

SUPPORTING INFORMATION

Effects of Conformational Restriction on A₁ Adenosine Receptor Modulation by 2-Amino-3-benzoylthiophenes

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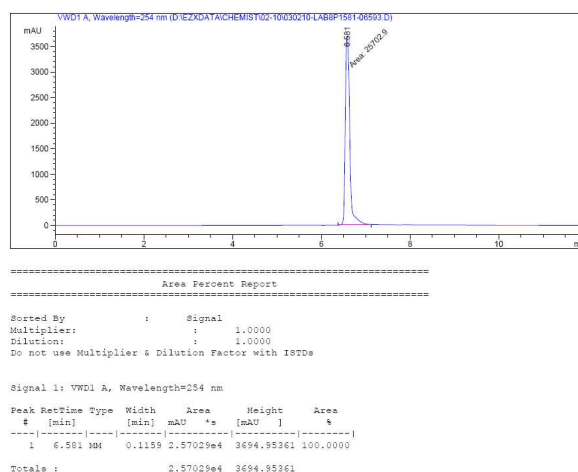
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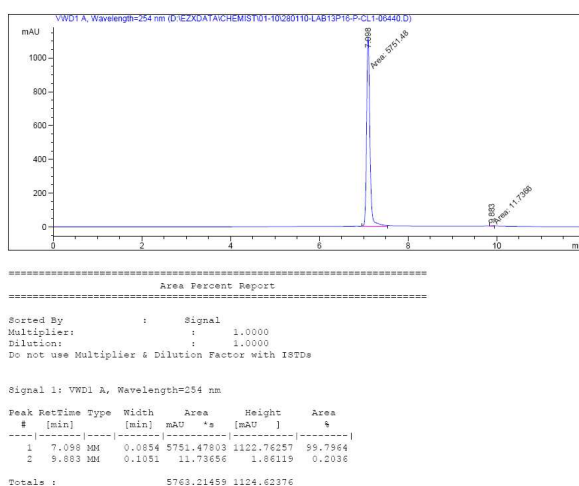
Compound Analysis

Compound purity was analysed on an Agilent 1200 Series LCMS system, incorporating a photodiode array detector (214/254 nm) coupled directly to an electrospray ionization source and a single quadrupole mass analyser (Agilent 6120 Quadrupole MS). Chromatograms show UV absorbance at 254 nm. RP-HPLC was carried out at 30 °C employing a Phenomenex column (Luna 5 μ m C8(2), 50 x 4.60 mm ID). The following buffers were used; buffer A 99.9% H₂O, 0.1% Formic acid and buffer B 99.9% CH₃CN, 0.1% formic acid. The following gradient was used with a flow rate of 0.5 mL/min and total run time of 12 min; 0–4 min 95% buffer A and 5% buffer B, 4–7 min 0% buffer A and 100% buffer B, 7–12 min 95% buffer A and 5% buffer B. Mass spectra were acquired in positive and negative ion mode with a scan range of 0–1000 m/z at 5V. All compounds were of $\geq 95\%$ purity.

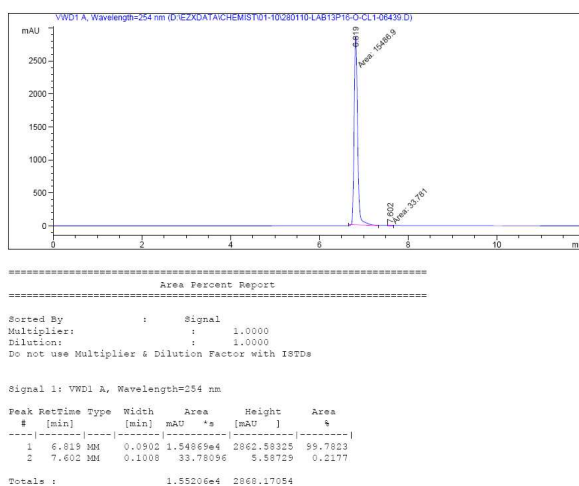
1-Amino-8*H*-indeno[1,2-*c*]thiophen-8-one (14a)



