Supporting Information:

Straightforward protocol for the efficient synthesis of varied N^1-acylated (aza)indole 2-/3-alkanoic acids and esters: optimization and scale-up

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Contents:

General. All commercial reagents, solvents and other materials were used as received without further purification. Flash chromatography was conducted on a Biotage SP1 automated flash chromatography system equipped with a fixed wavelength UV detector (λ = 254 nm) using prefabricated 'Flash KP-SIL' columns (size according to requirements). Thin-layer chromatography was performed on precoated fluorescent silica gel 60 F_{254} plates (250 um) from Whatman (Partisil® LK6D, Cat. No. 4865-821). Spots were visualized under natural light, and UV illumination at λ = 254 and 365 nm. Microwave reactions were performed in an automated Biotage Initiator Eight Synthesizer. NMR spectra were routinely recorded with a Bruker AV-400 instrument with sample changer (BACS 60) (400 MHz for ^{1}H, 100 MHz for ^{13}C) or a Bruker AV-300 system (282 MHz for ^{19}F) and calibrated with DMSO-d_6 or $CDCl_3$ as solvent and TMS as internal standard signal. Alternatively, ^{13}C NMR data were acquired on a Bruker DRX-500 instrument at 125 MHz or a Bruker AV-III-600 at 150 MHz. Chemical shifts (δ) are reported in parts per million (ppm). Coupling constants (*J*) are given in hertz (Hz). Low-resolution mass spectra were obtained on an Agilent 1200 series liquid chromatography – mass spectrometry (LCMS) system with electrospray ionization (ESI). High-resolution mass spectra (HRMS) were recorded on a Waters QTof–API–US Plus Acquity system with ES as the ion source. Analytical high-pressure liquid chromatography (HPLC) was performed on an Agilent 1200 analytical LCMS with UV detection at 214 nm and 254 nm along with ELSD detection. The purity of the target compounds was ≥95% (HPLC), if not denoted otherwise. NMR spectra were processed using Bruker TOPSPIN 2.1 or ACDLABS 1D NMR Processor software.

Synthetic procedures:

(Alternative) Synthetic procedures and detailed analytical data of compounds **2**, **9a**, **9b**, **10** and **30** have been already published elsewhere.

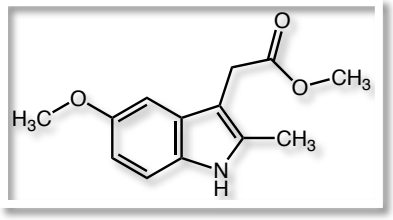
General Methods:

General Procedure A. Esterification of (2-aza-)indoleacetic acid derivatives.

General Procedure A_variant1: A reaction mixture containing the indoleacetic acid derivative (1 equivalent) and BOP-Cl (1 equivalent) in 3 mL/mmol of anhydrous CH_2Cl_2 is treated with triethylamine (2 equivalents) and aged at ambient temperature for 5 min. The mixture is combined with anhydrous methanol (0.14 mL/mmol) and then continuously stirred overnight at room temperature. Following dilution with dichloromethane (12 mL/mmol), the organic solution is washed with water (2x6 mL/mmol), dried over Na_2SO_4, and filtered. The organic filtrate is collected and concentrated *in vacuo* and the crude ester is purified by flash chromatography on silica gel (ethyl acetate/hexane gradient) to afford the title compound at first as viscous yellow oil, which stably crystallizes upon seeding and subsequent cold storage.

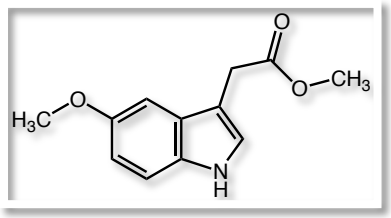
General Procedure A_variant 2: A solution of the (2-aza-)indoleacetic acid derivative (1 equivalent) in alcohol (preferentially methanol; 8.8 mL/mmol) containing 3 drops/mmol of concentrated sulfuric acid is refluxed overnight until the starting material is consumed. The progress of the conversion is monitored by TLC and/or LCMS. The reaction mixture is concentrated under reduced pressure to a low volume, and then diluted with ethyl acetate (5 mL/mmol). The organic layer is treated with water (2x3 mL/mmol) and 10% sodium bicarbonate solution (3 mL). The ethyl acetate phase is collected, dried over sodium sulfate, concentrated and then kept at high vacuum to obtain the title compound as an amorphous solid.

Examples:

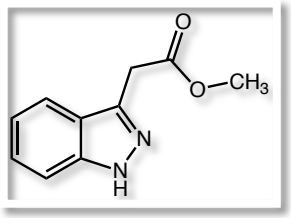


Methyl 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (9a). According to general procedure A_variant1, 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetic acid (1.0 g, 4.56 mmol) was subjected to reaction with BOP-Cl (1.16 g, 4.56 mmol), triethylamine (0.92 g, 9.12 mmol) and anhydrous methanol

(0.63 mL) in 12.5 mL of CH_2Cl_2 to afford the title compound as viscous yellow oil (1.06 g, 100%). $C_{13}H_{15}NO_3$, M_r = 233.26; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.28 (s, 3H), 3.57 (s, 3H), 3.62 (s, 2H), 3.72 (s, 3H), 6.62 (dd, *J*=2.4/8.4 Hz, 1H), 6.86 (d, *J*=2.4 Hz, 1H), 7.11 (d, *J*=8.8 Hz, 1H), 10.68 (s, 1H, indole-NH); LCMS (ESI) *t*R: 2.01 min (>99%, UV214, UV254, ELSD), *m/z*: 234.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{13}H_{15}NO_3$ $[M+H]^+$ calcd mass 234.1130, found 234.1131.



Methyl 2-(5-methoxy-1*H*-indol-3-yl)acetate (9b). According to general procedure A_variant1, 2-(5-methoxy-1*H*-indol-3-yl)acetic acid (0.5 g, 2.44 mmol) was subjected to reaction with BOP-Cl (0.62 g, 2.44 mmol), triethylamine (0.49 g, 4.87 mmol) and anhydrous methanol (0.34 mL) in 7 mL of CH_2Cl_2 to afford the title compound as viscous yellow oil (453 mg, 85%). $C_{12}H_{13}NO_3$, M_r = 219.24; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.60 (s, 3H), 3.70 (s, 2H), 3.74 (s, 3H), 6.72 (dd, *J*=2.4/8.8 Hz, 1H), 6.96 (d, *J*=2.4 Hz, 1H), 7.19 (d, *J*=2.4 Hz, 1H), 7.23 (d, *J*=8.8 Hz, 1H), 10.77 (s, 1H, indole-NH); LCMS (ESI) *t*R: 1.95 min (>99%, UV254), *m/z*: 220.1 $[M+H]^+$; HRMS (TOF, ES+) $C_{12}H_{13}NO_3$ $[M+H]^+$ calcd mass 220.0974, found 220.0975.



Methyl 2-(1*H*-indazol-3-yl)acetate (10). According to general procedure A_variant2, 2-(1*H*-indazol-3-yl)acetic acid (300 mg, 1.70 mmol) was refluxed in methanol (15 mL) for 14 h. The reaction mixture was worked up as described to quantitatively afford the title compound (250 mg, 77%). $C_{10}H_{10}N_2O_2$, M_r

= 190.20; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.62 (s, 3H), 4.01 (s, 2H), 7.09 (td, *J*=0.8/7.4 Hz, 1H), 7.33 (td, *J*=1.0/7.7 Hz, 1H), 7.48 (d, *J*=8.4 Hz, 1H), 7.69 (d, *J*=8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 33.04 (s, -CH_2-), 52.17 (s, -OCH_3), 110.49 (s, C7'), 120.29 (s), 120.43 (s), 122.20 (s, C4a'), 126.40 (s, C6'), 138.83 (s, C7a'), 141.20 (s, C3'), 171.03 (s, >C=O); LCMS (ESI) *t*R: 1.65 min (>99%, UV254), *m/z*: 191.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{10}H_{10}N_2O_2$ $[M+H]^+$ calcd mass 191.0821, found 191.0821.

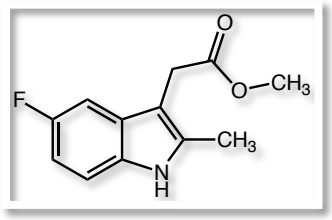
General Procedure B: (Simultanous) cyclization/esterification reaction of substituted aryl hydrazines with different ketoacids/esters.

General Procedure B_variant1: A mixture of the arylhydrazine hydrochloride (1 equivalent) and the methyl oxo(cyclo)alkanecarboxylate (1.1 equivalents) in acetic acid (1 mL/mmol) under argon is heated at 80 ˚C for 3 h. The course of the reaction is monitored by TLC. The reaction is cooled, diluted with water (2 mL/mmol) and the resulting precipitate is collected by filtration, gently washed with additional water and finally dried *in vacuo* to yield the pure cyclization product (indole alkanoic acid methyl ester). Alternatively the cold mixture is exhaustively extracted with CH_2Cl_2 (after H_2O addition), the organic solvent evaporated and the crude residue purified by flash chromatography to afford the desired solid product.

General Procedure B_variant2: A stirred mixture of the (substituted) arylhydrazine hydrochloride (1 equivalent), the respective ketoacid or its low alkyl ester (1.1 equivalents), 3 mL/mmol of methanol and 129 μL/mmol of concentrated sulfuric acid in a suitable microwave process vial is heated for 10 min at 120 ˚C under argon in a microwave synthesizer. The alcoholic solution is concentrated to about one-third of its original volume and then transferred to a phase separator syringe filled with cold water (2 mL). The organic compound is repeatedly extracted with dichloromethane (3x10 mL/mmol) and the combined organic phases are washed with brine (6-8 mL/mmol), dried over Na_2SO_4 and filtered. Removal of the organic solvent and treatment of the residue with a little hexane afford the respective

title compound as viscous mass at first that stably crystallizes upon rigorous drying in high vacuum and storage at low temperatures.

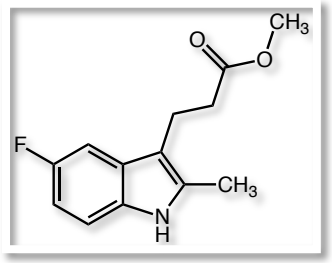
Examples:



Methyl 2-(5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (9c). According to general procedure B_variant2, the title compound was obtained from (4-fluorophenyl)hydrazine hydrochloride (50 mg, 0.31 mmol), 4-oxopentanoic acid (39.3 mg, 0.34 mmol)* and 40 μL H_2SO_4 in 1 mL methanol after 10 min at 120 °C in 84% yield (39 mg)** as brownish viscous mass. $C_{12}H_{12}FNO_2$, M_r = 221.23; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.31 (s, 3H), 3.57 (s, 3H), 3.65 (s, 2H), 6.81 (td, *J*=2.4/9.2 Hz, 1H), 7.10 (dd, *J*=2.4/10.0 Hz, 1H), 7.21 (dd, *J*=4.4/8.8 Hz, 1H), 10.97 (s, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -123.78 (5'-F); LCMS (ESI) *t*R: 2.18 min (95%, UV220, ELSD), *m/z*: 222.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{12}H_{12}FNO_2$ $[M+H]^+$ calcd mass 222.0930, found 222.0929.

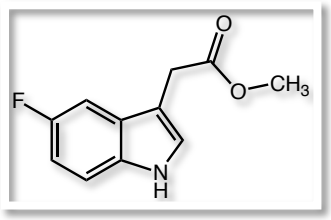
*) alternatively methyl 4-oxopentanoate (44 mg, 0.34 mmol) as cyclization reagent.

**) 59% (0.8 g) with conventional heating overnight [starting from: (4-fluorophenyl)hydrazine hydrochloride (1.0 g, 6.15 mmol), methyl 4-oxopentanoate (880 mg, 6.77 mmol) and 1.2 mL H_2SO_4 in 15 mL MeOH]

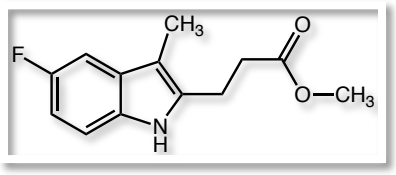


Methyl 3-(5-fluoro-2-methyl-1*H*-indol-3-yl)propanoate (9d). According to general procedure B_variant2, the title compound was obtained from (4-fluorophenyl)hydrazine hydrochloride (100 mg,

0.62 mmol), 5-oxohexanoic acid (88 mg, 0.68 mmol) and 100 μL H_2SO_4 in 3 mL methanol after 10 min at 120 °C in 76% yield (111 mg) as brownish viscous mass. $C_{13}H_{14}FNO_2$, M_r = 235.25; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.29 (s, 3H), 2.52 (t, *J*=7.6 Hz, 1H), 2.86 (t, *J*=7.4 Hz, 1H), 3.53 (s, 3H), 6.78 (td, *J*=2.4/9.2 Hz, 1H), 7.13 (dd, *J*=2.4/10.4 Hz, 1H), 7.17 (dd, *J*=4.4/8.6 Hz, 1H), 10.80 (bs, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -124.00 (5'-F); LCMS (ESI) *t*R: 2.39 min (>99%, UV220, ELSD), *m*/*z*: 236.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{13}H_{14}FNO_2$ $[M+H]^+$ calcd mass 236.1087, found 236.1086.

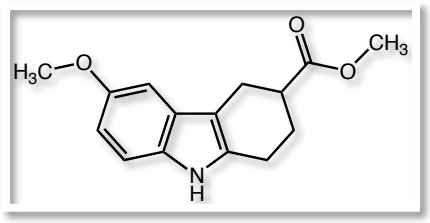


Methyl 2-(5-fluoro-1*H*-indol-3-yl)acetate (9e). According to general procedure B_variant2 (conventional heating), (4-fluorophenyl)hydrazine hydrochloride (100 mg, 0.62 mmol), 4-oxobutanoic acid (79 mg, 0.68 mmol) and 160 μL H_2SO_4 in 2 mL methanol were refluxed for 3 h under argon to afford 110 mg (86%) **9e** as brownish viscous mass. $C_{11}H_{10}FNO_2$, M_r = 207.20; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.60 (s, 3H), 3.72 (s, 2H), 6.91 (td, *J*=2.6/9.2 Hz, 1H), 7.22 (dd, *J*=2.4/10.0 Hz, 1H), 7.31-7.35 (m, 2H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -123.52 (5'-F); LCMS (ESI) *t*R: 2.16 min (>99%, ELSD), *m*/*z*: 208.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{11}H_{10}FNO_2$ $[M+H]^+$ calcd mass 208.0774, found 208.0772.

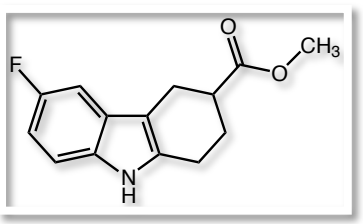


Methyl 3-(5-fluoro-3-methyl-1*H*-indol-2-yl)propanoate (14). According to general procedure B_variant2, the title compound was obtained from (4-fluorophenyl)hydrazine hydrochloride (100 mg,

0.62 mmol), 4-oxohexanoic acid (88.8 g, 0.68 mmol) and 80 μL H_2SO_4 in 3 mL methanol after 10 min at 120 ˚C in 46% yield (67 mg) as brownish viscous mass. $C_{13}H_{14}FNO_2$, M_r = 235.25; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.12 (s, 3H), 2.66 (t, *J*=8.0 Hz, 2H), 2.93 (t, *J*=7.6 Hz, 2H), 3.58 (s, 3H), 6.80 (td, *J*=2.8/9.2 Hz, 1H), 7.10 (dd, *J*=2.4/10.2 Hz, 1H), 7.20 (dd, *J*=4.6/8.6 Hz, 1H), 10.74 (bs, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -124.03 (5'-F); LCMS (ESI) *t*R: 2.58 min (>99%, UV220), *m/z*: 236.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{13}H_{14}FNO_2$ $[M+H]^+$ calcd mass 236.1087, found 236.1085.



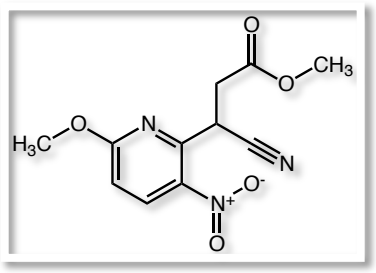
Methyl 6-methoxy-2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylate (15a). According to general procedure B_variant1, the title compound was obtained from (4-methoxyphenyl)hydrazine hydrochloride (80.0 mg, 0.46 mmol) and methyl 4-oxocyclohexanecarboxylate (85.9 mg, 0.55 mmol) in 0.5 mL glacial acetic acid after 3 h at 80 ˚C in 90% yield (107 mg) as an off-white solid. $C_{15}H_{17}NO_3$, M_r = 259.30; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.81-1.91 (m, 1H), 2.15-2.19 (m, 1H), 2.66-2.84 (m, 4H), 2.90 (dd, *J*=4.6/14.2 Hz, 1H), 3.65 (s, 3H), 3.72 (s, 3H), 6.61 (dd, *J*=2.4/8.8 Hz, 1H), 6.86 (d, *J*=2.4 Hz, 1H), 7.11 (d, *J*=8.8 Hz, 1H), 10.51 (s, 1H); LCMS (ESI) *t*R: 2.27 min (>99%, ELSD), *m/z*: 260.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{15}H_{17}NO_3$ $[M+H]^+$ calcd mass 260.1287, found 260.1285.



Methyl 6-fluoro-2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylate (15b). According to general procedure B_variant2, the title compound was obtained from (4-fluorophenyl)hydrazine hydrochloride

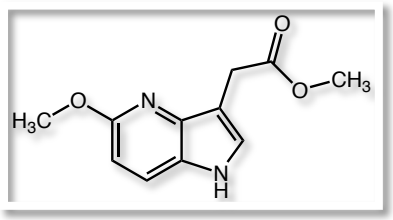
(100 mg, 0.62 mmol), 4-oxocyclohexanecarboxylic acid (96.2 g, 0.68 mmol) and 80 μL H_2SO_4 in 3 mL methanol after 10 min at 120 ˚C. When the alcoholic solution was progressively concentrated, an off-white product precipitation formed, which was filtered off and carefully washed with a little cold water. Alternatively the reaction mixture was poured onto chopped ice and water and the precipitation was collected by filtration to afford the title compound in 100% yield (152 mg). $C_{14}H_{14}FNO_2$, M_r = 247.26; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.84-1.92 (m, 1H), 2.16-2.20 (m, 1H), 2.66-2.85 (m, 4H), 2.90 (dd, *J*=4.8/14.6 Hz, 1H), 3.65 (s, 3H), 6.80 (td, *J*=2.8/9.2 Hz, 1H), 7.10 (dd, *J*=2.8/10.0 Hz, 1H), 7.20 (dd, *J*=4.6/8.6 Hz, 1H) 10.80 (bs, 1H); LCMS (ESI) *t*R: 2.54 min (>99%, UV254, ELSD), *m/z*: 248.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{14}H_{14}FNO_2$ $[M+H]^+$ calcd mass 248.1087, found 248.1086.

Synthesis of the 4-aza-indoleacetic acid ester derivative:



Methyl 3-cyano-3-(6-methoxy-3-nitropyridin-2-yl)propanoate (16). Under argon, 2-(6-methoxy-3-nitropyridin-2-yl)acetonitrile (500 mg, 2.59 mmol) was dissolved in acetonitrile (11 mL) in a flame dried round-bottom flask. Two equivalents of anhydrous potassium carbonate (0.72 g, 5.18 mmol) were added to this solution, and methyl 2-bromoacetate (245 μL, 2.59 mmol) was introduced dropwise. The reaction mixture was stirred at room temperature until the starting materials were consumed, approximately four hours. The crude material was combined with CH_2Cl_2 and inorganic debris was filtered off using a phase separator syringe equipped with a sodium sulfate drying cartridge. The filter cake was washed with small quantities of CH_2Cl_2 and all organic filtrates were collected and combined. The organic solvents were evaporated *in vacuo* at 40 ˚C and the resulting viscous dark brownish oil

either directly used in the next reaction step or purified by flash chromatography on a short silica-gel column (ethyl acetate/hexane gradient) prior to it's converion. $C_{11}H_{11}N_3O_5$, M_r = 265.22; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.15-3.29 (m, 2H), 3.64 (s, 3H), 3.99 (s, 3H), 5.22 (t, *J*=7.2 Hz, 1H), 7.08 (d, *J*=9.2 Hz, 1H), 8.48 (d, *J*=8.8 Hz, 1H); LCMS (ESI) *t*R: 1.98 min (96-100%, UV220, UV254, ELSD), *m/z*: 266.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{11}H_{11}N_3O_5$ $[M+H]^+$ calcd mass 266.0777, found 266.0775.



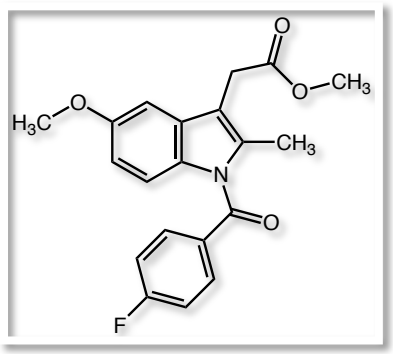
Methyl 2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)acetate (17). A 2 mL microwave process vial with a stir bar was charged with crude methyl 3-cyano-3-(6-methoxy-3-nitropyridin-2-yl)propanoate **16** (50 mg, 0.19 mmol), 10% Pd/C (5 mol %, 20 mg, 0.01 mmol), and methanol (1.5 mL). An excess of 1,4-cyclohexadiene (91 mg, 1.13 mmol) was added and the vessel flooded with argon, capped and heated under microwave conditions at 120 ˚C for 5 min. The reaction mixture was filtered through Celite® and the solvent was evaporated *in vacuo*. The crude material was purified by flash chromatography (SiO_2, ethyl acetate/hexane gradient) to yield the product as greenish oil (25 mg, 60%). $C_{11}H_{12}N_2O_3$, M_r = 220.22; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.61 (s, 3H), 3.72 (s, 2H), 3.83 (s, 3H), 6.53 (d, *J*=8.8 Hz, 1H), 7.38 (d, *J*=2.8 Hz, 1H), 7.66 (d, *J*=8.4 Hz, 1H), 11.01 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 29.41 (s, -CH_2-), 51.86 (s, -C(O)OCH_3), 52.83 (s, -OCH_3), 104.86 (s, C6'), 107.19 (s, C3'), 122.78 (s, C2'), 124.60 (s, C7a'), 126.80 (s, C7'), 141.29 (s, C3a'), 159.16 (s, C5'), 172.47 (s, >C=O); LCMS (ESI) *t*R: 0.69 min (>97%, UV220, ELSD), *m/z*: 221.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{11}H_{12}N_2O_3$ $[M+H]^+$ calcd mass 221.0926, found 221.0926.

General Procedure C: N^1-acylation reaction.

General procedure C_variant1: The indole precursor (1 equivalent) and fresh NaH (1.2 equivalents) are stirred in anhydrous DMF (4 mL/mmol) at 0 ˚C under argon for 30 min, at which time the acyl chloride reagent (1.2 equivalents) is added. The reaction mixture is stirred overnight at room temperature and is then poured into cold water (8 mL/mmol). The organic compound is immediately extracted with dichloromethane (2x8 mL/mmol), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue is purified on silica (ethyl acetate/hexane gradient) and, if necessary, recrystallized from hexane.

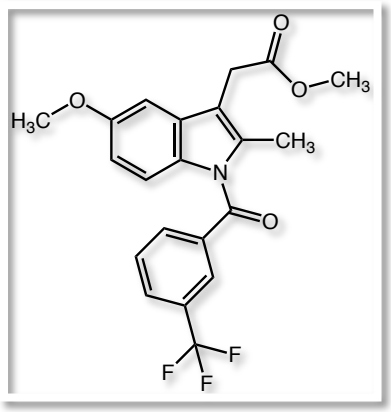
General procedure C_variant2: To a cooled solution (ice bath, 0-5 ˚C) of the (aza)indole precursor (1 equivalent) in anhydrous THF (6 mL/mmol) is added ^{t}BuONa (2 M in THF, 1.2 equivalents), and the mixture is stirred for 25 min at the low temperature. Then the acylation reagent (preferentially: acyl chloride) (1.2 equiv.) is added and the reaction is aged overnight at room temperature. The reaction is quenched with saturated aqueous NH_4Cl (provided in a commercial phase separator syringe) and the organic compound is extracted with CH_2Cl_2, washed with brine and water, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue is subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the title compound as yellow oil, which usually stably crystallizes upon drying at high vacuum and subsequent storage at -20 ˚C.

Examples:

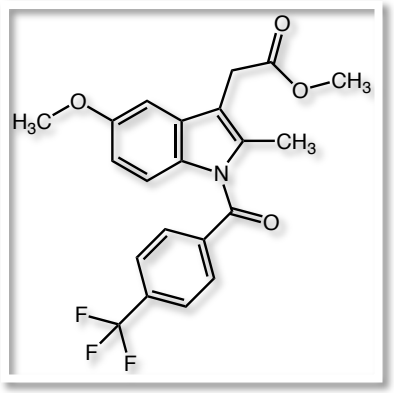


Methyl 2-(1-(4-fluorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (18a). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-2-

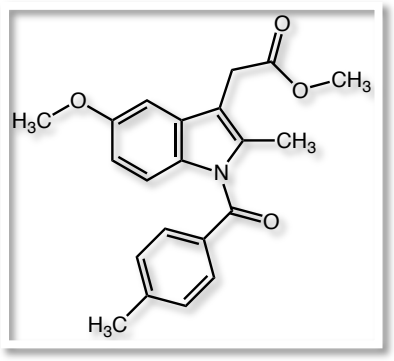
methyl-1*H*-indol-3-yl)acetate (80 mg, 0.34 mmol), 4-fluorobenzoyl chloride (65.3 mg, 0.41 mmol) and ^{t}BuONa (2 M in THF, 206 μL, 0.41 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 25% yield (31 mg). $C_{20}H_{18}FNO_4$, M_r = 355.36; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.21 (s, 3H), 3.62 (s, 3H), 3.75 (s, 3H), 3.78 (s, 2H), 6.70 (dd, *J*=2.6/9.0 Hz, 1H), 6.87 (d, *J*=8.8 Hz, 1H), 7.07 (d, *J*=2.4 Hz, 1H), 7.38-7.43 (m, 2H), 7.71-7.75 (m, 2H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -104.11 (4-F-benzoyl); LCMS (ESI) *t*R: 2.64 min (>95%, ELSD), *m/z*: 356.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{18}FNO_4$ $[M+H]^+$ calcd mass 356.1298, found 356.1297.



Methyl 2-(5-methoxy-2-methyl-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (18b). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.34 mmol), 4-fluorobenzoyl chloride (73 mg, 0.35 mmol) and ^{t}BuONa (2 M in THF, 175 μL, 0.35 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 32% yield (44 mg). $C_{21}H_{18}F_3NO_4$, M_r = 405.37; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.17 (s, 3H), 3.62 (s, 3H), 3.75 (s, 3H), 3.78 (s, 2H), 6.71 (dd, *J*=2.6/9.0 Hz, 1H), 6.93 (d, *J*=9.2 Hz, 1H), 7.03 (d, *J*=2.4 hz, 1H), 7.80 (t, *J*=7.8 Hz, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 8.00 (s, 1H), 8.06 (d, *J*=8.0 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.43 (*m*-CF_3); LCMS (ESI) *t*R: 2.82 min (>95%, ELSD), *m/z*: 406.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{18}F_3NO_4$ $[M+H]^+$ calcd mass 406.1266, found 406.1266.

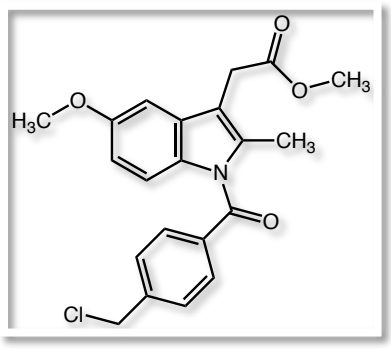


Methyl 2-(5-methoxy-2-methyl-1-(4-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (18c). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.34 mmol), 4-(trifluoromethyl)benzoyl chloride (85.8 mg, 0.41 mmol) and ^{t}BuONa (2 M in THF, 206 μL, 0.41 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 33% yield (46 mg). $C_{21}H_{18}F_3NO_4$, M_r = 405.37; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.16 (s, 3H), 3.62 (s, 3H), 3.75 (s, 3H), 3.78 (s, 2H), 6.73 (dd, *J*=2.6/9.0 Hz, 1H), 6.98 (d, *J*=9.2 Hz, 1H), 7.03 (d, *J*=2.4 Hz, 1h), 7.86 (d, *J*=8.4 Hz, 2H), 7.94 (d, *J*=8.4 Hz, 2H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.61 (*p*-CF_3); LCMS (ESI) *t*R: 2.85 min (>95%, ELSD), *m*/*z*: 406.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{18}F_3NO_4$ $[M+H]^+$ calcd mass 406.1266, found 406.1266.

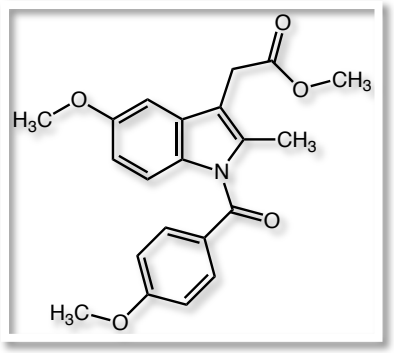


Methyl 2-(5-methoxy-2-methyl-1-(4-methylbenzoyl)-1*H*-indol-3-yl)acetate (18d). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.34 mmol), 4-methylbenzoyl chloride (63.6 mg, 0.41 mmol) and

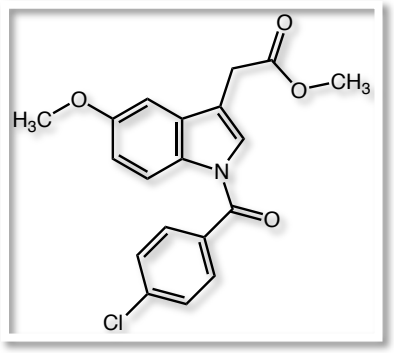
^{t}BuONa (2 M in THF, 206 μL, 0.41 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 57% yield (68.5 mg). $C_{21}H_{21}NO_4$, M_r = 351.40; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.22 (s, 3H), 2.42 (s, 3H), 3.62 (s, 3H), 3.74 (s, 3H), 3.77 (s, 2H), 6.68 (dd, *J*=2.6/9.0 Hz, 1H), 6.85 (d, *J*=8.8 Hz, 1H), 7.01 (d, *J*=2.4 Hz, 1H), 7.37 (d, *J*=8.0 Hz, 2H), 7.54 (pseudo-d, *J*=8.4 Hz, 2H); LCMS (ESI) *t*R: 2.74 min (>95%, ELSD), *m/z*: 352.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{21}NO_4$ $[M+H]^+$ calcd mass 352.1549, found 352.1548.



Methyl 2-(1-(4-(chloromethyl)benzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (18e). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.34 mmol), 4-(chloromethyl)benzoyl chloride (77.8 mg, 0.41 mmol) and ^{t}BuONa (2 M in THF, 206 μL, 0.41 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 42% yield (56 mg). $C_{21}H_{20}ClNO_4$, M_r = 385.84; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.19 9s, 3H), 3.62 (s, 3H), 3.75 (s, 3H), 3.78 (s, 2H), 4.88 (s, 2H), 6.69 (dd, *J*=2.6/9.0 Hz, 1H), 6.90 (d, *J*=9.2 Hz, 1H), 7.02 (d, *J*=2.4 Hz, 1H), 7.61-7.67 (m, 4H); LCMS (ESI) *t*R: 2.73 min (>95%, ELSD), *m/z*: 386.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{20}ClNO_4$ $[M+H]^+$ calcd mass 386.1159, found 386.1157.

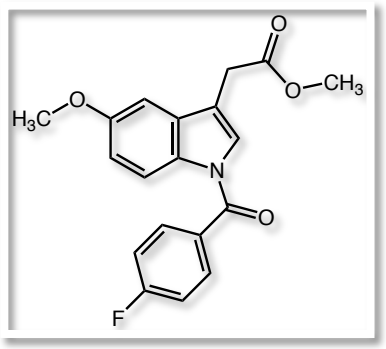


Methyl 2-(5-methoxy-1-(4-methoxybenzoyl)-2-methyl-1*H*-indol-3-yl)acetate (18f). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.34 mmol), 4-methoxybenzoyl chloride (70.2 mg, 0.41 mmol) and ^{t}BuONa (2 M in THF, 206 μL, 0.41 mmol) in anhydrous THF (2.5 mL). The crude material was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) and the residue (63 mg) recrystallized from EtOAc/hexane to afford the title compound in 32% yield (40 mg). $C_{21}H_{21}NO_5$, M_r = 367.40; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.24 (s, 3H), 3.62 (s, 3H), 3.75 (s, 3H), 3.77 (s, 2H), 3.86 (s, 3H), 6.68 (dd, *J*=2.6/9.0 Hz, 1H), 6.85 (d, *J*=9.2 Hz, 1H), 7.01 (d, *J*=2.4 Hz, 1H), 7.08-7.11 (m, 2H), 7.60-7.64 (m, 2H); LCMS (ESI) *t*R: 2.64 min (>95%, ELSD), *m/z*: 368.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{21}NO_5$ $[M+H]^+$ calcd mass 368.1498, found 368.1499.

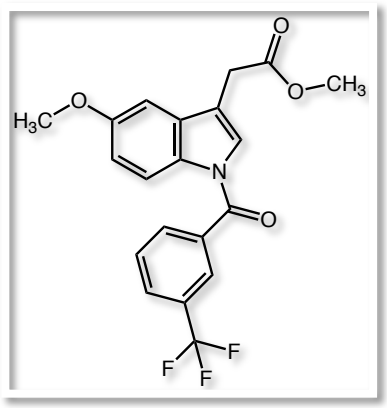


Methyl 2-(1-(4-chlorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetate (18g). According to general procedure C_variant1, methyl 2-(5-methoxy-1*H*-indol-3-yl)acetate (60 mg, 0.27 mmol) was subjected to reaction with 4-chlorobenzoyl chloride (57 mg, 0.33 mmol). The crude product was purified by flash

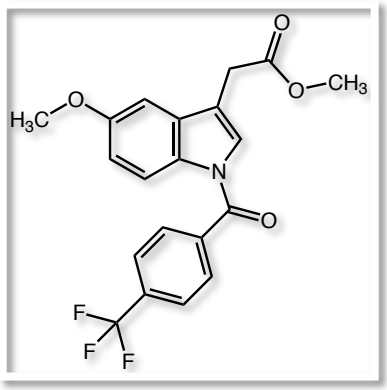
chromatography (SiO_2, ethyl acetate/hexane gradient) and recrystallized from hexane to afford 18 mg (18%) of the title compound as an off-white solid. $C_{19}H_{16}ClNO_4$, M_r = 357.79; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.61 (s, 3H), 3.78 (s, 2H), 3.81 (s, 3H), 7.00 (dd, *J*=2.4/9.0 Hz, 1H), 7.12 (d, *J*=2.4 Hz, 1H), 7.35 (s, 1H), 7.65-7.77 (m, 4H), 8.17 (d, *J*=8.8 Hz, 1H); LCMS (ESI) *t*R: 2.81 min (>99%, ELSD), *m/z*: 358.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{16}ClNO_4$ $[M+H]^+$ calcd mass 358.0846, found 358.0844.



Methyl 2-(1-(4-fluorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetate (18h). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-1*H*-indol-3-yl)acetate (80 mg, 0.36 mmol), 4-fluorobenzoyl chloride (69.4 mg, 0.44 mmol) and ^{t}BuONa (2 M in THF, 219 μL, 0.44 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 22% yield (27 mg). $C_{19}H_{16}FNO_4$, M_r = 341.33; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.61 (s, 3H, -CO-OCH_3), 3.79 (s, 2H, -CH_2-), 3.81 (s, 3H, -OCH_3), 6.99 (dd, *J*=2.4/8.8 Hz, 1H), 7.12 (d, *J*=2.8 Hz, 1H), 7.36 (s, 1H), 7.41-7.46 (m, 2H), 7.79-7.83 (m, 2H), 8.16 (d, *J*=8.8 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -105.87 (4-F-benzoyl); LCMS (ESI) *t*R: 2.62 min (>95%, ELSD), *m/z*: 342.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{16}FNO_4$ $[M+H]^+$ calcd mass 342.1142, found 342.1140.

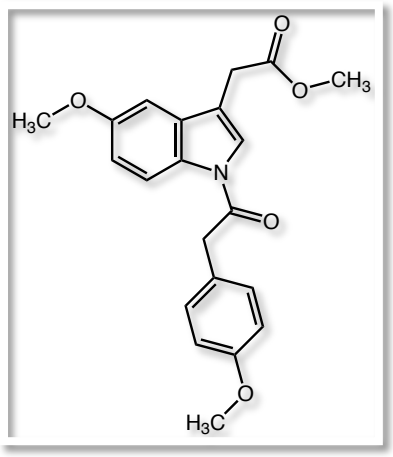


Methyl 2-(5-methoxy-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (18i). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-methoxy-1*H*-indol-3-yl)acetate (80 mg, 0.36 mmol), 3-(trifluoromethyl)benzoyl chloride (91.3 mg, 0.44 mmol) and NaH (17.5 mg, 0.44 mmol) in anhydrous DMF (1 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 13% yield (18.5 mg). $C_{20}H_{16}F_3NO_4$, M_r = 391.34; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.61 (s, 3H), 3.79 (s, 2H), 3.81 (s, 3H), 7.01 (dd, *J*=2.6/9.0 Hz, 1H), 7.13 (d, *J*=2.4 Hz, 1H), 7.31 (s, 1H), 7.83 (t, *J*=7.8 Hz, 1H), 8.01-8.05 (m, 2H), 8.09 (s, 1H), 8.19 (d, *J*=8.8 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.35 (*m*-CF_3); LCMS (ESI) *t*R: 2.75 min (>95%, ELSD), *m/z*: 392.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{16}F_3NO_4$ $[M+H]^+$ calcd mass 392.1110, found 392.1109.



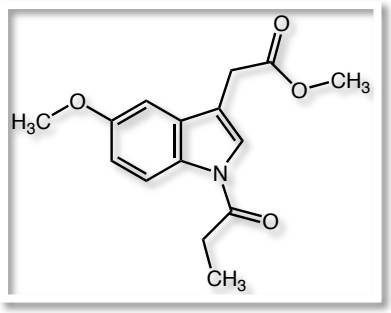
Methyl 2-(5-methoxy-1-(4-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (18j). According to general procedure C_variant2, the title compound was obtained from methyl 2-(5-methoxy-1*H*-indol-3-

yl)acetate (80 mg, 0.36 mmol), 4-(trifluoromethyl)benzoyl chloride (91.3 mg, 0.44 mmol) and ^{t}BuONa (2 M in THF, 219 uL, 0.44 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound as brownish oil in 29% yield (41 mg). $C_{20}H_{16}F_3NO_4$, M_r = 391.34; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.61 (s, 3H), 3.78 (s, 2H), 3.81 (s, 3H), 7.02 (dd, *J*=2.4/9.2 Hz, 1H), 7.13 (d, 2.4 Hz, 1H), 7.31 (s, 1H), 7.93-7.98 (m, 4H), 8.22 (d, *J*=8.8 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.61 (*p*-CF_3); LCMS (ESI) *t*R: 2.78 min (>99%, ELSD), *m/z*: 392.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{16}F_3NO_4$ $[M+H]^+$ calcd mass 392.1110, found 392.1110.

