Electronic Supplementary Information

Diastereoselective synthesis of pyrrolidine derivatives via a one-pot nitro-Mannich/hydroamination cascade using base and gold catalysis

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Contents

General Experimental

All non-aqueous reactions were conducted using oven-dried glassware under a positive pressure of dry nitrogen and were magnetically stirred unless otherwise stated. Yields refer to chromatographically purified and spectroscopically pure compounds, unless otherwise stated.

Solvents and Reagents

Concentration under reduced pressure was performed by rotary evaporation at 40 °C at the appropriate pressure. Reagents used were obtained from commercial suppliers or purified according to standard procedures. Petroleum ether (PE) refers to distilled light petroleum of fraction 30 - 40 °C. Anhydrous toluene, tetrahydrofuran, dichloromethane, diethyl ether and acetonitrile were dried by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic) columns. Dichloroethane and dimethyl sulfoxide were used as supplied. Deuterated solvents were used as supplied. Gold and silver catalysts are commercially available and were used as supplied. Silica gel treated with Et_3N was made by adding silica gel to a solution of petroleum ether (10% Et_3N), stirring at room temperature overnight and then concentrating under reduced pressure.

Chromatography

Reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F_{254} plates and visualised by fluorescence quenching under UV light. In addition, TLC plates were developed with potassium permanganate solution. Chromatographic purification was performed on VWR 60 silica gel 40-63 μm using technical grade solvents that were used as supplied.

Melting Points

Melting points were obtained on a Leica Galen III Hot-stage melting point apparatus and microscope and are reported uncorrected.

NMR Spectra

NMR spectra were recorded on a Bruker Spectrospin spectrometer operating at 400 MHz or 500 MHz (^{1}H acquisitions) and 100 MHz or 125 MHz (^{13}C acquisitions). Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard (e.g. Chloroform δ 7.27 ppm for ^{1}H and 77.0 ppm for ^{13}C). Coupling constants (*J*) are reported in hertz (Hz).

Data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, dd = doublet of doublets, ddd = doublet of doublets of doublets, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets, tq = triplet of quartets, qt = quartet of triplets, m = multiplet, br = broad, coupling constants in Hz, integration, assignment. The NMR spectra are reported as how the spectra are observed and do not take into account the theoretical NMR splitting. Two-dimensional spectroscopy (COSY, HMQC and HMBC) was used to assist in the assignment, which is not reported.

Mass Spectra

Low-resolution mass spectra (ESI) were recorded on a Waters LCT Premier XE Micromass mass spectrometer. High-resolution mass spectra (ESI) were recorded on Bruker Daltonics MicroTOF mass spectrometer. High-resolution mass spectra (FI) were recorded on a Bruker FT-ICR Apex III mass spectrometer. This method generates [M^+] ions, however the computer software reports the exact mass using [M], not [M^+].

Infrared Spectra

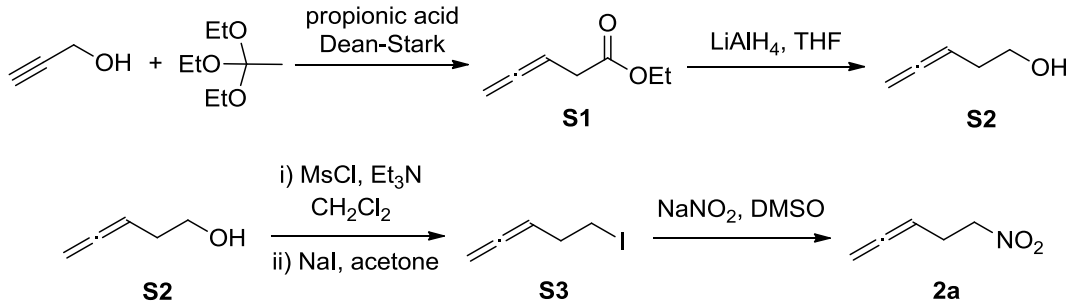
Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer equipped with a Diamond ATR module as a thin film. Only selected maximum absorbances are reported.

Synthesis and Characterisation of Starting Materials 1a-n and 2a-b

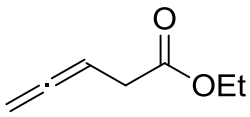
Synthesis of starting aldimines 1a-n

The starting *p*-methyl(phenylmethylene)benzenesulfonamide aldimines **1a** and **1d-n** were synthesised by condensation of the corresponding aldehyde with *p*-toluenesulfonamide using tetraethyl orthosilicate with azeotropic removal of ethanol.[1] The starting *p*-methyl(phenylmethylene)benzenesulfonamide aldimines **1b** and **1c** were synthesised by condensation of the corresponding aldehyde with *p*-toluenesulfonamide using $TiCl_4$ and Et_3N in CH_2Cl_2.[2]

Synthesis of nitro-allene 2a



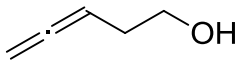
Synthesis and characterisation of ethyl penta-3,4-dienoate (S1)



Prepared according to a modified literature procedure described by Tamaru.[3] To a two-necked round bottom flask equipped with a Dean-Stark trap, was added propargyl alcohol (8.69 g, 155 mmol, 9.02 mL) and triethyl orthoacetate (53.0 g, 327 mmol, 59.9 mL). The resulting mixture was heated to 100 °C and then propionic acid (200 mg, 2.70 mmol, 201 µL) was added. The resulting mixture was stirred vigorously at 150 °C with removal of EtOH. After distillation of EtOH had ceased, propargyl alcohol (4.34 g, 77.5 mmol, 4.51 mL) was added dropwise and heating continued at 150 °C for a further 1 h. Then, two portions of propionic acid (200 mg, 2.70 mmol, 201 µL) were added into the reaction mixture at 30 min intervals until EtOH distillation had ceased. The reaction mixture was cooled to RT, quenched with 2M HCl (10 mL) and extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure to yield **S1** (17.2 g, 59%) as a yellow oil. The crude product was used

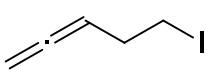
in the next step without further purification. **TLC**: R_f = 0.35 (PE/Et_2O 19:1, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 5.28 (qu, *J* = 7.0 Hz, 1H, CH_2=C=C**H**), 4.77 (dt, *J* = 7.0, 3.0 Hz, 2H, C**H_2**=C=CH), 4.17 (q, *J* = 7.0 Hz, 2H, CO_2C**H_2**CH_3), 3.05 (dt, *J* = 7.0, 3.0 Hz, 2H, C**H_2**CO_2), 1.28 (t, *J* = 7.0 Hz, 3H, CO_2CH_2C**H_3**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 209.3 (CH_2=**C**=CH), 171.4 (**C**=O), 83.5 (CH_2=C=**C**H), 75.8 (**C**H_2=C=CH), 60.8 (CO_2**C**H_2CH_3), 34.2 (**C**H_2CO_2), 14.2 (CO_2CH_2**C**H_3). Data was in accordance with that reported in the literature.[3]

Synthesis and characterisation of penta-3,4-dien-1-ol (S2)



Prepared according to a modified literature procedure described by Tamaru.[3] A solution of **S1** (17.2 g, 136 mmol) in THF (50 mL) at RT was added dropwise to a suspension of $LiAlH_4$ (5.17 g, 136 mmol) in THF (150 mL) at 0 °C. The resulting mixture was allowed to warm to RT and then stirred for 1 h. The reaction mixture was diluted with THF (100 mL) and quenched with a mixture of THF/H_2O (3:1) until a white solid formed. The residual solids were removed by filtration washing with THF (50 mL). The filtrate was dried over Na_2SO_4, filtered and concentrated under reduced pressure to yield **S2** (7.32 g, 64%) as a colourless oil. The crude product was used in the next step without further purification. **TLC**: R_f = 0.28 (PE/EtOAc 4:1, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 5.12 (qu, *J* = 6.5 Hz, 1H, CH_2=C=C**H**), 4.72 (dt, *J* = 6.5, 3.0 Hz, 2H, C**H_2**=C=CH), 3.70 (t, *J* = 6.5 Hz, 2H, CH_2C**H_2**OH), 2.26 (dtt, *J* = 6.5, 6.5, 3.0 Hz, 2H, C**H_2**CH_2OH), 1.88 (s, 1H, O**H**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 209.0 (CH_2=**C**=CH), 86.4 (CH_2=C=**C**H), 75.2 (**C**H_2=C=CH), 61.9 (CH_2**C**H_2OH), 31.6 (**C**H_2CH_2OH). Data was in accordance with that reported in the literature.[3]

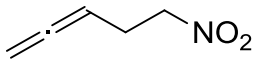
Synthesis and characterisation of 5-iodopenta-1,2-diene (S3)



Prepared according to a literature procedure described by Dauben.[4] To a stirred solution of **S2** (7.30 g, 86.8 mmol) and Et_3N (12.3 g, 122 mmol, 16.9 mL) in CH_2Cl_2 (180 mL) at –30 °C was added MsCl (9.94 g, 86.8 mmol, 6.72 mL). The resulting mixture was stirred at –10 °C for 1.5 h. The reaction was quenched with sat. aq. $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried over Na_2SO_4, filtered and

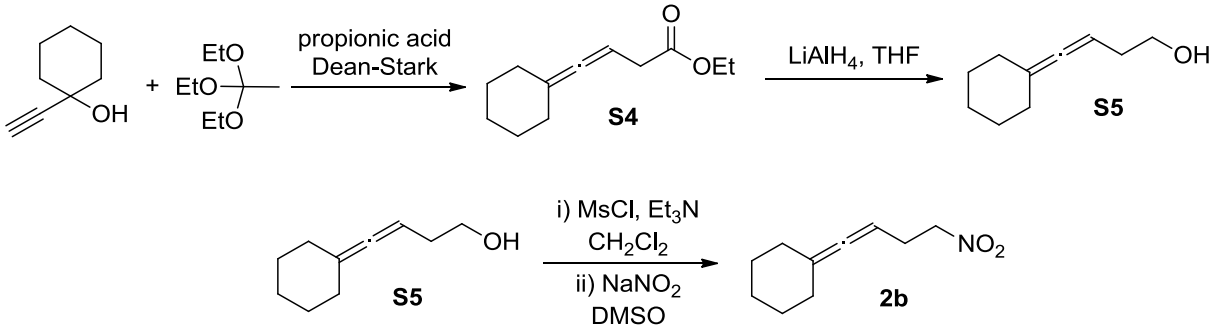
concentrated under reduced pressure to yield the crude mesylate as a yellow oil. The crude mesylate was dissolved in acetone (250 mL) at RT and NaI (32.6 g, 217 mmol) was added portionwise. The resulting mixture was heated to 70 °C for 12 h. The reaction mixture was cooled to RT, diluted with Et_2O (300 mL) and washed with sat. aq. Na_2SO_3 (100 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under a stream of nitrogen to yield **S3** (12.4 g, 73%) as a yellow oil. The crude product was used in the next step without further purification. **TLC**: R_f = 0.69 (PE 100%, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 5.14 (qu, *J* = 6.5 Hz, 1H, CH_2=C=C**H**), 4.75 (dt, *J* = 6.5, 3.0 Hz, 2H, C**H$_2$**=C=CH), 3.21 (t, *J* = 7.0 Hz, 2H, CH_2C**H$_2$**I), 2.57 (dtt, *J* = 7.0, 6.5, 3.0 Hz, 2H, C**H$_2$**CH_2I); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 208.8 (CH_2=**C**=CH), 89.5 (CH_2=C=**C**H), 76.2 (**C**H_2=C=CH), 32.3 (**C**H_2CH_2I), 4.5 (CH_2**C**H_2I). Data was in accordance with that reported in the literature.[4]

Synthesis and characterisation of 5-nitropenta-1,2-diene (2a)

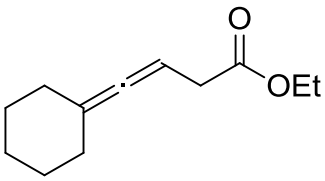


To a stirred solution of $NaNO_2$ (5.28 g, 76.4 mmol) in DMSO (80 mL) with a water bath at RT was added a solution of **S3** (12.4 g, 63.7 mmol) in DMSO (40 mL) dropwise. The resulting mixture was stirred at RT for 1.5 h. The reaction mixture was diluted with ice water (100 mL) and extracted with Et_2O (6 × 100 mL). The combined organic extracts were washed with ice water (200 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by flash column chromatography eluting with PE/Et_2O (19:1) yielded **2a** (3.85 g, 53%) as a colourless oil. **TLC**: R_f = 0.38 (PE/Et_2O 19:1, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 5.15 (qu, *J* = 6.5 Hz, 1H, CH_2=C=C**H**), 4.81 (dt, *J* = 6.5, 3.5 Hz, 2H, C**H$_2$**=C=CH), 4.47 (t, *J* = 7.0 Hz, 2H, CH_2C**H$_2$**NO_2), 2.69 (dtt, *J* = 7.0, 6.5, 3.5 Hz, 2H, C**H$_2$**CH_2NO_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 208.6 (CH_2=**C**=CH), 85.0 (CH_2=C=**C**H), 77.1 (**C**H_2=C=CH), 74.2 (CH_2**C**H_2NO_2), 25.5 (**C**$H_2CH_2NO_2$); **IR** (film/cm^{-1}): ν_{max} 2923, 1957, 1548, 1429, 1379, 1194, 1067, 851; **HRMS** (FI): exact mass calculated for $C_5H_7NO_2$ [(M – HNO_2)], 66.0470; found 66.0434.

Synthesis of nitro-allene 2b

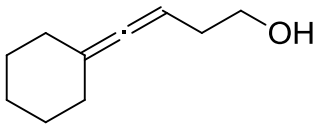


Synthesis and characterisation of ethyl 4-cyclohexylidenebut-3-enoate (S4)



Prepared in an analogous manner to compound **S1** on a 20.0 mmol scale using 1-ethynyl-1-cyclohexanol and triethyl orthoacetate, compound **S4** (6.71 g, 86%) was obtained as a yellow oil. The crude product was used in the next step without further purification. **TLC**: R_f = 0.55 (PE/Et_2O 19:1, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 5.09 (tt, *J* = 7.0, 2.0 Hz, 1H, C=C=C**H**), 4.15 (q, *J* = 7.0 Hz, 2H, $CO_2C\mathbf{H_2}CH_3$), 2.98 (d, *J* = 7.0 Hz, 1H, $C\mathbf{H_2}CO_2$), 2.15 - 2.06 (m, 4H, 2 × cyclohexyl $C\mathbf{H_2}$), 1.65 - 1.46 (m, 6H, 3 × cyclohexyl $C\mathbf{H_2}$), 1.27 (t, *J* = 7.0 Hz, 3H, $CO_2CH_2C\mathbf{H_3}$); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 199.6 (C=**C**=CH), 172.0 (**C**=O), 103.5 (**C**=C=CH), 81.7 (C=C=**C**H), 60.6 ($CO_2\mathbf{C}H_2CH_3$), 35.6 ($\mathbf{C}H_2CO_2$), 31.3 (2 × cyclohexyl $\mathbf{C}H_2$), 27.3 (2 × cyclohexyl $\mathbf{C}H_2$), 26.0 (cyclohexyl $\mathbf{C}H_2$), 14.2 ($CO_2CH_2\mathbf{C}H_3$). Data was in accordance with that reported in the literature.[5]

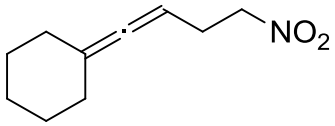
Synthesis and characterisation of 4-cyclohexylidenebut-3-en-1-ol (S5)



Prepared in an analogous manner to compound **S2** on a 34.0 mmol scale, compound **S5** (4.28 g, 83%) was obtained as a pale yellow oil after purification by flash column chromatography eluting with PE/EtOAc (4:1). **TLC**: R_f = 0.52 (PE/EtOAc 4:1, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 4.96 (tt, *J* = 6.5, 2.0 Hz, 1H, C=C=C**H**), 3.68 (t, *J* = 6.5 Hz, 2H, $C\mathbf{H_2}OH$), 2.22 (q, *J* = 6.5 Hz, 2H, $C\mathbf{H_2}CH_2OH$), 2.16 - 2.05 (m, 4H, 2 × cyclohexyl $C\mathbf{H_2}$), 1.65 - 1.45 (m, 6H, 3

× cyclohexyl C**H$_2$**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 199.0 (C=**C**=CH), 103.2 (**C**=C=CH), 84.9 (C=C=**C**H), 62.0 (CH_2**C**H_2OH), 32.5 (**C**H_2CH_2OH), 31.7 (2 × cyclohexyl **C**H_2), 27.4 (2 × cyclohexyl **C**H_2), 26.0 (cyclohexyl **C**H_2). Data was in accordance with that reported in the literature.[5]

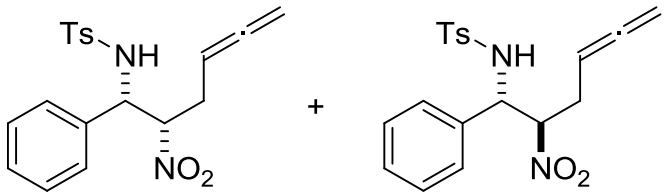
Synthesis and characterisation of (4-nitrobut-1-en-1-ylidene)cyclohexane (2b)



To a stirred solution of **S5** (2.28 g, 15.0 mmol) and Et_3N (2.13 g, 21.0 mmol, 2.92 mL) in CH_2Cl_2 (25 mL) at –30 °C was added MsCl (1.72 g, 15.0 mmol, 1.16 mL). The resulting mixture was stirred at –10 °C for 1.5 h. The reaction was quenched with sat. aq. $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to yield the crude mesylate as a yellow oil. The crude mesylate was added dropwise to a stirred solution of $NaNO_2$ (1.24 g, 18.0 mmol) in DMSO (15 mL) at RT maintained using a water bath and the resulting mixture was stirred at RT for 48 h. The reaction mixture was diluted with ice water (20 mL) and extracted with Et_2O (6 × 30 mL). The combined organic extracts were washed with ice water (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by flash column chromatography eluting with PE/Et_2O (98:2) yielded **2b** (531 mg, 20%) as a pale yellow oil. **TLC**: R_f = 0.22 (PE/Et_2O 98:2, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 5.00 (tt, *J* = 6.0, 2.0 Hz, 1H, C=C=C**H**), 4.45 (t, *J* = 6.5 Hz, 2H, CH_2C**H$_2$**NO_2), 2.69 - 2.61 (m, 2H, C**H$_2$**CH_2NO_2), 2.12 - 2.04 (m, 4H, 2 × cyclohexyl C**H$_2$**), 1.64 - 1.45 (m, 6H, 3 × cyclohexyl C**H$_2$**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 198.5 (C=**C**=CH), 105.4 (**C**=C=CH), 83.5 (C=C=**C**H), 74.4 (CH_2**C**H_2NO_2), 31.3 (2 × cyclohexyl **C**H_2), 27.2 (2 × cyclohexyl **C**H_2), 26.5 (**C**$H_2CH_2NO_2$), 25.9 (cyclohexyl **C**H_2); **IR** (film/cm^{-1}): ν_{max} 2927, 2854, 1551, 1433, 1375, 1341, 853, 768; **HRMS** (ESI): exact mass calculated for $C_{10}H_{15}NO_2$ [M], 181.1103; found 181.1108.

Synthesis and Characterisation of β-nitroamine 3

Synthesis and characterisation of *rac*-4-methyl-*N*-[(1*S*,2*S*)-2-nitro-1-phenylhexa-4,5-dien-1-yl]benzenesulfonamide and *rac*-4-methyl-*N*-[(1*S*,2*R*)-2-nitro-1-phenylhexa-4,5-dien-1-yl]benzenesulfonamide (3)

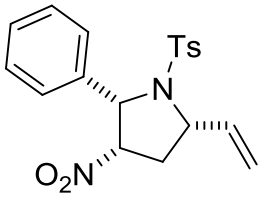


3

To a stirred mixture of aldimine **1a** (764 mg, 2.94 mmol) and nitro-allene **2a** (500 mg, 4.42 mmol) in PhMe (29.0 mL) at RT was added PS-BEMP (155 mg, 0.294 mmol). The resulting mixture was stirred at RT for 22 h. The reaction mixture was concentrated under a stream of nitrogen and the resulting solid was purified by flash column chromatography eluting with PE/EtOAc (6:1) to yield **3** (963 mg, 88%, mixture of diastereomers, dr 83:17) as an off-white solid. **TLC**: R_f = 0.19 (PE/EtOAc 6:1, UV, $KMnO_4$); **Melting Point**: 126 - 129 °C; ***Major diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.54 - 7.47 (m, *J* = 8.0 Hz, 2H, Ar**H**), 7.22 - 7.03 (m, 5H, Ar**H**), 7.02 - 6.96 (m, 2H, Ar**H**), 6.26 (d, *J* = 10.0 Hz, 1H, N**H**), 5.09 - 4.92 (m, 1H, C**H**=C=CH_2), 4.90 - 4.68 (m, 4H, C**H**N, C**H**NO_2 and CH=C=C**H$_2$**), 2.67 - 2.54 (m, 1H, C**H**H′), 2.37 - 2.25 (m, 4H, ArC**H$_3$** and CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 209.2 (CH=**C**=CH_2), 143.4 (Ar**C**), 136.8 (Ar**C**), 135.1 (Ar**C**), 129.3 (2 × Ar**C**H), 128.9 (2 × Ar**C**H), 128.5 (Ar**C**H), 126.9 (2 × Ar**C**H), 126.5 (2 × Ar**C**H), 91.3 (**C**HNO_2), 83.7 (**C**H=C=CH_2), 76.8 (CH=C=**C**H_2), 59.2 (**C**HN), 30.0 (**C**H_2), 21.4 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.85 (d, *J* = 8.5 Hz, 2H, Ar**H**), 7.31 (d, *J* = 8.5 Hz, 2H, Ar**H**), 6.95 - 6.90 (m, 2H, Ar**H**), 6.06 (d, *J* = 9.5 Hz, 1H, N**H**), 5.08 - 4.99 (m, 1H, C**H**=C=CH_2), 2.82 - 2.68 (m, 2H, C**HH′**), 2.33 (s, 3H, ArC**H$_3$**); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): 209.1 (CH=**C**=CH_2), 143.7 (Ar**C**), 136.5 (Ar**C**), 134.7 (Ar**C**), 129.5 (2 × Ar**C**H), 128.7 (2 × Ar**C**H), 128.6 (Ar**C**H), 127.0 (2 × Ar**C**H), 126.8 (2 × Ar**C**H), 90.6 (**C**HNO_2), 84.2 (**C**H=C=CH_2), 77.2 (CH=C=**C**H_2), 59.4 (**C**HN), 28.9 (**C**H_2), 21.4 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 3265, 2923, 1956, 1598, 1554, 1457, 1370, 1327, 1307, 1158, 1089, 910, 850, 813, 771; **MS** (ESI): *m/z* 395.1 [$(M + Na)^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{20}N_2NaO_4S$ [$(M + Na)^+$], 395.1036; found 395.1031.

