Supporting Information

First domino radical cyclisation / Smiles rearrangement combination

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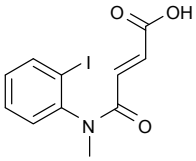
Experimental Section

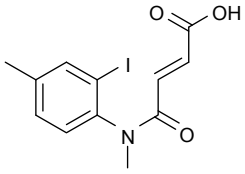
General : All solvents were dried and purified by standard literature methods prior to use. Commercials reagents are used without further purification. Melting points were determined on an hot-stage apparatus and are uncorrected. Reactions were monitored on silicagel plates (Kieselgel $60F_{254}$) and preparative column chromatography was carried out on silica gel 60 (70-230 mesh ASTM). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 300 apparatus at 300 and 75 MHz respectively, in $CDCl_3$, with TMS as internal standard. Coupling constants *J* are quoted in Hz. IR spectra (thin film or KBr pastille) were measured on a Perkin-Elmer SPECTRUM BX/RX Fourier transform spectrometer. Mass spectra were either recorded with an ESI-Q-TOF mass spectrometer or with a GCT Micromass Waters apparatus.

Experimental details and characterisation of new compounds:

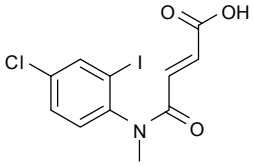


(*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid 1. To a suspension of (*E*)-3-(ethoxycarbonyl)-acrylic acid (5.0 g, 34.7 mmol) and DMTMM (9.59 g, 34.7 mmol) in THF (150 mL) was added NMM (3.81 mL, 34.7 mmol) and the suspension was stirred at r.t. for 20 min. A solution of *ortho*-iodoaniline (7.0 g 32.0 mmol) was then added and the suspension was stirred overnight. The reaction mixture was diluted with water, extracted with diethyl ether, successively washed with a saturated solution of $NaHCO_3$, water, solution of HCl 2%, brine, dried over magnesium sulfate and finally concentrated *in vacuo*. Crystallisation from diethyl ether gave the corresponding amide compound which was dissolved in dry THF and added to a suspension of NaH (288 mg, 12.0 mmol) in dry THF at 0°C. The suspension was stirred at 0°C for 30 min and at r.t. for 30 min more. A solution of iodomethane (1.9 mL, 12.5 mmol) in dry THF was then added at 0°C and the reaction mixture was stirred at r.t. until the completion of the reaction. The crude mixture was then quenched with water, THF was removed *in vacuo* and the mixture was treated successively with solutions of $NaHCO_3$ 5%, HCl 2%, and brine. Compound was crystallised in diethyl ether.

To a solution of (*E*)-ethyl 4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoate (2.83 g, 7.9 mmol) in ethanol (50 mL) at r.t. was added a solution of KOH 2N (16 mL, 31.4 mmol). After the disappearance of the starting material (TLC monitoring), the reaction mixture was diluted with water and washed with ethyl acetate. Aqueous layer was acidified and extracted with ethyl acetate. Crude mixture was dried over $MgSO_4$ and concentrated *in vacuo* to give compound **1** (4.30 g, total yield 62%) as a brownstone solid used without further purification. mp 157-159°C; ν_{max}(KBr)/ cm^{-1} 3427, 3048, 3013, 2978, 2925, 2528, 1714, 1626, 1591, 1560; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.27 (s, 3H), 6.63 (d, *J* = 15.2 Hz, 1H), 6.85 (d, *J* = 15.2 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.94 (d, 1H, *J* = 7.7 Hz); δ_C(75 MHz, $CDCl_3$, Me_4Si) 36.6, 99.1, 129.1, 130.1, 130.5, 130.9, 135.0, 140.4, 144.4, 163.9, 169.7; *m/z* (CI) 332 $[M+H]^+$, 233, 204, 159; HRMS (EI) calcd for $C_{11}H_{10}NO_3$ ($[M - I]^+$) 204.0661, found 204.0660.

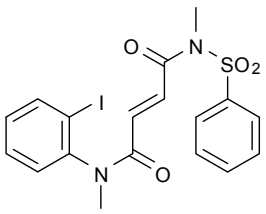


(*E*)-4-((2-iodo-4-methylphenyl)(methyl)amino)-4-oxobut-2-enoic acid 2. (*E*)-4-((2-iodo-4-methylphenyl)(methyl)amino)-4-oxobut-2-enoic acid was prepared according to previous process for **1**. The reaction was carried out with (*E*)-ethyl 4-((2-iodo-4-methylphenyl) (methyl)amino)-4-oxobut-2-enoate (2.70 g, 7.24 mmol), obtained from of (*E*)-3-(ethoxycarbonyl)-acrylic acid and 1 equivalent of 4-methyl-2-iodoaniline (3.5 g, 15.02 mmol) followed by treatment with NaH and MeI, and KOH 2N (10 mL, 28.95 mmol) in ethanol. Crude mixture was dried over $MgSO_4$ and concentrated *in vacuo* to give (*E*)-4-((2-iodo-4-methylphenyl)(methyl)amino)-4-oxobut-2-enoic acid (2.58 g, total yield 83%) as white crystals after crystallisation in diethyl ether. mp 172 °C; ν_{max}(KBr)/ cm^{-1} 2925, 2759, 2594, 2367, 1708, 1638, 1600, 1582, 1434, 1246, 969, 832; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.37 (s, 3H), 3.25 (s, 3H), 6.67 (d, *J* = 15.3 Hz, 1H), 6.85 (d, *J* = 15.3 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.22 (dd, *J* = 7.5 1.5 Hz, 1H), 7.76 (br d, *J* = 0.9 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 20.6, 36.7, 98.9, 128.5, 130.5, 130.9, 135.5, 140.7, 141.0, 141.8, 163.9, 169.9; *m/z* (CI) 345 $[M+H]^+$, 327, 247, 218, 201, 174, 128, 119, 99; HRMS (CI) calcd for $C_{12}H_{13}NO_3I$ $[M+H]^+$ 345.9940, found 345.9947.



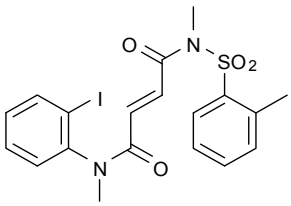
(*E*)-4-((4-chloro-2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid 3. (*E*)-4-((4-chloro-2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid was prepared according to previous process for **1**. The reaction was carried out with (*E*)-ethyl 4-((4-chloro-2-iodophenyl)(methyl)amino)-4-oxobut-2-enoate (930 mg, 2.36 mmol), obtained from of (*E*)-3-(ethoxycarbonyl)-acrylic acid and 1 equivalent of 4-chloro-2-iodoaniline (1.9 g, 7.49 mmol) followed by treatment with NaH and MeI, and KOH 2N (5 mL, 9.45 mmol) in ethanol. Crude mixture was dried over $MgSO_4$ and concentrated *in vacuo* to give (*E*)-4-((4-chloro-2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid (880 mg, total yield 87%) as a brownstone solid used without further purification. mp 185°C; ν_{max}(KBr)/ cm^{-1} 3075, 2925, 2599, 2362, 1706, 1641, 1594, 1473, 1390, 1279, 1243, 1215, 1135, 1099, 1055, 962; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.25 (s, 3H), 6.64 (d, J = 15.0 Hz, 1H), 6.88 (d, J = 15.0 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 7.43 (dd, J = 8.4 2.1 Hz, 1H), 7.94 (d, J = 2.1 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 36.9, 100.8, 131.3, 131.6, 133.3, 134.5, 136.5, 140.7, 144.9, 165.8, 168.1; *m/z* (CI) 366 $[M+H]^+$, 348, 267, 238, 221, 194, 127; HRMS (CI) calcd for $C_{11}H_{10}NO_3ClI$ $[M+H]^+$ 365.9394, found 365.9403.

Typical procedure for amidification. To a solution of acid **1, 2** or **3** (1 eq.) at 0°C in dry dichloromethane was added oxalyl chloride (1.2 eq.) and dry *N*,*N*-dimethylformamide (0.2 eq.). After 30 min, the temperature of the reaction mixture was raised to r.t. After completion of this step (TLC monitoring) the solvent was evaporated. The residue was diluted with dichloromethane and added to a solution of *N*-methylarylsulfonamide or N-isopropylarylsulfonamide (1 eq.) and triethylamine (4 eq.) at 0°C in dry dichloromethane. After 2-12 h (TLC monitoring) at r.t., the reaction mixture was washed with $NaHCO_3$ 5%, HCl 2% and brine. Product is obtained by column chromatography and/or crystallisation.

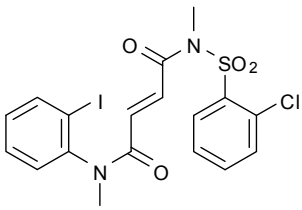


N^1-(2-iodophenyl)-N^1,N^4-dimethyl-N^4-(phenylsulfonyl)fumar-amide 4a. According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **1** (397 mg, 1.2 mmol), oxalyl chloride (144 µL, 1.68 mmol), dimethylformamide (20 µL) in dry dichloromethane (5 mL) and then *N*-methylphenylsulfonamide (171 mg, 1.0 mmol), triethylamine (561 µL, 4.0 mmol) in dry dichloromethane (5 mL). Compound **4a** was obtained after purification by

column chromatography (CH_2Cl_2 / MeOH : 99.5 / 0.5) as a beige oil (474 mg, 98%). ν_{max}(neat)/ cm^{-1} 3065, 2935, 1680, 1656, 1631, 1576, 1470, 1447, 1419, 1362, 1308, 1197, 1163, 1088, 1018, 967; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.27 (s, 3H), 3.32 (s, 3H), 6.53 (d, *J* = 14.8 Hz, 1H), 7.10 (td, *J* = 7.3 1.6 Hz, 1H), 7.23 (dd, *J* = 7.3 1.6 Hz, 1H), 7.42 (dt, *J* = 7.3 1.4 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.65 (tt, *J* = 7.4 1.8 Hz, 1H), 7.71 (d, *J* = 14.8 Hz, 1H), 7.91 (dd, *J* = 7.3 1.4 Hz, 1H), 7.91 (dd, *J* = 7.4 1.8 Hz, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 33.1, 36.6, 99.2, 127.5, 129.2, 129.4, 130.1, 130.4, 131.7, 133.5, 134.0, 138.7, 140.3, 144.5, 163.6, 165.1; *m/z* (CI) 485 $[M+H]^+$, 357, 314, 232; HRMS (CI) calcd for $C_{18}H_{18}IN_2O_4S$ $[M+H]^+$ 485.0032, found 485.0011.

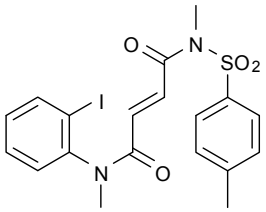


***N*¹-(2-iodophenyl)-*N*¹,*N*⁴-dimethyl-*N*⁴-(*o*-tolylsulfonyl) fumaramide 4b.** According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **1** (430 mg, 1.3 mmol), oxalyl chloride (228 µL, 2.6 mmol), dimethylformamide (39 µL) in dry dichloromethane (7 mL) and then *N*,2-dimethylbenzenesulfonamide (250 mg, 1.3 mmol), triethylamine (724 µL, 5.2 mmol) in dry dichloromethane (7 mL). Compound **4b** was obtained after purification by column chromatography (CH_2Cl_2 / MeOH : 99.5 / 0.5 to 95 / 5) as a white foam (364 mg, 56%). ν_{max}(neat)/ cm^{-1}3054, 2987, 2295, 1654, 1419, 1354, 1261, 1163, 892, 734; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.52 (s, 3H), 3.24 (s, 3H), 3.35 (s, 3H), 6.52 (d, *J* = 14.7 Hz, 1H), 7.09 (td, *J* = 7.7 1.2 Hz, 1H), 7.20 (dd, *J* = 7.7 1.2 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.40 (dt, *J* = 7.7 1.2 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 14.7 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 20.2, 32.9, 36.7, 99.3, 126.7, 129.2, 130.2, 130.3, 130.5, 131.6, 132.9, 133.7, 134.1, 137.4, 137.4, 137.5, 140.4, 144.5, 163.6, 165.2; *m/z* (ESI) 521 $[M+Na]^{+\cdot}$, 499; HRMS (ESI) calcd for $C_{19}H_{19}IN_2O_4SNa$ $[M+Na]^{+\cdot}$ 521.0008, found 521.0012.

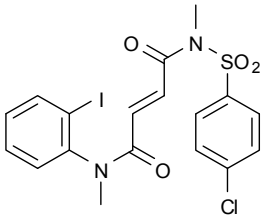


***N*¹-((2-chlorophenyl)sulfonyl)-*N*⁴-(2-iodophenyl)-*N*¹,*N*⁴-dimethyl fumaramide 4c.** According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **1** (438 mg, 1.46 mmol), oxalyl chloride (256 µL, 2.92 mmol), dimethylformamide (45 µL) in dry dichloromethane

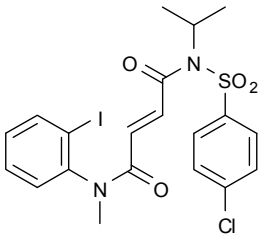
(7 mL) and then 2-chloro-*N*-methylbenzenesulfonamide (300 mg, 1.46 mmol), triethylamine (813 µL, 5.84 mmol) in dry dichloromethane (7 mL). Compound **4c** was obtained after purification by flash column chromatography (CH_2Cl_2 / MeOH : 100 / 0 to 99 / 1) and crystallised in diethyl ether as a white solid (485 mg, 64%). mp 154°C; ν_{max}(KBr)/ cm^{-1}, 2920, 2367, 1682, 1654, 1633, 1574, 1468, 1450, 1416, 1362, 1300, 1200, 1150, 1039, 1013, 931; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.24 (s, 3H), 3.45 (s, 3H), 6.53 (d, *J* = 14.7 Hz, 1H), 7.09 (td, *J* = 7.8 1.5 Hz, 1H), 7.20 (dd, *J* = 7.8 1.5 Hz, 1H), 7.40 (dt, *J* = 7.8 1.5 Hz, 1H), 7.45-7.58 (m, 3H), 7.48 (d, *J* = 14.7 Hz, 1H), 7.89 (dd, *J* = 8.1 1.5 Hz, 1H), 8.26 (dd, *J* = 8.4 1.5 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 33.3, 36.6, 99.2, 127.3, 129.1, 130.1, 130.4, 130.9, 131.9, 132.6, 134.0, 134.8, 136.6, 137.4, 140.3, 144.4, 163.4, 164.8; *m/z* (CI) 519 $[M+H]^+$, 391, 314, 233, 217; HRMS (CI) calcd for $C_{18}H_{17}IN_2O_4SCl$ $[M+H]^+$ 518.9642, found 518.9649.



***N*^{1}-(2-iodophenyl)-*N*^{1},*N*^{4}-dimethyl-*N*^{4}-tosylfumaramide 4d.** According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **1** (457 mg, 1.47 mmol), oxalyl chloride (154 µL, 1.76 mmol), dimethylformamide (25 µL, 0.29 mmol) in dry dichloromethane (8.5 mL) and then *N*,4-dimethylphenylsulfonamide (273 mg, 1.47 mmol) and triethylamine (818 µL, 5.88 mmol) in dry dichloromethane (8.5 mL). Compound **4d** was obtained by column chromatography (CH_2Cl_2 / MeOH : 99.5 / 0.5) as beige crystals (385 mg, 52%). mp 137-140 °C; ν_{max}(KBr)/ cm^{-1} 3057, 2916, 2846, 1652, 1467, 1419, 1362, 1265, 1194, 1128, 1084, 1014, 965, 838, 767, 657; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.43 (s, 3H), 3.27 (s, 3H), 3.31 (s, 3H), 6.53 (d, *J* = 14.8 Hz, 1H), 7.10 (td, *J* = 7.8 1.5 Hz, 1H), 7.23 (dd, *J* = 7.8 1.5 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.41 (td, *J* = 7.8 1.5 Hz, 1H), 7.71 (d, *J* = 14.8 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.87 (dd, *J* = 7.8 1.5 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.7, 33.0, 36.6, 99.3, 127.6, 129.2, 130.0, 130.1, 130.4, 131.9, 133.4, 135.8, 140.4, 144.5, 145.1, 163.7, 165.1; *m/z* (CI) 499 $[M+H]^+$, 371, 217, 186, 159; HRMS (CI) calcd for $C_{19}H_{20}IN_2O_4S$ ($[M+H]^+$) 499.0189, found 499.0125.

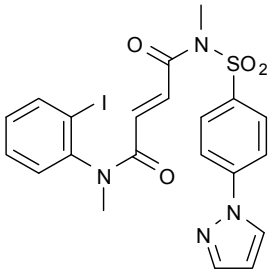


***N*⁴-(4-chlorophenylsulfonyl)-*N*¹-(2-iodophenyl)-*N*¹,*N*⁴-dimethyl fumaramide 4e.** According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **1** (331 mg, 1.0 mmol), oxalyl chloride (103 µL, 1.2 mmol), dimethyl formamide (25 µL) in dry dichloromethane (5 mL) and then 4-chloro-*N*-methylphenylsulfonamide (105.5 mg, 1.0 mmol), triethylamine (561 µL, 4.0 mmol) in dry dichloromethane (5 mL). Compound **4e** was obtained by column chromatography (CH_2Cl_2) and crystallisation in diethyl ether as a white solid (380 mg, 73 %). mp 126-128 °C; ν_{max}(KBr)/ cm^{-1} 3243, 3029, 2934, 1718, 1656, 1571, 1524 ; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.27 (s, 3H), 3.34 (s, 3H), 6.52 (d, *J* = 14.8 Hz, 1H), 7.11 (dt, *J* = 7.6 1.6 Hz, 1H), 7.23 (dd, *J* = 7.6 1.6 Hz, 1H), 7.42 (dt, *J* = 7.6 1.4, 1H), 7.51 (d, *J* = 8.7 Hz, 1H), 7.63 (d, *J* = 14.8 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 2H), 7.92 (dd, *J* = 7.6 1.4 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 33.2, 36.6, 99.2, 129.1, 129.2, 129.6, 130.1, 130.5, 131.4, 133.9, 137.1, 140.4, 140.7, 144.4, 163.5, 165.0; *m/z* (CI) 520 $[M+H]^+$, 393, 267, 231; HRMS (EI) calcd for $C_{18}H_{17}ClIN_2O_4S$ ($[M + H]^{+\cdot}$) 520.9601, found 520.9613.



***N*¹-((4-chlorophenyl)sulfonyl)-*N*⁴-(2-iodophenyl)-*N*¹-isopropyl-*N*⁴-methylfumaramide 4f.** According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **1** (708 mg, 2.14 mmol), oxalyl chloride (375 µL, 4.28 mmol), dimethylformamide (66 µL) in dry dichloromethane (15 mL) and then 4-chloro-*N*-isopropylbenzenesulfonamide (1 g, 4.28 mmol), triethylamine (1.19 mL, 8.56 mmol) in dry dichloromethane (15 mL). Compound **4f** was obtained after purification by flash column chromatography (CH_2Cl_2/AcOEt 100 / 0 to 90 / 10) and crystallisation in diethyl ether as a white solid (171 mg, 15%). mp 161-163 °C; ν_{max}(KBr)/ cm^{-1} 2966, 2925, 2372, 1687, 1656, 1631, 1473, 1421, 1381, 1354, 1303, 1181, 1163, 1130, 1088, 990, 954, 755; δ_H(300 MHz, $CDCl_3$, Me_4Si) 1.46 (d, *J* = 5.1 Hz, 3H), 1.48 (d, *J* = 5.4 Hz, 3H), 3.26 (s, 3H), 4.53 (sept, *J* = 6.9 Hz, 1H), 6.44 (d, *J* = 14.7 Hz, 1H), 7.11 (dt, *J* = 7.5 1.5 Hz, 1H), 7.23 (dd, *J* = 7.5 1.5 Hz, 1H), 7.43 (dt, *J* = 7.5 1.5 Hz, 1H), 7.49 (d, *J* = 14.7 Hz, 1H), 7.53 (d, *J* = 9 Hz, 2H), 7.89 (d, *J* = 8.7 Hz, 2H), 7.92 (dd, *J* = 8.1 1.5 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 20.6, 33.1, 36.6, 99.0, 127.6, 128.6, 129.4, 130.8, 131.5, 133.8, 134.0, 138.8, 140.7, 140.9, 141.9, 163.8, 165.2; *m/z* (CI) 547 $[M+H]^+$, 505, 419, 377, 373,

314, 245, 187, 174, 159, 145, 111, 91; HRMS (CI) calcd for $C_{20}H_{21}IN_2O_4SCl$ $[M+H]^+$ 546.9955, found 546.9959.

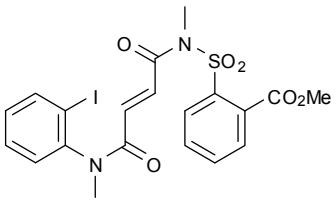


***N*^{1}-(4-(1*H*-pyrazol-1-yl)phenylsulfonyl)-*N*^{4}-(2-iodophenyl)-*N*^{1},*N*^{4}-dimethylfumaramide 4g.** According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **1** (245 mg, 0.8 mmol), oxalyl chloride (140 µL, 1.6 mmol), dimethylformamide (25 µL) in dry dichloromethane (10 mL) and then *N*-methyl-4-(1*H*-pyrazol-1-yl)benzenesulfonamide (189 mg, 0.8 mmol), triethylamine (445 µL, 3.2 mmol) in dry dichloromethane (10 mL).

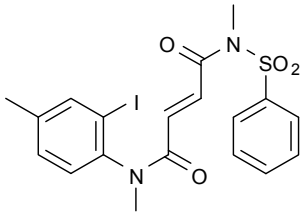
N-methyl-4-(1*H*-pyrazol-1-yl)benzenesulfonamide was previously prepared by reaction of 735 mg of 4-(1*H*-pyrazol-1-yl)benzene-1-sulfonyl chloride (3 mmol) and 138 mg of methanamine hydrochloride (2 mmol) suspended in 11 mL of water and vigorously stirred at room temperature. Then 4 mL of 1 N aqueous potassium hydroxide solution (4 mmol) is slowly added and the solution was heated to 50 °C for 5 h. After cooling to room temperature and pH monitoring (which must be inferior to 1 otherwise the solution had to be acidified with a 10 % HCl aqueous solution) the product was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford a white solid (189 mg, 40 %). mp 176 °C; ν_{max}(neat)/ cm^{-1} 3049, 2987, 2357, 2337, 1729, 1421, 1261, 1042, 895, 745; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.70 (s, 3H), 4.36 (Br s, 1H), 6.54 (t, *J* = 2.3 Hz, 1H), 7.78 (d, *J* = 2.3 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 2H), 7.96 (d, *J* = 8.9 Hz, 2H), 8.01 (d, *J* = 2.3 Hz, 1H); δ_C(75 MHz, $CDCl_3$+CD_3OD, Me_4Si) 28.6, 108.6, 118.8, 127.3, 128.6, 136.2, 142.0, 142.6; *m/z* (EI) 237 $[M]^{+\cdot}$, 207, 173, 159, 143, 116; HRMS (EI) calcd for $C_{10}H_{11}N_3O_2S$ $[M]^{+\cdot}$ 237.0583, found 237.0572.

Compound **4g** was finally obtained after purification by column chromatography (CH_2Cl_2 / MeOH : 99 / 1 to 90 / 10) as a white foam (211 mg, 48%). ν_{max}(KBr)/ cm^{-1} 3044, 2988, 2294, 1657, 1603, 1548, 1437, 1418, 1265; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.26 (s, 3H), 3.39 (s, 3H), 6.50 (d, *J* = 14.9 Hz, 1H), 6.53-6.55 (m, 1H), 7.09 (dt, *J* = 7.7 1.4 Hz, 1H), 7.22 (dd, *J* = 7.7 1.4 Hz, 1H), 7.40 (dt, *J* = 7.7 1.4 Hz, 1H), 7.69 (d, *J* = 14.9 Hz, 1H), 7.78 (fd, *J* = 1.2 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 2H), 7.88-7.91 (m, 1H), 7.99 (m, 1H), 8.00 (d, *J* = 8.9 Hz, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 33.1, 36.6, 99.3, 109.1 , 118.8, 126.9, 129.1, 129.5, 130.1, 130.4,

131.6, 133.6, 135.7, 140.3, 142.6, 143.8, 144.5, 163.5, 165.0; *m/z* (CI) 551 $[M+H]^+$, 423, 361, 345, 313, 238, 217, 207; HRMS (CI) calcd for $C_{21}H_{20}IN_4O_4SI$ $[M+H]^+$ 551.0250, found 551.0248.

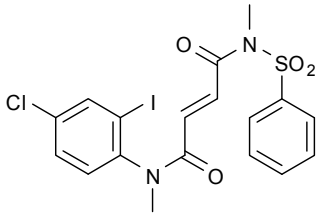


(*E*)-methyl-2-(*N*-(4-((2-iodophenyl)(methyl)amino)-4-oxo but-2-enoyl)-*N*-methylsulfamoyl)benzoate <u>4h</u>. According to general procedure for amidification from (*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid **<u>1</u>** (331 mg, 1.0 mmol), oxalyl chloride (103 µL, 1.2 mmol), dimethylformamide (25 µL) in dry dichloromethane (5 mL) and then methyl-2-methylsulfamoyl-benzoate **<u>2</u>** (229 mg, 1.0 mmol), triethylamine (561 µL, 4.0 mmol) in dry dichloromethane (5 mL). Compound was obtained by column chromatography (gradient elution CH_2Cl_2 / MeOH : 99.5 / 0.5 and 99 / 1) to give **<u>4h</u>** as a white solid (396 mg, 73 %); mp 67 °C; ν_{max}(KBr)/ cm^{-1} 3058, 2948, 1733, 1656, 1575; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.26 (s, 3H), 3.40 (s, 3H), 3.94 (s, 3H), 6.58 (d, *J* = 14.8 Hz, 1H), 7.09 (dt, *J* = 7.7 1.6 Hz, 1H), 7.21 (dd, *J* = 7.7 1.6 Hz, 1H), 7.40 (dt, *J* = 7.7 1.4 Hz, 1H), 7.50 (d, *J* = 14.8 Hz, 1H), 7.58-7.71 (m, 3H), 7.90 (dd, *J* = 7.7 1.4 Hz, 1H), 8.18-8.29 (m, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 33.3, 36.6, 53.3, 99.2, 129.1, 129.5, 130.1, 130.2, 130.4, 130.7, 131.4, 132.3, 133.6, 133.8, 137.0, 140.4, 144.4, 163.5, 165.0, 166.6; *m/z* (EI) 415 $[M-I]^{+\cdot}$, 362, 314, 264, 218; HRMS (EI) calcd for $C_{20}H_{19}N_2O_6S$ ($[M - I]^{+\cdot}$) 415.0964, found 415.0959.



***N*^{1}-(2-iodo-4-methylphenyl)-*N*^{1},*N*^{4}-dimethyl-*N*^{4}-(phenylsulfonyl) fumaramide <u>4i</u>.** According to general procedure for amidification from (*E*)-4-((2-iodo-4-methylphenyl) (methyl)amino)-4-oxobut-2-enoic acid (1.47 g, 4.26 mmol) acid **<u>2</u>**, oxalyl chloride (732 µL, 8.52 mmol), dimethylformamide (132 µL) in dry dichloromethane (30 mL) and then *N*-methylphenylsulfonamide (728 mg, 4.26 mmol), triethylamine (2.37 mL, 17.04 mmol) in dry dichloromethane (10 mL). Compound **<u>4i</u>** was obtained after purification by flash column chromatography (CH_2Cl_2) as a white foam (1.252 g, 59%). ν_{max}(neat)/ cm^{-1} 2920, 2372, 1656, 1631, 1486, 1447, 1367, 1305, 1197, 1166, 1083, 1018, 969, 931, 732; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.34 (s, 3H), 3.24 (s, 3H), 3.33 (s, 3H), 6.56 (d, *J* = 14.7 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 7.19 (dd, *J* = 8.7 1.2 Hz, 1H), 7.53-7.59

(m, 2H), 7.61-7.68 (m, 1H), 7.69 (d, J = 14.7 Hz, 1H), 7.72 (br d, J = 1.2 Hz, 1H), 7.90-7.94 (m, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 20.6, 33.1, 36.6, 99.0, 127.6, 128.6, 129.4, 130.8, 131.5, 133.8, 134.0, 138.8, 140.7, 140.9, 141.9, 163.8, 165.2; *m/z* (CI) 499 $[M+H]^+$, 371, 359, 327, 246, 231, 201, 172, 141, 111, 91, 77; HRMS (CI) calcd for $C_{19}H_{20}IN_2O_4S$ $[M+H]^+$ 499.0189, found 499.0187.

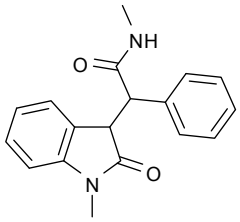


N^1-(4-chloro-2-iodophenyl)-N^1,N^4-dimethyl-N^4-(phenyl sulfonyl)fumaramide <u>4j</u>. According to general procedure for amidification from (*E*)-4-((4-chloro-2-iodophenyl) (methyl)amino)-4-oxobut-2-enoic acid **<u>3</u>** (1070 mg, 2.93 mmol), oxalyl chloride (503 µL, 5.86 mmol), dimethylformamide (90 µL) in dry dichloromethane (20 mL) and then *N*-methylphenylsulfonamide (501 mg, 2.93 mmol), triethylamine (1.63 mL, 11.72 mmol) in dry dichloromethane (15 mL). Compound **<u>4j</u>** was obtained after purification by flash column chromatography (CH_2Cl_2 / MeOH : 100 / 0 to 99 / 1) as a white foam (732 mg, 48%). ν_{max}(KBr)/ cm^{-1} 3070, 2925, 2848, 1656, 1625, 1468, 1447, 1359, 1308, 1197, 1163, 1099, 1088,1016, 969, 931, 838; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.24 (s, 3H), 3.32 (s, 3H), 6.52 (d, J = 14.7 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 8.4 2.4 Hz, 1H), 7.56 (dt, J = 7.5 1.5 Hz, 2H), 7.66 (tt, J = 7.5 2.4 Hz, 1H), 7.72 (d, J = 14.7 Hz, 1H), 7.90 (d, J = 1.8 Hz, 1H), 7.91 (dd, J = 7.5 1.8 Hz, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 33.1, 36.6, 99.6, 127.5, 129.4, 129.6, 130.3, 132.1, 133.1, 134.0, 135.4, 138.7, 139.7, 143.3, 163.6, 165.0; *m/z* (CI) 519 $[M+H]^+$, 391, 379, 348, 267, 251, 222, 193, 172, 141, 127, 77; HRMS (CI) calcd for $C_{18}H_{17}IN_2O_4SCl$ $[M+H]^+$ 518.9642, found 518.9650.

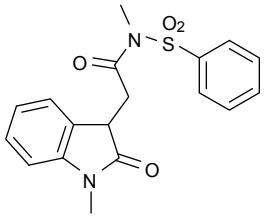
Typical procedure for domino radical cyclisations. In a flame-dried three-necked flask equipped with magnetic stirring, reflux condenser, Teflon valve with septum and curved glass-finger for first addition of solid initiator, a degassed dry solution of substrate was added by syringe. To this solution in reflux under argon atmosphere were added a first portion of solid initiator and a degassed solution of hydride dissolved in the reaction solvent. After 1 h, a second portion of initiator in solution was added. After completion of the reaction (TLC monitoring), solvent was evaporated and the residue was dissolved in acetonitrile and washed with hexane. The acetonitrile phase was dried over $MgSO_4$, filtered and evaporated to dryness

under reduced pressure. The residue was purified by column chromatography and in some cases compound was crystallised using appropriate solvent.

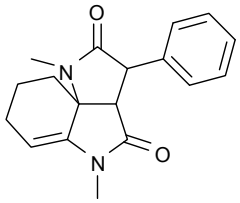
Compounds **5a**, **6a** and **7a** were prepared according to the typical procedure for domino radical cyclisations from N^1-(2-iodophenyl)-N^1,N^4-dimethyl-N^4-(phenylsulfonyl)fumaramide **4a** (135 mg, 0.31 mmol), TTMSS (115 µL, 0.372 mmol), ACCN (15 mg, 0.062 mmol, 0.4 eq.) in 2 portions at 1h interval, in decane (13 mL) at reflux over 3h. The crude product was purified by column chromatography (gradient elution CH_2Cl_2 / MeOH : 99 / 1 and 98.5 / 1.5) to give *N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-phenylacetamide **5a** (60 mg, 66%) (the diastereomers were partially separable by chromatography), *N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-*N*-(phenylsulfonyl)acetamide **6a** (12 mg, 11%) and the mixture of 1,5-dimethyl-3-phenyl-3,3a,8,9-tetrahydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione and 1,5-dimethyl-3-phenyl-3,3a-dihydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,9*H*)-dione **7a** (10 mg, 9%), as white oils.