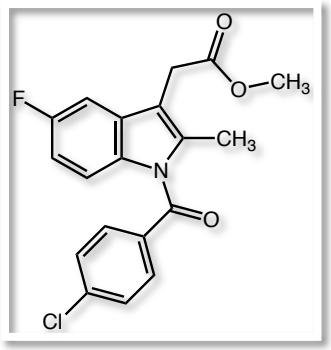


Methyl 2-(5-methoxy-1-(2-(4-methoxyphenyl)acetyl)-1*H*-indol-3-yl)acetate (18k). According to general procedure C_variant1, the title compound was obtained from from methyl 2-(5-methoxy-1*H*-indol-3-yl)acetate (80 mg, 0.36 mmol), 2-(4-chlorophenyl)acetyl chloride (81 mg, 0.44 mmol) and NaH (17.5 mg, 0.44 mmol) in anhydrous DMF (1 mL). The crude residue was repeatedly subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford a fifty-fifty mixture of the title compound and the *N*-unsubstituted indole starting material **20b**. Yield (mixture): 17 mg (13%).* $C_{21}H_{21}NO_5$, M_r = 367.40; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.64 (s, 3H), 3.72 (s, 3H), 3.78 (s, 3H), 3.79 (s, 2H), 4.26 (s, 2H), 6.92 (dd, *J*=2.8/9.2 Hz, 1H), 7.06 (d, *J*=2.4 Hz, 1H), 7.22-7.24 (m, 4H), 7.93 (s, 1H), 8.19 (d, *J*=9.2 Hz, 1H); LCMS (ESI) *t*R: 2.55 min (~50%, ELSD), *m/z*: 368.1 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{21}NO_5$ $[M+H]^+$ calcd mass 368.1498, found 368.1500.

*) title compound only about 50% pure (LCMS, ^{1}H NMR)

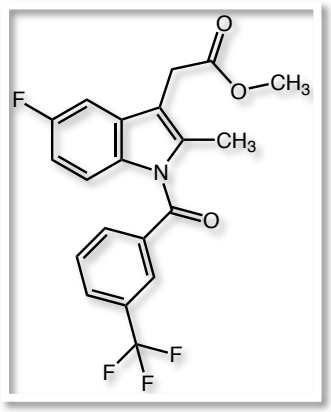


Methyl 2-(5-methoxy-1-propionyl-1*H*-indol-3-yl)acetate (18l). According to general procedure C_variant1, methyl 2-(5-methoxy-1*H*-indol-3-yl)acetate (60 mg, 0.27 mmol) was subjected to reaction with propionyl chloride (30 mg, 0.33 mmol). The crude product was purified by flash chromatography (SiO_2, ethyl acetate/hexane gradient) and recrystallized from hexane to afford 16 mg (21%) of the title compound as a white crystalline solid. $C_{15}H_{17}NO_4$, M_r = 275.30; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.16 (t, *J*=7.2 Hz, 3H), 2.98 (q, *J*=7.2 Hz, 2H), 3.64 (s, 3H, -$COOCH_3$), 3.78 (s, 5H, -OCH_3 & C3'-CH_2-), 6.93 (dd, *J*=2.8/9.0 Hz, 1H, C6'-H), 7.06 (d, *J*=2.8 Hz, 1H, C4'-H), 7.77 (s, 1H, C2'-H), 8.21 (d, *J*=9.2 Hz, 1H, C6'-H); LCMS (ESI) *t*R: 2.33 min (≥95%, ELSD, UV254), *m/z*: 276.1 $[M+H]^+$; HRMS (TOF, ES+) $C_{15}H_{17}NO_4$ $[M+H]^+$ calcd mass 276.1236, found 276.1238.

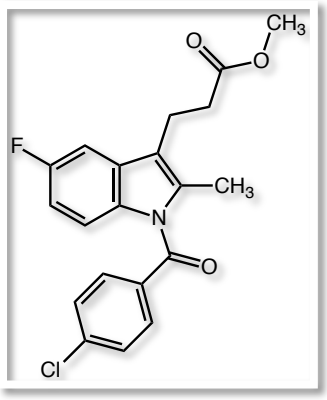


Methyl 2-(1-(4-chlorobenzoyl)-5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (18m). According to general procedure C_variant2, the title compound was obtained from methyl 2-(5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.36 mmol), 4-chlorobenzoyl chloride (75.9 mg, 0.43 mmol) and ^{t}BuONa (2 M in THF, 217 μL, 0.43 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound as clear yellow

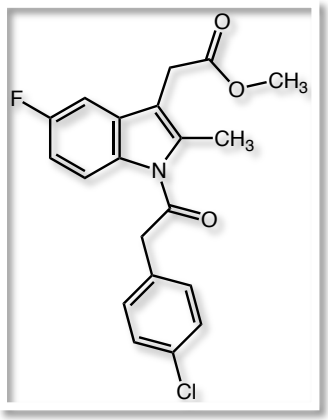
oil in 42% yield (54 mg). The viscous material partially crystallized upon storage at low temperatures. $C_{19}H_{15}ClFNO_3$, M_r = 359.78; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.21 (s, 3H), 3.62 (s, 3H), 3.80 (s, 2H), 6.96 (td, *J*=2.8/9.2 Hz, 1H), 7.05 (dd, *J*=4.4/9.2 Hz, 1H), 7.33 (dd, *J*=2.4/9.2 Hz, 1H), 7.64-7.71 (m, 4H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -118.7 (5'-F); LCMS (ESI) *t*R: 3.03 min (>99%, UV254, ELSD), *m/z*: 360.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{15}ClFNO_3$ $[M+H]^+$ calcd mass 360.0803, found 360.0802.



Methyl 2-(5-fluoro-2-methyl-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (18n). According to general procedure C_variant2, the title compound was obtained from methyl 2-(5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.36 mmol), 3-(trifluoromethyl)benzoyl chloride (90.5 mg, 0.43 mmol) and ^{t}BuONa (2 M in THF, 217 μL, 0.43 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound as yellow oil in 33% yield (47 mg). $C_{20}H_{15}F_4NO_3$, M_r = 393.33; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.17 (s, 3H), 3.62 (s, 3H), 3.80 (s, 2H), 6.97 (td, *J*=2.4/9.2 Hz, 1H), 7.10 (dd, *J*=4.4/9.0 Hz, 1H), 7.34 (dd, *J*=2.4/9.2 Hz, 1H), 7.81 (t, *J*=7.6 Hz, 1H), 7.95 (d, *J*=7.6 Hz, 1H), 8.03 (s, 1H), 8.08 (d, *J*=7.6 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -118.4 (5'-F), -59.5 (*m*-CF_3); LCMS (ESI) *t*R: 3.10 min (>95%, ELSD), *m/z*: 394.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{15}F_4NO_3$ $[M+H]^+$ calcd mass 394.1066, found 394.1068.

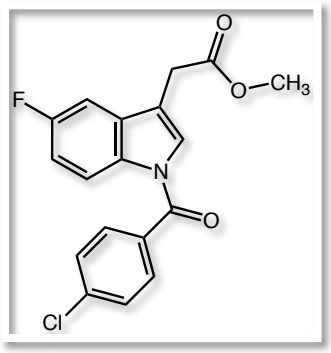


Methyl 3-(1-(4-chlorobenzoyl)-5-fluoro-2-methyl-1*H*-indol-3-yl)propanoate (18o). According to general procedure C_variant2, the title compound was obtained from methyl 3-(5-fluoro-2-methyl-1*H*-indol-3-yl)propanoate (80 mg, 0.34 mmol), 4-chlorobenzoyl chloride (71.4 mg, 0.41 mmol) and ^{t}BuONa (2 M in THF, 204 μL, 0.41 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound as yellow oil in 49% yield (62 mg). $C_{20}H_{17}ClFNO_3$, M_r = 373.81; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.19 (s, 3H), 2.59 (t, *J*=7.4 Hz, 2H), 2.92 (t, *J*=7.6 Hz, 2H), 3.56 (s, 3H), 6.94 (td, *J*=2.4/9.2 Hz, 1H), 7.08 (dd, *J*=4.6/9.0 Hz, 1H), 7.39 (dd, *J*=2.4/9.2 Hz, 1H), 7.63-7.68 (m, 4H); LCMS (ESI) *t*R: 3.21 min (>95%, ELSD), *m*/*z*: 374.3 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{17}ClFNO_3$ $[M+H]^+$ calcd mass 374.0959, found 374.0962.

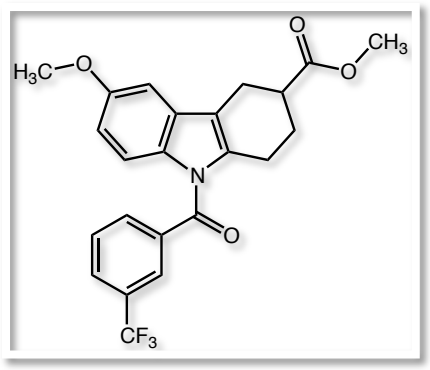


Methyl 2-(1-(2-(4-chlorophenyl)acetyl)-5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (18p). According to general procedure C_variant2, the title compound was obtained from from methyl 2-(5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (80 mg, 0.36 mmol), 2-(4-chlorophenyl)acetyl chloride (82 mg, 0.43 mmol) and

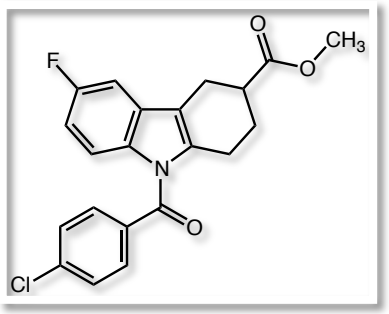
^{t}BuONa (2 M in THF, 217 μL, 0.43 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 4.5% yield (6 mg). $C_{20}H_{17}ClFNO_3$, M_r = 373.81; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.60 (s, 3H), 3.61 (s, 3H), 3.80 (s, 2H), 4.49 (s, 2H), 7.07 (td, *J*=2.8/9.2 Hz, 1H), 7.31 (dd, *J*=2.6/9.0 Hz, 1H), 7.33-7.41 (m, 4H), 8.12 (dd, *J*=4.4/9.2 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -98.1 (C5'-F); LCMS (ESI) *t*R: 3.01 min (>99%, ELSD), *m/z*: 374.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{17}ClFNO_3$ $[M+H]^+$ calcd mass 396.0779, found 396.0782.



Methyl 2-(1-(4-chlorobenzoyl)-5-fluoro-1*H*-indol-3-yl)acetate (18q). According to general procedure C_variant2, the title compound was obtained from methyl 2-(5-fluoro-1*H*-indol-3-yl)acetate (77.5 mg, 0.37 mmol), 4-chlorobenzoyl chloride (78.6 mg, 0.45 mmol) and ^{t}BuONa (2 M in THF, 224 μL, 0.45 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound as a light-orange solid in 42% yield (54 mg). $C_{18}H_{13}ClFNO_3$, M_r = 345.75; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.61 (s, 3H), 3.80 (s, 2H), 7.24 (td, *J*=2.4/9.2 Hz, 1H), 7.44 (dd, *J*=2.8/9.2 Hz, 1H), 7.47 (s, 1H), 7.66-7.79 (m, 4H), 8.29 (dd, *J*=4.8/8.8 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -116.6 (5'-F); LCMS (ESI) *t*R: 3.02 min (>99%, ELSD), *m/z*: 346.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{18}H_{13}ClFNO_3$ $[M+H]^+$ calcd mass 346.0646, found 346. 0644.

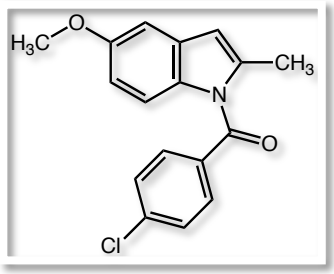


Methyl 6-methoxy-9-(3-(trifluoromethyl)benzoyl)-2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylate (19a). According to general procedure C_variant2, the title compound was obtained from from methyl 6-methoxy-2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylate (80 mg, 0.31 mmol), 3-(trifluoromethyl) benzoyl chloride (77.2 mg, 0.37 mmol) and ^{t}BuONa (2 M in THF, 185 μL, 0.37 mmol) in anhydrous THF (2.5 mL). The crude material was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) and the residue (59 mg) recrystallized from EtOAc/hexane to afford the pure title compound in 24% yield (32 mg). $C_{23}H_{20}F_3NO_4$, M_r = 431.40; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.70-1.80 (m, 1H), 2.03-2.07 (m, 1H), 2.47 (m, 2H, partly overlayed by DMSO signal), 2.73-2.79 (m, 1H), 2.82-2.89 (m, 1H), 2.94 (dd, *J*=5.0/15.8 Hz, 1H), 3.65 (s, 3H), 3.77 (s, 3H), 6.73 (dd, *J*=2.6/9.0 Hz, 1H), 7.04 (d, *J*=2.4 Hz, 1H), 7.08 (d, *J*=9.2 Hz, 1H), 7.79 (t, *J*=8.0 Hz, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 7.99 (s, 1H), 8.04 (d, *J*=8.0 Hz, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.41 (*m*-CF_3); LCMS (ESI) *t*R: 0.95 min (>95%, UV254), *m/z*: 432.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{23}H_{20}F_3NO_4$ $[M+H]^+$ calcd mass 432.1423, found 432.1422.

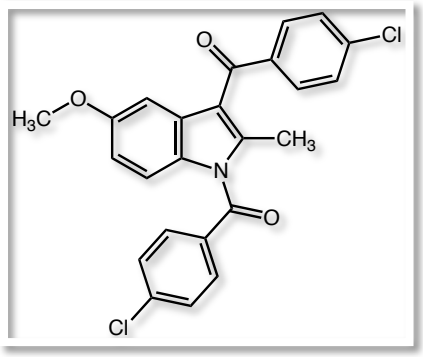


Methyl 9-(4-chlorobenzoyl)-6-fluoro-2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylate (19b). According to general procedure C_variant2, the title compound was obtained from methyl 6-fluoro-

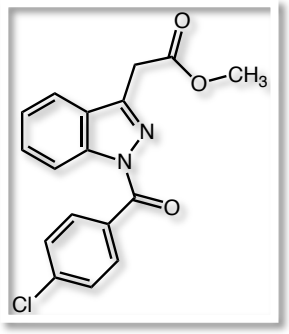
2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylate (80 mg, 0.32 mmol), 4-chlorobenzoyl chloride (67.9 mg, 0.39 mmol) and ^{t}BuONa (2 M in THF, 194 μL, 0.39 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound as white crystalline solid in 14% yield (17 mg). $C_{21}H_{17}ClFNO_3$, M_r = 385.82; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.72-1.79 (m, 1H), 2.06-2.10 (m, 1H), 2.54-2.56 (m, 2H), 2.72-2.78 (m, 1H), 2.83-2.89 (m, 1H), 2.95 (dd, *J*=5.2/15.4 Hz, 1H), 3.65 (s, 3H), 6.99 (td, *J*=2.4/9.2 Hz, 1H), 7.23 (dd, *J*=4.6/9.0 Hz, 1H), 7.34 (dd, *J*=2.4/9.0 Hz, 1H), 7.62-7.69 (m, 4H); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -123.87 (6'-F); LCMS (ESI) *t*R: 3.24 min (>99%, ELSD), *m/z*: 386.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{17}ClFNO_3$ $[M+H]^+$ calcd mass 386.0959, found 386.0961.



(4-chlorophenyl)(5-methoxy-2-methyl-1*H*-indol-1-yl)methanone (20a). According to general procedure C_variant2, the title compound was obtained from from 5-methoxy-2-methyl-1*H*-indole (100 mg, 0.62 mmol), 4-chlorobenzoyl chloride (130 mg, 0.74 mmol) and ^{t}BuONa (2 M in THF, 372 μL, 0.44 mmol) in anhydrous THF (2.5 mL). The crude residue was subjected to flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford the pure title compound in 25% yield (46 mg, yellow oil). $C_{17}H_{14}ClNO_2$, M_r = 299.75; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.26 (s, 3H, C2'-CH_3), 3.75 (s, 3H, -OCH_3), 6.51 (s, 1H, C3'-H), 6.69 (dd, *J*=3.1/12.0 Hz, 1H, C6'-H), 6.96 (d, *J*=12.0 Hz, 1H, C7'-H), 7.04 (d, *J*=2.9 Hz, 1H, C4'-H), 7.63-7.71 (m, 4H, ar-H 4-Cl-benzoyl); LCMS (ESI) *t*R: 2.93 min (>95%, ELSD), *m/z*: 300.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{17}H_{14}ClNO_2$ $[M+H]^+$ calcd mass 300.0791, found 300.0793.



(5-methoxy-2-methyl-1*H*-indole-1,3-diyl)bis((4-chlorophenyl)methanone) (20b). The title compound was formed as a side product in the synthesis of **20a** and could be isolated pure by flash chromatography in 8% yield (22 mg, white-yellow solid). Aside, a larger mixed fraction (56 mg) was separated containing residual **20b** and by the majority **20a**. $C_{24}H_{17}Cl_2NO_3$, M_r = 438.30; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.26 (s, 3H, C2'-CH_3), 3.64 (s, 3H, -OCH_3), 6.79 (dd, *J*=2.6/9.0 Hz, 1H, C6'-H), 6.85 (d, *J*=2.4 Hz 1H, C4'-H), 6.92 (d, *J*=9.2 Hz, 1H, C7'-H), 7.62-7.65 (m, 2H), 7.66-7.70 (m, 2H), 7.80-7.82 (m, 4H); LCMS (ESI) *t*R: 3.24 min (>95%, ELSD), *m/z*: 438.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{24}H_{17}Cl_2NO_3$ $[M+H]^+$ calcd mass 438.0664, found 438.0668.



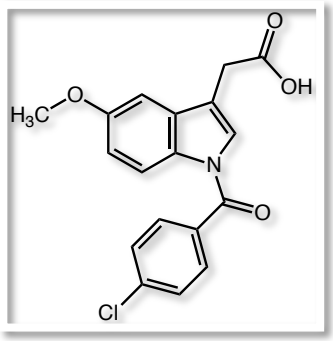
Methyl 2-(1-(4-chlorobenzoyl)-1*H*-indazol-3-yl)acetate (21). According to general procedure C_variant2, methyl 2-(1*H*-indazol-3-yl)acetate (80 mg, 0.42 mmol) was deprotonated with ^{t}BuONa (252 μL) and subjected to reaction with 4-chlorobenzoyl chloride (88.3 mg, 0.50 mmol). The crude product was purified by flash chromatography (SiO_2, ethyl acetate/hexane gradient) to afford 13.5 mg (52%) of the title compound as bright yellow solid. The compound permanently crystallized upon drying at high vacuum and storage at -20 °C. Yield: 51 mg (37%). $C_{17}H_{13}ClN_2O_3$, M_r = 328.75; ^{1}H NMR (400 MHz,

DMSO-d_6) δ: 3.65 (s, 3H), 4.16 (s, 2H), 7.50 (td, *J*=0.8/7.6 Hz, 1H), 7.63-7.66 (m, 2H), 7.71 (td, *J*=1.0/7.6 Hz, 1H), 7.91 (d, *J*=8.0 Hz, 1H), 8.00-8.03 (m, 2H), 8.41 (d, *J*=8.4 Hz, 1H); LCMS (ESI) *t*R: 2.80 min (>99%, ELSD), *m/z*: 329.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{17}H_{13}ClN_2O_3$ $[M+H]^+$ calcd mass 329.0693, found 329.0693.

General Procedure D for the anhydrous ester cleavage reaction with Me_3SnOH.

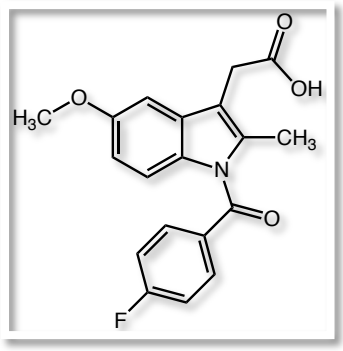
In a microwave process vial the (aza)indole alkylacid ester (1 equivalent) is dissolved in 1,2-dichloro ethane (36 mL/mmol) under argon and after addition of trimethyltin hydroxide (5 equivalents). The reaction mixture is heated for 30 min at 130 ˚C in a microwave (TLC analysis indicates complete reaction). Dichloromethane (36 mL/mmol) and 50% AcOH (70 mL/mmol) are added to the cold reaction solution and the resulting biphasic mixture is agitated until both layers are clear. The organic phase is collected, washed with brine, dried over Na_2SO_4 and filtered (using a phase separator syringe with drying cartridge). Removal of the solvent (dichloromethane) *in vacuo* and subsequent silica gel chromatography using ethyl acetate/hexane as eluent mixture (containing 0.5% AcOH) yields the pure title compound.

Examples:



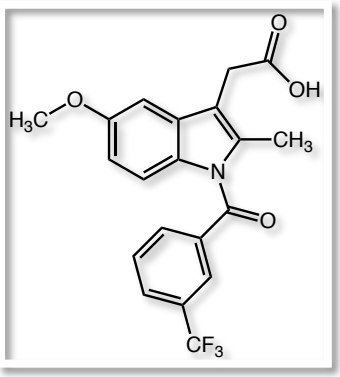
2-(1-(4-chlorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetic acid (2). According to general procedure D, methyl 2-(1-(4-chlorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetate (10 mg, 0.028 mmol) was subjected to reaction with trimethyltin hydroxide (25 mg, 0.14 mmol) in 1,2-DCE. The crude product was

chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to quantitatively afford the title compound as an off-white solid. Yield: 7.8 mg (81%). $C_{18}H_{14}ClNO_4$, M_r = 343.76; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.67 (s, 2H), 3.81 (s, 3H), 6.99 (dd, *J*=2.4/9.2 Hz, 1H), 7.12 (d, *J*=2.4 Hz, 1H), 7.32 (s, 1H), 7.65-7.77 (m, 4H), 8.17 (d, *J*=9.2 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 30.65 (s), 55.83 (s), 102.98 (s), 113.45 (s), 116.17 (s), 117.10 (s), 127.07 (s), 129.22 (s, 2C), 130.31 (s), 131.01 (s, 2C), 132.18 (s), 133.16 (s), 137.08 (s), 156.68 (s), 167.07 (s), 172.53 (s); LCMS (ESI) *t*R: 2.60 min (>99%, ELSD), *m/z*: 344.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{18}H_{14}ClNO_4$ $[M+H]^+$ calcd mass 344.0690, found 344.0693.

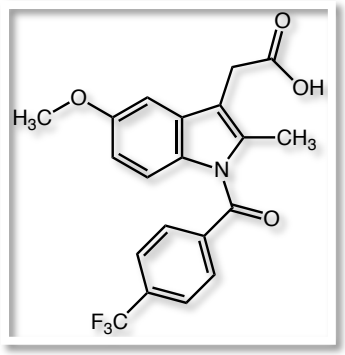


2-(1-(4-fluorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetic acid (22a). According to general procedure D, methyl 2-(1-(4-fluorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (15.0 mg, 0.042 mmol) was subjected to reaction with trimethyltin hydroxide (38 mg, 0.211 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an off-white solid. Yield: 12.9 mg (90%). $C_{19}H_{16}FNO_4$, M_r = 341.33; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.21 (s, 3H), 3.64 (bs, 2H), 3.75 (s, 3H), 6.69 (dd, *J*=2.6/9.0 Hz, 1H), 6.88 (d, *J*=8.8 Hz, 1H), 7.02 (d, *J*=2.4 Hz, 1H), 7.38-7.43 (m, 2H), 7.70-7.75 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 13.14 (s), 29.86 (s), 55.65 (s), 101.09 (s), 111.53 (s), 111.60 (s), 114.85 (s), 115.37 (d, *J*=130.5 Hz, 2C), 130.32 (s), 130.79 (s), 131.47 (s), 132.36 (d, *J*=9.3 Hz, 2C), 136.23 (s), 155.93 (s), ~165.5 (d, *J*=252 Hz, 1C), 168.14 (s), 176.19 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -104.19 (4-F-benzoyl); LCMS (ESI) *t*R: 2.41

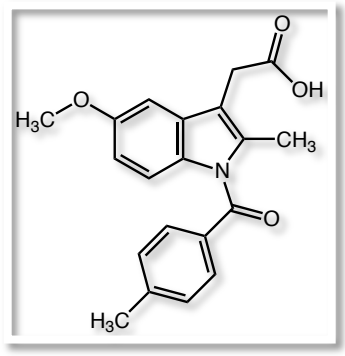
min (>99%, UV215, UV254, ELSD), *m/z*: 342.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{16}FNO_4$ $[M+H]^+$ calcd mass 342.1142, found 342.1143.



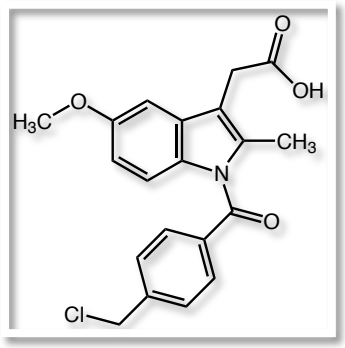
2-(5-methoxy-2-methyl-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetic acid (22b). According to general procedure D, methyl 2-(5-methoxy-2-methyl-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (15 mg, 0.037 mmol) was subjected to reaction with trimethyltin hydroxide (34 mg, 0.185 mmol) in 1,2-DCE (1.0 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to quantitatively afford the title compound as an off-white solid. Yield: 14.1 mg (97%). $C_{20}H_{16}F_3NO_4$, M_r = 391.34; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.17 (s, 3H), 3.66 (bs, 2H), 3.76 (s, 3H), 6.71 (dd, *J*=2.4/8.8 Hz, 1H), 6.94 (d, *J*=9.2 Hz, 1H), 7.04 (d, *J*=2.4 Hz, 1H), 7.80 (t, *J*=7.8 Hz, 1H), 7.94 (d, *J*=8.0 Hz, 1H), 8.00 (s, 1H), 8.06 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 13.48 (s), 29.93 (s), 55.71 (s), 101.34 (s), 111.89 (s), 112.37 (s), 114.99 (s), ~123.4 (q, *J*=272 Hz, 1C), 126.55 (d, *J*=3.9 Hz, 1C), 129.22 (s), 129.39 (s), 130.60 (s), 130.66 (s), 131.51 (d, *J*=33.0 Hz, 1C), 132.85 (s), 136.07 (s), 136.34 (s), 156.25 (s), 167.84 (s), 176.16 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.43 (*m*-CF_3); LCMS (ESI) *t*R: 2.60 min (>99%, UV215, UV254, ELSD), *m/z*: 392.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{16}F_3NO_4$ $[M+H]^+$ calcd mass 392.1110, found 392.1111.



2-(5-methoxy-2-methyl-1-(4-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetic acid (22c). According to general procedure D, methyl 2-(5-methoxy-2-methyl-1-(4-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (15 mg, 0.037 mmol) was subjected to reaction with trimethyltin hydroxide (33 mg, 0.183 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an off-white solid. Yield: 13.1 mg (90%). $C_{20}H_{16}F_3NO_4$, M_r = 391.34; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.16 (s, 3H), 3.64 (bs, 2H), 3.75 (s, 3H), 6.72 (dd, *J*=2.6/9.0 Hz, 1H), 6.99 (d, *J*=9.2 Hz, 1H), 7.04 (d, *J*=2.4 Hz, 1H), 7.86 (d, *J*=8.0 Hz, 2H), 7.94 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 13.47 (s), 29.88 (s), 55.68 (s), 101.40 (s), 111.77 (s), 112.31 (s), 115.07 (s), 123.43 (q, *J*=273 Hz, 1C), 125.79 (d, *J*= 3.7 Hz, 2C), 129.84 (s, 2C), 130.16 (d, *J*=32.9 Hz, 1C), 134.27 (s), 136.07 (s), 138.86 (s), 156.23 (s), 167.98 (s), 176.23 (s), one signal invisible; ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.60 (s, CF_3); LCMS (ESI) *t*R: 2.66 min (>99%, UV254), *m/z*: 392.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{16}F_3NO_4$ $[M+H]^+$ calcd mass 392.1110, found 392.1112.

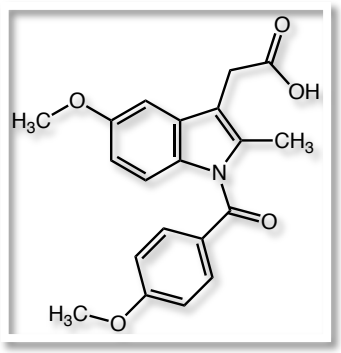


2-(5-methoxy-2-methyl-1-(4-methylbenzoyl)-1*H*-indol-3-yl)acetic acid (22d). According to general procedure D, methyl 2-(5-methoxy-2-methyl-1-(4-methylbenzoyl)-1*H*-indol-3-yl)acetate (15 mg, 0.043 mmol) was subjected to reaction with trimethyltin hydroxide (39 mg, 0.216 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an off-white solid. Yield: 11.8 mg (82%). $C_{20}H_{19}NO_4$, M_r = 337.37; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.21 (s, 3H), 2.42 (s, 3H), 3.64 (bs, 2H), 3.74 (s, 3H), 6.67 (dd, *J*=2.6/9.0 Hz, 1H), 6.85 (d, *J*=8.8 Hz, 1H), 7.01 (d, *J*=2.4 Hz, 1H), 7.37 (d, *J*=8.0 Hz, 2H), 7.54 (d, *J*=8.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 13.18 (s), 21.73 (s), 30.01 (s), 55.70 (s), 100.93 (s), 111.20 (s), 111.54 (s), 115.54 (s), 129.40 (s, 2C), 129.96 (s, 2C), 130.25 (s), 131.02 (s), 132.57 (s), 136.36 (s), 143.80 (s), 155.82 (s), 169.45 (s), 176.50 (s); LCMS (ESI) *t*R: 2.47 min (>99%, UV220, UV254), *m/z*: 338.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{19}NO_4$ $[M+H]^+$ calcd mass 338.1392, found 338.1390.



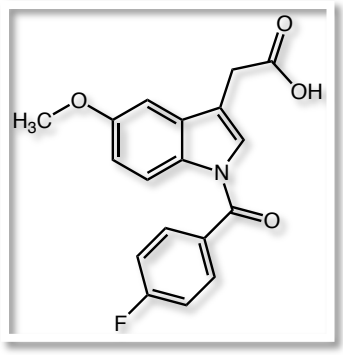
2-(1-(4-(chloromethyl)benzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetic acid (22e). According to general procedure D, methyl 2-(1-(4-(chloromethyl)benzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (15 mg, 0.039 mmol) was subjected to reaction with trimethyltin hydroxide (35 mg, 0.194 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an off-white solid. Yield: 14.1 mg (98%). $C_{20}H_{18}ClNO_4$, M_r = 371.81; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.19 (s, 3H), 3.65 (bs, 2H), 3.75 (s, 3H), 4.88 (s, 2H), 6.68 (dd,

J=2.4/9.2 Hz, 1H), 6.90 (d, *J*=8.8 Hz, 1H), 7.02 (d, *J*=2.4 Hz, 1H), 7.61-7.67 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 13.34 (s), 29.93 (s), 45.23 (s), 55.72 (s), 101.14 (s), 111.68 (s), 115.08 (s), 128.79 (s, 2C), 130.14 (s, 2C), 130.41 (s), 130.85 (s), 135.38 (s), 136.27 (s), 142.26 (s), 156.02 (s), 168.79 (s), ~176.3 (s), one signal invisible; LCMS (ESI) *t*R: 2.48 min (>99%, UV220, UV254), *m/z*: 372.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{18}ClNO_4$ $[M+H]^+$ calcd mass 372.1003, found 372.1003.

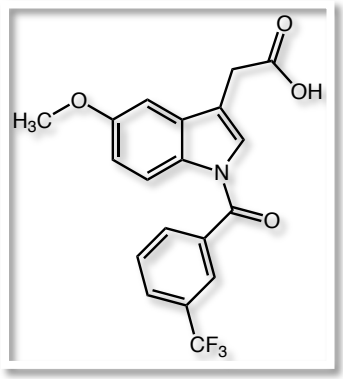


2-(5-methoxy-1-(4-methoxybenzoyl)-2-methyl-1*H*-indol-3-yl)acetic acid (22f). According to general procedure D, methyl 2-(5-methoxy-1-(4-methoxybenzoyl)-2-methyl-1*H*-indol-3-yl)acetate (20 mg,* 0.054 mmol) was subjected to reaction with trimethyltin hydroxide (49 mg, 0.272 mmol) in 1,2-DCE (1.0 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to quantitatively afford the title compound as an off-white solid. Yield: 8.9 mg (~93%).* $C_{20}H_{19}NO_5$, M_r = 353.37; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.24 (s, 3H), 3.65 (bs, 2H), 3.75 (s, 3H), 3.86 (s, 3H), 6.68 (dd, *J*=2.6/9.0 Hz, 1H), 6.85 (d, *J*=8.8 Hz, 1H), 7.02 (d, *J*=2.4 Hz, 1H), 7.08-7.11 (m, 2H), 7.61-7.64 (m, 2H); LCMS (ESI) *t*R: 2.34 min (>99%, UV254), *m/z*: 354.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{19}NO_5$ $[M+H]^+$ calcd mass 354.1341, found 354.1340.

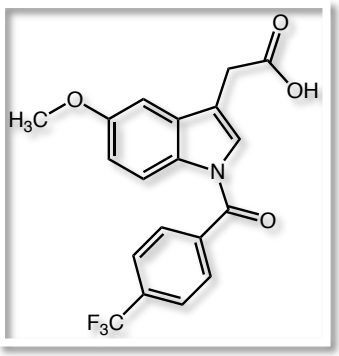
*) starting material ~50% pure (LCMS, ^{1}H NMR); impurity taken into consideration for the calculation of the percent yield!



2-(1-(4-fluorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetic acid (22g). According to general procedure D, methyl 2-(1-(4-fluorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetate (15.0 mg, 0.044 mmol) was subjected to reaction with trimethyltin hydroxide (40 mg, 0.220 mmol) in 1,2-DCE (1.0 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to quantitatively afford the title compound as an off-white/orange solid. Yield: 11 mg (76%). $C_{18}H_{14}FNO_4$, M_r = 327.31; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.67 (bs, 2H), 3.81 (s, 3H), 6.99 (dd, *J*=2.4/8.8 Hz, 1H), 7.12 (d, *J*=2.4 Hz, 1H), 7.32 (s, 1H), 7.40-7.46 (m, 2H), 7.78-7.83 (m, 2H), 8.16 (d, *J*=8.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 30.67 (s), 55.75 (s), 101.97 (s), 113.71 (s), 113.83 (s), 115.88 (d, *J*=22.1 Hz, 2C), 117.42 (s), 126.64 (s), 130.52 (d, *J*=3.1 Hz, 1C), 130.81 (s), 131.23 (s), 131.63 (d, *J*=9.1 Hz, 2C), 156.87 (s), 164.78 (d, *J*=254 Hz, 1C), 166.97 (s), 175.96 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -105.92 (4-F-benzoyl); LCMS (ESI) *t*R: 2.32 min (>99%, UV215, UV254, ELSD), *m/z*: 328.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{18}H_{14}FNO_4$ $[M+H]^+$ calcd mass 328.0985, found 328.0984.

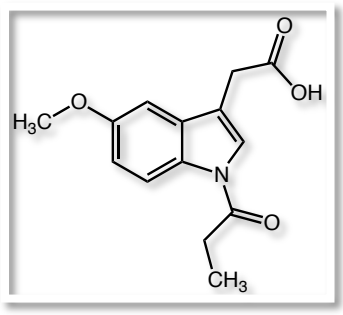


2-(5-methoxy-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetic acid (22h). According to general procedure D, methyl 2-(5-methoxy-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (7 mg, 0.018 mmol) was subjected to reaction with trimethyltin hydroxide (16 mg, 0.089 mmol) in 1,2-DCE (0.5 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to quantitatively afford the title compound as an off-white/bright orange solid. Yield: 6.5 mg (96%). $C_{19}H_{14}F_3NO_4$, M_r = 377.31; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.66 (bs, 2H), 3.81 (s, 3H), 7.00 (dd, *J*=2.6/9.0 Hz, 1H), 7.12 (d, *J*=2.4 hz, 1H), 7.27 (s, 1H), 7.83 (t, *J*=7.8 Hz, 1H), 8.02 (pseudo-t, *J*=7.2 Hz, 2H), 8.08 (s, 1H), 8.19 (d, *J*=8.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 30.56 (s), 55.74 (s), 102.09 (s), 113.89 (s), 114.55 (s), 117.52 (s), 123.47 (q, *J*=273 Hz, 1C), 125.98 (d, *J*=3.8 Hz, 1C), 126.21 (s), 128.38 (s), 129.26 (s), 130.69 (s), 131.34 (s), 131.36 (d, *J*=33.4 Hz, 1C), 132.11 (s), 135.27 (s), 157.08 (s), 166.47 (s), 175.51 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.35 (*m*-CF_3); LCMS (ESI) *t*R: 2.53 min (>99%, UV215, UV254, ELSD), *m/z*: 378.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{14}F_3NO_4$ $[M+H]^+$ calcd mass 378.0953, found 378.0954.

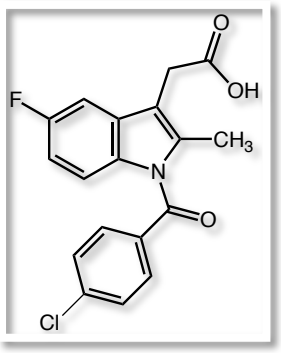


2-(5-methoxy-1-(4-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetic acid (22i). According to general procedure D, methyl 2-(5-methoxy-1-(4-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (15 mg, 0.038 mmol) was subjected to reaction with trimethyltin hydroxide (35 mg, 0.192 mmol) in 1,2-DCE (1.0 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to quantitatively afford the title

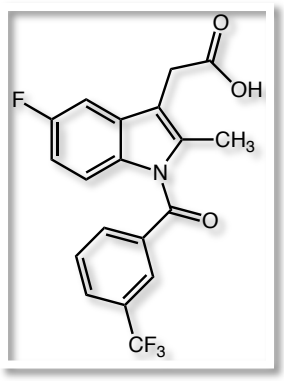
compound as an off-white solid. Yield: 14.4 mg (>99%). $C_{19}H_{14}F_3NO_4$, M_r = 377.31; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.66 (bs, 2H), 3.81 (s, 3H), 7.01 (dd, *J*=2.6/9.0 Hz, 1H), 7.13 (d, *J*=2.4 Hz, 1H), 7.28 (s, 1H), 7.93-7.98 (m, 4H), 8.21 (d, *J*=9.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 30.69 (s), 55.75 (s), 102.15 (s), 113.89 (s), 114.60 (s), 117.57 (s), 123.5 (q, *J*=270 Hz, 1C), 125.71 (d, *J*=3.6 Hz, 2C), 126.26 (s), 129.29 (s, 2C), 130.68 (s), 131.37 (s), 133.45 (d, *J*=31.5 Hz, 1C), 137.82 (s), 157.11 (s), 166.66 (s), 176.09 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.61 (*p*-CF_3); LCMS (ESI) *t*R: 2.53 min (>99%, UV215, UV254, ELSD), *m/z*: 378.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{14}F_3NO_4$ $[M+H]^+$ calcd mass 378.0953, found 378.0952.