Synthesis and Characterisation of Pyrrolidine 4

Synthesis and characterisation of *rac*-(2*S*,3*S*,5*S*)-1-[(4-methylphenyl)sulfonyl]-3-nitro-2-phenyl-5-vinylpyrrolidine (4)



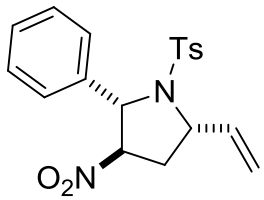
To a stirred mixture of aldimine **1a** (51.9 mg, 0.200 mmol) and nitro-allene **2a** (33.9 mg, 0.300 mmol) in PhMe (2.0 mL) at RT in a sealable vial was added KO^{t}Bu (1.1 mg, 0.010 mmol). The resulting mixture was stirred at RT for the 18 h. The reaction mixture was diluted with DCE (6.0 mL), then diphenylphosphate (10.0 mg, 0.040 mmol), Au(PPh$_3$)Cl (9.9 mg, 0.020 mmol) and AgSbF$_6$ (13.7 mg, 0.040 mmol) were added and the resulting mixture was heated to 70 °C for 4 h. The reaction mixture was filtered through a plug of celite and the filtrate was concentrated under a stream of nitrogen. The resulting solid was purified by recrystallisation from CH_2Cl_2/Et_2O to yield **4** (28 mg, 38%, dr >98:2) as a pale brown solid. **TLC**: R_f = 0.24 (PE/EtOAc 6:1, UV, KMnO4); **Melting Point**: 172 - 174 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.55 (d, *J* = 8.5 Hz, 2H, Ar**H**), 7.34 - 7.16 (m, 7H, Ar**H**), 6.12 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.50 (d, *J* = 9.0 Hz, 1H, C**H**N), 5.41 (d, *J* = 17.0 Hz, 1H, CH=CH$_{cis}$**H**$_{trans}$), 5.32 (d, *J* = 10.0 Hz, 1H, CH=C**H**$_{cis}$H$_{trans}$), 4.96 (ddd, *J* = 11.5, 8.5, 6.5 Hz, 1H, C**H**NO_2), 4.40 - 4.30 (m, 1H, N**C**HCH=CH_2), 2.78 - 2.65 (m, 1H, C**H**H′), 2.51 - 2.37 (m, 4H, ArC**H$_3$** and CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 144.1 (Ar**C**), 136.8 (**C**H=CH_2), 135.3 (Ar**C**), 134.8 (Ar**C**), 129.6 (2 × Ar**C**H), 128.9 (Ar**C**H), 128.4 (2 × Ar**C**H), 127.7 (2 × Ar**C**H), 127.5 (2 × Ar**C**H), 118.4 (CH=**C**H_2), 84.3 (**C**HNO_2), 64.9 (**C**HN), 60.5 (N**C**HCH=CH_2), 33.0 (**C**H_2), 21.5 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 2919, 1598, 1549, 1375, 1347, 1309, 1163, 1090, 1008, 971, 927, 814, 707, 662; **MS** (ESI): *m/z* 395.0 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{20}N_2NaO_4S$ [(M + Na)$^+$], 395.1036; found 395.1034.

Synthesis and Characterisation of Pyrrolidines 5a-o

General procedure for nitro-Mannich/hydroamination cascade:

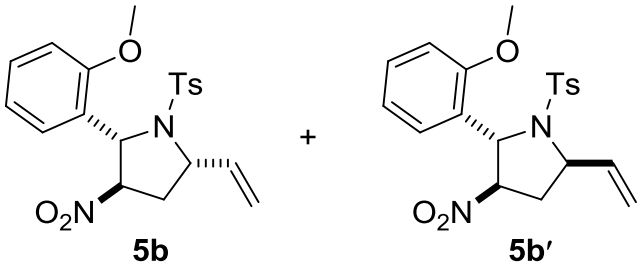
To a stirred mixture of the corresponding aldimine **1a-n** (0.200 mmol) and the corresponding nitro-allene **2a-b** (0.300 mmol) in PhMe (2.0 mL) at RT in a sealable vial was added KO^{t}Bu (1.1 mg, 0.010 mmol). The resulting mixture was stirred at RT for the indicated time. The reaction mixture was diluted with DCE (6.0 mL), then diphenylphosphate (10.0 mg, 0.040 mmol), Au(PPh$_3$)Cl (9.9 mg, 0.020 mmol) and AgSbF$_6$ (13.7 mg, 0.040 mmol) were added. The resulting mixture was heated to 70 °C for the indicated time. Silica gel (treated with Et$_3$N, 150 mg) was added and the resulting mixture was stirred at 70 °C for the indicated time. The reaction mixture was concentrated under a stream of nitrogen and the residue was purified by flash column chromatography to yield the desired products **5a-o**.

Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-1-[(4-methylphenyl)sulfonyl]-3-nitro-2-phenyl-5-vinylpyrrolidine (5a)



Prepared according to the general procedure, compound **5a** (60 mg, 81%) was obtained as a white solid after purification by flash column chromatography, eluting with PE/EtOAc (5:1). **TLC**: R_f = 0.45 (PE/EtOAc 5:1, UV, KMnO$_4$); **Melting Point**: 160 - 161 °C; **^{1}H NMR** (400 MHz, CDCl$_3$): δ_H 7.66 (d, *J* = 8.5 Hz, 2H, Ar**H**), 7.49 - 7.29 (m, 7H, Ar**H**), 6.10 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH$_2$), 5.60 (s, 1H, C**H**N), 5.38 (d, *J* = 17.0 Hz, 1H, CH=CH$_{cis}$**H**$_{\boldsymbol{trans}}$), 5.33 (d, *J* = 10.0 Hz, 1H, CH=C**H**$_{\boldsymbol{cis}}$H$_{trans}$), 4.75 - 4.69 (m, 1H, C**H**NO$_2$), 4.40 - 4.31 (m, 1H, NC**H**CH=CH$_2$), 2.61 (dd, *J* = 14.5, 7.0 Hz, 1H, C**H**H′), 2.46 (s, 3H, ArC**H$_3$**) 2.24 - 2.12 (m, 1H, CH**H′**); **^{13}C NMR** (100 MHz, CDCl$_3$): δ_C 144.2 (Ar**C**), 138.9 (Ar**C**), 137.4 (**C**H=CH$_2$), 134.1 (Ar**C**), 129.6 (2 × Ar**C**H), 128.9 (2 × Ar**C**H), 128.4 (Ar**C**H), 127.8 (2 × Ar**C**H), 126.1 (2 × Ar**C**H), 117.9 (CH=**C**H$_2$), 90.1 (**C**HNO$_2$), 68.9 (**C**HN), 62.1 (N**C**HCH=CH$_2$), 34.9 (**C**H$_2$), 21.6 (Ar**C**H$_3$); **IR** (film/cm^{-1}): ν_{max} 2918, 1549, 1344, 1313, 1162, 1129, 1096, 1024, 1011, 917, 814, 701; **MS** (ESI): *m/z* 395.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for C$_{19}$H$_{20}$N$_2$NaO$_4$S [(M + Na)$^+$], 395.1036; found 395.1029.

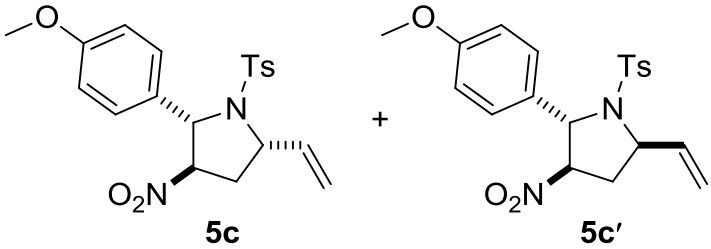
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(2-methoxyphenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5b) and *rac*-(2*S*,3*R*,5*R*)-2-(2-methoxyphenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5b′)



5b **5b′**

Prepared according to the general procedure, compounds **5b** and **5b′** (63 mg, 78%, mixture of diastereomers, dr 91:9) were obtained as a pale yellow solid after purification by flash column chromatography, eluting with PE/EtOAc (6:1). **TLC**: R_f = 0.27 (PE/EtOAc 6:1, UV, $KMnO_4$); **Melting Point**: 156 - 158 °C; ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.74 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.64 - 7.59 (m, 1H, Ar**H**), 7.39 - 7.28 (m, 3H, Ar**H**), 7.03 (t, *J* = 7.5 Hz, 1H, Ar**H**), 6.89 (d, *J* = 8.5 Hz, 1H, Ar**H**), 6.14 (ddd, *J* = 17.5, 10.0, 8.0 Hz, 1H, C**H**=CH_2), 5.77 (s, 1H, C**H**N), 5.33 (d, *J* = 17.5 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.31 (d, *J* = 10.0 Hz, 2H, CH=C**H_{cis}**H_{trans}), 4.73 (d, *J* = 6.0 Hz, 1H, C**H**NO_2), 4.30 - 4.21 (m, 1H, NC**H**CH=CH_2), 3.86 (s, 3H, ArOC**H_3**), 2.52 - 2.39 (m, 4H, ArC**H_3** and C**H**H′), 2.20 - 2.09 (m, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 155.5 (Ar**C**), 144.0 (Ar**C**), 137.6 (**C**H=CH_2), 134.0 (Ar**C**), 129.5 (2 × Ar**C**H), 129.5 (Ar**C**H), 128.0 (2 × Ar**C**H), 127.4 (Ar**C**H), 127.0 (Ar**C**), 120.7 (Ar**C**H), 117.6 (CH=**C**H_2), 110.2 (Ar**C**H), 88.3 (**C**HNO_2), 64.8 (**C**HN), 62.2 (N**C**HCH=CH_2), 55.3 (ArO**C**H_3), 36.0 (**C**H_2), 21.6 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.48 (d, *J* = 7.5 Hz, 1H, Ar**H**), 7.23 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.84 (d, *J* = 8.0 Hz, 1H, Ar**H**), 5.04 - 4.98 (m, 1H, CH=C**H**H′), 3.80 (s, 3H, ArOC**H_3**), 2.75 (ddd, *J* = 15.5, 9.0, 7.0 Hz, 1H, C**H**H′); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): δ_C 143.1 (Ar**C**), 136.3 (**C**H=CH_2), 129.0 (Ar**C**H), 127.7 (Ar**C**H), 120.9 (Ar**C**H), 118.5 (CH=**C**H_2), 110.3 (Ar**C**H), 88.2 (**C**HNO_2), 64.6 (**C**HN), 62.6 (N**C**HCH=CH_2), 55.2 (ArO**C**H_3), 36.2 (**C**H_2), 21.5 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 2919, 1552, 1370, 1343, 1286, 1250, 1156, 1091, 1027, 1003, 814, 756, 663; **MS** (ESI): *m/z* 425.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{20}H_{22}N_2NaO_5S$ [(M + Na)$^+$], 425.1142; found 425.1138.

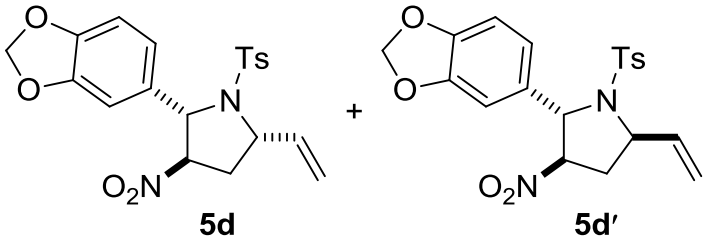
Synthesis of characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(4-methoxyphenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5c) and *rac*-(2*S*,3*R*,5*R*)-2-(4-methoxyphenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5c′)



5c **5c′**

Prepared according to the general procedure, compounds **5c** and **5c′** (25 mg, 31%, mixture of diastereomers, dr 93:7) were obtained as an off-white solid after purification by flash column chromatography, eluting with PE/EtOAc (4:1). **TLC**: R_f = 0.43 (PE/EtOAc 4:1, UV, $KMnO_4$); **Melting Point**: 129 - 132 °C; ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.65 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.36 (d, *J* = 8.5 Hz, 2H, Ar**H**), 7.31 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.92 (d, *J* = 8.5 Hz, 2H, Ar**H**), 6.08 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.52 (s, 1H, C**H**N), 5.37 (d, *J* = 17.0 Hz, 1H, CH=CH_{cis}**H**$_{trans}$), 5.31 (d, *J* = 10.0 Hz, 1H, CH=C**H**$_{cis}$H$_{trans}$), 4.72 - 4.64 (m, 1H, C**H**NO_2), 4.40 - 4.31 (m, 1H, NC**H**CH=CH_2), 3.83 (s, 3H, ArOC**H$_3$**), 2.59 (dd, *J* = 14.5, 7.0 Hz, 1H, C**H**H′), 2.46 (s, 3H, ArC**H$_3$**), 2.18 (ddd, *J* = 14.5, 9.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 159.6 (Ar**C**), 144.1 (Ar**C**), 137.5 (**C**H=CH_2), 134.2 (Ar**C**), 130.9 (Ar**C**), 129.6 (2 × Ar**C**H), 127.8 (2 × Ar**C**H), 127.4 (2 × Ar**C**H), 117.8 (CH=**C**H_2), 114.3 (2 × Ar**C**H), 90.2 (**C**HNO_2), 68.5 (**C**HN), 62.0 (N**C**HCH=CH_2), 55.4 (ArO**C**H_3), 34.9 (**C**H_2), 21.6 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.54 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.25 - 7.16 (m, 4H, Ar**H**), 6.87 (d, *J* = 8.5 Hz, 2H, Ar**H**), 5.87 (s, 1H, C**H**N), 5.05 (d, *J* = 10.0 Hz, 1H, CH=C**H**$_{cis}$H$_{trans}$), 2.84 (ddd, *J* = 15.5, 8.5, 7.0 Hz, 1H, C**H**H′), 2.41 (s, 3H, ArC**H$_3$**); **IR** (film/cm^{-1}): ν_{max} 2921, 1550, 1511, 1339, 1249, 1161, 1087, 1020, 1005, 839, 815, 665; **MS** (ESI): *m/z* 425.2 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{20}H_{22}N_2NaO_5S$ [(M + Na)$^+$], 425.1142; found 425.1139.

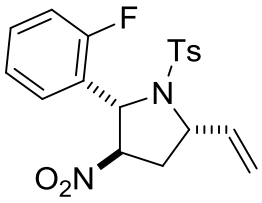
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(1,3-benzodioxol-5-yl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5d) and *rac*-(2*S*,3*R*,5*R*)-2-(1,3-benzodioxol-5-yl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5d′)



5d **5d′**

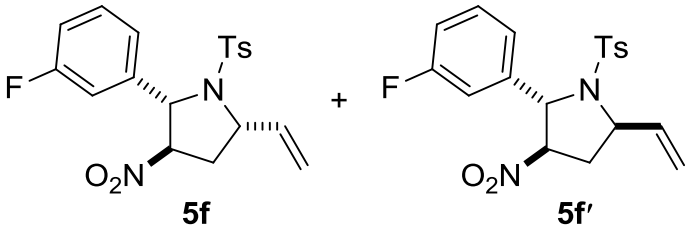
Prepared according to the general procedure on a 0.10 mmol scale, compounds **5d** and **5d′** (14 mg, 32%, mixture of diastereomers, dr 90:10) were obtained as an off-white solid after purification by flash column chromatography, eluting with PE/EtOAc (3:1). **TLC**: R_f = 0.47 (PE/EtOAc 3:1, UV, $KMnO_4$); **Melting Point**: 142 - 144 °C; ***Major Diastereomer*** **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.70 - 7.62 (m, 2H, Ar**H**), 7.32 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.94 - 6.88 (m, 2H, Ar**H**), 6.85 - 6.78 (m, 1H, Ar**H**), 6.08 (ddd, *J* = 17.5, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.99 (q, *J* = 1.5 Hz, 2H, OC**H_2**O), 5.45 (s, 1H, C**H**N), 5.37 (d, *J* = 17.5 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.33 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 4.69 - 4.64 (m, 1H, C**H**NO_2), 4.37 - 4.28 (m, 1H, NC**H**CH=CH_2), 2.58 (dddd, *J* = 14.5, 7.0, 2.5, 1.5 Hz, 1H, C**H**H′), 2.48 - 2.44 (m, 3H, ArC**H_3**), 2.19 (ddd, *J* = 15.0, 9.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 148.3 (Ar**C**), 147.7 (Ar**C**), 144.2 (Ar**C**), 137.4 (**C**H=CH_2), 134.0 (Ar**C**), 132.9 (Ar**C**), 129.7 (2 × Ar**C**H), 127.8 (2 × Ar**C**H), 119.7 (Ar**C**H), 117.9 (CH=**C**H_2), 108.5 (Ar**C**H), 106.6 (Ar**C**H), 101.4 (O**C**H_2O), 90.2 (**C**HNO_2), 68.7 (**C**HN), 62.0 (N**C**HCH=CH_2), 34.9 (**C**H_2), 21.6 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (500 MHz, $CDCl_3$, observable peaks): δ_H 7.59 - 7.53 (m, 2H, Ar**H**), 7.21 (d, *J* = 8.0 Hz, 2H, Ar**H**), 5.81 (s, 1H, C**H**N), 5.04 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 2.84 (ddd, *J* = 16.0, 9.5, 7.5 Hz, 1H, C**H**H′), 2.41 (s, 3H, ArC**H_3**); **^{13}C NMR** (125 MHz, $CDCl_3$, observable peaks): δ_C 147.7 (Ar**C**), 143.4 (Ar**C**), 138.1 (Ar**C**), 136.4 (**C**H=CH_2), 132.4 (Ar**C**), 129.1 (2 × Ar**C**H), 127.7 (2 × Ar**C**H), 119.9 (Ar**C**H), 118.5 (CH=**C**H_2), 108.3 (Ar**C**H), 106.5 (Ar**C**H), 102.1 (O**C**H_2O), 90.4 (**C**HNO_2), 68.0 (**C**HN), 62.6 (N**C**HCH=CH_2), 35.3 (**C**H_2), 21.5 (Ar**C**H_3); **IR** (film / cm^{-1}): ν_{max} 2887, 1548, 1487, 1348, 1231, 1162, 1098, 1028, 1013, 915, 819; **MS** (ESI): *m/z* 439.1 $[(M + Na)^+]$; **HRMS** (ESI): exact mass calculated for $C_{20}H_{20}N_2NaO_6S$ $[(M + Na)^+]$, 439.0934; found 439.0926.

Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(2-fluorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5e)



Prepared according to the general procedure, compound **5e** (62 mg, 79%) was obtained as an off-white solid after purification by flash column chromatography, eluting with PE/EtOAc (5:1). **TLC**: R_f = 0.39 (PE/EtOAc 5:1, UV, $KMnO_4$); **Melting Point**: 118 - 120 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.71 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.64 (t, *J* = 7.5 Hz, 1H, Ar**H**), 7.39 - 7.31 (m, 3H, Ar**H**), 7.23 (t, *J* = 7.5 Hz, 1H, Ar**H**), 7.14 - 7.05 (m, 1H, Ar**H**), 6.13 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.79 (s, 1H, C**H**N), 5.36 (d, *J* = 17.0 Hz, 1H, CH=CH_{cis}**H*$_{trans}$**), 5.34 (d, *J* = 10.0 Hz, 1H, CH=C**H*$_{cis}$**H_{trans}), 4.76 (d, *J* = 6.0 Hz, 1H, C**H**NO_2), 4.31 - 4.20 (m, 1H, NC**H**CH=CH_2), 2.59 (dd, *J* = 14.5, 6.5 Hz, 1H, C**H**H′), 2.47 (s, 3H, ArC**H$_3$**), 2.25 - 2.13 (m, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 159.3 (d, *J* = 247.0 Hz, Ar**C**F), 144.3 (Ar**C**), 137.2 (**C**H=CH_2), 133.5 (Ar**C**), 130.3 (d, *J* = 9.0 Hz, Ar**C**H), 129.7 (2 × Ar**C**H), 128.3 (d, *J* = 3.0 Hz, Ar**C**H), 127.9 (2 × Ar**C**H), 126.2 (d, *J* = 12.0 Hz, Ar**C**), 124.6 (d, *J* = 3.0 Hz, Ar**C**H), 118.0 (CH=**C**H_2), 115.6 (d, *J* = 21.0 Hz, Ar**C**H), 88.2 (**C**HNO_2), 63.6 (d, *J* = 2.5 Hz, **C**HN), 62.0 (N**C**HCH=CH_2), 35.6 (**C**H_2), 21.6 (Ar**C**H_3); **^{19}F NMR** (376.5 MHz, $CDCl_3$): δ_F –116.6 (Ar**F**); **IR** (film/cm^{-1}): ν_{max} 2922, 1552, 1485, 1368, 1345, 1159, 1090, 1027, 1021, 816, 766, 666; **MS** (ESI): *m/z* 413.0 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}FN_2NaO_4S$ [(M + Na)$^+$], 413.0942; found 413.0938.

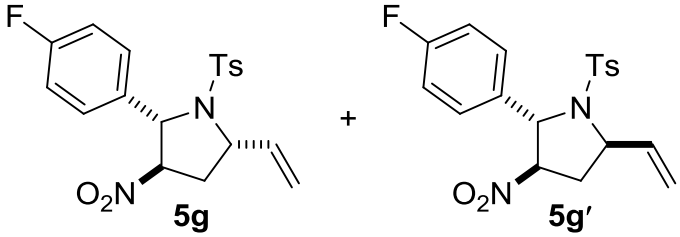
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(3-fluorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5f) and *rac*-(2*S*,3*R*,5*R*)-2-(3-fluorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5f′)



5f **5f′**

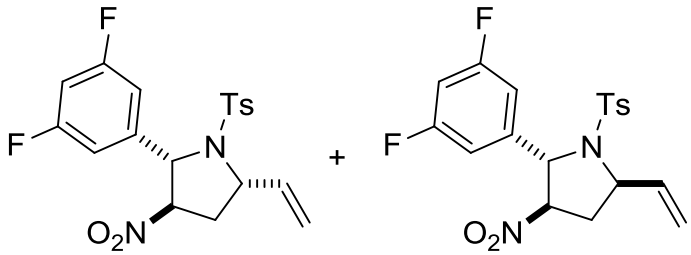
Prepared according to the general procedure, compounds **5f** and **5f′** (57 mg, 73%, mixture of diastereomer, dr 93:7) were obtained as a white solid after purification by flash column chromatography, eluting with PE/EtOAc (5:1). **TLC**: R_f = 0.42 (PE/EtOAc 5:1, UV, $KMnO_4$); **Melting Point**: 166 - 167 °C; ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.66 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.43 - 7.30 (m, 3H, Ar**H**), 7.29 - 7.13 (m, 2H, Ar**H**), 7.09 - 6.98 (m, 1H, Ar**H**), 6.08 (ddd, *J* = 17.5, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.57 (s, 1H, C**H**N), 5.38 (d, *J* = 17.5 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.34 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 4.76 - 4.63 (m, 1H, C**H**NO_2), 4.39 - 4.27 (m, 1H, NC**H**CH=CH_2), 2.61 (dd, *J* = 14.5, 7.0 Hz, 1H, C**H**H′), 2.46 (s, 3H, ArC**H_3**), 2.17 (ddd, *J* = 14.5, 9.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 163.0 (d, *J* = 247.5 Hz, Ar**C**F), 144.4 (Ar**C**), 141.6 (d, *J* = 6.5 Hz, Ar**C**), 137.1 (**C**H=CH_2), 133.7 (Ar**C**), 130.6 (d, *J* = 9.0 Hz, Ar**C**H), 129.7 (2 × Ar**C**H), 127.8 (2 × Ar**C**H), 121.8 (d, *J* = 3.0 Hz, Ar**C**H), 118.1 (CH=**C**H_2), 115.4 (d, *J* = 21.5 Hz, Ar**C**H), 113.4 (d, *J* = 23.0 Hz, Ar**C**H), 89.8 (**C**HNO_2), 68.3 (d, *J* = 1.5 Hz, **C**HN), 62.1 (N**C**HCH=CH_2), 34.9 (**C**H_2), 21.6 (Ar**C**H_3); **^{19}F NMR** (376.5 MHz, $CDCl_3$): δ_F –111.3 (Ar**F**); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.58 (d, *J* = 8.0 Hz, 2H, Ar**H**), 5.94 (s, 1H, C**H**N), 5.04 (d, *J* = 9.0 Hz, 1H), 2.88 - 2.75 (m, 1H, C**H**H′), 2.42 (s, 3H, ArC**H_3**); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): δ_C 143.6 (Ar**C**), 141.2 (Ar**C**), 137.9 (Ar**C**), 136.1 (**C**H=CH_2), 129.2 (2 × Ar**C**H), 127.6 (2 × Ar**C**H), 118.7 (CH=**C**H_2), 113.2 (d, *J* = 23.0 Hz, Ar**C**H), 90.0 (**C**HNO_2), 67.6 (**C**HN), 62.5 (N**C**HCH=CH_2), 35.3 (**C**H_2), 21.5 (Ar**C**H_3); **^{19}F NMR** (376.5 MHz, $CDCl_3$): δ_F –111.4 (Ar**F**); **IR** (film/cm^{-1}): ν_{max} 1543, 1369, 1342, 1164, 1119, 1090, 1029, 1013, 916, 816, 786, 698, 665; **MS** (ESI): *m/z* 413.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}FN_2NaO_4S$ [(M + Na)$^+$], 413.0942; found 413.0939.

Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(4-fluorophenyl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5g) and *rac*-(2*S*,3*R*,5*R*)-2-(4-fluorophenyl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5g′)



Prepared according to the general procedure, compounds **5g** and **5g′** (26 mg, 33%, mixture of diastereomer, dr 84:16) were obtained as an off-white solid after purification by flash column chromatography, eluting with PE/EtOAc (5:1). **TLC**: R_f = 0.35 (PE/EtOAc 5:1, UV, $KMnO_4$); **Melting Point:** 132 - 134 °C; ***Major Diastereomer*** **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.65 (AA′, part of AA′BB′ system, *J* = 8.0 Hz, 2H, Ar**H**), 7.47 - 7.40 (m, 2H, Ar**H**), 7.33 (BB′, part of AA′BB′ system, *J* = 8.0 Hz, 2H, Ar**H**), 7.12 - 7.02 (m, 2H, Ar**H**), 6.07 (ddd, *J* = 17.5, 10.5, 7.5 Hz, 1H, C**H**=CH_2), 5.54 (s, 1H, C**H**N), 5.37 (d, *J* = 17.5 Hz, 1H, CH=CH_{cis}**H*$_{trans}$**), 5.33 (d, *J* = 10.5 Hz, 1H, CH=C**H*$_{cis}$**H$_{trans}$), 4.70 - 4.66 (m, 1H, C**H**NO_2), 4.39 - 4.32 (m, 1H, NC**H**CH=CH_2), 2.66 - 2.57 (m, 1H, C**H**H′), 2.46 (s, 3H, ArC**H$_3$**), 2.18 (ddd, *J* = 15.0, 9.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 162.6 (d, *J* = 248.0 Hz, Ar**C**F), 144.4 (Ar**C**), 137.3 (**C**H=CH_2), 134.7 (d, *J* = 3.0 Hz, Ar**C**), 133.9 (Ar**C**), 129.7 (2 × Ar**C**H), 127.9 (d, *J* = 7.5 Hz, 2 × Ar**C**H), 127.8 (2 × Ar**C**H), 118.0 (CH=**C**H_2), 115.9 (d, *J* = 22.0 Hz, 2 × Ar**C**H), 90.0 (**C**HNO_2), 68.3 (**C**HN), 62.0 (N**C**HCH=CH_2), 34.9 (**C**H_2), 21.6 (Ar**C**H_3); **^{19}F NMR** (470.5 MHz, $CDCl_3$): δ_F –113.5 (Ar**F**); ***Minor Diastereomer*** **^{1}H NMR** (500 MHz, $CDCl_3$, observable peaks): δ_H 7.56 (AA′, part of AA′BB′ system, *J* = 8.0 Hz, 2H, Ar**H**), 7.31 - 7.28 (m, 2H, Ar**H**), 7.21 (BB′, part of AA′BB′ system, *J* = 8.0 Hz, 2H, Ar**H**), 5.91 (s, 1H, C**H**N), 5.47 - 5.40 (m, 1H, C**H**=CH_2), 5.05 (d, *J* = 10.0 Hz, 1H, CH=C**H*$_{cis}$**H$_{trans}$), 4.74 - 4.70 (m, 1H, NC**H**CH=CH_2), 4.66 - 4.63 (m, 1H, C**H**NO_2), 2.82 (ddd, *J* = 16.0, 9.5, 7.0 Hz, 1H, C**H**H′), 2.42 (m, 3H, ArC**H$_3$**); **^{13}C NMR** (125 MHz, $CDCl_3$, observable peaks): δ_C 143.6 (Ar**C**), 138.0 (Ar**C**), 136.2 (**C**H=CH_2), 134.5 (d, *J* = 3.0 Hz, Ar**C**), 129.2 (2 × Ar**C**H), 127.9 (d, *J* = 8.5 Hz, 2 × Ar**C**H), 127.7 (2 × Ar**C**H), 118.7 (CH=**C**H_2), 116.0 (d, *J* = 22.0 Hz, 2 × Ar**C**H), 90.2 (**C**HNO_2), 67.6 (**C**HN), 62.5 (N**C**HCH=CH_2), 35.3 (**C**H_2), 21.5 (Ar**C**H_3); **^{19}F NMR** (470.5 MHz, $CDCl_3$): δ_F –113.4 (Ar**F**); **IR** (film/cm^{-1}): ν_{max} 2923, 1605, 1553, 1509, 1349, 1225, 1163, 1095, 1027, 1012, 843, 814, 668; **MS** (ESI): *m/z* 413.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}FN_2NaO_4S$ [(M + Na)$^+$], 413.0942; found 413.0941.

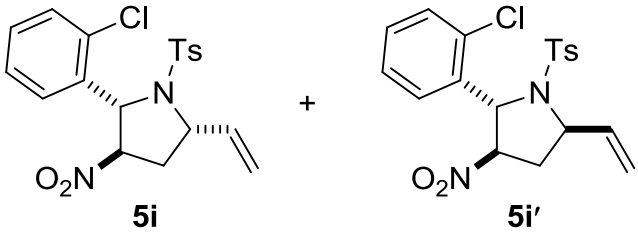
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(3,5-difluorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5h) and *rac*-(2*S*,3*R*,5*R*)-2-(3,5-difluorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5h′)



5h **5h′**

Prepared according to the general procedure, compounds **5h** and **5h′** (54 mg, 66%, mixture of diastereomers, dr 81:19) was obtained as a white solid after purification by flash column chromatography, eluting with PE/EtOAc (6:1). **TLC**: R_f = 0.41 (PE/EtOAc 6:1, UV, $KMnO_4$); **Melting Point**: 157 - 160 °C; ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.67 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.35 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.06 - 6.97 (m, 2H, Ar**H**), 6.83 - 6.73 (m, 1H, Ar**H**), 6.07 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.57 (s, 1H, C**H**N), 5.37 (d, *J* = 17.0 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.35 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 4.75 - 4.62 (m, 1H, C**H**NO_2), 4.34 - 4.25 (m, 1H, NC**H**CH=CH_2), 2.69 - 2.57 (m, 1H, C**H**H′), 2.47 (s, 3H, ArC**H_3**), 2.16 (ddd, *J* = 15.0, 9.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 163.2 (dd, *J* = 250.0, 13.0 Hz, 2 × Ar**C**F), 144.6 (Ar**C**), 143.1 (t, *J* = 8.5 Hz, Ar**C**), 136.9 (**C**H=CH_2), 133.4 (Ar**C**), 129.8 (2 × Ar**C**H), 127.8 (2 × Ar**C**H), 118.3 (CH=**C**H_2), 109.4 (dd, *J* = 19.0, 8.0 Hz, 2 × Ar**C**H), 104.0 (t, *J* = 25.0 Hz, Ar**C**H), 89.5 (**C**HNO_2), 67.9 (t, *J* = 2.5 Hz, **C**HN), 62.1 (N**C**HCH=CH_2), 34.9 (**C**H_2), 21.6 (Ar**C**H_3); **^{19}F NMR** (376.5 MHz, $CDCl_3$): δ_F –107.5 (2 × Ar**F**); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.60 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.24 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.92 - 6.85 (m, 2H, Ar**H**), 5.91 (s, 1H, C**H**N), 5.07 - 5.02 (m, 1H, CH=C**H**H′), 4.75 - 4.62 (m, 2H, NC**H**CH=CH_2 and C**H**NO_2), 2.80 (ddd, *J* = 15.5, 9.0, 7.0 Hz, 1H, C**H**H′), 2.42 (s, 3H, ArC**H_3**); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): δ_C 143.8 (Ar**C**), 142.8 (Ar**C**), 137.7 (Ar**C**), 135.7 (**C**H=CH_2), 129.2 (2 × Ar**C**H), 127.7 (2 × Ar**C**H), 119.0 (CH=**C**H_2), 103.9 (t, *J* = 25.5 Hz, Ar**C**H), 89.7 (C**H**NO_2), 67.2 (t, *J* = 2.5 Hz, **C**HN), 62.6 (N**C**HCH=CH_2), 35.2 (**C**H_2), 21.5 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 1598, 1551, 1346, 1166, 1116, 1011, 997, 918, 816, 666, 652; **MS** (ESI): *m/z* 431.0 [$(M + Na)^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{18}F_2N_2NaO_4S$ [$(M + Na)^+$], 431.0848; found 431.0850.

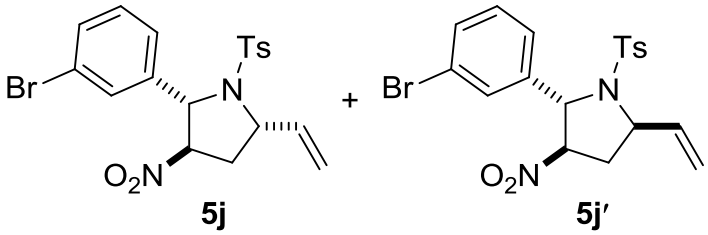
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(2-chlorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5i) and *rac*-(2*S*,3*R*,5*R*)-2-(2-chlorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5i′)



5i **5i′**

Prepared according to the general procedure, compounds **5i** and **5i′** (51 mg, 62%, mixture of diastereomers, dr 84:16) were obtained as a white solid after purification by flash column chromatography, eluting with PE/EtOAc (5:1). **TLC**: R_f = 0.24 (PE/EtOAc 5:1, UV, $KMnO_4$); **Melting Point**: 109 - 110 °C; ***Major Diastereomer*** **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.78 - 7.70 (m, 3H, Ar**H**), 7.45 - 7.25 (m, 5H, Ar**H**), 6.19 (ddd, *J* = 17.5, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.87 (s, 1H, C**H**N), 5.36 (d, *J* = 10.0 Hz, 1H, CH=C**H**$_{cis}$H$_{trans}$), 5.35 (d, *J* = 17.5 Hz, 1H, CH=CH$_{cis}$**H**$_{trans}$), 4.74 - 4.68 (m, 1H, C**H**NO_2), 4.18 (dt, *J* = 11.0, 7.0 Hz, 1H, NC**H**CH=CH_2), 2.58 - 2.50 (m, 1H, C**H**H′), 2.48 (s, 3H, ArC**H$_3$**), 2.19 (ddd, *J* = 14.5, 11.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 144.4 (Ar**C**), 137.2 (**C**H=CH_2), 136.4 (Ar**C**), 133.3 (Ar**C**), 131.9 (Ar**C**), 129.9 (Ar**C**H), 129.7 (3 × Ar**C**H), 128.3 (Ar**C**H), 128.1 (2 × Ar**C**H), 127.4 (Ar**C**H), 118.0 (CH=**C**H_2), 88.0 (**C**HNO_2), 66.2 (**C**HN), 62.3 (N**C**HCH=CH_2), 35.9 (**C**H_2), 21.7 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (500 MHz, $CDCl_3$, observable peaks): δ_H 7.66 - 7.52 (m, 2H, Ar**H**), 6.29 (s, 1H, C**H**N), 5.32 (dd, *J* = 17.0, 1.0 Hz, 1H, CH=CH$_{cis}$**H**$_{trans}$), 5.25 - 5.15 (m, 1H, C**H**=CH_2), 5.00 (dd, *J* = 10.0, 1.0 Hz, 1H, CH=C**H**$_{cis}$H$_{trans}$), 4.82 (td, *J* = 9.5, 1.0 Hz, 1H, NC**H**CH=CH_2), 2.77 (ddd, *J* = 15.5, 9.5, 7.0, Hz, 1H, C**H**H′), 2.44 (s, 3H, ArC**H$_3$**); **^{13}C NMR** (125 MHz, $CDCl_3$, observable peaks): δ_C 143.6 (Ar**C**), 138.2 (Ar**C**), 136.3 (Ar**C**), 135.7 (**C**H=CH_2), 131.4 (Ar**C**), 130.0 (Ar**C**H), 129.2 (2 × Ar**C**H), 127.9 (2 × Ar**C**H), 127.5 (Ar**C**H),119.3 (CH=**C**H_2), 88.2 (**C**HNO_2), 65.6 (**C**HN), 62.8 (N**C**HCH=CH_2), 35.7 (**C**H_2), 21.6 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 2923, 1598, 1553, 1444, 1353, 1163, 1095, 1027, 1013, 930, 815, 758, 669; **MS** (ESI): *m/z* 429.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}ClN_2NaO_4S$ [(M + Na)$^+$], 429.0646; found 429.0634.

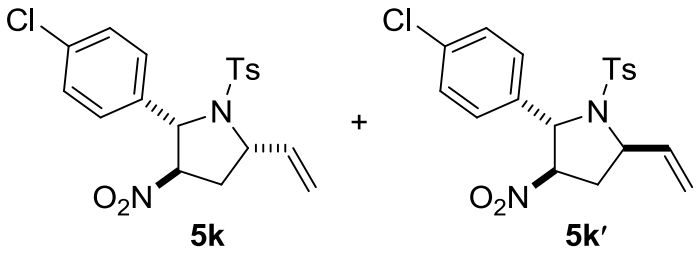
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(3-bromophenyl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5j) and *rac*-(2*S*,3*R*,5*R*)-2-(3-bromophenyl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5j′)



5j **5j′**

Prepared according to the general procedure, compounds **5j** and **5j′** (57 mg, 63%, mixture of diastereomers, dr 87:13) were obtained as an off-white solid after purification by flash column chromatography, eluting with PE/EtOAc (7:1). **TLC**: R_f = 0.30 (PE/EtOAc 7:1, UV, $KMnO_4$); **Melting Point**: 146 - 148 °C; ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.65 (d, *J* = 8.5 Hz, 2H, Ar**H**), 7.57 - 7.51 (m, 1H, Ar**H**), 7.50 - 7.37 (m, 2H, Ar**H**), 7.36 - 7.24 (m, 3H, Ar**H**), 6.07 (ddd, *J* = 17.5, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.54 (s, 1H, C**H**N), 5.39 (d, *J* = 17.5 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.35 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 4.70 - 4.66 (m, 1H, C**H**NO_2), 4.40 - 4.31 (m, 1H, NC**H**CH=CH_2), 2.70 - 2.57 (m, 1H, C**H**H′), 2.46 (s, 3H, ArC**H_3**), 2.17 (ddd, *J* = 15.0, 9.5, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 144.4 (Ar**C**), 141.1 (Ar**C**), 137.1 (**C**H=CH_2), 133.8 (Ar**C**), 131.6 (Ar**C**H), 130.5 (Ar**C**H), 129.7 (2 × Ar**C**H), 129.2 (Ar**C**H), 127.8 (2 × Ar**C**H), 124.9 (Ar**C**H), 123.1 (Ar**C**), 118.2 (CH=**C**H_2), 89.8 (**C**HNO_2), 68.1 (**C**HN), 62.1 (N**C**HCH=CH_2), 34.9 (**C**H_2), 21.6 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.21 (d, *J* = 8.0 Hz, 2H, Ar**H**), 5.89 (s, 1H, C**H**N), 5.52 - 5.43 (m, 1H, C**H**=CH_2), 5.08 (d, *J* = 10.0 Hz, 1H, CH=C**H**H'), 4.75 - 4.71 (m, 1H, NC**H**CH=CH_2), 4.66 - 4.62 (m, 1H, C**H**NO_2), 2.82 (ddd, *J* = 15.5, 9.0, 7.0 Hz, 1H, C**H**H′), 2.42 (s, ArC**H_3**); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): δ_C 136.3 (**C**H=CH_2), 129.1 (Ar**C**H), 127.5 (Ar**C**H), 125.1 (Ar**C**H), 118.6 (CH=**C**H_2), 90.0 (**C**HNO_2), 67.4 (**C**HN), 62.6 (N**C**HCH=CH_2), 35.3 (**C**H_2), 21.5 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 3065, 2919, 1548, 1422, 1366, 1340, 1312, 1159, 1091, 1014, 988, 922, 813, 782; **MS** (ESI): *m/z* 473.0 [$(M + Na)^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}BrN_2NaO_4S$ [$(M + Na)^+$], 473.0141; found 473.0137.

