

Synthesis of 4-Hydroxyquinolines as Potential Cytotoxic Agents

Oszkár Csuvik ¹, Nikoletta Szemerédi ², Gabriella Spengler ² and István Szatmári ^{1,3,*}

¹ Institute of Pharmaceutical Chemistry, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary

² Department of Medical Microbiology, Albert Szent-Györgyi Health Center and Albert Szent-Györgyi Medical School, University of Szeged, Semmelweis u. 6, H-6725 Szeged, Hungary

³ Stereochemistry Research Group, Eötvös Loránd Research Network, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary

* Correspondence: szatmari.istvan@szte.hu

Table S1. Physical-chemical properties of the synthesised 4-hydroxyquinolines.

Compound	Melting point (°C)	Molecular weight [M + H ⁺]
4a	211–214	218.0808
4b	208–210	232.0964
5	294–297	279.1126
7	>350	331.1441
12	199–202	407.1756
8	221–224	204.0659
9	>350	269.1651
10a	166–169	327.1702
10b	152–155	341.1854
13a	247–251	306.1119
13b	222–225	320.1277
20	257–260	365.1129
21	233–236	338.1182
22	224–227	334.1434
23	215–218	350.1384
24	256–259	363.1700
25	262–265	370.1435
26	177–180	370.1434
28	315–319	290.0808
29	295–298	340.0966
30	>350	340.0966
14	230–233	292.0968

¹H NMR, ¹³C NMR, and HRMS spectra of synthesised compounds

Methyl 2-(4-hydroxyquinolin-2-yl) acetate (4a)

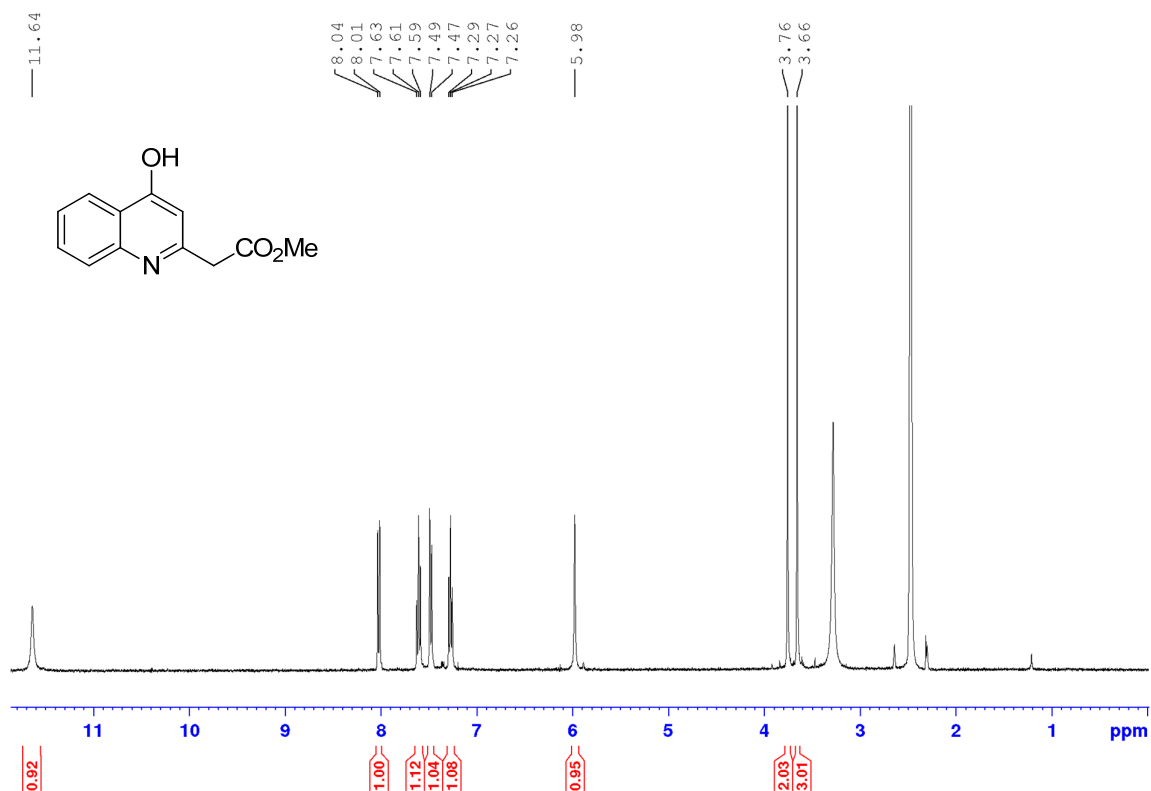


Figure S1. ¹H NMR spectrum of 4a

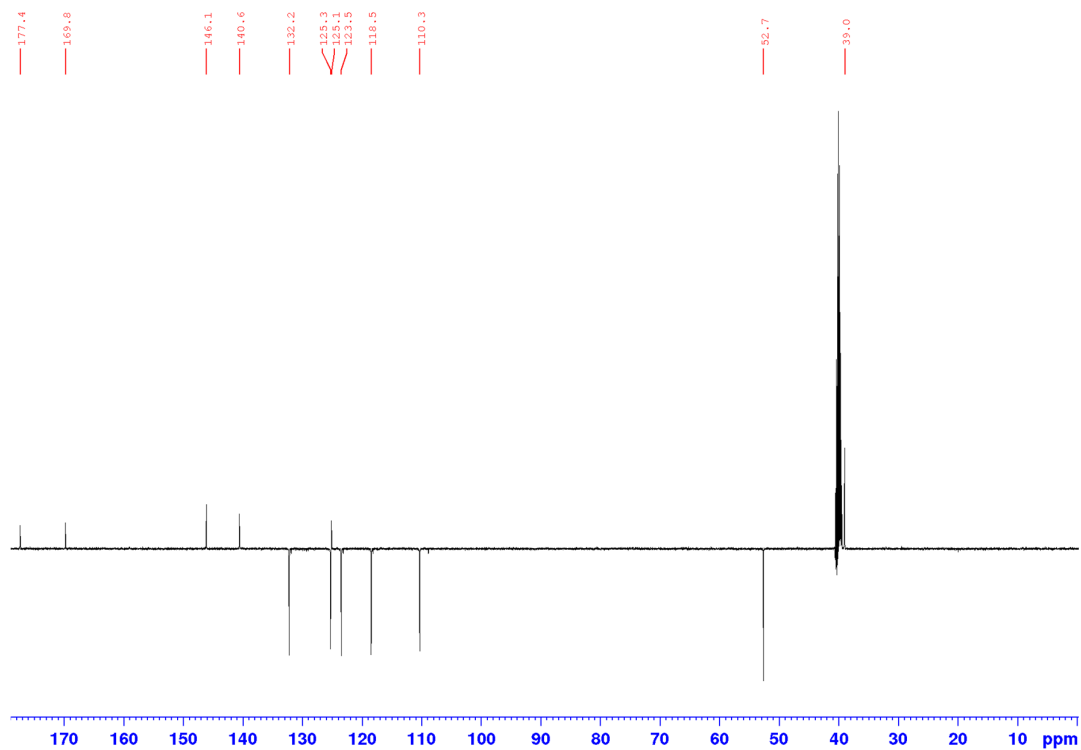


Figure S2. ¹³C NMR spectrum of 4a

SZP-20220523-POS #412-441 RT: 2.12-2.26 AV: 30 NL: 1.43E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

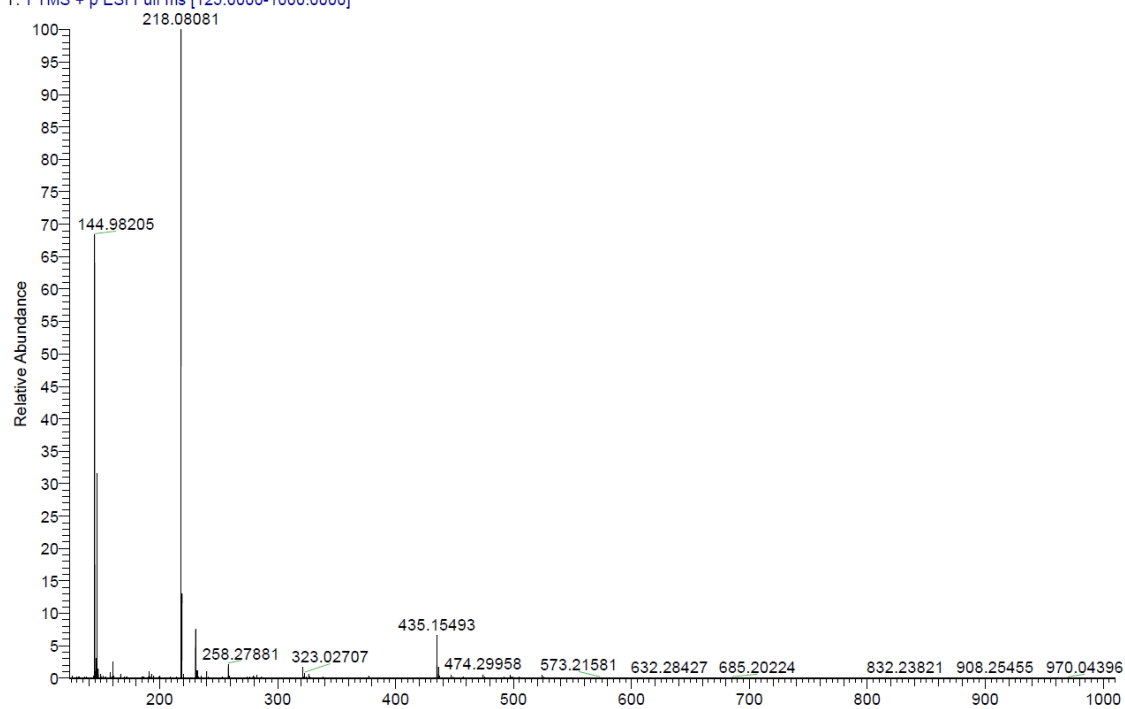


Figure S3. HRMS spectrum of **4a**

Ethyl 2-(4-hydroxyquinolin-2-yl) acetate (**4b**)

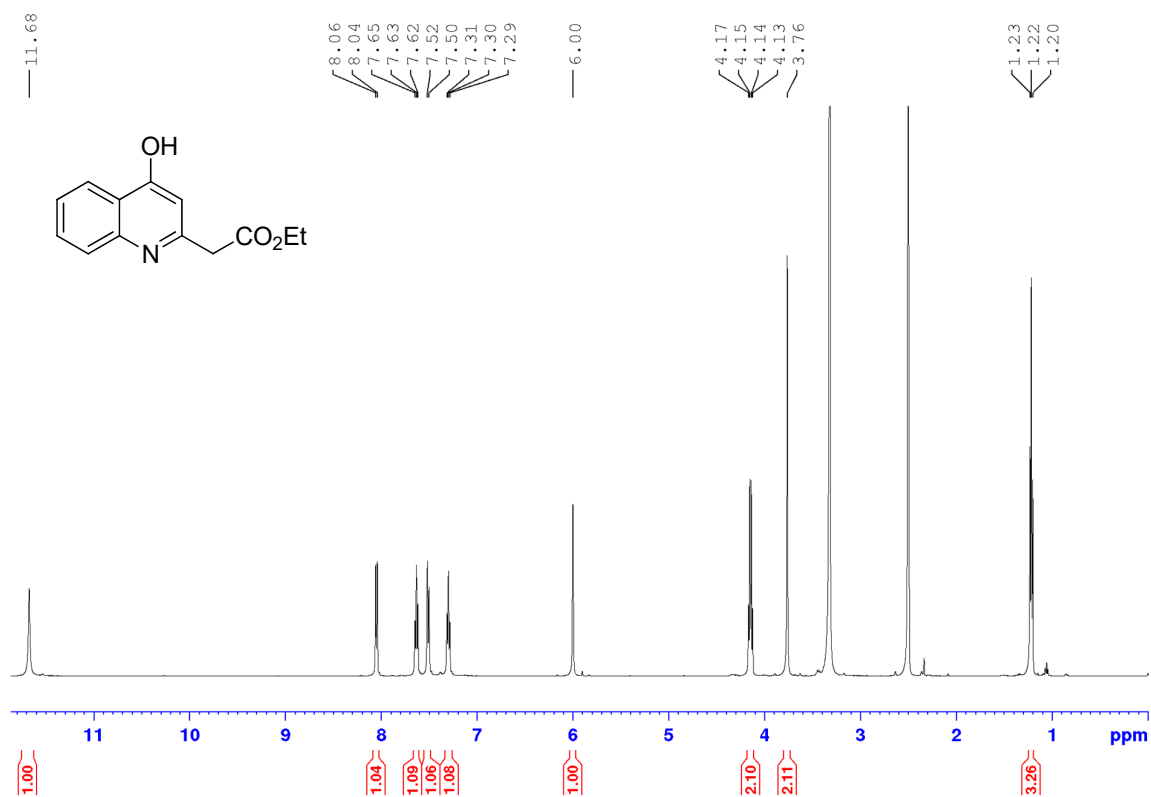


Figure S4. ¹H NMR spectrum of **4b**

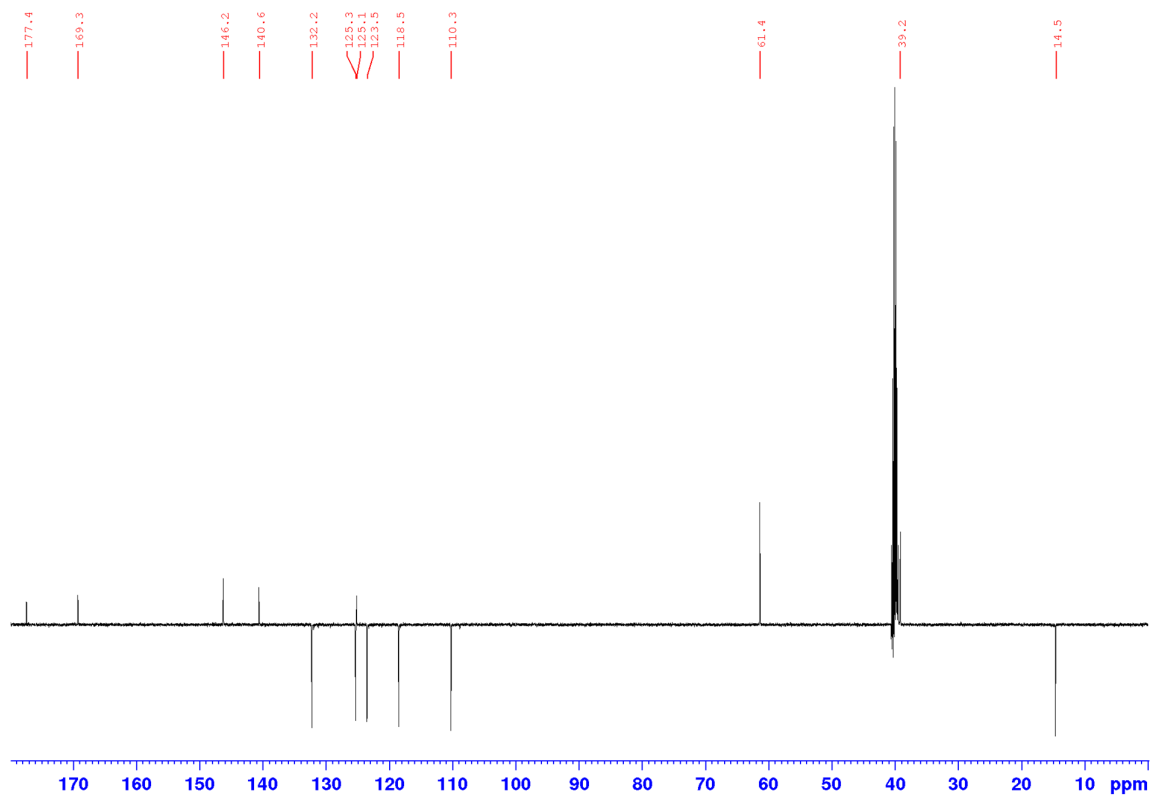


Figure S5. ¹³C NMR spectrum of **4b**

SZP-20220523-POS #901-923 RT: 4.63-4.75 AV: 23 NL: 1.96E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

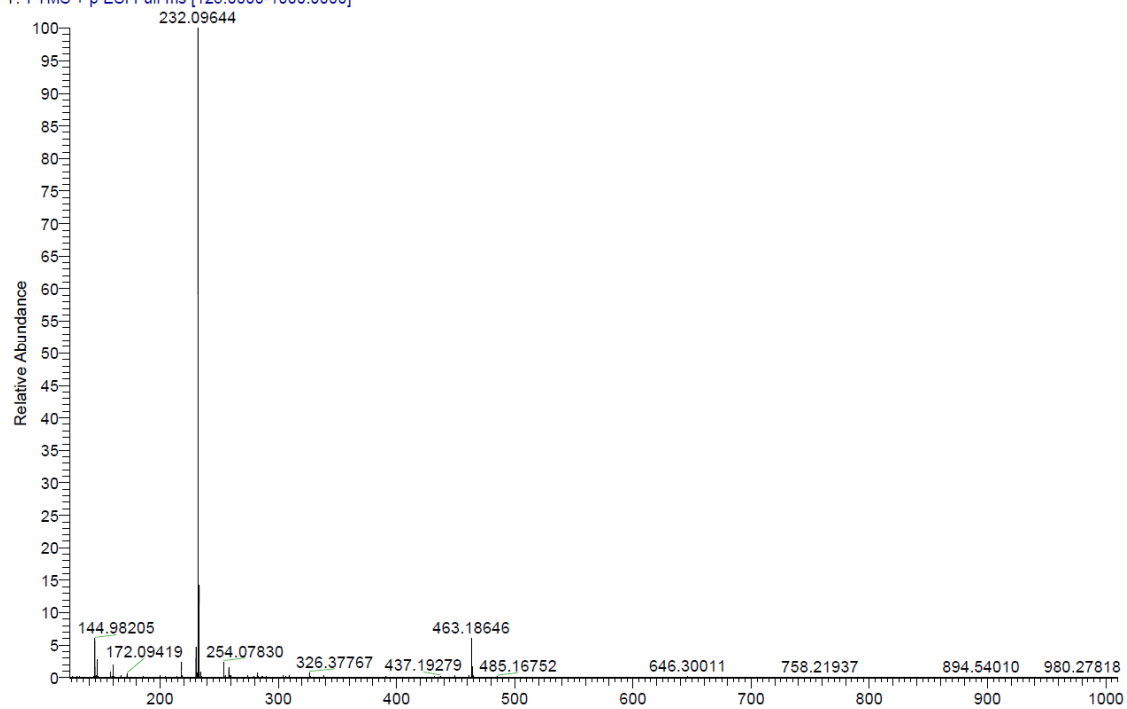


Figure S6. HRMS spectrum of **4b**

1-Phenyl-4-(phenylamino)pyridine-2,6(1*H*,3*H*)-dione (5)

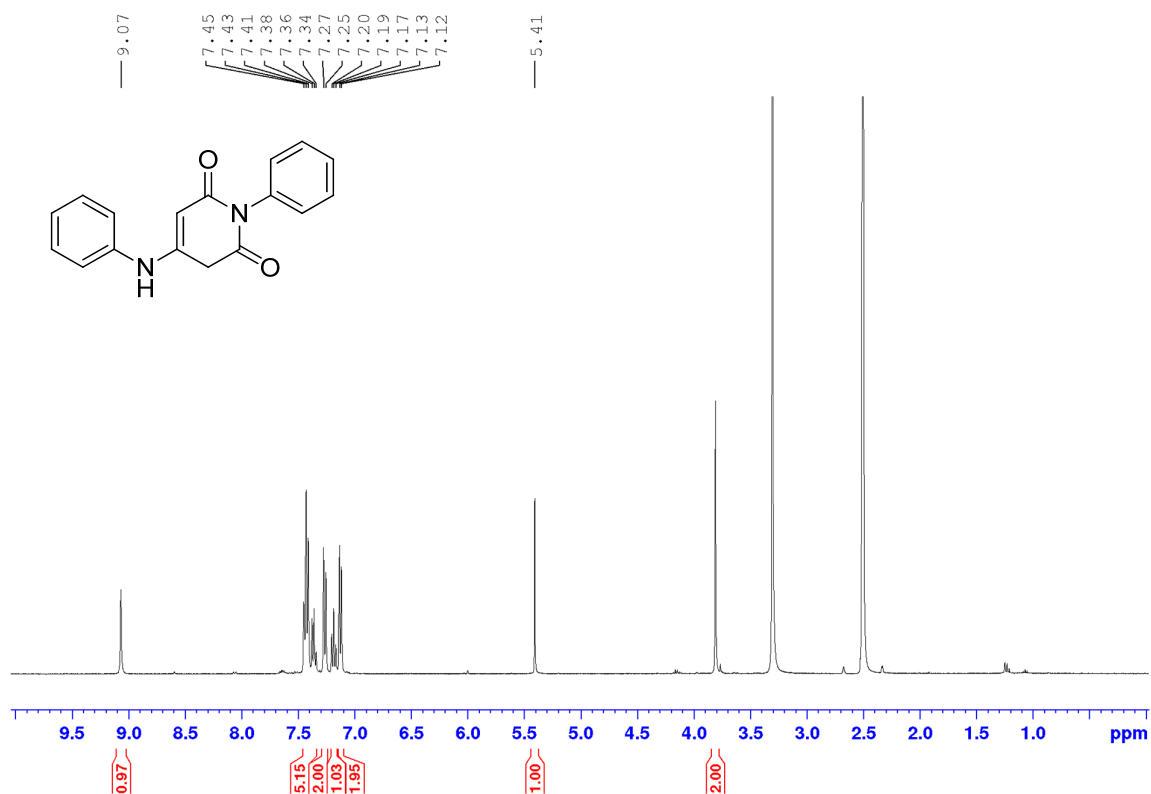


Figure S7. ¹H NMR spectrum of 5

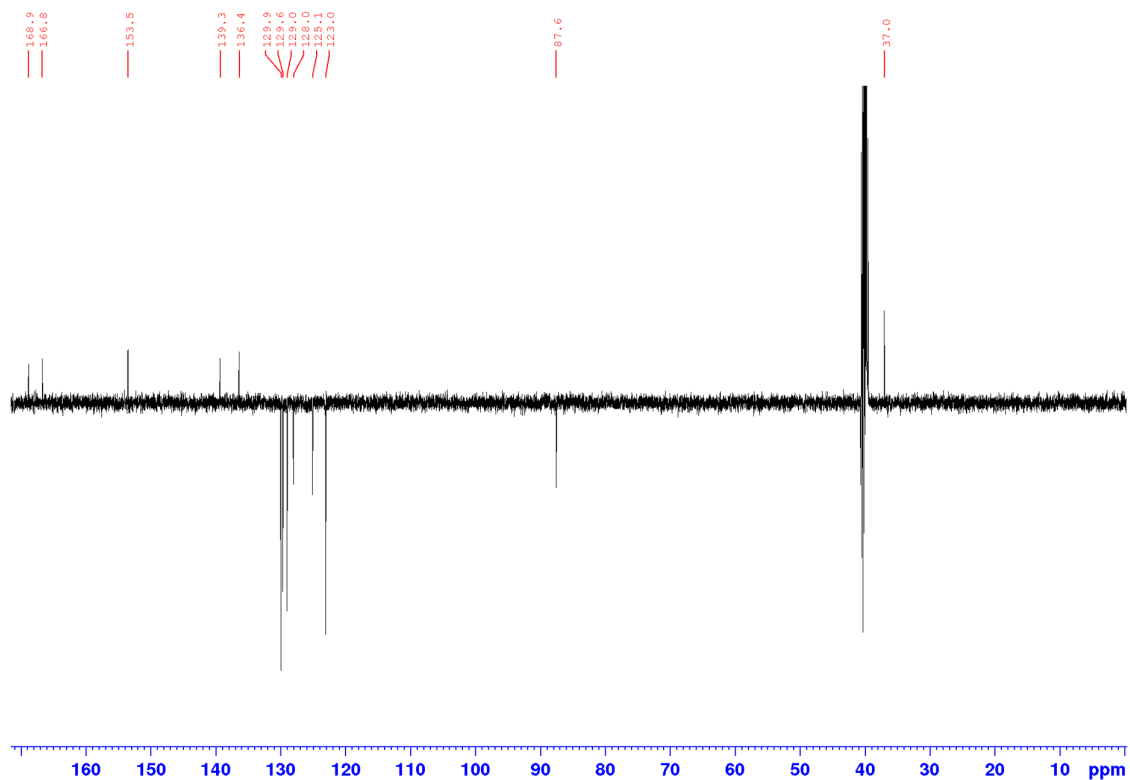


Figure S8. ¹³C NMR spectrum of 5

SZP-20220523-POS #2367-2385 RT: 12.25-12.34 AV: 19 NL: 6.45E8
T: FTMS + p ESI Full ms [125.0000-1000.0000]

