Supporting Information for:

Increasing Saturation: Development of Broadly Applicable Photocatalytic C_{sp2}-C_{sp3} Cross-Couplings of Alkyl Trifluoroborates and (Hetero)Aryl Bromides for Array Synthesis

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Reaction Guide

The following Data Guide was constructed based on observations and the data reported in the manuscript. Reaction parameters and substrate features are listed separately and contain references to the main text where appropriate. The notes have a particular focus on library synthesis; however, these recommendations can also be applied to single reactions. The Data Guide is intended to be a concise, digestible account of the work and should allow for wider adoption of this methodology in the medicinal chemistry community, specifically in a high-throughput setting.

Reaction Parameters			
Component	**Preferred**	**Acceptable**	**Not Compatible**
Ni Catalyst (see Figure 1)	Ni(dtbbpy)Br_2 (preformed) $Ni(NO_3)_2{\cdot}6H_2O$ $NiCl_2{\cdot}6H_2O$ $NiBr_2{\cdot}3H_2O$	$NiI_2{\cdot}xH_2O$ $Ni(OAc)_2{\cdot}4H_2O$	$Ni(acac)_2$
Photocatalyst (see Figure 2)	**[Ir(dF(CF$_3$)ppy)$_2$(bpy)]PF$_6$ (PC1)** **4CzIPN (PC2)** [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ [Ir(dF(Me)ppy)$_2$(dtbbpy)]PF$_6$ **Ir(p-F(t-Bu)ppy)$_3$ (PC3)**	$Ir(dF(t\text{-}Bu)ppy)_3$ $Ir(dFppy)_3$ **[9Mes-NPh-Me$_2$Acr]BF$_4$ (PC4)**	$Ir(ppy)_3$ [Ir(ppy)$_2$(dtbbpy)]PF$_6$ $[Ru(bpy)_3](PF6)_2$ $[Ru(phen)_3](Cl)_2{\cdot}xH_2O$ $[Ru(bpz)_3](PF_6)_2$ $[Ru(DIP)_3](Cl)_2$ [9Mes-NPh-Acr]BF_4 [9Mes-NMe-Acr]BF_4 Eosin Y Eosin B Fluorescein [Ph$_3$Pyryl]BF_4 Rose Bengal Benzophenone Rhodamine 6G
Solvent (see Figures 3 & 4)	Dioxane THF CPME 95:5 Dioxane/*t*-AmOH 80:20 Dioxane/DMAc 95:5 Dioxane/MeOH	*t*-AmOH DMAc NMP MeOH MEK 95:5 MEK/MeOH MeCN DMPU DMF	DMSO
Base (see Figures 3 & 4)	2,6-Lutidine Cs_2CO_3	Pyridine 2,4,6-Collidine K_2HPO_4	Morpholine DABCO DMAP TEA PMP DBU DBN TMG
Light Source	Blue (470 nm)	White (broad)	

(see Figure S2)	Purple (400-415 nm)		
Notes			
Ni Catalyst	• The active catalyst is formed *in situ* with dtbbpy as the ligand • Pre-formed Ni(dtbbpy)Br_2 is preferred for library synthesis • For libraries, the pre-formed Ni catalyst has good solubility in THF and the small amount as co-solvent will not affect the reaction • A Ni catalyst loading of 3 mol % is ideal		
Photocatalyst	• Generally, the preferred photocatalysts have good solubility in MeCN • For libraries, the small percentage of MeCN as a co-solvent should not affect the reaction outcome • The photocatalyst loading should stay around 2 mol % to give the best light penetration		
Solvent	• The reaction tolerates a wide variety of solvents, however, avoid DMSO as the major solvent • Reaction concentration should be ~0.05 M – increasing the concentration limits the trifluoroborate solubility and decreases light penetration • Vigorous stirring (750 RPM+) is required to achieve homogeneous distribution of the reaction components		
Base	• Increasing the equivalents of base (especially if increasing the equivalents of trifluoroborate) can often be beneficial		
Light Source	• Light source compatibility is based on the light sources used in this study with the intensities listed in Table S8 and "General Photoreactor Setup" (*vide infra*) • Purple LEDs (415 nm) give the highest P/IS ratios – the wavelength overlaps well with the photocatalyst absorbance, giving faster reactions rates and completed reactions in ~24 hours • Blue LEDs (470 nm) are comparable but can require extended reactions times (40+ hours) to achieve full conversion • White light (CFL bulb) has no advantages over the other light sources available		
Substrates			
Component	**High Conversion**	**Acceptable Conversion**	**Low to No Conversion**
Alkyl Trifluoroborate (see Figures 5 & 7)	Benzyl (**1a**) Isopropyl (**1c**) Cyclohexyl (**1f**) Tetrahydropyran-4-yl (**1i**) 2-(Trimethylsilyl) ethoxymethyl (**1j**) Benzyloxymethyl (**1k**) 4-Fluorobenzyl (**1n**) 4-Methoxybenzyloxymethyl (**1o**) Methoxymethyl (**1p**) Isopropoxymethyl (**1q**) 1-Boc-pyrrolidin-2-yl (**1u**)	1-Boc-piperdin-4-yl (**1b**) Cyclobutyl (**1g**) *tert*-Butoxymethyl (**1l**) Cyclopentyl (**1e**) *sec*-Butyl (**1m**) 4-(Tetrahydropyranyl methoxy)methyl (**1r**)	Cyclopropyl (**1d**) *tert*-Butyl (**1h**) Acetoxymethyl (**1t**) 2-(Dimethylamino) Ethoxymethyl (**1s**)
Aryl Halide (see Figure 6)	Electron neutral arenes Electron deficient arenes	Electron rich arenes	Certain basic heteroarenes
Functional Groups (see Figures 6 & 7;	Nitrile Trifluoromethyl Boc-protected amine	Terminal alkyne Aliphatic alcohol	Terminal alkene Tertiary anilide Primary aryl amine

Table 1)	Chloro Methyl ester Methyl Methoxy Alkyl chloride Ketone Internal alkyne Phenol Aromatic aldehyde		
Heterocycles (see Figures 6 & 7; Table 1)	Pyridine Quinoline Isoquinoline 2-Butylthiophene Benzofuran Benzo[d]thiazole 4-Methylthiazole 4H-Chromen-4-one	Indole *N*-Benzylpyrrole Benzo[d]oxazole	Unprotected pyrazole *N*-Pivaloylpyrrole 2-Chloropyrimidine 1-Methyl-1H-imidazole 1-Methyl-1H-indole 2-Chloroquinoline
Notes			
Alkyl Trifluoroborate	• For best results, use 2.0 or more equiv of trifluoroborate		
Aryl Halide	• Aryl bromides provide the highest RAP of product • For library reaction setup, if the aryl halide core has poor solubility, weighing individually into each reaction vessel or dosing as an adequately suspended slurry may be necessary – in this case, the base should be added individually to each reaction instead of adding to the stock solution		
Functional Groups	• Functional group compatibility was determined from considering both the substrate scope and robustness study; substrate analysis on a case-to-case basis can be extrapolated from the data provided		
Heterocycles	• Heterocycle compatibility was determined from considering both the substrate scope and robustness study; substrate analysis on a case-to-case basis can be extrapolated from the data provided		

Additional References

These references are provided to supplement those in the main body of the manuscript with reference numbers in parentheses corresponding to those included there.

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Abbreviations

96WP, 96-well plate; CFL, compact fluorescent light bulb; CPME, cyclopentyl methyl ether; DABCO, 1,4-diazabicyclo[2.2.2]octane; DBN, 1,5-diazabicyclo[4.3.0]non-5-ene; DBU, 1,8-diazabicycloundec-7-ene; DMAc, *N,N*-dimethylacetamide; DMAP, *N,N*-dimethylaminopyridine; DMF, *N,N*-dimethylformamide; DMPU, *N,N'*-dimethylpropyleneurea; DMSO, dimethyl sulfoxide; GC/FID, gas chromatography with flame-ionization detection; HTE, high-throughput experimentation; LED, light-emitting diode; MeCN, acetonitrile; MEK, methyl ethyl ketone or 2-butanone; MeOH, methanol; NMP, *N*-methylpyrrolidinone; PMP, 1,2,2,6,6-pentamethylpiperidine; RAP, UHPLC-MS relative area percent; SAR, structure-activity relationships; *t*-AmOH, *tert*-amyl alcohol or 2-methyl-2-butanol; TEA, trimethylamine; THF, tetrahydrofuran; TMG, 1,1,3,3-tetramethylguanidine; UHPLC-MS, ultra high performance liquid chromatography-mass spectrometry.

General Information

All reagents and catalysts were used as received from commercial sources. The preformed Ni(dtbbpy)Br_2 complex was prepared using literature procedures.[1] Potassium alkyl trifluoroborate salts were purchased from Combi-Blocks (**1a**, **1c**, **1d**, **1e**, **1f**, **1g**, **1h**, **1i**, **1j**, **1k**, **1l**, **1n**, **1o**, **1p**, **1q**, **1r**, **1s**, **1t**, **1u**), Frontier Scientific Services (**1b**), or Sigma-Aldrich (**1m**).

Ni Precatalyst Cost Information[2]

Name	CAS	MW	Vendor	Part No.	Quantity (g)	Cost ($)	Cost ($/g)	Cost ($/kg)	Cost ($/mol)
$Ni(COD)_2$	1295-35-8	275.06	Strem	28-0010	10	$298	$29.80	$29,800	$8,197
$NiCl_2$·DME	29046-78-4	219.72	AmBeed	A875498	25	$223	$8.92	$8,920	$1,960
$Ni(NO_3)_2·6H_2O$	13478-00-7	290.79	Chem-Impex	24615	5,000	$224	$0.04	$45	$13
$NiCl_2·6H_2O$	7791-20-0	237.69	Chem-Impex	01459	25,000	$1,848	$0.07	$74	$18
$NiBr_2·3H_2O$	7789-49-3	272.55	Aldrich	72243	1,000	$467	$0.47	$467	$127
$NiI_2·xH_2O$	7790-34-3	312.49	Combi-Blocks	HG-3944	25	$195	$7.80	$7,800	$2,437
$Ni(OAc)_2·4H_2O$	6018-89-9	248.84	Chem-Impex	30281	10,000	$830	$0.08	$88	$22
$Ni(acac)_2$	3264-82-2	256.91	Chem-Impex	26725	5,000	$1,596	$0.32	$319	$82

Equipment List

Microscale reactions (HTE, Robustness Study) were carried out in a Para-dox photoredox 96-well plate (Analytical Sales and Services, Cat. No. 96973) irradiated by a Lumidox or Lumidox UV 96-well LED array (Analytical Sales and Services; violet – 415 nm, LUM96-415; blue – 470 nm, LUM96B; white – broad spectrum, LUM96W) and controlled with a Lumidox controller (Analytical Sales and Services, LUMCON; operated at 30 mA current for blue and white LED arrays) or Lumidox UV controller (Analytical Sales and Services, LUMCON-UV; operated at 20 mA current for violet LED array). Solvent was removed from microscale reactions using a Genevac HT-4X evaporator. Solutions were dosed into vials with a digital microdispenser (VWR; 20-100 µL dispenser, 53506-201; 100 µL capillaries, 53508-499). Microscale reaction stirring was done on a Freeslate CM3 automation system. Shimadzu LCMS-2020 mass spectrometer was used for UHPLC-MS analysis. Absorbance measurements were recorded with a Shimadzu UV-2600 and spectral irradiances were measured with a Black-Comet SR concave grating spectrometer (StellarNet). Gas chromatography for the Robustness additives was carried out with an Agilent 6890 Plus GC with Autosampler. Chemical libraries were irradiated with Toogod Flexible Light LED Strip (5 m – 16.4 ft. DC 12V 300 pcs.) in either UV Black (purple) or Blue. Solvent was removed from chemical library reactions with a Zymark TurboVap or Genevac HT-12. Analytical LC-MS for chemical libraries was carried out on a Shimadzu Nexera Series 30 UHPLC with LCMS-2020 and purification was done using a Shimadzu Preparative LC-8A or LC-20 with LCMS-2020. Proton NMR spectra were recorded on a Bruker Avance III 500 MHz instrument, and are referenced to residual, undeuterated solvents (DMSO-d_6: δ 2.50). The following abbreviations are used to explain multiplicities: br = broad, s = singlet, d = doublet, t = triplet, m = multiplet. Flow photochemistry was conducted using a Vapourtec E series flow reactor (Part No. 50-1336) with UV-150 Photochemical Reactor (10 mL reactor coil, Part No. 50-1580) and standard high efficiency purple LEDs (420 nm, 18 W, Gen-1, Part No. 50-1445).

Safety Note

The lamps used to promote photocatalysis produce light at wavelengths that are potentially harmful. Appropriate eyewear that blocks the wavelength of light used and appropriately colored gels or plastic shields (orange for the blue and purple wavelengths used in this work) between the light source and the chemist are recommended.

General Analytical Methods

Microscale reactions (HTE, Robustness Study) and Flow Chemistry were analyzed by UHPLC-MS with detection by UV at 220 nm and low resolution mass spectrometry detection (positive ion mode). Injection conditions: Column: Waters Acquity BEH C8 1.7 um 2.1 x 50 mm; Injection Volume = 1.0 µL; Mobile Phase A: 5:95 MeCN:H_2O with 0.05% TFA; Mobile Phase B: 95:5 MeCN:H_2O with 0.05% TFA; Temp. = 40 °C; Gradient: 0% B to 100% B over 2 min., then a 0.5 min. hold at 100% B; Flow: 1 mL/min.

Robustness additives were analyzed by GC with detection by FID at 320 °C. Injection Conditions: Inlet Temp. = 250 °C; Column: Restek Rti-624Sil MS 20 m x 0.18 mm x 1.0 µm; Injection Volume = 0.50 µL; Carrier Gas/Flow Rate: Helium at 1.4 mL/min. constant flow; Injection Mode: Split injection, 70:1 split ratio; Inlet Liner: Restek Topaz Low Pressure Drop Liner, deactivated with wool; Run Time = 20 min.; Oven Program: 50 °C/0.5 min., 20 °C/min., 300 °C/7 min.

Chemical Libraries were purified via preparative LC-MS with the following conditions: Column: XBridge C18, 200 mm x 19 mm, 5 µm particles; Injection Volume = 2 mL; Mobile Phase A: 5:95 MeCN:H_2O with 10 mM ammonium acetate or 0.05% TFA; Mobile Phase B: 95:5 MeCN:H_2O with 10 mM ammonium acetate or 0.05% TFA; Gradient: a 0 min. hold at 20% B, 20-60% B over 20 mins., then a 0 min. hold at 100% B; Flow Rate: 20 mL/min.; Column Temp. = 25 °C; Detection: UV (220 nm) and fraction collection was triggered by MS signal. Fractions containing the desired product were combined and dried using a Genevac evaporator. Analytical LC-MS was used to determine the final purity of the chemical library compounds. Injection conditions: **Method A**: Column: Waters XBridge C18, 2.1 mm x 50 mm, 1.7 µm particles; Injection Volume = 2.0 µL; Mobile Phase A: 5:95 MeCN:H_2O with 10 mM ammonium acetate; Mobile Phase B: 95:5 MeCN:H_2O with 10 mM ammonium acetate; Temp. = 50 °C; Gradient: 0% B to 100% B over 3 min., then a 0.5 min. hold at 100% B; Flow: 1 mL/min.; Detection: MS and UV (220 nm). **Method B**: Column: Waters XBridge C18, 2.1 mm x 50 mm, 1.7 µm particles; Injection Volume = 2.0 µL; Mobile Phase A: 5:95 MeCN:H_2O with 0.1% TFA; Mobile Phase B: 95:5 MeCN:H_2O with 0.1% TFA; Temp. = 50 °C; Gradient: 0% B to 100% B over 3 min., then a 0.5 min. hold at 100% B; Flow: 1 mL/min.; Detection: MS and UV (220 nm).

Supplementary HTE Data

General Procedure for High-throughput Experimentation

Microscale high-throughput experiments were carried out in a nitrogen-filled glovebox. To a Para-dox plate containing empty 1 mL vials (borosilicate glass, 8 x 30 mm OD) in each well was added a stock solution of photocatalyst (0.002 M in DCM or MeCN, 100 µL, 2 mol %) and the solvent was removed using a Genevac evaporator. Stock solutions of Ni precatalyst (0.003 M in THF-inhibitor free, 3 mol %) and ligand (0.003 M in THF-inhibitor free, 3 mol %) were prepared and equal volumes of each solution were mixed and allowed to ligate for 20 min with gentle shaking. 100 µL of the combined solution was added along with a stock solution of aryl bromide (if solid; liquid aryl bromides were added with reaction solvent at the end of the setup; 0.100 M in THF-inhibitor free, 100 µL, 10 µmol) and the solvent was removed. Next, a stock solution of potassium alkyl trifluoroborate (0.120 M in acetone, 100 µL, 12 µmol) was added and the solvent removed using a Genevac. After completely drying, microstir bars were added. Then, solid inorganic base was added with a digital microdispenser. Finally, stock solutions of reaction solvent (100 µL) with liquid base (0.350 M) and in some cases, aryl bromide (0.100 M) were added to the appropriate wells. 100 µL of solvent was added to wells with inorganic base. The plate was then sealed under N_2 with a sheet of perfluoroalkoxy (PFA) film, two rubber mats and a metal lid, and the contents were stirred (300 RPM tumble stirring) on a Freeslate CM3 automation system at 20 °C for 16 h. The reactions were irradiated with a Lumidox or Lumidox UV 96-well LED array controlled by Lumidox or Lumidox UV controller. After reaction completion, 200 µL of a 2 mg/mL solution of 4,4'-dimethylbiphenyl in MeCN was added to the wells as internal standard (IS) and the mixture was further diluted with 50:50 MeCN:H_2O (200 µL). The contents were thoroughly mixed and an aliquot (25 µL) was added to a 96-well filter plate (0.7 µm PPE, Agilent 200937-100) and further diluted with 50:50 MeCN:H_2O (500 µL). The plate containing the filtered samples was then subject to UHPLC-MS analysis with results displayed as P/IS[3] or RAP.

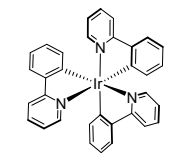
Table S1. $Ni(NO_3)_2$•$6H_2O$ vs. $Ni(COD)_2$ for 23 photocatalyst and no photocatalyst control reaction.[a]

Photocatalyst	**$Ni(COD)_2$**	**$Ni(NO_3)_2$•$6H_2O$**
No Photocatalyst	0.00	0.00
$Ir(ppy)_3$	0.07	0.29
$Ir(dFppy)_3$	0.42	3.74
$Ir(p\text{-}F(t\text{-}Bu)ppy)_3$	3.02	4.71
$Ir(dF(t\text{-}Bu)ppy)_3$	0.97	3.26
$[Ir(ppy)_2(dtbbpy)]PF_6$	1.34	2.42
$[Ir(dF(Me)ppy)_2(dtbbpy)]PF_6$	4.00	5.00
$[Ir(dF(CF_3)ppy)_2(bpy)]PF_6$	3.59	4.82
$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	4.95	4.58
$[Ru(bpy)_3](PF_6)_2$	0.08	0.05
$[Ru(phen)_3](Cl)_2 \cdot xH_2O$	0.09	0.07
$[Ru(bpz)_3](PF_6)_2$	0.39	0.83
$[Ru(DIP)_3](Cl)_2$	0.11	0.07

[9Mes-NPh-Acr]BF_4	0.22	0.35
[9Mes-NPh-Me_2Acr]BF_4	0.96	1.66
[9Mes-NMe-Acr]BF_4	0.46	0.86
Eosin Y	0.11	0.07
Eosin B	0.04	0.04
Fluorescein	0.79	0.49
[Ph_3Pyryl]BF_4	0.05	0.06
4CzIPN	2.69	4.63
Rose Bengal	0.01	0.06
Benzophenone	0.06	0.06
Rhodamine 6G	0.30	0.31

[a]Reaction conditions: 5-bromoquinoline (**2**, 10 μmol) and potassium benzyltrifluoroborate (**1a**, 1.2 equiv) with 2 mol % [PC], 3 mol % [Ni], 3 mol % 4,4'-di-*tert*-butyl-2,2'-bipyridine (dtbbpy), 2,6-lutidine (3.5 equiv), and dioxane (0.1 M). Reactions were monitored by UHPLC-MS with results displayed as P/IS.

Figure S1. Photoredox catalyst structures.[4]



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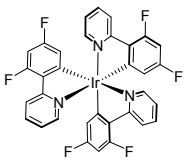

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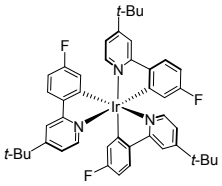

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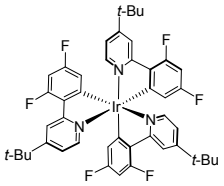

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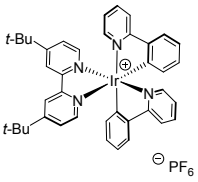

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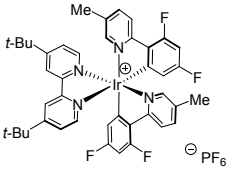

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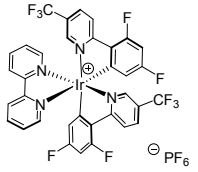

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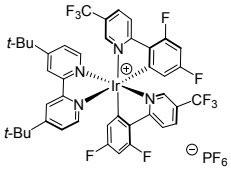

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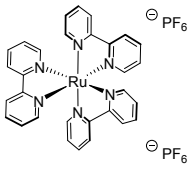

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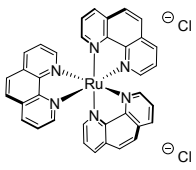
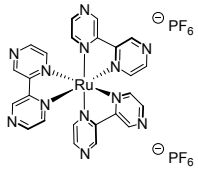
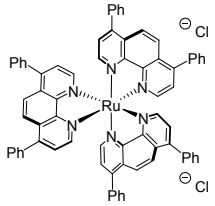


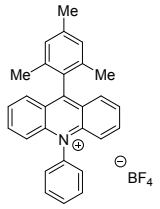
[Ru(phen)$_3$](Cl)$_2$ •H$_2$O
CAS 207802-45-7



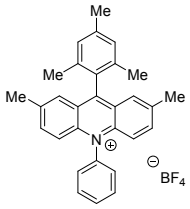
[Ru(bpz)$_3$](PF$_6$)$_2$
CAS 80907-56-8



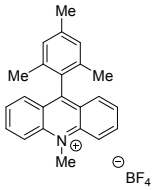
[Ru(DIP)$_3$](Cl)$_2$
CAS 36309-88-3



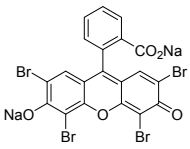
[9Mes-NPh-Acr]BF$_4$
CAS 1621019-96-2



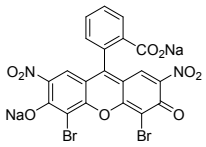
[9Mes-NPh-Me$_2$Acr]BF$_4$
CAS 1621020-00-5



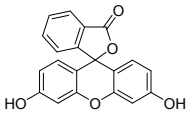
[9Mes-NMe-Acr]BF$_4$
CAS 1442433-71-7



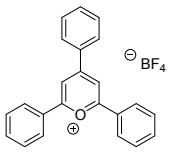
Eosin Y
CAS 17372-87-1



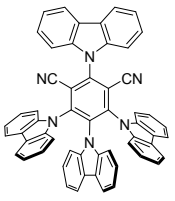
Eosin B
CAS 548-24-3



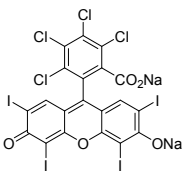
Fluorescein
CAS 2321-07-5



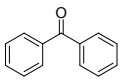
[Ph$_3$Pyryl]BF$_4$
CAS 448-61-3



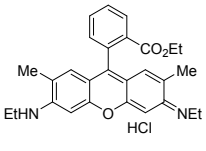
4CzIPN
CAS 1416881-52-1



Rose bengal
CAS 632-69-9

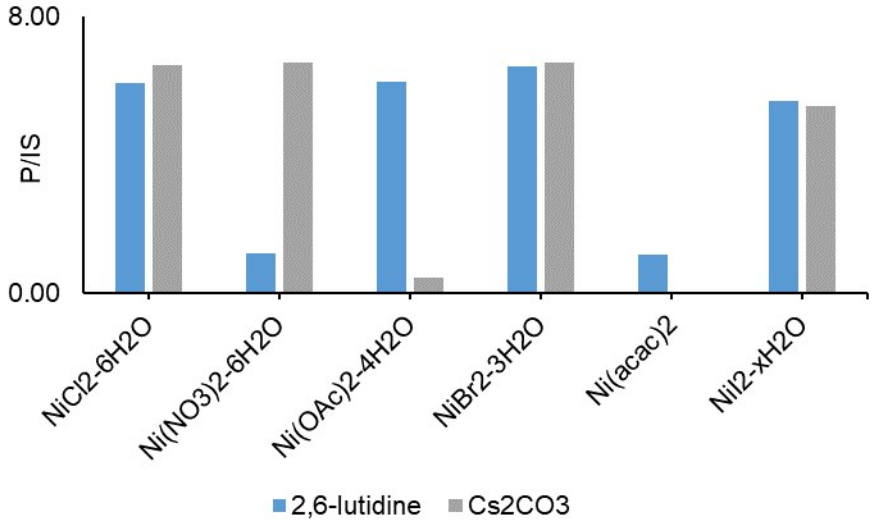


Benzophenone
CAS 119-61-9



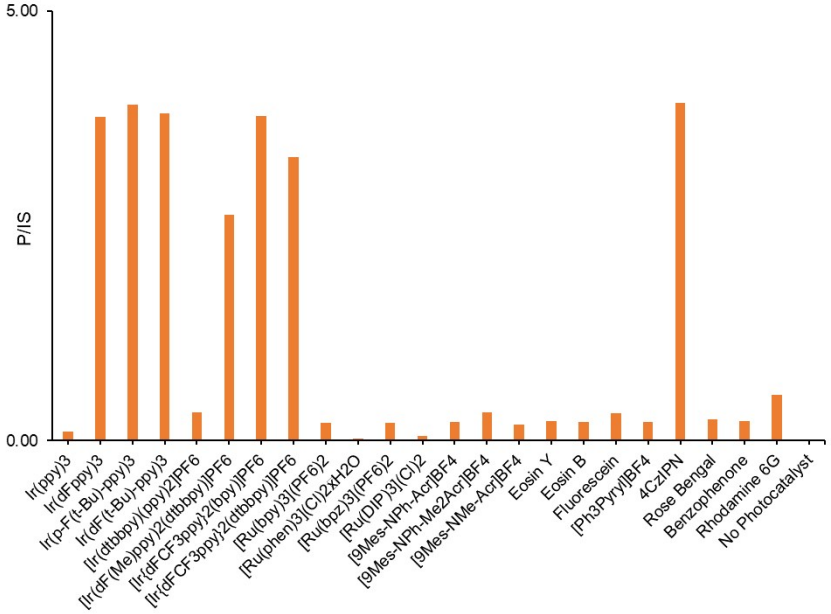
Rhodamine 6G
CAS 989-38-8

Table S2. Hydrated Ni(II) salts as Ni precatalysts with 4CzIPN as photocatalyst.[a]

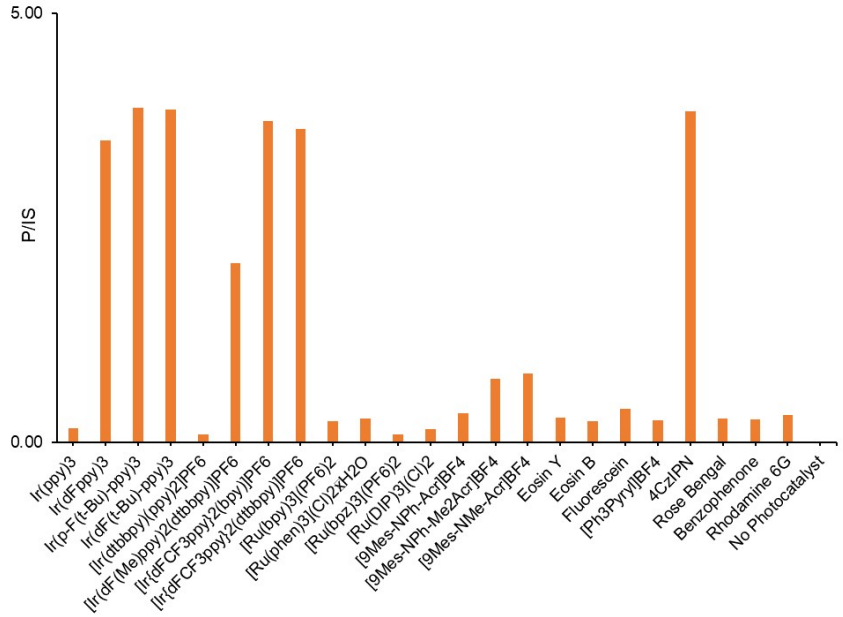


[a]Reaction conditions: **2** (10 μmol) and **1a** (1.2 equiv) with 2 mol % 4CzIPN, 3 mol % [Ni], 3 mol % dtbbpy, 2,6-lutidine (3.5 equiv) or Cs_2CO_3 (1.5 equiv), and dioxane (0.1 M). Reactions were monitored by UHPLC-MS with results displayed as P/IS.

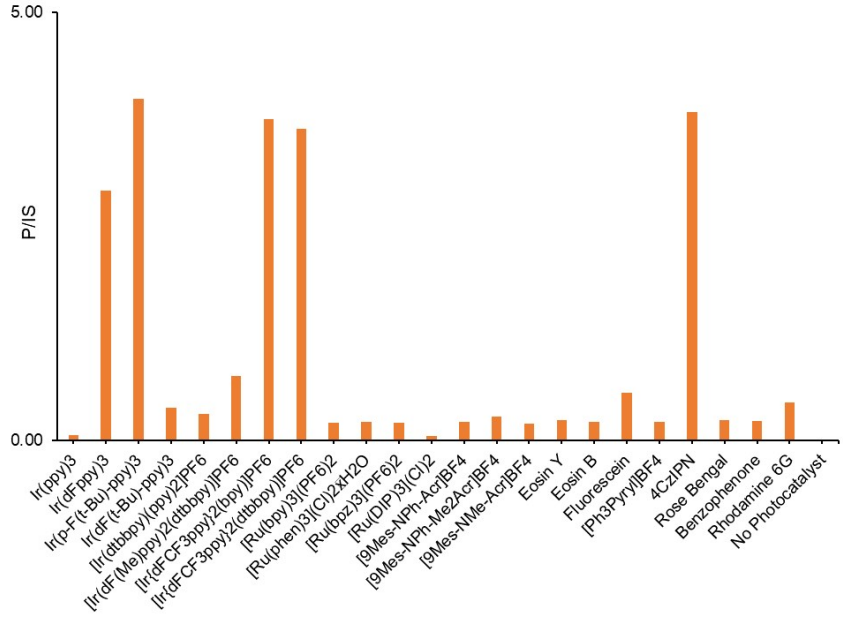
Table S3. Additional reaction conditions tested for photocatalyst screen.[a,b,c]



[a]Reaction conditions: **2** (10 μmol) and potassium 1-Boc-piperidin-4-yl trifluoroborate **1b** (1.2 equiv) with 2 mol % [PC], 3 mol % $Ni(NO_3)_2$•$6H_2O$, 3 mol % dtbbpy, Cs_2CO_3 (1.5 equiv), and dioxane (0.1 M) using blue LEDs (470 nm). Reactions were monitored by UHPLC-MS with results displayed as P/IS.



[b]Reaction conditions: **2** (10 μmol) and **1b** (1.2 equiv) with 2 mol % [PC], 3 mol % $Ni(NO_3)_2$•$6H_2O$, 3 mol % dtbbpy, 2,6-lutidine (3.5 equiv), and 95:5 dioxane/t-AmOH (0.1 M) using blue LEDs (470 nm). Reactions were monitored by UHPLC-MS with results displayed as P/IS.



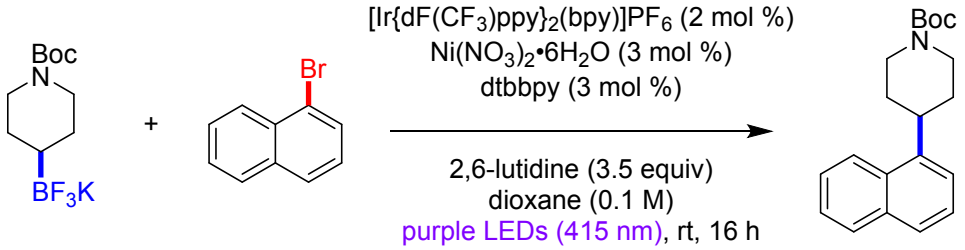
[c]Reaction conditions: **2** (10 μmol) and **1b** (1.2 equiv) with 2 mol % [PC], 3 mol % $Ni(NO_3)_2$•$6H_2O$, 3 mol % dtbbpy, Cs_2CO_3 (1.5 equiv), and 95:5 dioxane/t-AmOH (0.1 M) using blue LEDs (470 nm). Reactions were monitored by UHPLC-MS with results displayed as P/IS.

Table S4. Solvent polarities and base conjugate acid pKa values.

Solvent	**Polarity**
t-AmOH	2.8
THF	4.0
CPME	4.0
MEK	4.7
1,4-Dioxane	4.8
MeOH	5.1
MeCN	5.8
DMPU	6.0
DMF	6.4
DMAc	6.5
NMP	6.7
DMSO	7.2

Base	**pKa (conjugate acid)**
Pyridine	5.2
2,6-Lutidine	6.8
2,4,6-Collidine	7.4
Morpholine	8.4
DABCO	8.8
DMAP	9.2
Cs_2CO_3	10.3
TEA	10.8
DPA	11.1
PMP	11.3
K_2HPO_4	12.3
DBU	12.5
DBN	12.7
TMG	13.6

Table S5. Non-basic substrate control reactions.[5]



1b

Condition	P/IS
with 2,6-lutidine	12.3
without 2,6-lutidine	4.14

Table S6. Mixed solvent systems.[a]

Photocatalyst	Solvent	1a	1b
PC1	95:5 MEK/MeOH	2.90	0.82
	95:5 dioxane/MeOH	3.38	1.86
	95:5 dioxane/t-AmOH	3.43	3.01
	80:20 dioxane/DMAc	3.48	3.33
PC2	95:5 MEK/MeOH	1.69	0.88
	95:5 dioxane/MeOH	2.49	1.72
	95:5 dioxane/t-AmOH	2.61	3.18
	80:20 dioxane/DMAc	2.95	2.12
PC3	95:5 MEK/MeOH	1.72	1.21
	95:5 dioxane/MeOH	2.50	1.46
	95:5 dioxane/t-AmOH	2.47	2.95
	80:20 dioxane/DMAc	2.11	3.17
PC4	95:5 MEK/MeOH	2.08	0.87
	95:5 dioxane/MeOH	1.40	0.73
	95:5 dioxane/t-AmOH	1.87	0.59
	80:20 dioxane/DMAc	1.20	0.68

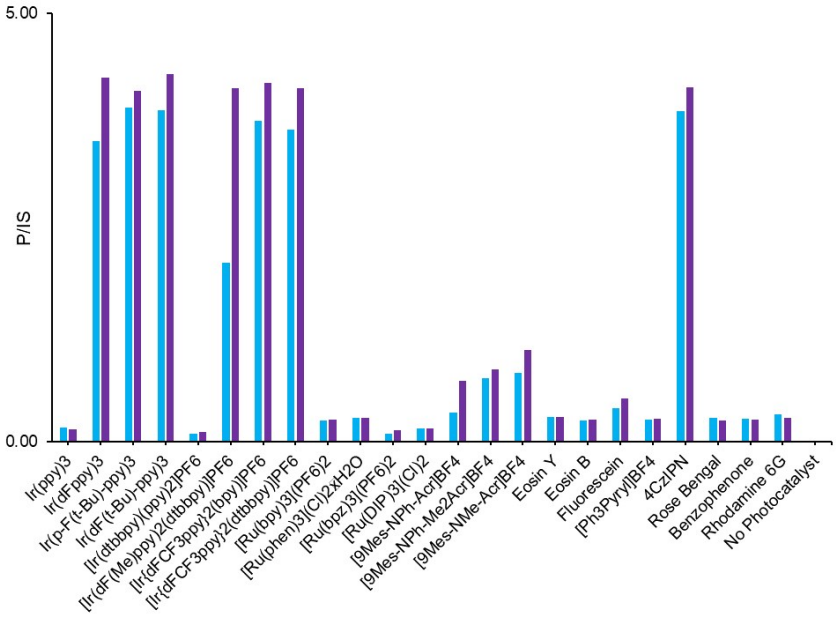
[a]Reaction conditions: **2** (10 µmol) and **1a** or **1b** (1.2 equiv) with 2 mol % [PC], 3 mol % $Ni(NO_3)_2$•$6H_2O$, 3 mol % dtbbpy, 2,6-lutidine (3.5 equiv), and solvent (0.1 M). Reactions were monitored by UHPLC-MS with results displayed as P/IS.

