

ELECTRONIC SUPPORTING INFORMATION

Synthesis and Spectroscopic Analysis of *Piperine* and *Piperlongumine*-Inspired Natural Product Scaffolds and their Molecular Docking with IL-1 β and NF- κ B proteins

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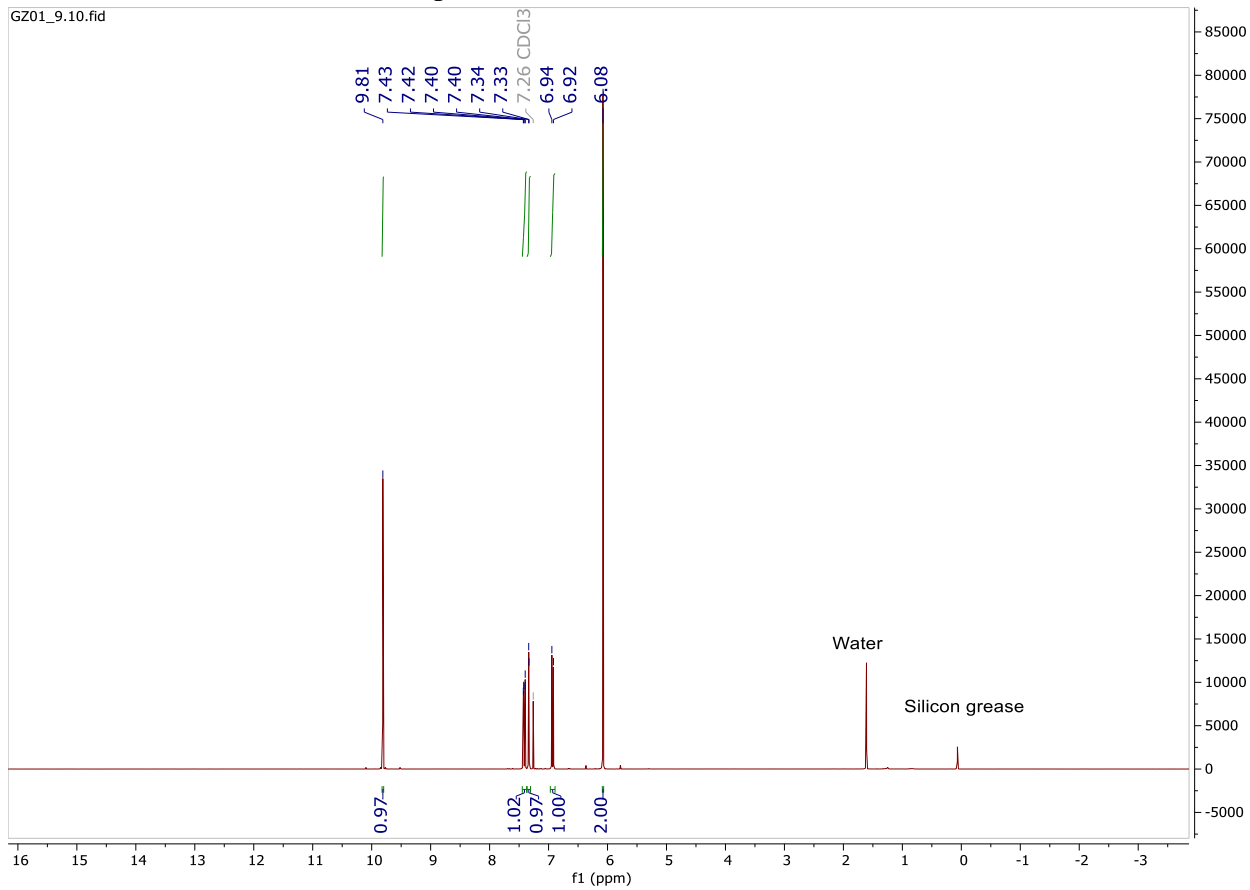
³ School of Chemistry, University of Birmingham, Edgbaston, B15 2TT, United Kingdom

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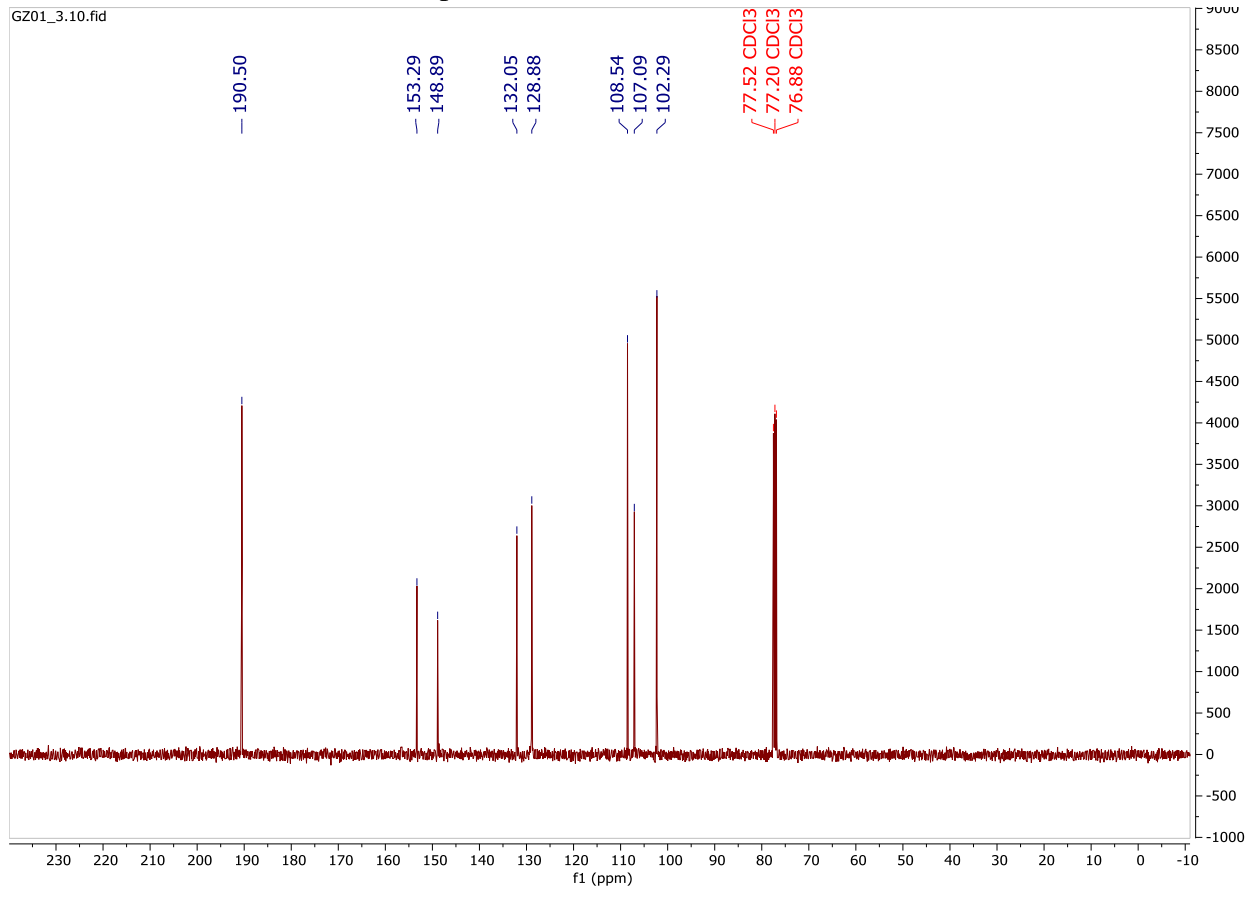
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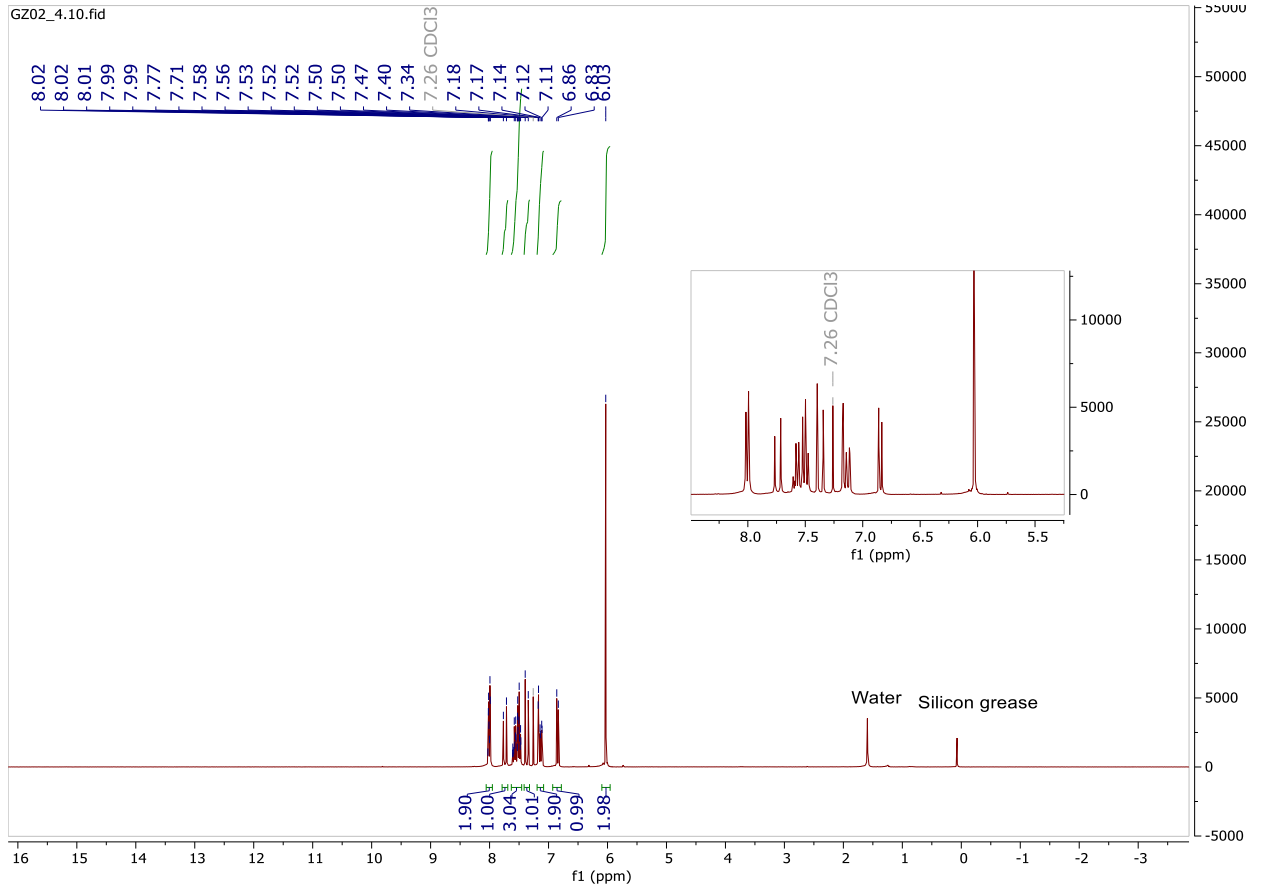
¹H NMR spectrum of **2** (300 MHz, CDCl₃)



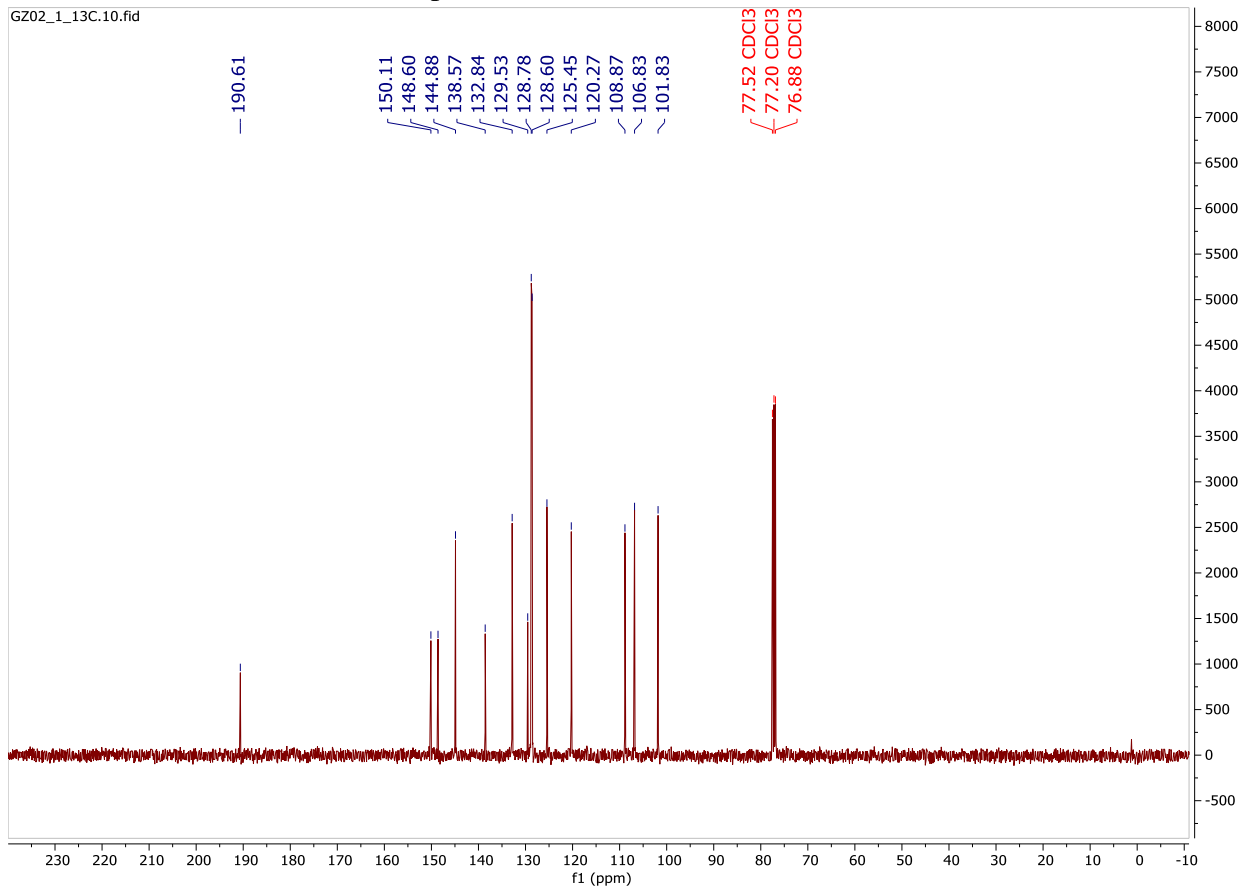
^{13}C NMR spectrum of **2** (101 MHz, CDCl_3)



¹H NMR spectrum of **3a** (300 MHz, CDCl₃)



¹³C NMR spectrum of **3a** (101 MHz, CDCl₃)

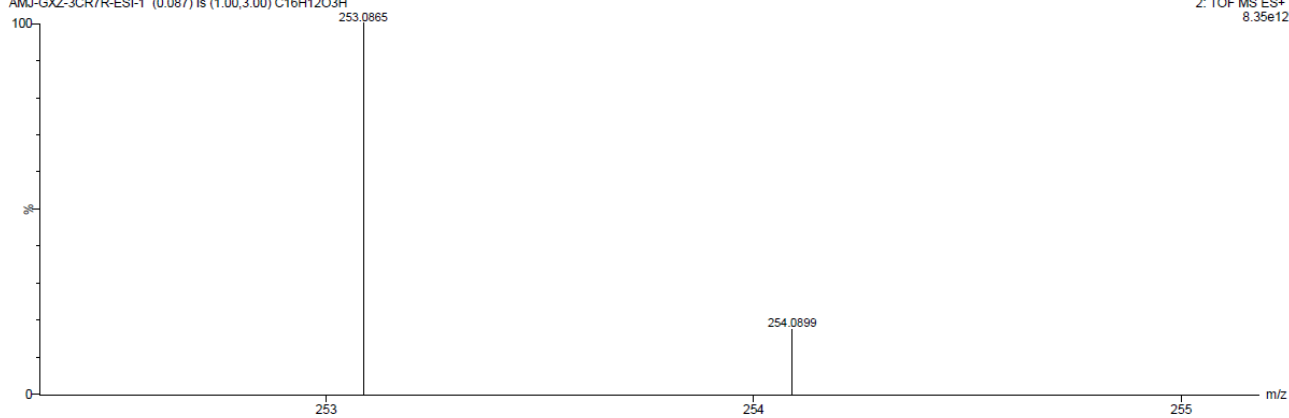


Mass Spectrometry of 3a

GZ02_4 C16H12O3 MW=25227
(DCM)/CH3OH:H2O:0.1% Formic Acid
AMJ-GXZ-3CR7R-ESI-1 (0.067) Is (1.00,3.00) C16H12O3H

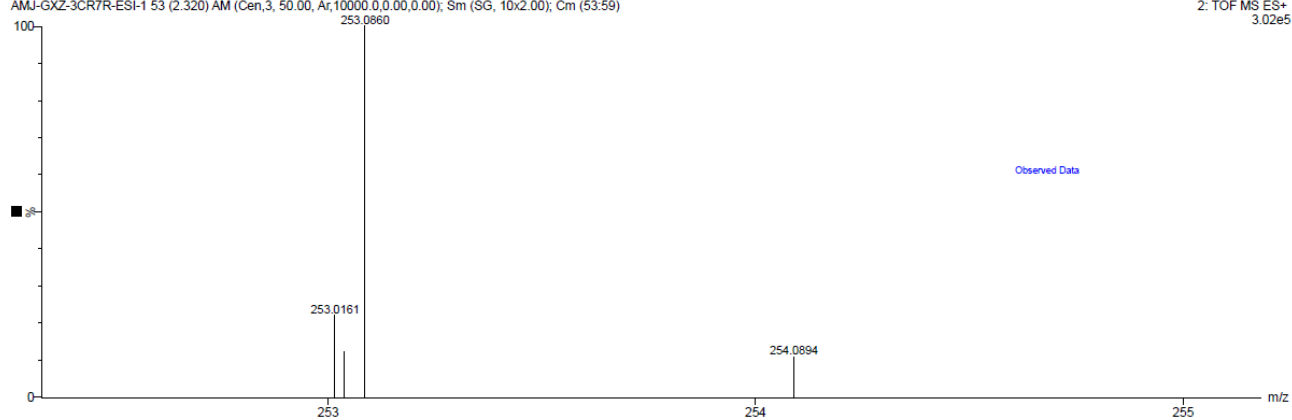
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Waters Xevo G2-XS

