Supporting Information for:

DL5050, A Selective Agonist for the Human Constitutive Androstane Receptor

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Contents:

1. General Procedures.

All reagents and solvents were of analytical grade and used without further purification. Reactions were monitored using thin-layer chromatography (TLC) on commercial silica-gel plates (GF254). UV spectra were obtained on a Nanodrop 2000c spectrophotometer. Flash column chromatography was performed on silica gel (200−300 mesh). NMR spectra were obtained on a Varian INOVA 400 MHz NMR spectrometer at 25 °C. Chemical shifts are reported as δ values (parts per million) using the residual solvent peak as an internal reference. Chemical shifts (δ) were reported in ppm referenced to the $CDCl_3$ residual peak (δ 7.264) for ^1H NMR. Chemical shifts of ^{13}C NMR were reported relative to CDCl3 (δ 77.04). Data for ^1H NMR were reported in the following order: chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; sept, septuplet; dd, double doublet; dt, double triplet; m, multiplet), coupling constant (Hz), number of protons. Data for ^{13}C NMR were reported as δ values (parts per million). High-resolution mass spectra (HRMS) were obtained on a JEOL AccuTOF with ESI/APCI ion sources coupled to an Agilent 1100 HPLC system. HPLC analysis was performed on a Shimadzu HPLC fitted with a C-18 reversed-phase column (Phenomenex, luna 5 μM C18(2) 4.6 mm ×100 mm) with a flow rate of 0.8 mL/min using CH_3CN−H_2O 8:2 mobile phase. The purity of final products is > 95%.

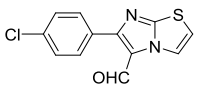
2. General Procedure for the Synthesis of Compounds **1-17**

A solution of 2-aminothiazole (5 mmol, 1 equiv) and bromomethyl ketone **30** (5 mmol, 1 equiv) in EtOH (30 mL) was heated under reflux for 16 h. The solvent was removed under reduced pressure, and saturated $NaHCO_3$ (30 mL) was added to the remaining solid. The mixture was then extracted with EtOAc (30 mL × 3), and the organic layers were combined, dried over Na_2SO_4. The concentrated crude product

dried overnight under vacuum to get the crude imidazothiazole **31** that was used directly in the next step.[1]

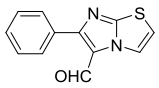
The Vilsmeier reagent was prepared by dropping of $POCl_3$ (16.5 mmol, 3.3 equiv) into a solution of DMF (5 mmol, 1.0 equiv) in $CHCl_3$ (5 mL) at 0 °C. To the resulting mixture at 0-5 °C was added a solution of imidazothiazole **31** (5 mmol) in $CHCl_3$ (30 mL) dropwise. The reaction was warmed to the room temperature over 1 h, and then heated under reflux for an additional 5 h. The solvent was removed under reduced pressure and the resulting residue was poured onto ice. The crude aldehyde **32** was collected by filtration and further purified using flash chromatography. [2]

*6-(4-Chlorophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32a**)*



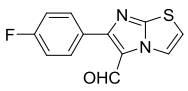
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.89 (s, 1H), 8.39 (d, J = 4.8 Hz, 1H), 7.74 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 156.8, 155.7, 136.0, 130.9, 130.2, 129.2, 124.0, 121.5, 114.9.

*6-Phenylimidazo[2,1-b]thiazole-5-carbaldehyde (**32b**)*



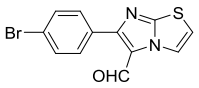
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.90 (s, 1H), 8.39 (d, J = 4.0 Hz, 1H), 7.79 (d, J = 6.8 Hz, 2H), 7.50 (d, J = 7.2 Hz, 3H), 7.05 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.1, 158.2, 155.6, 132.5, 129.7, 129.1, 128.9, 124.0, 121.5, 114.6.

*6-(4-Fluorophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32c**)*



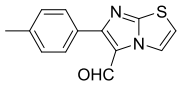
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86 (s, 1H), 8.38 (d, J = 4.8 Hz, 1H), 7.78 (t, J = 8.0 Hz, 2H), 7.19 (t, J = 7.6 Hz, 2H), 7.07 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 163.8 (J = 248.5 Hz), 156.6, 155.4, 130.9 (J = 7.4 Hz), 128.3, 123.8, 121.5, 116.2 (J = 20.8 Hz), 115.0.

*6-(4-Bromophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32d**)*



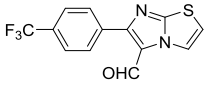
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.87 (s, 1H), 8.37 (d, J = 4.8 Hz, 1H), 7.67-7.61 (m, 4H), 7.07 (d, J = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 156.7, 155.7, 132.1, 131.4, 130.5, 124.3, 124.0, 121.5, 114.9.

*6-(p-Tolyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32e**)*



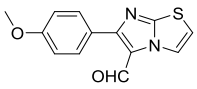
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.89 (s, 1H), 8.37 (d, J = 4.8 Hz, 1H), 7.69 (d, J = 8.0 Hz,2H), 7.31 (d, J = 8.0 Hz, 2H), 7.03 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.1, 158.4, 155.6, 139.9, 129.7, 129.0, 123.9, 121.5, 114.4, 21.4.

*6-(4-(Trifluoromethyl)phenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32f**)*



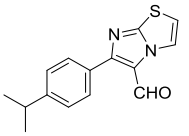
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.41 (d, J = 4.0 Hz, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 155.9, 155.6, 135.9, 131.1(J = 32.8 Hz), 129.3, 125.8 (J = 3.4 Hz), 124.3, 123.9 (J = 270.9 Hz), 121.4, 115.3.

*6-(4-Methoxyphenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32g**)*



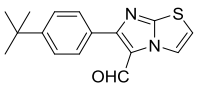
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 8.37 (d, J = 4.8 Hz, 1H), 7.75 (d, J = 8.8 Hz, 2H), 7.04-7.02 (m, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.0, 161.0, 158.0, 155.5, 130.4, 124.8, 123.6, 121.6, 114.4, 114.3, 55.4.

*6-(4-Isopropylphenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32h**)*



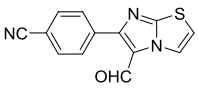
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.91 (s, 1H), 8.38 (d, J = 4.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 4.0 Hz, 1H), 3.02-2.95 (m, 1H), 1.30 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 158.5, 155.6, 150.8, 130.0, 129.1, 128.9, 127.1, 123.9, 121.5, 114.4, 34.0, 23.9.

*6-(4-(tert-Butyl)phenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32i**)*



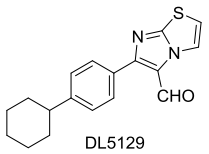
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H), 8.40 (d, J = 4.4 Hz, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 4.0 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 158.3, 155.6, 153.1, 129.5, 128.8, 125.9, 123.9, 121.5, 114.5, 34.8, 31.2.

*4-(5-Formylimidazo[2,1-b]thiazol-6-yl)benzonitrile (**32j**)*



^{1}H NMR (400 MHz, $CDCl_3$): δ 9.94 (s, 1H), 8.41 (d, J = 4.0 Hz, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 7.6 Hz, 2H), 7.13 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 155.8, 155.3, 136.8, 132.7, 129.5, 124.4, 121.5, 118.3, 115.6, 113.2.

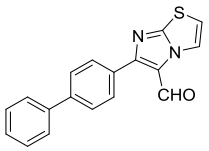
*6-(4-Cyclohexylphenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32k**)*



DL5129

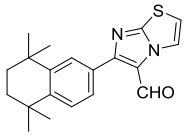
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.91 (s, 1H), 8.39 (d, J = 4.0 Hz, 1H), 7.72 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 7.6 Hz, 2H), 7.03 (d, J = 4.8 Hz, 1H), 2.60-2.56 (m, 1H), 1.94-1.76 (m, 5H), 1.52-1.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 158.5, 156.6, 150.0, 130.0, 129.1, 127.5, 123.9, 121.6, 114.4, 44.4, 34.3, 26.8, 26.1.

*6-([1,1'-Biphenyl]-4-yl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32l**)*



^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 8.42 (d, J = 4.8 Hz, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 7.6 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.40 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.0, 157.3, 155.4, 142.6, 140.1, 130.9, 129.5, 128.9, 127.9, 127.7, 127.124.0, 121.6, 114.9.

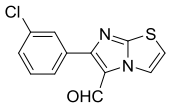
*6-(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32m**)*



^{1}H NMR (400 MHz, $CDCl_3$): δ 9.87 (s, 1H), 8.33 (d, J = 4.8 Hz, 1H), 7.71 (d, J = 1.6 Hz, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.41 (d, J = 8.8 Hz, 1H), 6.98 (d, J = 4.8 Hz, 1H),

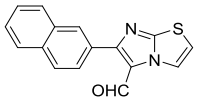
1.69 (s, 4H), 1.32 (s, 6H), 1.29 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.1, 158.8, 155.6, 146.8, 145.6, 129.7, 127.4, 127.2, 126.3, 123.9, 121.5, 114.4, 60.3, 34.9, 34.8, 34.4, 31.8, 31.7.

*6-(3-Chlorophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32n**)*



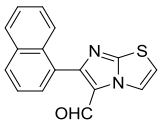
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.89 (s, 1H), 8.37 (d, J = 4.8 Hz, 1H), 7.79 (s, 1H), 7.65 (d, J = 6.4 Hz, 1H), 7.43-7.39 (m, 2H), 7.07 (d, J = 4.0 Hz, 1H), ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 156.2, 155.6, 135.0, 134.1, 130.2, 129.7, 129.0, 127.2, 124.1, 121.5, 115.1.

*6-(Naphthalen-2-yl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32o**)*



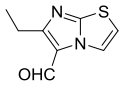
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.00 (s, 1H), 8.41 (d, J = 4.8 Hz, 1H), 8.27 (s, 1H), 7.99-7.89 (m, 4H), 7.56-7.54 (m, 2H), 7.07 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 158.1, 155.7, 133.7, 133.2, 129.7, 128.9, 128.8, 128.5, 127.8, 127.1, 126.8, 126.1, 124.2, 121.6, 114.8.

*6-(Naphthalen-1-yl)imidazo[2,1-b]thiazole-5-carbaldehyde (**32p**)*



^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (s, 1H), 8.44 (d, J = 3.6 Hz, 1H), 8.32-8.29 (m, 1H), 8.00-7.93 (m, 2H), 7.65 (d, 7.2 Hz, 1H), 7.60-7.54 (m, 3H), 7.12 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.3, 157.9, 155.5, 133.9, 132.0, 130.2, 129.7, 129.2, 128.3, 127.1, 126.4, 125.8, 125.5, 124.9, 121.3, 114.8.

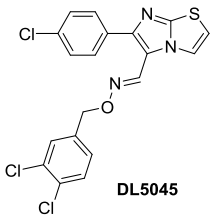
*6-Ethylimidazo[2,1-b]thiazole-5-carbaldehyde (**32q**)*



^{1}H NMR (400 MHz, $CDCl_3$): δ 9.81 (s, 1H), 8.26 (d, J = 3.6 Hz, 1H), 6.98 (d, J = 4.8 Hz, 1H), 2.99 (q, J = 8.0 Hz, 2H), 1.41 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6, 162.8, 155.6, 123.8, 121.2, 114.0, 21.7, 14.4.

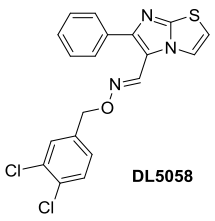
To a solution of aldehyde **32** (1 mmol) in EtOH (5 mL) was added hydroxylamine **33** (1 mmol) followed by AcOH (5 mmol, 5 equiv). The reaction mixture was heated under reflux overnight. After cooled to room temperature, a saturated aqueous solution of $NaHCO_3$ (30 mL) was added. The aqueous layer was extracted with EtOAc (30 mL × 3) and the combined organics were washed with brine (45 mL), dried (Na_2SO_4). The crude product was then purified by flash chromatography to give the desired product.

*(E)-6-(4-Chlorophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**1**)*



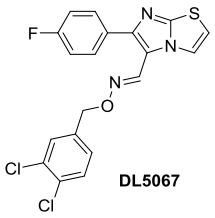
Yield 23%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.51 (s, 1H), 7.46-7.42 (m, 3H), 7.24 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 4.4 Hz, 1H), 5.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 149.3, 139.9, 137.7, 134.5, 132.6, 132.1, 131.9, 130.5, 130.1, 129.5, 129.0, 127.4, 121.5, 115.7, 113.0, 75.0; RMS (ESI): Exact mass calcd for $C_{19}H_{13}Cl_3N_3OS$ $[M+H]^+$ 435.9845, found 435.9855; HPLC analysis: retention time = 12.25 min, peak area 98.0%, 80:20 CH_3CN/H_2O.

*(E)-6-Phenylimidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**2**)*



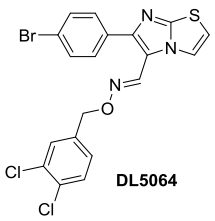
Yield 91%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 8.00 (d, J = 4.8 Hz, 1H), 7.66 (d, J = 6.8 Hz, 2H), 7.52-7.37 (m, 5H), 7.25 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 4.8 Hz, 1H), 5.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6, 150.6, 140.3, 137.9, 133.3, 132.6, 132.0, 130.5, 130.1, 128.8, 128.4, 127.4, 121.6, 115.6, 112.8, 74.9; RMS (ESI): Exact mass calcd for $C_{19}H_{14}Cl_2N_3OS$ $[M+H]^+$ 402.0234, found 402.0227; HPLC analysis: retention time = 8.01 min, peak area 97.4%, 80:20 CH_3CN/H_2O.

*(E)-6-(4-Fluorophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**3**)*



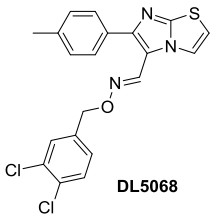
Yield 81%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.99 (d, J = 3.6 Hz, 1H), 7.64-7.61 (m, 2H), 7.51 (s, 1H), 7.44 (t, J = 4.8 Hz, 1H), 7.24 (J = 8.4 Hz, 1H), 7.17-7.12 (m, 2H), 6.91 (d, J = 4.8 Hz, 1H), 5.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9 (J = 247 Hz), 152.6, 149.5, 140.0, 137.8, 132.6, 132.0, 130.5, 130.14, 130.06, 129.5, 127.4, 121.5, 115.8 (J = 20.8 Hz), 115.5, 112.9, 74.9; HRMS (ESI): Exact mass calcd for $C_{19}H_{13}Cl_2FN_3OS$ [M+H]+ 420.0140, found 420.0137; HPLC analysis: retention time = 8.37 min, peak area 96.4%, 80:20 CH_3CN/H_2O.

*(E)-6-(4-Bromophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**4**)*



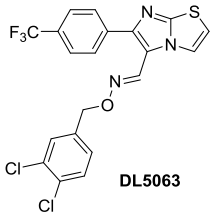
50% ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, 1H), 7.98 (d, J = 2.8 Hz, 1H), 7.56-7.44 (m, 6H), 7.24 (d, J = 7.6 Hz, 1H), 6.92 (d, J = 2.8 Hz, 1H), 5.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 149.2, 139.9, 137.7, 132.6, 132.5, 132.3, 131.9, 130.5, 130.1, 129.8, 127.4, 122.7, 121.5, 115.7, 113.1, 75.0; HRMS (ESI): Exact mass calcd for $C_{19}H_{13}BrN_3OS$ $[M+H]^+$ 479.9340, found 479.9454; HPLC analysis: retention time = 13.64 min, peak area 95.2%, 80:20 CH_3CN/H_2O.

*(E)-6-(p-Tolyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**5**)*



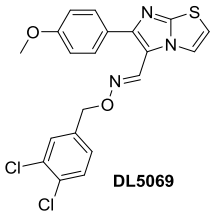
Yield 92%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (s, 1H), 7.99 (d, J = 4.0 Hz, 1H), 7.56-7.51 (m, 3H), 7.45 (d, J = 8.0 Hz, 1H), 7.28-7.24 (m, 3H), 6.89 (d, J = 4.0 Hz, 1H), 5.13 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 150.8, 140.4, 138.4, 137.9, 132.6, 132.0, 130.5, 130.1, 129.5, 128.3, 127.4, 121.6, 115.3, 112.6, 74.8, 21.3; HRMS (ESI): Exact mass calcd for $C_{20}H_{16}Cl_2N_3OS$ $[M+H]^+$ 416.0391, found 416.0384; HPLC analysis: retention time = 10.75 min, peak area 95.7%, 80:20 CH_3CN/H_2O.

*(E)-6-(4-(Trifluoromethyl)phenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**6**)*



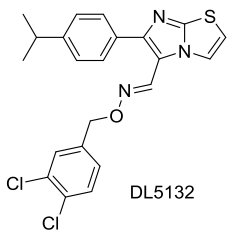
Yield 90%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.00 (d, J = 4.8 Hz, 1H), 7.78 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.52 (s, 1H), 7.45 (d, J = 8.8 Hz, 1H), 7.24 (d, J = 7.6 Hz, 1H), 6.95 (d, J = 4.8 Hz, 1H), 5.14 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 148.7, 139.7, 137.7, 136.9, 132.6, 132.1, 130.5, 130.3, 130.1, 128.5, 127.4, 126.8 (J = 270.9 Hz), 125.7, 121.5, 116.3, 113.4, 75.0; HRMS (ESI): Exact mass calcd for $C_{20}H_{13}Cl_2F_3N_3OS$ $[M+H]^+$ 470.0108, found 470.0100; HPLC analysis: retention time = 5.38 min, peak area 97.6%, 80:20 CH_3CN/H_2O.

*(E)-6-(4-Methoxyphenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**7**)*



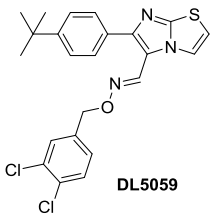
Yield 93%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.97 (d, J = 3.2 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.51 (s, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 6.98 (d, J = 7.6 Hz, 2H), 6.87 (d, J = 3.2 Hz, 1H), 5.12 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 152.5, 150.6, 140.4, 137.9, 132.5, 132.0, 130.5, 130.1, 129.6, 127.4, 126.0, 121.6, 115.0, 114.2, 112.4, 74.8, 55.3; HRMS (ESI): Exact mass calcd for $C_{20}H_{16}Cl_2N_3O_2S$ $[M+H]^+$ 432.0340, found 432.0346; HPLC analysis: retention time = 6.36 min, peak area 95.4%, 80:20 CH_3CN/H_2O.

*(E)-6-(4-Isopropylphenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**8**)*



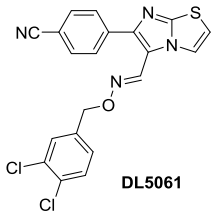
Yield 71%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.99 (d, J = 3.6 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.51 (s, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 3.6 Hz, 1H), 5.12 (s, 2H), 2.99-2.92 (m, 1H), 1.29 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 150.9, 149.3, 140.5, 137.9, 132.5, 132.0, 130.9, 130.5, 130.1, 128.4, 127.4, 126.9, 125.8, 121.6, 115.3, 112.5, 74.8, 33.9, 23.9; HRMS (ESI): Exact mass calcd for $C_{22}H_{20}Cl_2N_3OS$ $[M+H]^+$ 444.0704, found 444.0700; HPLC analysis: retention time = 15.80 min, peak area 95.2%, 80:20 CH_3CN/H_2O.

*(E)-6-(4-(tert-Butyl)phenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**9**)*



Yield 98%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.98 (d, J = 4.4 Hz, 1H), 7.60 (d, J = 8.8 Hz, 2H), 7.51-7.42 (m, 4H), 7.23 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 4.8 Hz, 1H), 5.12 (s, 2H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 151.6, 150.7, 140.5, 137.9, 132.5, 131.9, 130.5, 130.0, 128.1, 127.4, 125.7, 121.6, 115.4, 112.6, 74.8, 34.7, 31.3; HRMS (ESI): Exact mass calcd for $C_{23}H_{22}Cl_2N_3OS$ $[M+H]^+$ 458.0860, found 458.0864; HPLC analysis: retention time = 19.74 min, peak area 97.3%, 80:20 CH_3CN/H_2O.

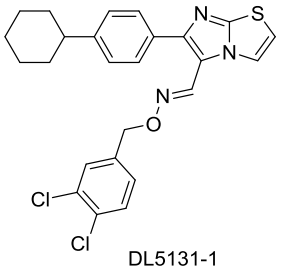
*(E)-4-(5-((((3,4-Dichlorobenzyl)oxy)imino)methyl)imidazo[2,1-b]thiazol-6-yl)benzoni trile (**10**)*



DL5061

Yield 80%,[1]H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 8.00 (d, J = 2.8 Hz, 1H), 7.76 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 7.6 Hz, 2H), 7.51 (s, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 4.0 Hz, 1H), 5.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 147.8, 139.4, 137.9, 137.6, 132.5, 132.2, 130.6, 130.1, 128.7, 128.1, 127.4, 121.5, 118.7, 116.6, 113.7, 111.7, 75.1; HRMS (ESI): Exact mass calcd for $C_{20}H_{13}Cl_2N_4OS$ $[M+H]^+$ 427.0184, found 427.0188; HPLC analysis: retention time = 12.64 min, peak area 96.8%, 80:20 CH_3CN/H_2O.

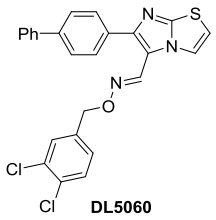
*(E)-6-(4-Cyclohexylphenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**11**)*



DL5131-1

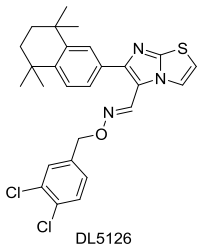
Yield 79%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.98 (d, J = 4.4 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.51 (s, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.30-7.23 (m, 3H), 6.87 (d, J = 4.8 Hz, 1H), 5.12 (s, 2H), 2.55 (t, J = 7.6 Hz, 1H), 1.92-1.75 (m, 5H), 1.50-1.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 150.9, 148.5, 140.5, 137.9, 132.5, 132.0, 130.9, 130.5, 130.1, 128.3, 127.4, 127.3, 121.6, 115.3, 112.5, 74.8, 44.4, 34.4, 26.9, 26.1; HRMS (ESI): Exact mass calcd for $C_{25}H_{24}Cl_2N_3OS$ $[M+H]^+$ 484.1017, found 384.1034; HPLC analysis: retention time = 43.23 min, peak area 96.5%, 80:20 CH_3CN/H_2O.

*(E)-6-([1,1'-Biphenyl]-4-yl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**12**)*



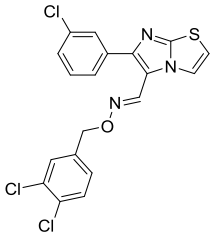
Yield 84%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.01 (d, J = 4.0 Hz, 1H), 7.76-7.64 (m, 6H), 7.49-7.44 (m, 4H), 7.38 (t, J = 7.2 Hz, 1H), 7.25 (d, J = 7.6 Hz, 1H), 6.90 (d, J = 4.0 Hz, 1H), 5.14 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 150.2, 141.1, 140.4, 140.3, 137.9, 132.6, 132.4, 132.0, 130.5, 130.1, 128.9, 128.7, 127.6, 127.44, 127.40, 127.1, 121.6, 115.6, 112.8.74.9; HRMS (ESI): Exact mass calcd for $C_{25}H_{18}Cl_2N_3OS$ $[M+H]^+$ 478.0547, found 478.0542; HPLC analysis: retention time = 17.33 min, peak area 97.0%, 80:20 CH_3CN/H_2O.

*(E)-6-(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**13**)*



Yield 59%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.99 (d, J = 3.6 Hz, 1H), 7.61 (s, 1H), 7.51 (s, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 2H), 7.24 (d, J = 8.4 Hz, 1H), 6.88 (d, J = 3.6 Hz, 1H), 5.13 (s, 2H), 1.72 (s, 4H), 1.35 (s, 6H), 1.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 151.3, 145.4, 140.7, 138.1, 132.5, 131.9, 130.5, 130.0, 127.3, 127.0, 126.6, 125.6, 121.6, 115.3, 112.5, 74.8, 35.1, 34.9, 34.4, 34.3, 31.9,31.8; HRMS (ESI): Exact mass calcd for $C_{27}H_{28}N_3OS$ $[M+H]^+$ 521.1330, found 512.1341; HPLC analysis: retention time = 52.94 min, peak area 96.4%, 80:20 CH_3CN/H_2O.

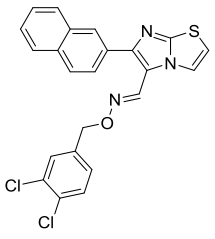
*(E)-6-(3-Chlorophenyl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**14**)*



DL5065

Yield 99%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.00 (d, J = 4.0 Hz, 1H), 7.68 (s, 1H), 7.52 (s, 2H), 7.46 (d, J = 8.8 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.25 (d, J = 8.4 Hz, 1H), 6.94 (d, J = 4.0 Hz, 1H), 5.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 148.8, 139.8, 137.7, 135.1, 134.8, 132.6, 132.1, 130.5, 130.1, 130.0, 128.5, 128.3, 127.4, 126.4, 121.6, 115.9, 113.2, 75.0; HRMS (ESI): Exact mass calcd for $C_{19}H_{13}Cl_3N_3OS$ $[M+H]^+$ 435.9874, found 435.9850; HPLC analysis: retention time = 12.90 min, peak area 97.2%, 80:20 CH_3CN/H_2O.

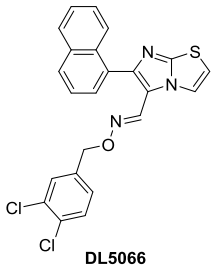
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**15**)*



DL5044

Yield 24%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (s, 1H), 8.11 (s, 1H), 8.03 (d, J = 4.4 Hz, 1H), 7.94-7.81 (m, 4H), 7.53-7.44 (m, 4H), 7.25 (d, J = 6.8 Hz, 1H), 6.93 (d, J = 4.4 Hz, 1H), 5.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 150.6, 140.4, 137.8, 133.3, 133.1, 132.0, 130.8, 130.5, 130.1, 128.5, 128.3, 127.7, 127.5, 127.4, 126.5, 126.0, 121.6, 115.8, 112.8, 74.9; HRMS (ESI): Exact mass calcd for $C_{23}H_{16}Cl_2N_3OS$ $[M+H]^+$ 452.0391, found 425.0397; HPLC analysis: retention time = 13.55 min, peak area 96.2%, 80:20 CH_3CN/H_2O.

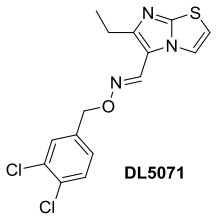
*(E)-6-(Naphthalen-1-yl)imidazo[2,1-b]thiazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**16**)*



DL5066

Yield 79%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (t, J = 5.6 Hz, 1H), 8.11 (s, 1H), 8.05 (d, J = 4.0 Hz, 1H), 7.94-7.91 (m, 2H), 7.90-7.41 (m, 6H), 7.19 (d, J = 7.6 Hz, 1H), 6.96 (d, J = 4.0 Hz, 1H), 5.08 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.4, 150.0, 140.2, 137.9, 133.9, 132.5, 132.1, 131.9, 130.5, 130.2, 130.0, 129.3, 128.8, 128.2, 127.3, 126.7, 126.13, 126.10, 125.0, 121.4, 112.9, 74.8; HRMS (ESI): Exact mass calcd for $C_{23}H_{16}Cl_2N_3OS$ $[M+H]^+$ 452.0391, found 452.0399; HPLC analysis: retention time = 9.87 min, peak area 95.7%, 80:20 CH_3CN/H_2O.

*(E)-N-(3,4-Dichlorophenethyl)-1-(6-ethylimidazo[2,1-b]thiazol-5-yl)methanimine (**17**)*



DL5071

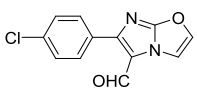
Yield 75%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.88 (d, J = 4.8 Hz, 1H), 7.51 (s, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.24 (d, J = 7.6 Hz, 1H), 6.83 (d, J = 3.6 Hz, 1H), 5.10 (s, 2H), 2.72 (q, J = 7.2 Hz, 2H), 1.31 (d, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1, 152.1, 138.9, 138.0, 132.5, 131.9, 130.4, 130.1, 127.5, 127.4, 121.2, 115.0, 112.0, 74.7, 21.3, 14.4; HRMS (ESI): Exact mass calcd for $C_{15}H_{14}Cl_2N_3OS$ $[M+H]^+$ 354.0234, found 354.0219; HPLC analysis: retention time = 4.85 min, peak area 98.9%, 80:20 CH_3CN/H_2O.

3. General Procedure for the Synthesis of Compounds **18-29**

A solution of oxazol-2-amine (5 mmol, 1 equiv) and bromomethyl ketone **30** (5 mmol, 1 equiv) in THF (20 mL) and CH_3CN (30 mL) was stirred at room temperature for 24 h. The precipitation from the reaction mixture was collected by filtration and then washed using CH_3CN. To a mixture of the resulting solid in toluene (50 mL) at 0 ^oC was added titanium (IV) chloride (0.94 g, 5 mmol) as a solution in toluene (5 mL) over 30 min. The reaction mixture was heated at 100 ^oC for an additional 3 h, and cooled. The solvent was removed by rotary evaporation, and ice was added to the residue. The pH value of the resulting mixture was adjusted to 9 using Na_2CO_3, and the resulting solution was extracted using EtOAc (30 mL × 3). The organic layers were combined, and dried over Na_2SO_4. The concentrated crude product was dried overnight under vacuum to get the imidazooxazole **35** that was used without further purification. [3]

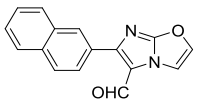
The Vilsmeier reagent was prepared by dropping of $POCl_3$ (16.5 mmol, 3.3 equiv) into a solution of DMF (5 mmol, 1.0 equiv) in $CHCl_3$ (5 mL) at 0 °C. To the resulting mixture at 0-5 °C was added a solution of imidazothiazole **35** (5 mmol) in $CHCl_3$ (30 mL) dropwise. The reaction was warmed to the room temperature over 1 h, and then heated under reflux for an additional 5 h. The solvent was removed under reduced pressure and the resulting residue was poured onto ice. The crude aldehyde **36** was collected by filtration and further purified using flash chromatography.

