Supporting information

Uracil as a Zn-Binding Bioisostere in the Design of Quinoline-Uracil Hybrids as Anticancer Carbonic Anhydrase Inhibitors.

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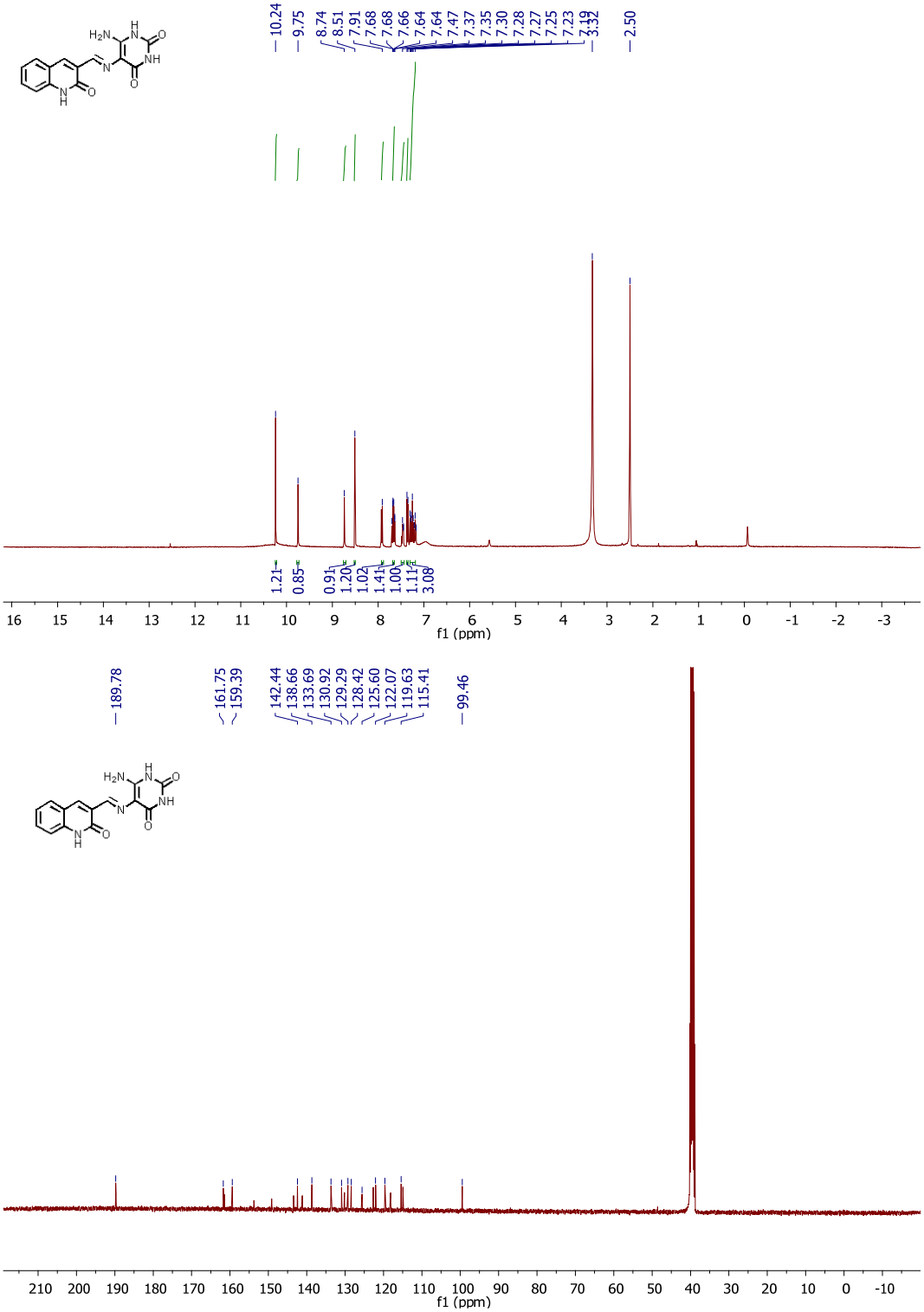
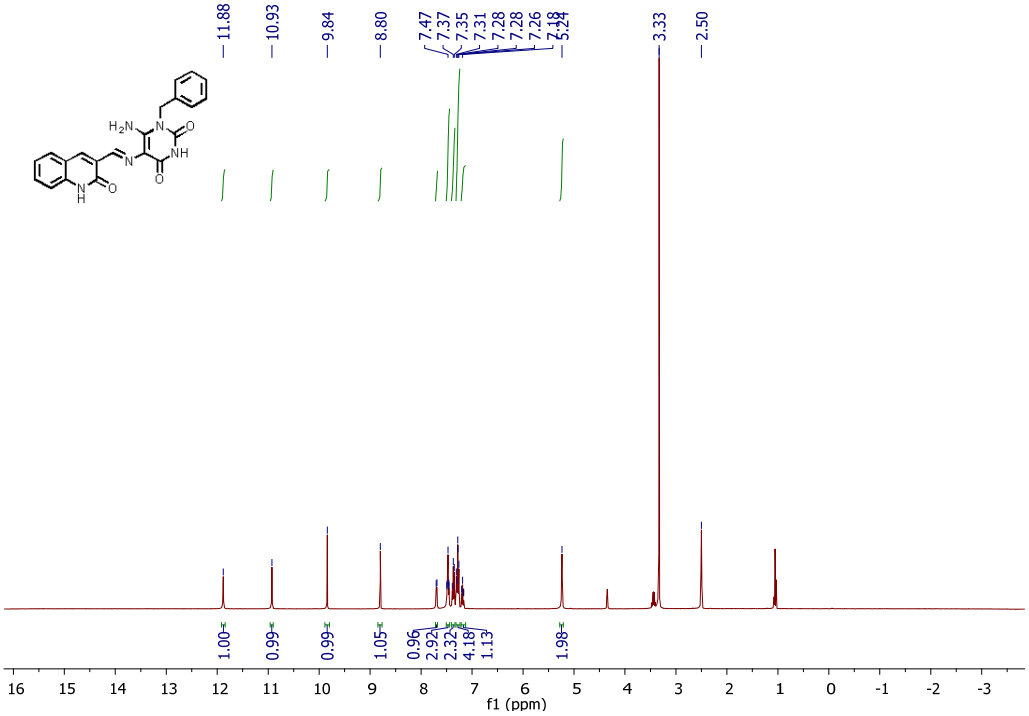


