

Supporting Information

Peptide Synthesis Beyond DMF: THF and ACN as Excellent and Friendlier Alternatives

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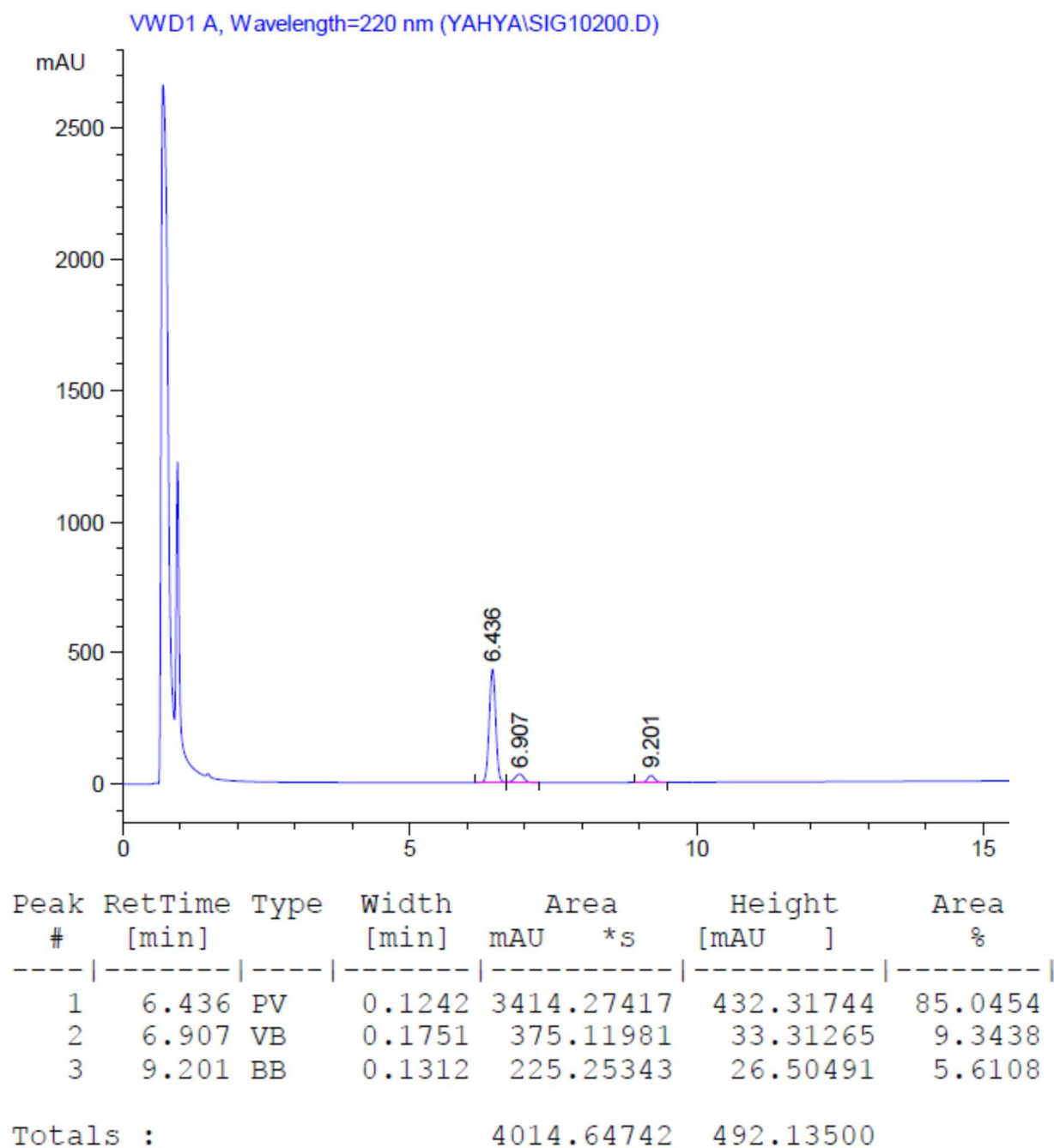
^f Department of Chemistry, College of Science, King Saud University P.O. Box 2455, Riyadh 11451, Saudi Arabia

^g School of Chemistry and Physics, University of Kwazulu-Natal, Durban 4001, South Africa

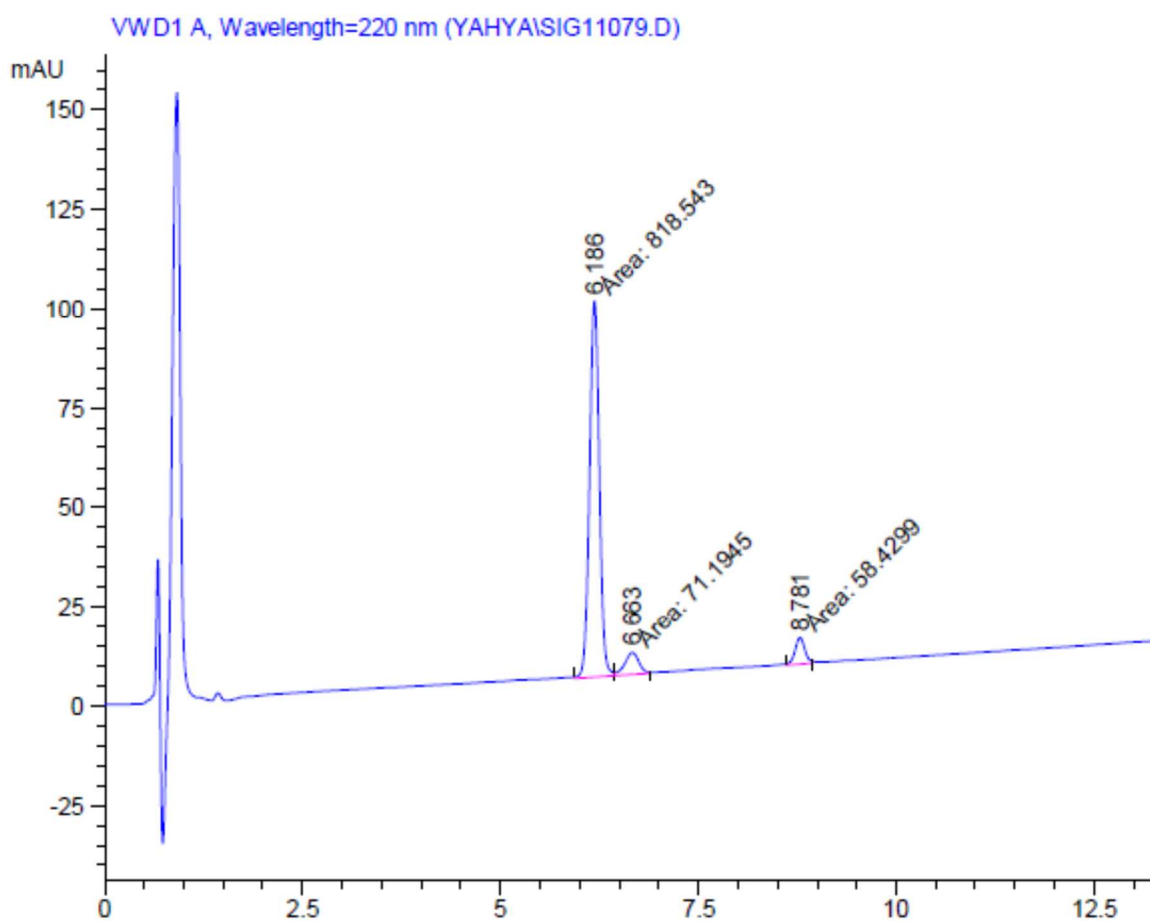
^h Department of Organic Chemistry, University of Barcelona, 08028-Barcelona, Spain

1- Z-Phg-Pro-NH₂ Racemization test:

1.1- HOBt in DMF



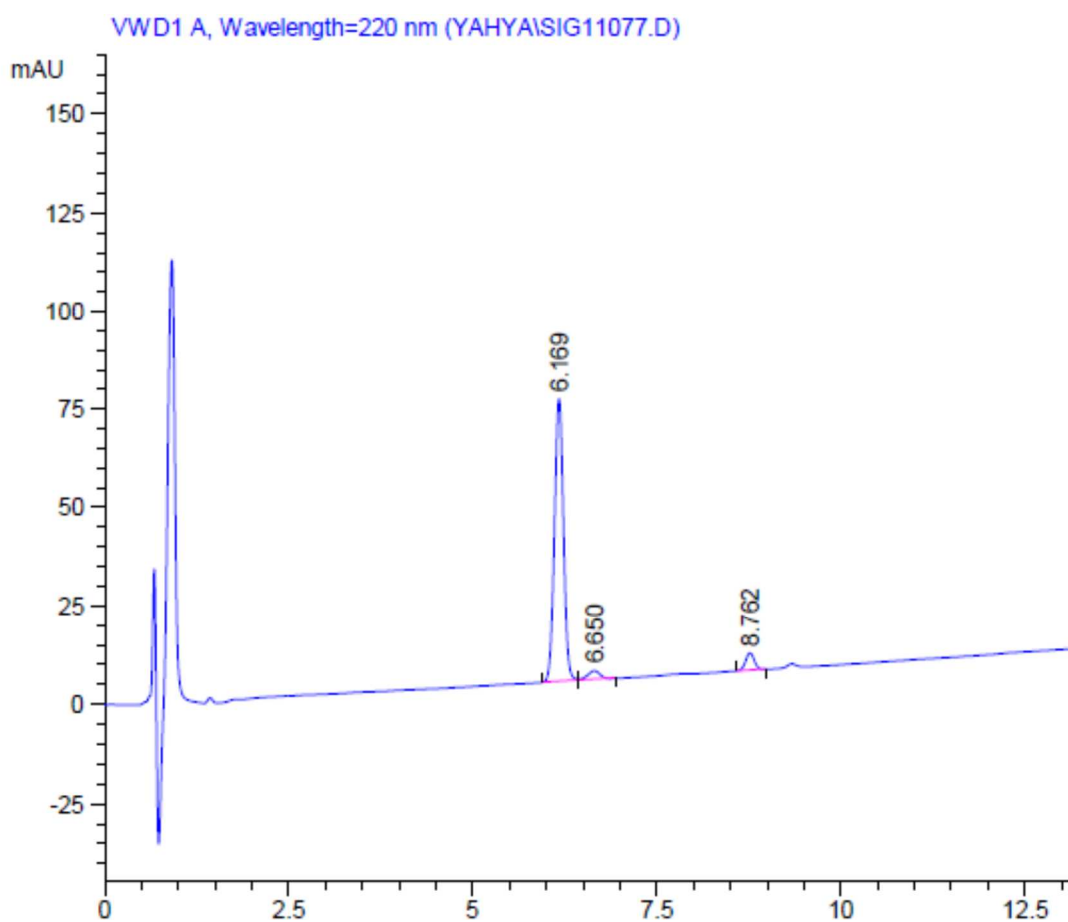
1.2- HOBt in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.186	MF	0.1435	818.54346	95.06696	86.3290
2	6.663	FM	0.2107	71.19449	5.63223	7.5086
3	8.781	MM	0.1449	58.42990	6.71888	6.1624

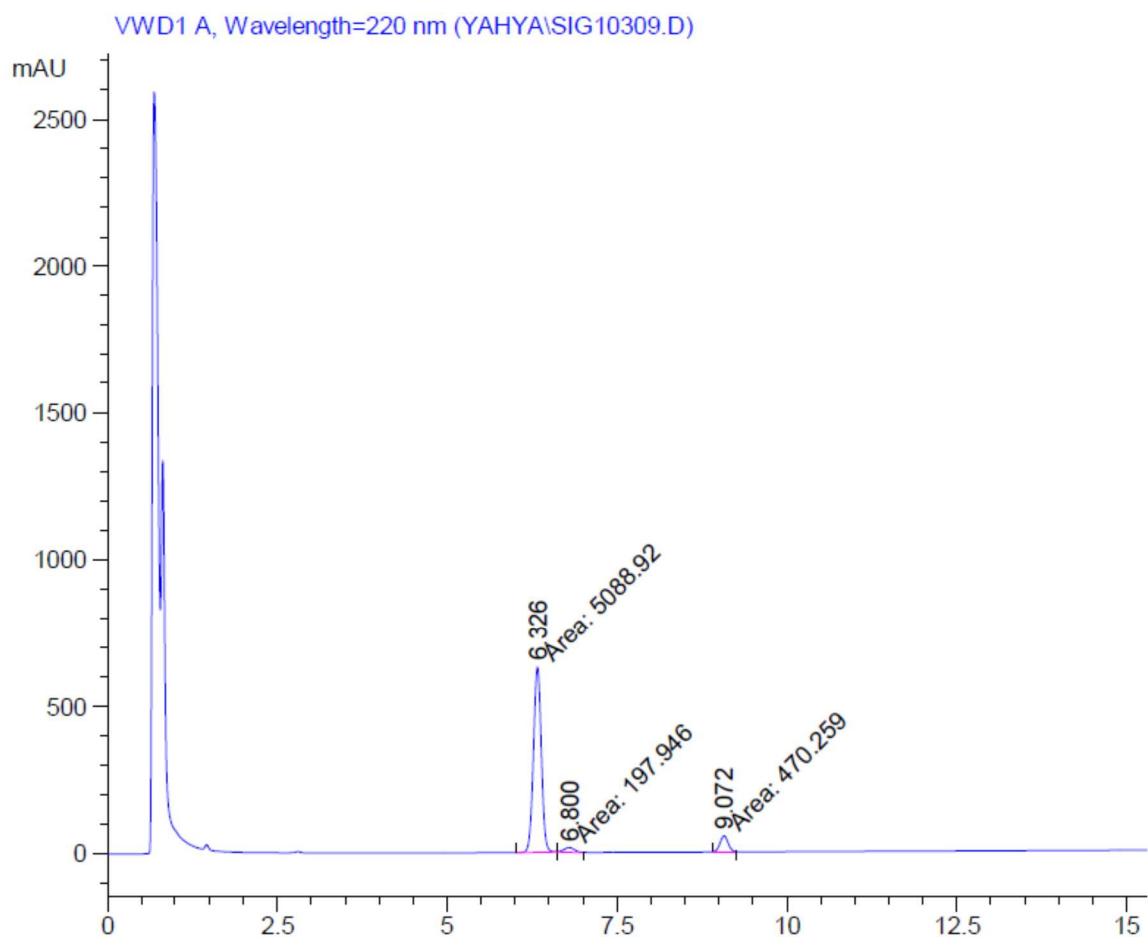
Totals : 948.16784 107.41807

1.2- HOBt in ACN



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.169	BB	0.1328	612.57001	71.94768	90.6859
2	6.650	BP	0.1825	26.65774	2.21760	3.9465
3	8.762	BB	0.1287	36.25735	4.37463	5.3676
Totals :				675.48510	78.53990	

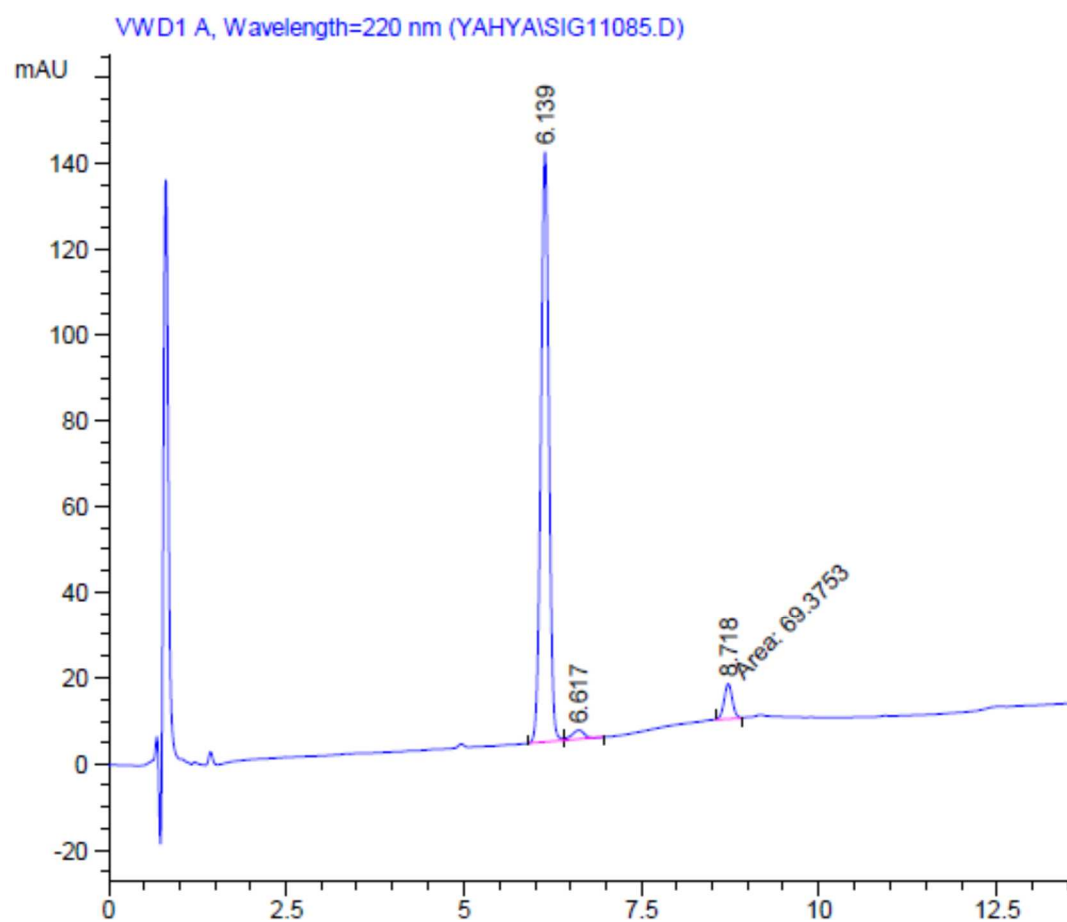
1.4-HOAt in DMF



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	6.326	MM	0.1349	5088.91650	628.60004	88.3934
2	6.800	MM	0.1974	197.94566	16.70938	3.4383
3	9.072	MM	0.1427	470.25909	54.91633	8.1683

Totals : 5757.12126 700.22575

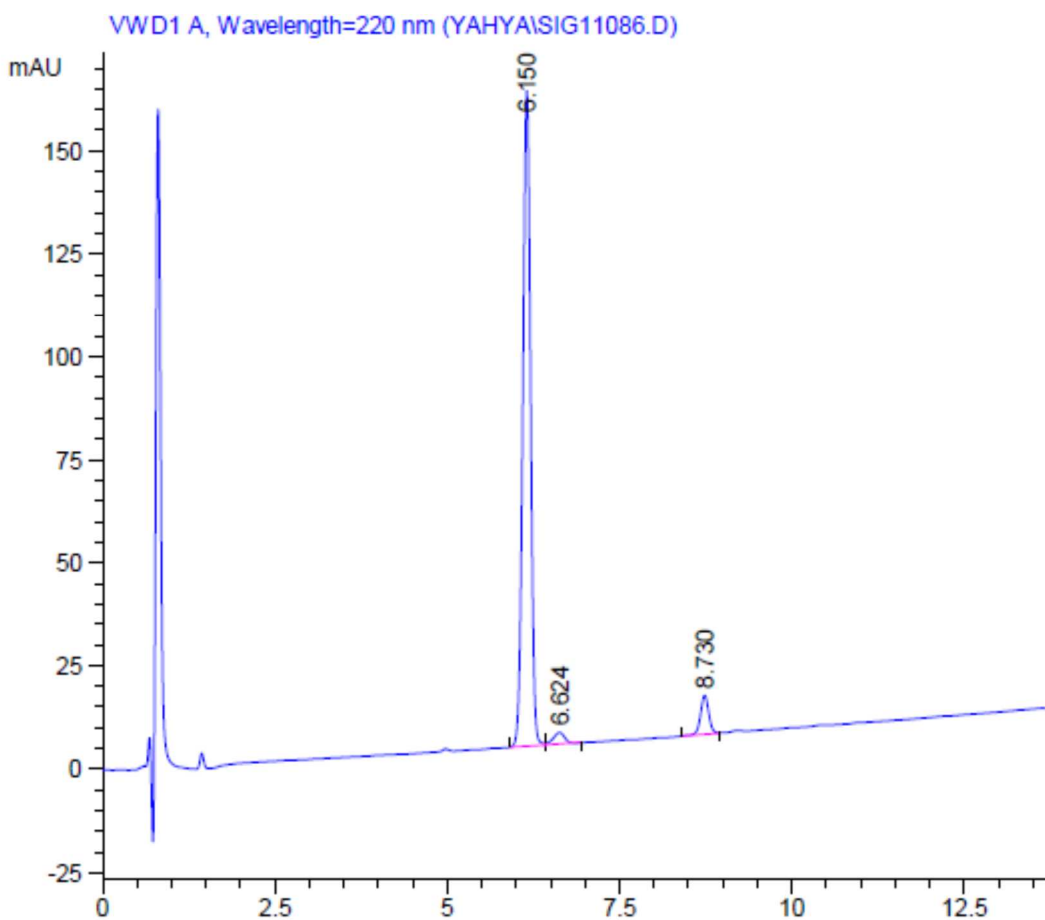
1.5-HOAt in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.139	BB	0.1216	1074.28430	137.72717	91.9310
2	6.617	BP	0.1844	24.91660	2.06585	2.1322
3	8.718	MM	0.1395	69.37532	8.28620	5.9367

Totals : 1168.57622 148.07922

1.6-HOAt in ACN

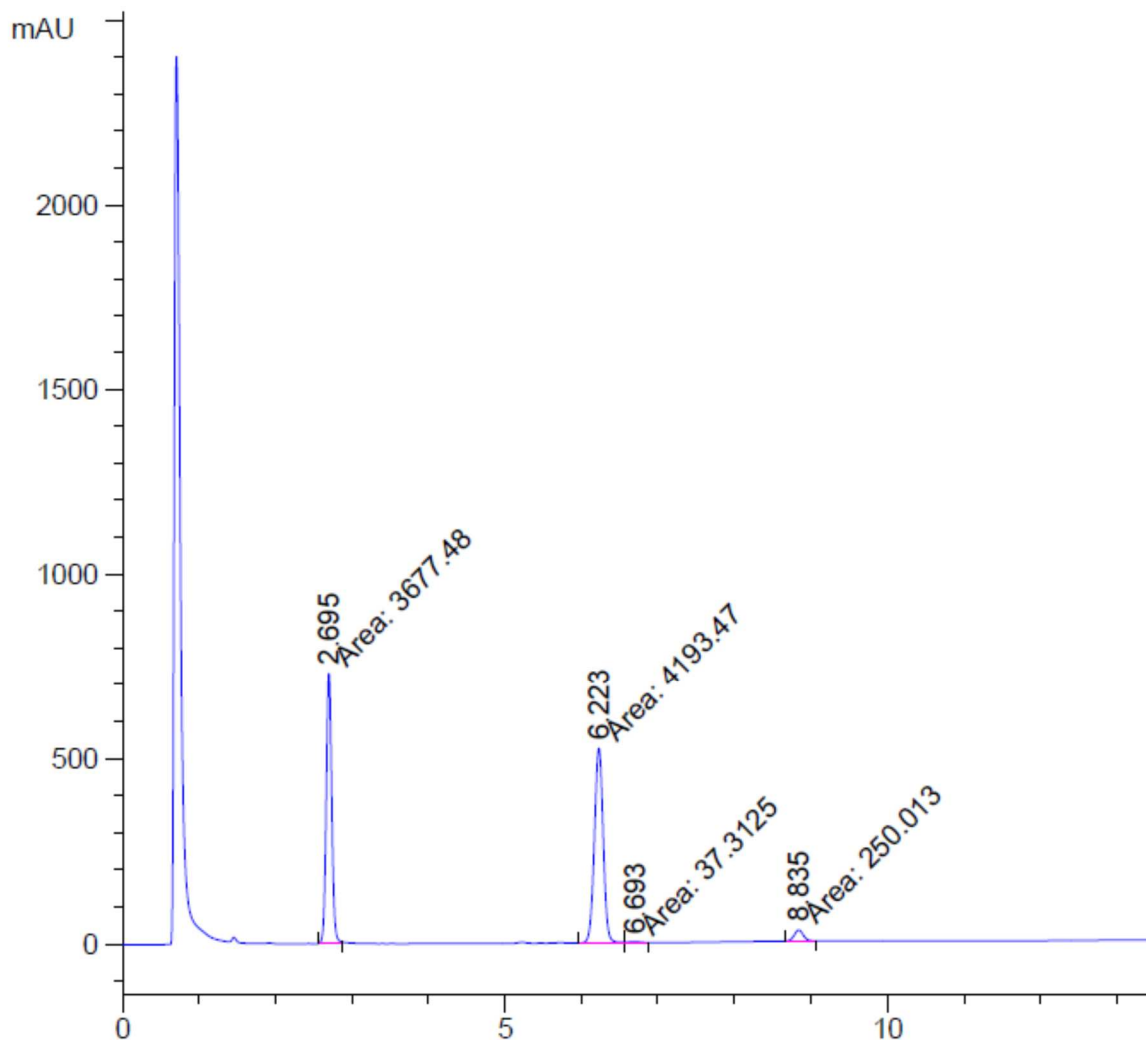


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.150	BB	0.1208	1229.13416	159.02092	91.6198
2	6.624	BP	0.1798	33.10896	2.80707	2.4679
3	8.730	BB	0.1306	79.31651	9.38959	5.9123

Totals : 1341.55962 171.21757

1.7-OxymaPure in DMF

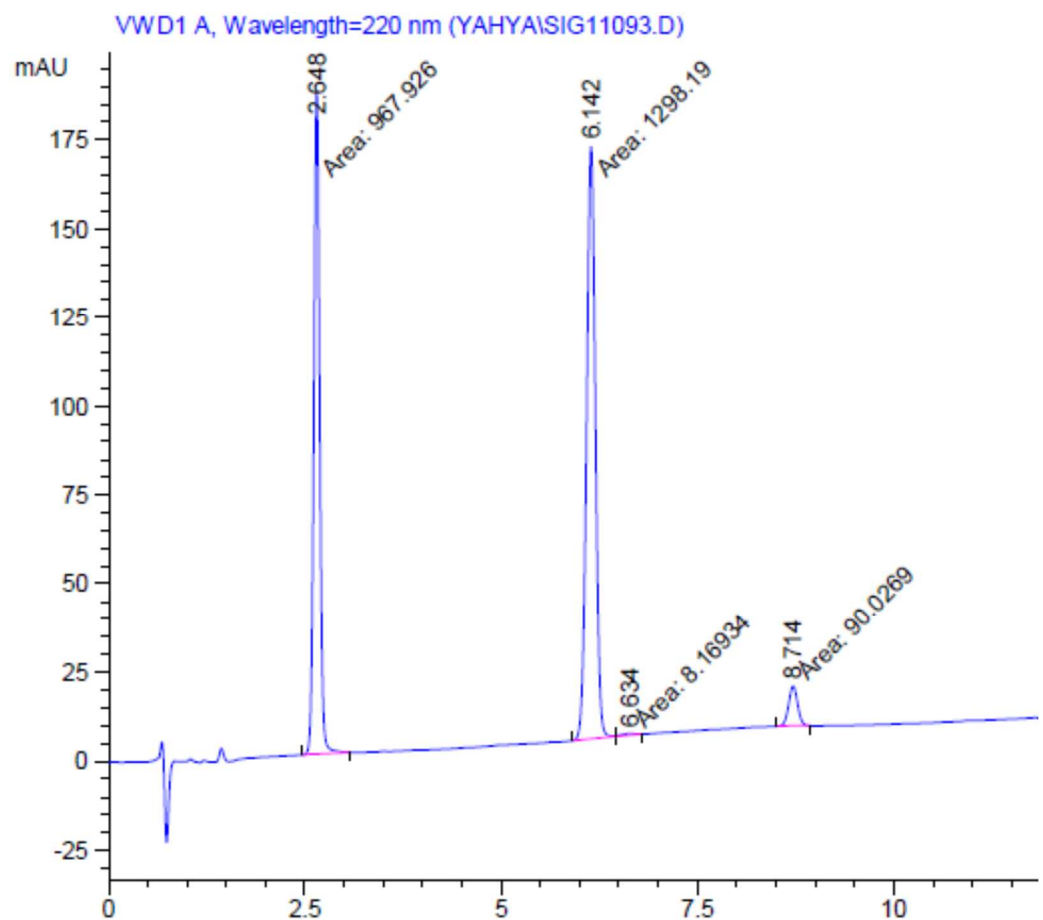
VWD1 A, Wavelength=220 nm (YAHYA\SIG10942.D)



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	2.695	MM	0.0834	3677.48315	735.30951	45.0767
2	6.223	MF	0.1329	4193.46582	525.72107	51.4014
3	6.693	FM	0.2116	37.31252	2.93868	0.4574
4	8.835	MM	0.1394	250.01295	29.89925	3.0645

Totals : 8158.27445 1293.86851

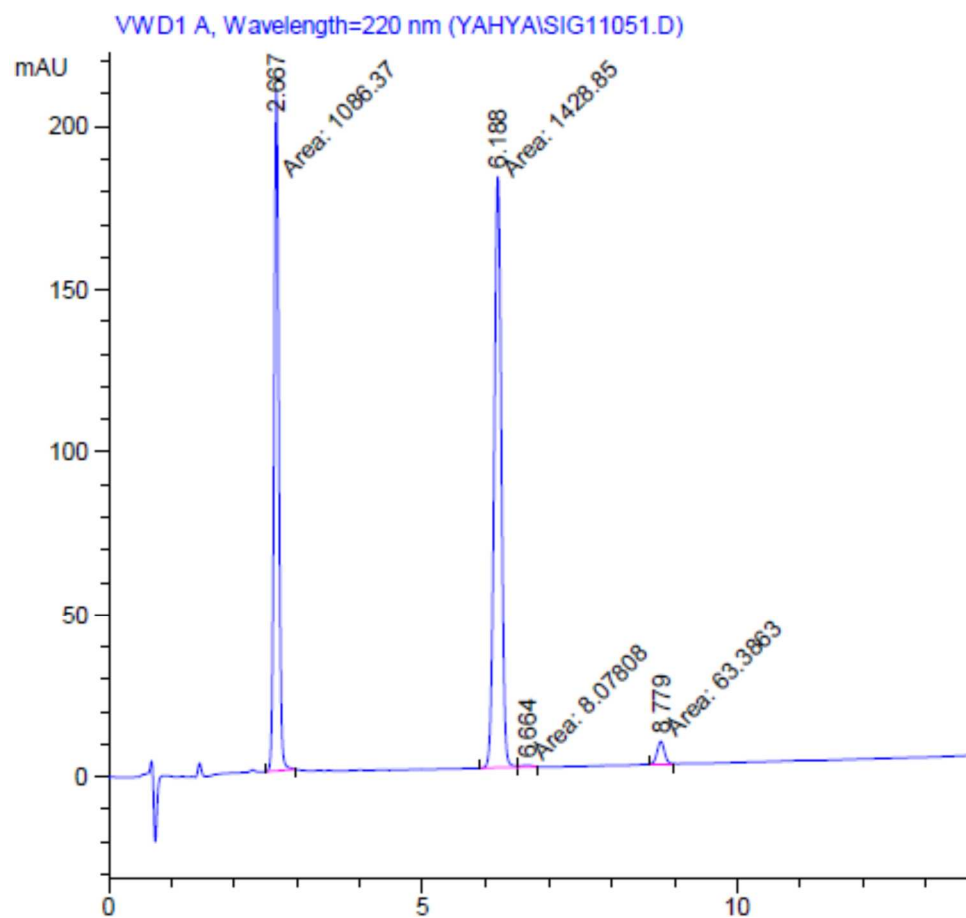
1.8-OxymaPure in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	2.648	MM	0.0860	967.92639	187.50903	40.9390
2	6.142	MF	0.1294	1298.19031	167.14500	54.9077
3	6.634	FM	0.2187	8.16934	6.22477e-1	0.3455
4	8.714	MM	0.1339	90.02687	11.20521	3.8077

