

Synthesis and Antibacterial Evaluation of Trisindolines against Methicillin-resistant *Staphylococcus aureus* Targeting Cell Membrane

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2. Results

2.1 Figure S16: Dose-Dependent Growth Inhibition of MRSA by the Active Trisindolines. (A-H) X-axis depicted the inhibitory concentration of active hits, and Y-axis represented percent growth in the presence of varying compound concentrations along with vancomycin (I).

2.2 Figure S17: LB Agar plates representing Minimum Bactericidal Concentration in $\mu\text{M}/\mu\text{g/ml}$.

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2.8 Table S5: GO analysis of DEGs of MRSA versus Compound 3g

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3.1 Table S8: KEGG analysis of DEGs of MRSA versus Compound 3g

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1. HRMS and NMR Spectra of trisindoline derivatives

1a Figure S1(a)...HRMS Spectrum (3a)

Single Mass Analysis

Tolerance = 50.0 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

8 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-17 N: 0-3 O: 0-1 Na: 0-1

3A

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

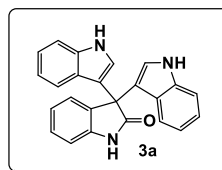
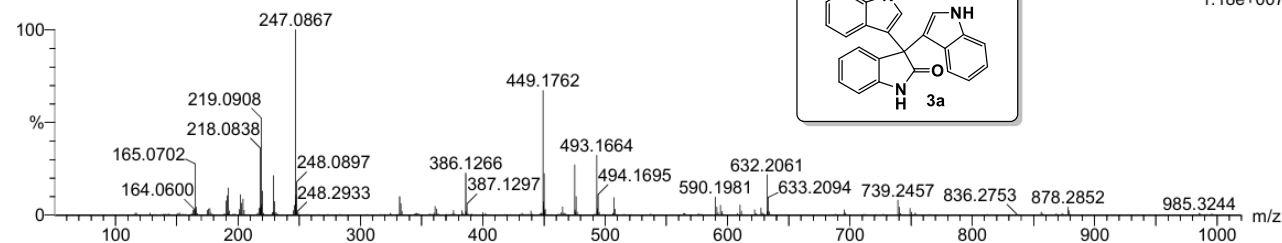
05-Nov-2024

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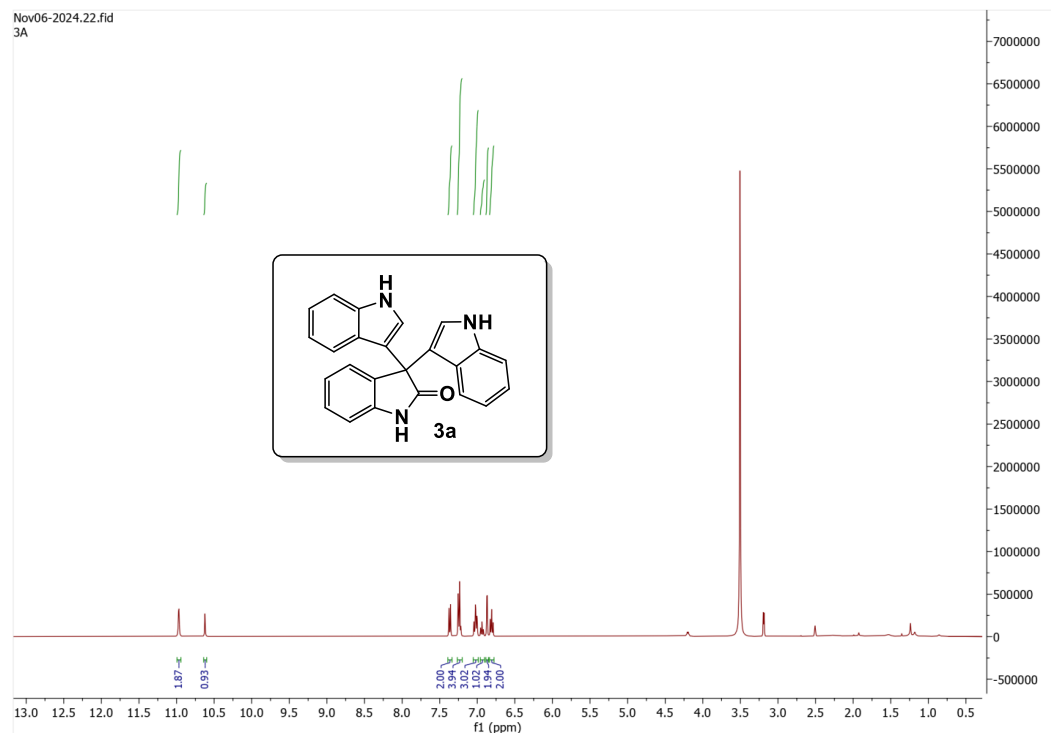
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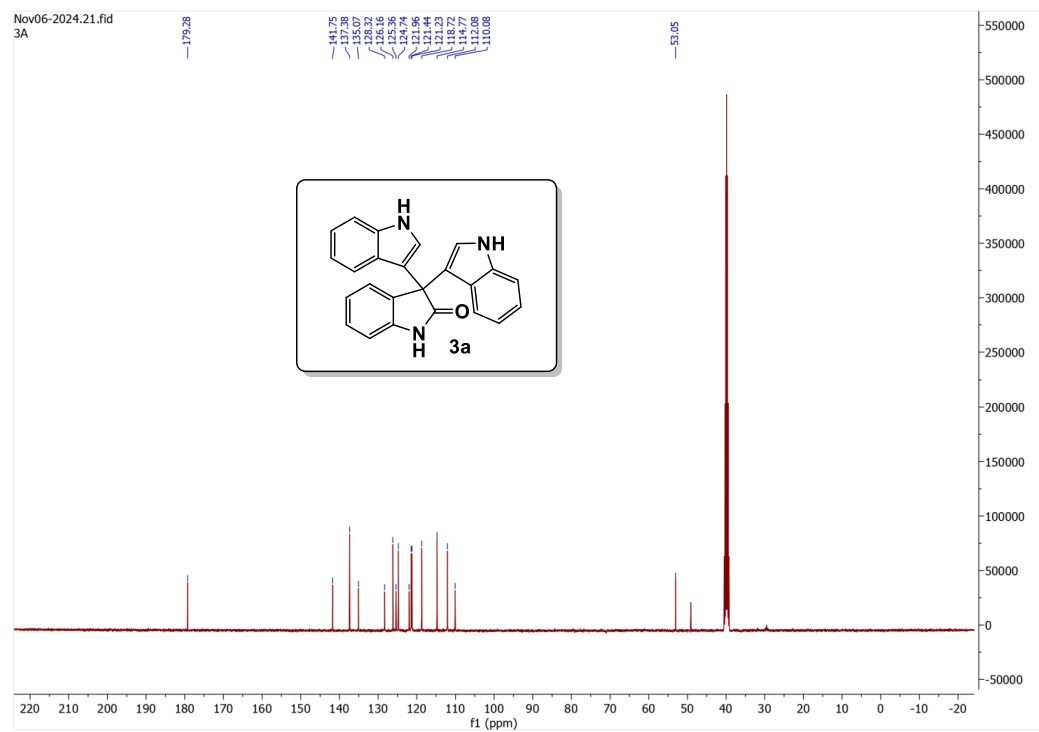
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Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
386.1266	386.1269	-0.3	-0.8	17.5	713.2	n/a	n/a	C ₂₄ H ₁₇ N ₃ O Na

1b Figure S1(b)...¹H NMR (400 MHz) of 3a in DMSO



1c Figure S1(c)...¹³C NMR{¹H} (101 MHz) of **3a** in DMSO



2a Figure S2(a)...HRMS Spectrum (3b)

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 = 3

Monoisotopic Mass, Even Electron Ions

36 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-1 F: 0-2

DMTIM-2

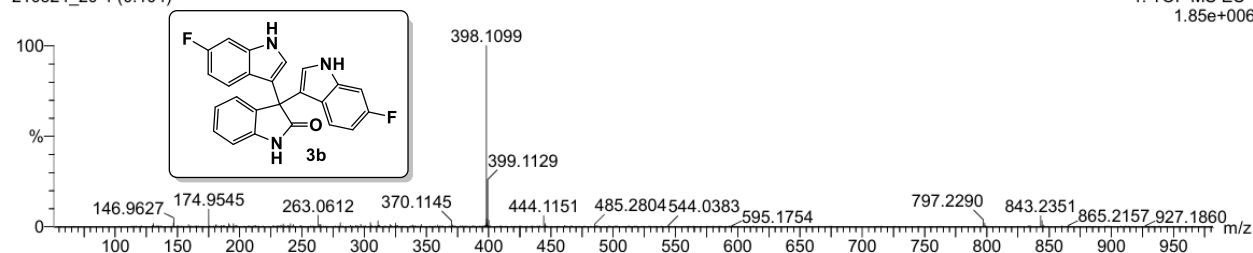
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21-Mar-2024

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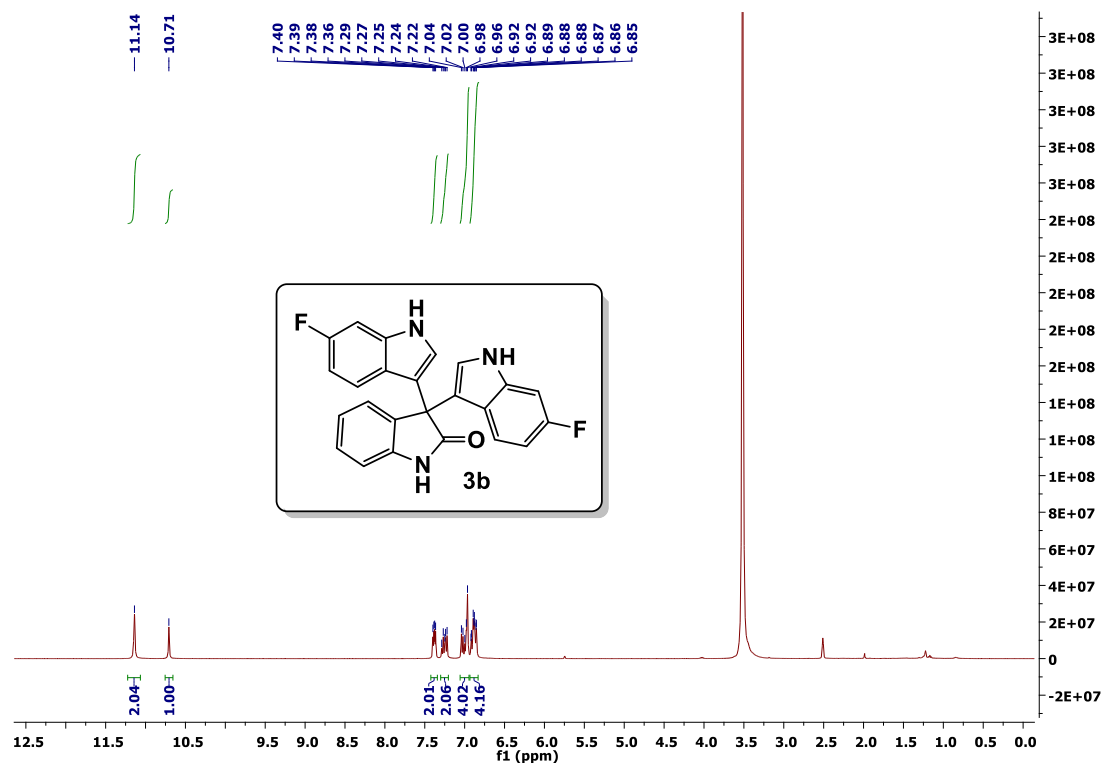
210324_20 4 (0.104)



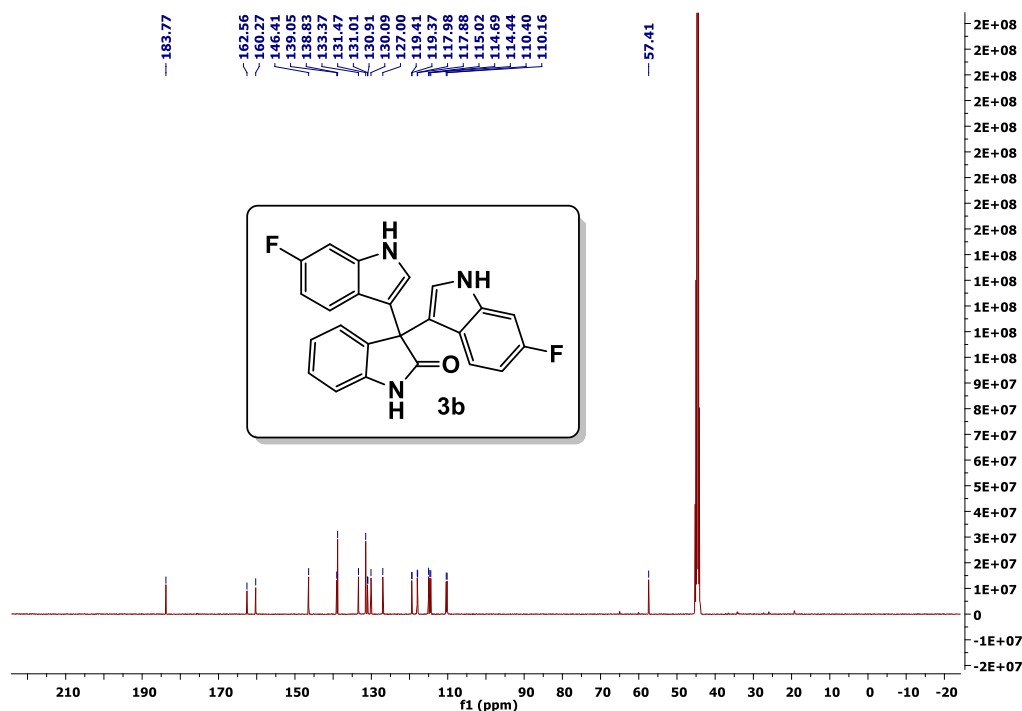
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Maximum: 2.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
398.1099	398.1105	-0.6	-1.5	18.5	1056.4	n/a	n/a	C24 H14 N3 O F2

2b Figure S2(b)...¹H NMR (400 MHz) of 3b in DMSO



2c Figure S2(c)...¹³C NMR{¹H} (101 MHz) of **3b** in DMSO



3a Figure S3(a)...HRMS Spectrum (**3c**)

Single Mass Analysis

Tolerance = 25.0 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

33 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-1 Cl: 0-2

DMTIM-4

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

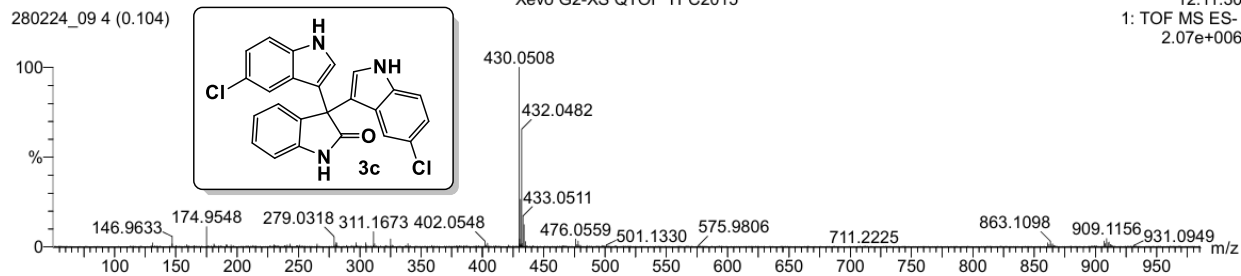
28-Feb-2024

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2.07e+006

280224_09 4 (0.104)

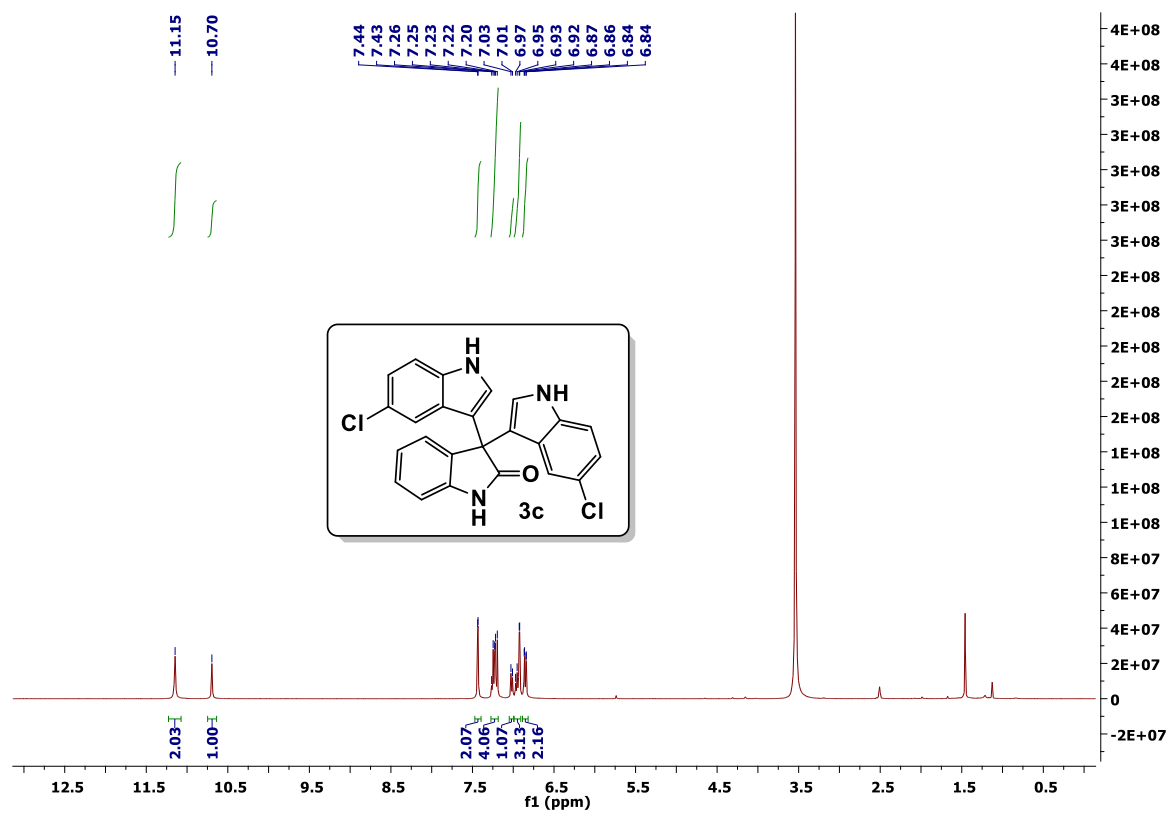


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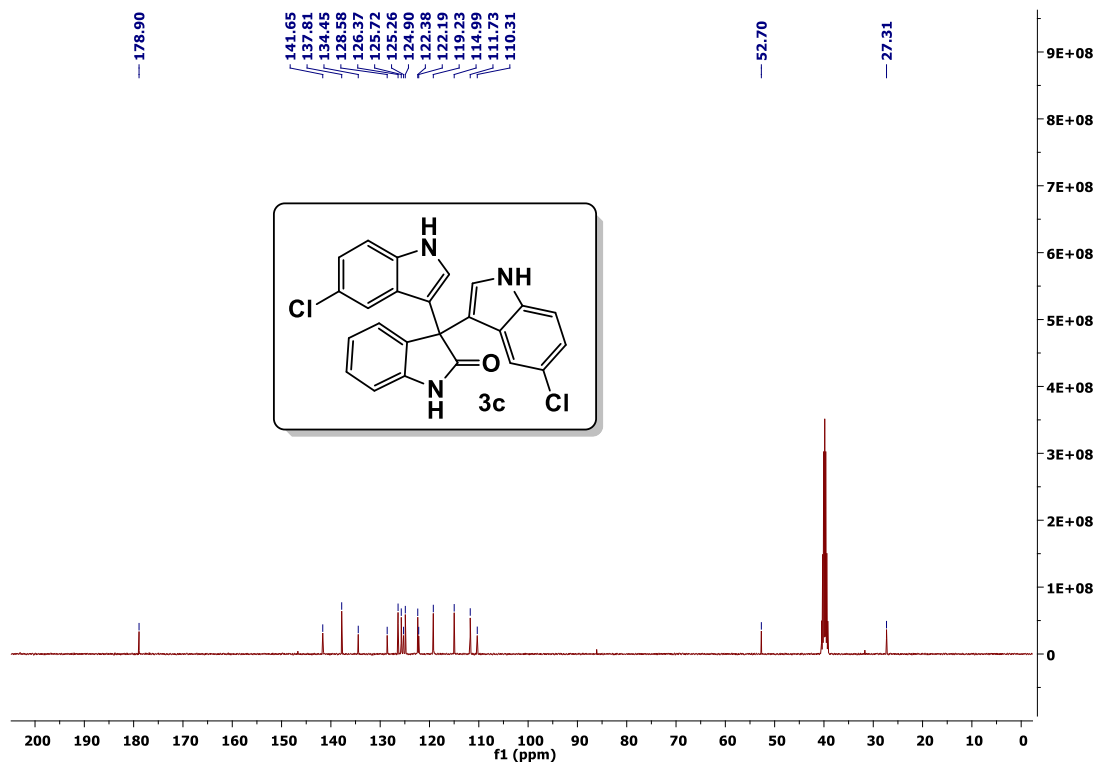
Maximum: 2.0 25.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
430.0508	430.0514	-0.6	-1.4	18.5	1095.2	n/a	n/a	C ₂₄ H ₁₄ N ₃ O Cl ₂

3b Figure S3(b)...¹H NMR (400 MHz) of **3c** in DMSO



3c Figure S3(c)... ^{13}C NMR{ ^1H } (101 MHz) of **3c** in DMSO



4a Figure S4(a)...HRMS Spectrum (**3d**)

Single Mass Analysis

Tolerance = 25.0 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

33 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-1 Cl: 0-2

DMTIM-3

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

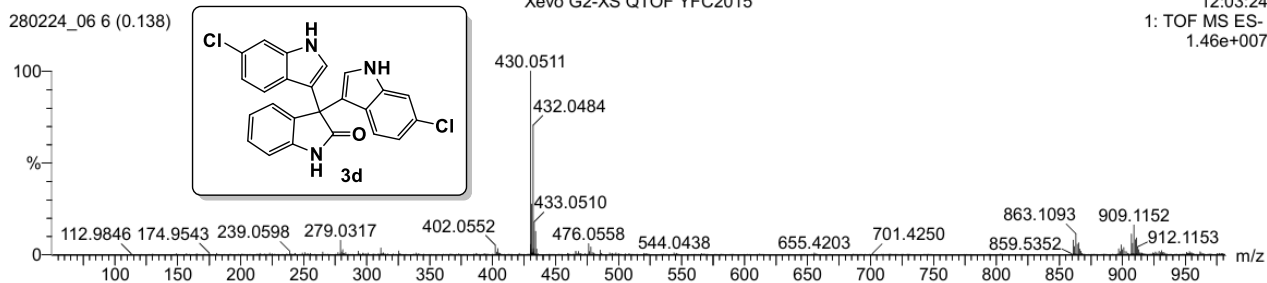
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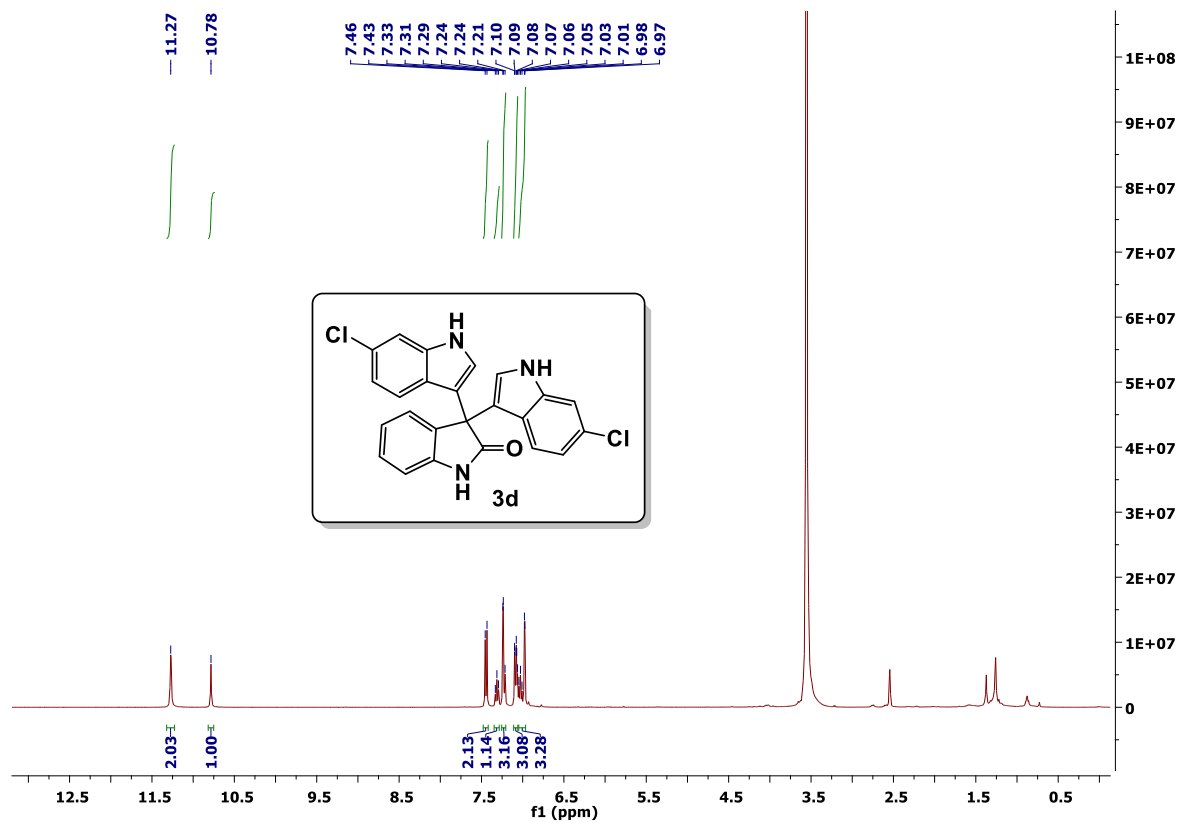
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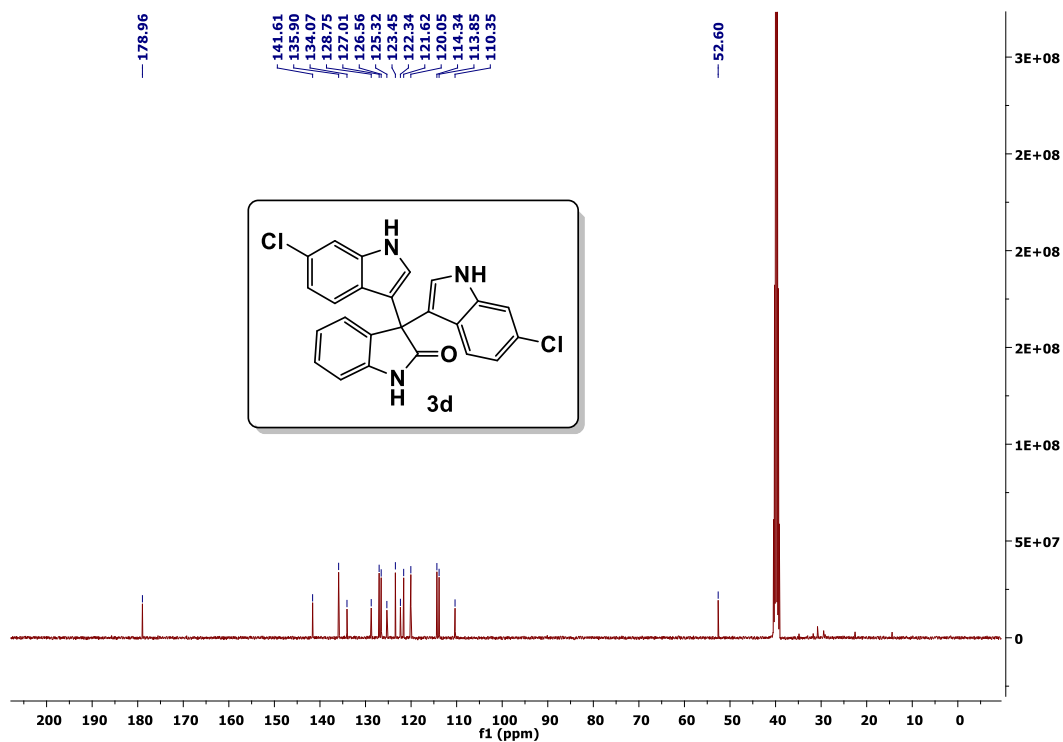
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Maximum: 2.0 25.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
430.0511	430.0514	-0.3	-0.7	18.5	1045.1	n/a	n/a	C ₂₄ H ₁₄ N ₃ O Cl ₂