Figure S2: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-1-benzyl-5-(((2-oxo-1,2-dihydroquinolin-3-yl)methylene)amino)pyrimidine-2,4(1H,3H)-dione (10b)



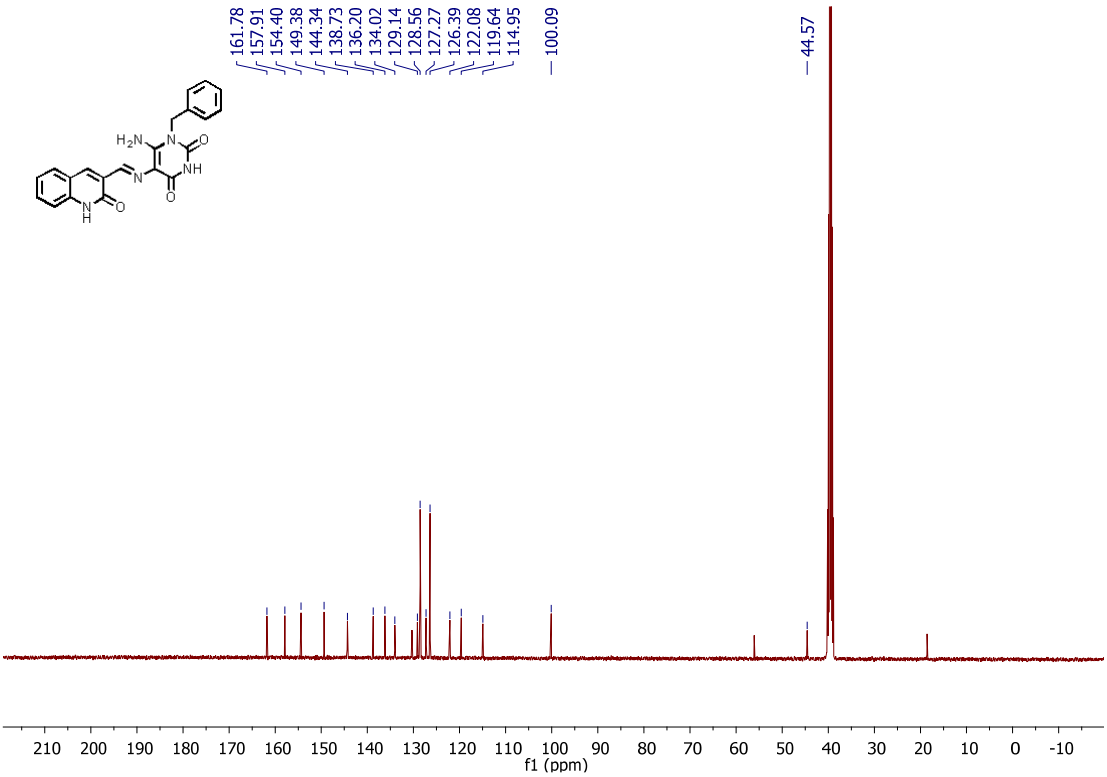


Figure S3: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-1-ethyl-5-(((2-