Totals : 2364.31291 366.48172

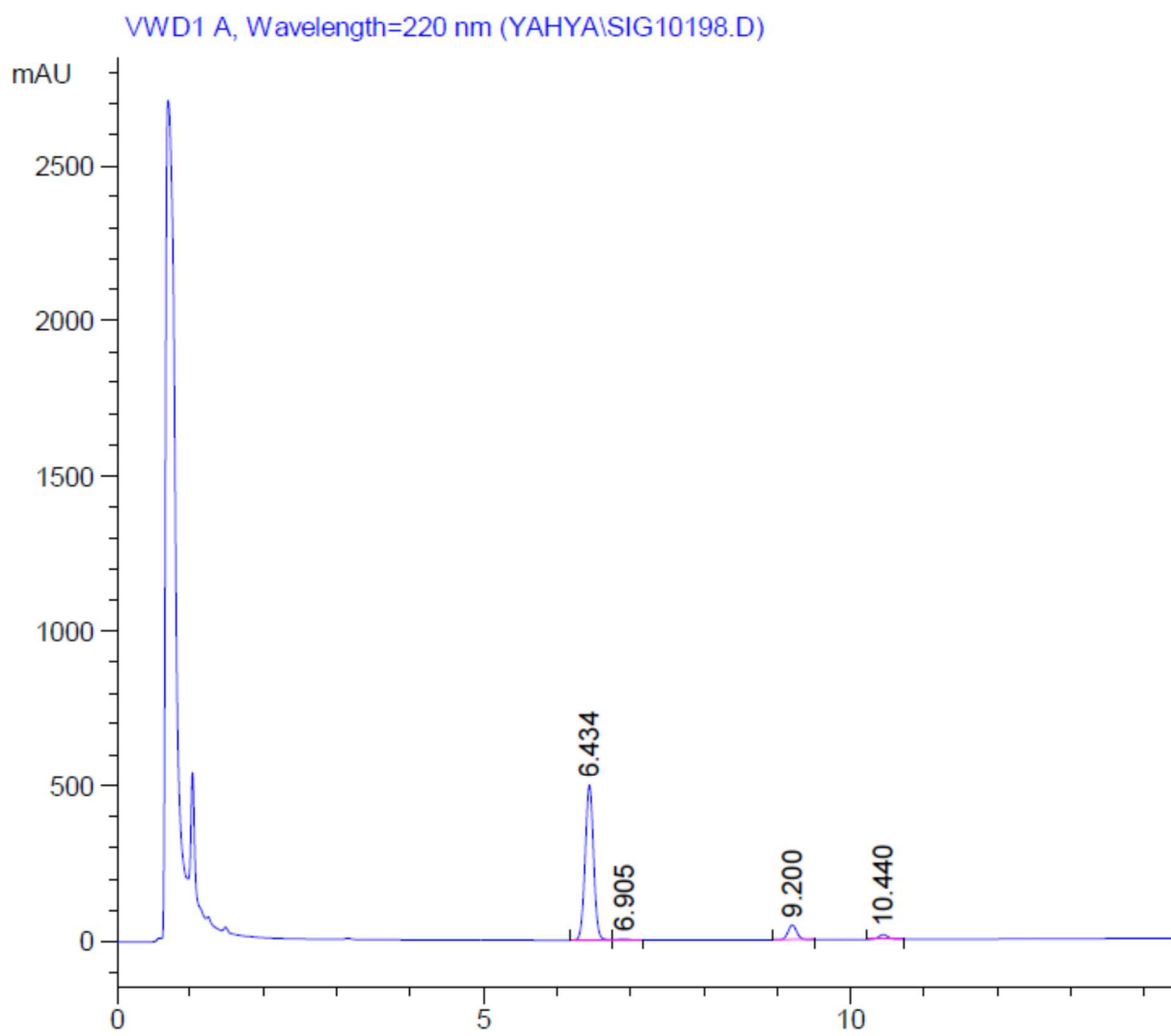
1.9-OxymaPure in ACN



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.667	MM	0.0860	1086.37109	210.44673	41.9986
2	6.188	MF	0.1305	1428.84729	182.46661	55.2386
3	6.664	FM	0.2152	8.07808	6.25771e-1	0.3123
4	8.779	MM	0.1456	63.38634	7.25517	2.4505

Totals : 2586.68281 400.79428

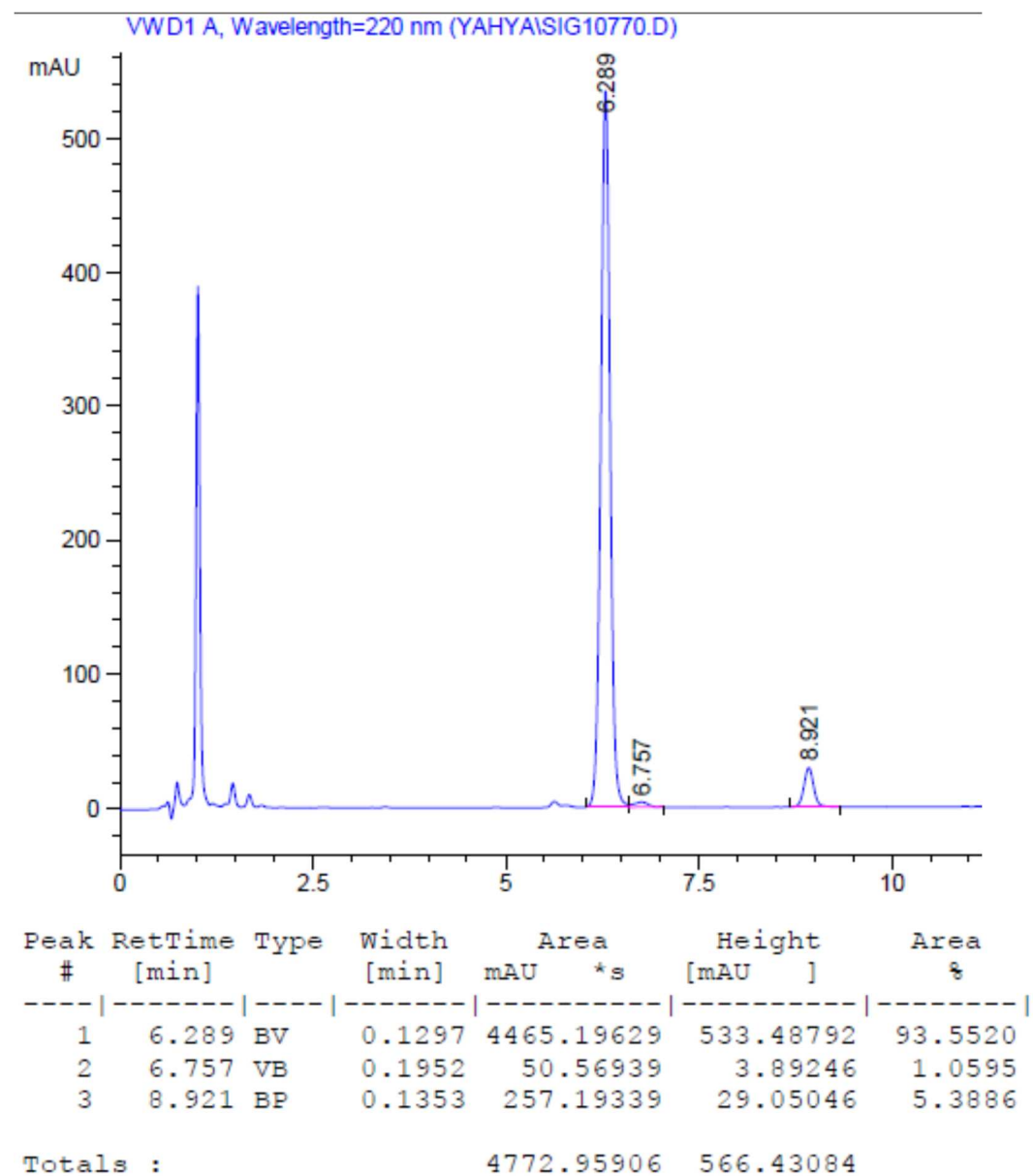
1.10-Oxyma-B in DMF



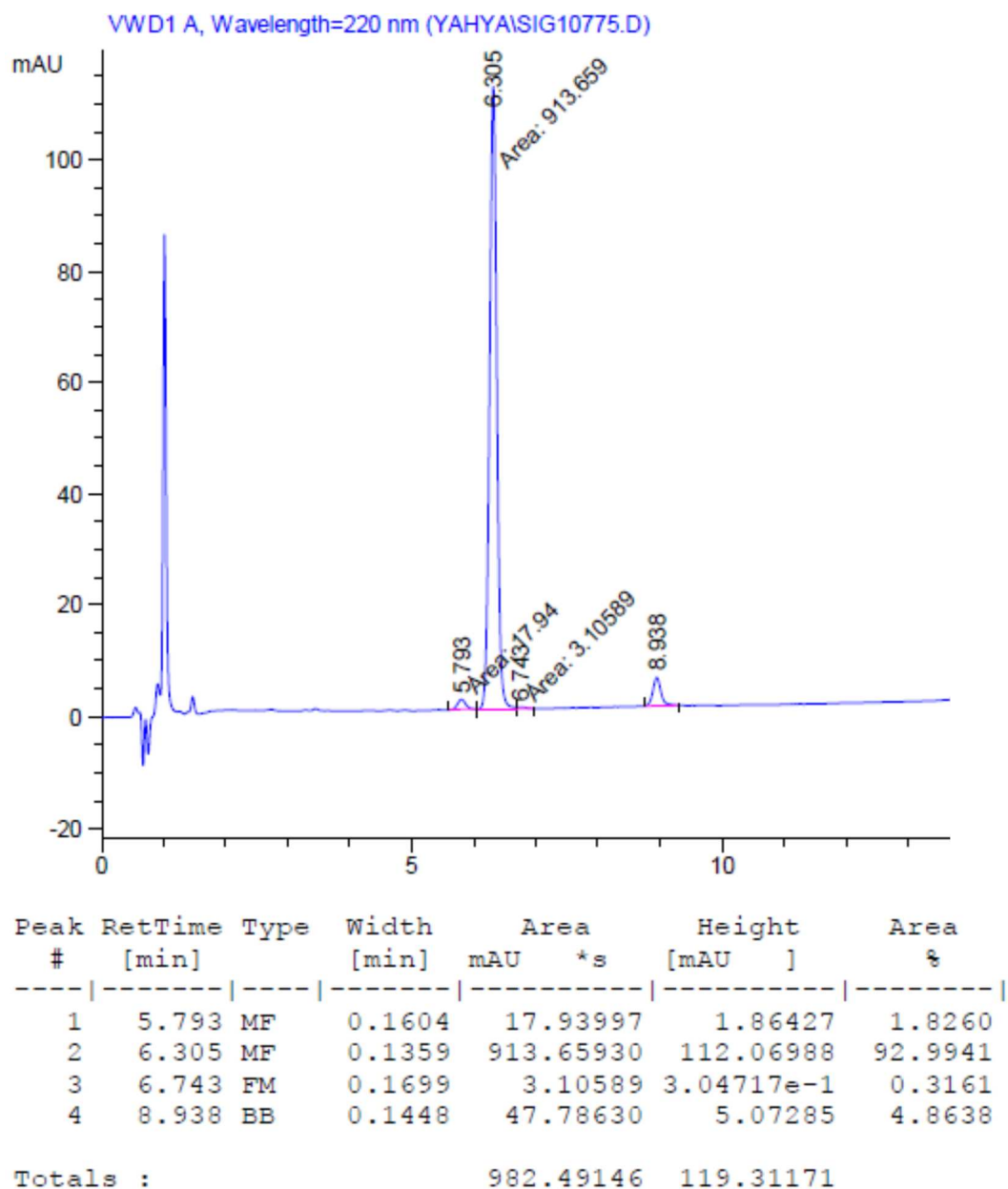
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.434	PV	0.1222	3953.95679	495.56058	87.3388
2	6.905	VV	0.1890	40.04154	3.15152	0.8845
3	9.200	BB	0.1298	394.05420	47.02825	8.7042
4	10.440	BB	0.1418	139.09808	15.18406	3.0725

Totals : 4527.15061 560.92440

1.11-Oxyma-B in THF

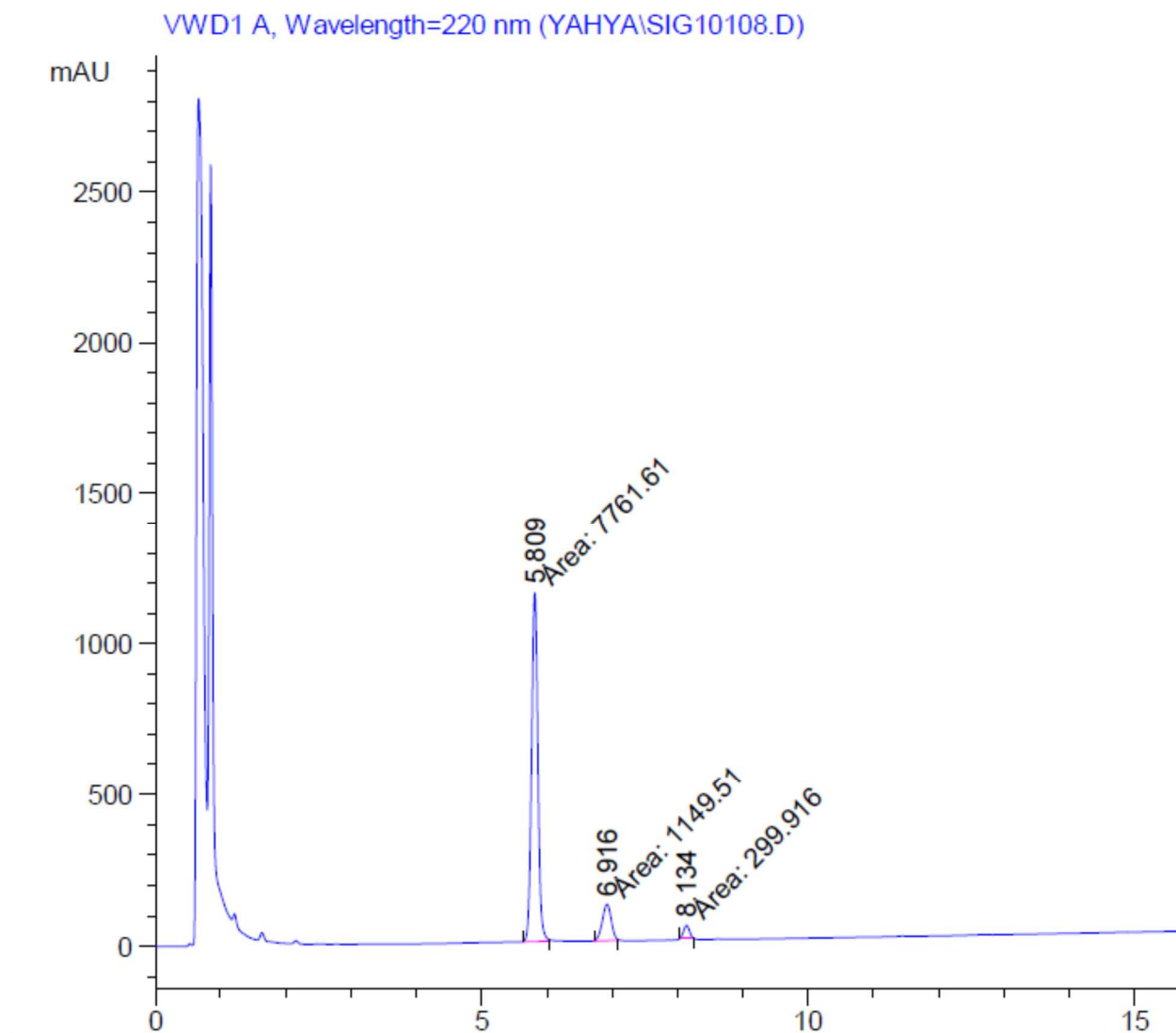


1.12-Oxyma-B in ACN



2-Z-Phe-Val-Pro-NH₂ Racemization test:

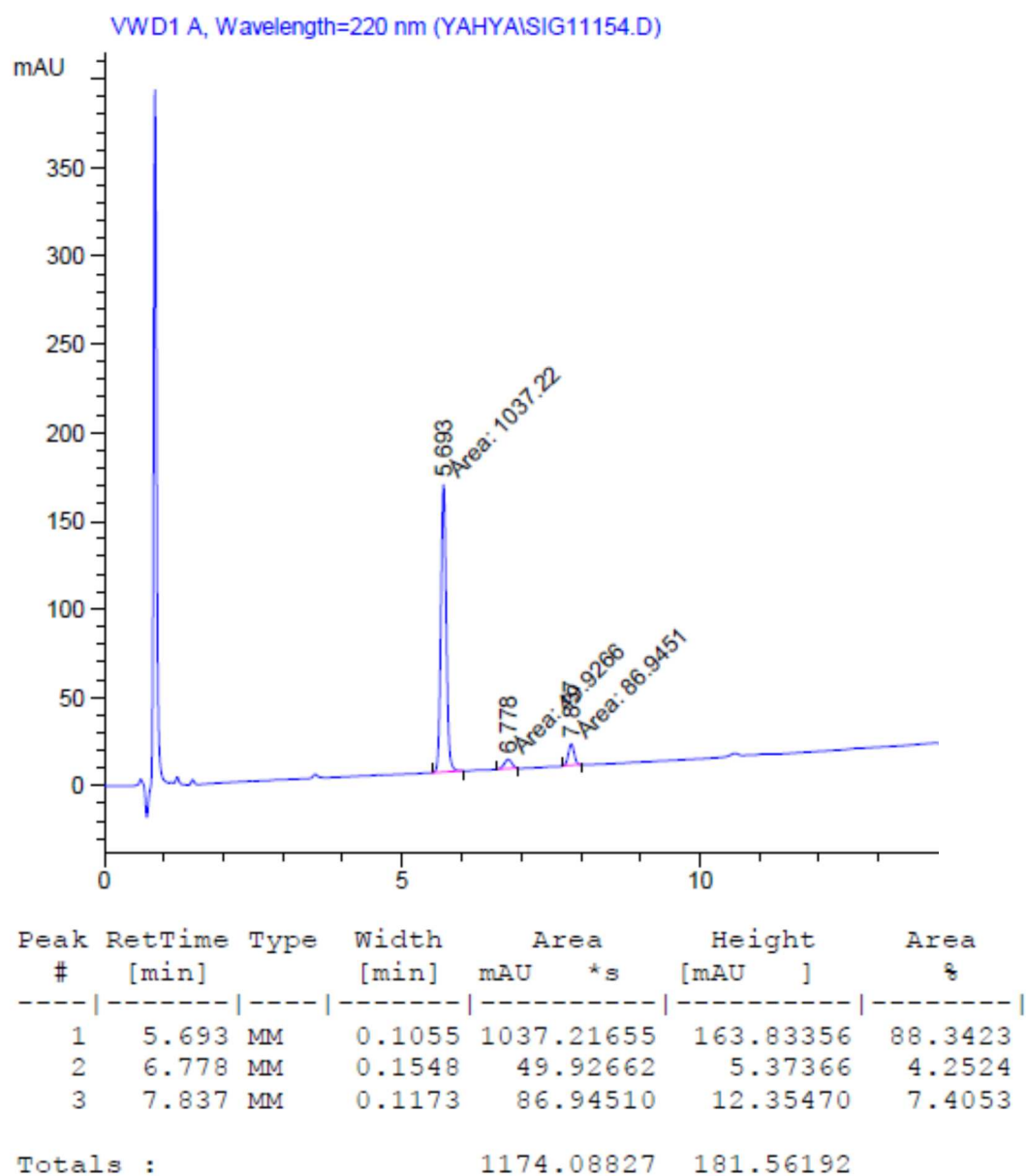
2.1- HOBt in DMF



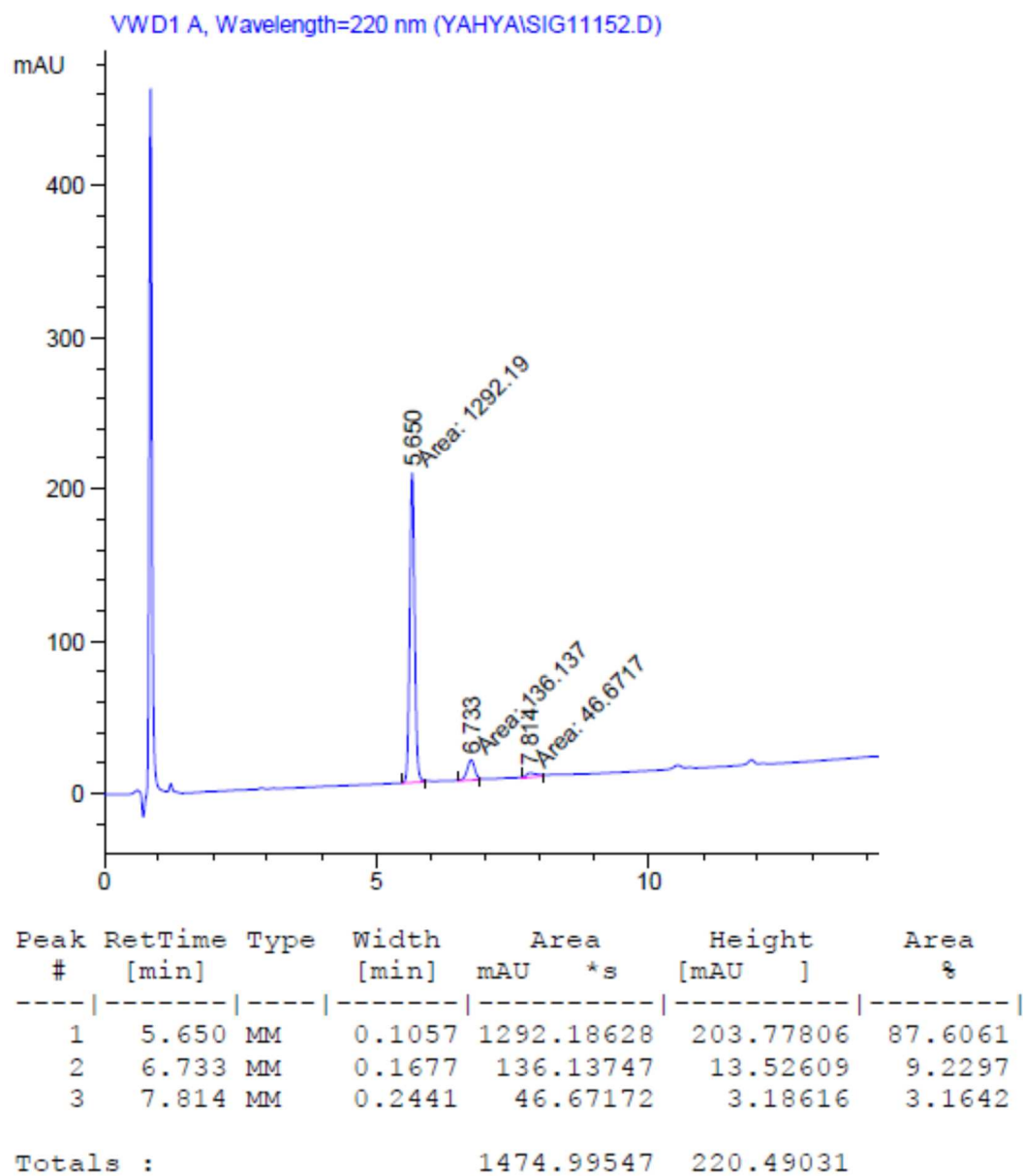
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	5.809	MM	0.1118	7761.60791	1156.86853	84.2642
2	6.916	MM	0.1590	1149.51404	120.45636	12.4797
3	8.134	MM	0.1096	299.91574	45.59239	3.2560

Totals : 9211.03769 1322.91728

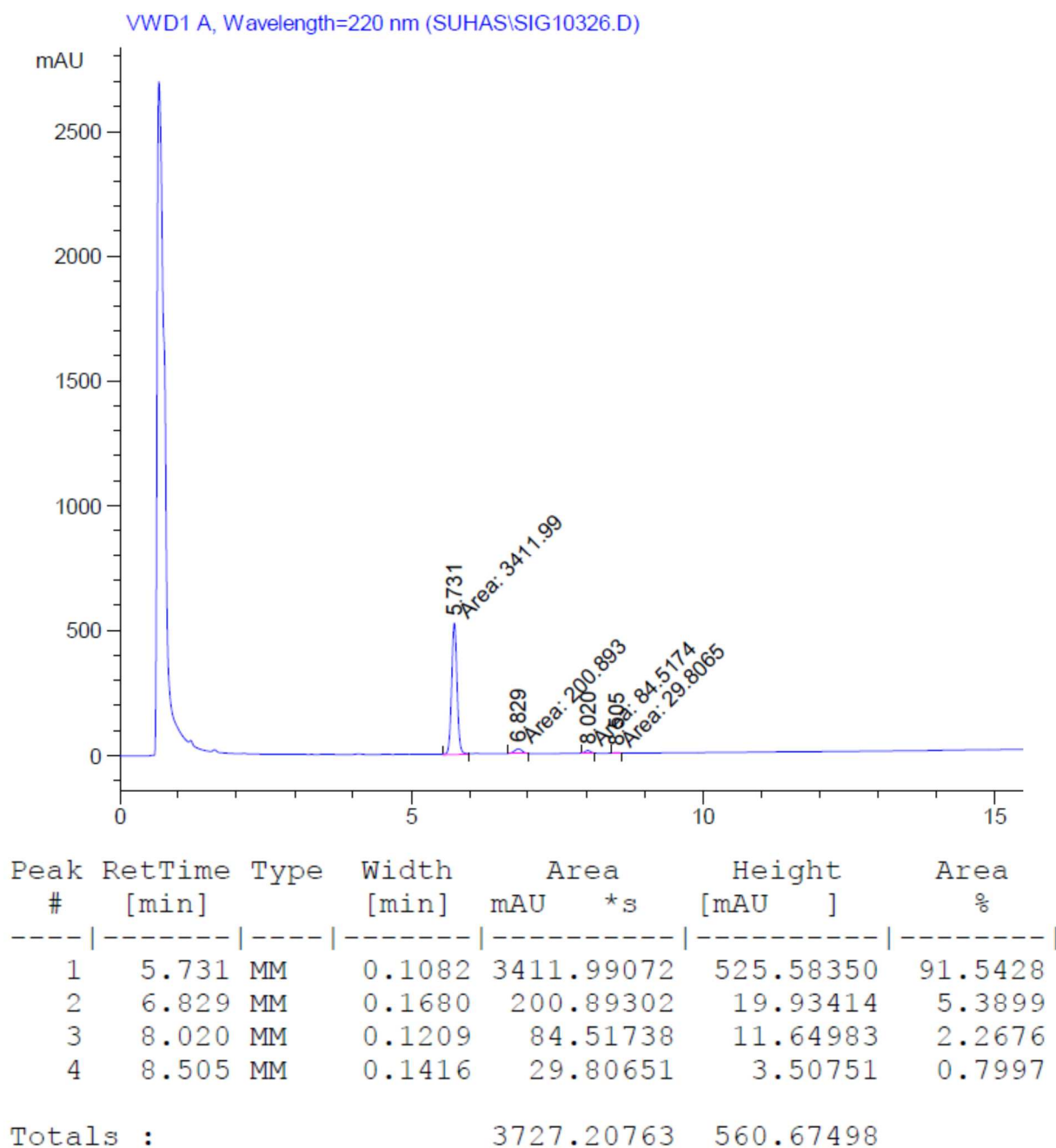
2.2- HOBt in THF



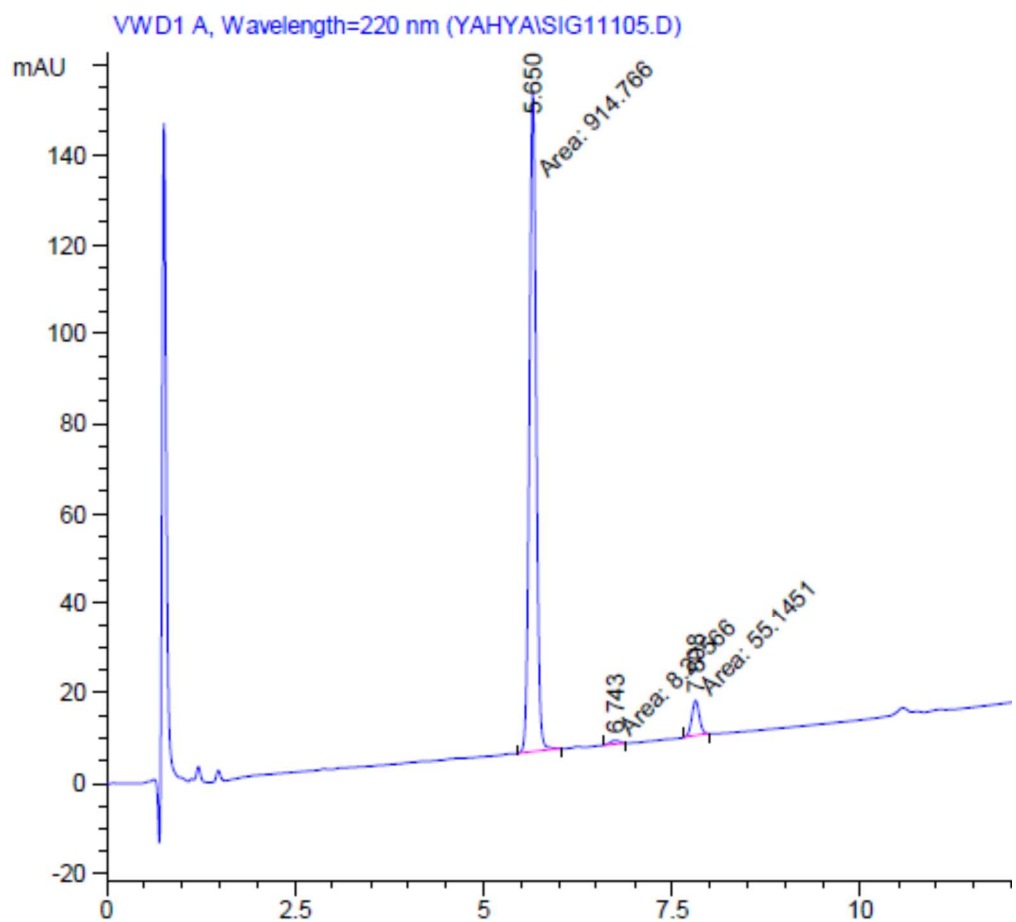
2.3- HOBt in ACN



2.4-HOAt in DMF



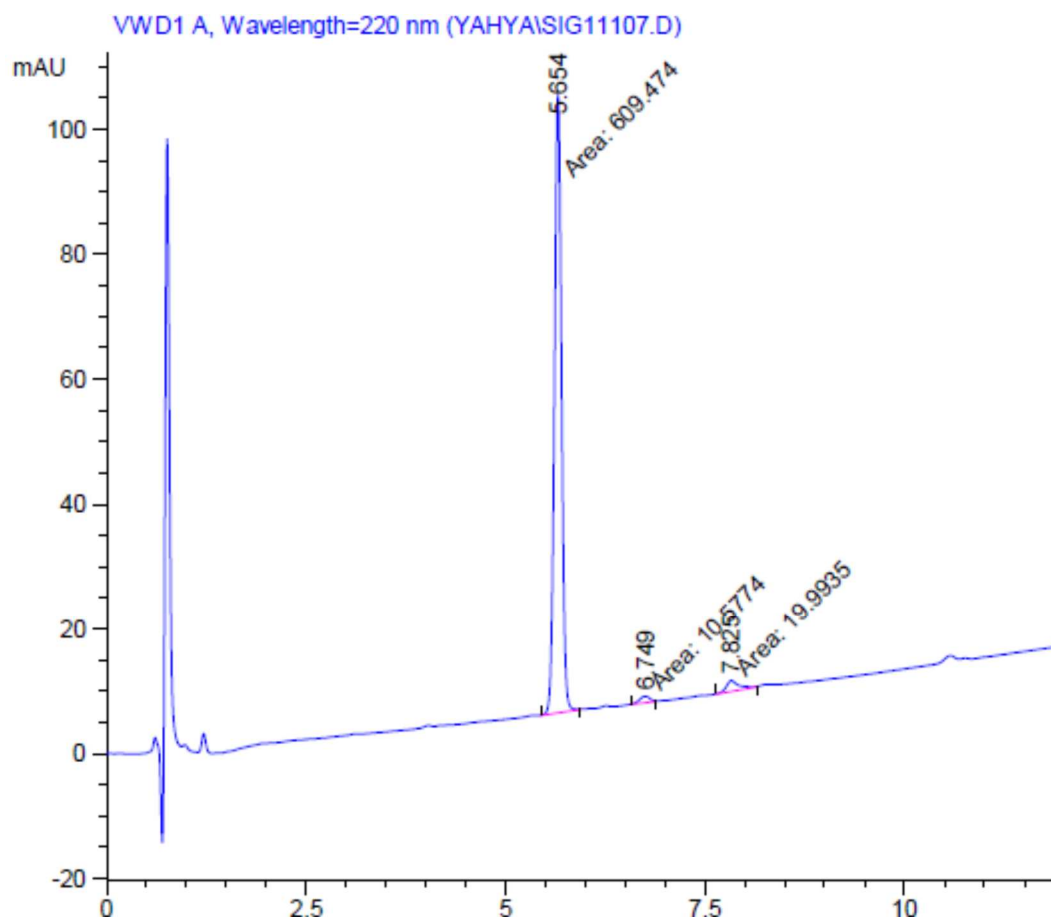
2.5-HOAt in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.650	MM	0.1035	914.76642	147.32126	93.5165
2	6.743	MM	0.1553	8.27566	8.87914e-1	0.8460
3	7.808	MM	0.1172	55.14510	7.83931	5.6375

