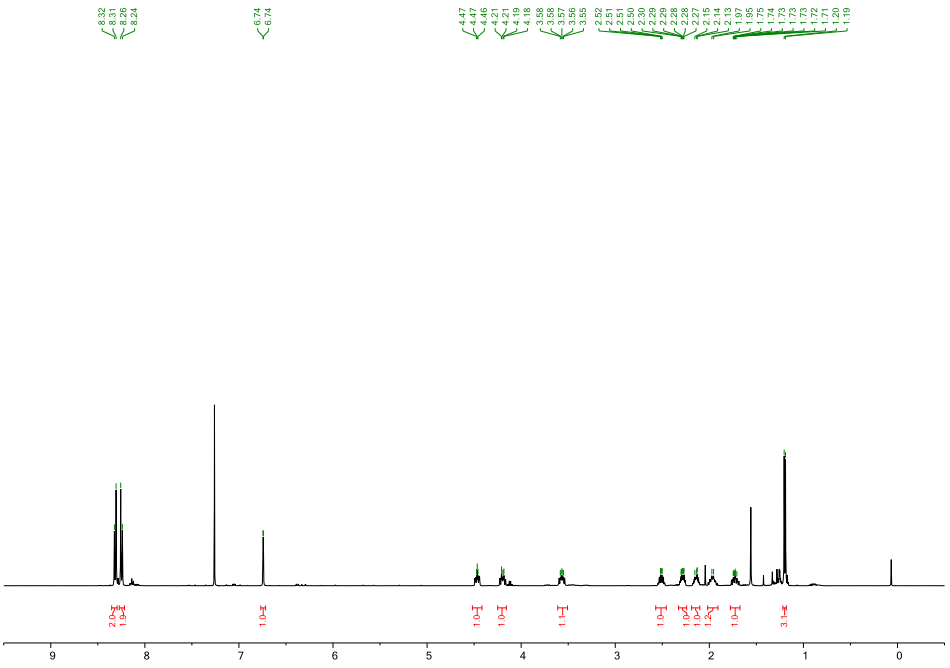
^{13}C NMR, $CDCl_3$, 101 MHz



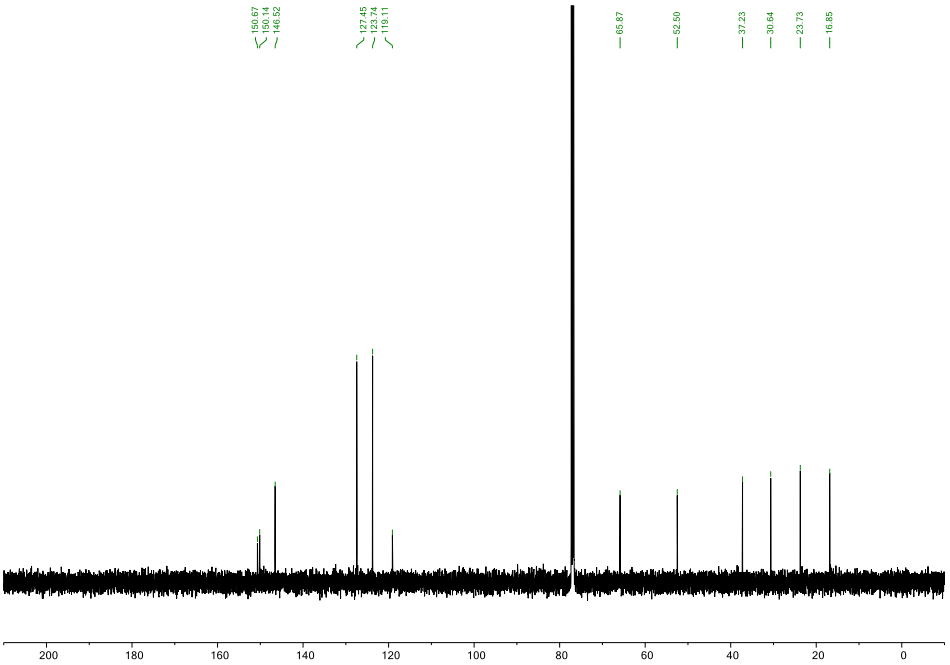


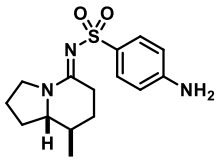
12d

^{1}H NMR, $CDCl_3$, 500 MHz



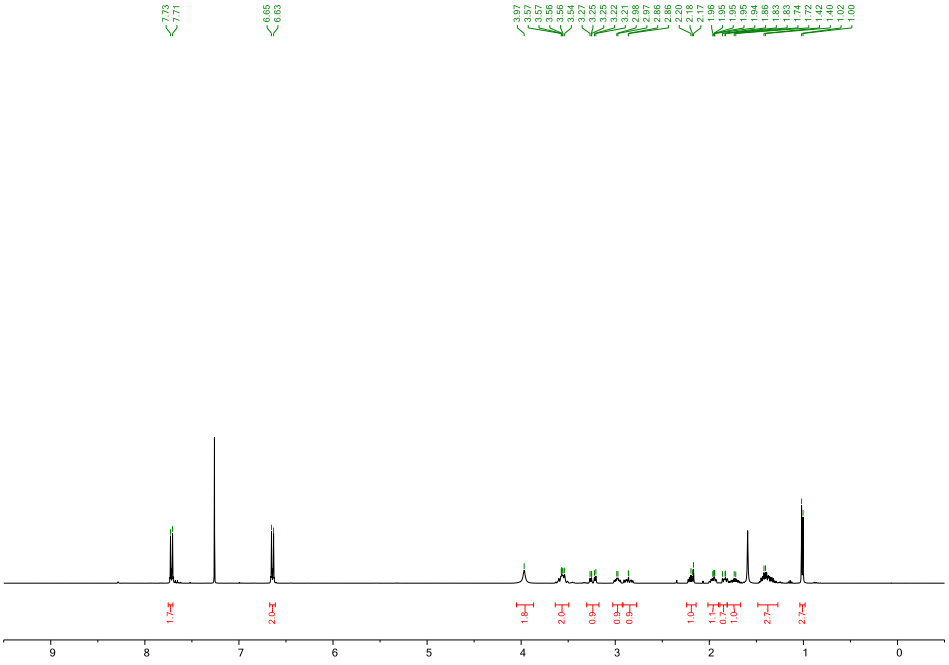
^{13}C NMR, $CDCl_3$, 126 MHz



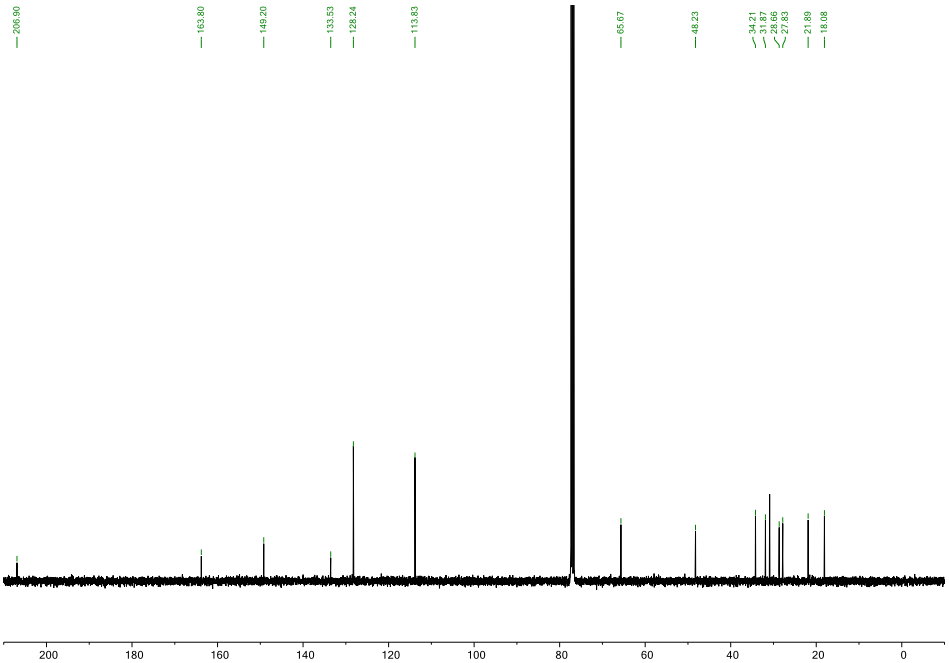


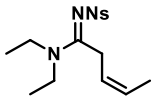
13d

^{1}H NMR, $CDCl_3$, 400 MHz



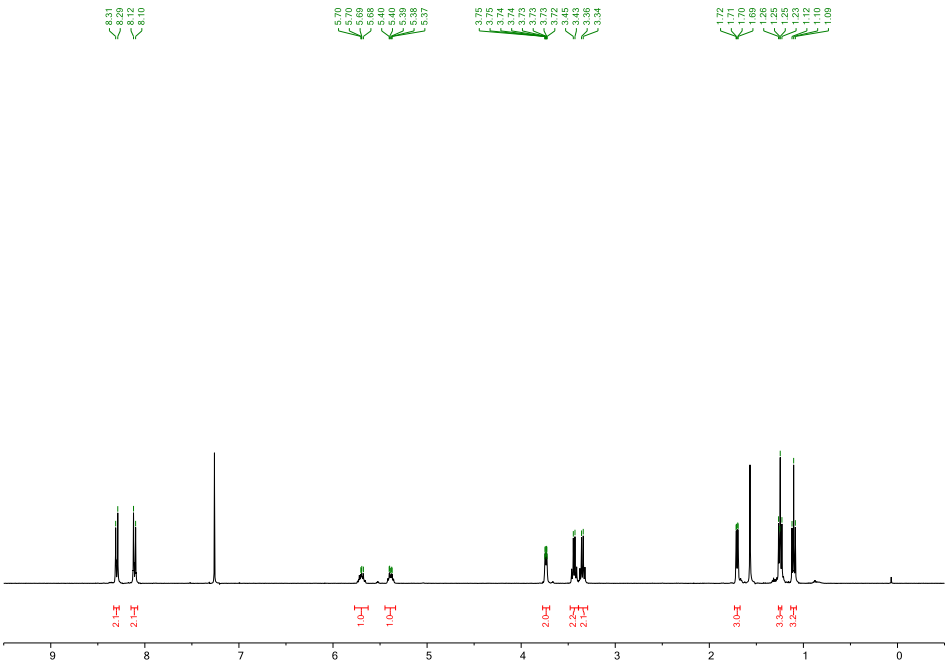