oxo-1,2-dihydroquinolin-3-yl)methylene)amino)pyrimidine-2,4(1H,3H)-dione (10c).

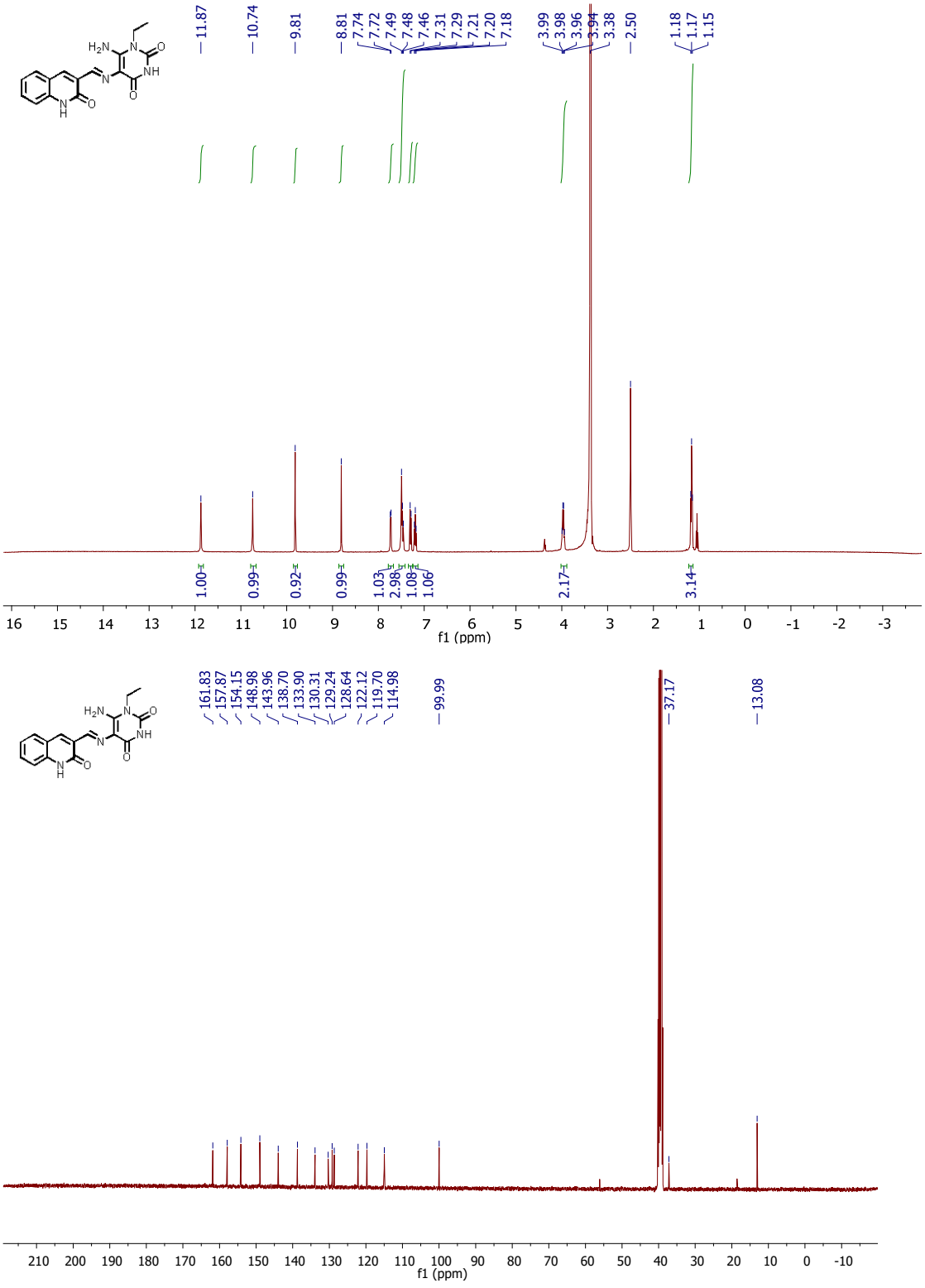


Figure S4: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-1-methyl-5-(((2-oxo-1,2-dihydroquinolin-3-yl)methylene)amino)pyrimidine-2,4(1H,3H)-dione (10d).