*6-(4-Chlorophenyl)imidazo[2,1-b]oxazole-5-carbaldehyde (**36a**)*



^1H NMR (400 MHz, $CDCl_3$): δ 9.85 (s, 1H), 7.97 (s, 1H), 7.74 (d, J = 8.8 Hz, 2H), 7.57 (s, 1H), 7.47 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.9, 154.7, 139.2 (2C), 136.0, 131.0, 130.1 (2C), 129.2 (2C), 120.4, 113.9.

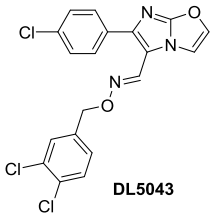
*6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde (**36b**)*



^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 8.28 (s, 1H), 8.00-7.89 (m, 5H), 7.58-7.55 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.5, 156.2, 139.2, 139.0, 133.8, 133.2, 129.9, 128.8, 128.6, 127.8, 127.2, 126.8, 125.9, 121.2, 114.0, 113.9.

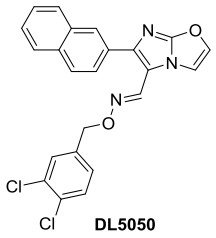
To a solution of aldehyde **36** (1 mmol) in EtOH (5ml) was added hydroxylamine **33** (1 mmol) followed by AcOH (5 mmol 5 equiv). The reaction mixture was heated under reflux over light. After cooled to room temperature, a saturated aqueous solution of $NaHCO_3$ (30 mL) was added. The aqueous layer was extracted with EtOAc (30 mL × 3) and the combined organics were washed with brine (45 mL), dried (Na_2SO_4). The crude product was then purified by flash column chromatography to give the desired product.

(E)-6-(4-Chlorophenyl)imidazo[2,1-b]oxazole-5-carbaldehyde
*O-(3,4-dichlorobenzyl) oxime (**18**)*



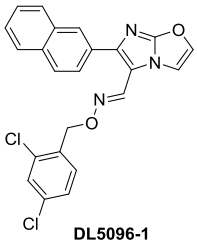
Yield 24%,^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 1H), 7.57 (d, J = 8.4 Hz, 3H), 7.50 (s, 1H), 7.46-7.39 (m, 4H), 7.23 (d, J = 8.8 Hz, 1H), 5.11 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 146.0, 139.9, 137.9, 137.7, 134.3, 132.6, 132.0, 130.5, 130.2, 130.1, 129.3, 129.0, 127.4, 113.8, 111.7, 74.9; HRMS (ESI): Exact mass calcd for $C_{19}H_{13}Cl_3N_3O_2$ $[M+H]^+$ 420.0073.0678, found 420.0069; HPLC analysis: retention time = 9.35 min, peak area 96.8%, 80:20 CH_3CN/H_2O.

*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(3,4-dichlorobenzyl) oxime (**19**)*



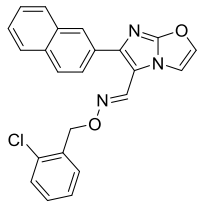
Yield 23%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.10 (s, 1H), 7.92-7.79 (m, 4H), 7.62 (s, 1H), 7.52-7.45 (m, 5H), 7.25 (d, J = 9.2 Hz, 1H), 5.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 147.3, 140.4, 137.9, 133.3, 133.1, 132.6, 132.0, 131.0, 130.5, 130.1, 128.5, 128.3, 127.7, 127.4 (2C), 127.2, 126.5 (2C), 125.8, 113.9, 111.9, 74.9; RMS (ESI): Exact mass calcd for $C_{23}H_{16}Cl_2N_3O_2$ $[M+H]^+$ 436.0619, found 436.0620; HPLC analysis: retention time = 10.04 min, peak area 95.4%, 80:20 CH_3CN/H_2O.

*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(2,4-dichlorobenzyl) oxime (**20**)*



Yield 46%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 8.10 (s, 1H), 7.91-7.79 (m, 4H), 7.65 (s, 1H), 7.53-7.48 (m, 2H), 4.43-7.41 (m, 3H), 7.27 (d, J = 8.8 Hz, 1H), 5.26 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 147.1, 140.4, 137.8, 134.3, 134.05, 133.97, 133.3, 133.0, 131.0, 130.8, 129.3, 128.5, 128.3, 127.7, 127.2, 127.16, 126.5, 126.4, 125.8, 114.0, 111.9, 72.8; HRMS (ESI): Exact mass calcd for $C_{23}H_{16}Cl_2N_3O_2$ $[M+H]^+$ 436.0619, found 436.624; HPLC analysis: retention time = 11.71 min, peak area 96.6%, 80:20 CH_3CN/H_2O.

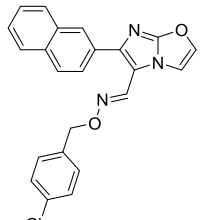
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(2-chlorobenzyl) oxime (**21**)*



DL5098-2

Yield 41%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (s, 1H), 8.11 (s, 1H), 7.91-7.80 (m, 4H), 7.68 (d, *J* = 1.6 Hz, 1H), 7.53-7.49 (m, 3H), 7.41 (d, *J* = 1.6 Hz, 2H), 7.31-7.27 (m, 2H), 5.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 146.9, 140.1, 137.8, 135.3, 133.5, 133.3, 133.0, 131.1, 130.2, 129.5, 129.3, 128.5, 128.3, 127.7, 127.2, 126.8, 126.44, 126.38, 125.8, 114.0, 112.1, 73.5; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}ClN_3O_2$ $[M+H]^+$ 402.1009, found 402.1015; HPLC analysis: retention time = 6.20 min, peak area 95.7%, 80:20 CH_3CN/H_2O.

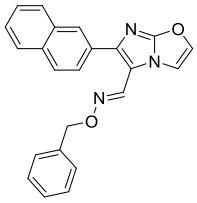
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(4-chlorobenzyl) oxime (**22**)*



DL5096-3

Yield 44%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.10 (s, 1H), 7.91-7.79 (m, 4H), 7.61 (s, 1H), 7.51-7.47 (m, 2H), 7.42 (s, 1H), 7.36 (s, 5H), 5.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 146.9, 140.1, 137.8, 136.0, 133.9, 133.3, 133.0, 131.0, 129.7, 128.7, 128.5, 128.3, 127.7, 127.2, 126.5, 126.4, 125.8, 113.9, 112.0, 75.7; HRMS (ESI): Exact mass calcd for $C_{25}H_{20}N_3O_2$ $[M+H]^+$ 402.1009, found 402.1000; HPLC analysis: retention time = 6.42 min, peak area 97.7%, 80:20 CH_3CN/H_2O.

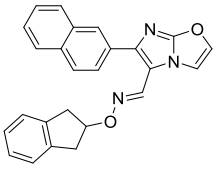
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-benzyl oxime (**23**)*



DL5098-3

Yield 71%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 8.10 (s, 1H), 7.91-7.79 (m, 4H), 7.67 (s, 1H), 7.53-7.33 (m, 8H), 5.21 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 146.7, 139.8, 137.7, 137.3, 133.3, 133.0, 131.1, 128.5, 128.4, 128.3, 128.1, 127.7, 127.1, 126.41, 126.37, 125.8, 114.0, 112.2, 76.6; HRMS (ESI): Exact mass calcd for $C_{23}H_{18}N_3O_2$ $[M+H]^+$ 368.1399, found 368.1397; HPLC analysis: retention time = 5.41 min, peak area 95.4%, 80:20 CH_3CN/H_2O.

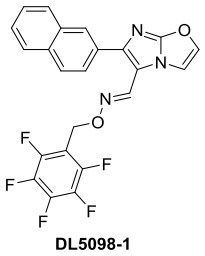
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(2,3-dihydro-1H-inden-2-yl) oxime (**24**)*



DL5090

Yield 64%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 8.08 (s, 1H), 7.87-7.77 (m, 4H), 4.9 (t, J = 4.8 Hz, 2H), 7.39 (d, J = 1.6 Hz, 2H), 7.28-7.20 (m, 4H), 5.16 (s, 1H), 3.37-3.23 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 146.3, 141.2, 139.7, 137.6, 133.3, 133.0, 1331.1, 128.4, 128.3, 127.7, 127.1, 126.6, 126.4, 126.3, 125.8, 124.6, 114.0, 83.4, 39.2; HRMS (ESI): Exact mass calcd for $C_{25}H_{20}N_3O_2$ $[M+H]^+$ 394.1555, found 394.1563; HPLC analysis: retention time = 6.67 min, peak area 96.3%, 80:20 CH_3CN/H_2O.

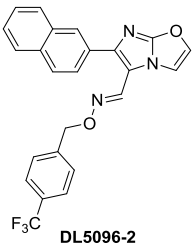
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-((perfluorophenyl)methyl) oxime (**25**)*



DL5098-1

Yield 35%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 8.06 (s, 1H), 7.99-7.83 (m, 3H), 7.76 (d, J = 7.6 Hz, 1H), 7.71 (s, 1H), 7.51-7.49 (m, 3H), 5.25 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 147.6, 147.0, 144.5, 142.8, 140.9, 138.7, 138.0, 133.3, 133.1, 130.8, 128.5, 128.3, 127.7, 127.2, 126.5, 125.7, 113.8, 111.6, 62.6; HRMS (ESI): Exact mass calcd for $C_{23}H_{13}F_5N_3O_2$ $[M+H]^+$ 458.0928, found 458.0935; HPLC analysis: retention time = 7.63 min, peak area 95.2%, 80:20 CH_3CN/H_2O.

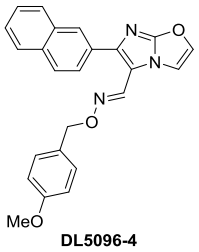
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(4-(trifluoromethyl)benzyl) oxime (**26**)*



DL5096-2

Yield 33%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.10 (s, 1H), 7.92-7.80 (m, 4H), 7.65 (d, J = 8.0 Hz, 2H), 7.60 (s, 1H), 7.54-7.50 (m, 4H), 7.43 (s, 1H), 5.25 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 147.2, 141.6, 140.3, 137.8, 133.3, 133.0, 131.0, 130.1 (J = 32.7 Hz),128.5, 128.3, 128.2, 127.7, 127.2, 126.5, 125.8, 125.5, 125.4, 124.1 (J = 270.8 Hz), 113.9, 111.9, 75.5; HRMS (ESI): Exact mass calcd for $C_{24}H_{17}F_3N_3O_2$ $[M+H]^+$ 436.1273, found 436.1264; HPLC analysis: retention time = 7.23 min, peak area 96.5%, 80:20 CH_3CN/H_2O.

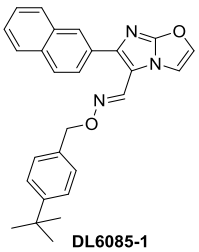
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(4-methoxybenzyl) oxime (**27**)*



DL5096-4

Yield 33%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.10 (s, 1H), 7.90-7.80 (m, 4H), 7.70 (s, 1H), 7.52-7.37 (m, 5H), 6.93 (d, J = 8.4 Hz, 2H), 5.14 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 156.2, 146.6, 139.7, 137.7, 133.3, 133.0, 131.1, 130.2, 129.3, 128.4, 128.3, 127.7, 127.1, 126.4, 126.3, 125.8, 114.0, 113.9, 112.3, 76.4, 55.3; HRMS (ESI): Exact mass calcd for $C_{24}H_{20}N_3O_3$ $[M+H]^+$ 398.1504, found 398.1514; HPLC analysis: retention time = 4.36 min, peak area 95.1%, 80:20 CH_3CN/H_2O.

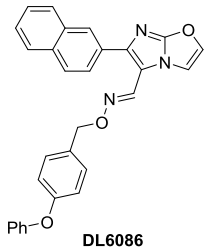
*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(4-(tert-butyl)benzyl) oxime (**28**)*



DL6085-1

Yield 31%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 8.10 (s, 1H), 7.90-7.80 (m, 4H), 7.70 (s, 1H), 7.51-7.38 (m, 7H), 5.19 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 151.2, 146.6, 139.7, 137.7, 134.2, 133.3, 133.0, 131.1, 128.4, 128.3, 127.7, 127.1, 126.41, 126.36, 125.8, 125.5, 114.0, 112.3, 75.5, 34.6, 31.3; HRMS (ESI): Exact mass calcd for $C_{27}H_{26}N_3O_2$ $[M+H]^+$ 424.2025, found 424.2018; HPLC analysis: retention time = 13.39 min, peak area 98.3%, 80:20 CH_3CN/H_2O.

*(E)-6-(Naphthalen-2-yl)imidazo[2,1-b]oxazole-5-carbaldehyde O-(4-phenoxybenzyl) oxime (**29**)*



DL6086

Yield 38%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 8.11 (s, 1H), 7.91-7.81 (m, 4H), 7.70 (s, 1H), 7.51 (t, *J* = 4.0 Hz, 2H), 7.43 (t, *J* = 4.4 Hz, 3H), 7.35 (t, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 8.0 Hz, 1H), 7.04 (t, *J* = 8.8 Hz, 4H), 5.18 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.3, 156.9, 156.2, 146.7, 139.9, 137.8, 133.3, 133.0, 132.0, 131.1, 130.3, 129.8, 128.5, 128.3, 127.7, 127.1, 126.5, 126.4, 125.8, 123.5, 119.1, 118.7, 114.0, 112.2, 76.2; HRMS (ESI): Exact mass calcd for $C_{29}H_{22}N_3O_3$ $[M+H]^+$ 460.1661, found 460.1659; HPLC analysis: retention time = 8.30 min, peak area 96.3%, 80:20 CH_3CN/H_2O.

4. CAR Agonist Luciferase Reporter Gene Assay

HepG2-CYP2B6-hCAR[4] cells were cultured in DMEM (Invitrogen, Carlsbad, CA) supplemented with 5 µg/mL blasticidin (Invitrogen), 0.5 mg/mL geneticin (Invitrogen), 10% Hyclone™ FBS (GE Healthcare Life Sciences, Logan, UT), and 100 U/mL penicillin and 100 µg/mL streptomycin (Invitrogen). For the assay, the HepG2-CYP2B6-hCAR cells were dispensed at 2,500 cells/4 µL/well in tissue culture–treated 1536-well white assay plates (Greiner Bio-One North America, Monroe, NC) using a Thermo Scientific Multidrop Combi (Thermo Fisher Scientific Inc., Waltham, MA). The media used for plating was DMEM supplemented with 10% Hyclone™ FBS and 100 U/mL penicillin and 100 µg/mL streptomycin. After the assay plates were incubated at 37ºC/5% CO_2 for 5 h, 23 nL of compounds dissolved in dimethyl sulfoxide (DMSO), CITCO (Sigma-Aldrich Corp., St. Louis, MO), or

DMSO were transferred to the assay plates by a Wako Pintool station (Wako Automation, San Diego, CA). One µL of PK11195 (Sigma-Aldrich Corp.) was added (final concentration of 0.75 µM PK11195) using a Flying Reagent Dispenser (FRD, Aurora Discovery, Carlsbad, CA). The final test compound concentrations in the 5 µL assay volume ranged from 6.41 pM to 92 µM in 16 different concentrations at a 1:3 dilution. The final concentration of DMSO (used for the negative control) was 0.46%. The plate format of the positive control is as follows: Column 1: concentration-response titration of CITCO from 2.81 nM to 92 µM at a 1:2 dilution with DMSO; Column 2 top half: 60 µM of CITCO; Column 2 bottom half: 48 µM of CITCO; Column 3 top half and Column 4: DMSO only; Column 3 bottom half: 92 µM of tetraoctyl ammonium bromide. After 23 h of incubation at 37 ºC/5% CO_2, One µL of CellTiter-Fluor™ (Promega, Madison, WI) was added, using the FRD, after which, all plates were put back into the incubator at 37 °C/5% CO_2 for another hour. The fluorescence intensity was then measured at 540 nm following excitation at 405 nm using a ViewLux plate reader (Perkin Elmer, Shelton, CT) to determine cell viability. Immediately after, 4 µL of ONE-Glo™ Luciferase reagent (Promega) was added to each well using the FRD and a 30 min incubation at room temperature occurred. Luminescence intensity was then measured using the ViewLux plate reader and data was expressed in relative luminescence units.

5. Cell Viability Assay[4]

The potential cytotoxicity of the compounds in HepG2-CYP2B6-hCAR cells was measured using a luciferase-coupled ATP quantitation assay (CellTiter-Glo viability assay, Promega). The change of intracellular ATP content indicates the number of metabolically competent cells. The cells were seeded at 2,500 cells/5 µL in 1536-well plates and were exposed to each test compound at concentrations and treatment duration as previously mentioned. The assay plates were incubated for 24 h at 37 ºC, followed by the addition of 4 µ/well of CellTiter-Glo reagent. After 30 min incubation at RT, the luminescence intensity of the plates was measured using a ViewLux plate

reader.

6. Experimental protocol for hPXR agonist HTS

HepG2-CYP3A4-hPXR cells were cultured in EMEM medium (ATCC, Manassas, VA) supplemented with 10% FBS (ThermoFisher Scientific, Waltham, MA), 100 U/mL of penicillin and 100 mg/mL of streptomycin (ThermoFisher Scientific), and 500 µg/mL geneticin (ThermoFisher Scientific) in collagen coated flasks (Corning Inc., Corning, NY). Cells were dispensed at 3,000 cells/well/5 µL in 1,536-well plates (Greiner Bio-One North America, Monroe, NC) using a Multidrop Combi (Thermo Fisher Scientific) in assay media which entailed phenol red free DMEM (ThermoFisher Scientific) supplemented with 5% charcoal/dextran treated FBS (Invitrogen, Carlsbad, CA), 1 mM sodium pyruvate (Invitrogen), 2 mM L-Glutamine (Invitrogen), and 100 U/mL of penicillin and 100 mg/mL of streptomycin (ThermoFisher Scientific). The assay plates were incubated at 37 °C/5% CO_2 for 5 hrs before 23 nL of each compound was transferred from the compound plate to the assay plate via a pin tool station (Kalypsys, San Diego, CA). After 23 hrs of incubation at 37°C/5% CO_2, 1 µL of CellTiter Fluor (Promega, Madison, WI) is added to each well for determination of cell viability. Plates were placed back in the incubator at 37 °C/5% CO_2 for another hour. Fluorescence intensity was then measured at 540 nm emission following excitation at 405 nm using a ViewLux plate reader (Perkin Elmer, Shelton, CT). Four µl of the ONE-Glo luciferase reagent (Promega) was then added followed by a 30 min incubation at room temperature. Finally, luminescence intensity was quantified using the ViewLux plate reader and data was expressed in relative luminescence units.

7. Culture and Treatment of HPH

Human primary Hepatocytes obtained from BioIVT (Baltimore, MD) were seeded at 0.75×10^6 cells/well in 12-well biocoat plate and cultured in sandwich format as

described previously[5] for 36 h before treatment with solvent (0.1% DMSO), PB (1 mM), RIF (10 µM), CITCO, compounds **18** and **19** (0.5, 1, 5 µM) for 24 h and 72 h before harvesting cells to detect RNA and protein, respectively.

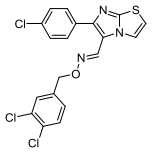
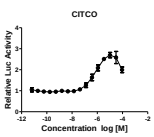
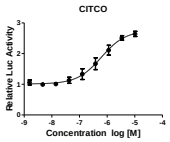
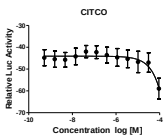
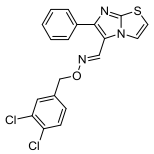
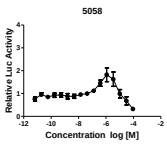
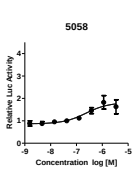
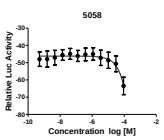
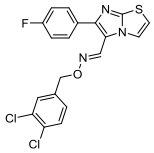
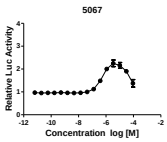
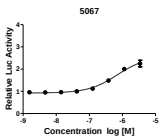
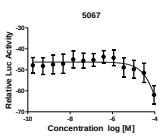
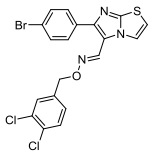
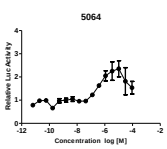
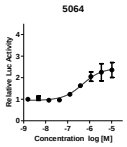
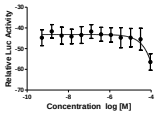
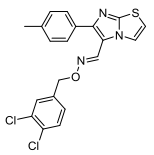
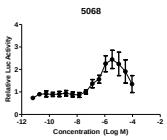
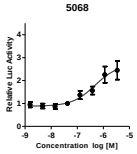
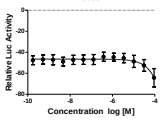
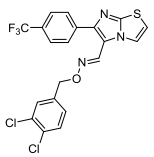
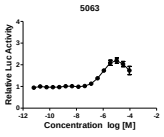
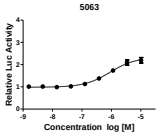
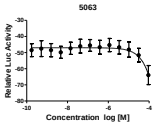
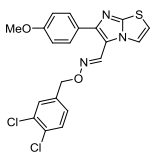
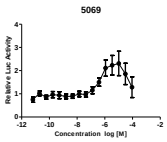
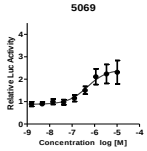
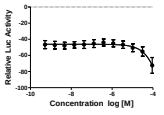
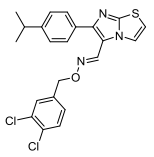
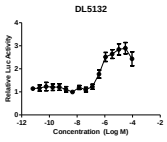
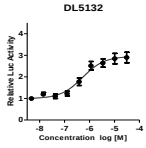
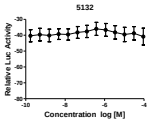
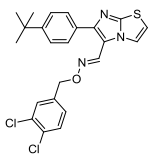
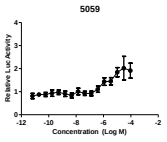
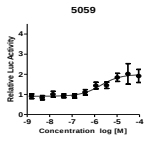
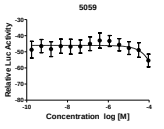
8. Real-Time PCR Analysis

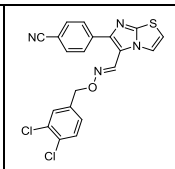
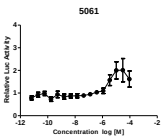
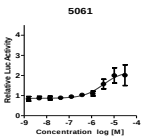
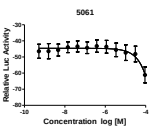
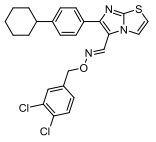
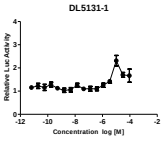
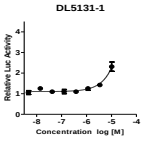
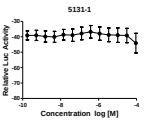
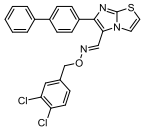
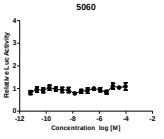
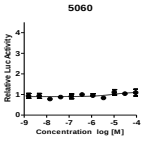
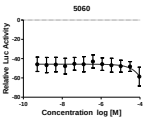
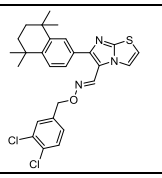
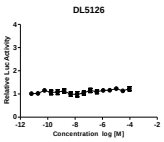
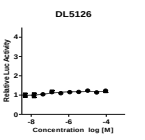
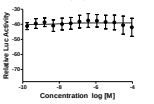
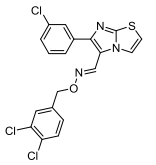
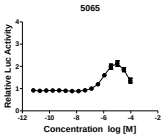
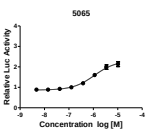
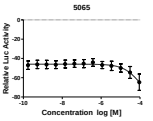
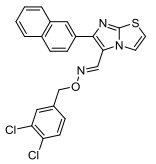
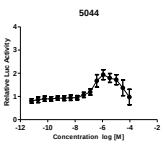
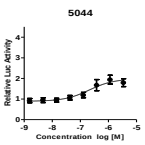
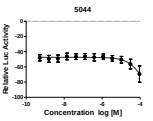
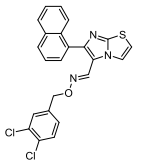
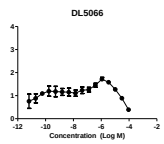
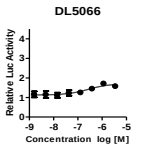
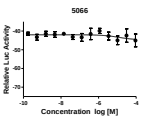
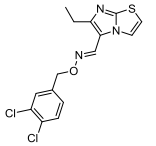
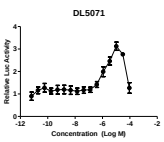
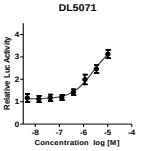
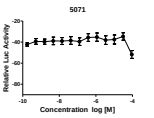
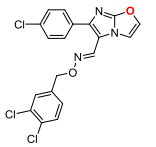
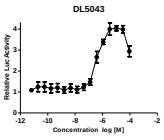
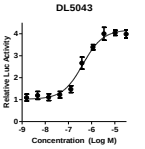
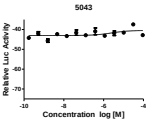
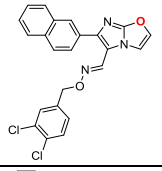
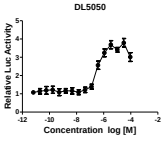
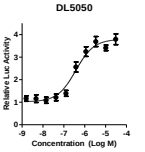
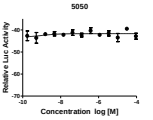
Total RNA from hepatocytes were isolated and reverse transcribed as described previously.[6] Real-Time PCR assay was performed on an ABI StepOnePlus Real-Time PCR system with SYBR Green PCR master mix from Qiagen (Germantown, MD). The primer sequences for CYP2B6, CYP3A4 and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) are as follows: CYP2B6, 5'-AGACGCCTTCAATCCTGACC-3' and 5'-CCTTCACCAAGACAAATCCGC-3'; CYP3A4, 5'-GTGGGGCTTTTATGATGGTCA-3' and 5'-GCCTCAGATTTCTCACCAACACA-3'; GAPDH, 5'-CCCATCACCATCTTCCAGGAG-3' and 5'-GTTGTCATGGATGACCTTGGC-3'. Induction values were calculated according to the previous description.[6]

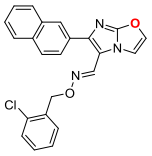
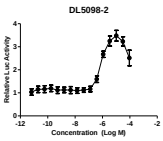
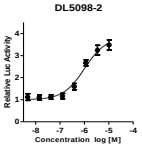
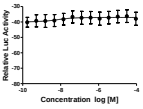
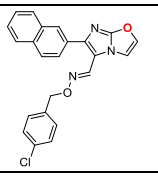
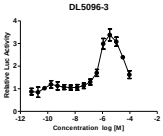
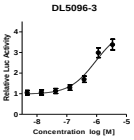
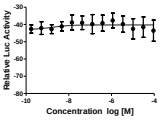
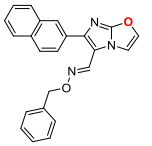
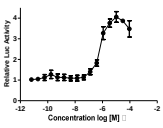
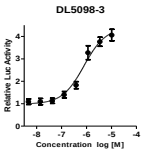
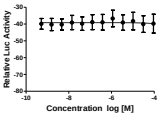
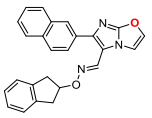
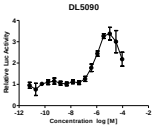
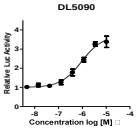
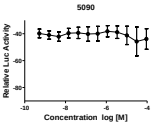
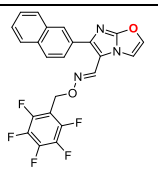
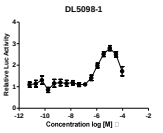
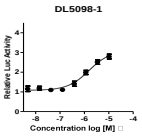
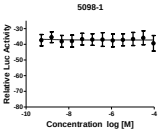
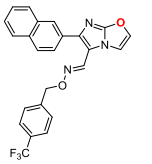
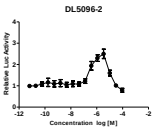
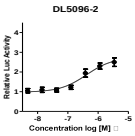
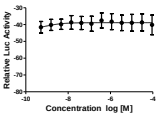
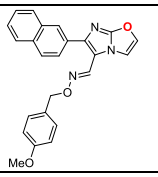
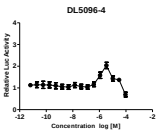
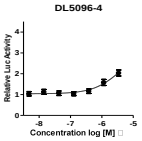
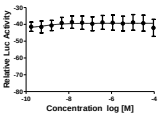
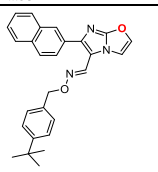
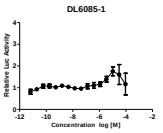
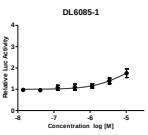
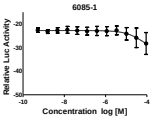
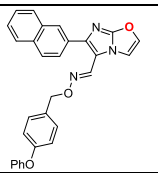
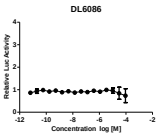
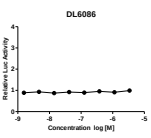
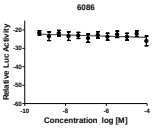
9. Western Blot Analysis

20 µg of cell homogenate proteins from hepatocytes were resolved on NuPAGE™ 4-12% Bis-Tris gels (Life Technologies) and electrophoretically transferred onto polyvinylidine fluoride membranes. Membranes were incubated with antibodies against CYP2B6 (Abcam), CYP3A4 (Millipore), or β-actin (Sigma-Aldrich), diluted at 1:500, 1:5000 and 1:5000, respectively at 4 °C overnight, followed by incubation with horseradish peroxidase secondary antibodies for 1 h at room temperature. Blots were developed with West Pico chemiluminescent substrates (ThermoFisher).