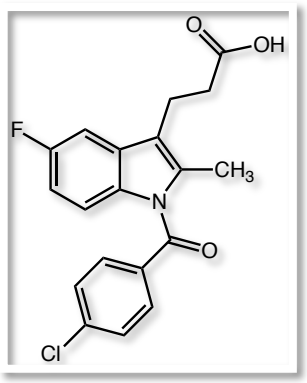
2-(5-methoxy-1-propionyl-1*H*-indol-3-yl)acetic acid (22j). According to general procedure D, methyl 2-(5-methoxy-1-propionyl-1*H*-indol-3-yl)acetate (4.7 mg, 0.017 mmol) was subjected to reaction with trimethyltin hydroxide (15 mg, 0.085 mmol) in 1,2-DCE (0.5 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to quantitatively afford the title compound as an off-white solid. Yield: 4.2 mg (94%). $C_{14}H_{15}NO_4$, M_r = 261.27; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.16 (t, *J*=7.2 Hz, 3H), 2.97 (q, *J*=7.2 Hz, 2H), 3.65 (bs, 2H), 3.78 (s, 3H), 6.92 (dd, *J*=2.4/8.8 Hz, 1H), 7.06 (d, *J*=2.8 Hz, 1H), 7.74 (s, 1H), 8.21 (d, *J*=9.2 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 8.71 (s), 28.87 (s), 30.67 (s), 55.65 (s), 101.78 (s), 113.71 (s), 113.80 (s), 117.58 (s), 123.93 (s), 130.51 (s), 130.72 (s), 156.47 (s), 171.65 (s), 175.96 (s); LCMS (ESI) *t*R: 1.90 min (>99%, UV254, ELSD), *m/z*: 262.2 $[M+H]^+$; HRMS (TOF, ES+) $C_{14}H_{15}NO_4$ $[M+H]^+$ calcd mass 262.1079, found 262.1081.



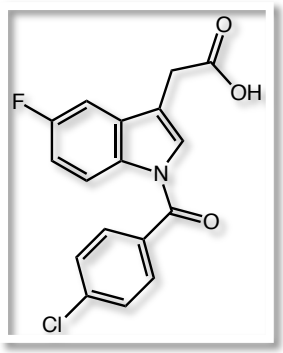
2-(1-(4-chlorobenzoyl)-5-fluoro-2-methyl-1*H*-indol-3-yl)acetic acid (22k). According to general procedure D, methyl 2-(1-(4-chlorobenzoyl)-5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (15 mg, 0.042 mmol) was subjected to reaction with trimethyltin hydroxide (38 mg, 0.21 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an off-white solid. Yield: 12.6 mg (87%). $C_{18}H_{13}ClFNO_3$, M_r = 345.75; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.21 (s, 3H), 3.67 (s, 2H), 6.95 (td, *J*=2.6/9.2 Hz, 1H), 7.06 (d, *J*=9.0 Hz, 1H), 7.32 (dd, *J*=2.6/9.4 Hz, 1H), 7.63-7.71 (m, 4H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 13.26 (s), 29.74 (s), 104.03 (d, *J*=24.2 Hz, 1C), 111.06 (d, *J*=25.3 Hz, 1C), 111.60 (d, *J*=3.5 Hz, 1C), 114.99 (d, *J*=9.0 Hz, 1C), 129.22 (s, 2C), 130.46 (d, *J*=9.4 Hz, 1C), 131.20 (s, 2C), 132.41 (s), 133.37 (s), 137.06 (s), 139.69 (s), 159.30 (d, *J*=240 Hz, 1C), 168.24 (s), 175.41 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -118.80 (5'-F); LCMS (ESI) *t*R: 2.67 min (>99%, UV254), *m/z*: 346.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{18}H_{13}ClFNO_3$ $[M+H]^+$ calcd mass 346.0646, found 346.0644.



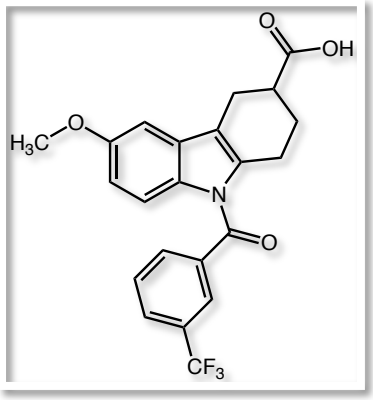
2-(5-fluoro-2-methyl-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetic acid (22l). According to general procedure D, methyl 2-(5-fluoro-2-methyl-1-(3-(trifluoromethyl)benzoyl)-1*H*-indol-3-yl)acetate (15 mg, 0.038 mmol) was subjected to reaction with trimethyltin hydroxide (35 mg, 0.19 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an orange-yellowish solid. Yield: 13.8 mg (95%). $C_{19}H_{15}ClFNO_3$, M_r = 359.78; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.16 (s, 3H), 3.68 (bs, 2H), 6.95 (td, *J*=2.6/9.0 Hz, 1H), 7.10 (dd, *J*=4.4/8.8 Hz, 1H), 7.33 (bd, *J*=8.8 Hz, 1H), 7.81 (t, *J*=7.8 Hz, 1H), 7.95 (d, *J*=7.6 Hz, 1H), 8.03 (s, 1H), 8.08 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 13.51 (s), 29.91 (s), 104.26 (d, *J*=24.3 Hz, 1C), 111.29 (d, *J*=25.2 Hz, 1C), 115.05 (d, *J*=9.2 Hz, 1C), 123.37 (q, *J*=276 Hz, 1C), 126.61 (s), 129.52 (s), 130.69 (d, *J*=8.4 Hz, 1C), 131.65 (d, *J*=32.2 Hz, 1C), 132.03 (s), 132.38 (s), 132.89 (s), 135.98 (s), 136.89 (s), 159.47 (d, *J*=241 Hz, 1C), 167.86 (s), 175.92 (s), one signal invisible; ^{19}F NMR (282 MHz, DMSO-d_6) δ: -118.49 (1F, 5'-F), -59.44 (s, 3F, *m*-CF_3); LCMS (ESI) *t*R: 2.61 min (>99%, UV215, UV254, ELSD), *m/z*: 380.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{15}ClFNO_3$ $[M+H]^+$ calcd mass 380.0910, found 380.0912.



3-(1-(4-chlorobenzoyl)-5-fluoro-2-methyl-1*H*-indol-3-yl)propanoic acid (22m). According to general procedure D, methyl 3-(1-(4-chlorobenzoyl)-5-fluoro-2-methyl-1*H*-indol-3-yl)propanoate (15 mg, 0.040 mmol) was subjected to reaction with trimethyltin hydroxide (36 mg, 0.20 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an off-white/yellowish solid. Yield: 13.7 mg (95%). $C_{19}H_{15}ClFNO_3$, M_r = 359.78; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.20 (s, 3H), 2.49 (t, *J*=7.2 Hz, 2H), 2.88 (t, *J*=7.2 Hz, 2H), 6.94 (td, *J*=2.4/9.2 Hz, 1H), 7.07 (dd, *J*=4.6/9.0 Hz, 1H), 7.39 (dd, *J*=2.0/9.2 Hz, 1H), 7.62-7.68 (m, 4H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 13.23 (s), 19.23 (s), 33.64 (s), 103.68 (d, *J*=23.7 Hz, 1C), 110.77 (d, *J*=25.1 Hz, 1C), 115.03 (d, *J*=9.1 Hz, 1C), 117.42 (s), 129.16 (s, 2C), 130.48 (d, *J*=9.2 Hz, 1C), 131.1294 (s, 2C), 132.60 (s), 133.65 (s), 135.50 (s), 139.47 (s), 159.23 (d, *J*=240 Hz, 1C), 168.31 (s), 178.04 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -118.67 (5'-F); LCMS (ESI) *t*R: 2.76 min (>99%, UV215, UV254), *m/z*: 360.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{19}H_{15}ClFNO_3$ $[M+H]^+$ calcd mass 360.0803, found 360.0805.



2-(1-(4-chlorobenzoyl)-5-fluoro-1*H*-indol-3-yl)acetic acid (22n). According to general procedure D, methyl 2-(1-(4-chlorobenzoyl)-5-fluoro-1*H*-indol-3-yl)acetate (15 mg, 0.043 mmol) was subjected to reaction with trimethyltin hydroxide (39 mg, 0.216 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as an off-white solid. Yield: 11.2 mg (78%). $C_{17}H_{11}ClFNO_3$, M_r = 331.73; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.66 (bs, 2H), 7.23 (td, *J*=2.6/9.2 Hz, 1H), 7.40-7.43 (m, 2H), 7.65-7.69 (m, 2H), 7.75-7.79 (m, 2H), 8.28 (dd, *J*=4.8/9.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 30.62 (s), 104.99 (d, *J*=24.3 Hz, 1C), 113.34 (d, *J*=24.9 Hz, 1C), 113.92 (s), 117.76 (d, *J*=8.9 Hz, 1C), 127.35 (s), 129.08 (s, 2C), 130.57 (s, 2C), 131.38 (d, *J*=9.7 Hz, 1C), 132.37 (s), 132.47 (s), 138.58 (s), 159.96 (d, *J*=242 Hz, 1C), 167.09 (s), 175.85 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -116.72 (5'-F); LCMS (ESI) *t*R: 2.54 min (>99%, UV215, UV254, ELSD), *m/z*: 332.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{17}H_{11}ClFNO_3$ $[M+H]^+$ calcd mass 332.0490, found 332.0490.

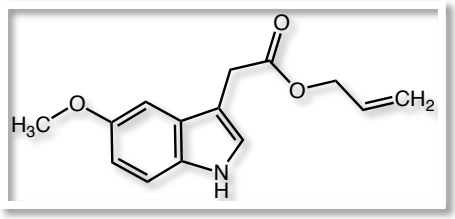


6-methoxy-9-(3-(trifluoromethyl)benzoyl)-2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylic acid (23). According to general procedure D, methyl 6-methoxy-9-(3-(trifluoromethyl)benzoyl)-2,3,4,9-tetrahydro-1*H*-carbazole-3-carboxylate, 15 mg,* 0.035 mmol) was subjected to reaction with trimethyltin hydroxide (31 mg, 0.174 mmol) in 1,2-DCE (1 mL). The crude product was chromatographed on a short silica gel column using 1:1 ethyl acetate/hexane (0.5% AcOH) mixtures of increasing polarity as eluants to afford the title compound quantitatively as a bright yellow solid. Yield:

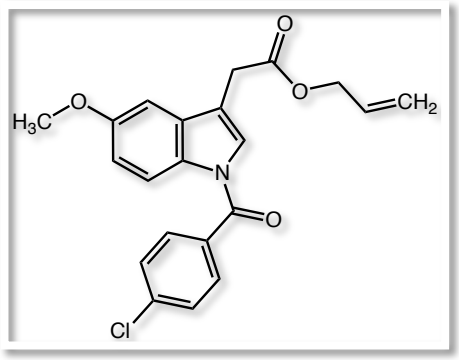
8.5 mg (98%). $C_{22}H_{18}F_3NO_4$, M_r = 417.38; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.69-1.75 (m, 1H), 2.02-2.06 (m, 1H), ~*2.47* (m, 2H, partially overlaid by DMSO signal), 2.71-2.74 (m, 2H), 2.89-2.92 (m, 1H), 3.78 (s, 3H), 6.73 (dd, *J*=2.6/9.0 Hz, 1H), 7.03 (d, *J*=2.4 Hz, 1H), 7.10 (d, *J*=9.2 Hz, 1H), 7.78 (t, *J*=7.8 Hz, 1H), 7.93 (d, *J*=7.6 Hz, 1H), 7.99 (s, 1H), 8.03 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 23.51 (s), 24.73 (s), 25.81 (s), 38.74 (s), 55.68 (s), 101.09 (s), 111.96 (s), 115.49 (s), 116.78 (s), 123.48 (d, *J*=272 Hz, 1C), 126.18 (s), 128.81 (s), 129.34 (s), 130.63 (s), 130.95 (s), 131.37 (d, *J*=29.0 Hz, 1C), 132.42 (s), 135.55 (s), 136.53 (s), 156.35 (s), 167.29 (s), 179.92 (s); ^{19}F NMR (282 MHz, DMSO-d_6) δ: -59.38 (*m*-CF_3); LCMS (ESI) *t*R: 2.74 min (>99%, UV254, ELSD), *m/z*: 418.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{22}H_{18}F_3NO_4$ $[M+H]^+$ calcd mass 418.1266, found 418.1267.

*) starting material ~60% pure (LCMS, ^{1}H NMR); impurity taken into consideration for the calculation of the percent yield!

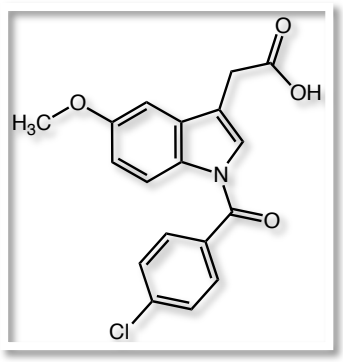
Large Scale Synthesis:



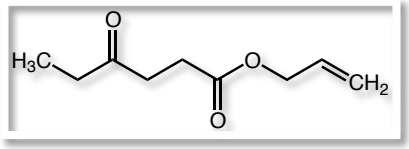
Allyl 2-(5-methoxy-1*H*-indol-3-yl)acetate (25). To a solution of 2-(5-methoxy-1*H*-indol-3-yl)acetic acid **7b** (15.25 g, 74.3 mmol) in 250 mL of acetone were added 29 g of cesium carbonate (89.2 mmol) and allyl bromide (7.1 mL, 81.74 mmol). The reaction mixture was stirred at room temperature for 12 h. The residual cesium carbonate was removed by filtration and solvent was concentrated *in vacuo*. The residue was purified by column chromatography using Hex/EtOAc (gradient: 0 to 30% EtOAc) to afford allyl 2-(5-methoxy-1H-indol-3-yl)acetate 25 (13.6 g, 75 %). $C_{14}H_{15}NO_3$, M_r = 245.27; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.8 (s, 2H), 3.89 (s, 3H), 4.64 (dt, *J* = 1.2, 5.7, 2H), 5.2 (dd, *J* = 1.2, 10.4, 1H), 5.32 (dd, *J* = 1.5, 17.2, 1H), 6.0-5.90 (m, 1H), 6.89 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.09 (d, *J* = 2.4 Hz, 1H), 7.17 (s, 1H), 7.26 (d, *J* = 8.8 Hz, 1H).



Allyl 2-(1-(4-chlorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetate (26). To a solution of allyl 2-(5-methoxy-1*H*-indol-3-yl)acetate 25 (10 g, 40.8 mmol) in dichloromethane (150 mL) were added triethylamine (17.1 mL, 122. 4 mmol) and DMAP (4.9 g, 40.8 mmol) at 0°C. After stirring 30 min, 4-chlorobenzoyl chloride (7.9 mL, 61.2 mmol) was added to the reaction mixture, which was allowed to warm to room temperature and stirred for 12 h. The reaction mixture was then quenched with saturated ammonium chloride (200 mL), extracted with dichloromethane (3 x 150 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography using Hex/EtOAc (gradient: 0 to 30% EtOAc) to afford a yellow solid of allyl 2-(1-(4-chlorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetate **26** (14.3 g, 92 %). $C_{21}H_{18}ClNO_4$, M_r = 383.82; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 2H), 3.88 (s, 3H), 4.62 (d, *J* = 6.0 Hz, 2H), 5.23 (dd, *J* = 1.2, 10.4 Hz, 1H), 5.29 (dd, *J* = 1.2, 17.2 Hz, 1H), 5.95-5.84 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 2H), 7.25 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 8.28 (d, *J* = 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.97 (s), 55.70 (s), 65.74 (s), 101.93 (s), 113.76 (s), 114.68 (s), 117.39 (s), 118.69 (s), 126.31 (s), 128.92 (s, 2C), 130.50 (s, 2C), 130.73 (s), 131.43 (s), 131.78 (s), 132.85 (s), 138.15 (s), 156.89 (s), 166.96 (s), 170.25 (s); LCMS (ESI), single peak, tR: 0.92 min (>99%, UV, ELSD), m/z:, 384.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{18}ClNO_4$ $[M+H]^+$ calcd mass 384.1003, found 384.1003.

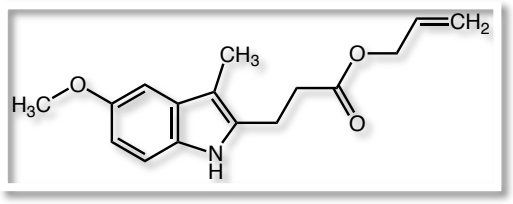


2-(1-(4-chlorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetic acid (2). To a solution of allyl 2-(1-(4-chlorobenzoyl)-5-methoxy-1*H*-indol-3-yl)acetate 3 (14.3 g, 37.3 mmol) in THF (200 mL) were added morpholine (32.5 mL, 373 mmol) and $Pd(PPh_3)_4$ (2.3 g, 1.9 mmol) under argon at room temperature. Stirring was continued until LCMS analysis indicated starting material has disappeared. The mixture was filtered and concentrated *in vacuo*. The residue was redissolved in dichloromethane and acidified with 2N HCl (50 mL) to afford white solid **2** (10 g, 79 %). $C_{18}H_{14}ClNO_4$, M_r = 343.76; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.67 (s, 2H), 3.81 (s, 3H), 6.99 (dd, *J*=2.4/9.2 Hz, 1H), 7.12 (d, *J*=2.4 Hz, 1H), 7.32 (s, 1H), 7.65-7.77 (m, 4H), 8.17 (d, *J*=9.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 30.15 (s), 55.47 (s), 102.70 (s), 113.05 (s), 115.70 (s), 116.70 (s), 126.84 (s), 128.82 (s, 2C), 129.99 (s), 130.69 (s, 2C), 131.87 (s), 133.00 (s), 136.57 (s), 156.30 (s), 166.60 (s), 171.97 (s); LCMS (ESI) tR: 2.60 min (>99%, ELSD), m/z: 344.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{18}H_{14}ClNO_4$ $[M+H]^+$ calcd mass 344.0690, found 344.0687.

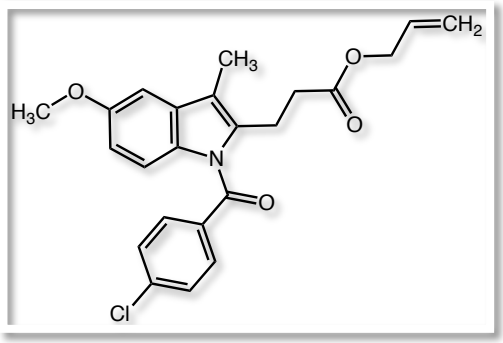


Allyl 4-oxohexanoate (27). Succinyl dichloride 4 (4.6 mL, 41.6 mmol) in dichloromethane (200 mL) was cooled to –40 ˚C and ethylaluminum dichloride (50 mL, 50 mmol) was added at –40 ˚C. The reaction mixture was stirred at –40 ˚C for 3.5 h and quenched with the addition of anhydrous allyl alcohol (100 mL). The reaction mixture was concentrated to dryness and redissolved in dichloromethane

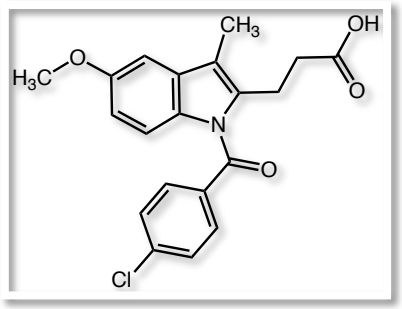
(100 mL). The organic layer was washed with aqueous sodium potassium tartrate (2 x 50 mL), water (50 mL) and saturated aqueous NaCl (50 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to provide pure allyl 4-oxohexanoate **27** (5.2 g, 73 %). $C_9H_{14}O_3$, M_r = 170.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, *J* = 7.2 Hz, 3H), 2.47 (q, *J* = 7.2 Hz, 2H), 2.62 (t, *J* = 6.4 Hz, 2H), 2.73 (t, *J* = 6.4 Hz, 2H), 4.57 (d, *J* = 5.6 Hz, 2H), 5.23 (dd, *J* = 1.2, 10.4 Hz, 1H), 5.31 (dd, *J* = 1.2, 18.0 Hz, 1H), 5.96-5.84 (m, 1H).



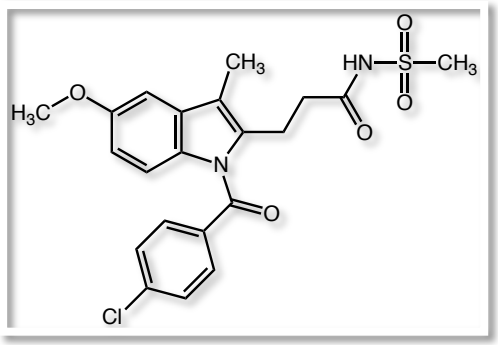
Allyl 3-(5-methoxy-3-methyl-1*H*-indol-2-yl)propanoate (28). To a mixture of (4-methoxyphenyl)hydrazine (10.4 g, 59.7 mmol) and allyl 4-oxohexanoate 5 (10.2 g, 59.7 mmol) in 1,4-dioxane (60 mL) was added acetic acid (30 mL) at room temperature. The reaction mixture was heated at 80 ˚C for 6 h then quenched with saturated $NaHCO_3$ (150 mL), extracted with EtOAc (3 x 60 mL), and dried over $MgSO_4$. The residue was purified by column chromatography using Hex/EtOAc (gradient: 0 to 40 % EtOAc) to afford brown oil allyl 3-(5-methoxy-3-methyl-1*H*-indol-2-yl)propanoate **28** (11.6 g, 71 %). $C_{16}H_{19}NO_3$, M_r = 273.33; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.68 (t, *J* = 6.4 Hz, 2H), 3.03 (t, *J* = 6.4 Hz, 2H), 3.86 (s, 3H), 4.60 (d, *J* = 7.2 Hz, 2H), 5.23 (dd, *J* = 1.2, 10.4 Hz, 1H), 5.29 (dd, *J* = 1.2, 17.2 Hz, 1H), 5.95- 5.83 (m, 1H), 6.78 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.43 (s), 20.91 (s), 34.09 (s), 55.95 (s), 65.47 (s), 100.50 (s), 106.91 (s), 111.04 (s), 111.08 (s), 118.54 (s), 129.32 (s), 130.39 (s), 131.85 (s), 134.45 (s), 153.73 (s), 173.45 (s); LCMS (ESI), single peak, tR: 0.79 min, m/z: 274.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{16}H_{19}NO_3$ $[M+H]^+$ calcd mass 274.1443, found 274.1441.



Allyl 3-(1-(4-chlorobenzoyl)-5-methoxy-3-methyl-1*H*-indol-2-yl)propanoate (29). To a solution of allyl 3-(5-methoxy-3-methyl-1*H*-indol-2-yl)propanoate **28** (16 g, 61.8 mmol) in 1,2-dichloroethane (200 mL) were added triethylamine (34.5 mL, 247.2 mmol) and DMAP (7.55 g, 61.8 mmol) at 0°C. After stirring for 30 min, 4-chlorobenzoyl chloride (19.7 mL, 154.6 mmol) was added to the reaction mixture, which was allowed to stir for 12 h under reflux condition. The reaction mixture was cooled down, quenched with saturated ammonium chloride (200 mL), extracted with dichloromethane (3 x 150 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography using Hex/EtOAc (gradient: 0 to 30% EtOAc) to afford brown oil of allyl 3-(1-(4-chlorobenzoyl)-5-methoxy-3-methyl-1*H*-indol-2-yl)propanoate **29** (22.2 g, 87 %). $C_{23}H_{22}ClNO_4$, M_r = 411.88; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (s, 3H), 2.69 (t, *J* = 7.6 Hz, 2H), 3.29 (t, *J* = 7.6 Hz, 2H), 3.83 (s, 3H), 4.53 (d, *J* = 6.0 Hz, 2H), 5.18 (dd, *J* = 1.2, 10.4 Hz, 1H), 5.25 (dd, *J* = 1.2, 17.2 Hz, 1H), 5.93-5.78 (m, 1H), 6.44 (d, *J* = 9.2 Hz, 1H), 6.59 (dd, *J* = 2.8, 8.4 Hz, 1H), 6.89 (d, *J* = 2.8 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.67 (s), 21.67 (s), 34.14 (s), 55.65 (s), 65.18 (s), 101.38 (s), 111.48 (s), 114.78 (s), 116.38 (s), 118.28 (s), 129.10 (s, 2C), 129.33 (s), 130.76 (s), 131.15 (s, 2C), 131.66 (s), 131.84 (s), 132.06 (s), 133.88 (s), 136.71 (s), 139.15 (s), 155.77 (s), 168.13 (s), 172.23 (s); LCMS ESI), single peak, tR: 0.99 min, m/z, 412.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{23}H_{22}ClNO_4$ $[M+H]^+$ calcd mass 412.1316, found 412.1320.



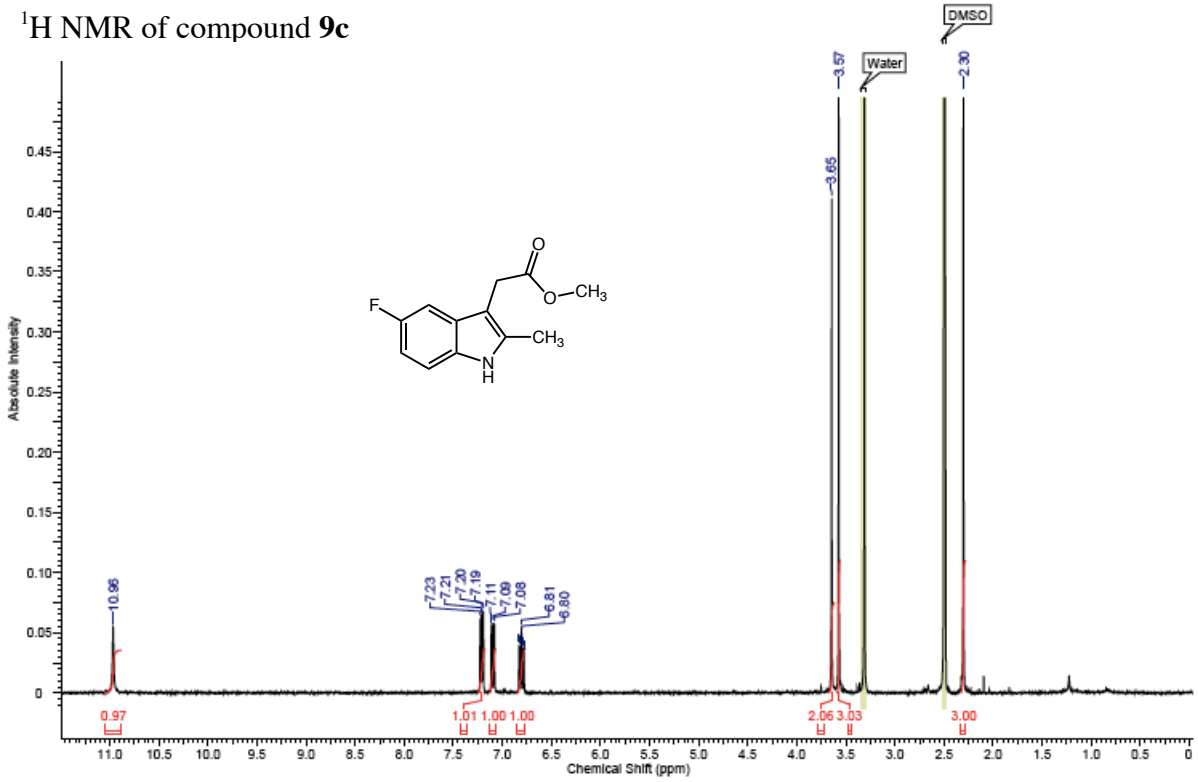
3-(1-(4-chlorobenzoyl)-5-methoxy-3-methyl-1*H*-indol-2-yl)propanoic acid (30). To a solution of allyl 3-(1-(4-chlorobenzoyl)-5-methoxy-3-methyl-1*H*-indol-2-yl)propanoate **29** (11.1 g, 26.9 mmol) in THF (200 mL) were added morpholine (23.0 mL, 269 mmol) and $Pd(PPh_3)_4$ (1.67 g, 1.35 mmol) under argon at room temperature. Stirring was continued until LCMS analysis indicated starting material has disappeared. The mixture was filtered and concentrated *in vacuo*. The residue was redissolved in dichloromethane, acidified with 2N HCl (50 mL), concentrated *in vacuo*, and purified by column chromatography using Hex/EtOAc (gradient: 0 to 100 % EtOAc) to afford yellow solid of 3-(1-(4-chlorobenzoyl)-5-methoxy-3-methyl-1*H*-indol-2-yl)propanoic acid **30** (7.9 g, 79%). $C_{20}H_{18}ClNO_4$, M_r = 371.81; ^{1}H NMR (400 MHz, $CDCl_3$,) δ 2.24 (s, 3H), 2.72 (t, *J* = 7.6 Hz, 2H), 3.29 (t, *J* = 7.6 Hz, 2H), 3.83 (s, 3H), 6.42 (d, *J* = 9.2 Hz, 1H), 6.59 (dd, *J* = 2.8, 9.2 Hz, 1H), 6.90 (d, *J* = 2.8 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 8.40 (s), 21.24 (s), 33.74 (s), 55.42 (s), 101.55 (s), 111.58 (s), 114.38 (s), 115.74 (s), 129.15 (s, 2C), 130.26 (s), 131.24 (s, 2C), 134.04 (s), 136.72 (s), 137.78 (s), 155.46 (s), 167.77 (s), 173.40 (s), one signal invisible; LCMS (ESI), single peak, tR: 0.82 min, m/z:, 372.0 $[M+H]^+$; HRMS (TOF, ES+) $C_{20}H_{18}ClNO_4$ $[M+H]^+$ calcd mass 372.1003, found 372.1005.



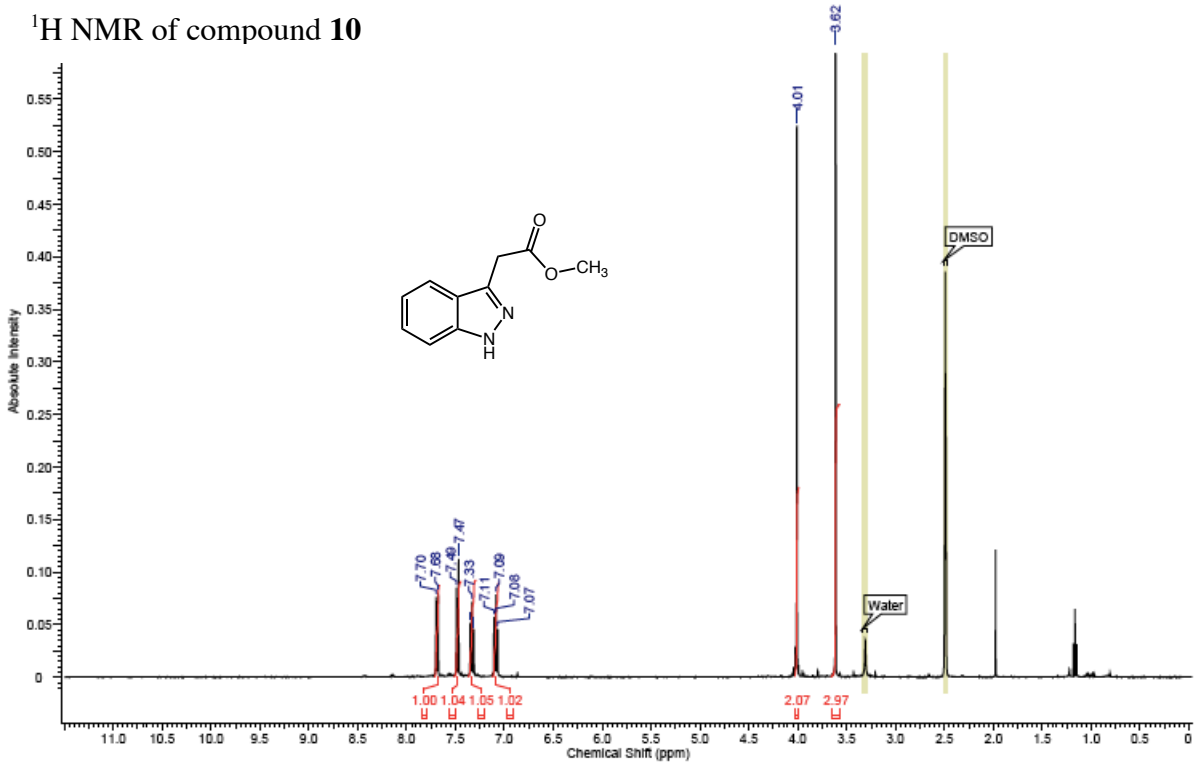
3-(1-(4-chlorobenzoyl)-5-methoxy-3-methyl-1*H*-indol-2-yl)-N-(methylsulfonyl)propanamide (31). The reaction mixture of 3-(1-(4-chlorobenzoyl)-5-methoxy-3-methyl-1*H*-indol-2-yl)propanoic acid **30** (7 g, 18.8 mmol) and methanesulfonamide (1.97 g, 20.7 mmol) in dichloromethane (94 mL) was treated with 1,1'-carbonyldiimidazole (3.05 g, 18.8 mmol) and DBU (3.4 mL, 22.6 mmol) at 0 ˚C. The reaction mixture was stirred at room temperature for 4h then quenched with acetic acid (5 mL) and washed with brine (3 x 40 mL). The organic layer was then dried over $MgSO_4$ and the solvent was removed *in vacuo*. The yellow solid **31** (5.6 g, 61 %) was obtained after column chromatography purification using Hex/EtOAc (gradient: 0 to 100 % EtOAc with 0.5 % of acetic acid). $C_{21}H_{21}ClN_2O_5S$, M_r = 170.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 2.54 (dd, *J* = 7.2, 7.6 Hz, 2H), 3.10 (dd, *J* = 7.2, 7.6 Hz, 2H), 3.14 (s, 3H), 3.75 (s, 3H), 6.42 (d, *J* = 9.2 Hz, 1H), 7.70-7.64 (m, 4H), 6.63 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.01 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 8.42 (s), 20.57 (s), 35.30 (s), 40.96 (s), 55.42 (s), 101.59 (s), 111.66 (s), 114.45 (s), 116.01 (s), 129.13 (s, 2C), 130.25 (s), 131.20 (s), 131.27 (s, 2C), 134.00 (s), 136.31 (s), 137.77 (s), 155.48 (s), 167.74 (s), 171.42 (s); LCMS (ESI), single peak, 0.81 min, m/z, 449.08 $[M+H]^+$; HRMS (TOF, ES+) $C_{21}H_{21}ClN_2O_5S$ $[M+H]^+$ calcd mass 449.0938, found 449.0941.