Gabriel Zazeri
29-Jan-2020
2: TOF MS ES+
8.35e12

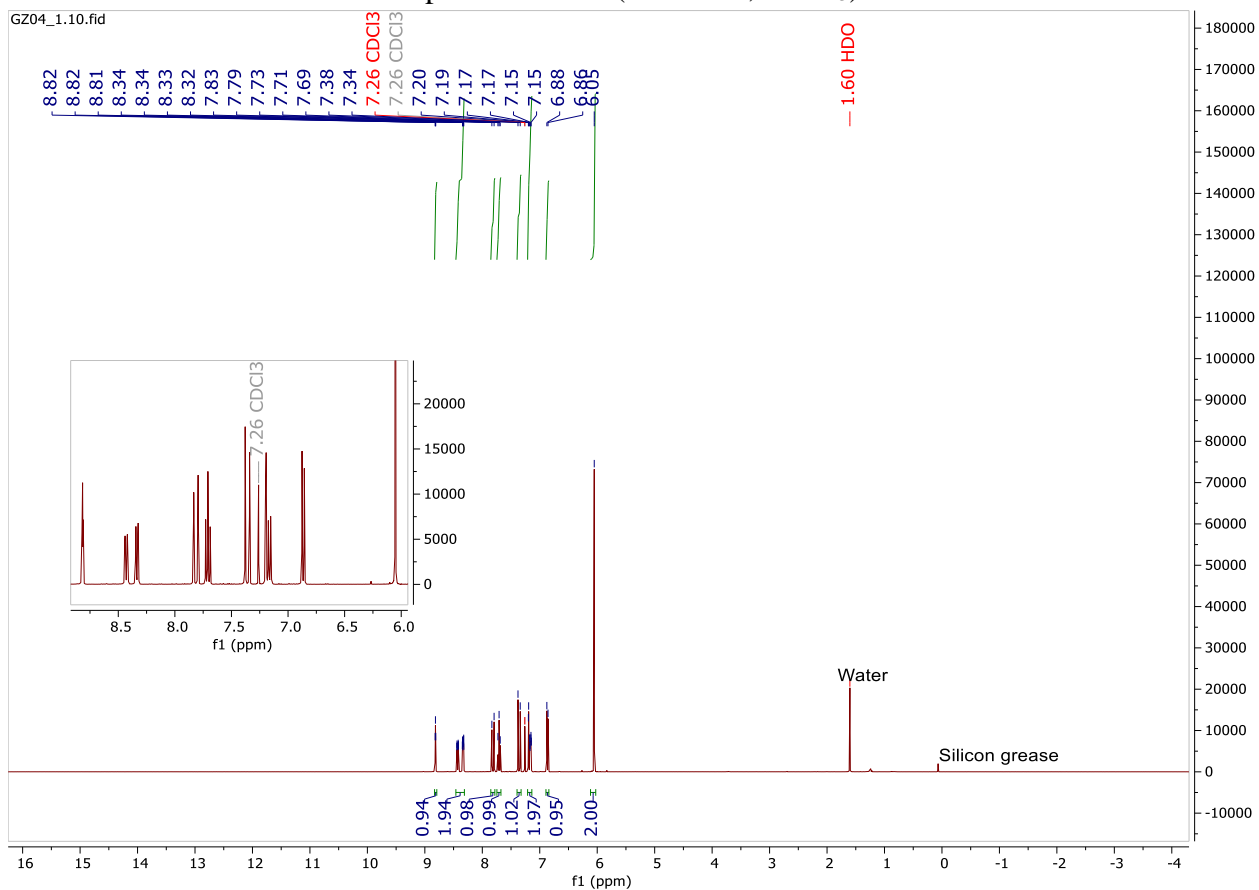


AMJ-GXZ-3CR7R-ESI-1 53 (2.320) AM (Cen,3, 50.00, Ar,10000.0,0.00,0.00); Sm (SG, 10x2.00); Cm (53:59)

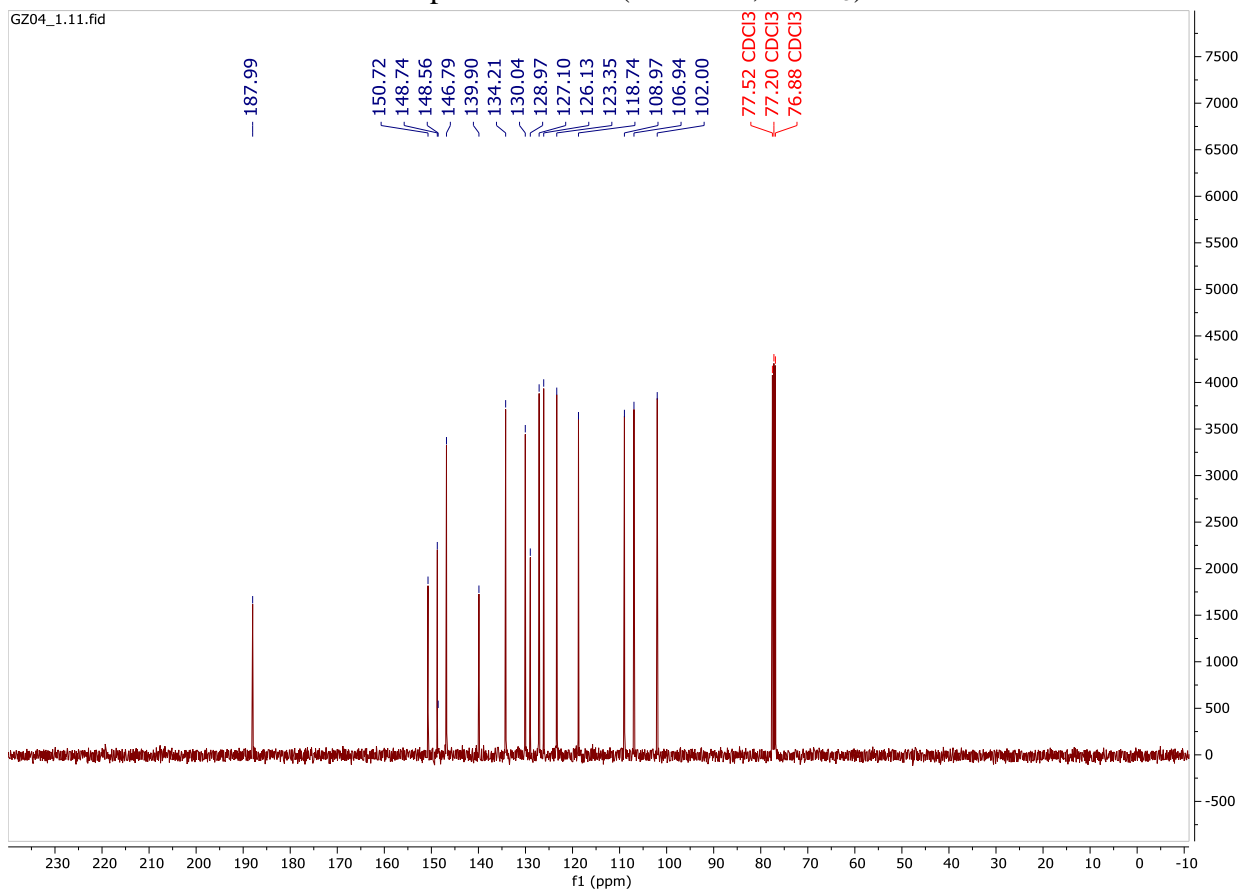
2: TOF MS ES+
3.02e5



¹H NMR spectrum of **3b** (400 MHz, CDCl₃)



¹³C NMR spectrum of **3b** (101 MHz, CDCl₃)

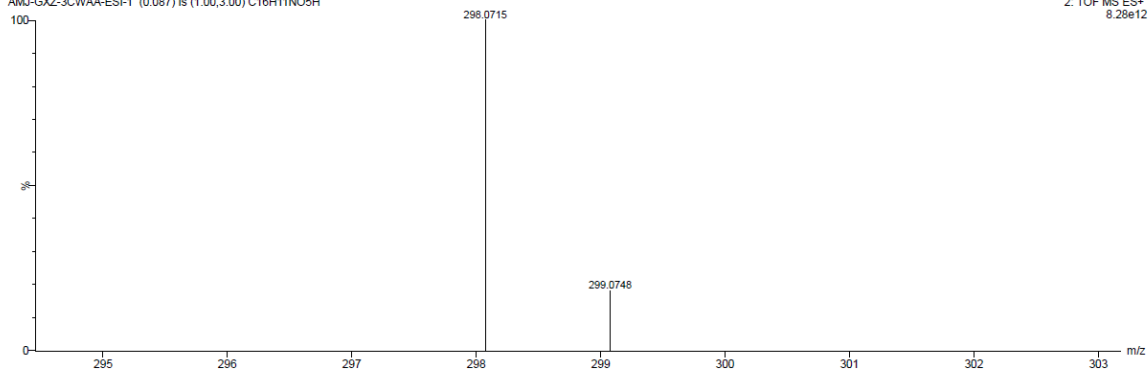


Mass Spectrometry of 3b

GZ04_1 C16H11NO5 MW=297
(DCM)/CH3OH:H2O:0.1% Formic Acid
AMJ-GXZ-3CWAA-ESI-1 (0.087) Is (1.00,3.00) C16H11NO5H

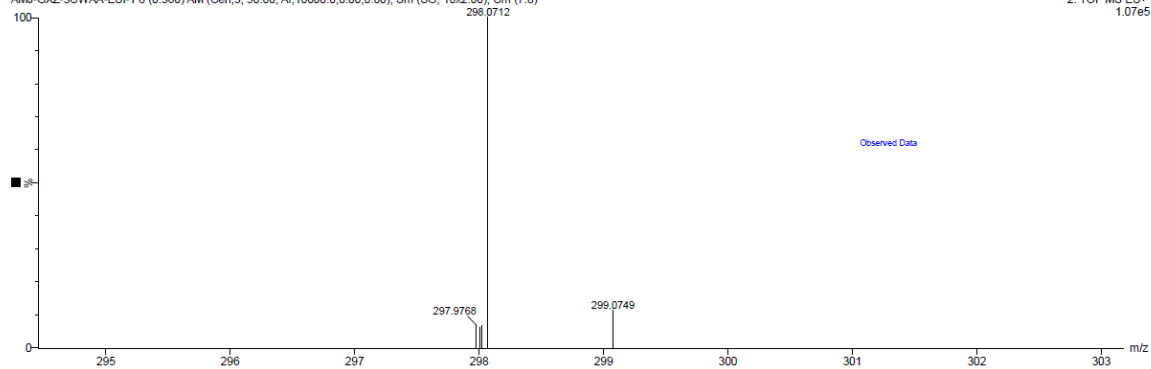
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Waters Xevo G2-XS

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30-Jan-2020
2: TOF MS ES+
8.28e12

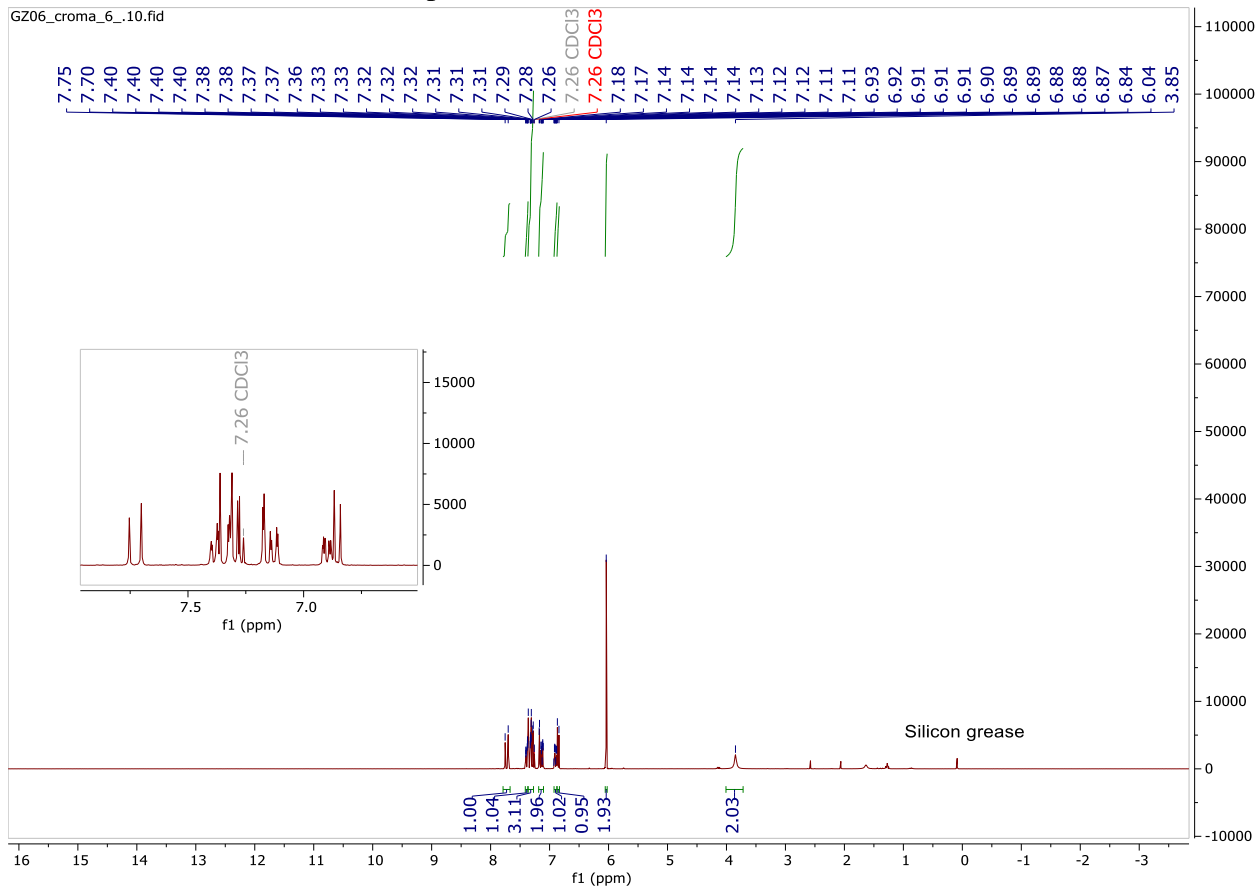


AMJ-GXZ-3CWAA-ESI-1 8 (0.360) AM (Cen,3, 50.00, Ar,10000.0,0.00,0.00); Sm (SG, 10x2.00); Cm (7.8)

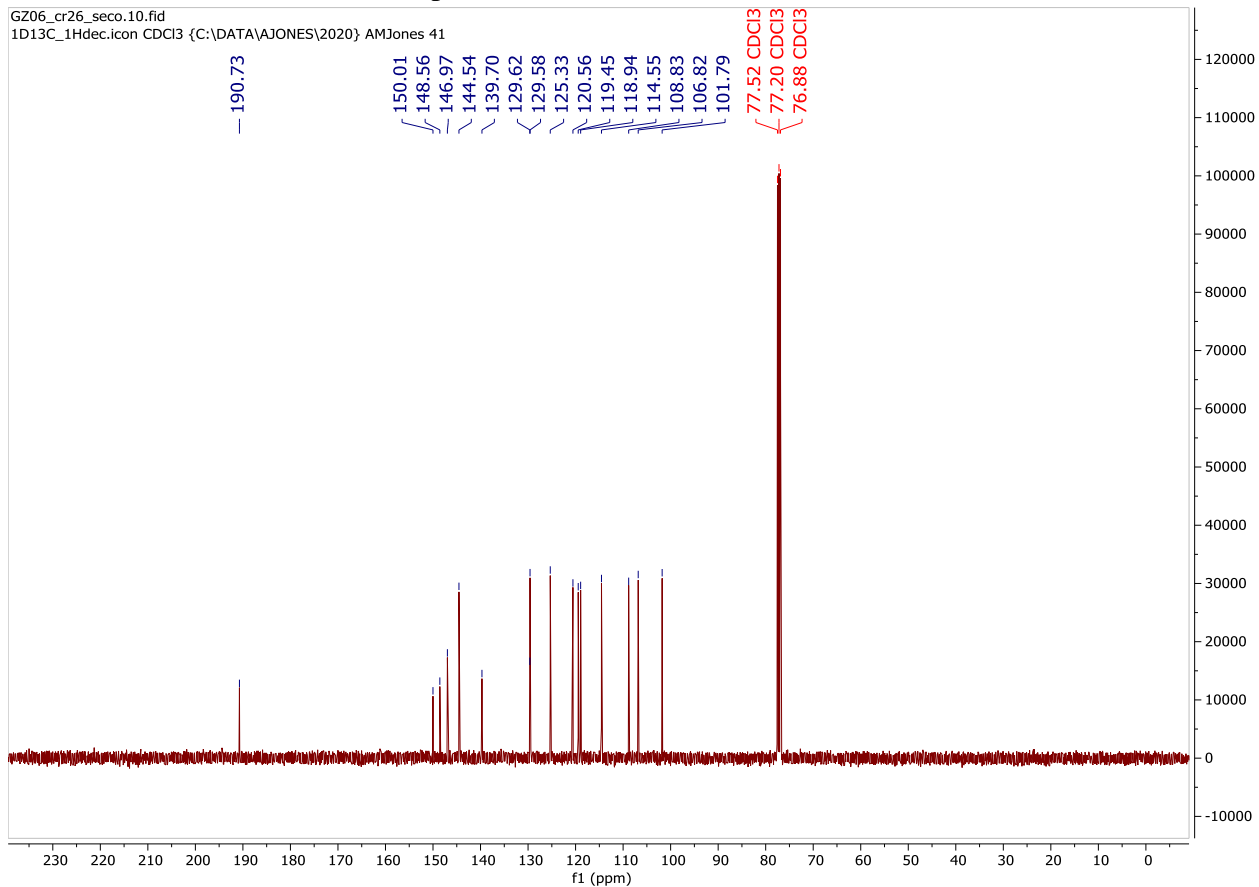
2: TOF MS ES+
1.07e5



¹H NMR spectrum of **3c** (300 MHz, CDCl₃)



