

Supporting Information

Miniaturized Click Chemistry and Direct Screening Facilitate the Discovery of Triazole Piperazine SARS-CoV-2 M^{pro} Inhibitors with Improved Metabolic Stability

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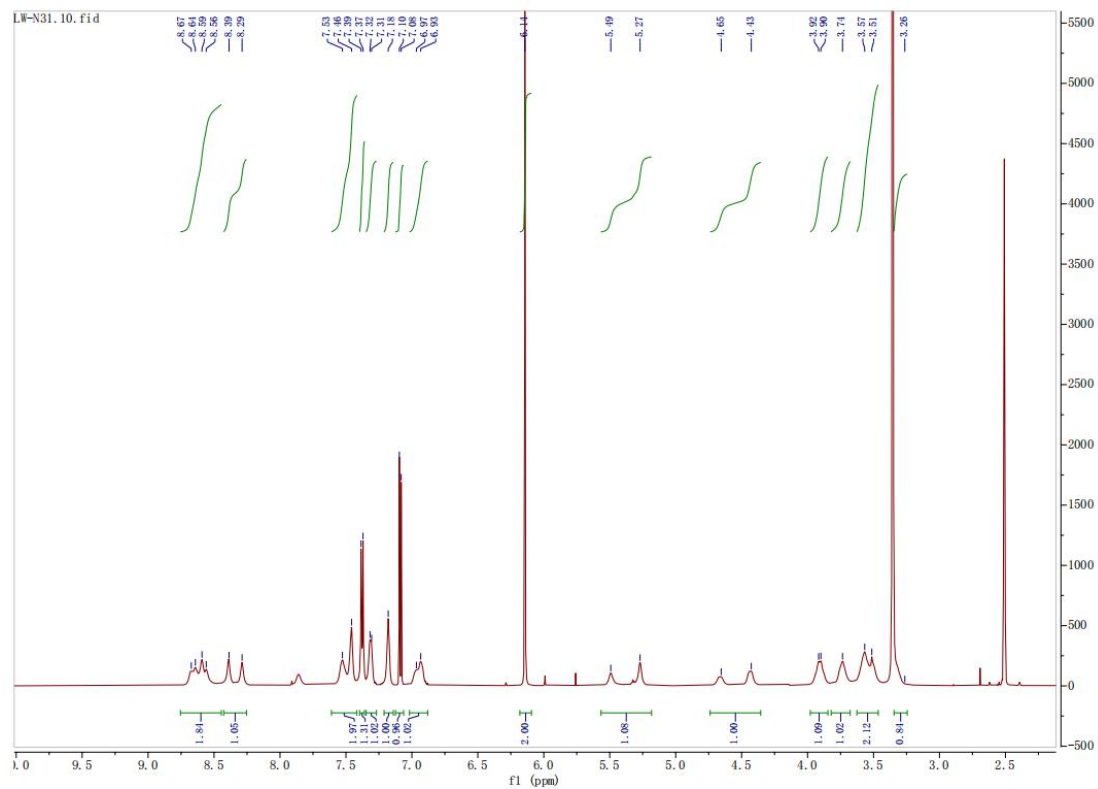
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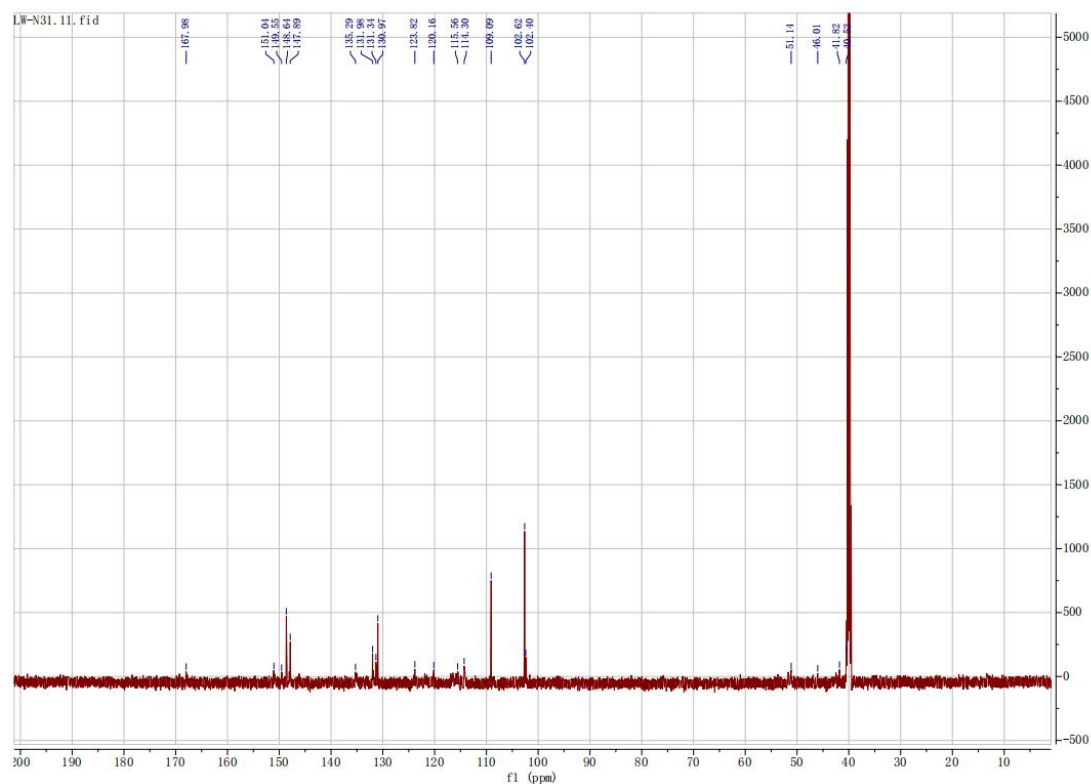
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^1H and ^{13}C NMR spectra of representative final compounds