Totals : 978.18717 156.04848

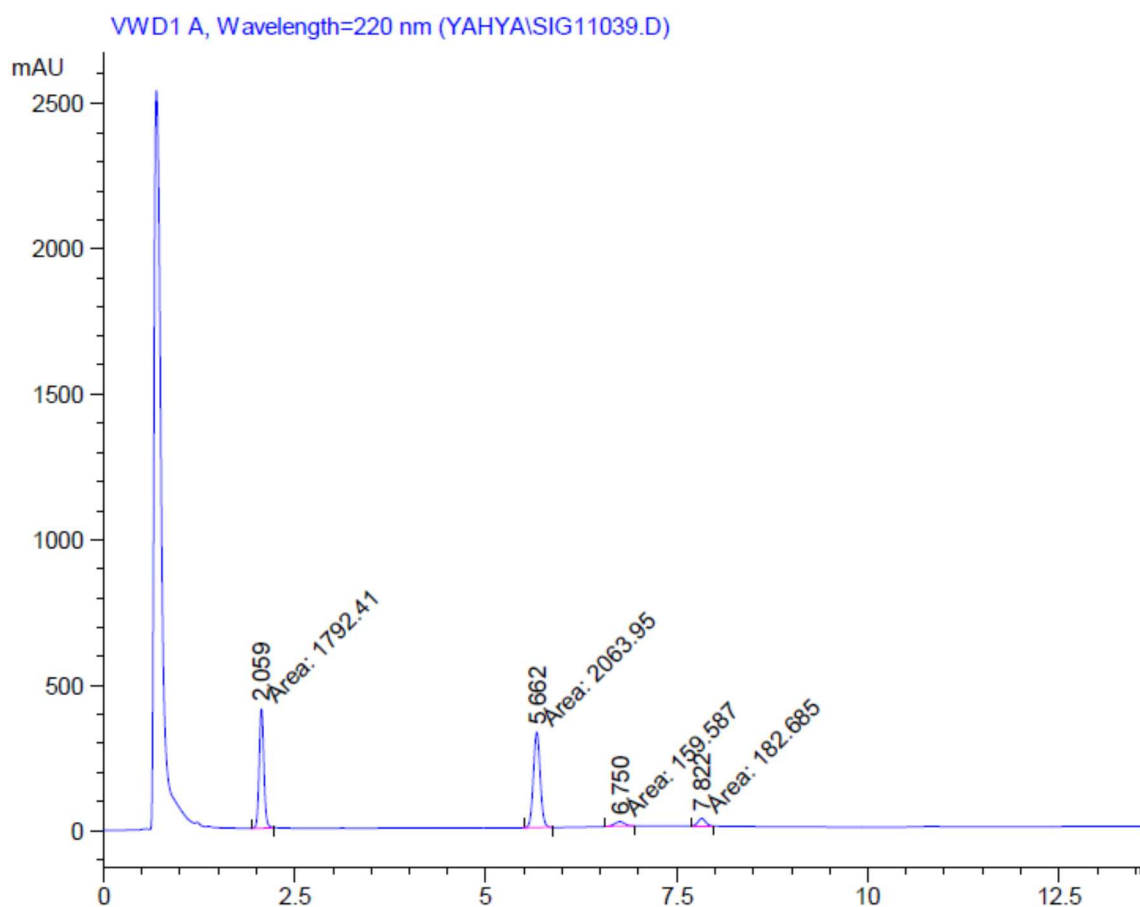
2.6-HOAt in ACN



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.654	MM	0.1023	609.47351	99.31754	95.2236
2	6.749	MM	0.1609	10.57745	1.09575	1.6526
3	7.825	MM	0.1868	19.99349	1.78424	3.1238

Totals : 640.04445 102.19752

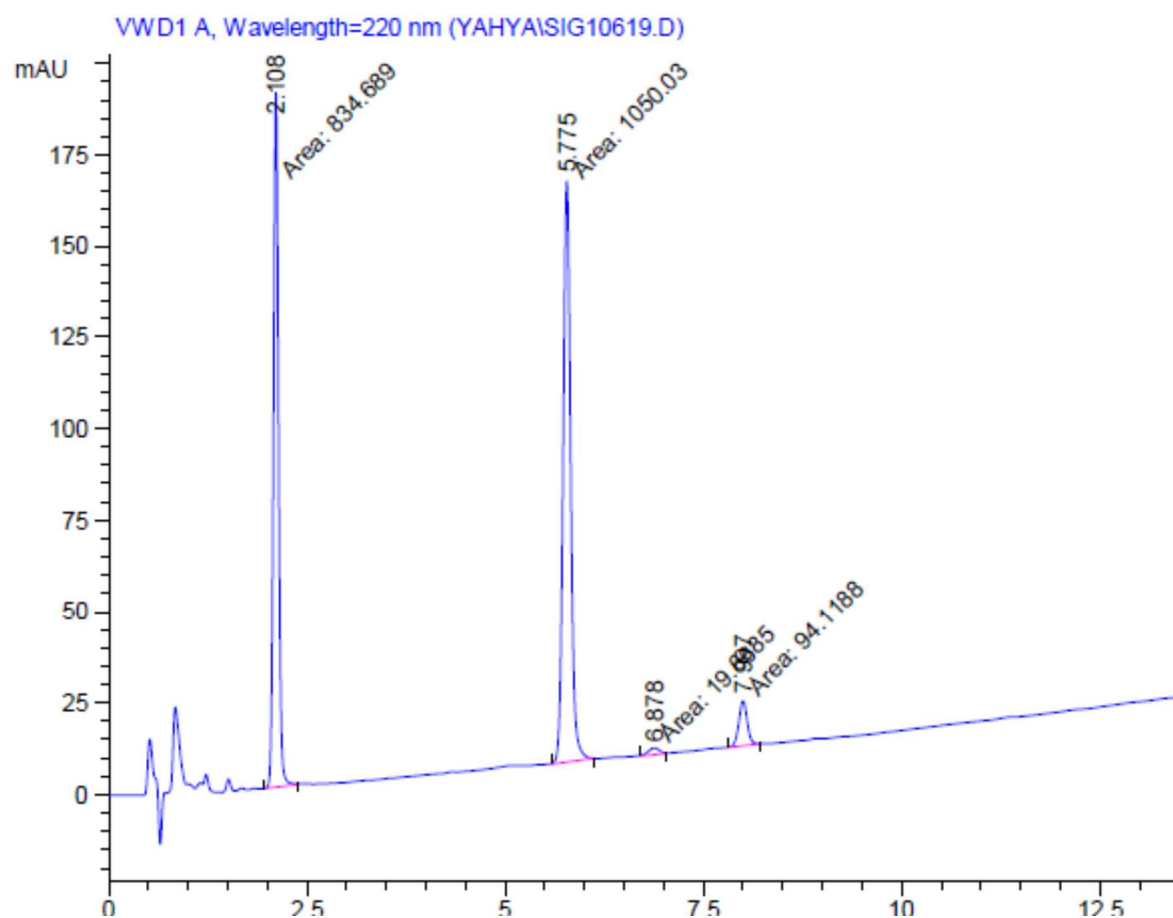
2.7-OxymaPure in DMF



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	2.059	MM	0.0720	1792.40674	414.90189	42.6902
2	5.662	MM	0.1045	2063.95459	329.12589	49.1578
3	6.750	MM	0.1629	159.58696	16.32829	3.8009
4	7.822	MM	0.1162	182.68468	26.21371	4.3511

Totals : 4198.63297 786.56978

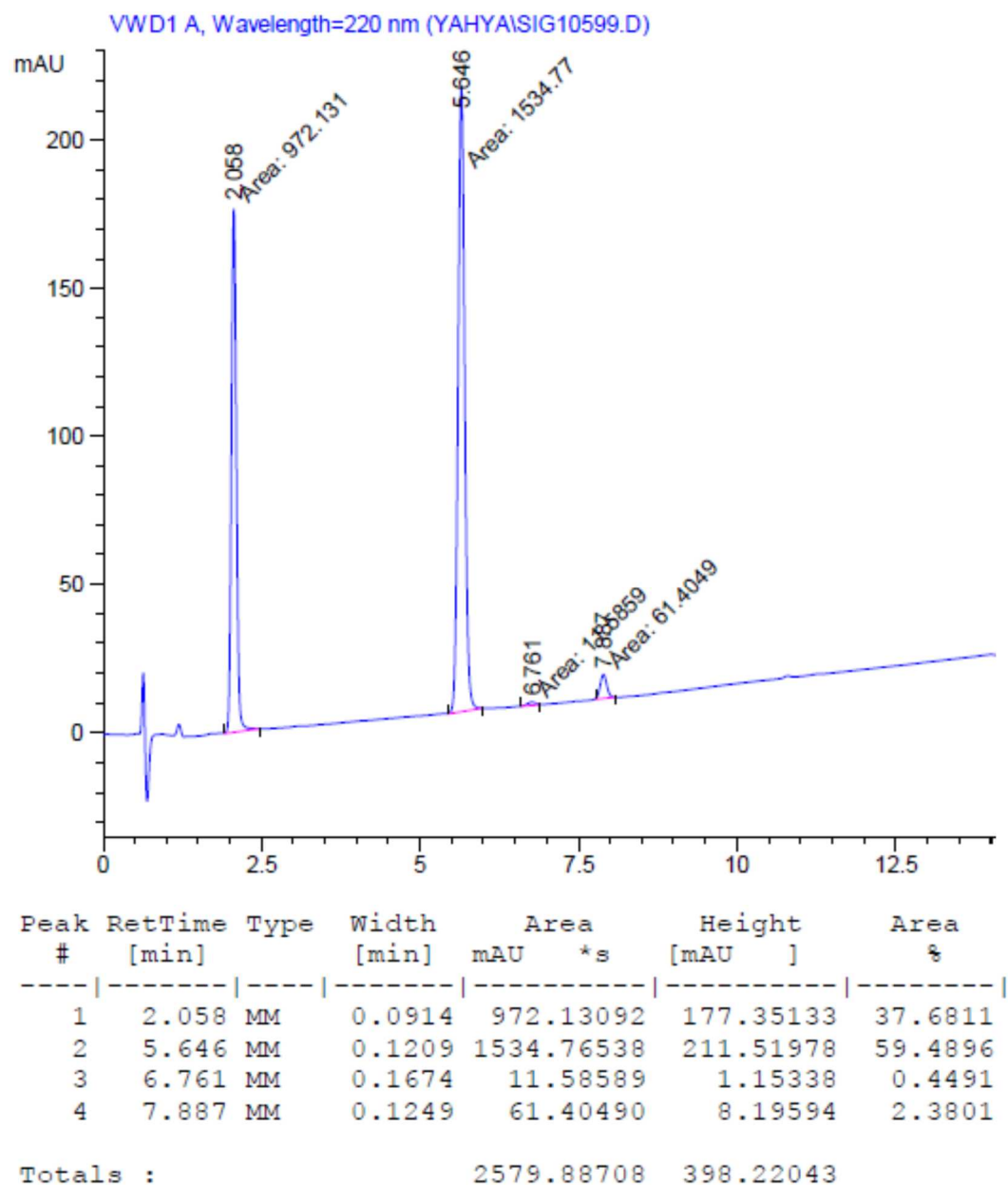
2.8-OxymaPure in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	2.108	MM	0.0727	834.68903	191.41022	41.7656
2	5.775	MM	0.1097	1050.03101	159.54111	52.5408
3	6.878	MM	0.1721	19.66851	1.90459	0.9842
4	7.997	MM	0.1266	94.11881	12.38939	4.7095

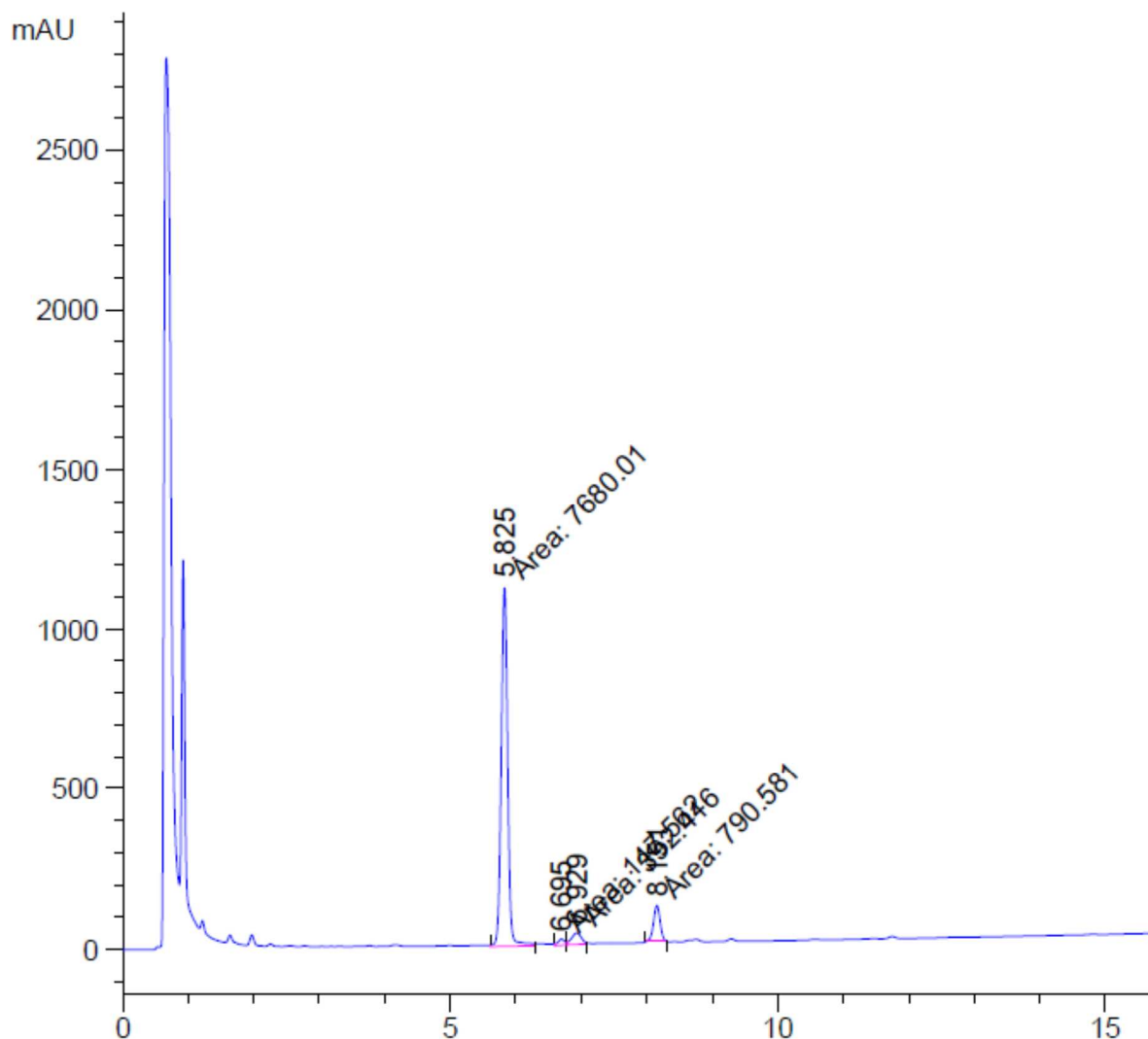
Totals : 1998.50736 365.24531

2.9-OxymaPure in ACN



2.10-Oxyma-B in DMF

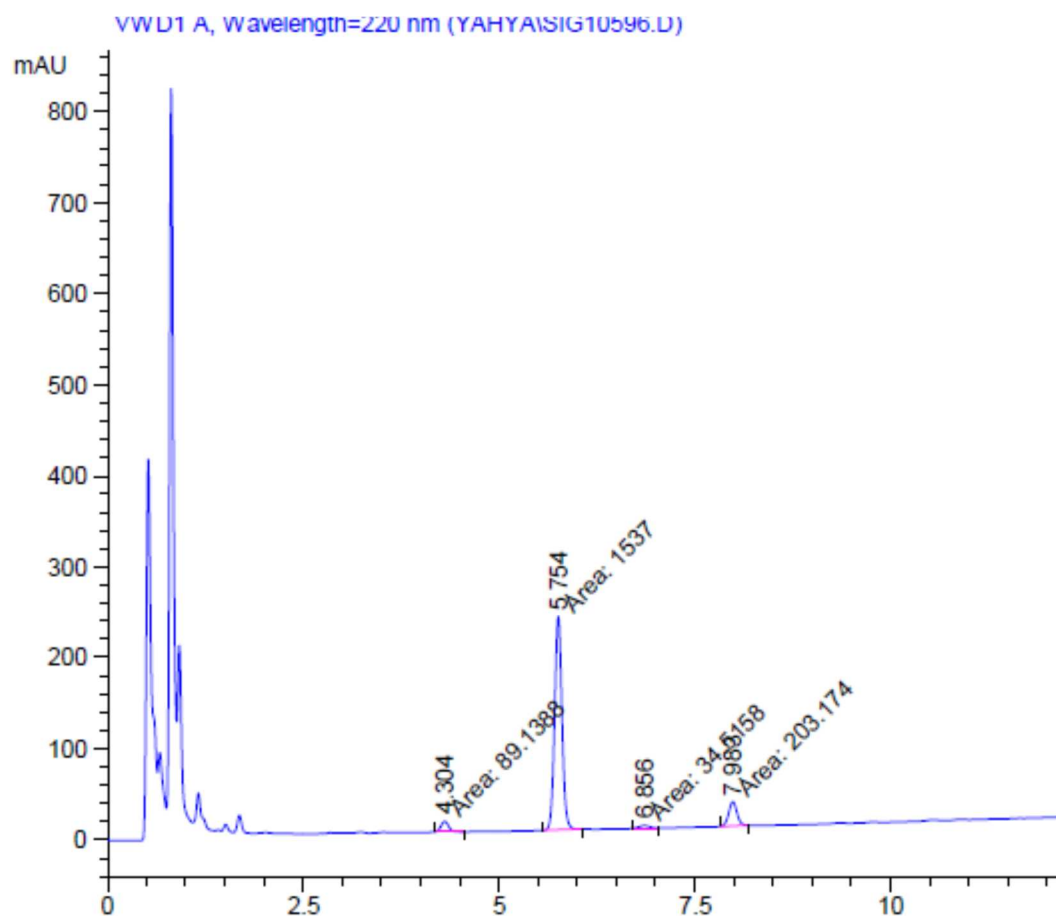
VWD1 A, Wavelength=220 nm (YAHYA\SIG10109.D)



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	5.825	MM	0.1138	7680.01074	1124.86694	85.2334
2	6.695	MF	0.1221	147.56154	20.13989	1.6376
3	6.929	FM	0.1768	392.41583	36.99476	4.3551
4	8.151	MM	0.1176	790.58063	112.03448	8.7739

Totals : 9010.56874 1294.03608

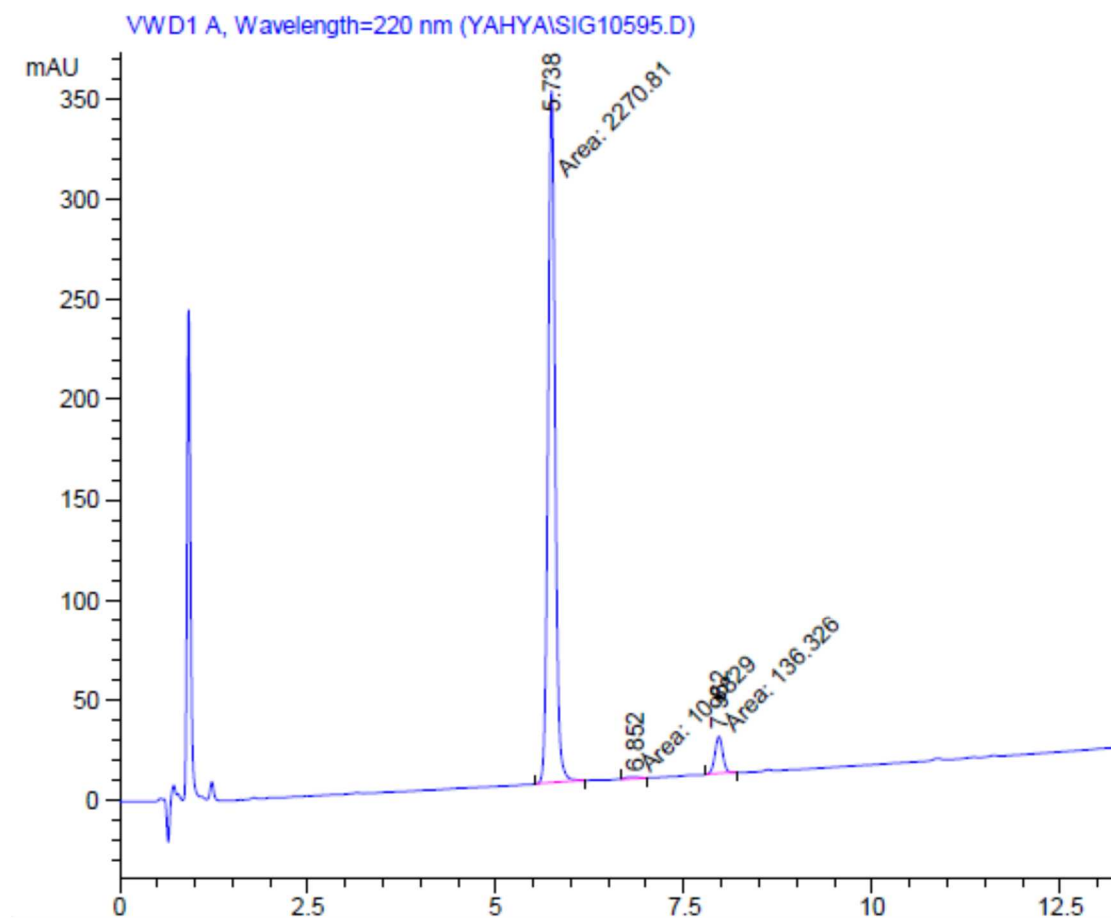
2.11- Oxyma-B in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	4.304	MM	0.1249	89.13880	11.89540	4.7826
2	5.754	MM	0.1094	1536.99585	234.20184	82.4646
3	6.856	MM	0.1735	34.51583	3.31647	1.8519
4	7.983	MM	0.1261	203.17403	26.85485	10.9009

Totals : 1863.82451 276.26856

2.12- Oxyma-B in ACN

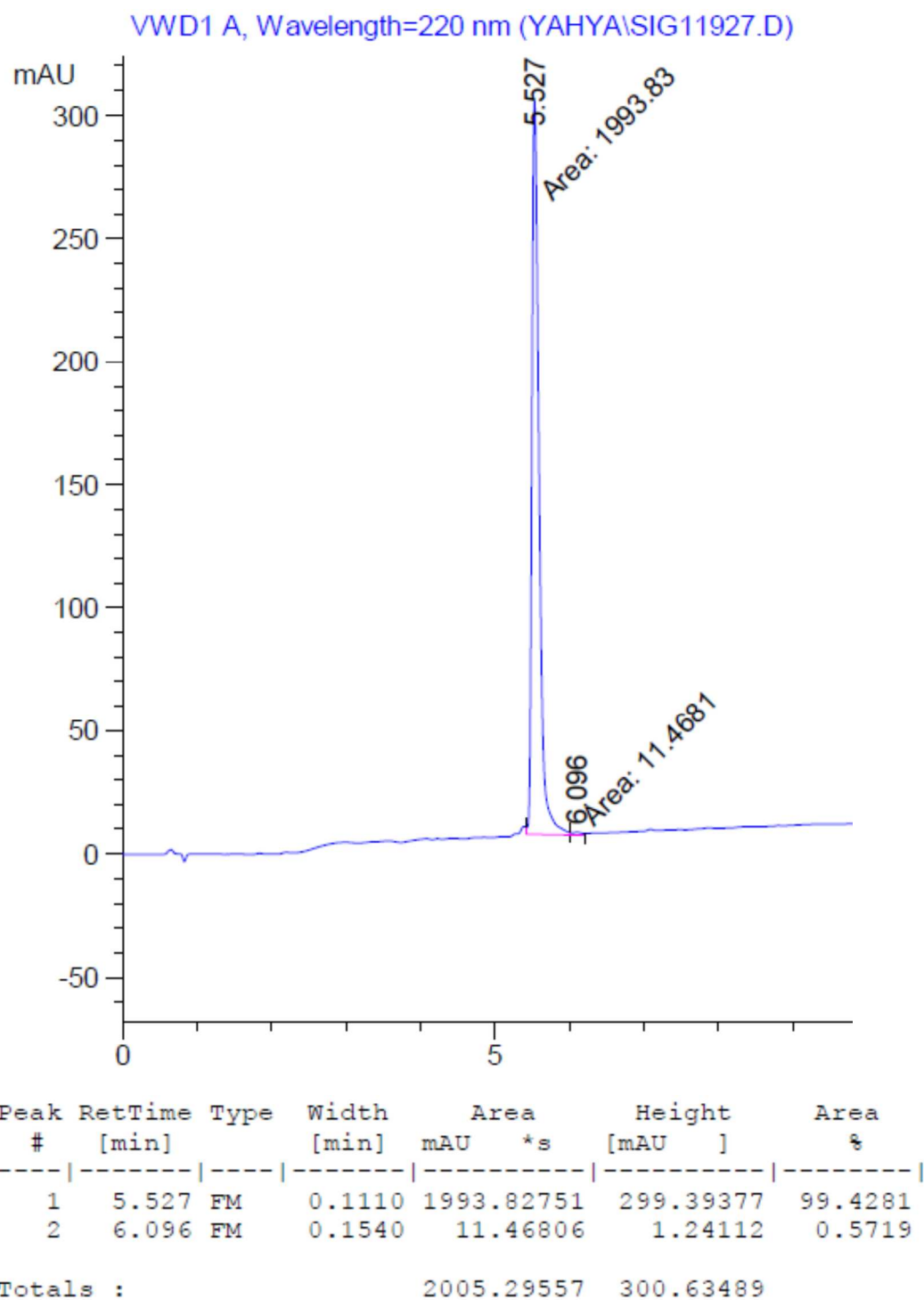


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	5.738	MM	0.1092	2270.80737		346.43256	93.9120
2	6.852	MM	0.2469	10.88295		7.34594e-1	0.4501
3	7.962	MM	0.1218	136.32571		18.65207	5.6379

