Angular Regioselective Synthesis of Varied Functionalized Hexahydro[1,2,4]triazolo[4,3-*a*]quinazolin-9-ones and Their Antiproliferative Action

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(4a*S**,8a*R**)-Ethyl 9-oxo-1-phenyl-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4a**) **S3**

(4a*S**,8a*R**)-Ethyl 9-oxo-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4b**) **S6**

(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-nitrophenyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4c**) **S9**

(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-methoxyphenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo-[4,3-*a*]quinazoline-3-carboxylate (**4d**) **S10**

(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-chlorophenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4e**) **S13**

(4a*S**,8a*R**)-Ethyl 9-oxo-1-(3-(trifluoromethyl)phenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo-[4,3-*a*]quinazoline-3-carboxylate (**4f**) **S14**

(4a*S**,8a*R**)-3-Acetyl-1-(*p*-tolyl)-4a,5,8,9-tetrahydro[1,2,4]triazolo[4,3-*a*]quinazoline-9(1*H*)-one (**4g**) .. **S15**

(4a*S**,8a*R**)-9-Oxo-*N*-Phenyl-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxamide (**4h**) **S16**

(4a*S**,8a*S**)-Ethyl 9-oxo-1-phenyl-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-a]quinazoline-3-carboxylate (**5a**) **S17**

(4a*S**,8a*S**)-Ethyl 9-oxo-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5b**) **S21**

(4a*S**,8a*S**)-Ethyl 1-(4-nitrophenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5c**) **S22**

(4a*S**,8a*S**)-Ethyl 1-(4-methoxyphenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo-[4,3-*a*]quinazoline-3-carboxylate (**5d**) **S23**

(4a*S**,8a*S**)-Ethyl 1-(4-chlorophenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5e**) **S24**

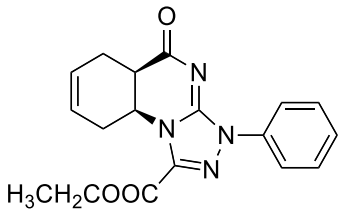
(4a*S**,8a*S**)-Ethyl 9-oxo-1-(3-(trifluoromethyl)phenyl)- 1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo-[4,3-*a*]quinazoline-3-carboxylate (**5f**) **S25**

(4a*S**,8a*S**)-3-Acetyl-1-(*p*-tolyl)-4a,5,8,9-tetrahydro-[1,2,4]triazolo[4,3-*a*]quinazolin-9(1*H*)-one (**5g**) ... **S26**

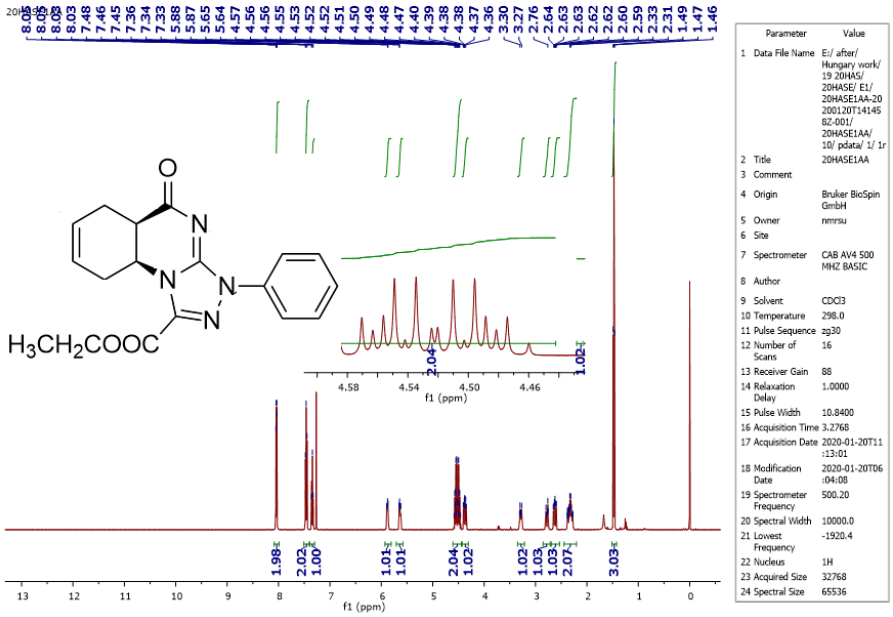
(4a*S**,8a*S**)-9-Oxo-*N*-phenyl-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxamide (**5h**) **S27**

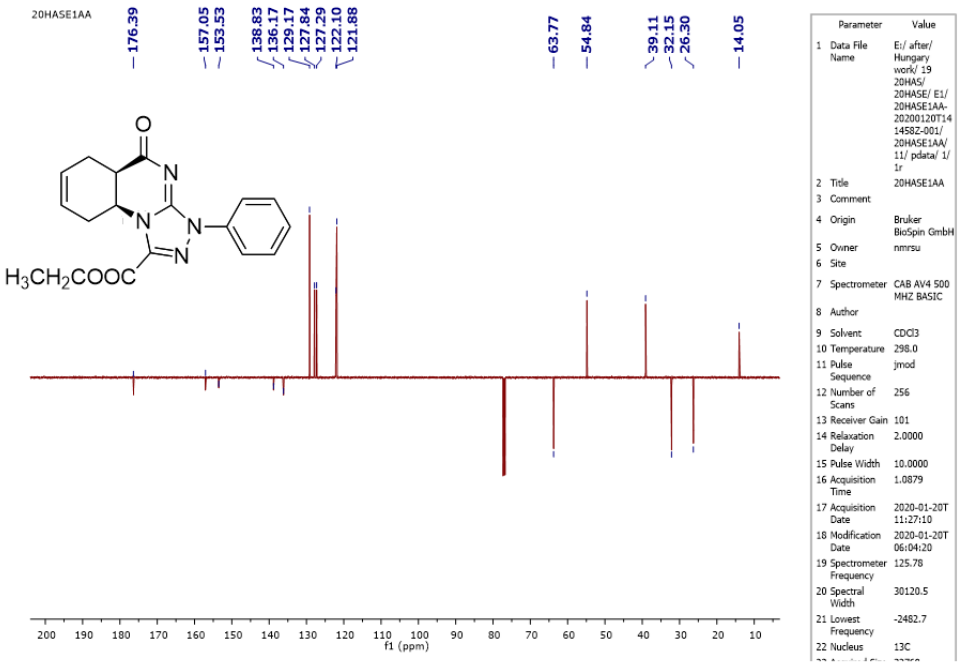
Crystallographic details of compound 5a **S28**

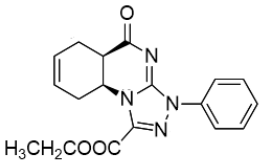
Copies of HRMS-ESI Spectra of compounds 4a-h and 5a-h **S29**



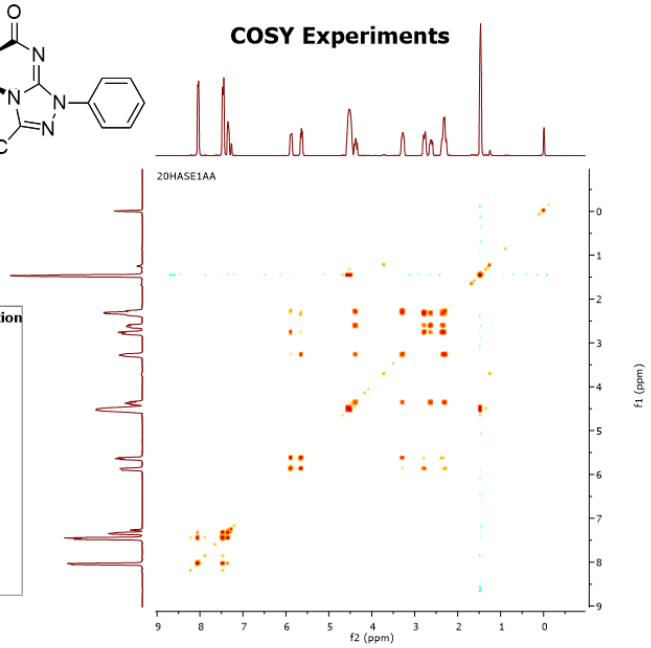
(4a*S**,8a*R**)-Ethyl 9-oxo-1-phenyl-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4a**)







COSY Experiments



H-H Correlation

f1 (ppm)	f2 (ppm)
4.36	2.29
4.38	2.63
2.62	2.34
4.54	1.48
7.45	7.33
5.88	2.81
4.28	3.26
5.64	3.29
2.79	2.33
5.90	5.63
3.27	2.30
8.04	7.44

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5	Owner	nmrsu
6	Site	
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8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	cosygpppqf
12	Number of Scans	1
13	Receiver Gain	101
14	Relaxation Delay	1.9508
15	Pulse Width	10.8400
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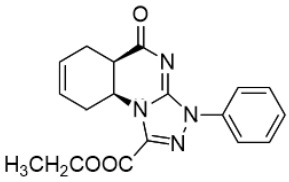
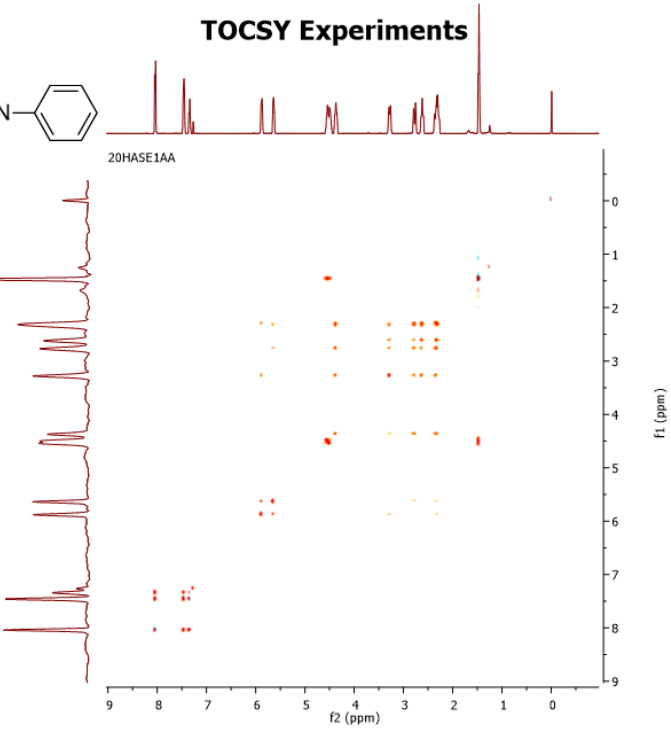
24	Spectral Size	(1024, 1024)



TOCSY Experiments



H-H Correction

f1 (ppm)	f2 (ppm)
5.88	2.75
4.52	1.46
5.64	3.28
4.37	2.77
4.37	2.33
8.04	7.35
4.37	2.62
5.64	2.62
4.52	1.48
4.37	3.28
5.64	2.77
5.88	2.79
8.04	7.46
5.88	2.30
5.64	2.34
5.88	3.28
5.88	2.62
5.88	5.64

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5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	mlevphpp
12	Number of Scans	8
13	Receiver Gain	101
14	Relaxation Delay	2.0000
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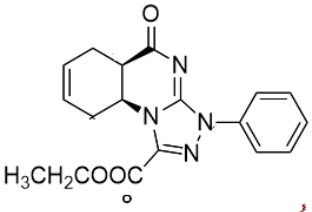
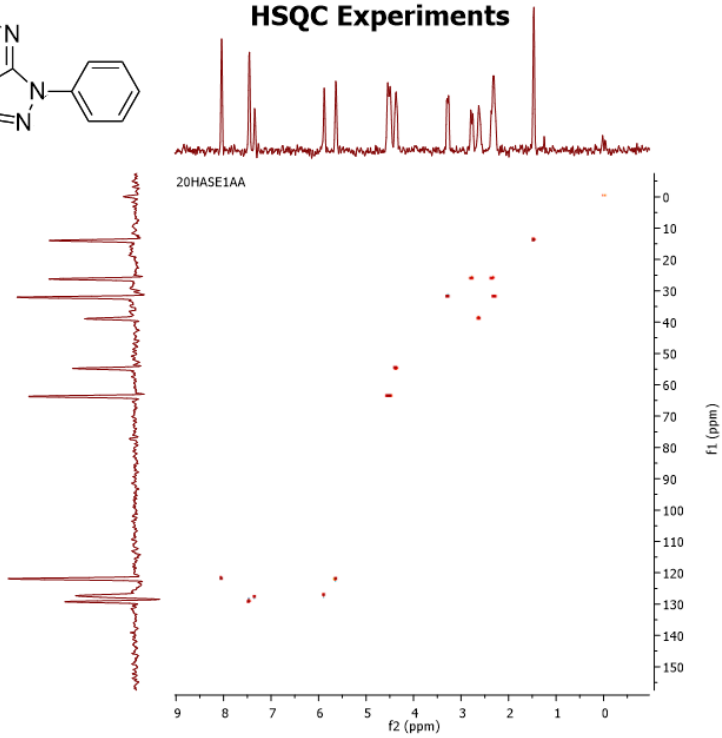


HSQC Experiments



C-H Correction

f1 (ppm)	f2 (ppm)
129.23	7.46
127.77	7.34
127.21	5.88
122.05	5.64
121.85	8.04
63.71	4.54
26.29	2.79
32.06	2.30
63.70	4.49
26.17	2.76
32.11	3.26
32.02	3.29
38.93	2.62
54.77	4.37
26.18	2.34
13.95	1.47

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9	Solvent	CDCl3
10	Temperature	298.0
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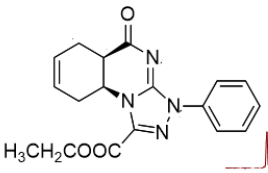

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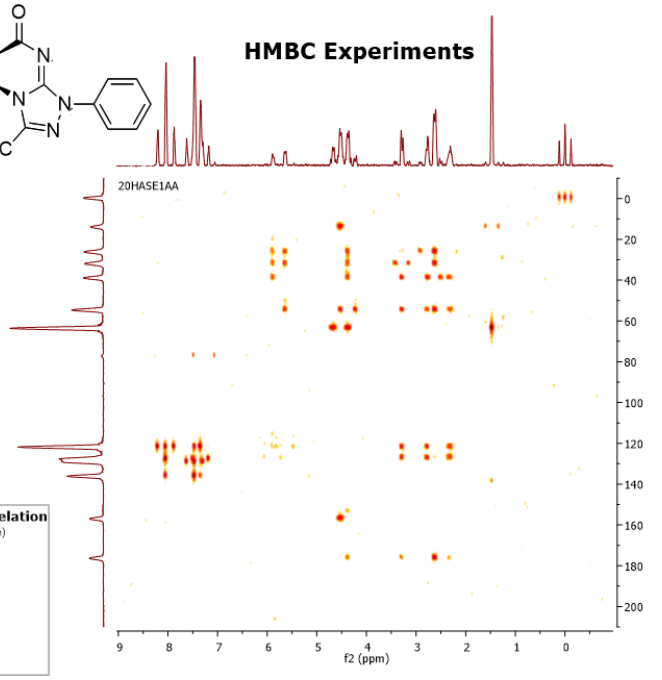

C-H^{3a} Correlation

f1 (ppm)	f2 (ppm)
174.21	4.38
156.13	4.38
63.54	4.38
38.67	4.38
31.93	4.38
26.13	4.38

	Parameter	Value (f2, f1)
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4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	hmbcgpndqf
12	Number of Scans	8
13	Receiver Gain	101
14	Relaxation Delay	1.5000
15	Pulse Width	10.8400
16	Acquisition Time	0.2048
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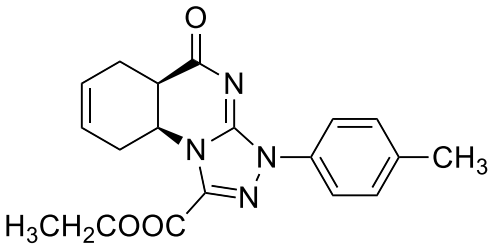
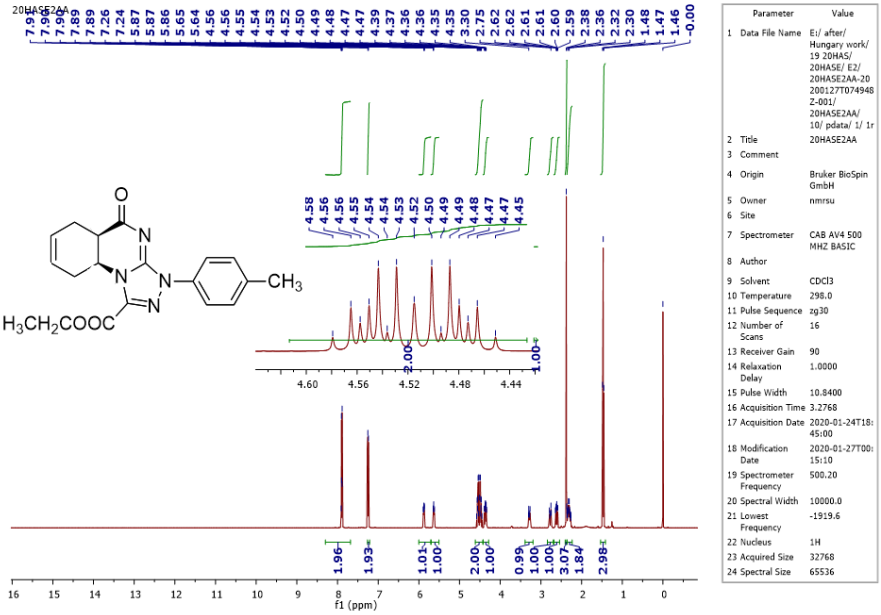


(4a*S**,8a*R**)-Ethyl 9-oxo-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4b**)



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8	Author	
9	Solvent	CDCl3
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12	Number of Scans	16
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14	Relaxation Delay	1.0000
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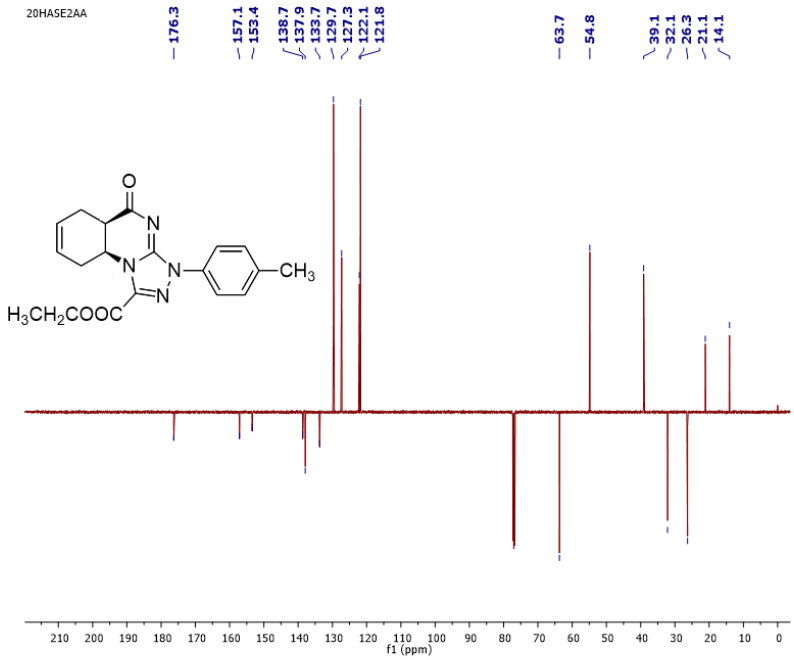

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5	Owner	nmrsu
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7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
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11	Pulse Sequence	jmod
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15	Pulse Width	10.0000
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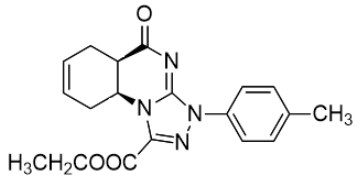
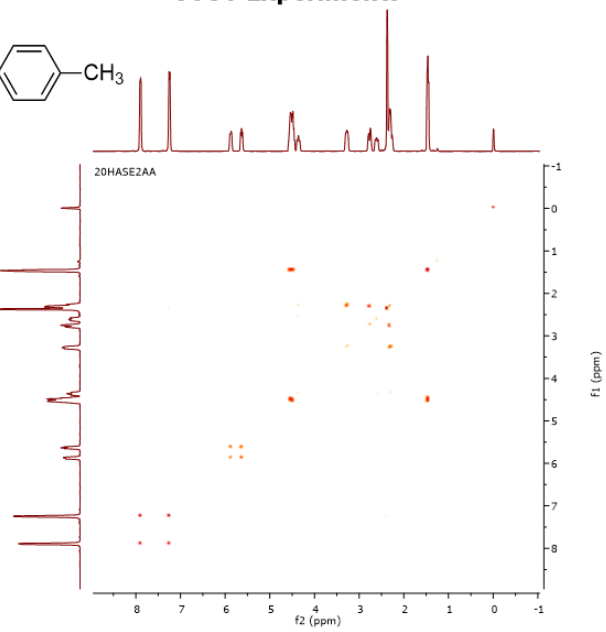


COSY Experiments



H-H Correlation	
f1 (ppm)	f2 (ppm)
2.78	2.32
3.28	2.29
4.51	1.46
5.88	5.63
7.89	7.25

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6	Site	
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8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	cosygpppqf
12	Number of Scans	1
13	Receiver Gain	101
14	Relaxation Delay	1.9488
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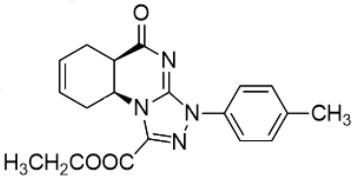
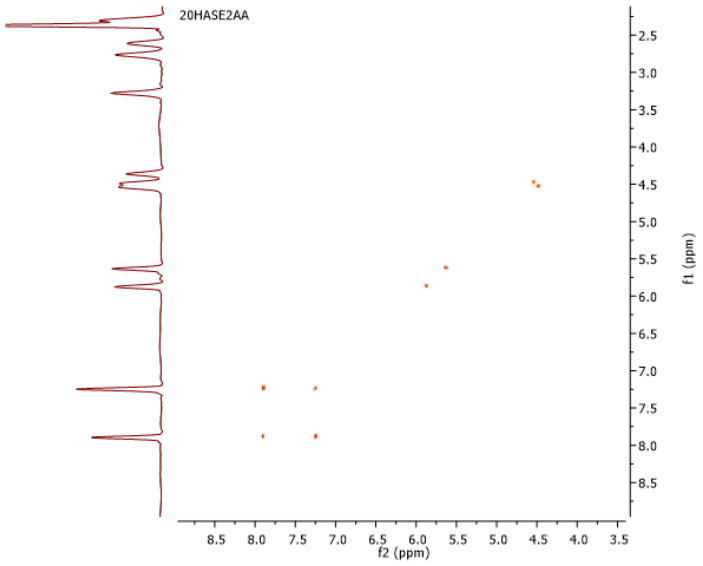


TOCSY Experiments



H-H Correlation	
f1 (ppm)	f2 (ppm)
4.36	3.27
4.36	2.76
4.36	2.60
4.36	2.32
4.51	1.46
4.53	1.46
5.63	4.36
5.63	3.28
5.63	2.32
5.63	2.60
5.63	2.76
5.88	5.63
5.88	4.36
5.88	2.29
5.88	2.61
5.88	2.77
5.88	3.27
7.89	7.25