***N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-phenylacetamide 5a.** Diastereoisomeric ratio 60/40 determined by NMR. ν_{max}(neat)/ cm^{-1} 3318, 2920, 1706, 1656, 1610, 1491, 1406, 1344, 1127, 1088, 840; *m/z* (CI) 295 $[M+H]^+$, 294, 236, 235, 218; HRMS (CI) calcd for $C_{18}H_{19}N_2O_2$ $[M+H]^+$ 295.1447, found 295.1438. **Major isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.84 (d, *J* = 4.8 Hz, 3H), 2.96 (s, 3H), 4.25 (d, *J* = 4.7 Hz, 1H), 4.48 (d, *J* = 4.7 Hz, 1H), 5.56 (br d, *J* = 4.8 Hz, 1H), 6.63 (d, *J* = 7.7 Hz, 1H), 6.96-7.01 (m, 3H), 7.08-7.18 (m, 3H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 25.9, 26.7, 48.3, 53.8, 107.7, 122.3, 126.2, 126.5, 127.9, 128.1, 128.3, 129.4, 135.1, 144.5, 172.2, 176.3; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.88 (d, *J* = 4.7 Hz, 3H), 3.05 (s, 3H), 4.15 (d, *J* = 4.0 Hz, 1H), 4.24 (d, *J* = 4.0 Hz, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 7.04 (dt, *J* = 7.7 0.9 Hz, 1H), 7.10 (dd, *J* = 6.6 3.1 Hz, 2H), 7.15-7.20 (m, 4H), 7.23 (dt, *J* = 8.7 0.9 Hz, 1H), 7.62 (br d, *J* = 4.7 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 25.9, 26.4, 48.1, 54.6, 107.9, 122.5, 123.7, 126.8, 127.5, 128.1, 128.2, 128.5, 135.2, 143.7, 171.6, 176.2.

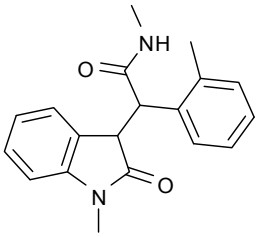


***N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-*N*-(phenylsulfonyl) acetamide 6a.** ν_{max}(neat)/ cm^{-1} 3369, 3297, 3054, 1705, 1609, 1356, 1261, 1160, 734; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.21 (dd, *J* = 18.0 8.4 Hz, 1H), 3.22 (s, 3H), 3.27 (s, 3H), 3.56 (dd, *J* = 17.9 3.6 Hz, 1H), 3.83 (dd, *J* = 8.4 3.3 Hz, 1H), 6.83 (d, *J* = 7.5 Hz, 1H), 6.97 (dt, *J* = 7.7 1.2 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.50-7.63 (m, 2H), 7.68 (tt, *J* = 7.5 1.2 Hz, 1H), 7.86-7.93 (m, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.3, 29.3, 33.1, 37.5, 41.6, 108.0, 122.5, 123.8, 127.1, 127.3, 128.2, 129.0, 129.4, 132.6, 133.9, 138.7, 144.1, 170.6, 176.9; *m/z* (EI) 358 $[M]^{+\cdot}$, 187, 159, 130, 117, 77; HRMS (EI) calcd for $C_{18}H_{18}N_2O_4S$ $[M]^{+\cdot}$ 358.0987, found 358.0999.



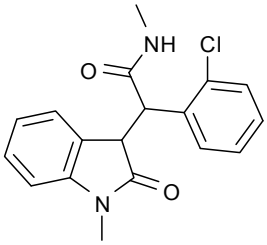
1,5-dimethyl-3-phenyl-3,3a,8,9-tetrahydro-1*H*-pyrrolo[3,2-*c*] indole-2,4(5*H*,7*H*)-dione 7a. ν_{max}(neat)/ cm^{-1} 3054, 2977, 2357, 2326 1713, 1685, 1416, 1261 ; δ_H (300 MHz, $CDCl_3$, Me_4Si) 1.88 (dd, *J* = 13.2 4.8 Hz, 1H), 1.93-1.97 (m, 2H), 2.25 (dd, *J* = 9.6 3.6 Hz, 1H), 2.34 (dt, *J* = 8.7 4.2 Hz, 1H), 2.40-2.50 (m, 1H), 2.87 (s, 3H), 3.01 (s, 3H), 3.05 (d, *J* = 8.4 Hz, 1H), 4.20 (d, *J* = 8.4 Hz, 1H), 5.24 (t, *J* = 3.9 Hz, 1H), 7.23 (dd, *J* = 8.1 1.8 Hz, 2H), 7.28-7.30 (m, 1H), 7.33 (dd, *J* = 8.1 1.8 Hz, 2H) ; δ_C(75 MHz, $CDCl_3$, Me_4Si) 18.4, 22.1, 26.2, 29.2, 31.6, 48.1, 52.5, 61.4, 102.7, 127.3, 127.9, 129.9, 134.1, 137.2, 170.3, 172.5; *m/z* (EI) 296 $[M]^{+\cdot}$, 267, 239, 211, 150; HRMS (EI) calcd for $C_{18}H_{20}N_2O_2$ $[M]^{+\cdot}$ 296.1525, found 296.1529.

Compound **5b** was prepared according to the typical procedure for domino radical cyclisations from N^1-(2-iodophenyl)-N^1,N^4-dimethyl-N^4-(*o*-tolylsulfonyl)fumaramide **4b** (200 mg, 0.4 mmol), TTMSS (154 µL, 0.5 mmol), ACCN (60 mg, 0.24 mmol) in 3 portions at 1h interval, in decane (16 mL) at reflux over 4h. The crude product was purified by column chromatography (gradient elution CH_2Cl_2 / MeOH : 99 / 1 and 98 / 2) to give *N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-*o*-tolylacetamide **5b** (71 mg, 62%) (the diastereomers were partially separable by chromatography) as a white oil.



***N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-*o*-tolylacetamide 5b.** Diastereoisomeric ratio 70/30 determined by NMR. ν_{max}(neat)/ cm^{-1} 3048, 2916, 2846, 1701, 1661, 1608, 1546, 1511, 1489, 1467, 1414, 1375, 1348, 1260, 1155, 1124; *m/z* (EI) 308 $[M]^{+\cdot}$, 250, 161, 105; HRMS (EI) calcd for $C_{19}H_{20}N_2O_2$ $[M]^{+\cdot}$ 308.1525, found 308.1508. **Major isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.29 (s, 3H), 2.82 (d, *J* = 4.8 Hz, 3H), 3.02 (s, 3H), 4.48 (d, *J* = 6.3 Hz, 1H), 4.54 (d, *J* = 6.3 Hz, 1H), 5.47 (br s, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.89-6.98 (m, 4H), 7.10-7.13 (m, 2H), 7.25 (dt, *J* = 6.9 1.2 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 20.3, 26.1, 26.9, 47.7, 48.4, 108.7, 122.4, 125.4, 126.2, 127.1, 127.9, 128.1, 128.3, 130.9, 134.4, 137.7, 144.6, 172.3, 176.4; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.37 (s, 3H), 2.73 (d, *J* = 4.8 Hz, 3H), 3.20 (s, 3H), 3.99 (d, *J* = 5.1 Hz, 1H), 4.57 (d, *J* = 5.1 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.89-6.98 (m, 2H), 7.17-7.18 (m, 3H), 7.22 (dt, *J* = 6.9 1.2 Hz, 1H), 7.33 (dd, *J* = 6.9 2.1 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 20.0, 26.4, 26.6, 47.1, 49.8, 108.1, 122.1, 122.4, 124.4, 126.4, 128.6, 128.6, 131.1, 135.1, 137.0, 143.8, 171.8, 176.7.

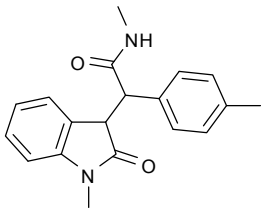
Compound **5c** was prepared according to the typical procedure for domino radical cyclisations from N^1-((2-chlorophenyl)sulfonyl)-N^4-(2-iodophenyl)-N^1,N^4-dimethylfumaramide **4c** (236 mg, 0.45 mmol), TTMSS (177 µL, 0.55 mmol), ACCN (66 mg, 0.27 mmol) in 3 portions at 1h interval, in decane (20 mL) at reflux over 6h. The crude product was purified by flash column chromatography (gradient elution CH_2Cl_2 / AcOEt : 95 / 5 and 80 / 20) to give 2-(2-chlorophenyl)-*N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)acetamide **5c** (81 mg, 59%) (the diastereomers were partially separable by chromatography) as a beige solid after crystallisation in diethyl ether.



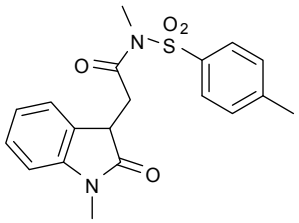
2-(2-chlorophenyl)-*N*-methyl-2-(1-methyl-2-oxoindolin-3-yl) acetamide.5c. Diastereoisomeric ratio 55/45 determined by NMR. mp 155 °C ν_{max}(KBr)/ cm^{-1} 3323, 3065, 2930, 2367, 1703, 1662, 1610, 1545, 1468, 1375, 1347, 1238, 1127, 1093, 1037, 758 *m/z* (EI) 328 $[M]^{+\cdot}$, 291, 271, 234; HRMS (EI) calcd for $C_{18}H_{17}N_2O_2Cl$ $[M]^{+\cdot}$ 328.0979, found 328.0991. **Major isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.83 (d, *J* = 4.8 Hz, 3H), 3.16 (s, 3H), 4.36 (d, *J* = 7.4 Hz, 1H), 4.57 (d, *J* = 7.4 Hz, 1H), 5.50 (br s, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.79 (t, *J* = 7.2 Hz, 1H), 6.87 (t, *J* = 7.5 Hz,

1H), 6.94 (d, *J* = 4.5 Hz, 1H), 7.22-7.30 (m, 2H), 7.33-7.41 (m, 1H), 7.55-7.61 (m, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.2, 26.6, 46.3, 49.1, 108.0, 122.1, 124.6, 126.9, 127.1, 128.2, 129.0, 129.6, 130.0, 134.3, 134.6, 144.3, 170.7, 175.7; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.79 (d, *J* = 4.8 Hz, 3H), 3.18 (s, 3H), 4.21 (d, *J* = 7.5 Hz, 1H), 4.61 (d, *J* = 7.5 Hz, 1H), 5.90 (br s, 1H), 6.80 (d, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 4.5 Hz, 1H), 7.22-7.31 (m, 4H), 7.36-7.41 (m, 1H), 7.55-7.61 (m, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.2, 26.8, 47.0, 49.7, 108.0, 122.2, 124.5, 126.6, 127.2, 128.2, 129.1, 129.7, 130.0, 134.2, 134.4, 144.2, 171.0, 176.0.

Compounds **5d** and **6d** were prepared according to the typical procedure for domino radical cyclisations from N^1-(2-iodophenyl)-*N*,*N*-dimethyl-N^4-(4-methylphenylsulfonyl)fumaramide **4d** (250 mg, 0.5 mmol), TTMSS (193 µL, 0.6 mmol), ACCN (75 mg, 0.2 mmol) in 2 portions at 1h30 interval in decane (20 mL) at reflux over 4h. The crude product was purified by column chromatography (gradient elution CH_2Cl_2 / MeOH : 99.5 / 0.5 and 98 / 2) to give *N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-*p*-tolylacetamide **5d** (99 mg, 64%) (the diastereomers were partially separable by chromatography) and *N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-*N*-tosylacetamide **6d** (25 mg, 13%) as a white powder and a yellow oil, respectively.

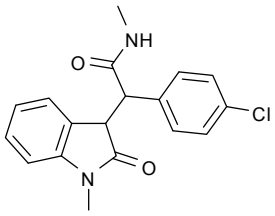


***N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-*p*-tolylacetamide 5d.** Diastereoisomeric ratio 62/38 determined by NMR. Mp 149-151 °C, ν_{max}(KBr)/ cm^{-1} 3048, 2916, 2846, 1701, 1661, 1608, 1546, 1511, 1489, 1414, 1375, 1260, 1124; *m/z* (EI) 308 $[M]^{+\cdot}$, 250, 161, 105; HRMS (EI) calcd for $C_{19}H_{20}N_2O_2$ $[M]^{+\cdot}$ 308.1508, found 308.1525. **Major isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.23 (s, 3H), 2.84 (d, *J* = 4.8 Hz, 3H), 2.98 (s, 3H), 4.24 (d, *J* = 4.7 Hz, 1H), 4.49 (d, *J* = 4.7 Hz, 1H), 5.46 (bs, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.99 (t, *J* = 7.8 Hz, 6-H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.0, 25.9, 26.7, 48.3, 53.4, 107.7, 122.2, 126.1, 126.7, 128.0, 129.0, 129.4, 132.0, 137.6, 144.5, 172.4, 176.4; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.24 (s, 3H), 2.89 (d, *J* = 4.8 Hz, 3H), 3.07 (s, 3H), 4.13 (d, *J* = 4.4 Hz, 1H), 4.17 (d, *J* = 4.4 Hz, 1H), 6.70 (d, *J* = 7.5 Hz, 1H), 6.94-7.02 (m, 1H), 6.98 (d, *J* = 9.3 Hz, 2H), 7.01 (d, *J* = 9.3 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.47 (bd, *J* = 3.9 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.0, 26.1, 26.6, 48.3, 54.3, 108.1, 122.6, 123.9, 126.7, 128.2, 128.5, 129.1, 132.4, 137.3, 144.0, 172.0, 176.5.



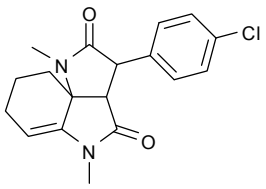
***N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)-*N*-tosylacetamide 6d.** ν_{max}(neat)/ cm^{-1} 3048, 2916, 1705, 1608, 1489, 1467, 1419, 1401, 1348, 1247, 1159; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.46 (s, 3H), 3.18 (dd, *J* = 18.0 8.5 Hz, 1H), 3.22 (s, 3H), 3.25 (s, 3H), 3.56 (dd, *J* = 18.0 3.4 Hz, 1H), 3.81 (dd, *J* = 8.5 3.4 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.7, 26.3, 33.1, 37.6, 41.7, 108.0, 122.4, 123.9, 127.4, 128.2, 128.3, 130.0, 135.8, 144.3, 145.1, 170.7, 177.0; *m/z* (EI) 372 $[M]^{+\cdot}$, 316, 159; HRMS (EI) calcd for $C_{19}H_{20}N_2O_4S$ $[M]^{+\cdot}$ 372.1149, found 372.1144.

Compounds **5e** and **7e** were prepared according to the typical procedure for domino radical cyclisations from N^1-(4-chlorophenylsulfonyl)-N^4-(2-iodophenyl)-N^1,N^4-dimethylfumaramide **4e** (148 mg, 0.285 mmol), TTMSS (106 µL, 0.342 mmol), ACCN (42 mg, 0.171 mmol) in 3 portions at 1h interval, in decane (12 mL) at reflux over 3h. The crude product was purified by column chromatography (CH_2Cl_2 / MeOH : 99.25 / 0.75)to give 2-(4-chlorophenyl)-*N*-methyl-2-(1'-methyl-2'-oxoindolin-3-yl)acetamide **5e** as a yellow oil (64 mg, 68%) (the diastereomers were partially separable by chromatography) and 3-(4'-chlorophenyl)-1,5-dimethyl-3,3a,8,9-tetrahydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione **7e1** (15 mg, 7 %) as white crystals after crystallisation in Et_2O and CH_2Cl_2.



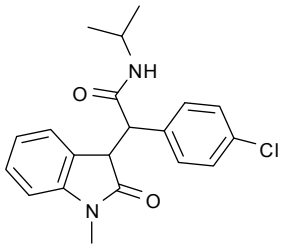
2-(4-chlorophenyl)-*N*-methyl-2-(1'-methyl-2'-oxoindolin-3-yl) acetamide 5e. Diastereoisomeric ratio 60/40 determined by NMR. ν_{max}(neat)/ cm^{-1} 3316, 3044, 2919, 1696, 1652, 1608, 1542; *m/z* (EI) 328 $[M]^{+\cdot}$, 270, 219, 177, 116; HRMS (EI) calcd for $C_{18}H_{17}N_2O_2Cl$ $[M]^{+\cdot}$ 328.0979, found 328.0914. **Major isomer** δ_H(300 MHz,, $CDCl_3$, Me_4Si) 2.91 (d, *J* = 4.7 Hz, 3H), 3.06 (s, 3H), 4.14 (d, J_{AB} = 17.7 Hz, 1H), 4.20 (d, J_{AB} = 17.7 Hz, 1H), 6.72 (d, *J* = 7.7 Hz, 1H), 7.02 (d, *J* = 8.5 Hz, 2H), 7.08 (t, *J* = 7.7 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.97 (d, *J* = 4.7 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.2, 26.7, 48.2, 54.4, 108.4, 123.0, 123.9, 126.6, 128.5, 128.9, 129.9, 133.6, 133.8, 143.8, 171.5, 176.4; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.86 (d, *J* = 4.8 Hz, 3H), 2.99 (s, 3H), 4.25 (d, *J* = 4.6 Hz, 1H), 4.44 (d, *J* = 4.6 Hz,

1H), 5.50 (br d, *J* = 4.8 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 2H), 7.00 (t, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 8.3 Hz, 1H), 7.23 (t, *J* = 7.7 Hz, 1H), 7.36 (d, *J* = 7.7 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.0, 26.8, 48.2, 53.1, 107.9, 122.4, 126.0, 126.2, 128.3, 128.5, 130.9, 133.6, 133.9, 144.4, 171.7, 176.1.



3-(4'-chlorophenyl)-1,5-dimethyl-3,3a,8,9-tetrahydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione 7e1. Mp 210-212°C ; ν_{max}(KBr)/ cm^{-1} 3044, 2912, 2846, 1722, 1681, 1384; δ_H (300 MHz, $CDCl_3$, Me_4Si) 1.88 (dd, *J* = 11.2 5.7 Hz, 1H), 1.91-2.00 (m, 2H), 2.24 (dd, *J* = 11.2 3.5 Hz, 1H), 2.34 (ddt, *J* = 8.6 8.4 3.7 Hz, 1H), 2.46 (tdd, *J* = 8.6 5.2 3.7 Hz, 1H), 2.88 (s, 3H), 3.00 (s, 3H), 3.04 (d, *J* = 8.4 Hz, 1H), 4.17 (d, *J* = 8.4 Hz, 1H), 5.26 (t, *J* = 3.7 Hz, 1H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H) ; δ_C(75 MHz, $CDCl_3$, Me_4Si) 18.4, 22.1, 26.2, 29.3, 31.5, 47.4, 52.3, 61.4, 103.1, 128.1, 131.3, 132.6, 133.2, 137.0, 170.2, 172.1; *m/z* (EI) 330 [$M^{+\bullet}$], 273, 220, 176; HRMS (CI) calcd for $C_{18}H_{20}N_2O_2Cl$ $[M+H]^+$ 331.1213, found 331.1213.

Compound **5f** was prepared according to the typical procedure for domino radical cyclisations from N^1-((4-chlorophenyl)sulfonyl)-N^4-(2-iodophenyl)-N^1-isopropyl-N^4-methylfumaramide **4f** (200 mg, 0.37 mmol), TTMSS (141 µL, 0.44 mmol), ACCN (54 mg, 0.22 mmol) in 3 portions at 1h interval, in decane (18 mL) at reflux over 7h. The crude product was purified by flash column chromatography (gradient elution CH_2Cl_2 / AcOEt : 98 / 2 and 80 / 20) to give 2-(4-chlorophenyl)-*N*-isopropyl-2-(1-methyl-2-oxoindolin-3-yl)acetamide **5f** (71 mg, 54%, conversion 88 %) (the diastereomers were partially separable by chromatography) as a white solid after crystallisation in diethyl ether.

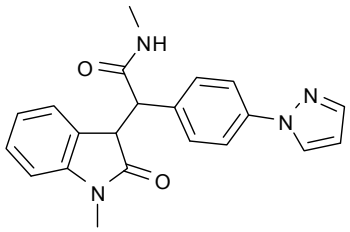


2-(4-chlorophenyl)-*N*-isopropyl-2-(1-methyl-2-oxoindolin-3-yl) acetamide 5f. Diastereoisomeric ratio 55/45 determined by NMR. mp 194 °C ν_{max}(KBr)/ cm^{-1} 3266, 3075, 2972, 2925, 2367, 1713, 1636, 1610, 1556, 1486, 1465, 1370, 1339, 1256, 1124, 1086, 1013, 752 *m/z* (EI) 356 [$M]^{+\cdot}$, 297, 270, 242, 234, 207, 146, 125, 118, 91; HRMS (EI) calcd for $C_{20}H_{21}N_2O_2Cl$ $[M]^{+\cdot}$ 356.1292, found 356.1301.

Major isomer δ_H(300 MHz, $CDCl_3$, Me_4Si) 1.21 (d, *J* = 6.3 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 3.06 (s, 3H), 4.15 (d, *J* = 6.5 Hz, 1H), 4.20 (d, *J* = 6.5 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H),

7.02-7.16 (m, 2H), 7.04 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 7.24 (t, J = 7.8 Hz, 1H), 7.86 (br d, J = 7.5 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 22.5, 26.0, 42.0, 48.4, 53.1, 107.9, 122.3, 126.0, 126.4, 128.2, 128.4, 130.8, 133.6, 133.8, 144.4, 170.1, 176.2; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 1.10 (d, J = 6.3 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H), 2.99 (s, 3H), 4.24 (d, J = 4.4 Hz, 1H), 4.42 (d, J = 4.4 Hz, 1H), 5.19 (br d, J = 7.5 Hz, 1H), 6.63 (d, J = 7.5 Hz, 1H), 6.96 (d, J = 8.4 Hz, 2H), 7.00 (t, J = 7.5 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 7.21 (t, J = 7.5 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 22.5, 26.2, 41.8, 48.2, 54.5, 108.3, 122.9, 126.4, 126.7, 128.0, 128.4, 128.5, 129.9, 130.8, 133.5, 134.0, 143.8, 169.9, 176.3.

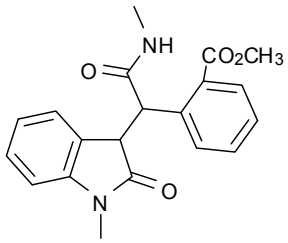
Compound **5g** was prepared according to the typical procedure for domino radical cyclisations from N^1-(4-(1*H*-pyrazol-1-yl)phenylsulfonyl)-N^4-(2-iodophenyl)-N^1,N^4-dimethyl fumaramide **4g** (130 mg, 0.24 mmol), TTMSS (93 µL, 0.29 mmol), ACCN (36 mg, 0.14 mmol) in 3 portions at 1h interval, in decane (10 mL) at reflux over 4h. The crude product was purified by flash column chromatography (gradient elution CH_2Cl_2 / AcOEt : 99 / 1 and 70 / 30) to give 2-(4-(1*H*-pyrazol-1-yl)phenyl)-*N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)acetamide **5g** (42 mg, 51%, conversion 89 %) (the diastereomers were partially separable by chromatography) as a yellow oil.



2-(4-(1*H*-pyrazol-1-yl)phenyl)-*N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)acetamide 5g. Diastereoisomeric ratio 75/25 determined by NMR. ν_{max}(neat)/ cm^{-1} 3437, 3323, 3106, 3013, 2935, 1706, 1667, 1610, 1520, 1489, 1465, 1390, 1375, 1349, 1191, 1122, 1091; *m/z* (ESI) 383 $[M+Na]^{+\cdot}$, 361; HRMS (ESI) for $C_{21}H_{20}N_4O_2Na$ $[M+Na]^{+\cdot}$ 383.1484, found 383.1487. **Major isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.94 (d, J = 4.6 Hz, 3H), 3.06 (s, 3H), 4.21 (d, J = 3.7 Hz, 1H), 4.32 (d, J = 4.6 Hz, 1H), 6.43-6.44 (m, 1H), 6.70 (d, J = 7.7 Hz, 1H), 7.08 (t, J = 7.7 Hz, 1H), 7.09 (d, J = 8.6 Hz, 2H), 7.25 (t, J = 7.7 Hz, 1H), 7.44 (d, J = 8.6 Hz, 2H), 7.48 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 1.8 Hz, 1H), 7.84 (d, J = 2.4 Hz, 1H), 8.15 (br s, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.0, 26.7, 48.3, 54.3, 107.7, 108.3, 118.8, 123.9, 126.1, 126.6, 128.4, 130.6, 133.3, 139.6, 141.2, 144.4, 171.9, 176.2; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.87 (d, J = 4.7 Hz, 3H), 2.99 (s, 3H), 4.32 (d, J = 4.5 Hz, 1H), 4.49 (d, J = 4.5 Hz, 1H), 5.53 (br s, 1H), 6.43-6.44 (m, 1H), 6.64 (d, J = 7.8 Hz, 1H), 7.01 (t, J = 7.5 Hz, 1H),

7.09 (d, *J* = 8.6 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 1.8 Hz, 1H), 7.84 (d, *J* = 2.4 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.2, 26.6, 48.1, 54.3, 107.7, 107.7, 118.9, 122.9, 126.1, 126.6, 126.7, 128.2, 130.6, 133.6, 139.4, 141.1, 143.8, 171.7, 176.3.

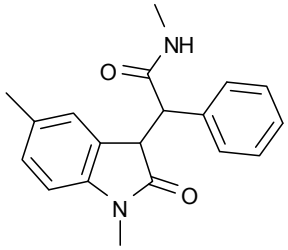
Compound **5h** was prepared according to the general procedure in 75% yield from (*E*)-methyl -2-(*N*-(4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoyl)-*N*-methylsulfamoyl) benzoate **4h** (136 mg, 0.25 mmol), TTMSS (96 µL, 0.30 mmol), ACCN (26 mg, 0.10 mmol) in 2 portions at 1h interval, in decane (10 mL) at reflux over 3h. The crude product was purified by column chromatography (gradient elution CH_2Cl_2 / MeOH : 99 / 1 and 98 / 2) to give **5h** as a white powder (66 mg, 75%) (the diastereomers were partially separable by chromatography).



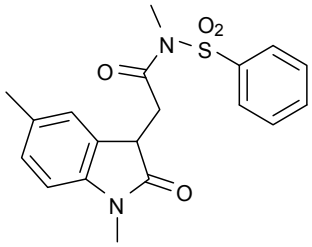
methyl 2-[1-(1-methyl-2-oxoindolin-3-yl)-2-(methylamino)-2-oxoethyl]benzoate 5h. Diastereoisomeric ratio 70/30 determined by NMR. mp 78-80°C. ν_{max}(neat)/ cm^{-1} 3338, 3044, 2948, 2912, 2846, 1711, 1670, 1608; *m/z* (EI) 352 $[M]^{+\cdot}$, 320, 262, 234; HRMS (EI) calcd for $C_{20}H_{20}N_2O_4$ $[M]^{+\cdot}$ 352.1423, found 352.1420. **Major isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.83 (d, *J* = 4.5 Hz, 3H), 3.12 (s, 3H), 3.84 (s, 3H), 4.47 (d, *J* = 7.9 Hz, 1H), 4.91 (d, *J* = 7.9 Hz, 1H), 6.43 (bs, 1H), 6.53 (d, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si)) 26.0, 26.5, 46.1, 47.7, 52.4, 107.7, 122.0, 125.1, 126.7, 127.1, 128.0, 129.3, 130.0, 130.3, 132.0, 138.1, 144.4, 169.0, 171.7, 175.6; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.80 (d, *J* = 4.8 Hz, 3H), 3.02 (s, 3H), 3.85 (s, 3H), 4.47 (d, *J* = 10.7 Hz, 1H), 4.73 (d, *J* = 10.7 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.90 (br d, *J* = 5.2 Hz, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 7.26-7.39 (m, 4H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.0, 26.5, 47.2, 48.4, 52.5, 107.7, 122.3, 125.2, 127.4, 127.5, 128.2, 129.3, 129.7, 130.5, 132.3, 138.7, 144.0, 168.4, 171.8, 175.6.

Compound **5i** was prepared according to the typical procedure for domino radical cyclisations from N^1-(2-iodo-4-methylphenyl)-N^1,N^4-dimethyl-N^4-(phenylsulfonyl)fumaramide **4i** (350 mg, 0.70 mmol), TTMSS (271 µL, 0.84 mmol), ACCN (108 mg, 0.42 mmol) in 3 portions at

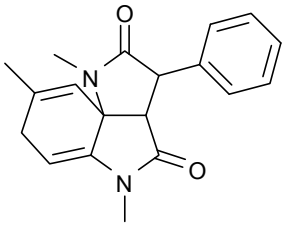
1h interval, in decane (28 mL) at reflux over 6h. The crude product was purified by flash column chromatography (gradient elution CH_2Cl_2 / AcOEt : 98 / 2 and 50/ 50) to give 2-(1,5-dimethyl-2-oxoindolin-3-yl)-*N*-methyl-2-phenylacetamide **5i** (76 mg, 35 %, conversion 80 %) (the diastereomers were separable by chromatography) as a white solid after crystallisation in diethyl ether, 2-(1,5-dimethyl-2-oxoindolin-3-yl)-*N*-methyl-*N*-(phenylsulfonyl)acetamide **6i** (30 mg, 15 %) as a white oil and 1,5,8-trimethyl-3-phenyl-3,3a-dihydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione **7i** (14 mg, 10 %) as a white solid.



2-(1,5-dimethyl-2-oxoindolin-3-yl)-*N*-methyl-2-phenylacetamide 5i. Diastereoisomeric ratio 65/35 determined by NMR. ν_{max}(KBr)/ cm^{-1} 3390, 3023, 2920, 2362, 1698, 1672, 1620, 1527, 1499, 1349, 1264, 1153, 1093, 804, 696 *m/z* (EI) 308 $[M]^{+\cdot}$, 277, 250, 222, 207, 160; HRMS (EI) calcd for $C_{19}H_{20}N_2O_2$ $[M]^{+\cdot}$ 308.1525, found 308.1534. **Major isomer** mp 184 °C; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.29 (s, 3H), 2.85 (d, *J* = 4.8 Hz, 3H), 2.94 (s, 3H), 4.25 (d, *J* = 4.8 Hz, 1H), 4.43 (d, *J* = 4.8 Hz, 1H), 5.56 (br d, *J* = 2.4 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 7.00 (d, *J* = 7.5 Hz,3H), 7.09-7.17 (m, 4H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.1, 25.9, 26.7, 48.3, 53.7, 107.4, 126.5, 126.9, 127.8, 128.3, 128.5, 129.5, 131.7, 135.2, 142.1, 172.2, 176.2; **Minor isomer** mp 195 °C; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.32 (s, 3H), 2.90 (d, *J* = 4.5 Hz, 3H), 3.02 (s, 3H), 4.12 (d, *J* = 3.6 Hz, 1H), 4.21 (d, *J* = 3.6 Hz, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 7.02 (s, 1H), 7.04-7.10 (m, 3H), 7.16-7.19 (m, 3H), 7.81 (br s, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.2, 26.2, 26.6, 48.3, 54.8, 107.9, 126.9, 127.0, 127.6, 128.3, 128.6, 129.6, 132.3, 135.4, 141.5, 172.2, 176.4.

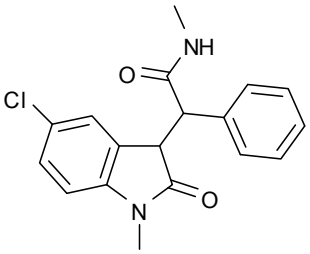


2-(1,5-dimethyl-2-oxoindolin-3-yl)-*N*-methyl-*N*-(phenylsulfonyl) acetamide 6i. ν_{max}(KBr)/ cm^{-1} 3044, 2987, 2357, 2331, 1734, 1708, 1367, 1261, 1166, 1042, 892, 719; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.27 (s, 3H), 3.20 (dd, *J* = 25.5 8.7 Hz, 1H), 3.20 (s, 3H), 3.28 (s, 3H), 3.53 (dd, *J* = 18.3 3.6 Hz, 1H), 3.79 (dd, *J* = 8.1 3.6 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.90 (s, 1H), 7.63 (dd, *J* = 8.1 0.6 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.1, 26.4, 31.2, 37.7, 41.7, 107.7, 124.8, 127.4, 128.3, 128.4, 129.4, 132.0, 134.0, 138.7, 141.9, 170.7, 176.8; *m/z* (EI) 372 $[M]^{+\cdot}$, 230, 201, 173, 144, 141, 110, 77; HRMS (EI) calcd for $C_{19}H_{20}N_2O_4S$ $[M]^{+\cdot}$ 372.1144, found 372.1136.



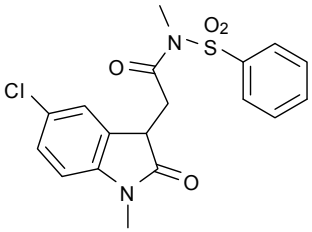
1,5,8-trimethyl-3-phenyl-3,3a-dihydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione 7i. Mp 123 °C ; ν_{max}(KBr)/ cm^{-1} 3059, 3028, 2920, 2853, 2367, 1716, 1690, 1662, 1613, 1427, 1380, 1323, 1150, 1114, 1062, 812, 721; δ_H (300 MHz, $CDCl_3$, Me_4Si) 1.87 (s, 3H), 2.35 (d, *J* = 17.4 Hz, 1H), 2.66 (d, *J* = 17.4 Hz, 1H), 2.80 (s, 3H), 2.97 (s, 1H), 3.05 (s, 3H), 4.17 (s, 1H), 5.56 (d, *J* = 6.0 Hz, 1H), 5.84-5.87 (m, 1H), 7.29-7.40 (m, 5H) ; δ_C(75 MHz, $CDCl_3$, Me_4Si) 22.6, 26.4, 26.8, 29.7, 31.5, 40.0, 49.6, 54.4, 100.3, 118.3, 127.3, 127.4, 128.9, 130.1, 136.0, 138.1, 171.8, 173.8; *m/z* (EI) 308 $[M]^{+\bullet}$, 251, 160; HRMS (EI) calcd for $C_{19}H_{20}N_2O_2$ $[M]^{+\bullet}$ 308.1525, found 308.1536.