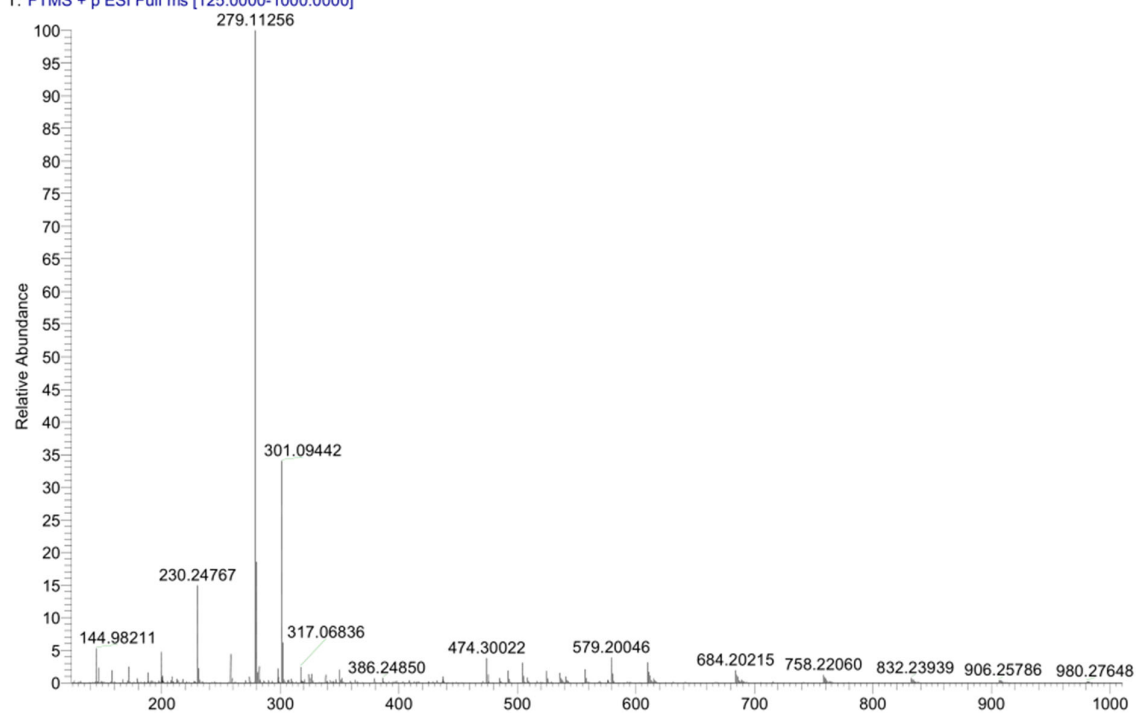


Figure S9. HRMS spectrum of 5

2,2'-(Propane-1,3-diyl)bis(quinolin-4-ol) (7)

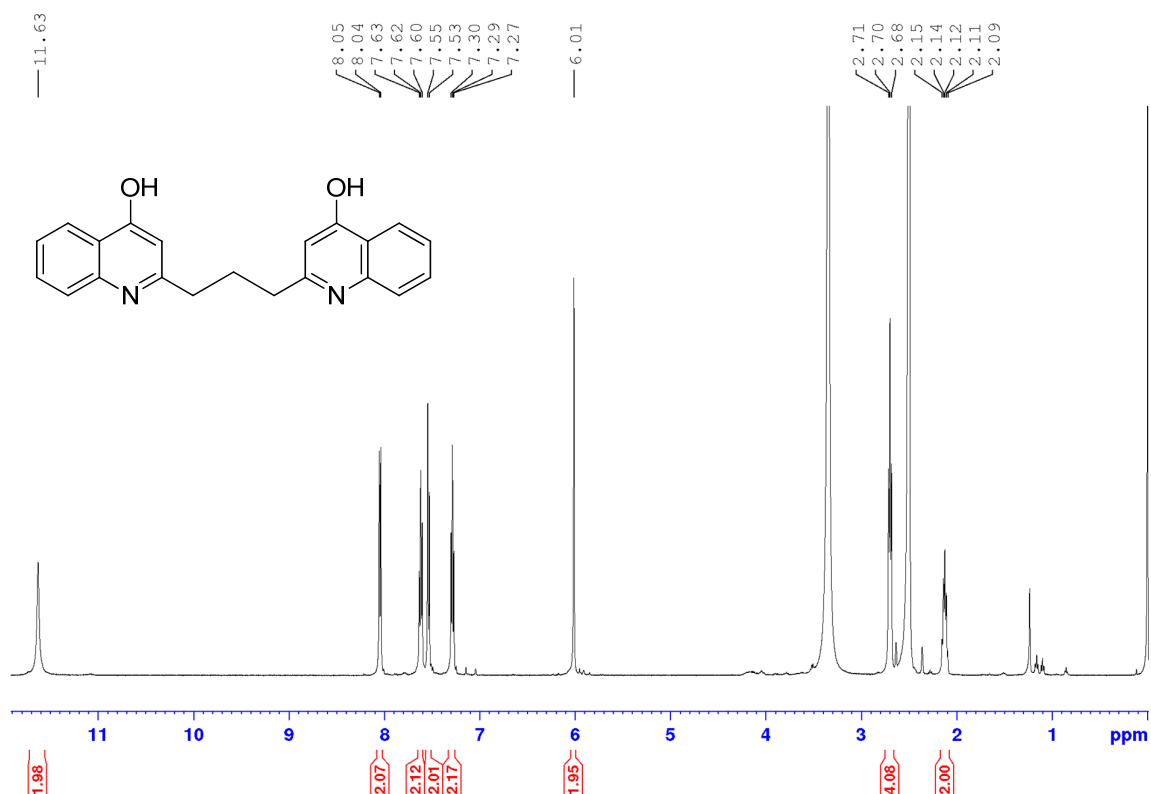


Figure S10. ¹H NMR spectrum of 7

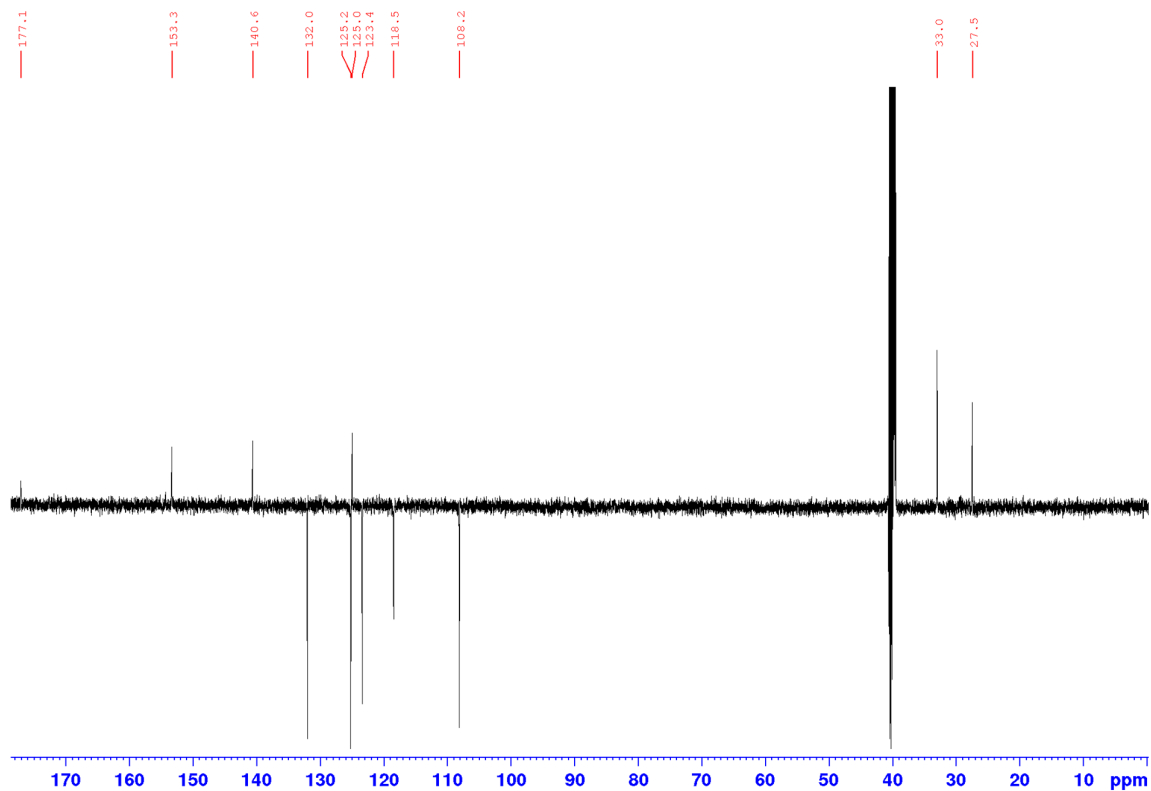


Figure S11. ¹³C NMR spectrum of 7

SZP-20220523-POS #4711-4725 RT: 24.46-24.53 AV: 15 NL: 1.09E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

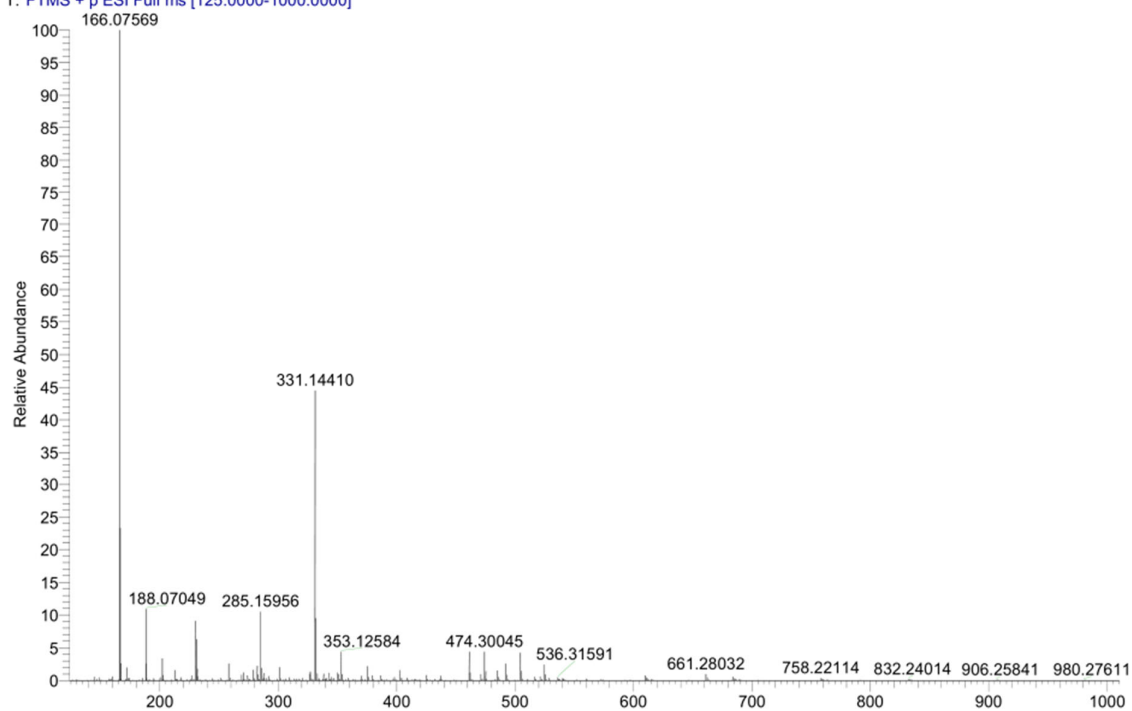


Figure S12. HRMS spectrum of 7

2,2'-(2-Phenylpropane-1,3-diyl)bis(quinolin-4-ol) (**12**)

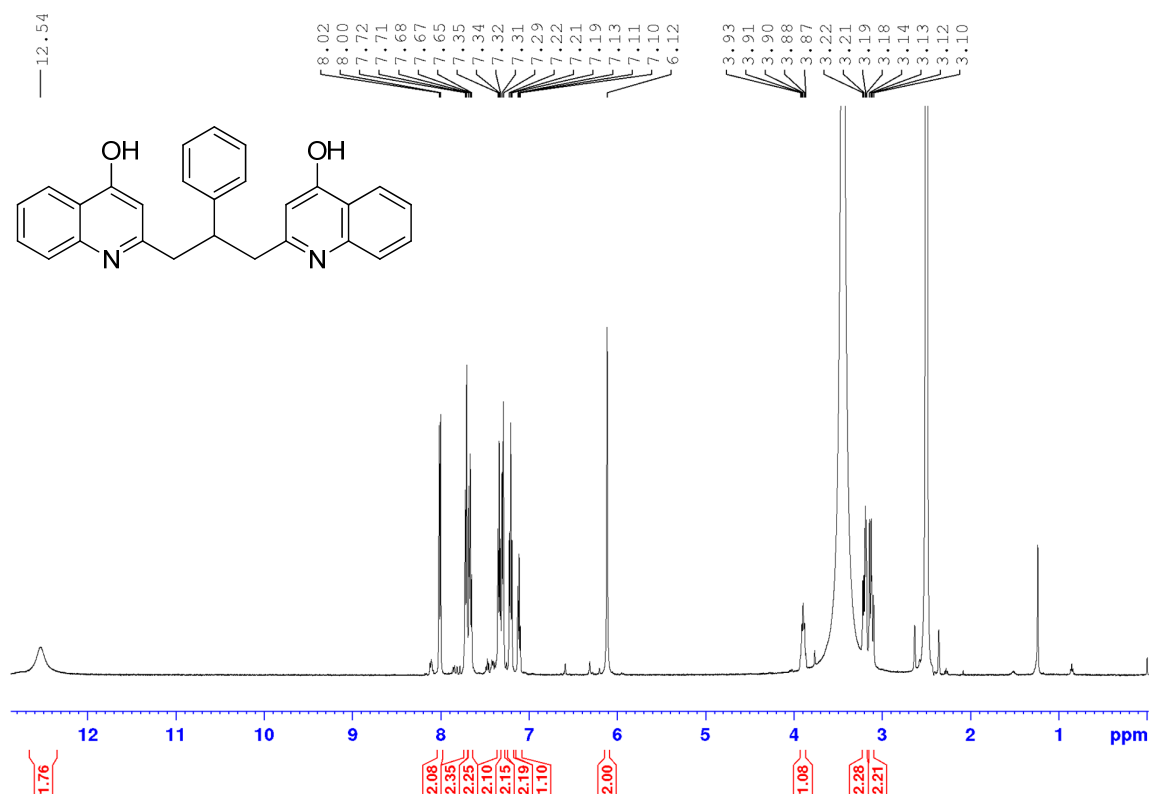


Figure S13. ¹H NMR spectrum of **12**

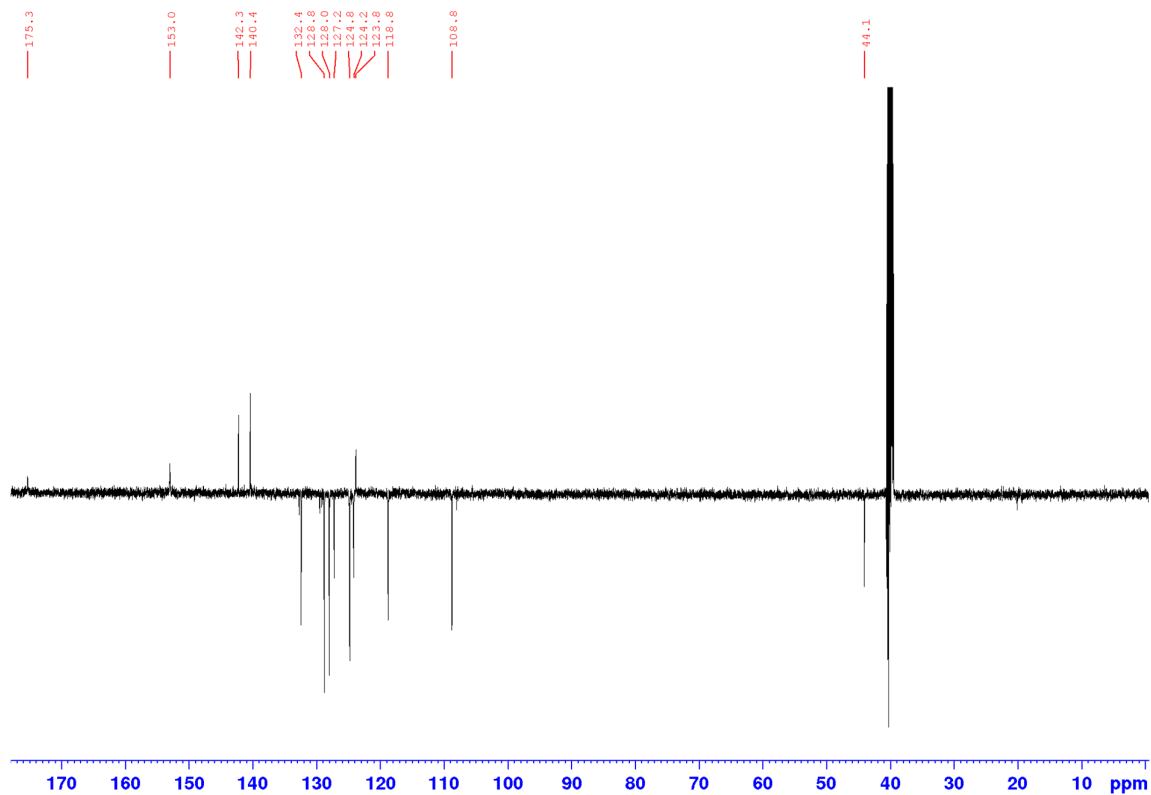


Figure S14. ¹³C NMR spectrum of **12**

SZP-20220523-POS #4848-4874 RT: 25.17-25.30 AV: 27 NL: 1.12E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

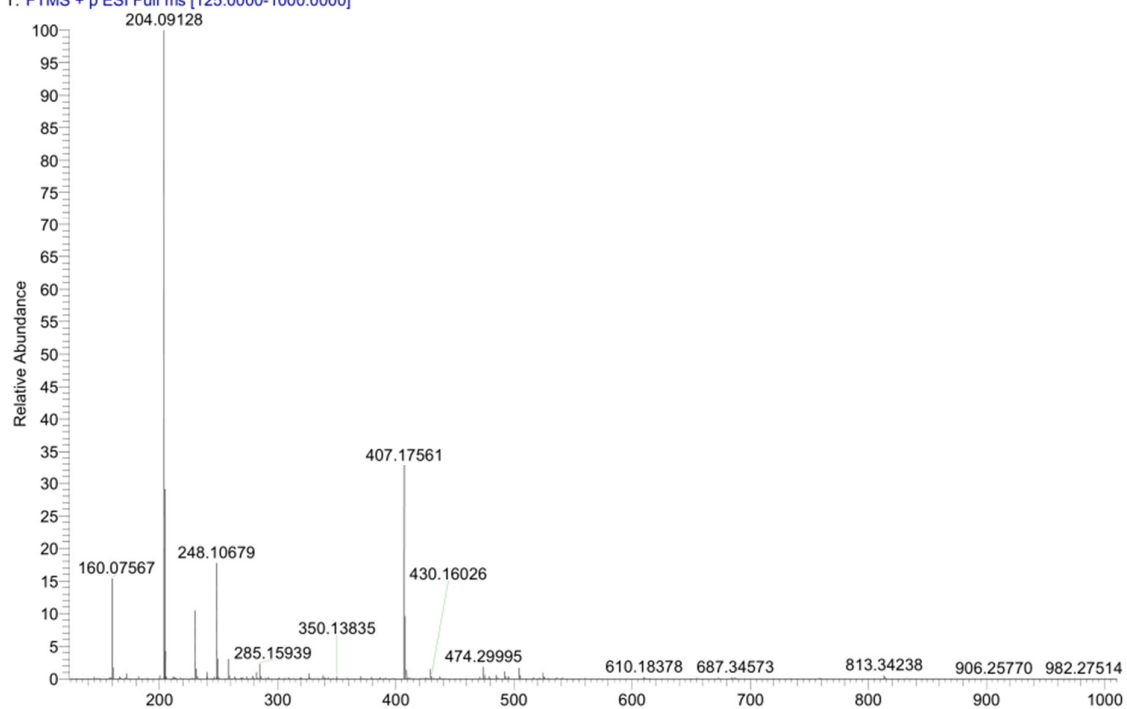


Figure S15. HRMS spectrum of 12

2-(4-hydroxyquinolin-2-yl)acetic acid (8)

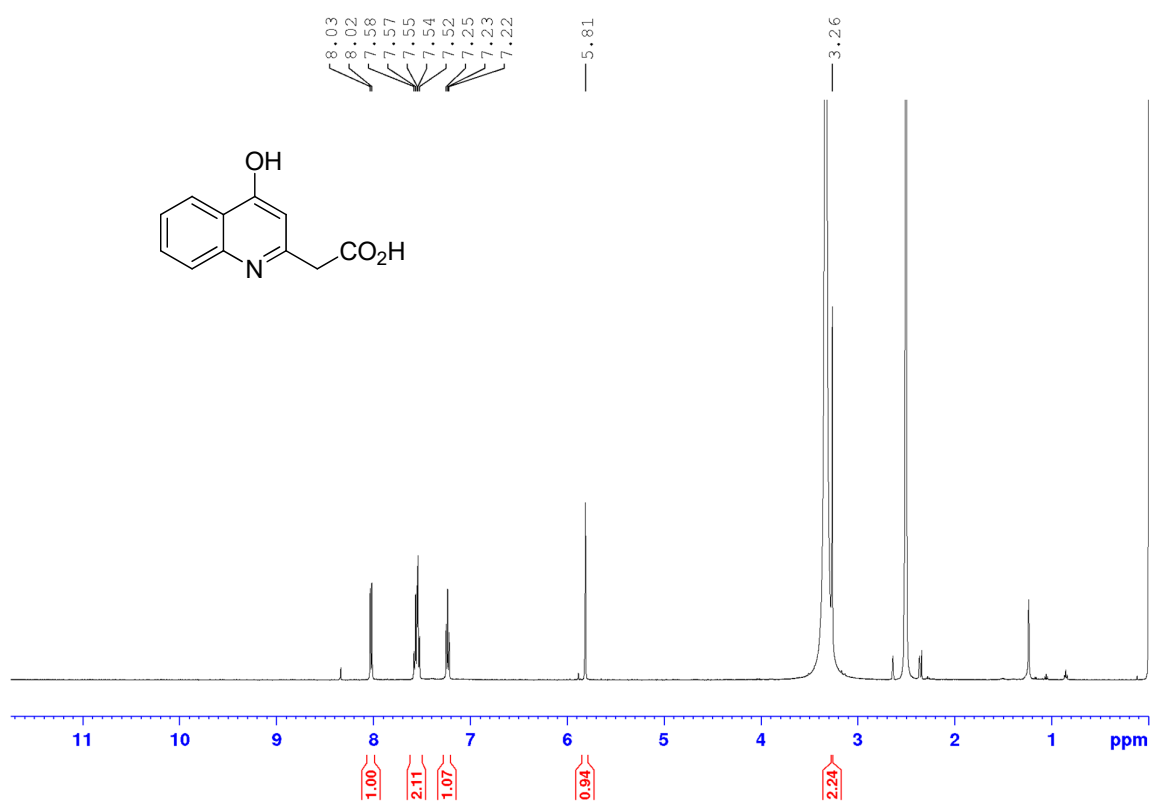


Figure S16. ¹H NMR spectrum of 8

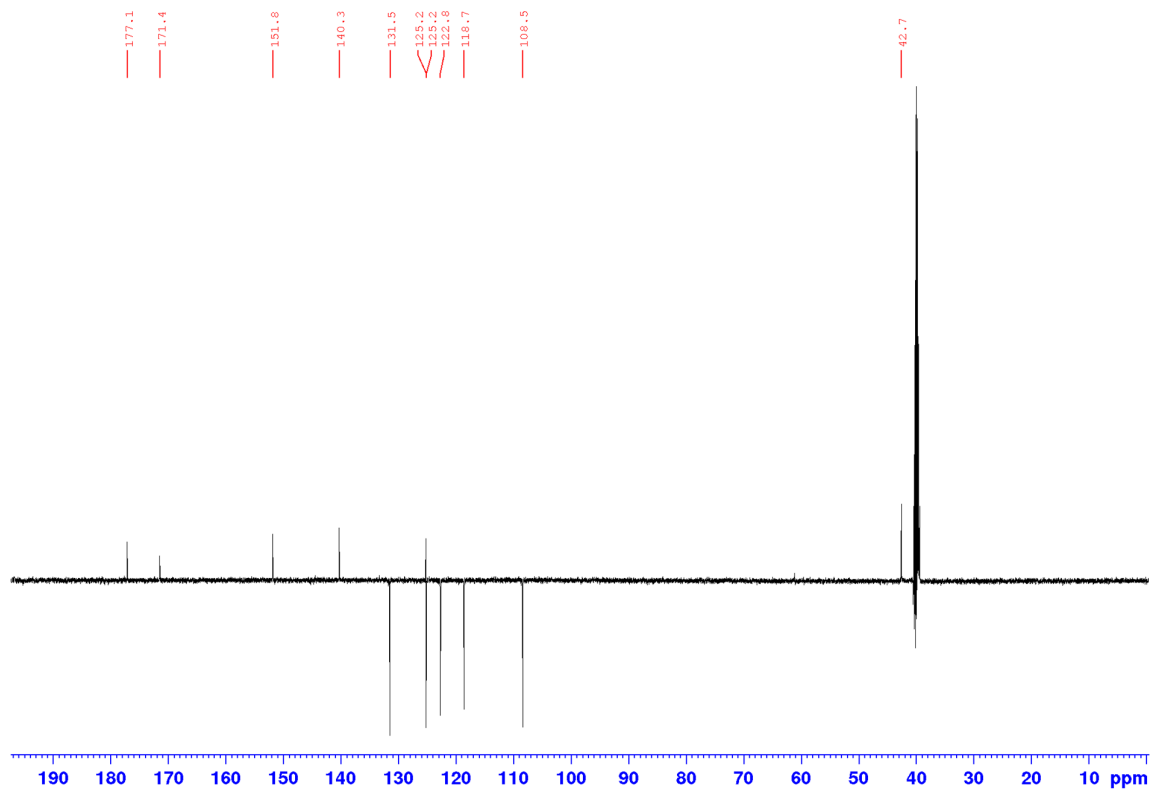


Figure S17. ¹³C NMR spectrum of 8

CSO-220617-POS #1478-1492 RT: 8.44-8.51 AV: 15 NL: 8.63E8
T: FTMS + p ESI Full lock ms [150.0000-1000.0000]

