

Supplementary materials

Exploring the antitubercular activity of anthranilic acid derivatives: from MabA (FabG1) inhibition to intrabacterial acidification

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† These authors contributed equally to this work.

Figure S1: 1D ¹⁹F NMR spectra of 4 compounds alone and in the presence of MabA

Figure S2: Western blot showing overexpression of MabA in H37Rv_pMV261-MabA, as compared to the parental control.

Figures S3-S40: ¹H NMR, ¹³C NMR and HRMS data of compounds **2-20**

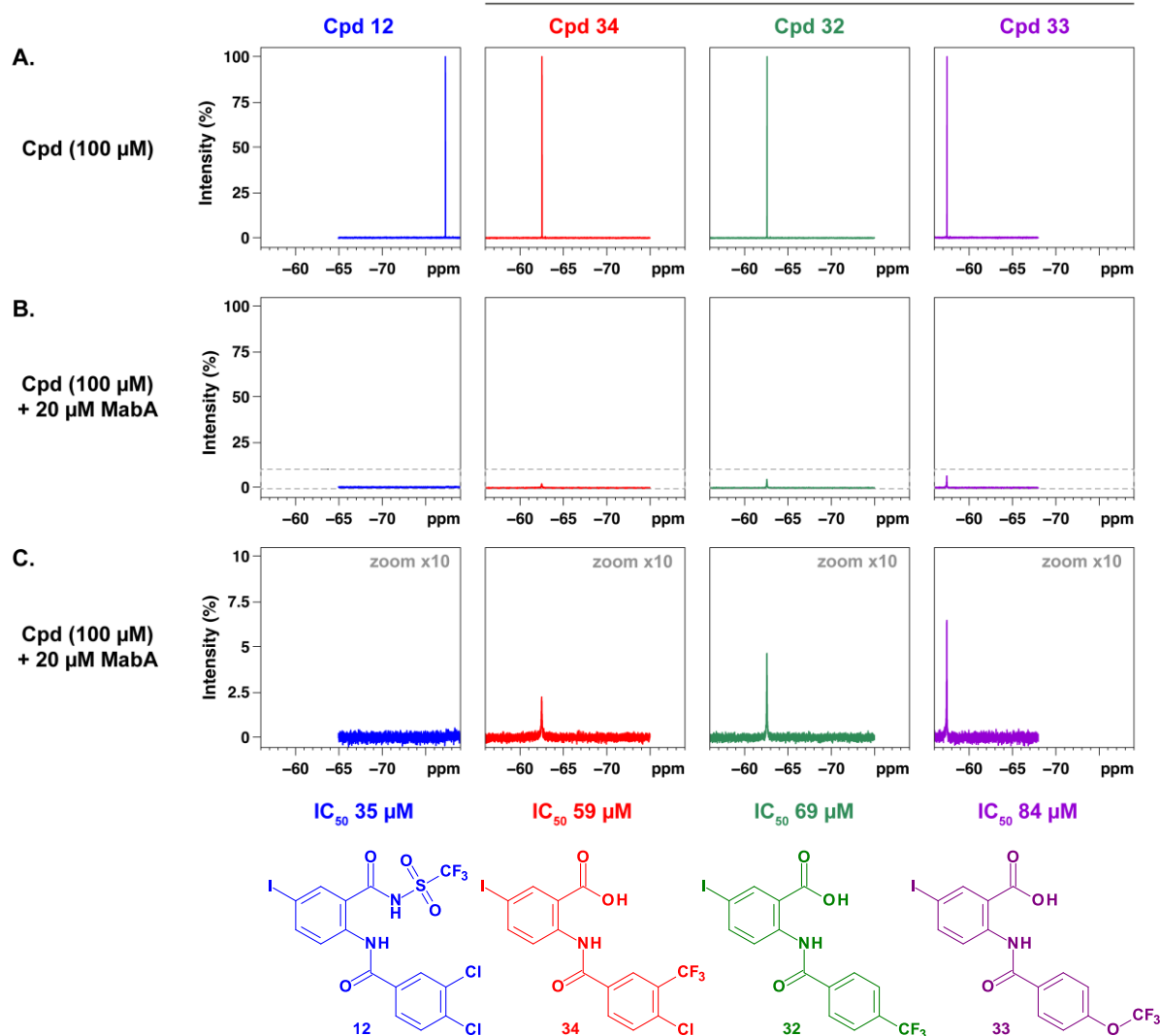


Figure S1: 1D ^{19}F NMR spectra of compound **12** (this study) and compounds **34**, **32** and **33** from Faion L. *et al.* [20] (in blue, red, green and violet, respectively) at 100 μM alone (**A.**) and in the presence of MabA at 20 μM (**B.** and **C.**). The spectra in **C.** correspond to the ones in **B.** with a 10x magnification of the y-axis. The IC_{50} for each compound is indicated at the bottom.

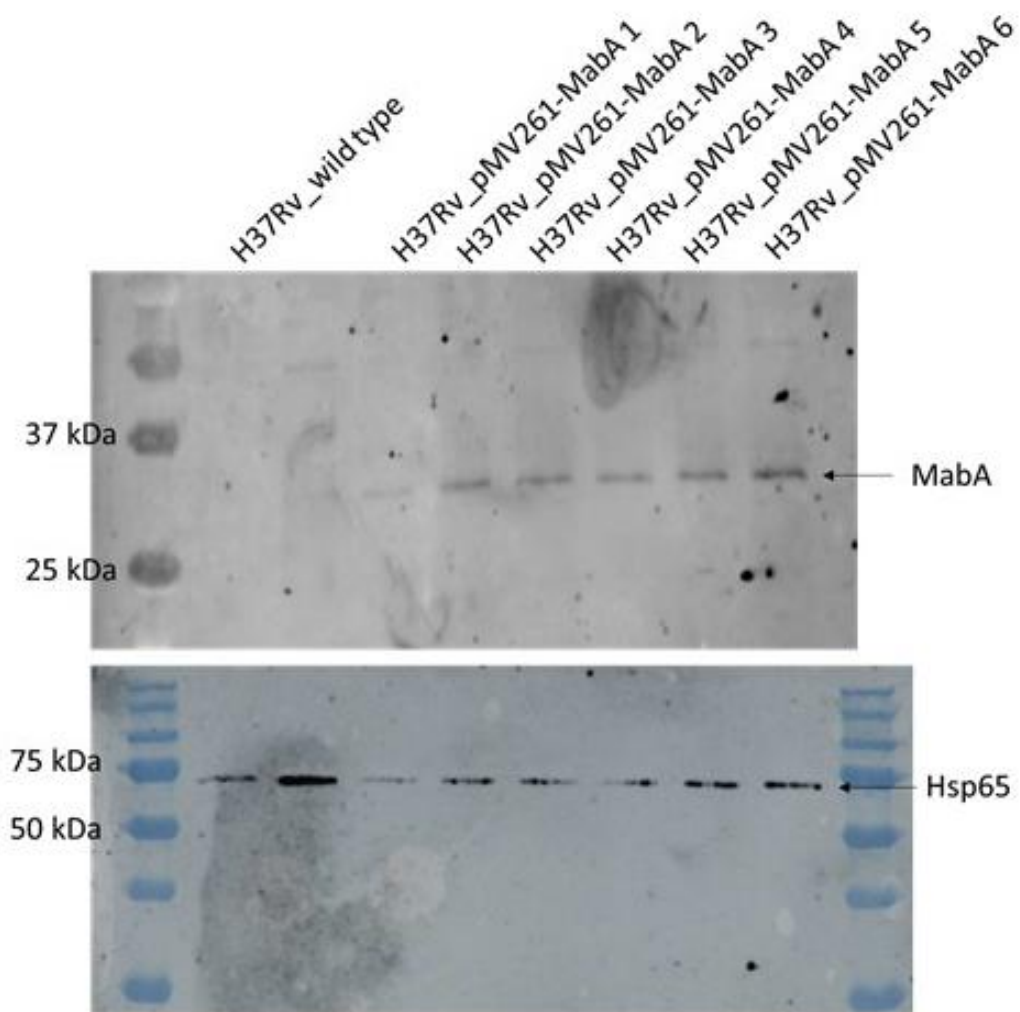
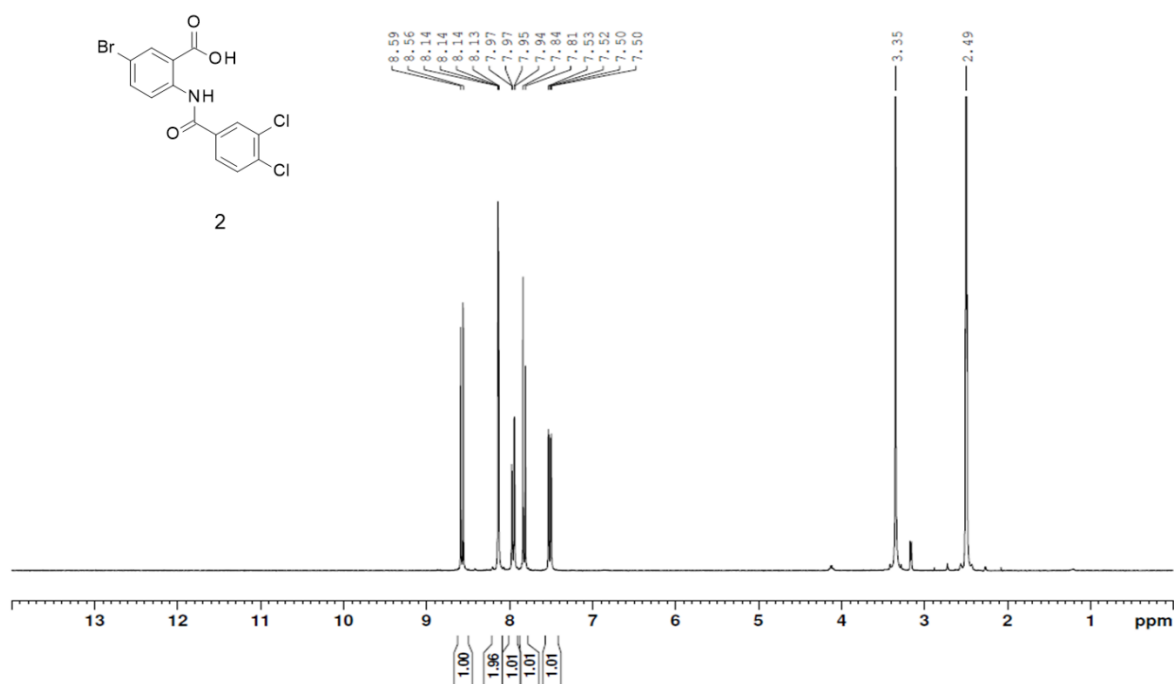


Figure S2: Western blot showing overexpression of MabA in H37Rv_pMV261-MabA, as compared to the parental control. H37Rv_pMV261-MabA 1 through 6 correspond to different clones tested.

¹H NMR of compound 2 (300 MHz, DMSO-d6)



¹³C NMR of compound 2 (75 MHz, DMSO-d6)

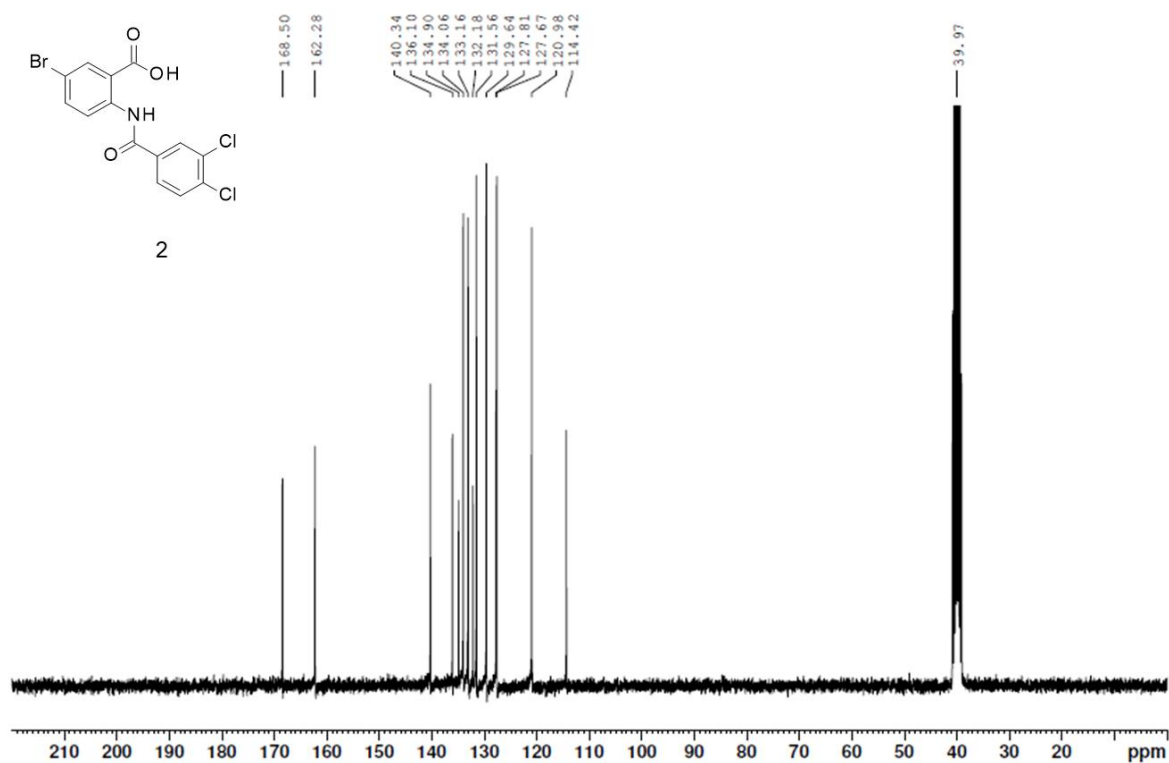


Figure S3: ¹H NMR and ¹³C NMR spectra of compound 2

Elemental Composition Report

Single Mass Analysis

Tolerance = 100.0 mDa / DBE: min = -1.5, max = 500.0

Element prediction: Off

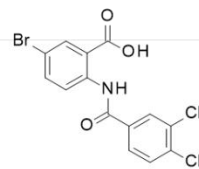
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

337 formula(e) evaluated with 55 results within limits (up to 10 best isotopic matches for each mass)

Elements Used:

C: 0-30 H: 0-40 N: 0-4 O: 0-6 Cl: 0-2 Br: 1-1



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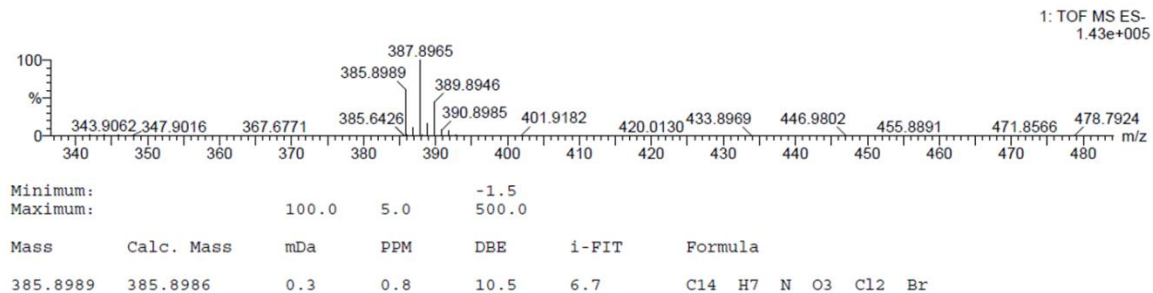