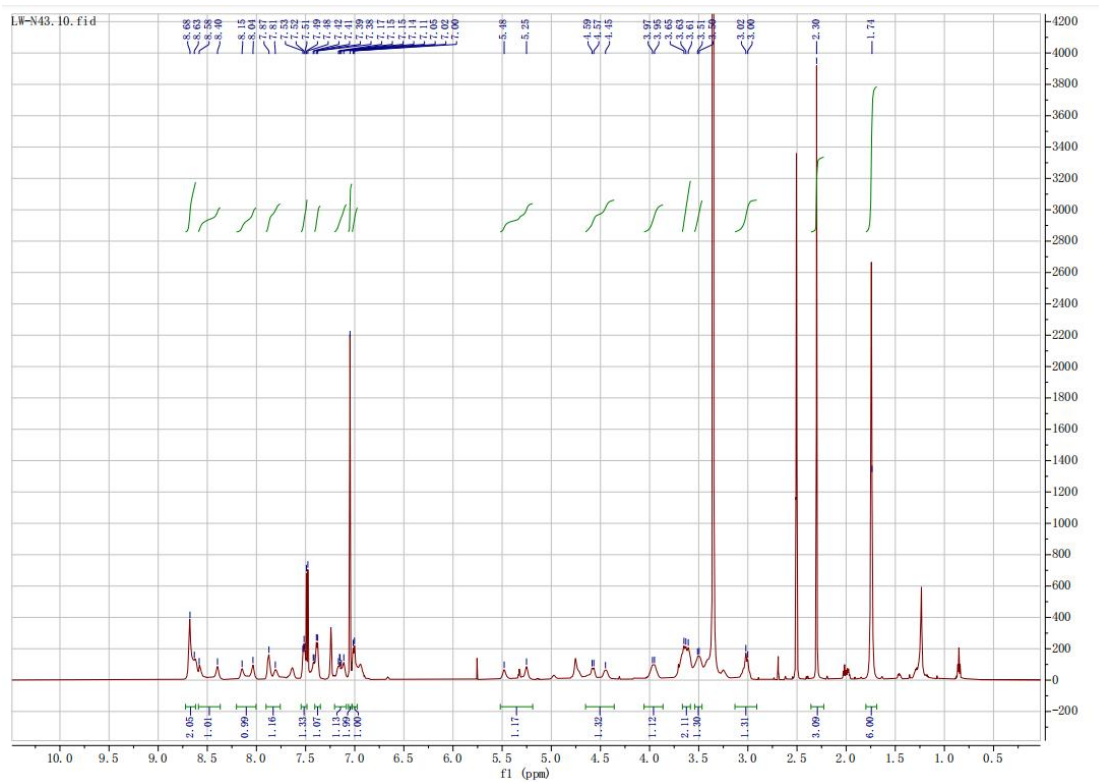
^1H NMR (600 MHz, $\text{DMSO}-d_6$) of **C1N31**