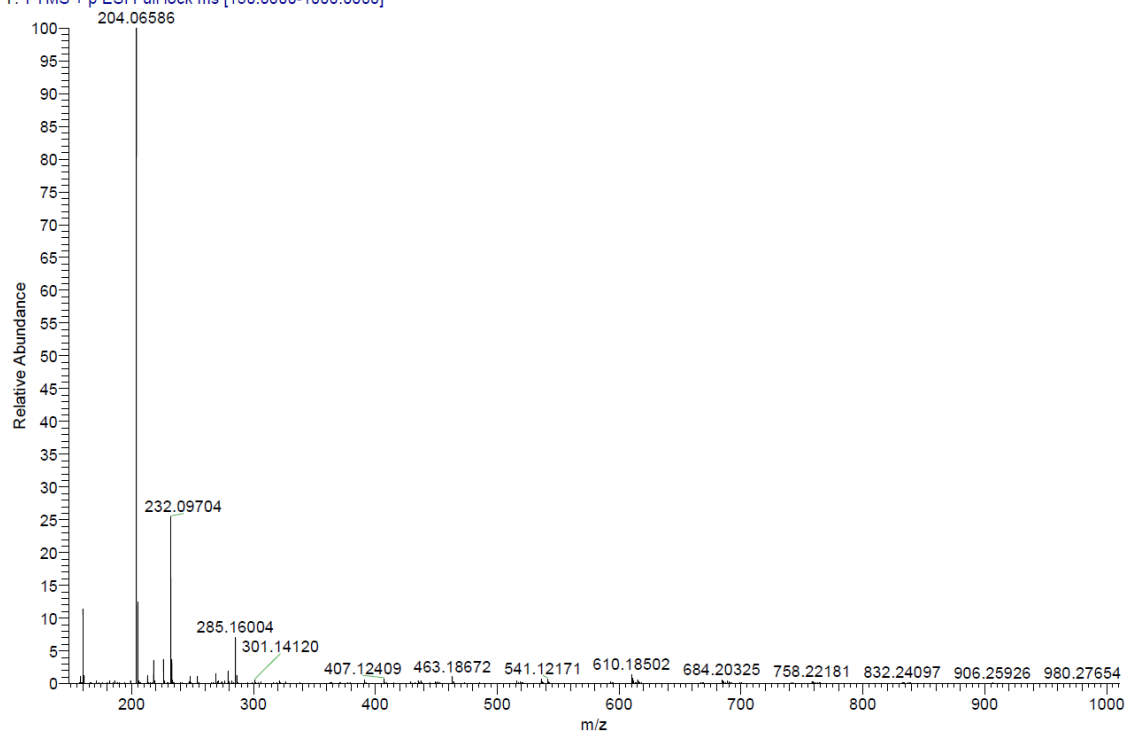


Figure S18. HRMS spectrum of 8

3-(Piperidin-1-ylmethyl)-1*H*-azeto[1,2-*a*]quinolin-4(2*H*)-one (9)

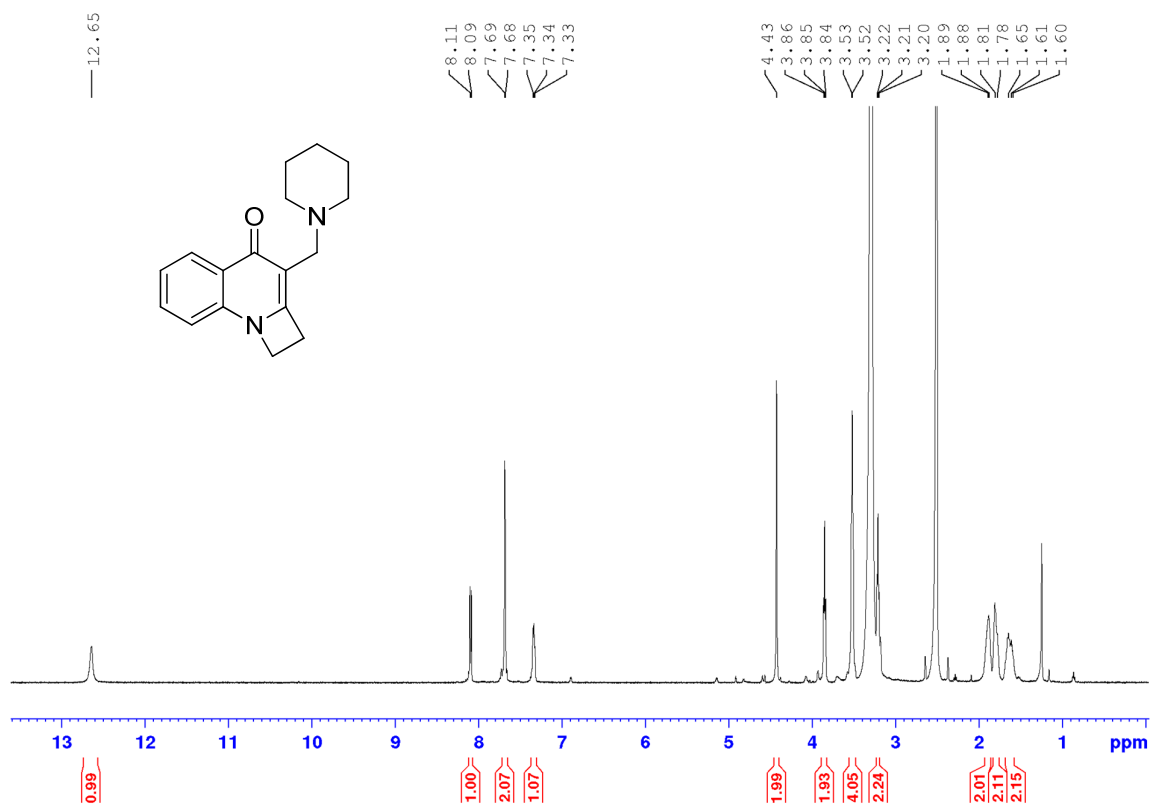


Figure S19. ¹H NMR spectrum of 9

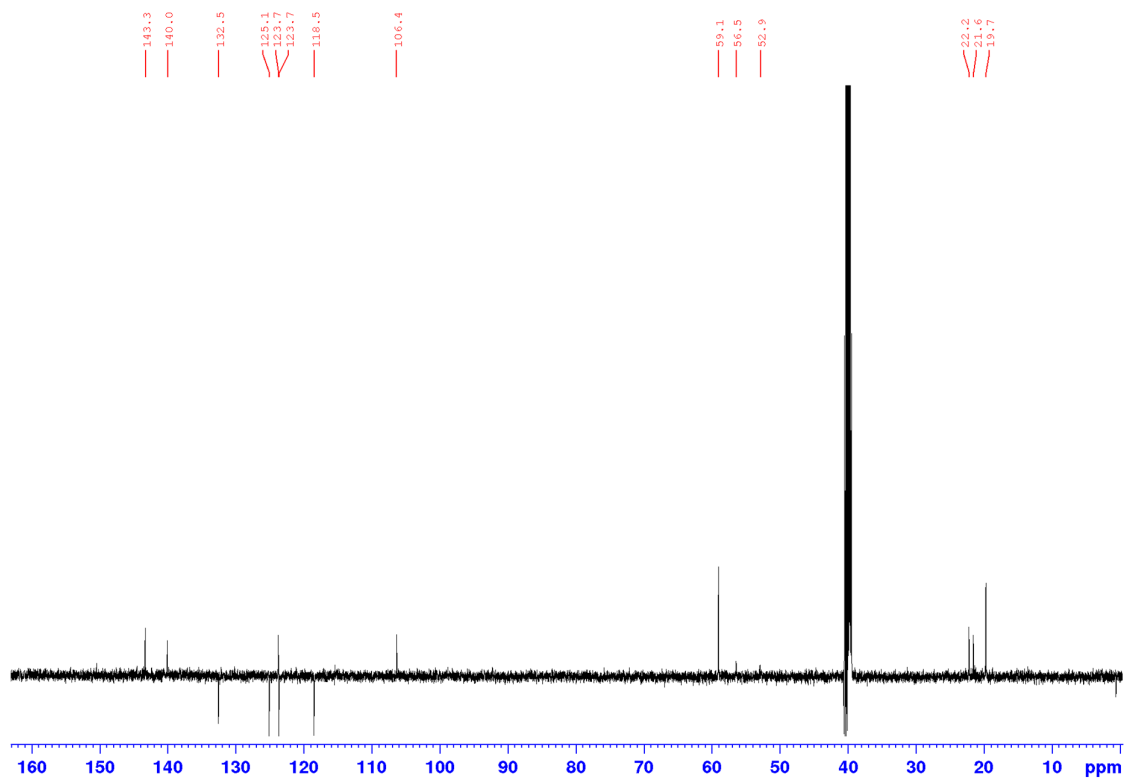


Figure S20. ¹³C NMR spectrum of 9

CSO-220617-POS #1310-1324 RT: 7.46-7.54 AV: 15 NL: 1.20E8
T: FTMS + p ESI Full lock ms [150.0000-1000.0000]

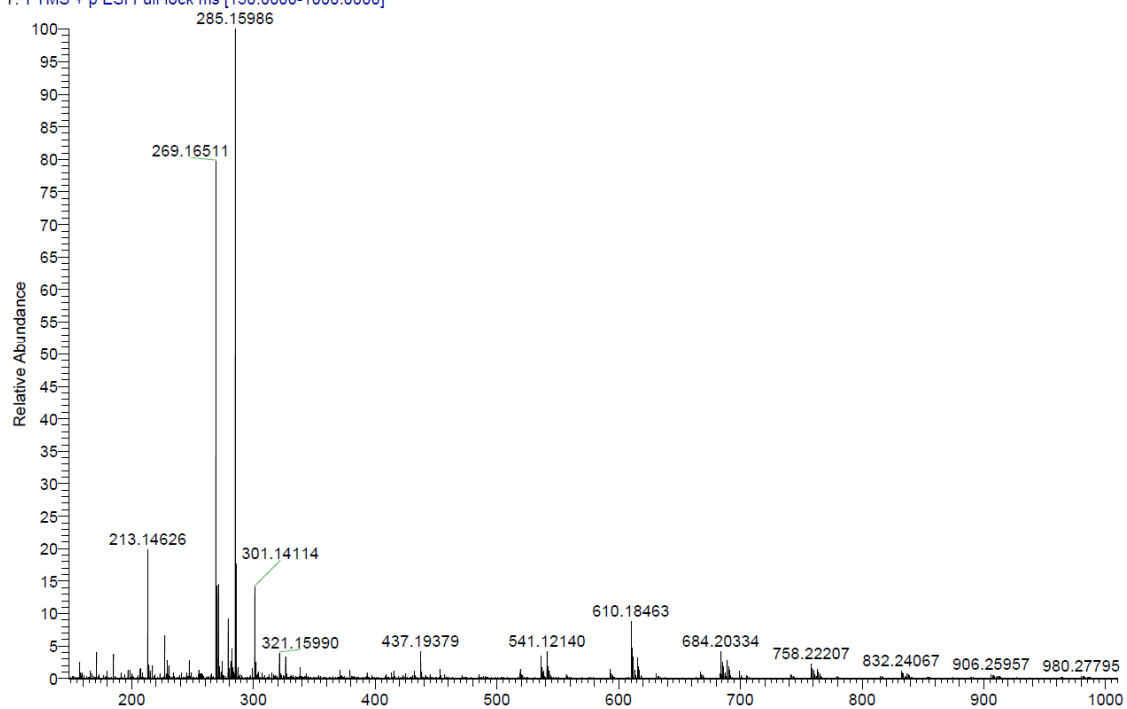


Figure S21. HRMS spectrum of **9**

Methyl 2-(4-hydroxy-3-(piperidin-1-ylmethyl)quinolin-2-yl) acetate (10a)

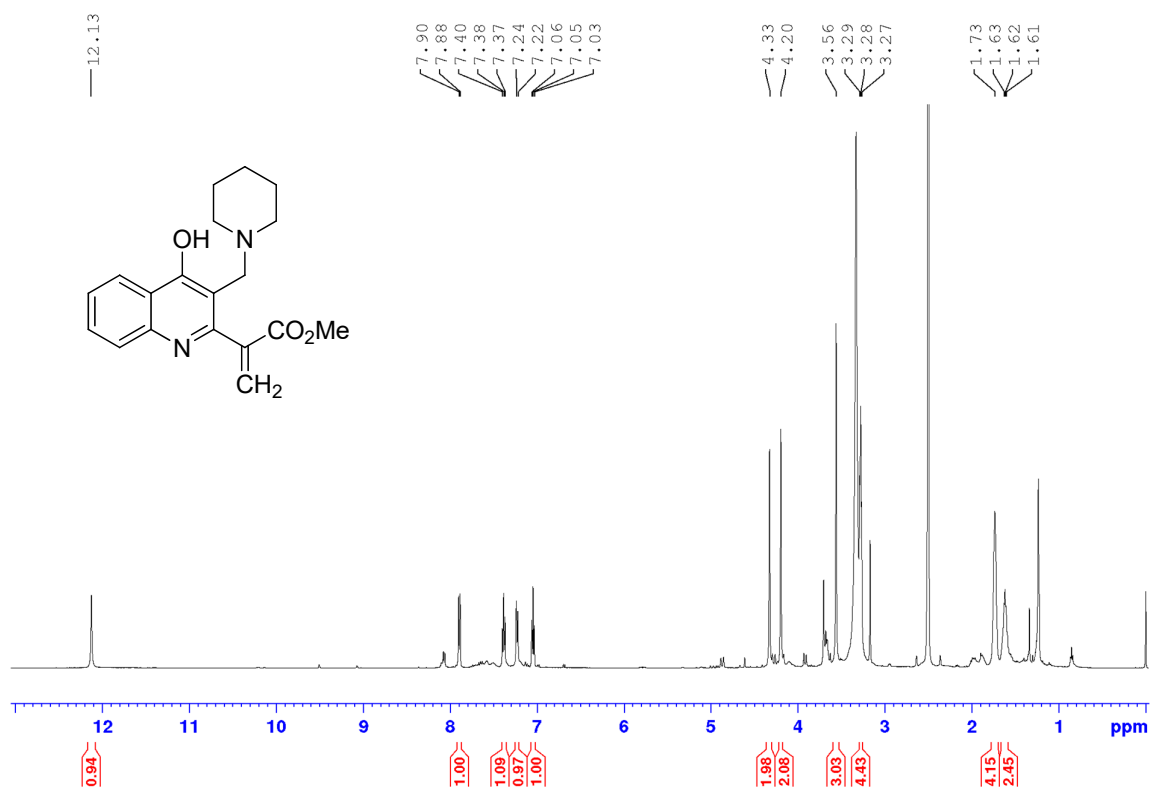


Figure S22. ¹H NMR spectrum of 10a

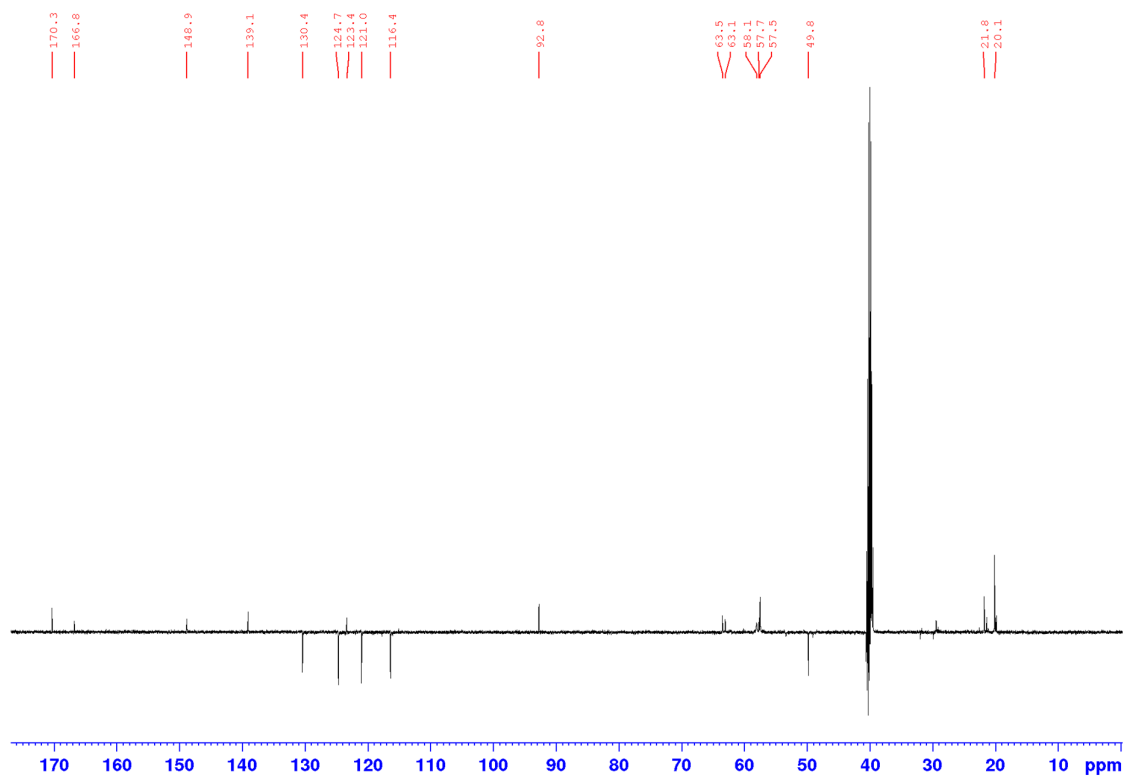


Figure S23. ¹³C NMR spectrum of 10a

SZP-20220523-POS #4552-4584 RT: 23.63-23.79 AV: 33 NL: 7.63E8
T: FTMS + p ESI Full ms [125.0000-1000.0000]

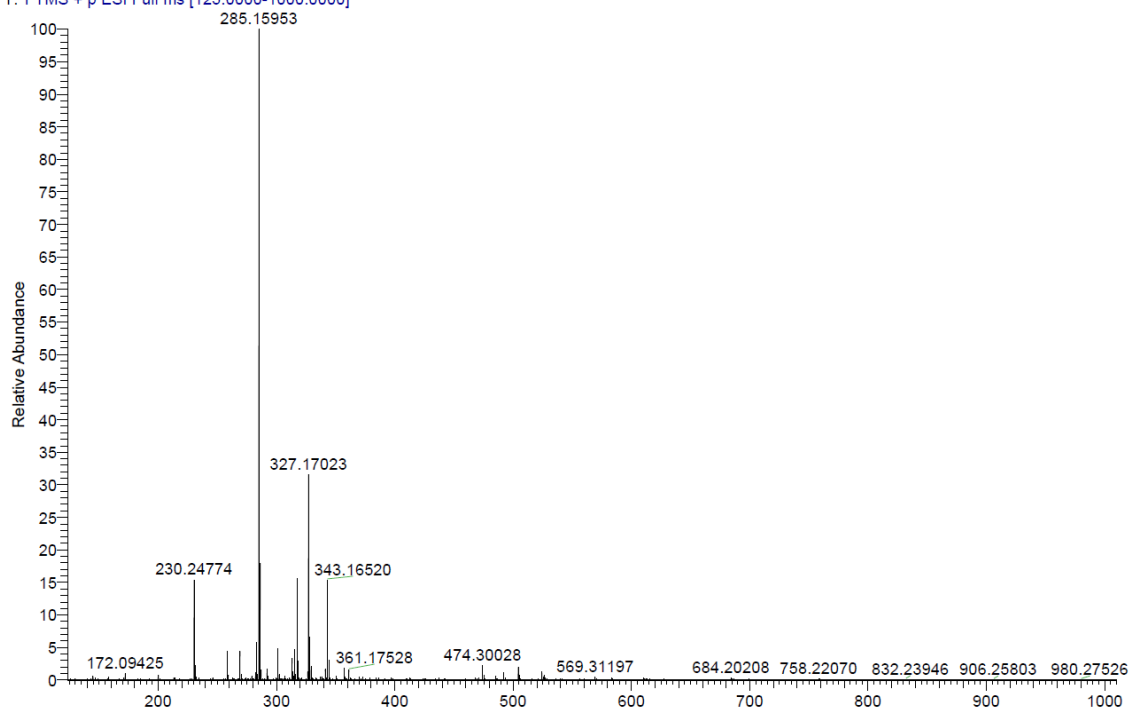


Figure S24. HRMS spectrum of 10a

Ethyl 2-(4-hydroxy-3-(piperidin-1-ylmethyl)quinolin-2-yl) acetate (**10b**)