Figure S4: HRMS spectrum of compound 2

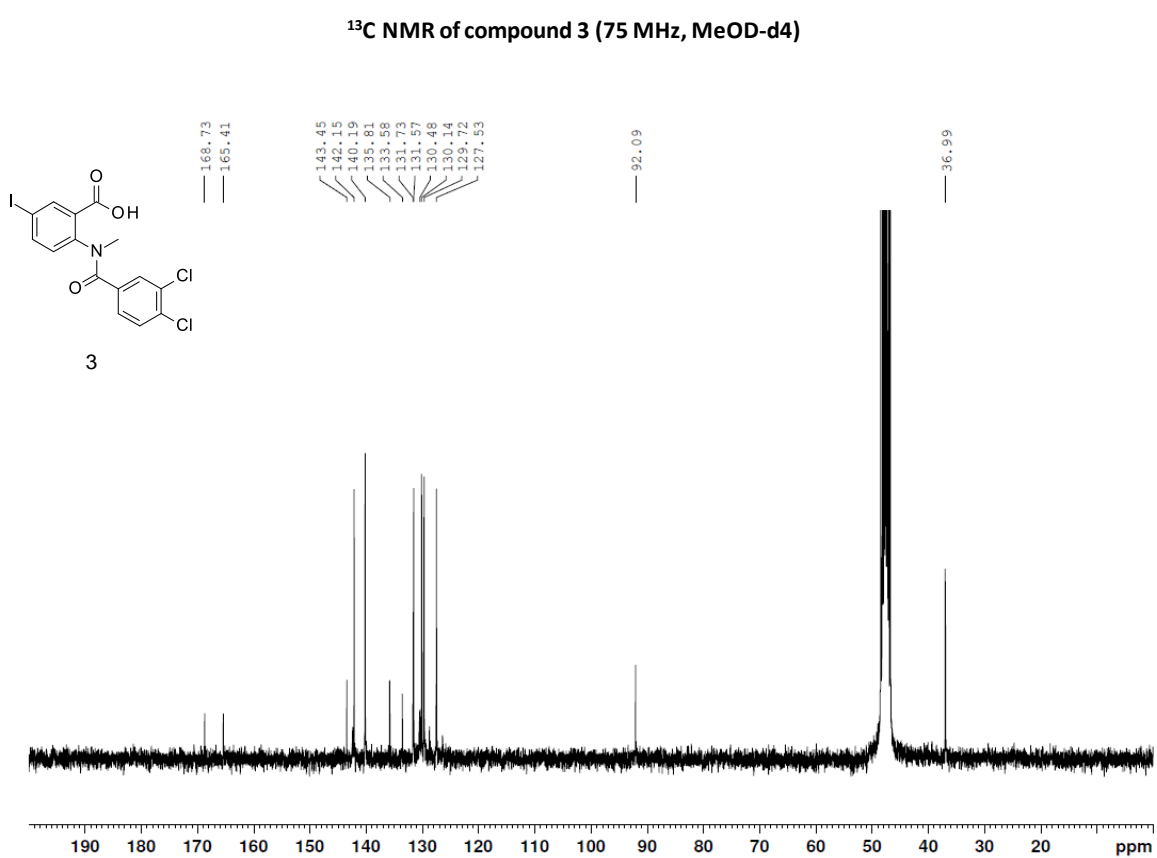
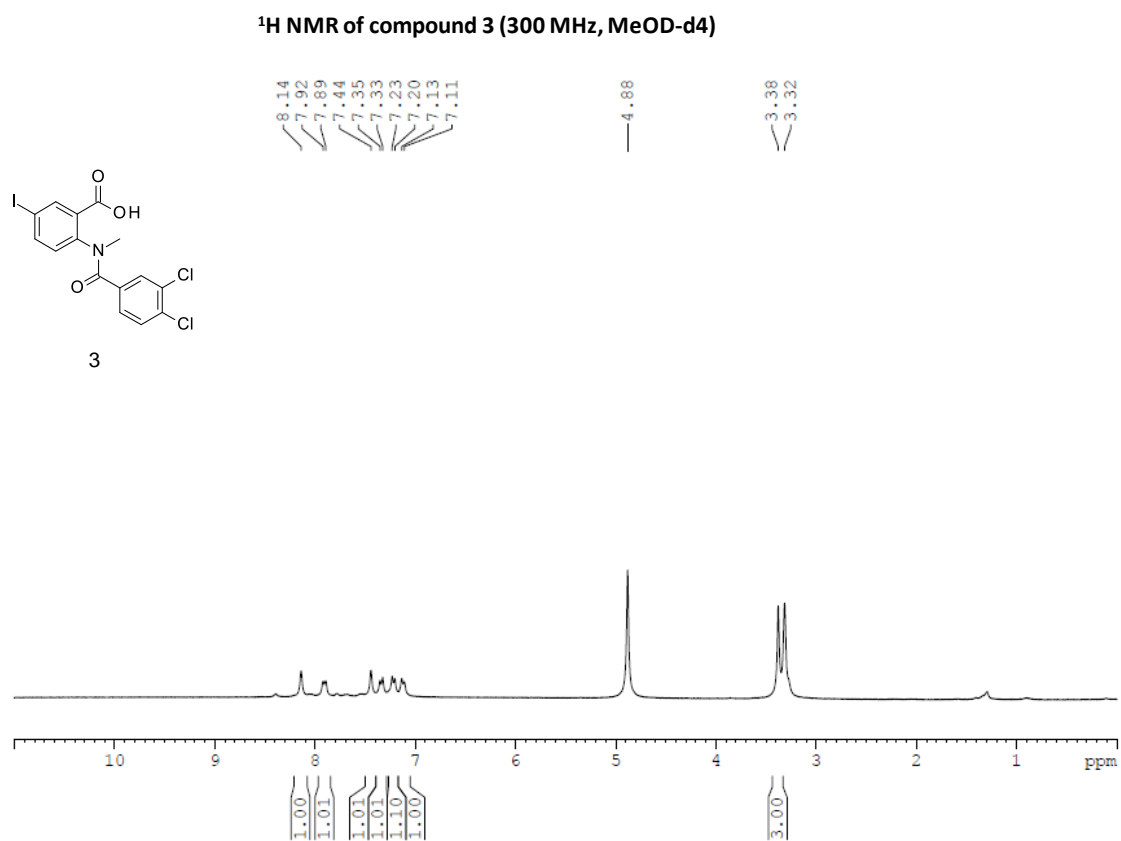
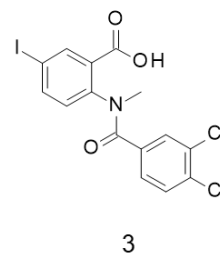


Figure S5: ¹H NMR and ¹³C NMR spectra of compound 3



Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

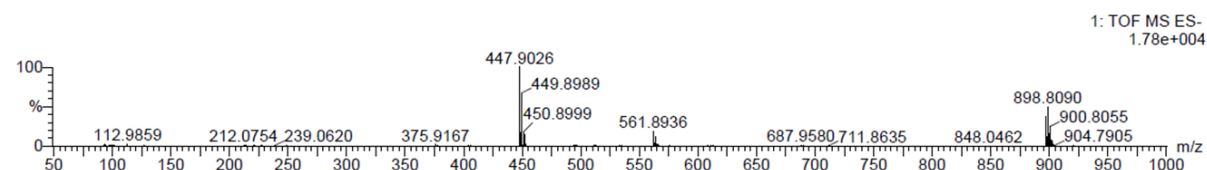
Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

768 formula(e) evaluated with 11 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

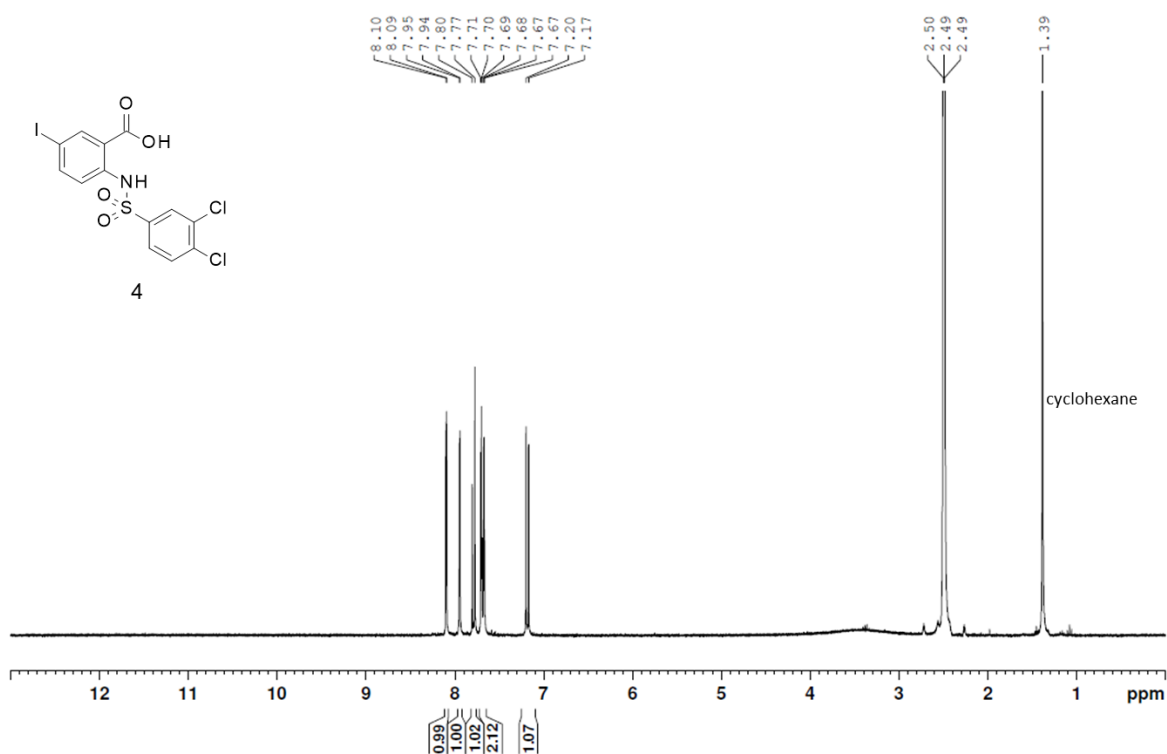
C: 6-40 H: 2-36 N: 0-5 O: 0-7 Cl: 1-3 I: 0-1



Minimum:				-1.5		
Maximum:		10.0	20.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
447.9026	447.9004	2.2	4.9	10.5	2.1	C15 H9 N O3 Cl2 I

Figure S6: HRMS spectrum of compound 3

¹H NMR of compound 4 (300 MHz, DMSO-d6)



¹³C NMR of compound 4 (75 MHz, DMSO-d6)

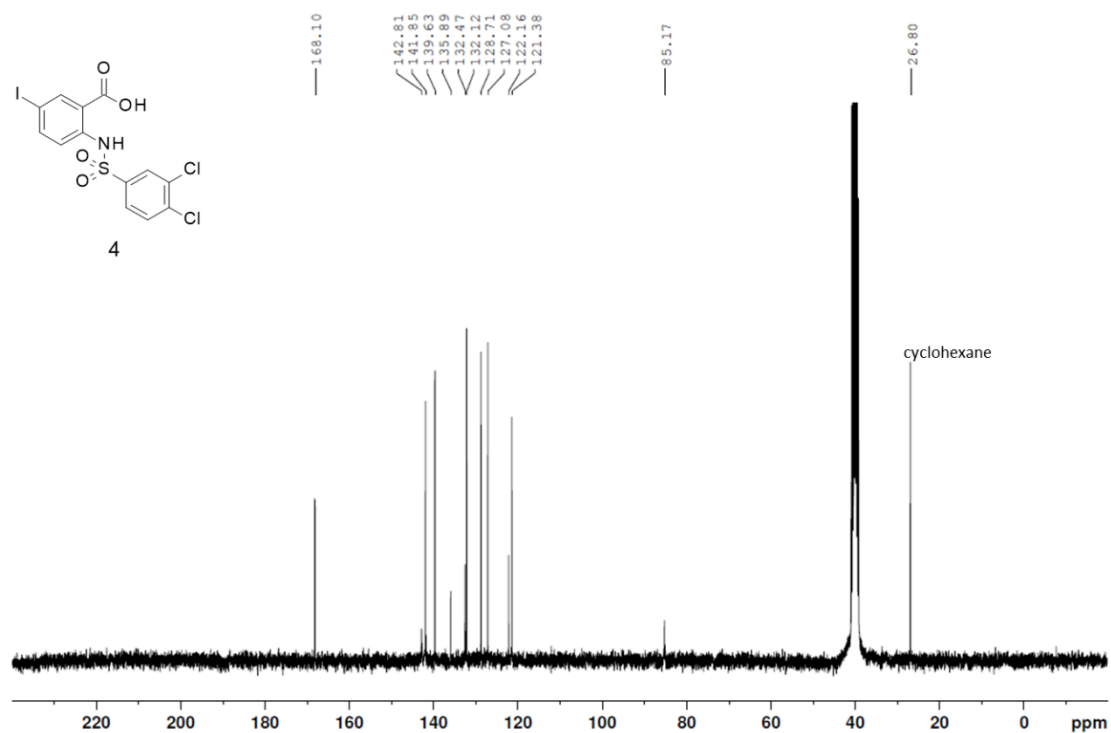


Figure S7: ¹H NMR and ¹³C NMR spectra of compound 4

Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

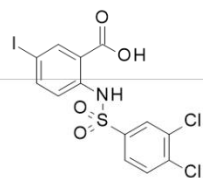
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

56 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 1-17 H: 1-17 N: 1-2 O: 0-4 S: 1-1 Cl: 0-2 I: 0-1



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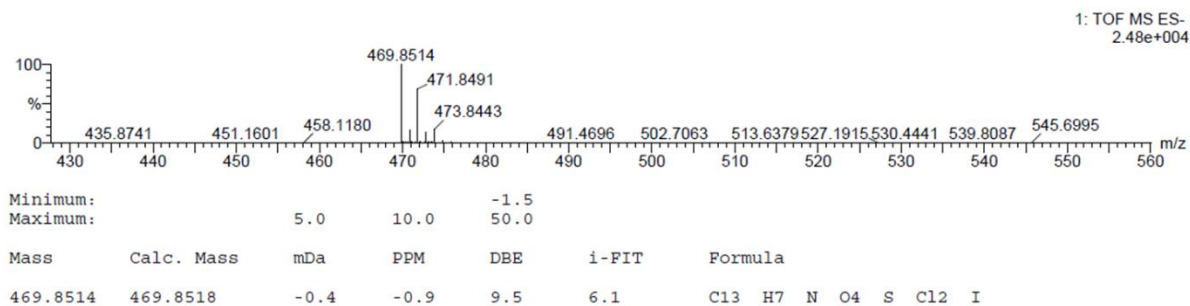
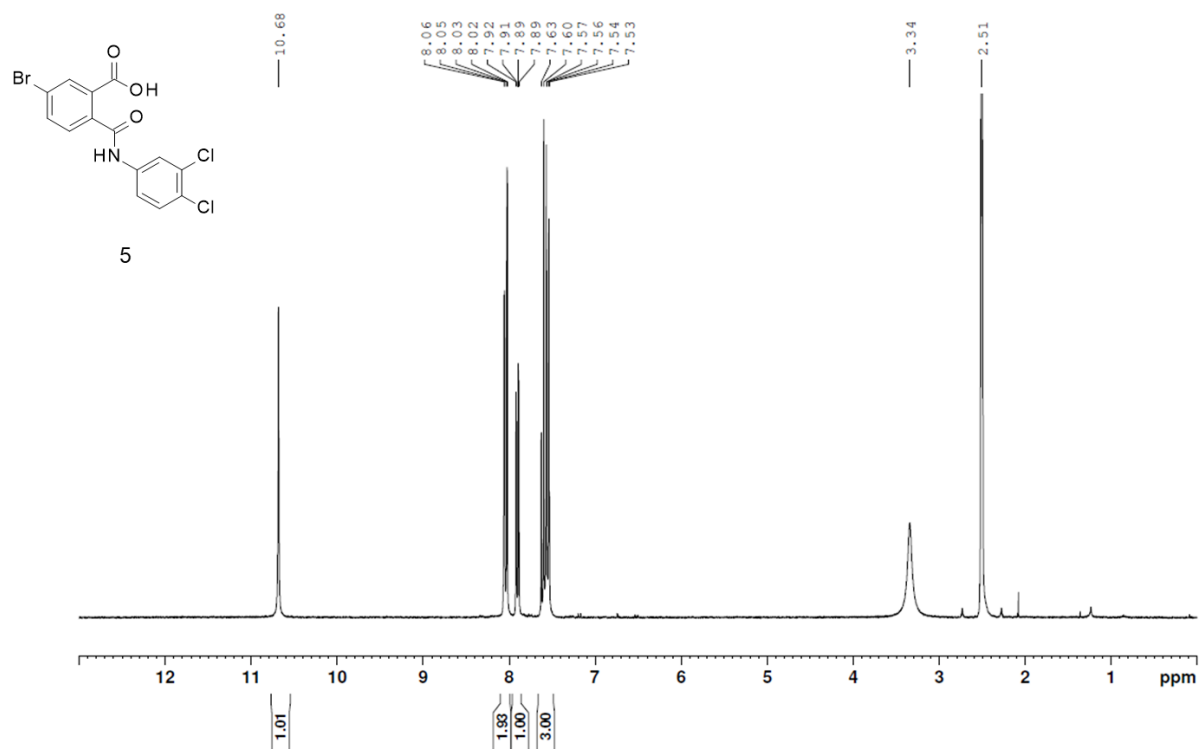


Figure S8: HRMS spectrum of compound 4

¹H NMR of compound 5 (300 MHz, DMSO-d6)



¹³C NMR of compound 5 (75 MHz, DMSO-d6)

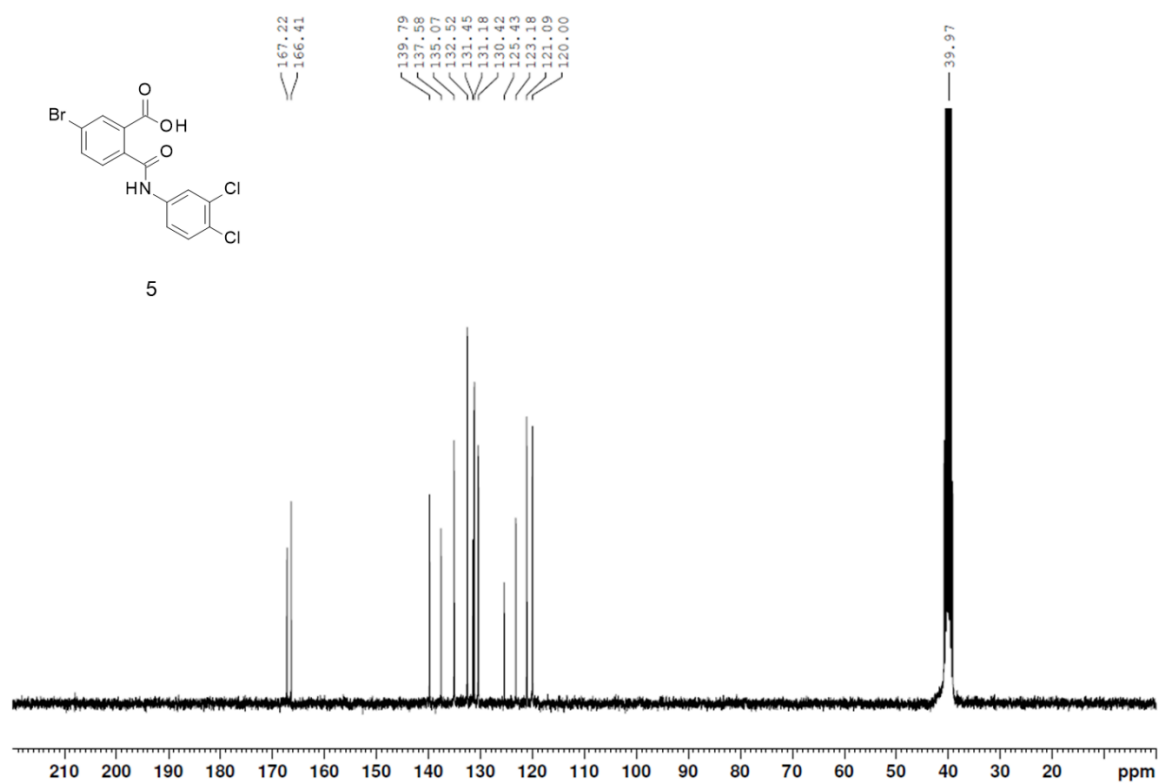
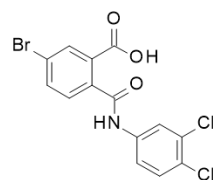


Figure S9: ¹H NMR and ¹³C NMR spectra of compound 5



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Elemental Composition Report

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Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

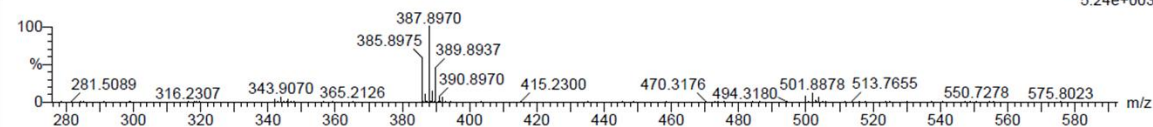
Monoisotopic Mass, Even Electron Ions

335 formula(e) evaluated with 7 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