10. Table S1 Original Data of Activity and Cytotoxicity for Cpd**1-29**

Cpd	Structure	All Curve	EC_{50} Curve	EC_{50} (μM)[a]	E_{max}	Cytotoxicity Curve
1 CITCO				0.62 ± 0.11	2.8	
2				0.58 ± 0.36	2.3	
3				0.67 ± 0.10	2.6	
4				0.48 ± 0.22	2. 4	
5				0.48 ± 0.23	2.7	
6				0.88 ± 0.09	2.3	
7				0.49 ± 0.27	2.4	
8				0.59 ± 0.13	3.0	
9				2.4 ± 0.30	2.0	

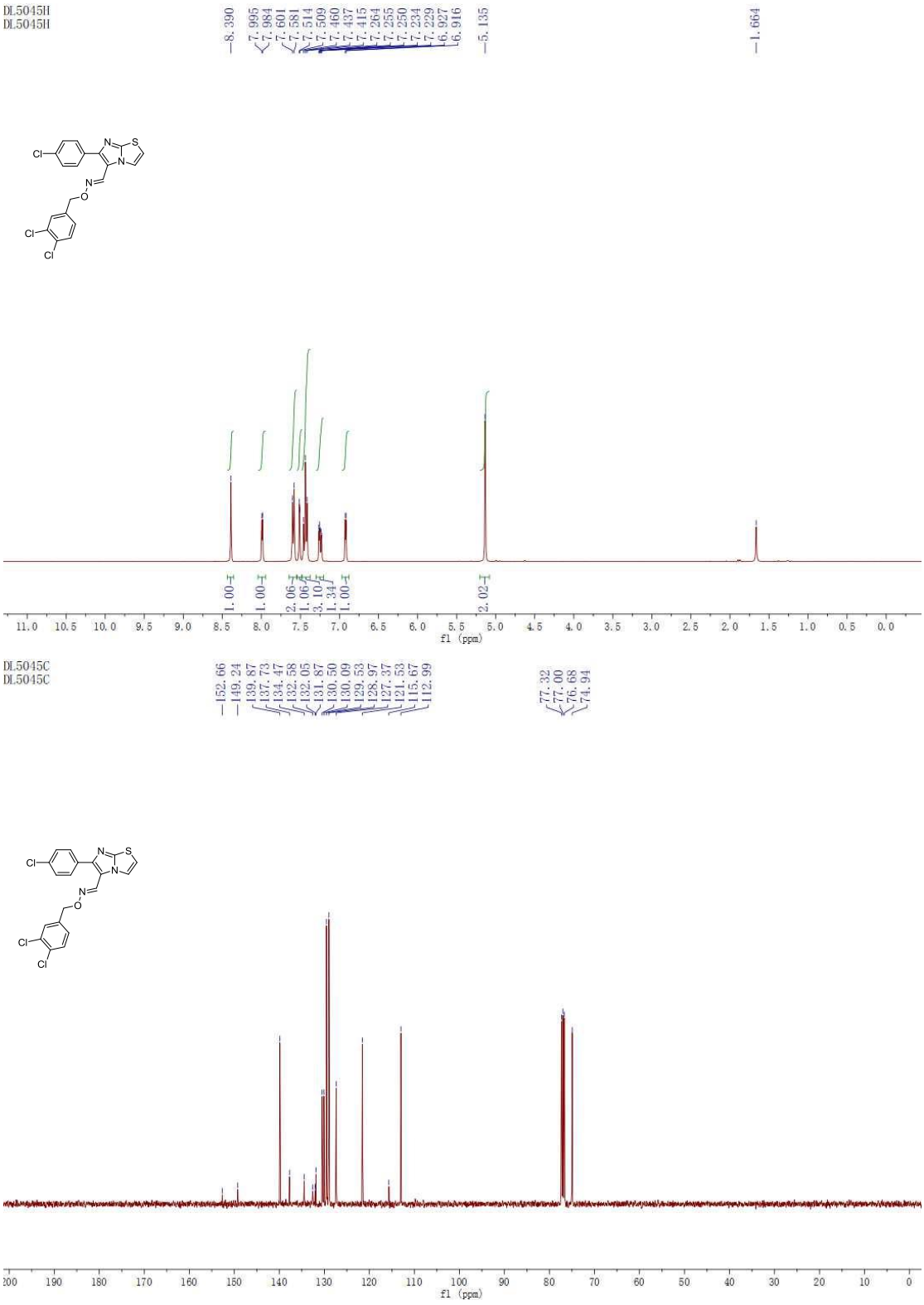
10				3.4 ± 0.29	2.2	
11				>100	2.3	
12				NC	1.1	
13				NC	1.2	
14				1.1 ± 0.08	2.3	
15				0.38 ± 0.31	2.3	
16				0.94 ± 0.73	2.2	
17				2.6 ± 0.16	3.6	
18				0.41 ± 0.09	4.2	
19				0.37 ± 0.11	3.8	
20				1.5 ± 0.12	3.5	

21				1.1 ± 0.11	3.8	
22				0.99 ± 0.15	4.2	
23				0.84 ± 0.10	4.4	
24				0.98 ± 0.11	3.7	
25				1.7 ± 0.13	3.1	
26				0.47 ± 0.18	2.8	
27				4.4 ± 0.44	3.3	
28				7.9 ± 0.48	2.3	
29				NC	1	

[a]EC_{50} and E_{max} values were calculated by nonlinear regression. Data are presented as mean ± SEM of at least three independent experiments in quadruplicate. NC (if the maximum concentration produced no effect).

11. ^{1}H, ^{13}C NMR and HPLC Spectra of Compounds **1-29**

Compound **1**

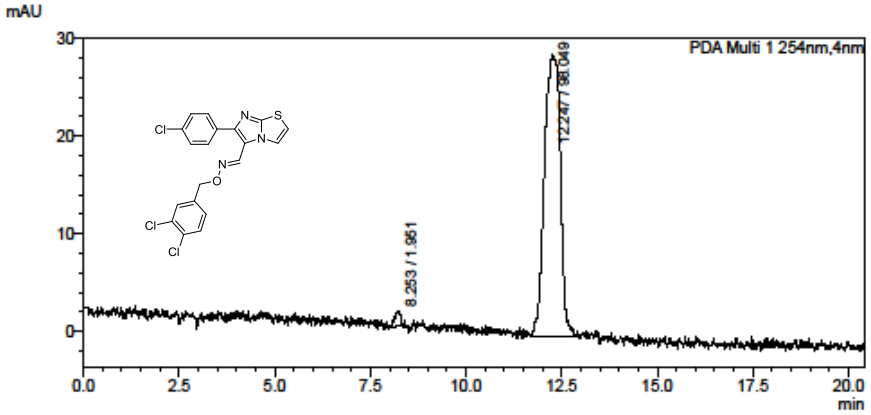


SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: 5045		
Sample ID	: 0.8/80		
Data Filename	: 7222.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/20/2018 5:22:53 PM	Acquired by	: System Administrator
Date Processed	: 7/20/2018 5:43:20 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

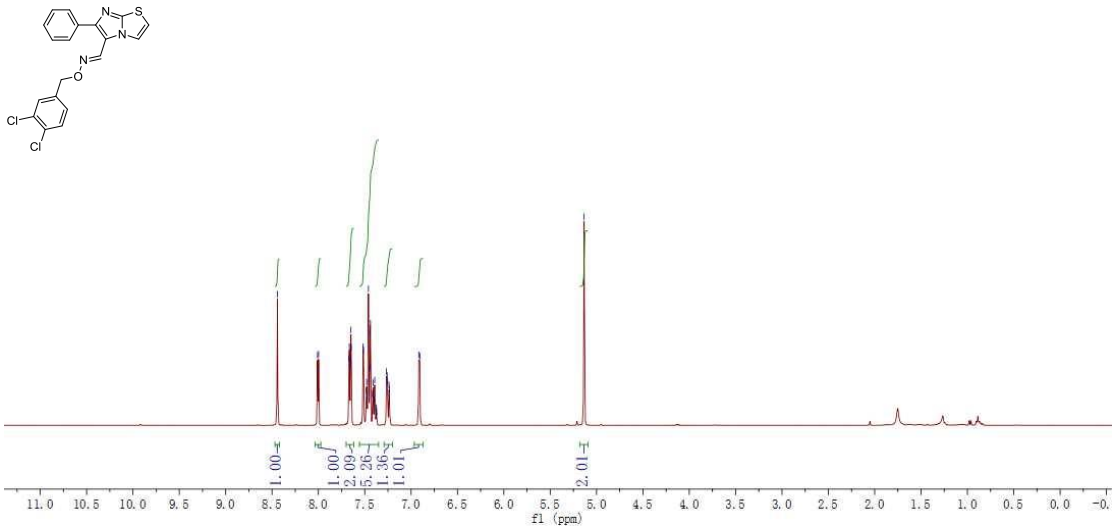
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	8.253	16465	1649	0.000		M	1.951
2	12.247	827306	28833	0.000		M	98.049
Total		843770	30483				100.000

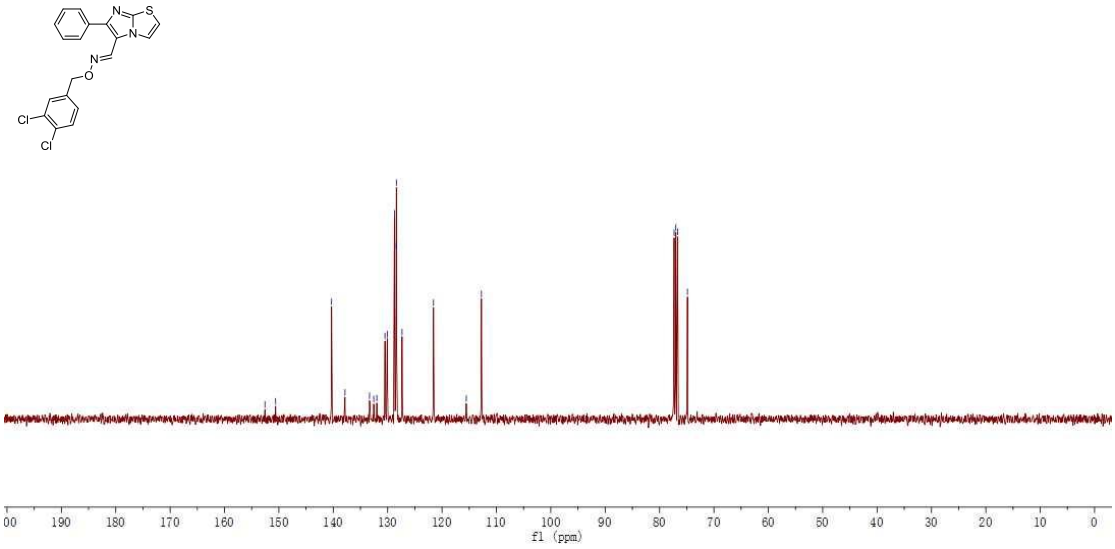
C:\Users\sop\Desktop\Xue Lab\Liang\7222.lcd

Compound **2**


DL5058H
8.442
8.009
7.998
7.671
7.666
7.653
7.649
7.646
7.518
7.513
7.482
7.479
7.475
7.460
7.446
7.442
7.439
7.415
7.411
7.408
7.398
7.393
7.378
7.374
7.371
7.266
7.259
7.254
7.238
7.233
6.917
6.906
5.134


N
S
N
O
Cl
Cl
1.00
1.00
2.09
5.26
1.36
1.01
2.01
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


DL5058C
DL5058C
152.56
150.60
140.31
137.84
133.33
132.55
131.99
130.48
130.07
128.75
128.42
128.39
127.36
121.57
115.54
112.76
77.33
77.01
76.69
74.87


N
S
N
O
Cl
Cl
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

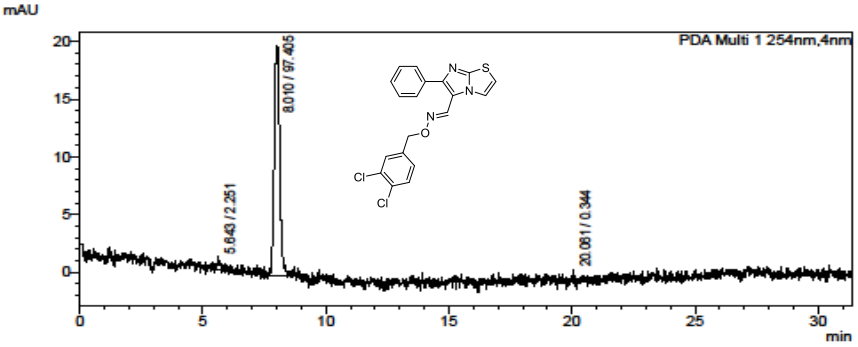
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5058		
Sample ID	: 0.8/80		
Data Filename	: 7223.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/20/2018 5:44:13 PM	Acquired by	: System Administrator
Date Processed	: 7/20/2018 6:15:37 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

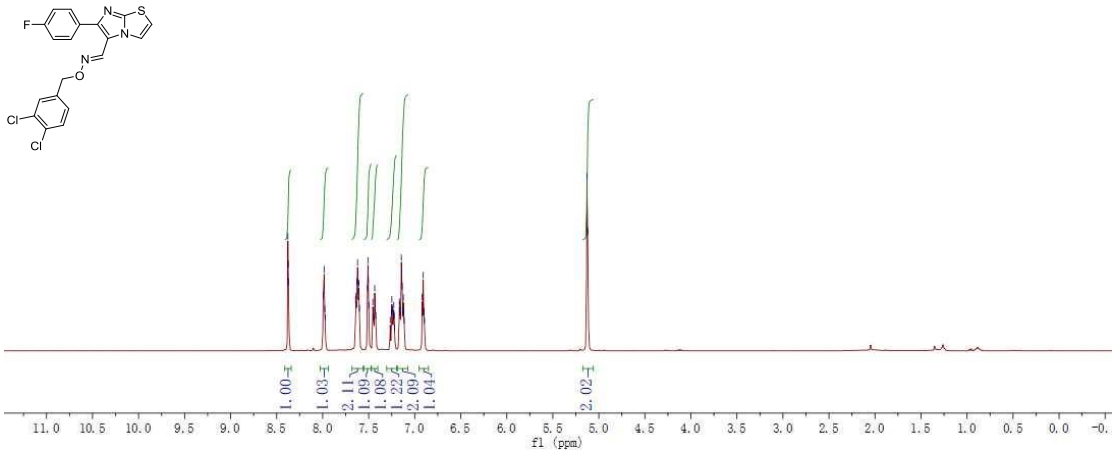
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	5.643	7035	1181	0.000		M	2.251
2	8.010	304362	19860	0.000		M	97.405
3	20.061	1074	980	0.000		M	0.344
Total		312470	22021				100.000

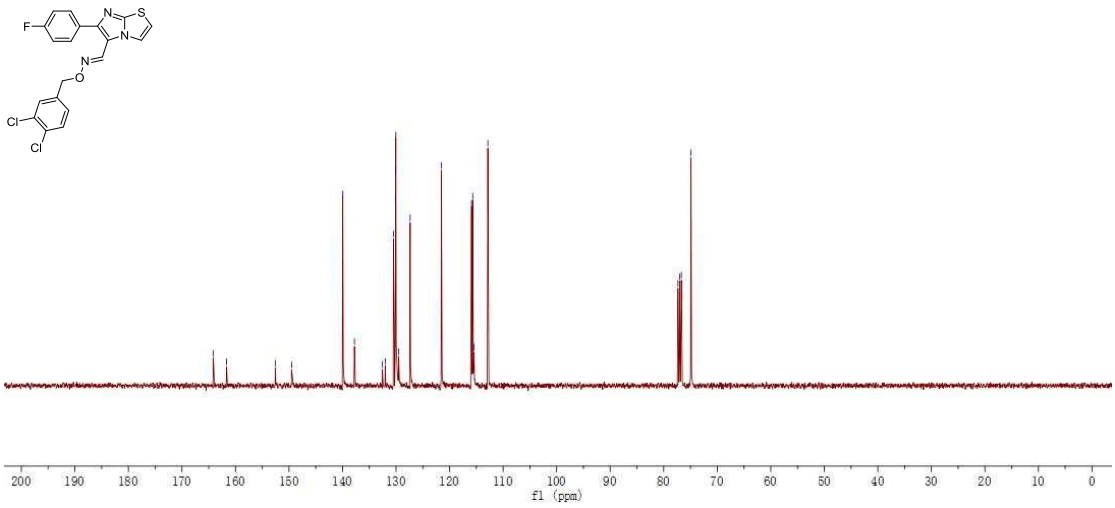
C:\Users\sop\Desktop\Xue Lab\Liang\7223.lcd

Compound **3**


DL5067H
DL5067H
8.378
8.373
8.369
7.995
7.984
7.977
7.972
7.642
7.637
7.629
7.621
7.613
7.607
7.601
7.514
7.508
7.504
7.499
7.455
7.446
7.435
7.428
7.423
7.266
7.253
7.248
7.243
7.233
7.228
7.223
7.218
7.167
7.162
7.157
7.146
7.140
7.136
7.129
7.124
7.118
7.114
6.919
6.908
6.900
6.894
5.129
5.121


F
N
S
N
O
Cl
Cl
1.00
1.03
2.11
1.09
1.08
1.22
2.09
1.04
2.02
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


DL5067C
DL5067C
164.13
161.66
152.54
149.52
139.95
137.77
132.55
132.02
130.48
130.13
130.08
130.04
129.51
127.37
121.53
115.90
115.68
115.44
112.85
77.34
77.02
76.71
74.90


F
N
S
N
O
Cl
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

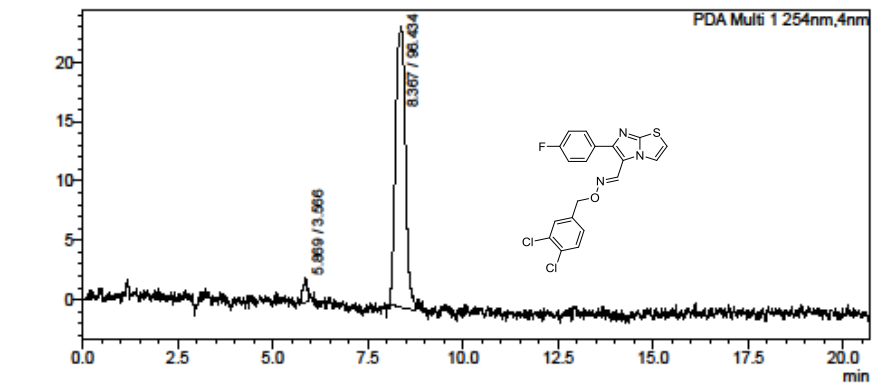
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5067		
Sample ID	: 0.8/80		
Data Filename	: 7191.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/18/2018 4:53:54 PM	Acquired by	: System Administrator
Date Processed	: 7/18/2018 5:14:39 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

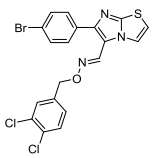
PDA Ch1 254nm

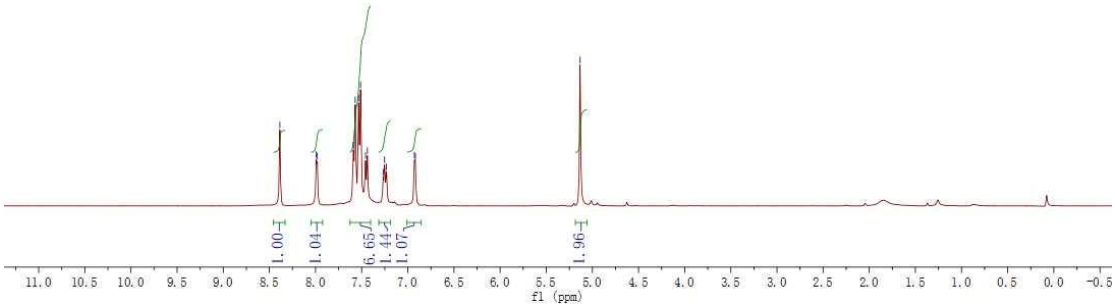
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	5.869	15680	2015	0.000		M	3.566
2	8.367	424045	23634	0.000		M	96.434
Total		439725	25648				100.000

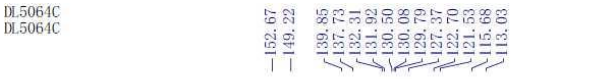
C:\Users\sop\Desktop\Xue Lab\Liang\7191.lcd

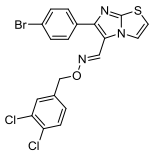
Compound **4**

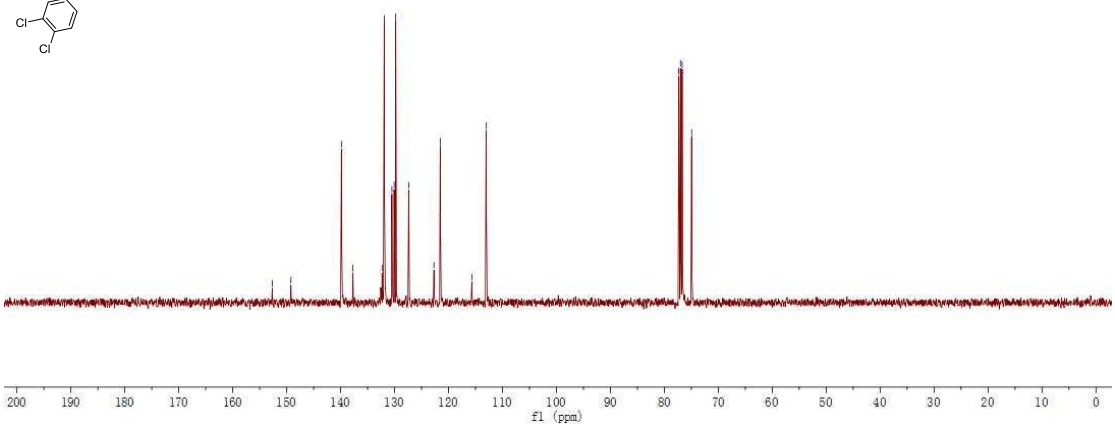

DL5064H
DL5064H
8.386
7.992
7.981
7.590
7.570
7.533
7.512
7.459
7.438
7.267
7.252
7.231
6.929
6.918
5.133


Br
N
S
N
O
Cl
Cl


1.00
1.04
6.65
1.44
1.07
1.96
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


DL5064C
DL5064C
152.67
149.22
139.85
137.73
132.31
131.92
130.50
130.08
129.79
127.37
122.70
121.53
115.68
113.03
77.33
77.01
76.70
74.94


Br
N
S
N
O
Cl
Cl

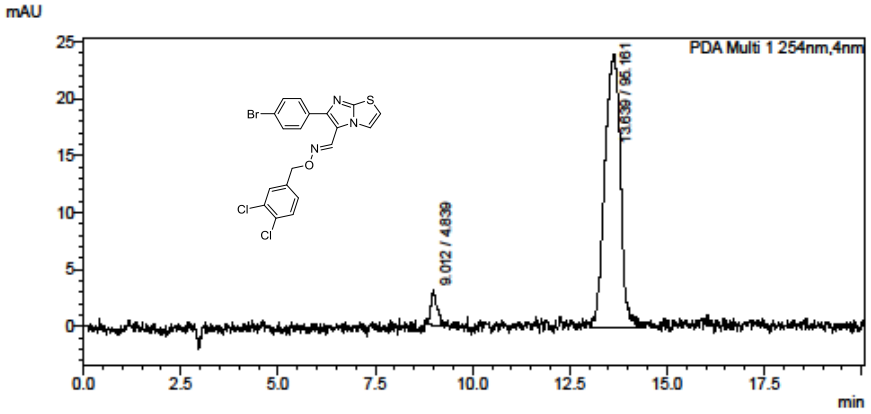

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: 5064		
Sample ID	: 0.8/80		
Data Filename	: 7232.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 4:29:10 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 4:49:17 PM	Processed by	: System Administrator

<Chromatogram>



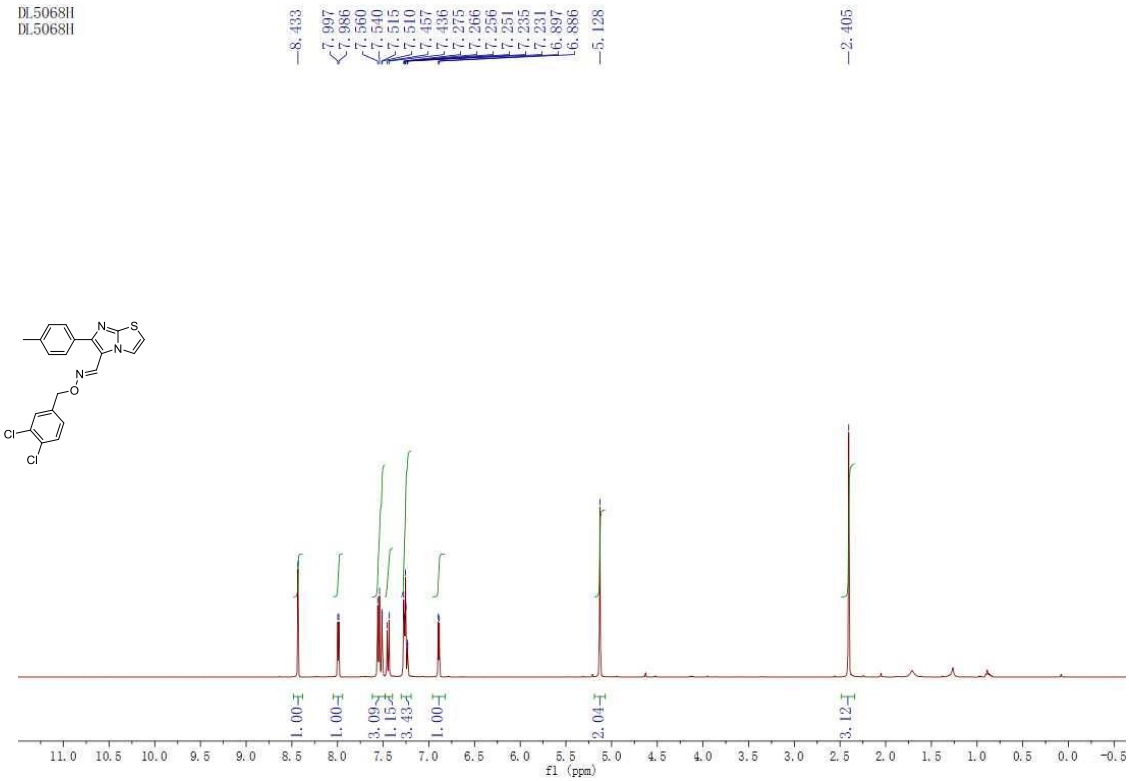
<Peak Table>

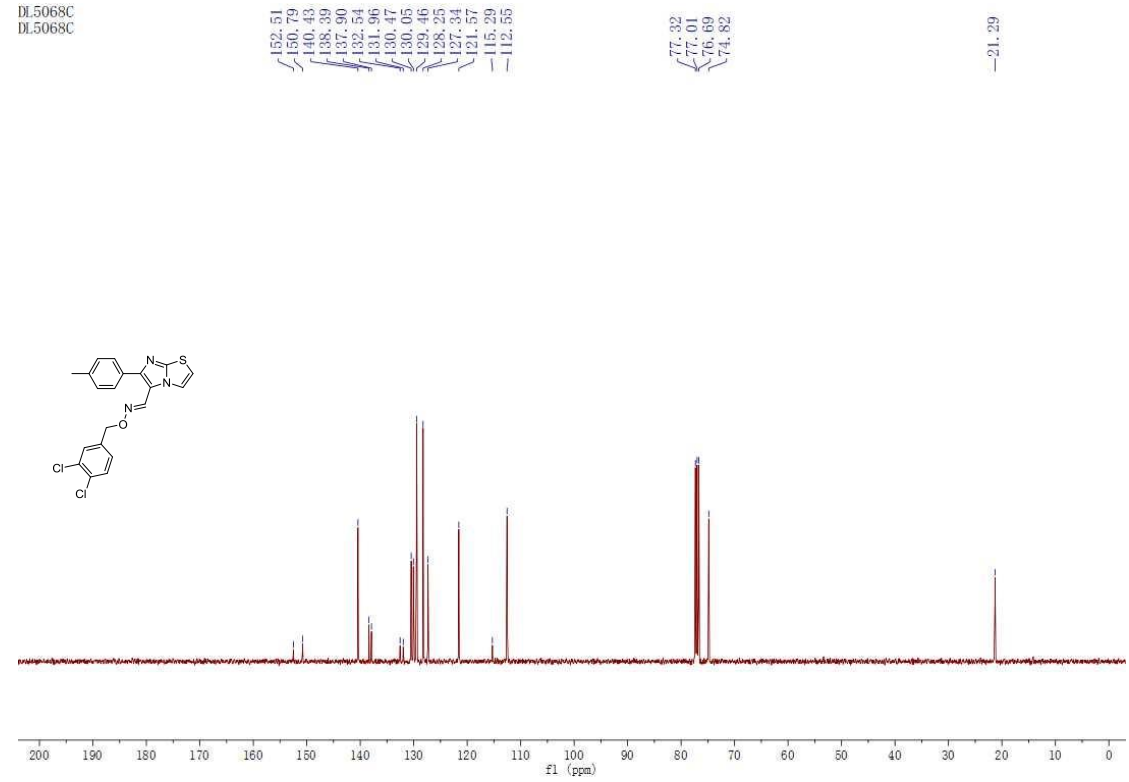
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	9.012	34300	3091	0.000		M	4.839
2	13.639	674544	23998	0.000		M	95.161
Total		708843	27089				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7232.lcd

Compound **5**


DL5068H
DL5068H
8.433
7.997
7.986
7.560
7.540
7.515
7.510
7.457
7.436
7.275
7.266
7.256
7.251
7.235
7.231
6.897
6.886
5.128
2.405
1.00
1.00
3.09
1.15
3.43
1.00
2.04
3.12
f1 (ppm)