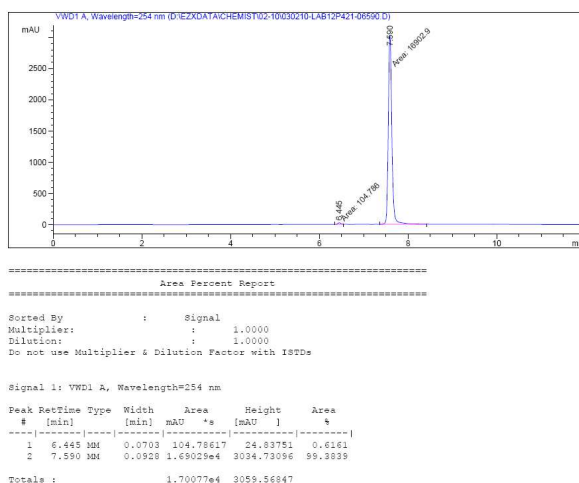
1-Amino-5-chloro-8*H*-indeno[1,2-*c*]thiophen-8-one (14b)



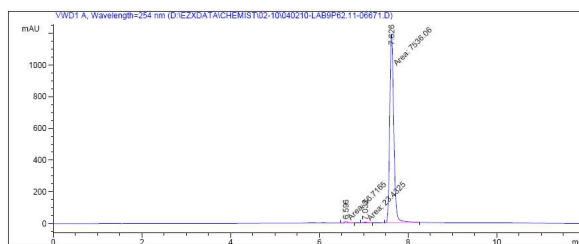
1-Amino-7-chloro-8*H*-indeno[1,2-*c*]thiophen-8-one (14c)



1-Amino-3-phenyl-8*H*-indeno[1,2-*c*]thiophen-8-one (17a)



1-Amino-3-(4-methoxyphenyl)-8*H*-indeno[1,2-*c*]thiophen-8-one (17b)



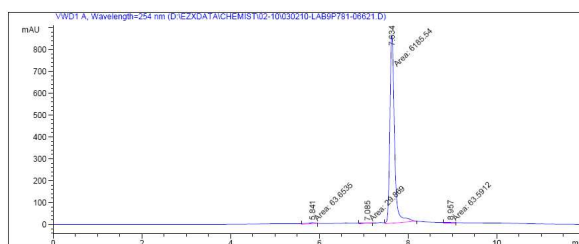
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Area Percent Report
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	6.596	HM	0.1114	56.71602	8.48223	0.7447
2	7.032	HM	0.1071	23.43254	3.64531	0.3077
3	7.626	HM	0.1053	7536.05559	1192.24170	98.9477
Totals :				7616.20766	1204.36924	

1-Amino-3-(4-(dimethylamino)phenyl)-8*H*-indeno[1,2-*c*]thiophen-8-one (17c)



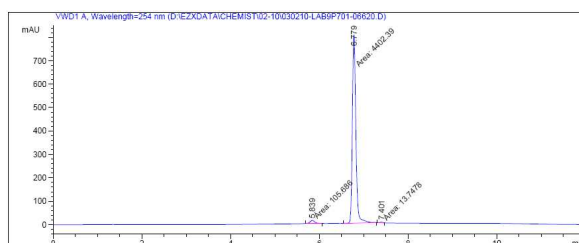
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	5.841	HM	0.2107	69.65954	5.03486	1.0036
2	7.085	HM	0.3105	29.86897	1.60325	0.4709
3	7.634	HM	0.1197	6185.54346	861.43536	97.5229
4	8.957	HM	0.2524	69.59125	4.19906	1.0026
Totals :				6342.65721	872.27258	

1-Amino-3-(pyrimidin-5-yl)-8*H*-indeno[1,2-*c*]thiophen-8-one (17d)



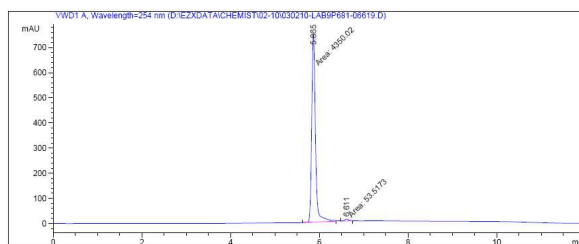
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Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	5.839	HM	0.1332	105.68593	13.22127	2.3372
2	6.779	HM	0.0912	4402.39404	804.93073	97.1557
3	7.401	HM	0.0796	13.74779	2.87723	0.3040
Totals :				4521.82777	821.02923	

