Supporting Information

Identification of 2-(4-(phenylsulfonyl)piperazine-1-yl)pyrimidine analogues as Novel Inhibitors of Chikungunya Virus

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Content

Cell lines and virus strain

Chikungunya virus, Indian Ocean strain 899, isolated in 2006 (Genbank FJ959103.1), was kindly provided by Prof. C. Drosten (Institute of Virology, University of Bonn, Germany). CHIKV was cultured on African green monkey kidney (Vero) cells (ATCC CCL-81) in minimum essential medium MEM Rega3 (Invitrogen, Belgium) supplemented with 10% Foetal Bovine Serum (FBS; Integro, The Netherlands), 1% L-glutamine and 1% sodium bicarbonate (Invitrogen). Antiviral assays were performed in MEM Rega-3 medium supplemented with 2% FBS.

Chikungunya virus-cell-based antiviral assay

Serial dilutions of compound were prepared in assay medium [MEM Rega3 (Cat. N°19993013; Invitrogen), 2% FCS (Integro), 5 ml 200 mM L-glutamine (25030024), and 5 ml 7.5% sodium bicarbonate (25080060)] that was added to empty wells of a 96-well microtiter plate (Falcon, BD). Subsequently, 50 µl of CHIKV dilution in assay medium was added (resulting in a MOI of 0.01), followed by 50 µl of Vero cell suspension (25 000 cells/50 µl). The assay plates were returned to the incubator for 5 days (37°C, 5% CO_2, 95-99% relative humidity), a time at which maximal virus-induced cell death or cytopathic effect (CPE) was observed in untreated, infected controls. Subsequently, the assay medium was aspirated, replaced with 75 µl of a 5% MTS (Promega) solution in phenol red-free medium and incubated for 1.5 hours. Absorbance was measured at a wavelength of 498 nm (Safire2, Tecan; optical densities (OD values) reached 0.6-0.8 for the untreated, uninfected controls). The EC_{50} (50% effective concentration or concentration which is calculated to inhibit virus-induced cell death by 50%) and CC_{50} (50% antimetabolic concentration or concentration which is calculated to inhibit the overall cell metabolism by 50%) values were derived from the dose-response curves. The 50% effective concentration (EC_{50}) and the 90%

effective concentration (EC_{90}) are the concentrations of compound that inhibit virus replication by 50% and 90%, respectively. The overall antimetabolic effect of the compounds is shown as Cytostatic/Cytotoxic Concentration (CC_{50}). The CC_{50} is the calculated concentration of compound that causes a 50% adverse effect on non-infected host cells (incorporates cytotoxic, cytostatic, and antimetabolic effect). All assay conditions producing an antiviral effect exceeding 50% were checked microscopically for minor signs of CPE or adverse effects on the host cell (i.e. altered cell morphology). A compound was only considered to elicit a selective antiviral effect on virus replication when, following microscopic quality control, at least at one concentration of the compound, no CPE nor any adverse effect is observed (image resembling untreated, uninfected cells). Multiple, independent experiments were performed.

Instrumental and General Analytical Methods

All reagents and solvents (of analytical and HPLC grades) were purchased from Sigma-Aldrich or other commercial suppliers like Fluka and Alfa Aesar and were used without further purification. Reactions that were moisture-sensitive were performed using anhydrous solvents and under argon atmosphere. EtOH, THF and DCM were dried before use. Disposable needles and syringes (B| Braun Inject and B| Braun Sterican®) were applied to transfer the solvents into the reaction flask. The solvents were removed under reduced pressure using the Heildolph Laborota 4000 efficient evaporator. Analytical thin-layer chromatography (TLC) was carried out on Polygram® SIL G/UV254 plates, layer 0.2 mm silica gel with fluorescent indicator. The spots were visualised by UV light (254 and/or 366nm) with UV light Vilmer Lourmat VL-6L. A part of the syntheses was performed in Cem Discover to obtain microwave conditions. Compounds were purified, performing a flash chromatography on a glass column using Merck silica gel (40−60 mesh). The solvent mixtures for chromatography are always referred to as a vol/vol ratio, and the melting points were determined on Cambridge Instruments.

NMR spectra were recorded on a Bruker Avance 500 NMR spectrometer (UltraShield) using a 5 mm switchable probe (TCI Prodigy Kryo-probe head, 5 mm, triple resonance-inverse-detection probe head) with z-axis gradients and automatic tuning and matching accessory (Bruker BioSpin). The resonance frequency for ^{1}H NMR was 500.13 MHz and for ^{13}C NMR 125.75 MHz. All measurements were performed for a solution in fully deuterated dimethylsulfoxide at 298 K. Standard 1D and gradient-enhanced 2D experiments, like double quantum filtered (DQF) COSY, HSQC, and HMBC, were used as supplied by the manufacturer. Chemical shifts are referenced internally to the residual, non-deuterated solvent signal 1H (δ 2.50 ppm) and the carbon signal 13C (δ 39.50 ppm) of dimethylsulfoxide. ^{19}F NMR spectra were recorded on a Bruker Avance III 400

NMR spectrometer (UltraShield) using a 5 mm switchable probe (BBFOPLUS, BB/19F – 1H/D) with z-axis gradients and automatic tuning and matching accessory (Bruker BioSpin). The resonance frequency for ^{1}H NMR was 400.23 MHz and for ^{19}F NMR 376.55 MHz. All measurements were performed for a solution in fully deuterated dimethylsulfoxide at 298 K. ^{19}F NMR spectra (broadband decoupled for 1H) were measured as supplied by the manufacturer using absolute referencing via Ξ ratio. Chemical shifts are given in ppm and are reported relative to TMS and referenced to the residual proton signal of d6-DMSO (2.49 ppm). d6-DMSO with 0.03% TMS (V/V), purchased at Euriso-top®, was used as a solvent for the samples. The specified abbreviations were used to characterize the signals: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, m = multiplet, and br = broad signal. The spectra were analysed by a computer using the software MestReNova 6 (Mestrelab research, 1994).

HRESIMS spectra were obtained on a maXis HD ESI-Qq-TOF mass spectrometer (Bruker Daltonics, Bremen, Germany). Samples were dissolved to 20 µg/mL in MeOH and directly infused into the ESI source at a flow rate of 3 µL/min with a syringe pump. The ESI ion source was operated as follows: capillary voltage: 0.9 to 4.0 kV (individually optimised), nebulizer: 0.4 bar (N_2), dry gas flow: 4 L/min (N_2), and dry temperature: 200 °C. Mass spectra were recorded in the range of *m/z* 50 – 1550 in the positive-ion mode. The sum formulas were determined using Bruker Compass DataAnalysis 4.2 based on the mass accuracy ($\Delta m/z \leq 2$ ppm) and isotopic pattern matching (SmartFormula algorithm).

The purity of the compounds was determined by HPLC on LC-2010A HT Liquid Chromatograph device (Shimadzu Corporation, Tokyo, Japan). The separation was carried out on an Acclaim 120 C18, 2.1 x 150 mm, 3 µm HPLC column (Thermo Fisher Scientific) using LC-MS-grade water with 0.1% FA and acetonitrile with 0.1% FA as mobile phase A and B,

respectively. The sample components were separated and eluted with a linear gradient from 5% to 95% B in 30 min, followed by an isocratic column cleaning and re-equilibration step. The flow rate was 0.1 mL/min, and the column oven temperature was set to 25 °C. The purity was determined from the UV chromatogram (254 nm) as the ratio of the peak area of the compound to the total peak area (i.e., the sum of the areas of all peaks that were not present in the solvent blank). Based on the HPLC data, all final compounds are ≥95% pure.

General Procedures

General Procedure A: Amine alkylation reaction for the synthesis of pyrimidine amines **2a**-**2j**. A stirred solution of pyrimidine (1 equiv) in anhydrous ethanol under an inert atmosphere was cooled to 0 °C before amine (2 equiv) was added dropwise. The reaction mixture was brought to room temperature and then stirred for 48 hours. After evaporation of the solvent, the residue was dissolved in dichloromethane and washed twice with water and with brine. The organic layer was dried over sodium sulphate, and then evaporated to dryness. The crude product was purified by column chromatography (SiO_2, eluent: hexane/EtOAc or DCM/MeOH) to afford the desired pyrimidine amines.

General Procedure B: Synthesis of compounds **3a**-**3l**. The pyrimidine amine (**2a**-**2j**, 1 equiv) and the Boc-protected pyridine (2 equiv) were dissolved/suspended in 1.5 ml dry ethanol. The mixture was heated to 155 °C for 30 minutes under microwave irradiation (250 Watt, 12 bars). After the solvent was evaporated, the resulting crude product was dissolved in dichloromethane and washed twice with K_2CO_3 solution (10% in water) and with water. The organic layer was dried over sodium sulphate, filtered, and then evaporated to dryness. The crude was purified by column chromatography (SiO_2, eluent: 80% dichloromethane/20% methanol), to obtain the pure product.

General Procedure C: Boc-deprotection reaction of compounds **4a-4b** and **4d-4m.** Carboxylate (1 equiv) was dissolved in dry tetrahydrofurane and stirred at room temperature, then the hydrochloric acid solution (4.0 M in dioxane, 10 equiv) was added dropwise. The mixture was stirred for 24 hours and evaporated to dryness. The residuum was dissolved in dichloromethane, washed twice with an aqueous solution of potassium carbonate (10%) and with water. The organic phase was dried over sodium sulphate, and filtered to obtain the desired product.

General Procedure D: Sulfonacylation reaction of nitrogen heterocycles. The pyrimidine (1 equiv) was dissolved in DCM. Sulfonyl chloride (1 equiv) and triethylamine (1 equiv) as a base was added and stirred overnight at room temperature. The mixture was diluted in DCM and washed twice with H_2O and with brine. The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by recrystallization (DIPE/EtOAc; DIPE/EtOH or Hexane/EtOAc) or by column chromatography (SiO_2, eluent: DCM/MeOH).

Characterization and Spectral Data of the Compounds

N-ethyl-6-methyl-2-(4-(4-fluorophenylsulfonyl)piperazin-1-yl)pyrimidin-4-amine (**1**). Compound **1** was prepared following general procedure D using **4a** (90 mg, 0.4 mmol), 4-fluorobenzenesulfonyl chloride (79 mg, 0.4 mmol) and TEA (42 mg, 0.42 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 50 mg of pure product (yield 33%). Mp 170.6−171.9 °C. Ret. time. 13.0 min, purity 96.9%. HRESIMS *m/z* 380.1555 $[M+H]^+$ (calcd for $C_{17}H_{23}FN_5O_2S^+$, 380.1551, Δ = -1.0 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.05 (t, 3H, CH_3), 2.00 (s, 3H, pyr-CH_3), 2.88 (m, 4H, pip-H3,5), 3.18 (br, 2H, NCH_2), 3.74 (m, 4H, pip-H2,6) 5.58 (s, 1H, pyr-H), 6.83 (br, 1H, NH), 7.48 (t, 2H, Ph-H3,5), 7.81 (q, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.61 (CH_3), 23.71 (pyr-CH_3), 34.60 (NCH_2), 42.43 (pip-C2,6), 45.78 (pip-C3,5), 116.68 ($^3J(^{13}C,^{19}F)$ = 22.6 Hz, (Ph-C3,5), 129.66 (pyr-C5), 130.69 ($^3J(^{13}C,^{19}F)$ = 9.7 Hz, Ph-C2,6), 131.11 ($^3J(^{13}C,^{19}F)$ = 3.1 Hz, Ph-C1), 160.62 (pyr-C2), 162.94 (pyr-C6), 164.72 ($^3J(^{13}C,^{19}F)$ = 253.9 Hz, Ph-C4), 174.42 (pyr-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.57 (Ph-F).

2-chloro-N-ethyl-6-methylpyrimidin-4-amine **(2a). 2a** was prepared following the general procedure A using 2,4-dichloro-6-methylpyrimidine (2.00 g, 12.27 mmol) and ethylamine (2.0 M in methanol, 12.27 ml, 24.54 mmol). The crude product was purified by column chromatography (SiO_2, eluent: either using a mixture of 50% hexane/50% ethyl acetate or 97.5% dichloromethane/2.5% methanol), resulting in 0.949 g of pure 2-chloro-N-ethyl-6-methylpyrimidin-4-amine (yield 45%).

[As a side product, 0.358 g of pure 4-chloro-N-ethyl-6-methylpyrimidin-2-amine **2f** (yield 17%) was obtained.]

2-chloro-N-isopropyl-6-methylpyrimidin-4-amine **(2b). 2b** was prepared following the general procedure A using 2,4-dichloro-6-methylpyrimidine (1.00 g, 6.13 mmol) and propan-2-amine

(1.00 ml, 12.27 mmol, diluted in 5 ml ethanol). The crude product was purified by column chromatography (SiO_2, eluent: 50% hexane/50% ethyl acetate), resulting in 0.608 g of pure 2-chloro-N-isopropyl-6-methylpyrimidin-4-amine (yield 53%).

[As a side product 0.239 g of pure 4-chloro-N-isopropyl-6-methylpyrimidin-2-amine **2j** (yield 21%) was obtained.]

N-(tert-butyl)-2-chloro-6-methylpyrimidin-4-amine **(2c). 2c** was prepared following the general procedure A using 2,4-dichloro-6-methylpyrimidine (1.00 g, 6.13 mmol) and 2-methylpropan-2-amine (1.29 ml, 12.34 mmol, diluted in 5 ml ethanol). The crude product was purified by column chromatography (SiO_2, eluent: 50% hexane/50% ethyl acetate), resulting in 0.200 g of pure N-(tert-butyl)-2-chloro-6-methylpyrimidin-4-amine (yield 16%).

2-chloro-4-ethoxy-6-methylpyrimidine **(2d). 2d** was prepared following the general procedure A using 2,4-dichloro-6-methylpyrimidine (1.00 g, 6.13 mmol) and sodium ethoxide solution (21% w/w in ethanol, 6.13 ml). The crude product was purified by column chromatography (SiO_2, eluent: dichloromethane) resulting in 0.353g of pure 2-chloro-4-ethoxy-6-methylpyrimidin (yield 33%).

2-chloro-4-methyl-6-(pyrrolidin-1-yl)pyrimidine **(2e). 2e** was prepared following the general procedure A using 2,4-dichloro-6-methylpyrimidine (0.50 g, 3.67 mmol) and pyrrolidine (0.435g, 6.12 mmol, diluted in 5 ml of dry ethanol). The crude product was purified by column chromatography (SiO_2, eluent: 50% hexane/50% ethyl acetate), resulting in 0.282 g of pure 2-chloro-4-methyl-6-(pyrrolidin-1-yl)pyrimidine (yield 39%).

[As a side product 0.109g of pure 4-chloro-6-methyl-2-(pyrrolidin-1-yl)pyrimidine (yield 15%) was obtained.]

***4-chloro-N-ethyl-6-methylpyrimidin-2-amine* (2f). 2f** was obtained as a side product from synthesis **2a** (yield 17%).

***6-chloro-N-ethyl-2-methylpyrimidin-4-amine* (2g). 2g** was prepared following the general procedure A using 4,6-dichloro-2-methylpyrimidine (1.00 g, 6.13 mmol) and ethylamine (2.0 M in methanol, 6.12 ml, 12.4 mmol). The crude product (0.95 g, 90% yield) was used without purification.

***2-chloro-N-ethylpyrimidin-4-amine* (2h). 2h** was prepared following the general procedure A using 2,4-dichloropyrimidine (3.50 g, 23.5 mmol) and ethylamine (2.0 M in methanol, 23.5 ml, 47 mmol). The crude product was purified by column chromatography (SiO_2, eluent: 50% hexane/50% ethyl actetate), resulting in 1.871g of pure 2-chloro-N-ethylpyrimidin-4-amine (yield 51%).

[As a side product 0.700 g of pure 4-chloro-N-ethylpyrimidin-2-amine **2i** (yield 19%) was obtained.]

***4-chloro-N-ethylpyrimidin-2-amine* (2i). 2i** was obtained in the first step of the synthesis of **2h** (yield 19%).

***4-chloro-N-isopropyl-6-methylpyrimidin-2-amine* (2j). 2j** was obtained in the first step of the synthesis of **2b** (yield 21%).

***tert-butyl 4-(4-(ethylamino)-6-methylpyrimidin-2-yl)piperazine-1-carboxylate* (3a). 3a** was prepared following the general procedure B using **2a** (0.86 g, 5.01 mmol) and tert-butyl piperazine-1-carboxylate (1.826 g, 9.8 mmol), to yield 1,365 g of pure product (yield 85%).

***tert-butyl 4-(4-(ethylamino)-6-methylpyrimidin-2-yl)-1,4-diazepane-1-carboxylate* (3b). 3b** was prepared following the general procedure B using **2a** (0.2 g, 1.17 mmol) and tert-butyl 1,4-diazepane-1-carboxylate (0.467 g, 2.3 mmol), to yield 0.333 g of pure product (yield 85%).

***tert-butyl 4-(4-(isopropylamino)-6-methylpyrimidin-2-yl)piperazine-1-carboxylate* (3c). 3c** was prepared following the general procedure B using **2b** (185 mg, 0.99 mmol) and tert-butyl piperazine-1-carboxylate (363 mg, 1.95 mmol), to yield 0.292 g of product (yield 87%).

***tert-butyl 4-(4-(tert-butylamino)-6-methylpyrimidin-2-yl)piperazine-1-carboxylate* (3d). 3d** was prepared following the general procedure B using **2c** (170 mg, 0.85 mmol) and tert-butyl piperazine-1-carboxylate (310 mg, 1.66 mmol), to yield 0.169 g of product (yield 57%).

***tert-butyl 4-(4-ethoxy-6-methylpyrimidin-2-yl)piperazine-1-carboxylate* (3e). 3e** was prepared following the general procedure B using **2d** (150 mg, 0.87 mmol) and tert-butyl piperazine-1-carboxylate (310 mg, 1.66 mmol), to yield 0.170 g of product (yield 61%).

***tert-butyl 4-(4-methyl-6-(pyrrolidin-1-yl)lpyrimidin-2-yl)piperazine-1-carboxylate* (3f). 3f** was prepared following the general procedure B using **2e** (231 mg, 1.17 mmol) and tert-butyl piperazine-1-carboxylate (425 mg, 2.28 mmol), to yield 0.305 g of product (yield 75%).

***tert-butyl 4-(2-(ethylamino)-6-methylpyrimidin-4-yl)piperazine-1-carboxylate* (3g). 3g** was prepared following the general procedure B using **2f** (304 mg, 1.78 mmol) and tert-butyl piperazine-1-carboxylate (646 mg, 3.47 mmol), to yield 0.542 g of product (yield 95%).

***tert-butyl 4-(6-(ethylamino)2-methylpyrimidin-4-yl)piperazine-1-carboxylate* (3h). 3h** was prepared following the general procedure B using **2g** (196 mg, 1.14 mmol) and tert-butyl piperazine-1-carboxylate (414 mg, 2.22 mmol), to yield 0.203 g of product (yield 55%).

***tert-butyl 4-(4-(ethylamino)pyrimidin-2-yl)piperazine-1-carboxylate* (3i). 3i** was prepared following the general procedure B using **2h** (180 mg, 1.14 mmol) and tert-butyl piperazine-1-carboxylate (440 mg, 2.36 mmol), to yield 0.256 g of product (yield 73%).

***tert-butyl 4-(2-(ethylamino)pyrimidin-4-yl)piperazine-1-carboxylate* (3j). 3j** was prepared following the general procedure B using **2i** (350 mg, 2.22 mmol) and tert-butyl piperazine-1-carboxylate (809 mg, 4.34 mmol), to yield 0.471 g of product (yield 69%).

***tert-butyl 4-(4-(cyclopropylamino)pyrimidin-2-yl)piperazine-1-carboxylate* (3k). 3k** was prepared following the general procedure B using 2-chloro-N-cyclopropylpyrimidin-4-amine (200 mg, 1.18 mmol) and tert-butyl piperazine-1-carboxylate (430 mg, 2.31 mmol), to yield 0.193 g of product (yield 52%).

***tert-butyl 4-(2-(isopropylamino)-6-methylpyrimidin-4-yl)piperazine-1-carboxylate* (3l). 3l** was prepared following the general procedure B using **2j** (250 mg, 1.34 mmol) and tert-butyl piperazine-1-carboxylate (491 mg, 2.63 mmol), to yield 0.256 g of product (yield 57%).

***N-ethyl-6-methyl-2-(piperazin-1-yl)pyrimidin-4-amine* (4a). 4a** was prepared following the general procedure C using **3a** (870 mg, 2.70 mmol), to yield 0.311 g of product (yield 52%).

***2-(1,4-diazepan-1-yl)-N-ethyl-6-methylpyrimidin-2-amine* (4b). 4b** was prepared following the general procedure C using **3b** (311 mg, 0.93 mmol), to yield 0.182 g of product (yield 83%).

***2-(3,4-dihydroquinoxaline-1(2H)-yl)-N-ethyl-6-methylpyrimidin-4-amine* (4c). 2a** (0.311 g, 1.81 mmol) and 1,2,3,4-tetrahydroquinoxaline (0.488 g, 3.64 mmol) were suspended in 1.5 ml dry ethanol. The mixture was heated to 155 °C for 30 minutes under microwave irradiation (250 Watt, 12 bars). After the solvent was evaporated, the resulting crude was dissolved in DCM and extracted twice with K_2CO_3 solution (10% in water). The organic layer was washed with water, dried with sodium sulphate, filtered, and then evaporated to dryness. The crude product was purified by column chromatography (SiO_2, eluent: 80% dichloromethane/20% methanol), to obtain 0.379 g of product (yield 78%).

N-isopropyl-6-methyl-2-(piperazin-1-yl)pyrimidin-4-amine **(4d). 4d** was prepared following the general procedure C using **3c** (278 mg, 0.83 mmol), to yield 190 mg of product (yield 97%).

N-(tert-butyl)-6-methyl-2-(piperazin-1-yl)pyrimidin-4-amine **(4e). 4e** was prepared following the general procedure C using **3d** (162 mg, 0.79 mmol), to yield 115 mg of product (yield 99%).

4-ethoxy-6-methyl-2-(piperazin-1-yl)pyrimidin-4-amine **(4f). 4f** was prepared following the general procedure C using **3e** (162 mg, 0.5 mmol), to yield 107 mg of product (yield 96%).

4-methyl-2-(piperazin-1-yl)-6-(pyrrolidin-1-yl)pyrimidine **(4g). 4g** was prepared following the general procedure C using **3f** (305 mg, 0.88 mmol), to yield 107 mg of product (yield 49%).

N-ethyl-4-methyl-6-(piperazin-1-yl)pyrimidin-2-amine **(4h). 4h** was prepared following the general procedure C using **3g** (300 mg, 0.93 mmol), to yield 200 mg of product (yield 97%).

N-ethyl-2-methyl-6-(piperazin-1-yl)pyrimidin-4-amine **(4i). 4i** was prepared following the general procedure C using **3h** (188 mg, 0.58 mmol), to yield 90 mg of product (yield 70%).

N-ethyl-2-(piperazin-1-yl)pyrimidin-4-amine **(4j). 4j** was prepared following the general procedure C using **3i** (244 mg, 0.79 mmol), to yield 110 mg of product (yield 67%).

N-ethyl-4-(piperazin-1-yl)pyrimidin-2-amine **(4k). 4k** was prepared following the general procedure C using **3j** (876 mg, 2.85 mmol), to yield 396 mg of product (yield 67%).

N-cyclopropyl-2-(piperazin-1-yl)pyrimidin-4-amine **(4l). 4l** was prepared following the general procedure C using **3k** (235 mg, 0.74 mmol), to yield 152 mg of product (yield 94%).

N-isopropyl-4-methyl-6-(piperazin-1-yl)pyrimidin-2-amine **(4m). 4m** was prepared following the general procedure C using **3l** (257 mg, 0.76 mmol), to yield 152 mg of product (yield 93%).

N-ethyl-6-methyl-2-(4-(phenylsulfonyl)piperazin-1-yl)pyrimidin-4-amine **(5a).** Compound **5a** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), benzenesulfonyl chloride (80 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was

purified by recrystallization (DIPE/EtOAc), resulting in 87 mg of pure product (yield 53%). Mp 120.3−124.4 °C. Ret. Time 13.80 min, purity 99.2%. HRESIMS *m/z* 362.1655 $[M+H]^+$ (calcd for $C_{17}H_{24}N_5O_2S^+$, 362.1654, Δ = -2.8 ppm). ^{1}H NMR (500 MHz, d$_6$DMSO) δ = 1.05 (t, 3H, CH_3), 2.00 (s, 3H, pyr-CH_3), 2.87 (m, 4H, pip-H3,5), 3.18 (br, 2H, NCH_2), 3.73 (m, 4H, pip-H2,6), 5.58 (s, 1H, pyr-H), 6.83 (br, 1H, NH), 7.64 (t, 2H, Ph-H3,5), 7.72 (m, 1H, Ph -H4), 7.74 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d$_6$DMSO) δ = 14.61 (CH_3), 23.71 (pyr-CH_3), 34.79 (NCH_2), 42.48 (pip-C2,6), 45.81 (pip- C3,5), 127.60 (Ph -C2,6), 129.46 (Ph -C3,5), 129.46 (pyr-C5), 133.35 (Ph -C4), 134.63 (Ph -C1), 160.65 (pyr-C2), 162.93 (pyr-C6), 174.29 (pyr-C4).

2-(4-((4-chlorophenyl)sulfonyl)piperazin-1-yl)-N-ethyl-6-methylpyrimidin-4-amine **(5b).** Compound **5b** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 4-chlorobenzenesulfonyl chloride (95 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (Hexane/EtOAc), resulting in 58 mg of pure product (yield 33%). Mp 132.0−133.6 °C. Ret. Time 15.28 min, purity 99.2%. HRESIMS *m/z* 396.1267 $[M+H]^+$ (calcd for $C_{17}H_{23}ClN_5O_2S^+$, 396.1256, Δ = -2.8 ppm). ^{1}H NMR (500 MHz, d$_6$DMSO) δ = 1.05 (t, 3H, CH_3), 2.00 (s, 3H, pyr-CH_3), 2.90 (m, 4H, pip-H3,5), 3.18 (br, 2H, NCH_2), 3.74 (m, 4H, pip-H2,6), 5.59 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.71 (m, 2H, Ph-H2,6), 7.75 (m, 2H, Ph-H3,5); ^{13}C NMR (125 MHz, d$_6$DMSO) δ = 14.61 (CH_3), 23.70 (pyr-CH_3), 34.53 (NCH_2), 42.43 (pip-C2,6), 45.75 (pip-C3,5), 129.50 (Ph-C3,5), 129.61 (Ph-C2,6), 129.61 (pyr-C5), 133.67 (Ph-C4), 138.30 (Ph-C1), 160.62 (pyr-C2), 162.93 (pyr-C6), 174.83 (pyr-C4).

2-(4-((4-bromophenyl)sulfonyl)piperazin-1-yl)-N-ethyl-6-methylpyrimidin-4-amine **(5c).** Compound **5c** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 4-bromobenzenesulfonyl chloride (115 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 62 mg of pure product

(yield 31%). Mp 147.2 °C. Ret. time 15.54 min, purity 99.3%. HRESIMS *m/z* 440.0763 $[M+H]^+$ (calcd for $C_{17}H_{23}BrN_5O_2S^+$, 440.0750, Δ = -2.8 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δc= 1.06 (t, 3H, CH_3), 2.01 (s, 3H, pyr-CH_3), 2.90 (m, 4H, pip-H3,5), 3.19 (br, 2H, NCH_2), 3.74 (m, 4H, pip-H2,6), 5.59 (s, 1H, pyr-H), 6.85 (br, 1H, NH), 7.67 (m, 2H, Ph-H2,6), 7.84 (m, 2H, Ph-H3,5); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.60 (CH_3), 23.71 (pyr-CH_3), 34.50 (NCH_2), 42.45 (pip-C2,6), 45.73 (pip-C3,5), 127.36 (Ph-C4), 129.55 (Ph-C2,6), 132.55 (Ph-C3,5), 134.09 (Ph-C1), 160.72 (pyr-C2), 162.94 (pyr-C4), 174.31(pyr-C6), n.d. (pyr-C5).

N-ethyl-2-(4-((4-iodophenyl)sulfonyl)piperazin-1-yl)-6-methylpyrimidin-4-amine **(5d).** Compound **5d** was prepared following general procedure D using **4a** (70 mg, 0.32 mmol), 4-iodobenzenesulfonyl chloride (96 mg, 0.32 mmol) and TEA (32 mg, 0.32 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 73 mg of pure product (yield 47%). Mp 159.4−160.4 °C. Ret. time 15.97 min, purity 99.0%. HRESIMS *m/z* 488.0625 $[M+H]^+$ (calcd for $C_{17}H_{23}IN_5O_2S^+$, 488.0612, Δ = -2.7 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.05 (t, 3H, CH_3), 2.01 (s, 3H, pyr-CH_3), 2.88 (m, 4H, pip-H3,5), 3.18 (br, 2H, NCH_2), 3.74 (m, 4H, pip-H2,6), 5.59 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.49 (m, 2H, Ph-H2,6), 8.01 (m, 2H, Ph-H3,5); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.61 (CH_3), 23.72 (pyr-CH_3), 34.52 (NCH_2), 42.44 (pip-2,6), 45.76 (pip-C3,5), 94.17 (pyr-C5), 101.87 (Ph-C4), 129.19 (Ph-C2,6), 134.38 (Ph-C1), 138.33 (Ph-C3,5), 160.62 (pyr-C2), 162.92 (pyr-C6), 174.34 (pyr-C4).

N-ethyl-6-methyl-2-(4-((4-trifluoromethyl)phenyl)sulfonyl)piperazin-1-yl)pyrimidin-4-amine **(5e).** Compound **5e** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 4-(trifluoromethyl)-benzenesulfonyl chlorid (115 mg, 0.47 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 62 mg of pure product (yield 32%). Mp 169.6−172.6 °C. Ret. time 16.13 min, purity 99.3%. HRESIMS

m/z 430.1528 $[M+H]^+$ (calcd for $C_{18}H_{23}F_3N_5O_2S^+$, 430.1519, Δ = -2.2 ppm). ^1H NMR (500 MHz, d_6DMSO) δ= 1.05 (t, 3H, CH_3), 2.00 (s, 3H, pyr-CH_3), 2.95 (m, 4H, pip-H3,5), 3.18 (br, 2H, NCH_2), 3.75 (m, 4H, pip-H2,6), 5.58 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.96 (m, 2H, Ph-H2,6), 8.02 (m, 2H, Ph-H3,5); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.61 (CH_3), 23.71 (pyr-CH_3), 34.54 (NCH_2), 42.43 (pip-2,6), 45.75 (pip-C3,5), 123.43 ($^3J(^{13}C,^{19}F)$ = 271.3 Hz, CF_3), 126.67 ($^3J(^{13}C,^{19}F)$ = 3.6 Hz, Ph-C3,5), 128.56 (Ph-C2,6), 129.65 (pyr-C5), 132.86 ($^3J(^{13}C,^{19}F)$ = 32.0 Hz, Ph-C4), 138.93 (Ph-C1), 160.59 (pyr-C2), 162.92 (pyr-C6), 173.33 (pyr-C4). ^{19}F NMR (400 MHz, d6DMSO) δ = -61.65 (CF_3).

N-ethyl-6-methyl-2-(4-((4-nitrophenyl)sulfonyl)piperazin-1-yl)pyrimidin-4-amine **(5f).** Compound **5f** was prepared following general procedure D using **4a** (200 mg, 0.9 mmol), 4-nitrobenzenesulfonyl chloride (200 mg, 0.9 mmol) and TEA (92 mg, 0.9 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 177 mg of pure product (yield 48%). Mp 172 °C. Ret. time 14.60 min, purity 96.2%. HRESIMS *m/z* 407.1503 $[M+H]^+$ (calcd for $C_{17}H_{23}N_6O_4S^+$, 407.1496, Δ = -1.7 ppm). ^1H NMR (500 MHz, d_6DMSO) δ = 1.04 (t, 3H, CH_3), 1.99 (s, 3H, pyr-CH_3), 2.96 (m, 4H, pip-H3,5), 3.17 (br, 2H, NCH_2), 3.75 (m, 4H, pip-H2,6), 5.58 (s, 1H, pyr-H), 6.83 (br, 1H, NH), 8.01 (m, 2H, Ph-H2,6), 8.42 (m, 2H, Ph-H3,5); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.66 (CH_3), 23.73 (pyr-CH_3), 34.61 (NCH_2), 42.49 (pip-C2,6), 45.77 (pip-C3,5), 124.80 (Ph-C3,5), 129.19 (Ph-C2,6), 140.54 (Ph-C1), 150.18 (Ph-C4), 160.61 (pyr-C2), 162.99 (pyr-C6), 170.56 (pyr-C4), n.d. (pyr-C5).

4-((4-(4-(ethylamino)-6-methylpyrimidin-2-yl)piperazin-1-yl)sulfonyl)benzonitrile **(5g).** Compound **5g** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 4-cyanobenzenesulfonyl chloride (91 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 36 mg of pure product

(yield 21%). Mp 180 °C. Ret. time 13.88 min, purity 97.6%. HRESIMS *m/z* 387.1607 $[M+H]^+$ (calcd for $C_{18}H_{23}N_6O_2S^+$, 387.1607, Δ = -2.5 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.05 (t, 3H, CH_3), 2.01 (s, 3H, pyr-CH_3), 2.95 (m, 4H, pip-H3,5), 3.19 (br, 2H, NCH_2), 3.75 (m, 4H, pip-H2,6), 5.59 (s, 1H, pyr-H), 6.85 (br, 1H, NH), 7.92 (m, 2H, Ph-H3,5), 8.11 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.59 (CH_3), 23.70 (pyr-CH_3), 34.61 (NCH_2), 42.47 (pip-C2,6), 45.70 (pip-C3,5), 94.45 (pyr-C5), 115.73 (Ph-C1), 117.65 (CN), 128.28 (Ph-C3,5), 133.61 (Ph-C2,6), 139.13 (Ph-C4), 160.50 (pyr-C2), 162.89 (pyr-C6), 174.30 (pyr-C4).

N-ethyl-2-(4-((4-methoxyphenyl)sulfonyl)piperazin-1-yl)-6-methylpyrimidin-4-amine **(5h).** Compound **5h** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 4-methoxybenzenesulfonyl chloride (93 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 32 mg of pure product (yield 18%). Mp 183.2-194.0 °C. Ret. time 14.24 min, purity 95.5%. HRESIMS *m/z* 392.1760 $[M+H]^+$ (calcd for $C_{18}H_{26}N_5O_3S^+$, 392.1751, Δ = -2.3 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.09 (t, 3H, CH_3), 2.18 (s, 3H, pyr-CH_3), 2.97 (m, 4H, pip-H3,5), 3.32 (br, 2H, NCH_2), 3.82 (m, 4H, pip-H2,6), 3.84 (s, 3H, OCH_3), 5.85 (s, 1H, pyr-H), 7.16 (m, 2H, Ph-H3,5), 7.69 (m, 2H, Ph-H2,6), n.d. (NH); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.00 (CH_3), 22.81 (pyr-CH_3), 35.30 (NCH_2), 43.60 (pip-C2,6), 45.27 (pip-C3,5), 55.76 (OCH_3), 96.43 (pyr-C5), 114.66 (Ph-C3,5), 126.00 (Ph-C1), 129.89 (Ph-C2,6), 162.94 (Ph-C4), n.d. (pyr-C2), n.d. (pyr-C4), n.d. (pyr-C6).

N-ethyl-6-methyl-2-(4-tosylpiperazin-1-yl)pyrimidin-4-amine **(5i).** Compound **5i** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 4-methylbenzenesulfonyl chloride (86 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 87 mg of pure product (yield 51%). Mp 170.6−171.9

°C. Ret. time 14.76 min, purity 95.5%. HRESIMS *m/z* 376.1807 $[M+H]^+$ (calcd for $C_{18}H_{26}N_5O_2S^+$, 376.1802, Δ = -1.5 ppm). ^{1}H NMR (500 MHz, d$_6$DMSO) δ = 1.05 (t, 3H, CH_3), 2.00 (s, 3H, pyr-CH_3), 2.39 (s, 3H, Ph-CH_3), 2.83 (m, 4H, pip-H3,5), 3.18 (br, 2H, NCH_2), 3.73 (m, 4H, pip-H2,6), 5.58 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.44 (m, 2H, Ph-H3,5), 7.62 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d$_6$DMSO) δ = 14.60 (CH_3), 21.03 (Ph-CH_3), 23.70 (pyr-CH_3), 34.64 (NCH_2), 42.46 (pip-2,6), 45.76 (pip-C3,5), 94.12 (pyr-C5), 127.65 (ph-C2,6), 129.88 (Ph-C3,5), 131.67 (Ph-C1), 143.78 (Ph-C4), 160.61 (pyr-C2), 162,92 (pyr-C6), n.d. (pyr-C4).

N-ethyl-2-(4-((2-fluorophenyl)sulfonyl)piperazin-1-yl)-6-methylpyrimidin-4-amine **(5j).** Compound **5j** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 2-fluorobenzenesulfonyl chloride (88 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 22 mg of pure product (yield 13%). Mp 170.6−171.9 °C. Ret. time 14.12 min, purity 98.1%. HRESIMS *m/z* 380.1559 $[M+H]^+$ (calcd for $C_{17}H_{23}FN_5O_2S^+$, 380.1551, Δ = -2.2 ppm). ^{1}H NMR (500 MHz, d$_6$DMSO) δ = 1.06 (t, 3H, CH_3), 2.02 (s, 3H, pyr-CH_3), 3.05 (m, 4H, pip-H3,5), 3.19 (br, 2H, NCH_2), 3.74 (m, 4H, pip-H2,6), 5.60 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.43 (m, 1H, Ph-H5), 7.48 (m, 1H, Ph-H3), 7.76 (m, 1H, Ph-H4), 7.78 (m, 1H, Ph-H6); ^{13}C NMR (125 MHz, d$_6$DMSO) δ = 14.61 (CH_3), 23.71 (pyr-CH_3), 34.53 (NCH_2), 42.72 (pip-C2,6), 45.43 (pip-C3,5), 94.24 (pyr-C5), 117.69 (^3J(^{13}C,^{19}F) = 21.6 Hz, Ph-C3), 123.64 (^3J(^{13}C,^{19}F) = 14.4 Hz, Ph-C1), 125.26 (^3J(^{13}C,^{19}F) = 3.4 Hz, Ph-C5), 130.98 (Ph-C6), 136.15 (^3J(^{13}C,^{19}F) = 8.7 Hz, Ph-C4), 158.26 (^3J(^{13}C,^{19}F) = 252.6 Hz, Ph-C2), 160.73 (pyr-C2), 162.94 (pyr-C6), n.d. (pyr-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -108.23 (Ph-F).

N-ethyl-2-(4-((3-fluorophenyl)sulfonyl)piperazin-1-yl)-6-methylpyrimidin-4-amine **(5k).** Compound **5k** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 3-

fluorobenzenesulfonyl chloride (88 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 62 mg of pure product (yield 36%). Mp 131.3−132.9 °C. Ret. time 14.45 min, purity 97.2%. HRESIMS *m/z* 380.1560 $[M+H]^+$ (calcd for $C_{17}H_{23}FN_5O_2S^+$, 380.1551, Δ = -2.5 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, CH_3), 2.01 (s, 3H, pyr-CH_3), 2.93 (m, 4H, pip-H3,5), 3.19 (br, 2H, NCH_2), 3.74 (m, 4H, pip-H2,6), 5.59 (s, 1H, pyr-H), 6.85 (br, 1H, NH), 7.58 (m, 1H, Ph-H2), 7.60 (m, 1H, Ph-H4), 7.60 (m, 1H, Ph-H6), 7.70 (m, 1H, Ph-H5); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.59 (CH_3), 23.69 (pyr-CH_3), 34.54 (NCH_2), 42.46 (pip-C2,6), 45.80 (pip-C3,5), 94.35 (pyr-C5), 114.63 (^3J(^{13}C,^{19}F) = 24.1 Hz, Ph-C2), 120.55 (^3J(^{13}C,^{19}F) = 21.2 Hz, Ph-C4), 123.84 (^3J(^{13}C,^{19}F) = 2.5 Hz, Ph-C6), 131.85 (^3J(^{13}C,^{19}F) = 8.0 Hz, Ph-C5), 136.90 (^3J(^{13}C,^{19}F) = 6.3 Hz, Ph-C1), 160.60 (pyr-C2), 161.87 (^3J(^{13}C,^{19}F) = 248.0 Hz, Ph-C3), 163.24 (pyr-C6), n.d. (pyr-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -110.01 (Ph-F).

2-(4-((3,4-difluorophenyl)sulfonyl)piperazin-1-yl)-N-ethyl-6-methylpyrimidin-4-amine **(5l).**

Compound **5l** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 3,4-difluorobenzenesulfonyl chloride (96 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 71 mg of pure product (yield 40%). Mp 108.8 °C. Ret. time 14.86 min, purity 98.1%. HRESIMS *m/z* 398.1464 $[M+H]^+$ (calcd for $C_{17}H_{22}F_2N_5O_2S^+$, 398.1457, Δ = -1.8 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, CH_3), 2.03 (s, 3H, pyr-CH_3), 2.95 (m, 4H, pip-H3,5), 3.21 (br, 2H, NCH_2), 3.76 (m, 4H, pip-H2,6), 5.62 (s, 1H, pyr-H), 6.90 (br, 1H, NH), 7.63 (m, 1H, Ph-H6), 7.71 (dt, 1H, J = 26.5 Hz, Ph-H5), 7.86 (ddd, 1H, J = 19.3 Hz, Ph-H2); 13C NMR (125 MHz, d_6DMSO) δ = 14.59 (CH_3), 23.51 (pyr-CH_3), 34.75 (NCH_2), 42.59 (pip-C2,6), 45.77 (pip-C3,5), 94.60 (pyr-C5), 117.63 (d, ^3J(^{13}C,^{19}F) = 19.6 Hz, Ph-C2), 118.96 (d, ^3J(^{13}C,^{19}F) = 18.3 Hz, Ph-C5), 125.62 (dd, ^3J(^{13}C,^{19}F) =

8.0 Hz, 3.5 Hz, Ph-C6), 132.05 (dd, $^{3}J(^{13}C,^{19}F)$ = 4.8 Hz, 3.5 Hz, Ph-C1), 149.55 (dd, $^{3}J(^{13}C,^{19}F)$ = 250.2 Hz, 13.2 Hz, Ph-C3), 152.62 (dd, $^{3}J(^{13}C,^{19}F)$ = 252.5 Hz, 12.3 Hz, Ph-C4), n.d. (pyr-C4), n.d. (pyr-C6), n.d. (pyr-C2); ^{19}F NMR (400 MHz, d6DMSO) δ = -130.60 (d, 21.8 HZ, Ph-F), -134.72 (d, 21.8 Hz, Ph-F).

***2-(4-((2,4-difluorophenyl)sulfonyl)piperazin-1-yl)-N-ethyl-6-methylpyrimidin-4-amine* (5m).** Compound **5m** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 2,4-difluorobenzenesulfonyl chloride (96 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 63 mg of pure product (yield 35%). Mp 134.2 °C. Ret. time 14.49 min, purity 98.5%. HRESIMS *m/z* 398.1465 $[M+H]^+$ (calcd for $C_{17}H_{22}F_2N_5O_2S^+$, 398.1457, Δ = -2.2 ppm). ^1H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, CH_3), 2.02 (s, 3H, pyr-CH_3), 3.05 (m, 4H, pip-H3,5), 3.20 (br, 2H, NCH_2), 3.75 (m, 4H, pip-H2,6), 5.60 (s, 1H, pyr-H), 6.85 (br, 1H, NH), 7.33 (dt, 1H, J = 19.3 Hz, Ph-H5), 7.59 (ddd, 1H, J = 22.3 Hz, Ph-H3), 7.85 (dt, 1H, J = 23.3 Hz, Ph-H6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.61 (CH_3), 23.72 (pyr-CH_3), 34.47 (NCH_2), 42.67 (pip-C2,6), 45.38 (pip-C3,5), 94.30 (pyr-C5), 106.42 (t, $^{3}J(^{13}C,^{19}F)$ = 26.4 Hz, Ph-C3), 112.69 (dd, $^{3}J(^{13}C,^{19}F)$ = 25.3 Hz, Ph-C5), 120.47 (dd, $^{3}J(^{13}C,^{19}F)$ = 18.1 Hz, Ph-C1), 133.06 (d, $^{3}J(^{13}C,^{19}F)$ = 11.1 Hz, Ph-C6), 159.19 (dd, $^{3}J(^{13}C,^{19}F)$ = 268.8 Hz, Ph-C2), 160.70 (pyr-C2), 162.94 (pyr-C6), 165.29 (dd, $^{3}J(^{13}C,^{19}F)$ = 265 Hz, Ph-C4), n.d. (pyr-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -100.98 (d, 12.5 HZ, Ph-F4), -102.98 (d, 12.5 Hz, Ph-F2).

***N-ethyl-6-methyl-2-(4-((3,4,5-trifluorophenyl)sulfonyl)piperazin-1-yl)pyrimidin-4-amine* (5n).** Compound **5n** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 3,4,5-trifluorobenzenesulfonyl chloride (105 mg, 0.46 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 72 mg of

pure product (yield 39%). Mp 112.1 °C. Ret. time 15.52 min, purity 96.7%. HRESIMS *m/z* 416.1374 $[M+H]^+$ (calcd for $C_{17}H_{21}F_3N_5O_2S^+$, 416.1363, Δ = -2.7 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, J = 7.2 Hz, CH_3), 2.01 (s, 3H, pyr-CH_3), 2.98 (m, 4H, pip-H3,5), 3.19 (br, 2H, NCH_2), 3.76 (m, 4H, pip-H2,6), 5.59 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.76 (t, 2H, J = 6.5 Hz, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.62 (CH_3), 23.69 (pyr-CH_3), 34.66 (NCH_2), 42.30 (pip-C2,6), 45.80 (pip-C3,5), 94.38 (pyr-C5), 113.31 (dd, $^3J(^{13}C,^{19}F)$ = 23.8 Hz, Ph-C2,6), 131.32 (Ph-C1), 142.26 (dt, $^3J(^{13}C,^{19}F)$ = 284.9 Hz, Ph-C4), 150.45 (dd, $^3J(^{13}C,^{19}F)$ = 262.6 Hz, Ph-C3,5), 160.50 (pyr-C2), 162.93 (pyr-C6), n.d. (pyr-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -131.07 (d, 21.2 HZ, Ph-F3,5), -153.14 (d, 21.2 Hz, Ph-F4).

