An Asymmetric Pericyclic Cascade Approach to Spirocyclic Oxindoles

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Supplementary Information

1. General Information

Reactions involving moisture sensitive reagents were carried out under an argon atmosphere using standard vacuum line techniques with freshly distilled solvents. All glassware used was flame dried and allowed to cool under vacuum. Solvents (THF, CH_2Cl_2, toluene, hexane and Et_2O) were obtained anhydrous and purified by an alumina column (Mbraun SPS-800). Petroleum ether is defined as petroleum ether 40-60 °C. All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise. Room temperature (rt) refers to 20-25 °C. Temperatures of 0 °C and -78 °C were obtained using ice/water and CO_2(s)/acetone baths respectively. Reflux conditions were obtained using DrySyn heating apparatus and a contact thermometer. *In vacuo* refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand CVC2 vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller. Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F254 silica). TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining with a 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated. ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance 300 (300 MHz, ^1H, 75 MHz ^{13}C), Bruker Avance II 400 (400 MHz, ^1H, 100 MHz, ^{13}C) or a Bruker Avance II 500 (500 MHz, ^1H, 125 MHz ^{13}C) spectrometer at ambient temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent as the internal standard. All coupling constants, *J*, are quoted in Hz. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), ABq (AB quartet), sept (septet), oct (octet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets, dt (doublet of triplets), dq (doublet of quartets), td (triplet of doublets), tq (triplet of quartets), qt (quartet of triplets) and qd (quartet of doublets). The abbreviation Ar is used to denote aromatic, br to denote broad and app. to denote apparent. Infrared spectra (ν_{max}) were either recorded on a Perkin-Elmer Spectrum GX FT-IR spectrometer using thin-films on NaCl plates/KBr discs or a Shimadzu ATR zinc-selenide cell FTIR 8400S. Only the characteristic peaks are quoted. Melting points were recorded on an Electrothermal apparatus and are uncorrected. The abbreviation (dec) denotes decomposition. HPLC analyses were obtained on a Gilson HPLC consisting of a Gilson 305 pump, Gilson 306 pump, Gilson 811C dynamic mixer, Gilson 805 manometric module, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118 UV/vis detector. Separation was achieved using Chiralcel OD-H and OJ-H columns or a Chiralpak AD-H and AS-H column. Mass spectrometry (m/z) data were acquired by electrospray ionisation (ES), electron impact (EI) or nanospray ionisation (NSI) either at the University of St Andrews or the EPSRC National Mass Spectrometry Service Centre, Swansea. At the University of St Andrews, low and high resolution ESI-MS were carried out on a Micromass LCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low resolution NSI MS was carried out on a Micromass Quattro II spectrometer and high resolution NSI-MS on a Thermofisher LTQ Orbitrap XL spectrometer. Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell.

2. General Procedures

General Procedure A for Hydroxylamine Preparation To a stirred solution of the requisite nitro compound (1.0 eq) and Rh/C (0.05 eq) in THF (ca. 10 mL per g) at 0 °C was added hydrazine monohydrate (1.2 eq) dropwise. The reaction was stirred for 2.5 h allowing to warm to rt before being filtered through a celite plug and the residue washed with THF. The filtrate was then concentrated *in vacuo* to yield a crude solid which was purified *via* recrystallisation (CH_2Cl_2 / petroleum ether) to yield the hydroxylamine as a white solid which was stored in the freezer.

General Procedure B for Nitrone Preparation To a stirred solution of the requisite nitro compound (1.0 eq), benzaldehyde (1.0 eq), NH_4Cl (1.3 eq) in EtOH/H_2O (1:1) at 0 °C was added zinc powder (2.0 eq) portionwise over 1 h and the reaction mixture stirred for 16 h, allowing to warm to rt. The reaction mixture was filtered through a celite plug, the filtrate collected and extracted (x4) with CH_2Cl_2. The combined organic phases were then dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a crude semi-solid which was purified *via* recrystallization (CH_2Cl_2 / petroleum ether) to give the nitrone as a white/off-white solid.

General Procedure C for Nitrone Preparation To a stirred solution of the requisite hydroxylamine (1.0 eq) and $MgSO_4$ (1.1 eq) in CH_2Cl_2 was added either benzaldehyde or aldehyde **23** and the reaction stirred at rt until complete by TLC. The reaction mixture was then filtered and concentrated *in vacuo* to yield the crude product which was purified *via* column chromatography over silica (0-40% EtOAc in petroleum ether) to yield the nitrone.

General Procedure D for Achiral Oxindole Synthesis To a stirred solution of the requisite nitrone in dry THF (0.15 mmol / 1 mL) under nitrogen was added the requisite ketene solution (1.0 mL) in dry THF (1 mL) and the reaction stirred at rt for 4 h. The reaction was then quenched with aq. 2M HCl (ca. 0.5 mL) and stirred for a further 15 min before being extracted with Et_2O (3 × 10 mL). The combined organic phases were then washed with sat. aq. $NaHCO_3$, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a crude oil which was purified by column chromatography over silica (0-40% EtOAc in petroleum ether) to yield the oxindole.

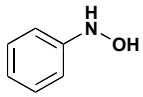
General Procedure E for Racemic Spirocyclic Oxindole Synthesis To a stirred solution of the requisite nitrone in dry THF (0.15 mmol / 1 mL) under nitrogen was added dropwise a solution of the requisite ketene (1.5 eq) in dry THF (1 mL) and the reaction stirred at rt for 1 h. The reaction was then quenched with aq. 2M HCl (ca. 0.5 mL) and stirred for a further 15 min before being extracted with Et_2O (3 × 10 mL). The combined organic phases were then washed with sat. aq. $NaHCO_3$, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a crude oil which was purified by column chromatography over silica (0-40% EtOAc in petroleum ether) to yield the oxindole.

General Procedure F for Asymmetric Spirocyclic Oxindole Synthesis To a stirred solution of the requisite chiral nitrone in dry THF (0.15 mmol / 1 mL) under nitrogen was added dropwise a solution of the requisite ketene (1.5 eq) in dry THF (1 mL) and the reaction stirred at -78 °C for 3 h. The reaction was then quenched with aq. 8M HCl (ca. 0.5 mL) and stirred for a further 4 h allowing to warm to rt before being extracted with Et_2O (3 × 10 mL). The combined organic phases were then

dried over Na_2SO_4, washed with sat. aq. $NaHCO_3$, filtered and concentrated *in vacuo* to give a crude oil which was purified by column chromatography over silica (0-40% EtOAc in petroleum ether) to yield the oxindole.

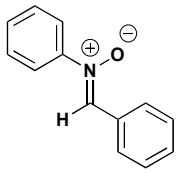
3. Achiral Nitrone Preparation

N-Phenylhydroxylamine 42



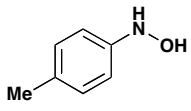
The hydroxylamine was obtained from nitrobenzene (2.00 g, 1.0 eq, 16.4 mmol), Rh/C (20 mg) and hydrazine monohydrate (0.88 mL, 1.2 eq, 19.7 mmol) in THF (20 mL) following **general procedure A** to yield **42** (1.47 g, 82%) as a white solid which was stored in the freezer; mp 82-83 °C {lit.[1] 80-81 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (2H, m, Ar*H*), 7.05-7.01 (3H, m, Ar*H*), 6.82 (1H, *br* s), 5.68 (1H, *br* s).

(*Z*)-*N*-Benzylideneaniline oxide 3



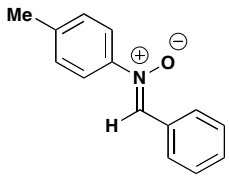
The nitrone was obtained from hydroxylamine **42** (0.309 g, 2.70 mmol), $MgSO_4$ (0.375 g, 1.1 eq, 2.97 mmol) and benzaldehyde (0.29 mL, 1.0 eq, 2.70 mmol) following **general procedure C** to yield **3** (0.34 g, 61%) as a white solid; mp 115-116 °C {lit.[2] 110 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42-8.39 (2H, m, Ar*H*), 7.93 (1H, s, $^+$N=C*H*), 7.80-7.77 (2H, m, Ar*H*), 7.51-7.47 (6H, m, Ar*H*).

N-(p-tolyl)hydroxylamine 43



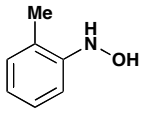
The hydroxylamine was obtained from 4-nitrotoluene (2.00 g, 1.0 eq, 14.5 mmol), Rh/C (20 mg) and hydrazine monohydrate (0.844 mL, 1.2 eq, 17.4 mmol) in THF (20 mL) following **general procedure A** to yield **43** (1.20 g, 67%) as a white solid which was stored in the freezer; mp 82-83 °C {lit.[3] 82-84 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (2H, d, *J* = 8.3, Ar*H*), 6.92 (2H, d, *J* = 8.3, Ar*H*), 6.70 (1H, br s), 5.48 (1H, br s), 2.30 (3H, s, *Me*).

(*Z*)-N-benzylidene-4-methylaniline oxide 9



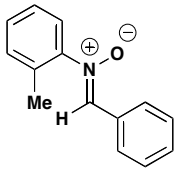
The nitrone was obtained from hydroxylamine **43** (0.234 g, 1.89 mmol), $MgSO_4$ (0.250 g, 1.1 eq, 2.08 mmol) and benzaldehyde (0.29 mL, 1.0 eq, 1.89 mmol) following **general procedure C** to yield **9** (0.340 g, 85%) as a white solid; mp 115-116 °C {lit.[4] 114-115 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41-8.37 (2H, m, Ar*H*), 7.90 (1H, s, $^+$N=C*H*), 7.67 (2H, d, *J* = 8.5, Ar*H*), 7.49-7.46 (3H, m, Ar*H*), 7.27 (2H, d, *J* = 7.6, Ar*H*), 2.42 (3H, s, *Me*).

***N*-(o-tolyl)hydroxylamine 44**



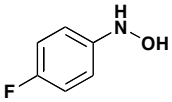
The hydroxylamine was obtained from o-nitrotoluene (2.00 g, 1.0 eq, 14.5 mmol), Rh/C (20 mg) and hydrazine monohydrate (0.844 mL, 1.2 eq, 17.4 mmol) in THF (20 mL) following **general procedure A** to yield **44** (1.25 g, 70%) as a white solid which was stored in the freezer; mp 36-37 °C {lit.[5] 44 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.26 (2H, m, Ar*H*), 7.13 (1H, d, *J* = 7.2, Ar*H*), 6.97 (1H, td, *J* = 7.2, 1.7, Ar*H*), 6.80 (1H, br s), 5.80 (1H, br s), 2.20 (3H, s, *Me*).

(*Z*)-N-benzylidene-2-methylaniline oxide 10



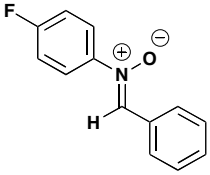
The nitrone was obtained from hydroxylamine **44** (0.234 g, 1.89 mmol), $MgSO_4$ (0.250 g, 1.1 eq, 2.08 mmol) and benzaldehyde (0.29 mL, 1.0 eq, 1.89 mmol) following **general procedure C** to yield **10** (0.406 g, quant.) as a white solid; mp 115-116 °C {lit.[6] 113-115 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38-8.34 (2H, m, Ar*H*), 7.57 (1H, s, $^+$N=C*H*), 7.50-7.47 (3H, m, Ar*H*), 7.39-7.30 (4H, m, Ar*H*), 2.43 (3H, s, *Me*).

***N*-(4-Fluorophenyl)hydroxylamine 45**



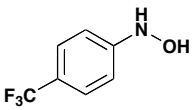
The hydroxylamine was obtained from 1-fluoro-4-nitrobenzene (7.00 g, 49.6 mmol), Rh/C (0.150 g, cat.) and hydrazine monohydrate solution (2.89 mL, 1.2 eq, 59.5 mmol) in THF (60 mL) following **general procedure A** to leave **45** (4.74 g, 92%) as a grey solid; mp 84-85 °C {lit.[7] 100 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03-6.99 (2H, m, Ar*H*), 6.97-6.94 (3H, m, Ar*H*).

(Z)-*N*-Benzylidene-4-fluoroaniline oxide 5



The nitrone was obtained from hydroxylamine **45** (4.74 g, 37.3 mmol), $MgSO_4$ (0.500 g, 1.1 eq, mmol) and benzaldehyde (3.69 mL, 0.97 eq, 36.2 mmol) in CH_2Cl_2 (35 mL) following **general procedure C** to yield **5** (5.17 g, 64%) as a silver solid which was used without further purification; mp 154-155 °C {lit.[8] 169.5-170.3 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42-8.40 (2H, m, Ar*H*), 7.91 (1H, s, $^+$N=C*H*), 7.83-7.80 (2H, m, Ar*H*), 7.52-7.51 (3H, m, Ar*H*), 7.22-7.17 (2H, m, Ar*H*).

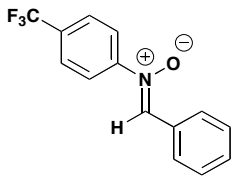
***N*-(4-(Trifluoromethyl)phenyl)hydroxylamine 46**



The hydroxylamine was obtained from 4-nitrobenzotrifluoride (6.00 g, 31.4 mmol), Rh/C (0.150 g, cat.) and hydrazine monohydrate solution (1.83 mL, 1.2 eq, 37.7 mmol) in THF (60

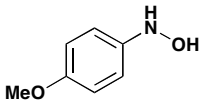
mL) following **general procedure A** to yield **46** (3.85 g, 69%) as a white solid; mp 83-84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (2H, d, *J* = 8.5, Ar*H*), 7.05 (2H, d, *J* = 8.5, Ar*H*).

(Z)-*N*-Benzylidene-4-(trifluoromethyl)aniline oxide 11



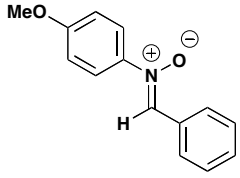
The nitrone was obtained from hydroxylamine **46** (3.0 g, 16.9 mmol), $MgSO_4$ (0.400g, 1.1 eq, mmol) and benzaldehyde (1.72 mL, 0.97 eq, 16.4 mmol) following **general procedure C** to yield **11** (4.38 g, 98%) as a white solid; mp 150-151 °C {lit.[9] 54-56 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42-8.39 (2H, m, Ar*H*), 7.91 (1H, s, $^+$N=C*H*), 7.83-7.80 (2H, m, Ar*H*), 7.52-7.51 (3H, m, Ar*H*), 7.22-7.17 (2H, m, Ar*H*).

***N*-(4-Methoxyphenyl)hydroxylamine 47**



The hydroxylamine was obtained from 4-nitroanisole (1.00 g, 6.53 mmol), Rh/C (0.100 g, cat.) and hydrazine monohydrate (0.69 mL, 1.2 eq, 7.84 mmol) following **general procedure A** to yield **47** (0.505 g, 56%) as an off-white solid; mp 84-85 °C {lit.[10] 86-94 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03-7.00 (2H, m, Ar*H*), 6.89-6.87 (2H, m, Ar*H*), 5.70 (1H, *br* s), 3.81 (3H, s, OCH_3).

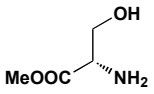
(Z)-*N*-Benzylidene-4-methoxyaniline oxide 4



The nitrone was obtained from hydroxylamine **47** (0.200 g, 1.44 mmol), $MgSO_4$ (0.191 g, 1.58 mmol) and benzaldehyde (0.15 mL, 1.44 mmol) in CH_2Cl_2 (5 mL) following **general procedure C** to yield **4** (0.062 g, 19%) as a grey solid; mp 122-123 °C {lit.[9] 132 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39-8.37 (2H, m, Ar*H*), 7.88 (1H, s, $^+$N=C*H*), 7.75-7.72 (2H, m, Ar*H*), 7.47 (3H, tdd, *J* = 5.4, 3.1, 2.2, Ar*H*), 6.99-6.95 (2H, m, Ar*H*), 3.87 (1H, s, OCH_3).

4. Chiral Nitrone Preparation

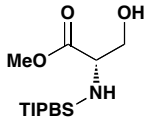
(*S*)-Methyl 2-amino-3-hydroxypropanoate hydrochloride 48



To a stirred solution of *(L)*-Serine (20.00 g, 0.19 mol) in MeOH (425 mL) cooled to < 0 °C using a salted ice bath was added thionyl chloride (69.0 mL, 6.0 eq, 1.14 mol) dropwise and the reaction stirred for 16 h allowing to warm to rt. The reaction mixture was then concentrated *in vacuo* and the residue taken up in Et_2O (200 mL) before being cooled with an ice bath to allow formation of a white precipitate. This precipitate was filtered and washed with cold Et_2O (3 × 50 mL) to yield **48** (28.70 g, 97%) as a white solid; mp 157-158 °C {lit.[11] 163-165 °C}; $[\alpha]_D^{20}$ +3.9 (*c* = 1.14, MeOH)

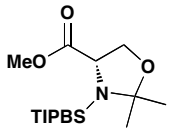
{lit.[11] $[\alpha]_D^{25}$ +3.7 (*c* = 4.00, MeOH)}; ^{1}H NMR (300 MHz, D_2O) δ 4.29 (1H, t, *J* = 3.8, C*H*(NH_2)), 4.08 (2H, dq, *J* = 12.5, 3.8, CH_2OH), 3.87 (3H, s, COO*Me*).

(*S*)-Methyl 3-hydroxy-2-(2,4,6-triisopropylphenylsulfonamido)propanoate 49



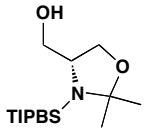
To a stirred solution of **48** (4.67 g, 0.030 mol) in CH_2Cl_2 (60 mL) was added dropwise Et_3N (9.98 mL, 2.4 eq, 0.07 mol) at 0 °C and the reaction mixture stirred for 5 min at 0 °C. After this time, 2,4,6-triisopropylbenzenesulfonyl chloride was added in one portion and the reaction stirred for 16 h allowing to warm to rt. The reaction was quenched with H_2O (100 mL) before being extracted with CH_2Cl_2 (3 × 120 mL). The combined organic layers were then washed in succession with sat. aq. $NaHCO_3$ (100 mL), 10% citric acid solution (100 mL), H_2O (100 mL) and brine (100 mL) before being dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield **49** (11.23 g, 97%) as an off-white solid; mp 109-111 °C; $[\alpha]_D^{20}$ +4.3° (*c* = 0.91, $CHCl_3$); ν_{max} cm^{-1} (KBr) 3359 (N-H), 3356 (O-H), 2959 (C-H), 1733 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (2H, s, Ar*H*), 4.12-4.06 (3H, m, *o*-*i*Pr*H* & C*H*NR), 3.91-3.90 (2H, m, CH_2), 3.66 (3H, s, COO*Me*), 2.90 (1H, dt, *J* = 13.8, 6.9), 1.29-1.24 (18H, m, *i*PrCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4 (*C*=O), 153.3 (4^{ry}Ar*C*(*p*-*i*Pr)), 150.3 (4^{ry}Ar*C*(*o*-*i*Pr)), 132.2 (4^{ry}Ar*C*SO_2), 124.0 (Ar*C*H), 101.3 (*C*Me_2), 63.7 (*C*H(COOMe), 57.2 (*C*H_2), 53.0 (COO*Me*), 34.2 (*p*-*i*Pr*C*(CH_3)$_2$), 30.0 (*o*-*i*Pr*C*(CH_3)$_2$), 24.9 (C*Me*$_2$, d, *J* = 12.9), 23.6 (*i*PrC(*C*H_3)$_2$), 23.6 (*i*PrC(*C*H_3)$_2$); *m*/*z* (EI$^+$) 386 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{19}H_{32}O_5NS^+$ ([M+H]$^+$) found 386.1998 requires 386.1996 (+ 0.2 ppm).

***(S)*-Methyl 2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidine-4-carboxylate 50**



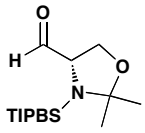
To a stirred solution of **49** (5.78 g, 0.015 mol) and pyridinium *para*-toluenesulfonate (0.94 g, 0.25 eq, 3.75 mmol) in toluene (200 mL) was added 2,2-dimethoxypropane (27.7 mL, 15.0 eq, 0.225 mol) and the reaction stirred at 80 °C for 16 h. After cooling, the reaction mixture was concentrated in vacuo to yield a crude light-brown oil which was purified by column chromatography over silica (petroleum ether / EtOAc 100:0 to 80:20) to yield **50** (3.00 g, 47 %) as a white solid; mp 106-107 °C; $[\alpha]_D^{20}$ -32.8° (*c* = 1.02, $CHCl_3$); ν_{max} cm^{-1} (KBr) 2963 (C-H), 1763 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (2H, s, Ar*H*), 4.40 (1H, dd, *J* = 7.4, 2.1, 1 × CH_2), 4.31-4.24 (3H, m, C*H*NR & *o*-*i*Pr*H*), 4.06 (1H, dd, *J* = 9.2, 2.1, 1 × CH_2), 3.23 (3H, s, COO*Me*), 2.89 (1H, dt, *J* = 13.8, 6.9, *p*-*i*Pr*H*), 1.80 (6H, d, *J* =11.6), 1.30-1.22 (18H, m, *i*PrCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4 (*C*=O), 153.8 (4^{ry}Ar*C*(*p*-*i*Pr)), 151.8 (4^{ry}Ar*C*(*o*-*i*Pr)), 131.9 (4^{ry} Ar*C*SO_2), 100.7 (*C*Me_2), 67.5 (*C*H(COOMe)), 59.1 (*C*H_2OR), 51.9 (COO*Me*), 34.2 (*p*-*i*Pr*C*(CH_3)$_2$), 29.5 (*o*-*i*Pr*C*(CH_3)$_2$), 27.6 (*p*-*i*PrC(*C*H_3)$_2$), 24.8 (C*Me*$_2$, d, *J* = 6.7), 23.6 (*o*-*i*PrC(*C*H_3)$_2$); *m*/*z* (EI$^+$) 426 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{22}H_{36}O_5NS^+$ ([M+H]$^+$) found 426.2312 requires 426.2309 (+ 0.3 ppm).

(*R*)-(2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methanol 51



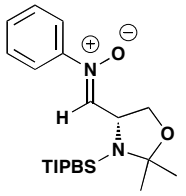
To a stirred solution of **50** (2.55 g, 6.00 mmol) in THF (18 mL) was added dropwise $LiAlH_4$ (2.0M in THF) (4.50 mL, 1.5 eq, 9.00 mmol) at 0 °C, and the reaction stirred at 0 °C for 30 min. The reaction was then quenched with dropwise addition of H_2O (1 mL), followed by addition of 40% KOH (1 mL), H_2O (3 mL) and EtOAc (5 mL). The resulting slurry was then stirred vigorously for 1 hr allowing to warm to rt before being filtered through a celite plug and the residue washed with EtOAc (30 mL). The reaction mixture was then dried over $MgSO_4$ before being filtered and concentrated *in vacuo* to yield **51** (2.39 g, quant.) as a very viscous colourless oil which crystallised as a white solid on standing; mp 80-82 °C; $[\alpha]_D^{20}$ +5.5° (*c* = 1.01, $CHCl_3$); ν_{max} cm^{-1} (thin-film) 3527 (O-H), 2960 (C-H); ^1H NMR (300 MHz, C_6D_6) δ 7.18 (2H, s, Ar*H*), 4.67 (2H, dt, *J* = 13.6, 6.8, *o*-*i*Pr*H*), 3.87-3.80 (3H, m, CH_2 & C*H*NR), 2.92 (1H, t, *J* = 9.3, 1 × CH_2OH), 2.70-2.58 (2H, m, *p*-*i*Pr*H* & 1 × CH_2OH), 1.88 (3H, s, C*Me*), 1.77 (3H, s, C*Me*), 1.36 (3H, d, *J* = 6.8, *o*-*i*PrCH_3), 1.30 (3H, d, *J* = 6.8, *o*-*i*PrCH_3), 1.09 (3H, d, *J* = 6.9, *p*-*i*PrCH_3); ^{13}C NMR (75 MHz, C_6D_6) δ 153.7 (4^{ry}Ar*C*), 151.9 (4^{ry}Ar*C*), 134.2 (4^{ry}Ar*C*SO_2), 124.3 (Ar*C*H), 99.8 (*C*Me_2), 66.2 (*C*H_2), 62.8 (*C*H(CH_2OH), 59.0 (*C*H_2OH), 34.3 (*p*-*i*Pr*C*(CH_3)), 29.3 (*o*-*i*Pr*C*(CH_3)$_2$), 28.8 (*p*-*i*PrC(*C*H_3)$_2$), 25.0 (C*Me*), 24.8 (C*Me*), 23.6 (*o*-*i*PrC(*C*H_3)), 23.6 (*o*-*i*PrC(*C*H_3)); *m*/*z* (EI^+) 398 ([M+H]$^+$, 100%); HRMS (EI^+) $C_{21}H_{36}O_4NS^+$ ([M+H]$^+$) found 398.2363 requires 398.2360 (+ 0.3 ppm).

***(S)*-2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidine-4-carbaldehyde 23**



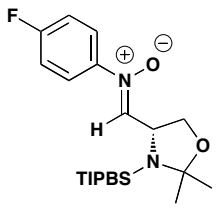
A solution of DMSO (1.43 mL, 4.0 eq, 201 mmol) in CH_2Cl_2 (25 mL) was added dropwise to a stirred solution of oxalyl chloride (0.88 mL, 2.0 eq, 101 mmol) in CH_2Cl_2 (15 mL) cooled to -78 °C using a dry ice/acetone bath and stirred at -78 °C for 15 min. A solution of **51** (2.00 g, 1.0 eq, 50.3 mmol) in CH_2Cl_2 (30 mL) was then added slowly and the reaction stirred for 35 min. At -78 °C was added DIPEA (5.22 mL, 6.0 eq, 302 mmol) and the reaction mixture stirred allowing to warm to rt before being quenched with sat. aq. NH_4Cl (25 mL). The organic phase was then separated and washed in succession with sat. aq. $NaHCO_3$ (30 mL) and brine (2 × 30 mL) before being dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield **23** (2.03 g, quant.) as a viscous yellow oil which was used without further purification; $[\alpha]_D^{20}$ -23.5° (*c* = 1.22, $CHCl_3$); ν_{max} cm^{-1} (thin-film) 2363 (C-H), 1701 (C=O); ^1H NMR (300 MHz, $CDCl_3$) δ 9.00 (1H, d, *J* = 2.7, C*H*O), 7.16 (2H, s, Ar*H*), 4.33-4.09 (5H, m, *o*-*i*Pr*H* & CH_2 & C*H*NR), 2.93-2.84 (1H, dt, *J* = 13.8, 7.1, *p*-*i*Pr*H*), 1.81 (6H, d, *J* = 3.7, C*Me*$_2$), 1.25 (18H, t, *J* = 7.1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.3 (*C*=O), 154.6 (4^{ry}Ar*C*(*p*-*i*Pr)), 151.4 (4^{ry}Ar*C*(*o*-*i*Pr)), 131.6 (4^{ry}Ar*C*SO_2), 124.4 (Ar*C*H), 100.7 (*C*Me_2), 65.8 (*C*H(CHO)), 64.6 (*C*H2), 34.2 (*p*-*i*Pr*C*(CH_3)), 29.3 (*o*-*i*Pr*C*(CH_3)), 27.9 (*p*-*i*PrC(*C*H_3)$_2$), 24.7 (C*Me*$_2$, d, *J* = 26.8), 23.5 (*p*-*i*PrC(*C*H_3)$_2$); *m*/*z* (CI^+) 396 ([M+H]$^+$, 100%); HRMS (CI^+) $C_{21}H_{33}NO_4S^+$ ([M+H]$^+$) found 396.2209 requires 396.2209 (+ 0.1 ppm).