C: 2-20 H: 2-36 N: 0-5 O: 0-7 Cl: 1-2 Br: 1-1 I: 0-1

1: TOF MS ES-
5.24e+003



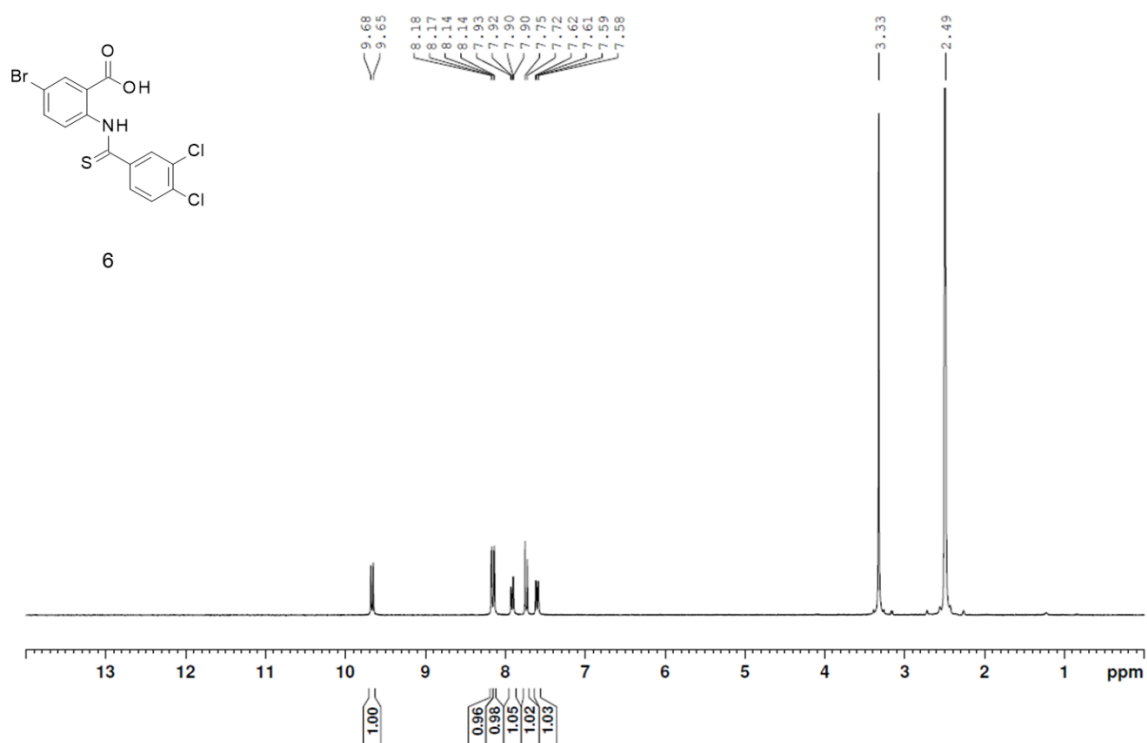
Minimum:
Maximum:

10.0 20.0 -1.5 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
385.8975	385.8986	-1.1	-2.9	10.5	0.2	C14 H7 N O3 Cl2 Br

Figure S10: HRMS spectrum of compound 5

¹H NMR of compound 6 (300 MHz, DMSO-d₆)



¹³C NMR of compound 6 (75 MHz, DMSO-d₆)

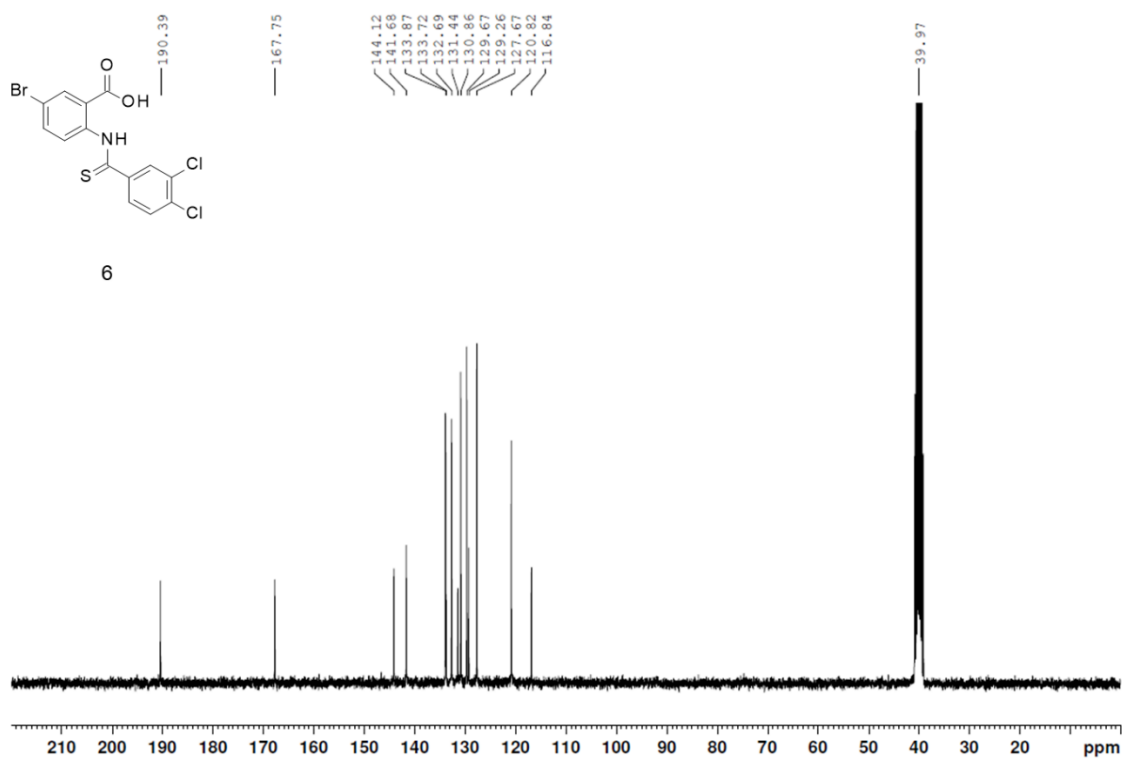
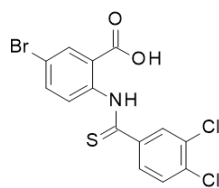


Figure S11: ¹H NMR and ¹³C NMR spectra of compound 6



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Elemental Composition Report

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Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

489 formula(e) evaluated with 16 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

C: 2-20 H: 2-36 N: 0-5 O: 0-7 S: 0-1 Cl: 1-2 Br: 1-1

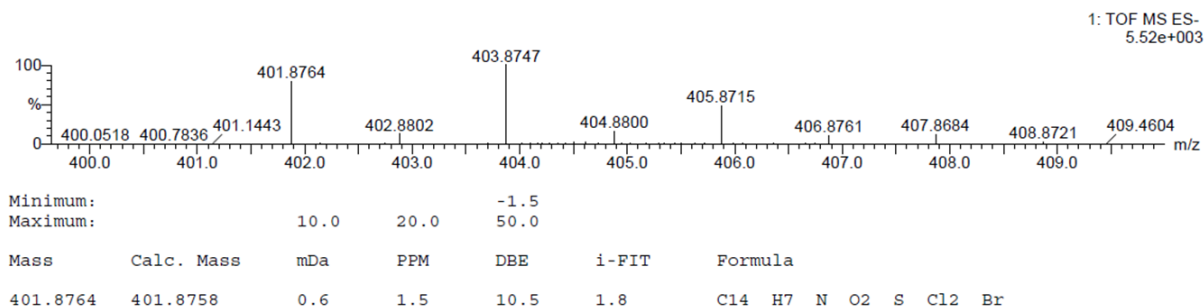
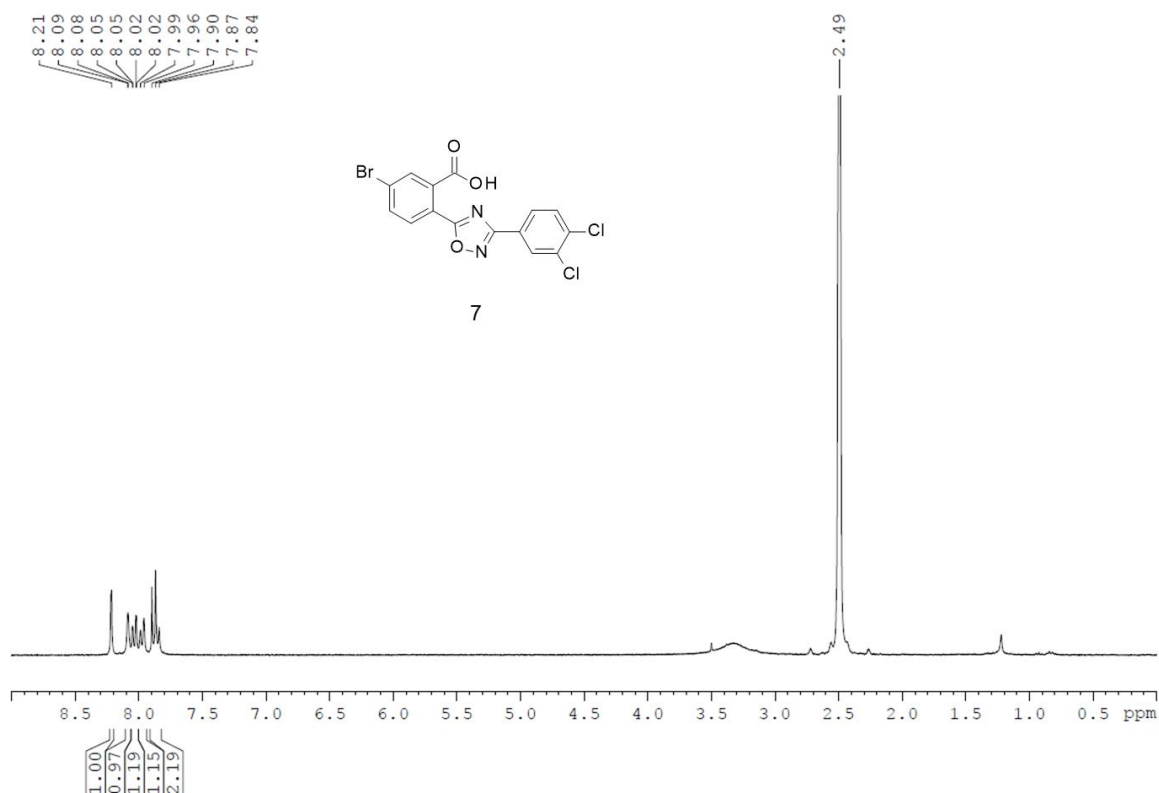


Figure S12: HRMS spectrum of compound 6

¹H NMR of compound 7 (300 MHz, DMSO-d₆)



¹³C NMR of compound 7 (75 MHz, DMSO-d₆)

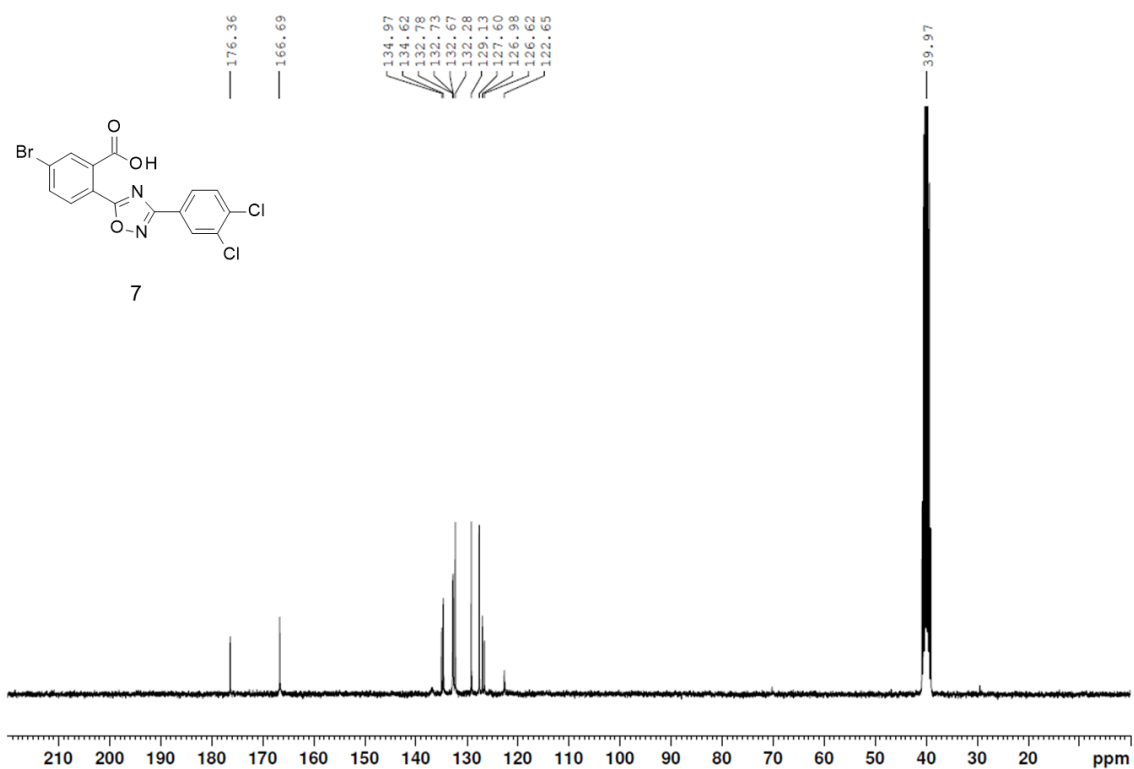


Figure S13: ¹H NMR and ¹³C NMR spectra of compound 7

Elemental Composition Report

Single Mass Analysis

Tolerance = 100.0 mDa / DBE: min = -1.5, max = 500.0

Element prediction: Off

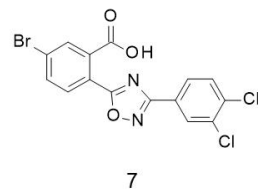
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

562 formula(e) evaluated with 159 results within limits (up to 10 best isotopic matches for each mass)

Elements Used:

C: 0-30 H: 0-40 N: 0-4 O: 0-6 Cl: 0-2 Br: 1-1 I: 0-1



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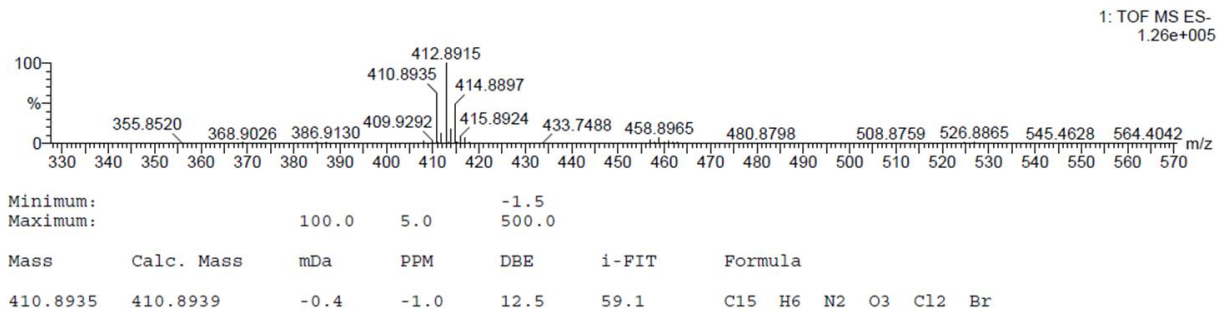


