Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications

Electronic Supplementary Information

Synthesis and antiproliferative activity of some 3-(pyrid-2-yl)-pyrazolines

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General Experimental

Chemicals, solvents and reagents used are commercially available and were used without further purification. PE refers to petroleum ether, bp 40-60 °C. TLCs were carried out on Merck Aluminium backed TLC plates Silica Gel 60 F254 and viewed using UV light of wavelength 254 nm and then stained with potassium permanganate. Merck Silica Gel (0.040-0.063 mm) was used for column chromatography. Compounds were loaded as an oil, CH_2Cl_2 solution or dry loaded by adsorption onto silica. Melting points were obtained using a Reichert-Jung heated-stage microscope. Infrared spectra were recorded on a Perkin-Elmer Spectrum RXI FT-IR system and all values are recorded in cm^{-1}.

NMR spectra were obtained on a Bruker Avance III (500 MHz) spectrometer. The chemical shifts are recorded in parts per million (ppm) with reference to tetramethylsilane. The coupling constants *J* are quoted to the nearest 0.5 Hz and are not corrected. The multiplicities are assigned as a singlet (s), doublet (d), triplet (t), doublet of doublets (dd), quartet (q) and multiplet (m). Mass spectra and high resolution mass spectra were obtained on a micrOTOF™ from Bruker Daltonics (Bremen, Germany) coupled with an electrospray source (ESI-TOF) using an autosampler in an Agilent 1100 LC system. Data was processed using external calibration with the Bruker Daltonics software, DataAnalysis™ as part of the overall hardware control software, Compass 1.1™.

X-ray Crystallography: Single crystals were analysed at 150(2) K using graphite monochromated Mo(Kα) radiation and a Nonius Kappa CCD diffractometer. The structures were solved using SHELXS-97 and refined using SHELXL-97. *In vitro* tubulin polymerisation assays were performed on a BMG labtech Fluostar plate reader prewarmed to 37 ^{o}C. Cell cycle analysis was performed on a Becton Dickinson flow cytometer FACSCanto™ and confocal microscopy was performed on a Zeiss LSM 510 META confocal microscope.

Analytical RP-HPLC was performed on a JASCO HPLC system equipped with a phenomenex Max-RP 80A 4 µm C-18 (150 × 4.6 mm) column with a flow rate of 1.0 mL/min. with detection at 274 nm and 254 nm shown. Mobile phase A was H_2O and mobile phase B was MeCN and all runs were performed with A:B 50:50 ratio.

MTS Cell Proliferation Assay[1]

Human cancer cell lines HT29 and MDA-MB-231 were supplied by Cancer Research UK. They were maintained in DMEM with high glucose (4.5 g/L) and $_{L}$-glutamine, supplemented with penicillin 100 U/mL, streptomycin 100 μg/mL and foetal bovine serum at 10%. All reagents supplied by Invitrogen.

1. Cells were maintained in 75 cm^2 tissue culture flasks (Nunc) with a weekly 1:10 split.

2. For the MTS assay, seed densities of 500 and 1000 cells per well in 50 μL were used for HT29 and MDA-MB-231 cell lines respectively. The seed densities had been determined previously to give an acceptable optical density value after 3 days incubation.

3. Plates were incubated at 37 ^{o}C, in humidified 5% CO_2 in air for 2-4 h.

4. Test agents were prepared at 100 × final concentration in DMSO (Sigma), diluted 1 in 50 in culture medium and 50 μL added to the appropriate wells, to give a final volume of 100 μL.

5. Quadruplicate samples were run as follows:
   Culture medium only (background)
   Cells only
   Cells + 1% DMSO
   Cells + test compound

6. Plates were incubated at 37 ^{o}C, in humidified 5% CO_2 in air.
   This exposure time appears to be adequate to demonstrate anti-proliferative activity, and is routinely used by other workers.

7. The MTS reagent was added, 20 μL per well. This is Promega Cell Titer® Aqueous One Solution Cell Proliferation Assay.

8. Plates were incubated at 37 ^{o}C, in humidified 5% CO_2 in air, for colour development.

9. Optical density readings at 490 nm were taken at 1-4 h, because the culture medium gives a high OD_{490nm} this was subtracted from all other OD_{490nm}.

10. Means and standard deviations were calculated from background corrected OD_{490nm} values.

11. IC_{50} values were calculated using the pharmacology function in SigmaPlot 8 (SPSS Inc). Each assay was repeated on three separate occasions.

Note: This assay is based upon the development of a coloured metabolite from viable cells. Therefore the inhibition of colour development by an active agent does not distinguish between inhibition of cell metabolism *ie* cytostasis and reduction in cell number *ie* cytotoxicity. Nevertheless, this assay provides a very quick and easy first approach for screening test compounds.

Cell Cycle Analysis

Following the procedure reported,[2] except using HT29 cells:

1. Cells were subcultured into a T25 flask (5×10^5 cells, 3 mL media) and grown for 24 h.

2. Fresh media containing required concentration of drug/control was added (3 mL) and the cells were incubated with drug for a further 24 h.

3. The supernatant media was collected, and combined with a PBS wash (5 mL). Trypsin (1 mL) was added and cells incubated for 5 min.

4. The trypsin was neutralised with media (2 mL) and this was combined with the supernatant and a further PBS wash (5 mL). The cell suspension was centrifuged (1000 rpm, 6 min), the supernatant was removed, and the cell pellet was resuspended in PBS (5 mL).

5. This was centrifuged (1000 rpm, 6 min), and the supernatant was removed. The cell pellet was resuspended in PBS (0.5 mL), and this suspension was carefully added to ice cold 70% ethanol solution (4.5 mL).The cells were fixed for a minimum of 2 h, before centrifuging (1000 rpm, 5 min).

6. The supernatant was removed and the cells resuspended in PBS (5 mL). The cells were washed *via* two centrifuging and resuspension cycles, and were finally resuspended in 1 mL of a solution of DNase-free RNase A (20 μg/mL) and propidium iodide (20 μg/mL) in 0.1% (v/v) Triton X-100 in PBS.

7. Cells were incubated at rt for 30 min in the dark. Cell fluorescence was determined using a FACSCanto™ (BDBiosciences), gating for mononuclear cells.

In Vitro Tubulin Polymerisation Assay

Performed using the Cytoskeleton BK004P *In Vitro* Tubulin Polymerisation Assay Kit.[3]

Following the manufacturer instructions (Cat # BK004P):

1. One 4 mg tube of tubulin (HTS03) was resuspended with 1 mL of cold G-PEM buffer (990 µl general tubulin buffer with 10 µl GTP stock) to give a final protein concentration of 4 mg/mL. The tube was placed on ice for 3 min until complete resuspension of the protein was observed.

2. A 96 well half area plate was prewarmed to 37 ^{o}C by placing in an incubator for 30 mins prior.

3. Pipette 10 µL of compound of interest at 10x strength in G-PEM buffer into two wells of the prewarmed 96 well half area plate and 10 µL of general tubulin buffer only into two of the control wells and incubate the plate for 2 min at 37 ^{o}C.

4. Remove the 96 well half area plate and pipette 100 µL of tubulin into the required wells and immediately place the plate into the spectrophotometer prewarmed to 37 ^{o}C and start recording using optical density reading at 340 nm at one reading per minute for one hour.

5. The optical density of each compound was plotted against time to obtain the tubulin polymerisation assay curves.

Confocal Microscopy

Following the procedure reported,[2] except using HT29 cells:

1. HT29 cells were subcultured in each well of a six well plate containing a glass coverslip and incubated at 37 ^{o}C for 24 h.

2. When the cells were approximately 50% confluent, the coverslips were removed and placed into a well of a new 6 well plate containing 450 µL medium. Drug solution in medium (50 µL, 10× concentrations to give appropriate 1× final concentrations) was then added along with a blank (50 µL of medium) and plates incubated for 24 h.

3. After 24 h the media was aspirated, the coverslips washed with PBS (500 µL per well) followed by fixation in freshly diluted 3% formaldehyde solution in PBS (500 µL) followed by incubation at 37 °C for 10 min.

4. After aspiration cells were permeabilised with PBS-T (0.1% Triton in PBS, 500 µL) for 5 min, and then incubated at 37 °C with blocking solution (10% bovine serum albumin (BSA) in PBS (500 µL)) for 5 min.

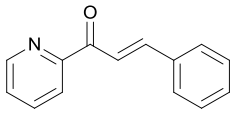
5. This was removed and Dm1A primary mouse antibody (purchased from Sigma, 1 in 200 in blocking solution, 500 µL) was added and incubated at 37 °C for 2 h.

6. The primary antibody solution was removed and the cells were washed 3 times (5 min at 37 °C) with PBS-T (500 µL). The appropriate Alexa Fluor® 546-coupled secondary antibody was then added as a solution in BSA in PBS (1 in 200 in blocking solution, 500 µL) and the plate returned to the incubator for a further 2 h ensuring minimal light exposure.

7. Cells washed 3 times (5 min at 37 °C) with PBS-T (500 µL), with a final wash in water (500 µL). The coverslips inverted onto microscope slides with mounting medium containing DAPI (4′,6-diamidino-2-phenylindole dihydrochloride) stain (30 µL) and allowed to dry at rt overnight and then stored at 4 °C until they were viewed using a Zeiss LSM510META confocal microscope.

Experimental

(*E*)-3-Phenyl-1-(pyridin-2-yl)prop-2-en-1-one (4)



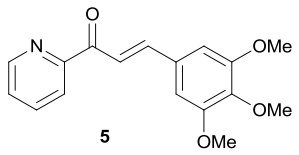
4

Following the procedure previously reported,[4] 2-acetylpyridine (1.33 g, 11.0 mmol) and benzaldehyde (1.06 g, 1.02 mL, 10.0 mmol) were added to distilled water (100 mL) cooled to 4 ^{o}C and shaken thoroughly forming a fine emulsion. 10 mL of 10% of NaOH aqueous solution was then added and shaken again for 30 seconds and the reaction left at 4 ^{o}C. After 24 h the solid product was filtered, dried and recrystallised from EtOH to give the chalcone **4** (2.02 g, 97%) as pale green crystals.

R_f [PE-EtOAc 4:6] 0.88; **Mp** 72-74 ^{o}C (EtOH); **IR** ν_{max}(film)/cm^{-1} 1667, 1601, 1337 and 1030; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 7.40-7.49 (4 H, m, Ph CH), 7.72-7.73 (2 H, m, Ph CH and py CH), 7.85-7.88 (1 H, m, py CH), 7.94 (1 H, d, *J* 16.0 Hz, COC*H*=CH), 8.18-8.19 (1 H, m, py CH), 8.30 (1 H, d, *J* 16.0 Hz, COCH=C*H*) and 8.74-8.76 (1 H, m, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 120.9 (CH), 122.9 (CH), 126.9 (CH), 128.8 (CH), 128.9 (CH), 130.6 (CH), 135.2 (Cq), 137.0 (CH), 144.8 (CH), 148.9 (CH), 154.3 (Cq) and 189.5 (Cq); **MS** m/z (ES$^+$) Found 232.0749 (MNa$^+$), $C_{14}H_{11}N_1NaO$ (MNa$^+$) requires 232.0738.

Consistent with the spectroscopic data previously reported for this compound.[4c]

(*E*)-1-(Pyridin-2-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (5)



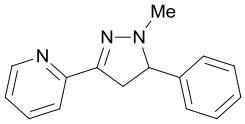
5

Crushed KOH pellets (5.0 mmol) were added to a rapidly stirred solution of 2-acetylpyridine (10.0 mmol) and 3,4,5-trimethoxybenzaldehyde (12.0 mmol) in EtOH (20 mL) and allowed to stir at rt (20 ^{o}C). After 24 h the solvent was removed under reduced pressure and the resulting solid purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the chalcone **5** as a yellow solid (2.54 g, 85%).

R_f [PE-EtOAc 4:6] 0.77; **Mp** 155-156 ^{o}C (MeOH); **IR** ν_{max}(film)/cm^{-1} 1605, 1217 and 791; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 3.89 (3 H, s, OCH_3), 3.92 (6 H, s, OCH_3), 6.94 (2 H, s, Ar CH), 7.45 (1 H, dt, *J* 8.0 and 1.0 Hz, py CH), 7.86 (1 H, d, *J* 16.0 Hz, COC*H*=CH), 7.87 (1 H, dt, *J* 7.5 and 1.5, py CH), 8.16 (1 H, d, *J* 16.0 Hz, COCH=C*H*), 8.18-8.19 (1 H, m, py CH) and 8.73-8.74 (1 H, m, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 56.2 (OCH_3), 60.9 (OCH_3), 106.0 (CH), 119.9 (CH), 122.9 (CH), 126.8 (CH), 130.6 (Cq), 137.0 (CH), 140.5 (Cq), 145.0 (CH), 148.7 (CH), 153.4 (Cq), 154.2 (Cq) and 189.2 (Cq); **MS** m/z (ES$^+$) Found 322.1074 (MNa$^+$), $C_{17}H_{17}NNaO_4$ (MNa$^+$) requires 322.1055; **Elemental Analysis** Found C (68.35%) H (5.79%) N (4.72%) requires C (68.21%) H (5.72%) N (4.68%); **HPLC** (analytical) t_R = 5.4 min.

Consistent with the spectroscopic data previously reported for this compound.[5]

2-(1-Methyl-5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)pyridine (8a)



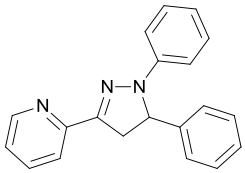
8a

Following the procedure previously reported,[4c] chalcone **4** (0.42 g, 2.0 mmol) was dissolved in EtOH (10 mL) and stirred for 10 min at rt until fully dissolved then methylhydrazine (0.37 g, 0.42 mL, 8.0 mmol) was added dropwise and stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the resulting yellow oil purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford pyrazoline **8a** (0.34 g, 72%) as a yellow oil, which solidified upon cooling and was recrystallised from Et_2O to give pale yellow crystals.

R_f [PE-EtOAc 4:6] 0.82; **Mp** 52-55 ^oC (Et_2O); **IR** ν_{max}(film)/cm^{-1} 2971, 1570, 1456 and 1122; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 2.88 (3 H, s, CH_3), 3.08 (1 H, dd, *J* 16.5 and 14.5 Hz, pyrazoline CH), 3.71 (1 H, dd, *J* 16.5 and 10.5 Hz, pyrazoline CH), 4.21 (1 H, dd, *J* 14.5 and 10.5 Hz, pyrazoline CH), 7.18 (1 H, dd, *J* 7.5 and 5.0 Hz, py CH), 7.29-7.34 (1 H, m, Ph CH), 7.35-7.40 (2 H, m, Ph CH), 7.45-7.48 (2 H, m, Ph), 7.66 (1 H, td, *J* 7.5 and 1.0 Hz, py CH), 7.91 (1 H, dt, *J* 8.0 and 1.0 Hz, py CH) and 8.56 (1 H, br.d, *J* 5.0 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 41.1 (CH_3), 42.6 (CH_2), 73.5 (CH), 120.4 (CH), 122.6 (CH), 127.4 (CH), 127.8 (CH), 128.6 (CH), 136.0 (CH), 140.2 (Cq), 149.1 (CH), 150.4 (Cq) and 152.1 (Cq); **MS** m/z (ES^+) Found 260.1158 (MNa^+), $C_{15}H_{15}N_3Na$ (MNa^+) requires 260.1164; **HPLC** (analytical) t_R = 18.3 min.

Consistent with the spectroscopic data previously reported for this compound.[4c]

2-(1,5-Diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)pyridine (8b)

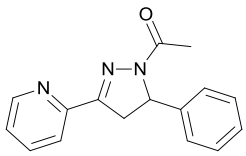


8b

Following a modified procedure to that reported,[6] phenyl hydrazine (10.0 mmol) was added to a rapidly stirred solution of chalcone **4** (5 mmol) in EtOH (10 mL) and heated to 70 ^{o}C for 18 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **8b** as an orange solid (0.73 g, 49%).

R_f [PE-EtOAc 4:6] 0.82; **Mp** 111-113 ^{o}C (EtOAc); **IR** ν_{max}(film)/cm^{-1} 1598, 1559, 1402 and 1132; **^{1}H NMR δ_H** (500 MHz; $CDCl_3$) 3.33 (1 H, dd, *J* 18.0 and 7.0 Hz, pyrazoline CH), 3.98 (1 H, dd, *J* 18.0 and 12.5 Hz, pyrazoline CH)), 5.36 (1 H, dd, *J* 12.5 and 7.0 Hz, pyrazoline CH), 6.79-6.83 (1 H, m, Ph CH), 7.10-7.20 (2 H, m, Ph CH), 7.21-7.34 (8 H, m, Ph CH and py CH), 7.70 (1 H, td, *J* 7.5 and 1.5 Hz, py CH), 8.15 (1 H, d, *J* 8.0, py CH), 8.53-8.54 (1 H, m, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 43.1 (CH_3), 64.6 (CH), 113.5 (CH), 119.5 (CH), 120.6 (CH), 122.6 (CH), 125.8 (CH), 127.5 (CH), 128.9 (CH), 129.1 (CH), 135.9 (CH), 142.2 (Cq), 144.2 (Cq), 147.9 (Cq), 149.0 (CH), 152.0 (Cq); **MS** m/z (ES$^+$) Found 300.1494 (MH^+) and 322.1319 (MNa^+), $C_{20}H_{18}N_3$ (MH^+) requires 300.1501 and $C_{20}H_{17}N_3Na$ (MNa^+) requires 322.1320; **HPLC** (analytical) t_R = 7.8 min.

1-(5-Phenyl-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethanone (8c)

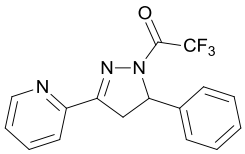


8c

Hydrazine monohydrate (20.0 mmol) was added to a rapidly stirred solution of chalcone **4** (5.0 mmol) in EtOH (20 mL) and heated to 80 ^{o}C for 2 h. The solvent was removed under reduced pressure and the resulting brown oil was dissolved in CH_2Cl_2 (20 mL) and acetyl chloride (10.0 mmol) added dropwise followed by NEt_3 (10.0 mmol) and the solution stirred at rt for 3 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **8c** as a white solid (0.95 g, 72%).

R_f [PE-EtOAc 4:6] 0.23; **Mp** 120-121 ^{o}C (EtOAc); **IR** ν_{max}(film)/cm^{-1} 1655, 1580, 1413 and 1335; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 3.38 (1 H, dd, *J* 18.5 and 5.0 Hz, pyrazoline CH), 3.84 (1 H, dd, *J* 18.5 and 12.0 Hz, pyrazoline CH), 5.60 (1 H, dd, *J* 12.0 and 5.0 Hz, pyrazoline CH), 7.21-7.31 (6 H, m, Ph CH and py CH), 7.71-7.75 (1 H, td, *J* 8.0 and 2.0 Hz, py CH), 8.08 (1 H, d, *J* 8.0 Hz, py CH) and 8.58 (1 H, d, *J* 5.0 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 21.8 (CH_3), 42.0 (CH_2), 60.1 (CH), 121.1 (CH), 124.2 (CH), 125.5 (CH), 127.5 (CH), 128.7 (CH), 136.2 (CH), 141.6 (CH), 149.3 (Cq), 150.6 (Cq), 155.3 (Cq) and 168.9 (Cq); **MS** m/z (ES$^+$) Found 288.1166 (MNa$^+$), $C_{16}H_{15}N_3NaO$ (MNa$^+$) requires 288.1113; **HPLC** (analytical) t_R = 6.1 min.

2,2,2-Trifluoro-1-(5-phenyl-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethanone (8d)

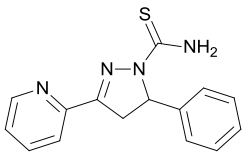


8d

Hydrazine monohydrate (10.0 mmol) was added to a rapidly stirred solution of chalcone **4** (2.5 mmol) in EtOH (20 mL) and heated to 80 ^{o}C for 2 h. The solvent was removed under reduced pressure and the resulting brown oil was dissolved in CH_2Cl_2 (20 mL) and trifluoroacetic anhydride (7.5 mmol) added dropwise followed by NEt_3 (7.5 mmol) and the solution stirred at rt for 3 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **8d** as a white solid (0.52 g, 65%).

R_f [PE-EtOAc 4:6] 0.87; **Mp** 143-145 ^{o}C (EtOH); **IR** ν_{max}(film)/cm^{-1} 1701, 1587, 1463 and 1171; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 3.50 (1 H, dd, *J* 19.0 and 5.0 Hz, pyrazoline CH), 3.92 (1 H, dd, *J* 19.0 and 11.5 Hz, pyrazoline CH), 5.64 (1 H, dd, *J* 11.5 and 4.5 Hz, pyrazoline CH), 7.24-7.38 (6 H, m, Ph CH and py CH), 7.80 (1 H, td, *J* 7.5 and 2.0 Hz, py CH), 8.19 (1 H, d, *J* 7.0 Hz, py CH) and 8.62 (1 H, d, *J* 6.0 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 41.7 (CH_2), 61.8 (CH), 116.2 ($COCF_3$, q, $J_{C\text{-}F}$ 287.0 Hz), 122.0 (CH), 125.2 (CH), 125.7 (CH), 128.4 (CH), 129.1 (CH), 136.5 (CH), 139.5 (Cq), 149.5 (Cq), 149.7 (CH), 154.2 ($COCF_3$, q, $J_{C\text{-}F}$ 38.5 Hz) and 159.6 (Cq); **^{19}F NMR** δ_F (470 MHz; $CDCl_3$) –71.35; **MS** m/z (ES$^+$) Found 320.1066 (MH^+) and 342.0888 (MNa^+), $C_{16}H_{13}F_3N_3O$ (MH^+) requires 320.1011 and $C_{16}H_{12}F_3N_3NaO$ (MNa^+) requires 342.0831; **HPLC** (analytical) t_R = 16.4 min.

5-Phenyl-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide (8e)



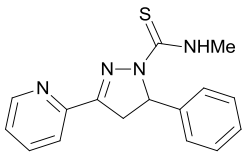
8e

Following a modified procedure to that reported,[7] chalcone **4** (5.0 mmol) and thiosemicarbazide (7.5 mmol) were added to EtOH (50 mL) followed by a solution of sodium hydroxide (5.0 mmol, 0.28 g) in water (10 mL) and refluxed for 6 h. The solvent was then concentrated and the product crystallised from ethanol to give the carbothioamide **8e** as yellow crystals (0.94 g, 67%).

R_f [PE-EtOAc 4:6] 0.55; **Mp** 185-189 ^oC (EtOH); **IR** ν_{max}(film)/cm^{-1} 3523, 3395, 1569, 1349 and 1195; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 3.45 (1 H, dd, *J* 20.0 and 4.0 Hz, pyrazoline CH), 3.96 (1 H, dd, *J* 20.0 and 12.0 Hz, pyrazoline CH), 6.10 (1 H, dd, *J* 12.0 and 4.0 Hz, pyrazoline CH), 6.30 (1 H, br. s, NH), 7.17 (1 H, br. s, NH), 7.26-7.35 (6 H, m, Ph CH and py CH), 7.78 (1 H, td, *J* 8.0 and 4.0 Hz, py CH), 8.07 (1 H, d, *J* 8.0 Hz, py CH) and 8.64 (1 H, d, *J* 8.0 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 42.9 (CH_2), 63.7 (CH), 121.5 (CH), 124.8 (CH), 125.3 (CH), 127.5 (CH), 128.8 (CH), 136.3 (CH), 141.6 (Cq), 149.7 (CH), 150.0 (Cq), 157.2 (Cq) and 177.3 (C=S); **MS** m/z (ES^+) Found 283.1004 (MH^+) and 305.0824 (MNa^+), $C_{15}H_{15}N_4S$ (MH^+) requires 283.1017 and $C_{15}H_{14}N_4NaS$ (MNa^+) requires 305.0837; **HPLC** (analytical) t_R = 6.1 min.

Consistent with the spectroscopic data previously reported for this compound.[7b]

_N_-Methyl-5-phenyl-3-(pyridin-2-yl)-4,5-dihydro-1_H_-pyrazole-1-carbothioamide (8f)

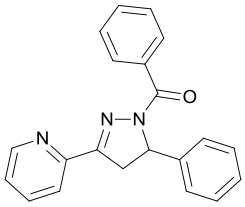


8f

Following a modified procedure to that reported,[8] carbothioamide **8e** (1.4 mmol) was added to a solution of potassium hydroxide (4.2 mmol) in THF (20 ml) and stirred for 15 min, methyl iodide (4.2 mmol) was then added and stirring continued for 2 h. Water (100 ml) was then added and stirring continued for 2 h resulting in the formation of a precipitate which was collected by filtration and recrystallised from EtOAc to afford carbothioamide **8f** as yellow crystals (0.37 g, 89%).

R_f [PE-EtOAc 4:6] 0.15; **Mp** 157-158 ^oC (EtOH); **IR** ν_{max}(film)/cm^{-1} 1604, 1566, 1320 and 1399; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 2.30 (3 H, s, CH_3), 3.34 (1 H, dd, *J* 18.5 and 6.0 Hz, pyrazoline CH), 3.93 (1 H, dd, *J* 18.5 and 12.0 Hz, pyrazoline CH), 5.63 (1 H, dd, *J* 12.0 and 6.0 Hz, pyrazoline CH), 7.24-7.35 (7 H, m, NH, Ph CH and py CH), 7.71 (1 H, td, *J* 7.5 and 1.5 Hz, py CH), 8.12 (1 H, d, *J* 7.5 Hz, py CH) and 8.55 (1 H, d, *J* 7.5 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 13.1 (CH_3), 42.8 (CH_2), 63.3 (CH), 121.1 (CH), 123.7 (CH), 125.5 (CH), 127.6 (CH), 128.9 (CH), 136.1 (CH), 149.1 (CH), 149.2 (Cq) 151.0 (Cq), 152.3 (Cq) and 160.0 (Cq); **MS** m/z (ES^+) Found 297.1182 (MH^+), $C_{16}H_{17}N_4S$ (MH^+) requires 297.1174; **HPLC** (analytical) t_R = 5.6 min.

Phenyl(5-phenyl-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)methanone (8h)

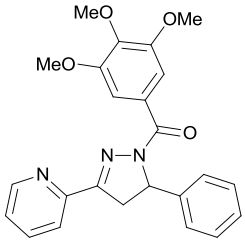


8h

Hydrazine monohydrate (20.0 mmol) was added to a rapidly stirred solution of chalcone **4** (5.0 mmol) in EtOH (20 mL) and heated to 80 ^{o}C for 2 h. The solvent was removed under reduced pressure and the resulting brown oil was dissolved in CH_2Cl_2 (20 mL) and benzoyl chloride (10.0 mmol) added dropwise followed by NEt_3 (10.0 mmol) and the solution stirred at rt for 3 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **8h** as a white solid (1.24 g, 76%).

R_f [PE-EtOAc 4:6] 0.76; **Mp** 139-140 ^{o}C (EtOAc); **IR** ν_{max}(film)/cm^{-1} 1641, 1577, 1413 and 1338; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 3.44 (1 H, dd, *J* 18.5 and 5.0 Hz, pyrazoline CH), 3.91 (1 H, dd, *J* 18.5 and 12.0 Hz, pyrazoline CH) 5.85 (1 H, dd, *J* 12.0 and 5.0 Hz, pyrazoline CH), 7.27-7.35 (6 H, m, Ph CH and py CH), 7.43-7.50 (3 H, m, Ph CH), 7.70 (1 H, td, *J* 7.5 and 1.5 Hz, py CH), 8.01-8.04 (3 H, m, Ph CH and py CH) and 8.59 (1 H, d, *J* 7.5 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 41.4 (CH_2), 61.5 (CH), 121.4 (CH), 124.3 (CH), 125.7 (CH), 127.5 (CH), 127.6 (CH), 128.8 (CH), 129.9 (CH), 130.9 (CH), 134.2 (Cq), 136.2 (CH), 141.6 (Cq), 149.3 (CH), 150.7 (Cq), 156.2 (Cq) and 166.6 (Cq); **MS** m/z (ES$^+$) Found 350.1282 (MNa^+), $C_{21}H_{17}N_3NaO$ (MNa^+) requires 350.1269; **HPLC** (analytical) t_R = 11.7 min.

(5-Phenyl-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)(3,4,5-trimethoxyphenyl)methanone (8i))

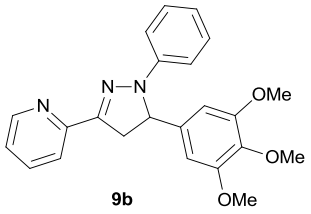


8i

Hydrazine monohydrate (20.0 mmol) was added to a rapidly stirred solution of chalcone **4** (5.0 mmol) in EtOH (20 mL) and heated to 80 ^{o}C for 2 h. The solvent was removed under reduced pressure and the resulting brown oil was dissolved in CH_2Cl_2 (20 mL) and 3,4,5-trimethoxybenzoyl chloride (10.0 mmol) added dropwise followed by NEt_3 (10.0 mmol) and the solution stirred at rt for 3 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **8i** as a white solid (1.56 g, 75%).

R_f [PE-EtOAc 4:6] 0.55; **Mp** 173-175 ^{o}C (EtOAc); **IR** ν_{max}(film)/cm^{-1} 1643, 1579, 1412 and 1341; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 3.44 (1 H, dd, *J* 18.5 and 5.0 Hz, pyrazoline CH), 3.88-3.94 (10 H, m, OCH_3 and pyrazoline CH), 5.82 (1 H, dd, *J* 12.0 and 5.0 Hz, pyrazoline CH), 7.25-7.33 (6 H, m, Ph CH and py CH), 7.40 (2 H, s, Ar CH), 7.74 (1 H, td, *J* 8.0 and 2.0 Hz, py CH), 8.05 (1 H, d, *J* 8.0 Hz, py CH) and 8.61 (1 H, d, *J* 7.5 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 41.2 (CH_2), 56.2 (CH), 60.9 (OCH_3), 62.0 (OCH_3), 108.0 (CH), 121.0 (CH), 124.4 (CH), 125.7 (CH), 127.6 (CH), 128.9 (CH), 136.2 (CH), 140.7 (Cq), 141.6 (Cq), 149.5 (CH), 150.8 (Cq), 152.3 (Cq), 156.0 (Cq), 156.5 (Cq) and 165.6 (Cq); **MS** m/z (ES$^+$) Found 418.1776 (MH^+) and 440.1587 (MNa^+), $C_{24}H_{24}N_3O_4$ (MH^+) requires 418.1767 and $C_{24}H_{23}N_3NaO_4$ (MNa^+) requires 440.1586; **Elemental Analysis** Found C (69.15%) H (5.37%) N (9.92%) requires C (69.05%) H (5.55%) N (10.07%); **HPLC** (analytical) t_R = 9.3 min.

2-(1-Phenyl-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl)pyridine (9b)

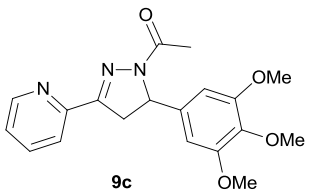


9b

Following a modified procedure to that reported,[6] phenyl hydrazine (5.0 mmol) was added to a rapidly stirred solution of chalcone **5** (2.5 mmol) in EtOH (20 mL) and heated to 80 ^{o}C for 3 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **9b** as a yellow solid (0.33 g, 34%).

R_f [PE-EtOAc 4:6] 0.70; **Mp** 75-77 ^{o}C (EtOAc); **IR** ν_{max}(film)/cm^{-1} 1601, 1502, 1214 and 1128; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 3.33 (1 H, dd, *J* 18.0 and 7.5 Hz, pyrazoline CH), 3.79 (6 H, s, OCH_3), 3.82 (3 H, s, OCH_3), 3.98 (1 H, dd, *J* 18.0 and 12.5 Hz, pyrazoline CH), 5.24 (1 H, dd, *J* 12.5 and 7.5 Hz, pyrazoline CH), 6.51 (2 H, s, Ar CH), 6.85 (1 H, td, *J* 7.0 and 1.0 Hz, py CH), 7.12 (2 H, d, *J* 8.5 Hz, Ph CH), 7.20-7.24 (3 H, m, Ph CH), 7.71 (1 H, td, *J* 7.5 and 1.5 Hz, py CH), 8.14 (1 H, d, *J* 8.0 Hz, py CH) and 8.54-8.55 (1 H, d, *J* 7.5 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 43.3 (CH_2), 55.9 (CH), 56.1 (OCH_3), 60.8 (OCH_3), 65.2 (CH), 102.4 (CH), 113.7 (CH), 119.8 (CH), 120.7 (CH), 122.7 (CH), 128.9 (CH), 130.0 (Cq), 136.1 (CH), 137.1 (Cq), 138.1 (Cq),140.3 (Cq) 144.6 (Cq) and 153.8 (Cq); **MS** m/z (ES$^+$) Found 390.1882 (MH^+) and 412.1649 (MNa^+), $C_{23}H_{24}N_3O_3$ (MH^+) requires 390.1818 and $C_{23}H_{23}N_3NaO_3$ (MNa^+) requires 412.1637; **HPLC** (analytical) t_R = 14.6 min.