***(R,Z)-N-((*2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)aniline oxide 19**



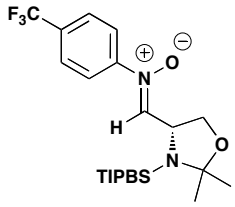
The nitrone was obtained from hydroxylamine **42** (0.330 g, 1.2 eq, 30.2 mmol), $MgSO_4$ (0.334 g, 1.1 eq, 27.7 mmol)) and aldehyde **23** (1.00 g, 25.2 mmol) in CH_2Cl_2 (10 mL) following **general procedure C** to yield a crude brown semi-solid which was triturated from Et_2O to yield **19** (0.558 g, 45%) as an off-white solid; mp 112-113 °C (decomp.); $[\alpha]_D^{20}$ -12.5° (*c* = 0.97, $CHCl_3$); ν_{max} cm^{-1} (KBr) 3274 (N-O), 2958 (C-H), 2959 (C-H), 1733 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.27 (3H, m, Ph*H*), 7.21 (2H, s, *i*PrAr*H*), 7.06-7.03 (2H, m, Ph*H*), 6.75 (1H, d, *J* = 5.3, *H*C=N$^+$), 5.11 (1H, ddd, *J* = 7.2, 5.3, 1.9, C*H*NR), 4.51-4.23 (4H, m, CH_2 & *o*-*i*PrH), 2.89 (1H, dt, *J* = 13.8, 6.9, *p*-*i*PrH), 1.84 (6H, d, *J* = 3.2, di*Me*), 1.29-1.20 (18H, m, *i*PrCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2 (4^{ry}Ar*C*), 151.8 (Ar*C*), 146.3 (4^{ry}Ar*C*), 139.1 (Ar*C*), 132.4 (H*C*=N$^+$), 130.4 (Ar*C*), 129.0 (Ar*C*), 124.4 (Ar*C*), 121.0 (Ar*C*), 100.2 (C*Me*$_2$), 68.0 (*C*H$_2$), 56.1 (*C*HNR), 34.2 (*p*-*i*Pr*C*), 29.2 (*p*-*i*Pr*C*H$_3$), 28.0 (*o*-*i*Pr*C*), 25.1 (C*Me*$_2$), 24.8 (C*Me*$_2$), 24.6 (*o*-*i*Pr*C*), 23.6 (*o*-*i*Pr*C*H$_3$); *m/z* (EI$^+$) 487 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{27}H_{39}O_4N_2S^+$ ([M+H]$^+$) found 487.2633 requires 487.2625 (+ 0.8 ppm).

(*R*,*Z*)-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-4-fluoroaniline oxide 24



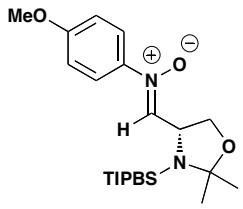
The nitrone was obtained from hydroxylamine **45** (0.106 g, 83.2 mmol), $MgSO_4$ (0.091 g, 83.2 mmol) and aldehyde **23** (0.300 g, 0.91 eq, 75.7 mmol) in CH_2Cl_2 (10 mL) following **general procedure C** to yield a crude brown foam which was purified by recrystallization from Et_2O followed by trituration from petroleum ether to yield **24** as a pale orange solid in > 90% purity; mp 138-140 °C; $[\alpha]_D^{20}$ -12.3° (*c* = 0.75, $CHCl_3$); ν_{max} cm^{-1} (thin-film) 2961, 2868, 1595, 1558, 1501, 1458; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (2H, s, Ar*H*), 7.07-7.02 (2H, m, Ar*H*), 6.99-6.93 (2H, m, Ar*H*), 6.71 (1H, d, *J* = 5.1, $^+$N=C*H*), 5.06 (1H, td, *J* = 5.1, 2.1, C*H*), 4.46 (1H, dd, *J* = 9.5, 7.3, 1 x C*H*$_2$), 4.35 (2H, quint., *J* = 6.8, ^{i}Pr*H*), 4.22 (1H, dd, *J* = 9.5, 2.1, 1 x C*H*$_2$), 2.88 (1H, dt, *J* = 13.8, 6.9, ^{i}Pr*H*), 1.83 (6H, d, *J* = 4.8, C*Me*$_2$), 1.27-1.20 (18H, m, ^{i}PrC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3 (d, *J* = 251.6), 153.2, 150.8, 141.5 (d, *J* = 3.0), 131.4, 123.3, 122.0 (d, *J* = 8.9), 114.9 (d, *J* = 23.3), 99.2, 66.9, 55.0, 33.2, 28.1, 27.0, 24.0, 23.7, 23.5, 22.6.

(*R*,*Z*)-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-4-(trifluoromethyl)aniline oxide 25



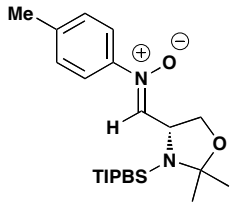
The nitrone was obtained from hydroxylamine **46** (0.268 g, 1.52 mmol), $MgSO_4$ (0.134 g, 1.11 mmol) and aldehyde **23** (0.400 g, 0.75 eq, 1.01 mmol) in CH_2Cl_2 (15 mL) following **general procedure C** and purified by column chromatography over silica (0-30% EtOAc in petroleum ether) followed by trituration from petroleum ether to yield **25** (0.350g, 63%) as an off-white solid; mp 52-54 °C; $[\alpha]_D^{20}$ -110.0° (*c* = 1.0, $CHCl_3$); ν_{max} cm^{-1} (thin-film) 2961, 2868, 1595, 1558, 1501, 1456; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26-7.21 (1H, m, Ar*H*), 7.18 (2H, s, Ar*H*), 7.00 (2H, d, *J* = 8.5, Ar*H*), 6.79 (1H, d, *J* = 5.4, $^+$N=C*H*), 5.12 (1H, ddd, *J* = 7.2, 5.4, 1.88, C*H*), 4.47 (1H, dd, *J* = 9.6, 7.3, 1 x CH_2), 4.35 (2H, dt, *J* = 13.7, 6.8, iPr*H*), 4.22 (1H, dd, *J* = 9.6, 2.0, 1 x CH_2), 2.86 (1H, dt, *J* = 13.7, 6.8, iPr*H*), 1.83 (6H, d, *J* = 7.8, CMe_2), 1.27-1.23 (12H, m, iPrCH_3), 1.17 (6H, dd, *J* = 6.8, 4.5, iPrCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 150.8, 147.4, 139.2, 131.5 (app. d, *J* = 33.2), 131.3, 125.3, 123.3, 123.3 (q, *J* = 267.5), 120.5, 99.3, 66.8, 55.1, 33.2, 28.1, 27.0, 24.1, 23.7, 23.5, 22.5 (d, *J* = 2.4); *m/z* (ESI$^+$) 577 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{37}O_4N_2SF_3^+$ ([M+Na]$^+$) found 577.2324 requires 577.2317 (-1.2 ppm).

(*R*,*Z*)-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-4-methoxyaniline oxide 26



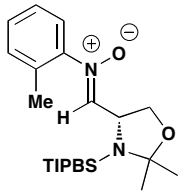
The nitrone was obtained from hydroxylamine **47** (0.116 g, 83.2 mmol), $MgSO_4$ (0.091 g, 83.2 mmol) and aldehyde **23** (0.300 g, 0.91 eq, 75.7 mmol) in CH_2Cl_2 (10 mL) following **general procedure C** to yield a crude brown foam which was purified by recrystallization from Et_2O followed by trituration from petroleum ether to yield **26** as a pale brown solid of > 90% purity; mp 103-104 °C; $[\alpha]_D^{20}$ -64.1° (*c* = 0.90, $CHCl_3$); ν_{max} cm^{-1} (thin-film) 2961, 1595, 1558, 1501, 1457; ^1H NMR (500 MHz, $CDCl_3$) δ 7.19 (2H, s, Ar*H*), 6.96 (2H app. qd, *J* = 4.6, 3.4, Ar*H*), 6.74 (2H, d, *J* = 9.0, Ar*H*), 6.67 (1H, d, *J* = 5.2, $^+$N=C*H*), 5.06 (1H, t, *J* = 5.2, C*H*), 4.45 (1H, dd, *J* = 9.3, 7.4, 1 x CH_2), 4.34 (2H, dt, *J* = 13.4, 6.7, iPr*H*), 4.22 (1H, dd, *J* = 9.3, 1.6, 1 x CH_2), 3.78 (3H, s, O*Me*), 2.88 (1H, dt, *J* = 13.7, 6.9, iPr*H*), 1.82 (6H, d, *J* = 8.4, CMe_2), 1.27-1.16 (18H, m, iPrCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 154.1, 151.7, 139.5, 138.0, 132.4, 127.8, 124.3, 122.3, 113.9, 100.1, 68.1, 56.0, 55.6, 34.1, 29.1, 28.0, 25.0, 24.9, 24.8, 24.6, 23.6.

(*R*,*Z*)-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-4-methylaniline oxide 27



The nitrone was obtained from hydroxylamine **43** (0.102 g, 83.2 mmol), $MgSO_4$ (0.091 g, 83.2 mmol) and aldehyde **23** (0.300 g, 0.91 eq, 75.7 mmol) in CH_2Cl_2 (10 mL) following **general procedure C** to yield a crude brown foam which was purified by recrystallization from Et_2O followed by trituration from petroleum ether to yield **27** (0.234 g, 56%) as an orange solid; mp 57-59 °C; $[\alpha]_D^{20}$ -53.6° (*c* = 0.50, $CHCl_3$); ν_{max} cm^{-1} (thin-film) 2957, 2888, 1599, 1560, 1502, 1462; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18 (2H, s, Ar*H*), 7.06 (2H, d, *J* = 8.2, Ar*H*), 6.91 (2H, d, *J* = 8.2, Ar*H*), 6.70 (1H, d, *J* = 5.3, $^+$N=C*H*), 5.07 (1H, t, *J* = 5.3, C*H*), 4.46 (1H, dd, *J* = 9.3, 7.4, 1 x CH_2), 4.35 (2H, dt, *J* = 13.5, 7.0, iPr*H*), 4.23 (1H, dd, *J* = 9.3, 1.7, 1 x CH_2), 2.88 (1H, dt, *J* = 13.8, 6.9, iPr*H*), 2.33 (3H, s, *Me*), 1.83 (6H, d, *J* = 4.8, CMe_2), 1.25 (12H, t, *J* = 7.0, iPrCH_3), 1.21 (6H, t, *J* = 6.9, iPrCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.1, 151.7, 144.1, 140.7, 138.5, 132.4, 129.5, 124.3 120.8, 100.1, 68.1, 56.0, 34.2, 29.1, 28.0, 25.0, 24.8, 24.6, 23.6, 23.6, 21.1.

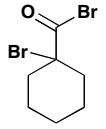
(*R*,*Z*)-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-2-methylaniline oxide 28



The nitrone was obtained from hydroxylamine **44** (0.102 g, 83.2 mmol), $MgSO_4$ (0.091g, 83.2 mmol) and aldehyde **23** (0.300 g, 0.91 eq, 75.7 mmol) in CH_2Cl_2 (10 mL) following **general procedure C** to yield a crude brown foam which was partially purified by attempted column chromatography followed by recrystallization from Et_2O, followed by trituration from petroleum ether to yield **28** (over 100%) as an impure brown oil after obvious decomposition. Therefore in subsequent preparations, the nitrone was prepared and immediately used crude in the next reaction step.

5. Achiral Oxindole Synthesis

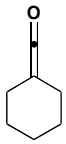
1-Bromocyclohexanecarbonyl bromide 1



To a stirred solution of neat cyclohexanoic acid (12.0 g, 93.6 mmol) was added PBr_3 (2.65 mL, 0.3 eq, 28.1 mmol) and the reaction mixture heated to 110 °C. Bromine (5.78 mL, 1.15 eq, 112 mmol) was then added dropwise until the reaction mixture retained the brown colour of the bromine. At this point, the reaction mixture was cooled, and whilst still stirring rapidly, was flushed with nitrogen into a saturated solution of sodium thiosulfate. The reaction mixture was then concentrated *in vacuo* to yield a crude pale brown liquid which was purified *via* kugelrohr distillation (120-122 °C,

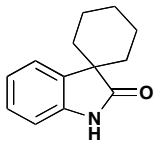
1mmHg) to give **1** (10.2 g, 43%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (4H, t, J = 5.7, CH_2), 1.86-1.73 (2H, m, CH_2), 1.67-1.53 (4H, m, CH_2).

Cyclopentamethyleneketene 2



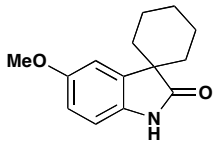
An excess of activated zinc (0.400 g) was suspended in THF (20 mL) at 0 °C. To this was added a solution of **1** (1.20 g, 4.45mmol) in THF (5 mL) dropwise over 30 mins. The reaction mixture was stirred at 0 °C for 30 min before a yellowy/green colour became apparent, stirring ceased and the reaction mixture allowed to settle. Ketene **2** was then used as an unquantified solution in THF in the next reaction.

Spiro[cyclohexane-1,3'-indolin]-2'-one 6



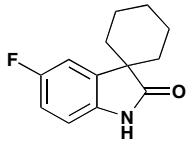
The oxindole was obtained from nitrone **3** (0.050 g, 0.254 mmol) and ketene solution **2** (3.0 mL) following **general procedure D**, to yield **6** (0.033 g, 65%) as a white solid; mp 110-111 °C {lit.[12] 119-121 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (1H, br s, N*H*), 7.45 (1H, d, J = 7.6, Ar*H*), 7.21 (1H, td, J = 7.7, 1.1, Ar*H*), 7.03 (1H, dd, J = 7.6, 1.1, Ar*H*), 6.90 (1H, d, J = 7.7, Ar*H*), 1.99-1.84 (4H, m, CH_2), 1.80-1.58 (6H, m, CH_2).

5'-Methoxyspiro[cyclohexane-1,3'-indolin]-2'-one 7



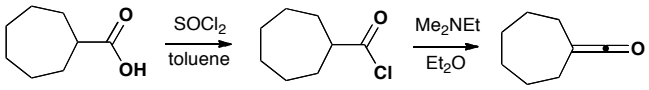
The oxindole was obtained from nitrone **4** (0.098 g, 0.431 mmol) and ketene solution **2** (5.0 mL) following **general procedure D**, to yield **7** (0.056 g, 56%) as an off-white solid; mp 208-209 °C {lit.[13] 226 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (1H, *br* s, N*H*), 7.05 (1H, d, J = 2.4, Ar*H*), 6.79 (1H, d, J = 8.4, Ar*H*), 6.73 (1H, d, J = 8.4, 2.4, Ar*H*), 3.80 (3H, s, O*Me*), 1.96-1.82 (4H, m, CH_2), 1.78-1.54 (6H, m, CH_2).

5'-Fluorospiro[cyclohexane-1,3'-indolin]-2'-one 8



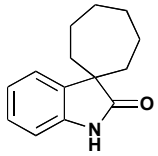
The oxindole was obtained from nitrone **5** (0.080 g, 0.372 mmol) and ketene solution **2** (4.5 mL) following **general procedure D**, to yield **8** (0.039 g, 48%) as an off-white solid; mp 101-102 °C {lit.[14] 114 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (1H, *br* s, N*H*), 7.18 (1H, dd, J = 8.7, 2.5, Ar*H*), 6.91 (1H, td, J = 8.7, 2.5, Ar*H*), 6.84 (1H, dd, J = 8.7, 4.6, Ar*H*), 1.98-1.83 (4H, m, CH_2), 1.77-1.56 (6H, m, CH_2); *m/z* (ESI$^+$) 219 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{13}H_{15}FON^+$ ([M+H]$^+$) found 220.1128 requires 220.1132 (- 0.7 ppm).

Cyclohexamethyleneketene 12



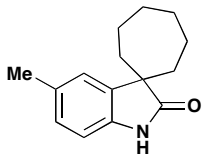
Cyclohexamethyleneketene **12** was prepared according to a literature procedure.[14] To a stirred solution of cycloheptanecarboxylic acid (5.00 g, 352 mmol) in toluene (50 mL) was added thionyl chloride (5.14 mL, 2.0 eq, 704 mmol) dropwise, and the reaction stirred at 80 °C for 16 h. The toluene and excess thionyl chloride were then removed under reduced pressure to leave a crude brown liquid which was purifed *via* Kugelrohr distillation (140 °C, 3 mmHg) to yield the intermediate acid chloride (5.34 g, 94%) as a colourless liquid. To a stirred solution of acid chloride (4.00 g, 249 mmol) in dry Et_2O (70 mL) under nitrogen was added dimethylethylamine (2.97 mL, 1.1 eq, 274 mmol) dropwise. The reaction was then stirred for 40 h at rt. After this time, the reaction was filtered under nitrogen to remove Et_3N salts. The Et_2O was then removed under reduced pressure to leave a yellow oil which was partially purified *via* Kugelrohr distillation (50 °C, 3 mmHg) to remove residual acid chloride and yield **12** as a yellow liquid which was taken up in THF (20 mL) and used immediately as a solution; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.25-2.21 (4H, m, C=CCH_2), 1.71-1.64 (4H, m, CH_2), 1.62-1.52 (4H, m, CH_2).

Spiro[cycloheptane-1,3'-indolin]-2'-one 13



The oxindole was obtained from nitrone **3** (0.050 g, 0.254 mmol) and ketene solution **12** (1.0 mL) following **general procedure D**, to yield **13** (0.043 g, 79%) as a white solid; mp 140-142 °C; ν_{max} cm^{-1} (KBr) 3165 (N-H), 2932 (C-H) 1700 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (1H, *br* s, N*H*), 7.35 (1H, dd, *J* = 7.5, 0.4, Ar*H*), 7.20 (1H, td, *J* = 7.7, 1.2, Ar*H*), 7.03 (1H, td, *J* = 7.5, 1.2, Ar*H*), 6.88 (1H, dd, *J* = 7.7, 0.4, Ar*H*), 2.08-1.93 (4H, m, CH_2), 1.82-1.68 (8H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.1 (*C*=O), 139.4 (*C*(3a)), 137.9 (*C*(7a)), 127.4 (Ar*C*), 123.2 (Ar*C*), 122.4 (Ar*C*), 109.4 (Ar*C*), 50.5 (*C*(3)), 36.9 (*C*H$_2$), 31.3 (*C*H$_2$), 23.8 (*C*H$_2$); *m/z* (ESI$^+$) 216 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{14}H_{18}ON^+$ ([M+H]$^+$) found 216.1383 requires 216.1383 (+ 0.0 ppm).

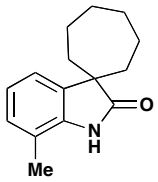
5'-Methylspiro[cycloheptane-1,3'-indolin]-2'-one 14



The oxindole was obtained from nitrone **9** (0.026 g, 0.123 mmol) and ketene solution **12** (1.0 mL) following **general procedure D**, to yield **14** (0.023 g, 82%) as a white solid; mp 163-164°C; ν_{max} cm^{-1} (KBr) 3162 (NH), 2920, 2852, 1698 (C=O), 1625, 1492, 1457, 1354, 1321; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1H, *br* s, N*H*), 7.14 (1H, t, *J* = 0.6, Ar*H*), 6.98 (1H, ddd, *J* = 7.9, 1.6, 0.6), 6.76 (1H, d, *J* = 7.9, Ar*H*), 2.34 (3H, s, *Me*), 2.05-1.95 (4H, m, CH_2), 1.79-1.71 (8H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.5, 138.0, 137.0, 131.7, 127.6, 124.0, 109.2, 50.5, 36.9, 31.4, 23.9, 21.3;

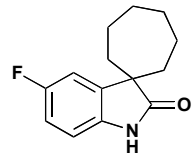
m/z (ESI$^+$) 230 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{15}H_{20}ON^+$ ([M+H]$^+$) found 230.1541 requires 230.1539 (+ 0.7 ppm).

7'-methylspiro[cycloheptane-1,3'-indolin]-2'-one 15



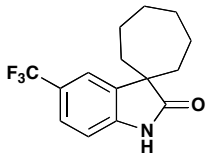
The oxindole was obtained from nitrone **10** (0.023 g, 0.109 mmol) and ketene solution **12** (1.0 mL) following **general procedure D**, to yield **15** (0.017 g, 68%) as a white solid; mp 218-221 °C; ν_{max} cm^{-1} (KBr) 3155 (NH), 3097, 2963, 2904, 1719 (C=O), 1698, 1631, 1604, 1489, 1465, 1438, 1350, 1328, 1320; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (1H, br s, N*H*), 7.18 (1H, d, *J* = 7.2, Ar*H*), 7.02-6.92 (2H, m, Ar*H*), 2.26 (3H, s, *Me*), 2.06-1.91 (4H, m, CH_2), 1.80-1.66 (8H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.4, 138.1, 137.5, 128.7, 122.3, 120.6, 118.6, 50.9, 37.0, 31.3, 23.8; *m/z* (ESI$^+$) 230 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{15}H_{20}ON^+$ ([M+H]$^+$) found 230.1541 requires 230.1539 (+ 0.7 ppm).

5'-Fluorospiro[cycloheptane-1,3'-indolin]-2'-one 16



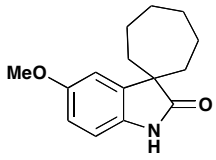
The oxindole was obtained from nitrone **5** (0.028 g, 0.130 mmol) and ketene solution **12** (1.0 mL) following **general procedure D**, to yield **16** (0.022g, 79%) as a white solid; mp 151-152°C; ν_{max} cm^{-1} (KBr) 3192 (NH), 3081, 2923, 2852, 1696, 1625, 1608, 1482, 1348, 1319; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (1H, *br* s, N*H*), 7.06 (1H, dd, *J* =8.4, 2.5, Ar*H*), 6.91-6.81 (2H, m, Ar*H*), 2.05-1.93 (4H, m, CH_2), 1.78-1.69 (8H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.3 (*C*=O), 159.3 (*C*5, d, *J* = 239.8), 139.4 (*C*3a, d, *J* = 7.6), 135.3 (*C*7a), 113.6 (*C*4, d, *J* = 23.5), 111.2 (*C*6, d, *J* = 24.5), 109.9 (*C*7, d, *J* = 8.2), 51.1 (*C*3), 36.8, 31.3, 23.8; *m/z* (ESI$^+$) 234 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{14}H_{17}FON^+$ ([M+H]$^+$) found 234.1291 requires 234.1289 (+ 1.0 ppm).

5'-(trifluoromethyl)spiro[cycloheptane-1,3'-indolin]-2'-one 17



The oxindole was obtained from nitrone **11** (0.031 g, 0.117 mmol) and ketene solution **12** (1.0 mL) following **general procedure D**, to yield **17** (0.027 g, 82%) as a white solid; mp 146-147 °C; ν_{max} cm^{-1} (KBr) 3168 (NH), 3076, 2900, 2847, 1712 (C=O), 1689, 1633, 1598, 1485, 1463; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (1H, br s, N*H*), 7.53 (1H, s, Ar*H*), 7.48 (1H, ddd, *J* = 8.1, 1.7, 0.8, Ar*H*), 6.94 (1H, d, *J* = 8.1, Ar*H*), 2.07-1.94 (4H, m, CH_2), 1.82-1.69 (8H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.7, 142.4, 138.3, 125.2 (d, *J* = 3.7), 120.1 (d, *J* = 3.7), 109.2, 50.5, 36.8, 31.2, 23.8; *m/z* (ESI$^+$) 284 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{15}H_{17}F_3ON^+$ ([M+H]$^+$) found 284.1255 requires 284.1257 (- 0.6 ppm).

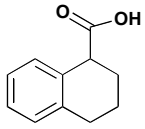
5'-Methoxyspiro[cycloheptane-1,3'-indolin]-2'-one 18



The oxindole was obtained from nitrone **4** (0.036 g, 0.158 mmol) and ketene solution **12** (1.0 mL) following **general procedure D**, to yield **18** (0.036 g, 92%) as a white solid; mp 162-163°C; ν_{max} cm^{-1} (KBr) 3174 (NH), 3088, 2947, 2907, 2847, 1714 (C=O), 1687, 1633, 1601, 1484, 1456, 1438, 1350, 1328, 1311; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (1H, *br* s, N*H*), 6.94 (1H, d, *J* = 2.4, Ar*H*), 6.77 (1H, d, *J* = 8.4, Ar*H*), 6.71 (1H, dd, *J* = 8.4, 2.4, Ar*H*), 3.80 (3H, s, O*Me*), 2.05-1.91 (4H, m, CH_2), 1.79-1.68 (8H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.2, 155.7, 139.3, 132.9, 111.2, 111.0, 109.6, 55.9, 50.9, 36.9, 31.3, 23.8; *m/z* (ESI^+) 246 ($[M+H]^+$, 100%); HRMS (EI^+) $C_{15}H_{20}O_2N^+$ ($[M+H]^+$) found 246.1491 requires 230.1491 (+ 1.0 ppm).

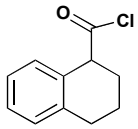
6. Ketene Preparation

1,2,3,4-Tetrahydronaphthalene-1-carboxylic acid 52



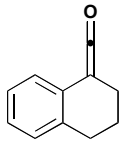
52 was prepared according to a known two-step literature procedure[15] from 1-naphthoic acid (11.5 g, 668 mmol) and isolated as a light brown solid (3.46 g, 33% over 2 steps) which was used without any further purification and with analytical data in accordance with the literature values; mp 110-112 °C {lit.[16] 82-84 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.05 (1H, *br* s), 7.25-7.11 (4H, m, Ar*H*), 3.86-3.84 (1H, m, C*H*), 2.89-2.73 (2H, m, CH_2), 2.24-2.18 (1H, m, 1 x CH_2), 2.08-1.95 (2H, m, CH_2), 1.83-1.77 (1H, m, 1 x CH_2).

1,2,3,4-Tetrahydronaphthalene-1-carbonyl chloride 53



To a stirred solution of **52** (3.45 g, 1.96 mmol) in toluene (40 mL) was added thionyl chloride (2.86 mL, 2.0 eq, 3.96 mmol) and the reaction stirred at 80 °C for 5h. After this time, the reaction mixture was concentrated *in vacuo* and purified *via* Kugelrohr distillation (230 °C; 3 mmHg) {lit.[17] 142.5-143 °C; 18 mmHg}; to yield **53** (2.55 g, 67%) as a pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.20 (1H, m, Ar*H*), 7.19-7.14 (3H, m, Ar*H*), 4.26 (1H, t, *J* = 6.1, C*H*), 2.90-2.74 (2H, m, CH_2), 2.36 (1H, dddd, *J* = 13.4, 7.9, 5.7, 3.2, CH_2), 2.19 (1H, dddd, *J* = 13.4, 9.9, 6.5, 3.2, CH_2), 1.99-1.89 (1H, m, 1 x CH_2), 1.87-1.80 (1H, m, 1 x CH_2).

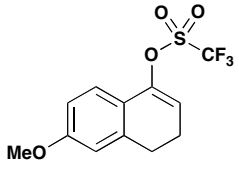
1,2,3,4-Tetrahydronaphthalene-1-ketene 20



To a stirred solution of acyl chloride **53** (3.10 g, 15.9 mmol) in dry Et_2O (45 mL) at 0 °C under nitrogen was added N,N-dimethylethylamine (1.90 mL, 1.1 eq, 17.5 mmol) dropwise over 15 min. The reaction was then stirred for 16 h at 0 °C. After this time, the reaction mixture was allowed to

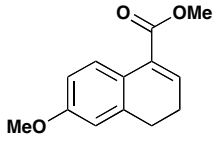
warm to rt before being filtered under nitrogen to remove the hydrochloride salts. The Et_2O was then removed under reduced pressure to leave a yellow oil which was purified *via* Kugelrohr distillation (154-160 °C, 3 mmHg) {lit.[18] 52-53 °C; 0.001 mmHg} to yield **20** (1.14 g, 45 %) a dark yellow/orange liquid which was stored in the freezer under nitrogen and used within two weeks of preparation; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15-7.08 (2H, m, Ar*H*), 7.00-6.94 (2H, m, Ar*H*), 2.77 (2H, t, J = 6.2, CH_2), 2.68-2.64 (2H, m, CH_2), 1.96-1.87 (2H, m, CH_2).