¹³C NMR spectrum of **3c** (101 MHz, CDCl₃)

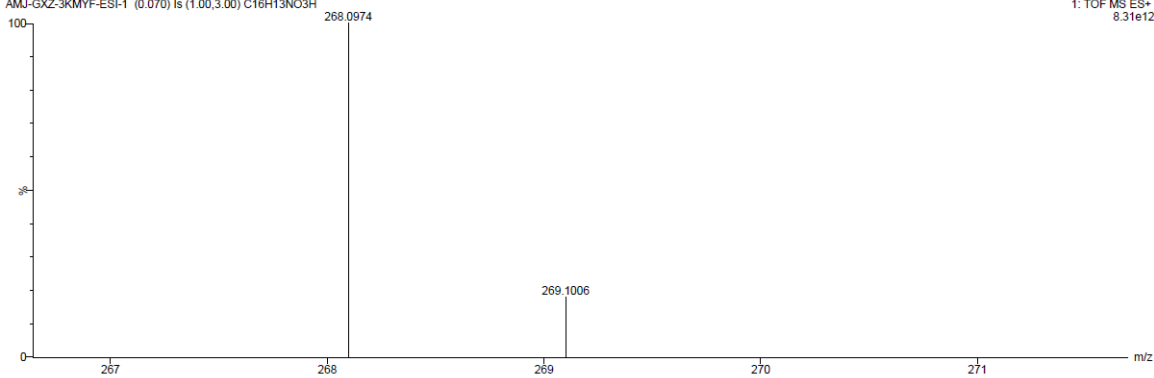


Mass Spectrometry of 3c

GZ06 C16H13NO3 MW=267
(DCM)/CH3OH:H2O:0.1% Formic Acid
AMJ-GXZ-3KMYF-ESI-1 (0.070) Is (1.00,3.00) C16H13NO3H

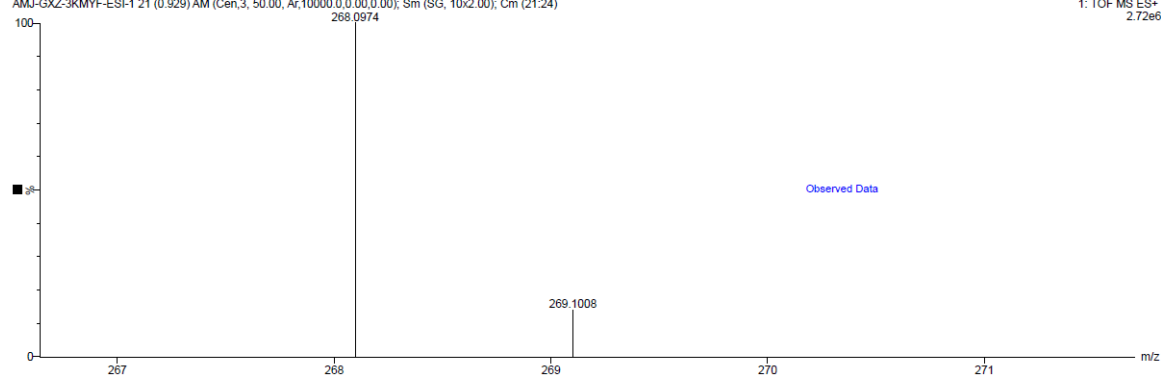
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13-Mar-2020
1: TOF MS ES+
8.31e12

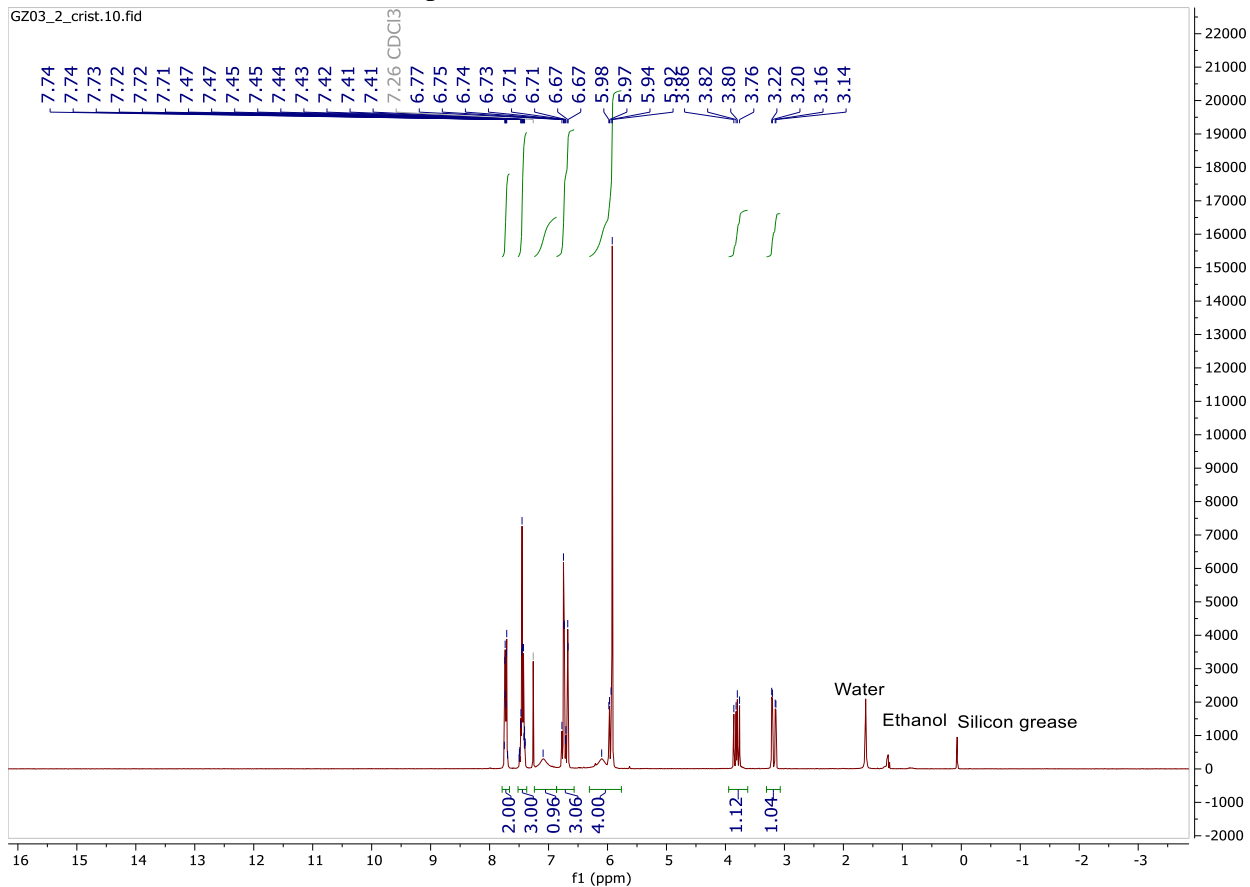


AMJ-GXZ-3KMYF-ESI-1 21 (0.929) AM (Cen,3, 50.00, Ar,10000.0,0.00,0.00); Sm (SG, 10x2.00); Cm (21:24)

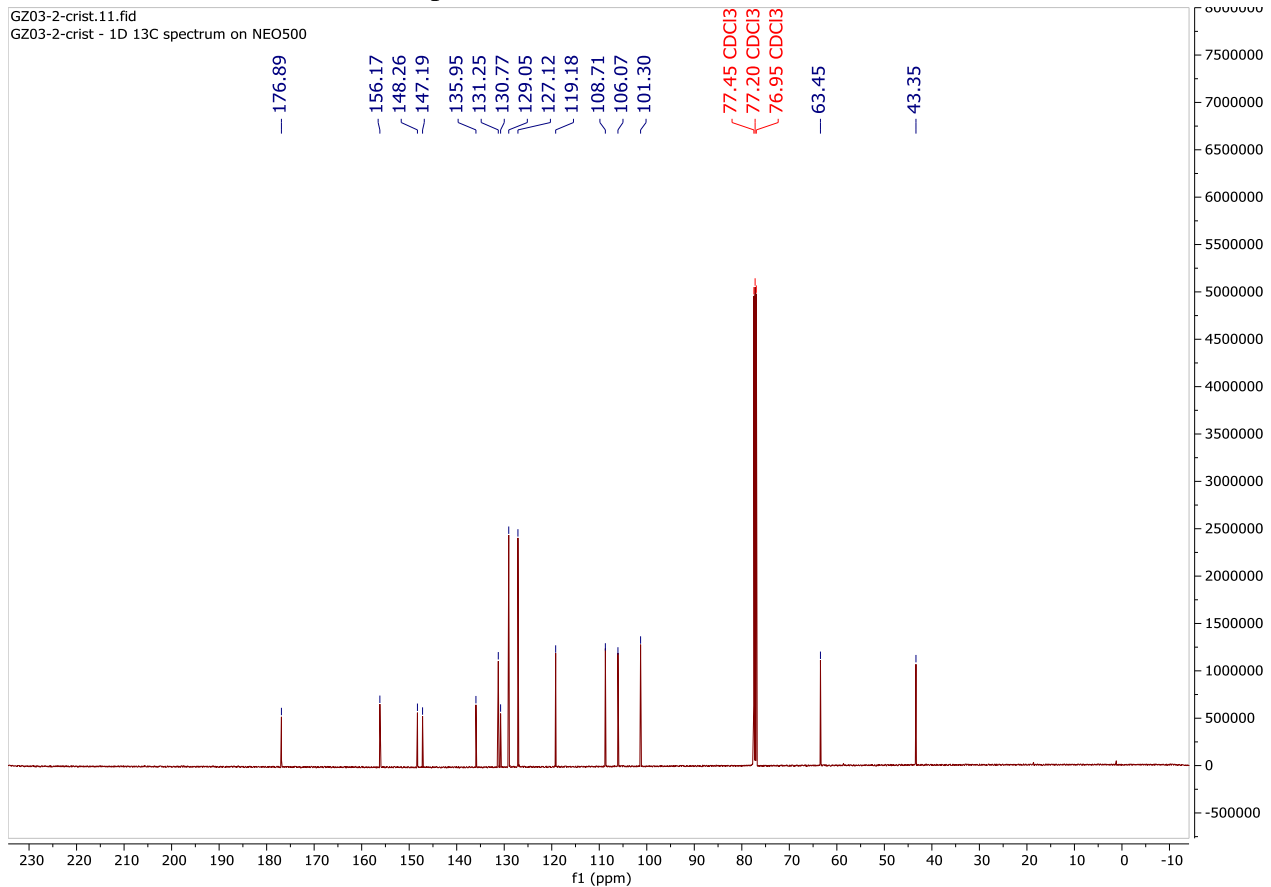
1: TOF MS ES+
2.72e8



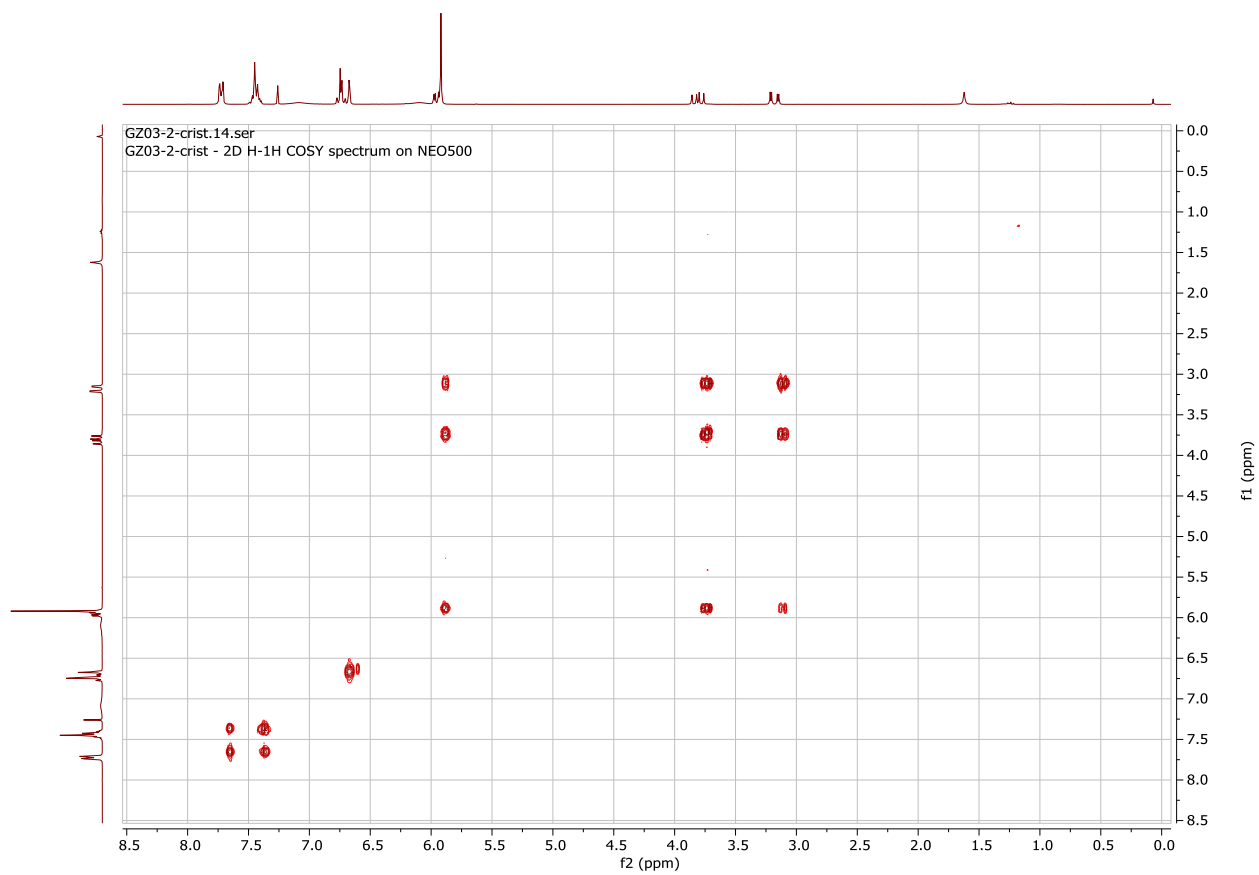
¹H NMR spectrum of **4a** (300 MHz, CDCl₃)



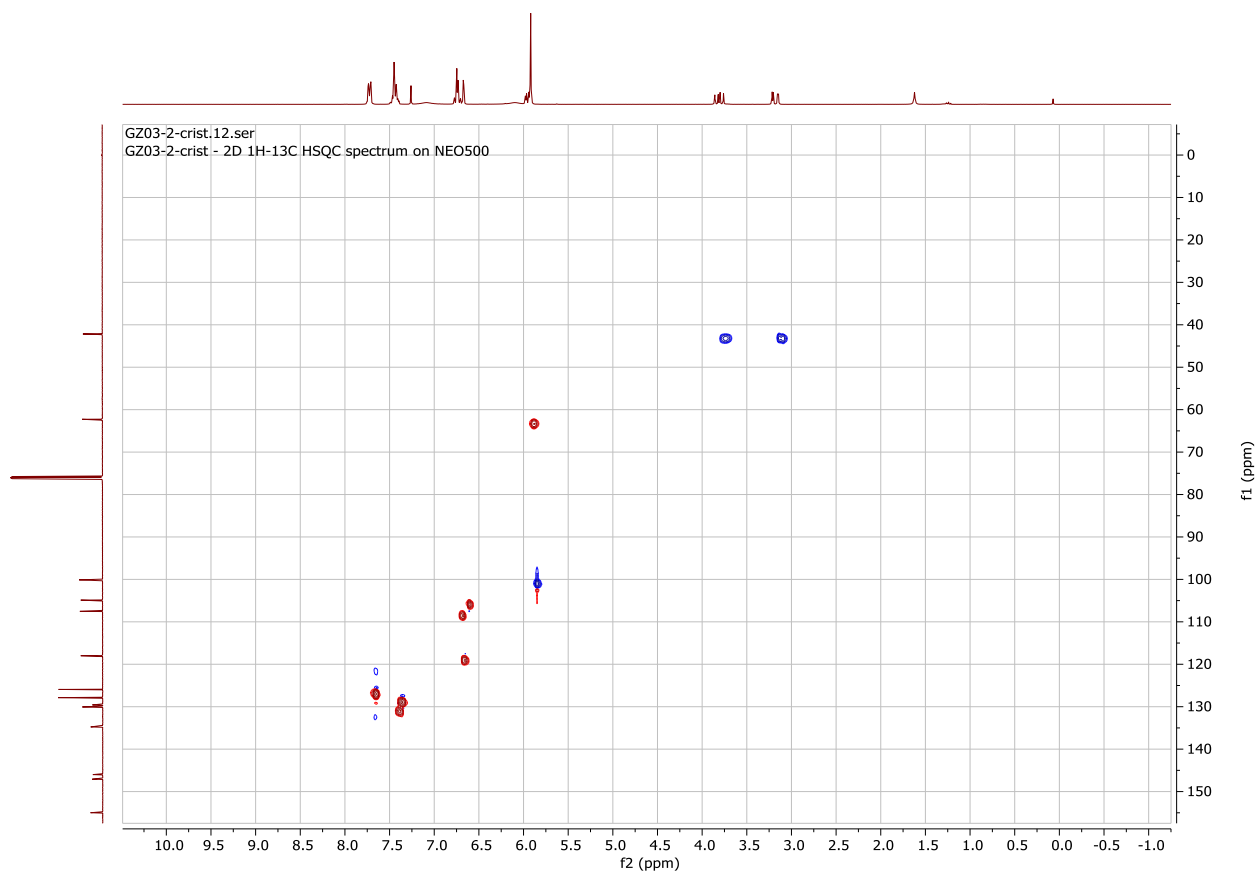
¹³C NMR spectrum of **4a** (126 MHz, CDCl₃)