Figure S14: HRMS spectrum of compound 7

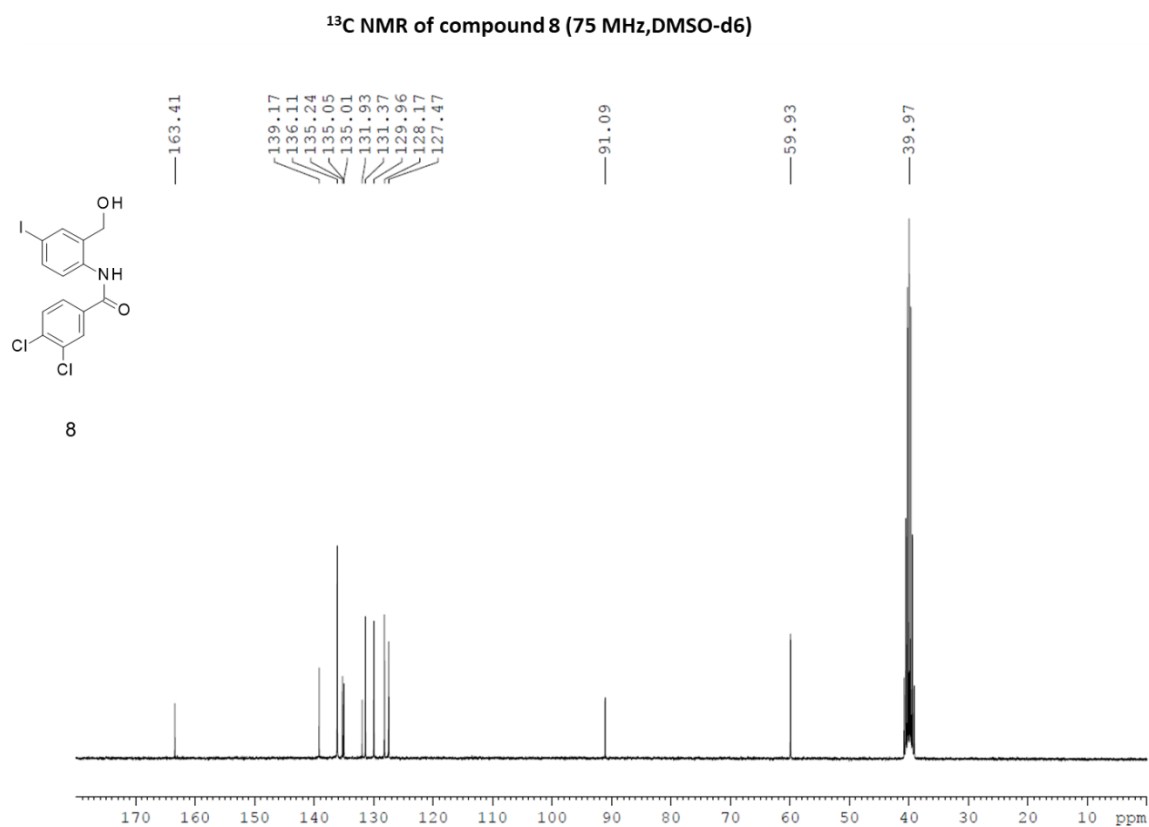
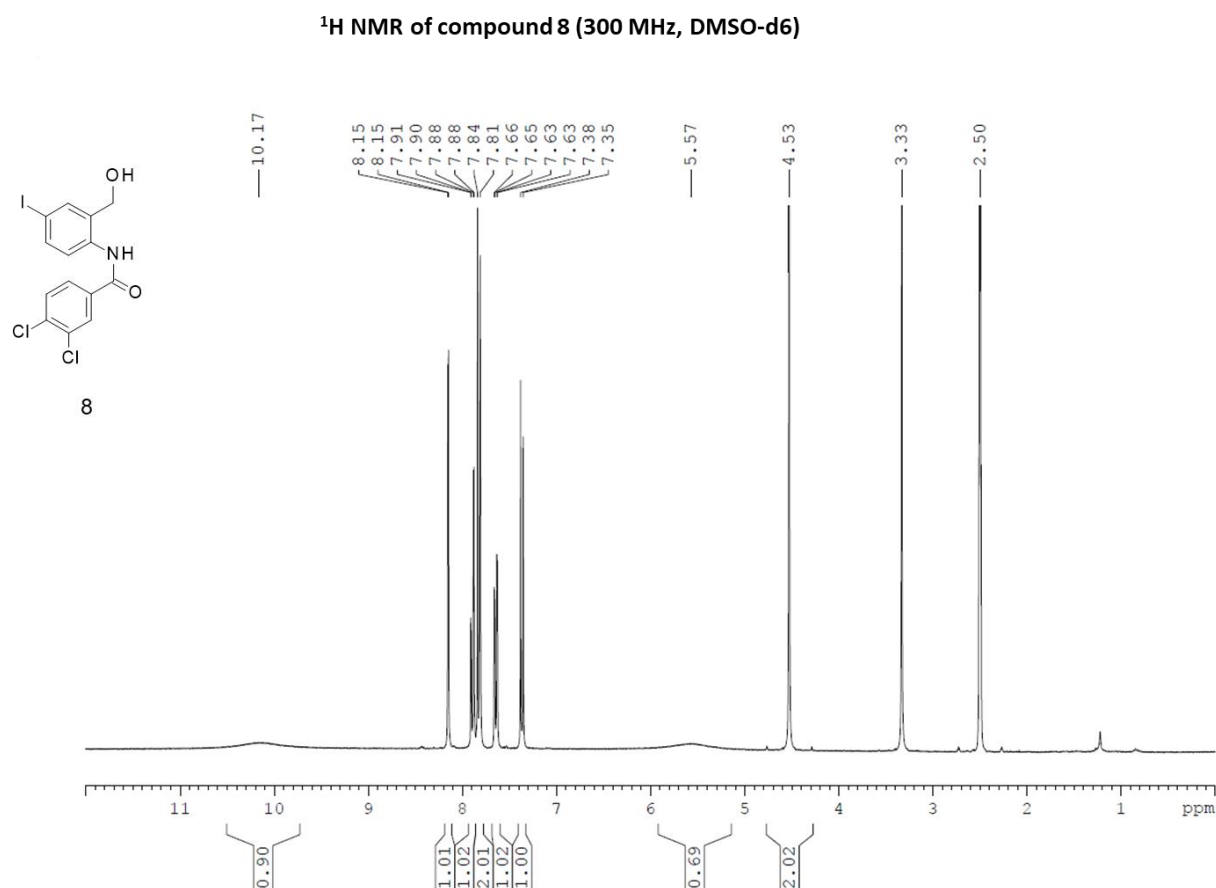
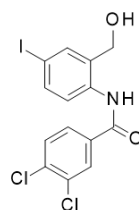


Figure S15: ¹H NMR and ¹³C NMR spectra of compound 8



Elemental Composition Report

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Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

8

Monoisotopic Mass, Even Electron Ions

391 formula(e) evaluated with 10 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

C: 2-20 H: 2-36 N: 0-5 O: 0-7 Cl: 1-2 I: 0-1

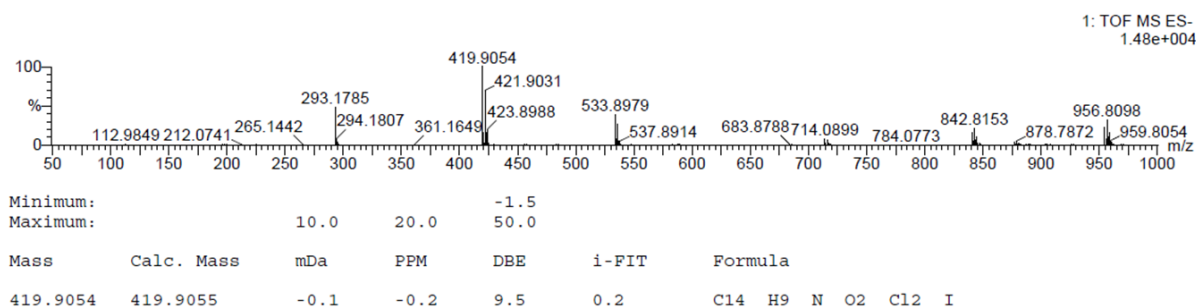
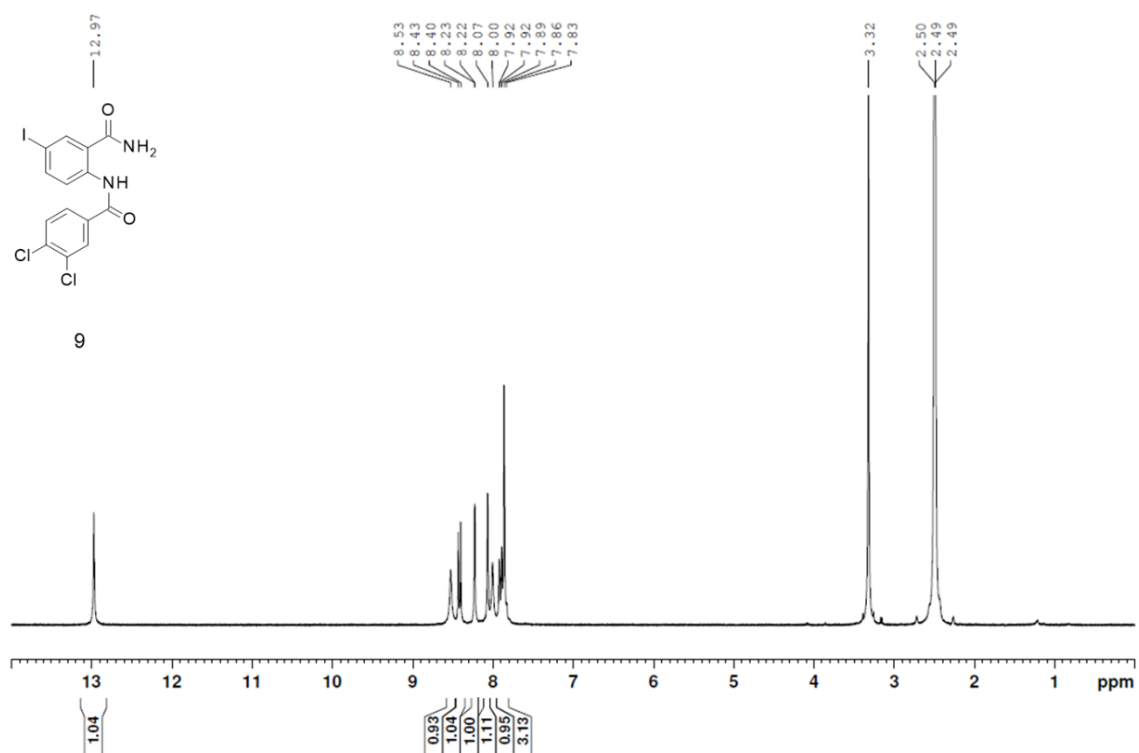


Figure S16: HRMS spectrum of compound 8

¹H NMR of compound 9 (300 MHz, DMSO-d₆)



¹³C NMR of compound 9 (75 MHz, DMSO-d₆)

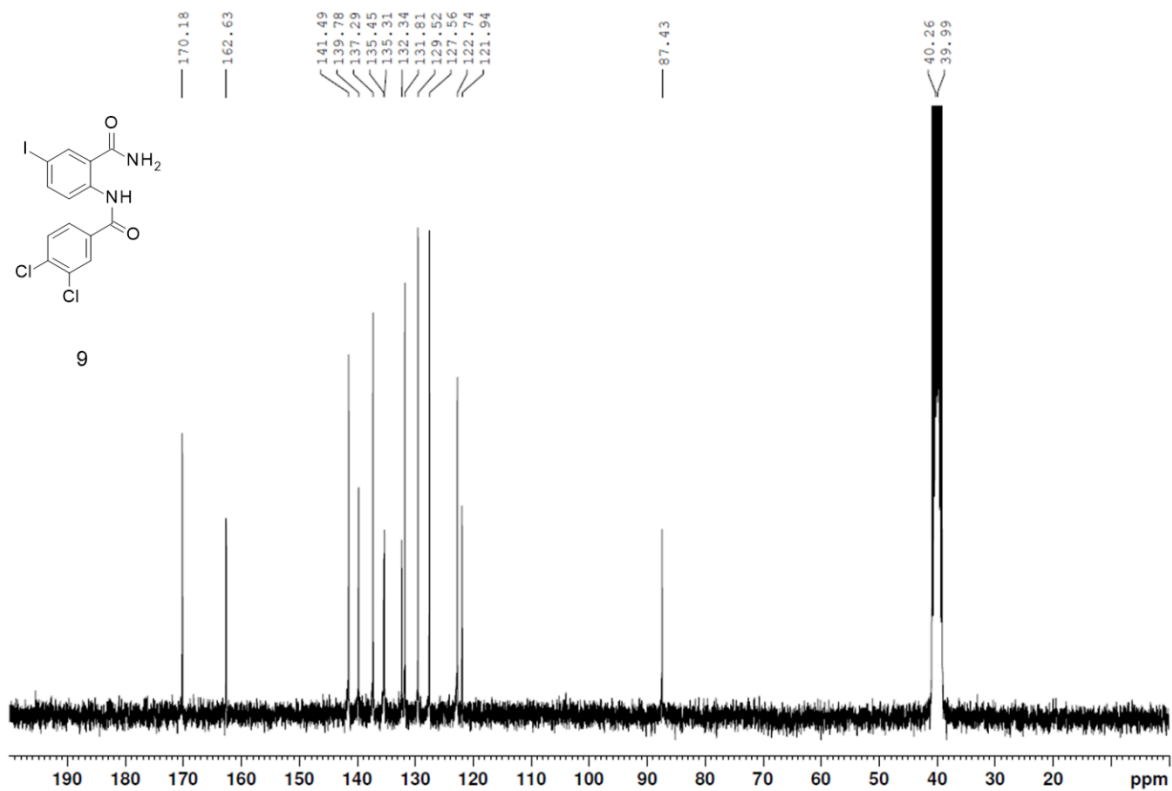


Figure S17: ¹H NMR and ¹³C NMR spectra of compound 9

Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

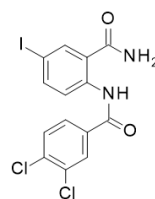
Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

635 formula(e) evaluated with 12 results within limits (up to 1 closest results for each mass)

Elements Used:

C: 6-40 H: 2-36 N: 0-4 O: 0-7 Cl: 1-3 I: 0-1



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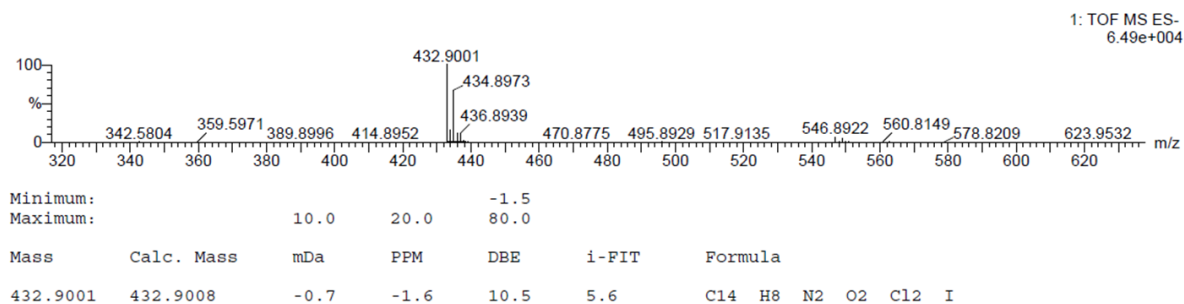
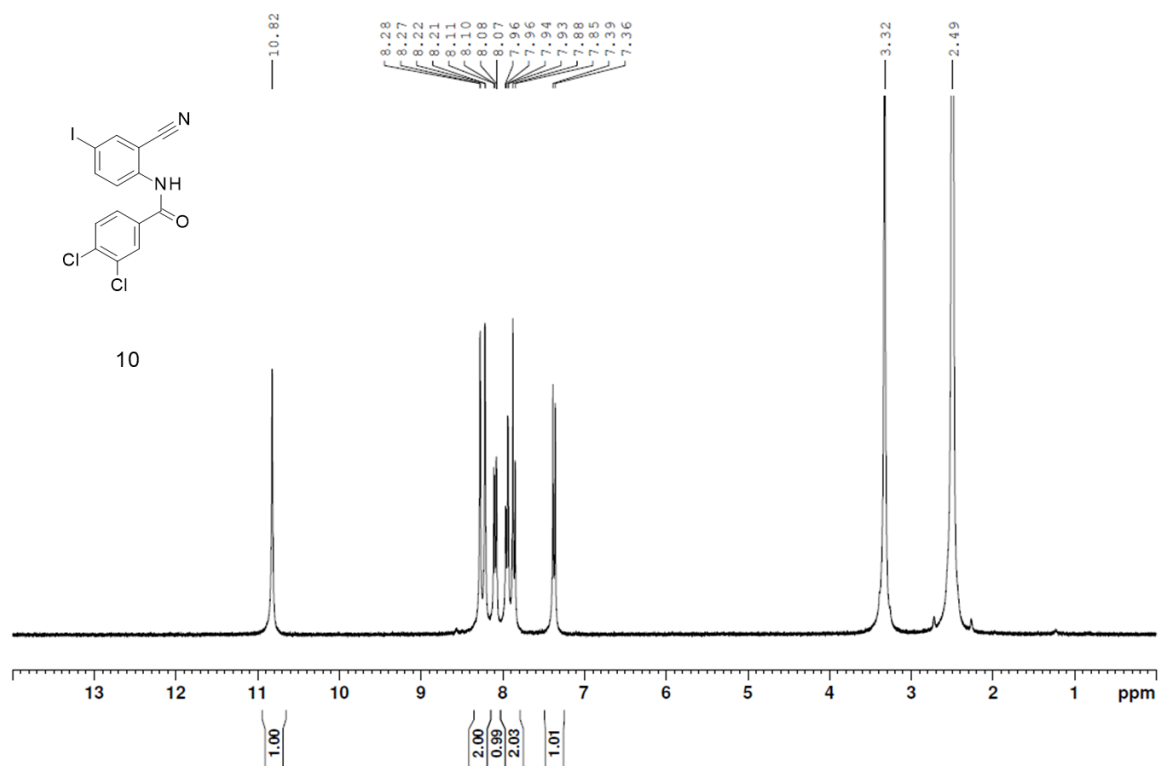


Figure S18: HRMS spectrum of compound 9

¹H NMR of compound 10 (300 MHz, DMSO-d₆)



¹³C NMR of compound 10 (75 MHz, DMSO-d₆)

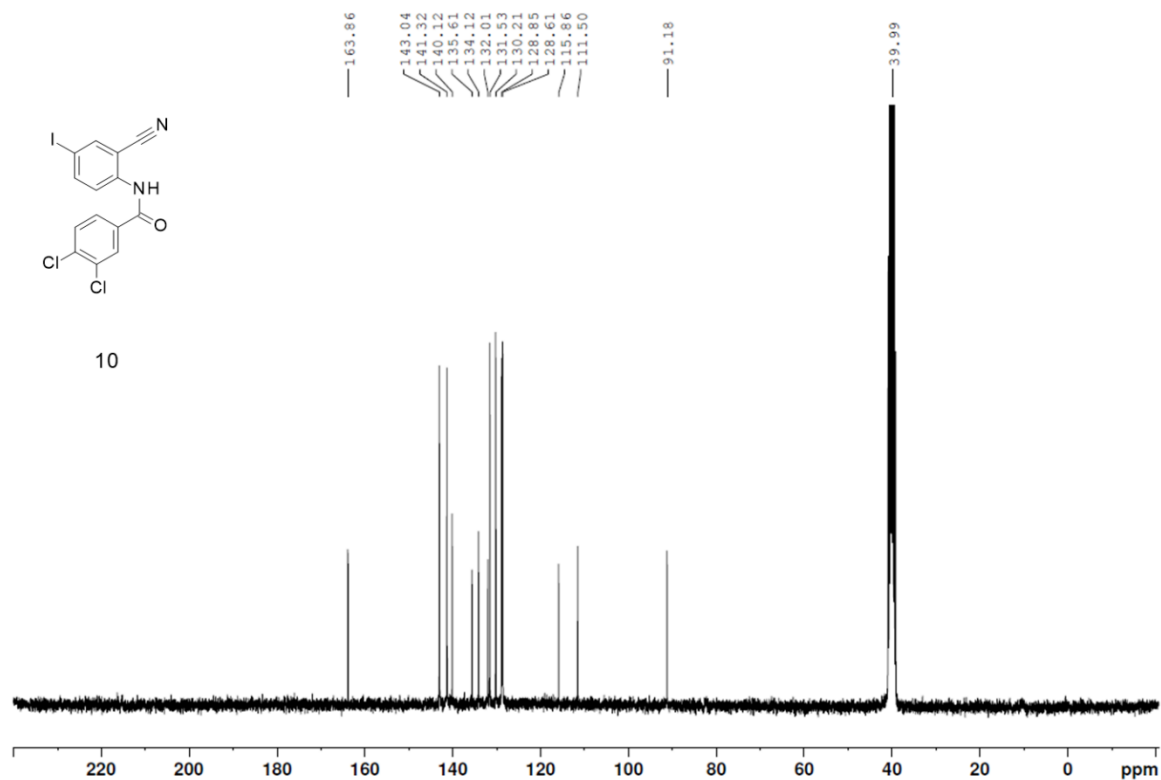
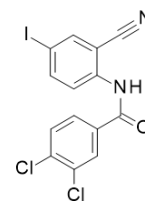


Figure S19: ¹H NMR and ¹³C NMR spectra of compound 10



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Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