6-Methoxy-3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate 54



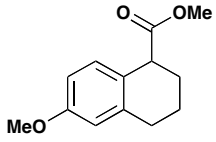
To a stirred solution of 6-methoxytetralone (12.21 g, 69.3 mmol) in THF (80 mL) at -78 °C was added LHMDS (1.0 M in THF, 69.0 mL, 1.10 eq) dropwise and the reaction mixture stirred at -78 °C for 45 min. A solution of N,N-bis(trifluoromethylsulfonyl)aniline (25.0 g, 1.01 eq, 70.0 mmol) in THF (35 mL) was then added dropwise and upon completion of addition, the reaction was warmed to 0°C and stirred for 3 h before quenching with H_2O (50 mL). The reaction mixture was then partitioned between Et_2O (120 mL) and H_2O (100 mL), the aqueous layer collected and extracted with Et_2O (70 mL x 3). The combined organic layers were then washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude brown oil. The crude product was purified *via* rapid flash column chromatography over silica (20% EtOAc in petroleum ether) to yield **54** (22.6 g, quant.) as an orange oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (1H, s, Ar*H*), 6.64 (1H, dd, J = 8.5, 2.5, Ar*H*), 6.60 (1H, d, J = 2.5, Ar*H*), 5.73 (1H, t, J = 4.8, C*H*), 3.69 (3H, s, O*Me*), 2.70 (2H, t, J = 8.1, CH_2), 2.35 (2H, td, J = 8.1, 4.8, CH_2).

Methyl 6-methoxy-3,4-dihydronaphthalene-1-carboxylate 55



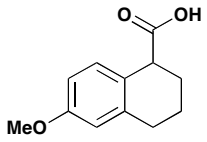
To a stirred solution of **54** (10.0 g, 32.5 mmol) in DMF (80 mL) was added sequentially MeOH (60 mL), Et_3N (7.20 mL, 1.6 eq, 52.0 mmol), PPh_3 (3.41 g, 0.4 eq, 13.0 mmol) and $Pd(OAc)_2$ (0.73 g, 0.1 eq, 3.25 mmol) under nitrogen. A balloon of carbon monoxide gas was then introduced to the reaction, the reaction vessel purged and heated to 65 °C. The reaction vessel was then sealed under an atmosphere of carbon monoxide and heated at 65 °C for 16 h. After this time, the reaction mixture was allowed to cool to rt before being partitioned between EtOAc (250 mL) and H2O (150 mL). The layers were then separated and the organic layer washed with 1M HCl (100 mL) and brine (100 mL) before being dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude brown oil which was purified by flash column chromatography over silica (20% EtOAc in petroleum ether) to yield **55** (3.03 g, 43%) as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (1H, d, J = 8.6, Ar*H*), 7.03 (1H, t, J = 4.9, C*H*), 6.76 (1H, dd, J = 8.6, 2.8, Ar*H*), 6.72 (1H, d, J = 2.6, Ar*H*), 3.84 (3H, s, O*Me*), 3.81 (3H, s, O*Me*), 2.74 (2H, t, J = 7.9, CH_2), 2.38 (2H, ddd, J = 8.6, 7.2, 4.9, CH_2).

Methyl 6-methoxy-1,2,3,4-tetrahydronaphthalene-1-carboxylate 56



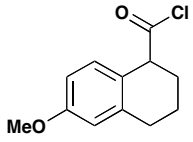
To a stirred solution of **55** (3.03 g, 13.9 mmol) in EtOH (150 mL) was added 10 mol % Pd/C (0.225 g) at rt. A balloon of hydrogen gas was then introduced to the reaction mixture, the vessel purged and then sealed before being stirred under an atmosphere of hydrogen and stirred at rt for 16 h. The reaction mixture was then filtered through a celite plug, the residue washed with EtOAc, and the filtrate concentrated *in vacuo* to yield **56** (3.01 g, quant.) as a colourless oil which was used without any further purification; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (1H, d, *J* = 8.5, Ar*H*), 6.71 (1H, dd, *J* = 8.5, 2.8, Ar*H*), 6.63 (1H, d, *J* = 2.7, Ar*H*), 3.79-3.76 (1H, m, C*H*), 3.77 (3H, s, O*Me*), 3.71 (3H, s, O*Me*), 2.87-2.67 (2H, m, CH_2), 2.18-2.09 (1H, m, 1 x CH_2), 2.03-1.91 (1H, m, 1 x CH_2), 1.80-1.69 (2H, m, CH_2).

6-Methoxy-1,2,3,4-tetrahydronaphthalene-1-carboxylic acid 57



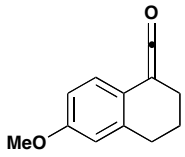
To a stirred solution of **56** (3.00 g, 13.6 mmol) in H_2O/MeOH (4/30 mL) was added LiOH (1.63 g, 5 eq., 68.0 mmol) and the reaction stirred at rt for 16 h. The reaction mixture was then concentrated *in vacuo* to give a white semi-solid which was taken up in H_2O (25 mL) and the acid precipitated by dropwise addition of 2M HCl. The white precipitate was then collected by filtration and dried under high vacuum to yield **57** (2.80 g, quant.) as a white solid; mp 78-80 °C {lit.[19] 83-84 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (1H, d, *J* = 8.5, Ar*H*), 6.73 (1H, dd, *J* = 8.5, 2.7, Ar*H*), 6.64 (1H, d, *J* = 2.7, Ar*H*), 3.81-3.78 (1H, m, C*H*), 3.78 (3H, s, O*Me*), 2.87-2.65 (2H, m, 1 x CH_2), 2.24-2.09 (1H, m, 1 x CH_2), 2.06-1.86 (2H, m, CH_2), 1.85-1.70 (1H, m, 1 x CH_2).

6-Methoxy-1,2,3,4-tetrahydronaphthalene-1-carbonyl chloride 58



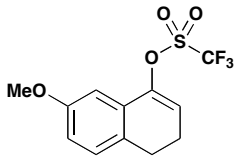
To a stirred solution of **57** (2.80 g, 13.6 mmol) in toluene (30 mL) was added DMF (0.212 mL, 0.2 eq, 2.72 mmol) followed by dropwise addition of oxalyl chloride (2.37 mL, 2.0 eq, 27.2 mmol). The reaction mixture was then stirred for 3 h at rt before being concentrated *in vacuo* multiple times with additional toluene (to remove excess oxalyl chloride) to yield **58** as a yellow oil (2.29 g, 75%) which was used without further purification; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (1H, d, *J* = 8.5, Ar*H*), 6.75 (1H, dd, *J* = 8.5, 2.7, Ar*H*), 6.66 (1H, d, *J* = 2.7, Ar*H*), 4.19 (1H, t, *J* = 6.0, C*H*), 3.79 (3H, s, O*Me*), 2.91-2.69 (2H, m, CH_2), 2.39-2.29 (1H, m, 1 x CH_2), 2.21-2.10 (1H, m, 1 x CH_2), 1.98-1.74 (2H, m, CH_2).

6-Methoxy-1,2,3,4-tetrahydronaphthalene-1-ketene 59



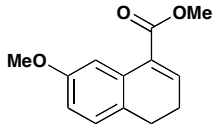
To a stirred solution of **58** (1.0 g, 4.45 mmol) in Et_2O (18 mL) at 0 °C was added N,N-dimethylethylamine (0.531 mL, 1.1 eq, 4.90 mmol) dropwise and the reaction mixture stirred at 0°C for 16h. After such time, the reaction mixture was filtered under argon to remove amine hydrochloride salts and the reaction mixture concentrated under reduced pressure to yield a dark yellow oil. The crude ketene was suspended in THF (10 mL) and used as a crude solution in all further reactions. ***This ketene was not distilled, but used as a crude solution in THF assumed to be 40 mg per 1 mL of THF.*** As such, only limited spectroscopic data was obtained for this species; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (1H, d, *J* = 8.5, Ar*H*), 6.72 (1H, dd, *J* = 8.5, 2.7, Ar*H*), 6.66 (1H, d, *J* = 2.7, Ar*H*), 3.77 (3H, s, O*Me*), 2.73 (2H, t, *J* = 6.2, CH_2), 2.64-2.61 (2H, m, CH_2), 1.92-1.84 (2H, m, CH_2).

7-Methoxy-3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate 60



To a stirred solution of 7-methoxytetralone (12.00 g, 68.0 mmol) in THF (100 mL) at -78 °C was added LHMDS (1.0 M in THF, 74.8 mL, 1.10 eq) dropwise and the reaction mixture stirred at -78 °C for 45 min. A solution of N,N-bis(trifluoromethylsulfonyl)aniline (25.0 g, 1.01 eq, 70.0 mmol) in THF (35 mL) was then added dropwise and upon completion of addition, the reaction was warmed to 0°C and stirred for 3 h before quenching with H_2O (50 mL). The reaction mixture was then partitioned between Et_2O (120 mL) and H_2O (100 mL), the aqueous layer collected and extracted with Et_2O (70 mL x 3). The combined organic layers were then washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude brown oil. The crude product was purified *via* rapid flash column chromatography over silica (20% EtOAc in petroleum ether) to yield **60** (22.4 g, quant.) as an orange oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (1H, d, *J* = 8.2, Ar*H*), 6.91 (1H, d, *J* = 2.6, Ar*H*), 6.80 (1H, dd, *J* = 8.2, 2.6, Ar*H*), 6.03 (1H, t, *J* = 4.8, C*H*), 3.81 (3H, s, O*Me*), 2.80 (2H, *J* = 8.2, CH_2), 2.53-2.45 (2H, m, CH_2).

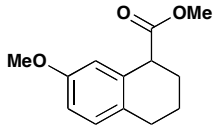
Methyl 7-methoxy-3,4-dihydronaphthalene-1-carboxylate 61



To a stirred solution of **60** (17.0 g, 55.2 mmol) in DMF (135mL) was added sequentially MeOH (110 mL), Et_3N (12.24 mL, 1.6 eq, 88.3 mmol), PPh_3 (5.79 g, 0.4 eq, 22.1 mmol) and $Pd(OAc)_2$ (1.24 g, 0.1 eq, 5.52 mmol) under nitrogen. A balloon of carbon monoxide gas was then introduced to the reaction, the reaction vessel purged and heated to 65 °C. The reaction vessel was then sealed under an atmosphere of carbon monoxide and heated at 65 °C for 16 h. After this time, the reaction mixture was allowed to cool to rt before being partitioned between EtOAc (250 mL) and H2O (150 mL). The layers were then separated and the organic layer washed with 1M HCl (100 mL) and brine (100 mL) before being dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude

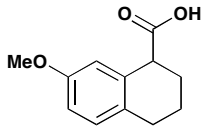
brown oil which was purified by flash column chromatography over silica (20% EtOAc in petroleum ether) to yield **61** (7.43 g, 62%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (1H, d, *J* = 2.7, Ar*H*), 7.20 (1H, t, *J* = 4.9, C*H*), 7.07 (1H, d, *J* = 8.2, Ar*H*), 6.75 (1H, dd, *J* = 8.2, 2.7, Ar*H*), 3.85 (3H, s, O*Me*), 3.81 (3H, s, O*Me*), 2.70 (2H, t, *J* = 7.9, CH_2), 2.41-2.36 (2H, m, CH_2).

Methyl 7-methoxy-1,2,3,4-tetrahydronaphthalene-1-carboxylate 62



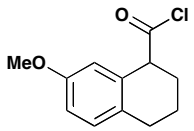
To a stirred solution of **61** (7.43 g, 34.0 mmol) in EtOH (250 mL) was added 10 mol % Pd/C (0.440 g) at rt. A balloon of hydrogen gas was then introduced to the reaction mixture, the vessel purged and then sealed before being stirred under an atmosphere of hydrogen and stirred at rt for 16 h. The reaction mixture was then filtered through a celite plug, the residue washed with EtOAc, and the filtrate concentrated *in vacuo* to yield **62** (7.40 g, quant.) as a colourless oil which was used without any further purification; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (1H, d, *J* = 8.3, Ar*H*), 6.77-6.71 (2H, m, Ar*H*), 3.81 (1H, t, *J* = 5.7, C*H*), 3.79 (3H, s, O*Me*), 3.72 (3H, s, O*Me*), 2.82-2.63 (2H, m, CH_2), 2.14-2.08 (1H, m, 1 x CH_2), 2.00-1.93 (2H, m, CH_2), 1.79-1.73 (1H, m, 1 x CH_2).

7-Methoxy-1,2,3,4-tetrahydronaphthalene-1-carboxylic acid 63



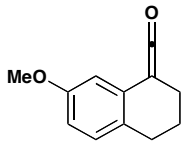
To a stirred solution of **63** (7.40 g, 33.6 mmol) in H_2O/MeOH (10/75 mL) was added LiOH (4.02 g, 5 eq., 170.2 mmol) and the reaction stirred at rt for 16 h. The reaction mixture was then concentrated *in vacuo* to give a white semi-solid which was taken up in H_2O (75 mL) and the acid precipitated by dropwise addition of 2M HCl. The white precipitate was then collected by filtration and dried under high vacuum to yield **63** (6.20 g, 89%) as a white solid; mp 120-121 °C {lit.[20] 137-138 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (1H, d, *J* = 9.2, Ar*H*), 6.78-6.75 (2H, m, Ar*H*), 3.82 (1H, t, *J* = 5.5, C*H*), 3.77 (3H, s, O*Me*), 2.83-2.63 (2H, m, CH_2), 2.22-2.11 (1H, m, 1 x CH_2), 2.06-1.90 (2H, m, CH_2), 1.81-1.71 (1H, m 1 x CH_2).

7-Methoxy-1,2,3,4-tetrahydronaphthalene-1-carbonyl chloride 64



To a stirred solution of **63** (6.20 g, 30.1 mmol) in toluene (65 mL) was added DMF (0.47 mL, 0.2 eq, 6.02 mmol) followed by dropwise addition of oxalyl chloride (5.25 mL, 2.0 eq, 60.2 mmol). The reaction mixture was then stirred for 3 h at rt before being filtered and concentrated *in vacuo* multiple times with additional toluene (to remove excess oxalyl chloride) to yield **64** as a yellow oil (5.10 g, 78%) which was used without further purification; ν_{max} cm^{-1} (thin-film) 2351, 1786, 1599, 1585, 1489; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (1H, d, *J* = 8.5, Ar*H*), 6.81 (1H, dd, *J* = 8.5, 2.6, Ar*H*), 6.68 (1H, d, *J* = 2.6, Ar*H*), 4.21 (1H, t, *J* = 6.1, C*H*), 3.78 (3H, s, O*Me*), 2.84–2.65 (2H, m, CH_2), 2.38-2.28 (1H, m, 1 x CH_2), 2.22-2.11 (1H, m, 1 x CH_2), 1.99-1.74 (2H, m, 1 x CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 157.8, 131.8, 130.6, 129.3, 114.5, 114.3, 56.6, 55.4, 28.1, 26.7, 20.4.

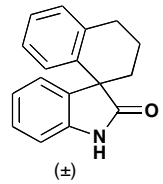
7-Methoxy-1,2,3,4-tetrahydronaphthalene-1-ketene 65



To a stirred solution of **64** (1.0 g, 4.45 mmol) in Et_2O (18 mL) at 0°C was added N,N-dimethylethylamine (0.531 mL, 1.1 eq, 4.90 mmol) dropwise and the reaction mixture stirred at 0°C for 16h. After such time, the reaction mixture was filtered under argon to remove amine hydrochloride salts and the reaction mixture concentrated under reduced pressure to yield a dark yellow oil. The crude ketene was suspended in THF (10 mL) and used as a crude solution in all further reactions. ***This ketene was not distilled, but used as a crude solution in THF assumed to be 40 mg per 1 mL of THF.*** As such, only limited spectroscopic data was obtained for this species; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (1H, d, *J* = 8.4, Ar*H*), 6.54 (1H, dd, *J* = 8.4, 2.6, Ar*H*), 6.44 (1H, d, *J* = 2.6, Ar*H*), 3.75 (3H, s, O*Me*), 2.68 (2H, t, *J* = 6.1, CH_2), 2.63-2.60 (2H, m, CH_2), 1.86-1.84 (2H, m, CH_2).

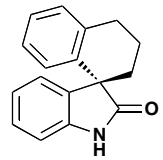
7. Asymmetric Spirocyclic Oxindoles

(±)-3',4'-Dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one (±)22

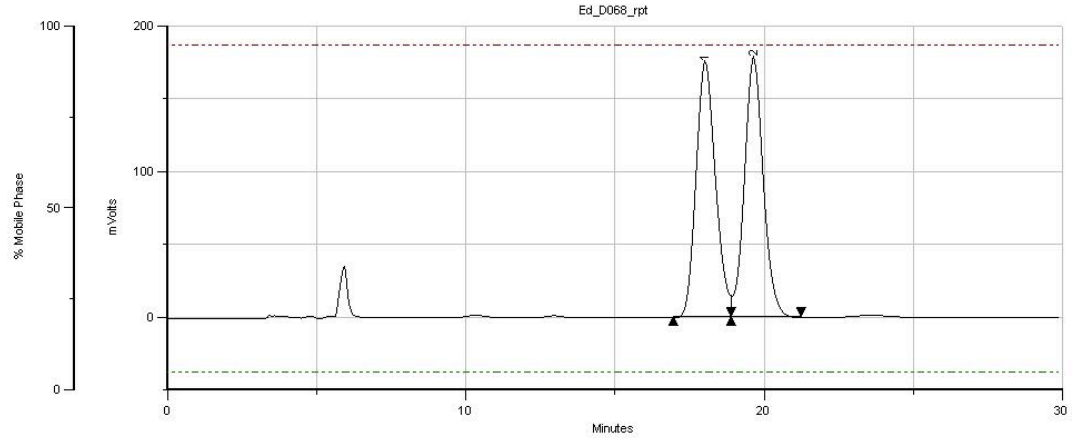


The oxindole was obtained from nitrone **3** (0.050 g, 0.254 mmol) and ketene **20** (0.040 g, 0.279 mmol) following **general procedure E** to yield **(±)22** (0.047 g, 74%) as a white solid; mp 211-213 °C {lit.[21] 213-215 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (1H, br s, Ar*H*), 7.26-7.11 (3H, m, Ar*H*), 7.05-6.94 (4H, m, Ar*H*), 6.61 (1H, dd, *J* = 7.8, 0.7, Ar*H*), 3.07-2.92 (2H, m, CH_2), 2.39-2.22 (2H, m, CH_2), 2.07-1.97 (2H, m, CH_2).

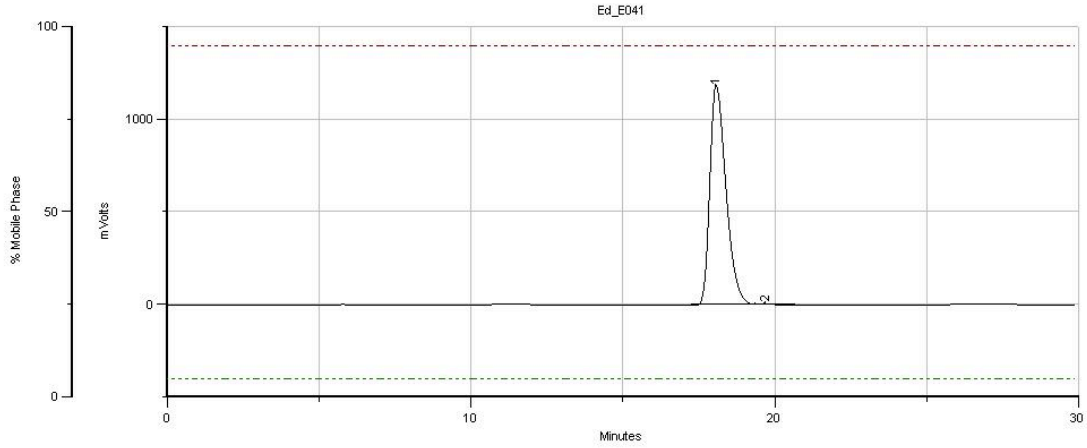
(*S*)-3',4'-Dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one 22



The oxindole was obtained from chiral nitrone **19** (0.110g, 22.6 mmol) and ketene **20** (0.054 g, 33.9 mmol) following **general procedure F** to yield **22** (0.054 g, 96%) as an off-white solid; $[\alpha]_D^{20}$ +0.8° (*c* = 0.75, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 18.0 min (major) and 19.6 min (minor)).

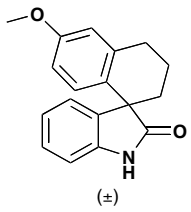


Peak	tR (min)	Area (%)
1	18.02	50.33
2	19.64	49.67



Peak	tR (min)	Area (%)
1	18.09	99.41
2	19.69	0.59

(±)-6'-Methoxy-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one (±)29

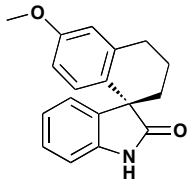


(±)

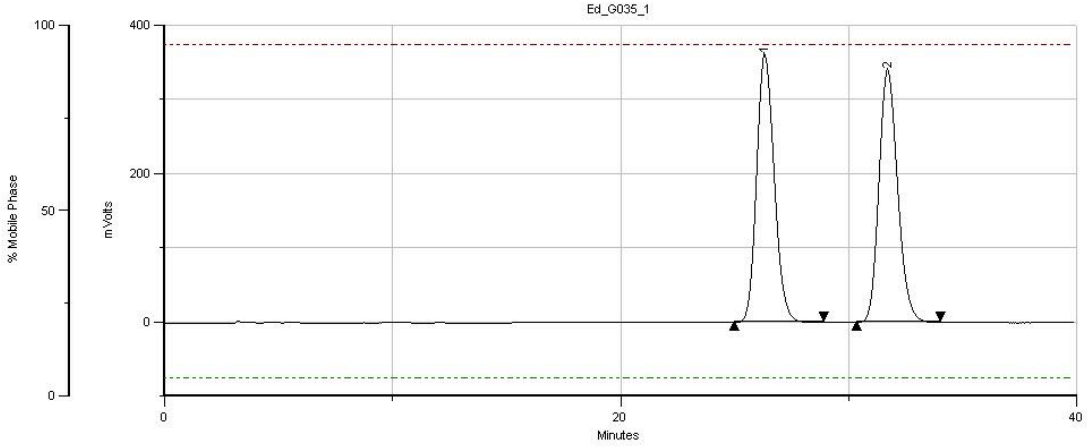
The oxindole was obtained from nitrone **3** (0.084 g, 0.353 mmol) and ketene solution **59** (0.080 g, 0.425 mmol) following **general procedure E** to yield **(±)29** (0.093 g, 94%) as a white solid; mp 149-150 °C; ν_{max} cm^{-1} (thin-film) 3130, 3080, 2934, 1697, 1620, 1499, 1474; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (1H, br s, N*H*), 7.21 (1H, td, *J* = 7.5, 1.5, Ar*H*), 7.03-6.92 (3H, m, Ar*H*), 6.70 (1H, d, *J* = 2.4, Ar*H*), 6.57-6.50 (2H, m, Ar*H*), 3.75 (3H, s, O*Me*), 3.04-2.88 (2H, m, CH_2), 2.42-2.30 (1H, m, 1 x CH_2), 2.26-2.18 (1H, m, 1 x CH_2), 2.03-1.95 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ

181.5, 157.4, 138.9, 138.2, 136.9, 128.2, 126.7, 126.0, 123.3, 121.8, 112.8, 112.1, 108.5, 54.2, 50.9, 33.3, 28.6, 17.7; *m/z* (ESI$^+$) 280 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{18}H_{17}NO_2^+$ ([M+H]$^+$) found 280.1334 requires 280.1332 (+ 0.2 ppm).

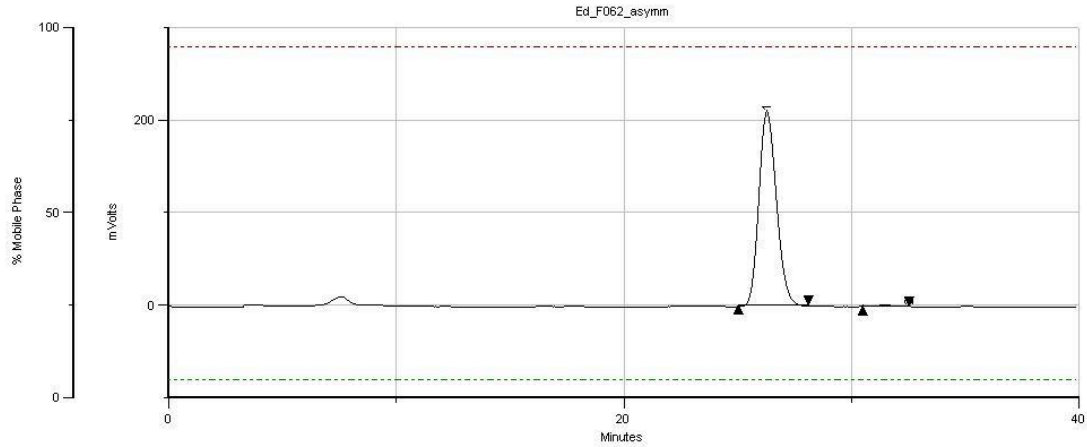
(*S*)-6'-Methoxy-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one 29



The oxindole was obtained from chiral nitrone **19** (0.104 g, 0.214 mmol) and ketene solution **59** (1.6 mL) following **general procedure F** to yield **29** (0.036 g, 85%) as an off-white solid; $[\alpha]_D^{20}$ -8.8° (*c* = 0.50, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 26.3 min (major) and 31.7 min (minor)).