1-Amino-3-(pyridin-4-yl)-8H-indeno[1,2-c]thiophen-8-one (17e)



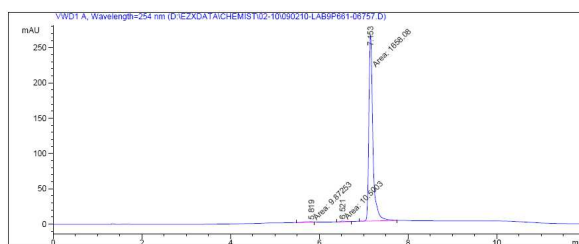
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height *s	Area [mAU]	%
1	5.865	HM	0.0966	4350.02100	750.44495	58.7847	
2	6.611	HM	0.1116	53.51729	7.59510	1.2153	
Totals :				4403.53829	758.44005		

4-(1-Amino-8-oxo-8H-indeno[1,2-c]thiophen-3-yl)benzoic acid (17f)



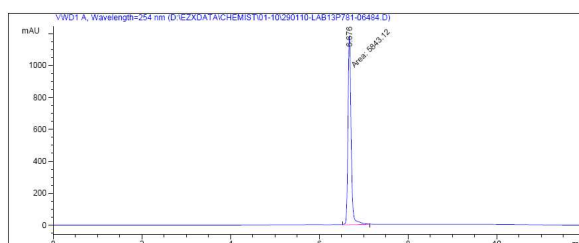
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height *s	Area [mAU]	%
1	5.819	HM	0.3045	5.87253	5.40330e-1	0.5882	
2	6.521	HM	0.1593	10.50029	1.09983	0.6256	
3	7.153	HM	0.1090	1658.07849	263.6376	98.7862	
Totals :				1678.45130	264.90292		

(2-Aminothiophen-3-yl)(phenyl)methanone (20a)



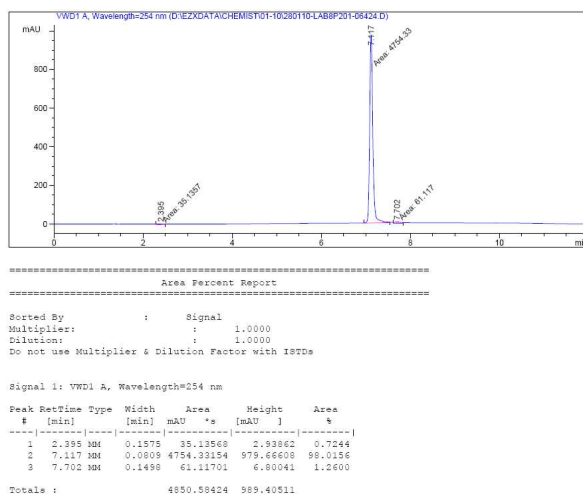
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Do not use Multiplier & Dilution Factor with ISTDs

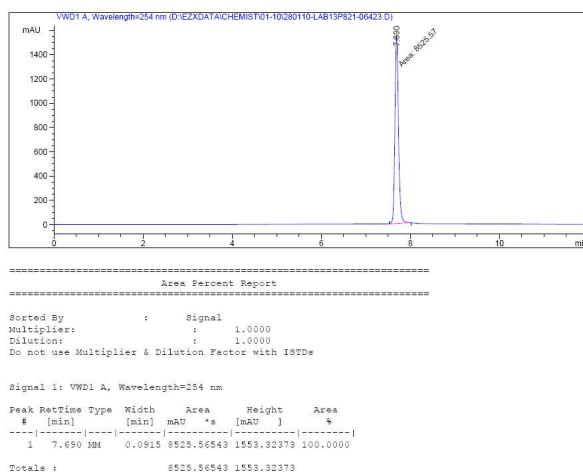
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height *s	Area [mAU]	%
1	6.676	HM	0.0620	5843.11768	1187.27930	100.0000	
Totals :				5843.11768	1187.27930		