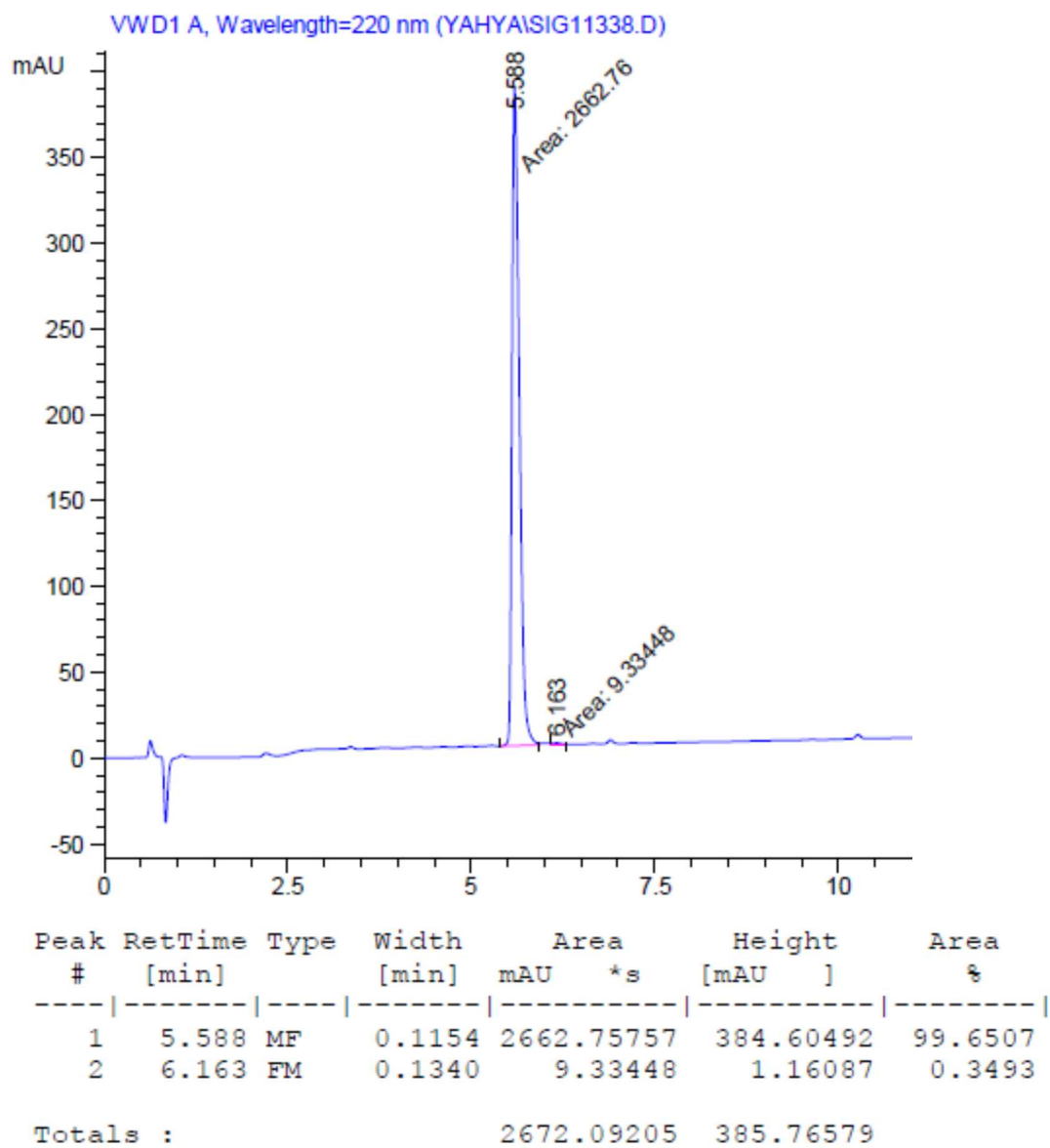
Totals : 2418.01604 365.81922

3- H-Gly-Ser-Phe-NH₂ racemization Experiments

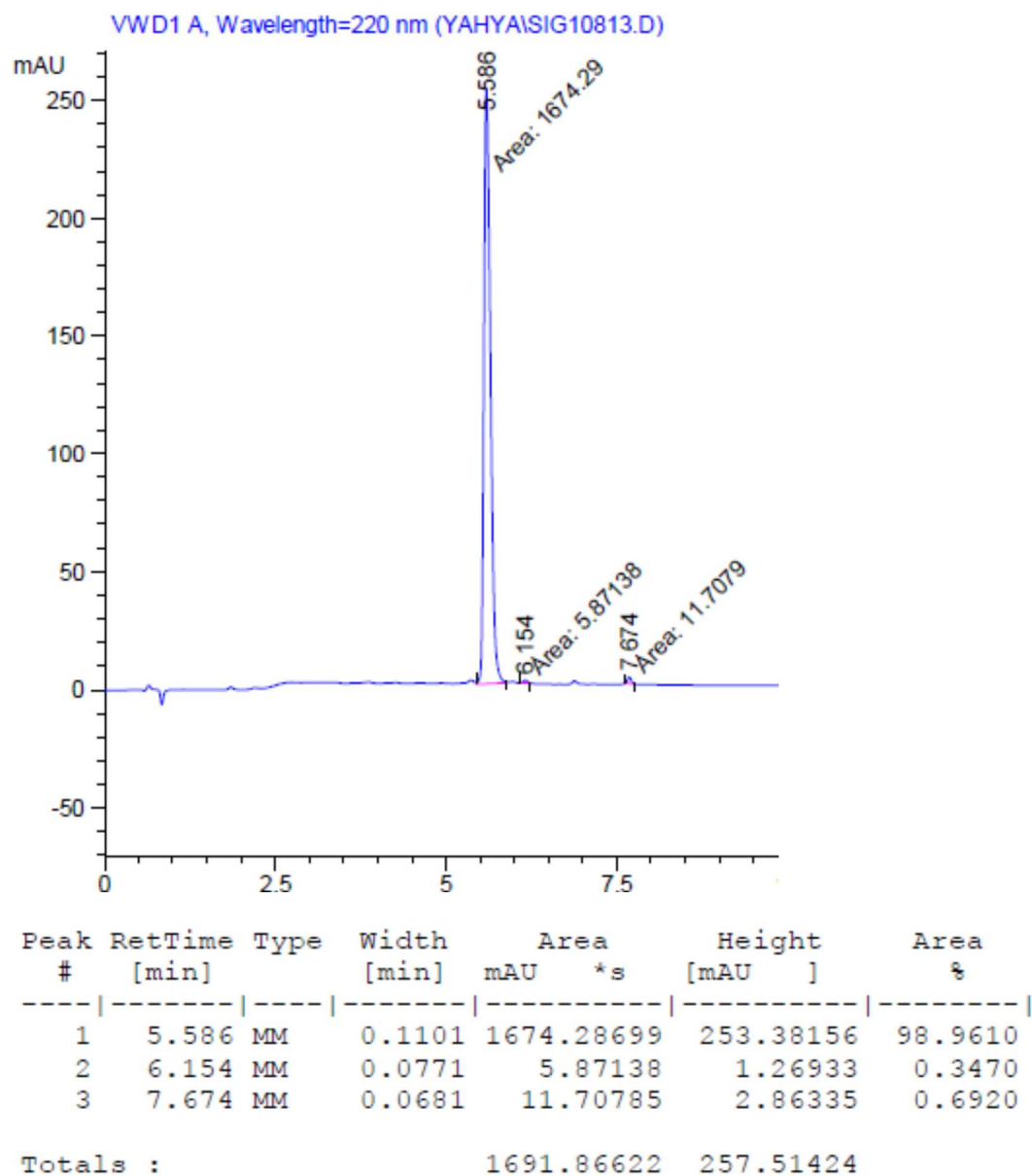
3.1-HOBt in DMF



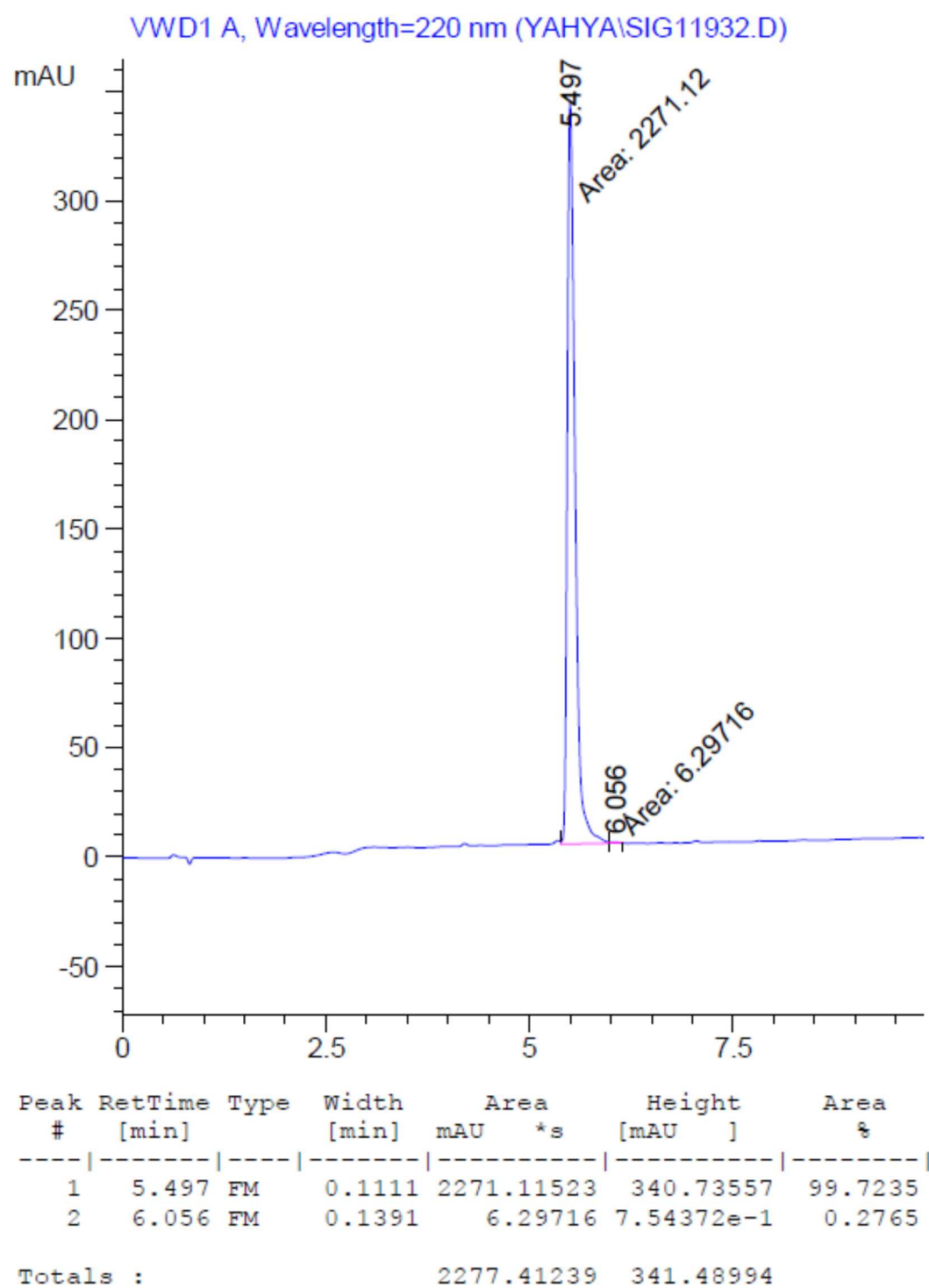
3.2-HOBt in THF



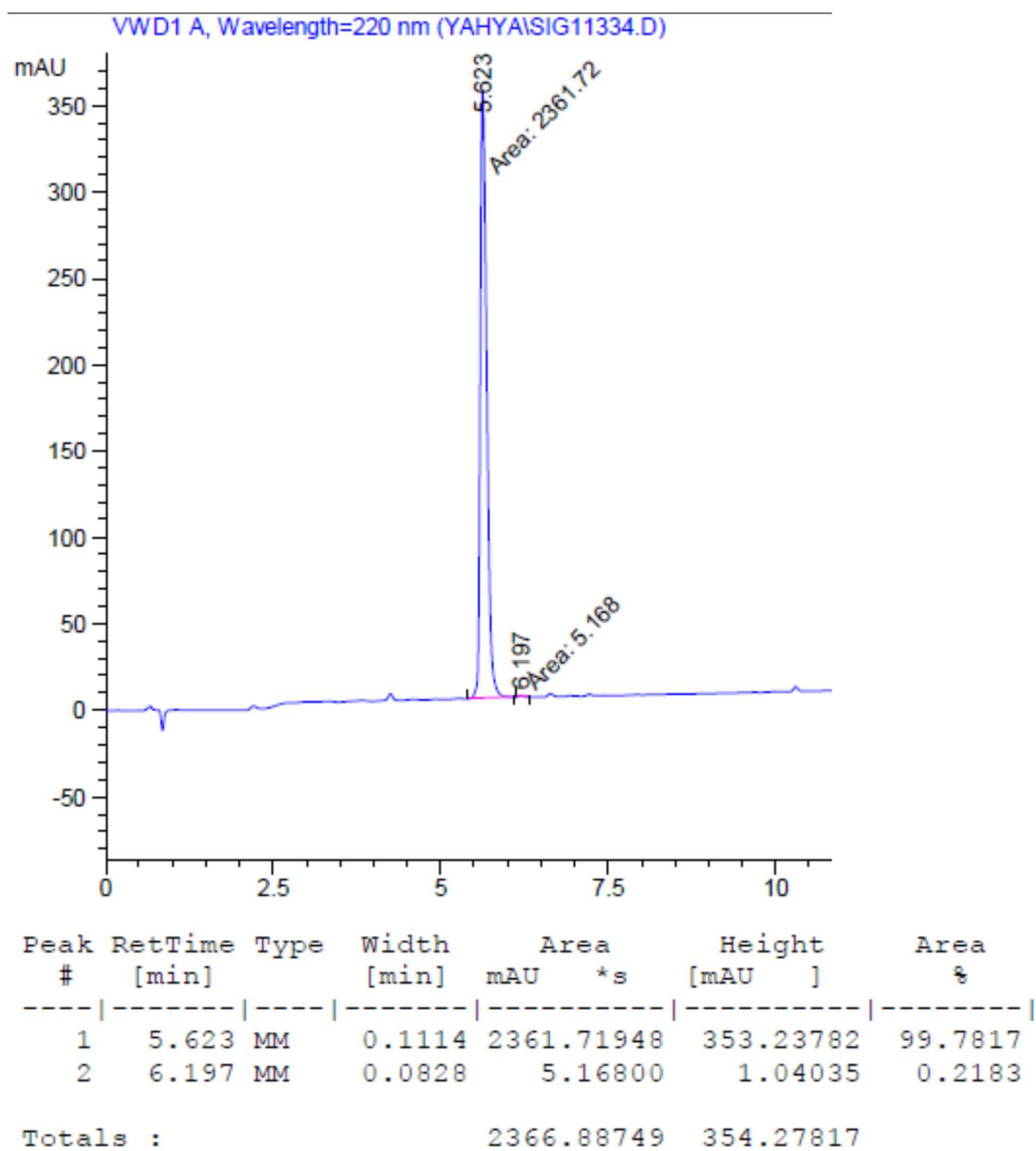
3.2-HOBt in ACN



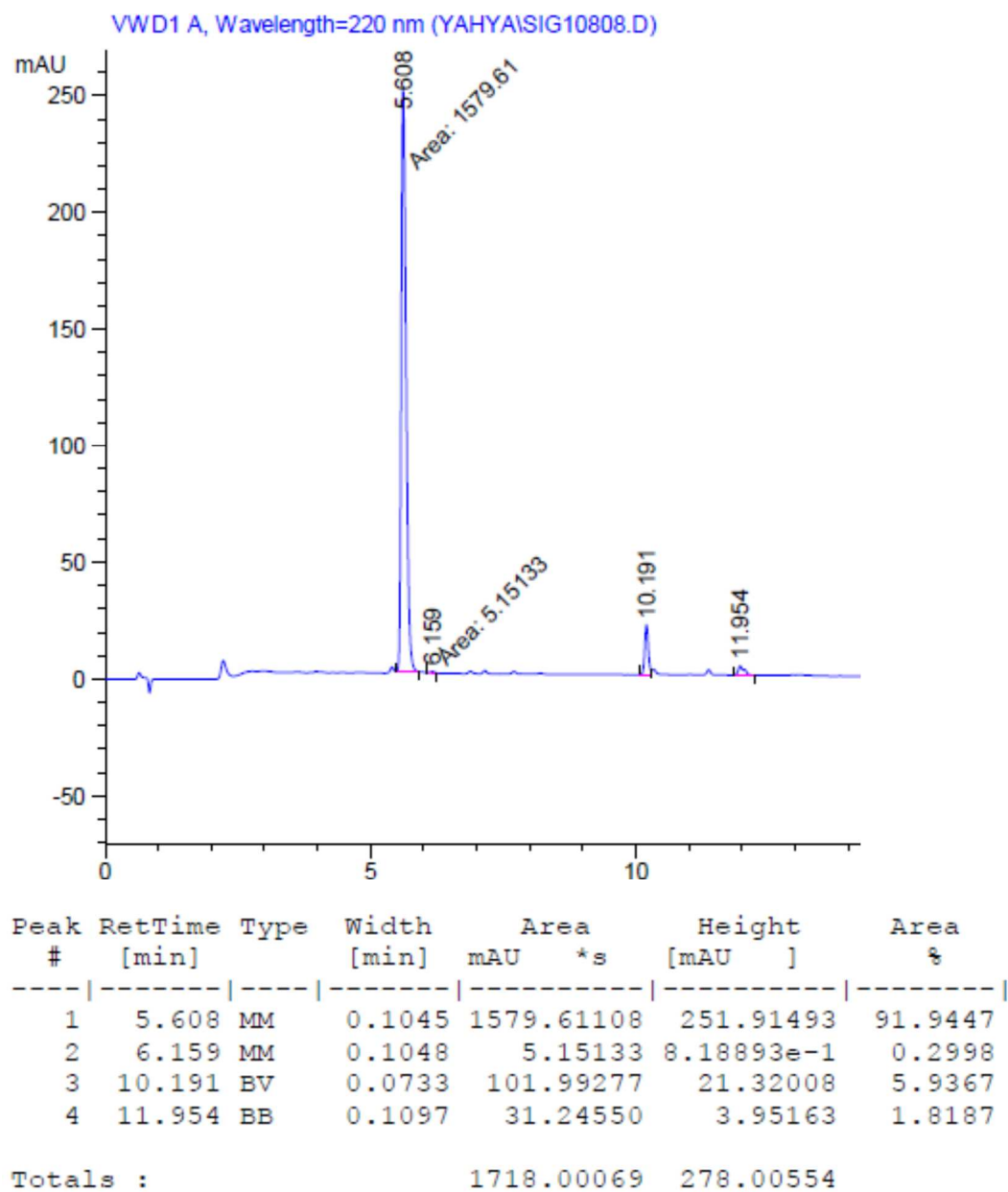
3.4-HOAt in DMF



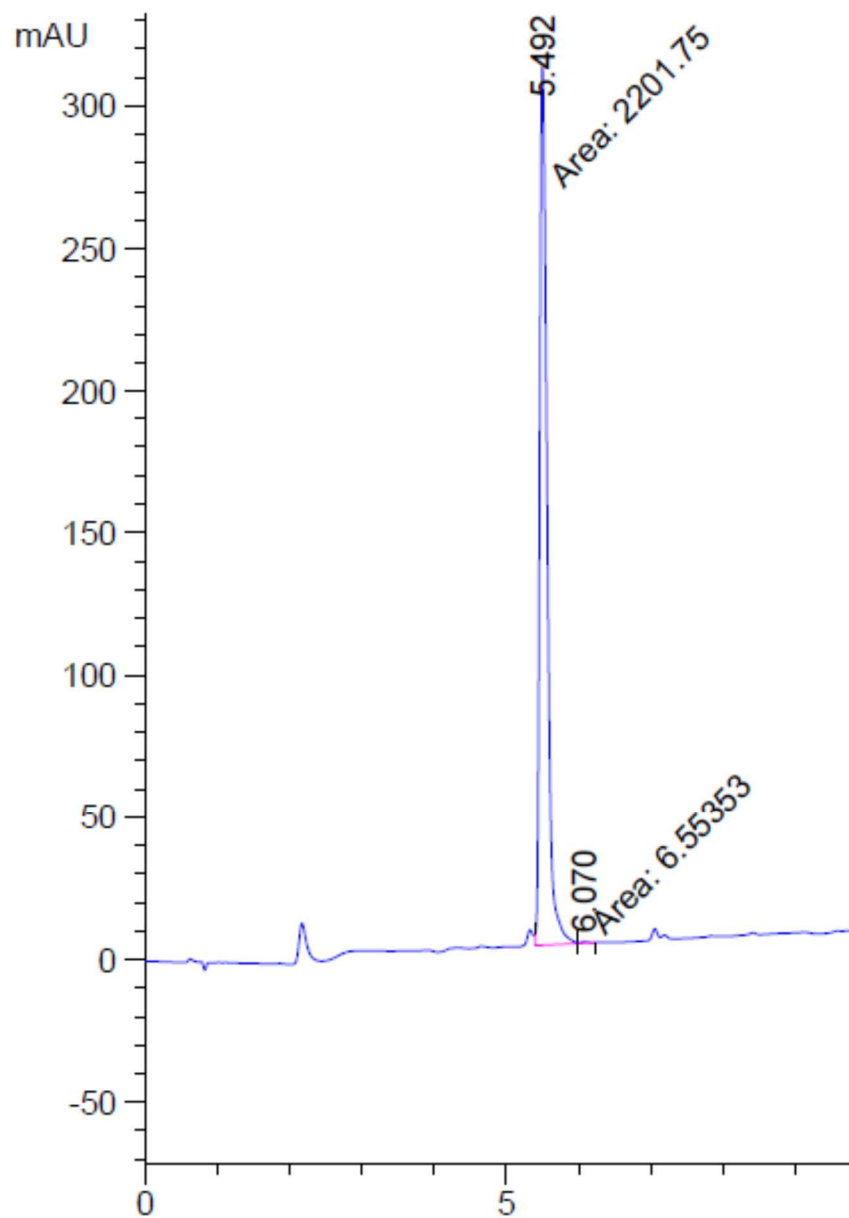
3.5-HOAt in THF



3.6-HOAt in ACN

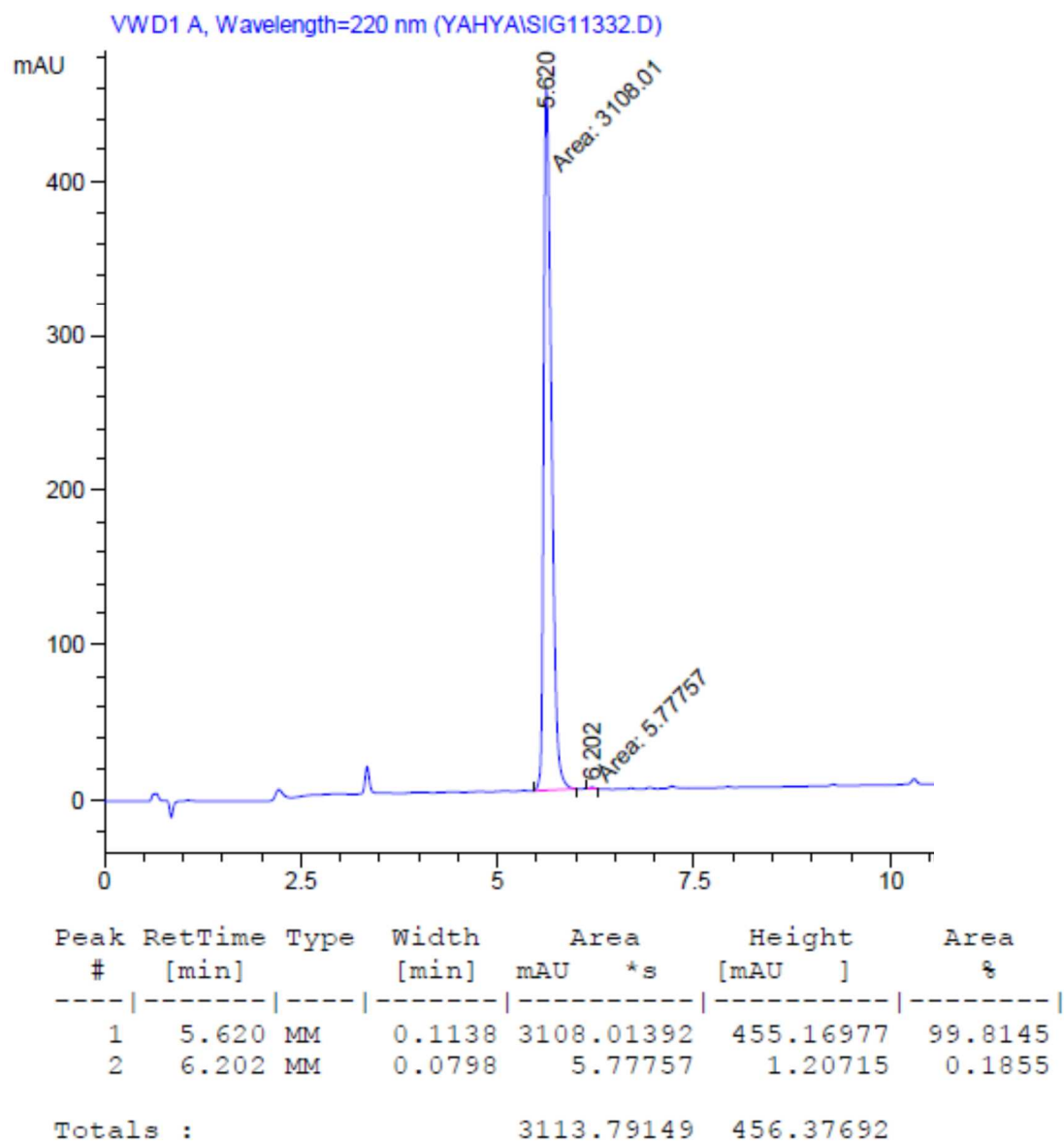


3.7-OxymaPure in DMF

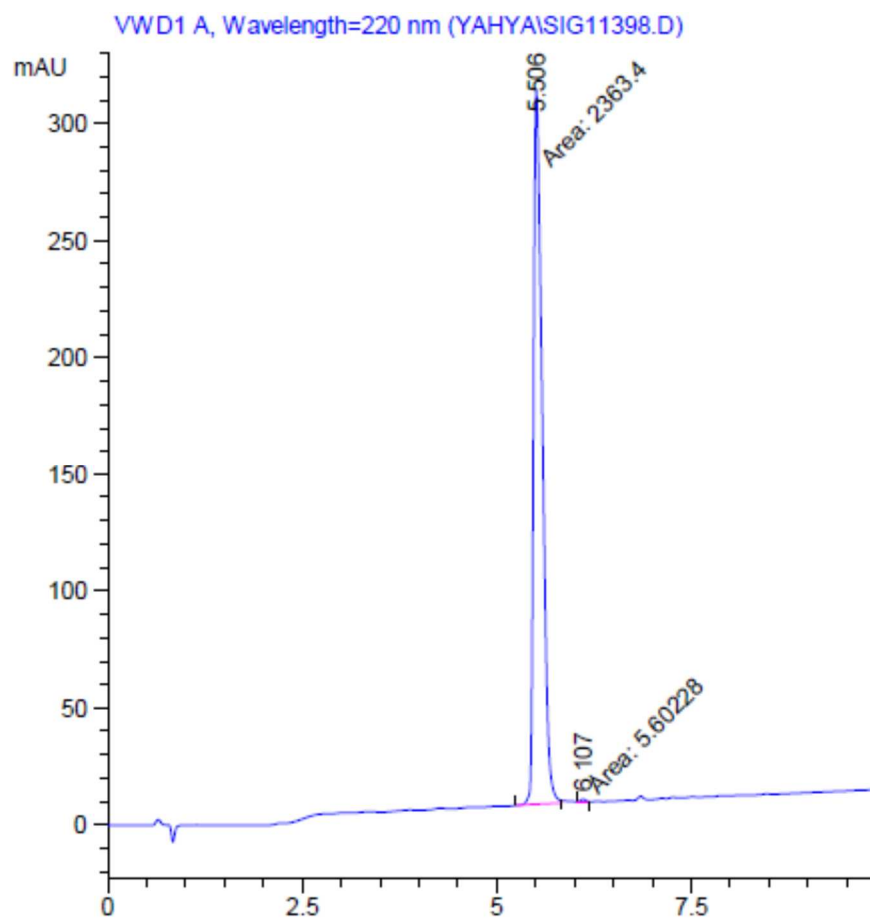


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.492	FM	0.1184	2201.74780	310.03635	99.7032
2	6.070	FM	0.1490	6.55353	7.33042e-1	0.2968
Totals :				2208.30133	310.76939	

3.8-OxymaPure in THF



3.9-OxymaPure in ACN

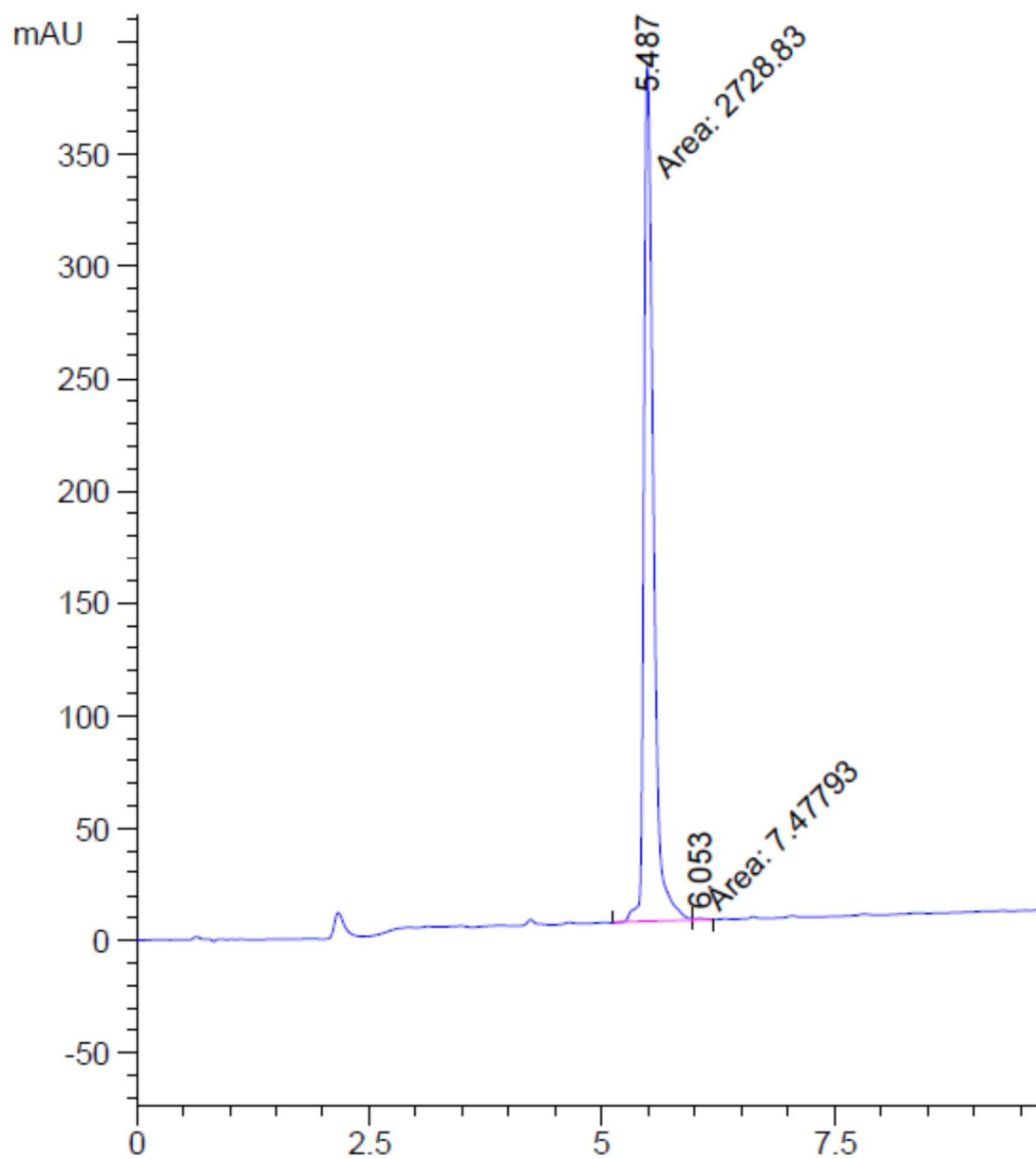


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.506	MF	0.1285	2363.39551	306.42755	99.7635
2	6.107	FM	0.0795	5.60228	1.17441	0.2365

Totals : 2368.99779 307.60196

3.10- Oxyma-B in DMF

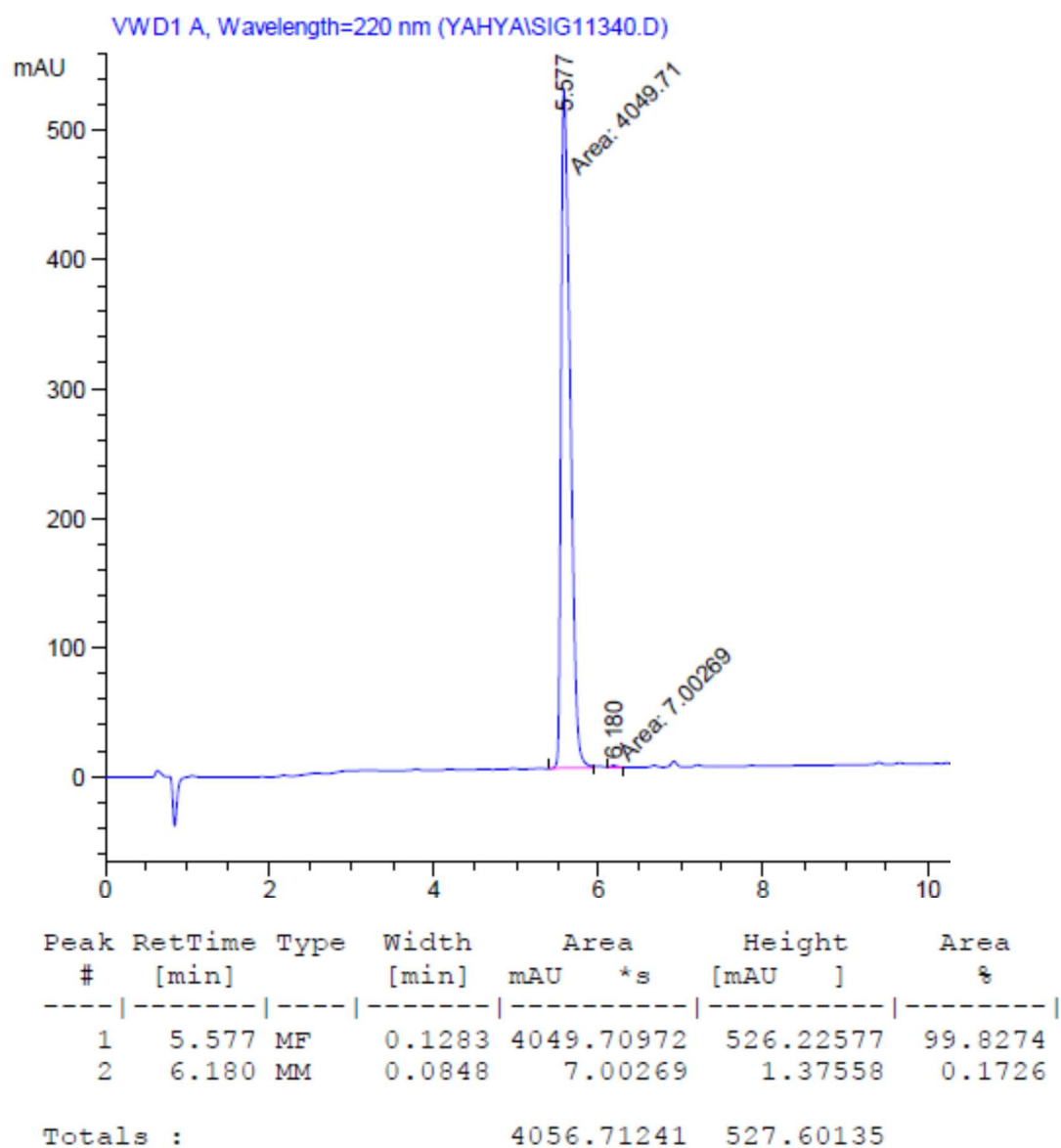
VWD1 A, Wavelength=220 nm (YAHYA\SIG11933.D)



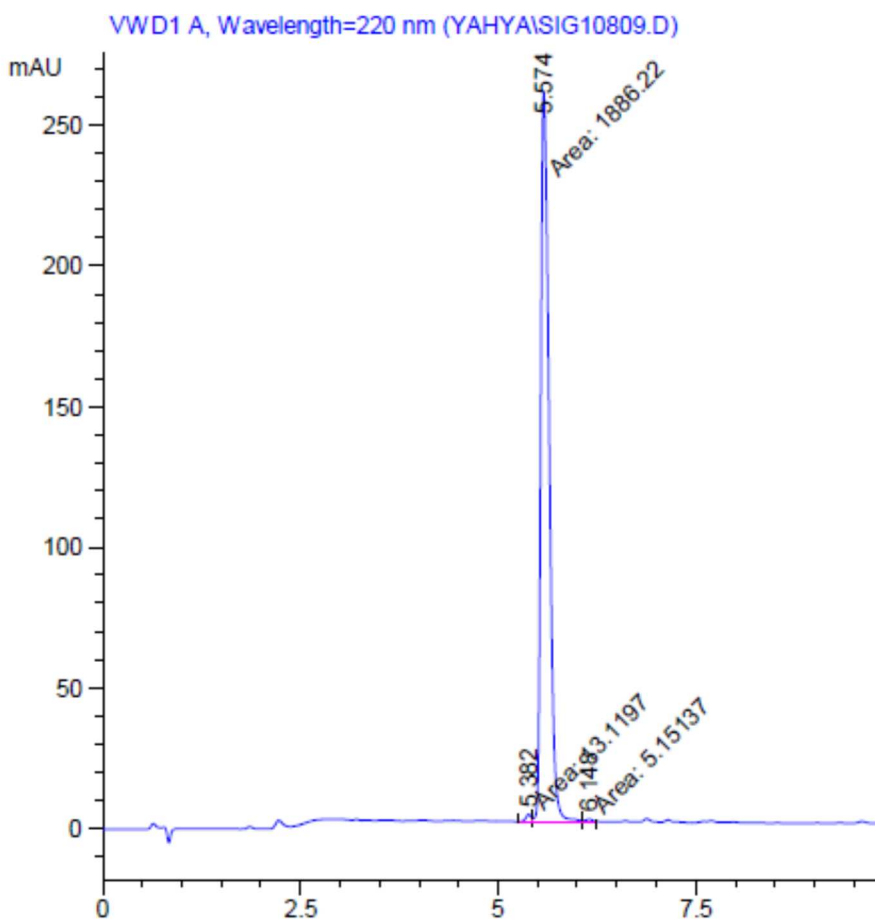
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.487	MF	0.1186	2728.83398	383.47549	99.7267
2	6.053	FM	0.1387	7.47793	8.98371e-1	0.2733