Compound **5j** was prepared according to the typical procedure for domino radical cyclisations from N^1-(4-chloro-2-iodophenyl)-N^1,N^4-dimethyl-N^4-(phenylsulfonyl)fumaramide **4j** (180 mg, 0.35 mmol), TTMSS (137 µL, 0.44 mmol), ACCN (57 mg, 0.22 mmol) in 3 portions at 1h interval, in decane (15 mL) at reflux over 5h. The crude product was purified by flash column chromatography (gradient elution CH_2Cl_2 / AcOEt : 95 / 5 and 80 / 20) to give 2-(5-chloro-1-methyl-2-oxoindolin-3-yl)-*N*-methyl-2-phenylacetamide **5j** (61 mg, 55%) (the diastereomers were partially separable by chromatography) as a yellow solid after crystallisation in diethyl ether, and 2-(5-chloro-1-methyl-2-oxoindolin-3-yl)-*N*-methyl-*N*-(phenylsulfonyl)acetamide **6j** (11 mg, 8%) as a white solid after crystallisation in diethyl ether, and 8-chloro-1,5-dimethyl-3-phenyl-3,3a-dihydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione **7j** (6 mg, 5%) as a yellow solid after crystallisation in diethyl ether.

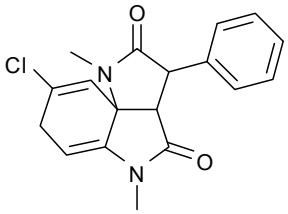


2-(5-chloro-1-methyl-2-oxoindolin-3-yl)-*N*-methyl-2-phenyl acetamide 5j. Diastereoisomeric ratio 70/30 determined by NMR. mp 190°C; ν_{max}(KBr)/ cm^{-1} 3276, 3085, 2930, 2362, 1700, 1636, 1607, 1486, 1359, 1349, 1266, 1106, 817, 706 *m/z* (EI) 328 $[M]^{+\cdot}$, 270, 242, 207; HRMS (EI) calcd for $C_{18}H_{17}N_2O_2Cl$ $[M]^{+\cdot}$ 328.0979, found 328.0985. **Major isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.86 (d, *J* = 4.8 Hz, 3H), 2.95 (s, 3H), 4.31 (d, *J* = 4.5 Hz, 1H), 4.46 (d, *J* = 4.5 Hz, 1H), 5.41 (br d, *J* = 3.3 Hz, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 6.97-7.01 (m, 1H), 6.98 (dd, *J* = 7.5 1.5 Hz, 1H), 7.11-7.22 (m, 4H), 7.44 (d, *J* = 2.1 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.0, 27.8, 48.4, 53.7, 108.5, 124.5, 126.7, 127.7, 128.0, 128.2, 128.4, 129.4, 134.7, 143.0, 171.9,

175.9; **Minor isomer** δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.84 (d, *J* = 4.5 Hz, 3H), 3.09 (s, 3H), 4.08 (d, *J* = 4.2 Hz, 1H), 4.26 (d, *J* = 4.5 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.91 (br s, 1H), 6.98 (dd, *J* = 6 1.8 Hz, 1H), 7.11-7.22 (m, 5H), 7.40 (d, *J* = 1.2 Hz, 1H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.3, 26.6, 48.4, 54.2, 108.9, 124.3, 126.7, 127.7, 128.0, 128.2, 128.7, 128.8, 134.7, 142.8, 171.9, 175.9.



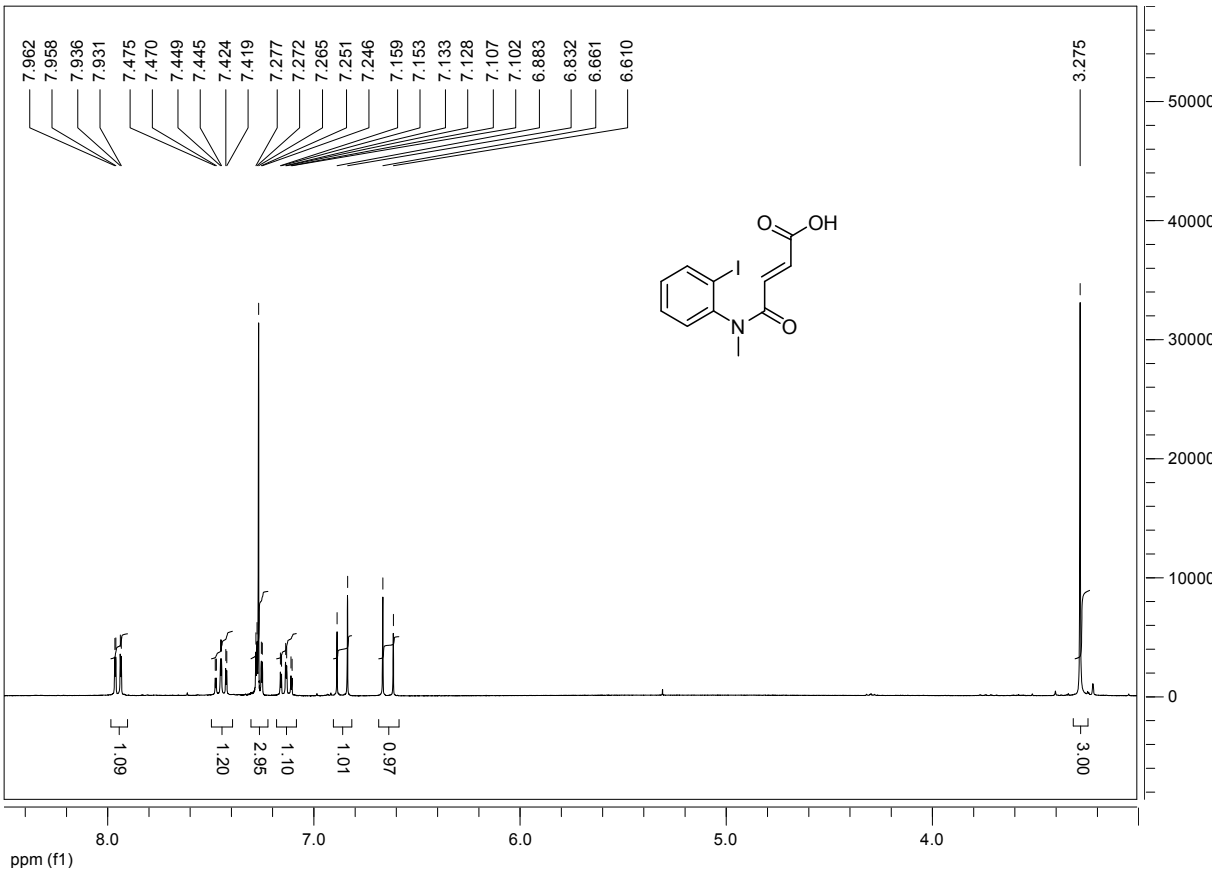
2-(5-chloro-1-methyl-2-oxoindolin-3-yl)-*N*-methyl-*N*-(phenyl sulfonyl)acetamide 6j. mp 82°C; ν_{max}(KBr)/ cm^{-1} 3059, 2935, 2362, 1718, 1695, 1659, 1486, 1390, 1359, 1207, 1166, 1099, 1086, 1024, 987, 925, 826, 731; δ_H(300 MHz, $CDCl_3$, Me_4Si) 3.21 (s, 3H), 3.24 (dd, *J* = 18.3 8.1 Hz, 1H), 3.27 (s, 3H), 3.57 (dd, *J* = 18.3 3.3 Hz, 1H), 3.78 (dd, *J* = 8.1 3.3 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 7.02 (d, *J* = 1.2 Hz, 1H), 7.24 (dd, *J* = 9.9 2.1 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.5, 33.2, 37.5, 41.8, 108.9, 124.3, 127.3, 127.8, 128.1, 129.6, 130.0, 134.2, 138.6, 142.9, 170.4, 176.4; *m/z* (EI) 392 $[M]^{+\cdot}$, 250, 221, 193, 171, 164, 141, 110, 77; HRMS (EI) calcd for $C_{18}H_{17}N_2O_4SCl$ $[M]^{+\cdot}$ 392.0598, found 392.0603.

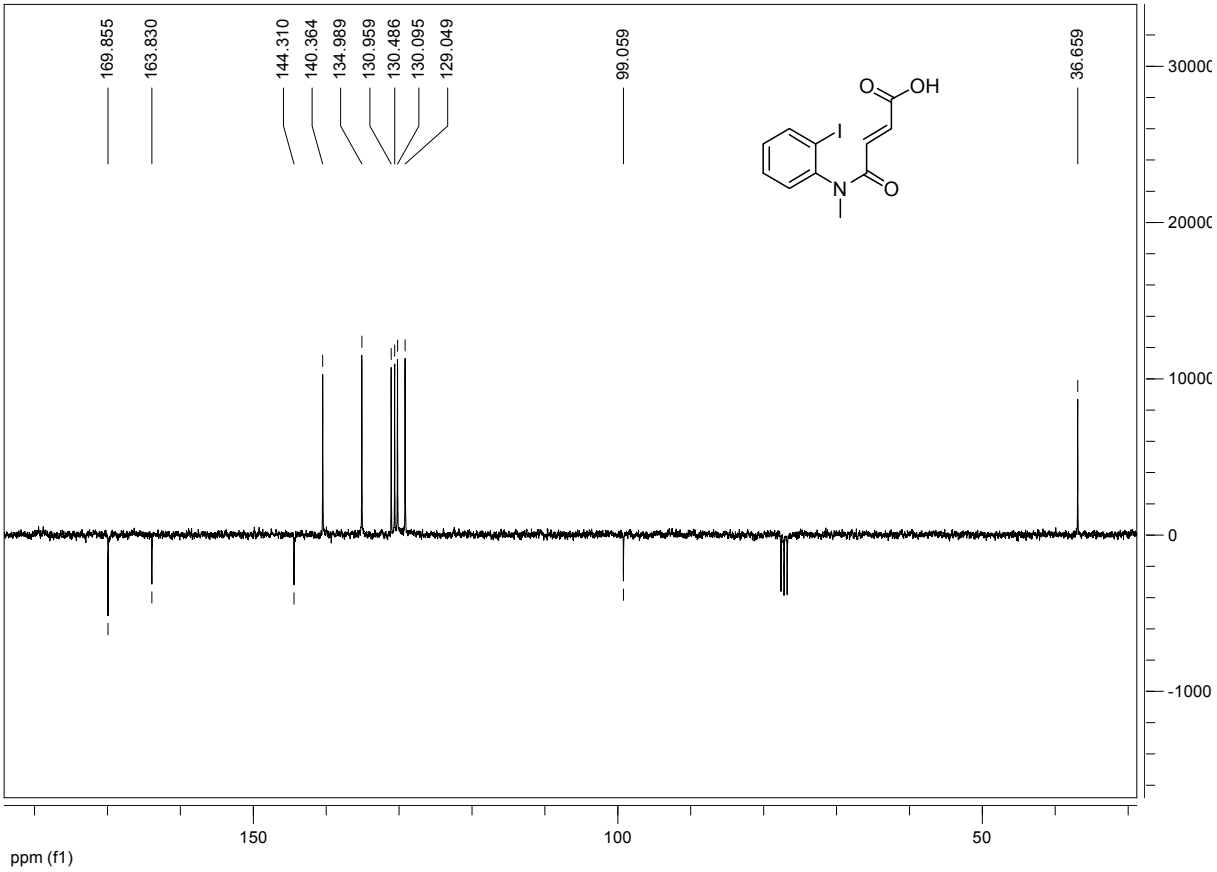


8-chloro-1,5-dimethyl-3-phenyl-3,3a-dihydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione 7j. Mp 100 °C ; ν_{max}(neat)/ cm^{-1} 3044, 2982, 2300, 1729, 1695, 1656, 1419, 1372, 1264, 1044, 889, 727; δ_H (300 MHz, $CDCl_3$, Me_4Si) 2.75 (d, *J* = 24 Hz, 1H), 2.94 (s, 3H), 2.94 (s, 3H), 3.13 (d, *J* = 24 Hz, 1H), 3.13 (d, *J* = 9.9 Hz, 1H), 4.22 (d, *J* = 9.6 Hz, 1H), 5.49 (d, *J* = 6.3 Hz, 1H), 6.25 (dd, *J* = 6.3, 3.0 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 2H), 7.30-7.35 (m, 1H), 7.34 (d, *J* = 7.5 Hz, 2H); δ_C(75 MHz, $CDCl_3$, Me_4Si) 26.6, 40.8, 48.5, 51.6, 60.9, 97.8, 121.2, 125.2, 127.6, 128.1, 129.8, 133.8, 136.9, 170.6, 171.2; *m/z* (EI) 328 $[M]^{+\bullet}$, 271, 236, 208, 182, 131, 103, 91, 77; HRMS (EI) calcd for $C_{18}H_{17}N_2O_2Cl$ $[M]^{+\bullet}$ 328.0979, found 328.0991.

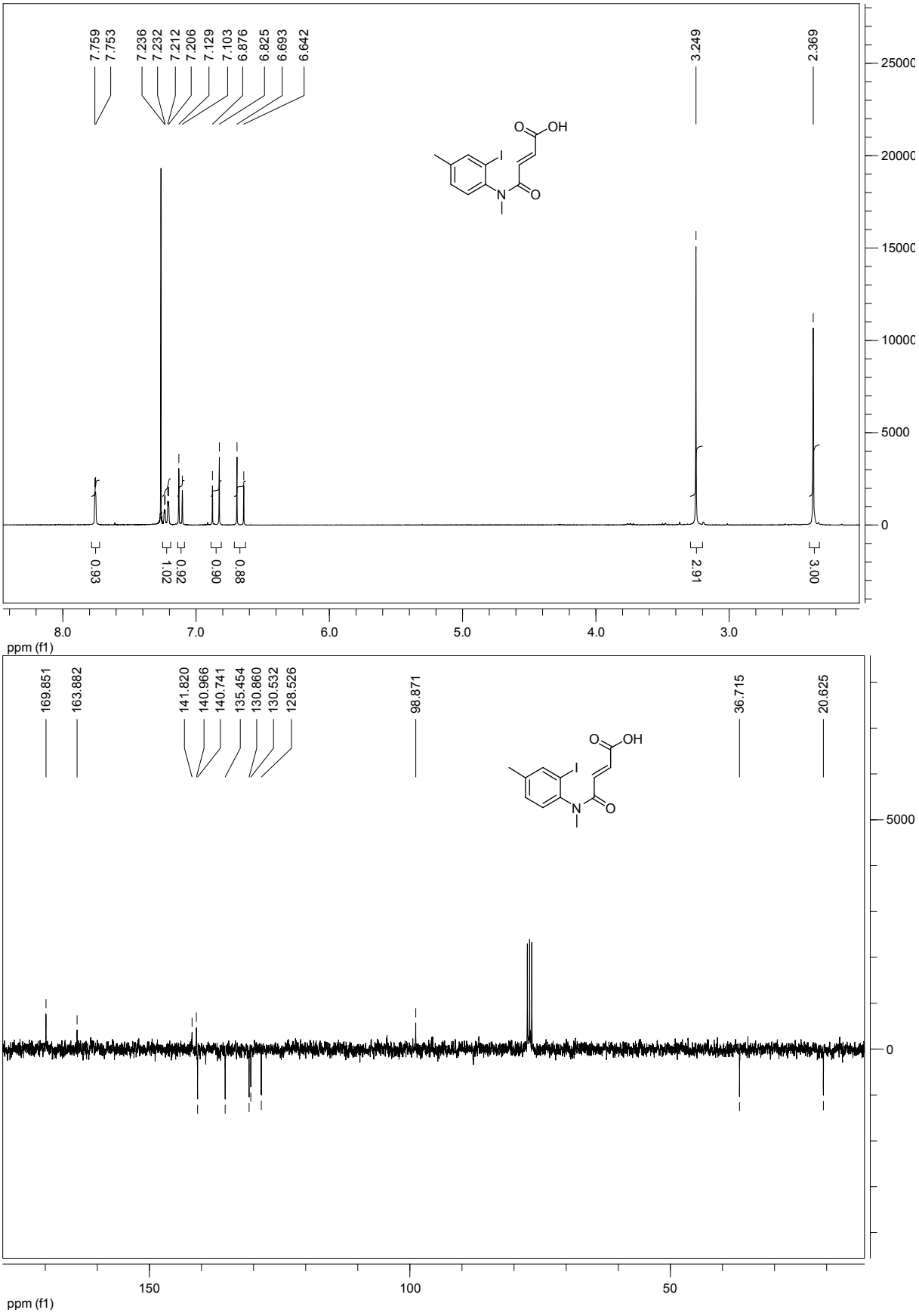
Copies of ^{1}H and ^{13}C NMR SPECTRA for Compounds 1 - 7

(*E*)-4-((2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid 1

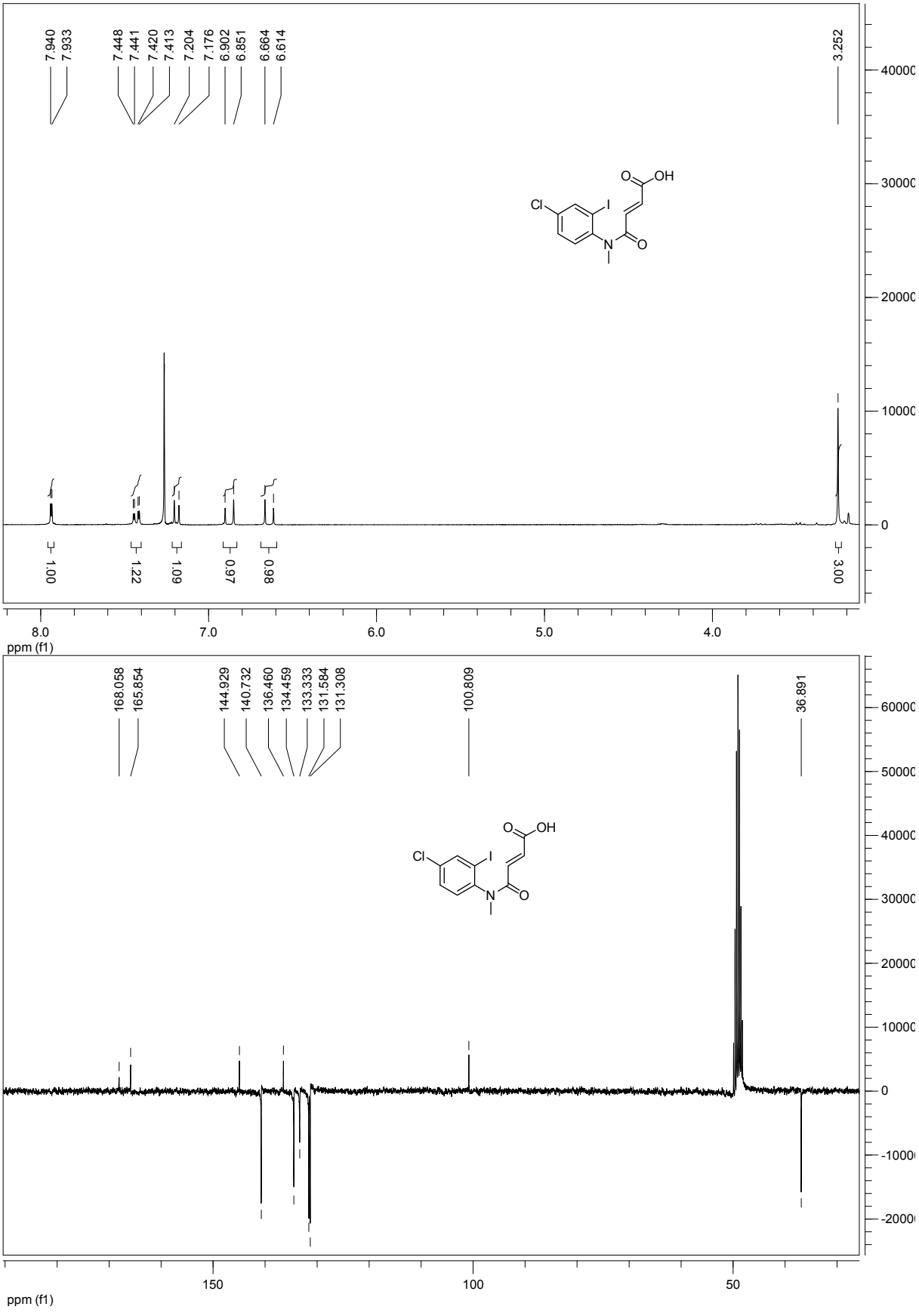




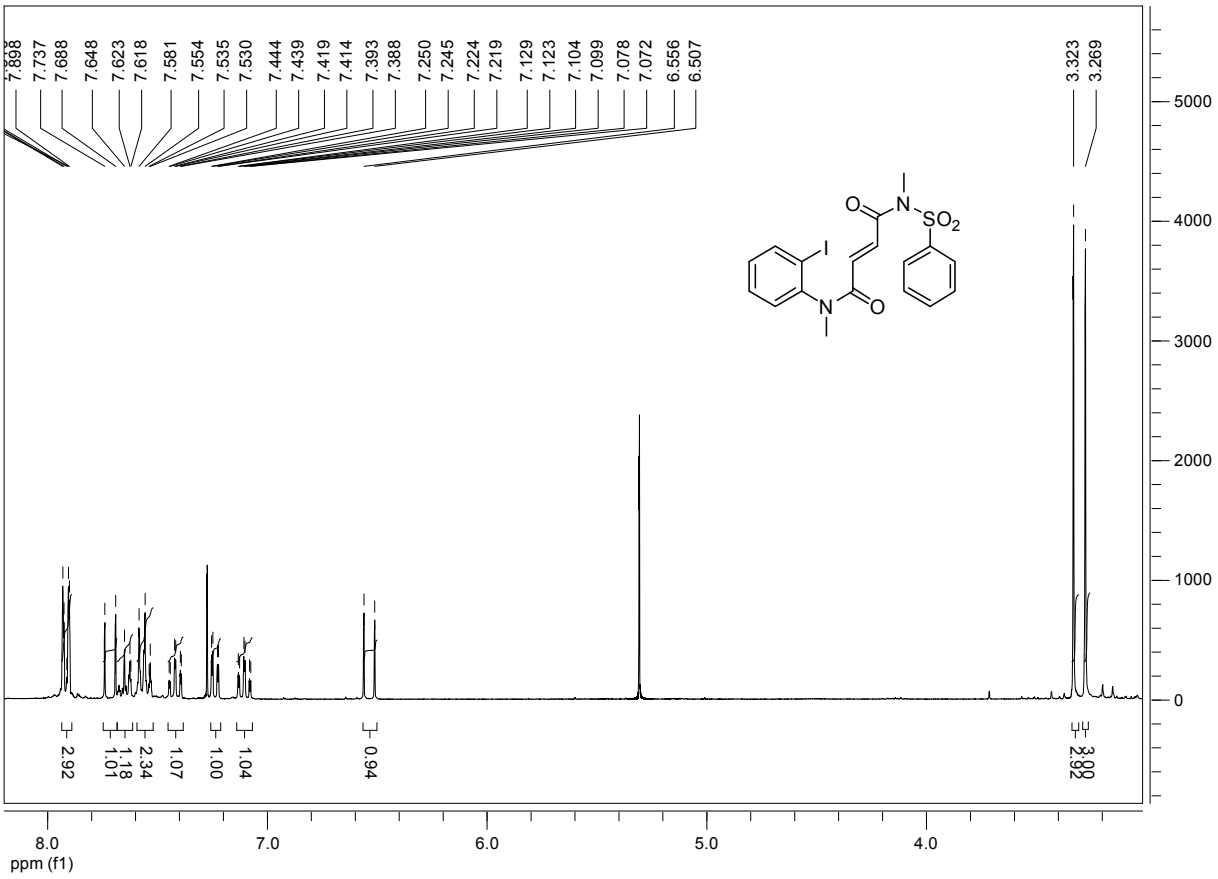
(*E*)-4-((2-iodo-4-methylphenyl)(methyl)amino)-4-oxobut-2-enoic acid 2

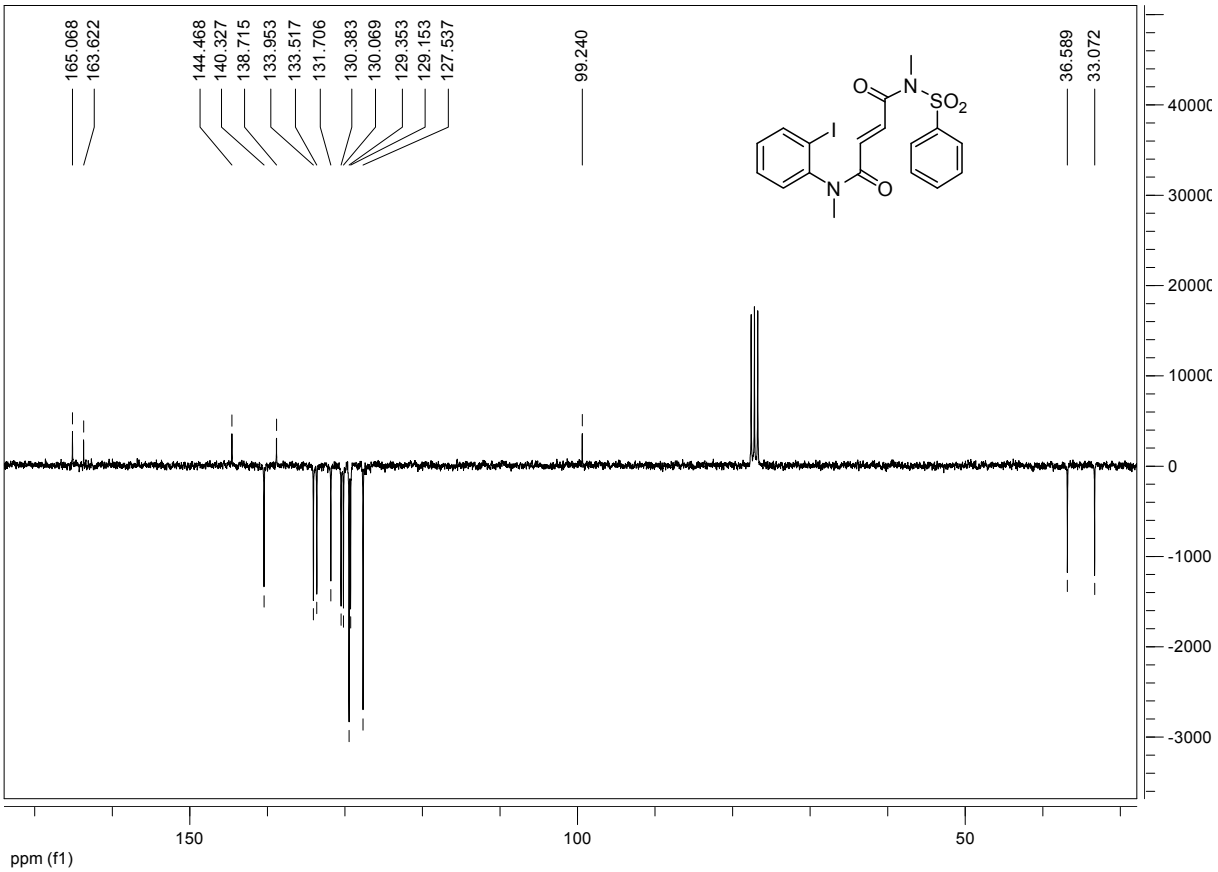


(*E*)-4-((4-chloro-2-iodophenyl)(methyl)amino)-4-oxobut-2-enoic acid 3

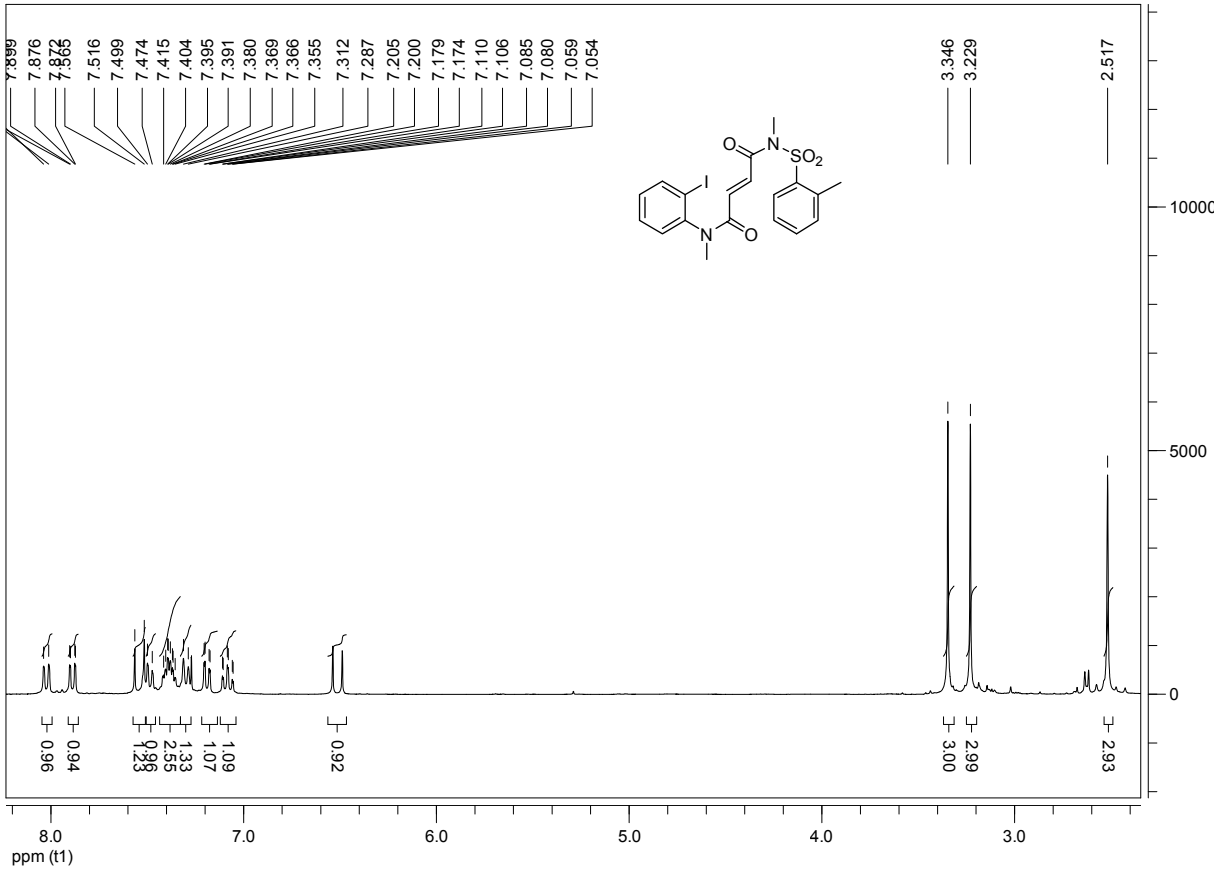


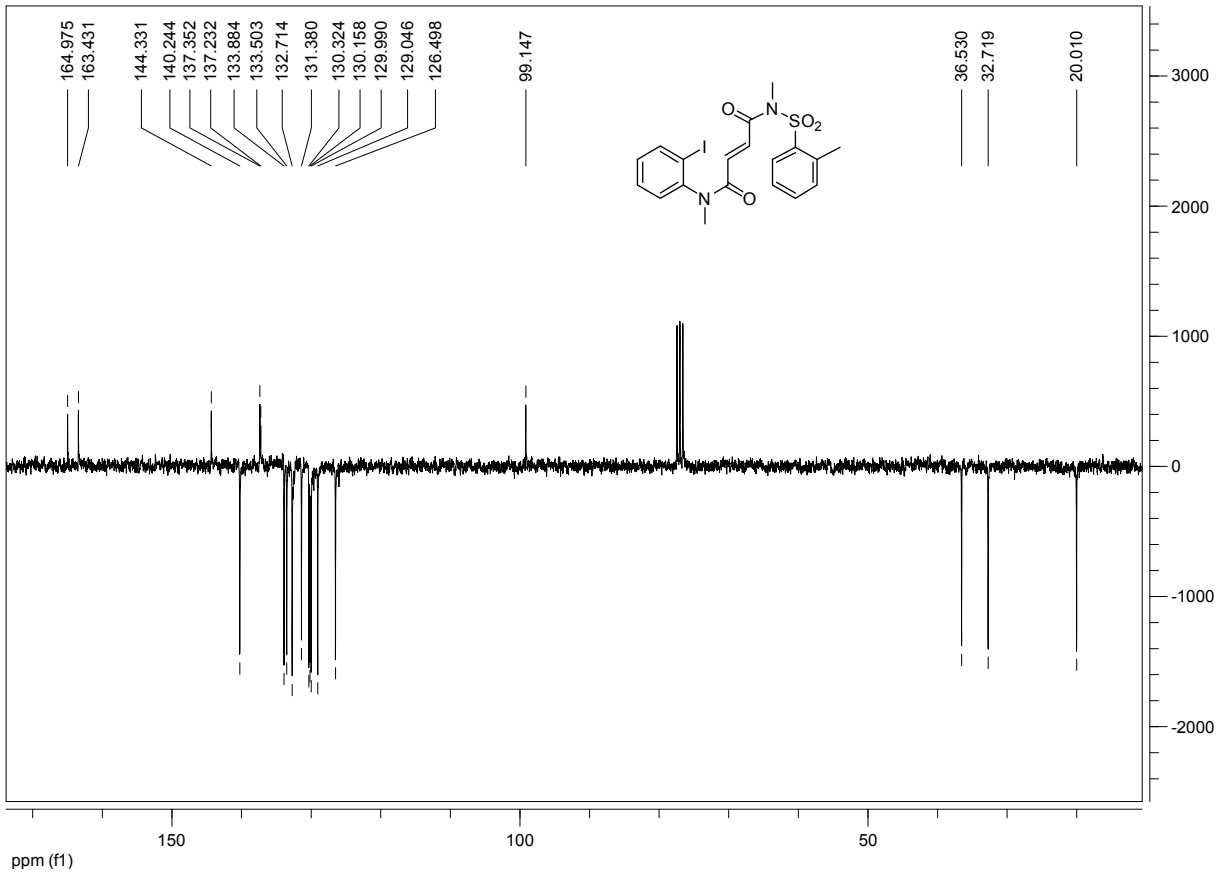
N^1-(2-iodophenyl)-N^1,N^4-dimethyl-N^4-(phenylsulfonyl)fumaramide 4a