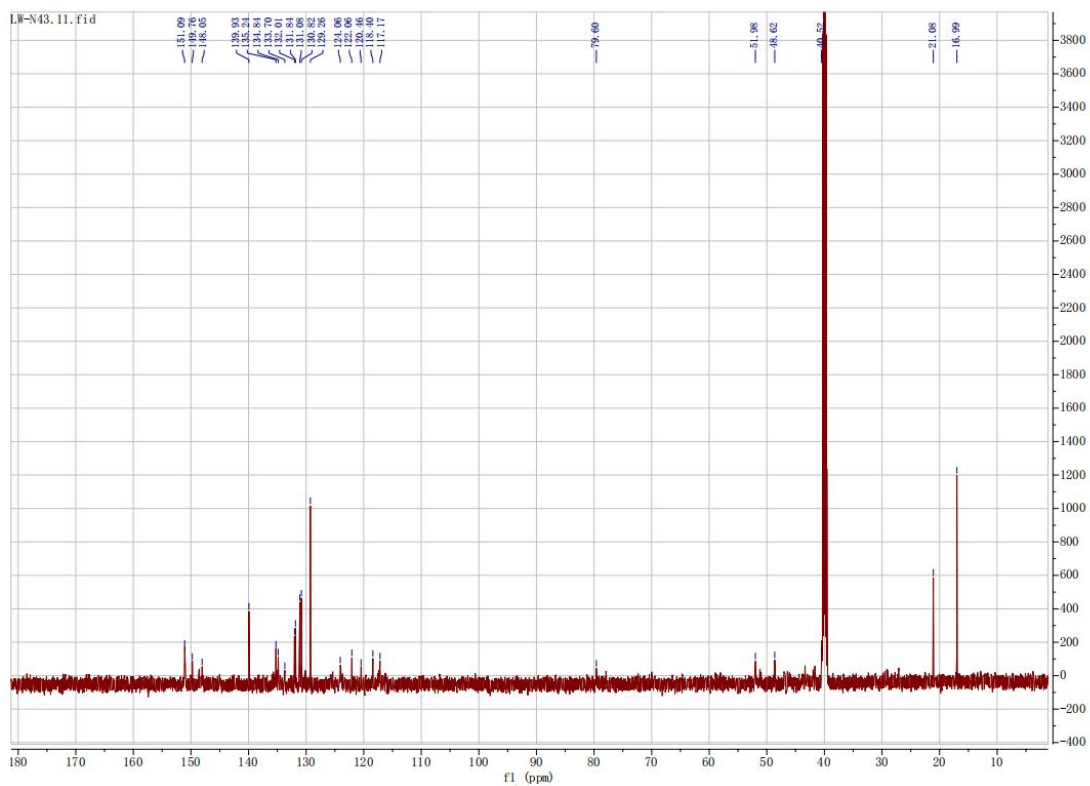
^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) of **C1N31**



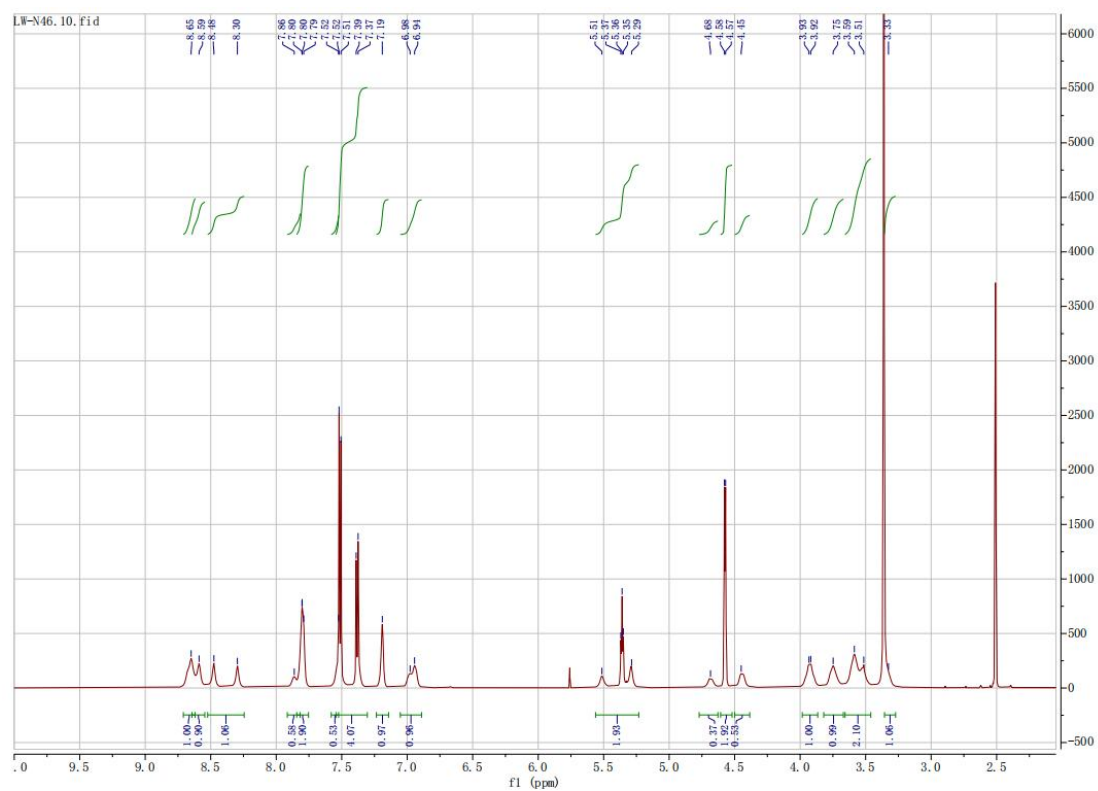
^1H NMR (600 MHz, $\text{DMSO}-d_6$) of **C1N43**