Totals : 2736.31191 384.37387

3.11- Oxyma-B in THF



3.12- Oxyma-B in ACN

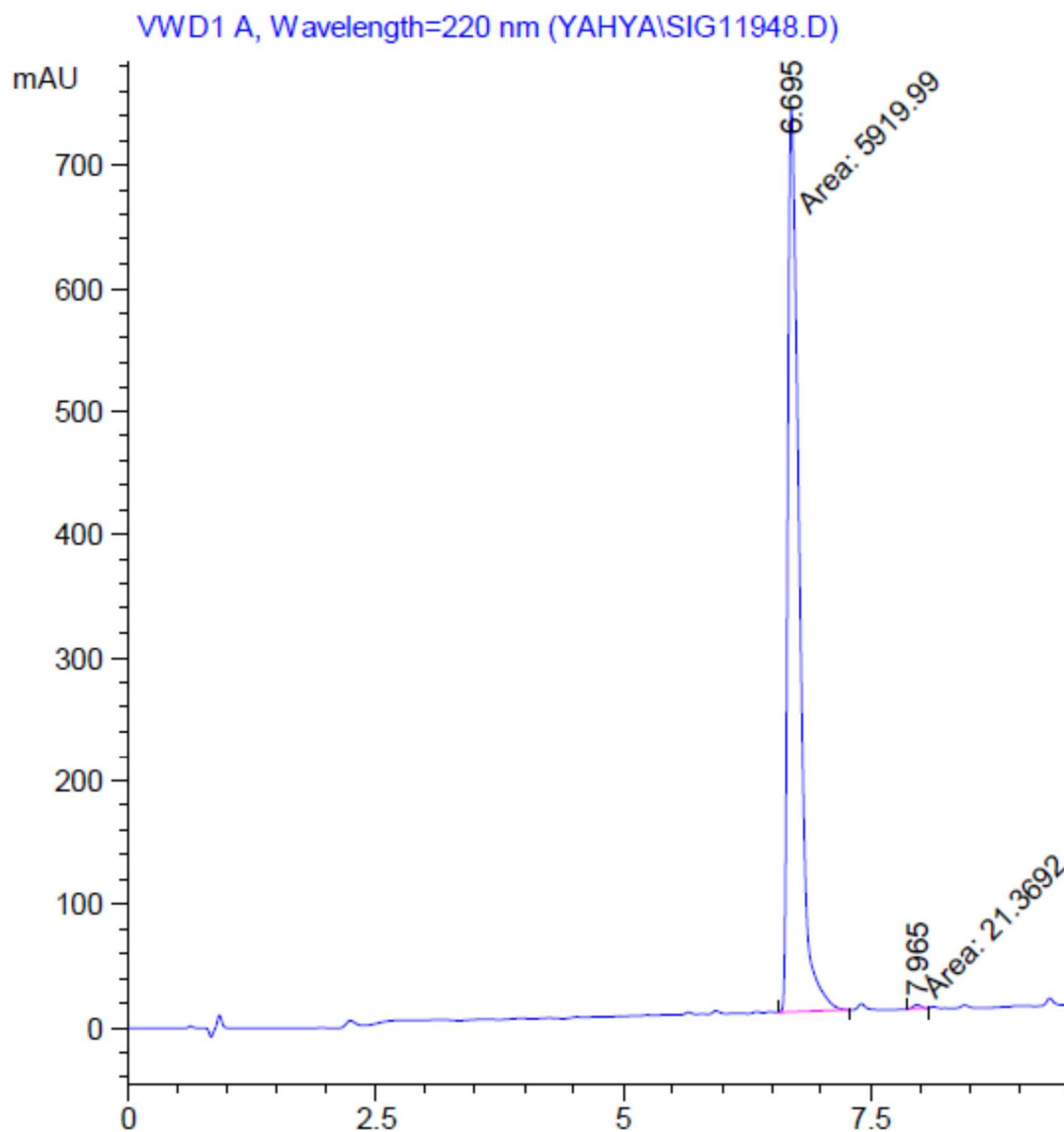


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	5.382	MF	0.0832	13.11968		2.62848	0.6889
2	5.574	FM	0.1209	1886.22241		259.94125	99.0406
3	6.148	FM	0.1006	5.15137		8.53031e-1	0.2705

Totals : 1904.49346 263.42276

4- H-Gly-Cys-Phe-NH₂ racemization experiments

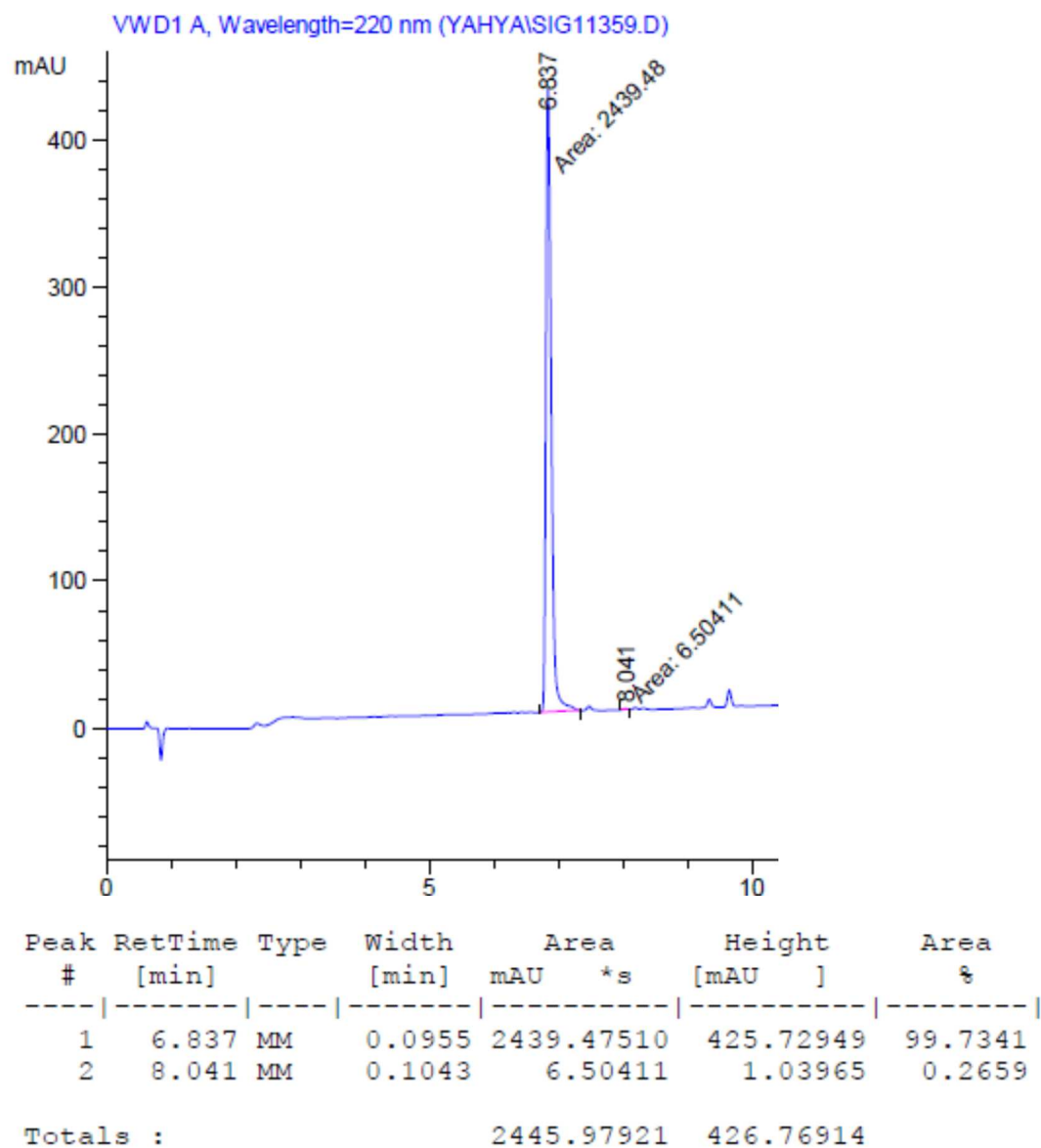
4.1-HOBt in DMF



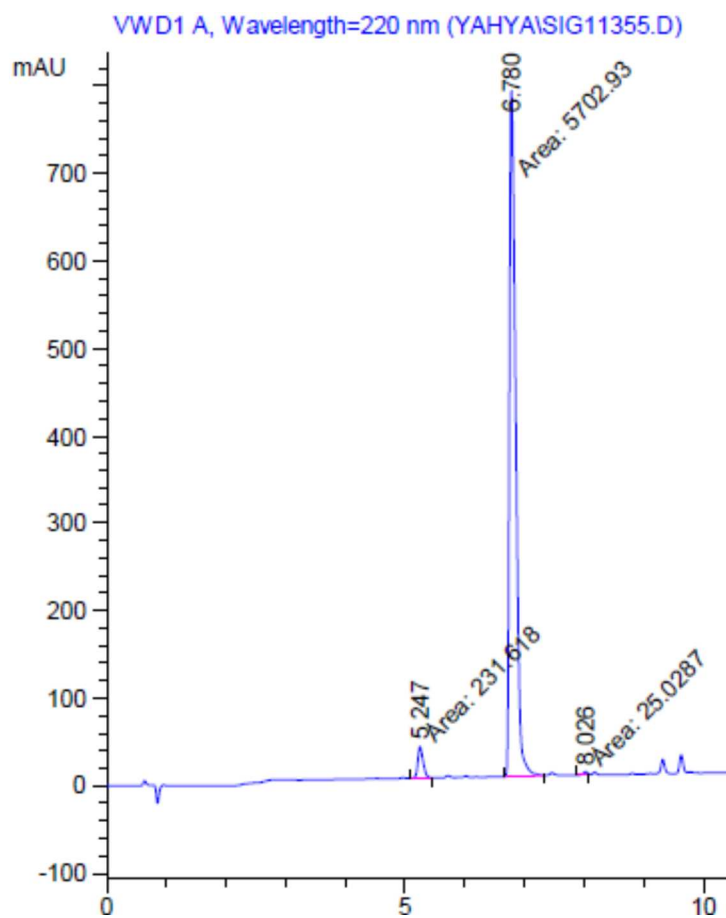
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	6.695	MM	0.1340	5919.99268	736.52924	99.6403
2	7.965	MM	0.0989	21.36915	3.60116	0.3597

Totals : 5941.36183 740.13040

4.2-HOBt in THF



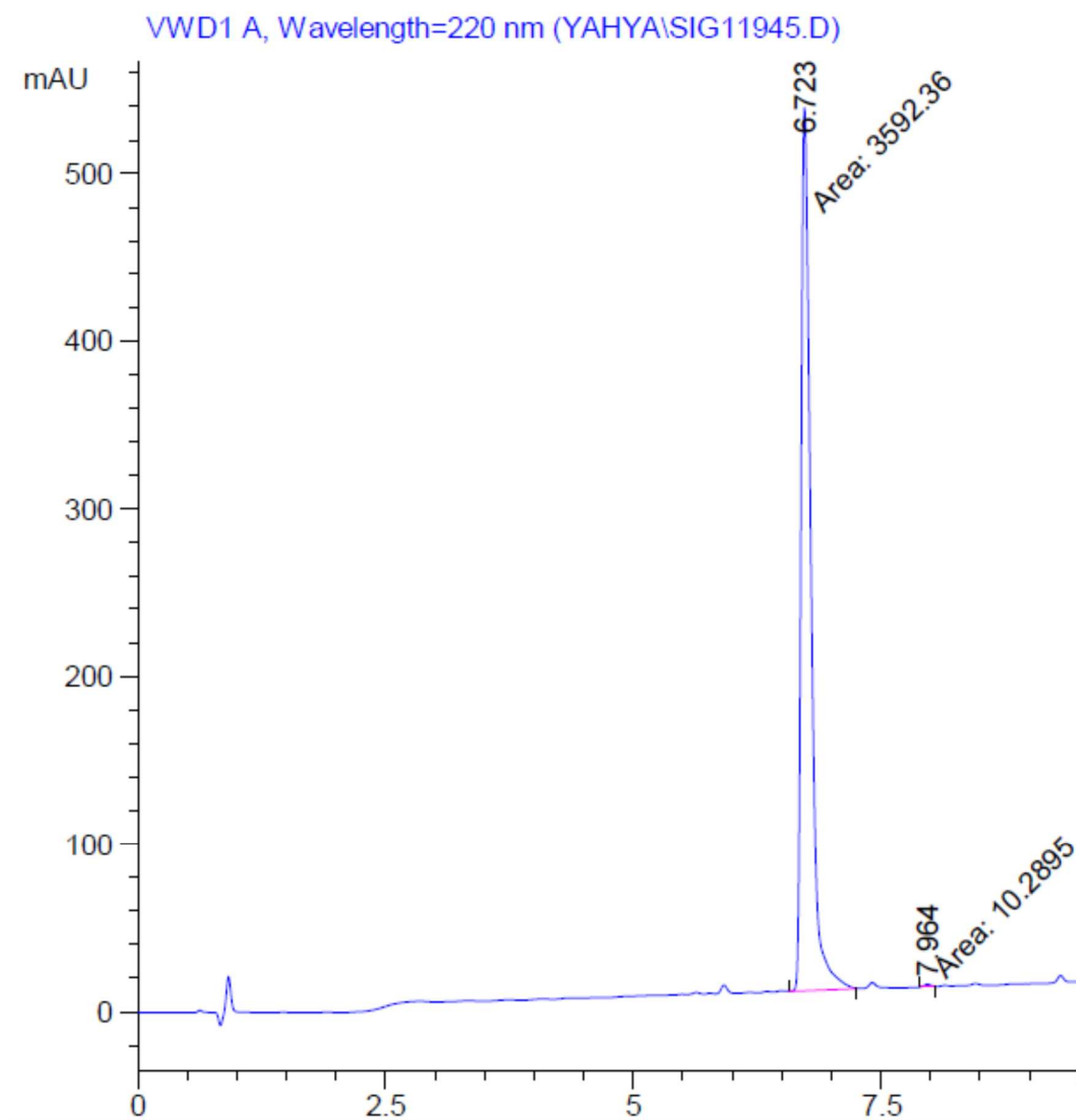
4.3-HOBt in ACN



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.247	MM	0.1060	231.61769	36.42426	3.8865
2	6.780	MM	0.1209	5702.93359	785.86230	95.6935
3	8.026	MF	0.0993	25.02871	4.20064	0.4200

Totals : 5959.58000 826.48721

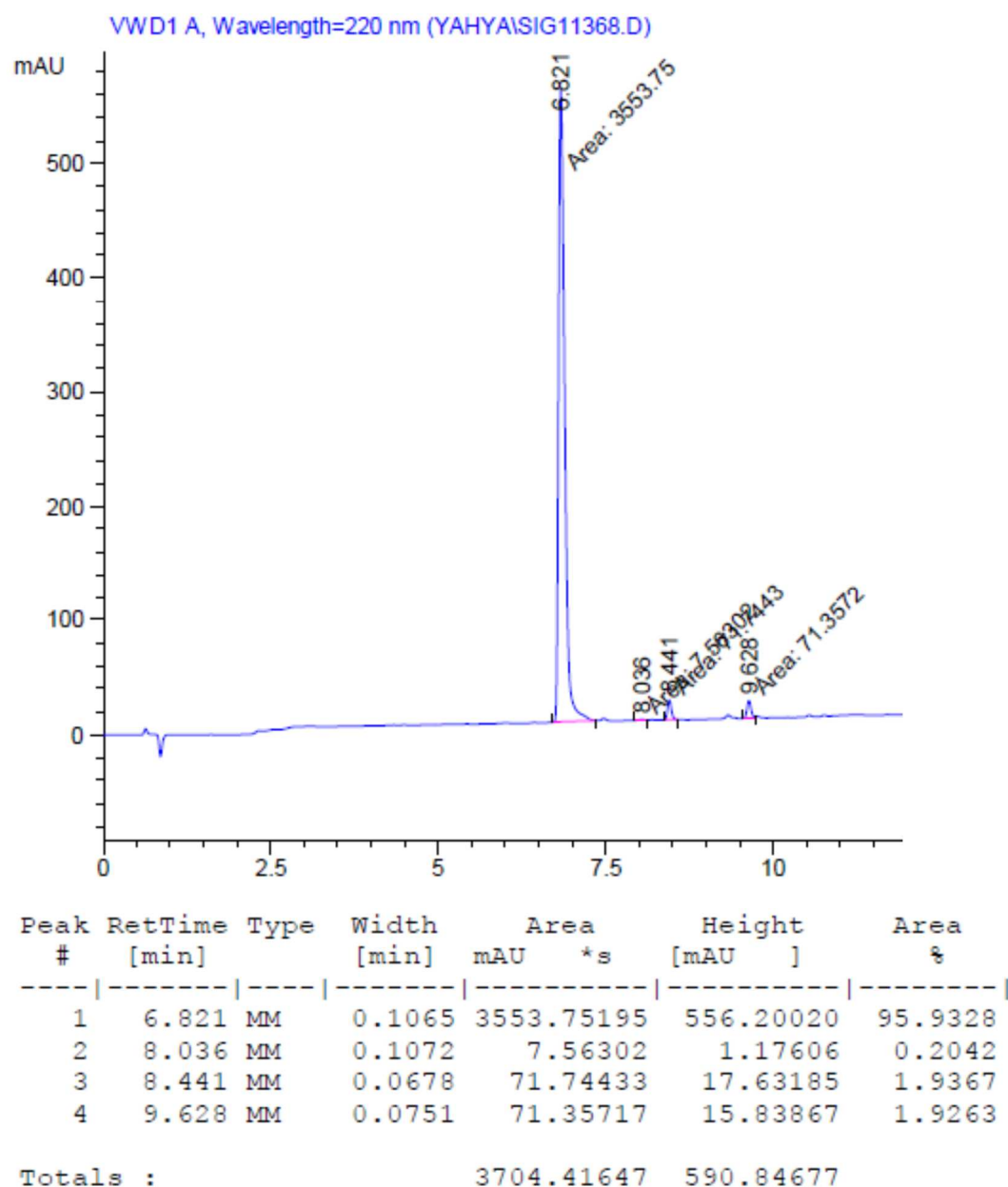
4.4-HOAt in DMF



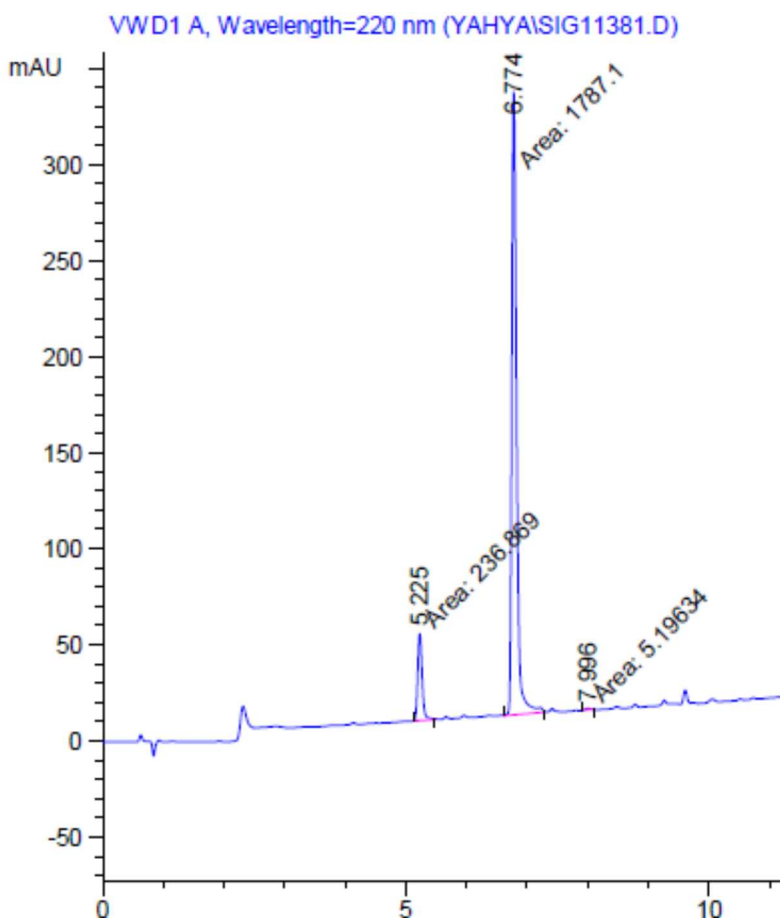
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.723	MM	0.1132	3592.36328	528.82007	99.7144
2	7.964	MM	0.0931	10.28946	1.84258	0.2856

Totals : 3602.65274 530.66265

4.5-HOAt in THF



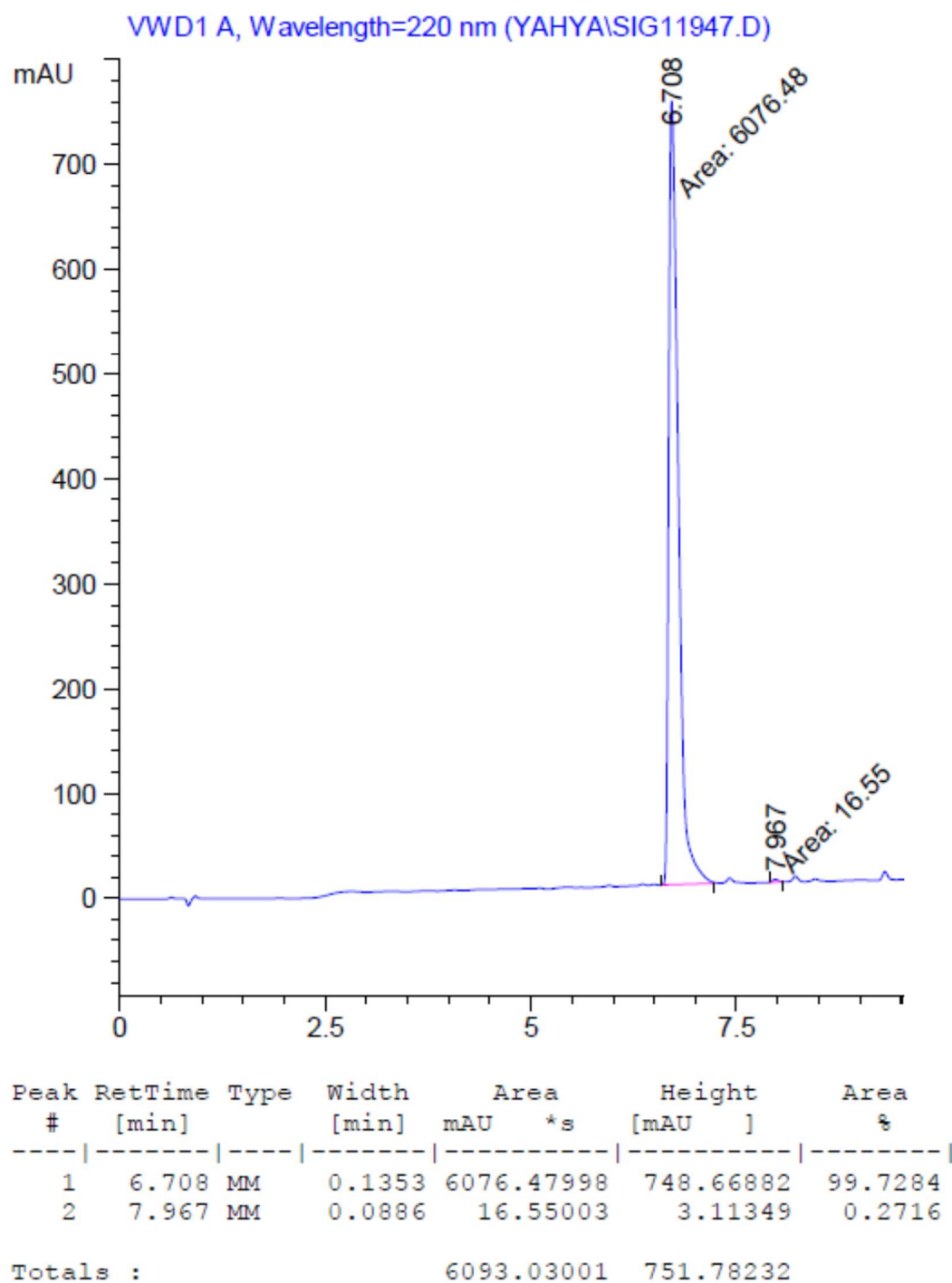
4.6-HOAt in ACN



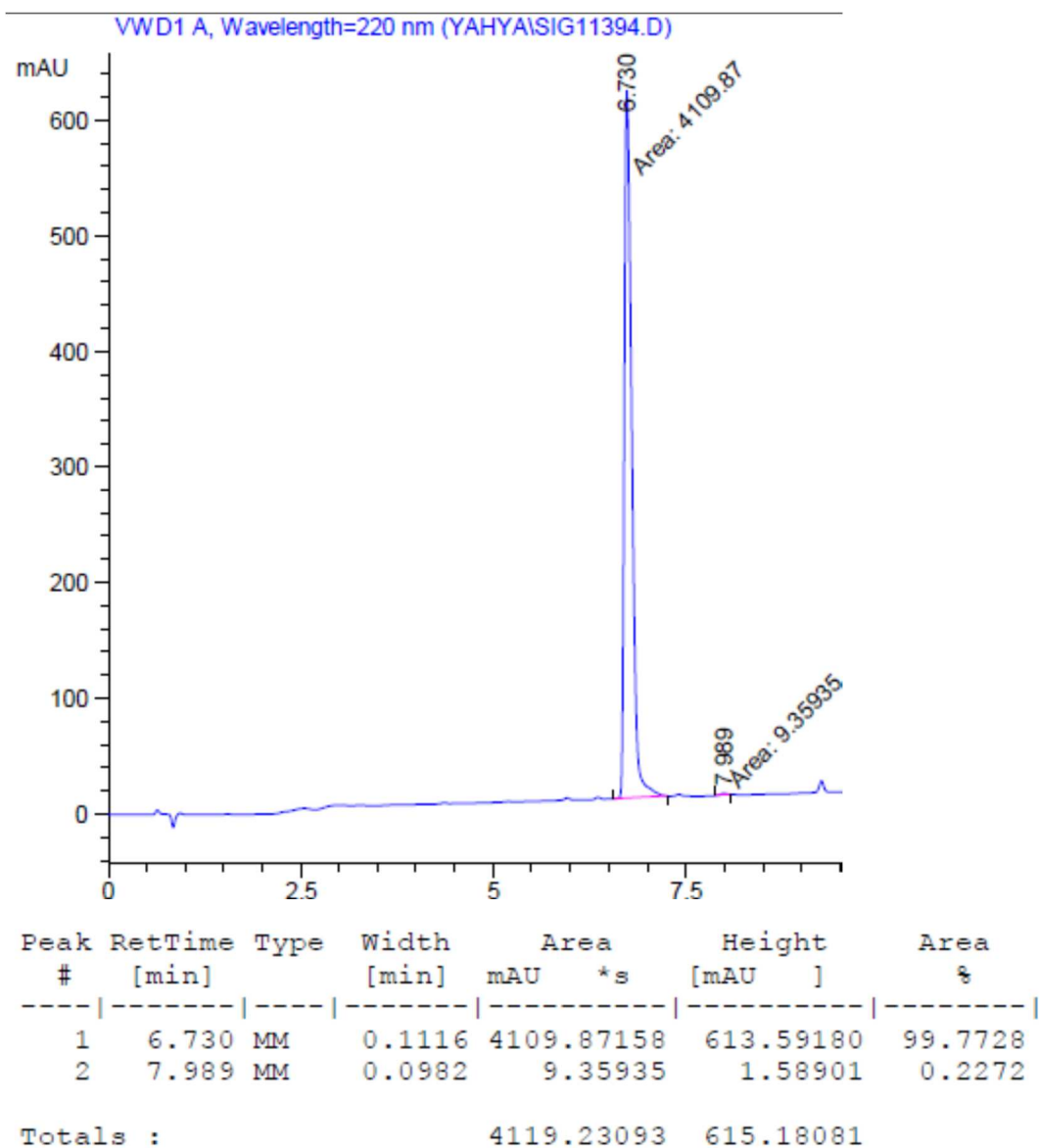
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	5.225	MM	0.0868	236.86908	45.48138	11.6732
2	6.774	MM	0.0913	1787.09766	326.34229	88.0707
3	7.996	MM	0.1049	5.19634	8.25580e-1	0.2561