1-(3-(Pyridin-2-yl)-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethanone (9c)

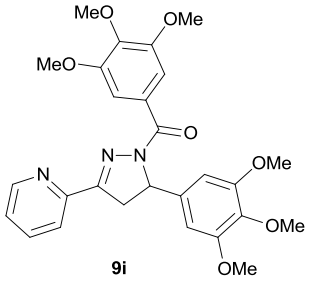


9c

Hydrazine monohydrate (8.0 mmol) was added to a rapidly stirred solution of chalcone **5** (4.0 mmol) in EtOH (20 mL) and heated to 80 ^{o}C for 2 h. The solvent was removed under reduced pressure and the resulting brown oil was dissolved in CH_2Cl_2 (20 mL) and acetyl chloride (8.0 mmol) added dropwise followed by NEt_3 (8.0 mmol) and the solution stirred at rt for 3 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **9c** as a white solid (1.14 g, 80%).

R_f [PE-EtOAc 4:6] 0.24; **Mp** 173-174 ^{o}C (EtOH); **IR** ν_{max}(film)/cm^{-1} 1662, 1594, 1416, 1327 and 1132; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 3.34 (1 H, dd, *J* 18.5 and 5.0 Hz, pyrazoline CH), 3.77 (3 H, s, OCH_3), 3.79-3.87 (7 H, m, OCH_3 and pyrazoline CH), 5.51 (1 H, dd, *J* 12.0 and 5.0 Hz, pyrazoline CH), 6.40 (2 H, s, Ar CH), 7.26-7.30 (1 H, m, py CH), 7.73 (1 H, td, *J* 7.5 and 1.5 Hz, py CH), 8.06 (1 H, d, *J* 8.0 Hz, py CH) and 8.57 (1 H, d, *J* 4.5 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 21.8 (C=O*C*H_3), 42.2 (CH_2), 56.0 (CH), 60.3 (OCH_3), 60.6 (OCH_3), 102.3 (CH), 121.1 (CH), 124.3 (CH), 136.2 (CH), 137.2 (Cq), 137.4 (Cq), 149.4 (CH), 150.5 (Cq), 153.4 (Cq), 155.4 (Cq) and 169.1 (Cq); **MS** m/z (ES$^+$) Found 378.1481 (MNa$^+$), $C_{19}H_{21}N_3NaO_4$ (MNa$^+$) requires 378.1430; **HPLC** (analytical) t_R = 4.2 min.

(3-(Pyridin-2-yl)-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)(3,4,5-trimethoxyphenyl)methanone (9i)



9i

Hydrazine monohydrate (8.0 mmol) was added to a rapidly stirred solution of chalcone **5** (2.0 mmol) in EtOH (20 mL) and heated to 80 ^{o}C for 2 h. The solvent was removed under reduced pressure and the resulting brown oil was dissolved in CH_2Cl_2 (20 mL) and 3,4,5-trimethoxybenzoyl chloride (4.0 mmol) added dropwise followed by NEt_3 (4.0 mmol) and the solution stirred at rt for 3 h. The solvent was then removed under reduced pressure and the solid was purified by column chromatography with silica gel using PE:EtOAc 6:4 to afford the desired pyrazoline **9i** as a white solid (0.85 g, 84%).

R_f [PE-EtOAc 4:6] 0.41; **Mp** 174-175 ^{o}C (EtOH); **IR** ν_{max}(film)/cm^{-1} 1641, 1580, 1416 and 1128; **^{1}H NMR** δ_H (500 MHz; $CDCl_3$) 3.42 (1 H, dd, *J* 19.0 and 5.0 Hz, pyrazoline CH), 3.81 (3 H, s, OCH_3), 3.82 (6 H, s, OCH_3), 3.85-3.93 (10 H, m, OCH_3 and pyrazoline CH), 5.75 (1 H, dd, *J* 12.0 and 5.0 Hz, pyrazoline CH), 6.52 (2 H, s, Ar CH), 7.32 (1 H, td, *J* 5.0 and 1.0 Hz, py CH), 7.40 (2 H, s, Ar CH), 7.74 (1 H, td, *J* 7.5 and 1.5 Hz, py CH), 8.04 (1 H, d, *J* 8.0 Hz, py CH) and 8.61 (1 H, d, *J* 5.5 Hz, py CH); **^{13}C NMR** δ_C (125 MHz; $CDCl_3$) 41.4 (CH_2), 56.1 (OCH_3), 56.2 (OCH_3), 56.3 (OCH_3) 60.7 (OCH_3), 62.2 (CH), 102.5 (CH), 108.0 (CH), 121.1 (CH), 124.5 (CH), 128.9 (CH), 136.3 (CH), 137.4 (Cq), 137.5 (Cq), 140.9 (Cq), 149.6 (Cq), 150.7 (Cq), 152.5 (Cq), 153.6 (Cq), 156.7 (Cq) and 165.8 (C=O); **MS** m/z (ES$^+$) Found 508.2078 (MH^+) and 530.1898 (MNa^+), $C_{27}H_{30}N_3O_7$ (MH^+) requires 508.2084 and $C_{27}H_{29}N_3NaO_7$ (MNa^+) requires 530.1903; **HPLC** (analytical) t_R = 5.4 min.

References

1. MTS is 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium. A. H. Cory, T. C. Owen, J. A. Barltrop and J. G. Cory, *Cancer Commum.*, 1991, **3**, 207.

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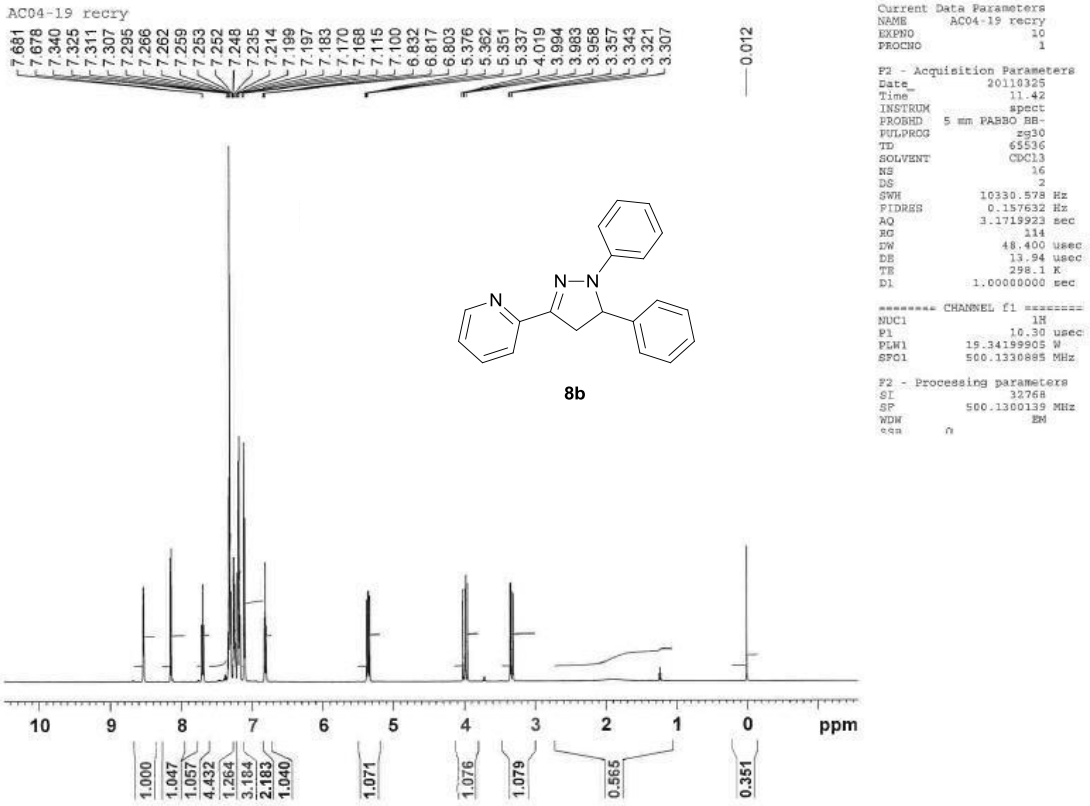
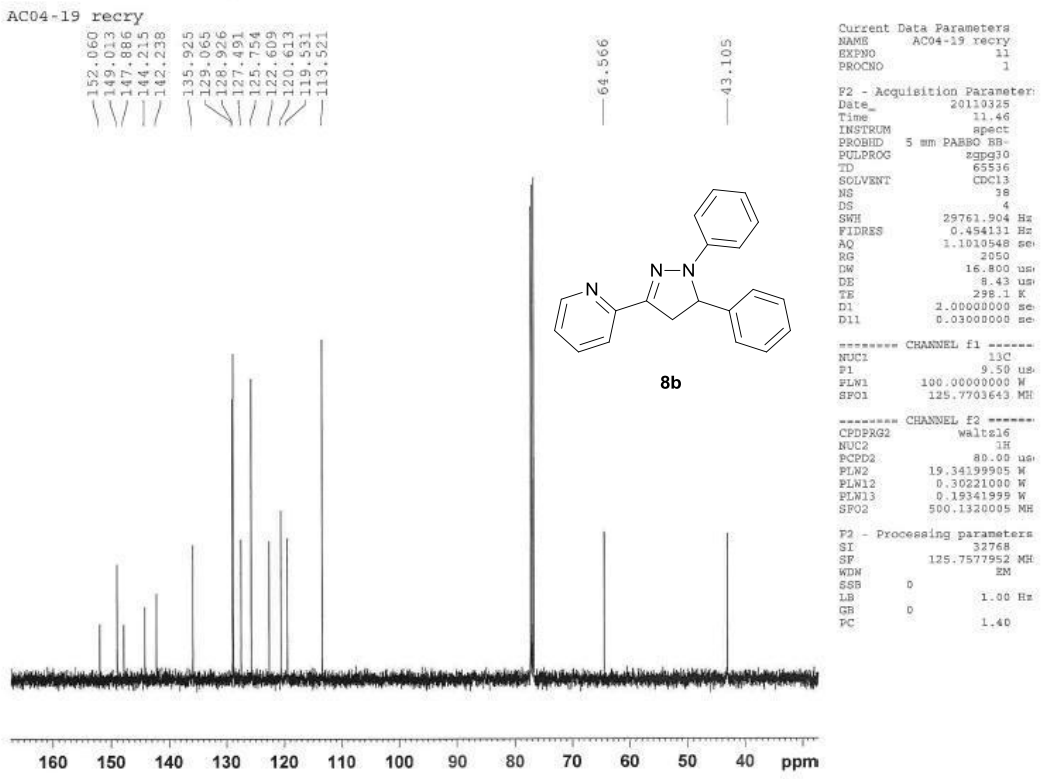
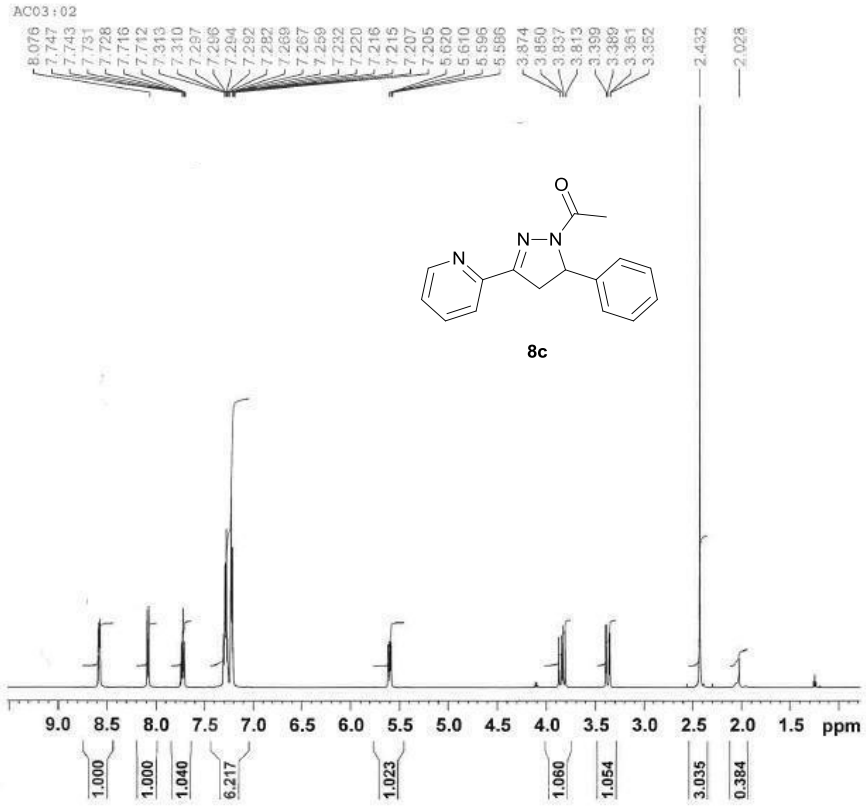
8. S. Wang, B. Shi, Y. Li, *Syn. Comm.*, 2003, **33**, 1449-1457.

^{1}H and ^{13}C NMR Spectra

^{1}H and ^{13}C NMR spectra of compound **8a** was previously published.[4c]





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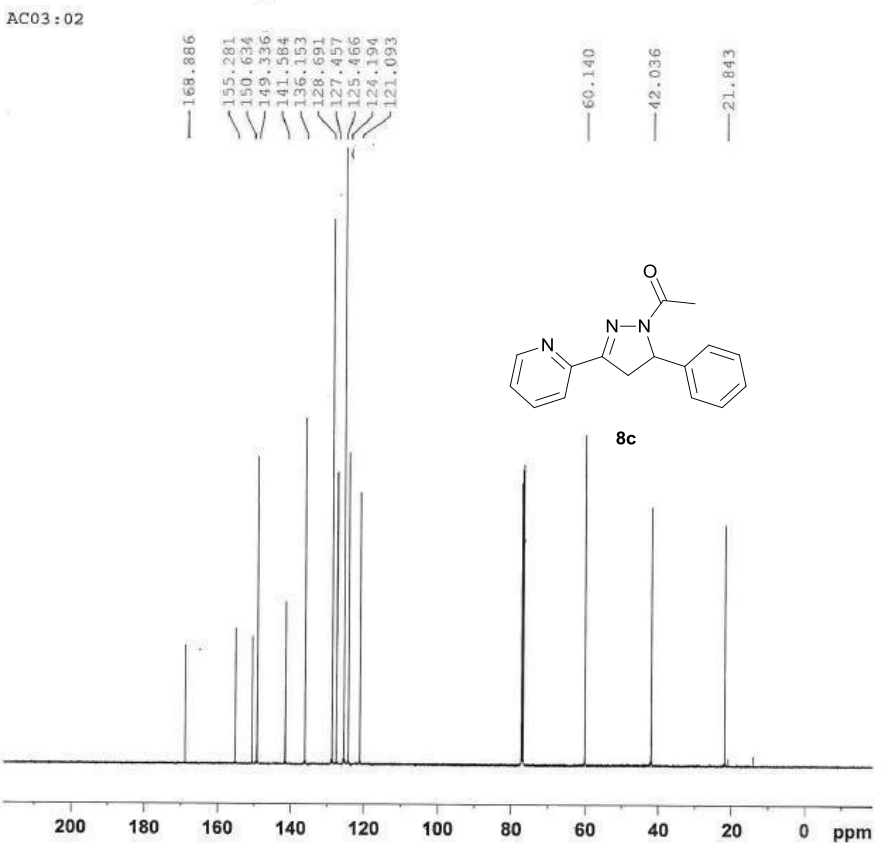


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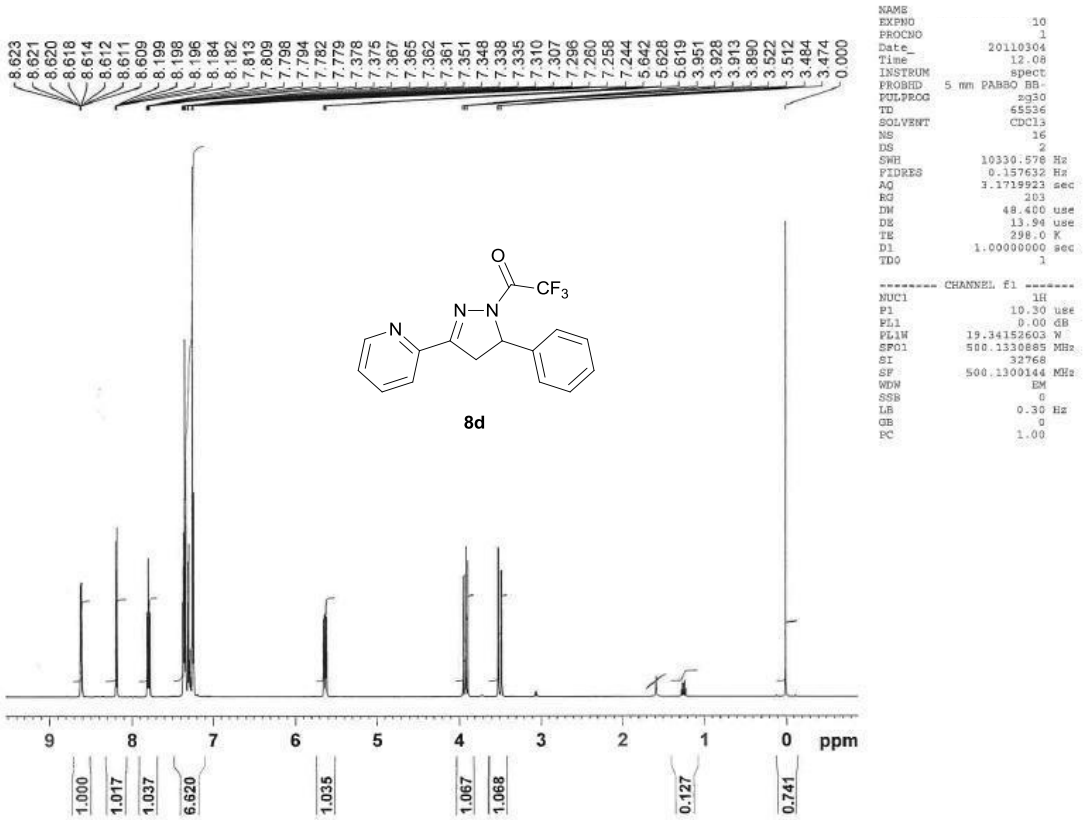
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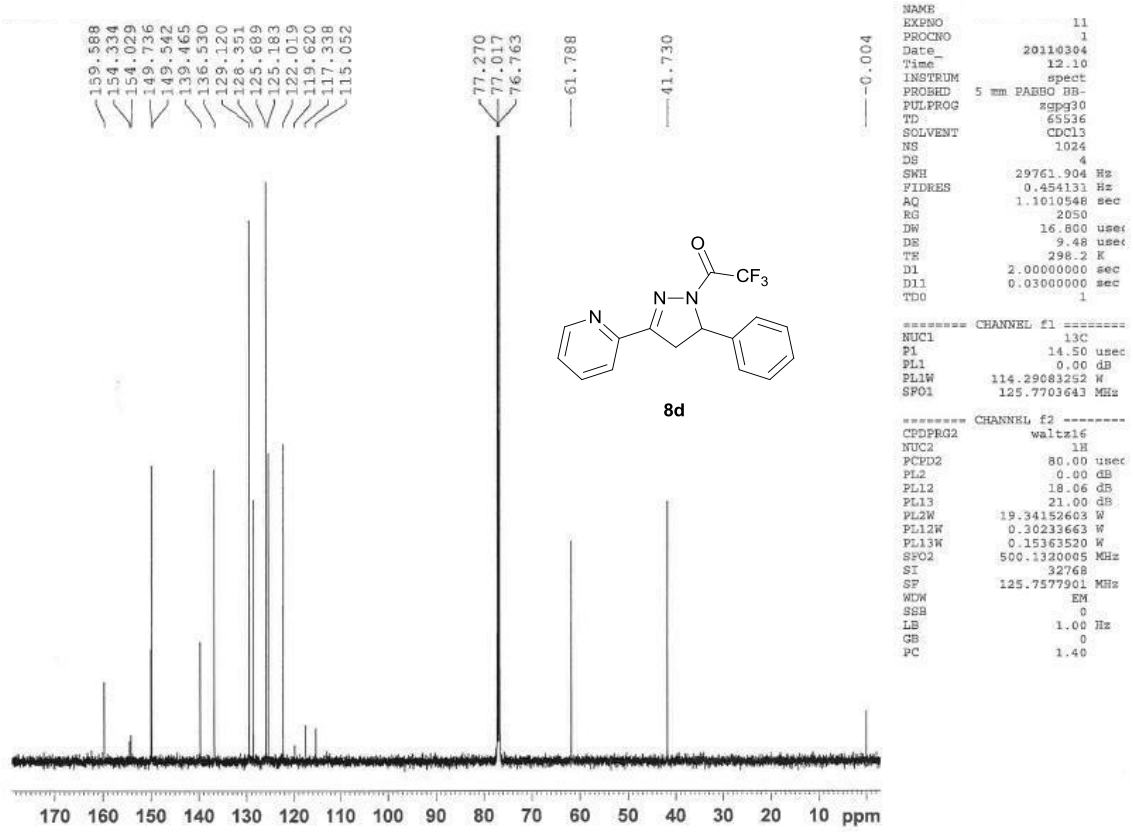
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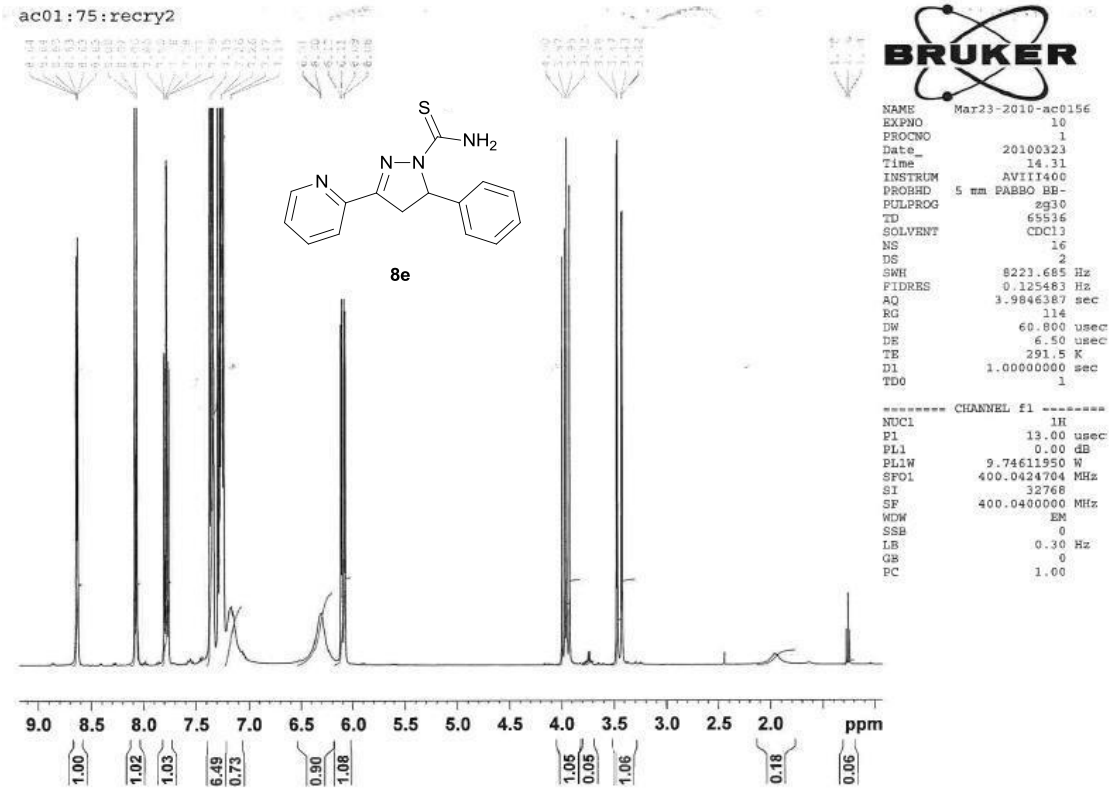
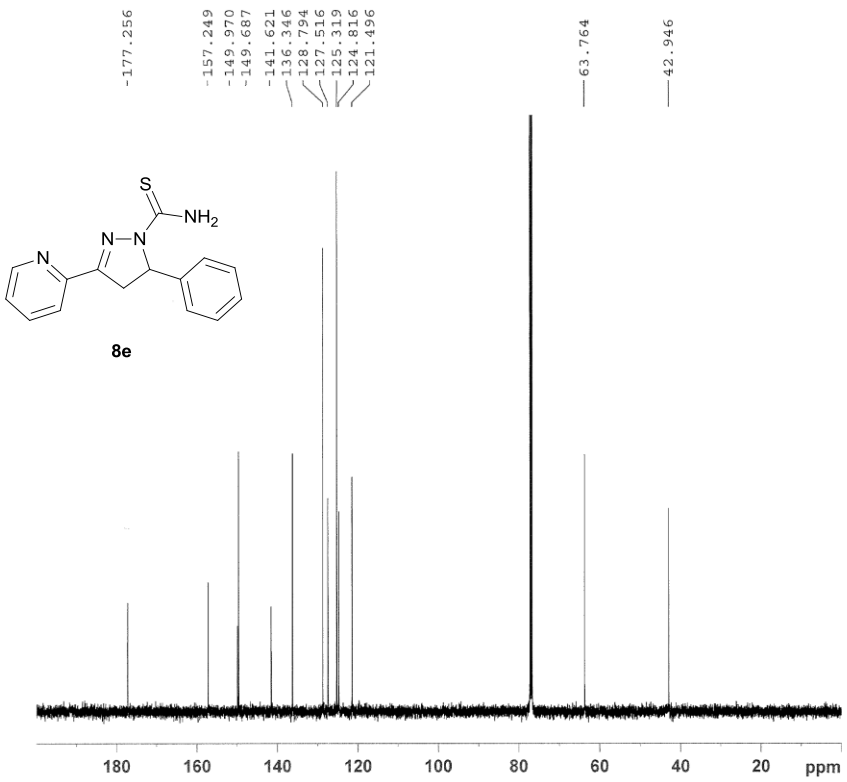
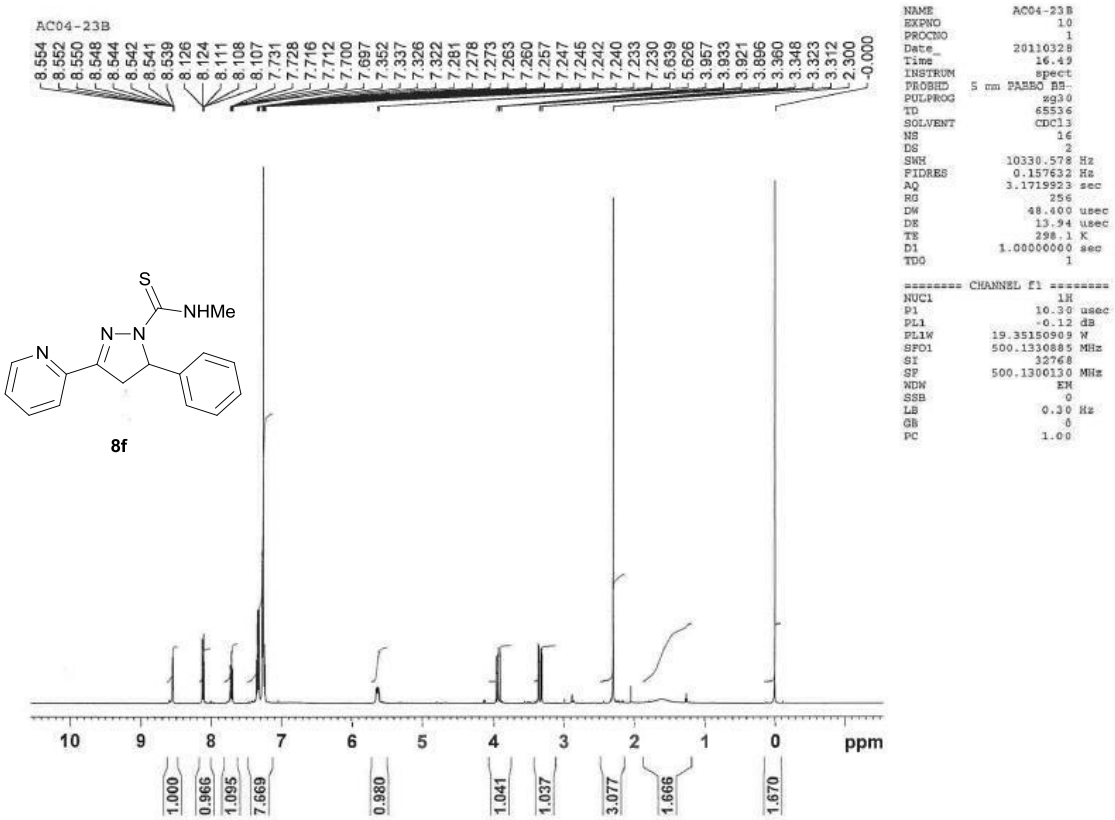
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010548 sec
RG 2050
DW 16.800 usec
DE 9.48 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 14.50 usec
PL1 0.00 dB
PL1W 114.29083252 W
SFO1 125.7703643 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 18.06 dB
PL13 21.00 dB
PL2W 19.34152603 W
PL12W 0.30233663 W
PL13W 0.15363520 W
SFO2 500.1320005 MHz
SI 32768
SF 125.7577901 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