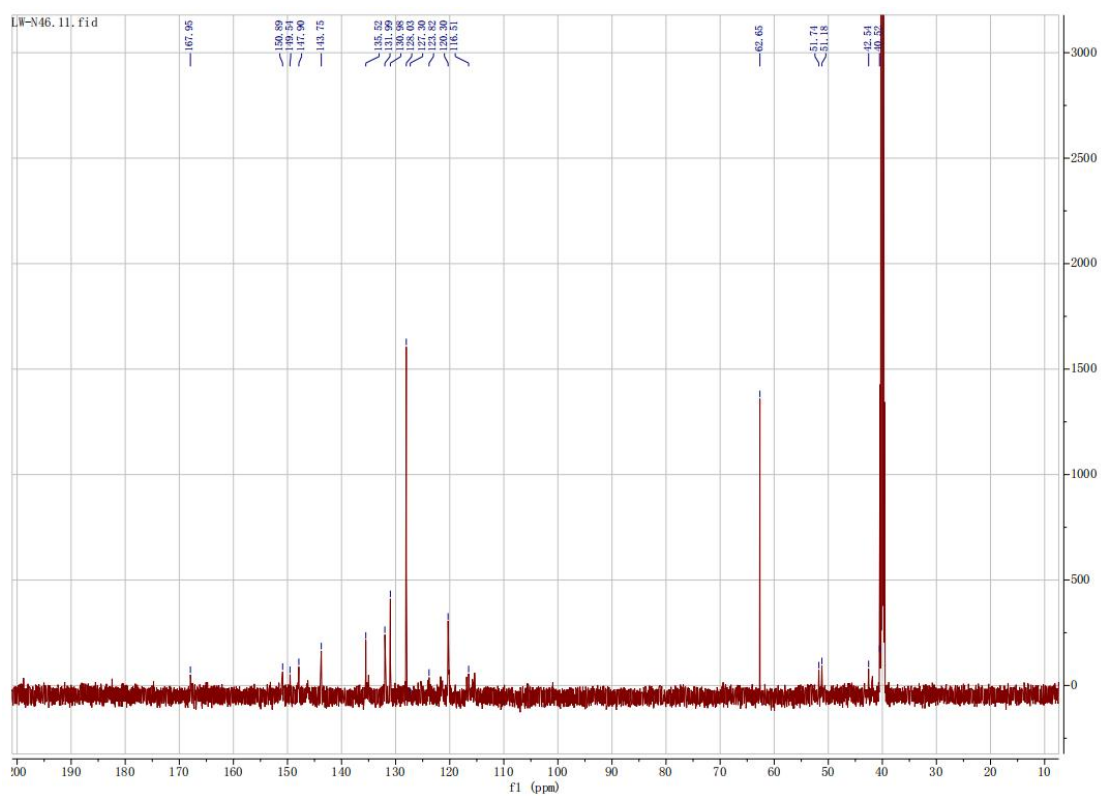
^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) of **C1N43**