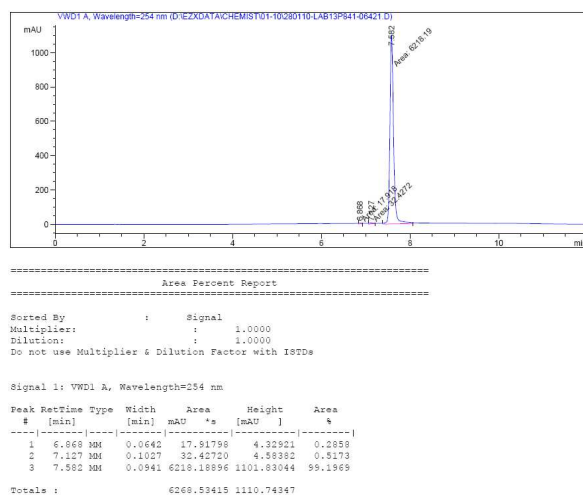
(2-Aminothiophen-3-yl)(4-chlorophenyl)methanone (20b)



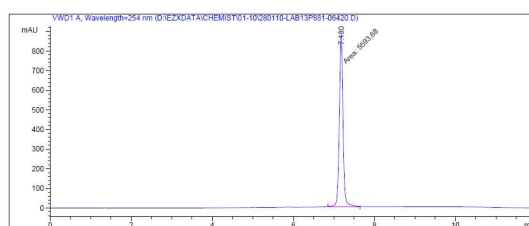
(2-Amino-5-phenylthiophen-3-yl)(phenyl)methanone (22a)



(2-Amino-5-(4-methoxyphenyl)thiophen-3-yl)(phenyl)methanone (22b)



(2-Amino-5-(4-(dimethylamino)phenyl)thiophen-3-yl)(phenyl)methanone (22c)



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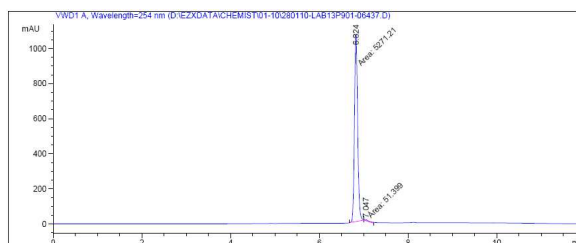
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Dilution:      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type Width Area Height Area
# [min] [min] [min] mAU %s [mAU ] %
-----
1 7.160 NM 0.1062 5593.67529 878.16022 100.0000
Totals :                5593.67529 878.16022

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(2-Amino-5-(pyrimidin-5-yl)thiophen-3-yl)(phenyl)methanone (22d)



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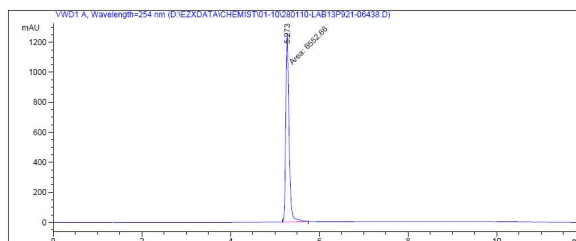
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Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type Width Area Height Area
# [min] [min] [min] mAU %s [mAU ] %
-----
1 6.824 NM 0.0821 5271.20605 1069.82849 99.0343
2 7.047 NM 0.1301 51.39905 6.58260 0.9657
Totals :                5322.60510 1076.41109

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(2-Amino-5-(pyridin-4-yl)thiophen-3-yl)(phenyl)methanone (22e)