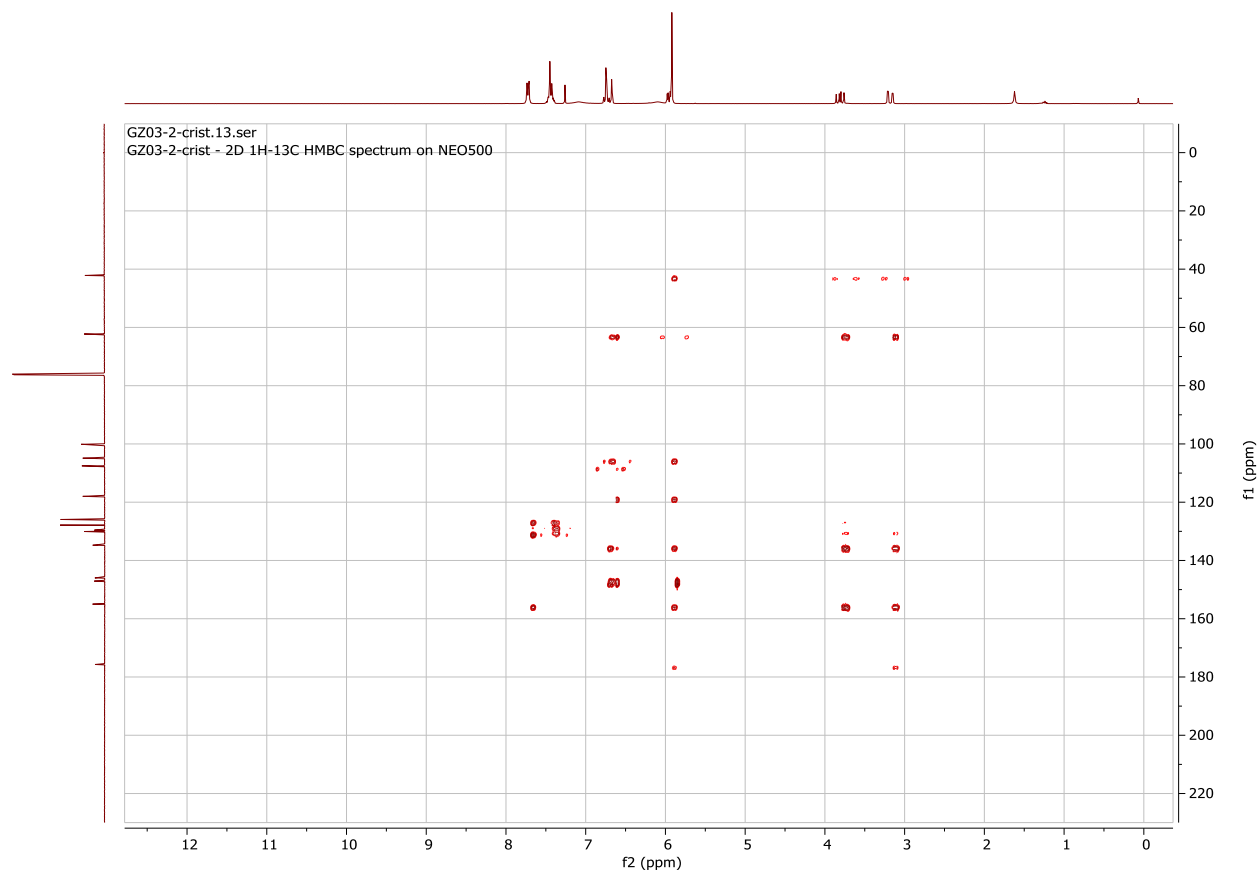
^1H - ^1H COSY NMR spectrum of **4a**



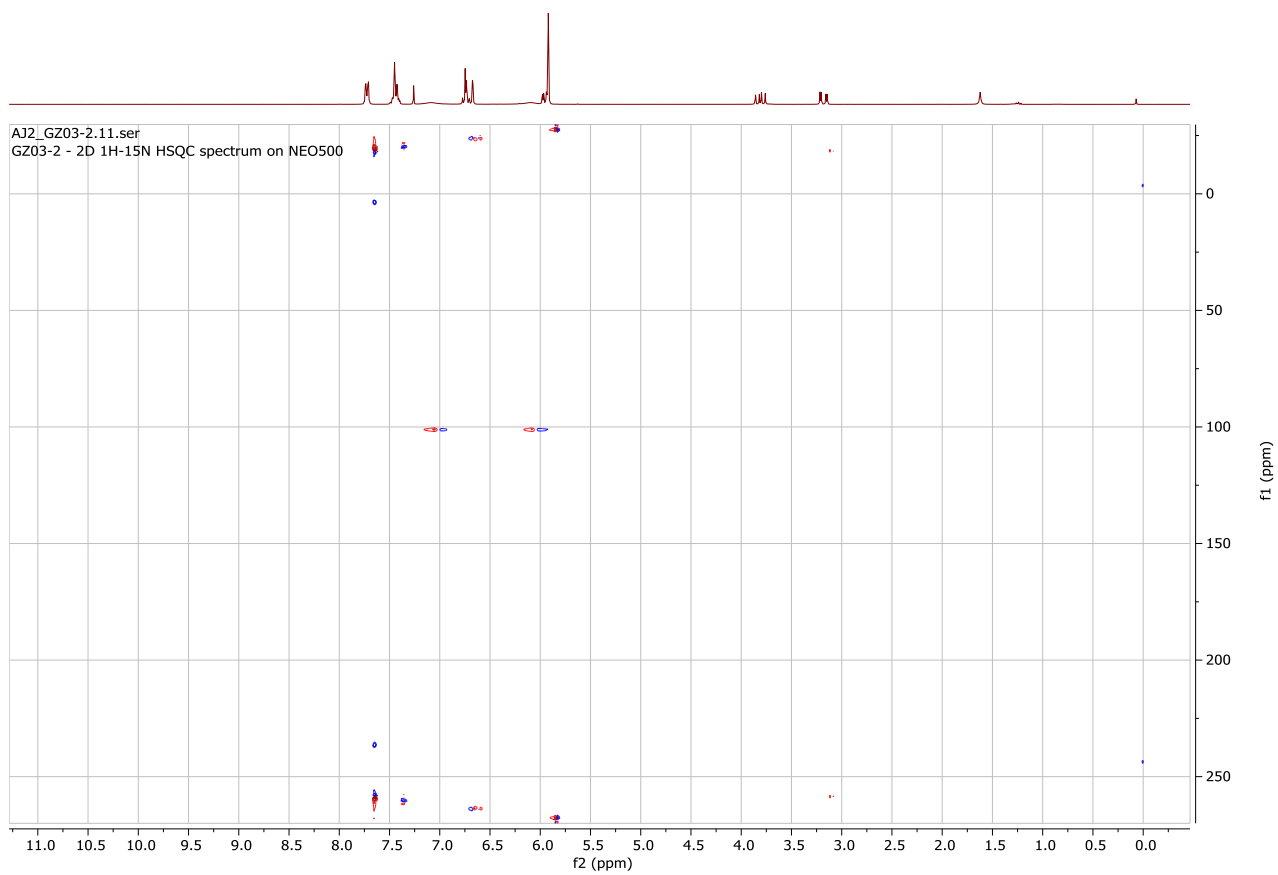
^1H - ^{13}C HSQC NMR spectrum of **4a**



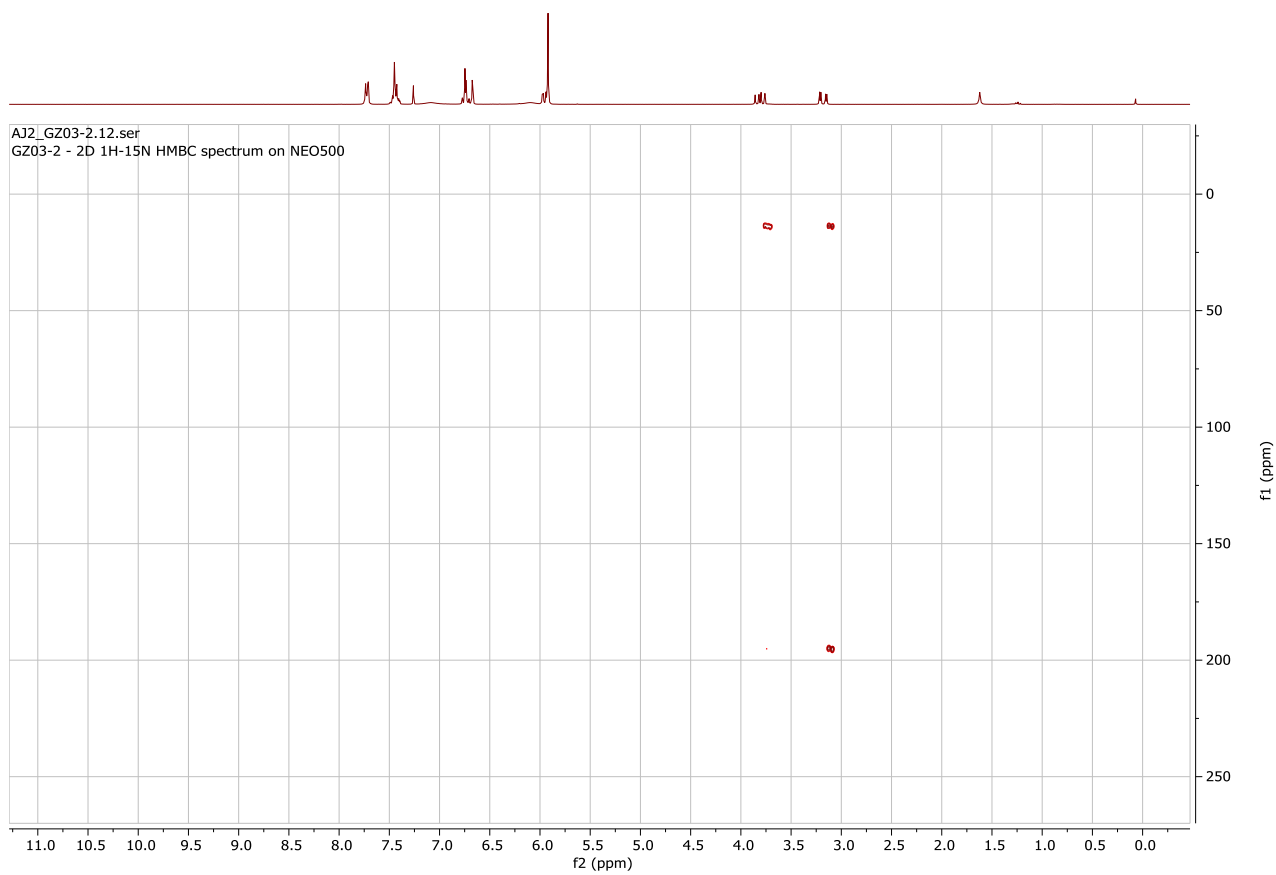
^1H - ^{13}C HMBC NMR spectrum of **4a**



^1H - ^{15}N HSQC NMR spectrum of **4a**



^1H - ^{15}N HMBC NMR spectrum of **4a**

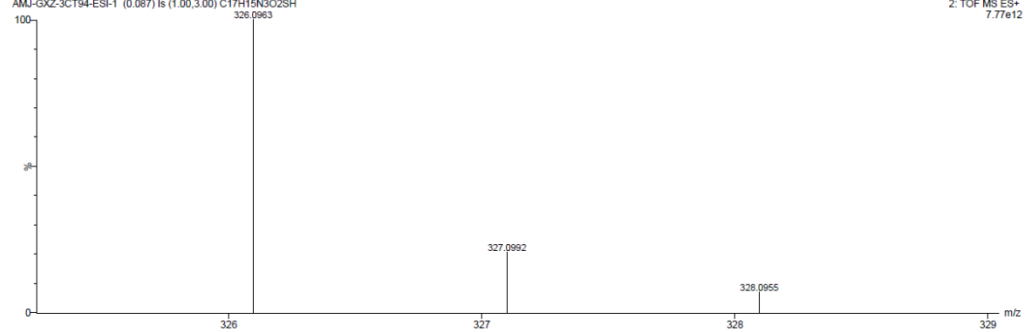


Mass Spectrometry of 4a

GZ03_2 C17H15N3O2S MW=325
(DCM)/CH3OH:H2O:0.1% Formic Acid
AMU-GXZ-3CT94-ESI-1 (0.087) Is (1.00,3.00) C17H15N3O2SH

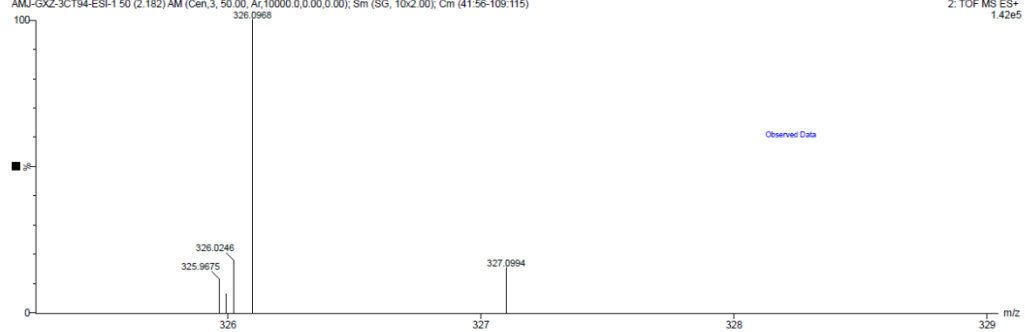
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Gabriel Zazeni
29-Jan-2020
2: TOF MS ES+
7.77e12

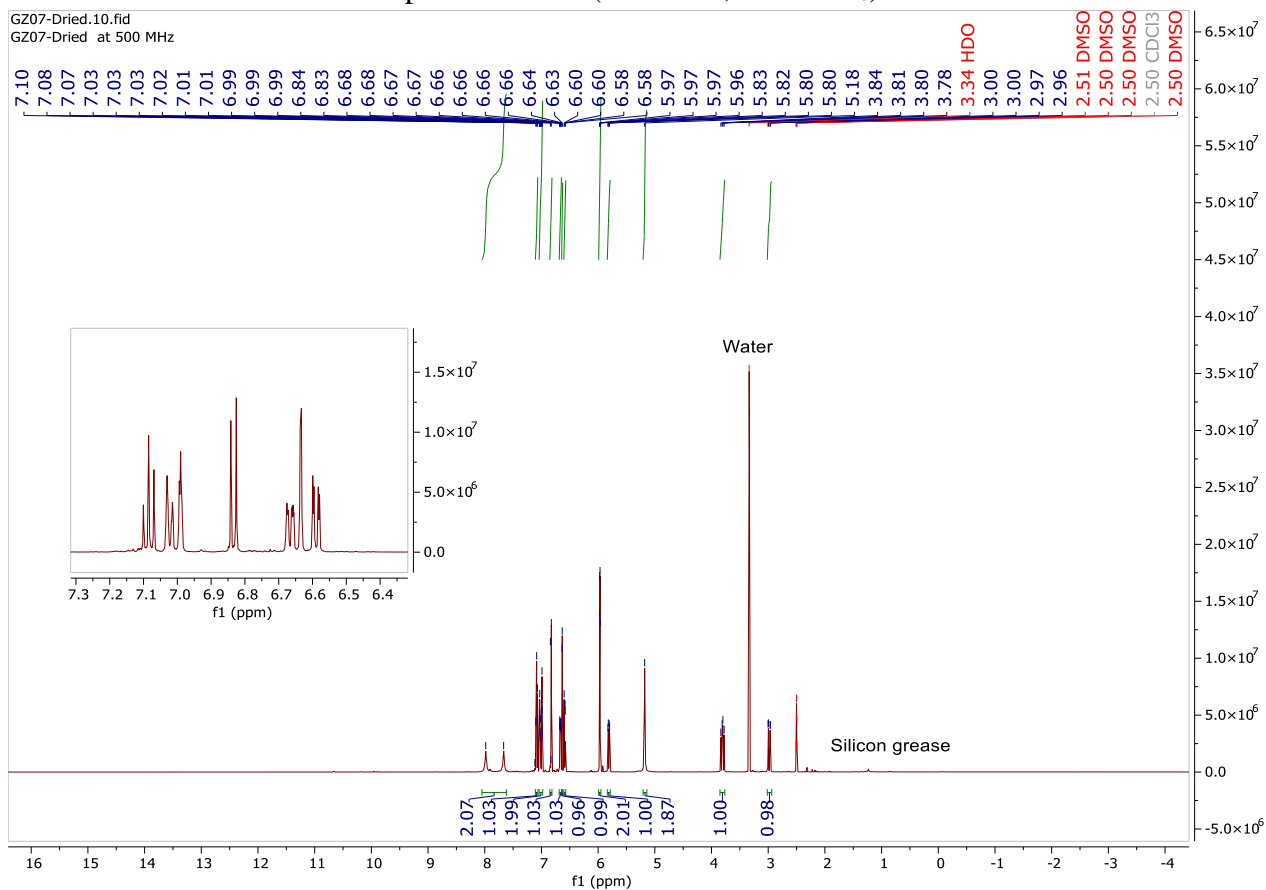


AMU-GXZ-3CT94-ESI-1 50 (2.182) AM (Cen,3, 50.00, Ar,100000.0,0.00,0.00); Sm (SG, 10x2.00); Cm (41.56-109-115)