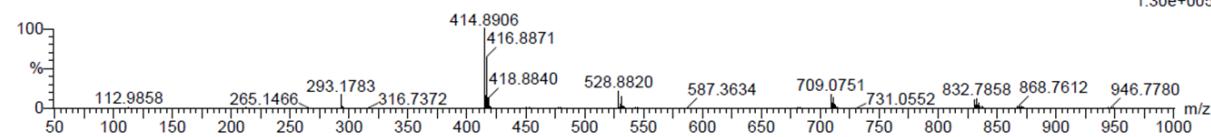
Monoisotopic Mass, Even Electron Ions

603 formula(e) evaluated with 12 results within limits (up to 1 closest results for each mass)

Elements Used:

C: 6-40 H: 2-36 N: 0-4 O: 0-7 Cl: 1-3 I: 0-1

1: TOF MS ES-
1.30e+005

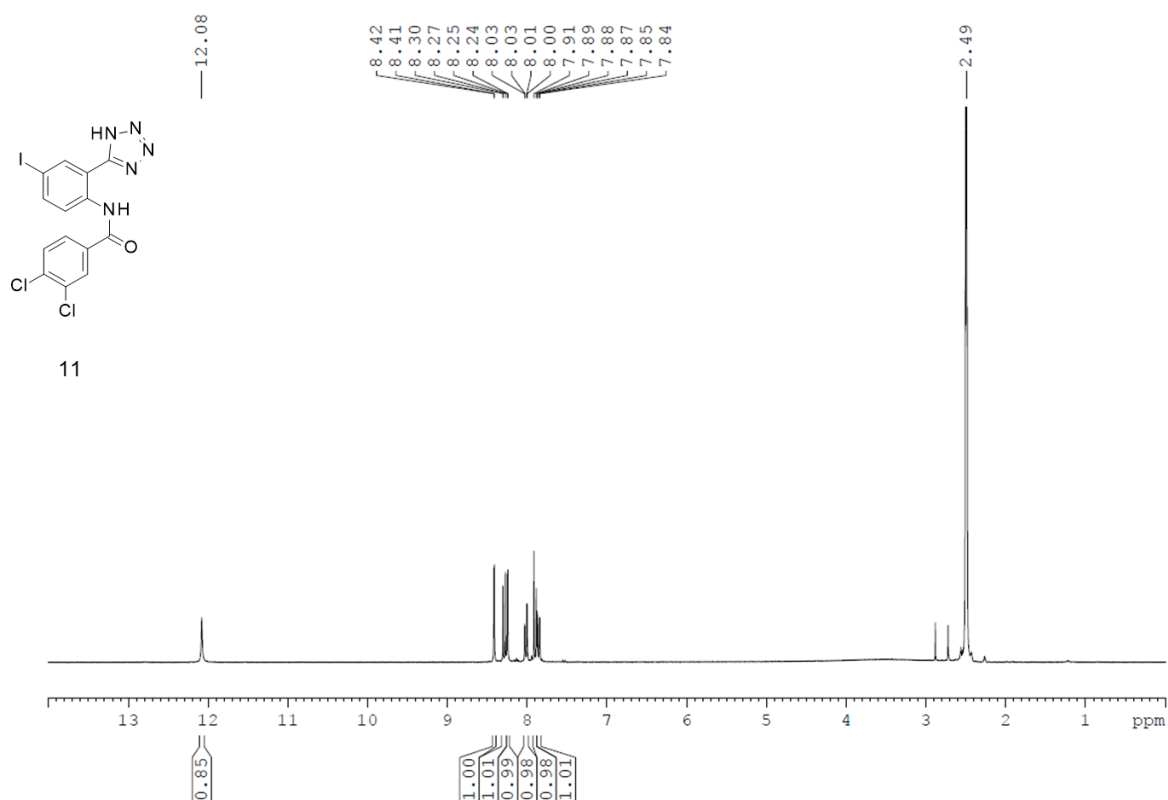


Minimum: -1.5
Maximum: 10.0 20.0 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
414.8906	414.8902	0.4	1.0	11.5	1.1	C14 H6 N2 O Cl2 I

Figure S20: HRMS spectrum of compound 10

¹H NMR of compound 11 (300 MHz, DMSO-d₆)



¹³C NMR of compound 11 (75 MHz, DMSO-d₆)

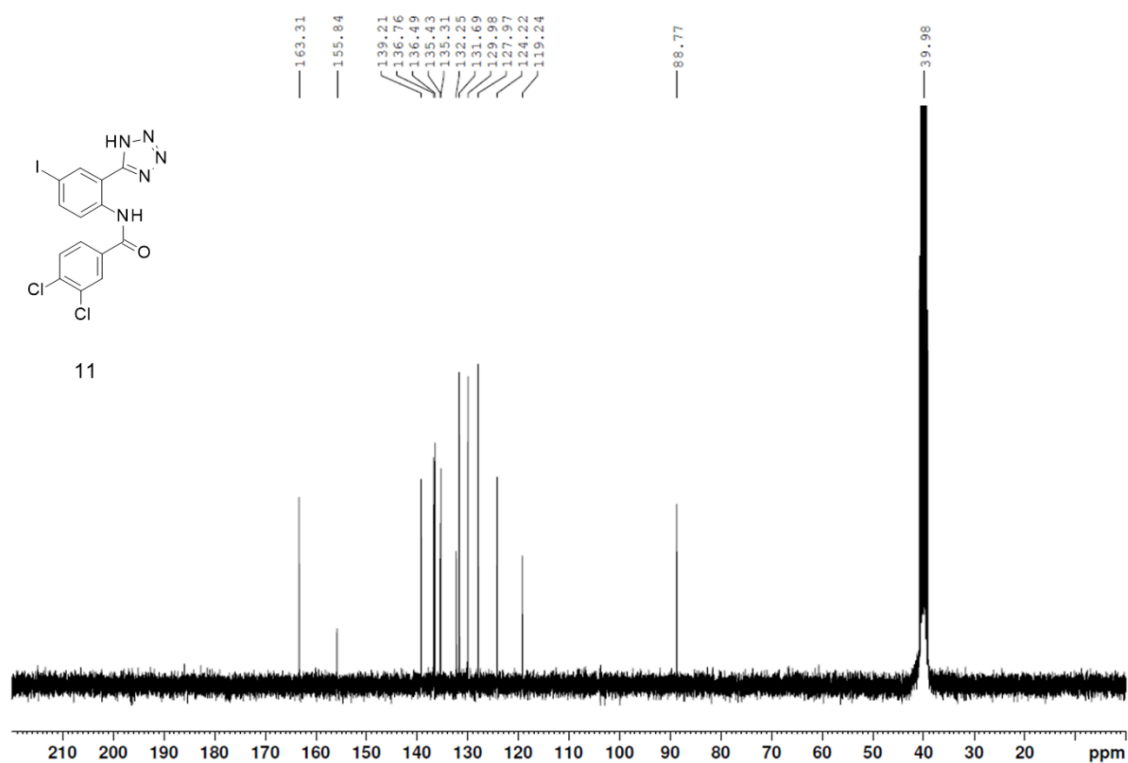


Figure S21: ¹H NMR and ¹³C NMR spectra of compound 11

Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

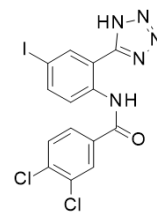
Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

783 formula(e) evaluated with 17 results within limits (up to 1 closest results for each mass)

Elements Used:

C: 6-40 H: 2-36 N: 0-5 O: 0-7 Cl: 1-3 I: 0-1



11

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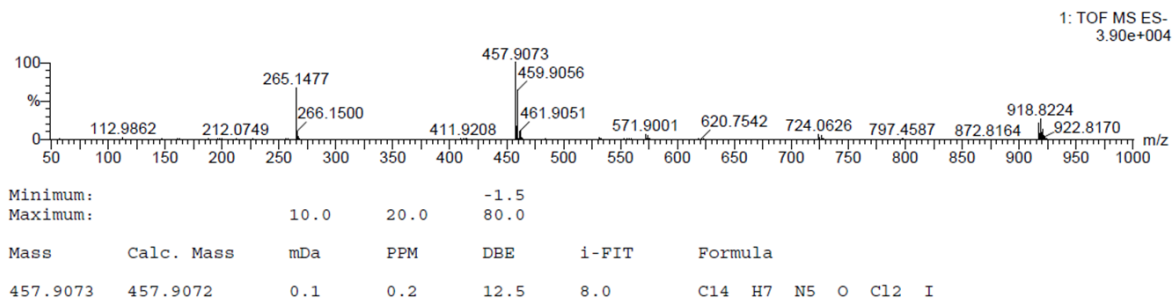


Figure S22: HRMS spectrum of compound 11

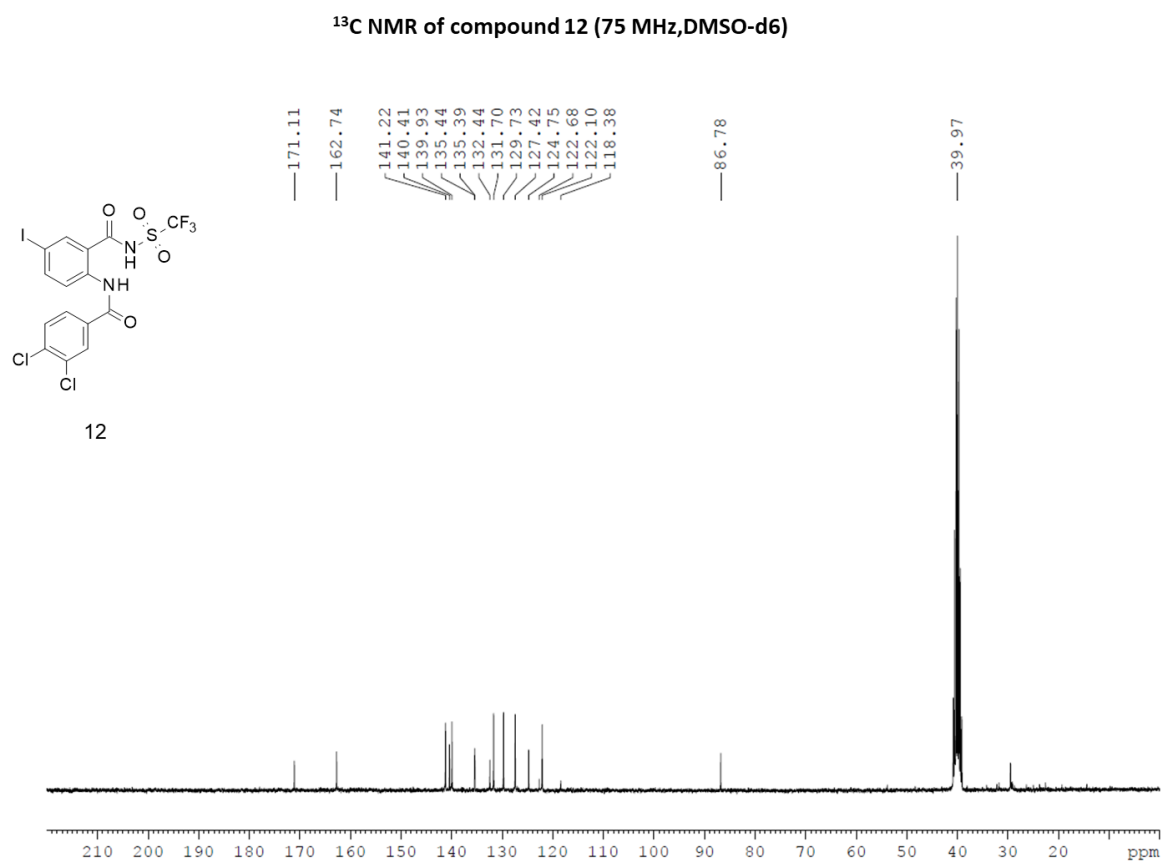
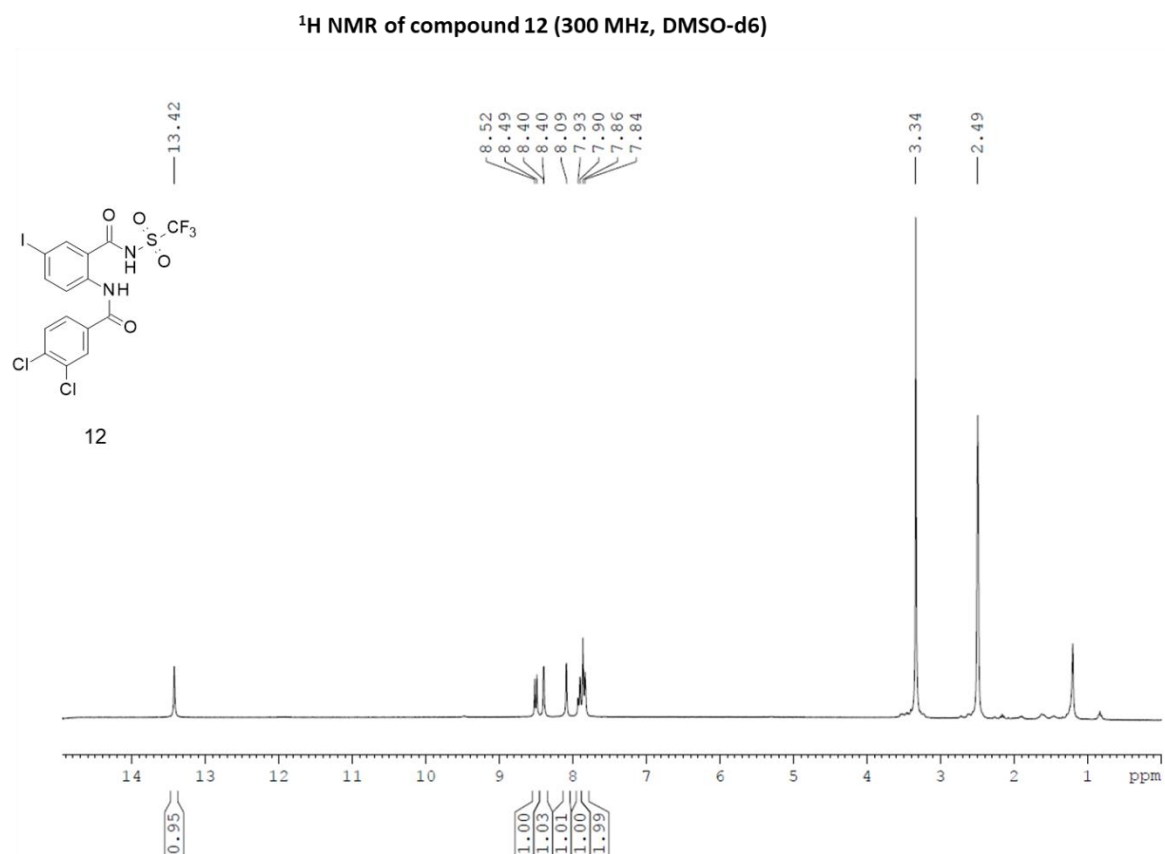


Figure S23: ¹H NMR and ¹³C NMR spectra of compound 12

Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

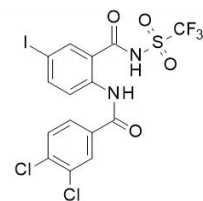
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

11796 formula(e) evaluated with 19 results within limits (up to 5 closest results for each mass)

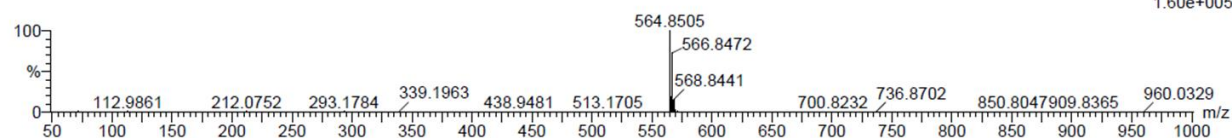
Elements Used:

C: 15-15 H: 0-60 N: 0-10 O: 0-15 F: 1-3 S: 0-3 Cl: 0-2 I: 0-1



12

1: TOF MS ES-
1.60e+005

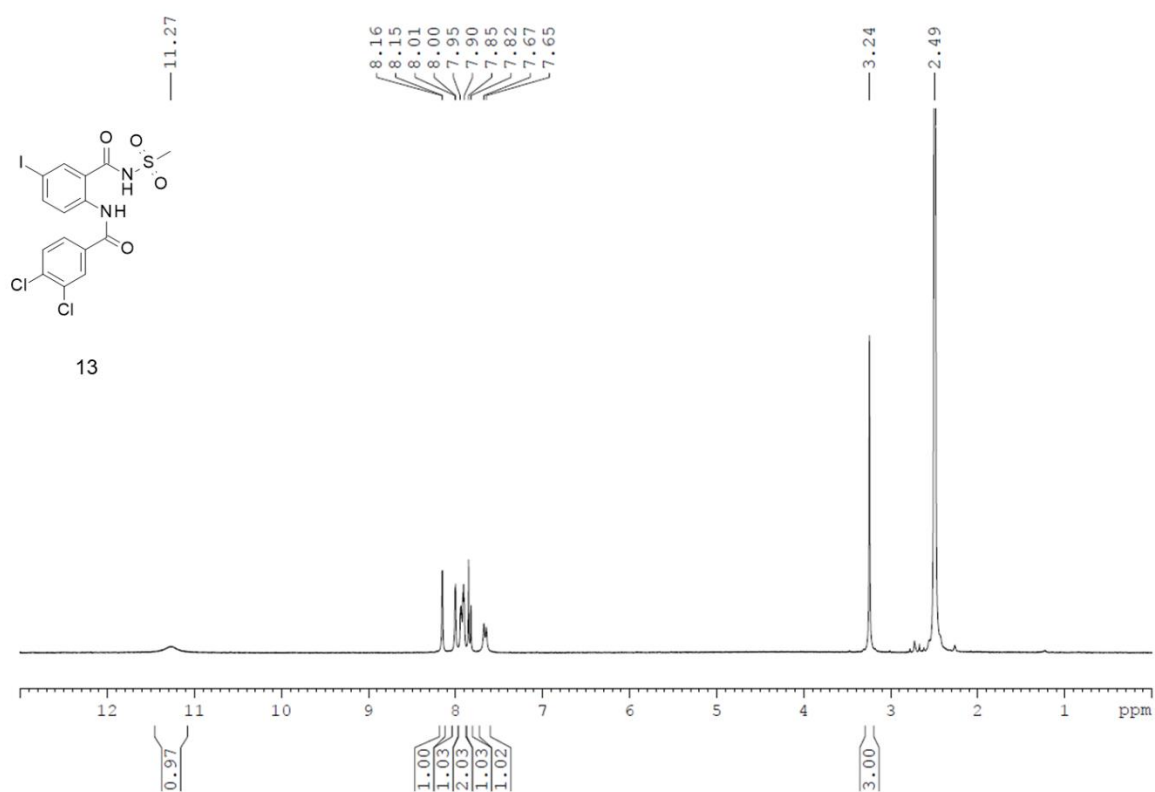


Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
564.8505	564.8500	0.5	0.9	10.5	35.5	C15 H7 N2 O4 F3 S Cl2 I