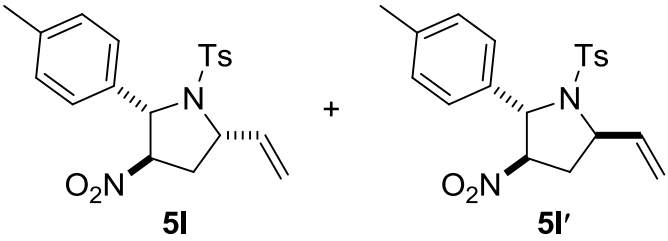
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(4-chlorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5k) and *rac*-(2*S*,3*R*,5*R*)-2-(4-chlorophenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5k′)



5k **5k′**

Prepared according to the general procedure, compounds **5k** and **5k′** (45 mg, 56%, mixture of diastereomers, dr 63:37) were obtained as an off-white solid after purification by flash column chromatography, eluting with PE/EtOAc (3:1). **TLC**: R_f = 0.36 (PE/EtOAc 3:1, UV, $KMnO_4$); **Melting Point**: 126 - 127 °C; **^{1}H NMR** (400 MHz, $CDCl_3$, mixture of diastereomers): δ_H 7.65 (d, *J* = 8.0 Hz, 2H, Ar**H**, *major*), 7.56 (d, *J* = 8.0 Hz, 2H, Ar**H**, *minor*), 7.44 - 7.30 (m, Ar**H**, 6H *major* and 2H *minor*), 7.29 - 7.25 (m, 2H, Ar**H**, *minor*), 7.22 (d, *J* = 8.0 Hz, 2H, Ar**H**, *minor*), 6.07 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH_2, *major*), 5.90 (s, 1H, C**H**N, *minor*), 5.53 (s, 1H, C**H**N, *major*), 5.47 - 5.27 (m, CH=C$\mathbf{H}_{cis}\mathbf{H}_{trans}$, 2H *major*; C**H**=$CH_{cis}\mathbf{H}_{trans}$, 2H *minor*), 5.04 (d, *J* = 9.5 Hz, 1H, CH=C$\mathbf{H}_{cis}H_{trans}$, *minor*), 4.76 - 4.61 (m, 3H, C**H**NO_2, 1H *major* and 1H *minor*; NC**H**CH=CH_2, 1H *minor*), 4.38 - 4.29 (m, 1H, NC**H**CH=CH_2, *major*), 2.86 - 2.74 (m, 1H, C**H**H′, *minor*), 2.67 - 2.55 (m, 2H, CH**H′**, 1H *major* and 1H *minor*), 2.46 (s, 3H, ArC$\mathbf{H}_3$, *major*), 2.42 (s, 3H, ArC$\mathbf{H}_3$, *minor*), 2.21 - 2.11 (m, 1H, C**H**H', *major*); **^{13}C NMR** (100 MHz, $CDCl_3$, mixture of diastereomers): δ_C 144.4 (Ar**C**), 143.6 (Ar**C**), 138.0 (Ar**C**), 137.5 (Ar**C**), 137.2 (**C**H=CH_2, *major*), 137.2 (Ar**C**), 136.0 (**C**H=CH_2, *minor*), 134.4 (Ar**C**), 134.3 (Ar**C**), 133.8 (Ar**C**), 129.7 (2 × Ar**C**H, *major*), 129.2 (4 × Ar**C**H, *minor*), 129.1 (2 × Ar**C**H, *major*), 127.8 (2 × Ar**C**H, *major*), 127.7 (2 × Ar**C**H, *minor*), 127.6 (2 × Ar**C**H, *major*), 127.5 (2 × Ar**C**H, *minor*), 118.8 (CH=**C**H_2, *minor*), 118.1 (CH=**C**H_2, *major*), 90.1 (**C**HNO_2, *minor*), 89.8 (**C**HNO_2, *major*), 68.3 (**C**HN, *major*), 67.6 (**C**HN, *minor*), 62.5 (N**C**HCH=CH_2, *minor*), 62.0 (N**C**HCH=CH_2, *major*), 35.2 (**C**H_2, *minor*), 34.9 (**C**H_2, *major*), 21.6 (Ar**C**H_3, *major*), 21.5 (Ar**C**H_3, *minor*); **IR** (film/cm^{-1}): ν_{max} 2922, 1551, 1488, 1365, 1344, 1161, 1092, 1027, 1009, 927, 868, 812, 731, 666; **MS** (ESI): *m/z* 429.0 [$(M + Na)^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{19}ClN_2NaO_4S$ [$(M + Na)^+$], 429.0646; found 429.0645.

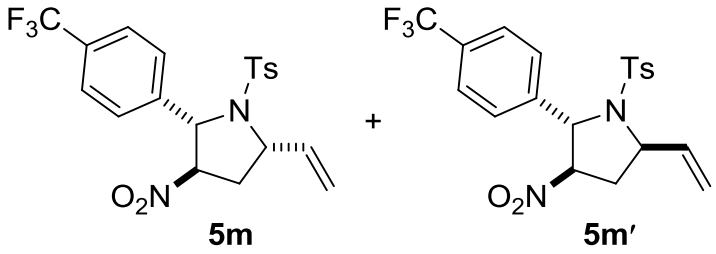
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-2-(4-methylphenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5l) and *rac*-(2*S*,3*R*,5*R*)-2-(4-methylphenyl)-1-[(4-methyl phenyl)sulfonyl]-3-nitro-5-vinylpyrrolidine (5l′)



5l **5l′**

Prepared according to the general procedure, compounds **5l** and **5l′** (50 mg, 64%, mixture of diastereomers, dr 90:10) were obtained as a pale yellow solid after purification by flash column chromatography, eluting with PE/EtOAc (6:1). **TLC**: R_f = 0.39 (PE/EtOAc 6:1, UV, $KMnO_4$); **Melting Point**: 151 - 153 °C; ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.66 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.33 (t, *J* = 8.5 Hz, 4H, Ar**H**), 7.21 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.09 (ddd, *J* = 17.5, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.55 (s, 1H, C**H**N), 5.37 (d, *J* = 17.0 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.32 (d, *J* = 10.0 Hz, 2H, CH=C**H_{cis}**H_{trans}), 4.74 - 4.64 (m, 1H, C**H**NO_2), 4.40 - 4.30 (m, 1H, NC**H**CH=CH_2), 2.59 (dd, *J* = 14.5, 7.0 Hz, 1H, C**H**H′), 2.46 (s, 3H, ArC**H_3**), 2.37 (s, 3H, ArC**H_3**), 2.17 (ddd, *J* = 14.5, 9.5, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 144.1 (Ar**C**), 138.2 (Ar**C**), 137.5 (**C**H=CH_2), 136.0 (Ar**C**), 134.1 (Ar**C**), 129.6 (4 × Ar**C**H), 127.8 (2 × Ar**C**H) 126.0 (2 × Ar**C**H), 117.8 (CH=**C**H_2), 90.1 (**C**HNO_2), 68.8 (**C**HN), 62.1 (N**C**HCH=CH_2), 34.9 (**C**H_2), 21.6 (Ar**C**H_3), 21.0 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.56 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.16 (d, *J* = 8.0 Hz, 2H, Ar**H**), 5.90 (s, 1H, C**H**N), 5.50 - 5.41 (m, 1H, C**H**=CH_2), 5.03 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 2.83 (ddd, *J* = 15.5, 9.0, 7.0 Hz, 1H, C**H**H′), 2.41 (s, 3H, ArC**H_3**); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): δ_C 136.5 (**C**H=CH_2), 129.1 (Ar**C**H), 127.7 (Ar**C**H), 126.0 (Ar**C**H), 90.4 (**C**HNO_2), 68.2 (**C**HN), 62.4 (N**C**HCH=CH_2); **IR** (film/cm^{-1}): ν_{max} 2922, 1546, 1513, 1351, 1163, 1096, 1028, 1013, 916, 817, 806, 664; **MS** (ESI): *m/z* 409.1 [$(M + Na)^+$]; **HRMS** (ESI): exact mass calculated for $C_{20}H_{22}N_2NaO_4S$ [$(M + Na)^+$], 409.1192; found 409.1186.

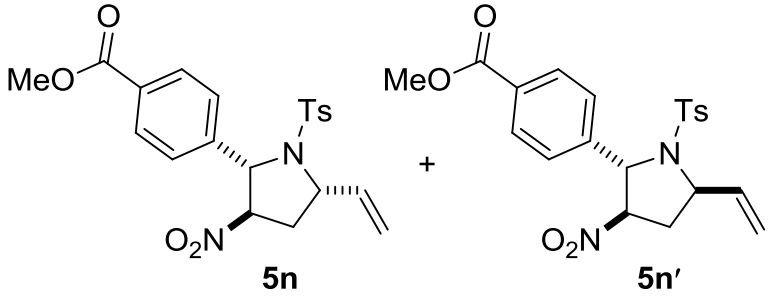
Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-1-[(4-methylphenyl)sulfonyl]-3-nitro-2-[4-(trifluoromethyl)phenyl]-5-vinylpyrrolidine (5m) and *rac*-(2*S*,3*R*,5*R*)-1-[(4-methylphenyl)sulfonyl]-3-nitro-2-[4-(trifluoromethyl)phenyl]-5-vinylpyrrolidine (5m′)



5m **5m′**

Prepared according to the general procedure, compounds **5m** and **5m′** (45 mg, 56%, mixture of diastereomers, dr 92:8) were obtained as a white solid after purification by flash column chromatography, eluting with PE/EtOAc (5:1). **TLC**: R_f = 0.38 (PE/EtOAc 5:1, UV, $KMnO_4$), **Melting Point**: 145 - 147 °C; ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.71 - 7.63 (m, 4H, Ar**H**), 7.60 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.34 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.09 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.61 (s, 1H, C**H**N), 5.38 (d, *J* = 17.5 Hz, 1H, CH=CH_{cis}**H*$_{trans}$**), 5.35 (d, *J* = 10.0 Hz, 2H, CH=**C*$_{cis}$**H_{trans}), 4.73 - 4.67 (m, 1H, C**H**NO_2), 4.40 - 4.31 (m, 1H, NC**H**CH=CH_2), 2.67 - 2.58 (m, 1H, C**H**H′), 2.47 (s, 3H, ArC**H$_3$**), 2.17 (ddd, *J* = 15.0, 9.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 144.6 (Ar**C**), 142.9 (Ar**C**), 137.1 (**C**H=CH_2), 133.6 (Ar**C**), 130.7 (q, *J* = 33.0 Hz, Ar**C**), 129.8 (2 × Ar**C**H), 127.8 (2 × Ar**C**H), 126.7 (2 × Ar**C**H), 126.4 (q, *J* = 251.5 Hz, Ar**C**F_3), 126.0 (q, *J* = 4.0 Hz, 2 × Ar**C**H), 118.2 (CH=**C**H_2), 89.7 (**C**HNO_2), 68.3 (**C**HN), 62.1 (N**C**HCH=CH_2), 34.9 (**C**H_2), 21.6 (Ar**C**H_3); **^{19}F NMR** (376.5 MHz, $CDCl_3$): δ_F –62.6 (ArC**F$_3$**); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 7.57 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.47 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.21 (d, *J* = 8.0 Hz, 2H, Ar**H**), 5.99 (s, 1H, C**H**N), 5.06 (d, *J* = 10.0 Hz, 1H, CH=C**H*$_{cis}$**H_{trans}), 4.76 (td, *J* = 9.0, 2.0 Hz, 1H, NC**H**CH=CH_2), 4.66 (d, *J* = 7.0 Hz, 1H, C**H**NO_2), 2.81 (ddd, *J* = 15.5, 9.0, 7.0 Hz, C**H**H′), 2.41 (s, 3H, ArC**H$_3$**); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): δ_C 135.9 (**C**H=CH_2), 129.2 (Ar**C**H), 126.6 (Ar**C**H), 35.2 (**C**H_2), 21.5 (Ar**C**H_3); **^{19}F NMR** (376.5 MHz, $CDCl_3$): δ_F –62.7 (ArC**F$_3$**); **IR** (film/cm^{-1}): ν_{max} 1554, 1416, 1344, 1324, 1160, 1115, 1066, 1006, 930, 845, 813, 665; **MS** (ESI): *m/z* 463.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{20}H_{19}F_3N_2NaO_4S$ [(M + Na)$^+$], 463.0910; found 463.0905.

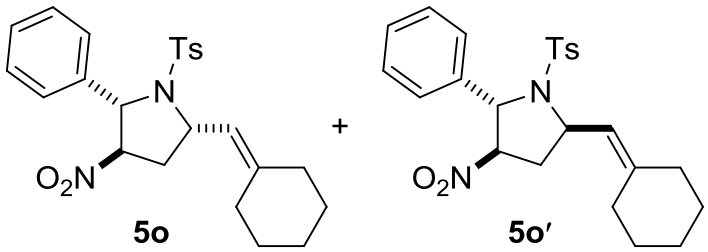
Synthesis and characterisation of *rac*-methyl 4-{(2*S*,3*R*,5*S*)-1-[(4-methylphenyl) sulfonyl]-3-nitro-5-vinylpyrrolidin-2-yl}benzoate (5n) and *rac*-methyl 4-{(2*S*,3*R*,5*R*)-1-[(4-methylphenyl) sulfonyl]-3-nitro-5-vinylpyrrolidin-2-yl}benzoate (5n′)



5n **5n′**

Prepared according to the general procedure on a 0.10 mmol scale, compounds **5n** and **5n′** (32 mg, 73%, mixture of diastereomers, dr 86:14) were obtained as an off-white solid after purification by flash column chromatography, eluting with PE/EtOAc (5:1). **TLC**: R_f = 0.27 (PE/EtOAc 5:1, UV, $KMnO_4$); **Melting Point**: 183 - 185 °C (decomp); ***Major Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 8.07 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.66 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.55 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.33 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.09 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1H, C**H**=CH_2), 5.63 (s, 1H, C**H**N), 5.38 (d, *J* = 17.0 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.34 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 4.72 - 4.68 (m, 1H, C**H**NO_2), 4.39 - 4.29 (m, 1H, NC**H**CH=CH_2), 3.94 (s, 3H, CO_2C**H_3**), 2.62 (dd, *J* = 15.0, 7.0 Hz, 1H, C**H**H′), 2.46 (s, 3H, Ar**C**H_3), 2.16 (ddd, *J* = 15.0, 9.0, 6.0 Hz, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 166.4 (**C**=O), 144.5 (Ar**C**), 143.8 (Ar**C**), 137.1 (**C**H=CH_2), 133.8 (Ar**C**), 130.3 (Ar**C**),130.3 (2 × Ar**C**H), 129.8 (2 × Ar**C**H), 127.8 (2 × Ar**C**H), 126.2 (2 × Ar**C**H), 118.2 (CH=**C**H_2), 89.7 (**C**HNO_2), 68.6 (**C**HN), 62.1 (N**C**HCH=CH_2), 52.3 (CO_2**C**H_3), 35.0 (**C**H_2), 21.6 (Ar**C**H_3); ***Minor Diastereomer*** **^{1}H NMR** (400 MHz, $CDCl_3$, observable peaks): δ_H 8.04 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.59 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.43 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.21 (d, *J* = 8.0 Hz, 2H, Ar**H**), 6.00 (s, 1H, C**H**N), 5.04 (d, *J* = 10.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 4.79 - 4.63 (m, 2H, NC**H**CH=CH_2 and C**H**NO_2), 2.81 (ddd, *J* = 15.5, 9.0, 7.0 Hz, 1H, C**H**H′), 2.41 (s, 3H, Ar**C**H_3); **^{13}C NMR** (100 MHz, $CDCl_3$, observable peaks): δ_C 130.3 (2 × Ar**C**H), 129.2 (2 × Ar**C**H), 127.7 (2 × Ar**C**H), 126.1 (2 × Ar**C**H), 90.0 (**C**HNO_2), 62.6 (N**C**HCH=CH_2), 21.5 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 2923, 1722, 1546, 1367, 1344, 1275, 1183, 1160, 1104, 1014, 819, 669; **MS** (ESI): *m/z* 453.1 [(M + $Na)^+$]; **HRMS** (ESI): exact mass calculated for $C_{21}H_{22}N_2NaO_6S$ [(M + $Na)^+$], 453.1091; found 453.1079.

Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-5-(cyclohexylidenemethyl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-2-phenylpyrrolidine (5o) and *rac*-(2*S*,3*R*,5*R*)-5-(cyclohexylidenemethyl)-1-[(4-methylphenyl)sulfonyl]-3-nitro-2-phenylpyrrolidine (5o′)



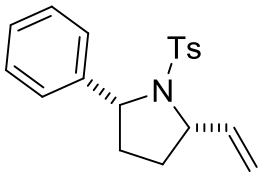
5o **5o′**

Prepared according to the general procedure, compounds **5o** and **5o′** (21 mg, 24%, mixture of diastereomers, dr 77:23) were obtained as a white solid after purification by flash column chromatography, eluting with PE/EtOAc (6:1). **TLC**: R_f = 0.36 (PE/EtOAc 6:1, UV, $KMnO_4$); **Melting Point**: 119 - 122 °C; **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of diastereomers): δ_H 7.68 - 7.63 (m, 2H, Ar**H**, *minor*), 7.62 - 7.56 (m, 2H, Ar**H**, *major*), 7.48 - 7.37 (m, Ar**H**, 4H *major* and 4H *minor*), 7.36 - 7.25 (m, Ar**H**, 3H *major* and 1H *minor*), 7.23 (d, *J* = 8.0 Hz, 2H, Ar**H**, *minor*), 6.00 (s, 1H, C**H**N, *minor*), 5.65 (s, 1H, C**H**N, *major*), 5.26 (d, *J* = 9.0 Hz, 1H, C**H**=C, *major*), 5.12 (td, *J* = 10.0, 2.0 Hz, 1H, NC**H**CH=C, *minor*) 4.77 - 4.65 (m, C**H**NO_2, *major* and *minor*; NC**H**CH=C, *major*), 4.51 (d, *J* = 10.0 Hz, C**H**=C, *minor*), 2.78 (ddd, *J* = 15.5, 9.5, 7.0 Hz, 1H, C**H**H′, *minor*), 2.55 (dd, *J* = 15.0, 6.5 Hz, 1H, C**H**H′, *major*), 2.51 - 2.45 (m, 1H, CH**H′**, *minor*), 2.44 (s, 3H, ArC**H$_3$**, *major*), 2.42 (s, 3H, ArC**H$_3$**, *minor*), 2.35 - 2.25 (m, cyclohexyl **H**, 1H *major* and 2H *minor*), 2.24 - 2.09 (m, 3H, cyclohexyl **H**, *major*), 2.05 (ddd, *J* = 15.0, 10.0, 6.0 Hz, 1H, CH**H′**, *major*), 1.87 - 1.45 (m, cyclohexyl **H**, 6H *major* and 8H *minor*); **^{13}C NMR** (125 MHz, $CDCl_3$, mixture of diastereomers): δ_C 143.9 (Ar**C**), 143.8 (Ar**C**), 143.8 (CH=**C**), 143.1 (CH=**C**), 139.2 (Ar**C**), 135.1 (Ar**C**), 129.4 (2 × Ar**C**H, *major*), 129.0 (2 × Ar**C**H, *minor*), 128.9 (2 × Ar**C**H, *minor*), 128.9 (2 × Ar**C**H, *major*), 128.3 (Ar**C**H, *major*), 128.2 (Ar**C**H, *minor*), 127.7 (2 × Ar**C**H, *major*), 127.5 (2 × Ar**C**H, *minor*), 126.2 (2 × Ar**C**H, *major*), 125.8 (2 × Ar**C**H, *minor*), 120.8 (**C**H=C, *major*), 119.8 (**C**H=C, *minor*), 90.6 (**C**HNO_2, minor), 90.2 (**C**HNO_2, *major*), 68.5 (**C**HN, *major*), 68.0 (**C**HN, *minor*), 57.1 (N**C**HCH=C, *major*), 56.1 (N**C**HCH=C, *minor*), 37.0 (cyclohexyl **C**H_2, *major*), 36.7 (cyclohexyl **C**H_2, *minor*), 36.0 (**C**H_2, *major*), 35.9 (**C**H_2, *minor*), 29.3 (cyclohexyl **C**H_2, *major*), 28.7 (cyclohexyl **C**H_2, *minor*), 28.2 (cyclohexyl **C**H_2, *major*), 27.6 (cyclohexyl **C**H_2, *major*), 27.3 (cyclohexyl **C**H_2, *minor*), 26.6 (cyclohexyl **C**H_2, *major*), 26.5 (cyclohexyl **C**H_2, *minor*), 21.6 (Ar**C**H_3, *major*), 21.5 (Ar**C**H_3, *minor*); **IR** (film/cm^{-1}): ν_{max} 2929, 2854, 1599, 1552, 1495, 1449, 1351, 1159, 1093, 1011, 814, 702, 670;

MS (ESI): *m/z* 441.2 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{24}H_{28}N_2NaO_4S$ [(M + Na)$^+$], 463.1662; found 463.1685.