UV-Vis and Irradiance Measurements

Absorbance measurements were performed using a UV-Visible spectrometer with 1-mm quartz cuvette. Catalyst solutions (0.5 mM) were prepared in DCM or MeCN for collecting the absorbance data.

Spectral irradiances of the LEDs were measured with a concave grating spectrometer by placing the detector probe directly on top of the individual LEDs on the 96-well photomat. Average irradiance (W/m^2) was calculated by integrating the area underneath the spectral irradiance shown in Figure 5. Measurements were performed through the bottom of a glass vial to account for scattering through the reactor vials during the HTE studies. Average irradiances corresponding to the applied current settings are summarized in Table S8.

Table S7. Blue (470 nm) vs. Purple (415 nm) LEDs for photocatalyst screen.[a,b]



[a]Reaction conditions: **2** (10 μmol) and **1b** (1.2 equiv) with 2 mol % [PC], 3 mol % $Ni(NO_3)_2•6H_2O$, 3 mol % dtbbpy, 2,6-lutidine (3.5 equiv), and 95:5 dioxane/t-AmOH (0.1 M). Reactions were monitored by UHPLC-MS with results displayed as P/IS. [b]Similar impurity profiles were observed for reactions conducted under both blue and purple LEDs.

Table S8. Average irradiance of each light source at the current used for conducting reactions.

Light Source	Current (mA)	Average Irradiance (W/m^2)
White (broad)	30	320
Blue (470 nm)	30	394
Purple (415 nm)	20	281

Robustness Study of Ni/photoredox Organoboron Cross-coupling

General Procedure for the Robustness Study

Stock solutions of additive (0.2 M) were prepared in 1,4-dioxane. To a Para-dox plate containing 1 mL reaction vials in a glovebox was added a stock solution of photocatalyst (0.002 M in DCM, 100 μL, 2 mol %) and the solvent was removed using a Genevac evaporator. Stock solutions of $Ni(NO_3)_2 \cdot 6H_2O$ (0.003 M in THF-inhibitor free, 3 mol %) and dtbbpy (0.003 M in THF-inhibitor free, 3 mol %) were prepared and equal volumes of each solution were mixed and allowed to ligate for 20 mins. with gentle shaking. After removing the plate from the Genevac, 100 μL of the combined solution was added along with a stock solution of **2** (0.100 M in THF-inhibitor free, 100 μL, 10 μmol) and the solvent was removed. Next, a stock solution of **1b** (0.120 M in acetone, 100 μL, 12 μmol) was added and the solvent removed. After completely drying in the Genevac, microstir bars were added. Then, Cs_2CO_3 was added with a solid dispenser. Finally, a stock solution of 2,6-lutidine (0.350 M) in 1,4-dioxane (50 μL) was added to the appropriate wells. Fifty μL of solvent was added to wells with inorganic base. Lastly, 50 μL of the additive solutions were placed in the appropriate wells. The plate was sealed and the contents were stirred (300 RPM) at 20 °C for 16 h. The reactions were irradiated with Lumidox UV 96-well LED array (violet – 415 nm) controlled by a Lumidox UV (20 mA intensity) controller. After completion, a 2 mg/mL solution of internal standard (4,4'-dimethylbiphenyl) in MeCN was added to the vials (100 μL). An aliquot (100 μL) of the resulting mixture was further diluted in 1,4-dioxane (100 μL) and subjected to GC-FID analysis. The reactions were further diluted with 50:50 MeCN:H_2O (300 μL) and the contents were thoroughly mixed. An aliquot (25 μL) was added to an HPLC plate and further diluted with 50:50 MeCN:H_2O (500 μL). The plate was then subject to UHPLC-MS analysis. The percent additive remaining using GC was calculated by analyzing the stock solution to determine the additive/internal standard ratio and comparing that to the additive/internal standard ratio for the standard reaction.

Figure S2. Additives tested in the robustness study.

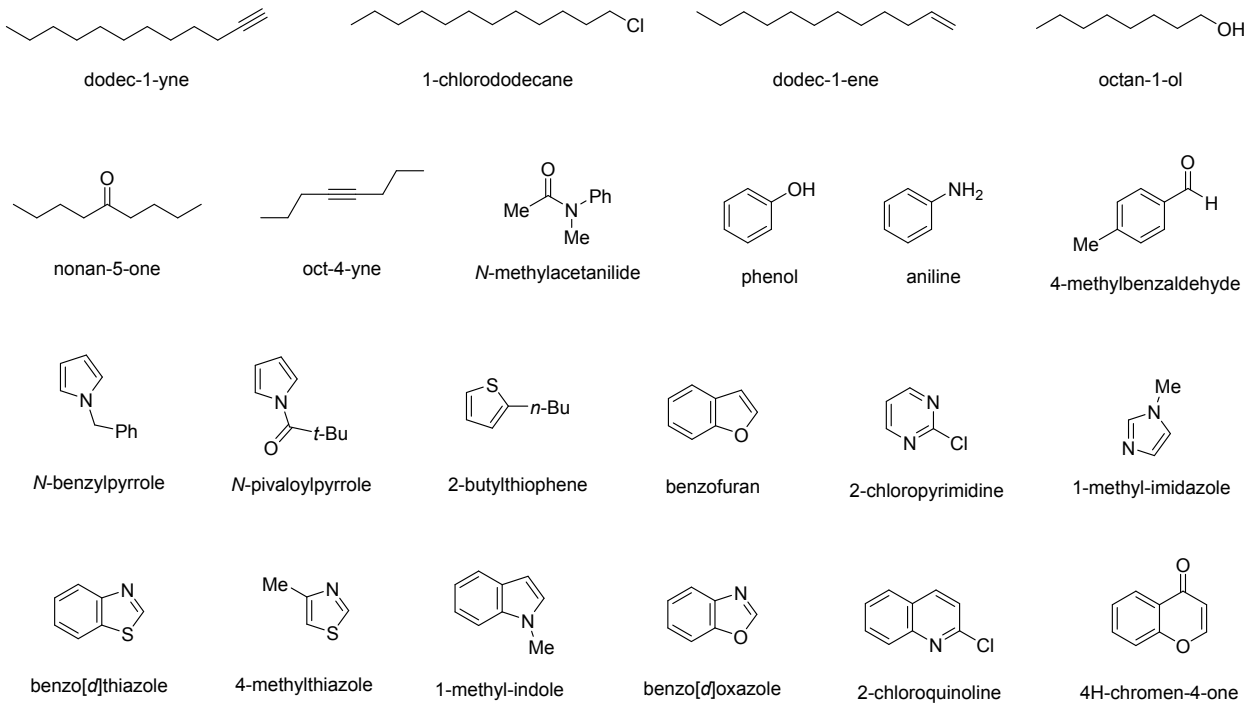


Table S9. Complete Robustness Study for the Photocatalytic Cross-Coupling of **1b** and **2**.[a]

Entry	Additive	*PC1 + 2,6-lutidine*			*PC1 + Cs_2CO_3*			*PC2 + 2,6-lutidine*			*PC2 + Cs_2CO_3*		
		RAP Prod	RAP SM	% Additive Remaining	RAP Prod	RAP SM	% Additive Remaining	RAP Prod	RAP SM	% Additive Remaining	RAP Prod	RAP SM	% Additive Remaining
1	None	94	6.4	N/A	55	45	N/A	87	13	N/A	100	0.0	N/A
2	dodec-1-yne	87	13	67	93	7.3	58	85	15	61	96	3.6	61
3	1-chlorododecane	91	9.0	99	100	0.0	99	88	12	99	100	0.0	99
4	dodec-1-ene	9.9	90	99	10	90	99	1.5	99	99	2.5	98	99
5	octan-1-ol	94	6.4	0.0	100	0.0	18	68	32	0.0	4.5	95	17
6	nonan-5-one	92	8.1	99	99	1.0	99	93	7.0	99	100	0.0	99
7	oct-4-yne	90	9.7	90	100	0.0	85	91	8.6	86	100	0.0	85
8	N-methylacetanilide	10	90	99	10	90	99	1.5	98	99	5.0	95	99
9	phenol	100	0.0	91	100	0.0	91	91	8.7	77	8.8	91	85
10	aniline	8.0	92	84	11	89	87	1.5	99	92	1.3	99	97
11	4-methylbenzaldehyde	93	6.7	91	100	0.0	96	91	8.5	92	100	0.0	97
12	N-benzylpyrrole	89	11	60	100	0.0	92	80	20	89	100	0.0	99
13	N-pivaloylpyrrole	1.4	99	89	4.7	95	74	1.5	99	99	4.4	96	68
14	2-butylthiophene	90	9.6	99	100	0.0	99	86	14	99	100	0.0	99
15	benzofuran	91	8.5	99	100	0.0	99	91	8.6	99	100	0.0	99
16	2-chloropyrimidine	5.3	95	88	1.6	98	95	1.4	99	94	0.0	100	99
17	1-methyl-1H-imidazole	1.9	98	5.5	2.1	98	99	2.6	97	95	0.0	100	99
18	benzo[d]thiazole	82	18	95	91	8.8	98	88	12	96	100	0.0	97
19	4-methylthiazole	83	17	97	86	14	95	88	12	97	100	0.0	97
20	1-methyl-1H-indole	5.8	94	94	9.1	91	95	1.5	99	99	4.7	95	99
21	benzo[d]oxazole	93	6.8	98	64	36	99	94	6.0	98	64	36	98
22	2-chloroquinoline	3.6	96	97	3.5	96	97	4.2	96	99	0.0	100	99
23	4H-chromen-4-one	95	5.3	96	100	0.0	96	93	6.6	96	100	0.0	99

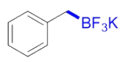
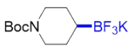
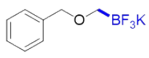
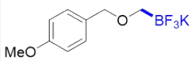
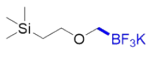
[a]Reactions were run in a 96WP format with the following conditions: **2** (10 μmol) and **1b** (1.2 equiv) with 2 mol % [PC], 3 mol % $Ni(NO_3)_2$•$6H_2O$, 3 mol % dtbbpy, 2,6-lutidine (3.5 equiv) or Cs_2CO_3 (1.5 equiv) and dioxane (0.1 M) in the presence of 1 molar equivalent of the additive. The yield of the product (green) and remaining starting material (blue) are given as an UHPLC-MS RAP. The amount of additive remaining (red) is provided as a percentage as determined by gas chromatography with flame-ionization detection (GC/FID).

Flow Chemistry

General procedure for Flow Chemistry

Reaction solutions were prepared in a nitrogen-filled glovebox and kept under nitrogen during the reaction. Stock solutions of $Ni(NO_3)_2$•$6H_2O$ (0.03 M in THF-inhibitor free, 3 mol %) and dtbbpy (0.033 M in THF-inhibitor free, 3.3 mol %) were prepared and 0.5 mL of each solution were added to a 20 mL vial and allowed to ligate for 20 mins. with gentle shaking. The solvent was removed with a Genevac evaporator and once dry, a stir bar was added. Then, $[Ir(dF(CF_3)ppy)_2(bpy)]PF_6$ (10 mg, 0.01 mmol, 2 mol %), **2** (104 mg, 0.5 mmol), and **1b** (291 mg, 1.0 mmol, 2.0 equiv) were added to the reaction vial. Finally, 10.0 mL (0.05 M) or 12.5 mL (0.04 M) of 4:1 dioxane:DMAc stock solution and 206 µL of 2,6-lutidine were added. The reaction mixture was stirred for approximately 5 min. to give a completely homogeneous solution. The reaction was conducted using a Vapourtec flow photoreactor (details above). The pump was primed and reactor pre-equilibrated with blank solvent (4:1 dioxane:DMAc). The temperature was maintained at 35 °C and 4.0 mL of reaction solution was pumped at different flow rates (1.00 mL/min., 10 min residence time; 0.5 mL/min., 20 min. residence time; 0.25 mL/min., 40 min. residence time; 0.166 mL/min., 60 min. residence time) while irradiating with purple LEDs. After the entire reaction had entered the reactor, it was followed by blank solvent at the same flow rate. The pressure was kept between 0-2 bar and ~2.0 mL of steady-state reaction mixture was collected for each timepoint and subject to UHPLC-MS analysis.

Table S10. Solubility data for selected potassium trifluoroborate salts.[a]

		Dosing Solvents						Reaction Solvents					
Entry	**Substrate**	THF	2-Me THF	DCM	MeCN	acetone	MeOH	DMAc	1,4-dioxane	95% dioxane/ t-AmOH	50% dioxane/ t-AmOH	80% dioxane/ DMAc	50% dioxane/ DMAc
1		>95.4	2.2	0.1	74.1	>94.8	37.5	15.8	27.3	25.4	6.2	17.3	32.2
2		24.8	1.1	not detected	63.0	>99.5	68.3	>98.0	9.6	7.3	2.8	42.6	>91.5
3		21.2	0.5	0.4	9.9	40.2	25.8	>99.5	2.5	2.2	1.0	61.1	82.8
4		12.6	0.4	not detected	17.9	50.9	>104.6	>100.0	not detected	not detected	0.2	>100.0	>100.0
5		1.3	0.1	2.1	6.5	8.2	5.3	70.5	1.2	0.7	0.7	21.4	45.4
6		not detected	not detected	not detected	2.9	1.6	1.5	>103.8	0.1	0.1	not detected	4.6	47.5
7		0.8	not detected	not detected	4.4	5.1	11.5	>100.0	not detected	not detected	not detected	8.6	65.4

[a]Solubility at rt (20-25 °C) in mg/mL

Chemical Libraries Synthesis

General Procedure for Chemical Library Synthesis

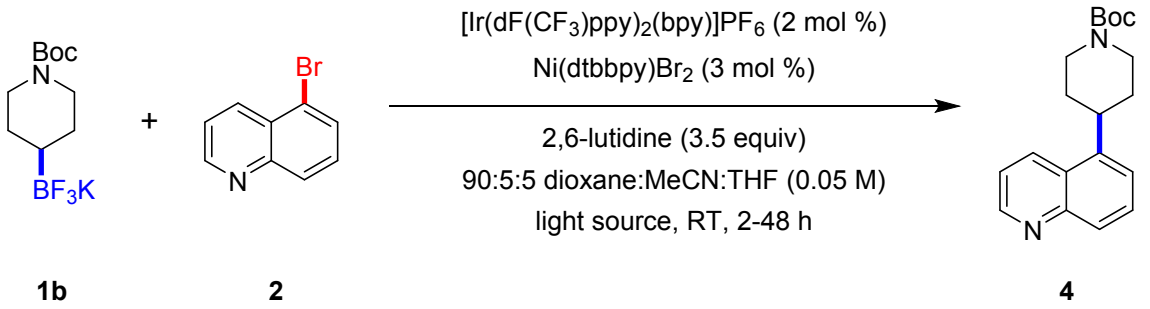
To each 4 mL, round bottom, screw-cap vial was added potassium alkyl trifluoroborate (0.100 mmol, 2.0 equiv) and a stir bar. A 900 μL portion of a solution of aryl bromide (0.055 M, 0.050 mmol) and 2,6-lutidine (0.192 M, 3.5 equiv) in 1,4-dioxane was placed in the corresponding vials. Then, 50 μL of a solution of $[Ir(dF(CF_3)ppy)_2(bpy)]PF_6$ (0.018 M, 0.001 mmol, 2 mol %) in MeCN and 50 μL of a solution of $Ni(dtbbpy)Br_2$ (0.025 M, 0.0015 mmol, 3 mol %) in THF were added to the vials. The reactions were degassed and capped under N_2 atmosphere. The reactions were irradiated with purple LEDs (400 nm) for 24 h with stirring at 750 RPM. After completion, the reaction solvent was removed via a Zymark evaporator. The crude solid was dissolved in DMF (2.0 mL) and filtered through a 0.45 μm PTFE syringe filter into a clean vial. The crude material was purified via preparative LC-MS. The purified material was then subject to LC-MS analysis using either Method A or B.

General Photoreactor Setup[6]

For reactions conducted in 2-dram vials, either purple or blue LED strips were used as the light source. For blue (waterproof), the surface mounted diode (SMD) 5050 chip LEDs produce an individual LED irradiance of 206 ± 15 W/m^2 measured at 10 mm away from the LED with a peak intensity wavelength of 450 nm. For purple (non-waterproof), the SMD 5050 chip LEDs produce an individual LED irradiance of 175 ± 24 W/m^2 measured at 6 mm away from the LED with a peak intensity wavelength of 400 nm. The measurements were taken at different distances due to detector saturation. Reaction vials were placed at a distance of 10 mm from the light source to the face of the vial.

O_2 Sensitivity Experiments

Table S11. O_2 sensitivity experiments varying time and light source.

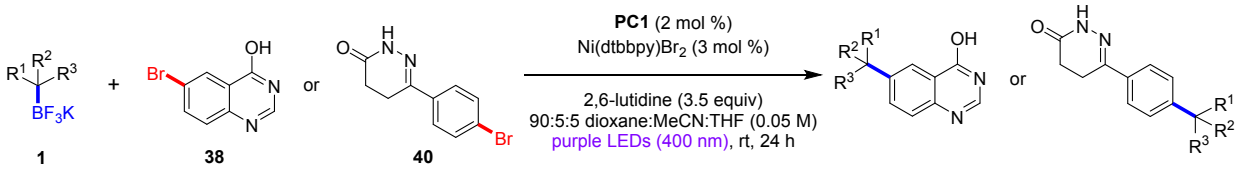


1b **2** **4**

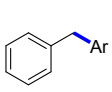
Technique	Time (h)	Light Source	2 RAP	4 RAP
Setup in glovebox[a]	24	Blue LEDs (450 nm)	19	81
No degassing[b]	24	Blue LEDs (450 nm)	63	37
Direct sparging with N_2[c]	24	Blue LEDs (450 nm)	43	57
Evacuate/refill with Ar[d]	24	Blue LEDs (450 nm)	56	44
Antechamber degas[e]	24	Blue LEDs (450 nm)	33	67
Setup in glovebox	48	Blue LEDs (450 nm)	0.0	100
No degassing	48	Blue LEDs (450 nm)	0.0	100
Evacuate/refill with Ar	48	Blue LEDs (450 nm)	0.0	100
Setup in glovebox	2	Purple LEDs (400 nm)	76	24
Setup in glovebox	4	Purple LEDs (400 nm)	63	37
Setup in glovebox	6	Purple LEDs (400 nm)	36	64
Setup in glovebox	8	Purple LEDs (400 nm)	32	68
Setup in glovebox	24	Purple LEDs (400 nm)	0.0	100
No degassing	24	Purple LEDs (400 nm)	10	90
Direct sparging with N_2	24	Purple LEDs (400 nm)	0.0	100
Evacuate/refill with Ar	24	Purple LEDs (400 nm)	0.0	100
Antechamber degas	24	Purple LEDs (400 nm)	0.0	100

[a]Reactions set up in glovebox under inert N_2 atmosphere; [b]reactions set up on benchtop with no effort to exclude O_2; [c]reactions were directly sparged with N_2 for 10-20 mins.; [d]reactions were vented with a needle and degassed in a desiccator by evacuating and refilling with Ar (3x Ar fill, 2x evacuated); [e]reactions were degassed in a glovebox antechamber by evacuating and refilling with N_2 (5x evacuated and refilled with N_2) and subsequently capped under inert N_2 atmosphere. Reaction success was determined based on the UHPLC-MS RAP of the cross-coupled product from the crude reaction mixture.

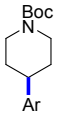
Table S12. Fourteen- and Twenty-member Photocatalytic Cross-Coupling Chemical Libraries.



1 38 40



core 38 - 52, 84% yield
core 40 - 80, 75% yield



core 38 - 53, 38% yield
core 40 - 81, 45% yield

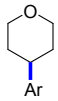
core 38 - 54, 56% yield
core 40 - 82, 50% yield

core 38 - 55, 36% yield
core 40 - 83, 42% yield

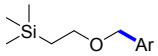
core 38 - 56, 55% yield
core 40 - 84, 55% yield

core 38 - 57, 35% yield
core 40 - 85, 39% yield

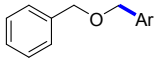
core 38 - 58, 0% yield
core 40 - 86, 0% yield



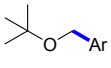
core 38 - 59, 37% yield
core 40 - 87, 57% yield



core 38 - 60, 65% yield
core 40 - 88, 62% yield

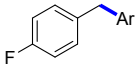


core 38 - 61, 48% yield
core 40 - 89, 57% yield

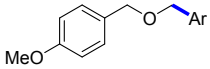


core 38 - 62, 64% yield
core 40 - 90, 45% yield

core 38 - 63, 41% yield
core 40 - 91, 49% yield

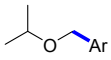


core 38 - 64, 65% yield
core 40 - 92, 65% yield



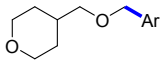
core 38 - 65, 32% yield
core 40 - 93, 50% yield

core 40 - 122, 68% yield

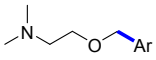


core 40 - 123, 63% yield

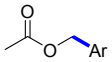
core 40 - 124, 63% yield



core 40 - 125, 25% yield

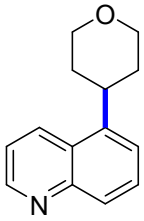


core 40 - 126, <5% yield

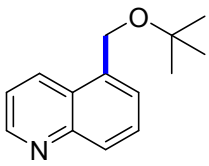


core 40 - 127, 0% yield

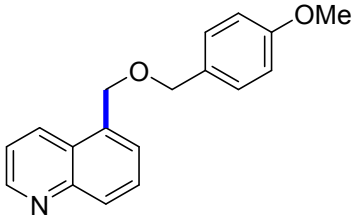
Characterization Data for Chemical Library Compounds



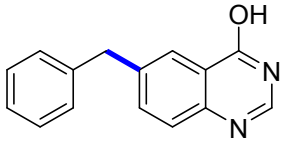
5-(tetrahydro-2H-pyran-4-yl)quinoline (45): 0.6 mg (6% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.99–8.82 (m, 1H), 8.69 (br d, *J*=8.5 Hz, 1H), 7.90 (br d, *J*=8.2 Hz, 1H), 7.82–7.66 (m, 1H), 7.64–7.47 (m, 2H), 4.00 (br d, *J*=9.9 Hz, 3H), 3.75–3.57 (m, 1H), 1.93–1.72 (m, 5H); **LC** Method B: Purity = 98%, Retention Time = 0.90 min.; Method A: Purity = 100%, Retention Time = 1.36 min.; **MS (ESI)** 214.12 $(M + H)^+$.



5-(tert-butoxymethyl)quinoline (48): 1.2 mg (11% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.93 (br d, *J*=3.1 Hz, 1H), 8.54 (br d, *J*=8.2 Hz, 1H), 7.97 (d, *J*=8.2 Hz, 1H), 7.74 (t, *J*=7.8 Hz, 1H), 7.65 (d, *J*=7.1 Hz, 2H), 7.60 (q, *J*=7.9 Hz, 1H), 4.89 (s, 2H), 1.33 (s, 9H); **LC** Method B: Purity = 91%, Retention Time = 1.19 min.; Method A: Purity = 99%, Retention Time = 1.76 min.; **MS (ESI)** 216.13 $(M + H)^+$.

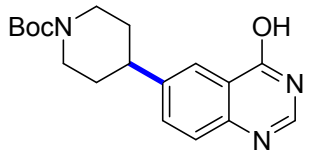


5-(((4-methoxybenzyl)oxy)methyl)quinoline (51): 3.9 mg (28% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.93 (br d, *J*=2.7 Hz, 1H), 8.53 (br d, *J*=8.2 Hz, 1H), 8.01 (d, *J*=8.5 Hz, 1H), 7.75 (t, *J*=7.8 Hz, 1H), 7.64 (d, *J*=7.1 Hz, 1H), 7.62–7.57 (m, 1H), 7.35–7.25 (m, *J*=8.5 Hz, 2H), 6.97–6.89 (m, *J*=8.5 Hz, 2H), 4.97 (s, 2H), 4.55 (s, 2H), 3.75 (s, 3H); **LC** Method A: Purity = 100%, Retention Time = 1.81 min.; Method B: Purity = 97%, Retention Time = 1.33 min.; **MS (ESI)** 280.13 $(M + H)^+$.

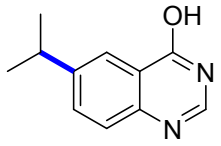


6-benzylquinazolin-4-ol (52): 9.9 mg (84% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.96 (s, 1H), 7.72 (br d, *J*=6.7 Hz, 1H), 7.62 (d, *J*=8.5 Hz, 1H), 7.35–7.21 (m, 5H), 4.12 (s,

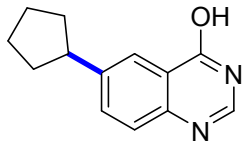
2H); **LC** Method A: Purity = 99%, Retention Time = 1.46 min.; Method B: Purity = 99%, Retention Time = 1.48 min.; **MS (ESI)** 237.10 $(M + H)^+$.



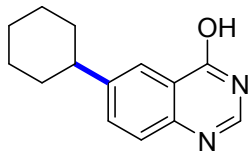
tert-butyl 4-(4-hydroxyquinazolin-6-yl)piperidine-1-carboxylate (53): 6.3 mg (38% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.06 (s, 1H), 7.95 (s, 1H), 7.75 (d, *J*=7.8 Hz, 1H), 7.64 (d, *J*=8.5 Hz, 1H), 4.11 (br d, *J*=11.9 Hz, 2H), 2.96–2.75 (m, 3H), 1.84 (br d, *J*=12.8 Hz, 2H), 1.61–1.47 (m, 2H), 1.44 (s, 9H); **LC** Method A: Purity = 100%, Retention Time = 1.66 min.; Method B: Purity = 100%, Retention Time = 1.62 min.; **MS (ESI)** 330.17 $(M + H)^+$.



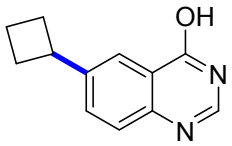
6-isopropylquinazolin-4-ol (54): 5.3 mg (56% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.97 (s, 1H), 7.75 (dd, *J*=8.5, 1.8 Hz, 1H), 7.63 (d, *J*=8.5 Hz, 1H), 3.08 (dt, *J*=13.7, 6.8 Hz, 2H), 1.28 (d, *J*=7.0 Hz, 6H); **LC** Method B: Purity = 100%, Retention Time = 1.33 min.; Method A: Purity = 100%, Retention Time = 1.36 min.; **MS (ESI)** 189.10 $(M + H)^+$.



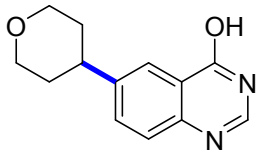
6-cyclopentylquinazolin-4-ol (55): 3.9 mg (36% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.97 (s, 1H), 7.74 (d, *J*=8.2 Hz, 1H), 7.62 (d, *J*=8.5 Hz, 1H), 3.16 (br t, *J*=7.9 Hz, 1H), 2.10 (br s, 2H), 1.82 (br s, 2H), 1.71 (br dd, *J*=7.2, 4.7 Hz, 2H), 1.67–1.51 (m, 2H); **LC** Method A: Purity = 96%, Retention Time = 1.52 min.; Method B: Purity = 95%, Retention Time = 1.52 min.; **MS (ESI)** 215.11 $(M + H)^+$.



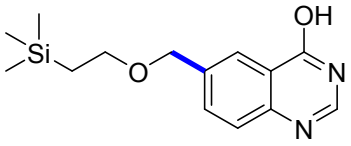
6-cyclohexylquinazolin-4-ol (56): 6.3 mg (55% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.95 (s, 1H), 7.73 (br d, *J*=8.2 Hz, 1H), 7.62 (d, *J*=8.2 Hz, 1H), 2.82–2.62 (m, 1H), 1.85 (br t, *J*=11.6 Hz, 4H), 1.74 (br d, *J*=12.2 Hz, 1H), 1.52–1.37 (m, 4H), 1.35–1.14 (m, 1H); **LC** Method A: Purity = 99%, Retention Time = 1.67 min.; Method B: Purity = 98%, Retention Time = 1.67 min.; **MS (ESI)** 229.12 $(M + H)^+$.



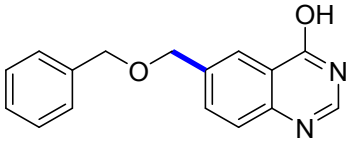
6-cyclobutylquinazolin-4-ol (57): 3.5 mg (35% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.06 (s, 1H), 7.94 (s, 1H), 7.76–7.68 (m, 1H), 7.63 (d, *J*=8.5 Hz, 1H), 3.69 (br t, *J*=8.7 Hz, 1H), 2.44–2.31 (m, 2H), 2.19–2.10 (m, 2H), 2.08–1.99 (m, 1H), 1.93–1.83 (m, 1H); **LC** Method A: Purity = 100%, Retention Time = 1.39 min.; Method B: Purity = 100%, Retention Time = 1.39 min.; **MS (ESI)** 201.10 $(M + H)^+$.



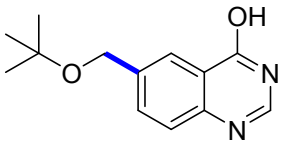
6-(tetrahydro-2H-pyran-4-yl)quinazolin-4-ol (59): 4.3 mg (37% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.06 (br s, 1H), 7.97 (s, 1H), 7.77 (dd, *J*=8.5, 1.8 Hz, 1H), 7.65 (d, *J*=8.2 Hz, 1H), 3.99 (br dd, *J*=11.1, 3.5 Hz, 3H), 2.96 (br t, *J*=11.9 Hz, 1H), 1.82–1.66 (m, 5H); **LC** Method A: Purity = 100%, Retention Time = 1.05 min.; Method B: Purity = 100%, Retention Time = 1.07 min.; **MS (ESI)** 231.11 $(M + H)^+$.



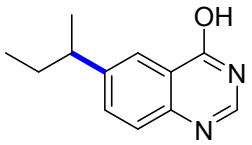
6-((2-(trimethylsilyl)ethoxy)methyl)quinazolin-4-ol (60): 9.0 mg (65% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.06 (s, 2H), 7.74 (br d, *J*=8.2 Hz, 1H), 7.65 (d, *J*=8.2 Hz, 1H), 4.56 (s, 2H), 3.58 (t, *J*=7.9 Hz, 2H), 0.94 (t, *J*=7.9 Hz, 2H), 0.00 (s, 9H); **LC** Method A: Purity = 100%, Retention Time = 1.82 min.; Method B: Purity = 100%, Retention Time = 1.84 min.; **MS (ESI)** 277.13 $(M + H)^+$.



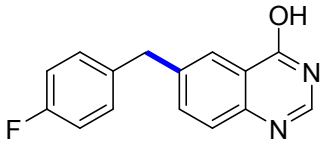
6-((benzyloxy)methyl)quinazolin-4-ol (61): 6.4 mg (48% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.12 (s, 1H), 8.10 (br s, 1H), 7.81 (br d, *J*=6.7 Hz, 1H), 7.69 (d, *J*=8.2 Hz, 1H), 7.40 (d, *J*=4.3 Hz, 4H), 7.37–7.30 (m, 1H), 4.70 (s, 2H), 4.60 (s, 2H); **LC** Method A: Purity = 100%, Retention Time = 1.56 min.; Method B: Purity = 100%, Retention Time = 1.53 min.; **MS (ESI)** 267.11 $(M + H)^+$.



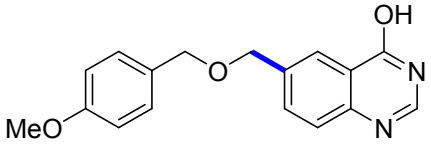
6-(tert-butoxymethyl)quinazolin-4-ol (62): 7.4 mg (64% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.08 (s, 2H), 7.76 (br d, *J*=7.9 Hz, 1H), 7.65 (d, *J*=8.5 Hz, 1H), 4.56 (s, 2H), 1.28 (s, 9H); **LC** Method A: Purity = 99%, Retention Time = 1.33 min.; Method B: Purity = 99%, Retention Time = 1.36 min.; **MS (ESI)** 233.12 $(M + H)^+$.



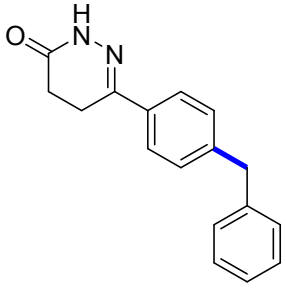
6-(sec-butyl)quinazolin-4-ol (63): 4.1 mg (41% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.93 (s, 1H), 7.71 (dd, *J*=8.4, 1.7 Hz, 1H), 7.63 (d, *J*=8.2 Hz, 1H), 2.83–2.67 (m, 1H), 1.71–1.54 (m, 2H), 1.26 (d, *J*=6.7 Hz, 3H), 0.79 (t, *J*=7.3 Hz, 3H); **LC** Method A: Purity = 99%, Retention Time = 1.45 min.; Method B: Purity = 97%, Retention Time = 1.45 min.; **MS (ESI)** 203.11 $(M + H)^+$.



6-(4-fluorobenzyl)quinazolin-4-ol (64): 8.2 mg (65% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.06 (s, 1H), 7.96 (s, 1H), 7.71 (d, *J*=8.2 Hz, 1H), 7.63 (d, *J*=8.2 Hz, 1H), 7.33 (t, *J*=6.6 Hz, 2H), 7.15 (t, *J*=8.9 Hz, 2H), 4.12 (s, 2H); **LC** Method A: Purity = 99%, Retention Time = 1.49 min.; Method B: Purity = 99%, Retention Time = 1.52 min.; **MS (ESI)** 255.09 $(M + H)^+$.