***N-ethyl-6-methyl-2-(4-((2,3,4-trifluorophenyl)sulfonyl)piperazin-1-yl)pyrimidin-4-amine* (5o).** Compound **5o** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 2,3,4-trifluorobenzenesulfonyl chloride (105 mg, 0.46 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 78 mg of pure product (yield 42%). Mp 142.7 °C. Ret. time 15.31 min, purity 98.2%. HRESIMS *m/z* 416.1373 $[M+H]^+$ (calcd for $C_{17}H_{21}F_3N_5O_2S^+$, 416.1363, Δ = -2.5 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, CH_3), 2.02 (s, 3H, pyr-CH_3), 3.08 (m, 4H, pip-H3,5), 3.20 (br, 2H, NCH_2), 3.77 (m, 4H, pip-H2,6), 5.60 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.54 (m, 1H, Ph-H5), 7.63 (m, 1H, Ph-H6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.63 (CH_3), 23.72 (pyr-CH_3), 35.00 (NCH_2), 42.54 (pip-C2,6), 45.32 (pip-C3,5), 113.37 (Ph-C5), 121.60 (Ph-C1), 125.66 (Ph-C6), 140.03 (d, $^3J(^{13}C,^{19}F)$ = 252.2 Hz, Ph-C3), 147.77 (d, $^3J(^{13}C,^{19}F)$ = 250.3 Hz, Ph-C2), 153.44 (d, $^3J(^{13}C,^{19}F)$ = 253.2 Hz, Ph-C4), 160.61 (pyr-C2), 162.94 (pyr-C6), 174.20 (pyr-C4), n.d. (pyr-C5); ^{19}F NMR (400 MHz, d6DMSO) δ = -125.97 (Ph-F), -129.01 (Ph-F), -156.91 (Ph-F).

N-ethyl-6-methyl-2-(4-((2,4,6-trifluorophenyl)sulfonyl)piperazin-1-yl)pyrimidin-4-amine **(5p).** Compound **5p** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 2,3,4-trifluorobenzenesulfonyl chloride (100 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by column chromatography (dichloromethane/20% methanol), resulting in 85 mg of pure product (yield 45%). Mp 140.3 °C. Ret. time 13.16 min, purity 96.5%. HRESIMS *m/z* 416.1364 $[M+H]^+$ (calcd for $C_{17}H_{21}F_3N_5O_2S^+$, 416.1363, Δ = -0.4 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.07 (t, 3H, CH_3), 2.02 (s, 3H, pyr-CH_3), 3.12 (m, 4H, pip-H3,5), 3.20 (br, 2H, NCH_2), 3.77 (m, 4H, pip-H2,6), 5.61 (s, 1H, pyr-H), 6.85 (br, 1H, NH), 7.47 (m, 1H, Ph-H3,5); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.64 (CH_3), 23.73 (pyr-CH_3), 34.61 (NCH_2), 42.59 (pip-C2,6), 45.14 (pip-C3,5), 94.47 (pyr-C5), 102.97 (t, $^3J(^{13}C,^{19}F)$ = 28.4 Hz, Ph-C3,5), 110.78 (Ph-C1), 160.07 (ddd, $^3J(^{13}C,^{19}F)$ = 255.8, 16.6 and 7.4 Hz, Ph-C2,6), 160.70 (pyr-C2), 162.97 (pyr-C4), 163.31 (pyr-C6), 164.93 (dt, $^3J(^{13}C,^{19}F)$ = 250.4, 15.7 and 15.7 Hz, Ph-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -101.84 (t, 10.6 Hz, Ph-F2,6), -98.90 (m, Ph-F4).

N-ethyl-6-methyl-2-(4-((perfluorophenyl)sulfonyl)piperazin-1-yl)pyrimidin-4-amine **(5q).** Compound **5q** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), pentafluorobenzenesulfonyl chloride (120 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 33 mg of pure product (yield 16%). Mp 175.2−177.5 °C. Ret. time 16.15 min, purity 97.4%. HRESIMS *m/z* 452.1189 $[M+H]^+$ (calcd for $C_{17}H_{19}F_5N_5O_2S^+$, 452.1174, Δ = -3.3 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.07 (t, 3H, CH_3), 2.03 (s, 3H, pyr-CH_3), 3.18 (m, 4H, pip-H3,5), 3.21 (br, 2H, NCH_2), 3.81 (m, 4H, pip-H2,6), 5.61 (s, 1H, pyr-H), 6.85 (br, 1H, NH); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.67 (CH_3), 23.71 (pyr-CH_3), 34.64 (NCH_2), 42.45 (pip-C2,6), 45.15 (pip-C3,5), 160.63 (pyr-C2), 163.05 (pyr-C6), n.d. (pyr-C4), n.d. (pyr-C5), n.d. (Ph-C1), n.d. (Ph-C2), n.d.

(Ph-C3), n.d. (Ph-C4), n.d. (Ph-C5), n.d. (Ph-C6); ^{19}F NMR (400 MHz, d6DMSO) δ = -135.43 (d, J = 18.9 Hz, F-2, F6), -146.86 (t, J = 22.3 Hz, F-4), -159.44 (dd, J = 22.3 and 18.9 Hz, F-3, F-5).

2-(4-((3,4-dichlorophenyl)sulfonyl)piperazin-1-yl)-N-ethyl-6-methylpyrimidin-4-amine **(5r).** Compound **5r** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 3,4-dichlorobenzoyl chloride (94 mg, 0.45 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 70 mg of pure product (yield 36%). Mp 116.5 °C. Ret. time 13.14 min, purity 90.8%. HRESIMS *m/z* 430.0870 $[M+H]^+$ (calcd for $C_{17}H_{22}Cl_2N_5O_2S^+$, 430.0866, Δ = -0.9 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, CH_3), 2.02 (s, 3H, pyr-CH_3), 2.97 (m, 4H, pip-H3,5), 3.19 (br, 2H, NCH_2), 3.76 (m, 4H, pip-H2,6), 5.60 (s, 1H, pyr-H), 6.84 (br, 1H, NH), 7.71 (dd, 8.4 and 2.1 Hz, 1H, Ph-H6), 7.90 (d, 8.4 Hz, 1H, Ph-H5), 7.94 (d, 2.1 Hz, 1H, Ph-H2); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.59 (CH_3), 23.70 (pyr-CH_3), 35.43 (NCH_2), 42.43 (pip-C2,6), 45.72 (pip-C3,5), 127.65 (Ph-C6), 129.20 (Ph-C2), 131.84 (Ph-C5), 132.55 (Ph-C2), 135.32 (Ph-C3), 136.55 (Ph-C4), n.d. (pyr-C2), n.d. (pyr-C4), n.d. (pyr-C5), n.d. (pyr-C6).

2-(4-((4-aminophenyl)sulfonyl)piperazin-1-yl)-N-ethyl-6-methylpyrimidin-4-amine **(5s).** Compound **5f** (200 mg, 0.49 mmol) and tin (II) chloride dihydrate (800 mg, 3.55 mmol) were dissolved in EtOAc and heated to 80 °C for 48 h under reflux. The mixture was diluted in ethyl acetate and extracted with saturated sodium hydrogen carbonate solution. The organic layer dried over sodium sulphate, filtered and concentrated in vacuum. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 122 mg of pure product (yield 66%). Mp 159.8 °C. Ret. time 12.19 min, purity 95.2%. HRESIMS *m/z* 377.1762 $[M+H]^+$ (calcd for $C_{17}H_{25}N_6O_2S^+$, 377.1754, Δ = -2.0 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, CH_3), 2.01 (s, 3H, pyr-CH_3), 2.77 (m, 4H, pip-H3,5), 3.19 (br, 2H, NCH_2), 3.71 (m, 4H, pip-H2,6), 5.58 (s, 1H, pyr-H),

6.08 (s, 2H, NH_2), 6.62 (m, 2H, Ph-H3,5), 6.82 (br, 1H, NH), 7.34 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.61 (CH_3), 23.74 (pyr-CH_3), 34.57 (NCH_2), 42.47 (pip-C2,6), 45.79 (pip-C3,5), 93.99 (pyr-C5), 112.64 (Ph-C3,5), 118.94 (Ph-C1), 129.64 (Ph-C2,6), 153.26 (Ph-C4), 160.71 (pyr-C2), 162.93 (pyr-C6), n.d. (pyr-C4).

(4-(4-(ethylamino)-6-methylpyrimidin-2-yl)piperazin-1-yl)(4-fluorophenyl)methanone **(6a).** Compound **6a** was prepared following general procedure D using **4a** (120 mg, 0.54 mmol), 4-fluorobenzoyl chloride (86 mg, 0.54 mmol) and TEA (55 mg, 0.54 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 90 mg of pure product (yield 49%). Mp 131.6−134.2 °C. Ret. time 12.39 min, purity 98.4%. HRESIMS *m/z* 344.1891 $[M+H]^+$ (calcd for $C_{18}H_{23}FN_5O^+$, 344.1881, Δ = -2.8 ppm). ^1H NMR (500 MHz, d_6DMSO) δ = 1.08 (t, 3H, CH_3), 2.05 (s, 3H, pyr-CH_3), 3.22 (br, 2H, NCH_2), 3.68 (br, 4H, pip-H3,5), 3.68 (br, 4H, pip-H2,6), 5.63 (s, 1H, pyr-H), 6.84 (br, 2H, NH_2), 7.29 (m, 2H, Ph-H3,5), 7.50 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.67 (CH_3), 23.78 (pyr-CH_3), 34.65 (NCH_2), 43.36 (pip-C2,6), 43.36 (pip-C3,5), 94.21 (pyr-C5), 115.39 ($^3J(^{13}C,^{19}F)$ = 21.2 Hz, Ph-C3,5), 129.66 ($^3J(^{13}C,^{19}F)$ = 8.6 Hz, Ph-C2,6), 132.32 ($^3J(^{13}C,^{19}F)$ = 3.2 Hz, Ph-C1), 161.07 (pyr-C2), 162.54 ($^3J(^{13}C,^{19}F)$ = 244.9 Hz, Ph-C4), 162.96 (pyr-C6), 168.25 (amide-C), n.d. (pyr-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -111.17 (Ph-F).

N-ethyl-2-(4-(4-fluorobenzyl)piperazin-1-yl)-6-methylpyrimidin-4-amine **(6b).** Compound **6b** was prepared following general procedure D using **4a** (100 mg, 0.45 mmol), 4-fluorobenzyl chloride (66 mg, 0.46 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by column chromatography (SiO2, eluent: 80% DCM, 20% MeOH), resulting in 40 mg of pure product (yield 27%). Mp 124−127 °C, Ret. time 7.79 min, purity 94.5%. HRESIMS *m/z* 330.2098 $[M+H]^+$ (calcd for $C_{18}H_{25}FN_5^+$, 330.2089, Δ = -2.8 ppm). ^1H NMR (500 MHz, d_6DMSO)

δ = 1.07 (t, 3H, CH_3), 2.03 (s, 3H, pyr-CH_3), 2.35 (m, 4H, pip-H3,5), 3.20 (br, 2H, NCH_2), 3.47 (s, 2H, Bn-CH_2), 3.63 (m, 4H, pip-H2,6), 5.58 (s, 1H, pyr-H), 6.78 (br, 2H, NH_2), 7.15 (m, 2H, Ph-H3,5), 7.35 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.72 (CH_3), 23.77 (pyr-CH_3), 34.66 (NCH_2), 43.31 (pip-C2,6), 52.54 (pip-C3,5), 61.29 (Bn-C), 114.99 (d, $^3J(^{13}C,^{19}F)$ = 21.2 Hz, Ph-C3,5), 130.87 (d, $^3J(^{13}C,^{19}F)$ = 7.4 Hz, Ph-C2,6), 134.27 (Ph-C1), 161.35 (d, $^3J(^{13}C,^{19}F)$ = 240.6 Hz, Ph-C4), 162.98 (pyr-C6), n.d. (pyr-C2), n.d. (pyr-C4), n.d. (pyr-C5); ^{19}F NMR (400 MHz, d6DMSO) δ = -115.97 (Ph-F).

N-ethyl-2-(4-((4-fluorophenyl)sulfonyl)-1,4-diazepan-1-yl)-6-methylpyrimidin-4-amine **(7a).** Compound **7a** was prepared following general procedure D using **4b** (146 mg, 0.62 mmol), 4-fluorobenzenesulfonyl chloride (79 mg, 0.62 mmol) and TEA (63 mg, 0.62 mmol) in DCM. The crude product was column chromatography (SiO_2, eluent: 80% DCM, 20% MeOH), resulting in 134 mg of pure product (yield 55%). Mp resinous substance, Ret. time 13.66 min, purity 97.9%. HRESIMS *m/z* 394.1721 $[M+H]^+$ (calcd for $C_{18}H_{25}FN_5O_2S^+$, 394.1708, Δ = -3.5 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.07 (t, 3H, J = 7.2 Hz, CH_3), 1.73 (m, 2H, dia-H6), 2.00 (s, 3H, pyr-CH_3), 3.18 (br, 2H, NCH_2), 3.22 (m, 2H, dia-H5), 3.34 (m, 2H, dia-H3), 3.64 (t, 2H, dia-H7), 3.76 (t, 2H, dia-H2), 5.56 (s, 1H, pyr-H), 6.76 (br, 1H, NH), 7.33 (t, 2H, Ph-H3,5), 7.77 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.79 (CH_3), 23.93 (pyr-CH_3), 28.11 (dia-C6), 34.62 (NCH_2), 45.29 (dia-C7), 47.06 (dia-C2), 47.06 (dia-C5), 47.93 (dia-C3), 93.67 (pyr-C5), 116.41 (d, $^3J(^{13}C,^{19}F)$ = 22.5 Hz, Ph-C3,5), 129.67 (d, $^3J(^{13}C,^{19}F)$ = 9.4 Hz, Ph-C2,6), 135.43 (d, $^3J(^{13}C,^{19}F)$ = 2.8 Hz, Ph-C1), 160.36 (pyr-C2), 163.01 (pyr-C4), 163.01. (pyr-C6), 164.25 (d, $^3J(^{13}C,^{19}F)$ = 249.9 Hz, Ph-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -106.68 (Ph-F).

N-ethyl-2-(4-((4-fluorophenyl)sulfonyl)-3,4-dihydroquinoxalin-1(2H)-yl)-6-methylpyrimidin-4-amine **(7b).** Compound **7b** was prepared following general procedure D using

4c (345 mg, 1.28 mmol), 4-fluorobenzenesulfonyl chloride (249 mg, 1.28 mmol) and TEA (130 mg, 1.28 mmol) in DCM. The crude product was purified by column chromatography (SiO_2, eluent: 80% DCM, 20% MeOH), resulting in 154 mg of pure product (yield 28%). Mp 124-127 °C, Ret. time 15.08 min, purity 95.0%. HRESIMS *m/z* 428.1569 $[M+H]^+$ (calcd for $C_{21}H_{23}FN_5O_2S^+$, 428.1551, Δ = -4.1 ppm). ^{1}H NMR (500 MHz, d$_6$DMSO) δ = 1.06 (t, 3H, CH_3), 2.03 (s, 3H, pyr-CH_3), 3.13 (quint, 2H, NCH_2), 3.71 (m, 2H, qu-H3), 3.90 (m, 2H, qu-H2), 5.74 (s, 1H, pyr-H), 6.95 (br, 1H, NH), 7.04 (m, 2H, Ph-H3,5), 7.05 (m, 1H, qu-H7), 7.16 (m, 1H, qu-H6), 7.44 (m, 2H, Ph-H2,6), 7.50 (d, 1H, qu-H8), 7.70 (d, 1H, qu-H5); ^{13}C NMR (125 MHz, d$_6$DMSO) δ = 14.71 (CH_3), 23.68 (pyr-CH_3), 34.71 (NCH_2), 44.02 (qu-C3), 47.44 (qu-C2), 96.74 (pyr-C5), 116.10 (d, $^3J(^{13}C,^{19}F)$ = 22.7 Hz, Ph-C3,5), 122.61 (qu-C7), 125.55 (qu-C8), 125.70 (qu-C6), 126.11 (qu-C5), 129.60 (qu-8a), 129.62 (d, $^3J(^{13}C,^{19}F)$ = 9.6 Hz, Ph-C2,6), 134.10 (Ph-C1), 136.64 (qu-C4a), 158.94 (pyr-C2), 162.49 (pyr-C4), 162.52 (d, $^3J(^{13}C,^{19}F)$ = 250.7 Hz, Ph-C4), n.d. (pyr-C6). ^{19}F NMR (400 MHz, d6DMSO) δ = -105.49 (Ph-F).

2-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)-N-isopropyl-6-methylpyrimidin-4-amine (**8a**). Compound **8a** was prepared following general procedure D using **4d** (180 mg, 0.76 mmol), 4-fluorobenzenesulfonyl chloride (143 mg, 0.73 mmol) and TEA (77 mg, 0.45 mmol) in DCM. The crude product was by column chromatography (SiO_2, eluent: 45 % Hexane, 45 % EtOAC and 10 % EtOH), resulting in 94 mg of pure product (yield 33 %). Mp 180.7 °C, Ret. time 15.12 min, purity 96.5%. HRESIMS *m/z* 394.1719 $[M+H]^+$ (calcd for $C_{18}H_{25}FN_5O_2S^+$, 394.1708, Δ = -2.9 ppm). ^{1}H NMR (500 MHz, d$_6$DMSO) δ = 1.07 (d, 3H, ipr-CH_3), 1.99 (s, 3H, pyr-CH_3), 2.88 (m, 4H, pip-H3,5), 3.73 (m, 4H, pip-H2,6), 3.95 (br, 1H, ipr-CH), 5.57 (s, 1H, pyr-H), 6.71 (br, 1H, NH), 7.47 (m, 2H, Ph-H3,5), 7.81 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d$_6$DMSO) δ = 22.49 (ipr-CH_3), 23.74 (pyr-CH_3), 41.24 (ipr-CH), 42.50 (pip-C2,6), 45.83 (pip-C3,5), 94.50 (pyr-C5),

116.75 ($^{3}J(^{13}C,^{19}F)$ = 22.7 Hz, Ph-C3,5), 130.77 ($^{3}J(^{13}C,^{19}F)$ = 9.5 Hz, Ph-C2,6), 131.14 ($^{3}J(^{13}C,^{19}F)$ = 2.9 Hz, Ph-C1), 160.70 (pyr-C2), 162.36 (pyr-C4), 163.30 (pyr-C6), 164.76 ($^{3}J(^{13}C,^{19}F)$ = 250.5 Hz, Ph-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.57 (Ph-F).

N-(tert-butyl)-6-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)-2-methylpyrimidin-4-amine (**8b**). Compound **8b** was prepared following general procedure D using **4e** (110 mg, 0.44 mmol), 4-fluorobenzenesulfonyl chloride (86 mg, 0.44 mmol) and TEA (45 mg, 0.44 mmol) in DCM. The crude product was purified by recrystallization (DIPE/ethyl acetate), resulting in 78 mg of N-(tert-butyl)-6-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)-2-methylpyrimidin-4-amine (yield 41%). Mp 144.7 °C Ret. time 14.36 min, purity 96.8%. HRESIMS *m/z* 408.1877 $[M+H]^+$ (calcd for $C_{19}H_{27}FN_5O_2S^+$, 408.1864, Δ = -3.1 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.32 (s, 9H, tBu-CH_3), 1.99 (s, 3H, pyr-CH_3), 2.92 (s, 4H, pip-H3,5), 3.74 (m, 4H, pip-H2,6), 5.65 (s, 1H, pyr-H), 6.57 (br, 1H, NH), 7.48 (m, 2H, Ph-H3,5), 7.82 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 28.84 (tBu-CH_3), 42.74 (pip-C2,6), 45.67 (pip-C3,5), 50.36 (tBu-C), 95.68 (pyr-C5), 116.70 (d, $^{3}J(^{13}C,^{19}F)$ = 22.7 Hz, Ph-C3,5), 130.72 (d, $^{3}J(^{13}C,^{19}F)$ = 9.4 Hz, Ph-C2,6), 131.13 (d, $^{3}J(^{13}C,^{19}F)$ = 3.2 Hz, Ph-C1), 164.72 (d, $^{3}J(^{13}C,^{19}F)$ = 250.8 Hz, Ph-C4), n.d. (pyr-CH_3), n.d. (pyr-C2), n.d. (pyr-C4), n.d. (pyr-C6); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.56 (Ph-F).

4-ethoxy-2-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)-6-methylpyrimidine **(8c).** Compound **8c** was prepared following general procedure D using **4f** (107 mg, 0.48 mmol), 4-fluorobenzenesulfonyl chloride (91 mg, 0.47 mmol) and TEA (45 mg, 0.44 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 88 mg of pure product (yield 53%). Mp 156.5 °C. Ret. time 25.03 min, purity 98.6%. HRESIMS *m/z* 381.1396 $[M+H]^+$ (calcd for $C_{17}H_{22}FN_4O_3S^+$, 381.1391, Δ = -1.2 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.25 (t, 3H, CH_3), 2.14 (s, 3H, pyr-CH_3), 2.93 (m, 4H, pip-H3,5), 3.80 (m, 4H, pip-H2,6), 4.23 (q, 2H,

OCH_2), 5.93 (s, 1H, pyr-H), 7.48 (m, 2H, Ph-H3,5), 7.82 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.30 (CH_3), 23.66 (pyr-CH_3), 42.50 (pip-C3,5), 45.68 (pip-C2,6), 61.14 (OCH_2), 95.24 (pyr-C5), 116.71 ($^3J(^{13}C,^{19}F)$ = 22.8 Hz, Ph-C3,5), 130.69 ($^3J(^{13}C,^{19}F)$ = 9.9 Hz, Ph-C2,6), 131.12 ($^3J(^{13}C,^{19}F)$ = 2.6 Hz, Ph-C1), 160.43 (pyr-C2), 164.72 ($^3J(^{13}C,^{19}F)$ = 250.4 Hz, Ph-C4), 167.85 (pyr-C6), 169.58 (pyr-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.58 (Ph-F).

2-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)-4-methyl-6-(pyrrolidin-1-yl)pyrimidine **(8d).** Compound **8d** was prepared following general procedure D using **4g** (208 mg, 0.84 mmol), 4-fluorobenzenesulfonyl chloride (164 mg, 0.84 mmol) and TEA (86 mg, 0.85 mmol) in DCM. The crude product was purified by column chromatography (SiO_2, eluent: 80 % DCM, 20 % MeOH), resulting in 251 mg of pure product (yield 74 %). Mp 147 °C. Ret. time 15.21 min, purity 96.4%. HRESIMS *m/z* 406.1718 $[M+H]^+$ (calcd for $C_{19}H_{25}FN_5O_2S^+$, 406.1708, Δ = -2.6 ppm). ^1H NMR (500 MHz, d_6DMSO) δ = 1.85 (br, 4H, pyrrolidine-H3,4), 2.06 (s, 3H, pyr-CH_3), 3.30 (br, 4H, pyrrolidine-H2,5), 2.88 (m, 4H, pip-H3,5), 3.76 (m, 4H, pip-H2,6), 5.65 (s, 1H, pyr-H), 7.47 (m, 2H, Ph-H3,5), 7.81 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 23.90 (pyr-CH_3), 24.78 (pyrrolidine-C3,4), 42.58 (pip-C2,6), 45.77 (pip-C3,5), 45.83 (pyrrolidine-C2,5), 92.83 (pyr-C5), 116.76 ($^3J(^{13}C,^{19}F)$ = 22.7 Hz, Ph-C3,5), 130.77 ($^3J(^{13}C,^{19}F)$ = 9.4 Hz, Ph-C2,6), 131.13 ($^3J(^{13}C,^{19}F)$ = 2.7 Hz, Ph-C1), 160.28 (pyr-C2), 160.62 (pyr-C6), 164.43 (pyr-C4), 164.76 ($^3J(^{13}C,^{19}F)$ = 250.6 Hz, Ph-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.56 (Ph-F).

N-ethyl-4-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)-6-methylpyrimidin-2-amine **(9a).** Compound **9a** was prepared following general procedure D using **4h** (109 mg, 0.49 mmol), 4-fluorobenzenesulfonyl chloride (96 mg, 0.49 mmol) and TEA (50 mg, 0.49 mmol) in DCM. The crude product was purified by column chromatography (SiO_2, eluent: 87.5 % DCM, 12.5 % MeOH), resulting in 165 mg of pure product (yield 89%). Mp 158.1-159.9 °C. Ret. time 14.20

min, purity 98.5%. HRESIMS *m/z* 380.1560 $[M+H]^+$ (calcd for $C_{17}H_{23}FN_5O_2S^+$, 380.1551, Δ = -2.5 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.03 (t, 3H, CH_3), 2.04 (s, 3H, pyr-CH_3), 2.90 (m, 4H, pip-H3,5), 3.17 (m, 2H, NCH_2), 3.62 (m, 4H, pip-H2,6), 5.85 (s, 1H, pyr-H), 6.45 (br, 1H, NH), 7.48 (m, 2H, Ph-H3,5), 7.82 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.94 (CH_3), 23.89 (pyr-CH_3), 35.18 (NCH_2), 42.59 (pip-C2,6), 45.51 (pip-C3,5), 90.99 (pyr-C5), 116.74 (^3J(^{13}C,^{19}F) = 22.5 Hz, Ph-C3,5), 130.69 (^3J(^{13}C,^{19}F) = 9.6 Hz, Ph-C2,6), 131.06 (^3J(^{13}C,^{19}F) = 2.4 Hz, Ph-C1), 161.62 (pyr-C2), 162.40 (pyr-C4), 164.74 (d, ^3J(^{13}C,^{19}F) = 250.5 Hz, Ph-C4), 165.91 (pyr-C6);^{19}F NMR (400 MHz, d6DMSO) δ = -105.45 (Ph-F).

N-ethyl-6-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)-2-methylpyrimidin-4-amine **(9b).** Compound **9b** was prepared following general procedure D using **4i** (86 mg, 0.39 mmol), 4-fluorobenzenesulfonyl chloride (76 mg, 0.39 mmol) and TEA (39 mg, 0.39 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 72 mg of pure product (yield 49%). Mp 166.1-168.6 °C. Ret. time 13.97 min, purity 97.1%. HRESIMS *m/z* 380.1561 $[M+H]^+$ (calcd for $C_{17}H_{23}FN_5O_2S^+$, 380.1551, Δ = -2.7 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.04 (t, 3H, CH_3), 2.13 (s, 3H, pyr-CH_3), 2.91 (m, 4H, pip-H3,5), 3.13 (m, 2H, NCH_2), 3.55 (m, 4H, pip-H2,6), 5.37 (s, 1H, pyr-H), 6.57 (t, 1H, NH), 7.48 (t, 2H, Ph-H3,5), 7.82 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.65 (CH_3), 25.88 (pyr-CH_3), 35.13 (NCH_2), 42.93 (pip-C2,6), 45.60 (pip-C3,5), 116.80 (^3J(^{13}C,^{19}F) = 22.3 Hz, Ph-C3,5), 130.77 (^3J(^{13}C,^{19}F) = 9.5 Hz, Ph-C2,6), 131.11 (^3J(^{13}C,^{19}F) = 2.2 Hz, Ph-C1), 162.04 (pyr-C6), 163.55 (pyr-C4), 164.80 (^3J(^{13}C,^{19}F) = 250.5 Hz, Ph-C4), 165.44 (pyr-C2), n.d. (pyr-C5); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.45 (Ph-F).

N-ethyl-2-(4-(4-fluorophenylsulfonyl)piperazin-1-yl)pyrimidin-4-amine **(9c).** Compound **9c** was prepared following general procedure D using **4j** (117 mg, 0.56 mmol), 4-

fluorobenzenesulfonyl chloride (94 mg, 0.48 mmol) and TEA (57 mg, 0.56 mmol) in DCM. The crude product was purified by recrystallization (DIPE/EtOAc), resulting in 89 mg of pure product (yield 51%). Mp 123.0-124.5 °C. Ret. time 13.75 min, purity 97.1%. HRESIMS *m/z* 366.1404 $[M+H]^+$ (calcd for $C_{16}H_{21}FN_5O_2S^+$, 366.1395, Δ = -2.6 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, CH_3), 2.89 (m, 4H, pip-H3,5), 3.20 (br, 2H, NCH_2), 3.74 (m, 4H, pip-H2,6), 5.72 (d, 1H, pyr-H), 7.02 (br, 1H, NH), 7.48 (m, 2H, Ph-H3,5), 7.65 (br, 1H, pyr-H6), 7.82 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.47 (CH_3), 34.31 (NCH_2), 42.44 (pip-C2,6), 45.71 (pip-C3,5), 96.36 (pyr-C5), 116.69 ($^3J(^{13}C,^{19}F)$ = 22.3 Hz, Ph-C3,5), 130.68 ($^3J(^{13}C,^{19}F)$ = 9.4 Hz, Ph-C2,6), 131.11 ($^3J(^{13}C,^{19}F)$ = 2.2 Hz, Ph-C1), 154.44 (pyr-C6), 160.72 (pyr-C2), 162.23 (pyr-C4), 164.69 ($^3J(^{13}C,^{19}F)$ = 250.5 Hz, Ph-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.57 (Ph-F).

N-ethyl-4-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)pyrimidin-2-amine **(9d).** Compound **9d** was prepared following general procedure D using **4k** (95 mg, 0.46 mmol), 4-fluorobenzenesulfonyl chloride (90 mg, 0.46 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by column chromatography (SiO_2, eluent: 80% DCM, 20% MeOH), resulting in 140 mg of pure product (yield 83%). Mp 188-189 °C. Ret. time 13.65 min, purity 95.3%. HRESIMS *m/z* 366.1404 $[M+H]^+$ (calcd for $C_{16}H_{21}FN_5O_2S^+$, 366.1395, Δ = -2.6 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.03 (t, 3H, CH_3), 2.91 (m, 4H, pip-H3,5), 3.18 (m, 2H, NCH_2), 3.62 (m, 4H, pip-H2,6), 5.95 (d, 1H, pyr-H), 6.50 (br, 1H, NH), 7.48 (t, 2H, Ph-H3,5), 7.76 (d, 1H, pyr-H6), 7.82 (m, 2H, Ph-H2,6); ^{13}C NMR (125 MHz, d_6DMSO) δ = 14.96 (CH_3), 35.27 (NCH_2), 42.52 (pip-C2,6), 45.59 (pip-C3,5), 92.57 (pyr-C5), 116.81 ($^3J(^{13}C,^{19}F)$ = 22.6 Hz, Ph-C3,5), 130.77 ($^3J(^{13}C,^{19}F)$ = 9.5 Hz, Ph-C2,6), 131.09 ($^3J(^{13}C,^{19}F)$ = 3.0 Hz, Ph-C1), 157.04 (pyr-C6), 161.73 (pyr-C2), 161.78 (pyr-C4), 164.82 (d, $^3J(^{13}C,^{19}F)$ = 250.8 Hz, Ph-C4); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.43 (Ph-F).

N-cyclopropyl-2-(4-((4-fluorophenyl)sulfonyl)piperazin-1-yl)pyrimidin-4-amine **(10).** Compound **10** was prepared following general procedure D using **4l** (148 mg, 0.67 mmol), 4-fluorobenzenesulfonyl chloride (131 mg, 0.67 mmol) and TEA (68 mg, 0.64 mmol) in DCM. The crude product was purified by recrystallization (DIPE / ethyl acetate), resulting in 81 mg of pure product (yield 32%). Mp 174.4 °C. Ret. time 14.11 min, purity 97.5%. HRESIMS *m/z* 378.1403 $[M+H]^+$ (calcd for $C_{17}H_{21}FN_5O_2S^+$, 378.1395, Δ = -2.3 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 0.41 (m, 2H, CH_2), 0.68 (m, 2H, CH_2), 2.92 (m, 4H, pip-H3,5), 3.76 (m, 4H, pip-H2,6), 5.94 (br, 1H, pyr-H), 5.94 (br, 1H, NH), 7.48 (t, 2H, Ph-H3,5), 7.74 (m, 1H, pyr-H6), 7.82 (m, 2H, Ph-H2,6), n.d. (NCH); ^{13}C NMR (125 MHz, d_6DMSO) δ = 6.78 (CH_2), 42.75 (pip-C2,6), 45.60 (pip-C3,5), 116.79 (^3J(^{13}C,^{19}F) = 22.6 Hz, Ph-C3,5), 130.77 (^3J(^{13}C,^{19}F) = 9.5 Hz, Ph-C2,6), 131.16 (^3J(^{13}C,^{19}F) = 3.0 Hz, Ph-C1), n.d. (pyr-C2), n.d. (pyr-C4), n.d. (pyr-C5), n.d. (pyr-C6), n.d. (Ph-C4), n.d. (NCH); ^{19}F NMR (400 MHz, d6DMSO) δ = -105.51 (Ph-F).

(3-chlorophenyl)(4-(2-(ethylamino)-6-methylpyrimidin-4-yl)piperazin-1-yl)methanone **(11a).** Compound **11a** was prepared following general procedure D using **4h** (169 mg, 0.76 mmol), 4-chlorobenzoyl chloride (134 mg, 0.76 mmol) and TEA (77 mg, 0.76 mmol) in DCM. The crude product was purified by column chromatography (dichloromethane/20% methanol), resulting in 178 mg of pure product (yield 65%). Mp 181 °C. Ret. Time 13.74 min, purity 99.9 %. HRESIMS *m/z* 360.1593 $[M+H]^+$ (calcd for $C_{18}H_{23}ClN_5O^+$, 360.1586, Δ = -2.0 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, NCH_3), 2.08 (s, 3H, pyr-CH_3), 3.22 (br, 2H, NCH_2), 3.37/3.54 (br, 4H, pip-H2,6), 3.64 (br, 4H, pip-H3,5), 5.91 (s, 1H, pyr-H5), 6.48 (br, 1H, NH), 7.47 (m, 2H, ph-2,6), 7.53 (m, 2H, ph-H3,5); ^{13}C NMR (500 MHz, d_6DMSO) δ = 14.99 (CH_3), 23.86 (pyr-CH_3), 35.22 (NCH_2), 43.20 (pip- C3,5), 43.20 (pip-C2,6), 91.20 (pyr-C5), 128.55 (ph-C3,5), 129.09 (ph-C2,6),

134.30 (ph-C4), 134.56 (ph-C1), 161.48 (pyr-C2), 162.72 (pyr-C4), 165.54 (pyr-C6), 168.12 (amide-C).

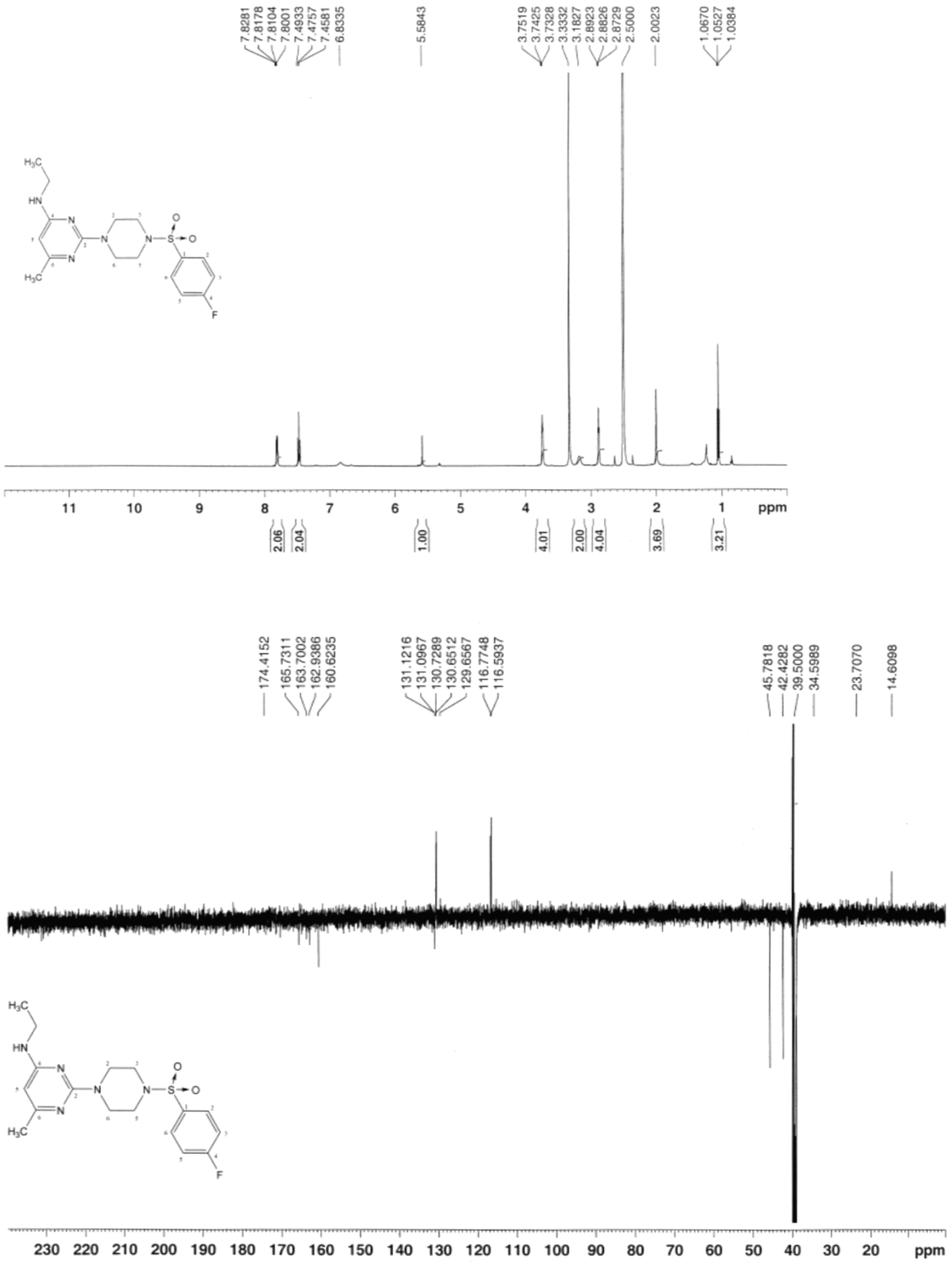
***(4-chlorophenyl)(4-(2-(ethylamino)pyrimidin-4-yl)piperazin-1-yl)methanone* (11b).** Compound **11b** was prepared following general procedure D using **4k** (95 mg, 0.46 mmol), 4-chlorobenzoyl chloride (85 mg, 0.46 mmol) and TEA (46 mg, 0.45 mmol) in DCM. The crude product was purified by column chromatography (dichloromethane/20% methanol), resulting in 53 mg of pure product (yield 34%). Mp 180 °C. Ret. Time 13.13 min, purity 96.2%. HRESIMS *m/z* 346.1435 $[M+H]^+$ (calcd for $C_{17}H_{21}ClN_5O^+$, 346.1429, Δ = -1.7 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.06 (t, 3H, NCH_3), 3.21 (quint, 2H, NCH_2), 3.37/3.54 (br, 4H, pip-H2,6), 3.64/3.65 (br, 4H, pip-H3,5), 6.01 (s, 1H, pyr-H5), 6.52 (br, 1H, NH), 7.47 (m, 2H, ph-2,6), 7.53 (m, 2H, ph-H3,5), 7.81 (d, 1H, pyr-H6); ^{13}C NMR (500 MHz, d_6DMSO) δ = 15.01 (NCH_3), 35.31 (NCH_2), 41.48/43.13 (pip- C3,5), 43.13/46.87 (pip-C2,6), 92.84 (pyr-C5), 128.63 (ph-C3,5), 129.16 (ph-C2,6), 134.39 (ph-C4), 134.58 (ph-C1), 156.86 (pyr-C6), 161.74 (pyr-C2), 162.11 (pyr-C4), 168.26 (amide-C).

***(4-fluorophenyl)(4-(2-(isopropylamino)-6-methylpyrimidin-4-yl)piperazin-1-yl)methanone* (11c).** Compound **11c** was prepared following general procedure D using **4m** (176 mg, 0.75 mmol), 4-chlorobenzoyl chloride (119 mg, 0.68 mmol) and TEA (76 mg, 0.75 mmol) in DCM. The crude product was purified by column chromatography (dichloromethane/20% methanol), resulting in 140 mg of pure product (yield 52%). Mp 74-75 °C. Ret. Time 13.37 min, purity 98.4%. HRESIMS *m/z* 358.2044 $[M+H]^+$ (calcd for $C_{19}H_{25}FN_5O^+$, 358.2038, Δ = -1.7 ppm). ^{1}H NMR (500 MHz, d_6DMSO) δ = 1.08 (d, 6H, iPr-CH_3), 2.08 (s, 3H, pyr-CH_3), 3.61 (br, 4H, pip-H2,6), 3.61 (br, 4H, pip-H3,5), 3.98 (m, 1H, iPr-CH), 5.90 (s, 1H, pyr-H5), 6.31 (br, 1H, NH), 7.29 (m, 2H, ph-3,5), 7.51 (m, 2H, ph-H2,6); ^{13}C NMR (500 MHz, d_6DMSO) δ = 22.68 (iPr-CH_3), 41.72

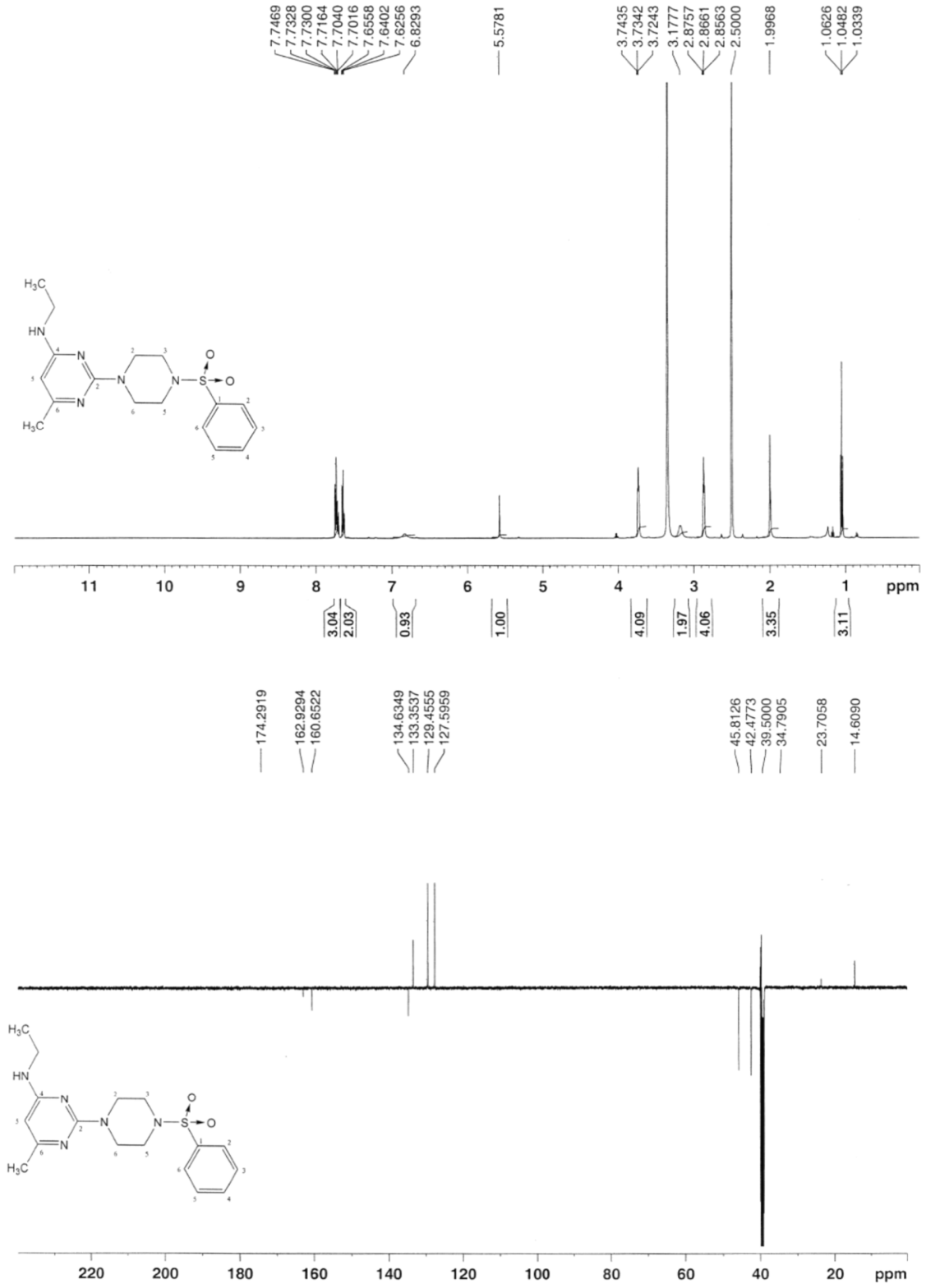
(iPr-CH), 115.50 (^{3}J(^{13}C,^{19}F) = 21.6 Hz, Ph-C3,5), 129.76 (^{3}J(^{13}C,^{19}F) = 8.3 Hz, Ph-C2,6), 132.20 (^{3}J(^{13}C,^{19}F) = 3.0 Hz, Ph-C1), 161.01 (pyr-C2), 162.67 (d, ^{3}J(^{13}C,^{19}F) = 245.1 Hz, Ph-C4), 162.81 (pyr-C4), 165.62 (pyr-C6), 168.42 (amide-C), n.d. (pyr-CH_3), n.d. (pip- C3,5), n.d. (pip-C2,6), n.d. (pyr-C5); ^{19}F NMR (400 MHz, d6DMSO) δ = -111.00 (Ph-F).