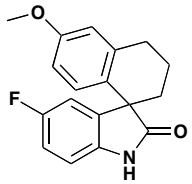


Peak	tR (min)	Area (%)
1	26.32	50.06
2	31.71	49.94



Peak	tR (min)	Area (%)
1	26.29	98.60
2	31.46	1.40

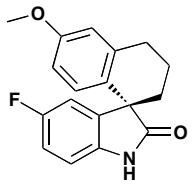
(±)-5-Fluoro-6'-methoxy-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one (±)30



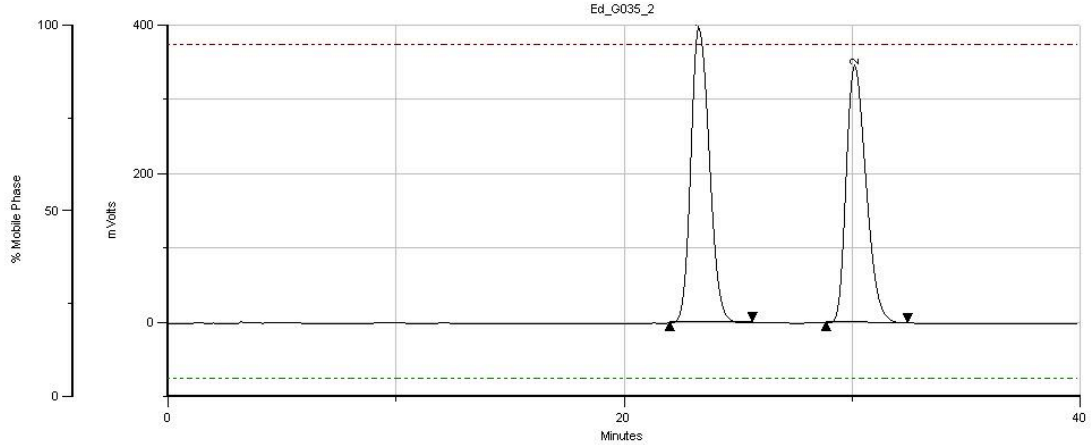
(±)

The oxindole was obtained from nitrone **5** (0.091 g, 0.353 mmol) and ketene solution **59** (0.080 g, 0.425 mmol) following **general procedure E** to yield **(±)30** (0.093 g, 89%) as a white solid; mp 71-73 °C; ν_{max} cm^{-1} (thin-film) 3067, 2930, 1699, 1609, 1503, 1472; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (1H, br s, N*H*), 6.95-6.83 (2H, m, Ar*H*), 6.78 (1H, dd, *J* = 8.1, 2.5, Ar*H*), 6.70 (1H, d, *J* = 2.5, Ar*H*), 6.60 (1H, dd, *J* = 8.6, 2.5, Ar*H*), 6.51 (1H, d, *J* = 8.6, Ar*H*), 3.76 (3H, s, O*Me*), 3.03-2.90 (2H, m, CH_2), 2.42-2.30 (1H, m, 1 x CH_2), 2.23-2.18 (1H, m, 1 x CH_2), 2.01-1.93 (2H, m, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.5, 158.9 (d, *J* = 237.5), 158.6, 139.5, 139.4, 139.2, 136.1, 129.2, 126.4, 114.1 (d, *J* = 25.0), 114.1, 113.3, 112.0 (d, *J* = 25.0), 110.5 (d, *J* = 7.9), 55.2, 52.7, 34.2, 29.6, 18.7; *m/z* (ESI$^+$) 298 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{18}H_{16}FNO_2^+$ ([M+H]$^+$) found 298.1241 requires 280.1238 (+ 0.3 ppm).

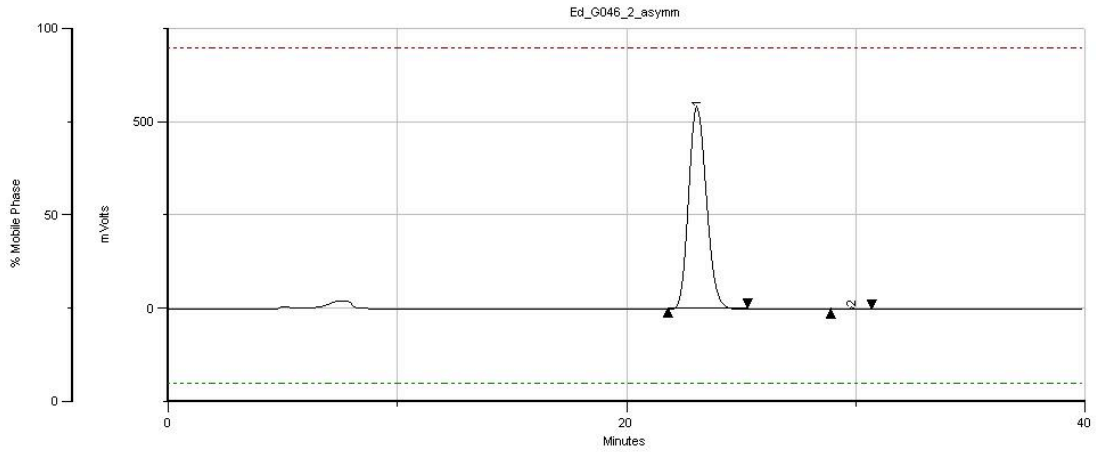
(*S*)-5-Fluoro-6'-methoxy-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one 30



The oxindole was obtained from chiral nitrone **24** (0.108 g, 0.214 mmol) and ketene solution **59** (1.6 mL) following **general procedure F** to yield **30** (0.063 g, 99%) as a white solid; $[\alpha]_D^{20}$ -6.7° (*c* = 0.55, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 23.3 min (major) and 30.1 min (minor)).

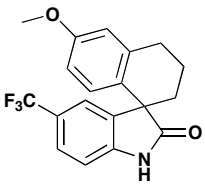


Peak	tR (min)	Area (%)
1	23.28	51.67
2	30.12	48.33



Peak	tR (min)	Area (%)
1	23.07	98.78
2	29.81	1.22

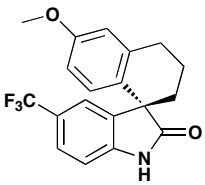
(±)-6'-Methoxy-5-(trifluoromethyl)-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one (±)31



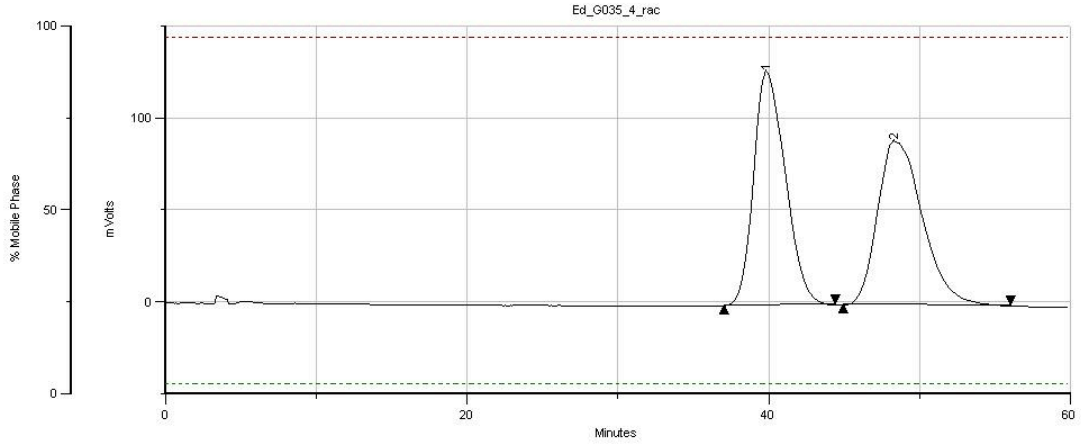
(±)

The oxindole was obtained from nitrone **11** (0.113 g, 0.353 mmol) and ketene solution **59** (0.080 g, 0.425 mmol) following **general procedure E** to yield **(±)31** (0.101 g, 82%) as a white solid; mp 70-71 °C; ν_{max} cm^{-1} (thin-film) 3157, 2934, 2841, 1694, 1622, 1497; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (1H, br s, N*H*), 7.52 (1H, dd, *J* = 8.2, 0.9, Ar*H*), 7.04 (1H, d, *J* = 8.2, Ar*H*), 6.75 (1H, d, *J* = 2.7, Ar*H*), 6.62 (1H, dd, *J* = 8.6, 2.7, Ar*H*), 6.50 (1H, d, *J* = 8.6, Ar*H*), 3.79 (3H, s, O*Me*), 3.01 (2H, app. br t, *J* = 6.3, CH_2), 2.45-2.36 (1H, m, 1 x CH_2), 2.28-2.20 (1H, m, 1 x CH_2), 2.07-1.96 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 158.8, 143.5, 139.4, 138.3, 129.1, 125.9, 125.6 (app. t, *J* = 5.0), 125.1 (d, *J* = 40.3), 121.2 (d, *J* = 3.9), 114.1, 113.4, 109.9, 55.2, 52.2, 34.3, 29.6, 18.6; *m/z* (ESI^+) 348 ($[M+H]^+$, 100%); HRMS (EI^+) $C_{19}H_{16}F_3NO_2^+$ ($[M+H]^+$) found 348.1205 requires 348.1206 (+ 0.1 ppm).

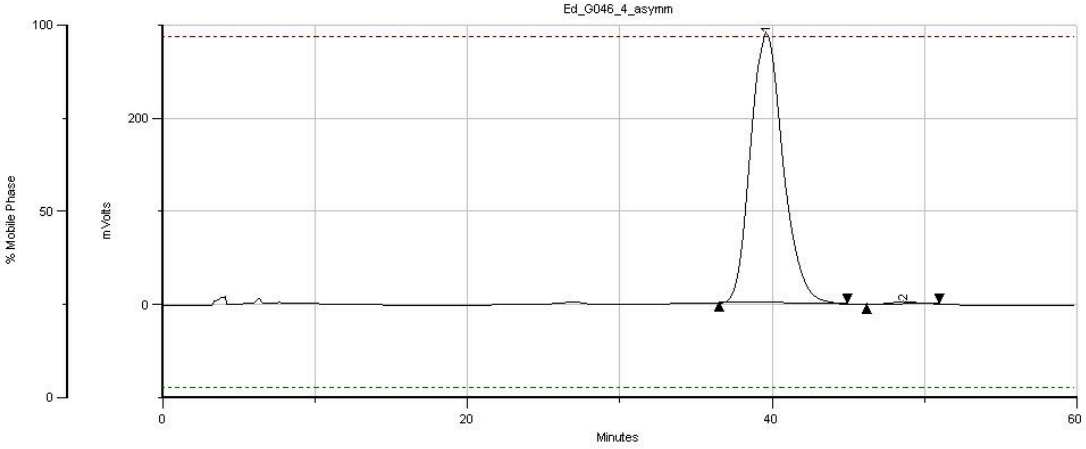
(*S*)-6'-Methoxy-5-(trifluoromethyl)-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one 31



The oxindole was obtained from chiral nitrone **25** (0.119 g, 0.214 mmol) and ketene solution **59** (1.6 mL) following **general procedure F** to yield **31** (0.036 g, 48%) as a white solid; $[\alpha]_D^{20}$ -52.0° (*c* = 0.40, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 39.8 min (major) and 49.0 min (minor)).

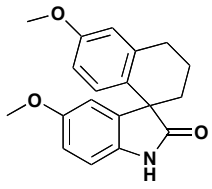


Peak	tR (min)	Area (%)
1	39.85	50.08
2	49.30	49.92



Peak	tR (min)	Area (%)
1	39.61	98.66
2	48.65	1.34

(±)-5,6'-Dimethoxy-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one (±)32

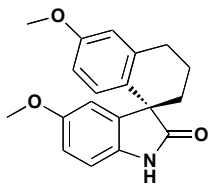


(±)

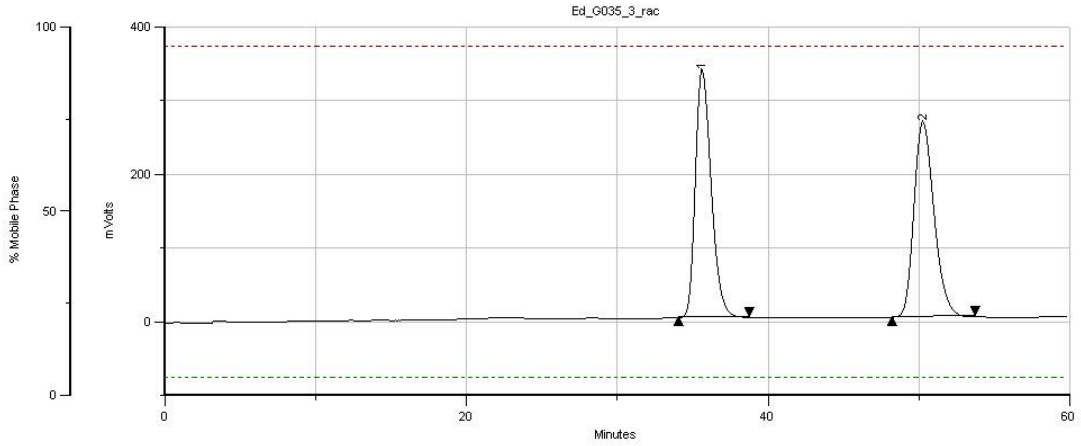
The oxindole was obtained from nitrone **4** (0.074 g, 0.326 mmol) and ketene solution **59** (0.080 g, 0.425 mmol) following **general procedure E** to yield **(±)32** (0.078 g, 77%) as a white solid; mp 109-110 °C; ν_{max} cm^{-1} (thin-film) 3190, 2934, 1683, 1605, 1495; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (1H, br s, N*H*), 6.84 (1H, d, *J* = 8.5, Ar*H*), 6.74 (1H, dd, *J* = 8.5, 2.5, Ar*H*), 6.69 (1H, d, *J* = 2.5, Ar*H*), 6.63 (1H, d, *J* = 2.5, Ar*H*), 6.59 (1H, dd, *J* = 8.5, 2.5, Ar*H*), 6.53 (1H, d, *J* = 8.5, Ar*H*), 3.75 (3H, s, O*Me*), 3.72 (3H, s, O*Me*), 3.05-2.87 (2H, m, CH_2), 2.43-2.30 (1H, m, 1 x CH_2), 2.26-2.16 (2H, m, CH_2), 2.03-1.92 (1H, m, 1 x CH_2); ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.5, 158.4, 156.0, 139.2, 133.4, 129.3, 127.0, 113.8, 113.1, 112.4, 111.4, 109.8, 55.8, 55.2, 52.4, 34.4, 29.6, 18.7, 14.2; *m/z*

(ESI$^+$) 310 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{19}H_{19}NO_3^+$ ([M+H]$^+$) found 310.1441 requires 310.1438 (+ 0.3 ppm).

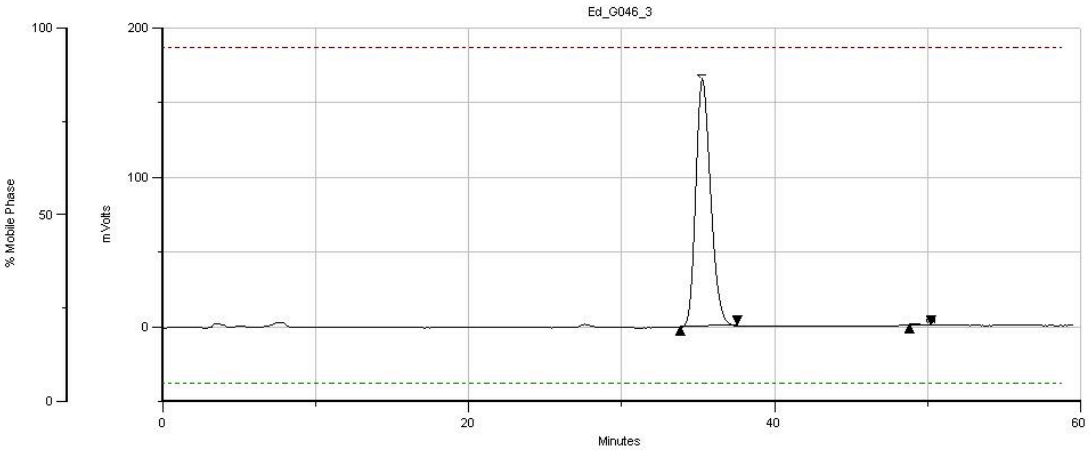
(*S*)-5,6'-Dimethoxy-3',4'-dihydro-2'*H*-spiro[indoline-3,1'-naphthalen]-2-one 32



The oxindole was obtained from chiral nitrone **26** (0.111 g, 0.214 mmol) and ketene solution **59** (1.6 mL) following **general procedure F** to yield **32** (0.034 g, 52%) as a white solid; $[\alpha]_D^{20}$ -75.2° (c = 0.25, $CHCl_3$); HPLC analysis: 99% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 35.6 min (major) and 50.3 min (minor)).

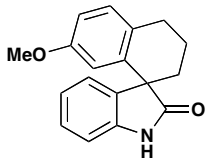


Peak	tR (min)	Area (%)
1	35.62	49.95
2	50.26	50.05



Peak	tR (min)	Area (%)
1	35.27	99.72
2	49.30	0.28

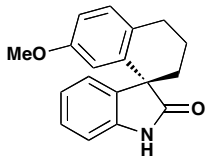
(±)-7'-methoxy-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one (±)33



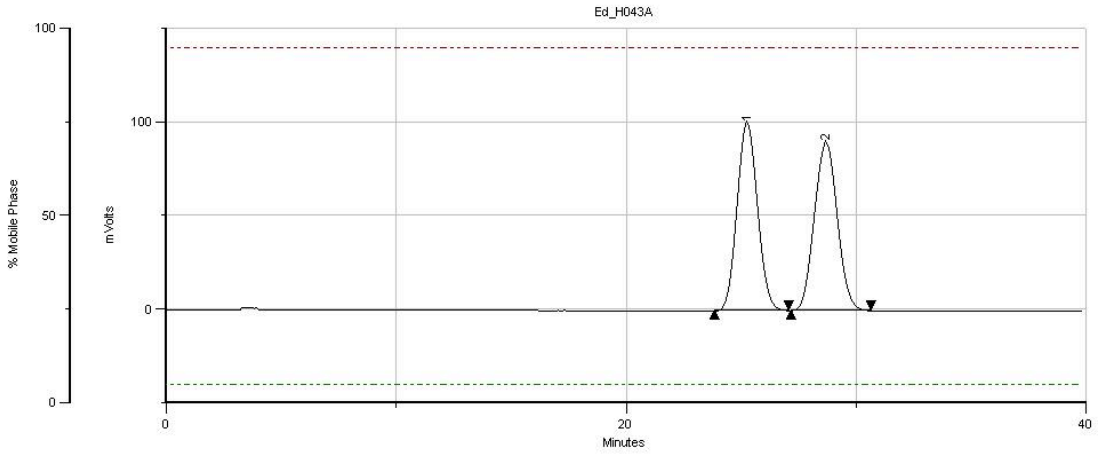
(±)

The oxindole was obtained from nitrone **3** (0.028 g, 0.142 mmol) and ketene solution **65** (2.0 mL) following **general procedure E** to yield **(±)33** (0.033 g, 83%) as a white solid; mp 101-103 °C; ν_{max} cm^{-1} (thin-film) 3179, 2934, 2836, 1687, 1620, 1497; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (1H, br s, N*H*), 7.21 (1H, td, *J* = 7.6, 1.5, Ar*H*), 7.10 (1H, d, *J* = 8.5, Ar*H*), 7.06-7.03 (1H, m, Ar*H*), 6.99 (1H, dd, *J* = 7.4, 1.0, Ar*H*), 6.93 (1H, d, *J* = 7.7, Ar*H*), 6.73 (1H, dd, *J* = 8.5, 2.7, Ar*H*), 6.12 (1H, d, *J* = 2.7, Ar*H*), 3.61 (3H, s, O*Me*), 2.99-2.84 (2H, m, CH_2), 2.35-2.17 (2H, m, CH_2), 2.05-1.95 (2H, m, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.6, 157.8, 140.1, 137.7, 135.7, 130.5, 130.1, 127.9, 124.3, 122.8, 113.3, 113.1, 109.8, 55.2, 52.8, 34.1, 28.5, 18.9; *m/z* (ESI$^+$) 280 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{18}H_{17}NO_2^+$ ([M+H]$^+$) found 280.1336 requires 280.1332 (+ 0.4 ppm).

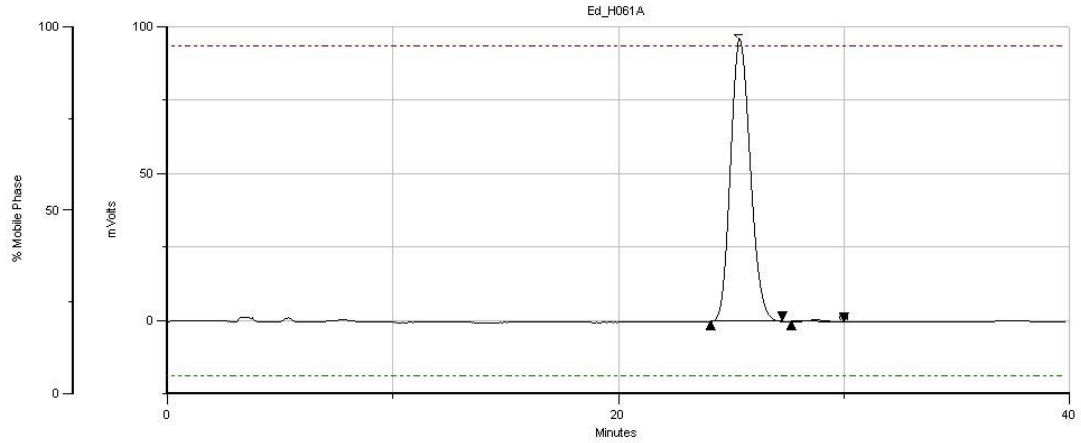
(*S*)-7'-methoxy-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one 33



The oxindole was obtained from chiral nitrone **19** (0.075 g, 0.154 mmol) and ketene solution **65** (2.0 mL) following **general procedure F** to yield **33** (0.034 g, 79%) as a white solid; $[\alpha]_D^{20}$ -9.4° (*c* = 0.70, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 25.3 min (major) and 28.7 min (minor)).

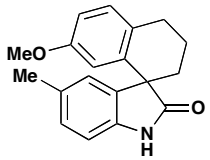


Peak	tR (min)	Area (%)
1	25.26	49.86
2	28.70	50.14



Peak	tR (min)	Area (%)
1	25.38	98.98
2	28.83	1.02

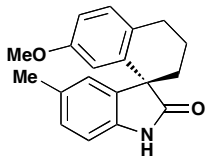
(±)-7'-methoxy-5-methyl-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one (±)34



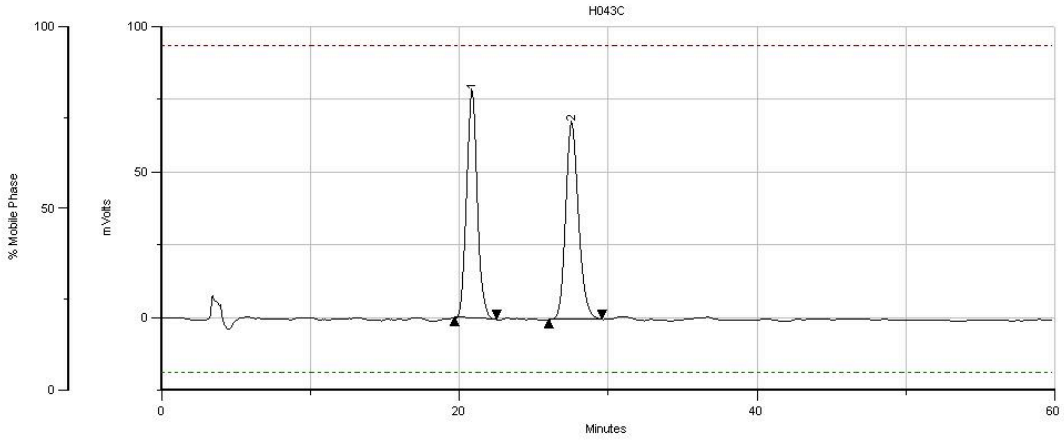
(±)

The oxindole was obtained from nitrone **9** (0.031 g, 0.106 mmol) and ketene solution **65** (2.0 mL) following **general procedure E** to yield **(±)34** (0.036 g, 84%) as a white solid; mp 180-181 °C; ν_{max} cm^{-1} (thin-film) 3146, 3024, 2833, 1689, 1610, 1499; ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (1H, br s, N*H*), 7.10 (1H, d, *J* = 8.5, Ar*H*), 7.00 (1H, dd, *J* = 7.9, 0.6, Ar*H*), 6.86 (1H, s, Ar*H*), 6.82 (1H, d, *J* = 7.9, Ar*H*), 6.73 (1H, dd, *J* = 8.5, 2.6, Ar*H*), 6.13 (1H, d, *J* = 2.6, Ar*H*), 3.62 (3H, s, O*Me*), 2.96-2.87 (2H, m, CH_2), 2.36-2.28 (1H, m, 1 x CH_2), 2.25 (3H, s, *Me*), 2.23-2.18 (1H, m, 1 x CH_2), 2.03-1.95 (2H, m, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.3, 157.8, 137.7, 137.4, 135.9, 132.3, 130.5, 130.1, 128.2, 125.1, 113.3, 113.1, 109.3, 55.2, 52.8, 34.1, 28.4, 18.9; *m/z* (ESI^+) 294 ($[M+H]^+$, 100%); HRMS (EI^+) $C_{19}H_{19}NO_2^+$ ($[M+H]^+$) found 294.1492 requires 294.1492 (+ 0.0 ppm).

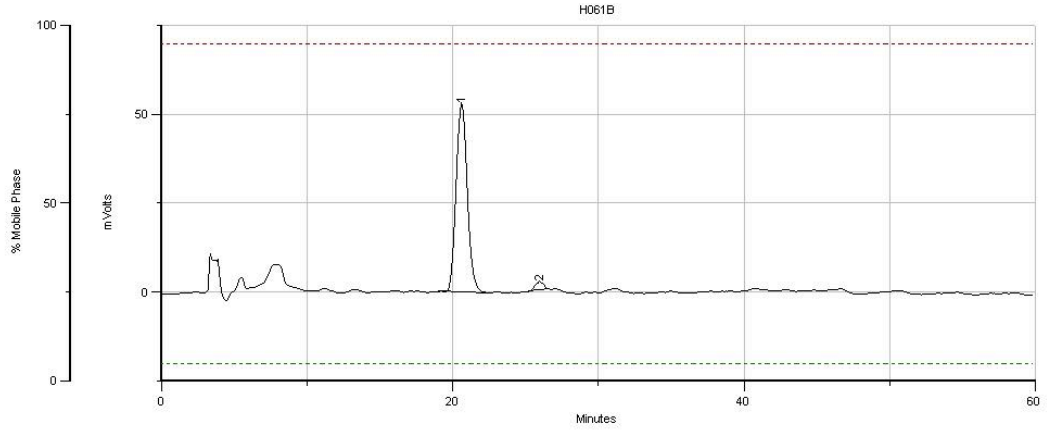
(*S*)-7'-methoxy-5-methyl-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one 34



The oxindole was obtained from chiral nitrone **27** (0.075 g, 0.150 mmol) and ketene solution **65** (2.0 mL) following **general procedure F** to yield **34** (0.039 g, 89%) as a white semi-solid; $[\alpha]_D^{20}$ +39.5° (*c* = 0.45, $CHCl_3$); HPLC analysis: 94% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 20.7 min (major) and 26.2 min (minor)).