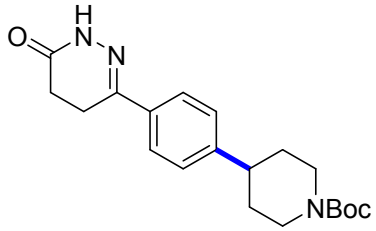


6-(((4-methoxybenzyl)oxy)methyl)quinazolin-4-ol (65): 4.8 mg (32% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.10 (s, 2H), 7.79 (br d, *J*=8.2 Hz, 1H), 7.68 (d, *J*=8.2 Hz, 1H), 7.37–7.27 (m, *J*=8.5 Hz, 2H), 6.99–6.92 (m, *J*=8.5 Hz, 2H), 4.66 (s, 2H), 4.52 (s, 2H), 3.78 (s, 3H); **LC** Method A: Purity = 99%, Retention Time = 1.44 min.; Method B: Purity = 99%, Retention Time = 1.47 min.; **MS (ESI)** 297.12 $(M + H)^+$.

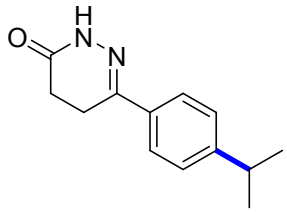


6-(4-benzylphenyl)-4,5-dihydropyridazin-3(2H)-one (80): 9.9 mg (75% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.87 (s, 1H), 7.67 (d, *J*=8.3 Hz, 2H), 7.32–7.27 (m, 4H), 7.24–7.17 (m, 3H),

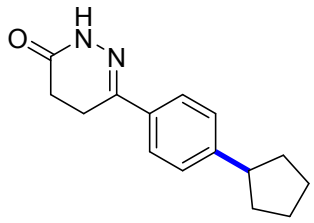
3.97 (s, 2H), 2.92 (t, *J*=8.3 Hz, 2H), 2.45–2.40 (m, 2H); **LC** Method B: Purity = 100%, Retention Time = 1.79 min.; Method A: Purity = 100%, Retention Time = 1.78 min.; **MS (ESI)** 265.13 $(M + H)^+$.



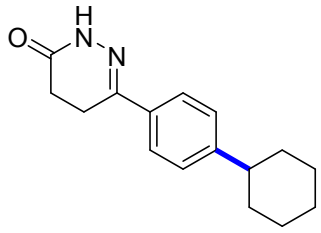
Tert-butyl 4-(4-(6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)phenyl)piperdine-1-carboxylate (81): 8.1 mg (45% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.93 (s, 1H), 7.74 (d, *J*=8.2 Hz, 2H), 7.36 (br d, *J*=8.2 Hz, 2H), 4.13 (br s, 2H), 2.99 (t, *J*=8.2 Hz, 2H), 2.87 (br s, 1H), 2.78 (br t, *J*=12.2 Hz, 2H), 2.55–2.44 (m, 2H), 1.81 (br d, *J*=12.8 Hz, 2H), 1.58–1.45 (m, 2H), 1.48 (s, 9H); **LC** Method B: Purity = 95%, Retention Time = 1.81 min.; Method A: Purity = 100%, Retention Time = 1.92 min.; **MS (ESI)** 358.21 $(M + H)^+$.



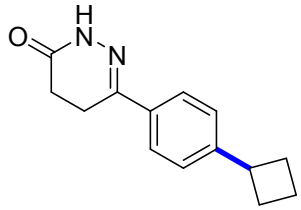
6-(4-(isopropylphenyl)-4,5-dihydropyridazin-3(2H)-one (82): 5.4 mg (50% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.88 (s, 1H), 7.74–7.65 (m, *J*=8.2 Hz, 2H), 7.36–7.28 (m, *J*=8.2 Hz, 2H), 3.01–2.88 (m, 3H), 2.51–2.40 (m, 2H), 1.23 (d, *J*=7.0 Hz, 6H); **LC** Method A: Purity = 100%, Retention Time = 1.74 min.; Method B: Purity = 100%, Retention Time = 1.73 min.; **MS (ESI)** 217.13 $(M + H)^+$.



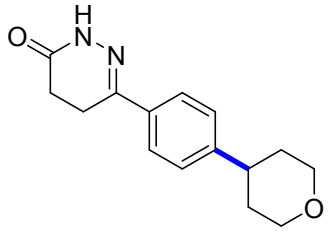
6-(4-cyclopentylphenyl)-4,5-dihydropyridazin-3(2H)-one (83): 5.0 mg (42% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.86 (s, 1H), 7.69–7.63 (m, *J*=8.3 Hz, 2H), 7.33–7.27 (m, *J*=8.2 Hz, 2H), 3.04–2.97 (m, 1H), 2.95–2.89 (m, 2H), 2.49–2.37 (m, 2H), 2.07–1.96 (m, 2H), 1.82–1.72 (m, 2H), 1.70–1.61 (m, 2H), 1.57–1.50 (m, 2H); **LC** Method A: Purity = 97%, Retention Time = 1.88 min.; Method B: Purity = 98%, Retention Time = 1.92 min.; **MS (ESI)** 243.14 $(M + H)^+$.



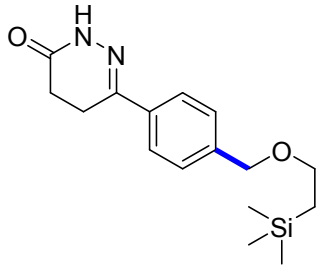
6-(4-cyclohexylphenyl)-4,5-dihydropyridazin-3(2H)-one (84): 7.1 mg (55% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.87 (s, 1H), 7.67 (d, *J*=8.2 Hz, 2H), 7.29 (d, *J*=8.2 Hz, 2H), 2.94 (t, *J*=8.2 Hz, 2H), 2.50–2.37 (m, 2H), 1.93–1.76 (m, 4H), 1.72 (br d, *J*=11.6 Hz, 1H), 1.48–1.30 (m, 4H), 1.25 (br d, *J*=12.2 Hz, 2H); **LC** Method B: Purity = 99%, Retention Time = 2.03 min.; Method A: Purity = 100%, Retention Time = 2.12 min.; **MS (ESI)** 257.16 $(M + H)^+$.



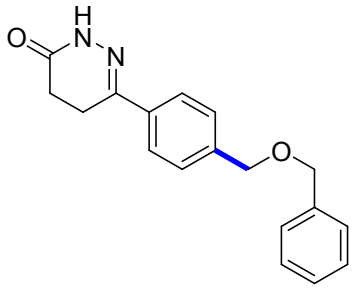
6-(4-cyclobutylphenyl)-4,5-dihydropyridazin-3(2H)-one (85): 4.3 mg (39% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.86 (s, 1H), 7.72–7.64 (m, *J*=8.3 Hz, 2H), 7.32–7.24 (m, *J*=8.2 Hz, 2H), 3.71–3.50 (m, 1H), 2.93 (t, *J*=8.3 Hz, 2H), 2.49–2.40 (m, 2H), 2.37–2.24 (m, 2H), 2.13–2.05 (m, 2H), 2.03–1.94 (m, 1H), 1.82 (q, *J*=9.7 Hz, 1H); **LC** Method A: Purity = 96%, Retention Time = 1.75 min.; Method B: Purity = 99%, Retention Time = 1.78 min.; **MS (ESI)** 229.13 $(M + H)^+$.



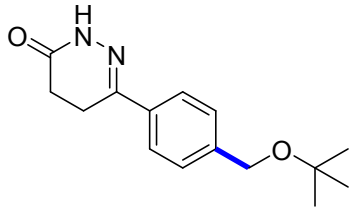
6-(4-(tetrahydro-2H-pyran-4-yl)phenyl)-4,5-dihydropyridazin-3(2H)-one (87): 7.3 mg (57% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.89 (s, 1H), 7.74–7.68 (m, *J*=8.2 Hz, 2H), 7.37–7.29 (m, *J*=8.2 Hz, 2H), 3.97 (br d, *J*=10.7 Hz, 2H), 3.47 (br d, *J*=7.9 Hz, 1H), 2.95 (t, *J*=8.2 Hz, 2H), 2.82 (dt, *J*=10.0, 5.2 Hz, 1H), 2.51–2.40 (m, 3H), 1.74–1.64 (m, 4H); **LC** Method A: Purity = 100%, Retention Time = 1.39 min.; Method B: Purity = 100%, Retention Time = 1.38 min.; **MS (ESI)** 259.14 $(M + H)^+$.



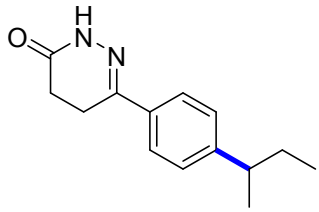
6-(4-((2-trimethylsilyl)ethoxy)methyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (88): 9.5 mg (62% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.90 (s, 1H), 7.72 (d, *J*=8.2 Hz, 2H), 7.36 (d, *J*=8.3 Hz, 2H), 4.46 (s, 2H), 3.55 (t, *J*=8.0 Hz, 2H), 2.94 (t, *J*=8.3 Hz, 2H), 2.49–2.42 (m, 2H), 0.93 (t, *J*=7.9 Hz, 2H), 0.00 (s, 9H); **LC** Method A: Purity = 100%, Retention Time = 2.12 min.; Method B: Purity = 100%, Retention Time = 2.15 min.; **MS (ESI)** 305.16 $(M + H)^+$.



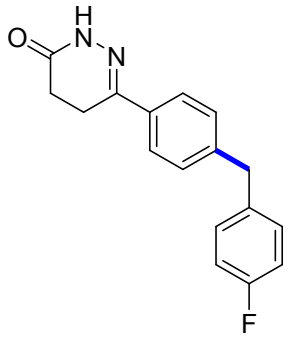
6-(4-((benzyloxy)methyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (89): 8.5 mg (57% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.91 (s, 1H), 7.74 (d, *J*=8.4 Hz, 2H), 7.43–7.34 (m, 6H), 7.34–7.16 (m, 1H), 4.56 (s, 2H), 4.54 (s, 2H), 2.95 (t, *J*=8.3 Hz, 2H), 2.49–2.39 (m, 2H); **LC** Method A: Purity = 99%, Retention Time = 1.71 min.; Method B: Purity = 100%, Retention Time = 1.75 min.; **MS (ESI)** 295.14 $(M + H)^+$.



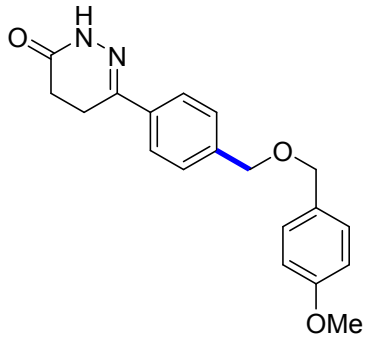
6-(4-(tert-butoxymethyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (90): 5.8 mg (45% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.90 (s, 1H), 7.73 (d, *J*=8.2 Hz, 2H), 7.38 (br d, *J*=7.9 Hz, 2H), 4.45 (s, 2H), 2.96 (t, *J*=8.1 Hz, 2H), 2.51–2.41 (m, 2H), 1.25 (s, 9H); **LC** Method A: Purity = 100%, Retention Time = 1.72 min.; Method B: Purity = 100%, Retention Time = 1.71 min.; **MS (ESI)** 261.15 $(M + H)^+$.



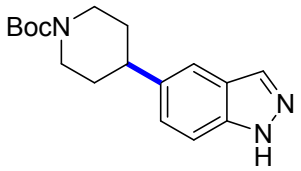
6-(4-(sec-butyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (91): 5.9 mg (49% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.86 (s, 1H), 7.70–7.64 (m, *J*=8.4 Hz, 2H), 7.29–7.21 (m, *J*=8.3 Hz, 2H), 2.93 (t, *J*=8.3 Hz, 2H), 2.66–2.52 (m, 1H), 2.49–2.37 (m, 2H), 1.62–1.50 (m, 2H), 1.19 (d, *J*=6.9 Hz, 3H), 0.76 (t, *J*=7.4 Hz, 3H); **LC** Method A: Purity = 100%, Retention Time = 1.81 min.; Method B: Purity = 97%, Retention Time = 1.85 min.; **MS (ESI)** 231.14 $(M + H)^+$.



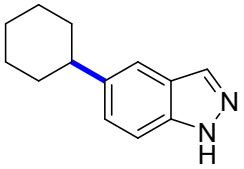
6-(4-(4-fluorobenzyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (92): 9.2 mg (65% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.89 (s, 1H), 7.69 (d, *J*=8.2 Hz, 2H), 7.36–7.22 (m, 4H), 7.13 (br t, *J*=8.9 Hz, 2H), 3.98 (s, 2H), 2.94 (t, *J*=8.2 Hz, 2H), 2.50–2.38 (m, 2H); **LC** Method A: Purity = 100%, Retention Time = 1.85 min.; Method B: Purity = 99%, Retention Time = 1.77 min.; **MS (ESI)** 283.12 $(M + H)^+$.



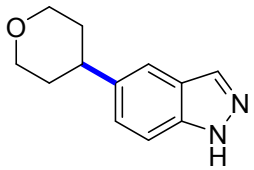
6-(4-(((4-methoxybenzyl)oxy)methyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (93): 8.1 mg (50% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.93 (s, 1H), 7.79–7.72 (m, *J*=8.2 Hz, 2H), 7.46–7.37 (m, *J*=8.2 Hz, 2H), 7.35–7.26 (m, *J*=8.5 Hz, 2H), 6.98–6.92 (m, *J*=8.5 Hz, 2H), 4.55 (s, 2H), 4.48 (s, 2H), 3.77 (s, 3H), 2.97 (t, *J*=8.2 Hz, 2H), 2.51–2.43 (m, 2H); **LC** Method A: Purity = 100%, Retention Time = 1.75 min.; Method B: Purity = 99%, Retention Time = 1.68 min.; **MS (ESI)** 325.15 $(M + H)^+$.



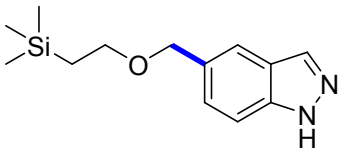
tert-butyl 4-(1H-indazol-5-yl)piperidine-1-carboxylate (95): 2.7 mg (18% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.98 (s, 1H), 7.57 (s, 1H), 7.46 (d, *J*=8.5 Hz, 1H), 7.26 (br d, *J*=8.4 Hz, 1H), 4.10 (br s, 2H), 2.86–2.66 (m, 3H), 1.80 (br d, *J*=13.1 Hz, 2H), 1.56–1.49 (m, 2H), 1.43 (s, 9H); **LC** Method B: Purity = 98%, Retention Time = 1.84 min.; Method A: Purity = 97%, Retention Time = 1.91 min.; **MS (ESI)** 302.18 $(M + H)^+$.



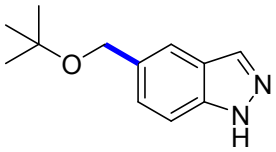
5-cyclohexyl-1H-indazole (98): 2.8 mg (28% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.91 (br s, 1H), 7.99 (s, 1H), 7.55 (s, 1H), 7.46 (d, *J*=8.9 Hz, 1H), 7.26 (br d, *J*=8.2 Hz, 1H), 2.67–2.55 (m, 1H), 1.84 (br t, *J*=11.7 Hz, 4H), 1.74 (br d, *J*=12.8 Hz, 1H), 1.52–1.36 (m, 4H), 1.34–1.13 (m, 1H); **LC** Method A: Purity = 100%, Retention Time = 2.18 min.; Method B: Purity = 99%, Retention Time = 2.09 min.; **MS (ESI)** 201.13 $(M + H)^+$.



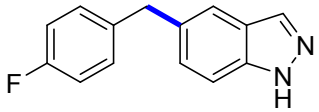
5-(tetrahydro-2H-pyran-4-yl)-1H-indazole (101): 1.2 mg (12% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.00 (s, 1H), 7.57 (s, 1H), 7.47 (d, *J*=8.6 Hz, 1H), 7.37–7.24 (m, 1H), 4.03–3.90 (m, 3H), 3.00–2.80 (m, 1H), 1.81–1.66 (m, 5H); **LC** Method A: Purity = 100%, Retention Time = 1.21 min.; Method B: Purity = 100%, Retention Time = 1.28 min.; **MS (ESI)** 203.11 $(M + H)^+$.



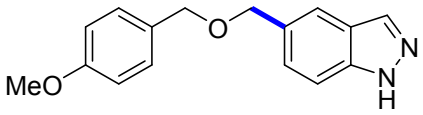
5-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole (102): 3.2 mg (26% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.68 (s, 1H), 7.52 (br d, *J*=8.5 Hz, 1H), 7.32 (br d, *J*=8.6 Hz, 1H), 4.51 (s, 2H), 3.58–3.53 (m, 2H), 0.92 (t, *J*=7.9 Hz, 2H), 0.00 (s, 9H); **LC** Method A: Purity = 100%, Retention Time = 1.99 min.; Method B: Purity = 100%, Retention Time = 2.06 min.; **MS (ESI)** 249.13 $(M + H)^+$.



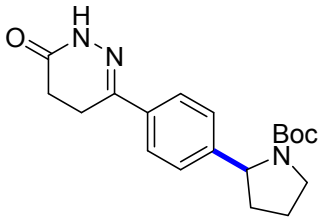
5-(tert-butoxymethyl)-1H-indazole (104): 4.7 mg (46% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.02 (s, 1H), 7.67 (s, 1H), 7.48 (d, *J*=8.3 Hz, 1H), 7.29 (d, *J*=8.4 Hz, 1H), 4.47 (s, 2H), 1.24 (s, 9H); **LC** Method B: Purity = 98%, Retention Time = 1.59 min.; Method A: Purity = 99%, Retention Time = 1.66 min.; **MS (ESI)** 205.13 $(M + H)^+$.



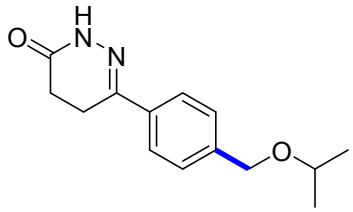
5-(4-fluorobenzyl)-1H-indazole (106): 2.8 mg (25% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.99 (s, 1H), 7.57 (s, 1H), 7.45 (d, *J*=8.5 Hz, 1H), 7.27 (t, *J*=6.7 Hz, 2H), 7.21 (d, *J*=8.0 Hz, 1H), 7.09 (t, *J*=8.9 Hz, 2H), 4.02 (s, 2H); **LC** Method A: Purity = 100%, Retention Time = 1.71 min.; Method B: Purity = 100%, Retention Time = 1.79 min.; **MS (ESI)** 227.09 $(M + H)^+$.



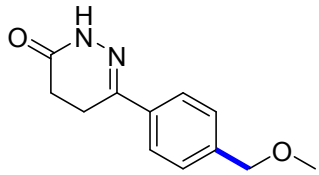
5-(((4-methoxybenzyl)oxy)methyl)-1H-indazole (107): 3.6 mg (28% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.71 (s, 1H), 7.52 (d, *J*=8.5 Hz, 1H), 7.34 (d, *J*=8.5 Hz, 1H), 7.28 (d, *J*=8.6 Hz, 2H), 6.92 (d, *J*=7.6 Hz, 2H), 4.57 (s, 2H), 4.45 (s, 2H), 3.74 (s, 3H); **LC** Method A: Purity = 100%, Retention Time = 1.58 min.; Method B: Purity = 100%, Retention Time = 1.67 min.; **MS (ESI)** 269.12 $(M + H)^+$.



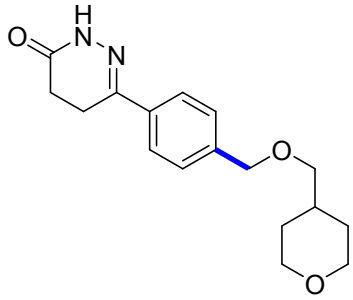
Tert-butyl 2-(4-(6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)phenyl)pyrrolidine-1-carboxylate (122): 11.7 mg (68% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.88 (s, 1H), 7.75–7.64 (m, 2H), 7.21 (br d, *J*=7.9 Hz, 2H), 2.94 (t, *J*=8.2 Hz, 2H), 2.44 (br t, *J*=8.2 Hz, 2H), 2.31 (br s, 1H), 1.81 (br d, *J*=6.3 Hz, 2H), 1.69 (br s, 1H), 1.39 (br s, 3H), 1.11 (br s, 9H); **LC-MS** Method A: Purity = 100%, Retention Time = 1.74 min.; Method B: Purity = 100%, Retention Time = 1.77 min.; **MS (ESI)** 344.19 $(M + H)^+$.



6-(4-(isopropoxymethyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (123): 7.8 mg (63% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.90 (s, 1H), 7.75–7.70 (m, *J*=8.2 Hz, 2H), 7.40–7.34 (m, *J*=8.3 Hz, 2H), 4.49 (s, 2H), 3.64 (dt, *J*=12.2, 6.1 Hz, 1H), 2.94 (t, *J*=8.3 Hz, 2H), 2.50–2.42 (m, 2H), 1.15 (d, *J*=6.1 Hz, 6H); **LC** Method A: Purity = 100%, Retention Time = 1.54 min.; Method B: Purity = 100%, Retention Time = 1.57 min.; **MS (ESI)** 247.14 $(M + H)^+$.



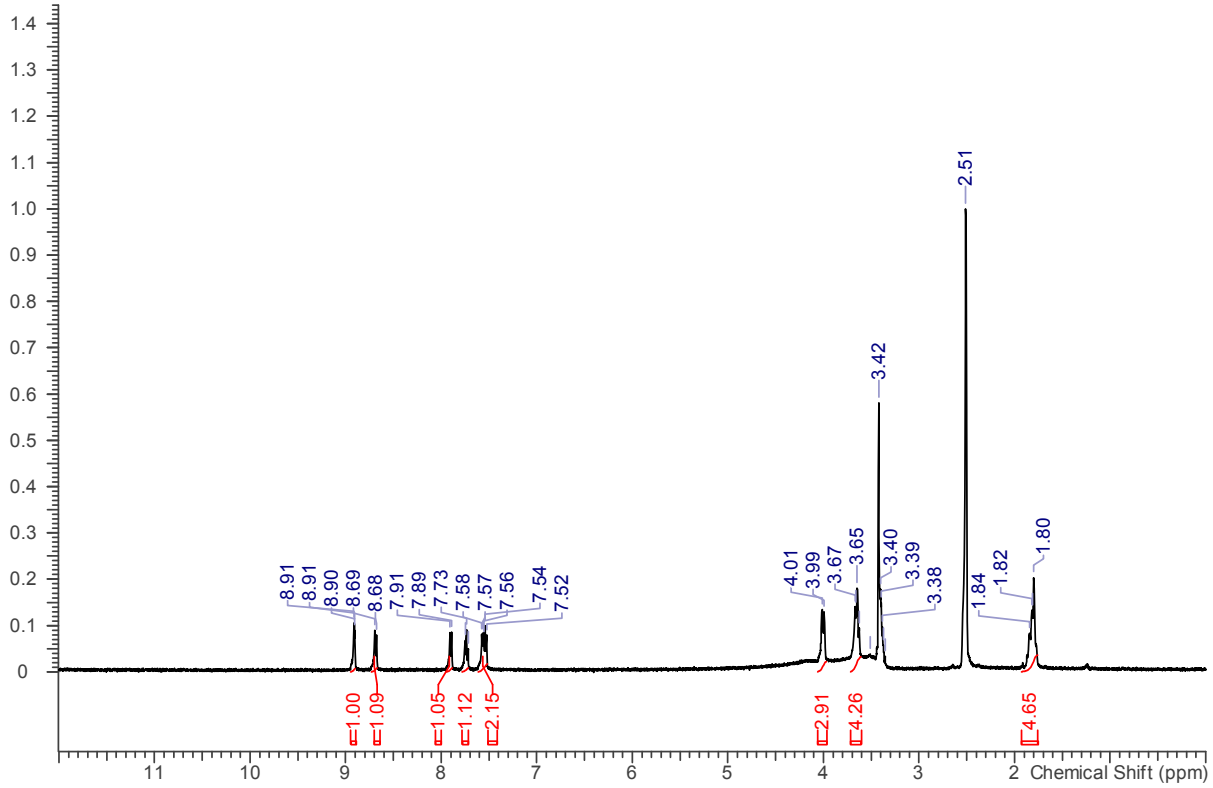
6-(4-(methoxymethyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (124): 6.9 mg (63% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.93 (s, 1H), 7.76 (d, *J*=8.2 Hz, 2H), 7.39 (d, *J*=8.2 Hz, 2H), 4.46 (s, 2H), 2.97 (t, *J*=8.2 Hz, 2H), 2.53 (s, 3H), 2.51–2.44 (m, 2H); **LC** Method A: Purity = 100%, Retention Time = 1.23 min.; Method B: Purity = 96%, Retention Time = 1.16 min.; **MS (ESI)** 219.11 $(M + H)^+$.



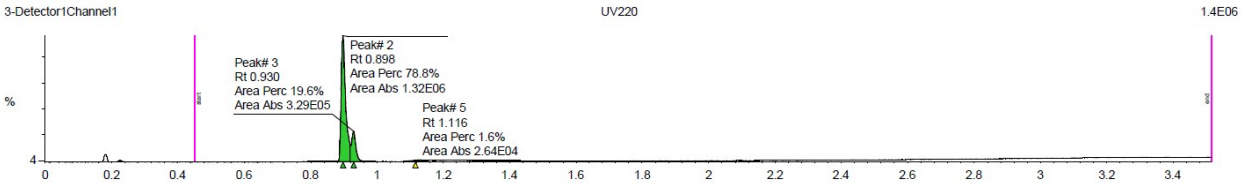
6-(4-(((tetrahydro-2H-pyran-4-yl)methoxy)methyl)phenyl)-4,5-dihydropyridazin-3(2H)-one (125): 3.8 mg (25% yield); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.90 (s, 1H), 7.78–7.68 (m, *J*=8.3 Hz, 2H), 7.43–7.31 (m, *J*=8.2 Hz, 2H), 4.49 (s, 2H), 3.83 (br dd, *J*=11.3, 2.9 Hz, 2H), 2.95 (t, *J*=8.3 Hz, 2H), 2.49–2.40 (m, 2H), 1.91–1.74 (m, 1H), 1.59 (br d, *J*=12.4 Hz, 2H), 1.28–1.15 (m, 2H); **LC** Method A: Purity = 100%, Retention Time = 1.45 min.; Method B: Purity = 100%, Retention Time = 1.48 min.; **MS (ESI)** 303.16 $(M + H)^+$.

Spectral Data

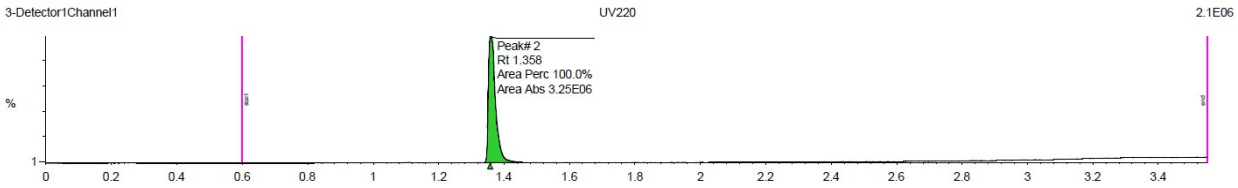
^{1}H NMR (DMSO-d_6, 500 MHz) of **45**



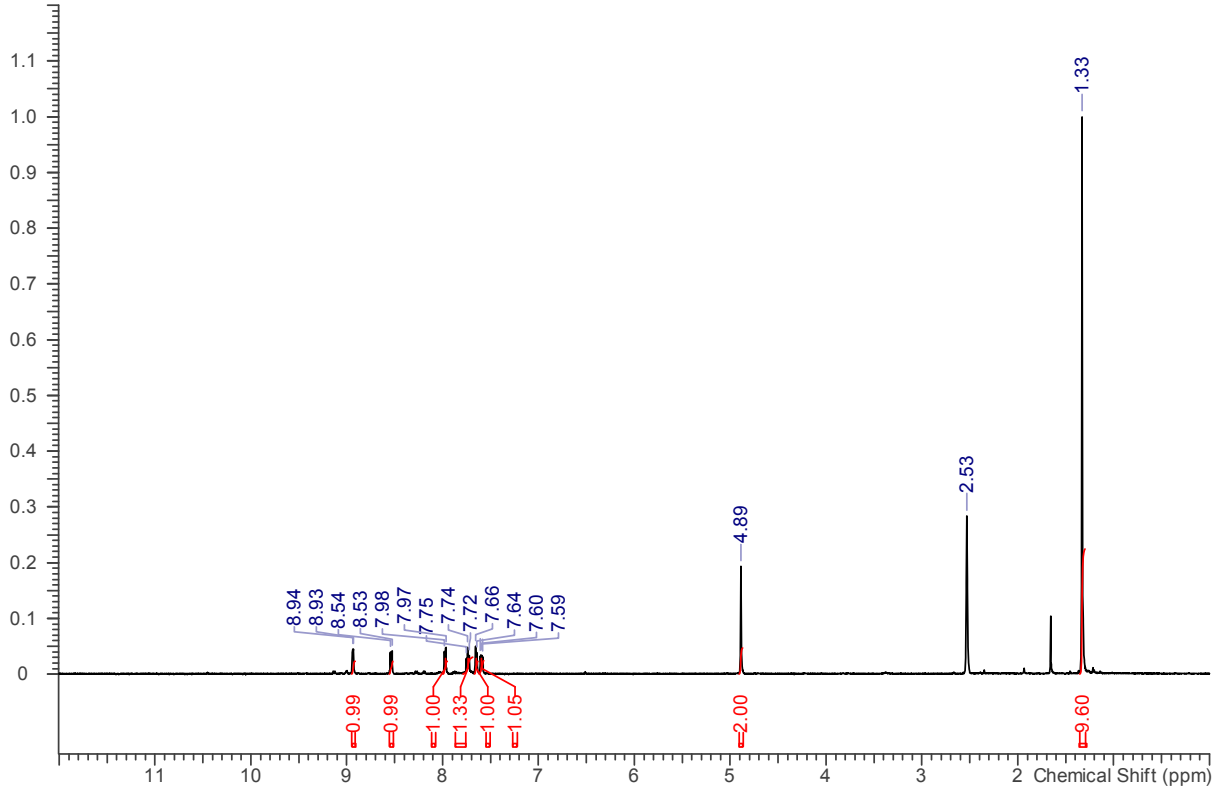
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **45**



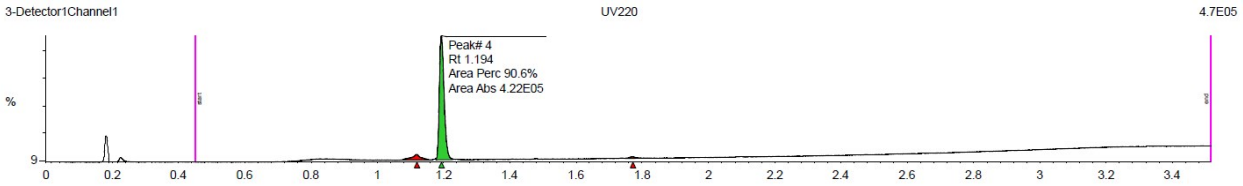
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **45**



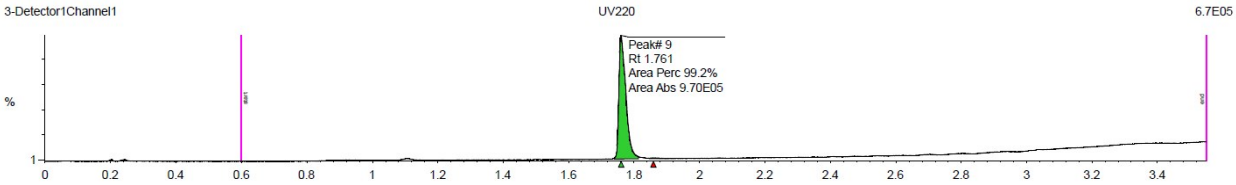
^{1}H NMR (DMSO-d_6, 500 MHz) of **48**



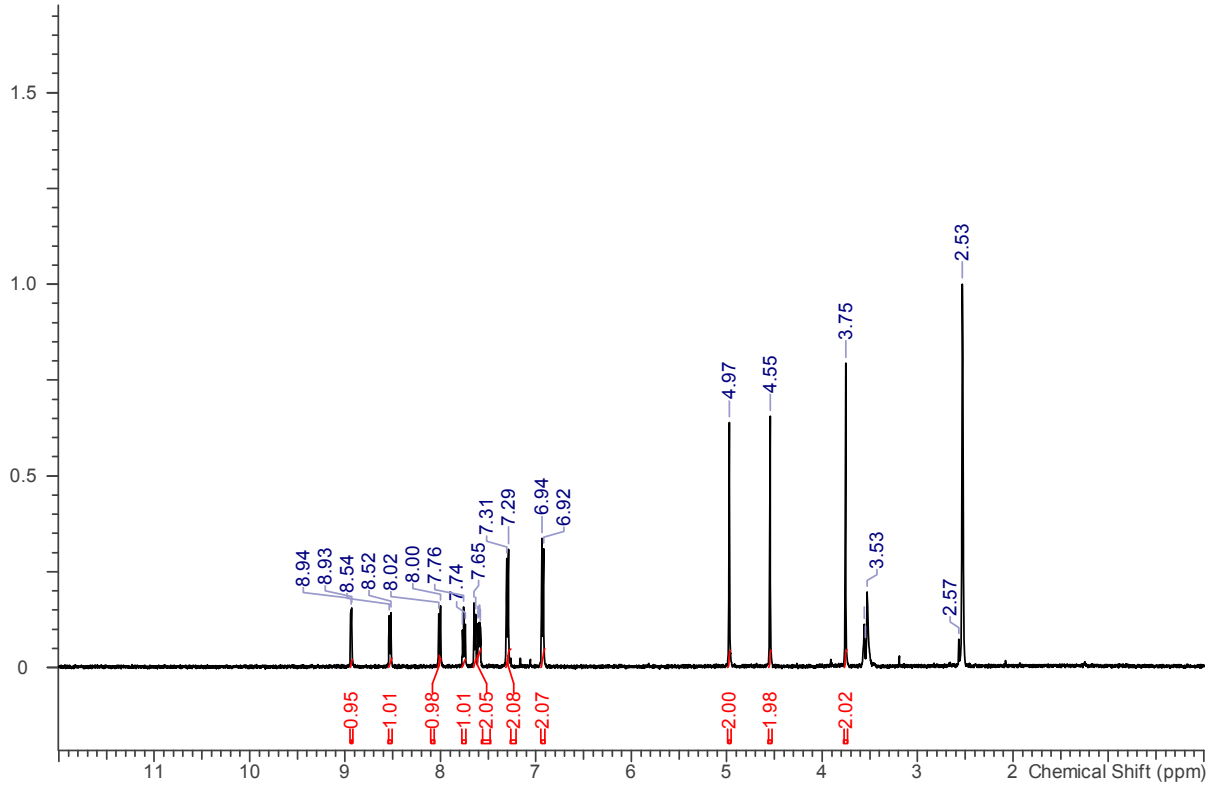
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **48**



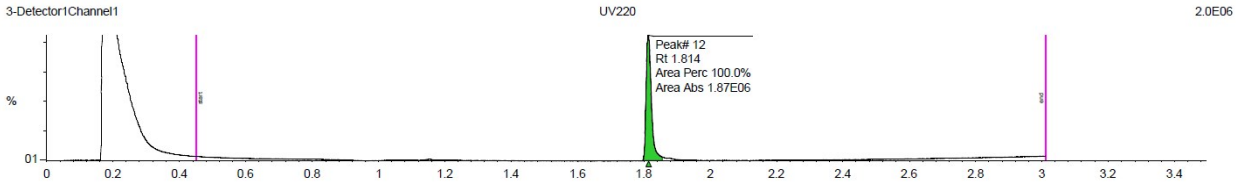
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **48**



