

Synthesis and Antibacterial Evaluation of Quinoline-Sulfonamide Hybrid Compounds: A Promising Strategy Against Bacterial Resistance

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Table S1: Minimum inhibitory concentration (MIC) of compound QS-3 and standard drug CIP in µg/mL.

| Compound | <i>E. coli</i> | <i>E. faecalis</i> | <i>P. aeruginosa</i> | <i>K. pneumoniae</i> | <i>Salmonella typhi</i> |
|----------|----------------|--------------------|----------------------|----------------------|-------------------------|
| QS-3 | 128 | 128 | 64 | 256 | 512 |
| CIP | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |

Table S2: Zone of inhibition (mm) against environmental Multidrug-resistant bacterial isolates.

| S. No. | Isolate Name | QS-3 | AMP | CIP |
|--------|--------------|------|-----|-----|
| 1. | EJH01 | - | - | 15 |
| 2. | EJH02 | - | 30 | 26 |
| 3. | EJH04 | - | - | - |
| 4. | EJH05 | - | 20 | 25 |
| 5. | EJH07 | - | 25 | 22 |
| 6. | EJH11 | - | 21 | 26 |
| 7. | EJH12 | - | - | 25 |
| 8. | EJH13 | - | - | 20 |
| 9. | EJH14 | - | - | 22 |
| 10. | EJH15 | - | 20 | 17 |
| 11. | EJH18 | - | 17 | 25 |
| 12. | EJH19 | - | 17 | 21 |
| 13. | EJH20 | - | 20 | 19 |
| 14. | EJH21 | - | 18 | 26 |
| 15. | EJH22 | - | 32 | 14 |
| 16. | EJH23 | - | 20 | 24 |
| 17. | EJH24 | - | 23 | 28 |
| 18. | EJH25 | -- | 22 | 21 |
| 19. | A200 | - | - | 18 |
| 20. | AA 201 | - | - | 16 |

| | | | | |
|-----|--------|---|----|----|
| 21. | AA 202 | 8 | - | - |
| 22. | AA 209 | - | 30 | 21 |
| 23. | AA 216 | - | - | 24 |
| 24. | AA 221 | - | - | 21 |
| 25. | AA 224 | - | - | 11 |
| 26. | AA 237 | - | 26 | 25 |
| 27. | AA 240 | - | 23 | 25 |
| 28. | AA 243 | - | 20 | 19 |
| 29. | AA 245 | - | 18 | 22 |
| 30. | AA 248 | - | 25 | 27 |
| 31. | AA 261 | - | 25 | 29 |
| 32. | AA 269 | - | - | - |
| 33. | AA 273 | - | 15 | 14 |
| 34. | AA 276 | - | 22 | 23 |
| 35. | AA 290 | 8 | - | - |

Table S3. Drug ability or Lipinski's 'rule-of-five' data of compounds QS1-QS12.

| Compounds | Molecular Wt. | No. of HBA | No. of HBD | Mol log P | Molar Refractivity (MR) | Lipinski violation |
|-----------|---------------|------------|------------|-----------|-------------------------|--------------------|
| QS-1 | 460.94 | 4 | 2 | 3.13 | 128.71 | 0 |
| QS-2 | 427.88 | 4 | 2 | 3.59 | 113.37 | 0 |
| QS-3 | 439.91 | 4 | 2 | 2.88 | 119.9 | 0 |
| QS-4 | 459.95 | 3 | 2 | 3.88 | 130.92 | 0 |
| QS-5 | 451.97 | 3 | 2 | 3.85 | 127.99 | 0 |

| | | | | | | |
|-------|--------|---|---|------|--------|---|
| QS-6 | 485.98 | 3 | 2 | 4.25 | 138.85 | 1 |
| QS-7 | 460.94 | 4 | 2 | 3.13 | 128.71 | 0 |
| QS-8 | 427.88 | 4 | 2 | 3.59 | 113.37 | 0 |
| QS-9 | 439.91 | 4 | 2 | 2.88 | 119.9 | 0 |
| QS-10 | 459.95 | 3 | 2 | 3.88 | 130.92 | 0 |
| QS-11 | 451.97 | 3 | 2 | 3.85 | 127.99 | 0 |
| QS-12 | 485.98 | 3 | 2 | 4.25 | 138.85 | 1 |

NMR spectrum of compound QS1-QS12

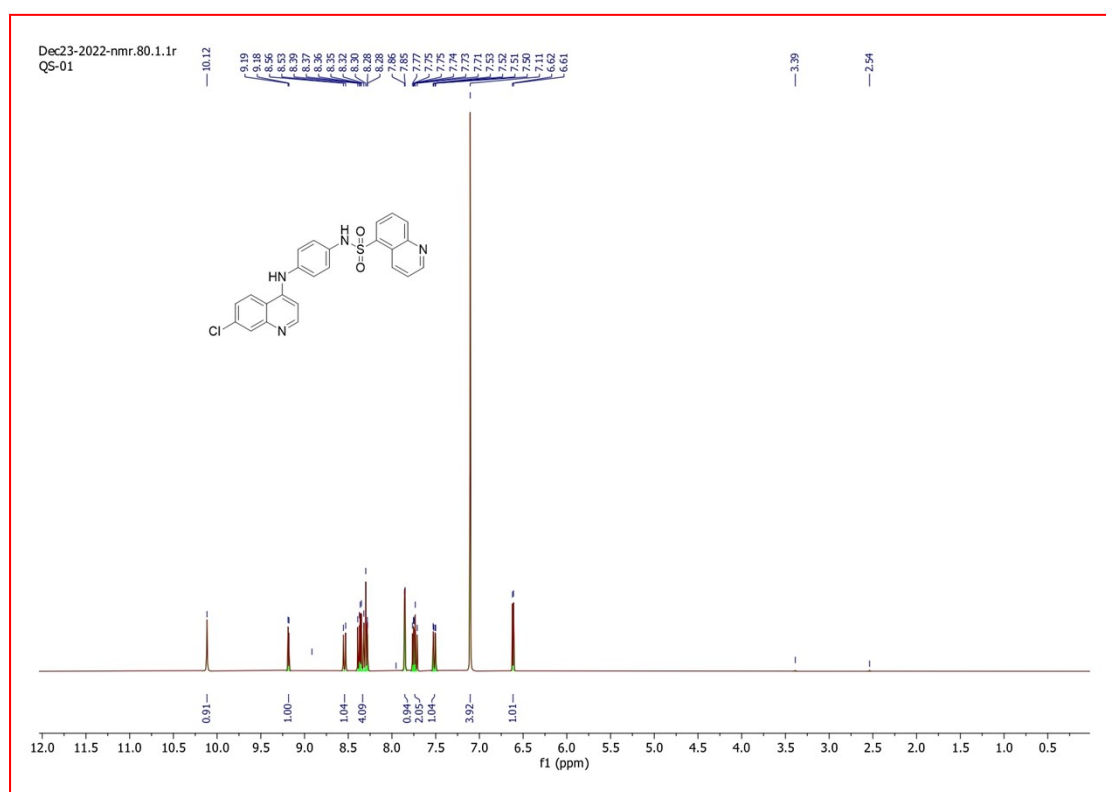


Figure.- S1. ¹H NMR Spectrum of compound (QS-1)

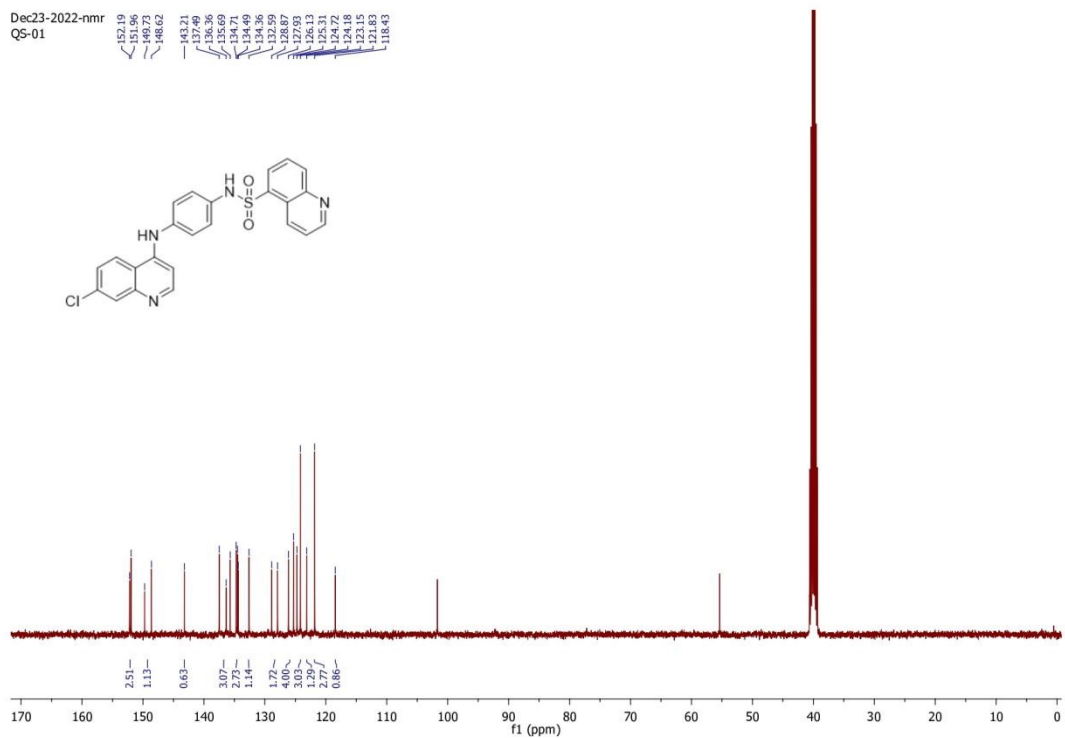


Figure.- S2. ¹³C NMR Spectrum of compound (QS-1)

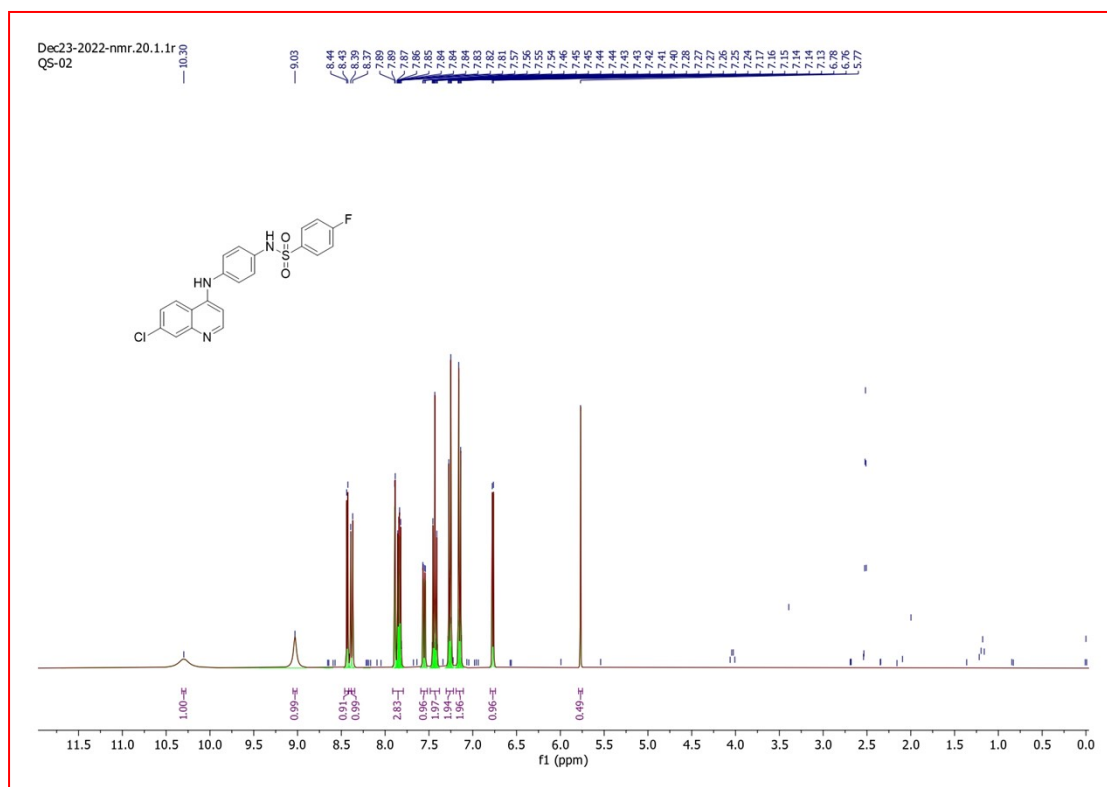


Figure-S3. ¹H NMR Spectrum of compound (QS-2)

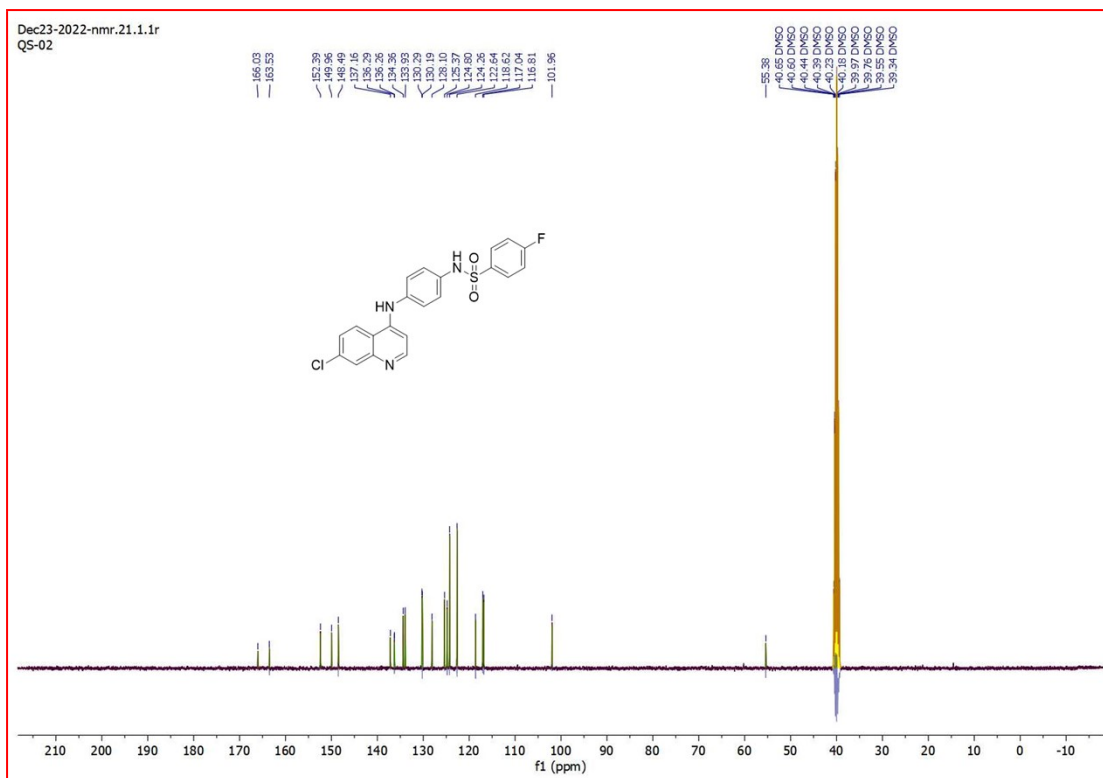


Figure-S4. ^{13}C NMR Spectrum of compound (QS-2)

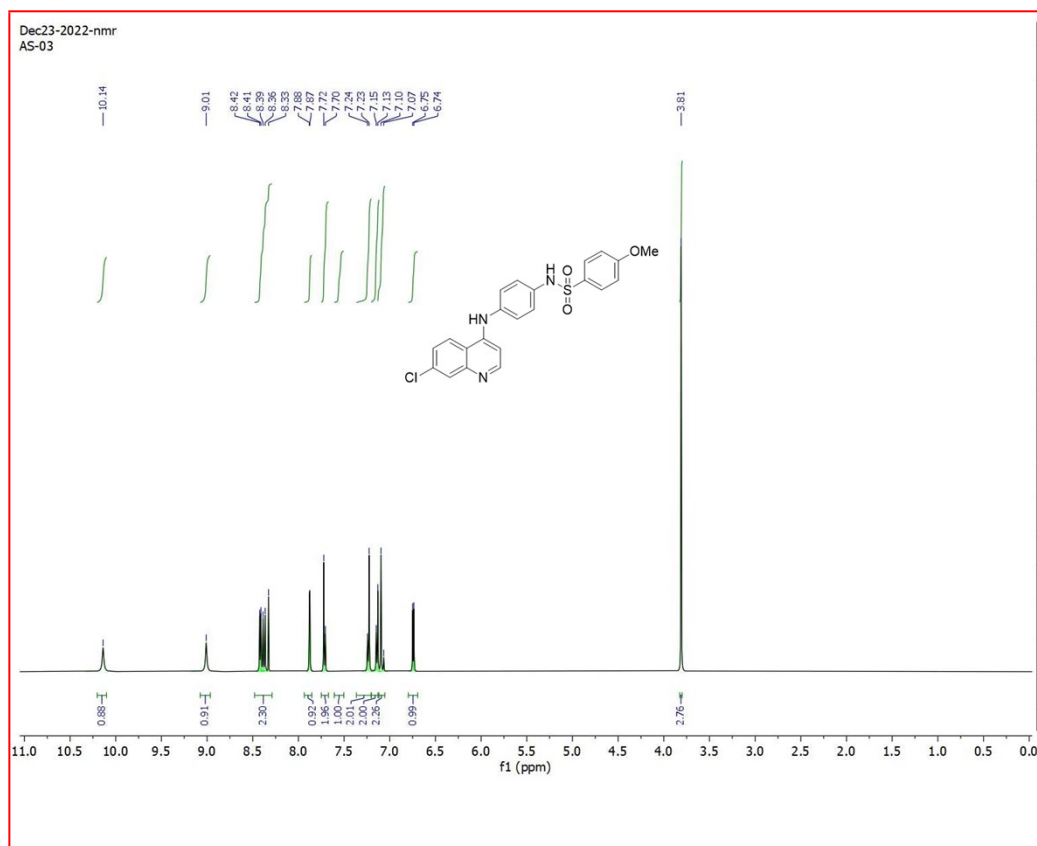


Figure-S5. ^1H NMR Spectrum of compound (QS-3)