Figure S24: HRMS spectrum of compound 12

¹H NMR of compound 13 (300 MHz, DMSO-d₆)



¹³C NMR of compound 13 (75 MHz, DMSO-d₆)

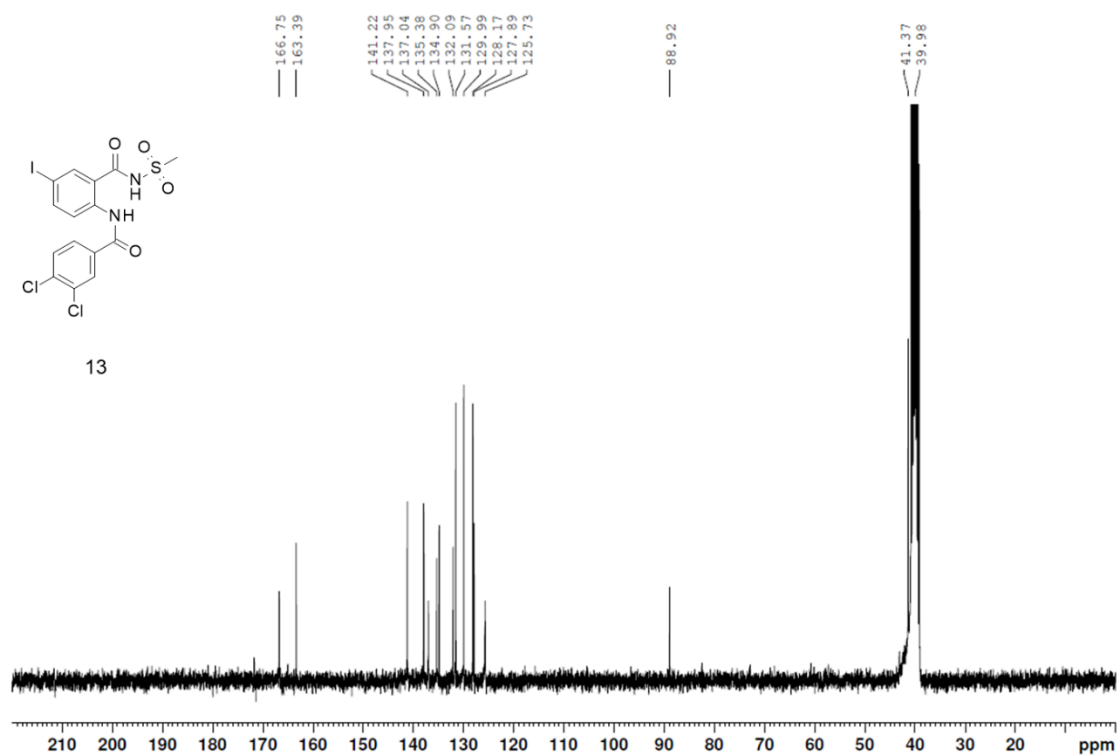
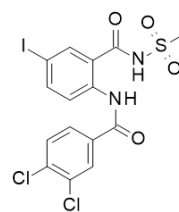


Figure S25: ¹H NMR and ¹³C NMR spectra of compound 13



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Elemental Composition Report

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Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

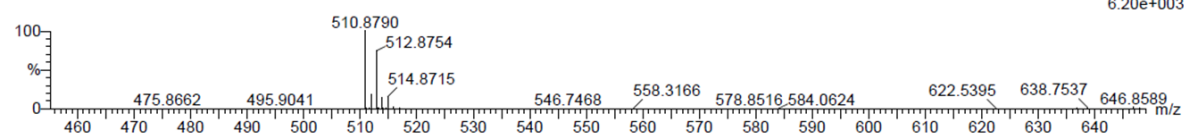
Monoisotopic Mass, Even Electron Ions

1636 formula(e) evaluated with 30 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

C: 6-40 H: 2-36 N: 0-5 O: 0-7 S: 0-1 Cl: 1-3 I: 0-1

1: TOF MS ES-
6.20e+003



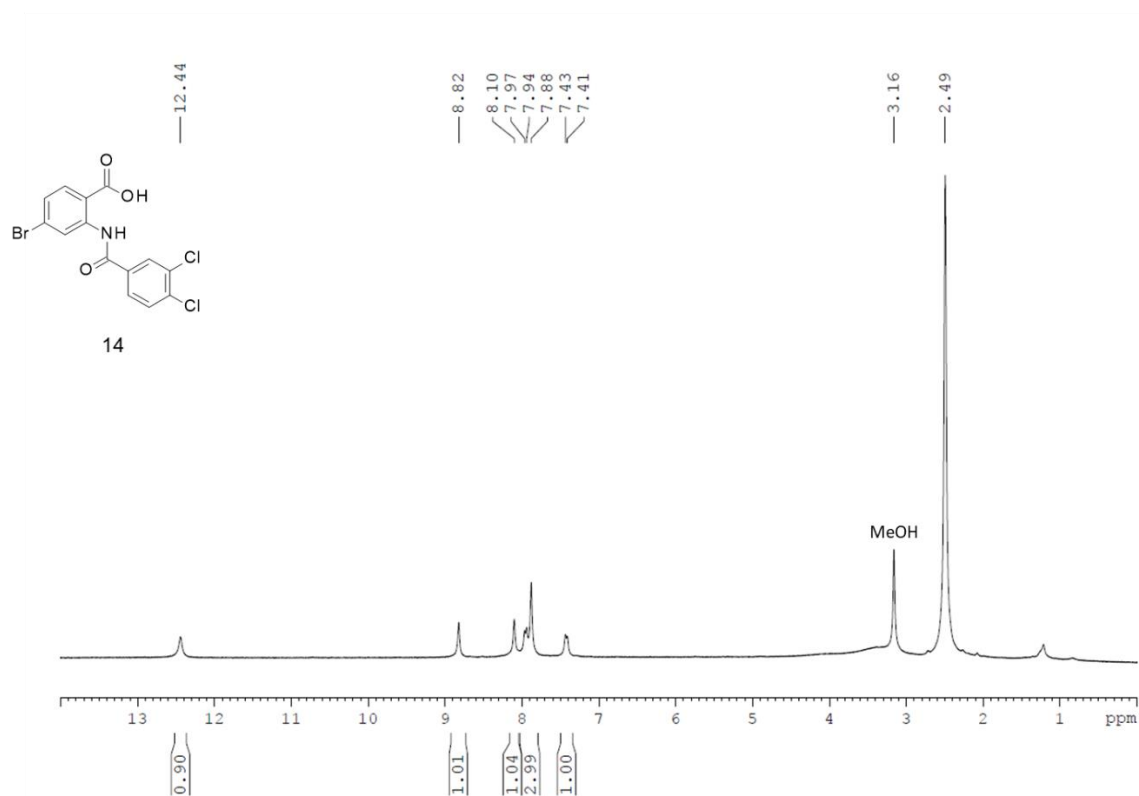
Minimum:

Maximum: 10.0 20.0 -1.5 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
510.8790	510.8783	0.7	1.4	10.5	0.2	C15 H10 N2 O4 S Cl2 I

Figure S26: HRMS spectrum of compound 13

¹H NMR of compound 14 (300 MHz, DMSO-d₆)



¹³C JMOD NMR of compound 14 (75 MHz, DMSO-d₆)

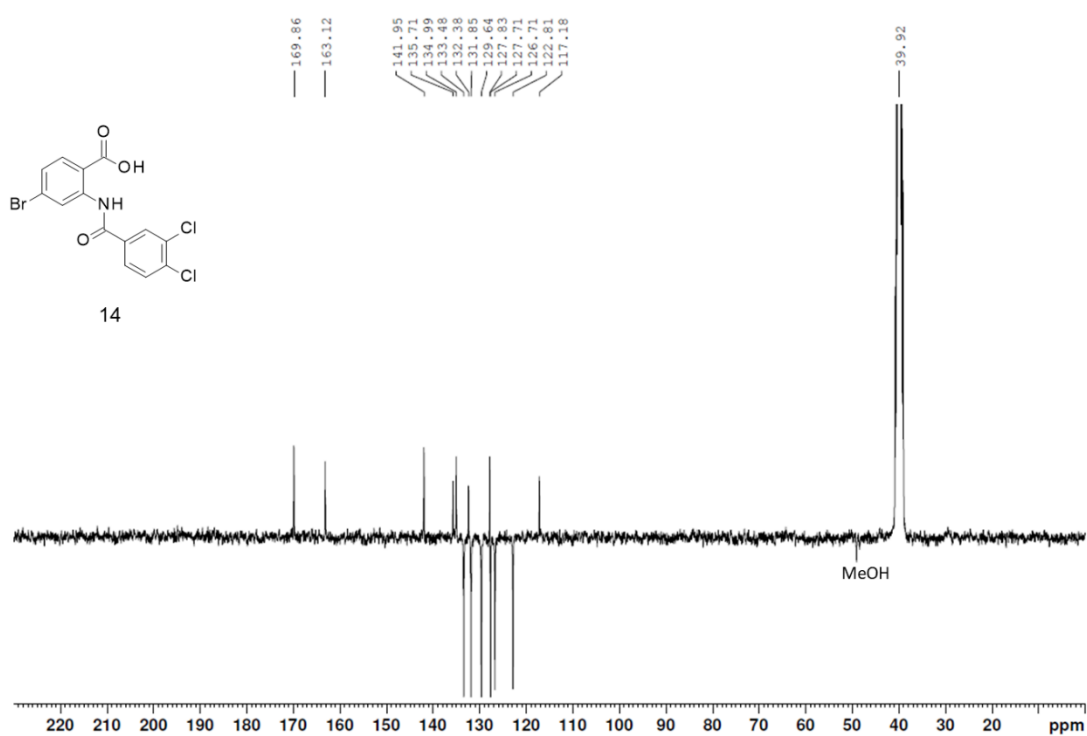


Figure S27: ¹H NMR and ¹³C NMR spectra of compound 14

Elemental Composition Report

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Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

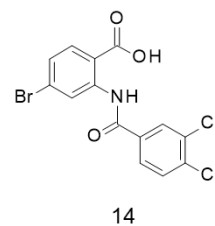
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

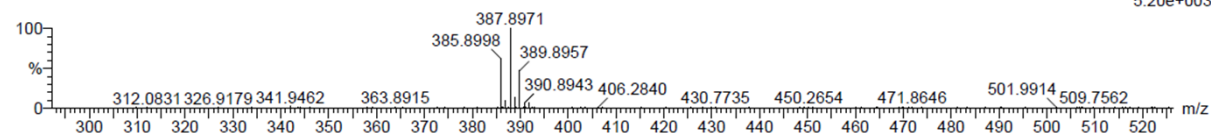
2876 formula(e) evaluated with 6 results within limits (up to 5 closest results for each mass)

Elements Used:

C: 10-50 H: 0-60 N: 0-10 O: 0-15 Cl: 0-2 Br: 0-1 I: 0-1



1: TOF MS ES-
5.20e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
385.8998	385.8986	1.2	3.1	10.5	1.8	C14 H7 N O3 Cl2 Br

Figure S28: HRMS spectrum of compound 14

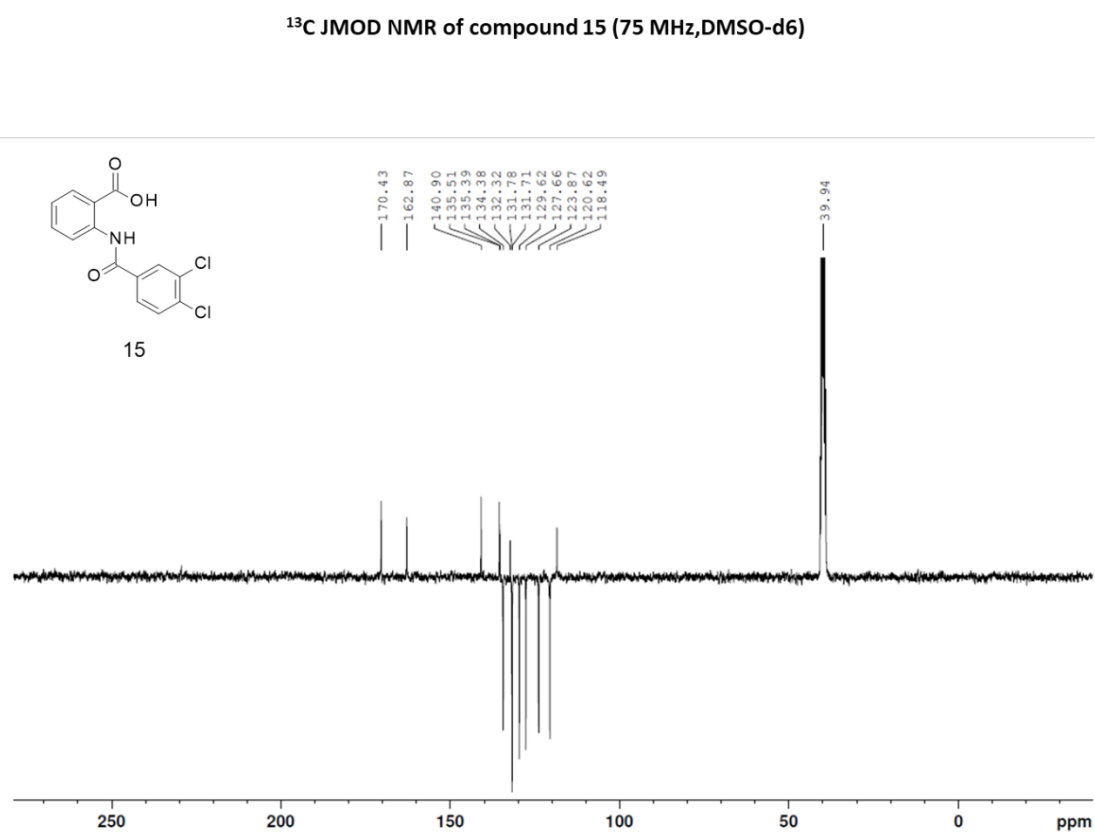
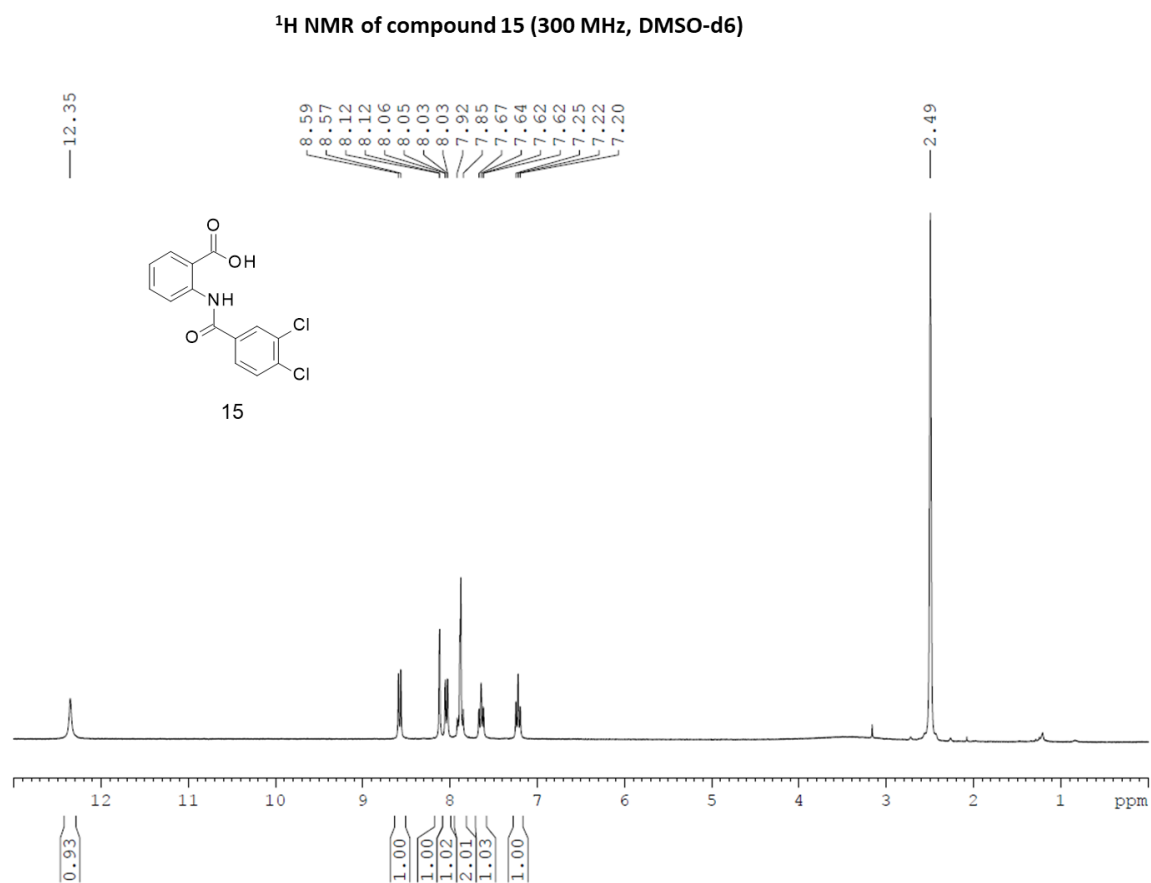


Figure S29: ¹H NMR and ¹³C NMR spectra of compound 15

Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

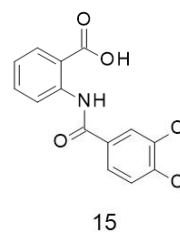
Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

343 formula(e) evaluated with 5 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