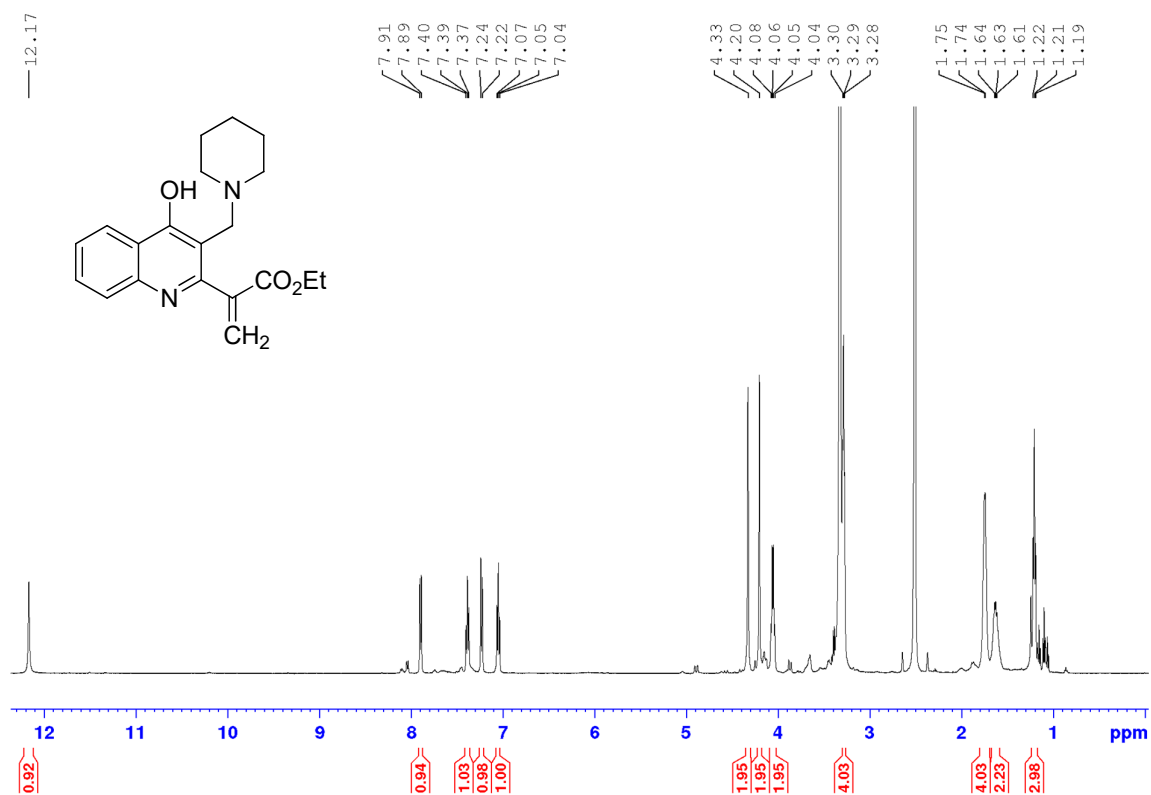


Figure S25. ¹H NMR spectrum of **10b**

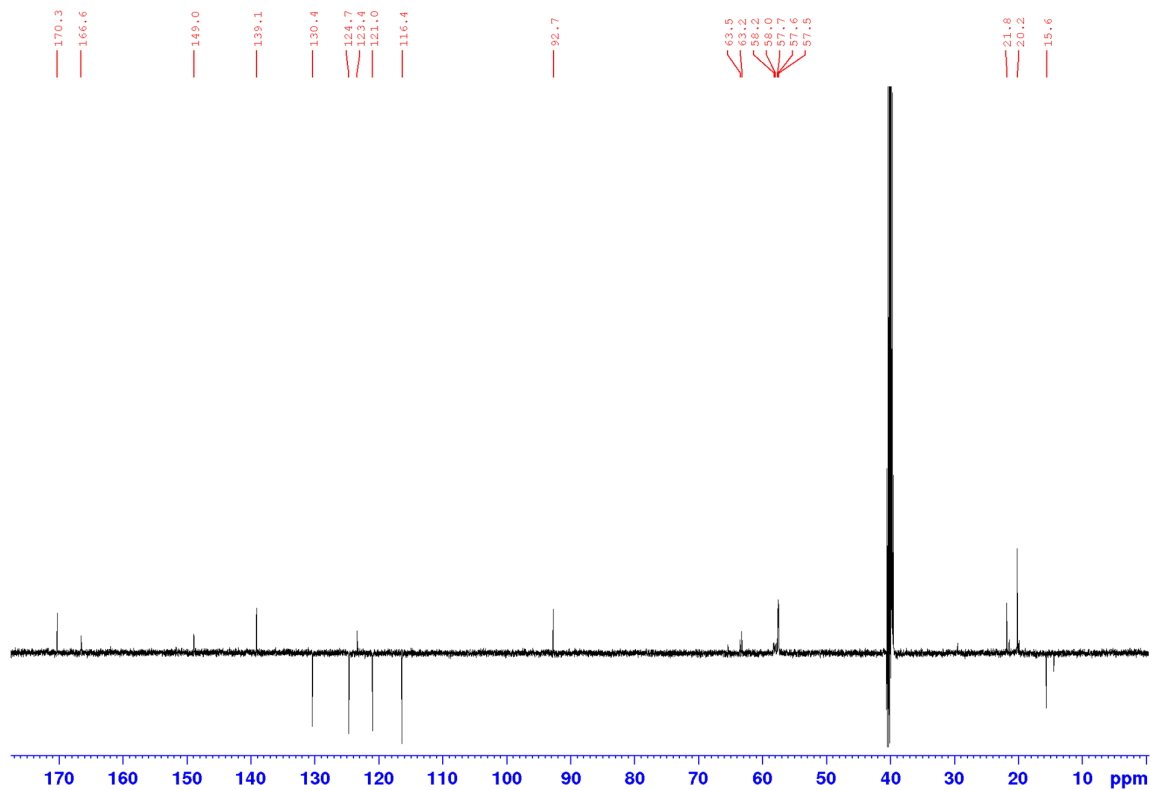


Figure S26. ¹³C NMR spectrum of **10b**

SZP-20220523-POS #4037-4073 RT: 20.95-21.13 AV: 37 NL: 9.87E8
T: FTMS + p ESI Full ms [125.0000-1000.0000]

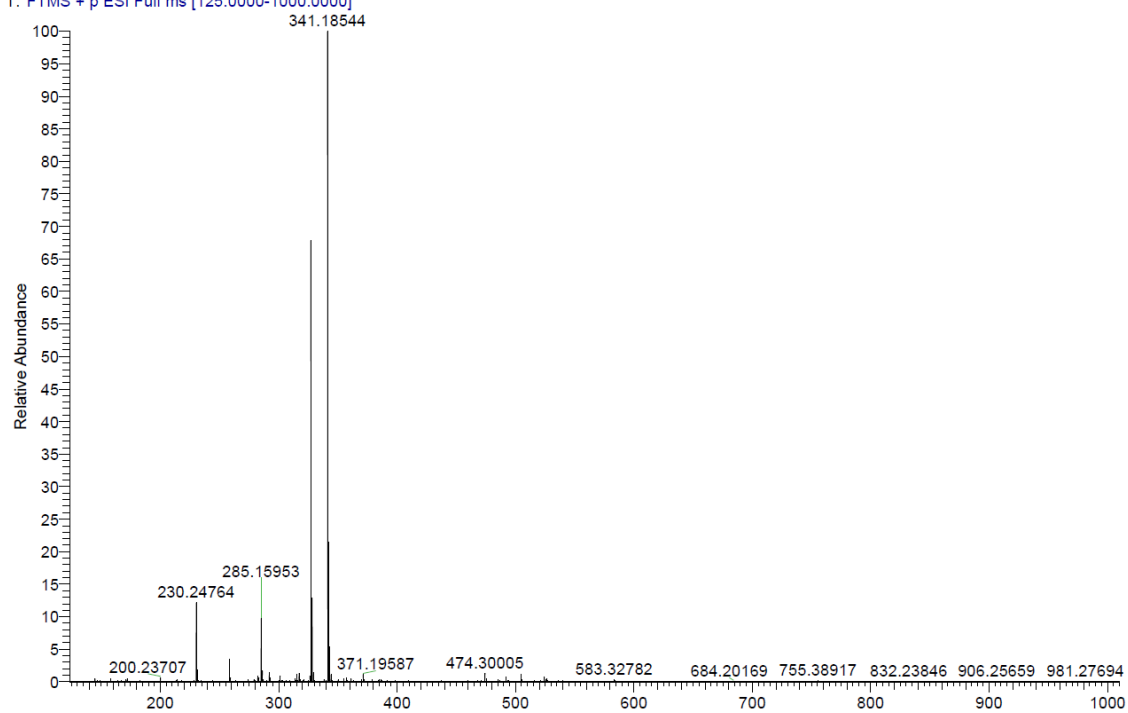


Figure S27. HRMS spectrum of **10b**

(Z)-methyl 2-(4-hydroxyquinolin-2-yl)-3-phenylacrylate (13a)

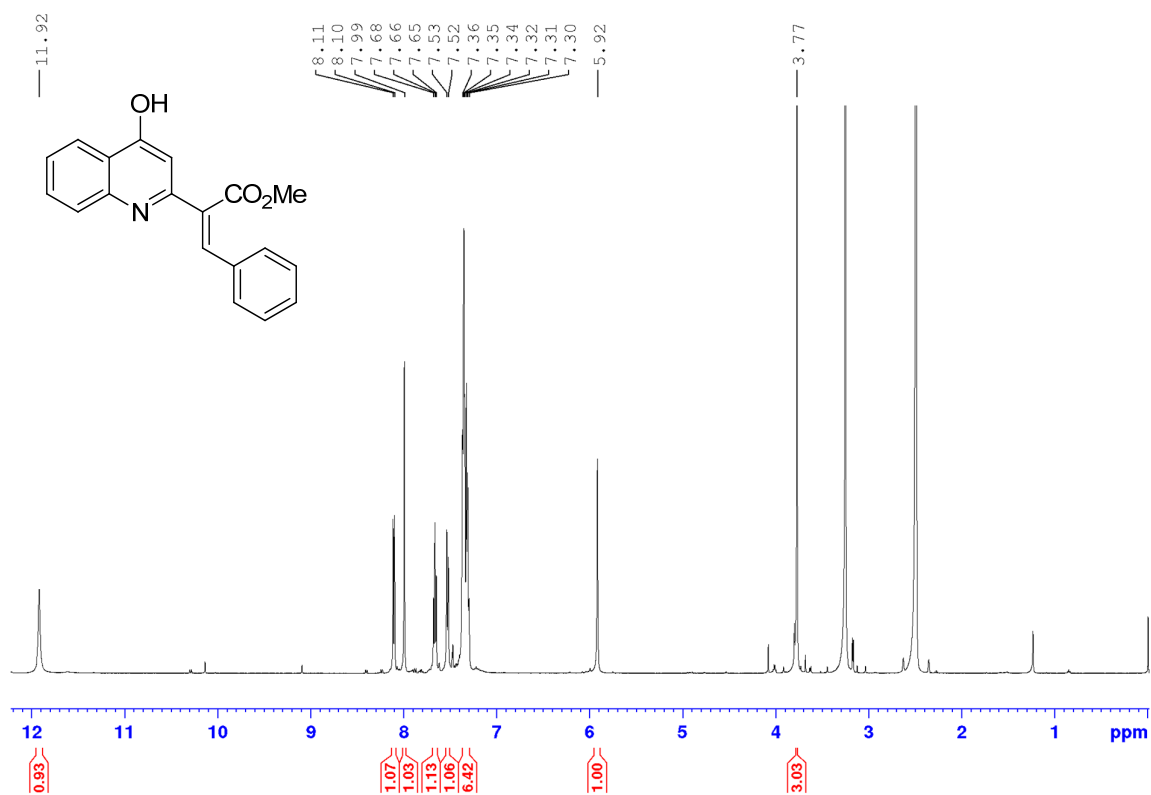


Figure S28. ¹H NMR spectrum of **13a**

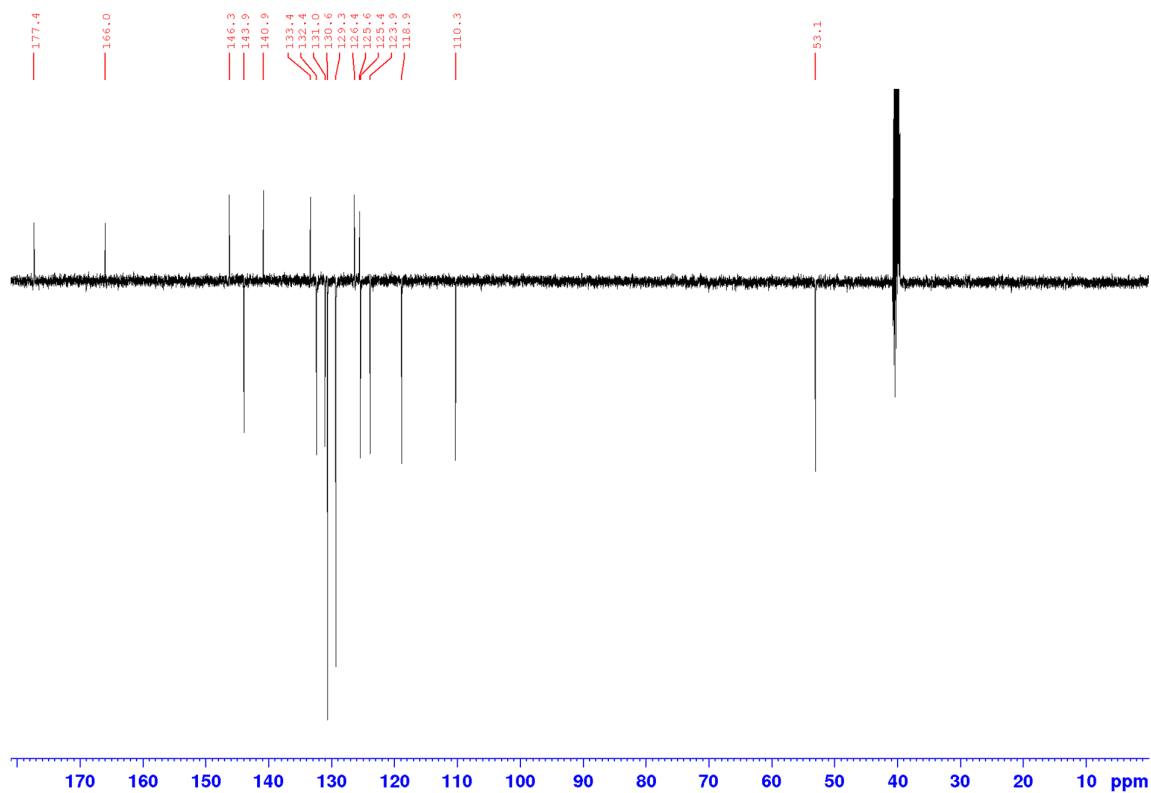


Figure S29. ¹³C NMR spectrum of **13a**

SZP-20220523-POS #652-684 RT: 3.35-3.51 AV: 33 NL: 1.88E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

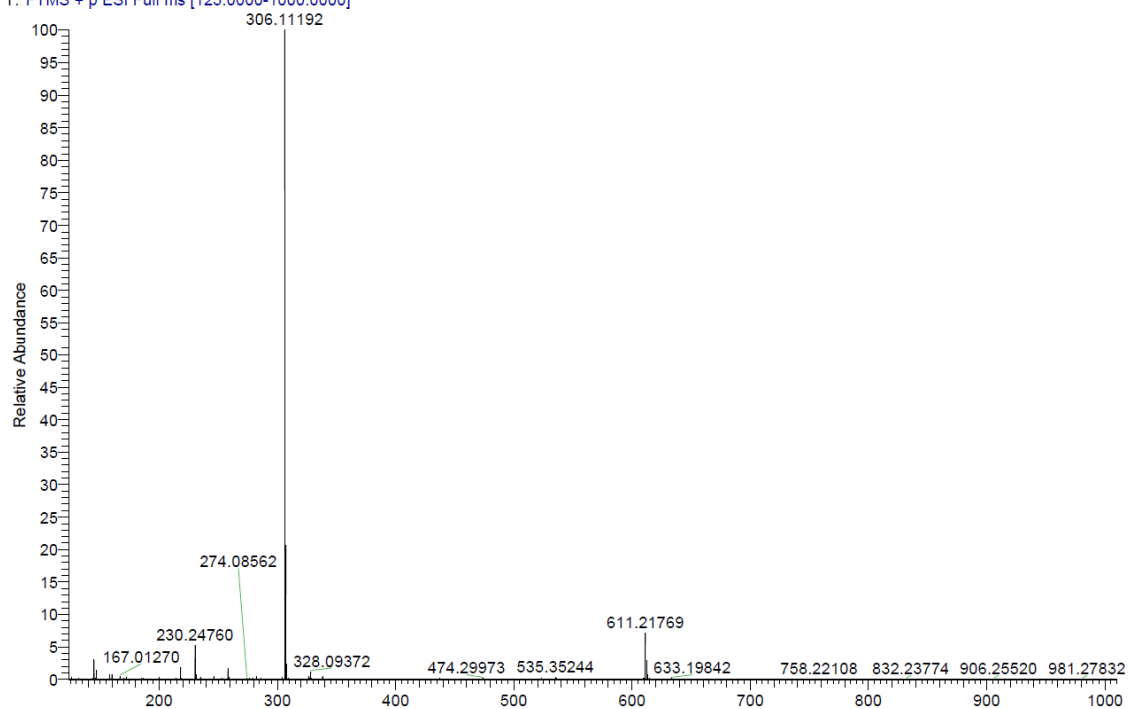


Figure S30. HRMS spectrum of **13a**

(Z)-ethyl 2-(4-hydroxyquinolin-2-yl)-3-phenylacrylate (13b)

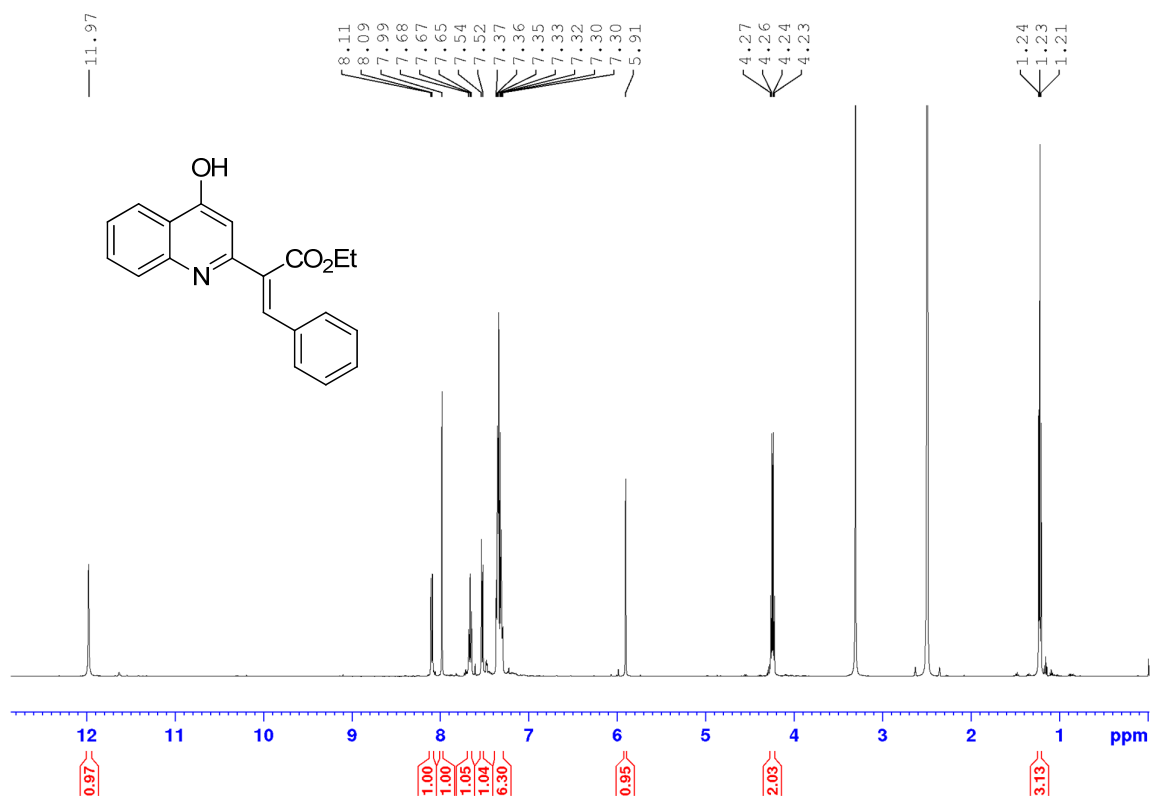


Figure S31. ¹H NMR spectrum of **13b**

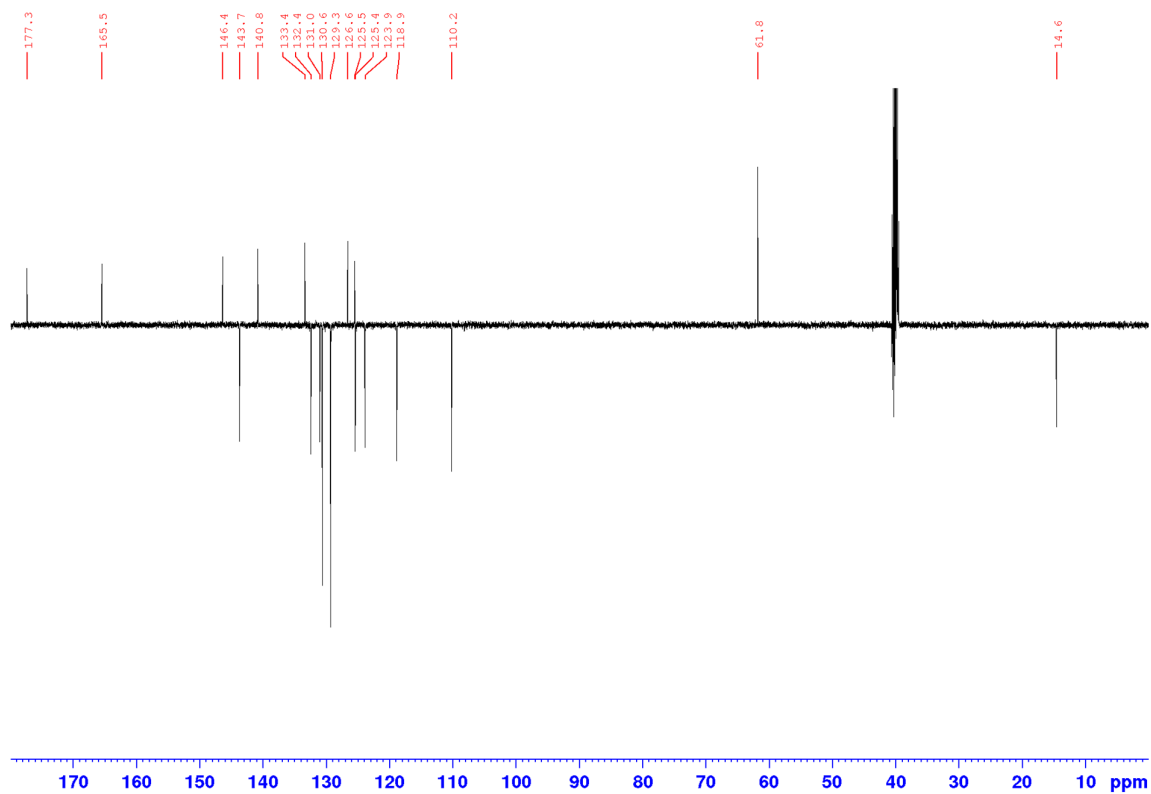


Figure S32. ¹³C NMR spectrum of **13b**

SZP-20220523-POS #1103-1132 RT: 5.68-5.83 AV: 30 NL: 2.07E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

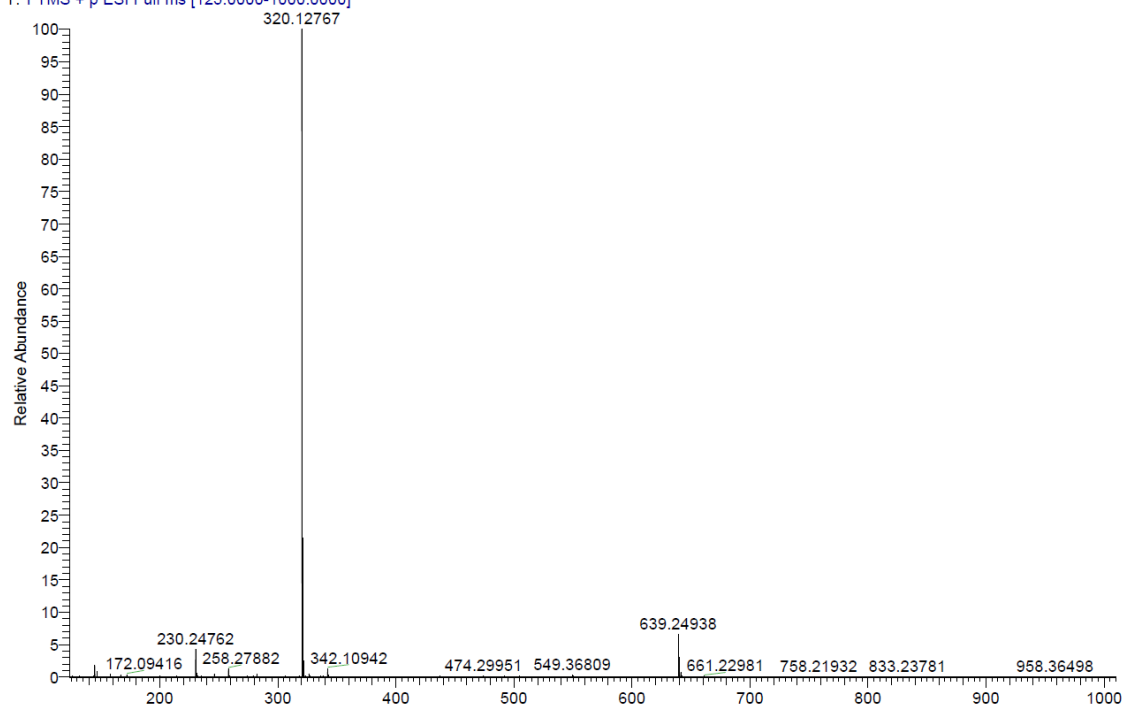


Figure S33. HRMS spectrum of **13b**

(Z)-ethyl 2-(4-hydroxyquinolin-2-yl)-3-(4-nitrophenyl)acrylate (**20**)