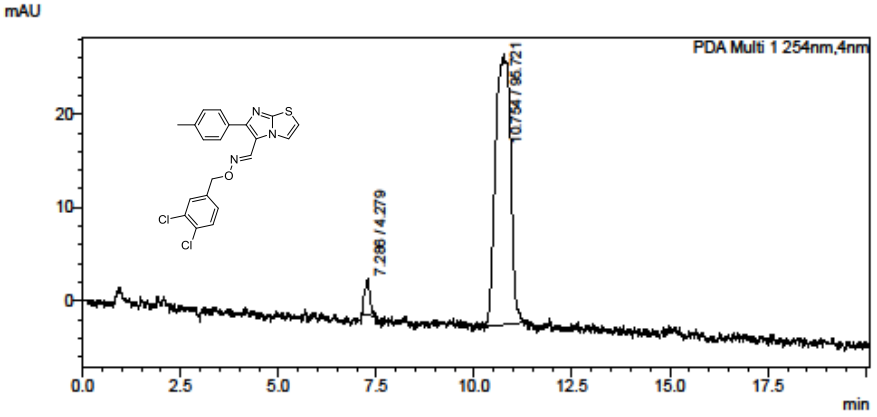

DL5068C
DL5068C
152.51
150.79
140.43
138.39
137.90
132.54
131.96
130.47
130.05
129.46
128.25
127.34
121.57
115.29
112.55
77.32
77.01
76.69
74.82
21.29
f1 (ppm)

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: 5068		
Sample ID	: 0.8/80		
Data Filename	: 7211.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/20/2018 12:20:47 PM	Acquired by	: System Administrator
Date Processed	: 7/20/2018 12:40:59 PM	Processed by	: System Administrator

<Chromatogram>

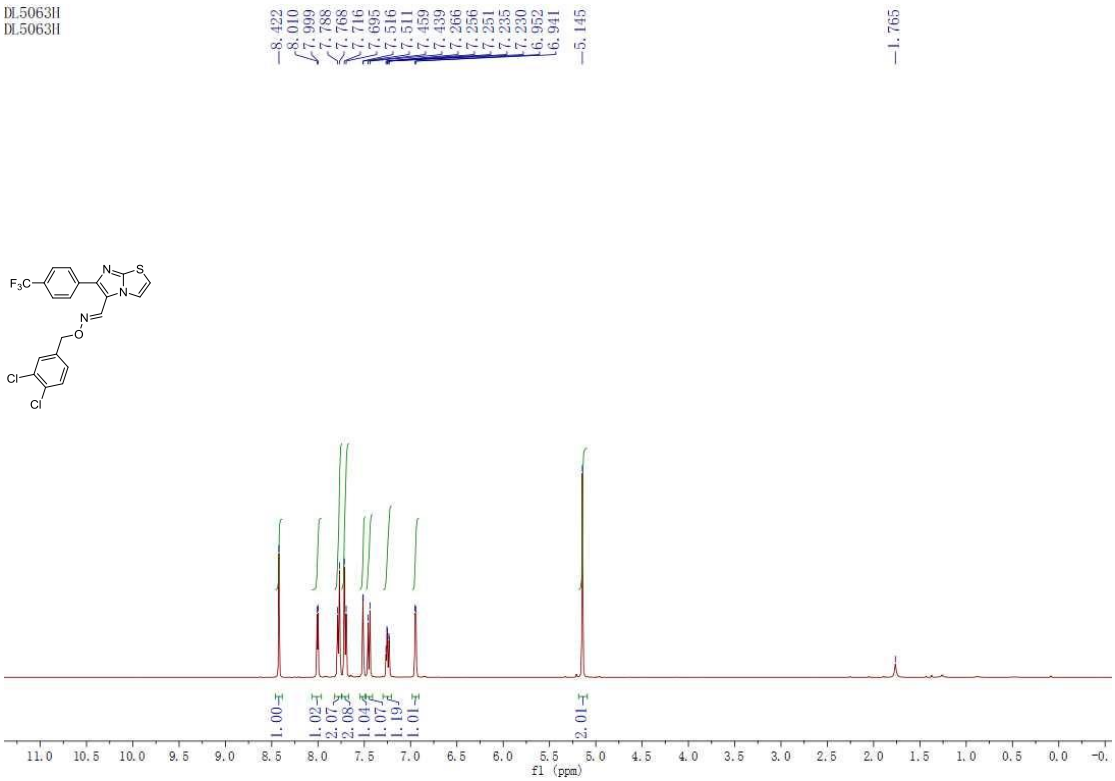


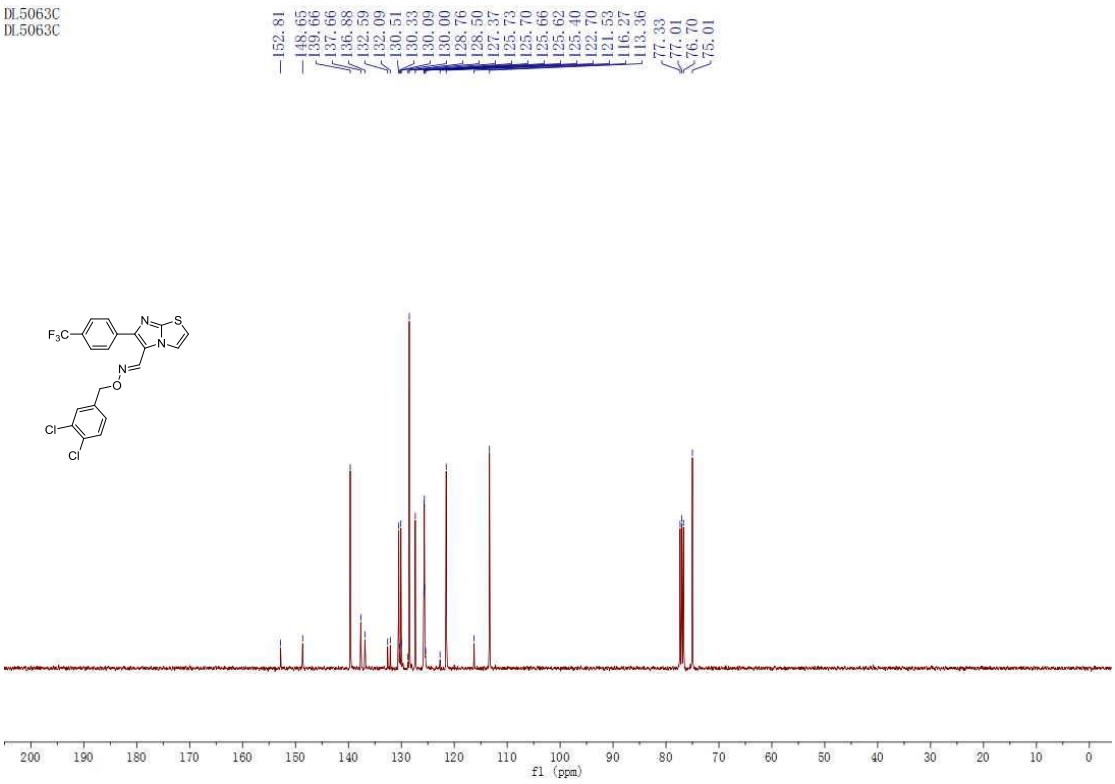
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	7.286	34692	3800	0.000		M	4.279
2	10.754	776045	28942	0.000		M	95.721
Total		810736	32742				100.000

Compound **6**


DL5063H
DL5063H
8.422
8.010
7.999
7.788
7.768
7.716
7.695
7.516
7.511
7.459
7.439
7.266
7.256
7.251
7.235
7.230
6.952
6.941
5.145
1.765
1.00
1.02
2.07
2.08
1.04
1.07
1.19
1.01
2.01
f1 (ppm)


DL5063C
DL5063C
152.81
148.65
139.66
137.66
136.88
132.59
132.09
130.51
130.33
130.09
130.00
128.76
128.50
127.37
125.73
125.70
125.66
125.62
125.40
122.70
121.53
116.27
113.36
77.33
77.01
76.70
75.01
f1 (ppm)

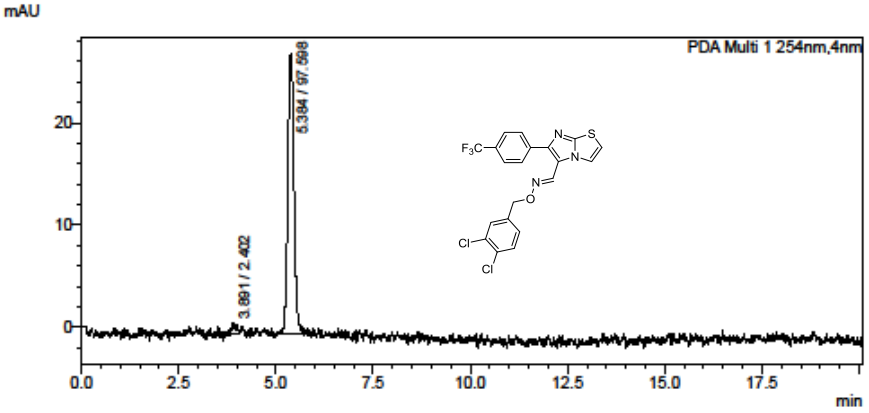
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5063		
Sample ID	: 0.8/80		
Data Filename	: 7278.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 5 uL		
Date Acquired	: 7/26/2018 2:08:25 PM	Acquired by	: System Administrator
Date Processed	: 7/26/2018 2:28:33 PM	Processed by	: System Administrator

<Chromatogram>

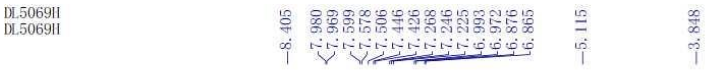


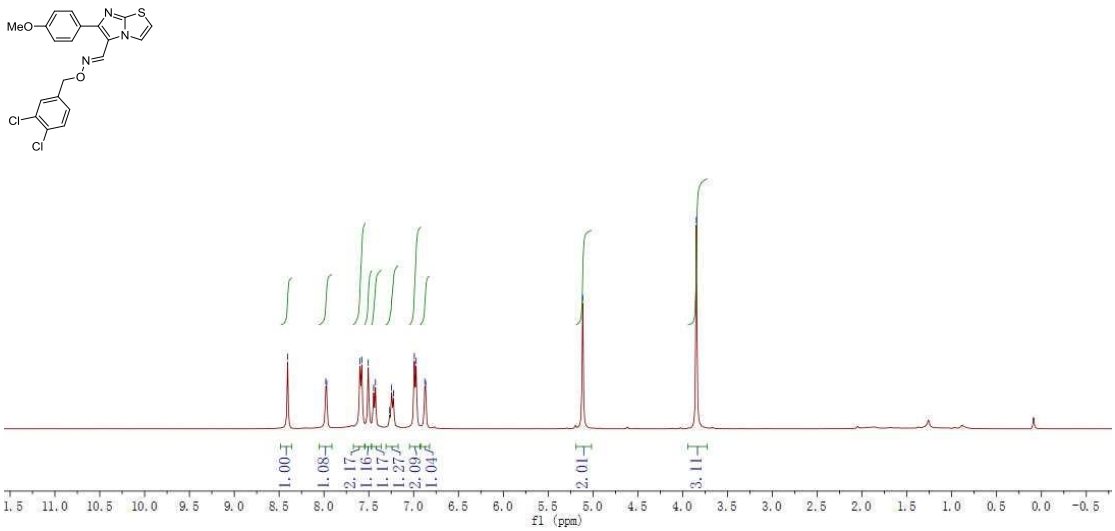
<Peak Table>

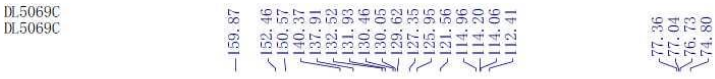
PDA Ch1 254nm

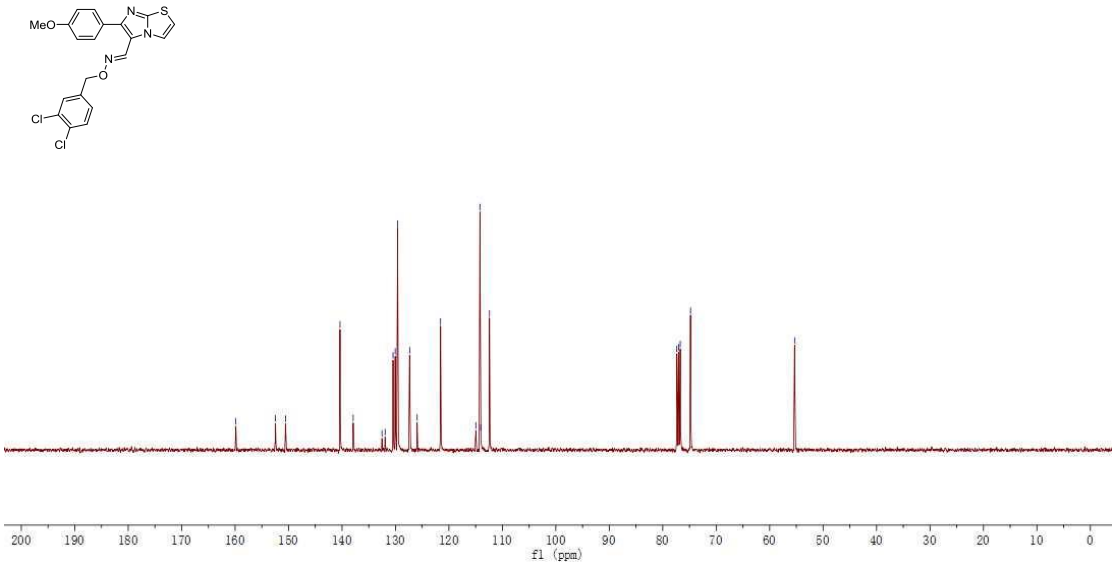
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	3.891	7371	1054	0.000		M	2.402
2	5.384	299456	27386	0.000		M	97.598
Total		306828	28440				100.000

Compound **7**


DL5069H
DL5069H
8.405
7.980
7.969
7.599
7.578
7.506
7.446
7.426
7.268
7.246
7.225
6.993
6.972
6.876
6.865
5.115
3.848


MeO
N
S
N
O
Cl
Cl
1.00
1.08
2.17
1.16
1.17
1.27
2.09
1.04
2.01
3.11
f1 (ppm)


DL5069C
DL5069C
159.87
152.46
150.57
140.37
137.91
132.52
131.93
130.46
130.05
129.62
127.35
125.95
121.56
114.96
114.20
114.06
112.41
77.36
77.04
76.73
74.80
55.33


MeO
N
S
N
O
Cl
Cl
f1 (ppm)

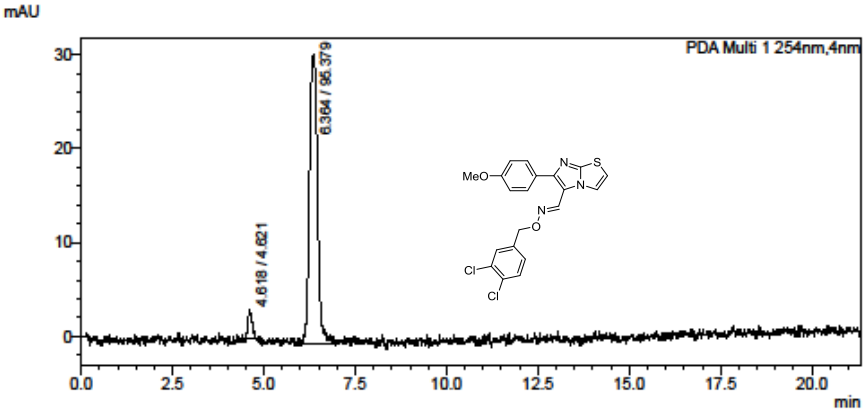
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5069		
Sample ID	: 0.8/80		
Data Filename	: 7238.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/23/2018 3:34:23 PM	Acquired by	: System Administrator
Date Processed	: 7/23/2018 3:55:45 PM	Processed by	: System Administrator

<Chromatogram>



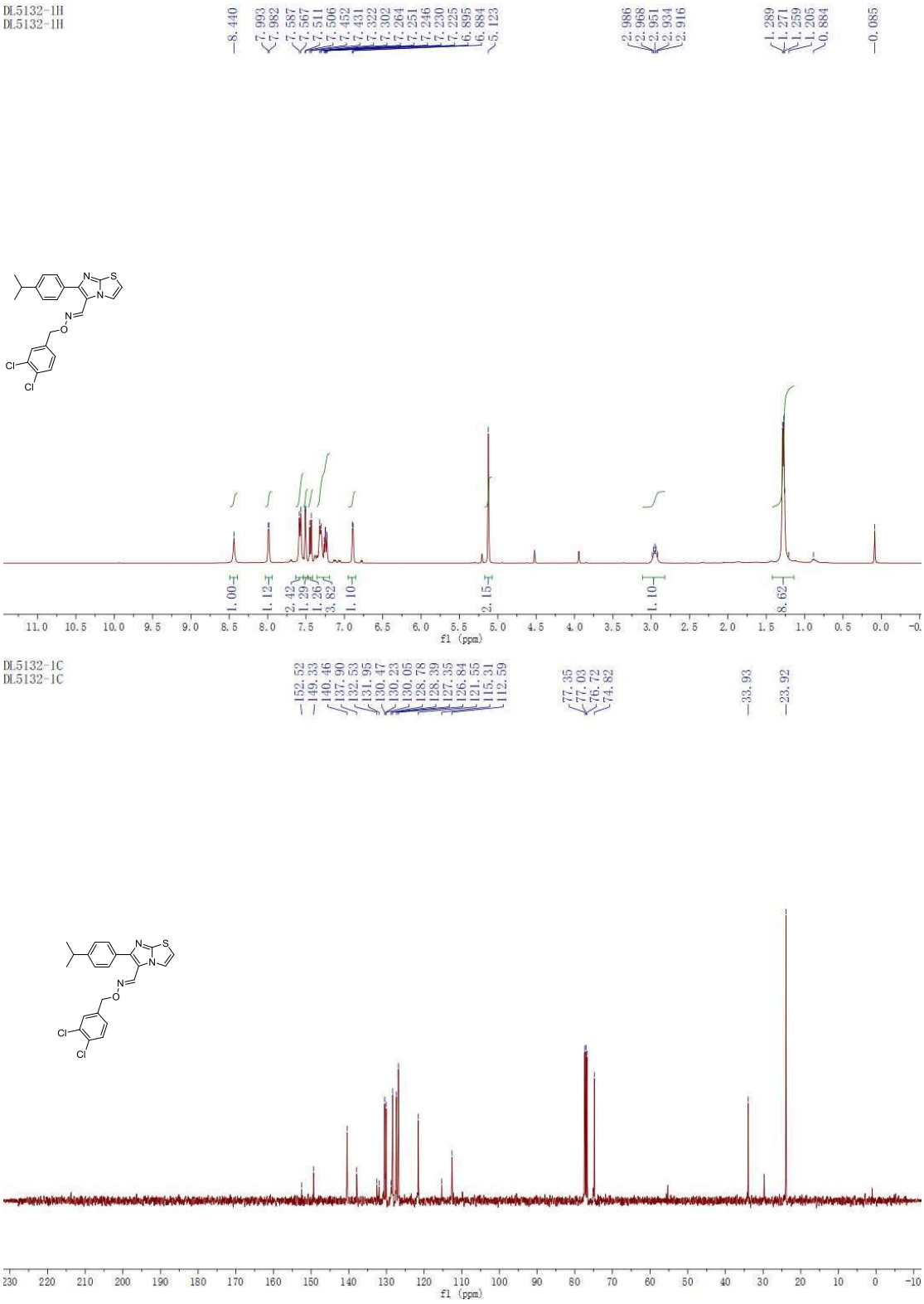
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	4.618	22992	3025	0.000		M	4.621
2	6.364	474545	30701	0.000		M	95.379
Total		497537	33726				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7238.lcd

Compound **8**


DL5132-1H
DL5132-1H
8.440
7.993
7.982
7.587
7.567
7.511
7.506
7.452
7.431
7.322
7.302
7.264
7.251
7.246
7.230
7.225
6.895
6.884
5.123
2.986
2.968
2.951
2.934
2.916
1.289
1.271
1.259
1.205
0.884
0.085
1.00
1.12
2.42
1.29
1.26
3.82
1.10
2.15
1.10
8.62
f1 (ppm)
DL5132-1C
DL5132-1C
152.52
149.33
140.46
137.90
132.53
131.95
130.47
130.23
130.05
128.78
128.39
127.35
126.84
121.55
115.31
112.59
77.35
77.03
76.72
74.82
33.93
23.92
f1 (ppm)

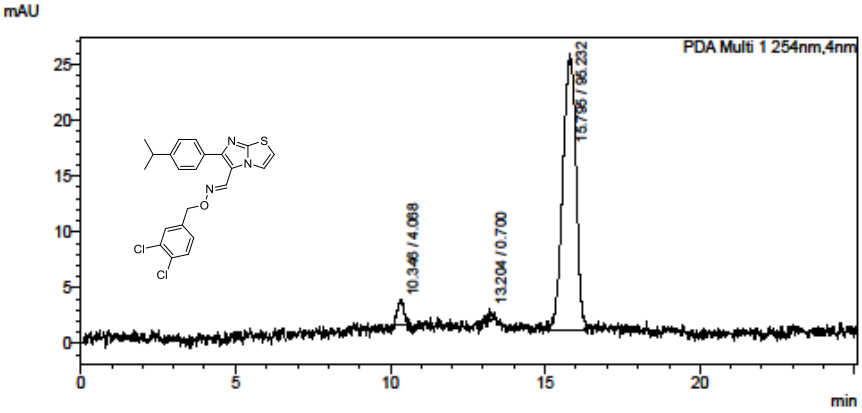
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 6132		
Sample ID	: 0.8/80		
Data Filename	: 7275.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 5 uL		
Date Acquired	: 7/26/2018 12:48:37 PM	Acquired by	: System Administrator
Date Processed	: 7/26/2018 1:13:42 PM	Processed by	: System Administrator

<Chromatogram>



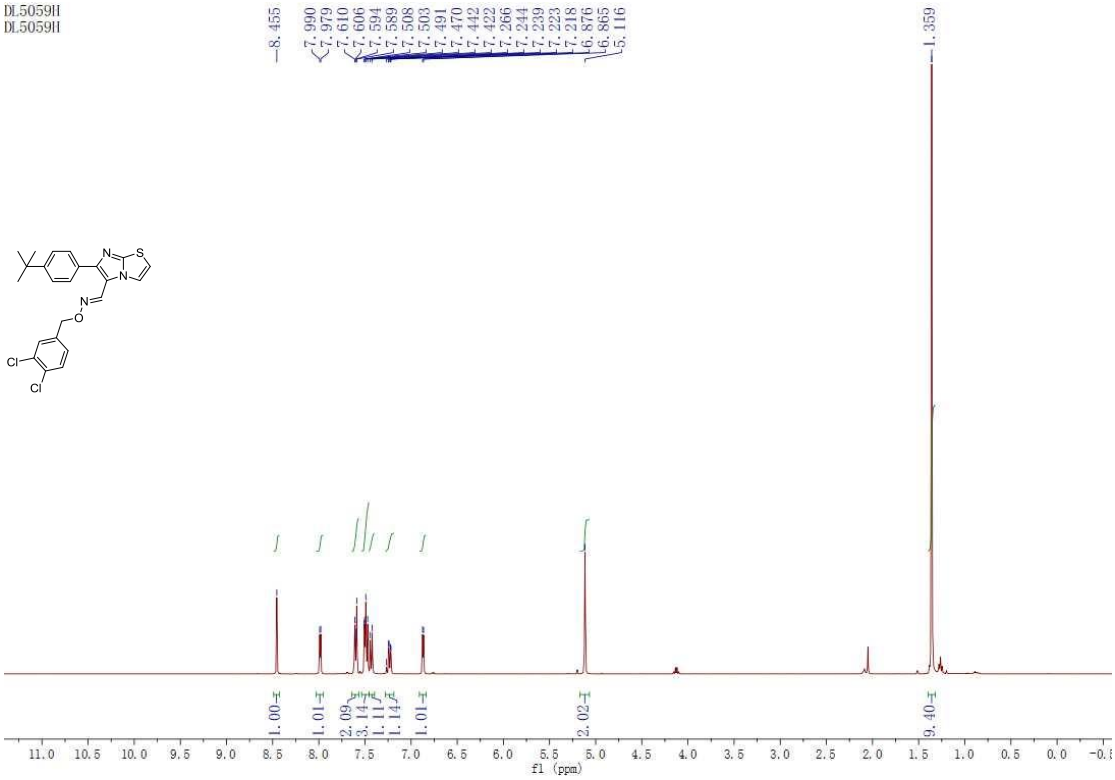
<Peak Table>

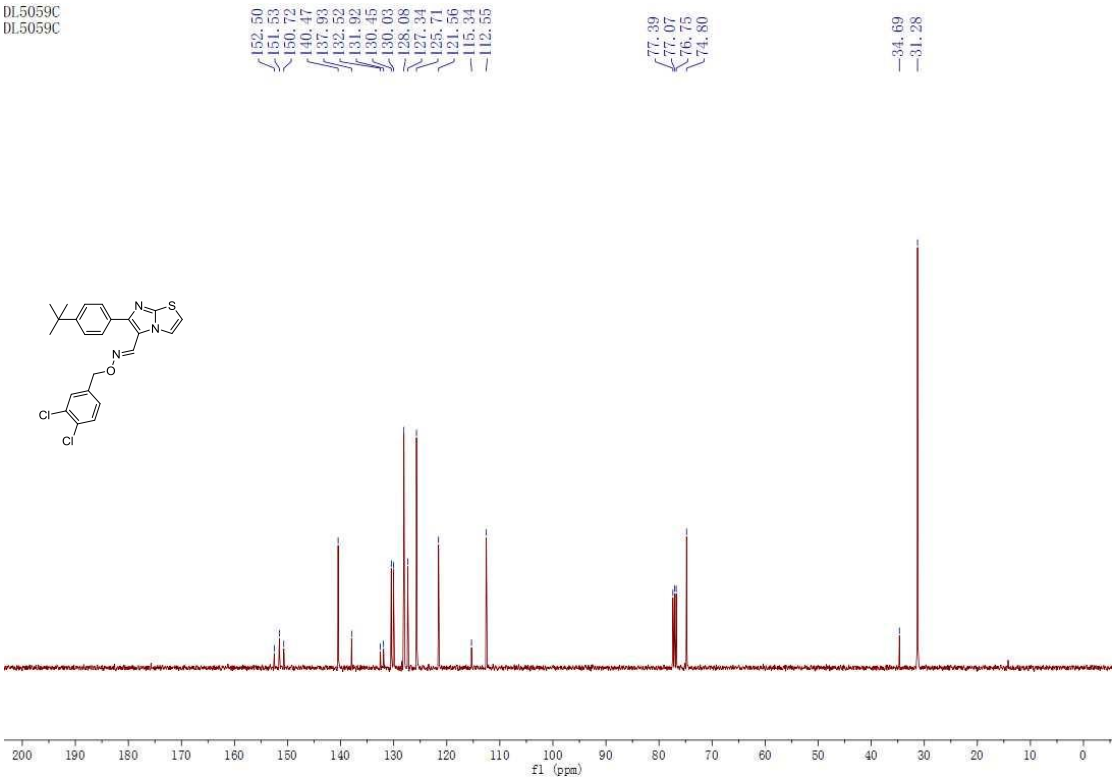
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	10.346	31402	2272	0.000		M	4.068
2	13.204	5407	1146	0.000		M	0.700
3	15.795	735171	24649	0.000		M	95.232
Total		771980	28068				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7275.lcd

Compound **9**


DL5059H
DL5059H
8.455
7.990
7.979
7.610
7.606
7.594
7.589
7.508
7.503
7.491
7.470
7.442
7.422
7.266
7.244
7.239
7.223
7.218
6.876
6.865
5.116
1.359
1.00
1.01
2.09
3.14
1.11
1.14
1.01
2.02
9.40
f1 (ppm)


DL5059C
DL5059C
152.50
151.53
150.72
140.47
137.93
132.52
131.92
130.45
130.03
128.08
127.34
125.71
121.56
115.34
112.55
77.39
77.07
76.75
74.80
34.69
31.28
f1 (ppm)

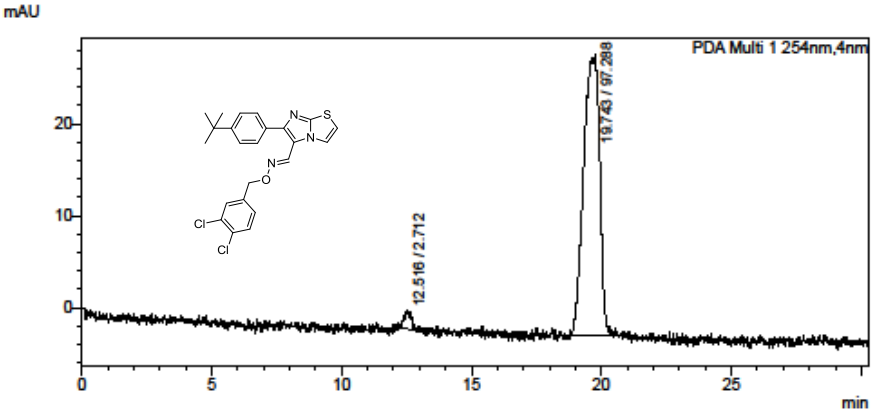
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5059		
Sample ID	: 0.8/80		
Data Filename	: 7284.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/26/2018 9:48:13 PM	Acquired by	: System Administrator
Date Processed	: 7/26/2018 10:18:32 PM	Processed by	: System Administrator