Totals : 2029.16307 372.64924

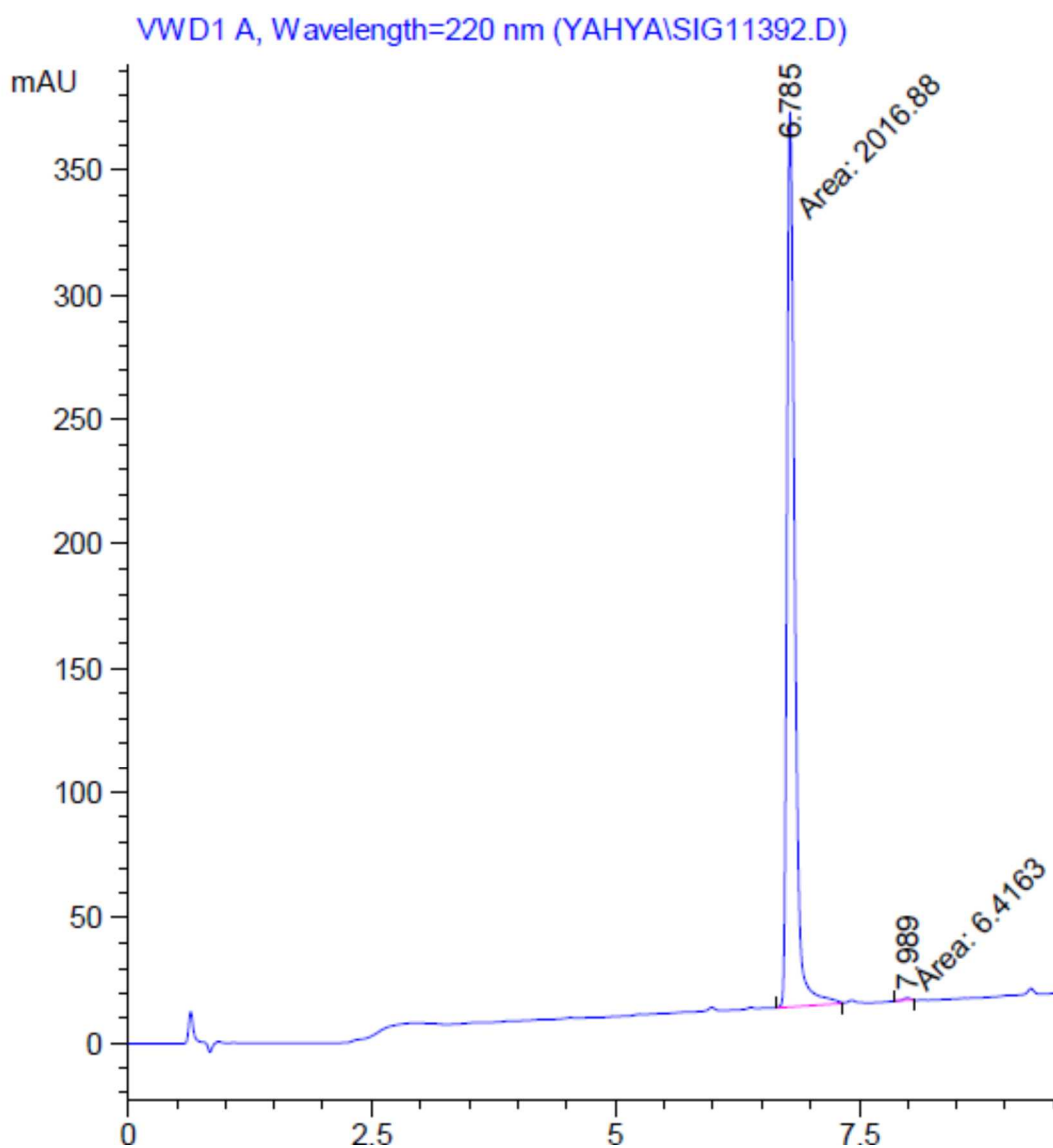
4.7-OxymaPure in DMF



4.8-OxymaPure in THF



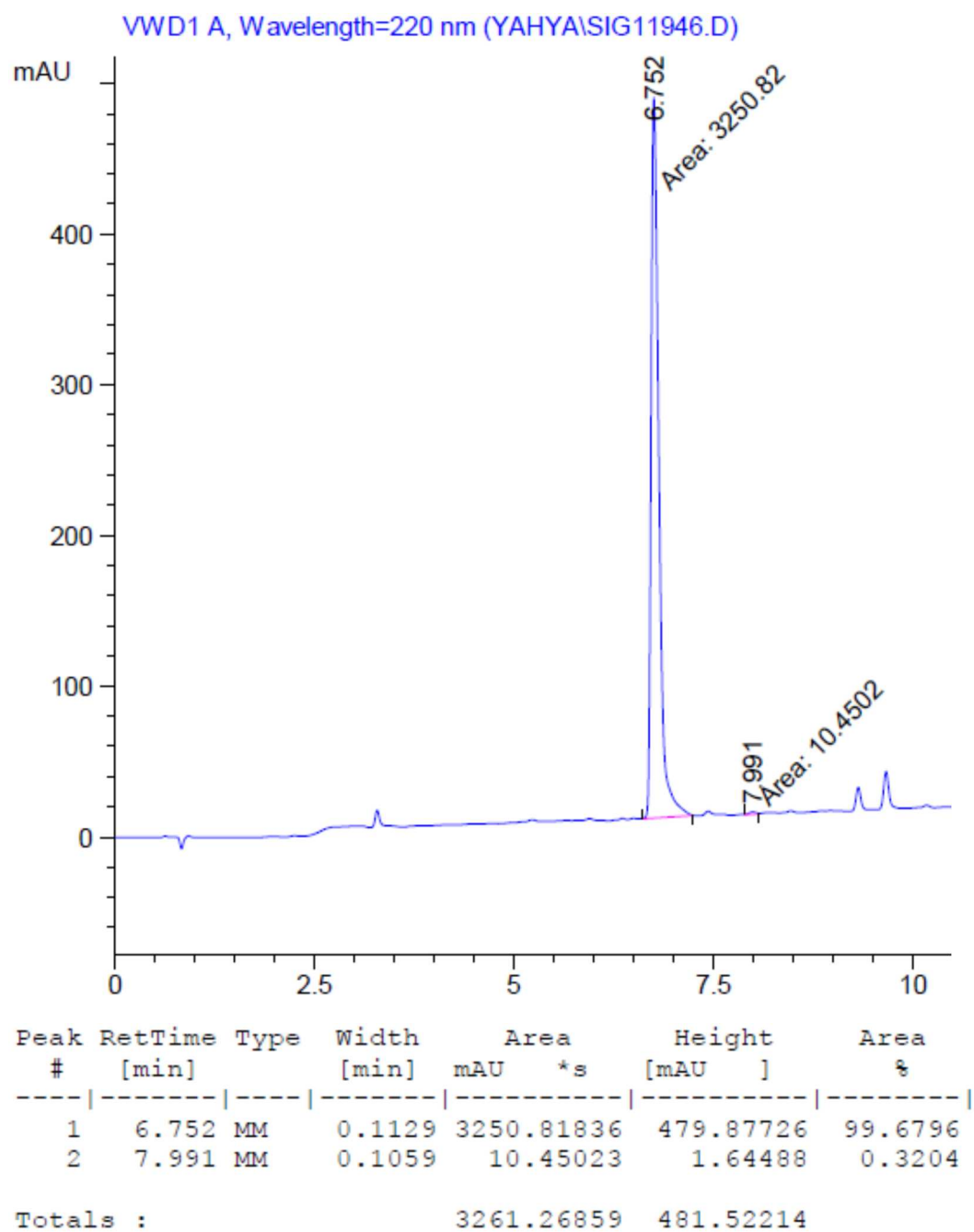
4.9-OxymaPure in ACN



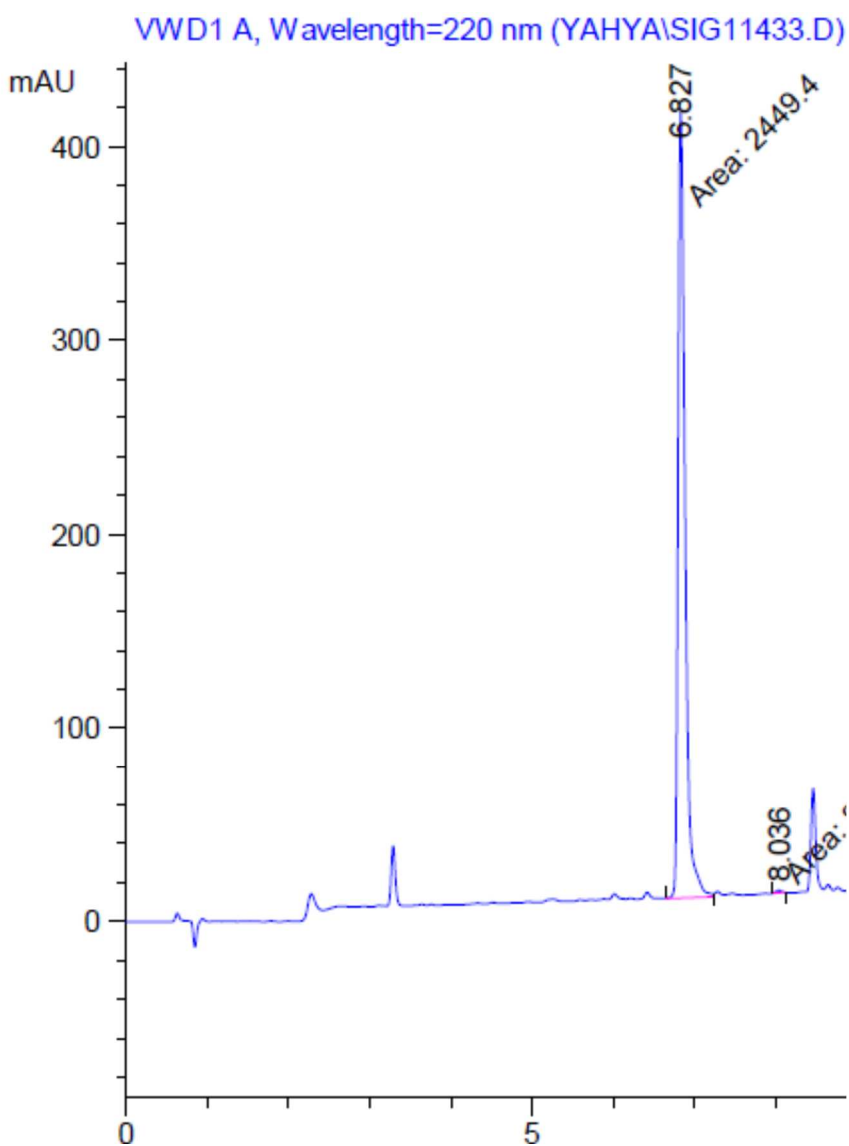
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.785	MM	0.0932	2016.87634	360.57712	99.6829
2	7.989	MM	0.0926	6.41630	1.15442	0.3171

Totals : 2023.29264 361.73154

4.10- Oxyma-B in DMF



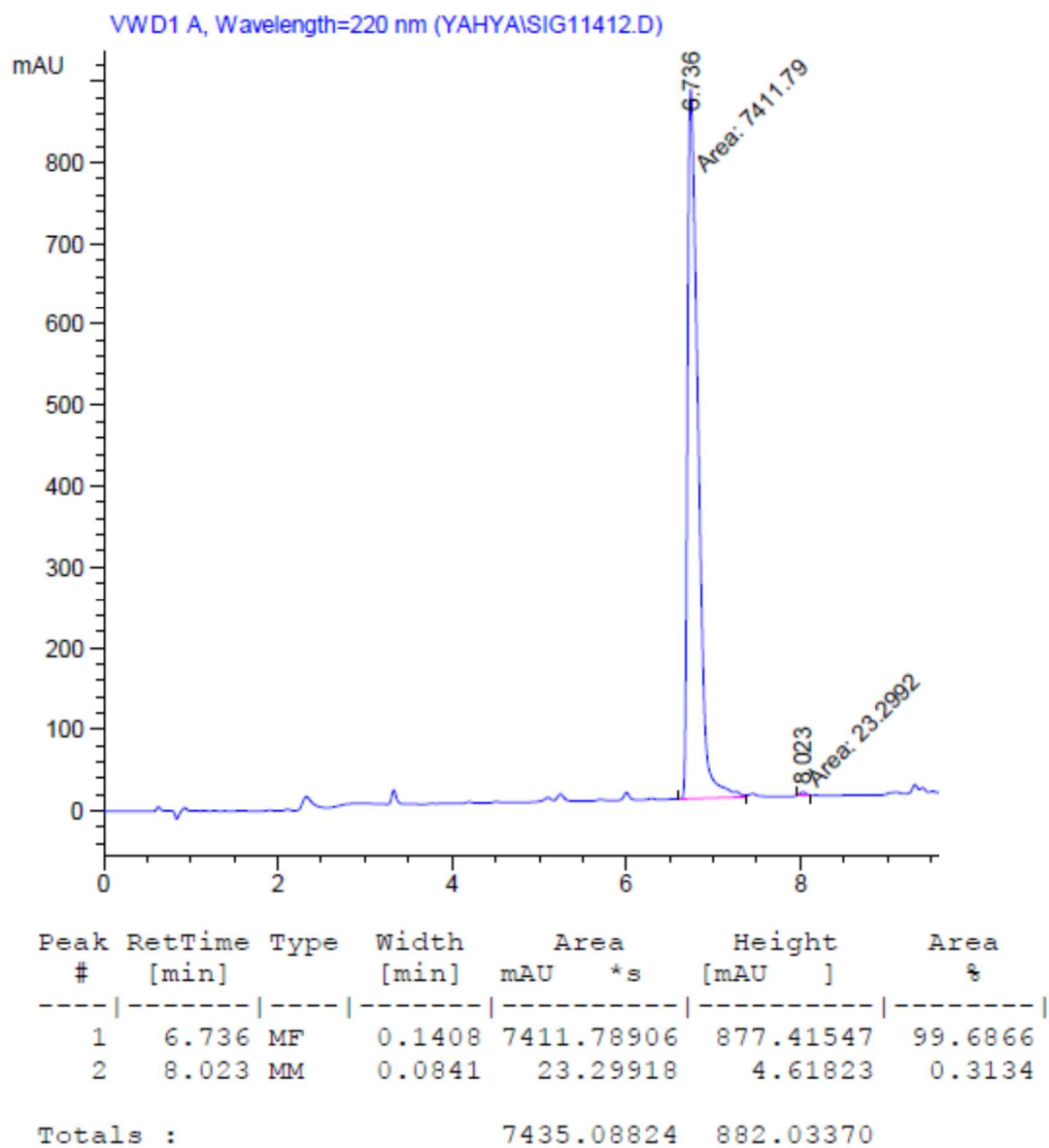
4.11- Oxyma-B in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.827	MM	0.0998	2449.40479	408.85620	99.6601
2	8.036	MM	0.0882	8.35345	1.57886	0.3399

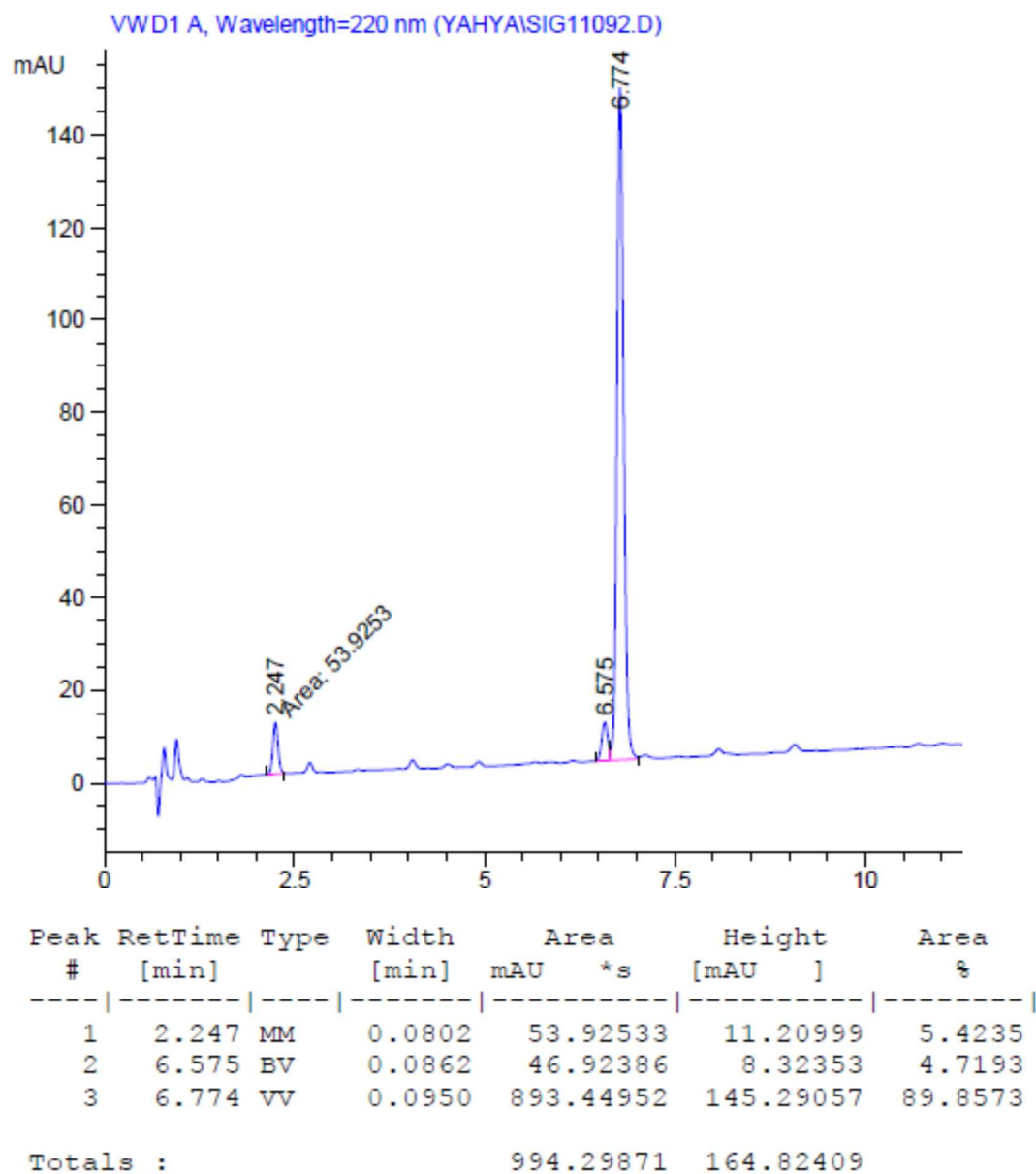
Totals : 2457.75824 410.43507

4.12- Oxyma-B in ACN

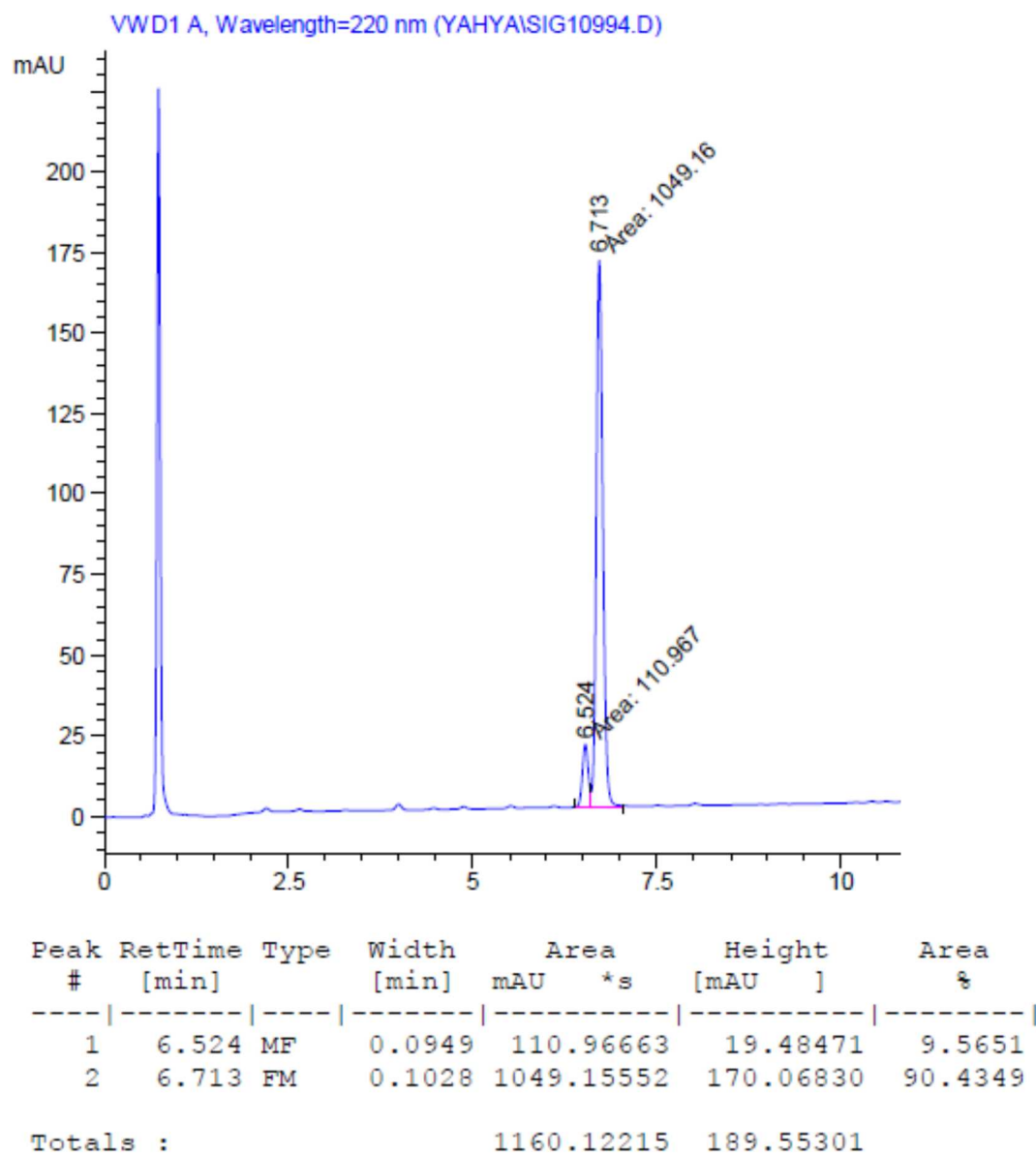


5- Peptide synthesis experiments (Synthesis of H-Tyr-Aib-Aib-Phe-Leu-NH₂)

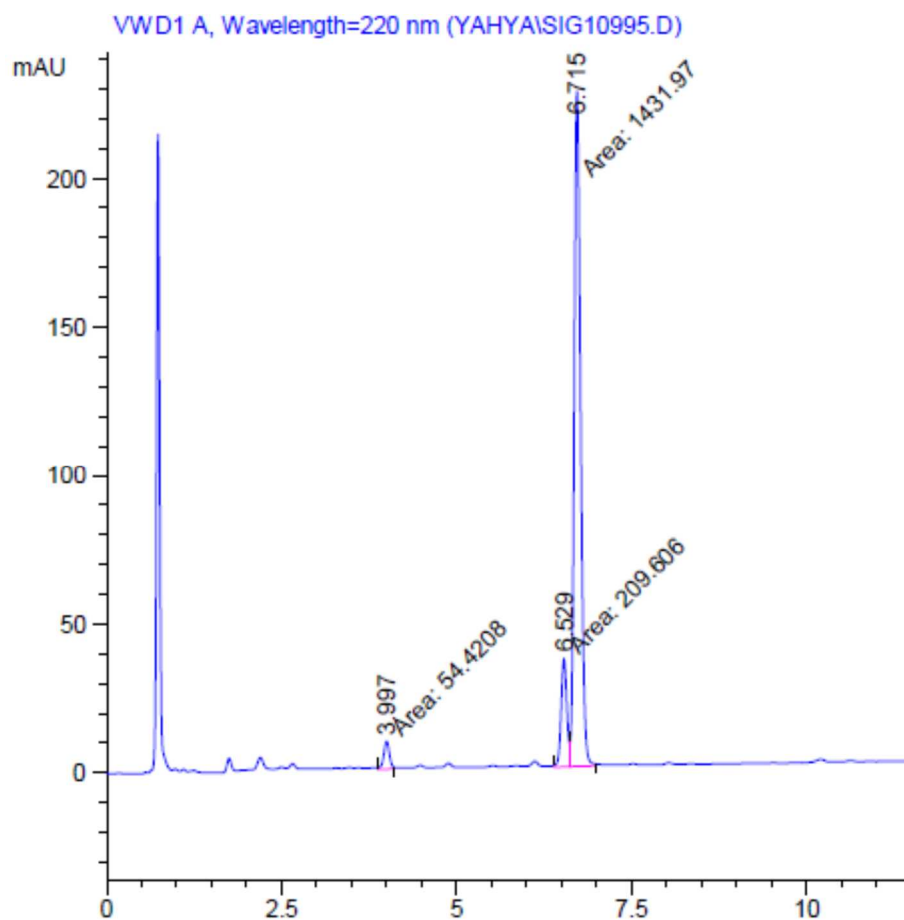
5.1- HOBt in DMF



5.2- HOBt in THF



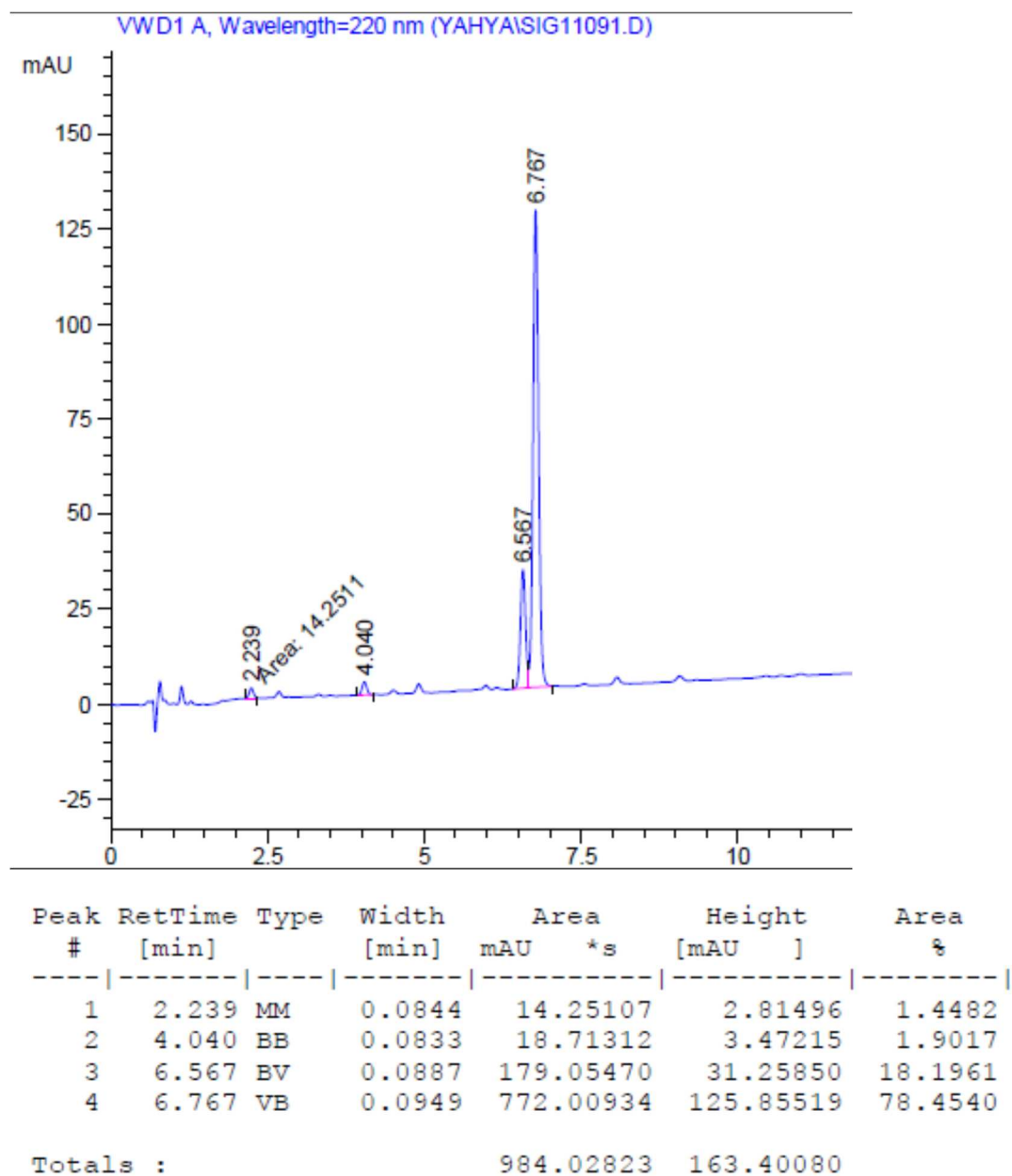
5.3- HOBt in ACN



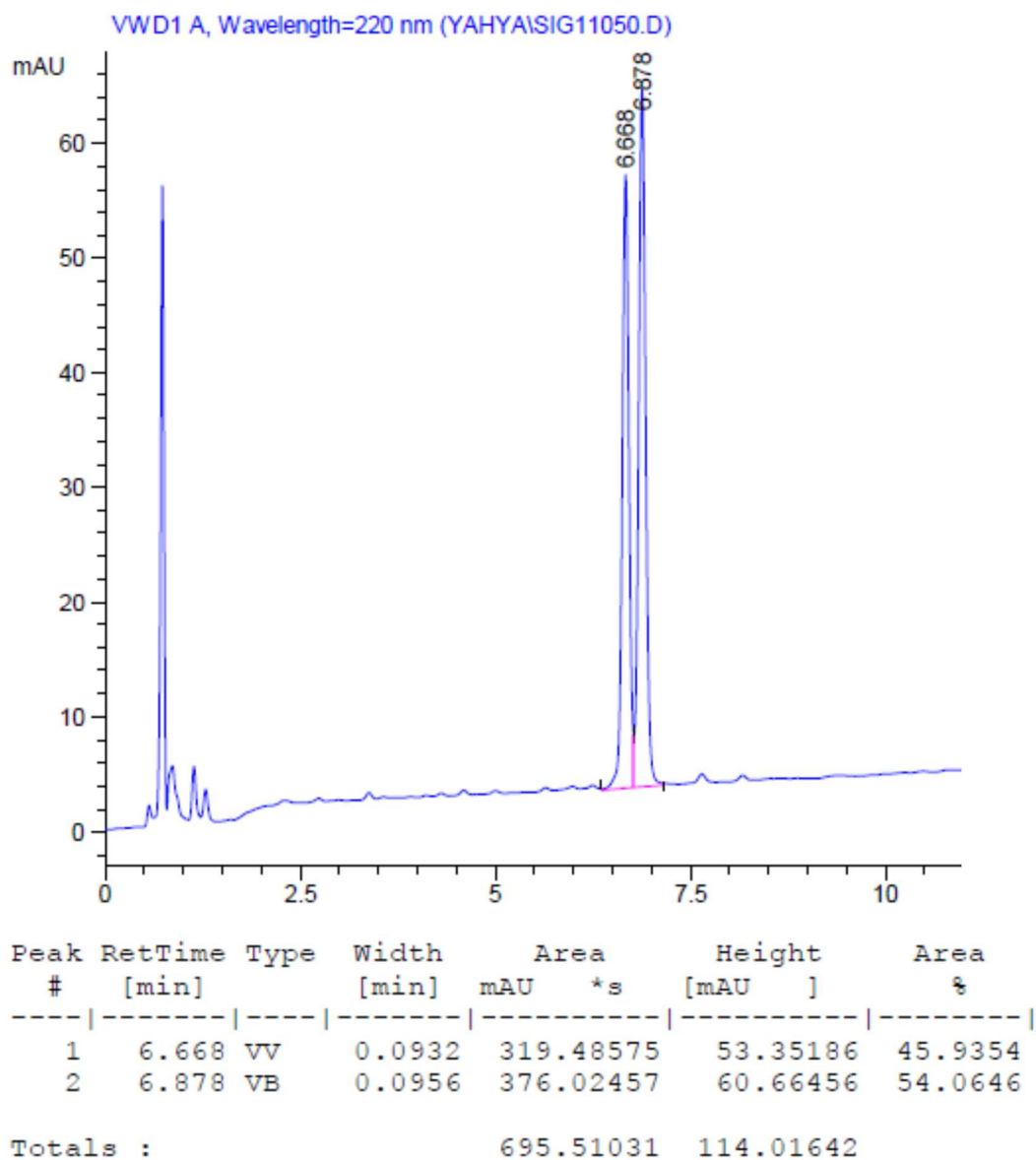
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	3.997	MM	0.0959	54.42081	9.46010	3.2088
2	6.529	MF	0.0959	209.60553	36.42484	12.3588
3	6.715	FM	0.1048	1431.97473	227.80069	84.4324

Totals : 1696.00107 273.68564

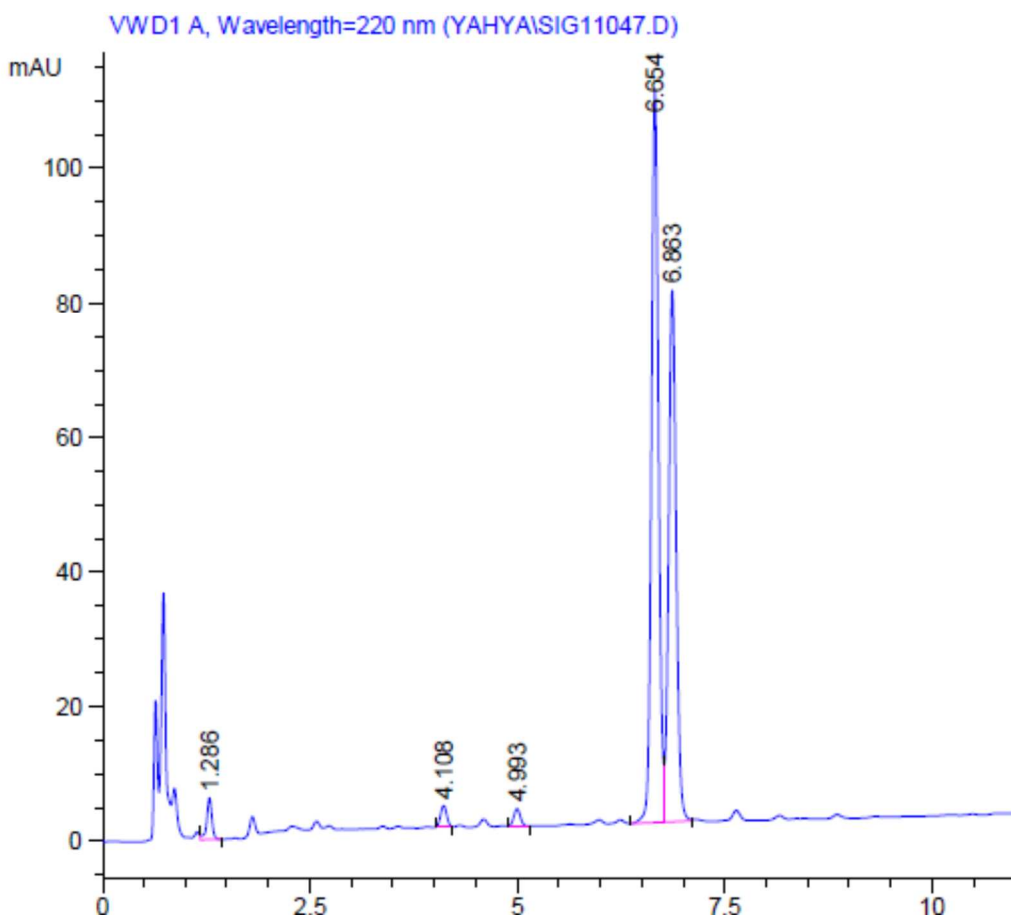
5.4- HOAt in DMF



5.5- HOAt in THF



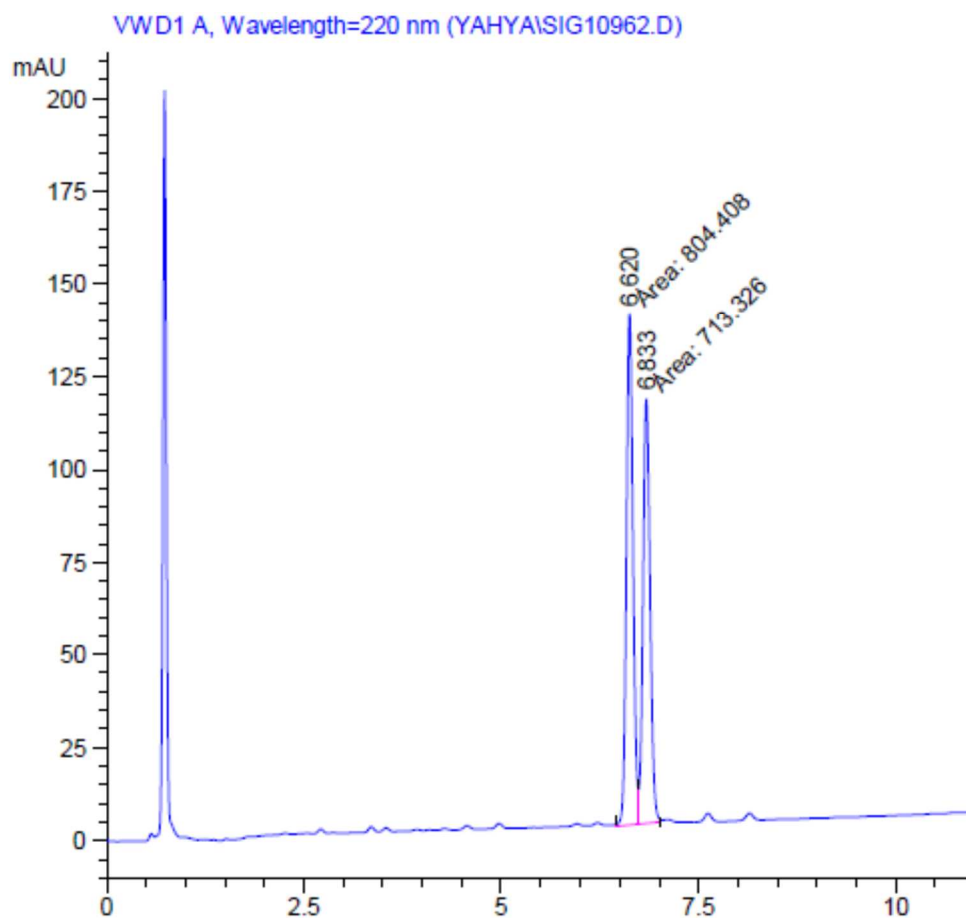
5.6- HOAt in ACN



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	1.286	VP	0.0664	26.90536	6.22871	2.2345
2	4.108	BV	0.0827	17.32223	3.24201	1.4386
3	4.993	BP	0.0861	14.46956	2.62754	1.2017
4	6.654	VV	0.0911	645.20673	108.71227	53.5851
5	6.863	VB	0.0970	500.17480	79.16366	41.5400