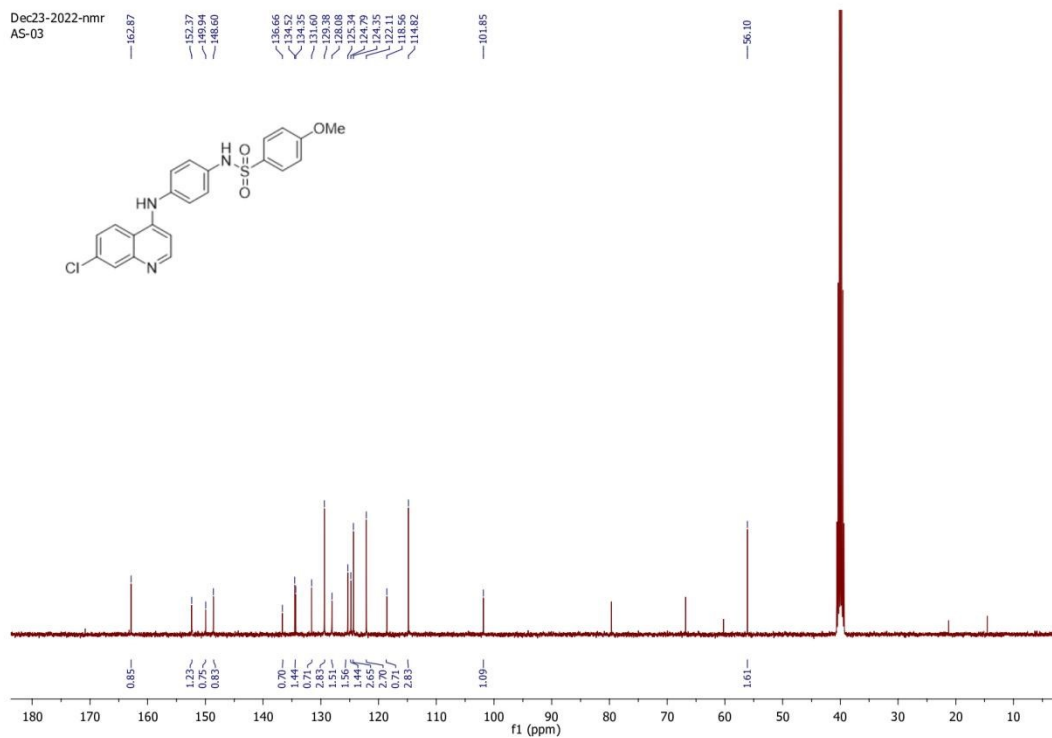


Figure-S6. ¹³C NMR Spectrum of compound (QS-3)

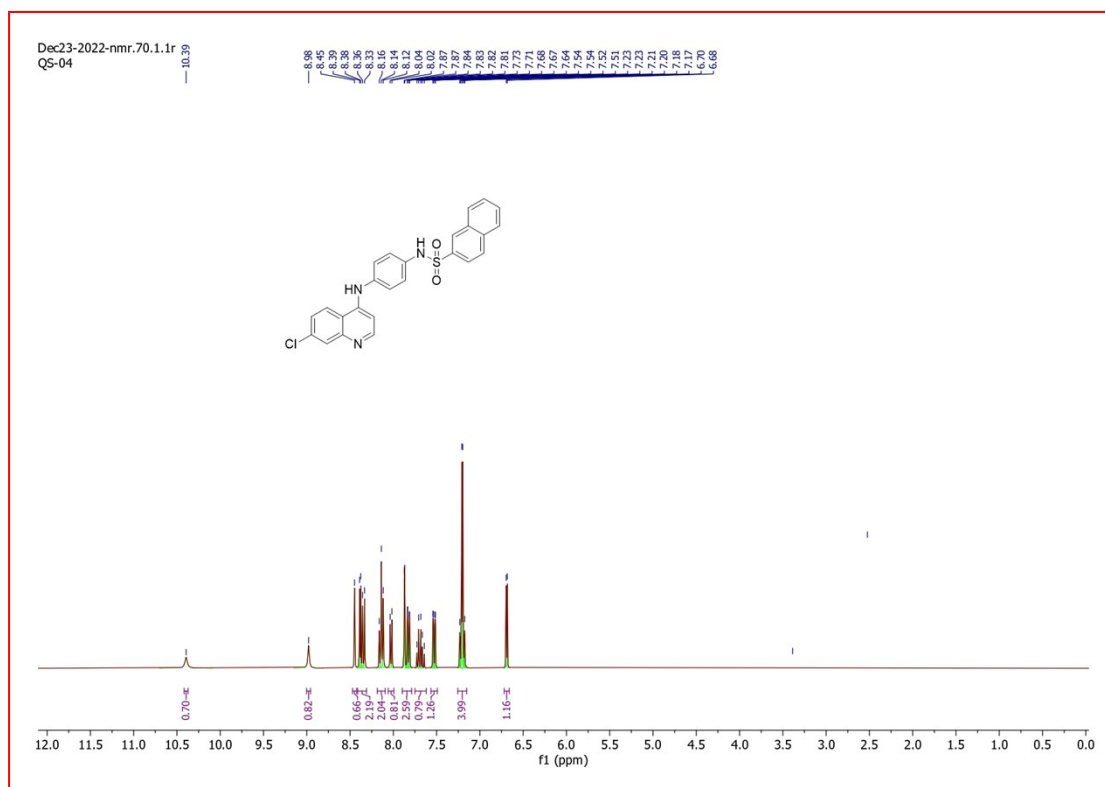


Figure.- S7. ¹H NMR Spectrum of compound (QS-4)

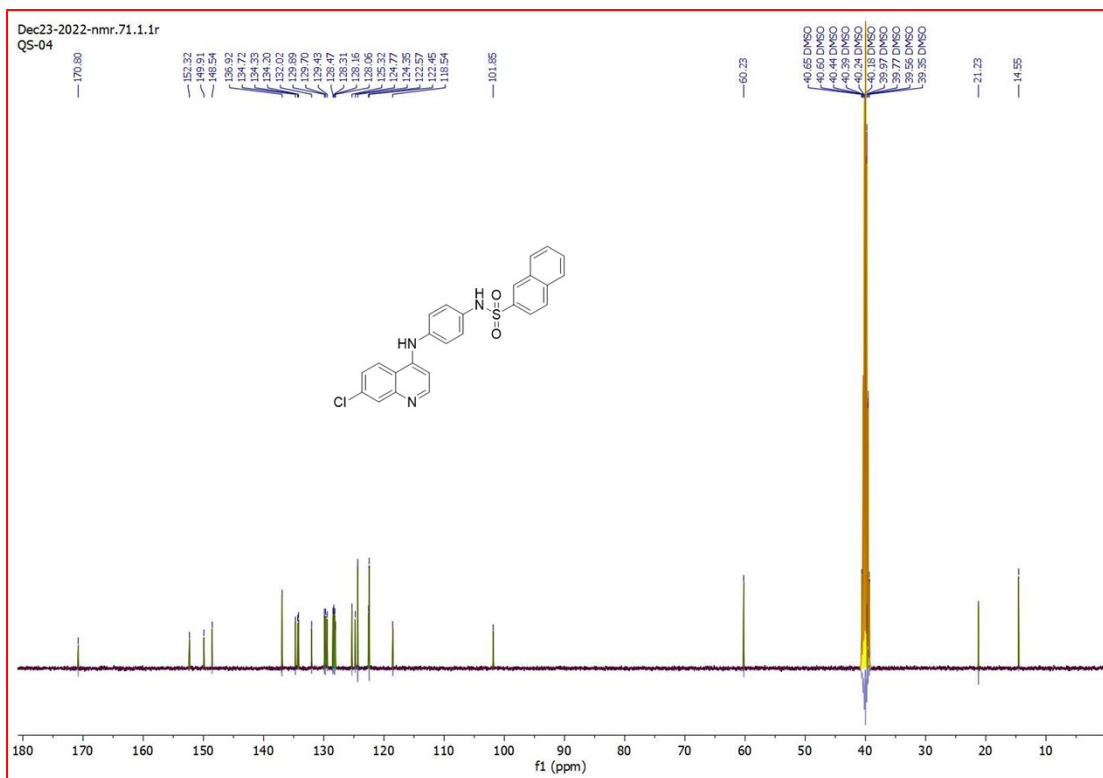


Figure.- S8. ¹³C NMR Spectrum of compound (QS-4)

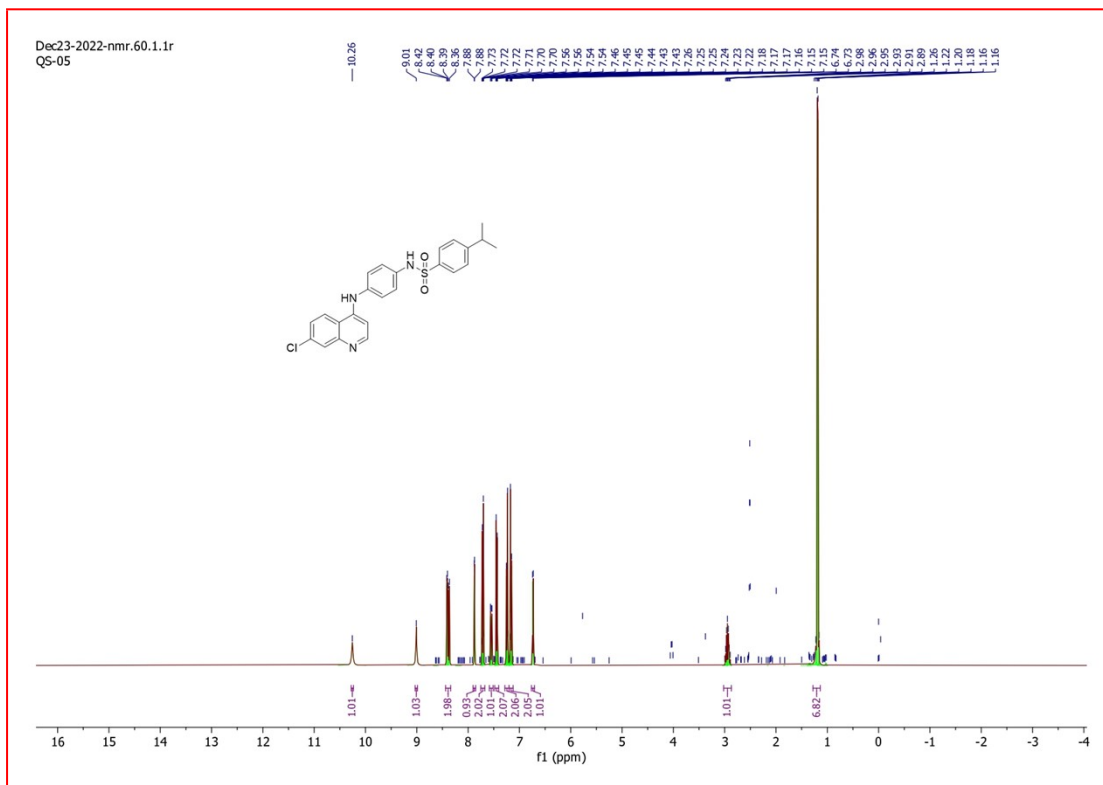


Figure.- S9. ¹H NMR Spectrum of compound (QS-5)

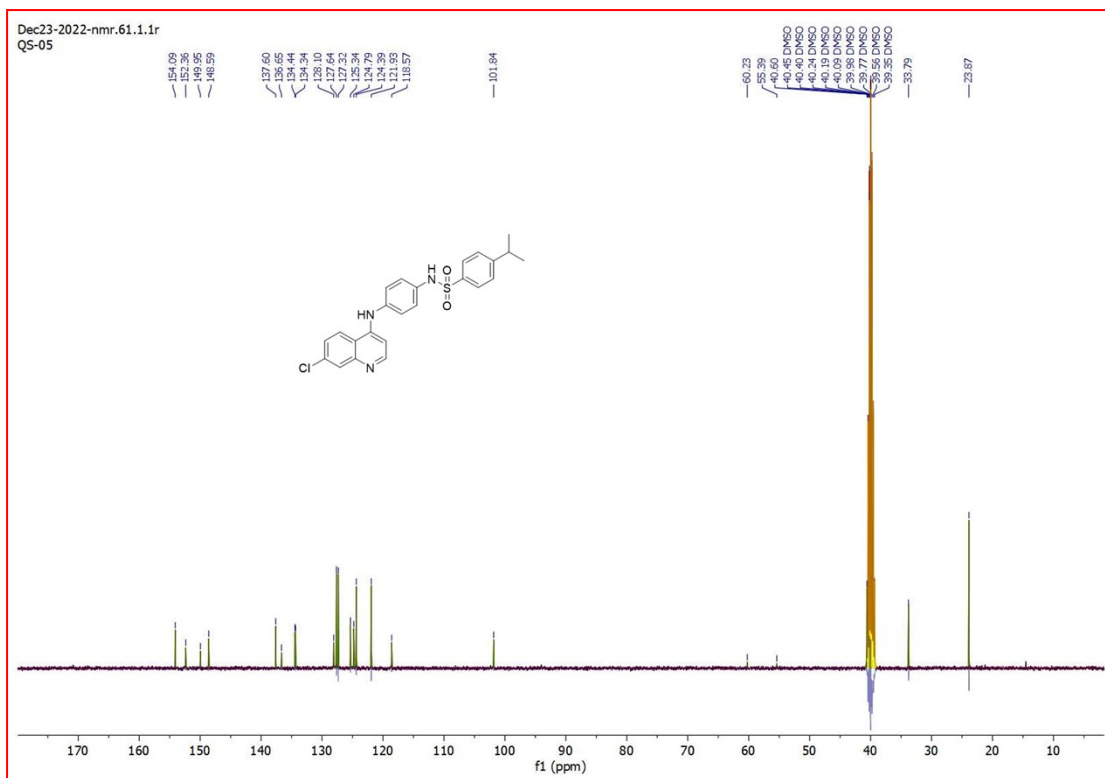


Figure.- S10. ¹³C NMR Spectrum of compound (QS-5)

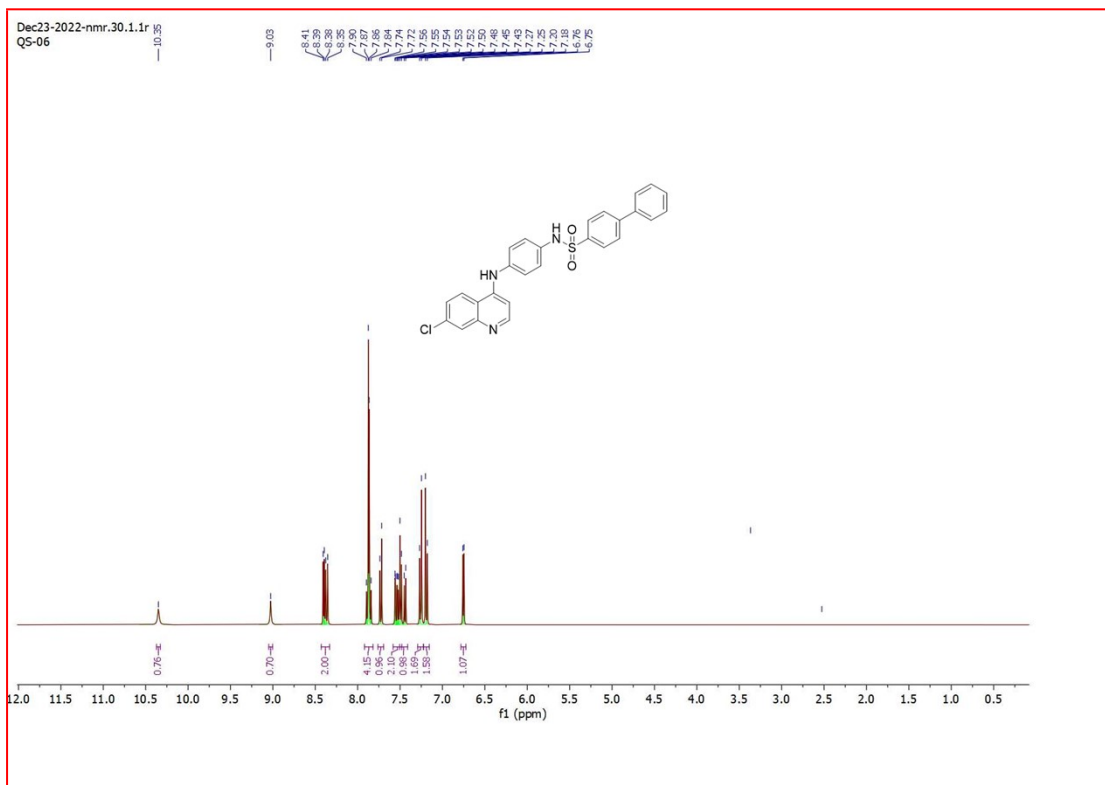


Figure.- S11. ¹H NMR Spectrum of compound (QS-6)