Copies of 1H- and 13C-NMR Spectra

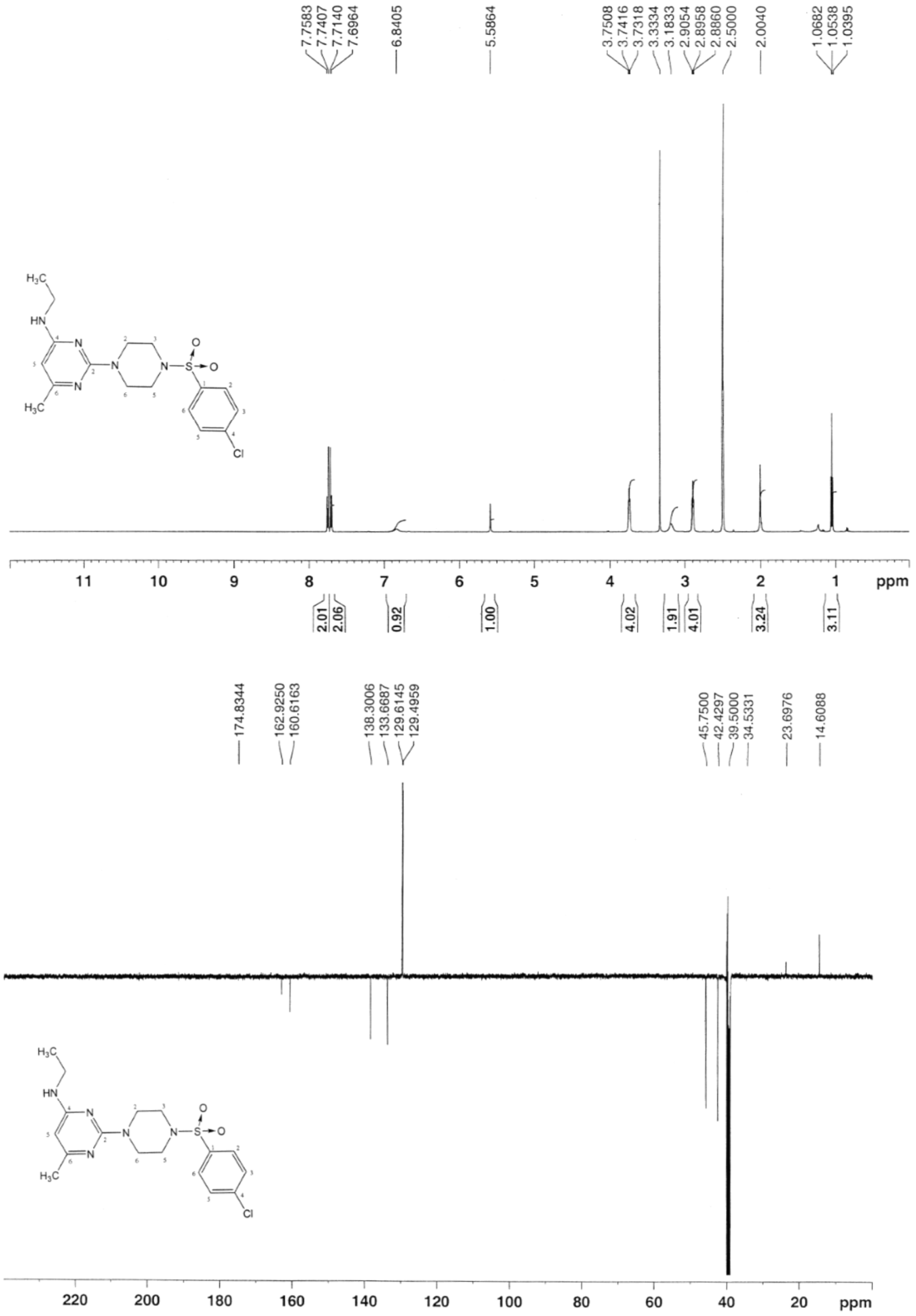
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 1



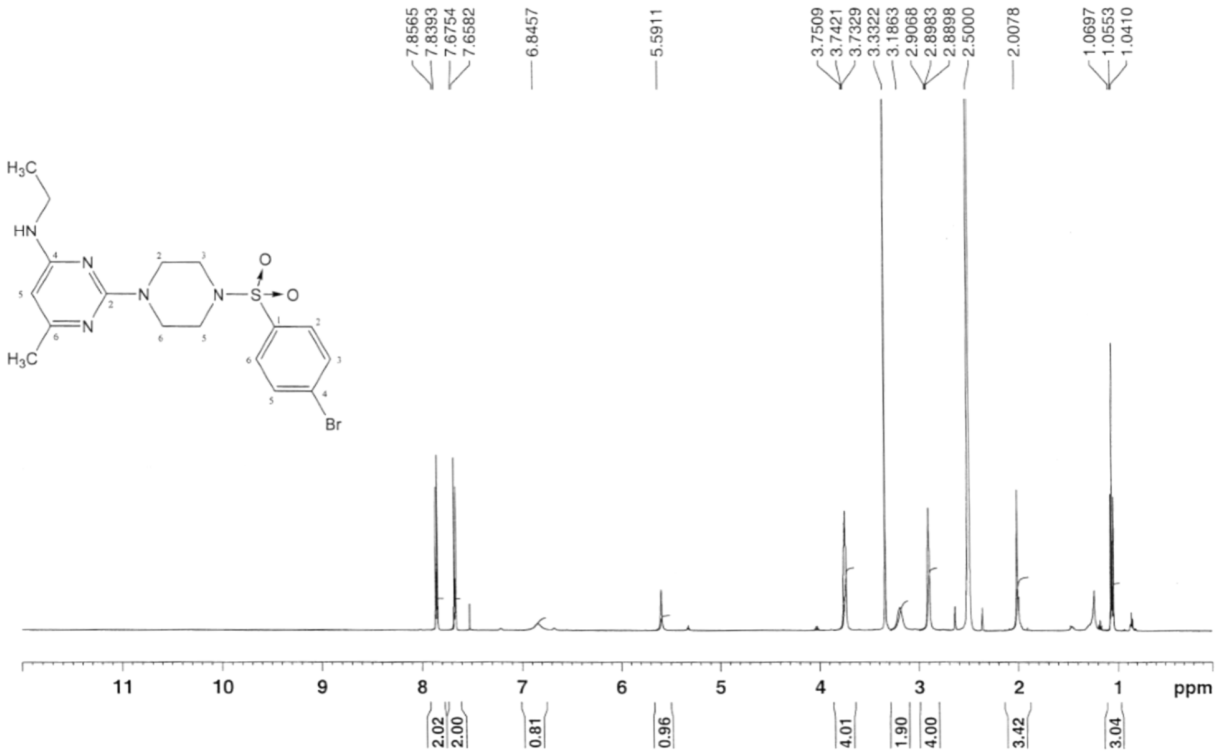
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5a

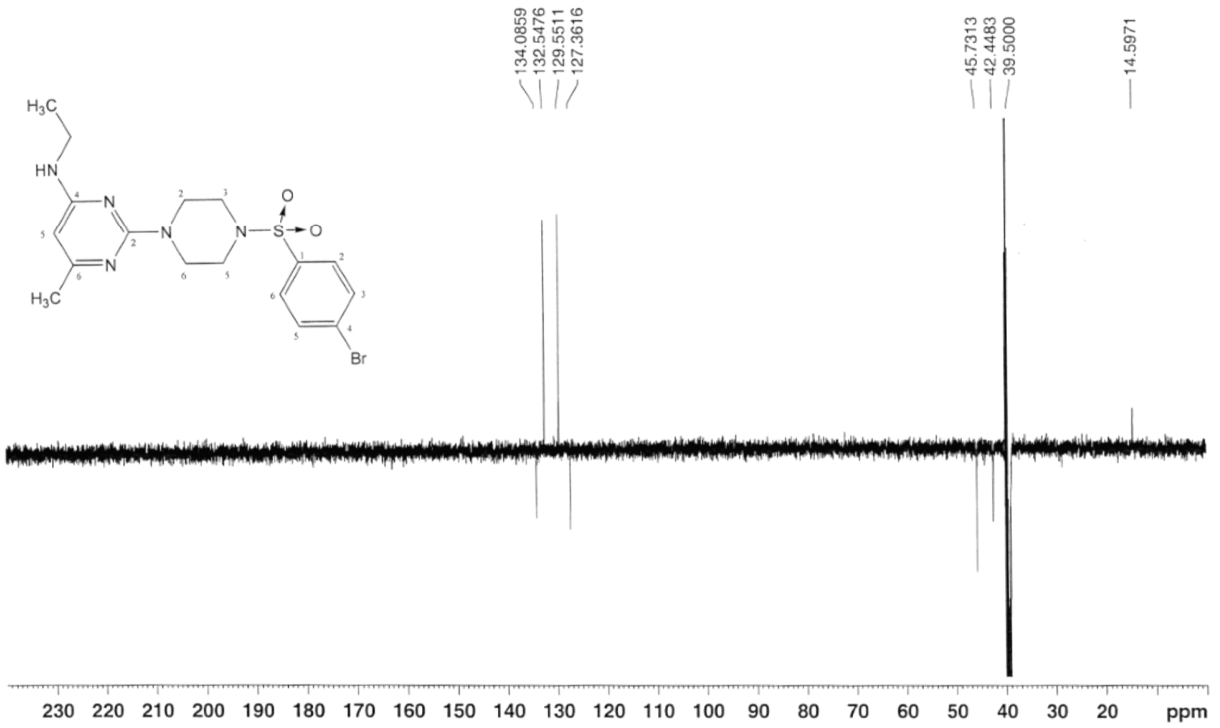


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5b

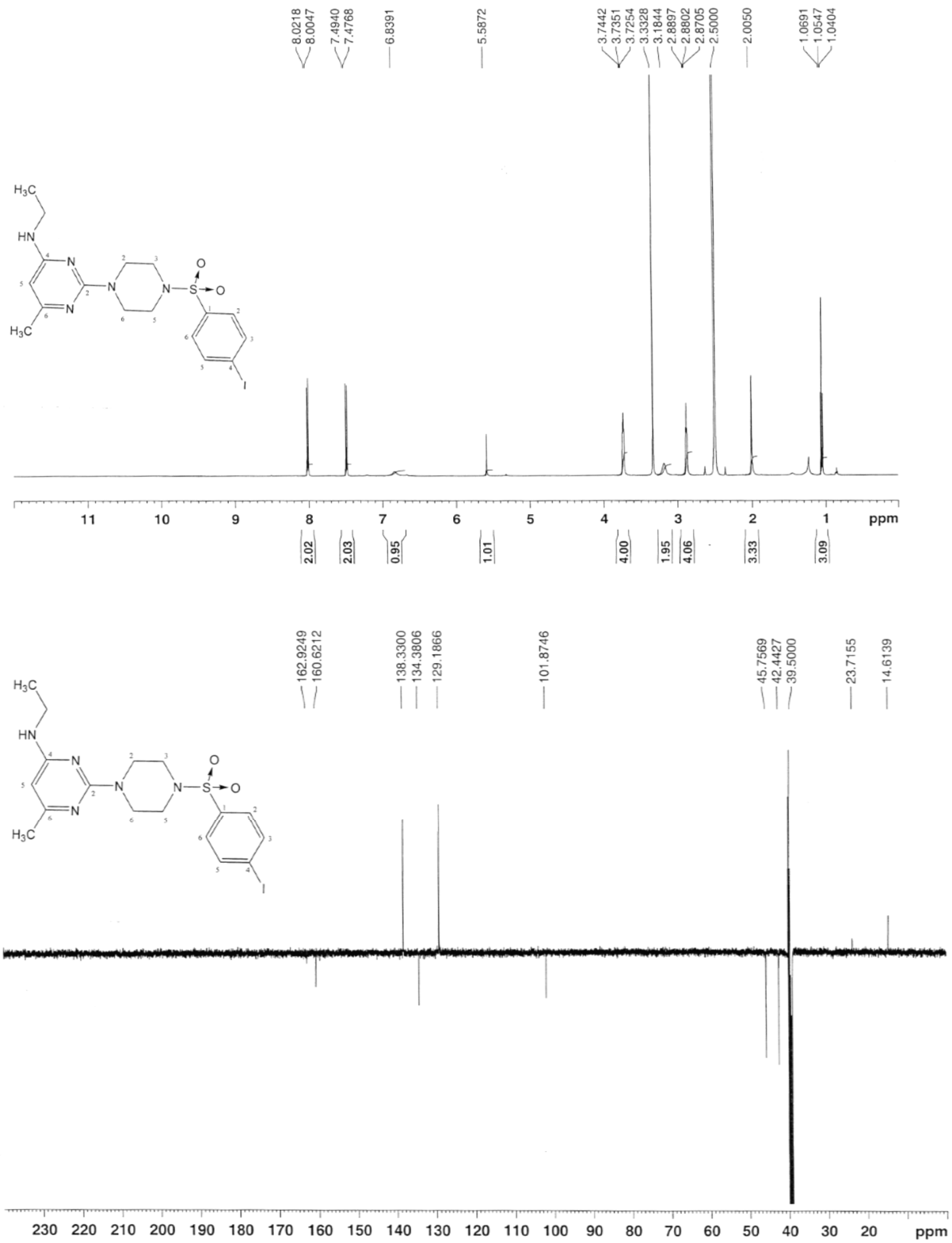


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5c

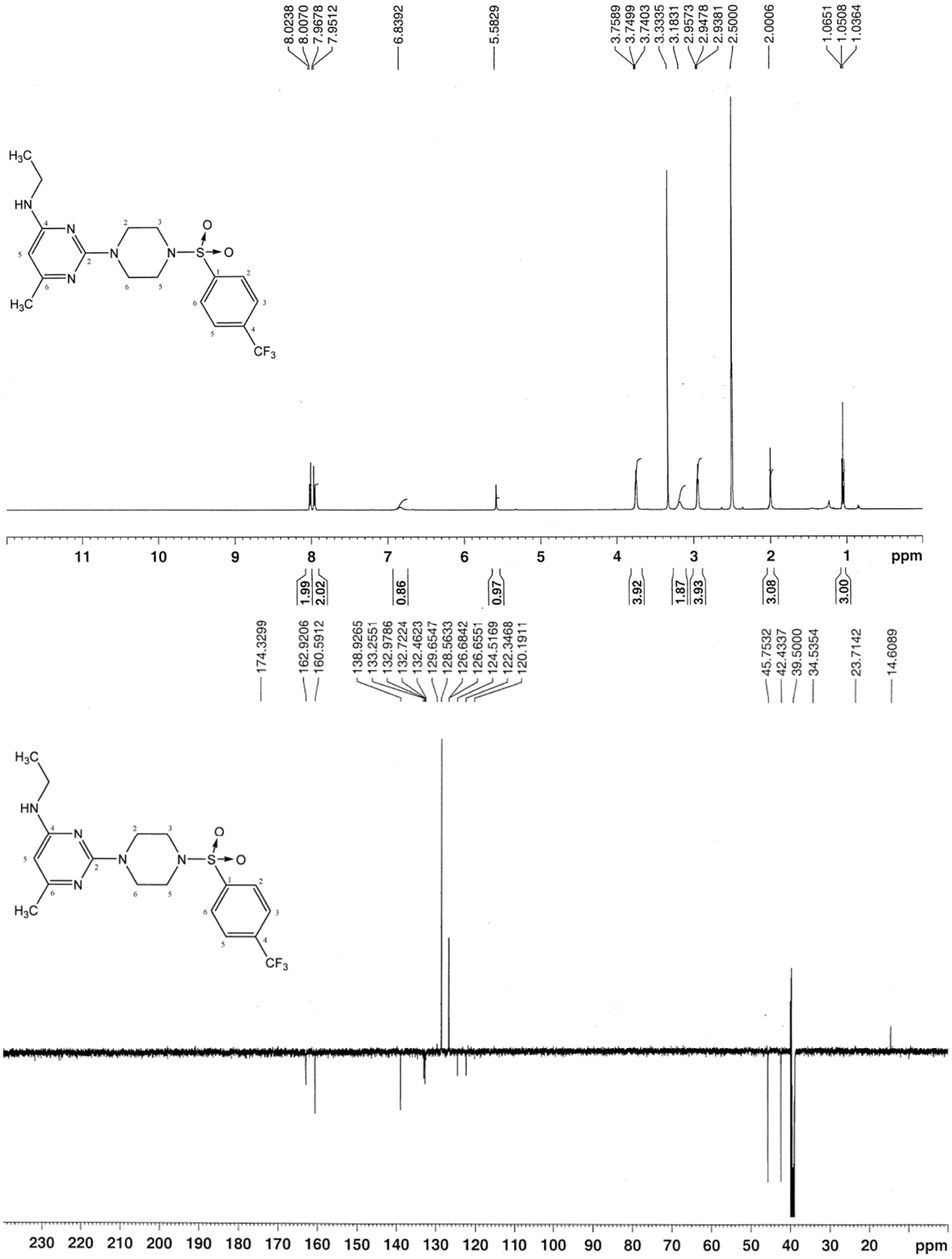




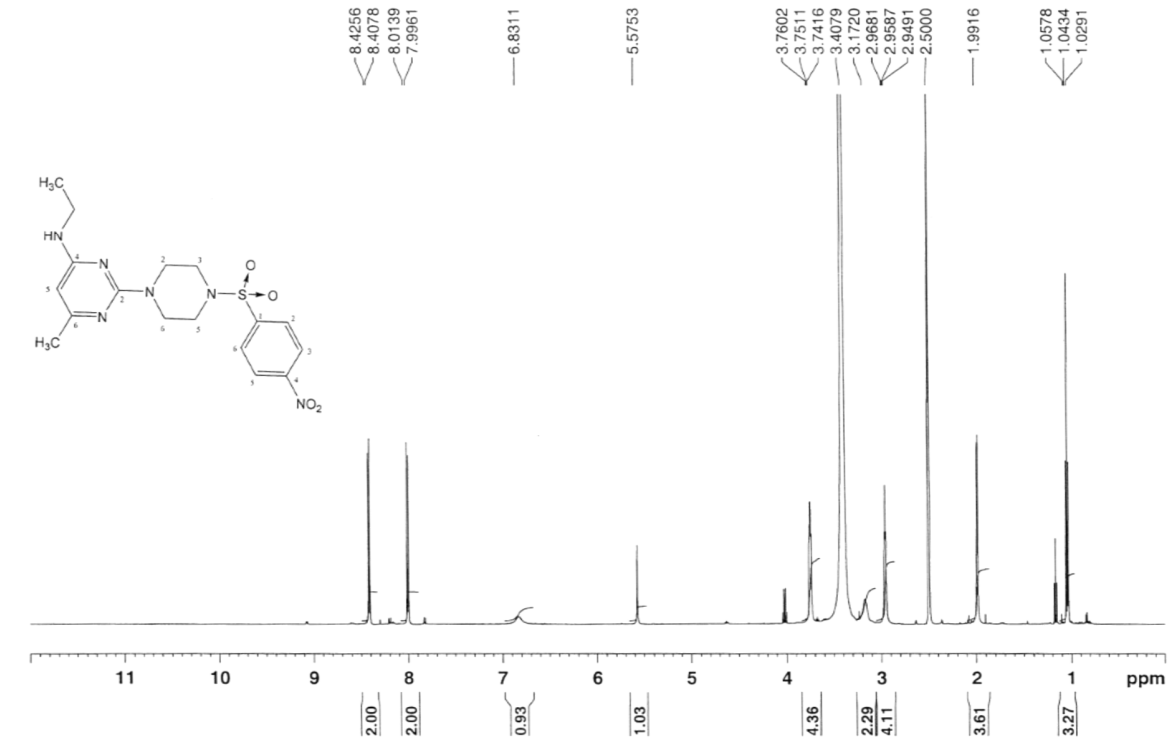
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5d

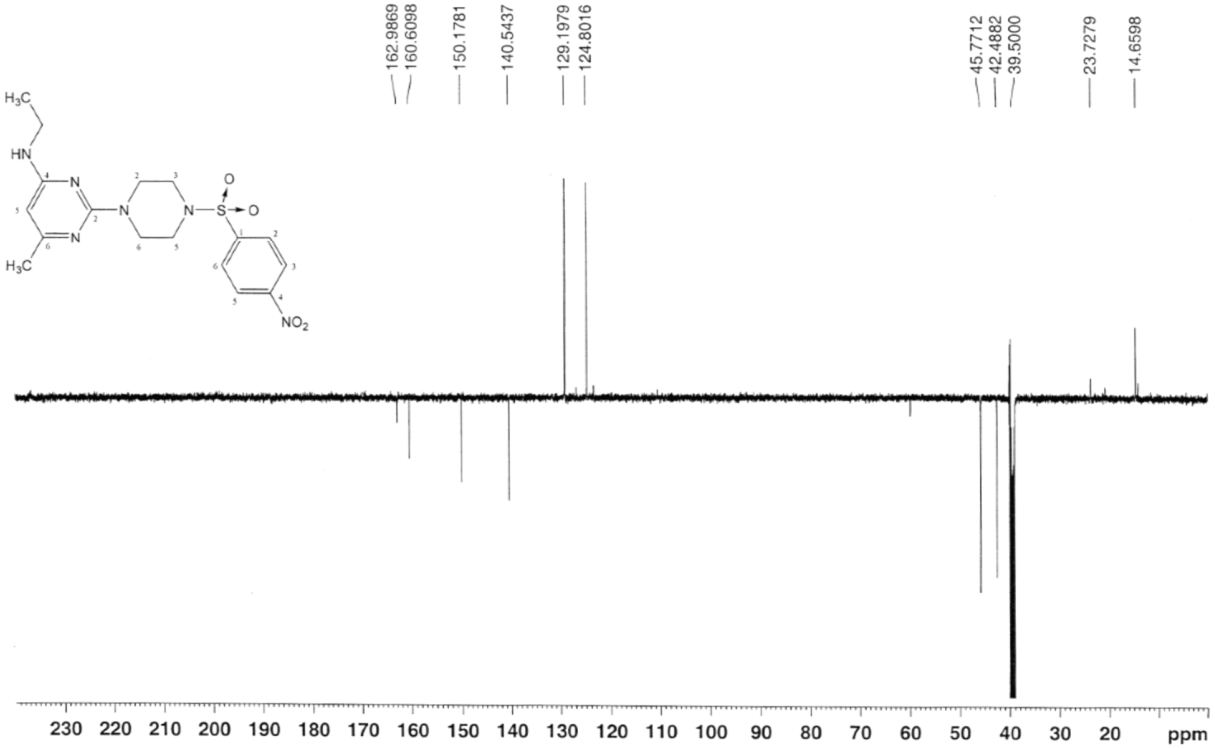


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5e

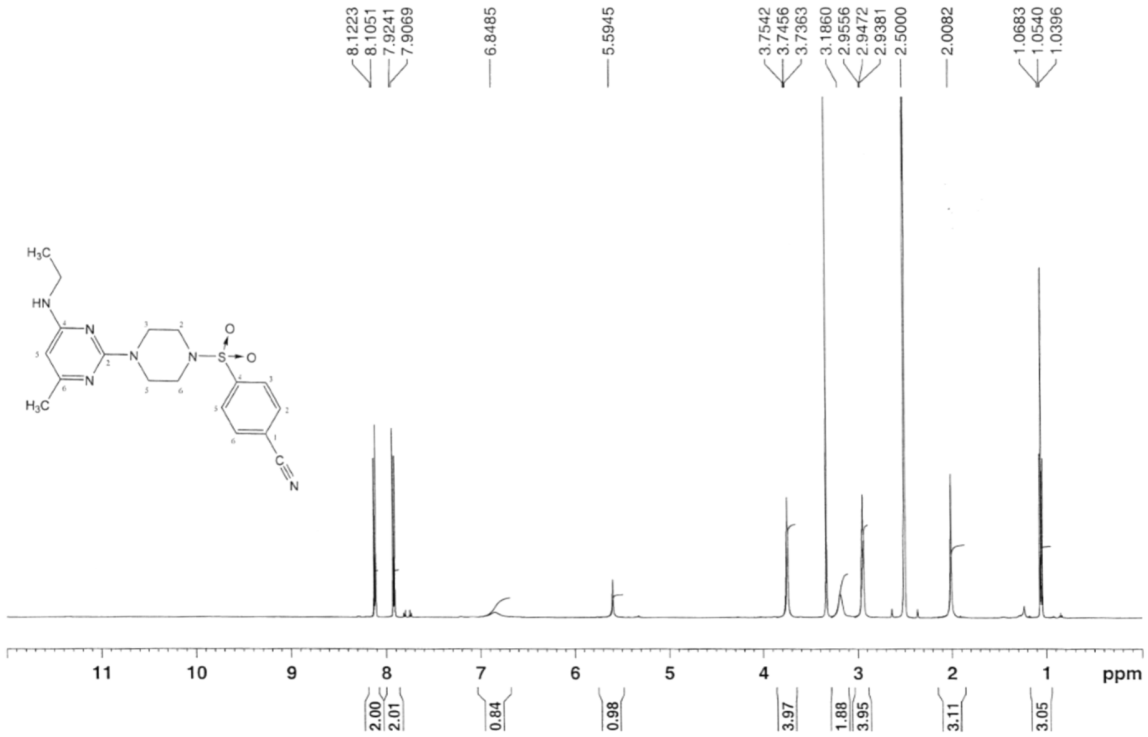


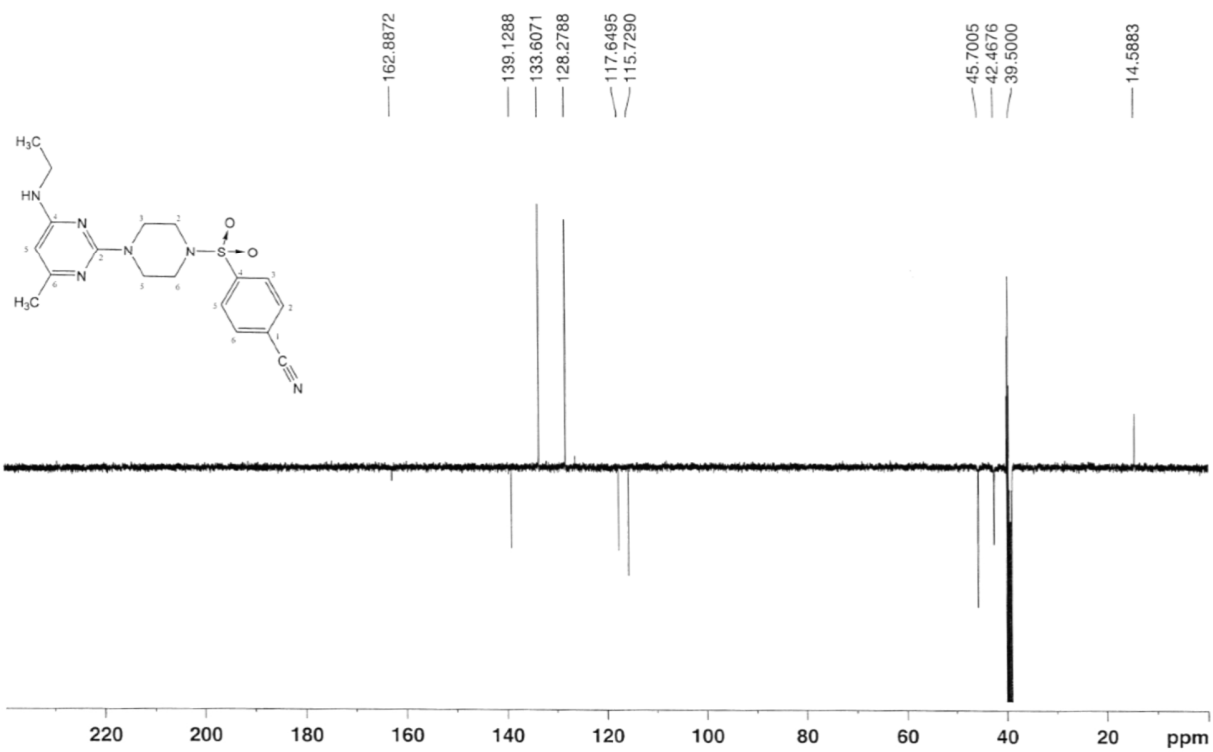
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5f



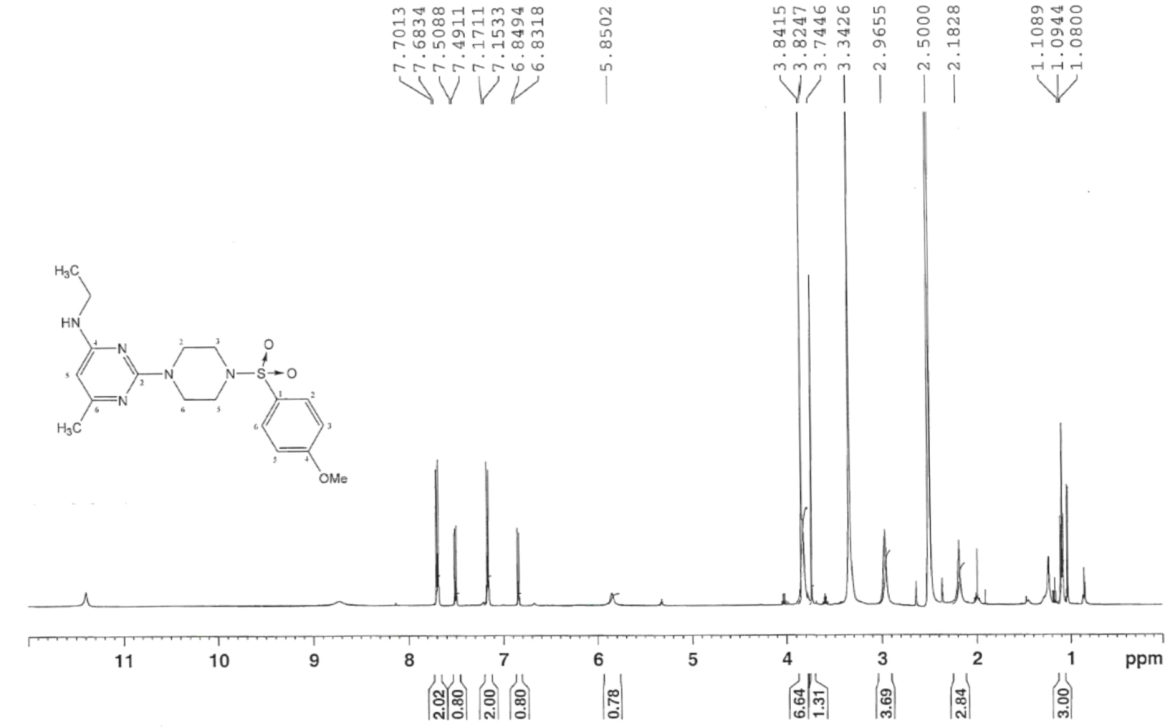


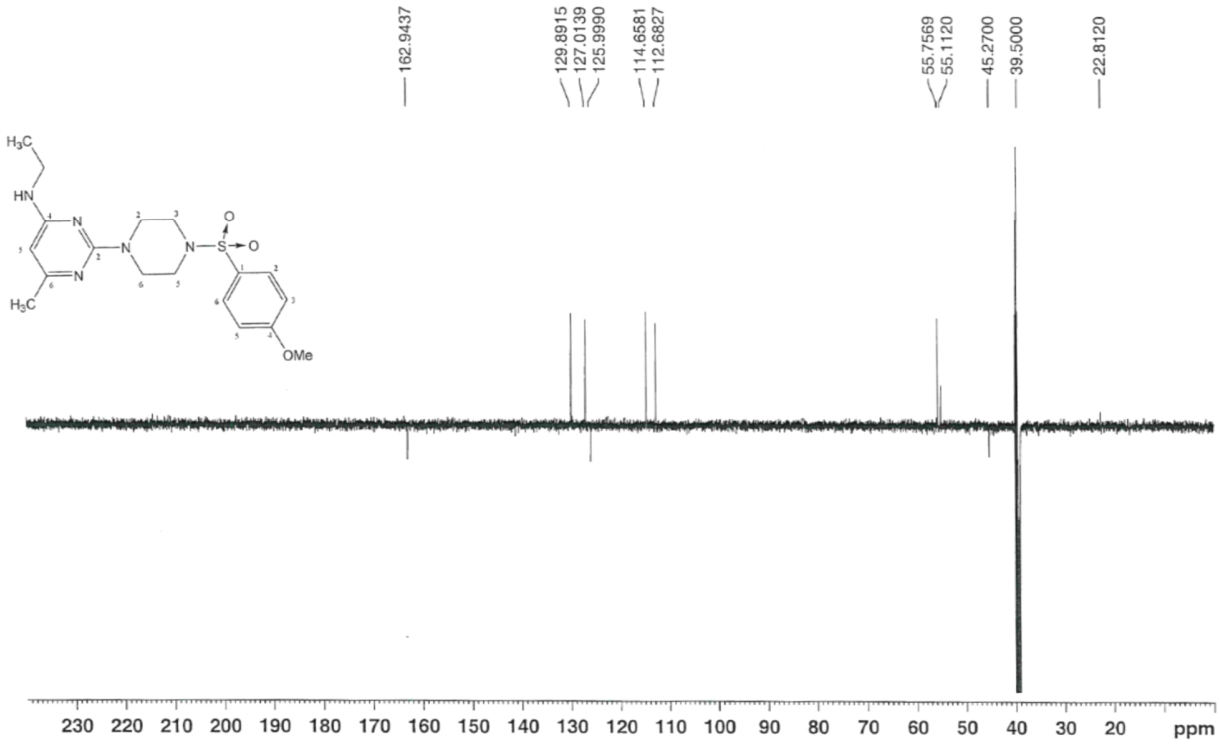
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5g



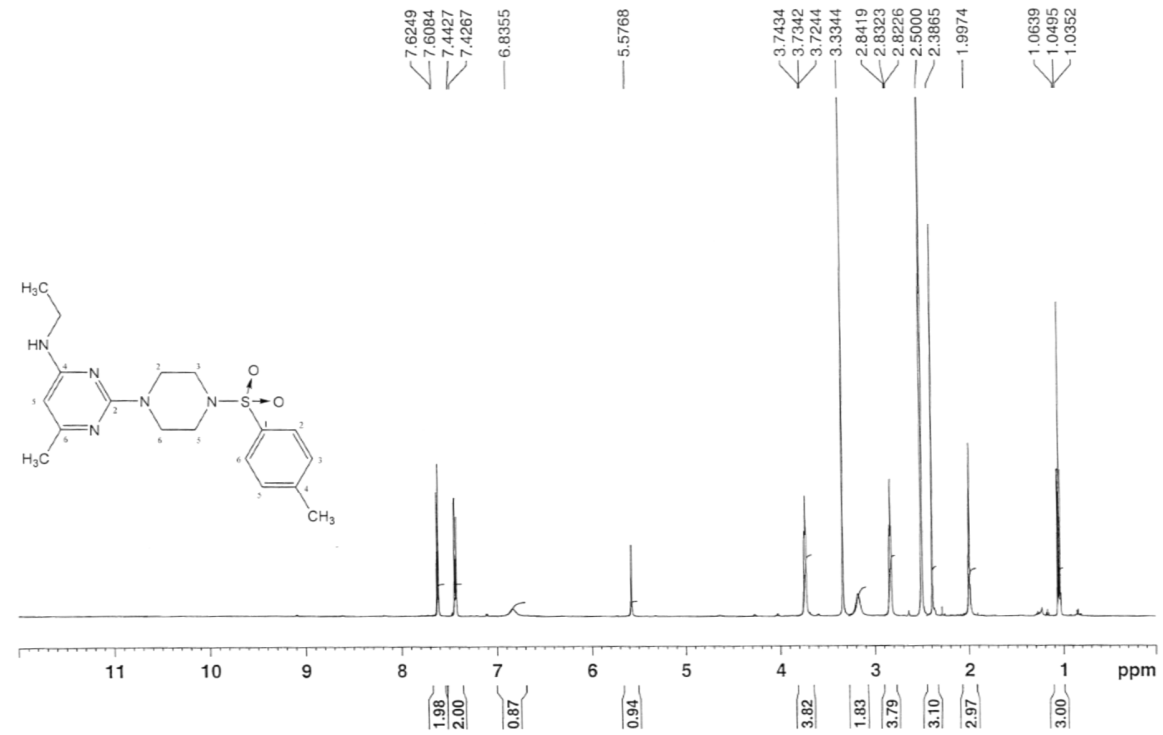


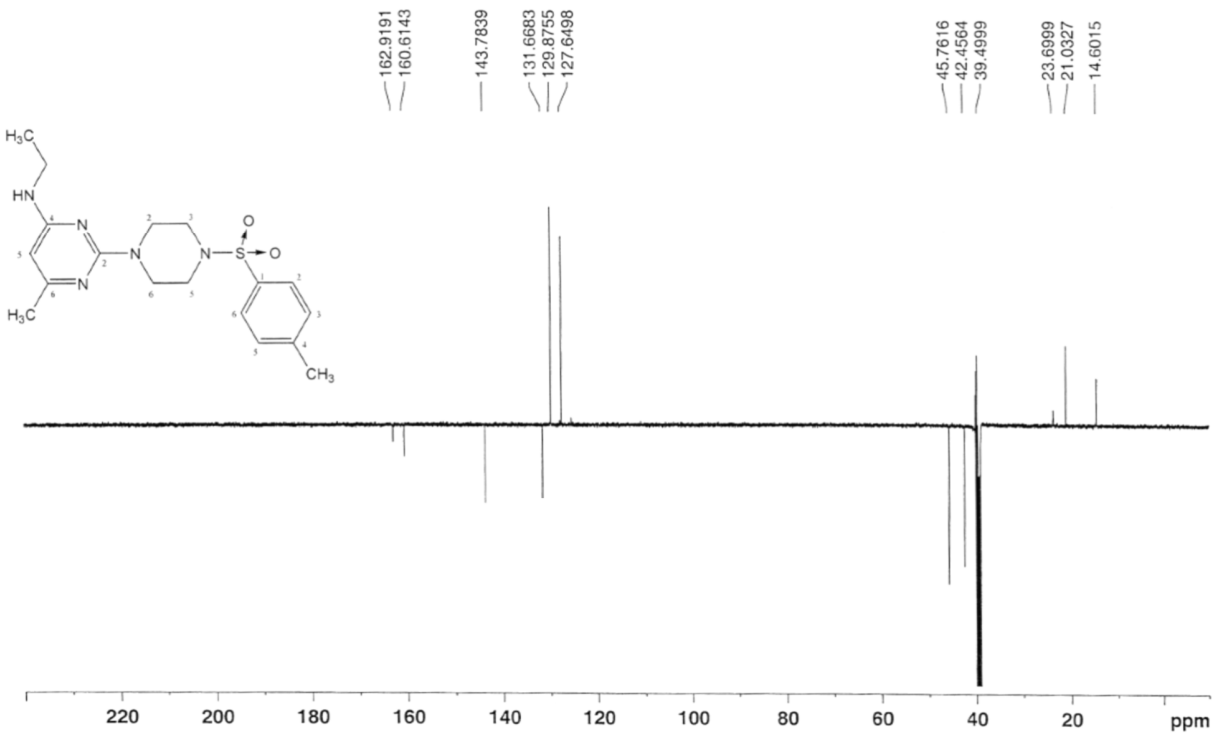
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5h



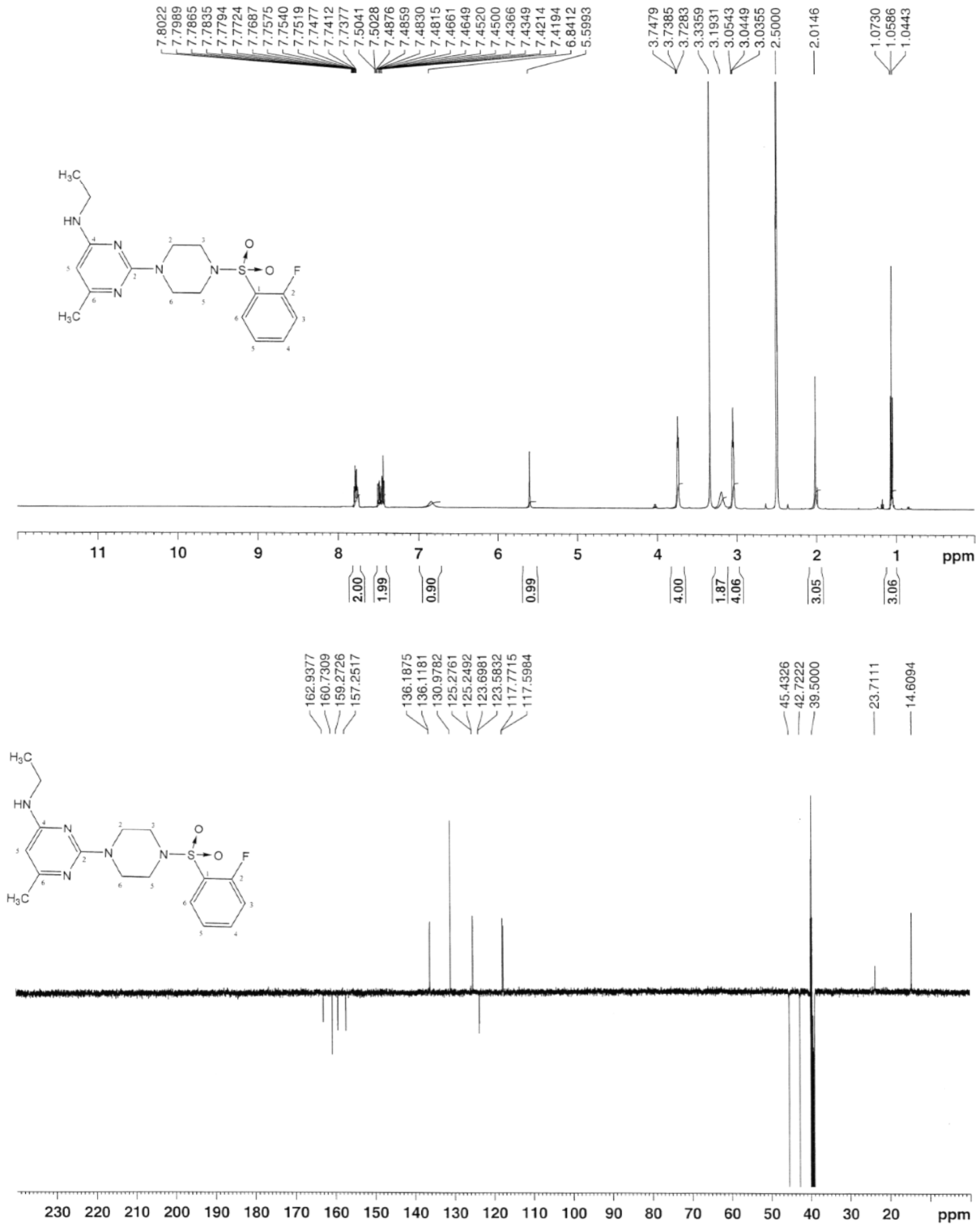


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5i

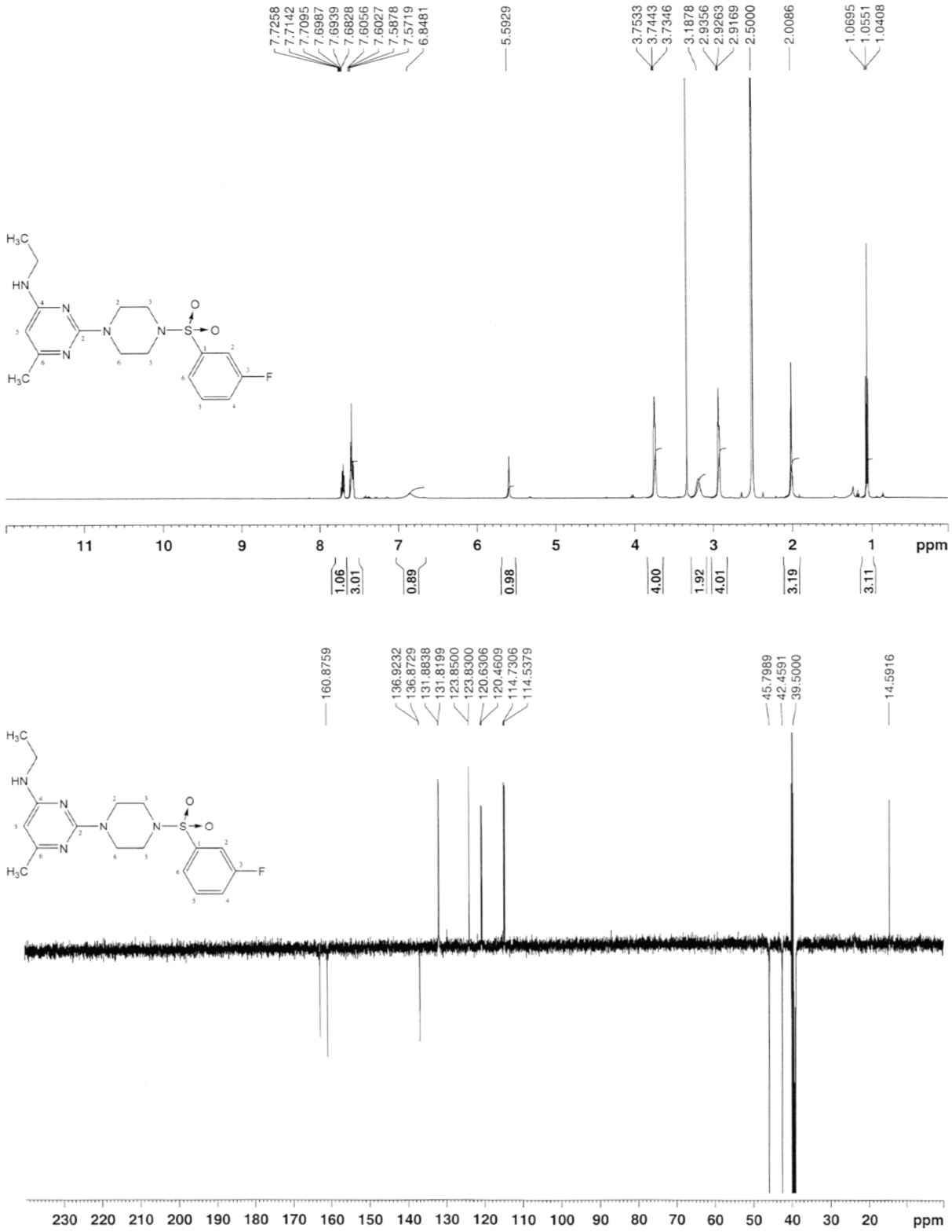




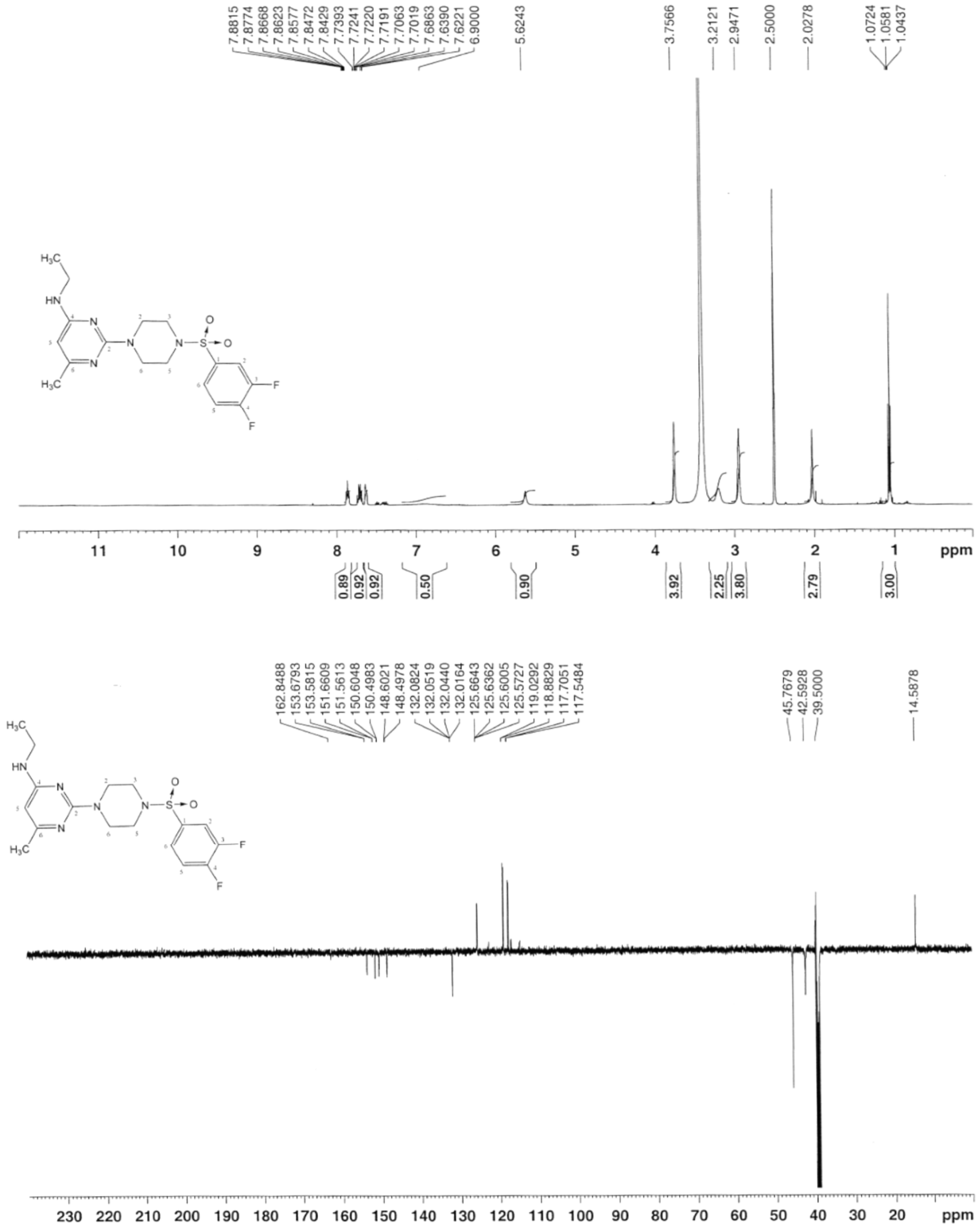
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5j