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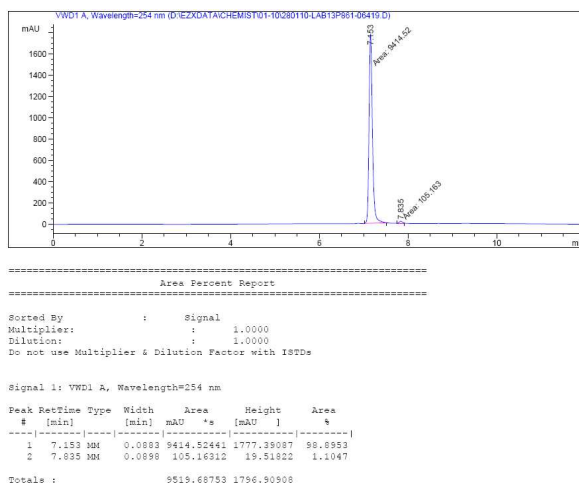
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Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

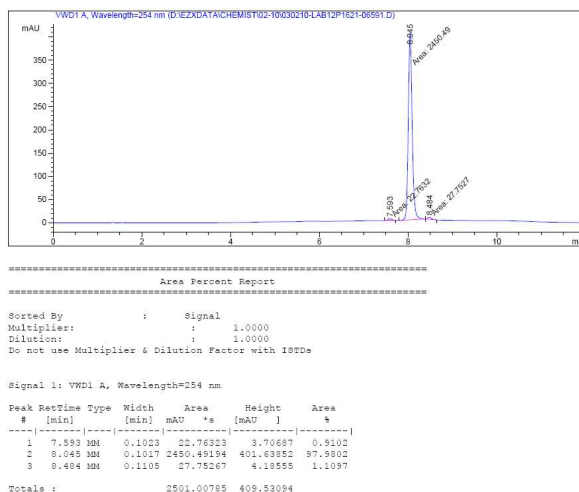
Peak RetTime Type Width Area Height Area
# [min] [min] [min] mAU %s [mAU ] %
-----
1 5.273 NM 0.0864 6552.66064 1264.05383 100.0000
Totals :                6552.66064 1264.05383

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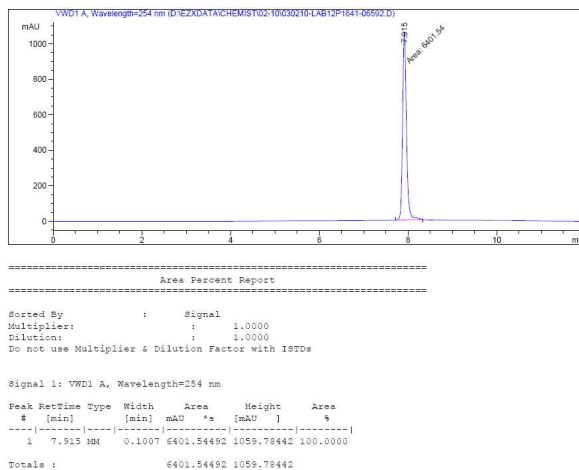
4-(5-Amino-4-benzoylthiophen-2-yl)benzoic acid (22f)



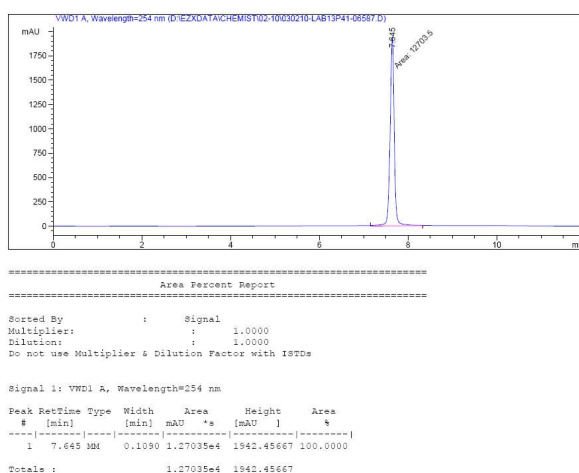
(2-Amino-5-phenylthiophen-3-yl)(4-chlorophenyl)methanone (23a)