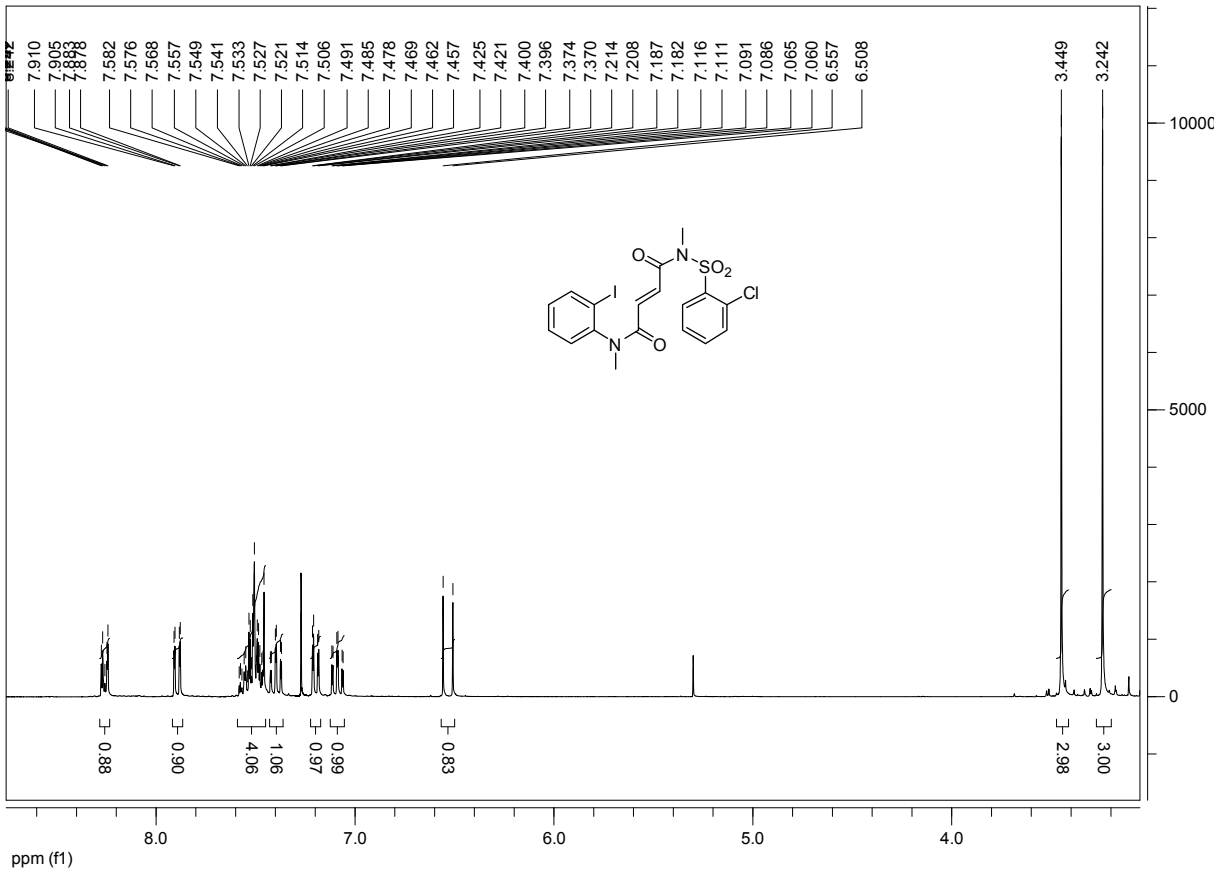


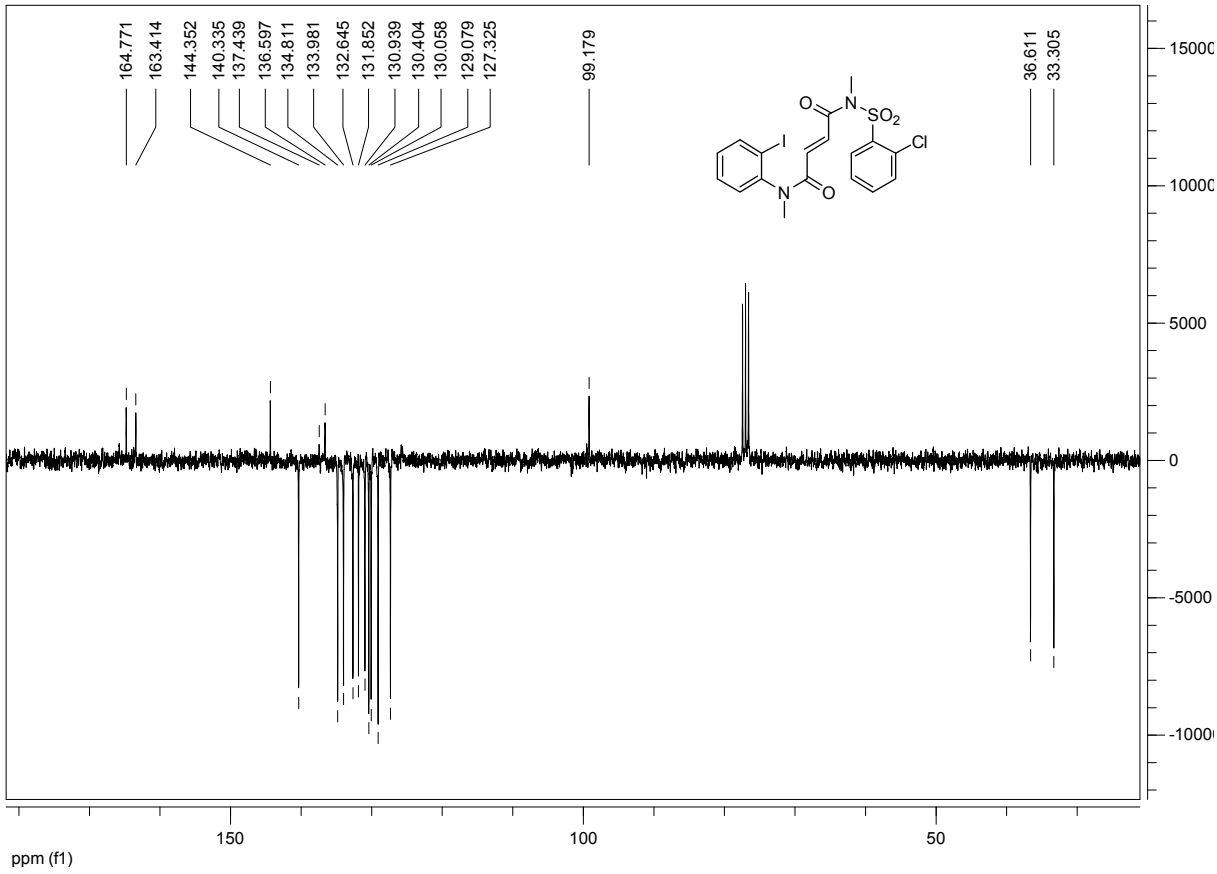
N^1-(2-iodophenyl)-N^1,N^4-dimethyl-N^4-(*o*-tolylsulfonyl)fumaramide **4b**



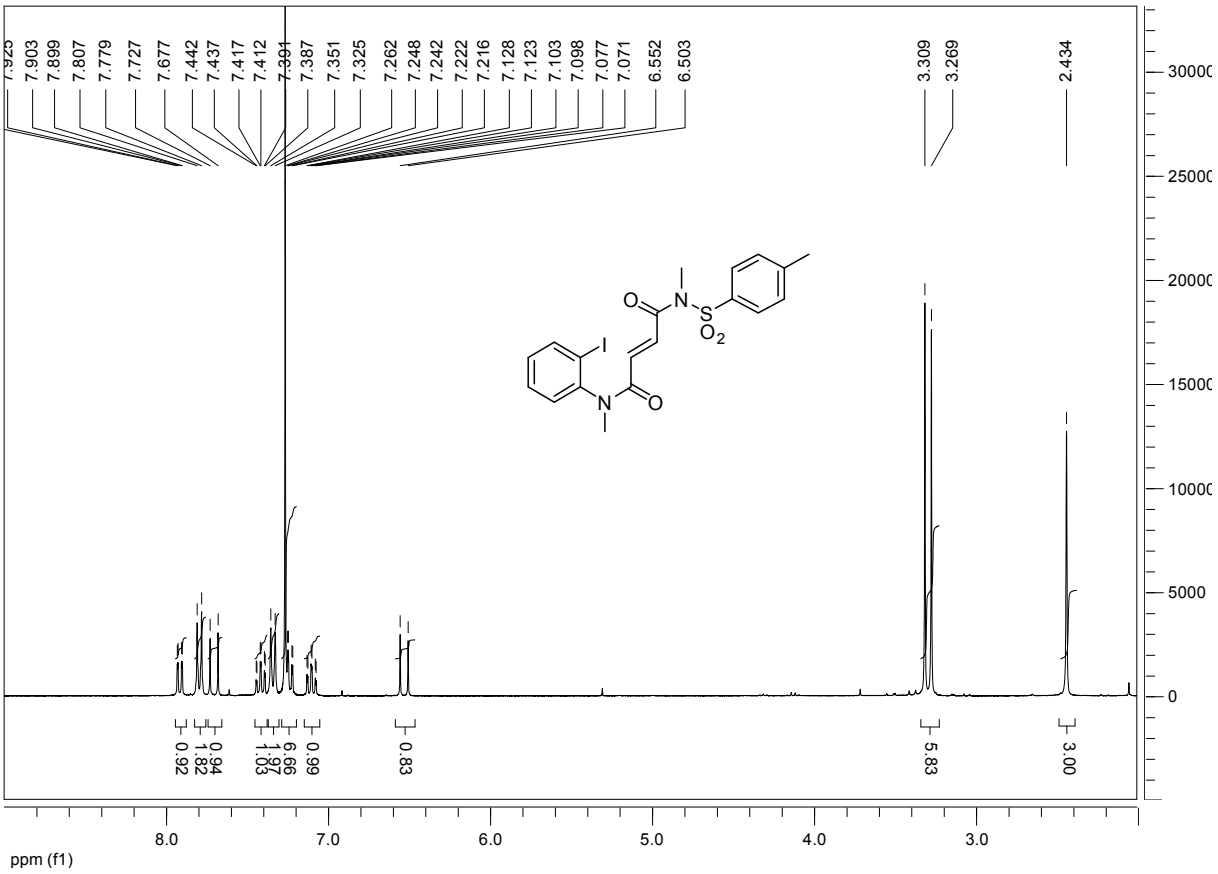


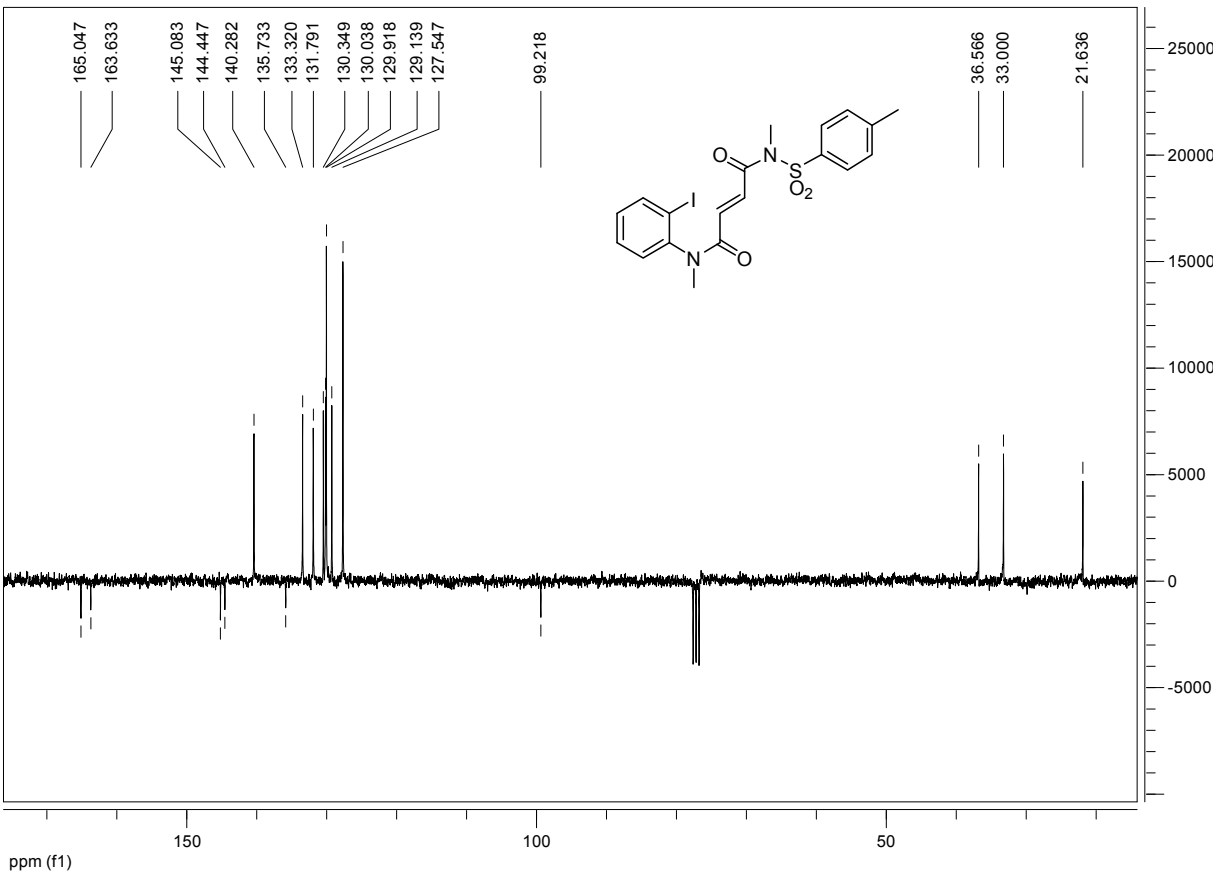
N^1-((2-chlorophenyl)sulfonyl)-N^4-(2-iodophenyl)-N^1,N^4-dimethylfumaramide 4c



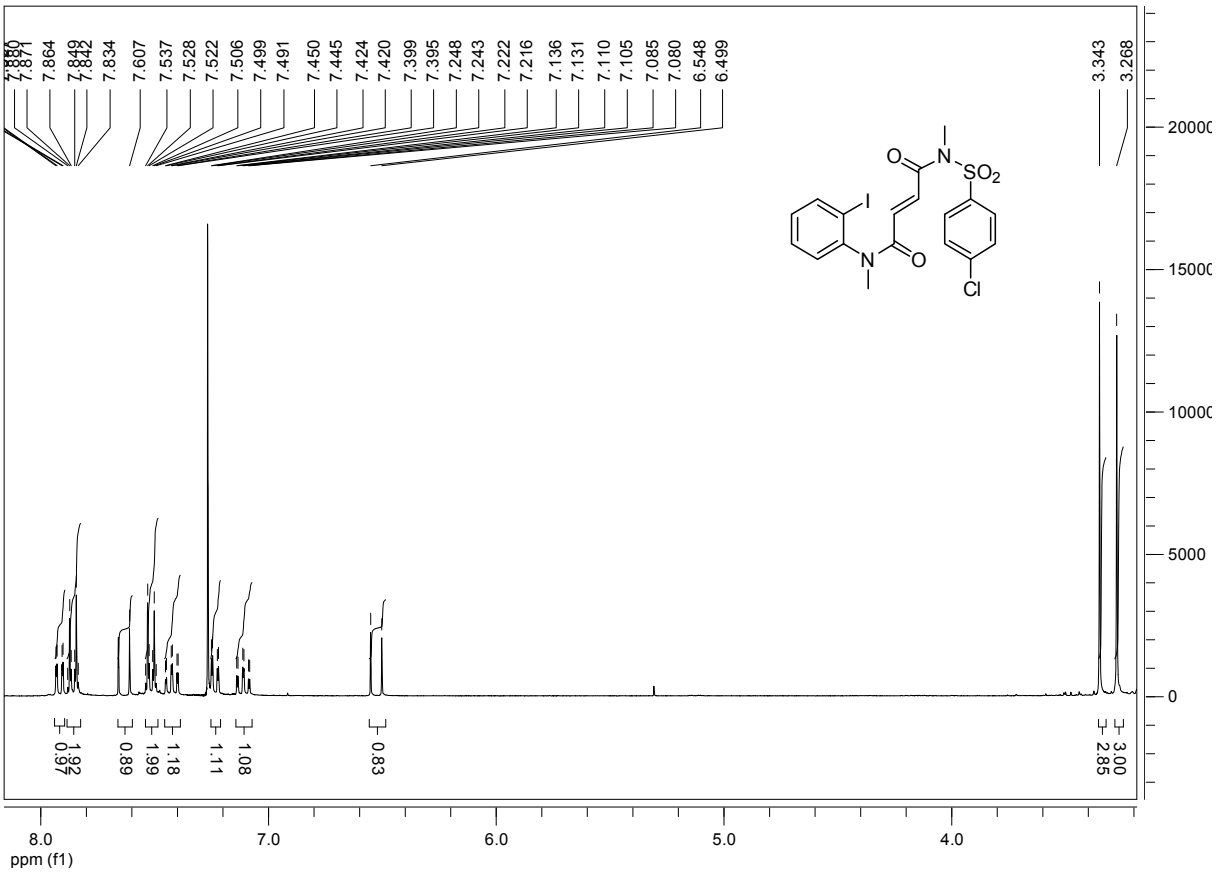


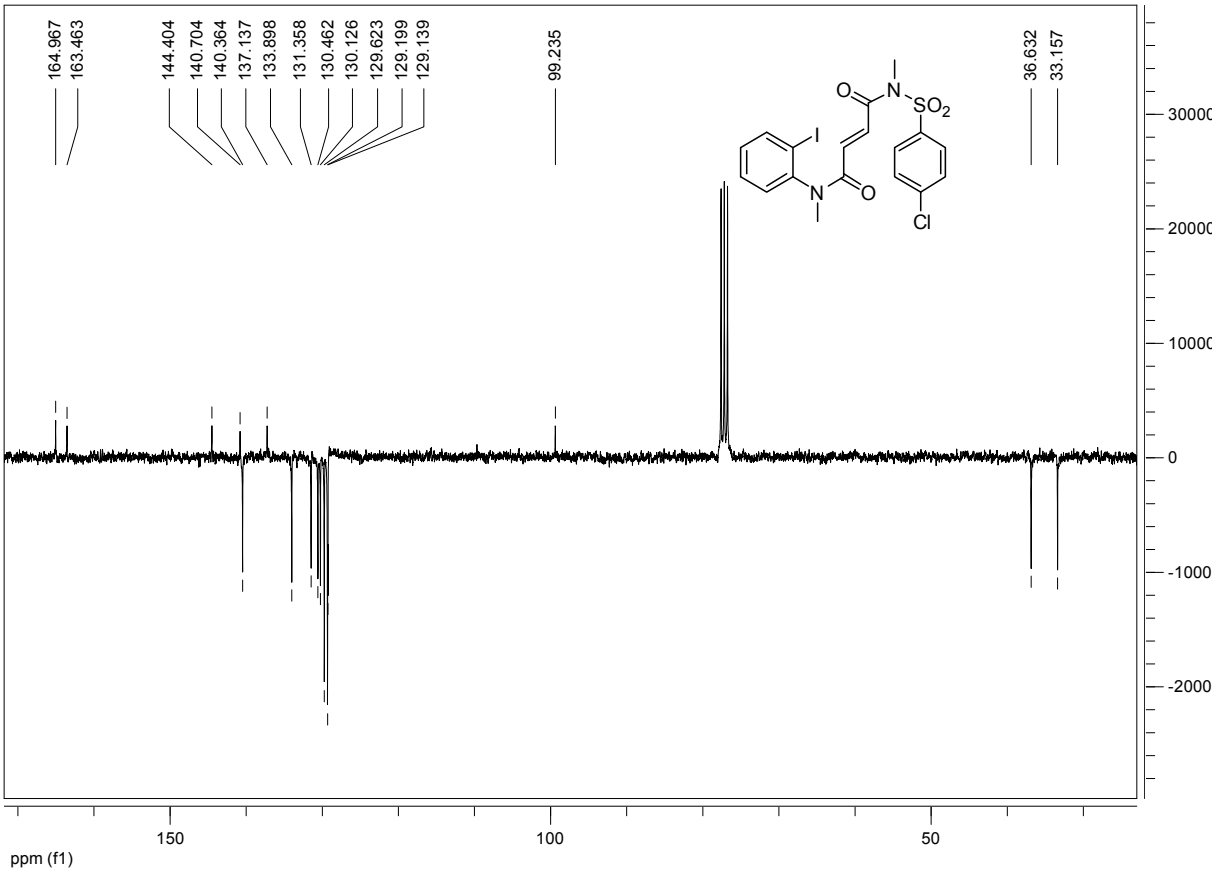
N^1-(2-iodophenyl)-N^1,N^4-dimethyl-N^4-(tosyl)fumaramide 4d



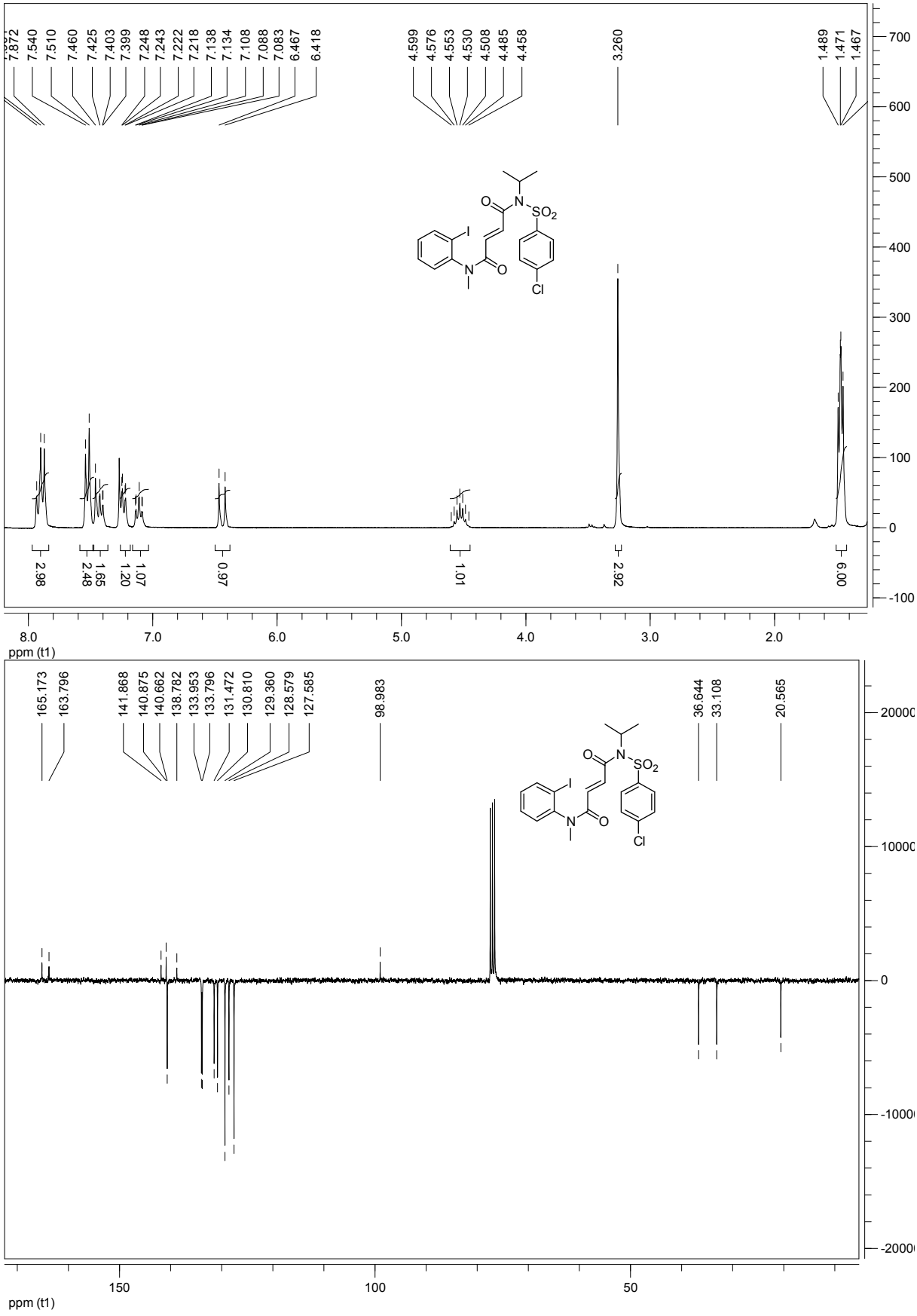


N^4-(4-chlorophenylsulfonyl)-N^1-(2-iodophenyl)-N^1,N^4-dimethylfumaramide <u>4e</u>



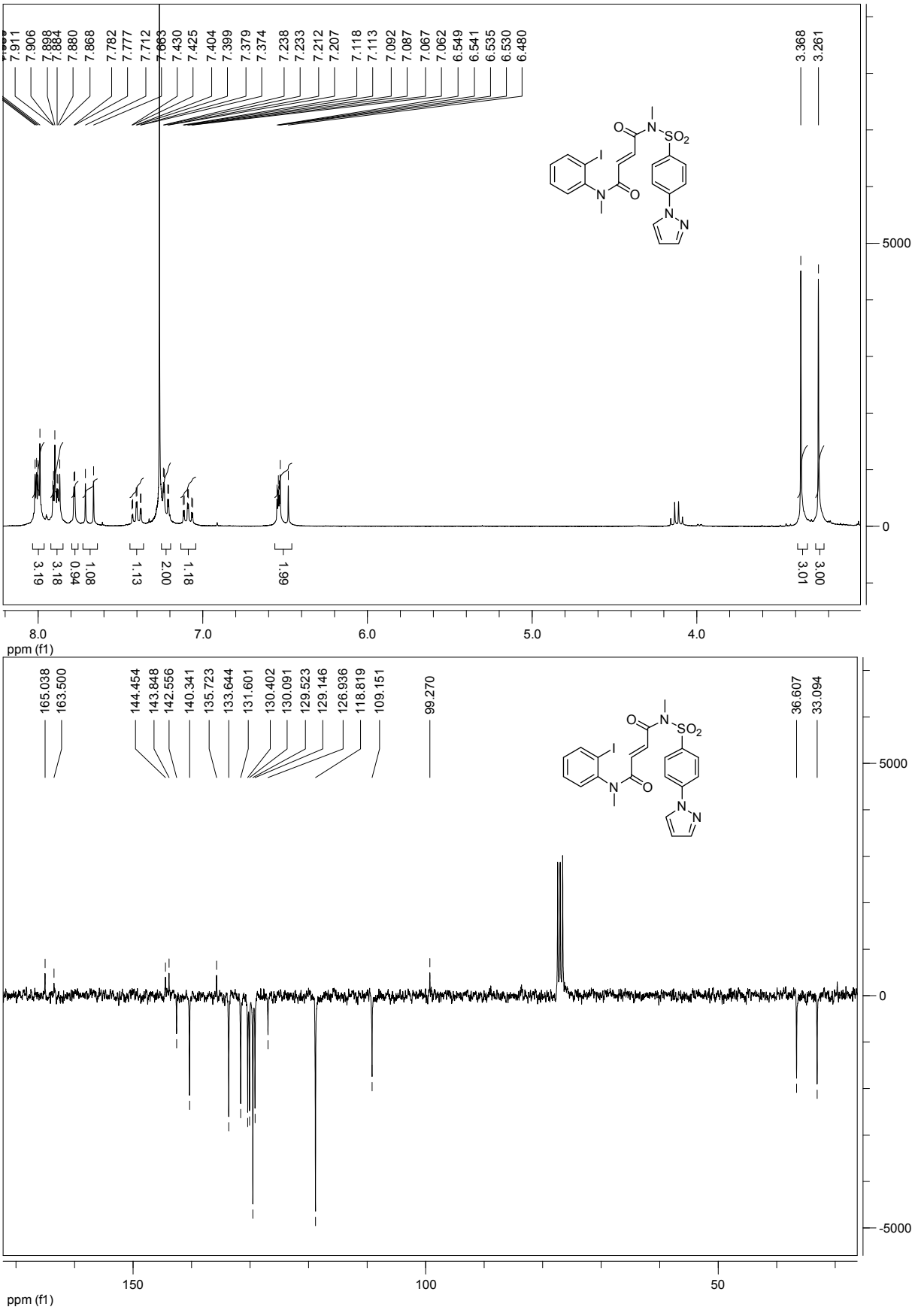


N^1-((4-chlorophenyl)sulfonyl)-N^4-(2-iodophenyl)-N^1-isopropyl-N^4-methylfumaramide <u>4f</u>