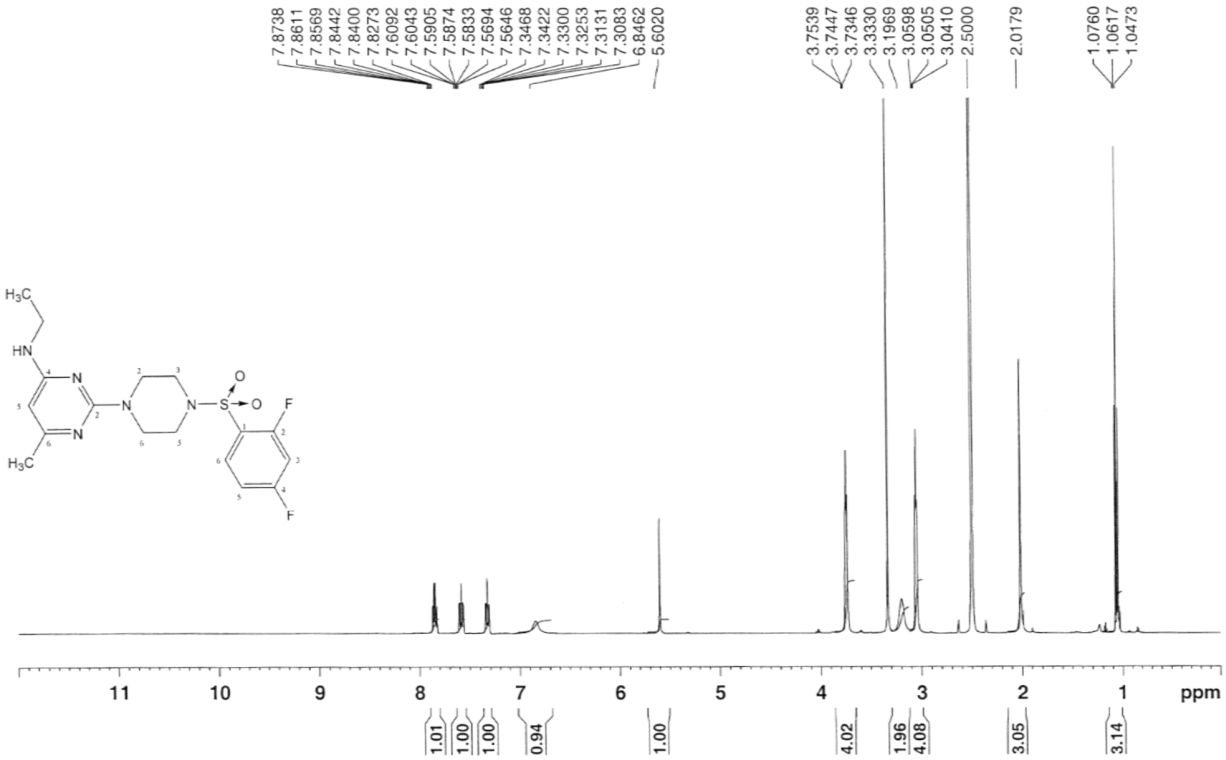
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5k

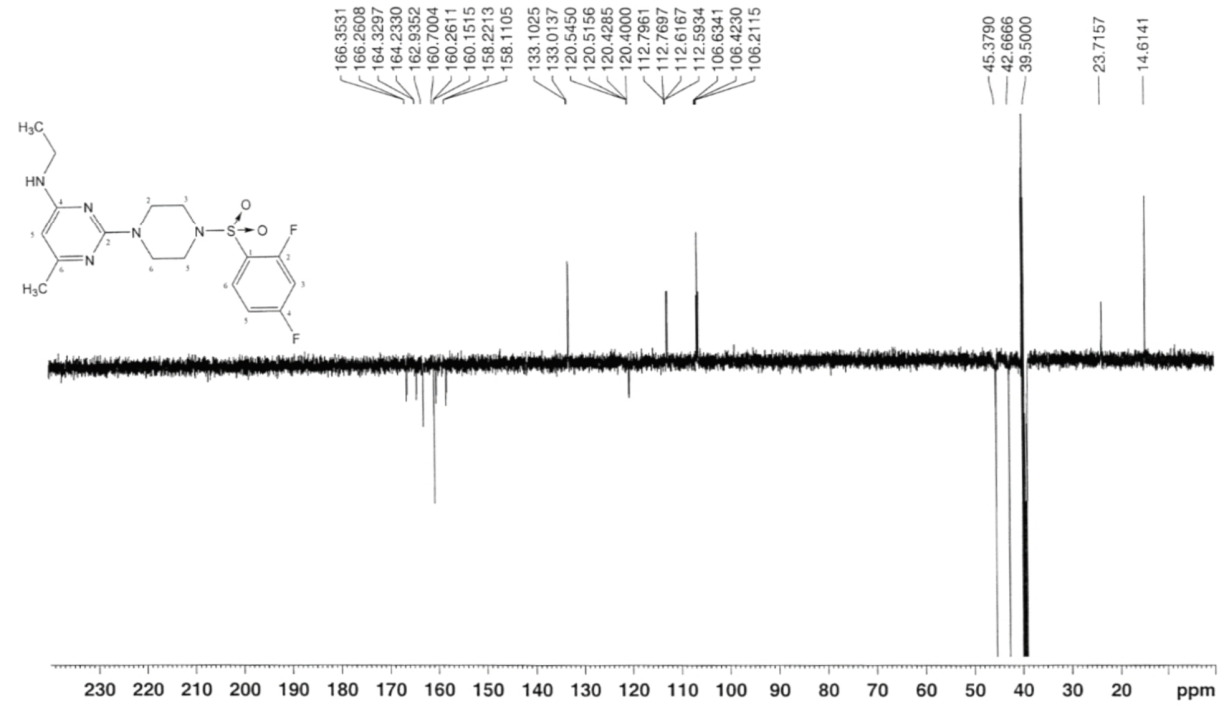


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5l

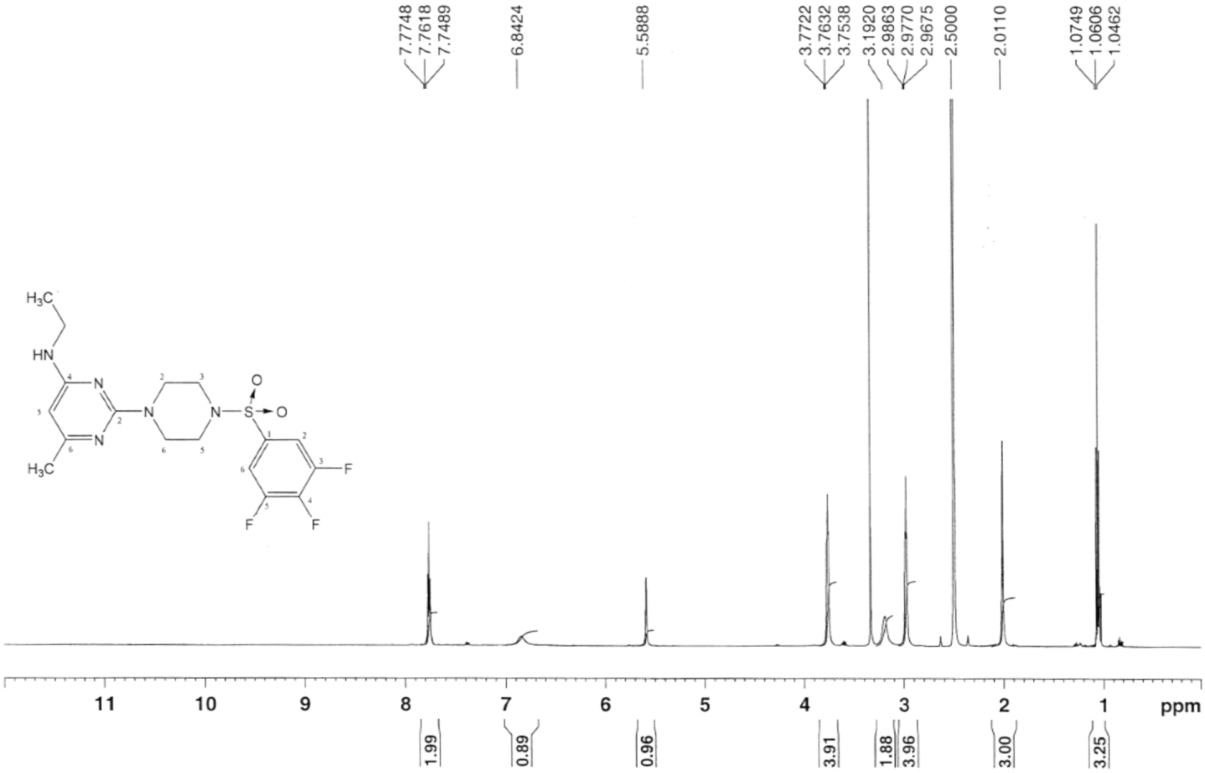


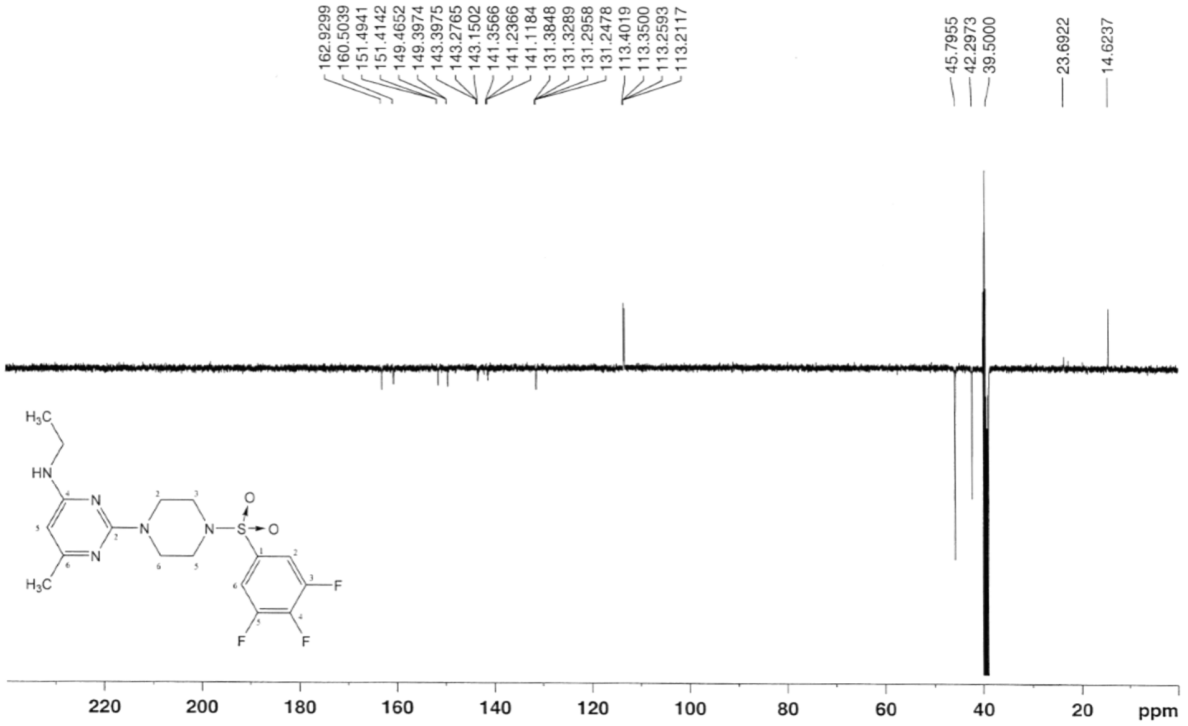
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5m



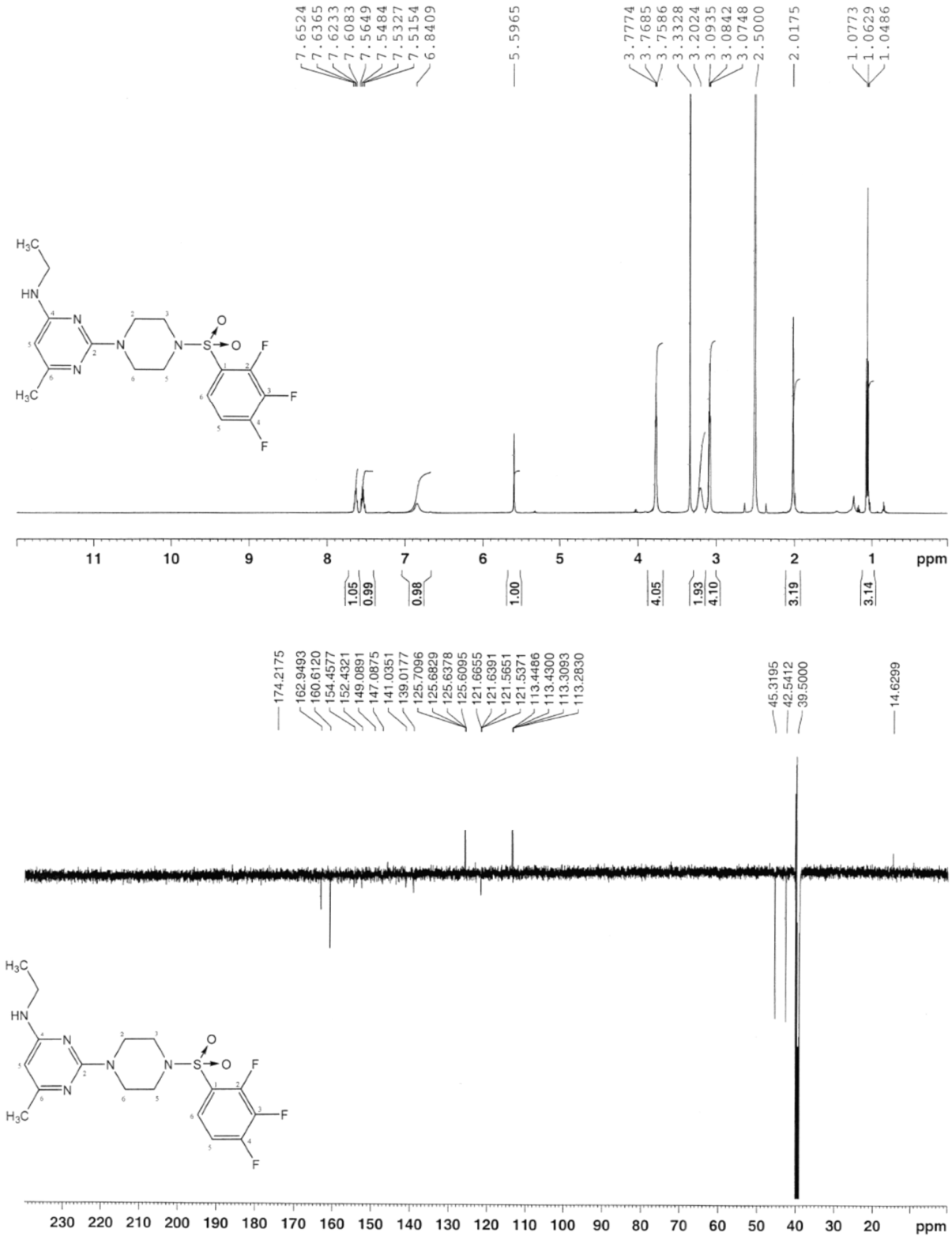


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5n

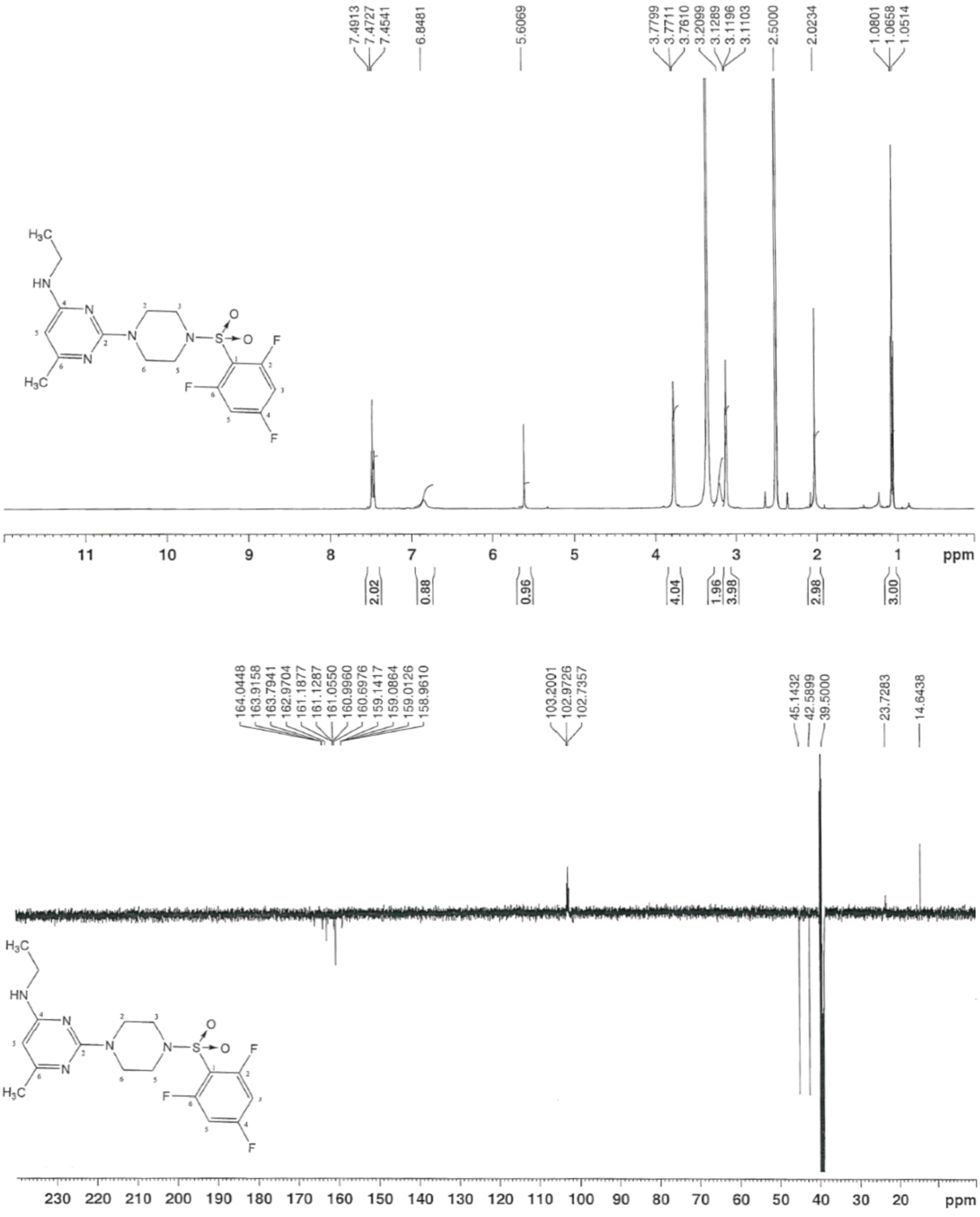




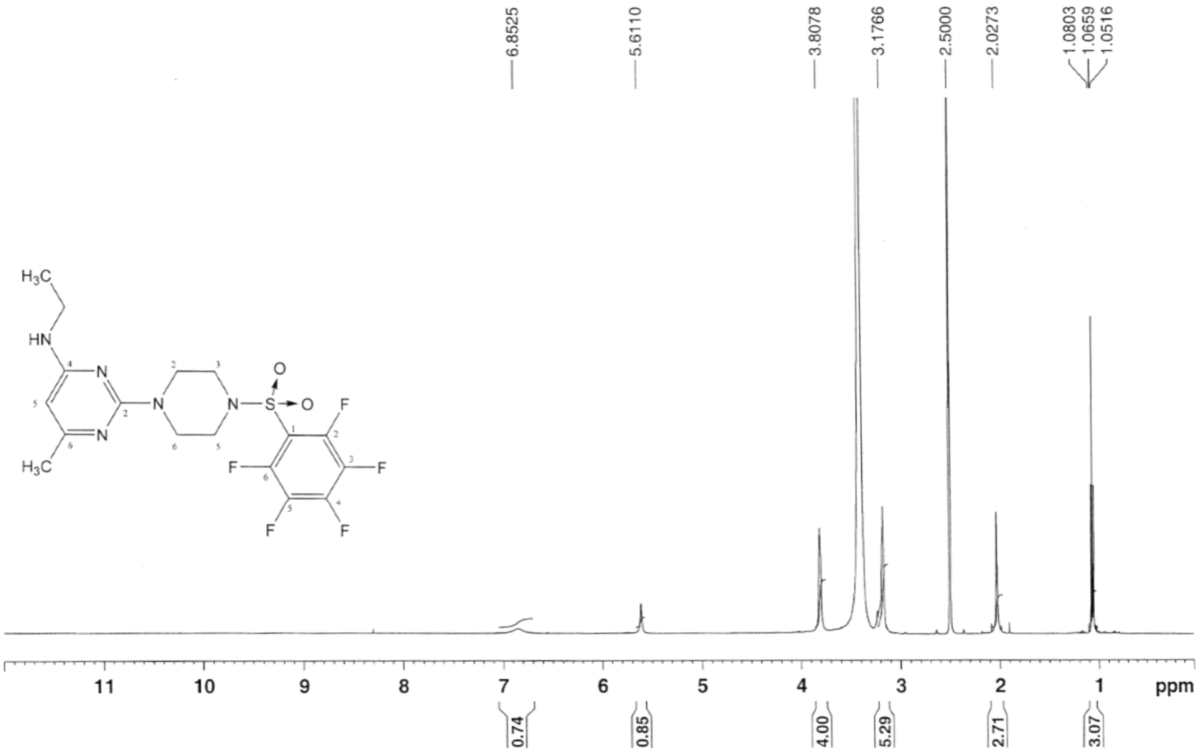
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5o

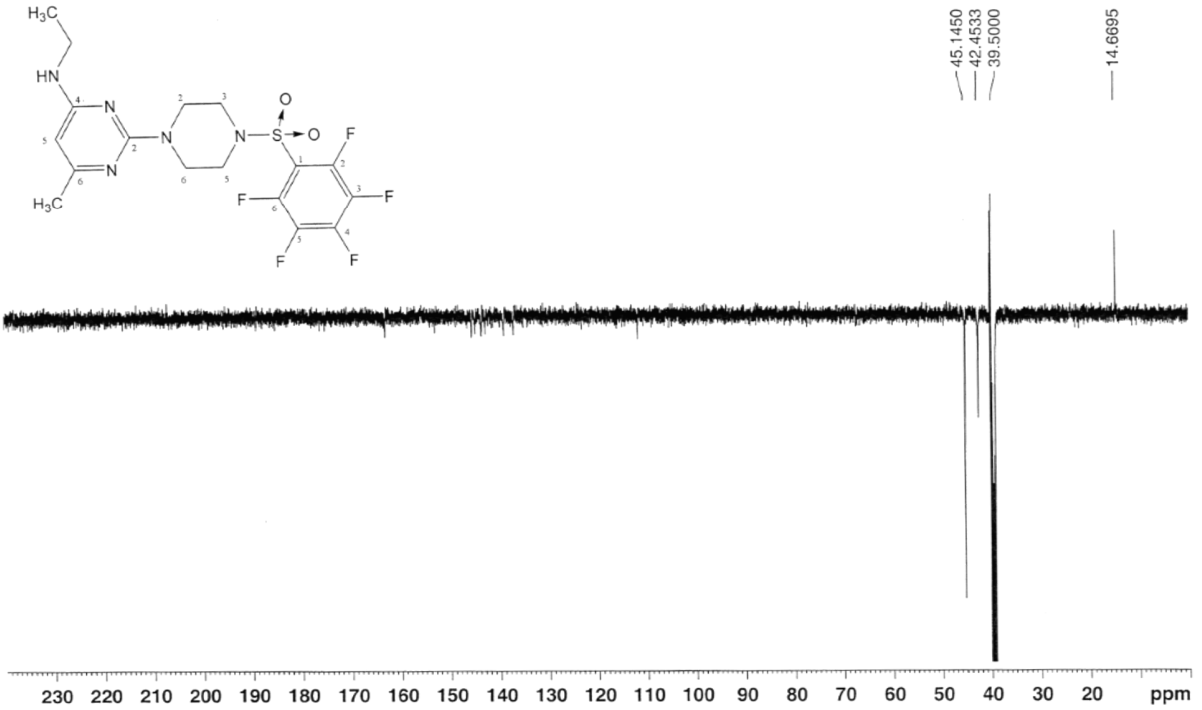


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5p

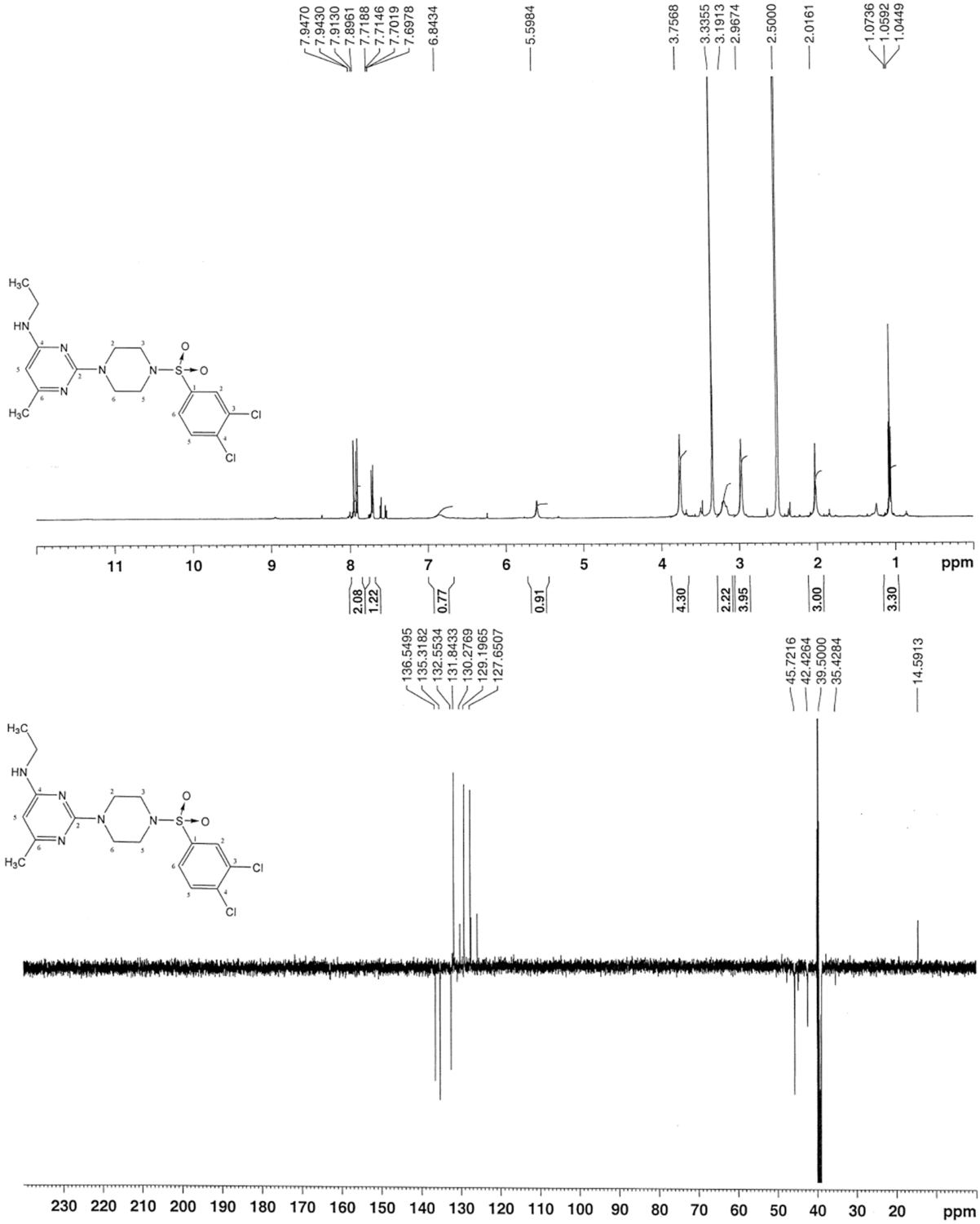


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5q

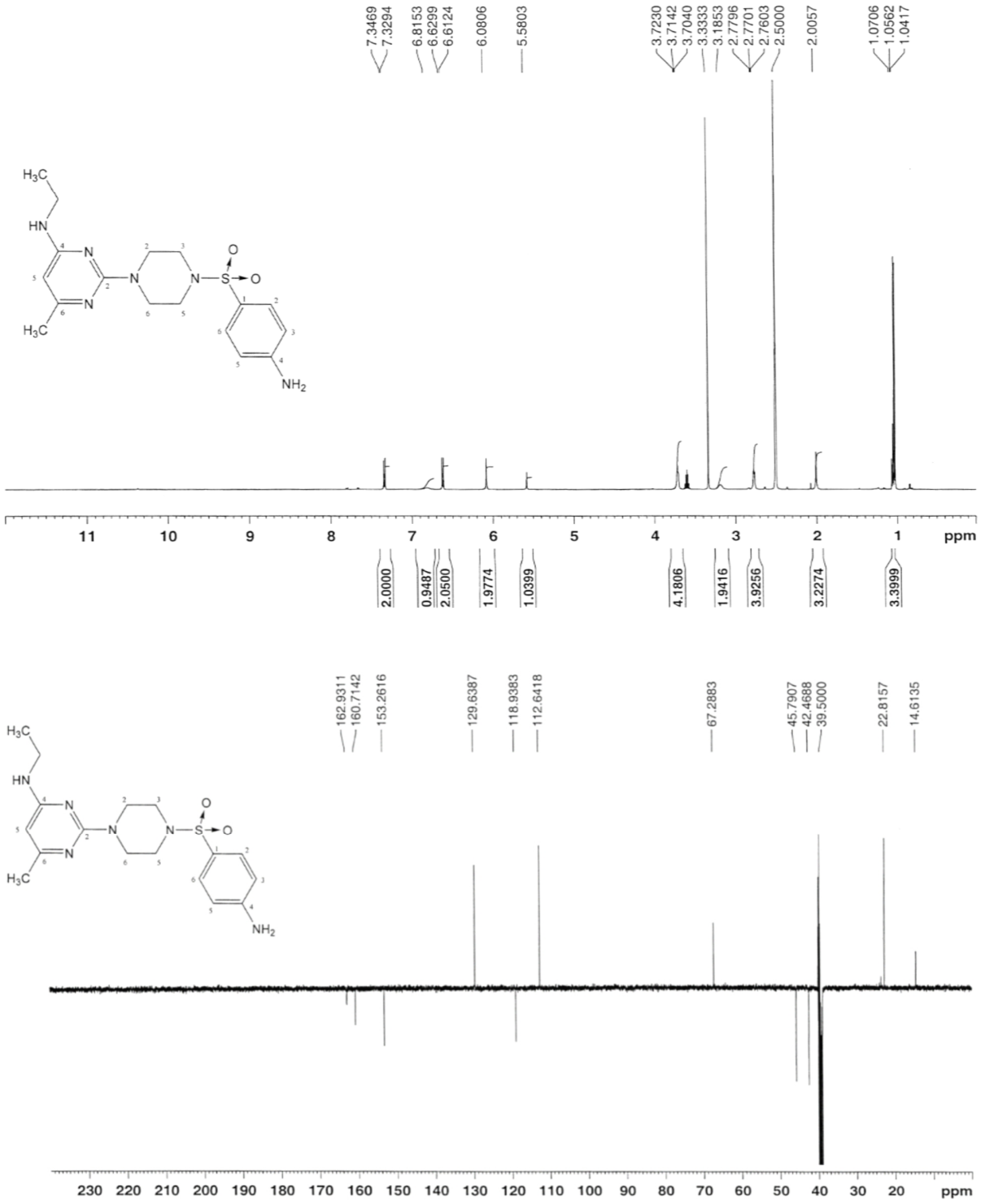




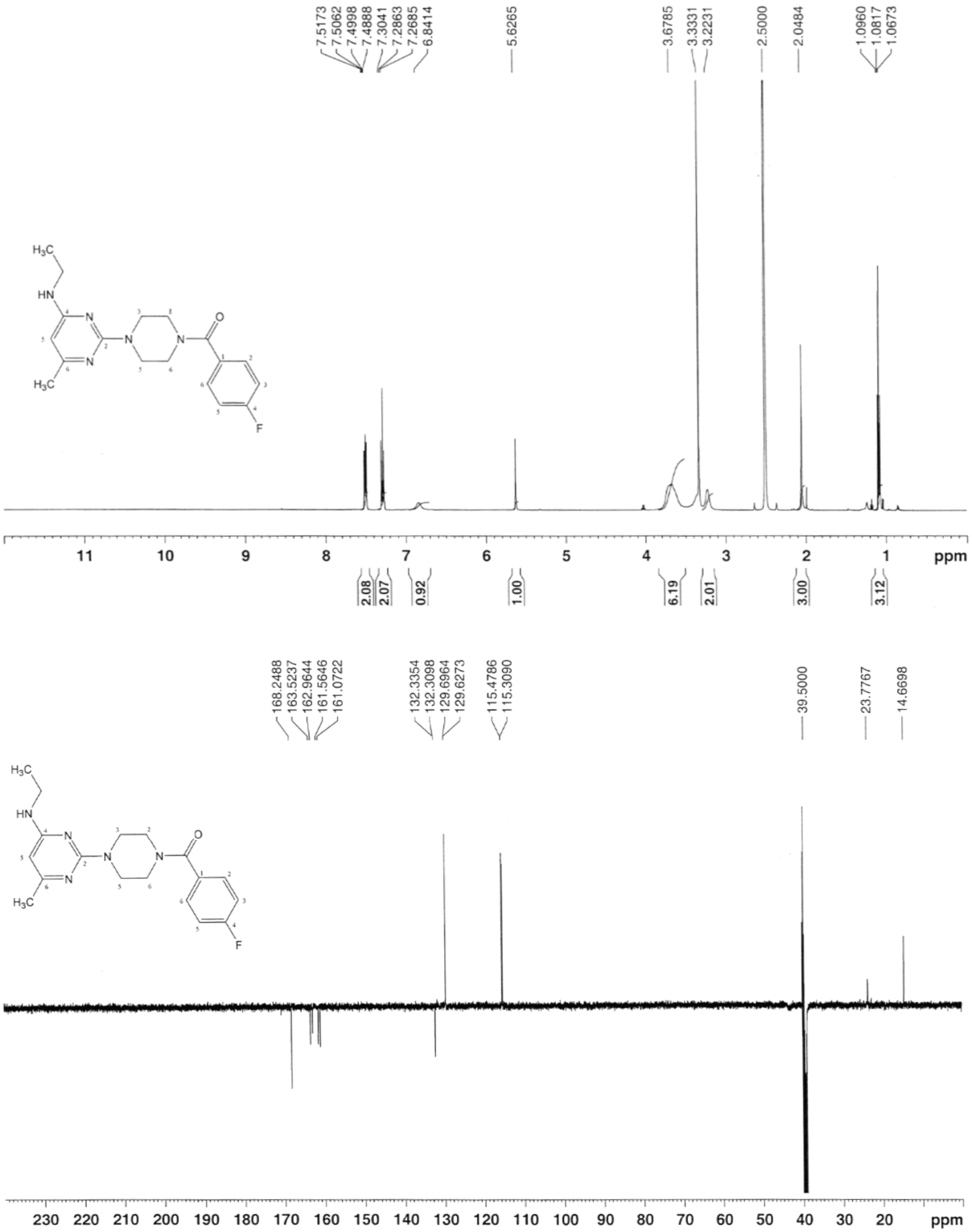
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5r



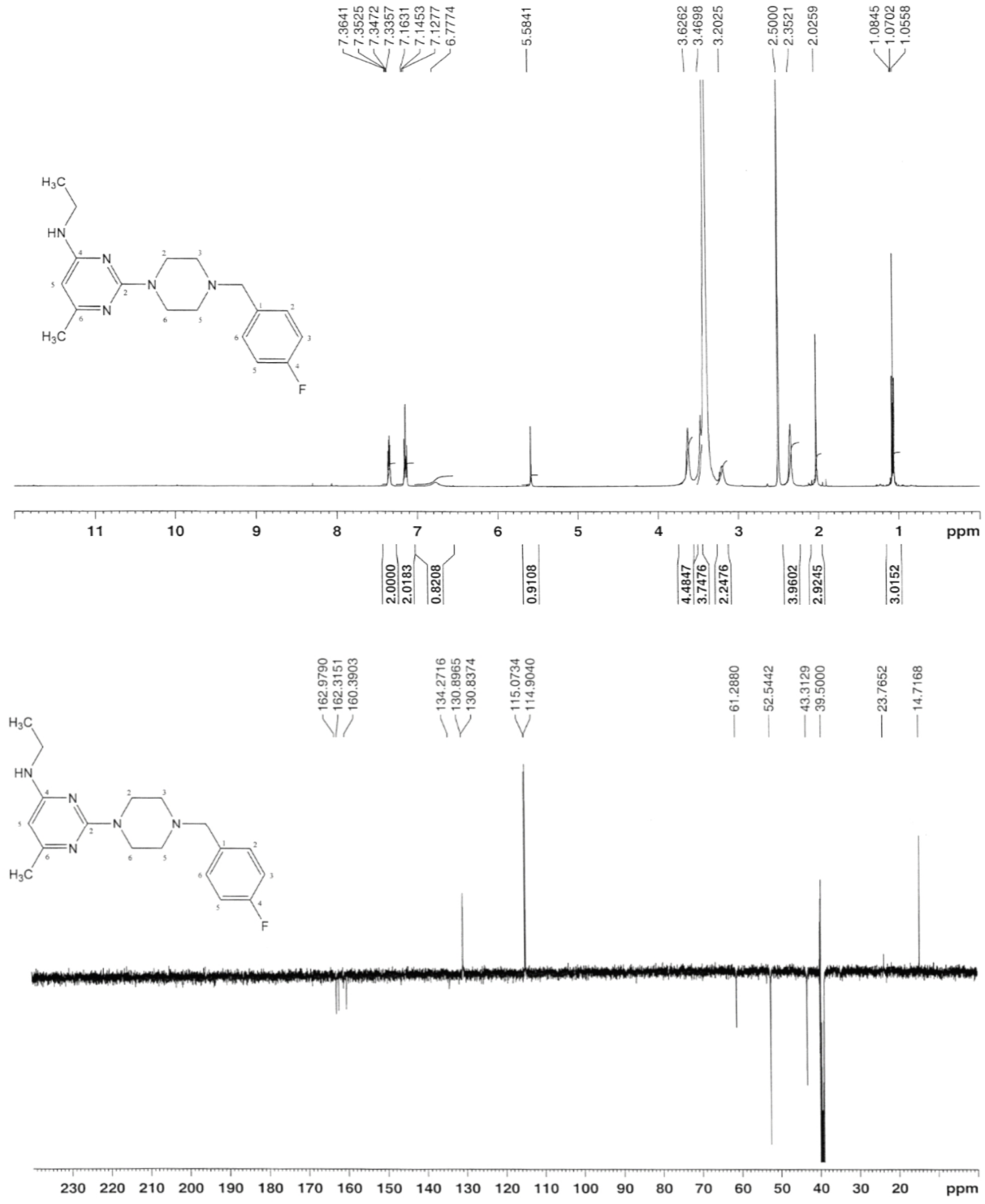
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 5s



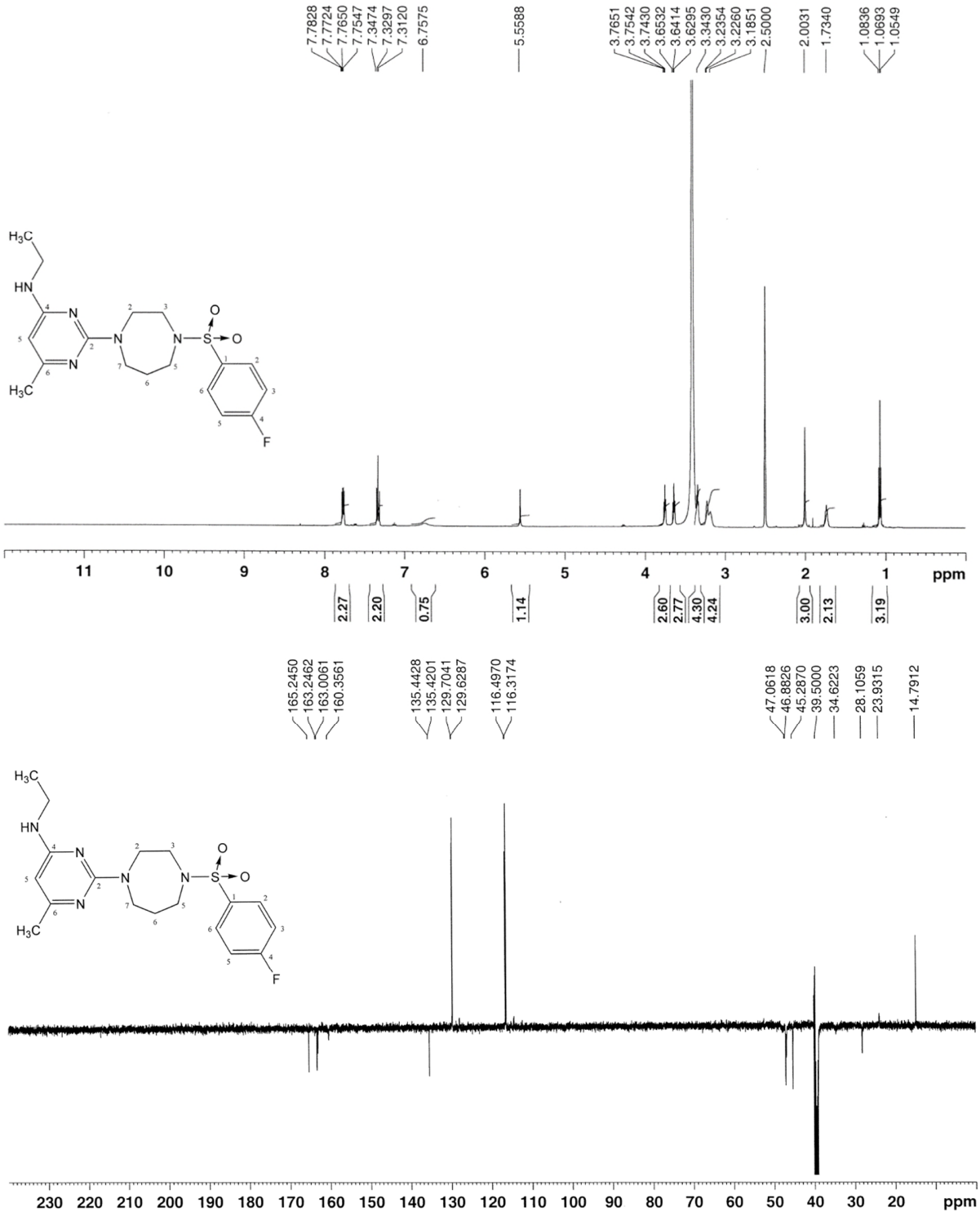
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 6a