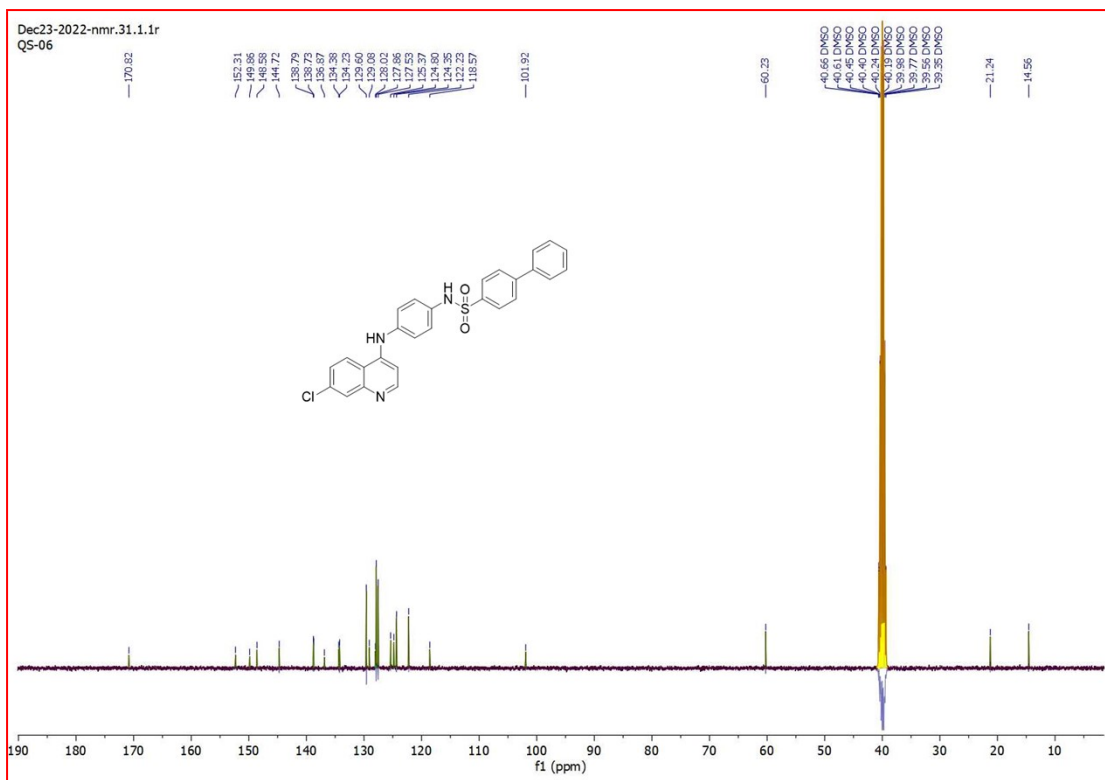


Figure.- S12. ¹³C NMR Spectrum of compound (QS-6)

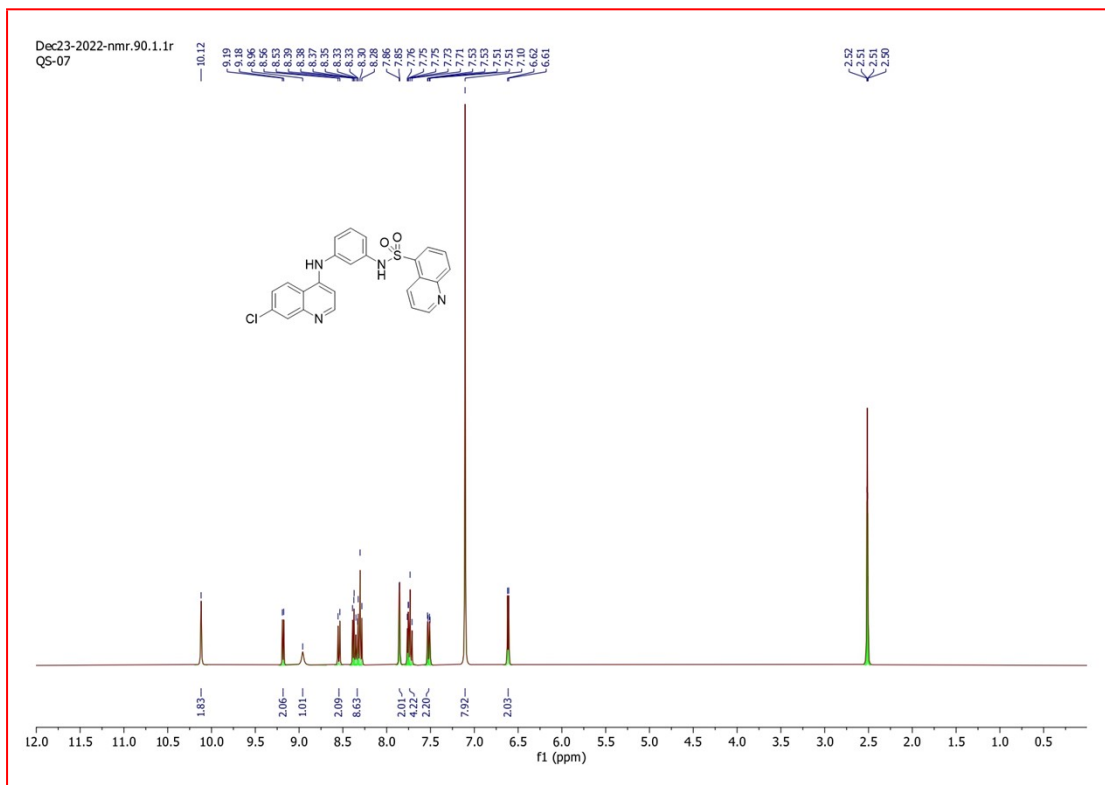


Figure.- S13. ¹H NMR Spectrum of compound (QS-7)

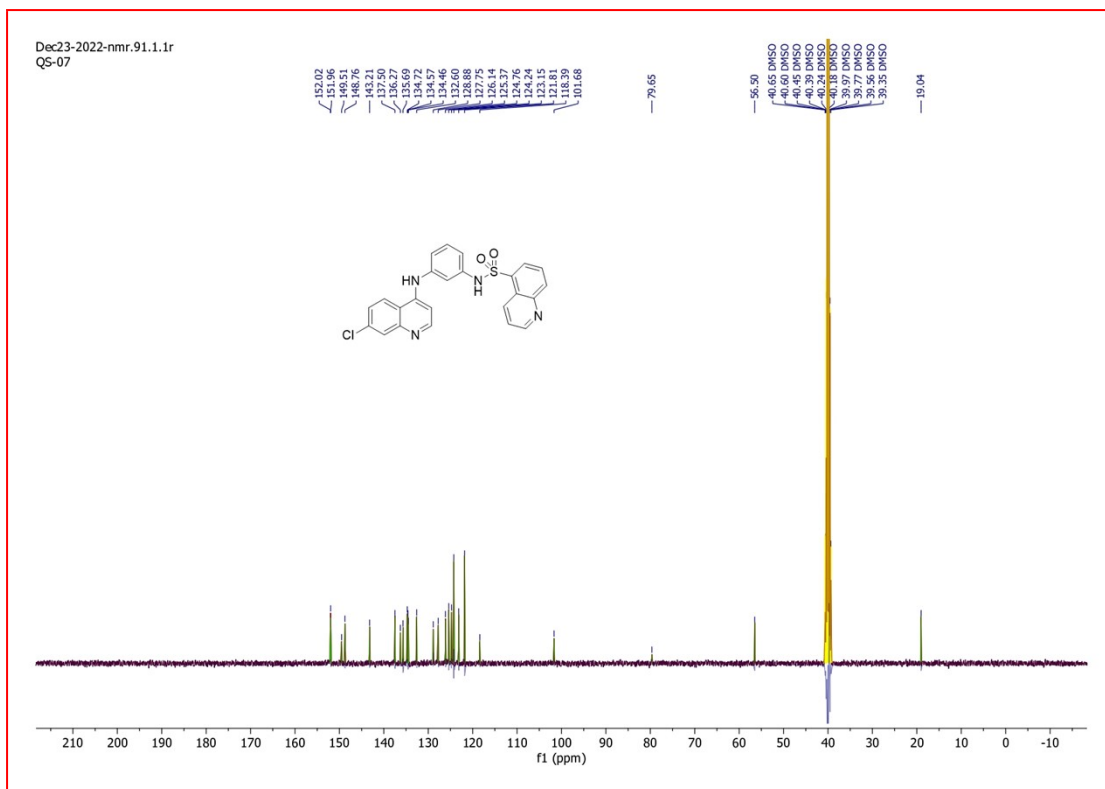


Figure.- S14. ¹³C NMR Spectrum of compound (QS-7)

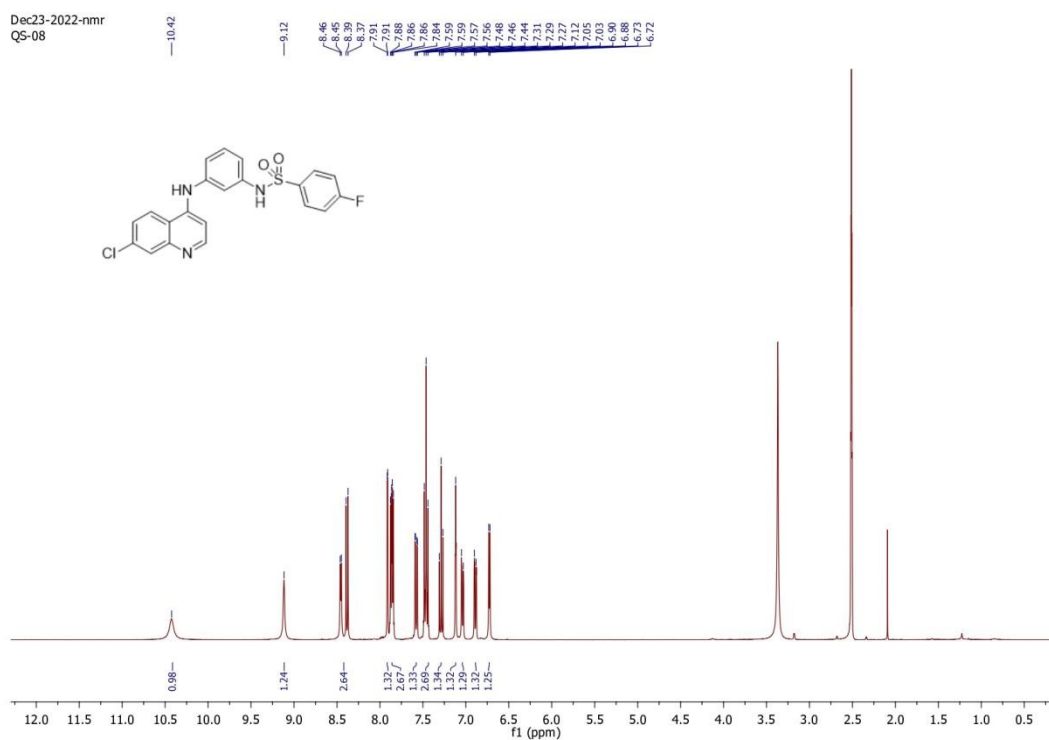


Figure.- S15. ¹H NMR Spectrum of compound (QS-8)

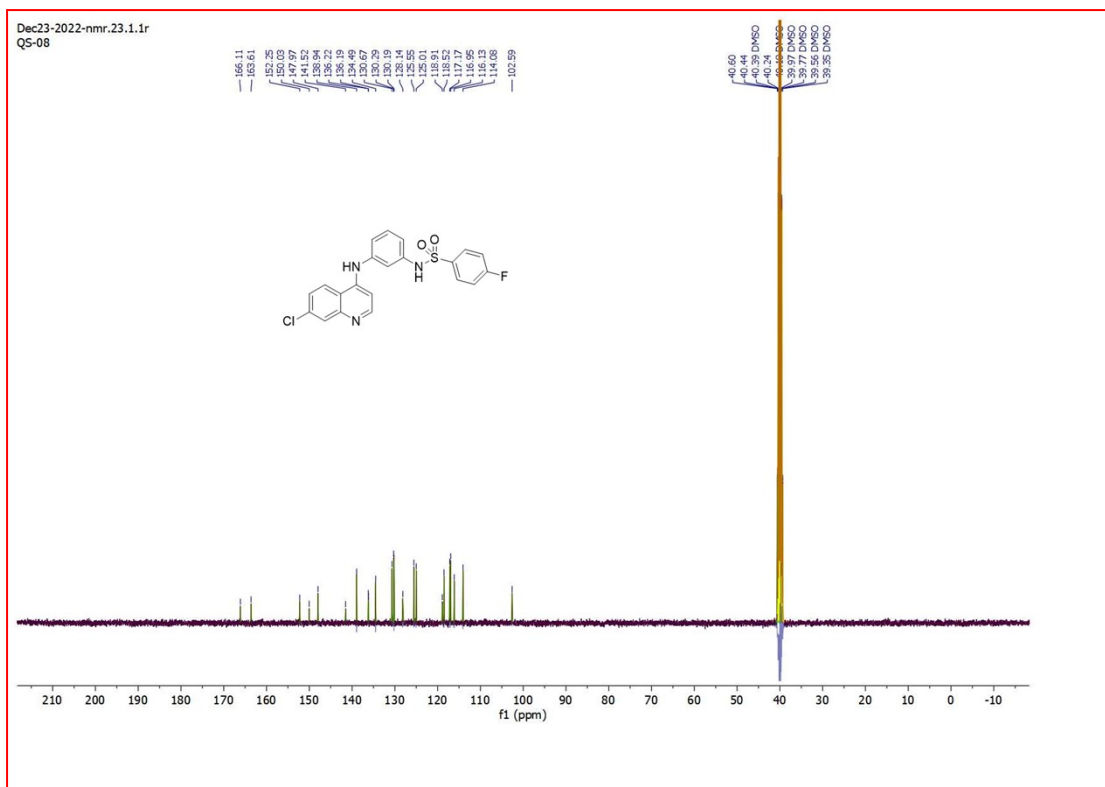


Figure.- S16. ^{13}C NMR Spectrum of compound (QS-8)

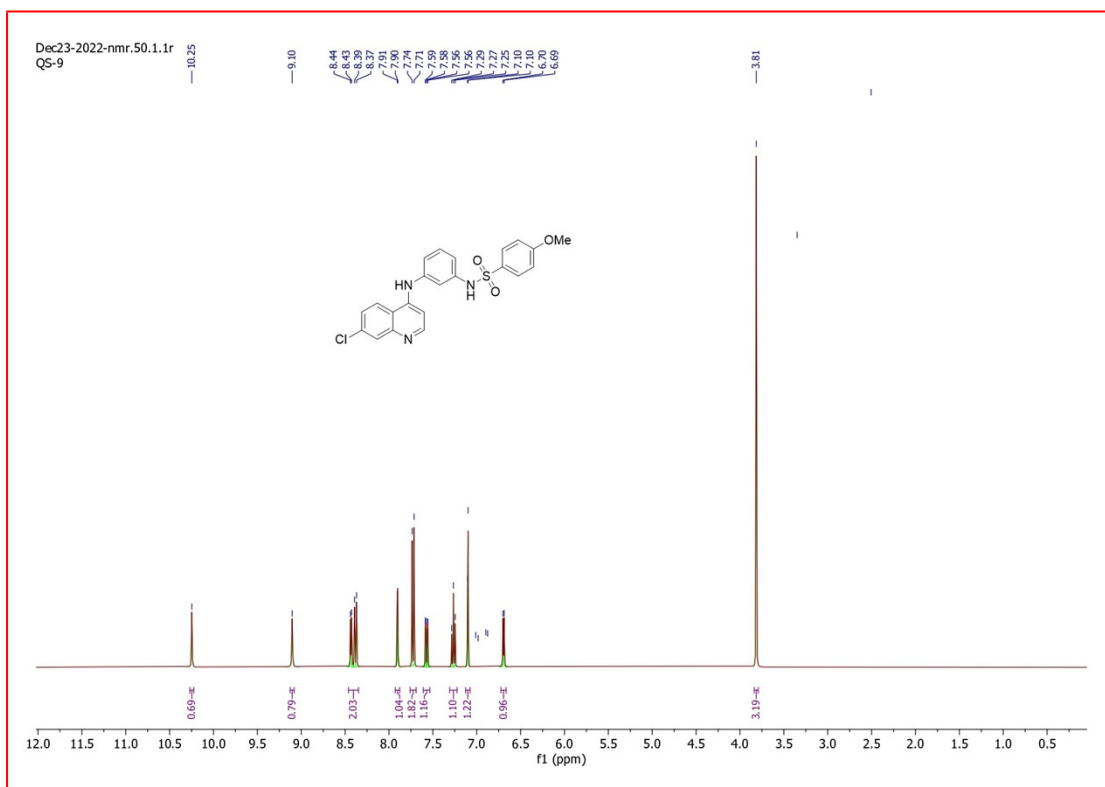


Figure.- S17. ^1H NMR Spectrum of compound (QS-9)