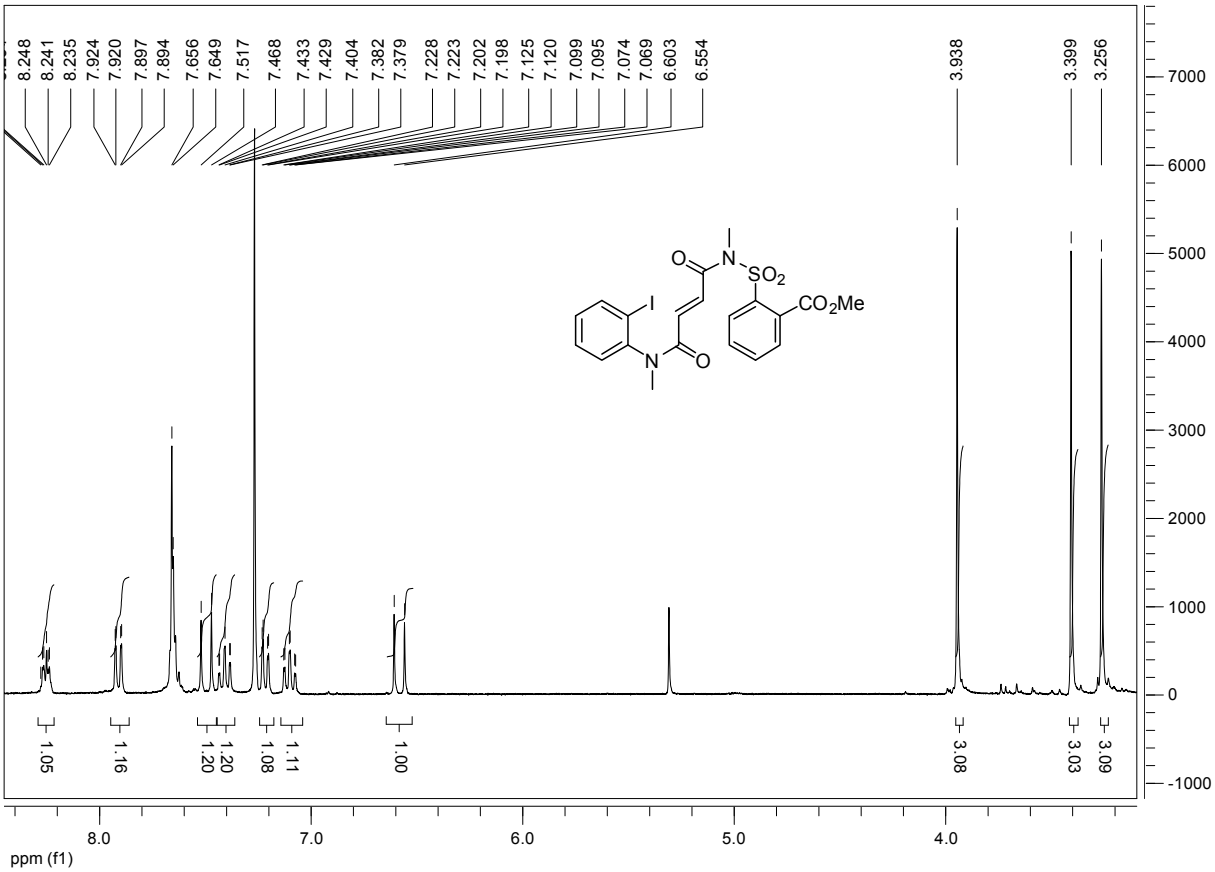


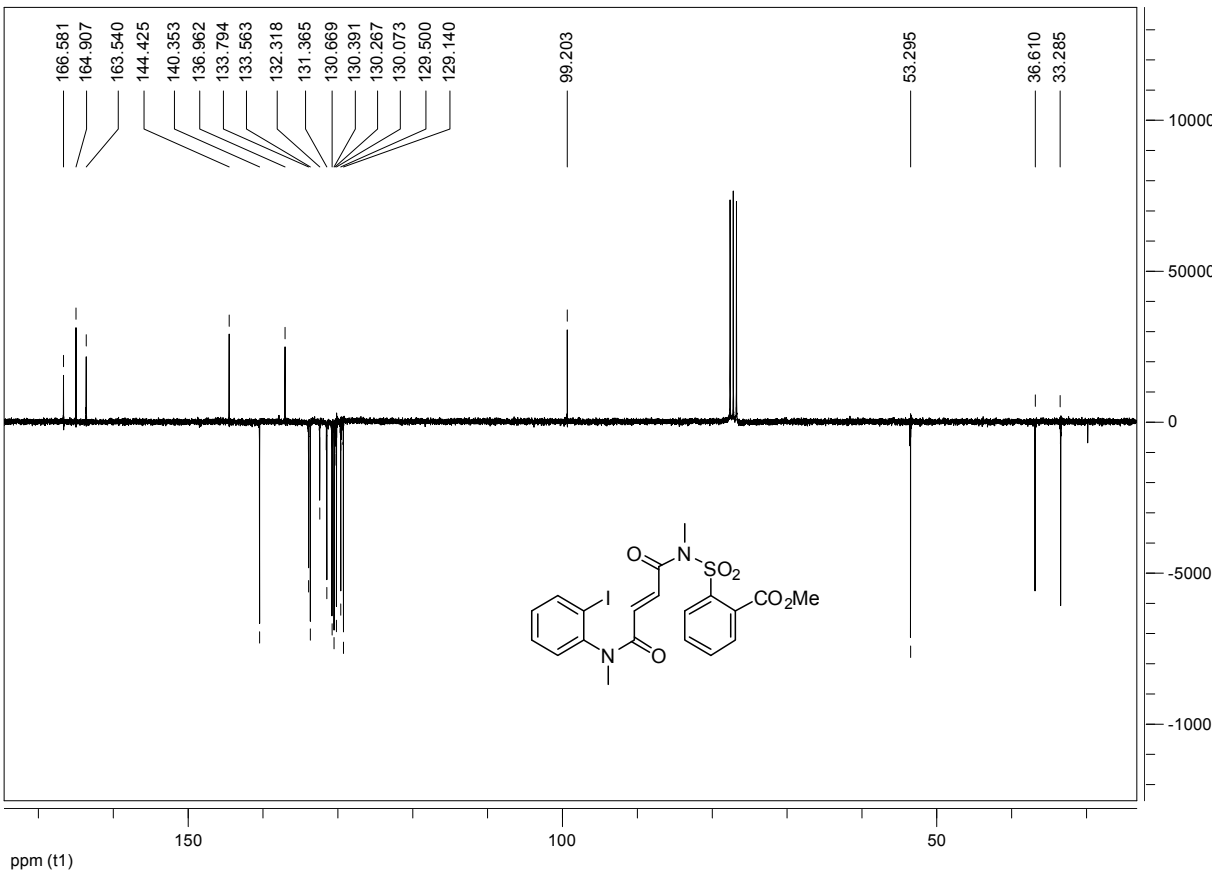
N^1-(4-(1*H*-pyrazol-1-yl)phenylsulfonyl)-N^4-(2-iodophenyl)-N^1,N^4-dimethylfumaramide

4g

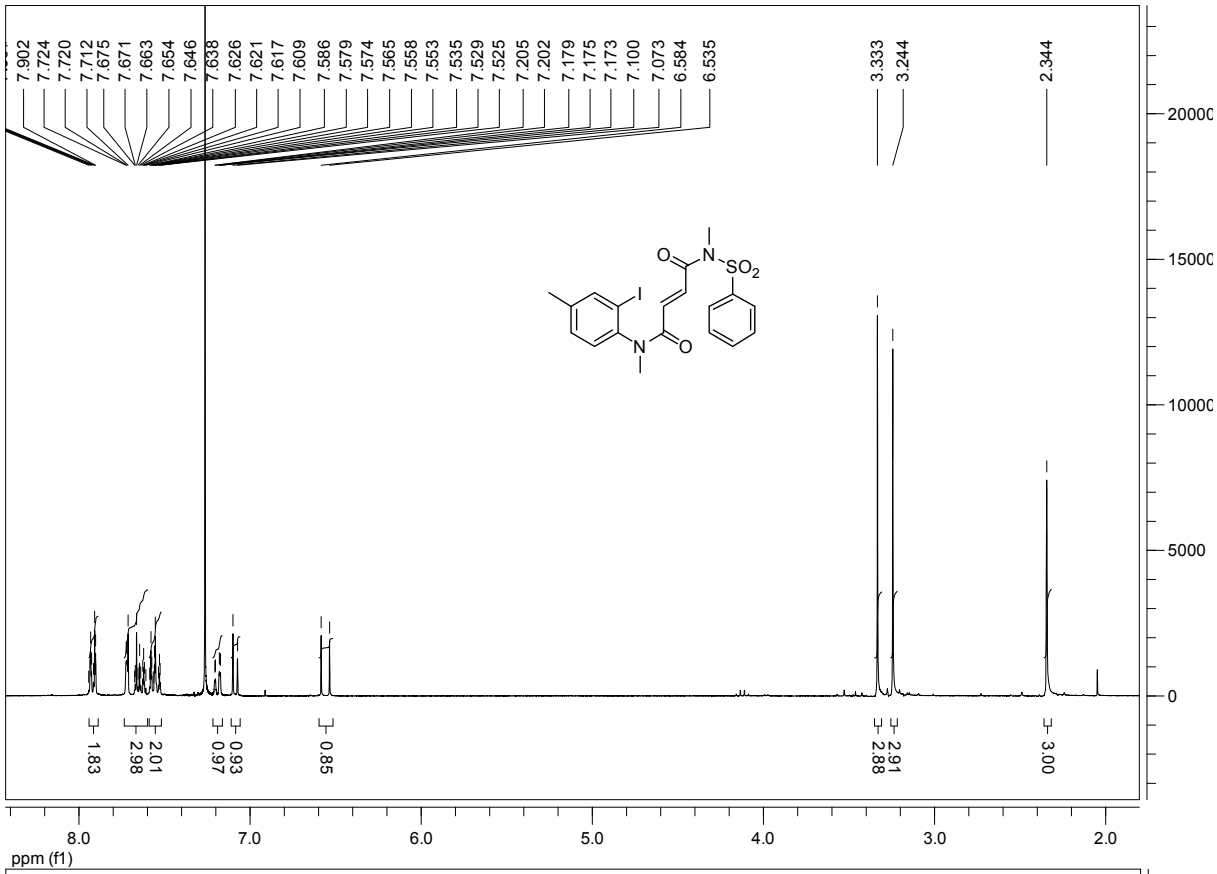


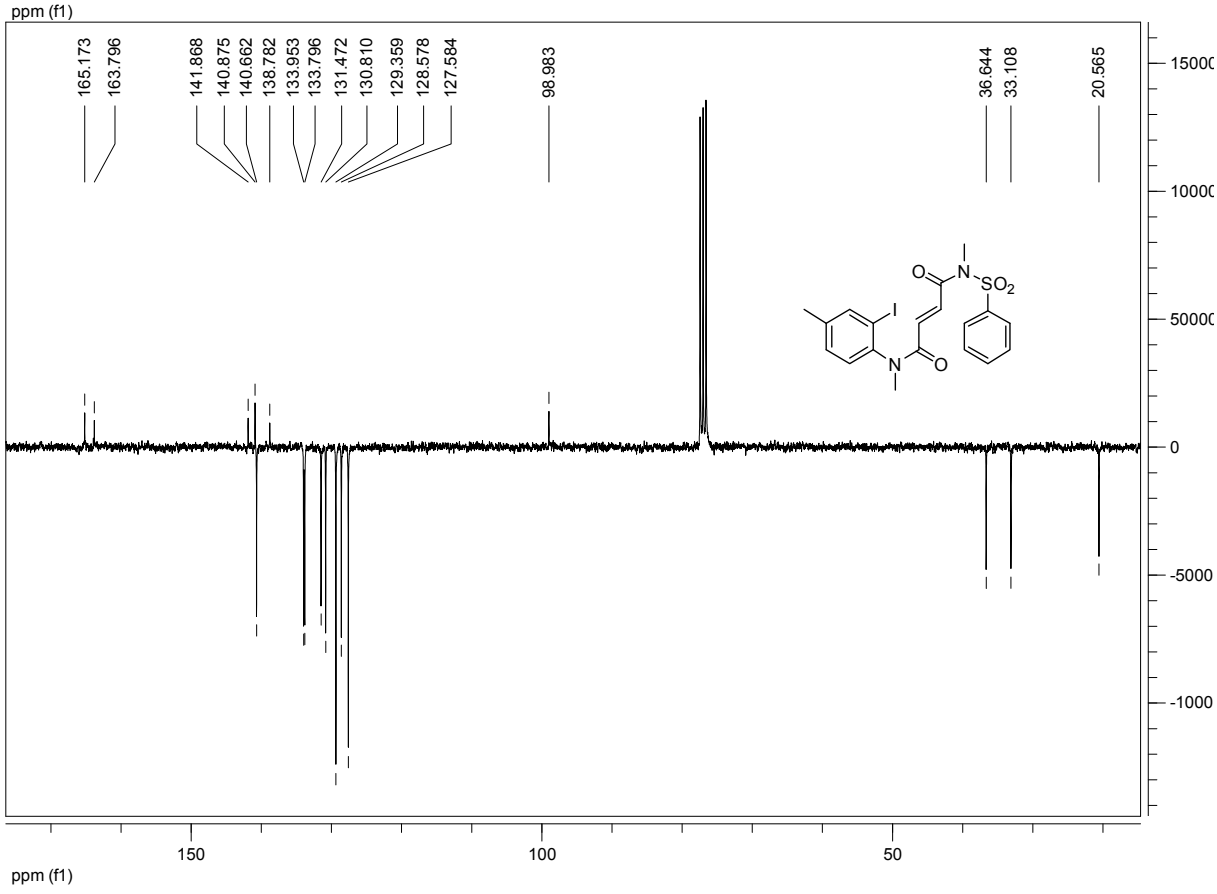
(*E*)-methyl-2-(*N*-(4-((2-iodophenyl)(methyl)amino)-4-oxo but-2-enoyl)-*N*-methyl sulfamoyl)benzoate <u>4h</u>



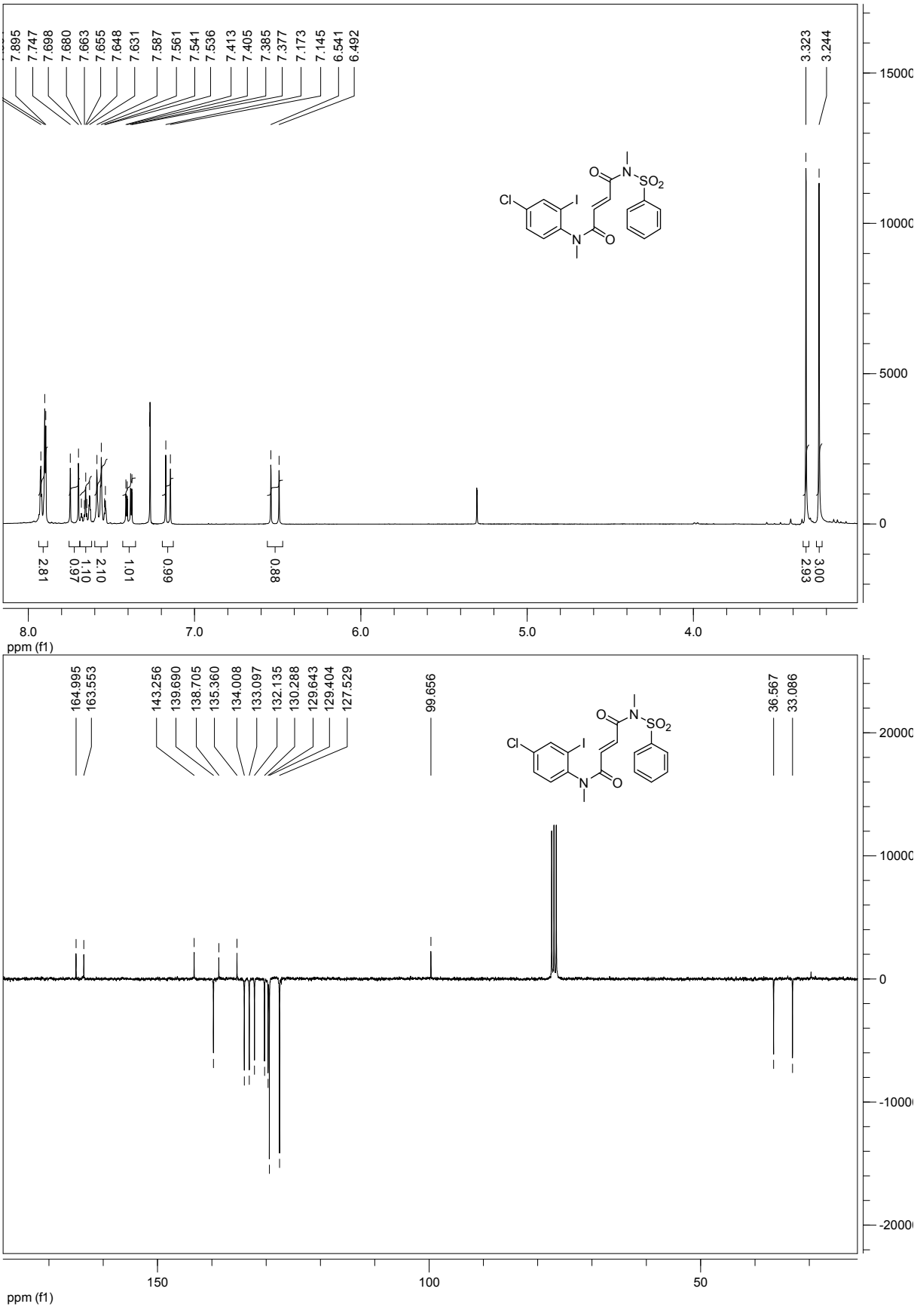


N^1-(2-iodo-4-methylphenyl)-N^1,N^4-dimethyl-N^4-(phenylsulfonyl)fumaramide 4i

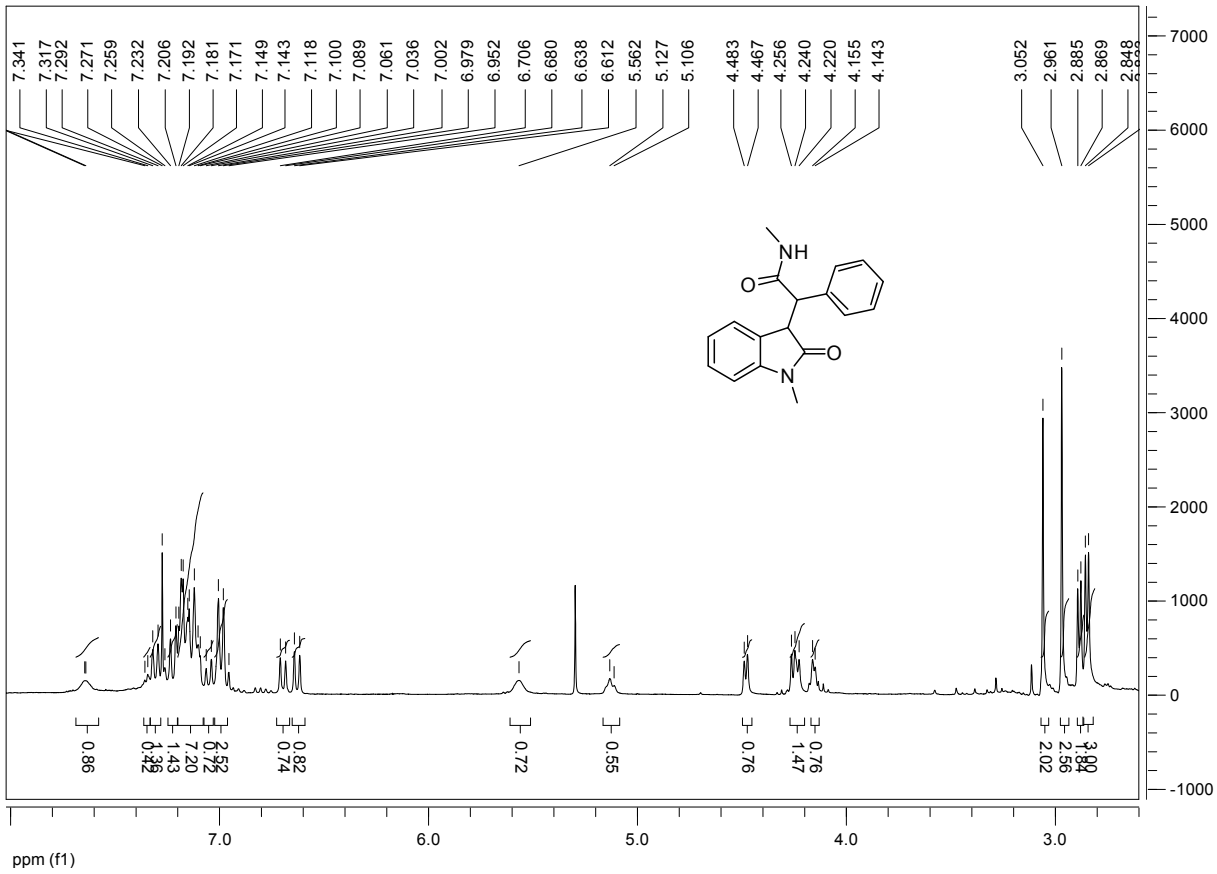


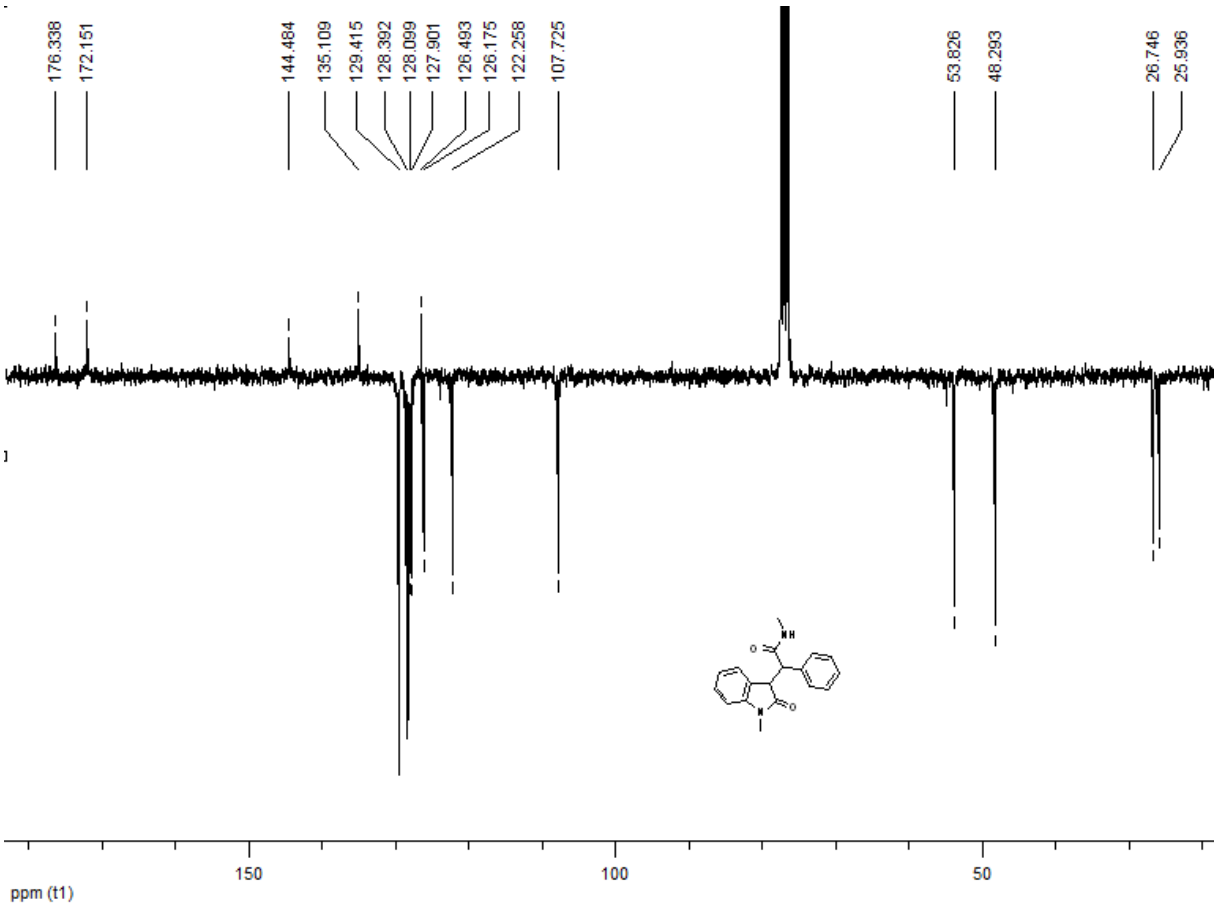


N^1-(4-chloro-2-iodophenyl)-N^1,N^4-dimethyl-N^4-(phenylsulfonyl)fumaramide **4j**

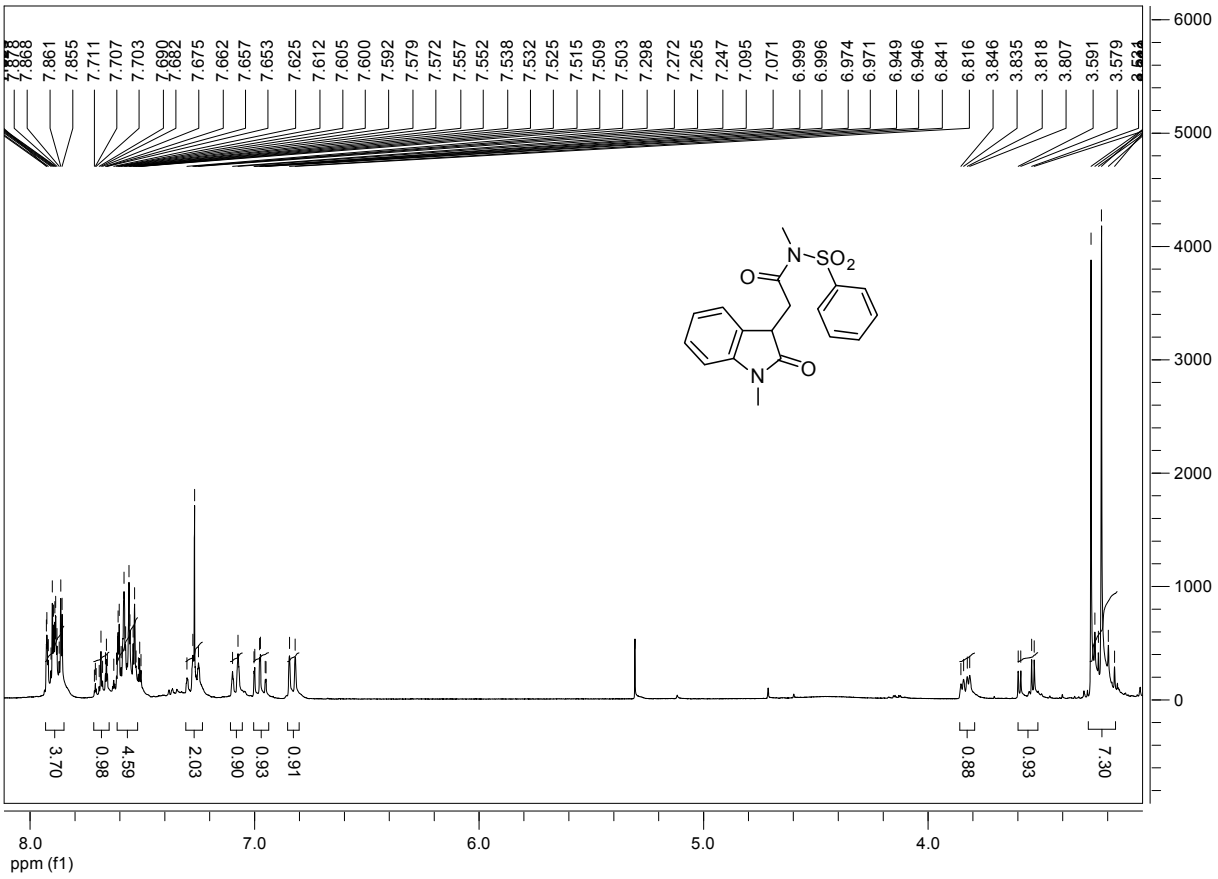


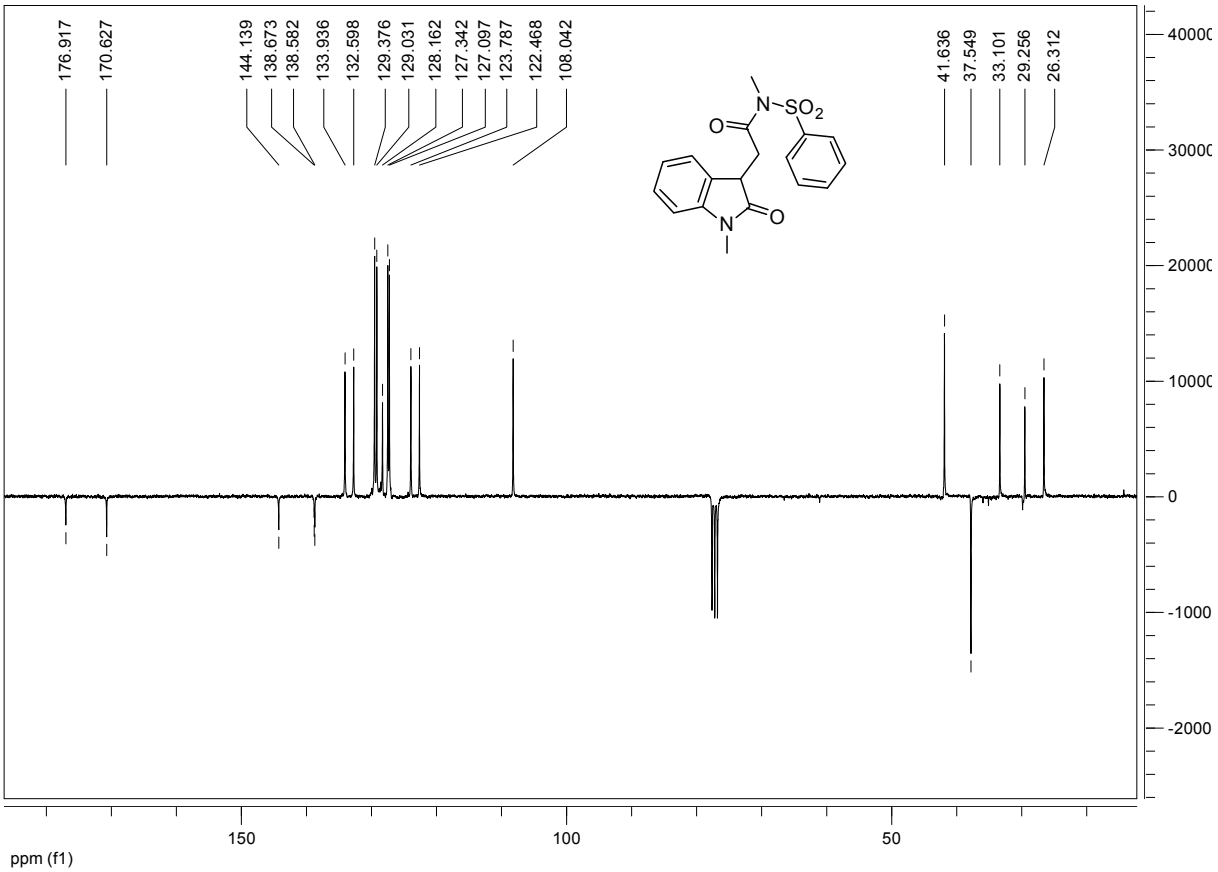
N-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-phenylacetamide **5a**



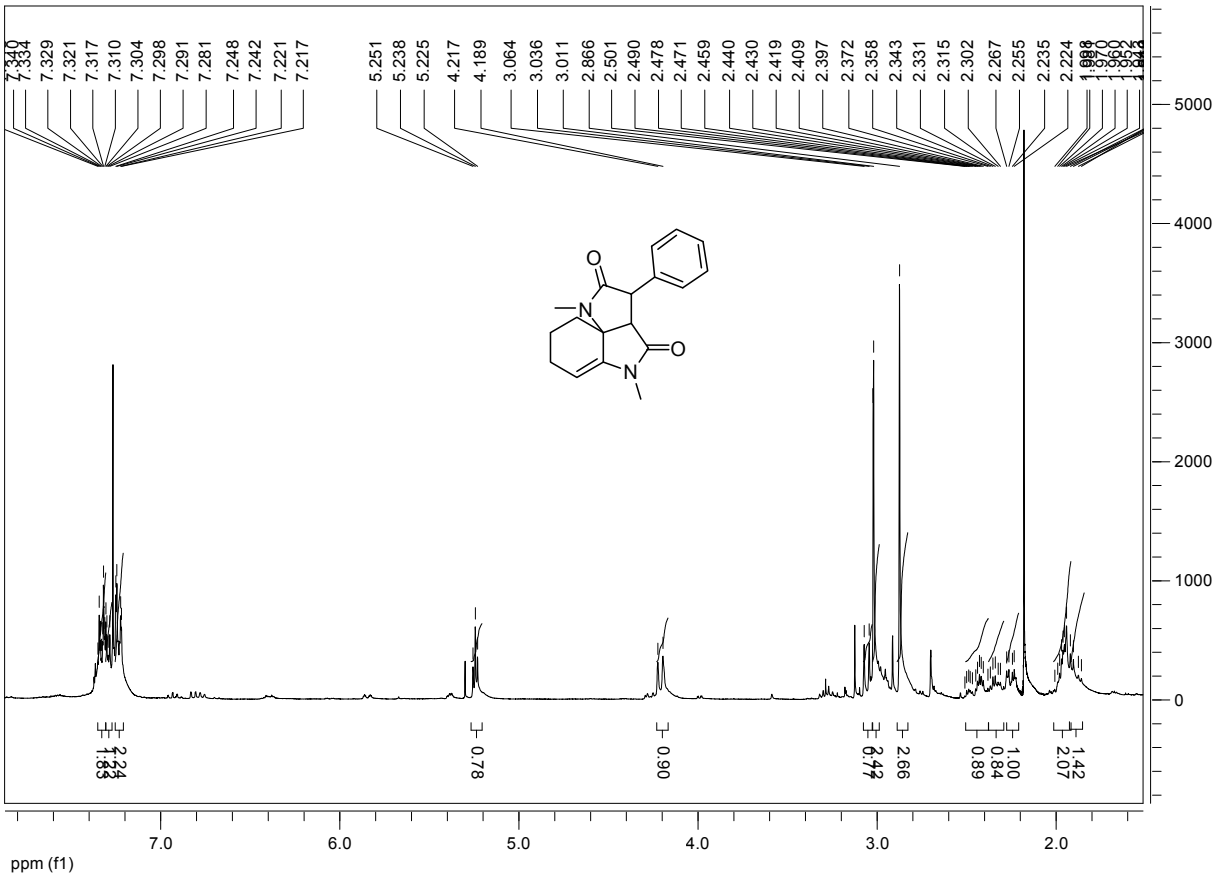


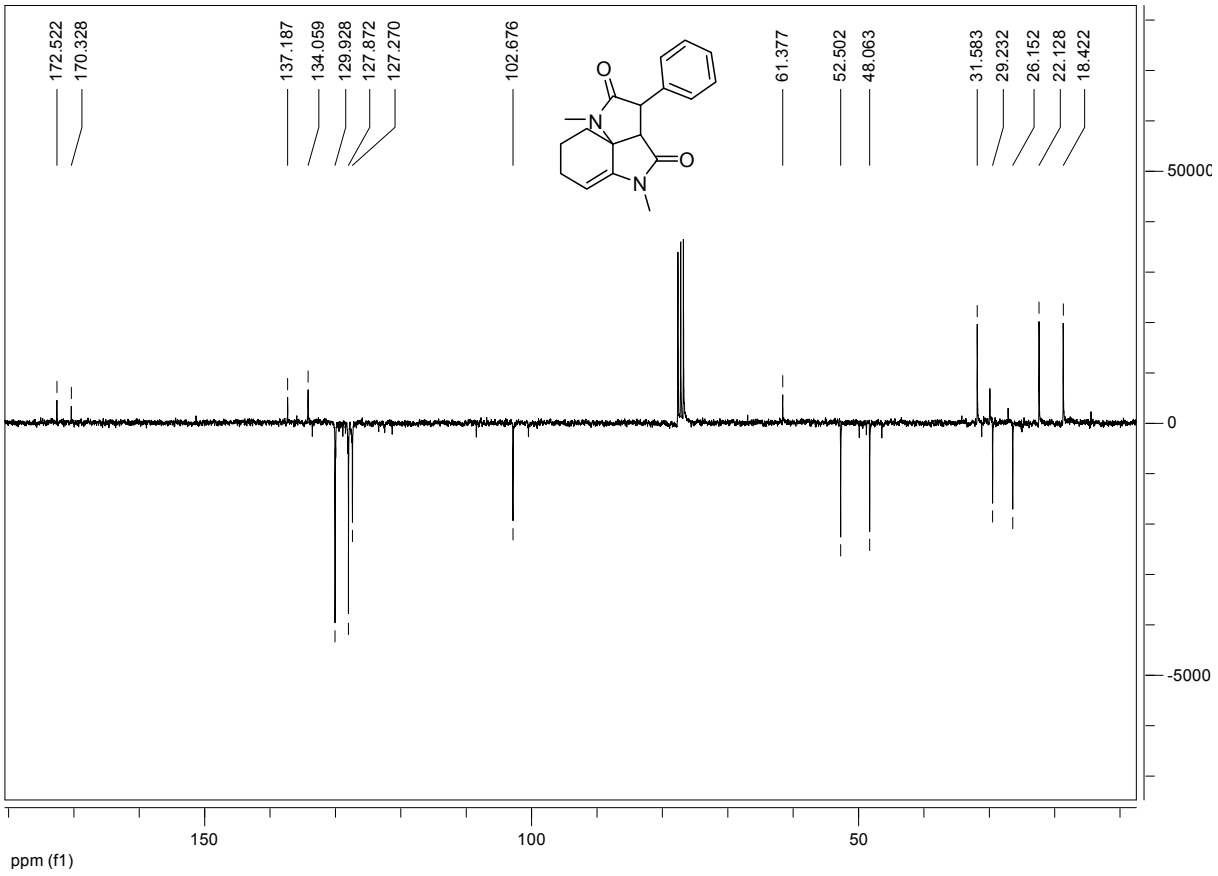
_N_-methyl-2-(1-methyl-2-oxoindolin-3-yl)-_N_-(phenylsulfonyl)acetamide <u>6a</u>