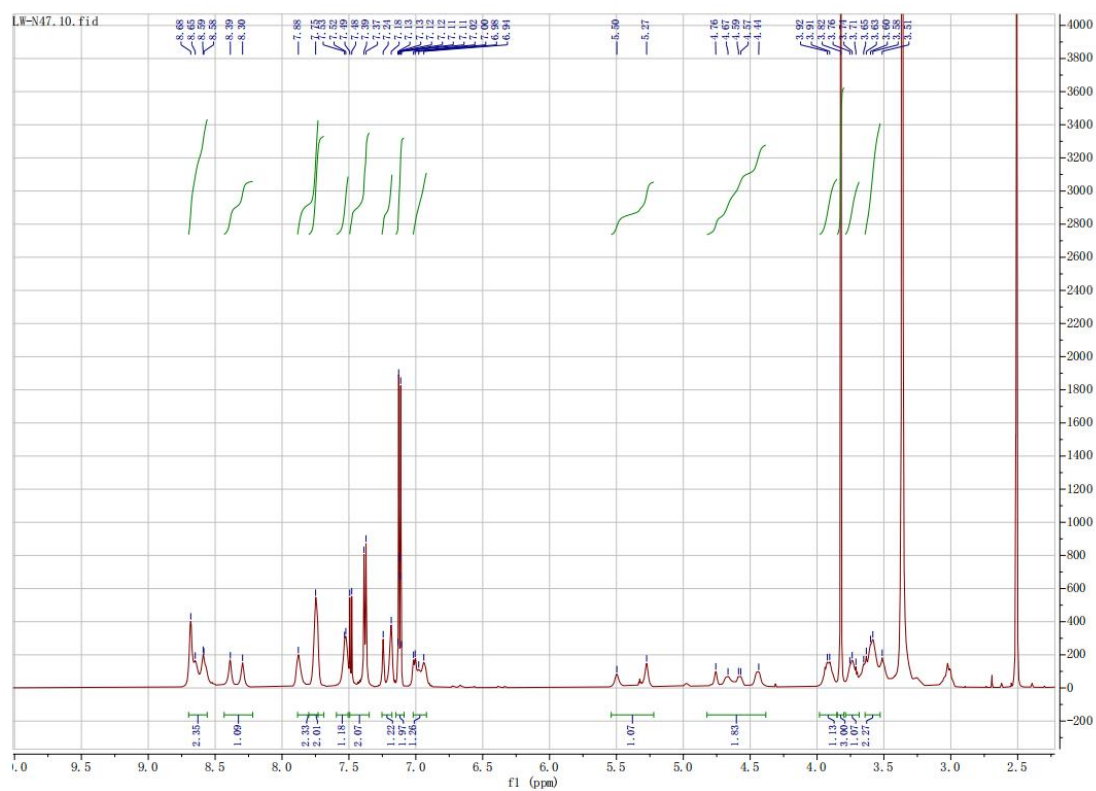
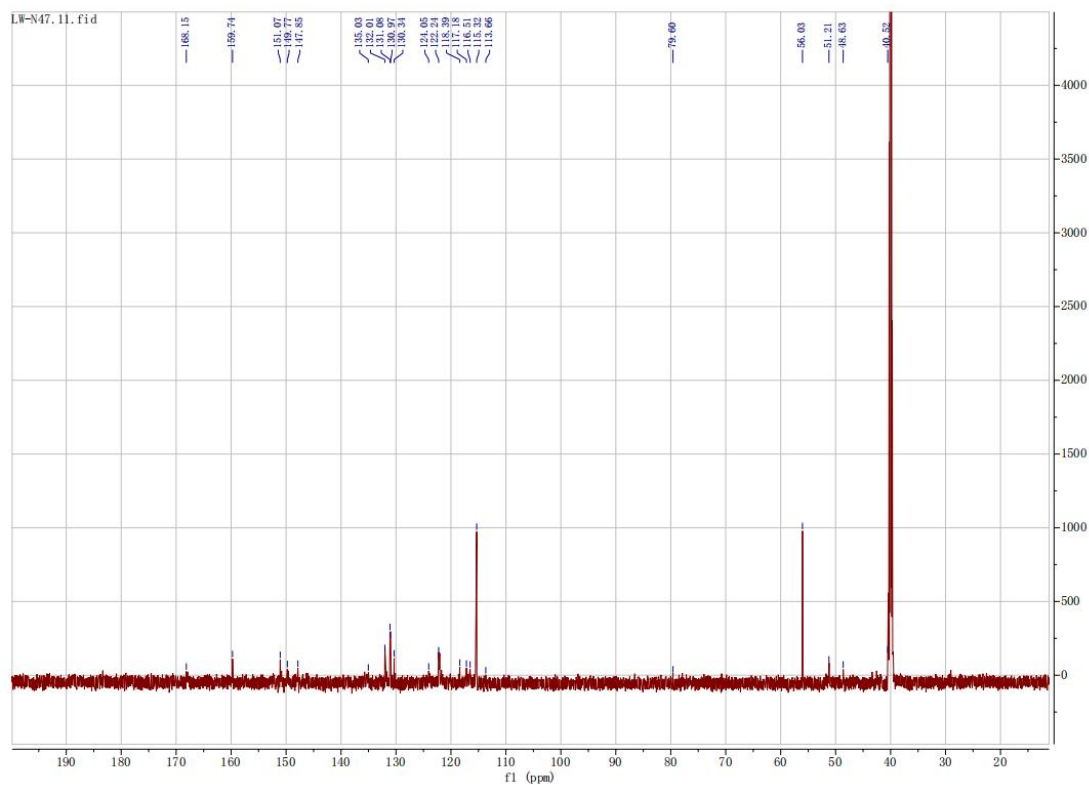
^1H NMR (600 MHz, $\text{DMSO}-d_6$) of **C1N46**