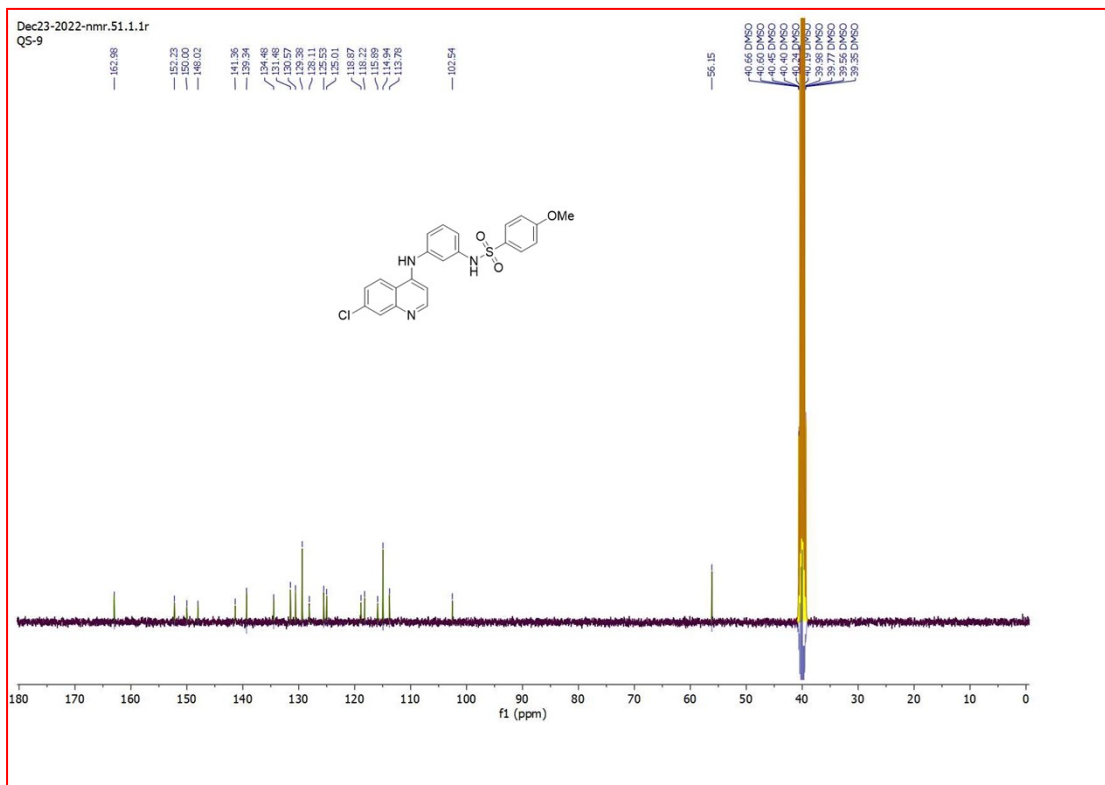


Figure.- S18. ^{13}C NMR Spectrum of compound (QS-9)

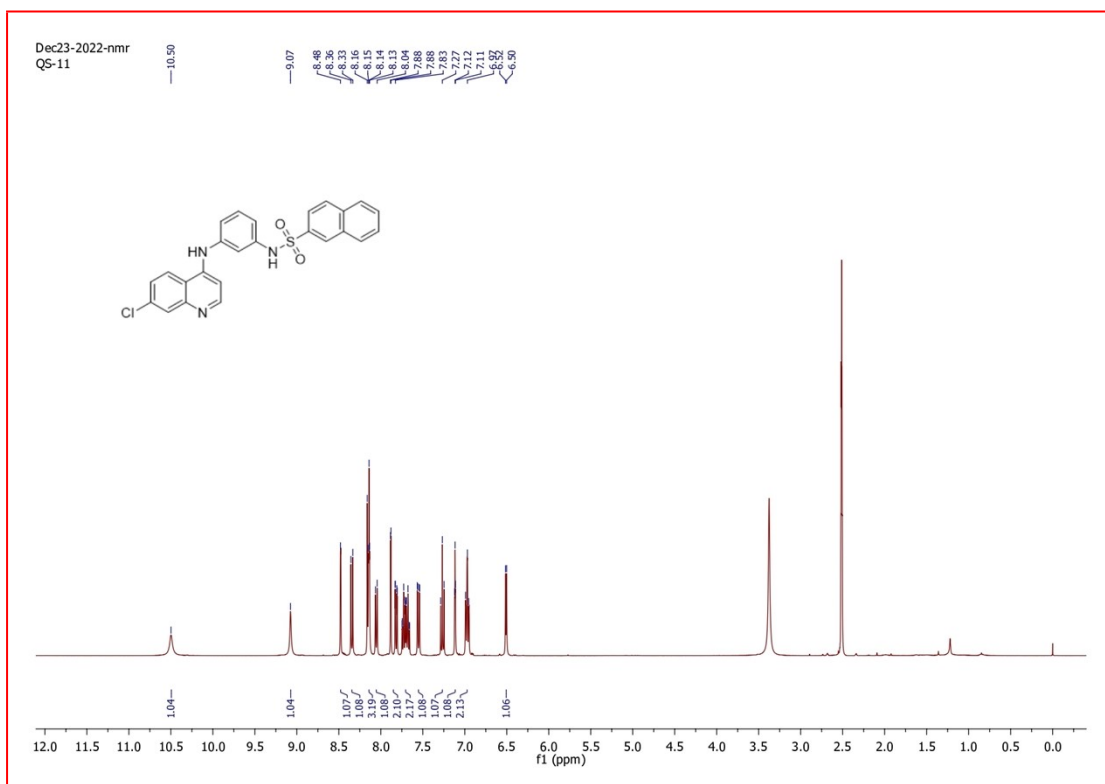


Figure.- S19. ^1H NMR Spectrum of compound (QS-10)

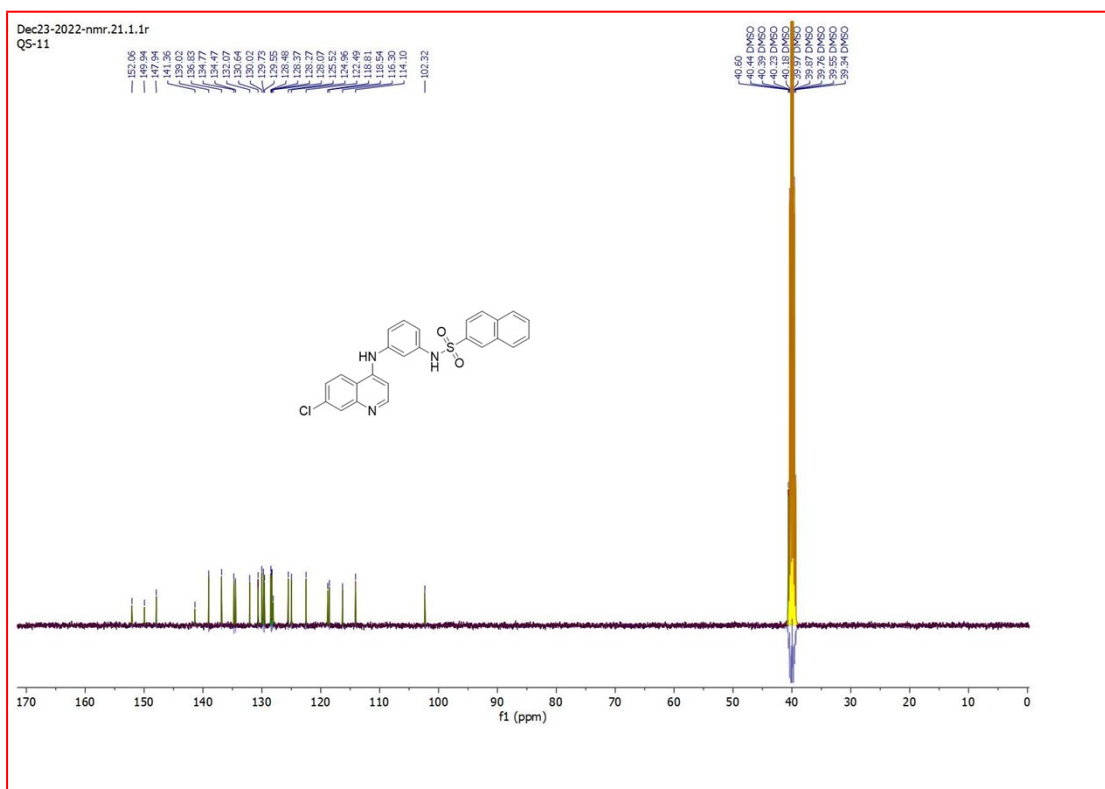


Figure.- S20. ¹³C NMR Spectrum of compound (QS-10)

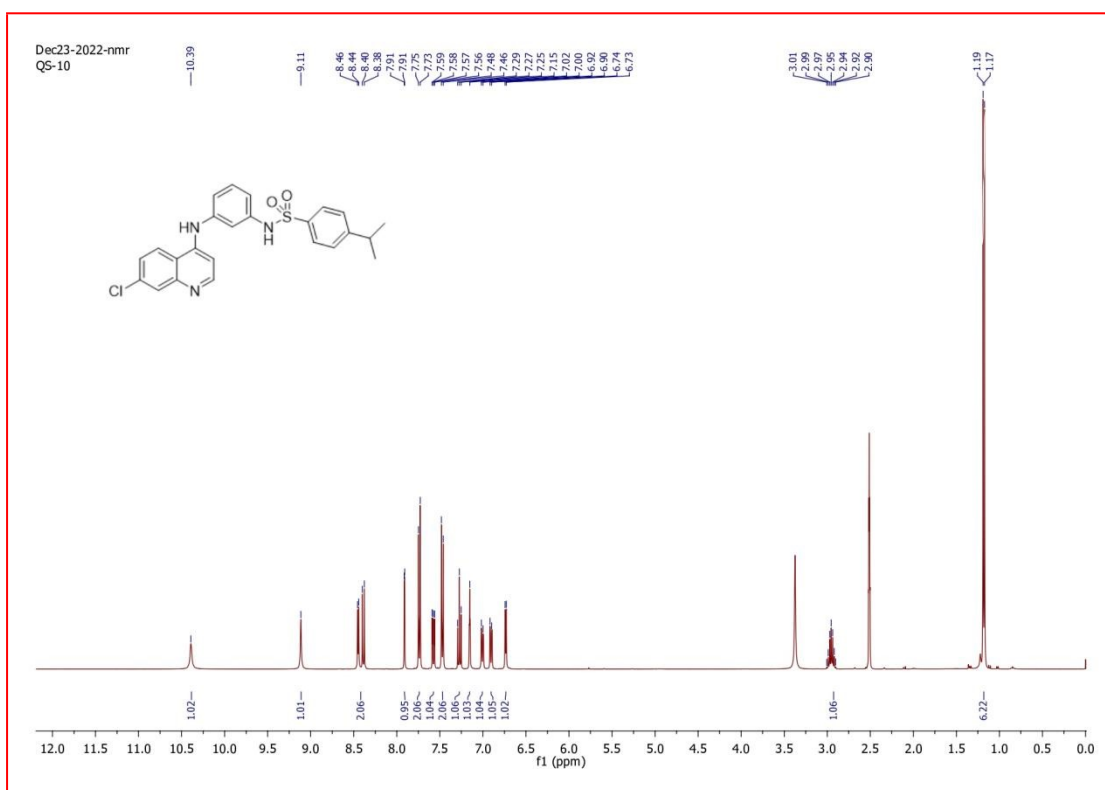


Figure.- S21. ¹H NMR Spectrum of compound (QS-11)

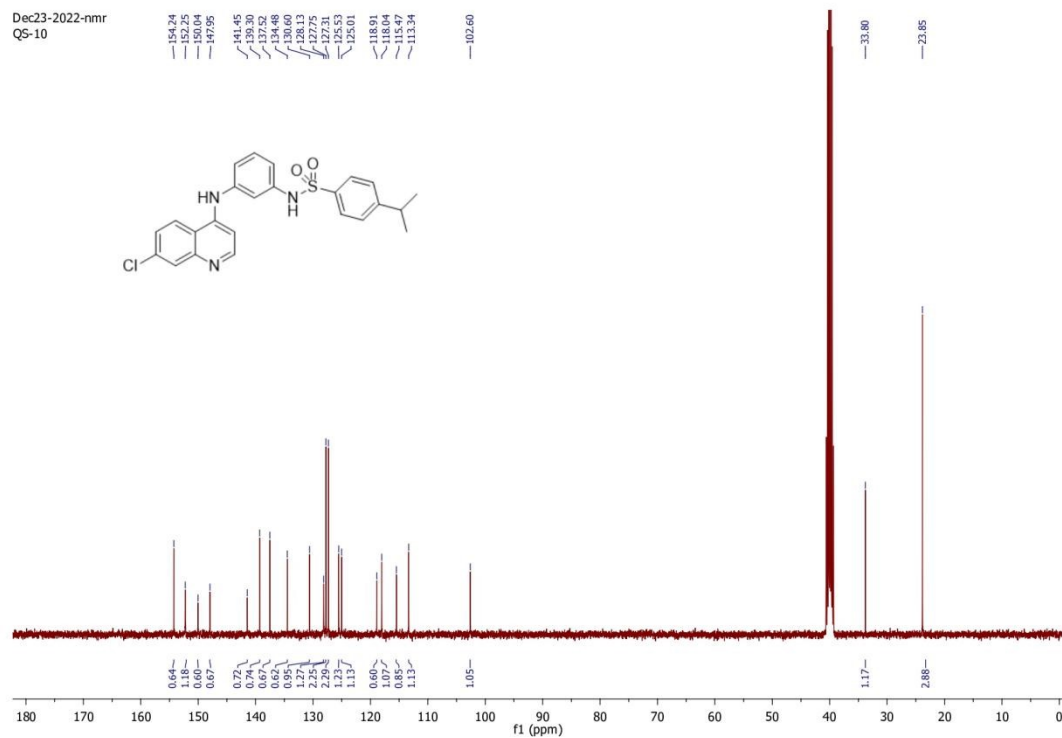


Figure.- S22. ¹³C NMR Spectrum of compound (QS-11)

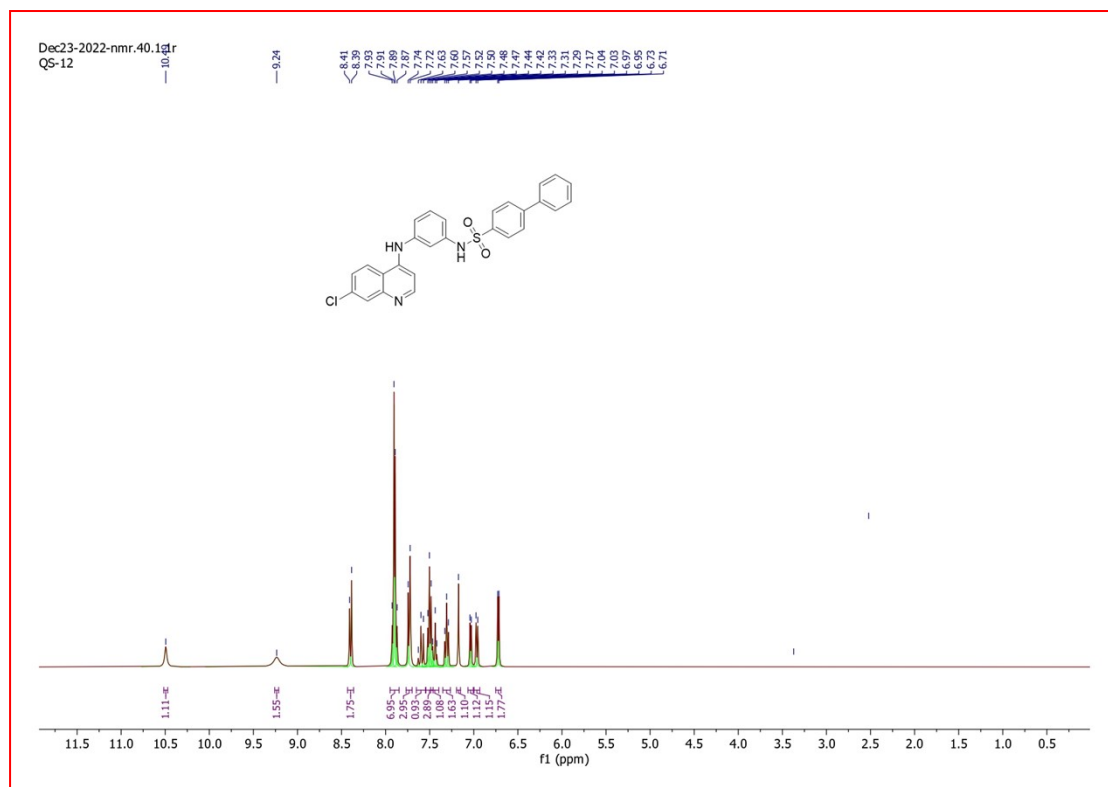


Figure.- S23. ¹H NMR Spectrum of compound (QS-12)