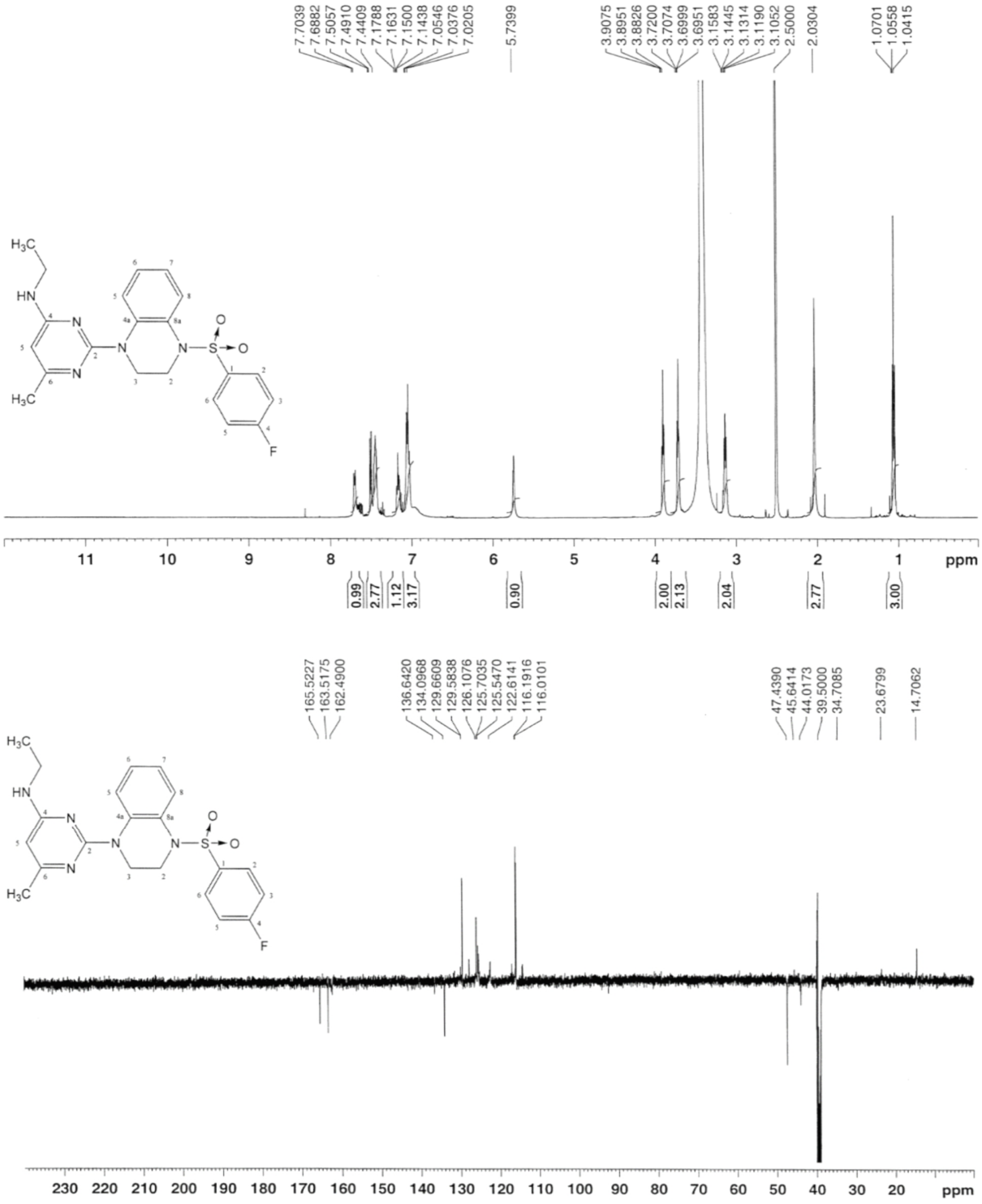
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 6b



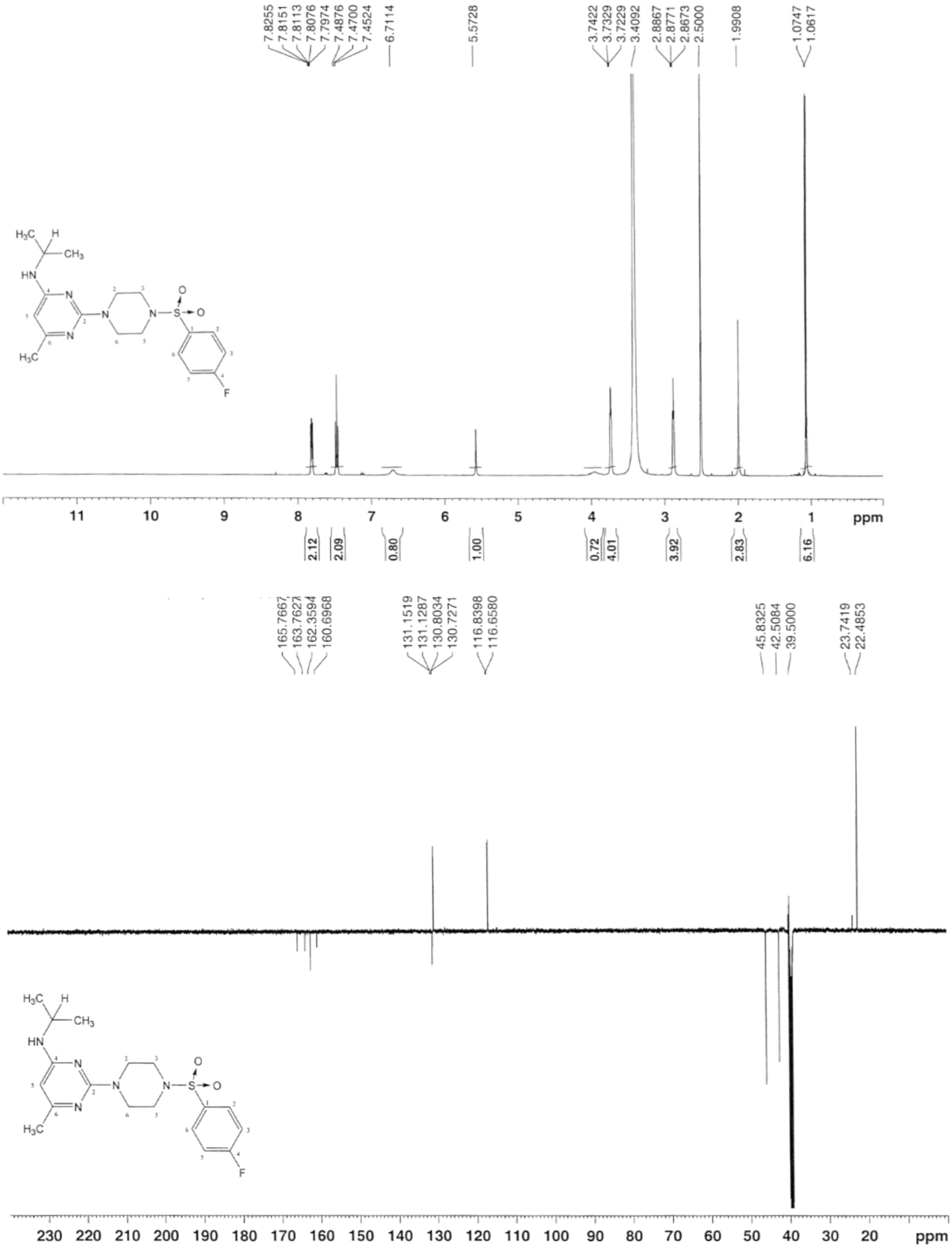
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 7a



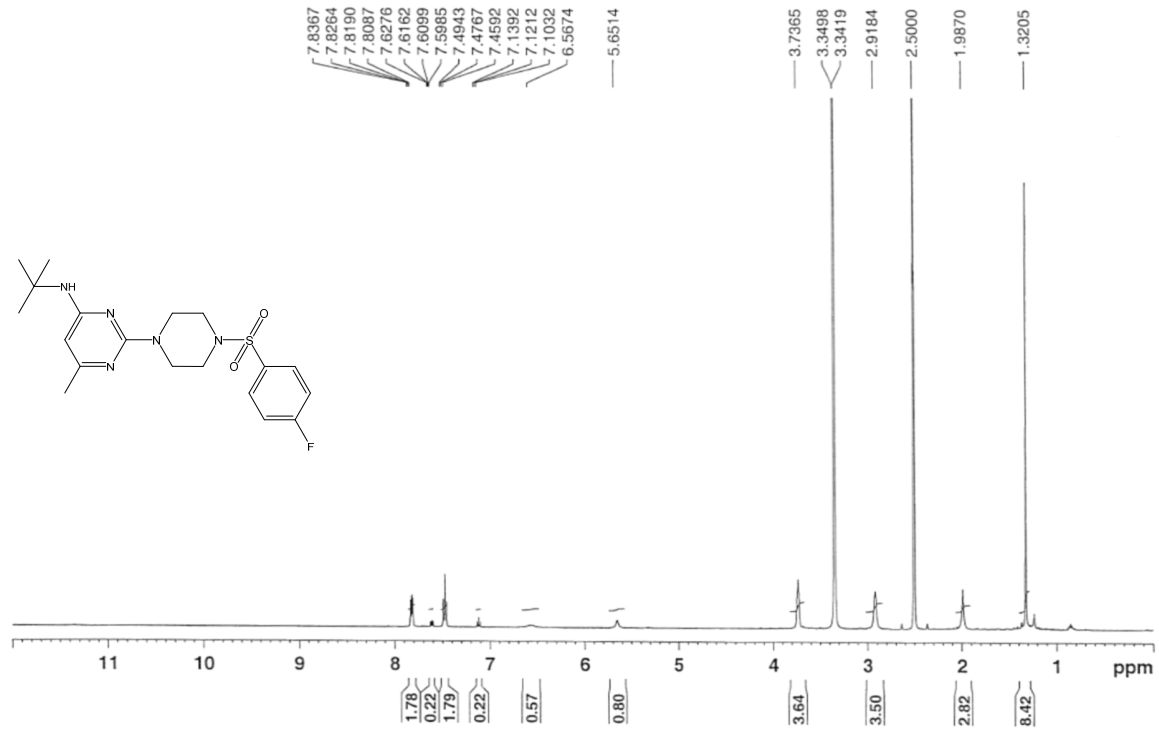
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 7b

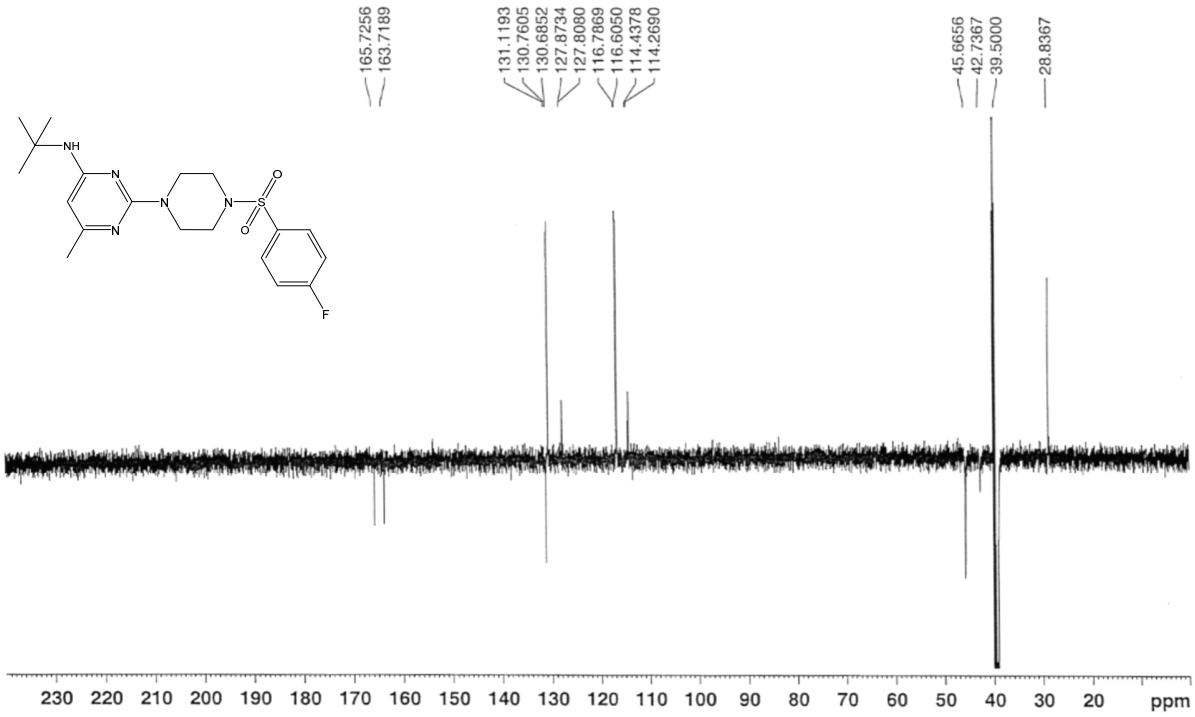


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 8a

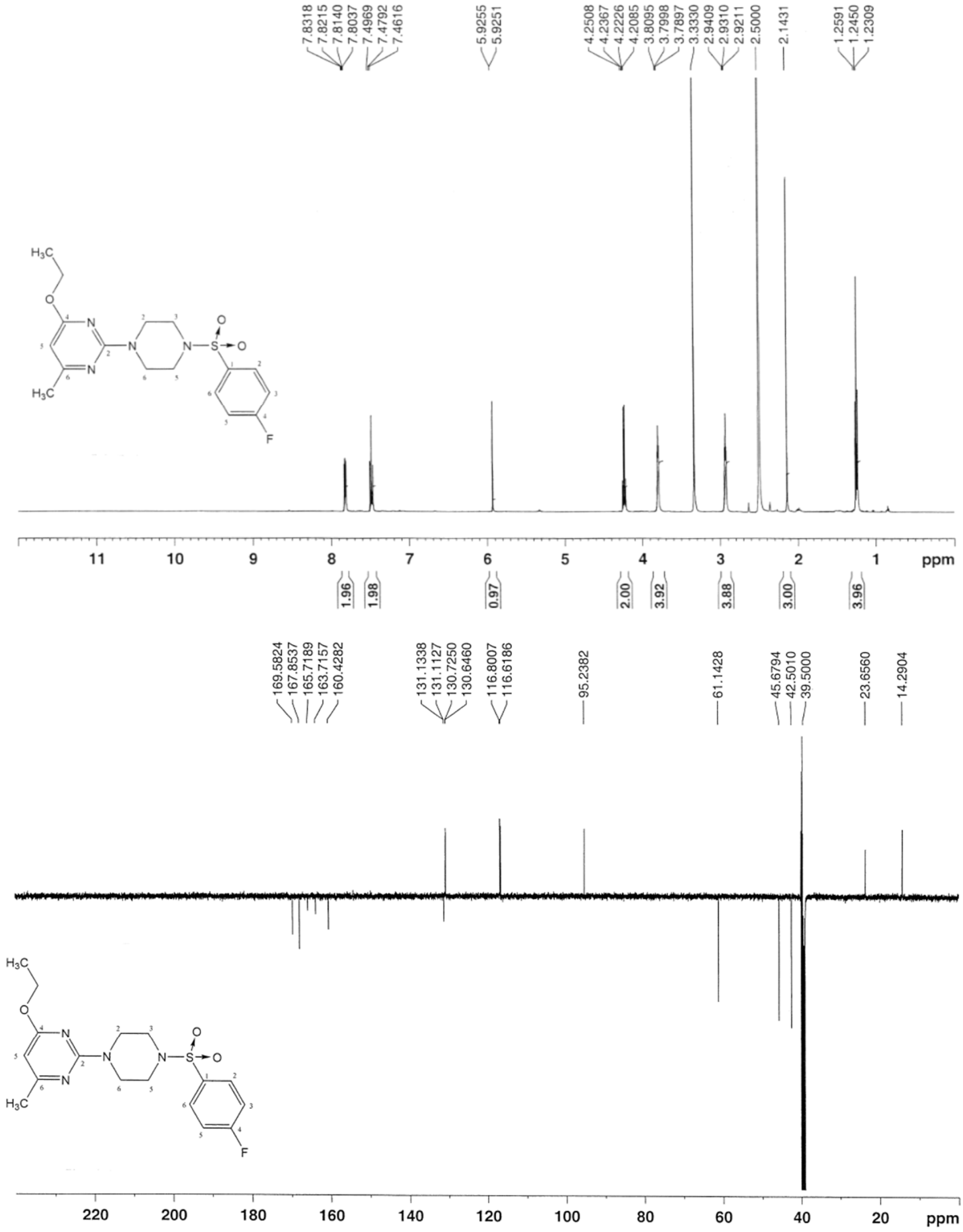


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 8b

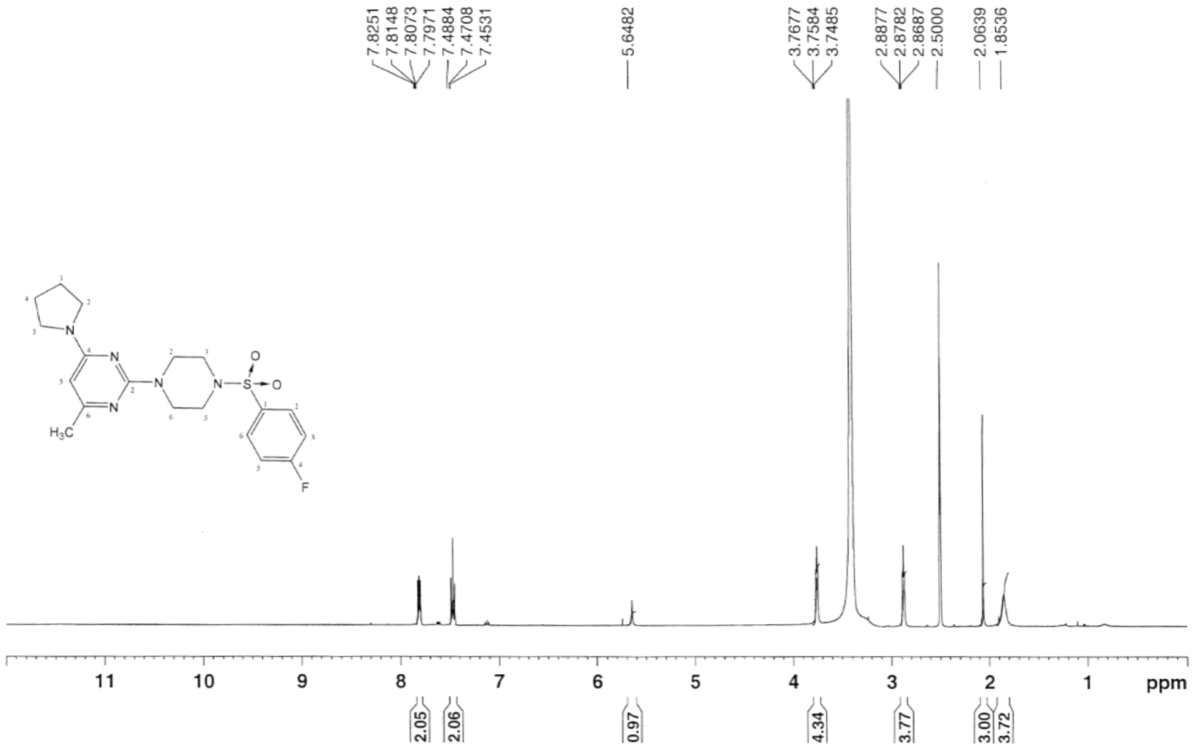


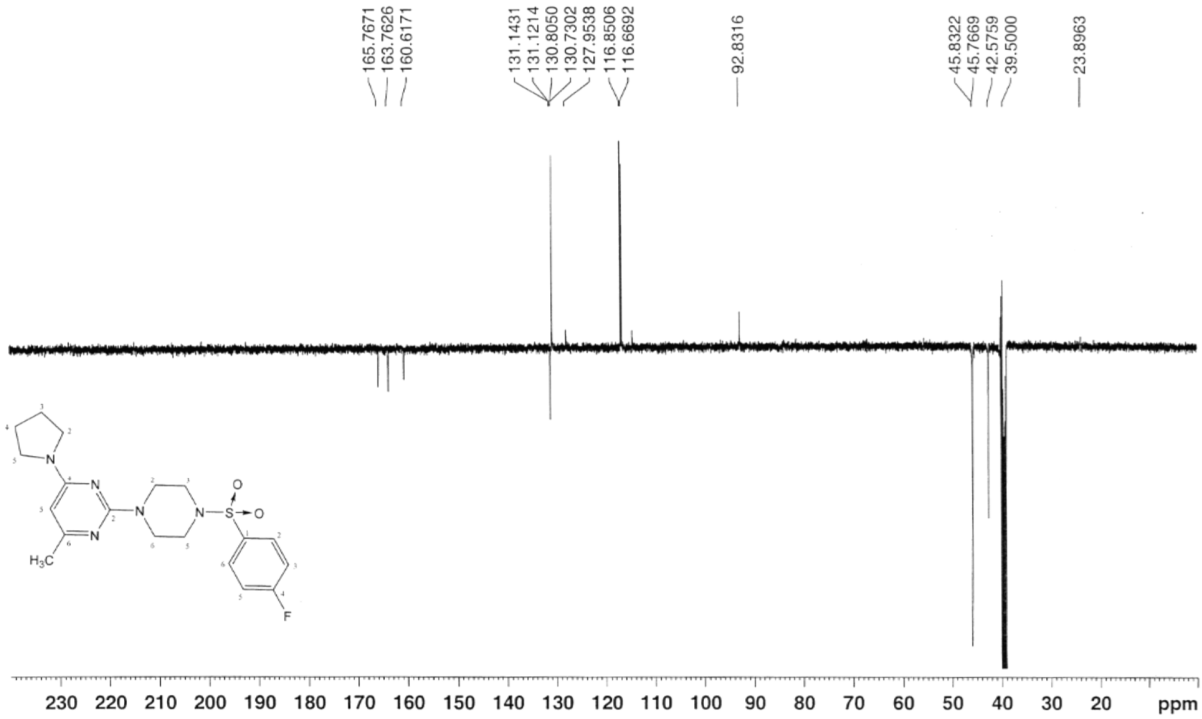


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 8c

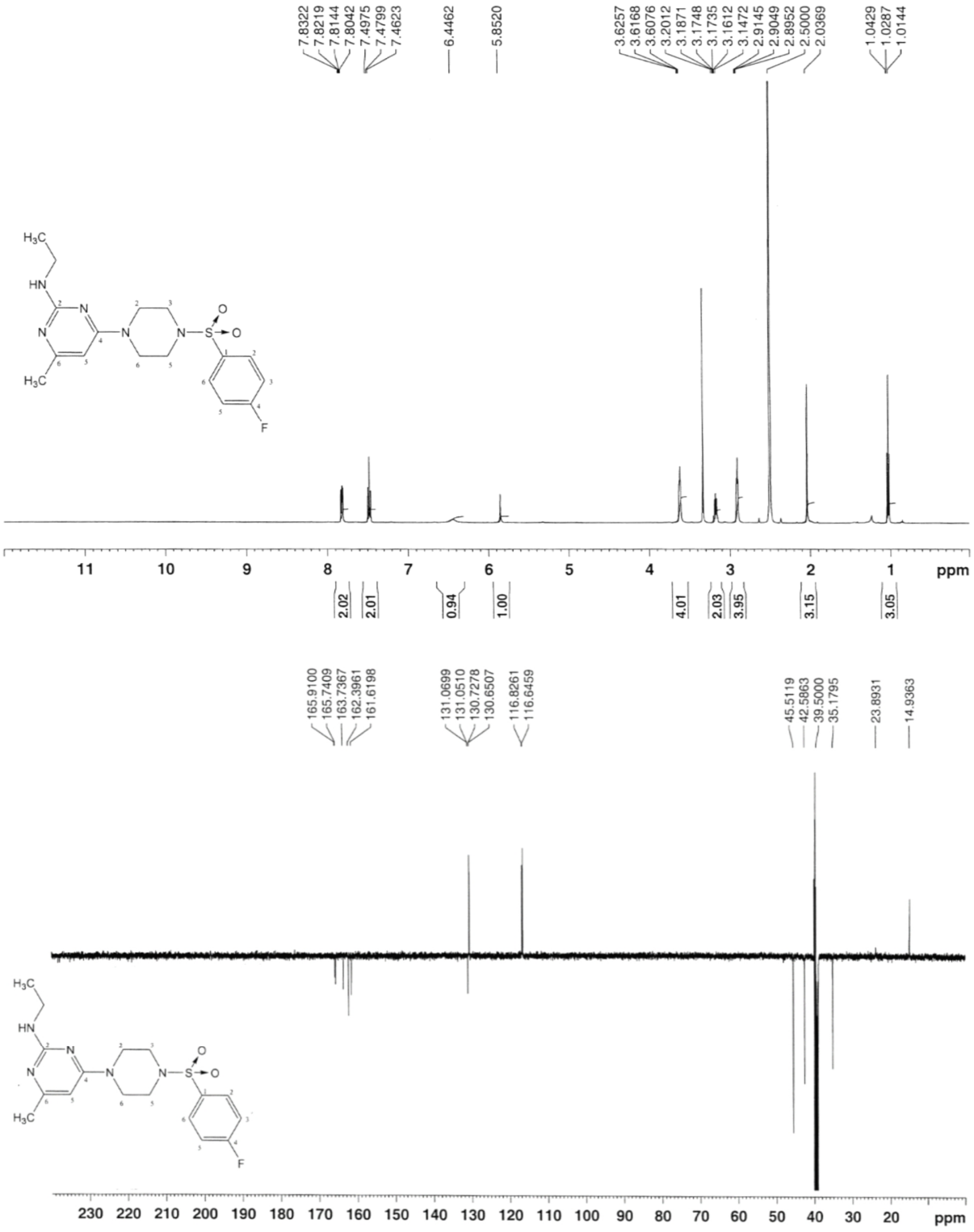


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 8d

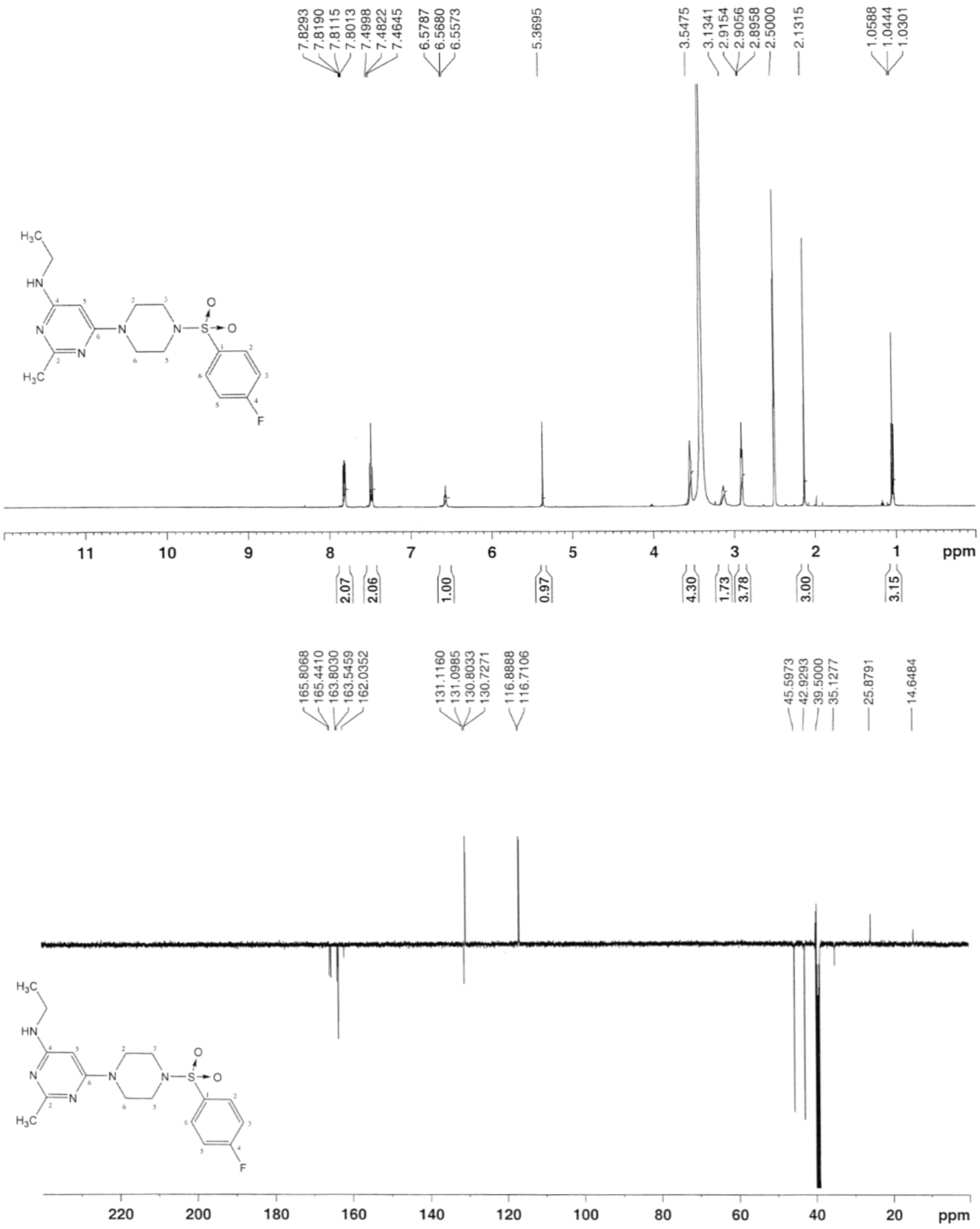




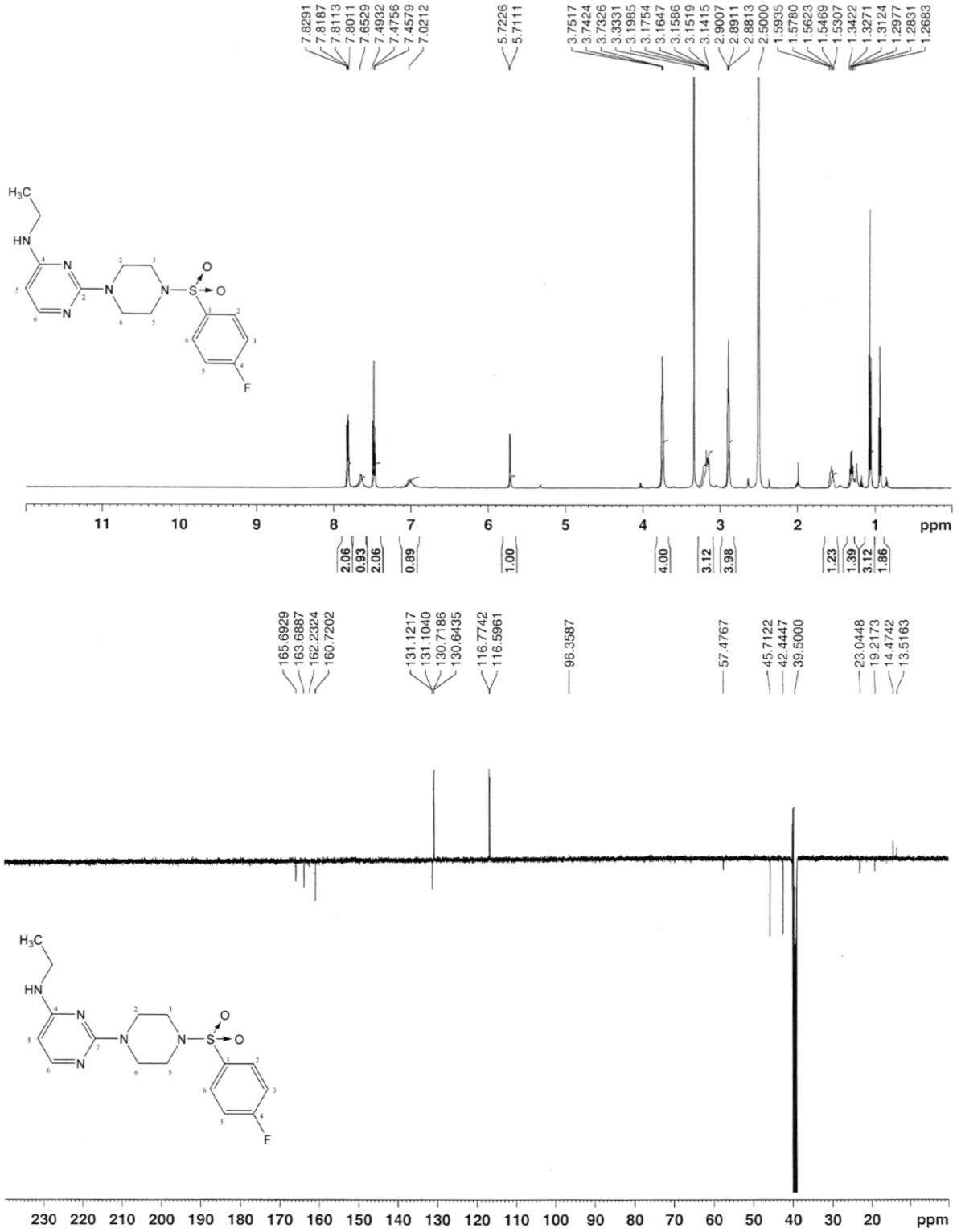
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 9a



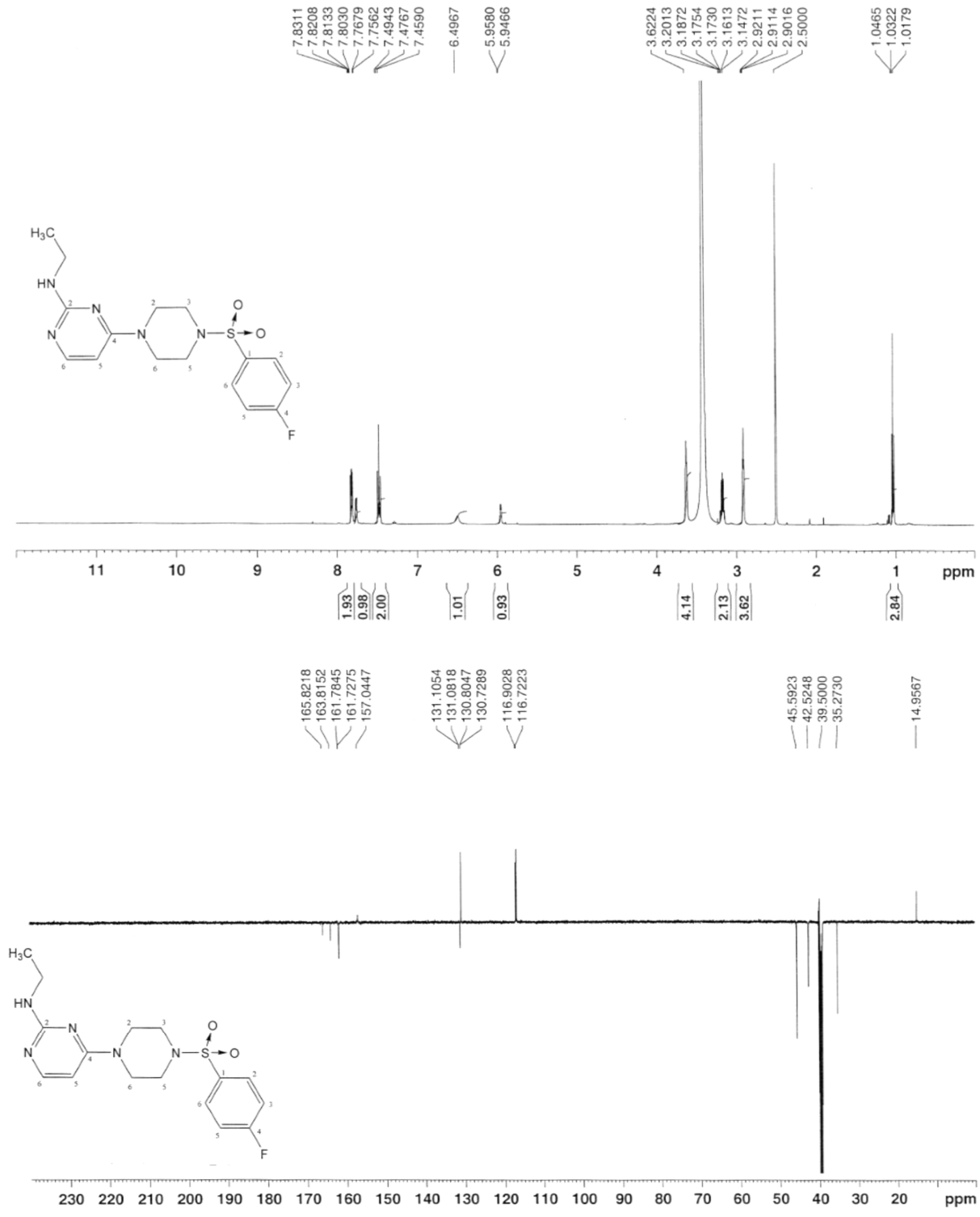
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 9b



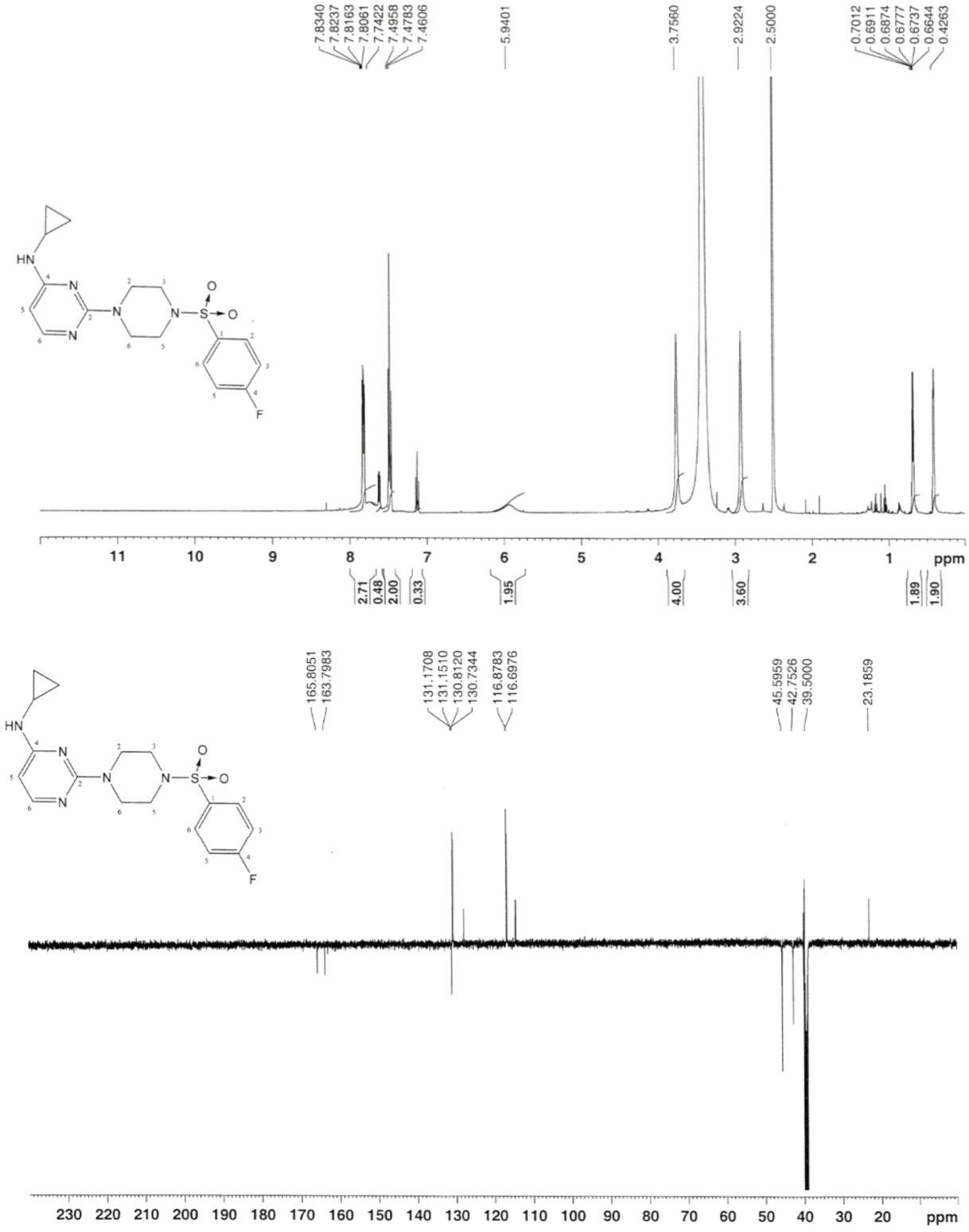
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 9c



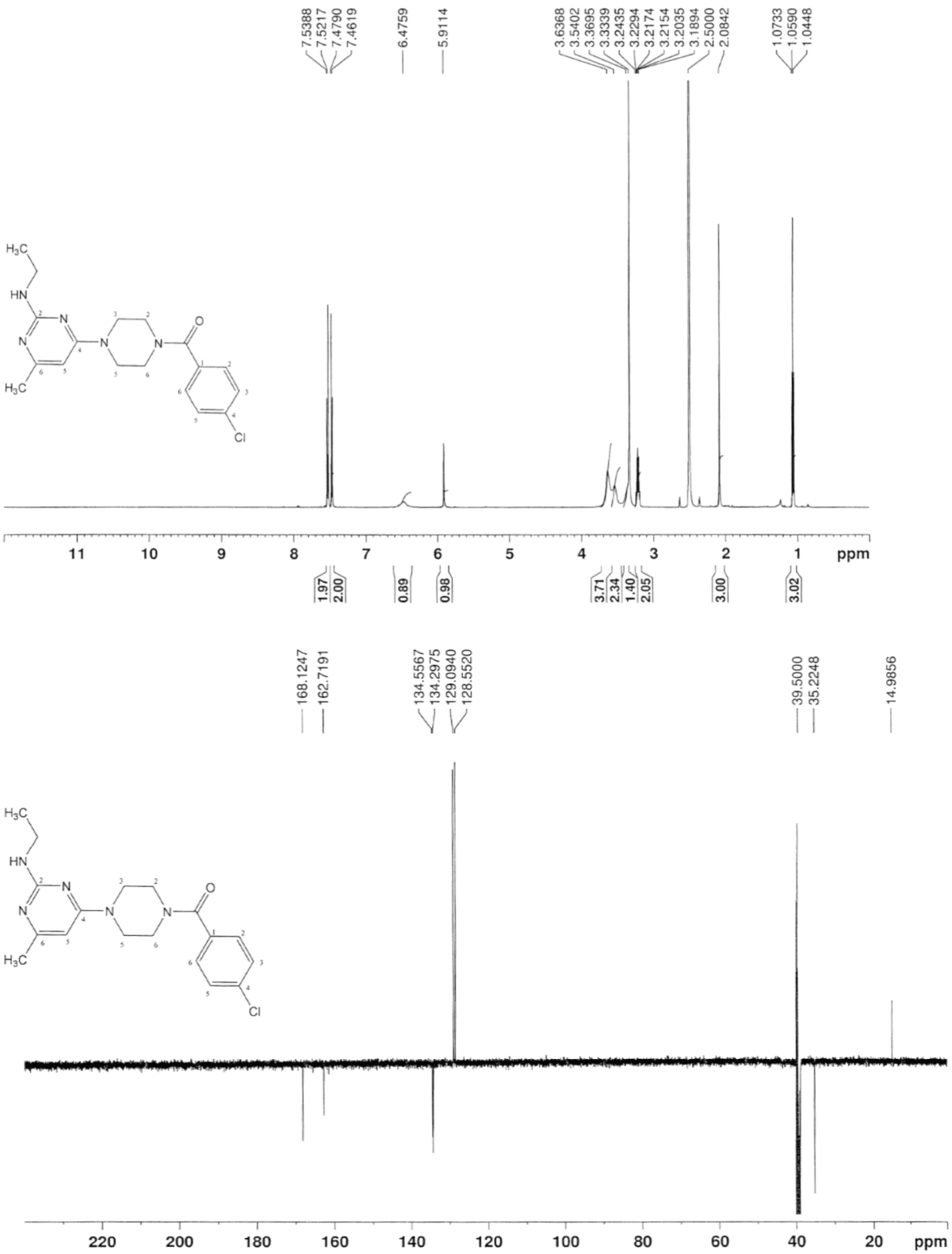
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 9d