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4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	mlevphpp
12	Number of Scans	8
13	Receiver Gain	101
14	Relaxation Delay	1.9980
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22	Nucleus	(1H, 1H)
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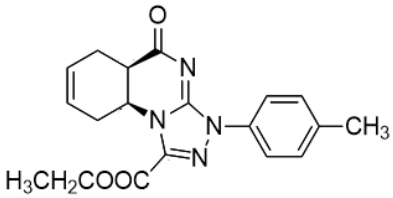
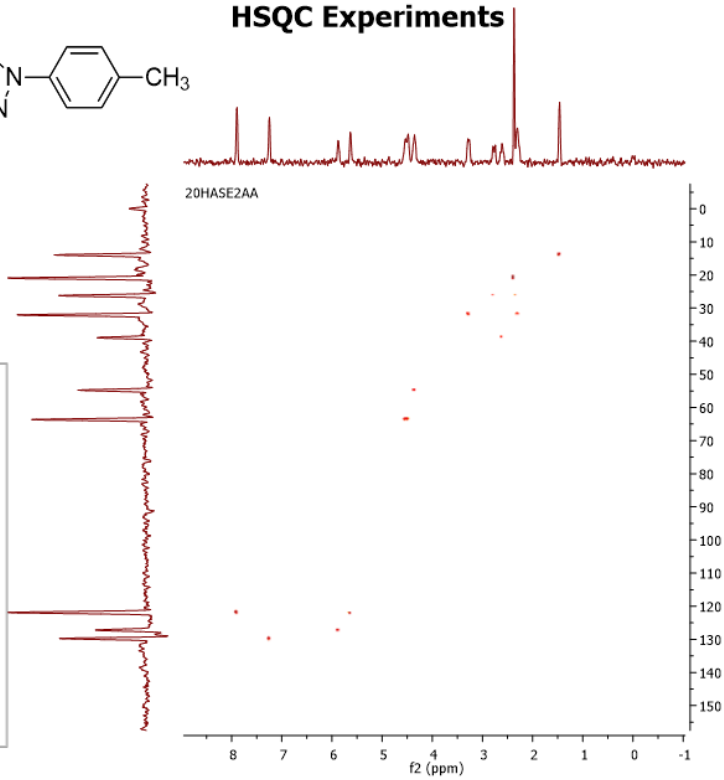


HSQC Experiments



C-H Correlation	
f1 (ppm)	f2 (ppm)
13.95	1.46
20.89	2.37
26.21	2.77
26.21	2.33
32.02	2.29
32.03	3.29
38.95	2.61
54.76	4.35
63.63	4.48
121.85	7.89
122.01	5.63
127.18	5.87
129.76	7.25

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6	Site	
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8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	hsqcetgp
12	Number of Scans	2
13	Receiver Gain	101
14	Relaxation Delay	1.5000
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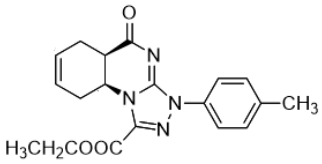
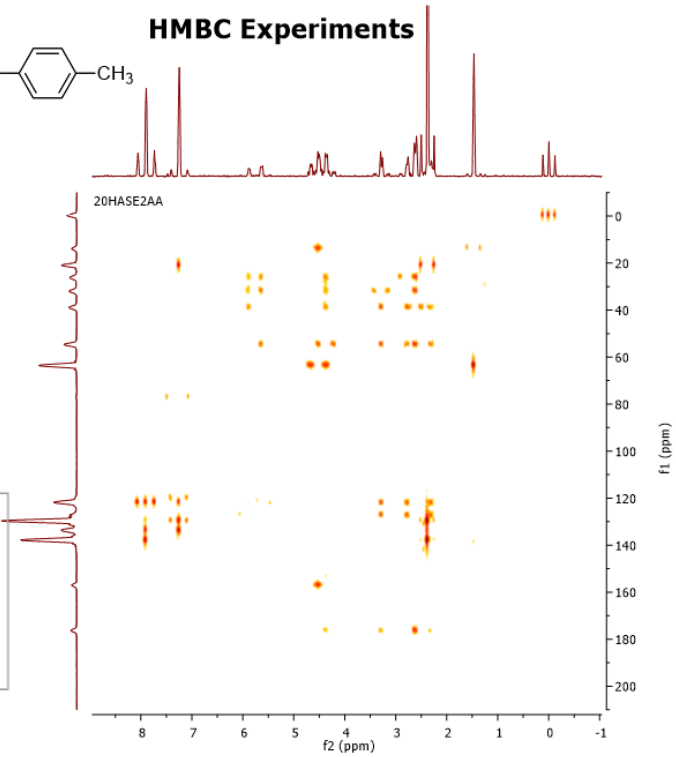
19	Spectrometer Frequency	(500.20, 125.78)
20	Spectral Width	(5000.0, 20752.3)
21	Lowest Frequency	(-520.2, -943.0)
22	Nucleus	(1H, 13C)
23	Acquired Size	(512, 256)
24	Spectral Size	(1024, 1024)

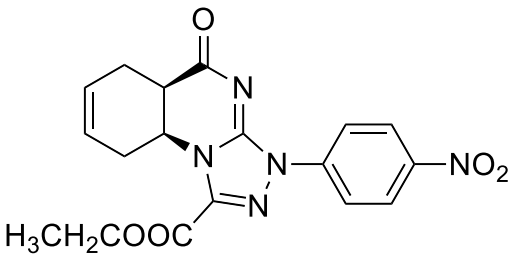


HMBC Experiments

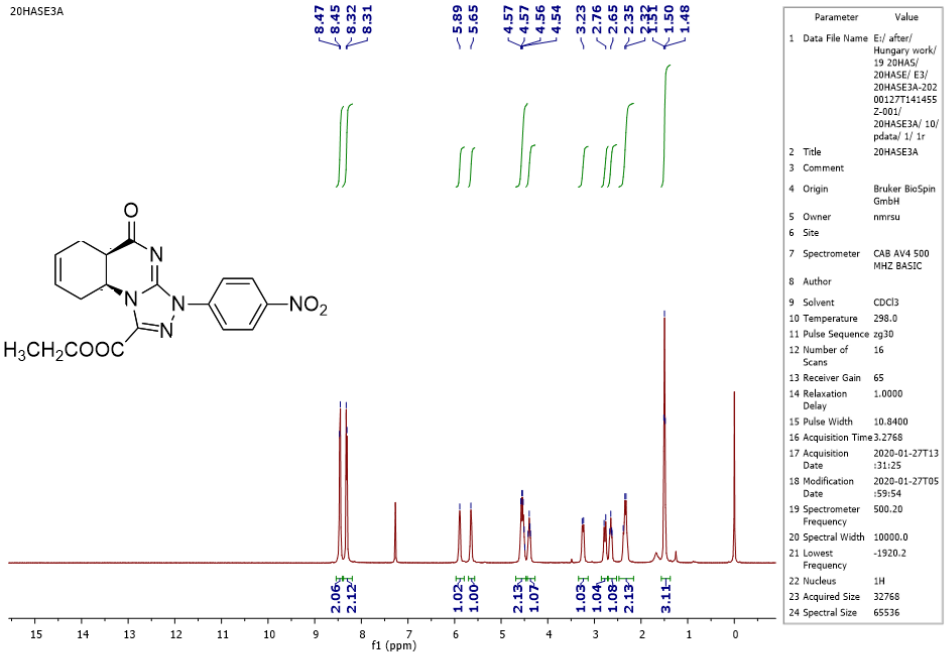


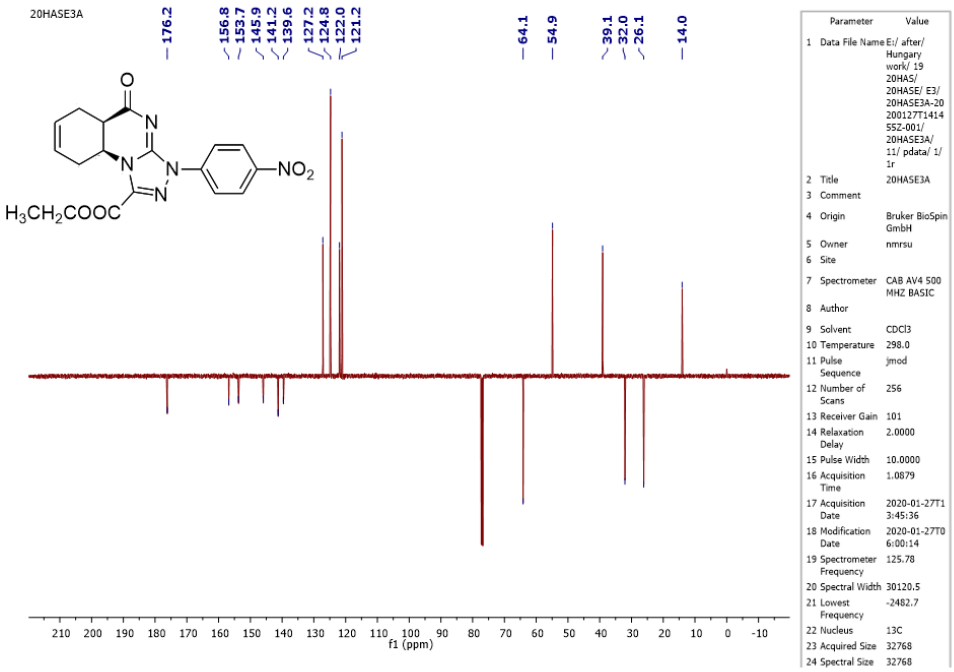
C-H9a Correlation	
f1 (ppm)	f2 (ppm)
26.24	4.35
31.78	4.36
38.70	4.36
61.12	4.37
153.31	4.36
176.19	4.36

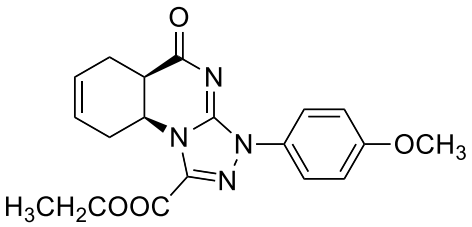
	Parameter	Value (f2, f1)
1	Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E2/ 20HASE2AA-20 200127T074948 Z-001/ 20HASE2AA/ 16/ pdata/ 1/ 2rr
2	Title	20HASE2AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	hmbcgpndqf
12	Number of Scans	8
13	Receiver Gain	101
14	Relaxation Delay	1.5000
15	Pulse Width	10.8400
16	Acquisition Time	0.2048
17	Acquisition Date	2020-01-24T21:57:30
18	Modification Date	2020-01-27T00:15:44
19	Spectrometer Frequency	(500.20, 125.78)
20	Spectral Width	(5000.0, 27672.1)
21	Lowest Frequency	(-520.2, -1258.5)
22	Nucleus	(1H, 13C)
23	Acquired Size	(1024, 128)
24	Spectral Size	(2048, 1024)



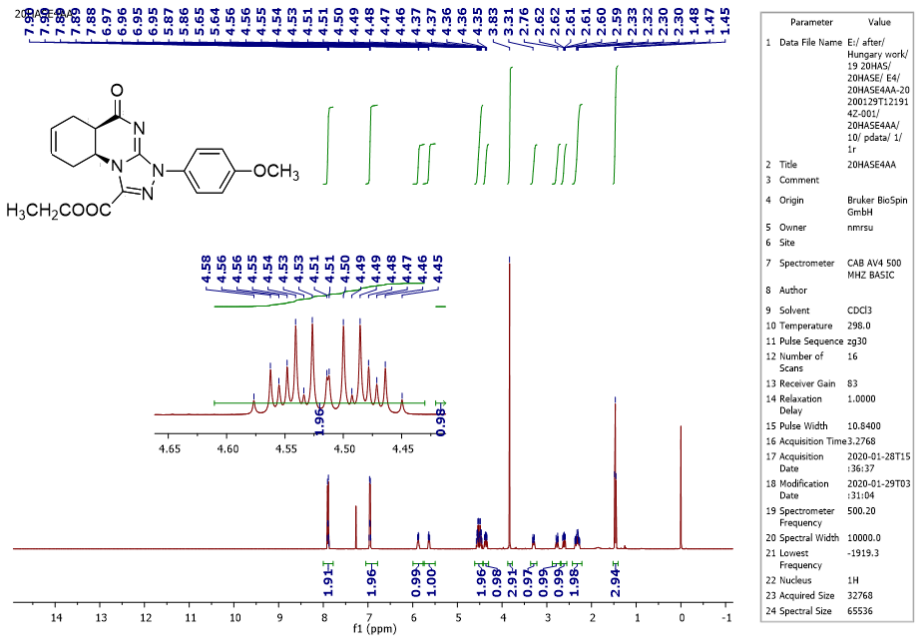
(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-nitrophenyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4c**)



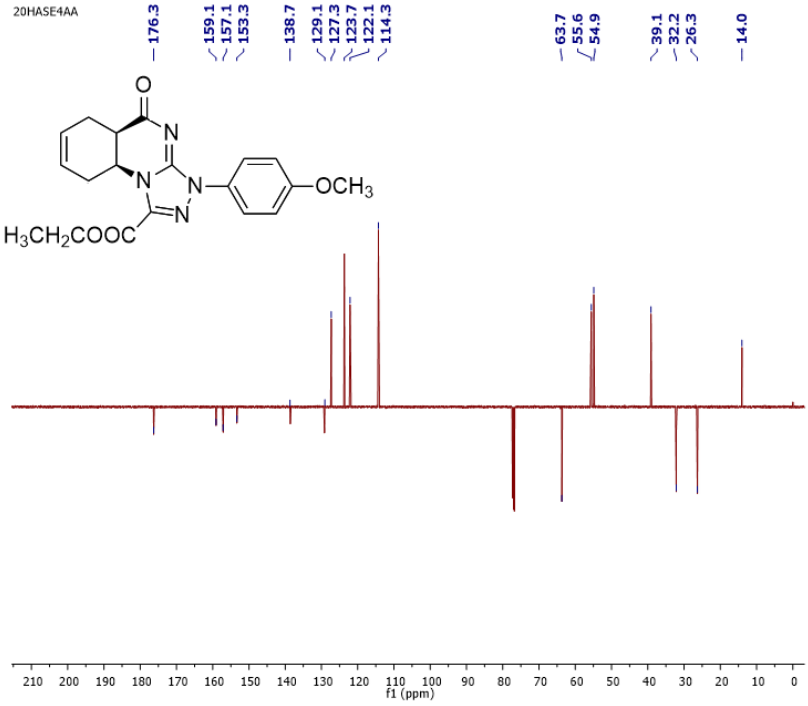




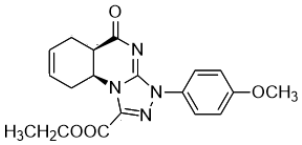
(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-methoxyphenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo-[4,3-*a*]quinazoline-3-carboxylate (**4d**)



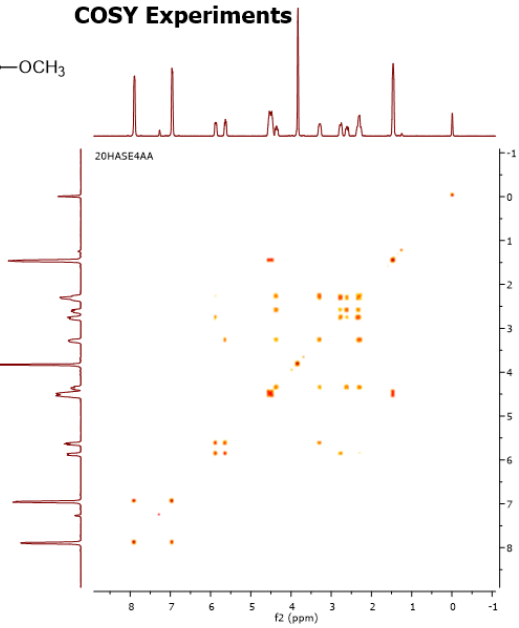
	Parameter	Value
1	Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E4/ 20HASE4AA-20200129T121914Z-001/ 20HASE4AA/ 10/ pdata/ 1/ 1r
2	Title	20HASE4AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	zg30
12	Number of Scans	16
13	Receiver Gain	83
14	Relaxation Delay	1.0000
15	Pulse Width	10.8400
16	Acquisition Time	3.2768
17	Acquisition Date	2020-01-28T15:36:37
18	Modification Date	2020-01-29T03:31:04
19	Spectrometer Frequency	500.20
20	Spectral Width	10000.0
21	Lowest Frequency	-1919.3
22	Nucleus	1H
23	Acquired Size	32768
24	Spectral Size	65536



	Parameter	Value
1	Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E4/ 20HASE4AA-20200129T121914Z-001/ 20HASE4AA/ 11/ pdata/ 1/ 1r
2	Title	20HASE4AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	jmod
12	Number of Scans	256
13	Receiver Gain	101
14	Relaxation Delay	2.0000
15	Pulse Width	10.0000
16	Acquisition Time	1.0879
17	Acquisition Date	2020-01-28T15:50:47
18	Modification Date	2020-01-29T03:29:24
19	Spectrometer Frequency	125.78
20	Spectral Width	30120.5
21	Lowest Frequency	-2482.7
22	Nucleus	13C
23	Acquired Size	32768
24	Spectral Size	32768

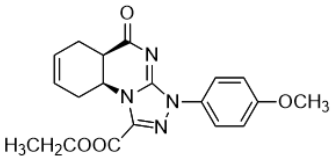


COSY Experiments

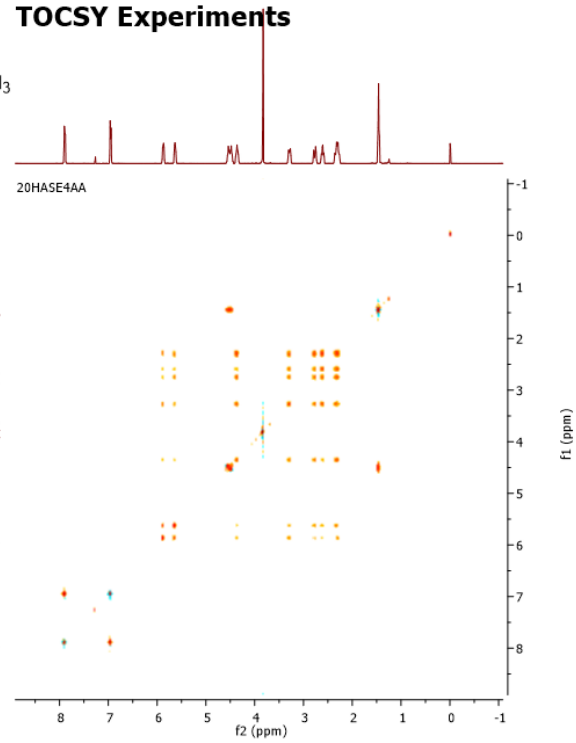


H-H correlation	
f1 (ppm)	f2 (ppm)
2.61	2.32
2.77	2.60
2.77	2.34
3.29	2.29
4.35	3.29
4.36	2.30
4.36	2.61
4.51	1.46
5.63	3.29
5.86	2.28
5.88	2.77
5.88	5.63
7.90	6.95

	Parameter	Value (f2, f1)
1	Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E4/ 20HASE4AA-20200129T121914Z-001/ 20HASE4AA/ 12/ pdata/ 1/ 2rr
2	Title	20HASE4AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	cosygpppqf
12	Number of Scans	1
13	Receiver Gain	101
14	Relaxation Delay	1.9508
15	Pulse Width	10.8400
16	Acquisition Time	0.2048
17	Acquisition Date	2020-01-28T15:56:36
18	Modification Date	2020-01-29T03:29:34
19	Spectrometer Frequency	(500.20, 500.20)
20	Spectral Width	(5000.0, 5000.0)
21	Lowest Frequency	(-544.7, -544.7)
22	Nucleus	(1H, 1H)
23	Acquired Size	(1024, 128)
24	Spectral Size	(1024, 1024)

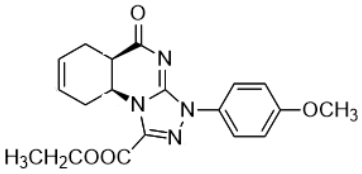


TOCSY Experiments

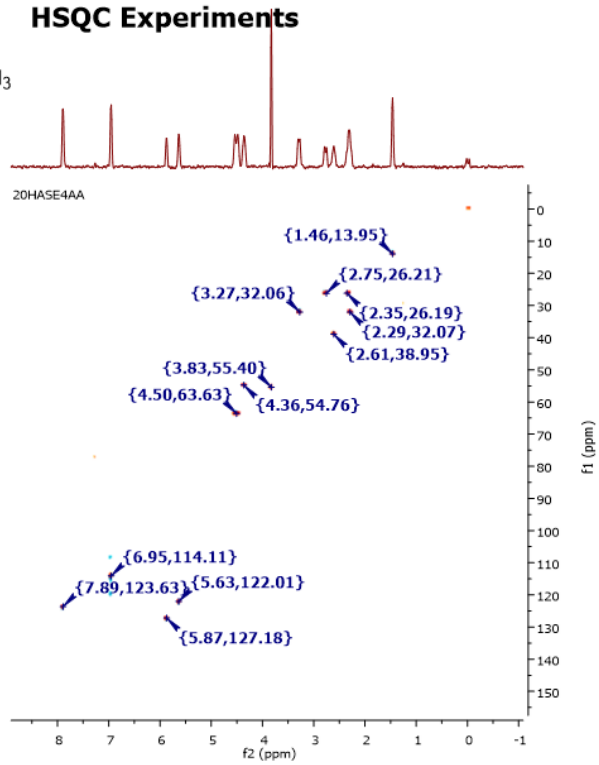


f1 (ppm)	f2 (ppm)
2.61	2.31
2.77	2.32
3.26	2.29
3.29	2.32
3.29	2.60
3.29	2.76
4.36	3.28
4.36	2.32
4.36	2.77
4.37	2.59
4.52	1.46
5.63	2.32
5.63	2.61
5.63	2.77
5.63	3.29
5.88	3.28
5.88	2.77
5.88	2.60
5.88	2.30
6.96	7.89
7.89	6.95

	Parameter	Value (f2, f1)
1	Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E4/ 20HASE4AA-20200129T121914Z-001/ 20HASE4AA/ 14/ pdata/ 1/ 2rr
2	Title	20HASE4AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	mlevphpp
12	Number of Scans	8
13	Receiver Gain	101
14	Relaxation Delay	2.0000
15	Pulse Width	10.8400
16	Acquisition Time	0.2048
17	Acquisition Date	2020-01-28T18:02:47
18	Modification Date	2020-01-29T03:31:22
19	Spectrometer Frequency	(500.20, 500.20)
20	Spectral Width	(5000.0, 5000.0)
21	Lowest Frequency	(-544.7, -544.7)
22	Nucleus	(1H, 1H)
23	Acquired Size	(1024, 256)
24	Spectral Size	(1024, 1024)



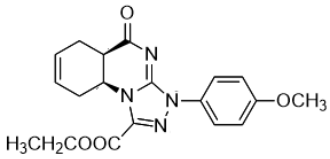
HSQC Experiments



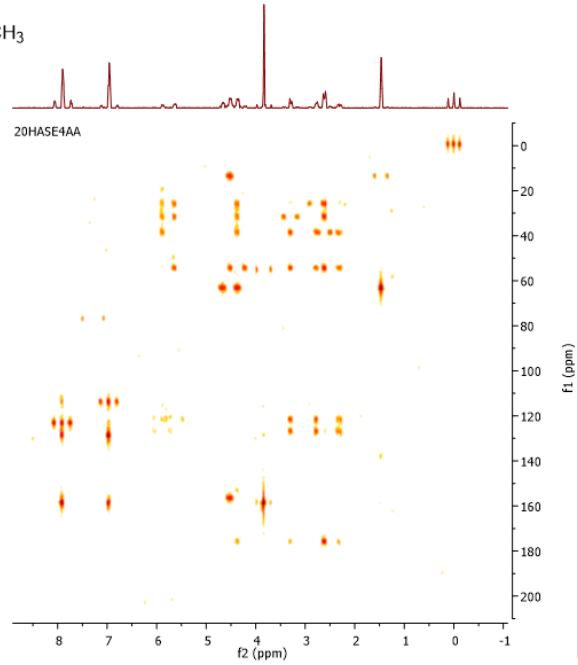
H-H Correlation

f1 (ppm)	f2 (ppm)
13.95	1.46
26.19	2.35
26.21	2.75
32.06	3.27
32.07	2.29
38.95	2.61
54.76	4.36
55.40	3.83
63.63	4.50
114.11	6.95
122.01	5.63
123.63	7.89
127.18	5.87

	Parameter	Value (f2, f1)
1	Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E4/ 20HASE4AA-20 200129T121914 Z-001/ 20HASE4AA/ 15/ pdata/ 1/ 2rr
2	Title	20HASE4AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	hsqcetgp
12	Number of Scans	2
13	Receiver Gain	101
14	Relaxation Delay	1.5000
15	Pulse Width	10.8400
16	Acquisition Time	0.1024
17	Acquisition Date	2020-01-28T18: 17:44
18	Modification Date	2020-01-29T03: 32:10
19	Spectrometer Frequency	(500.20, 125.78)
20	Spectral Width	(5000.0, 20752.3)
21	Lowest Frequency	(-544.7, -943.0)
22	Nucleus	(1H, 13C)
23	Acquired Size	(512, 256)
24	Spectral Size	(1024, 1024)