4b Figure S4(b)...¹H NMR (400 MHz) of **3d** in DMSO



4c Figure S4(c)...¹³C NMR{¹H} (101 MHz) of **3d** in DMSO



5a Figure S5(a)...HRMS Spectrum (**3e**)

Single Mass Analysis

Tolerance = 25.0 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

33 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-1 Br: 0-2

I5BI

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

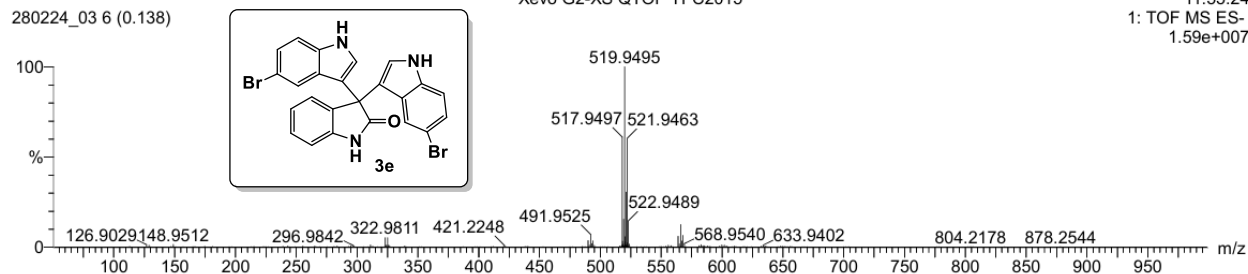
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1.59e+007

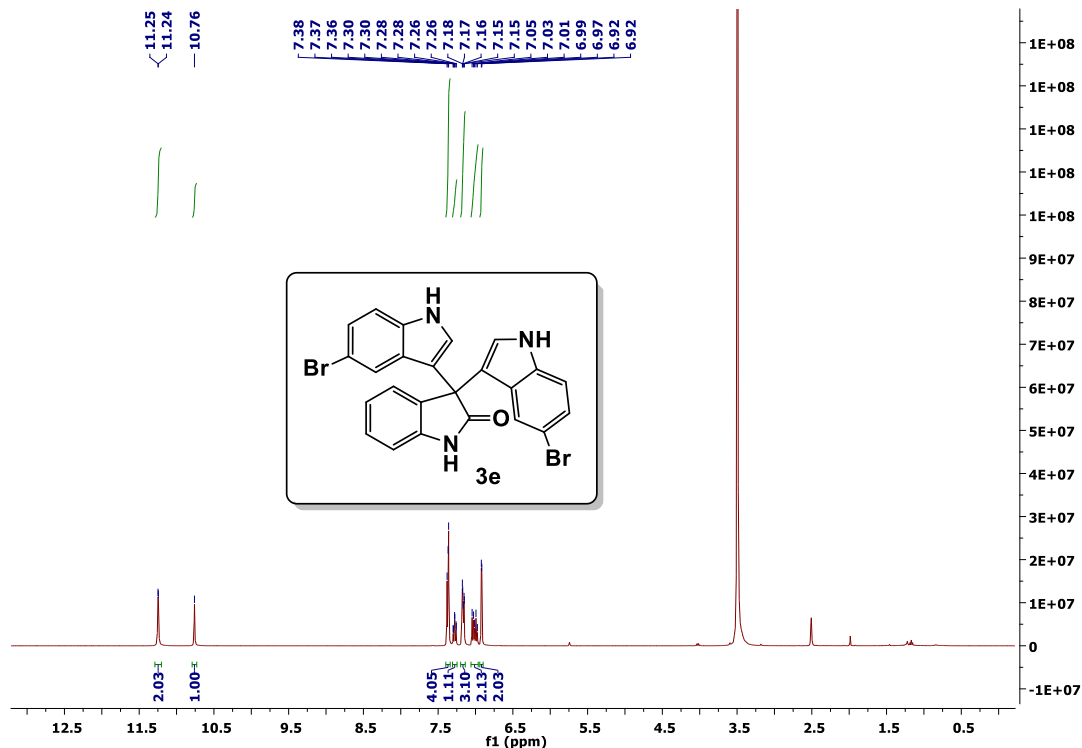
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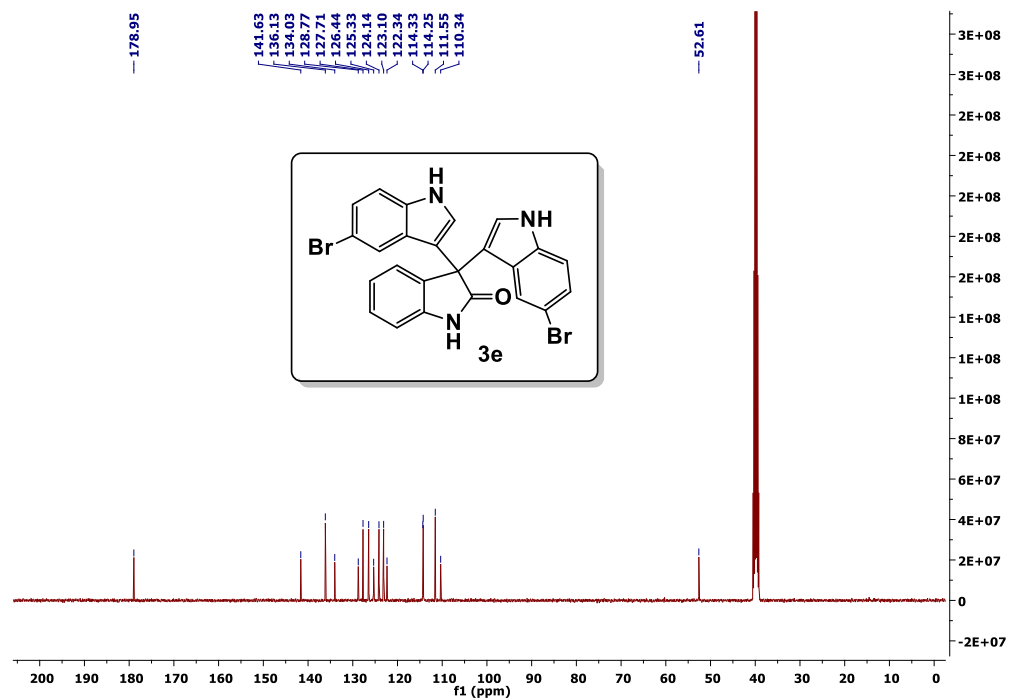
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Maximum: 2.0 25.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
517.9497	517.9504	-0.7	-1.4	18.5	991.1	n/a	n/a	C ₂₄ H ₁₄ N ₃ O Br ₂

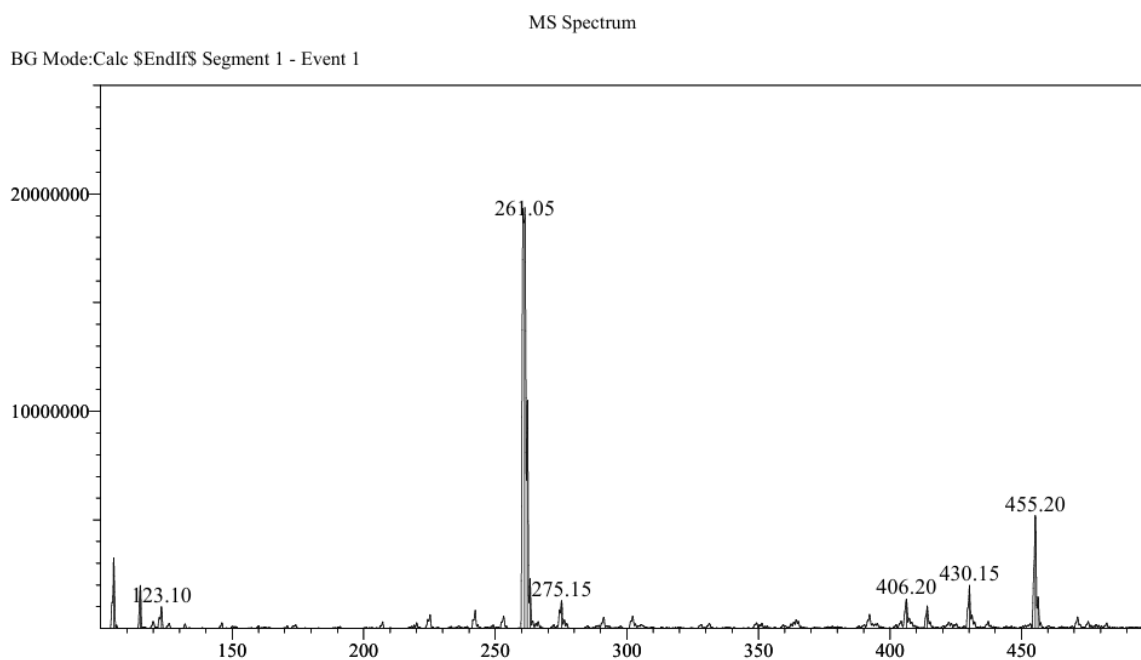
5b Figure S5(b)...¹H NMR (400 MHz) of 3e in DMSO



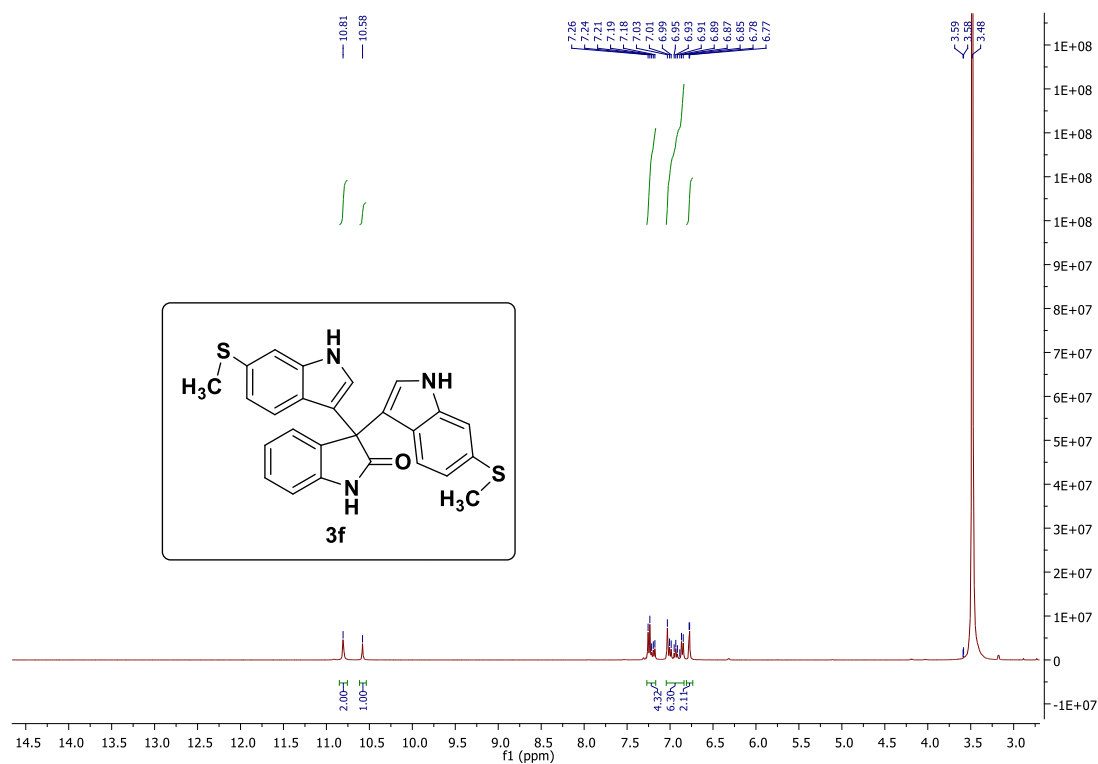
5c Figure S5(c)...¹³C NMR{¹H} (101 MHz) of 3e in DMSO



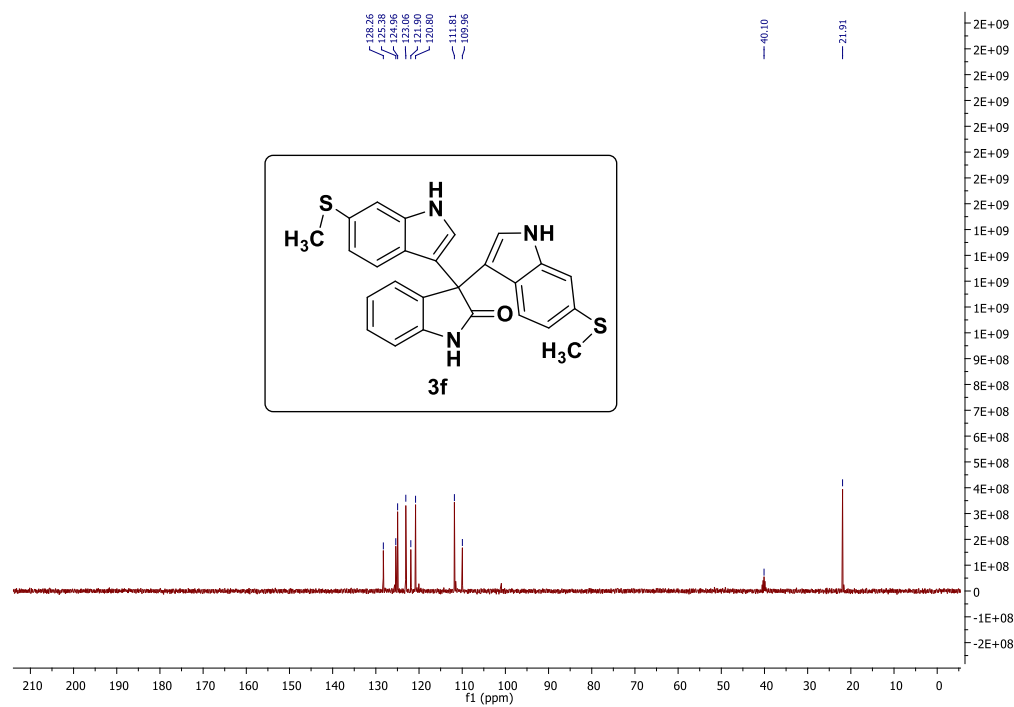
6a Figure S6(a)...LCMS Spectrum (3f)



6b Figure S6(b)...¹H NMR (400 MHz) of **3f** in DMSO

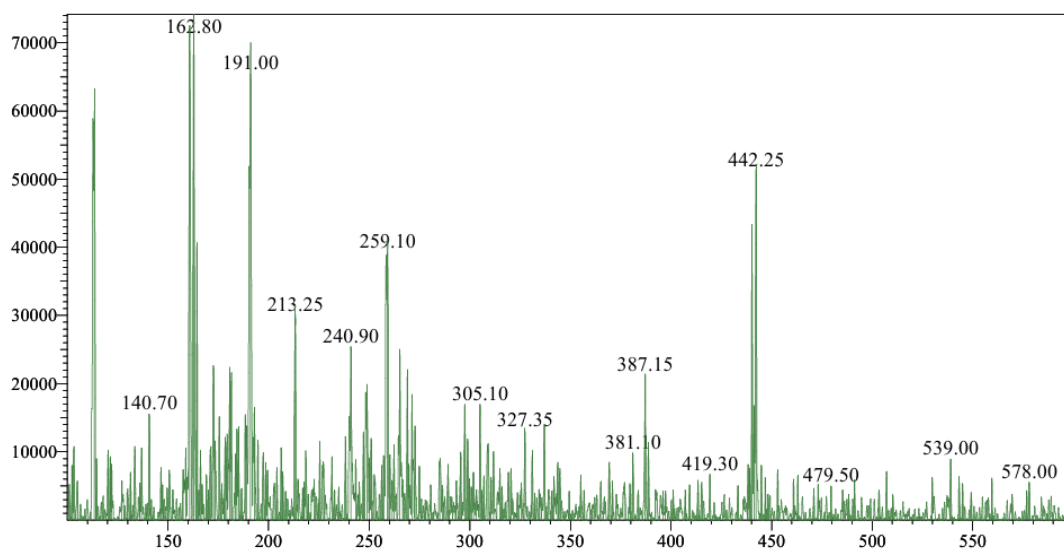


6c Figure S6(c)...¹³C NMR {¹H} (101 MHz) of **3f** in DMSO

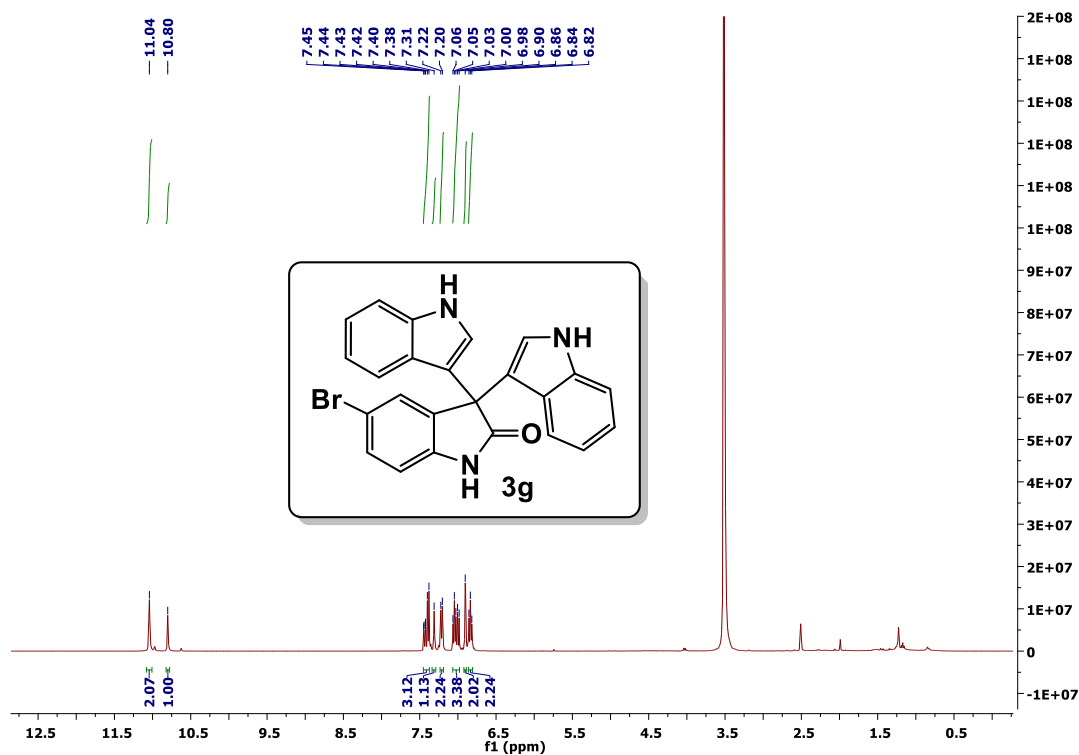


7a Figure S7(a)...LCMS Spectrum (**3g**)

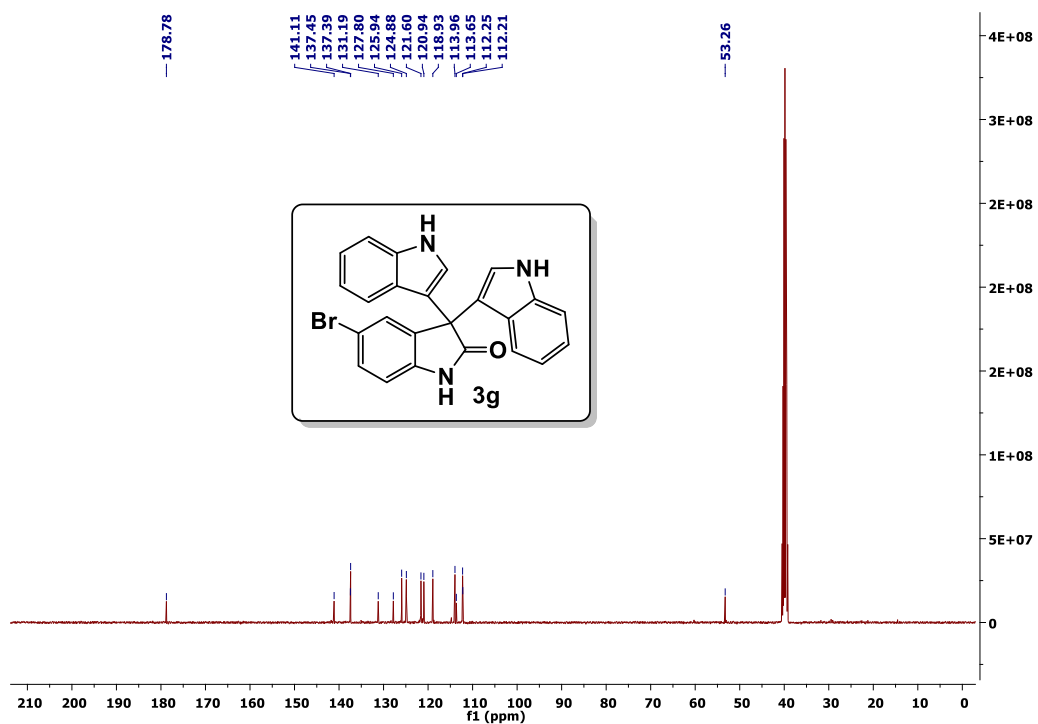
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7b Figure S7(b)...¹H NMR (400 MHz) of 3g in DMSO



7c Figure S7(c)...¹³C NMR{¹H} (101 MHz) of 3g in DMSO



8a Figure S8(a)...HRMS Spectrum (3h)

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 = 3

Monoisotopic Mass, Even Electron Ions

28 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

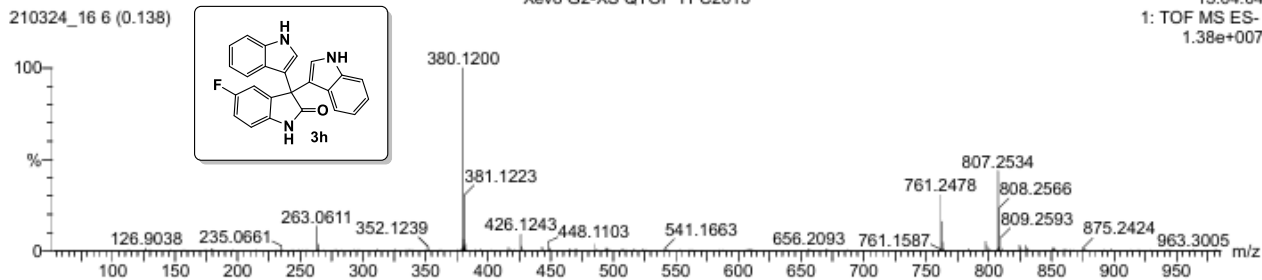
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5FII

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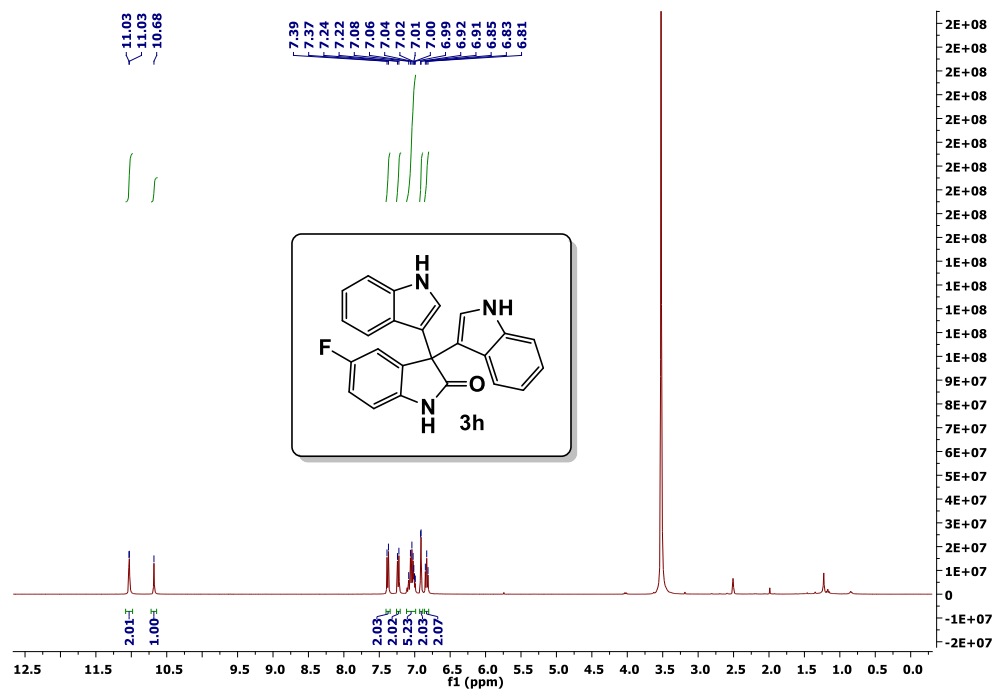
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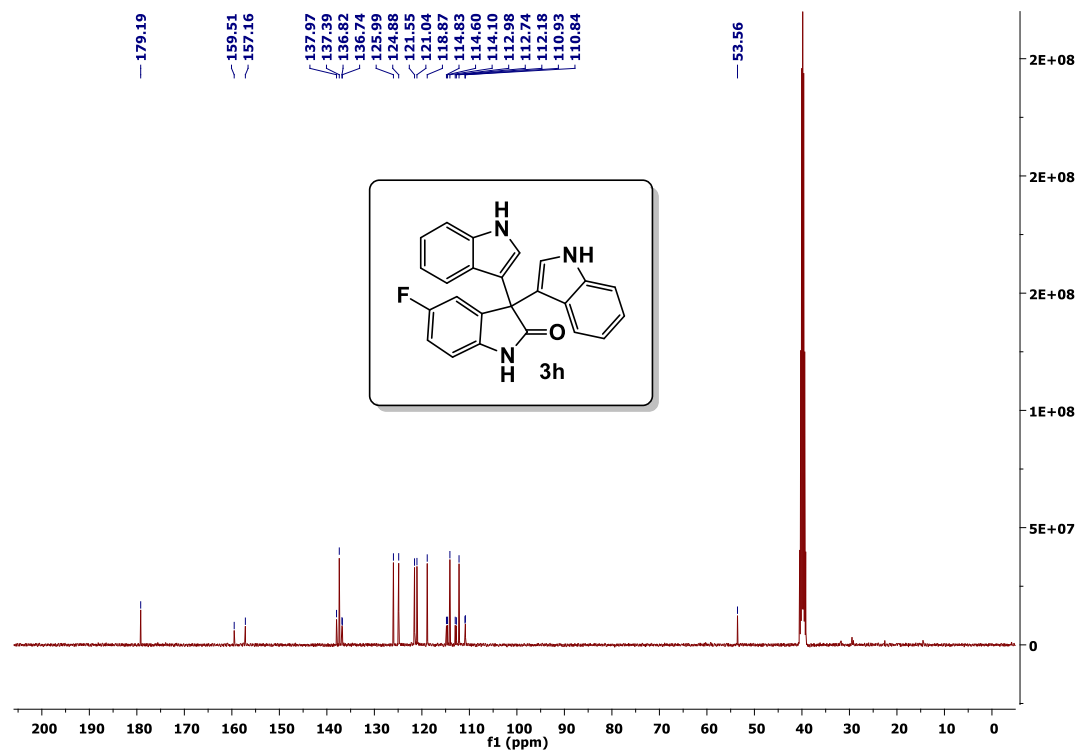
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Maximum: 2.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
380.1200	380.1199	0.1	0.3	18.5	1166.2	n/a	n/a	C ₂₄ H ₁₅ N ₃ O F