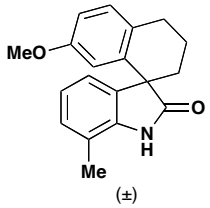


Peak	tR (min)	Area (%)
1	20.85	49.14
2	26.42	50.86



Peak	tR (min)	Area (%)
1	20.61	96.58
2	25.97	3.42

(±)-7'-methoxy-7-methyl-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one (±)35

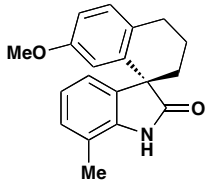


(±)

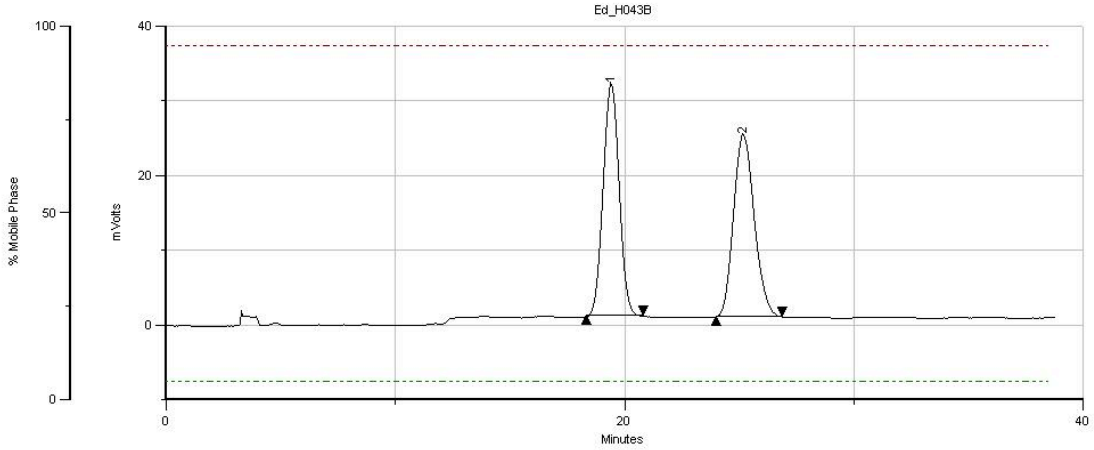
The oxindole was obtained from nitrone **28** (0.031 g, 0.106 mmol) and ketene solution **65** (2.0 mL) following **general procedure E** to yield **(±)35** (0.038 g, 88%) as a white solid; mp 216-218 °C; ν_{max} cm^{-1} (thin-film) 3173, 3148, 2936, 2837, 1690, 1624, 1601, 1497; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (1H, br s, N*H*), 7.10 (1H, d, *J* = 8.5, Ar*H*), 7.02 (1H, d, *J* = 6.6, Ar*H*), 6.91-6.86 (2H, m, Ar*H*), 6.73 (1H, dd, *J* = 8.5, 2.6, Ar*H*), 6.13 (1H, d, *J* = 2.6, Ar*H*), 3.59 (3H, s, O*Me*), 2.98-2.87 (2H, m, CH_2), 2.37-2.33 (1H, m, 1 x CH_2), 2.29 (3H, s, *Me*), 2.24-2.19 (1H, m, 1 x CH_2), 2.00-1.98 (2H, m, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.0, 157.8, 138.9, 137.3, 135.9, 130.5, 130.0,

129.2, 122.7, 121.7, 119.1, 113.2, 113.1, 55.2, 53.2, 34.1, 28.5, 18.8, 16.6; *m/z* (ESI$^+$) 294 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{19}H_{19}NO_2^+$ ([M+H]$^+$) found 294.1492 requires 294.1489 (+ 0.3 ppm).

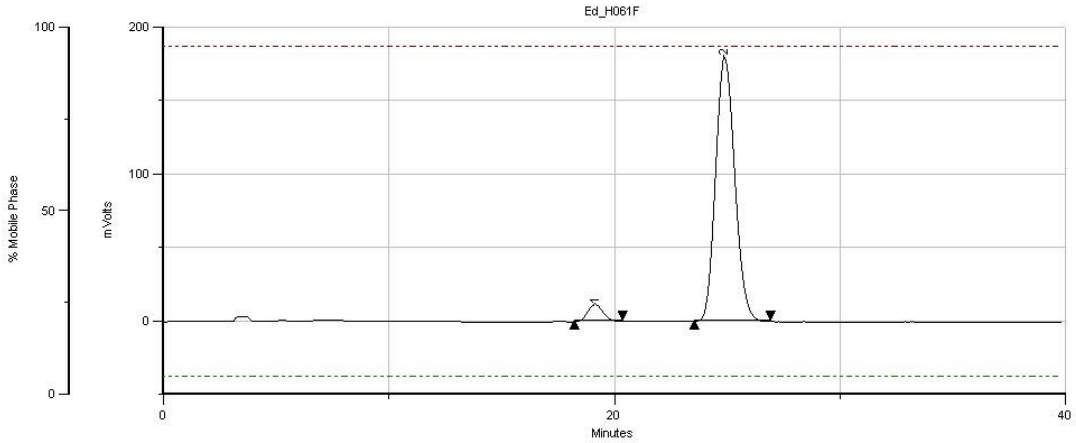
(*S*)-7'-methoxy-7-methyl-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one 35



The oxindole was obtained from chiral nitrone **28** (0.057 g, 0.113 mmol) and ketene solution **65** (2.0 mL) following **general procedure F** to yield **35** (0.018 g, 55%) as a white solid; $[\alpha]_D^{20}$ -3.0° (*c* = 0.40, $CHCl_3$); HPLC analysis: 90% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 19.2 min (minor) and 25.1 min (major)).

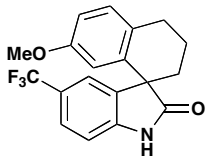


Peak	tR (min)	Area (%)
1	19.42	49.64
2	25.18	50.36



Peak	tR (min)	Area (%)
1	19.14	4.97
2	24.89	95.03

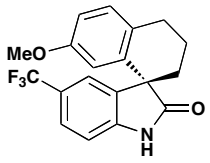
(±)-7'-methoxy-5-(trifluoromethyl)-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one (±)36



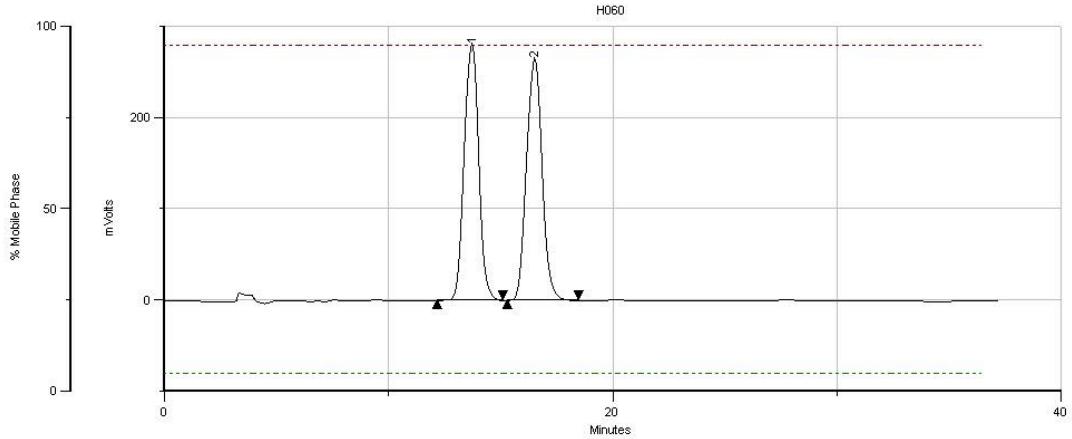
(±)

The oxindole was obtained from nitrone **11** (0.040 g, 0.151 mmol) and ketene solution **65** (2.0 mL) following **general procedure E** to yield **(±)36** (0.034 g, 65%) as a colourless oil; ν_{max} cm^{-1} (thin-film) 2849, 1701, 1466; ^1H NMR (300 MHz, $CDCl_3$) δ 8.22 (1H, br s, N*H*), 7.51 (1H, dt, *J* = 8.2, 0.8, Ar*H*), 7.28 (1H, t, *J* = 8.5, Ar*H*), 7.14 (1H, d, *J* = 8.5, Ar*H*), 7.02 (1H, d, *J* = 8.2, Ar*H*), 6.77 (1H, dd, *J* = 8.5, 2.7, Ar*H*), 6.07 (1H, d, *J* = 2.7, Ar*H*), 3.62 (3H, s, O*Me*), 2.94 (1H, t, *J* = 6.4, 1 x CH_2), 2.39-2.32 (1H, m, 1 x CH_2), 2.27-2.18 (1H, m, 1 x CH_2), 2.04-1.95 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$); 182.6, 158.0, 143.2, 138.1, 134.6, 130.8, 130.1, 125.7 (d, *J* = 2.3), 125.4 app. d, *J* = 25.7), 121.4 (d, *J* = 4.0), 113.4, 113.2, 109.8, 55.2, 52.8, 34.1, 28.3, 18.8; *m/z* (ESI^+) 348 ($[M+H]^+$, 100%); HRMS (EI^+) $C_{19}H_{17}NO_2F_3^+$ ($[M+H]^+$) found 348.1209 requires 348.1206 (+ 0.9 ppm).

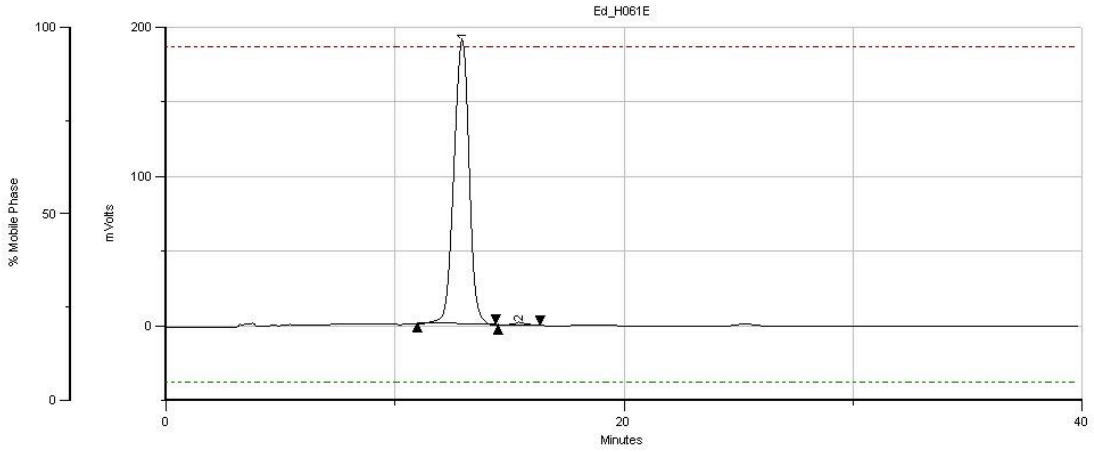
(*S*)-7'-methoxy-5-(trifluoromethyl)-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one 36



The oxindole was obtained from chiral nitrone **25** (0.075 g, 0.135 mmol) and ketene solution **65** (2.0 mL) following **general procedure F** to yield **36** (0.032 g, 64%) as a colourless oil; $[\alpha]_D^{20}$ -3.1° (*c* = 0.60, $CHCl_3$); HPLC analysis: 97% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 13.0 min (major) and 15.8 min (minor)).

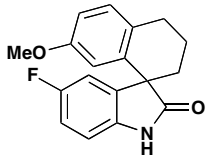


Peak	tR (min)	Area (%)
1	13.51	49.59
2	16.20	50.41



Peak	tR (min)	Area (%)
1	12.94	98.67
2	15.45	1.33

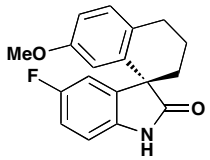
(±)-5-Fluoro-7'-methoxy-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one (±)37



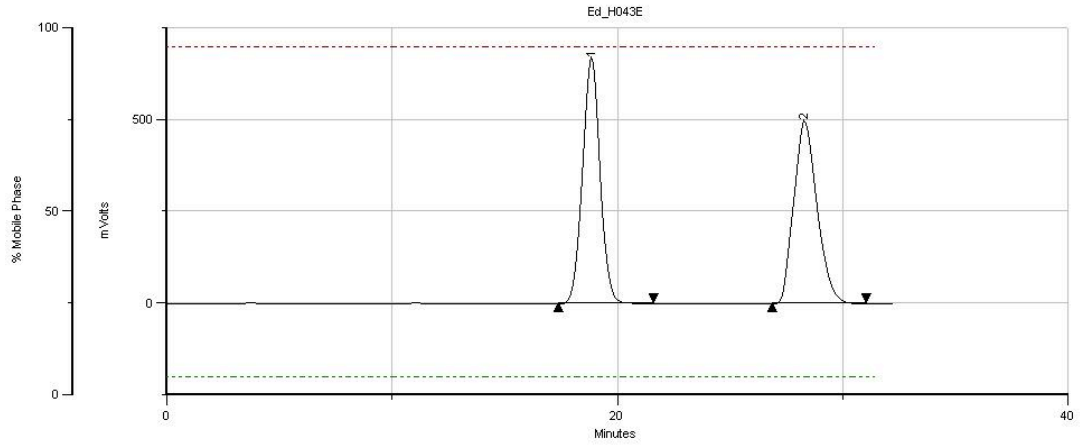
(±)

The oxindole was obtained from nitrone **5** (0.028 g, 0.094 mmol) and ketene solution **65** (2.0 mL) following **general procedure E** to yield **(±)37** (0.025 g, 65%) as a white solid; mp 104-106 °C; ν_{max} cm^{-1} (thin-film) 3146, 3024, 2849, 1691, 1611, 1500, 1487; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (1H, br s, N*H*), 7.11 (1H, d, *J* = 8.5, Ar*H*), 6.91 (1H, td, *J* = 8.7, 2.5, Ar*H*), 6.87 (1H, dd, *J* = 8.5, 4.5, Ar*H*), 6.79 (1H, dd, *J* = 8.1, 2.5, Ar*H*), 6.75 (1H, dd, *J* = 8.5, 2.6, Ar*H*), 6.11 (1H, d, *J* = 2.6, Ar*H*), 3.63 (3H, s, O*Me*), 2.97-2.86 (2H, m, CH_2), 2.37-2.30 (1H, m, 1 x CH_2), 2.25-2.17 (2H, m, 1 x CH_2), 2.01-1.94 (1H, m, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.4, 159.1 (d, *J* = 239.3), 158.3, 139.2 (d, *J* = 7.9), 135.9, 135.9 135.0, 130.7, 130.0, 114.3 (d, *J* = 23.3), 113.2 (d, *J* = 27.2), 112.3 (d, *J* = 24.7), 110.3 (d, *J* = 8.1), 55.2, 53.3, 34.0, 28.3, 18.8; *m/z* (ESI^+) 298 ($[M+H]^+$, 100%); HRMS (EI^+) $C_{18}H_{16}FNO_2^+$ ($[M+H]^+$) found 298.1242 requires 298.1238 (+ 0.4 ppm).

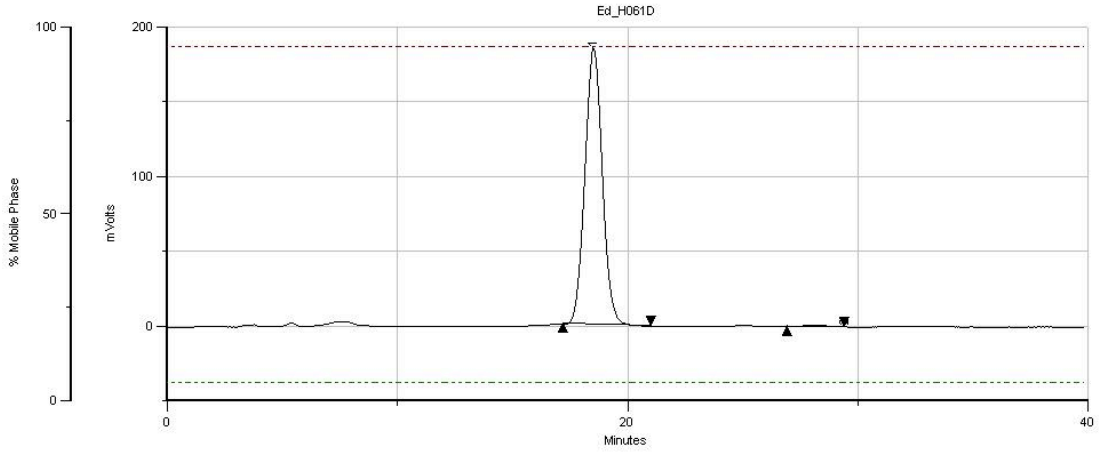
(*S*)-5-fluoro-7'-methoxy-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one 37



The oxindole was obtained from chiral nitrone **24** (0.059 g, 0.149 mmol) and ketene solution **65** (2.0 mL) following **general procedure F** to yield **37** (0.033 g, 74%) as a off-white solid; $[\alpha]_D^{20}$ -4.4° (*c* = 0.65, $CHCl_3$); HPLC analysis: 97% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 18.9 min (major) and 28.3 min (minor)).

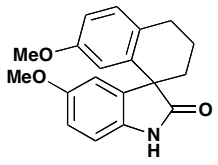


Peak	tR (min)	Area (%)
1	18.85	50.33
2	28.31	49.67



Peak	tR (min)	Area (%)
1	18.53	98.63
2	28.07	1.37

(±)-5,7'-dimethoxy-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one (±)38

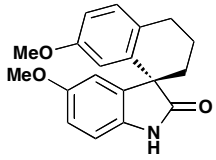


(±)

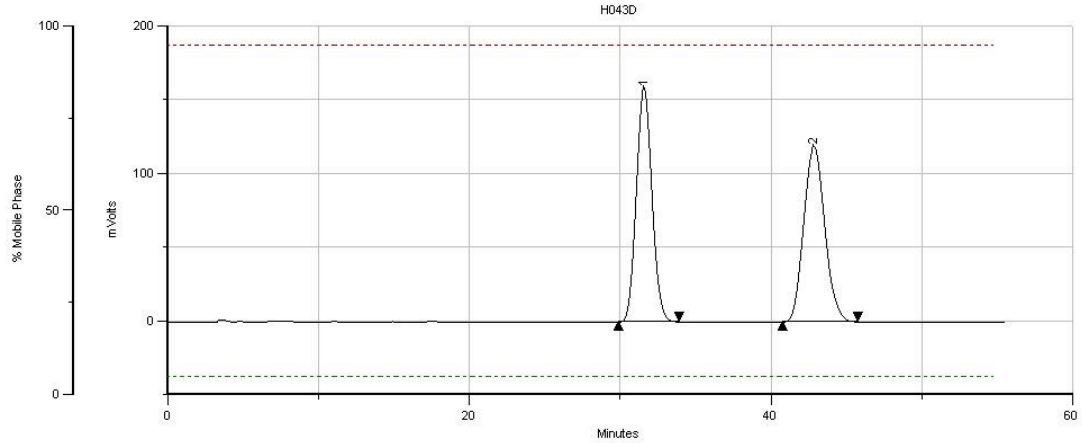
The oxindole was obtained from nitrone **4** (0.029 g, 0.094 mmol) and ketene solution **65** (2.0 mL) following **general procedure E** to yield **(±)38** (0.036 g, 92%) as a white solid; mp 136-137 °C; ν_{max} cm^{-1} (thin-film) 3154, 3024, 2833, 1693, 1612, 1499, 1485; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (1H, br s, N*H*), 7.10 (1H, d, *J* = 8.5, Ar*H*), 6.85 (1H, d, *J* = 8.5, Ar*H*), 6.74 (1H, dd, *J* = 8.5, 2.5, Ar*H*), 6.64 (1H, d, *J* = 2.3, Ar*H*), 6.14 (1H, d, *J* = 2.5, Ar*H*), 3.72 (3H, s, O*Me*), 3.62 (3H, s, O*Me*), 2.98-2.86 (2H, m, CH_2), 2.38-2.30 (1H, m, 1 x CH_2), 2.24–2.17 (2H, m, CH_2), 2.02-1.95 (1H, m, 1 x CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.7, 157.9, 156.0, 139.0, 135.6, 133.5, 130.5, 130.0, 113.3,

113.2, 112.4, 111.4, 110.1, 55.8, 55.2, 53.3, 34.1, 28.4, 18.8; *m/z* (ESI^+) 310 ($[M+H]^+$, 100%); HRMS (EI^+) $C_{19}H_{19}NO_3^+$ ($[M+H]^+$) found 310.1441 requires 310.1438 (+ 0.3 ppm).

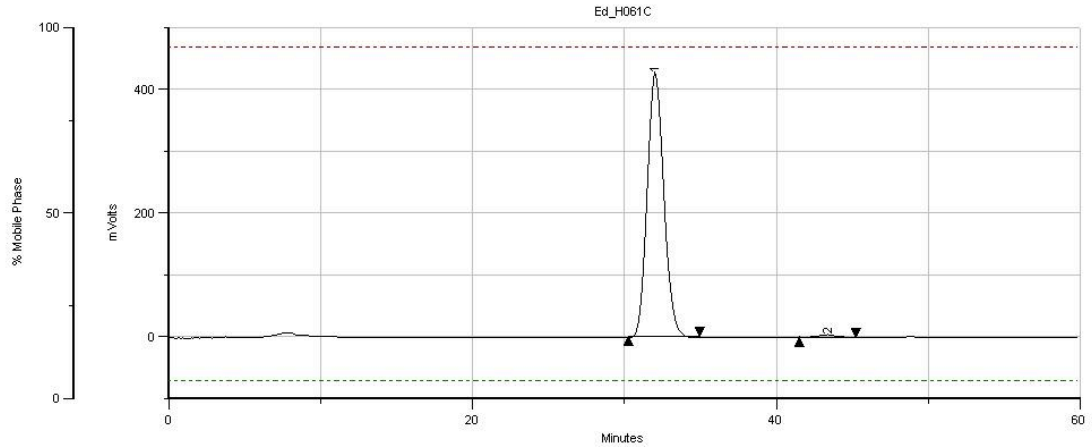
(*S*)-5,7'-dimethoxy-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-2-one 38



The oxindole was obtained from chiral nitrone **26** (0.075 g, 0.145 mmol) and ketene solution **65** (2.0 mL) following **general procedure F** to yield **38** (0.043 g, 96%) as a very viscous orange oil; $[\alpha]_D^{20}$ -13.3° (*c* = 0.95, $CHCl_3$); HPLC analysis: 97% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 31.6 min (major) and 43.0 min (minor)).



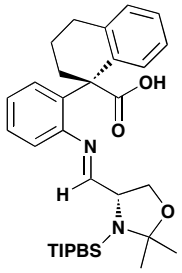
Peak	tR (min)	Area (%)
1	31.58	49.73
2	42.85	50.27



Peak	tR (min)	Area (%)
1	32.01	97.84
2	43.41	2.16

8. Intermediate Isolation

(*S*)-1-(2-((*E*)-(((*R*)-2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene) amino)phenyl)-1,2,3,4-tetrahydronaphthalene-1-carboxylic acid 21



To a stirred solution of nitrone **19** (0.050 g, 0.103 mmol) in THF (3 mL) was added ketene **20** (0.020g, 1.2 eq, 0.124 mmol) and the reaction stirred at rt for 1h 30 min before quenching with aq. NH_4Cl (sat.) (1 mL). The reaction mixture was extracted with Et_2O (10 mL) and washed with brine (10 mL) before being dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude yellow oil which was purified *via* column chromatography over silica (0-20% EtOAc in petroleum ether) to yield **21** (0.017 g, 26%) as a colourless oil; ν_{max} cm^{-1} (thin-film) 3441, 1697, 1653; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 (1H, d, *J* = 8.0, Ar*H*), 7.22-7.11 (4H, m, Ar*H* & C*H*=N), 7.15 (2H, s, Ar*H*), 6.93 (2H, dt, *J* = 24.1, 7.5, Ar*H*), 6.40 (1H, d, *J* = 7.6, Ar*H*), 5.78 (d, *J* = 7.6, Ar*H*), 4.47-4.45 (1H, m, C*H*), 4.34 (2H, dt, *J* = 13.4, 6.7, iPr*H*), 4.25 (1H, dd, *J* = 9.2, 2.0, 1 x CH_2), 4.14 (1H, dd, *J* = 9.0, 7.3, 1 x CH_2), 2.88-2.84 (2H, m, 1 x CH_2 & 1 x iPr*H*), 2.76-2.73 (1H, m, 1 x CH_2), 2.59-2.54 (1H, m, 1 x CH_2), 2.46-2.43 (1H, m, 1 x CH_2), 1.80 (6H, s, CMe_2), 1.29-1.19 (18H, m, CH_2 & iPrCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.8, 163.1, 154.1, 151.6, 147.5, 139.2, 138.8, 135.0, 132.6, 130.1, 129.9, 129.6, 127.6, 127.4, 126.1, 125.7, 124.2, 117.6, 100.4, 67.3, 61.2, 54.8, 34.2, 32.3, 29.2, 28.1, 25.1, 24.5, 23.5, 22.7, 19.5; *m/z* (ESI^+) 667.42 ($[M+Na]^+$, 100%).

9. References

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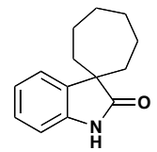

13

^{13}C, $CDCl_3$, 75 MHz

7.669
7.347
7.345
7.212
7.208
7.187
7.182
7.161
7.157
7.047
7.044
7.022
7.019
6.997
6.993
6.879
6.877
6.853
6.852

2.065
2.033
2.029
2.014
1.985
1.979
1.960
1.950
1.920
1.810
1.779
1.762
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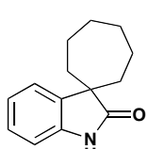
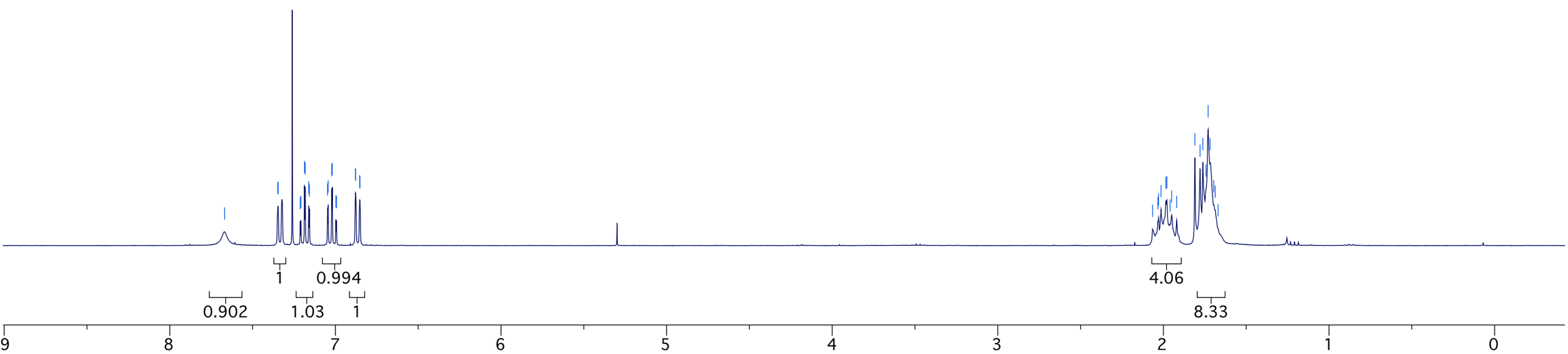
1.730
1.718
1.696
1.687
1.670

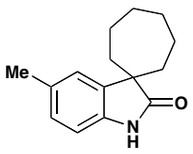


13

^{1}H, $CDCl_3$, 300 MHz

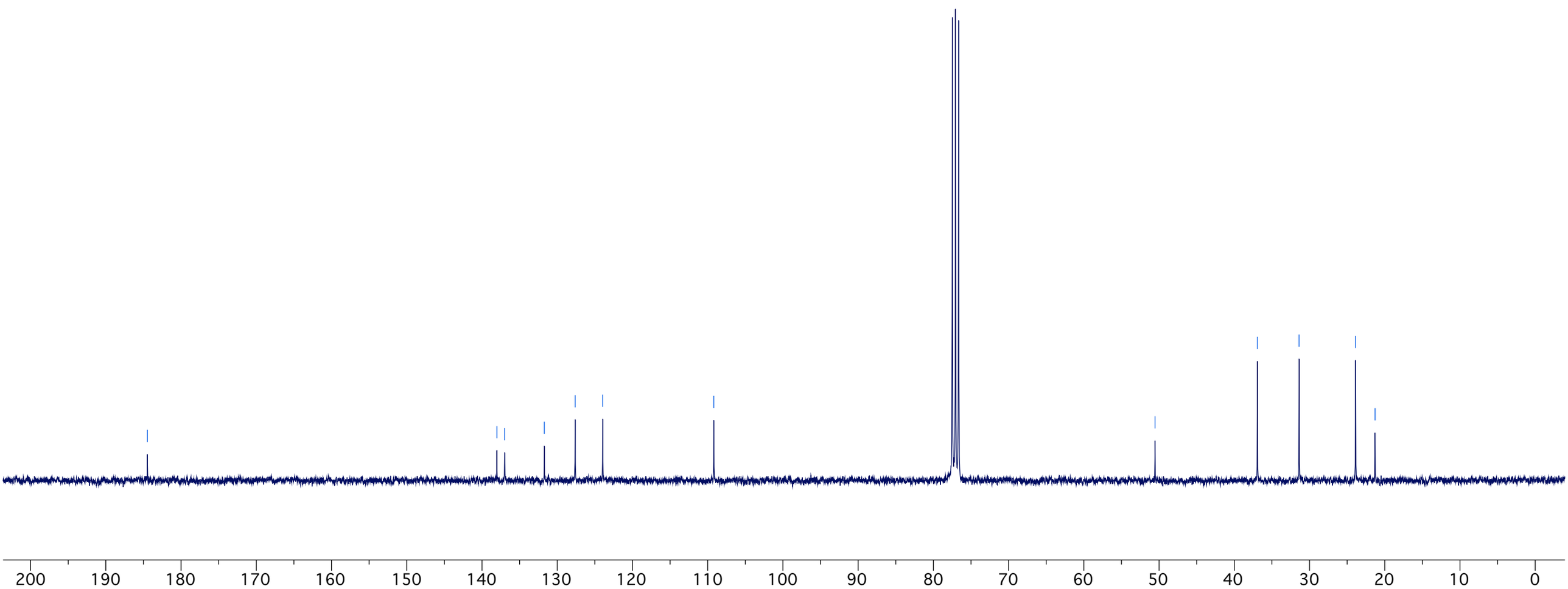


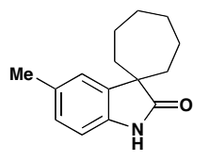
184.477
138.014
136.984
131.717
127.612
123.954
109.183
50.534
36.931
31.390
23.885
21.293