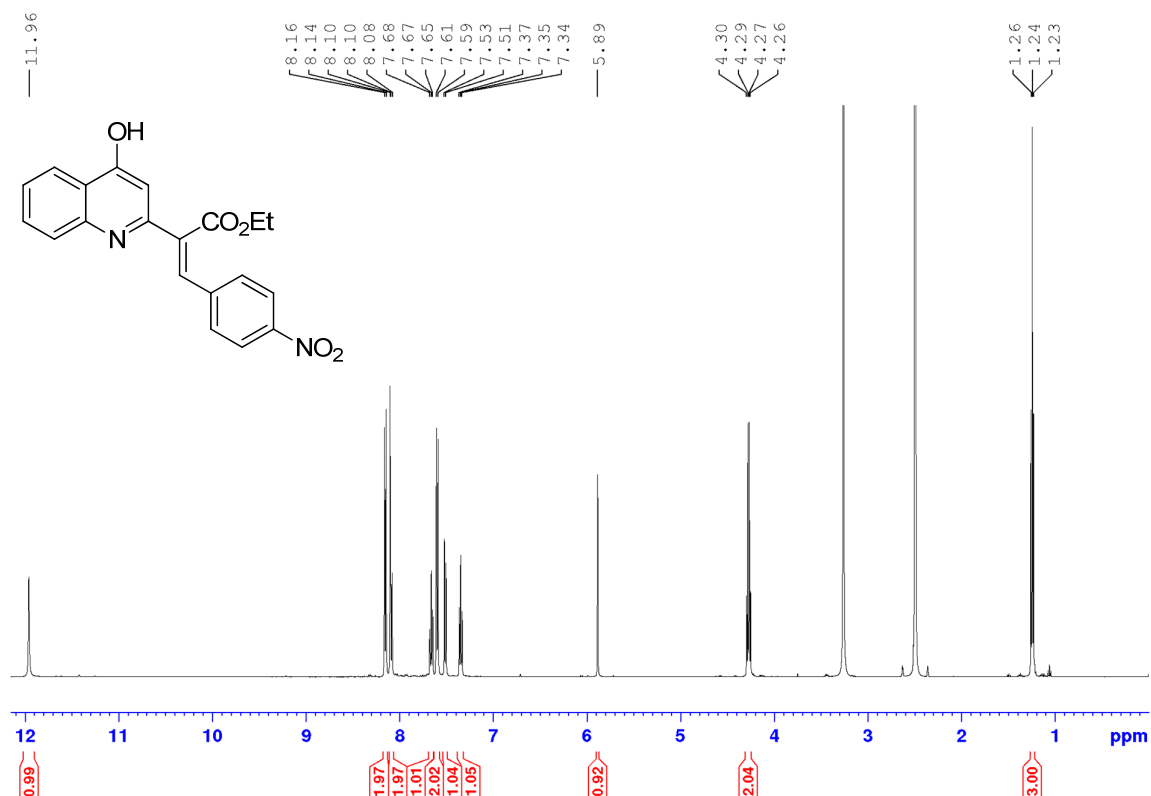


Figure S34. ¹H NMR spectrum of **20**

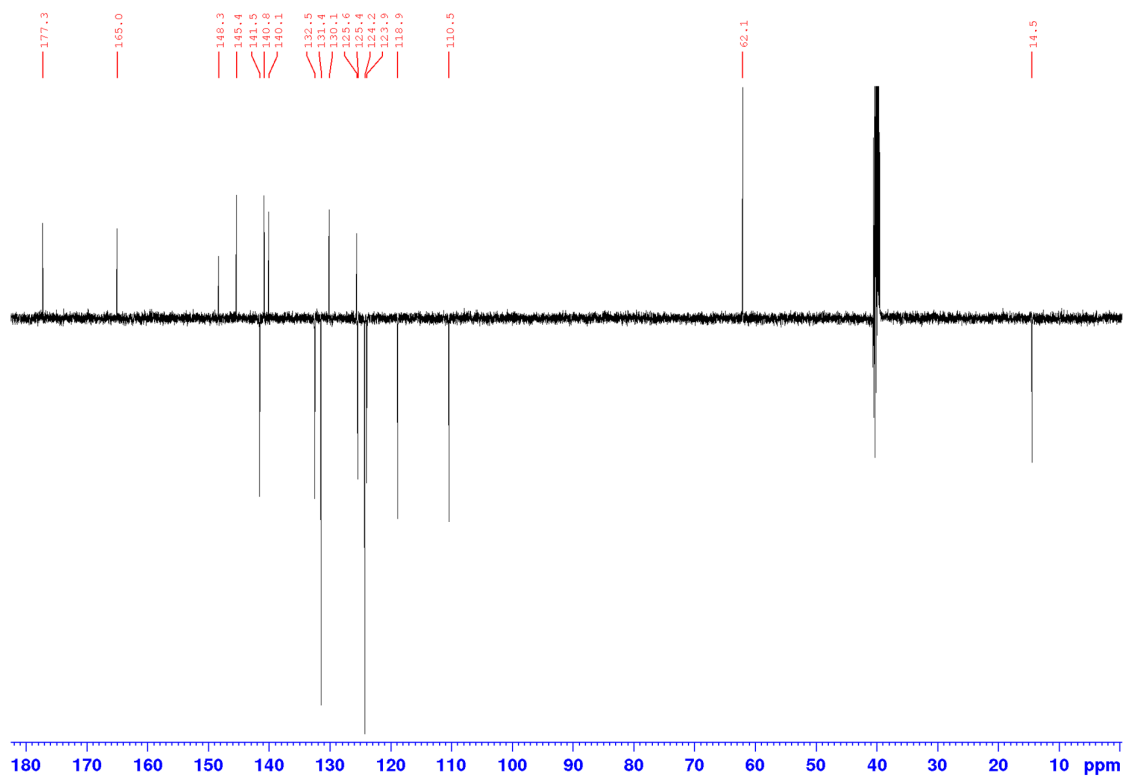


Figure S35. ¹³C NMR spectrum of **20**

SZP-20220523-POS #1811-1833 RT: 9.36-9.47 AV: 23 NL: 1.25E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

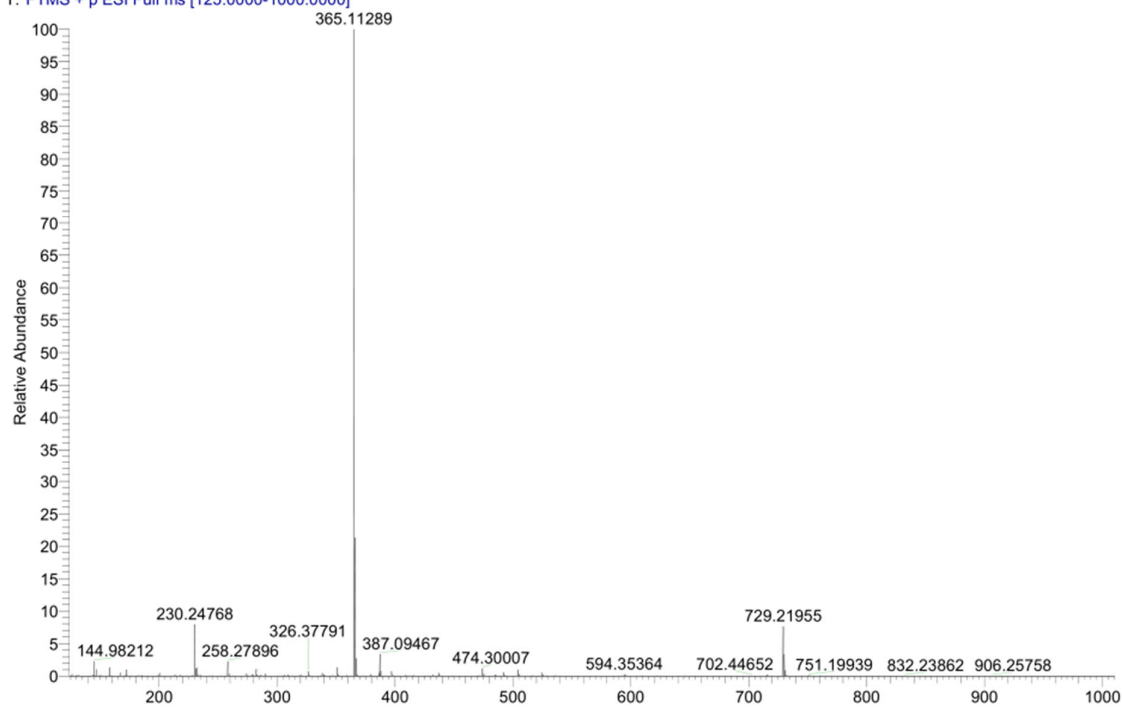


Figure S36. HRMS spectrum of 20

(Z)-ethyl 3-(4-fluorophenyl)-2-(4-hydroxyquinolin-2-yl)acrylate (**21**)

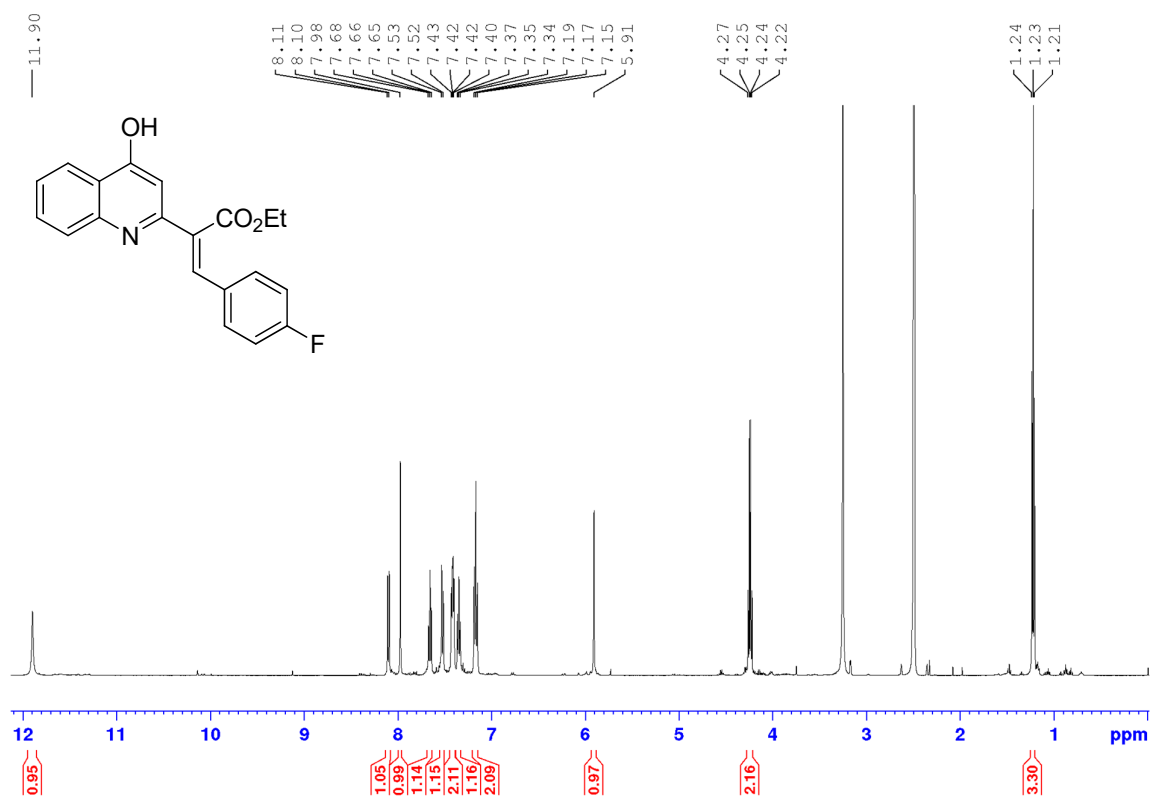


Figure S37. ¹H NMR spectrum of **21**

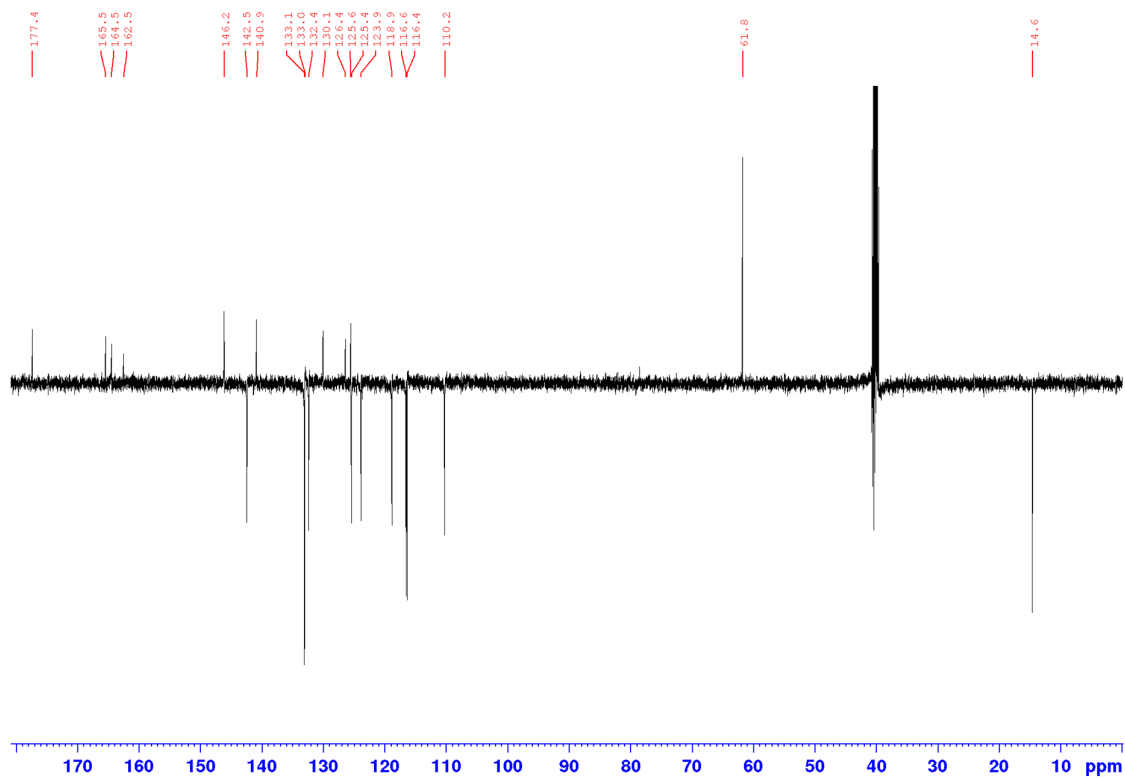


Figure S38. ¹³C NMR spectrum of **21**

SZP-20220523-POS #2526-2547 RT: 13.08-13.18 AV: 22 NL: 2.63E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

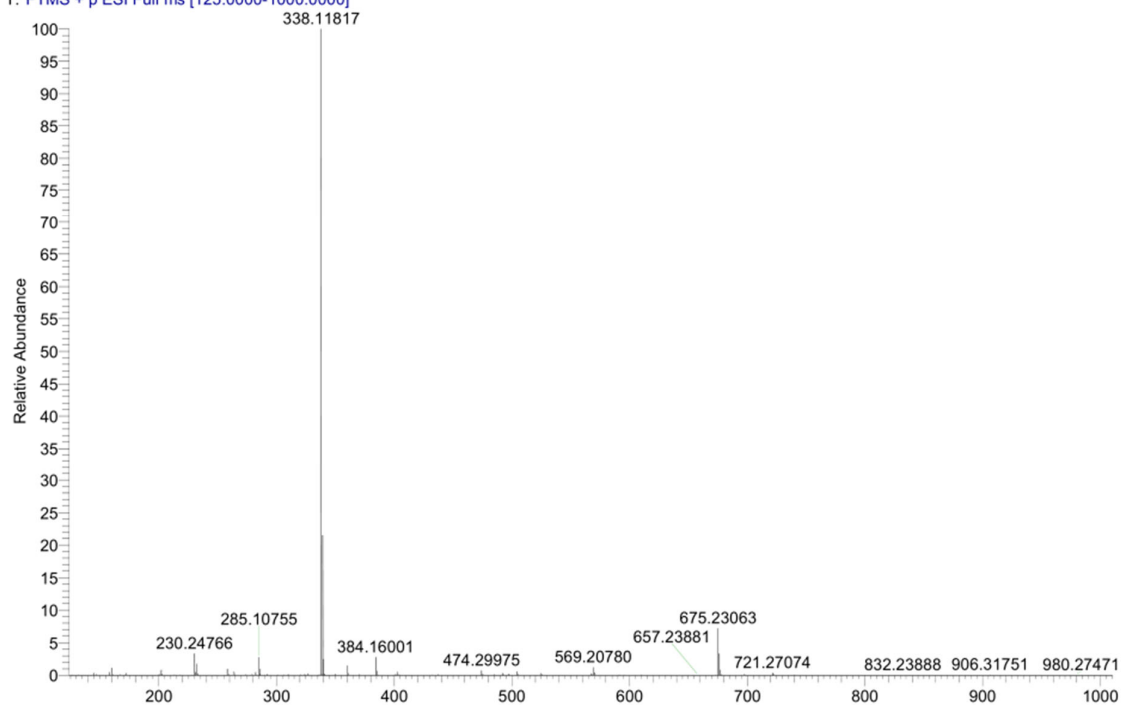


Figure S39. HRMS spectrum of **21**

(Z)-ethyl 2-(4-hydroxyquinolin-2-yl)-3-(*p*-tolyl)acrylate (**22**)

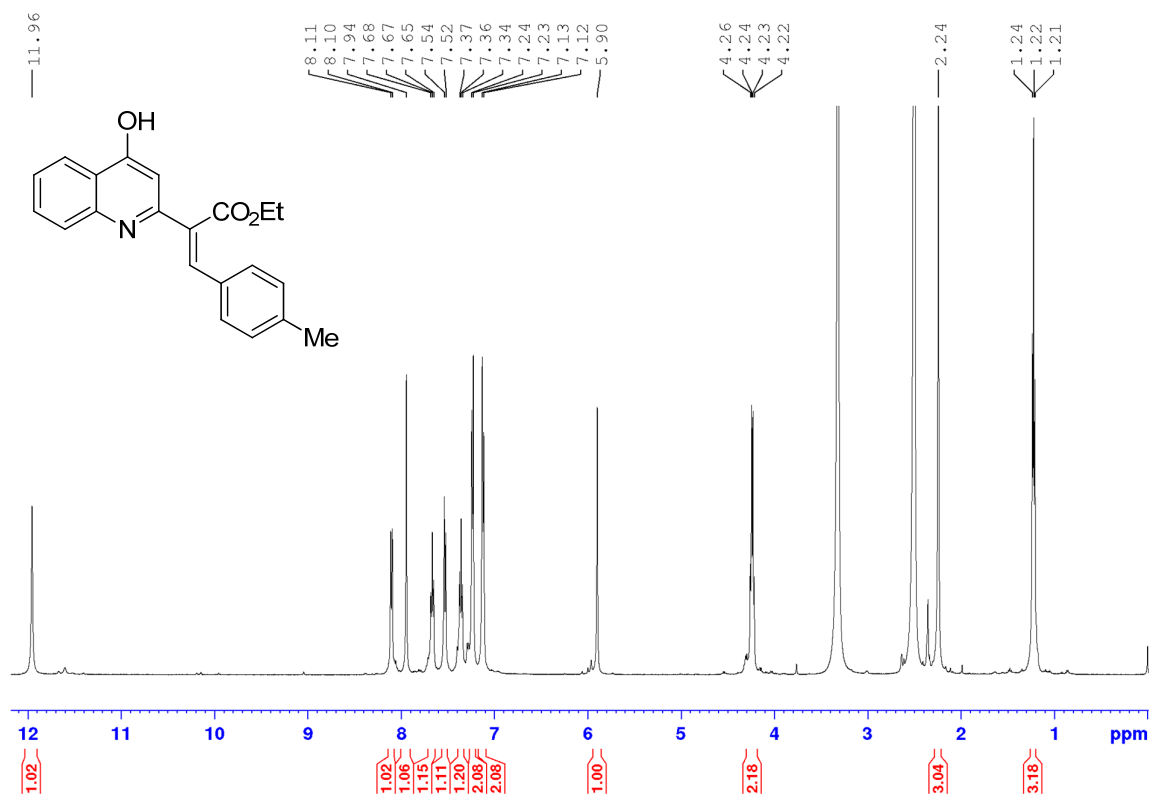


Figure S40. ¹H NMR spectrum of **22**

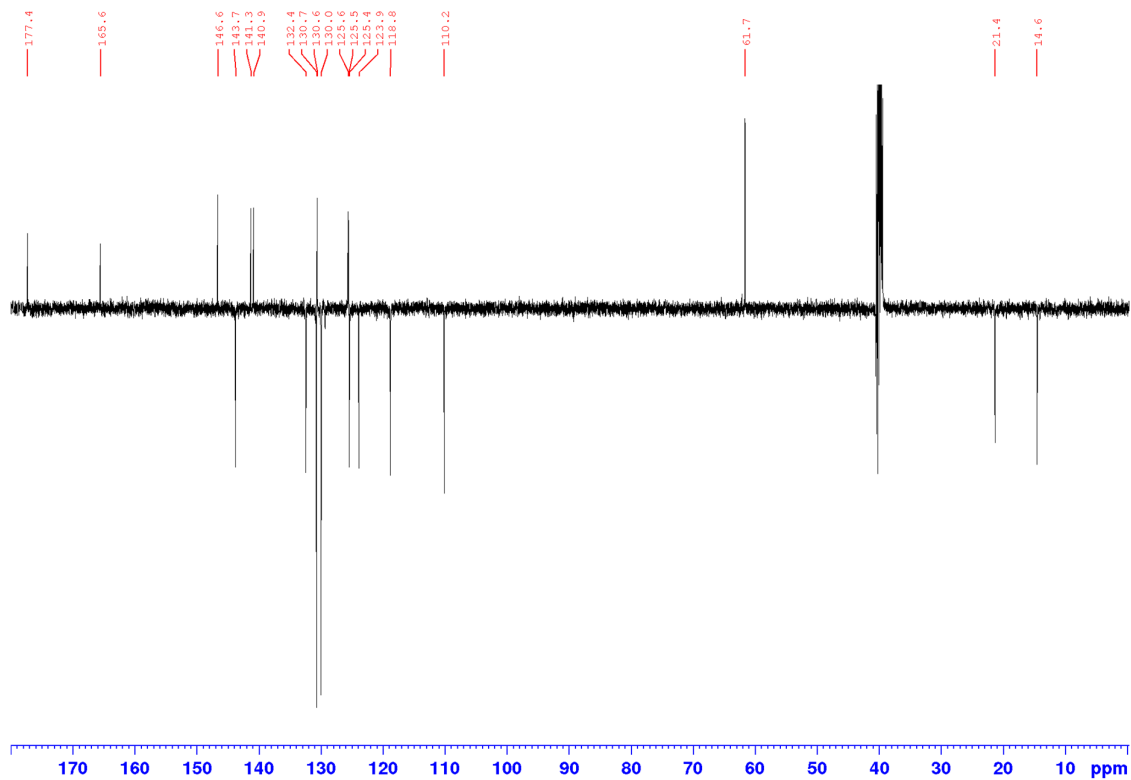


Figure S41. ¹³C NMR spectrum of **22**

SZP-20220523-POS #2702-2738 RT: 13.99-14.17 AV: 37 NL: 1.55E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