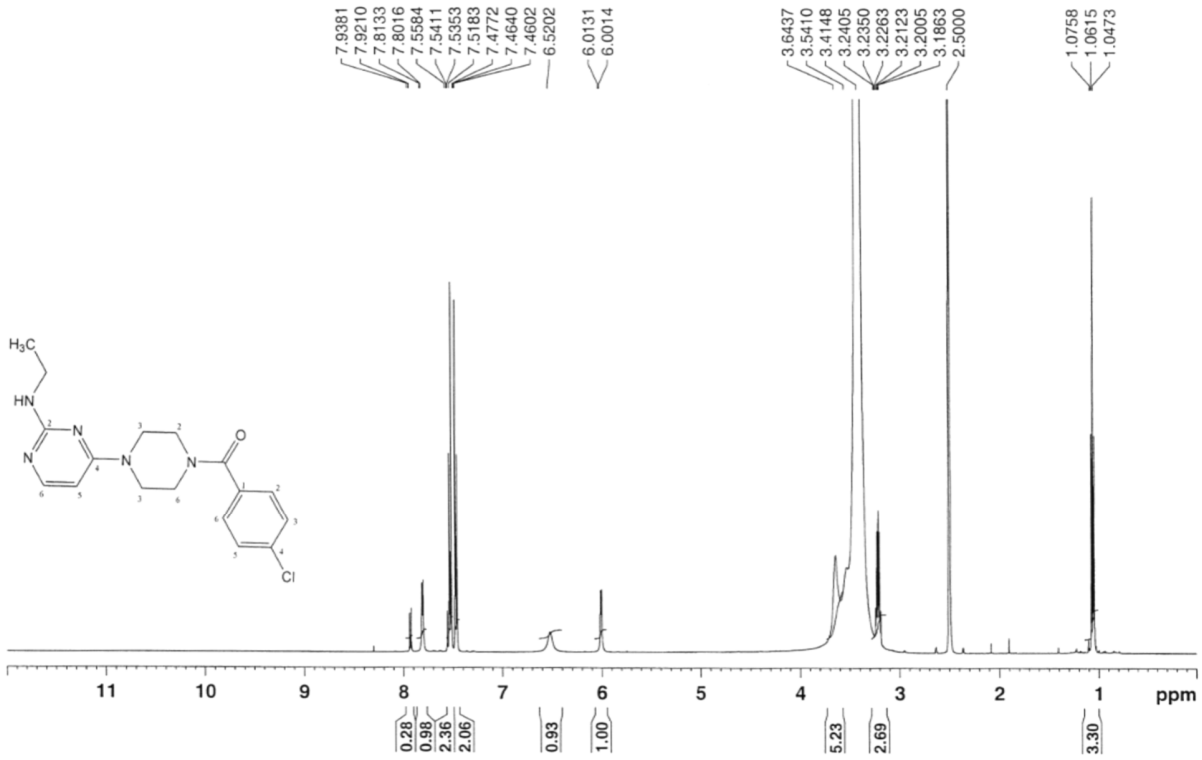
^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 10

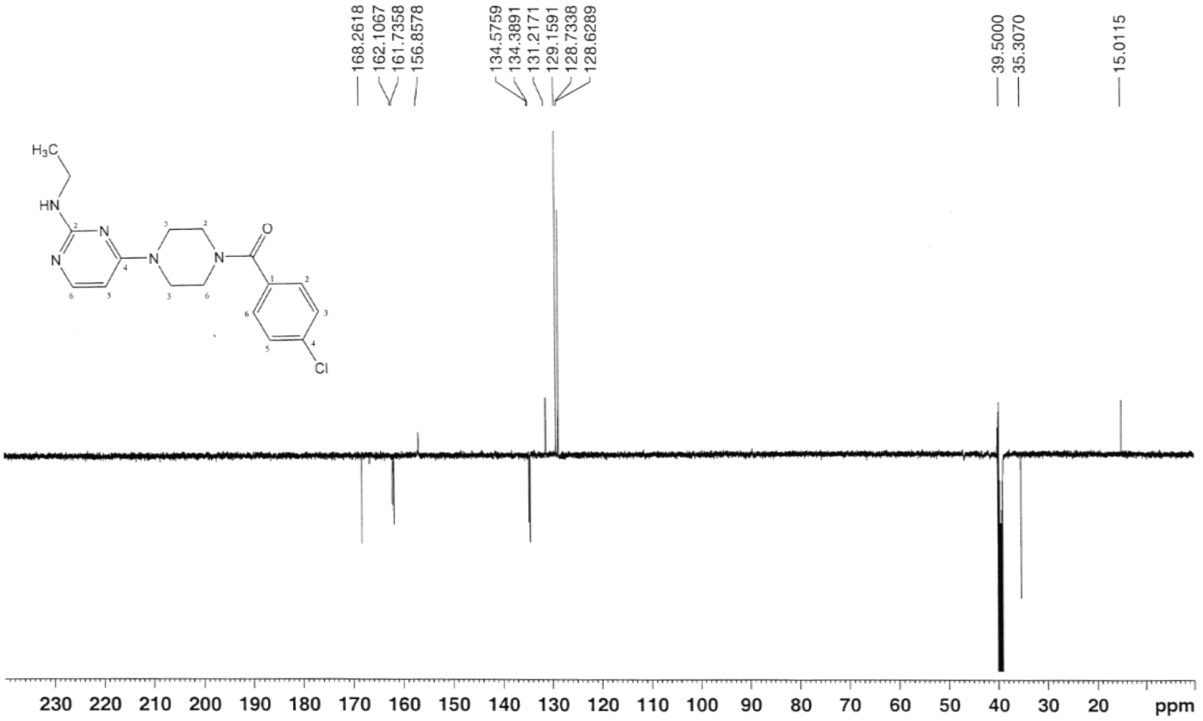


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 11a

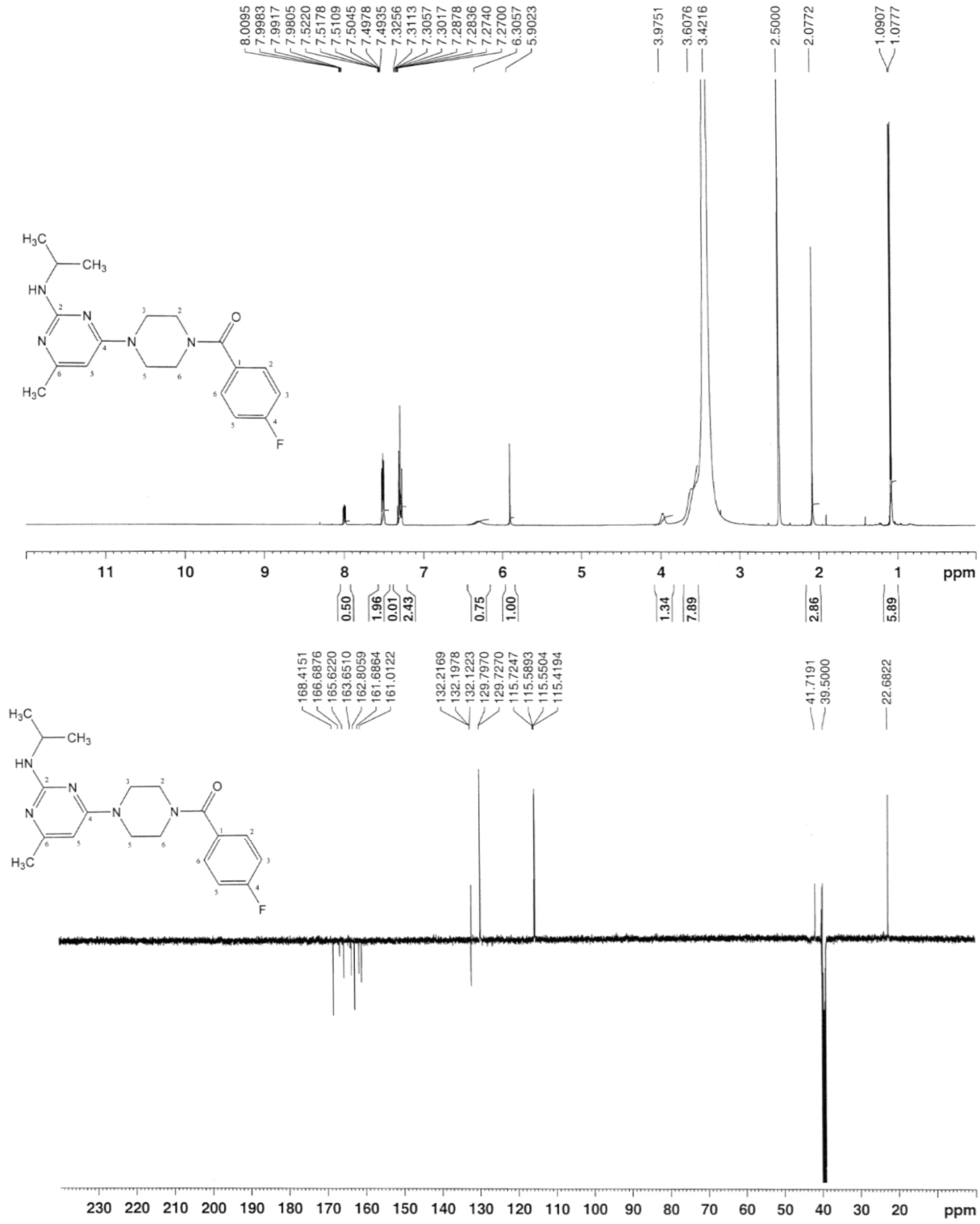


^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 11b





^{1}H- and ^{13}C-NMR Spectra in DMSO-d6 of compound 11c



HPLC determined purity of the Compounds

HPLC determined purity of compound 1

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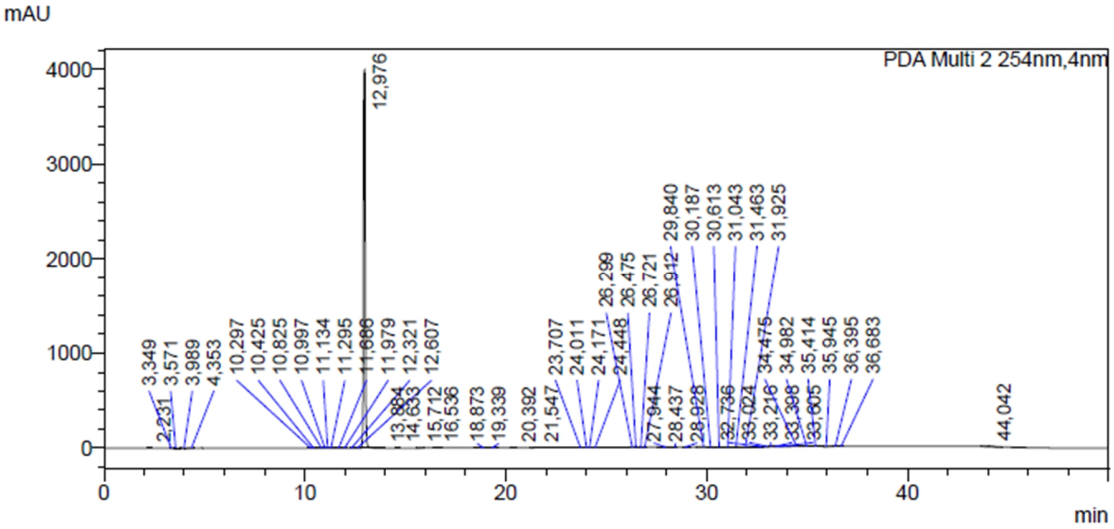


<Peak Table>

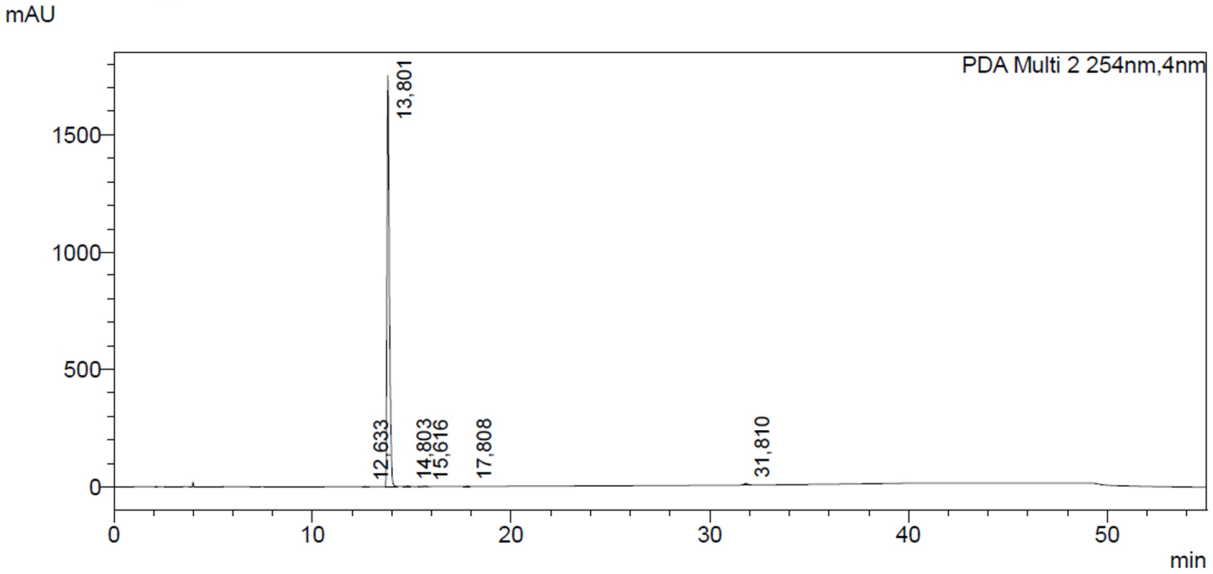
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	2,231	2154	536	0,013	0,008
2	3,349	6329	418	0,010	0,023
3	3,571	56294	3805	0,094	0,207
4	3,989	31352	6215	0,154	0,115
5	4,353	42499	1261	0,031	0,156
6	10,297	2868	349	0,009	0,011
7	10,425	2180	271	0,007	0,008
8	10,825	1647	193	0,005	0,006
9	10,997	1678	213	0,005	0,006
10	11,134	2553	370	0,009	0,009
11	11,295	3515	682	0,017	0,013
12	11,686	3437	336	0,008	0,013
13	11,979	1086	66	0,002	0,004
14	12,321	1189	204	0,005	0,004
15	12,607	4699	1089	0,027	0,017
16	12,976	26360640	3995065	98,732	96,910
17	13,884	1086	264	0,007	0,004
18	14,633	1824	337	0,008	0,007
19	15,712	1027	81	0,002	0,004
20	16,536	9246	865	0,021	0,034
21	18,873	6915	418	0,010	0,025
22	19,339	1760	96	0,002	0,006

Peak#	Ret. Time	Area	Height	Height%	Area%
23	20,392	1212	164	0,004	0,004
24	21,547	1120	66	0,002	0,004
25	23,707	8307	672	0,017	0,031
26	24,011	2303	242	0,006	0,008
27	24,171	1704	197	0,005	0,006
28	24,448	1112	91	0,002	0,004
29	26,299	6916	642	0,016	0,025
30	26,475	4958	540	0,013	0,018
31	26,721	6958	850	0,021	0,026
32	26,912	1365	170	0,004	0,005
33	27,944	6057	536	0,013	0,022
34	28,437	1030	52	0,001	0,004
35	28,928	2373	190	0,005	0,009
36	29,840	9552	696	0,017	0,035
37	30,187	2801	163	0,004	0,010
38	30,613	5574	339	0,008	0,020
39	31,043	6999	423	0,010	0,026
40	31,463	28190	1843	0,046	0,104
41	31,925	10232	584	0,014	0,038
42	32,736	34217	875	0,022	0,126
43	33,024	20136	1402	0,035	0,074
44	33,216	12140	1231	0,030	0,045
45	33,398	13870	1343	0,033	0,051
46	33,605	25365	1952	0,048	0,093
47	34,475	115010	2146	0,053	0,423
48	34,982	38882	2114	0,052	0,143
49	35,414	98547	5715	0,141	0,362
50	35,945	42994	2117	0,052	0,158
51	36,395	8296	662	0,016	0,030
52	36,683	2879	189	0,005	0,011
53	44,042	134145	5022	0,124	0,493
Total		27201220	4046360	100,000	100,000

HPLC determined purity of compound 5a

<Chromatogram>



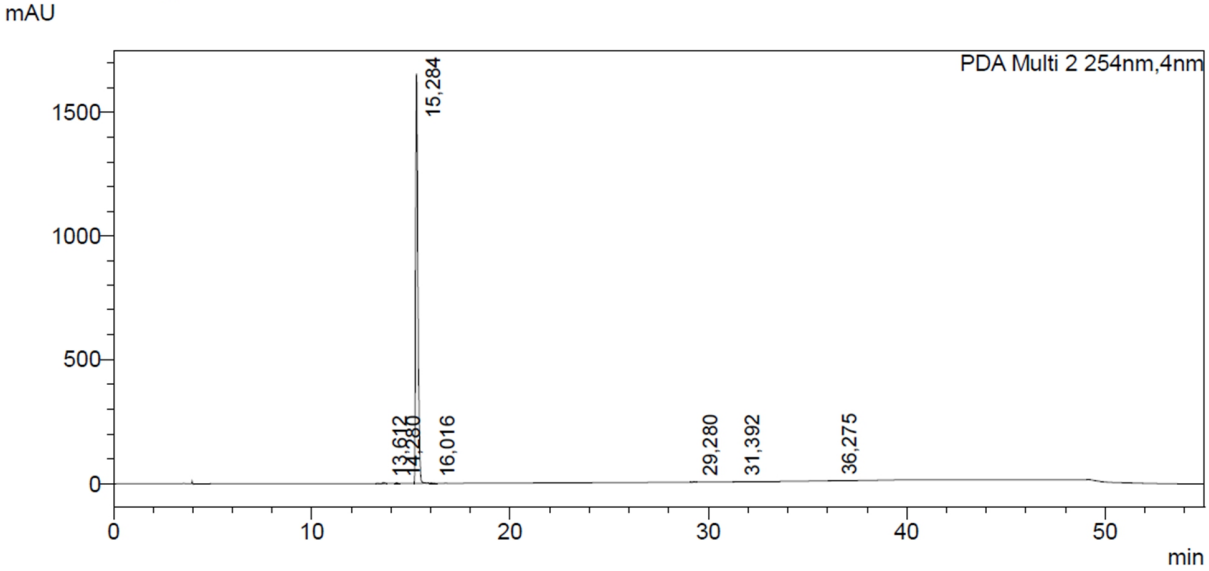
<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Height%
1	12,633	8558	1237	0,058	0,058	0,070
2	13,801	14585087	1749773	99,169	99,169	99,184
3	14,803	15141	2452	0,103	0,103	0,139
4	15,616	13076	1910	0,089	0,089	0,108
5	17,808	8283	1829	0,056	0,056	0,104
6	31,810	77144	6965	0,525	0,525	0,395
Total		14707288	1764166		100,000	100,000

HPLC determined purity of compound 5b

<Chromatogram>



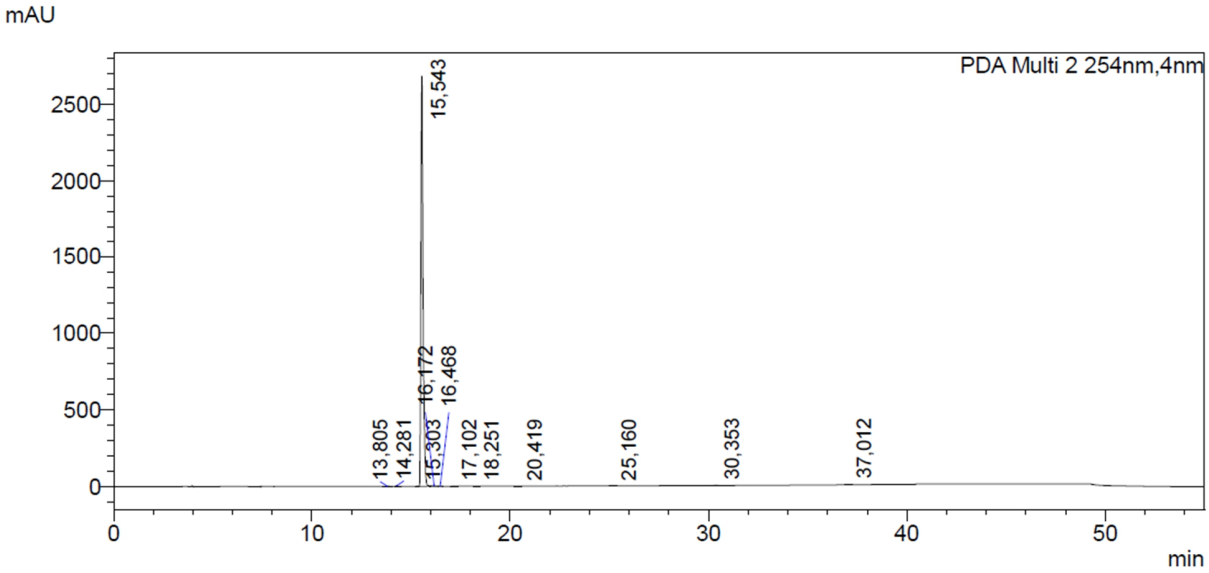
<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Height%
1	13,612	36296	4654	0,000	0,276	0,279
2	14,280	21581	2997	0,000	0,164	0,180
3	15,284	13024787	1654000	0,000	99,072	99,176
4	16,016	20486	1996	0,000	0,156	0,120
5	29,280	15761	1497	0,000	0,120	0,090
6	31,392	11653	1259	0,000	0,089	0,075
7	36,275	16213	1331	0,000	0,123	0,080
Total		13146778	1667734		100,000	100,000

HPLC determined purity of compound 5c

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	13,805	19254	1800	0,000	0,067	0,096
2	14,281	33931	4911	0,000	0,182	0,170
3	15,303	7071	1243	0,000	0,046	0,035
4	15,543	19818058	2684918	0,000	99,414	99,306
5	16,172	13444	1783	0,000	0,066	0,067
6	16,468	5961	1024	0,000	0,038	0,030
7	17,102	6634	672	0,000	0,025	0,033
8	18,251	4655	438	0,000	0,016	0,023
9	20,419	9645	784	0,000	0,029	0,048
10	25,160	8832	650	0,000	0,024	0,044
11	30,353	15376	1310	0,000	0,049	0,077
12	37,012	13734	1221	0,000	0,045	0,069
Total		19956594	2700755		100,000	100,000

HPLC determined purity of compound 5d

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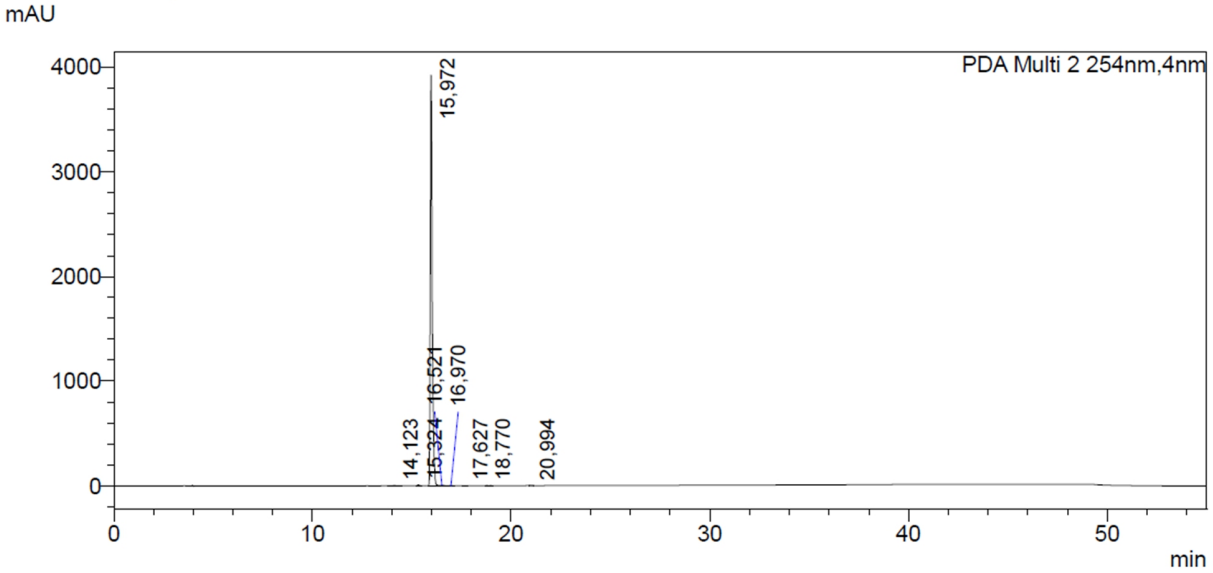

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	14,123	72174	4361	0,000	0,110	0,265
2	15,324	52360	8289	0,000	0,210	0,193
3	15,972	26932955	3919907	0,000	99,299	99,047
4	16,521	41400	5080	0,000	0,129	0,152
5	16,970	36177	3697	0,000	0,094	0,133
6	17,627	18770	1717	0,000	0,044	0,069
7	18,770	25995	2172	0,000	0,055	0,096
8	20,994	12190	2361	0,000	0,060	0,045
Total		27192021	3947583		100,000	100,000

HPLC determined purity of compound 5e

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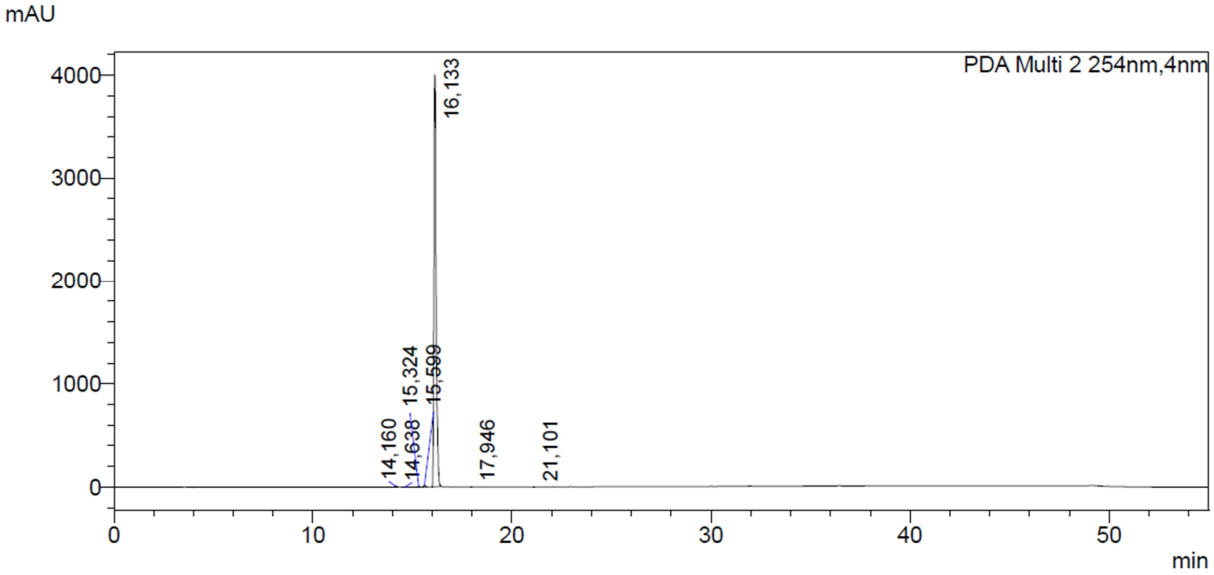


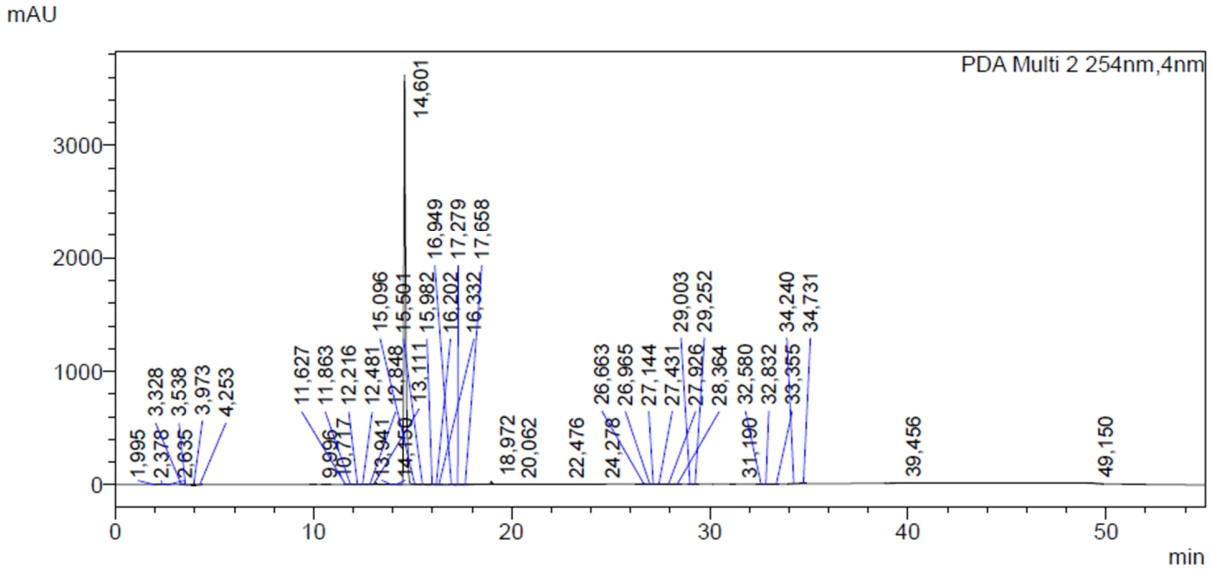
<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	14,160	76196	11658	0,000	0,289	0,246
2	14,638	10011	1650	0,000	0,041	0,032
3	15,324	37121	6262	0,000	0,155	0,120
4	15,599	90774	15556	0,000	0,385	0,293
5	16,133	30757004	3996922	0,000	99,035	99,258
6	17,946	9381	2419	0,000	0,060	0,030
7	21,101	6501	1413	0,000	0,035	0,021
Total		30986988	4035881		100,000	100,000

HPLC determined purity of compound 5f

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	1,995	1362	129	0,003	0,005
2	2,378	8351	1240	0,033	0,033
3	2,635	1107	126	0,003	0,004
4	3,328	1694	139	0,004	0,007
5	3,538	27138	2322	0,062	0,107
6	3,973	57193	23170	0,620	0,226
7	4,253	5662	335	0,009	0,022
8	9,996	1789	242	0,006	0,007
9	10,717	2759	227	0,006	0,011
10	11,627	1023	128	0,003	0,004
11	11,863	1556	181	0,005	0,006
12	12,216	4262	384	0,010	0,017
13	12,481	5978	773	0,021	0,024
14	12,848	4479	483	0,013	0,018
15	13,111	183548	25263	0,676	0,726
16	13,941	3755	281	0,008	0,015
17	14,150	4090	373	0,010	0,016
18	14,601	24314318	3618423	96,820	96,210
19	15,096	51314	6438	0,172	0,203
20	15,501	13507	1927	0,052	0,053
21	15,982	20035	2869	0,077	0,079
22	16,202	1849	332	0,009	0,007

Peak#	Ret. Time	Area	Height	Height%	Area%
23	16,332	2854	324	0,009	0,011
24	16,949	6617	909	0,024	0,026
25	17,279	1315	161	0,004	0,005
26	17,658	5467	583	0,016	0,022
27	18,972	166826	25728	0,688	0,660
28	20,062	3695	476	0,013	0,015
29	22,476	4359	509	0,014	0,017
30	24,278	1081	111	0,003	0,004
31	26,663	72951	5863	0,157	0,289
32	26,965	43524	3324	0,089	0,172
33	27,144	55745	3514	0,094	0,221
34	27,431	45751	2644	0,071	0,181
35	27,926	17339	1448	0,039	0,069
36	28,364	3834	377	0,010	0,015
37	29,003	1813	195	0,005	0,007
38	29,252	6561	638	0,017	0,026
39	31,190	1594	166	0,004	0,006
40	32,580	2742	257	0,007	0,011
41	32,832	2585	174	0,005	0,010
42	33,355	1321	113	0,003	0,005
43	34,240	3730	230	0,006	0,015
44	34,731	1748	159	0,004	0,007
45	39,456	4240	208	0,006	0,017
46	49,150	97666	3365	0,090	0,386
Total		25272127	3737263	100,000	100,000

HPLC determined purity of compound 5g

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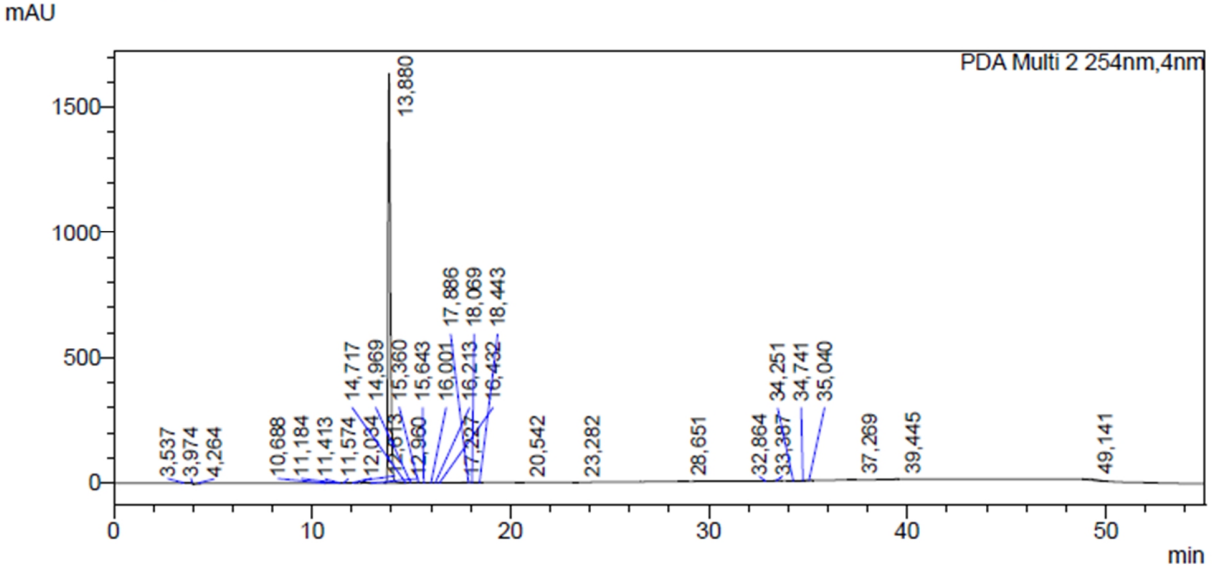


<Peak Table>

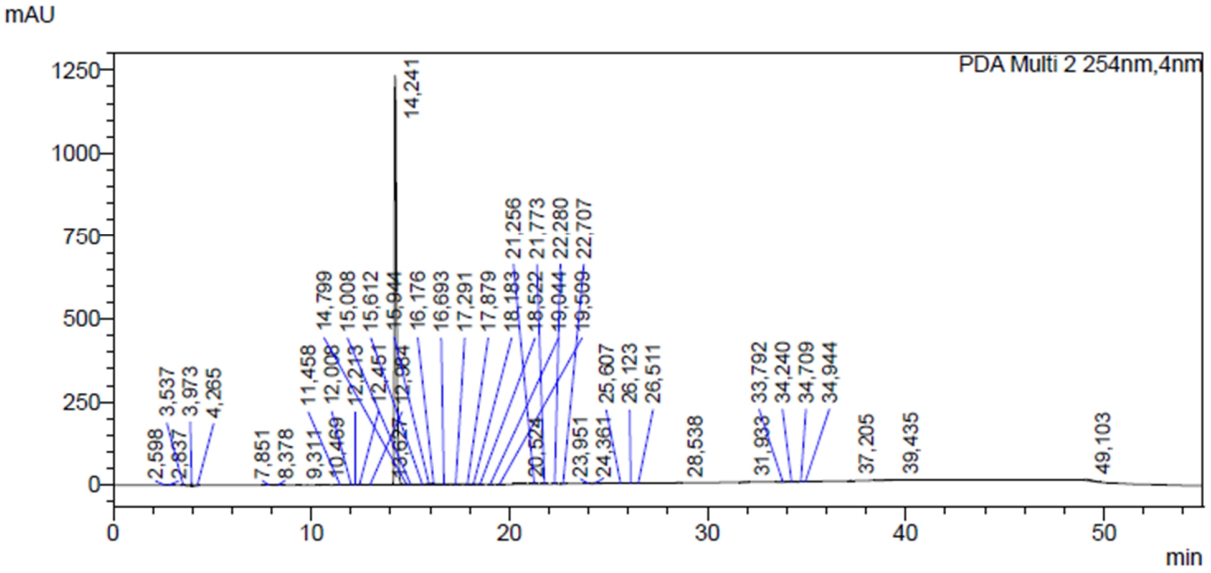
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,537	15924	1943	0,115	0,117	0,115
2	3,974	8180	4389	0,059	0,263	0,059
3	4,264	21812	856	0,158	0,051	0,158
4	10,688	1232	74	0,009	0,004	0,009
5	11,184	8720	739	0,063	0,044	0,063
6	11,413	1130	152	0,008	0,009	0,008
7	11,574	3587	339	0,026	0,020	0,026
8	12,034	9530	1104	0,069	0,066	0,069
9	12,613	76387	10158	0,553	0,610	0,553
10	12,960	1494	169	0,011	0,010	0,011
11	13,880	13486001	1634141	97,584	98,071	97,584
12	14,717	1502	242	0,011	0,015	0,011
13	14,969	5848	870	0,042	0,052	0,042
14	15,360	20428	2930	0,148	0,176	0,148
15	15,643	2235	314	0,016	0,019	0,016
16	16,001	1598	171	0,012	0,010	0,012
17	16,213	1112	204	0,008	0,012	0,008
18	16,432	1355	194	0,010	0,012	0,010
19	17,227	1259	77	0,009	0,005	0,009
20	17,886	16321	1042	0,118	0,063	0,118
21	18,069	8883	875	0,064	0,052	0,064
22	18,443	3598	388	0,026	0,023	0,026

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	20,542	3676	332	0,027	0,020	0,027
24	23,282	1365	166	0,010	0,010	0,010
25	28,651	1168	99	0,008	0,006	0,008
26	32,864	2676	157	0,019	0,009	0,019
27	33,387	1589	78	0,012	0,005	0,012
28	34,251	4083	236	0,030	0,014	0,030
29	34,741	2398	205	0,017	0,012	0,017
30	35,040	1338	74	0,010	0,004	0,010
31	37,269	1874	114	0,014	0,007	0,014
32	39,445	2718	151	0,020	0,009	0,020
33	49,141	98824	3304	0,715	0,198	0,715
Total		13819845	1666290		100,000	100,000

HPLC determined purity of compound 5h

<Chromatogram>



<Peak Table>

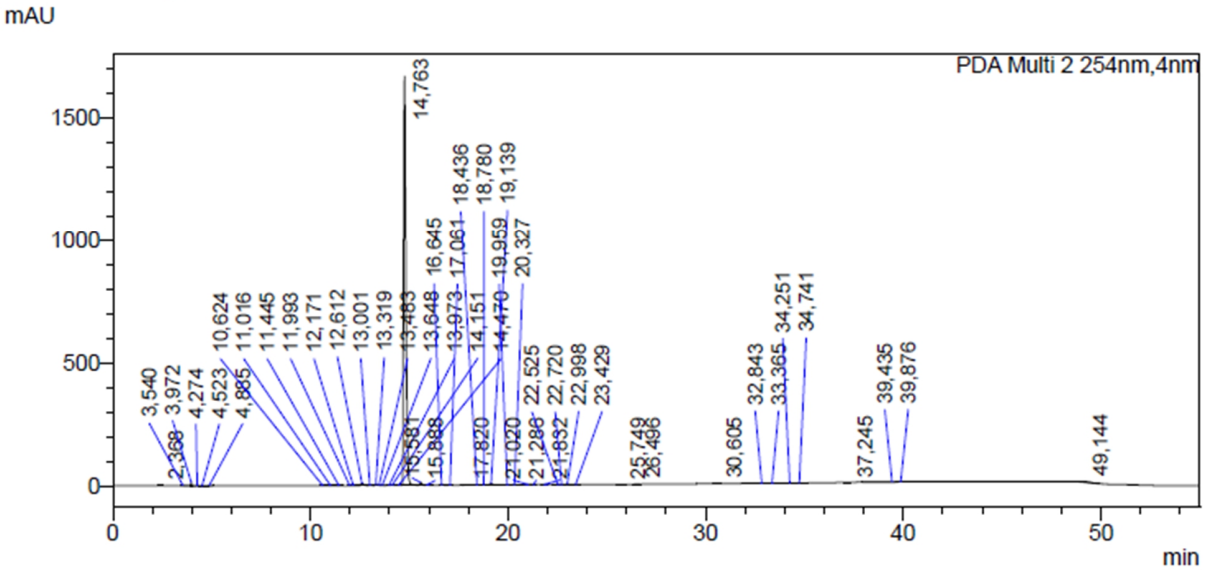
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	2,598	1452	172	0,015	0,013	0,015
2	2,837	3391	464	0,034	0,036	0,034
3	3,537	42565	2396	0,427	0,188	0,427
4	3,973	19037	7154	0,191	0,562	0,191
5	4,265	17706	727	0,178	0,057	0,178
6	7,851	11904	860	0,119	0,068	0,119
7	8,378	8151	1174	0,082	0,092	0,082
8	9,311	1208	174	0,012	0,014	0,012
9	10,469	8409	886	0,084	0,070	0,084
10	11,458	1956	163	0,020	0,013	0,020
11	12,008	15427	1882	0,155	0,148	0,155
12	12,213	1650	286	0,017	0,022	0,017
13	12,451	23441	2949	0,235	0,232	0,235
14	12,984	5488	787	0,055	0,062	0,055
15	13,627	1684	201	0,017	0,016	0,017
16	14,241	9519087	1232386	95,551	96,837	95,551
17	14,799	6710	1234	0,067	0,097	0,067
18	15,008	7059	1001	0,071	0,079	0,071
19	15,612	6559	1090	0,066	0,086	0,066
20	15,944	47319	2487	0,475	0,195	0,475
21	16,176	20778	2145	0,209	0,169	0,209
22	16,693	3874	175	0,039	0,014	0,039

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	17,291	1326	104	0,013	0,008	0,013
24	17,879	1426	164	0,014	0,013	0,014
25	18,183	1873	328	0,019	0,026	0,019
26	18,522	1611	233	0,016	0,018	0,016
27	19,044	1940	332	0,019	0,026	0,019
28	19,509	1606	115	0,016	0,009	0,016
29	20,524	7403	483	0,074	0,038	0,074
30	21,256	5878	638	0,059	0,050	0,059
31	21,773	2313	285	0,023	0,022	0,023
32	22,280	1815	249	0,018	0,020	0,018
33	22,707	3167	392	0,032	0,031	0,032
34	23,951	4622	502	0,046	0,039	0,046
35	24,361	26676	2563	0,268	0,201	0,268
36	25,607	1149	111	0,012	0,009	0,012
37	26,123	1333	92	0,013	0,007	0,013
38	26,511	2126	187	0,021	0,015	0,021
39	28,538	2490	204	0,025	0,016	0,025
40	31,933	7801	730	0,078	0,057	0,078
41	33,792	1084	75	0,011	0,006	0,011
42	34,240	3884	211	0,039	0,017	0,039
43	34,709	2012	186	0,020	0,015	0,020
44	34,944	1600	126	0,016	0,010	0,016
45	37,205	3108	287	0,031	0,023	0,031
46	39,435	5838	191	0,059	0,015	0,059
47	49,103	93327	3054	0,937	0,240	0,937
Total		9962261	1272633		100,000	100,000

HPLC determined purity of compound 5i

<Chromatogram>



<Peak Table>

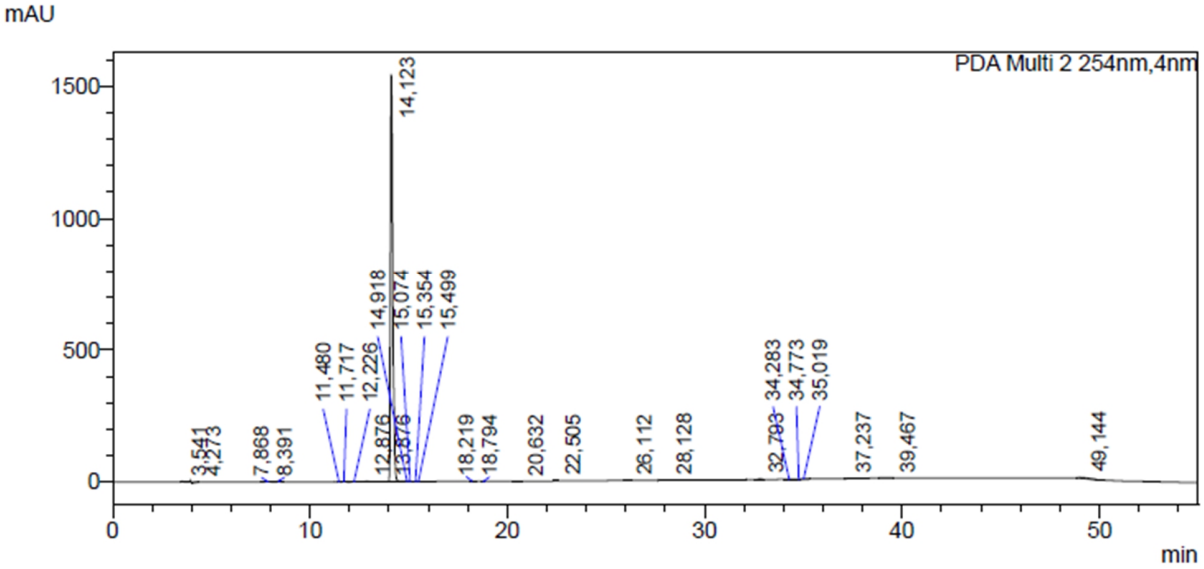
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	2,368	5743	938	0,040	0,054	0,040
2	3,540	32697	2303	0,230	0,132	0,230
3	3,972	35299	14780	0,248	0,847	0,248
4	4,274	17255	979	0,121	0,056	0,121
5	4,523	15743	684	0,111	0,039	0,111
6	4,885	1853	202	0,013	0,012	0,013
7	10,624	1576	83	0,011	0,005	0,011
8	11,016	1937	239	0,014	0,014	0,014
9	11,445	1002	78	0,007	0,004	0,007
10	11,993	3896	494	0,027	0,028	0,027
11	12,171	1466	188	0,010	0,011	0,010
12	12,612	71524	8964	0,503	0,514	0,503
13	13,001	12321	1444	0,087	0,083	0,087
14	13,319	29070	3916	0,204	0,224	0,204
15	13,483	7899	1285	0,056	0,074	0,056
16	13,648	15179	2034	0,107	0,117	0,107
17	13,973	2658	346	0,019	0,020	0,019
18	14,151	14595	1685	0,103	0,097	0,103
19	14,470	9684	883	0,068	0,051	0,068
20	14,763	13590755	1670194	95,543	95,720	95,543
21	15,581	68551	10369	0,482	0,594	0,482
22	15,888	10003	1353	0,070	0,078	0,070