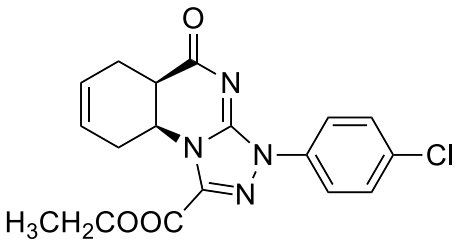
HMBC Experiments



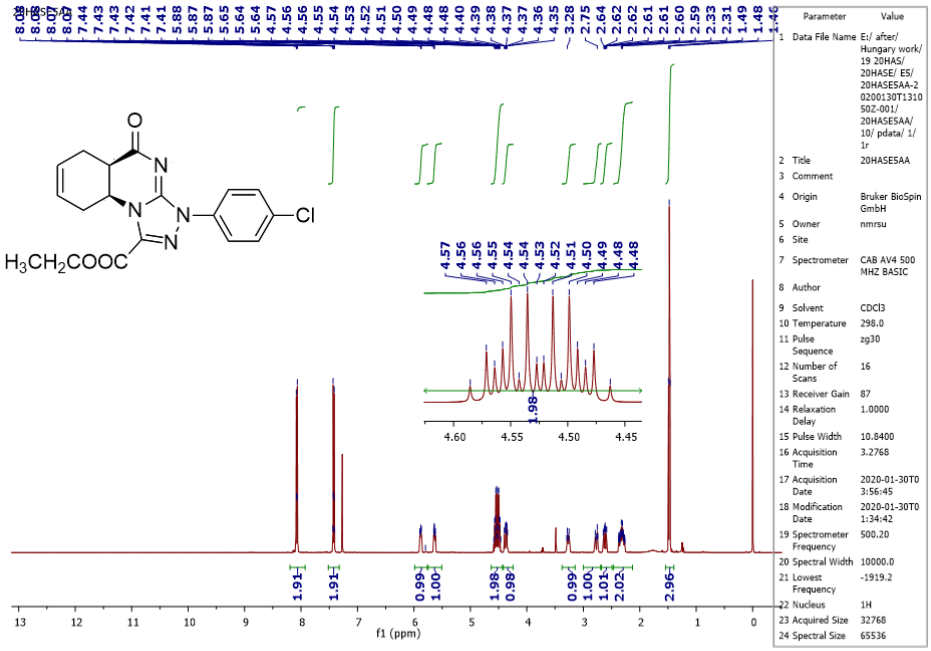
C-H9a Correlation

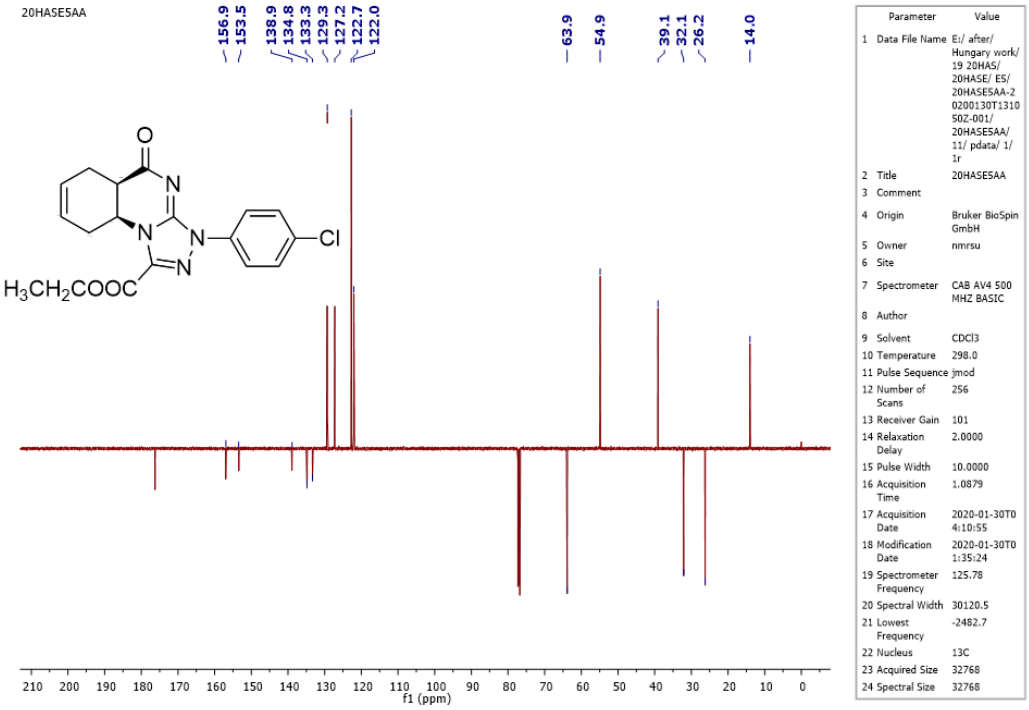
f1 (ppm)	f2 (ppm)
26.32	4.37
31.77	4.37
38.71	4.37
63.48	4.37
155.44	4.37
178.42	4.37

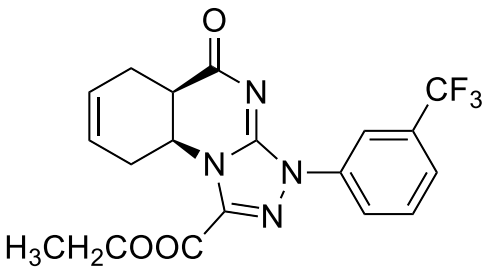
	Parameter	Value (f2, f1)
1	Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E4/ 20HASE4AA-20 200129T12191 4Z-001/ 20HASE4AA/ 16/ pdata/ 1/ 2rr
2	Title	20HASE4AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	298.0
11	Pulse Sequence	hmbcgpndqf
12	Number of Scans	8
13	Receiver Gain	101
14	Relaxation Delay	1.5000
15	Pulse Width	10.8400
16	Acquisition Time	0.2048
17	Acquisition Date	2020-01-28T18 :49:12
18	Modification Date	2020-01-29T03 :32:20
19	Spectrometer Frequency	(500.20, 125.78)
20	Spectral Width	(5000.0, 27672.1)
21	Lowest Frequency	(-544.7, -1258.5)
22	Nucleus	(1H, 13C)
23	Acquired Size	(1024, 128)
24	Spectral Size	(2048, 1024)



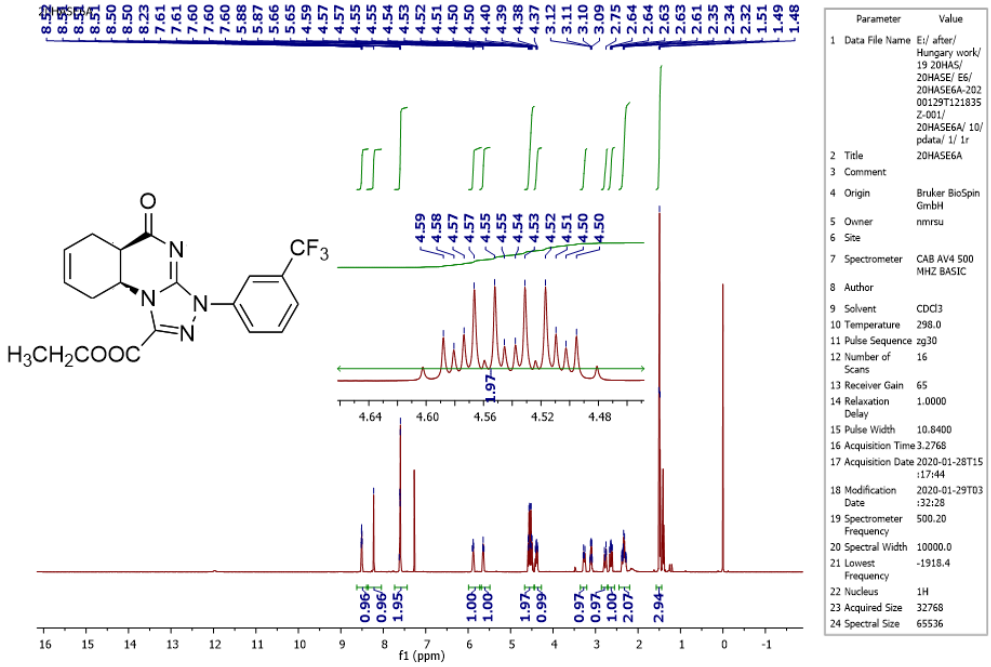
(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-chlorophenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4e**)



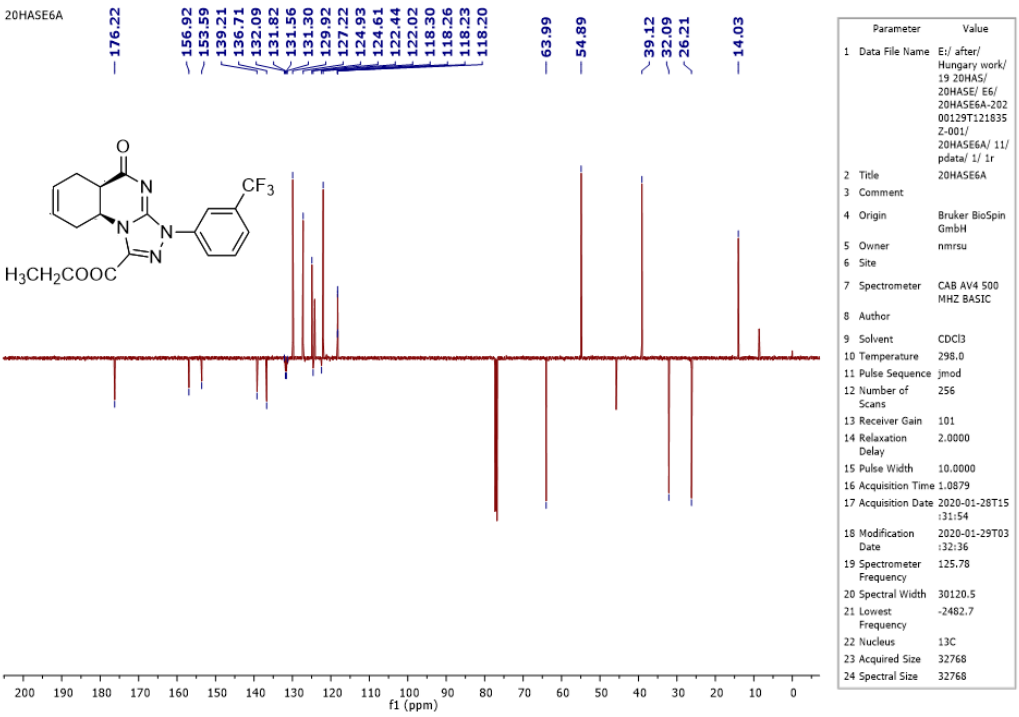




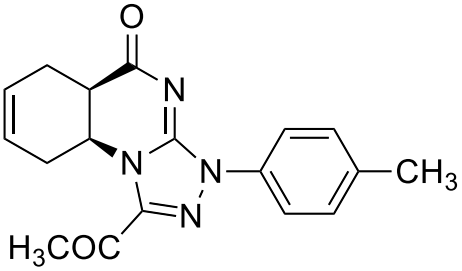
(4a*S**,8a*R**)-Ethyl 9-oxo-1-(3-(trifluoromethyl)phenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4f**)



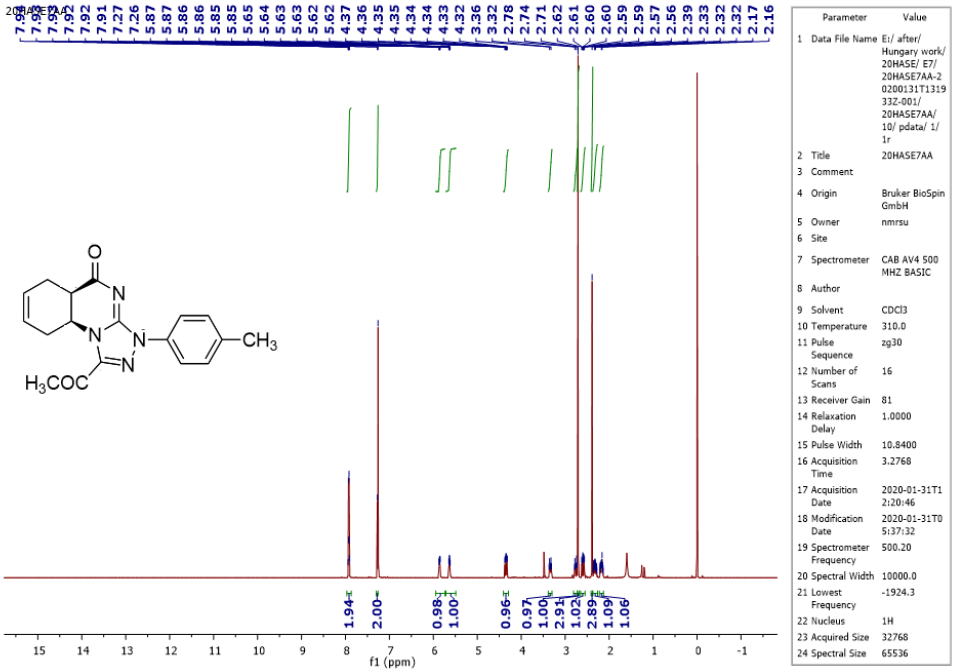
Parameter	Value
1 Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E6/ 20HASE6A-202 00129T121835 Z-001/ 20HASE6A/ 10/ pdata/ 1/ 1r
2 Title	20HASE6A
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmrsu
6 Site	
7 Spectrometer	CAB AV4 500 MHZ BASIC
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zg30
12 Number of Scans	16
13 Receiver Gain	65
14 Relaxation Delay	1.0000
15 Pulse Width	10.8400
16 Acquisition Time	3.2768
17 Acquisition Date	2020-01-28T15:17:44
18 Modification Date	2020-01-29T03:32:28
19 Spectrometer Frequency	500.20
20 Spectral Width	10000.0
21 Lowest Frequency	-1918.4
22 Nucleus	1H
23 Acquired Size	32768
24 Spectral Size	65536

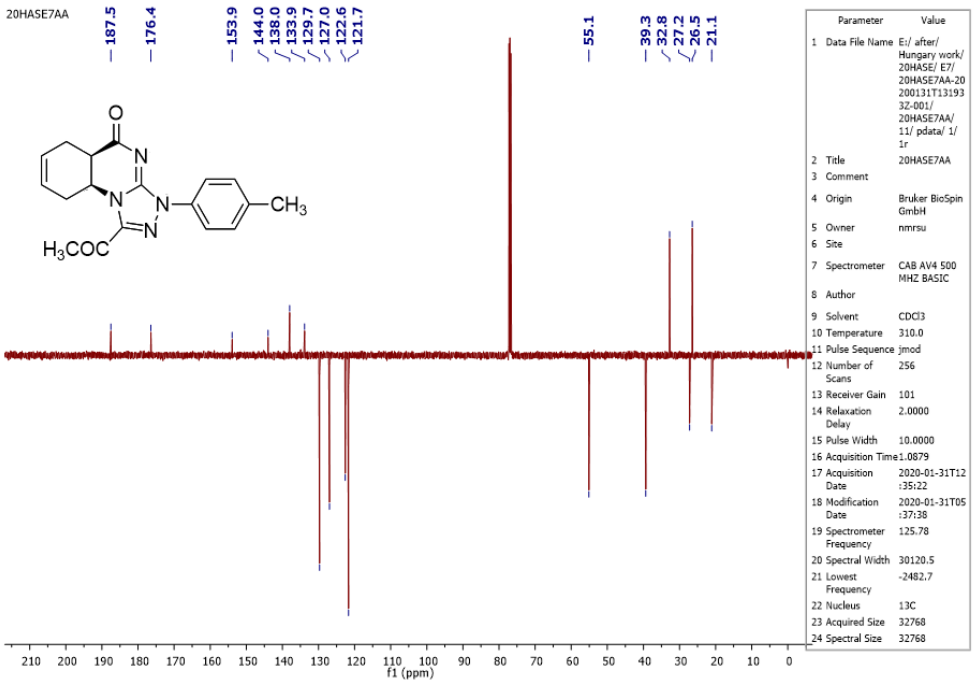


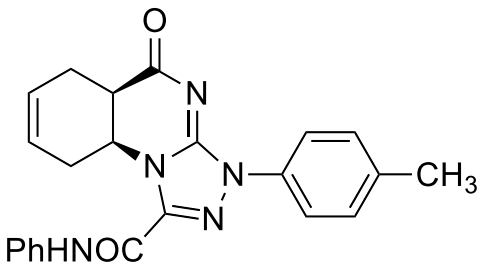
Parameter	Value
1 Data File Name	E:/ after/ Hungary work/ 19 20HAS/ 20HASE/ E6/ 20HASE6A-202 00129T121835 Z-001/ 20HASE6A/ 11/ pdata/ 1/ 1r
2 Title	20HASE6A
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmrsu
6 Site	
7 Spectrometer	CAB AV4 500 MHZ BASIC
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	jmod
12 Number of Scans	256
13 Receiver Gain	101
14 Relaxation Delay	2.0000
15 Pulse Width	10.0000
16 Acquisition Time	1.0879
17 Acquisition Date	2020-01-28T15:31:54
18 Modification Date	2020-01-29T03:32:36
19 Spectrometer Frequency	125.78
20 Spectral Width	30120.5
21 Lowest Frequency	-2482.7
22 Nucleus	13C
23 Acquired Size	32768
24 Spectral Size	32768



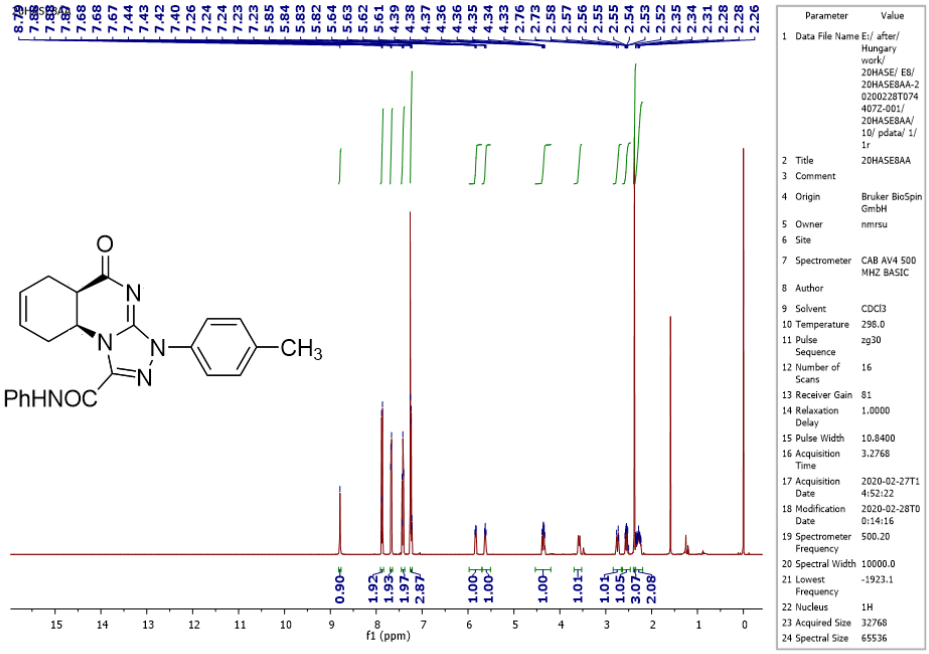
(4a*S**,8a*R**)-3-Acetyl-1-(*p*-tolyl)-4a,5,8,9-tetrahydro[1,2,4]triazolo[4,3-*a*]quinazoline-9(1*H*)-one (**4g**)

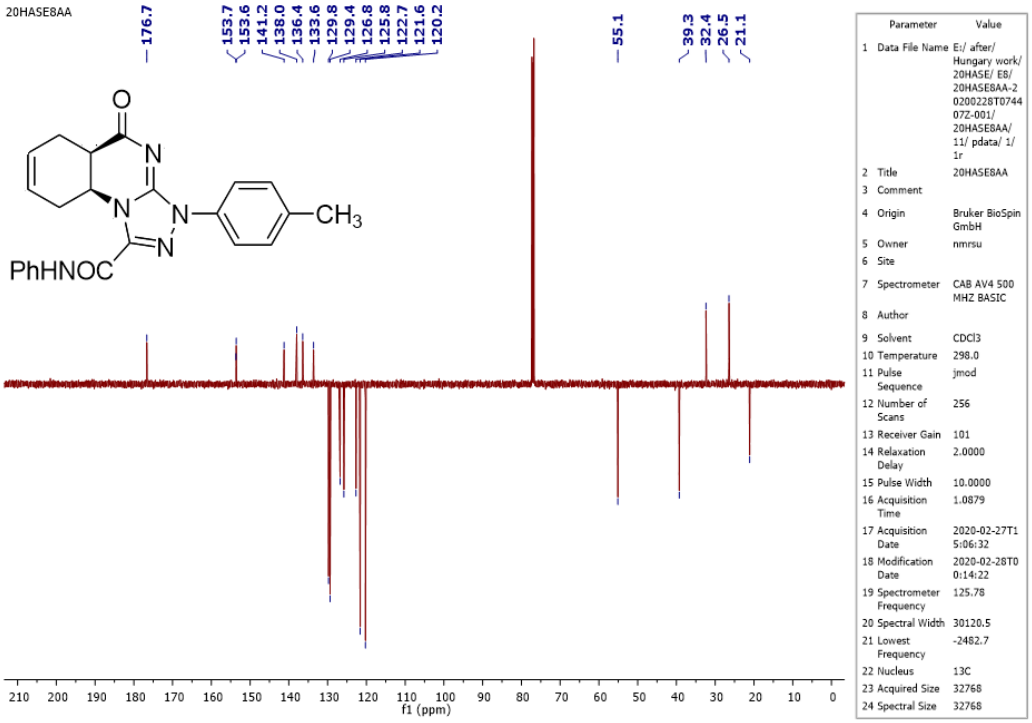


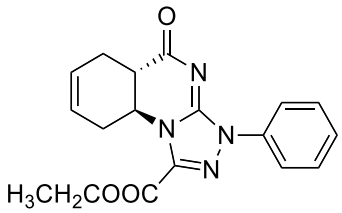




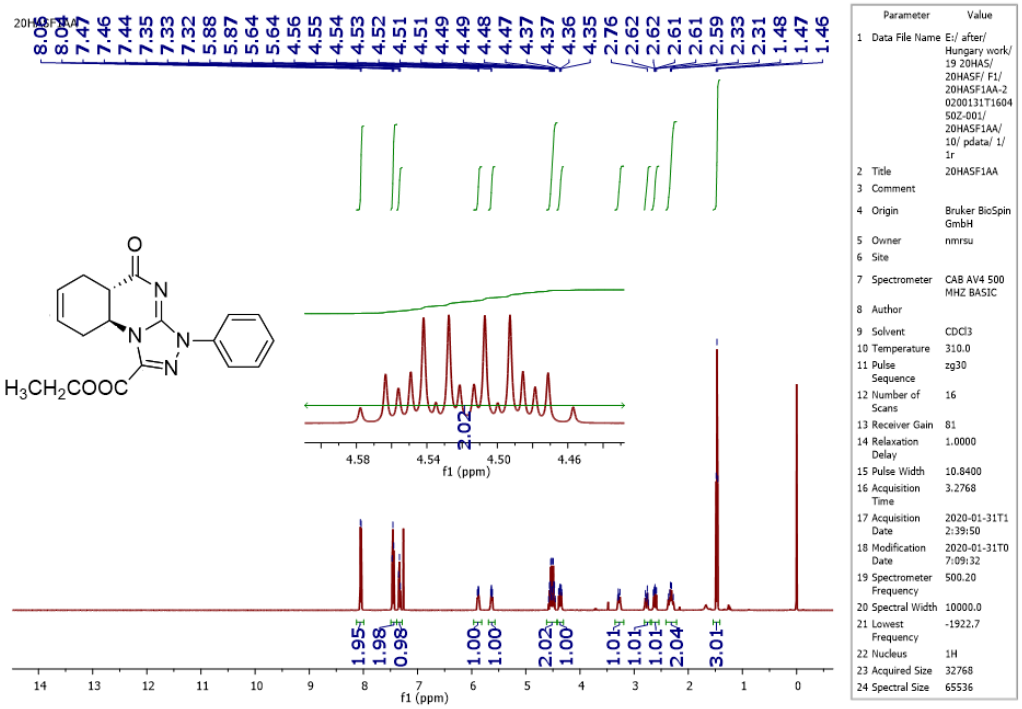
(4a*S**,8a*R**)-9-Oxo-*N*-Phenyl-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxamide (**4h**)