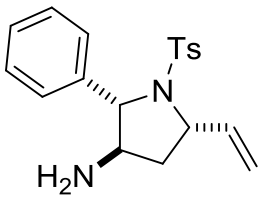
Synthetic Elaboration of Pyrrolidine 5a

Synthesis and characterisation of *rac*-(2*R*,5*S*)-1-[(4-methylphenyl)sulfonyl]-2-phenyl-5-vinylpyrrolidine (6)



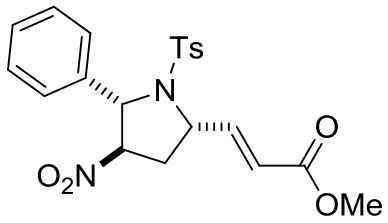
Compound **6** was prepared according to a literature procedure described by Ono.[6] To a solution of **5a** (37.2 mg, 0.100 mmol) in PhMe (2.5 mL) in a microwave vial at RT was added AIBN (3.3 mg, 0.020 mmol) and Bu_3SnH (146 mg, 0.500 mmol, 135 μL). The resulting mixture was degassed and flushed with nitrogen several times (ca. × 5), then rapidly heated to 120 °C and stirred for 2.5 h. The reaction mixture was allowed to cool to RT and then directly purified by flash column chromatography eluting with PE/EtOAc (9:1) to yield **6** (17 mg, 53%, dr 96:4) as a colourless oil. On standing the product crystallised into a white solid. **TLC**: R_f = 0.29 (PE/EtOAc 9:1, UV, $KMnO_4$); **Melting Point**: 69 - 71 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ_H 7.65 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.38 - 7.21 (m, 7H, Ar**H**), 6.02 (ddd, *J* = 17.0, 10.5, 6.5 Hz, 1H, C**H**=CH_2), 5.35 (dt, *J* = 17.5, 1.0 Hz, 1H, CH=CH_{cis}**H**$_{\boldsymbol{trans}}$), 5.21 (dt, *J* = 10.5, 1.0 Hz, 1H, CH=C**H**$_{\boldsymbol{cis}}$$H_{trans}$), 4.83 (t, *J* = 6.5 Hz, 1H, C**H**N), 4.34 (q, *J* = 6.5 Hz, 1H, NC**H**CH=CH_2), 2.43 (s, 3H, ArC**H**$_3$), 2.04 - 1.95 (m, 1H, PhCHC**H**H′CHH′), 1.92 - 1.72 (m, 3H, PhCHCH**H′**C**HH′**); **^{13}C NMR** (125 MHz, $CDCl_3$): δ_C 143.2 (Ar**C**), 142.4 (Ar**C**), 139.0 (**C**H=CH_2), 135.5 (Ar**C**), 129.4 (2 × Ar**C**H), 128.2 (2 × Ar**C**H), 127.7 (2 × Ar**C**H), 127.1 (Ar**C**H), 126.5 (2 × Ar**C**H), 116.1 (CH=**C**H_2), 64.9 (**C**HN), 63.6 (N**C**HCH=CH_2), 34.5 (PhCH**C**H_2CH_2), 30.9 (PhCHCH_2**C**H_2), 21.5 (Ar**C**H_3); **MS** (ESI): *m/z* 350.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{21}NNaO_2S$ [(M + Na)$^+$], 350.1185; found 350.1171. Data was in accordance with that reported in the literature.[7]

Synthesis and characterisation of *rac*-(2*S*,3*R*,5*S*)-1-[(4-methylphenyl)sulfonyl]-2-phenyl-5-vinylpyrrolidin-3-amine (7)



Compound **7** was prepared according to a literature procedure described by Takemoto.[8] To a stirred solution of **5a** (37.2 mg, 0.100 mmol) in THF (1.0 mL) at RT was added zinc powder (157 mg, 2.40 mmol) and acetic acid (0.3 mL). The resulting mixture was stirred at RT for 36 h. The reaction was quenched with sat. aq. $NaHCO_3$ (30 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with CH_2Cl_2/MeOH (97:3) to yield **7** (30 mg, 88%, dr 94:6) as an off-white solid. **TLC**: R_f = 0.28 (CH_2Cl_2/MeOH 97:3, UV, $KMnO_4$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.60 (AA′, part of AA′BB′ system, *J* = 8.5 Hz, 2H, Ar**H**), 7.37 - 7.20 (m, 7H, Ar**H**), 6.02 (ddd, *J* = 17.0, 10.5, 6.5 Hz, 1H, C**H**=CH_2), 5.38 (dt, *J* = 17.0, 1.0 Hz, 1H, CH=CH_{cis}**H_{trans}**), 5.23 (dt, *J* = 10.5, 1.0 Hz, 1H, CH=C**H_{cis}**H_{trans}), 4.55 (q, *J* = 6.5 Hz, 1H, C**H**NH_2), 4.38 (d, *J* = 5.0 Hz, 1H, C**H**N), 3.44 - 3.34 (m, 1H, NC**H**CH=CH_2), 2.40 (s, 3H, ArC**H_3**), 2.25 (br s, 2H, N**H_2**), 2.01 (dt, *J* = 13.0, 5.5 Hz, 1H, C**H**H′), 1.83 - 1.72 (m, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 143.4 (Ar**C**), 139.9 (Ar**C**), 138.7 (**C**H=CH_2), 135.3 (Ar**C**), 129.4 (2 × Ar**C**H), 128.4 (2 × Ar**C**H), 127.7 (2 × Ar**C**H), 127.6 (Ar**C**H), 126.8 (2 × Ar**C**H), 116.3 (CH=**C**H_2), 72.8 (**C**HNH_2), 61.1 (**C**HN), 59.3 (N**C**HCH=CH_2), 38.5 (**C**H_2), 21.5 (Ar**C**H_3); **IR** (film/cm^{-1}): ν_{max} 3375, 3063, 3030, 2926, 1598, 1494, 1451, 1342, 1156, 1092, 1004, 921; **MS** (ESI): *m/z* 343.2 [(M + H)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{19}H_{23}N_2O_2S$ [(M + H)$^+$], 343.1475; found 343.1472.

Synthesis and characterisation of *rac*-methyl (2*E*)-3-{(2*S*,4*R*,5*S*)-1-[(4-methylphenyl)sulfonyl]-4-nitro-5-phenylpyrrolidin-2-yl}acrylate (8)



To a stirred solution of **5a** (37.2 mg, 0.100 mmol) in CH_2Cl_2 (1.0 mL) at RT in a sealable vial was added methyl arcylate (34.4 mg, 0.400 mmol, 36.0 uL) Hoveyda Grubbs II catalyst (3.20 mg, 0.005 mmol). The resulting mixture was heated to 45 °C for 24 h. The reaction mixture was allowed to cool to RT and then directly purified by flash column chromatography eluting with PE/EtOAc (4:1) to yield **8** (32 mg, 74%, dr 97:3) as a white solid. **TLC**: R_f = 0.18 (PE/EtOAc 4:1, UV, $KMnO_4$); **Melting Point**: 177 - 179 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H 7.63 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.49 - 7.29 (m, 7H, Ar**H**), 7.08 (dd, *J* = 15.5, 7.5 Hz, 1H, C**H**=CHCO$_2$), 6.12 (d, *J* = 15.5 Hz, 1H, CH=C**H**CO$_2$), 5.58 (s, 1H, C**H**N), 4.73 (d, *J* = 5.5 Hz, 1H, C**H**NO$_2$), 4.54 - 4.44 (m, 1H, NC**H**CH=CH), 3.81 (s, 3H, CO$_2$C**H$_3$**), 2.66 (dd, *J* = 14.5, 7.0 Hz, 1H, C**H**H′), 2.46 (s, 3H, ArC**H$_3$**), 2.24 - 2.12 (m, 1H, CH**H′**); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C 166.0 (**C**=O), 145.9 (**C**H=CHCO$_2$), 144.6 (Ar**C**), 138.3 (Ar**C**), 133.5 (Ar**C**), 129.8 (2 × Ar**C**H), 129.1 (2 × Ar**C**H), 128.6 (Ar**C**H), 127.7 (2 × Ar**C**H), 126.0 (2 × Ar**C**H), 123.4 (CH=**C**HCO$_2$), 89.9 (**C**HNO$_2$), 69.1 (**C**HN), 60.3 (N**C**HCH=CH), 51.9 (CO$_2$**C**H$_3$), 34.5 (**C**H$_2$), 21.6 (Ar**C**H$_3$); **IR** (film/cm^{-1}): ν_{max} 3034, 2952, 1706, 1495, 1355, 1333, 1112, 1096, 1012, 825, 737, 672; **MS** (ESI): *m/z* 453.1 [(M + Na)$^+$]; **HRMS** (ESI): exact mass calculated for $C_{21}H_{22}N_2NaO_6S$ [(M + Na)$^+$], 453.1091; found 453.1086.

Assignment of Stereochemistry

The relative stereochemistry of compound **5a** was determined by nOe analysis and single crystal X-Ray analysis, all other major pyrrolidine diastereomers **5** were assigned by analogy. The relative stereochemistry of compound **5k** was assigned by nOe analysis and by comparison of the ^{1}H NMR spectrum with that of compound **5a**, giving further supporting evidence for the relative stereochemistry of compounds **5**. The relative stereochemistry of compound **5k′** was assigned by nOe analysis and by comparison of the ^{1}H NMR spectrum with that of compound **5a** and **5k**, all other minor pyrrolidine diastereomers **5′** were assigned by analogy.

The relative stereochemistry of compound **4** was determined by nOe analysis and by comparison of the ^{1}H NMR spectrum with that of compound **5a** and similar compounds reported in the literature.[9] The relative stereochemistry of compounds **3** and **3′** were assigned by analogy to compound **4**.

The relative stereochemistry of compounds **6**, **7** and **8** were assigned by analogy to the nOe analysis and single crystal X-Ray analysis of compound **5a**.

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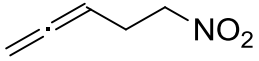
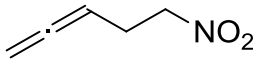
^{1}H NMR of compound **2a**



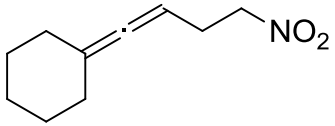
400 MHz, $CDCl_3$

^{13}C NMR of compound **2a**



100 MHz, $CDCl_3$

^{1}H NMR of compound **2b**



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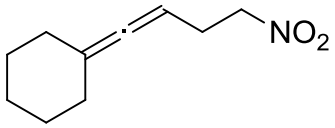
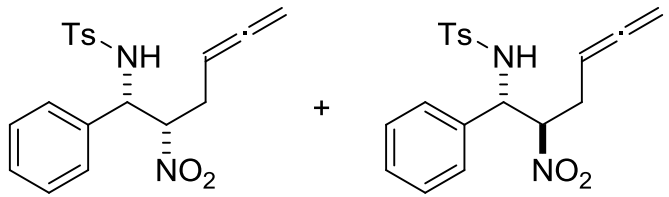
^{13}C NMR of compound **2b**



100 MHz, $CDCl_3$

^{1}H NMR of compound **3**



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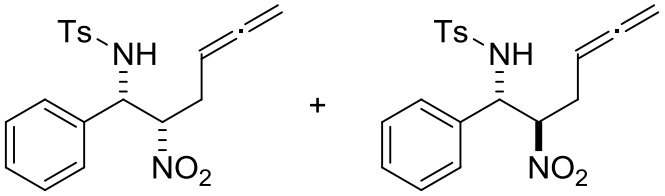
^{13}C NMR of compound **3**



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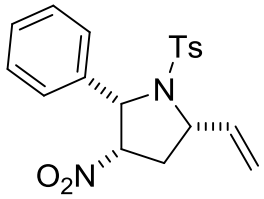
^{1}H NMR of compound **4**



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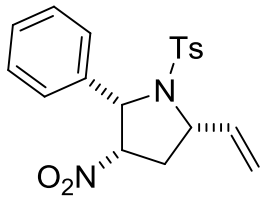
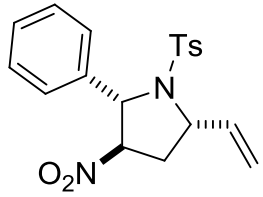
^{13}C NMR of compound **4**



100 MHz, $CDCl_3$

^{1}H NMR of compound **5a**



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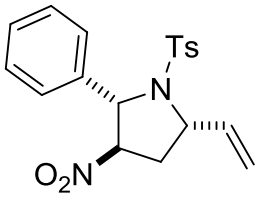
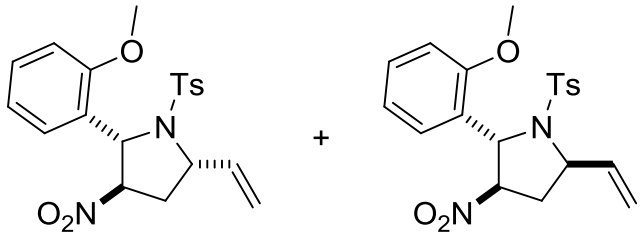


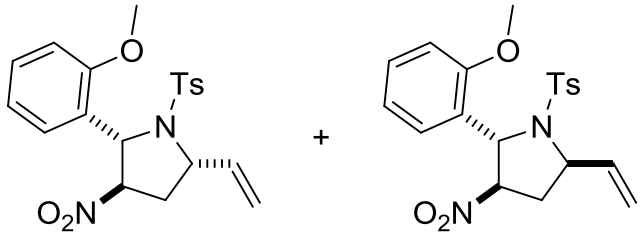
100 MHz, $CDCl_3$

^{1}H NMR of compounds **5b** and **5b′**



400 MHz, $CDCl_3$

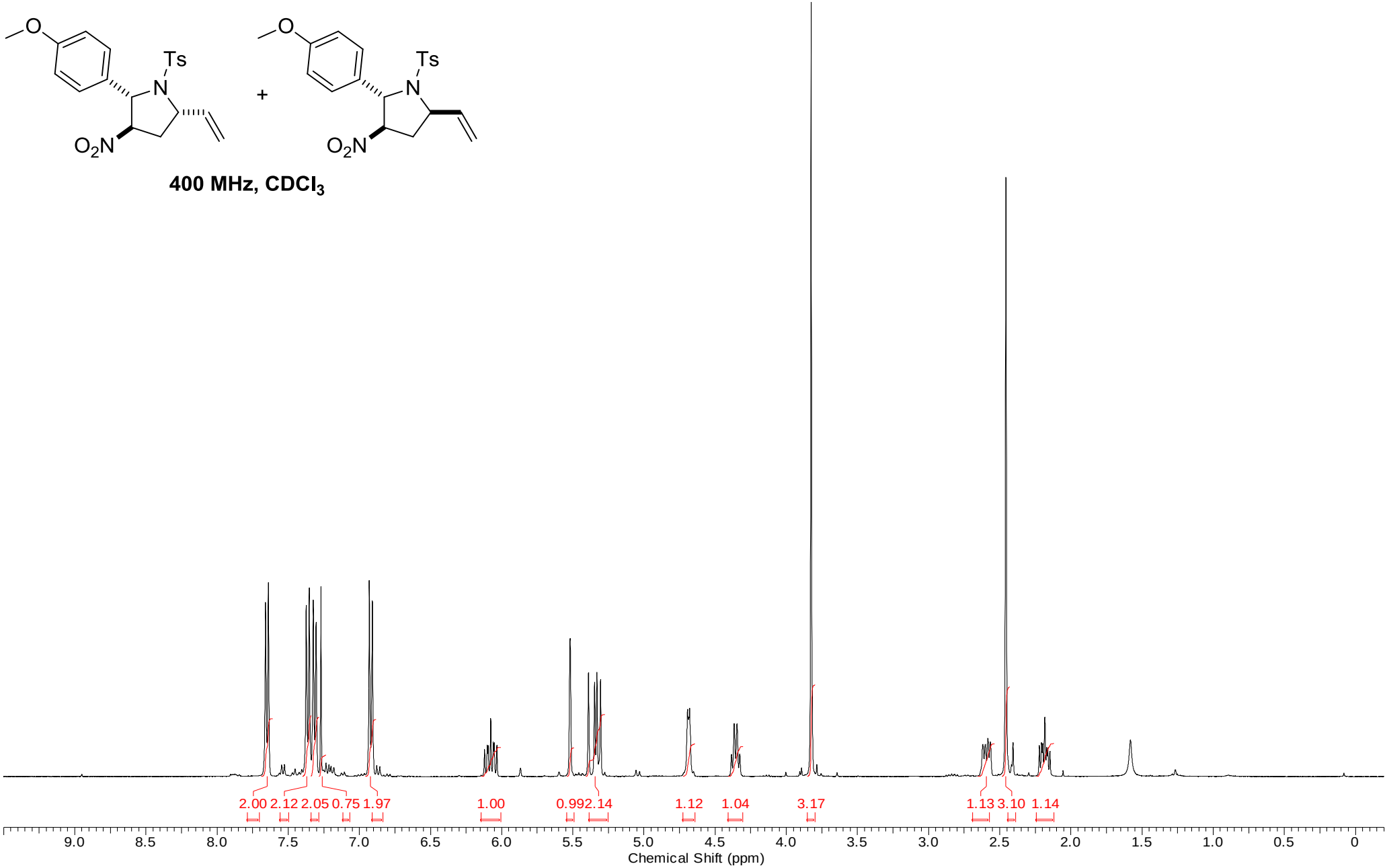
^{13}C NMR of compounds **5b** and **5b′**



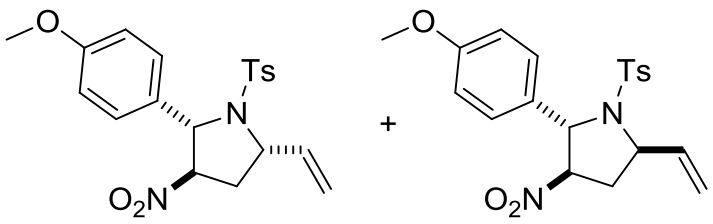
+

100 MHz, $CDCl_3$

^{1}H NMR of compounds **5c** and **5c′**



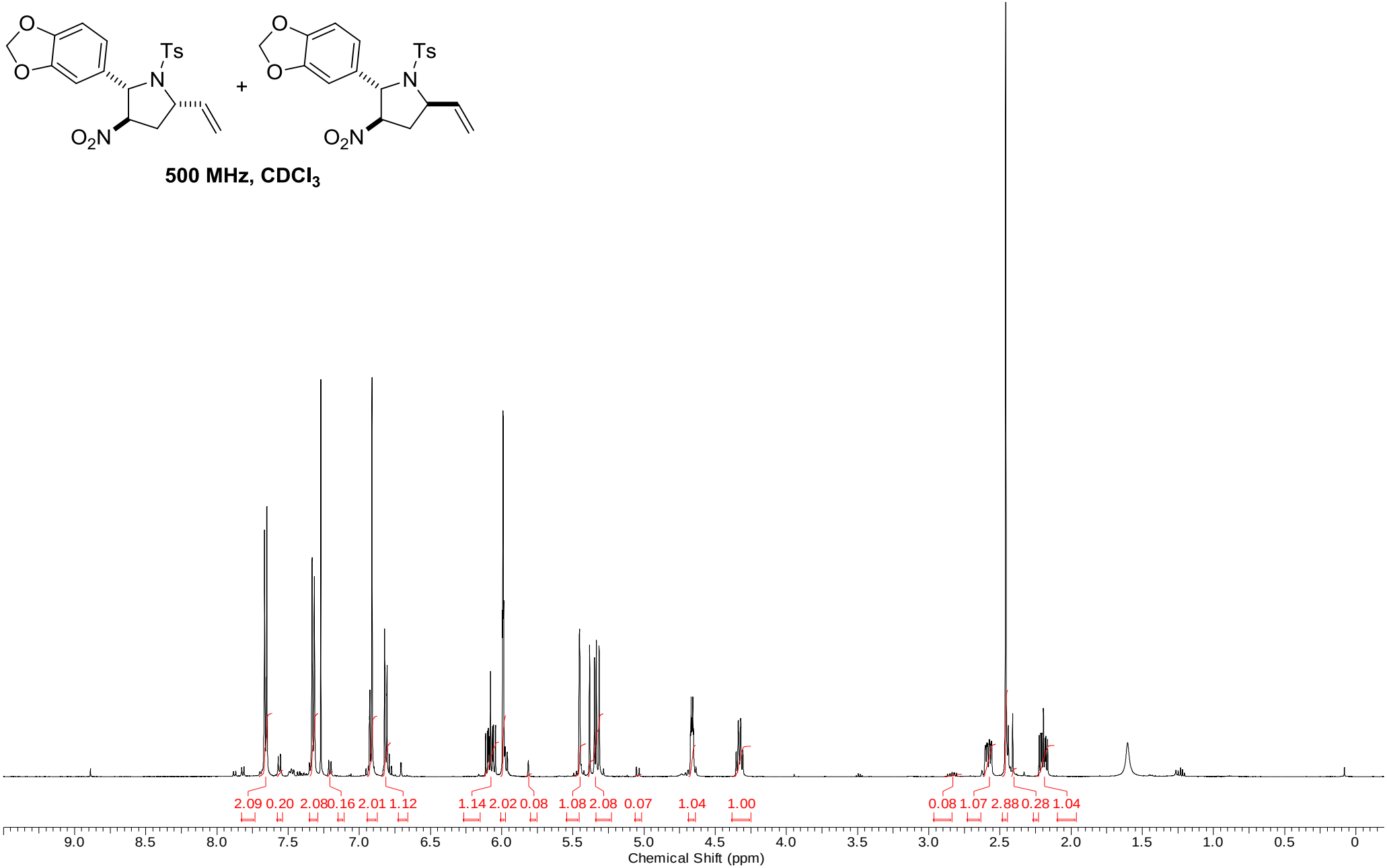
^{13}C NMR of compounds **5c** and **5c′**