^{13}C NMR, $CDCl_3$, 101 MHz



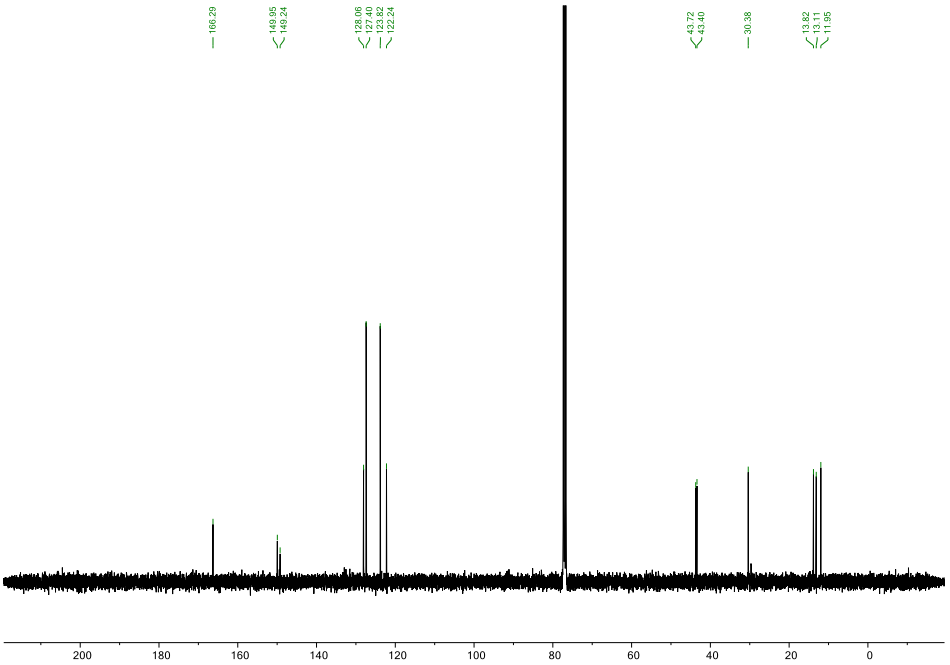


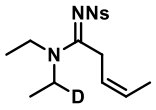
15a

^{1}H NMR, $CDCl_3$, 400 MHz



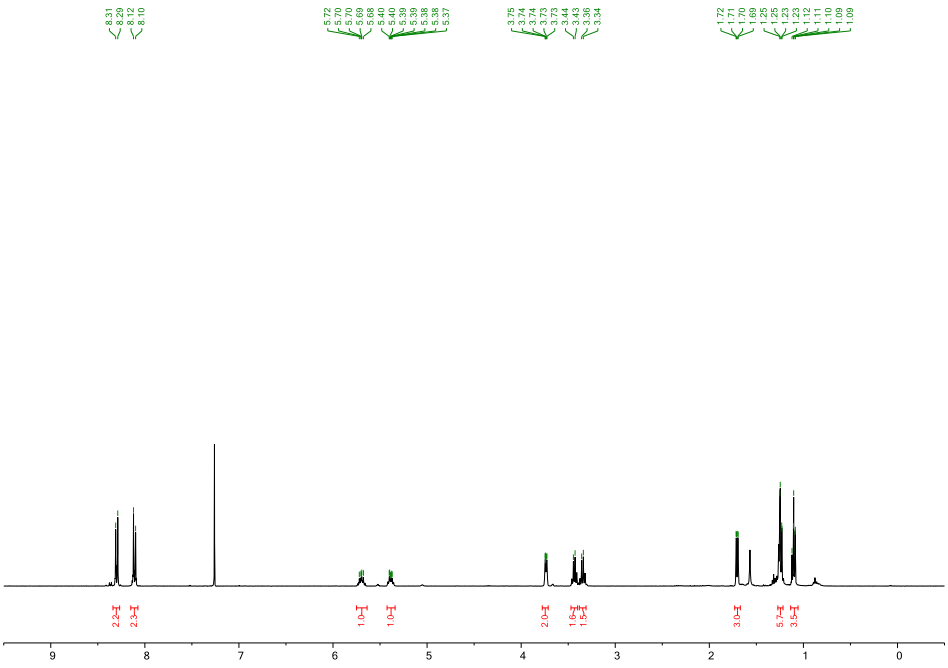
^{13}C NMR, $CDCl_3$, 101 MHz



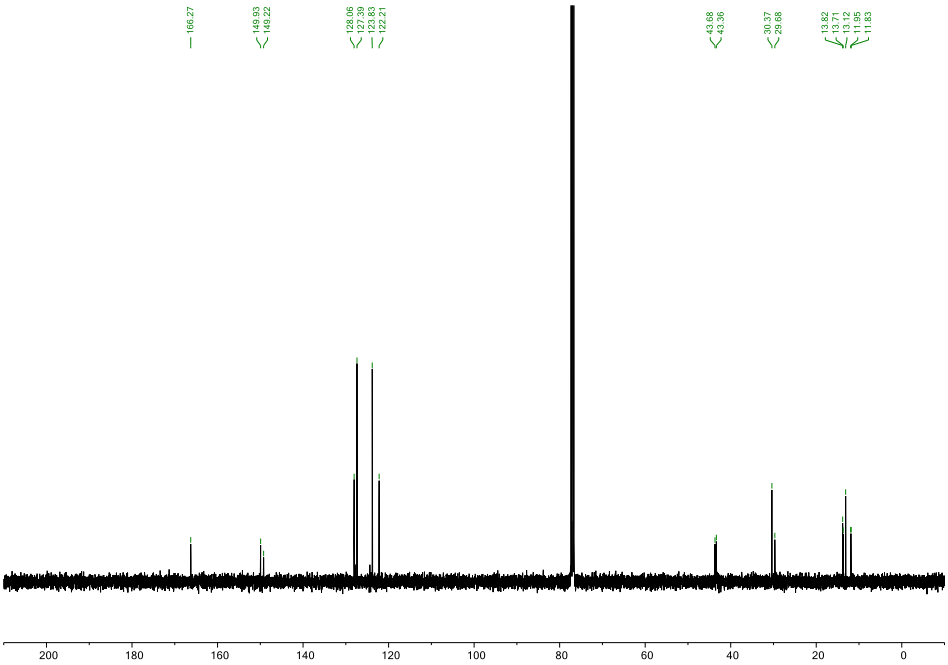


***d*-15a**

^{1}H NMR, $CDCl_3$, 400 MHz

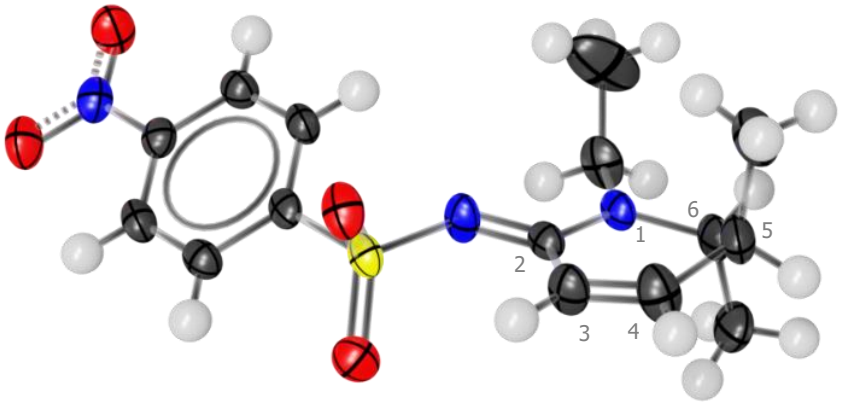


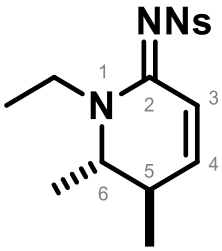
^{13}C NMR, $CDCl_3$, 101 MHz



Crystallography experimental details for 9a

Deposition number 2118194.





Structure of **9a**. Atomic displacement ellipsoids drawn at 50% probability level, hydrogen atoms drawn at 0.30 Å, minor disorder component omitted.

Crystal Data	
Chemical formula	$C_{15}H_{19}N_3O_4S$
M_r	337.39
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	150
a, b, c (Å)	7.4133 (13), 26.128 (5), 8.6554 (16)
β (°)	103.592 (7)
V (Å^3)	1629.5 (5)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.22
Crystal size (mm)	0.4 × 0.26 × 0.06

Data collection	
Diffractometer	Bruker D8 VENTURE
Absorption correction	Multi-scan *SADABS2016*/2 (Bruker,2016/2) was used for absorption correction. wR2(int) was 0.1305 before and 0.0737 after correction. The Ratio of minimum to maximum transmission is 0.7826. The λ/2 correction factor is Not present.
T_{min}, T_{max}	0.584, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	14811, 4057, 2841
R_{int}	0.059
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.668

Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.074, 0.169, 1.10
No. of reflections	4057
No. of parameters	246
No. of restraints	8
H-atom treatment	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.45, -0.35