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	16,645	18342	2263	0,129	0,130	0,129
24	17,061	3380	486	0,024	0,028	0,024
25	17,820	1186	126	0,008	0,007	0,008
26	18,436	5754	689	0,040	0,039	0,040
27	18,780	1295	199	0,009	0,011	0,009
28	19,139	38771	5786	0,273	0,332	0,273
29	19,959	2924	336	0,021	0,019	0,021
30	20,327	3379	256	0,024	0,015	0,024
31	21,020	2946	318	0,021	0,018	0,021
32	21,286	1048	139	0,007	0,008	0,007
33	21,832	5794	662	0,041	0,038	0,041
34	22,525	2754	274	0,019	0,016	0,019
35	22,720	1437	135	0,010	0,008	0,010
36	22,998	24777	2442	0,174	0,140	0,174
37	23,429	10214	987	0,072	0,057	0,072
38	25,749	1659	137	0,012	0,008	0,012
39	26,496	6581	674	0,046	0,039	0,046
40	30,605	3444	294	0,024	0,017	0,024
41	32,843	4792	241	0,034	0,014	0,034
42	33,365	1570	91	0,011	0,005	0,011
43	34,251	3460	203	0,024	0,012	0,024
44	34,741	2967	303	0,021	0,017	0,021
45	37,245	2587	231	0,018	0,013	0,018
46	39,435	23044	523	0,162	0,030	0,162
47	39,876	7802	349	0,055	0,020	0,055
48	49,144	92151	3276	0,648	0,188	0,648
Total		14224764	1744866		100,000	100,000

HPLC determined purity of compound 5j

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,541	15340	1974	0,117	0,126	0,117
2	4,273	21392	753	0,164	0,048	0,164
3	7,868	21799	1521	0,167	0,097	0,167
4	8,391	14411	2081	0,110	0,133	0,110
5	11,480	1130	154	0,009	0,010	0,009
6	11,717	2506	269	0,019	0,017	0,019
7	12,226	9320	1024	0,071	0,066	0,071
8	12,876	11804	1506	0,090	0,096	0,090
9	13,876	2463	336	0,019	0,021	0,019
10	14,123	12807480	1543587	98,093	98,811	98,093
11	14,918	2275	445	0,017	0,029	0,017
12	15,074	2313	408	0,018	0,026	0,018
13	15,354	1802	307	0,014	0,020	0,014
14	15,499	1478	203	0,011	0,013	0,011
15	18,219	5901	962	0,045	0,062	0,045
16	18,794	1028	152	0,008	0,010	0,008
17	20,632	2634	211	0,020	0,013	0,020
18	22,505	1817	206	0,014	0,013	0,014
19	26,112	1066	83	0,008	0,005	0,008
20	28,128	1246	122	0,010	0,008	0,010
21	32,793	18370	1653	0,141	0,106	0,141
22	34,283	3425	201	0,026	0,013	0,026

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	34,773	2257	193	0,017	0,012	0,017
24	35,019	1962	101	0,015	0,006	0,015
25	37,237	3057	279	0,023	0,018	0,023
26	39,467	3376	154	0,026	0,010	0,026
27	49,144	94836	3281	0,726	0,210	0,726
Total		13056488	1562164		100,000	100,000

HPLC determined purity of compound 5k

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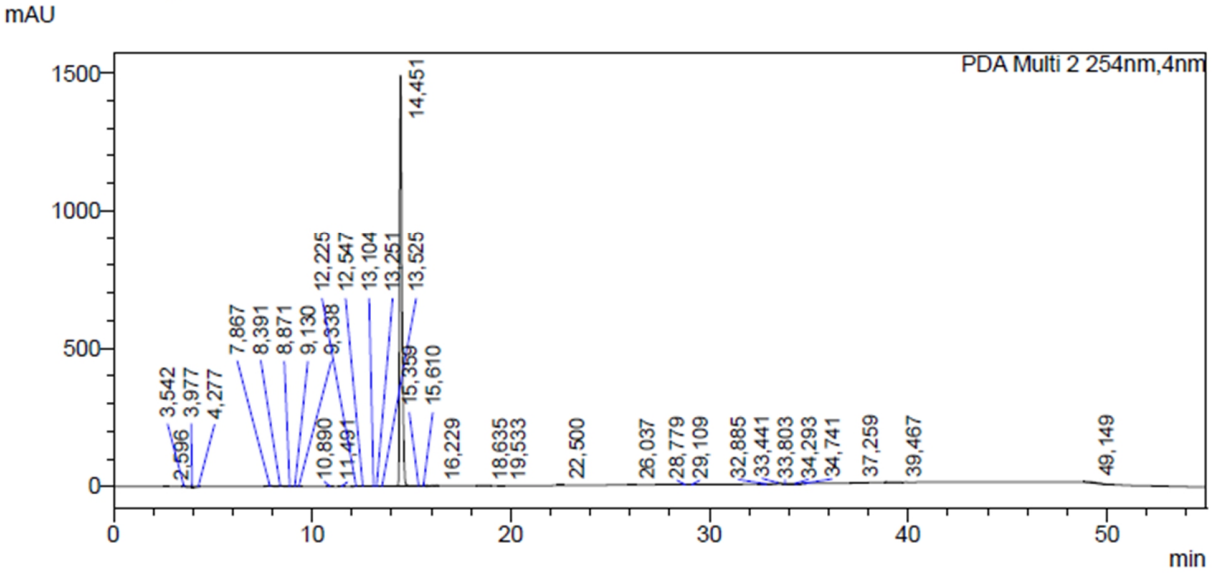

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	2,596	1092	135	0,009	0,009
2	3,542	50324	2567	0,169	0,399
3	3,977	17533	6282	0,413	0,139
4	4,277	21017	748	0,049	0,167
5	7,867	33091	2363	0,155	0,262
6	8,391	22534	3079	0,202	0,179
7	8,871	2683	370	0,024	0,021
8	9,130	1891	203	0,013	0,015
9	9,338	2308	302	0,020	0,018
10	10,890	2569	252	0,017	0,020
11	11,491	2038	287	0,019	0,016
12	12,225	3286	327	0,021	0,026
13	12,547	2479	205	0,013	0,020
14	13,104	2873	408	0,027	0,023
15	13,251	2640	353	0,023	0,021
16	13,525	4196	585	0,038	0,033
17	14,451	12266466	1491405	98,045	97,193
18	15,359	12792	1732	0,114	0,101
19	15,610	1892	246	0,016	0,015
20	16,229	1689	269	0,018	0,013
21	18,635	14165	568	0,037	0,112
22	19,533	1439	195	0,013	0,011

Peak#	Ret. Time	Area	Height	Height%	Area%
23	22,500	1741	203	0,013	0,014
24	26,037	2396	210	0,014	0,019
25	28,779	2410	150	0,010	0,019
26	29,109	1243	95	0,006	0,010
27	32,885	4043	210	0,014	0,032
28	33,441	35659	3166	0,208	0,283
29	33,803	3891	282	0,019	0,031
30	34,293	3283	192	0,013	0,026
31	34,741	1299	140	0,009	0,010
32	37,259	2570	240	0,016	0,020
33	39,467	5881	262	0,017	0,047
34	49,149	85270	3119	0,205	0,676
Total		12620682	1521150	100,000	100,000

HPLC determined purity of compound 5l

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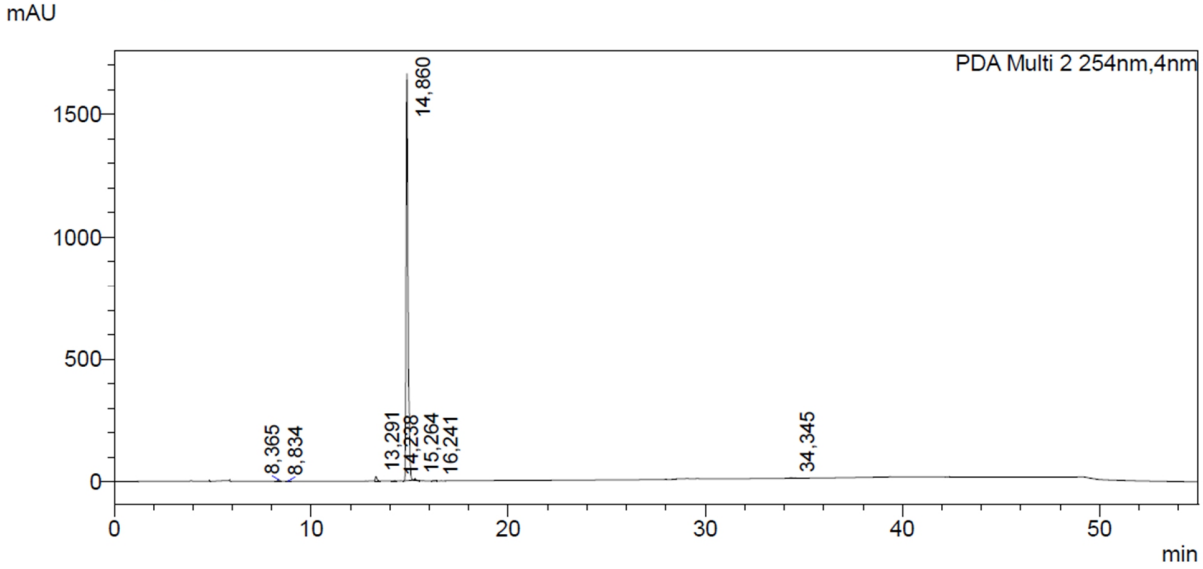


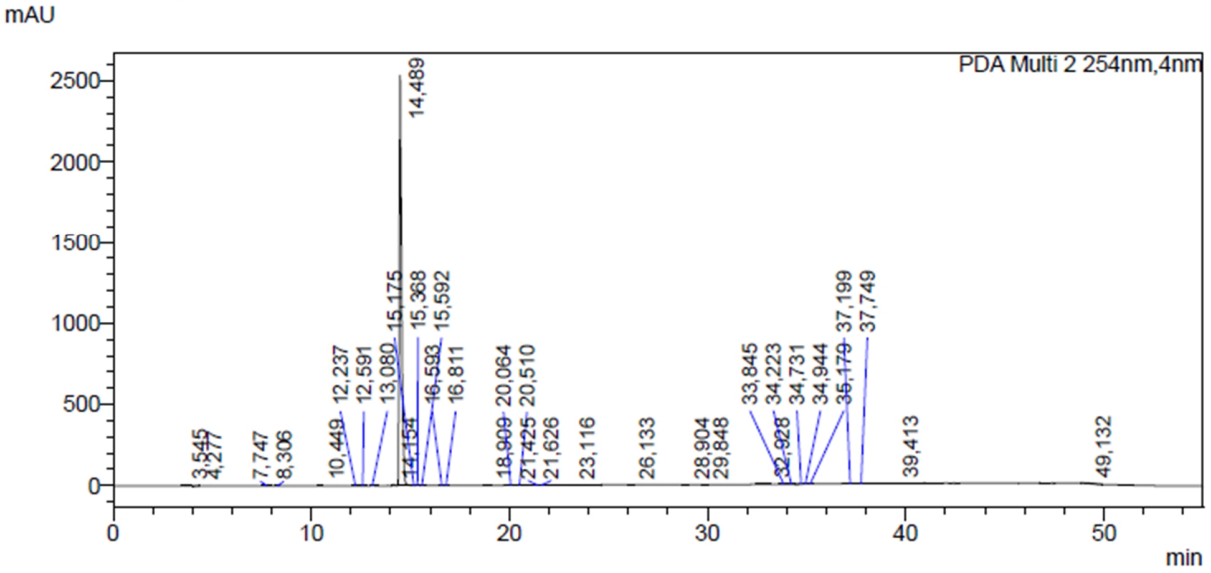
<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	8,365	45376	6107	0,360	0,385
2	8,834	8438	1131	0,067	0,072
3	13,291	113067	18907	1,114	0,959
4	14,238	7509	1154	0,068	0,064
5	14,860	11567300	1661295	97,889	98,066
6	15,264	31421	5038	0,297	0,266
7	16,241	8134	1372	0,081	0,069
8	34,345	14234	2118	0,125	0,121
Total		11795480	1697124	100,000	100,000

HPLC determined purity of compound 5m

<Chromatogram>



<Peak Table>

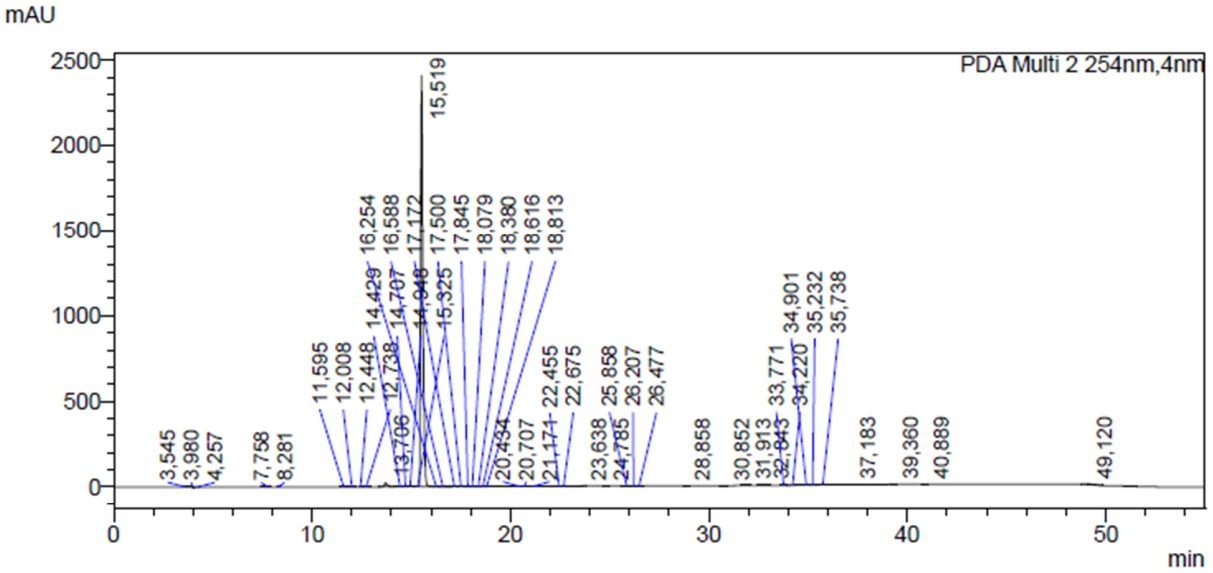
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,545	13678	1743	0,067	0,068	0,067
2	4,277	24311	911	0,119	0,036	0,119
3	7,747	3695	256	0,018	0,010	0,018
4	8,306	3056	422	0,015	0,017	0,015
5	10,449	1300	191	0,006	0,007	0,006
6	12,237	2973	351	0,015	0,014	0,015
7	12,591	2066	293	0,010	0,011	0,010
8	13,080	12068	1575	0,059	0,062	0,059
9	14,154	45489	6709	0,223	0,262	0,223
10	14,489	20089223	2533589	98,539	98,970	98,539
11	15,175	2551	484	0,013	0,019	0,013
12	15,368	25037	3795	0,123	0,148	0,123
13	15,592	8599	1336	0,042	0,052	0,042
14	16,593	4261	561	0,021	0,022	0,021
15	16,811	1391	156	0,007	0,006	0,007
16	18,909	3235	431	0,016	0,017	0,016
17	20,064	1868	166	0,009	0,006	0,009
18	20,510	2589	185	0,013	0,007	0,013
19	21,425	2974	403	0,015	0,016	0,015
20	21,626	5300	631	0,026	0,025	0,026
21	23,116	1386	146	0,007	0,006	0,007
22	26,133	1120	93	0,005	0,004	0,005

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	28,904	2969	259	0,015	0,010	0,015
24	29,848	3195	308	0,016	0,012	0,016
25	32,928	2936	149	0,014	0,006	0,014
26	33,845	2494	179	0,012	0,007	0,012
27	34,223	6426	362	0,032	0,014	0,032
28	34,731	2028	138	0,010	0,005	0,010
29	34,944	1712	157	0,008	0,006	0,008
30	35,179	1651	115	0,008	0,004	0,008
31	37,199	3360	340	0,016	0,013	0,016
32	37,749	1617	121	0,008	0,005	0,008
33	39,413	1768	117	0,009	0,005	0,009
34	49,132	98793	3279	0,485	0,128	0,485
Total		20387119	2559949		100,000	100,000

HPLC determined purity of compound 5n

<Chromatogram>



<Peak Table>

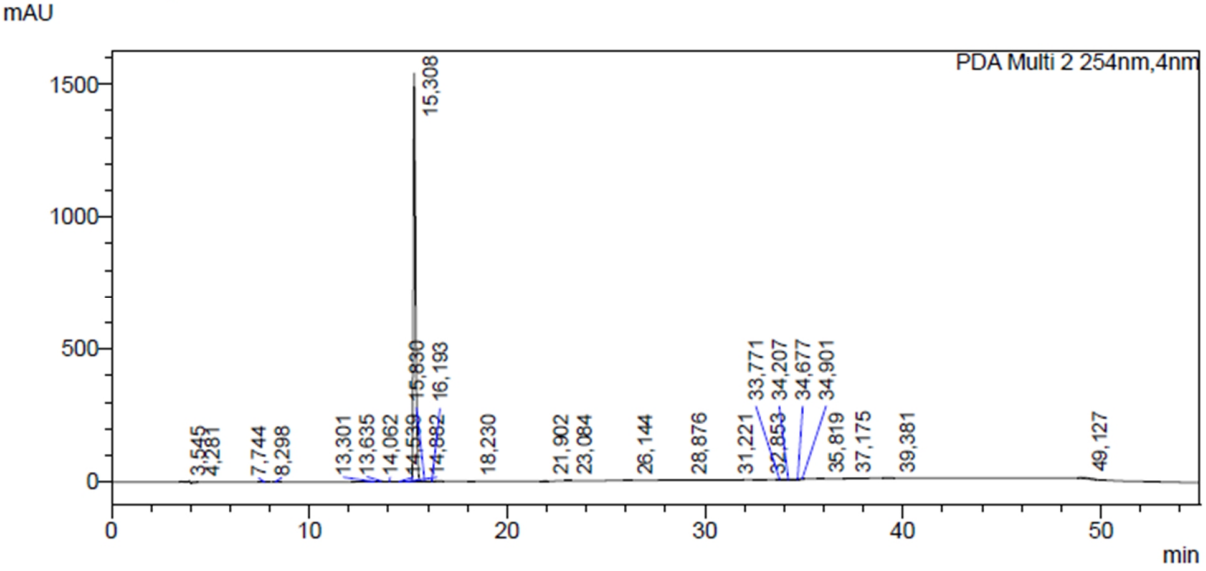
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,545	13550	1747	0,069	0,071	0,069
2	3,980	6465	4015	0,033	0,162	0,033
3	4,257	23952	1015	0,123	0,041	0,123
4	7,758	1502	94	0,008	0,004	0,008
5	8,281	1098	151	0,006	0,006	0,006
6	11,595	3401	376	0,017	0,015	0,017
7	12,008	1878	210	0,010	0,009	0,010
8	12,448	1321	107	0,007	0,004	0,007
9	12,738	3234	383	0,017	0,015	0,017
10	13,706	213344	21825	1,092	0,883	1,092
11	14,429	3801	353	0,019	0,014	0,019
12	14,707	2401	256	0,012	0,010	0,012
13	14,948	37768	4927	0,193	0,199	0,193
14	15,325	12887	2201	0,066	0,089	0,066
15	15,519	18904450	2409165	96,722	97,421	96,722
16	16,254	10411	1349	0,053	0,055	0,053
17	16,588	10815	1608	0,055	0,065	0,055
18	17,172	28298	3838	0,145	0,155	0,145
19	17,500	20748	2776	0,106	0,112	0,106
20	17,845	4122	441	0,021	0,018	0,021
21	18,079	3100	492	0,016	0,020	0,016
22	18,380	2293	141	0,012	0,006	0,012

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	18,616	1970	319	0,010	0,013	0,010
24	18,813	29531	3150	0,151	0,127	0,151
25	20,434	4325	374	0,022	0,015	0,022
26	20,707	1628	211	0,008	0,009	0,008
27	21,171	1871	220	0,010	0,009	0,010
28	22,455	2785	298	0,014	0,012	0,014
29	22,675	8522	917	0,044	0,037	0,044
30	23,638	3544	338	0,018	0,014	0,018
31	24,785	2389	264	0,012	0,011	0,012
32	25,858	11569	1052	0,059	0,043	0,059
33	26,207	2316	176	0,012	0,007	0,012
34	26,477	5590	548	0,029	0,022	0,029
35	28,858	2469	257	0,013	0,010	0,013
36	30,852	1352	117	0,007	0,005	0,007
37	31,913	6547	455	0,033	0,018	0,033
38	32,843	2892	160	0,015	0,006	0,015
39	33,771	1281	130	0,007	0,005	0,007
40	34,220	5496	309	0,028	0,012	0,028
41	34,901	3565	153	0,018	0,006	0,018
42	35,232	2417	156	0,012	0,006	0,012
43	35,738	24411	1817	0,125	0,073	0,125
44	37,183	3934	355	0,020	0,014	0,020
45	39,360	1667	155	0,009	0,006	0,009
46	40,889	1523	137	0,008	0,006	0,008
47	49,120	100719	3405	0,515	0,138	0,515
Total		19545157	2472943		100,000	100,000

HPLC determined purity of compound 5o

<Chromatogram>



<Peak Table>

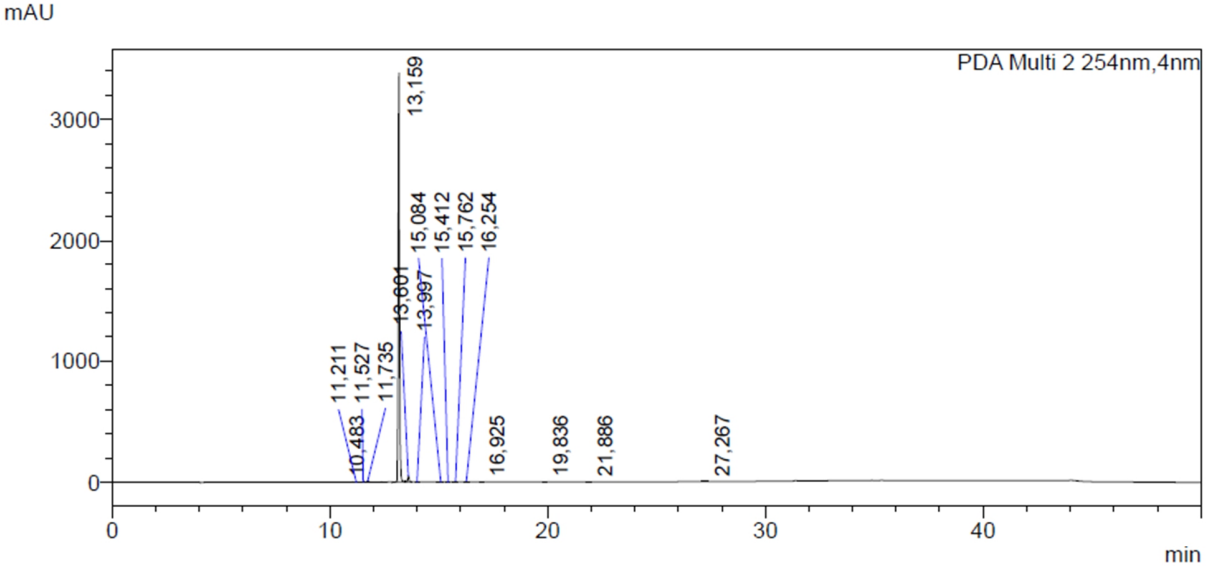
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,545	13957	1760	0,112	0,113	0,112
2	4,281	26205	973	0,209	0,063	0,209
3	7,744	4558	281	0,036	0,018	0,036
4	8,298	3894	452	0,031	0,029	0,031
5	13,301	1819	153	0,015	0,010	0,015
6	13,635	20100	2177	0,161	0,140	0,161
7	14,062	7254	983	0,058	0,063	0,058
8	14,539	1467	219	0,012	0,014	0,012
9	14,882	3602	427	0,029	0,027	0,029
10	15,308	12290732	1539513	98,228	99,006	98,228
11	15,830	10340	1691	0,083	0,109	0,083
12	16,193	1107	141	0,009	0,009	0,009
13	18,230	1159	172	0,009	0,011	0,009
14	21,902	3708	416	0,030	0,027	0,030
15	23,084	2328	267	0,019	0,017	0,019
16	26,144	1336	87	0,011	0,006	0,011
17	28,876	2696	251	0,022	0,016	0,022
18	31,221	1417	144	0,011	0,009	0,011
19	32,853	3005	165	0,024	0,011	0,024
20	33,771	1347	132	0,011	0,009	0,011
21	34,207	5619	330	0,045	0,021	0,045
22	34,677	1424	116	0,011	0,007	0,011

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	34,901	1763	147	0,014	0,009	0,014
24	35,819	1550	152	0,012	0,010	0,012
25	37,175	3874	363	0,031	0,023	0,031
26	39,381	2640	162	0,021	0,010	0,021
27	49,127	93571	3296	0,748	0,212	0,748
Total		12512472	1554966		100,000	100,000

HPLC determined purity of compound 5p

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	10,483	8864	1361	0,039	0,062
2	11,211	40132	2259	0,065	0,282
3	11,527	15688	3300	0,095	0,110
4	11,735	58383	11879	0,342	0,410
5	13,159	13738507	3380101	97,232	96,508
6	13,601	218966	49736	1,431	1,538
7	13,997	21209	3602	0,104	0,149
8	15,084	18025	3950	0,114	0,127
9	15,412	7032	1186	0,034	0,049
10	15,762	43876	5898	0,170	0,308
11	16,254	25795	6040	0,174	0,181
12	16,925	16431	3977	0,114	0,115
13	19,836	5711	1119	0,032	0,040
14	21,886	10497	985	0,028	0,074
15	27,267	6510	930	0,027	0,046
Total		14235625	3476324	100,000	100,000

HPLC determined purity of compound 5q

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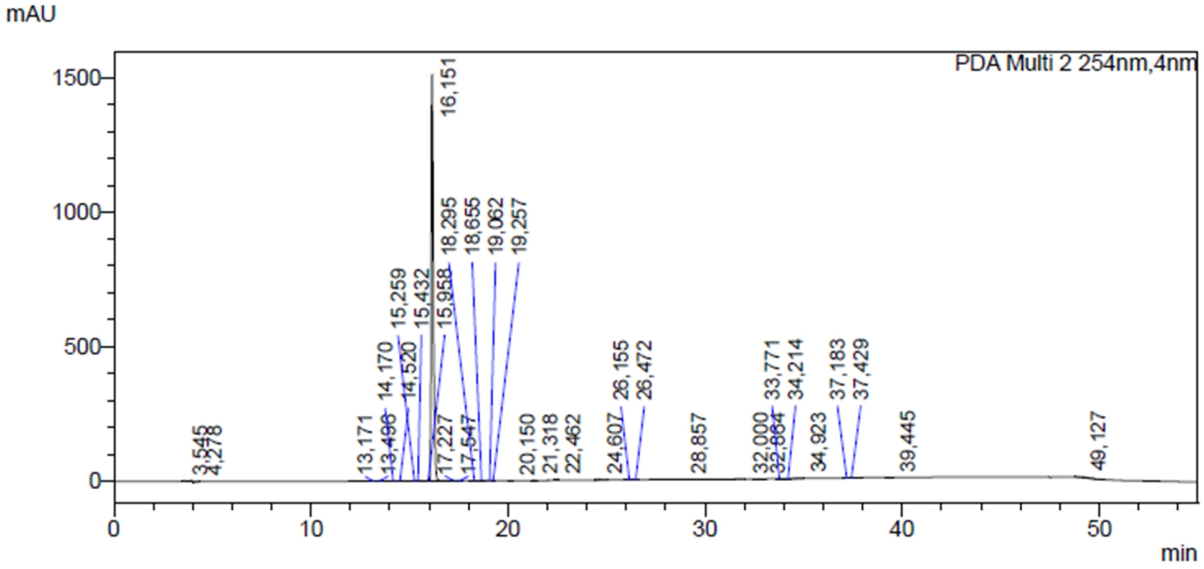

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,545	13843	1759	0,114	0,115	0,114
2	4,278	25709	936	0,212	0,061	0,212
3	13,171	1685	232	0,014	0,015	0,014
4	13,496	7889	1073	0,065	0,070	0,065
5	14,170	7403	729	0,061	0,047	0,061
6	14,520	14171	1902	0,117	0,124	0,117
7	15,259	7253	980	0,060	0,064	0,060
8	15,432	11712	1436	0,097	0,093	0,097
9	15,958	7207	1286	0,060	0,084	0,060
10	16,151	11792788	1510500	97,406	98,319	97,406
11	17,227	7220	810	0,060	0,053	0,060
12	17,547	2663	394	0,022	0,026	0,022
13	18,295	5877	729	0,049	0,047	0,049
14	18,655	9708	1364	0,080	0,089	0,080
15	19,062	4153	582	0,034	0,038	0,034
16	19,257	1133	149	0,009	0,010	0,009
17	20,150	2906	381	0,024	0,025	0,024
18	21,318	7339	1000	0,061	0,065	0,061
19	22,462	2472	317	0,020	0,021	0,020
20	24,607	42738	3985	0,353	0,259	0,353
21	26,155	1282	80	0,011	0,005	0,011
22	26,472	2701	245	0,022	0,016	0,022

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	28,857	2253	237	0,019	0,015	0,019
24	32,000	1250	23	0,010	0,001	0,010
25	32,864	3584	140	0,030	0,009	0,030
26	33,771	1294	129	0,011	0,008	0,011
27	34,214	5256	308	0,043	0,020	0,043
28	34,923	2701	129	0,022	0,008	0,022
29	37,183	4145	401	0,034	0,026	0,034
30	37,429	5602	618	0,046	0,040	0,046
31	39,445	1726	103	0,014	0,007	0,014
32	49,127	99204	3367	0,819	0,219	0,819
Total		12106871	1536323		100,000	100,000

HPLC determined purity of compound 5r

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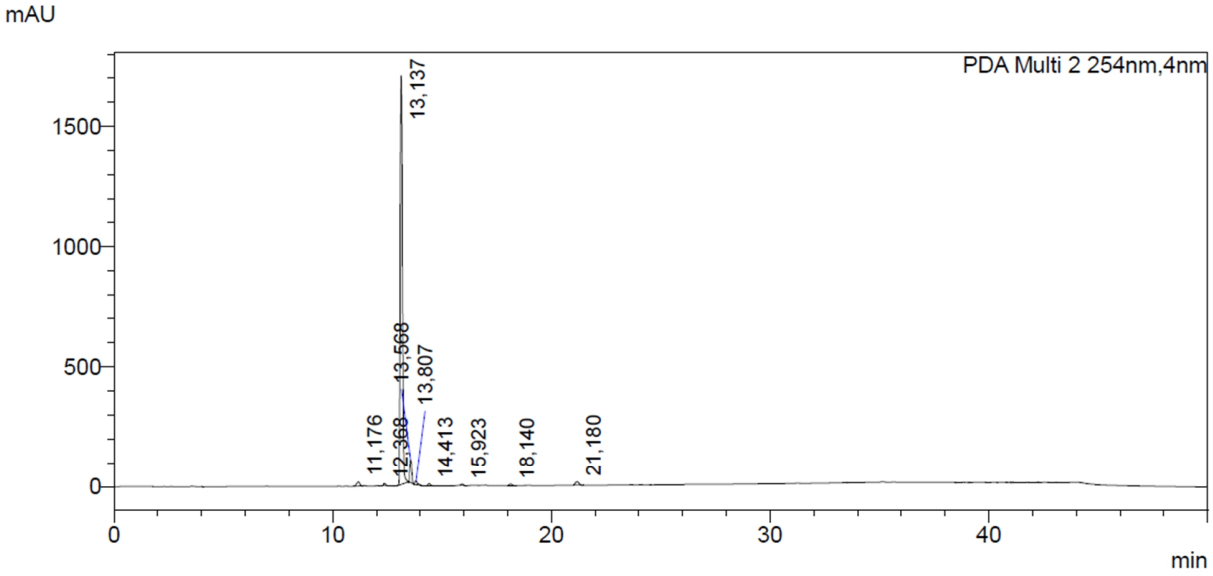

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	11,176	162052	18165	0,971	1,214
2	12,368	44250	7854	0,420	0,331
3	13,137	12124945	1701507	90,941	90,818
4	13,568	589804	95901	5,126	4,418
5	13,807	120926	14823	0,792	0,906
6	14,413	66662	8523	0,456	0,499
7	15,923	26831	4461	0,238	0,201
8	18,140	53119	5649	0,302	0,398
9	21,180	162274	14116	0,754	1,215
Total		13350862	1870998	100,000	100,000

HPLC determined purity of compound 5s

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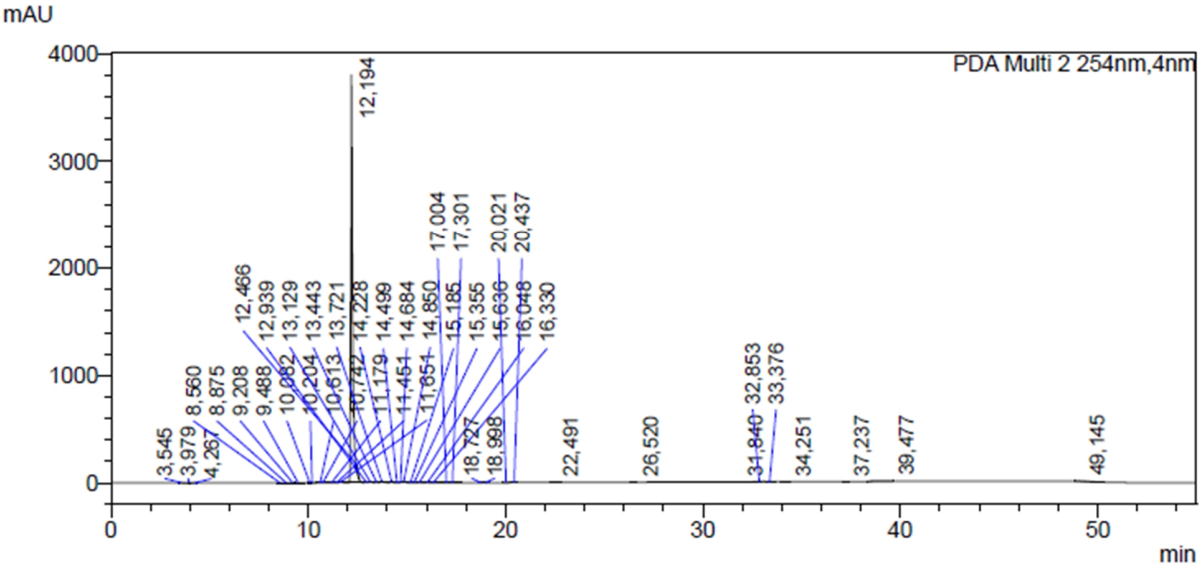

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,545	51278	2485	0,198	0,063	0,198
2	3,979	14776	6241	0,057	0,157	0,057
3	4,267	20743	827	0,080	0,021	0,080
4	8,560	6569	693	0,025	0,017	0,025
5	8,875	5615	735	0,022	0,018	0,022
6	9,208	8281	803	0,032	0,020	0,032
7	9,488	18075	2126	0,070	0,054	0,070
8	10,082	3196	455	0,012	0,011	0,012
9	10,204	5028	655	0,019	0,016	0,019
10	10,613	2983	356	0,012	0,009	0,012
11	10,742	3114	447	0,012	0,011	0,012
12	11,179	1192	124	0,005	0,003	0,005
13	11,451	10131	1173	0,039	0,030	0,039
14	11,651	90653	9171	0,350	0,231	0,350
15	12,194	24680318	3801893	95,169	95,733	95,169
16	12,466	309486	66326	1,193	1,670	1,193
17	12,939	33299	4050	0,128	0,102	0,128
18	13,129	76197	10045	0,294	0,253	0,294
19	13,443	51878	8035	0,200	0,202	0,200
20	13,721	127341	13408	0,491	0,338	0,491
21	14,228	73333	9819	0,283	0,247	0,283
22	14,499	1770	347	0,007	0,009	0,007

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	14,684	32533	5056	0,125	0,127	0,125
24	14,850	103931	13757	0,401	0,346	0,401
25	15,185	1557	264	0,006	0,007	0,006
26	15,355	3992	559	0,015	0,014	0,015
27	15,636	22393	2339	0,086	0,059	0,086
28	16,048	19240	2021	0,074	0,051	0,074
29	16,330	10375	582	0,040	0,015	0,040
30	17,004	1402	195	0,005	0,005	0,005
31	17,301	1170	92	0,005	0,002	0,005
32	18,727	4056	433	0,016	0,011	0,016
33	18,998	1071	126	0,004	0,003	0,004
34	20,021	1423	115	0,005	0,003	0,005
35	20,437	3704	399	0,014	0,010	0,014
36	22,491	7200	517	0,028	0,013	0,028
37	26,520	2213	216	0,009	0,005	0,009
38	31,840	1639	71	0,006	0,002	0,006
39	32,853	5515	253	0,021	0,006	0,021
40	33,376	1791	89	0,007	0,002	0,007
41	34,251	3274	197	0,013	0,005	0,013
42	37,237	3253	282	0,013	0,007	0,013
43	39,477	7471	201	0,029	0,005	0,029
44	49,145	98810	3382	0,381	0,085	0,381
Total		25933271	3971355		100,000	100,000

HPLC determined purity of compound 6a

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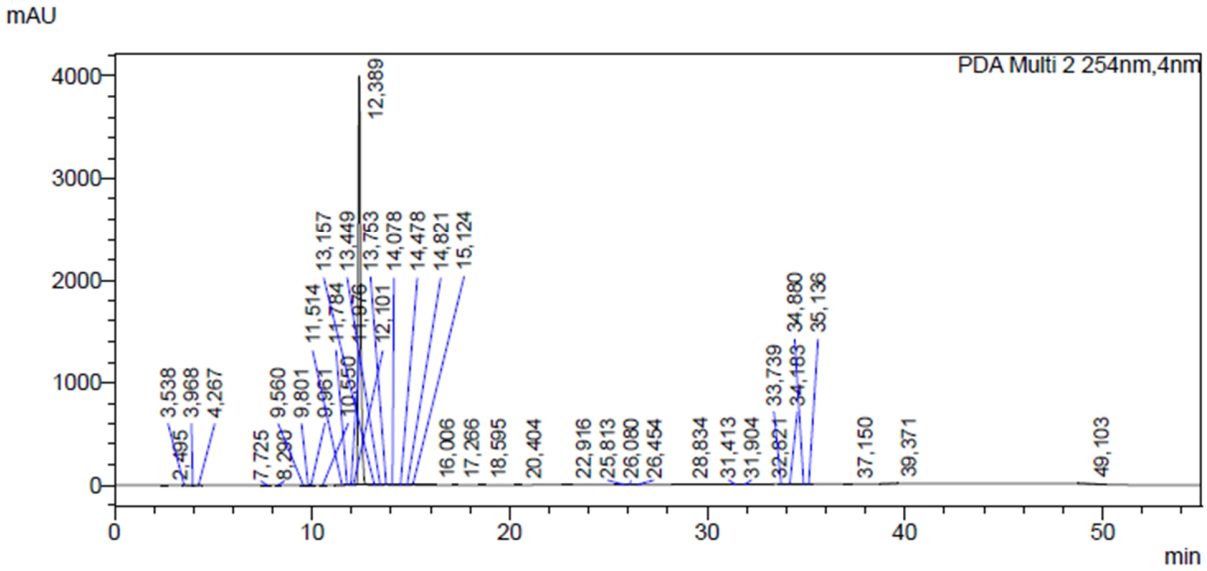

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	2,495	2278	314	0,006	0,008	0,006
2	3,538	53159	2339	0,149	0,058	0,149
3	3,968	11966	5354	0,033	0,132	0,033
4	4,267	26543	1059	0,074	0,026	0,074
5	7,725	2628	152	0,007	0,004	0,007
6	8,290	1870	235	0,005	0,006	0,005
7	9,560	1914	237	0,005	0,006	0,005
8	9,801	7460	916	0,021	0,023	0,021
9	9,961	10459	1333	0,029	0,033	0,029
10	10,550	2977	346	0,008	0,009	0,008
11	11,514	6070	405	0,017	0,010	0,017
12	11,784	59502	8068	0,166	0,199	0,166
13	11,976	19222	2853	0,054	0,070	0,054
14	12,101	14760	1985	0,041	0,049	0,041
15	12,389	35168954	3999084	98,349	98,460	98,349
16	13,157	3694	580	0,010	0,014	0,010
17	13,449	24327	3685	0,068	0,091	0,068
18	13,753	75484	9446	0,211	0,233	0,211
19	14,078	3236	411	0,009	0,010	0,009
20	14,478	7454	748	0,021	0,018	0,021
21	14,821	1188	196	0,003	0,005	0,003
22	15,124	94424	14158	0,264	0,349	0,264

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	16,006	5881	697	0,016	0,017	0,016
24	17,266	1610	222	0,005	0,005	0,005
25	18,595	2251	279	0,006	0,007	0,006
26	20,404	2212	202	0,006	0,005	0,006
27	22,916	6869	673	0,019	0,017	0,019
28	25,813	1372	85	0,004	0,002	0,004
29	26,080	1156	105	0,003	0,003	0,003
30	26,454	2001	193	0,006	0,005	0,006
31	28,834	3022	278	0,008	0,007	0,008
32	31,413	1249	60	0,003	0,001	0,003
33	31,904	1004	37	0,003	0,001	0,003
34	32,821	2999	158	0,008	0,004	0,008
35	33,739	1378	143	0,004	0,004	0,004
36	34,183	5906	330	0,017	0,008	0,017
37	34,880	3700	158	0,010	0,004	0,010
38	35,136	1384	90	0,004	0,002	0,004
39	37,150	4586	418	0,013	0,010	0,013
40	39,371	5261	215	0,015	0,005	0,015
41	49,103	105979	3402	0,296	0,084	0,296
Total		35759393	4061647		100,000	100,000

HPLC determined purity of compound 6b

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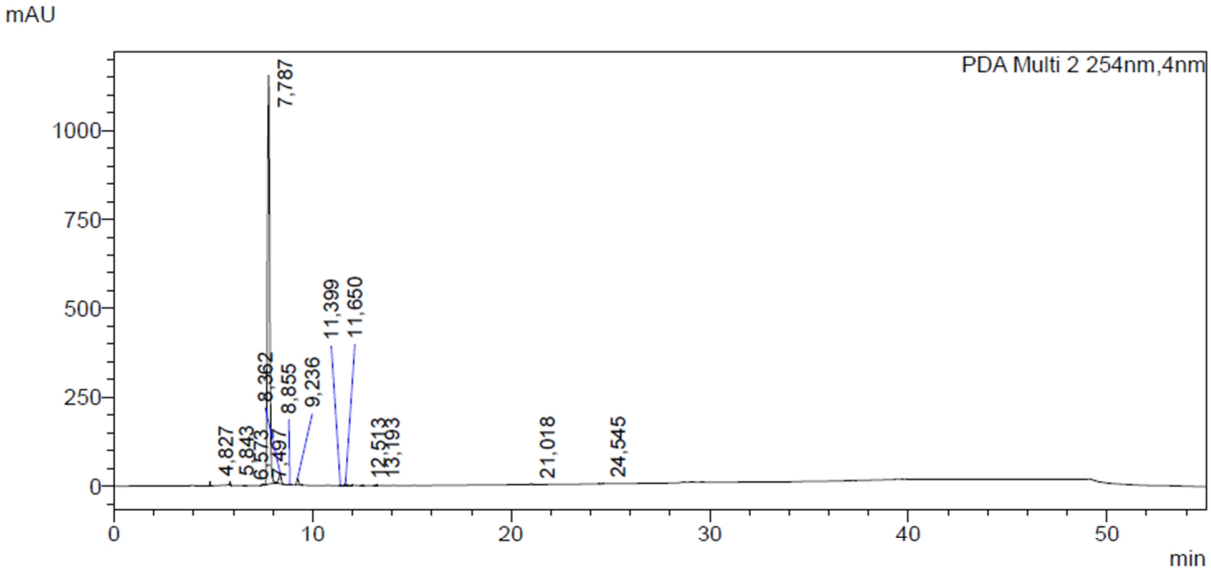

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	4,827	25773	12016	0,972	0,261
2	5,843	22994	10552	0,854	0,233
3	6,573	9188	1274	0,103	0,093
4	7,497	14131	2085	0,169	0,143
5	7,787	9313930	1148618	92,934	94,467
6	8,362	254509	30955	2,505	2,581
7	8,855	8173	1456	0,118	0,083
8	9,236	130720	18462	1,494	1,326
9	11,399	6445	1017	0,082	0,065
10	11,650	38319	4675	0,378	0,389
11	12,513	10519	1422	0,115	0,107
12	13,193	11001	1672	0,135	0,112
13	21,018	8804	1138	0,092	0,089
14	24,545	4919	610	0,049	0,050
Total		9859425	1235952	100,000	100,000