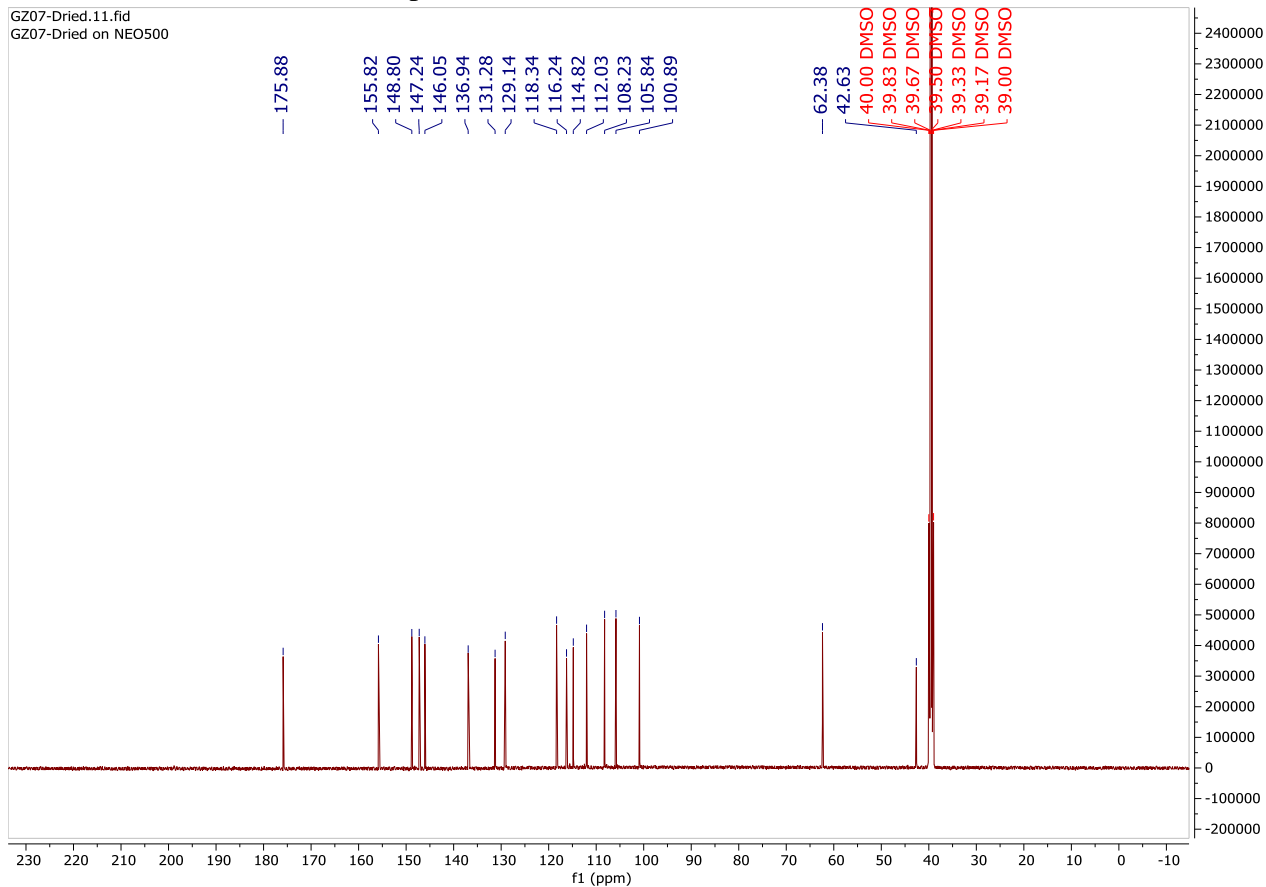
2: TOF MS ES+
1.42e5



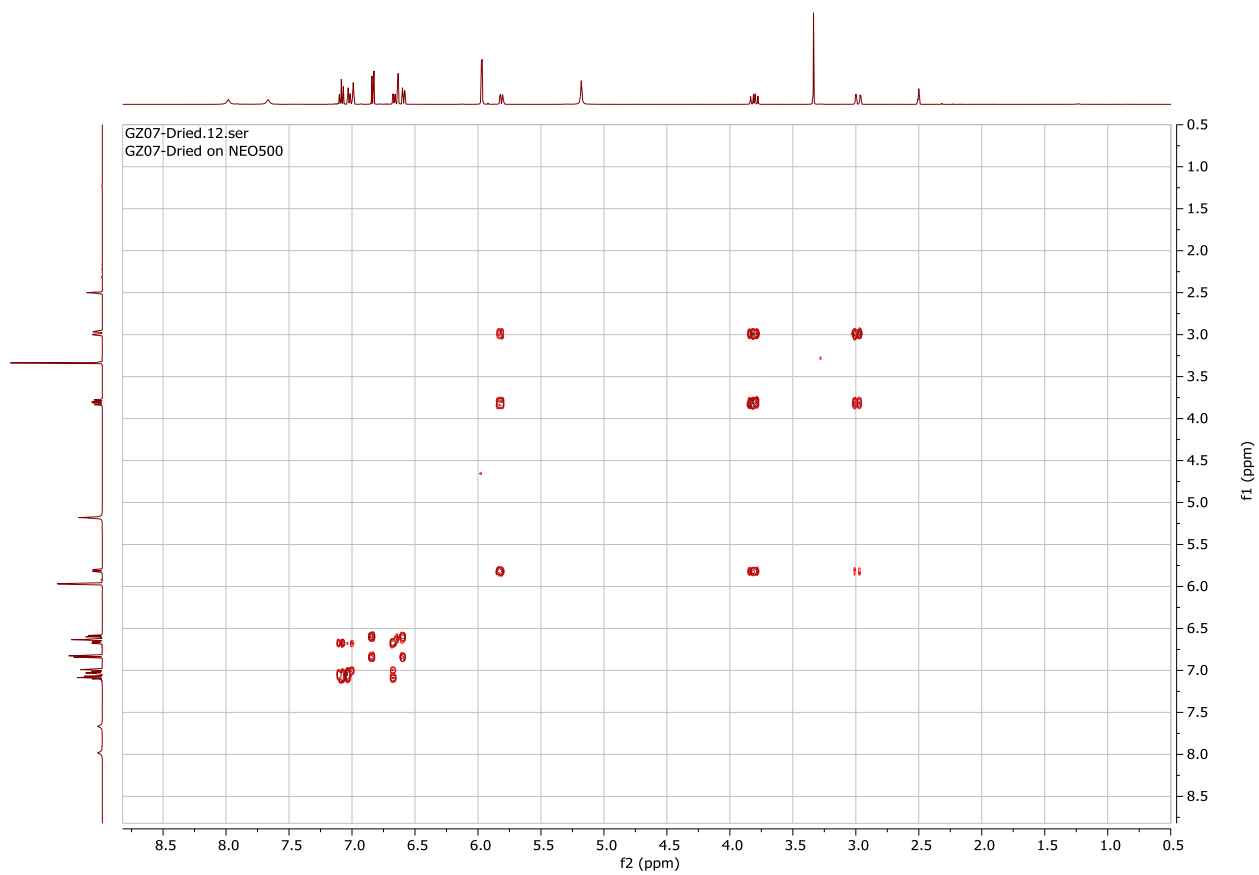
¹H NMR spectrum of 4c (500 MHz, DMSO-d₆)



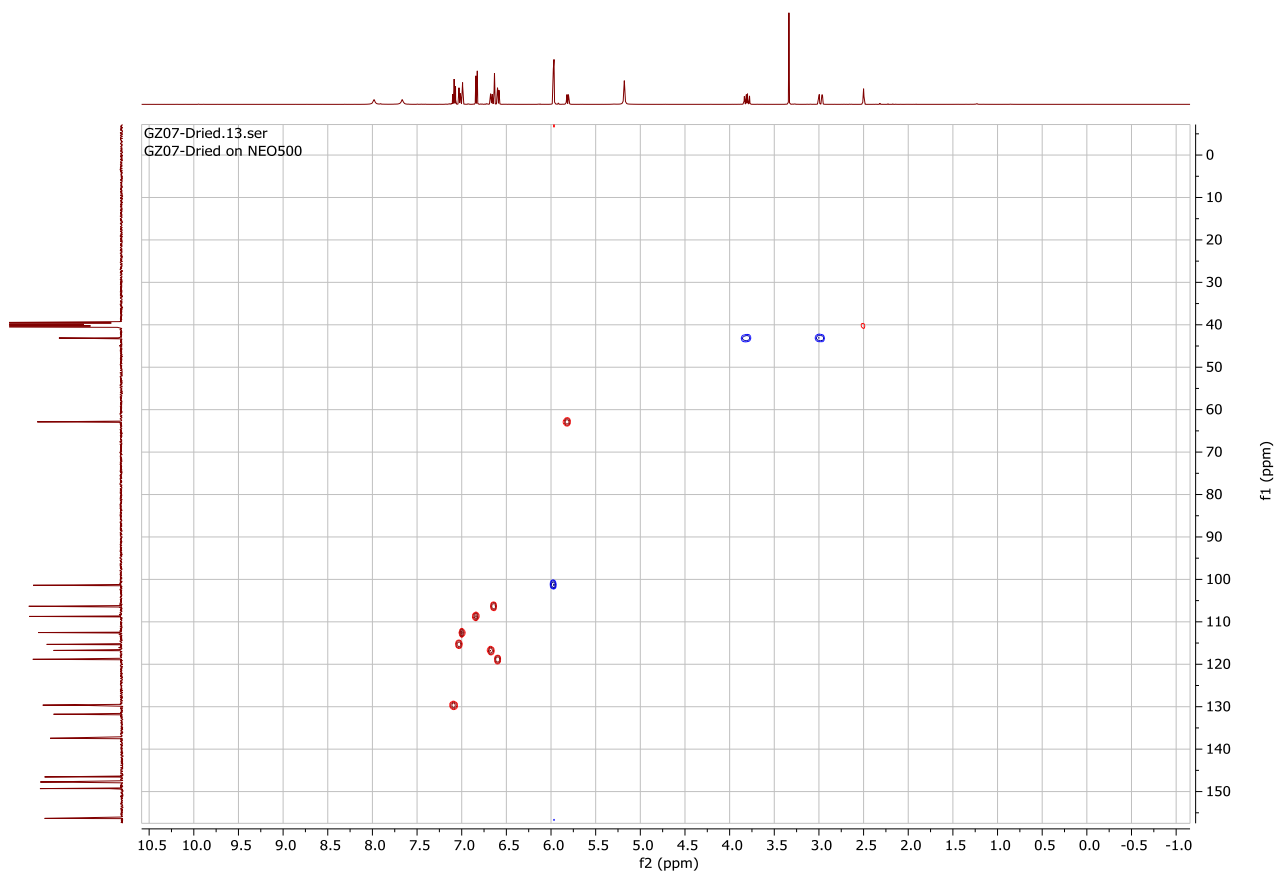
¹³C NMR spectrum of **4c** (126 MHz, DMSO-d₆)



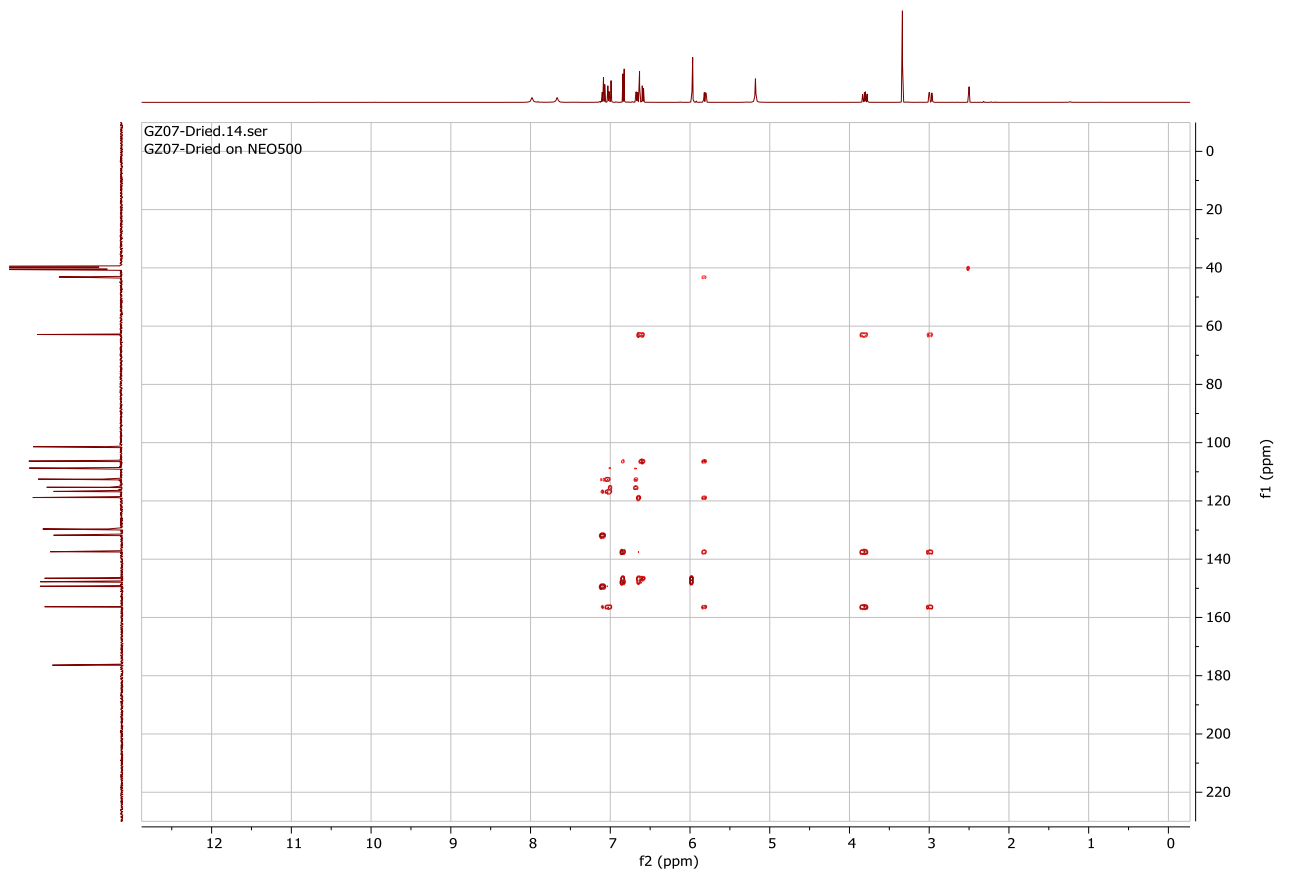
^1H - ^1H COSY NMR spectrum of **4c**



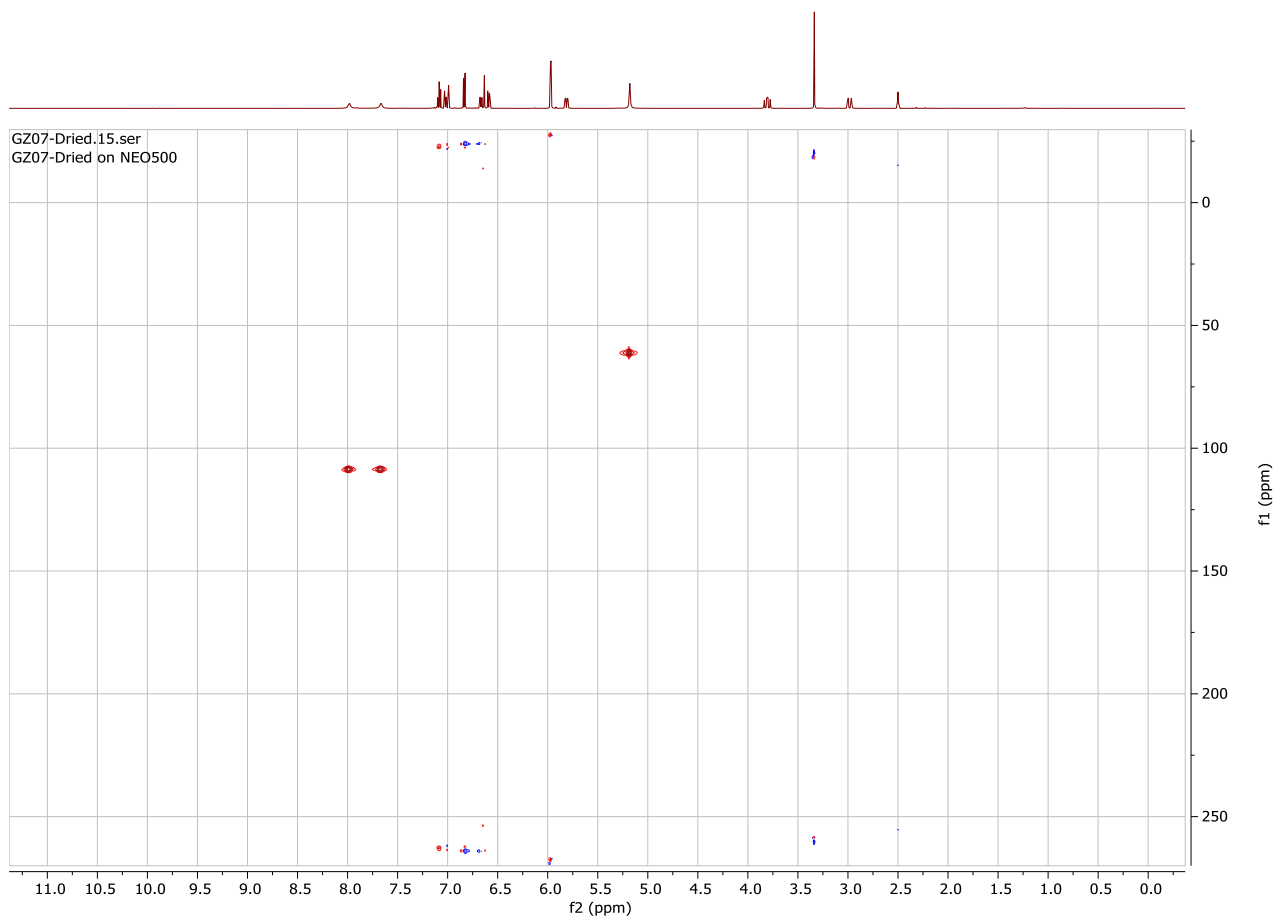
^1H - ^{13}C HSQC NMR spectrum of **4c**