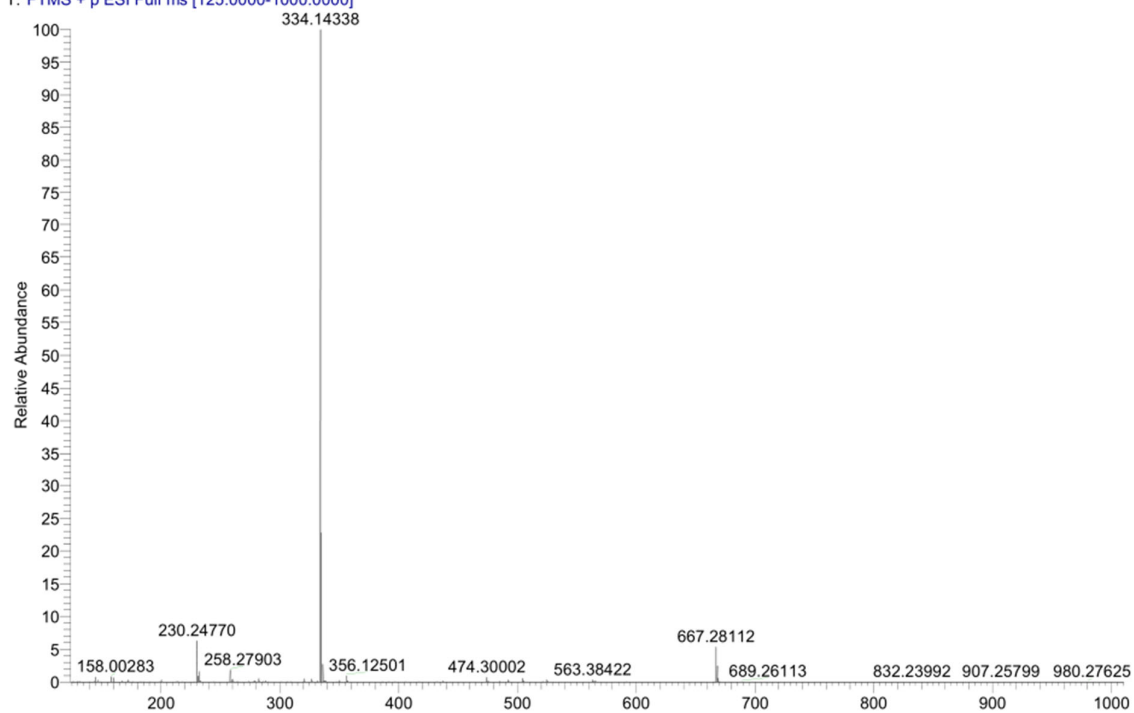


Figure S42. HRMS spectrum of **22**

(Z)-ethyl 2-(4-hydroxyquinolin-2-yl)-3-(4-methoxyphenyl)acrylate (**23**)

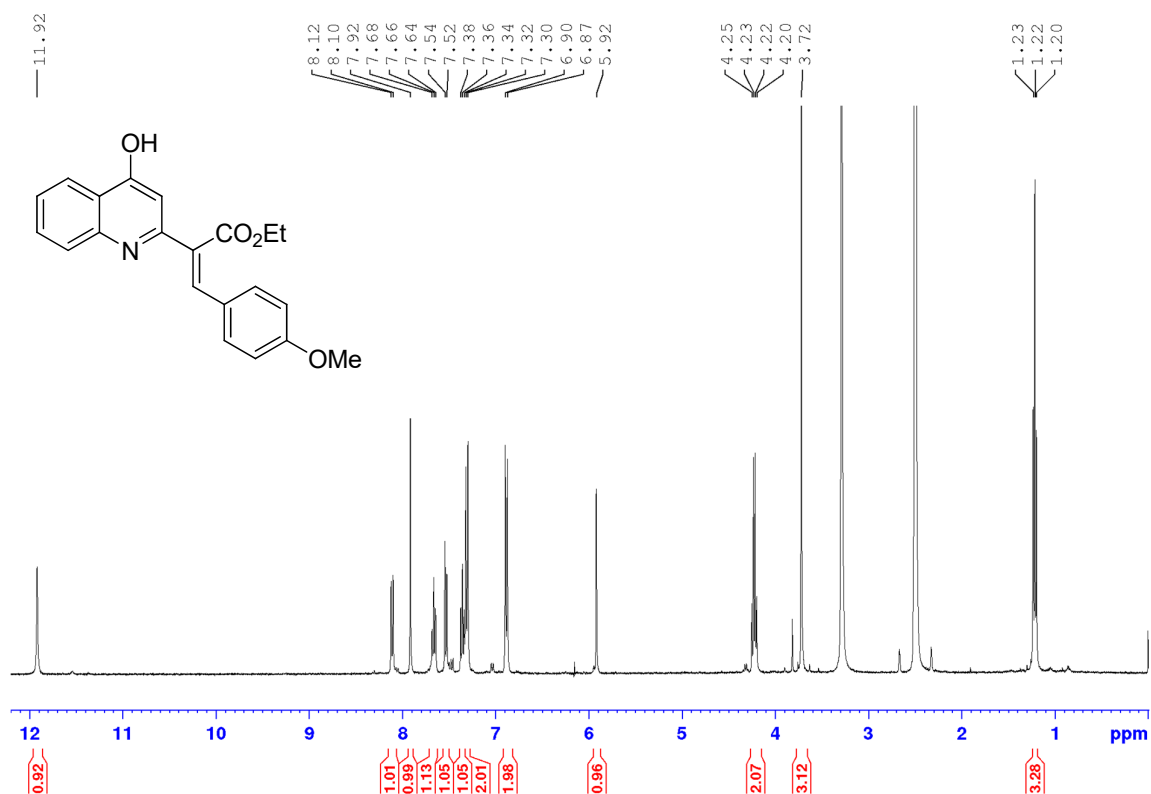


Figure S43. ¹H NMR spectrum of **23**

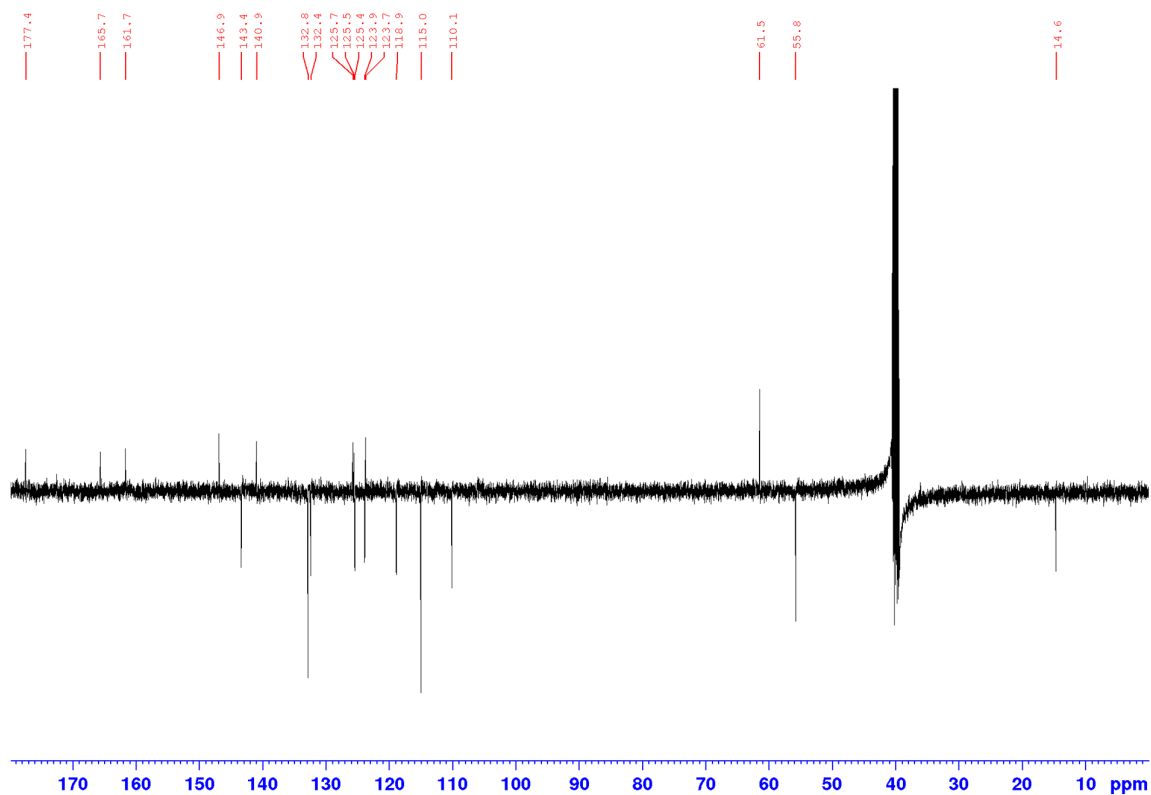


Figure S44. ¹³C NMR spectrum of **23**

SZP-20220523-POS #2080-2120 RT: 10.76-10.96 AV: 41 NL: 1.94E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

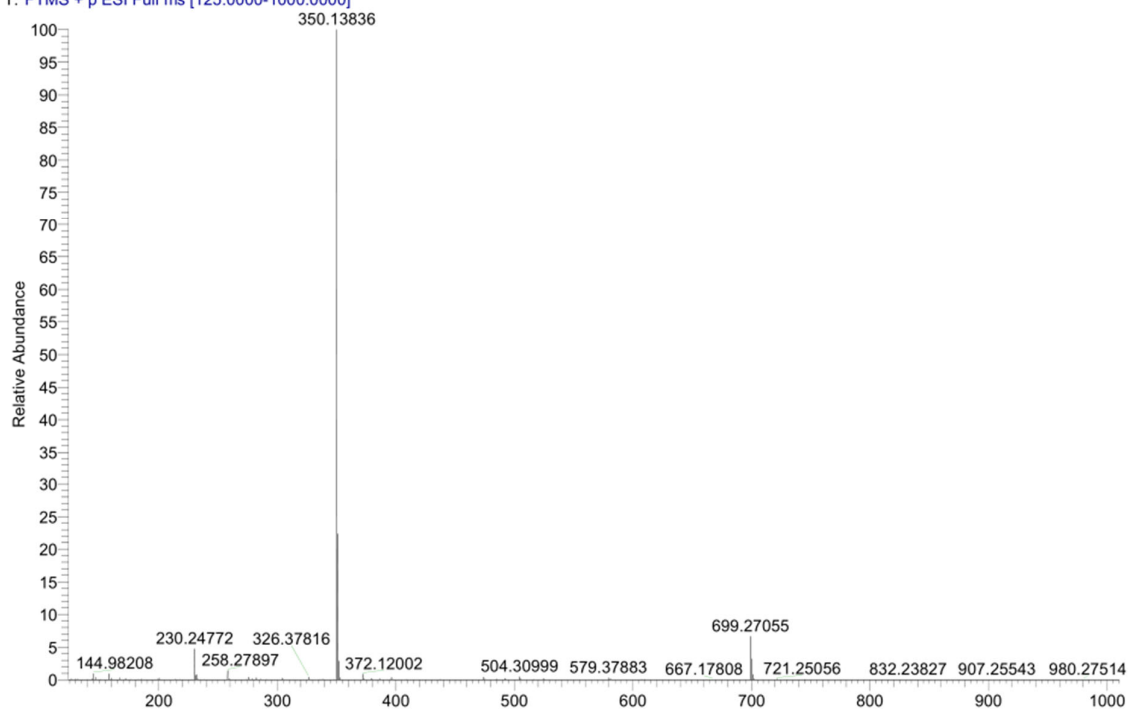


Figure S45. HRMS spectrum of **23**

(Z)-ethyl 3-(4-(dimethylamino)phenyl)-2-(4-hydroxyquinolin-2-yl)acrylate (**24**)

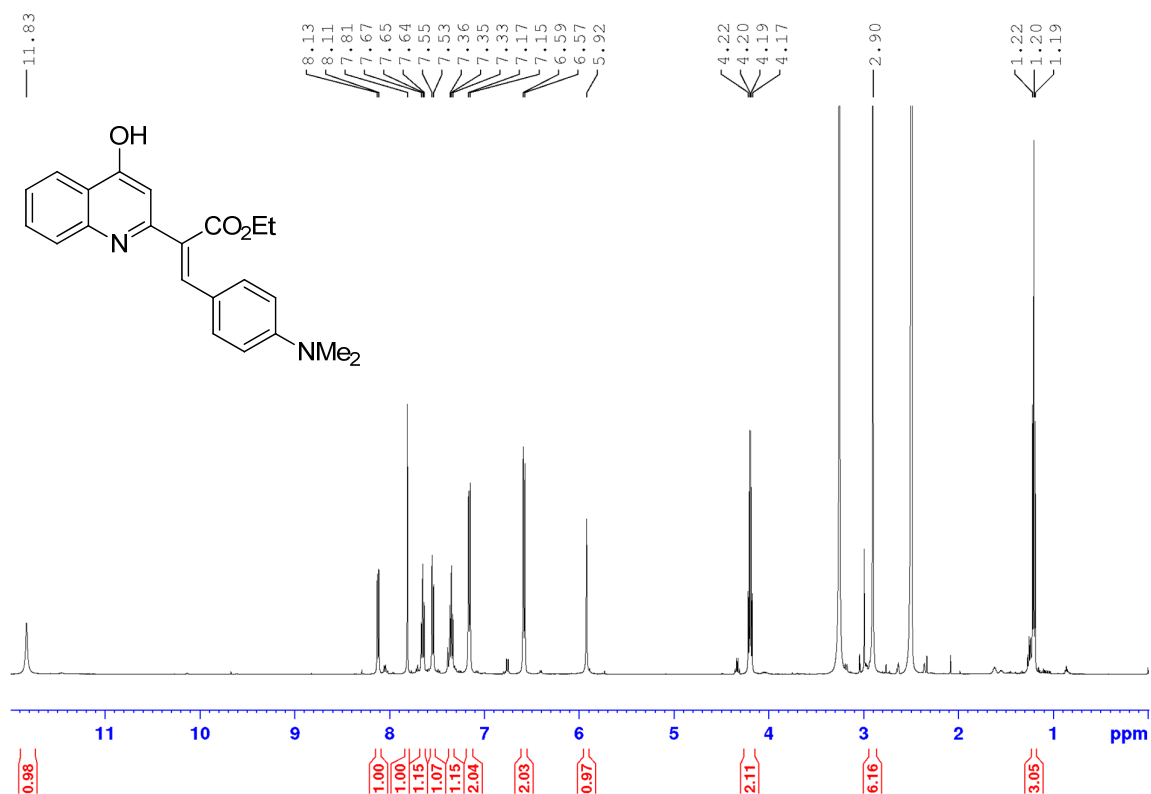


Figure S46. ¹H NMR spectrum of **24**

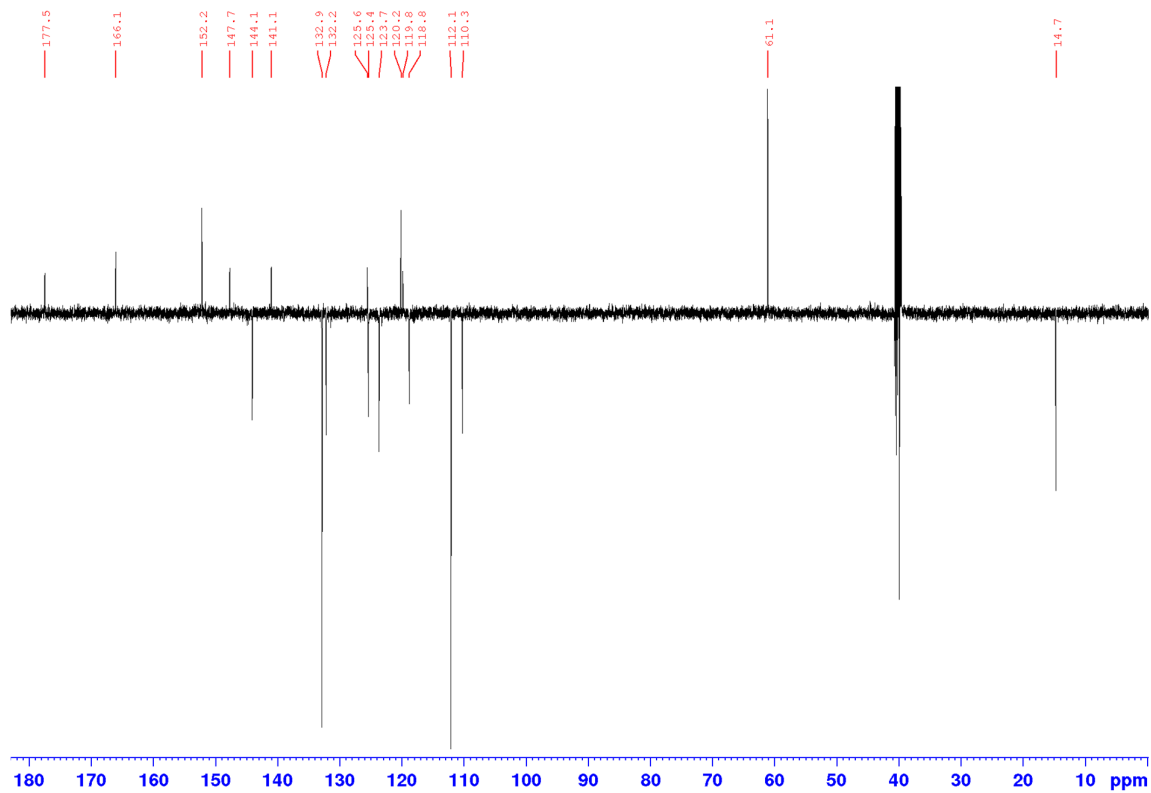


Figure S47. ¹³C NMR spectrum of **24**

SZP-20220523-POS #3086-3122 RT: 16.00-16.18 AV: 37 NL: 1.71E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

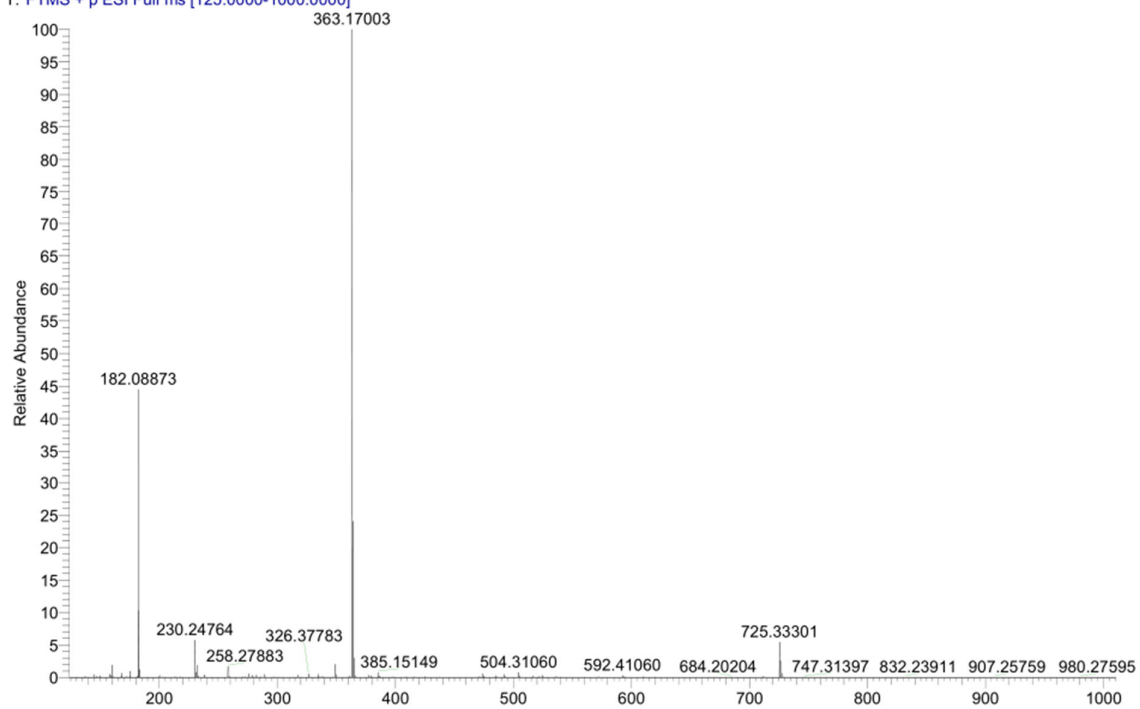


Figure S48. HRMS spectrum of **24**

(Z)-ethyl 2-(4-hydroxyquinolin-2-yl)-3-(naphthalen-1-yl)acrylate (**25**)

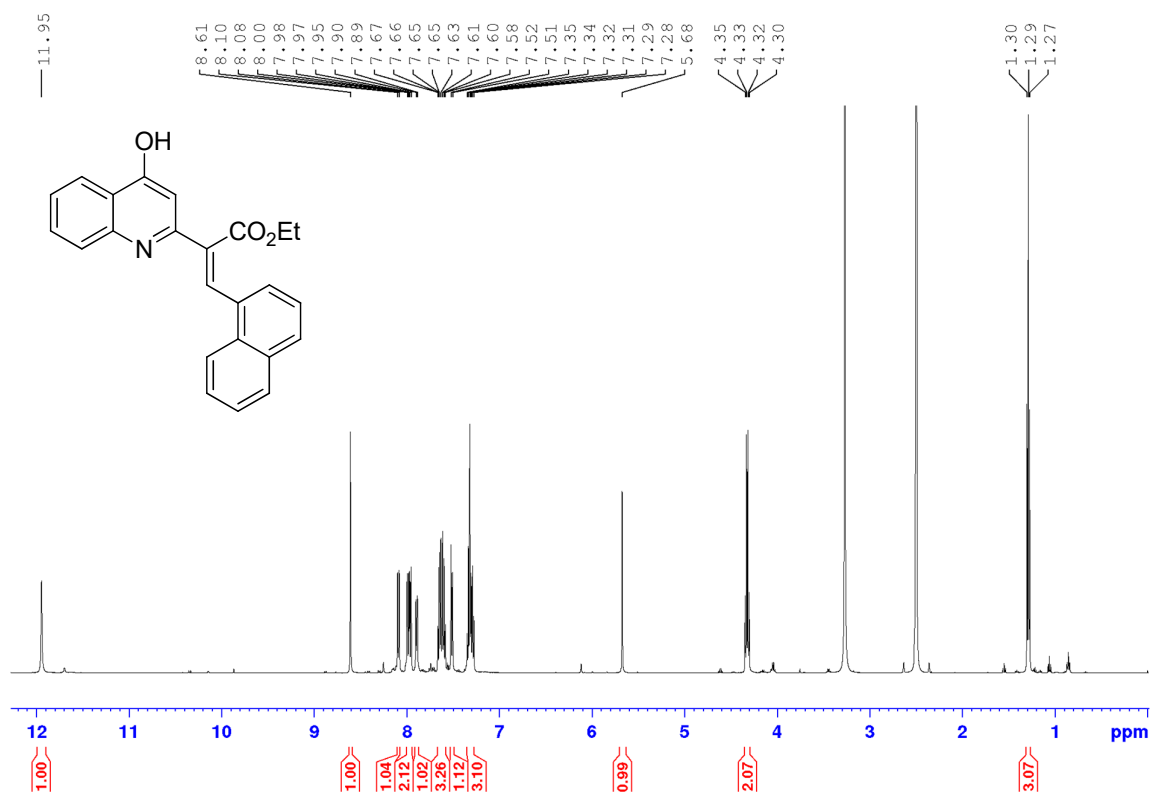


Figure S49. ¹H NMR spectrum of **25**

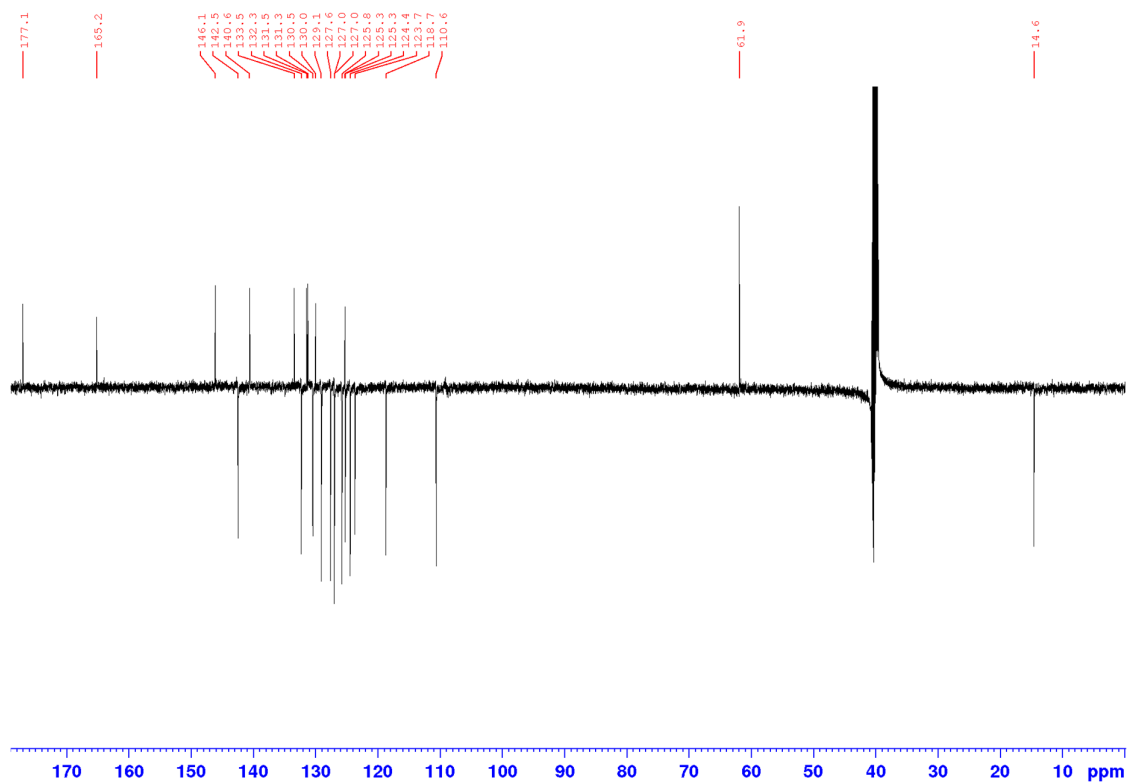


Figure S50. ¹³C NMR spectrum of **25**

SZP-20220523-POS #3507-3536 RT: 18.18-18.33 AV: 30 NL: 1.79E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