14

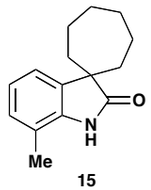
^{13}C, $CDCl_3$, 75 MHz





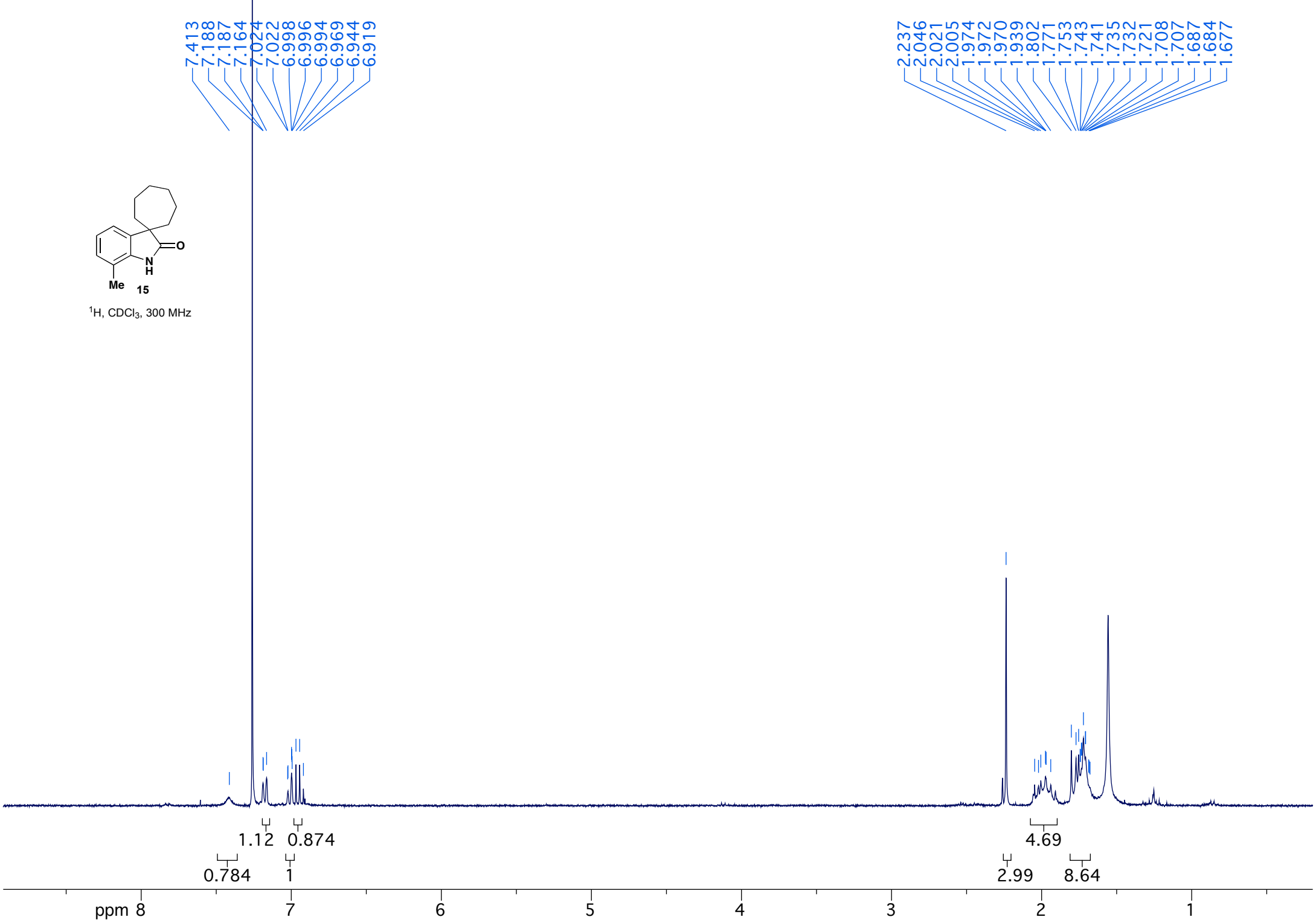
14

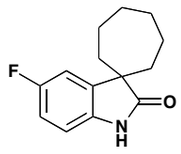
^{1}H, $CDCl_3$, 300 MHz



15

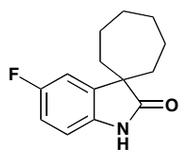
^{13}C, $CDCl_3$,125 MHz


7.413
7.188
7.187
7.164
7.024
7.022
6.998
6.996
6.994
6.969
6.944
6.919
2.237
2.046
2.021
2.005
1.974
1.972
1.970
1.939
1.802
1.771
1.753
1.743
1.741
1.735
1.732
1.721
1.708
1.707
1.687
1.684
1.677
O
N
H
Me
15
1H, CDCl3, 300 MHz
1.12
0.874
0.784
1
4.69
2.99
8.64
ppm 8
7
6
5
4
3
2
1



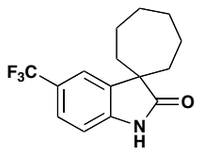
16

^{13}C, $CDCl_3$, 75 MHz



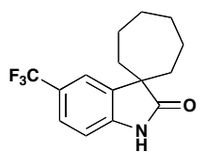
16

^{1}H, $CDCl_3$, 300 MHz



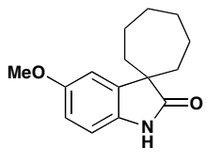
17

^{13}C, $CDCl_3$, 75 MHz



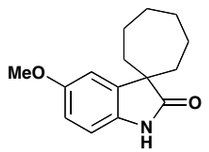
17

^{1}H, $CDCl_3$, 300 MHz



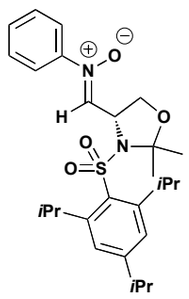
18

^{13}C, $CDCl_3$, 75 MHz



18

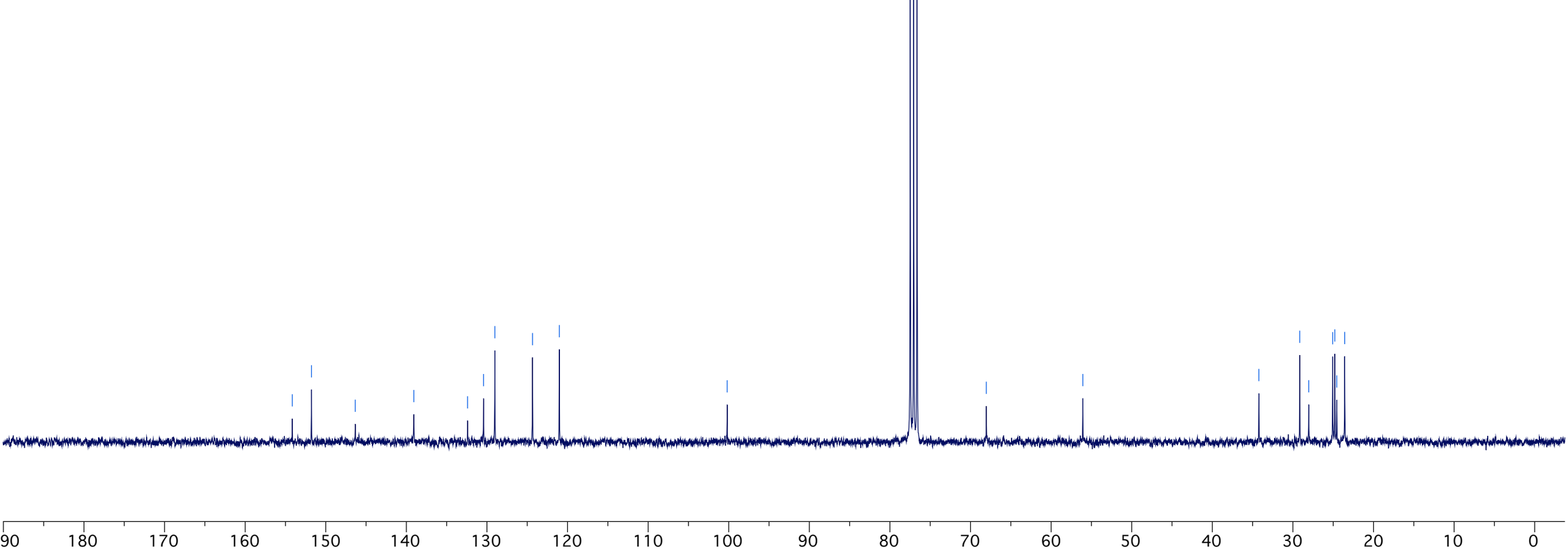
^{1}H, $CDCl_3$, 300 MHz

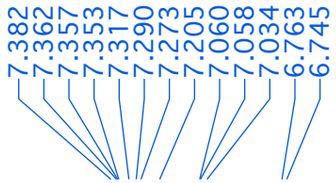


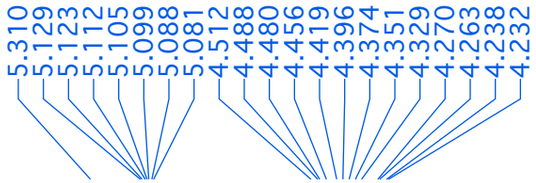
19

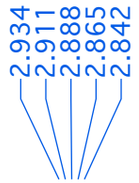
^{13}C, $CDCl_3$, 75 MHz

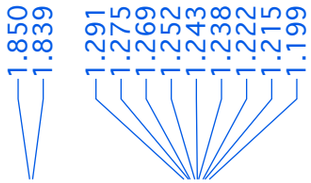
154.150
151.774
146.343
139.075
132.404
130.424
129.017
124.349
121.021
100.197
68.040
56.064
34.224
29.152
28.035
25.062
24.804
24.560
23.577

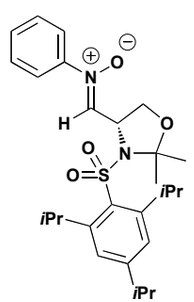






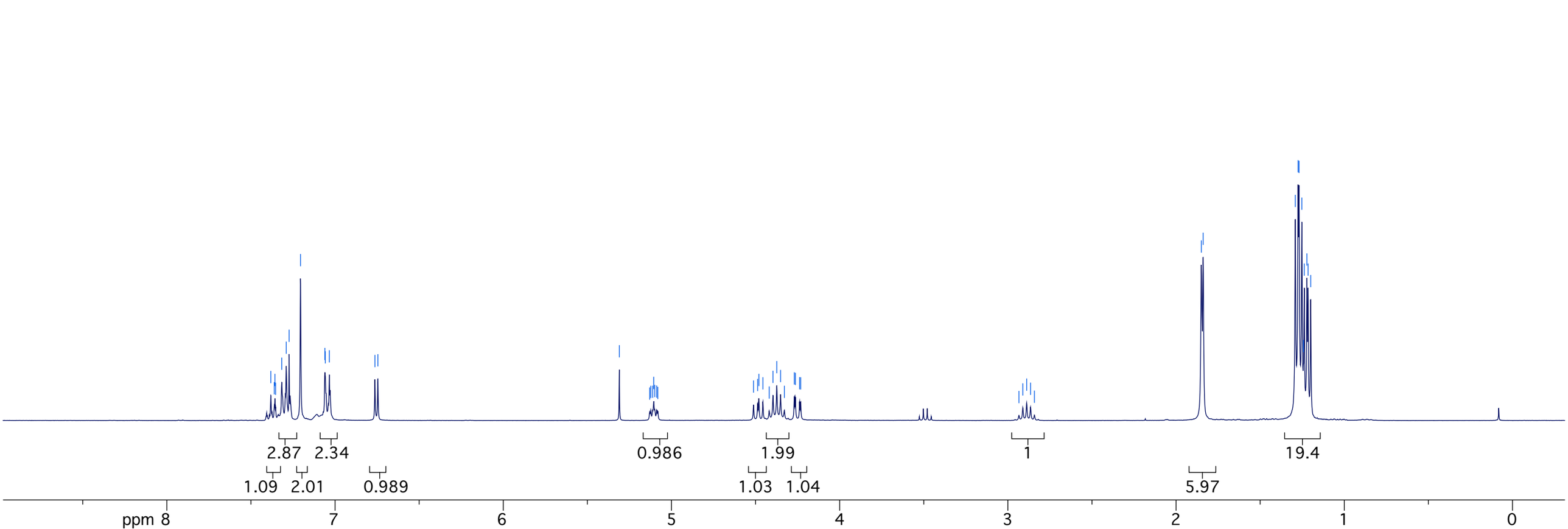


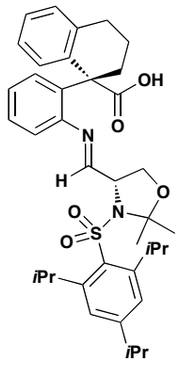




19

^{1}H, $CDCl_3$, 300 MHz

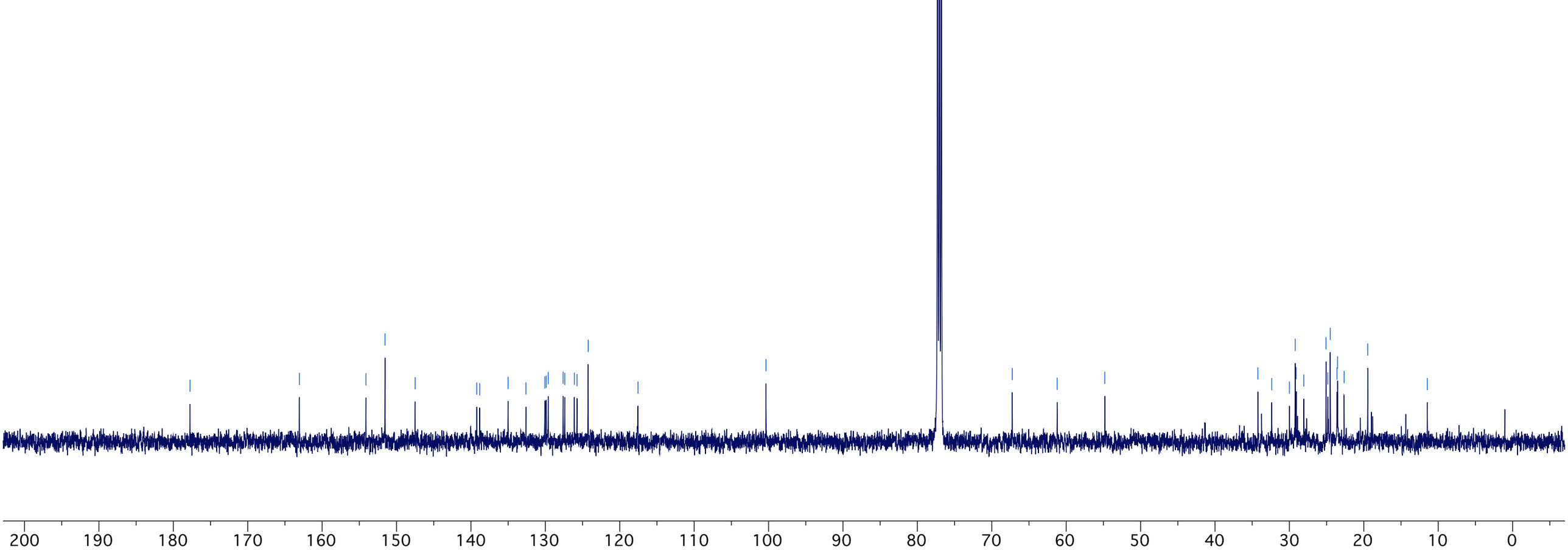


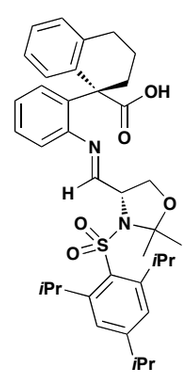


21

^{13}C, $CDCl_3$, 125 MHz

177.757
163.054
154.111
151.550
147.499
139.215
138.820
135.006
132.607
130.056
129.873
129.616
127.613
127.386
126.097
125.743
124.243
117.552
100.352
67.248
61.214
54.807
34.240
32.373
29.994
29.224
29.086
28.072
25.083
24.846
24.510
23.609
23.530
22.651
19.468
11.469

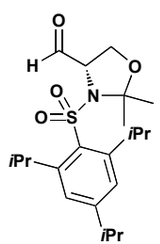




21

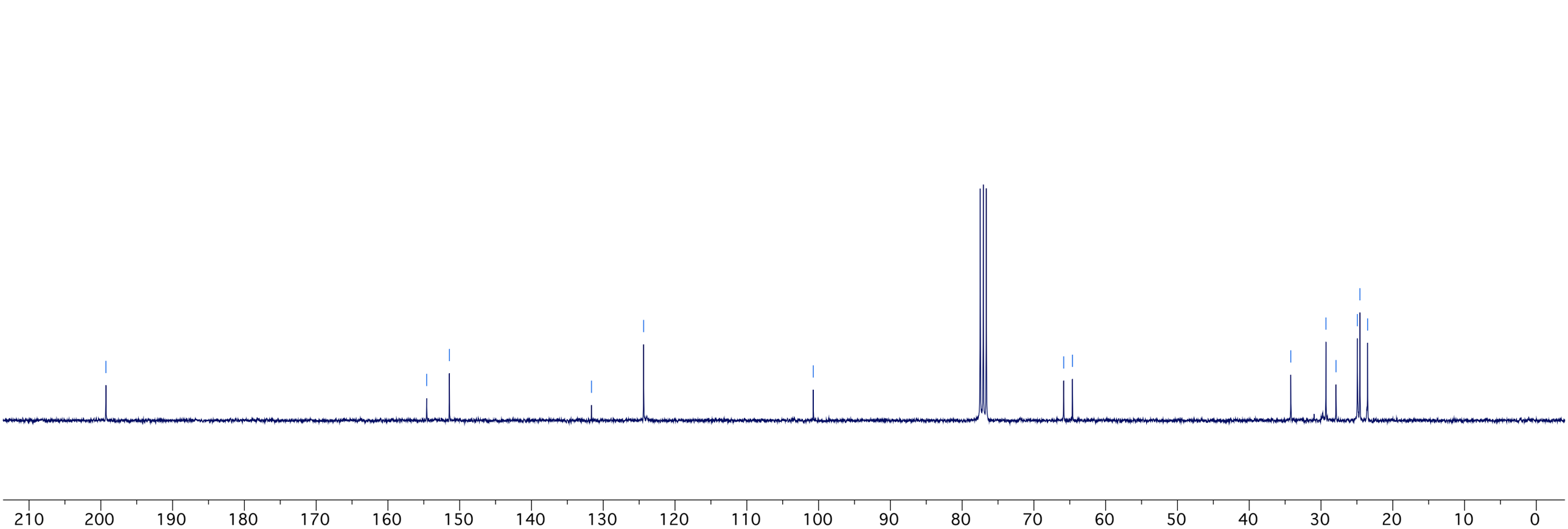
^{1}H, $CDCl_3$, 500 MHz

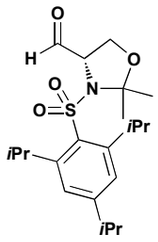
199.288
154.600
151.434
131.640
124.374
100.737
65.847
64.632
34.204
29.313
27.911
24.934
24.577
23.505



23

^{13}C, $CDCl_3$, 75 MHz

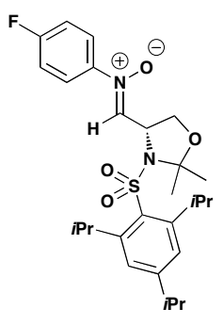




23

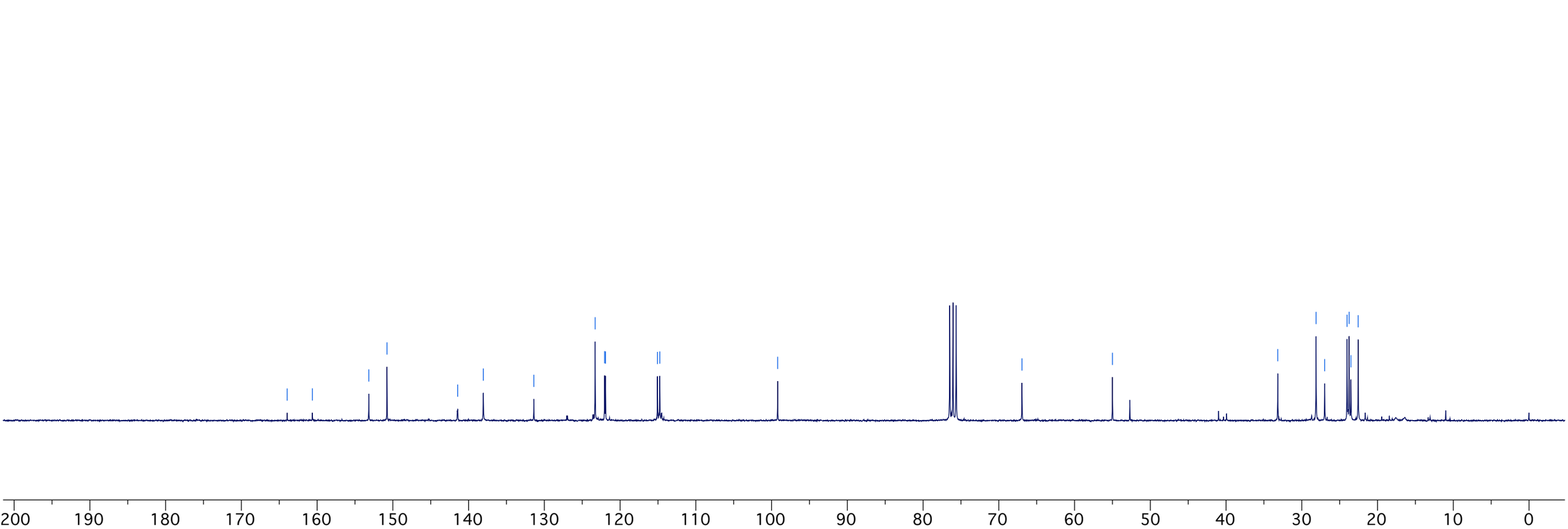
^{1}H, $CDCl_3$, 300 MHz

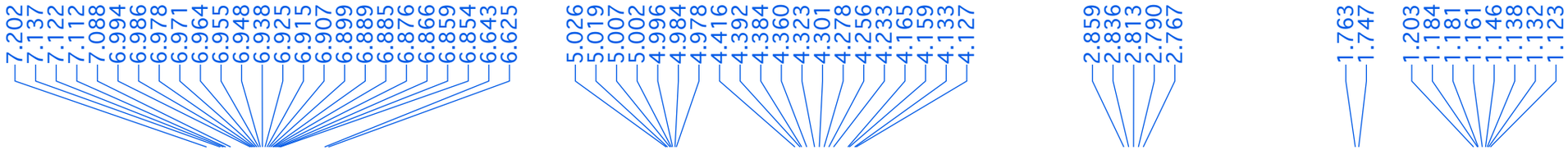
163.956
160.622
153.173
150.774
141.441
138.059
131.386
123.295
122.043
121.926
115.068
114.760
99.200
66.946
54.999
33.172
28.117
26.977
24.027
23.748
23.514
22.556