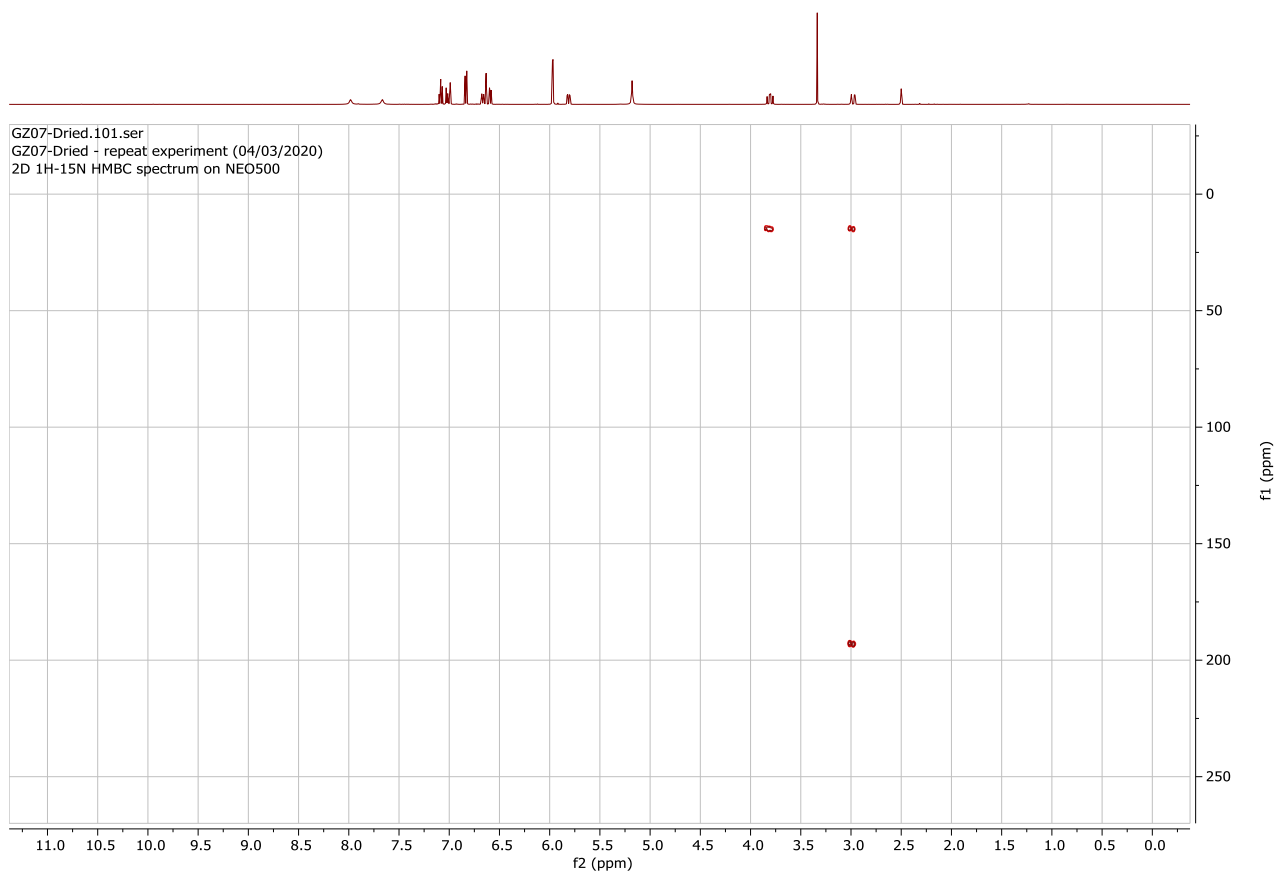
^1H - ^{13}C HMBC NMR spectrum of **4c**



^1H - ^{15}N HSQC NMR spectrum of **4c**



^1H - ^{15}N HMBC NMR spectrum of **4c**

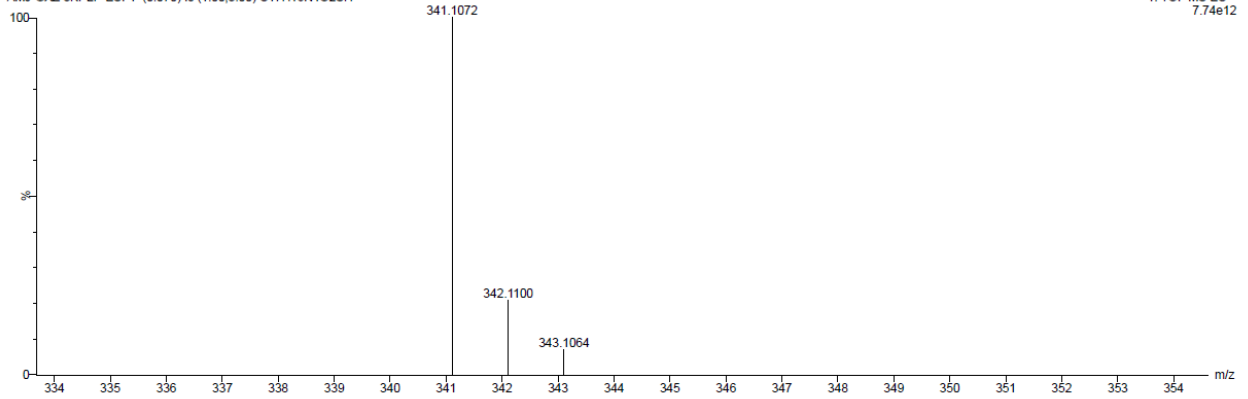


Mass Spectrometry of 4c

GZ07 C17H16N4O2S MW=340
(DCM)/CH3OH:H2O:0.1% Formic Acid
AMJ-GXZ-3KPLP-ESI-1 (0.070) Is (1.00,3.00) C17H16N4O2SH

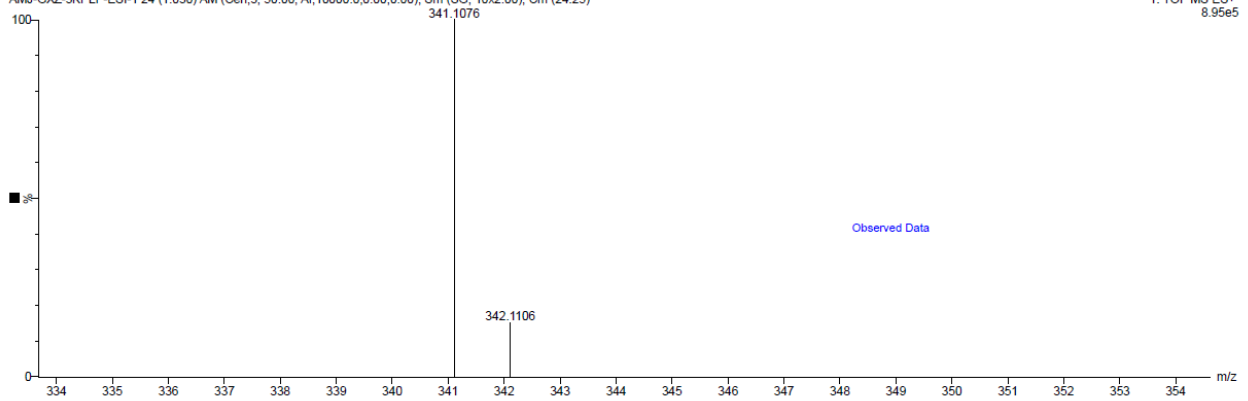
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1: TOF MS ES+
7.74e12

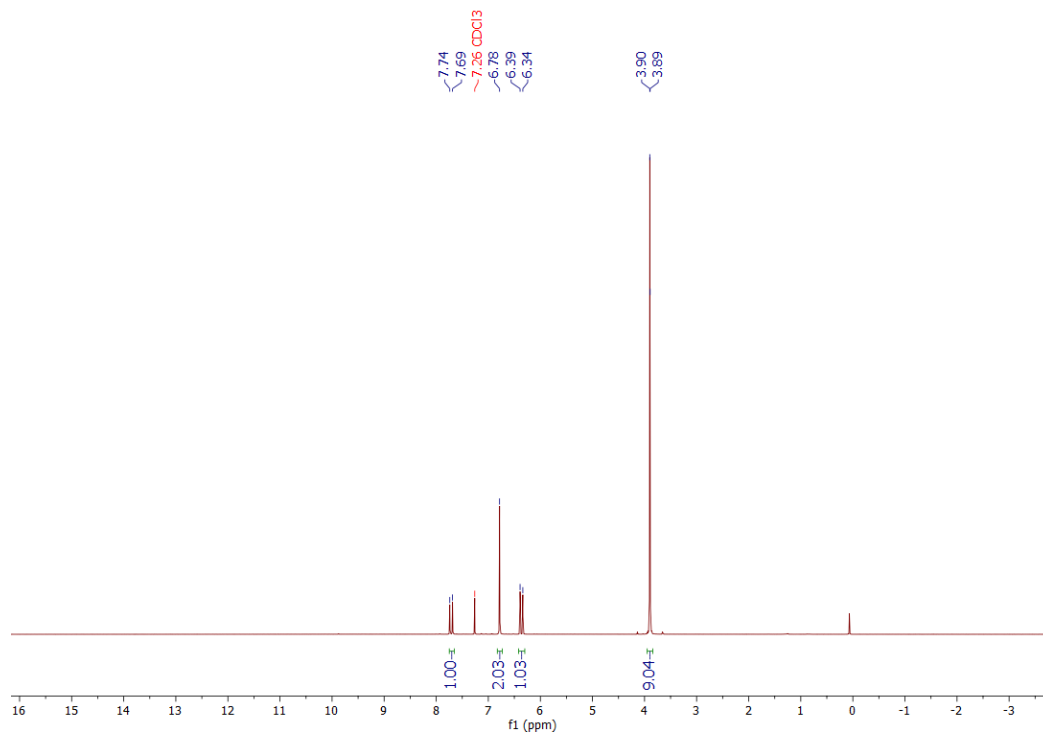


AMJ-GXZ-3KPLP-ESI-1 24 (1.030) AM (Cen,3, 50.00, Ar,10000.0,0.00,0.00); Sm (SG, 10x2.00); Cm (24:25)

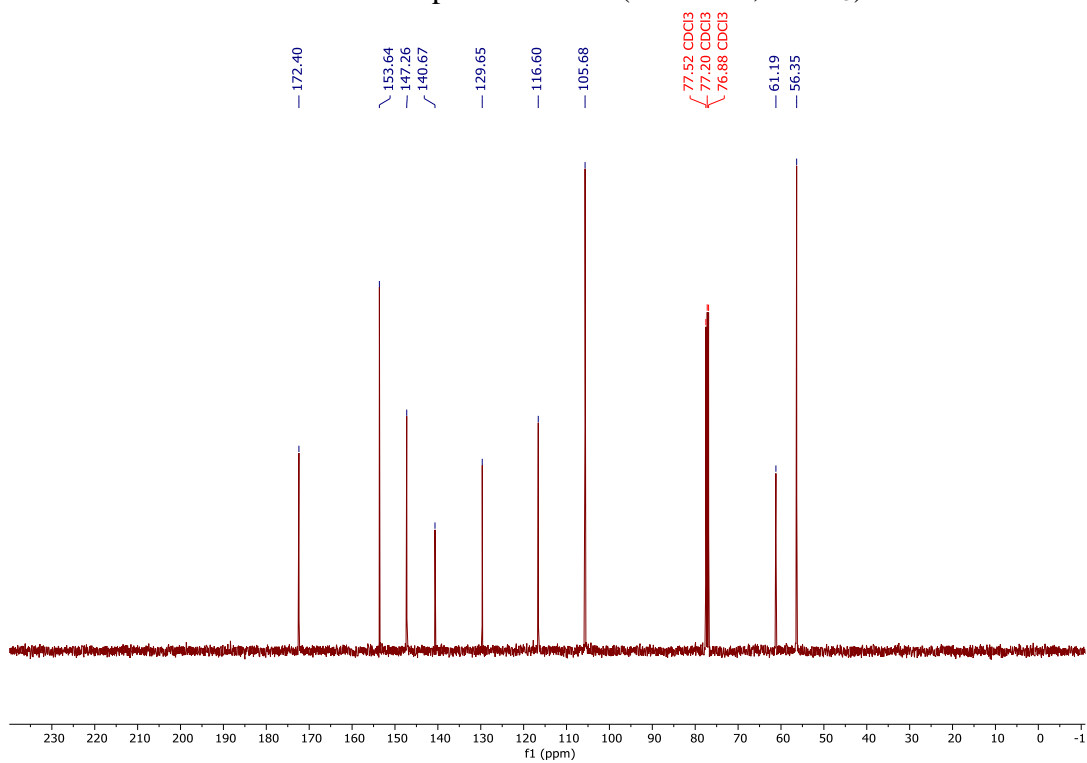
1: TOF MS ES+
8.95e5



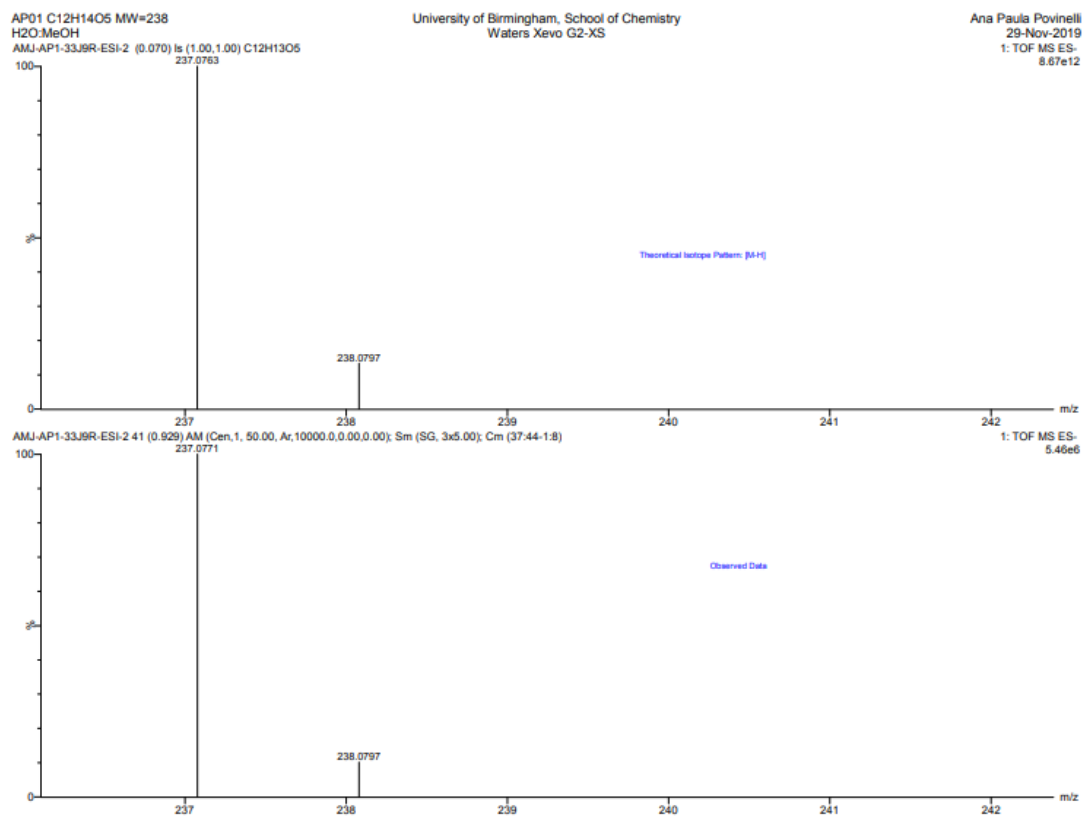
^1H NMR spectrum of **7a** (300 MHz, CDCl_3)



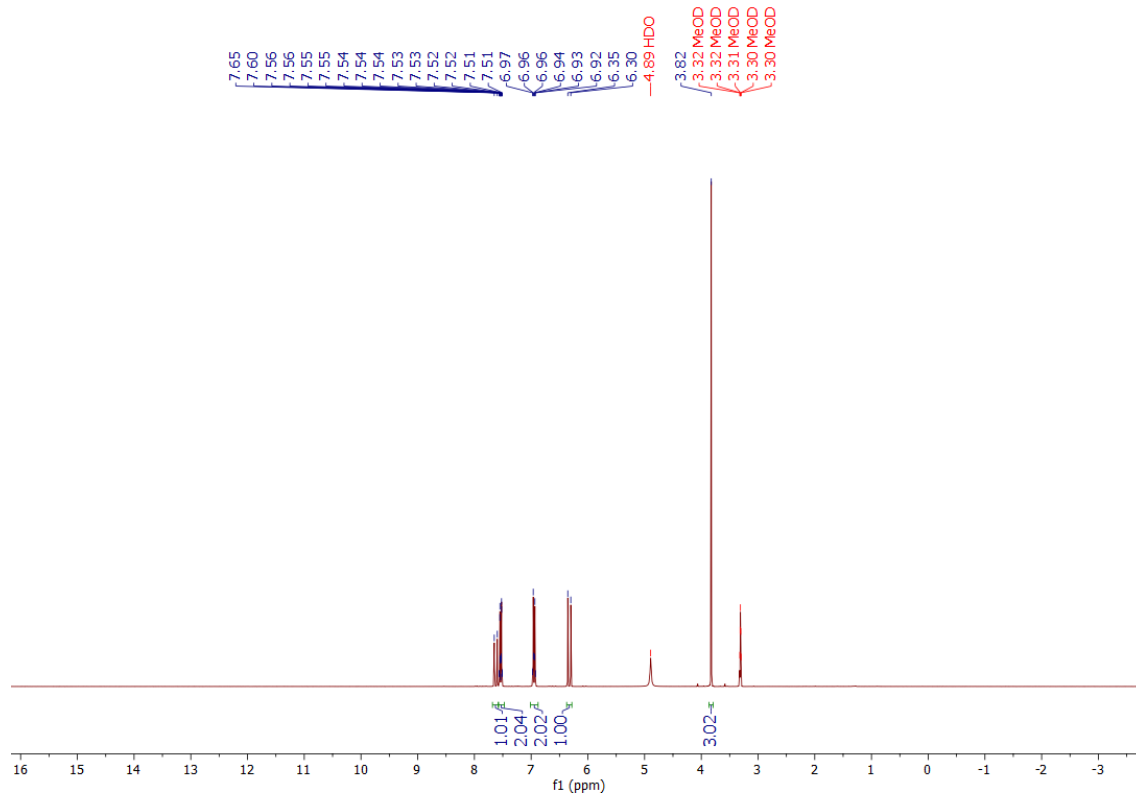
^{13}C NMR spectrum of **7a** (101 MHz, CDCl_3)