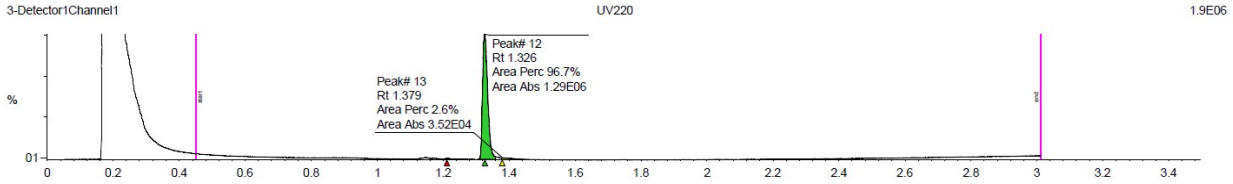
^{1}H NMR (DMSO-d_6, 500 MHz) of **51**



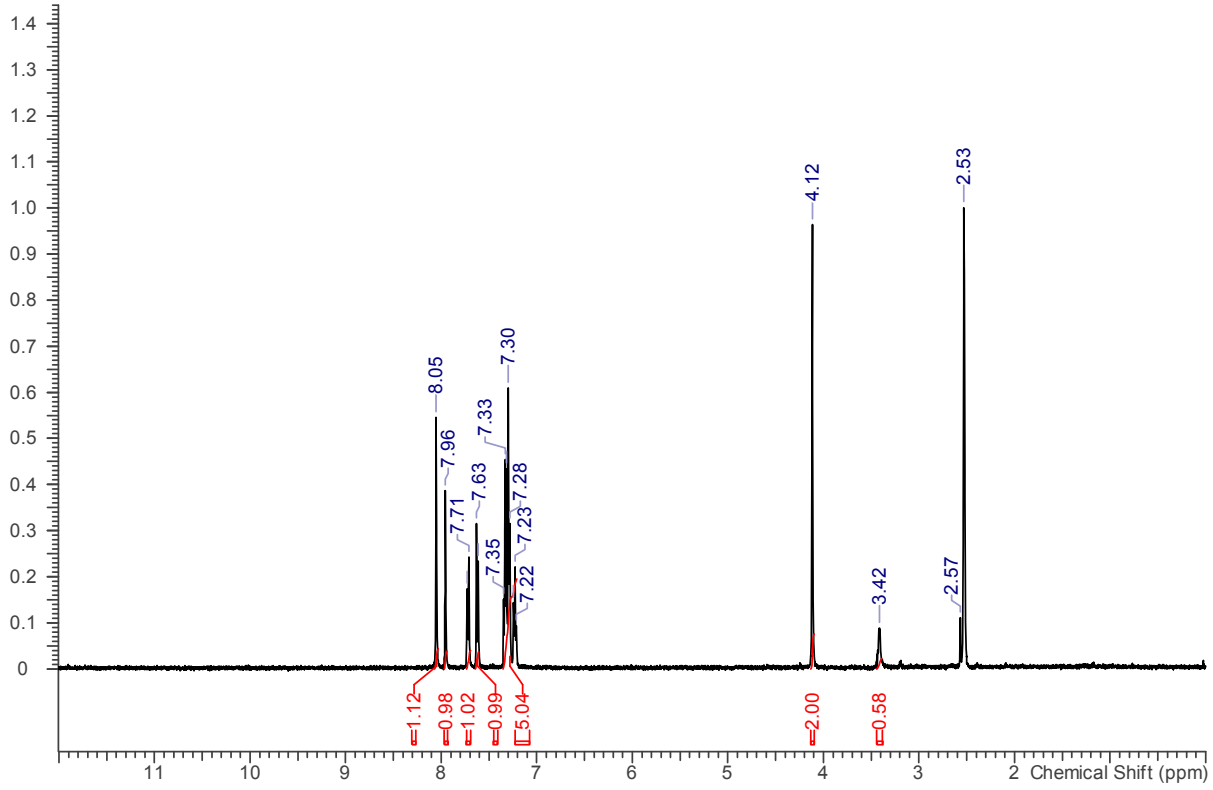
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **51**



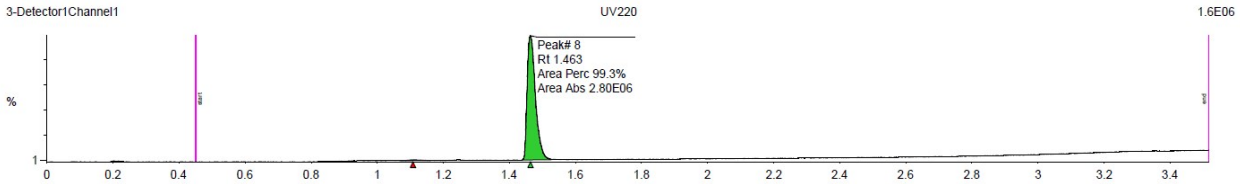
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **51**



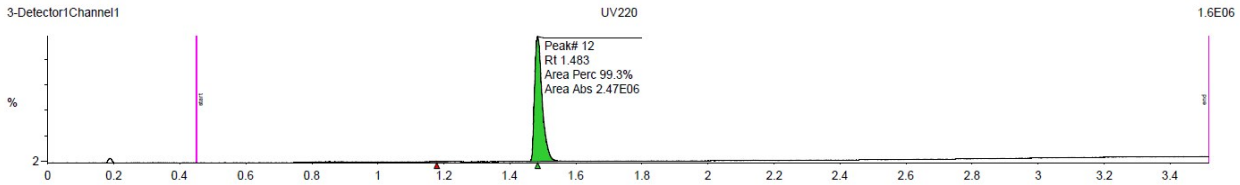
^{1}H NMR (DMSO-d_6, 500 MHz) of **52**



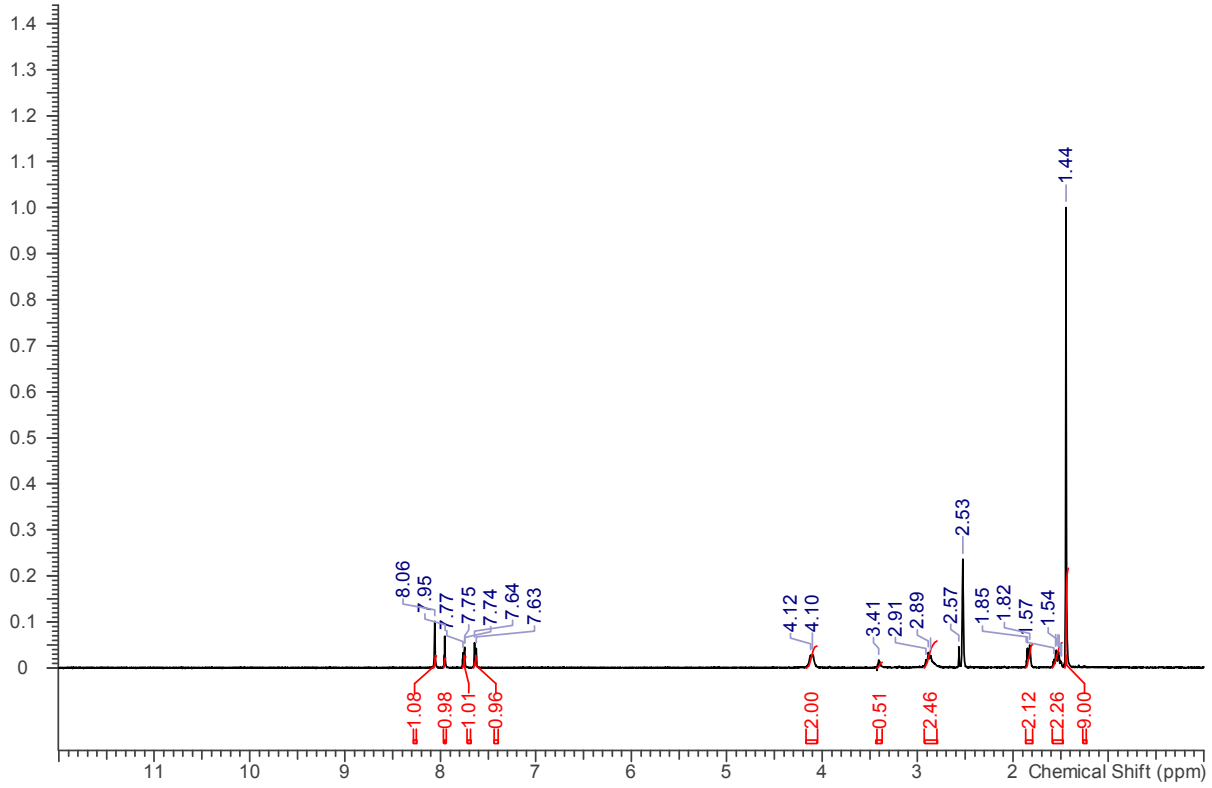
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **52**



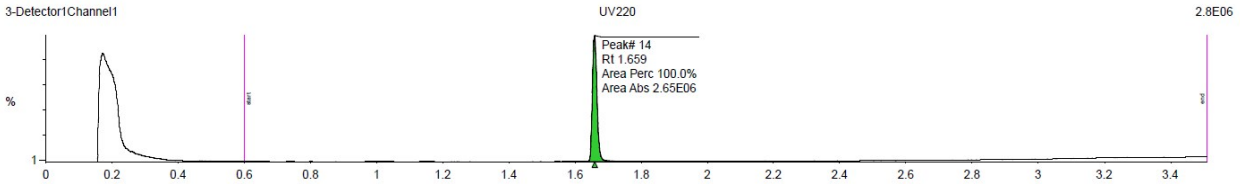
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **52**



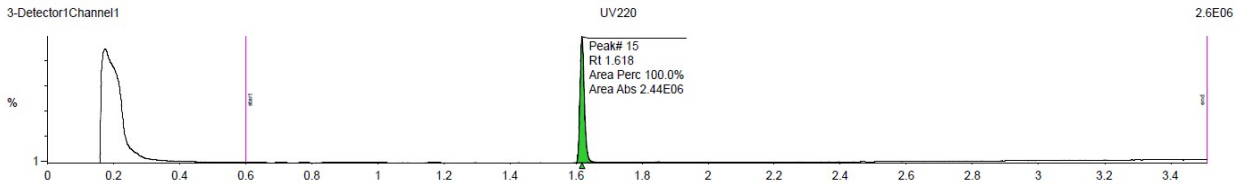
^{1}H NMR (DMSO-d_6, 500 MHz) of **53**



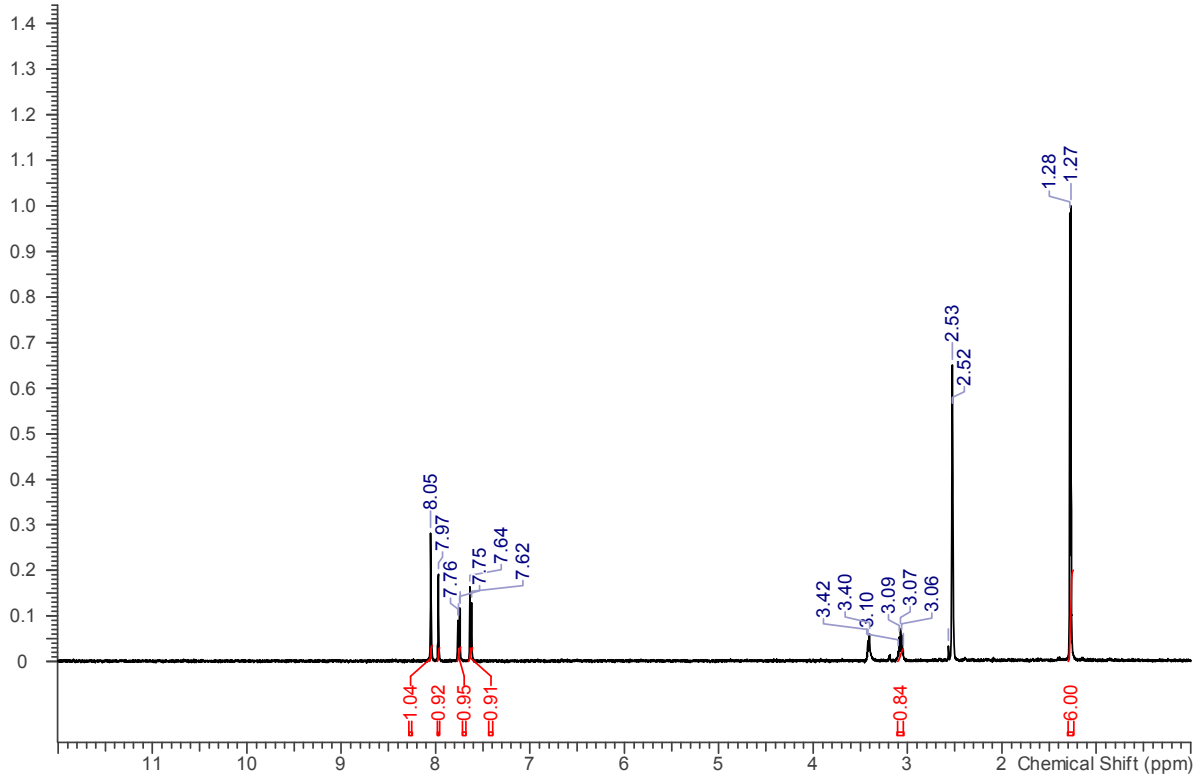
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **53**



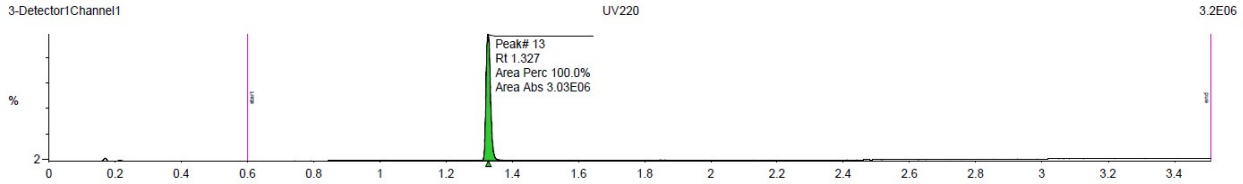
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **53**



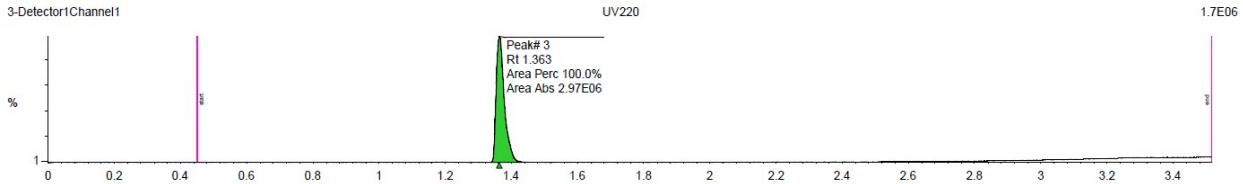
^{1}H NMR (DMSO-d_6, 500 MHz) of **54**



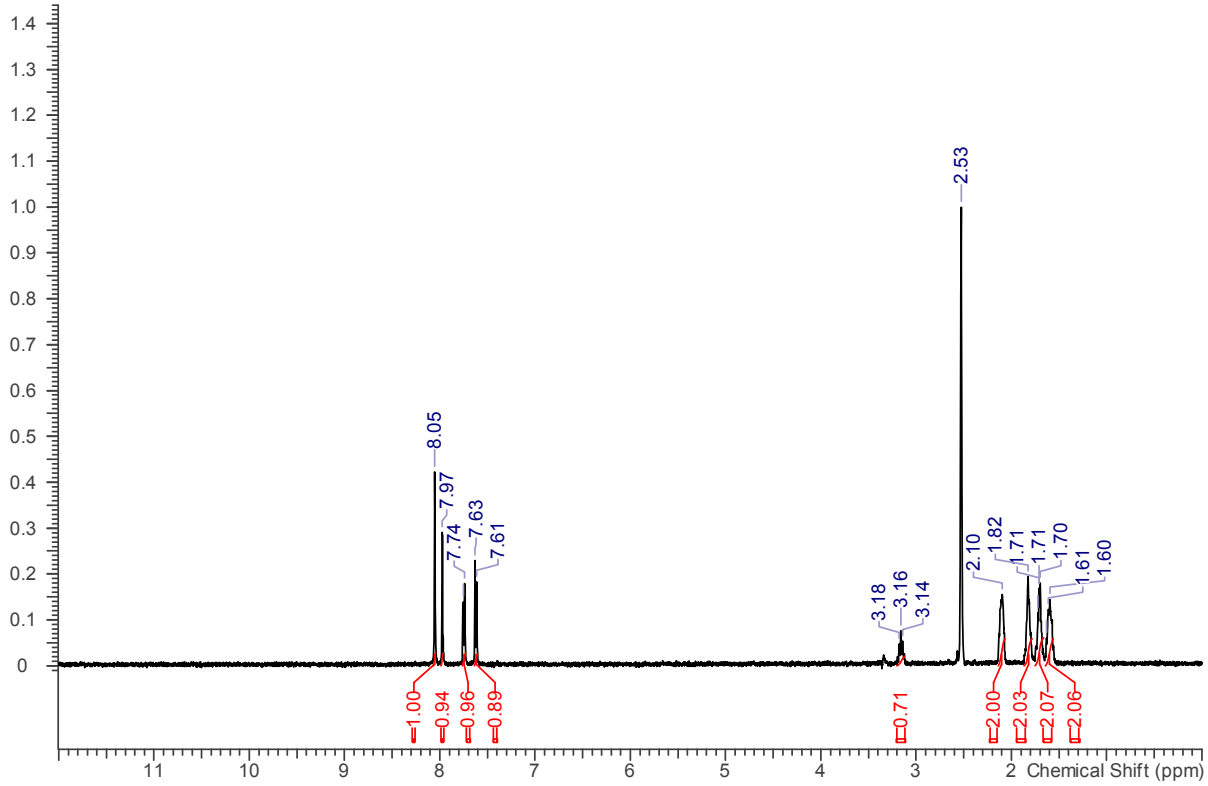
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **54**



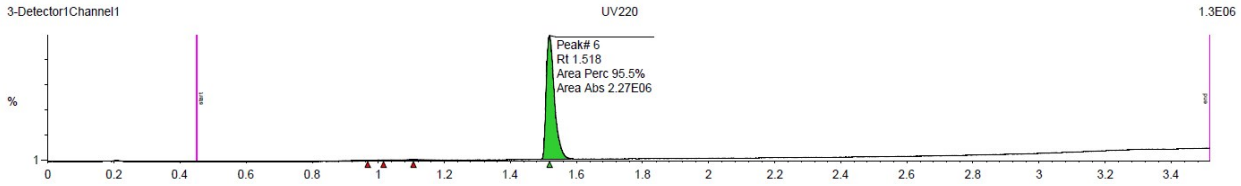
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **54**



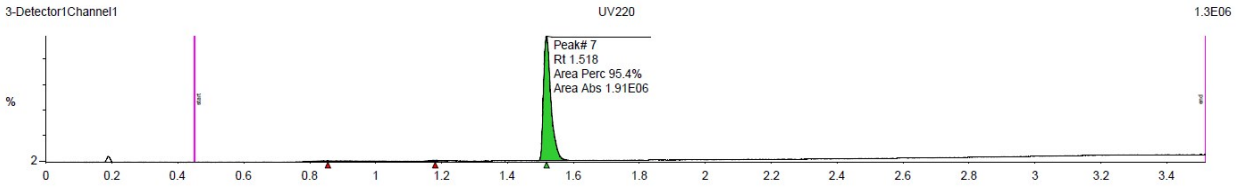
^{1}H NMR (DMSO-d_6, 500 MHz) of **55**



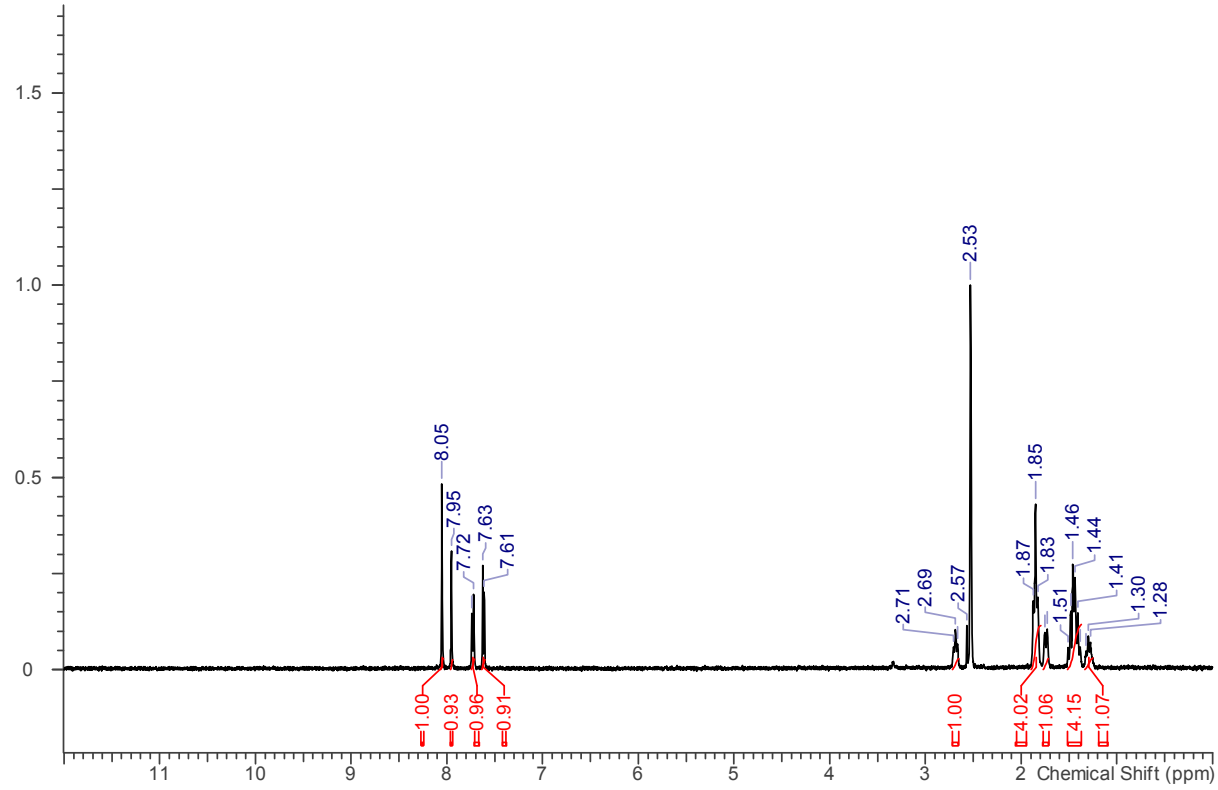
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **55**



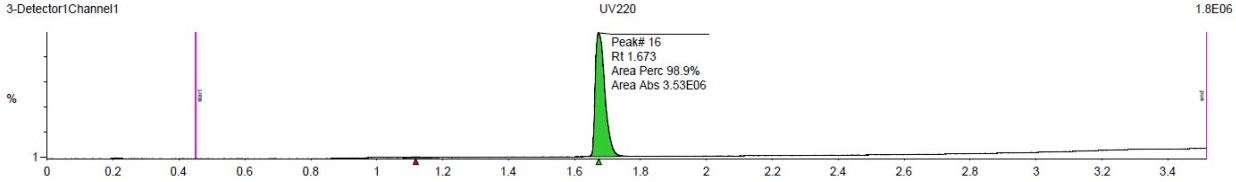
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **55**



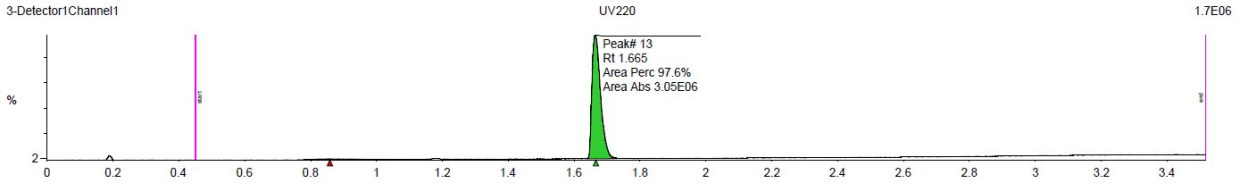
^{1}H NMR (DMSO-d_6, 500 MHz) of **56**



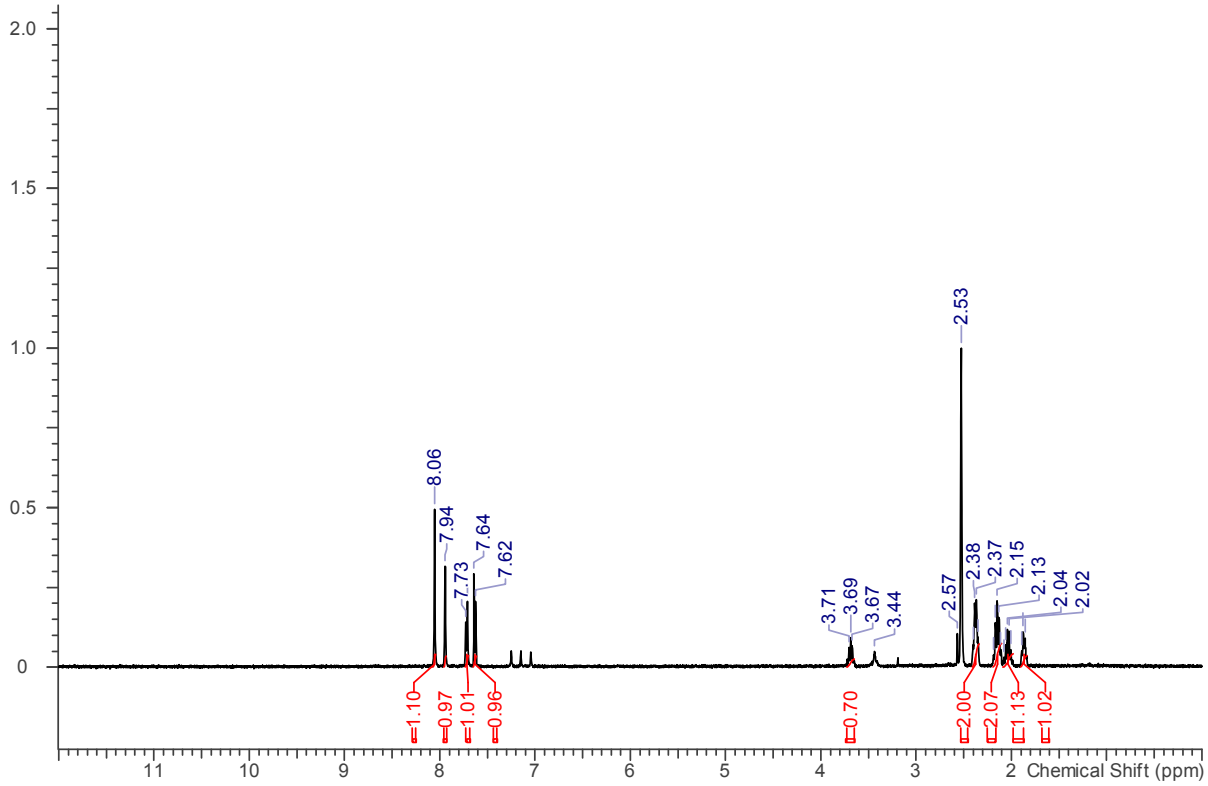
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **56**



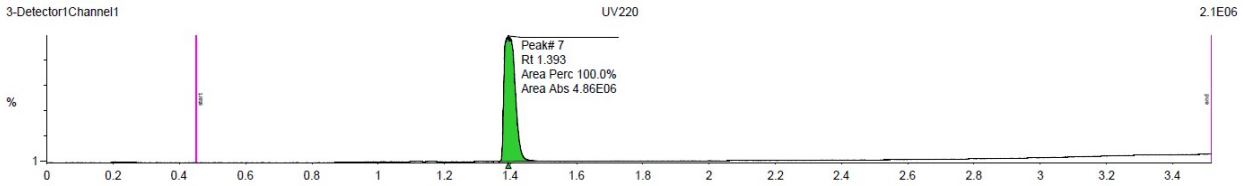
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **56**



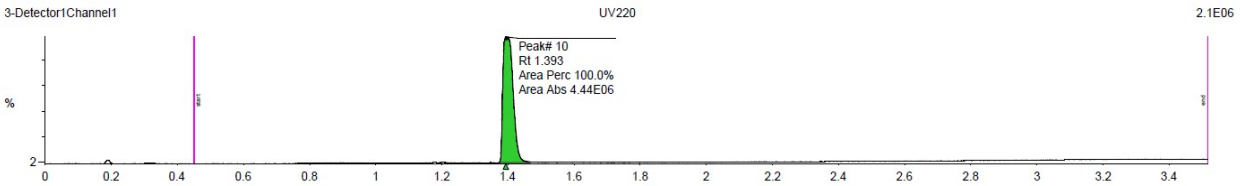
^{1}H NMR (DMSO-d_6, 500 MHz) of **57**



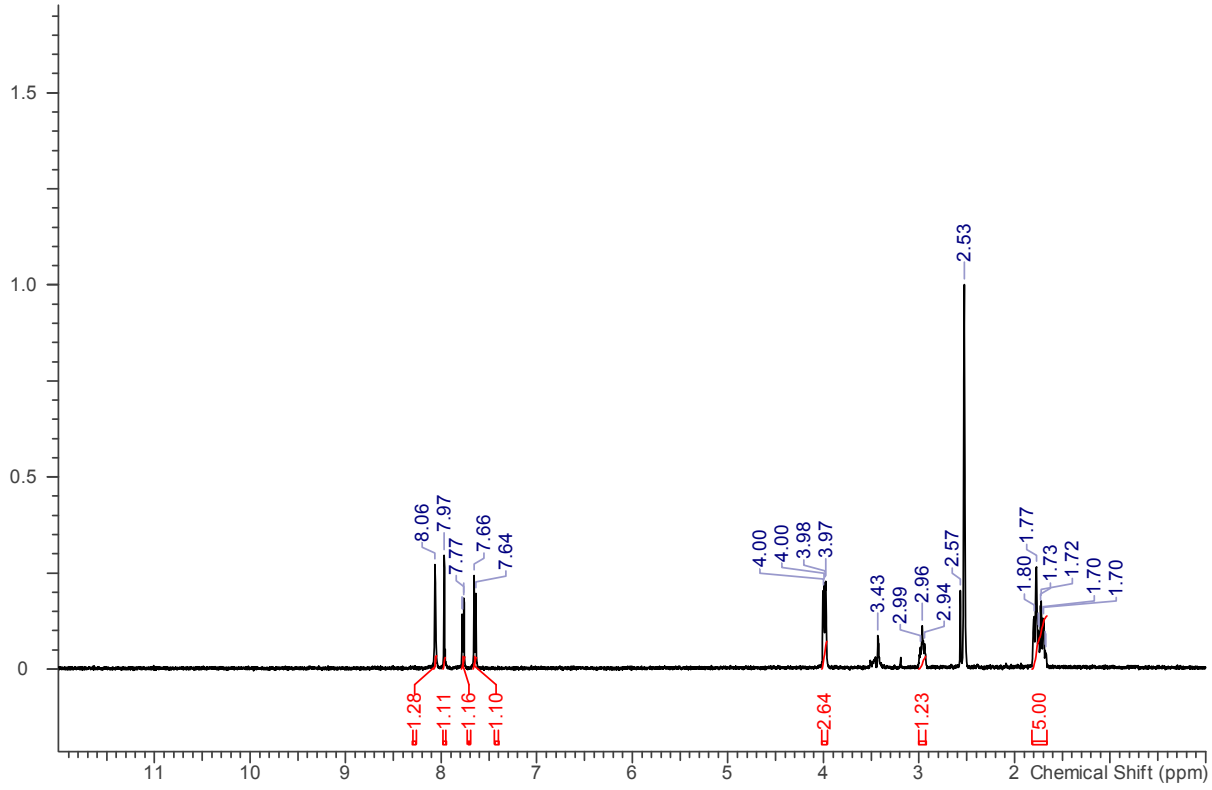
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **57**



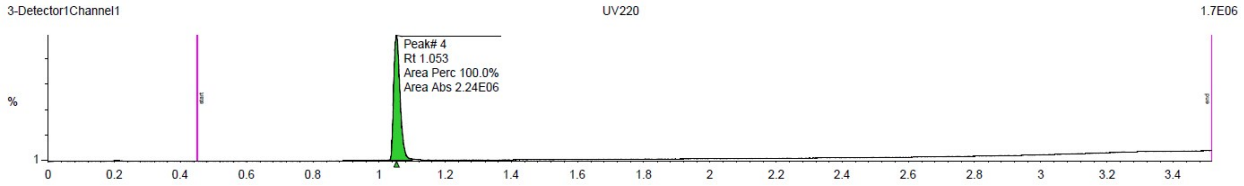
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **57**



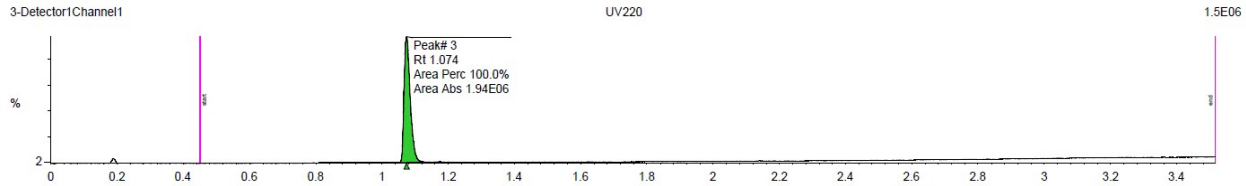
^{1}H NMR (DMSO-d_6, 500 MHz) of **59**



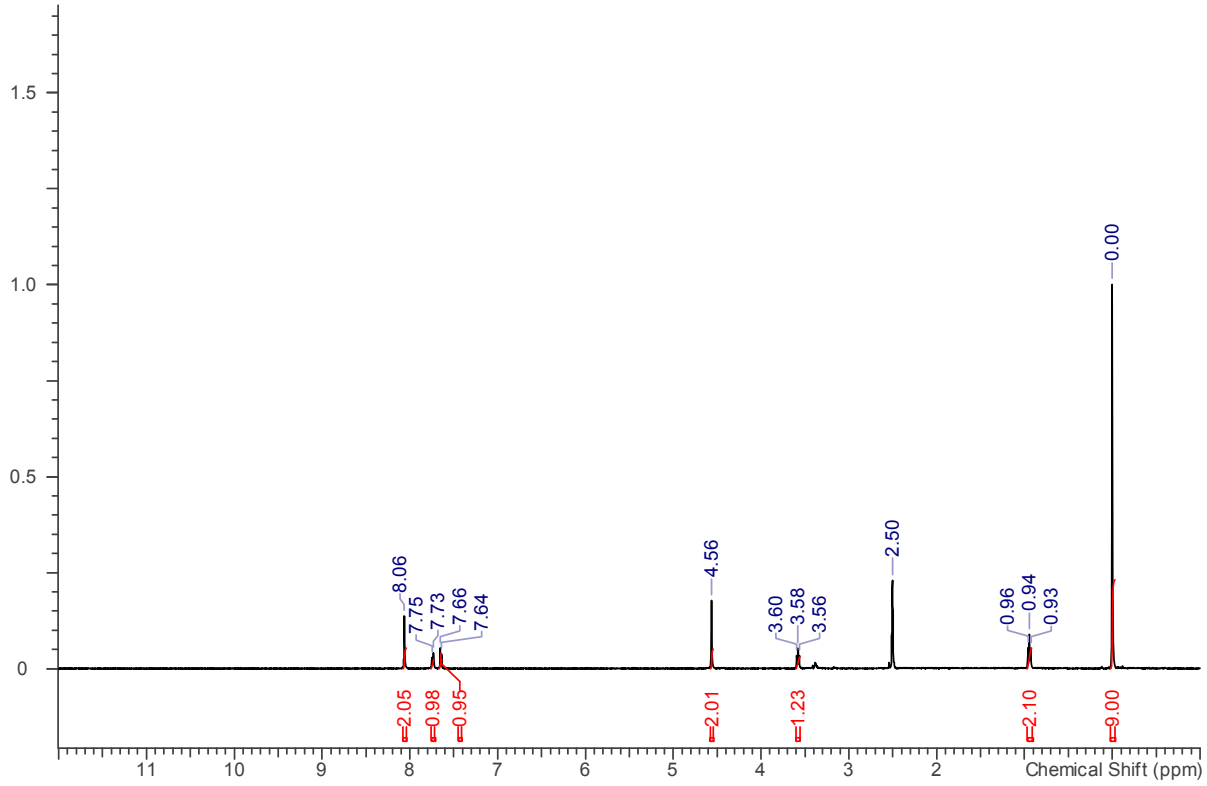
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **59**