(4a*S**,8a*S**)-Ethyl 9-oxo-1-phenyl-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-a]quinazoline-3-carboxylate (**5a**)



	Parameter	Value
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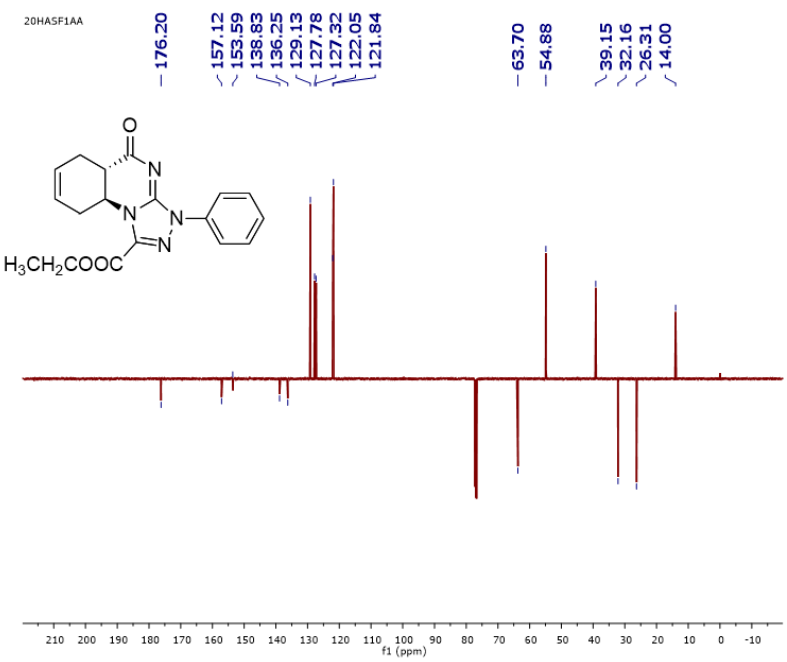
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	310.0
11	Pulse Sequence	zg30
12	Number of Scans	16
13	Receiver Gain	81
14	Relaxation Delay	1.0000
15	Pulse Width	10.8400
16	Acquisition Time	3.2768
17	Acquisition Date	2020-01-31T12:39:50
18	Modification Date	2020-01-31T07:09:32
19	Spectrometer Frequency	500.20
20	Spectral Width	10000.0
21	Lowest Frequency	-1922.7
22	Nucleus	1H
23	Acquired Size	32768
24	Spectral Size	65536



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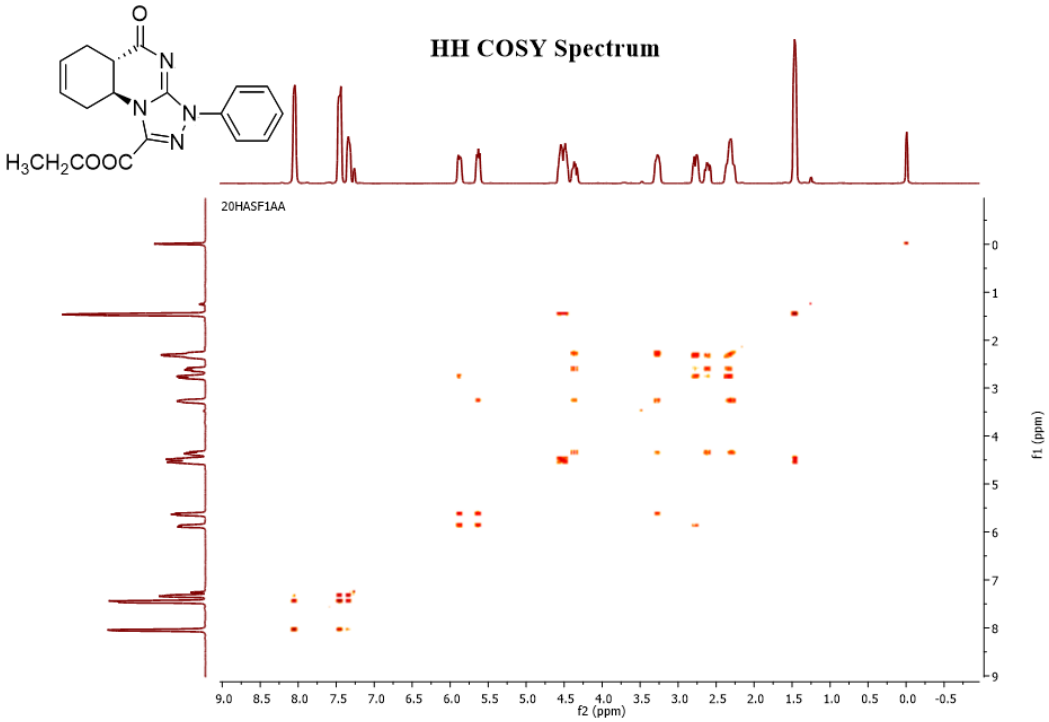
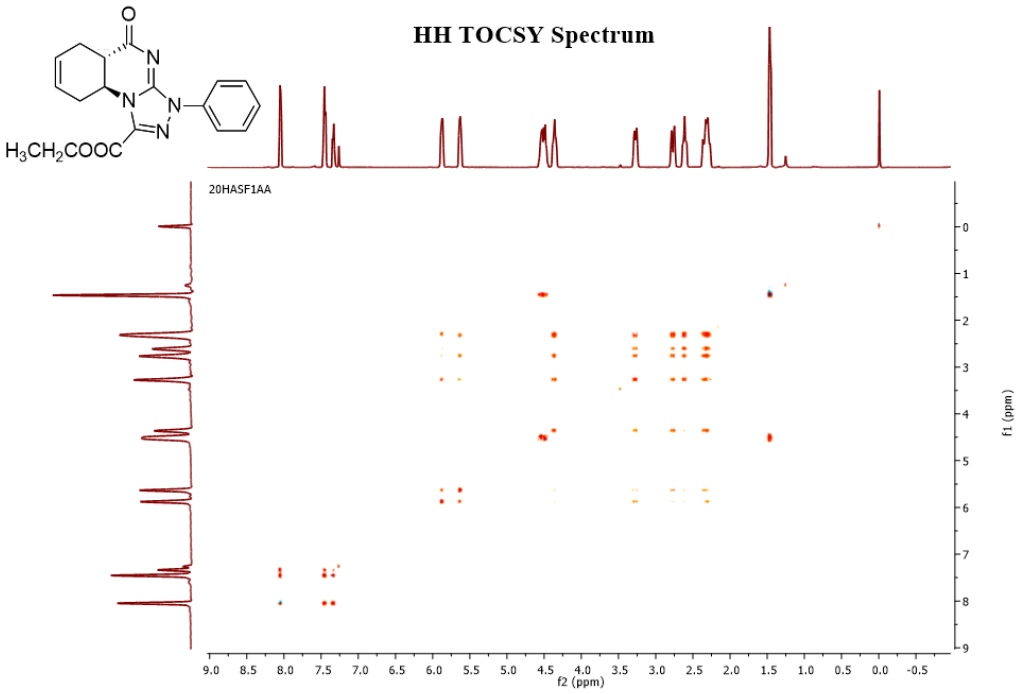
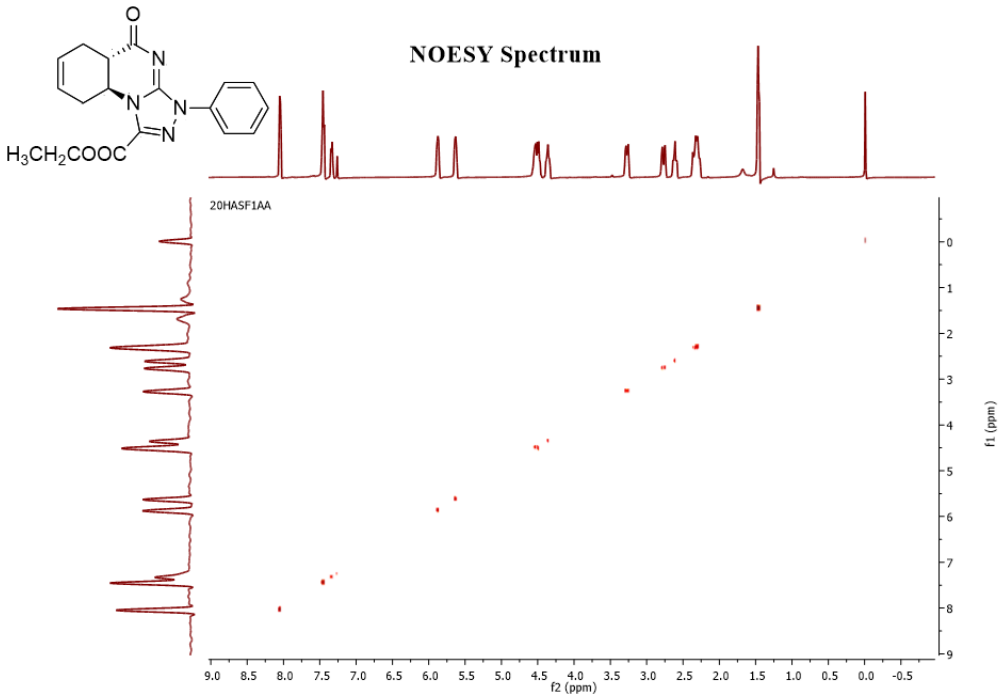
2	Title	20HASF1AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	310.0
11	Pulse Sequence	jmod
12	Number of Scans	256
13	Receiver Gain	101
14	Relaxation Delay	2.0000
15	Pulse Width	10.0000
16	Acquisition Time	1.0879
17	Acquisition Date	2020-01-31T12:54:15
18	Modification Date	2020-01-31T07:09:40
19	Spectrometer Frequency	125.78
20	Spectral Width	30120.5
21	Lowest Frequency	-2482.7
22	Nucleus	13C
23	Acquired Size	32768
24	Spectral Size	32768


HH COSY Spectrum
20HASF1AA
f2 (ppm)
f1 (ppm)


HH TOCSY Spectrum
20HASF1AA
f2 (ppm)
f1 (ppm)


NOESY Spectrum
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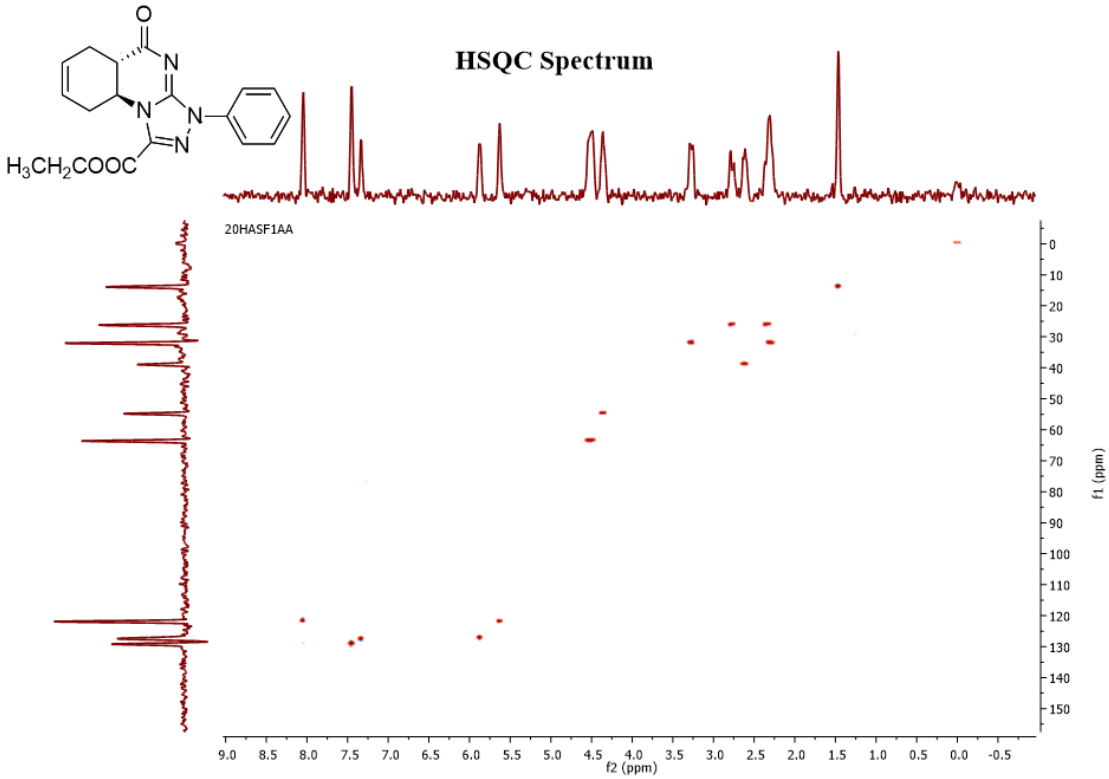
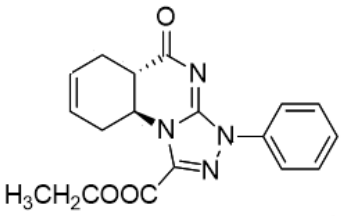
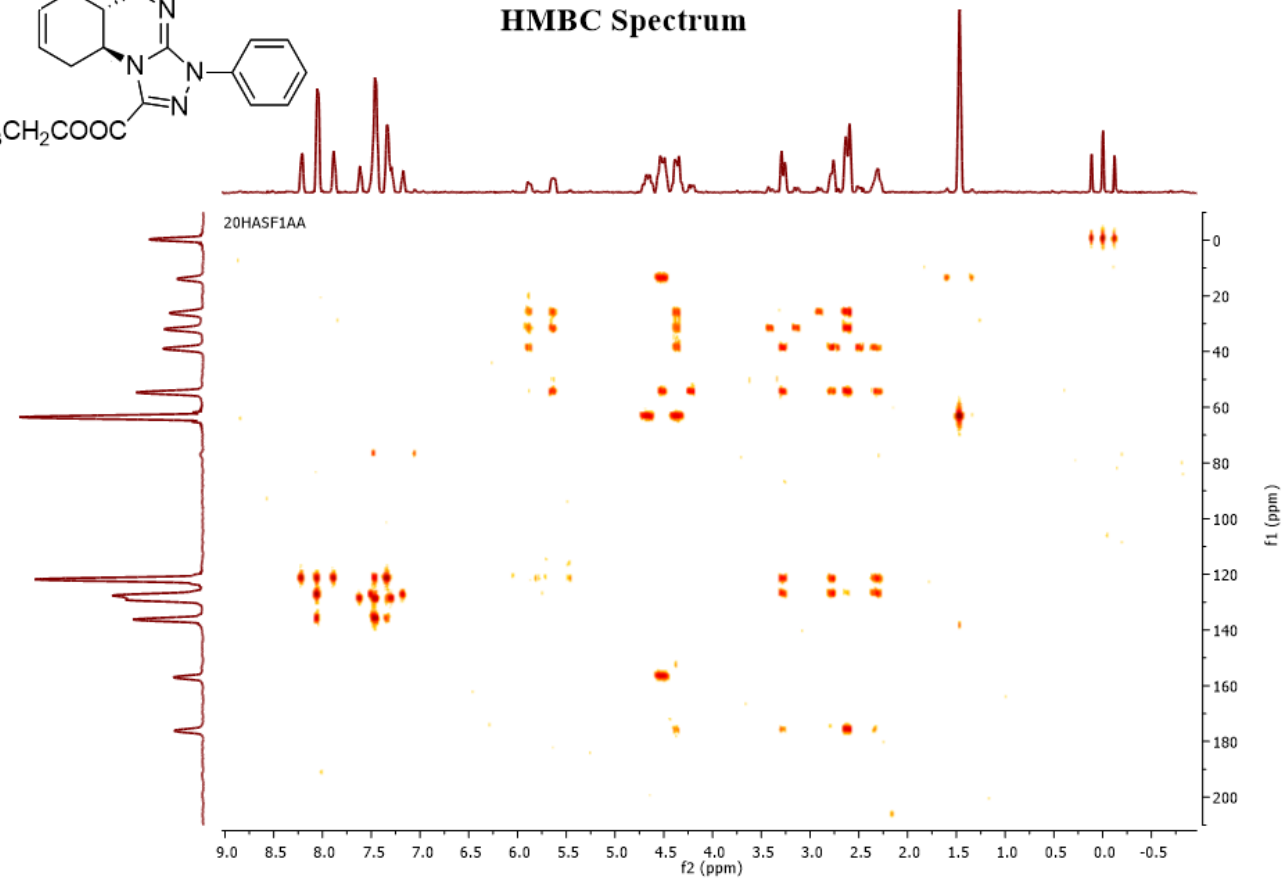
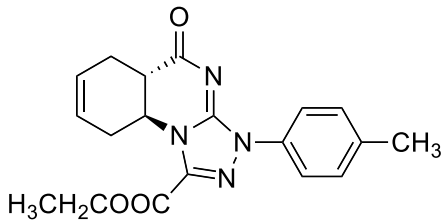
f2 (ppm)
f1 (ppm)


HSQC Spectrum
20HASF1AA
f2 (ppm)
f1 (ppm)

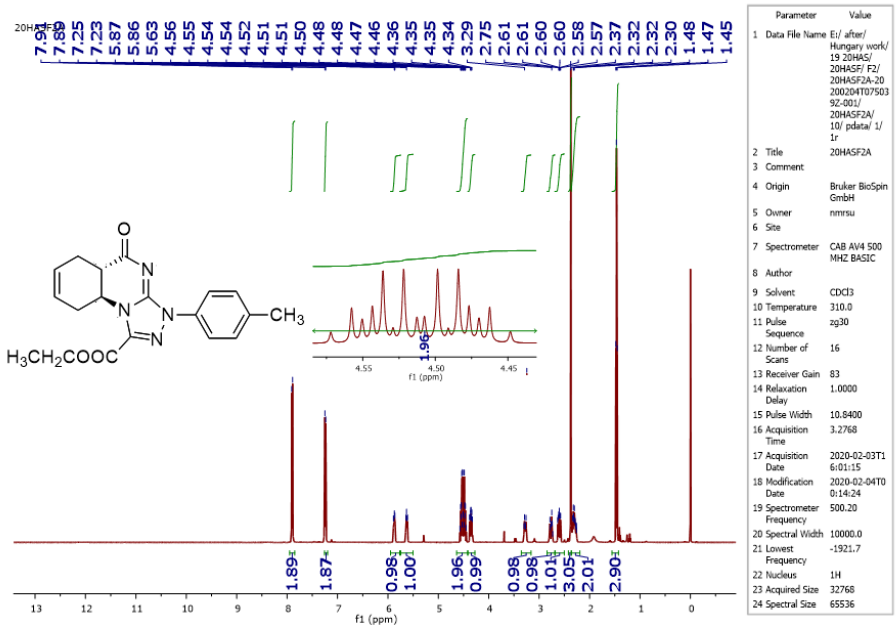


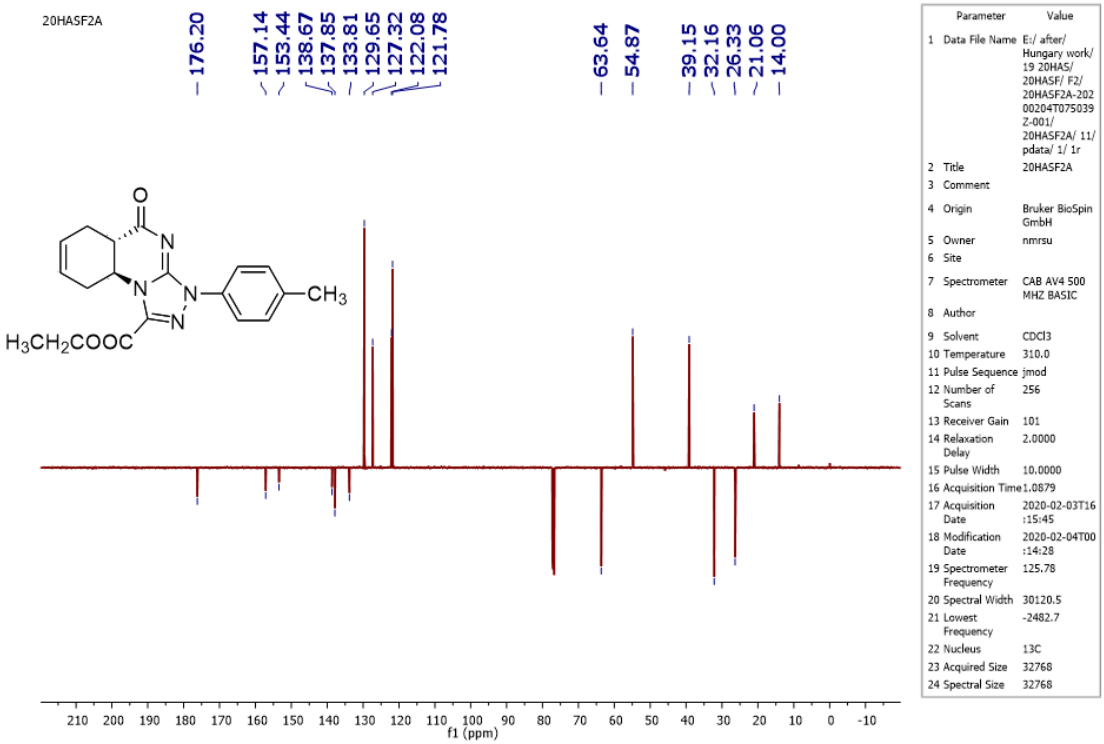
HMBC Spectrum

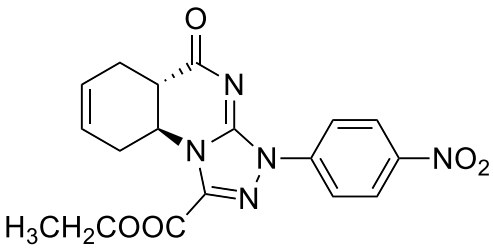




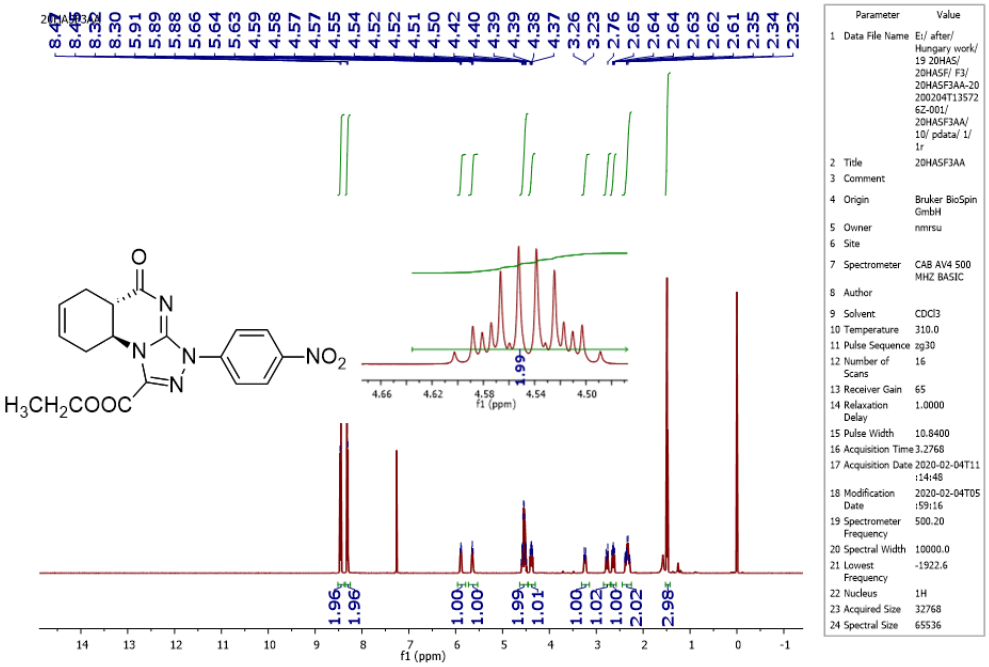
(4a*S**,8a*S**)-Ethyl 9-oxo-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5b**)