8b Figure S8(b)...¹H NMR (400 MHz) of 3h in DMSO



8c Figure S8(c)...¹³C NMR{¹H} (101 MHz) of **3h** in DMSO



9a Figure S9(a)...HRMS Spectrum (**3i**)

Single Mass Analysis

Tolerance = 25.0 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

30 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-4 O: 0-3

5NII

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

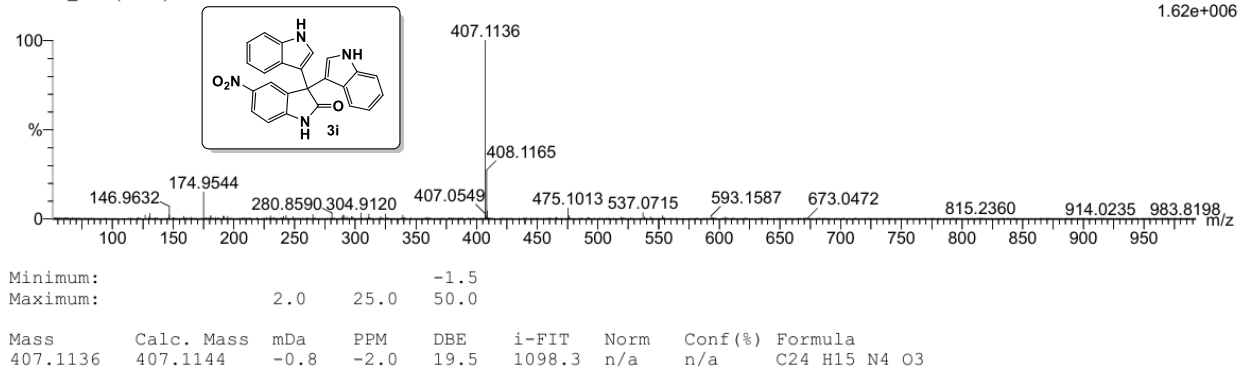
28-Feb-2024

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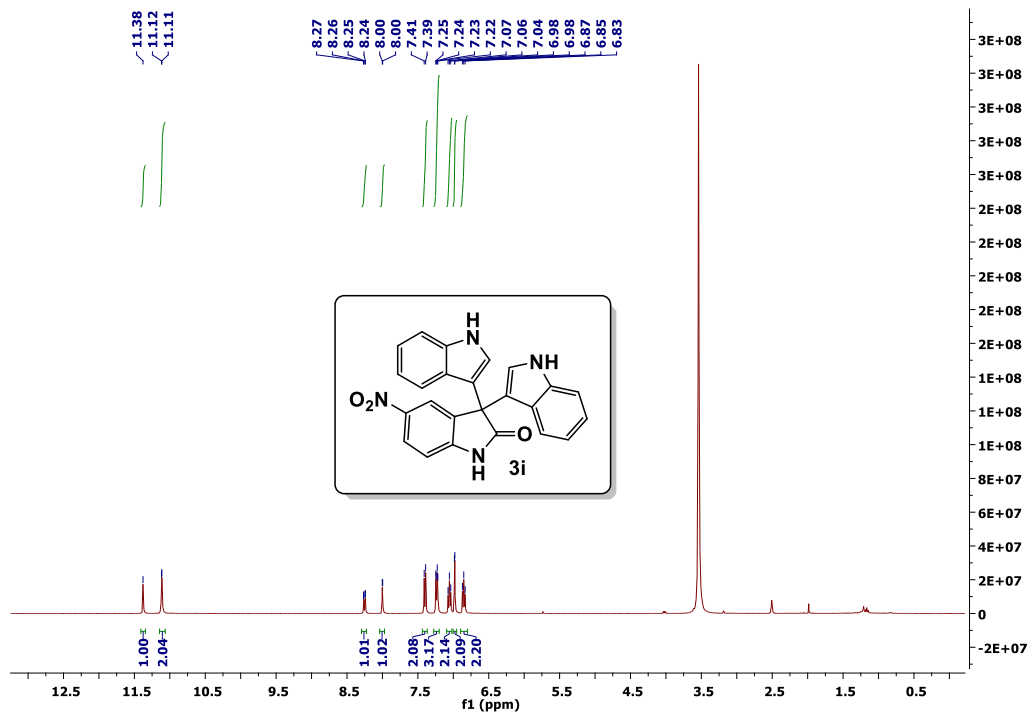
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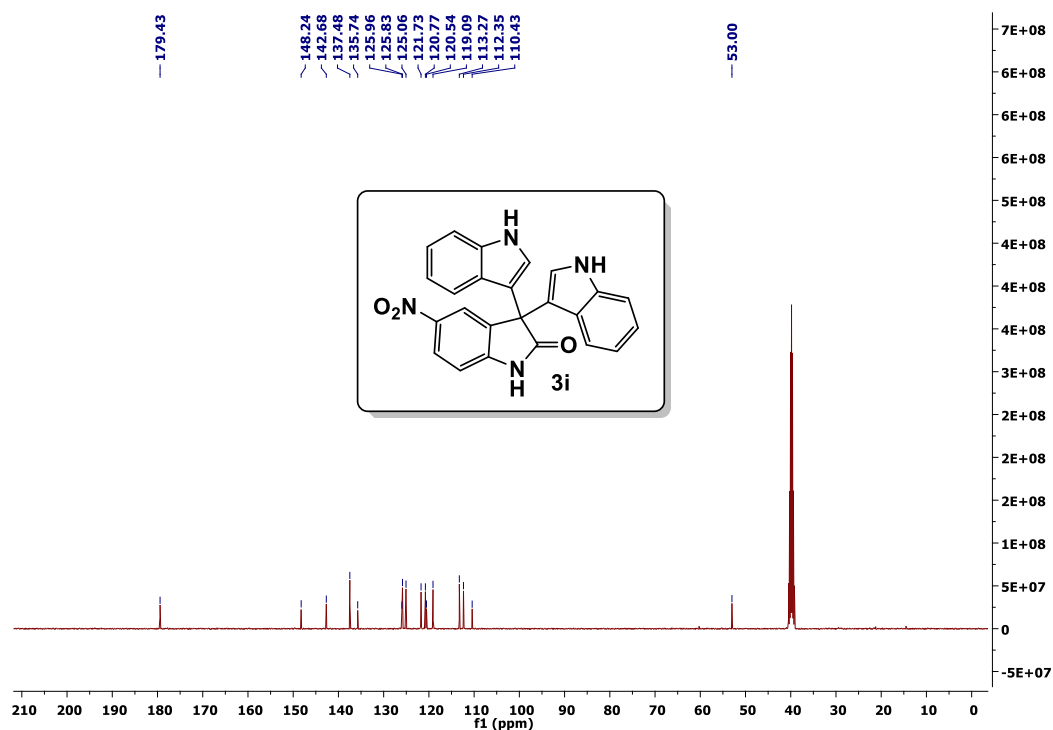
280224_08 9 (0.208)



9b Figure S9(b)...¹H NMR (400 MHz) of 3i in DMSO



9c Figure S9(c)...¹³C NMR{¹H} (101 MHz) of 3i in DMSO



10a Figure S10(a)...HRMS Spectrum (3j)

Single Mass Analysis

Tolerance = 25.0 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

17 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-25 H: 0-100 N: 0-3 O: 0-1

5MII

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

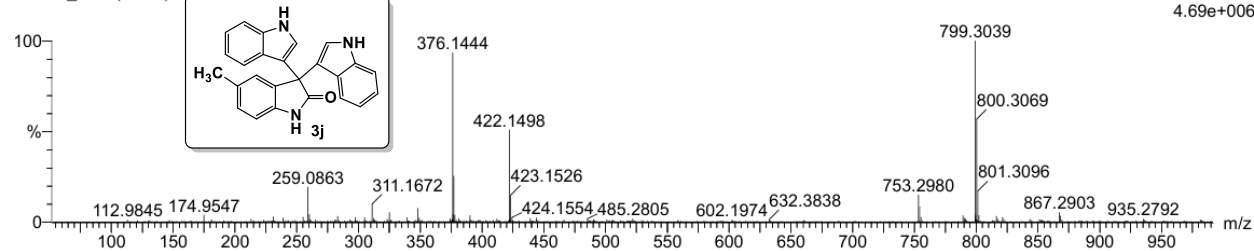
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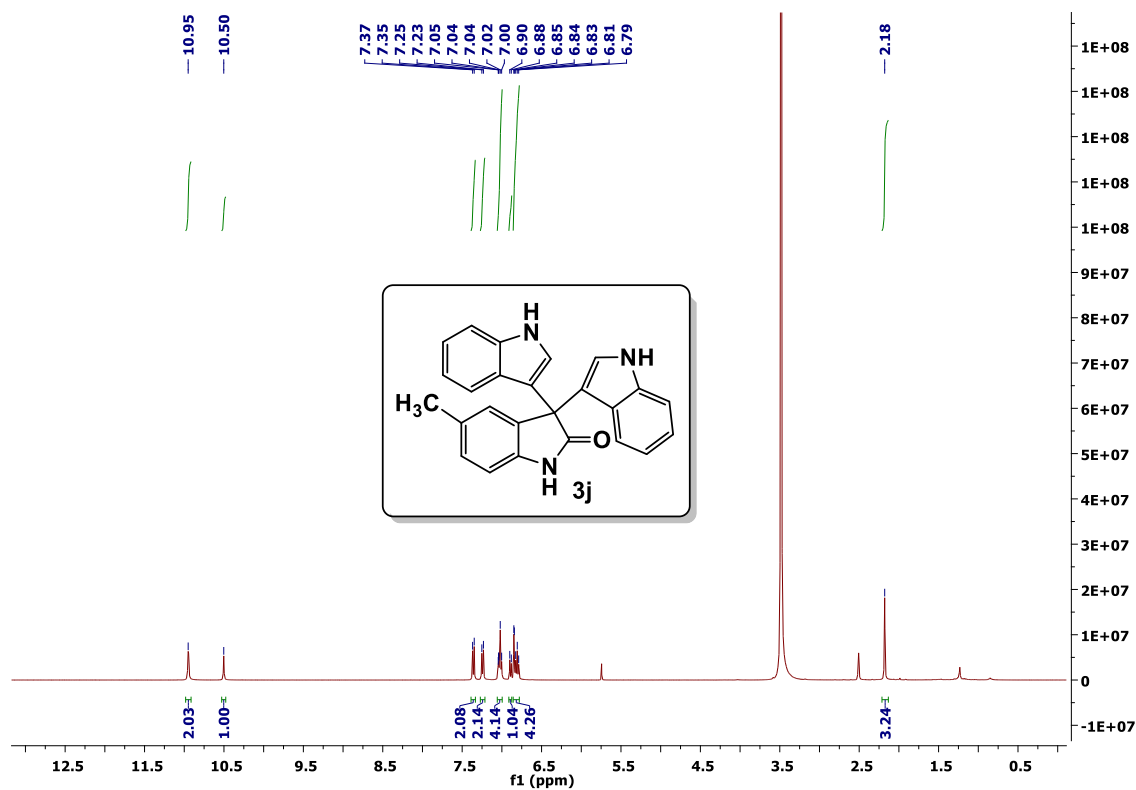
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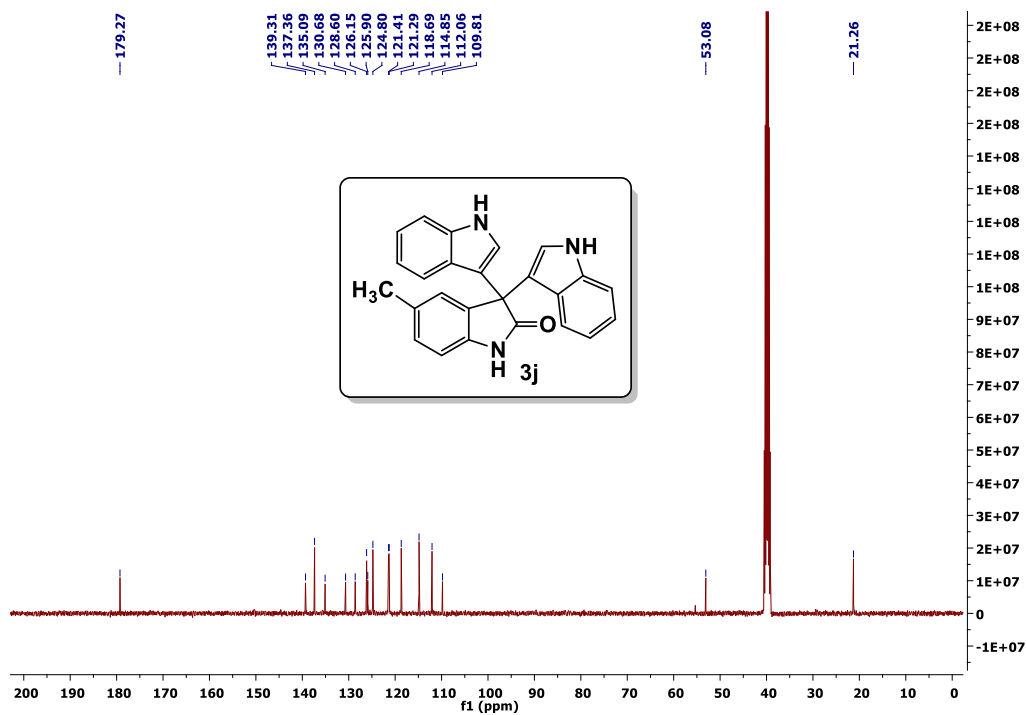
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Maximum: 2.0 25.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
376.1444	376.1450	-0.6	-1.6	18.5	1266.4	n/a	n/a	C25 H18 N3 O

10b Figure S10(b)...¹H NMR (400 MHz) of 3j in DMSO



10c Figure S10(c)... ^{13}C NMR $\{^1\text{H}\}$ (101 MHz) of **3j** in DMSO



11a Figure S11(a)...HRMS Spectrum (**3k**)

Single Mass Analysis

Tolerance = 25.0 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

25 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-1 Cl: 0-1

7Cl

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

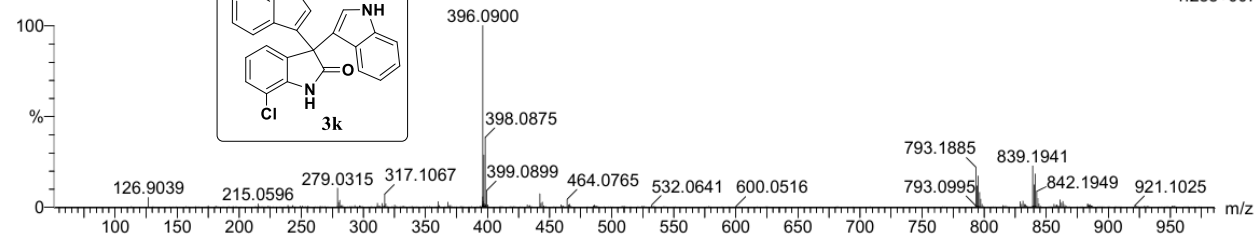
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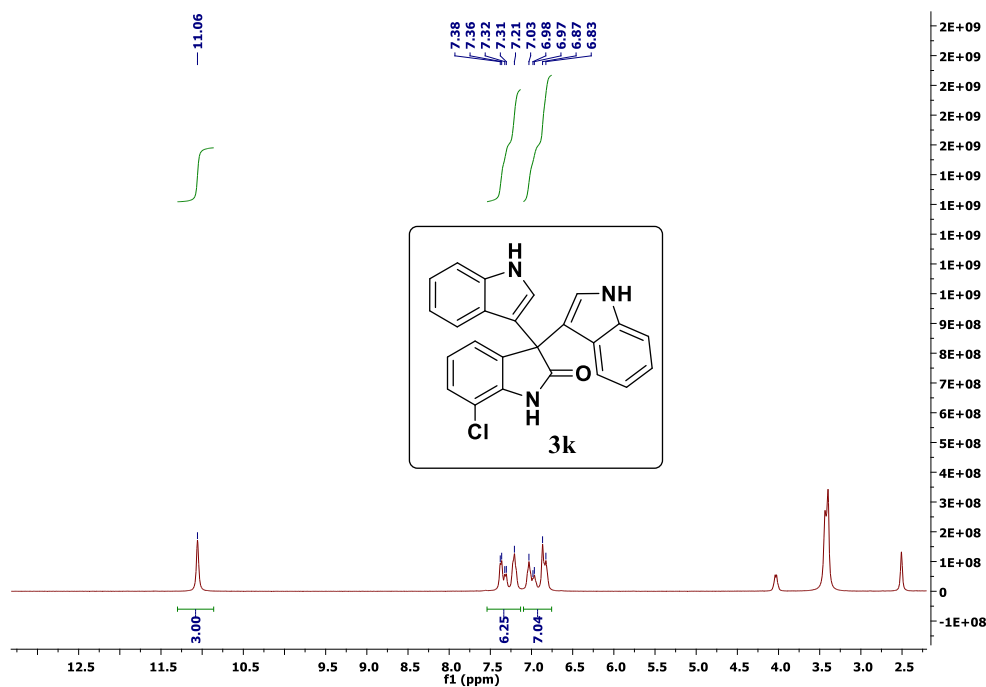
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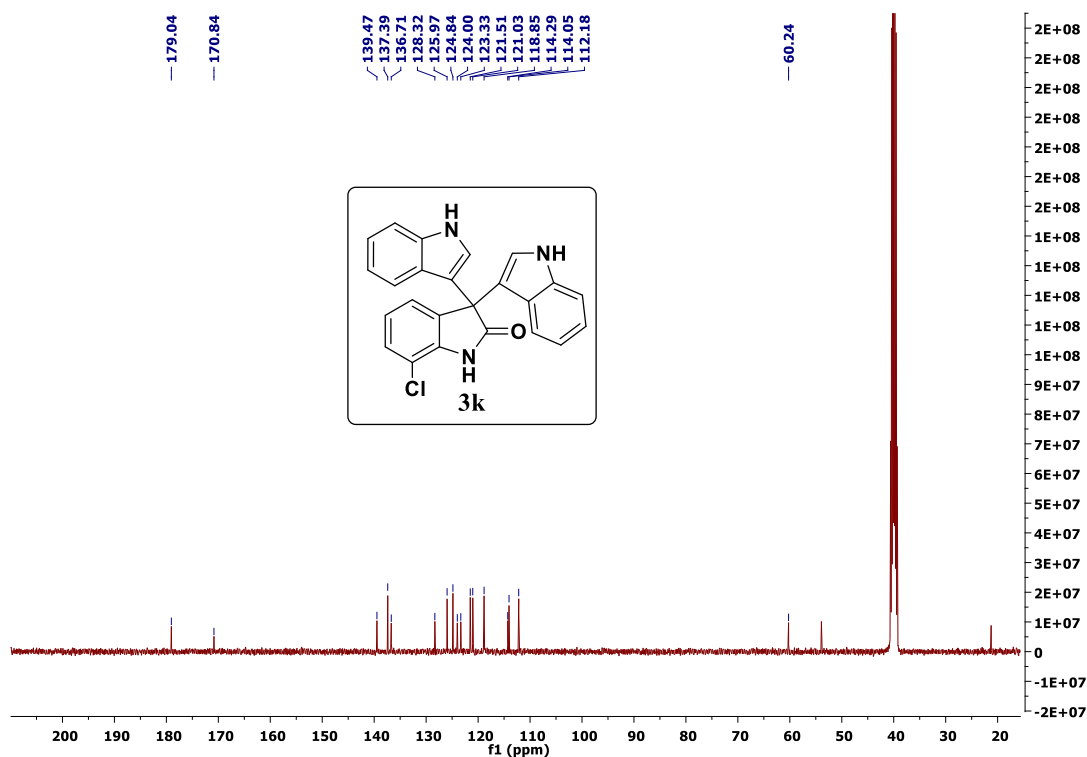
Minimum: -1.5
Maximum: 2.0 25.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
396.0900	396.0904	-0.4	-1.0	18.5	1177.9	n/a	n/a	C ₂₄ H ₁₅ N ₃ O Cl

11b Figure S11(b)...¹H NMR (400 MHz) of 3k in DMSO



11c Figure S11(c)...¹³C NMR {¹H} (101 MHz) of 3k in DMSO



12a Figure S12(a)...HRMS Spectrum (3l)

Single Mass Analysis

Tolerance = 25.0 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

60 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-1 F: 0-1 Cl: 0-2

5F16Cl

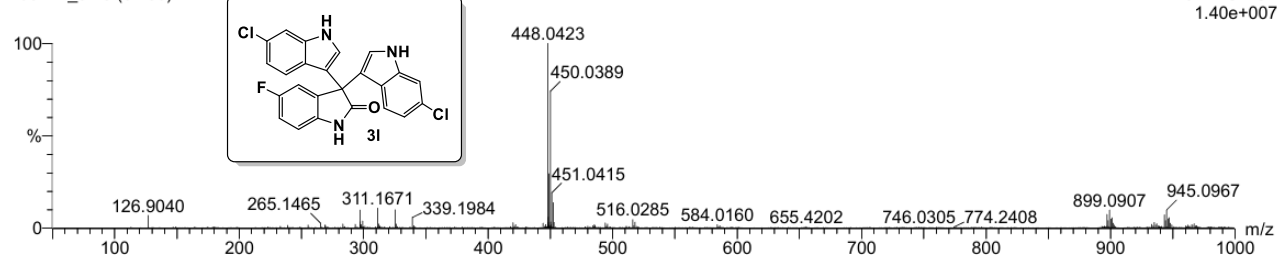
QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

28-Feb-2024

11:58:06

1: TOF MS ES-
1.40e+007

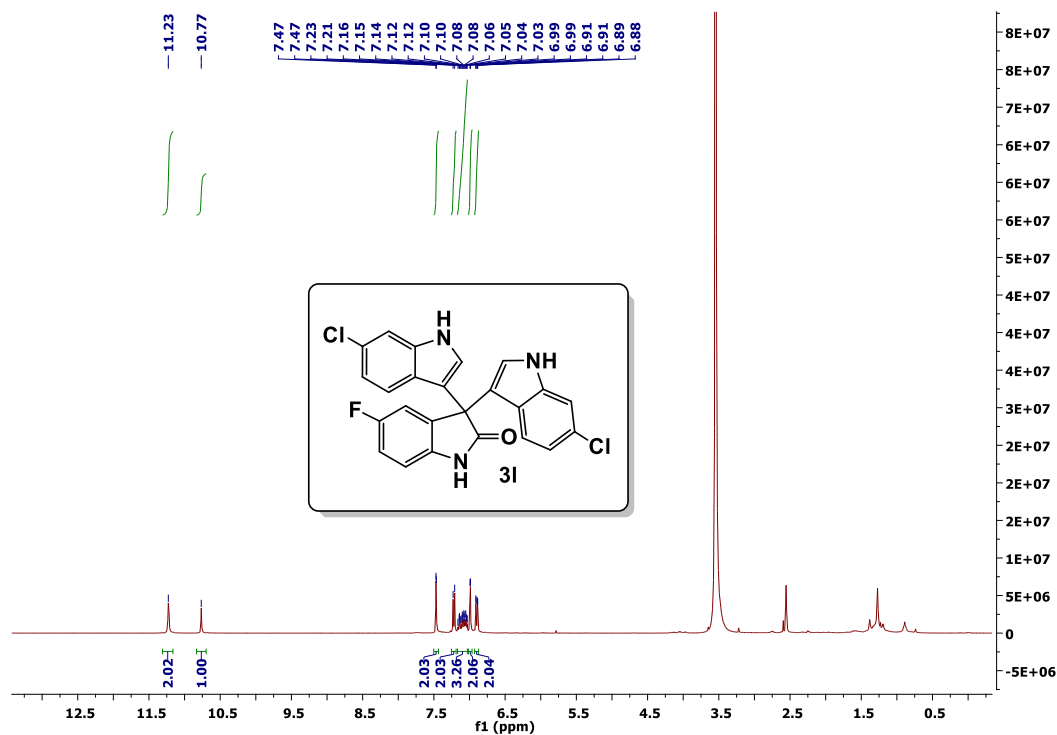
280224_04 6 (0.138)