NMR spectra of selected intermediates:

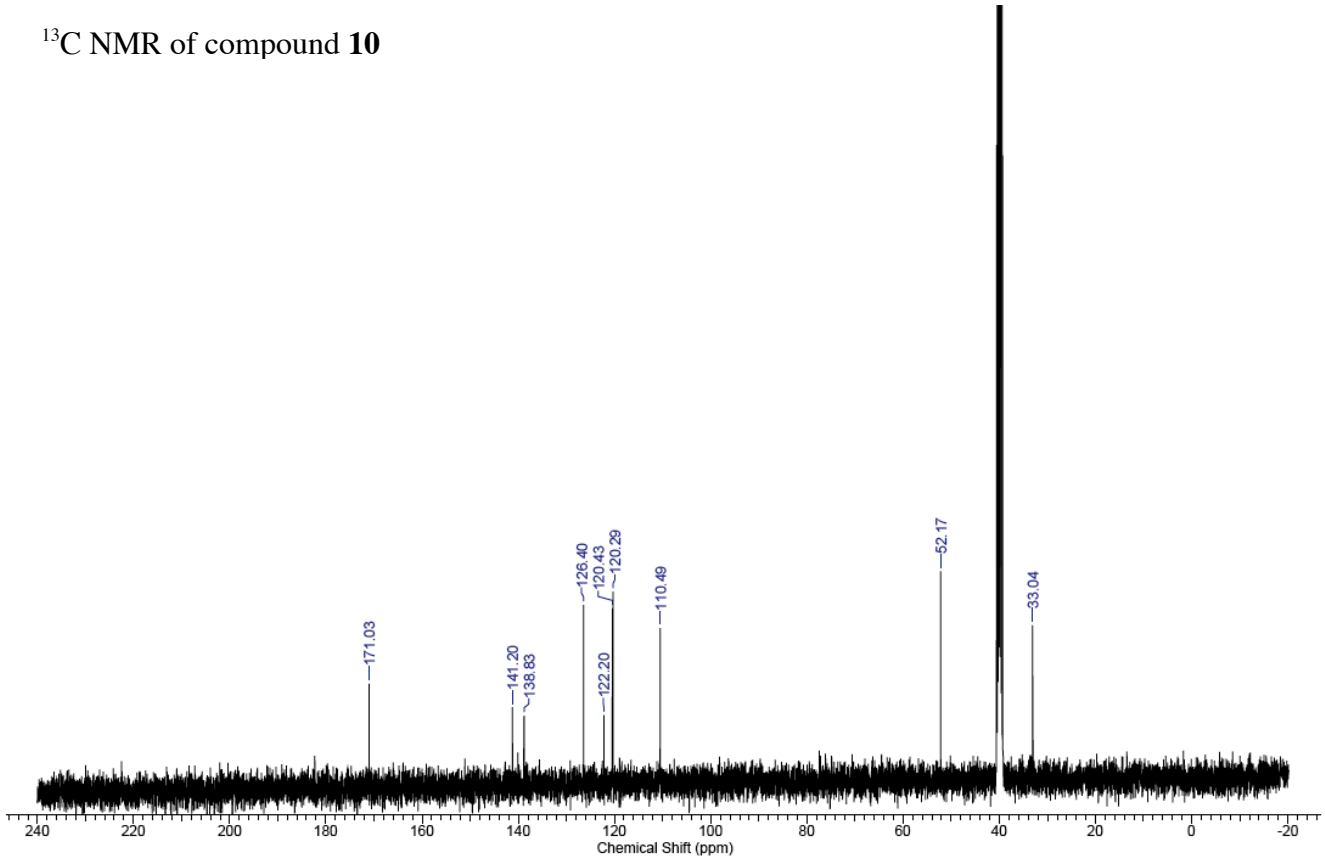
^{1}H NMR of compound **9c**



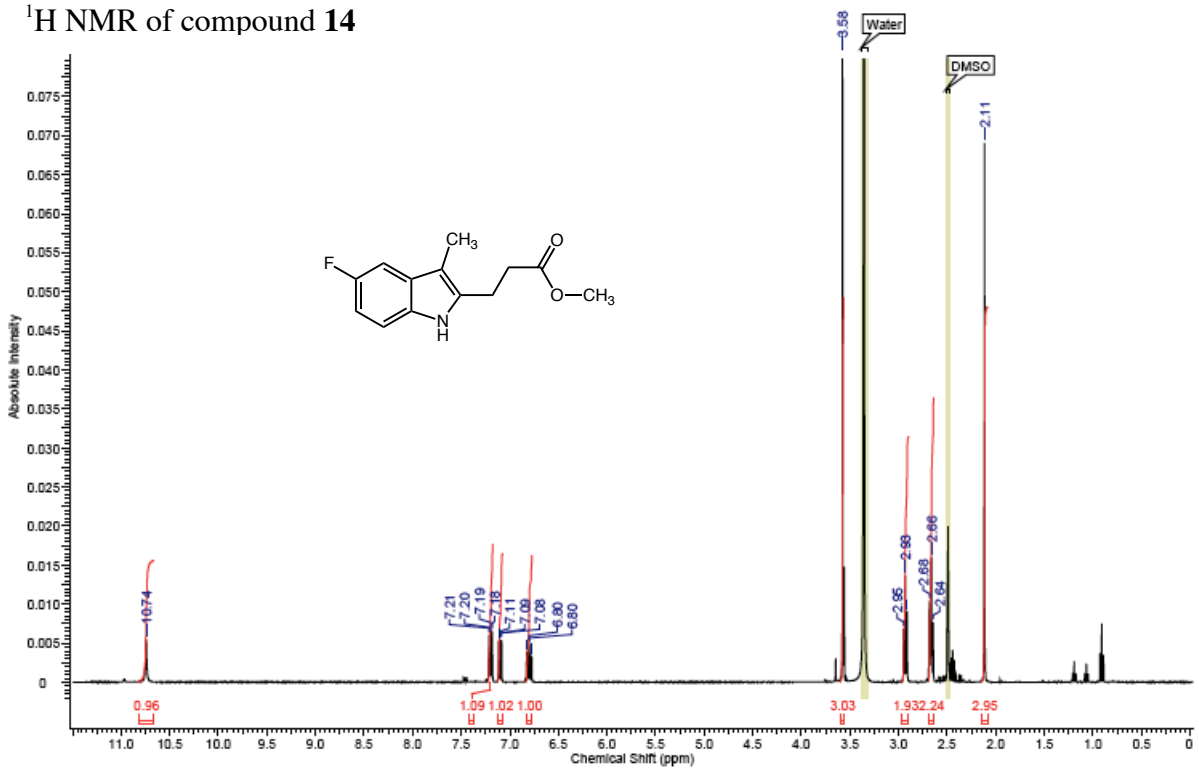
^{1}H NMR of compound **10**



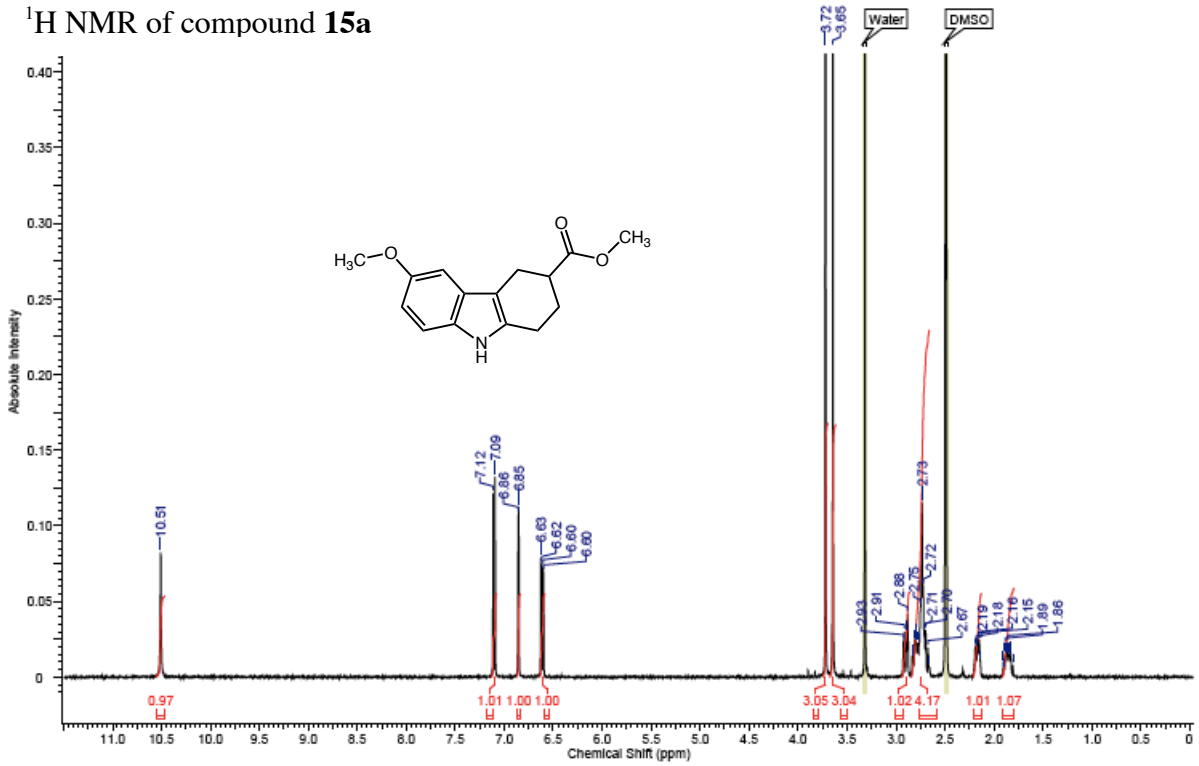
^{13}C NMR of compound **10**



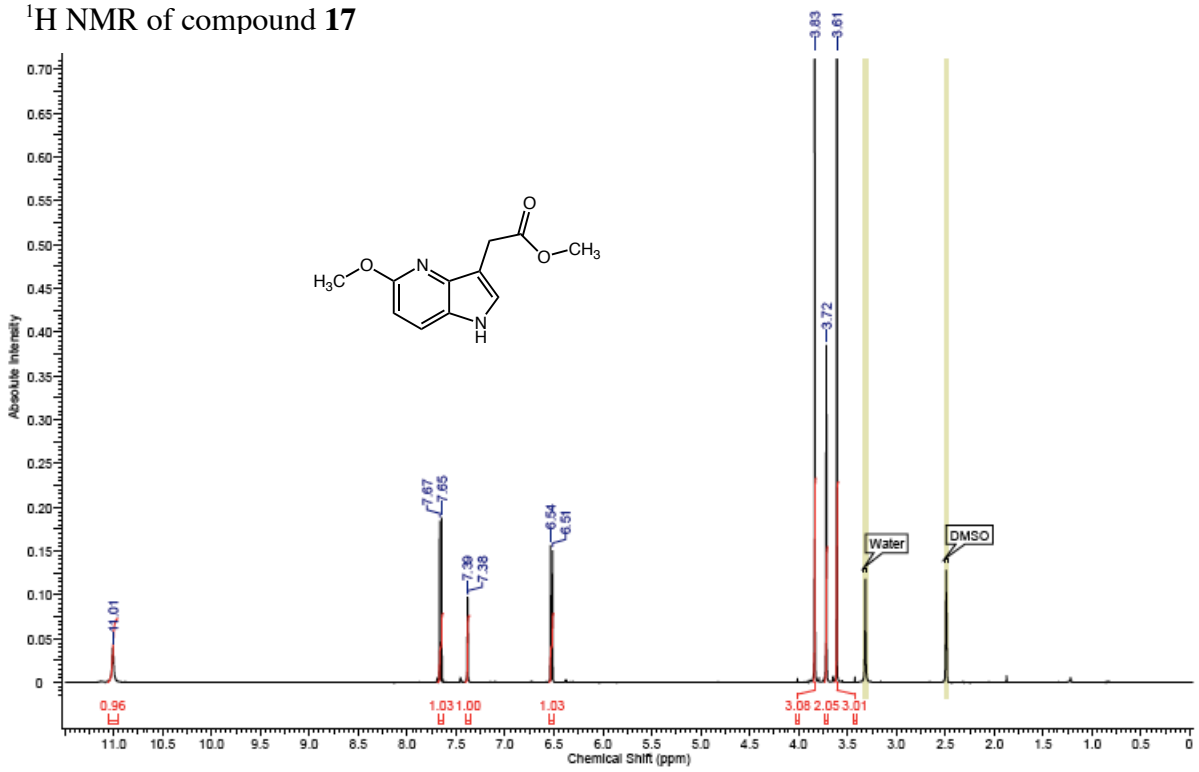
^{1}H NMR of compound **14**



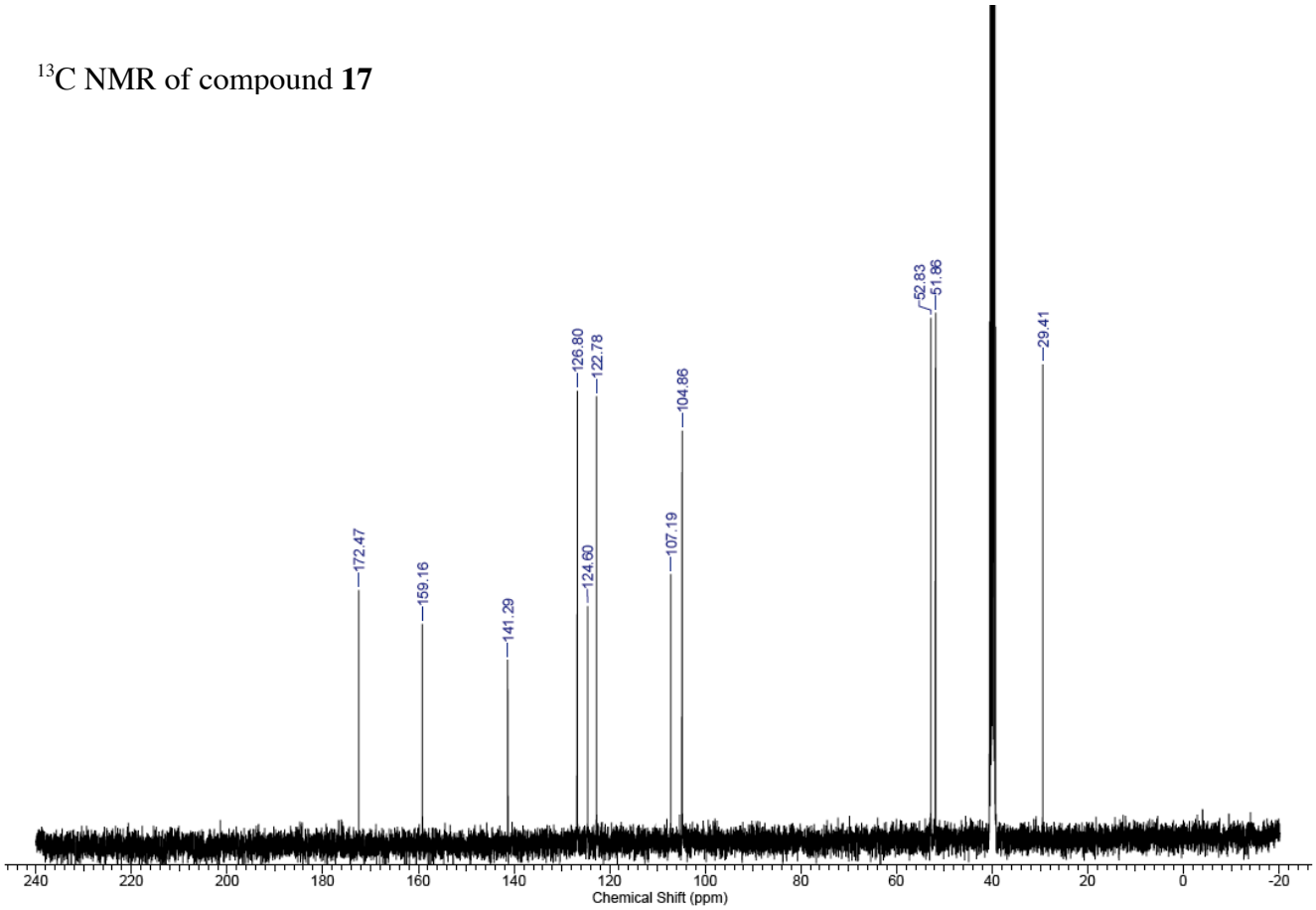
^{1}H NMR of compound **15a**



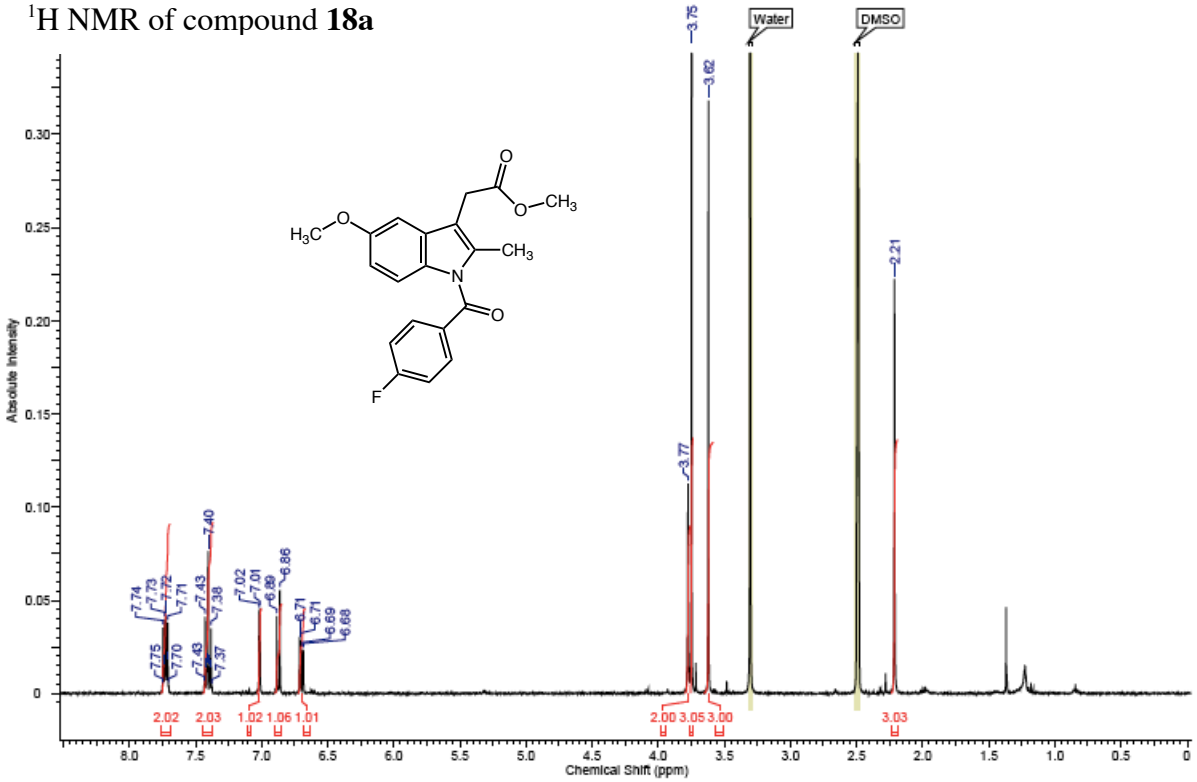
^{1}H NMR of compound **17**



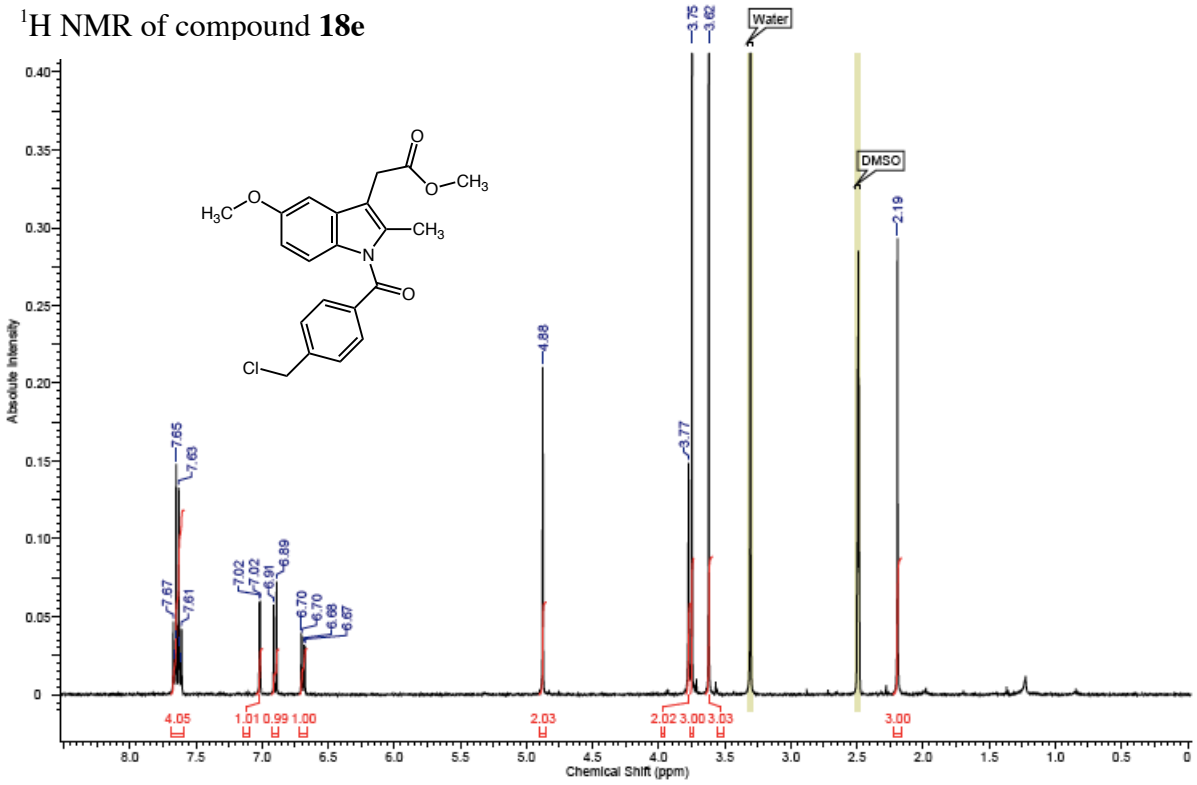
^{13}C NMR of compound **17**



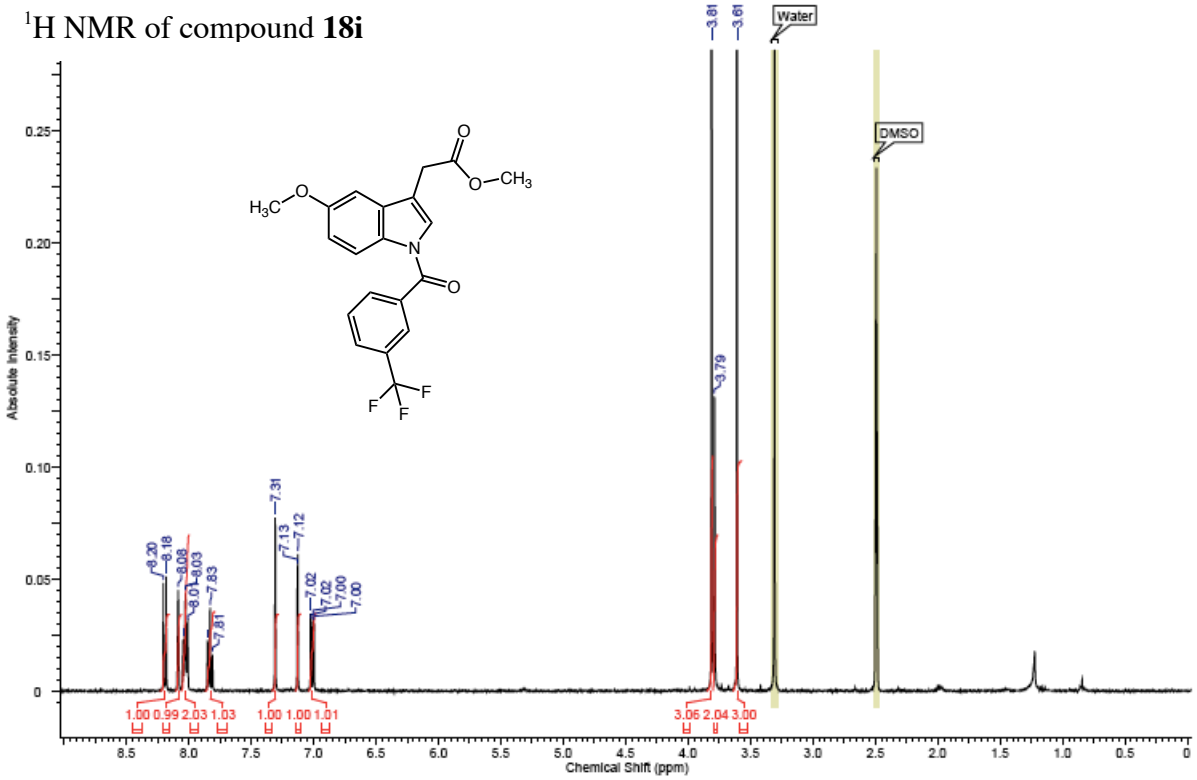
^{1}H NMR of compound **18a**



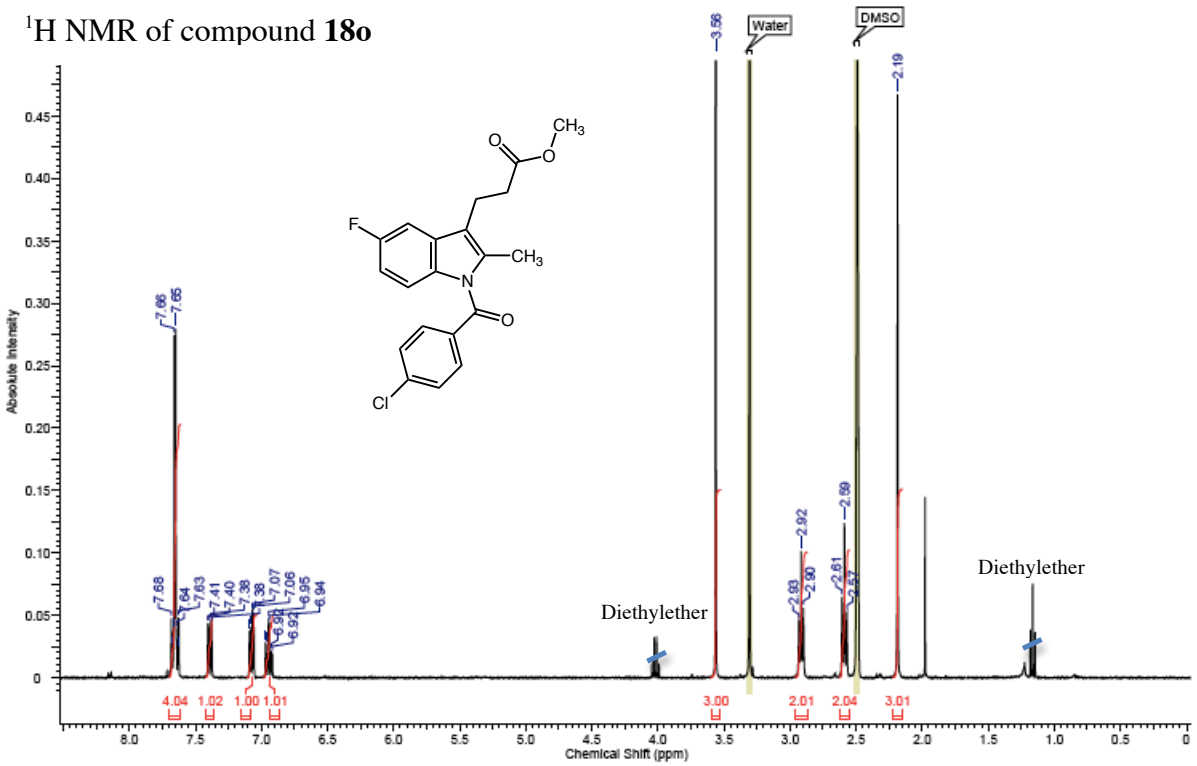
^{1}H NMR of compound **18e**



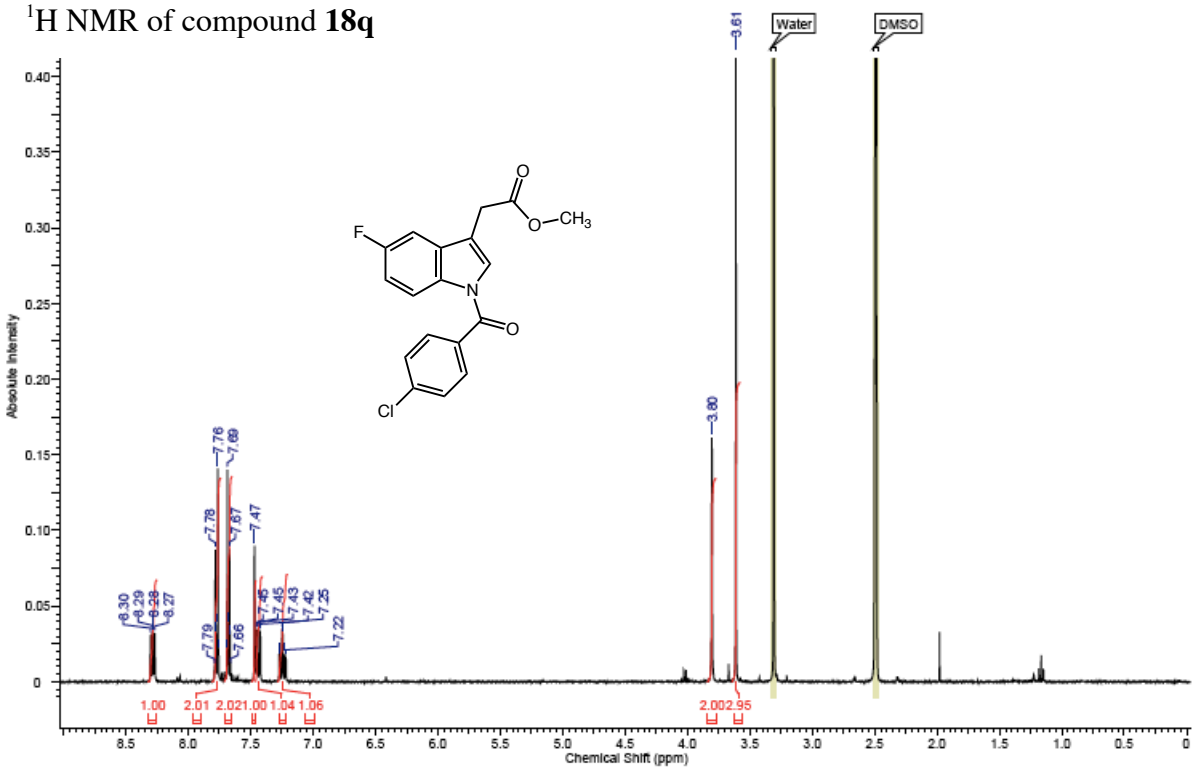
^{1}H NMR of compound **18i**



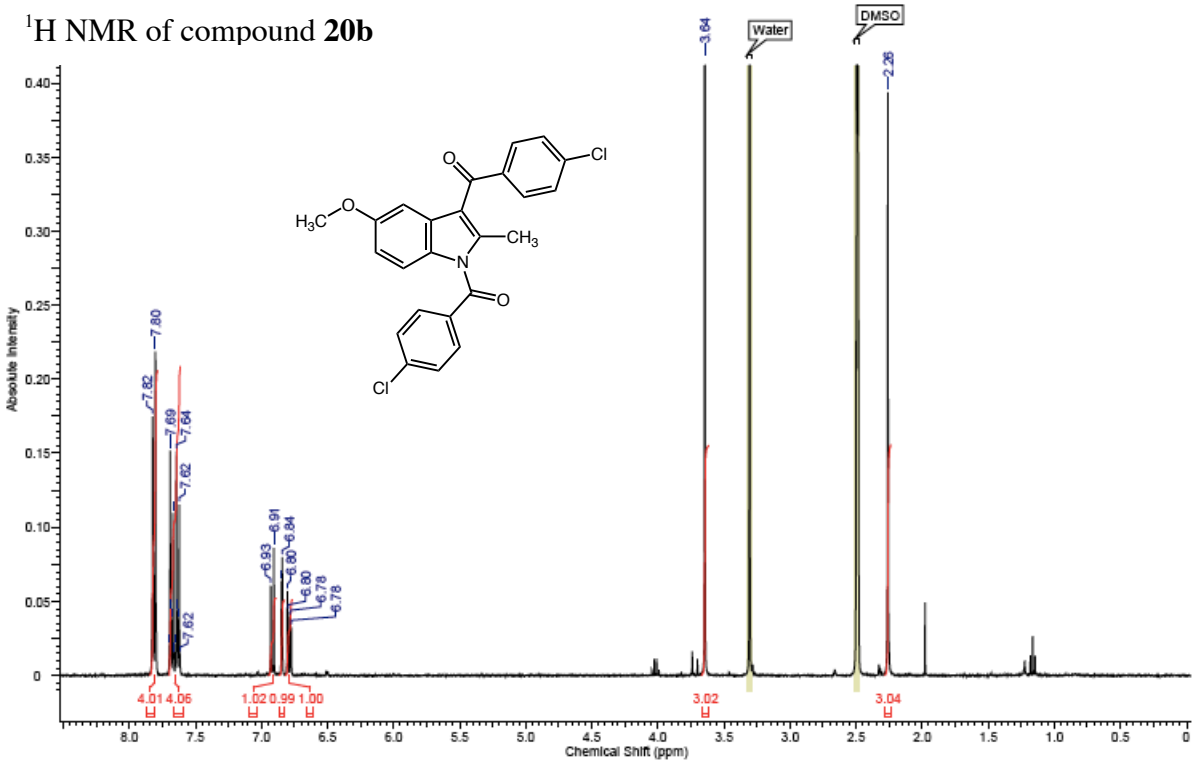
^{1}H NMR of compound **18o**



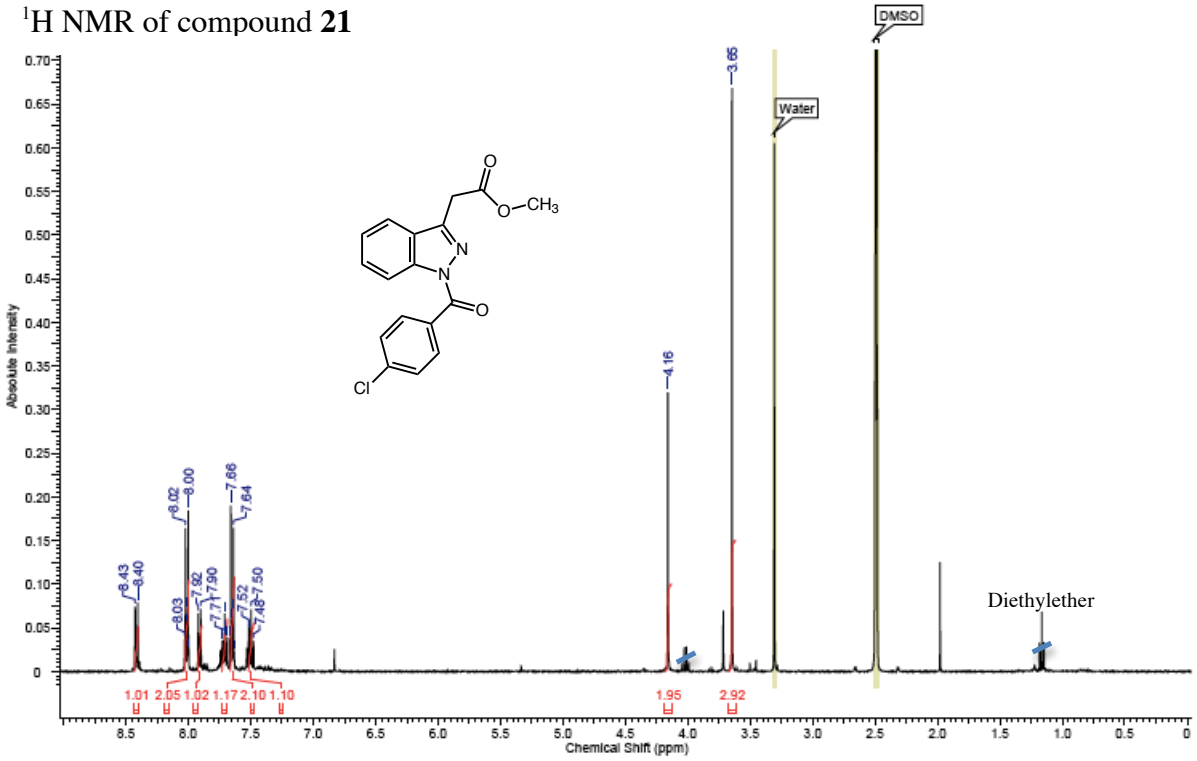
^{1}H NMR of compound **18q**



^{1}H NMR of compound **20b**

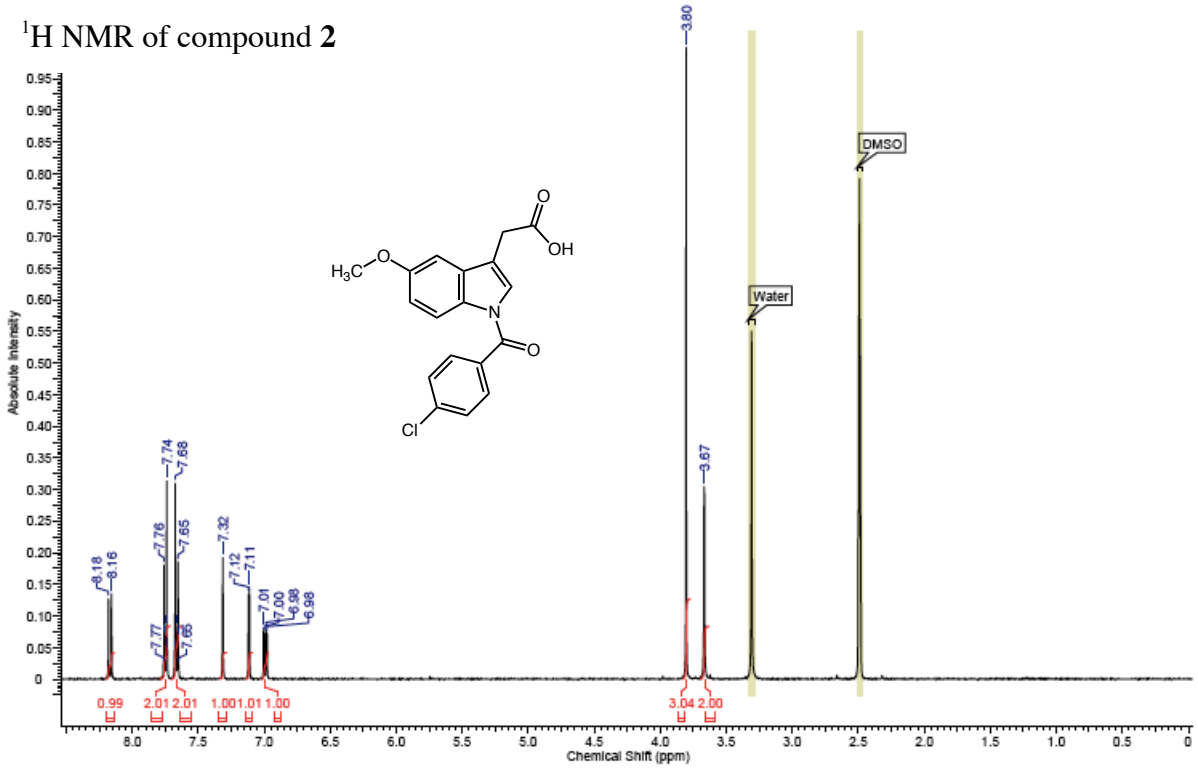


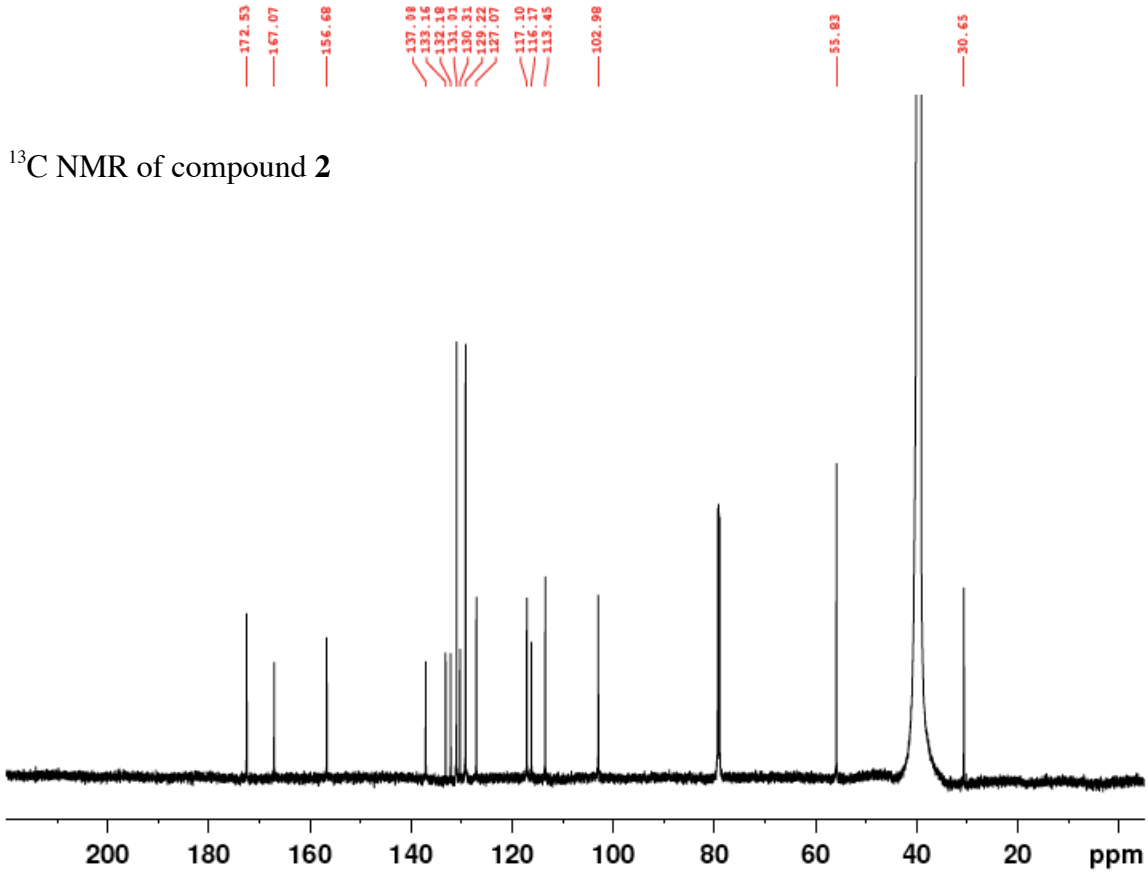
^{1}H NMR of compound **21**



NMR spectra of all final compounds (free acids):