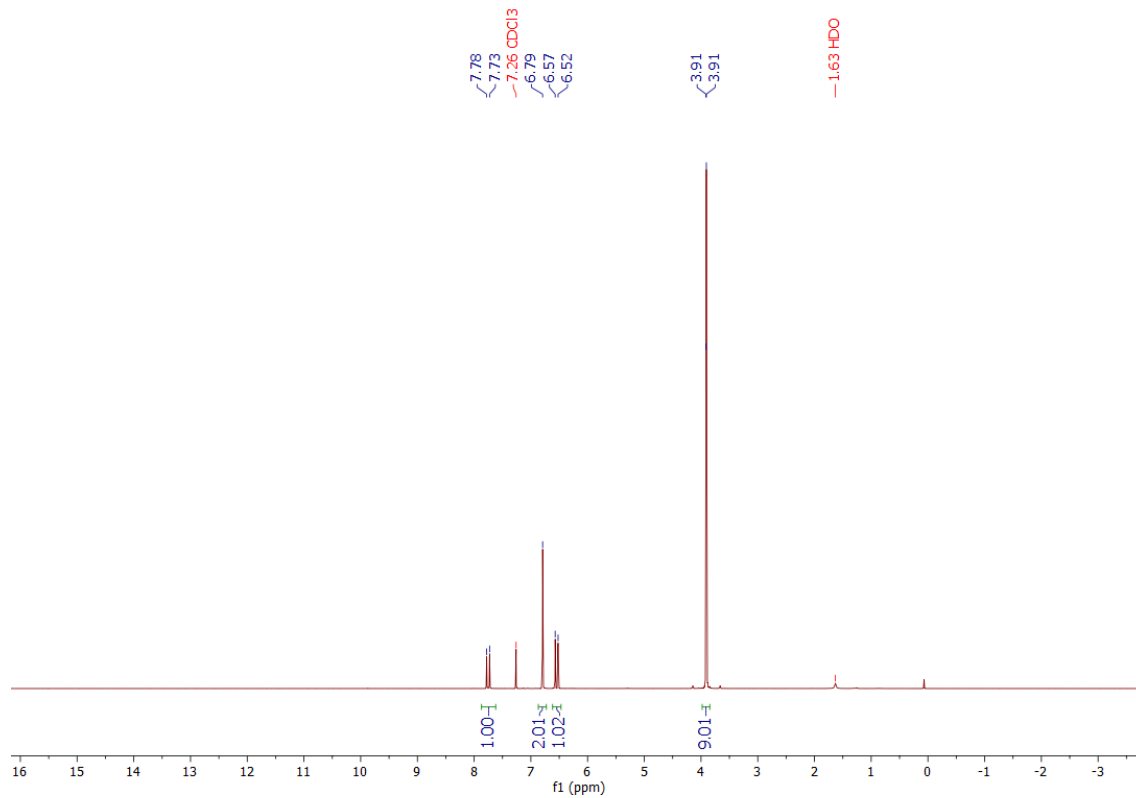
Mass Spectrometry of 7a



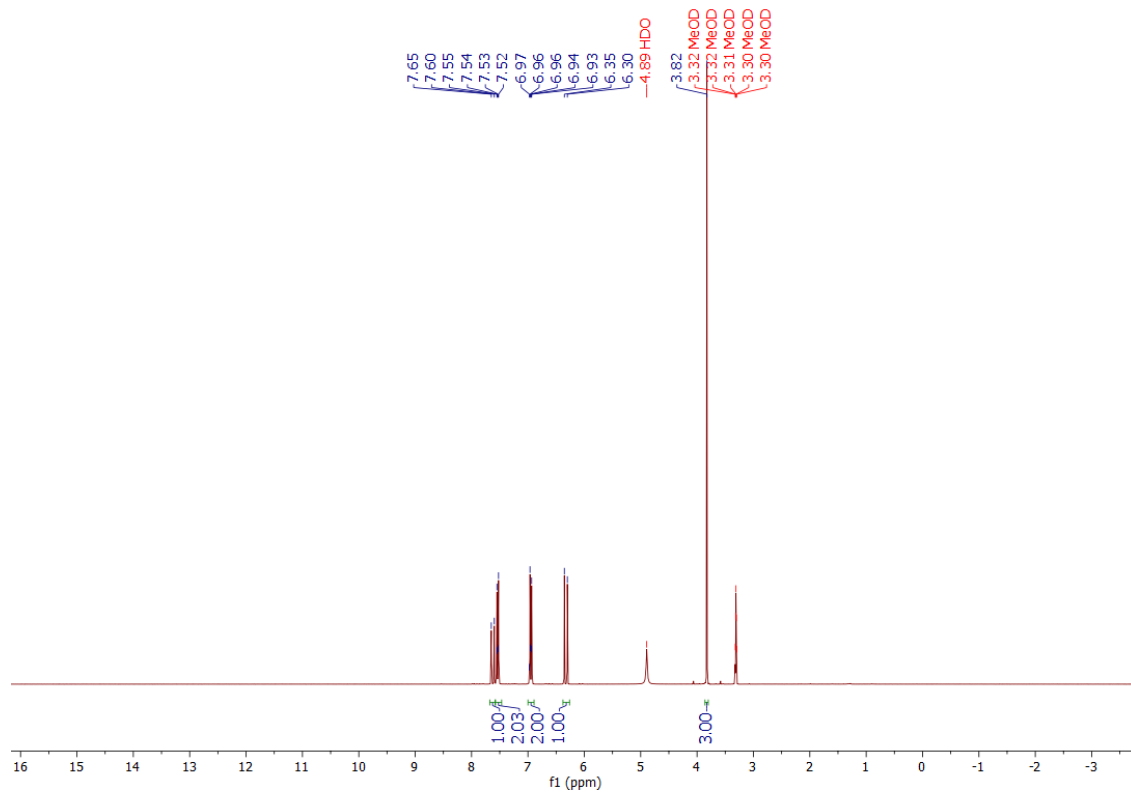
¹H NMR spectrum of **7b** (300 MHz, CD₃OD)



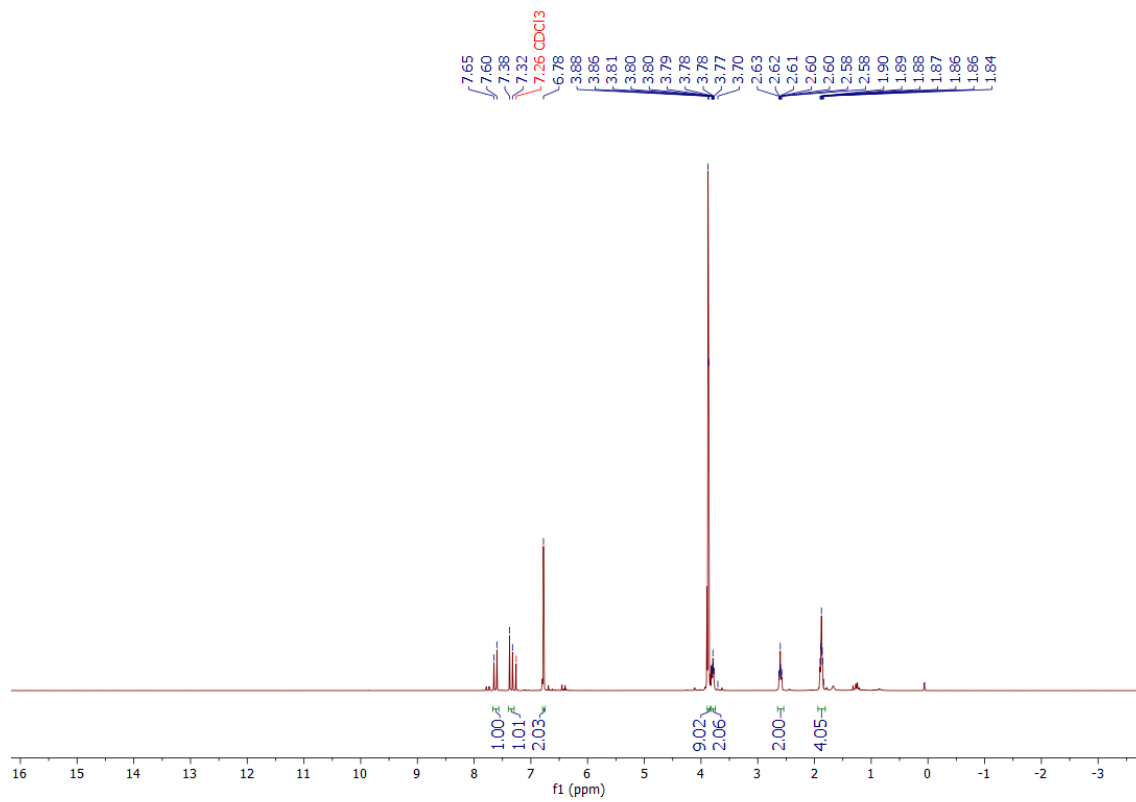
^1H NMR spectrum of **8a** (300 MHz, CDCl_3)



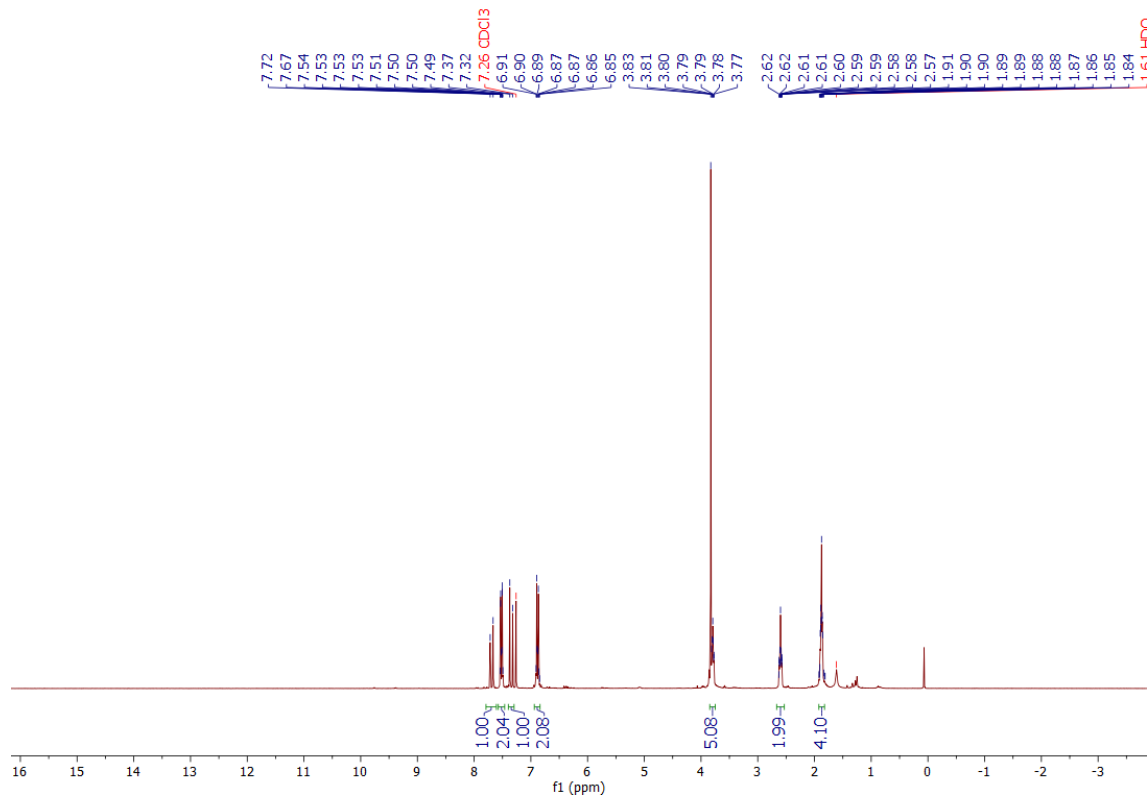
¹H NMR spectrum of **8b** (300 MHz, CD₃OD)



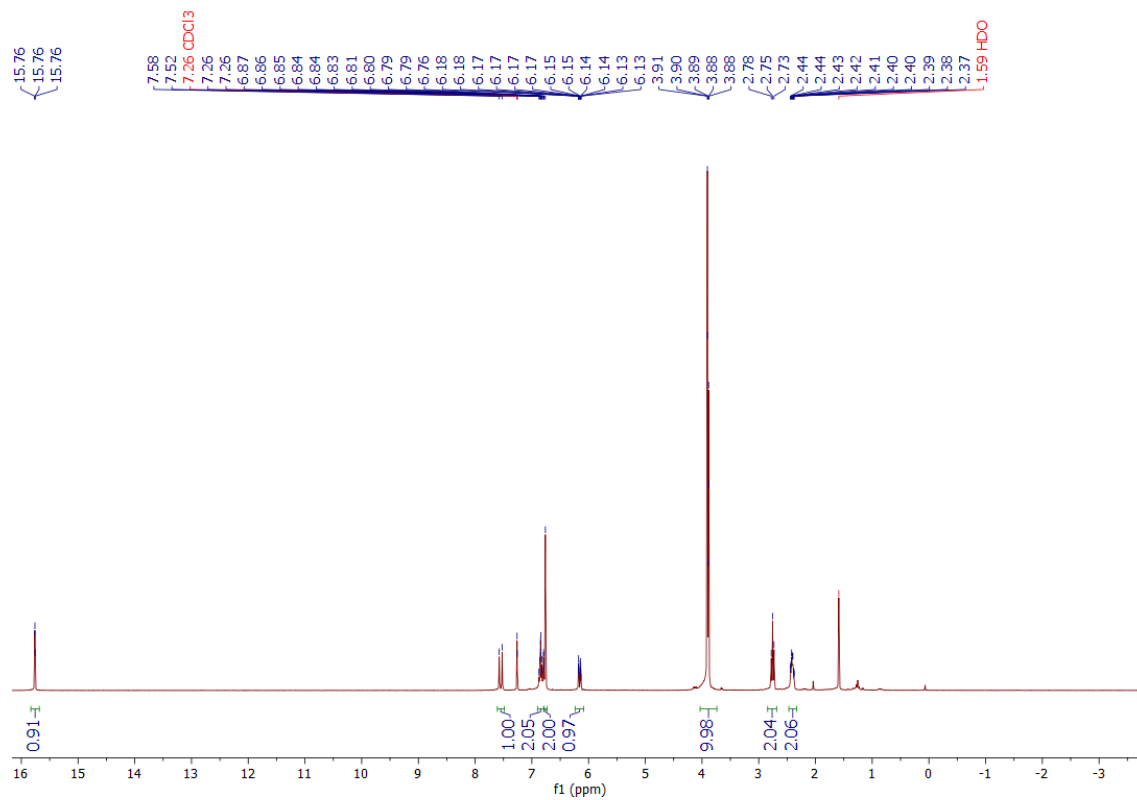
^1H NMR spectrum of **9a** (300 MHz, CDCl_3)



¹H NMR spectrum of **9b** (300 MHz, CDCl₃)



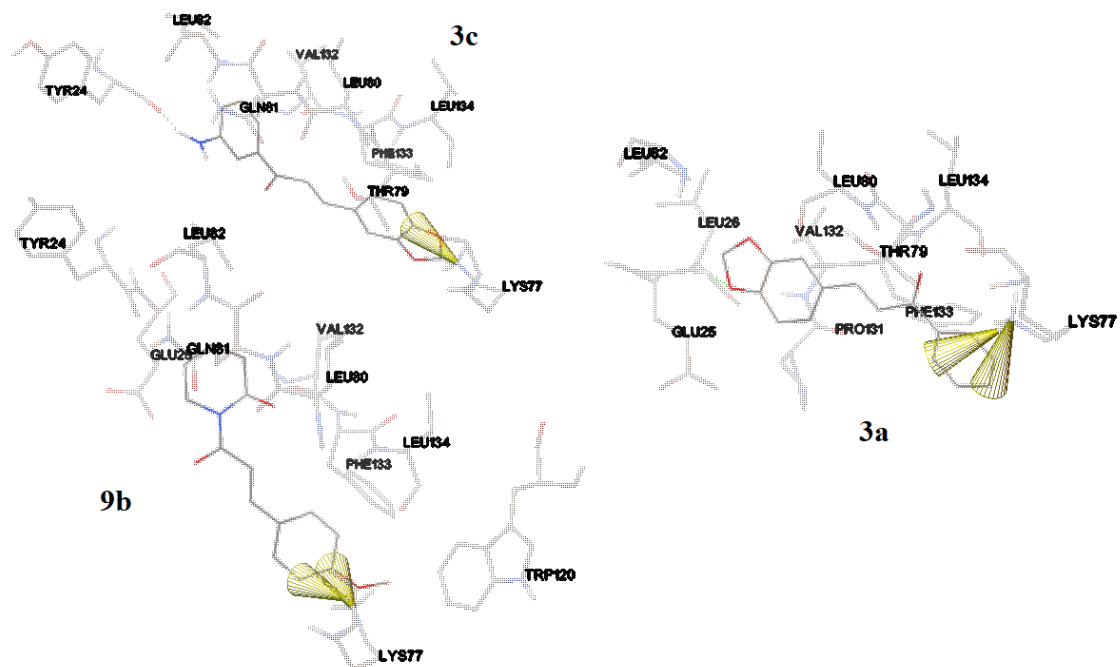
¹H NMR spectrum of **10** (300 MHz, CDCl₃)



Computational Models

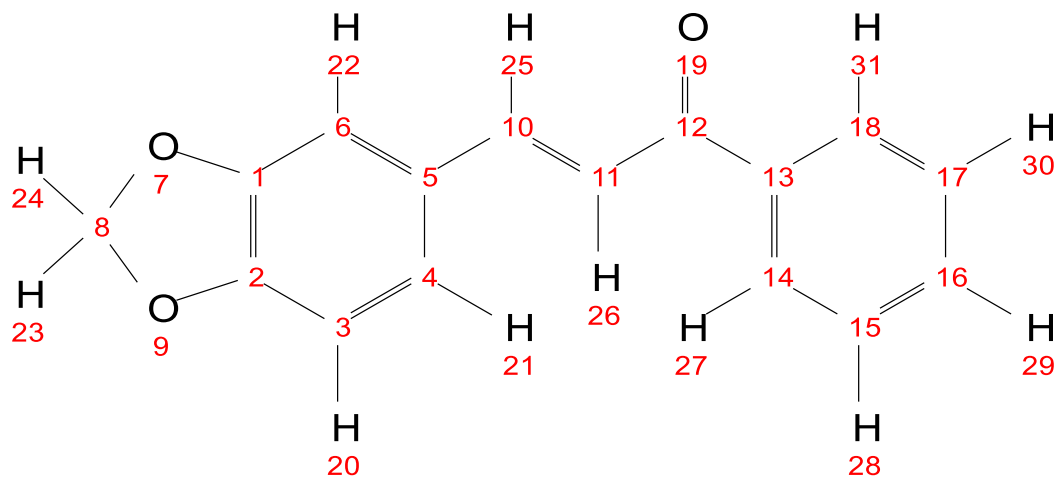
Molecular docking

cation- π interaction between Lys77 of IL-1B and **3a**, **3c** and **9b**.