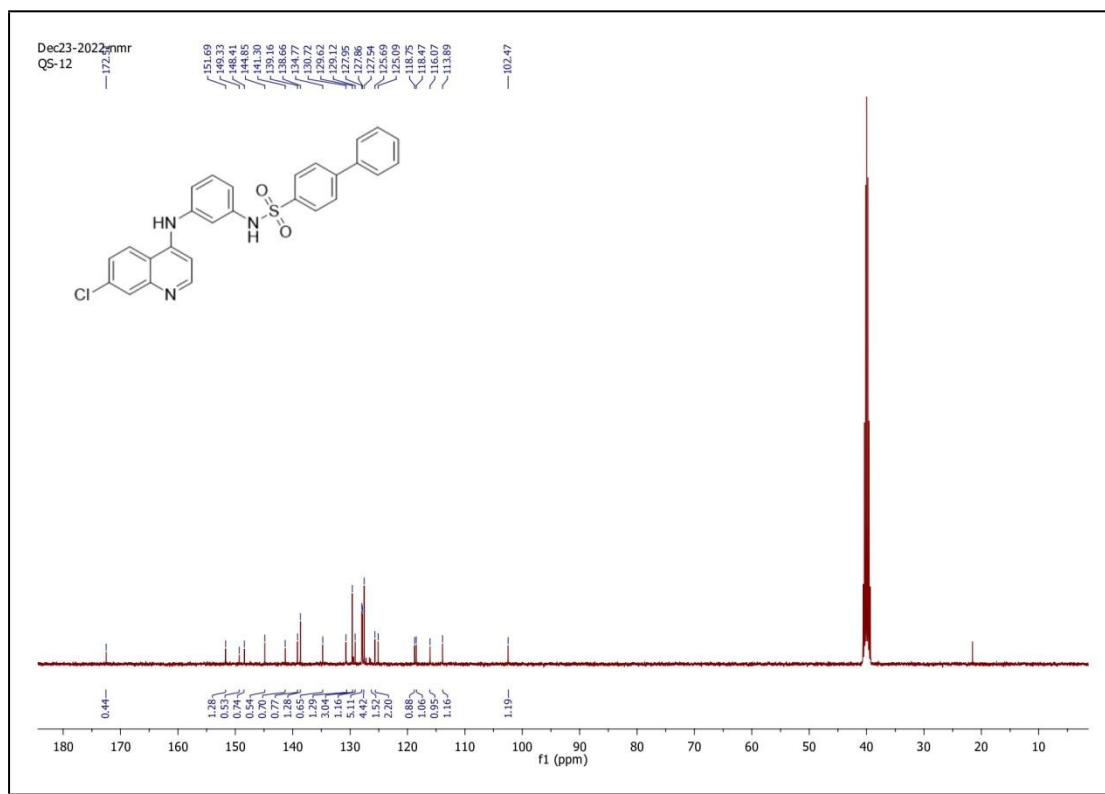


Figure - S24. ¹³C NMR Spectrum of compound (QS-12)

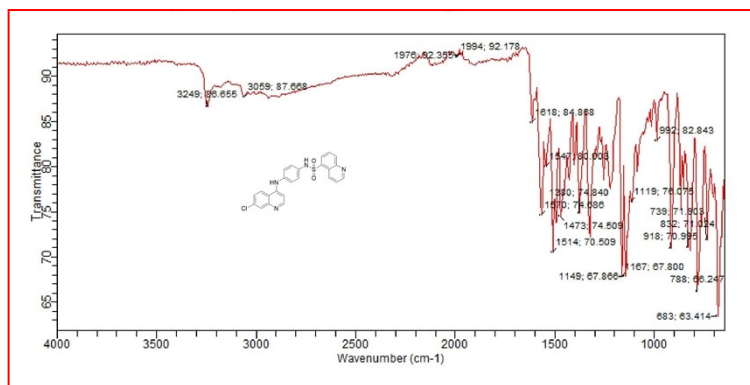


Figure - S25. FTIR Spectrum of compound (QS-1)

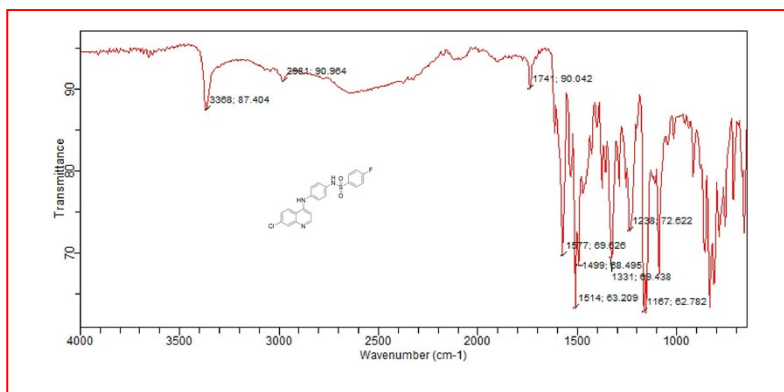


Figure - S26. FTIR Spectrum of compound (QS-2)

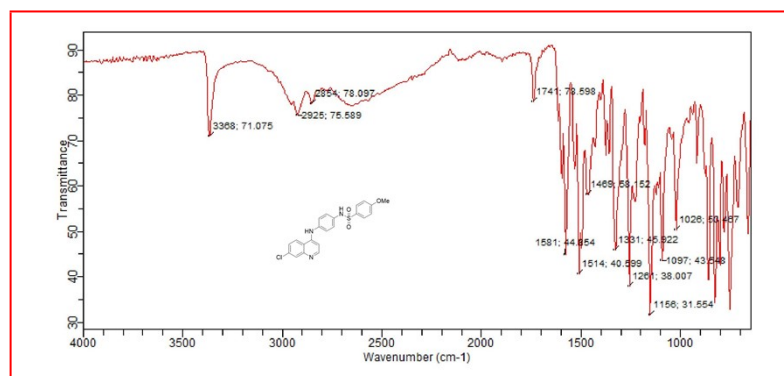


Figure - S27. FTIR Spectrum of compound (QS-3)

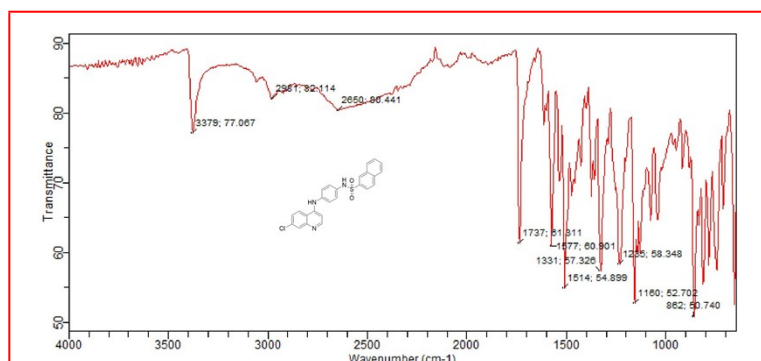


Figure - S28. FTIR Spectrum of compound (QS-4)

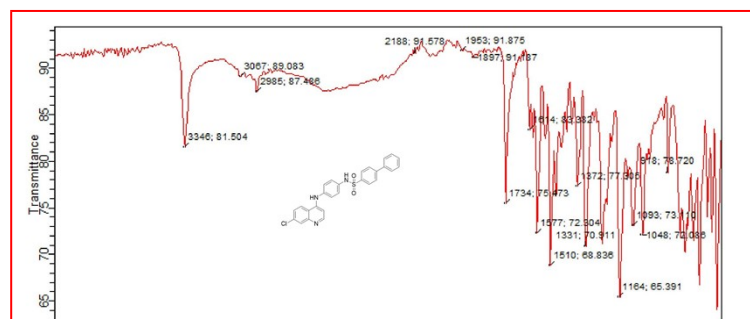


Figure - S29. FTIR Spectrum of compound (QS-5)

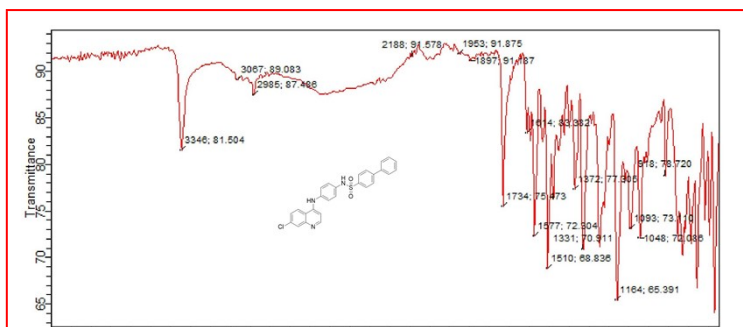


Figure - S30. FTIR Spectrum of compound (QS-6)

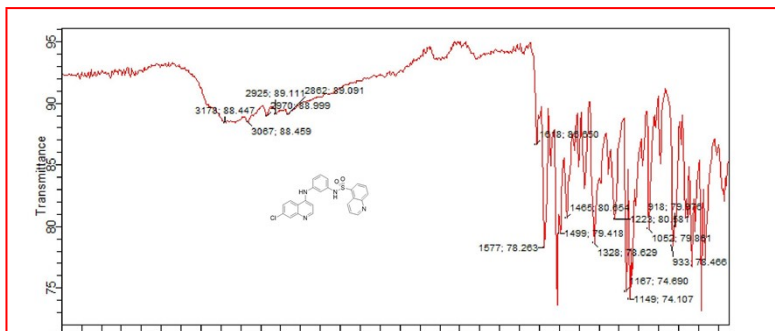


Figure - S31. FTIR Spectrum of compound (QS-7)

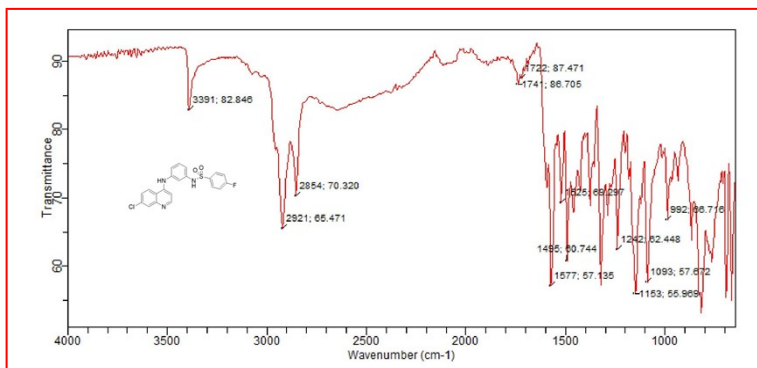


Figure - S32. FTIR Spectrum of compound (QS-8)

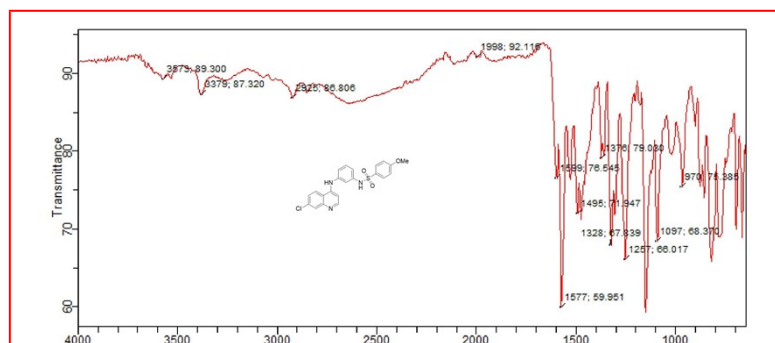


Figure - S33. FTIR Spectrum of compound (QS-9)

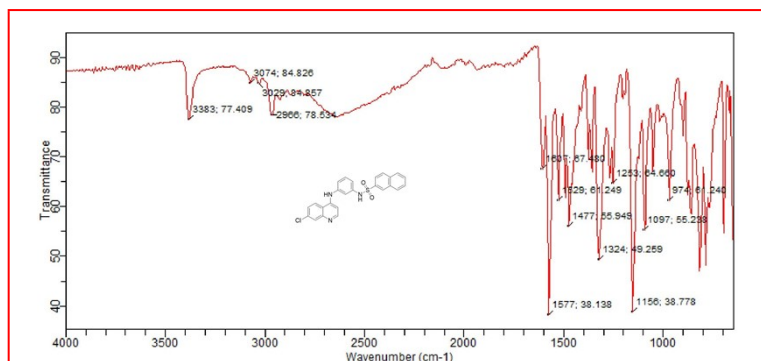


Figure - S34. FTIR Spectrum of compound (QS-10)

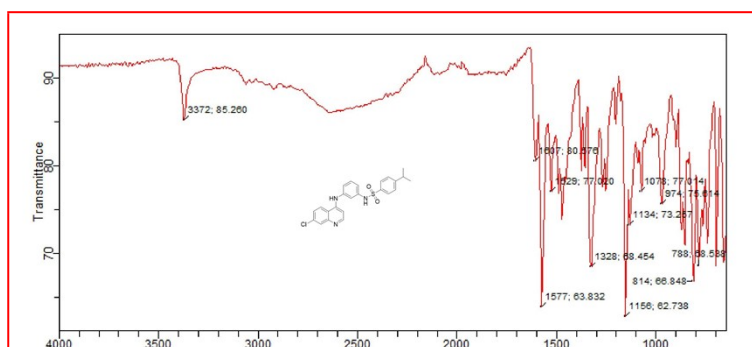


Figure - S35. FTIR Spectrum of compound (QS-11)

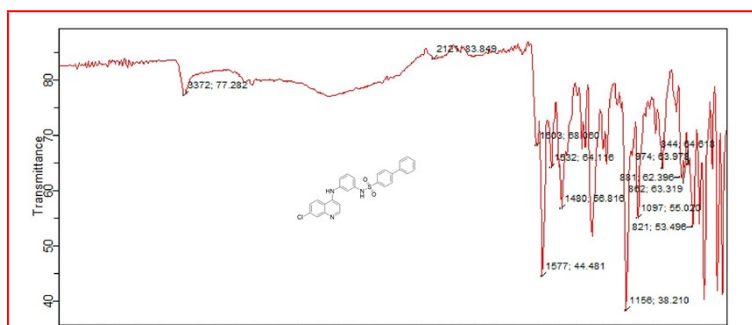


Figure - S36. FTIR Spectrum of compound (QS-12)

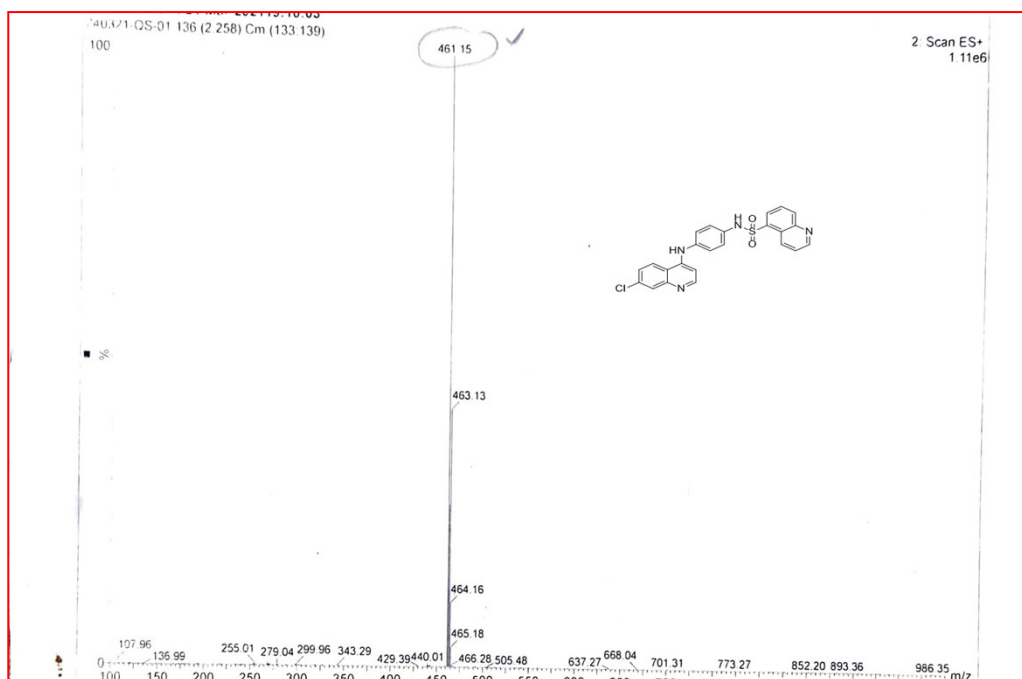


Figure - S37. Mass spectrum of compound (QS-1)

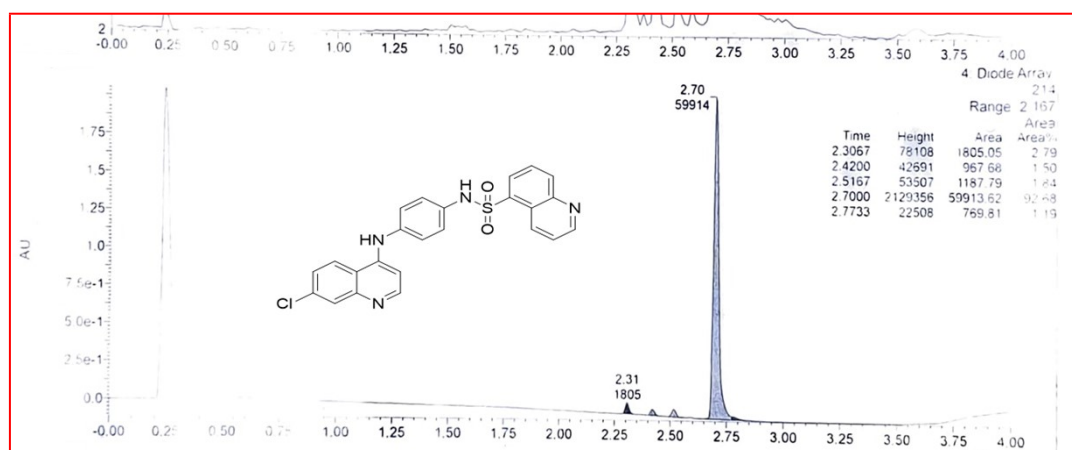


Figure - S38. Purity of compound (QS-1)