<Chromatogram>



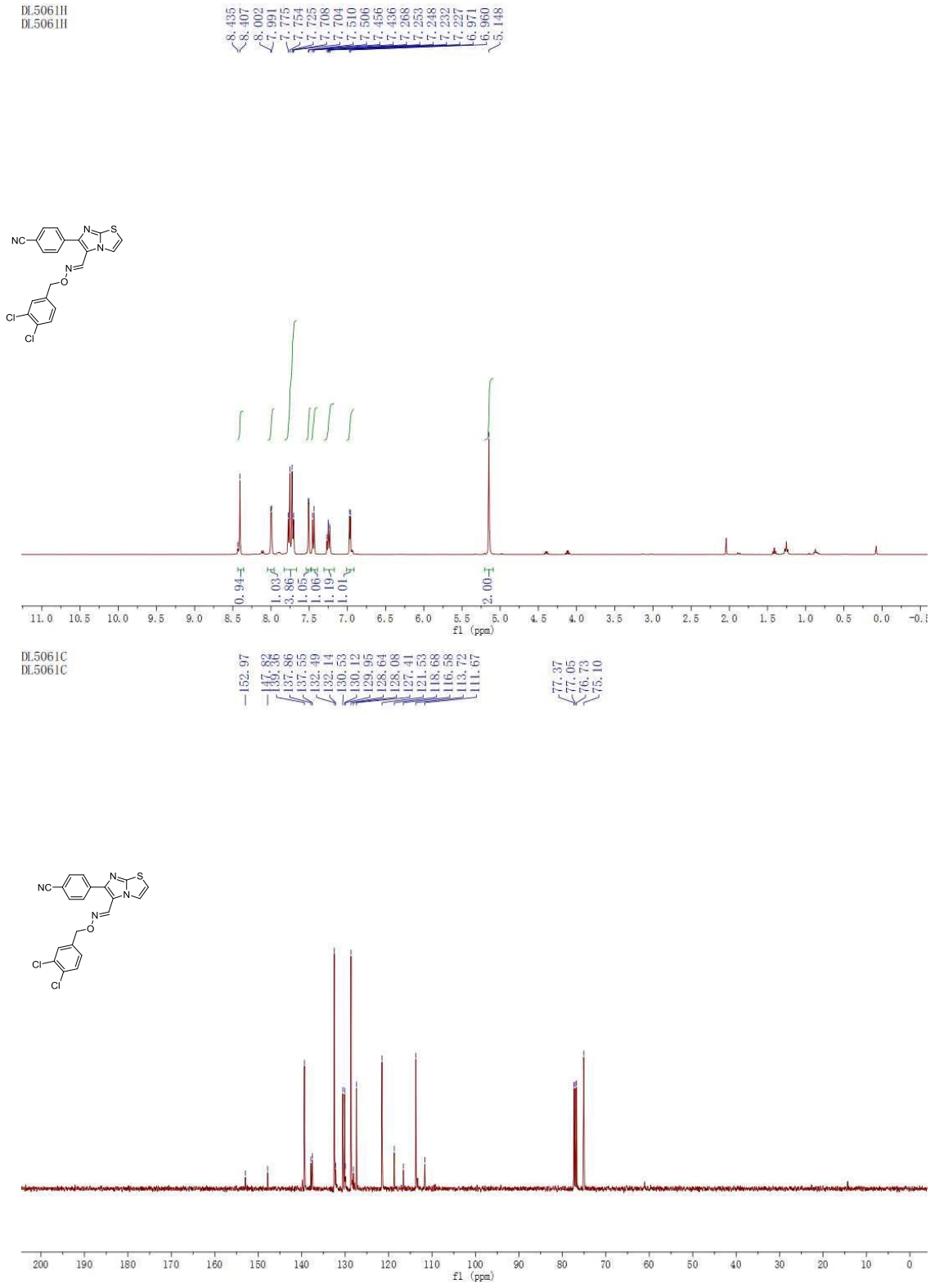
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	12.516	36706	2080	0.000		M	2.712
2	19.743	1316959	30590	0.000		M	97.288
Total		1353666	32670				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7284.lcd

Compound **10**


DL5061H
DL5061H
8.435
8.407
8.002
7.991
7.775
7.754
7.725
7.708
7.704
7.510
7.506
7.456
7.436
7.268
7.253
7.248
7.232
7.227
6.971
6.960
5.148
NC
N
S
N
O
Cl
Cl
0.94
1.03
3.86
1.05
1.06
1.19
1.01
2.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
DL5061C
DL5061C
152.97
147.82
139.36
137.86
137.55
132.49
132.14
130.53
130.12
129.95
128.64
128.08
127.41
121.53
118.68
116.58
113.72
111.67
77.37
77.05
76.73
75.10
NC
N
S
N
O
Cl
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

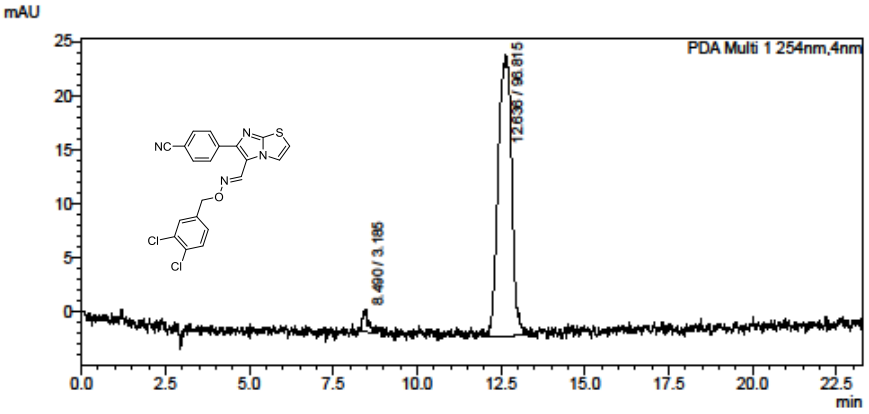
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5061		
Sample ID	: 0.8/80		
Data Filename	: 7224.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 12:47:35 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 1:10:54 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

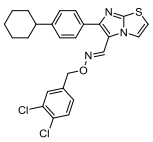
PDA Ch1 254nm

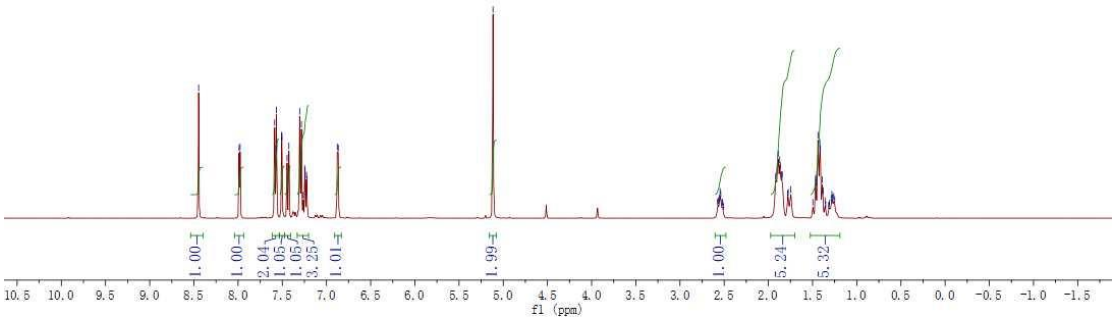
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	8.490	23888	2069	0.000		M	3.185
2	12.636	726170	25982	0.000		M	96.815
Total		750058	28052				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7224.lcd

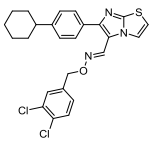
Compound **11**

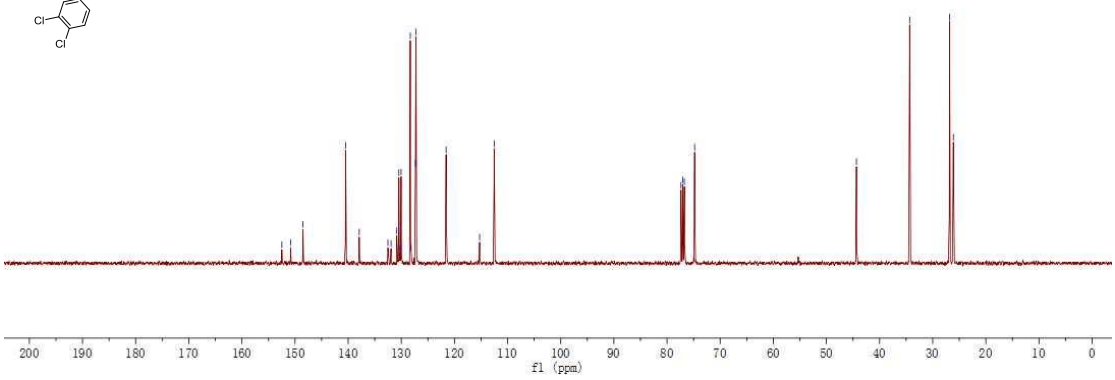

DL5131-1H
DL5131-1H
8.446
7.988
7.977
7.587
7.571
7.566
7.508
7.503
7.446
7.425
7.303
7.283
7.264
7.247
7.242
7.226
7.221
6.878
6.867
5.116
2.575
2.567
2.554
2.546
2.539
2.525
2.517
2.509
1.917
1.890
1.872
1.865
1.852
1.843
1.782
1.775
1.746
1.467
1.461
1.439
1.418
1.412
1.390
1.382
1.358
1.289
1.281
1.273
1.260
1.249




1.00
1.00
2.04
1.05
1.05
3.25
1.01
1.99
1.00
5.24
5.32
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


DL5131-1C
DL5131-1C
152.49
150.84
148.52
140.49
137.92
132.52
131.93
130.86
130.46
130.22
130.04
128.31
128.16
127.35
127.25
121.57
115.27
112.53
77.37
77.05
76.74
74.80
44.35
34.34
26.84
26.11



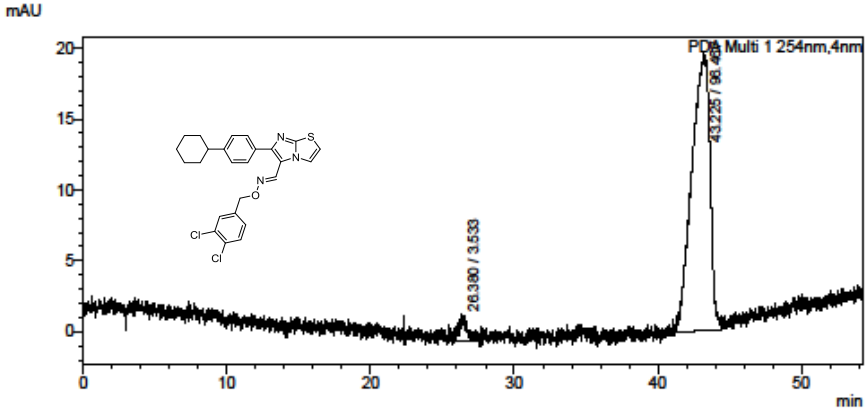

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: 5131-1		
Sample ID	: 0.8/80		
Data Filename	: 7228.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 2:19:27 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 3:13:44 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

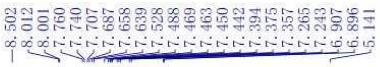
PDA Ch1 254nm

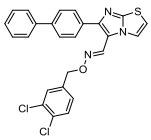
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	26.380	63131	1815	0.000		M	3.533
2	43.225	1723798	19506	0.000		M	96.467
Total		1786929	21321				100.000

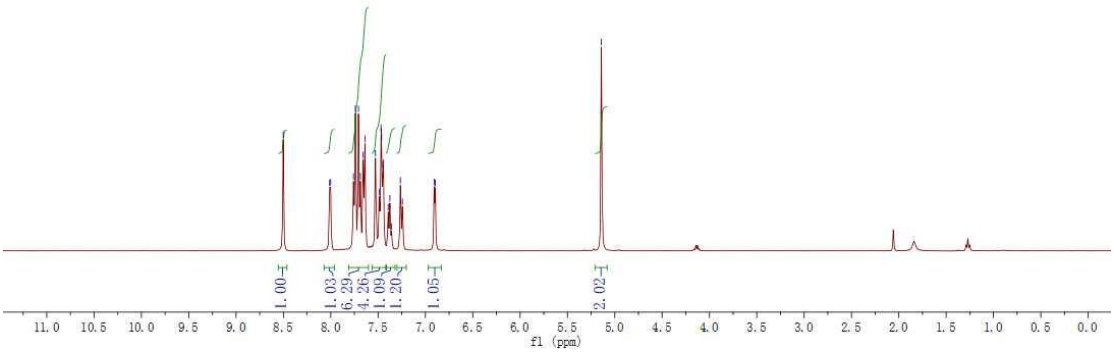
C:\Users\sop\Desktop\Xue Lab\Liang\7228.lcd

Compound **12**

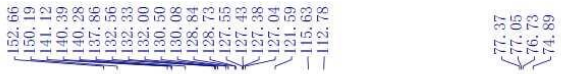
DL5060H
DL5060H

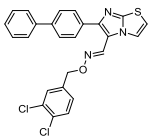






DL5060C
DL5060C





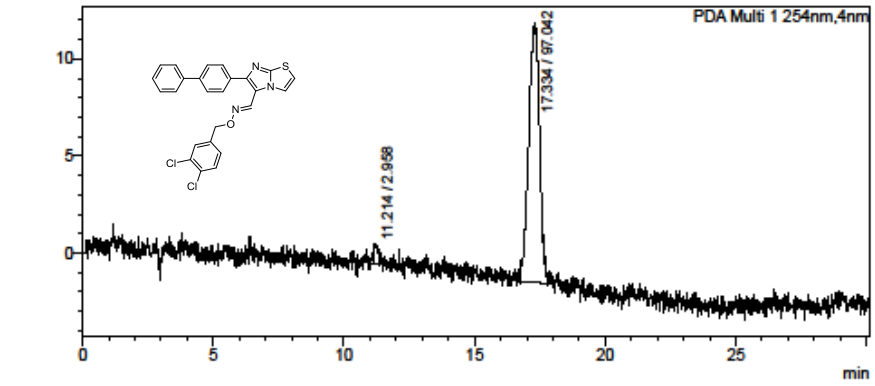
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5060		
Sample ID	: 0.8/80		
Data Filename	: 7229.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 3:14:54 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 3:45:03 PM	Processed by	: System Administrator

<Chromatogram>



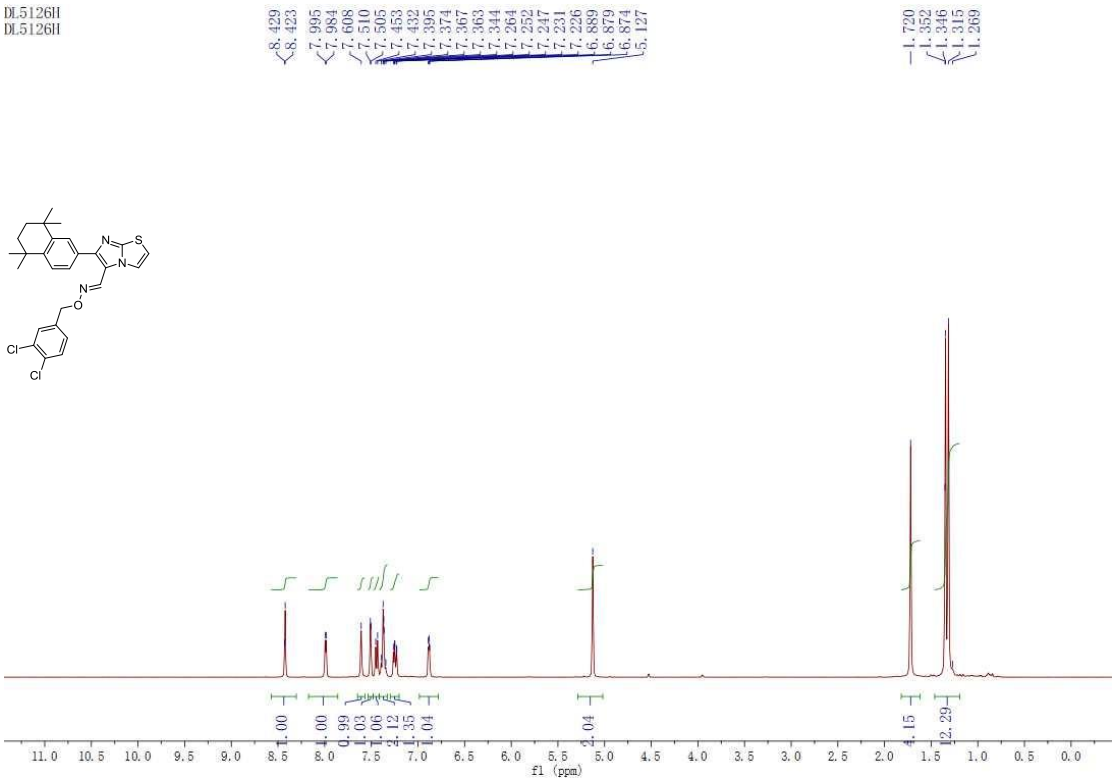
<Peak Table>

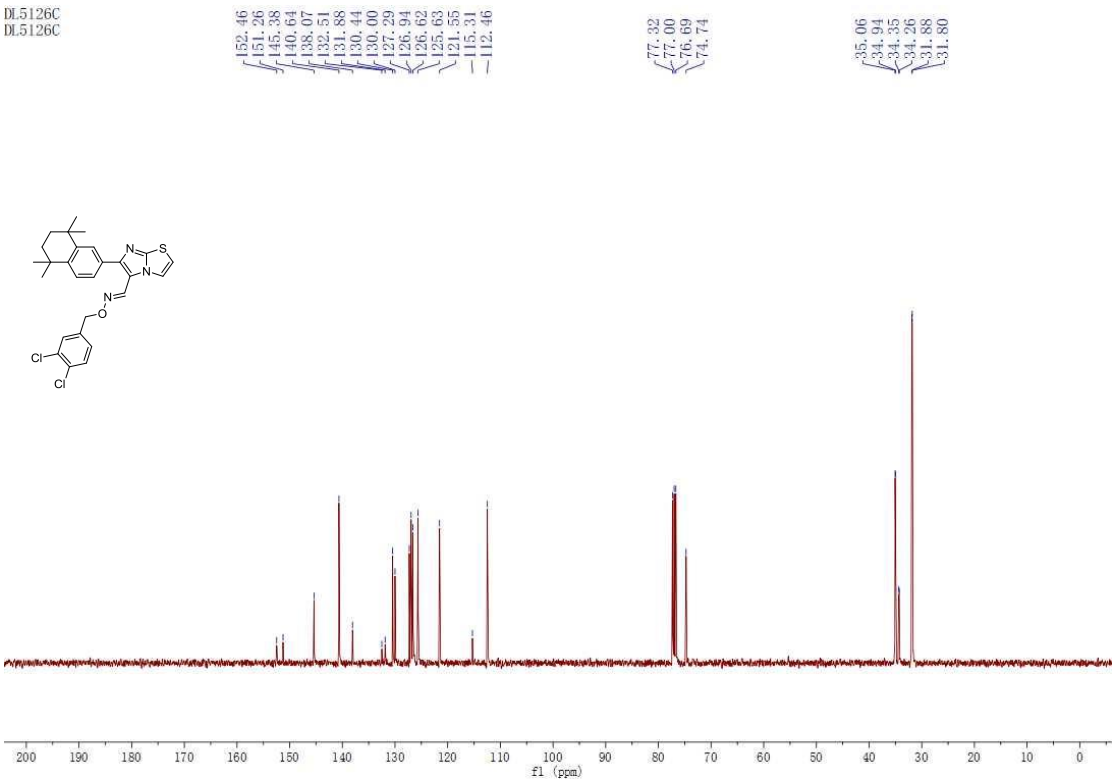
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	11.214	11845	1034	0.000		M	2.958
2	17.334	388588	13365	0.000		M	97.042
Total		400433	14399				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7229.lcd

Compound **13**


DL5126H
DL5126H
8.429
8.423
7.995
7.984
7.608
7.510
7.505
7.453
7.432
7.395
7.374
7.367
7.363
7.344
7.264
7.252
7.247
7.231
7.226
6.889
6.879
6.874
5.127
1.720
1.352
1.346
1.315
1.269
Cl
Cl
1.00
1.00
0.99
1.03
1.06
1.12
1.35
1.04
1.04
4.15
12.29
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


DL5126C
DL5126C
152.46
151.26
145.38
140.64
138.07
132.51
131.88
130.44
130.00
127.29
126.94
126.62
125.63
121.55
115.31
112.46
77.32
77.00
76.69
74.74
35.06
34.94
34.35
34.26
31.88
31.80
Cl
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

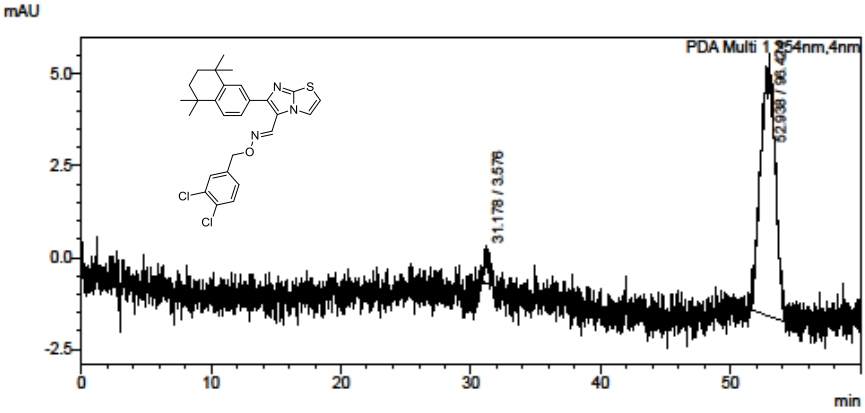
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5126		
Sample ID	: 0.8/80		
Data Filename	: 7194.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/18/2018 6:09:11 PM	Acquired by	: System Administrator
Date Processed	: 7/18/2018 7:09:14 PM	Processed by	: System Administrator

<Chromatogram>

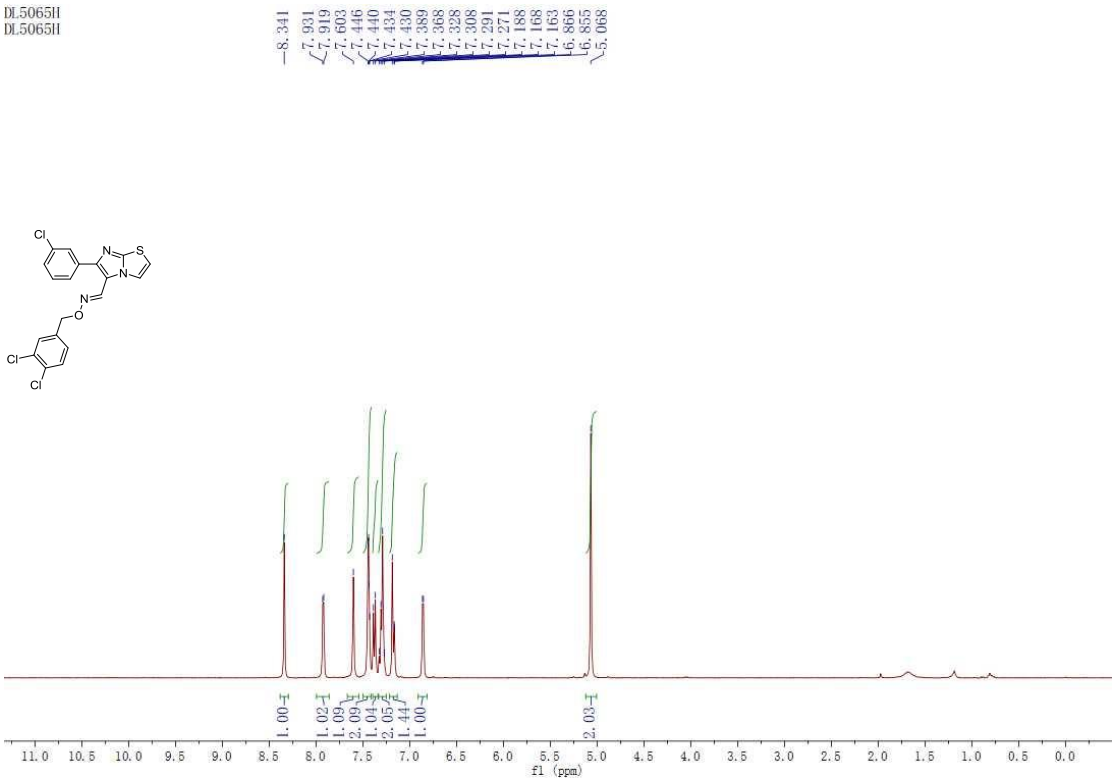


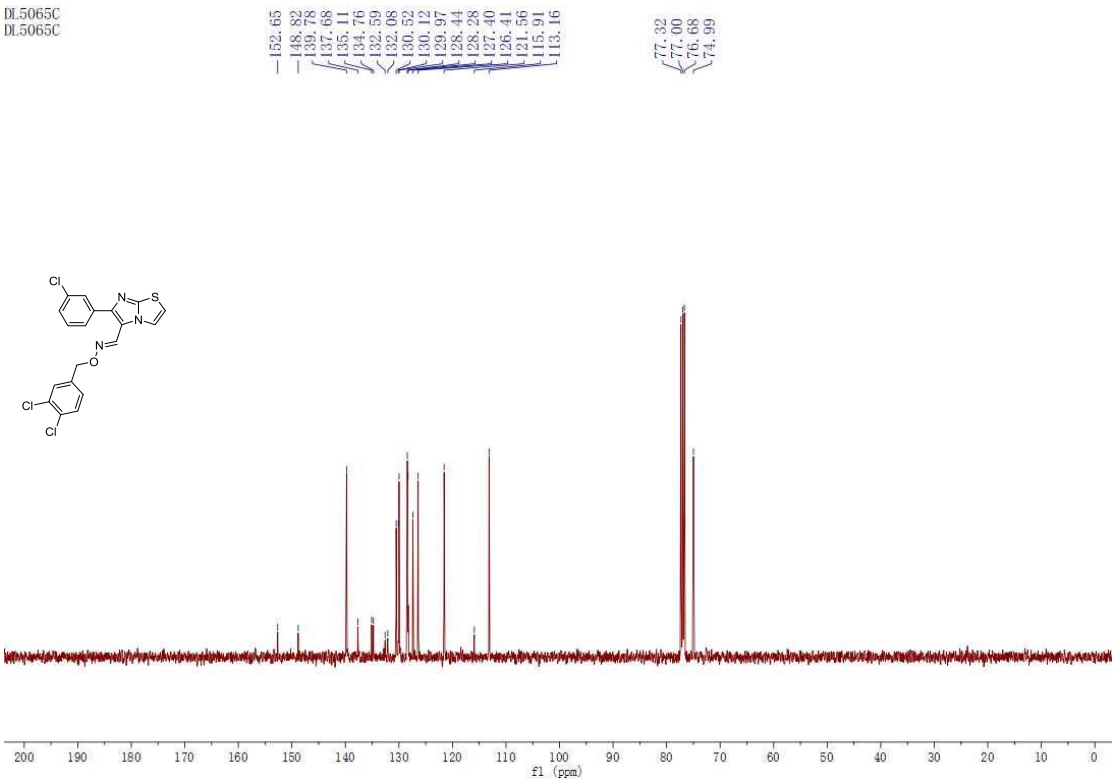
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	31.178	20337	996	0.000		M	3.576
2	52.938	548383	7112	0.000		M	96.424
Total		568720	8109				100.000

Compound **14**


DL5065H
DL5065H
8.341
7.931
7.919
7.603
7.446
7.440
7.434
7.430
7.389
7.368
7.328
7.308
7.291
7.271
7.188
7.168
7.163
6.866
6.855
5.068
1.00
1.02
1.09
2.09
1.04
2.05
1.44
1.00
2.03
f1 (ppm)


DL5065C
DL5065C
152.65
148.82
139.78
137.68
135.11
134.76
132.59
132.08
130.52
130.12
129.97
128.44
128.28
127.40
126.41
121.56
115.91
113.16
77.32
77.00
76.68
74.99
f1 (ppm)

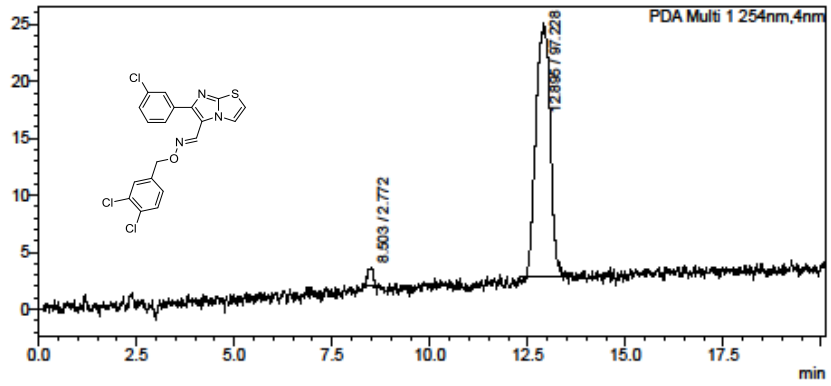
SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: 5065		
Sample ID	: 0.8/80		
Data Filename	: 7193.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/18/2018 5:44:59 PM	Acquired by	: System Administrator
Date Processed	: 7/18/2018 6:05:07 PM	Processed by	: System Administrator

<Chromatogram>

mAU



<Peak Table>

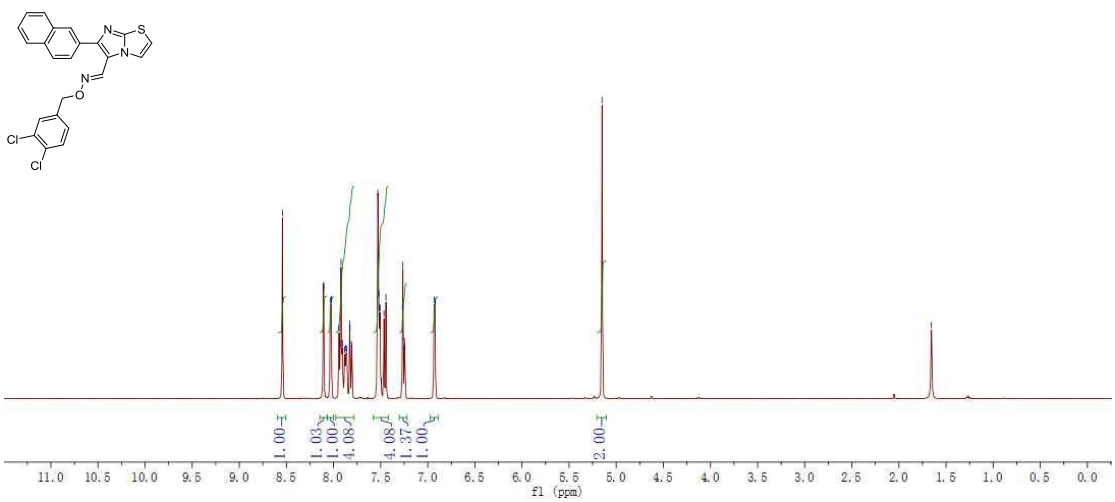
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	8.503	15986	1711	0.000		M	2.772
2	12.895	560698	22227	0.000		M	97.228
Total		576684	23938				100.000