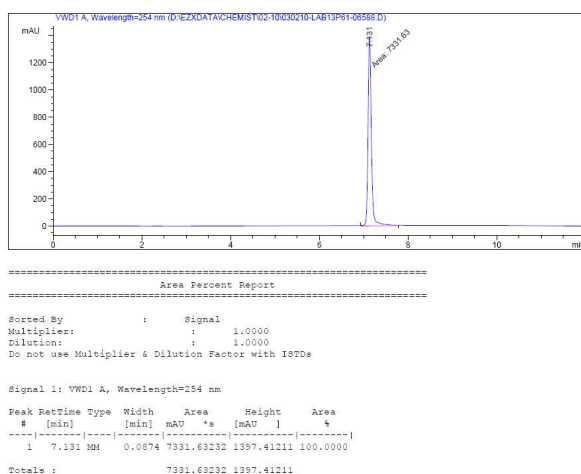
(2-Amino-5-(4-methoxyphenyl)thiophen-3-yl)(4-chlorophenyl)methanone (23b)



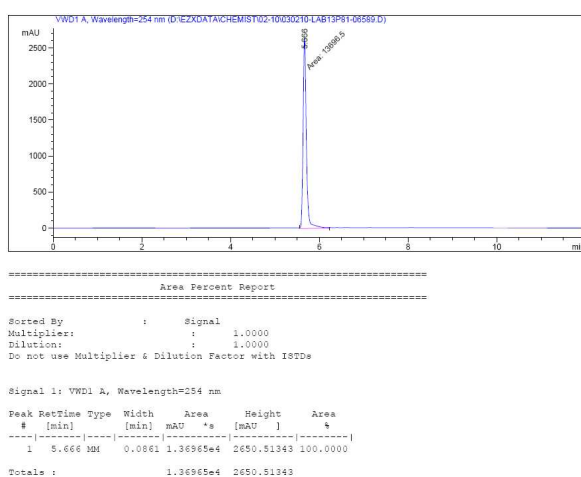
(2-Amino-5-(4-(dimethylamino)phenyl)thiophen-3-yl)(4-chlorophenyl)methanone (23c)



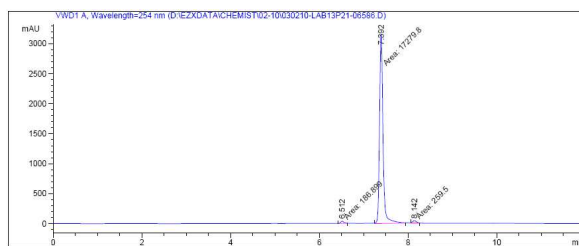
(2-Amino-5-(pyrimidin-5-yl)thiophen-3-yl)(4-chlorophenyl)methanone (23d)



(2-Amino-5-(pyridin-4-yl)thiophen-3-yl)(4-chlorophenyl)methanone (23e)



4-(5-Amino-4-(4-chlorobenzoyl)thiophen-2-yl)benzoic acid (23f)



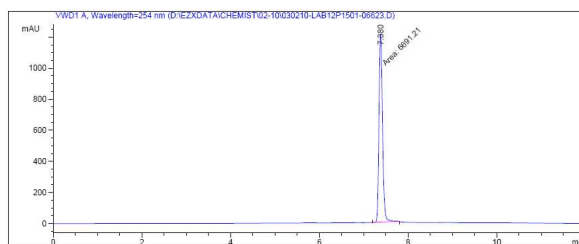
Area Percent Report

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Dilution: 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height *s	Area [mAU]	%
1	6.512	NM	0.0812	186.89851	38.34509	1.0544	
2	7.392	NM	0.0911	1.72798e4	3161.96975	97.4817	
3	8.142	NM	0.1039	258.45951	41.63106	1.4639	
Totals				1.77262e4	3241.94492		

(2-Amino-8H-indeno[2,1-b]thiophen-3-yl)(phenyl)methanone (25a)



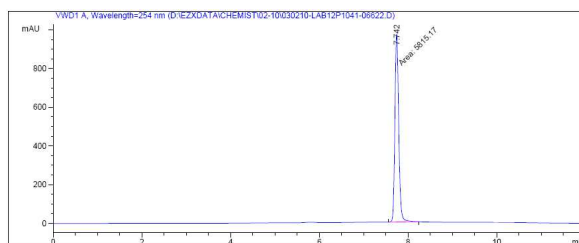
Area Percent Report

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Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height *s	Area [mAU]	%
1	7.380	NM	0.0919	6691.20752	1213.28845	100.0000	
Totals				6691.20752	1213.28845		