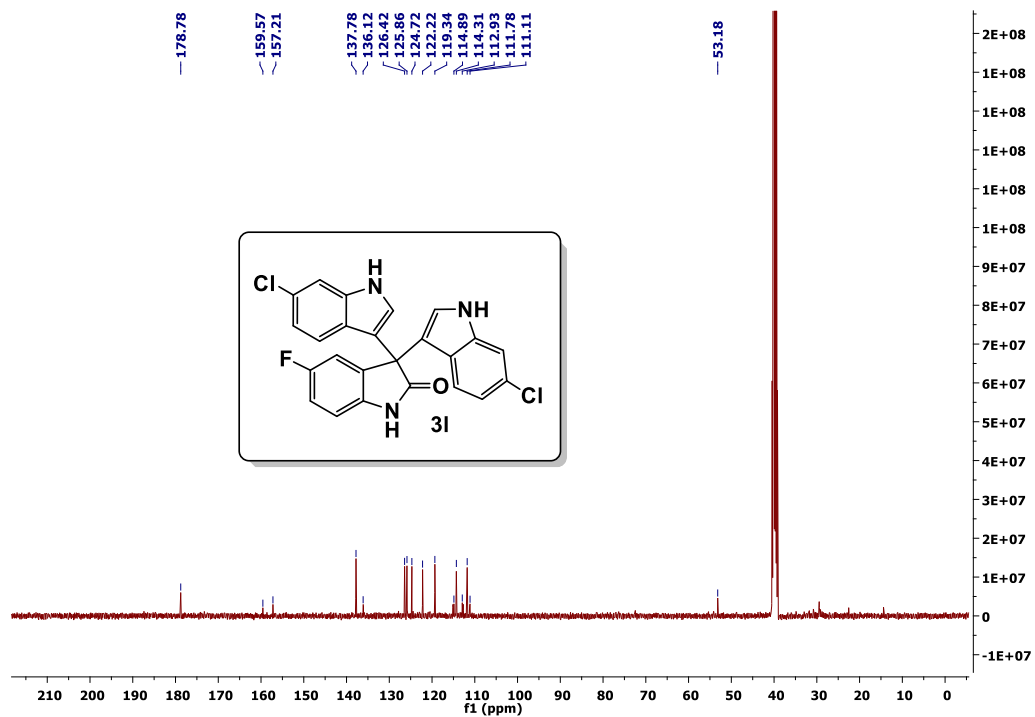
Minimum: -1.5
Maximum: 2.0 25.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
448.0423	448.0420	0.3	0.7	18.5	962.8	n/a	n/a	C ₂₄ H ₁₃ N ₃ O F Cl ₂

12b Figure S12(b)...¹H NMR (400 MHz) of 3l in DMSO



12c Figure S12(c)...¹³C NMR{¹H} (101 MHz) of 3I in DMSO



13a Figure S13(a)...HRMS Spectrum (3m)

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 = 3

Monoisotopic Mass, Even Electron Ions

33 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-25 H: 0-100 N: 0-3 O: 0-1 Br: 0-2

5MI5BI

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

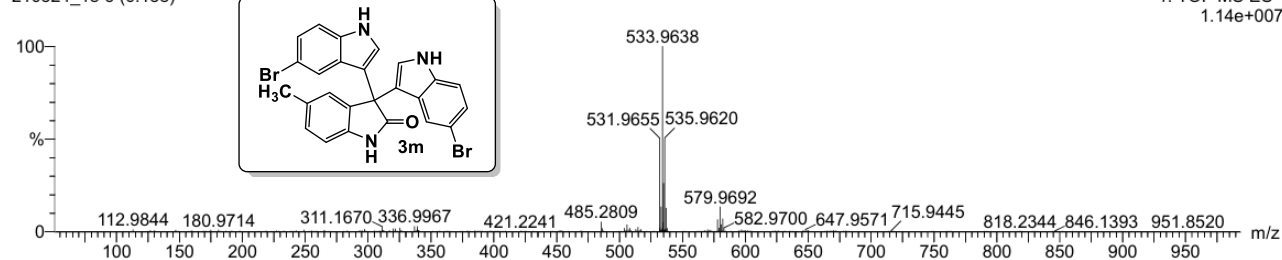
21-Mar-2024

15:09:30

1: TOF MS ES-

1.14e+007

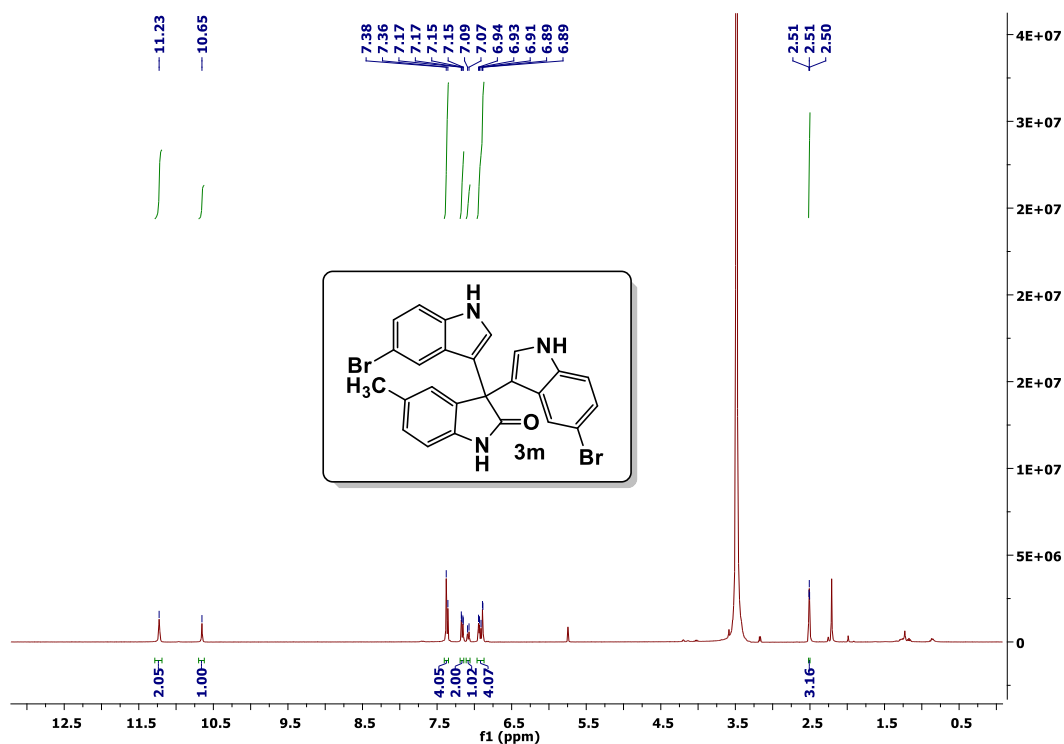
210324_18 6 (0.138)



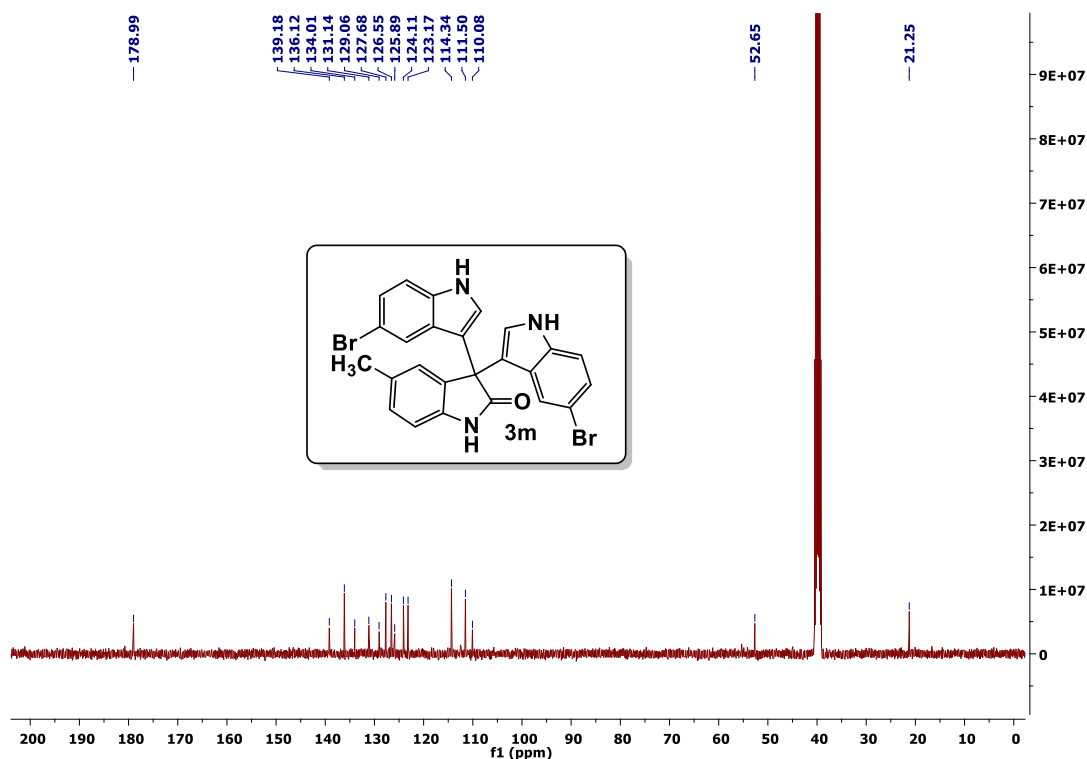
Minimum: -1.5
Maximum: 2.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
531.9655	531.9660	-0.5	-0.9	18.5	1014.4	n/a	n/a	C25 H16 N3 O Br2

13b Figure S13(b)...¹H NMR (400 MHz) of 3m in DMSO



13c Figure S13(c)...¹³C NMR {¹H} (101 MHz) of 3m in DMSO



14a Figure S14(a)...HRMS Spectrum (**3n**)

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 = 3

Monoisotopic Mass, Even Electron Ions

33 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-25 H: 0-100 N: 0-3 O: 0-1 Cl: 0-2

5MI5Cl

210324_21 5 (0.121)

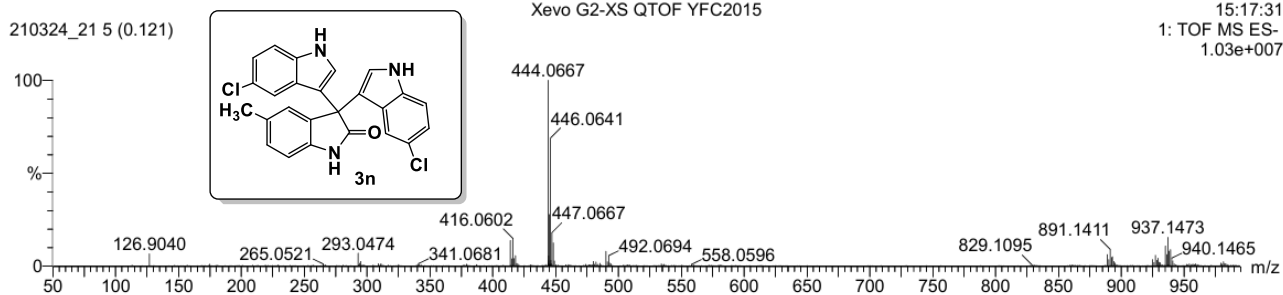
QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

21-Mar-2024

15:17:31

1: TOF MS ES-

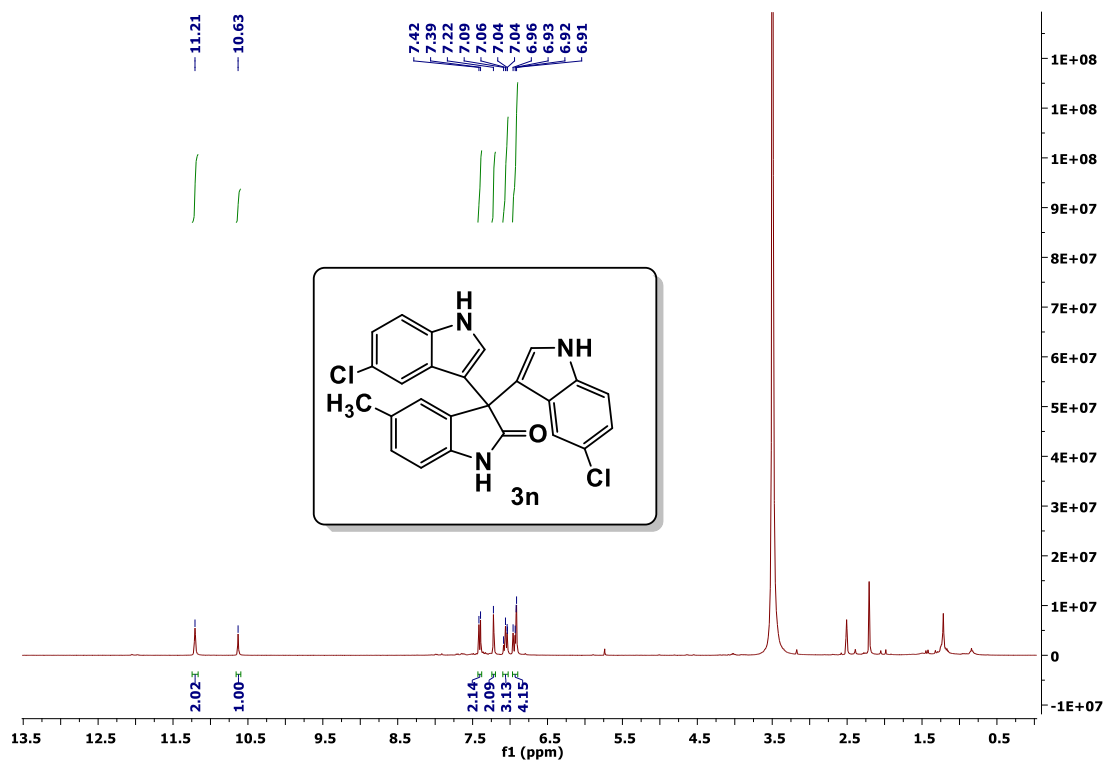
1.03e+007



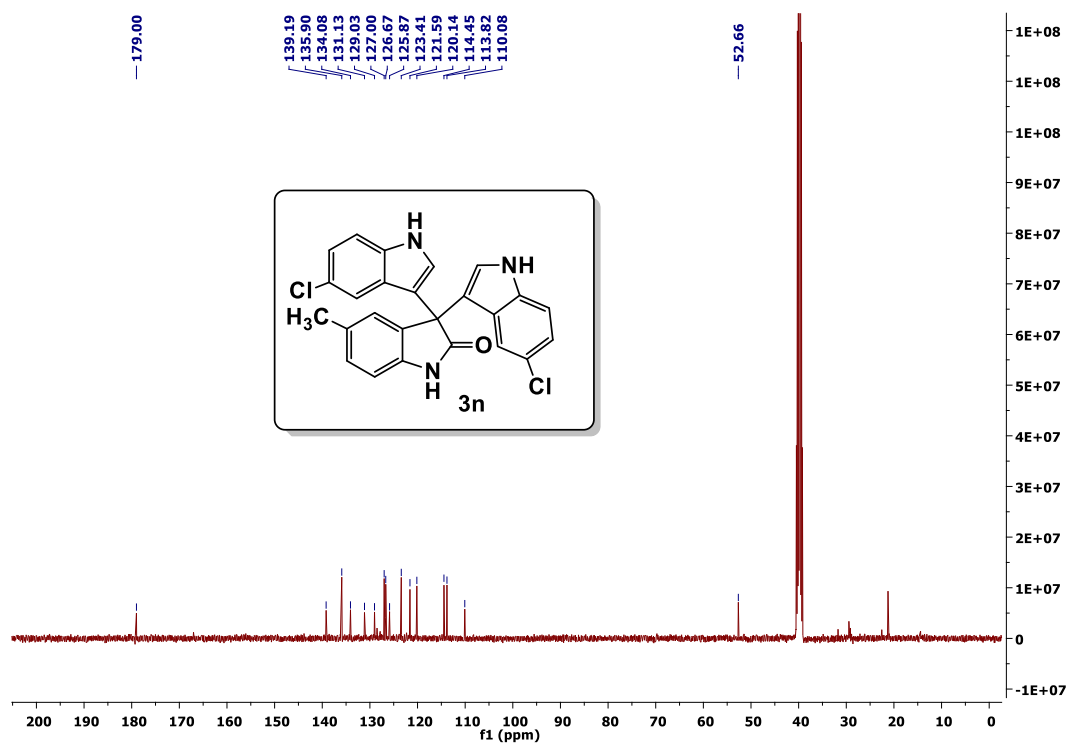
Minimum: -1.5
Maximum: 2.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
444.0667	444.0670	-0.3	-0.7	18.5	1092.3	n/a	n/a	C25 H16 N3 O Cl2

14b Figure S14(b)...¹H NMR (400 MHz) of **3n** in DMSO



14c Figure S14(c)... ^{13}C NMR $\{^1\text{H}\}$ (101 MHz) of **3n** in DMSO



15a Figure S15(a)...HRMS Spectrum (**3o**)

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 = 3

Monoisotopic Mass, Even Electron Ions

41 formula(e) evaluated with 1 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 0-24 H: 0-100 N: 0-3 O: 0-1 Cl: 0-3

7Cl5Cl

QMI DIVISION, CSIR-IIIM JAMMU
Xevo G2-XS QTOF YFC2015

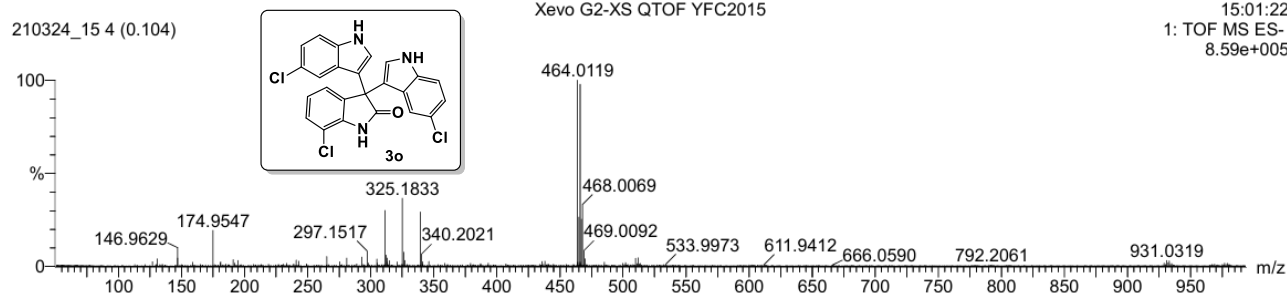
21-Mar-2024

15:01:22

1: TOF MS ES-

8.59e+005

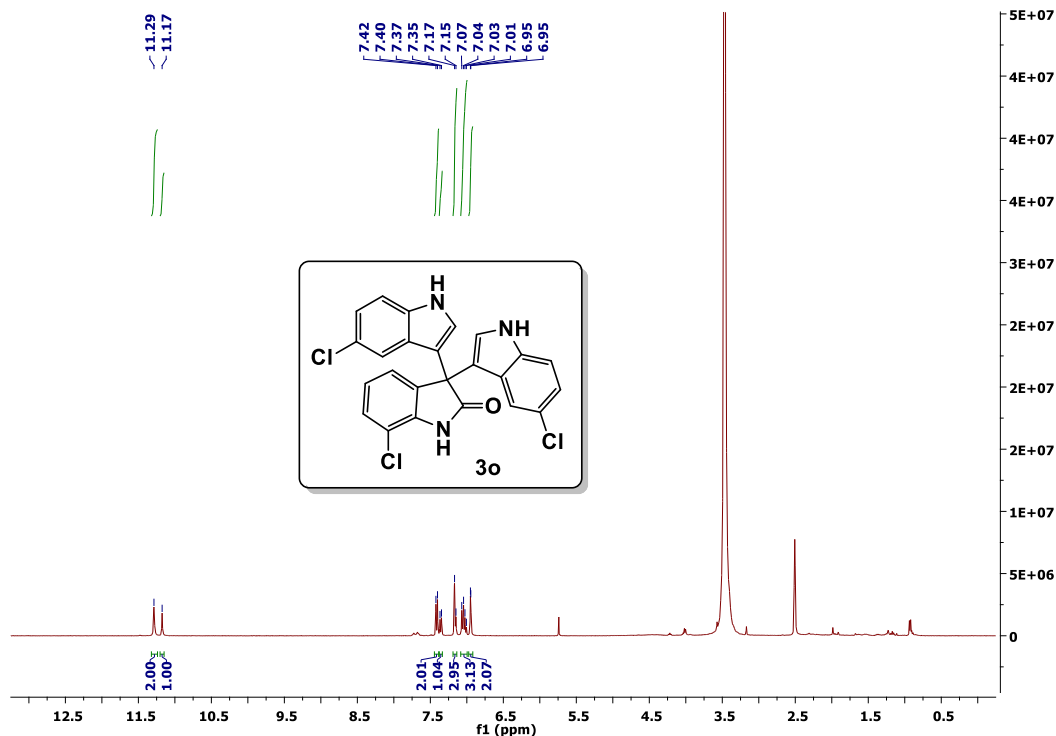
210324_15 4 (0.104)



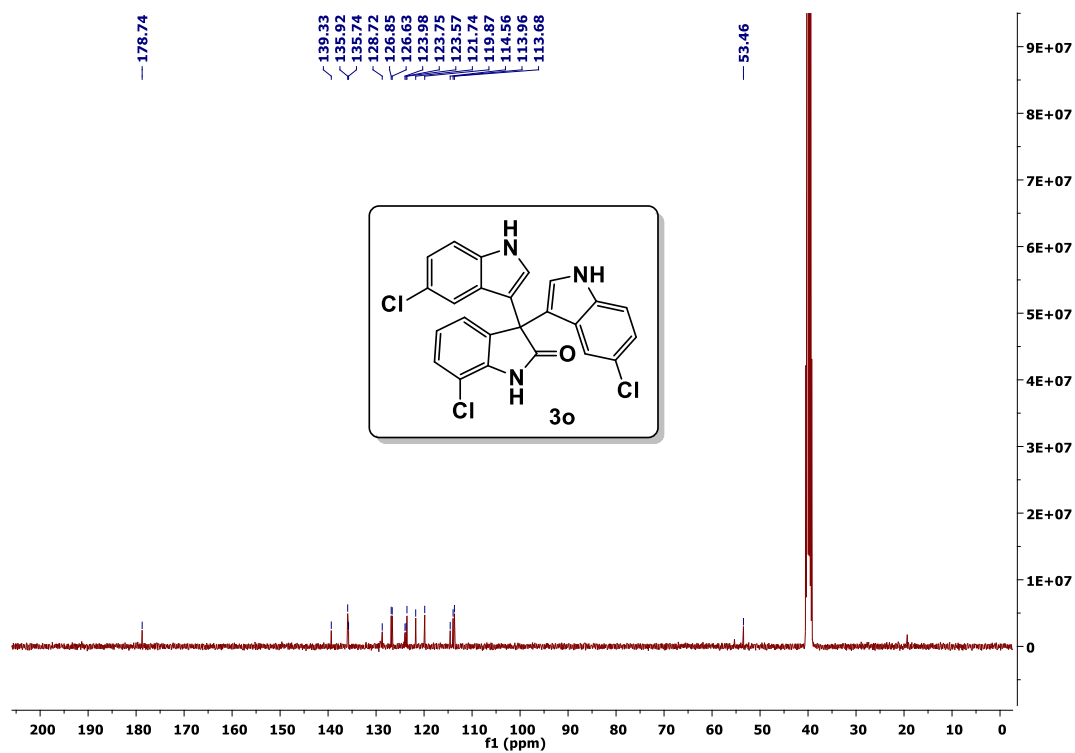
Minimum: -1.5
Maximum: 2.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
464.0119	464.0124	-0.5	-1.1	18.5	948.1	n/a	n/a	C ₂₄ H ₁₃ N ₃ O Cl ₃

15b Figure S15(b)...¹H NMR (400 MHz) of **3o** in DMSO



15c Figure S15(c)...¹³C NMR{¹H} (101 MHz) of **3o** in DMSO



Results

2.1 Minimum Inhibitory Concentration

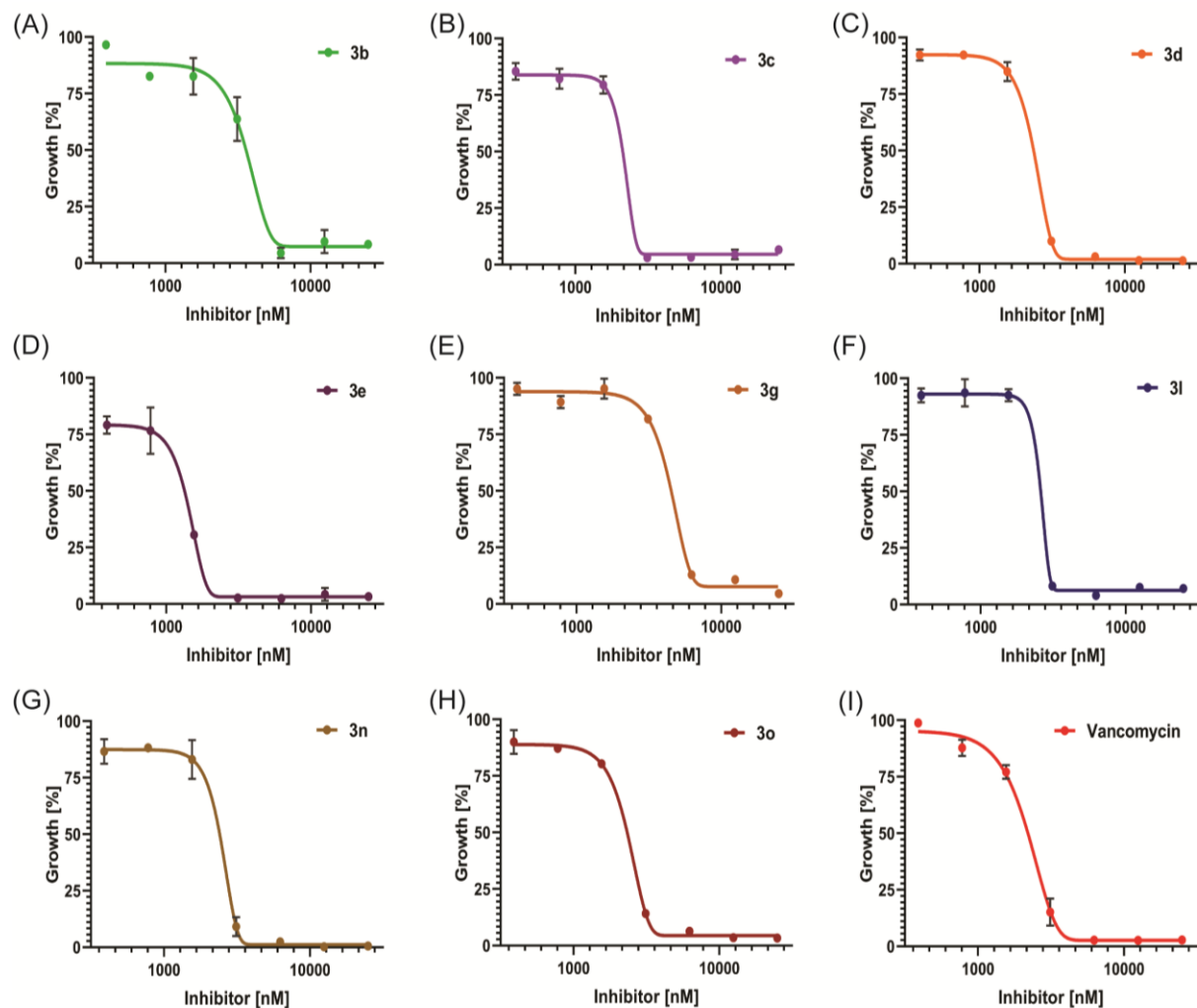


Figure S16. Dose-Dependent Growth Inhibition of MRSA by the Active Trisindolines. (A-H) X-axis depicted the inhibitory concentration of active hits, and Y-axis represented percent growth in the presence of varying compound concentrations along with vancomycin (I).