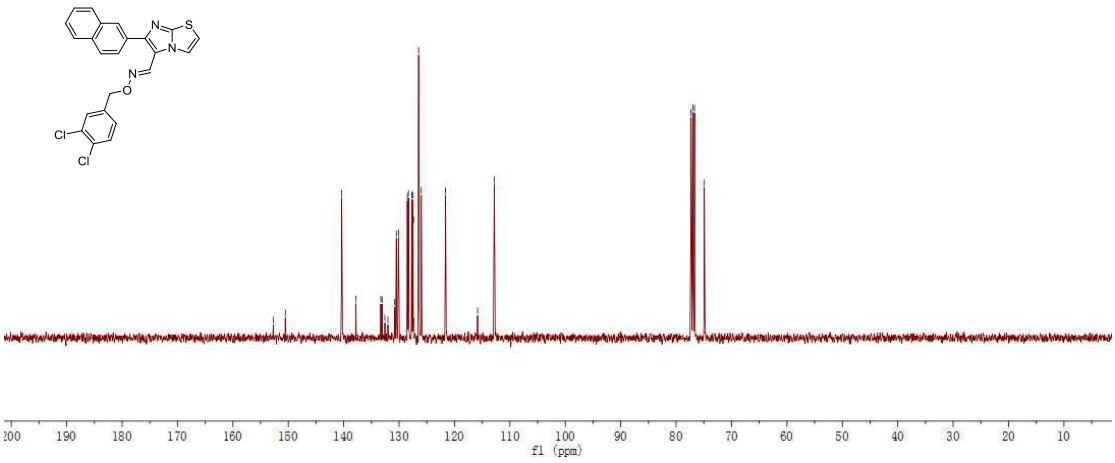
C:\Users\sop\Desktop\Xue Lab\Liang\7193.lcd

Compound **15**


DL5044H
DL5044H
8.543
8.108
8.104
8.035
8.024
7.942
7.929
7.920
7.906
7.882
7.869
7.859
7.830
7.825
7.808
7.804
7.530
7.525
7.519
7.516
7.511
7.506
7.494
7.464
7.444
7.268
7.264
7.248
7.243
6.933
6.922
5.150
1.655


1.00
1.03
1.00
4.08
4.08
1.37
1.00
2.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


DL5044C
DL5044C
152.73
150.54
140.37
137.81
133.31
133.08
132.57
132.02
130.79
130.50
130.10
128.51
128.32
127.71
127.51
127.38
126.47
126.01
121.63
115.84
112.82
77.32
77.01
76.69
74.92


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

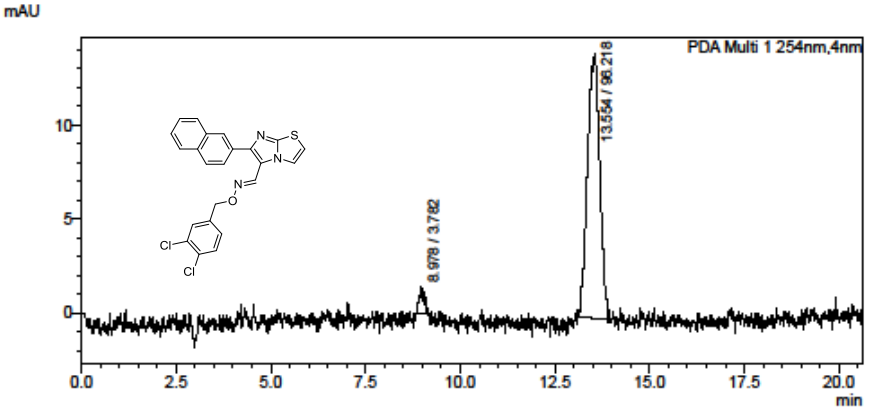
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5044		
Sample ID	: 0.8/80		
Data Filename	: 7189.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/18/2018 3:30:12 PM	Acquired by	: System Administrator
Date Processed	: 7/18/2018 3:50:52 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

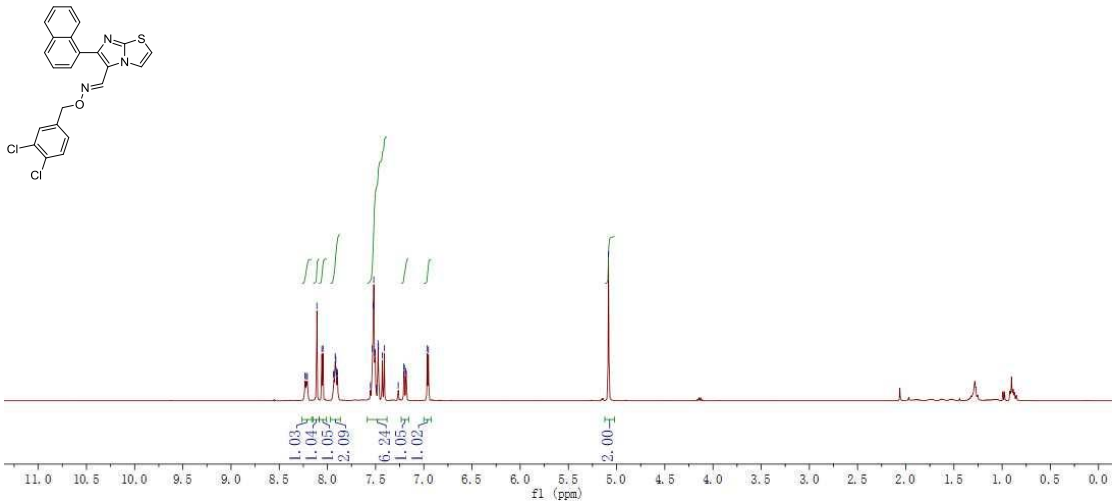
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	8.978	12351	1445	0.000		M	3.782
2	13.554	314174	14041	0.000		M	96.218
Total		326524	15486				100.000

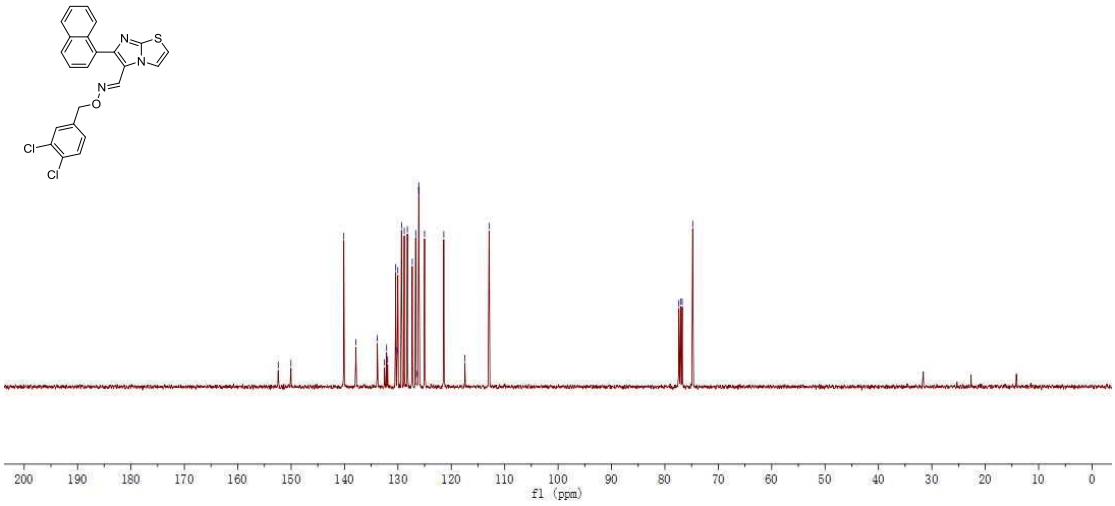
C:\Users\sop\Desktop\Xue Lab\Liang\7189.lcd

Compound **16**


DL5066H
DL5066H
8.233
8.219
8.209
8.109
8.058
8.046
7.938
7.931
7.920
7.913
7.908
7.900
7.895
7.554
7.536
7.527
7.519
7.509
7.503
7.491
7.475
7.470
7.431
7.410
7.265
7.207
7.202
7.186
7.181
6.964
6.952
5.084


1.03
1.04
1.05
2.09
6.24
1.05
1.02
2.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


DL5066C
DL5066C
152.41
150.03
140.14
137.89
133.86
132.51
132.12
131.92
130.45
130.15
130.01
129.33
128.81
128.23
127.32
126.67
126.50
126.12
126.09
125.01
121.41
117.47
112.92
77.39
77.07
76.75
74.79


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

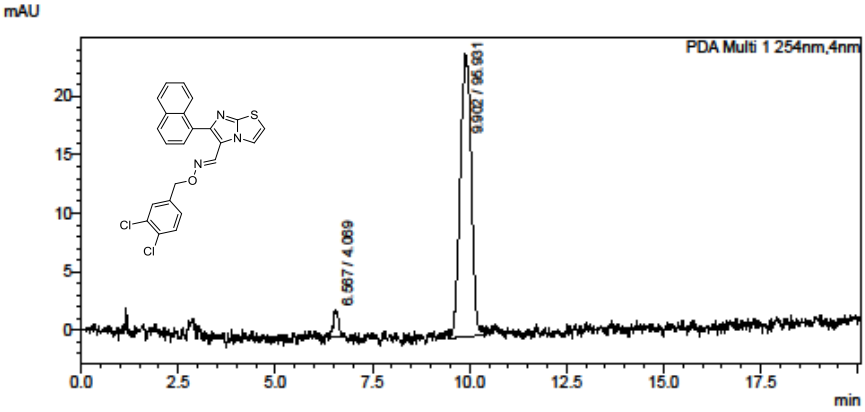
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5066		
Sample ID	: 0.8/80		
Data Filename	: 7297.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 80 uL		
Date Acquired	: 8/5/2018 12:37:33 PM	Acquired by	: System Administrator
Date Processed	: 8/5/2018 12:57:40 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	6.567	20460	2312	0.000		M	4.069
2	9.902	482418	24135	0.000		M	95.931
Total		502878	26447				100.000

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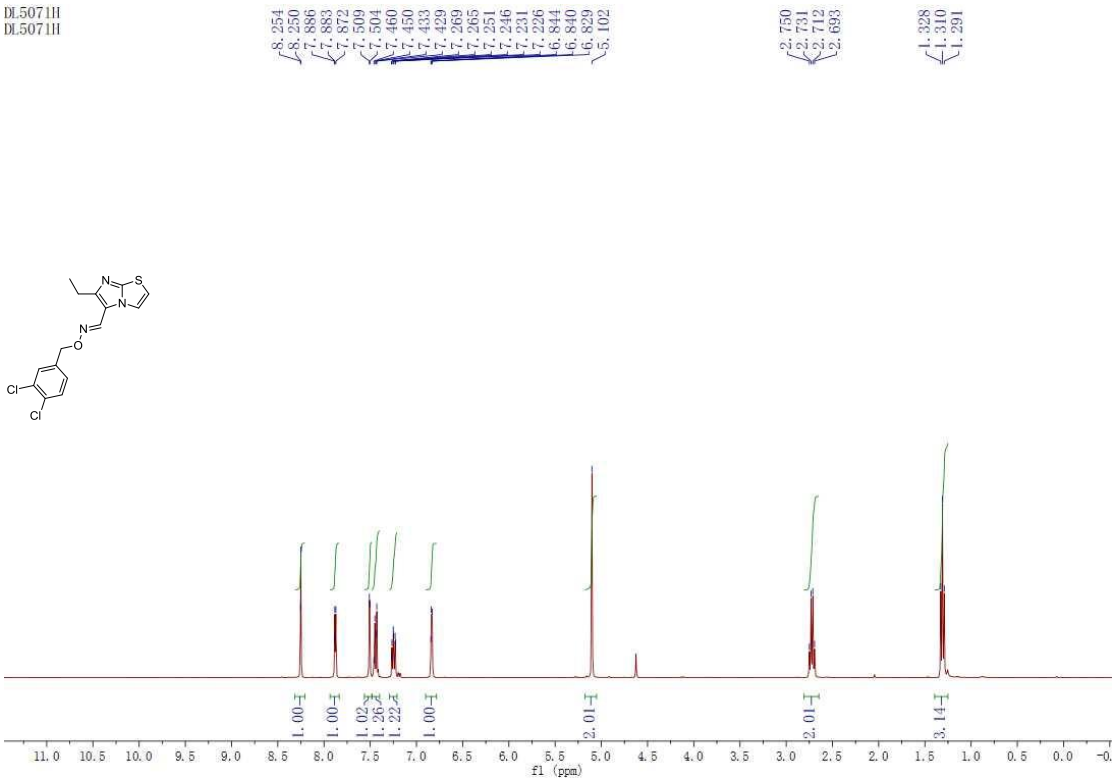
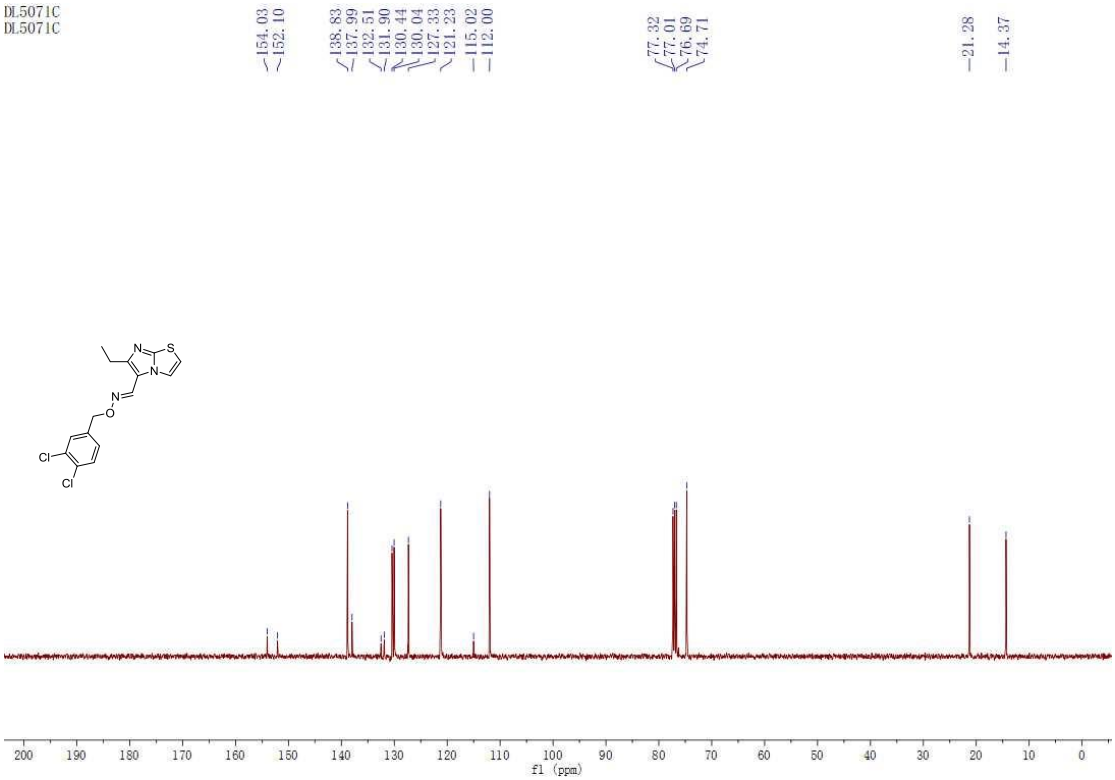
Compound **17**


DL5071H
DL5071H
8.254
8.250
7.886
7.883
7.872
7.509
7.504
7.460
7.450
7.433
7.429
7.269
7.265
7.251
7.246
7.231
7.226
6.844
6.840
6.829
5.102
2.750
2.731
2.712
2.693
1.328
1.310
1.291
1.00
1.00
1.02
1.26
1.22
1.00
2.01
2.01
3.14
f1 (ppm)


DL5071C
DL5071C
154.03
152.10
138.83
137.99
132.51
131.90
130.44
130.04
127.33
121.23
115.02
112.00
77.32
77.01
76.69
74.71
21.28
14.37
f1 (ppm)

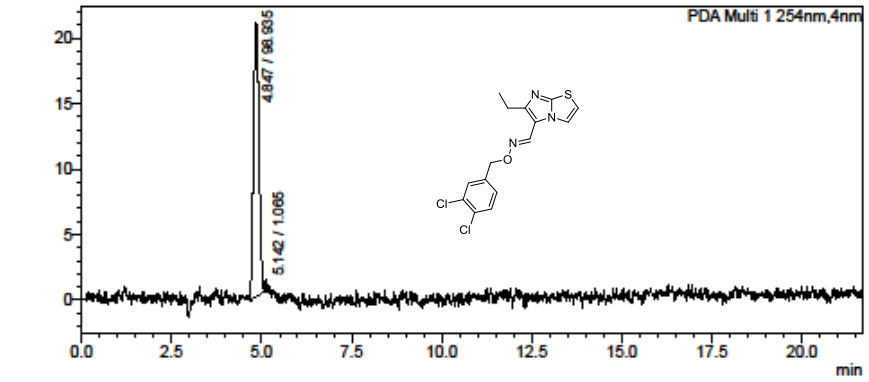
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5071		
Sample ID	: 0.8/80		
Data Filename	: 7225.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 1:12:11 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 1:33:54 PM	Processed by	: System Administrator

<Chromatogram>



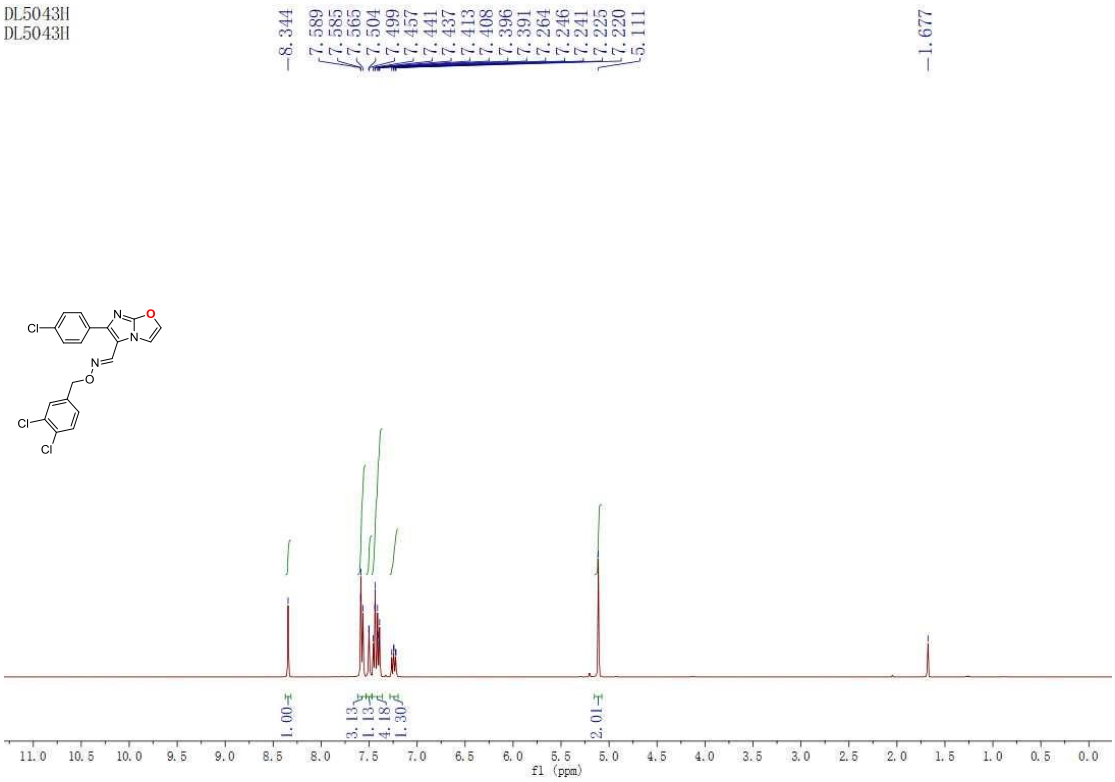
<Peak Table>

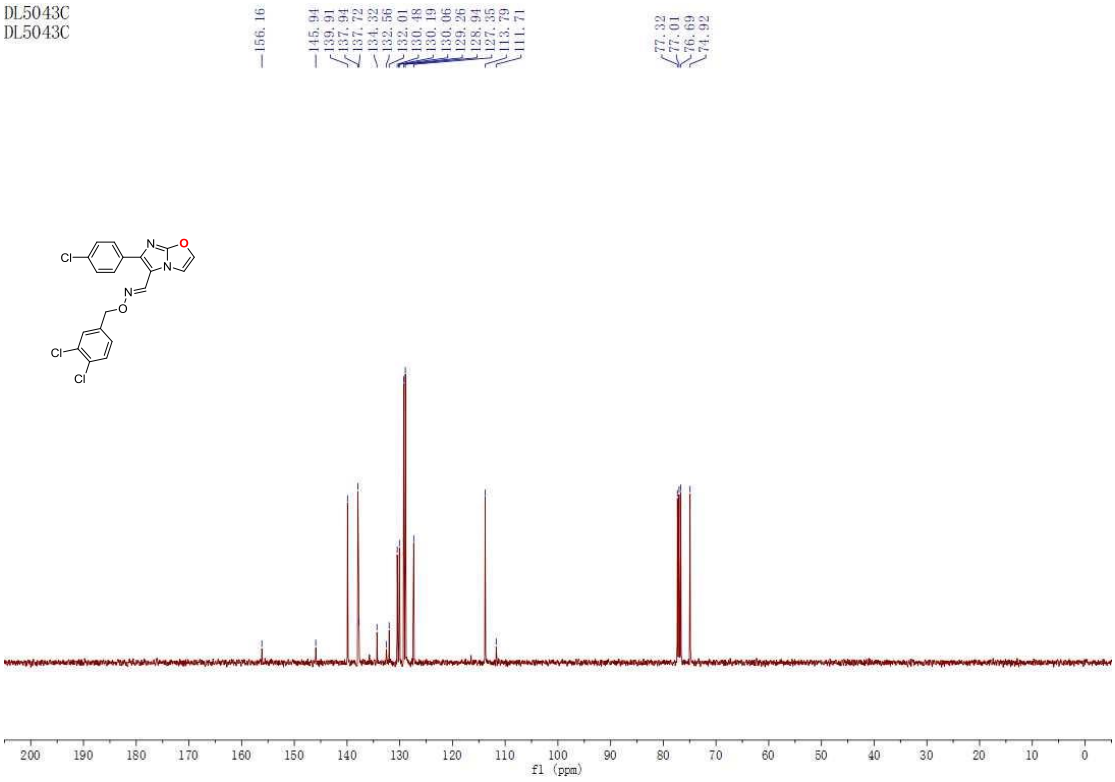
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	4.847	222277	20930	0.000		M	98.935
2	5.142	2392	940	0.000		M	1.065
Total		224669	21870				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7225.lcd

Compound **18**


DL5043H
DL5043H
8.344
7.589
7.585
7.565
7.504
7.499
7.457
7.441
7.437
7.413
7.408
7.396
7.391
7.264
7.246
7.241
7.225
7.220
5.111
1.677
1.00
3.13
1.13
4.18
1.30
2.01
f1 (ppm)


DL5043C
DL5043C
156.16
145.94
139.91
137.94
137.72
134.32
132.56
132.01
130.48
130.19
130.06
129.26
128.94
127.35
113.79
111.71
77.32
77.01
76.69
74.92
f1 (ppm)

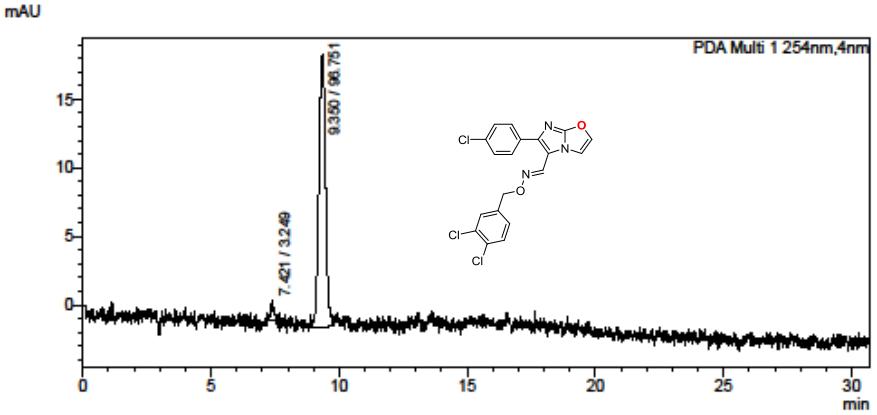
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5043		
Sample ID	: 0.8/80		
Data Filename	: 7188.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/18/2018 2:51:41 PM	Acquired by	: System Administrator
Date Processed	: 7/18/2018 3:22:25 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	7.421	12000	1479	0.000		M	3.249
2	9.350	357345	19829	0.000		M	96.751
Total		369345	21308				100.000

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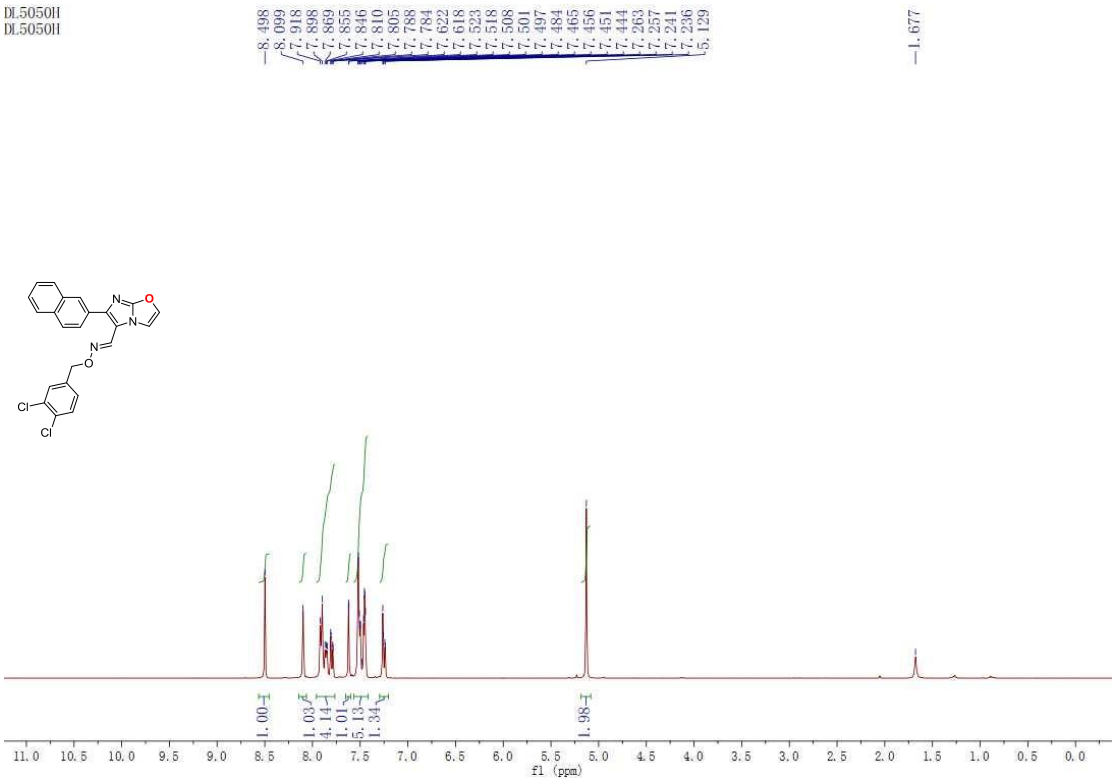
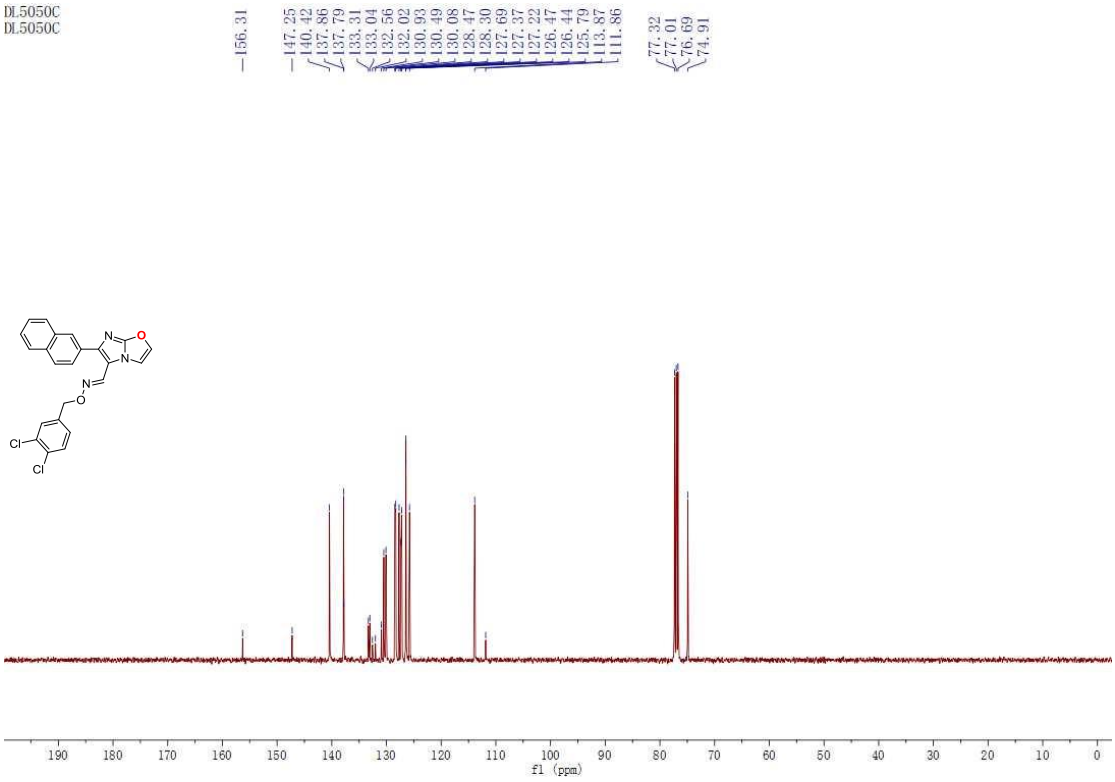
Compound **19**