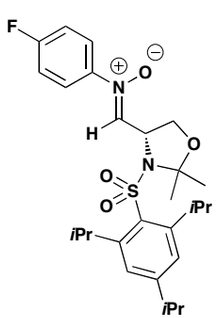


24

^{13}C, $CDCl_3$,75 MHz

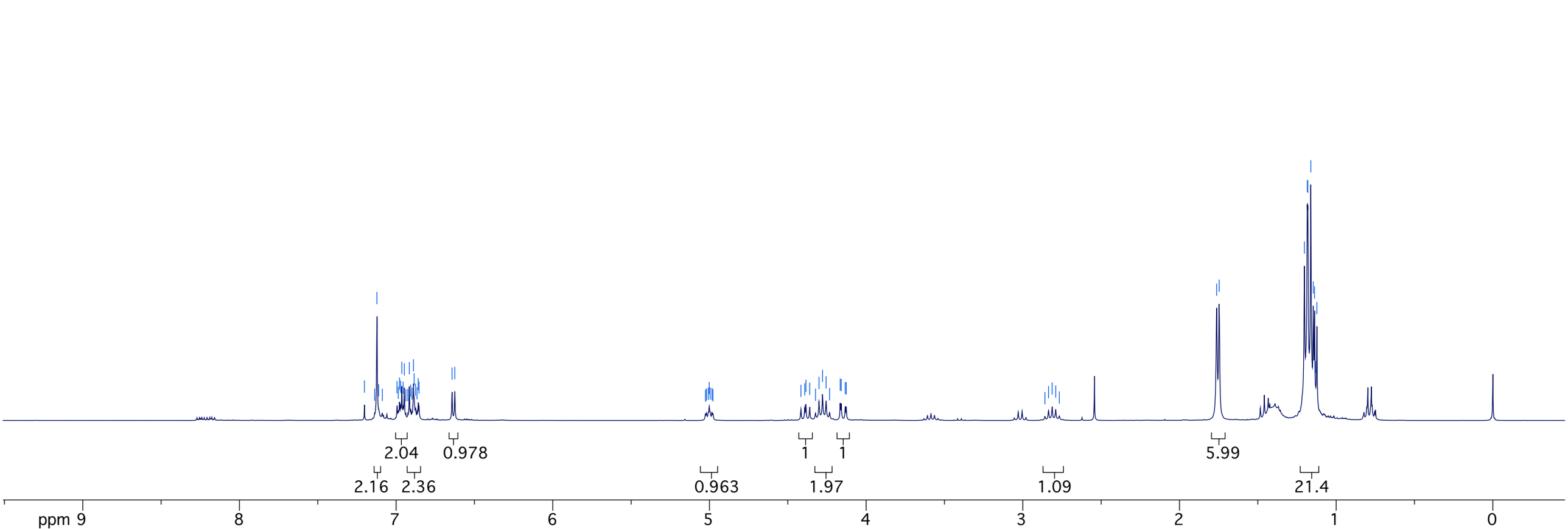


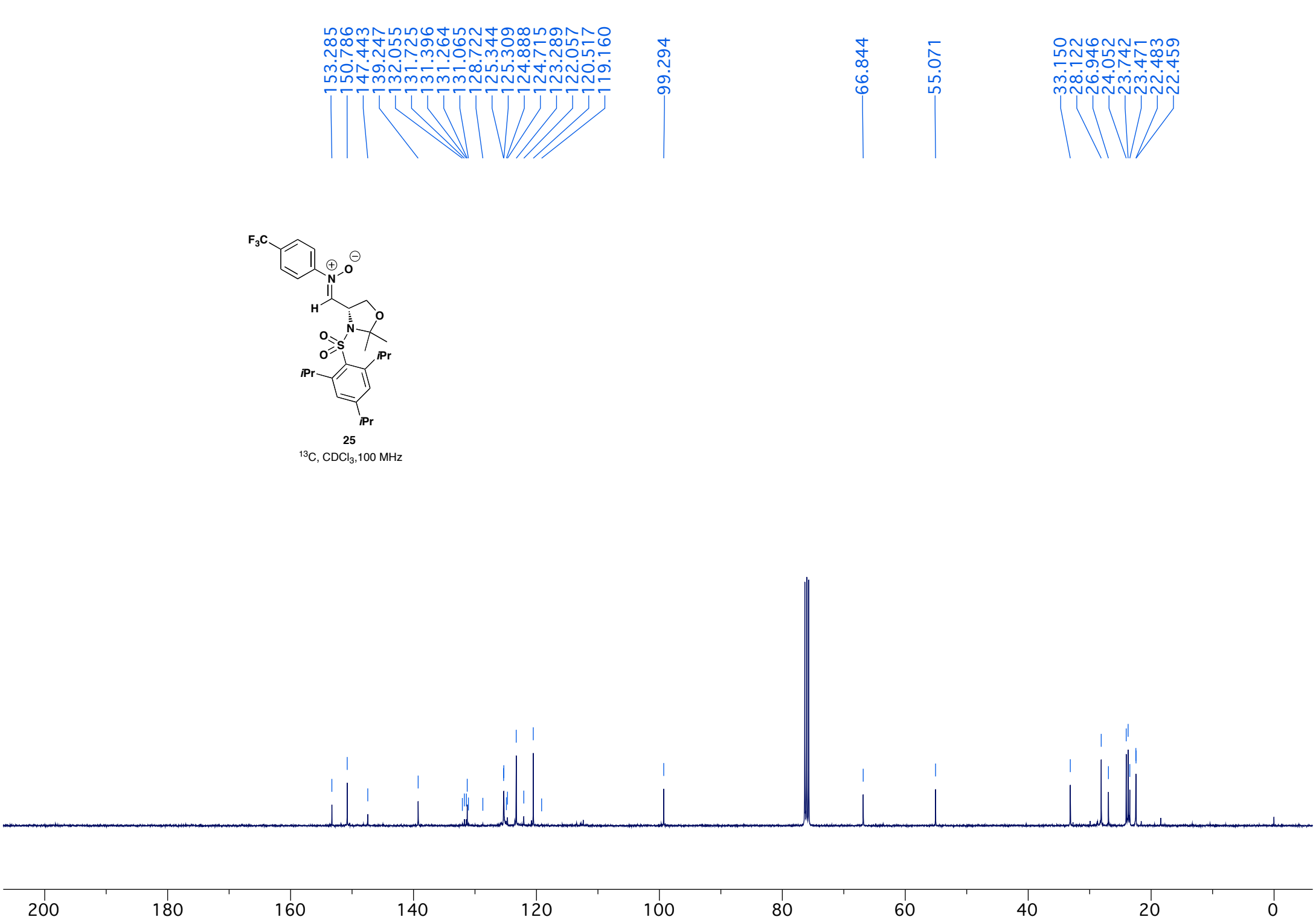




24

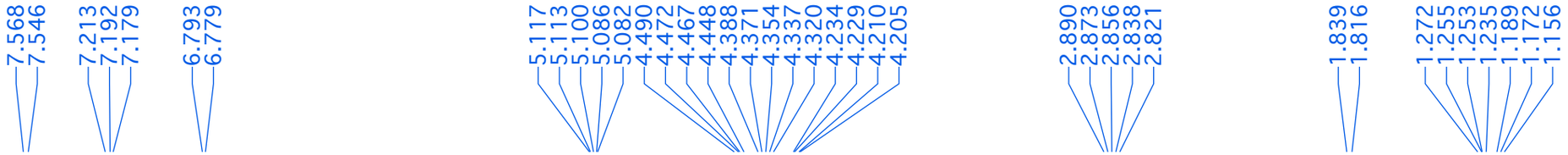
^{1}H, $CDCl_3$, 300 MHz

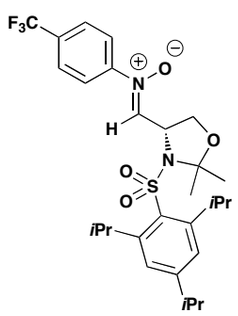




25

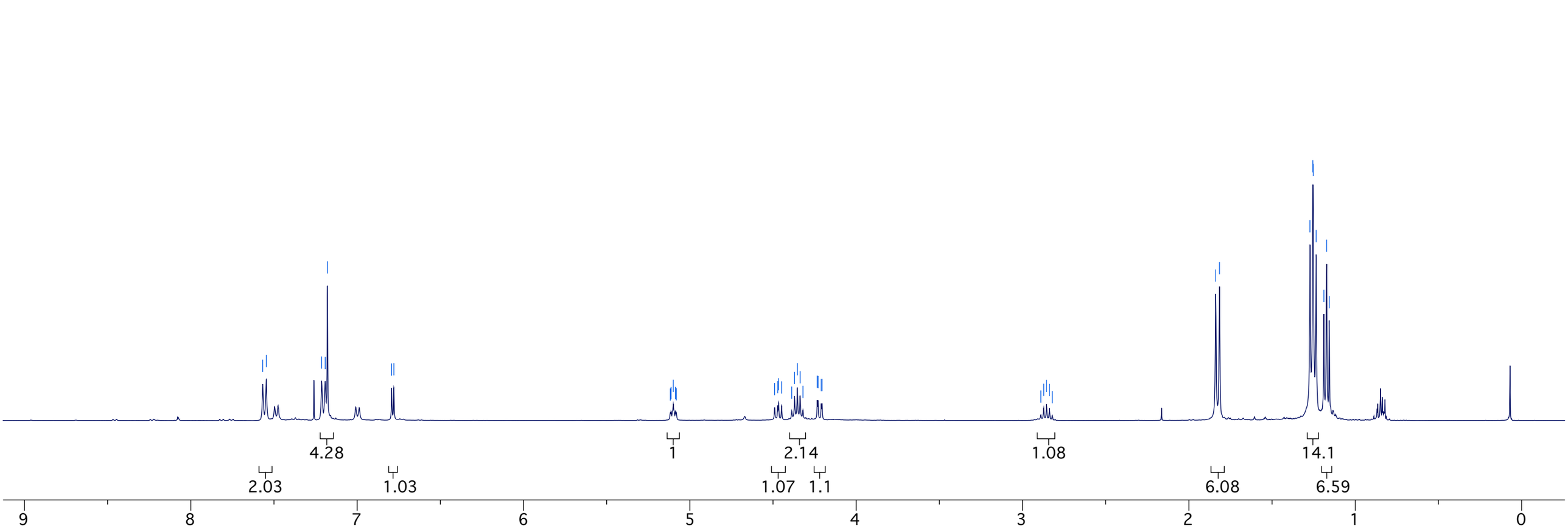
^{13}C, $CDCl_3$,100 MHz

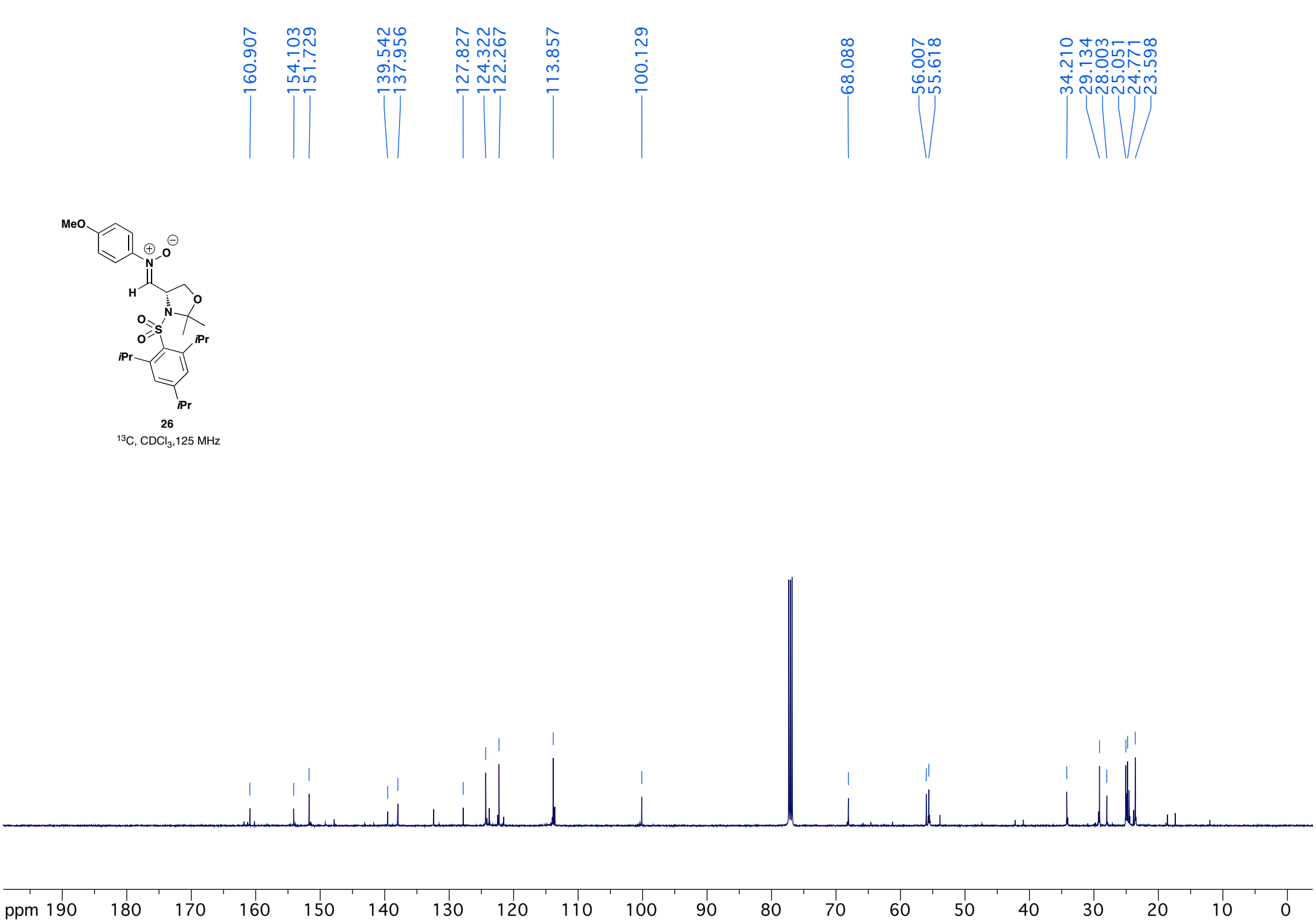




25

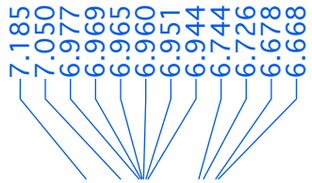
^{1}H, $CDCl_3$, 400 MHz

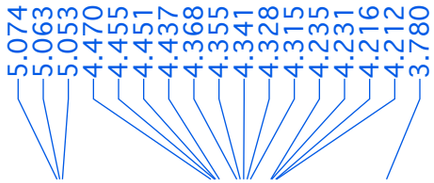


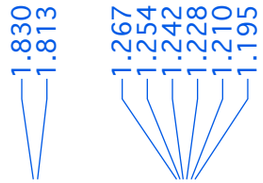


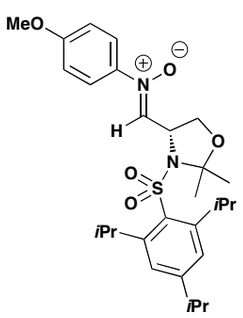
26

^{13}C, $CDCl_3$,125 MHz



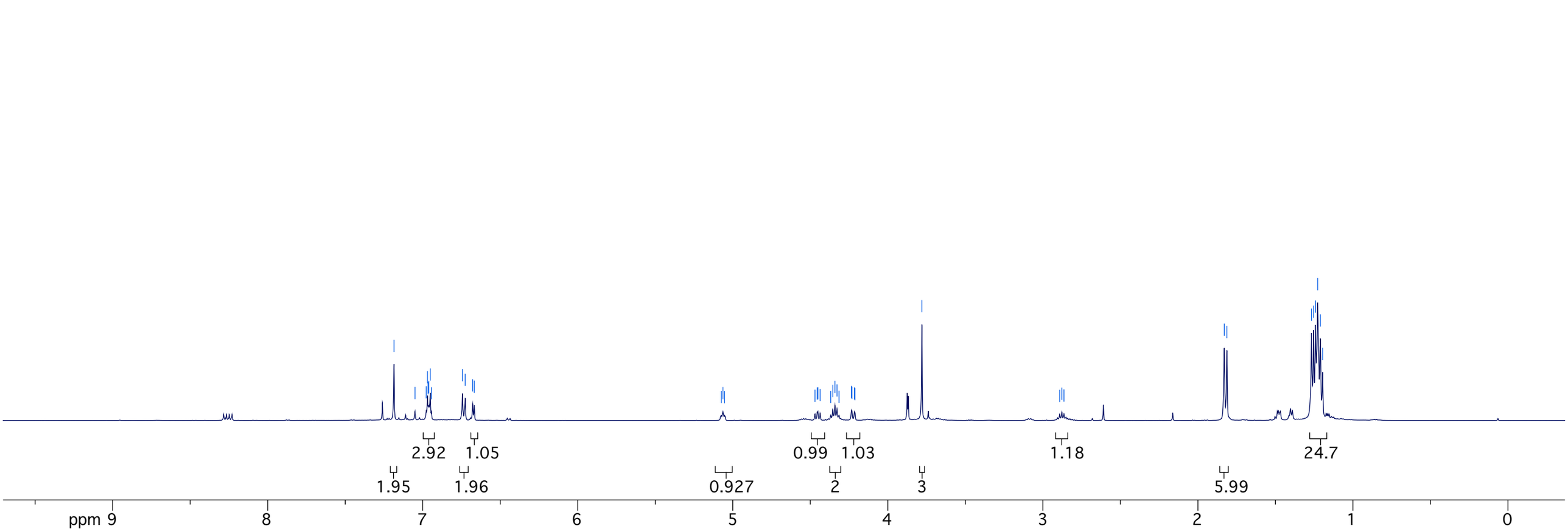




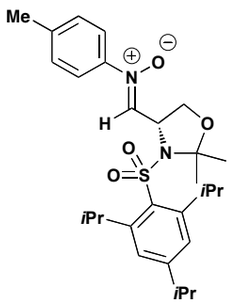


26

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

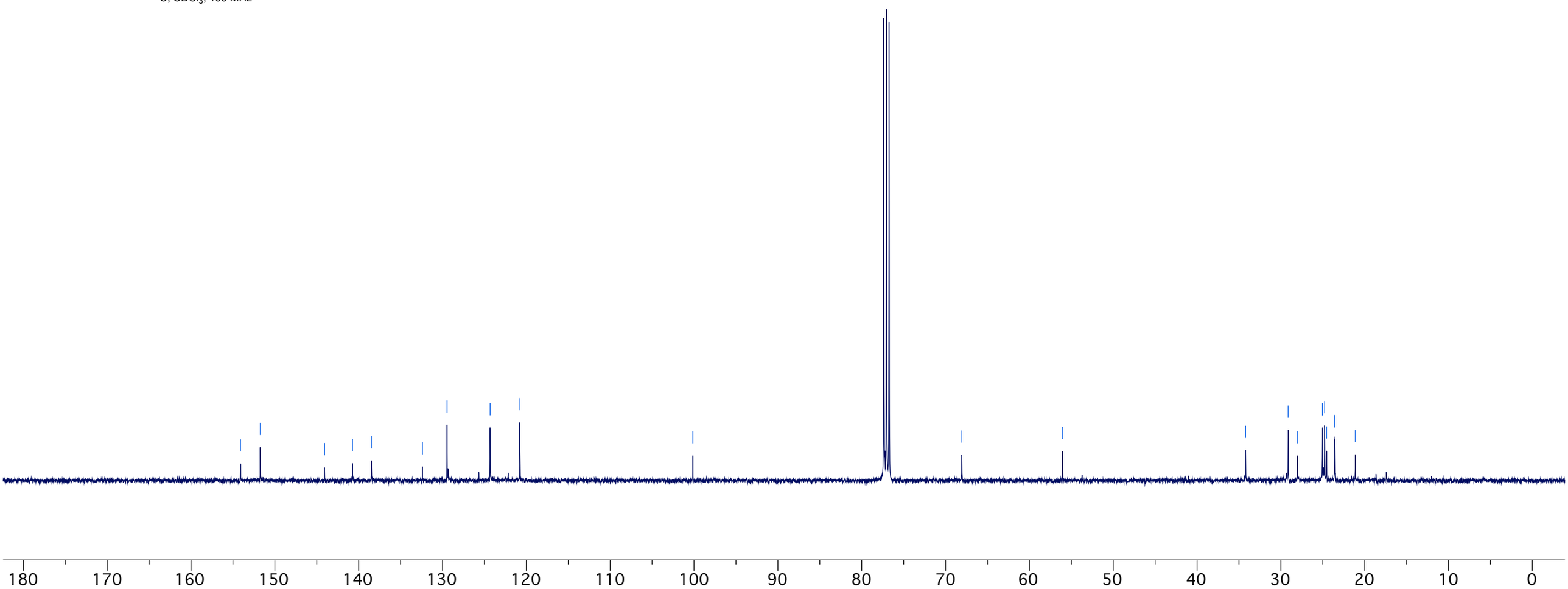


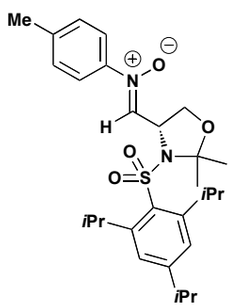
154.097
151.731
144.071
140.737
138.479
132.398
129.458
124.320
120.768
100.139
68.056
56.037
34.212
29.132
28.017
25.042
24.782
24.555
23.567
23.554
21.123



27

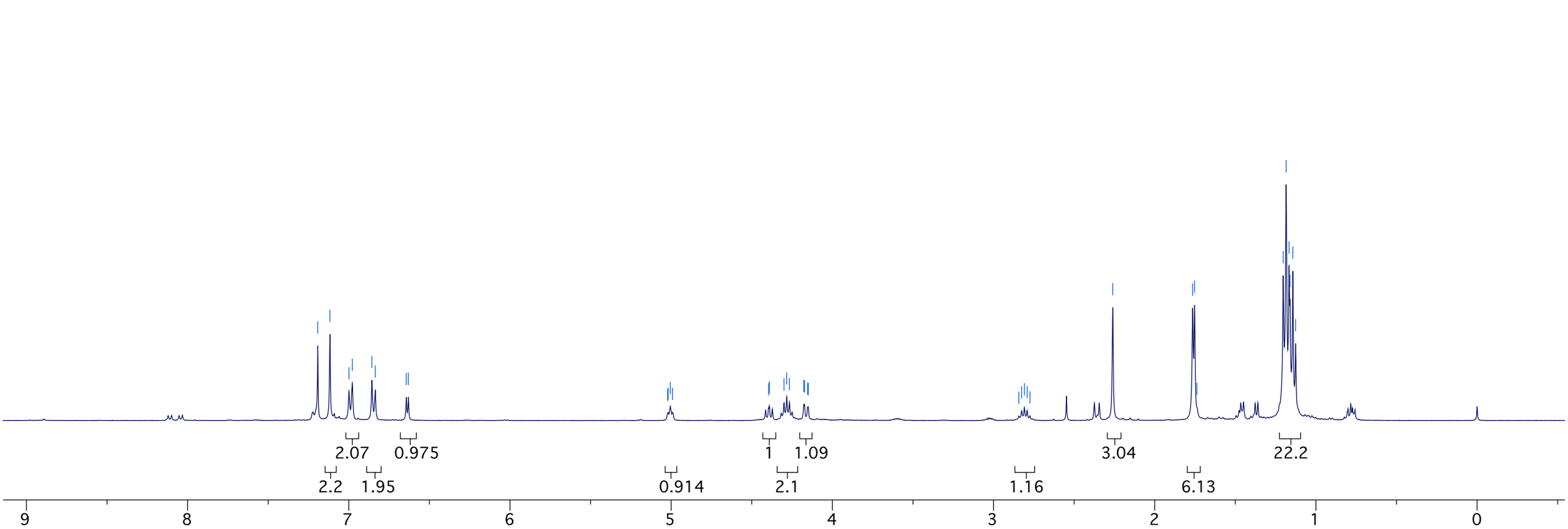
^{13}C, $CDCl_3$, 100 MHz

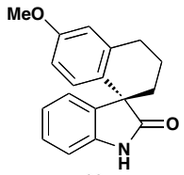




27

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





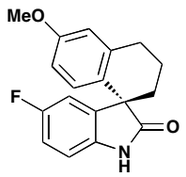
29

^{13}C NMR 100MHz

29

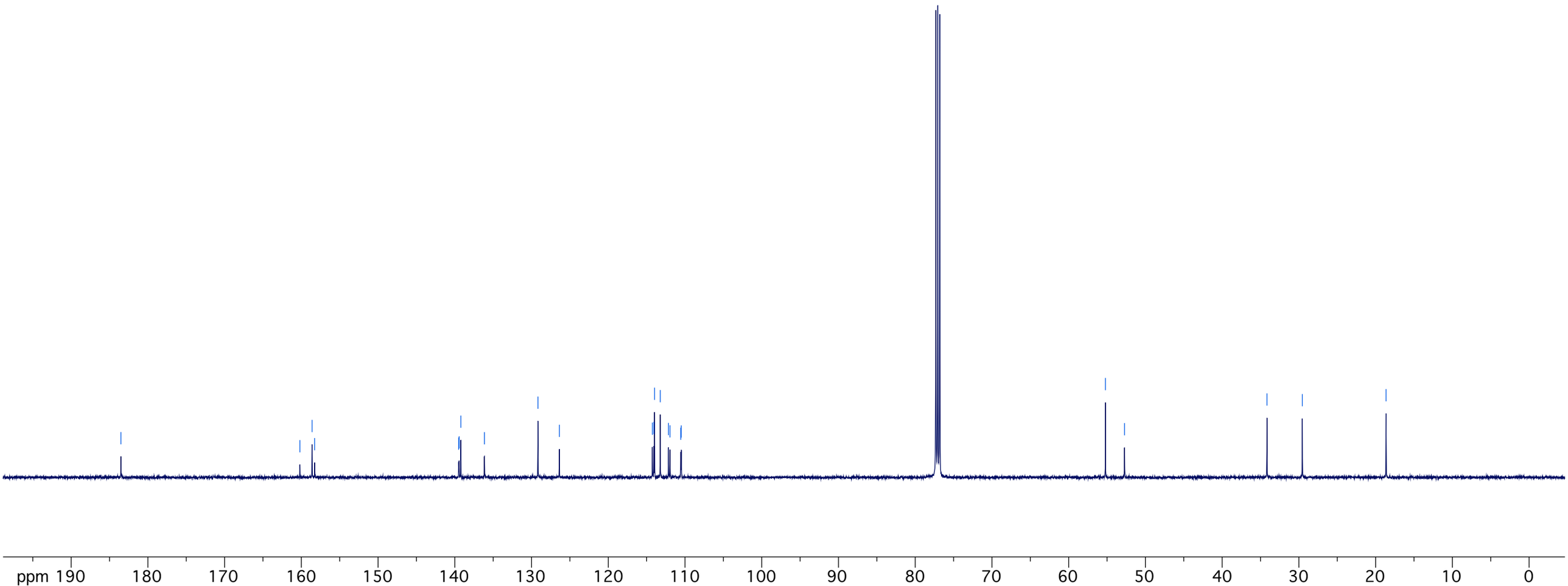
^{1}H NMR 300MHz

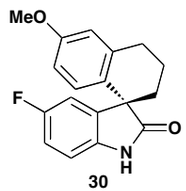
183.514
160.185
158.601
158.273
139.495
139.434
139.212
136.142
129.161
126.373
114.252
114.064
113.967
113.226
112.157
111.961
110.553
110.490
55.208
52.721
34.160
29.552
18.640



30

^{13}C, $CDCl_3$, 125 MHz

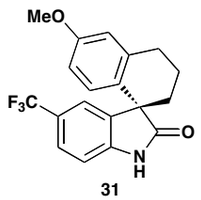




30

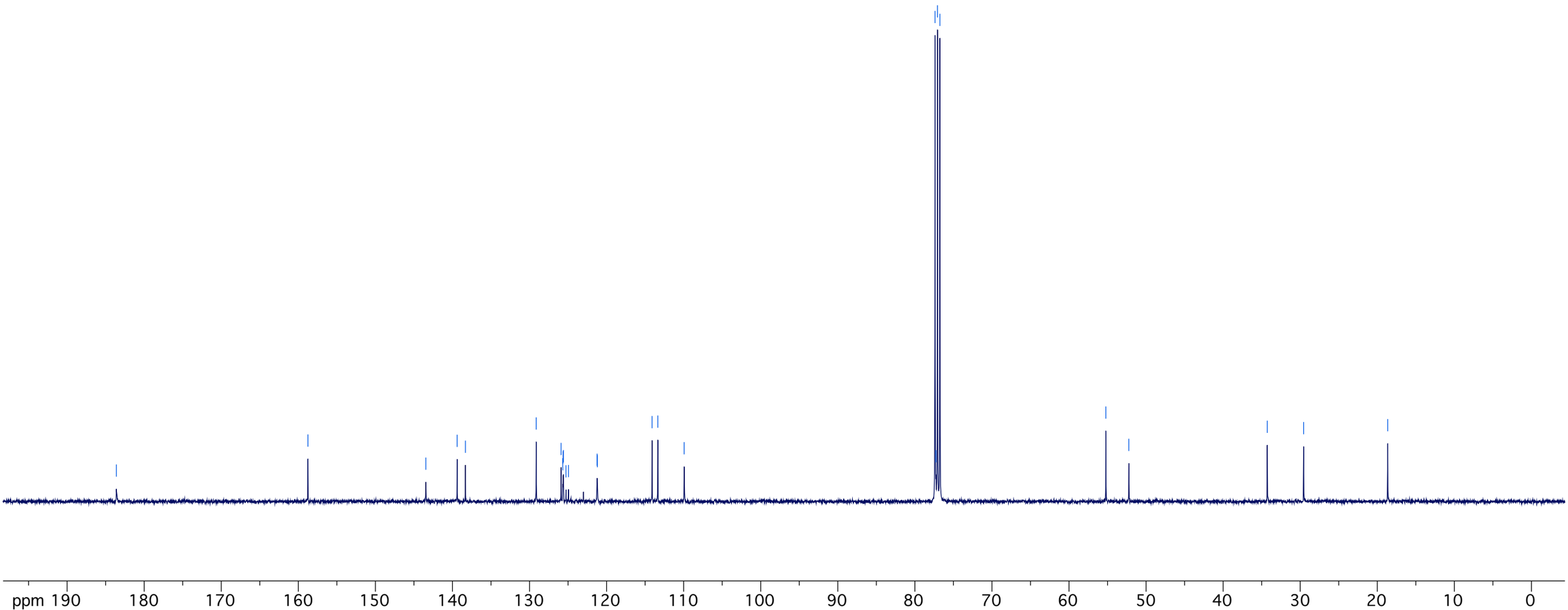
^{1}H NMR 300MHz

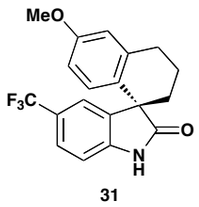
183.607
158.755
143.456
139.390
138.318
129.132
125.909
125.692
125.647
125.607
125.271
124.949
121.229
121.198
114.099
113.354
109.936
77.383
77.270
77.065
76.748
55.219
52.241
34.276
29.559
18.646