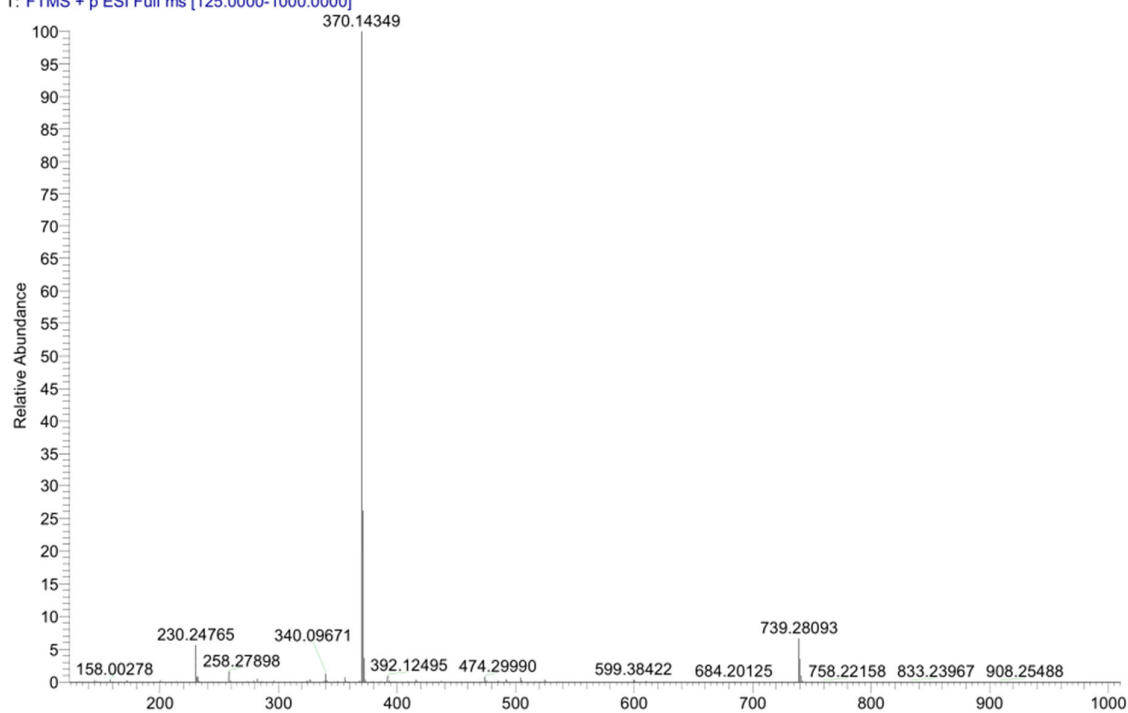


Figure S51. HRMS spectrum of 25

(Z)-ethyl 2-(4-hydroxyquinolin-2-yl)-3-(naphthalen-2-yl)acrylate (**26**)

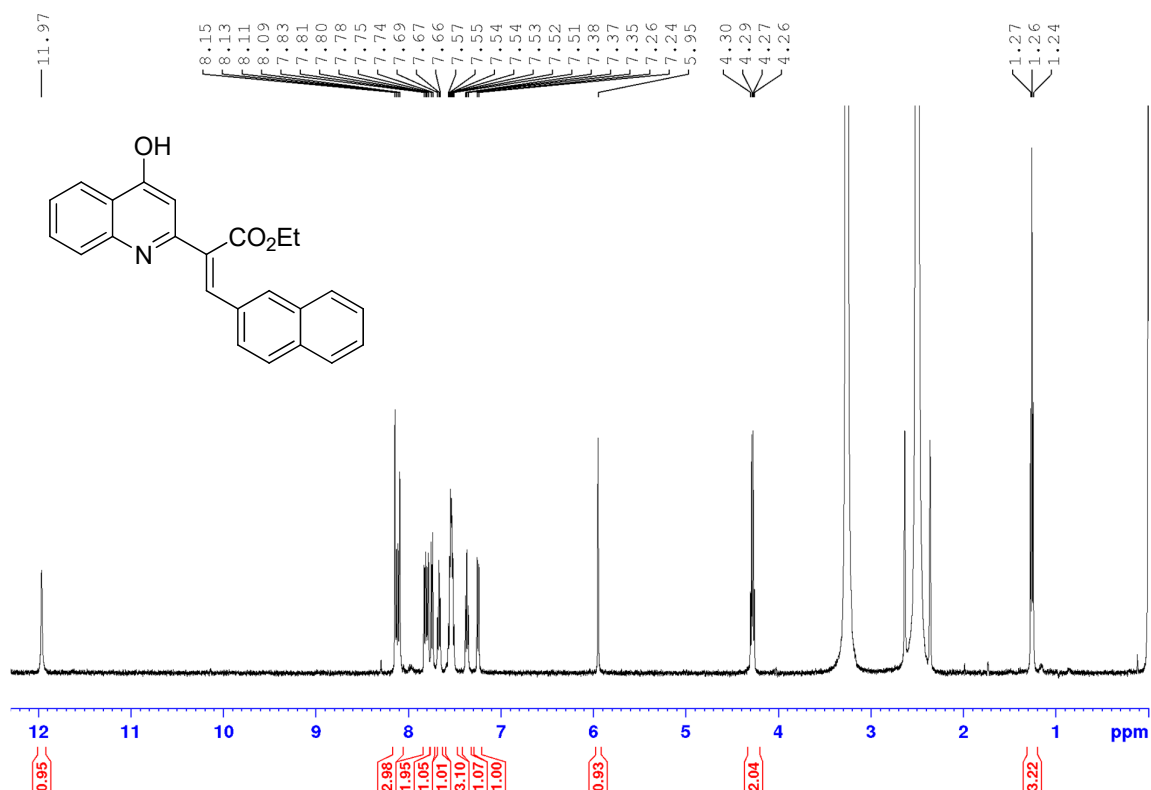


Figure S52. ¹H NMR spectrum of **26**

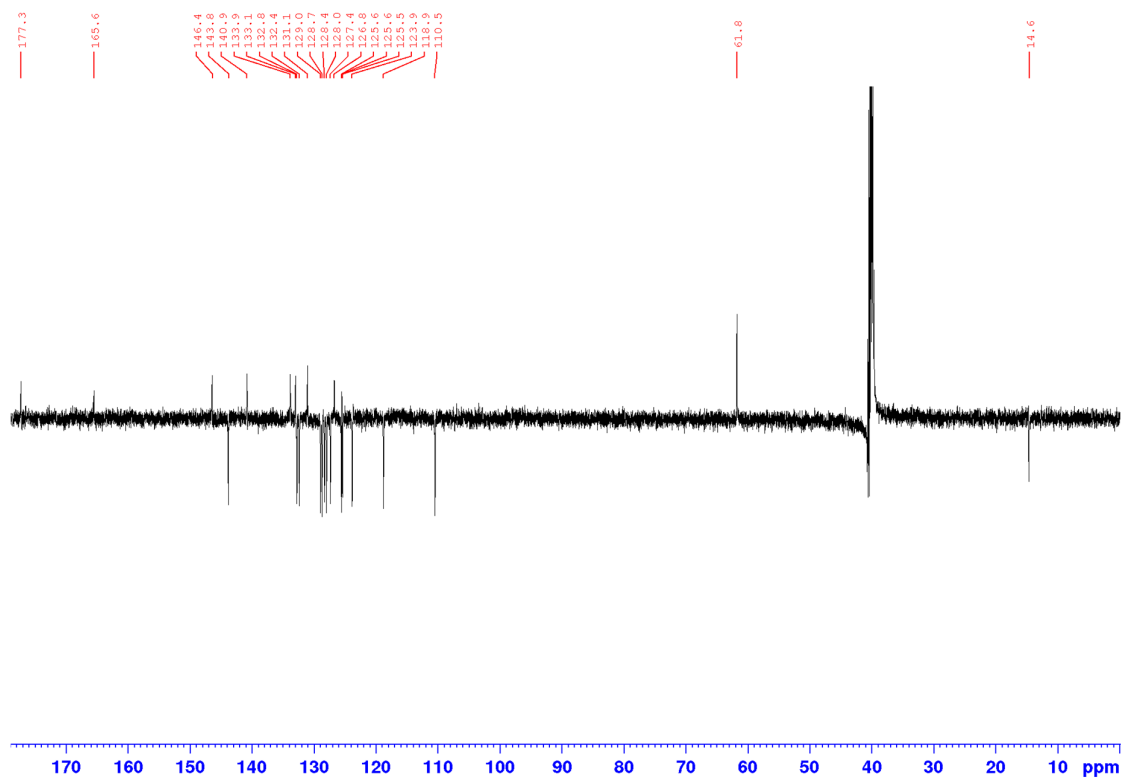


Figure S53. ¹³C NMR spectrum of **26**

SZP-20220523-POS #3659-3692 RT: 18.97-19.14 AV: 34 NL: 1.13E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

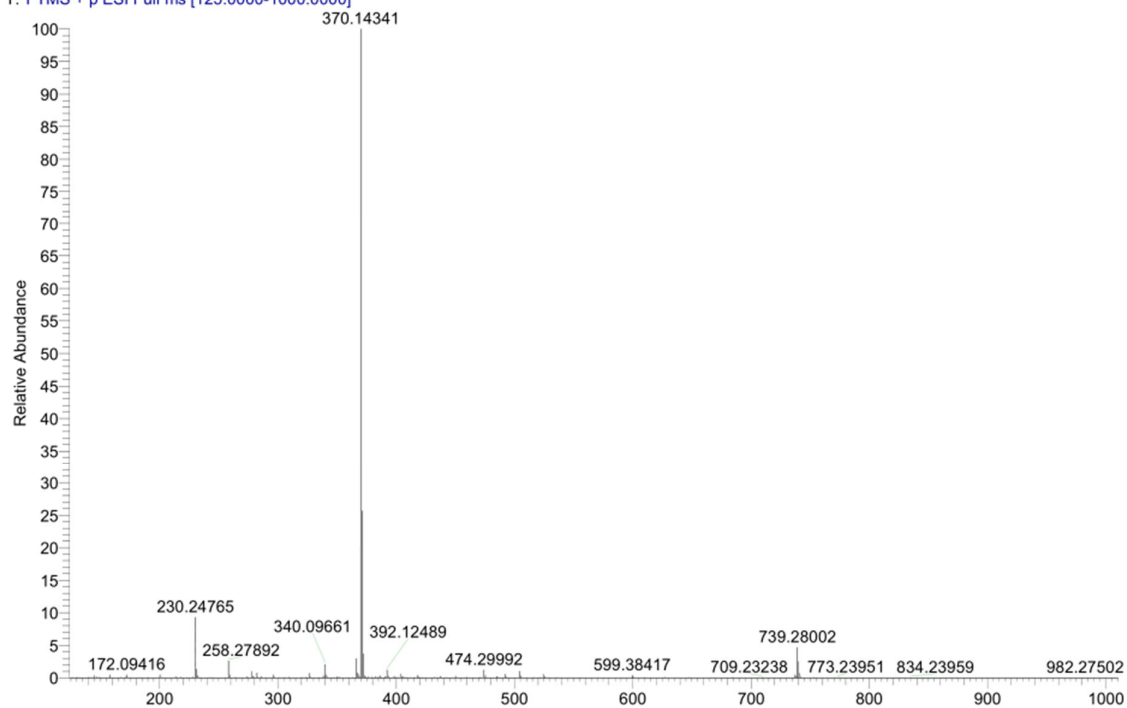


Figure S54. HRMS spectrum of 26

3-(4-Hydroxyquinolin-2-yl)-2H-chromen-2-one (28)

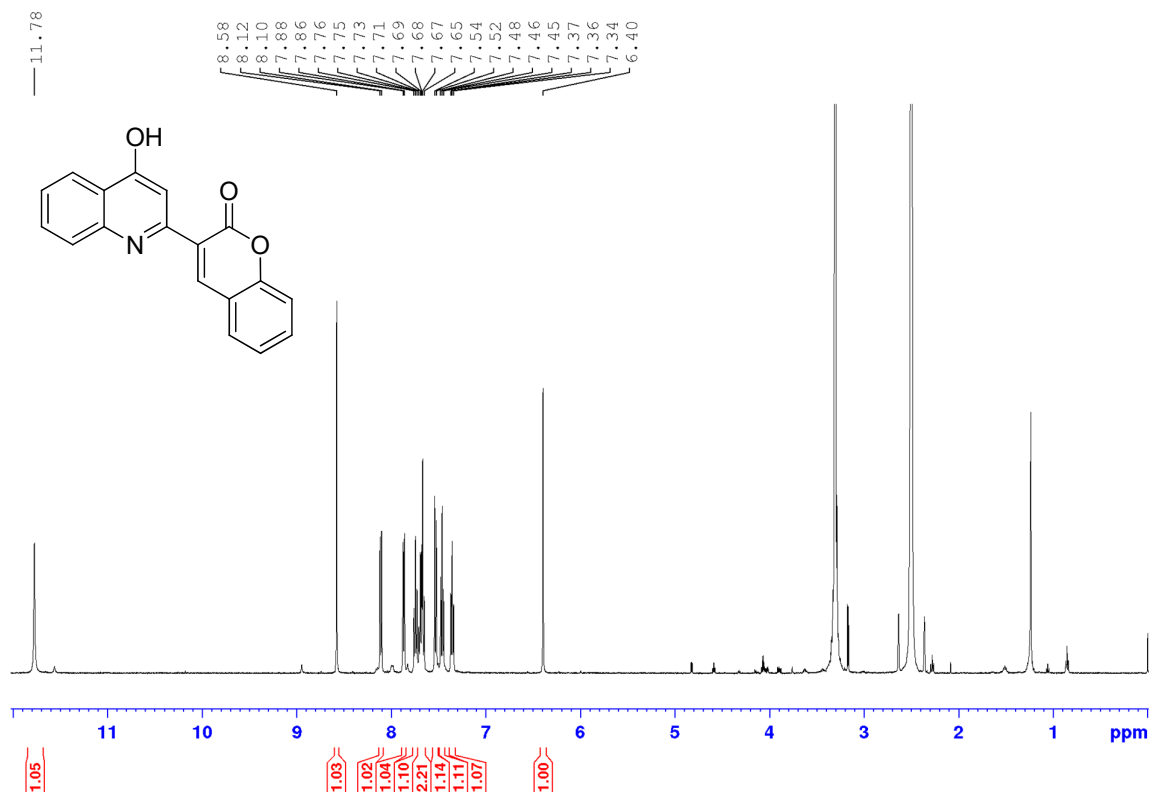


Figure S55. ¹H NMR spectrum of 28

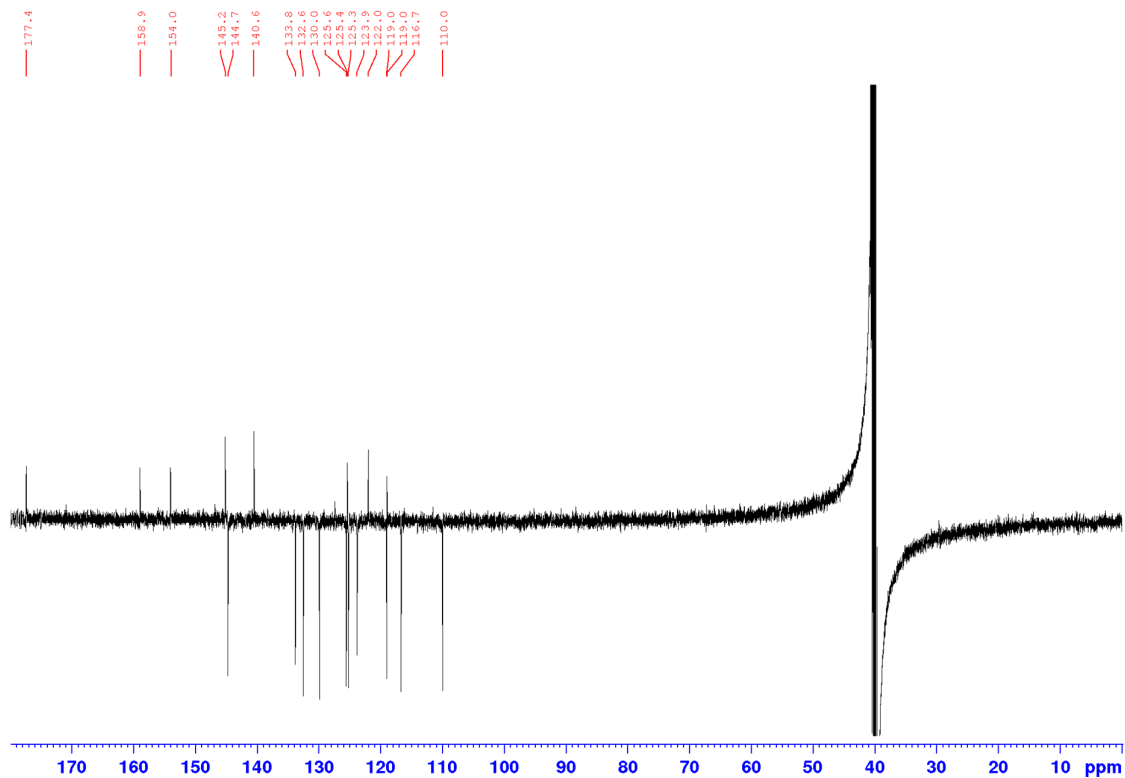


Figure S56. ¹³C NMR spectrum of 28

SZP-20220523-POS #1365-1390 RT: 7.04-7.17 AV: 26 NL: 1.19E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

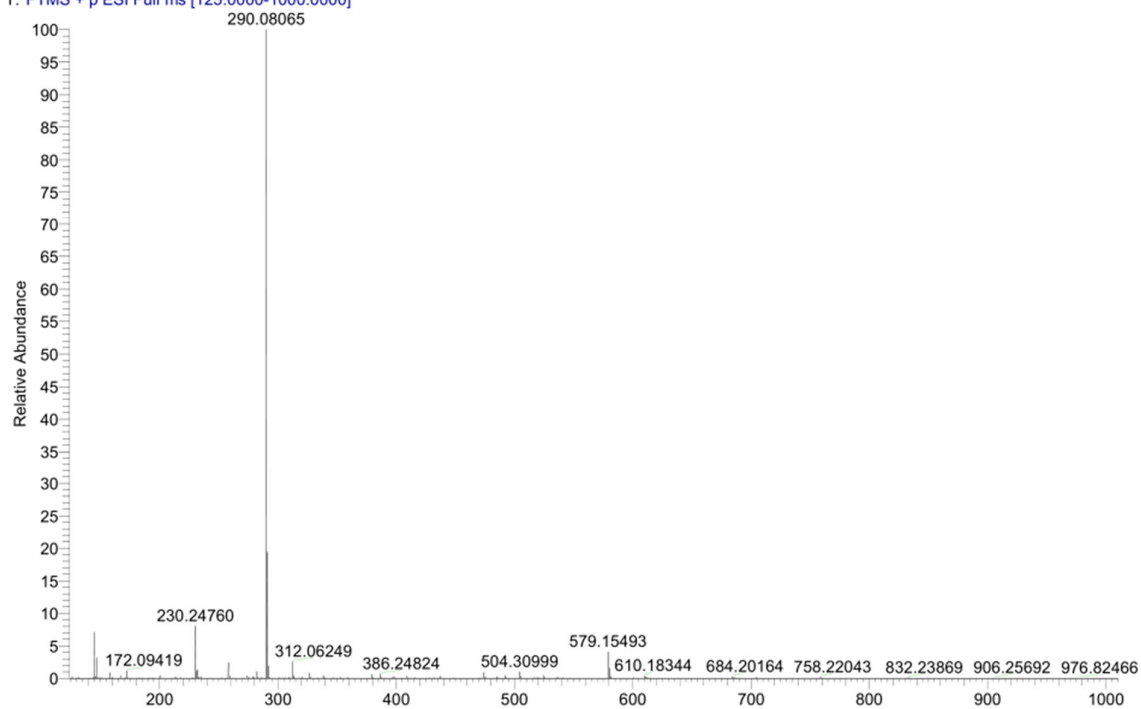


Figure S57. HRMS spectrum of 28

2-(4-Hydroxyquinolin-2-yl)-3H-benzo[*f*]chromen-3-one (29)