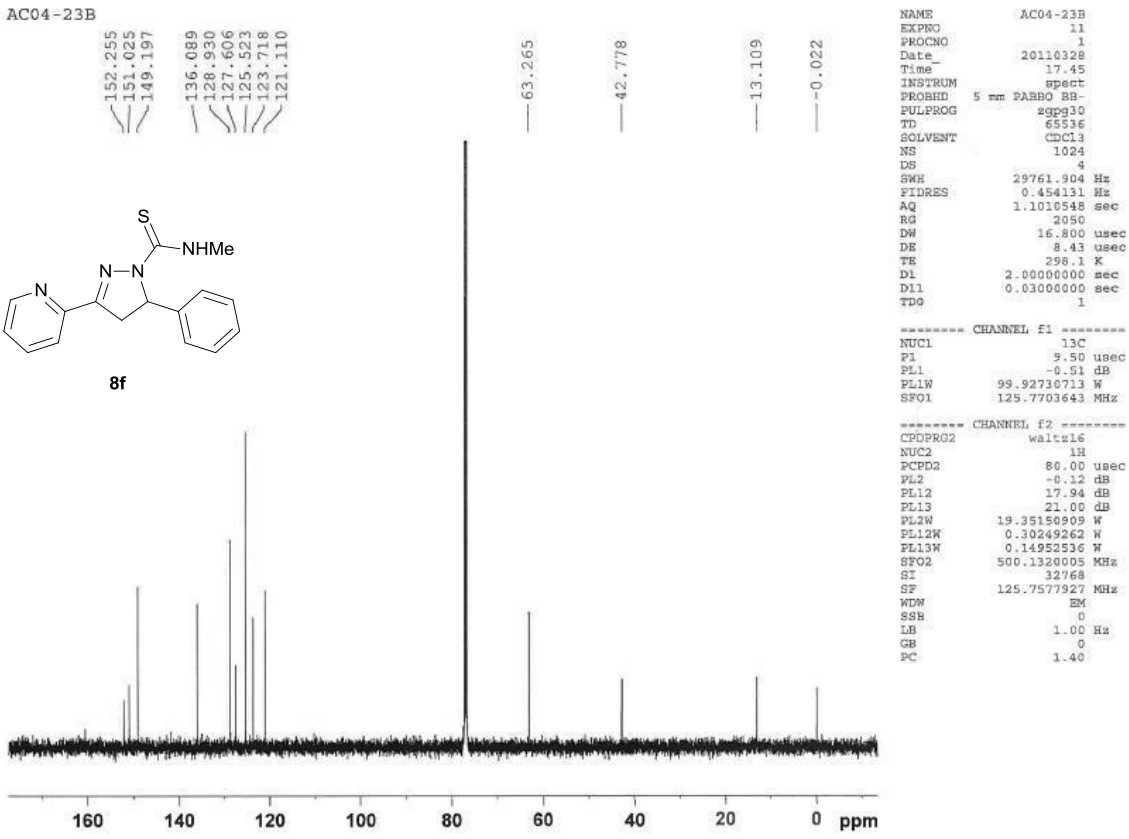


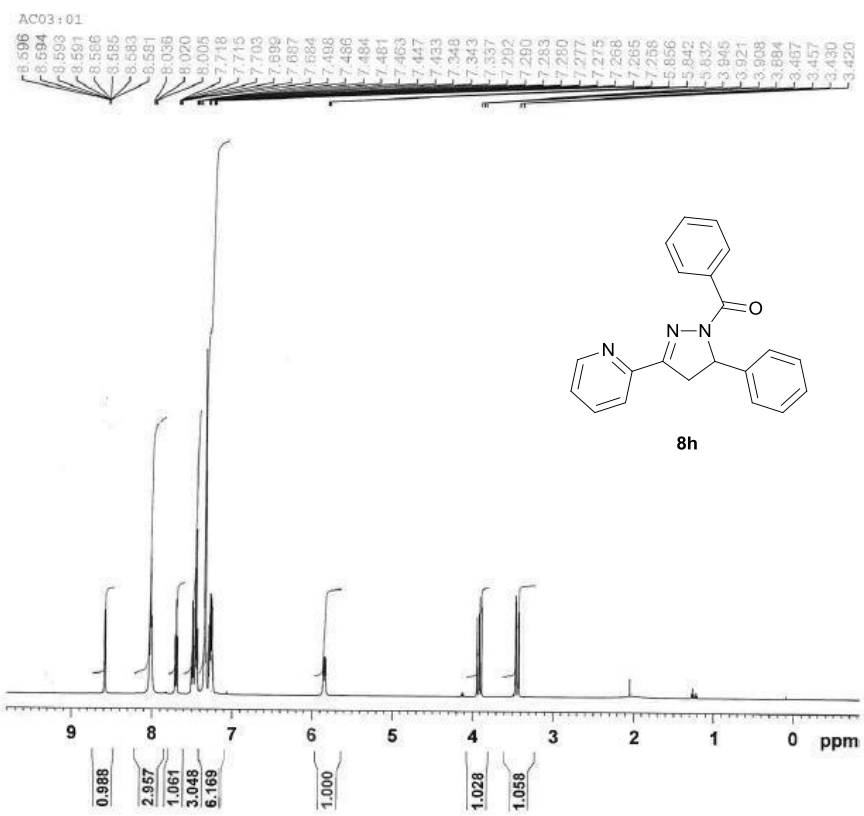

```
NAME          Mar23-2010-ac0156
EXPNO                        10
PROCNO                        1
Date_                  20100323
Time                      14.31
INSTRUM                AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                 8223.685 Hz
FIDRES              0.125483 Hz
AQ                  3.9846387 sec
RG                         114
DW                    60.800 usec
DE                     6.50 usec
TE                     291.5 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       1H
P1                    13.00 usec
PL1                    0.00 dB
PL1W             9.74611950 W
SFO1           400.0424704 MHz
SI                       32768
SF             400.0400000 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                     1.00
```



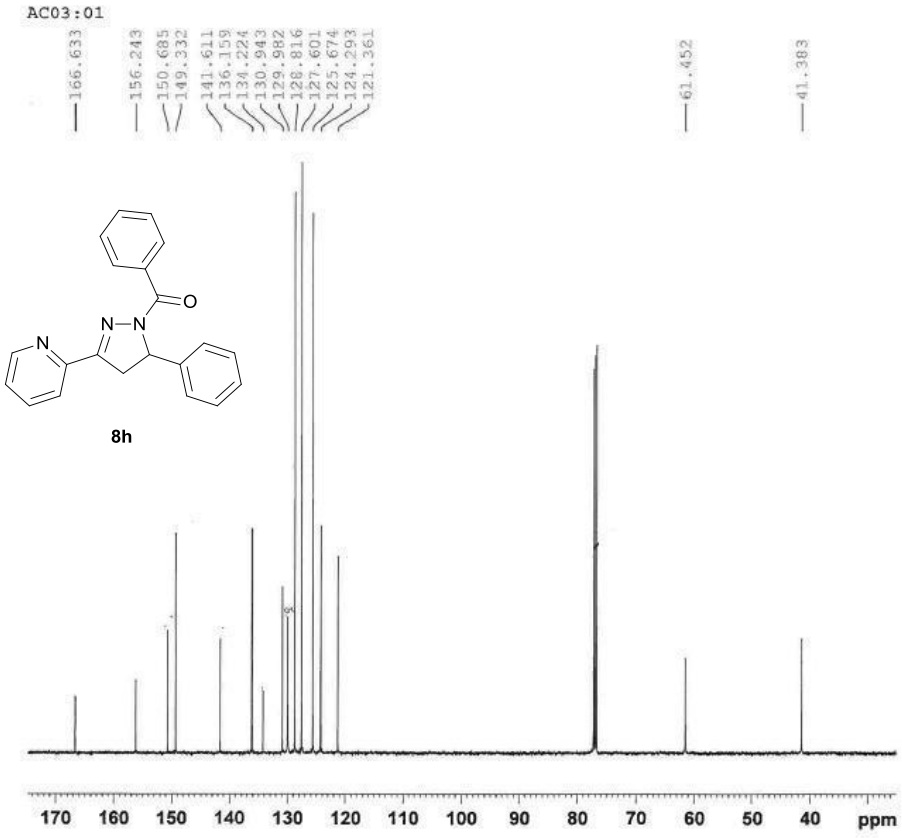

```
NAME
EXPNO                        11
PROCNO                        1
Date_                  20130214
Time                      11.52
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                         227
DS                           4
SWH                29761.904 Hz
FIDRES              0.454131 Hz
AQ                  1.1010548 sec
RG                        2050
DW                    16.800 usec
DE                     8.45 usec
TE                     298.3 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                     9.40 usec
PL1                   -0.51 dB
PL1W            99.92730713 W
SFO1           125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 80.00 usec
PL2                   -0.12 dB
PL12                  17.94 dB
PL13                  21.00 dB
PL2W            19.35150909 W
PL12W            0.30249262 W
PL13W            0.14952536 W
SFO2           500.1320005 MHz
SI                       32768
SF             125.7577966 MHz
WDW                        EM
SSB                         0
LB                     1.00 Hz
GB                          0
PC                     1.40
```


AC04-23B
8.554 8.552 8.550 8.548 8.544 8.542 8.541 8.539 8.126 8.124 8.111 8.108 8.107 7.731 7.728 7.716 7.712 7.700 7.697 7.352 7.337 7.326 7.322 7.281 7.278 7.273 7.263 7.260 7.257 7.247 7.245 7.242 7.240 7.233 7.230 5.639 5.626 3.957 3.933 3.921 3.896 3.360 3.348 3.323 3.312 2.300 -0.000
S
NHMe
N
N
N
8f
10 9 8 7 6 5 4 3 2 1 0 ppm
1.000 0.966 1.095 7.669 0.980 1.041 1.037 3.077 1.666 1.670
NAME AC04-23B
EXPNO 10
PROCNO 1
Date_ 20110328
Time 16.49
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10330.578 Hz
FIDRES 0.157632 Hz
AQ 3.1719923 sec
RG 256
DW 48.400 usec
DE 13.94 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.30 usec
PL1 -0.12 dB
PL1W 19.35150909 W
SFO1 500.1330885 MHz
SI 32768
SF 500.1300130 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

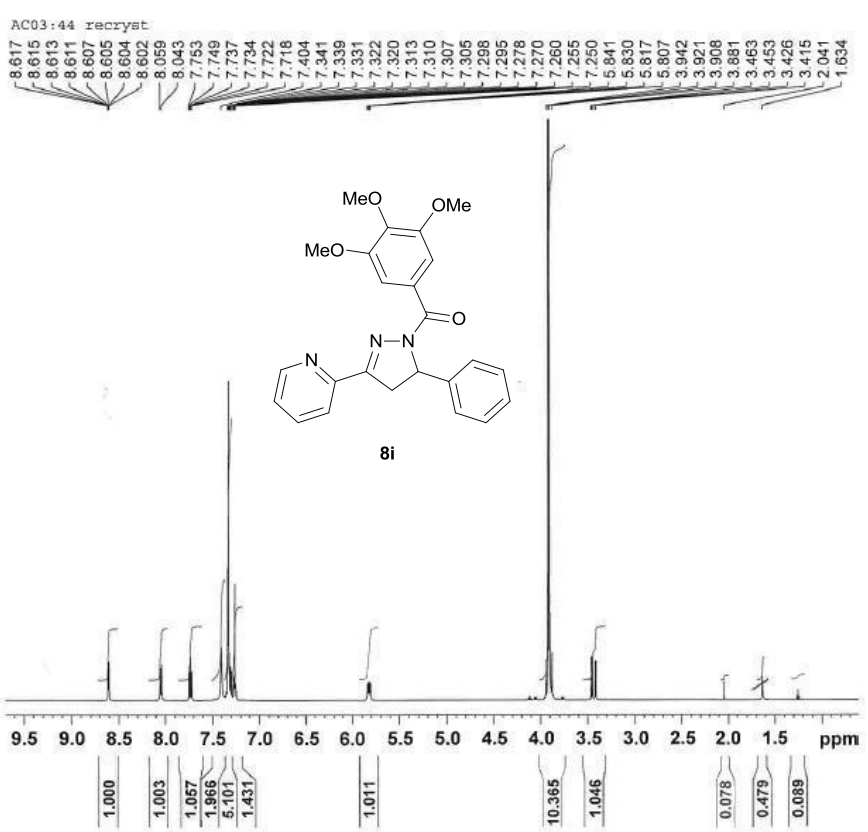

AC04-23B
152.255 151.025 149.197 136.089 128.930 127.606 125.523 123.718 121.110 63.265 42.778 13.109 -0.022
S
NHMe
N
N
N
8f
160 140 120 100 80 60 40 20 0 ppm
NAME AC04-23B
EXPNO 11
PROCNO 1
Date_ 20110328
Time 17.45
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010548 sec
RG 2050
DW 16.800 usec
DE 8.43 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.50 usec
PL1 -0.51 dB
PL1W 99.92730713 W
SFO1 125.7703643 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -0.12 dB
PL12 17.94 dB
PL13 21.00 dB
PL2W 19.35150909 W
PL12W 0.30249262 W
PL13W 0.14952536 W
SFO2 500.1320005 MHz
SI 32768
SF 125.7577927 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



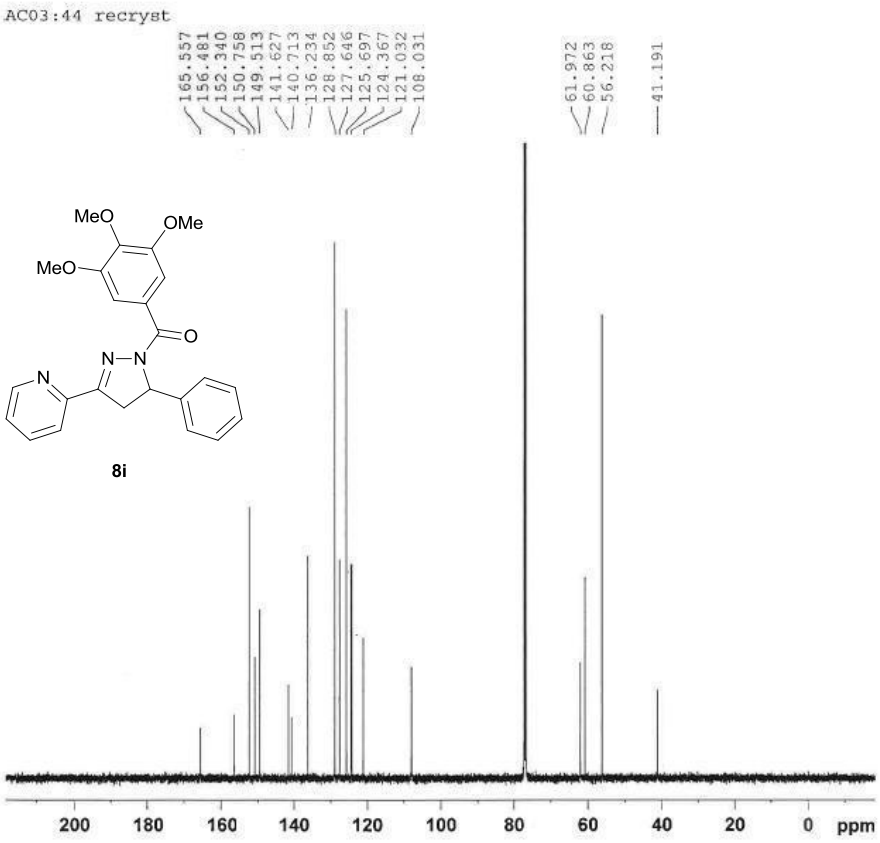
NAME	AC03-01
EXPNO	10
PROCNO	1
Date_	20101011
Time	12.54
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578
FIDRES	0.157632
AQ	3.1719923
RG	64
DW	48.400
DE	12.94
TE	300.0
D1	1.00000000
TD0	1
======== CHANNEL f1 ====	
NUC1	1H
P1	10.30
PL1	0.00
PL1W	19.34152603
SFO1	500.1330885
SI	32768
SF	500.1300143
WDW	EM
SSB	0
LB	0.30
GB	0
PC	1.00



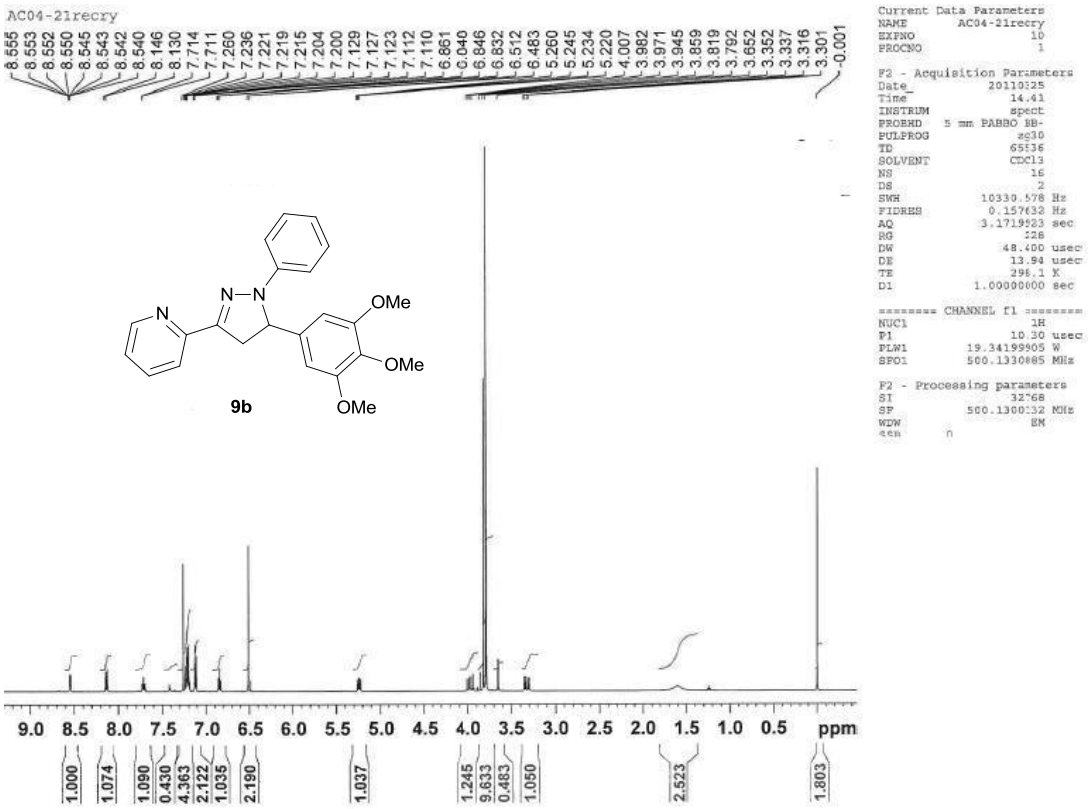
NAME	AC03-01
EXPNO	11
PROCNO	1
Date_	20101011
Time	13.30
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	604
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	2050
DW	16.800 usec
DE	9.53 usec
TE	300.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.50 usec
PL1	0.00 dB
PL1W	114.29083252 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	16.06 dB
PL13	21.00 dB
PL2W	19.34152603 W
PL12W	0.30233663 W
PL13W	0.15363520 W
SFO2	500.1320005 MHz
SI	32768
SF	125.7578010 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40



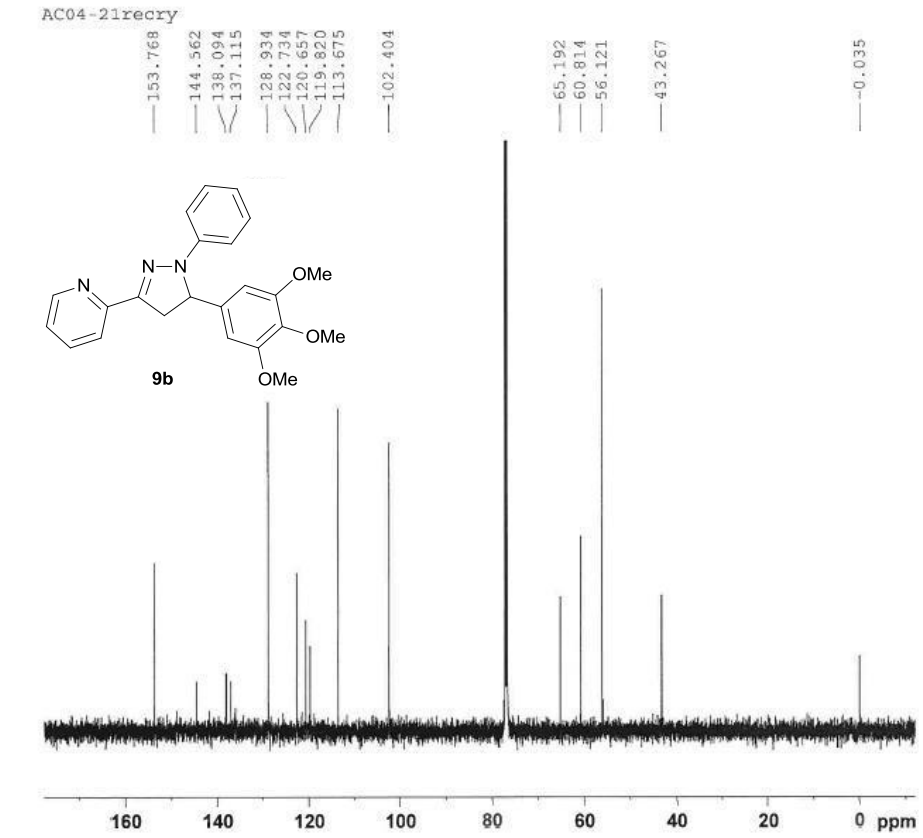
NAME	AC03-44
EXPNO	10
PROCNO	1
Date_	20101130
Time	2.54
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	128
DW	48.400 usec
DE	13.94 usec
TE	300.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	10.30 usec
PL1	0.00 dB
PL1W	19.34152603 W
SFO1	500.1330885 MHz
SI	32768
SF	500.1300132 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



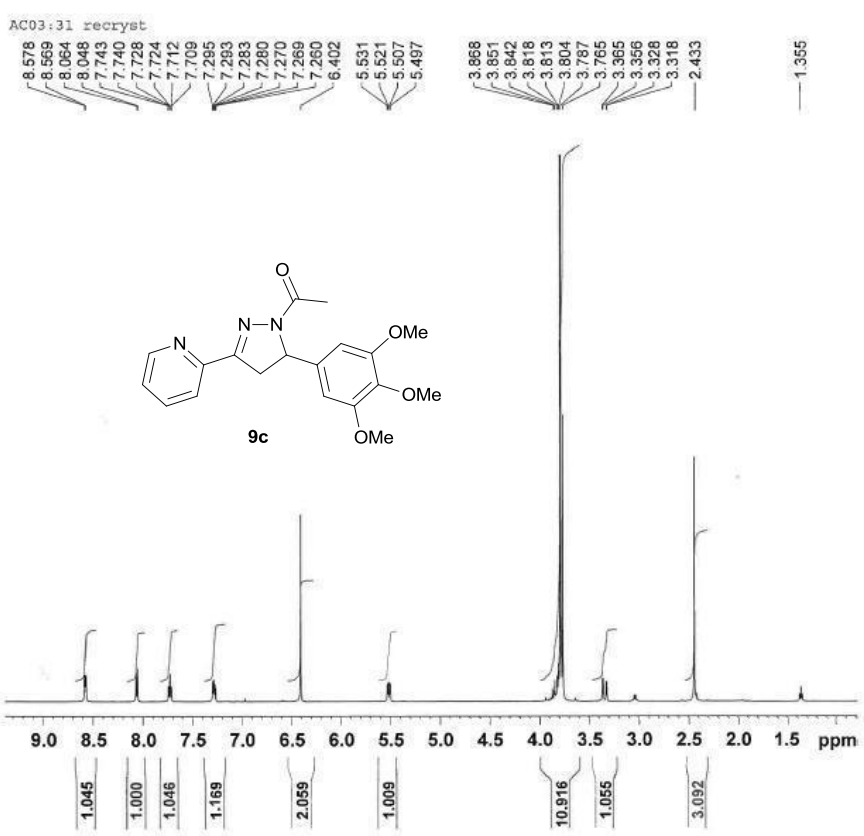
NAME	AC03-44
EXPNO	11
PROCNO	1
Date_	20101130
Time	3.50
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1024
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	2050
DW	16.800 usec
DE	9.48 usec
TE	300.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	0.00 dB
PL1W	114.29083252 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	18.06 dB
PL13	21.00 dB
PL2W	19.34152603 W
PL12W	0.30233663 W
PL13W	0.15363520 W
SFO2	500.1320005 MHz
SI	32768
SF	125.7577963 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40



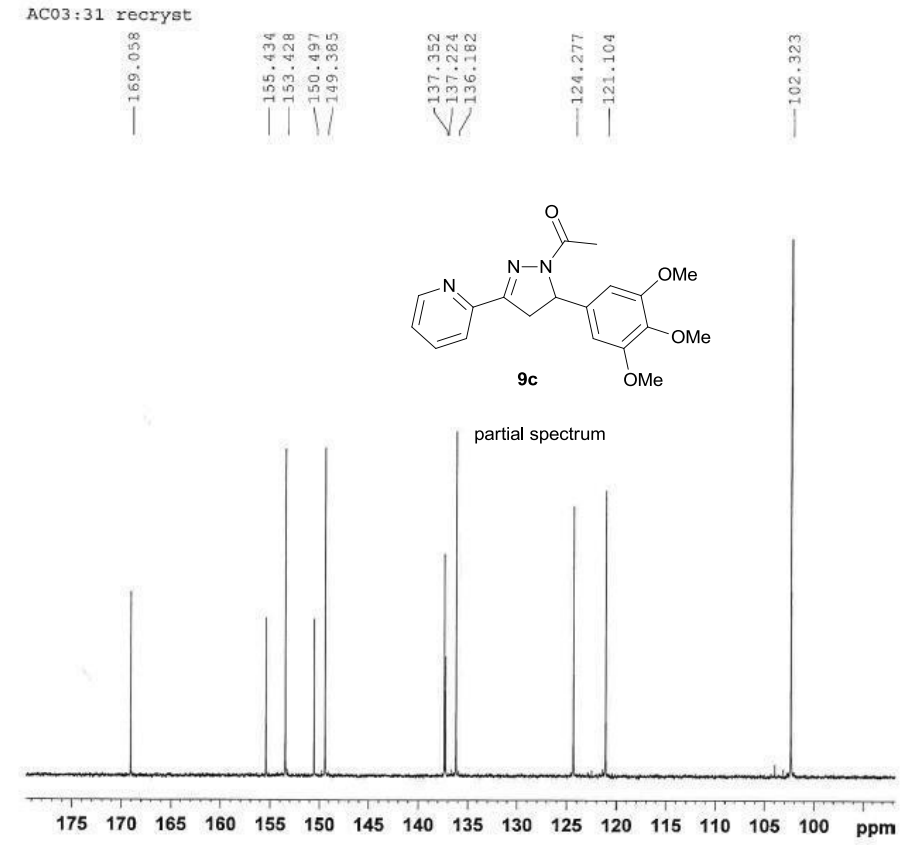

```
Current Data Parameters
NAME         AC04-21recry
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20110325
Time               14.41
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10330.578 Hz
FIDRES         0.157632 Hz
AQ             3.1719923 sec
RG                   228
DW                48.400 usec
DE                13.94 usec
TE                298.1 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.30 usec
PLW1          19.34199905 W
SFO1         500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF           500.1300032 MHz
WDW                   EM
SSB                    0
```



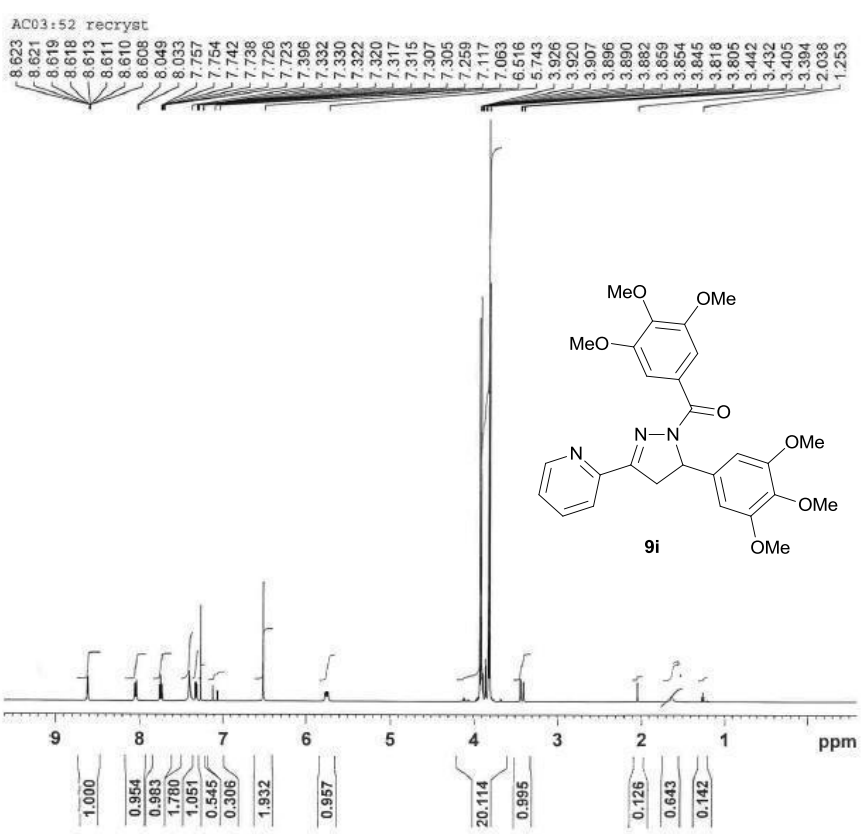

```
Current Data Parameters
NAME         AC04-21recry
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20110325
Time               14.56
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            29761.904 Hz
FIDRES         0.454131 Hz
AQ             1.1010548 sec
RG                  2050
DW                16.800 usec
DE                 8.43 usec
TE                298.1 K
D1             2.00000000 sec
D11            0.03000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.50 usec
PLW1         100.00000000 W
SFO1         125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             80.00 usec
PLW2          19.34199905 W
PLW12          0.30221000 W
PLW13          0.19341999 W
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                 32768
SF           125.7577940 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```



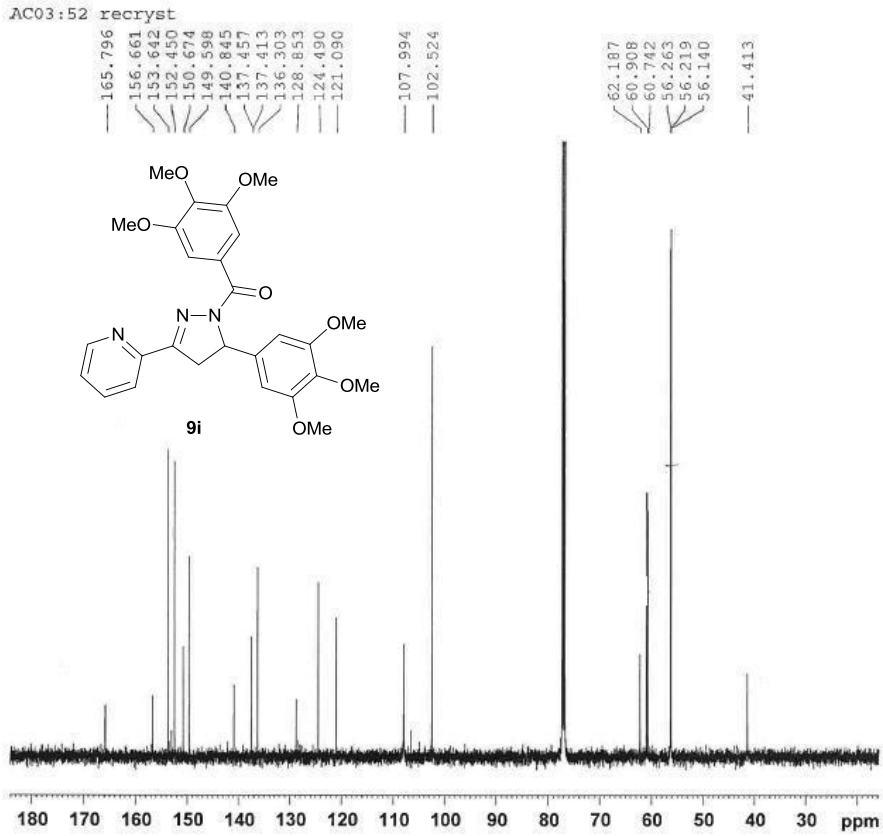