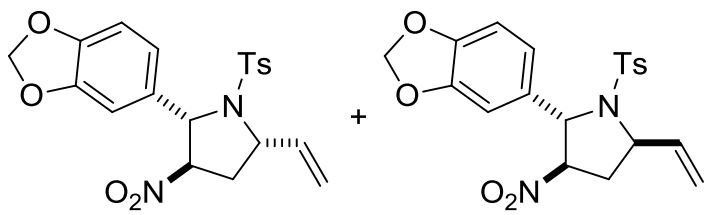
+

100 MHz, $CDCl_3$

^{1}H NMR of compounds **5d** and **5d′**



^{13}C NMR of compounds **5d** and **5d′**



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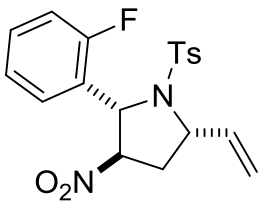

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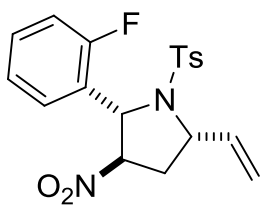
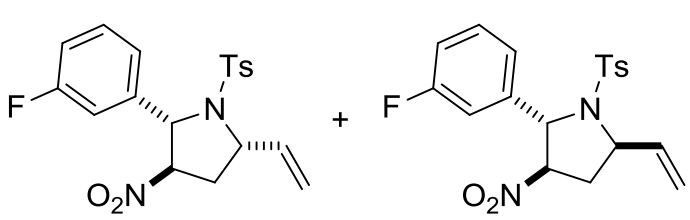
^{13}C NMR of compound **5e**



100 MHz, $CDCl_3$

^{1}H NMR of compounds **5f** and **5f′**



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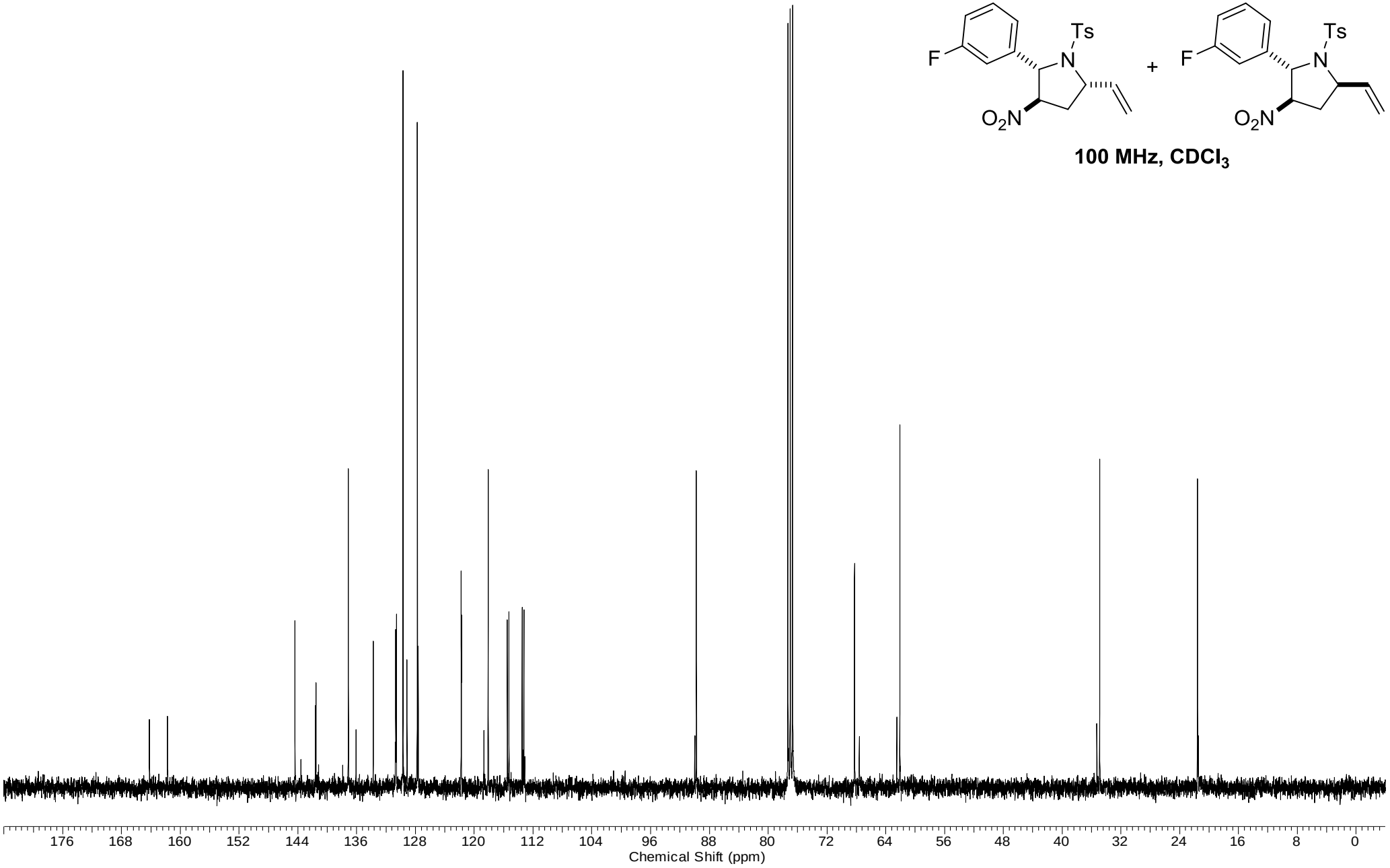
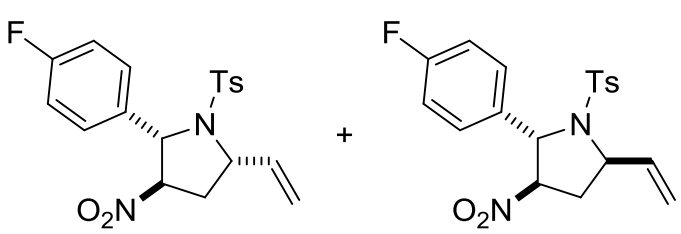


^{1}H NMR of compounds **5g** and **5g′**



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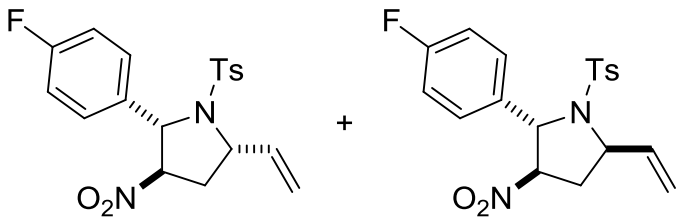
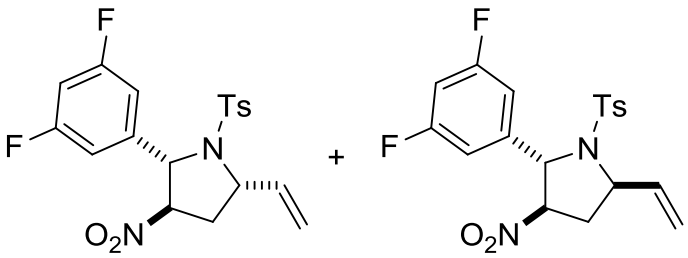
^{13}C NMR of compounds **5g** and **5g′**



125 MHz, $CDCl_3$

^{1}H NMR of compounds **5h** and **5h′**



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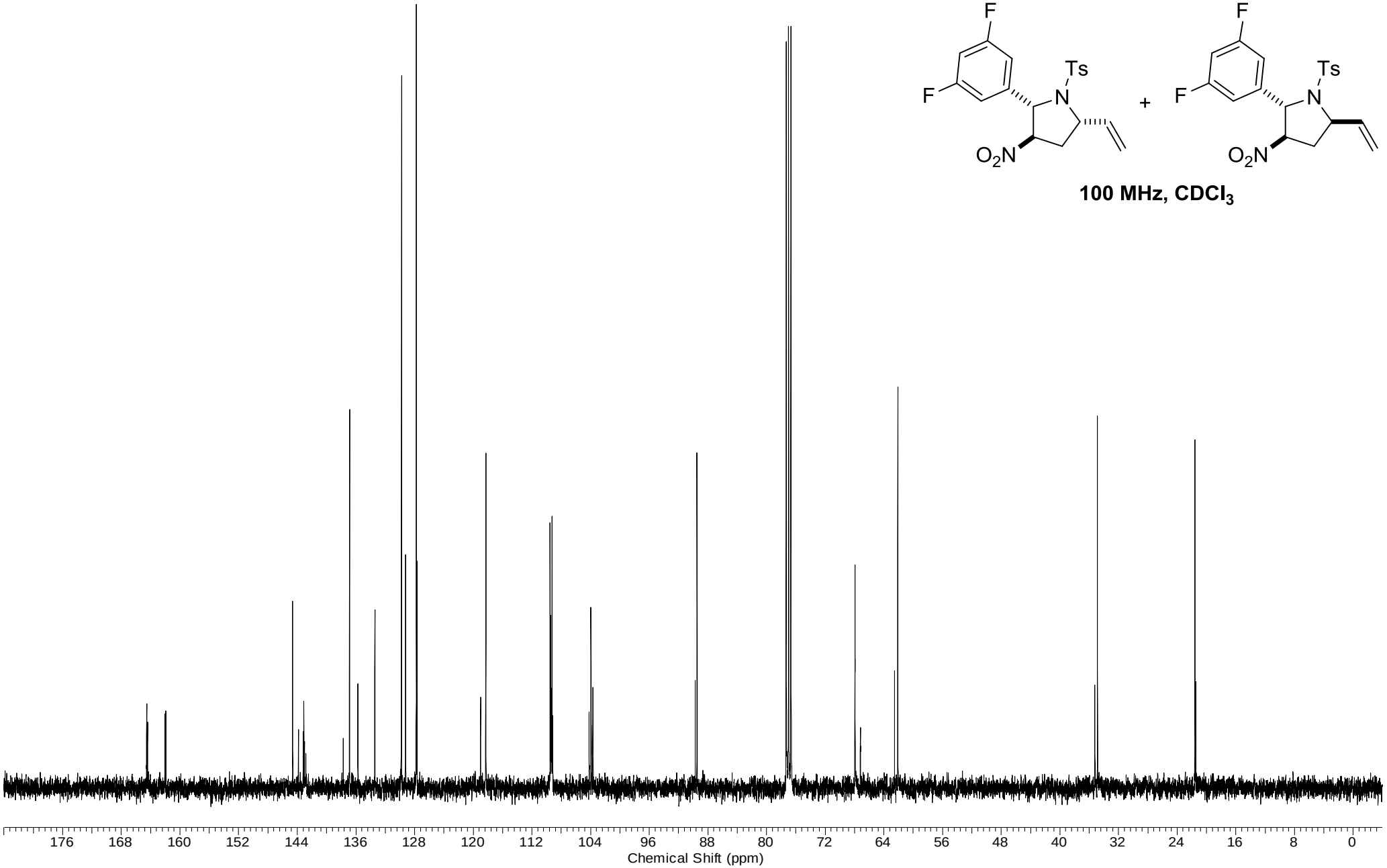
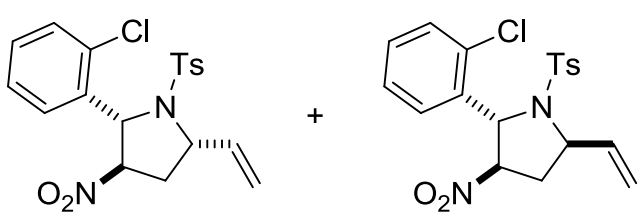
^{13}C NMR of compounds **5h** and **5h′**



^{1}H NMR of compounds **5i** and **5i′**



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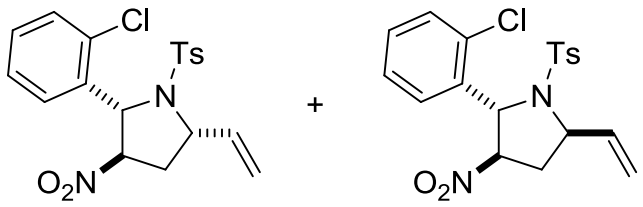
^{13}C NMR of compounds **5i** and **5i′**



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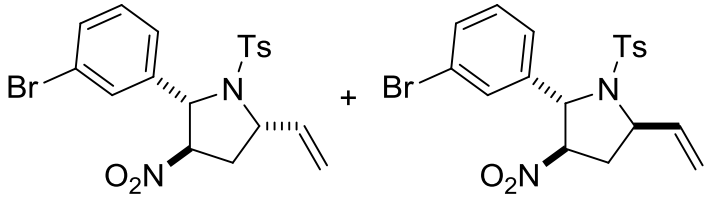
^{1}H NMR of compounds **5j** and **5j′**



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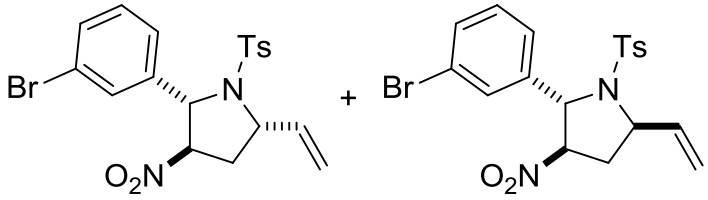
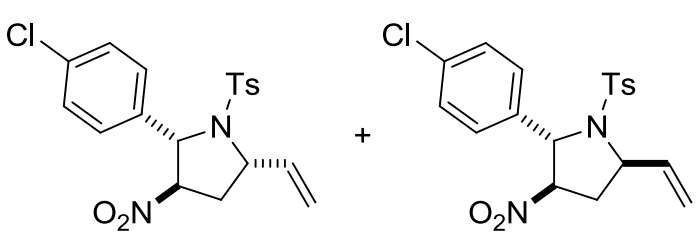
^{13}C NMR of compounds **5j** and **5j′**