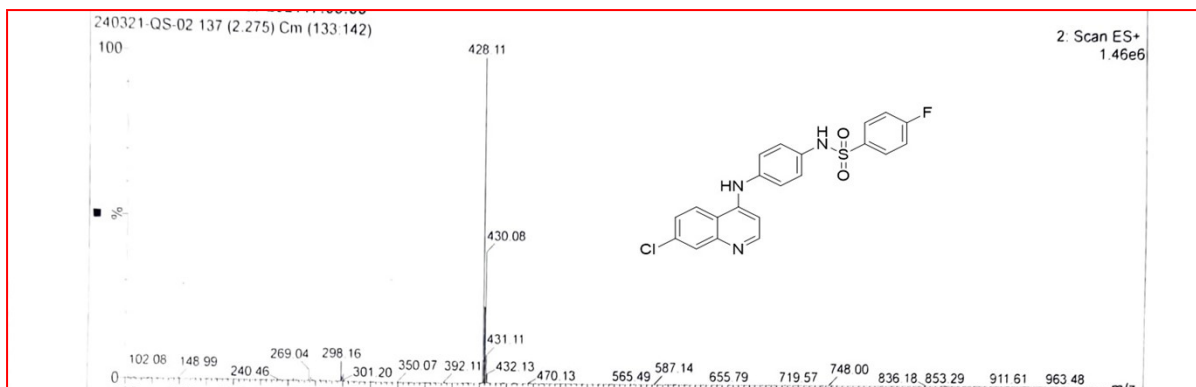


Figure - S39. Mass spectrum of compound (QS-2)

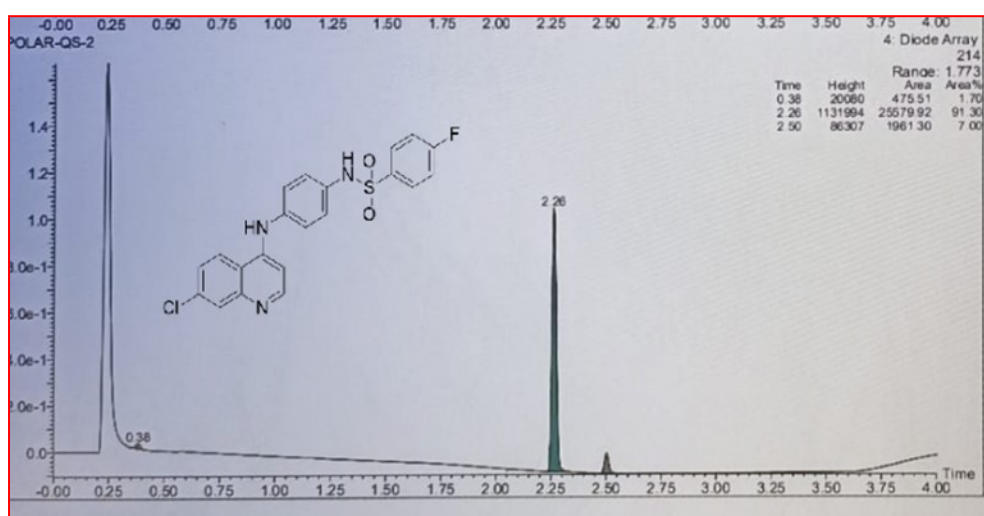


Figure - S40. Purity of compound (QS-2)

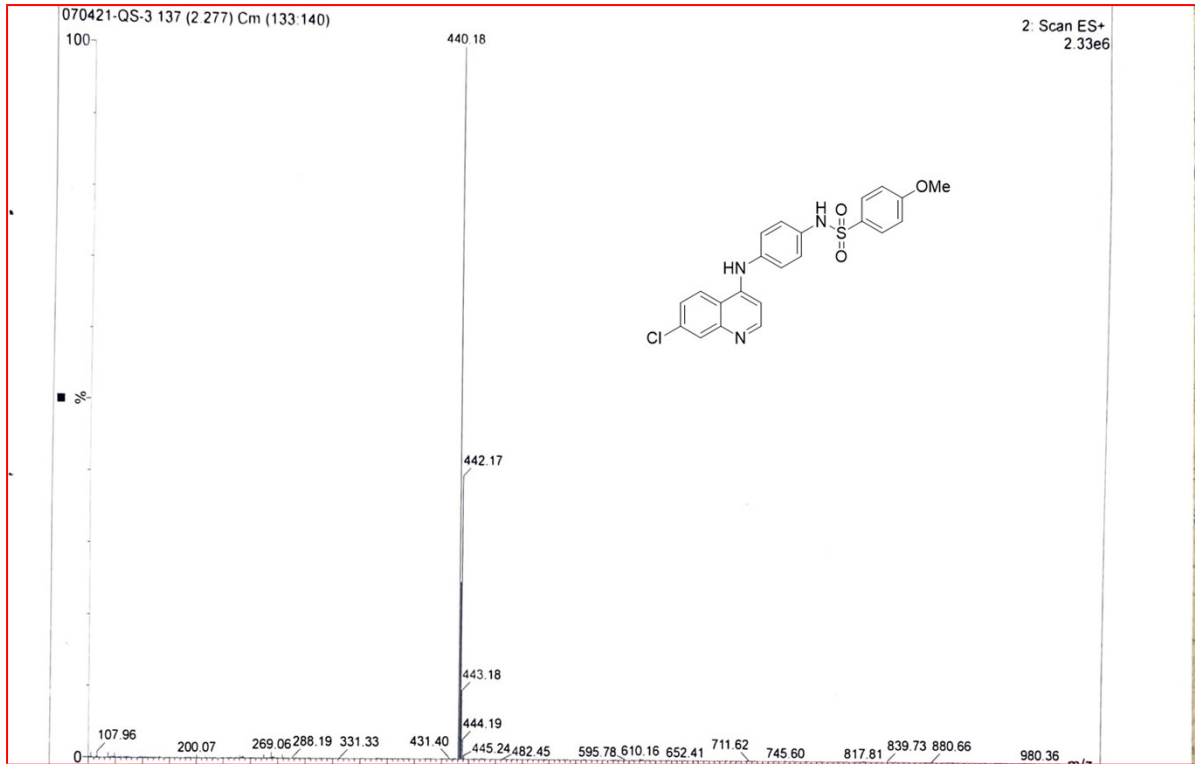


Figure - S41. Mass spectrum of compound (QS-3)

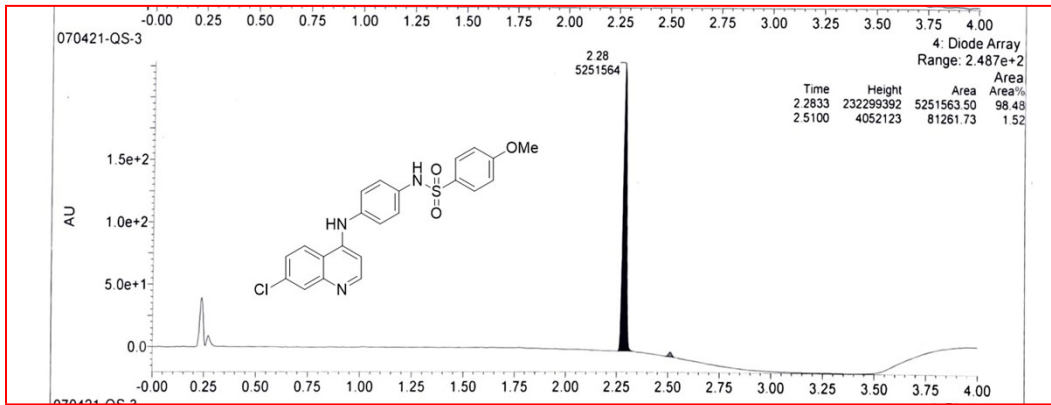


Figure - S42. Purity of compound (QS-3)

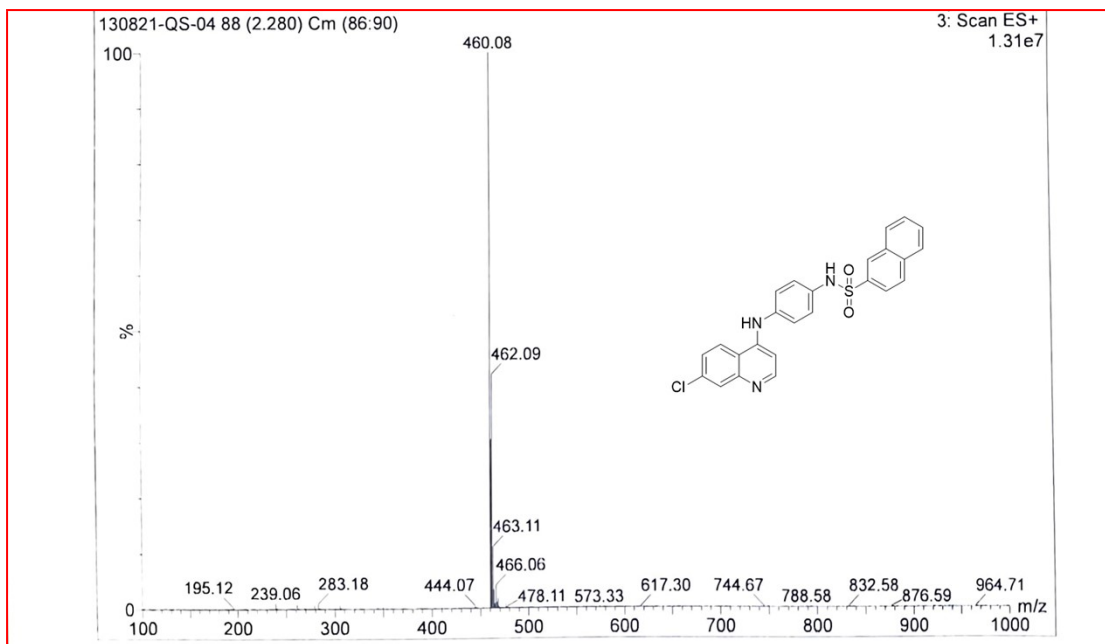


Figure - S43. Mass spectrum of compound (QS-4)

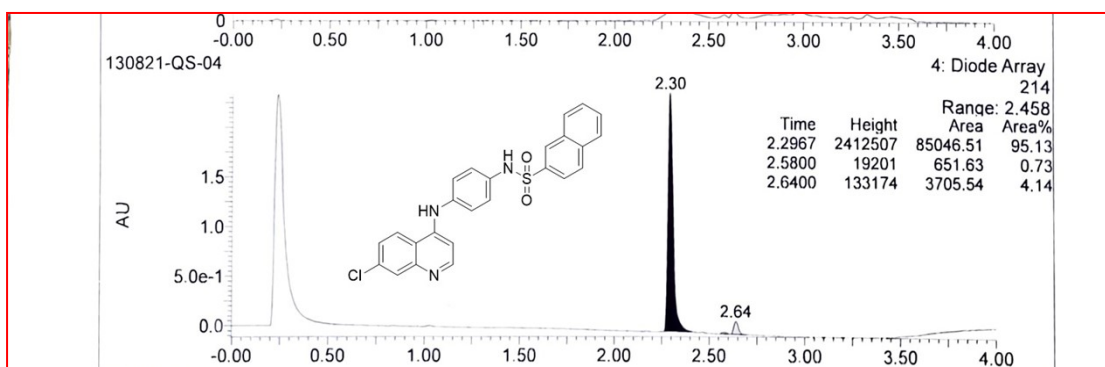


Figure - S44. Purity of compound (QS-4)

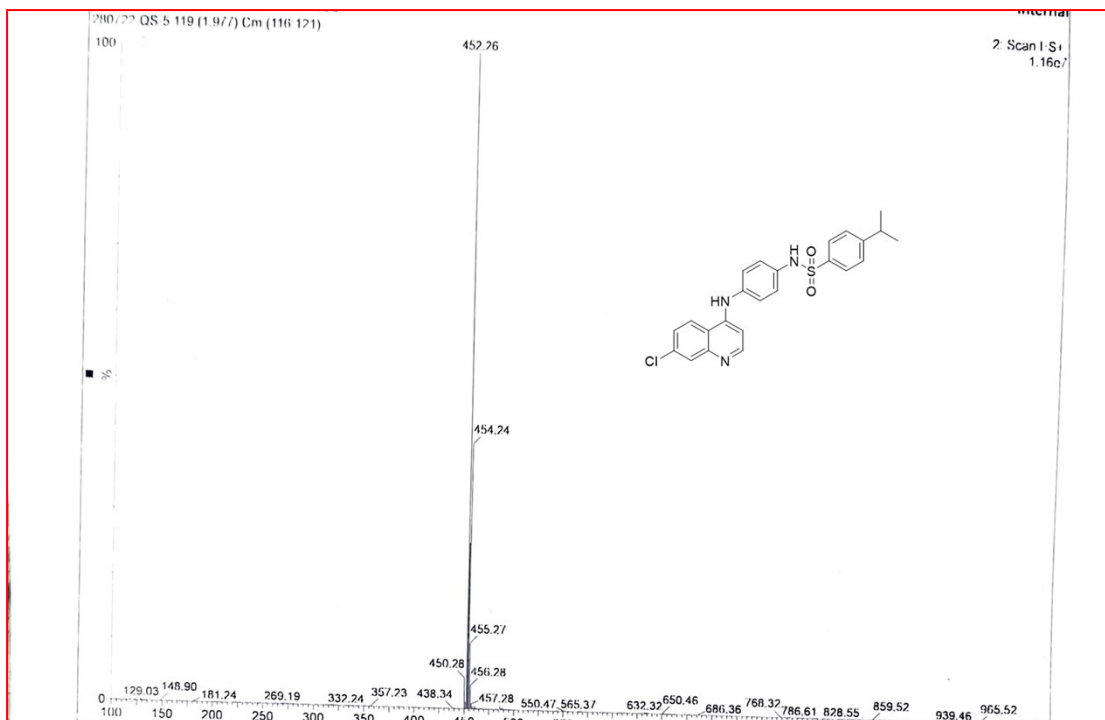


Figure - S45. Mass spectrum of compound (QS-5)

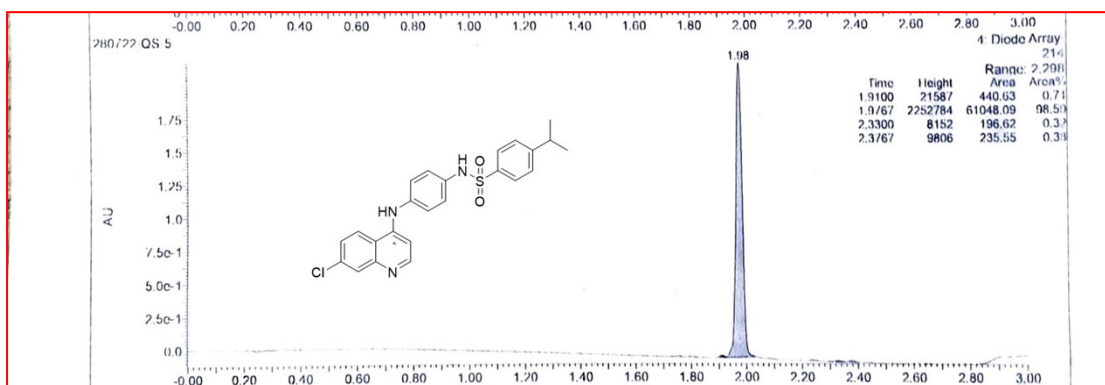


Figure - S46. Purity of compound (QS-5)

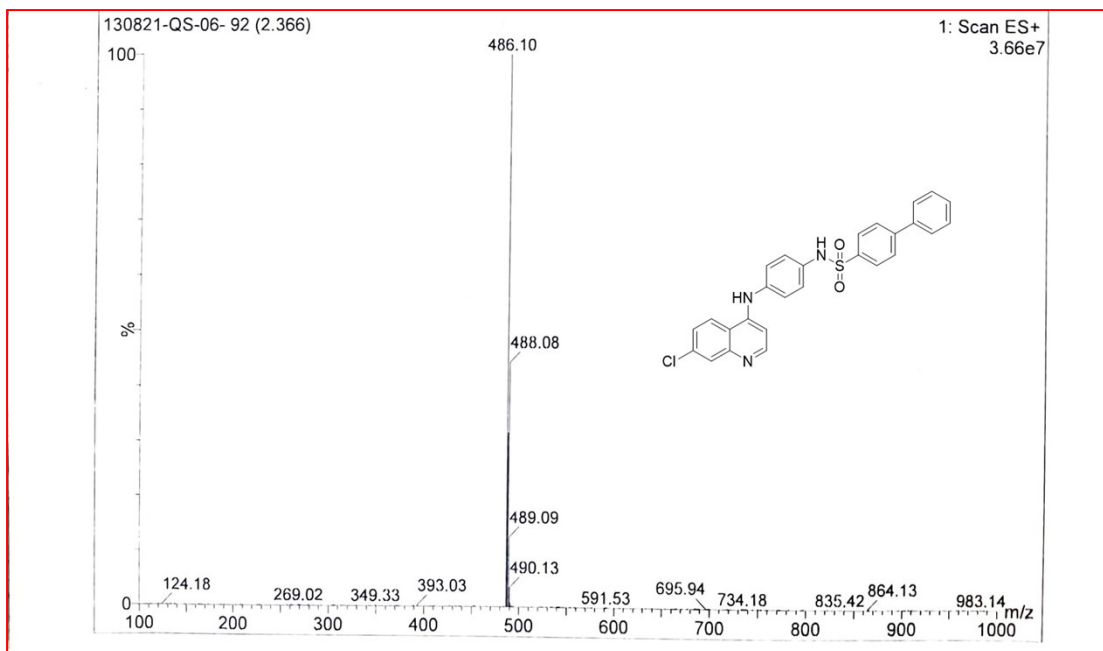


Figure - S47. Mass spectrum of compound (QS-6)