```
NAME          AC03-31 recryst
EXPNO                      20
PROCNO                      1
Date_                20101118
Time                    13.23
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG                 zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                 10330.578 Hz
FIDRES              0.157632 Hz
AQ                  3.1719923 sec
RG                         32
DW                     48.400 usec
DE                     13.94 usec
TE                     300.0 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      10.30 usec
PL1                      0.00 dB
PL1W                19.34152603 W
SFO1                500.1330885 MHz
SI                       32768
SF                  500.1300138 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```




```
NAME          AC03-31 recryst
EXPNO                      21
PROCNO                      1
Date_                20101118
Time                    13.27
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG              zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       1024
DS                          4
SWH                 29761.904 Hz
FIDRES              0.454131 Hz
AQ                  1.1010548 sec
RG                       2050
DW                     16.800 usec
DE                      9.48 usec
TE                     300.0 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       13C
P1                      14.50 usec
PL1                      0.00 dB
PL1W               114.29083252 W
SFO1                125.7703543 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   80.00 usec
PL2                      0.00 dB
PL12                    18.06 dB
PL13                    21.00 dB
PL2W                19.34152603 W
PL12W               0.30233563 W
PL13W               0.15363520 W
SFO2                500.1320905 MHz
SI                       32766
SF                  125.7578055 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```



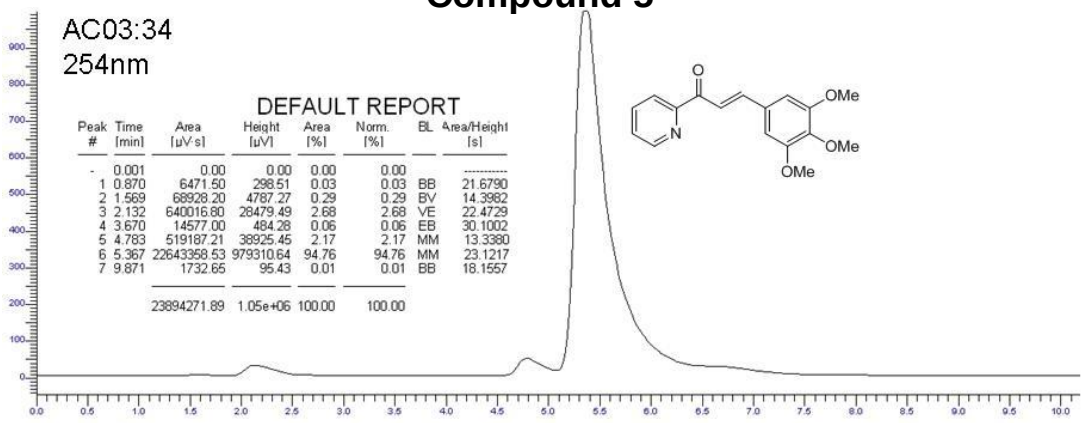
NAME	AC03-52
EXPNO	10
PROCNO	1
Date_	20101203
Time	23.35
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	161
DW	48.400 use
DE	13.94 use
TE	300.1 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	10.30 use
PL1	0.00 dB
PL1W	19.34152603 W
SFO1	500.1330885 MHz
SI	32768
SF	500.1300140 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



NAME	AC03-52
EXPNO	11
PROCNO	1
Date_	20101204
Time	0.31
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1024
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	2050
DW	16.800 usec
DE	9.48 usec
TE	300.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	0.00 dB
PL1W	114.29083252 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	18.06 dB
PL13	21.00 dB
PL2W	19.34152603 W
PL12W	0.30233663 W
PL13W	0.15363520 W
SFO2	500.1320005 MHz
SI	32768
SF	125.7577924 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

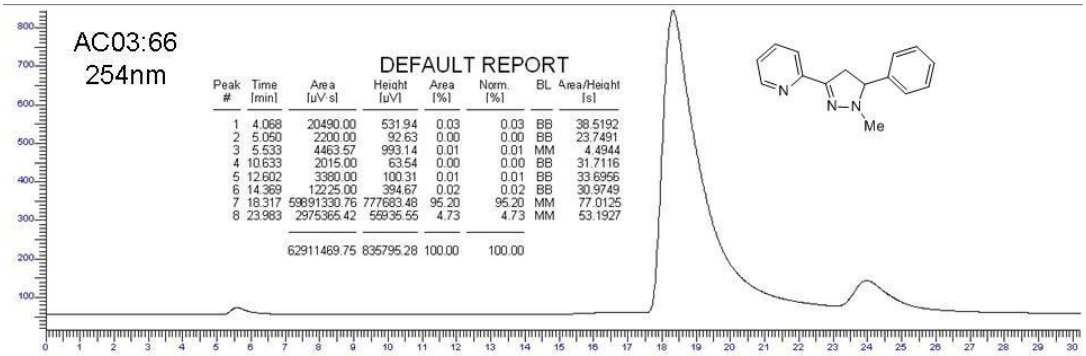
HPLC traces at 254nm

Compound 5



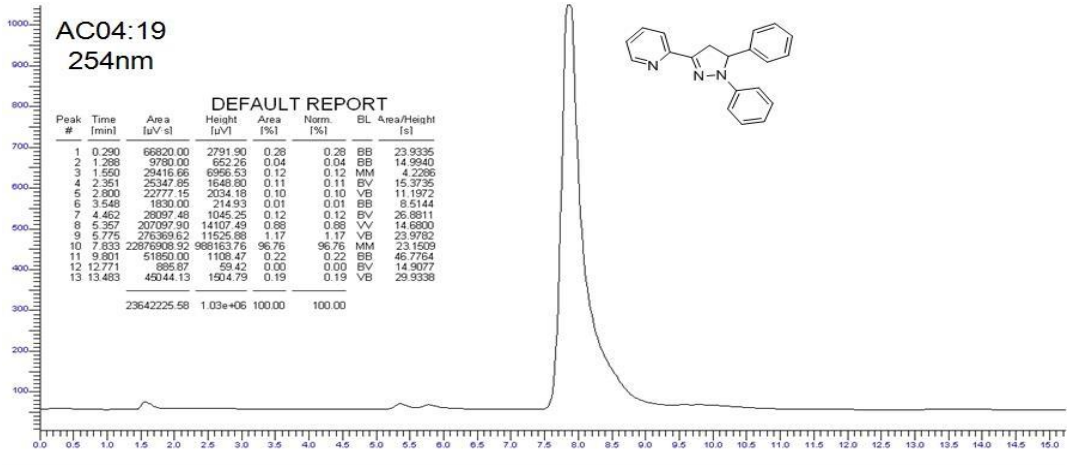
Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	0.870	6471.50	298.51	0.03	0.03	BB	21.6790
2	1.569	68928.20	4787.27	0.29	0.29	BV	14.3982
3	2.132	640016.80	28479.49	2.68	2.68	VE	22.4729
4	3.670	14577.00	484.28	0.06	0.06	EB	30.1002
5	4.783	519187.21	38925.45	2.17	2.17	MM	13.3380
6	5.367	22643358.53	979310.64	94.76	94.76	MM	23.1217
7	9.871	1732.65	95.43	0.01	0.01	BB	18.1557
		23894271.89	1.05e+06	100.00	100.00		

Compound 8a



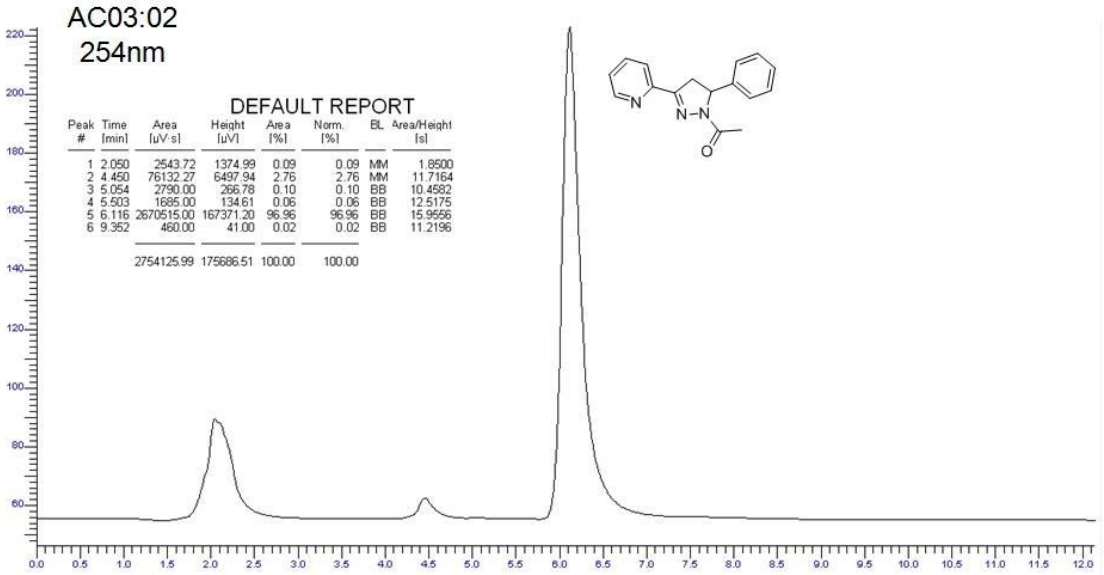
Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	4.068	20490.00	531.94	0.03	0.03	BB	38.5192
2	5.050	2200.00	92.63	0.00	0.00	BB	23.7491
3	5.533	4463.57	993.14	0.01	0.01	MM	4.4944
4	10.633	2015.00	63.54	0.00	0.00	BB	31.7116
5	12.602	3380.00	100.31	0.01	0.01	BB	33.6956
6	14.369	12225.00	394.67	0.02	0.02	BB	30.9749
7	18.317	59891330.76	777683.48	95.20	95.20	MM	77.0125
8	23.983	2975365.42	55935.55	4.73	4.73	MM	53.1927
		62911469.75	835795.28	100.00	100.00		

Compound 8b

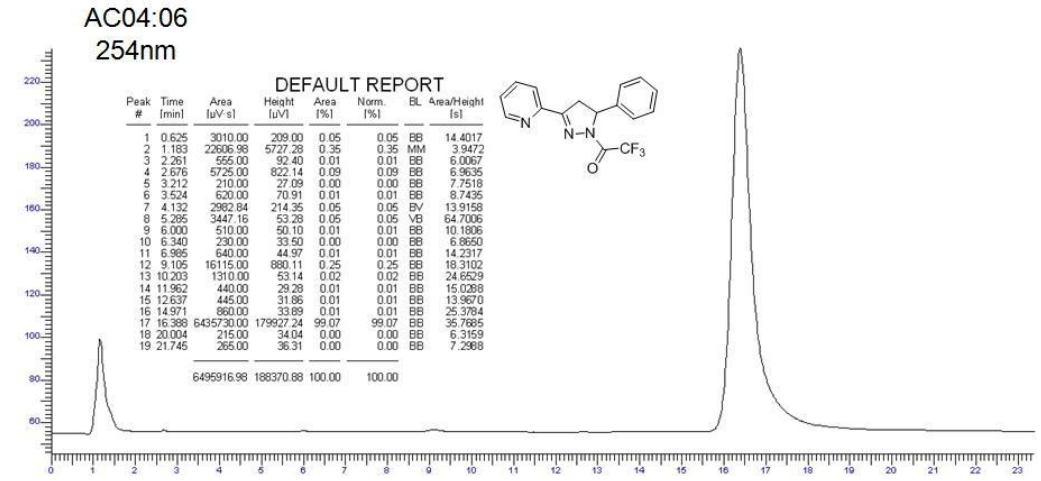


Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.290	66820.00	2791.90	0.28	0.28	BB	23.9335
2	1.288	9780.00	652.26	0.04	0.04	BB	14.9940
3	1.550	29416.66	6956.53	0.12	0.12	MM	4.2286
4	2.351	25347.85	1648.80	0.11	0.11	BV	15.3735
5	2.800	22777.15	2034.18	0.10	0.10	VB	11.1972
6	3.548	1830.00	214.93	0.01	0.01	BB	8.5144
7	4.462	28097.48	1045.25	0.12	0.12	BV	26.8811
8	5.357	207097.90	14107.49	0.88	0.88	VV	14.6800
9	5.775	276369.62	11525.88	1.17	1.17	VB	23.9782
10	7.833	22876908.92	988163.76	96.76	96.76	MM	23.1509
11	9.801	51850.00	1108.47	0.22	0.22	BB	46.7764
12	12.771	885.87	59.42	0.00	0.00	BV	14.9077
13	13.483	45044.13	1504.79	0.19	0.19	VB	29.9338
		23642225.58	1.03e+06	100.00	100.00		

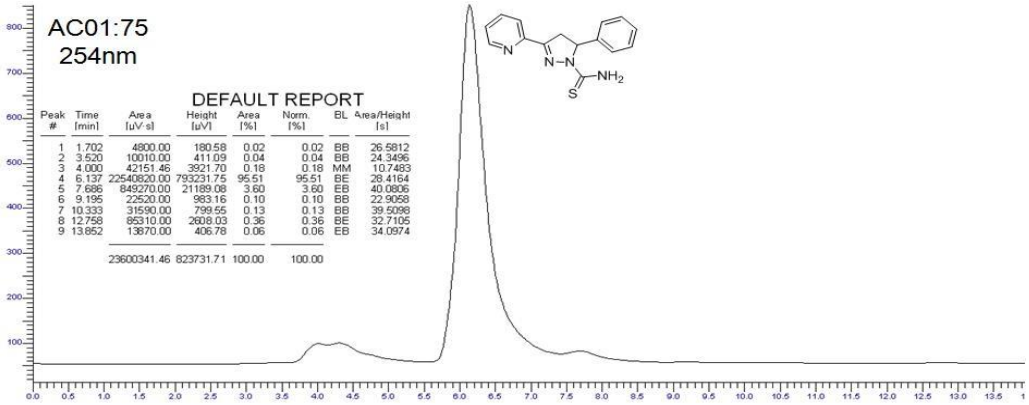
Compound 8c



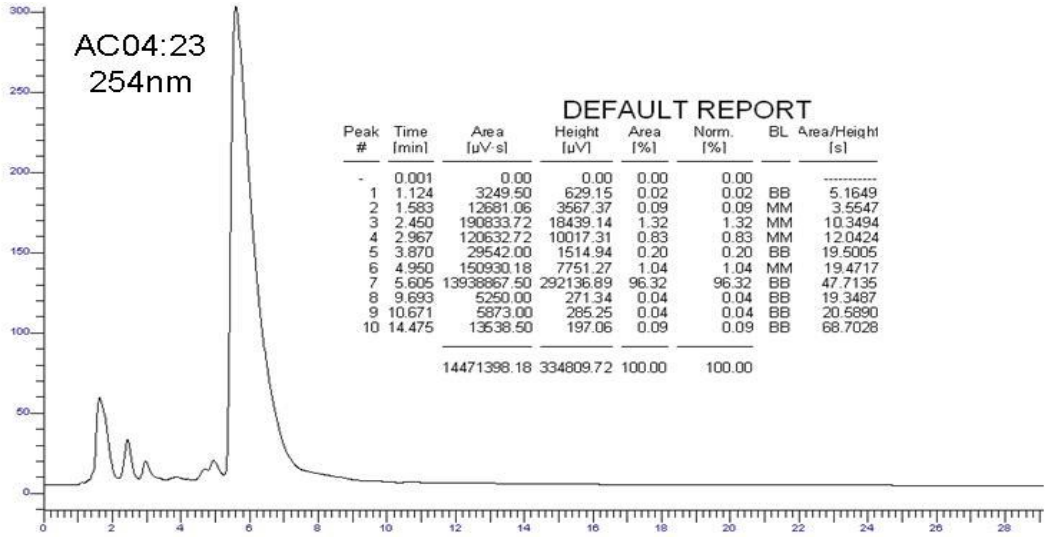
Compound 8d



Compound 8e



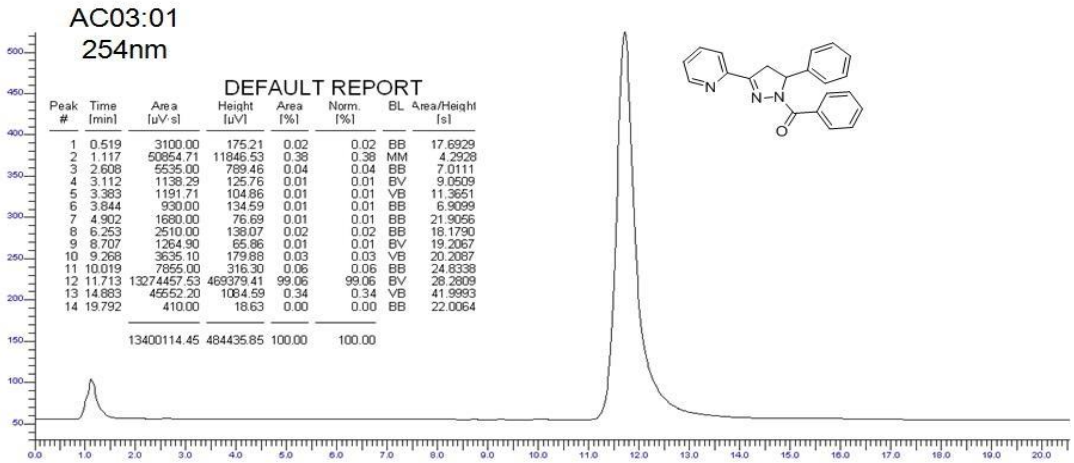
Compound 8f



DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	1.124	3249.50	629.15	0.02	0.02	BB	5.1649
2	1.583	12681.06	3567.37	0.09	0.09	MM	3.5547
3	2.450	190833.72	18439.14	1.32	1.32	MM	10.3494
4	2.967	120632.72	10017.31	0.83	0.83	MM	12.0424
5	3.870	29542.00	1514.94	0.20	0.20	BB	19.5005
6	4.950	150930.18	7751.27	1.04	1.04	MM	19.4717
7	5.605	13938867.50	292136.89	96.32	96.32	BB	47.7135
8	9.693	5250.00	271.34	0.04	0.04	BB	19.3487
9	10.671	5873.00	285.25	0.04	0.04	BB	20.5890
10	14.475	13538.50	197.06	0.09	0.09	BB	68.7028
		14471398.18	334809.72	100.00	100.00		

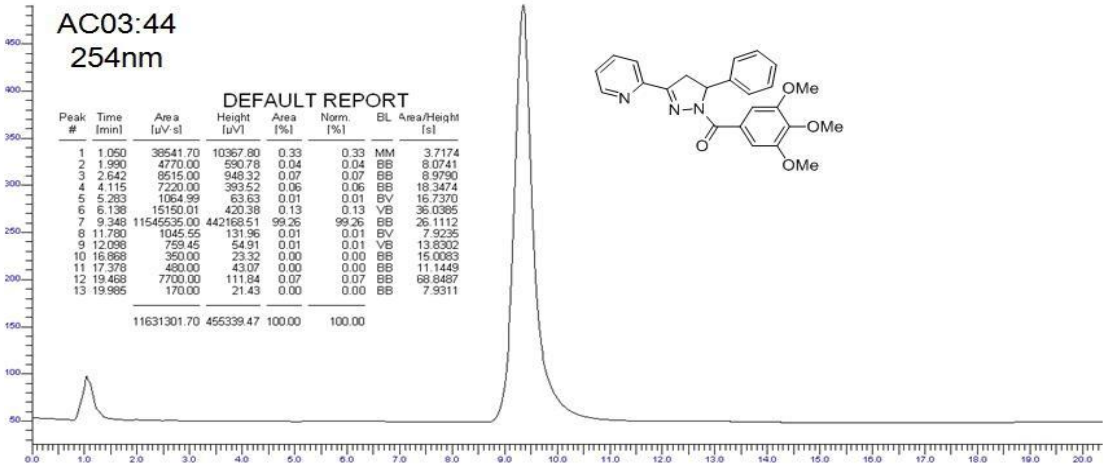
Compound 8h



DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.519	3100.00	175.21	0.02	0.02	BB	17.6929
2	1.117	50854.71	11846.53	0.38	0.38	MM	4.2928
3	2.608	5535.00	789.46	0.04	0.04	BB	7.0111
4	3.112	1138.29	125.76	0.01	0.01	BV	9.0509
5	3.383	1191.71	104.86	0.01	0.01	VB	11.3651
6	3.844	930.00	134.59	0.01	0.01	BB	6.9099
7	4.902	1680.00	76.69	0.01	0.01	BB	21.9056
8	6.253	2510.00	138.07	0.02	0.02	BB	18.1790
9	8.707	1264.90	65.86	0.01	0.01	BV	19.2067
10	9.268	3635.10	179.88	0.03	0.03	VB	20.2087
11	10.019	7855.00	316.30	0.06	0.06	BB	24.8338
12	11.713	13274457.53	469379.41	99.06	99.06	BV	28.2809
13	14.883	45552.20	1084.59	0.34	0.34	VB	41.9993
14	19.792	410.00	18.63	0.00	0.00	BB	22.0064
		13400114.45	484435.85	100.00	100.00		

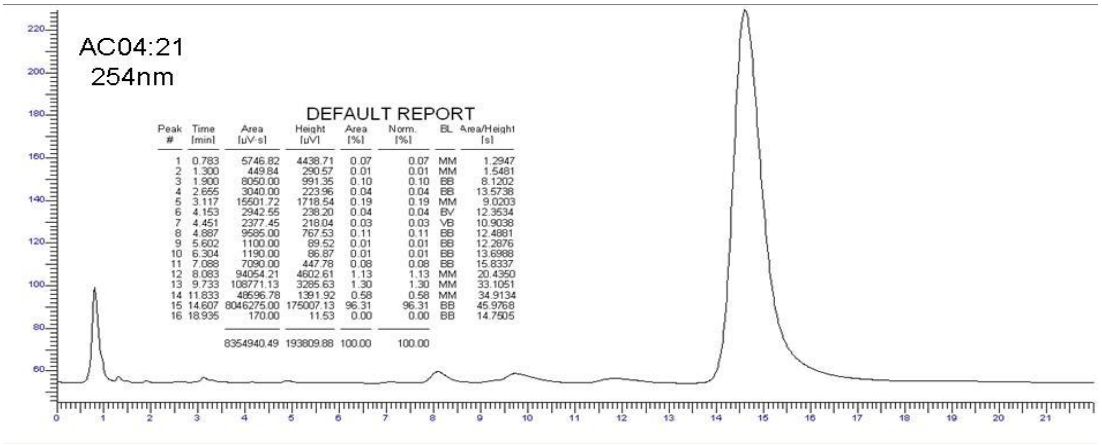
Compound 8i



DEFAULT REPORT

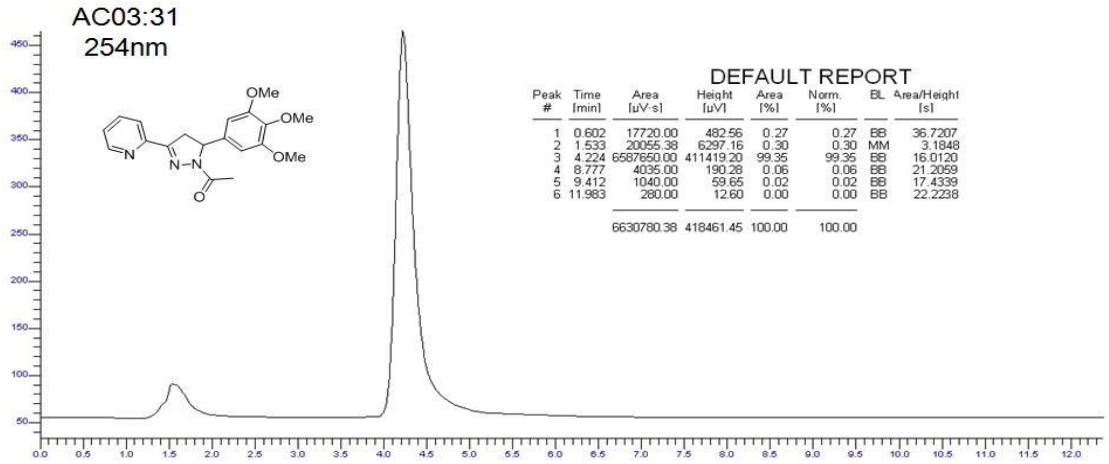
Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	1.050	38541.70	10367.80	0.33	0.33	MM	3.7174
2	1.990	4770.00	590.78	0.04	0.04	BB	8.0741
3	2.642	9515.00	948.32	0.07	0.07	BB	8.9790
4	4.115	7220.00	393.52	0.06	0.06	BB	18.3474
5	5.283	1064.99	63.63	0.01	0.01	BV	16.7370
6	6.138	15150.01	420.38	0.13	0.13	VB	36.0385
7	9.348	11545535.00	442168.51	99.26	99.26	BB	26.1112
8	11.780	1045.55	131.96	0.01	0.01	BV	7.9235
9	12.098	759.45	54.91	0.01	0.01	VB	13.8302
10	16.868	350.00	23.32	0.00	0.00	BB	15.0083
11	17.378	480.00	43.07	0.00	0.00	BB	11.1449
12	19.468	7700.00	111.84	0.07	0.07	BB	68.8487
13	19.985	170.00	21.43	0.00	0.00	BB	7.9311
		11631301.70	455339.47	100.00	100.00		

Compound 9b



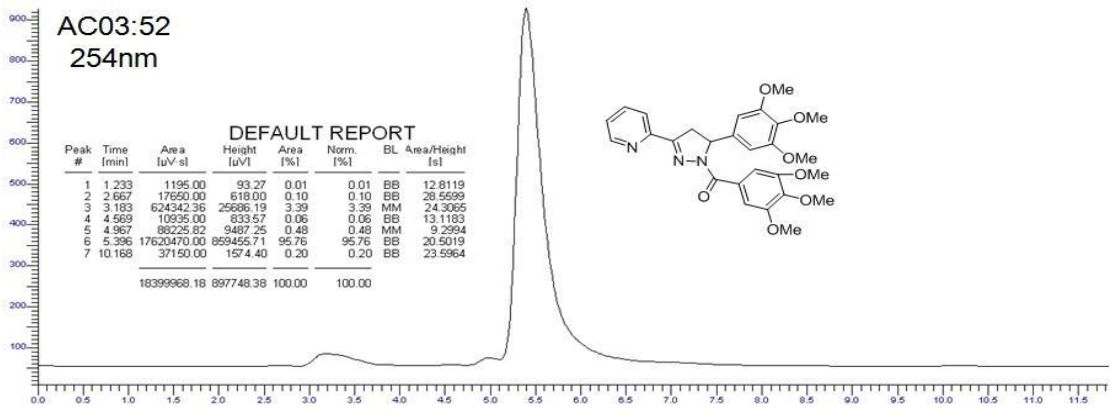
Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.783	5746.82	4438.71	0.07	0.07	MM	1.2947
2	1.300	449.84	290.57	0.01	0.01	MM	1.5481
3	1.900	8050.00	991.35	0.10	0.10	BB	8.1202
4	2.655	3040.00	223.96	0.04	0.04	BB	13.5738
5	3.117	15501.72	1718.54	0.19	0.19	MM	9.0203
6	4.153	2942.55	238.20	0.04	0.04	BV	12.3534
7	4.451	2377.45	218.04	0.03	0.03	VB	10.9038
8	4.887	9585.00	767.53	0.11	0.11	BB	12.4881
9	5.602	1100.00	89.52	0.01	0.01	BB	12.2876
10	6.304	1190.00	86.87	0.01	0.01	BB	13.6988
11	7.088	7090.00	447.78	0.08	0.08	BB	15.8337
12	8.083	94054.21	4602.61	1.13	1.13	MM	20.4350
13	9.733	108771.13	3285.63	1.30	1.30	MM	33.1051
14	11.833	48596.78	1391.92	0.58	0.58	MM	34.9134
15	14.607	8046275.00	175007.13	96.31	96.31	BB	45.9768
16	18.935	170.00	11.53	0.00	0.00	BB	14.7505
		8354940.49	193809.88	100.00	100.00		

Compound 9c



Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.602	17720.00	482.56	0.27	0.27	BB	36.7207
2	1.533	20055.38	6297.16	0.30	0.30	MM	3.1848
3	4.224	6587650.00	411419.20	99.35	99.35	BB	16.0120
4	8.777	4035.00	190.28	0.06	0.06	BB	21.2059
5	9.412	1040.00	59.65	0.02	0.02	BB	17.4339
6	11.983	280.00	12.60	0.00	0.00	BB	22.2238
		6630780.38	418461.45	100.00	100.00		

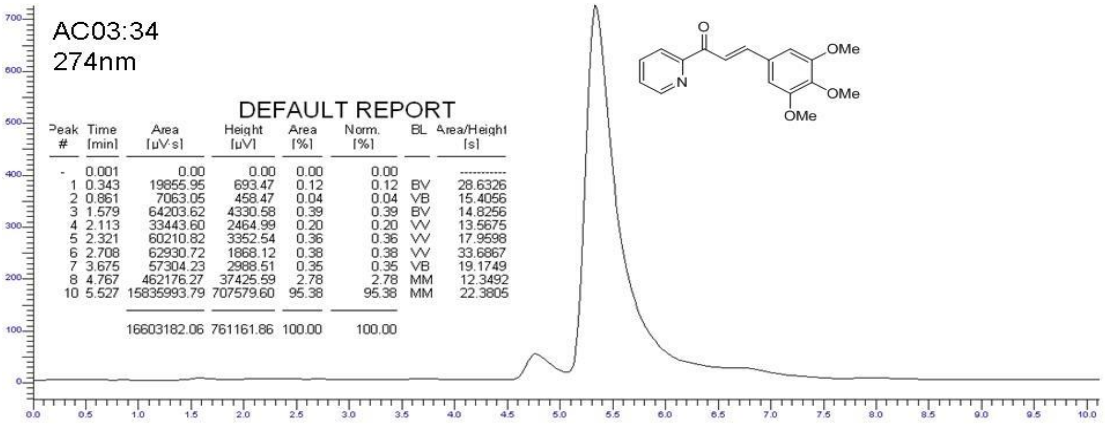
Compound 9i



Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	1.233	1195.00	93.27	0.01	0.01	BB	12.8119
2	2.667	17650.00	618.00	0.10	0.10	BB	28.5599
3	3.183	624342.36	25686.19	3.39	3.39	MM	24.3065
4	4.569	10935.00	833.57	0.06	0.06	BB	13.1183
5	4.967	88225.82	9487.25	0.48	0.48	MM	9.2994
6	5.396	17620470.00	859455.71	95.76	95.76	BB	20.5019
7	10.168	37150.00	1574.40	0.20	0.20	BB	23.5964
		18399968.18	897748.38	100.00	100.00		

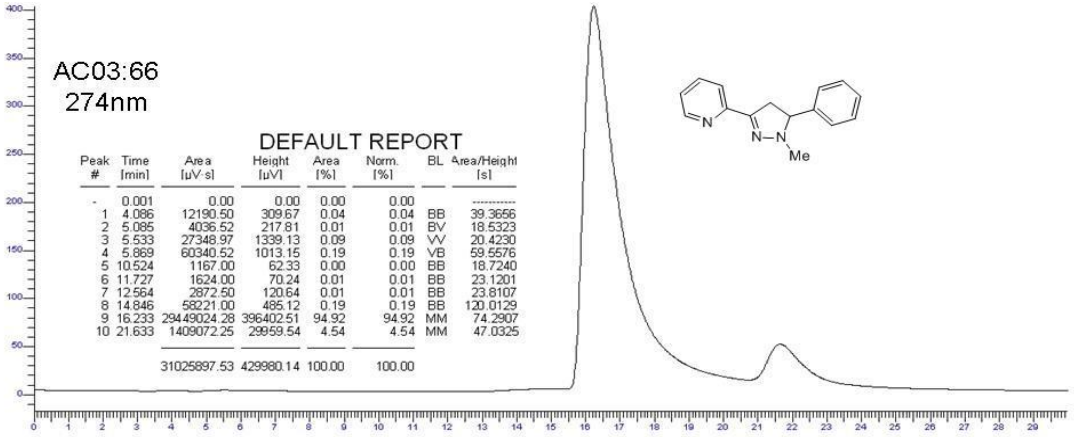
HPLC traces at 274 nm

Compound 5



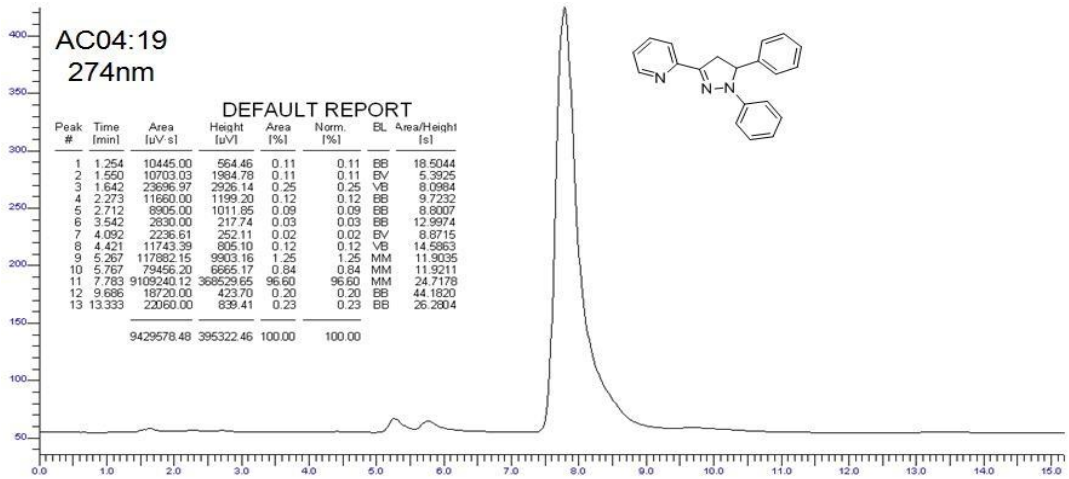
Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	0.343	19855.95	693.47	0.12	0.12	BV	28.6326
2	0.861	7063.05	458.47	0.04	0.04	VB	15.4056
3	1.579	64203.62	4330.58	0.39	0.39	BV	14.8256
4	2.113	33443.60	2464.99	0.20	0.20	VV	13.5675
5	2.321	60210.82	3352.54	0.36	0.36	VV	17.9598
6	2.708	62930.72	1868.12	0.38	0.38	VV	33.6867
7	3.675	57304.23	2988.51	0.35	0.35	VB	19.1749
8	4.767	462176.27	37425.59	2.78	2.78	MM	12.3492
10	5.527	15835993.79	707579.60	95.38	95.38	MM	22.3805
		16603182.06	761161.86	100.00	100.00		

Compound 8a



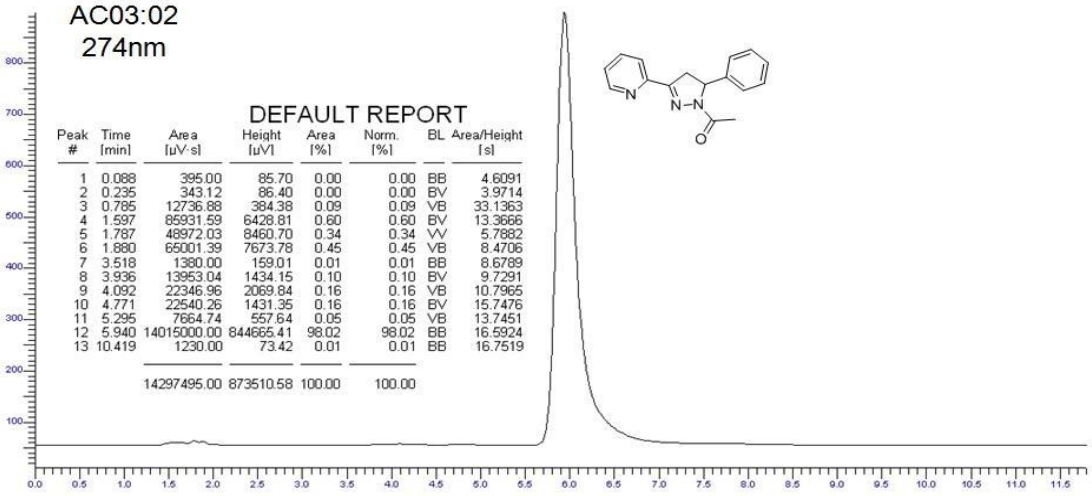
Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	4.086	12190.50	309.67	0.04	0.04	BB	39.3656
2	5.085	4036.52	217.81	0.01	0.01	BV	18.5323
3	5.533	27348.97	1339.13	0.09	0.09	VV	20.4230