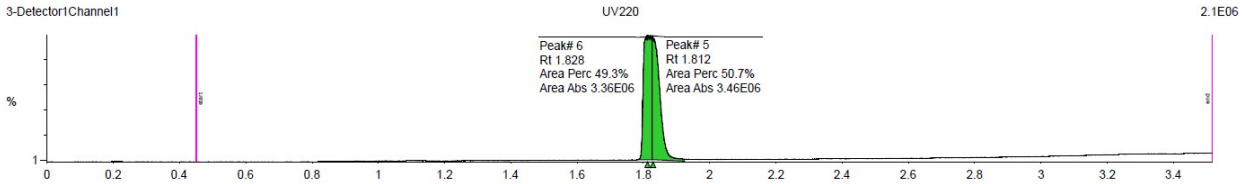
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **59**



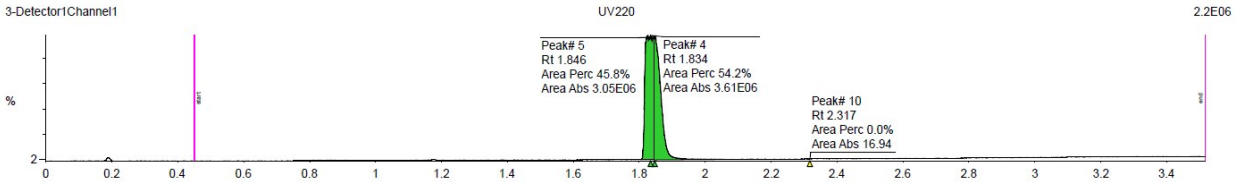
^{1}H NMR (DMSO-d_6, 500 MHz) of **60**



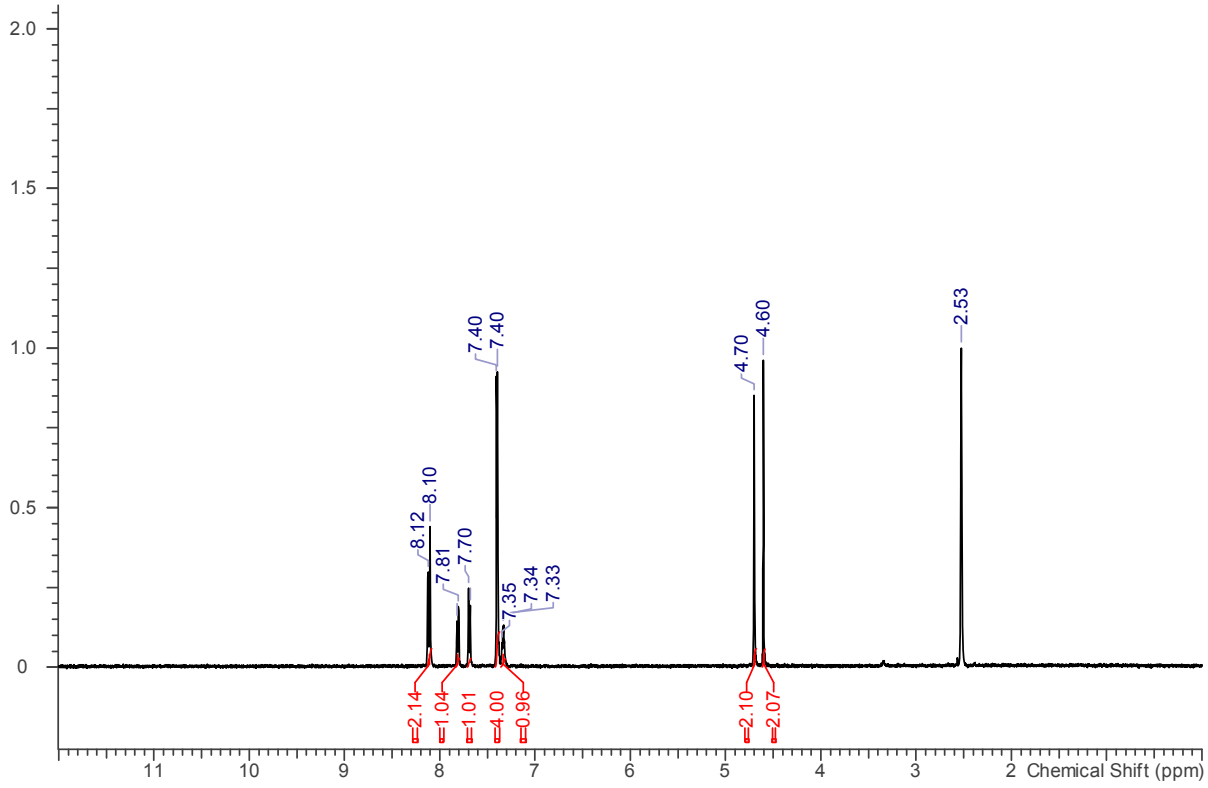
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **60**



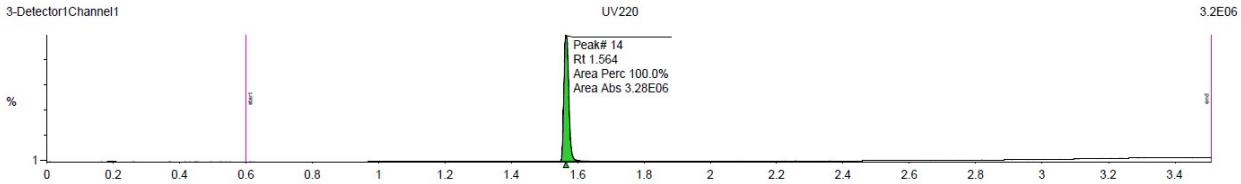
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **60**



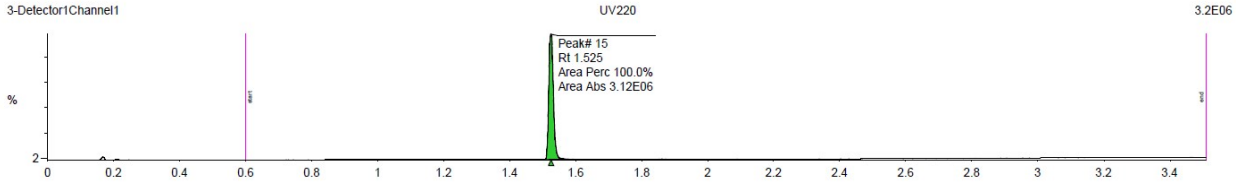
^{1}H NMR (DMSO-d_6, 500 MHz) of **61**



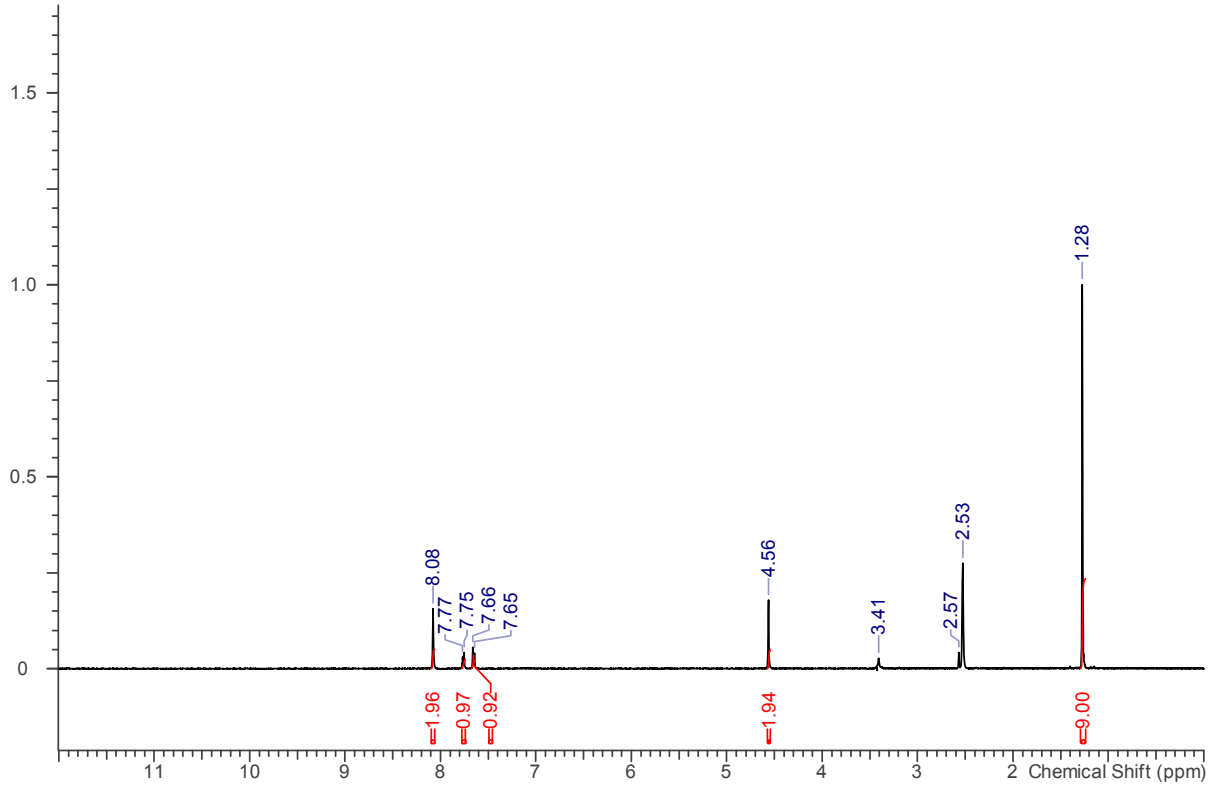
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **61**



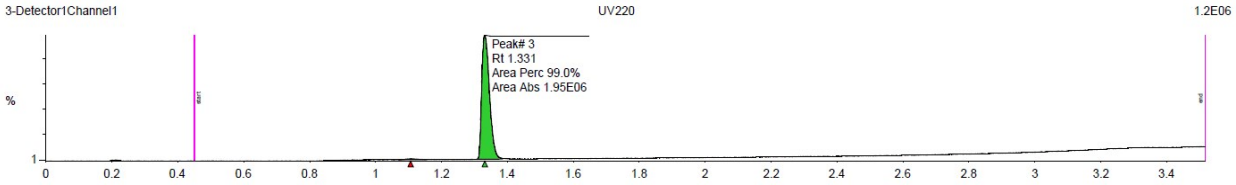
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **61**



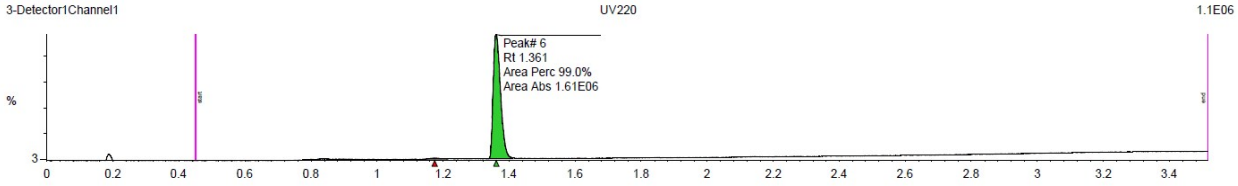
^{1}H NMR (DMSO-d_6, 500 MHz) of **62**



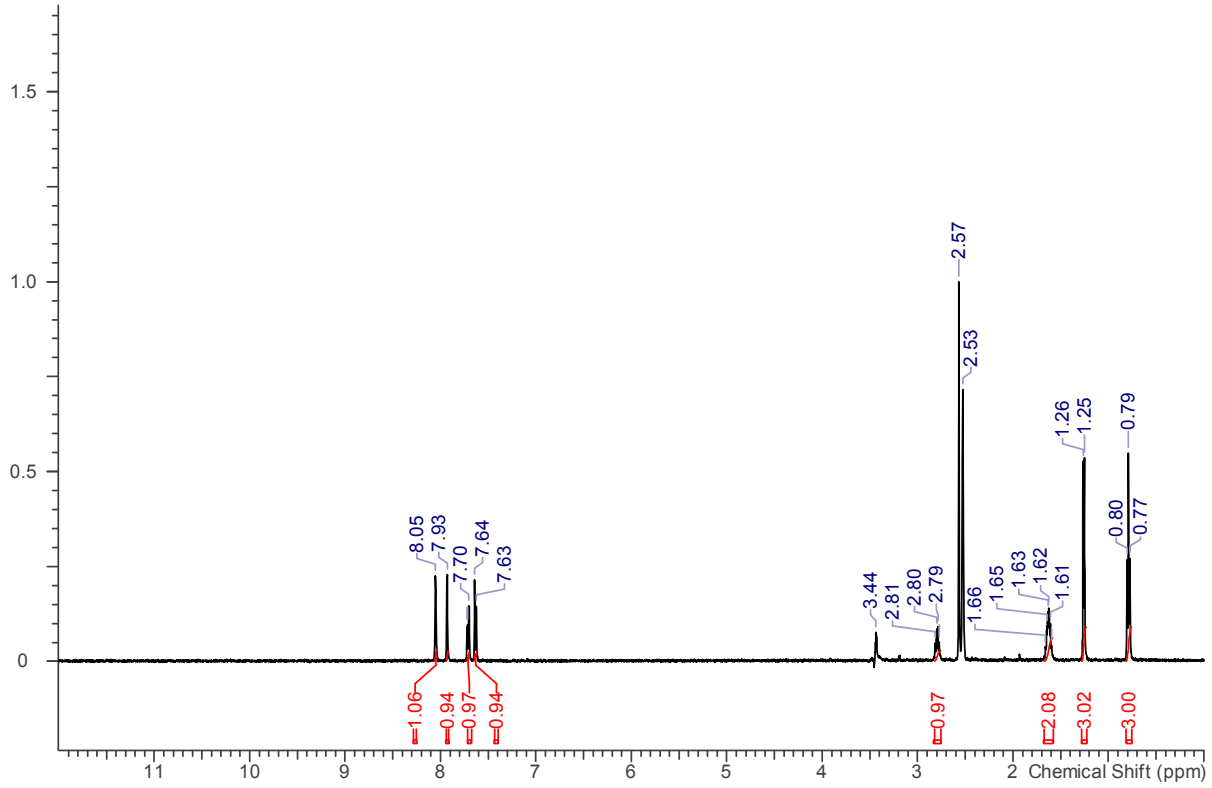
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **62**



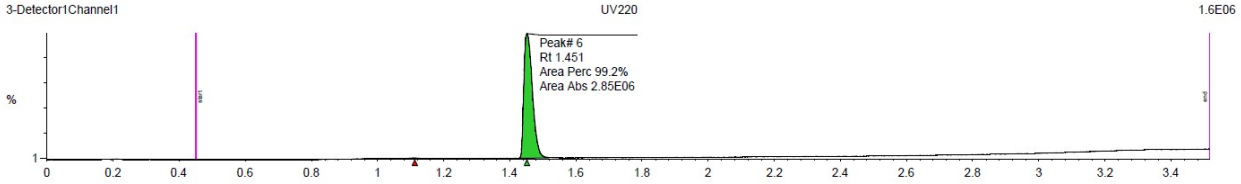
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **62**



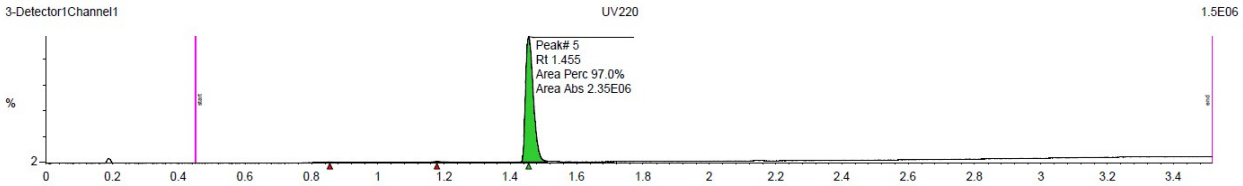
^{1}H NMR (DMSO-d_6, 500 MHz) of **63**



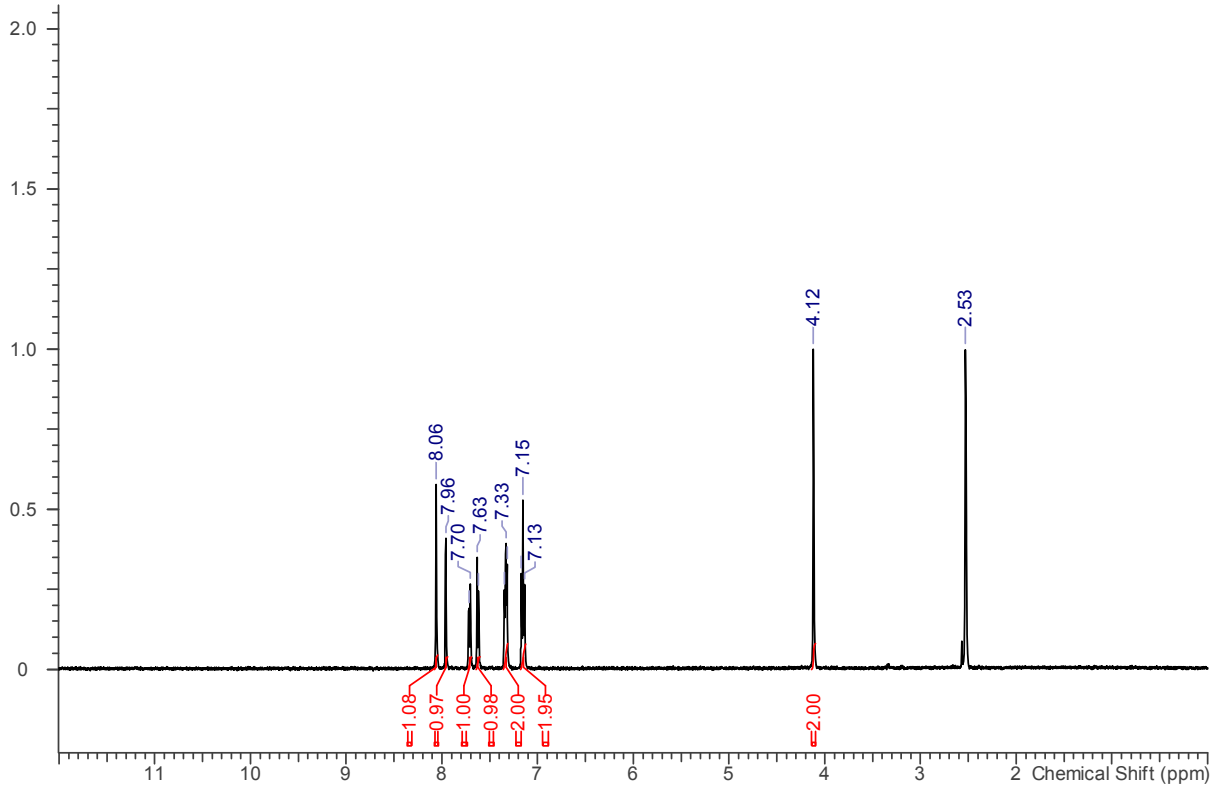
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **63**



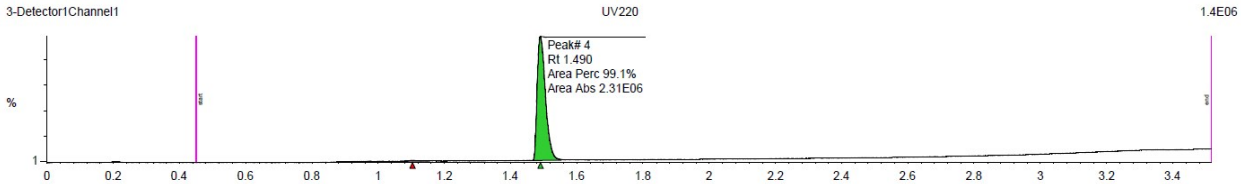
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **63**



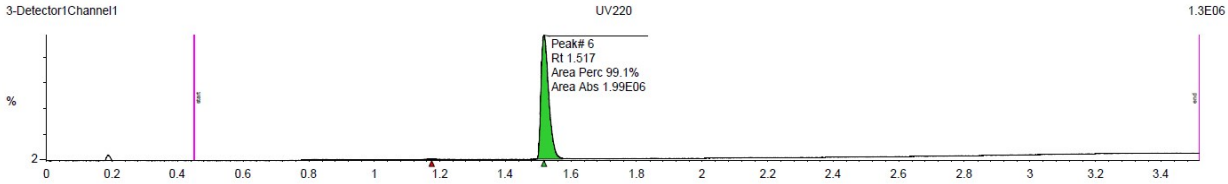
^{1}H NMR (DMSO-d_6, 500 MHz) of **64**



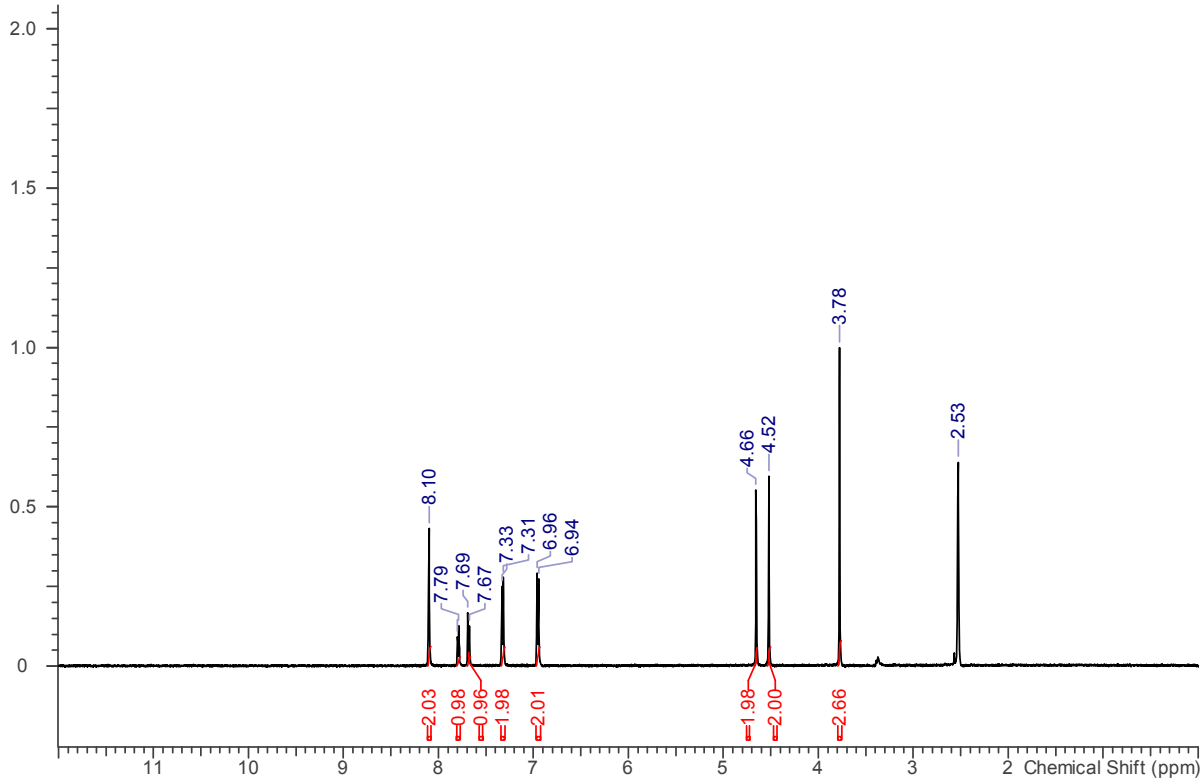
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **64**



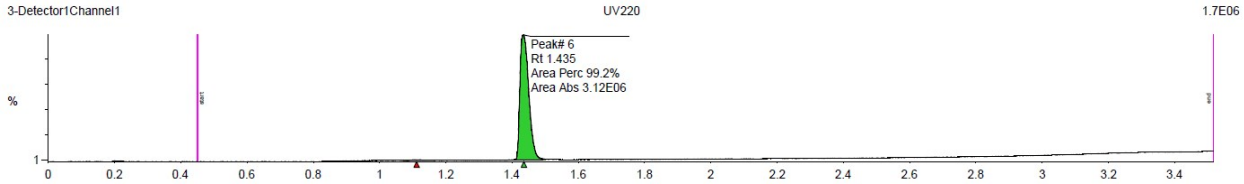
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **64**



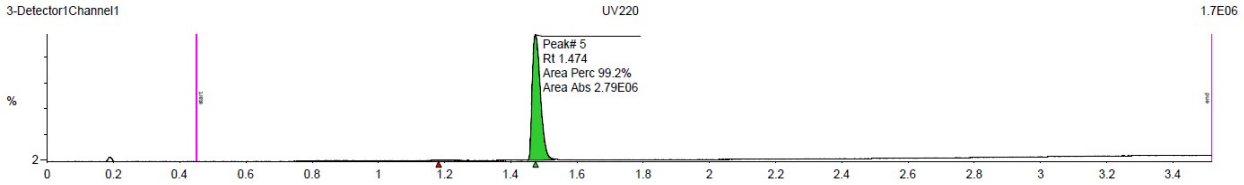
^{1}H NMR (DMSO-d_6, 500 MHz) of **65**



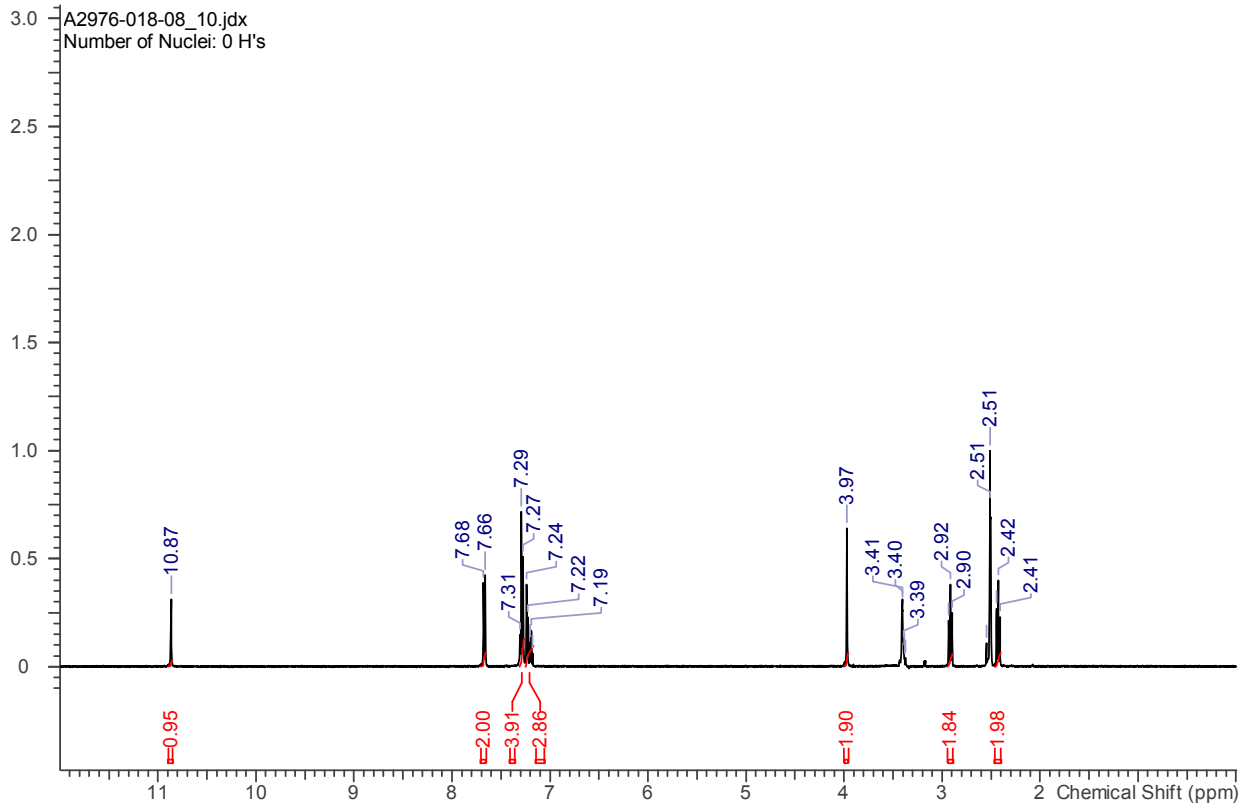
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **65**



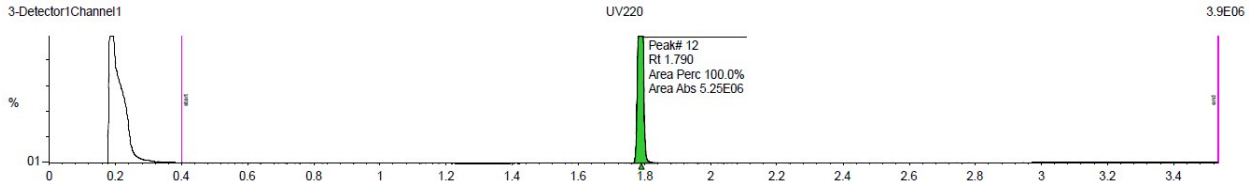
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **65**



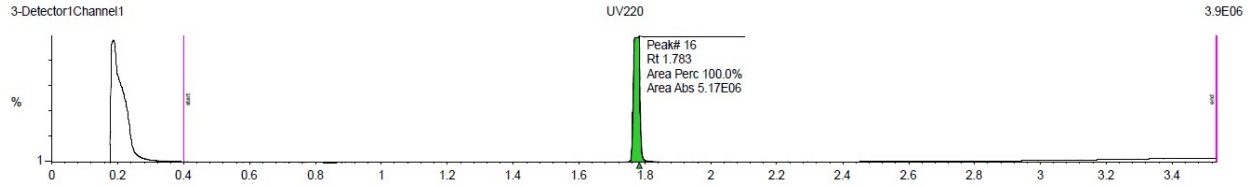
^{1}H NMR (DMSO-d_6, 500 MHz) of **80**



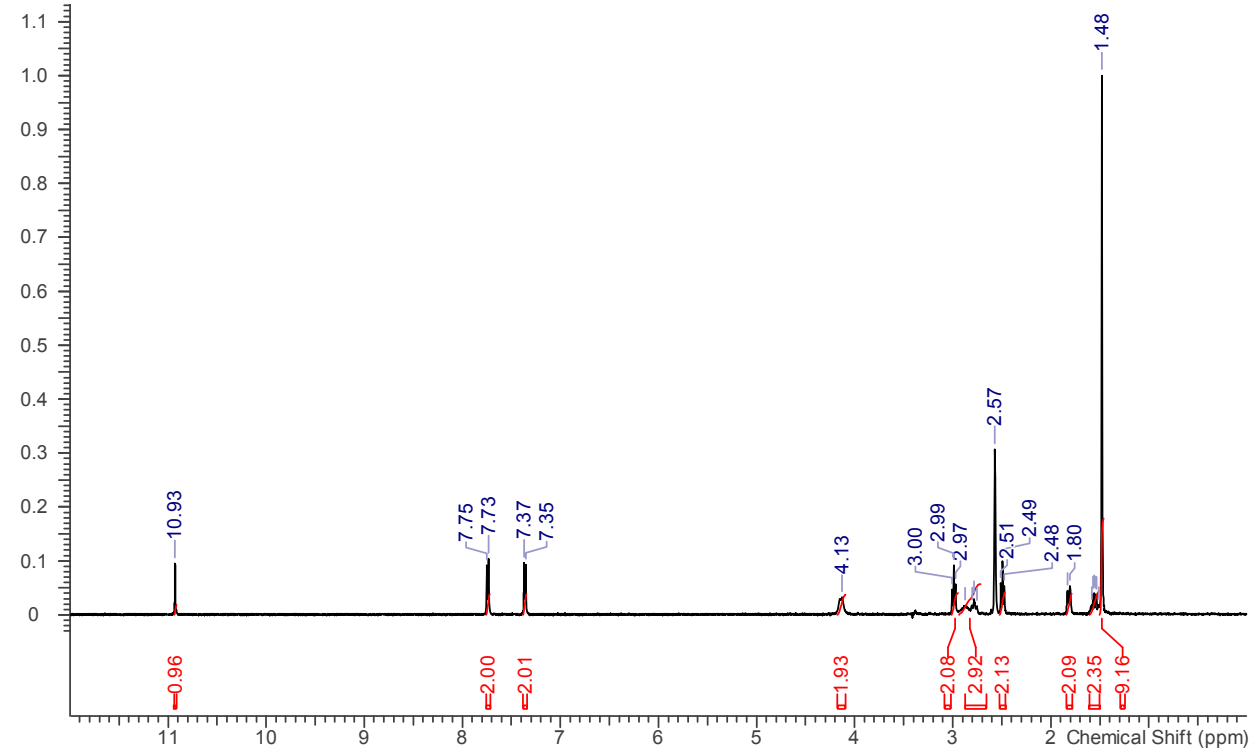
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **80**



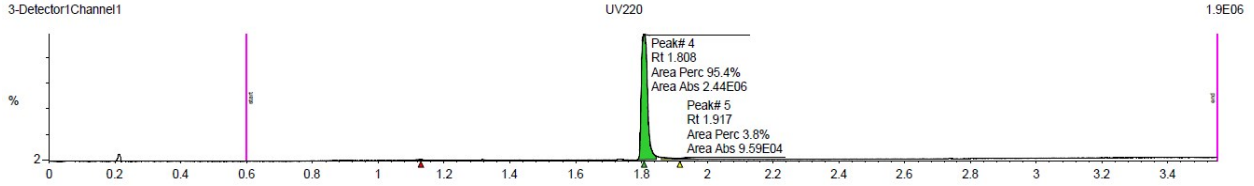
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **80**