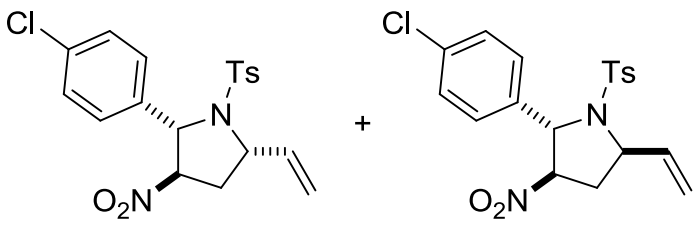
100 MHz, $CDCl_3$

^{1}H NMR of compounds **5k** and **5k′**



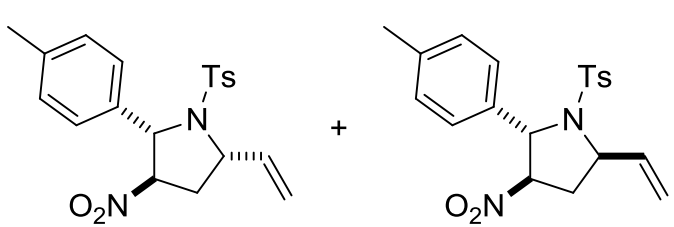
400 MHz, $CDCl_3$

^{13}C NMR of compounds **5k** and **5k′**



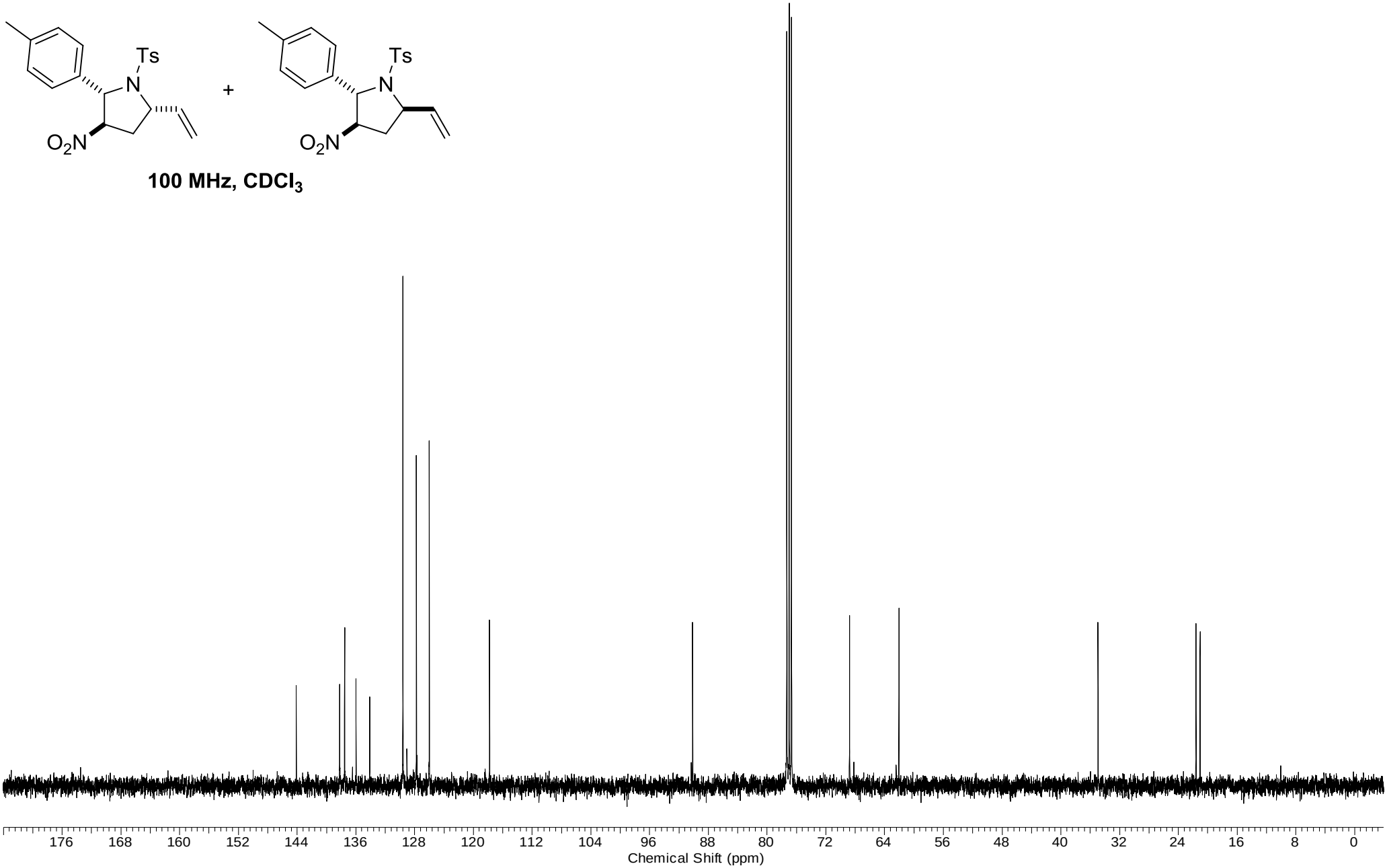
100 MHz, $CDCl_3$

^{1}H NMR of compounds **5l** and **5l′**

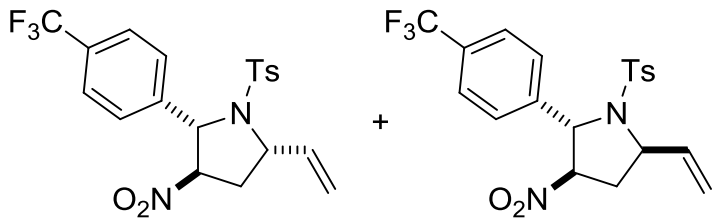


400 MHz, $CDCl_3$

^{13}C NMR of compounds **5l** and **5l′**

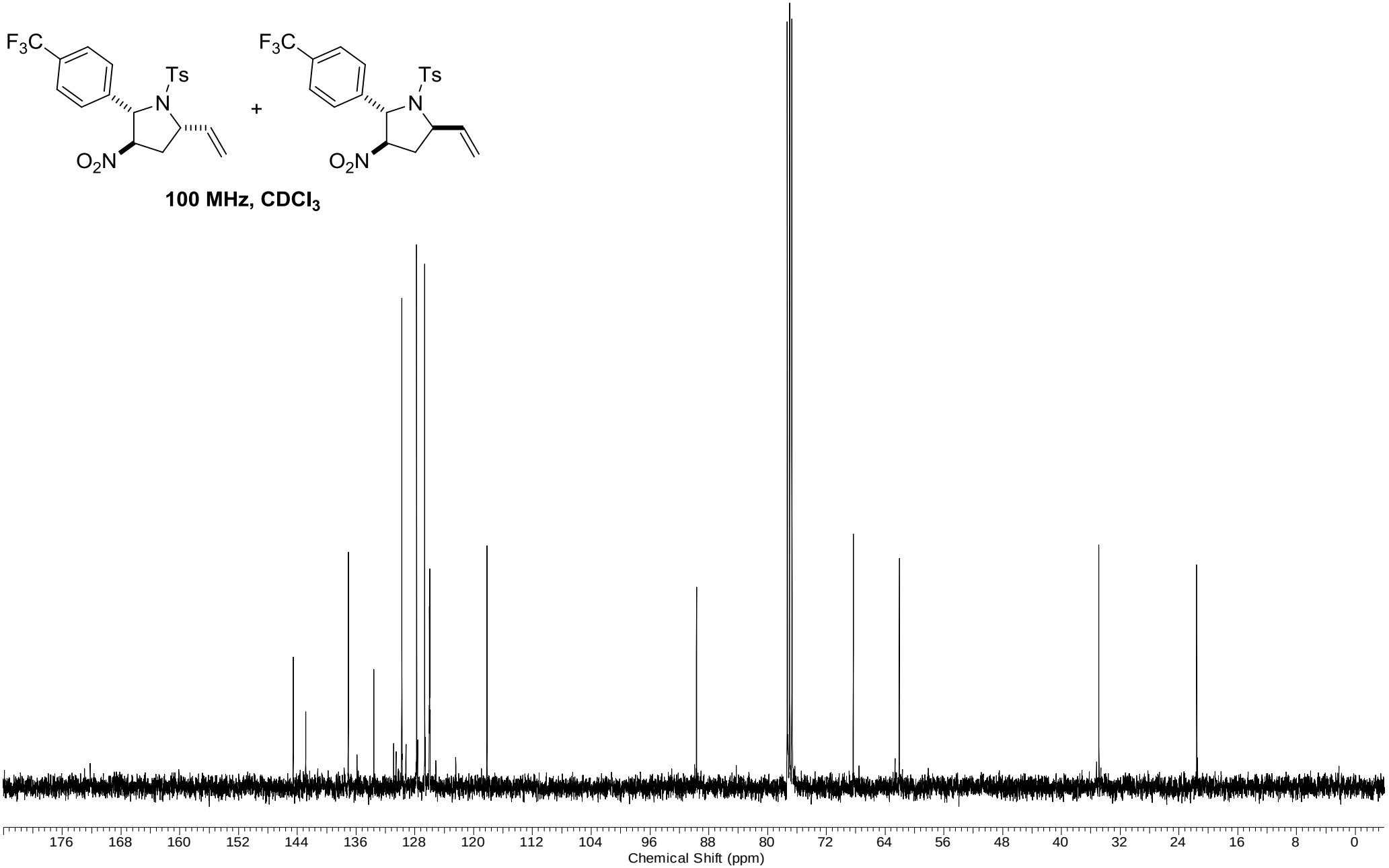


^{1}H NMR of compounds **5m** and **5m′**

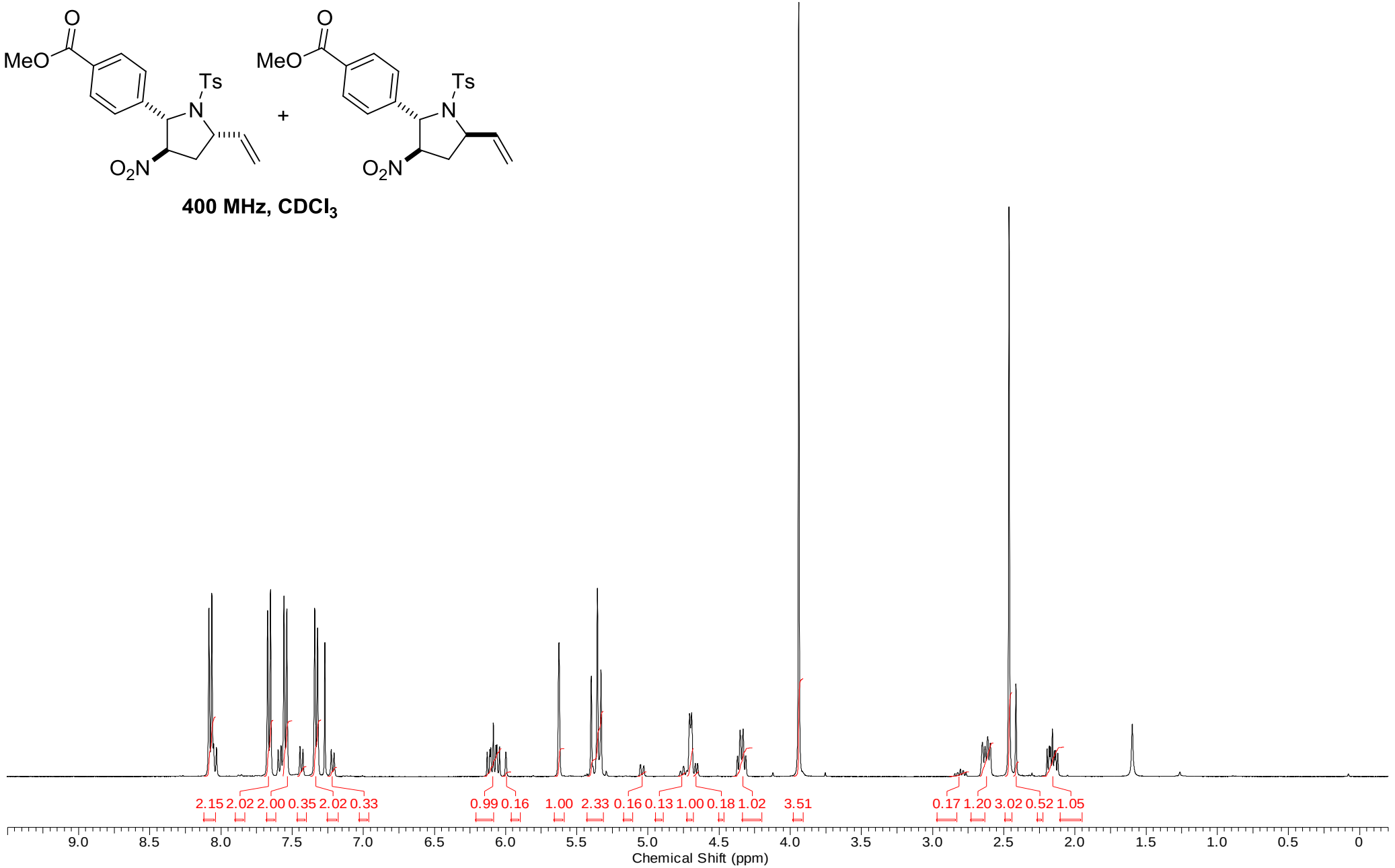


400 MHz, $CDCl_3$

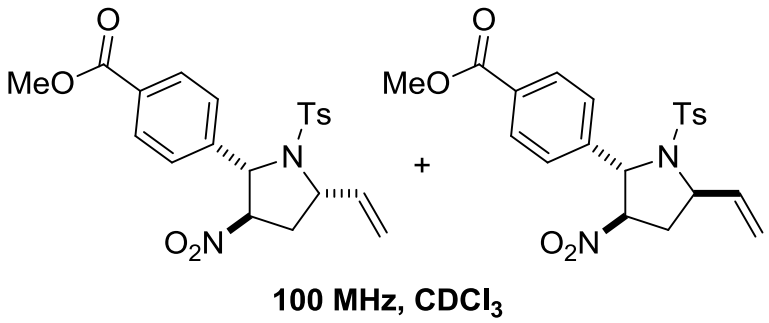
^{13}C NMR of compounds **5m** and **5m′**



^{1}H NMR of compounds **5n** and **5n′**

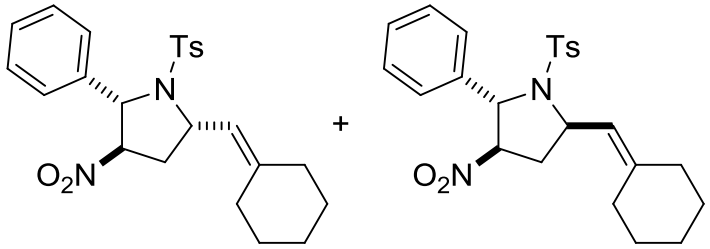


^{13}C NMR of compounds **5n** and **5n′**



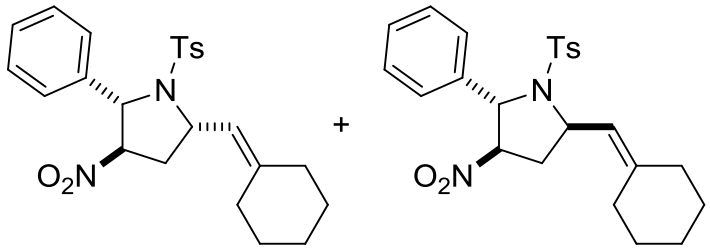
100 MHz, $CDCl_3$

^{1}H NMR of compounds **5o and 5o′**



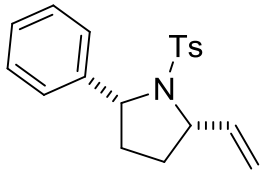
500 MHz, $CDCl_3$

^{13}C NMR of compounds **5o** and **5o′**



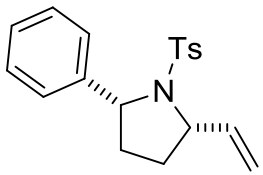
125 MHz, $CDCl_3$

^{1}H NMR of compound **6**



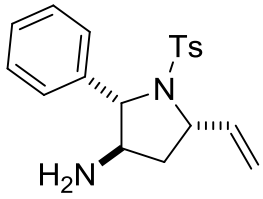
500 MHz, $CDCl_3$

^{13}C NMR of compound **6**



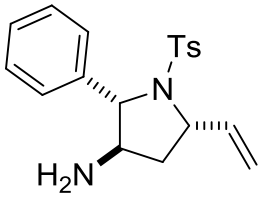
125 MHz, $CDCl_3$

^{1}H NMR of compound **7**



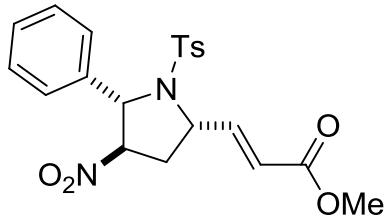
400 MHz, $CDCl_3$

^{13}C NMR of compound **7**



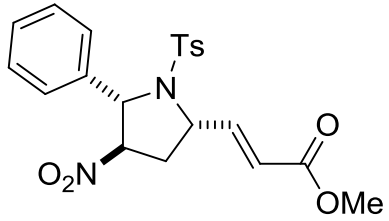
100 MHz, $CDCl_3$

^{1}H NMR of compound **8**



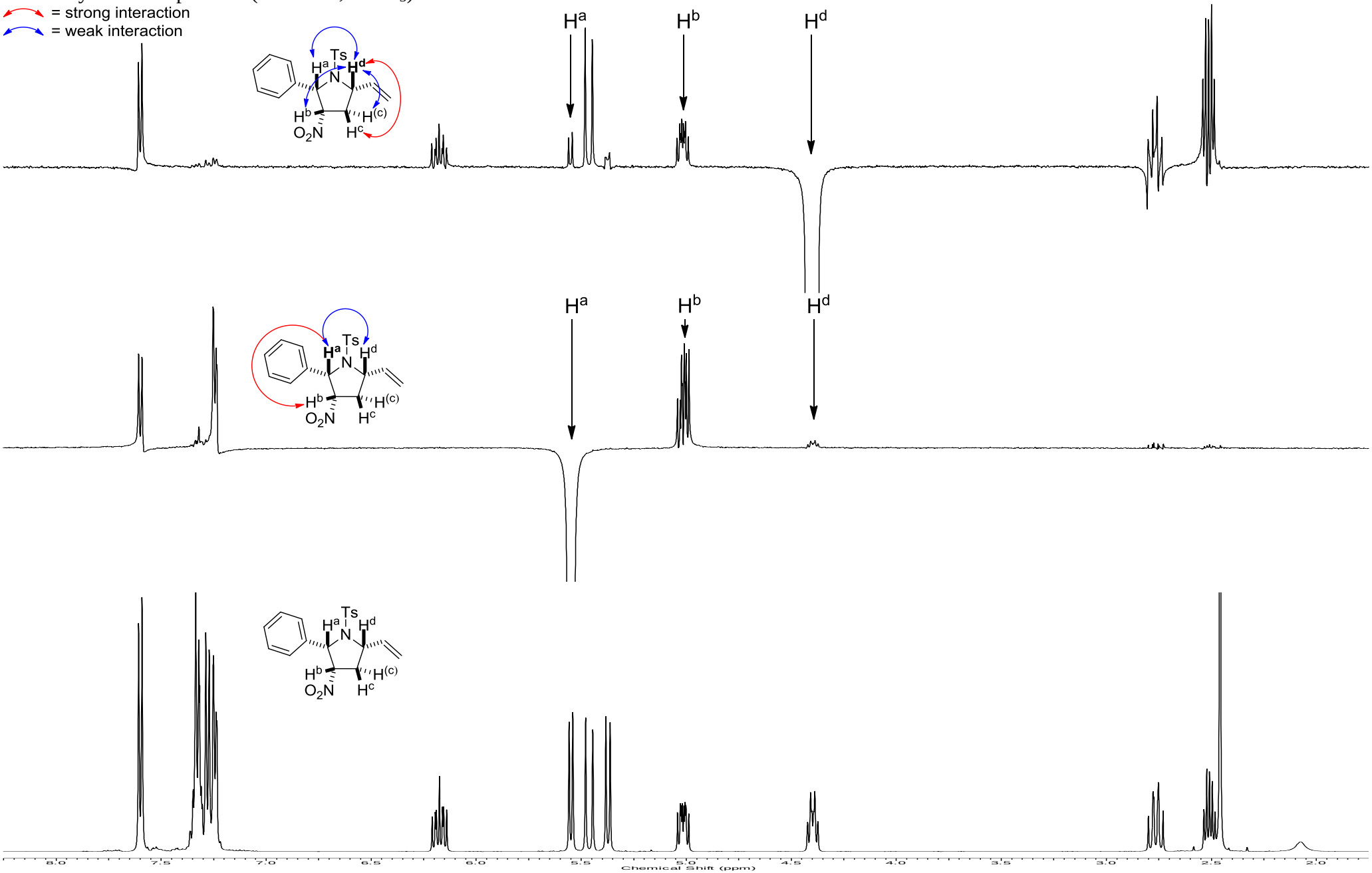
400 MHz, $CDCl_3$

^{13}C NMR of compound **8**

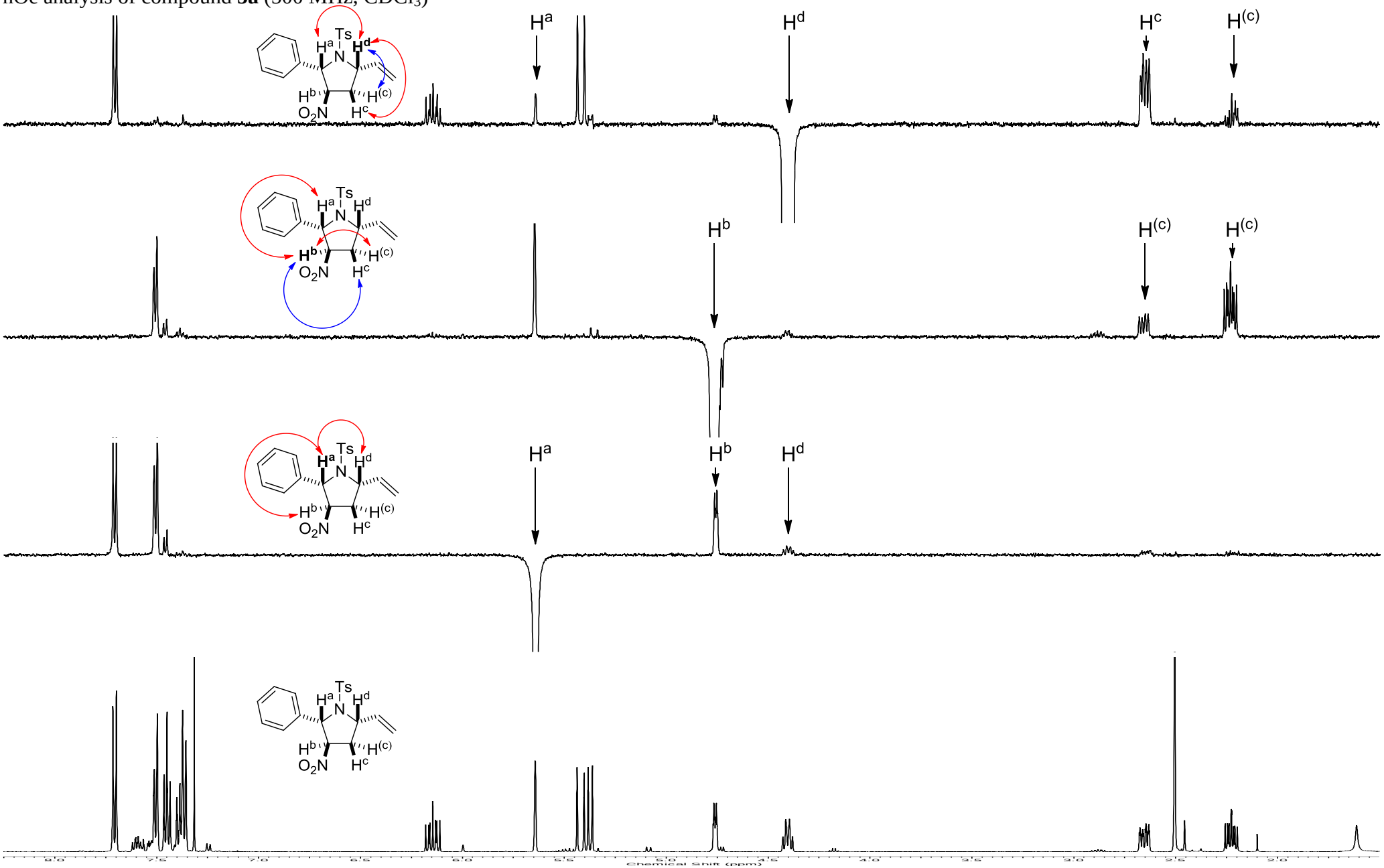


100 MHz, $CDCl_3$

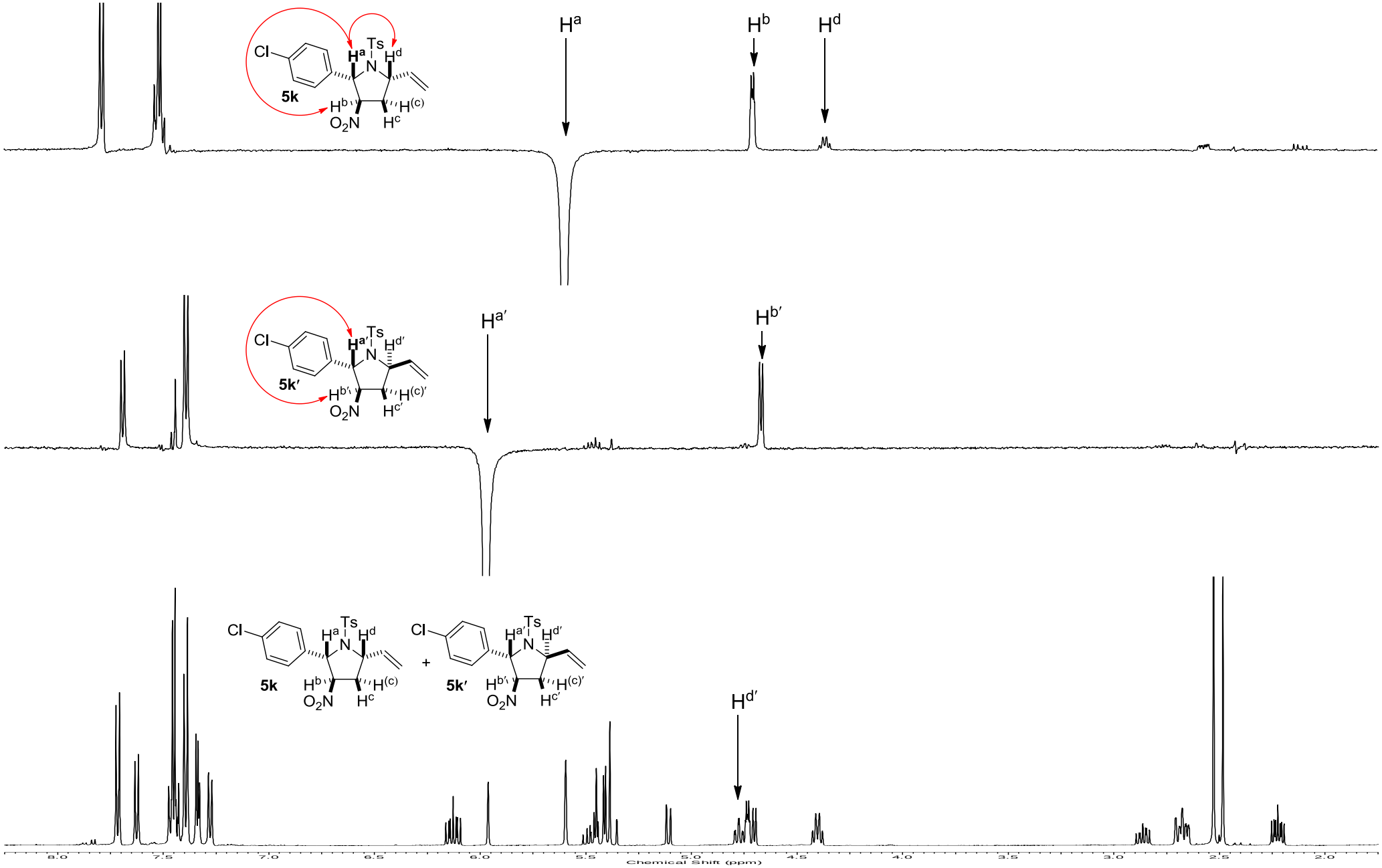
nOe analysis of compound **4** (500 MHz, $CDCl_3$)