Totals : 1204.07869 199.97419

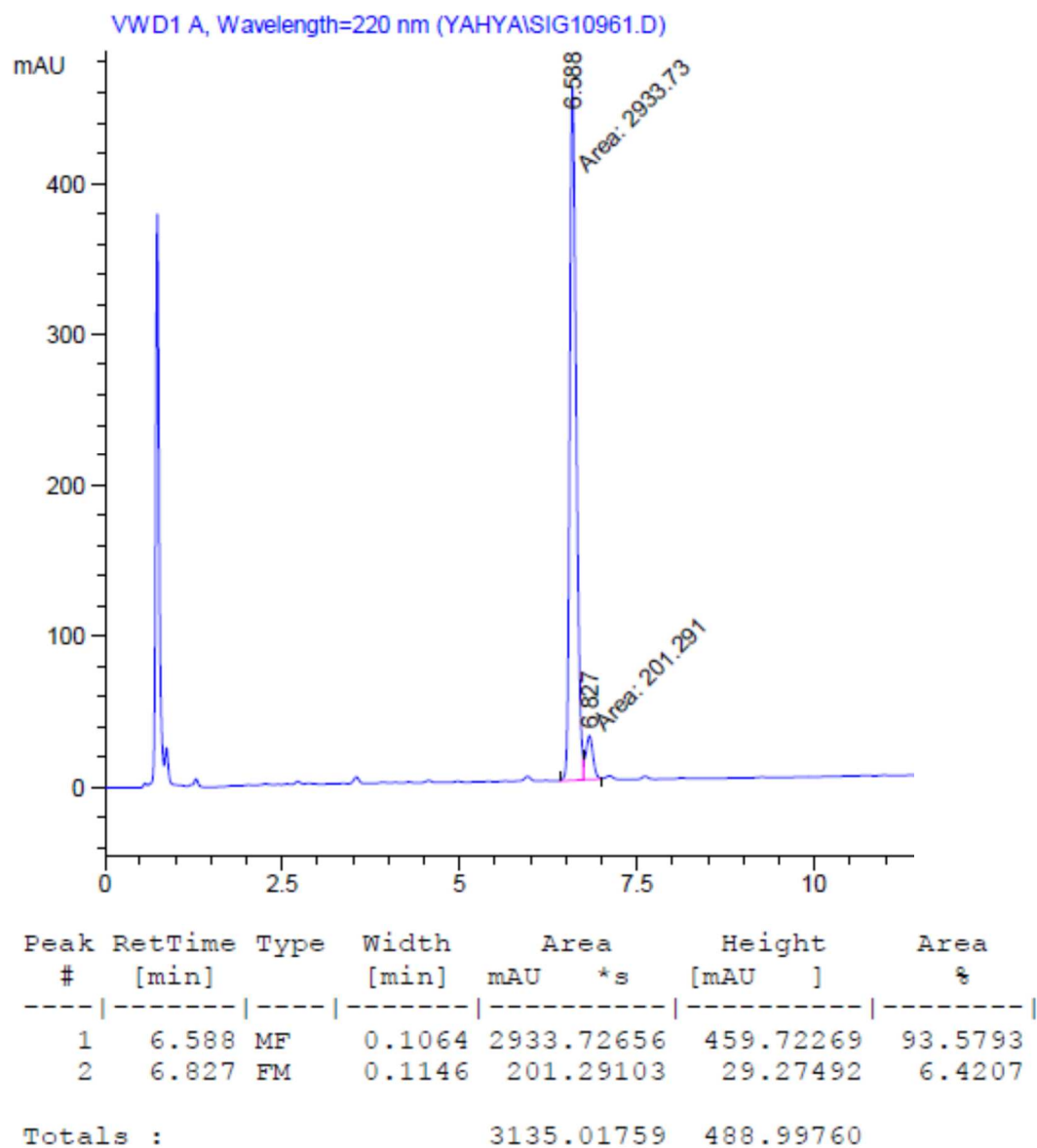
5.7- OxymaPure in DMF



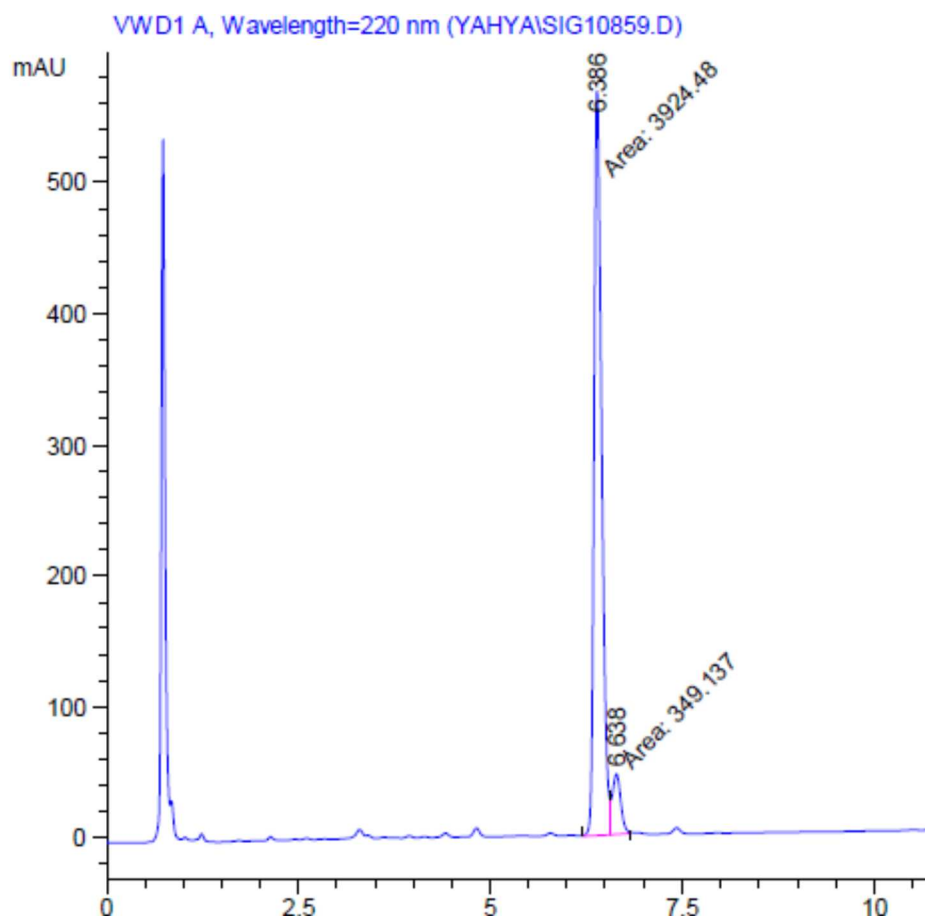
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	6.620	MF	0.0969	804.40753		138.30249	53.0006
2	6.833	FM	0.1036	713.32593		114.76675	46.9994

Totals : 1517.73346 253.06924

5.8- OxymaPure in THF

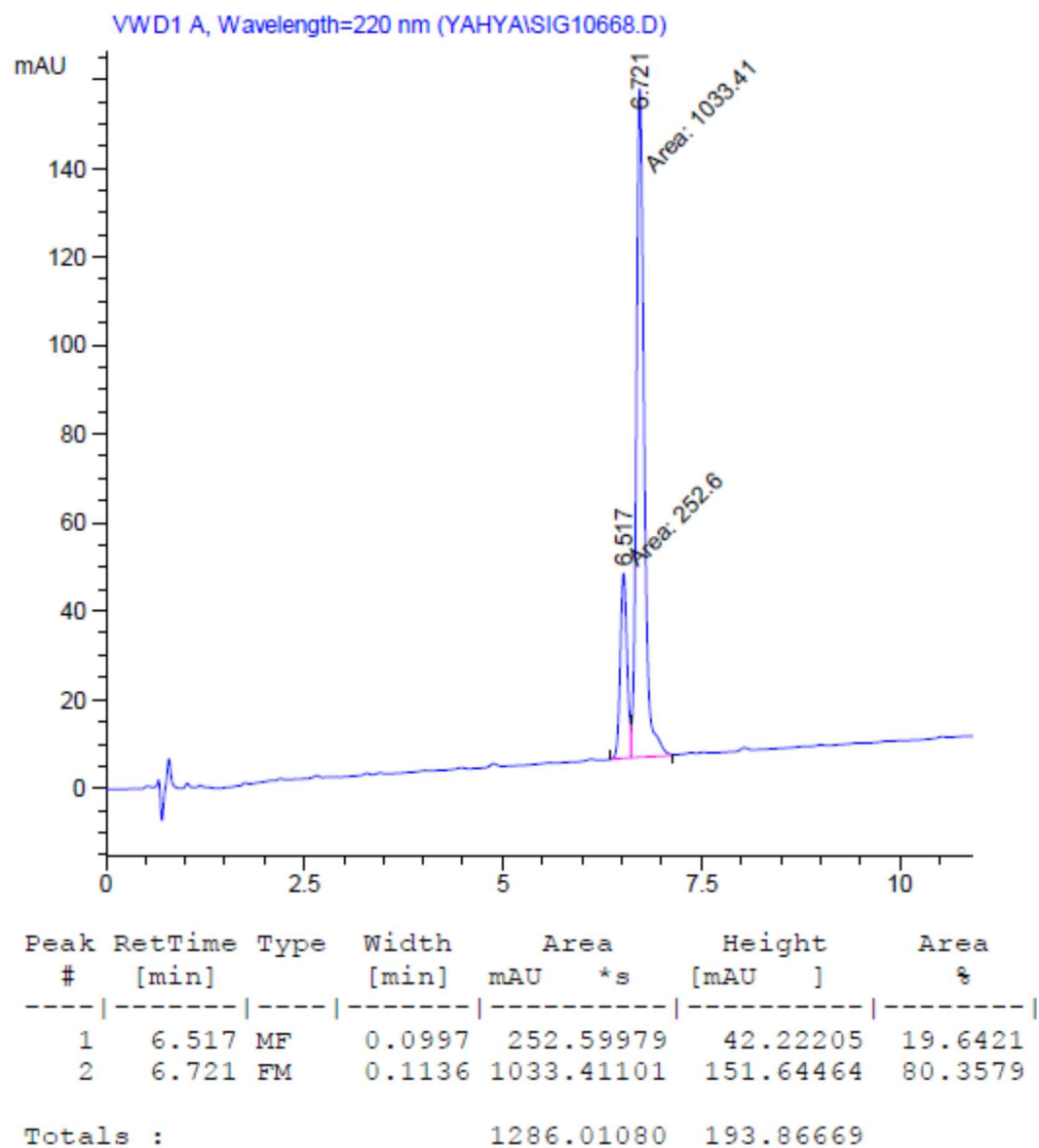


5.9- OxymaPure in ACN

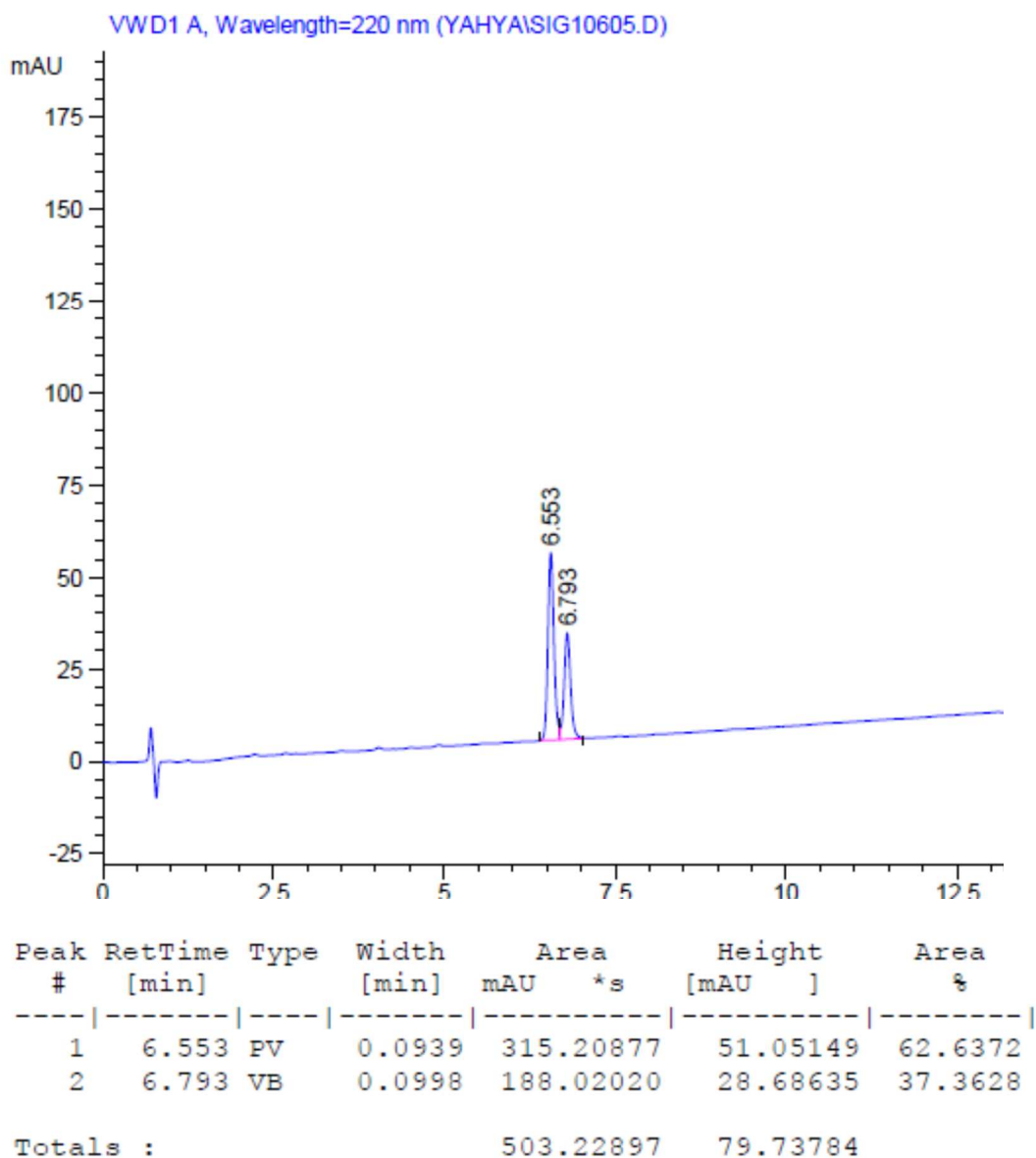


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	6.386	MF	0.1149	3924.47827	569.50177	91.8304
2	6.638	FM	0.1257	349.13699	46.29751	8.1696
Totals :				4273.61526	615.79928	

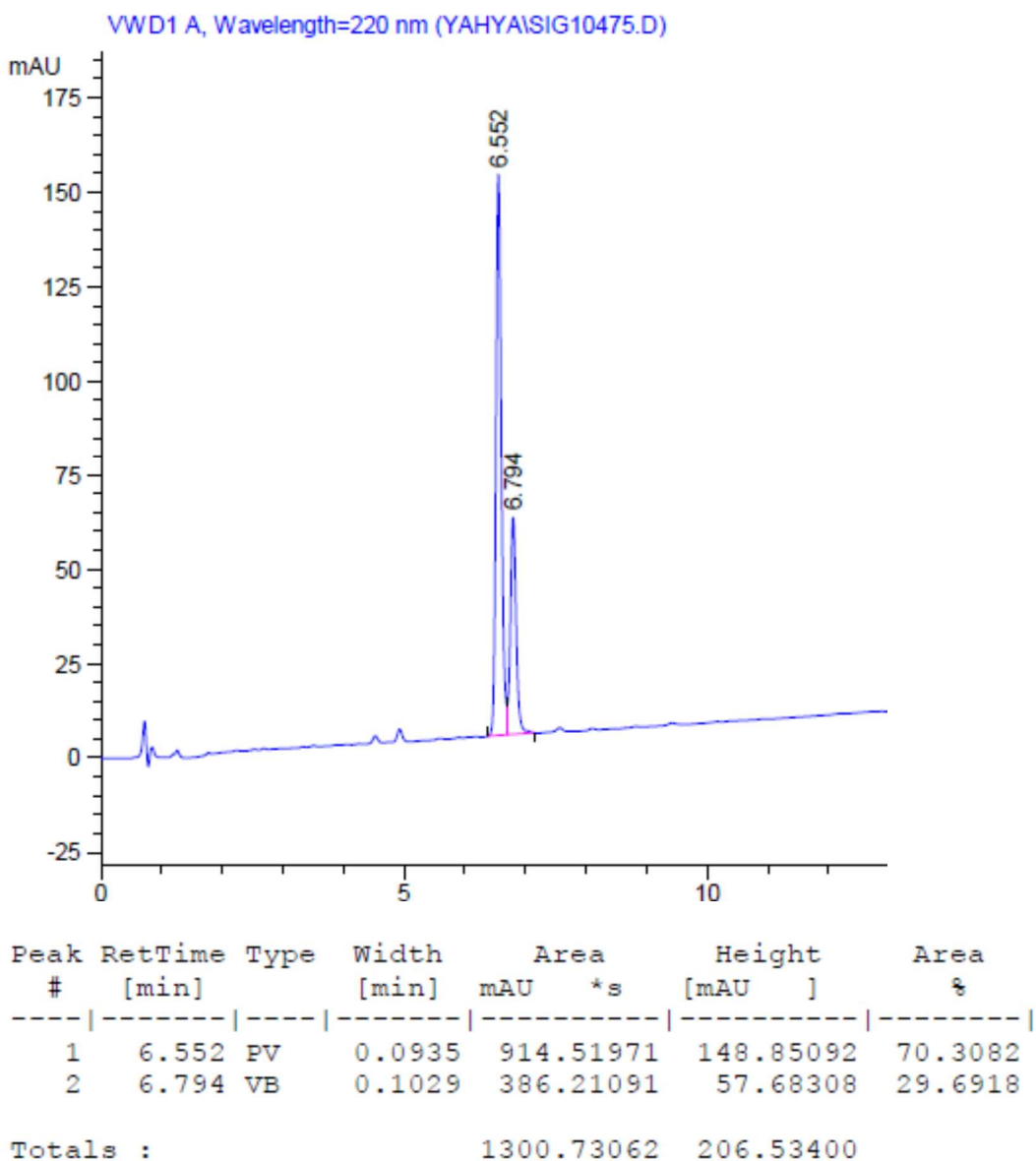
5.10- Oxyma-B in DMF



5.11- Oxyma-B in THF

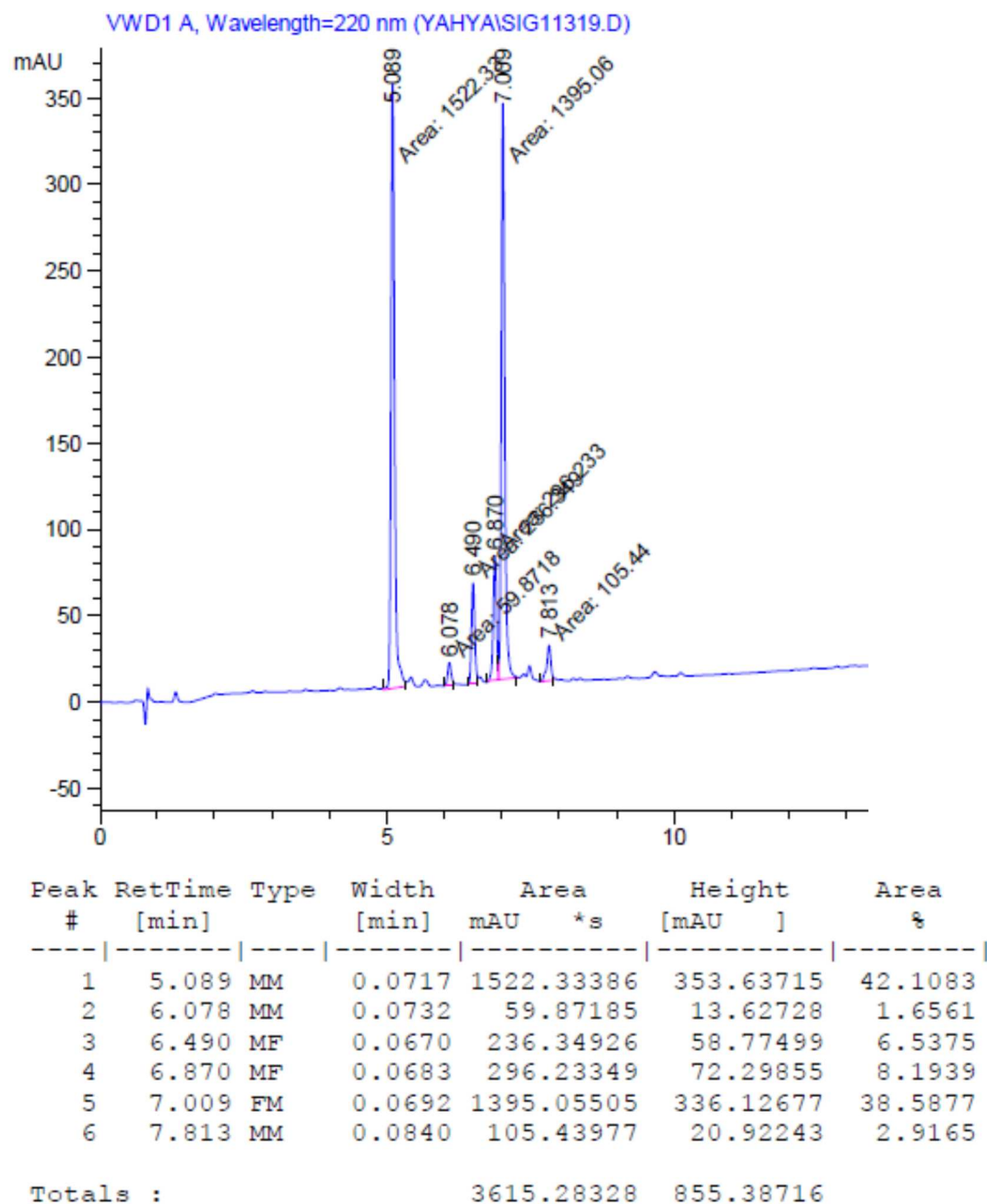


5.12- Oxyma-B in ACN

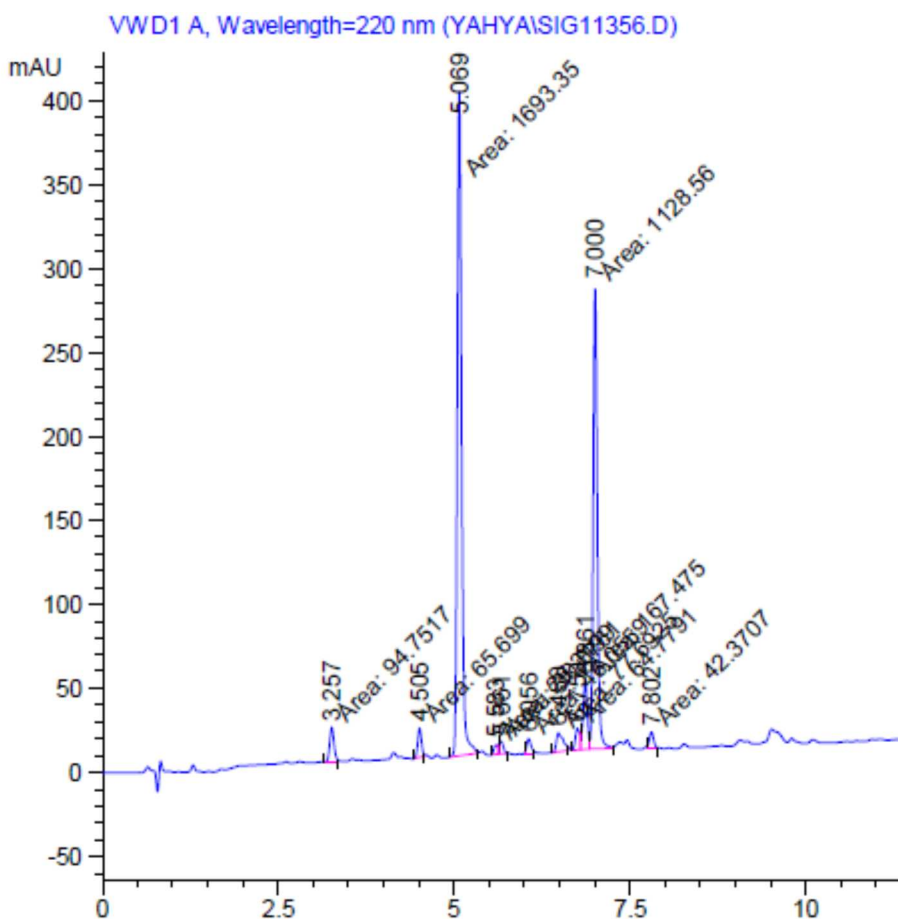


6- Peptide synthesis experiments (Synthesis of Aib-modified ACP decapeptide)

6.1- HOBt in DMF



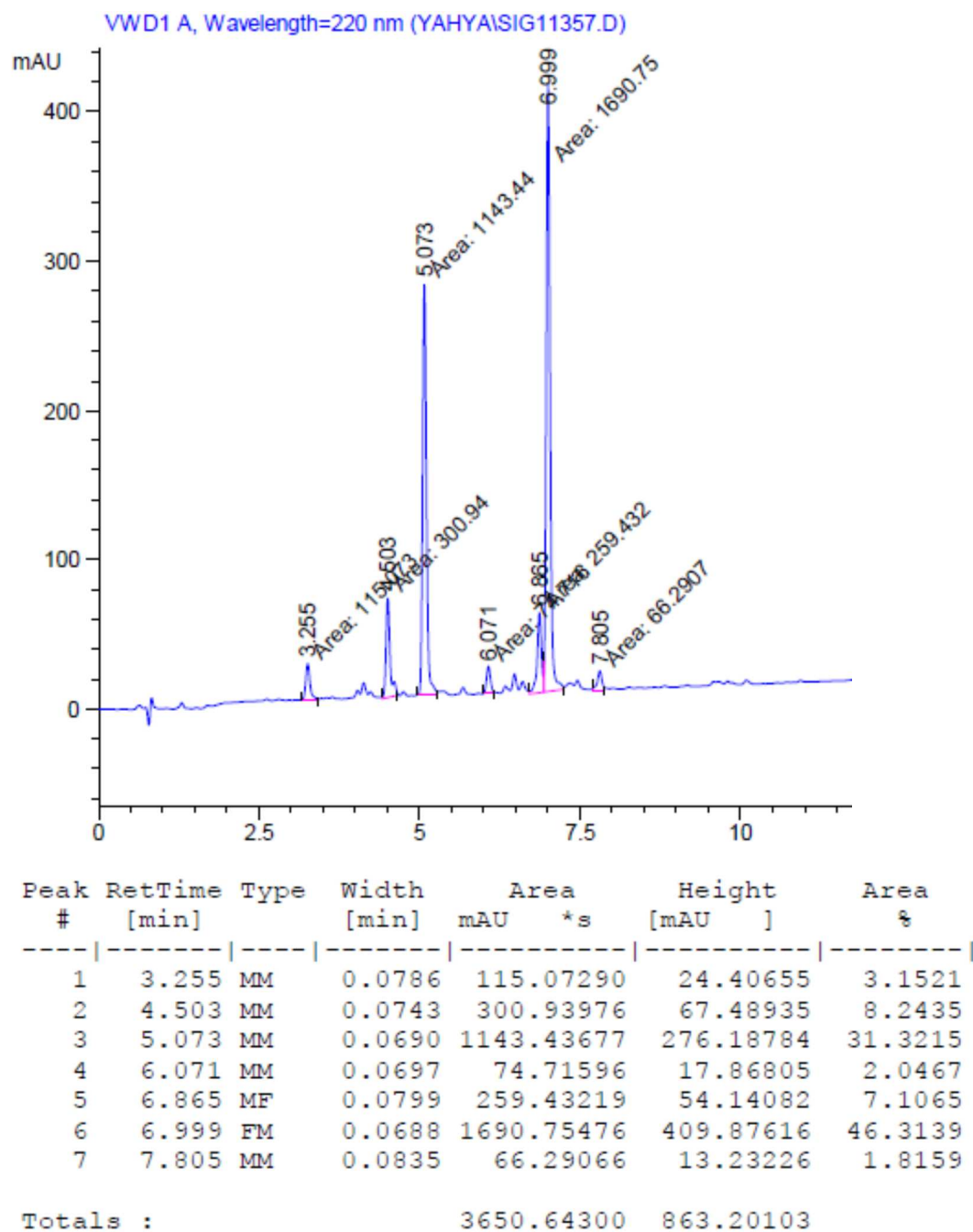
6.2- HOBt in THF



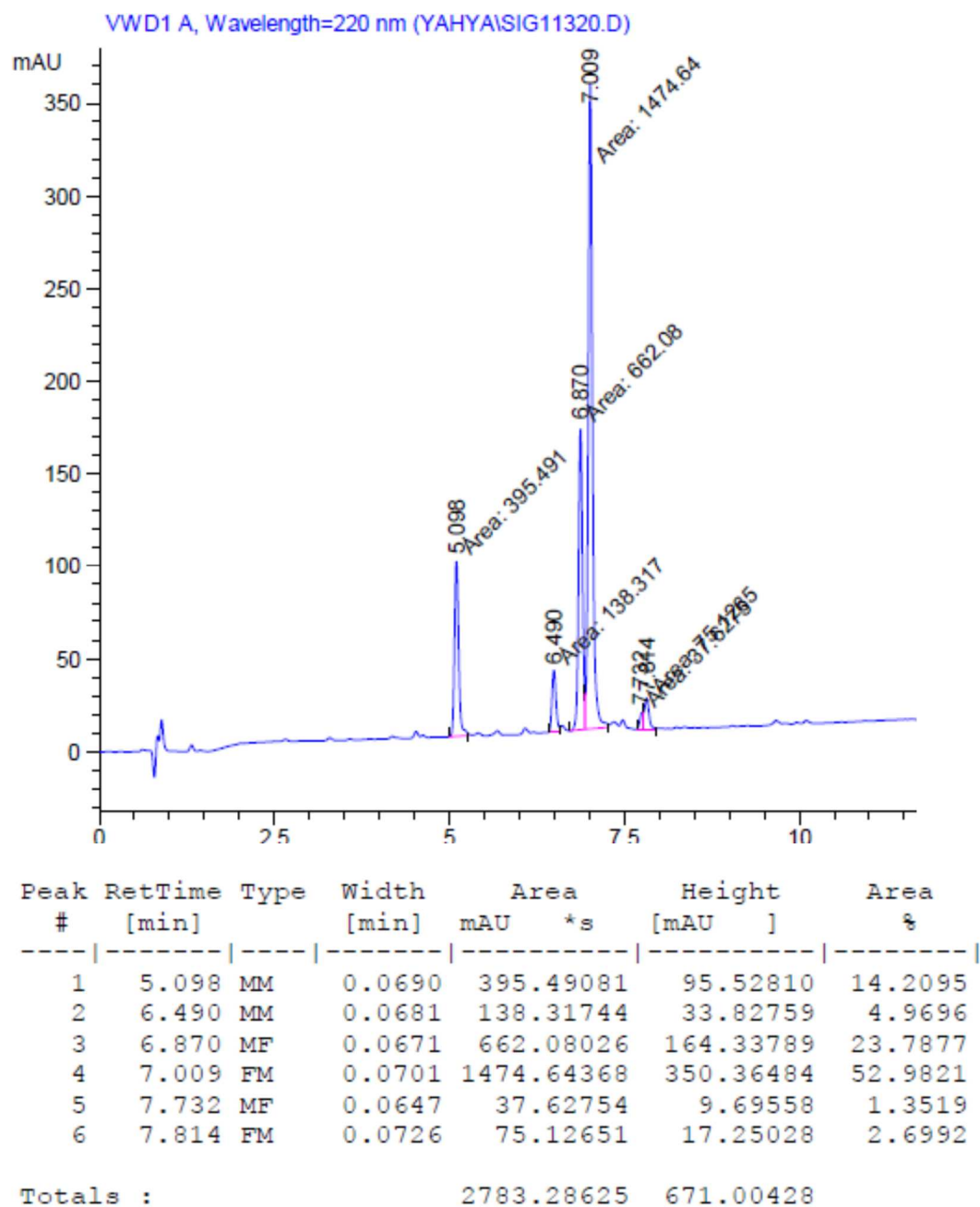
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	3.257	MM	0.0748	94.75173	21.12108	2.7569
2	4.505	MM	0.0623	65.69898	17.57346	1.9116
3	5.069	MM	0.0707	1693.34741	399.26398	49.2693
4	5.583	MF	0.0740	25.31987	5.70302	0.7367
5	5.661	FM	0.0660	30.87609	7.79360	0.8984
6	6.056	MM	0.0789	46.05588	9.72683	1.3400
7	6.480	MM	0.1135	77.69253	11.40971	2.2605
8	6.750	MF	0.0827	64.77909	13.05362	1.8848
9	6.861	FM	0.0680	167.47545	41.03422	4.8728
10	7.000	FM	0.0681	1128.55688	276.34662	32.8362
11	7.802	MM	0.0710	42.37067	9.94491	1.2328