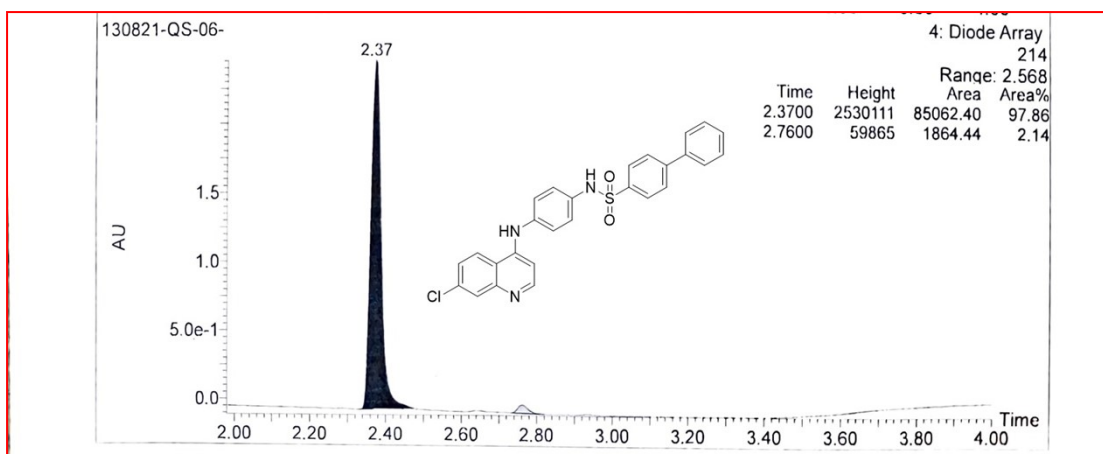


Figure - S48. Purity of compound (QS-6)

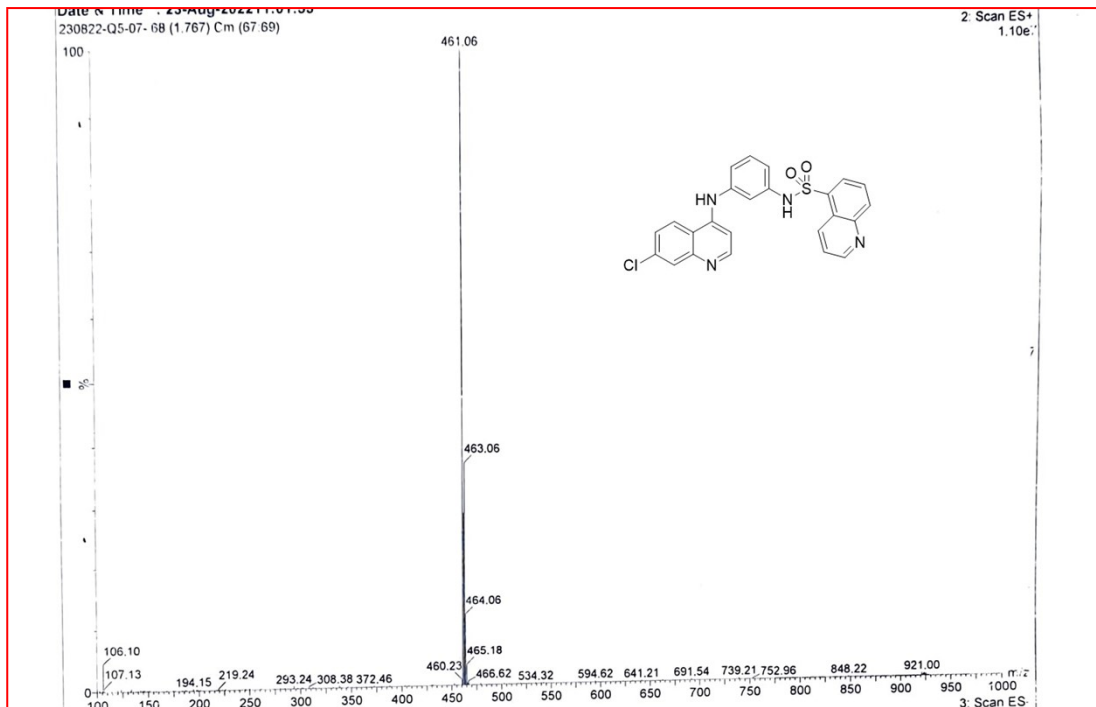


Figure - S49. Mass spectrum of compound (QS-7)

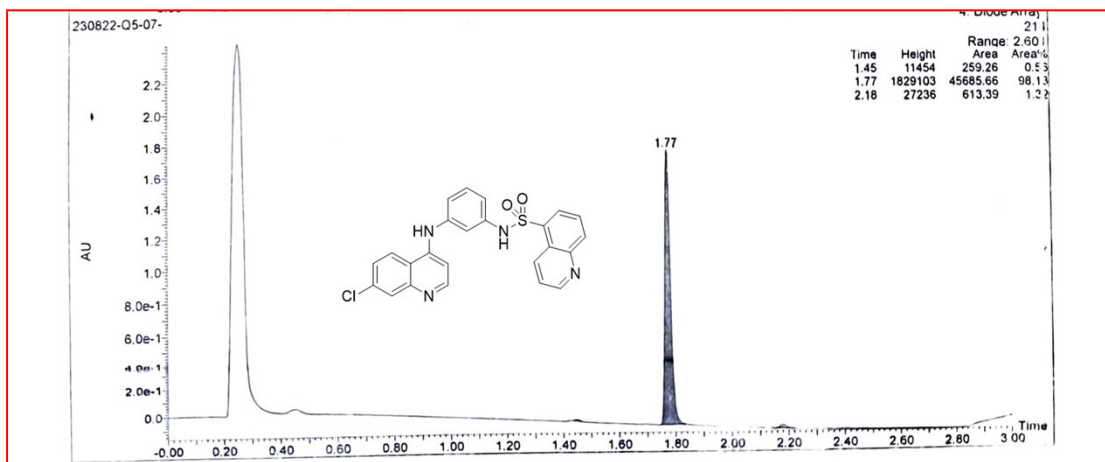


Figure - S50. Purity of compound (QS-7)

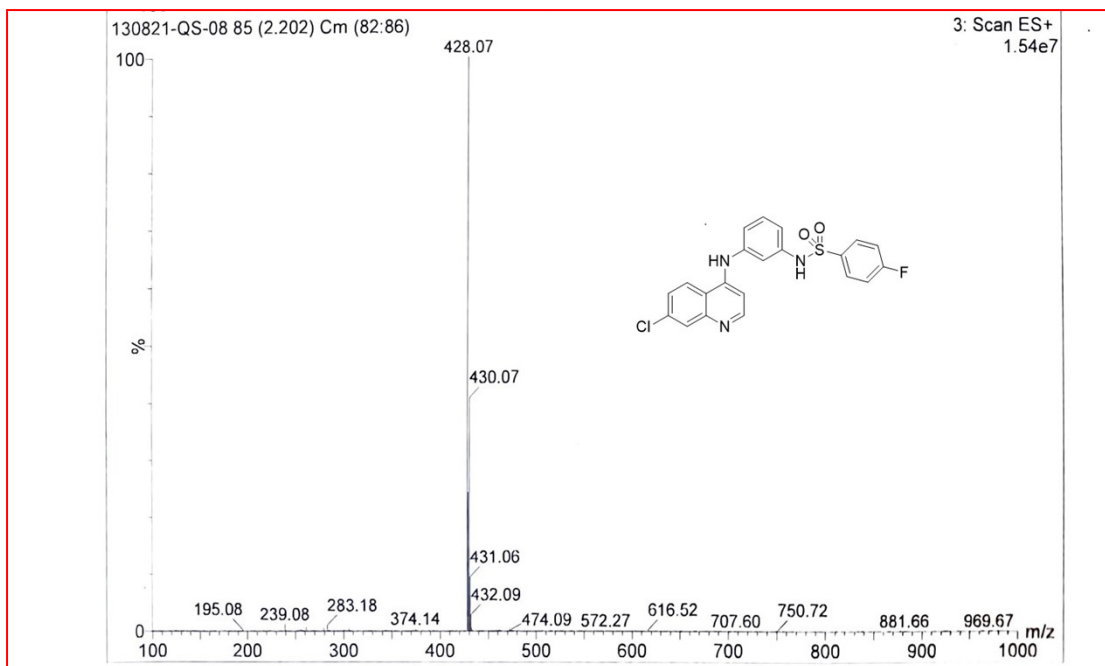


Figure - S51. Mass spectrum of compound (QS-8)

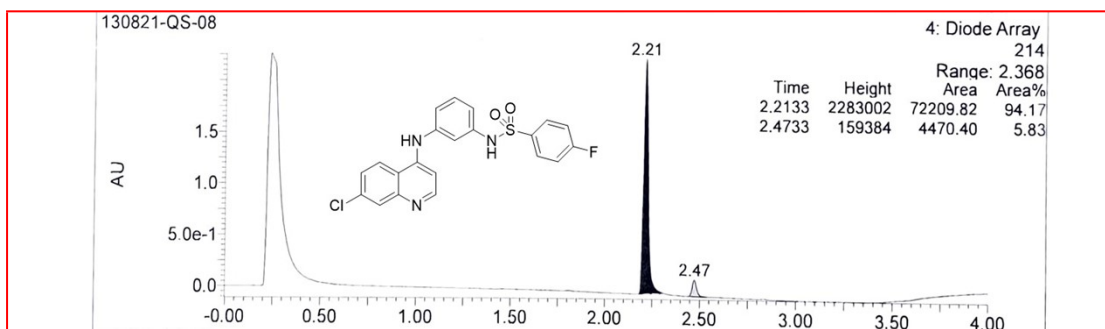


Figure - S52. Purity of compound (QS-8)

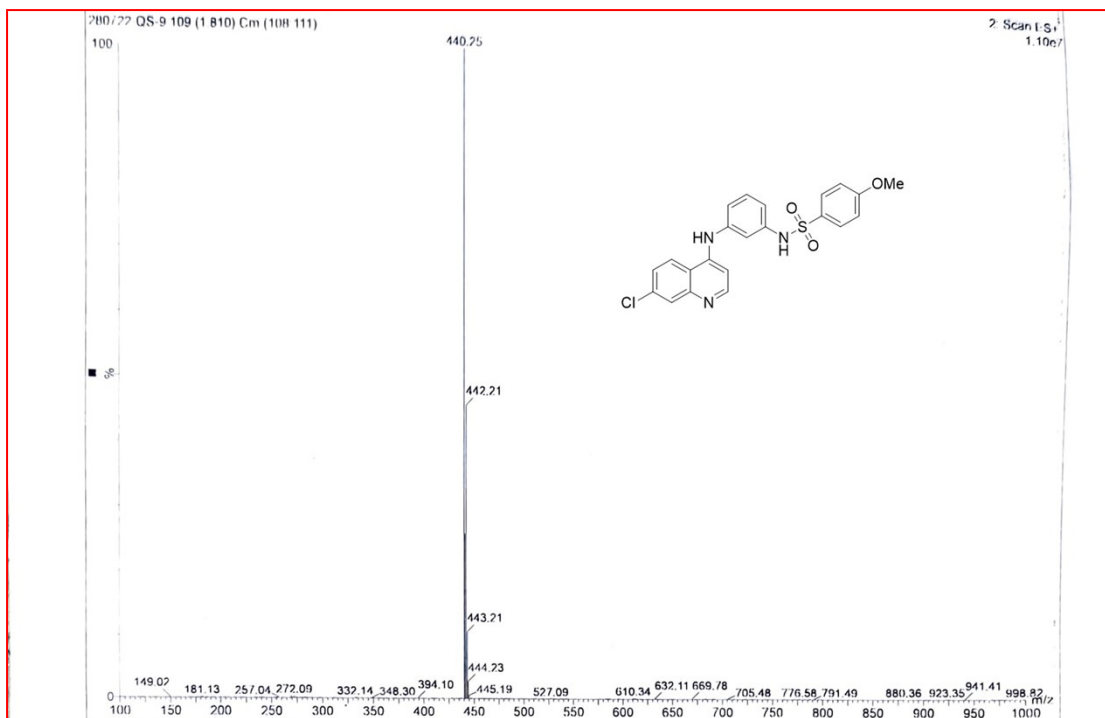


Figure - S53. Mass spectrum of compound (QS-9)

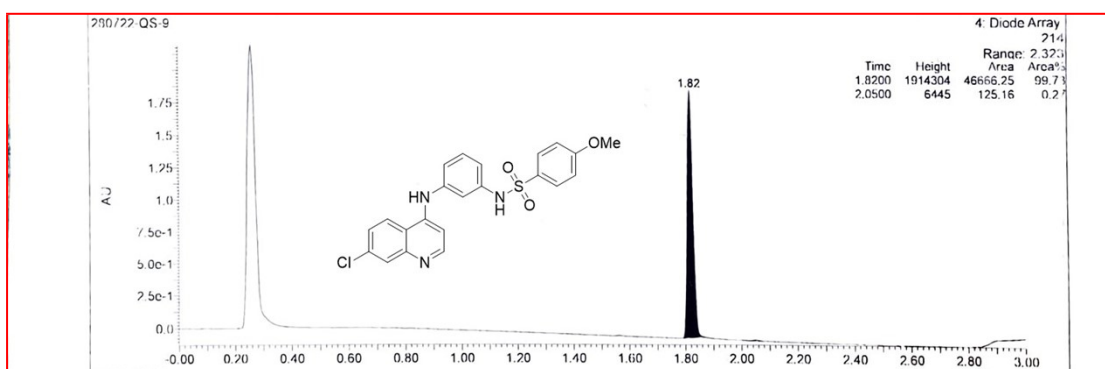


Figure - S54. Purity of compound (QS-9)

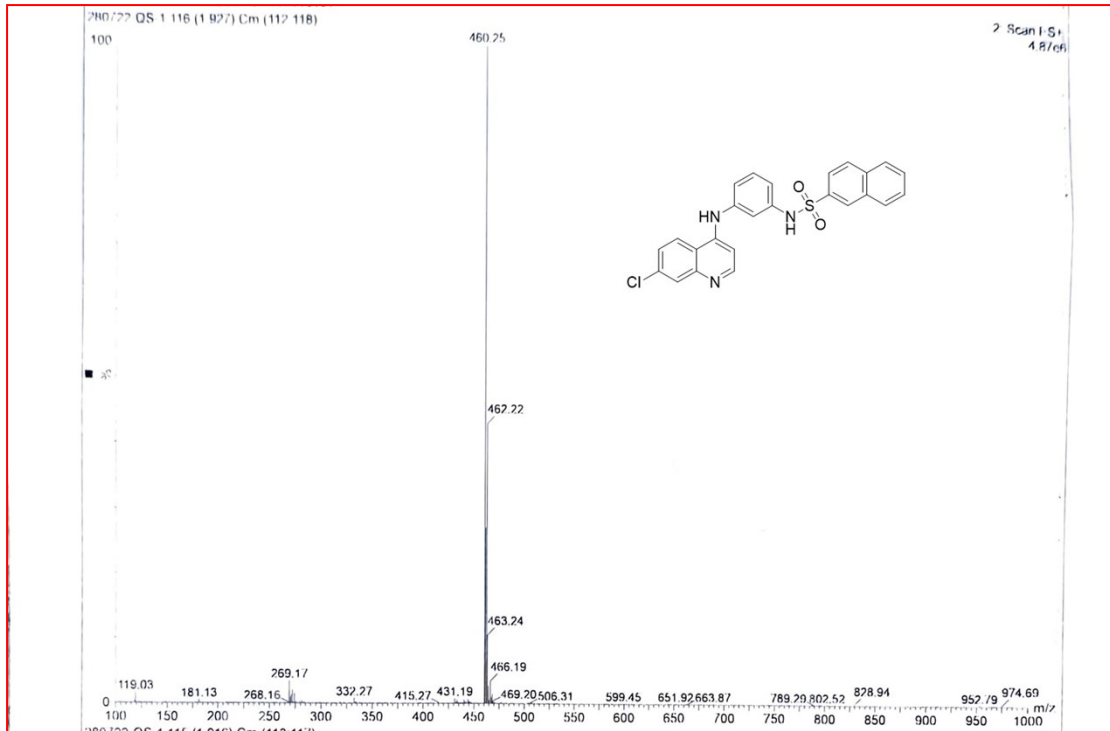


Figure - S55. Mass spectrum of compound (QS-10)