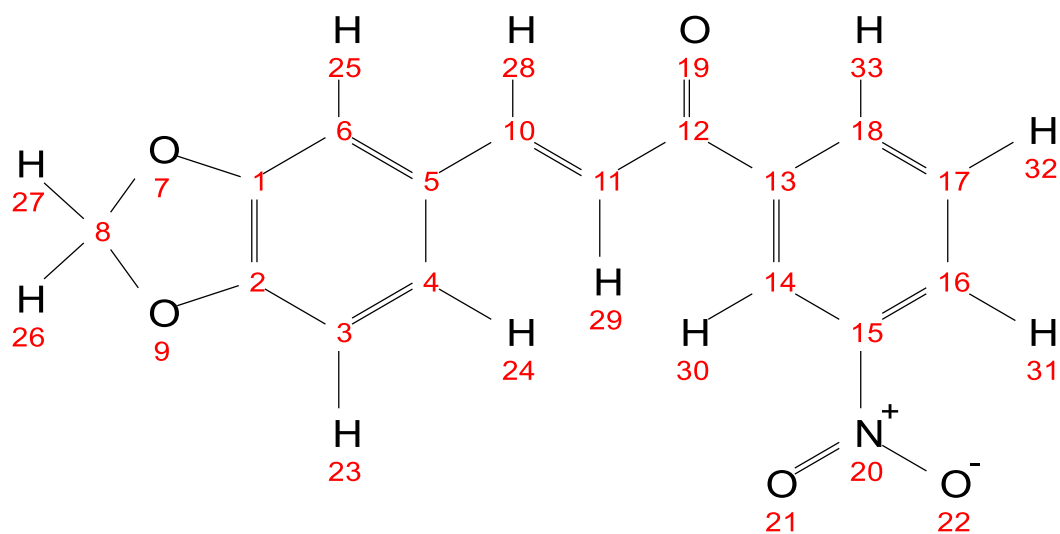
Ab initio Calculation of selected dihedral torsional angles

3a



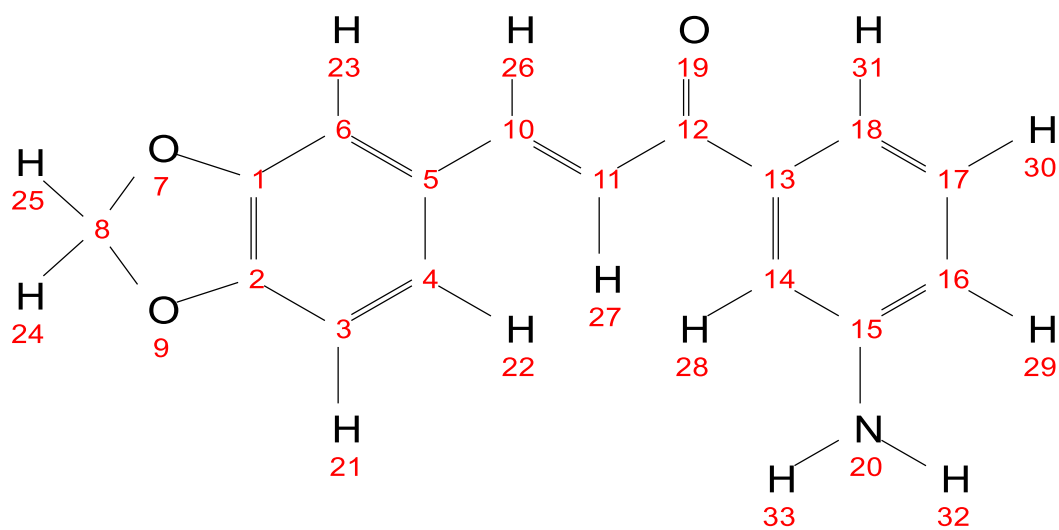
Dihedral	Torsional angle
14-15-16-17	0.228
18-13-12-11	168.513
19-12-11-10	-5.721
10-5-6-1	179.978
7-8-9-2	-8.186
2-3-4-5	0.087

3b



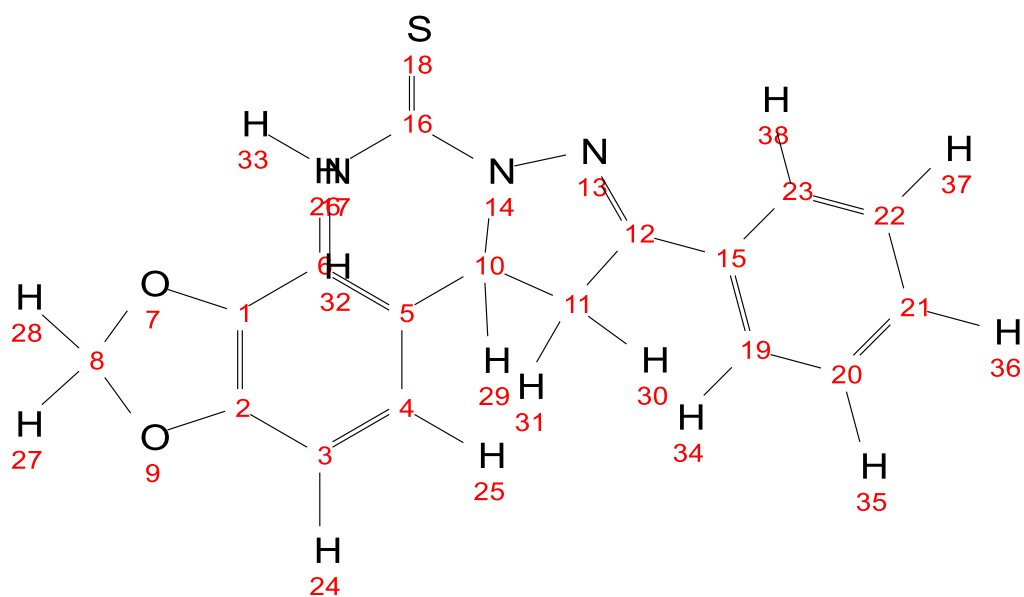
Dihedral	Torsional angle
21-15-22-20	-0.036
22-20-15-16	-2.658
16-17-18-13	0.112
18-13-12-19	-0.218
18-13-12-11	179.987
11-10-5-6	178.969
6-1-7-8	177.766
8-9-2-3	-177.792

3c



Dihedral	Torsional angle
20-15-16-17	-179.849
16-17-18-13	0.012
18-13-12-19	-0.793
18-13-12-11	179.225
11-10-5-6	179.596
5-6-1-7	-179.991
8-9-2-3	-179.961

4a



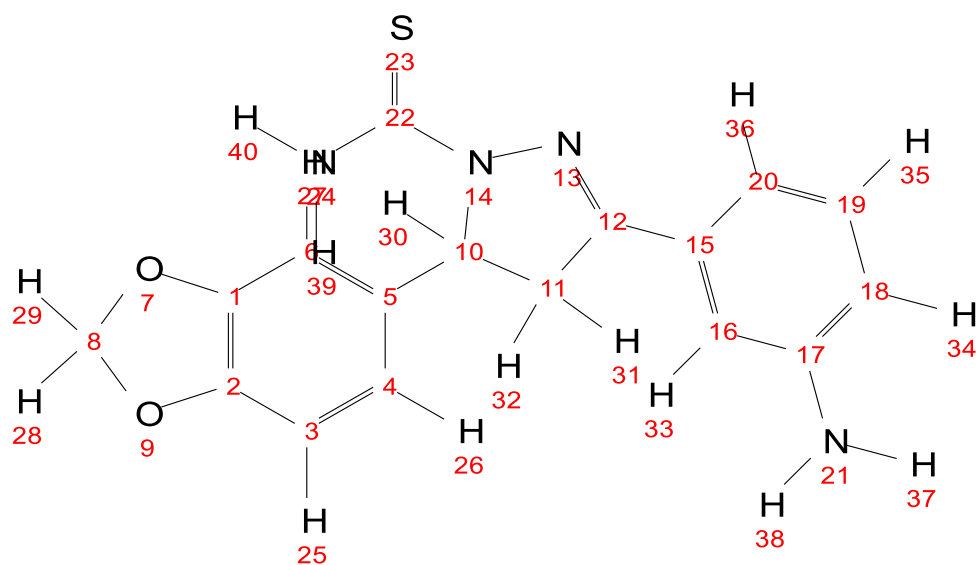
Torsional angle of the dihedral of **4a** simulated in H₂O

Dihedral	Torsional angle
19-20-21-22	-0.067
23-15-12-11	177.810
12-13-14-10	0.626
13-14-10-11	-1.407
14-11-13-10	-0.950
14-17-16-18	-178.286
11-10-5-4	-74.257
11-12-15-19	-2.859
4-3-2-9	176.492
8-7-1-32	-176.820

Torsional angle of the dihedral of 5-membered ring of **4a** simulated in CDCl₃

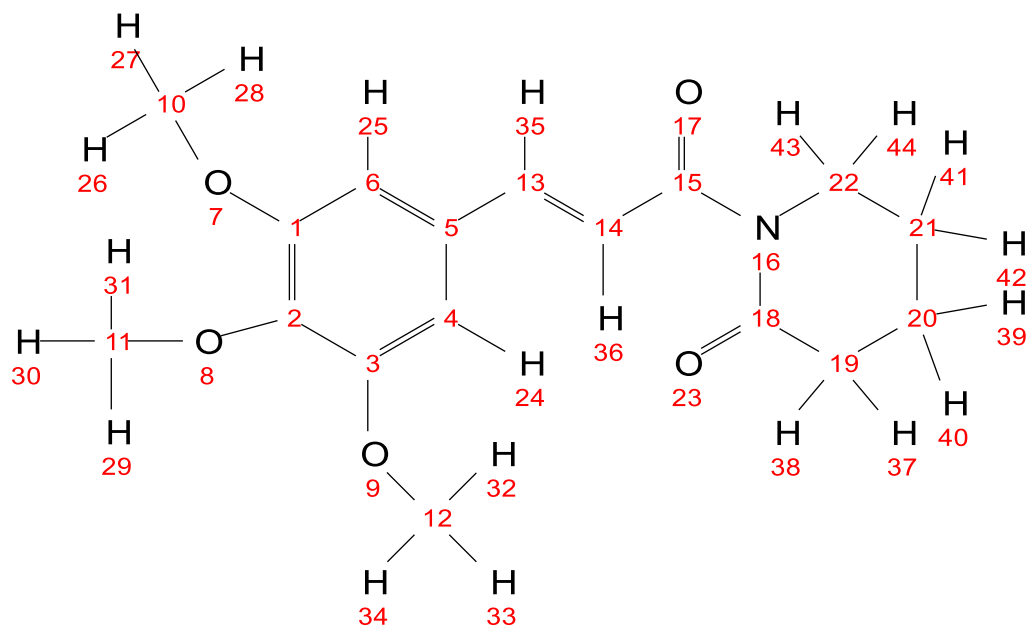
Dihedral	Torsional angle
13-14-10-11	4.838
14-11-13-10	-3.046
12-13-14-10	-2.841

4c



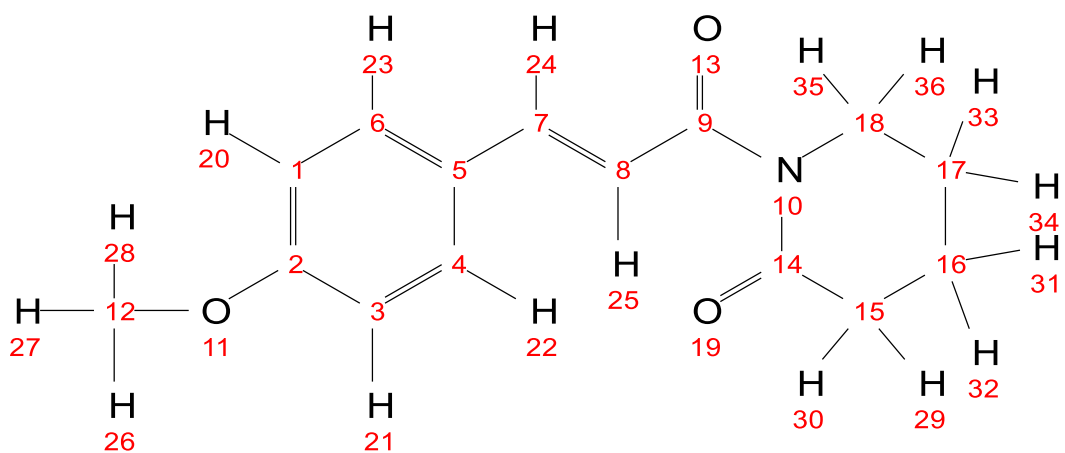
Dihedral	Torsional angle
21-17-18-19	176.732
20-15-12-11	-172.194
12-13-14-10	0.626
13-10-14-11	-1.407
13-14-10-11	102.997
6-1-7-8	173.361
8-9-2-3	-178.833
6-5-4-3	0.268

9a



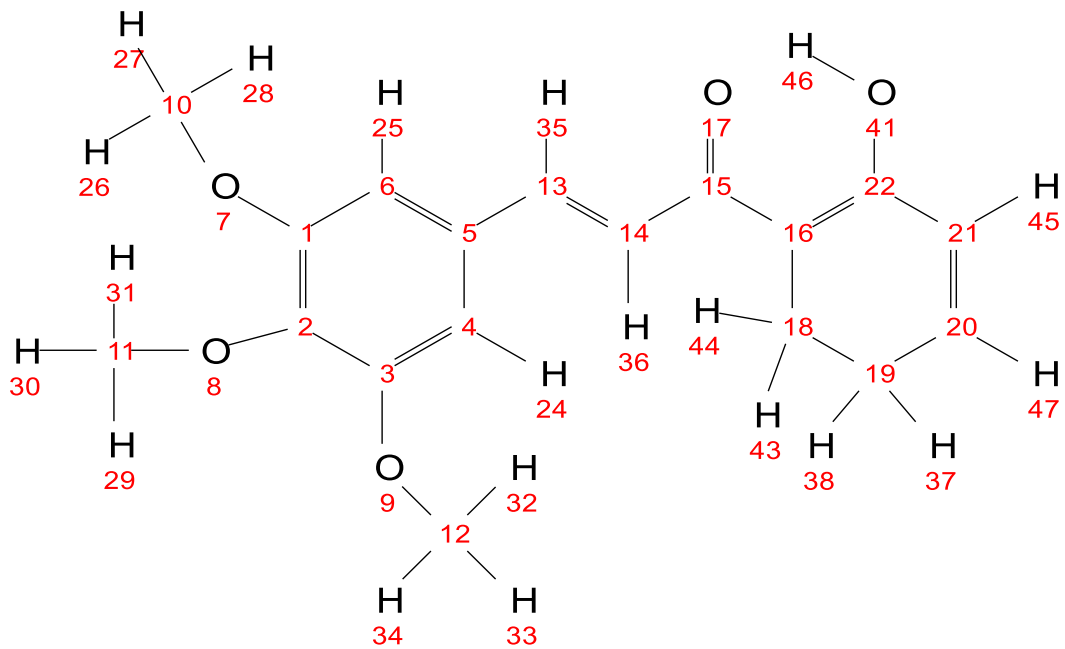
Dihedral	Torsional angle
20-21-22-16	-48.558
22- 16-15-17	9.655
16-15-14-13	-173.008
13-5-6-1	179.762
10-7-1-2	73.431
11-8-2-3	-119.435
9- 12-3-4	-134.562
15-16-22-21	-167.467

9b



Dihedral	Torsional angle
19-14-15-16	-173.441
17-18-10-9	-168.002
13-9-8-7	12.815
5-5-1-2	0.191
12-11-2-3	-179.427
8-7-5-6	179.783
19-14-15-16	-173.441
17-18-10-9	-168.002

10



Dihedral	Torsional angle
18-19-20-21	28.591
41-22-16-15	1.471
17-15-14-13	-5.019
15-14-13-5	179.702
10-7-1-2	72.840
11-8-2-3	-106.728
12-9-3-4	112.209
14-15-16-22	176.508

References

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