(4a*S**,8a*S**)-Ethyl 1-(4-nitrophenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5c**)



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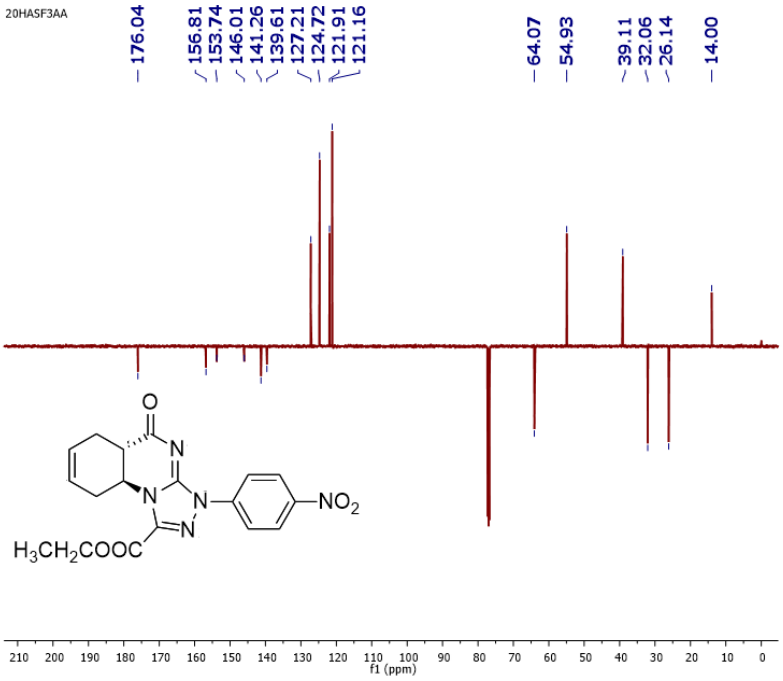
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	310.0
11	Pulse Sequence	zg30
12	Number of Scans	16
13	Receiver Gain	65
14	Relaxation Delay	1.0000
15	Pulse Width	10.8400
16	Acquisition Time	3.2768
17	Acquisition Date	2020-02-04T11:14:48
18	Modification Date	2020-02-04T05:59:16
19	Spectrometer Frequency	500.20
20	Spectral Width	10000.0
21	Lowest Frequency	-1922.6
22	Nucleus	1H
23	Acquired Size	32768
24	Spectral Size	65536



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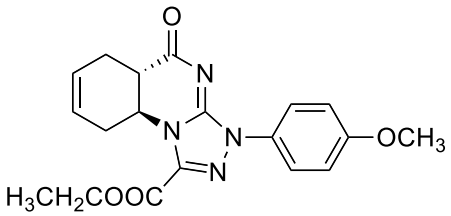
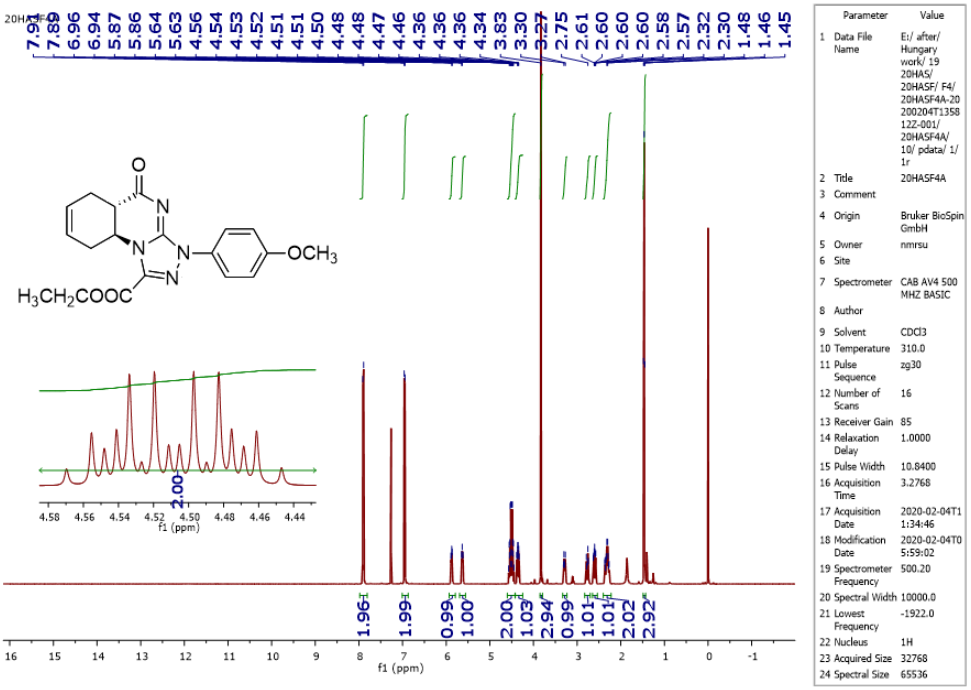
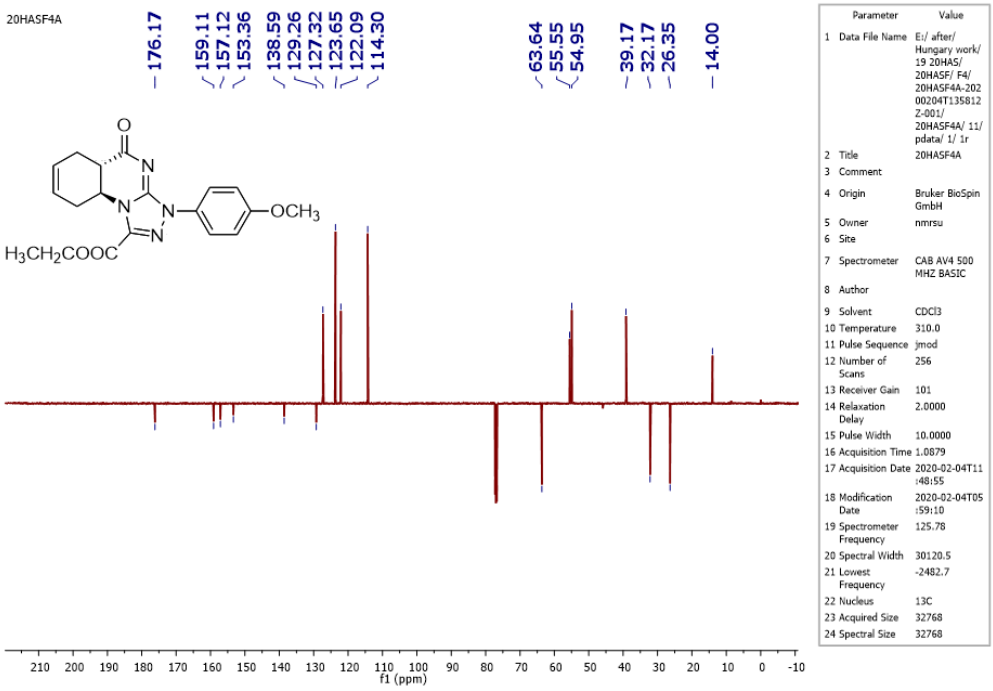
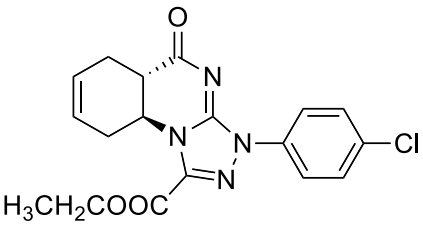
2	Title	20HASF3AA
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	310.0
11	Pulse Sequence	jmod
12	Number of Scans	256
13	Receiver Gain	101
14	Relaxation Delay	2.0000
15	Pulse Width	10.0000
16	Acquisition Time	1.0879
17	Acquisition Date	2020-02-04T11:29:31
18	Modification Date	2020-02-04T05:59:22
19	Spectrometer Frequency	125.78
20	Spectral Width	30120.5
21	Lowest Frequency	-2482.7
22	Nucleus	13C
23	Acquired Size	32768
24	Spectral Size	32768



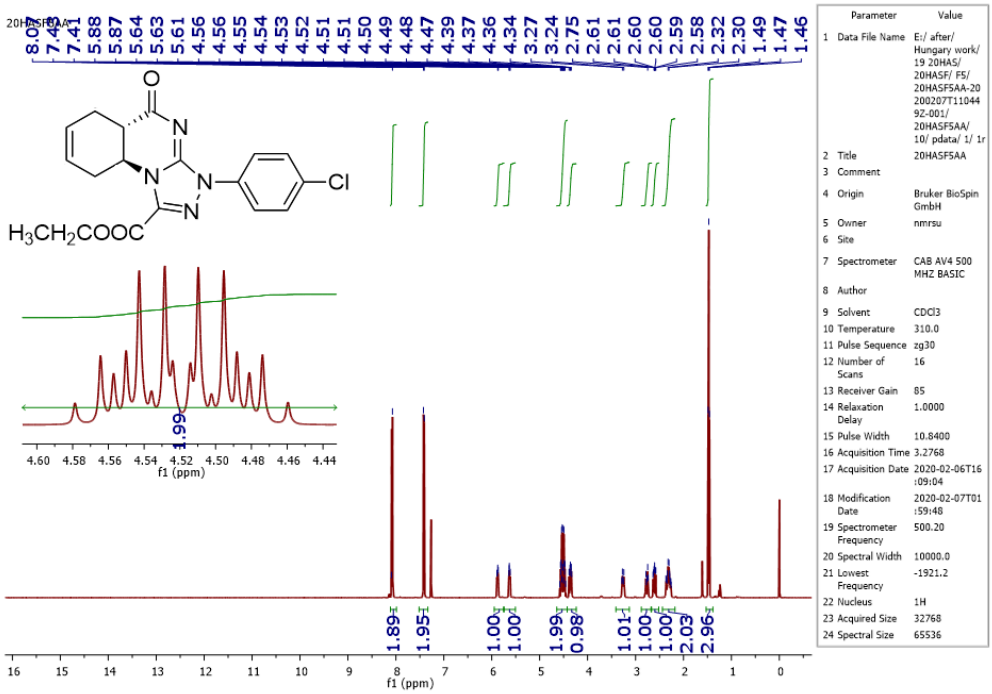
(4a*S**,8a*S**)-Ethyl 1-(4-methoxyphenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5d**)

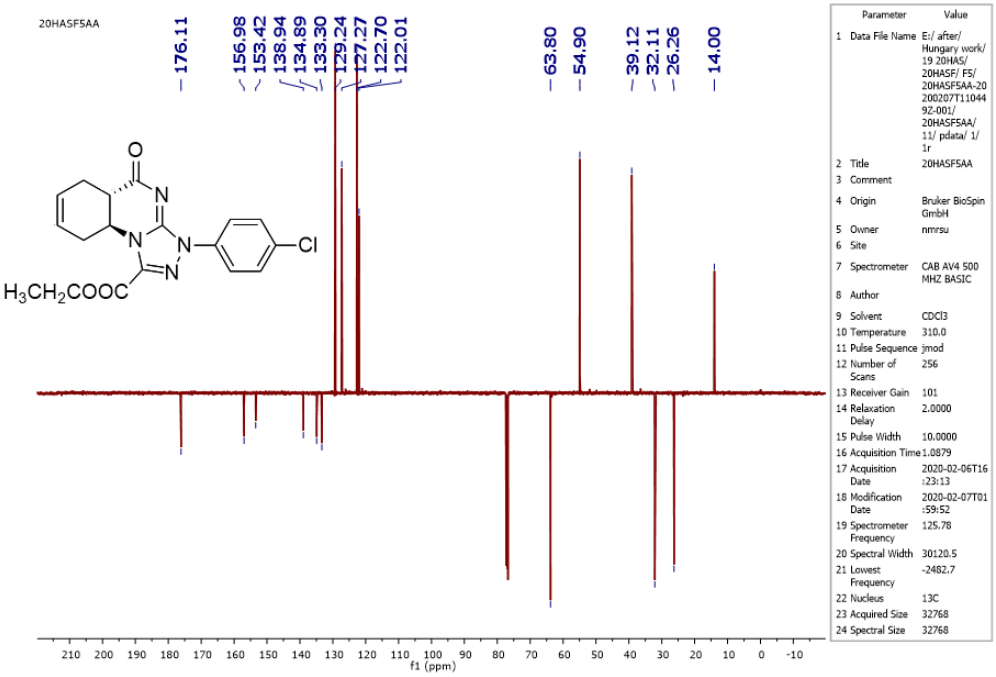


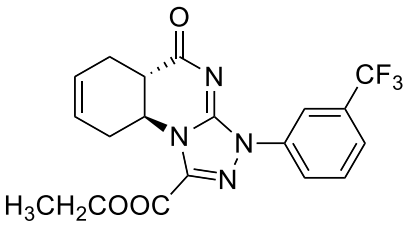




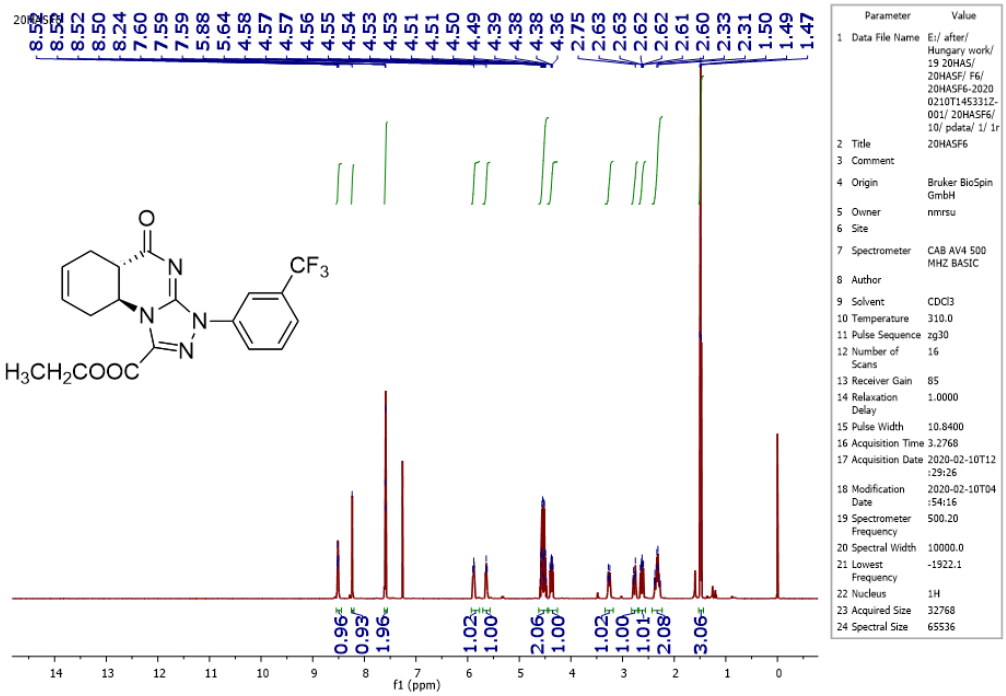
(4a*S**,8a*S**)-Ethyl 1-(4-chlorophenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5e**)

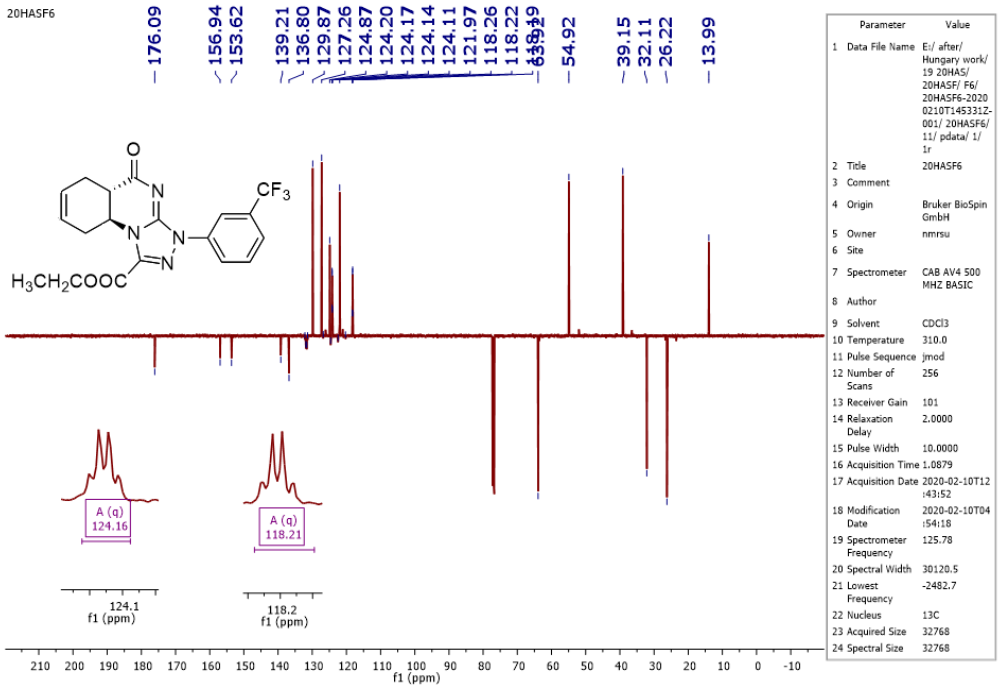


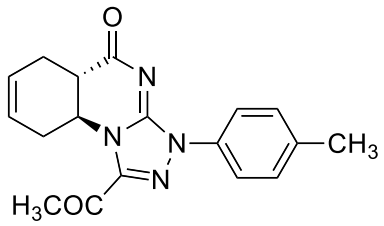




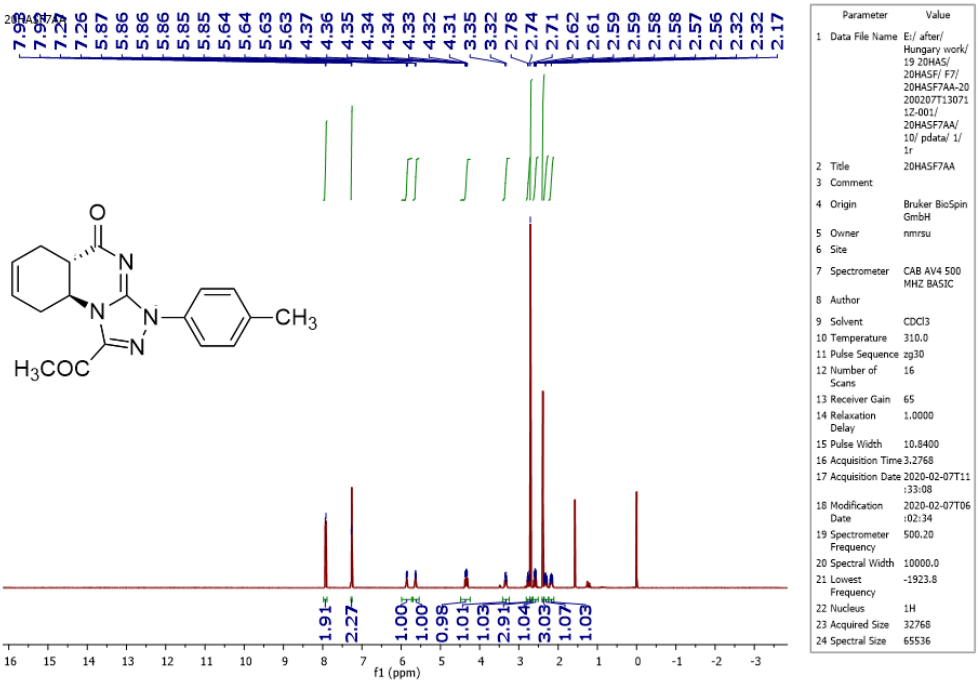
(4a*S**,8a*S**)-Ethyl 9-oxo-1-(3-(trifluoromethyl)phenyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5f**)

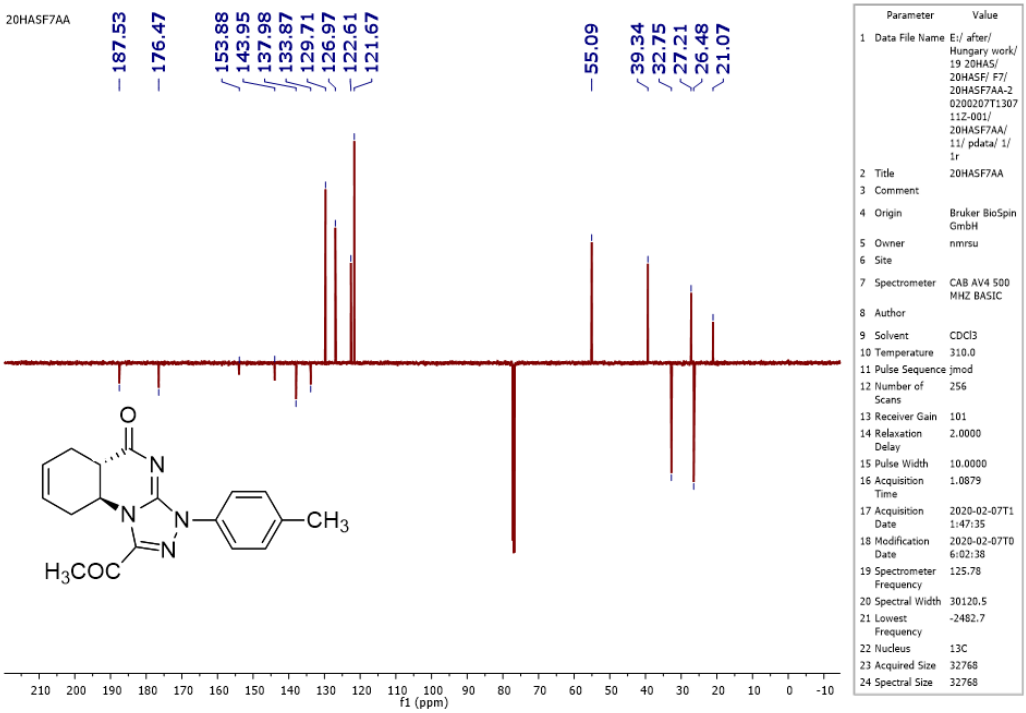


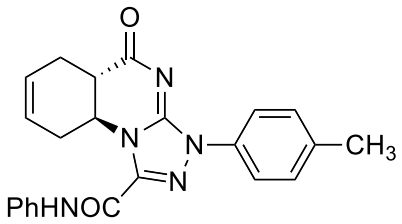




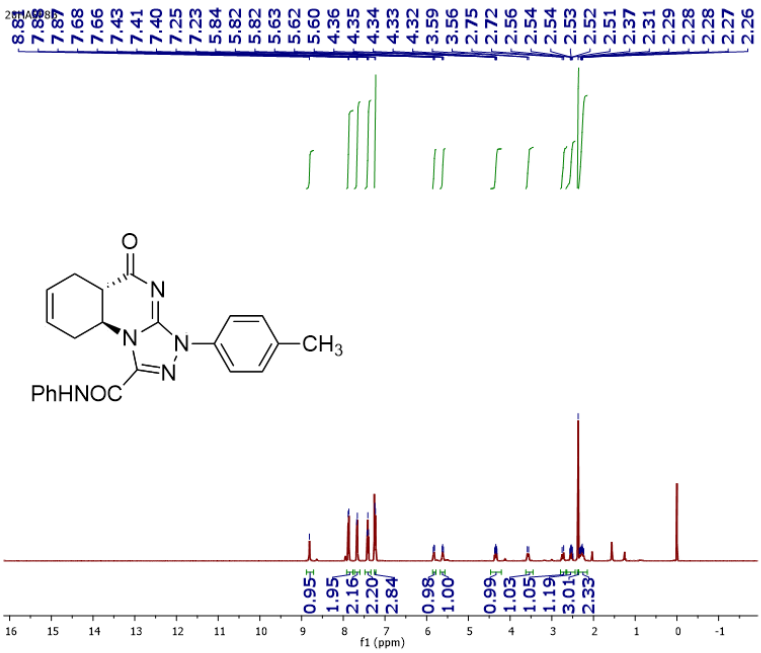
(4a*S**,8a*S**)-3-Acetyl-1-(*p*-tolyl)-4a,5,8,9-tetrahydro-[1,2,4]triazolo[4,3-*a*]quinazolin-9(1*H*)-one (**5g**)