31

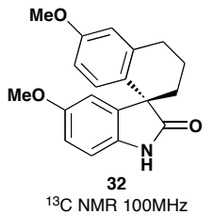
^{13}C, $CDCl_3$, 100 MHz





31

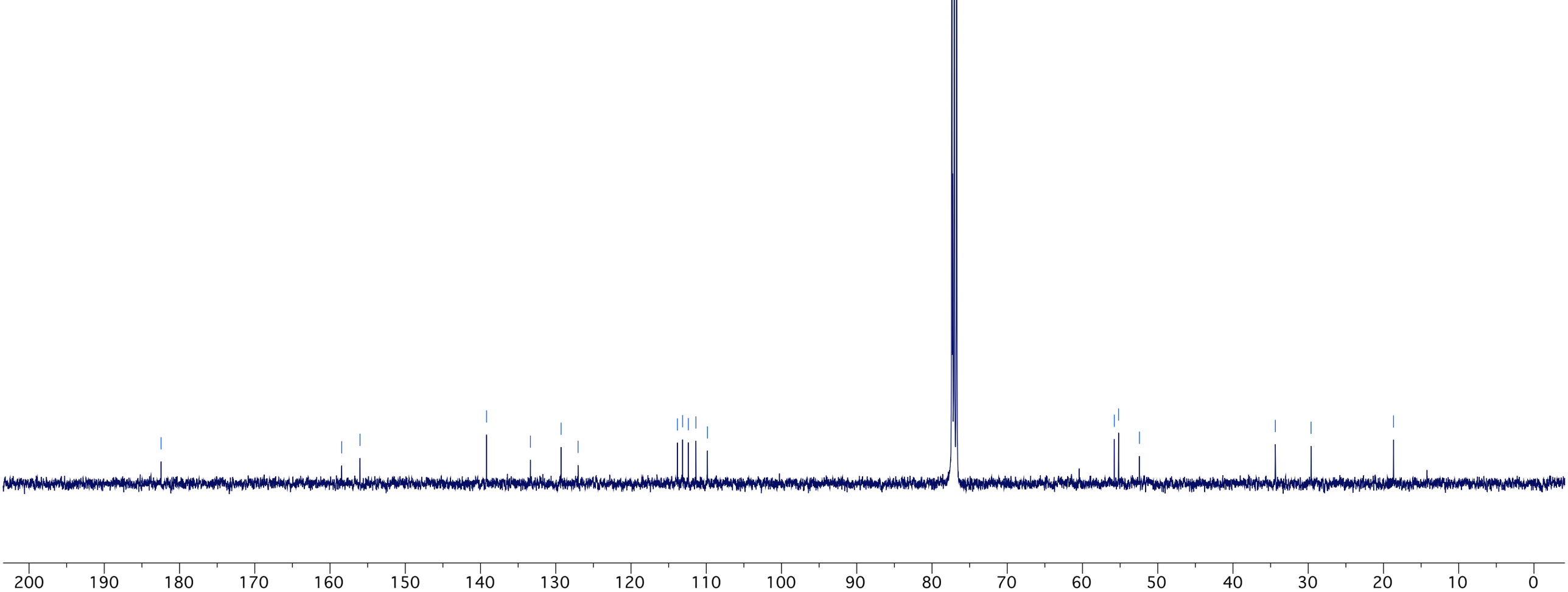
^{1}H, $CDCl_3$, 300 MHz

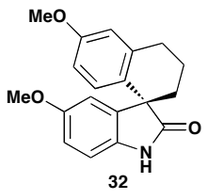


32

^{13}C NMR 100MHz

182.457
158.447
156.012
139.194
133.370
129.294
127.037
113.836
113.144
112.382
111.373
109.846
55.771
55.206
52.437
34.371
29.622
18.665

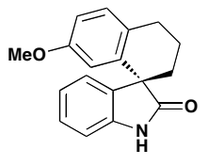




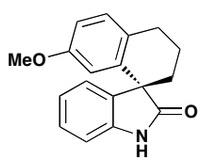
32

^{1}H NMR 300MHz

182.616
157.831
140.052
137.675
135.727
130.540
130.061
127.859
124.331
122.820
113.251
113.143
109.763
55.198
52.824
34.096
28.451
18.860



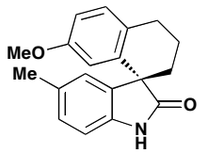
33
^{13}C NMR 125MHz



33

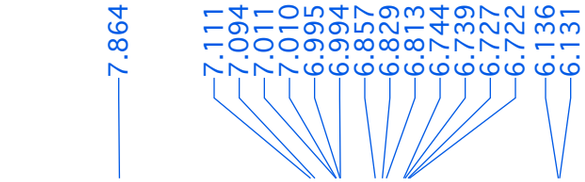
^{1}H NMR 300MHz

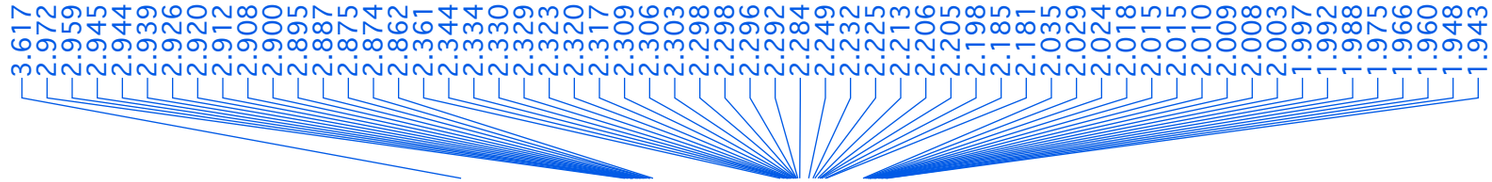
182.282
157.804
137.735
137.420
135.925
132.334
130.495
130.078
128.189
125.106
113.282
113.136
109.293
55.212
52.765
34.143
28.480
21.162
18.902

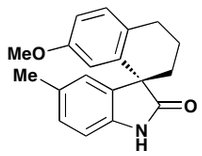


34

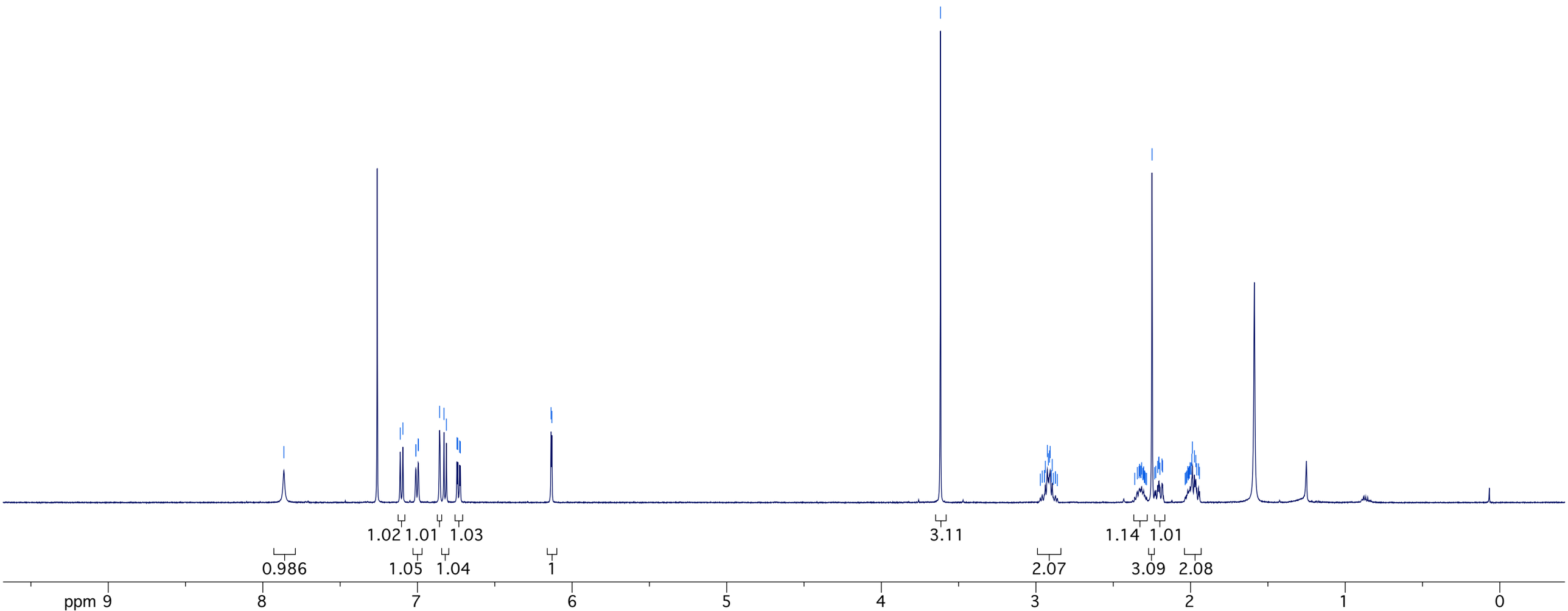
^{13}C NMR 125MHz

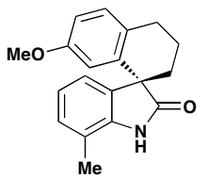






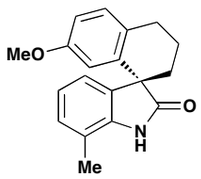
34
^{1}H NMR 500MHz





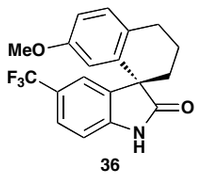
35
^{13}C NMR 125MHz

183.035
157.790
138.913
137.297
135.940
130.466
130.026
129.158
122.717
121.657
119.102
113.233
113.085
55.207
53.212
34.111
28.466
18.809
16.593



35

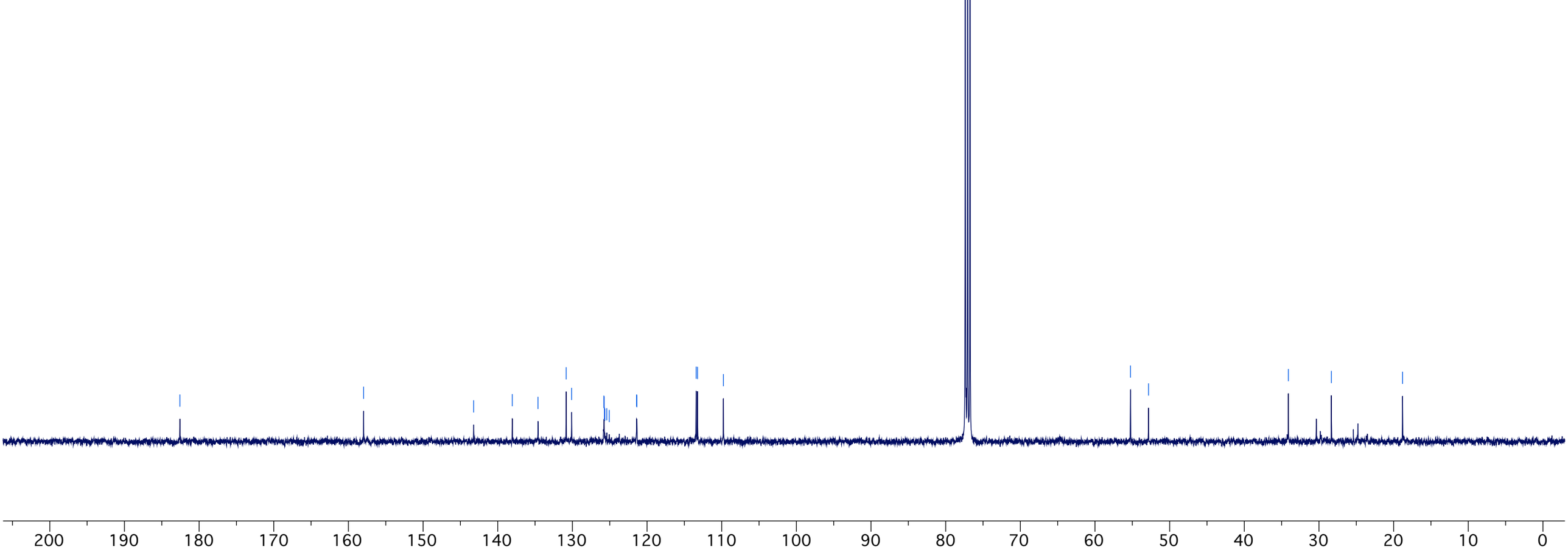
^{1}H NMR 500MHz

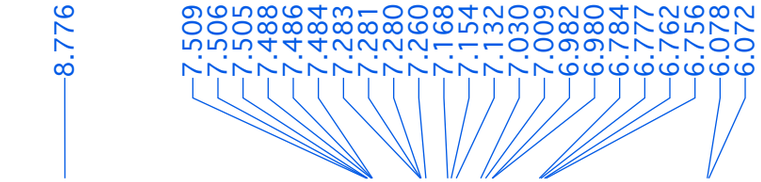


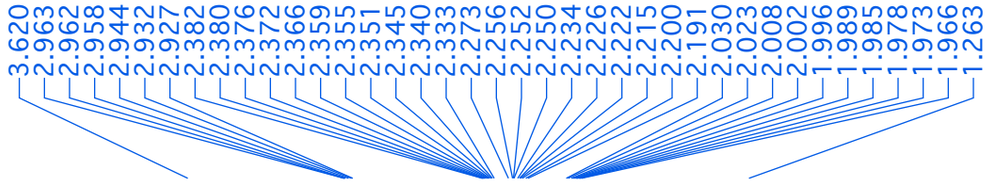
36

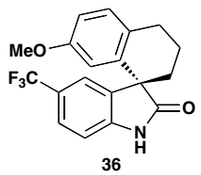
^{13}C, $CDCl_3$, 100 MHz

182.574
157.967
143.226
138.053
134.607
130.830
130.104
125.783
125.746
125.710
125.647
125.390
125.066
121.397
121.361
113.429
113.242
109.771
55.247
52.829
34.095
28.336
18.804



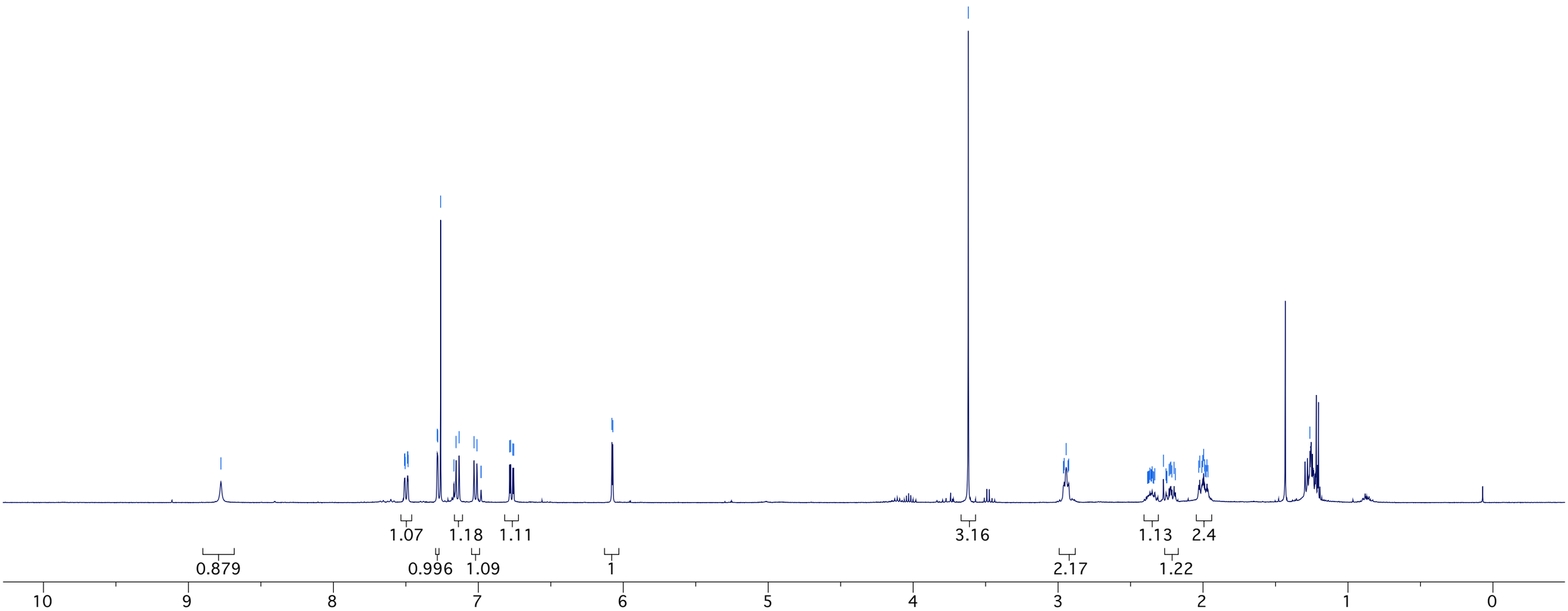




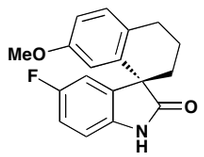


36

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

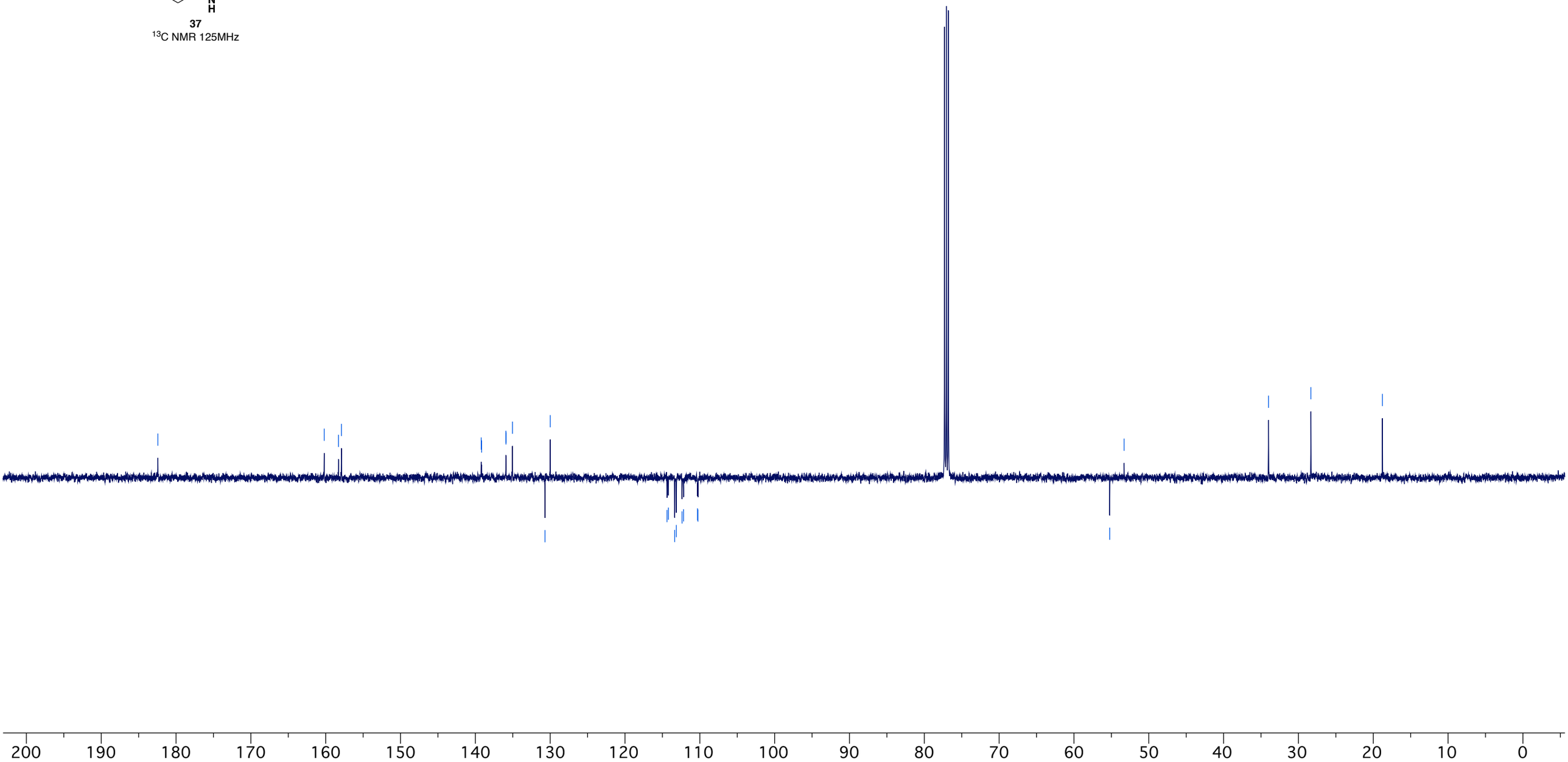


182.428
160.202
158.288
157.893
139.220
139.158
135.916
135.907
135.041
130.691
129.991
114.388
114.203
113.358
113.141
112.373
112.176
110.317
110.252
55.224
53.298
34.000
28.334
18.779

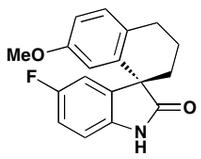


37

^{13}C NMR 125MHz

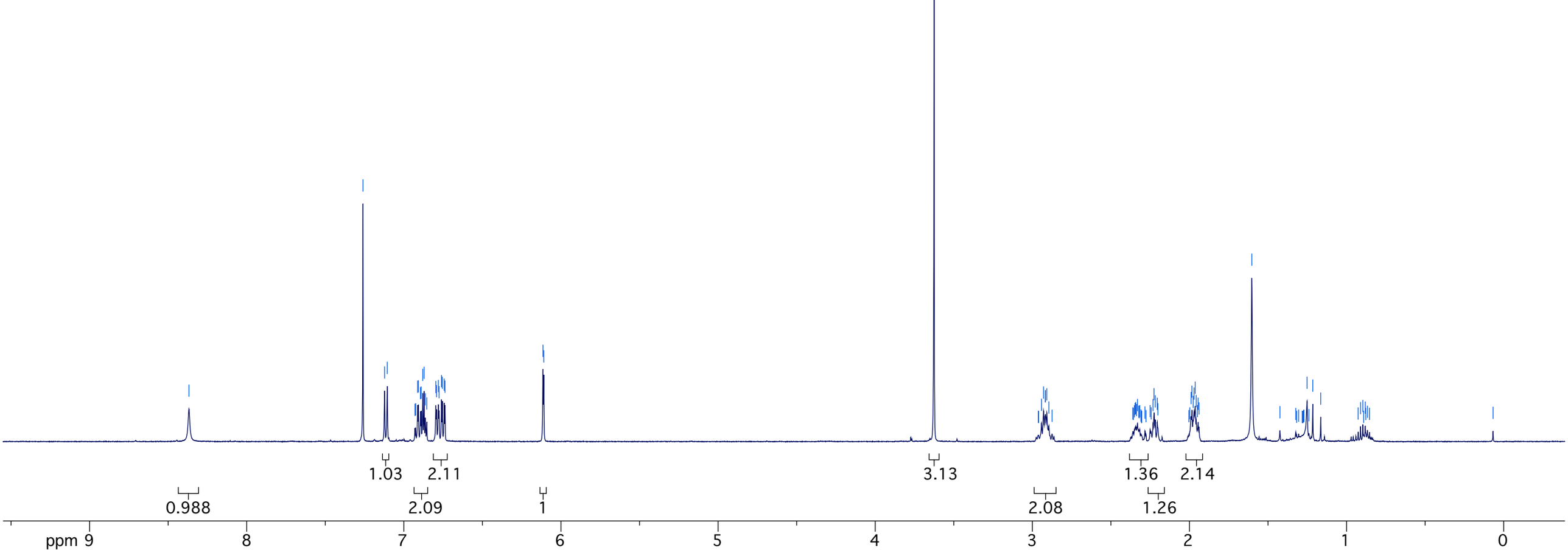


8.368
7.260
7.123
7.106
6.929
6.924
6.912
6.907
6.894
6.889
6.880
6.871
6.863
6.854
6.797
6.792
6.780
6.776
6.760
6.755
6.743
6.738
6.114
6.109
3.626
2.962
2.960
2.942
2.929
2.917
2.917
2.908
2.895
2.874
2.360
2.357
2.350
2.346
2.342
2.337
2.331
2.323
2.320
2.316
2.309
2.306
2.305
2.304
2.283
2.277
2.251
2.244
2.232
2.226
2.217
2.205
2.201
2.004
1.998
1.990
1.984
1.976
1.971
1.963
1.957
1.950
1.945
1.939
1.603
1.424
1.323
1.318
1.305
1.282
1.280
1.278
1.277
1.273
1.272
1.252
1.240
1.215
1.165
0.926
0.911
0.897
0.891
0.881
0.878
0.867
0.854
0.068

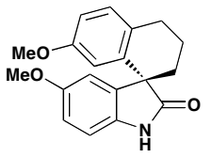


37

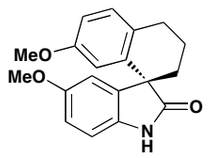
^{1}H NMR 500MHz



182.678
157.853
156.000
138.979
135.646
133.475
130.540
130.033
113.265
113.206
112.444
111.388
110.134
55.759
55.217
53.287
34.121
28.438
18.844

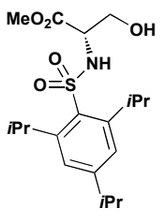


38
^{13}C NMR 125MHz



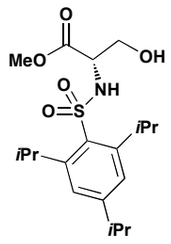
38

^{1}H NMR 500MHz



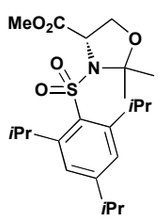
15

^{13}C, $CDCl_3$, 75 MHz



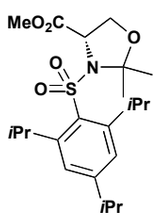
49

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



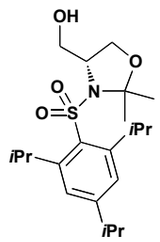
50

^{13}C, $CDCl_3$, 75 MHz



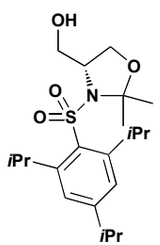
50

^{1}H, $CDCl_3$, 300 MHz



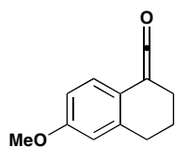
51

^{13}C, C_6D_6, 75 MHz



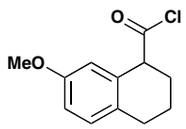
51

^{1}H, C_6D_6, 300 MHz

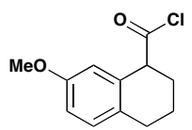


59

^{1}H NMR 400MHz

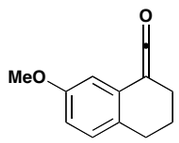


64
^{13}C NMR 75MHz



64

^{1}H NMR 300MHz



65
^{1}H NMR 400MHz