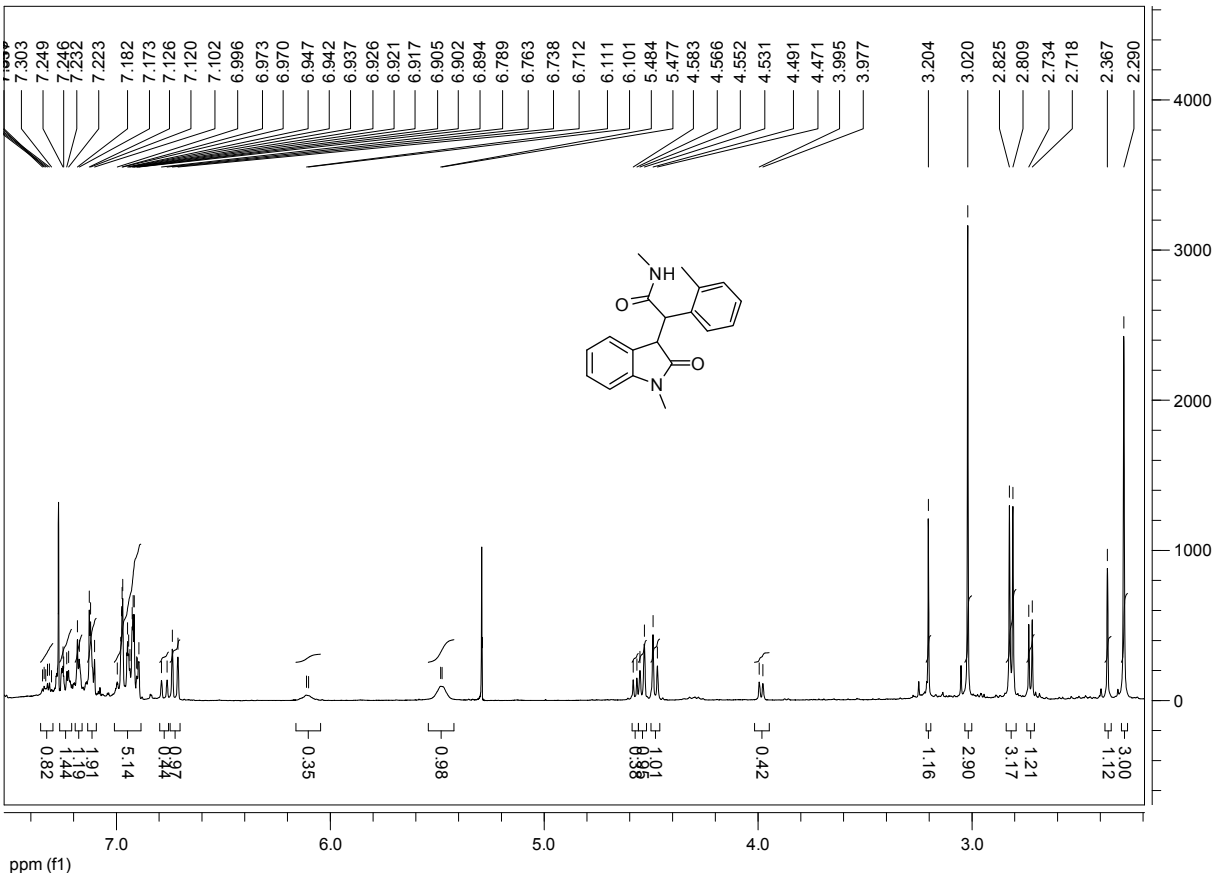


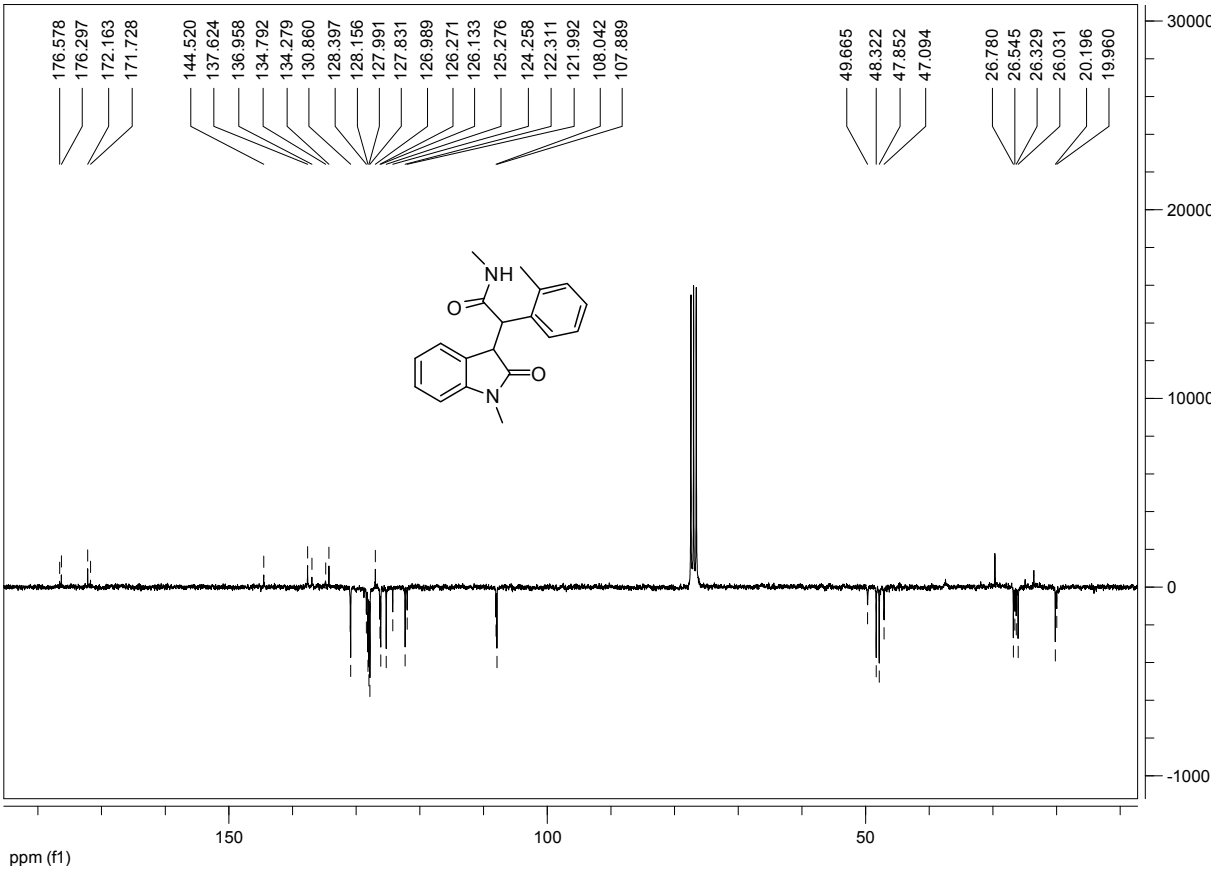
1,5-dimethyl-3-phenyl-3,3a,8,9-tetrahydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione 7a



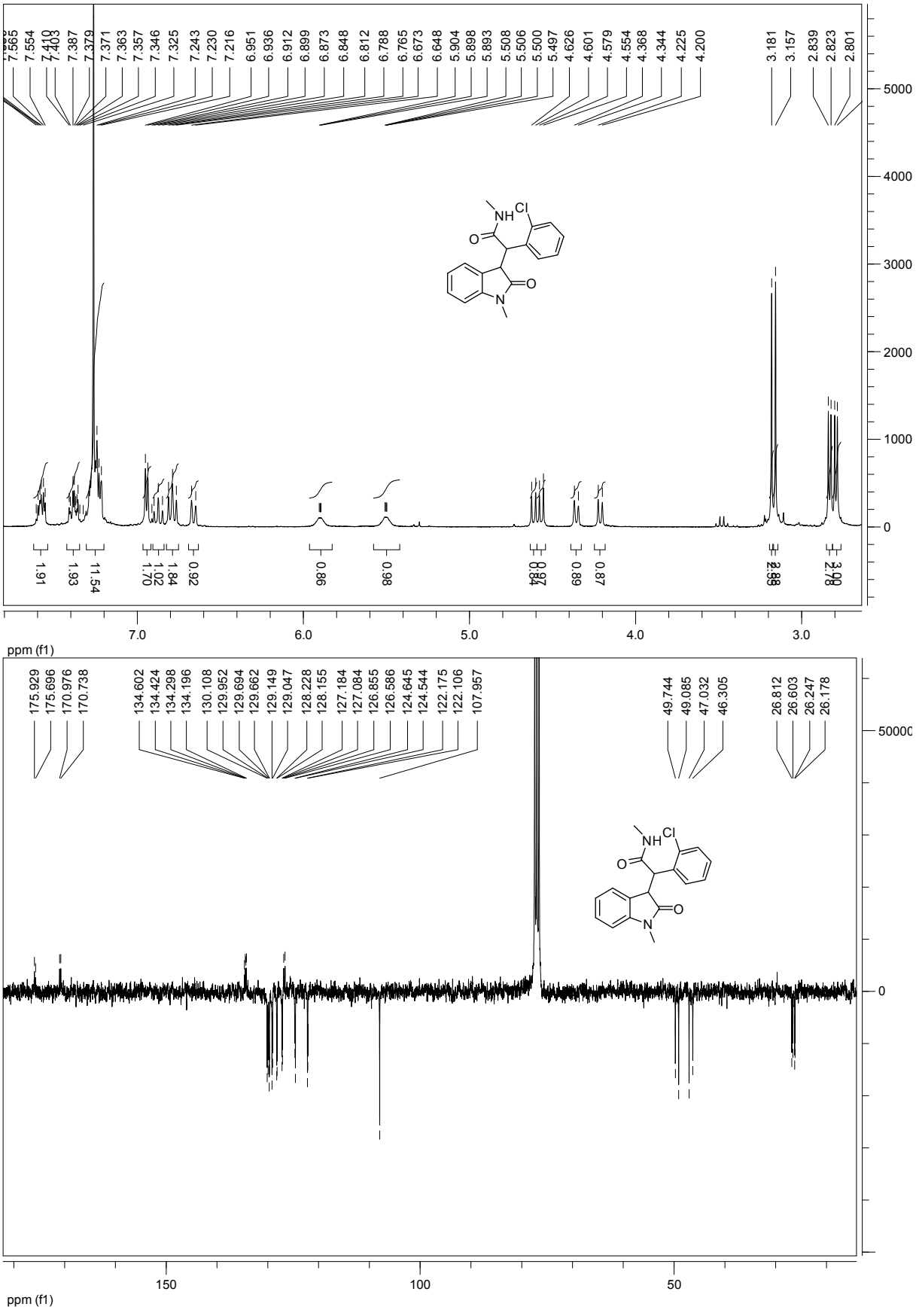


N-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-*o*-tolylacetamide **5b**

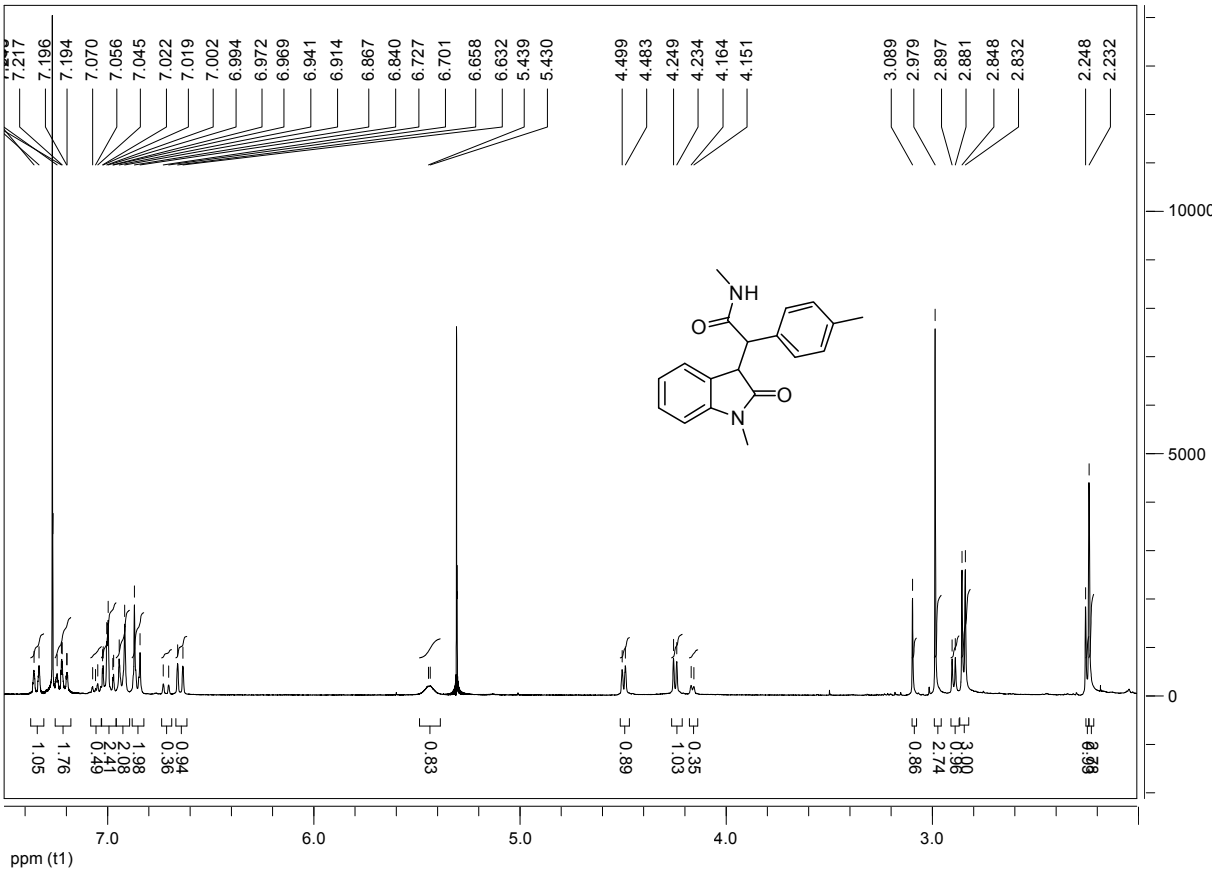


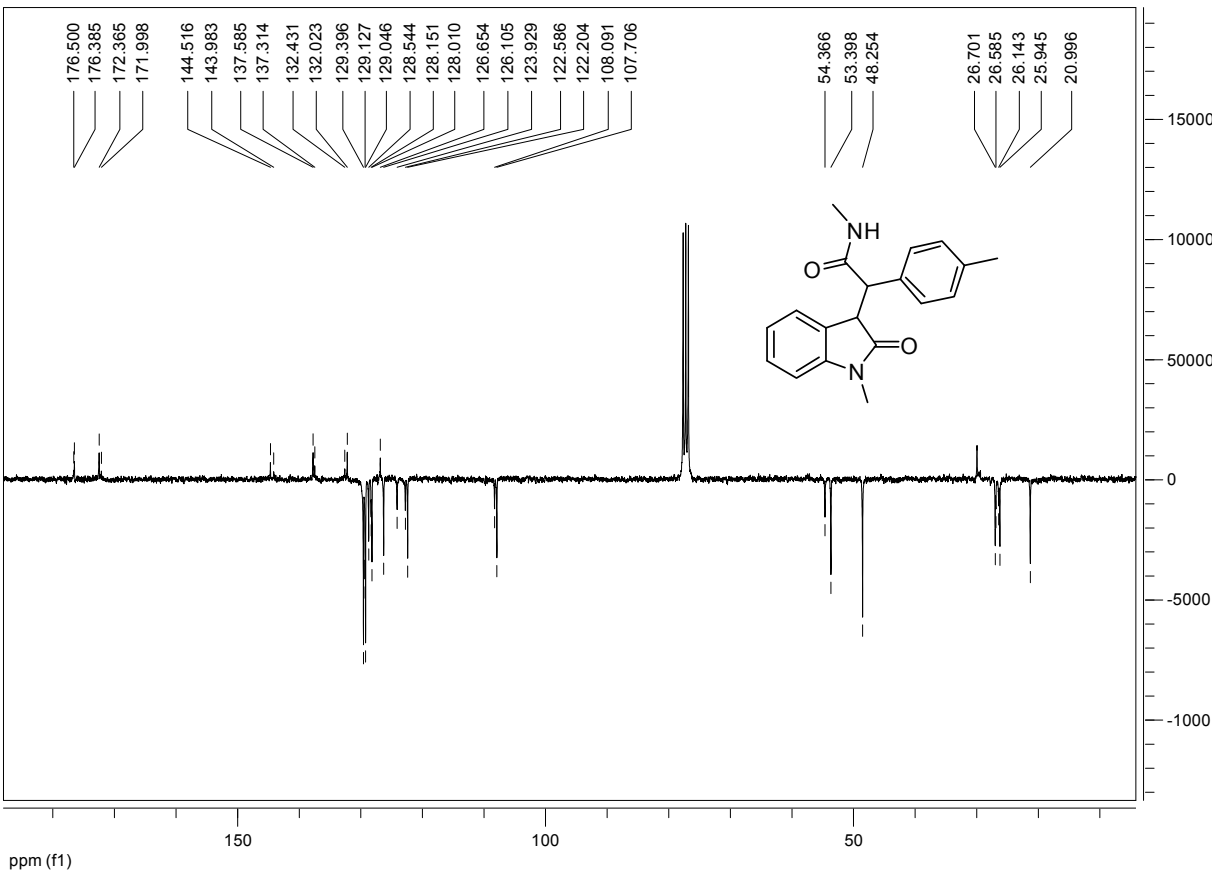


2-(2-chlorophenyl)-*N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)acetamide.5c

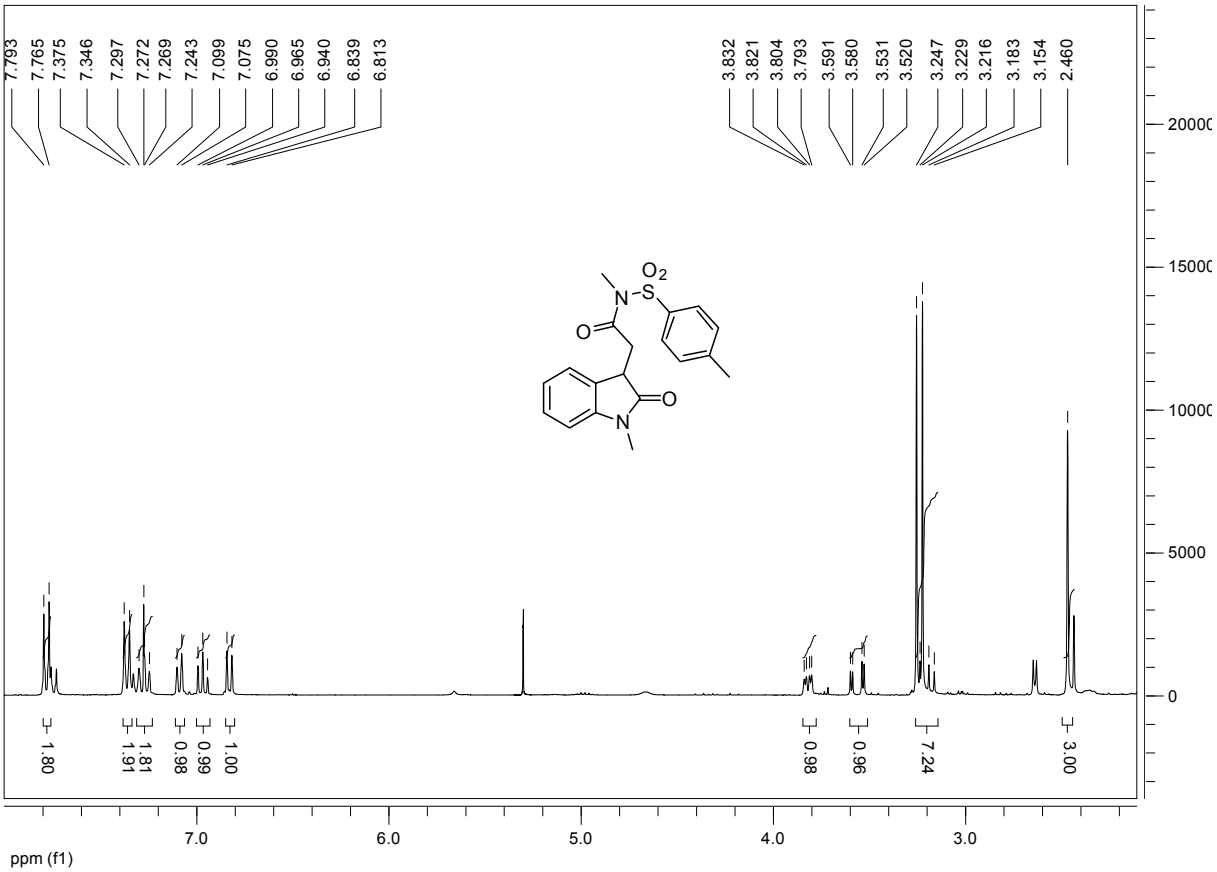


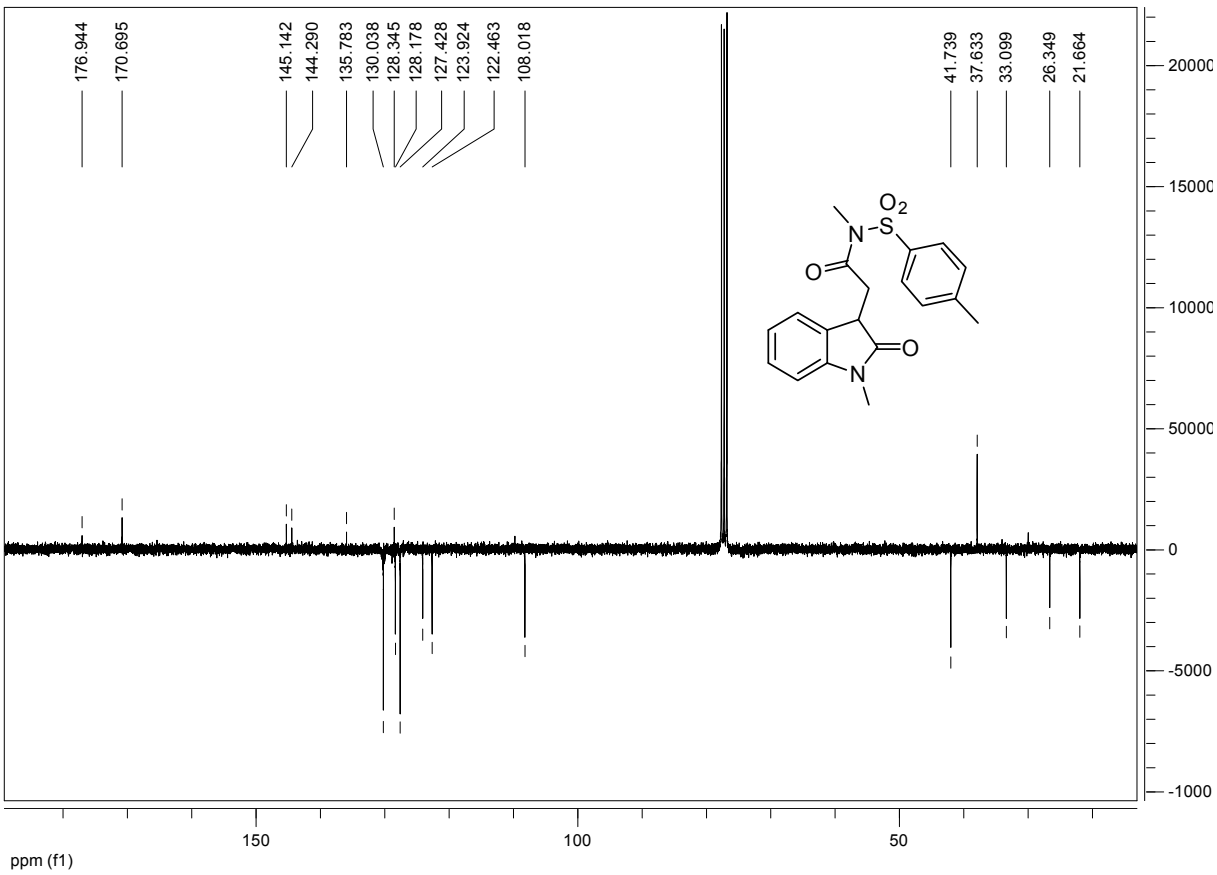
N-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-*p*-tolylacetamide **5d**



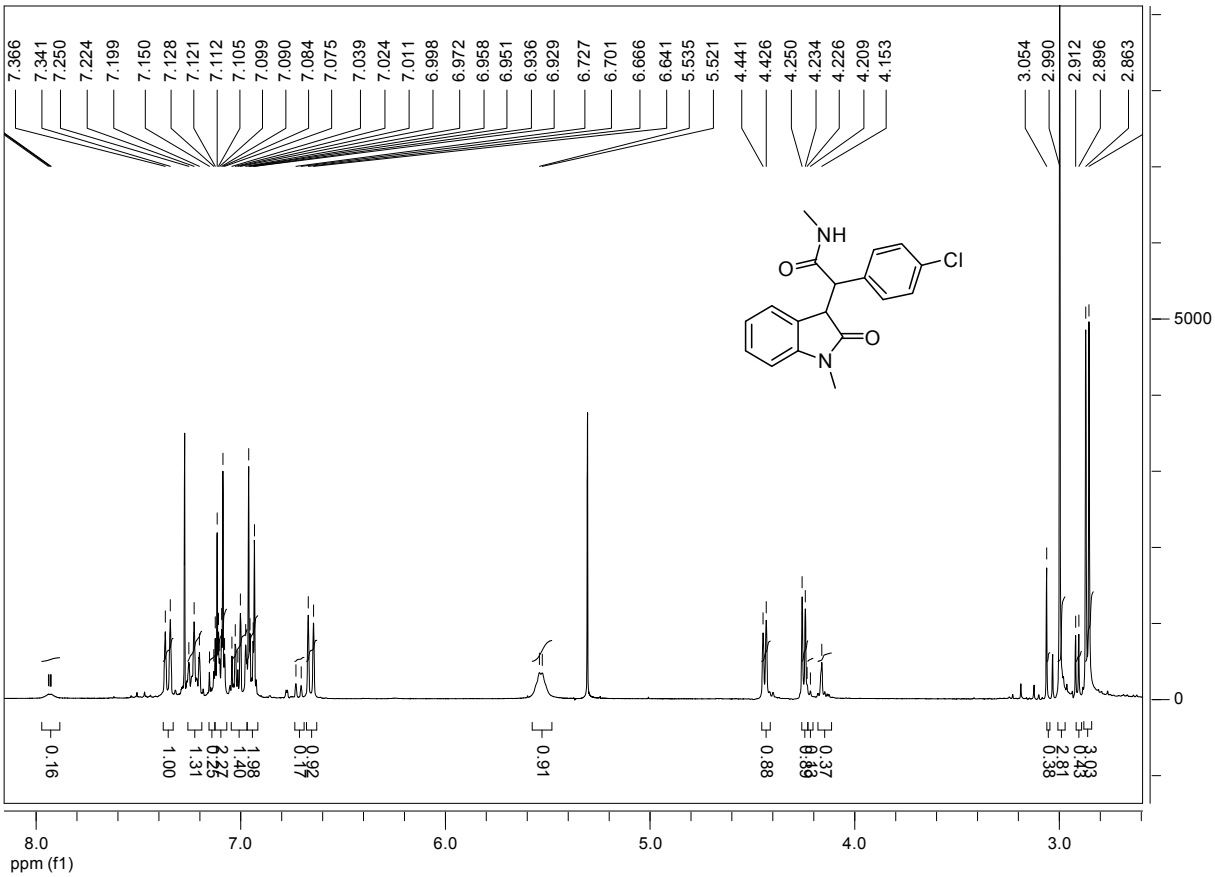


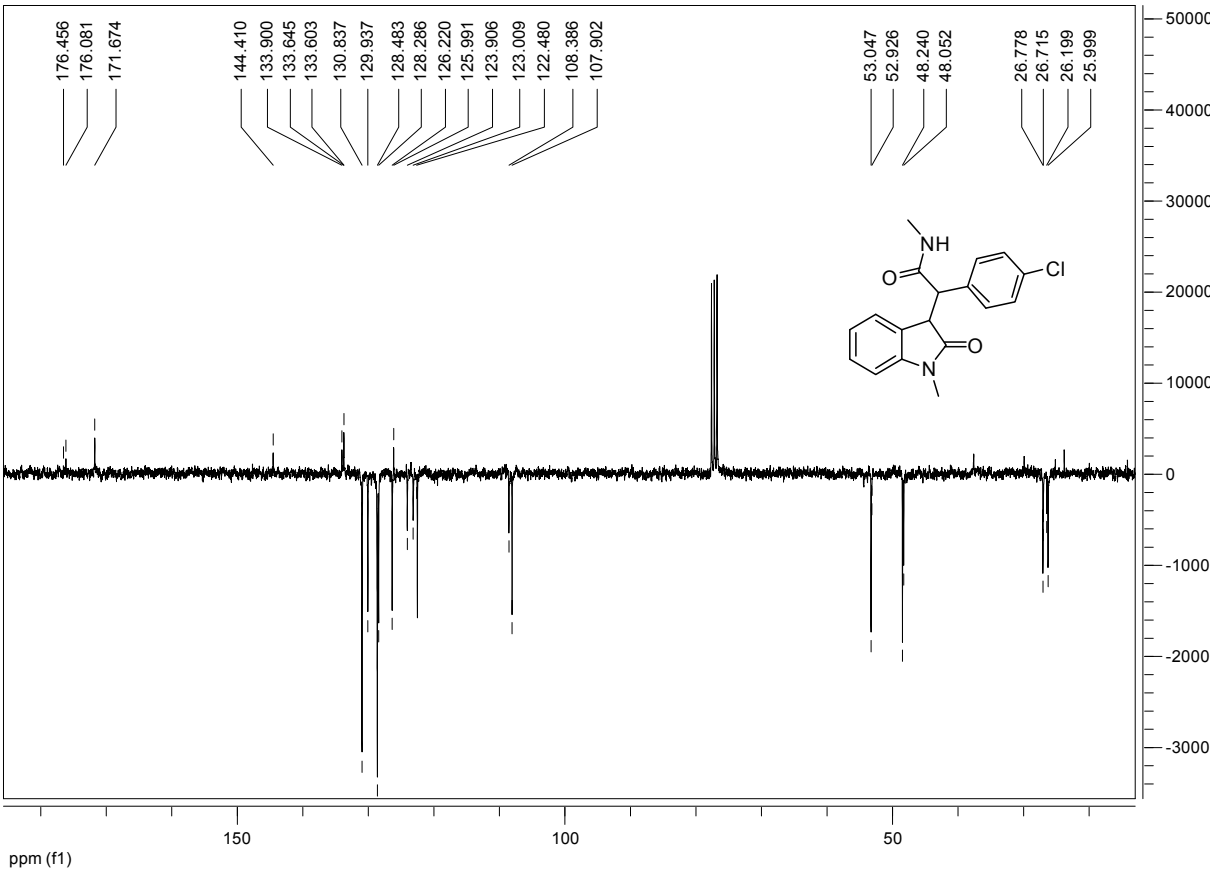
N-methyl-2-(1-methyl-2-oxoindolin-3-yl)-2-tosylacetamide **6d**