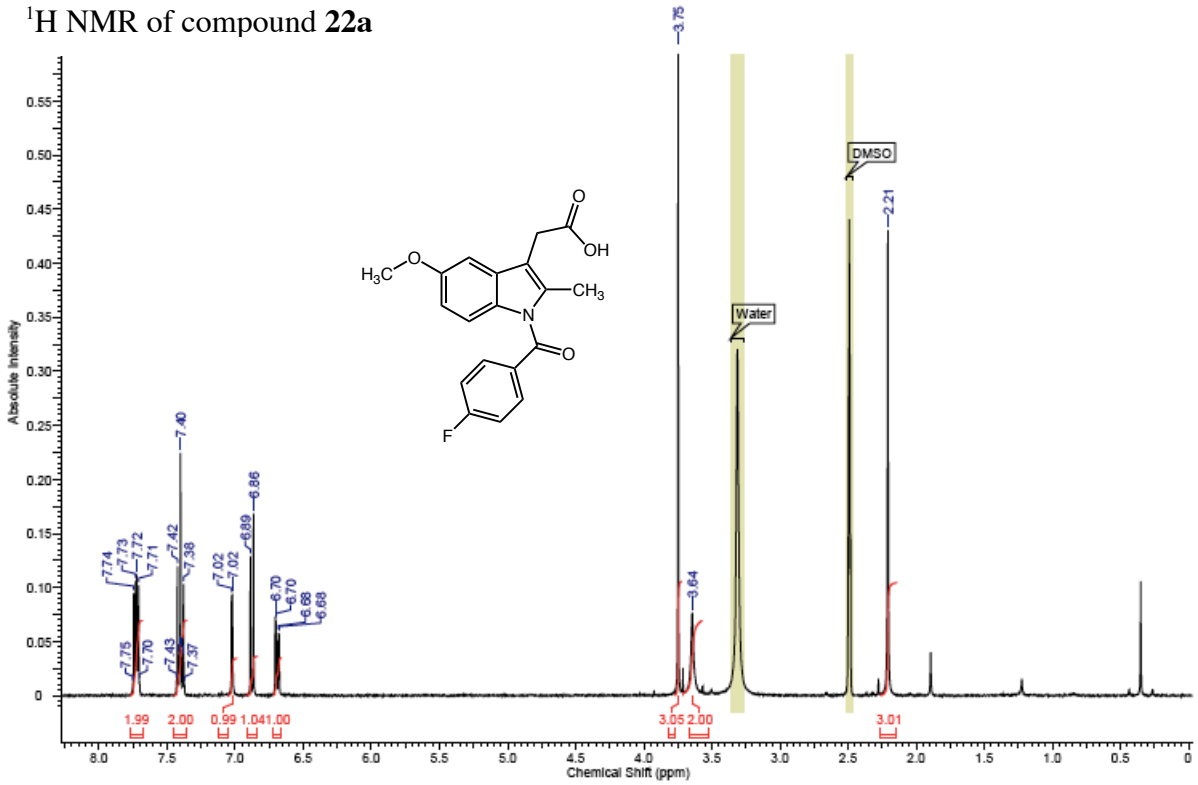
^{1}H NMR of compound **2**



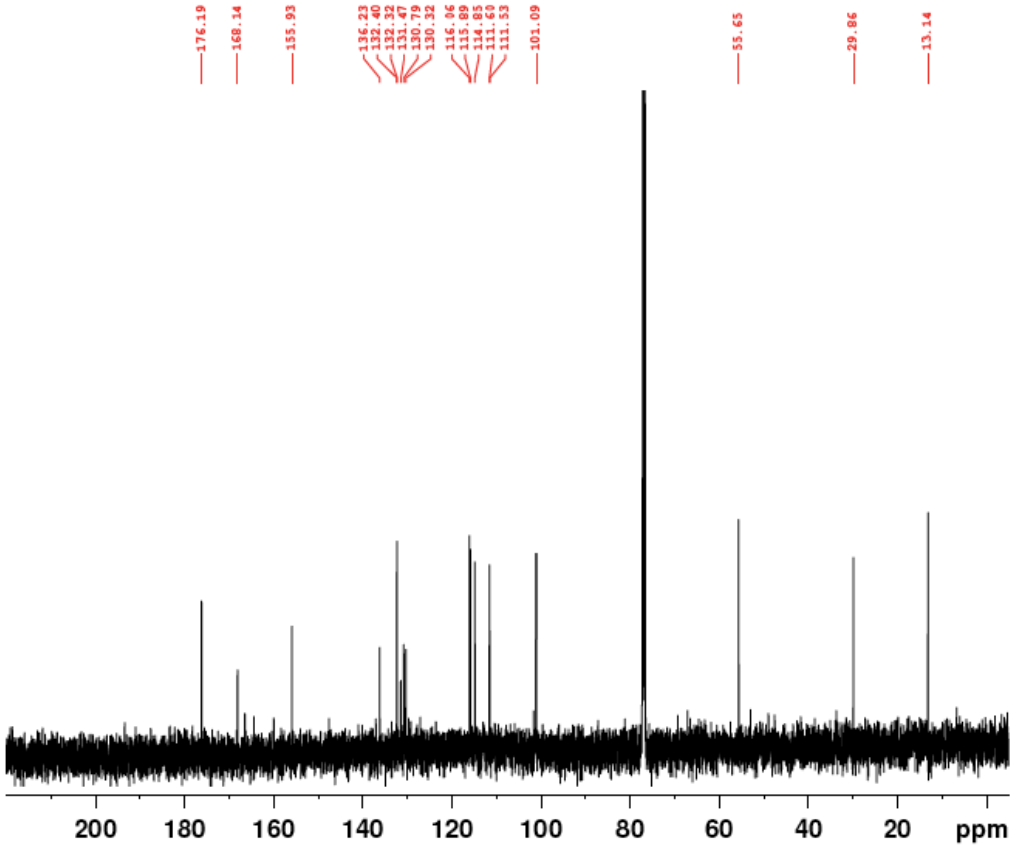


^{13}C NMR of compound **2**

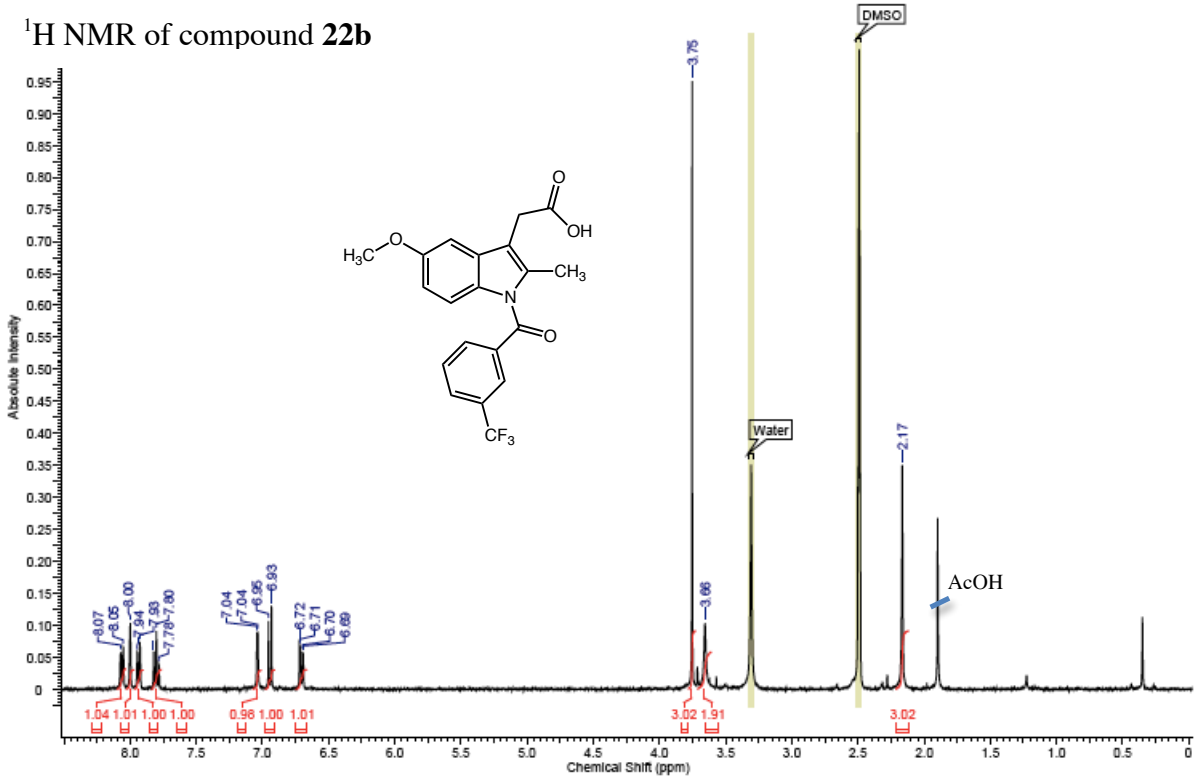
[1]H NMR of compound **22a**



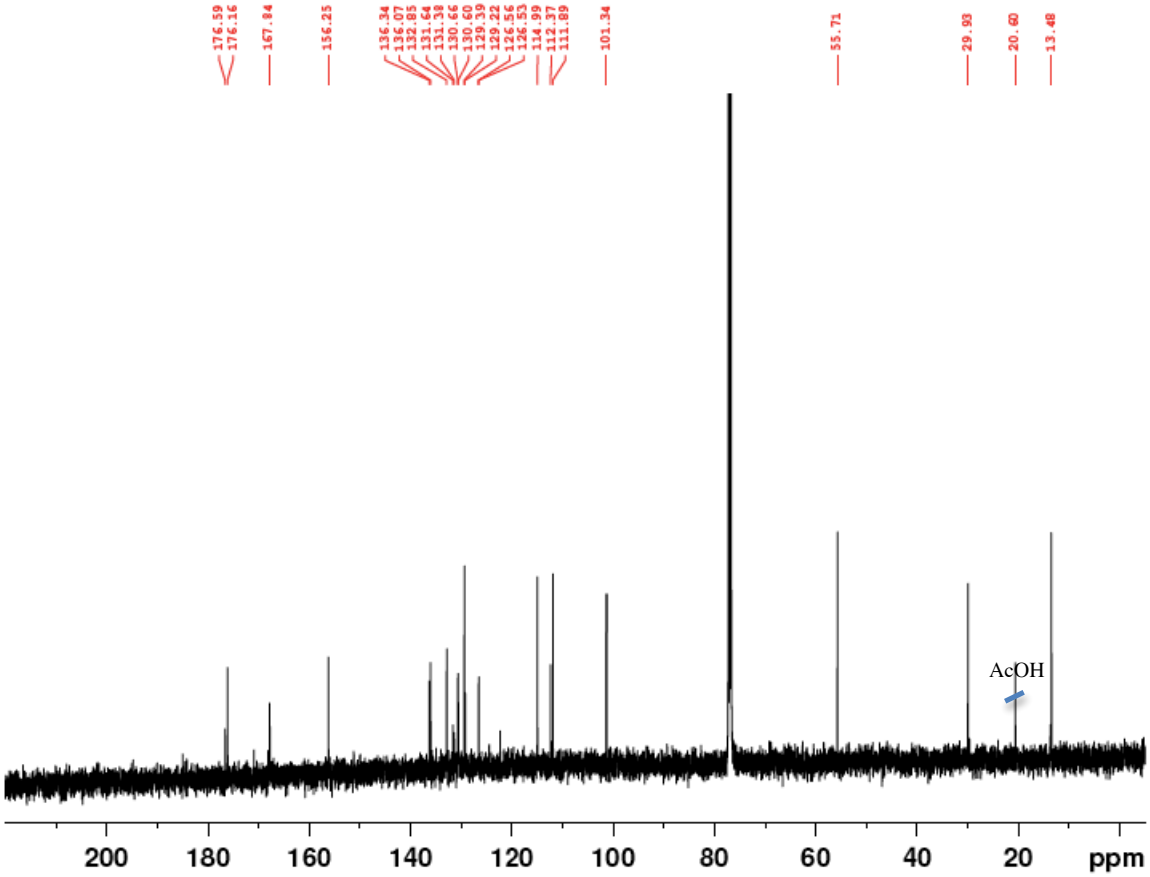
[13]C NMR of compound **22a**



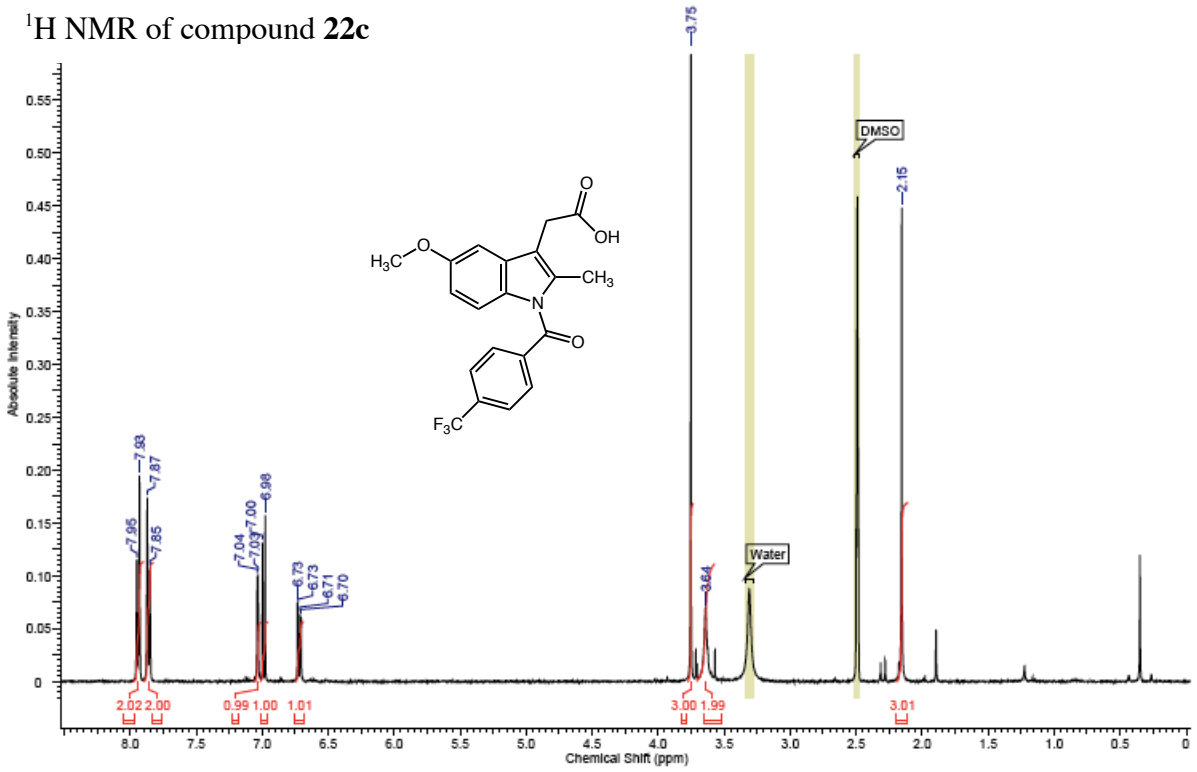
[1]H NMR of compound **22b**



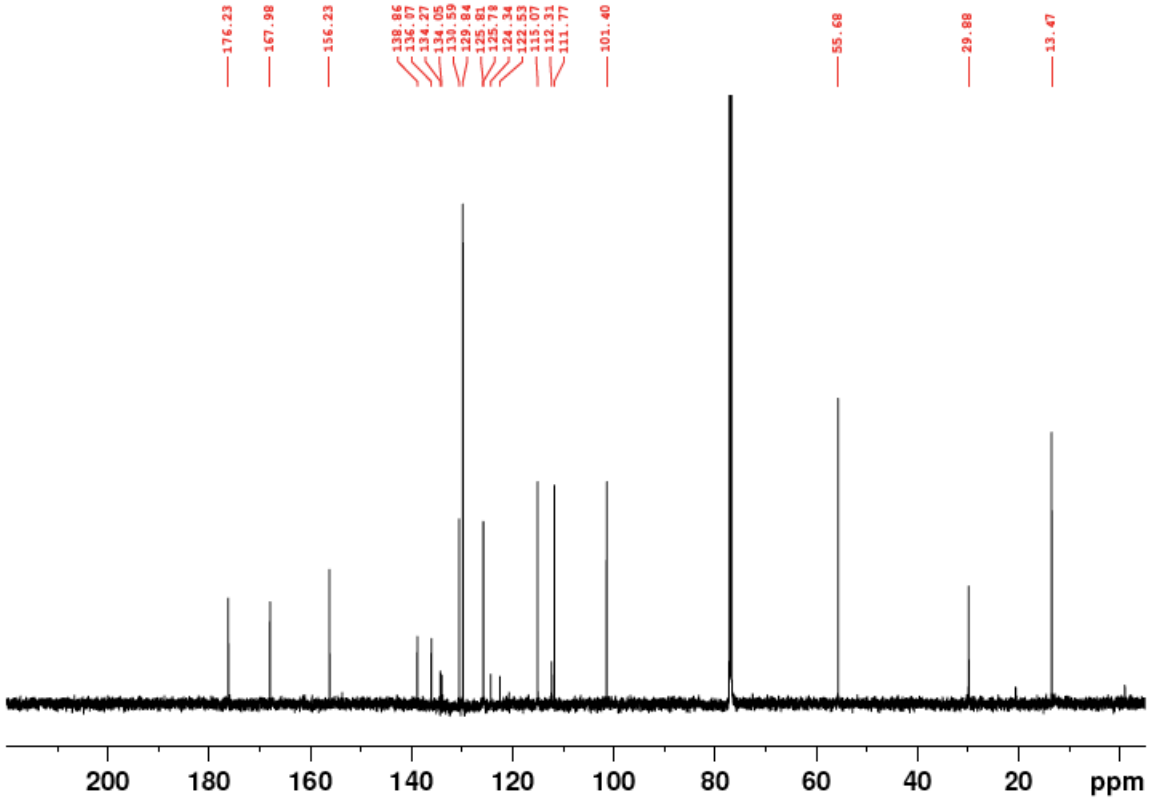
[13]C NMR of compound **22b**



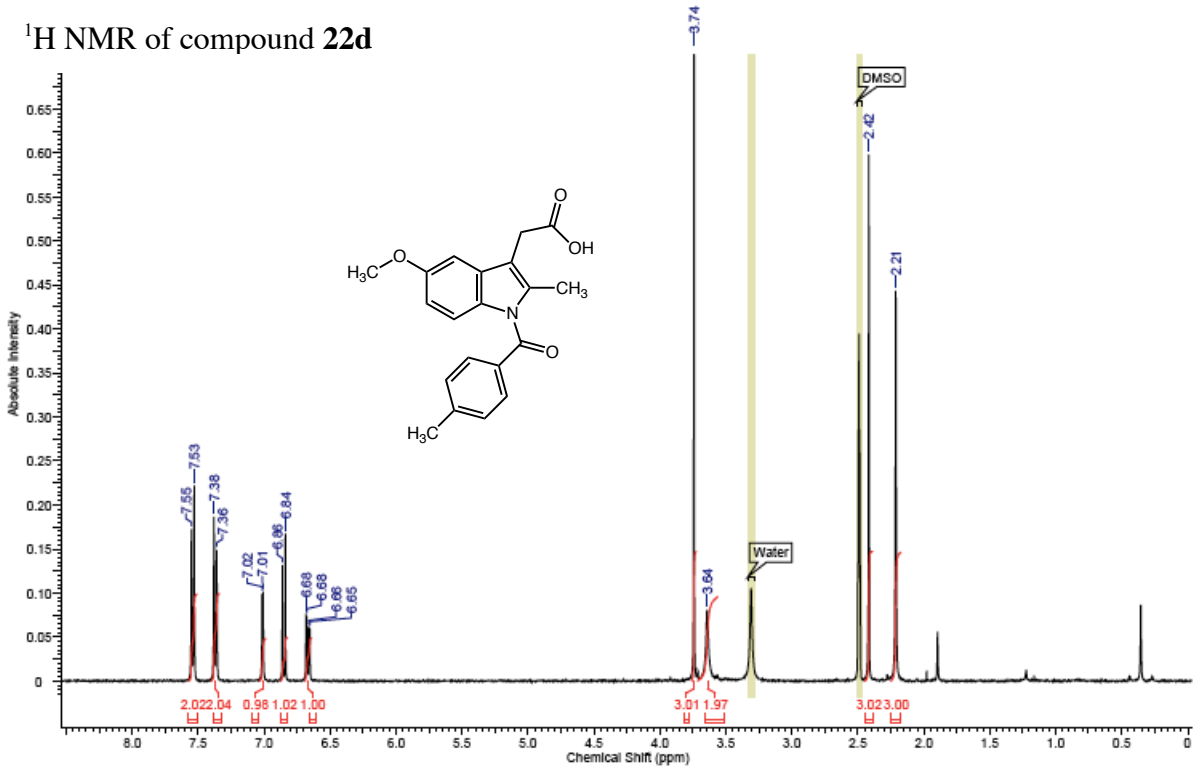
^{1}H NMR of compound **22c**



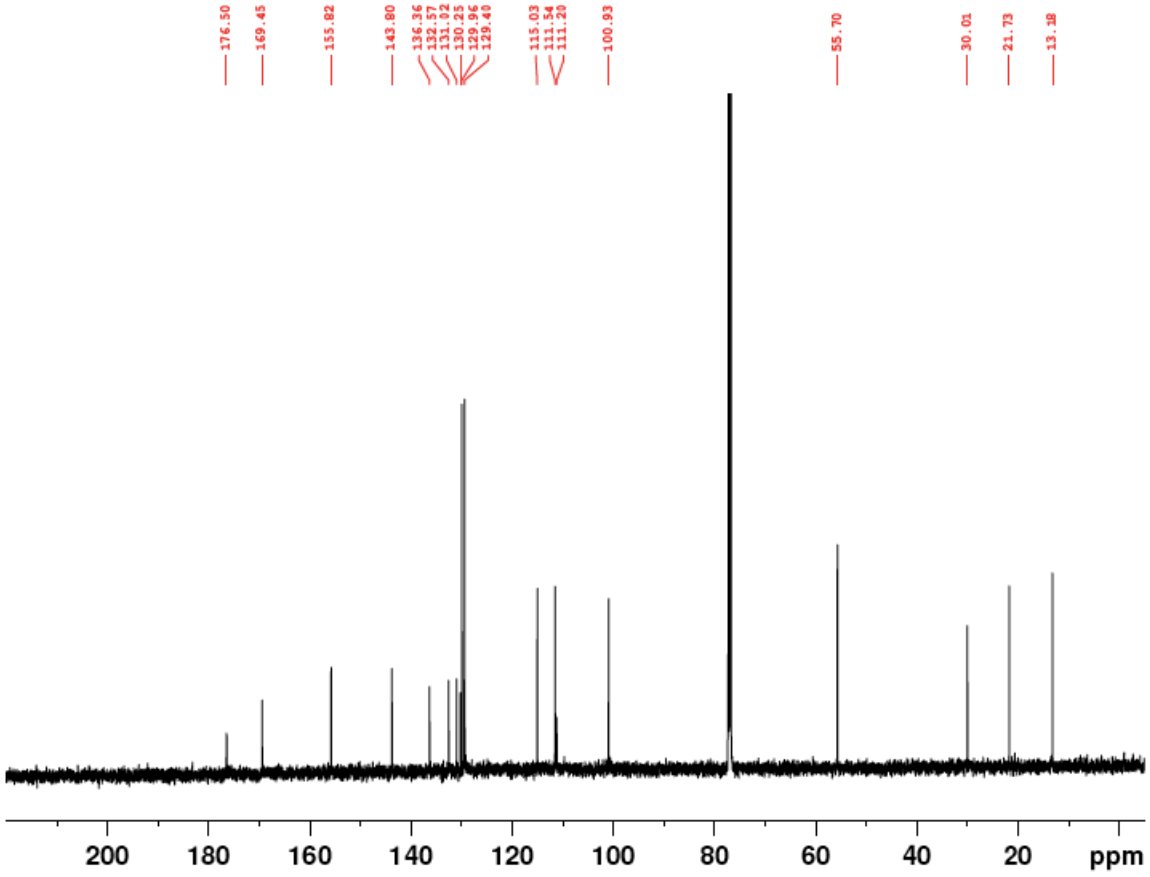
^{13}C NMR of compound **22c**



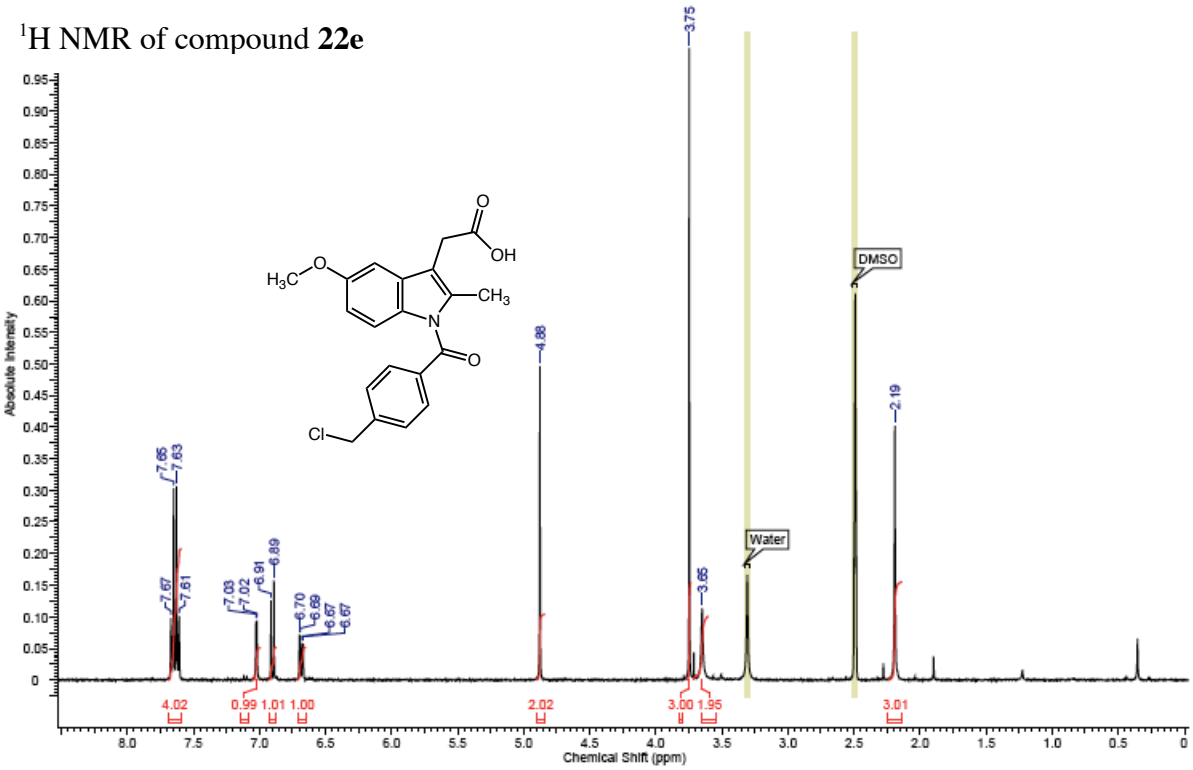
^{1}H NMR of compound **22d**



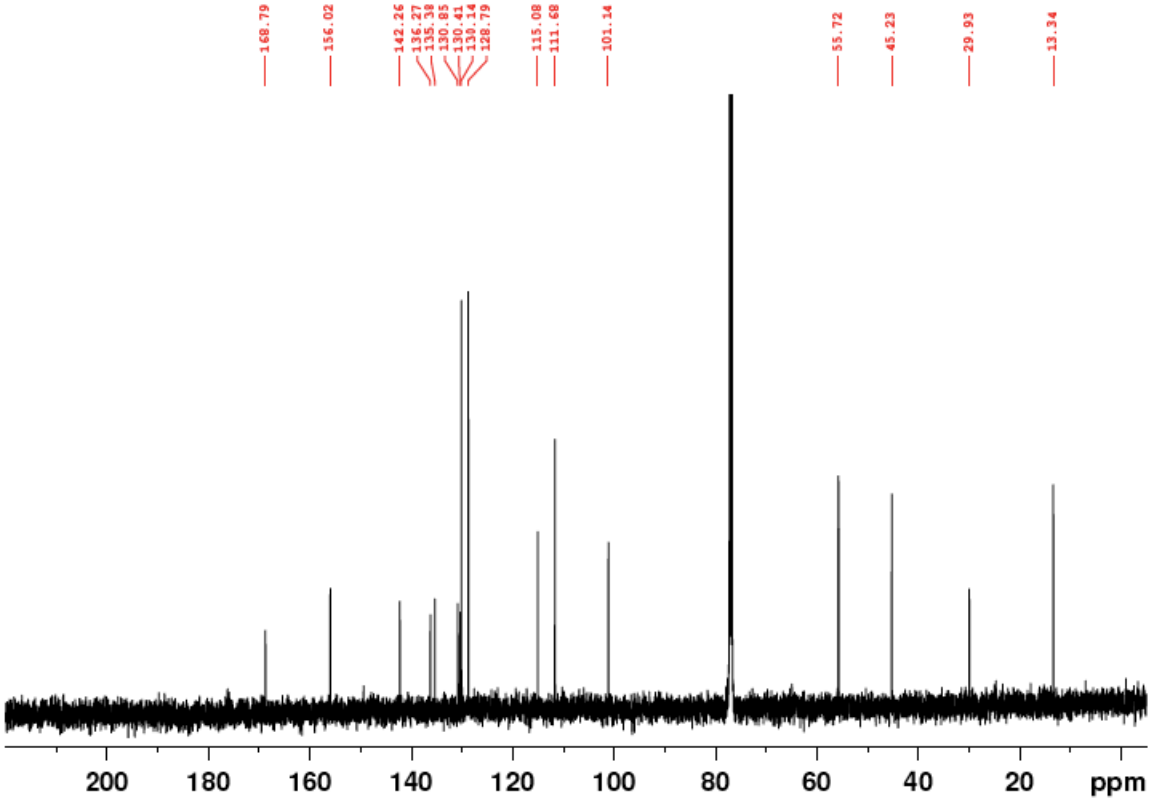
^{13}C NMR of compound **22d**



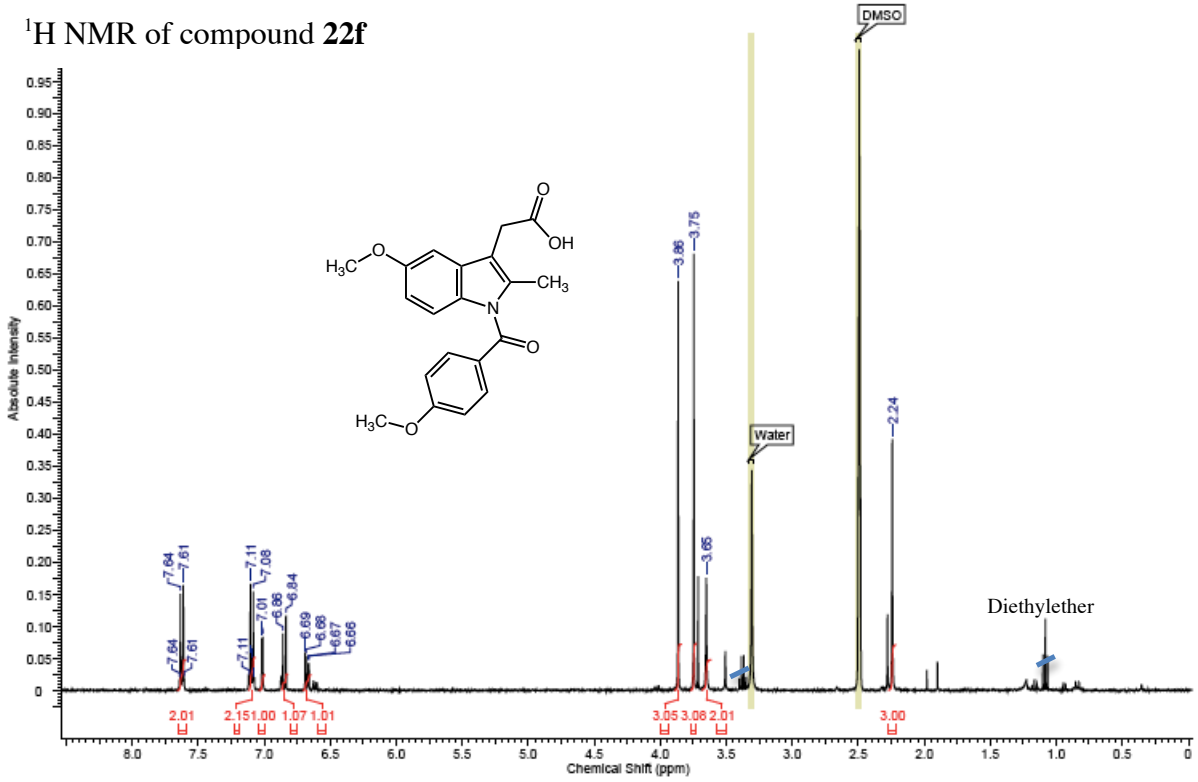
^{1}H NMR of compound **22e**



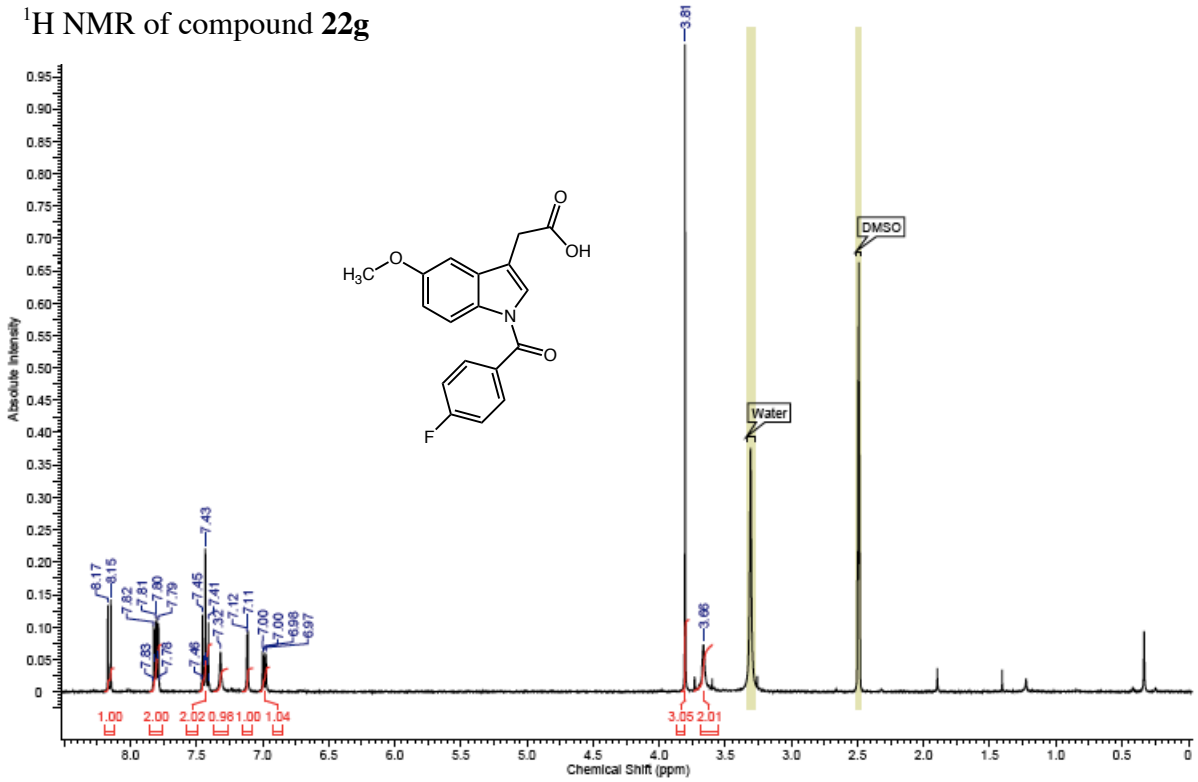
^{13}C NMR of compound **22e**



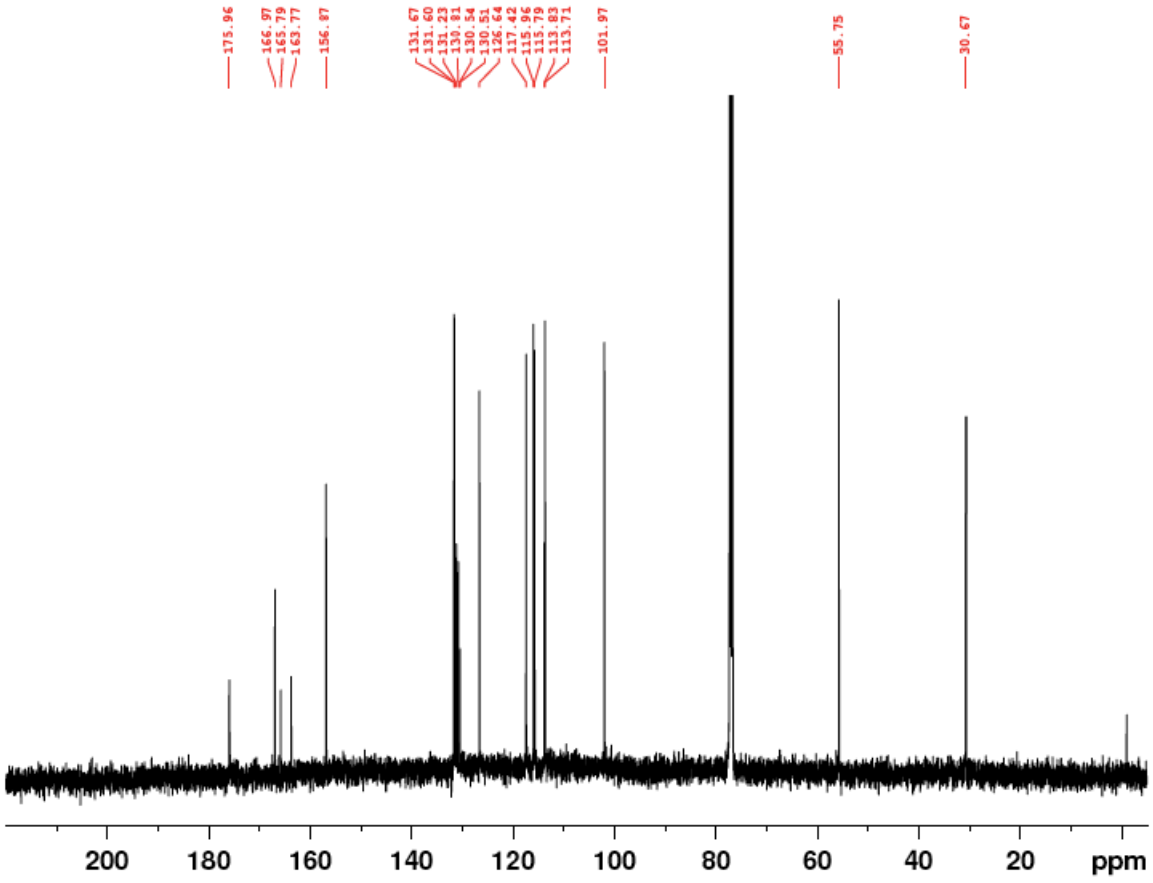