DL5050H
DL5050H
8.498
8.099
7.918
7.898
7.869
7.855
7.846
7.810
7.805
7.788
7.784
7.622
7.618
7.523
7.518
7.508
7.501
7.497
7.484
7.465
7.456
7.451
7.444
7.263
7.257
7.241
7.236
5.129
1.677
Cl
Cl
1.00
1.03
4.14
1.01
5.13
1.34
1.98
f1 (ppm)


DL5050C
DL5050C
156.31
147.25
140.42
137.86
137.79
133.31
133.04
132.56
132.02
130.93
130.49
130.08
128.47
128.30
127.69
127.37
127.22
126.47
126.44
125.79
113.87
111.86
77.32
77.01
76.69
74.91
Cl
Cl
f1 (ppm)

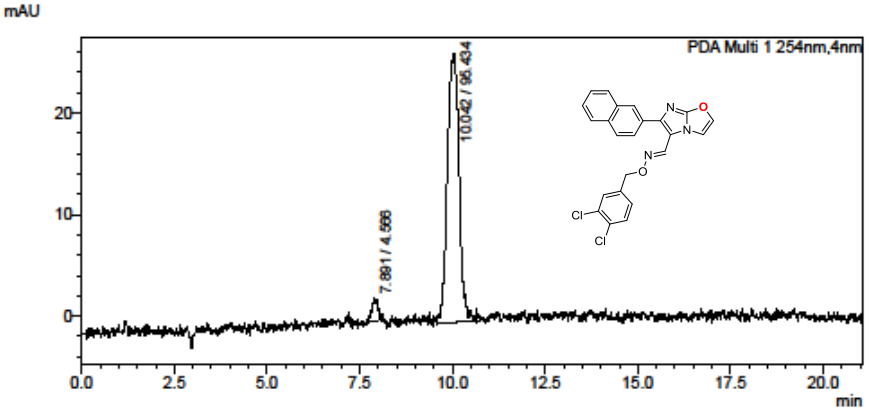
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5050		
Sample ID	: 0.8/80		
Data Filename	: 7230.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 3:46:02 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 4:07:07 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	7.891	27786	2327	0.000		M	4.566
2	10.042	580782	26370	0.000		M	95.434
Total		608568	28696				100.000

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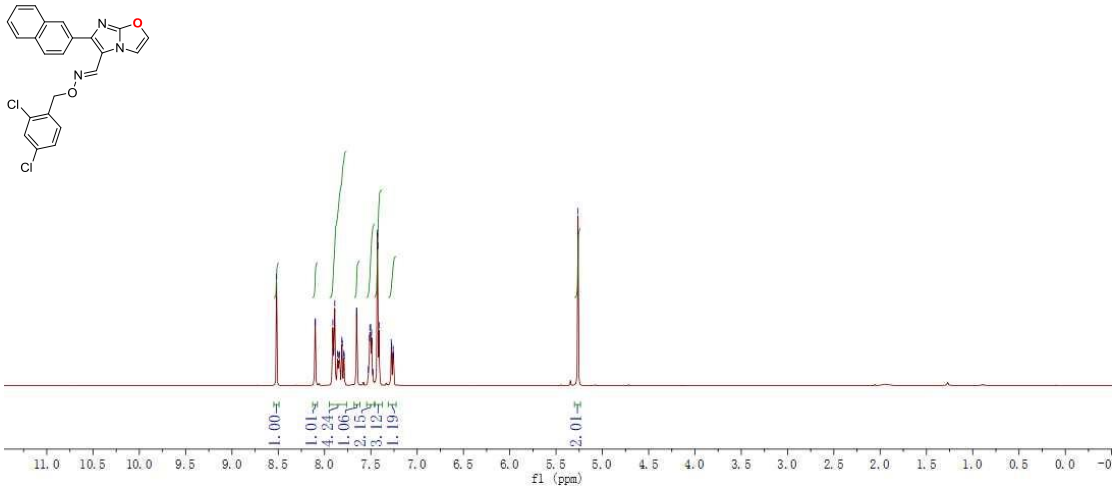
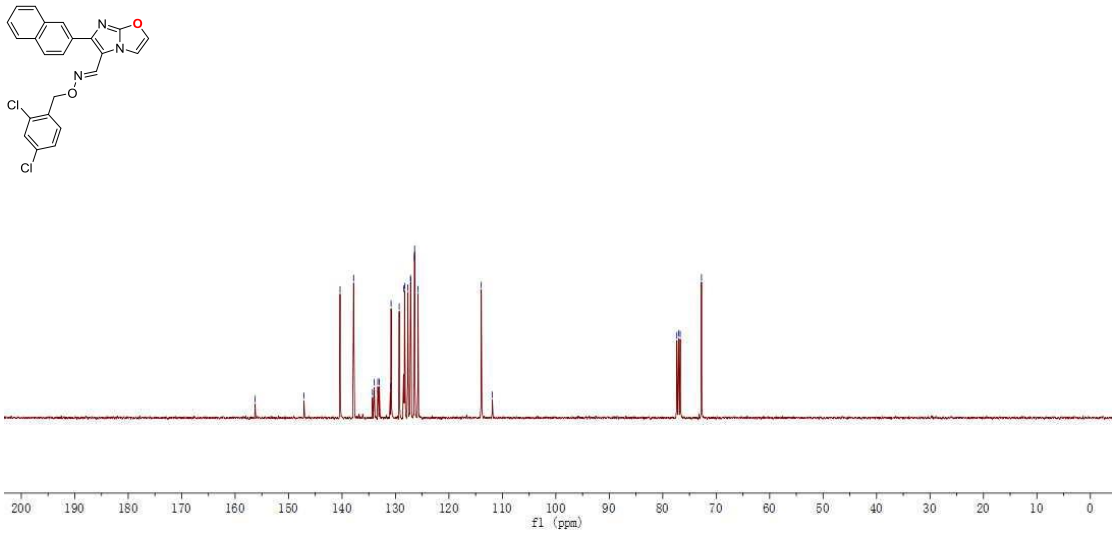
Compound **20**


DL5096-1H
DL5096-1H
8.518
8.103
8.099
7.911
7.901
7.890
7.860
7.847
7.837
7.813
7.809
7.792
7.787
7.655
7.651
7.527
7.515
7.511
7.502
7.492
7.488
7.476
7.429
7.424
7.411
7.280
7.275
7.263
7.259
7.254
5.263


1.00
1.01
4.24
1.06
2.15
3.12
1.19
2.01
f1 (ppm)


DL5096-1C
DL5096-1C
156.28
147.13
140.37
137.83
134.31
134.03
133.96
133.31
133.03
130.96
130.82
129.30
128.46
128.30
127.69
127.19
127.14
126.46
126.42
125.79
113.95
111.88
77.36
77.04
76.73
72.75

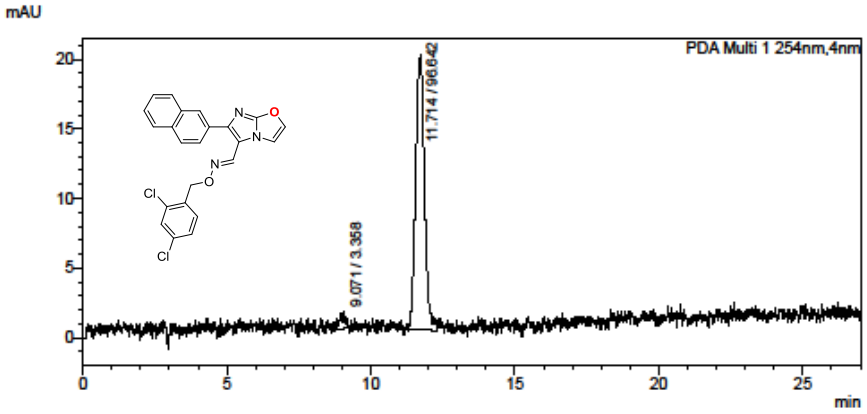

f1 (ppm)

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: 5096-1		
Sample ID	: 0.8/80		
Data Filename	: 7221.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/20/2018 4:19:13 PM	Acquired by	: System Administrator
Date Processed	: 7/20/2018 4:46:17 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

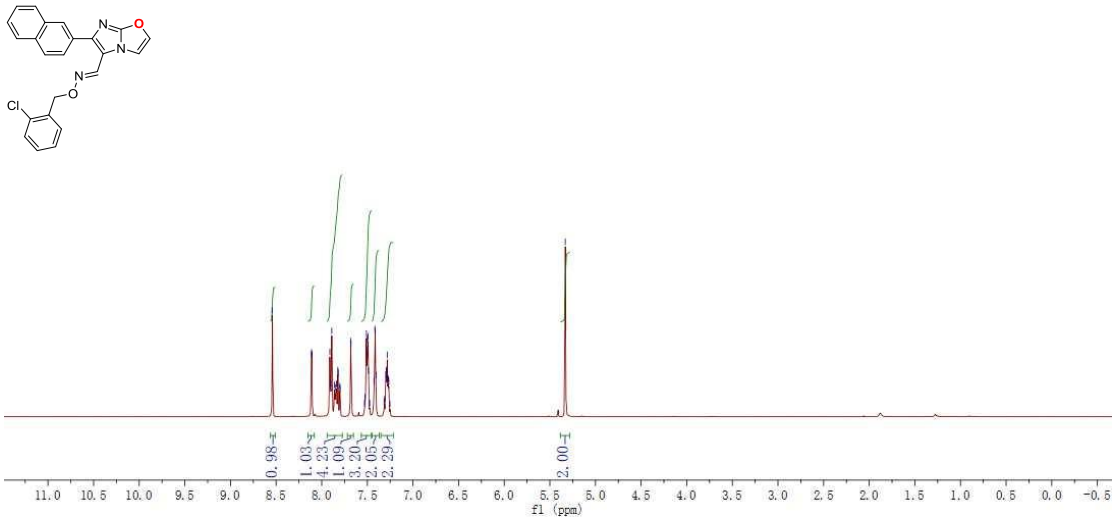
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	9.071	14668	1282	0.000		M	3.358
2	11.714	422166	19748	0.000		M	96.642
Total		436834	21029				100.000

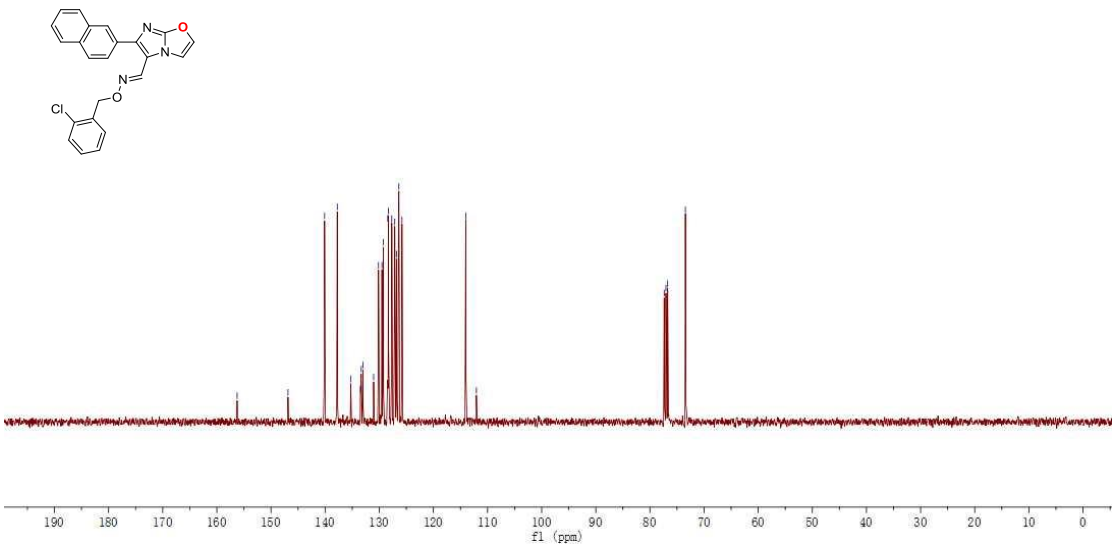
C:\Users\sop\Desktop\Xue Lab\Liang\7221.lcd

Compound **21**


DL5098-2H
DL5098-2H
8.540
8.112
8.108
7.911
7.903
7.890
7.861
7.847
7.838
7.823
7.819
7.802
7.798
7.683
7.679
7.531
7.527
7.515
7.510
7.500
7.491
7.487
7.475
7.428
7.418
7.413
7.405
7.316
7.312
7.298
7.293
7.289
7.282
7.275
7.271
7.265
7.252
5.331


0.98
1.03
4.23
1.09
3.20
2.05
2.29
2.00
f1 (ppm)


DL5098-2C
DL5098-2C
156.25
146.86
140.10
137.76
135.24
133.48
133.33
133.01
131.04
130.14
129.51
129.26
128.44
128.30
127.69
127.14
126.82
126.43
126.38
125.80
114.02
112.06
77.37
77.05
76.73
73.45


f1 (ppm)

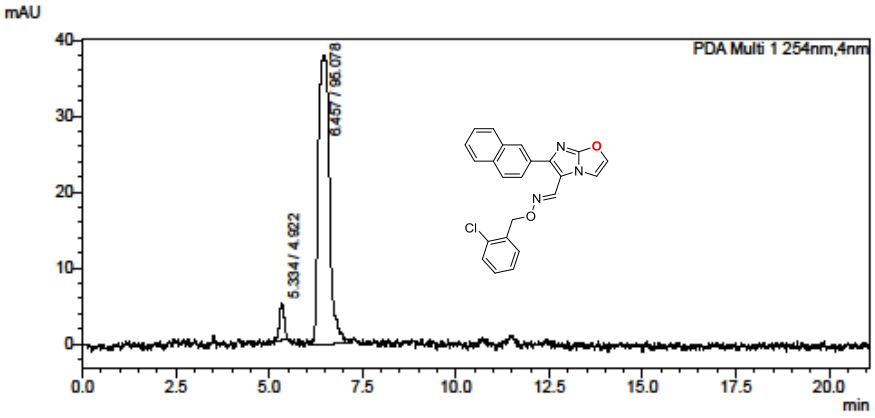
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5098-2		
Sample ID	: 0.8/80		
Data Filename	: 7244.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/23/2018 5:30:52 PM	Acquired by	: System Administrator
Date Processed	: 7/23/2018 5:52:00 PM	Processed by	: System Administrator

<Chromatogram>



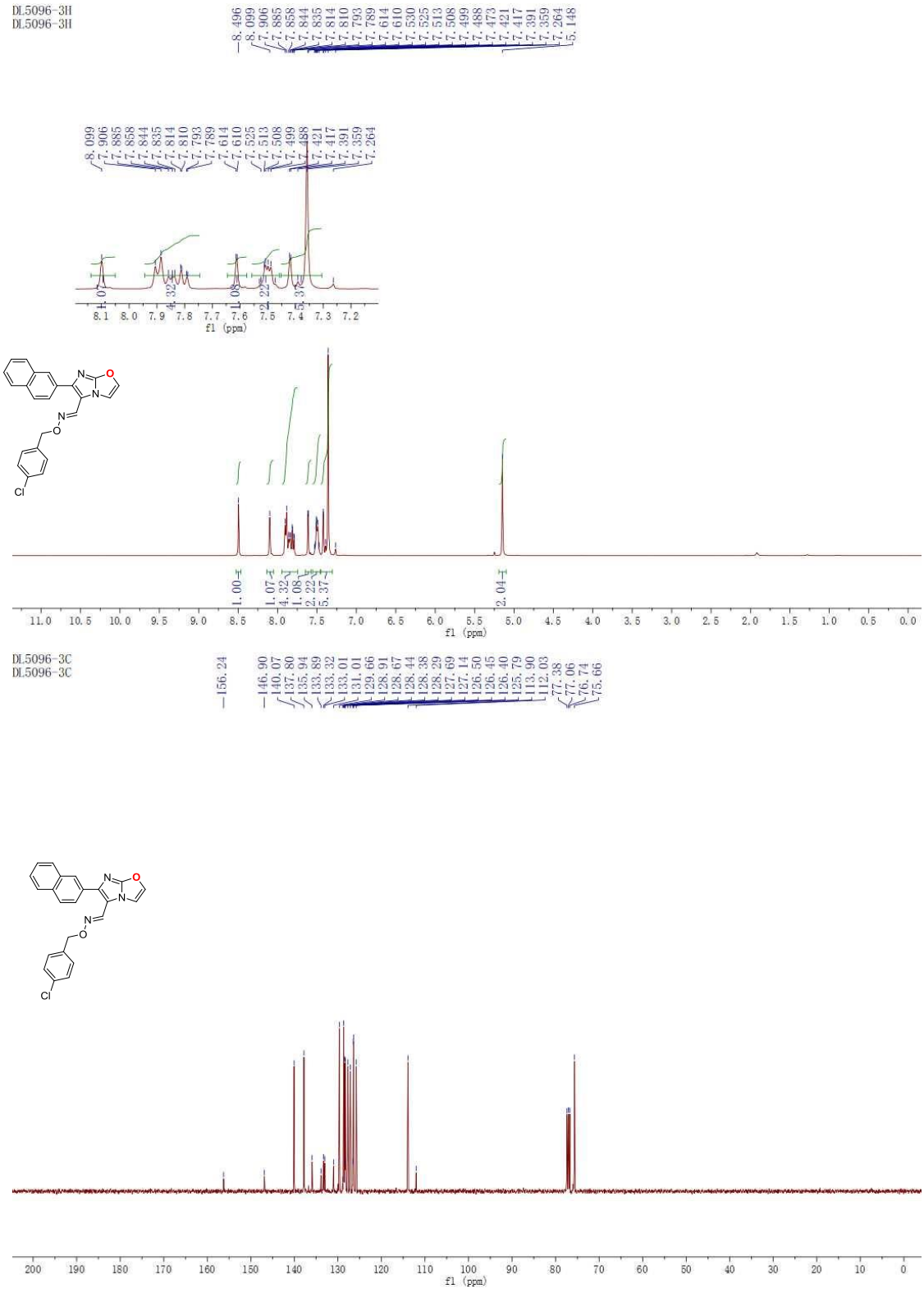
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	5.334	41004	4955	0.000		M	4.922
2	6.457	792005	37940	0.000		M	95.078
Total		833008	42894				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7244.lcd

Compound **22**



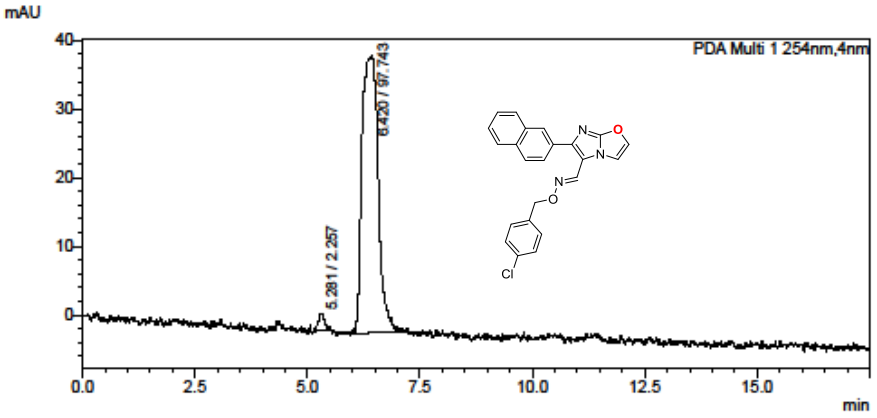
SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: 5096-3		
Sample ID	: 0.8/80		
Data Filename	: 7252.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/25/2018 5:44:00 PM	Acquired by	: System Administrator
Date Processed	: 7/25/2018 6:01:33 PM	Processed by	: System Administrator

<Chromatogram>



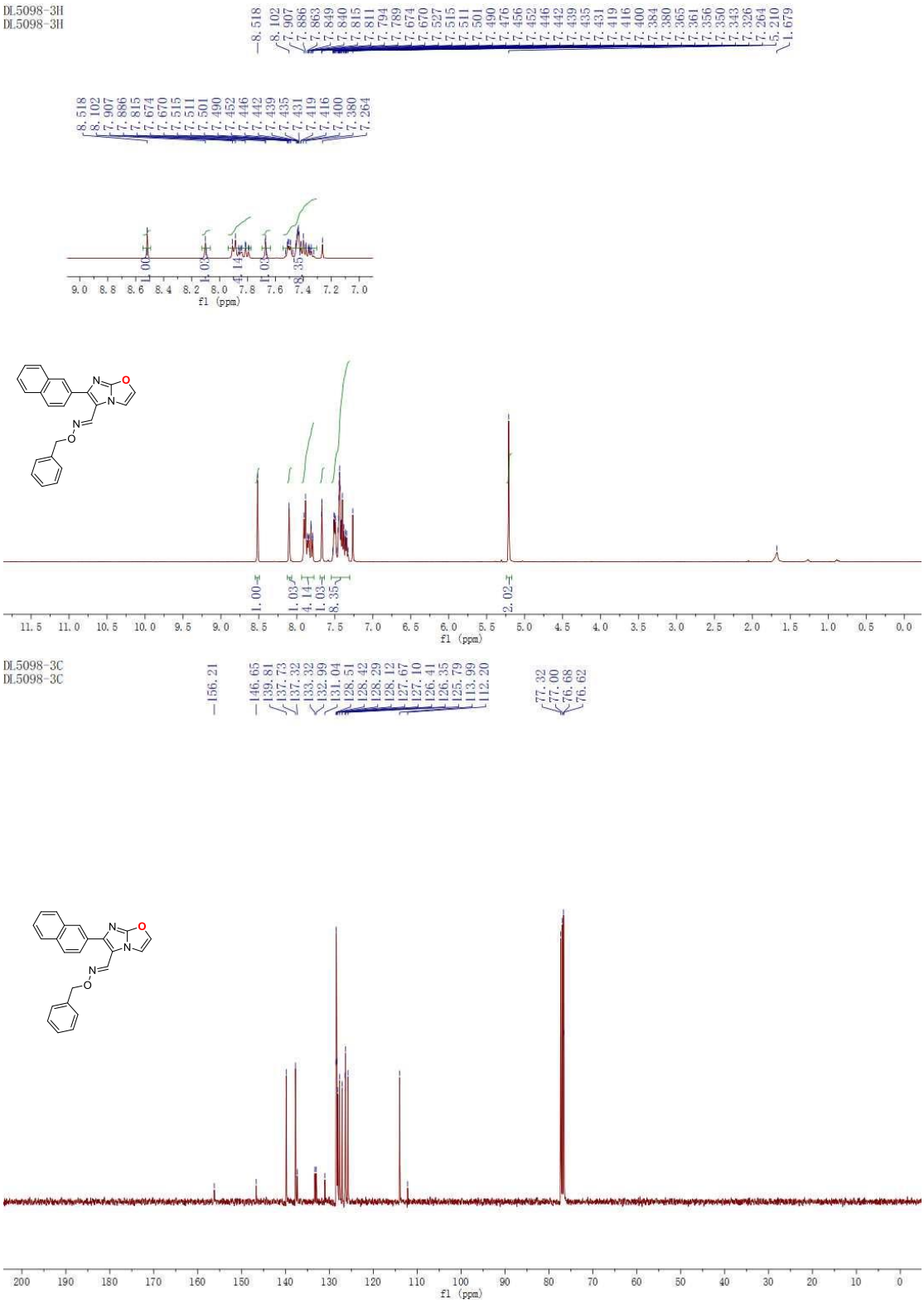
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	5.281	23235	2434	0.000		M	2.257
2	6.420	1006255	40354	0.000		M	97.743
Total		1029490	42788				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7252.lcd

Compound **23**



SHIMADZU LabSolutions

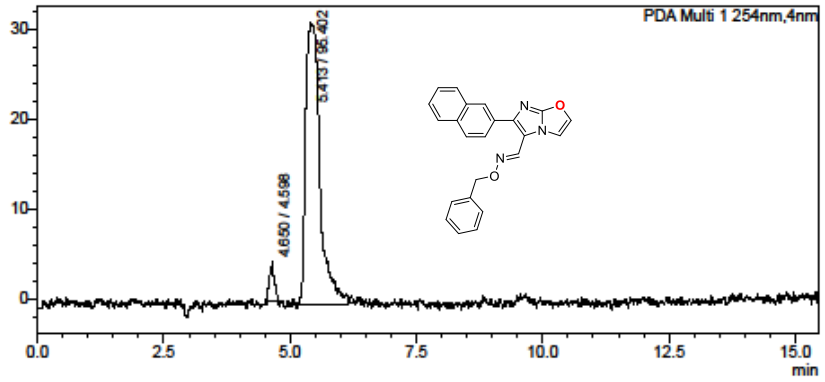
Analysis Report

<Sample Information>

Sample Name	: 5098-3		
Sample ID	: 0.8/80		
Data Filename	: 7235.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 5:55:52 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 6:11:22 PM	Processed by	: System Administrator

<Chromatogram>

mAU



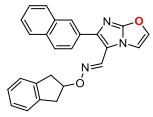
<Peak Table>

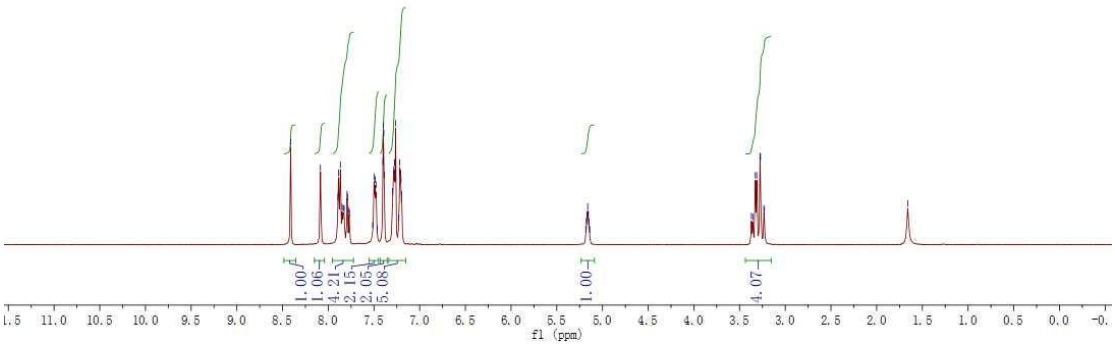
PDA Ch1 254nm

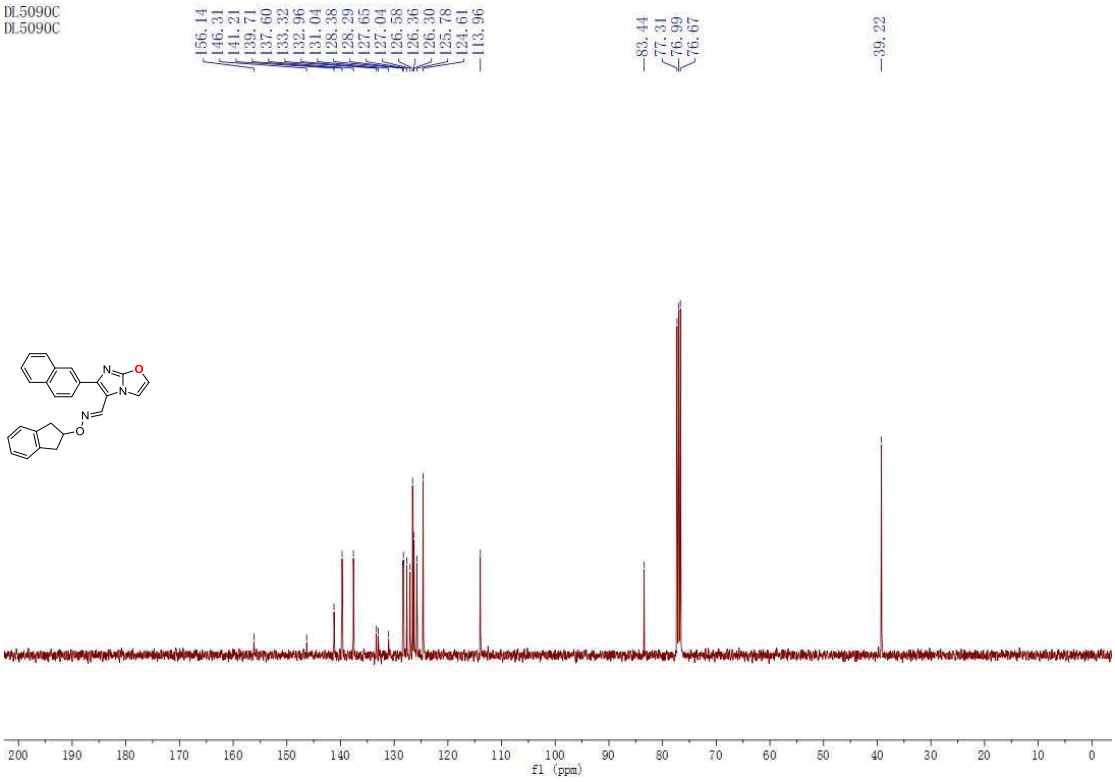
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	4.650	29884	4456	0.000		M	4.598
2	5.413	620116	31292	0.000		M	95.402
Total		650000	35748				100.000