4	5.869	60340.52	1013.15	0.19	0.19	VB	59.5576
5	10.524	1167.00	62.33	0.00	0.00	BB	18.7240
6	11.727	1624.00	70.24	0.01	0.01	BB	23.1201
7	12.564	2872.50	120.64	0.01	0.01	BB	23.8107
8	14.846	58221.00	485.12	0.19	0.19	BB	120.0129
9	16.233	29449024.28	396402.51	94.92	94.92	MM	74.2907
10	21.633	1409072.25	29959.54	4.54	4.54	MM	47.0325
		31025897.53	429980.14	100.00	100.00		

Compound 8b



Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	1.254	10445.00	564.46	0.11	0.11	BB	18.5044
2	1.550	10703.03	1984.78	0.11	0.11	BV	5.3925
3	1.642	23696.97	2926.14	0.25	0.25	VB	8.0984
4	2.273	11660.00	1199.20	0.12	0.12	BB	9.7232
5	2.712	8805.00	1011.85	0.09	0.09	BB	8.8007
6	3.542	2830.00	217.74	0.03	0.03	BB	12.9974
7	4.092	2236.61	252.11	0.02	0.02	BV	8.8715
8	4.421	11743.39	805.10	0.12	0.12	VB	14.5863
9	5.267	117882.15	9903.16	1.25	1.25	MM	11.9035
10	5.767	79456.20	6665.17	0.84	0.84	MM	11.9211
11	7.783	9109240.12	368529.65	96.60	96.60	MM	24.7178
12	9.686	18720.00	423.70	0.20	0.20	BB	44.1820
13	13.333	22060.00	839.41	0.23	0.23	BB	26.2804
		9429578.48	395322.46	100.00	100.00		

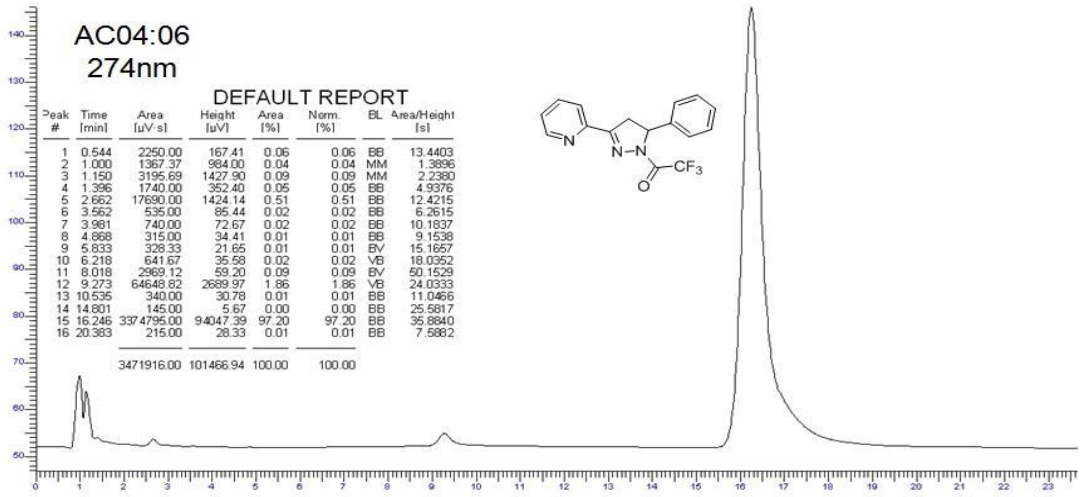
Compound 8c



DEFAULT REPORT

Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.088	395.00	85.70	0.00	0.00	BB	4.6091
2	0.235	343.12	86.40	0.00	0.00	BV	3.9714
3	0.785	12736.88	384.38	0.09	0.09	VB	33.1363
4	1.597	85931.59	6428.81	0.60	0.60	BV	13.3666
5	1.787	48972.03	8460.70	0.34	0.34	VV	5.7882
6	1.880	65001.39	7673.78	0.45	0.45	VB	8.4706
7	3.518	1380.00	159.01	0.01	0.01	BB	8.6789
8	3.936	13953.04	1434.15	0.10	0.10	BV	9.7291
9	4.092	22346.96	2069.84	0.16	0.16	VB	10.7965
10	4.771	22540.26	1431.35	0.16	0.16	BV	15.7476
11	5.295	7664.74	557.64	0.05	0.05	VB	13.7451
12	5.940	14015000.00	844665.41	98.02	98.02	BB	16.5924
13	10.419	1230.00	73.42	0.01	0.01	BB	16.7519
		14297495.00	873510.58	100.00	100.00		

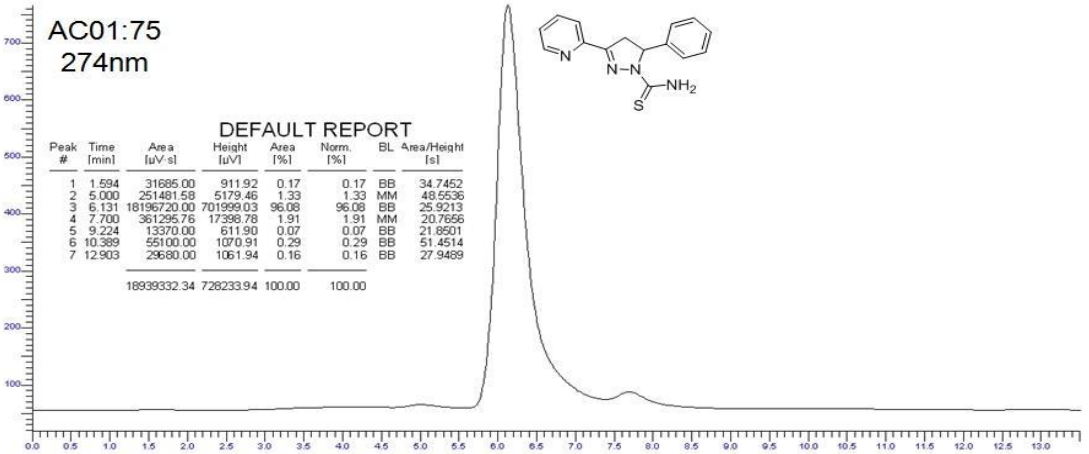
Compound 8d



DEFAULT REPORT

Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.544	2250.00	167.41	0.06	0.06	BB	13.4403
2	1.000	1367.37	984.00	0.04	0.04	MM	1.3896
3	1.150	3195.69	1427.90	0.09	0.09	MM	2.2380
4	1.396	1740.00	352.40	0.05	0.05	BB	4.9376
5	2.662	17690.00	1424.14	0.51	0.51	BB	12.4215
6	3.562	535.00	85.44	0.02	0.02	BB	6.2615
7	3.981	740.00	72.67	0.02	0.02	BB	10.1837
8	4.868	315.00	34.41	0.01	0.01	BB	9.1538
9	5.833	328.33	21.65	0.01	0.01	BV	15.1657
10	6.218	641.67	35.58	0.02	0.02	VB	18.0352
11	8.018	2969.12	59.20	0.09	0.09	BV	50.1529
12	9.273	64648.82	2689.97	1.86	1.86	VB	24.0333
13	10.535	340.00	30.78	0.01	0.01	BB	11.0466
14	14.801	145.00	5.67	0.00	0.00	BB	25.5817
15	16.246	3374795.00	94047.39	97.20	97.20	BB	35.8840
16	20.383	215.00	28.33	0.01	0.01	BB	7.5882
		3471916.00	101466.94	100.00	100.00		

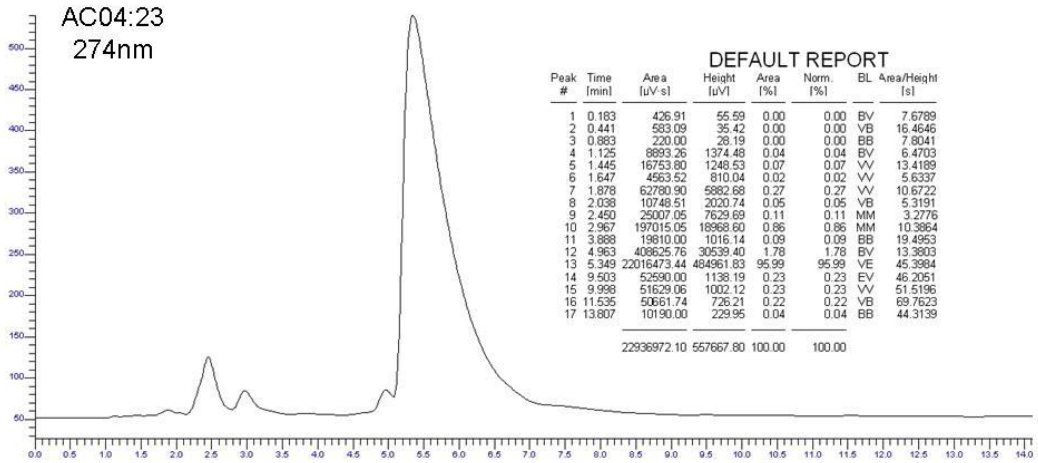
Compound 8e



DEFAULT REPORT

Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	1.594	31685.00	911.92	0.17	0.17	BB	34.7452
2	5.000	251481.58	5179.46	1.33	1.33	MM	48.5536
3	6.131	18196720.00	701999.03	96.08	96.08	BB	25.9213
4	7.700	361296.76	17398.78	1.91	1.91	MM	20.7656
5	9.224	13370.00	611.90	0.07	0.07	BB	21.8501
6	10.389	55100.00	1070.91	0.29	0.29	BB	51.4514
7	12.903	29680.00	1061.94	0.16	0.16	BB	27.9489
		18939332.34	728233.94	100.00	100.00		

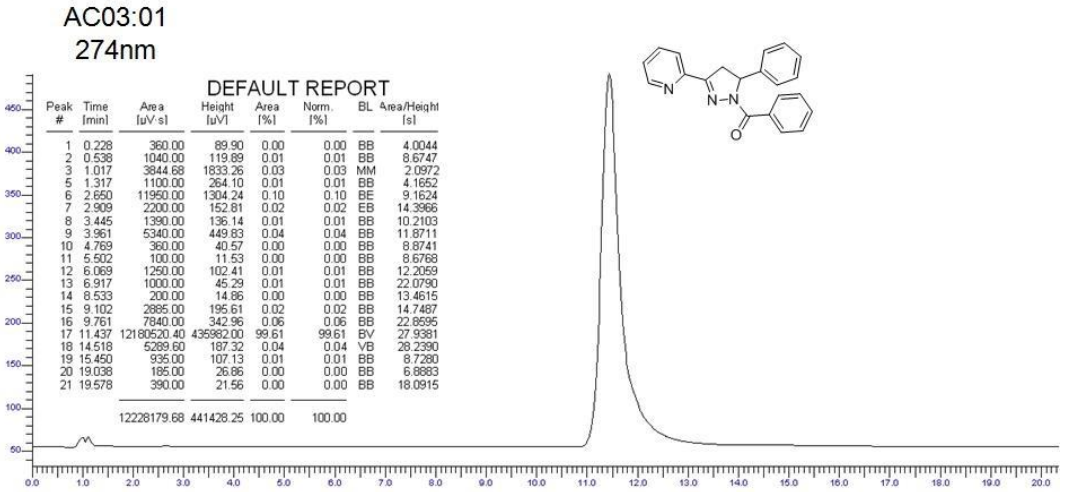
Compound 8f



DEFAULT REPORT

Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.183	426.91	55.59	0.00	0.00	BV	7.6789
2	0.441	583.09	35.42	0.00	0.00	VB	16.4646
3	0.883	220.00	28.19	0.00	0.00	BB	7.8041
4	1.125	8893.26	1374.48	0.04	0.04	BV	6.4703
5	1.445	16753.80	1248.53	0.07	0.07	VV	13.4189
6	1.647	4563.52	810.04	0.02	0.02	VV	5.6337
7	1.878	62780.90	5882.68	0.27	0.27	VV	10.6722
8	2.038	10748.51	2020.74	0.05	0.05	VB	5.3191
9	2.450	25007.05	7629.69	0.11	0.11	MM	3.2776
10	2.967	197015.05	18968.60	0.86	0.86	MM	10.3864
11	3.888	19810.00	1016.14	0.09	0.09	BB	19.4953
12	4.963	408625.76	30539.40	1.78	1.78	BV	13.3803
13	5.349	22016473.44	484961.83	95.99	95.99	VE	45.3984
14	9.503	52590.00	1138.19	0.23	0.23	EV	46.2051
15	9.998	51629.06	1002.12	0.23	0.23	VV	51.5196
16	11.535	50661.74	726.21	0.22	0.22	VB	69.7623
17	13.807	10190.00	229.95	0.04	0.04	BB	44.3139
		22936972.10	557667.80	100.00	100.00		

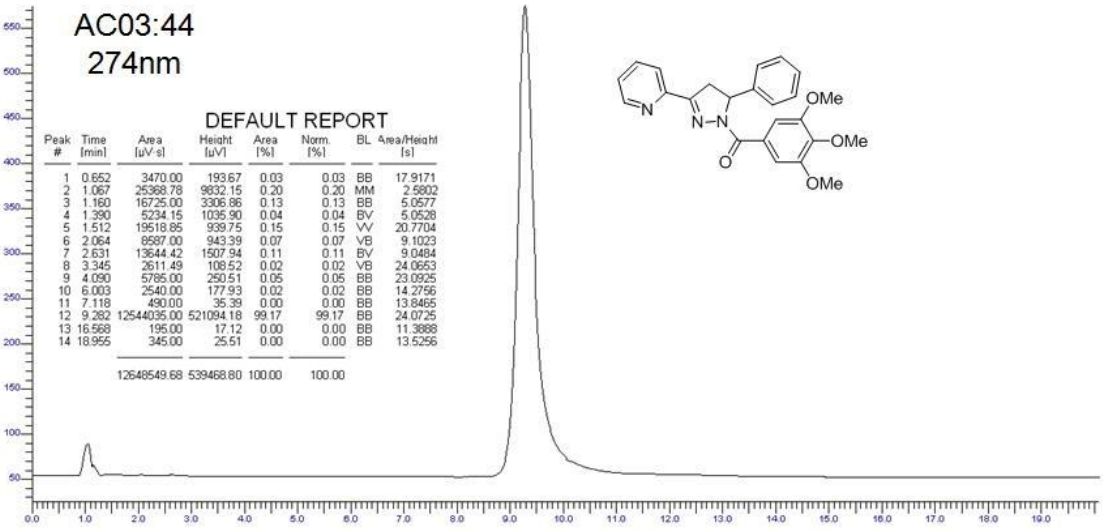
Compound 8h



DEFAULT REPORT

Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.228	360.00	89.90	0.00	0.00	BB	4.0044
2	0.538	1040.00	119.89	0.01	0.01	BB	8.6747
3	1.017	3844.68	1833.26	0.03	0.03	MM	2.0972
5	1.317	1100.00	264.10	0.01	0.01	BB	4.1652
6	2.650	11950.00	1304.24	0.10	0.10	BE	9.1624
7	2.909	2200.00	152.81	0.02	0.02	EB	14.3966
8	3.445	1390.00	136.14	0.01	0.01	BB	10.2103
9	3.961	5340.00	449.83	0.04	0.04	BB	11.8711
10	4.769	360.00	40.57	0.00	0.00	BB	8.8741
11	5.502	100.00	11.53	0.00	0.00	BB	8.6768
12	6.069	1250.00	102.41	0.01	0.01	BB	12.2059
13	6.917	1000.00	45.29	0.01	0.01	BB	22.0790
14	8.533	200.00	14.86	0.00	0.00	BB	13.4615
15	9.102	2885.00	195.61	0.02	0.02	BB	14.7487
16	9.761	7840.00	342.96	0.06	0.06	BB	22.8595
17	11.437	12180520.40	435982.00	99.61	99.61	BV	27.9381
18	14.518	5289.60	187.32	0.04	0.04	VB	28.2390
19	15.450	935.00	107.13	0.01	0.01	BB	8.7280
20	19.038	185.00	26.86	0.00	0.00	BB	6.8883
21	19.578	390.00	21.56	0.00	0.00	BB	18.0915
		12228179.68	441428.25	100.00	100.00		

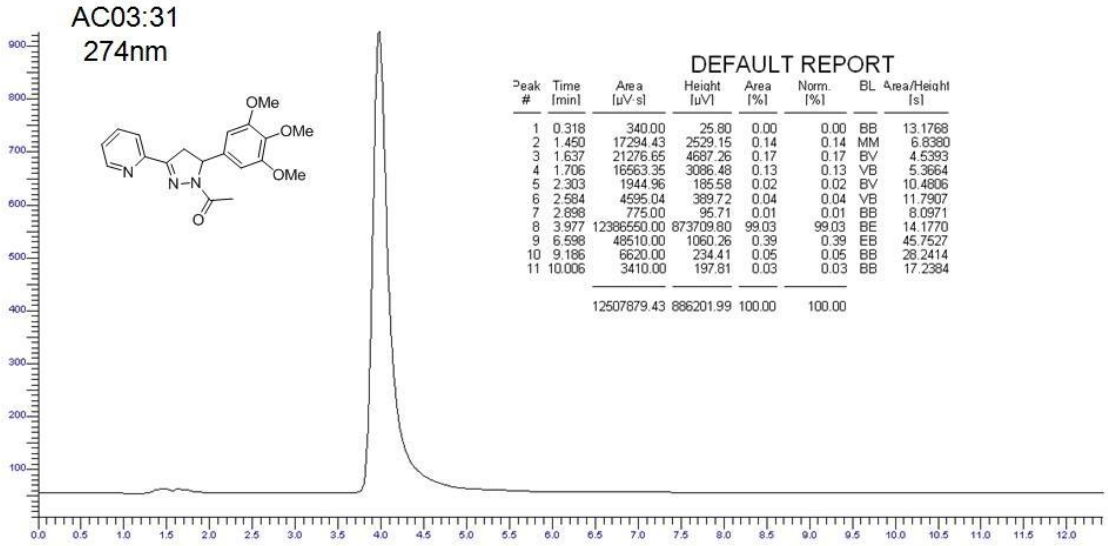
Compound 8i



DEFAULT REPORT

Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.652	3470.00	193.67	0.03	0.03	BB	17.9171
2	1.067	25368.78	9832.15	0.20	0.20	MM	2.5802
3	1.160	16725.00	3306.86	0.13	0.13	BB	5.0577
4	1.390	5234.15	1035.90	0.04	0.04	BV	5.0528
5	1.512	19518.85	939.75	0.15	0.15	VV	20.7704
6	2.064	8587.00	943.39	0.07	0.07	VB	9.1023
7	2.631	13644.42	1507.94	0.11	0.11	BV	9.0484
8	3.345	2611.49	108.52	0.02	0.02	VB	24.0653
9	4.090	5785.00	250.51	0.05	0.05	BB	23.0925
10	6.003	2540.00	177.93	0.02	0.02	BB	14.2756
11	7.118	490.00	35.39	0.00	0.00	BB	13.8465
12	9.282	12544035.00	521094.18	99.17	99.17	BB	24.0725
13	16.568	195.00	17.12	0.00	0.00	BB	11.3888
14	18.955	345.00	25.51	0.00	0.00	BB	13.5256
		12648549.68	539468.80	100.00	100.00		

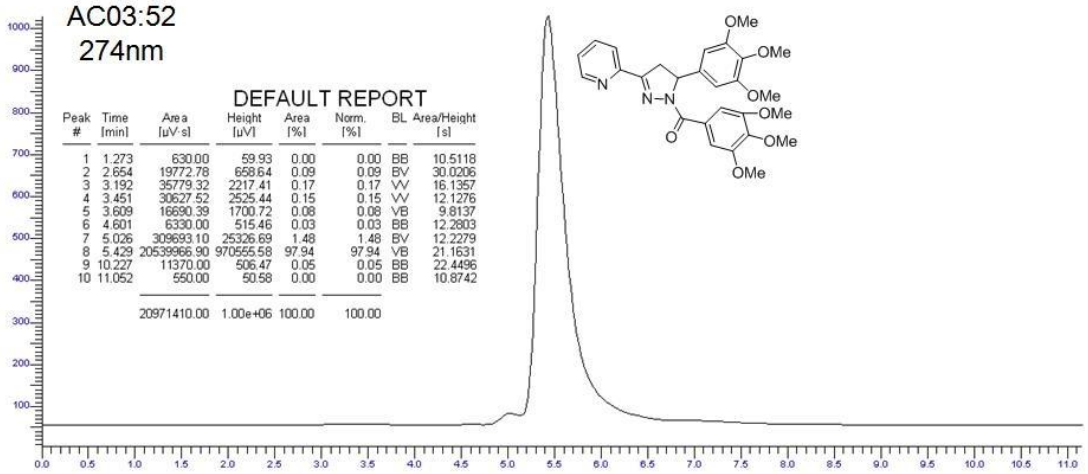
Compound 9c



DEFAULT REPORT

Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	0.318	340.00	25.80	0.00	0.00	BB	13.1768
2	1.450	17294.43	2529.15	0.14	0.14	MM	6.8380
3	1.637	21276.65	4687.26	0.17	0.17	BV	4.5393
4	1.706	16563.35	3086.48	0.13	0.13	VB	5.3664
5	2.303	1944.96	185.58	0.02	0.02	BV	10.4806
6	2.584	4595.04	389.72	0.04	0.04	VB	11.7907
7	2.898	775.00	95.71	0.01	0.01	BB	8.0971
8	3.977	12386550.00	873709.80	99.03	99.03	BE	14.1770
9	6.598	48510.00	1060.26	0.39	0.39	EB	45.7527
10	9.186	6620.00	234.41	0.05	0.05	BB	28.2414
11	10.006	3410.00	197.81	0.03	0.03	BB	17.2384
		12507879.43	886201.99	100.00	100.00		

Compound 9i

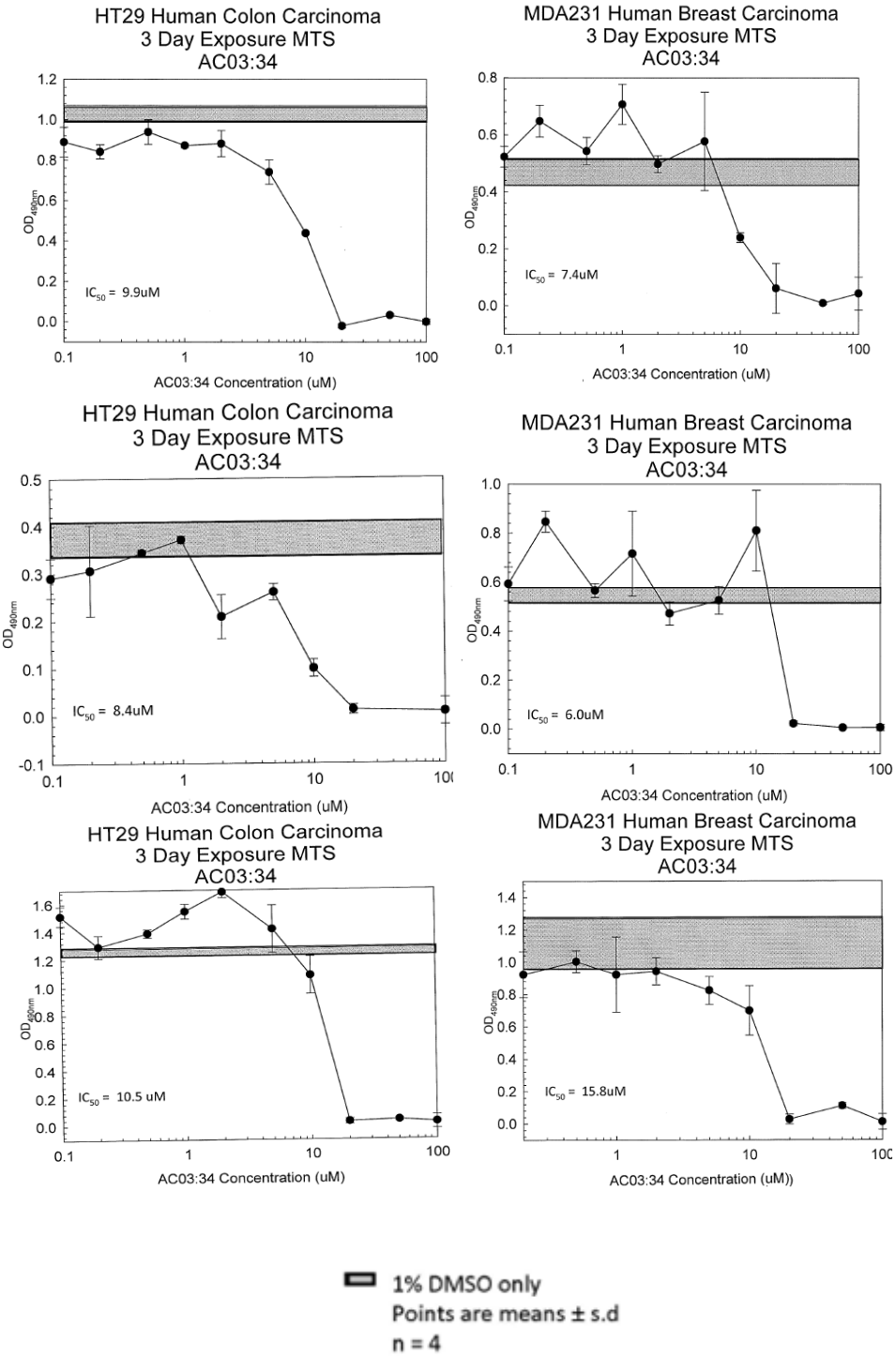


DEFAULT REPORT

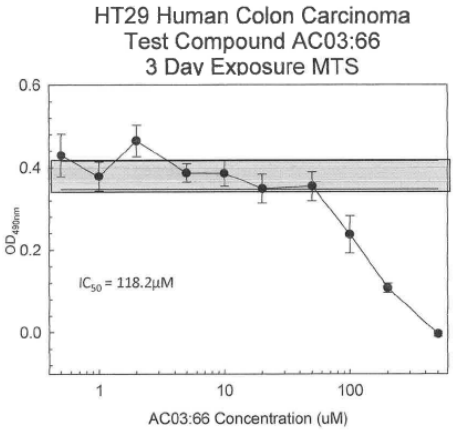
Peak #	Time [min]	Area [uV·s]	Height [uV]	Area [%]	Norm. [%]	BL	Area/Height [s]
1	1.273	630.00	59.93	0.00	0.00	BB	10.5118
2	2.654	19772.78	658.64	0.09	0.09	BV	30.0206
3	3.192	35779.32	2217.41	0.17	0.17	VV	16.1357
4	3.451	30627.52	2525.44	0.15	0.15	VV	12.1276
5	3.609	16690.39	1700.72	0.08	0.08	VB	9.8137
6	4.601	6330.00	515.46	0.03	0.03	BB	12.2803
7	5.026	309693.10	25326.69	1.48	1.48	BV	12.2279
8	5.429	20539966.90	970555.58	97.94	97.94	VB	21.1631
9	10.227	11370.00	506.47	0.05	0.05	BB	22.4496
10	11.052	550.00	50.58	0.00	0.00	BB	10.8742
		20971410.00	1.00e+06	100.00	100.00		

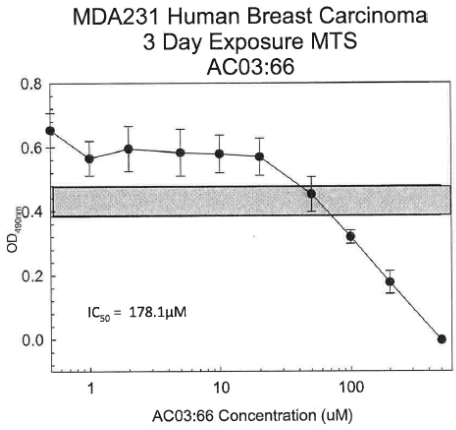
MTS Assays

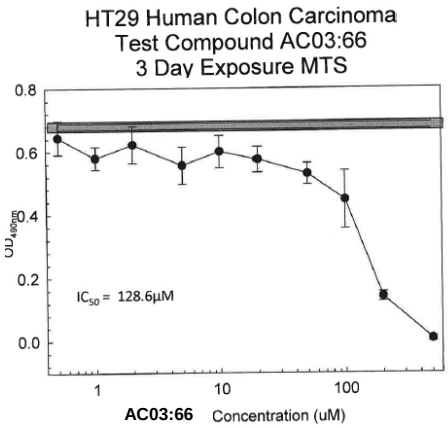
Compound 5

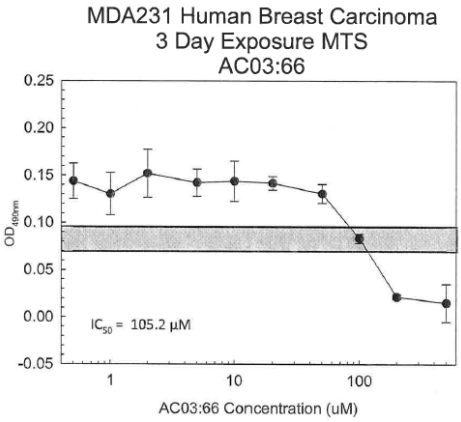


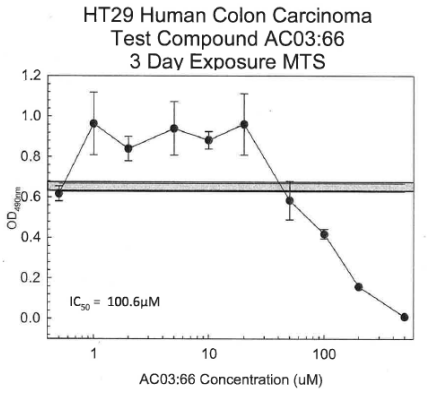
Compound 8a

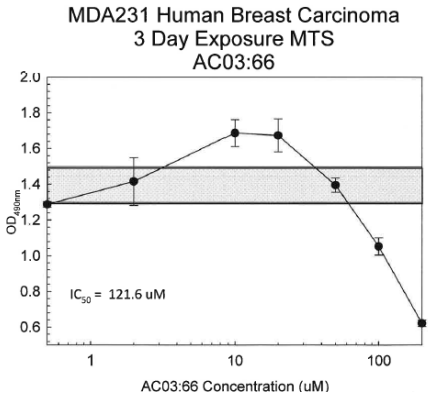






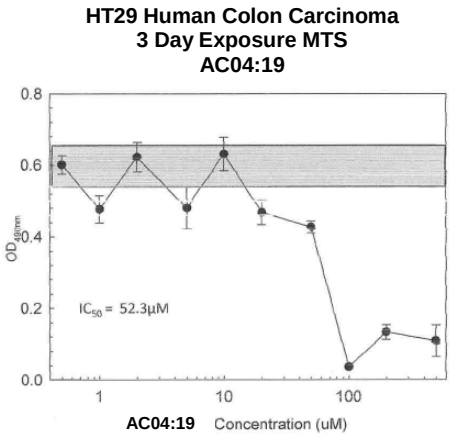


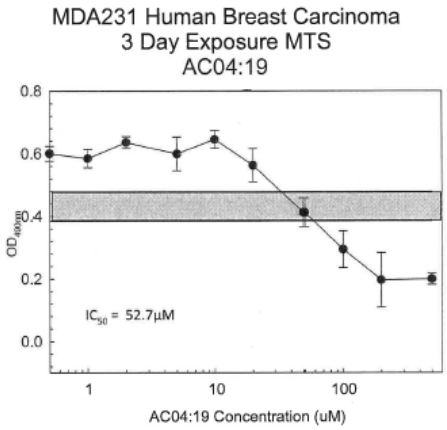


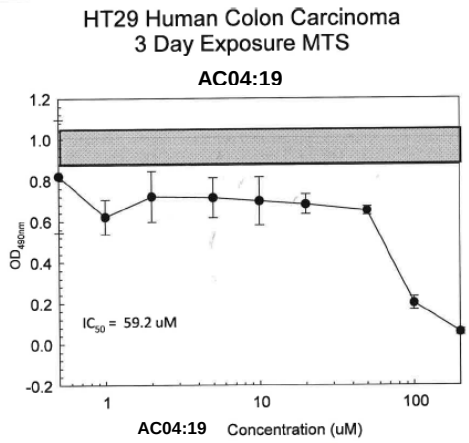


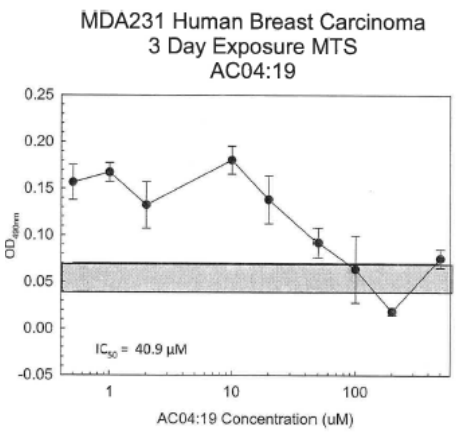
1% DMSO only
Points are means ± s.d
n = 4

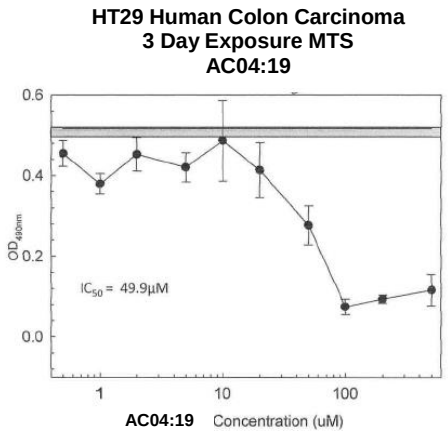
Compound 8b

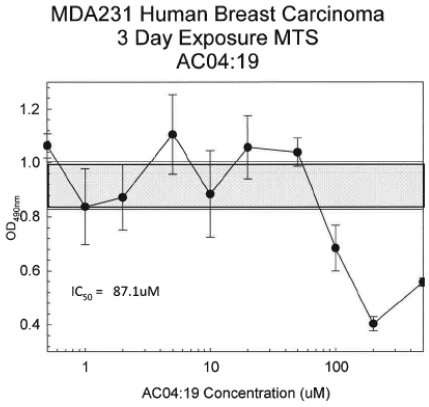






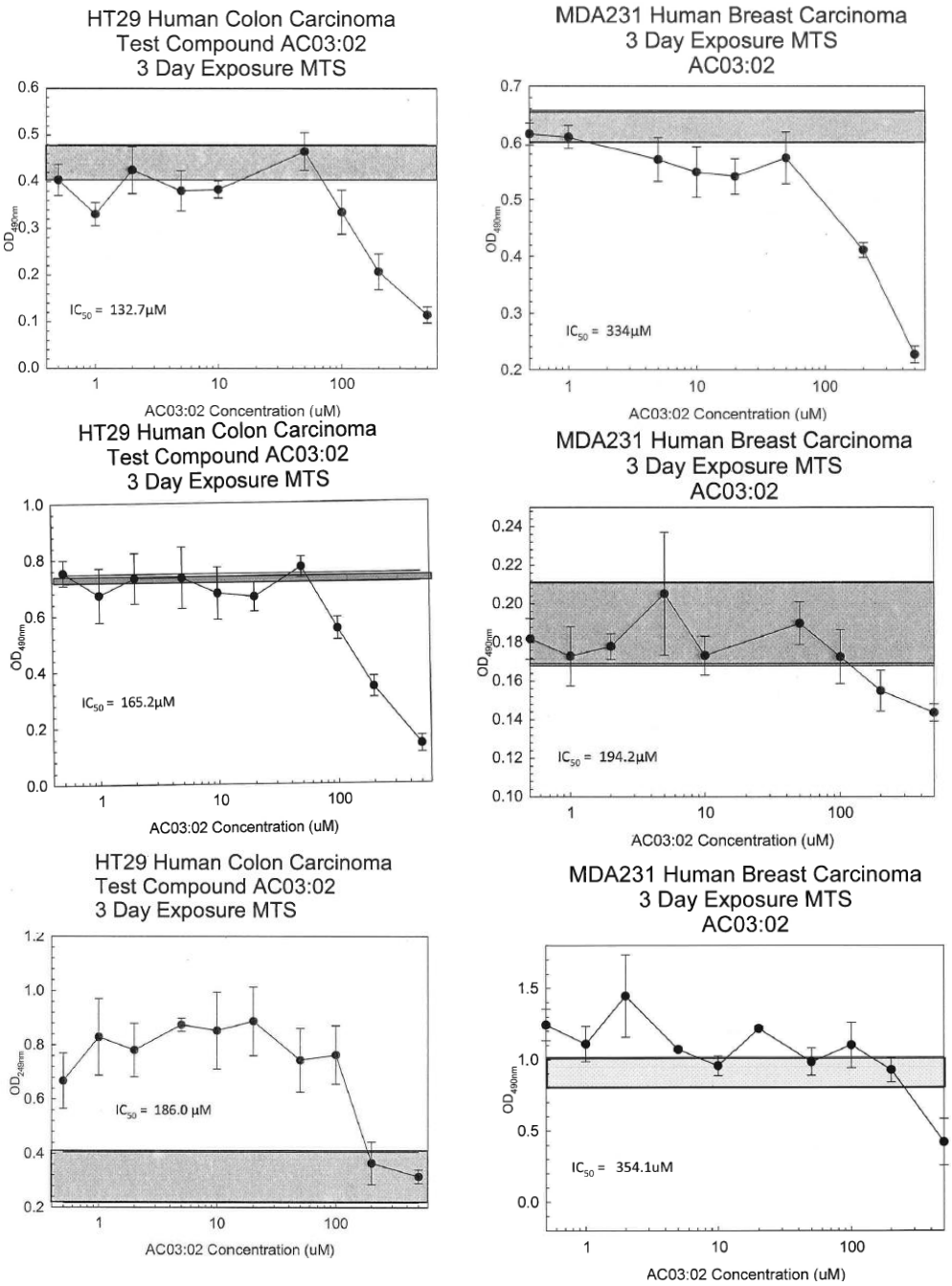




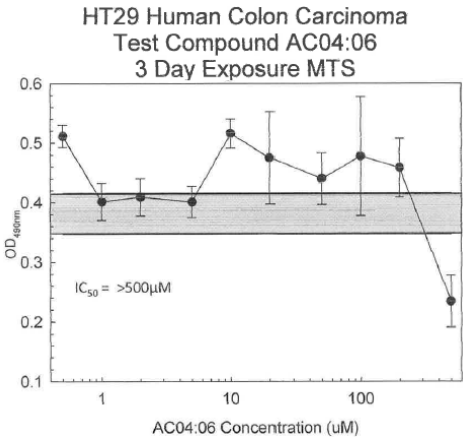


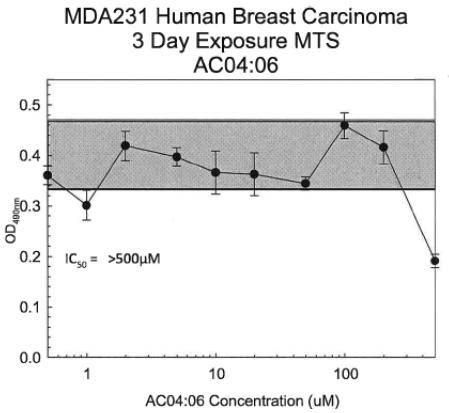
1% DMSO only
Points are means ± s.d
n = 4

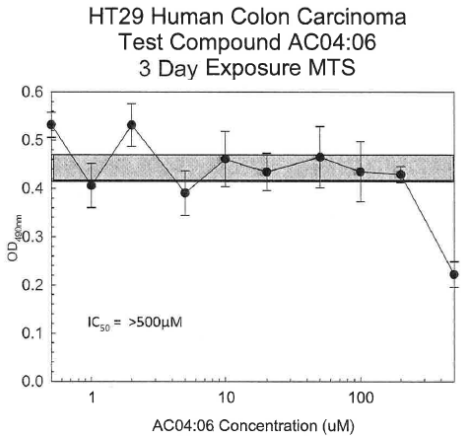
Compound 8c

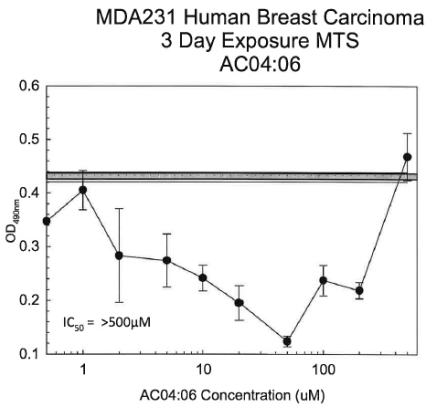


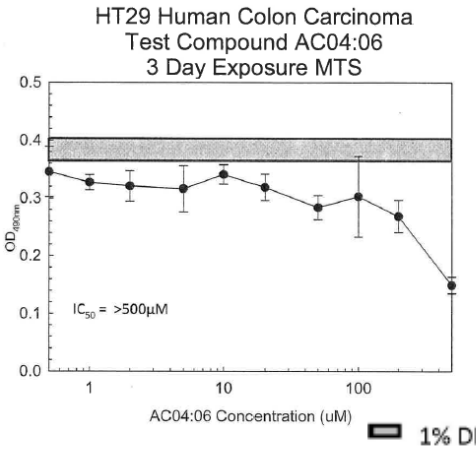
Compound 8d

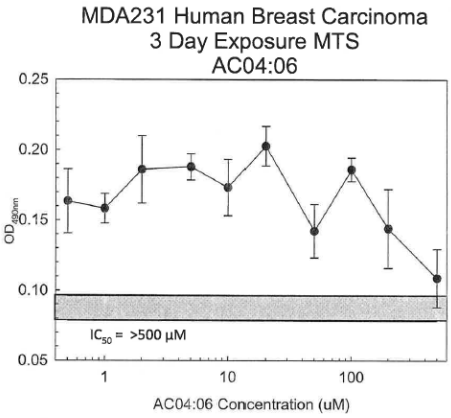






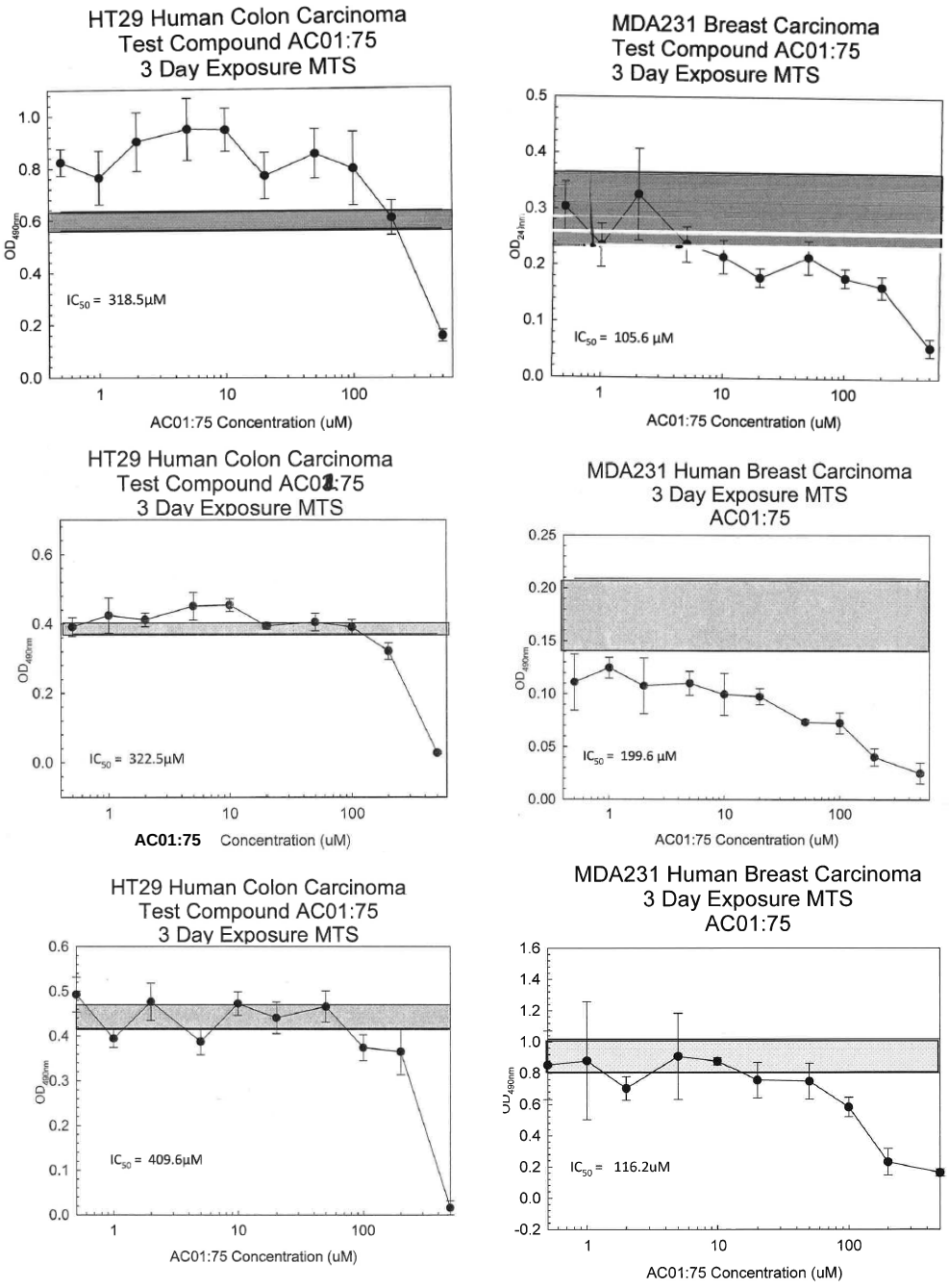




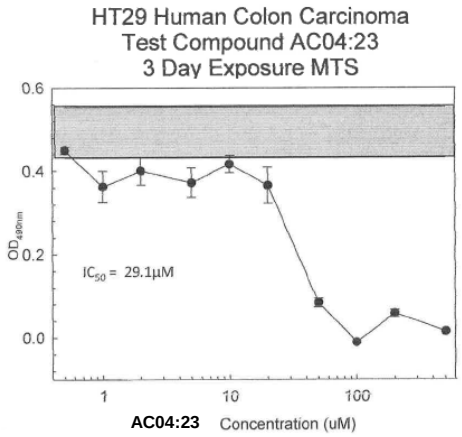


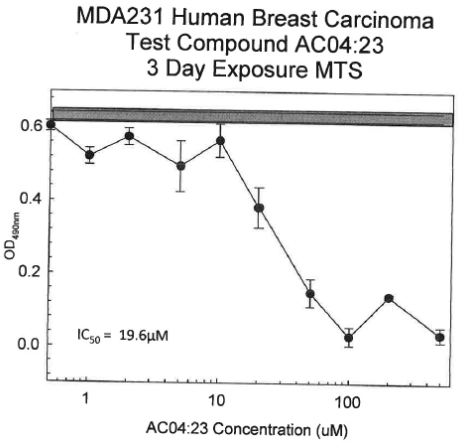
1% DMSO only
Points are means ± s.d
n = 4

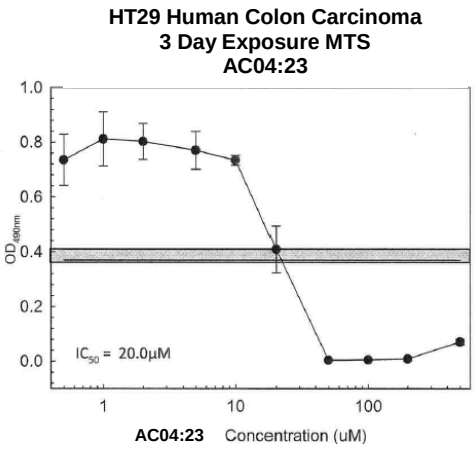
Compound 8e

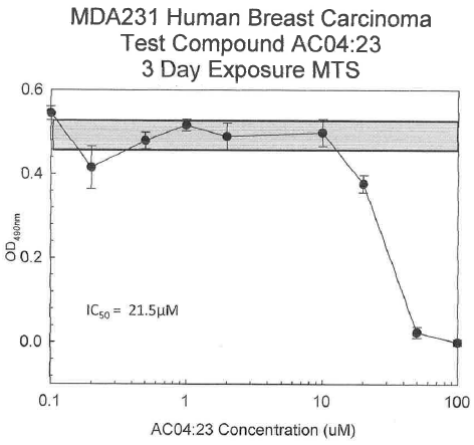


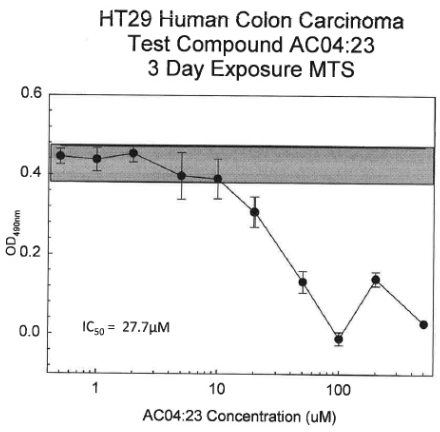
Compound 8f

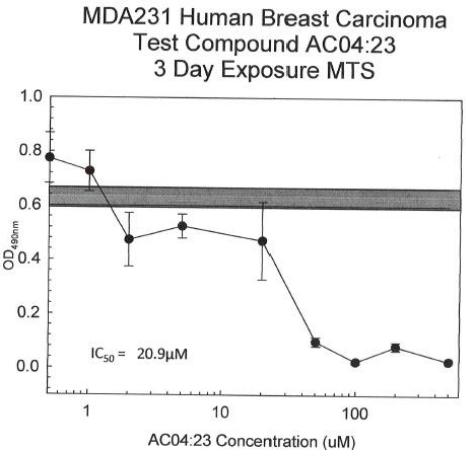






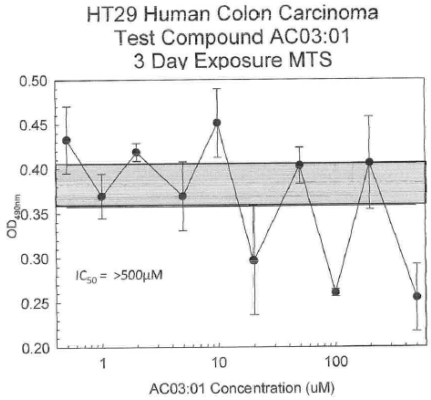


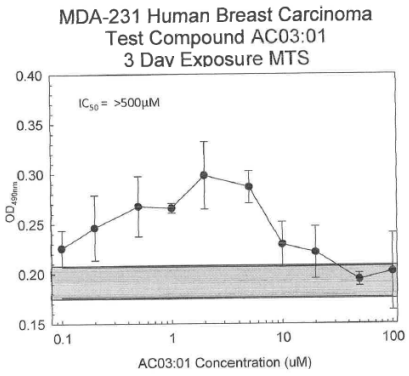


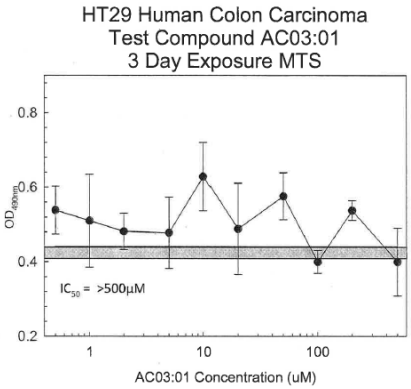


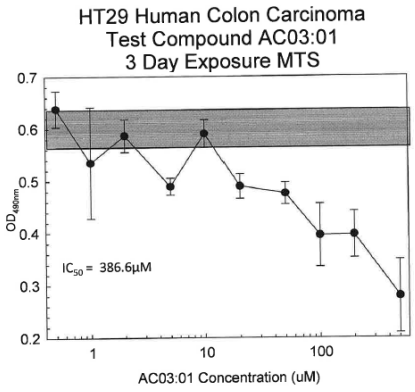
1% DMSO only
Points are means ± s.d
n = 4

Compound 8h



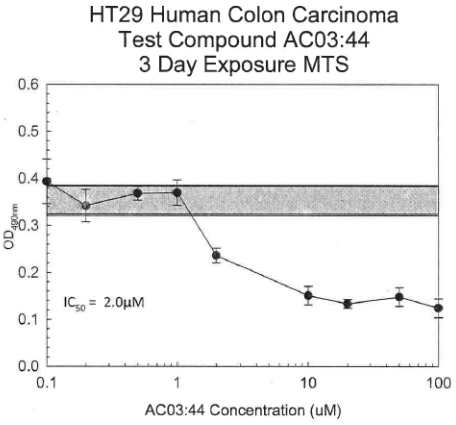


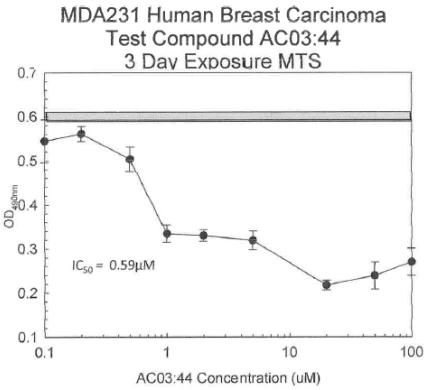


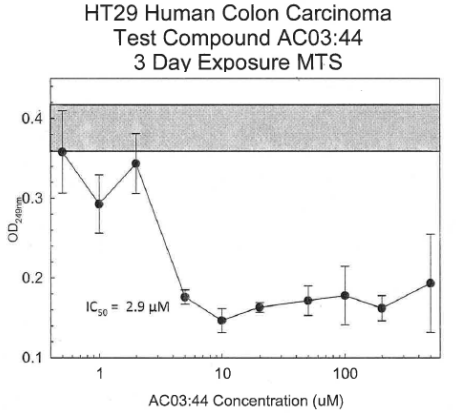


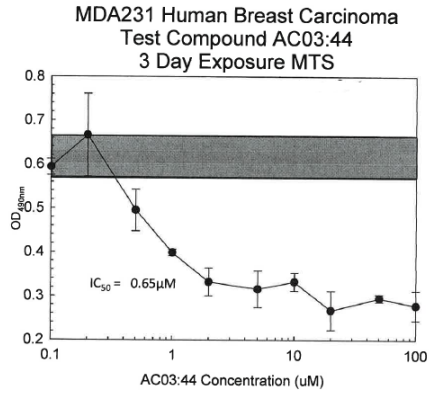
1% DMSO only
Points are means ± s.d
n = 4

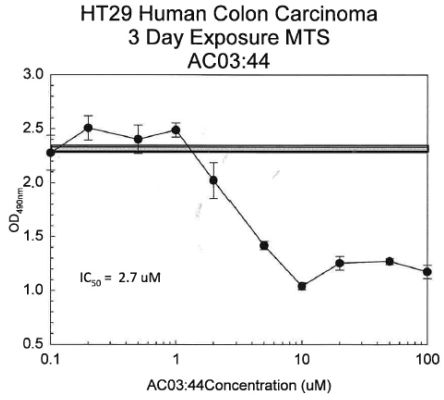
Compound 8i

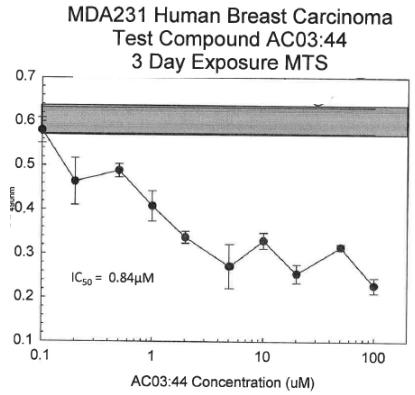






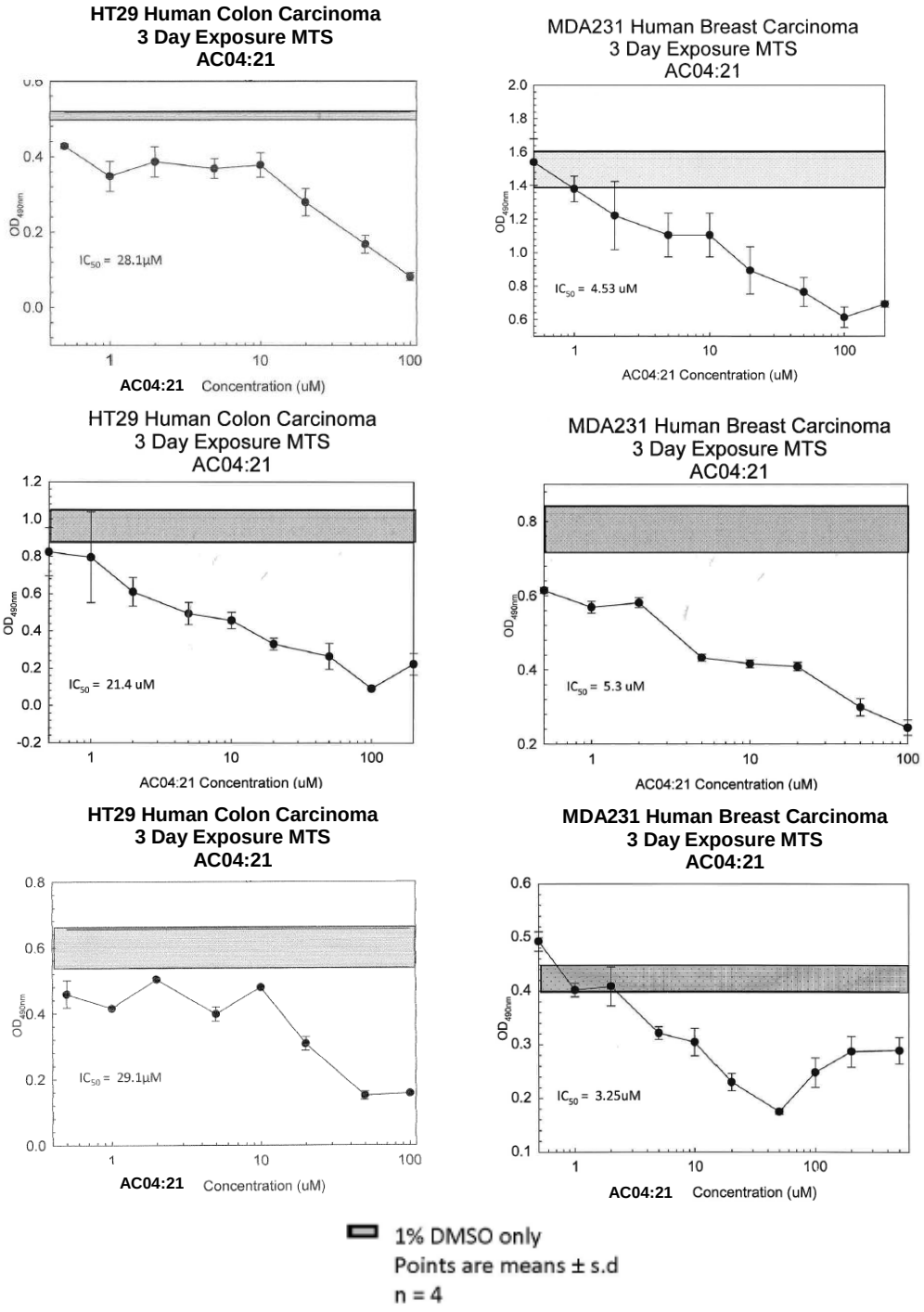




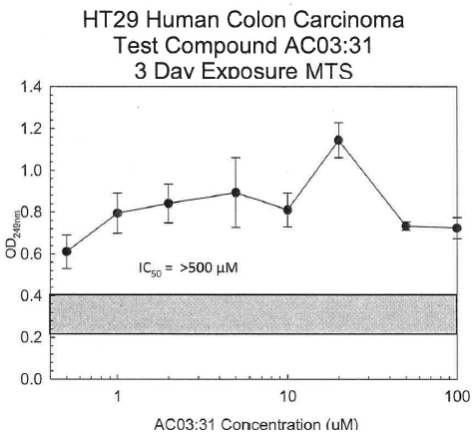


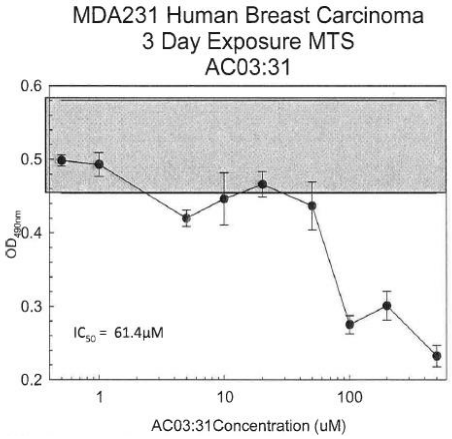
1% DMSO only
Points are means ± s.d
n = 4

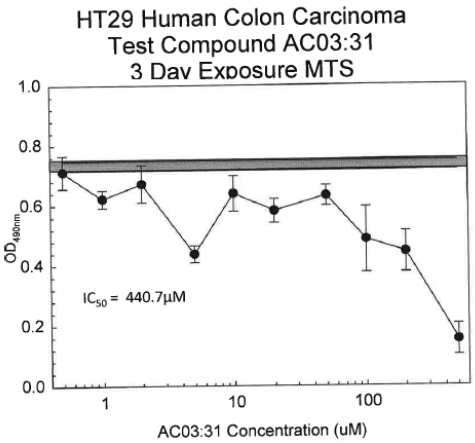
Compound 9b

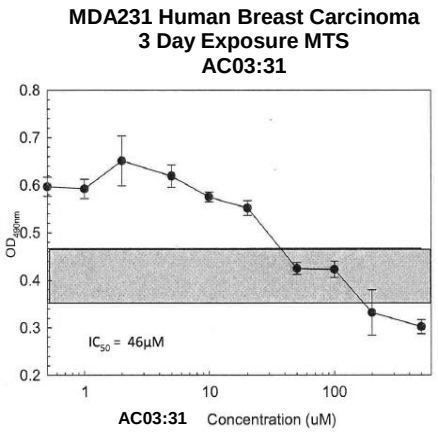

HT29 Human Colon Carcinoma
3 Day Exposure MTS
AC04:21
OD490nm
IC50 = 28.1µM
AC04:21 Concentration (uM)
MDA231 Human Breast Carcinoma