^{1}H NMR of compound **22f**



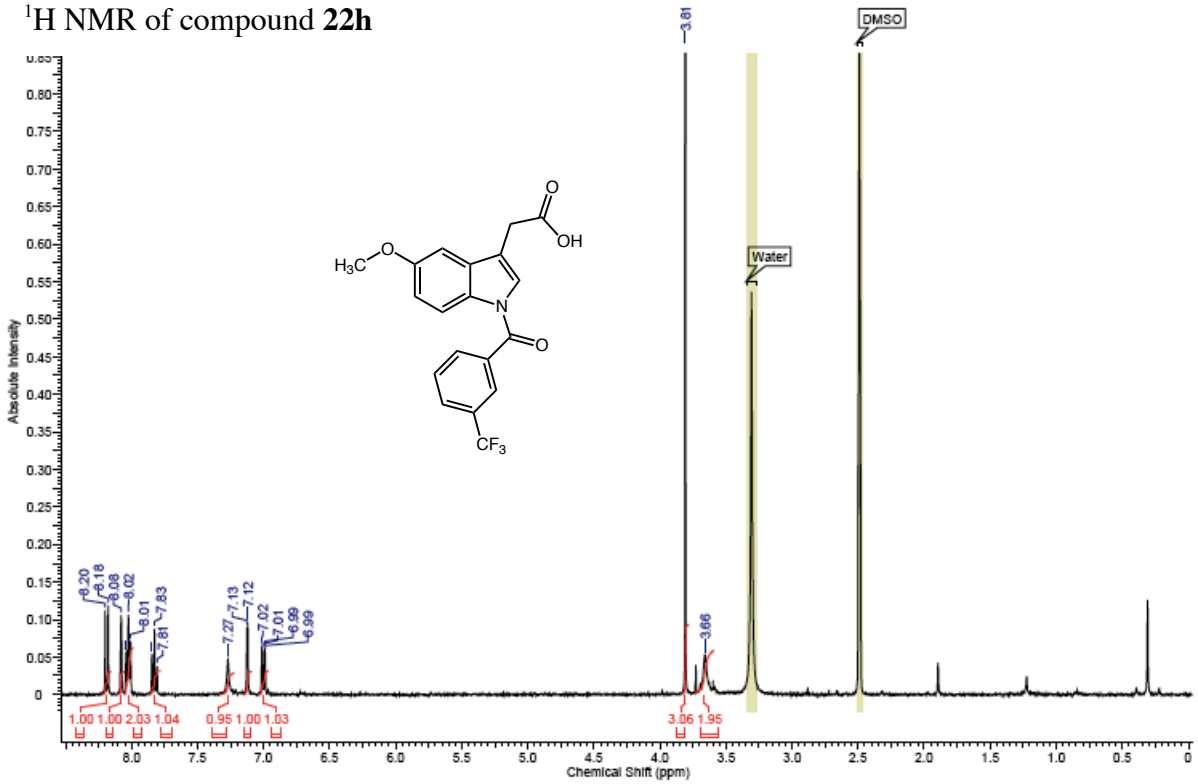
[1]H NMR of compound **22g**



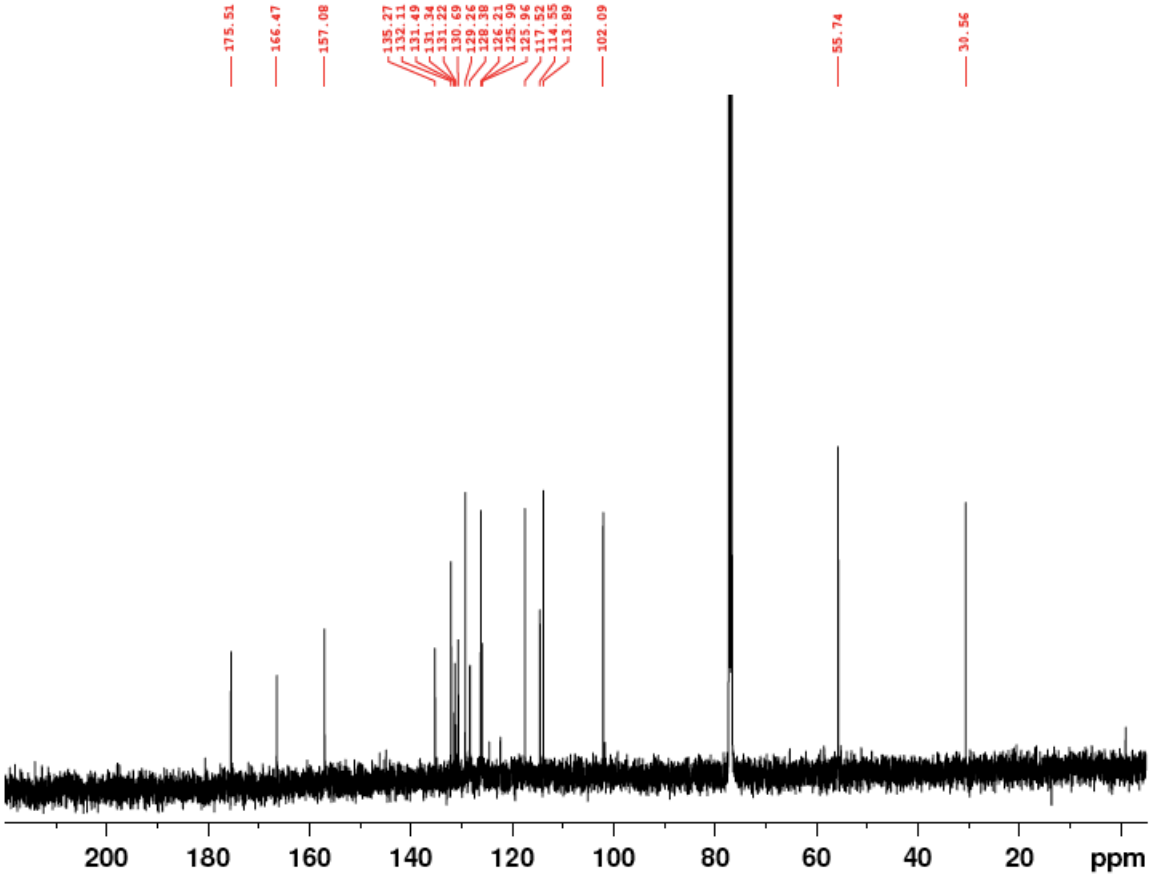
[13]C NMR of compound **22g**



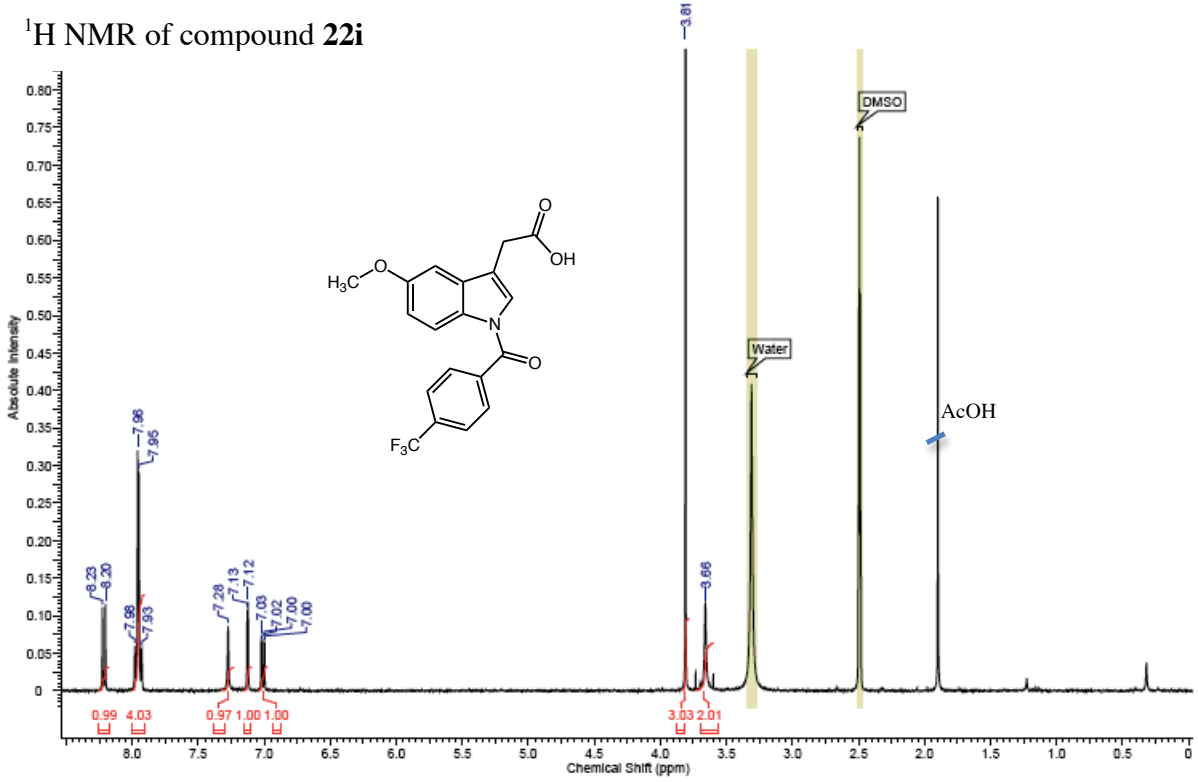
^{1}H NMR of compound **22h**



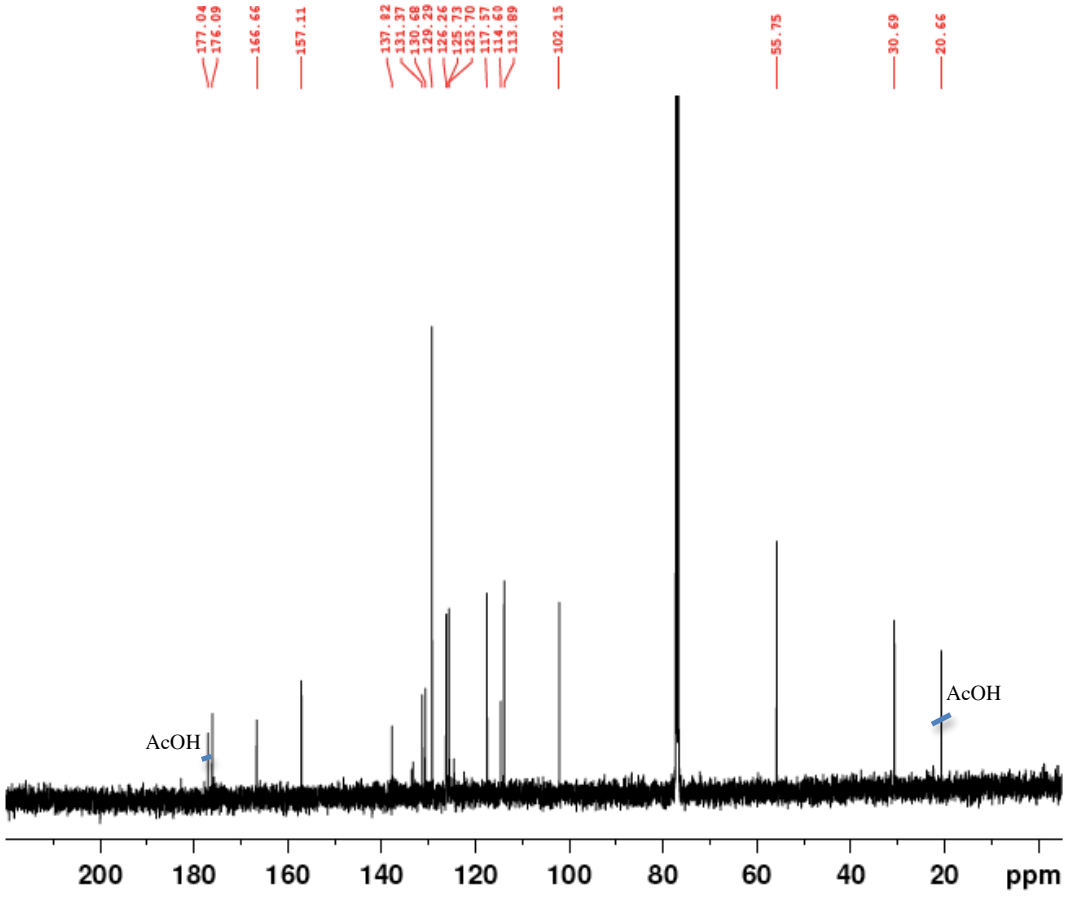
^{13}C NMR of compound **22h**



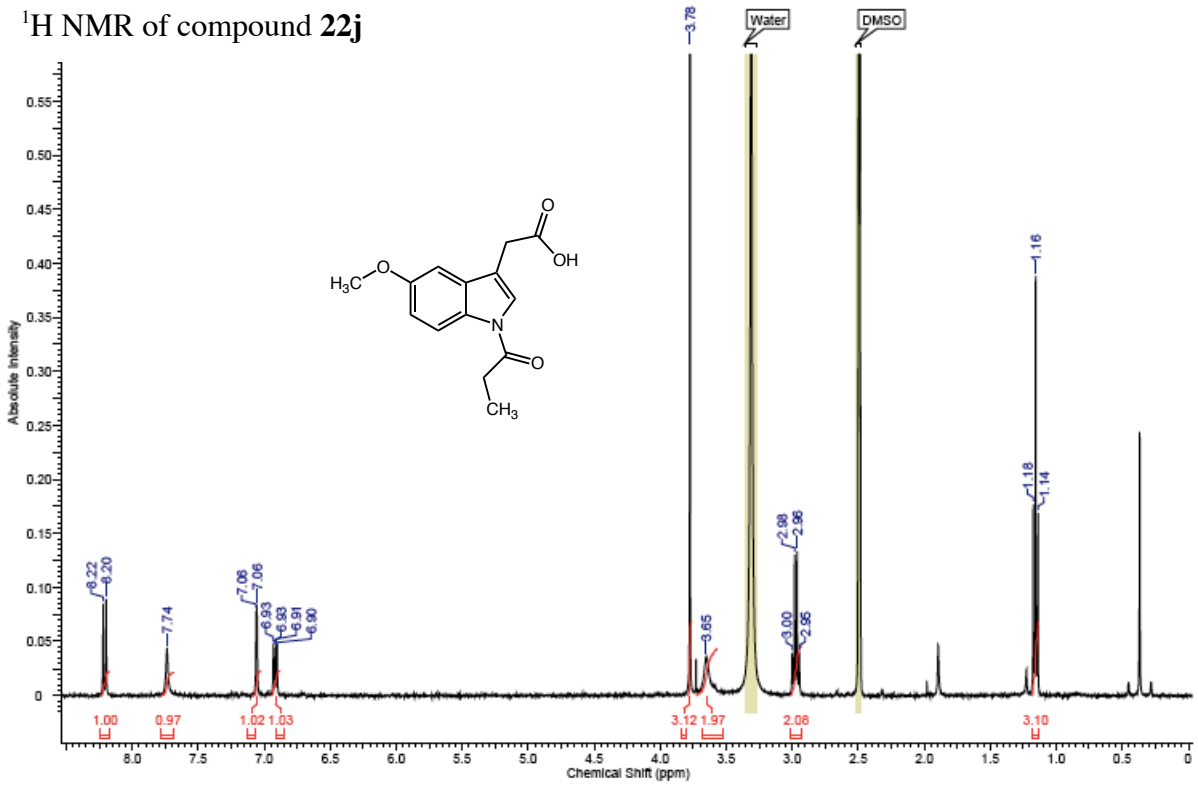
^{1}H NMR of compound **22i**



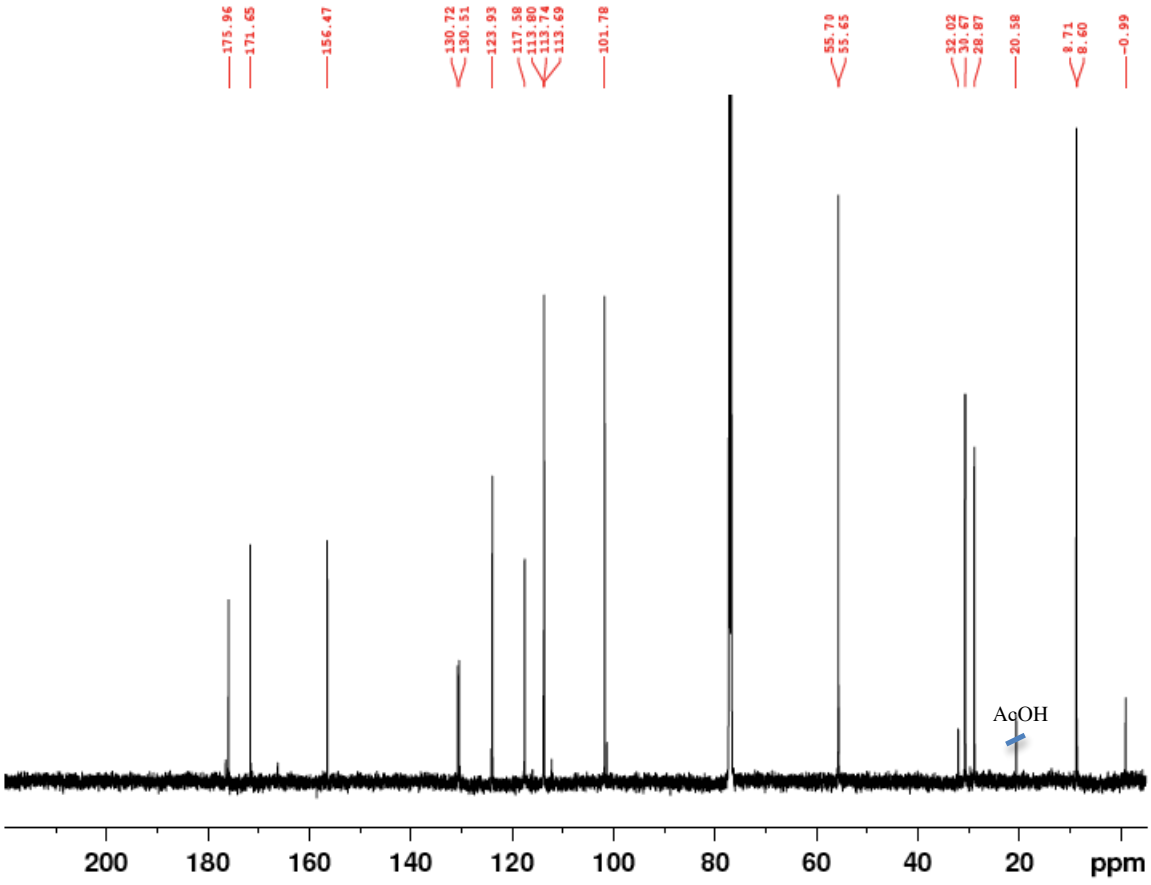
^{13}C NMR of compound **22i**



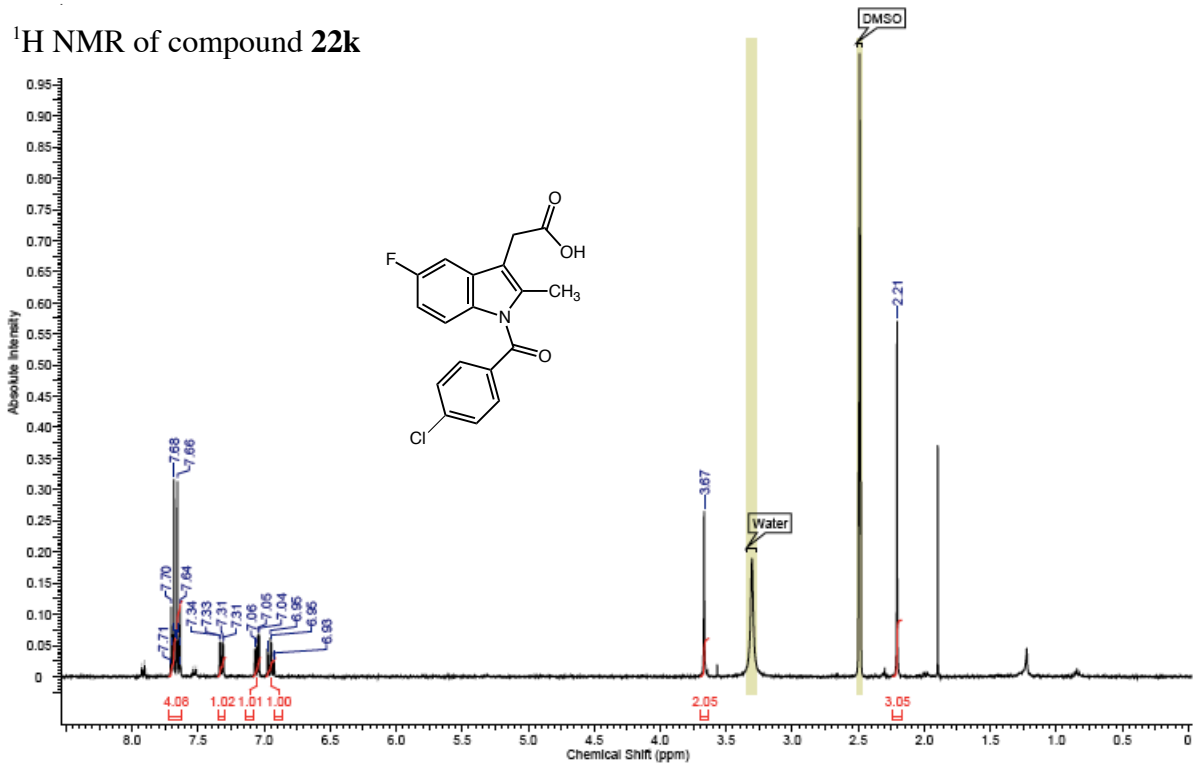
^{1}H NMR of compound **22j**



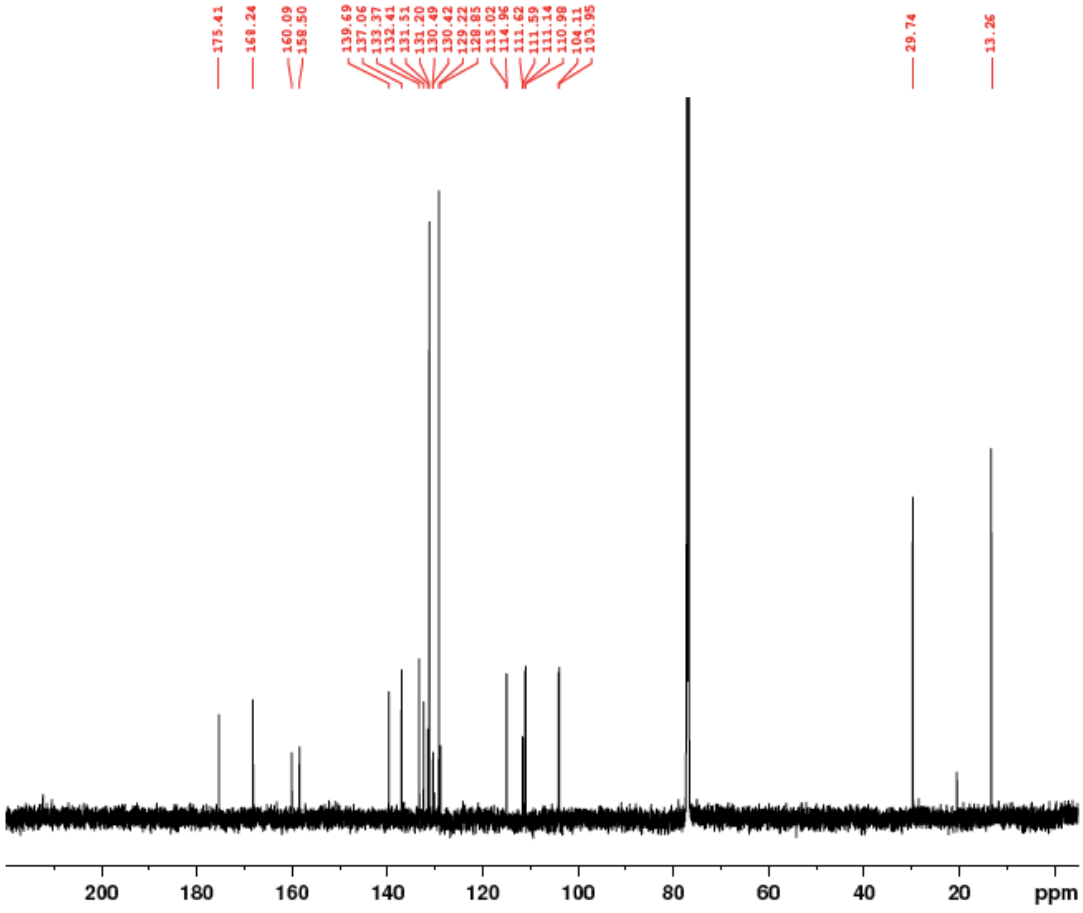
^{13}C NMR of compound **22j**



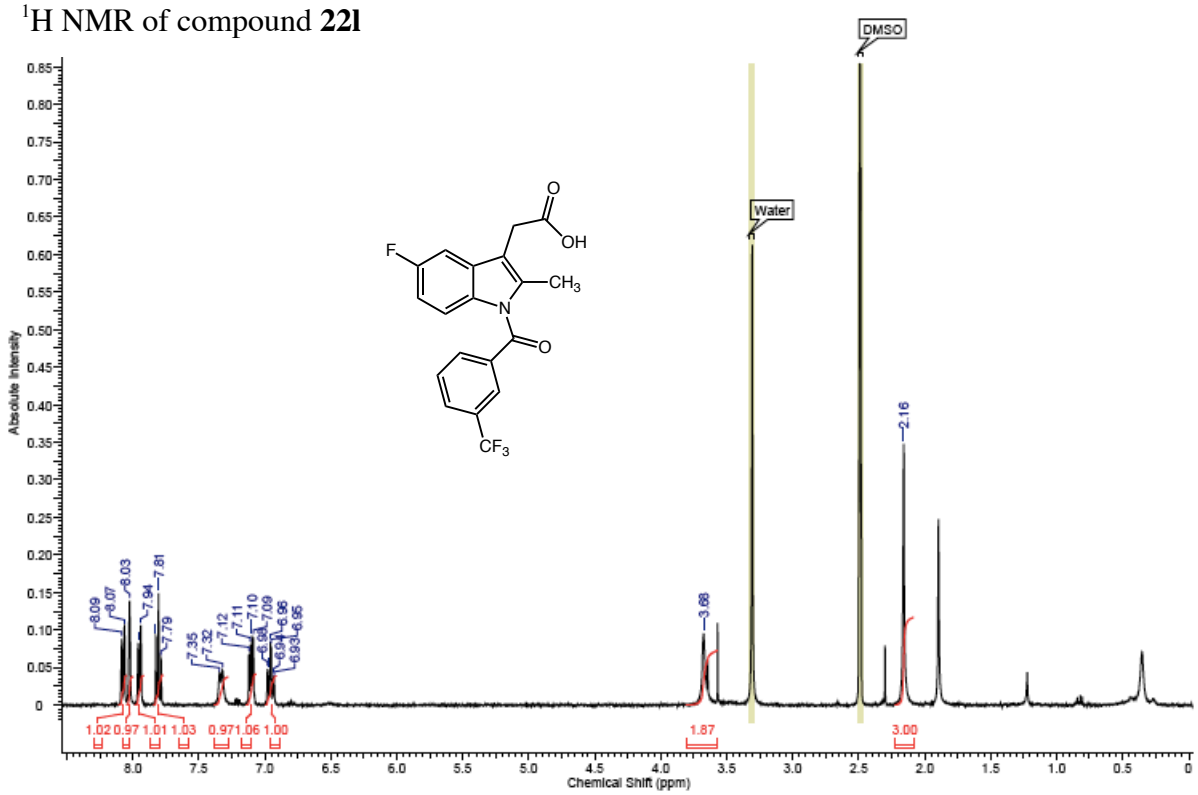
^{1}H NMR of compound **22k**



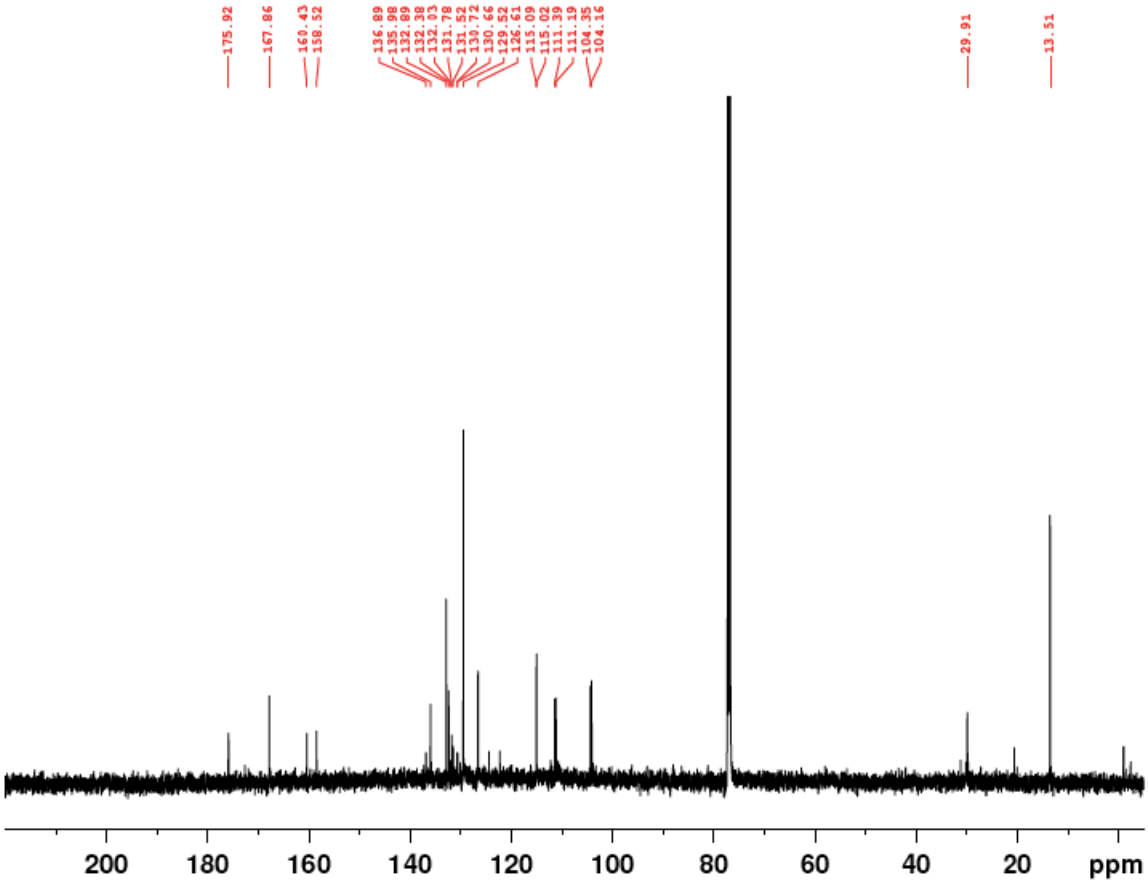
^{13}C NMR of compound **22k**



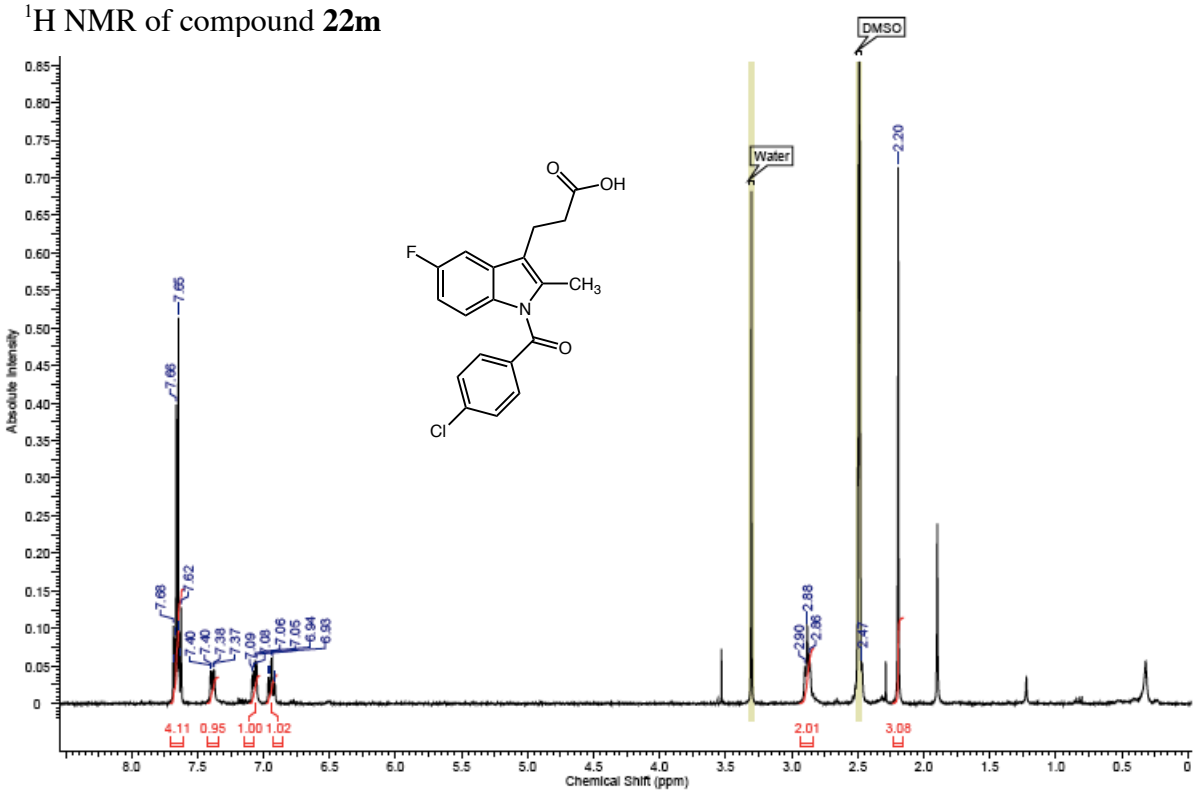
^{1}H NMR of compound **22l**



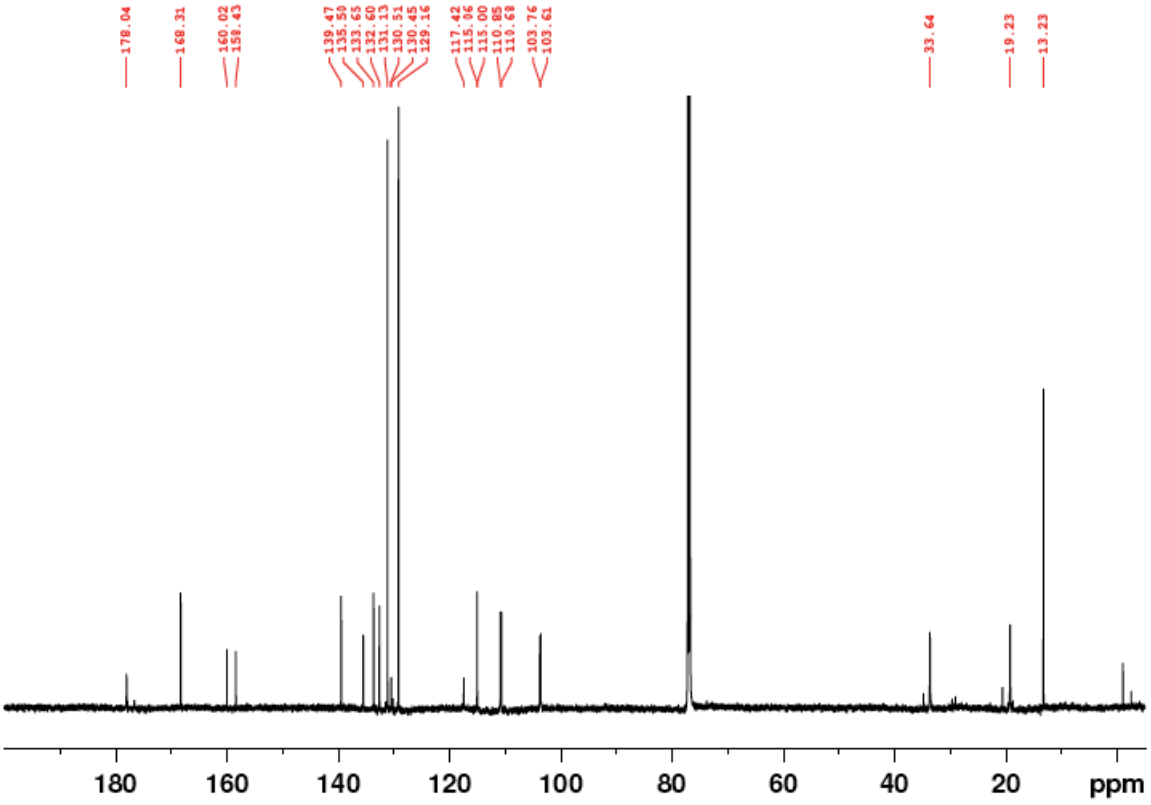