C: 2-20 H: 2-36 N: 0-5 O: 0-7 Cl: 1-2 I: 0-1



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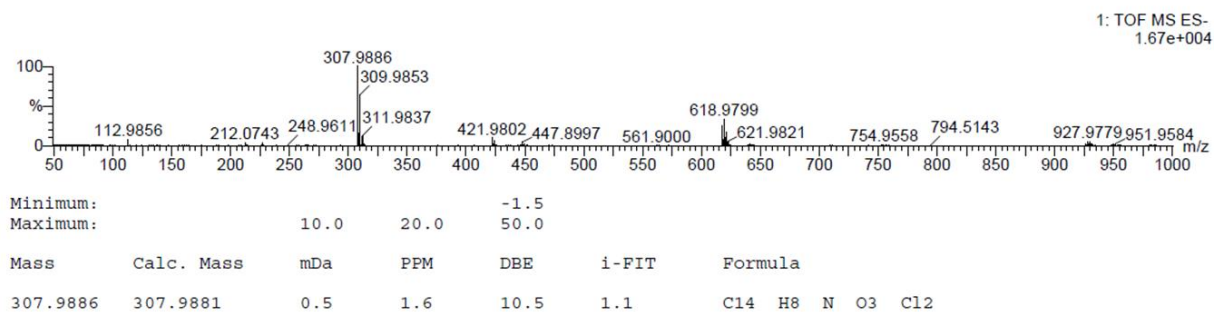
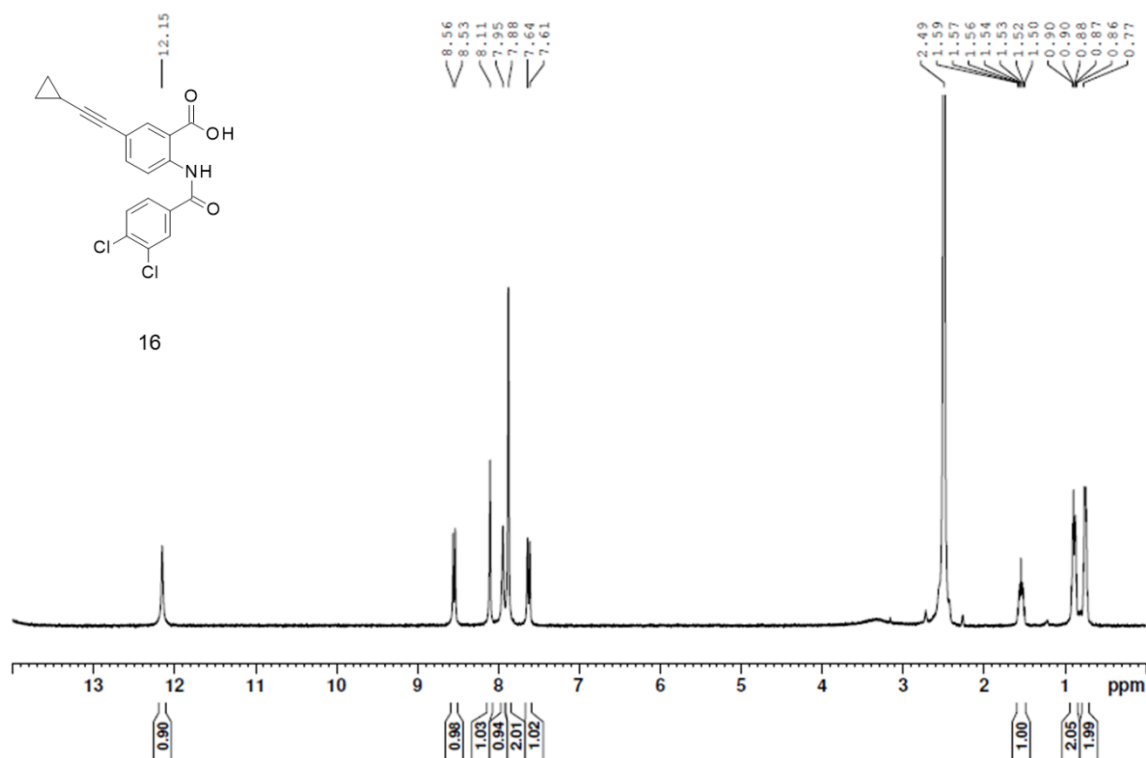


Figure S30: HRMS spectrum of compound 15

¹H NMR of compound 16 (300 MHz, DMSO-d₆)



¹³C NMR of compound 16 (75 MHz, DMSO-d₆)

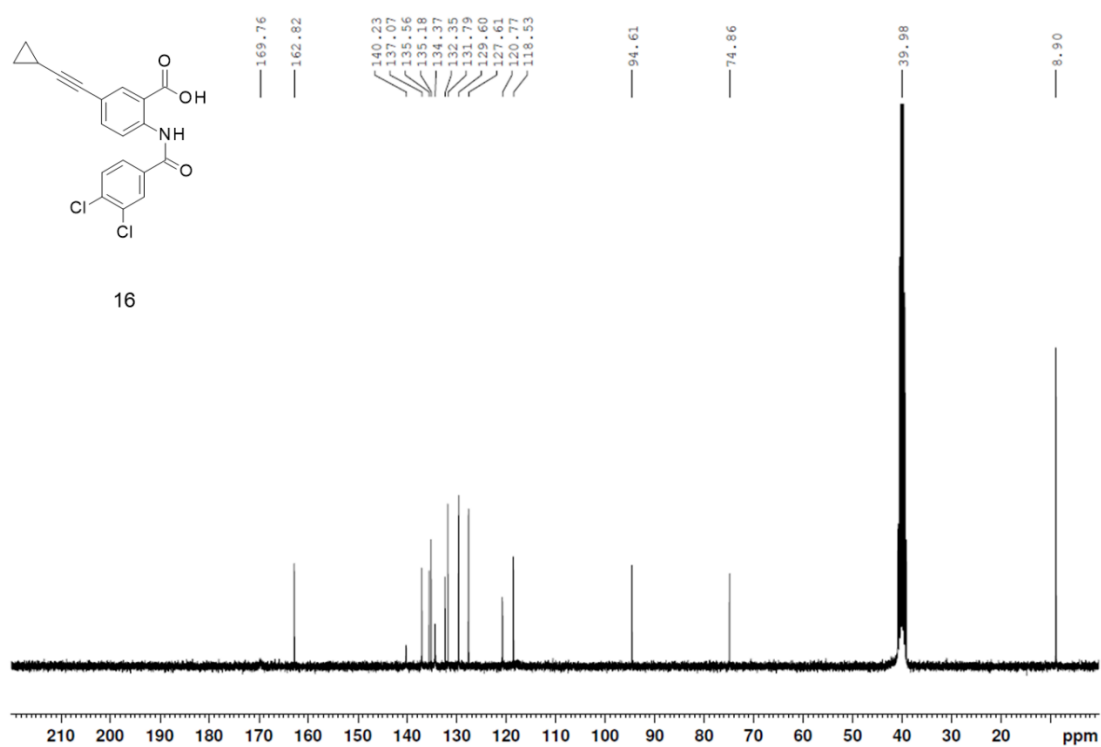
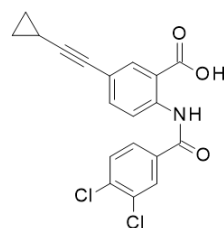


Figure S31: ¹H NMR and ¹³C NMR spectra of compound 16



16

Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

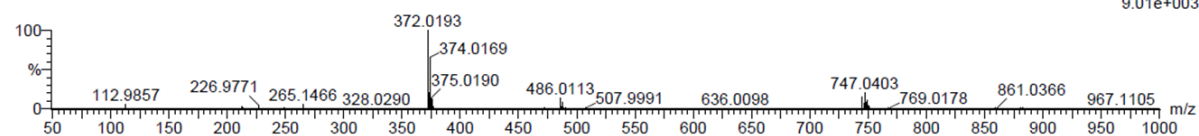
Monoisotopic Mass, Even Electron Ions

221 formula(e) evaluated with 5 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

C: 2-20 H: 2-36 N: 0-5 O: 0-7 Cl: 1-2

1: TOF MS ES-
9.01e+003



Minimum: -1.5
Maximum: 10.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
372.0193	372.0194	-0.1	-0.3	13.5	1.1	C19 H12 N O3 Cl2

Figure S32: HRMS spectrum of compound 16

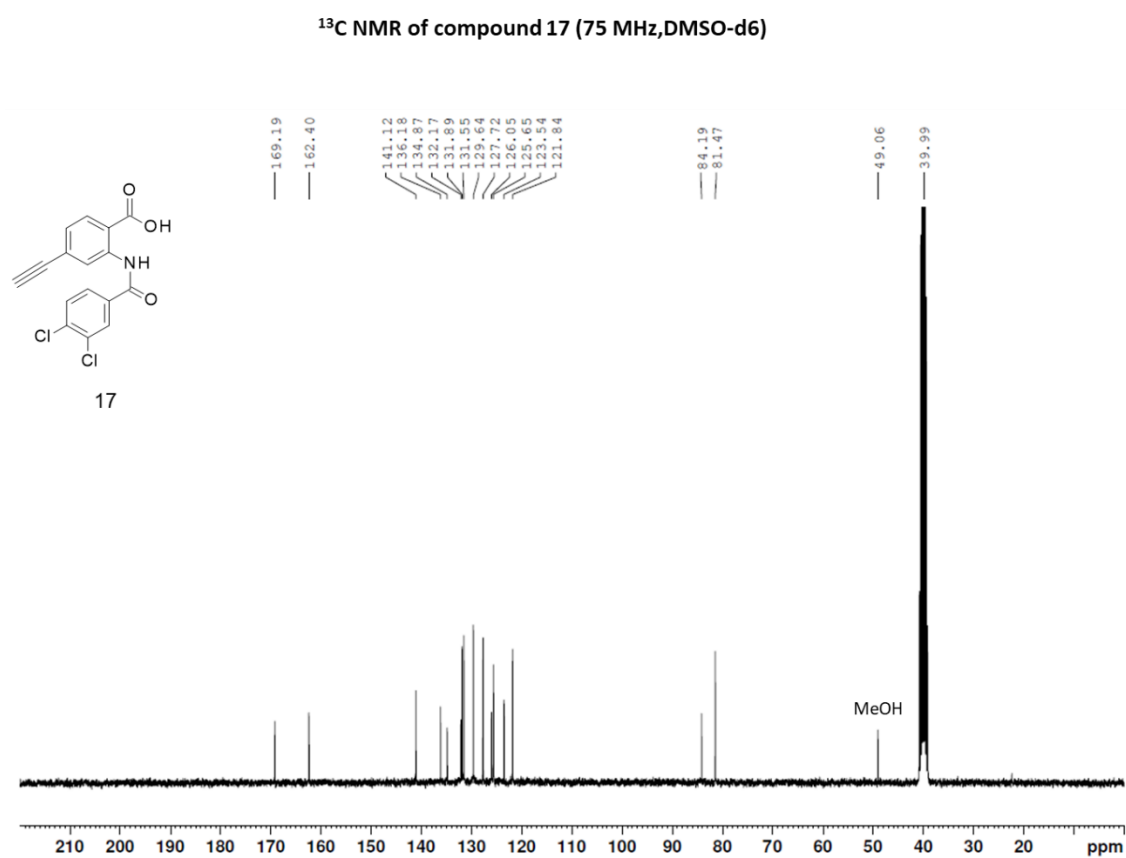
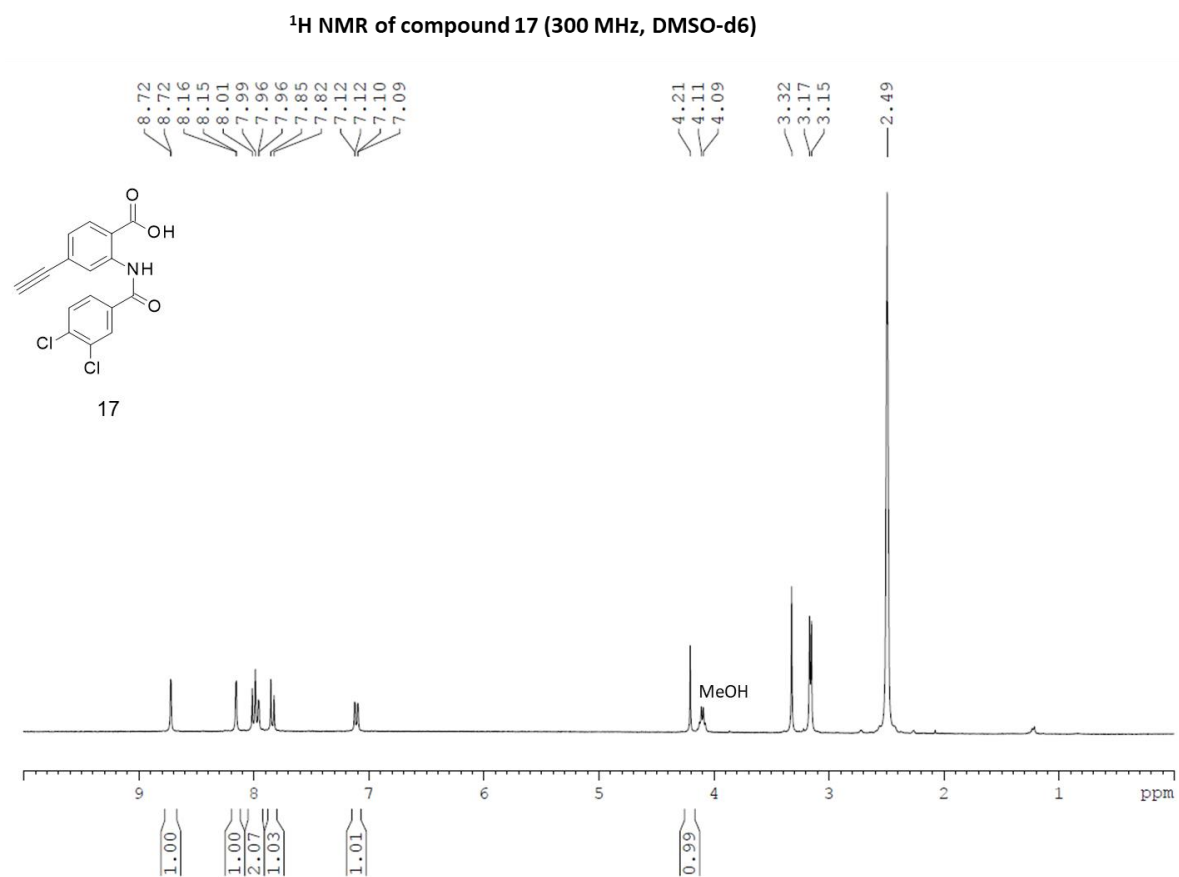


Figure S33: ¹H NMR and ¹³C NMR spectra of compound 17

Elemental Composition Report

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Single Mass Analysis

Tolerance = 100.0 mDa / DBE: min = -1.5, max = 500.0

Element prediction: Off

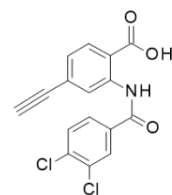
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

350 formula(e) evaluated with 59 results within limits (up to 10 best isotopic matches for each mass)

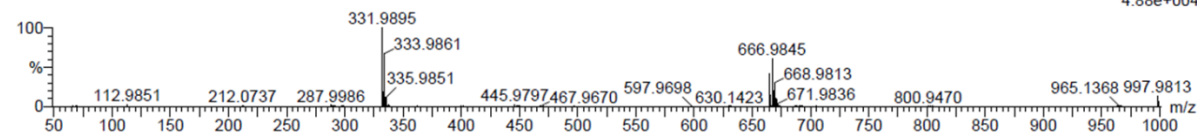
Elements Used:

C: 0-30 H: 0-40 N: 0-4 O: 0-6 Cl: 0-2



17

1: TOF MS ES-
4.88e+004



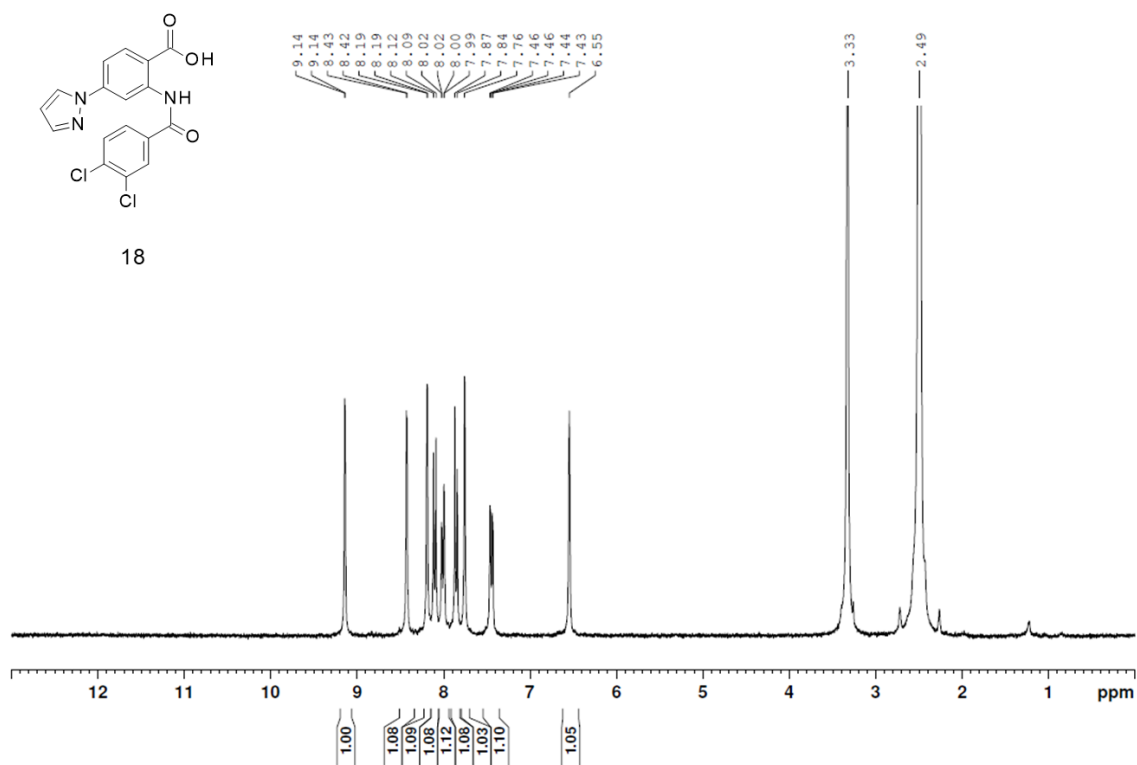
Minimum:

Maximum: 100.0 5.0 -1.5 500.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
331.9895	331.9881	1.4	4.2	12.5	9.8	C16 H8 N O3 Cl2

Figure S34: HRMS spectrum of compound 17

¹H NMR of compound 18 (300 MHz, DMSO-d6)



¹³C JMOD NMR of compound 18 (75 MHz, DMSO-d6)