HPLC determined purity of compound 7a

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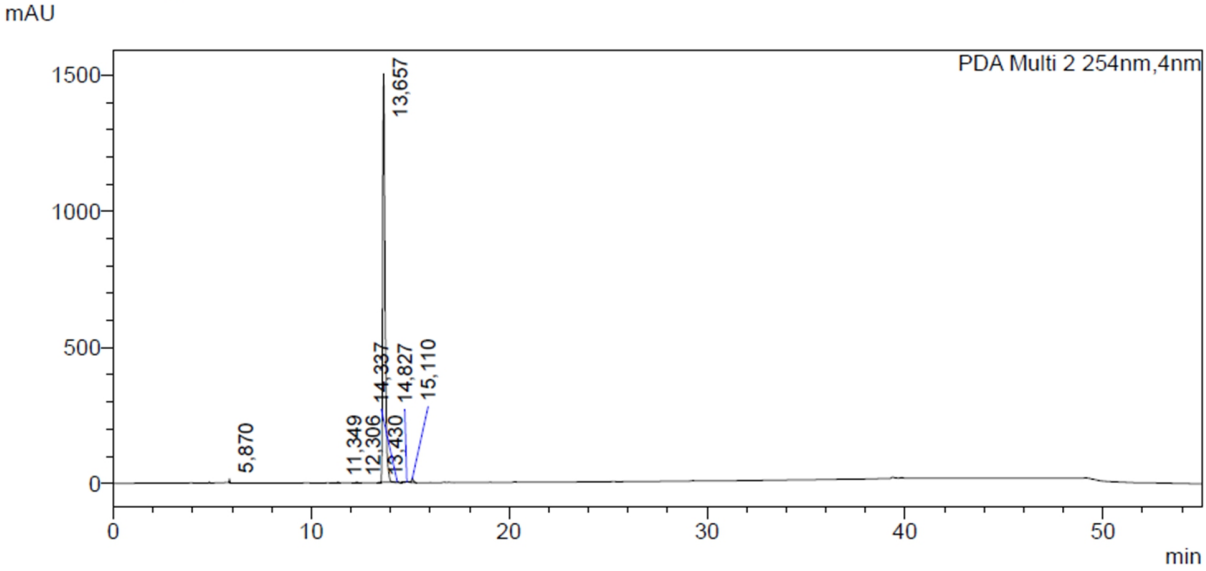

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	5,870	30035	16000	1,036	0,239
2	11,349	41419	3617	0,234	0,329
3	12,306	39298	3914	0,253	0,312
4	13,430	11134	1909	0,124	0,088
5	13,657	12327961	1499389	97,073	97,899
6	14,337	25391	3111	0,201	0,202
7	14,827	35554	3111	0,201	0,282
8	15,110	81796	13541	0,877	0,650
Total		12592588	1544592	100,000	100,000

HPLC determined purity of compound 7b

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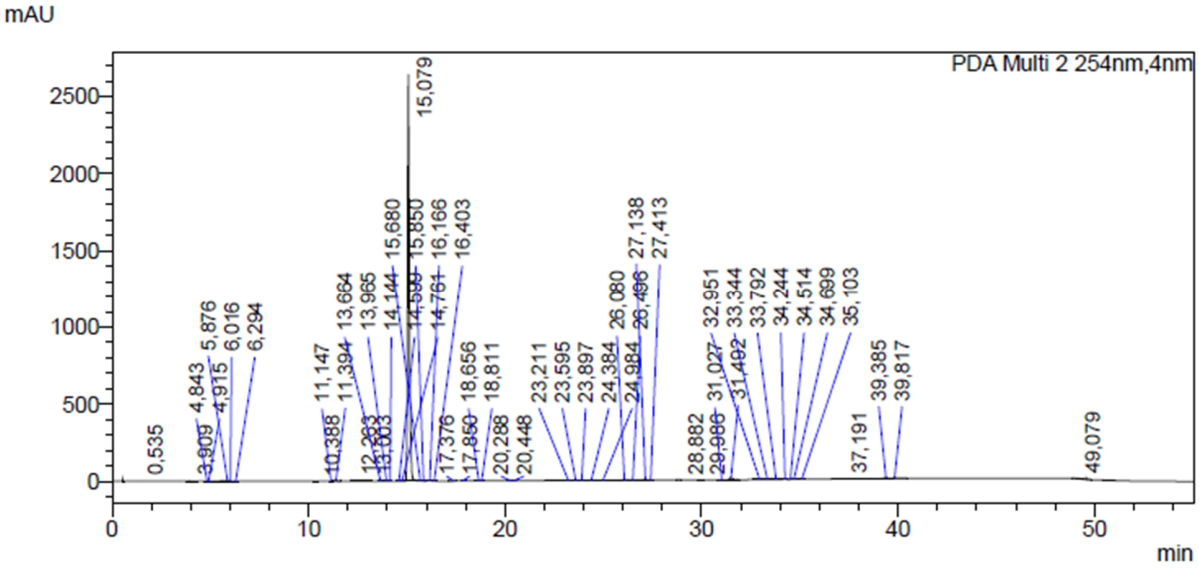


<Peak Table>

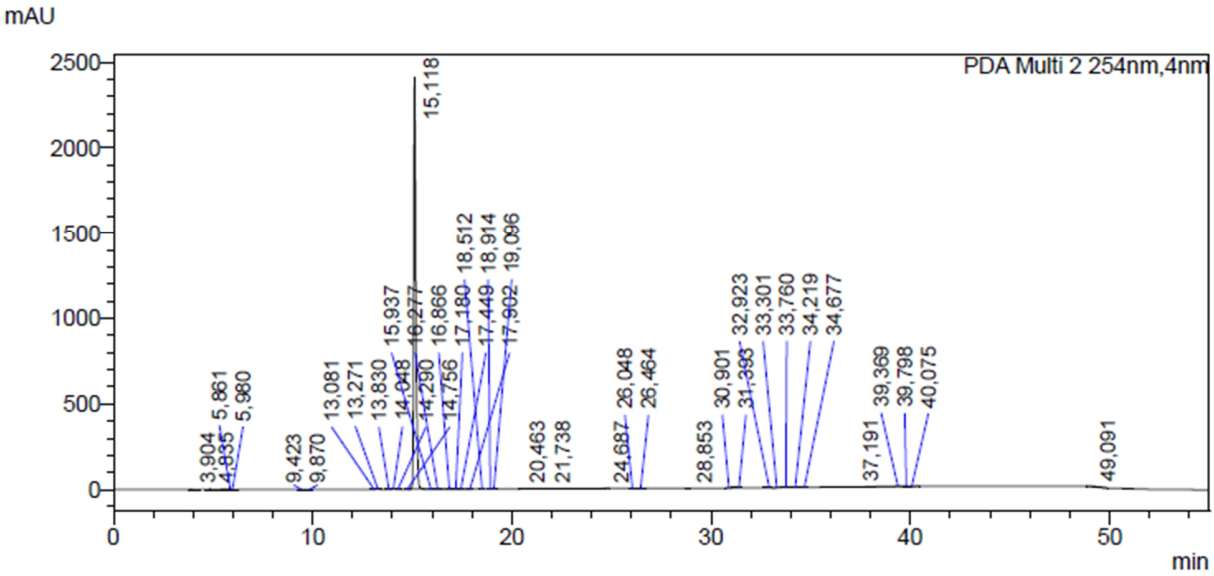
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	0,535	8332	8082	0,297	0,047
2	3,909	21837	2660	0,098	0,122
3	4,843	4774	1820	0,067	0,027
4	4,915	3199	657	0,024	0,018
5	5,876	162209	10512	0,386	0,906
6	6,016	15258	1250	0,046	0,085
7	6,294	7231	547	0,020	0,040
8	10,388	1236	164	0,006	0,007
9	11,147	2734	412	0,015	0,015
10	11,394	46651	6979	0,256	0,260
11	12,263	5739	848	0,031	0,032
12	13,003	13048	1130	0,042	0,073
13	13,664	5911	879	0,032	0,033
14	13,965	6507	1101	0,040	0,036
15	14,144	3896	607	0,022	0,022
16	14,599	5640	860	0,032	0,031
17	14,761	3258	477	0,018	0,018
18	15,079	17014379	2640710	96,990	94,999
19	15,680	9039	1794	0,066	0,050
20	15,850	3309	744	0,027	0,018
21	16,166	32258	3281	0,120	0,180

Peak#	Ret. Time	Area	Height	Height%	Area%
22	16,403	2747	504	0,019	0,015
23	17,376	1316	84	0,003	0,007
24	17,850	3836	554	0,020	0,021
25	18,656	3436	259	0,010	0,019
26	18,811	2068	209	0,008	0,012
27	20,288	1979	209	0,008	0,011
28	20,448	2126	234	0,009	0,012
29	23,211	2355	163	0,006	0,013
30	23,595	1145	84	0,003	0,006
31	23,897	7434	853	0,031	0,042
32	24,384	2238	197	0,007	0,012
33	24,984	1351	166	0,006	0,008
34	26,080	2077	173	0,006	0,012
35	26,496	5116	241	0,009	0,029
36	27,138	48472	5289	0,194	0,271
37	27,413	3239	377	0,014	0,018
38	28,882	1863	194	0,007	0,010
39	29,986	7914	914	0,034	0,044
40	31,027	4126	321	0,012	0,023
41	31,492	137782	12961	0,476	0,769
42	32,951	7786	490	0,018	0,043
43	33,344	2927	139	0,005	0,016
44	33,792	1381	135	0,005	0,008
45	34,244	7722	446	0,016	0,043
46	34,514	3184	307	0,011	0,018
47	34,699	3291	251	0,009	0,018
48	35,103	5687	580	0,021	0,032
49	37,191	7886	596	0,022	0,044
50	39,385	120222	4973	0,183	0,671
51	39,817	48221	2664	0,098	0,269
52	49,079	82683	2581	0,095	0,462
Total		17910053	2722661	100,000	100,000

HPLC determined purity of compound 8a

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,904	22010	2693	0,121	0,109	0,121
2	4,835	9502	2681	0,052	0,109	0,052
3	5,861	136431	10111	0,752	0,411	0,752
4	5,980	8619	734	0,047	0,030	0,047
5	9,423	3986	586	0,022	0,024	0,022
6	9,870	1218	195	0,007	0,008	0,007
7	13,081	1584	196	0,009	0,008	0,009
8	13,271	34309	5476	0,189	0,223	0,189
9	13,830	1372	140	0,008	0,006	0,008
10	14,048	28060	4071	0,155	0,166	0,155
11	14,290	6076	983	0,033	0,040	0,033
12	14,756	1850	350	0,010	0,014	0,010
13	15,118	17515941	2410482	96,511	97,991	96,511
14	15,937	3055	584	0,017	0,024	0,017
15	16,277	4937	725	0,027	0,029	0,027
16	16,866	3843	646	0,021	0,026	0,021
17	17,180	8286	1177	0,046	0,048	0,046
18	17,449	3938	351	0,022	0,014	0,022
19	17,902	1002	141	0,006	0,006	0,006
20	18,512	2609	417	0,014	0,017	0,014
21	18,914	1016	147	0,006	0,006	0,006
22	19,096	5928	979	0,033	0,040	0,033

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	20,463	3144	351	0,017	0,014	0,017
24	21,738	3456	318	0,019	0,013	0,019
25	24,687	5014	521	0,028	0,021	0,028
26	26,048	2274	178	0,013	0,007	0,013
27	26,464	2853	166	0,016	0,007	0,016
28	28,853	1506	192	0,008	0,008	0,008
29	30,901	2135	190	0,012	0,008	0,012
30	31,393	5408	403	0,030	0,016	0,030
31	32,923	6875	459	0,038	0,019	0,038
32	33,301	3282	142	0,018	0,006	0,018
33	33,760	1246	140	0,007	0,006	0,007
34	34,219	8283	467	0,046	0,019	0,046
35	34,677	2921	200	0,016	0,008	0,016
36	37,191	6680	567	0,037	0,023	0,037
37	39,369	121316	4882	0,668	0,198	0,668
38	39,798	40651	2635	0,224	0,107	0,224
39	40,075	12775	991	0,070	0,040	0,070
40	49,091	113708	3248	0,627	0,132	0,627
Total		18149098	2459913		100,000	100,000

HPLC determined purity of compound 8b

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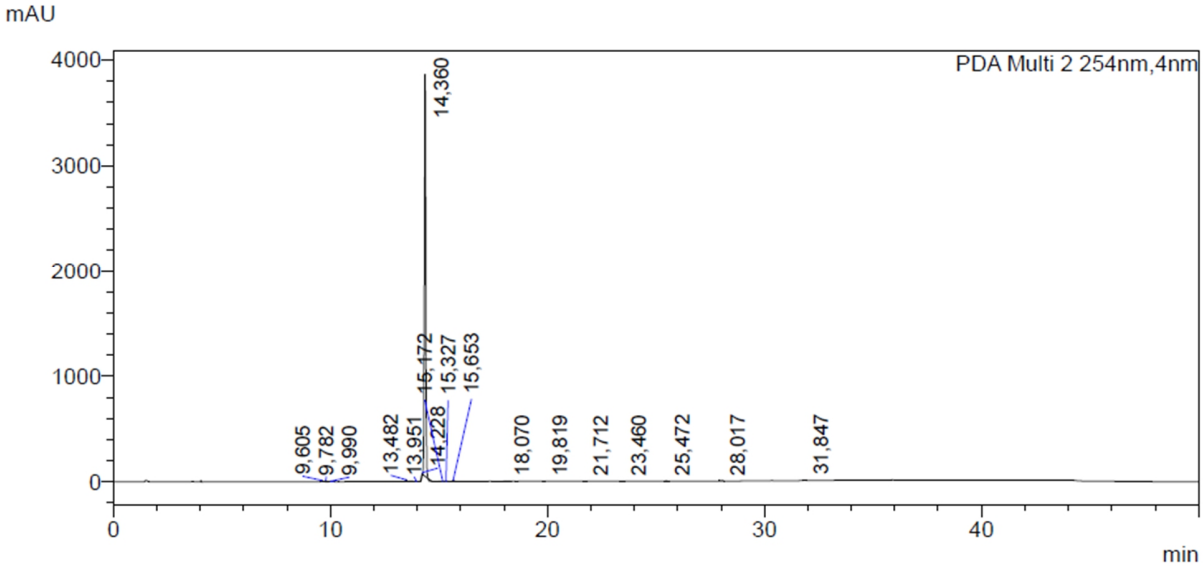

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	9,605	70886	14299	0,365	0,413
2	9,782	32395	8655	0,221	0,189
3	9,990	27881	3214	0,082	0,162
4	13,482	118948	17050	0,435	0,693
5	13,951	15286	3057	0,078	0,089
6	14,228	29279	13463	0,344	0,171
7	14,360	16620292	3813811	97,400	96,849
8	15,172	26622	6304	0,161	0,155
9	15,327	10273	2202	0,056	0,060
10	15,653	67219	13990	0,357	0,392
11	18,070	11093	2926	0,075	0,065
12	19,819	8146	1644	0,042	0,047
13	21,712	5728	1409	0,036	0,033
14	23,460	30368	3634	0,093	0,177
15	25,472	40082	3698	0,094	0,234
16	28,017	17035	2407	0,061	0,099
17	31,847	29480	3843	0,098	0,172
Total		17161011	3915605	100,000	100,000

HPLC determined purity of compound 8c

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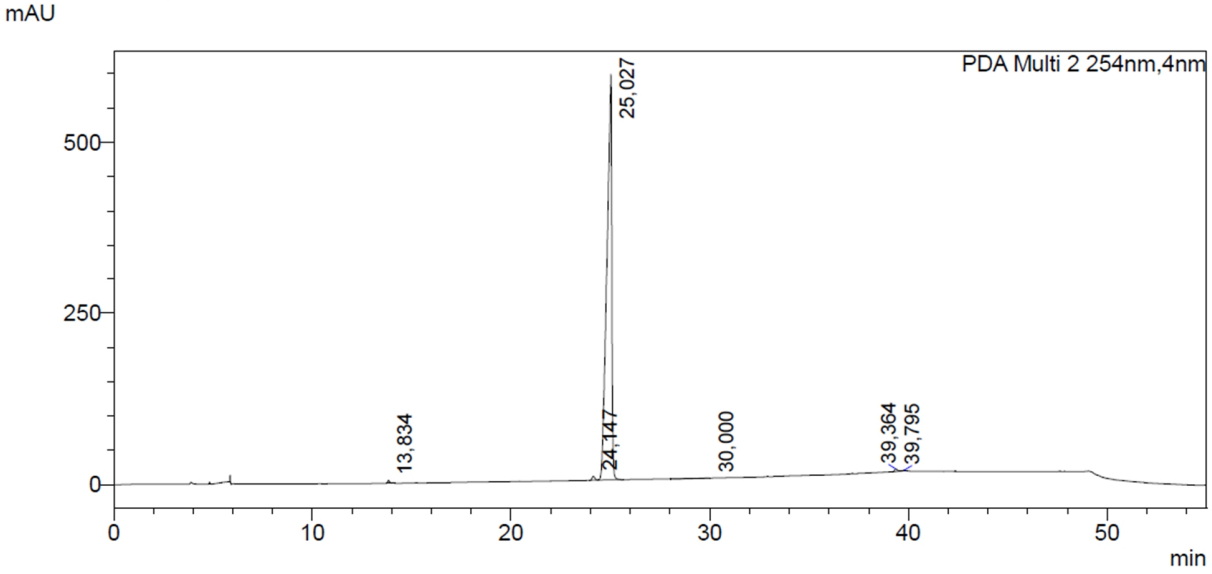

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	13,834	33057	4440	0,732	0,324
2	24,147	54784	5746	0,947	0,536
3	25,027	10067019	591373	97,491	98,550
4	30,000	11728	0	0,000	0,115
5	39,364	37837	3769	0,621	0,370
6	39,795	10695	1265	0,209	0,105
Total		10215121	606593	100,000	100,000

HPLC determined purity of compound 8d

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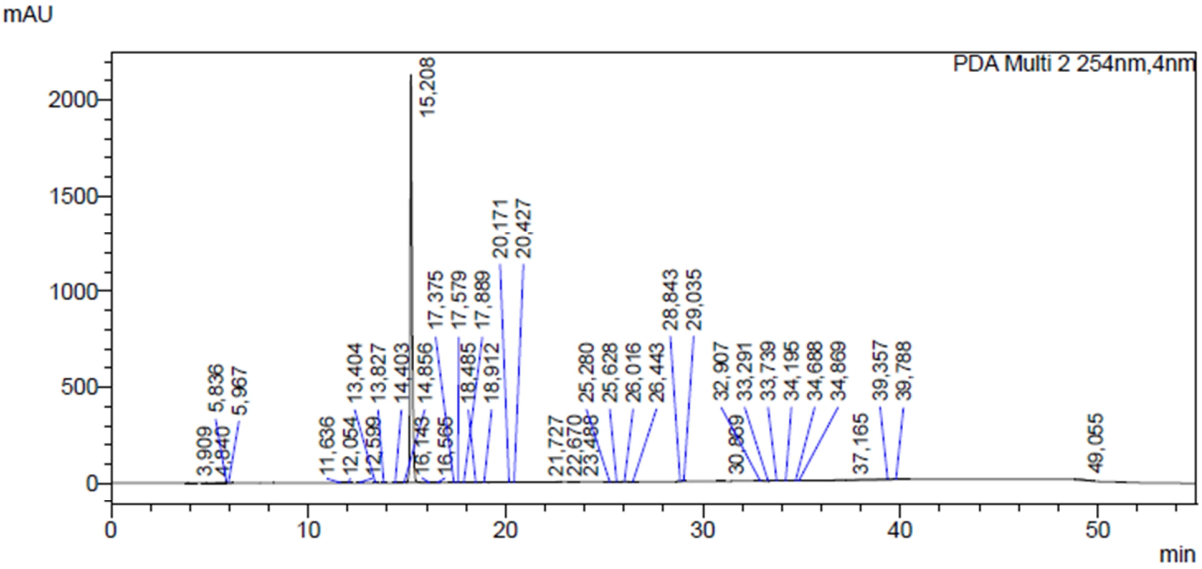


<Peak Table>

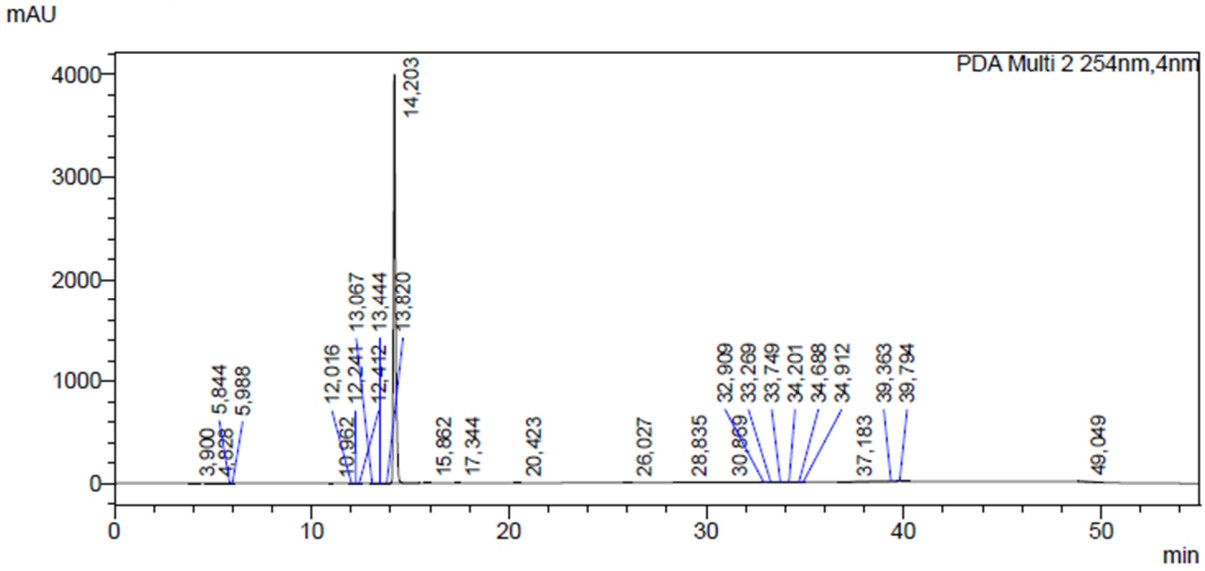
PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,909	21722	2658	0,140	0,122	0,140
2	4,840	11601	3209	0,075	0,148	0,075
3	5,836	149123	13357	0,962	0,615	0,962
4	5,967	9135	925	0,059	0,043	0,059
5	11,636	2083	304	0,013	0,014	0,013
6	12,054	1764	257	0,011	0,012	0,011
7	12,599	8810	1373	0,057	0,063	0,057
8	13,404	7976	1238	0,051	0,057	0,051
9	13,827	2351	362	0,015	0,017	0,015
10	14,403	1642	285	0,011	0,013	0,011
11	14,856	4077	422	0,026	0,019	0,026
12	15,208	14935388	2130177	96,374	98,092	96,374
13	16,143	2816	291	0,018	0,013	0,018
14	16,565	1430	267	0,009	0,012	0,009
15	17,375	2347	208	0,015	0,010	0,015
16	17,579	1561	151	0,010	0,007	0,010
17	17,889	1630	185	0,011	0,008	0,011
18	18,485	1707	125	0,011	0,006	0,011
19	18,912	4347	223	0,028	0,010	0,028
20	20,171	1010	91	0,007	0,004	0,007
21	20,427	3679	352	0,024	0,016	0,024
22	21,727	1364	208	0,009	0,010	0,009

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	22,670	7899	921	0,051	0,042	0,051
24	23,488	1354	68	0,009	0,003	0,009
25	25,280	1233	80	0,008	0,004	0,008
26	25,628	8962	828	0,058	0,038	0,058
27	26,016	2495	199	0,016	0,009	0,016
28	26,443	3261	166	0,021	0,008	0,021
29	28,843	2772	286	0,018	0,013	0,018
30	29,035	1047	114	0,007	0,005	0,007
31	30,869	1995	176	0,013	0,008	0,013
32	32,907	6470	430	0,042	0,020	0,042
33	33,291	2892	144	0,019	0,007	0,019
34	33,739	2067	150	0,013	0,007	0,013
35	34,195	8503	473	0,055	0,022	0,055
36	34,688	2867	189	0,018	0,009	0,018
37	34,869	1791	153	0,012	0,007	0,012
38	37,165	9426	671	0,061	0,031	0,061
39	39,357	123552	4767	0,797	0,220	0,797
40	39,788	48483	2543	0,313	0,117	0,313
41	49,055	82711	2590	0,534	0,119	0,534
Total		15497340	2171615		100,000	100,000

HPLC determined purity of compound 9a

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,900	21549	2630	0,070	0,065	0,070
2	4,828	9835	2920	0,032	0,072	0,032
3	5,844	147722	13055	0,478	0,324	0,478
4	5,988	6481	716	0,021	0,018	0,021
5	10,962	1361	204	0,004	0,005	0,004
6	12,016	2000	210	0,006	0,005	0,006
7	12,241	3140	492	0,010	0,012	0,010
8	12,412	1141	184	0,004	0,005	0,004
9	13,067	1564	70	0,005	0,002	0,005
10	13,444	1123	152	0,004	0,004	0,004
11	13,820	4508	686	0,015	0,017	0,015
12	14,203	30441488	3997565	98,515	99,160	98,515
13	15,862	2016	238	0,007	0,006	0,007
14	17,344	1215	106	0,004	0,003	0,004
15	20,423	2071	214	0,007	0,005	0,007
16	26,027	1991	166	0,006	0,004	0,006
17	28,835	1611	207	0,005	0,005	0,005
18	30,869	1700	175	0,006	0,004	0,006
19	32,909	6892	458	0,022	0,011	0,022
20	33,269	3063	166	0,010	0,004	0,010
21	33,749	1180	142	0,004	0,004	0,004
22	34,201	8298	469	0,027	0,012	0,027

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	34,688	2944	188	0,010	0,005	0,010
24	34,912	1098	102	0,004	0,003	0,004
25	37,183	8032	603	0,026	0,015	0,026
26	39,363	106910	4634	0,346	0,115	0,346
27	39,794	41194	2377	0,133	0,059	0,133
28	49,049	68335	2302	0,221	0,057	0,221
Total		30900462	4031432		100,000	100,000

HPLC determined purity of compound 9b

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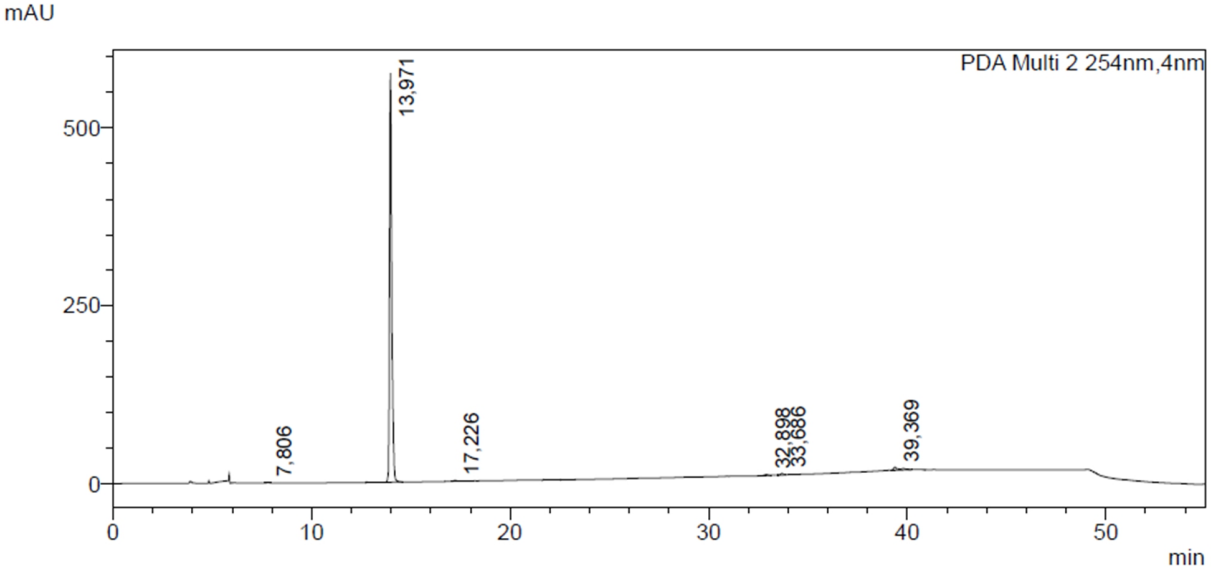


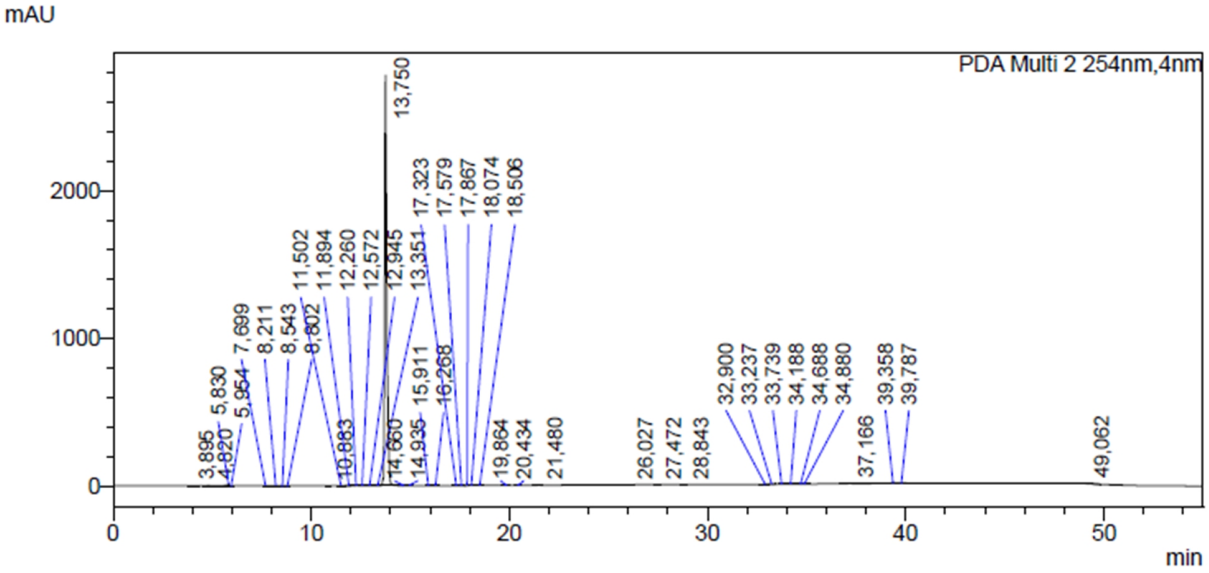
<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	7,806	4667	757	0,130	0,100
2	13,971	4525060	574241	98,341	97,060
3	17,226	12285	1436	0,246	0,263
4	32,898	15010	1290	0,221	0,322
5	33,686	21105	1999	0,342	0,453
6	39,369	84018	4204	0,720	1,802
Total		4662145	583928	100,000	100,000

HPLC determined purity of compound 9c

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	3,895	21960	2639	0,104	0,093	0,104
2	4,820	13553	3872	0,064	0,137	0,064
3	5,830	138709	14363	0,654	0,508	0,654
4	5,954	4733	601	0,022	0,021	0,022
5	7,699	6263	684	0,030	0,024	0,030
6	8,211	5709	695	0,027	0,025	0,027
7	8,543	1397	125	0,007	0,004	0,007
8	8,802	1081	136	0,005	0,005	0,005
9	10,883	1364	132	0,006	0,005	0,006
10	11,502	6233	904	0,029	0,032	0,029
11	11,894	2735	375	0,013	0,013	0,013
12	12,260	26790	3536	0,126	0,125	0,126
13	12,572	1184	158	0,006	0,006	0,006
14	12,945	4676	513	0,022	0,018	0,022
15	13,351	3402	512	0,016	0,018	0,016
16	13,750	20611382	2777050	97,146	98,224	97,146
17	14,660	3267	552	0,015	0,020	0,015
18	14,935	10220	1677	0,048	0,059	0,048
19	15,911	4571	573	0,022	0,020	0,022
20	16,268	3421	202	0,016	0,007	0,016
21	17,323	2238	132	0,011	0,005	0,011
22	17,579	1081	130	0,005	0,005	0,005

Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
23	17,867	1994	201	0,009	0,007	0,009
24	18,074	14536	2226	0,069	0,079	0,069
25	18,506	4912	479	0,023	0,017	0,023
26	19,864	4521	507	0,021	0,018	0,021
27	20,434	2539	261	0,012	0,009	0,012
28	21,480	8038	942	0,038	0,033	0,038
29	26,027	1784	172	0,008	0,006	0,008
30	27,472	4953	545	0,023	0,019	0,023
31	28,843	1724	203	0,008	0,007	0,008
32	32,900	7069	446	0,033	0,016	0,033
33	33,237	2214	158	0,010	0,006	0,010
34	33,739	1189	145	0,006	0,005	0,006
35	34,188	8775	490	0,041	0,017	0,041
36	34,688	3440	225	0,016	0,008	0,016
37	34,880	2202	155	0,010	0,005	0,010
38	37,166	9101	669	0,043	0,024	0,043
39	39,358	118272	4639	0,557	0,164	0,557
40	39,787	44522	2456	0,210	0,087	0,210
41	49,062	99150	2776	0,467	0,098	0,467
Total		21216902	2827255		100,000	100,000

HPLC determined purity of compound 9d

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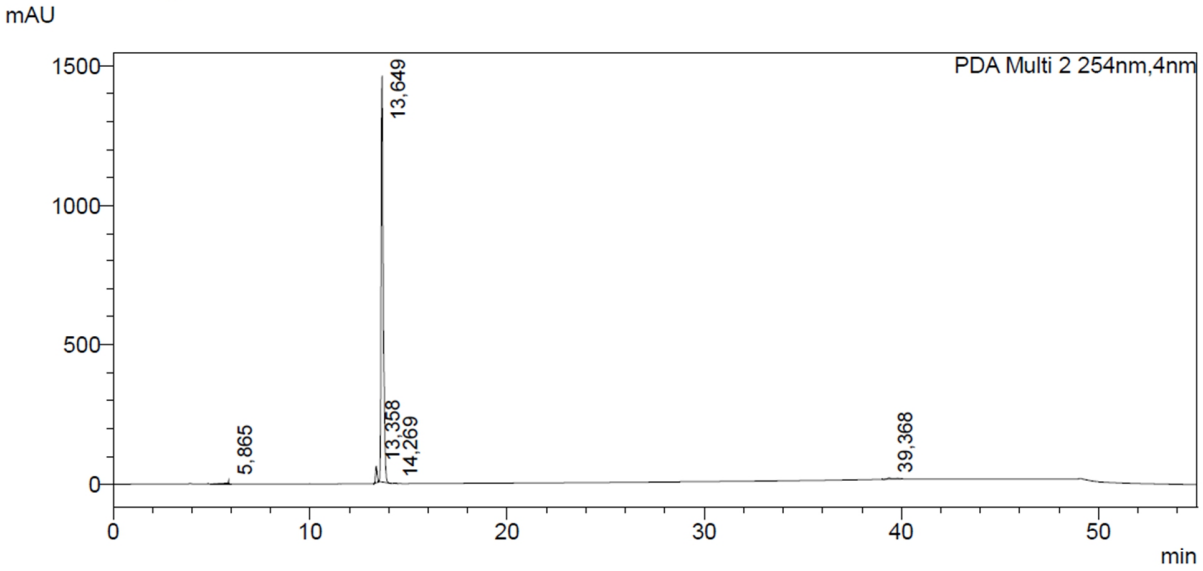

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	5,865	119788	12383	0,808	1,024
2	13,358	341003	59373	3,875	2,914
3	13,649	11155650	1454774	94,936	95,325
4	14,269	9997	1686	0,110	0,085
5	39,368	76321	4155	0,271	0,652
Total		11702760	1532373	100,000	100,000

HPLC determined purity of compound 10

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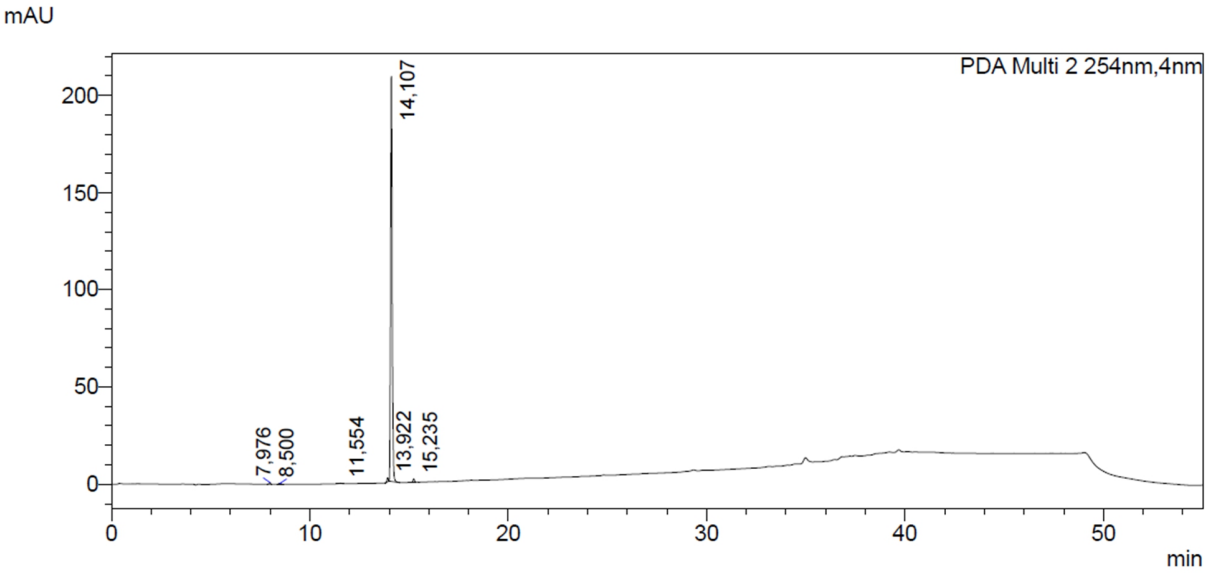

<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	7,976	5171	1031	0,482	0,418
2	8,500	4864	477	0,223	0,393
3	11,554	2321	239	0,112	0,188
4	13,922	8533	2017	0,943	0,690
5	14,107	1205555	208282	97,400	97,501
6	15,235	10014	1796	0,840	0,810
Total		1236458	213842	100,000	100,000

HPLC determined purity of compound 11a

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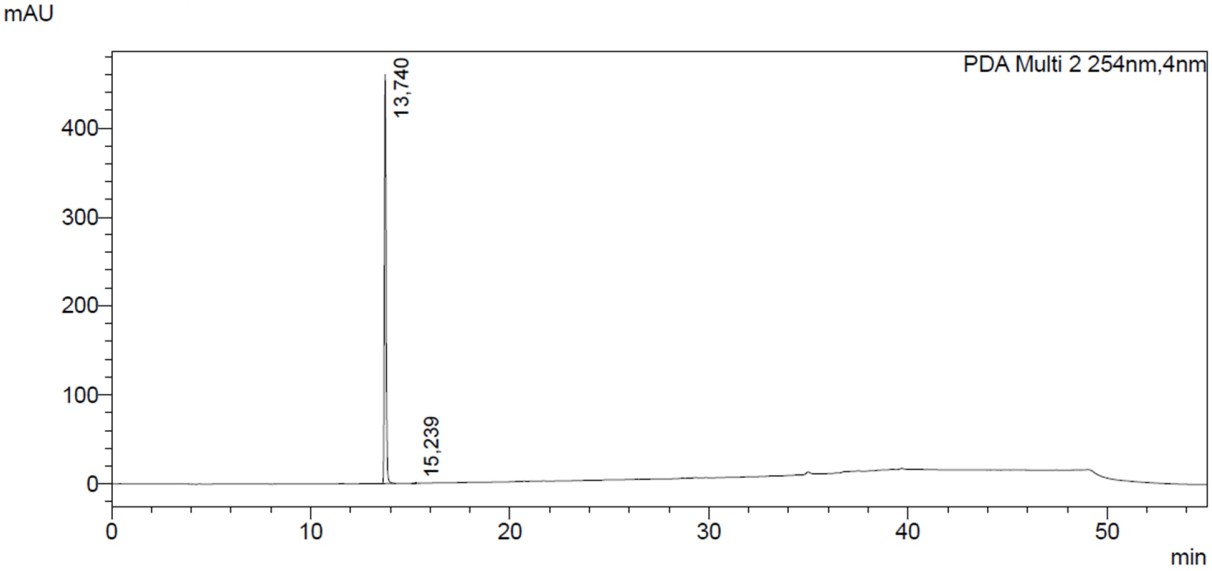


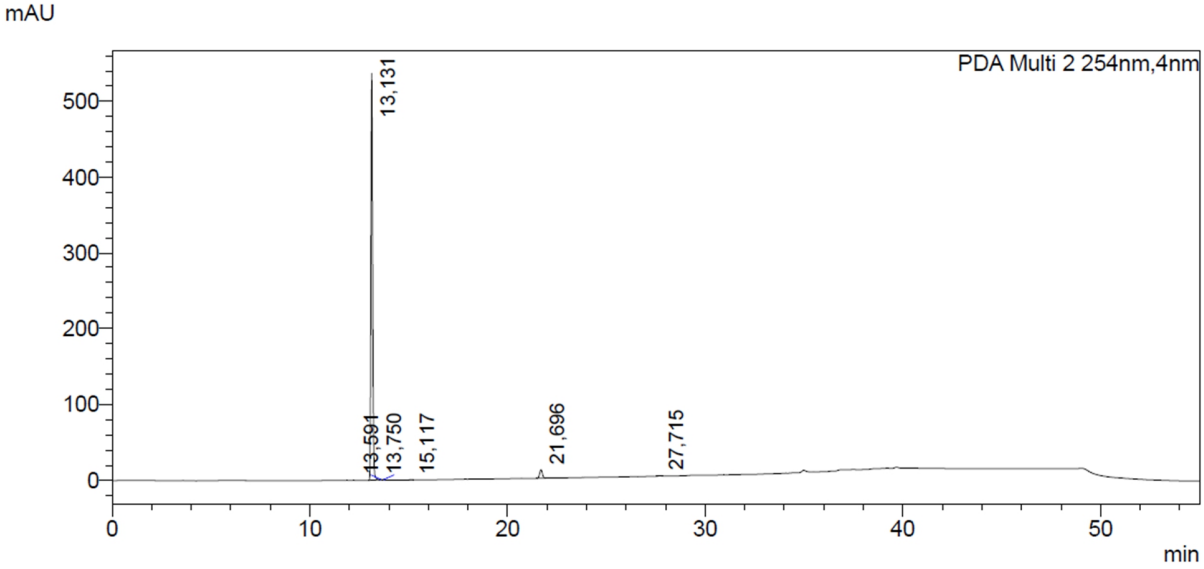
<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	13,740	2655235	459390	99,944	99,931
2	15,239	1833	257	0,056	0,069
Total		2657068	459647	100,000	100,000

HPLC determined purity of compound 11b

<Chromatogram>



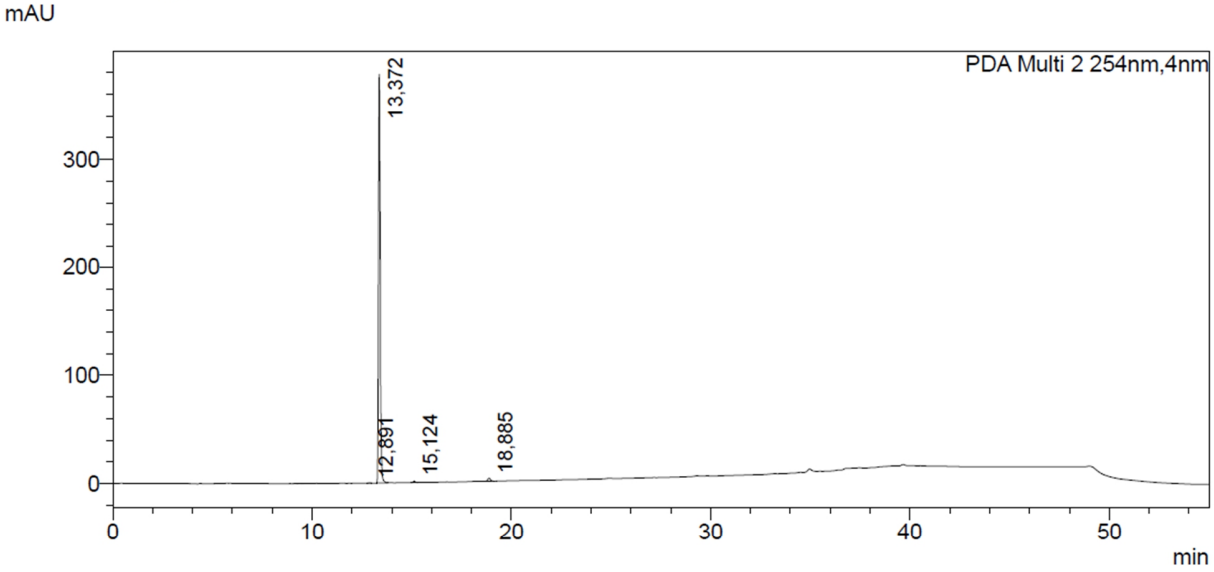
<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	13,131	3203156	536018	97,508	96,229
2	13,591	2631	572	0,104	0,079
3	13,750	4329	795	0,145	0,130
4	15,117	2487	304	0,055	0,075
5	21,696	108371	11309	2,057	3,256
6	27,715	7702	722	0,131	0,231
Total		3328675	549719	100,000	100,000

HPLC determined purity of compound 11c

<Chromatogram>



<Peak Table>

PDA Ch2 254nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	12,891	2477	328	0,086	0,107
2	13,372	2281492	378016	98,781	98,416
3	15,124	8301	1469	0,384	0,358
4	18,885	25941	2867	0,749	1,119
Total		2318212	382680	100,000	100,000