(2-Amino-8H-indeno[2,1-b]thiophen-3-yl)(4-chlorophenyl)methanone (25b)



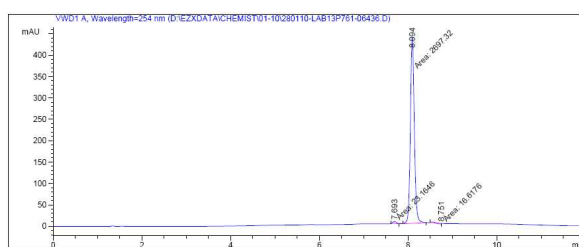
Area Percent Report

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Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height *s	Area [mAU]	%
1	7.742	NM	0.0996	5815.17188	972.98468	100.0000	
Totals				5815.17188	972.98468		

(2-Amino-7-(trifluoromethyl)-8*H*-indeno[2,1-*b*]thiophen-3-yl)(phenyl)methanone (25c)



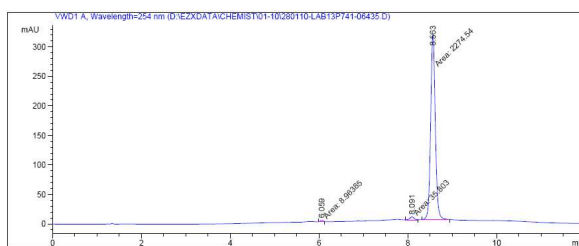
Area Percent Report

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Dilution: 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height	Area %
1	7.693	NM	0.0828	23.16458	4.66454	0.8463
2	8.094	NM	0.1030	2697.31665	436.31332	58.5466
3	8.751	NM	0.1402	16.41759	1.87556	0.6071
Totals:				2737.09683	442.95382	

(2-Amino-7-(trifluoromethyl)-8*H*-indeno[2,1-*b*]thiophen-3-yl)(4-chlorophenyl)methanone (25d)



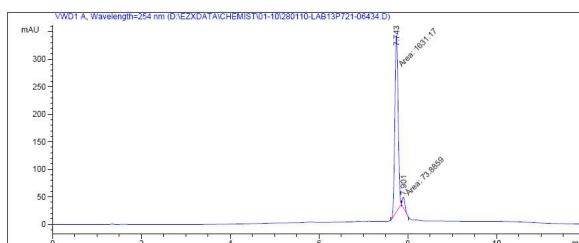
Area Percent Report

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Dilution: 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height	Area %
1	8.059	NM	0.0661	8.56385	2.25920	0.3865
2	8.091	NM	0.1149	35.80302	5.19439	1.5437
3	8.563	NM	0.1212	2274.54370	312.77423	98.0698
Totals:				2319.31056	320.22782	

(2-Amino-5-(trifluoromethyl)-8*H*-indeno[2,1-*b*]thiophen-3-yl)(phenyl)methanone (25e)



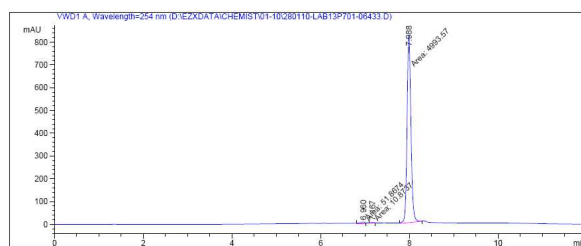
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Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height	Area %
1	7.743	NM	0.0845	1631.17273	321.61270	55.6667
2	7.901	NM	0.0631	73.88591	19.50391	4.3333
Totals:				1705.05864	341.11651	

(2-Amino-5-(trifluoromethyl)-8*H*-indeno[2,1-*b*]thiophen-3-yl)(4-chlorophenyl)methanone (25f)



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Area Percent Report
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Dilution: : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area %	Height [mAU]	Area %
1	6.960	MM	0.1296	51.86741	6.57173	1.0258	
2	7.167	MM	0.0924	10.87365	1.36156	0.2151	
3	7.988	MM	0.1009	4593.57129	824.62311	98.7592	

Totals : 5056.31235 833.25640