2.2 Minimum Bactericidal Concentration

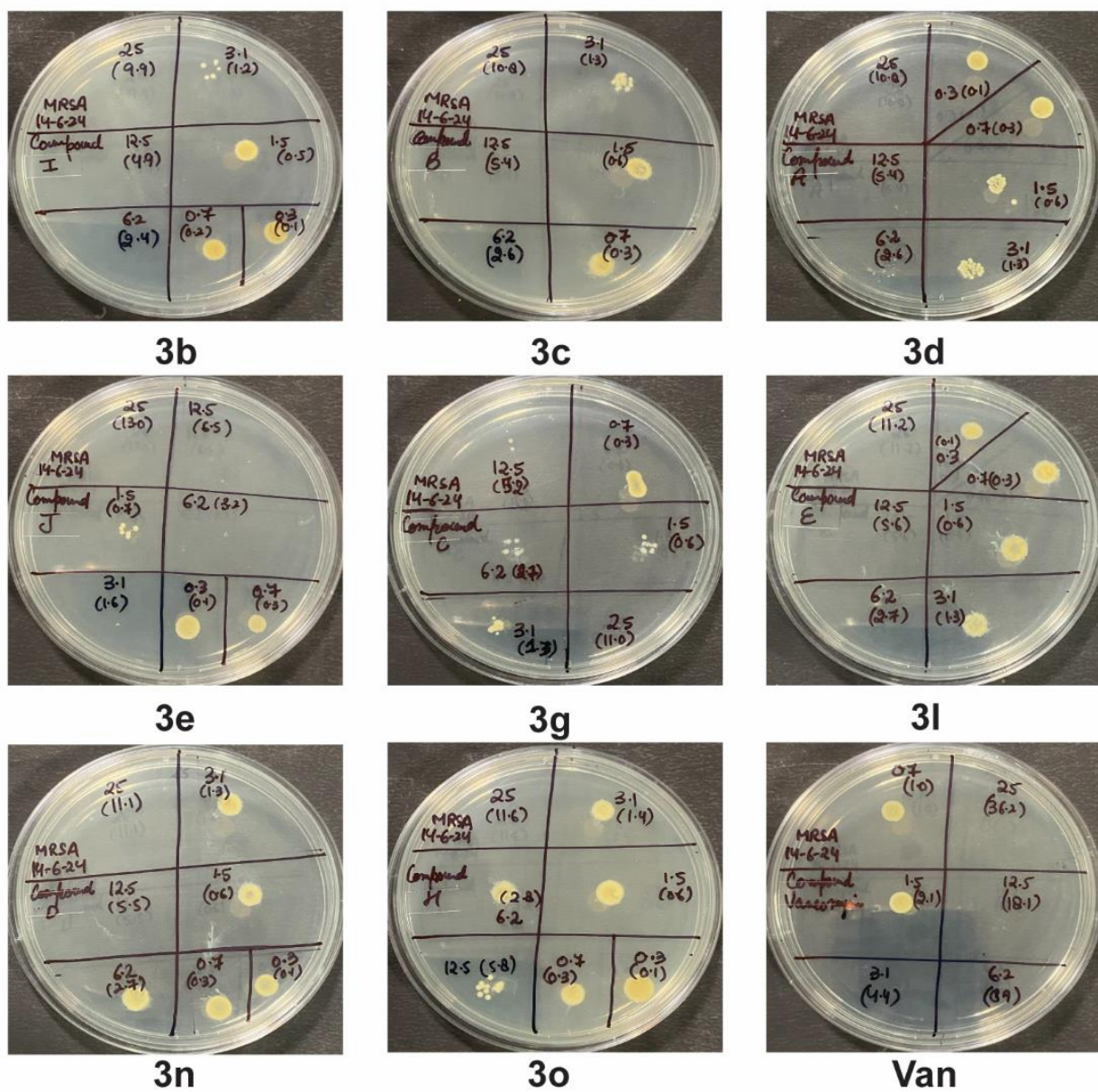


Figure S17: LB Agar plates representing Minimum Bactericidal Concentration in $\mu\text{M}/\mu\text{g/ml}$

2.3 Biocompatibility Studies with active trisindolines

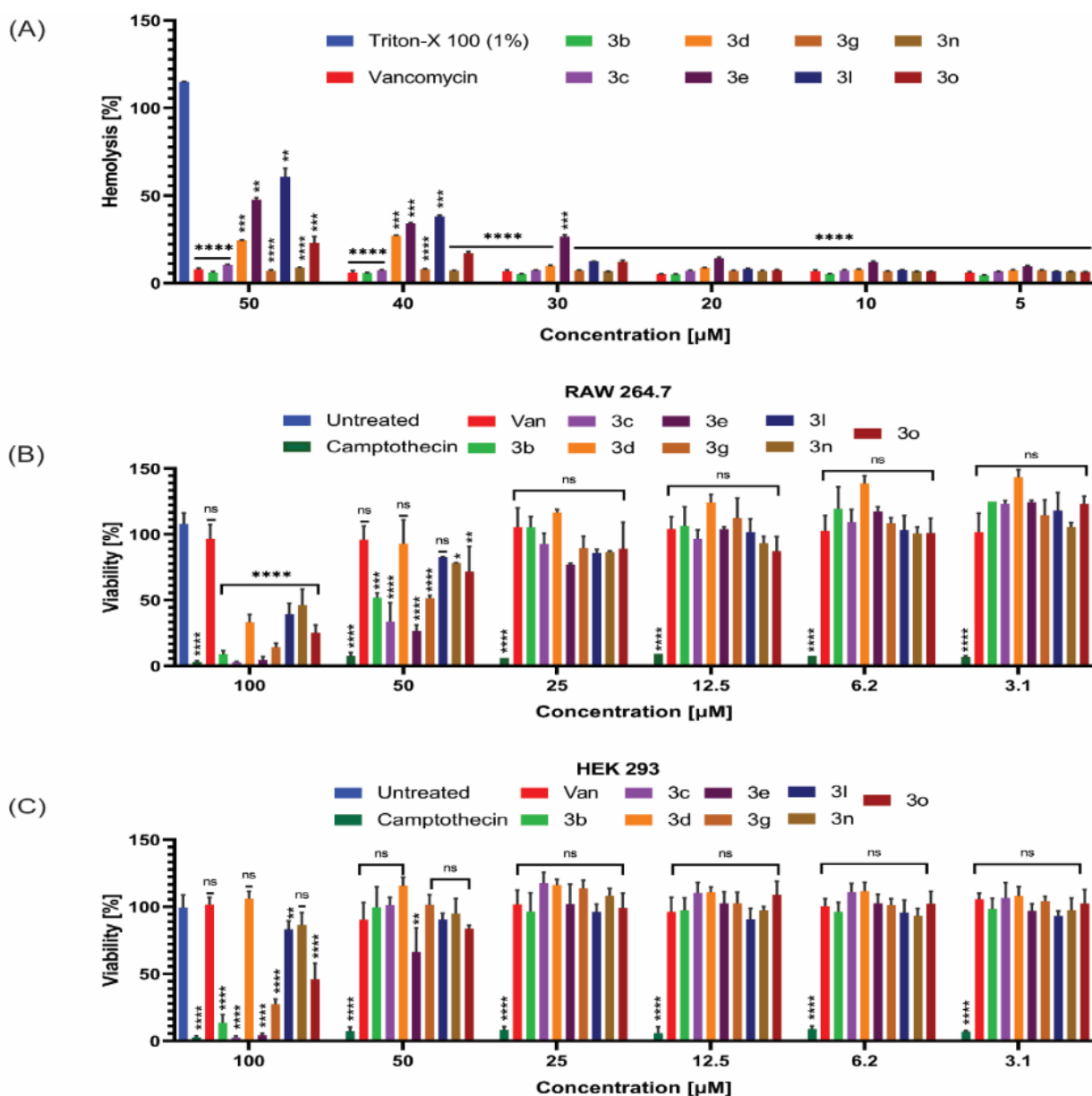
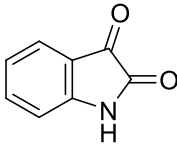
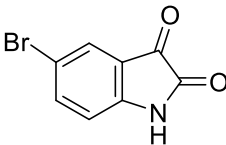
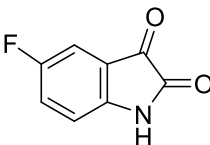
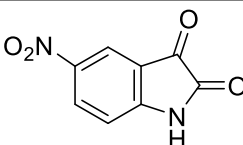
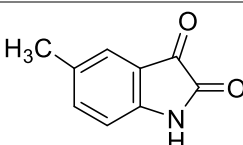
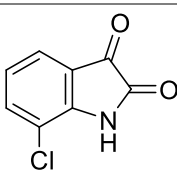
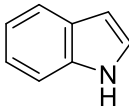
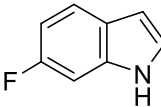
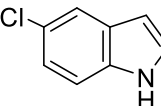
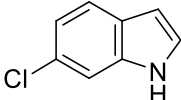
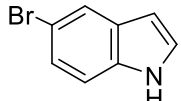
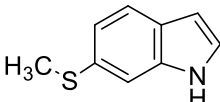


Figure S18. Biocompatibility Studies of the active Trisindolines. (A) Hemolysis assay on rabbit's RBCs in the presence of active molecules with Triton X-100 (1%) as positive control. (B & C) Cytotoxicity profiling on three different cell lines RAW 264.7 & HEK 293 in the presence of potential hits with reference drug vancomycin and positive control camptothecin (where ns-non-significant, *P < 0.05, ** P < 0.01, *** P < 0.001 & **** P < 0.0001).

2.4 Table S1: Chemical structures and antimicrobial efficacy (MIC value in $\mu\text{g/mL}$) of starting reactants (indoles and isatins) against methicillin-resistant *Staphylococcus aureus*.

S. No.	Compound	Chemical structure	Anti-staphylococcal susceptibility ($\mu\text{g/mL}$)		
			MIC	IC ₅₀	MBC
1	1a		>100	>100	>100
2	1b		>100	>100	>100
3	1c		>100	>100	>100
4	1d		>100	>100	>100
5	1e		>100	>100	>100
6	1f		>100	>100	>100
7	2a		>100	>100	>100
8	2b		>100	>100	>100
9	2c		>100	>100	>100

10	2d		>100	>100	>100
11	2e		>100	>100	>100
12	2f		>100	>100	>100

2.5 Table S2: Best possible synergistic combinations of Tris-indolines with standard drug Vancomycin

S. No.	Code	MIC (μM)		FICI value	Result
		alone	combination		
1	3b	6.2	0.15	0.22	Synergy
	Vancomycin	3.1	0.62		
2	3c	3.1	0.62	0.20	Synergy
	Vancomycin	3.1	0.01		
3	3d	3.1	0.62	0.20	Synergy
	Vancomycin	3.1	0.009		
4	3e	1.5	1.25	0.39	Synergy
	Vancomycin	3.1	0.009		
5	3g	6.2	0.15	0.22	Synergy
	Vancomycin	3.1	0.62		
6	3l	6.2	1.25	0.39	Synergy
	Vancomycin	3.1	0.009		
7	3n	3.1	1.25	0.39	Synergy
	Vancomycin	3.1	0.009		
8	3o	3.1	0.15	0.25	Synergy
	Vancomycin	3.1	0.62		

2.6 Table S3: ADME constraints depicting physiochemical and pharmacokinetic assets of prioritized trisindoline derivatives.

Physiochemical properties	3b	3c	3d	3e	3g	3l	3n	3o
Formula	C ₂₄ H ₁₅ F ₂ N ₃ O	C ₂₄ H ₁₅ C _l ₂ N ₃ O	C ₂₄ H ₁₅ C _l ₂ N ₃ O	C ₂₄ H ₁₅ B _r ₂ N ₃ O	C ₂₄ H ₁₆ B _r ₂ N ₃ O	C ₂₄ H ₁₄ Cl ₂ FN ₃ O	C ₂₅ H ₁₇ C _l ₂ N ₃ O	C ₂₄ H ₁₅ C _l ₂ N ₃ O
Molecular Weight (g/mol)	399.39	432.30	432.30	521.20	442.31	450.29	446.33	466.75
H-bond acceptors	3	1	1	1	1	2	1	1
H-bond donors	3	3	3	3	3	3	3	3
Rotatable bonds	2	2	2	2	2	2	2	2
Stereocenters	0	0	0	0	0	0	0	0
Log Po/w (iLOGP)	2.38	2.65	2.70	2.85	2.45	2.77	2.92	2.91
Solubility (mg/ml)	1.62e ⁻⁰³	1.39e ⁻⁰⁴	1.39e ⁻⁰⁴	1.23e ⁻⁰⁴	5.44e ⁻⁰⁴	1.14e ⁻⁰⁴	6.09e ⁻⁰⁵	3.34e ⁻⁰⁵
Log S (Ali)	-5.39	-6.49	-6.49	-6.63	-5.91	-6.60	-6.86	-7.15
Class	Moderately soluble	Poorly soluble	Poorly soluble	Poorly soluble	Moderately soluble	Poorly soluble	Poorly soluble	Poorly soluble
GI absorption	High	High	High	High	High	High	High	High
BBB permeant	No	No	No	No	Yes	No	No	No
CYP1A2 inhibitor	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CYP2C19 inhibitor	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Drug-likeness Lipinski (Violation)	Yes (0)	Yes (1)	Yes (1)	No (2)	Yes (0)	Yes (1)	Yes (1)	Yes (1)
Drug-likeness Ghose	Yes	No (1)	No (1)	No (2)	Yes	No (1)	No (1)	No (1)

Bioavailability score	0.55	0.55	0.55	0.17	0.55	0.55	0.55	0.55
Leadlikeness (Violation)	No (2)	No (2)	No (2)	No (2)	No (2)	No (2)	No (2)	No (2)

2.7 Table S4: GO analysis of DEGs of MRSA versus Compound 3e

Membrane (MRSA versus compound 3e)			
S. No	Gene Id	Annotation	Regulation
1	SAOUHSC_02469	Uncharacterized protein	Up
2	SAOUHSC_02616	Uncharacterized protein	Up
3	SAOUHSC_A02450	Uncharacterized protein	Up
4	SAOUHSC_00602	DUF443 domain-containing protein	Up
5	SAOUHSC_00409	Uncharacterized protein	Up
6	SAOUHSC_00701	DUF1361 domain-containing protein	Up
7	SAOUHSC_A01081	Uncharacterized protein	Up
8	SAOUHSC_00971	Uncharacterized protein	Up
9	SAOUHSC_00040	Uncharacterized protein	Up
10	SAOUHSC_00823	Mid2-like cell wall stress sensor domain protein	Up
11	SAOUHSC_00868	Teichoic acid D-Ala incorporation-associated protein DltX	Up
12	SAOUHSC_01068	Uncharacterized protein	Up
13	SAOUHSC_00966	Holin-like toxin	Up
14	SAOUHSC_01603	Uncharacterized protein	Up
15	SAOUHSC_02145	Phage protein	Up
16	SAOUHSC_01902	Uncharacterized protein	Up
17	SAOUHSC_02925	Uncharacterized protein	Up
18	SAOUHSC_00697	Uncharacterized protein	Up
19	SAOUHSC_02156	Uncharacterized protein	Up
20	SAOUHSC_00682	DUF456 domain-containing protein	Up
21	SAOUHSC_00978	TM2 domain-containing protein	Up
22	SAOUHSC_00725	DUF1146 domain-containing protein	Up
23	SAOUHSC_01971	DUF3267 domain-containing protein	Up
24	SAOUHSC_02176	Conserved hypothetical phage protein	Up
25	SAOUHSC_01900	CPBP family intramembrane metalloprotease SdpA	Up
26	SAOUHSC_00047	Uncharacterized protein	Up
27	SAOUHSC_02629	Drug resistance transporter, EmrB	Up
28	SAOUHSC_00700	QacA subfamily, putative	Up

29	SAOUHSC_00334	Uncharacterized protein	Up
30	SAOUHSC_02148	ABC-2 transporter permease	Up
31	SAOUHSC_00431	DUF1700 domain-containing protein	Up
32	SAOUHSC_01113	YibE/F family protein	Down
33	SAOUHSC_02930	Uncharacterized protein	Down
34	SAOUHSC_00775	Signal transduction protein TRAP (Target of RNAIII-activating protein)	Down
35	SAOUHSC_00174	DUF2198 family protein	Down
36	SAOUHSC_00716	lysostaphin (EC 3.4.24.75)	Down
37	SAOUHSC_02794	DoxX family protein	Down
38	SAOUHSC_02338	Uncharacterized protein	Down
39	SAOUHSC_00428	DUF1146 domain-containing protein	Down
40	SAOUHSC_00182	Cytosolic protein	Down
41	SAOUHSC_01334	Isoprenylcysteine carboxyl methyltransferase family protein	Down
42	SAOUHSC_00253	Secreted protein	Down
43	SAOUHSC_00844	Uncharacterized protein	Down
44	SAOUHSC_01084	Lipoprotein	Down
45	SAOUHSC_00818	Thermonuclease (EC 3.1.31.1) (Micrococcal nuclease) (Staphylococcal nuclease)	Down
		Heme ABC transporter permease	
ATP-binding cassette (ABC) transporter complex			
S. No	Gene Id	Annotation	Regulation
1	SAOUHSC_01312	ABC transmembrane type-2 domain-containing protein	up
2	SAOUHSC_01991	ABC transporter, permease protein, putative	up
3	SAOUHSC_00927	Oligopeptide ABC transporter, substrate-binding protein, putative	down
4	SAOUHSC_03019	ABC transporter, ATP-binding protein, putative	down
5	SAOUHSC_02832	ABC transporter domain-containing protein	down
6	SAOUHSC_00637	ABC transporter domain-containing protein	down
7	SAOUHSC_00105	Phosphonate ABC transporter, substrate-binding protein, putative	down
phosphoenolpyruvate-dependent sugar phosphotransferase system			
S. No	Gene Id	Annotation	Regulation
1	SAOUHSC_02400	PTS system mannitol-specific EIICB component (EC 2.7.1.197) (EIICB-Mtl)	up
2	SAOUHSC_02661	PTS system sucrose-specific IIBC component, putative (EC 2.7.1.69)	up

3	SAOUHSC_02401	Uncharacterized protein	up
4	SAOUHSC_02402	Mannitol-specific phosphotransferase enzyme IIA component (EIIA) (EIII) (PTS system mannitol-specific EIIA component)	up
5	SAOUHSC_00216	PTS system component	up
6	SAOUHSC_00311	PTS EIIB type-2 domain-containing protein	up
7	SAOUHSC_02888	Phosphotransferase system EIIC domain-containing protein	down
8	SAOUHSC_02974	Uncharacterized protein	down
protein-N(PI)-phosphohistidine-sugar phosphotransferase activity			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02661	PTS system sucrose-specific IIBC component, putative (EC 2.7.1.69)	up
2	SAOUHSC_02401	Uncharacterized protein	up
3	SAOUHSC_00311	PTS EIIB type-2 domain-containing protein	up
4	SAOUHSC_02888	Phosphotransferase system EIIC domain-containing protein	Down
5	SAOUHSC_02974	Uncharacterized protein	Down
ATPase-coupled transmembrane transporter activity			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_03019	ABC transporter, ATP-binding protein, putative	Down
2	SAOUHSC_02832	ABC transporter domain-containing protein	Down
3	SAOUHSC_00637	ABC transporter domain-containing protein	Down

2.8 Table S5: GO analysis of DEGs of MRSA versus Compound 3g

Membrane (MRSA versus compound 3g)			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00701	DUF1361 domain-containing protein	Up
2	SAOUHSC_00700	Uncharacterized protein	Up
3	SAOUHSC_02842	Uncharacterized protein	Up
4	SAOUHSC_01484	Uncharacterized protein	Up
5	SAOUHSC_01971	DUF3267 domain-containing protein	Up
6	SAOUHSC_01899	Staphylococcal protein	Up
7	SAOUHSC_00991	Acyltransferase 3 domain-containing protein	Up
8	SAOUHSC_A02450	Uncharacterized protein	Up
9	SAOUHSC_02616	Uncharacterized protein	Up
10	SAOUHSC_01761	DUF4930 family protein	Up

11	SAOUHSC_01607	Stressosome-associated protein Prli42	Up
12	SAOUHSC_00868	Teichoic acid D-Ala incorporation-associated protein DltX	Up
13	SAOUHSC_01902	Uncharacterized protein	Up
14	SAOUHSC_02948	Uncharacterized protein	Up
15	SAOUHSC_00218	Uncharacterized protein	Up
16	SAOUHSC_02469	Uncharacterized protein	Up
17	SAOUHSC_00971	Uncharacterized protein	Up
18	SAOUHSC_01984	DUF2975 domain-containing protein	Up
19	SAOUHSC_02796	Uncharacterized protein	Up
20	SAOUHSC_02588	Transmembrane protein	Up
21	SAOUHSC_00697	Uncharacterized protein	Up
22	SAOUHSC_02528	Uncharacterized protein	Up
23	SAOUHSC_02153	Phenol-soluble modulins export ABC transporter permease subunit PmtB	Up
24	SAOUHSC_00683	DUF1129 family protein	Up
25	SAOUHSC_01900	CPBP family intramembrane metalloprotease SdpA	Up
26	SAOUHSC_00355	YxeA family protein	Up
27	SAOUHSC_00639	M50 family metalloprotease	Up
28	SAOUHSC_00718	Uncharacterized protein	Up
29	SAOUHSC_01382	Permease	Up
30	SAOUHSC_00602	DUF443 domain-containing protein	Up
31	SAOUHSC_00123	Capsular polysaccharide biosynthesis protein Cap5J, putative	Up
32	SAOUHSC_01489	Uncharacterized protein	Up
33	SAOUHSC_00085	MFS transporter	Up
34	SAOUHSC_02112	Permease	Up
35	SAOUHSC_01155	YggT family protein	Up
36	SAOUHSC_00661	Alpha/beta hydrolase fold-3 domain-containing protein	Up
37	SAOUHSC_02164	Conserved hypothetical phage protein	Up
38	SAOUHSC_02704	Cation efflux protein cytoplasmic domain-containing protein	Up
39	SAOUHSC_A01081	Uncharacterized protein	Up
40	SAOUHSC_01025	Uncharacterized protein	Up
41	SAOUHSC_00040	Uncharacterized protein	Up
42	SAOUHSC_00965	CPBP family intramembrane metalloprotease	Up
43	SAOUHSC_02587	CPBP family intramembrane metalloprotease SdpB	Up
44	SAOUHSC_02522	AEC family transporter	Up
45	SAOUHSC_02928	Uncharacterized protein	Up
46	SAOUHSC_02100	Cell wall-active antibiotics response LiaF-like C-terminal domain-containing protein	Up

47	SAOUHSC_01945	Membrane protein, putative	Up
48	SAOUHSC_00823	Mid2-like cell wall stress sensor domain protein	Up
49	SAOUHSC_01068	Uncharacterized protein	Up
50	SAOUHSC_02390	Lytic regulatory protein, putative	Up
51	SAOUHSC_00978	TM2 domain-containing protein	Up
52	SAOUHSC_00591	DUF443 domain-containing protein	Up
53	SAOUHSC_00660	Branched-chain amino acid transport system II carrier protein	Up
54	SAOUHSC_01704	Uncharacterized protein	Up
55	SAOUHSC_01603	Uncharacterized protein	Up
56	SAOUHSC_01407	5-bromo-4-chloroindolyl phosphate hydrolase	Up
57	SAOUHSC_02156	Uncharacterized protein	Up
58	SAOUHSC_00922	DUF3899 domain-containing protein	Up
59	SAOUHSC_02688	Uncharacterized protein	Up
60	SAOUHSC_02660	Magnesium transporter CorA family protein	Up
61	SAOUHSC_02256	Abortive infection protein	Up
62	SAOUHSC_01340	DUF1453 family protein	Up
63	SAOUHSC_00047	Uncharacterized protein	Up
64	SAOUHSC_00270	DUF5079 family protein	Up
65	SAOUHSC_01050	DUF4064 domain-containing protein	Up
66	SAOUHSC_01908	NERD domain-containing protein	Up
67	SAOUHSC_00335	Low temperature requirement protein A	Up
68	SAOUHSC_01097	CvpA family protein	Up
69	SAOUHSC_02925	Uncharacterized protein	Up
70	SAOUHSC_02724	Uncharacterized protein	Up
71	SAOUHSC_02863	FeoB-associated Cys-rich membrane protein	Up
72	SAOUHSC_00704	Lipoprotein	Up
73	SAOUHSC_02145	Phage protein	Up
74	SAOUHSC_00592	DUF443 domain-containing protein	Up
75	SAOUHSC_02595	Bile acid:sodium symporter family protein	Up
76	SAOUHSC_02008	Teichoic acid translocation permease protein TagG	Up
77	SAOUHSC_02773	Transporter, putative	Up
78	SAOUHSC_02309	YdbS-like PH domain-containing protein	Up
79	SAOUHSC_01213	YfhO family protein	Up
80	SAOUHSC_01467	peptidoglycan glycosyltransferase (EC 2.4.99.28)	Up
81	SAOUHSC_01895	Mannosyl-glycoprotein endo-beta-N-acetylglucosamidase-like domain-containing protein	Up
82	SAOUHSC_00117	Capsular polysaccharide biosynthesis protein Cap5D, putative	Up
83	SAOUHSC_01706	Fido domain-containing protein	Up

84	SAOUHSC_02628	Uncharacterized protein	Up
85	SAOUHSC_02629	Drug resistance transporter, EmrB	Up
86	SAOUHSC_00725	QacA subfamily, putative	Up
87	SAOUHSC_02575	DUF1146 domain-containing protein	Up
88	SAOUHSC_00433	DUF4870 domain-containing protein	Up
89	SAOUHSC_00775	YibE/F family protein	Up
90	SAOUHSC_00968	DUF2198 family protein	Up
91	SAOUHSC_02668	Bacteriocin-associated integral membrane family protein	Up
92	SAOUHSC_01628	DUF3139 domain-containing protein	Up
93	SAOUHSC_01517	Uncharacterized protein	Up
94	SAOUHSC_02166	Conserved hypothetical phage protein	Up
95	SAOUHSC_00431	Hypothetical phage protein	Up
96	SAOUHSC_00174	YibE/F family protein	Up
97	SAOUHSC_01051	lysostaphin (EC 3.4.24.75)	Up
98	SAOUHSC_02761	DUF4064 domain-containing protein	Up
99	SAOUHSC_00802	CPBP family intramembrane metalloprotease	Up
100	SAOUHSC_00853	Carboxylesterase, putative (EC 3.1.1.1)	Up
101	SAOUHSC_01071	Uncharacterized protein	Up
102	SAOUHSC_01478	Glycerophosphoryl diester phosphodiesterase, putative (EC 3.1.4.46)	Up
103	SAOUHSC_02149	DUF1405 domain-containing protein	Up
104	SAOUHSC_01119	Uncharacterized protein	Up
105	SAOUHSC_02176	DUF4044 domain-containing protein	Up
106	SAOUHSC_02666	Conserved hypothetical phage protein	Up
107	SAOUHSC_02810	DUF4889 domain-containing protein	Up
108	SAOUHSC_01427	HTH merR-type domain-containing protein	Up
109	SAOUHSC_02603	Probable CtpA-like serine protease	Up
110	SAOUHSC_00584	Uncharacterized protein	Up
111	SAOUHSC_00026	LXG domain-containing protein	Up
112	SAOUHSC_00271	Uncharacterized protein	Up
113	SAOUHSC_01882	DUF5080 family protein	Up
114	SAOUHSC_01762	Serine aminopeptidase S33 domain-containing protein	Up
115	SAOUHSC_01279	MW1603 protein	Up
116	SAOUHSC_01693	Hydrolase, alpha/beta fold family domain protein	Up
117	SAOUHSC_02718	Helix-hairpin-helix DNA-binding motif class 1 domain-containing protein	Up
118	SAOUHSC_00012	ABC transporter ATP-binding protein	Down
119	SAOUHSC_00381	AzID domain-containing protein	Down
120	SAOUHSC_01067	DUF1304 domain-containing protein	Down
121	SAOUHSC_02426	DUF420 domain-containing protein	Down