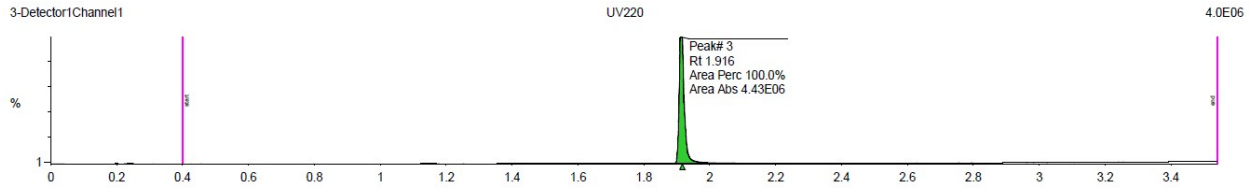
^{1}H NMR (DMSO-d_6, 500 MHz) of **81**



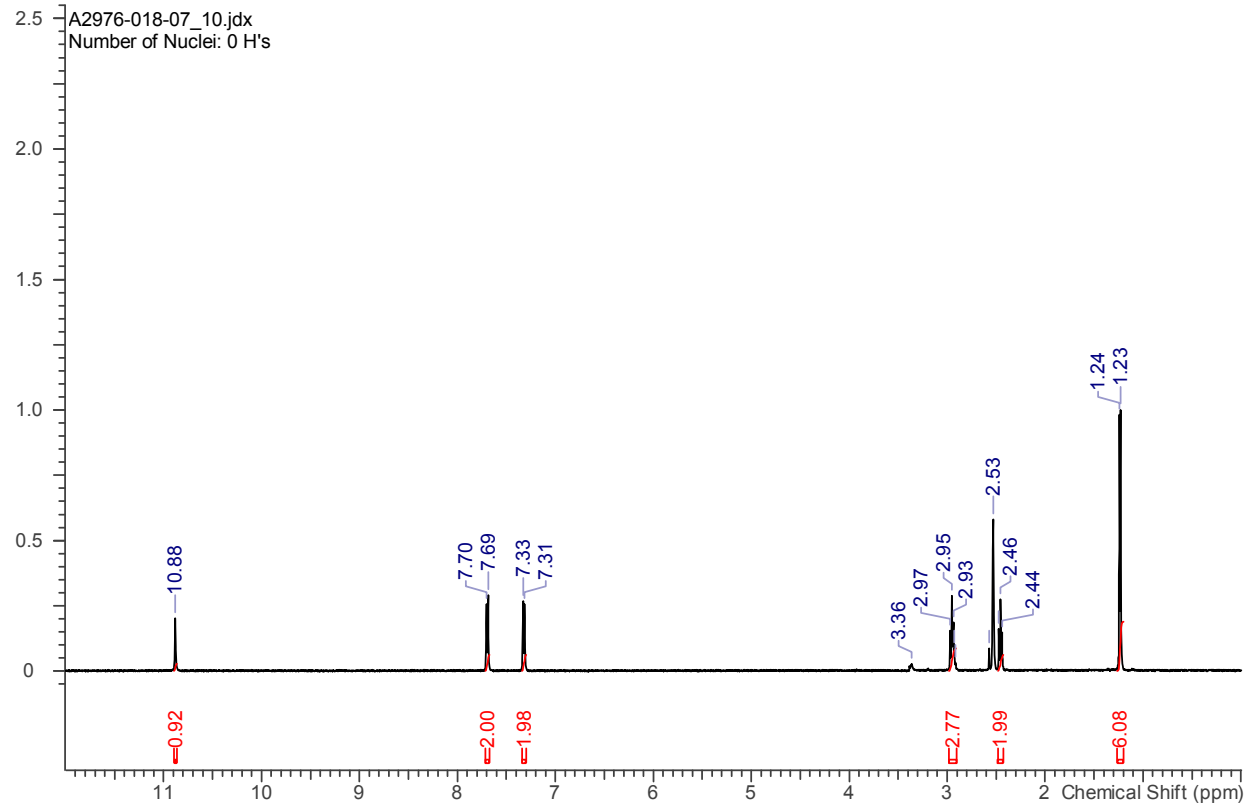
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **81**



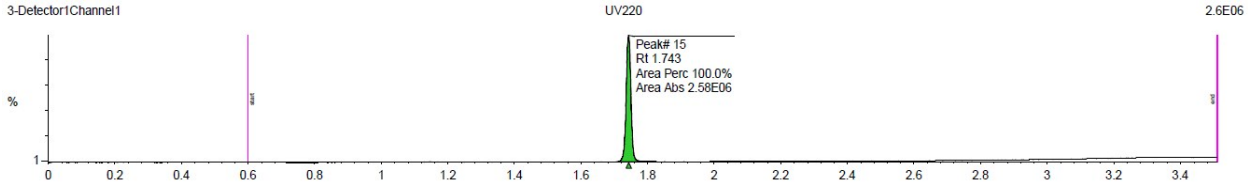
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **81**



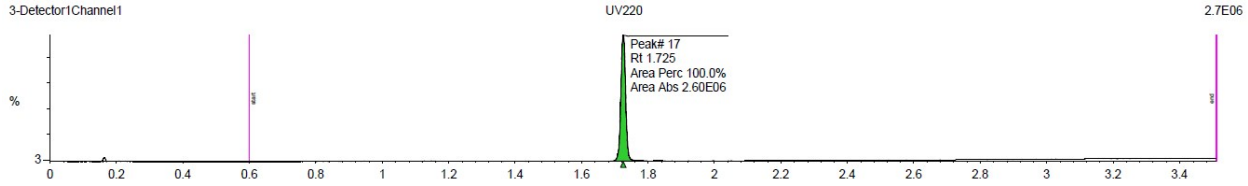
^{1}H NMR (DMSO-d_6, 500 MHz) of **82**



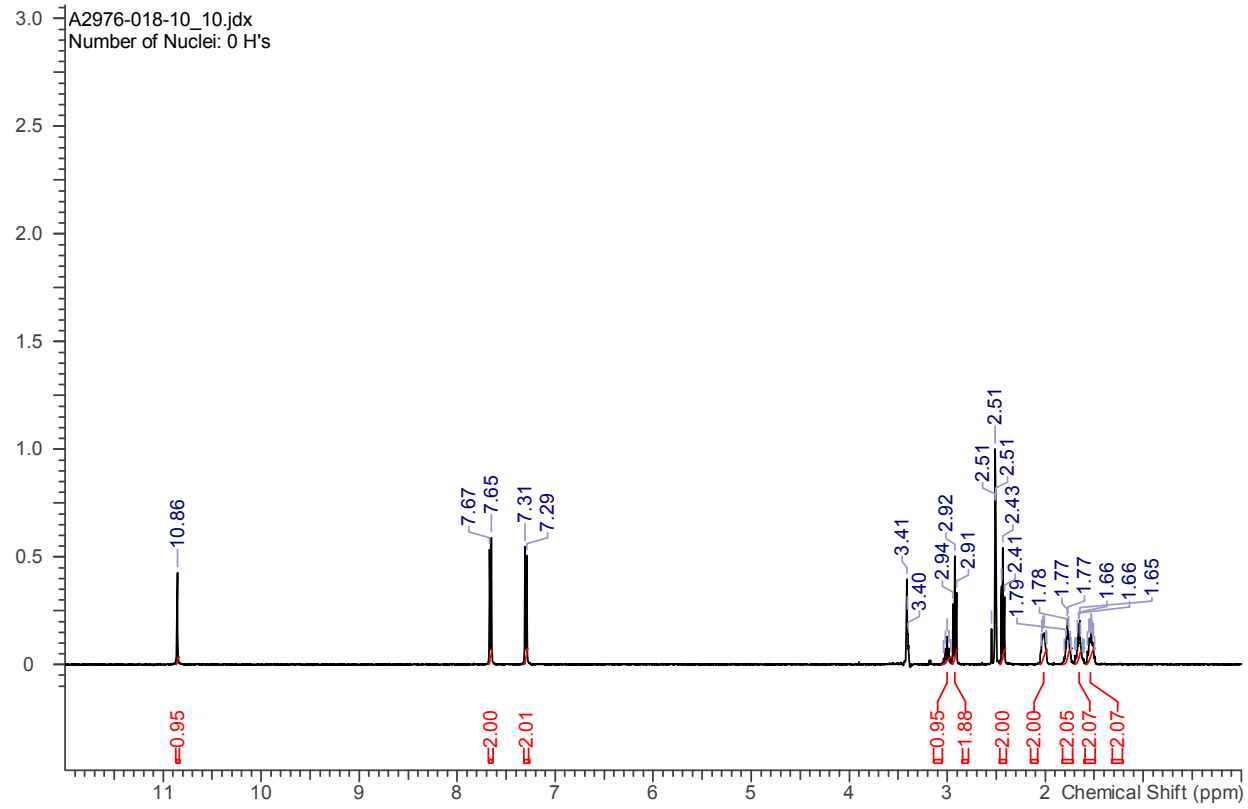
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **82**



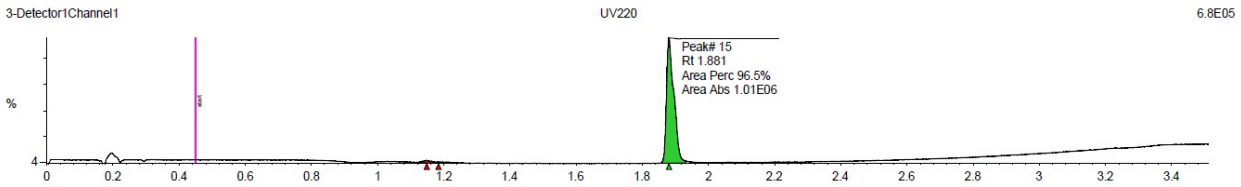
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **82**



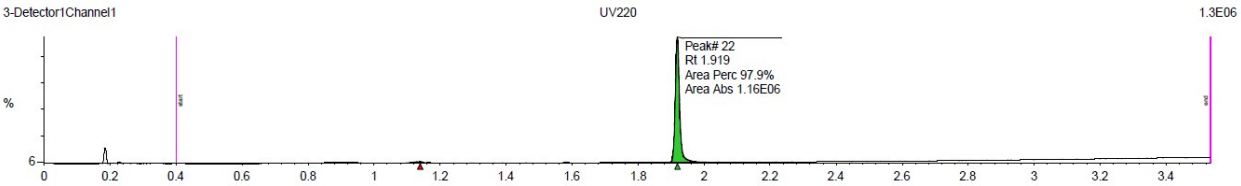
^{1}H NMR (DMSO-d_6, 500 MHz) of **83**



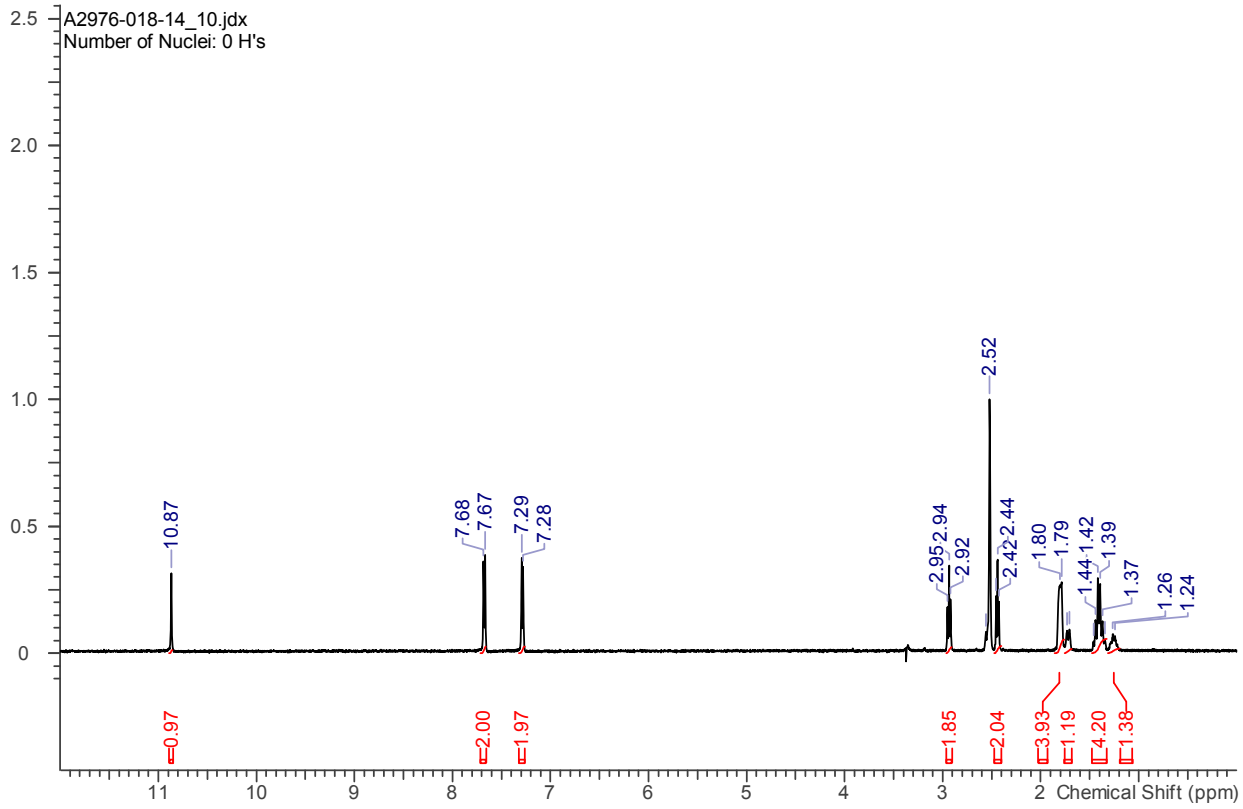
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **83**



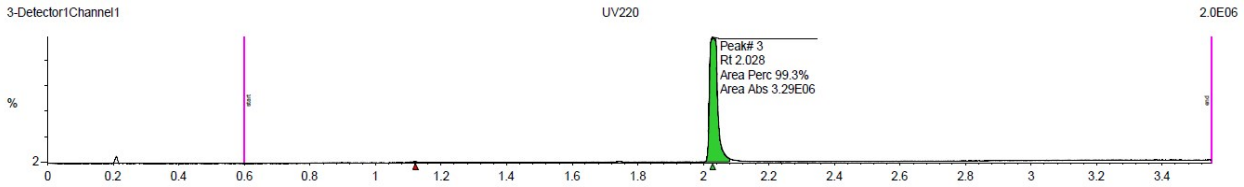
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **83**



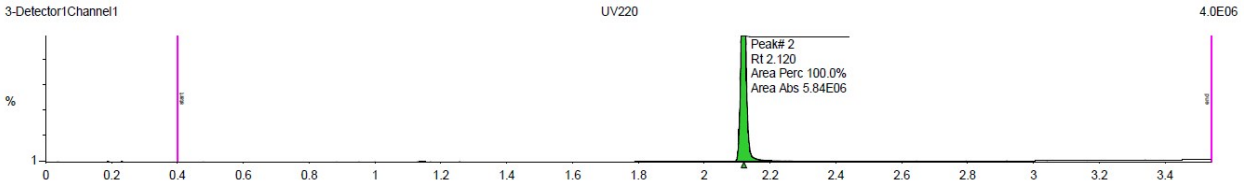
^{1}H NMR (DMSO-d_6, 500 MHz) of **84**



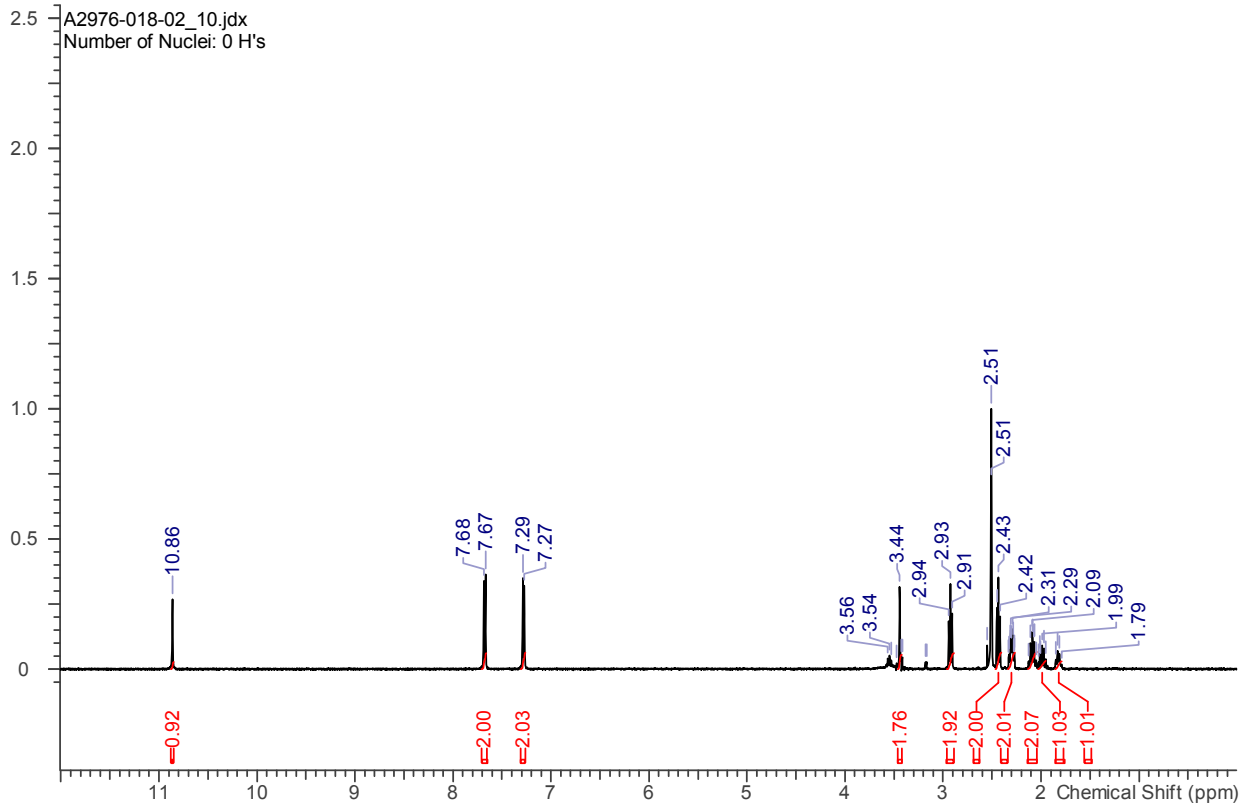
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **84**



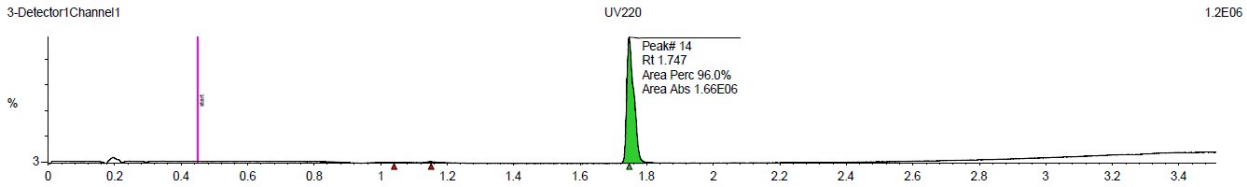
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **84**



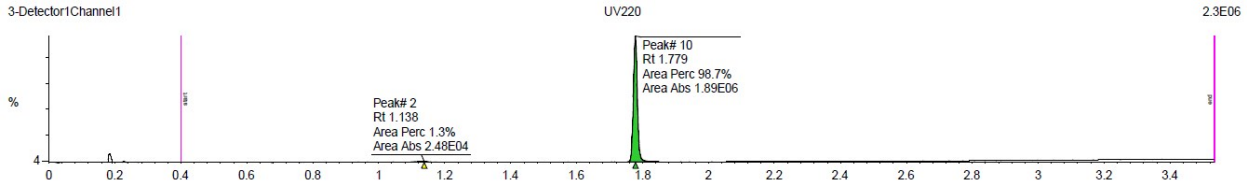
^{1}H NMR (DMSO-d_6, 500 MHz) of **85**



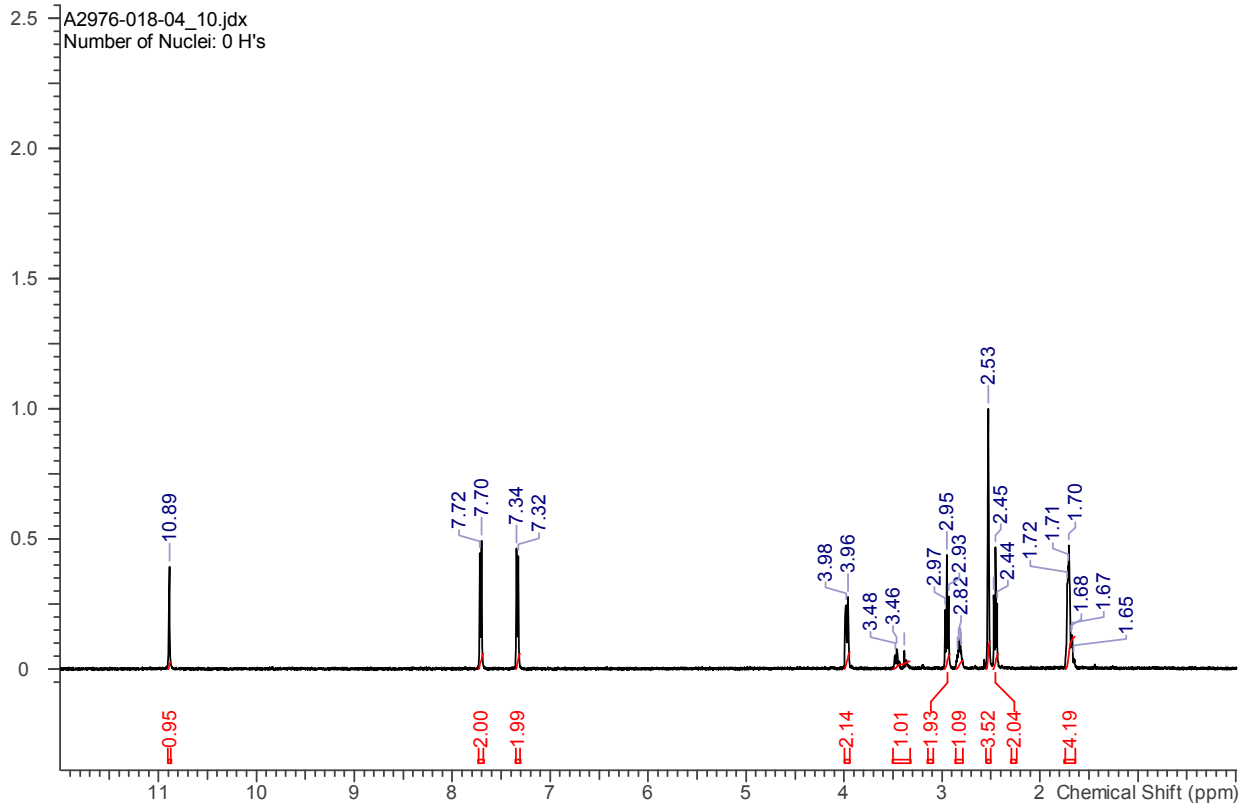
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **85**



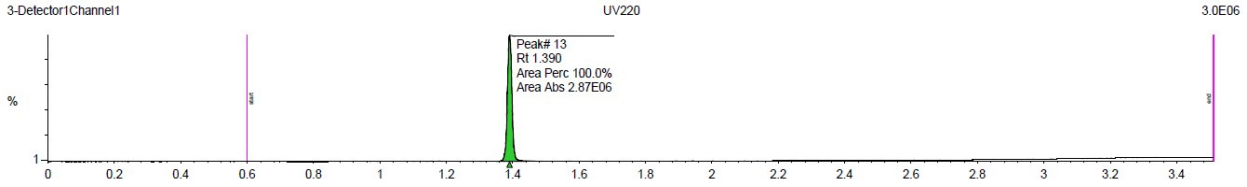
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **85**



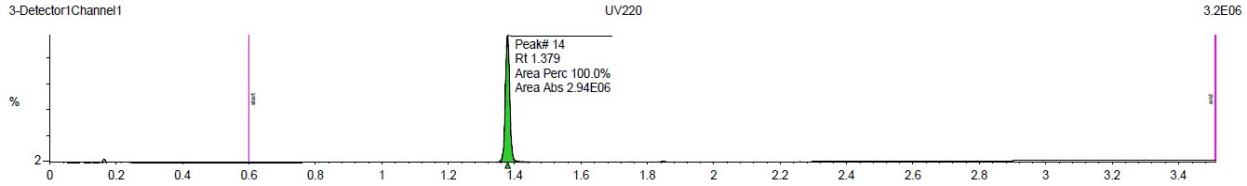
^{1}H NMR (DMSO-d_6, 500 MHz) of **87**



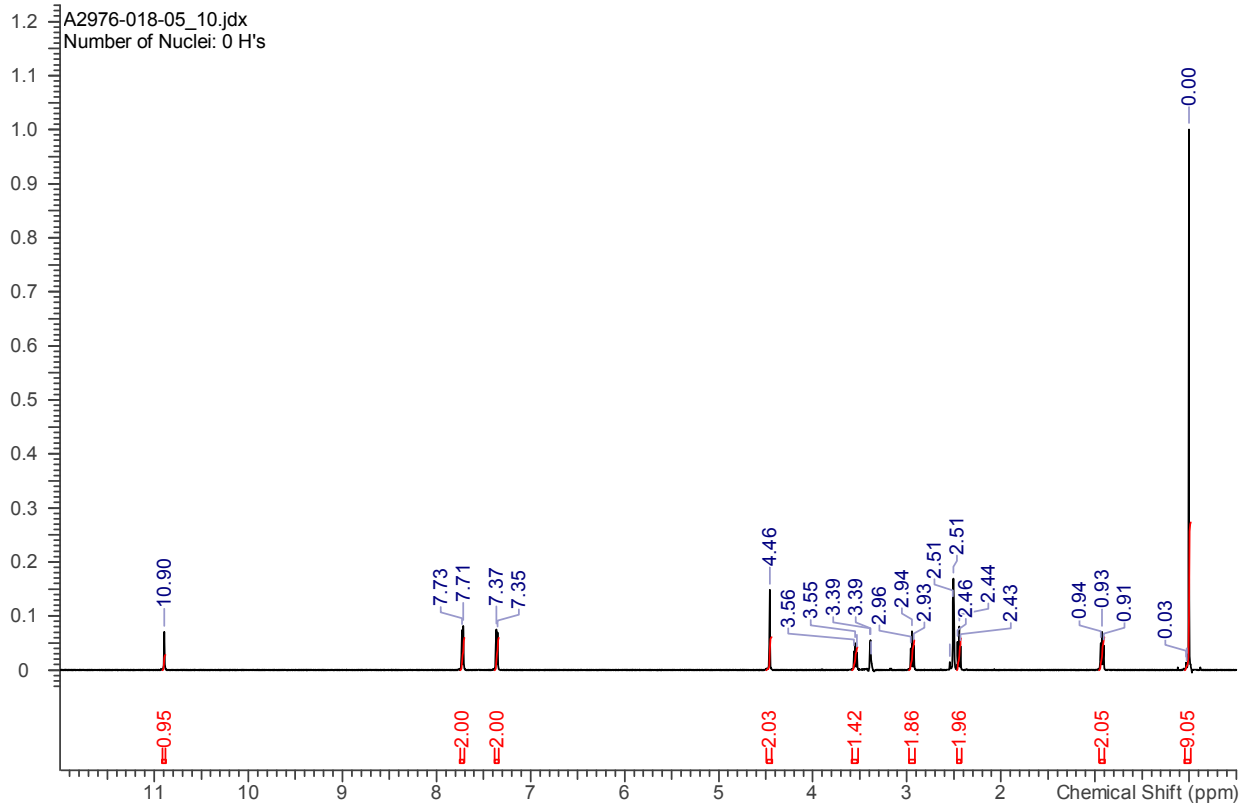
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **87**



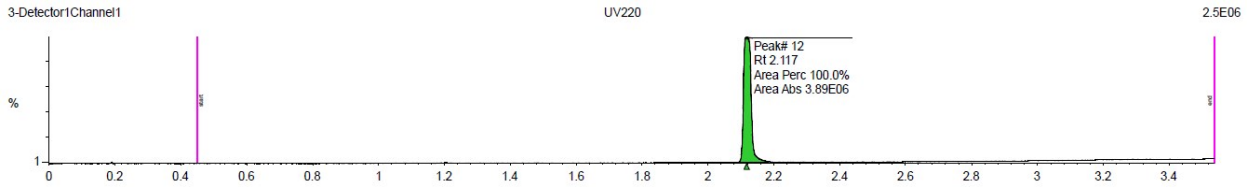
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **87**



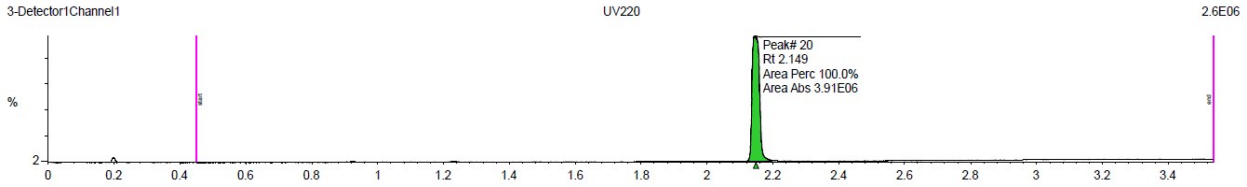
^{1}H NMR (DMSO-d_6, 500 MHz) of **88**



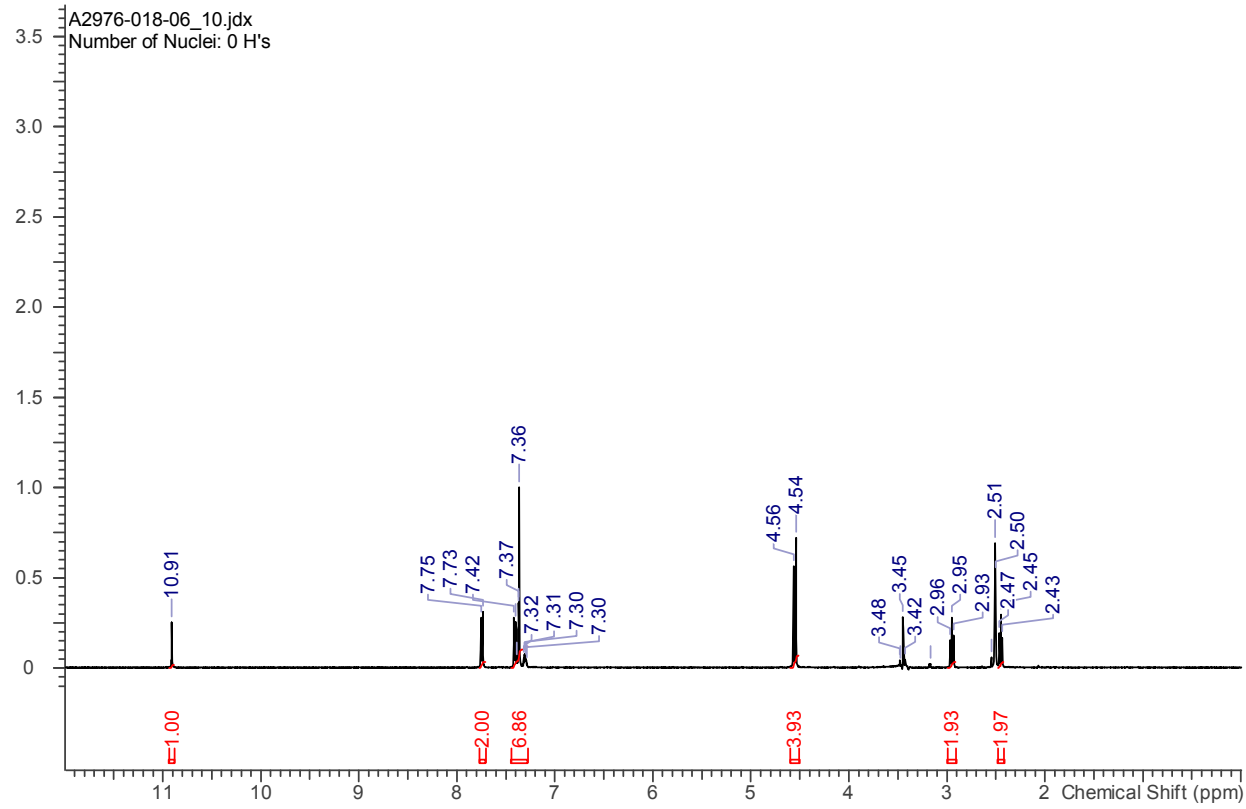
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **88**



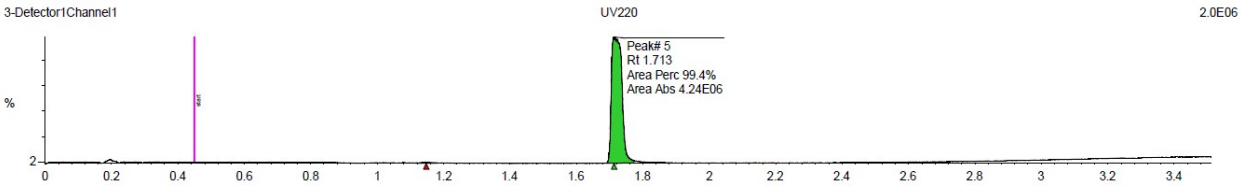
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **88**