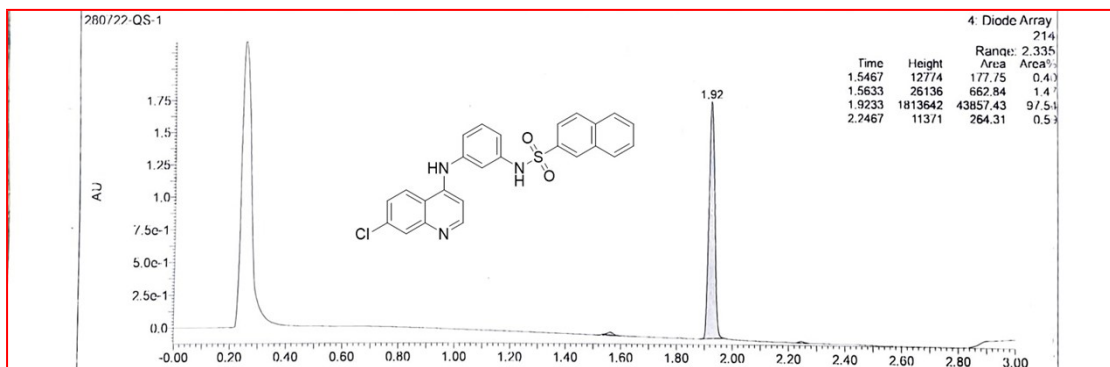


Figure - S56. Purity of compound (QS-10)

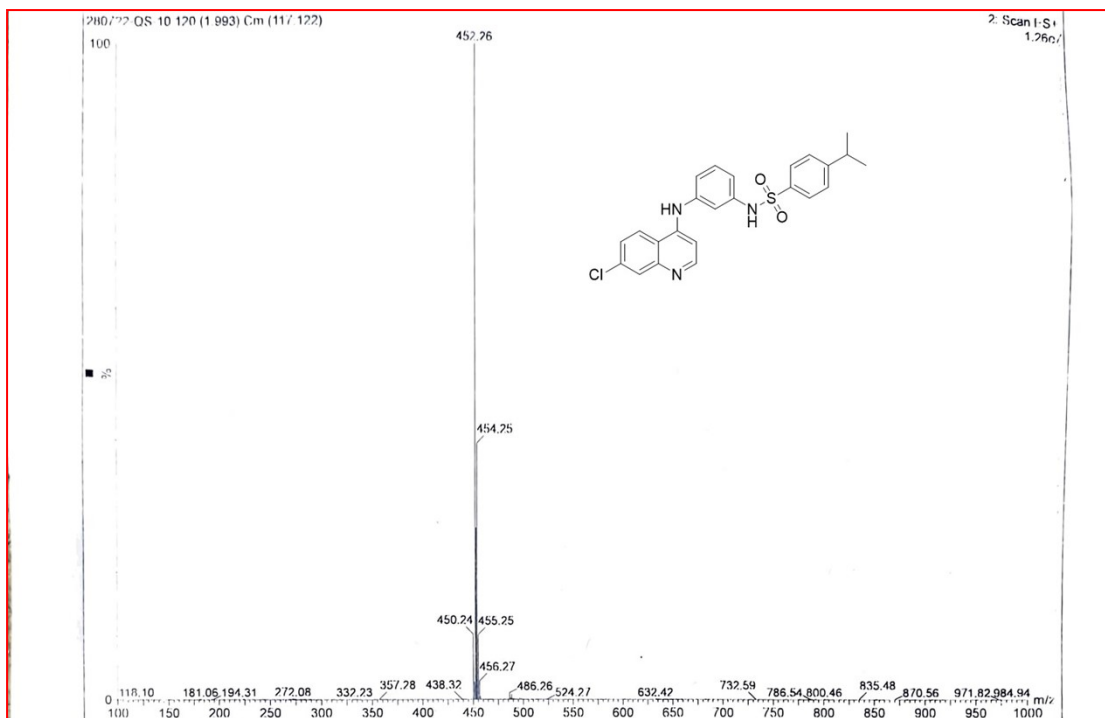


Figure - S57. Mass spectrum of compound (QS-11)

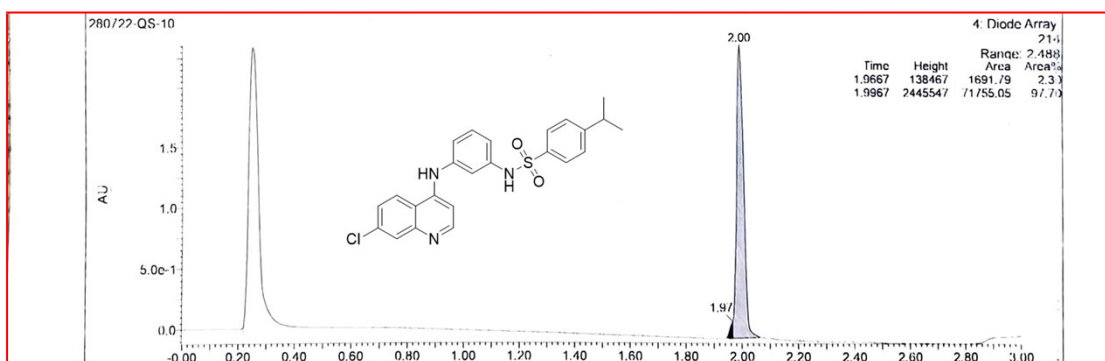


Figure - S58. Purity of compound (QS-11)

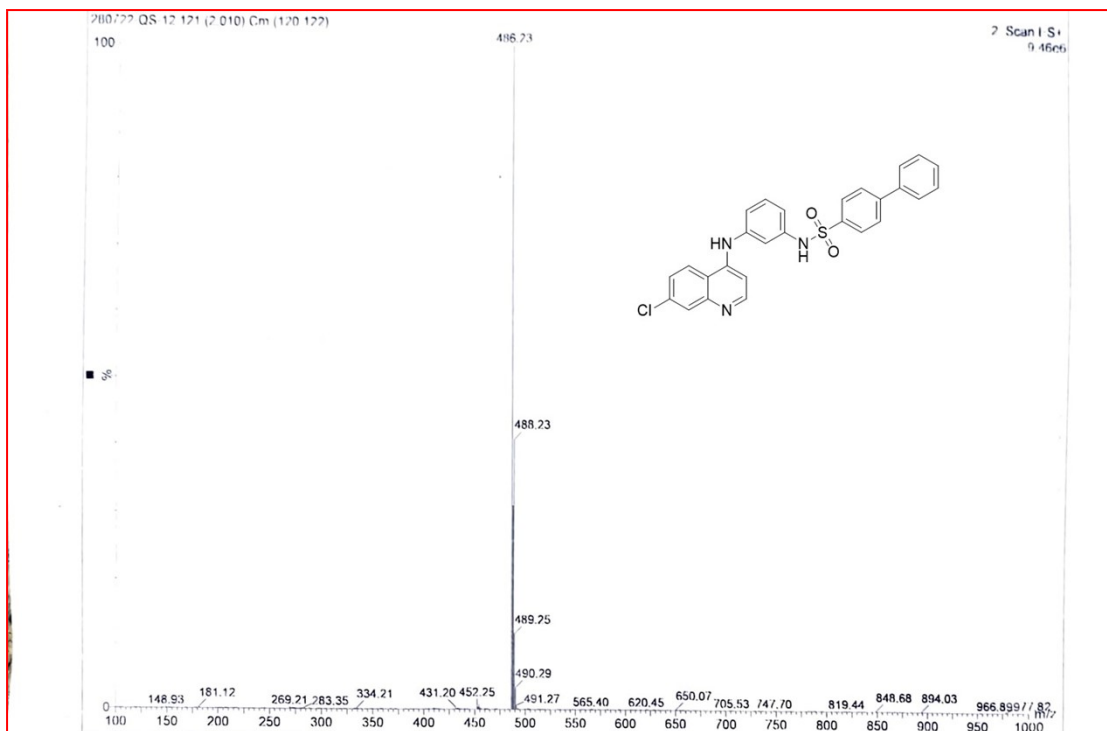


Figure - S59. Mass spectrum of compound (QS-12)

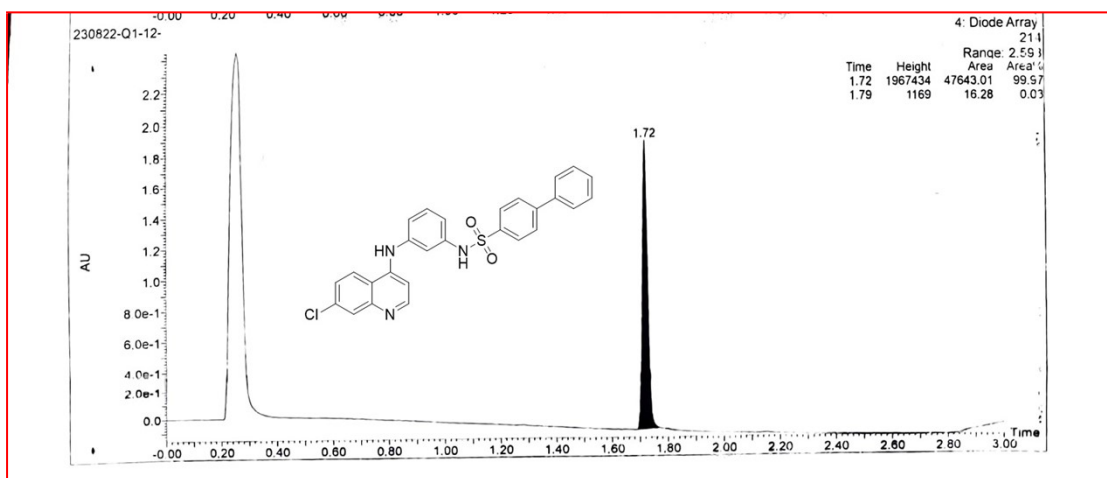


Figure - S60. Purity of compound (QS-12)

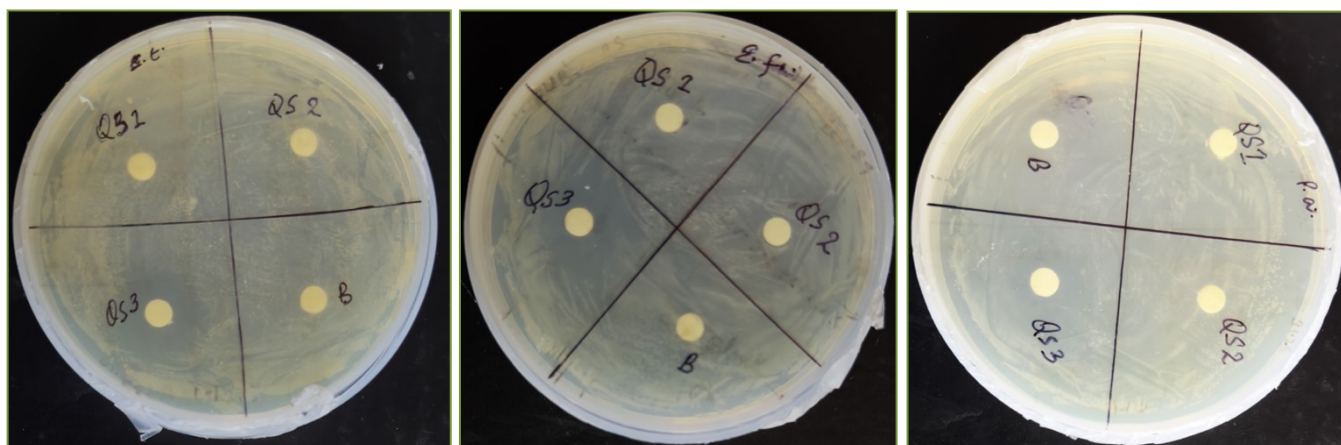


Figure – S61. Clearance zone in the bacterial lawn on treating with compounds

Combination Assay raw data:

Reading 1:

| Bacterial Strain | MIC in combination (µg/mL) | |
|----------------------|----------------------------|-------|
| | Comp | CIP |
| <i>E. coli</i> | 4 | 0.125 |
| <i>E. faecalis</i> | 2 | 0.125 |
| <i>P. aeruginosa</i> | 4 | 0.5 |
| <i>S. typhi</i> | 2 | 0.25 |

Reading 2:

| Bacterial Strain | MIC in combination (µg/mL) | |
|----------------------|----------------------------|-------|
| | Comp | CIP |
| <i>E. coli</i> | 2 | 0.25 |
| <i>E. faecalis</i> | 2 | 0.125 |
| <i>P. aeruginosa</i> | 8 | 0.25 |
| <i>S. typhi</i> | 2 | 0.25 |

Reading 3:

| Bacterial Strain | MIC in combination (µg/mL) | |
|------------------|----------------------------|-----|
| | Comp | CIP |

| | | |
|----------------------|---|-------|
| <i>E. coli</i> | 2 | 0.125 |
| <i>E. faecalis</i> | 8 | 0.5 |
| <i>P. aeruginosa</i> | 4 | 0.5 |
| <i>S. typhi</i> | 2 | 0.25 |

Disk diffusion Assay raw data:

Reading 1:

| | Zone of Inhibition (in mm) at different concentrations of Test Compound. | | |
|----------------------|--|-----|------|
| Isolates | ½ MIC | MIC | 2MIC |
| <i>E. coli</i> | 6 | 7 | 7 |
| <i>E. faecalis</i> | 7 | 6 | 7 |
| <i>P. aeruginosa</i> | 6 | 8 | 12 |
| <i>S. typhi</i> | 7 | 5 | 8 |

Reading 2:

| | Zone of Inhibition (in mm) at different concentrations of Test Compound. | | |
|----------------------|--|-----|------|
| Isolates | ½ MIC | MIC | 2MIC |
| <i>E. coli</i> | 6 | 9 | 8 |
| <i>E. faecalis</i> | 8 | 10 | 8 |
| <i>P. aeruginosa</i> | 5 | 6 | 8 |
| <i>S. typhi</i> | 7 | 9 | 5 |

Reading 3:

| | Zone of Inhibition (in mm) at different concentrations of Test Compound. | | |
|----------------------|--|-----|------|
| Isolates | ½ MIC | MIC | 2MIC |
| <i>E. coli</i> | 6 | 6 | 7 |
| <i>E. faecalis</i> | 6 | 8 | 9 |
| <i>P. aeruginosa</i> | 7 | 10 | 10 |
| <i>S. typhi</i> | 7 | 7 | 11 |

Environmental strains raw data:

| Isolates Name | Reading 1 | Reading 2 | Reading 3 | Reading 4 |
|---------------|-----------|-----------|-----------|-----------|
| EJH01 | 0 | 0 | 0 | 0 |
| EJH02 | 0 | 0 | 0 | 0 |
| EJH04 | 0 | 0 | 0 | 0 |
| EJH05 | 0 | 0 | 0 | 0 |

| | | | | |
|--------|---|----|---|---|
| EJH07 | 0 | 0 | 0 | 0 |
| EJH11 | 0 | 0 | 0 | 0 |
| EJH12 | 0 | 0 | 0 | 0 |
| EJH13 | 0 | 0 | 0 | 0 |
| EJH14 | 0 | 0 | 0 | 0 |
| EJH15 | 0 | 0 | 0 | 0 |
| EJH18 | 0 | 0 | 0 | 0 |
| EJH19 | 0 | 0 | 0 | 0 |
| EJH20 | 0 | 0 | 0 | 0 |
| EJH21 | 0 | 0 | 0 | 0 |
| EJH22 | 0 | 0 | 0 | 0 |
| EJH23 | 0 | 0 | 0 | 0 |
| EJH24 | 0 | 0 | 0 | 0 |
| EJH25 | 0 | 0 | 0 | 0 |
| A200 | 0 | 0 | 0 | 0 |
| AA 201 | 0 | 0 | 0 | 0 |
| AA 202 | 8 | 9 | 6 | 9 |
| AA 209 | 0 | 0 | 0 | 0 |
| AA 216 | 0 | 0 | 0 | 0 |
| AA 221 | 0 | 0 | 0 | 0 |
| AA 224 | 0 | 0 | 0 | 0 |
| AA 237 | 0 | 0 | 0 | 0 |
| AA 240 | 0 | 0 | 0 | 0 |
| AA 243 | 0 | 0 | 0 | 0 |
| AA 245 | 0 | 0 | 0 | 0 |
| AA 248 | 0 | 0 | 0 | 0 |
| AA 261 | 0 | 0 | 0 | 0 |
| AA 269 | 0 | 0 | 0 | 0 |
| AA 273 | 0 | 0 | 0 | 0 |
| AA 276 | 0 | 0 | 0 | 0 |
| AA 290 | 8 | 10 | 7 | 7 |

Hemolysis raw data:

| Control | 0.05 | 0.1 | 0.25 | 0.5 | 1 |
|---------|------|------|------|-----|------|
| 0.6 | 1.23 | 2.62 | 2.8 | 2.9 | 3.24 |
| 0.88 | 1.43 | 1.9 | 2.5 | 3.1 | 3.9 |
| 0.9 | 1.33 | 2.26 | 2.6 | 3.2 | 4.2 |

MIC raw data:

| QS-3 | <i>E. coli</i> | <i>E. faecalis</i> | <i>P. aeruginosa</i> | <i>K. pneumoniae</i> | <i>S. typhi</i> |
|-----------|----------------|--------------------|----------------------|----------------------|-----------------|
| Reading 1 | 128 | 128 | 64 | 256 | 512 |
| Reading 2 | 128 | 64 | 64 | 128 | 512 |
| Reading 3 | 128 | 128 | 32 | 256 | 512 |