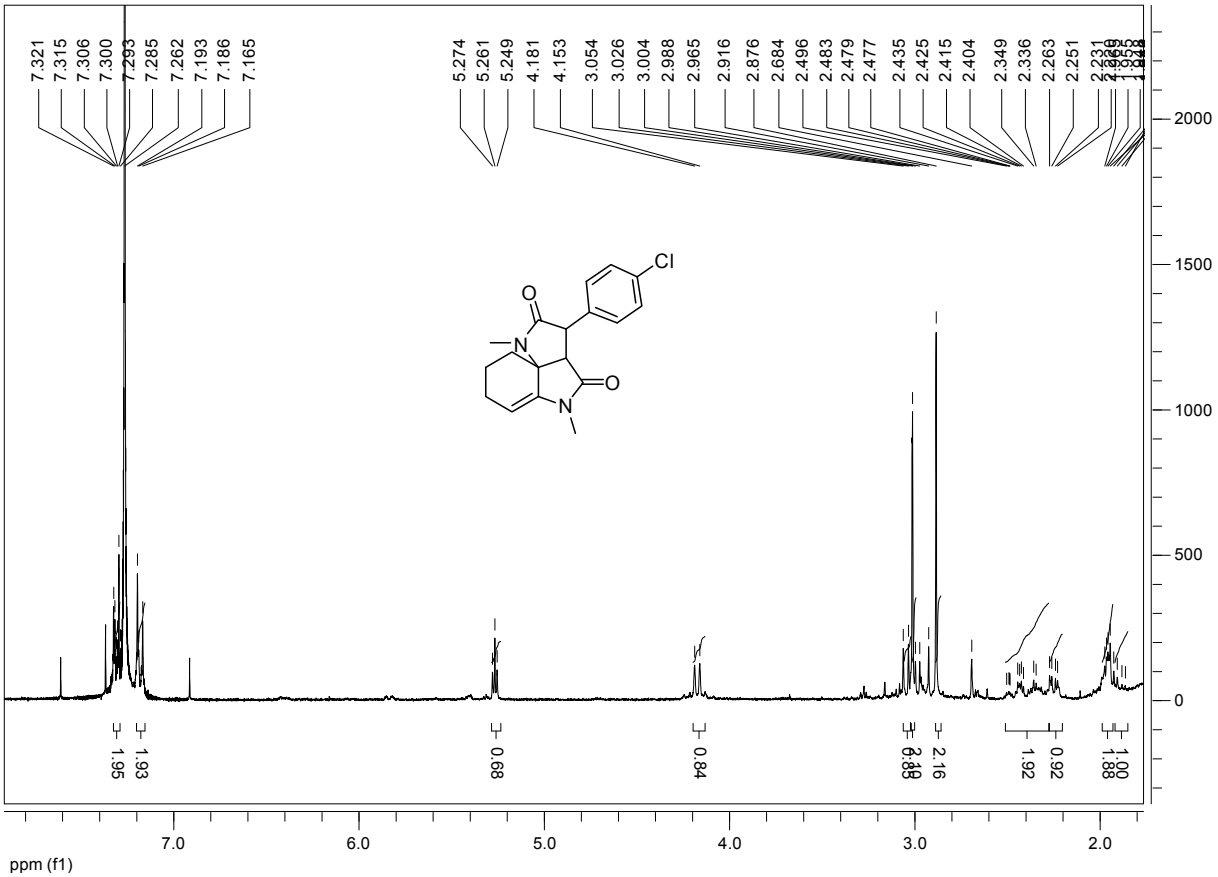


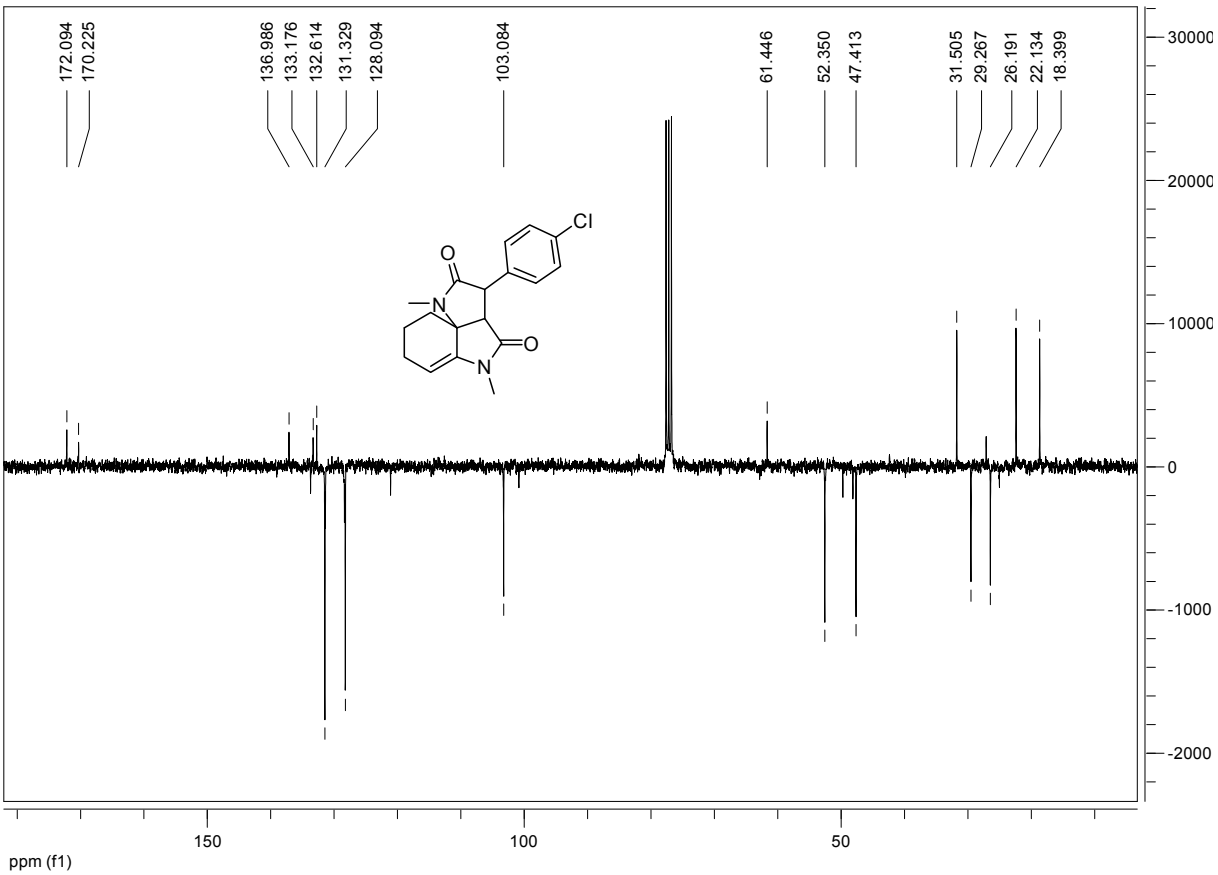
2-(4-Chlorophenyl)-*N*-methyl-2-(1'-methyl-2'-oxoindolin-3-yl)acetamide 5e



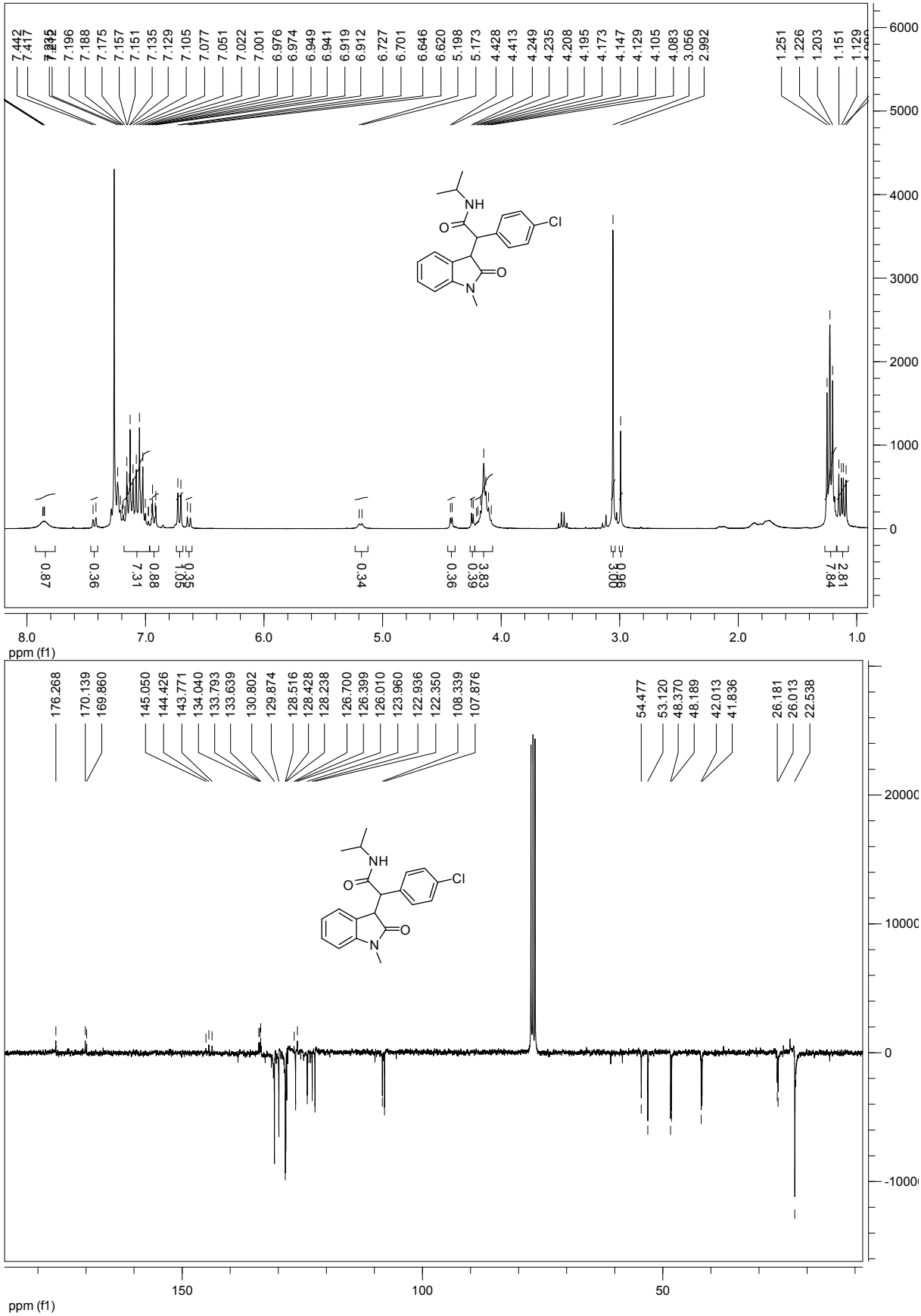


3-(4'-chlorophenyl)-1,5-dimethyl--3,3a,8,9-tetrahydro-1*H*-pyrrolo[3,2-*c*]indole-2,4 (5*H*,7*H*)-dione 7e

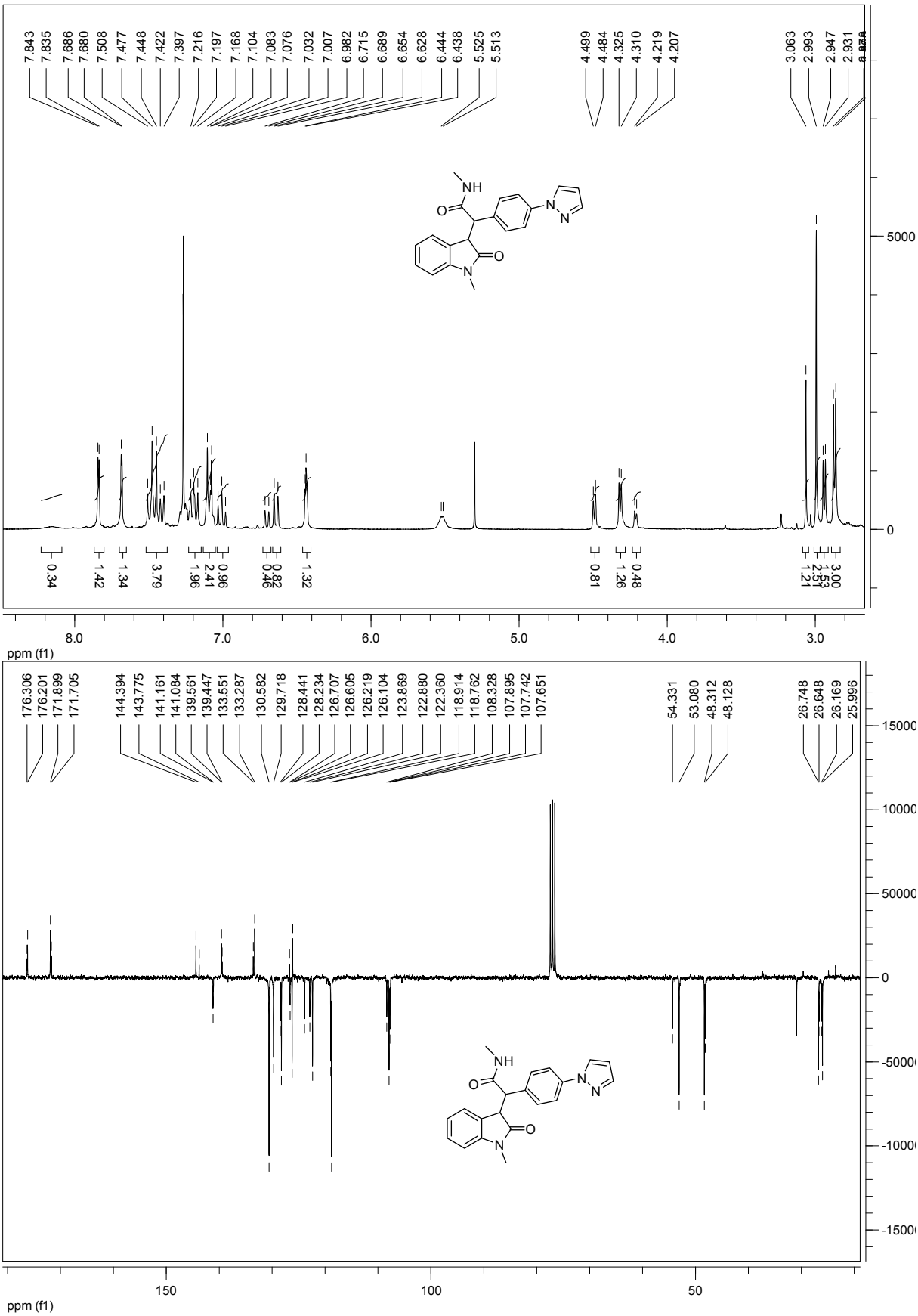




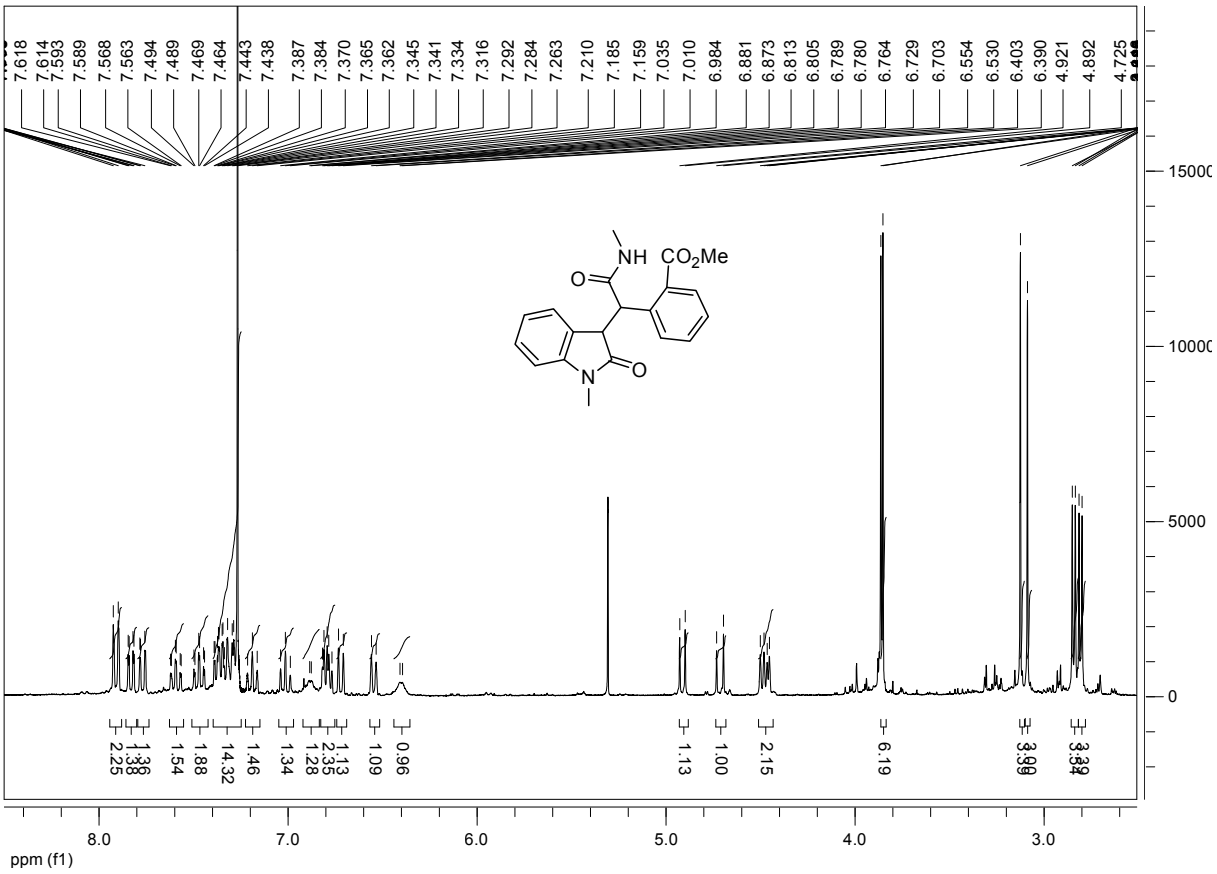
2-(4-chlorophenyl)-*N*-isopropyl-2-(1-methyl-2-oxoindolin-3-yl)acetamide <u>5f</u>

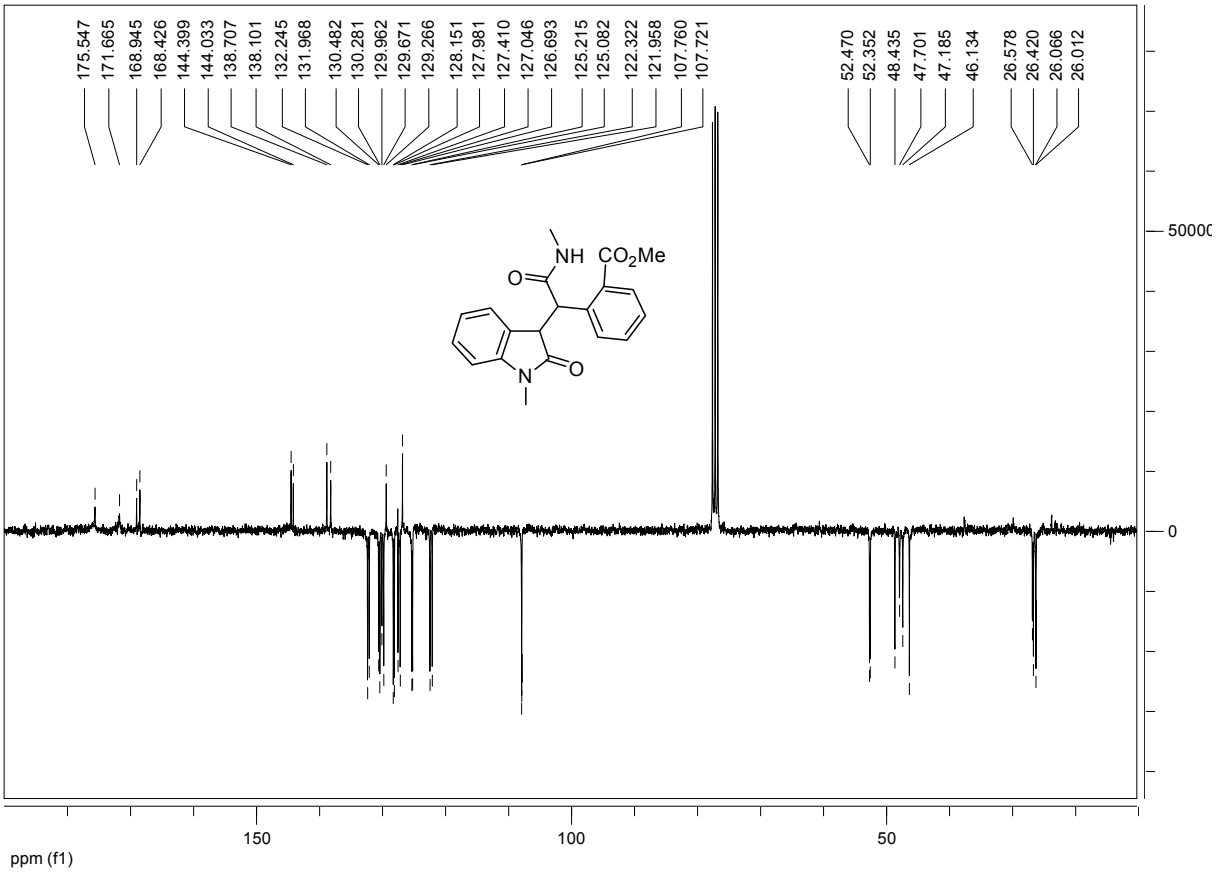


2-(4-(1*H*-pyrazol-1-yl)phenyl)-*N*-methyl-2-(1-methyl-2-oxoindolin-3-yl)acetamide 5g

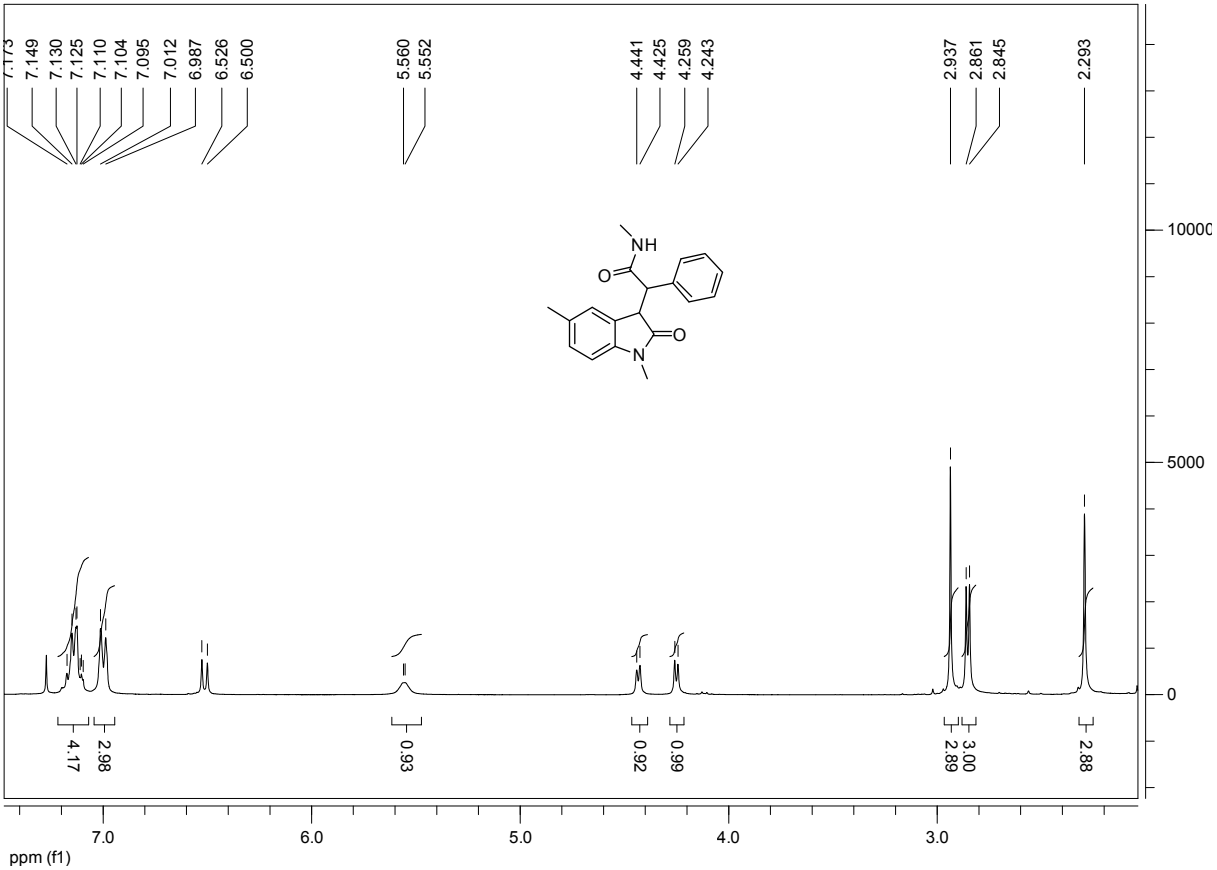


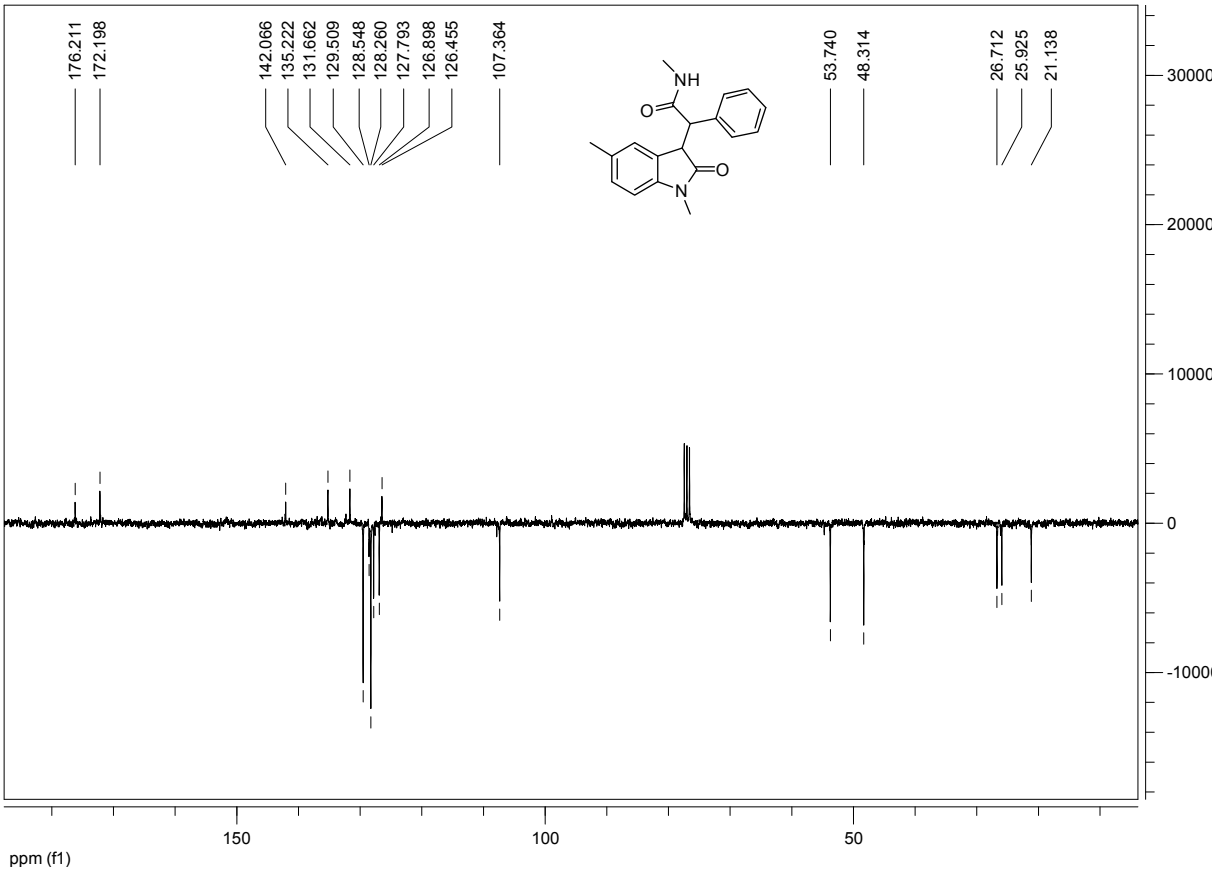
Methyl 2-[1-(1-methyl-2-oxoindolin-3-yl)-2-(methylamino)-2-oxoethyl]benzoate 5h



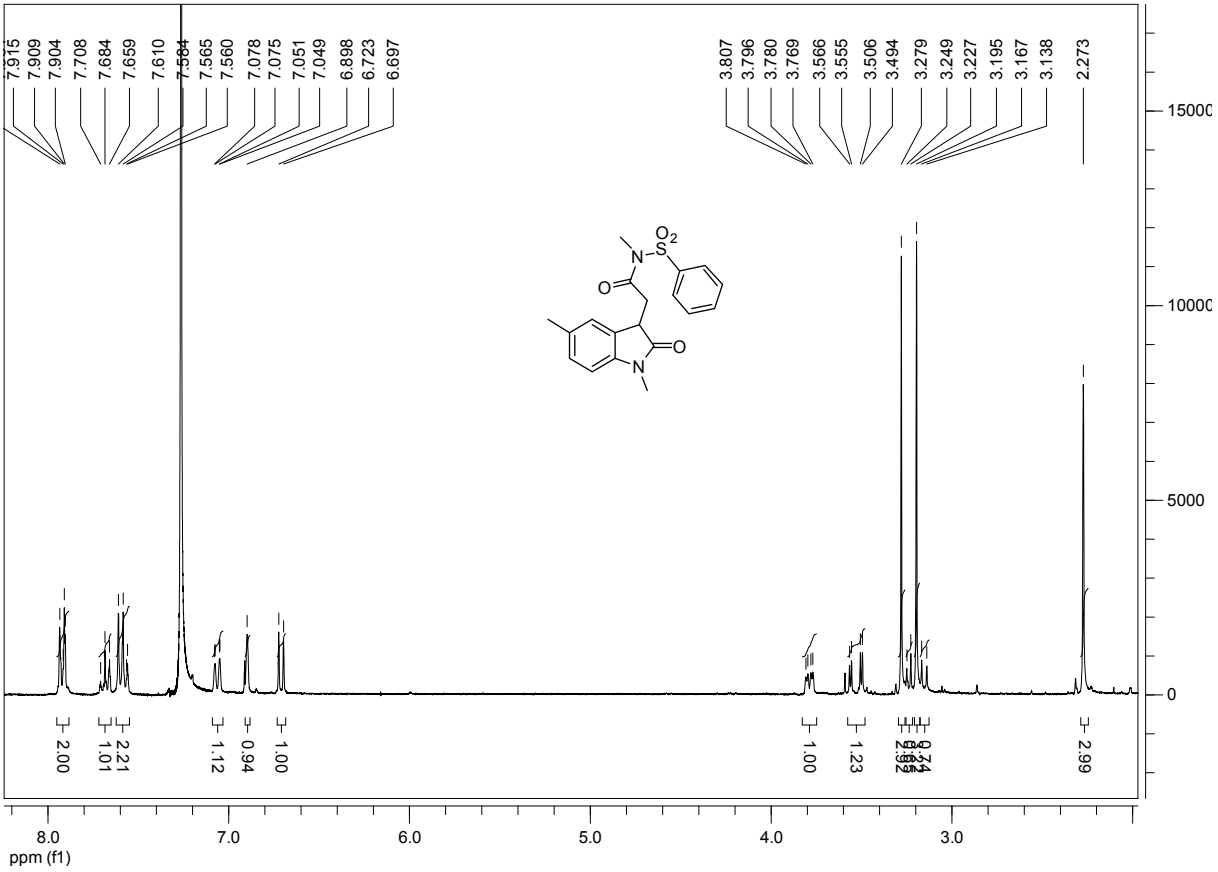


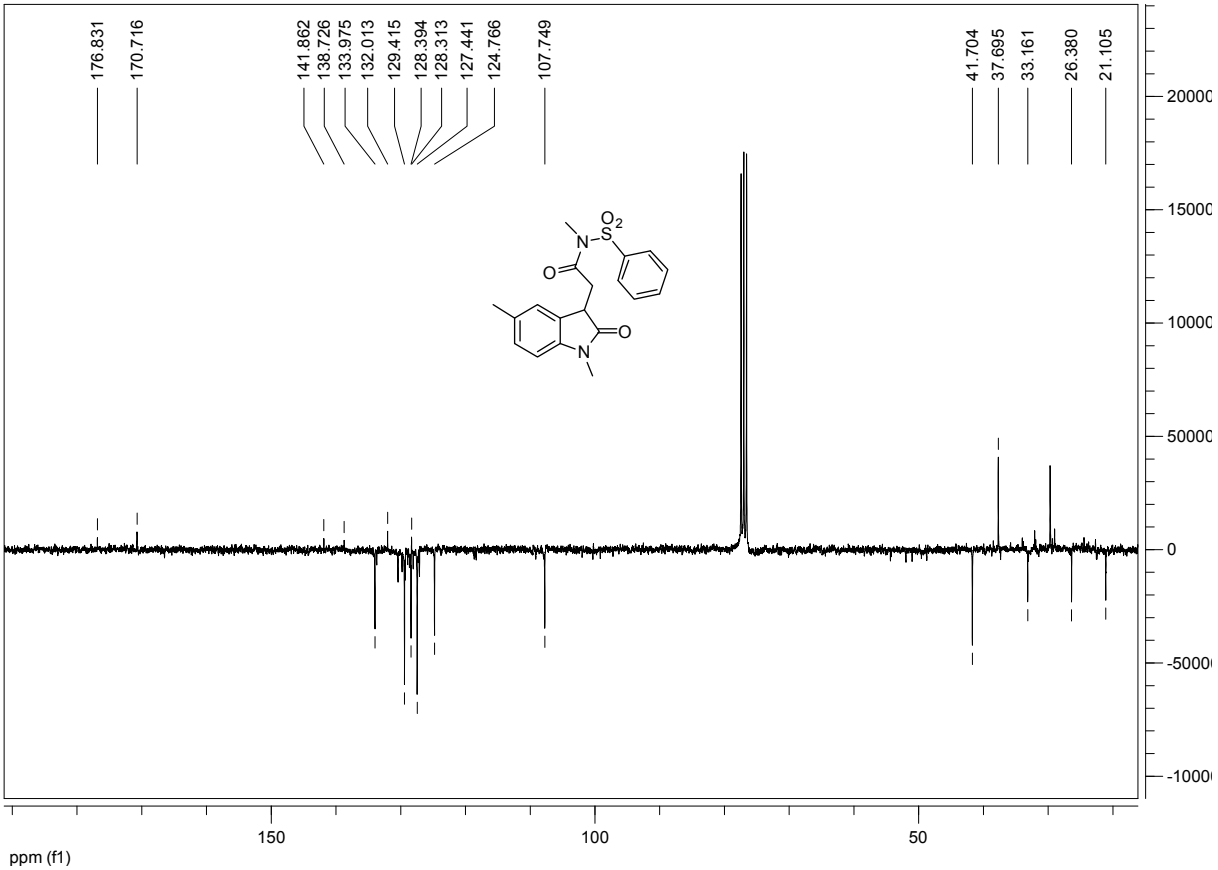
2-(1,5-dimethyl-2-oxoindolin-3-yl)-*N*-methyl-2-phenylacetamide <u>5i</u>