¹³C NMR (150 MHz, DMSO-*d*₆) of C1N46

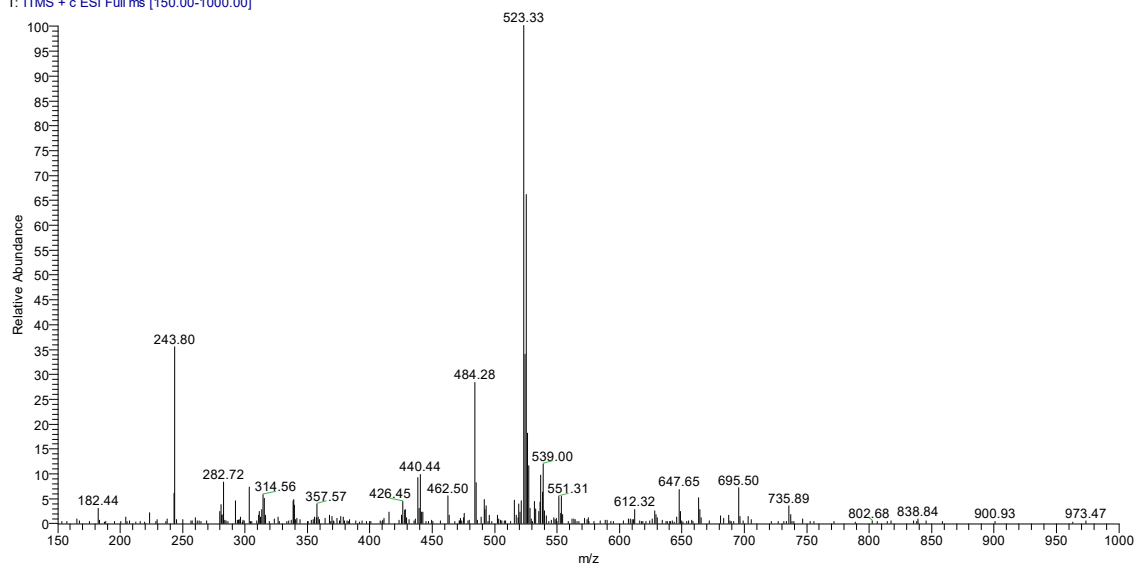


¹H NMR (600 MHz, DMSO-*d*₆) of C1N47

 ^{13}C NMR (150 MHz, DMSO- d_6) of **C1N47**

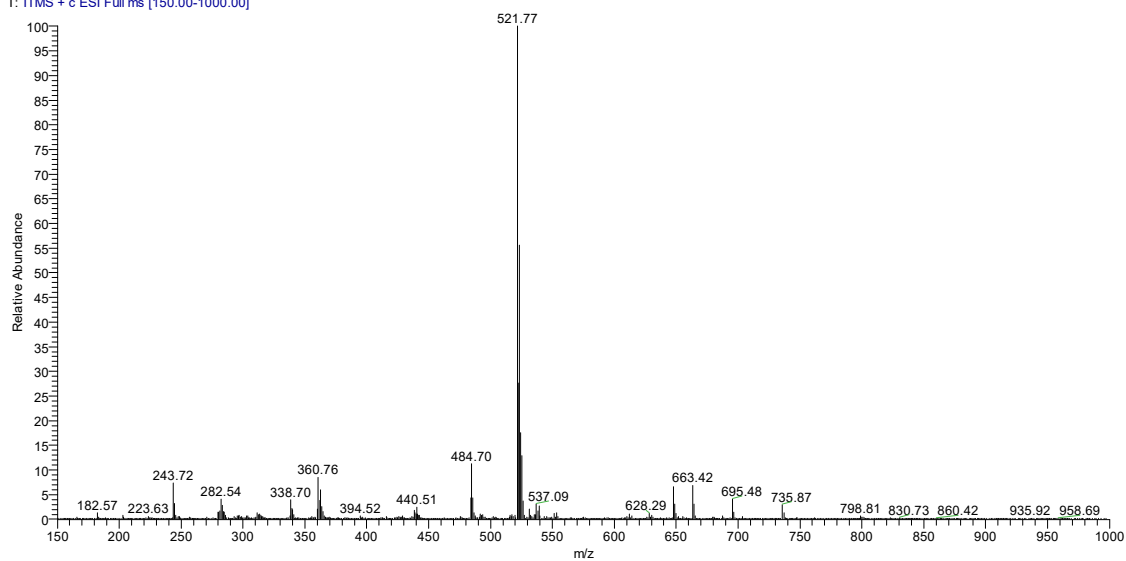
Mass spectrometry of C1N31

N31 #2228 RT: 6.03 AV: 1 NL: 8.31E3
T: ITMS + c ESI Full ms [150.00-1000.00]



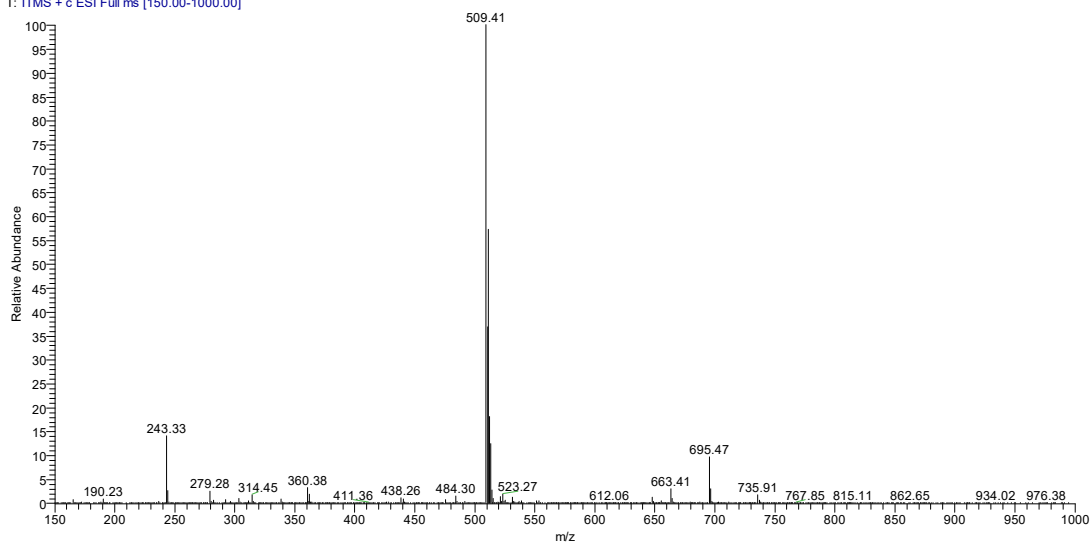
Mass spectrometry of C1N43

N43 #2327-2358 RT: 6.30-6.38 AV: 32 NL: 2.46E4
T: ITMS + c ESI Full ms [150.00-1000.00]