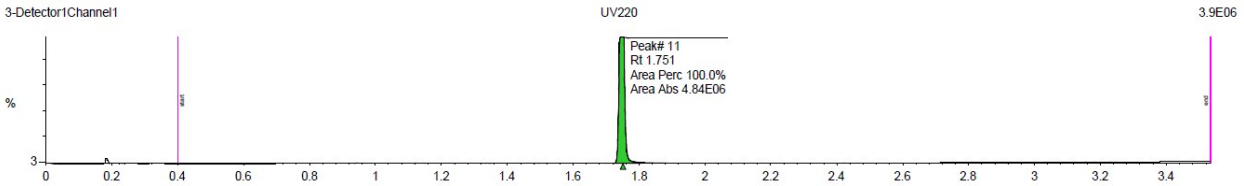
^{1}H NMR (DMSO-d_6, 500 MHz) of **89**



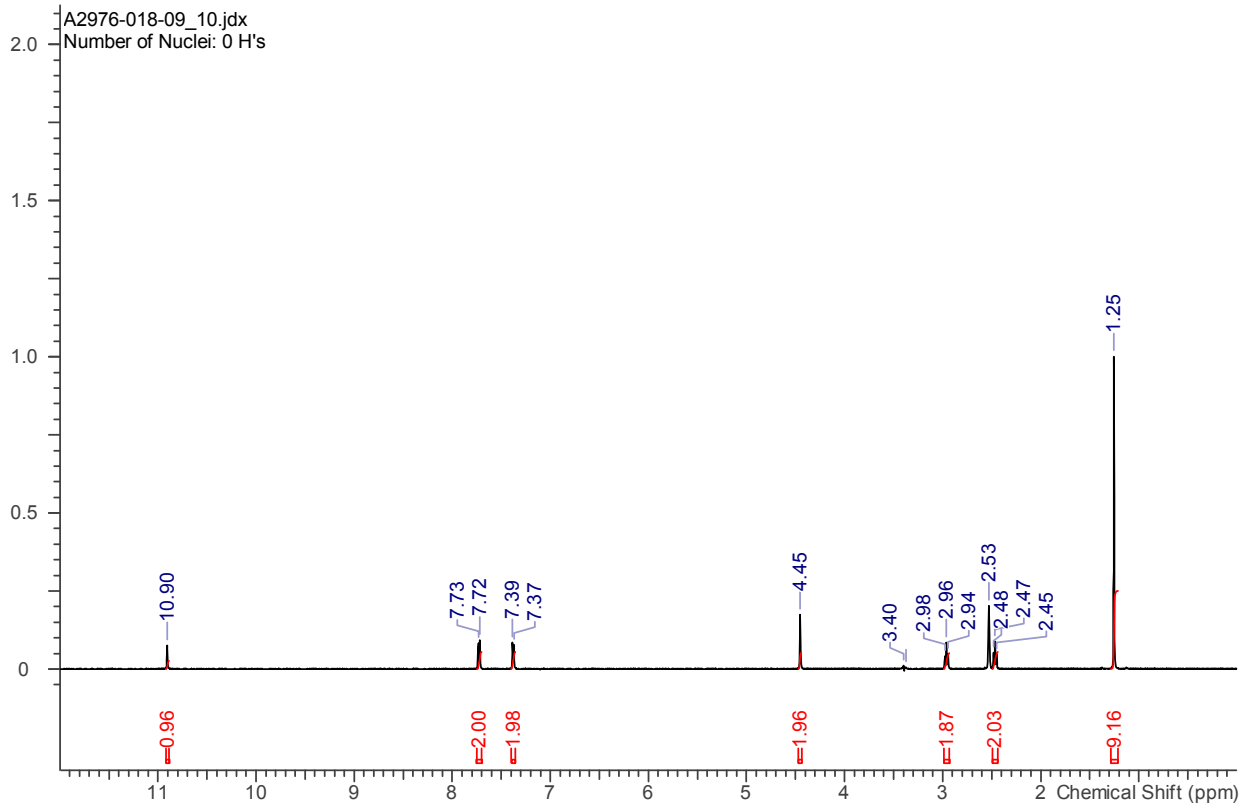
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **89**



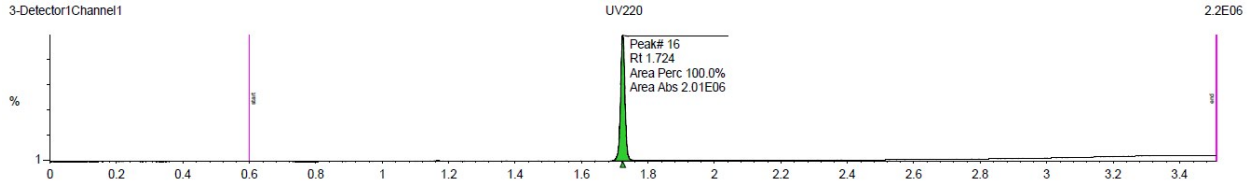
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **89**



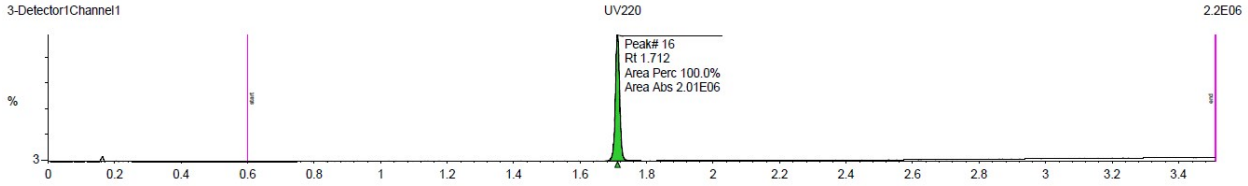
^{1}H NMR (DMSO-d_6, 500 MHz) of **90**



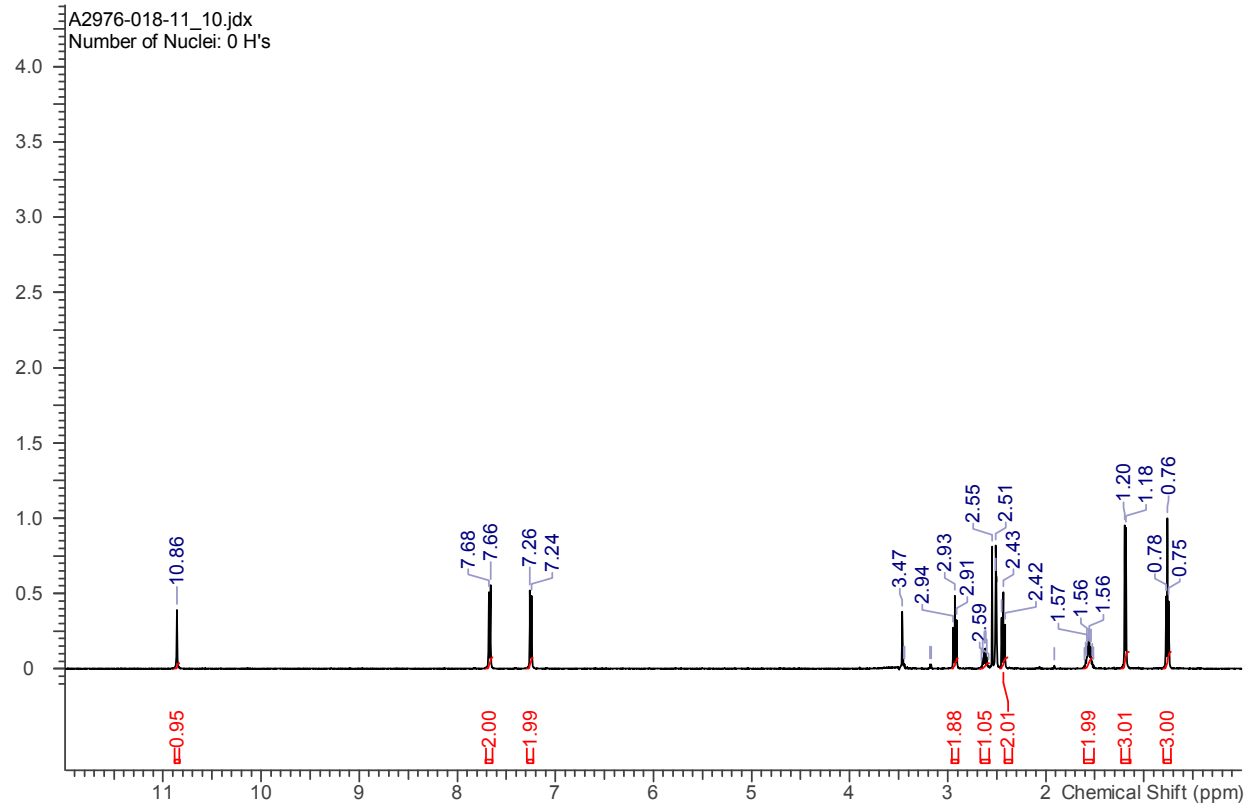
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **90**



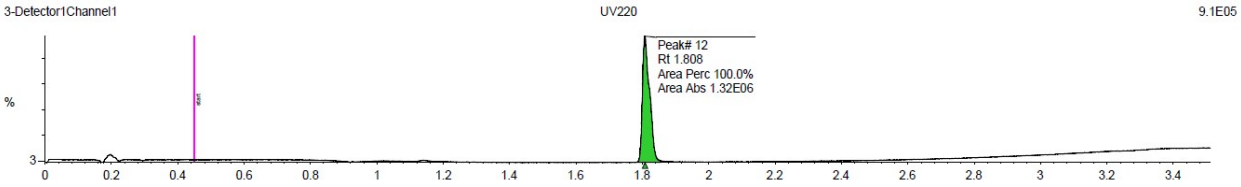
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **90**



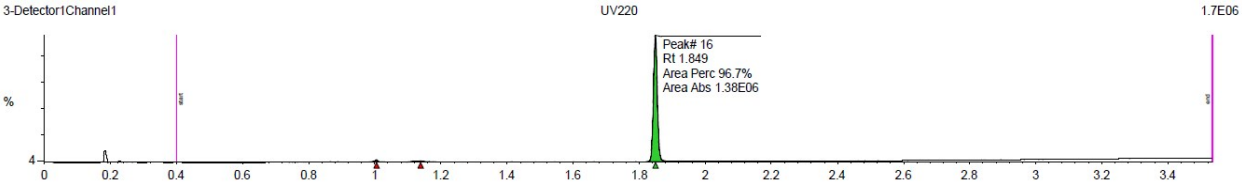
^{1}H NMR (DMSO-d_6, 500 MHz) of **91**



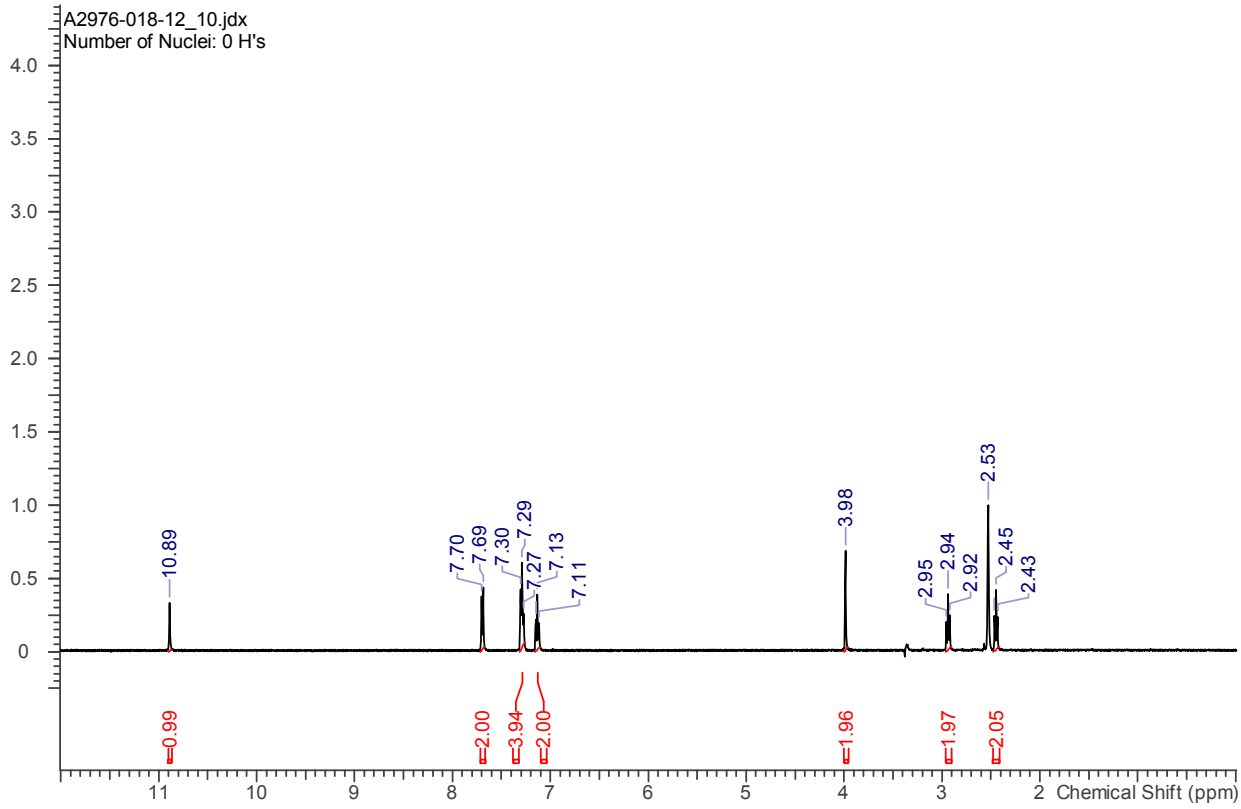
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **91**



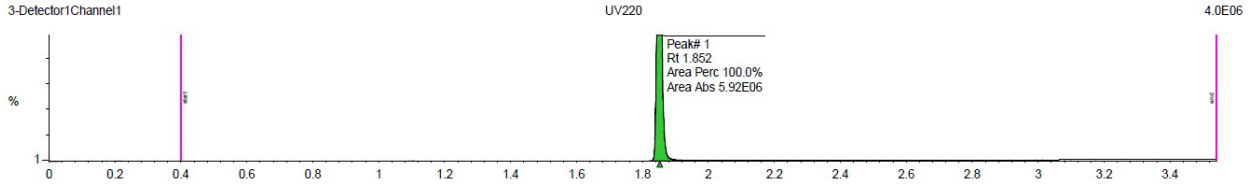
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **91**



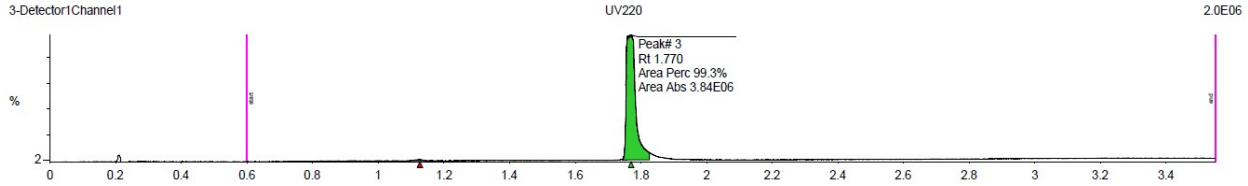
^{1}H NMR (DMSO-d_6, 500 MHz) of **92**



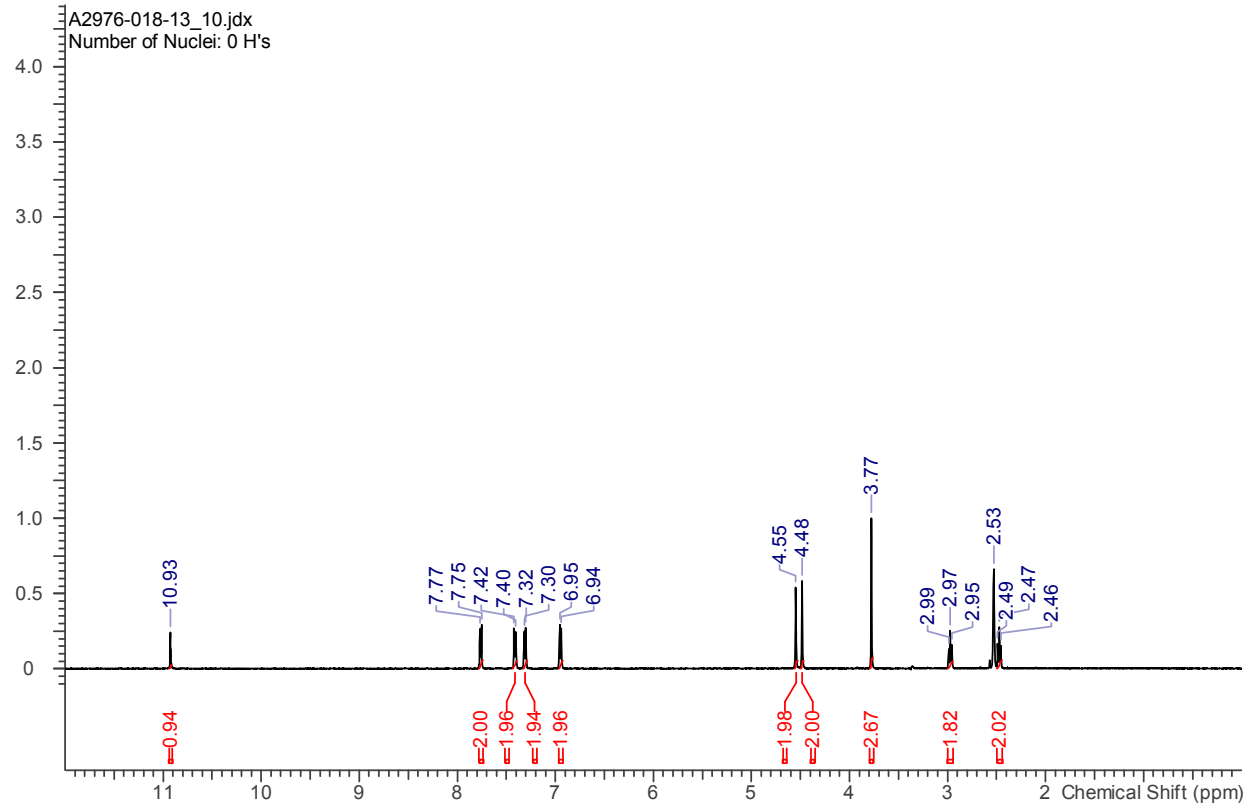
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **92**



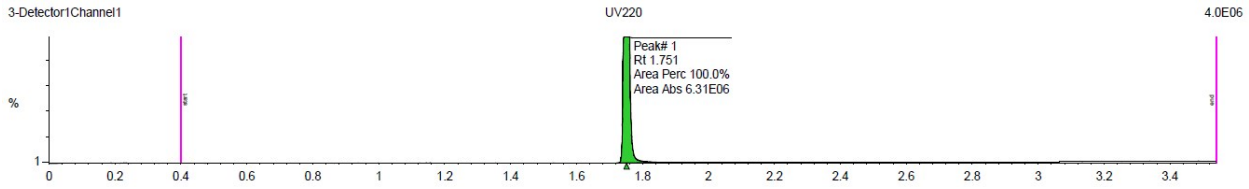
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **92**



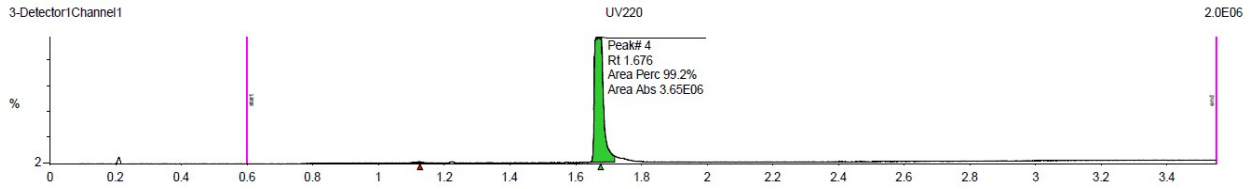
^{1}H NMR (DMSO-d_6, 500 MHz) of **93**



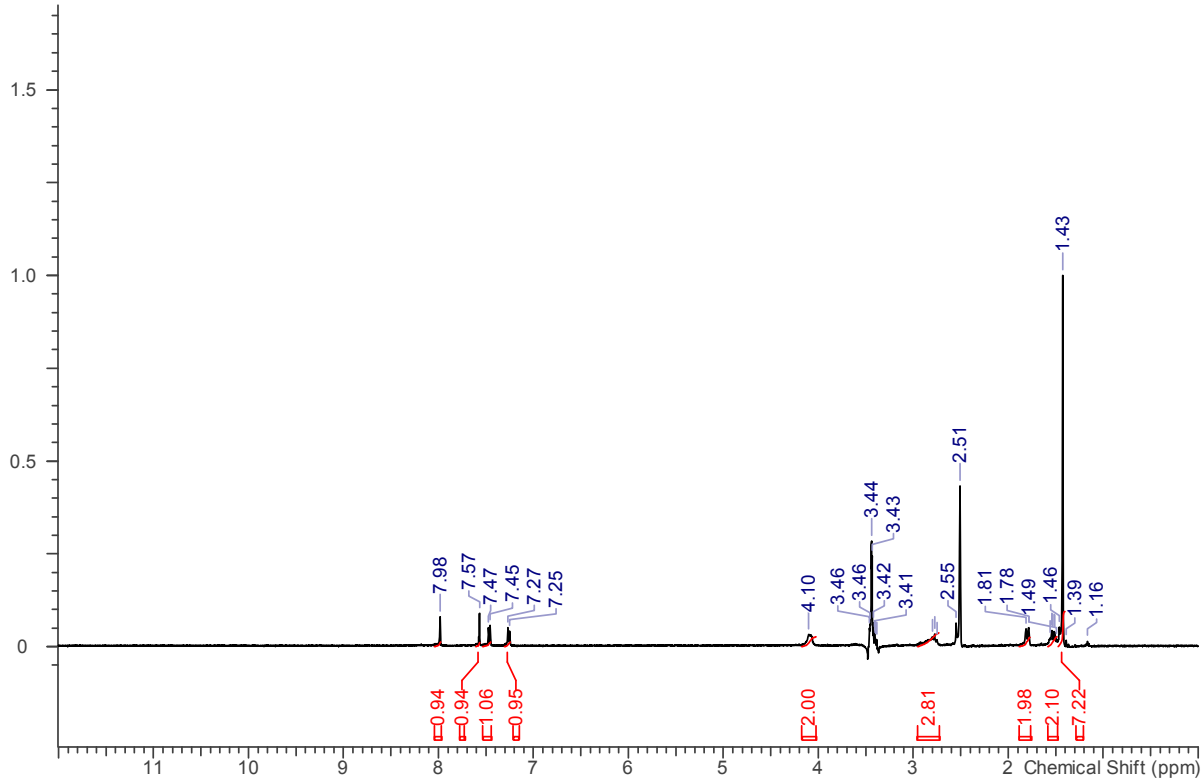
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **93**



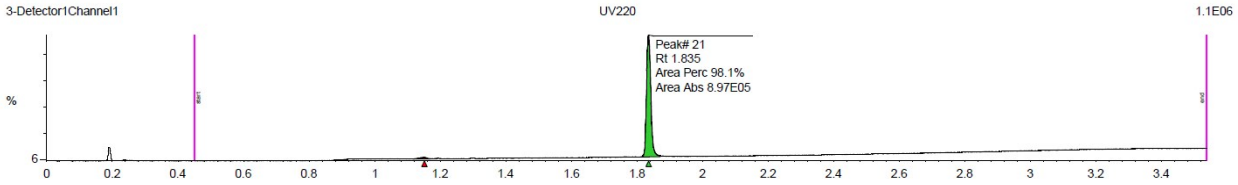
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **93**



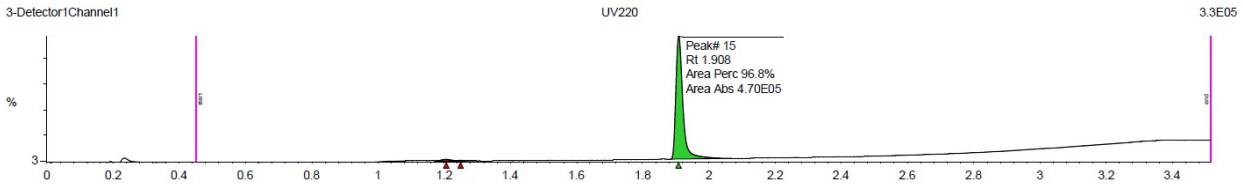
^{1}H NMR (DMSO-d_6, 500 MHz) of **95**



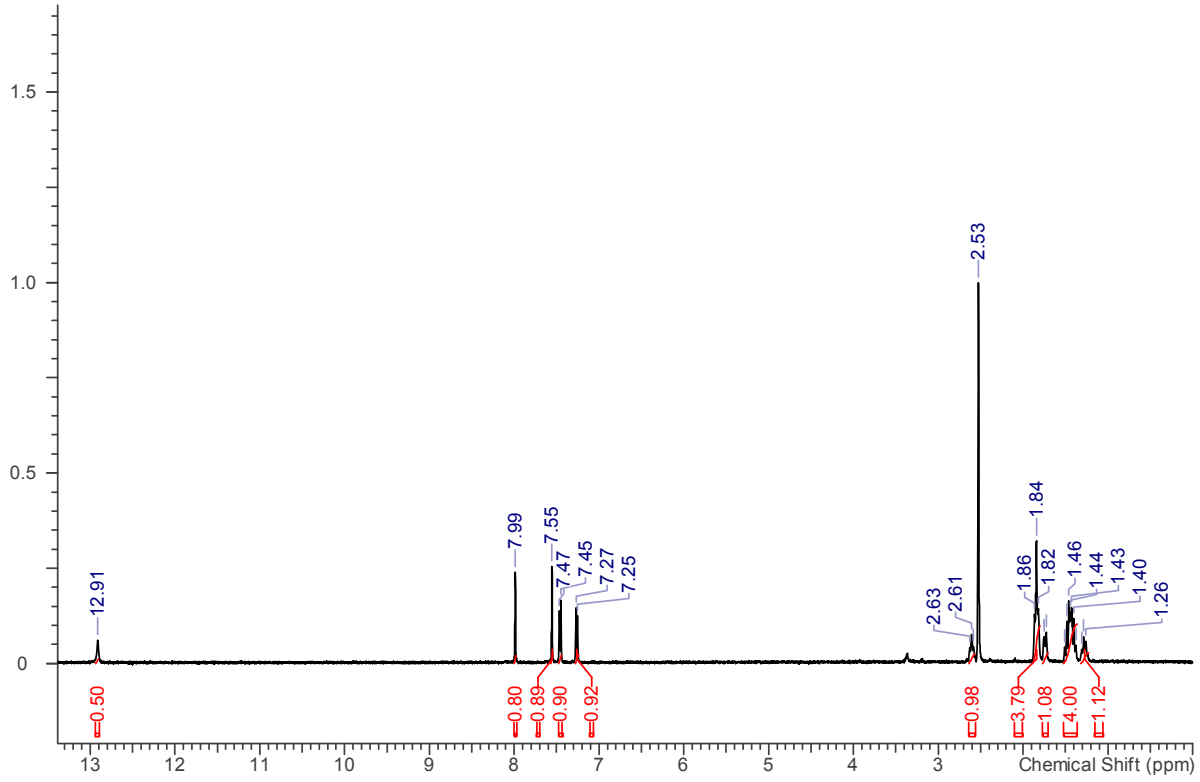
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **95**



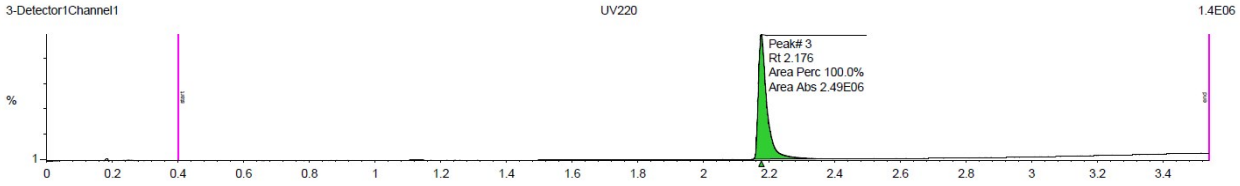
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **95**



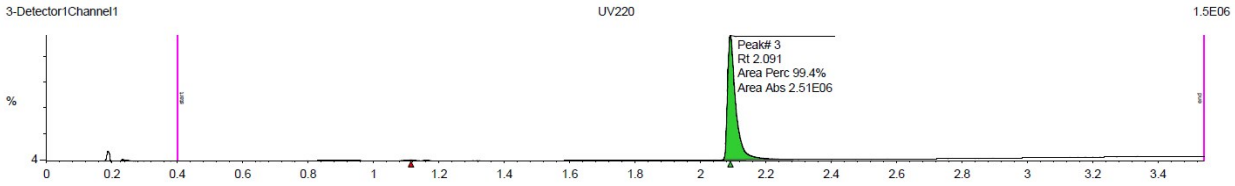
^{1}H NMR (DMSO-d_6, 500 MHz) of **98**



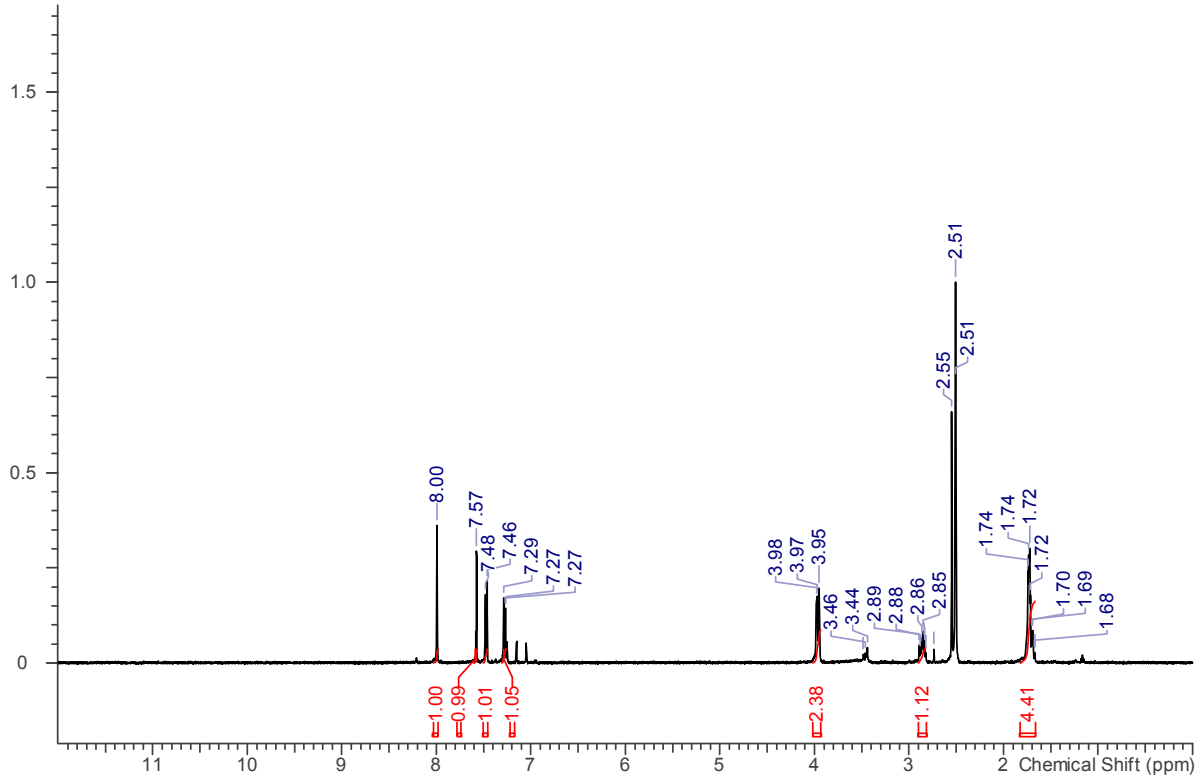
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **98**



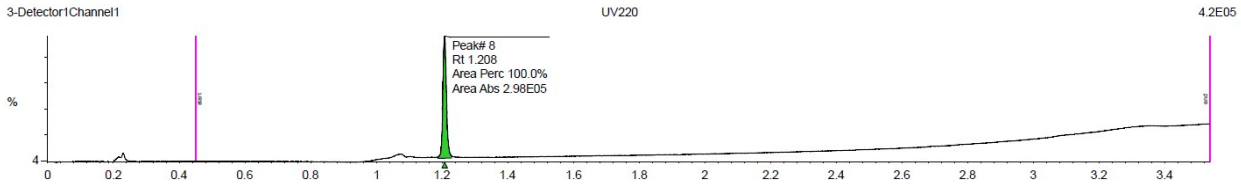
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **98**



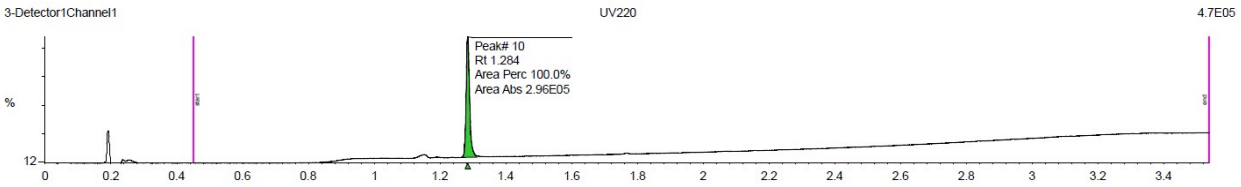
^{1}H NMR (DMSO-d_6, 500 MHz) of **101**



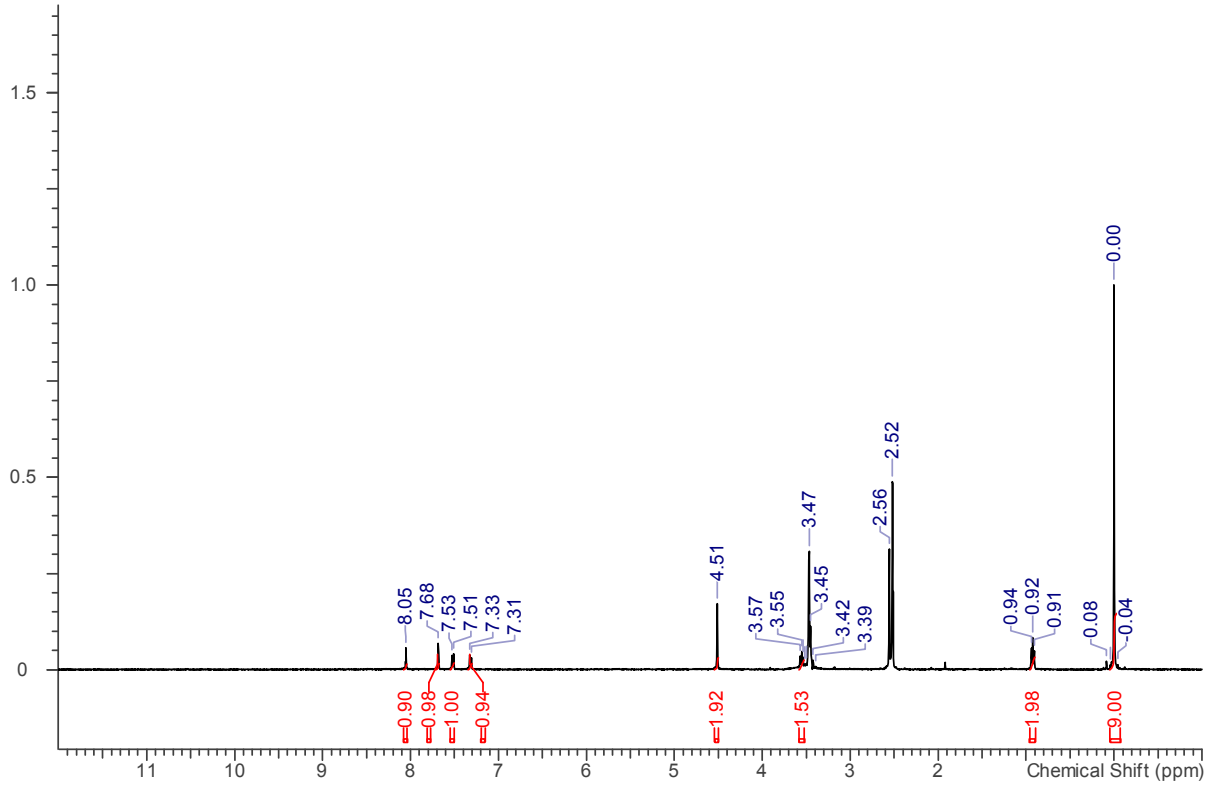
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **101**



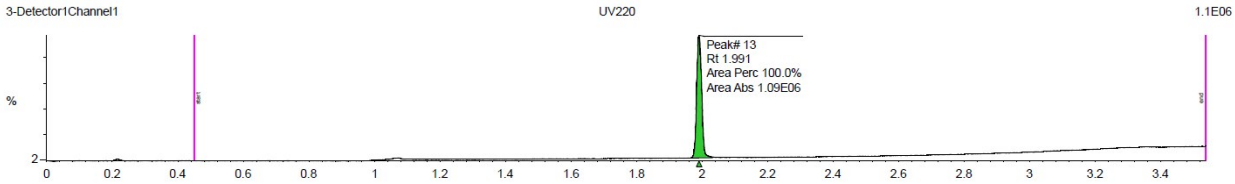
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **101**