3 Day Exposure MTS
AC04:21
IC50 = 4.53 uM
AC04:21 Concentration (uM)
HT29 Human Colon Carcinoma
3 Day Exposure MTS
AC04:21
IC50 = 21.4 uM
AC04:21 Concentration (uM)
MDA231 Human Breast Carcinoma
3 Day Exposure MTS
AC04:21
IC50 = 5.3 uM
AC04:21 Concentration (uM)
HT29 Human Colon Carcinoma
3 Day Exposure MTS
AC04:21
IC50 = 29.1µM
AC04:21 Concentration (uM)
MDA231 Human Breast Carcinoma
3 Day Exposure MTS
AC04:21
IC50 = 3.25uM
AC04:21 Concentration (uM)
1% DMSO only
Points are means ± s.d
n = 4

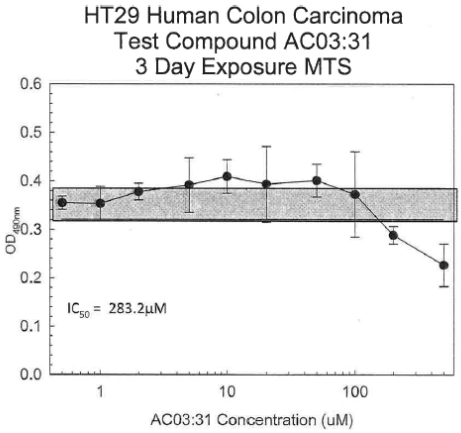
Compound 9c

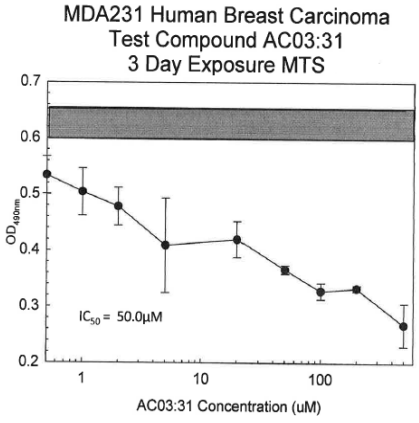






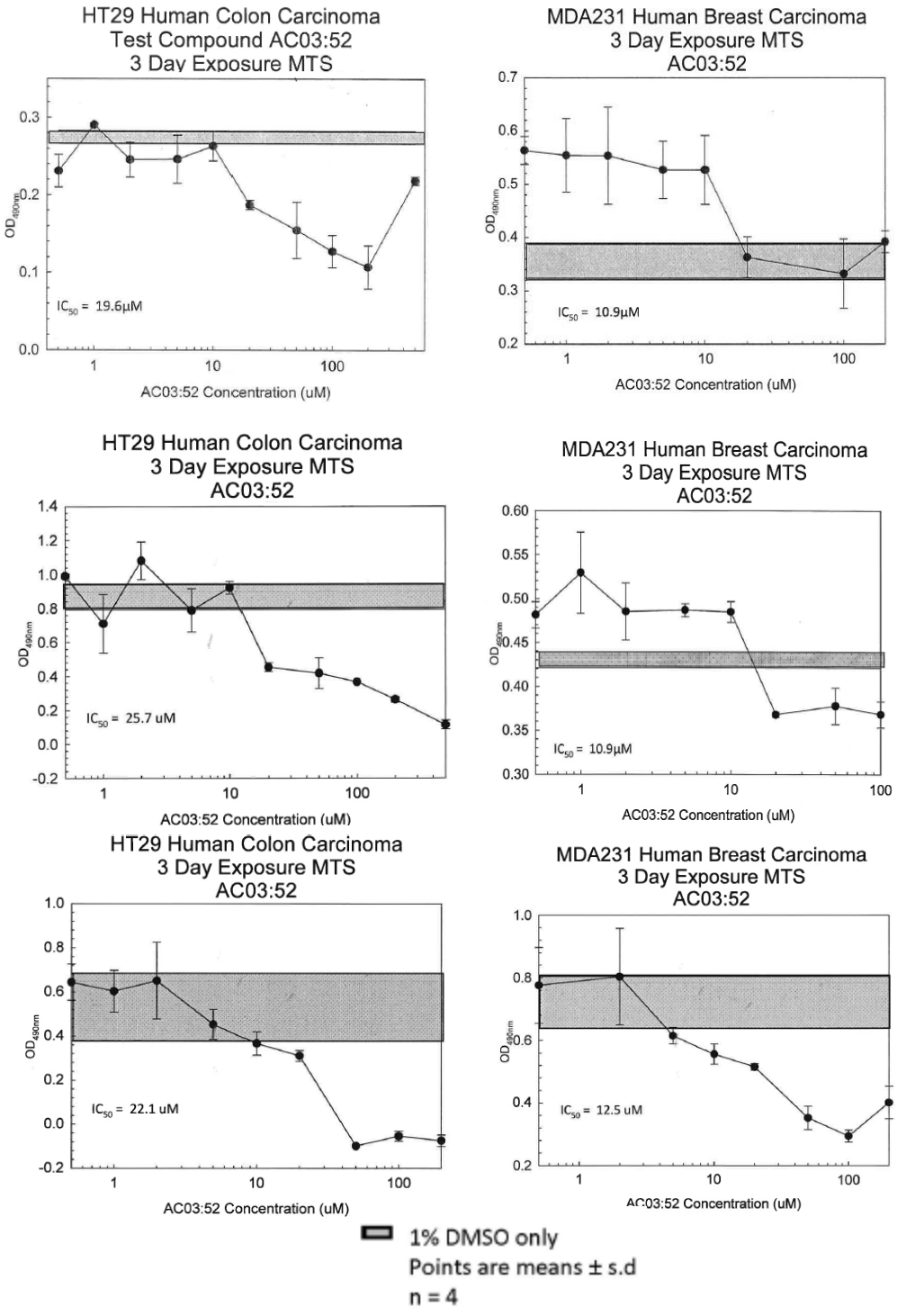




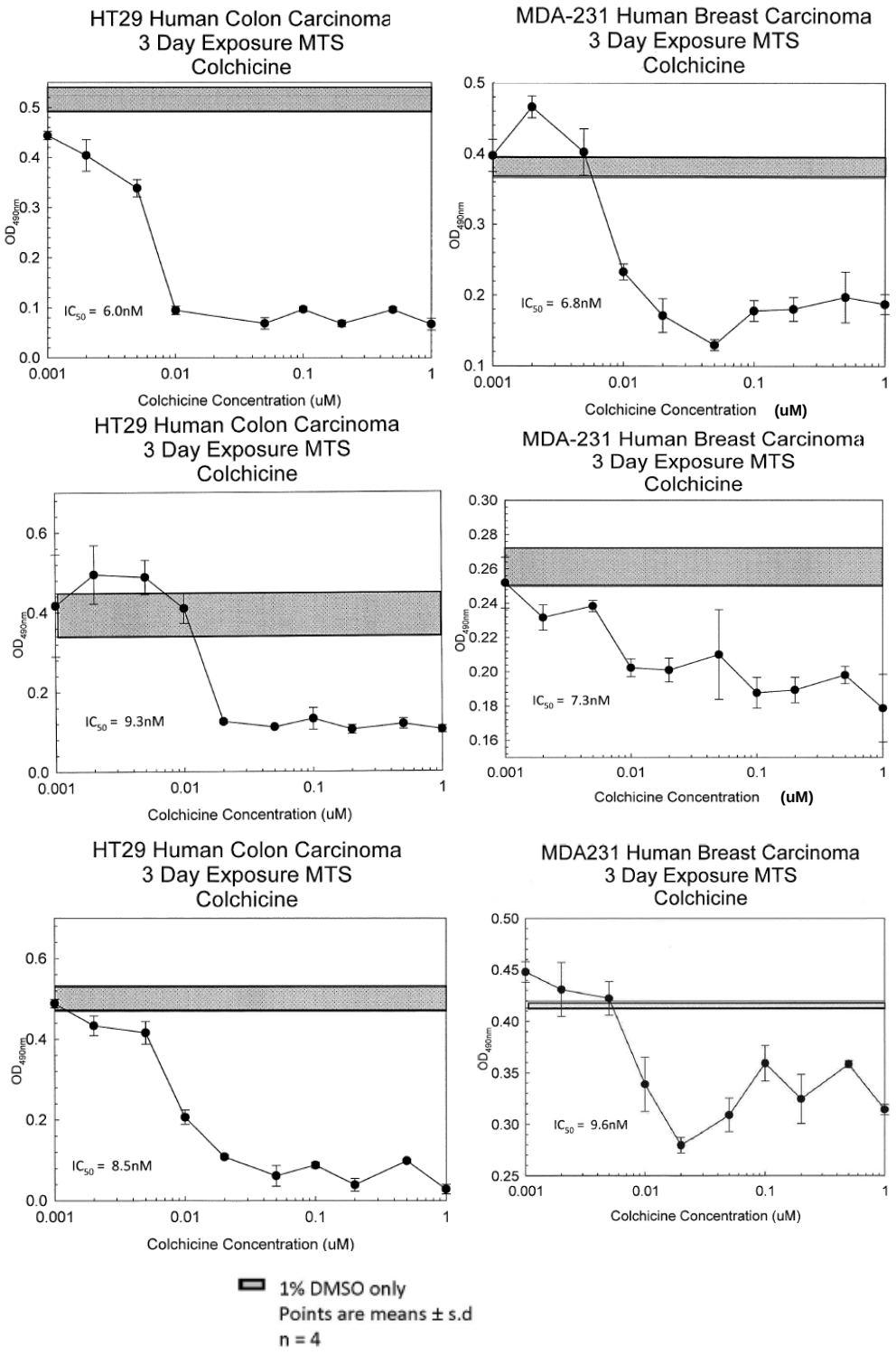


1% DMSO only
Points are means ± s.d
n = 4

Compound 9i



Colchicine



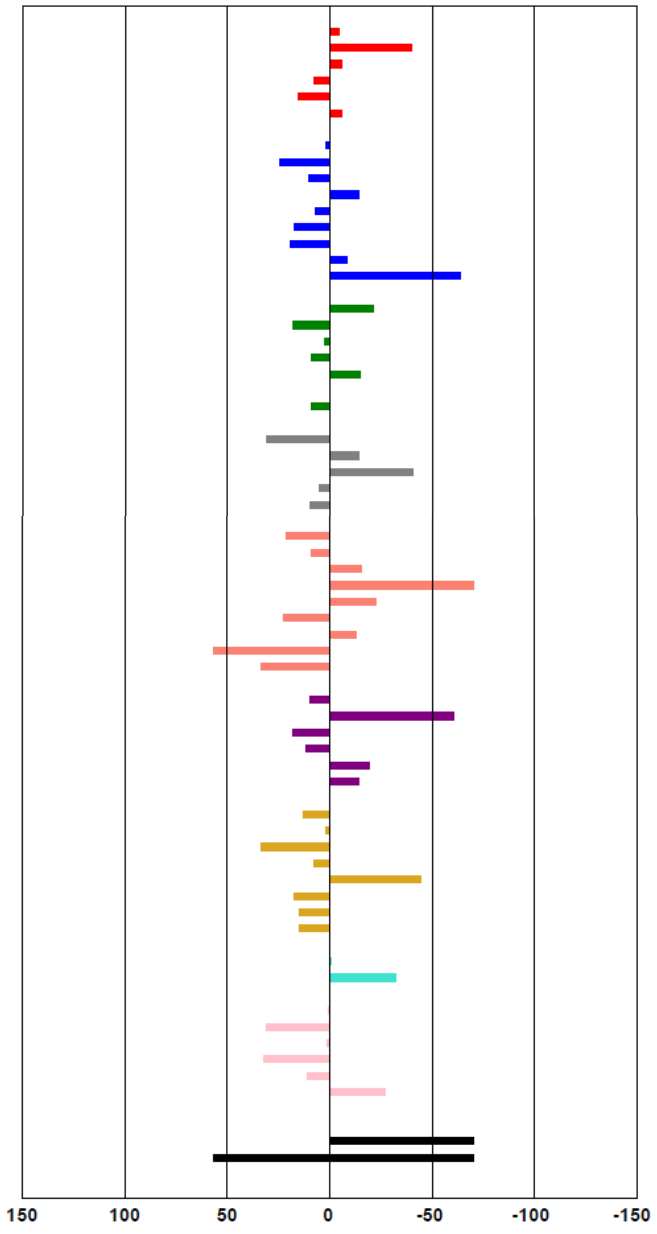
NCI Data

Pyrazoline 8i – Single Dose

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-761258 / 1	Conc: 1.00E-5 Molar	Test Date: Aug 22, 2011
Experiment ID: 1108OS12		Report Date: Sep 12, 2011

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	15.28
HL-60(TB)	-19.74
K-562	13.92
MOLT-4	27.77
RPMI-8226	35.40
SR	14.19
Non-Small Cell Lung Cancer	
A549/ATCC	22.14
EKVX	44.62
HOP-62	29.96
HOP-92	5.44
NCI-H226	27.06
NCI-H23	37.40
NCI-H322M	39.12
NCI-H460	11.46
NCI-H522	-43.64
Colon Cancer	
COLO 205	-1.56
HCC-2998	38.08
HCT-116	22.61
HCT-15	28.98
HT29	5.17
KM12	20.19
SW-620	29.02
CNS Cancer	
SF-268	50.59
SF-295	5.51
SF-539	-20.52
SNB-19	25.23
U251	29.87
Melanoma	
LOX IMVI	40.94
MALME-3M	28.74
M14	4.20
MDA-MB-435	-50.29
SK-MEL-2	-2.85
SK-MEL-28	42.61
SK-MEL-5	6.98
UACC-257	76.69
UACC-62	53.39
Ovarian Cancer	
IGROV1	29.81
OVCAR-3	-40.78
OVCAR-5	37.71
OVCAR-8	31.28
NCI/ADR-RES	0.62
SK-OV-3	5.62
Renal Cancer	
786-0	32.68
A498	21.66
ACHN	53.41
CAKI-1	27.53
RXF 393	-24.74
SN12C	37.15
TK-10	34.84
UO-31	34.80
Prostate Cancer	
PC-3	19.36
DU-145	-12.00
Breast Cancer	
MCF7	20.41
MDA-MB-231/ATCC	51.03
HS 578T	20.94
BT-549	51.91
T-47D	31.13
MDA-MB-468	-7.41
Mean	19.84
Delta	70.13
Range	126.98



Pyrazoline 8i – Five Dose

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 761258 / 1	Experiment ID : 1109NS21	Test Type : 08	Units : Molar
Report Date : October 26, 2011	Test Date : September 12, 2011	QNS :	MC :
COMI : AC03:44 (109726)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0Y8X	

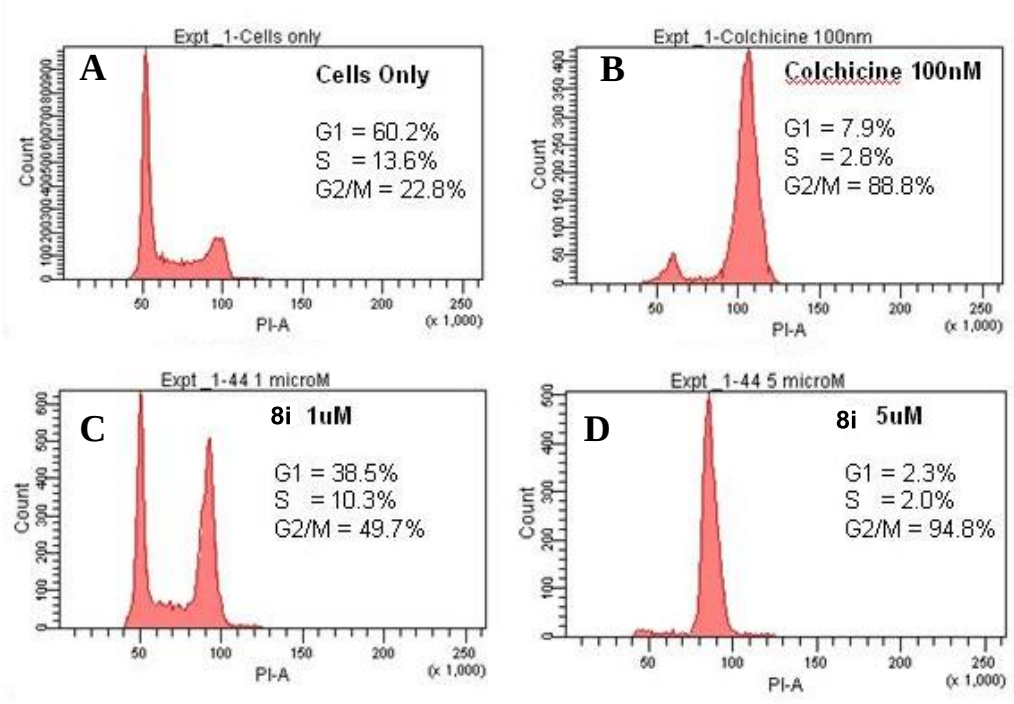
			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.380	1.644	1.659	1.714	1.206	0.596	0.533	101	106	65	17	12	2.08E-6	> 1.00E-4	> 1.00E-4
HL-60(TB)	0.695	2.424	2.467	2.384	1.440	0.703	0.586	102	98	43	.	-16	7.47E-7	1.07E-5	> 1.00E-4
MOLT-4	0.518	2.348	2.443	2.465	2.096	1.075	0.807	105	106	86	30	16	4.46E-6	> 1.00E-4	> 1.00E-4
RPMI-8226	0.673	2.632	2.607	2.555	2.361	1.769	1.627	99	96	86	56	49	6.63E-5	> 1.00E-4	> 1.00E-4
SR	0.449	2.410	2.379	2.292	0.896	0.760	0.707	98	94	23	16	13	4.15E-7	> 1.00E-4	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.410	1.844	1.794	1.773	1.113	0.772	0.710	96	95	49	25	21	9.52E-7	> 1.00E-4	> 1.00E-4
EKVX	0.836	2.041	1.957	1.925	1.746	1.473	1.440	93	90	75	53	50	> 1.00E-4	> 1.00E-4	> 1.00E-4
HOP-62	0.407	1.042	1.029	1.028	0.772	0.589	0.573	98	98	57	29	26	1.82E-6	> 1.00E-4	> 1.00E-4
HOP-92	0.903	2.203	2.125	2.055	1.855	1.707	1.611	94	89	73	62	54	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H226	0.668	1.606	1.527	1.493	1.195	0.733	0.745	92	88	56	7	8	1.33E-6	> 1.00E-4	> 1.00E-4
NCI-H23	0.445	1.402	1.384	1.354	1.093	0.778	0.719	98	95	68	35	29	3.45E-6	> 1.00E-4	> 1.00E-4
NCI-H322M	0.717	1.919	1.958	1.914	1.766	1.486	1.487	103	100	87	64	64	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H460	0.172	1.991	2.027	1.955	0.714	0.358	0.285	102	98	30	10	6	5.05E-7	> 1.00E-4	> 1.00E-4
NCI-H522	0.798	1.713	1.732	1.709	1.168	0.838	0.801	102	100	40	4	.	6.88E-7	> 1.00E-4	> 1.00E-4
Colon Cancer															
COLO 205	0.315	1.241	1.314	1.333	0.610	0.239	0.254	108	110	32	-24	-20	5.85E-7	3.71E-6	> 1.00E-4
HCC-2998	0.424	1.711	1.699	1.663	1.303	0.658	0.625	99	96	68	18	16	2.32E-6	> 1.00E-4	> 1.00E-4
HCT-116	0.194	1.504	1.597	1.552	0.637	0.445	0.269	107	104	34	19	6	5.86E-7	> 1.00E-4	> 1.00E-4
HCT-15	0.395	1.905	1.888	1.806	1.099	0.696	0.572	99	93	47	20	12	8.48E-7	> 1.00E-4	> 1.00E-4
HT29	0.216	1.256	1.318	1.344	0.386	0.263	0.241	106	108	16	5	2	4.31E-7	> 1.00E-4	> 1.00E-4
KM12	0.322	2.445	2.591	2.570	1.177	0.966	0.792	107	106	40	30	22	7.11E-7	> 1.00E-4	> 1.00E-4
SW-620	0.196	1.788	1.737	1.724	0.753	0.601	0.599	97	96	35	25	25	5.67E-7	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	0.280	1.747	1.814	1.797	1.262	1.114	0.922	105	103	67	57	44	3.34E-5	> 1.00E-4	> 1.00E-4
SF-539	0.713	1.970	2.023	2.122	1.362	0.634	0.663	104	112	52	-11	-7	1.06E-6	6.64E-6	> 1.00E-4
SNB-19	0.476	1.593	1.549	1.497	1.145	0.745	0.804	96	91	60	24	29	1.89E-6	> 1.00E-4	> 1.00E-4
SNB-75	0.863	1.553	1.427	1.423	0.938	0.762	1.041	82	81	11	-12	26	2.77E-7	.	> 1.00E-4
U251	0.365	1.638	1.578	1.544	0.966	0.641	0.568	95	93	47	22	16	8.68E-7	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.247	1.585	1.488	1.476	0.924	0.763	0.505	93	92	51	39	19	1.13E-6	> 1.00E-4	> 1.00E-4
MALME-3M	0.602	1.465	1.451	1.455	1.102	1.034	1.077	98	99	58	50	55	> 1.00E-4	> 1.00E-4	> 1.00E-4
M14	0.317	1.167	1.165	1.170	0.697	0.398	0.480	100	100	45	10	19	8.01E-7	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.551	2.497	2.488	2.250	0.588	0.275	0.304	100	87	2	-50	-45	2.73E-7	1.09E-6	.
SK-MEL-2	0.821	1.506	1.576	1.598	1.083	0.830	0.915	110	114	38	1	14	6.99E-7	> 1.00E-4	> 1.00E-4
SK-MEL-28	0.533	1.401	1.385	1.338	1.002	0.807	0.811	98	93	54	32	32	1.51E-6	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.497	2.284	2.204	2.074	0.999	0.799	0.558	96	88	28	17	3	4.32E-7	> 1.00E-4	> 1.00E-4
UACC-257	0.874	1.786	1.727	1.705	1.433	1.520	1.496	94	91	61	71	68	> 1.00E-4	> 1.00E-4	> 1.00E-4
UACC-62	0.563	1.932	1.835	1.787	1.052	1.070	0.957	93	89	36	37	29	5.41E-7	> 1.00E-4	> 1.00E-4
Ovarian Cancer															
IGROV1	0.570	1.803	1.895	1.933	1.365	1.156	0.918	107	111	64	48	28	7.13E-6	> 1.00E-4	> 1.00E-4
OVCAR-3	0.235	1.764	1.918	1.887	0.851	0.656	0.566	110	108	40	28	22	7.19E-7	> 1.00E-4	> 1.00E-4
OVCAR-4	0.580	1.192	1.178	1.136	0.984	0.858	0.703	98	91	66	45	20	5.95E-6	> 1.00E-4	> 1.00E-4
OVCAR-5	0.521	1.401	1.385	1.404	1.257	0.767	0.758	98	100	84	28	27	4.01E-6	> 1.00E-4	> 1.00E-4
OVCAR-8	0.498	1.977	1.968	1.900	1.564	0.932	0.832	99	95	72	29	23	3.28E-6	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.500	1.581	1.559	1.515	0.851	0.480	0.543	98	94	32	-4	4	5.19E-7	.	> 1.00E-4
SK-OV-3	0.563	1.262	1.300	1.279	0.864	0.509	0.495	105	102	43	-10	-12	7.62E-7	6.57E-6	> 1.00E-4
Renal Cancer															
786-0	0.661	2.219	2.186	2.202	1.542	1.001	0.985	98	99	57	22	21	1.54E-6	> 1.00E-4	> 1.00E-4
A498	0.701	1.890	1.702	1.621	1.287	1.154	1.116	84	77	49	38	35	9.43E-7	> 1.00E-4	> 1.00E-4
ACHN	0.346	1.359	1.432	1.386	0.994	0.771	0.596	107	103	64	42	25	4.29E-6	> 1.00E-4	> 1.00E-4
CAKI-1	0.638	2.038	1.947	1.883	1.097	0.962	0.854	94	89	33	23	15	4.93E-7	> 1.00E-4	> 1.00E-4
RXF 393	0.511	1.095	1.073	1.043	0.810	0.364	0.495	96	91	51	-29	-3	1.03E-6	4.36E-6	> 1.00E-4
SN12C	0.473	1.790	1.691	1.660	1.403	0.908	0.755	93	90	71	33	21	3.53E-6	> 1.00E-4	> 1.00E-4
TK-10	0.909	1.799	1.815	1.848	1.645	1.530	1.490	102	106	83	70	65	> 1.00E-4	> 1.00E-4	> 1.00E-4
UO-31	0.370	1.389	1.329	1.352	1.131	0.772	0.642	94	96	75	39	27	5.01E-6	> 1.00E-4	> 1.00E-4
Prostate Cancer															
PC-3	0.364	1.552	1.514	1.432	1.177	0.991	0.988	97	90	68	53	53	> 1.00E-4	> 1.00E-4	> 1.00E-4
DU-145	0.173	1.526	1.659	1.698	1.267	0.603	0.545	110	113	81	32	27	4.26E-6	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.280	1.531	1.438	1.357	0.474	0.470	0.444	93	86	15	15	13	3.24E-7	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.638	1.692	1.648	1.576	1.163	1.101	0.982	96	89	50	44	33	9.89E-7	> 1.00E-4	> 1.00E-4
HS 578T	0.449	1.874	1.827	1.769	1.518	1.148	1.141	97	93	75	49	49	9.18E-6	> 1.00E-4	> 1.00E-4
BT-549	0.868	1.836	1.862	1.899	1.512	1.287	0.874	103	107	67	43	1	5.13E-6	> 1.00E-4	> 1.00E-4
T-47D	0.549	1.229	1.247	1.241	0.956	0.928	0.908	103	102	60	56	53	> 1.00E-4	> 1.00E-4	> 1.00E-4
MDA-MB-468	0.579	1.175	1.133	1.080	0.753	0.545	0.579	93	84	29	-6	.	4.17E-7	6.80E-6	> 1.00E-4

COMPARE Analysis of Pyrazoline 8i

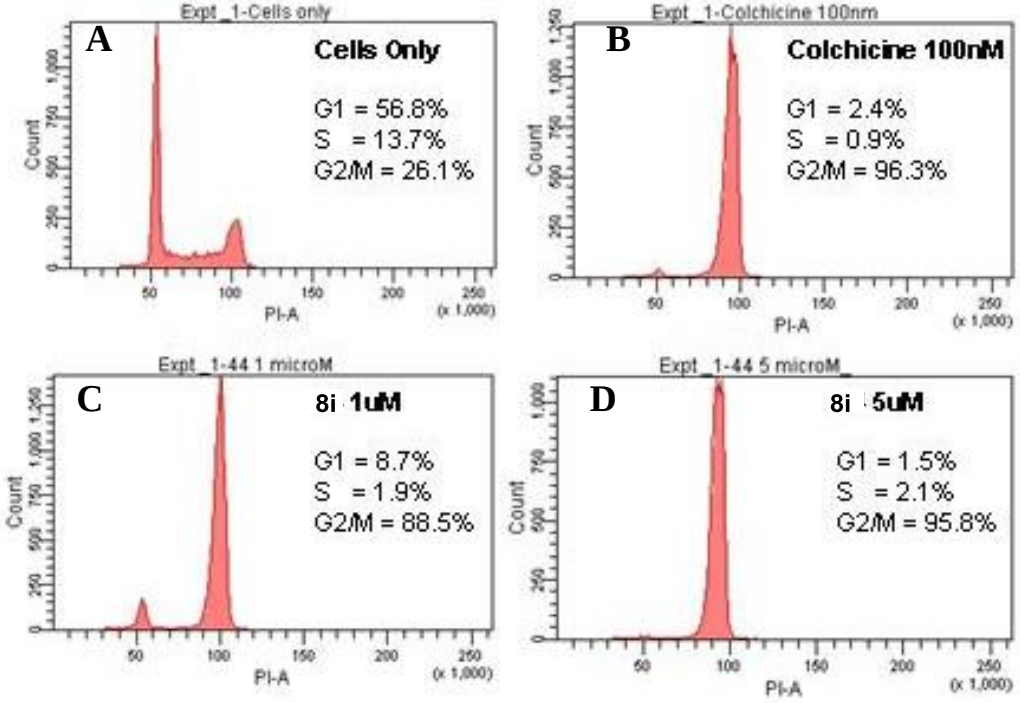
Rank	Correlation	namecode	Seed Vector ident For Display	Seed Vector descriptor For Display	Target Vector ident For Display	Target Vector descriptor For Display	Count Common Cell Lines	Seed Standard Deviation	Target Standard Deviation
1	0.49	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S357704 Endpt:GI50 ExpId:AVGDATA hiConc:-7.7	cyanomorpholino-ADR	57	0.795	0.416
2	0.43	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S150014 Endpt:GI50 ExpId:AVGDATA hiConc:-2.5	hydrazine sulfate	55	0.797	0.381
3	0.413	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S237020 Endpt:GI50 ExpId:AVGDATA hiConc:2.6	largomycin	57	0.795	0.327
4	0.406	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S26980 Endpt:GI50 ExpId:AVGDATA hiConc:-4.6	mitomycin C	58	0.794	0.556
5	0.39	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S67574 Endpt:GI50 ExpId:AVGDATA hiConc:-3.0	vincristine sulfate	57	0.795	0.657
6	0.381	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S332598 Endpt:GI50 ExpId:AVGDATA hiConc:-4.3	rhizoxin	45	0.755	0.848
7	0.372	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S182986 Endpt:GI50 ExpId:AVGDATA hiConc:-3.6	AZQ	50	0.765	0.466
8	0.371	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S375575 Endpt:GI50 ExpId:AVGDATA hiConc:-5.0	cyclopentenylcytosine	51	0.788	0.89