Totals : 3436.92459 812.97104

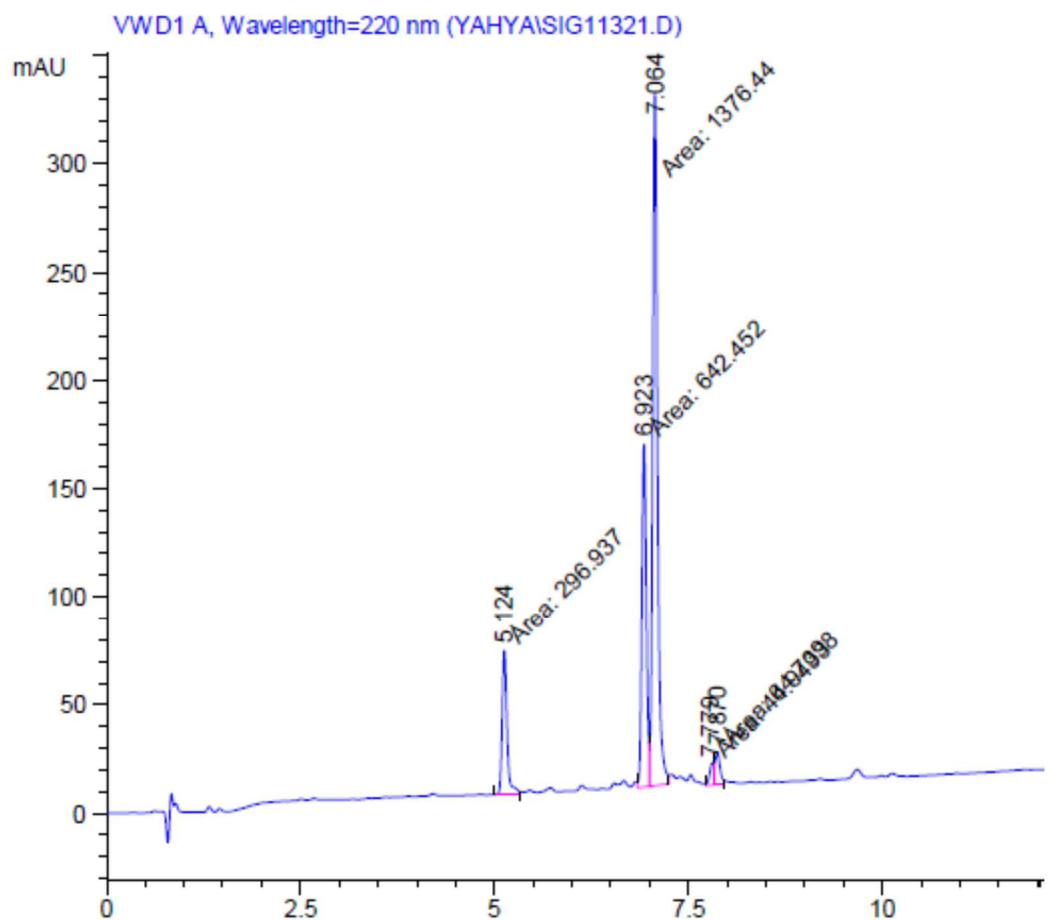
6.3- HOBt in ACN



6.4- HOAt in DMF



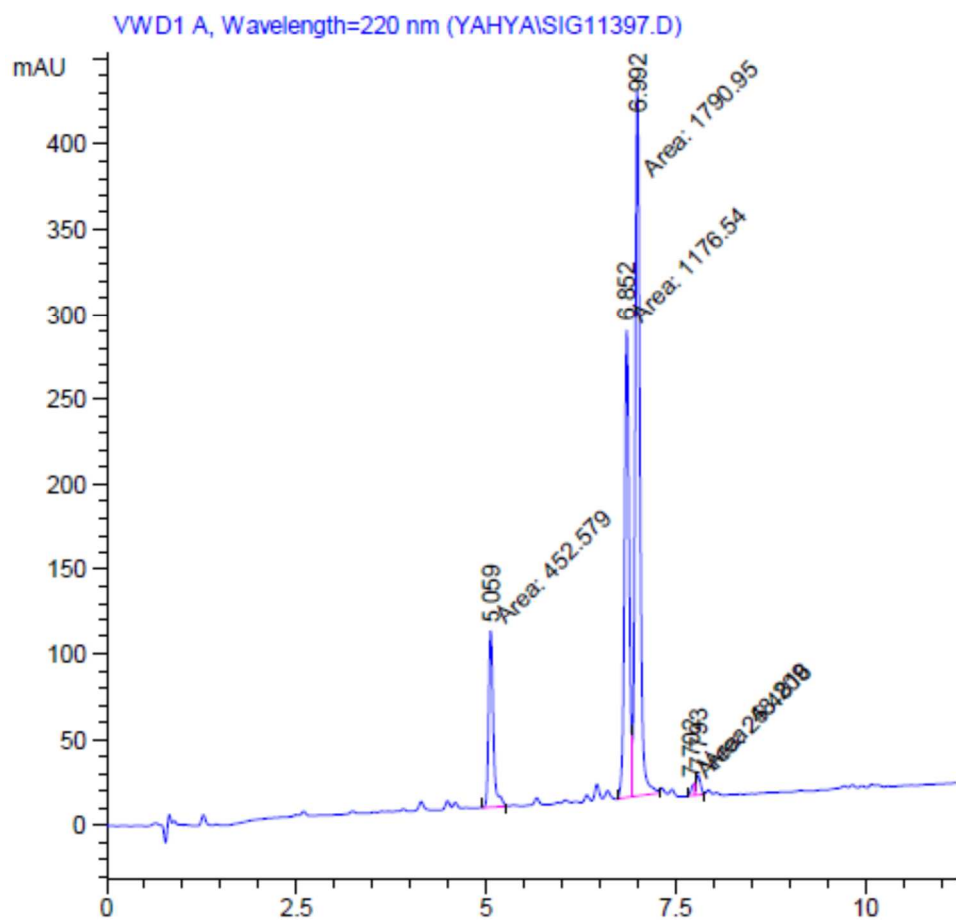
6.5- HOAt in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU*s	Height [mAU]	Area %
1	5.124	MM	0.0738	296.93680	67.06278	12.2422
2	6.923	FM	0.0671	642.45160	159.64384	26.4871
3	7.064	MF	0.0709	1376.44446	323.46533	56.7484
4	7.779	MF	0.0720	44.94930	10.39900	1.8532
5	7.870	FM	0.0710	64.73981	15.20530	2.6691

Totals : 2425.52197 575.77626

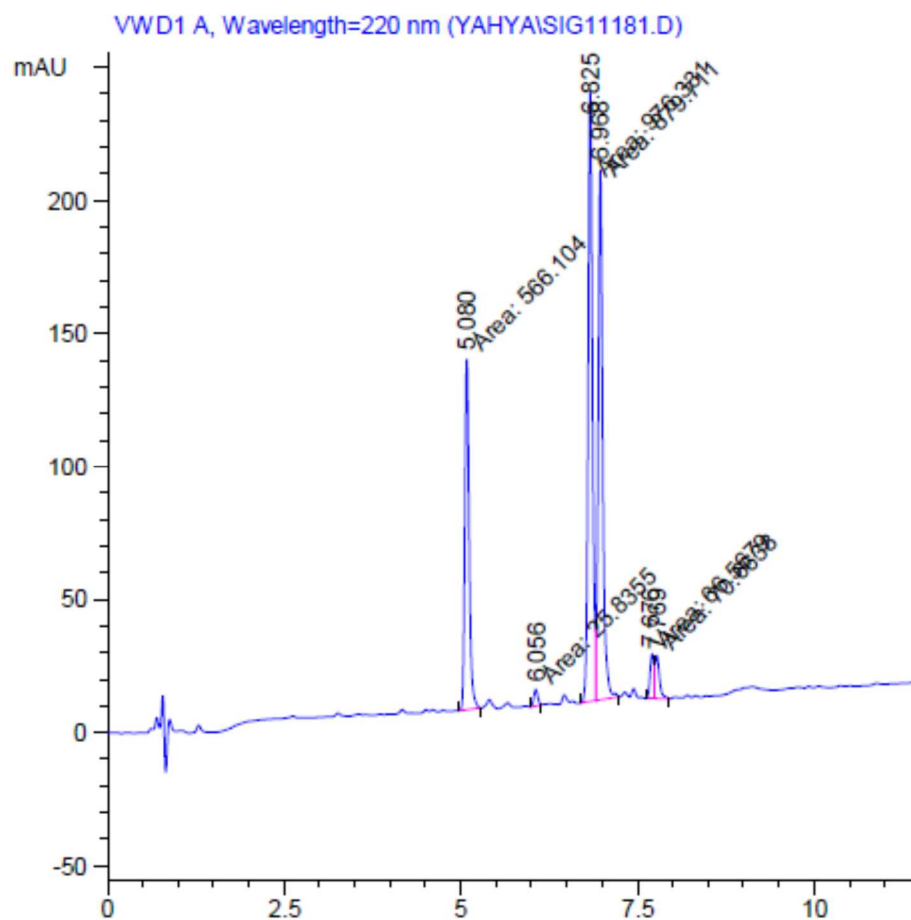
6.6- HOAt in ACN



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.059	MM	0.0727	452.57864	103.81384	12.9539
2	6.852	MF	0.0710	1176.54395	276.24612	33.6755
3	6.992	FM	0.0714	1790.95044	417.95383	51.2614
4	7.702	MF	0.0608	25.48162	6.99078	0.7293
5	7.793	FM	0.0693	48.20901	11.59882	1.3799

Totals : 3493.76367 816.60339

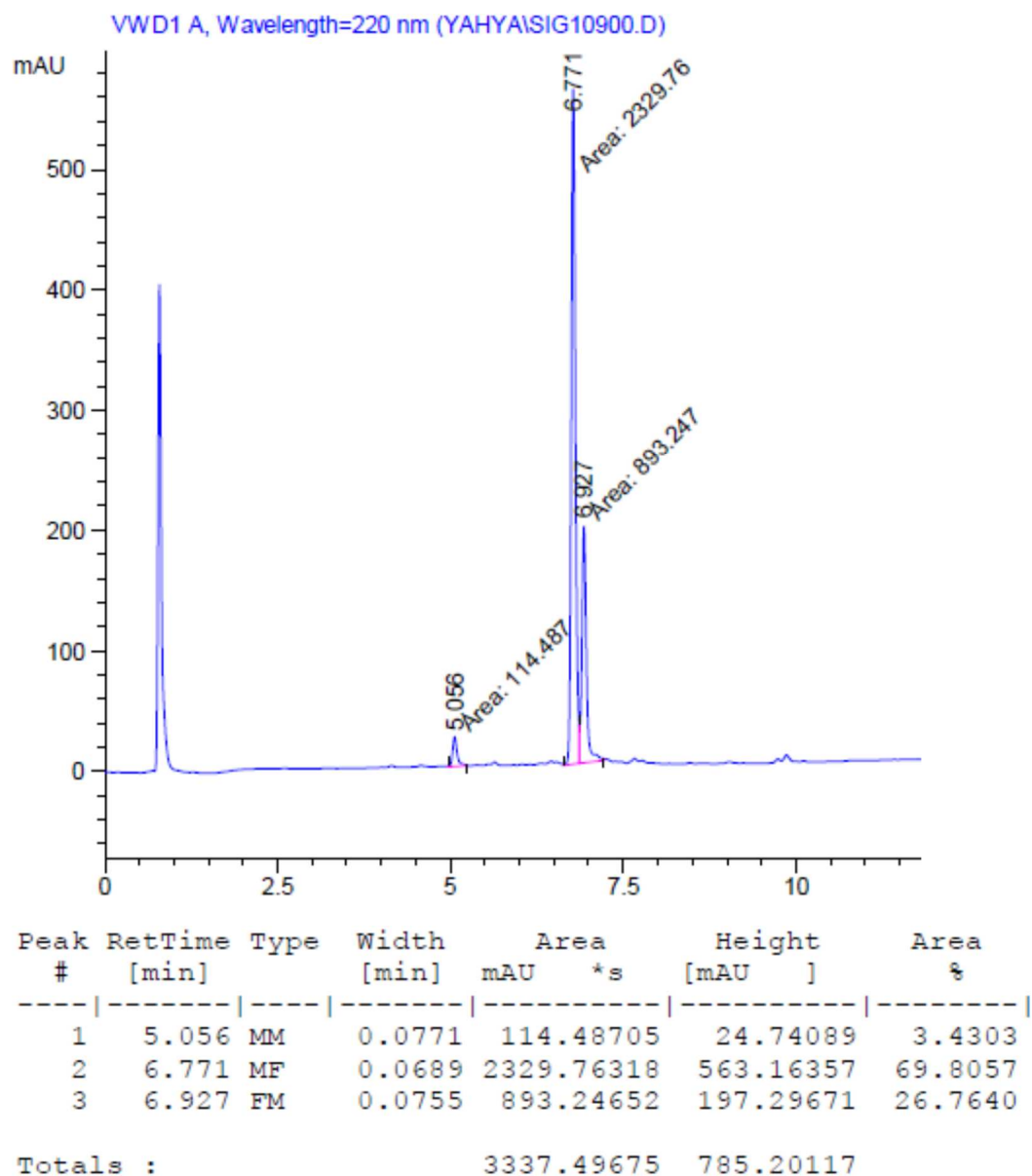
6.7- OxymaPure in DMF



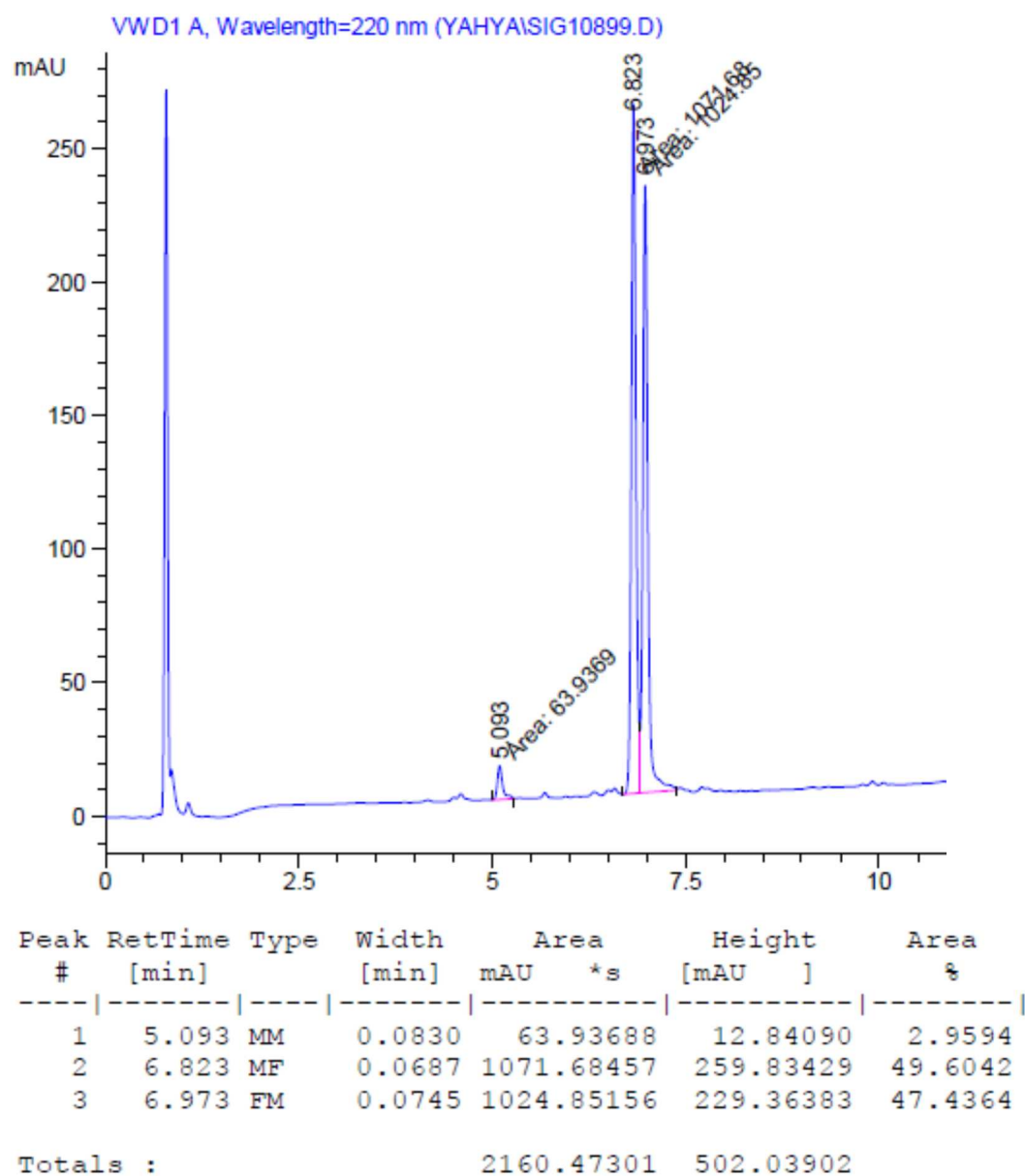
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	5.080	MM	0.0709	566.10370	133.08109	21.8978
2	6.056	MM	0.0675	25.83551	6.38302	0.9994
3	6.825	MF	0.0706	976.33081	230.47884	37.7660
4	6.968	FM	0.0731	879.71143	200.51784	34.0286
5	7.676	MF	0.0660	66.56786	16.82010	2.5749
6	7.769	FM	0.0727	70.66376	16.19696	2.7334

Totals : 2585.21306 603.47785

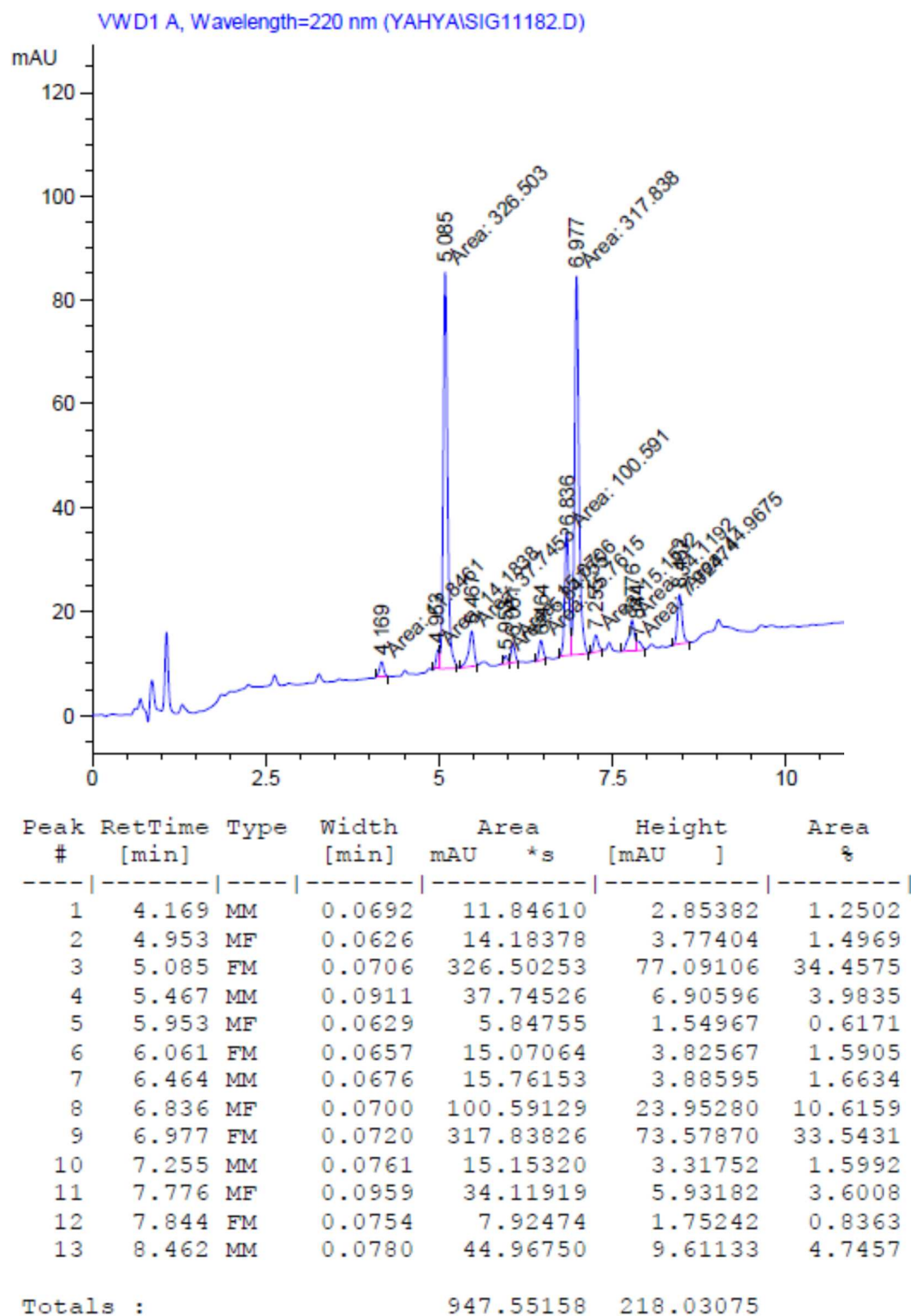
6.8- OxymaPure in THF



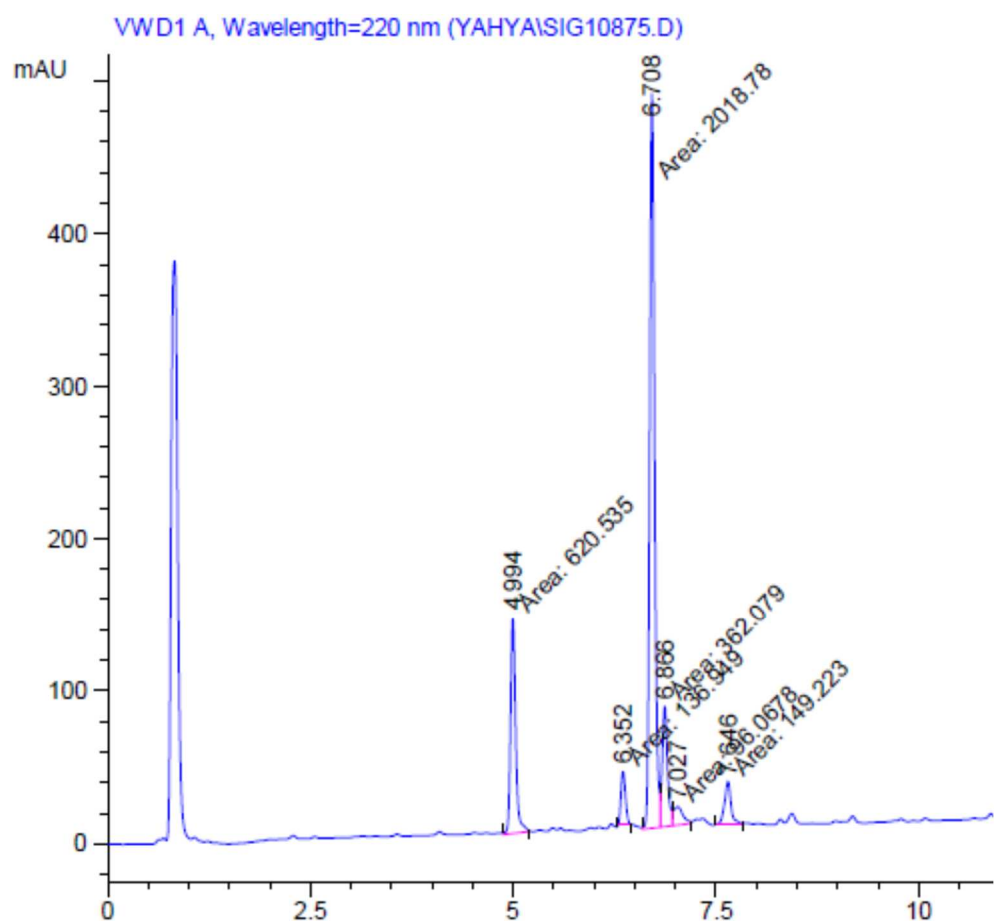
6.9- OxymaPure in ACN



6.10- Oxyma-B in DMF



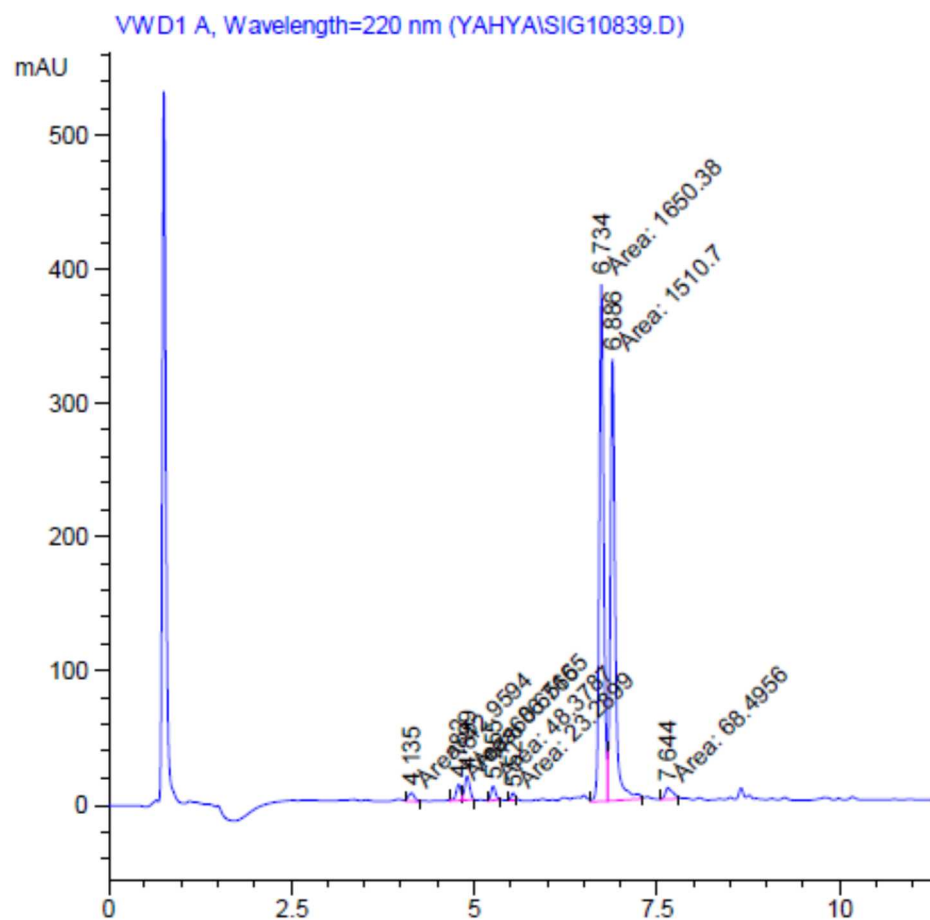
6.11- Oxyma-B in THF



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	4.994	MM	0.0728	620.53467	142.10287	18.3393
2	6.352	MM	0.0647	136.94949	35.28719	4.0474
3	6.708	MF	0.0694	2018.78015	484.92331	59.6631
4	6.866	MF	0.0758	362.07907	79.57053	10.7009
5	7.027	FM	0.1308	96.06782	12.23791	2.8392
6	7.646	MM	0.0894	149.22276	27.82842	4.4101

Totals : 3383.63396 781.95024

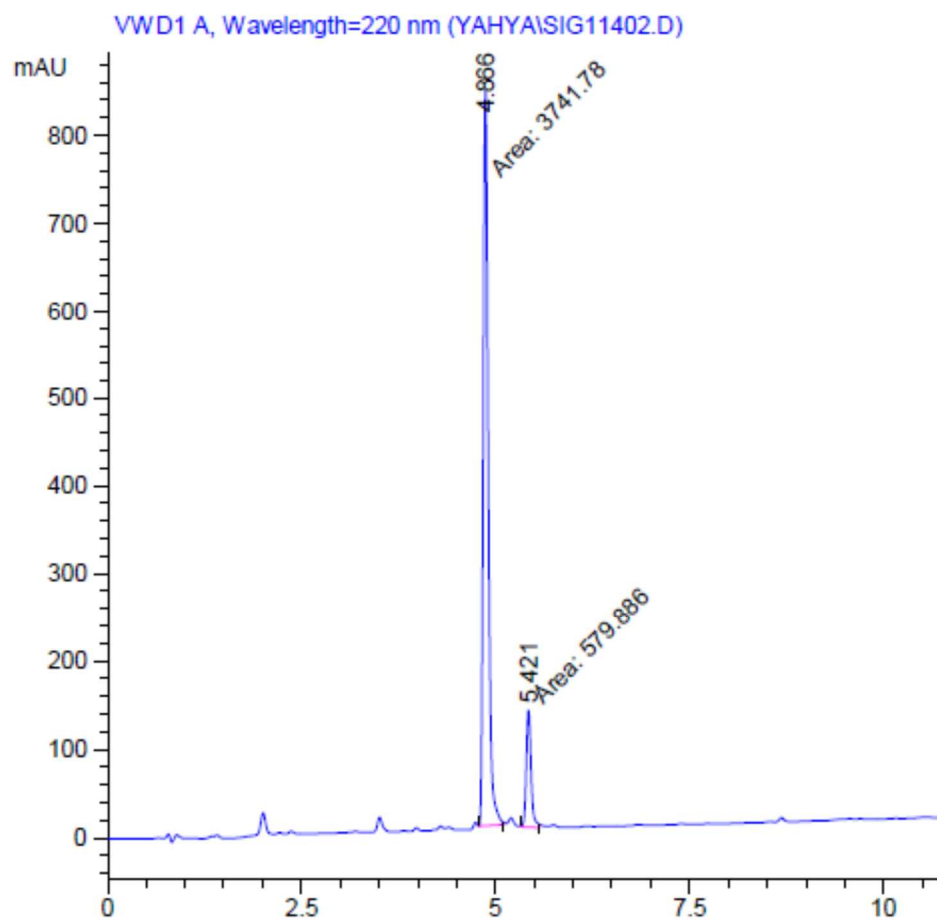
6.12- Oxyma-B in ACN



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	4.135	MM	0.1092	42.95938	6.55540	1.2304
2	4.782	MF	0.0814	60.65647	12.41274	1.7372
3	4.899	FM	0.0792	86.71651	18.24301	2.4836
4	5.255	MM	0.0737	48.37871	10.94215	1.3856
5	5.528	MM	0.0626	23.28985	6.19931	0.6670
6	6.734	MF	0.0706	1650.38013	389.50598	47.2675
7	6.886	FM	0.0758	1510.69861	332.12930	43.2670
8	7.644	MM	0.1268	68.49562	9.00487	1.9617

Totals : 3491.57527 784.99276

6.13- des-Aib-Ile⁷²-Asn



6.14- des-Aib-Ile⁷²-Asn mixed with Aib-modified ACP decapeptide obtained from HOBt and THF