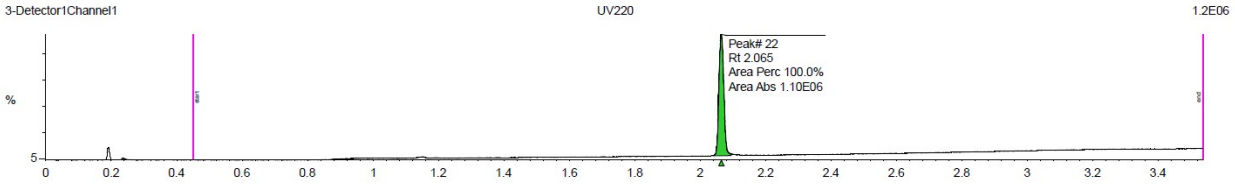
^{1}H NMR (DMSO-d_6, 500 MHz) of **102**



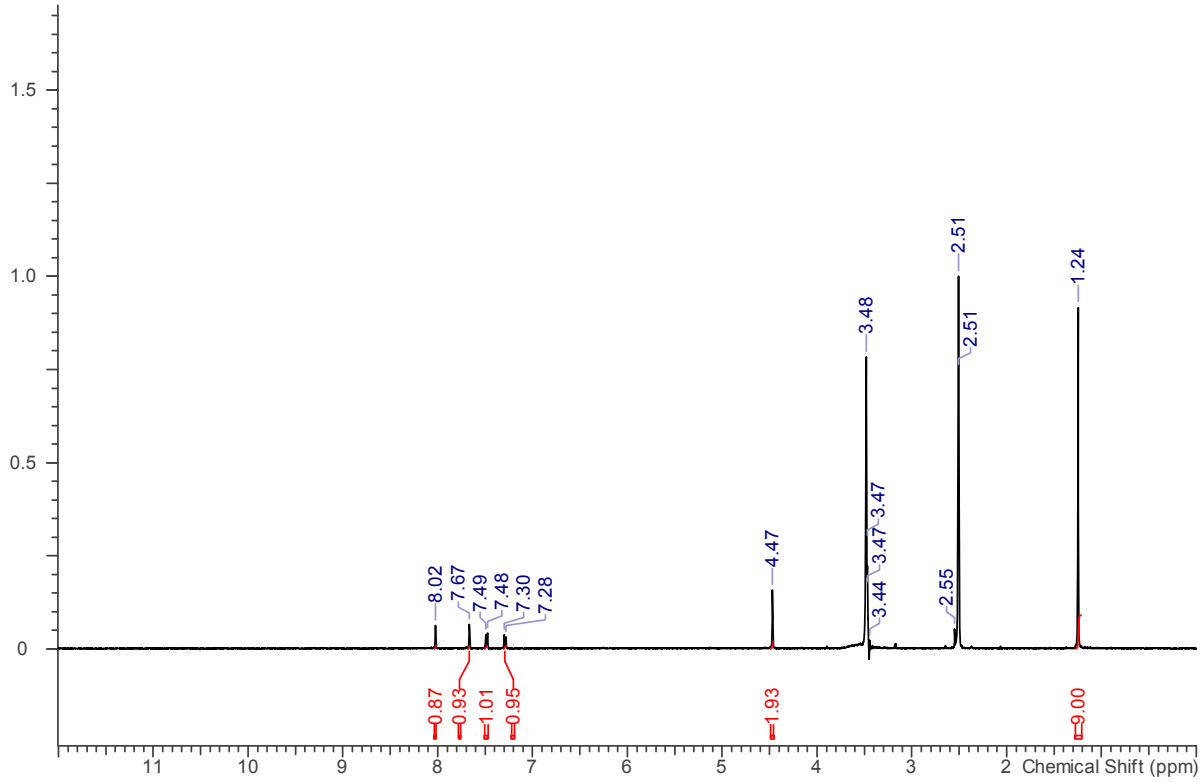
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **102**



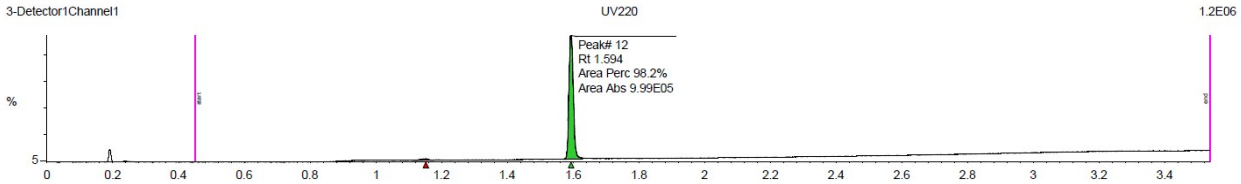
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **102**



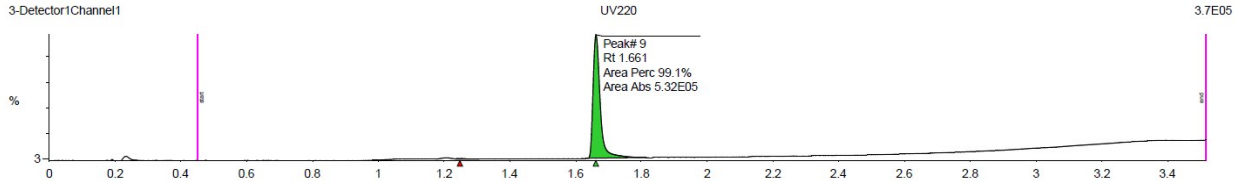
^{1}H NMR (DMSO-d_6, 500 MHz) of **104**



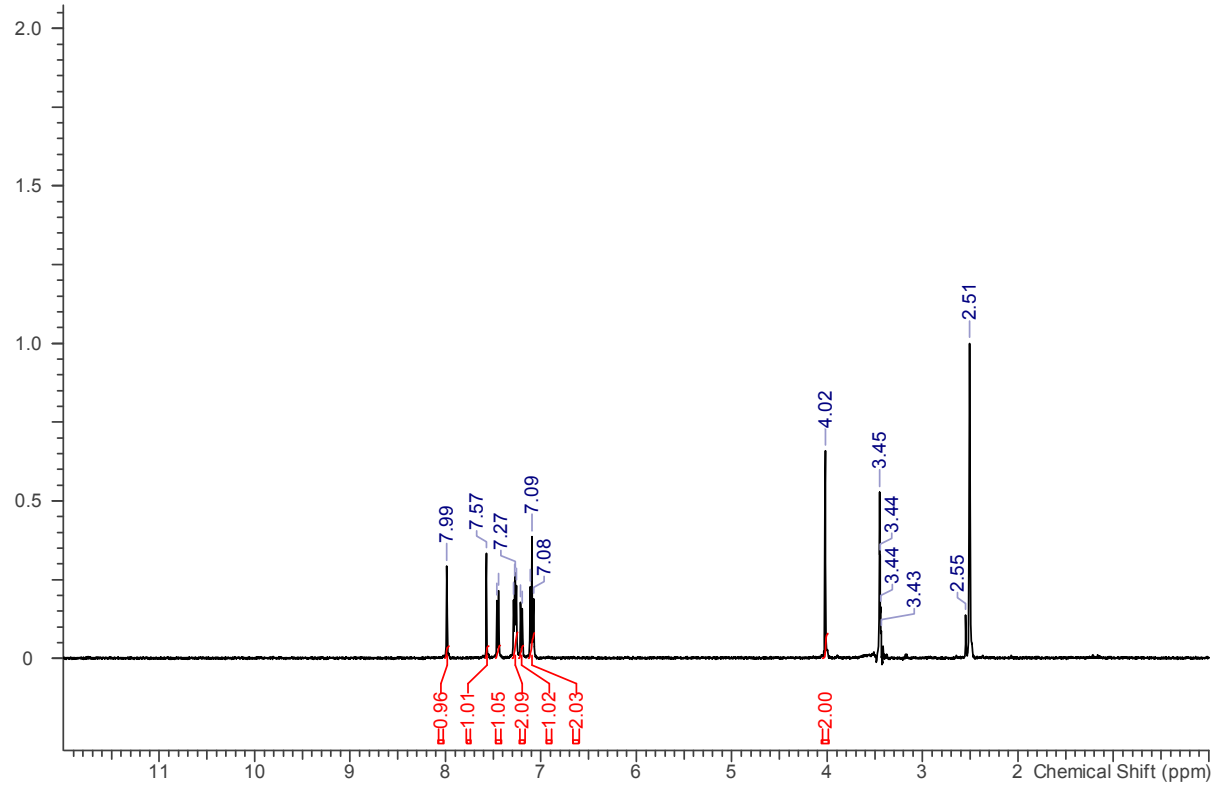
LC-MS (Injection 1: MeCN:H_2O with 0.1% TFA) of **104**



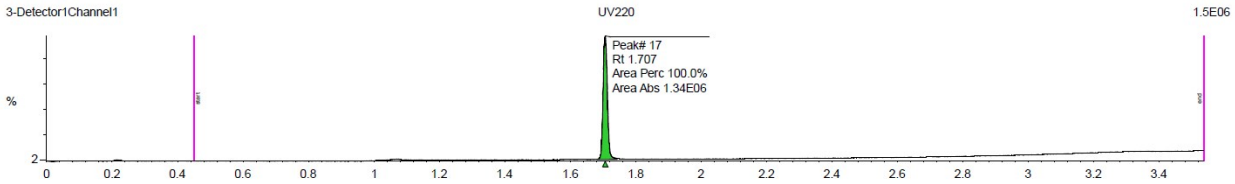
LC-MS (Injection 2: MeCN:H_2O with 10 mM ammonium acetate) of **104**



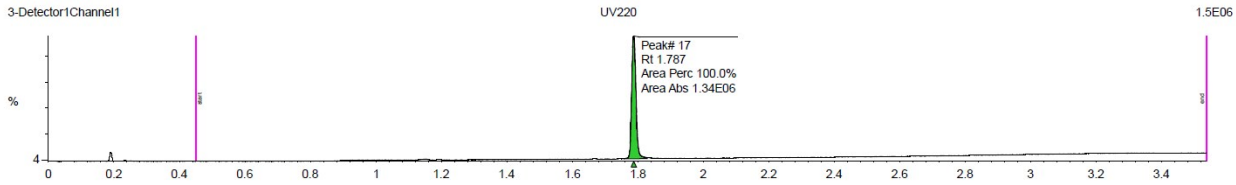
^{1}H NMR (DMSO-d_6, 500 MHz) of **106**



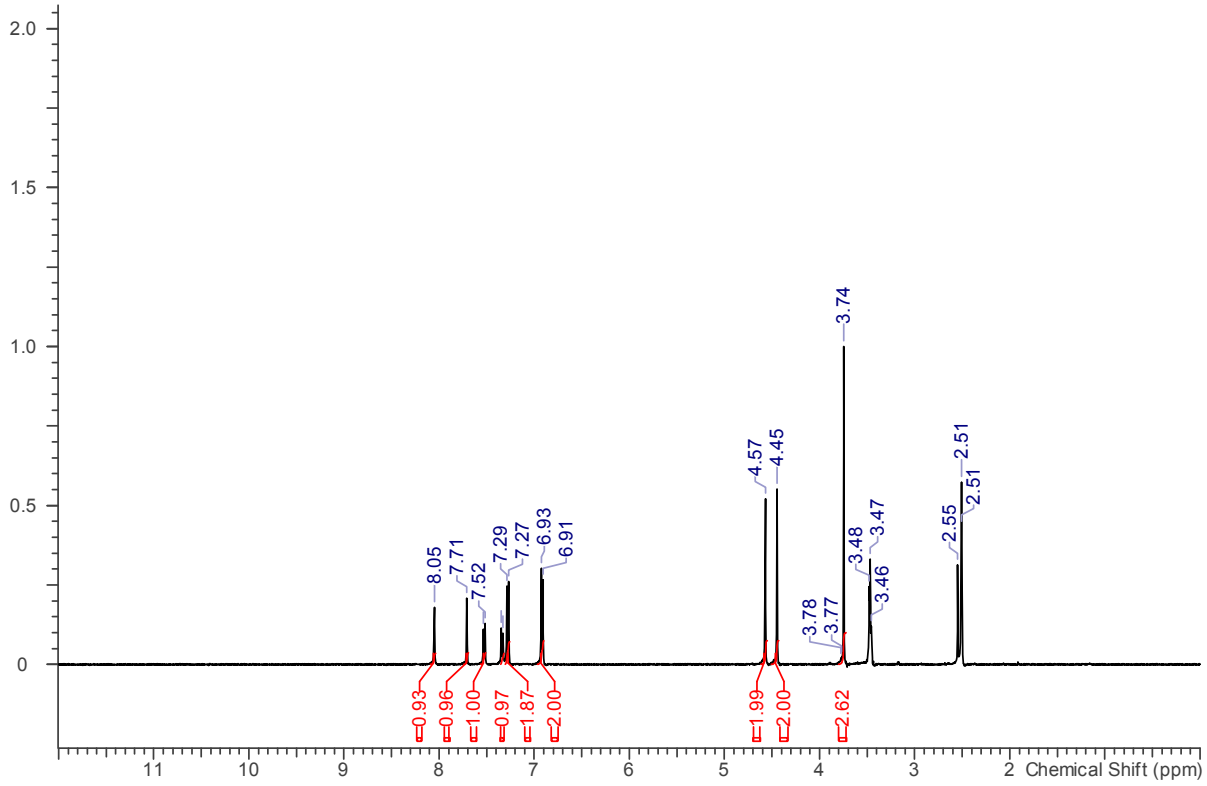
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **106**



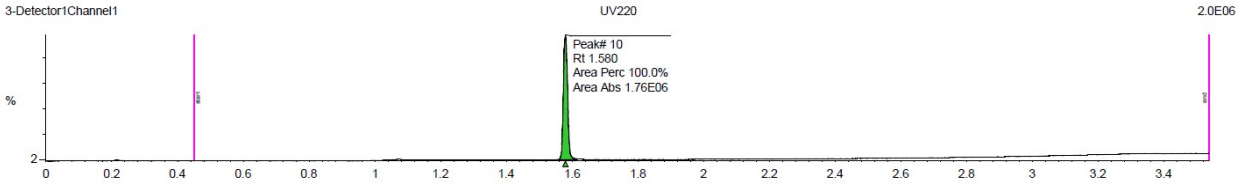
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **106**



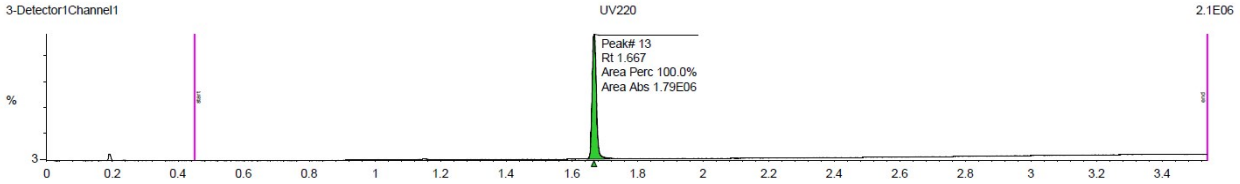
^{1}H NMR (DMSO-d_6, 500 MHz) of **107**



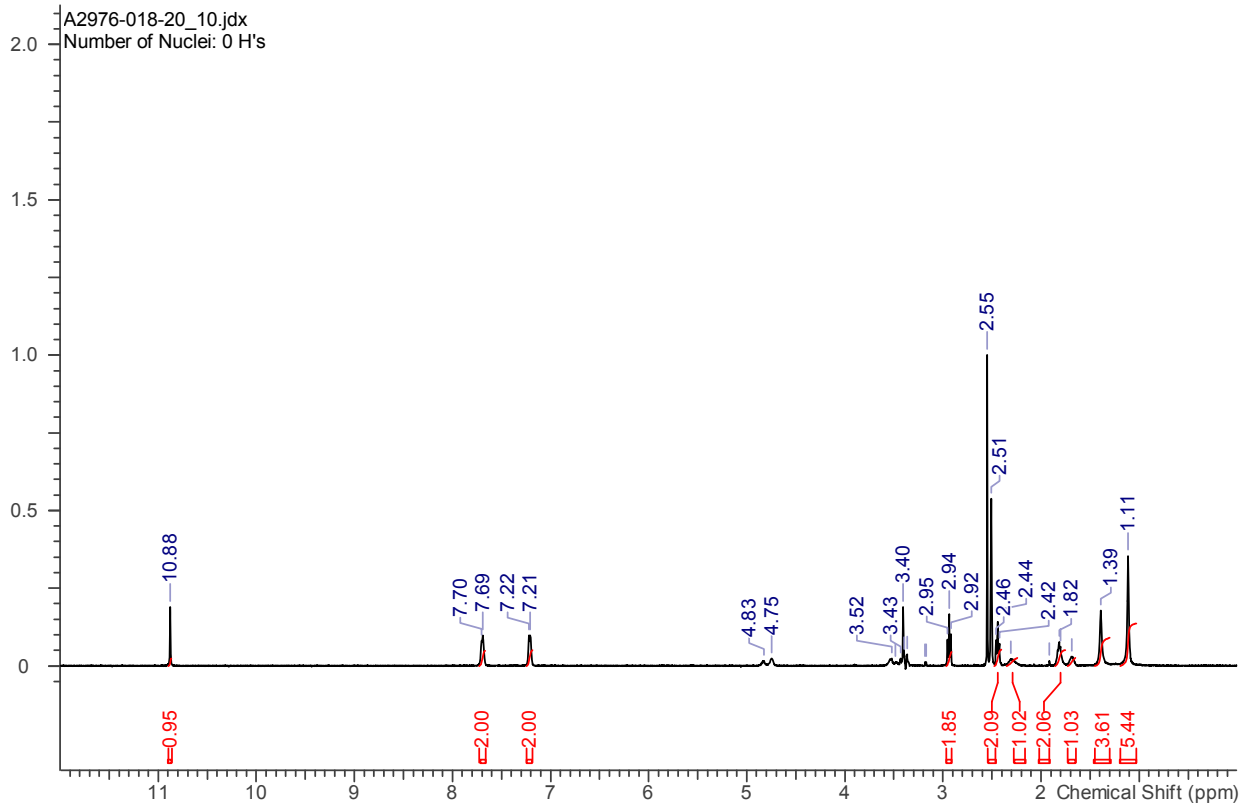
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **107**



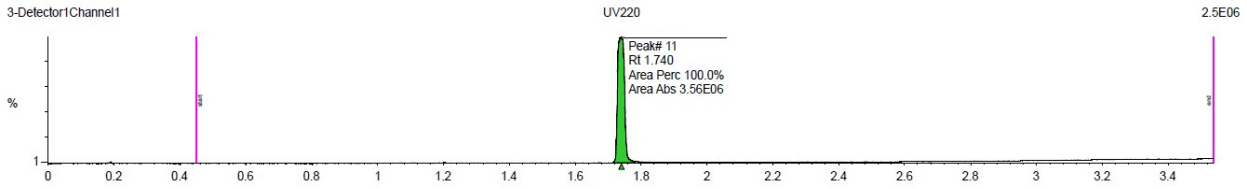
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **107**



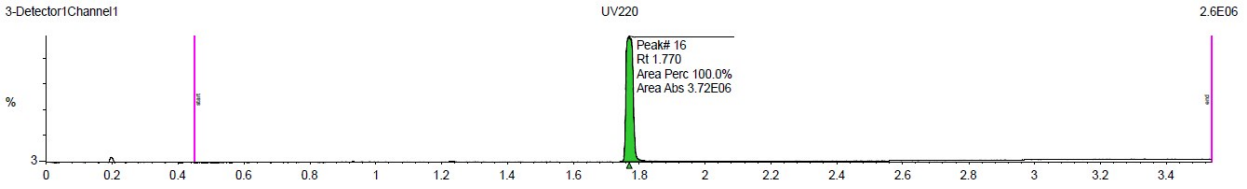
^{1}H NMR (DMSO-d_6, 500 MHz) of **122**



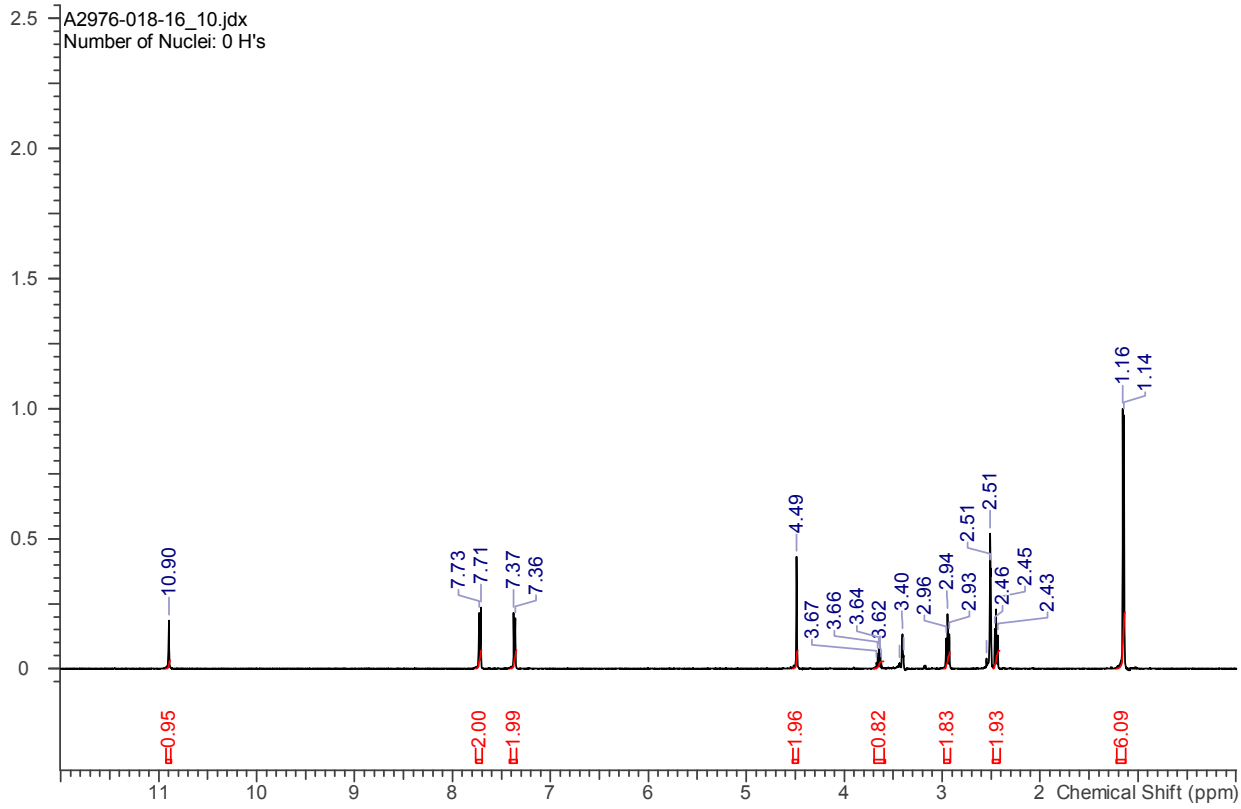
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **122**



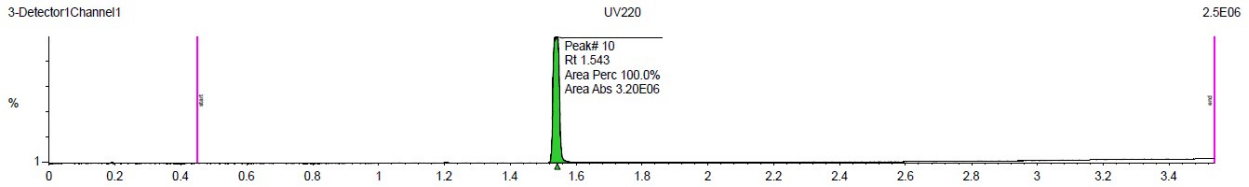
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **122**



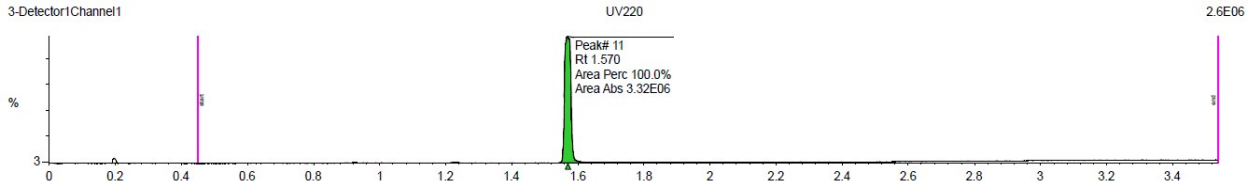
^{1}H NMR (DMSO-d_6, 500 MHz) of **123**



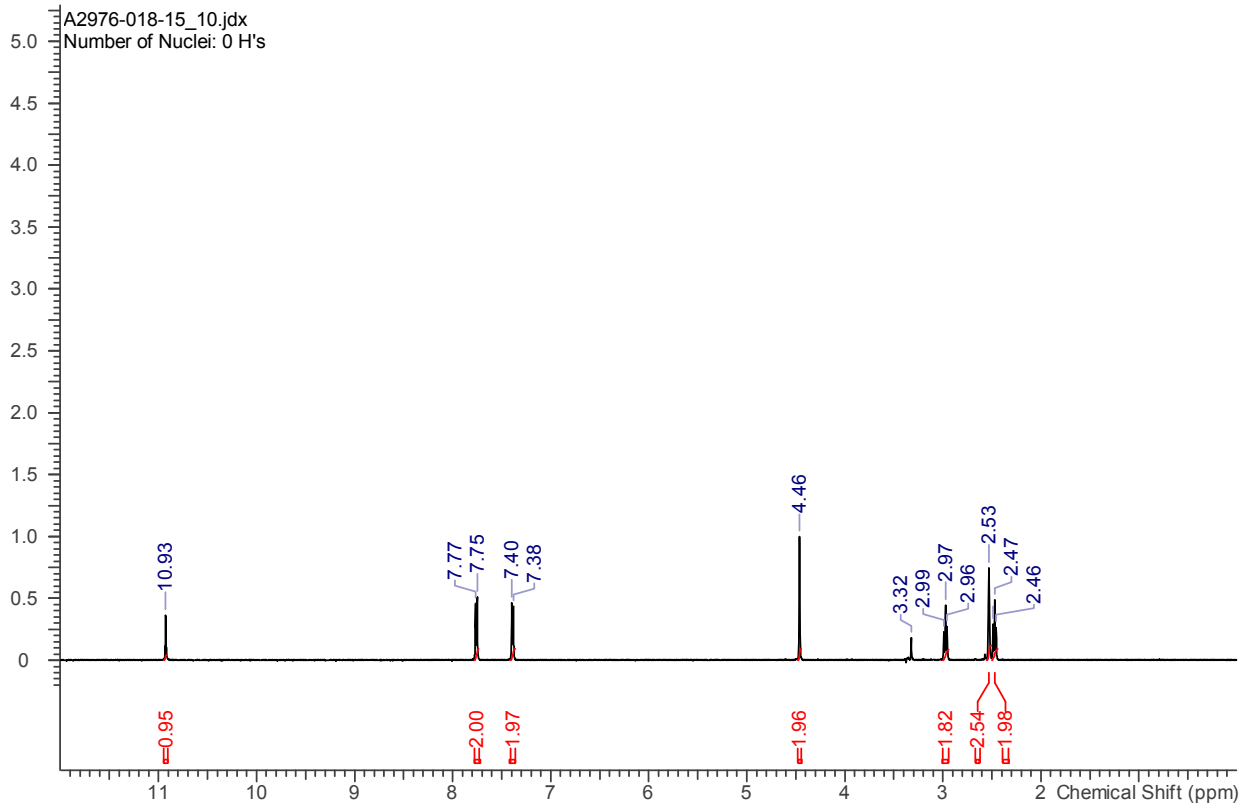
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **123**



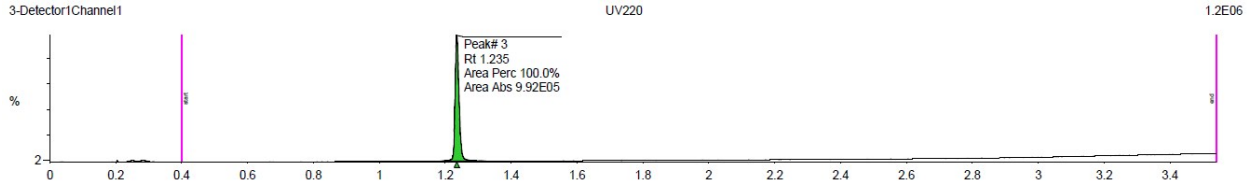
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **123**



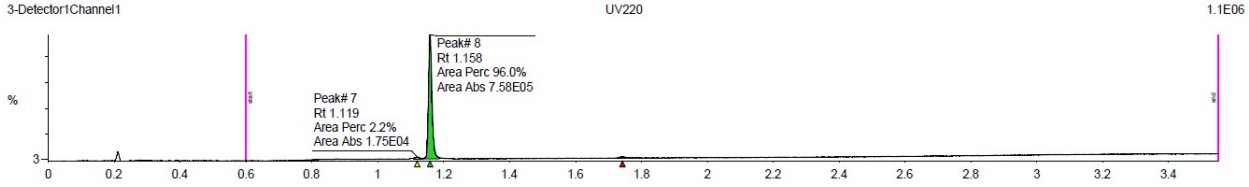
^{1}H NMR (DMSO-d_6, 500 MHz) of **124**



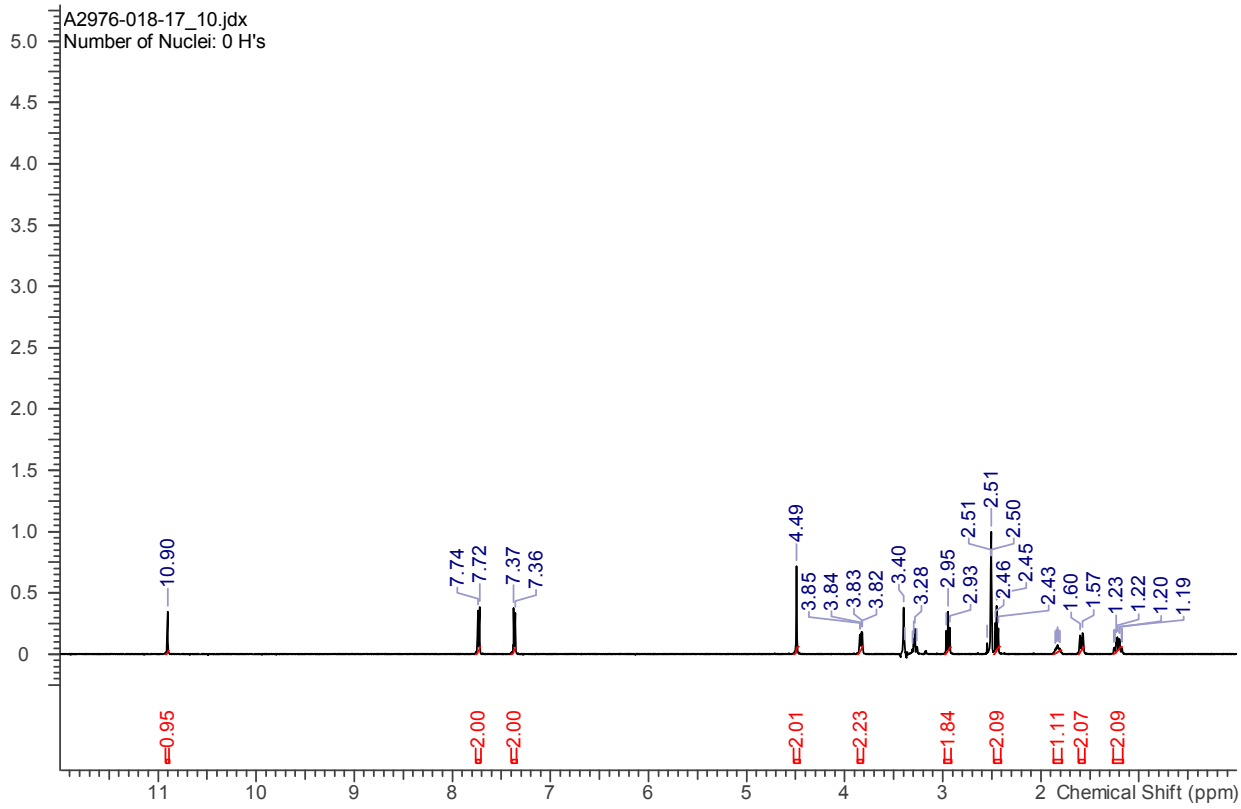
LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **124**



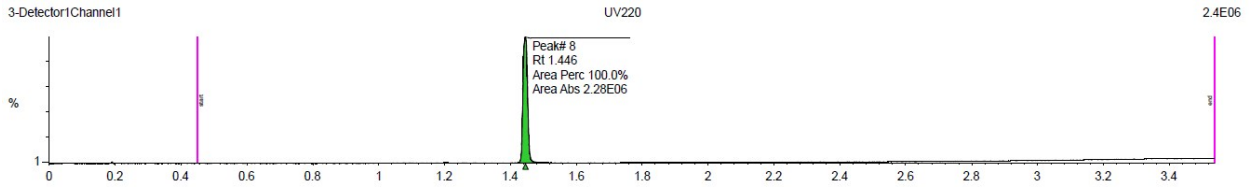
LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **124**



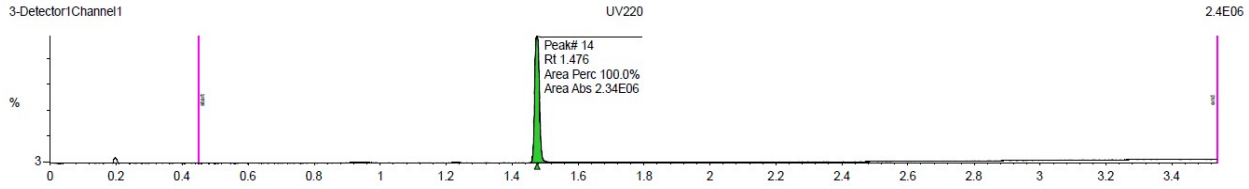
^{1}H NMR (DMSO-d_6, 500 MHz) of **125**



LC-MS (Injection 1: MeCN:H_2O with 10 mM ammonium acetate) of **125**



LC-MS (Injection 2: MeCN:H_2O with 0.1% TFA) of **125**



References for the Supplemental Information

1. L. L. Anka-Lufford, K. M. Huihui, N. J. Gower, L. K. Ackerman and D. J. Weix, *Chemistry*, 2016, **22**, 11564-11567.
2. Nickel precatalyst costs are based on the cheapest listed catalog prices (on a per gram basis) from commercial vendor websites as of 5/31/2021.
3. The P/IS is intended to compare the reaction outcome within a data set, and not meant to compare across data sets.
4. In the case of Ir complexes, commercial availability was also considered when choosing photocatalysts for subsequent studies.
5. It is hypothesized in the literature (see ref. 10 in the main text) that the base is needed to sequester the BF3 by-product that is generated throughout the course of the reaction, although this has not been proven experimentally.
6. A manuscript describing the capabilities of the Bristol Myers Squibb (BMS) Photoreactor is in progress.