(4a*S**,8a*S**)-9-Oxo-*N*-phenyl-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxamide (**5h**)



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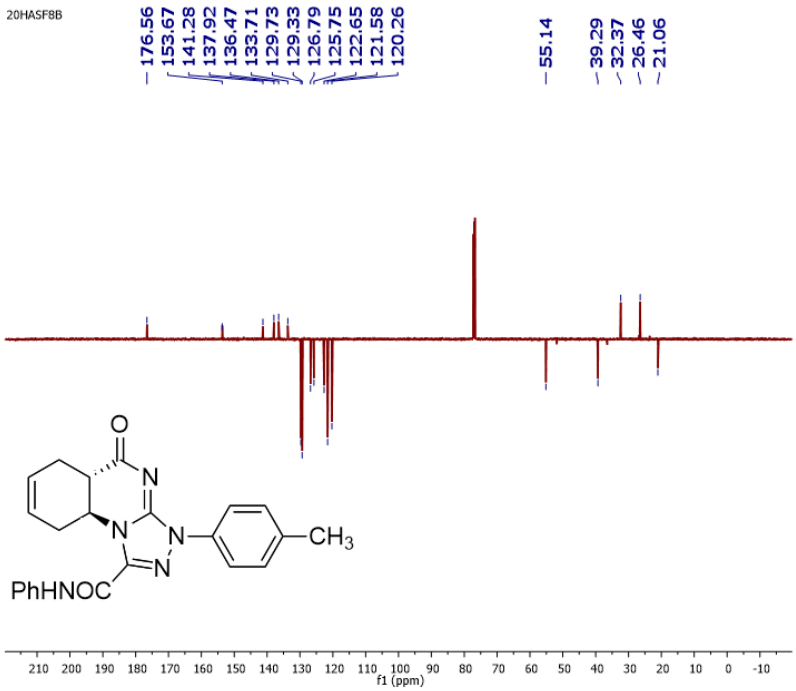
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	310.0
11	Pulse Sequence	zg30
12	Number of Scans	16
13	Receiver Gain	81
14	Relaxation Delay	1.0000
15	Pulse Width	10.8400
16	Acquisition Time	3.2768
17	Acquisition Date	2020-02-10T12:49:06
18	Modification Date	2020-02-11T00:08:50
19	Spectrometer Frequency	500.20
20	Spectral Width	10000.0
21	Lowest Frequency	-1925.1
22	Nucleus	1H
23	Acquired Size	32768
24	Spectral Size	65536



	Parameter	Value
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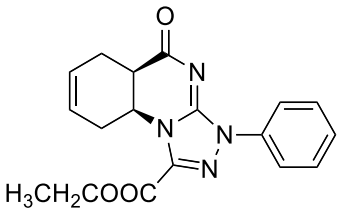
2	Title	20HASF8B
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Spectrometer	CAB AV4 500 MHZ BASIC
8	Author	
9	Solvent	CDCl3
10	Temperature	310.0
11	Pulse Sequence	jmod
12	Number of Scans	256
13	Receiver Gain	101
14	Relaxation Delay	2.0000
15	Pulse Width	10.0000
16	Acquisition Time	1.0879
17	Acquisition Date	2020-02-10T13:03:31
18	Modification Date	2020-02-11T00:08:56
19	Spectrometer Frequency	125.78
20	Spectral Width	30120.5
21	Lowest Frequency	-2482.7
22	Nucleus	13C
23	Acquired Size	32768
24	Spectral Size	32768

Crystallographic details of compound 5a

Table S1. Crystal Data.

	5a
CCDC	
empirical formula	$C_{18}H_{18}N_4O_3$
fw	338.36
temp (K)	120(2)
λ(Å)	1.54184
cryst syst	Triclinic
space group	$P\bar{1}$
a (Å)	9.5332(3)
b (Å)	10.4081(3)
c (Å)	16.8864(5)
α (deg)	89.227(2)
β (deg)	81.130(2)
γ (deg)	74.199(3)
V (Å^3)	1592.20(9)
Z	4
ρ_{calc} (Mg/m^3)	1.412
μ(Mo Kα) (mm^{-1})	0.812
No. reflns.	42738
Unique reflns.	6682
Completeness to θ=67.684°	100%
GOOF (F^2)	1.029
R_{int}	0.0503
R1[a] ($I \geq 2\sigma$)	0.0377
wR2[b] ($I \geq 2\sigma$)	0.0932

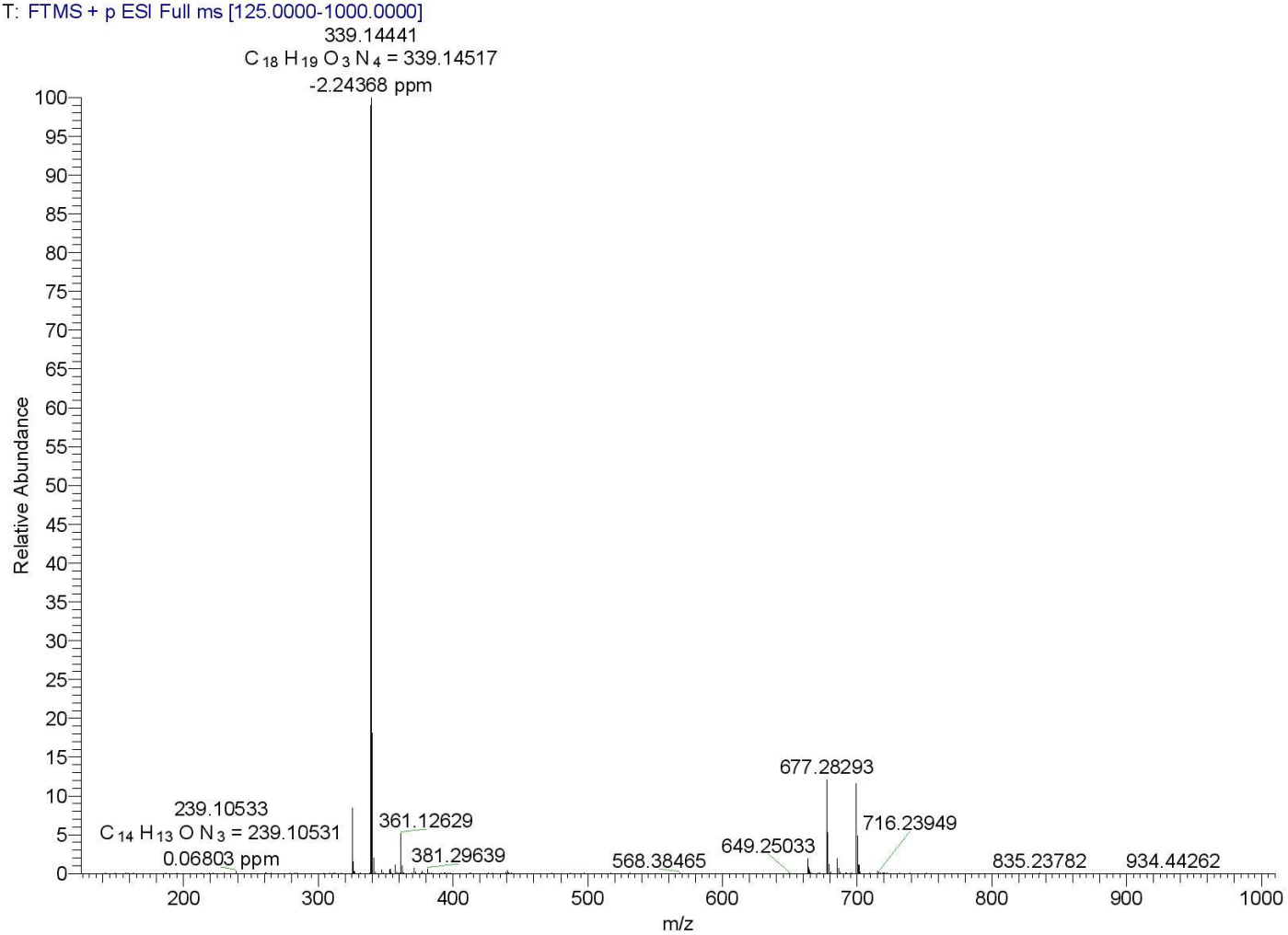
[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$

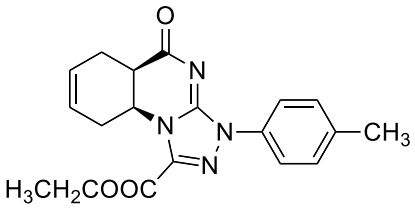


(4a*S**,8a*R**)-Ethyl 9-oxo-1-phenyl-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4a**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #76-89 RT: 0.39-0.45 AV: 14 NL: 5.62E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

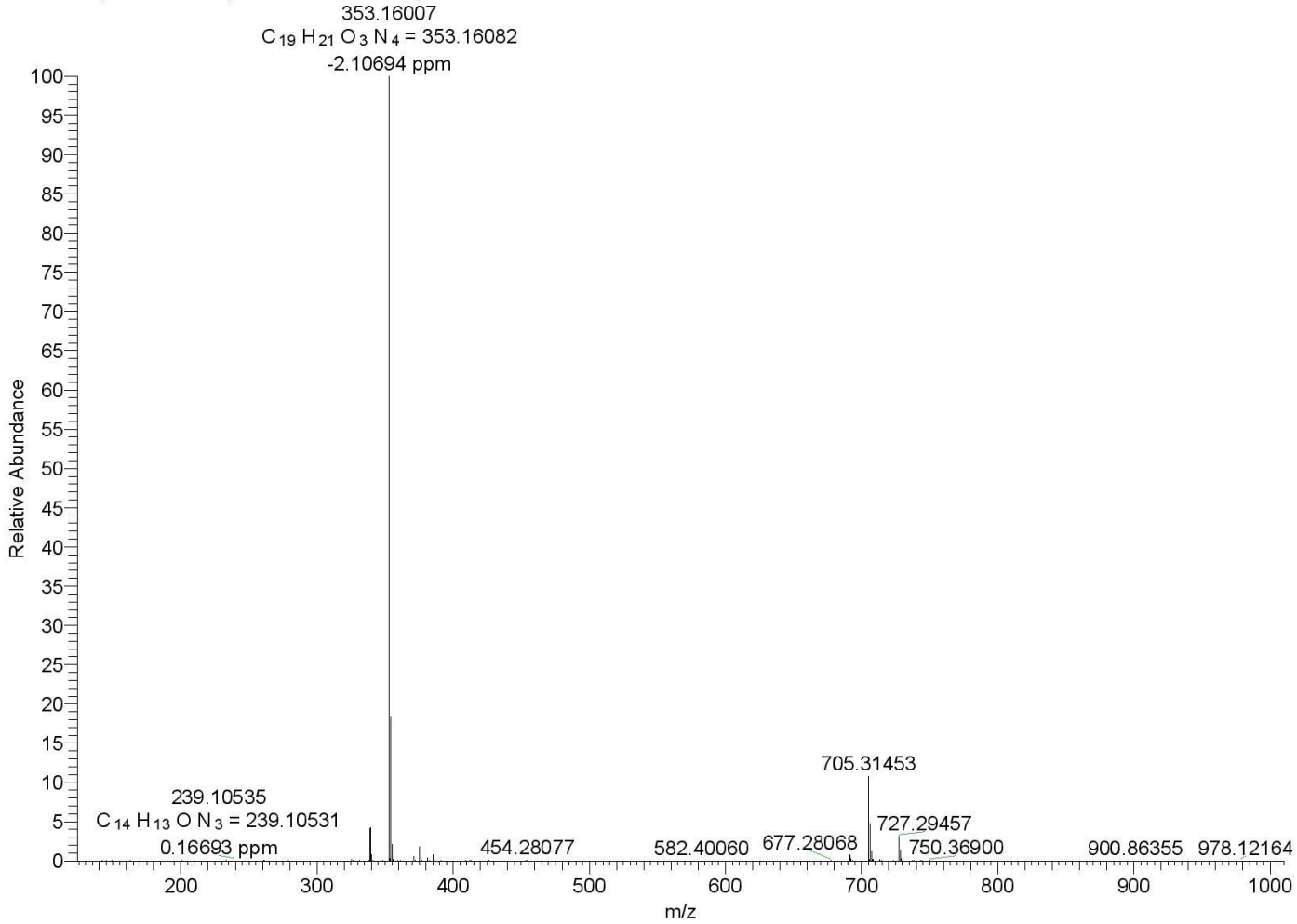


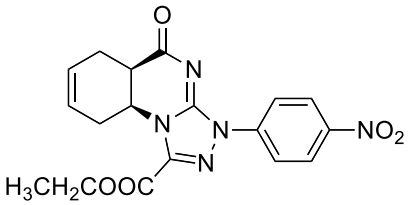


(4a*S**,8a*R**)-Ethyl 9-oxo-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4b**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #332-348 RT: 1.72-1.80 AV: 17 NL: 6.17E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

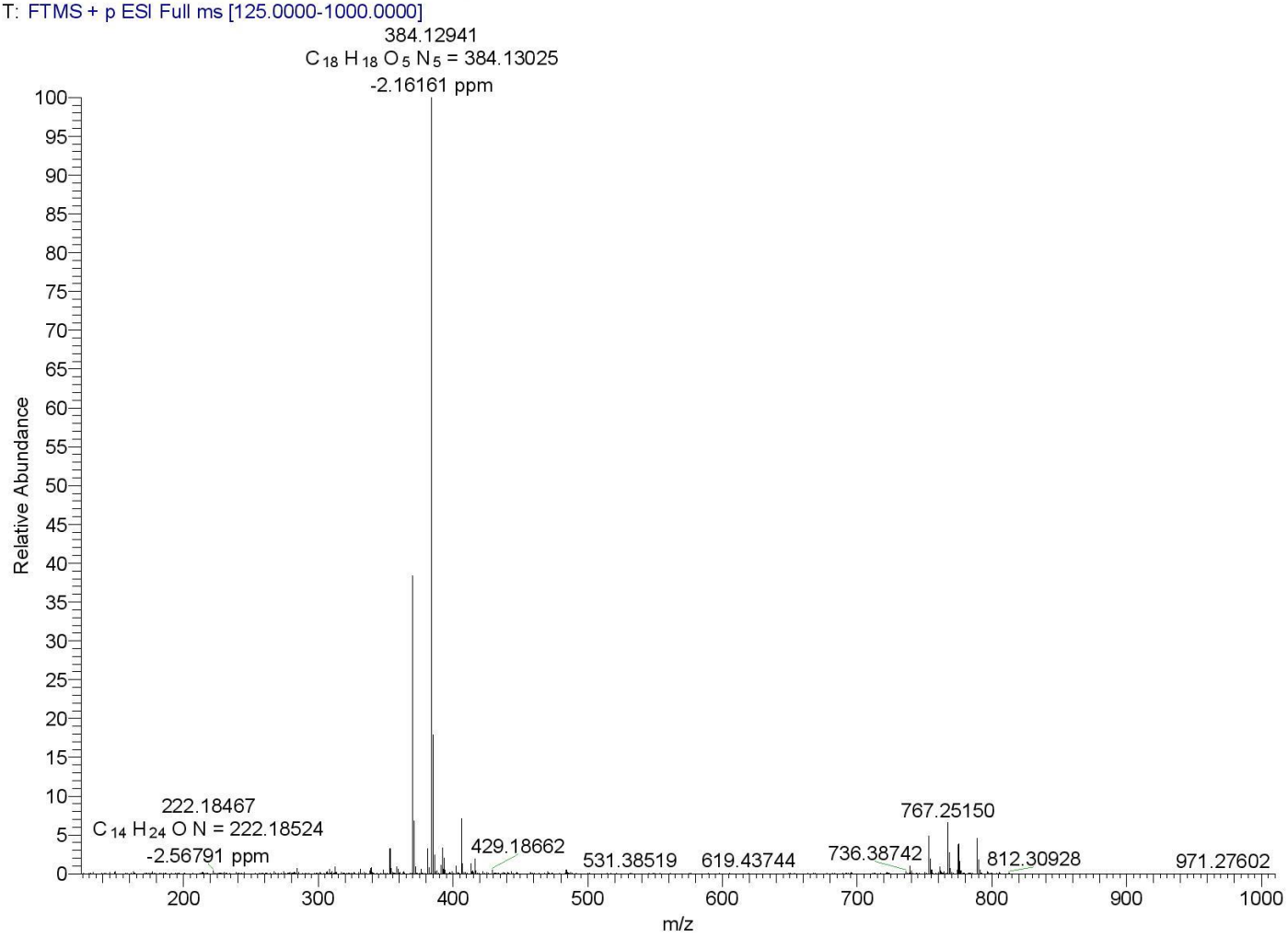


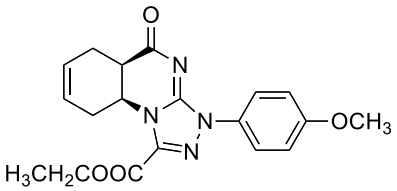


(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-nitrophenyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4c**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #529-549 RT: 2.73-2.83 AV: 21 NL: 1.70E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

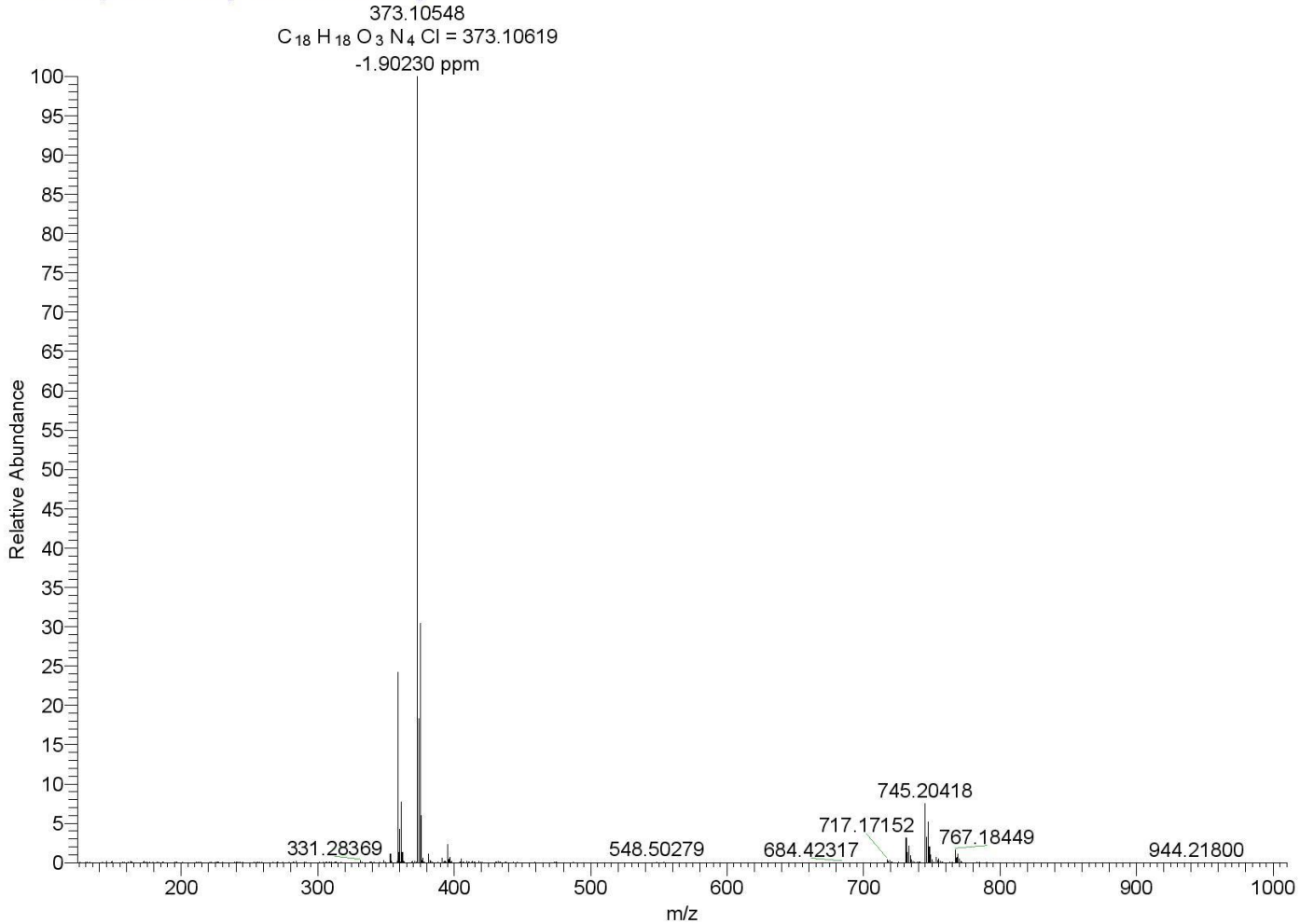


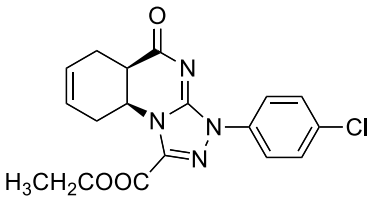


(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-methoxyphenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4d**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #901-936 RT: 4.63-4.81 AV: 36 NL: 2.51E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

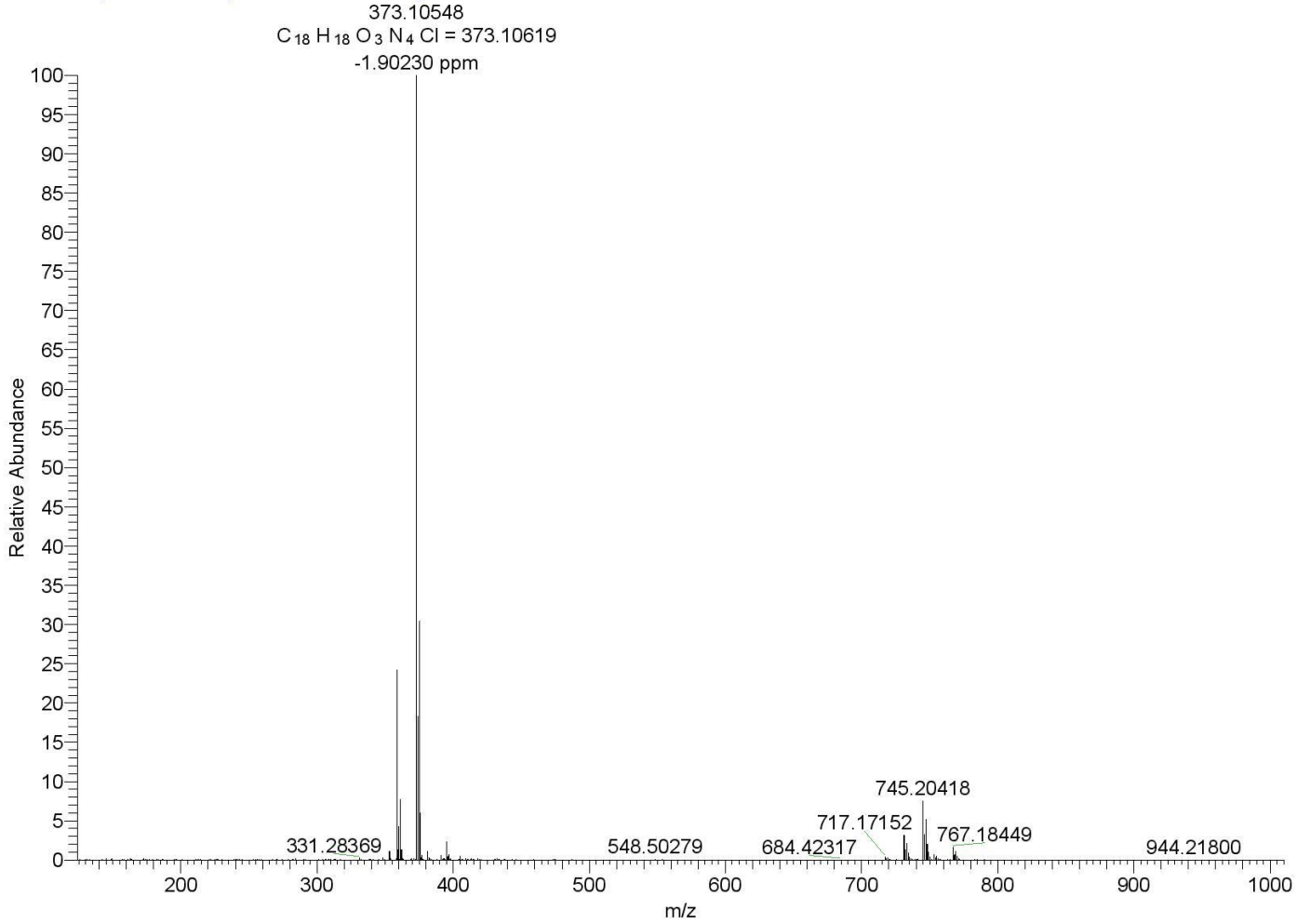


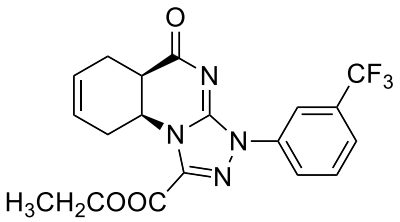


(4a*S**,8a*R**)-Ethyl 9-oxo-1-(4-chlorophenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4e**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #901-936 RT: 4.63-4.81 AV: 36 NL: 2.51E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