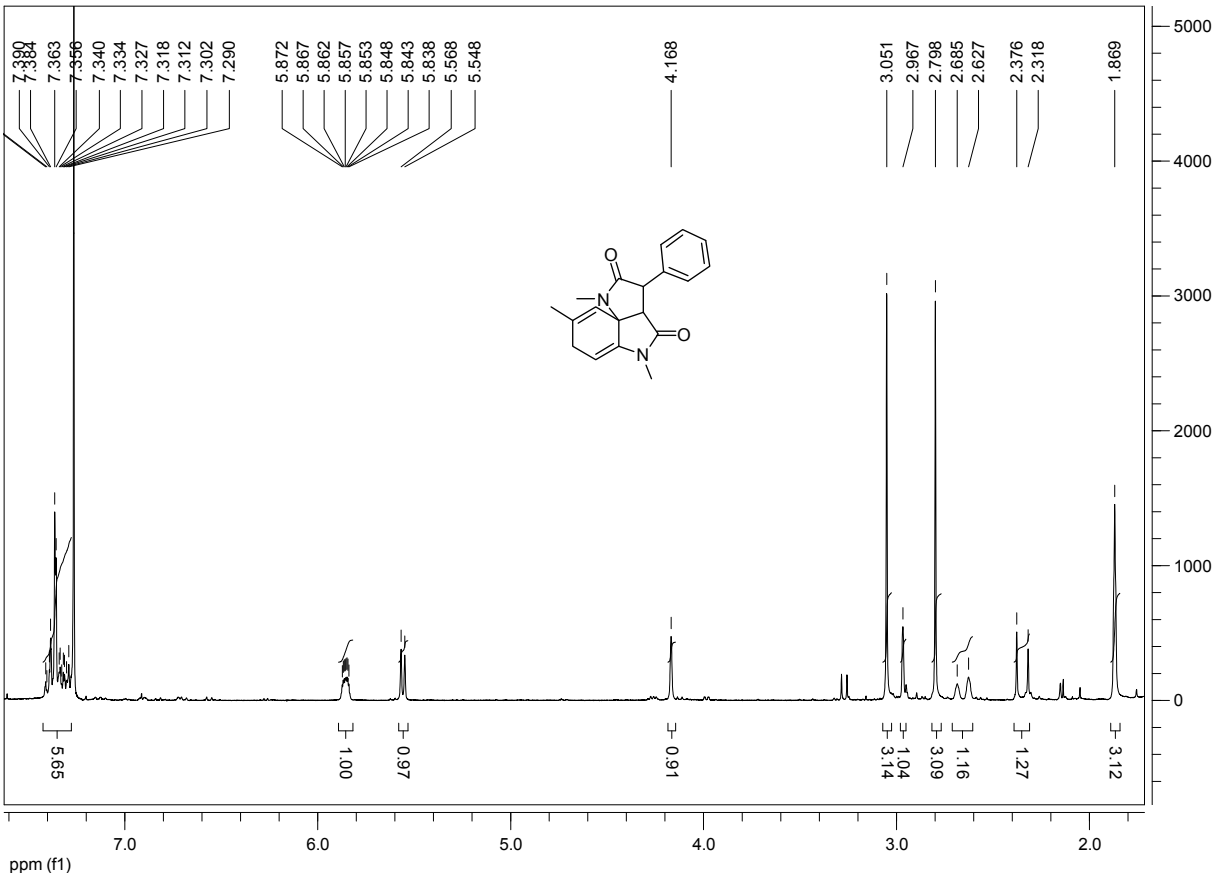


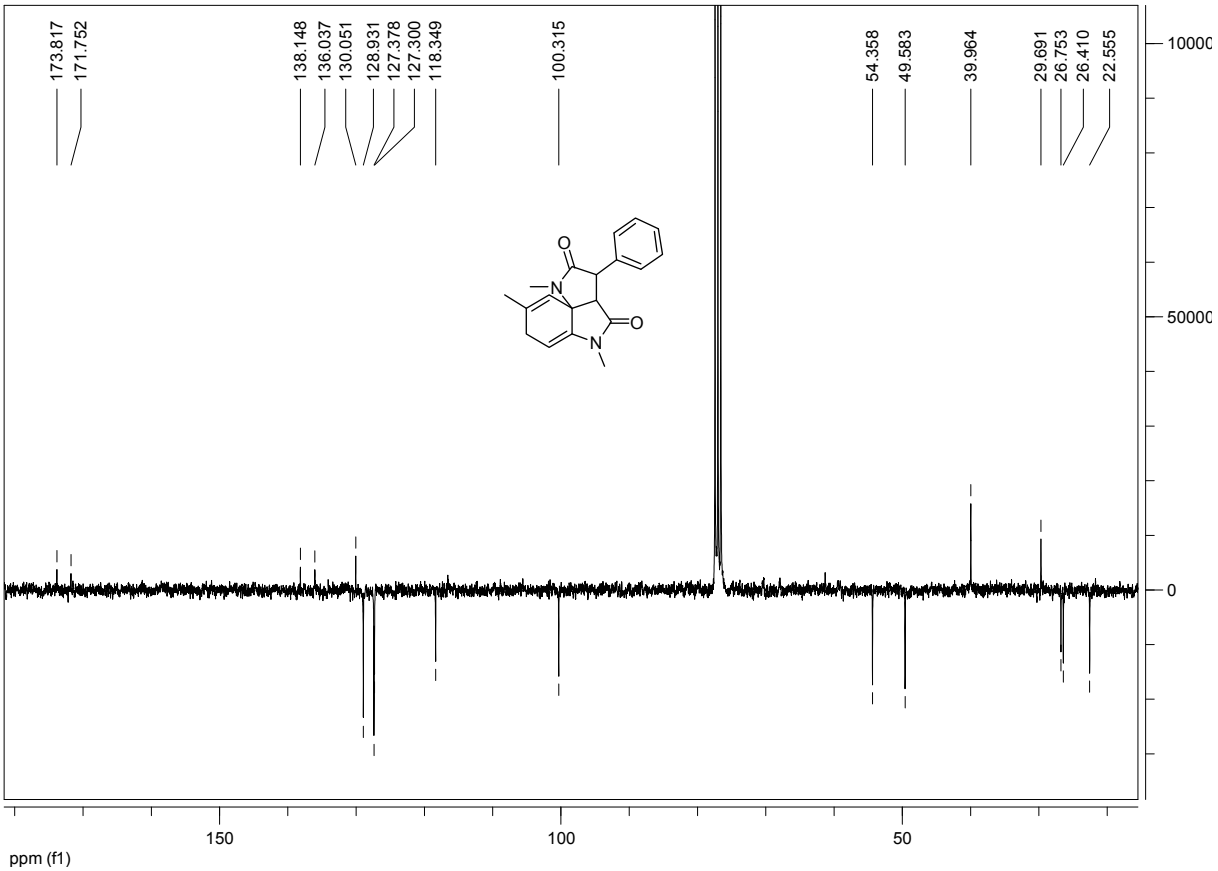
2-(1,5-dimethyl-2-oxoindolin-3-yl)-*N*-methyl-*N*-(phenylsulfonyl)acetamide <u>6i</u>



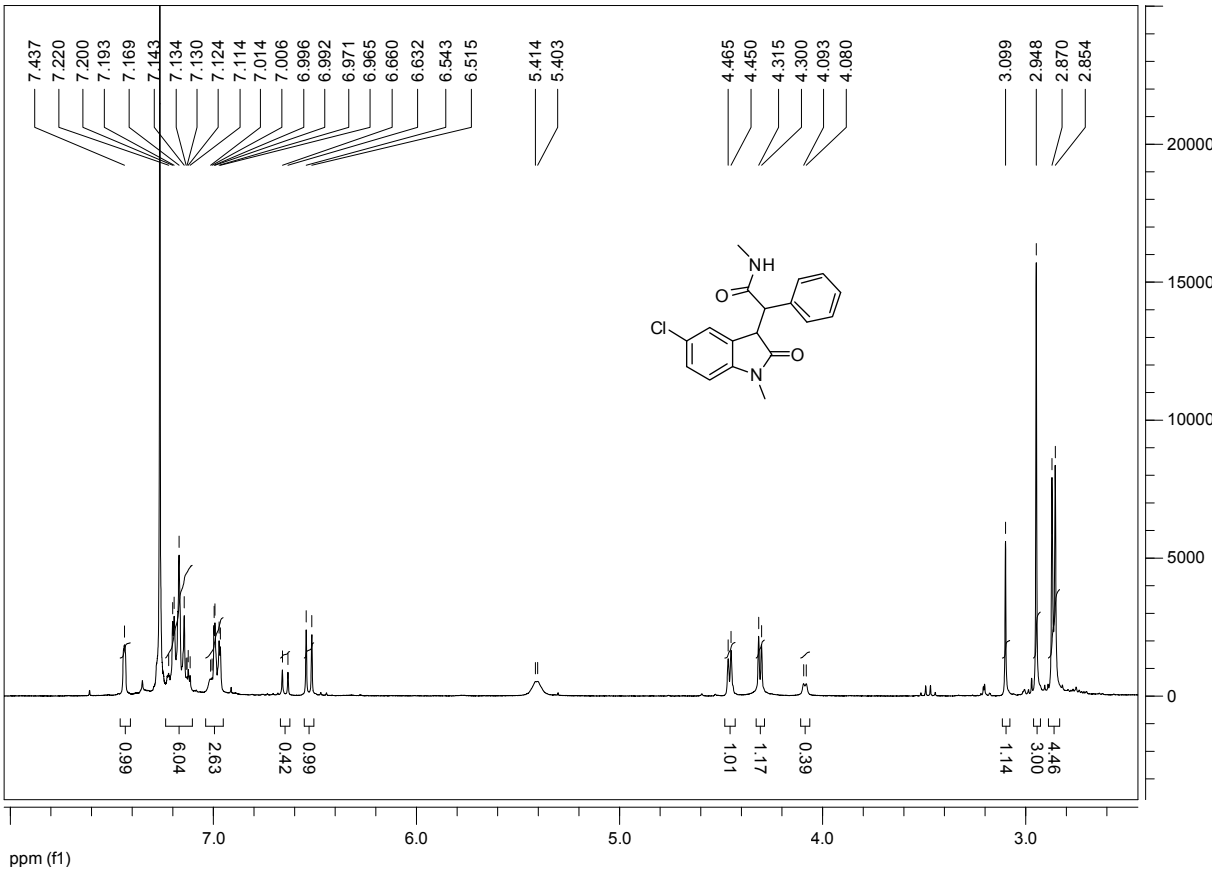


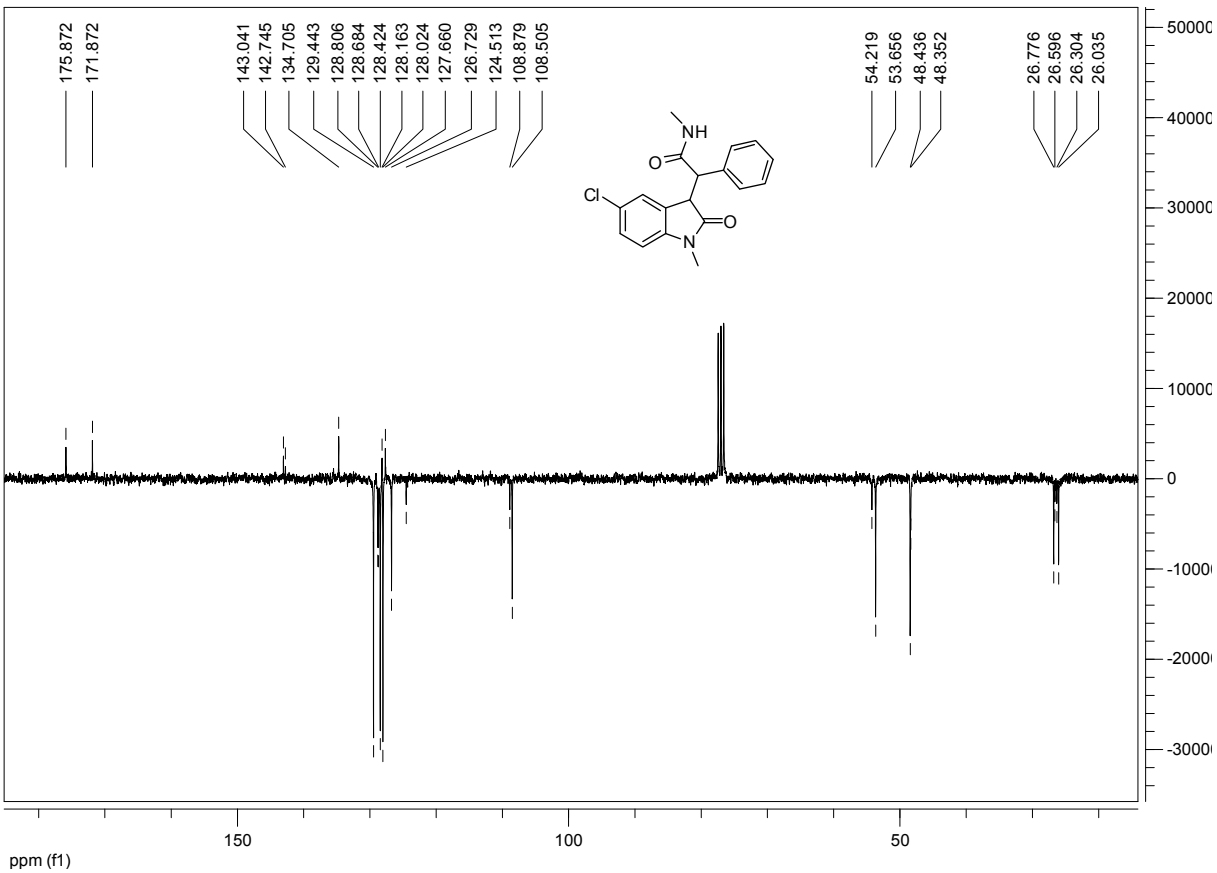
1,5,8-trimethyl-3-phenyl-3,3a-dihydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione 7i



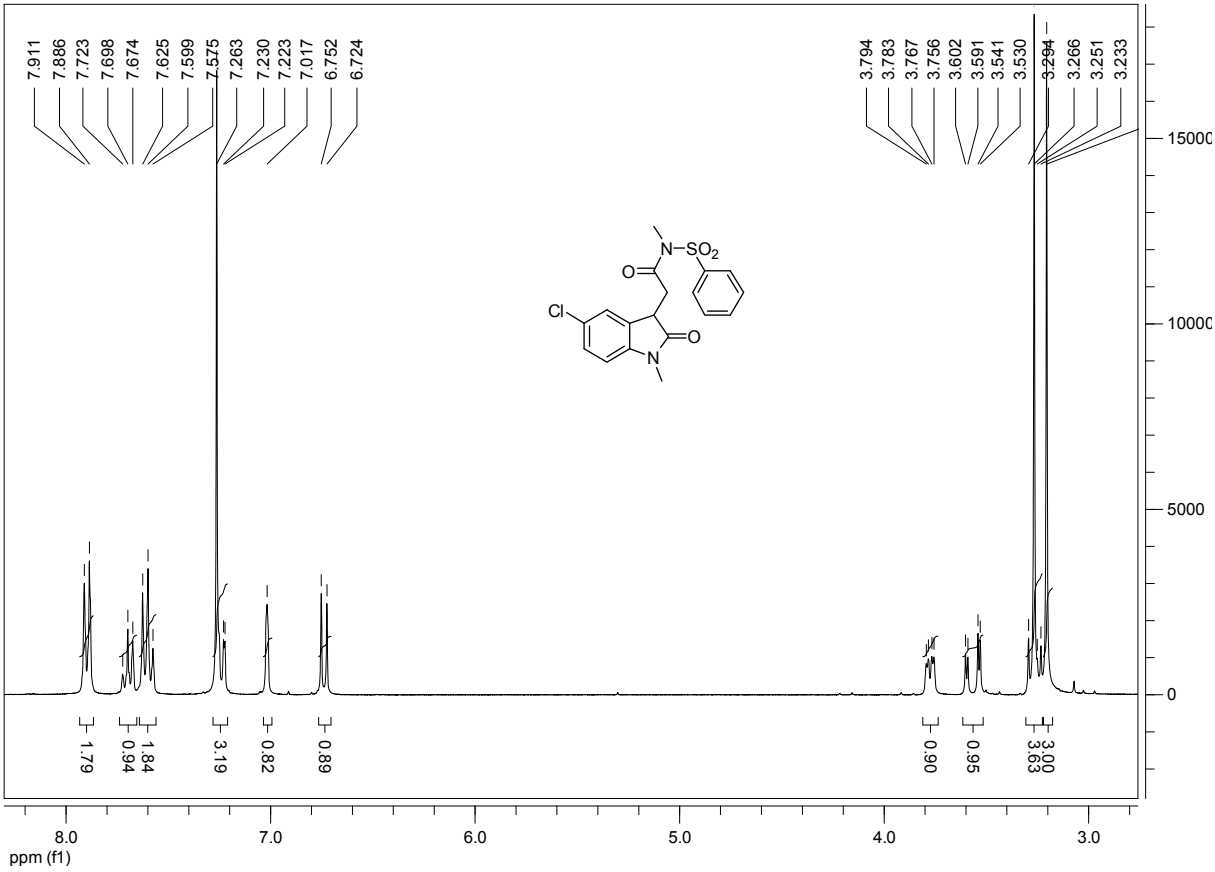


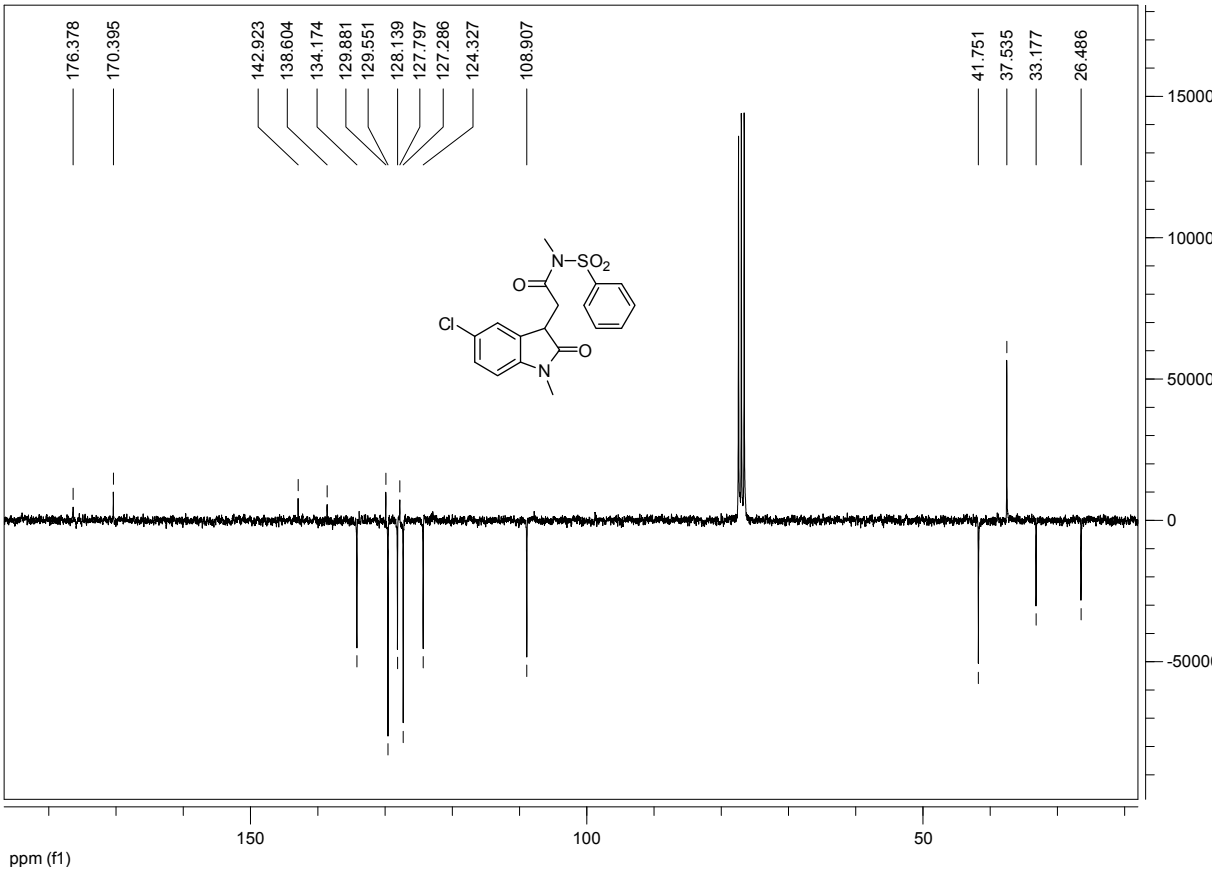
2-(5-chloro-1-methyl-2-oxoindolin-3-yl)-*N*-methyl-2-phenylacetamide 5j





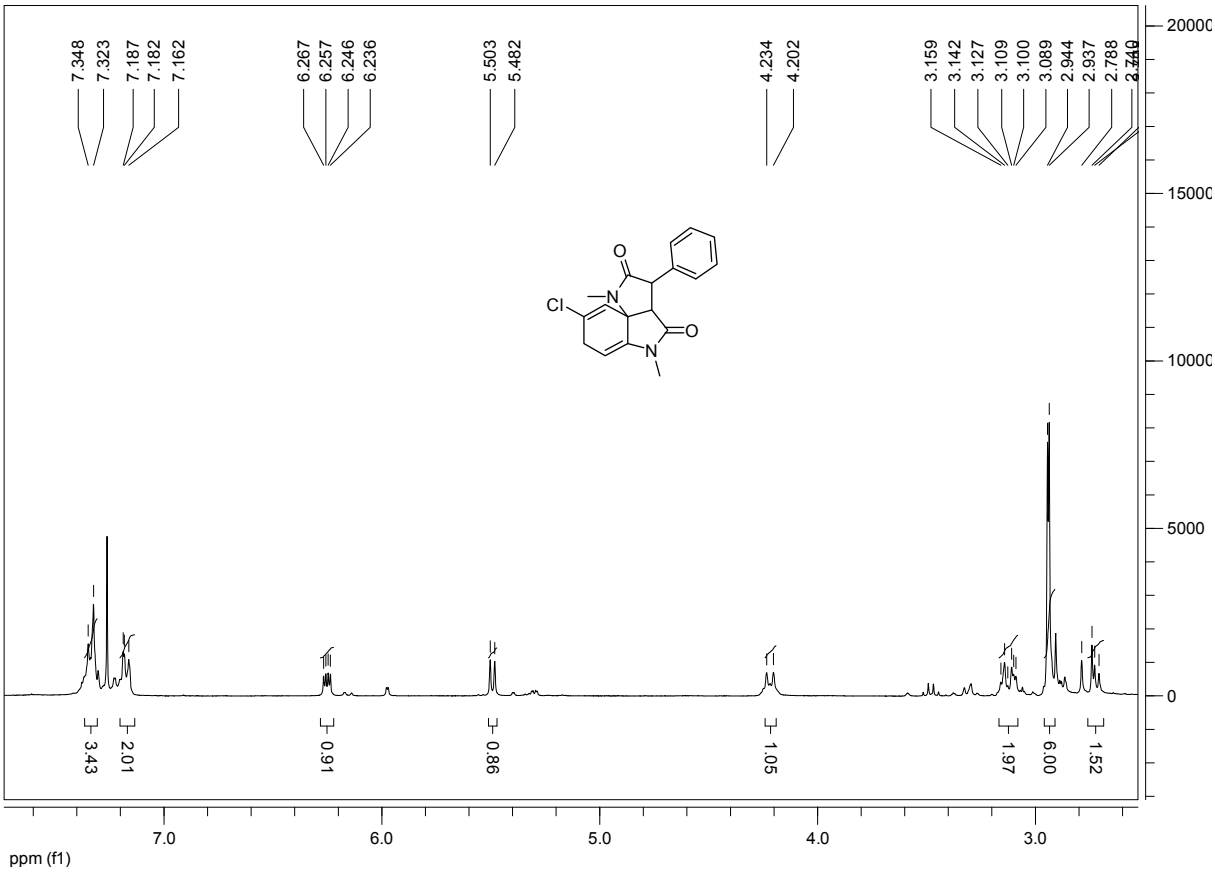
2-(5-chloro-1-methyl-2-oxoindolin-3-yl)-*N*-methyl-*N*-(phenyl sulfonyl)acetamide 6j

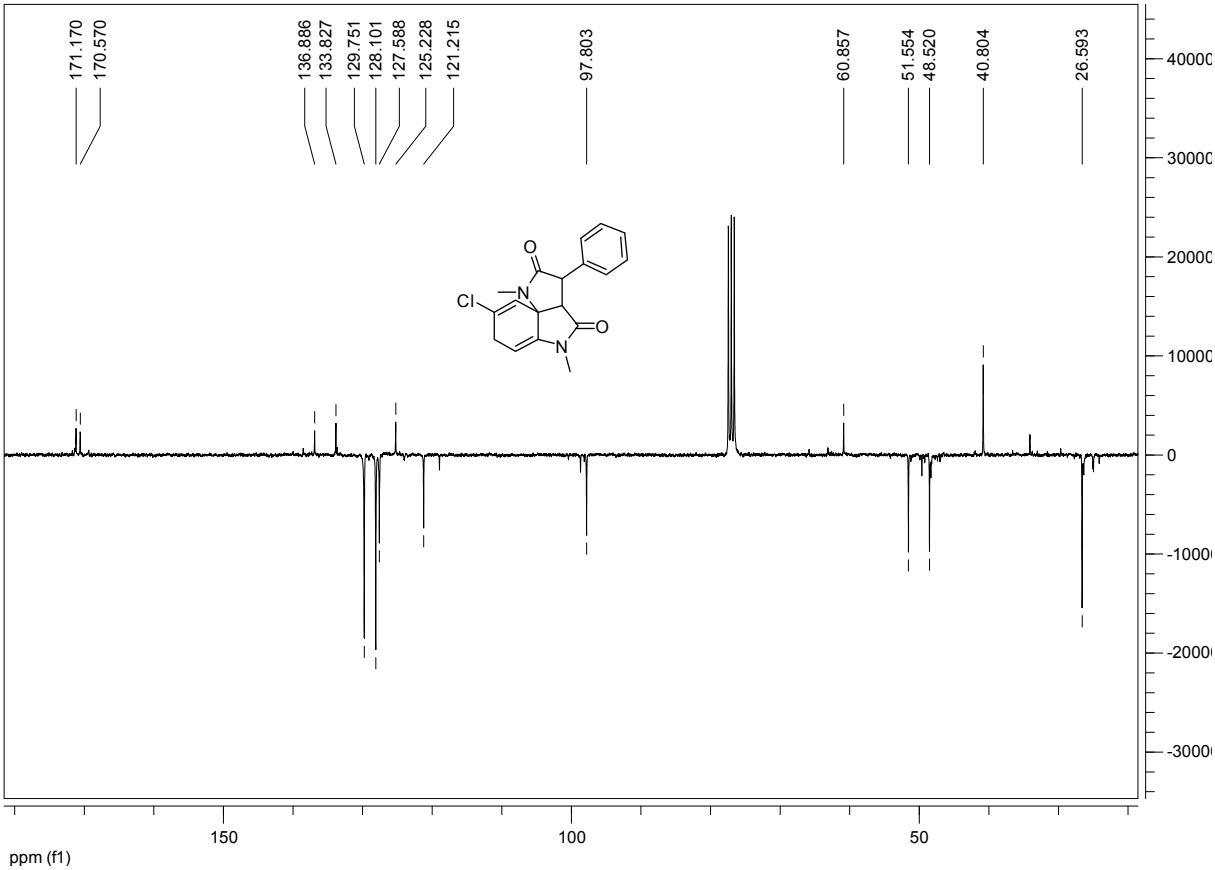




8-chloro-1,5-dimethyl-3-phenyl-3,3a-dihydro-1*H*-pyrrolo[3,2-*c*]indole-2,4(5*H*,7*H*)-dione

7i





Crystallographic data

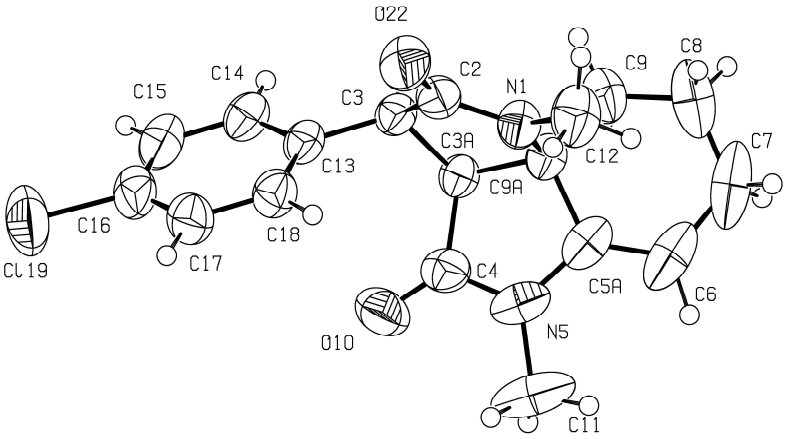


Figure 1 ORTEP view and atom labelling of **7e1**

Colourless crystals were obtained by slow diffusion of pentane on a benzene/methanol solution. Molecular formula = $C_{18}H_{19}ClN_2O_2$, Mr = 330.80, triclinic, P -1, *a* = 9.071(3), *b* = 9.395(3), *c* = 10.422(3) Å, α = 88.77(2)°, β = 72.15(3)°, γ = 77.04(2)°, *V* = 822.8(4) $Å^3$, Z = 2, Dx = 1.33 gcm^{-3}, μ = 0.24 mm^{-1}, F(000) = 348 , T = 296K.

A total of 15453 reflections were collected using a MAR345 image plate detector and Mo Kα radiation (λ = 0.71069 Å). 2792 independent refection (Rint = 0.038). The structure was solved by direct methods with SHELXS-97 [1] and refined by least square using F^2 values and anisotropic thermal parameters for non-hydrogen atoms with SHELXL-97 [1]. Some H atoms were localized by Fourier difference synthesis, the other ones were calculated with AFIX. The H atoms were included in the refinement with a common isotropic temperature factor. Final R values are: R 0.068 for 2503 observed reflections, R (all data) = 0.073, wR = 0.194, S = 1.07. The data have been deposited with the Cambridge Crystallographic Data Centre (Nr CCDC 825601)

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[1] Sheldrick GM. 1997; SHELXS-97 and SHELXL-97. Program for the Solution and Refinement of Crystal Structures. University of Göttingen, Germany.

[2] Spek, A. : PLATON, Molecular Geometry Program University of Utrecht, The Netherlands 1998.