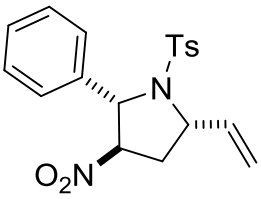
nOe analysis of compound **5a** (500 MHz, $CDCl_3$)

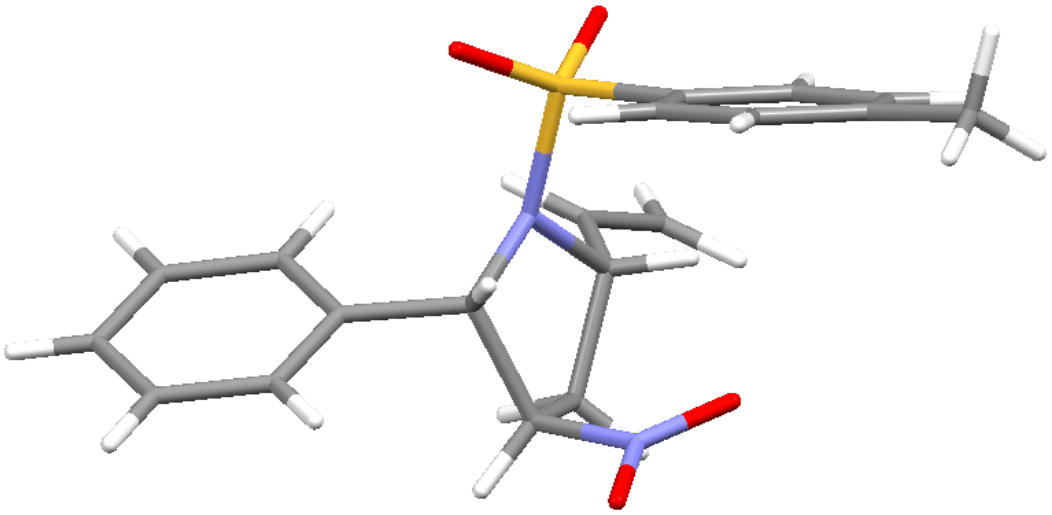


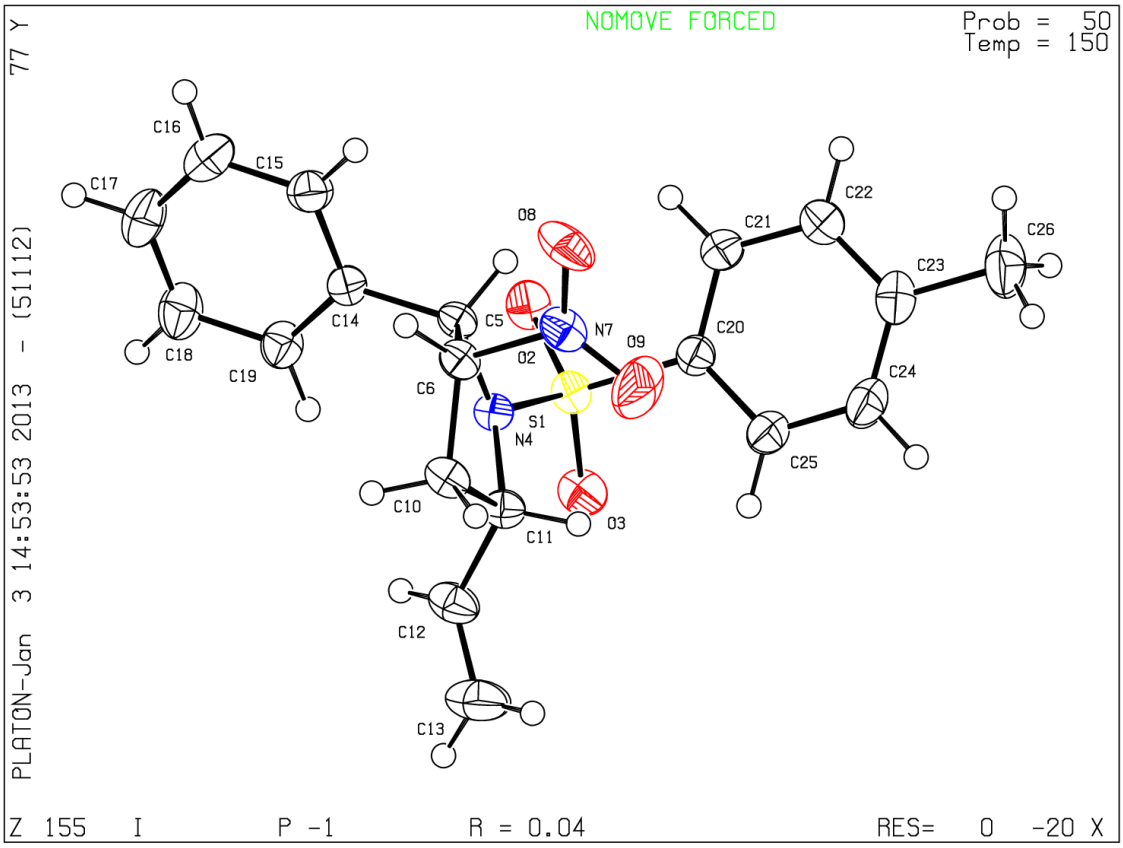
nOe analysis of compounds **5k** and **5k′** (500 MHz, $CDCl_3$)



X-Ray data for compound **5a**







Crystal data

$C_{19}H_{20}N_2O_4S$	Z = 2
M_r = 372.44	F(000) = 392
Triclinic, $P\bar{1}$	D_x = 1.367 Mg m^{-3}
Hall symbol: -P 1	Melting point: not measured K
a = 7.4965 (2) Å	Mo $K\alpha$ radiation, λ = 0.71073 Å
b = 10.6303 (2) Å	Cell parameters from 3794 reflections
c = 11.6630 (3) Å	θ = 5–27°
α = 100.5307 (9)°	μ = 0.21 mm^{-1}
β = 94.2654 (9)°	T = 150 K
γ = 96.0409 (10)°	Block, Colourless
V = 904.52 (4) Å^3	0.60 × 0.40 × 0.40 mm

Data collection

Nonius KappaCCD diffractometer	3495 reflections with $I > 2.0\sigma(I)$
Graphite monochromator	R_{int} = 0.020
ω scans	θ_{max} = 27.5°, θ_{min} = 5.3°
Absorption correction: Multi-scan *DENZO*/*SCALEPACK* (Otwinowski & Minor, 1997)	h = –8→9
T_{min} = 0.71, T_{max} = 0.92	k = –13→13
14483 measured reflections	l = –15→15
4113 independent reflections	

Refinement

Refinement on F^2	Primary atom site location: Structure-invariant direct methods
Least-squares matrix: Full	Hydrogen site location: Difference Fourier map
$R[F^2 > 2\sigma(F^2)]$ = 0.044	H-atom parameters constrained
$wR(F^2)$ = 0.120	Method, part 1, Chebychev polynomial, (Watkin, 1994, *P*rince, 1982) [*w*eight] = 1.0/[A_0*T_0(x) + A_1*T_1(x) ⋯ + A_{n-1}]*T_{n-1}(x)] where A_i are the Chebychev coefficients listed below and x = *F* /*F*max Method = Robust Weighting (*P*rince, 1982) W = [*w*eight] * [1-(delta*F*/6*sigma*F*)^2]^2 A_i are: 44.2 71.4 41.9 17.3 4.09
S = 0.93	$(\Delta/\sigma)_{max}$ = 0.0003
4112 reflections	$\Delta\rho_{max}$ = 0.42 e Å^{-3}
235 parameters	$\Delta\rho_{min}$ = –0.45 e Å^{-3}
0 restraints	

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.55334 (5)	0.12705 (4)	0.26737 (4)	0.0261
O2	0.44650 (16)	0.01585 (12)	0.29030 (11)	0.0332
O3	0.48276 (17)	0.19987 (14)	0.18587 (11)	0.0352
N4	0.73437 (17)	0.07592 (13)	0.21554 (11)	0.0232

C5	0.8258 (2)	−0.01530 (15)	0.27387 (13)	0.0235
C6	1.0281 (2)	0.02994 (16)	0.27095 (14)	0.0254
N7	1.0959 (2)	0.12085 (16)	0.38478 (13)	0.0318
O8	1.1594 (2)	0.07306 (17)	0.46296 (12)	0.0483
O9	1.0835 (3)	0.23438 (16)	0.39365 (16)	0.0750
C10	1.0334 (2)	0.09702 (18)	0.16698 (14)	0.0281
C11	0.8593 (2)	0.16147 (17)	0.16200 (14)	0.0263
C12	0.7924 (2)	0.1680 (2)	0.03847 (16)	0.0350
C13	0.8470 (3)	0.2623 (3)	−0.0141 (2)	0.0534
C14	0.7812 (2)	−0.15481 (16)	0.21057 (14)	0.0256
C15	0.8396 (3)	−0.25086 (18)	0.26582 (17)	0.0339
C16	0.8040 (3)	−0.37917 (19)	0.2100 (2)	0.0420
C17	0.7120 (3)	−0.41260 (19)	0.0986 (2)	0.0440
C18	0.6545 (3)	−0.3175 (2)	0.04399 (19)	0.0419
C19	0.6880 (2)	−0.18887 (18)	0.09974 (16)	0.0325
C20	0.6147 (2)	0.23403 (16)	0.40182 (15)	0.0269
C21	0.6072 (3)	0.18978 (18)	0.50645 (16)	0.0336
C22	0.6499 (3)	0.27649 (19)	0.61211 (17)	0.0382
C23	0.7021 (3)	0.40646 (19)	0.61478 (18)	0.0379
C24	0.7120 (3)	0.44856 (18)	0.50867 (19)	0.0425
C25	0.6664 (3)	0.36374 (18)	0.40225 (18)	0.0372
C26	0.7405 (4)	0.5001 (2)	0.7306 (2)	0.0528
H51	0.7955	−0.0083	0.3545	0.0284*
H61	1.1014	−0.0420	0.2665	0.0304*
H101	1.1411	0.1601	0.1720	0.0334*
H102	1.0285	0.0298	0.0953	0.0338*
H111	0.8797	0.2490	0.2103	0.0318*
H121	0.7070	0.0986	−0.0043	0.0440*
H131	0.9335	0.3335	0.0290	0.0686*
H132	0.8028	0.2606	−0.0915	0.0676*
H151	0.9039	−0.2271	0.3425	0.0421*
H161	0.8454	−0.4449	0.2498	0.0517*
H171	0.6885	−0.5013	0.0596	0.0529*
H181	0.5893	−0.3398	−0.0315	0.0504*
H191	0.6434	−0.1227	0.0619	0.0397*
H211	0.5733	0.0990	0.5042	0.0404*
H221	0.6435	0.2463	0.6852	0.0459*
H241	0.7499	0.5378	0.5085	0.0499*
H251	0.6665	0.3934	0.3284	0.0451*
H263	0.8326	0.5684	0.7229	0.0796*
H262	0.7848	0.4570	0.7904	0.0788*
H261	0.6320	0.5359	0.7507	0.0795*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.01957 (19)	0.0305 (2)	0.0275 (2)	0.00296 (14)	0.00305 (14)	0.00384 (15)
O2	0.0235 (6)	0.0347 (7)	0.0381 (7)	−0.0047 (5)	0.0067 (5)	0.0018 (5)
O3	0.0282 (6)	0.0459 (8)	0.0347 (7)	0.0145 (5)	0.0015 (5)	0.0111 (6)
N4	0.0197 (6)	0.0263 (7)	0.0245 (6)	0.0039 (5)	0.0026 (5)	0.0066 (5)

C5	0.0218 (7)	0.0286 (8)	0.0199 (7)	0.0022 (6)	−0.0005 (5)	0.0053 (6)
C6	0.0209 (7)	0.0310 (8)	0.0227 (7)	0.0012 (6)	−0.0025 (6)	0.0041 (6)
N7	0.0251 (7)	0.0408 (8)	0.0259 (7)	−0.0048 (6)	−0.0034 (5)	0.0043 (6)
O8	0.0515 (9)	0.0724 (11)	0.0224 (6)	0.0138 (8)	−0.0018 (6)	0.0115 (6)
O9	0.1239 (19)	0.0343 (8)	0.0523 (10)	−0.0038 (10)	−0.0360 (11)	−0.0043 (7)
C10	0.0209 (7)	0.0390 (9)	0.0250 (8)	0.0031 (6)	0.0026 (6)	0.0077 (7)
C11	0.0213 (7)	0.0302 (8)	0.0285 (8)	0.0025 (6)	0.0050 (6)	0.0082 (6)
C12	0.0313 (9)	0.0494 (11)	0.0295 (9)	0.0135 (8)	0.0061 (7)	0.0147 (8)
C13	0.0573 (14)	0.0679 (15)	0.0500 (13)	0.0250 (12)	0.0176 (10)	0.0356 (12)
C14	0.0222 (7)	0.0269 (8)	0.0272 (8)	0.0009 (6)	0.0032 (6)	0.0044 (6)
C15	0.0362 (9)	0.0338 (9)	0.0336 (9)	0.0056 (7)	0.0042 (7)	0.0103 (7)
C16	0.0428 (11)	0.0300 (9)	0.0558 (12)	0.0050 (8)	0.0073 (9)	0.0135 (9)
C17	0.0402 (11)	0.0277 (9)	0.0587 (13)	−0.0023 (8)	0.0034 (9)	−0.0014 (9)
C18	0.0387 (10)	0.0361 (10)	0.0436 (11)	0.0000 (8)	−0.0078 (8)	−0.0038 (8)
C19	0.0303 (8)	0.0312 (9)	0.0331 (9)	0.0028 (7)	−0.0047 (7)	0.0022 (7)
C20	0.0258 (8)	0.0259 (8)	0.0290 (8)	0.0027 (6)	0.0057 (6)	0.0045 (6)
C21	0.0403 (10)	0.0279 (8)	0.0325 (9)	0.0000 (7)	0.0048 (7)	0.0072 (7)
C22	0.0472 (11)	0.0368 (10)	0.0299 (9)	0.0051 (8)	0.0015 (8)	0.0055 (7)
C23	0.0384 (10)	0.0331 (9)	0.0387 (10)	0.0073 (8)	0.0012 (8)	−0.0028 (8)
C24	0.0533 (12)	0.0243 (9)	0.0480 (11)	0.0013 (8)	0.0084 (9)	0.0023 (8)
C25	0.0474 (11)	0.0273 (9)	0.0385 (10)	0.0042 (8)	0.0122 (8)	0.0073 (7)
C26	0.0624 (14)	0.0429 (12)	0.0448 (12)	0.0117 (10)	−0.0061 (10)	−0.0115 (9)

Geometric parameters (Å, º)

S1—O2	1.4348 (13)	C14—C19	1.390 (2)
S1—O3	1.4364 (13)	C15—C16	1.389 (3)
S1—N4	1.6309 (13)	C15—H151	0.961
S1—C20	1.7591 (17)	C16—C17	1.392 (3)
N4—C5	1.4780 (19)	C16—H161	0.971
N4—C11	1.486 (2)	C17—C18	1.378 (3)
C5—C6	1.547 (2)	C17—H171	0.961
C5—C14	1.521 (2)	C18—C19	1.390 (3)
C5—H51	0.975	C18—H181	0.951
C6—N7	1.511 (2)	C19—H191	0.971
C6—C10	1.516 (2)	C20—C21	1.388 (2)
C6—H61	0.984	C20—C25	1.391 (2)
N7—O8	1.213 (2)	C21—C22	1.391 (3)
N7—O9	1.206 (2)	C21—H211	0.967
C10—C11	1.539 (2)	C22—C23	1.390 (3)
C10—H101	0.985	C22—H221	0.968
C10—H102	0.991	C23—C24	1.395 (3)
C11—C12	1.506 (2)	C23—C26	1.513 (3)
C11—H111	0.986	C24—C25	1.391 (3)
C12—C13	1.314 (3)	C24—H241	0.962
C12—H121	0.959	C25—H251	0.970
C13—H131	0.977	C26—H263	0.969
C13—H132	0.935	C26—H262	0.961
C14—C15	1.394 (2)	C26—H261	0.960
O2—S1—O3	120.16 (8)	C5—C14—C15	118.18 (15)

O2—S1—N4	106.13 (7)	C5—C14—C19	122.41 (15)
O3—S1—N4	105.90 (7)	C15—C14—C19	119.39 (16)
O2—S1—C20	107.83 (8)	C14—C15—C16	119.86 (18)
O3—S1—C20	107.45 (8)	C14—C15—H151	119.3
N4—S1—C20	109.01 (7)	C16—C15—H151	120.9
S1—N4—C5	118.39 (10)	C15—C16—C17	120.48 (19)
S1—N4—C11	120.26 (11)	C15—C16—H161	118.8
C5—N4—C11	113.44 (12)	C17—C16—H161	120.7
N4—C5—C6	103.38 (12)	C16—C17—C18	119.58 (18)
N4—C5—C14	113.25 (12)	C16—C17—H171	120.5
C6—C5—C14	109.97 (13)	C18—C17—H171	119.9
N4—C5—H51	110.5	C17—C18—C19	120.31 (19)
C6—C5—H51	110.6	C17—C18—H181	120.0
C14—C5—H51	109.1	C19—C18—H181	119.6
C5—C6—N7	108.78 (13)	C18—C19—C14	120.37 (18)
C5—C6—C10	104.25 (12)	C18—C19—H191	119.8
N7—C6—C10	112.04 (14)	C14—C19—H191	119.8
C5—C6—H61	112.0	S1—C20—C21	120.19 (13)
N7—C6—H61	105.6	S1—C20—C25	119.34 (14)
C10—C6—H61	114.2	C21—C20—C25	120.45 (17)
C6—N7—O8	116.62 (16)	C20—C21—C22	119.46 (17)
C6—N7—O9	119.42 (15)	C20—C21—H211	119.1
O8—N7—O9	123.96 (17)	C22—C21—H211	121.4
C6—C10—C11	106.01 (13)	C21—C22—C23	121.14 (18)
C6—C10—H101	113.3	C21—C22—H221	119.8
C11—C10—H101	111.5	C23—C22—H221	119.1
C6—C10—H102	107.7	C22—C23—C24	118.50 (17)
C11—C10—H102	108.1	C22—C23—C26	120.3 (2)
H101—C10—H102	110.1	C24—C23—C26	121.17 (19)
C10—C11—N4	101.98 (13)	C23—C24—C25	121.14 (18)
C10—C11—C12	112.06 (14)	C23—C24—H241	119.9
N4—C11—C12	112.53 (14)	C25—C24—H241	119.0
C10—C11—H111	109.9	C20—C25—C24	119.27 (18)
N4—C11—H111	110.4	C20—C25—H251	119.2
C12—C11—H111	109.7	C24—C25—H251	121.5
C11—C12—C13	123.4 (2)	C23—C26—H263	108.9
C11—C12—H121	118.0	C23—C26—H262	110.1
C13—C12—H121	118.6	H263—C26—H262	108.2
C12—C13—H131	119.0	C23—C26—H261	109.1
C12—C13—H132	119.8	H263—C26—H261	109.7
H131—C13—H132	121.2	H262—C26—H261	110.7

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C5—H51···O8^{i}	0.98	2.37	3.235 (3)	148 (1)
C10—H101···O3^{ii}	0.99	2.54	3.408 (3)	147 (1)
C18—H181···O3^{iii}	0.95	2.60	3.301 (3)	131 (1)

Symmetry codes: (i) –*x*+2, –*y*, –*z*+1; (ii) *x*+1, *y*, *z*; (iii) –*x*+1, –*y*, –*z*.