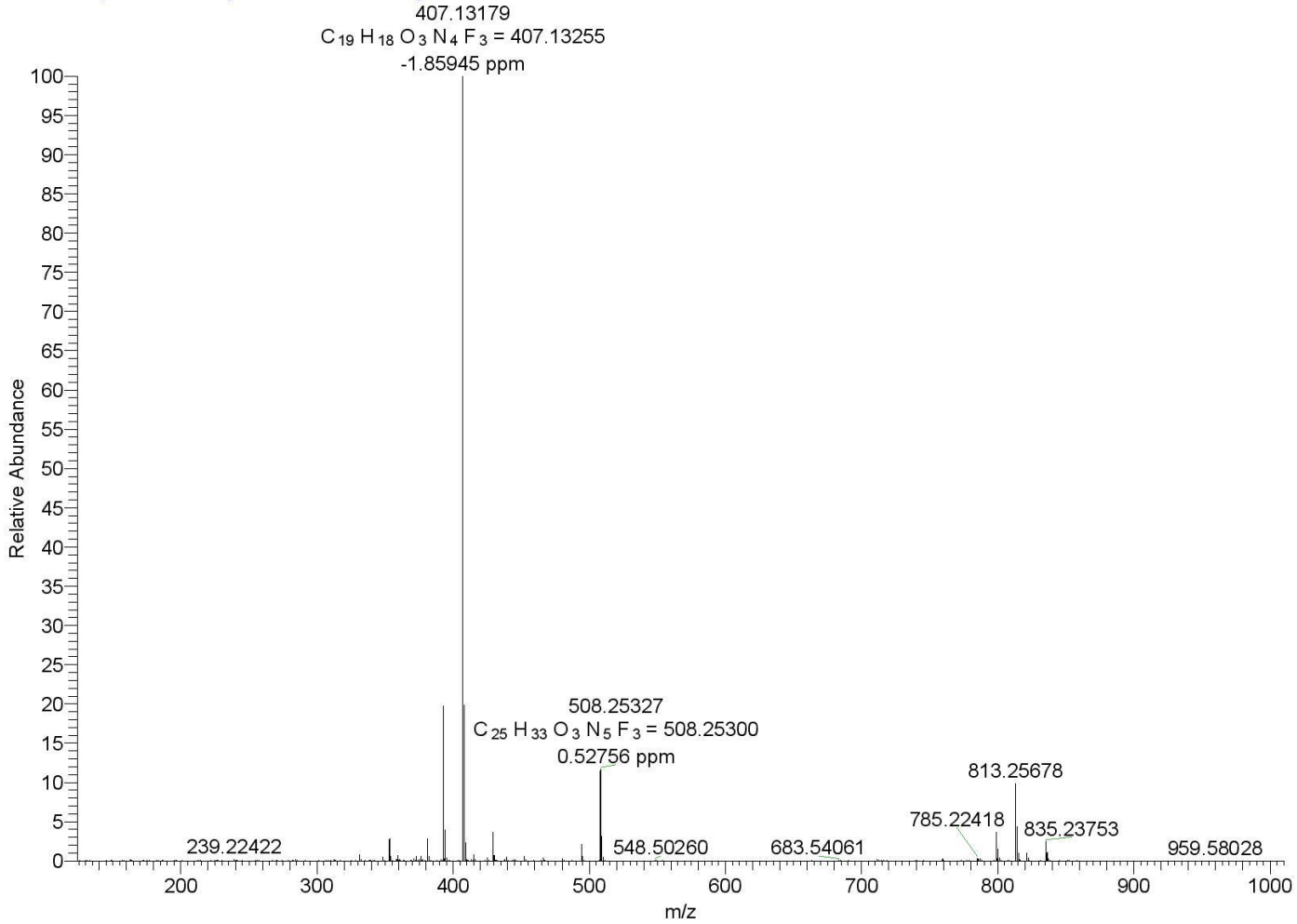


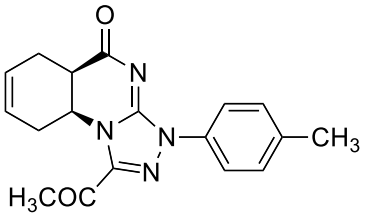


(4a*S**,8a*R**)-Ethyl 9-oxo-1-(3-(trifluoromethyl)phenyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**4f**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #1060-1088 RT: 5.44-5.59 AV: 29 NL: 2.95E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

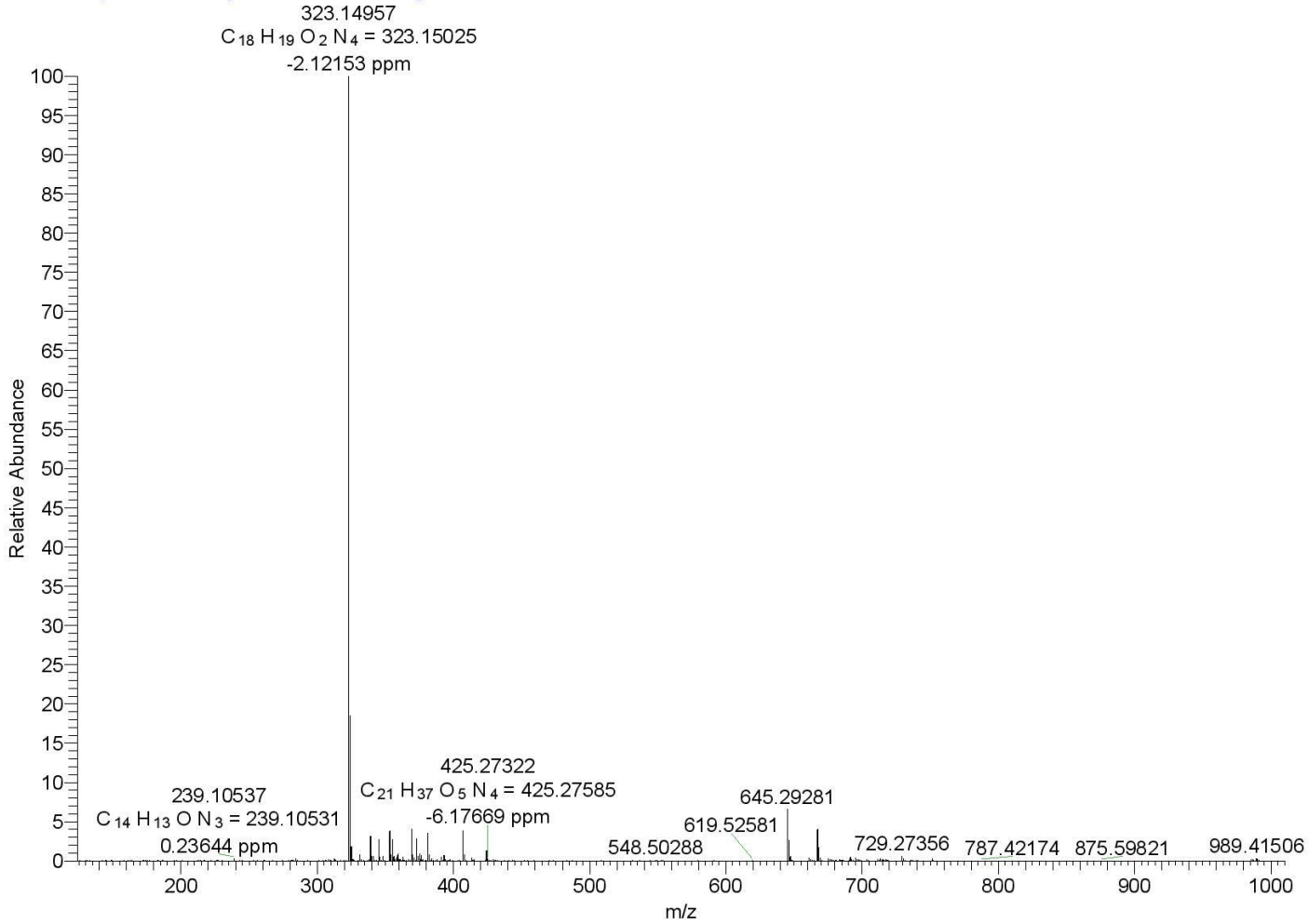


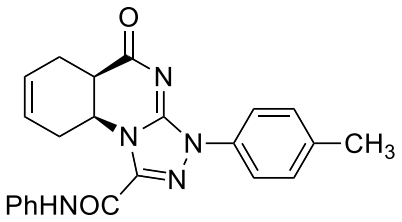


(4a*S**,8a*R**)-3-Acetyl-1-(*p*-tolyl)-4a,5,8,9-tetrahydro[1,2,4]triazolo[4,3-*a*]quinazoline-9(1*H*)-one (**4g**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #1224-1244 RT: 6.28-6.38 AV: 21 NL: 3.22E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

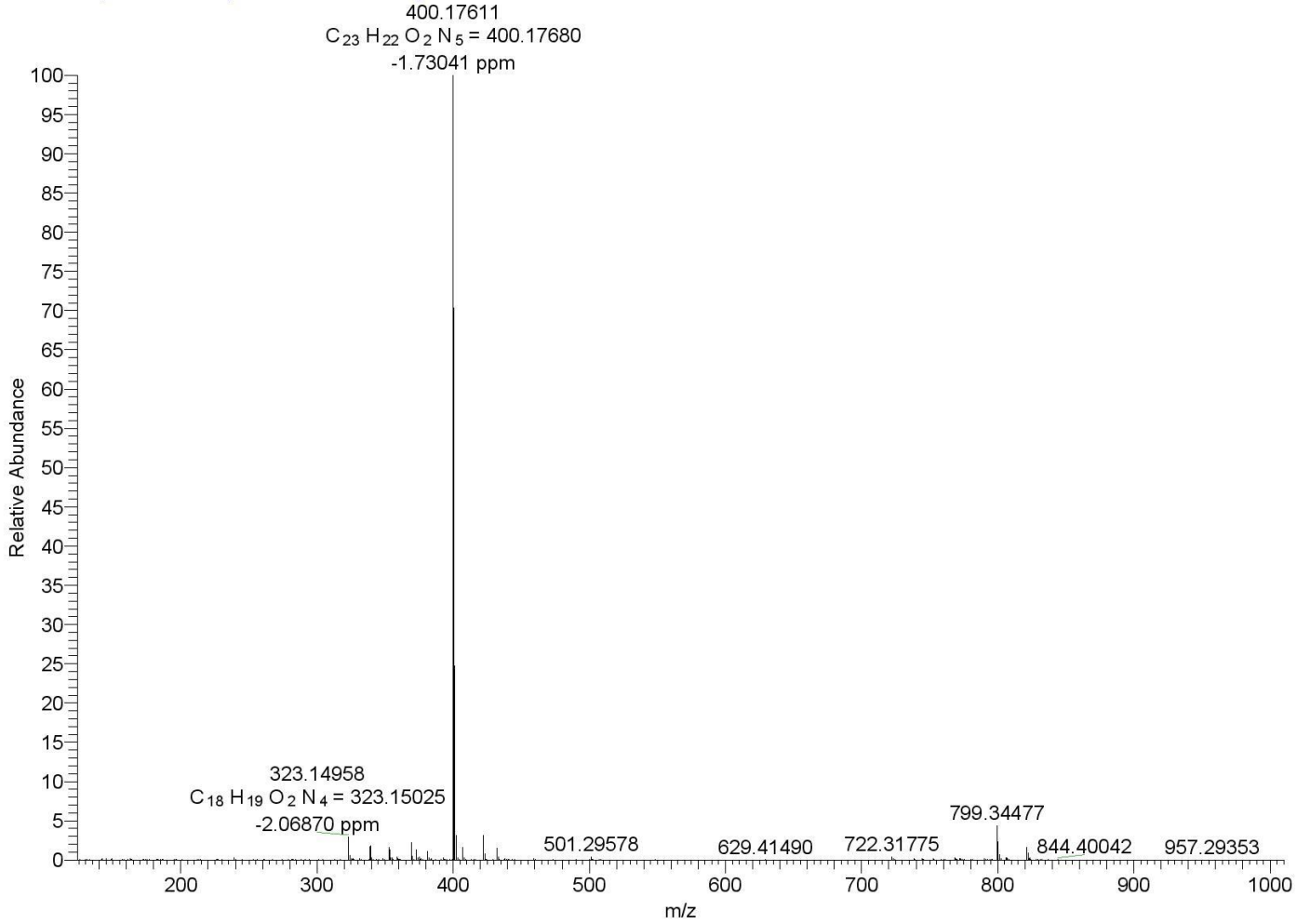


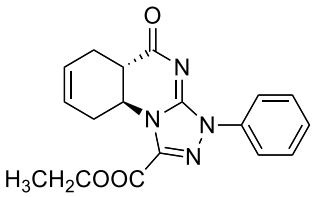


(4a*S**,8a*R**)-9-Oxo-*N*-Phenyl-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxamide (**4h**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #1365-1385 RT: 7.01-7.11 AV: 21 NL: 2.82E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

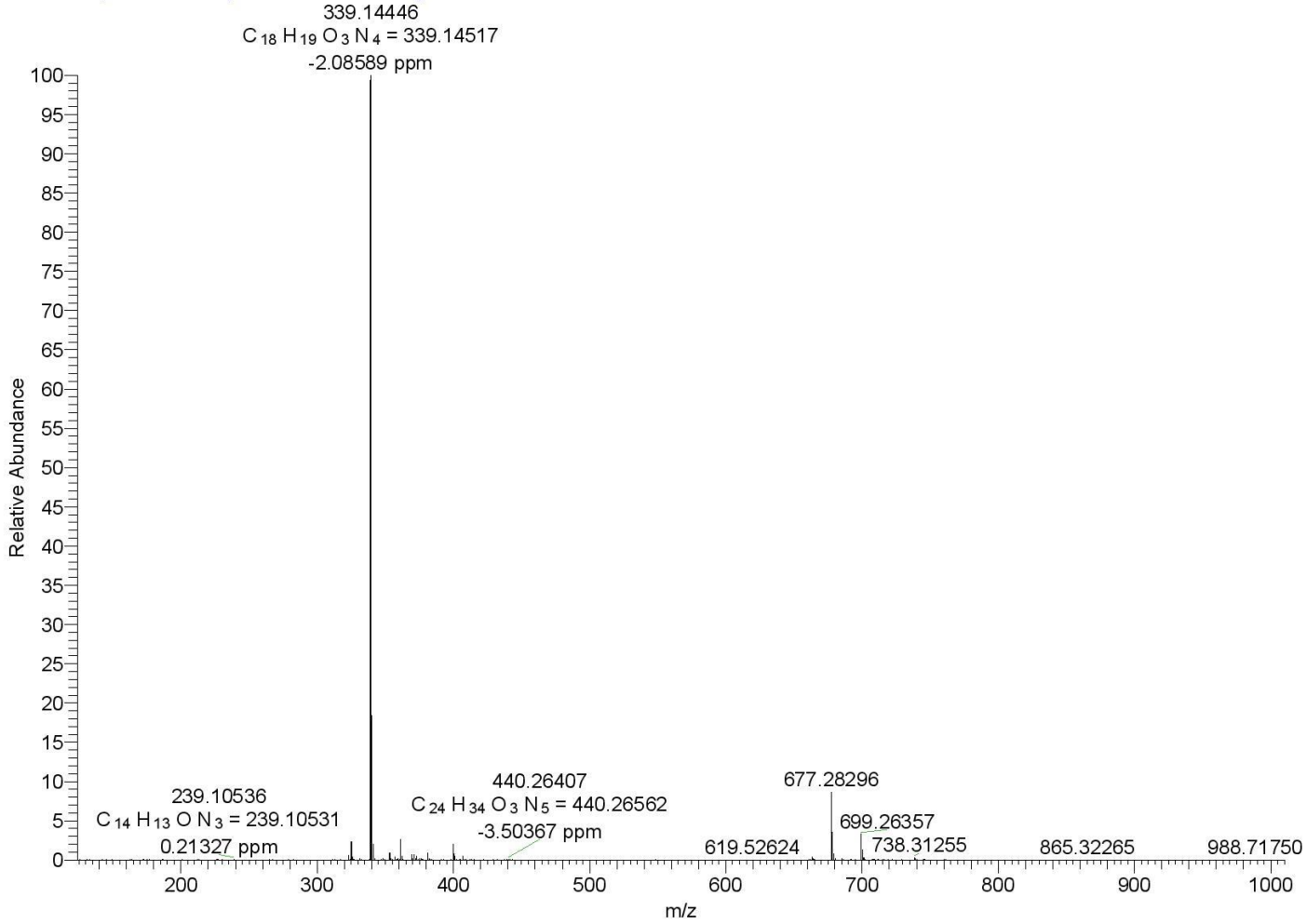


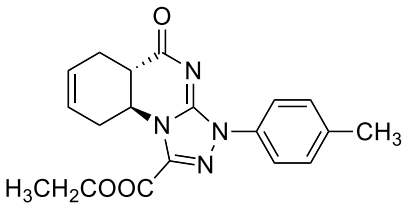


(4a*S**,8a*S**)-Ethyl 9-oxo-1-phenyl-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-a]quinazoline-3-carboxylate (**5a**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #1512-1538 RT: 7.76-7.89 AV: 27 NL: 4.48E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

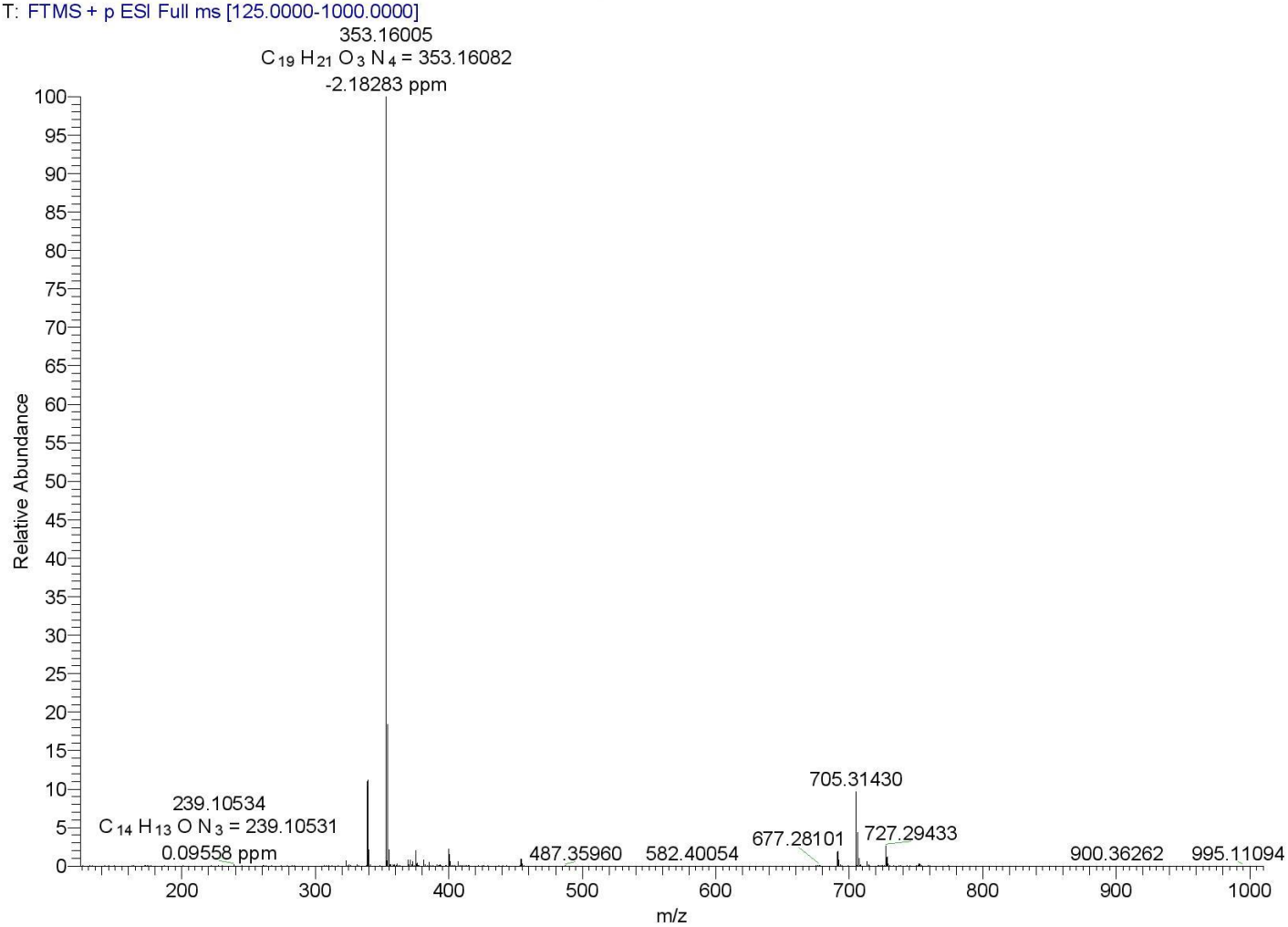


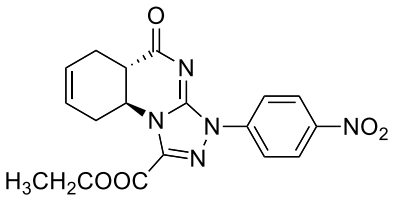


(4a*S**,8a*S**)-Ethyl 9-oxo-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5b**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #1696-1716 RT: 8.70-8.80 AV: 21 NL: 5.09E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