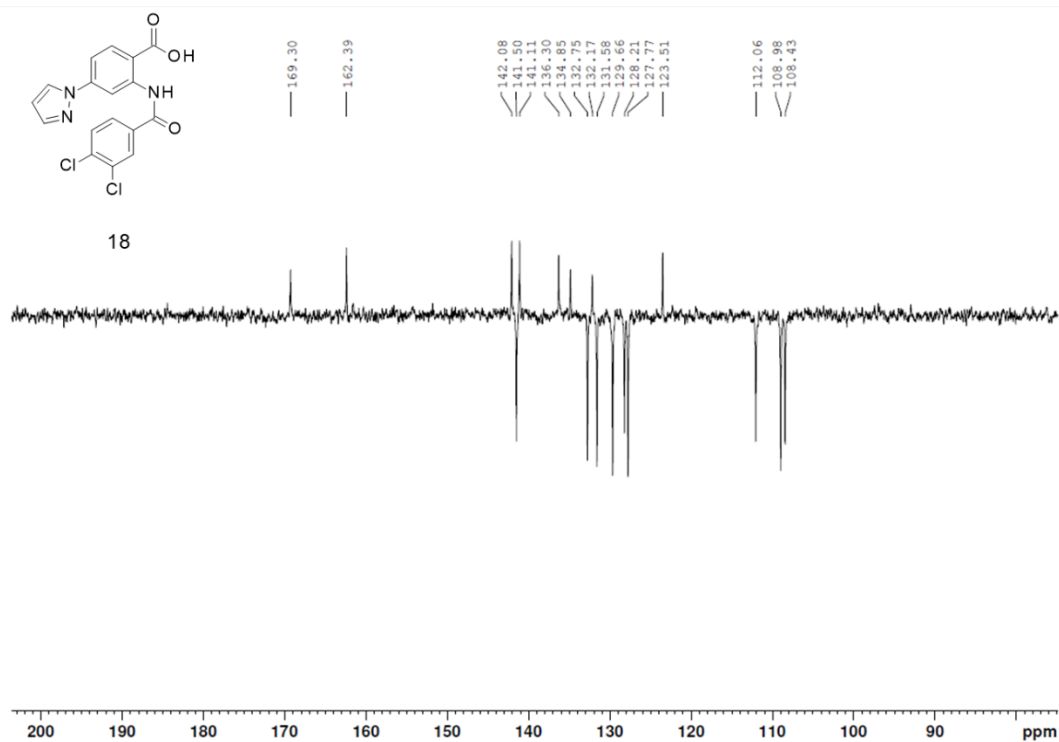


Figure S35: ¹H NMR and ¹³C NMR spectra of compound 18

Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

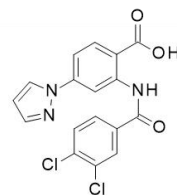
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

2596 formula(e) evaluated with 22 results within limits (up to 5 closest results for each mass)

Elements Used:

C: 10-50 H: 0-60 N: 0-10 O: 0-15 Cl: 0-2 Br: 0-1 I: 0-1



18

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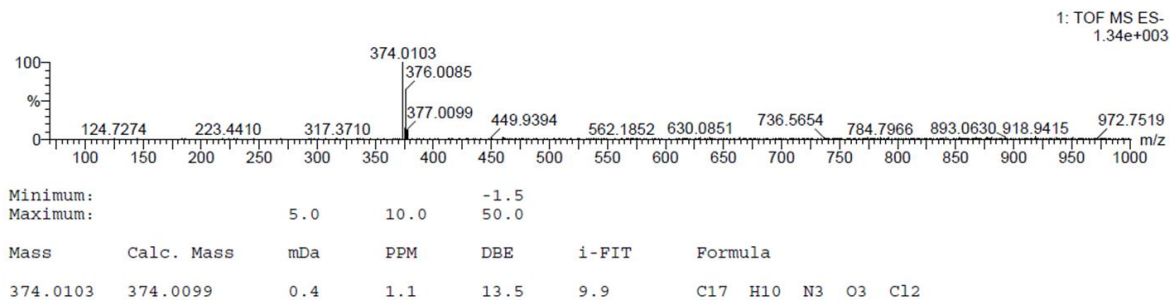


Figure S36: HRMS spectrum of compound 18

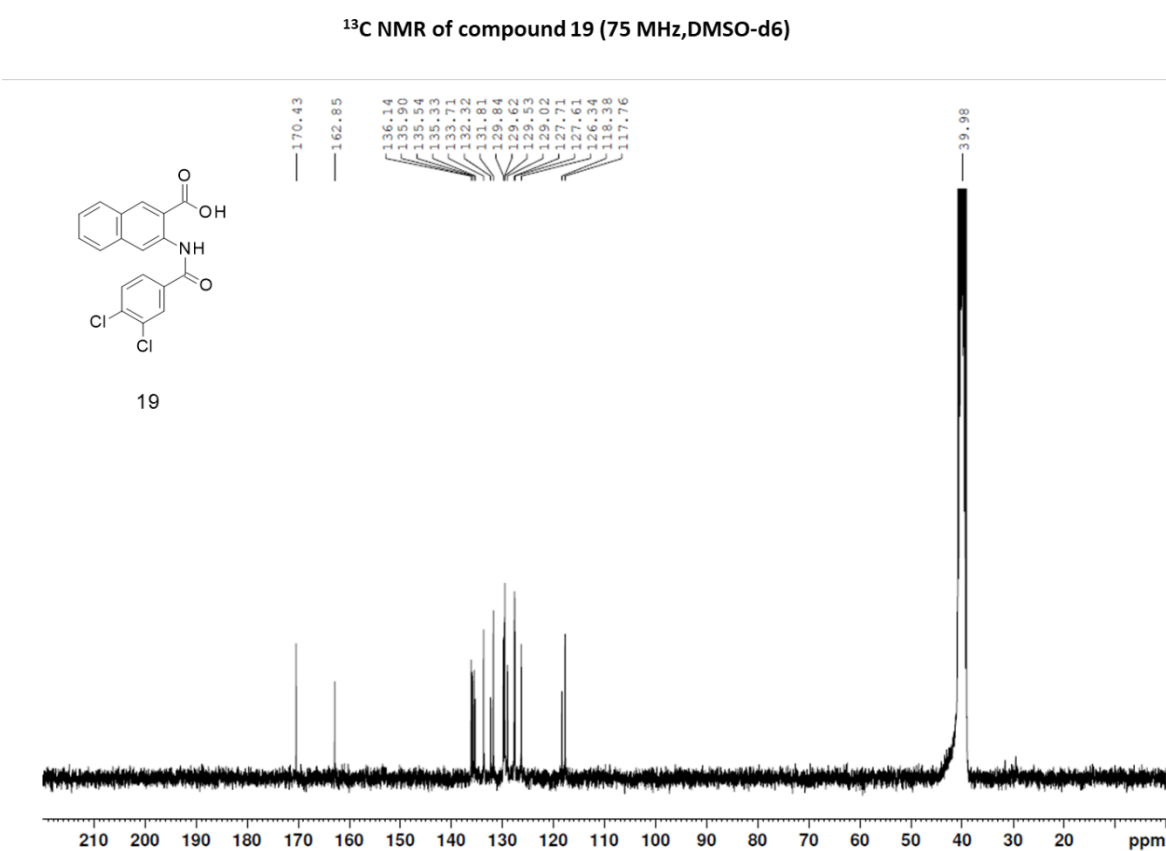
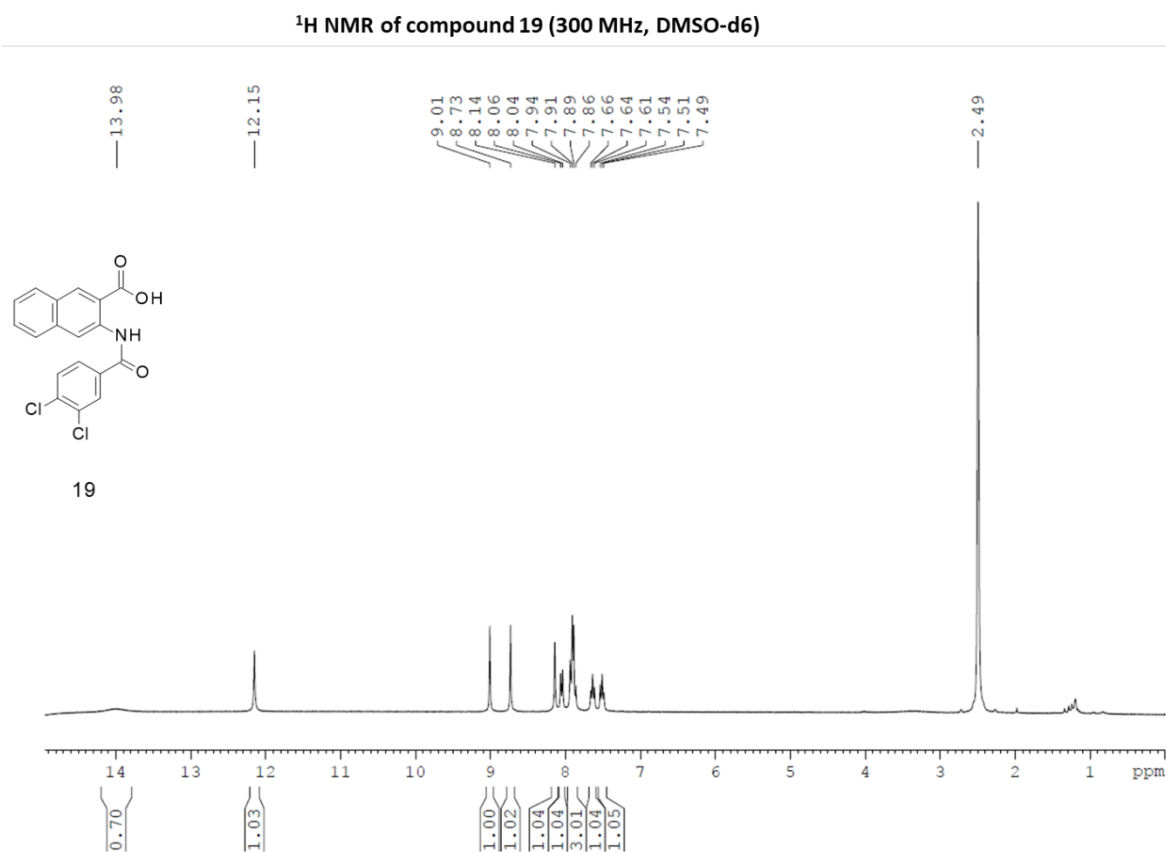
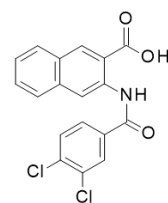


Figure S37: ¹H NMR and ¹³C NMR spectra of compound 19



19

Elemental Composition Report

Single Mass Analysis

Tolerance = 100.0 mDa / DBE: min = -1.5, max = 500.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

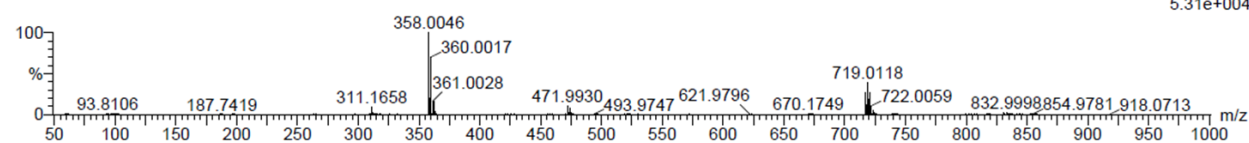
Monoisotopic Mass, Even Electron Ions

360 formula(e) evaluated with 67 results within limits (up to 10 best isotopic matches for each mass)

Elements Used:

C: 0-30 H: 0-40 N: 0-4 O: 0-6 Cl: 0-2

1: TOF MS ES-
5.31e+004

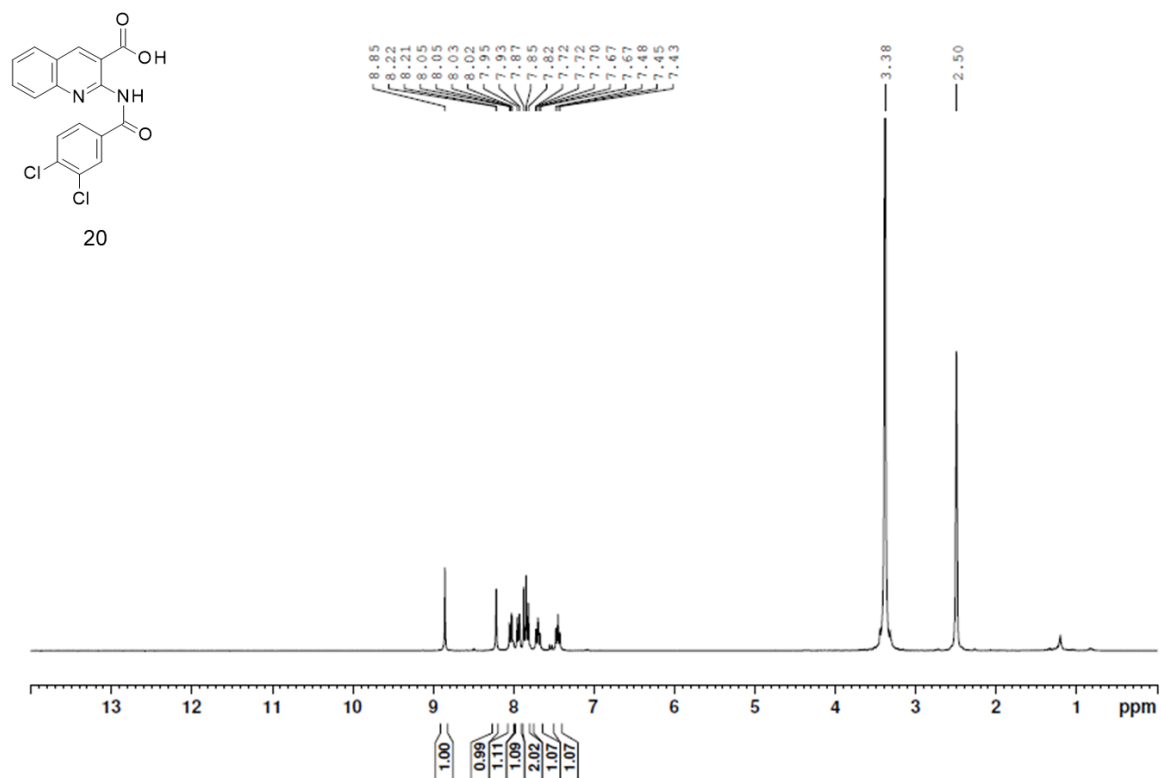


Minimum: -1.5
Maximum: 100.0 5.0 500.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
358.0046	358.0038	0.8	2.2	13.5	54.2	C18 H10 N O3 Cl2

Figure S38: HRMS spectrum of compound 19

¹H NMR of compound 20 (300 MHz, DMSO-d6)



¹³C NMR of compound 20 (75 MHz, DMSO-d6)

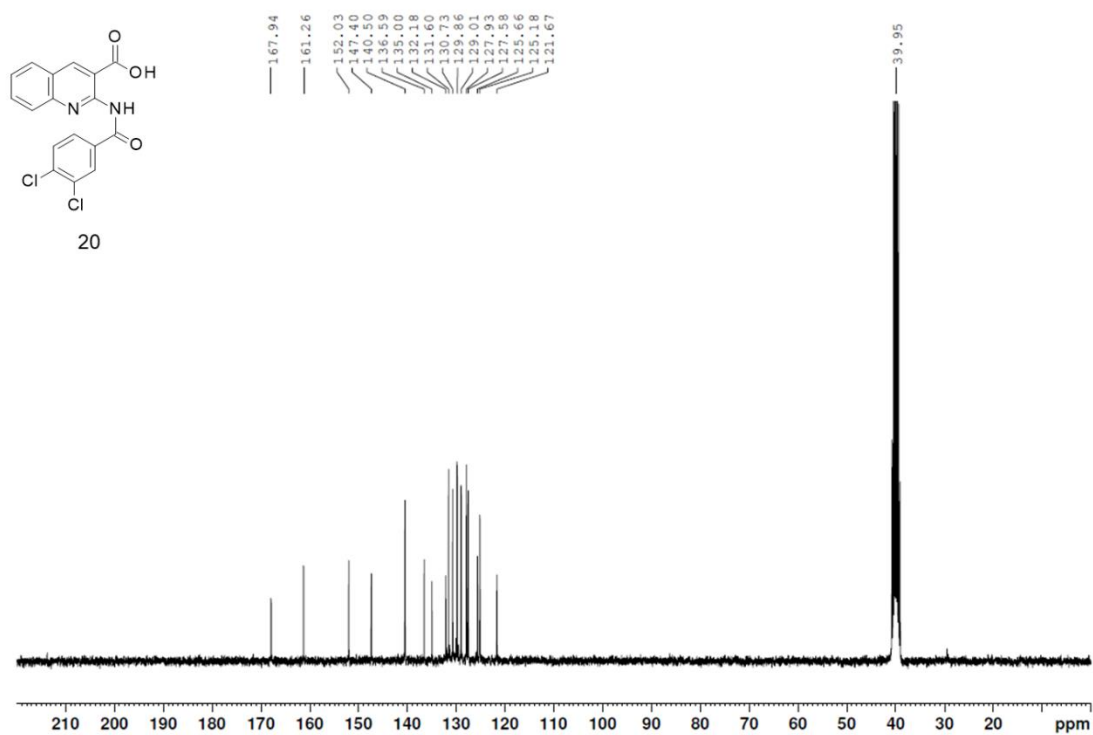
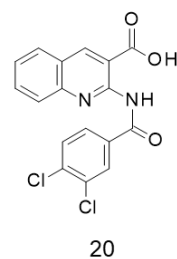


Figure S39: ¹H NMR and ¹³C NMR spectra of compound 20



Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

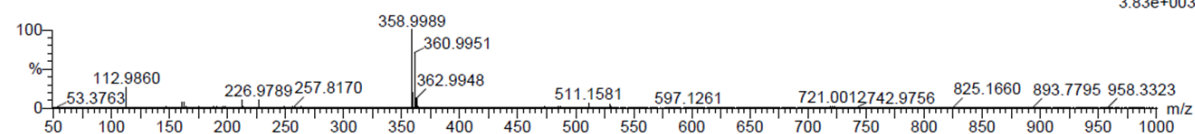
Monoisotopic Mass, Even Electron Ions

403 formula(e) evaluated with 6 results within limits (up to 1 best isotopic matches for each mass)

Elements Used:

C: 2-20 H: 2-36 N: 0-5 O: 0-7 Cl: 1-2 I: 0-1

1: TOF MS ES-
3.83e+003



Minimum: -1.5
Maximum: 10.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
358.9989	358.9990	-0.1	-0.3	13.5	0.0	C17 H9 N2 O3 Cl2

Figure S40: HRMS spectrum of compound 20