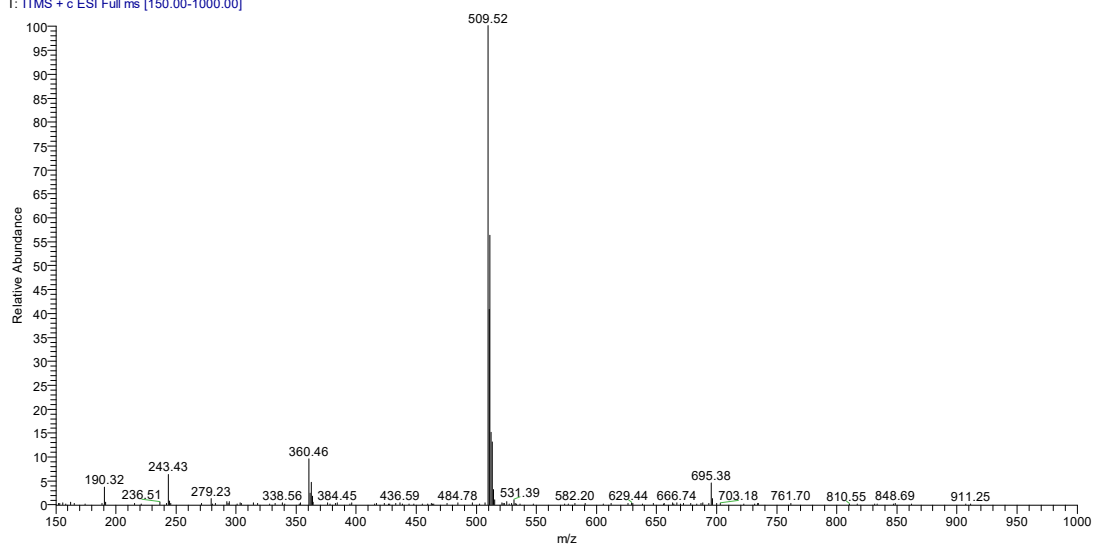
Mass spectrometry of C1N46

N46 #1971-2004 RT: 5.33-5.42 AV: 34 NL: 1.15E4
T: ITMS + c ESI Full ms [150.00-1000.00]



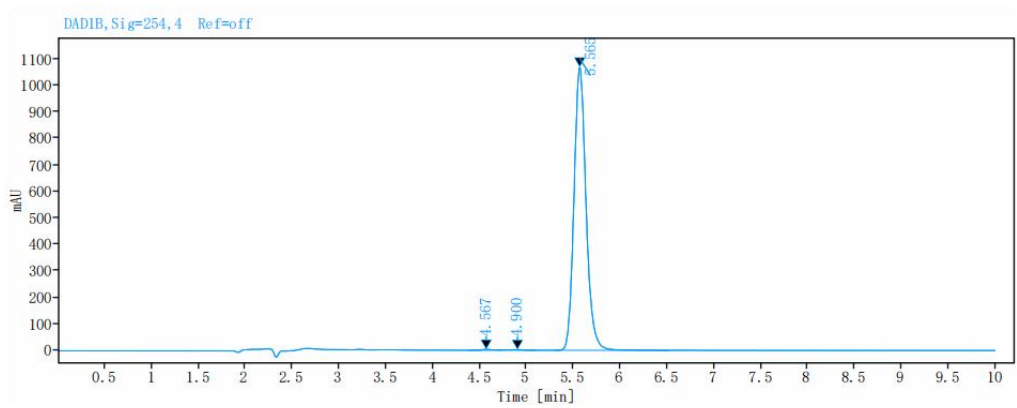
Mass spectrometry of C1N47

N47 #2205 RT: 5.97 AV: 1 NL: 1.98E4
T: ITMS + c ESI Full ms [150.00-1000.00]



HPLC chromatogram report of C1N31

Sample name: N31
Data file: 2024-06-19 16-00-23+08-00-01. dx
Instrument: Agilent1260 Prime
Sample volume 10. 000
Collection method: 20240604-80%-10min. amx

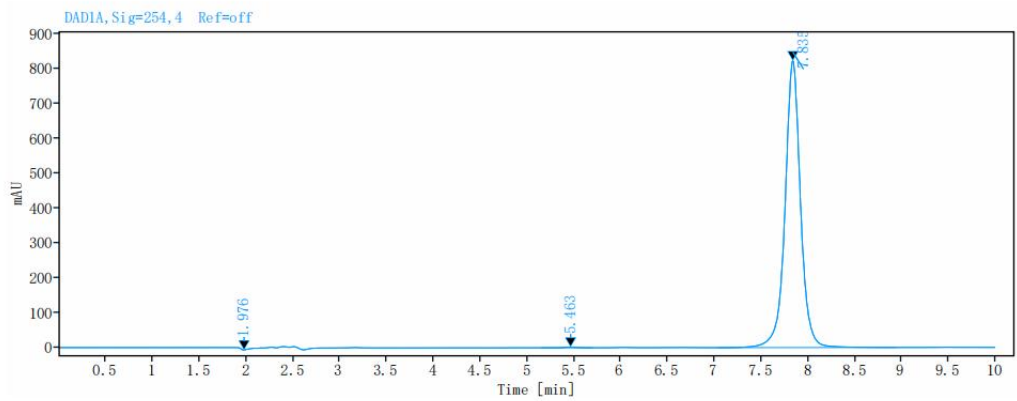


Signal DAD1B, Sig=254, 4 Ref=off

Retention time (min)	type	Pike width [min]	Peak area	Peak height	Peak area%	Name
4.567	BV	0.3345	27.2437	3.4919	0.2843	
4.900	VV	0.3873	28.9105	2.6289	0.3017	
5.565	BV	1.2161	9527.9185	1066.5046	99.4141	
总和			9584.0727			