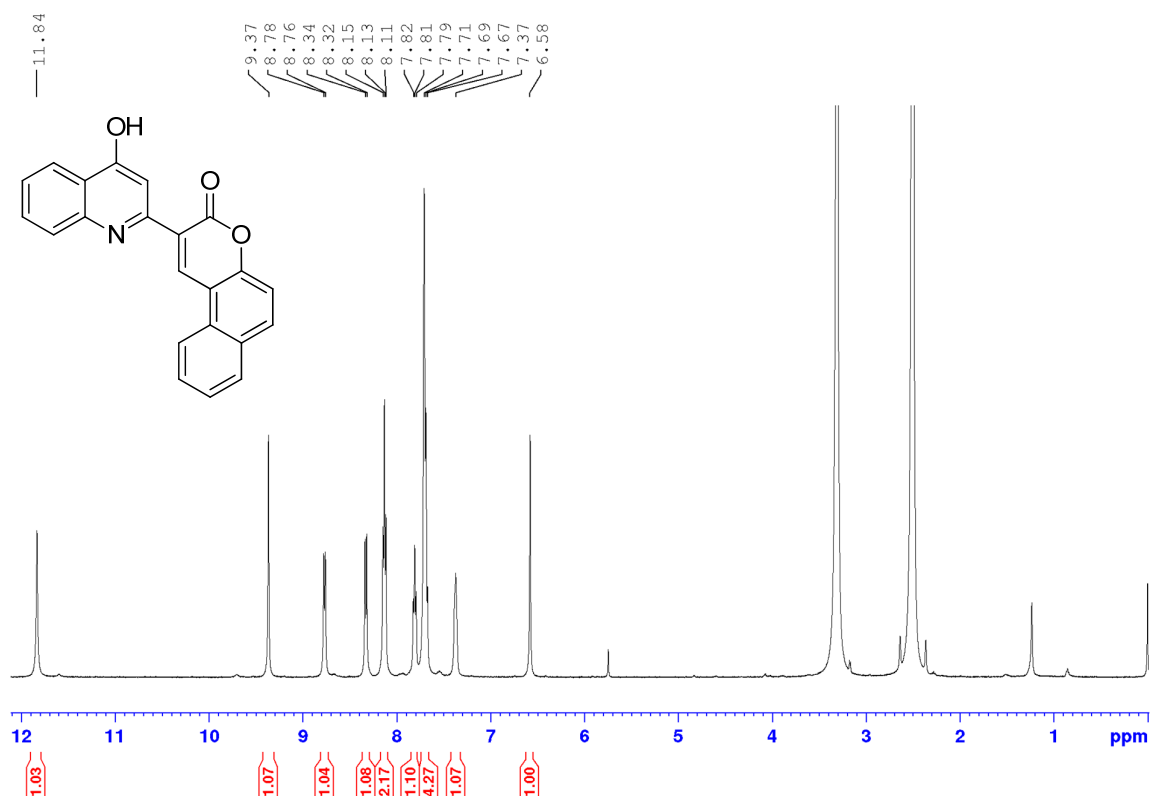


Figure S58. ¹H NMR spectrum of 29

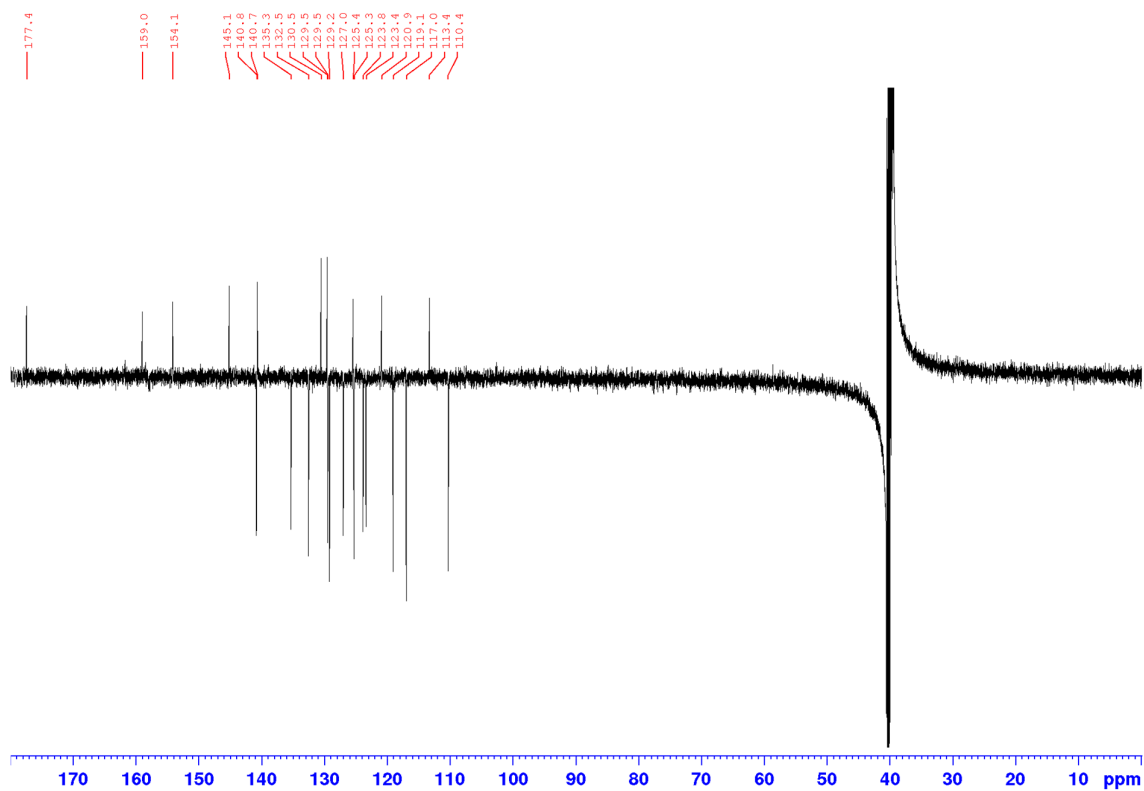


Figure S59. ¹³C NMR spectrum of 29

SZP-20220523-POS #1581-1603 RT: 8.16-8.28 AV: 23 NL: 7.78E8
T: FTMS + p ESI Full ms [125.0000-1000.0000]

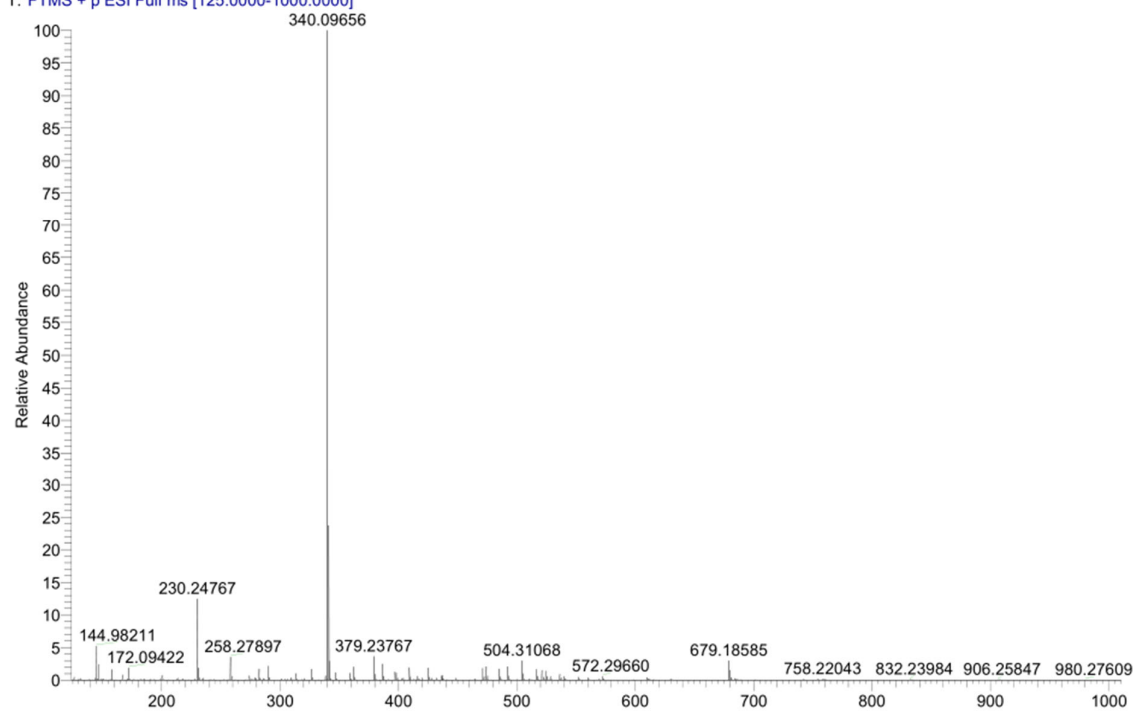


Figure S60. HRMS spectrum of **29**

3-(4-Hydroxyquinolin-2-yl)-2H-benzo[h]chromen-2-one (30)

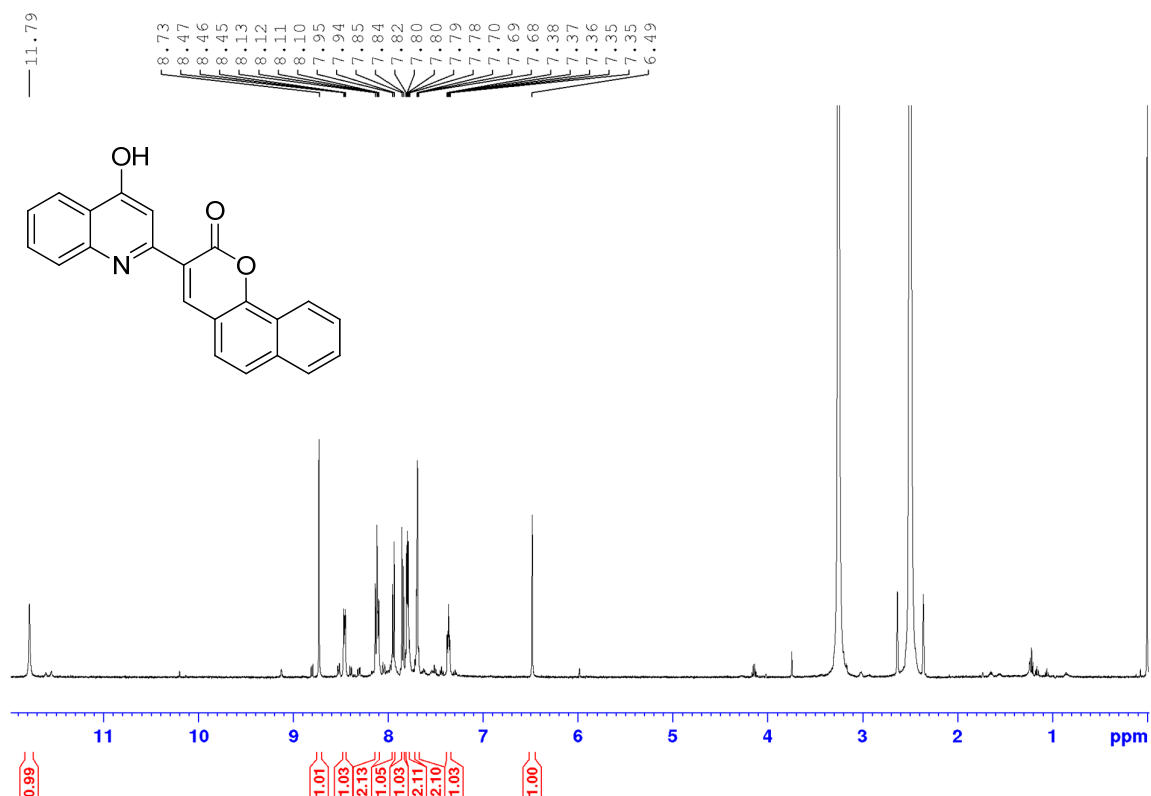


Figure S61. ¹H NMR spectrum of 30

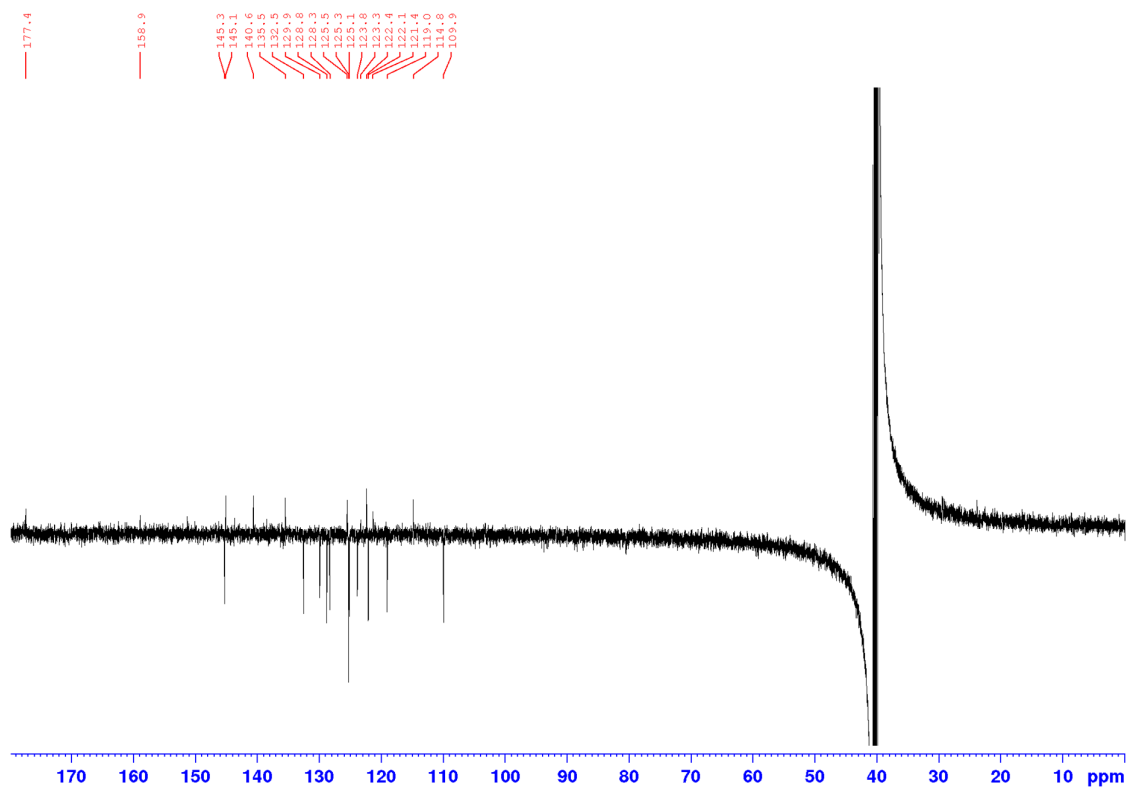


Figure S62. ¹³C NMR spectrum of 30

SZP-20220523-POS #3284-3310 RT: 17.03-17.16 AV: 27 NL: 1.17E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

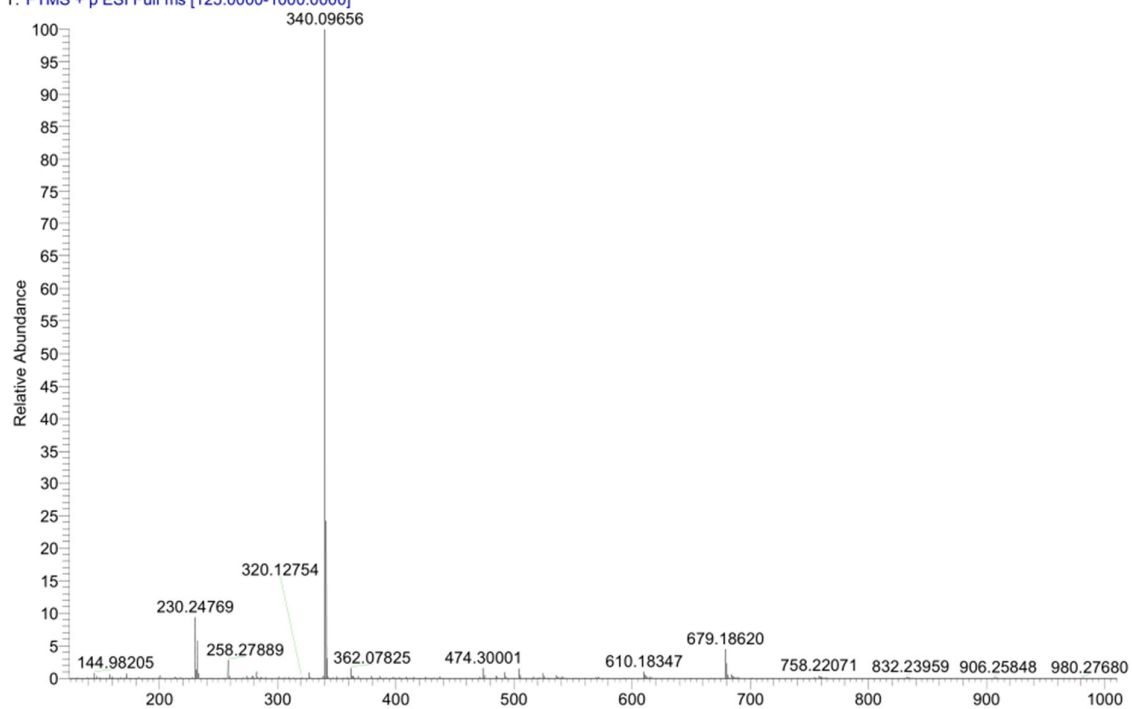


Figure S63. HRMS spectrum of 30

2-(4-Hydroxyquinolin-2-yl)-3-phenylacrylic acid (14)

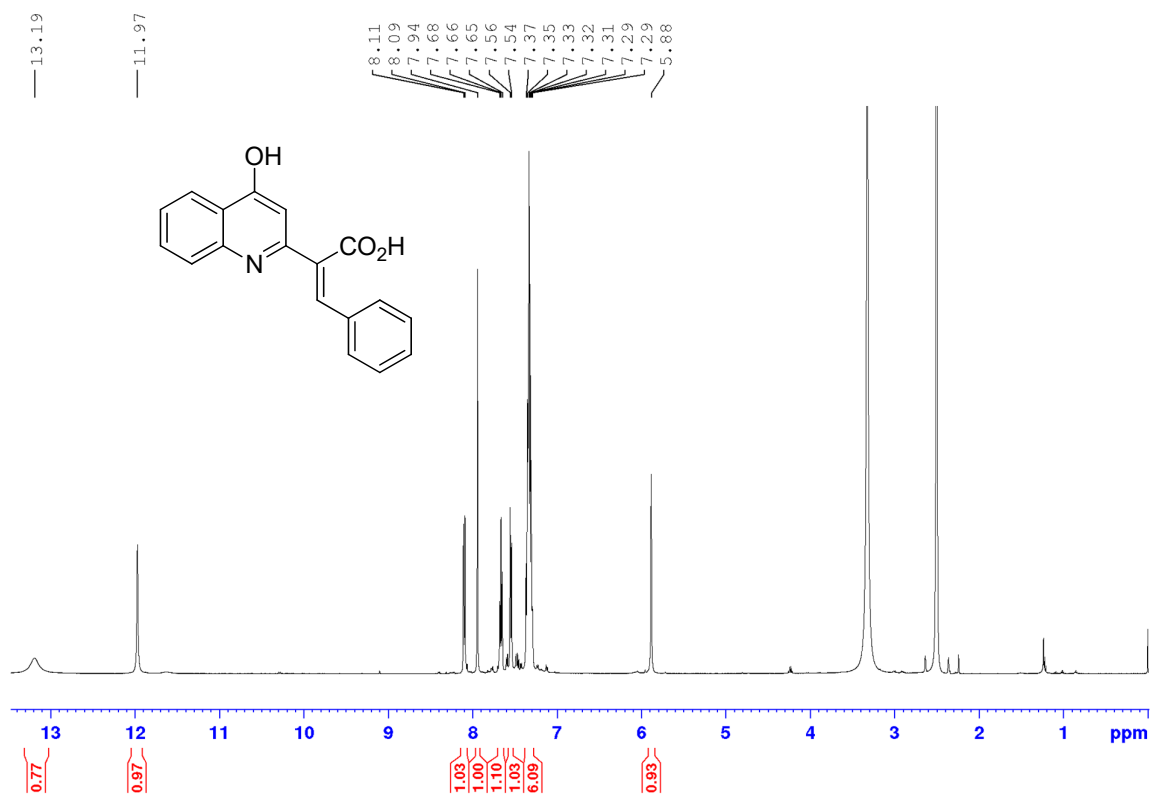


Figure S64. ¹H NMR spectrum of **14**

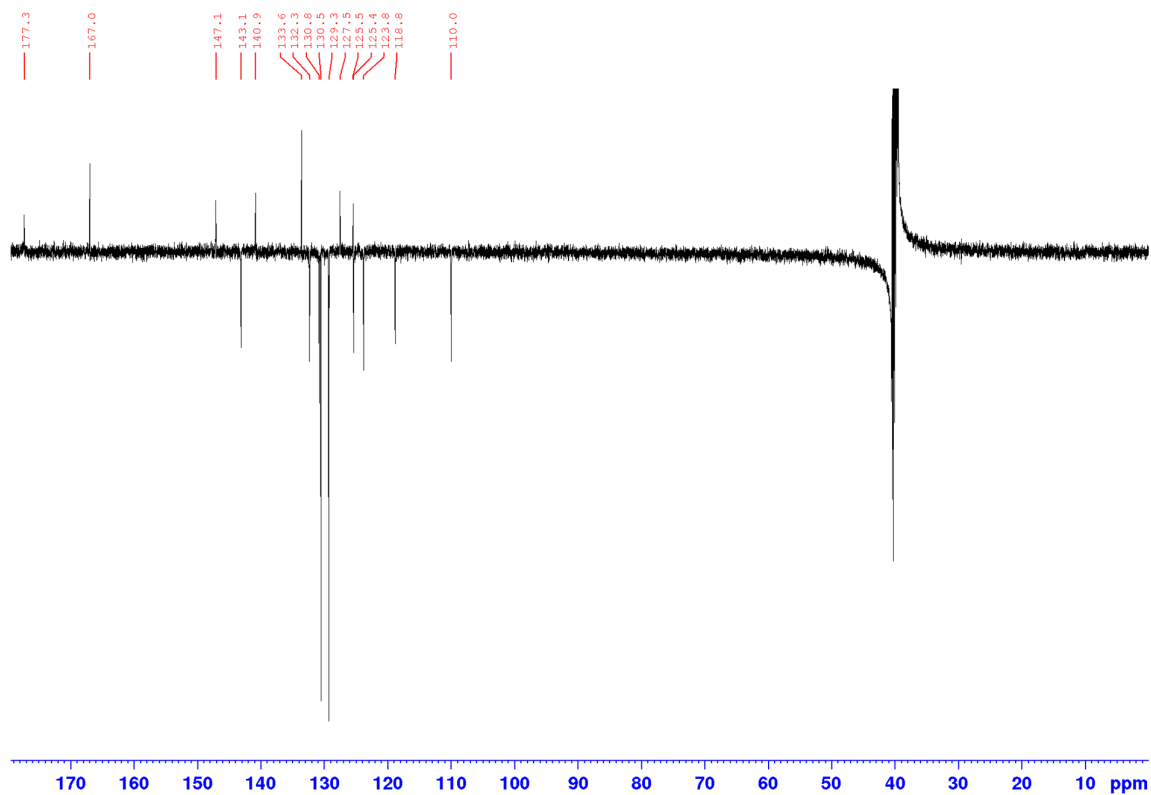


Figure S65. ¹³C NMR spectrum of **14**

SZP-20220523-POS #4210-4235 RT: 21.85-21.97 AV: 26 NL: 1.46E9
T: FTMS + p ESI Full ms [125.0000-1000.0000]

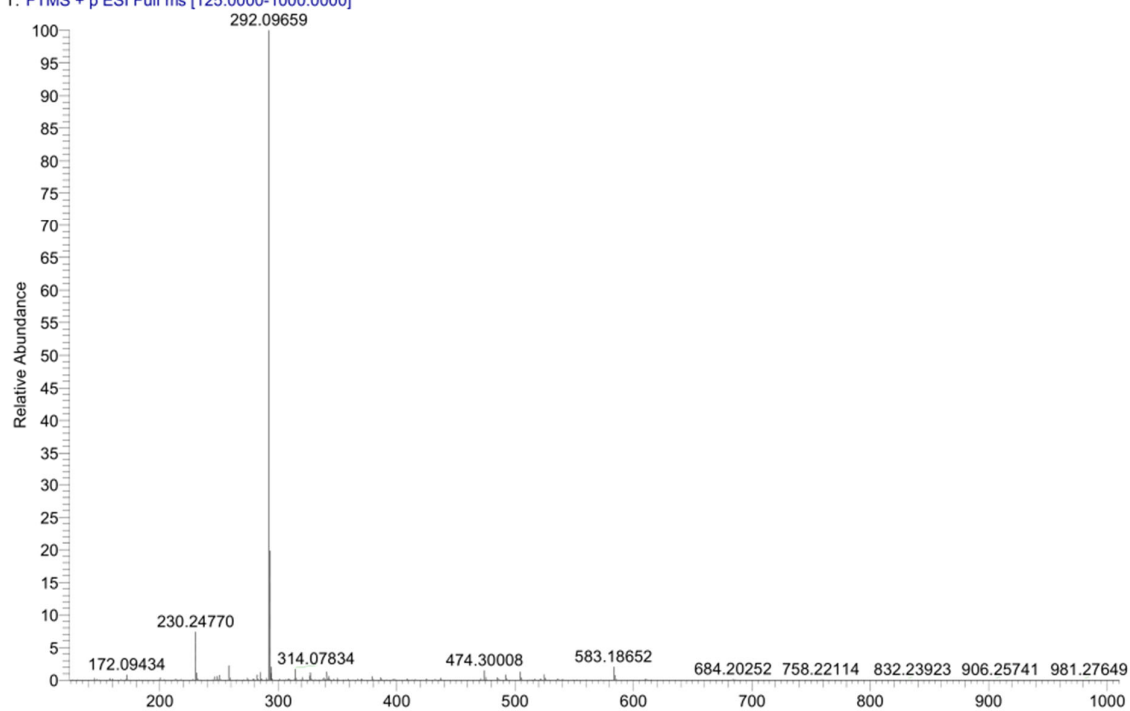


Figure S66. HRMS spectrum of **14**