9	0.37	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S224131 Endpt:GI50 ExpId:AVGDATA hiConc:-2.0	PALA	56	0.791	0.715
10	0.369	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S157365 Endpt:GI50 ExpId:AVGDATA hiConc:2.3	neocarzinostatin	54	0.775	0.243
11	0.359	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S237020 Endpt:GI50 ExpId:AVGDATA hiConc:1.6	largomycin	52	0.797	0.466
12	0.356	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S153858 Endpt:GI50 ExpId:AVGDATA hiConc:-7.0	maytansine	56	0.8	0.724
13	0.35	PUBLIC	NSC:S761258 Endpt:GI50 ExpId:1109NS21 hiConc:-4.0		NSC:S619003 Endpt:GI50 ExpId:AVGDATA hiConc:-4.0	MX2 HCl	45	0.755	0.473

Cell Cycle Analysis

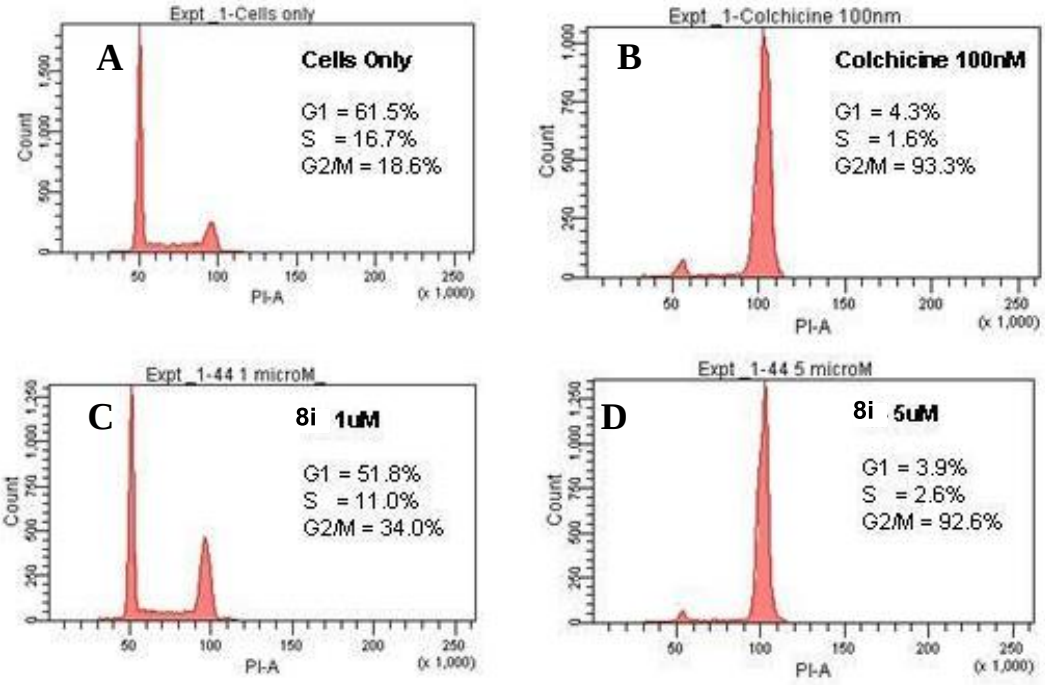
1st Experiment



2nd Experiment

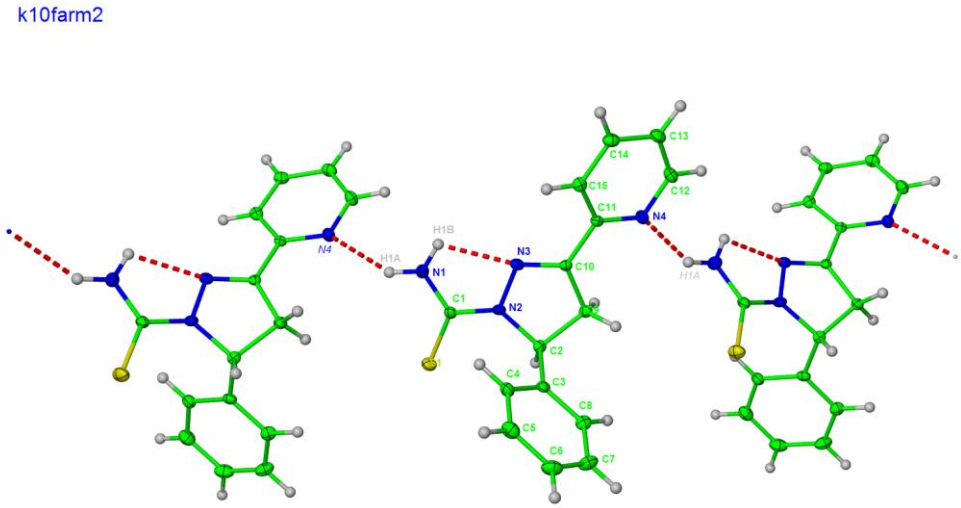


3rd Experiment



X-Ray Data

X-ray Structure Determination of Pyrazoline (8e) CCDC 926530



X-ray crystal structure of compound **8e** shown here is in a different orientation to that given in Fig. 2 in the paper, however it is of the same crystal structure (data below)

Table 1. Crystal data and structure refinement for **8e**.

Identification code	k10farm2
Empirical formula	C15 H14 N4 S
Formula weight	282.36
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P21/n
Unit cell dimensions	a = 9.7950(2)Å α = 90°
	b = 14.7280(3)Å β = 107.768(1)°
	c = 10.0360(2)Å γ = 90°
Volume	1378.74(5) $Å^3$
Z	4
Density (calculated)	1.360 Mg/m^3
Absorption coefficient	0.230 mm^{-1}
F(000)	592
Crystal size	0.35 x 0.35 x 0.12 mm
Theta range for data collection	3.52 to 27.52°
Index ranges	-12<=h<=12; -19<=k<=19; -13<=l<=13
Reflections collected	24456
Independent reflections	3152 [R(int) = 0.0669]
Reflections observed (>2σ)	2385
Data Completeness	0.996
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.938 and 0.716

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3152 / 2 / 190
Goodness-of-fit on F^2	1.025
Final R indices [I>2σ(I)]	R1 = 0.0392 wR2 = 0.0883
R indices (all data)	R1 = 0.0608 wR2 = 0.0979
Largest diff. peak and hole	0.249 and -0.250 eÅ^{-3}

Notes:

H1A and H1B located and refined at a distance of 0.98Å from N1.

Hydrogen bonding in the lattice.

Hydrogen bonds with H..A < r(A) + 2.000 Angstroms and <DHA > 110 deg.

D-H	d(D-H)	d(H..A)	<DHA	d(D..A)	A
N1-H1A	0.974	2.131	151.06	3.020	N4 [x-1/2, -y+1/2, z+1/2]
N1-H1B	0.973	2.685	153.02	3.579	S1 [x-1/2, -y+1/2, z-1/2]

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **8e**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
S(1)	4628(1)	1778(1)	10745(1)	31(1)
N(1)	2367(2)	2474(1)	8805(2)	29(1)
N(2)	4541(1)	2782(1)	8521(1)	22(1)
N(3)	3811(1)	3255(1)	7308(1)	21(1)
N(4)	4898(1)	3550(1)	4307(1)	24(1)
C(1)	3790(2)	2369(1)	9288(2)	22(1)
C(2)	6091(2)	2733(1)	8703(2)	21(1)
C(3)	6924(2)	3463(1)	9689(2)	21(1)
C(4)	6280(2)	4048(1)	10399(2)	27(1)
C(5)	7078(2)	4704(1)	11299(2)	35(1)
C(6)	8530(2)	4781(1)	11503(2)	39(1)
C(7)	9185(2)	4210(1)	10789(2)	36(1)
C(8)	8388(2)	3558(1)	9887(2)	27(1)
C(9)	6100(2)	2885(1)	7186(2)	22(1)
C(10)	4676(2)	3346(1)	6575(2)	19(1)
C(11)	4195(2)	3800(1)	5208(2)	19(1)
C(12)	4427(2)	3897(1)	3010(2)	28(1)
C(13)	3310(2)	4510(1)	2582(2)	28(1)
C(14)	2626(2)	4782(1)	3531(2)	27(1)
C(15)	3063(2)	4417(1)	4866(2)	24(1)

Table 3. Bond lengths [Å] and angles [°] for **8e**.

S(1)-C(1)	1.6842(16)	N(1)-C(1)	1.338(2)
N(1)-H(1A)	0.974(5)	N(1)-H(1B)	0.973(5)
N(2)-C(1)	1.359(2)	N(2)-N(3)	1.3960(17)
N(2)-C(2)	1.4748(19)	N(3)-C(10)	1.2870(19)
N(4)-C(12)	1.343(2)	N(4)-C(11)	1.3440(19)
C(2)-C(3)	1.519(2)	C(2)-C(9)	1.541(2)
C(2)-H(2)	1.0000	C(3)-C(4)	1.386(2)
C(3)-C(8)	1.393(2)	C(4)-C(5)	1.390(2)
C(4)-H(4)	0.9500	C(5)-C(6)	1.379(3)
C(5)-H(5)	0.9500	C(6)-C(7)	1.384(3)
C(6)-H(6)	0.9500	C(7)-C(8)	1.385(2)
C(7)-H(7)	0.9500	C(8)-H(8)	0.9500
C(9)-C(10)	1.504(2)	C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900	C(10)-C(11)	1.468(2)
C(11)-C(15)	1.394(2)	C(12)-C(13)	1.382(2)
C(12)-H(12)	0.9500	C(13)-C(14)	1.380(2)
C(13)-H(13)	0.9500	C(14)-C(15)	1.384(2)
C(14)-H(14)	0.9500	C(15)-H(15)	0.9500
C(1)-N(1)-H(1A)	117.5(13)	C(1)-N(1)-H(1B)	120.9(12)
H(1A)-N(1)-H(1B)	120.4(17)	C(1)-N(2)-N(3)	119.74(12)
C(1)-N(2)-C(2)	128.48(13)	N(3)-N(2)-C(2)	111.48(11)
C(10)-N(3)-N(2)	107.42(12)	C(12)-N(4)-C(11)	116.95(14)
N(1)-C(1)-N(2)	115.28(14)	N(1)-C(1)-S(1)	123.48(12)
N(2)-C(1)-S(1)	121.23(12)	N(2)-C(2)-C(3)	111.95(12)
N(2)-C(2)-C(9)	100.77(11)	C(3)-C(2)-C(9)	112.13(12)
N(2)-C(2)-H(2)	110.5	C(3)-C(2)-H(2)	110.5
C(9)-C(2)-H(2)	110.5	C(4)-C(3)-C(8)	118.34(15)
C(4)-C(3)-C(2)	122.43(14)	C(8)-C(3)-C(2)	119.23(14)
C(3)-C(4)-C(5)	120.80(16)	C(3)-C(4)-H(4)	119.6
C(5)-C(4)-H(4)	119.6	C(6)-C(5)-C(4)	120.29(17)
C(6)-C(5)-H(5)	119.9	C(4)-C(5)-H(5)	119.9
C(5)-C(6)-C(7)	119.55(17)	C(5)-C(6)-H(6)	120.2
C(7)-C(6)-H(6)	120.2	C(6)-C(7)-C(8)	120.13(16)
C(6)-C(7)-H(7)	119.9	C(8)-C(7)-H(7)	119.9
C(7)-C(8)-C(3)	120.87(16)	C(7)-C(8)-H(8)	119.6
C(3)-C(8)-H(8)	119.6	C(10)-C(9)-C(2)	100.62(12)
C(10)-C(9)-H(9A)	111.6	C(2)-C(9)-H(9A)	111.6
C(10)-C(9)-H(9B)	111.6	C(2)-C(9)-H(9B)	111.6
H(9A)-C(9)-H(9B)	109.4	N(3)-C(10)-C(11)	120.13(13)
N(3)-C(10)-C(9)	114.22(13)	C(11)-C(10)-C(9)	125.43(13)
N(4)-C(11)-C(15)	123.04(14)	N(4)-C(11)-C(10)	114.83(13)
C(15)-C(11)-C(10)	122.10(13)	N(4)-C(12)-C(13)	123.74(15)
N(4)-C(12)-H(12)	118.1	C(13)-C(12)-H(12)	118.1
C(14)-C(13)-C(12)	118.66(15)	C(14)-C(13)-H(13)	120.7
C(12)-C(13)-H(13)	120.7	C(13)-C(14)-C(15)	118.95(15)
C(13)-C(14)-H(14)	120.5	C(15)-C(14)-H(14)	120.5
C(14)-C(15)-C(11)	118.61(14)	C(14)-C(15)-H(15)	120.7
C(11)-C(15)-H(15)	120.7		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **8e**. The anisotropic displacement factor exponent takes the form: -2 gpi^2 [h^2 a^{*2} U11 + ... + 2 h k a* b* U.

Atom	U11	U22	U33	U23	U13	U12
S(1)	28(1)	36(1)	25(1)	10(1)	4(1)	-5(1)
N(1)	21(1)	42(1)	25(1)	8(1)	8(1)	-4(1)
N(2)	17(1)	28(1)	20(1)	4(1)	5(1)	-1(1)
N(3)	21(1)	23(1)	16(1)	0(1)	4(1)	-2(1)
N(4)	25(1)	28(1)	20(1)	1(1)	11(1)	0(1)
C(1)	22(1)	25(1)	20(1)	-1(1)	7(1)	-5(1)
C(2)	17(1)	23(1)	22(1)	3(1)	6(1)	1(1)
C(3)	22(1)	23(1)	17(1)	6(1)	4(1)	1(1)
C(4)	28(1)	33(1)	21(1)	1(1)	9(1)	-2(1)
C(5)	43(1)	36(1)	26(1)	-7(1)	11(1)	-1(1)
C(6)	40(1)	34(1)	35(1)	-5(1)	-1(1)	-8(1)
C(7)	24(1)	32(1)	44(1)	2(1)	-1(1)	-4(1)
C(8)	24(1)	24(1)	33(1)	3(1)	6(1)	2(1)
C(9)	21(1)	25(1)	21(1)	-2(1)	7(1)	0(1)
C(10)	20(1)	20(1)	18(1)	-3(1)	7(1)	-2(1)
C(11)	19(1)	20(1)	17(1)	-3(1)	7(1)	-5(1)
C(12)	33(1)	34(1)	21(1)	1(1)	13(1)	0(1)
C(13)	31(1)	29(1)	21(1)	7(1)	4(1)	-3(1)
C(14)	23(1)	24(1)	29(1)	2(1)	3(1)	1(1)
C(15)	24(1)	24(1)	25(1)	-3(1)	9(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **8e**.

Atom	x	y	z	U(eq)
H(2)	6473	2117	9040	25
H(4)	5280	3999	10268	32
H(5)	6621	5101	11775	42
H(6)	9078	5224	12130	47
H(7)	10184	4264	10918	43
H(8)	8845	3171	9396	33
H(9A)	6905	3280	7147	27
H(9B)	6150	2303	6708	27
H(12)	4889	3712	2349	34
H(13)	3018	4739	1653	33
H(14)	1868	5212	3272	32
H(15)	2600	4585	5535	28
H(1A)	1791(19)	2159(13)	9300(20)	55(6)
H(1B)	1915(19)	2747(13)	7894(11)	47(6)

Table 6. Dihedral angles [°] for **8e**.

Atom1 - Atom2 - Atom3 - Atom4	Dihedral
C(1) - N(2) - N(3) - C(10)	-161.42(14)
C(2) - N(2) - N(3) - C(10)	12.75(16)
N(3) - N(2) - C(1) - N(1)	-1.3(2)
C(2) - N(2) - C(1) - N(1)	-174.40(14)
N(3) - N(2) - C(1) - S(1)	179.10(11)
C(2) - N(2) - C(1) - S(1)	6.0(2)
C(1) - N(2) - C(2) - C(3)	-89.28(18)
N(3) - N(2) - C(2) - C(3)	97.19(14)
C(1) - N(2) - C(2) - C(9)	151.37(15)
N(3) - N(2) - C(2) - C(9)	-22.16(15)
N(2) - C(2) - C(3) - C(4)	4.7(2)
C(9) - C(2) - C(3) - C(4)	117.11(16)
N(2) - C(2) - C(3) - C(8)	-174.86(13)
C(9) - C(2) - C(3) - C(8)	-62.44(18)
C(8) - C(3) - C(4) - C(5)	-0.8(2)
C(2) - C(3) - C(4) - C(5)	179.62(15)
C(3) - C(4) - C(5) - C(6)	-0.2(3)
C(4) - C(5) - C(6) - C(7)	1.0(3)
C(5) - C(6) - C(7) - C(8)	-0.7(3)
C(6) - C(7) - C(8) - C(3)	-0.4(3)
C(4) - C(3) - C(8) - C(7)	1.2(2)
C(2) - C(3) - C(8) - C(7)	-179.28(15)
N(2) - C(2) - C(9) - C(10)	21.41(14)
C(3) - C(2) - C(9) - C(10)	-97.81(14)
N(2) - N(3) - C(10) - C(11)	178.38(12)
N(2) - N(3) - C(10) - C(9)	3.41(17)
C(2) - C(9) - C(10) - N(3)	-16.74(16)
C(2) - C(9) - C(10) - C(11)	168.61(13)
C(12) - N(4) - C(11) - C(15)	-2.5(2)
C(12) - N(4) - C(11) - C(10)	175.33(13)
N(3) - C(10) - C(11) - N(4)	-154.21(14)
C(9) - C(10) - C(11) - N(4)	20.1(2)
N(3) - C(10) - C(11) - C(15)	23.7(2)
C(9) - C(10) - C(11) - C(15)	-161.97(14)
C(11) - N(4) - C(12) - C(13)	2.2(2)
N(4) - C(12) - C(13) - C(14)	-0.3(3)
C(12) - C(13) - C(14) - C(15)	-1.4(2)
C(13) - C(14) - C(15) - C(11)	1.0(2)
N(4) - C(11) - C(15) - C(14)	1.0(2)
C(10) - C(11) - C(15) - C(14)	-176.75(14)

Symmetry transformations used to generate equivalent atoms:

X-ray Structure Determination of pyrazoline (8i) CCDC 926531

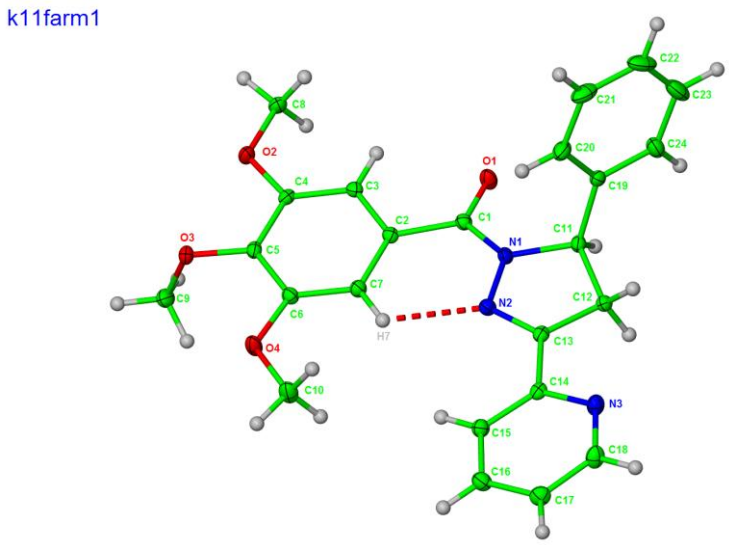


Table 1. Crystal data and structure refinement for pyrazoline **(8i)**.

Identification code	k11farm1
Empirical formula	C24 H23 N3 O4
Formula weight	417.45
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	a = 6.9770(1)Å $\alpha = 90^o$
	b = 22.0950(2)Å $\beta = 90^o$
	c = 26.6010(3)Å $\gamma = 90^o$
Volume	4100.73(8) $Å^3$
Z	8
Density (calculated)	1.352 Mg/m^3
Absorption coefficient	0.093 mm^{-1}
F(000)	1760
Crystal size	0.40 x 0.25 x 0.25 mm
Theta range for data collection	3.54 to 27.47^o
Index ranges	-8<=h<=9; -28<=k<=27; -34<=l<=34
Reflections collected	56599
Independent reflections	4679 [R(int) = 0.0645]
Reflections observed (>2σ)	3531
Data Completeness	0.997
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.982 and 0.893
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4679 / 0 / 283
Goodness-of-fit on F^2	1.051
Final R indices [I>2σ(I)]	R1 = 0.0422 wR2 = 0.0882
R indices (all data)	R1 = 0.0649 wR2 = 0.0991