HPLC chromatogram report of C1N43

Sample name: N43
Data file: 2024-06-19 19-56-36+08-00-04. dx
Instrument: Agilent1260 Prime
Sample volume 10. 000
Collection method: 75%-80%-10MIN. amx

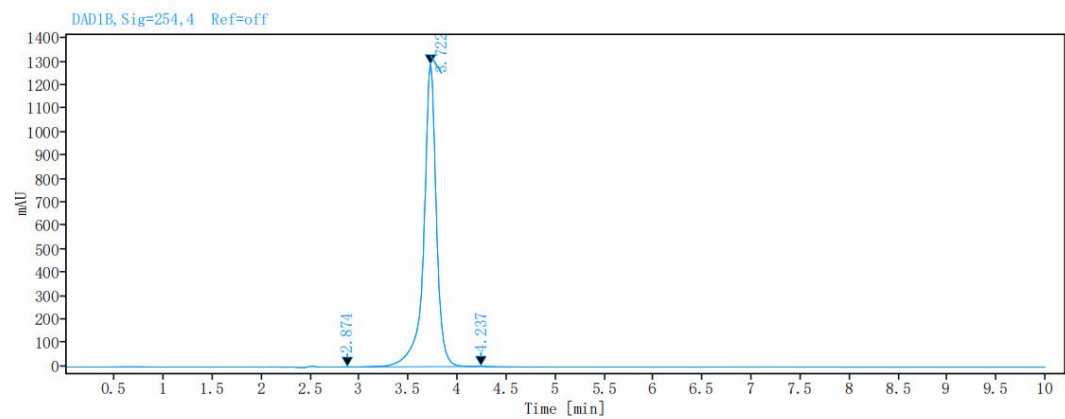


Signal DAD1A, Sig=254, 4 Ref=off

Retention time (min)	type	Pike width [min]	Peak area	Peak height	Peak area%	Name
1.976	BM m	0.0000	0.0000	0.0000	0.0000	
5.463	BB	0.5500	18.5748	2.1456	0.1957	
7.835	BB	1.9044	9473.1640	821.7384	99.8043	
总和			9491.7388			

HPLC chromatogram report of C1N46

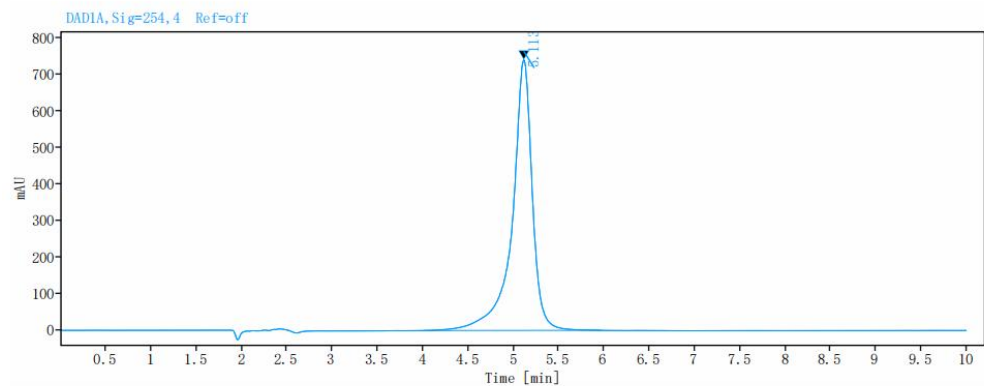
Sample name: N46
Data file: 2024-06-19 16-24-26+08-00-03. dx
Instrument: Agilent1260 Prime
Sample volume 10.000
Collection method: 20240604-80%-10min. amx



Signal DAD1B, Sig=254, 4 Ref=off						
Retention time (min)	type	Pike width [min]	Peak area	Peak height	Peak area%	Name
2.874	MM m	0.0973	1.3261	0.2171	0.0115	
3.722	MM m	0.1304	11537.4858	1288.7469	99.8837	
4.237	MM m	0.0843	12.1069	2.2673	0.1048	
总和			11550.9188			

HPLC chromatogram report of C1N47

Sample name: N47
Data file: 2024-06-19 20-07-29+08-00-05. dx
Instrument: Agilent1260 Prime
Sample volume 10.000
Collection method: 75%-80%-10MIN. amx



Signal DAD1A, Sig=254, 4 Ref=off						
Retention time (min)	type	Pike width [min]	Peak area	Peak height	Peak area%	Name
5.113	MM m	0.2244	11474.4860	741.9293	100.0000	
总和			11474.4860			