122	SAOUHSC_01131	Membrane protein, putative	Down
123	SAOUHSC_00065	Uncharacterized protein	Down
124	SAOUHSC_00023	DUF1648 domain-containing protein	Down
125	SAOUHSC_02422	Regulatory protein YchH-like domain-containing protein	Down
126	SAOUHSC_01516	Hemolysin III	Down
127	SAOUHSC_01103	Holin protein	Down
128	SAOUHSC_01787	Succinate dehydrogenase cytochrome b-558 subunit, putative	Down
129	SAOUHSC_02443	Amino acid permease	Down
130	SAOUHSC_00050	SLC12A domain-containing protein	Down
131	SAOUHSC_02592	Alkaline shock response membrane anchor protein AmaP	Down
132	SAOUHSC_02391	DUF3278 domain-containing protein	Down
133	SAOUHSC_00793	Mid2-like cell wall stress sensor domain protein	Down
134	SAOUHSC_00844	Holin-like toxin	Down
135	SAOUHSC_02760	DUF4887 domain-containing protein	Down
136	SAOUHSC_02833	Lipoprotein	Down
137	SAOUHSC_02930	Glutamate synthase alpha subunit, putative (EC 1.4.1.13)	Down
138	SAOUHSC_02663	Peptide ABC transporter permease	Down
139	SAOUHSC_02729	Signal transduction protein TRAP (Target of RNAIII-activating protein)	Down
140	SAOUHSC_00280	DUF1722 domain-containing protein	Down
141	SAOUHSC_02721	Amino acid ABC transporter-like protein, putative	Down
142	SAOUHSC_02821	DUF4064 domain-containing protein	Down
143	SAOUHSC_00195	Type I toxin-antitoxin system Fst family toxin	Down
144	SAOUHSC_02754	Membrane spanning protein, putative	Down
145	SAOUHSC_00200	Probable acetyl-CoA acyltransferase (EC 2.3.1.16) (Putative acetyl-CoA C-acetyltransferase VraB)	Down
146	SAOUHSC_02923	ABC transporter, ATP-binding protein, putative	Down
147	SAOUHSC_02656	Membrane protein, putative	Down
148	SAOUHSC_03046	Amino acid permease	Down
149	SAOUHSC_00658	DUF2871 domain-containing protein	Down
150	SAOUHSC_02424	Helix-turn-helix domain protein	Down
151	SAOUHSC_01334	phosphoenolpyruvate--glycerone phosphotransferase (EC 2.7.1.121)	Down
152	SAOUHSC_01181	Metal-dependent hydrolase	Down
153	SAOUHSC_02662	Secreted protein	Down
154	SAOUHSC_00818	TM2 domain-containing protein	Down

155	SAOUHSC_02376	PTS system sucrose-specific IIBC component (EC 2.7.1.69)	Down
156	SAOUHSC_02837	Thermonuclease (EC 3.1.31.1) (Micrococcal nuclease) (Staphylococcal nuclease)	Down
157	SAOUHSC_02910	DoxX family membrane protein	Down
158	SAOUHSC_02868	Uncharacterized protein	Down
159	SAOUHSC_03048	Uncharacterized protein	Down
160	SAOUHSC_02384	Uncharacterized protein	Down
161	SAOUHSC_01918	Permease	Down
162	SAOUHSC_00716	Integral membrane protein	Down
163	SAOUHSC_00146	Excalibur calcium-binding domain-containing protein	Down
164	SAOUHSC_00182	DoxX family protein	Down
165	SAOUHSC_01919	DUF1440 domain-containing protein	Down
166	SAOUHSC_03047	Isoprenylcysteine carboxyl methyltransferase family protein	Down
167	SAOUHSC_01884	DUF4352 domain-containing protein	Down
168	SAOUHSC_02680	DUF3147 family protein	Down
169	SAOUHSC_00203	proline dehydrogenase (EC 1.5.5.2)	Down
170	SAOUHSC_02681	Nitrate reductase, beta subunit (EC 1.7.99.4)	Down
Plasma membrane			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02313	K(+)-transporting ATPase subunit F	up
2	SAOUHSC_01387	Phosphate transport system permease protein	up
3	SAOUHSC_01764	Prepilin peptidase A24 N-terminal domain-containing protein	up
4	SAOUHSC_00124	Capsular polysaccharide biosynthesis protein Cap5K, putative	up
5	SAOUHSC_01386	Phosphate transport system permease protein PstA	up
6	SAOUHSC_02151	Phenol-soluble modulins export ABC transporter permease subunit PmtD	up
7	SAOUHSC_00901	Putative undecaprenyl phosphate transporter SAOUHSC_00901	up
8	SAOUHSC_00344	Mechanosensitive ion channel family protein	up
9	SAOUHSC_00916	MFS transporter	up
10	SAOUHSC_00931	Oligopeptide ABC transporter, permease protein, putative	up
11	SAOUHSC_00762	Undecaprenyl/decaprenyl-phosphate alpha-N-acetylglucosaminyl 1-phosphate transferase	up
12	SAOUHSC_00703	Quinolone resistance protein NorA	up
13	SAOUHSC_02099	Sensor protein VraS (EC 2.7.13.3)	up
14	SAOUHSC_01758	Uncharacterized protein	up
15	SAOUHSC_00373	Xanthine permease, putative	up

16	SAOUHSC_01893	Arsenical pump membrane protein	up
17	SAOUHSC_01047	Spermidine/putrescine ABC transporter, permease protein, putative	up
18	SAOUHSC_00033	Probable membrane transporter protein	up
19	SAOUHSC_00402	Uncharacterized lipoprotein SAOUHSC_00402	up
20	SAOUHSC_00621	DMT family transporter	up
21	SAOUHSC_00672	Transporter/	up
22	SAOUHSC_01346	Glycine betaine transporter, putative	up
23	SAOUHSC_01063	Probable peptidoglycan glycosyltransferase FtsW (EC 2.4.99.28) (Cell division protein FtsW) (Cell wall polymerase) (Peptidoglycan polymerase)	up
24	SAOUHSC_02740	Quinolone resistance protein NorB	up
25	SAOUHSC_00880	Na ⁺ /H ⁺ antiporter family protein	up
26	SAOUHSC_01871	Polysaccharide biosynthesis protein, putative	up
27	SAOUHSC_00405	Uncharacterized lipoprotein SAOUHSC_00405	up
28	SAOUHSC_02557	Urea transporter, putative	up
29	SAOUHSC_01313	Histidine kinase-, DNA gyrase B-, and HSP90-like ATPase domain protein	up
30	SAOUHSC_02797	MFS transporter	up
31	SAOUHSC_01838	Serine protease HtrA-like/GtrA/	up
32	SAOUHSC_02722	DPMS transmembrane domain-containing protein	up
33	SAOUHSC_00930	Nickel import system ATP-binding protein NikE (EC 7.2.2.11)	up
34	SAOUHSC_00870	Teichoic acid D-alanyltransferase (EC 2.3.1.-)	up
35	SAOUHSC_03000	Capsular polysaccharide biosynthesis, capA, putative	up
36	SAOUHSC_02638	DUF218 domain-containing protein	up
37	SAOUHSC_00614	Uncharacterized protein	up
38	SAOUHSC_01048	Spermidine/putrescine ABC transporter, permease protein, putative	up
39	SAOUHSC_00143	Major facilitator superfamily (MFS) profile domain-containing pro+F219:F252tein	up
40	SAOUHSC_01656	Metal ABC transporter permease	up
41	SAOUHSC_00060	PhoU domain-containing protein	up
42	SAOUHSC_02001	Aromatic acid exporter family protein	up
43	SAOUHSC_01992	Phosphotransferase system, EIIC domain protein	up
44	SAOUHSC_00903	Signal peptidase I (EC 3.4.21.89)	up
45	SAOUHSC_02629	Drug resistance transporter, EmrB/QacA subfamily, putative	up
46	SAOUHSC_00932	Oligopeptide ABC transporter, permease protein, putative	up

47	SAOUHSC_01759	Cell shape-determining protein MreC (Cell shape protein MreC)	up
48	SAOUHSC_02866	SSD domain-containing protein	up
49	SAOUHSC_00556	Putative proline/betaine transporter	up
50	SAOUHSC_00114	Capsular polysaccharide biosynthesis protein, putative	up
51	SAOUHSC_00172	Uncharacterized protein SAOUHSC_00172	up
52	SAOUHSC_00642	Transport permease protein	up
53	SAOUHSC_02520	Sugar transporter, putative	up
54	SAOUHSC_00711	HlyC/CorC family transporter	up
55	SAOUHSC_01354	Sodium:alanine symporter family protein, putative	up
56	SAOUHSC_02731	Cation/H ⁺ exchanger domain-containing protein	up
57	SAOUHSC_01358	AI-2E family transporter	up
58	SAOUHSC_01238	Phosphatidate cytidyltransferase (EC 2.7.7.41)	up
59	SAOUHSC_00618	Uncharacterized protein	up
60	SAOUHSC_00668	ABC transporter permease, putative	up
61	SAOUHSC_02955	histidine kinase (EC 2.7.13.3) (Glycopeptide resistance-associated protein S)	up
62	SAOUHSC_01978	UPF0754 membrane protein SAOUHSC_01978	up
63	SAOUHSC_01691	DNA internalization-related competence protein ComEC/Rec2/Cytochrome d ubiquinol oxidase, subunit II, putative (EC 1.10.3.-)	up
64	SAOUHSC_01032	Glycosyltransferase 2-like domain-containing protein	up
65	SAOUHSC_00713	Putative multidrug export ATP-binding	up
66	SAOUHSC_02003	permease protein SAOUHSC_02003 (EC 7.6.2.-)	up
67	SAOUHSC_01411	Putative branched-chain amino acid carrier protein SAOUHSC_01411	up
68	SAOUHSC_01440	Probable queuosine precursor transporter (Q precursor transporter)	up
69	SAOUHSC_01876	Major facilitator superfamily (MFS) profile domain-containing protein	up
70	SAOUHSC_00828	Amino acid transporter	up
71	SAOUHSC_02420	Major facilitator superfamily (MFS) profile domain-containing protein	up
72	SAOUHSC_01310	Cardiolipin synthase (CL synthase) (EC 2.7.8.-)	up
73	SAOUHSC_00760	Uncharacterized membrane protein SAOUHSC_00760	up
74	SAOUHSC_01031	Cytochrome d ubiquinol oxidase, subunit I, putative	up

75	SAOUHSC_00653	Ferrichrome transport permease fluB, putative	up
76	SAOUHSC_02622	Sodium/glutamate symporter	up
77	SAOUHSC_02319	Rod shape-determining protein RodA	up
78	SAOUHSC_00975	DoxX family protein	up
79	SAOUHSC_00102	Phosphonates ABC transporter, permease protein CC0363, putative	Down
80	SAOUHSC_00058	Quinolone resistance protein NorB	Down
81	SAOUHSC_00158	PTS system MurNAc-GlcNAc-specific EIIBC component [Includes: MurNAc-GlcNAc-specific phosphotransferase enzyme IIB component (EC 2.7.1.-) (PTS system MurNAc-GlcNAc-specific EIIB component); MurNAc-GlcNAc permease IIC component (PTS system MurNAc-GlcNAc-specific EIIC component)]	Down
82	SAOUHSC_02909	Dihydroorotate dehydrogenase (quinone) (EC 1.3.5.2)	Down
83	SAOUHSC_02954	ABC transporter, ATP-binding protein, putative	Down
84	SAOUHSC_02590	Amino acid permease	Down
85	SAOUHSC_03035	SLC12A domain-containing protein	Down
86	SAOUHSC_00235	HdeD family acid-resistance protein	Down
87	SAOUHSC_02547	PTS system glucose-specific EIIA component (EIIA-Glc) (EIII-Glc) (Glucose-specific phosphotransferase enzyme IIA component)	Down
88	SAOUHSC_03031	Molybdenum transport system permease	Down
89	SAOUHSC_00287	EamA domain-containing protein	Down
90	SAOUHSC_00071	Putative hemin import ATP-binding protein HrtA	Down
91	SAOUHSC_00138	Lipoprotein, SirC, putative	Down
92	SAOUHSC_02400	ABC transmembrane type-1 domain-containing protein	Down
93	SAOUHSC_00801	PTS system mannitol-specific EIICB component (EC 2.7.1.197) (EIICB-Mtl)	Down
94	SAOUHSC_00072	Protein translocase subunit SecG	Down
95	SAOUHSC_00358	Lipoprotein, SirB, putative	Down
96	SAOUHSC_01991	GlsB/YeaQ/YmgE family stress response membrane protein	Down
97	SAOUHSC_01643	ABC transporter, permease protein, putative	Down
98	SAOUHSC_00923	Bacterial type II secretion system protein E domain-containing protein//////////	Down
99	SAOUHSC_00131	ABC transmembrane type-1 domain-containing protein	Down
100	SAOUHSC_00698	DUF454 domain-containing protein	Down
101	SAOUHSC_00924	Sodium-dependent dicarboxylate transporter SdcS (Na ⁽⁺⁾)/dicarboxylate symporter)	Down

102	SAOUHSC_02687	ABC transmembrane type-1 domain-containing protein	Down
103	SAOUHSC_00501	Formate/nitrite transporter, putative	Down
104	SAOUHSC_00926	NupC/NupG family nucleoside CNT transporter	Down
105	SAOUHSC_00367	Oligopeptide ABC transporter, ATP-binding protein, putative	Down
106	SAOUHSC_01640	L-cystine uptake protein TcyP (Transporter of cystine TcyP)	Down
107	SAOUHSC_03030	ComG operon protein 3	Down
108	SAOUHSC_00259	Sodium, sulfate symporter, putative	Down
109	SAOUHSC_02661	ESAT-6 secretion machinery protein EssA	Down
110	SAOUHSC_00843	PTS system sucrose-specific IIBC component, putative (EC 2.7.1.69)	Down
111	SAOUHSC_02450	ABC transmembrane type-1 domain-containing protein	Down
112	SAOUHSC_02888	PTS system lactose-specific EIICB component (EC 2.7.1.207) (EIICB-Lac)	Down
113	SAOUHSC_00099	Phosphotransferase system EIIC domain-containing protein	Down
114	SAOUHSC_00241	Tetracycline resistance protein	Down
115	SAOUHSC_01104	Ribose transporter RbsU	Down
116	SAOUHSC_02597	succinate dehydrogenase (EC 1.3.5.1)	Down
117	SAOUHSC_02678	PTS system component, putative	Down
118	SAOUHSC_02841	Respiratory nitrate reductase, gamma subunit (EC 1.7.99.4)	Down
119	SAOUHSC_01133	Phosphotransferase system EIIC domain-containing protein	Down
120	SAOUHSC_01914	Permease, Putative membrane protein insertion efficiency factor	Down
121	SAOUHSC_00925	ABC transporter domain-containing protein	Down
122	SAOUHSC_01130	YfcC family protein	Down
123	SAOUHSC_00209	PTS system, glucose-specific IIBC component, putative (EC 2.7.1.69)	Down
124	SAOUHSC_02753	Membrane protein, putative	Down
125	SAOUHSC_00178	Maltose ABC transporter, permease protein	Down
126	SAOUHSC_02975	PTS system, fructose-specific IIABC component, putative	Down
127	SAOUHSC_02806	Gluconate permease, putative	Down
128	SAOUHSC_02815	Major facilitator superfamily (MFS) profile domain-containing protein	Down
129	SAOUHSC_00437	Uncharacterized protein	Down
130	SAOUHSC_00294	Na ⁺ /proline symporter	Down
131	SAOUHSC_00183	Membrane protein, putative	Down

132	SAOUHSC_00317	Glycerol-3-phosphate transporter	Down
133	SAOUHSC_00281	Formate/nitrite transporter	Down
134	SAOUHSC_00310	Ascorbate-specific PTS system EIIC component (Ascorbate-specific permease IIC component UlaA)	Down
135	SAOUHSC_02967	Arginine-ornithine antiporter	Down
136	SAOUHSC_02648	L-lactate permease	Down
137	SAOUHSC_00636	Iron (Chelated) ABC transporter, permease protein, putative	Down
138	SAOUHSC_02681	nitrate reductase (quinone) (EC 1.7.5.1)	Down
139	SAOUHSC_01450	Amino acid permease	Down
Transmembrane transport			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00931	Oligopeptide ABC transporter, permease protein, putative	up
2	SAOUHSC_02522	AEC family transporter	up
3	SAOUHSC_01047	Spermidine/putrescine ABC transporter, permease protein, putative	up
4	SAOUHSC_02740	Quinolone resistance protein NorB	up
5	SAOUHSC_01048	Spermidine/putrescine ABC transporter, permease protein, putative	up
6	SAOUHSC_01656	Metal ABC transporter permease/Oligopeptide ABC transporter, permease protein, putative	up
7	SAOUHSC_00932	AI-2E family transporter	up
8	SAOUHSC_01358	ABC transporter permease, putative	up
9	SAOUHSC_00668	Putative multidrug export ATP-binding permease protein SAOUHSC_02003 (EC 7.6.2.-)	up
10	SAOUHSC_02003	Major facilitator superfamily (MFS) profile domain-containing protein	up
11	SAOUHSC_02420	ABC transporter ATP-binding protein	up
12	SAOUHSC_02718	Quinolone resistance protein NorB	down
13	SAOUHSC_00058	ABC transporter, ATP-binding protein, putative	down
14	SAOUHSC_02954	Amino acid permease	down
15	SAOUHSC_02590	SLC12A domain-containing protein	down
16	SAOUHSC_00287	Putative hemin import ATP-binding protein HrtA	down
17	SAOUHSC_00138	ABC transmembrane type-1 domain-containing protein	down
18	SAOUHSC_00923	Amino acid ABC transporter-like protein, putative	down
19	SAOUHSC_02729	ABC transmembrane type-1 domain-containing protein	down
20	SAOUHSC_00924		

21	SAOUHSC_00099	Tetracycline resistance protein	down
22	SAOUHSC_00925	ABC transporter domain-containing protein	down
23	SAOUHSC_00636	Iron (Chelated) ABC transporter, permease protein, putative	down
phosphoenolpyruvate-dependent sugar phosphotransferase system			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01992	Phosphotransferase system, EIIC domain protein	up
2	SAOUHSC_00158	PTS system MurNAc-GlcNAc-specific EIIBC component [Includes: MurNAc-GlcNAc-specific phosphotransferase enzyme IIB component (EC 2.7.1.-) (PTS system MurNAc-GlcNAc-specific EIIB component); MurNAc-GlcNAc permease IIC component (PTS system MurNAc-GlcNAc-specific EIIC component)]	down
3	SAOUHSC_00235	PTS system glucose-specific EIIA component (EIIA-Glc) (EIII-Glc) (Glucose-specific phosphotransferase enzyme IIA component)	down
4	SAOUHSC_02400	PTS system mannitol-specific EIICB component (EC 2.7.1.197) (EIICB-Mtl)	down
5	SAOUHSC_02661	PTS system sucrose-specific IIBC component, putative (EC 2.7.1.69)	down
6	SAOUHSC_00658	phosphoenolpyruvate--glycerone phosphotransferase (EC 2.7.1.121)	down
7	SAOUHSC_02450	PTS system lactose-specific EIICB component (EC 2.7.1.207) (EIICB-Lac)	down
8	SAOUHSC_02888	Phosphotransferase system EIIC domain-containing protein	down
9	SAOUHSC_02662	PTS system sucrose-specific IIBC component (EC 2.7.1.69)	down
10	SAOUHSC_02597	PTS system component, putative	down
11	SAOUHSC_02841	Phosphotransferase system EIIC domain-containing protein	down
12	SAOUHSC_02974	Uncharacterized protein	down
13	SAOUHSC_00209	PTS system, glucose-specific IIBC component, putative (EC 2.7.1.69)	down
14	SAOUHSC_02975	PTS system, fructose-specific IIABC component, putative	down
15	SAOUHSC_00437	Uncharacterized protein	down
16	SAOUHSC_02451	PTS system lactose-specific EIIA component (EIIA-Lac) (EIII-Lac) (Lactose-specific phosphotransferase enzyme IIA component)	down
17	SAOUHSC_00310	Ascorbate-specific PTS system EIIC component (Ascorbate-specific permease IIC component UlaA)	down

18	SAOUHSC_00311	PTS EIIB type-2 domain-containing protein	down
19	SAOUHSC_00313	Uncharacterized protein	down
Nickel cation transport			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01387	Phosphate transport system permease protein	up
2	SAOUHSC_01386	Phosphate transport system permease protein PstA	up
3	SAOUHSC_00931	Oligopeptide ABC transporter, permease protein, putative	up
4	SAOUHSC_01047	Spermidine/putrescine ABC transporter, permease protein, putative	up
5	SAOUHSC_00930	Nickel import system ATP-binding protein Nike (EC 7.2.2.11)	up
6	SAOUHSC_01048	Spermidine/putrescine ABC transporter, permease protein, putative	up
7	SAOUHSC_00932	Oligopeptide ABC transporter, permease protein, putative	up
8	SAOUHSC_00102	Phosphonates ABC transporter, permease protein CC0363, putative	down
9	SAOUHSC_02547	Molybdenum transport system permease	down
10	SAOUHSC_00138	ABC transmembrane type-1 domain-containing protein	down
11	SAOUHSC_01991	ABC transporter, permease protein, putative	down
12	SAOUHSC_00923	ABC transmembrane type-1 domain-containing protein	down
13	SAOUHSC_00924	ABC transmembrane type-1 domain-containing protein	down
14	SAOUHSC_00926	Oligopeptide ABC transporter, ATP-binding protein, putative	down
15	SAOUHSC_00843	ABC transmembrane type-1 domain-containing protein	down
16	SAOUHSC_00178	Maltose ABC transporter, permease protein	down
17	SAOUHSC_00177	Maltose/maltodextrin transport system permease protein	down
protein-N(PI)-phosphohistidine-sugar phosphotransferase activity			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01992	Phosphotransferase system, EIIC domain protein	up
2	SAOUHSC_00158	PTS system MurNAc-GlcNAc-specific EIIBC component [Includes: MurNAc-GlcNAc-specific phosphotransferase enzyme IIB component (EC 2.7.1.-) (PTS system MurNAc-GlcNAc-specific EIIB component); MurNAc-GlcNAc permease IIC component (PTS system MurNAc-GlcNAc-specific EIIC component)]	down

3	SAOUHSC_00235	PTS system glucose-specific EIIA component (EIIA-Glc) (EIII-Glc) (Glucose-specific phosphotransferase enzyme IIA component)	down
4	SAOUHSC_02661	PTS system sucrose-specific IIBC component, putative (EC 2.7.1.69)	down
5	SAOUHSC_02888	Phosphotransferase system EIIC domain-containing protein	down
6	SAOUHSC_02662	PTS system sucrose-specific IIBC component (EC 2.7.1.69)	down
7	SAOUHSC_02597	PTS system component, putative	down
8	SAOUHSC_02841	Phosphotransferase system EIIC domain-containing protein	down
9	SAOUHSC_02974	Uncharacterized protein	down
10	SAOUHSC_00209	PTS system, glucose-specific IIBC component, putative (EC 2.7.1.69)	down
11	SAOUHSC_00437	Uncharacterized protein	down
12	SAOUHSC_00311	PTS EIIB type-2 domain-containing protein	down
13	SAOUHSC_00313	Uncharacterized protein	down
acyltransferase activity, transferring groups other than amino-acyl groups			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00991	Acyltransferase 3 domain-containing protein	up
2	SAOUHSC_00979	N-acetyltransferase domain-containing protein	up
3	SAOUHSC_02651	N-acetyltransferase domain-containing protein	up
4	SAOUHSC_00684	N-acetyltransferase domain-containing protein	up
5	SAOUHSC_02997	N-acetyltransferase domain-containing protein	up
6	SAOUHSC_00811	N-acetyltransferase domain-containing protein	up
7	SAOUHSC_02551	N-acetyltransferase domain-containing protein	down
8	SAOUHSC_00430	N-acetyltransferase domain-containing protein	down
9	SAOUHSC_03017	N-acetyltransferase domain-containing protein	down
10	SAOUHSC_01847	N-acetyltransferase domain-containing protein	down
11	SAOUHSC_02686	N-acetyltransferase domain-containing protein	down
12	SAOUHSC_02836	N-acetyltransferase domain-containing protein	down
13	SAOUHSC_02827	Uncharacterized protein	down
peptide transport			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00929	Oligopeptide ABC transporter, ATP-binding protein, putative	up
2	SAOUHSC_00930	Nickel import system ATP-binding protein Nike (EC 7.2.2.11)	up
3	SAOUHSC_00170	Solute-binding protein family 5 domain-containing protein	down
4	SAOUHSC_00927	Oligopeptide ABC transporter, substrate-binding protein, putative	down
5	SAOUHSC_00924	ABC transmembrane type-1 domain-containing	down

		protein	
6	SAOUHSC_00926	Oligopeptide ABC transporter, ATP-binding protein, putative	down
7	SAOUHSC_00925	ABC transporter domain-containing protein	down

2.9 Table S6: GO analysis of DEGs of MRSA versus Compound 3n

Membrane (MRSA versus compound 3n)			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02469	Uncharacterized protein	up
2	SAOUHSC_00701	DUF1361 domain-containing protein	up
3	SAOUHSC_00971	Uncharacterized protein	up
4	SAOUHSC_02732	Uncharacterized protein	up
5	SAOUHSC_00602	DUF443 domain-containing protein	up
6	SAOUHSC_00334	ABC-2 transporter permease	up
7	SAOUHSC_02176	Conserved hypothetical phage protein	up
8	SAOUHSC_02145	Phage protein	up
9	SAOUHSC_02470	Uncharacterized protein	up
10	SAOUHSC_01902	Uncharacterized protein	up
11	SAOUHSC_00040	Uncharacterized protein	up
12	SAOUHSC_A02450	Uncharacterized protein	up
13	SAOUHSC_00823	Mid2-like cell wall stress sensor domain protein	up
14	SAOUHSC_01068	Uncharacterized protein	up
15	SAOUHSC_00978	TM2 domain-containing protein	up
16	SAOUHSC_01761	DUF4930 family protein	up
17	SAOUHSC_01900	CPBP family intramembrane metalloprotease SdpA	up
18	SAOUHSC_A01081	Uncharacterized protein	up
19	SAOUHSC_00639	M50 family metallopeptidase	up
20	SAOUHSC_02925	Uncharacterized protein	up
21	SAOUHSC_02700	Quinolone resistance protein NorB	up
22	SAOUHSC_00700	Uncharacterized protein	up
23	SAOUHSC_00682	DUF456 domain-containing protein	up
24	SAOUHSC_02629	Drug resistance transporter, EmrB/QacA subfamily, putative	up
25	SAOUHSC_02868	Uncharacterized protein	up
26	SAOUHSC_02704	Cation efflux protein cytoplasmic domain-containing protein	up
27	SAOUHSC_02680	Nitrate reductase, beta subunit (EC 1.7.99.4)	up