C:\Users\sop\Desktop\Xue Lab\Liang\7235.lcd

Compound **24**







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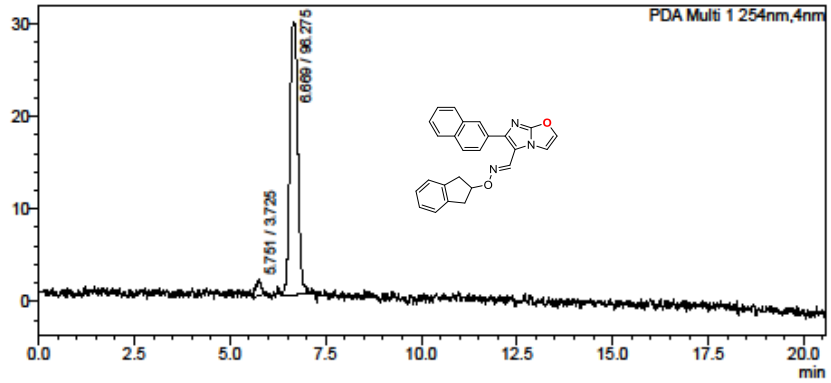
Analysis Report

<Sample Information>

Sample Name	: 5090		
Sample ID	: 0.8/80		
Data Filename	: 7239.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/23/2018 3:56:48 PM	Acquired by	: System Administrator
Date Processed	: 7/23/2018 4:17:23 PM	Processed by	: System Administrator

<Chromatogram>

mAU



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	5.751	16614	1804	0.000		M	3.725
2	6.669	429361	29414	0.000		M	96.275
Total		445975	31218				100.000

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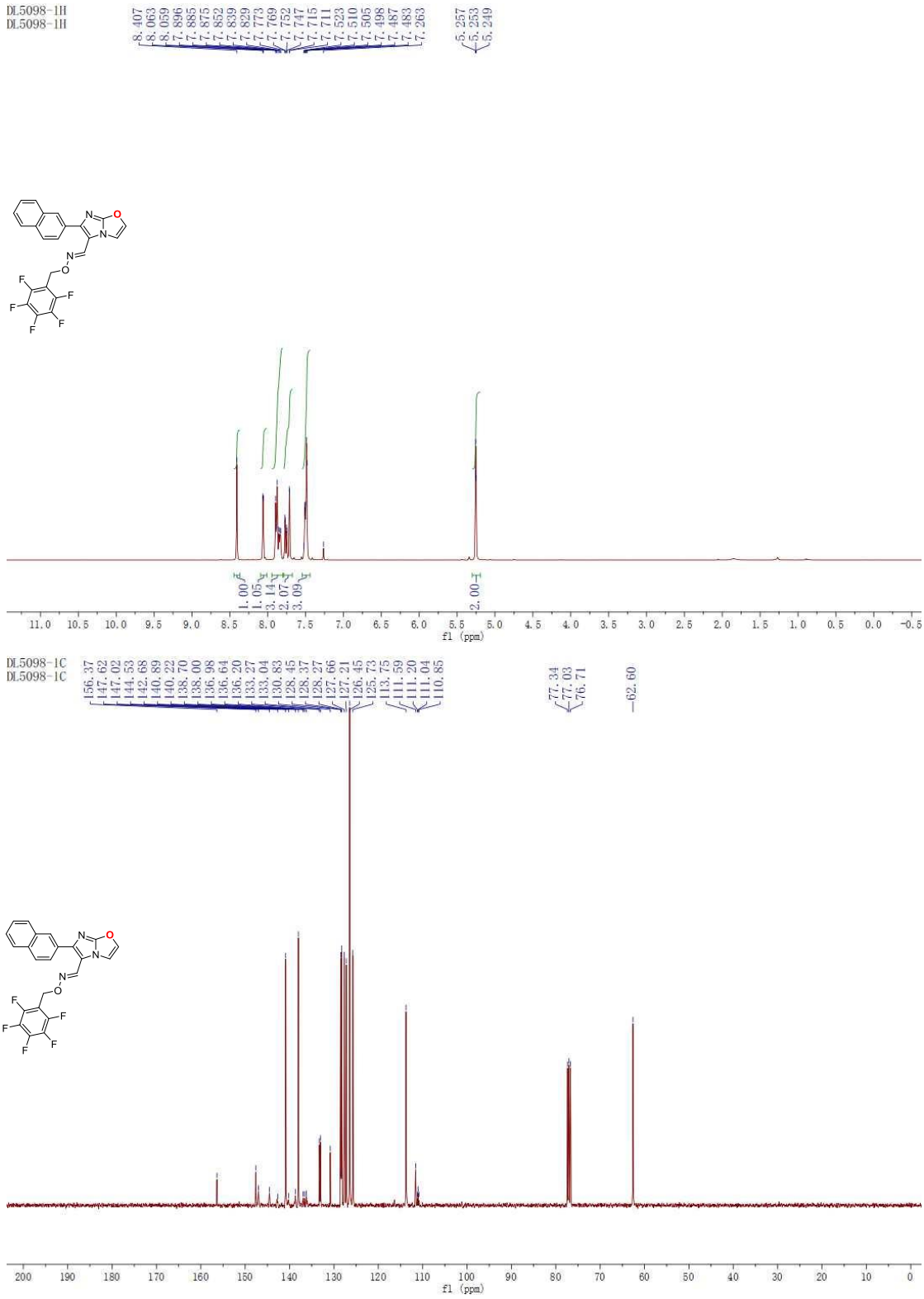
Compound **25**


DL5098-1H
DL5098-1H
8.407
8.063
8.059
7.896
7.885
7.875
7.852
7.839
7.829
7.773
7.769
7.752
7.747
7.715
7.711
7.523
7.510
7.505
7.498
7.487
7.483
7.263
5.257
5.253
5.249
1.00
1.05
3.14
2.07
3.09
2.00
f1 (ppm)
DL5098-1C
DL5098-1C
156.37
147.62
147.02
144.53
142.68
140.89
140.22
138.70
138.00
136.98
136.64
136.20
133.27
133.04
130.83
128.45
128.37
128.27
127.66
127.21
126.45
125.73
113.75
111.59
111.20
111.04
110.85
77.34
77.03
76.71
62.60
f1 (ppm)

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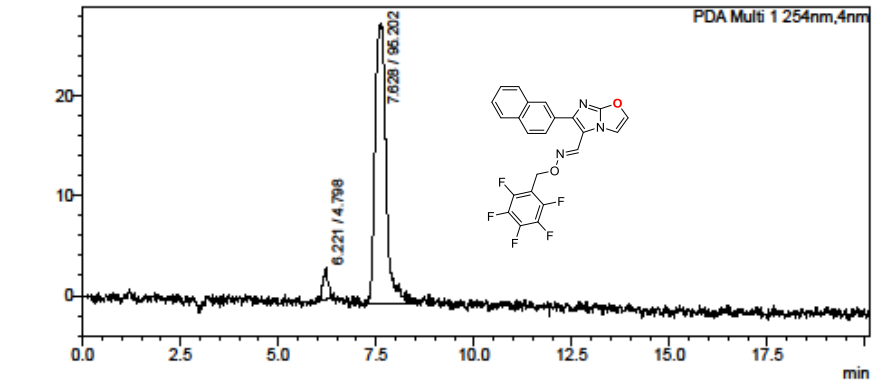
Analysis Report

<Sample Information>

Sample Name	: 5098-1		
Sample ID	: 0.8/80		
Data Filename	: 7234.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 5:34:52 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 5:55:00 PM	Processed by	: System Administrator

<Chromatogram>

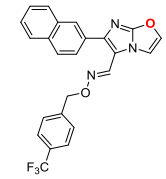


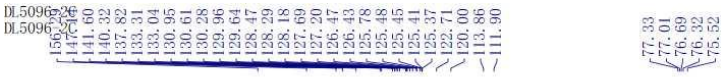
<Peak Table>

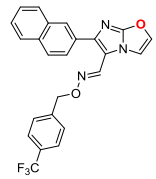
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	6.221	28429	3117	0.000		M	4.798
2	7.628	564032	28063	0.000		M	95.202
Total		592461	31180				100.000

Compound **26**





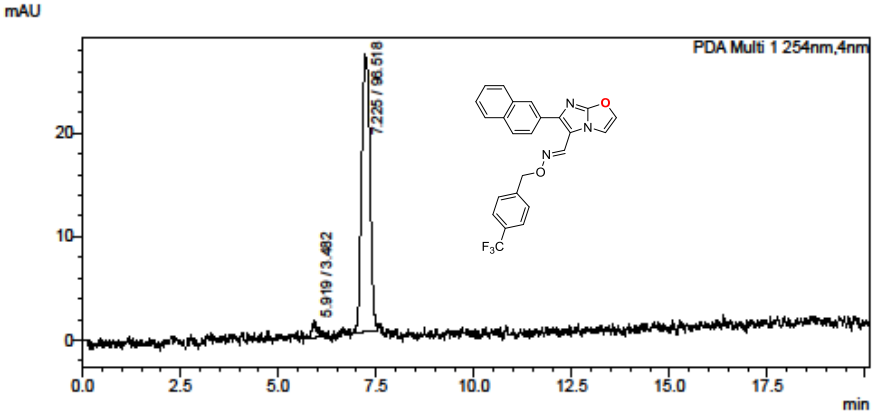


Analysis Report

<Sample Information>

Sample Name	: 5096-2		
Sample ID	: 0.8/80		
Data Filename	: 7217.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/20/2018 2:39:05 PM	Acquired by	: System Administrator
Date Processed	: 7/20/2018 2:59:14 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	5.919	14209	1599	0.000		M	3.482
2	7.225	393901	26812	0.000		M	96.518
Total		408110	28411				100.000

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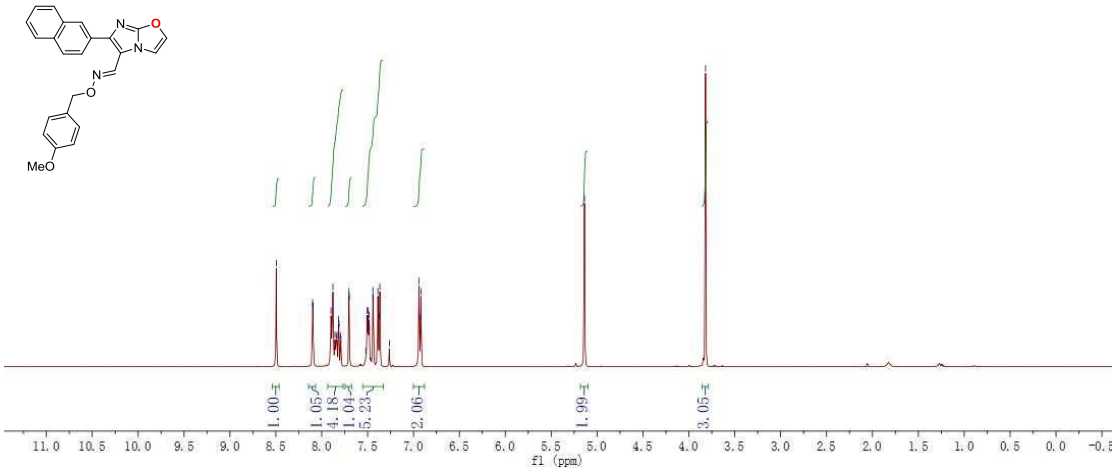
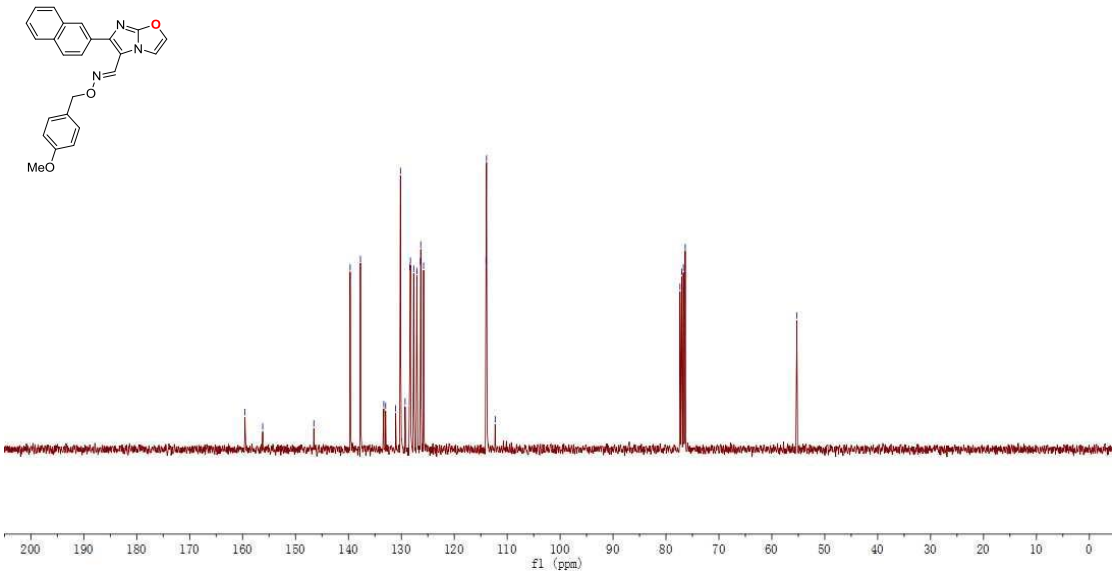
Compound **27**


DL5096-4H
DL5096-4H
8.495
8.100
8.095
7.899
7.878
7.856
7.842
7.833
7.816
7.812
7.795
7.790
7.704
7.700
7.520
7.508
7.504
7.495
7.485
7.481
7.443
7.439
7.388
7.372
7.367
7.263
6.940
6.923
6.919
5.137
3.818


MeO
1.00
1.05
4.18
1.04
5.23
2.06
1.99
3.05
f1 (ppm)


DL5096-4C
DL5096-4C
159.57
156.20
146.54
139.67
137.73
133.32
132.97
131.08
130.17
129.29
128.39
128.29
127.67
127.07
126.40
126.33
125.80
114.01
113.91
112.27
77.35
77.03
76.72
76.36
55.28


MeO
f1 (ppm)

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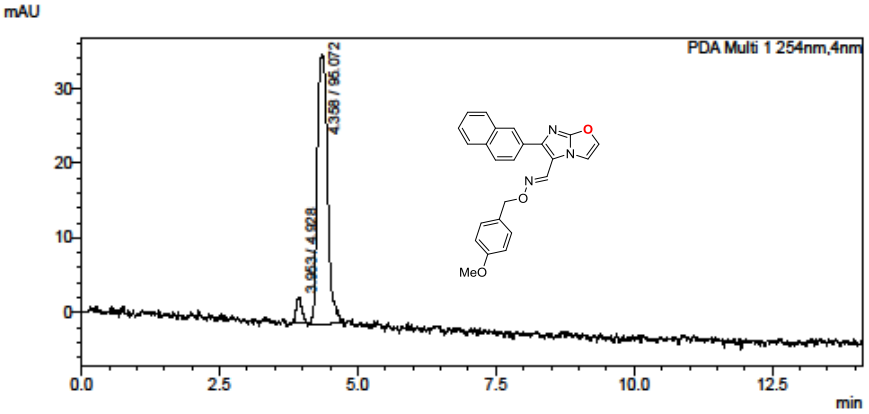
Analysis Report

<Sample Information>

Sample Name	: 5096-4		
Sample ID	: 0.8/80		
Data Filename	: 7268.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 5 uL		
Date Acquired	: 7/26/2018 11:15:05 AM	Acquired by	: System Administrator
Date Processed	: 7/26/2018 11:29:15 AM	Processed by	: System Administrator

<Chromatogram>

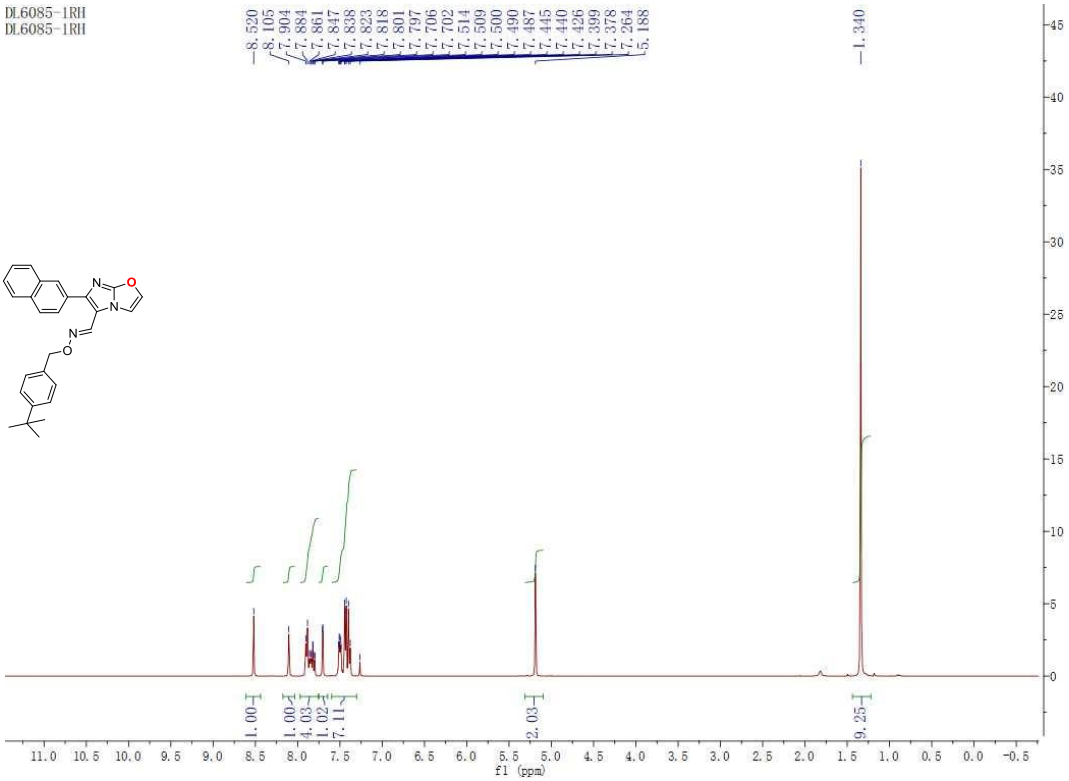


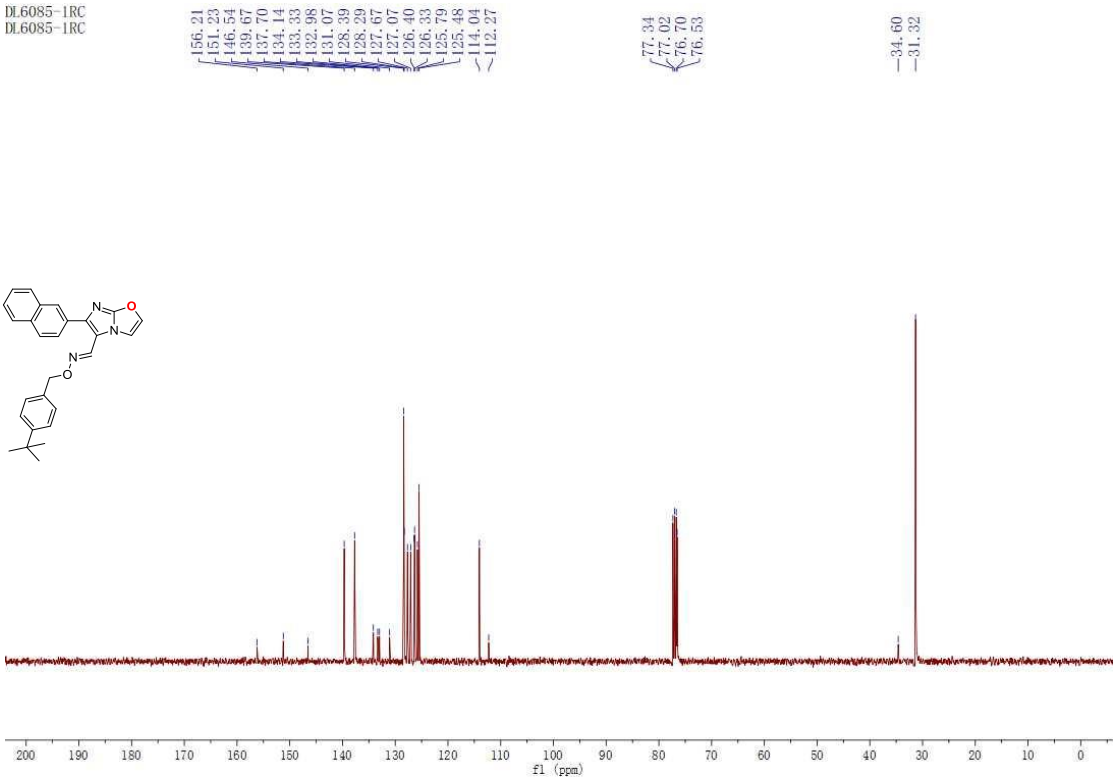
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	3.953	24086	3402	0.000		M	4.928
2	4.358	464707	36073	0.000		M	95.072
Total		488793	39475				100.000

Compound **28**


DL6085-1RH
DL6085-1RH
8.520
8.105
7.904
7.884
7.861
7.847
7.838
7.823
7.818
7.801
7.797
7.706
7.702
7.514
7.509
7.500
7.490
7.487
7.445
7.440
7.426
7.399
7.378
7.264
5.188
1.340
1.00
1.00
4.03
1.02
7.11
2.03
9.25
f1 (ppm)


DL6085-1RC
DL6085-1RC
156.21
151.23
146.54
139.67
137.70
134.14
133.33
132.98
131.07
128.39
128.29
127.67
127.07
126.40
126.33
125.79
125.48
114.04
112.27
77.34
77.02
76.70
76.53
34.60
31.32
f1 (ppm)

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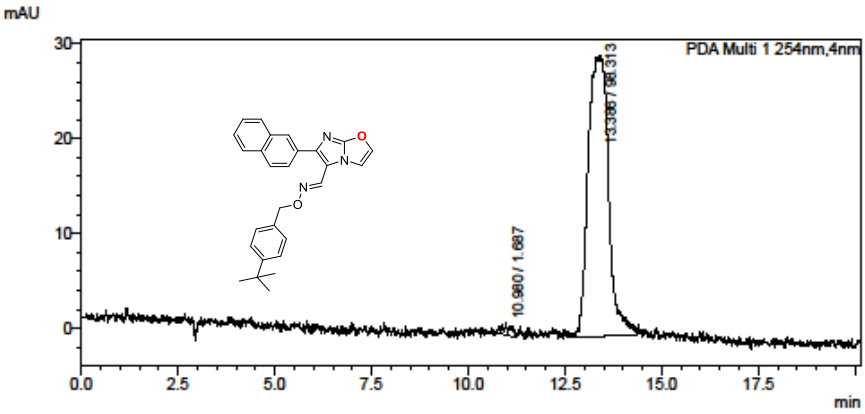
Analysis Report

<Sample Information>

Sample Name	: 6085-1		
Sample ID	: 0.8/80		
Data Filename	: 7231.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 7/22/2018 4:08:10 PM	Acquired by	: System Administrator
Date Processed	: 7/22/2018 4:28:19 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	10.980	18572	1264	0.000		M	1.687
2	13.386	1082286	29564	0.000		M	98.313
Total		1100858	30828				100.000

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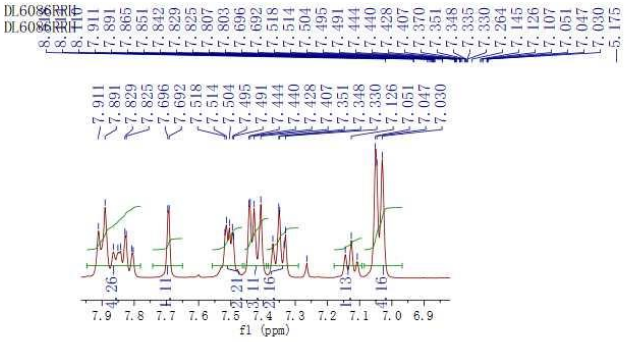
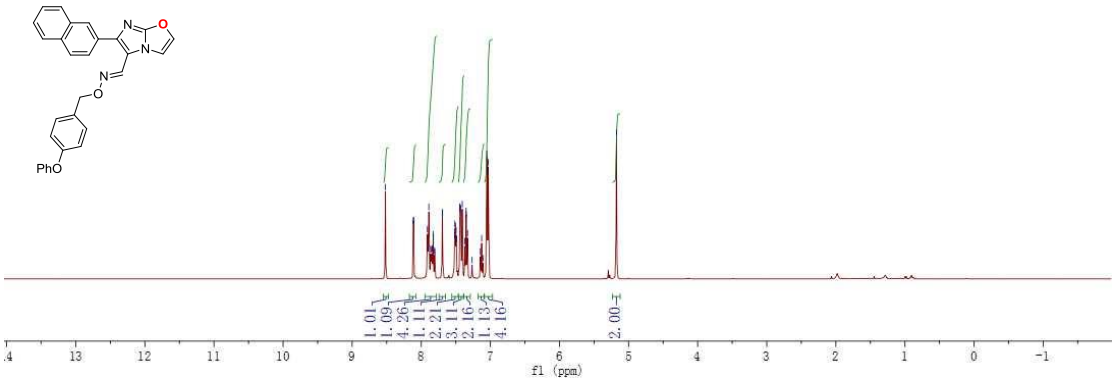
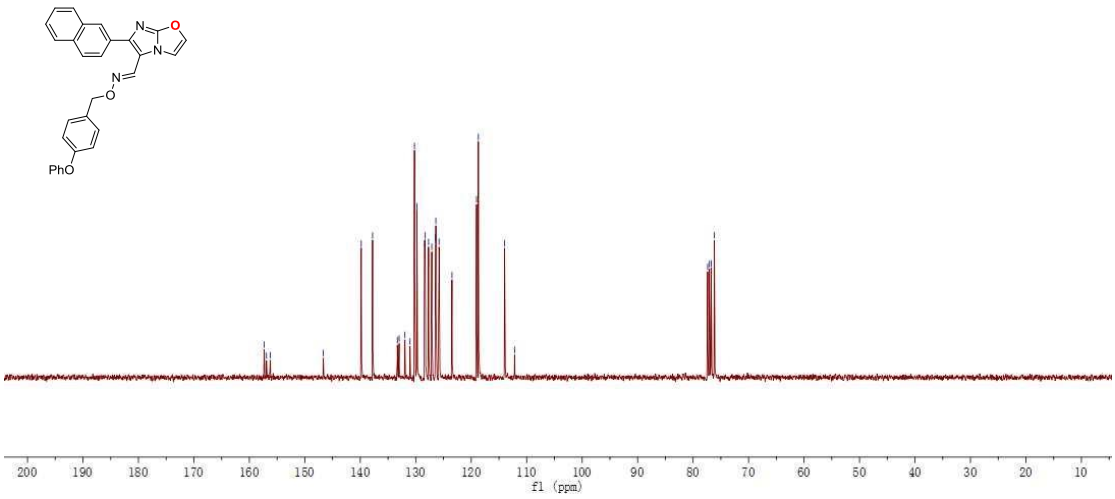
Compound **29**







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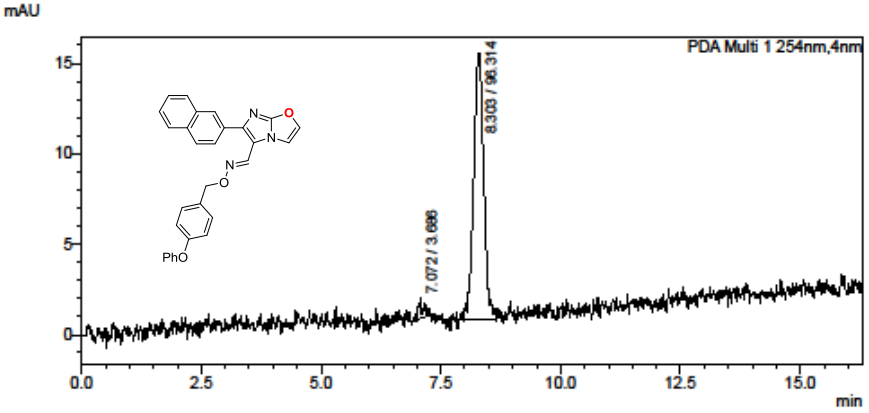
Analysis Report

<Sample Information>

Sample Name	: 6086		
Sample ID	: 0.8/80		
Data Filename	: 7274.lcd		
Method Filename	: DL single run.lcm		
Batch Filename	:		
Vial #	: 1-4	Sample Type	: Unknown
Injection Volume	: 5 uL		
Date Acquired	: 7/26/2018 12:26:15 PM	Acquired by	: System Administrator
Date Processed	: 7/26/2018 12:42:36 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Area%
1	7.072	8338	1188	0.000		M	3.686
2	8.303	217859	14650	0.000		M	96.314
Total		226198	15837				100.000

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12. References

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(2) Andreani, A.; Granaiola, M.; Leoni, A.; Locatelli, A.; Morigi, R.; Rambaldi, M.; Lenaz, G.; Fato, R.; Bergamini, C.; Farruggia, G. *J. Med. Chem.* **2005**, *48*, 3085-3089.

(3) Mekonnen, B.; Crank, G.; Craig, D. *J. Heterocyclic Chem.* **1997**, *34*, 589-599.

(4) Lynch, C.; Zhao, J.; Huang, R.; Xiao, J.; Li, L.; Heyward, S.; Xia, M.; Wang, H. *Sci. Rep.* **2015**, *5*, 10405.

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(6) Mackowiak, B.; Li, L.; Welch, M. A.; Li, D.; Jones, J. W.; Heyward, S.; Kane, M. A.; Swaan, P. W.; Wang, H. *Mol. Pharmacol.* **2017**, *92*, 75-87.