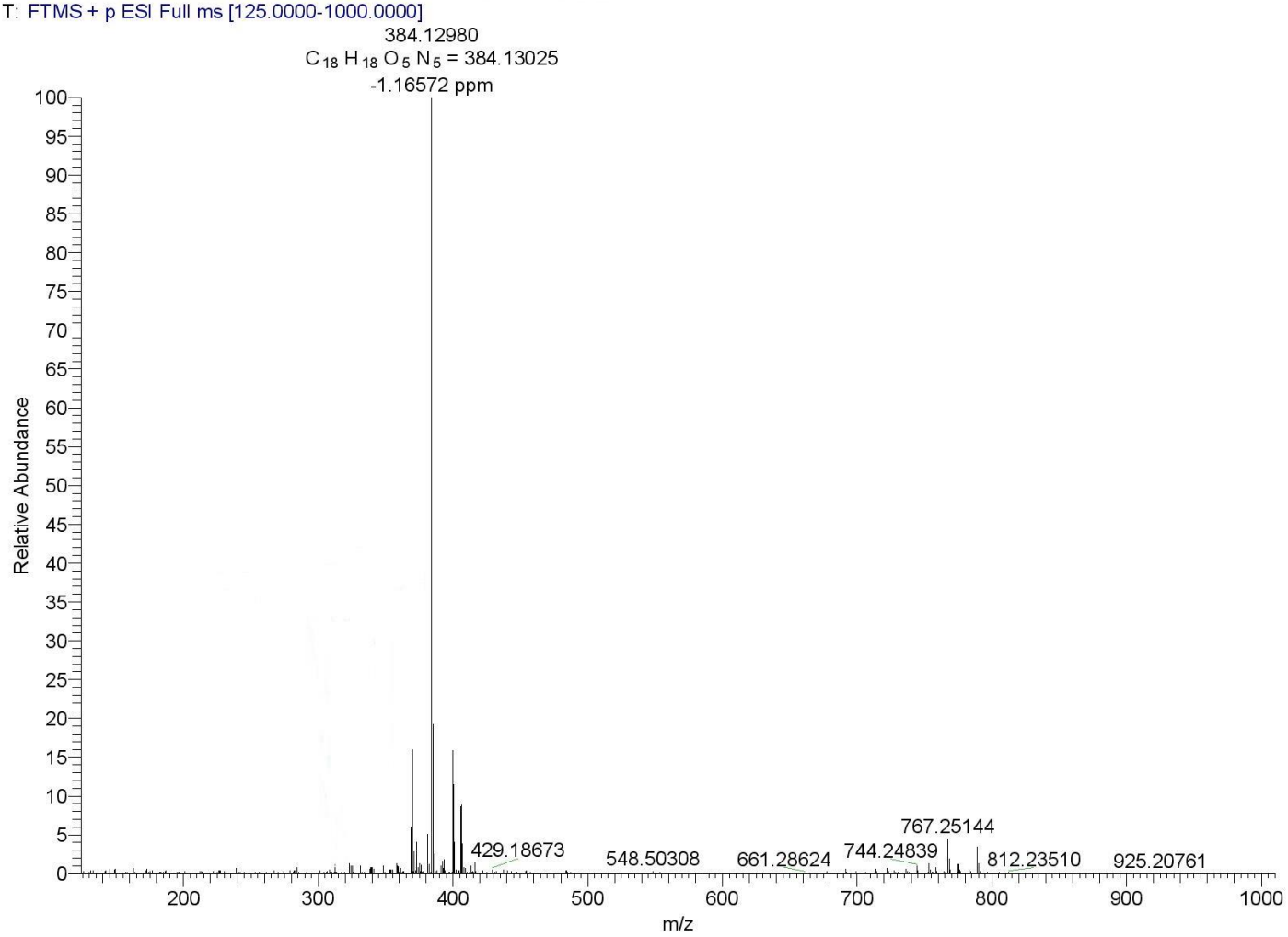


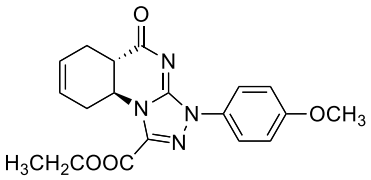


(4a*S**,8a*S**)-Ethyl 1-(4-nitrophenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5c**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #1830-1863 RT: 9.39-9.55 AV: 34 NL: 8.36E8
T: FTMS + p ESI Full ms [125.0000-1000.0000]

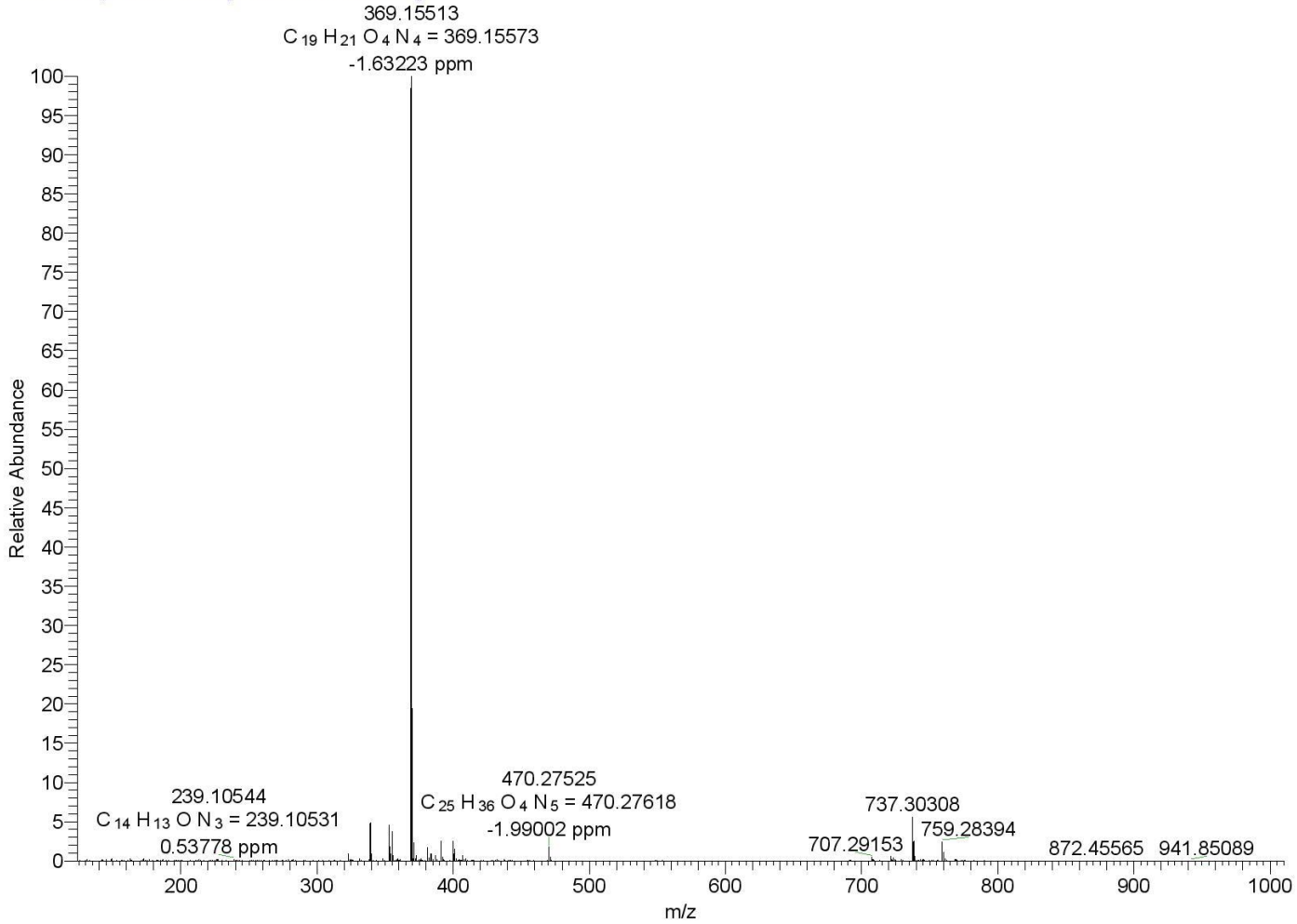


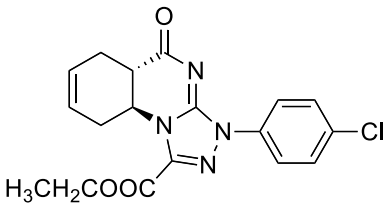


(4a*S**,8a*S**)-Ethyl 1-(4-methoxyphenyl)-9-oxo-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5d**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #1973-2006 RT: 10.12-10.29 AV: 34 NL: 1.99E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

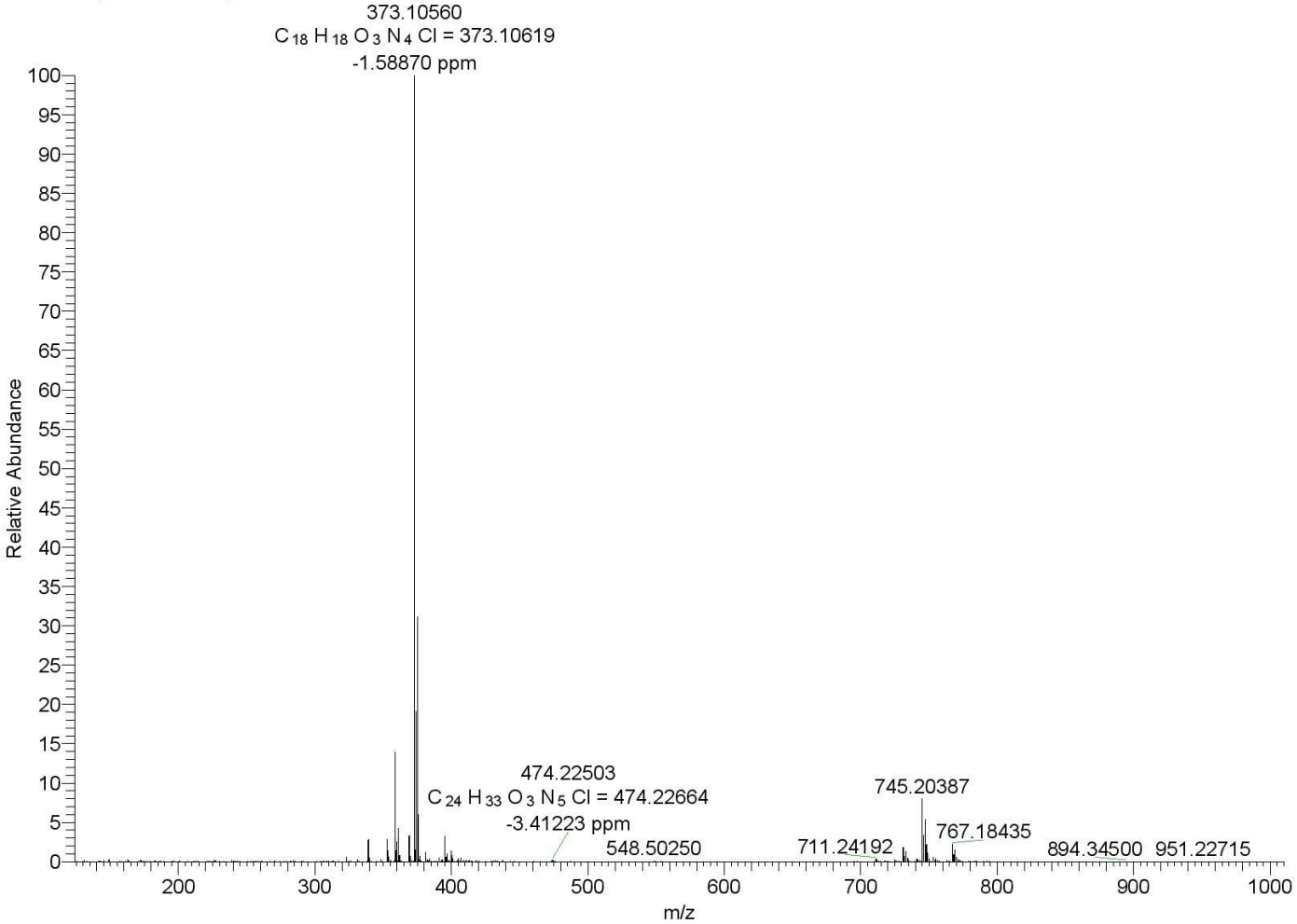


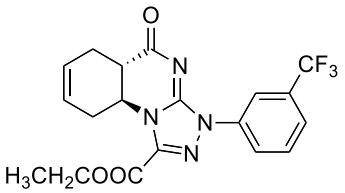


(5a*S**,9a*S**)-Ethyl 3-(4-chlorophenyl)-5-oxo-3,5,5a,6,9,9a-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-1-carboxylate (**5e**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #2129-2162 RT: 10.92-11.09 AV: 34 NL: 1.95E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

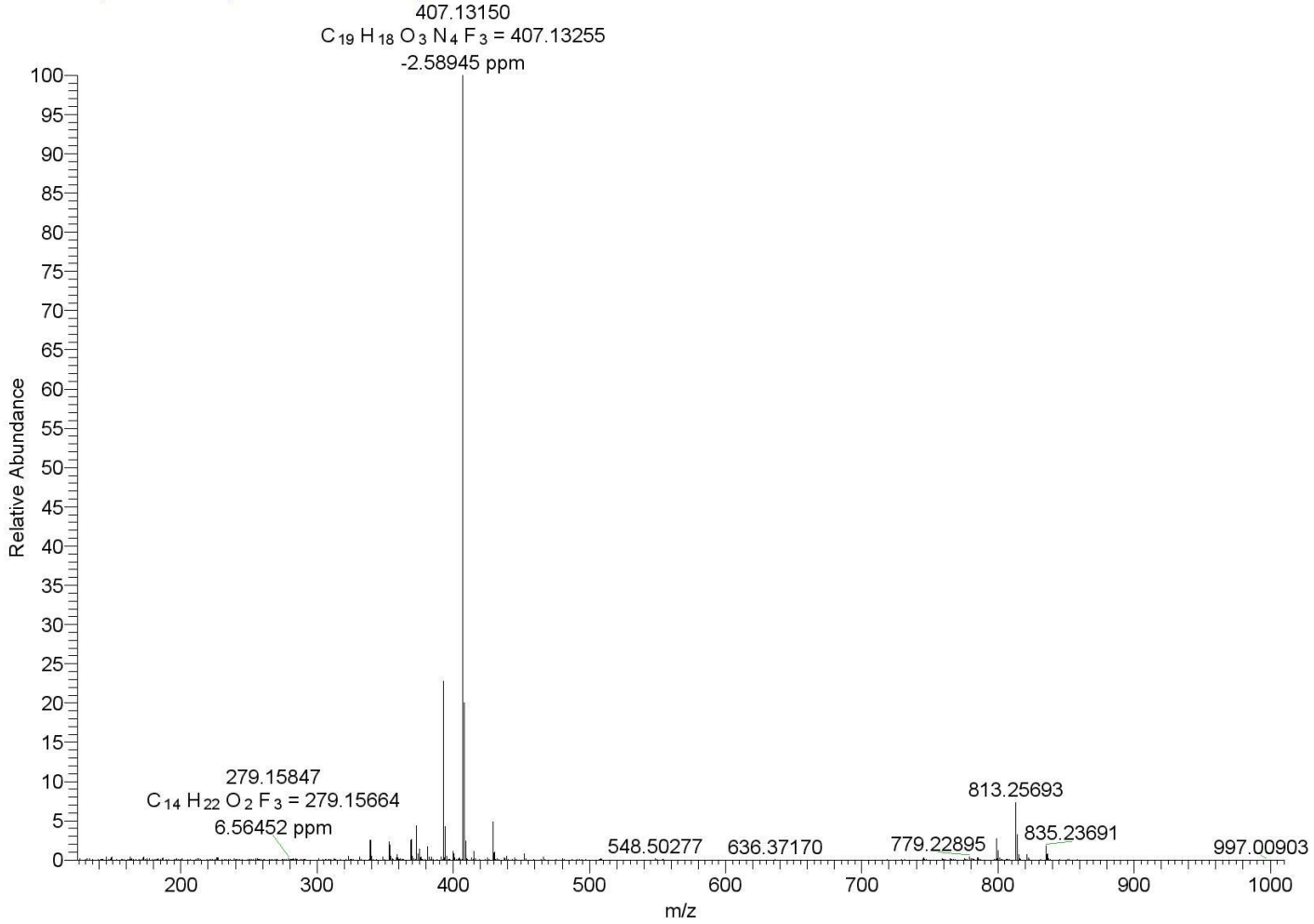


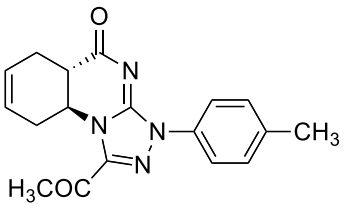


(4a*S**,8a*S**)-Ethyl 9-oxo-1-(3-(trifluoromethyl)phenyl)- 1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxylate (**5f**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #2291-2324 RT: 11.75-11.92 AV: 34 NL: 1.45E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

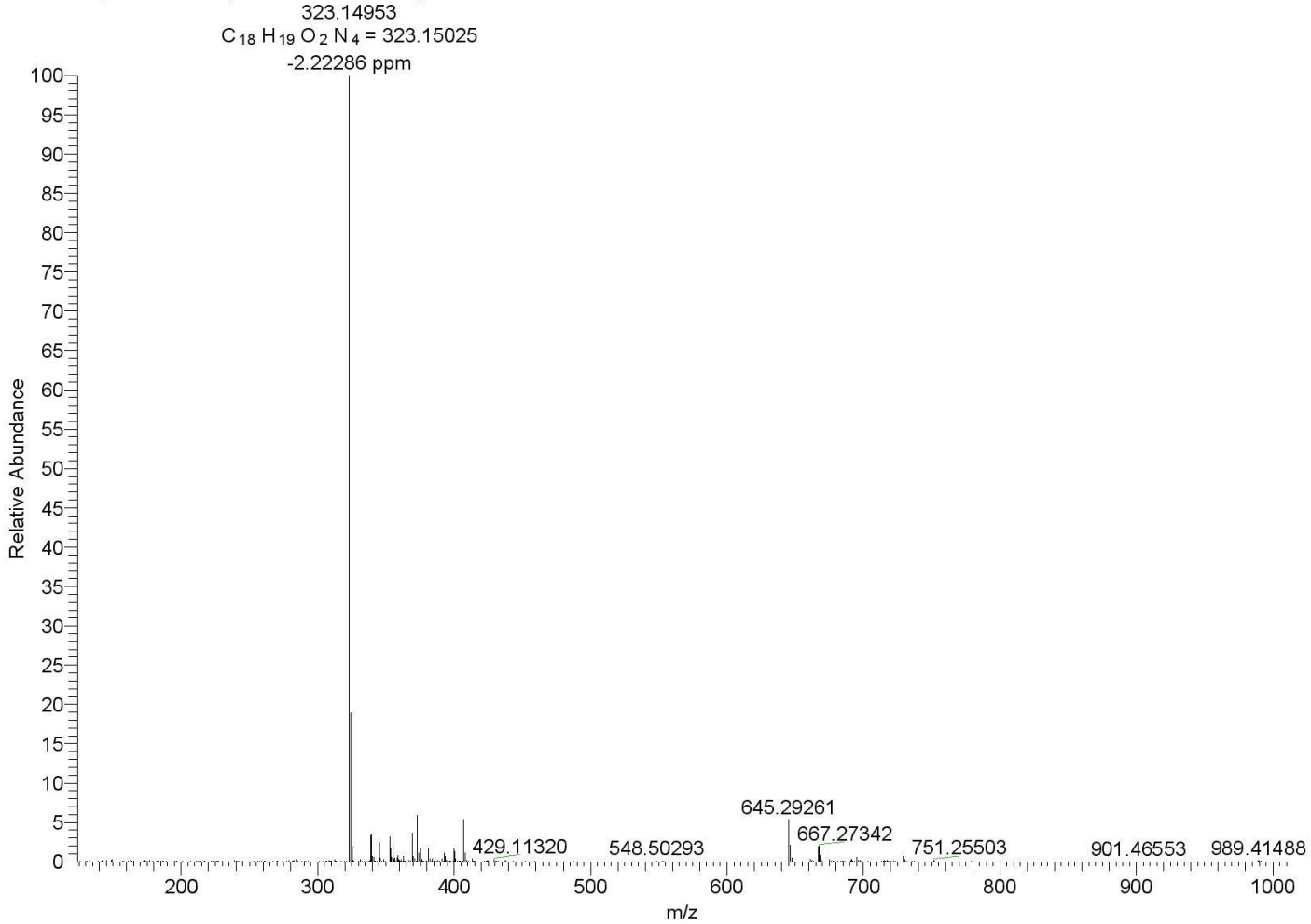


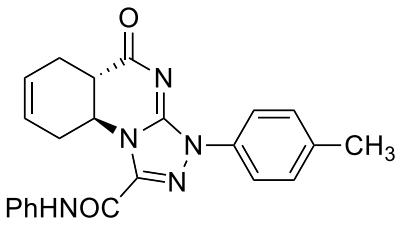


(4a*S**,8a*S**)-3-Acetyl-1-(*p*-tolyl)-4a,5,8,9-tetrahydro-[1,2,4]triazolo[4,3-*a*]quinazolin-9(1*H*)-one (**5g**)

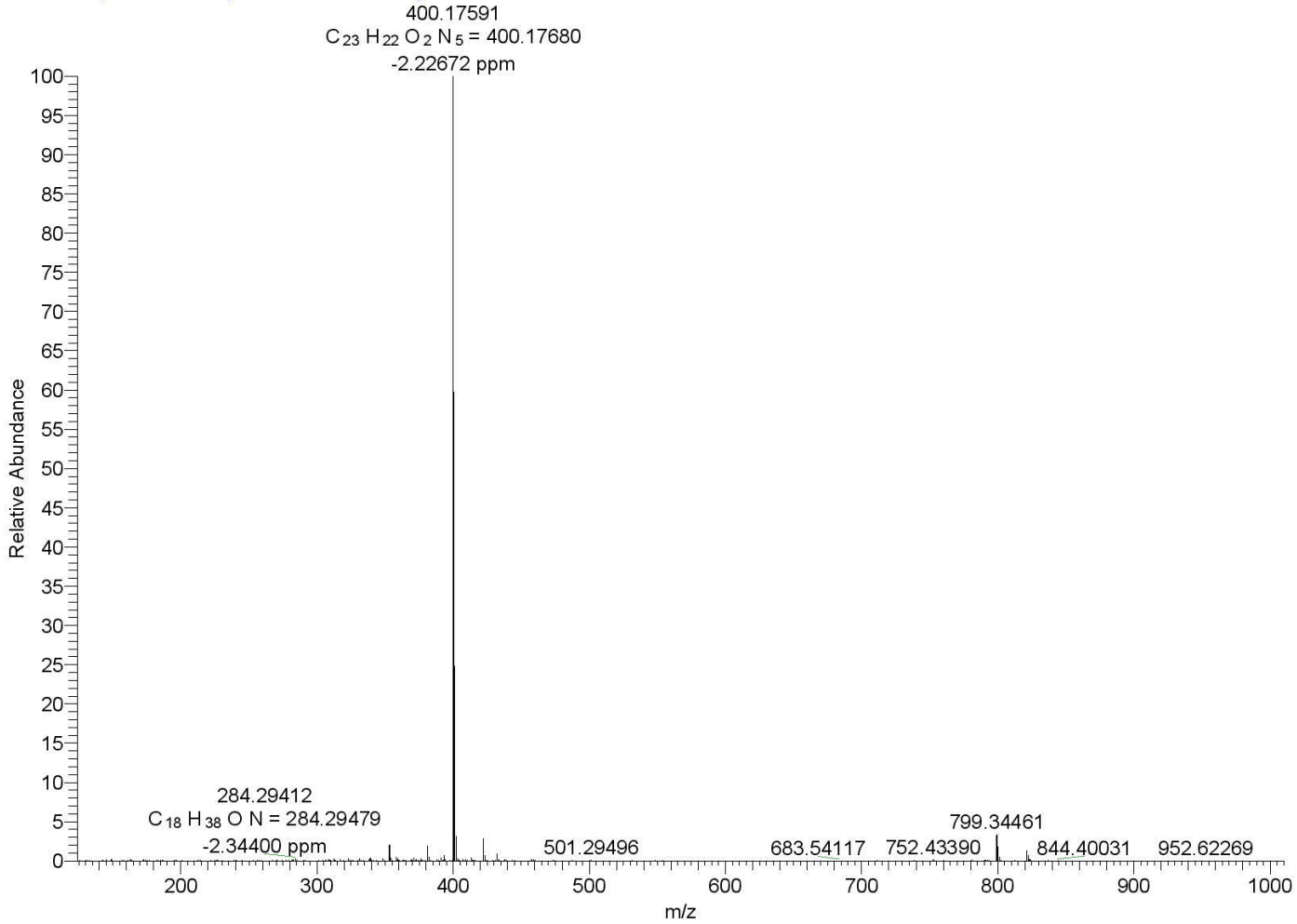
D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #2438-2455 RT: 12.50-12.59 AV: 18 NL: 2.13E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]





(4a*S**,8a*S**)-9-Oxo-*N*-phenyl-1-(*p*-tolyl)-1,4a,5,8,8a,9-hexahydro-[1,2,4]triazolo[4,3-*a*]quinazoline-3-carboxamide (**5h**)

D:\DATA\...\20230126\PM-20230126-POS 01/26/23 11:18:13 4A

PM-20230126-POS #2580-2602 RT: 13.23-13.34 AV: 23 NL: 2.33E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]