^{13}C NMR of compound **22l**



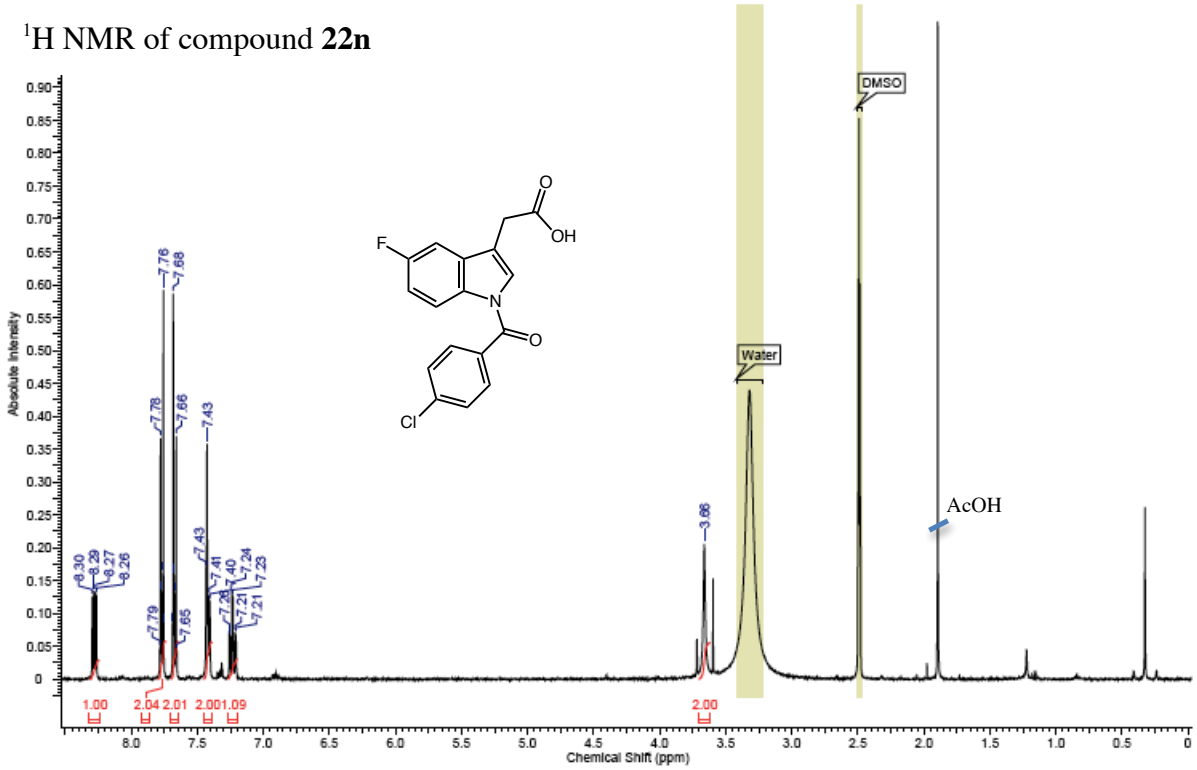
[1]H NMR of compound **22m**



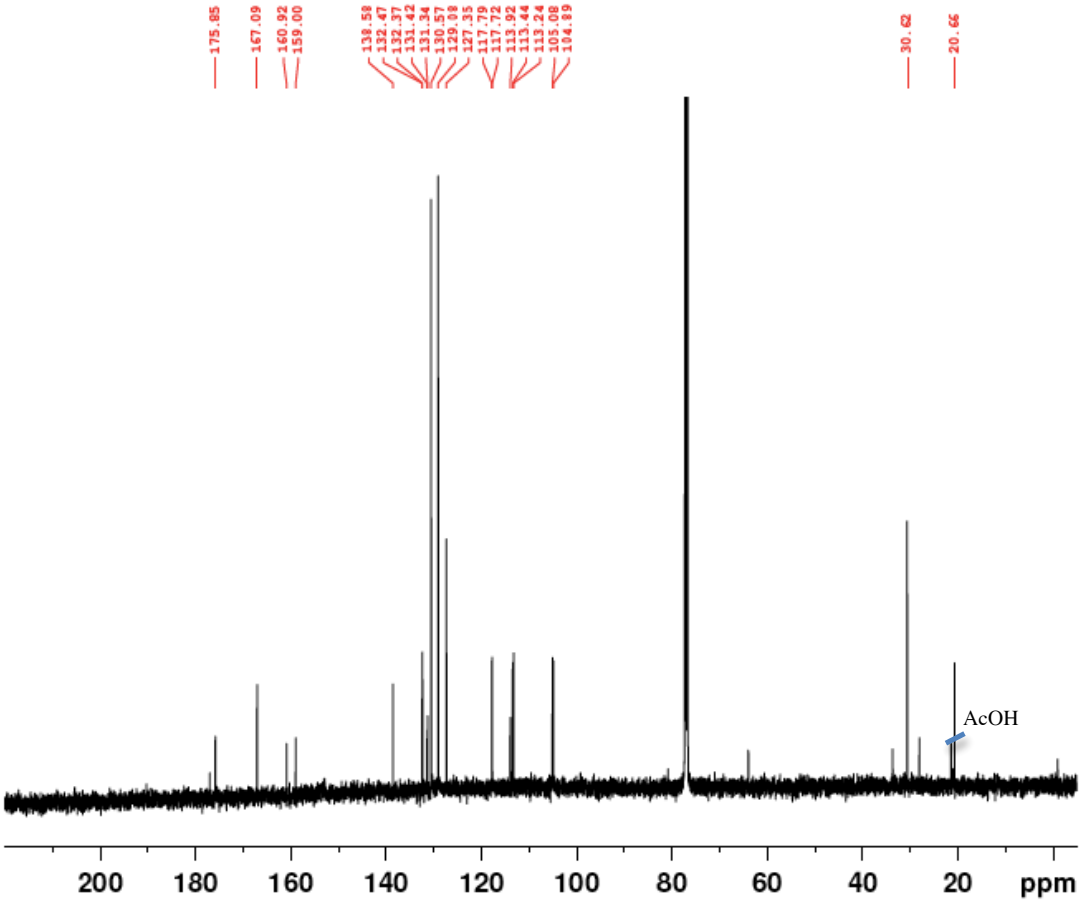
[13]C NMR of compound **22m**



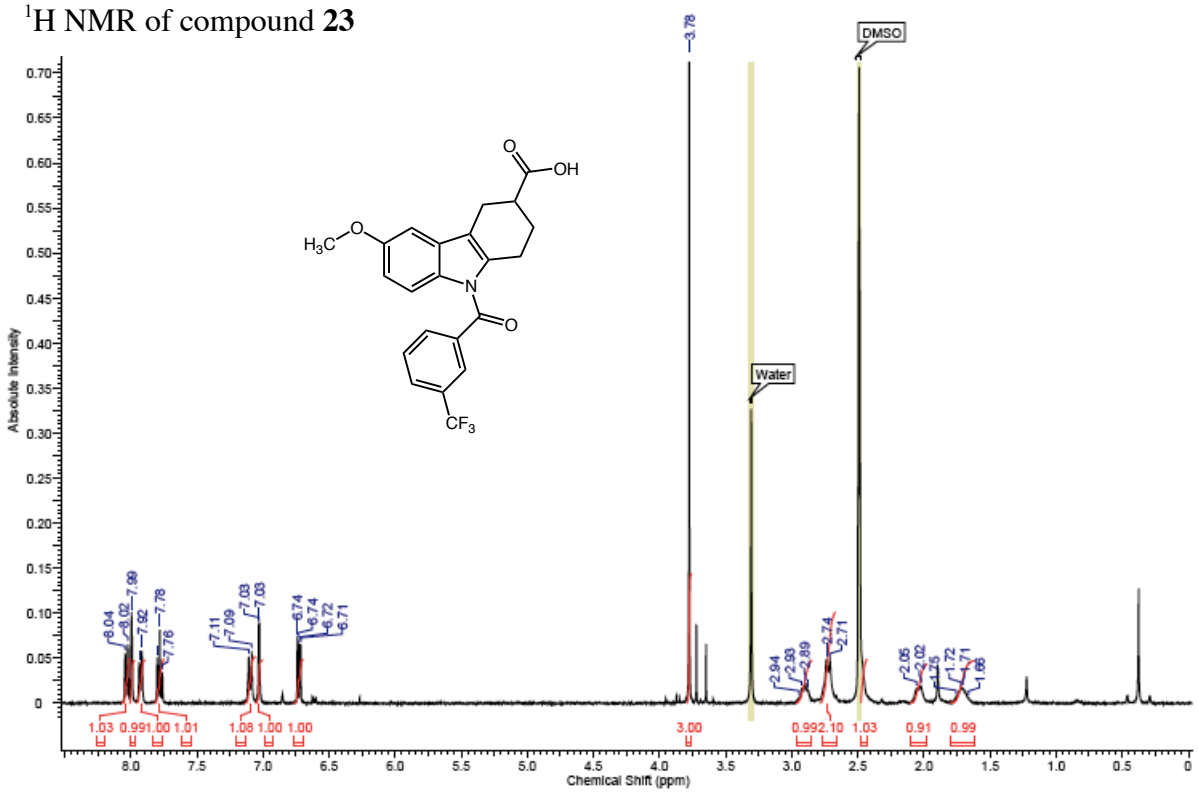
[1]H NMR of compound **22n**



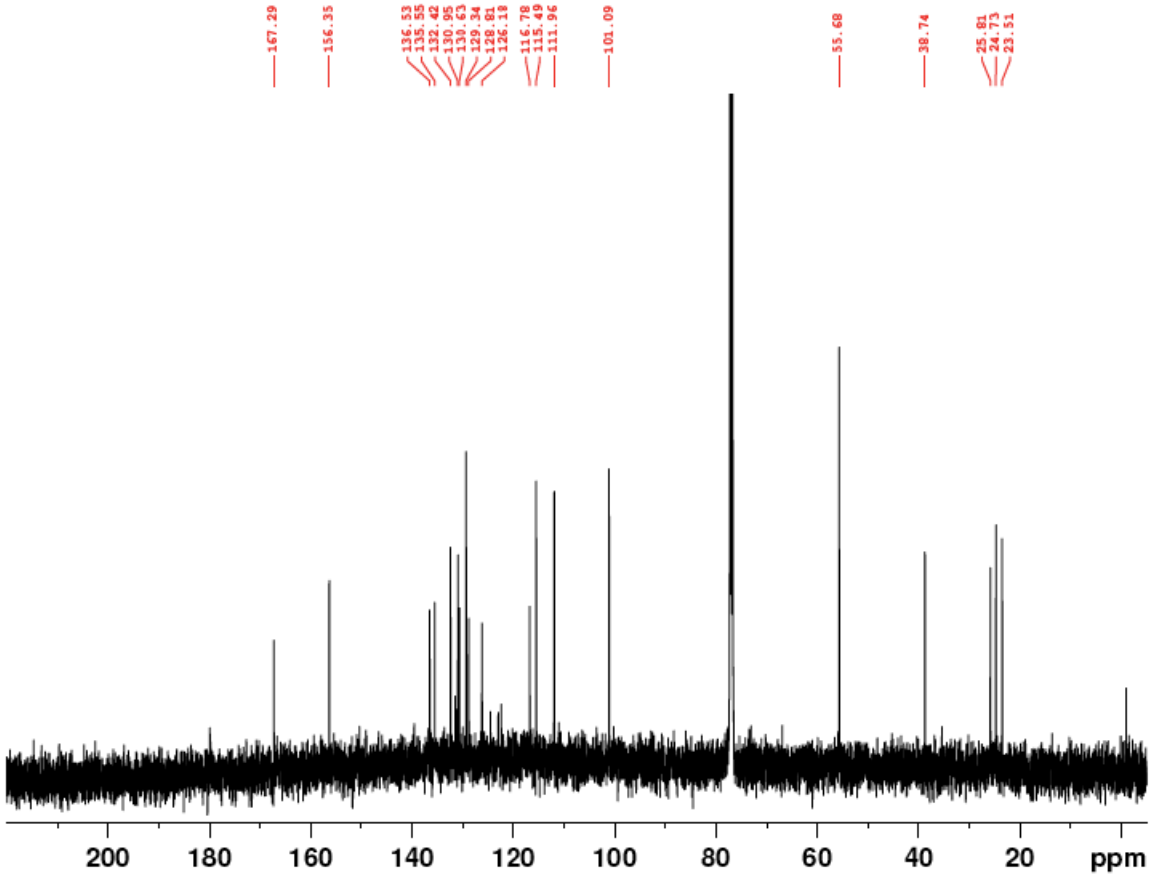
[13]C NMR of compound **22n**



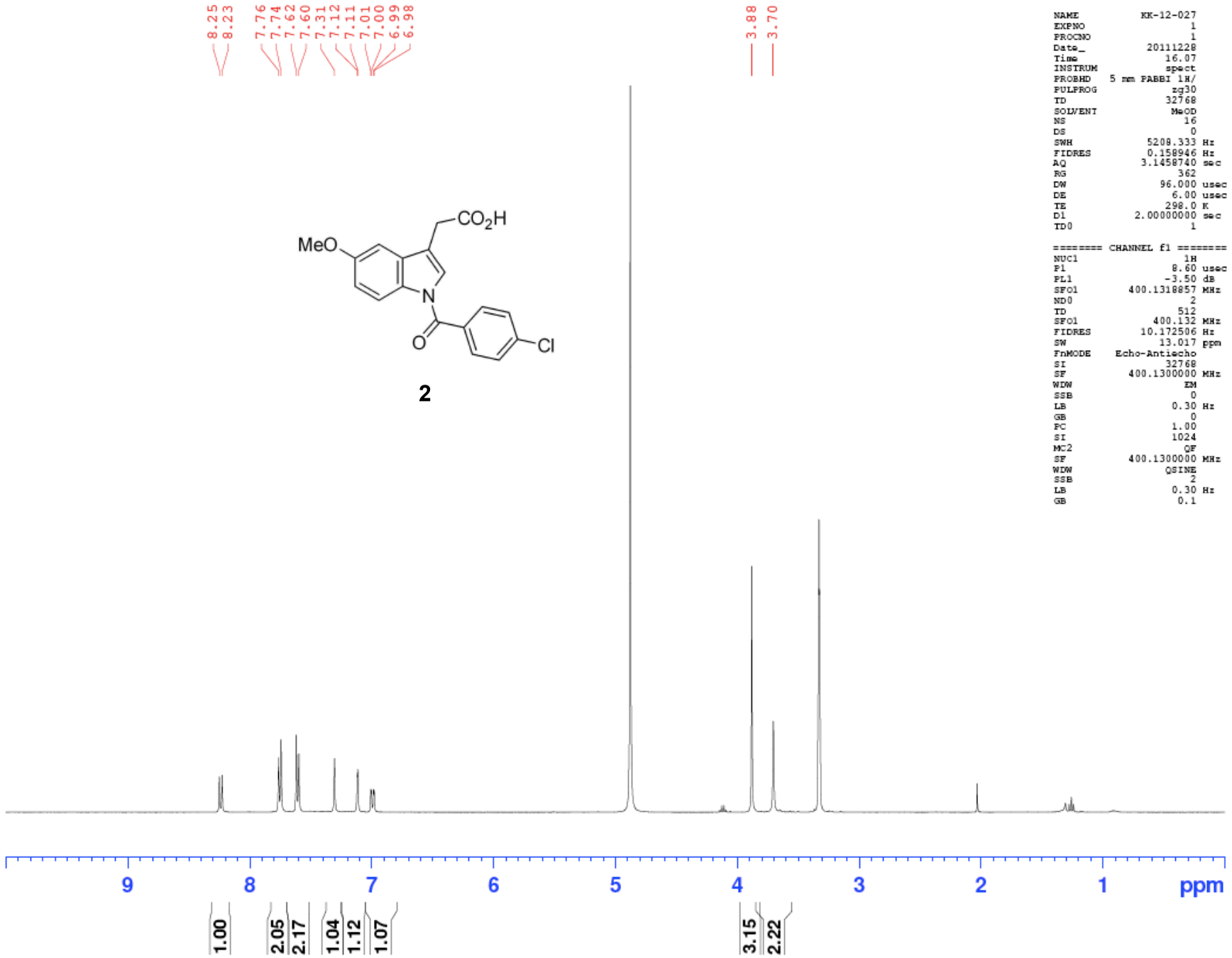
^{1}H NMR of compound **23**



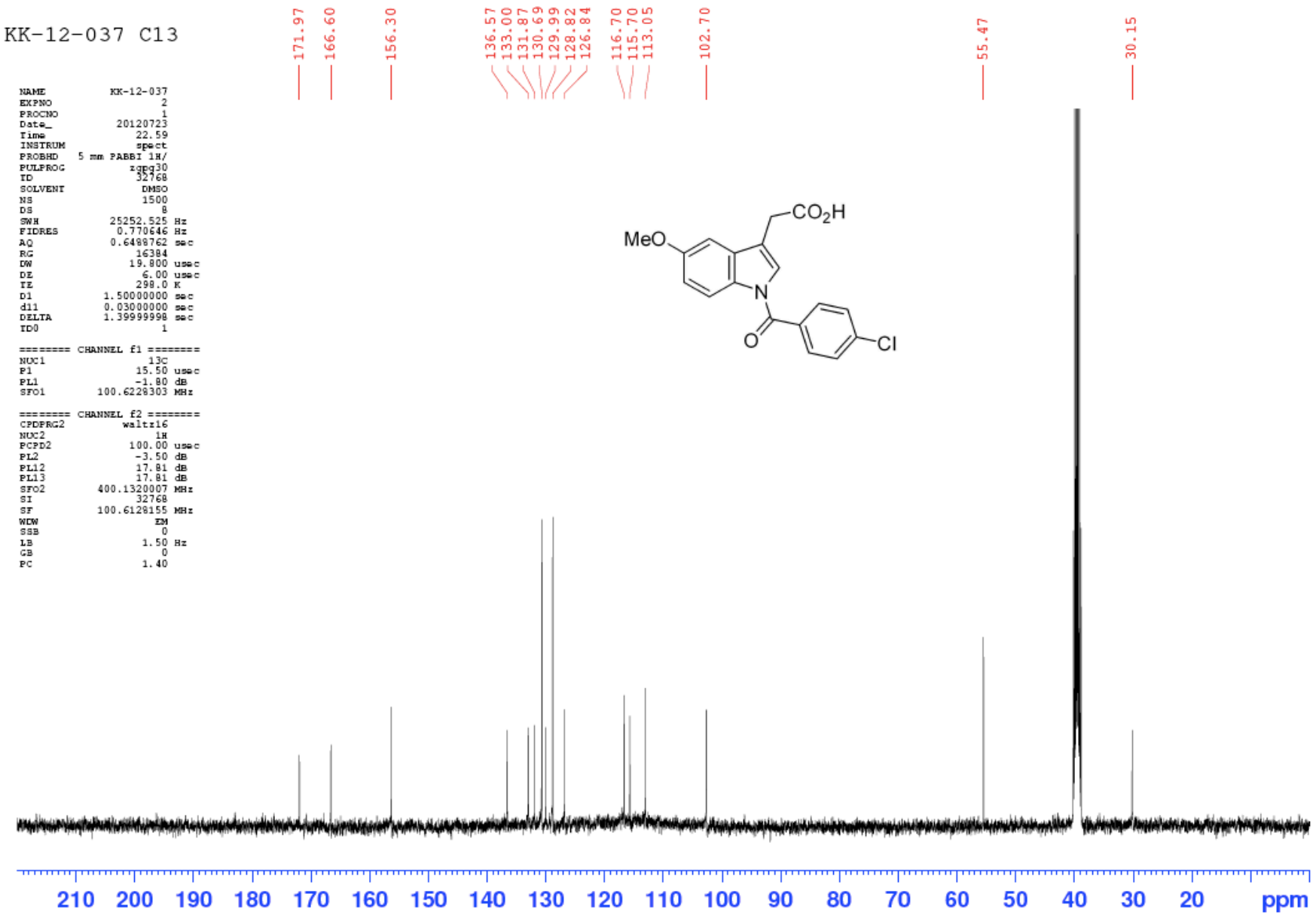
^{13}C NMR of compound **23**



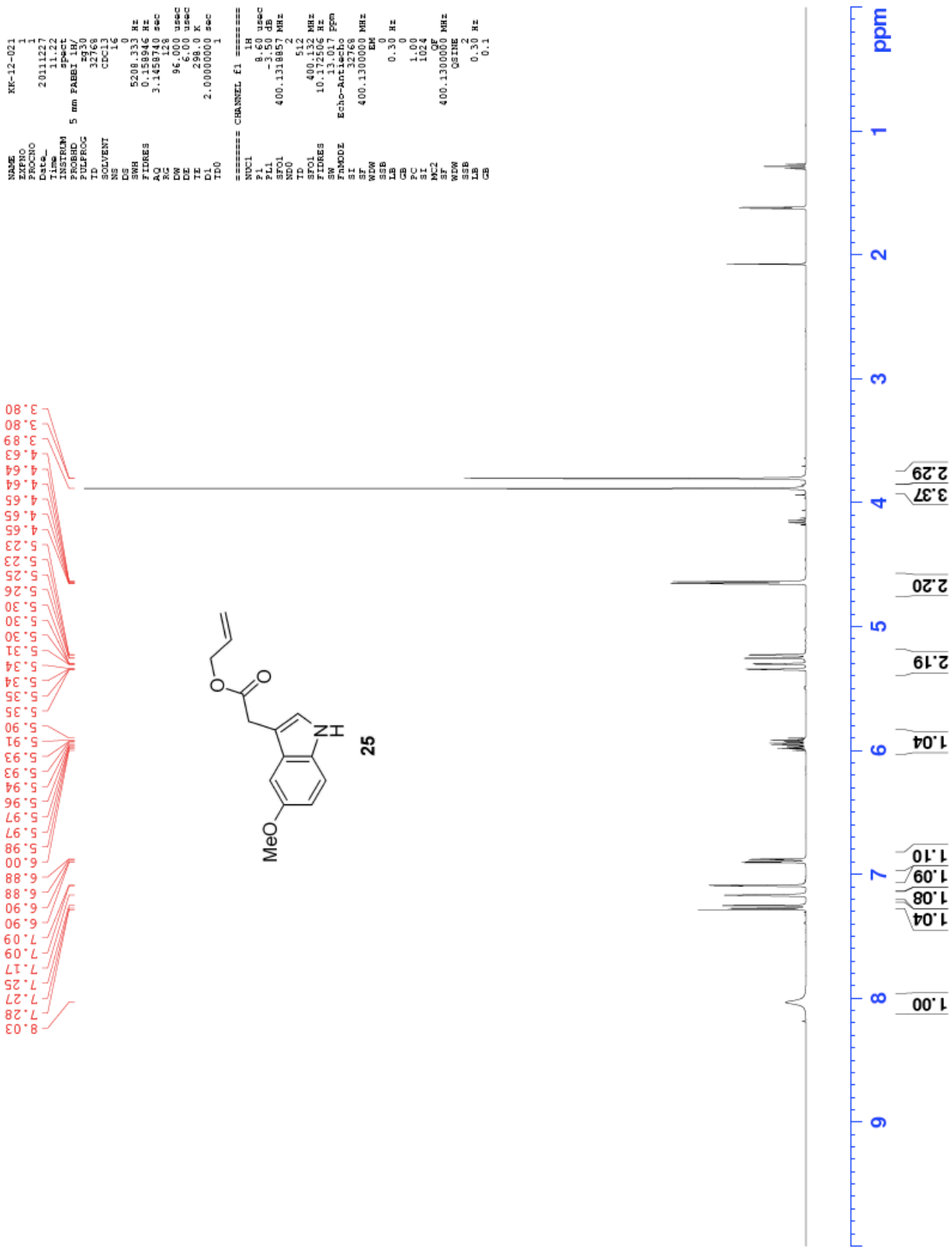
^{1}H NMR of compound **2** (large scale)



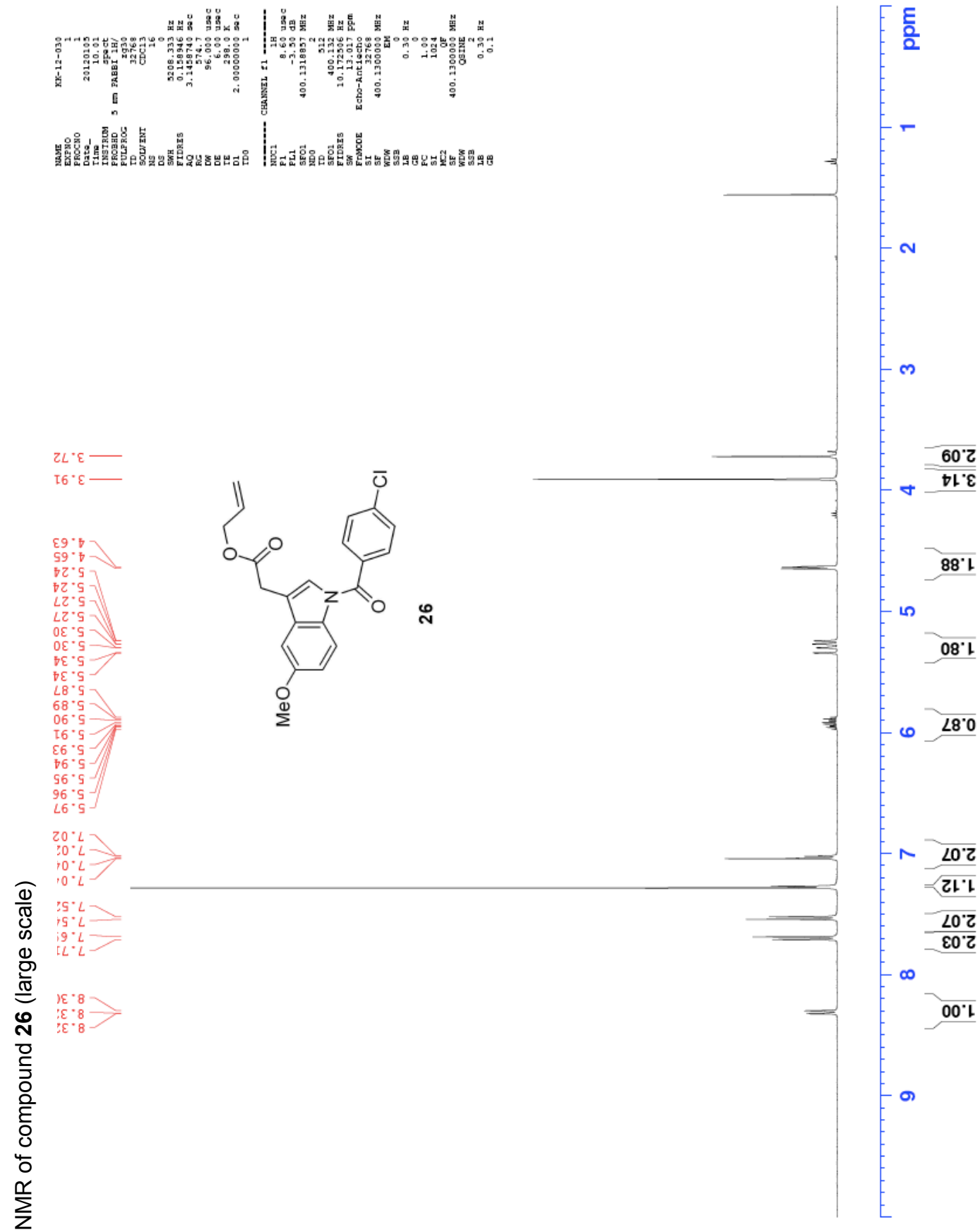
^{13}C NMR of compound **2** (large scale)



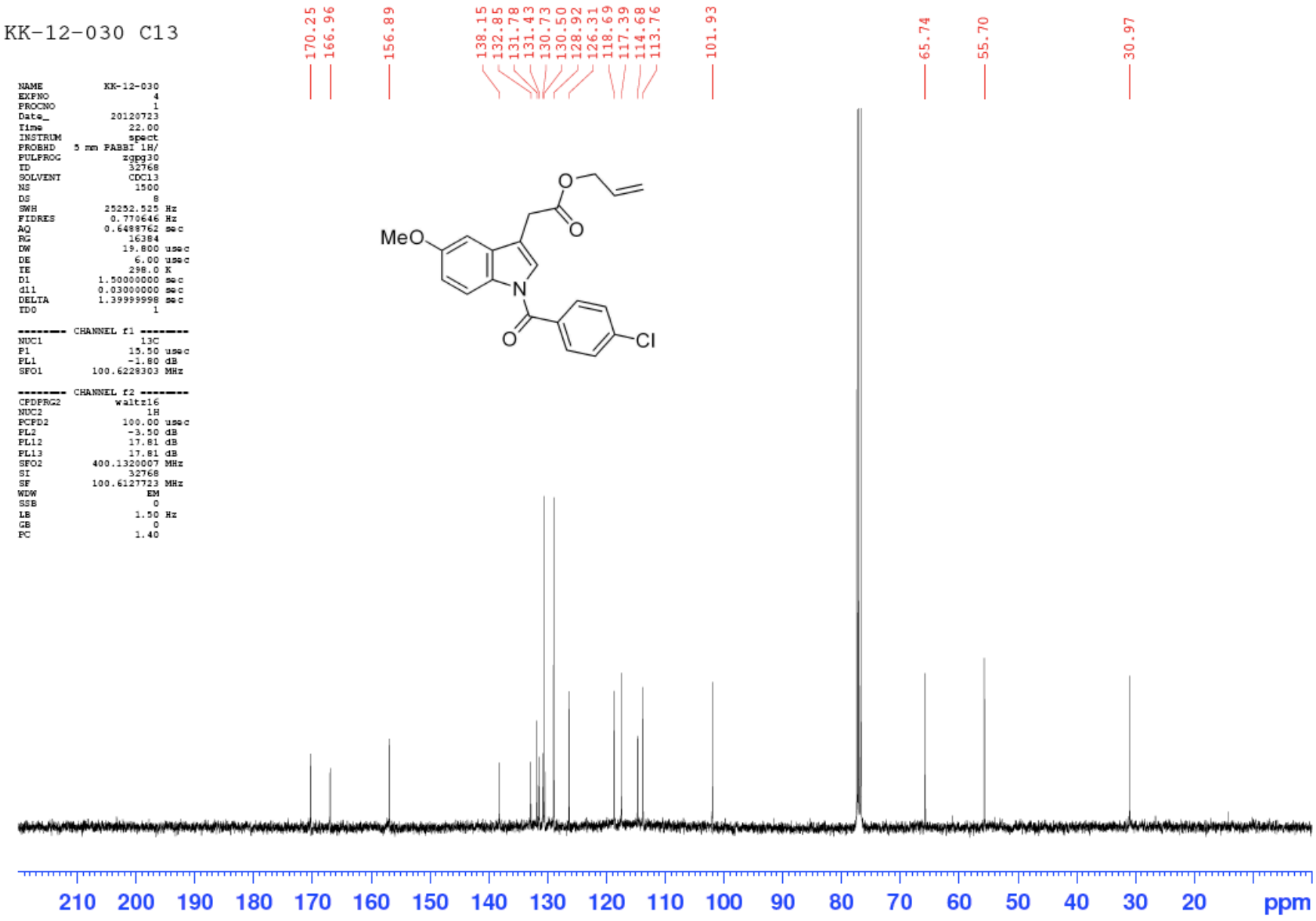
^{1}H NMR of compound **25** (large scale)



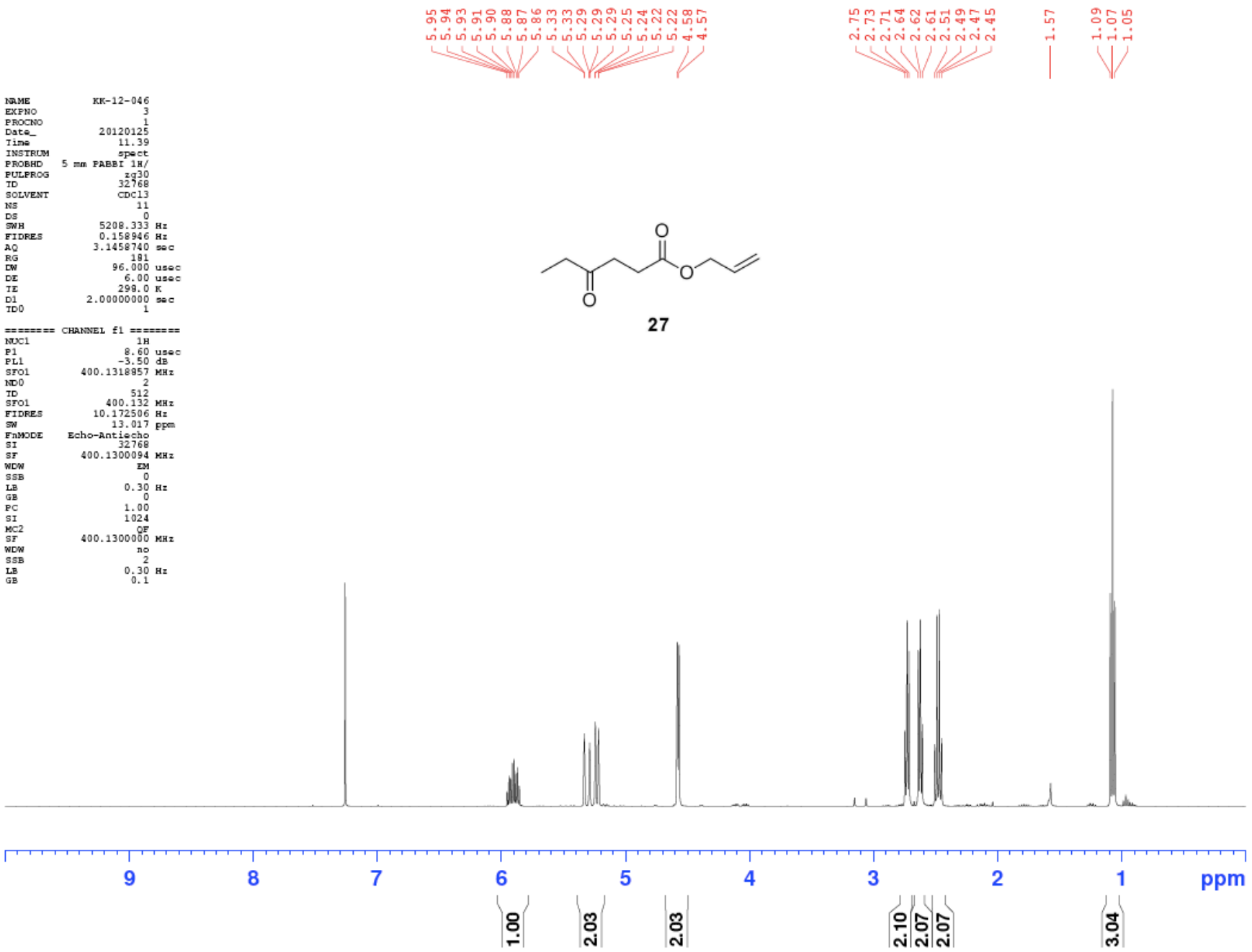
^{1}H NMR of compound **26** (large scale)



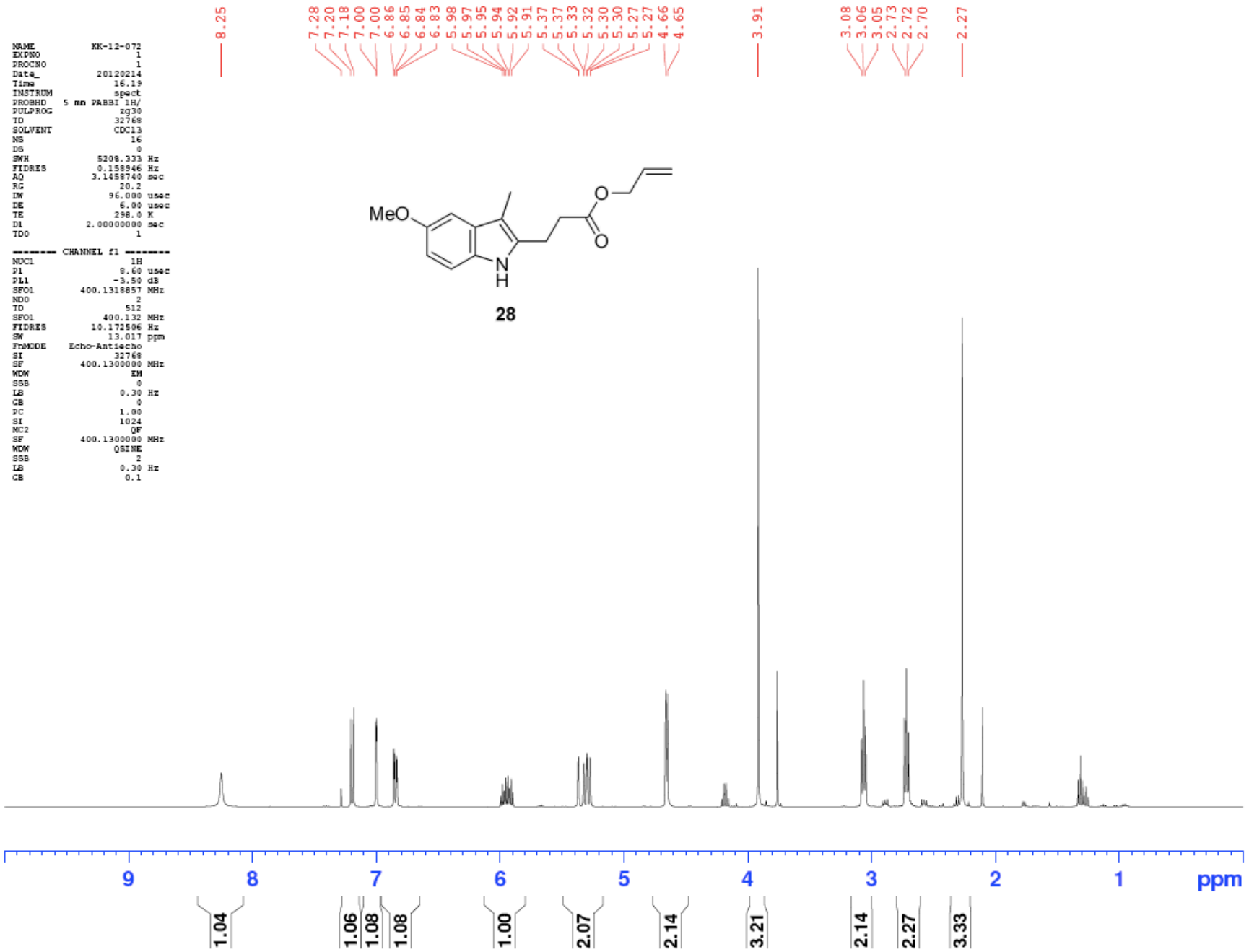
^{13}C NMR of compound **26** (large scale)