28	SAOUHSC_02264	Accessory gene regulator protein C	up
29	SAOUHSC_01803	Amino acid permease	up
30	SAOUHSC_01025	SLC12A domain-containing protein	up
31	SAOUHSC_00591	Uncharacterized protein	up
32	SAOUHSC_00026	DUF443 domain-containing protein	up
33	SAOUHSC_02699	Uncharacterized protein	up
34	SAOUHSC_00117	Amino acid ABC transporter substrate-binding protein	up
35	SAOUHSC_00991	Capsular polysaccharide biosynthesis protein Cap5D, putative	up
36	SAOUHSC_01971	Acyltransferase 3 domain-containing protein	up
37	SAOUHSC_00793	DUF3267 domain-containing protein	up
38	SAOUHSC_01919	DUF4887 domain-containing protein	up
39	SAOUHSC_00089	DUF4352 domain-containing protein	up
40	SAOUHSC_00946	Bacterial sugar transferase domain-containing protein	up
41	SAOUHSC_00592	Sodium:proton antiporter	up
42	SAOUHSC_02773	DUF443 domain-containing protein	up
43	SAOUHSC_00426	Transporter, putative	Down
44	SAOUHSC_02724	Lipoprotein	Down
45	SAOUHSC_00911	Uncharacterized protein	Down
46	SAOUHSC_01326	Acyltransferase 3 domain-containing protein	Down
47	SAOUHSC_00844	Amino acid permease	Down
48	SAOUHSC_01103	SLC12A domain-containing protein	Down
49	SAOUHSC_01840	Lipoprotein	Down
50	SAOUHSC_02147	Succinate dehydrogenase cytochrome b-558 subunit, putative	Down
51	SAOUHSC_00200	Transglycosylase domain protein	Down
52	SAOUHSC_02733	DUF4097 domain-containing protein	Down
53	SAOUHSC_00253	Membrane protein, putative/)	Down
54	SAOUHSC_00810	Membrane protein, putative	Down
55	SAOUHSC_01423	Uncharacterized protein	Down
56	SAOUHSC_01609	Uncharacterized protein	Down
57	SAOUHSC_01316	Phosphatidic acid phosphatase type 2	Down
58	SAOUHSC_02777	haloperoxidase domain-containing protein	Down
59	SAOUHSC_00428	Putative aromatic acid exporter C-terminal domain-containing protein	Down
60	SAOUHSC_03046	Thermonuclease (EC 3.1.31.1) (Micrococcal nuclease) (Staphylococcal nuclease)	Down
61	SAOUHSC_02666	DUF1433 domain-containing protein	Down

62	SAOUHSC_02338	Cytosolic protein	Down
63	SAOUHSC_02930	Helix-turn-helix domain protein	Down
64	SAOUHSC_01984	DUF4889 domain-containing protein	Down
65	SAOUHSC_00716	DUF1146 domain-containing protein	Down
66	SAOUHSC_03047	Signal transduction protein TRAP (Target of RNAIII-activating protein)	Down
67	SAOUHSC_02821	DUF2975 domain-containing protein	Down
68	SAOUHSC_01084	DoxX family protein	Down
69	SAOUHSC_02910	DUF3147 family protein	Down
70	SAOUHSC_00203	Membrane spanning protein, putative//Uncharacterized protein/Uncharacterized protein/	Down
71	SAOUHSC_02656	Heme ABC transporter permease	Down
72	SAOUHSC_00818	Uncharacterized protein	Down
73	SAOUHSC_00182	Uncharacterized protein	Down
Transmembrane transporter activity			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_03036	ABC transporter, ATP-binding protein, putative	up
2	SAOUHSC_00747	Uncharacterized protein	up
3	SAOUHSC_02444	Osmoprotectant transporter, BCCT family, opuD-like protein, putative	up
4	SAOUHSC_00072	Lipoprotein, SirB, putative	up
5	SAOUHSC_00654	Ferrichrome ABC transporter (Permease), putative	up
6	SAOUHSC_00246	Quinolone resistance protein NorB	up
7	SAOUHSC_02700	Quinolone resistance protein NorB	up
8	SAOUHSC_02740	Quinolone resistance protein NorB	up
9	SAOUHSC_00569	APC family permease	up
10	SAOUHSC_02762	Major facilitator superfamily (MFS) profile domain-containing protein	up
11	SAOUHSC_02629	Drug resistance transporter, EmrB/QacA subfamily, putative	up
12	SAOUHSC_01346	Glycine betaine transporter, putative	up
13	SAOUHSC_00653	Ferrichrome transport permease fhuB, putative	up
14	SAOUHSC_02427	Uncharacterized protein	up
15	SAOUHSC_02428	Uncharacterized protein	up
16	SAOUHSC_00071	Lipoprotein, SirC, putative	up
17	SAOUHSC_00732	Amino acid ABC transporter, permease protein, putative	up
18	SAOUHSC_00681	Major facilitator superfamily protein superfamily	up
19	SAOUHSC_02733	Membrane protein, putative	down

Phosphoenolpyruvate-dependent sugar phosphotransferase system			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02400	PTS system mannitol-specific EIICB component (EC 2.7.1.197) (EIICB-Mtl)/	up
2	SAOUHSC_00216	PTS system component/	up
3	SAOUHSC_00708	Fructose specific permease, putative/	up
4	SAOUHSC_02401	Uncharacterized protein/	up
5	SAOUHSC_02661	PTS system sucrose-specific IIBC component, putative (EC 2.7.1.69)/	up
6	SAOUHSC_01028	Phosphocarrier protein HPr (Histidine-containing protein)/	up
7	SAOUHSC_00311	PTS EIIB type-2 domain-containing protein/	down
8	SAOUHSC_00209	PTS system, glucose-specific IIBC component, putative (EC 2.7.1.69)/	down
9	SAOUHSC_00313	Uncharacterized protein/	down
10	SAOUHSC_02974	Uncharacterized protein	down
nucleic acid binding			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00483	S1 RNA binding domain protein/	up
2	SAOUHSC_00819	Cold shock protein CspA/	up
3	SAOUHSC_00892	S1 motif domain-containing protein/	up
4	SAOUHSC_01543	Phi related protein/	down
5	SAOUHSC_01074	Uncharacterized protein/	down
6	SAOUHSC_01316	Thermonuclease (EC 3.1.31.1) (Micrococcal nuclease) (Staphylococcal nuclease)/	down
7	SAOUHSC_01576	Exonuclease family/	down
8	SAOUHSC_00818	Thermonuclease (EC 3.1.31.1) (Micrococcal nuclease) (Staphylococcal nuclease)	down
siderophore-dependent iron import into cell			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00747	Uncharacterized protein	up
2	SAOUHSC_00072	Lipoprotein, SirB, putative	up
3	SAOUHSC_00654	Ferrichrome ABC transporter (Permease), putative	up
4	SAOUHSC_00653	Ferrichrome transport permease fhuB, putative	up
5	SAOUHSC_02427	Uncharacterized protein	up
6	SAOUHSC_02428	Uncharacterized protein	up
7	SAOUHSC_00071	Lipoprotein, SirC, putative	up
ABC-type transporter activity			
S. No.	Gene Id	Annotation	Regulation

1	SAOUHSC_01312	ABC transmembrane type-2 domain-containing protein/	up
2	SAOUHSC_02658	Membrane protein, putative/	up
3	SAOUHSC_02151	Phenol-soluble modulins export ABC transporter permease subunit PmtD/Putative multidrug export ATP-binding/	up
4	SAOUHSC_02003	permease protein SAOUHSC_02003 (EC 7.6.2.-)/	up
5	SAOUHSC_00693	Amino acid ABC transporter ATP-binding/permease protein	up

3.0 Table S7: KEGG analysis of DEGs of MRSA versus Compound 3e

Metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00899	Argininosuccinate synthase (EC 6.3.4.5) (Citrulline--aspartate ligase)/	up
2	SAOUHSC_00798	2,3-bisphosphoglycerate-independent phosphoglycerate mutase (BPG-independent PGAM) (Phosphoglyceromutase) (iPGM) (EC 5.4.2.12)/	up
3	SAOUHSC_00898	Argininosuccinate lyase (ASAL) (EC 4.3.2.1) (Arginosuccinase)/	up
4	SAOUHSC_00797	Triosephosphate isomerase (TIM) (TPI) (EC 5.3.1.1) (Triose-phosphate isomerase)/	up
5	SAOUHSC_00421	Tryptophan synthase beta chain-like PALP domain-containing protein/	up
6	SAOUHSC_00796	Phosphoglycerate kinase (EC 2.7.2.3)/	up
7	SAOUHSC_00795	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.-)/	up
8	SAOUHSC_00554	SIS domain protein/	up
9	SAOUHSC_01367	Anthranilate synthase component II, putative/	up
10	SAOUHSC_01635	Shikimate kinase (SK) (EC 2.7.1.71)/	down
11	SAOUHSC_00989	Aminotransferase (EC 2.6.1.-)/	down
12	SAOUHSC_02703	2,3-bisphosphoglycerate-dependent phosphoglycerate mutase (BPG-dependent PGAM) (PGAM) (Phosphoglyceromutase) (dPGM) (EC 5.4.2.11)/	down
13	SAOUHSC_02840	L-serine deaminase/Transaldolase/	down
14	SAOUHSC_01901	Aromatic amino acid beta-eliminating lyase/	down
15	SAOUHSC_01307	threonine aldolase domain-containing protein/	down
16	SAOUHSC_02285	2-isopropylmalate synthase (EC 2.3.3.13) (Alpha-IPM synthase) (Alpha-	down

		isopropylmalate synthase)/	
17	SAOUHSC_01322	Homoserine kinase (HK) (HSK) (EC 2.7.1.39)/	down
18	SAOUHSC_00339	Hcy-binding domain-containing protein/	down
19	SAOUHSC_01794	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.-)/	down
20	SAOUHSC_02284	Ketol-acid reductoisomerase (NADP(+)) (KARI) (EC 1.1.1.86) (Acetohydroxy-acid isomeroreductase) (AHIR) (Alpha-keto-beta-hydroxylacyl reductoisomerase) (Ketol-acid reductoisomerase type 1) (Ketol-acid reductoisomerase type I)/	down
21	SAOUHSC_02281	Dihydroxy-acid dehydratase (DAD) (EC 4.2.1.9)/	down
22	SAOUHSC_01321	Threonine synthase (EC 4.2.3.1)/	down
23	SAOUHSC_02282	Acetolactate synthase (EC 2.2.1.6)/	down
24	SAOUHSC_01451	L-threonine dehydratase catabolic TdcB (EC 4.3.1.19) (Threonine deaminase)/	down
25	SAOUHSC_00340	Trans-sulfuration enzyme family protein/	down
26	SAOUHSC_00341	Cystathionine gamma-synthase/	down
27	SAOUHSC_02283	acetolactate synthase (EC 2.2.1.6)/	down
28	SAOUHSC_01320	Homoserine dehydrogenase (EC 1.1.1.3)/	down
29	SAOUHSC_01319	Aspartokinase (EC 2.7.2.4)	down
Human Diseases			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00812	Clumping factor A (Fibrinogen receptor A) (Fibrinogen-binding protein A)/	up
2	SAOUHSC_00069	Immunoglobulin G-binding protein A (IgG-binding protein A) (Staphylococcal protein A) (SpA)/	down
3	SAOUHSC_00544	Serine-aspartate repeat-containing protein C/	down
4	SAOUHSC_02971	Neutral metalloproteinase (EC 3.4.24.-)/	down
5	SAOUHSC_02709	Gamma-hemolysin component C (Leukocidins subunit)/	down
6	SAOUHSC_02710	Gamma-hemolysin component B (H-gamma-1) (H-gamma-I) (Leukocidin f subunit)/	down
7	SAOUHSC_02708	Gamma-hemolysin h-gamma-ii subunit, putative/	down
8	SAOUHSC_01112	FPRL1 inhibitory protein (FLIPr)/	down
9	SAOUHSC_01114	Fibrinogen-binding protein/	down
10	SAOUHSC_00191	Staphylococcal complement inhibitor/	down
11	SAOUHSC_01115	Staphylococcal complement inhibitor/	down
12	SAOUHSC_02706	Immunoglobulin-binding protein Sbi/	down
13	SAOUHSC_02167	Staphylococcal complement inhibitor (SCIN)/	down

14	SAOUHSC_02241	Uncharacterized leukocidin-like protein 1/	down
15	SAOUHSC_02243	Uncharacterized leukocidin-like protein 2/	down
16	SAOUHSC_00399	Staphylococcal superantigen-like 11/	down
17	SAOUHSC_02169	Chemotaxis inhibitory protein (CHIPS)	down
Metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02285	2-isopropylmalate synthase (EC 2.3.3.13) (Alpha-IPM synthase) (Alpha-isopropylmalate synthase)/	down
2	SAOUHSC_02284	Ketol-acid reductoisomerase (NADP(+)) (KARI) (EC 1.1.1.86) (Acetohydroxy-acid isomeroreductase) (AHIR) (Alpha-keto-beta-hydroxylacyl reductoisomerase) (Ketol-acid reductoisomerase type 1) (Ketol-acid reductoisomerase type I)/	down
3	SAOUHSC_02281	Dihydroxy-acid dehydratase (DAD) (EC 4.2.1.9)/	down
4	SAOUHSC_02282	Acetolactate synthase (EC 2.2.1.6)/	down
5	SAOUHSC_01451	L-threonine dehydratase catabolic TdcB (EC 4.3.1.19) (Threonine deaminase)/	down
6	SAOUHSC_02283	acetolactate synthase (EC 2.2.1.6)	down
Metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00421	Tryptophan synthase beta chain-like PALP domain-containing protein/	up
2	SAOUHSC_02840	L-serine deaminase/	Down
3	SAOUHSC_01322	Homoserine kinase (HK) (HSK) (EC 2.7.1.39)/	Down
4	SAOUHSC_00339	Hcy-binding domain-containing protein/	Down
5	SAOUHSC_00340	Trans-sulfuration enzyme family protein/	Down
6	SAOUHSC_00341	Cystathionine gamma-synthase/	Down
7	SAOUHSC_01320	Homoserine dehydrogenase (EC 1.1.1.3)/	Down
8	SAOUHSC_01319	Aspartokinase (EC 2.7.2.4)	Down
Metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00798	2,3-bisphosphoglycerate-independent phosphoglycerate mutase (BPG-independent PGAM) (Phosphoglyceromutase) (iPGM) (EC 5.4.2.12)/	up
2	SAOUHSC_02703	2,3-bisphosphoglycerate-dependent phosphoglycerate mutase (BPG-dependent PGAM) (PGAM) (Phosphoglyceromutase) (dPGM) (EC 5.4.2.11)/	down
3	SAOUHSC_02840	L-serine deaminase/	down

4	SAOUHSC_01307	Aromatic amino acid beta-eliminating lyase/	down
5	SAOUHSC_01322	threonine aldolase domain-containing protein/	down
6	SAOUHSC_01321	Homoserine kinase (HK) (HSK) (EC 2.7.1.39)/	down
7	SAOUHSC_01451	Threonine synthase (EC 4.2.3.1)/	down
8	SAOUHSC_01320	L-threonine dehydratase catabolic TdcB (EC 4.3.1.19) (Threonine deaminase)/	down
9	SAOUHSC_01319	Homoserine dehydrogenase (EC 1.1.1.3)/Aspartokinase (EC 2.7.2.4)	down
Metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00797	Triosephosphate isomerase (TIM) (TPI) (EC 5.3.1.1) (Triose-phosphate isomerase)/	up
2	SAOUHSC_00796	Phosphoglycerate kinase (EC 2.7.2.3)/	up
3	SAOUHSC_00795	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.-)/	up
4	SAOUHSC_01901	Transaldolase/	Down
5	SAOUHSC_01794	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.-)	Down
Membrane Transport			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00177	Maltose/maltodextrin transport system permease protein/	up
2	SAOUHSC_00178	Maltose ABC transporter, permease protein/	up
3	SAOUHSC_02743	Amino acid ABC transporter, permease protein, putative/	up
4	SAOUHSC_02765	Metal-staphylopine import system permease protein CntC/	up
5	SAOUHSC_01991	ABC transporter, permease protein, putative/	up
6	SAOUHSC_02552	Biotin transporter/	up
7	SAOUHSC_02552	Oligopeptide ABC transporter, substrate-binding protein, putative/	up
8	SAOUHSC_02552	ABC transporter domain-containing protein/	up
9	SAOUHSC_02552	Oligopeptide ABC transporter, ATP-binding protein, putative/	up
10	SAOUHSC_02552	ABC transporter domain-containing protein/	up
11	SAOUHSC_02552	Energy-coupling factor transporter transmembrane protein EcfT/	up
12	SAOUHSC_02552	ABC transporter domain-containing protein/	up
13	SAOUHSC_02552	Phosphonate ABC transporter, substrate-binding protein, putative/	up
14	SAOUHSC_02552	Molybdenum ABC transporter, periplasmic molybdate-binding protein/	up
15	SAOUHSC_02552	ABC transporter, substrate-binding protein,	up

		putative/	
16	SAOUHSC_02552	Methionine import ATP-binding protein MetN 2 (EC 7.4.2.11)/	up
17	SAOUHSC_02552	Lipoprotein/	up
18	SAOUHSC_02552	ABC transmembrane type-1 domain-containing protein	up
Membrane Transport			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02848	PTS system glucoside-specific EIICBA component [Includes: Glucoside permease IIC component (PTS system glucoside-specific EIIC component); Glucoside-specific phosphotransferase enzyme IIB component (EC 2.7.1.-) (PTS system glucoside-specific EIIB component); Glucoside-specific phosphotransferase enzyme IIA component (PTS system glucoside-specific EIIA component)]/	up
2	SAOUHSC_02400	PTS system mannitol-specific EIICB component (EC 2.7.1.197) (EIICB-Mtl)/	up
3	SAOUHSC_00155	PTS system glucose-specific EIICBA component (EC 2.7.1.199) (EIICBA-Glc) (EII-Glc) (EIICBA-Glc 1) [Includes: Glucose permease IIC component (PTS system glucose-specific EIIC component); Glucose-specific phosphotransferase enzyme IIB component (PTS system glucose-specific EIIB component); Glucose-specific phosphotransferase enzyme IIA component (PTS system glucose-specific EIIA component)]/	up
4	SAOUHSC_02661	PTS system sucrose-specific IIBC component, putative (EC 2.7.1.69)/	up
5	SAOUHSC_02402	Mannitol-specific phosphotransferase enzyme IIA component (EIIA) (EIII) (PTS system mannitol-specific EIIA component)/	up
6	SAOUHSC_00216	PTS system component/	up
7	SAOUHSC_00311	PTS EIIB type-2 domain-containing protein	up

3.1 Table S8: KEGG analysis of DEGs of MRSA versus Compound 3g

Carbohydrate metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01266	2-oxoacid:acceptor oxidoreductase subunit alpha	up

2	SAOUHSC_01267	2-oxoacid:ferredoxin oxidoreductase subunit beta	up
3	SAOUHSC_00196	enoyl-CoA hydratase (EC 4.2.1.17)/	down
4	SAOUHSC_01103	Succinate dehydrogenase cytochrome b-558 subunit, putative/	down
5	SAOUHSC_02282	Acetolactate synthase (EC 2.2.1.6)/	down
6	SAOUHSC_02921	Alpha-acetolactate decarboxylase (EC 4.1.1.5)/	down
7	SAOUHSC_02283	acetolactate synthase (EC 2.2.1.6)/	down
8	SAOUHSC_00336	Probable acetyl-CoA acyltransferase (EC 2.3.1.9) (Acetoacetyl-CoA thiolase)/	down
9	SAOUHSC_01105	Succinate dehydrogenase iron-sulfur subunit (EC 1.3.5.1)/	down
10	SAOUHSC_01104	succinate dehydrogenase (EC 1.3.5.1)/	down
11	SAOUHSC_02468	Acetolactate synthase, putative (EC 2.2.1.6)/	down
12	SAOUHSC_00086	Diacetyl reductase [(S)-acetoin forming] (EC 1.1.1.304) (Acetoin(diacetyl) reductase) (Meso-2,3-butanediol dehydrogenase)/	down
13	SAOUHSC_02924	Aspartate aminotransferase family protein/	down
14	SAOUHSC_02467	Alpha-acetolactate decarboxylase (EC 4.1.1.5)/	down
15	SAOUHSC_00113	Aldehyde-alcohol dehydrogenase/	down
16	SAOUHSC_00187	Formate acetyltransferase (EC 2.3.1.54) (Pyruvate formate-lyase)	down
Infectious disease: bacterial			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01359	Phosphatidylglycerol lysyltransferase (EC 2.3.2.3) (Lysylphosphatidylglycerol synthase) (LPG synthase) (Multiple peptide resistance factor)/	up
2	SAOUHSC_00392	Staphylococcal superantigen-like 7/	up
3	SAOUHSC_00870	Teichoic acid D-alanyltransferase (EC 2.3.1.-)/	up
4	SAOUHSC_00668	ABC transporter permease, putative/	up
5	SAOUHSC_00871	D-alanyl carrier protein (DCP) (D-alanine--poly(phosphoribitol) ligase subunit 2)/	up
6	SAOUHSC_00869	D-alanine--D-alanyl carrier protein ligase (DCL) (EC 6.2.1.54) (D-alanine--poly(phosphoribitol) ligase subunit 1) (D-alanine-activating enzyme) (DAE)/	up
7	SAOUHSC_00872	Protein DltD/	up
8	SAOUHSC_00545	Serine-aspartate repeat-containing protein D/	down
9	SAOUHSC_01112	FPRL1 inhibitory protein (FLIPr)/	down
10	SAOUHSC_02710	Gamma-hemolysin component B (H-gamma-1) (H-gamma-I) (Leukocidin f subunit)/	down

11	SAOUHSC_02963	Clumping factor B (Fibrinogen receptor B) (Fibrinogen-binding protein B)/	down
12	SAOUHSC_02971	Neutral metalloproteinase (EC 3.4.24.-)/	down
13	SAOUHSC_00544	Serine-aspartate repeat-containing protein C/	down
14	SAOUHSC_00191	Staphylococcal complement inhibitor/	down
15	SAOUHSC_02167	Staphylococcal complement inhibitor (SCIN)/	down
16	SAOUHSC_02798	Surface protein G/	down
17	SAOUHSC_01133	Permease/	down
18	SAOUHSC_01114	Fibrinogen-binding protein/	down
19	SAOUHSC_01115	Staphylococcal complement inhibitor/	down
20	SAOUHSC_02241	Uncharacterized leukocidin-like protein 1/	down
21	SAOUHSC_02171	Staphylokinase/	down
22	SAOUHSC_02243	Uncharacterized leukocidin-like protein 2/	down
23	SAOUHSC_02708	Gamma-hemolysin h-gamma-ii subunit, putative/	down
24	SAOUHSC_02709	Gamma-hemolysin component C (Leukocidin s subunit)/	down
25	SAOUHSC_02169	Chemotaxis inhibitory protein (CHIPS)/	down
26	SAOUHSC_02706	Immunoglobulin-binding protein Sbi/	down
27	SAOUHSC_00069	Immunoglobulin G-binding protein A (IgG-binding protein A) (Staphylococcal protein A) (SpA)/	down
28	SAOUHSC_00399	Staphylococcal superantigen-like 11	down
Amino acid metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02375	S-ribosylhomocysteine lyase (EC 4.4.1.21) (AI-2 synthesis protein) (Autoinducer-2 production protein LuxS)/5'-methylthioadenosine/	up
2	SAOUHSC_01702	S-adenosylhomocysteine nucleosidase (MTA/SAH nucleosidase) (MTAN) (EC 3.2.2.9) (5'-deoxyadenosine nucleosidase) (DOA nucleosidase) (dAdo nucleosidase) (5'-methylthioadenosine nucleosidase) (MTA nucleosidase) (S-adenosylhomocysteine nucleosidase) (AdoHcy nucleosidase) (SAH nucleosidase) (SRH nucleosidase)/	up
3	SAOUHSC_01152	Purine nucleoside phosphorylase/	up
4	SAOUHSC_00422	Trans-sulfuration enzyme family protein, putative/	up
5	SAOUHSC_00421	Tryptophan synthase beta chain-like PALP domain-containing protein/	up
6	SAOUHSC_00013	AB hydrolase-1 domain-containing protein/	down
7	SAOUHSC_01394	Aspartokinase (EC 2.7.2.4)/	down