Largest diff. peak and hole	0.182 and -0.215 $eÅ^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **8i**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
O(1)	8672(2)	1985(1)	7146(1)	34(1)
O(2)	13646(1)	441(1)	6698(1)	32(1)
O(3)	12242(1)	-195(1)	5936(1)	29(1)
O(4)	8769(2)	32(1)	5556(1)	36(1)
N(1)	6394(2)	2016(1)	6564(1)	25(1)
N(2)	5409(2)	1815(1)	6142(1)	25(1)
N(3)	982(2)	2382(1)	5679(1)	31(1)
C(1)	8030(2)	1763(1)	6756(1)	25(1)
C(2)	9030(2)	1235(1)	6514(1)	23(1)
C(3)	10824(2)	1096(1)	6719(1)	24(1)
C(4)	11870(2)	613(1)	6532(1)	23(1)
C(5)	11148(2)	263(1)	6140(1)	24(1)
C(6)	9351(2)	399(1)	5941(1)	26(1)
C(7)	8287(2)	882(1)	6126(1)	26(1)
C(8)	14362(2)	728(1)	7139(1)	32(1)
C(9)	11790(2)	-777(1)	6138(1)	38(1)
C(10)	6969(2)	171(1)	5328(1)	41(1)
C(11)	5385(2)	2514(1)	6834(1)	24(1)
C(12)	3449(2)	2530(1)	6551(1)	26(1)
C(13)	3785(2)	2096(1)	6126(1)	24(1)
C(14)	2400(2)	1975(1)	5720(1)	25(1)
C(15)	2544(2)	1469(1)	5410(1)	29(1)
C(16)	1184(2)	1382(1)	5039(1)	34(1)
C(17)	-269(2)	1802(1)	4988(1)	34(1)
C(18)	-314(2)	2286(1)	5315(1)	35(1)
C(19)	6439(2)	3111(1)	6804(1)	26(1)
C(20)	7541(2)	3265(1)	6388(1)	37(1)
C(21)	8358(2)	3836(1)	6354(1)	51(1)
C(22)	8092(3)	4255(1)	6730(1)	58(1)
C(23)	7013(3)	4104(1)	7147(1)	55(1)
C(24)	6190(2)	3533(1)	7187(1)	38(1)

Table 3. Bond lengths [Å] and angles [°] for **8i**.

O(1)-C(1)	1.2310(17)	O(2)-C(4)	1.3690(17)
O(2)-C(8)	1.4238(18)	O(3)-C(5)	1.3787(16)
O(3)-C(9)	1.4294(18)	O(4)-C(6)	1.3670(17)
O(4)-C(10)	1.4276(19)	N(1)-C(1)	1.3705(18)
N(1)-N(2)	1.3873(16)	N(1)-C(11)	1.4921(17)
N(2)-C(13)	1.2918(18)	N(3)-C(18)	1.341(2)
N(3)-C(14)	1.3421(18)	C(1)-C(2)	1.5041(19)
C(2)-C(7)	1.393(2)	C(2)-C(3)	1.400(2)
C(3)-C(4)	1.3843(19)	C(3)-H(3)	0.9500
C(4)-C(5)	1.394(2)	C(5)-C(6)	1.394(2)
C(6)-C(7)	1.389(2)	C(7)-H(7)	0.9500
C(8)-H(8A)	0.9800	C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800	C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800	C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9800	C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800	C(11)-C(19)	1.5117(19)

C(11)-C(12)	1.5468(19)	C(11)-H(11)	1.0000
C(12)-C(13)	1.500(2)	C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900	C(13)-C(14)	1.473(2)
C(14)-C(15)	1.395(2)	C(15)-C(16)	1.381(2)
C(15)-H(15)	0.9500	C(16)-C(17)	1.380(2)
C(16)-H(16)	0.9500	C(17)-C(18)	1.379(2)
C(17)-H(17)	0.9500	C(18)-H(18)	0.9500
C(19)-C(20)	1.389(2)	C(19)-C(24)	1.391(2)
C(20)-C(21)	1.387(2)	C(20)-H(20)	0.9500
C(21)-C(22)	1.375(3)	C(21)-H(21)	0.9500
C(22)-C(23)	1.382(3)	C(22)-H(22)	0.9500
C(23)-C(24)	1.391(3)	C(23)-H(23)	0.9500
C(24)-H(24)	0.9500		
C(4)-O(2)-C(8)	117.34(11)	C(5)-O(3)-C(9)	113.00(11)
C(6)-O(4)-C(10)	116.84(11)	C(1)-N(1)-N(2)	125.76(11)
C(1)-N(1)-C(11)	120.92(11)	N(2)-N(1)-C(11)	113.05(11)
C(13)-N(2)-N(1)	107.96(11)	C(18)-N(3)-C(14)	116.80(13)
O(1)-C(1)-N(1)	117.08(12)	O(1)-C(1)-C(2)	120.08(13)
N(1)-C(1)-C(2)	122.84(12)	C(7)-C(2)-C(3)	119.87(13)
C(7)-C(2)-C(1)	125.41(13)	C(3)-C(2)-C(1)	114.70(12)
C(4)-C(3)-C(2)	120.04(13)	C(4)-C(3)-H(3)	120.0
C(2)-C(3)-H(3)	120.0	O(2)-C(4)-C(3)	125.15(13)
O(2)-C(4)-C(5)	114.44(12)	C(3)-C(4)-C(5)	120.40(13)
O(3)-C(5)-C(4)	120.14(12)	O(3)-C(5)-C(6)	120.46(13)
C(4)-C(5)-C(6)	119.33(12)	O(4)-C(6)-C(7)	124.25(13)
O(4)-C(6)-C(5)	115.03(12)	C(7)-C(6)-C(5)	120.71(13)
C(6)-C(7)-C(2)	119.63(13)	C(6)-C(7)-H(7)	120.2
C(2)-C(7)-H(7)	120.2	O(2)-C(8)-H(8A)	109.5
O(2)-C(8)-H(8B)	109.5	H(8A)-C(8)-H(8B)	109.5
O(2)-C(8)-H(8C)	109.5	H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5	O(3)-C(9)-H(9A)	109.5
O(3)-C(9)-H(9B)	109.5	H(9A)-C(9)-H(9B)	109.5
O(3)-C(9)-H(9C)	109.5	H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5	O(4)-C(10)-H(10A)	109.5
O(4)-C(10)-H(10B)	109.5	H(10A)-C(10)-H(10B)	109.5
O(4)-C(10)-H(10C)	109.5	H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5	N(1)-C(11)-C(19)	112.84(11)
N(1)-C(11)-C(12)	101.14(11)	C(19)-C(11)-C(12)	112.32(11)
N(1)-C(11)-H(11)	110.1	C(19)-C(11)-H(11)	110.1
C(12)-C(11)-H(11)	110.1	C(13)-C(12)-C(11)	102.50(11)
C(13)-C(12)-H(12A)	111.3	C(11)-C(12)-H(12A)	111.3
C(13)-C(12)-H(12B)	111.3	C(11)-C(12)-H(12B)	111.3
H(12A)-C(12)-H(12B)	109.2	N(2)-C(13)-C(14)	120.86(13)
N(2)-C(13)-C(12)	114.72(12)	C(14)-C(13)-C(12)	124.40(12)
N(3)-C(14)-C(15)	122.79(13)	N(3)-C(14)-C(13)	115.03(13)
C(15)-C(14)-C(13)	122.17(13)	C(16)-C(15)-C(14)	118.97(14)
C(16)-C(15)-H(15)	120.5	C(14)-C(15)-H(15)	120.5
C(17)-C(16)-C(15)	118.79(14)	C(17)-C(16)-H(16)	120.6
C(15)-C(16)-H(16)	120.6	C(18)-C(17)-C(16)	118.43(14)
C(18)-C(17)-H(17)	120.8	C(16)-C(17)-H(17)	120.8
N(3)-C(18)-C(17)	124.20(14)	N(3)-C(18)-H(18)	117.9
C(17)-C(18)-H(18)	117.9	C(20)-C(19)-C(24)	119.25(14)
C(20)-C(19)-C(11)	121.66(13)	C(24)-C(19)-C(11)	118.94(14)
C(21)-C(20)-C(19)	120.06(17)	C(21)-C(20)-H(20)	120.0
C(19)-C(20)-H(20)	120.0	C(22)-C(21)-C(20)	120.71(19)
C(22)-C(21)-H(21)	119.6	C(20)-C(21)-H(21)	119.6
C(21)-C(22)-C(23)	119.58(17)	C(21)-C(22)-H(22)	120.2

C(23)-C(22)-H(22)	120.2	C(22)-C(23)-C(24)	120.34(18)
C(22)-C(23)-H(23)	119.8	C(24)-C(23)-H(23)	119.8
C(19)-C(24)-C(23)	120.05(18)	C(19)-C(24)-H(24)	120.0
C(23)-C(24)-H(24)	120.0		

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **8i**. The anisotropic displacement factor exponent takes the form: $-2\ gpi^2\ [\ h^2\ a^{*2}\ U11 + ... + 2\ h\ k\ a^*\ b^*\ U$.

Atom	U11	U22	U33	U23	U13	U12
O(1)	36(1)	34(1)	32(1)	-10(1)	-10(1)	9(1)
O(2)	22(1)	35(1)	39(1)	-10(1)	-7(1)	7(1)
O(3)	26(1)	28(1)	33(1)	-4(1)	3(1)	5(1)
O(4)	34(1)	37(1)	37(1)	-15(1)	-14(1)	11(1)
N(1)	24(1)	22(1)	28(1)	-4(1)	-3(1)	3(1)
N(2)	25(1)	24(1)	24(1)	1(1)	-3(1)	1(1)
N(3)	31(1)	33(1)	29(1)	1(1)	-4(1)	9(1)
C(1)	25(1)	22(1)	26(1)	0(1)	-2(1)	1(1)
C(2)	24(1)	21(1)	24(1)	2(1)	0(1)	0(1)
C(3)	23(1)	23(1)	25(1)	0(1)	-1(1)	-2(1)
C(4)	18(1)	25(1)	26(1)	3(1)	0(1)	0(1)
C(5)	23(1)	23(1)	26(1)	0(1)	4(1)	2(1)
C(6)	28(1)	25(1)	25(1)	-2(1)	-2(1)	0(1)
C(7)	25(1)	25(1)	28(1)	-1(1)	-4(1)	4(1)
C(8)	22(1)	36(1)	38(1)	-6(1)	-5(1)	1(1)
C(9)	31(1)	25(1)	59(1)	-3(1)	-1(1)	3(1)
C(10)	38(1)	44(1)	42(1)	-15(1)	-18(1)	11(1)
C(11)	23(1)	23(1)	27(1)	-1(1)	3(1)	3(1)
C(12)	23(1)	22(1)	33(1)	-2(1)	0(1)	0(1)
C(13)	23(1)	21(1)	27(1)	4(1)	2(1)	0(1)
C(14)	23(1)	25(1)	26(1)	6(1)	2(1)	1(1)
C(15)	28(1)	26(1)	35(1)	1(1)	-3(1)	3(1)
C(16)	37(1)	29(1)	36(1)	-2(1)	-5(1)	0(1)
C(17)	32(1)	38(1)	31(1)	2(1)	-9(1)	2(1)
C(18)	34(1)	40(1)	32(1)	1(1)	-6(1)	12(1)
C(19)	20(1)	23(1)	34(1)	-1(1)	-4(1)	3(1)
C(20)	28(1)	32(1)	50(1)	3(1)	8(1)	1(1)
C(21)	28(1)	43(1)	82(2)	19(1)	2(1)	-7(1)
C(22)	43(1)	29(1)	103(2)	7(1)	-26(1)	-11(1)
C(23)	58(1)	30(1)	77(2)	-17(1)	-26(1)	3(1)
C(24)	39(1)	32(1)	43(1)	-11(1)	-7(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **8i**.

Atom	x	y	z	U(eq)
H(3)	11325	1333	6987	28
H(7)	7060	970	5990	31
H(8A)	14436	1166	7083	48
H(8B)	15643	571	7215	48
H(8C)	13502	645	7422	48
H(9A)	12140	-789	6495	57
H(9B)	12509	-1089	5956	57
H(9C)	10413	-853	6103	57
H(10A)	5941	115	5575	62
H(10B)	6755	-100	5042	62
H(10C)	6975	591	5212	62
H(11)	5175	2400	7194	29
H(12A)	2385	2393	6769	32
H(12B)	3162	2941	6424	32
H(15)	3561	1187	5452	35
H(16)	1248	1040	4823	40
H(17)	-1215	1758	4734	41
H(18)	-1328	2570	5280	42
H(20)	7736	2978	6126	44
H(21)	9110	3938	6069	61
H(22)	8646	4646	6702	70
H(23)	6833	4391	7408	66
H(24)	5456	3430	7475	46

Table 6. Dihedral angles [°] for **8i**.

Atom1 - Atom2 - Atom3 - Atom4	Dihedral
C(1) - N(1) - N(2) - C(13)	169.20(13)
C(11) - N(1) - N(2) - C(13)	-4.79(15)
N(2) - N(1) - C(1) - O(1)	-177.09(13)
C(11) - N(1) - C(1) - O(1)	-3.5(2)
N(2) - N(1) - C(1) - C(2)	2.6(2)
C(11) - N(1) - C(1) - C(2)	176.19(12)
O(1) - C(1) - C(2) - C(7)	168.54(14)
N(1) - C(1) - C(2) - C(7)	-11.2(2)
O(1) - C(1) - C(2) - C(3)	-9.42(19)
N(1) - C(1) - C(2) - C(3)	170.87(13)
C(7) - C(2) - C(3) - C(4)	0.9(2)
C(1) - C(2) - C(3) - C(4)	179.01(12)
C(8) - O(2) - C(4) - C(3)	8.8(2)
C(8) - O(2) - C(4) - C(5)	-172.17(12)
C(2) - C(3) - C(4) - O(2)	179.03(13)
C(2) - C(3) - C(4) - C(5)	0.0(2)
C(9) - O(3) - C(5) - C(4)	97.25(16)
C(9) - O(3) - C(5) - C(6)	-85.70(16)
O(2) - C(4) - C(5) - O(3)	-2.82(19)
C(3) - C(4) - C(5) - O(3)	176.28(12)
O(2) - C(4) - C(5) - C(6)	-179.90(12)
C(3) - C(4) - C(5) - C(6)	-0.8(2)

C(10) - O(4) - C(6) - C(7)	1.5(2)
C(10) - O(4) - C(6) - C(5)	-177.62(14)
O(3) - C(5) - C(6) - O(4)	2.7(2)
C(4) - C(5) - C(6) - O(4)	179.79(13)
O(3) - C(5) - C(6) - C(7)	-176.46(13)
C(4) - C(5) - C(6) - C(7)	0.6(2)
O(4) - C(6) - C(7) - C(2)	-178.76(14)
C(5) - C(6) - C(7) - C(2)	0.3(2)
C(3) - C(2) - C(7) - C(6)	-1.1(2)
C(1) - C(2) - C(7) - C(6)	-178.97(13)
C(1) - N(1) - C(11) - C(19)	73.16(16)
N(2) - N(1) - C(11) - C(19)	-112.52(13)
C(1) - N(1) - C(11) - C(12)	-166.64(12)
N(2) - N(1) - C(11) - C(12)	7.68(14)
N(1) - C(11) - C(12) - C(13)	-7.14(13)
C(19) - C(11) - C(12) - C(13)	113.43(13)
N(1) - N(2) - C(13) - C(14)	-179.52(12)
N(1) - N(2) - C(13) - C(12)	-0.65(16)
C(11) - C(12) - C(13) - N(2)	5.34(16)
C(11) - C(12) - C(13) - C(14)	-175.84(12)
C(18) - N(3) - C(14) - C(15)	-0.7(2)
C(18) - N(3) - C(14) - C(13)	-179.71(13)
N(2) - C(13) - C(14) - N(3)	-165.69(13)
C(12) - C(13) - C(14) - N(3)	15.6(2)
N(2) - C(13) - C(14) - C(15)	15.3(2)
C(12) - C(13) - C(14) - C(15)	-163.49(14)
N(3) - C(14) - C(15) - C(16)	0.6(2)
C(13) - C(14) - C(15) - C(16)	179.55(14)
C(14) - C(15) - C(16) - C(17)	0.2(2)
C(15) - C(16) - C(17) - C(18)	-0.8(2)
C(14) - N(3) - C(18) - C(17)	0.0(2)
C(16) - C(17) - C(18) - N(3)	0.8(3)
N(1) - C(11) - C(19) - C(20)	31.53(19)
C(12) - C(11) - C(19) - C(20)	-82.02(17)
N(1) - C(11) - C(19) - C(24)	-153.00(13)
C(12) - C(11) - C(19) - C(24)	93.45(16)
C(24) - C(19) - C(20) - C(21)	-0.8(2)
C(11) - C(19) - C(20) - C(21)	174.63(15)
C(19) - C(20) - C(21) - C(22)	0.0(3)
C(20) - C(21) - C(22) - C(23)	0.6(3)
C(21) - C(22) - C(23) - C(24)	-0.4(3)
C(20) - C(19) - C(24) - C(23)	1.0(2)
C(11) - C(19) - C(24) - C(23)	-174.57(15)
C(22) - C(23) - C(24) - C(19)	-0.4(3)