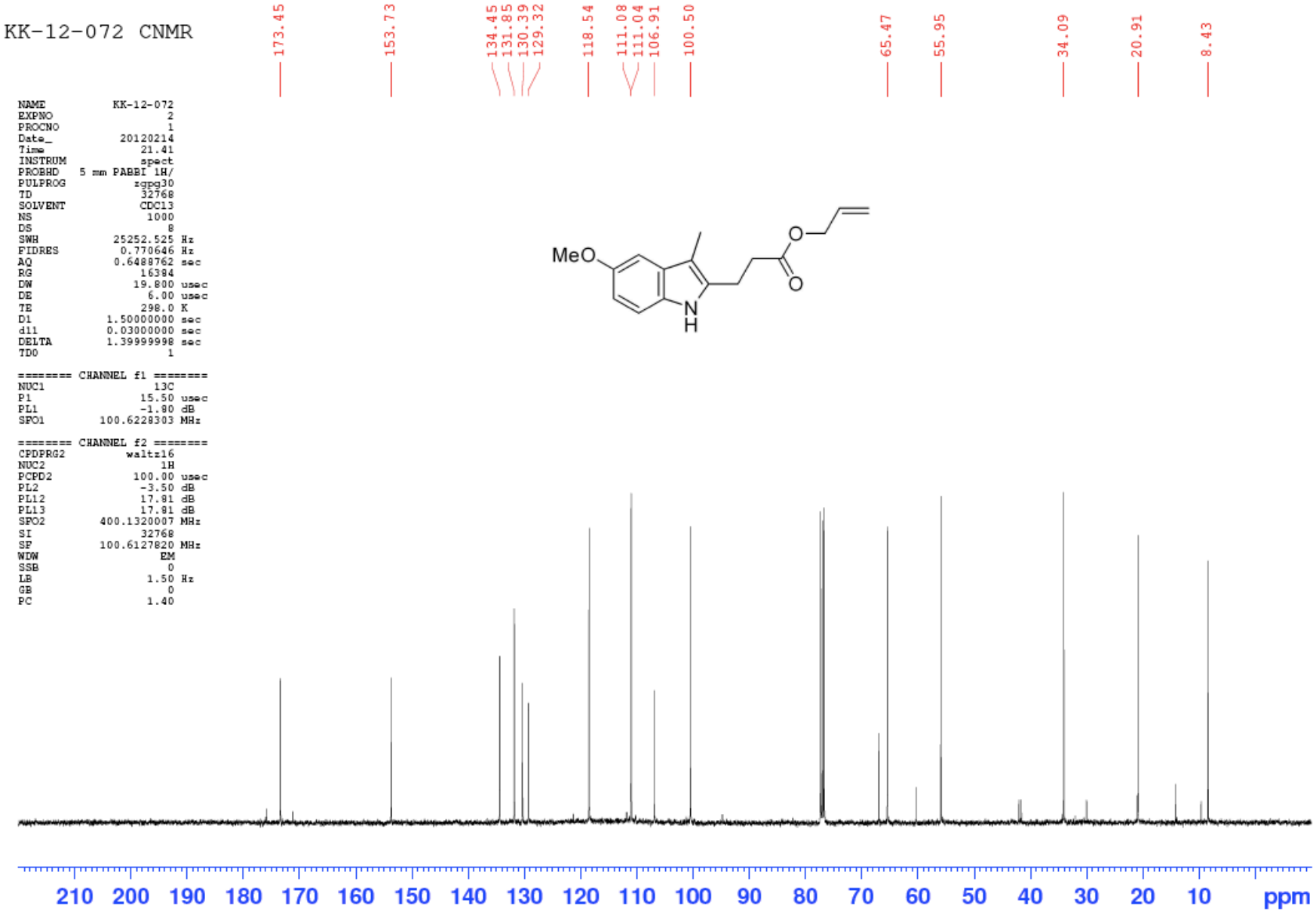
^{1}H NMR of compound **27** (large scale)



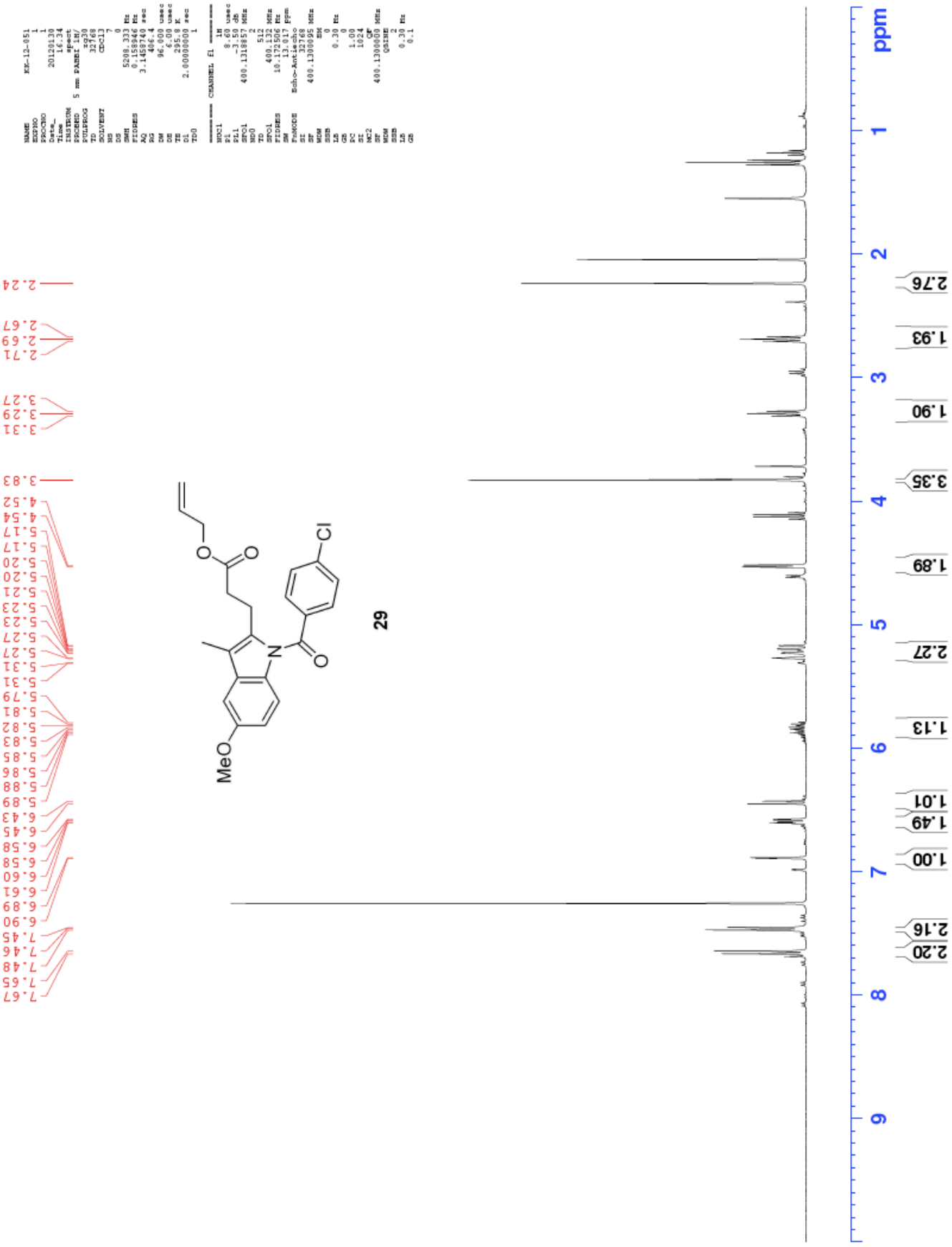
^{1}H NMR of compound **28** (large scale)



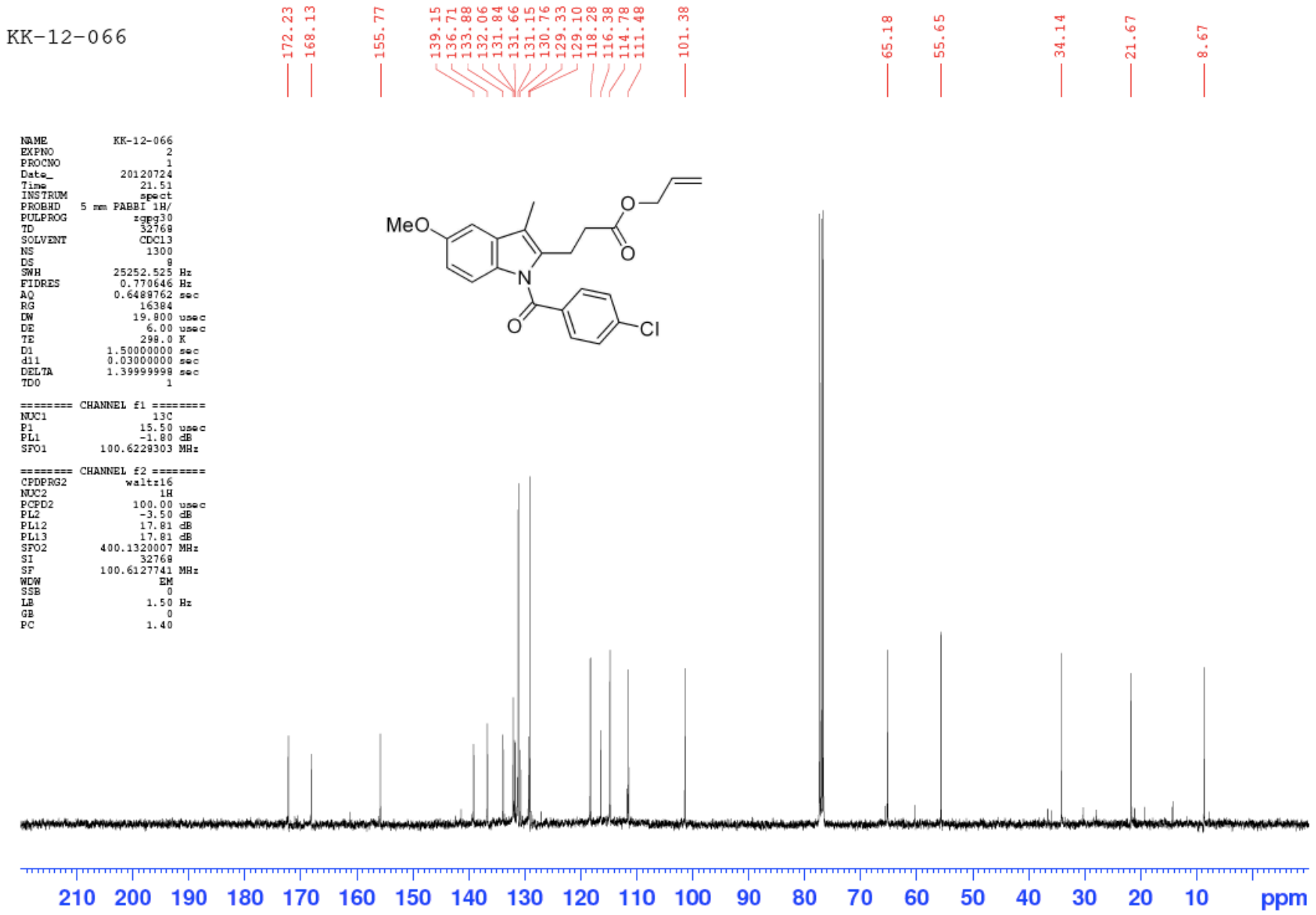
^{13}C NMR of compound **28** (large scale)



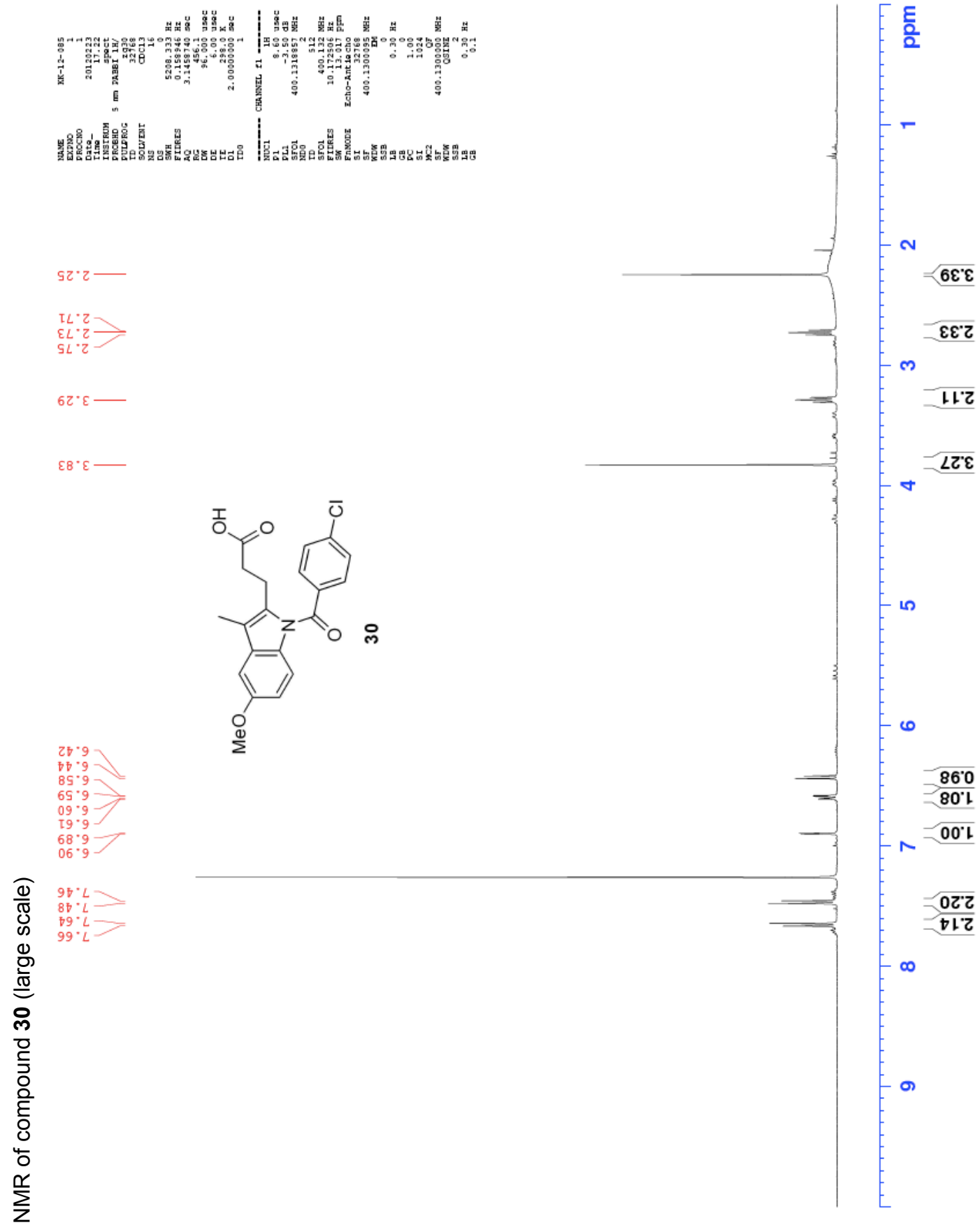
^{1}H NMR of compound **29** (large scale)



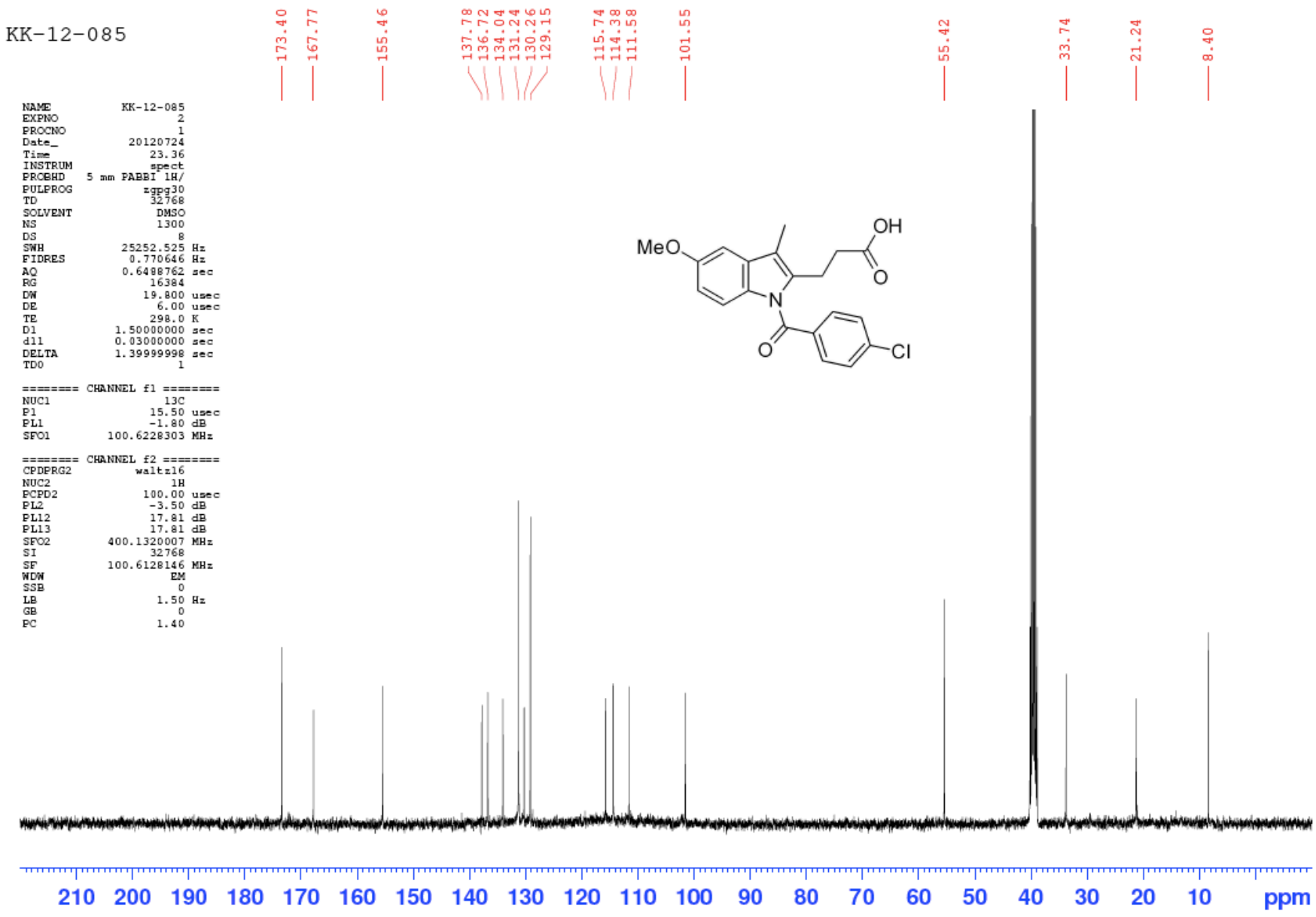
^{13}C NMR of compound **29** (large scale)



^{1}H NMR of compound **30** (large scale)

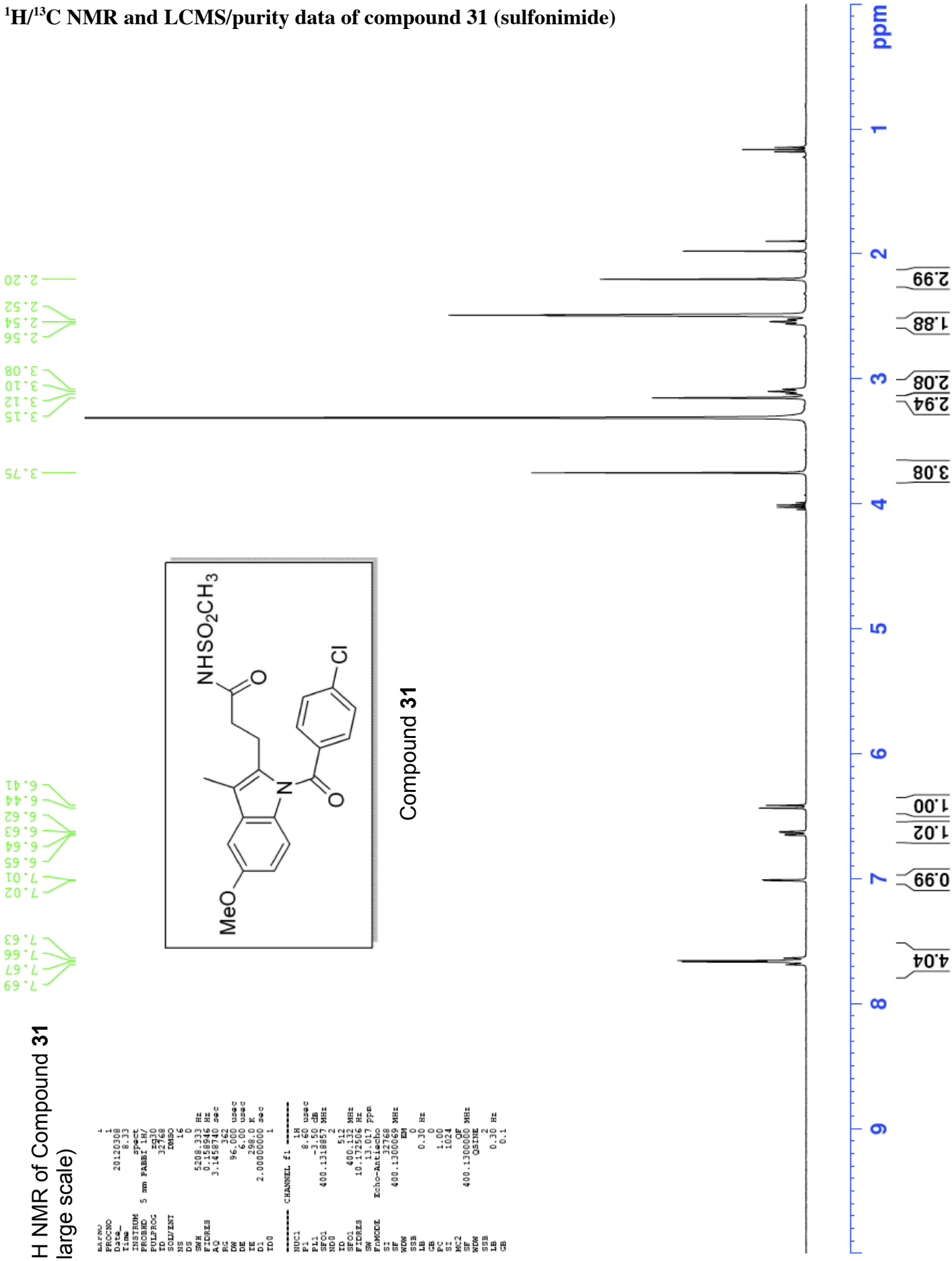


^{13}C NMR of compound **30** (large scale)



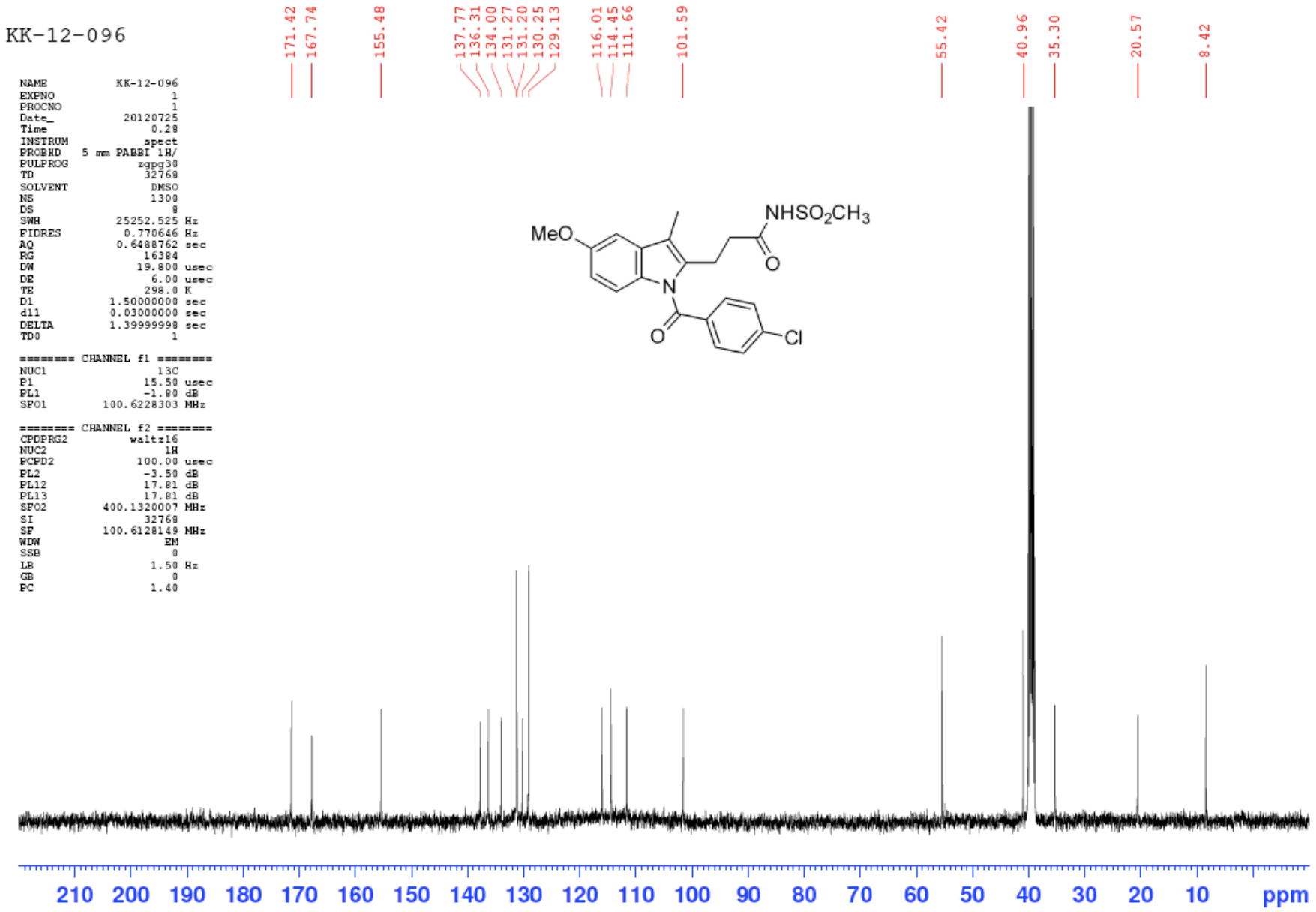
$^{1}H/^{13}C$ NMR and LCMS/purity data of compound 31 (sulfonimide)

^{1}H NMR of Compound **31** (large scale)



Compound **31**

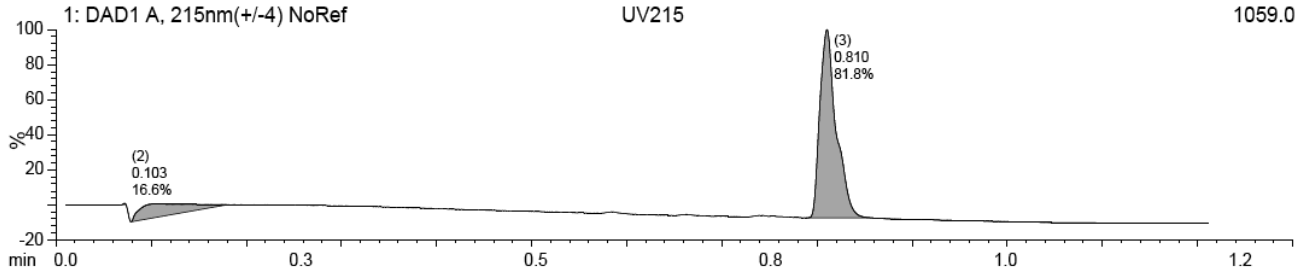
^{13}C NMR of Compound **31** (large scale)

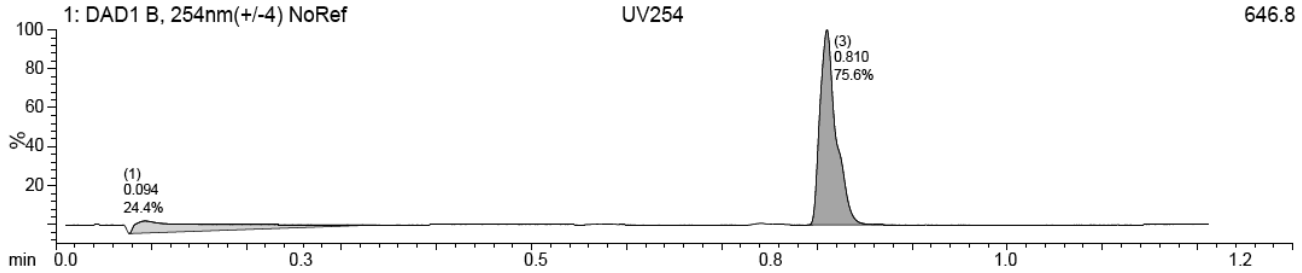


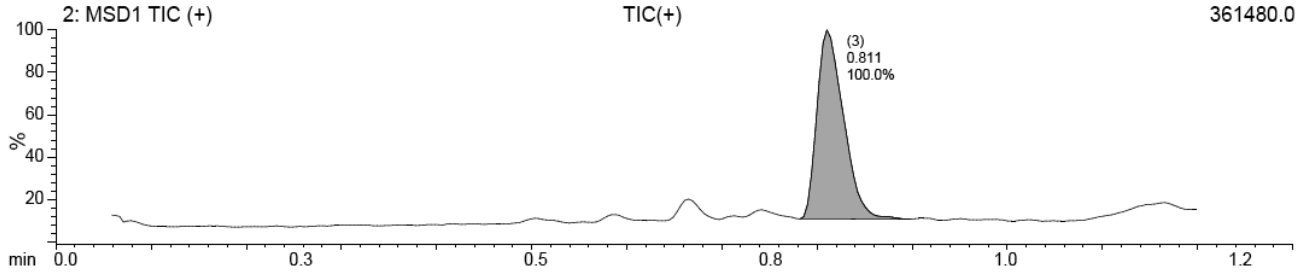
VCNDD 12410 Agilent 1200 LCMS

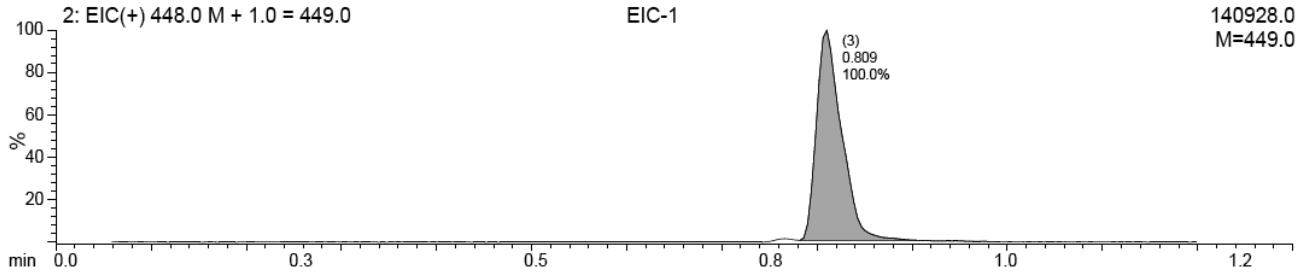
Sample Name: # 31 **Acquired:** 3/7/2012 2:55 PM **Method:** KINETEX NEW1.M **Description:** Easy-Access Method: 'Kinetex 1 Minute' ,448.00, 371.00
User: kimk3 **Filename:** **Location:** 1,2:E,9

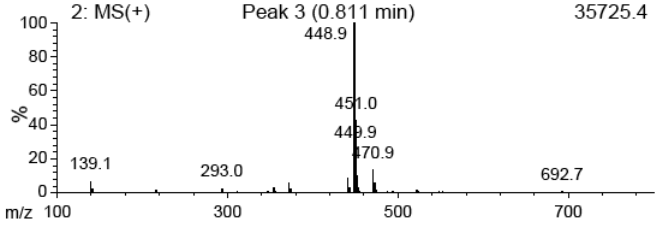
Peak #	Time	Area % UV215	Area % UV254	Area % TIC(+)	Area % ELSD	BPM	Area Abs UV215	Area Abs UV254	Area Abs TIC(+)	Area Abs ELSD
1	0.083	1.6	24.4	0.0	0.0	214.2	28.35	247.41	0	0
1	0.083	1.6	24.4	0.0	0.0	214.2	28.35	247.41	0	0
2	0.103	16.6	0.0	0.0	0.0	236.0	285.38	0	0	0
2	0.103	16.6	0.0	0.0	0.0	236.0	285.38	0	0	0
3	0.810	81.8	75.6	100.0	0.0	448.9	1405.84	768.19	626740.25	0
3	0.810	81.8	75.6	100.0	0.0	448.9	1405.84	768.19	626740.25	0

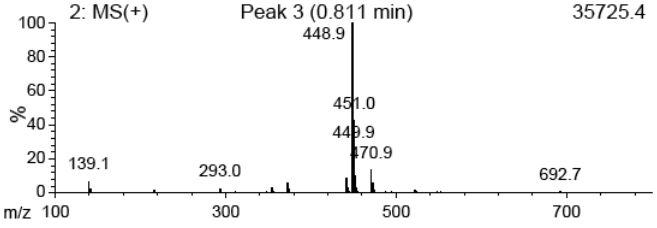








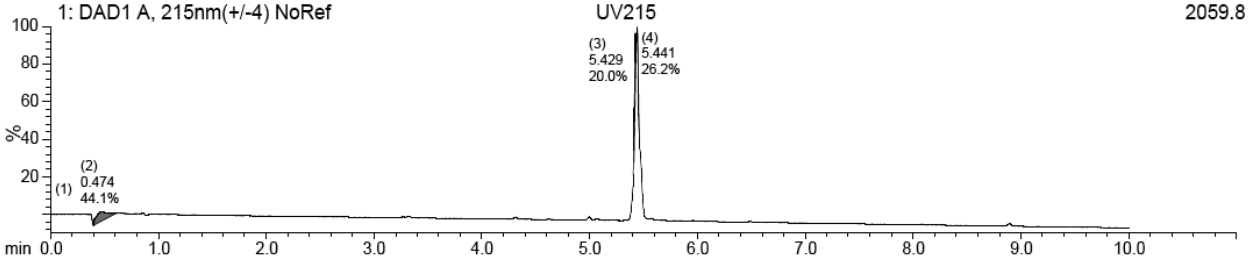


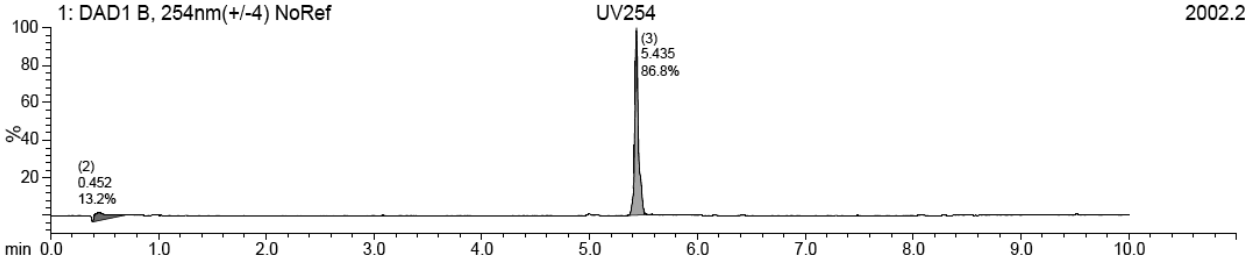


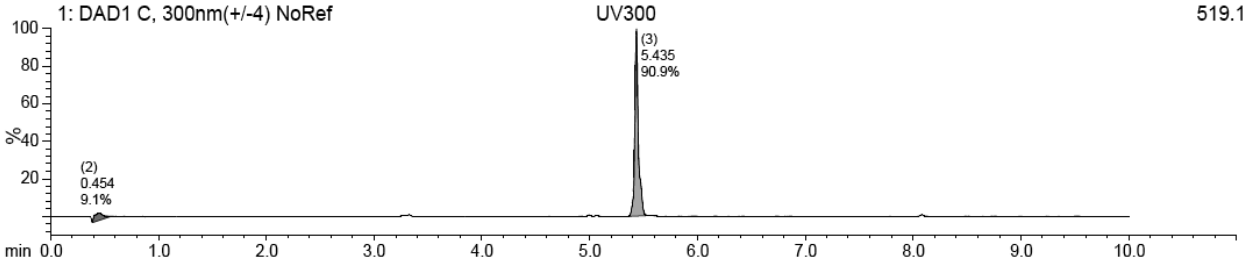
VCNDD 12410 Agilent 1200 LCMS

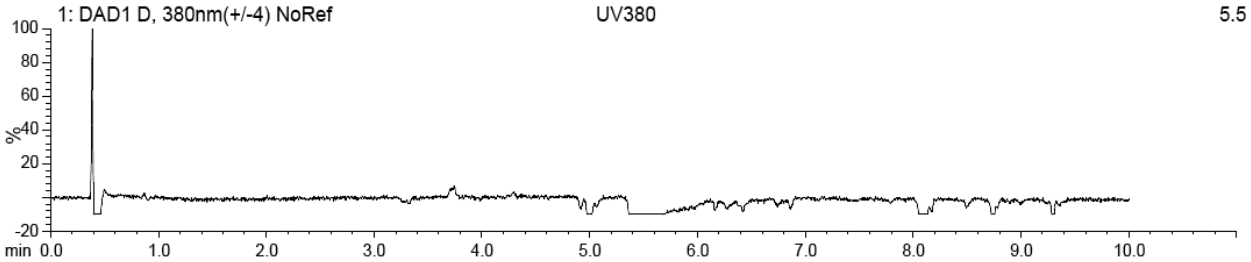
Sample Name: # **31** **Acquired:** 3/7/2012 3:03 PM **Method:** KINETEX_10_MIN.M **Description:** Easy-Access Method: '10 Minute Purity Analysis' ,448.00
User: kimk3 **Filename:** **Location:** 1,2:F,1

Peak #	Time	Area % UV215	Area % UV254	Area % UV300	Area % UV380	Area % UV300	Area % TIC(+)	BPM	Area Abs UV215	Area Abs UV254	Area Abs UV300
1	0.373	9.7	0.0	0.0	0.0	0.0	0.0	130.2	162.58	0	0
2	0.457	44.1	13.2	9.1	0.0	13.5	100.0	186.2	740.31	720.67	118.25
3	5.434	20.0	86.8	90.9	0.0	86.5	0.0	448.9	336.73	4736.62	1179.17
4	5.441	26.2	0.0	0.0	0.0	0.0	0.0	448.9	440.82	0	0









VCNDD 12410 Agilent 1200 LCMS

Sample Name: # **31** **Acquired:** 3/7/2012 3:03 PM **Method:** KINETEX_10_MIN.M **Description:** Easy-Access Method: '10 Minute Purity Analysis' ,448.00
User: kimk3 **Filename:** **Location:** 1,2:F,1