8	SAOUHSC_01395	Aspartate-semialdehyde dehydrogenase (ASA dehydrogenase) (ASADH) (EC 1.2.1.11) (Aspartate-beta-semialdehyde dehydrogenase)/	down
9	SAOUHSC_00488	Cysteine synthase (EC 2.5.1.47)/	down
10	SAOUHSC_02840	L-serine deaminase/	down
11	SAOUHSC_01320	Homoserine dehydrogenase (EC 1.1.1.3)/	down
12	SAOUHSC_00339	Hcy-binding domain-containing protein/	down
13	SAOUHSC_00341	Cystathionine gamma-synthase/	down
14	SAOUHSC_01322	Homoserine kinase (HK) (HSK) (EC 2.7.1.39)/	down
15	SAOUHSC_02839	L-serine dehydratase (EC 4.3.1.17)/	down
16	SAOUHSC_00340	Trans-sulfuration enzyme family protein/	down
17	SAOUHSC_02922	L-lactate dehydrogenase 2 (L-LDH 2) (EC 1.1.1.27)/	down
18	SAOUHSC_01319	Aspartokinase (EC 2.7.2.4)/	down
19	SAOUHSC_00206	L-lactate dehydrogenase 1 (L-LDH 1) (EC 1.1.1.27)	down
Drug resistance: antimicrobial			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01359	Phosphatidylglycerol lysyltransferase (EC 2.3.2.3) (Lysylphosphatidylglycerol synthase) (LPG synthase) (Multiple peptide resistance factor)/	up
2	SAOUHSC_01838	Serine protease HtrA-like/	up
3	SAOUHSC_00870	Teichoic acid D-alanyltransferase (EC 2.3.1.-)/	up
4	SAOUHSC_00665	Response regulator protein GraR (Glycopeptide resistance-associated protein R)/	up
5	SAOUHSC_00668	ABC transporter permease, putative/	up
6	SAOUHSC_00871	D-alanyl carrier protein (DCP) (D-alanine--poly(phosphoribitol) ligase subunit 2)/	up
7	SAOUHSC_01739	Probable cell wall amidase LytH (EC 3.5.1.-)/	up
8	SAOUHSC_00869	D-alanine--D-alanyl carrier protein ligase (DCL) (EC 6.2.1.54) (D-alanine--poly(phosphoribitol) ligase subunit 1) (D-alanine-activating enzyme) (DAE)/	up
9	SAOUHSC_00872	Protein DltD/	up
10	SAOUHSC_02971	Neutral metalloproteinase (EC 3.4.24.-)/	down
11	SAOUHSC_02171	Staphylokinase	down
Amino acid metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_02558	Urease subunit gamma (EC 3.5.1.5) (Urea	up

		amidohydrolase subunit gamma)/	
2	SAOUHSC_02559	Urease subunit beta (EC 3.5.1.5) (Urea amidohydrolase subunit beta)/	up
3	SAOUHSC_02561	Urease subunit alpha (EC 3.5.1.5) (Urea amidohydrolase subunit alpha)/	up
4	SAOUHSC_00148	Arginine biosynthesis bifunctional protein ArgJ [Cleaved into: Arginine biosynthesis bifunctional protein ArgJ alpha chain; Arginine biosynthesis bifunctional protein ArgJ beta chain] [Includes: Glutamate N-acetyltransferase (EC 2.3.1.35) (Ornithine acetyltransferase) (OATase) (Ornithine transacetylase); Amino-acid acetyltransferase (EC 2.3.1.1) (N-acetylglutamate synthase) (AGSase)]/	down
5	SAOUHSC_01169	Carbamoyl phosphate synthase small chain (EC 6.3.5.5) (Carbamoyl phosphate synthetase glutamine chain)/	down
6	SAOUHSC_01170	Carbamoyl phosphate synthase large chain (EC 6.3.4.16) (EC 6.3.5.5) (Carbamoyl phosphate synthetase ammonia chain)/	down
7	SAOUHSC_00895	Glutamate dehydrogenase/	down
8	SAOUHSC_02134	Nitric oxide synthase oxygenase (EC 1.14.14.47)/	down
9	SAOUHSC_00899	Argininosuccinate synthase (EC 6.3.4.5) (Citrulline--aspartate ligase)/	down
10	SAOUHSC_00898	Argininosuccinate lyase (ASAL) (EC 4.3.2.1) (Argininosuccinase)/	down
11	SAOUHSC_02965	Carbamate kinase 2 (EC 2.7.2.2)/	down
12	SAOUHSC_02968	Ornithine carbamoyltransferase (OTCase) (EC 2.1.3.3)/	down
13	SAOUHSC_01129	Carbamate kinase 1 (EC 2.7.2.2)/	down
14	SAOUHSC_01128	Ornithine carbamoyltransferase (OTCase) (EC 2.1.3.3)/	down
15	SAOUHSC_02969	Arginine deiminase (ADI) (EC 3.5.3.6) (Arginine dihydrolase) (AD)	down
Carbohydrate metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01266	2-oxoacid:acceptor oxidoreductase subunit alpha/	up
2	SAOUHSC_01267	2-oxoacid:ferredoxin oxidoreductase subunit beta/	up
3	SAOUHSC_01983	Fumarate hydratase class II (Fumarase C) (EC 4.2.1.2) (Aerobic fumarase) (Iron-independent fumarase)/	down

4	SAOUHSC_01064	Pyruvate carboxylase (EC 6.4.1.1)/	down
5	SAOUHSC_01103	Succinate dehydrogenase cytochrome b-558 subunit, putative/	down
6	SAOUHSC_01040	Pyruvate dehydrogenase E1 component subunit alpha (EC 1.2.4.1)/	down
7	SAOUHSC_01041	Pyruvate dehydrogenase E1 component subunit beta (EC 1.2.4.1)/	down
8	SAOUHSC_02927	Probable malate:quinone oxidoreductase (EC 1.1.5.4) (MQO) (Malate dehydrogenase [quinone])/	down
9	SAOUHSC_02647	Probable malate:quinone oxidoreductase (EC 1.1.5.4) (MQO) (Malate dehydrogenase [quinone])/	down
10	SAOUHSC_01042	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex (EC 2.3.1.-)/	down
11	SAOUHSC_01416	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex (EC 2.3.1.61) (2-oxoglutarate dehydrogenase complex component E2) (OGDC-E2) (Dihydrolipoamide succinyltransferase component of 2-oxoglutarate dehydrogenase complex)/	down
12	SAOUHSC_01418	2-oxoglutarate dehydrogenase E1 component (EC 1.2.4.2) (Alpha-ketoglutarate dehydrogenase)/	down
13	SAOUHSC_01218	Succinate--CoA ligase [ADP-forming] subunit alpha (EC 6.2.1.5) (Succinyl-CoA synthetase subunit alpha) (SCS-alpha)/Succinate dehydrogenase iron-sulfur subunit (EC 1.3.5.1)/succinate dehydrogenase (EC 1.3.5.1)/Phosphoenolpyruvate carboxykinase (ATP) (PCK) (PEP carboxykinase) (PEPCK) (EC 4.1.1.49)	down
14	SAOUHSC_01105	Succinate--CoA ligase [ADP-forming] subunit alpha (EC 6.2.1.5) (Succinyl-CoA synthetase subunit alpha) (SCS-alpha)/	down
15	SAOUHSC_01104	Succinate dehydrogenase iron-sulfur subunit (EC 1.3.5.1)/	down
16	SAOUHSC_01910	succinate dehydrogenase (EC 1.3.5.1)/Phosphoenolpyruvate carboxykinase (ATP) (PCK) (PEP carboxykinase) (PEPCK) (EC 4.1.1.49)	down
Metabolism			

S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00796	Phosphoglycerate kinase (EC 2.7.2.3)/	up
2	SAOUHSC_02558	Urease subunit gamma (EC 3.5.1.5) (Urea amidohydrolase subunit gamma)/	up
3	SAOUHSC_02559	Urease subunit beta (EC 3.5.1.5) (Urea amidohydrolase subunit beta)/	up
4	SAOUHSC_00798	2,3-bisphosphoglycerate-independent phosphoglycerate mutase (BPG-independent PGAM) (Phosphoglyceromutase) (iPGM) (EC 5.4.2.12)/	up
5	SAOUHSC_01266	2-oxoacid:acceptor oxidoreductase subunit alpha/	up
6	SAOUHSC_02561	Urease subunit alpha (EC 3.5.1.5) (Urea amidohydrolase subunit alpha)/	up
7	SAOUHSC_01267	2-oxoacid:ferredoxin oxidoreductase subunit beta/	up
8	SAOUHSC_01868	Putative dipeptidase SAOUHSC_01868 (EC 3.4.13.-)/	up
9	SAOUHSC_00797	Triosephosphate isomerase (TIM) (TPI) (EC 5.3.1.1) (Triose-phosphate isomerase)/	up
10	SAOUHSC_00359	phosphoglycerate mutase (2,3-diphosphoglycerate-dependent) (EC 5.4.2.11)/	up
11	SAOUHSC_00795	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.-)/	up
12	SAOUHSC_01160	VOC domain-containing protein/	up
13	SAOUHSC_02143	Uncharacterized protein SAOUHSC_02143/	up
14	SAOUHSC_00196	enoyl-CoA hydratase (EC 4.2.1.17)/	down
15	SAOUHSC_01901	Transaldolase/	down
16	SAOUHSC_01983	Fumarate hydratase class II (Fumarase C) (EC 4.2.1.2) (Aerobic fumarase) (Iron-independent fumarase)/	down
17	SAOUHSC_01394	Aspartokinase (EC 2.7.2.4)/	down
18	SAOUHSC_01064	Pyruvate carboxylase (EC 6.4.1.1)/	down
19	SAOUHSC_01395	Aspartate-semialdehyde dehydrogenase (ASA dehydrogenase) (ASADH) (EC 1.2.1.11) (Aspartate-beta-semialdehyde dehydrogenase)/	down
20	SAOUHSC_02875	D-lactate dehydrogenase (EC 1.1.1.28) (D-specific 2-hydroxyacid dehydrogenase)/S	down
21	SAOUHSC_01103	Succinate dehydrogenase cytochrome b-558 subunit, putative/	down
22	SAOUHSC_02793	Phosphoglucomutase (PGM) (EC 5.4.2.2) (Alpha-phosphoglucomutase) (Glucose phosphomutase)/	down
23	SAOUHSC_00488	Cysteine synthase (EC 2.5.1.47)/	down

24	SAOUHSC_01040	Pyruvate dehydrogenase E1 component subunit alpha (EC 1.2.4.1)/	down
25	SAOUHSC_01041	Pyruvate dehydrogenase E1 component subunit beta (EC 1.2.4.1)/	down
26	SAOUHSC_00472	Ribose-phosphate pyrophosphokinase (RPPK) (EC 2.7.6.1) (5-phospho-D-ribosyl alpha-1-diphosphate synthase) (Phosphoribosyl diphosphate synthase) (Phosphoribosyl pyrophosphate synthase) (P-Rib-PP synthase) (PRPP synthase) (PRPPase)/	down
27	SAOUHSC_00574	Phosphate acetyltransferase (EC 2.3.1.8) (Phosphotransacetylase)/	down
28	SAOUHSC_02927	Probable malate:quinone oxidoreductase (EC 1.1.5.4) (MQO) (Malate dehydrogenase [quinone])/	down
29	SAOUHSC_01007	Bifunctional protein FolD [Includes: Methylene tetrahydrofolate dehydrogenase (EC 1.5.1.5); Methenyl tetrahydrofolate cyclohydrolase (EC 3.5.4.9)]/	down
30	SAOUHSC_01397	4-hydroxy-tetrahydrodipicolinate reductase (HTPA reductase) (EC 1.17.1.8)/	down
31	SAOUHSC_00037	FAD/NAD(P)-binding domain-containing protein/	down
32	SAOUHSC_02647	Probable malate:quinone oxidoreductase (EC 1.1.5.4) (MQO) (Malate dehydrogenase [quinone])/	down
33	SAOUHSC_01406	Acylphosphatase (EC 3.6.1.7) (Acylphosphate phosphohydrolase)/	down
34	SAOUHSC_01042	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex (EC 2.3.1.-)/	down
35	SAOUHSC_01416	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex (EC 2.3.1.61) (2-oxoglutarate dehydrogenase complex component E2) (OGDC-E2) (Dihydrolipoamide succinyltransferase component of 2-oxoglutarate dehydrogenase complex)/	down
36	SAOUHSC_02582	Putative formate dehydrogenase SAOUHSC_02582 (EC 1.17.1.9)/	down
37	SAOUHSC_01820	Acetate kinase (EC 2.7.2.1) (Acetokinase)/	down
38	SAOUHSC_00895	Glutamate dehydrogenase/	down
39	SAOUHSC_01320	Homoserine dehydrogenase (EC 1.1.1.3)/	down
40	SAOUHSC_00339	Hcy-binding domain-containing protein/	down

41	SAOUHSC_00336	Probable acetyl-CoA acyltransferase (EC 2.3.1.9) (Acetoacetyl-CoA thiolase)/	down
42	SAOUHSC_01321	Threonine synthase (EC 4.2.3.1)/	down
43	SAOUHSC_00195	Probable acetyl-CoA acyltransferase (EC 2.3.1.16) (Putative acetyl-CoA C-acetyltransferase VraB)/	down
44	SAOUHSC_01418	2-oxoglutarate dehydrogenase E1 component (EC 1.2.4.2) (Alpha-ketoglutarate dehydrogenase)/	down
45	SAOUHSC_01322	Homoserine kinase (HK) (HSK) (EC 2.7.1.39)/	down
46	SAOUHSC_01218	Succinate--CoA ligase [ADP-forming] subunit alpha (EC 6.2.1.5) (Succinyl-CoA synthetase subunit alpha) (SCS-alpha)/	down
47	SAOUHSC_01105	Succinate dehydrogenase iron-sulfur subunit (EC 1.3.5.1)/	down
48	SAOUHSC_02830	D-lactate dehydrogenase (EC 1.1.1.28) (D-specific 2-hydroxyacid dehydrogenase)/	down
49	SAOUHSC_02822	Fructose-1,6-bisphosphatase class 3 (FBPase class 3) (EC 3.1.3.11) (D-fructose-1,6-bisphosphate 1-phosphohydrolase class 3)/	down
50	SAOUHSC_01104	succinate dehydrogenase (EC 1.3.5.1)/	down
51	SAOUHSC_02678	Respiratory nitrate reductase, gamma subunit (EC 1.7.99.4)/	down
52	SAOUHSC_01846	Putative long chain fatty acid-CoA ligase VraA (EC 6.2.1.1) (Acyl-CoA synthetase)/	down
53	SAOUHSC_02965	Carbamate kinase 2 (EC 2.7.2.2)/	down
54	SAOUHSC_01910	Phosphoenolpyruvate carboxykinase (ATP) (PCK) (PEP carboxykinase) (PEPCK) (EC 4.1.1.49)/	down
55	SAOUHSC_01794	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.-)/	down
56	SAOUHSC_02924	Aspartate aminotransferase family protein/	down
57	SAOUHSC_02922	L-lactate dehydrogenase 2 (L-LDH 2) (EC 1.1.1.27)/	down
58	SAOUHSC_01319	Aspartokinase (EC 2.7.2.4)/	down
59	SAOUHSC_00716	DoxX family protein/	down
60	SAOUHSC_02703	2,3-bisphosphoglycerate-dependent phosphoglycerate mutase (BPG-dependent PGAM) (PGAM) (Phosphoglyceromutase) (dPGM) (EC 5.4.2.11)/	down
61	SAOUHSC_00113	Aldehyde-alcohol dehydrogenase/	down
62	SAOUHSC_02808	Gluconate kinase (EC 2.7.1.12)/	down
63	SAOUHSC_00310	Ascorbate-specific PTS system EIIC component (Ascorbate-specific permease IIC	down

		component UlaA)/	
64	SAOUHSC_02684	Assimilatory nitrite reductase [NAD(P)H], large subunit, putative (EC 1.7.1.4)/	down
65	SAOUHSC_00132	Putative aldehyde dehydrogenase AldA (EC 1.2.1.3)/	down
66	SAOUHSC_02682	uroporphyrinogen-III C-methyltransferase (EC 2.1.1.107)/	down
67	SAOUHSC_02680	Nitrate reductase, beta subunit (EC 1.7.99.4)/	down
68	SAOUHSC_01129	Carbamate kinase 1 (EC 2.7.2.2)/	down
69	SAOUHSC_02681	nitrate reductase (quinone) (EC 1.7.5.1)/	down
70	SAOUHSC_00311	PTS EIIB type-2 domain-containing protein/	down
71	SAOUHSC_00312	PTS EIIA type-2 domain-containing protein/	down
72	SAOUHSC_02683	Assimilatory nitrite reductase [NAD(P)H], small subunit, putative (EC 1.7.1.4)/	down
73	SAOUHSC_00608	Alcohol dehydrogenase (ADH) (EC 1.1.1.1)/	down
74	SAOUHSC_00206	L-lactate dehydrogenase 1 (L-LDH 1) (EC 1.1.1.27)/	down
75	SAOUHSC_00187	Formate acetyltransferase (EC 2.3.1.54) (Pyruvate formate-lyase)	down
Energy metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01032	Cytochrome d ubiquinol oxidase, subunit II, putative (EC 1.10.3.-)/	up
2	SAOUHSC_01031	Cytochrome d ubiquinol oxidase, subunit I, putative/	up
3	SAOUHSC_00999	Probable quinol oxidase subunit 4 (EC 1.10.3.-) (Quinol oxidase polypeptide IV)/	down
4	SAOUHSC_02347	ATP synthase subunit b (ATP synthase F(0) sector subunit b) (ATPase subunit I) (F-type ATPase subunit b) (F-ATPase subunit b)/	down
5	SAOUHSC_02345	ATP synthase subunit alpha (EC 7.1.2.2) (ATP synthase F1 sector subunit alpha) (F-ATPase subunit alpha)/	down
6	SAOUHSC_02343	ATP synthase gamma chain (ATP synthase F1 sector gamma subunit) (F-ATPase gamma subunit)/	down
7	SAOUHSC_01103	Succinate dehydrogenase cytochrome b-558 subunit, putative/	down
8	SAOUHSC_01000	Probable quinol oxidase subunit 3 (EC 1.10.3.-) (Quinol oxidase polypeptide III)/	down
9	SAOUHSC_01002	Probable quinol oxidase subunit 2 (EC 1.10.3.-) (Quinol oxidase polypeptide II)/	down
10	SAOUHSC_01001	Probable quinol oxidase subunit 1 (EC 1.10.3.-) (Quinol oxidase polypeptide I)/	down
11	SAOUHSC_02349	ATP synthase subunit c (ATP synthase F(0)	down

		sector subunit c) (F-type ATPase subunit c) (F-ATPase subunit c) (Lipid-binding protein)/	
12	SAOUHSC_02341	ATP synthase subunit beta (EC 7.1.2.2) (ATP synthase F1 sector subunit beta) (F-ATPase subunit beta)/	down
13	SAOUHSC_02340	ATP synthase epsilon chain (ATP synthase F1 sector epsilon subunit) (F-ATPase epsilon subunit)/	down
14	SAOUHSC_01105	Succinate dehydrogenase iron-sulfur subunit (EC 1.3.5.1)/	down
15	SAOUHSC_01104	succinate dehydrogenase (EC 1.3.5.1)	down
Glycan biosynthesis and metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00762	Undecaprenyl/decaprenyl-phosphate alpha-N-acetylglucosaminyl 1-phosphate transferase/	up
2	SAOUHSC_00691	Undecaprenyl-diphosphatase (EC 3.6.1.27) (Bacitracin resistance protein) (Undecaprenyl pyrophosphate phosphatase)/	up
3	SAOUHSC_01361	Regulatory protein MsrR/	up
4	SAOUHSC_00223	Teichoic acid glycerol-phosphate transferase (EC 2.7.8.45)/	up
5	SAOUHSC_00997	Uncharacterized protein SAOUHSC_00997 (ORF1)/	up
6	SAOUHSC_00870	Teichoic acid D-alanyltransferase (EC 2.3.1.-)/	up
7	SAOUHSC_00728	Lipoteichoic acid synthase [Cleaved into: Glycerol phosphate lipoteichoic acid synthase (LTA synthase) (EC 2.7.8.-) (Polyglycerol phosphate synthase); Processed glycerol phosphate lipoteichoic acid synthase]/	up
8	SAOUHSC_01213	YfhO family protein/	up
9	SAOUHSC_00117	Capsular polysaccharide biosynthesis protein Cap5D, putative/	up
10	SAOUHSC_00227	Teichoic acid ribitol-phosphate polymerase TarL (EC 2.7.8.14) (Poly(ribitol phosphate) polymerase TarL) (Ribitol-phosphate polymerase TarL) (Tar polymerase TarL)/	up
11	SAOUHSC_00871	D-alanyl carrier protein (DCP) (D-alanine--poly(phosphoribitol) ligase subunit 2)/	up
12	SAOUHSC_00713	Glycosyltransferase 2-like domain-containing protein/	up
13	SAOUHSC_00953	Processive diacylglycerol beta-glucosyltransferase (EC 2.4.1.315) (Beta-diglucosyldiacylglycerol synthase) (Beta-DGS) (DGlcDAG synthase) (Glc2-DAG	up

		synthase) (Beta-gentiobiosyldiacylglycerol synthase) (Beta-monoglucosyldiacylglycerol synthase) (Beta-MGS) (MGlcDAG synthase) (Diglucosyl diacylglycerol synthase (1,6-linking)) (Glucosyl-beta-1,6-glucosyldiacylglycerol synthase) (UDP glucosyltransferase) (UDP-glucose:1,2-diacylglycerol-3-beta-D-glucosyltransferase)/	
14	SAOUHSC_00869	D-alanine--D-alanyl carrier protein ligase (DCL) (EC 6.2.1.54) (D-alanine--poly(phosphoribitol) ligase subunit 1) (D-alanine-activating enzyme) (DAE)/	up
15	SAOUHSC_00872	Protein DltD/	up
16	SAOUHSC_00222	Teichoic acid ribitol-phosphate polymerase TarK (EC 2.7.8.14) (Poly(ribitol phosphate) polymerase TarK) (Ribitol-phosphate polymerase TarK) (Tar polymerase TarK)	down
Metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00914	2-isopropylmalate synthase (EC 2.3.3.13)/	up
2	SAOUHSC_01266	2-oxoacid:acceptor oxidoreductase subunit alpha/	up
3	SAOUHSC_01267	2-oxoacid:ferredoxin oxidoreductase subunit beta/	up
4	SAOUHSC_02286	3-isopropylmalate dehydrogenase (EC 1.1.1.85) (3-IPM-DH) (Beta-IPM dehydrogenase) (IMDH)/	down
5	SAOUHSC_01611	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex (EC 2.3.1.-)/	down
6	SAOUHSC_00148	Arginine biosynthesis bifunctional protein ArgJ [Cleaved into: Arginine biosynthesis bifunctional protein ArgJ alpha chain; Arginine biosynthesis bifunctional protein ArgJ beta chain] [Includes: Glutamate N-acetyltransferase (EC 2.3.1.35) (Ornithine acetyltransferase) (OATase) (Ornithine transacetylase); Amino-acid acetyltransferase (EC 2.3.1.1) (N-acetylglutamate synthase) (AGSase)]/	down
7	SAOUHSC_01394	Aspartokinase (EC 2.7.2.4)/	down
8	SAOUHSC_01395	Aspartate-semialdehyde dehydrogenase (ASA dehydrogenase) (ASADH) (EC 1.2.1.11) (Aspartate-beta-semialdehyde dehydrogenase)/	down
9	SAOUHSC_01612	2-oxoisovalerate dehydrogenase, E1	down

		component, beta subunit, putative (EC 1.2.4.1)/	
10	SAOUHSC_01040	Pyruvate dehydrogenase E1 component subunit alpha (EC 1.2.4.1)/	down
11	SAOUHSC_01041	Pyruvate dehydrogenase E1 component subunit beta (EC 1.2.4.1)/	down
12	SAOUHSC_02282	Acetolactate synthase (EC 2.2.1.6)/	down
13	SAOUHSC_01042	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex (EC 2.3.1.-)/	down
14	SAOUHSC_02921	Alpha-acetolactate decarboxylase (EC 4.1.1.5)/	down
15	SAOUHSC_01613	2-oxoisovalerate dehydrogenase subunit alpha (EC 1.2.4.4) (Branched-chain alpha-keto acid dehydrogenase E1 component alpha chain)/	down
16	SAOUHSC_02283	acetolactate synthase (EC 2.2.1.6)/	down
17	SAOUHSC_01416	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex (EC 2.3.1.61) (2-oxoglutarate dehydrogenase complex component E2) (OGDC-E2) (Dihydrolipoamide succinyltransferase component of 2-oxoglutarate dehydrogenase complex)/	down
18	SAOUHSC_01418	2-oxoglutarate dehydrogenase E1 component (EC 1.2.4.2) (Alpha-ketoglutarate dehydrogenase)/	down
19	SAOUHSC_02468	Acetolactate synthase, putative (EC 2.2.1.6)/	down
20	SAOUHSC_02281	Dihydroxy-acid dehydratase (DAD) (EC 4.2.1.9)/	down
21	SAOUHSC_02467	Alpha-acetolactate decarboxylase (EC 4.1.1.5)/	down
22	SAOUHSC_01319	Aspartokinase (EC 2.7.2.4)	down

3.2 Table S9: KEGG analysis of DEGs of MRSA versus Compound 3n

Infectious disease: bacterial			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_00812	Clumping factor A (Fibrinogen receptor A) (Fibrinogen-binding protein A)	up
2	SAOUHSC_02963	Clumping factor B (Fibrinogen receptor B) (Fibrinogen-binding protein B)	up
3	SAOUHSC_01081	Iron-regulated surface determinant protein A (Fur-regulated protein A) (Staphylococcal transferrin-binding protein A)	down

4	SAOUHSC_00871	D-alanyl carrier protein (DCP) (D-alanine--poly(phosphoribitol) ligase subunit 2)	down
5	SAOUHSC_00390	Staphylococcal superantigen-like 5	down
6	SAOUHSC_02971	Neutral metalloproteinase (EC 3.4.24.-)	down
7	SAOUHSC_02161	MHC class II analog protein	down
8	SAOUHSC_02710	Gamma-hemolysin component B (H-gamma-1) (H-gamma-I) (Leukocidin f subunit)	down
9	SAOUHSC_01114	Fibrinogen-binding protein	down
10	SAOUHSC_02709	Gamma-hemolysin component C (Leukocidin s subunit)	down
11	SAOUHSC_00191	Staphylococcal complement inhibitor	down
12	SAOUHSC_02171	Staphylokinase	down
13	SAOUHSC_01115	Staphylococcal complement inhibitor	down
14	SAOUHSC_02708	Gamma-hemolysin h-gamma-ii subunit, putative	down
15	SAOUHSC_01112	FPRL1 inhibitory protein (FLIPr)	down
16	SAOUHSC_00069	Immunoglobulin G-binding protein A (IgG-binding protein A) (Staphylococcal protein A) (SpA)	down
17	SAOUHSC_02706	Immunoglobulin-binding protein Sbi	down
18	SAOUHSC_02167	Staphylococcal complement inhibitor (SCIN)	down
19	SAOUHSC_02243	Uncharacterized leukocidin-like protein 2	down
20	SAOUHSC_02241	Uncharacterized leukocidin-like protein 1	down
21	SAOUHSC_02169	Chemotaxis inhibitory protein (CHIPS)	down
22	SAOUHSC_00399	Staphylococcal superantigen-like 11	down
Amino acid metabolism			
S. No.	Gene Id	Annotation	Regulation
1	SAOUHSC_01012	Phosphoribosylformylglycinamide synthase subunit PurQ (FGAM synthase) (EC 6.3.5.3) (Formylglycinamide ribonucleotide amidotransferase subunit I) (FGAR amidotransferase I) (FGAR-AT I) (Glutaminase PurQ) (EC 3.5.1.2) (Phosphoribosylformylglycinamide synthase subunit I)	up
2	SAOUHSC_00899	Argininosuccinate synthase (EC 6.3.4.5) (Citrulline--aspartate ligase)	up
3	SAOUHSC_02558	Urease subunit gamma (EC 3.5.1.5) (Urea amidohydrolase subunit gamma)	up
4	SAOUHSC_02559	Urease subunit beta (EC 3.5.1.5) (Urea amidohydrolase subunit beta)	up
5	SAOUHSC_02561	Urease subunit alpha (EC 3.5.1.5) (Urea amidohydrolase subunit alpha)	up
6	SAOUHSC_01170	Carbamoyl phosphate synthase large chain	down

		(EC 6.3.4.16) (EC 6.3.5.5) (Carbamoyl phosphate synthetase ammonia chain)	
7	SAOUHSC_02965	Carbamate kinase 2 (EC 2.7.2.2)	down
8	SAOUHSC_01128	Ornithine carbamoyltransferase (OTCase) (EC 2.1.3.3)	down
9	SAOUHSC_01129	Carbamate kinase 1 (EC 2.7.2.2)	down
10	SAOUHSC_02969	Arginine deiminase (ADI) (EC 3.5.3.6) (Arginine dihydrolase) (AD)	down
11	SAOUHSC_02968	Ornithine carbamoyltransferase (OTCase) (EC 2.1.3.3)	down