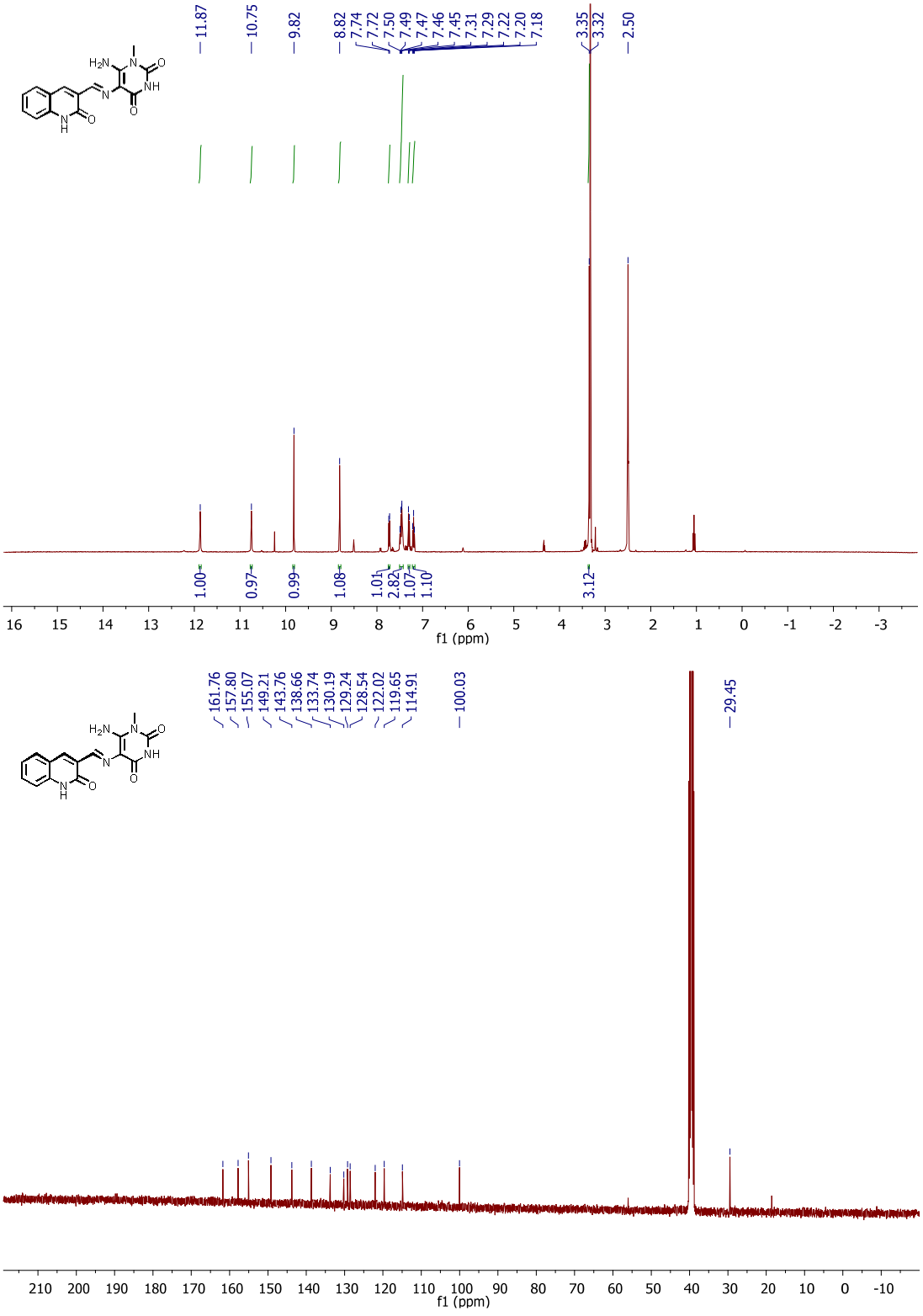


Figure S5: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-3-(((6-amino-1-methyl-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)imino)methyl) quinolin-2(1H)-one (10e)

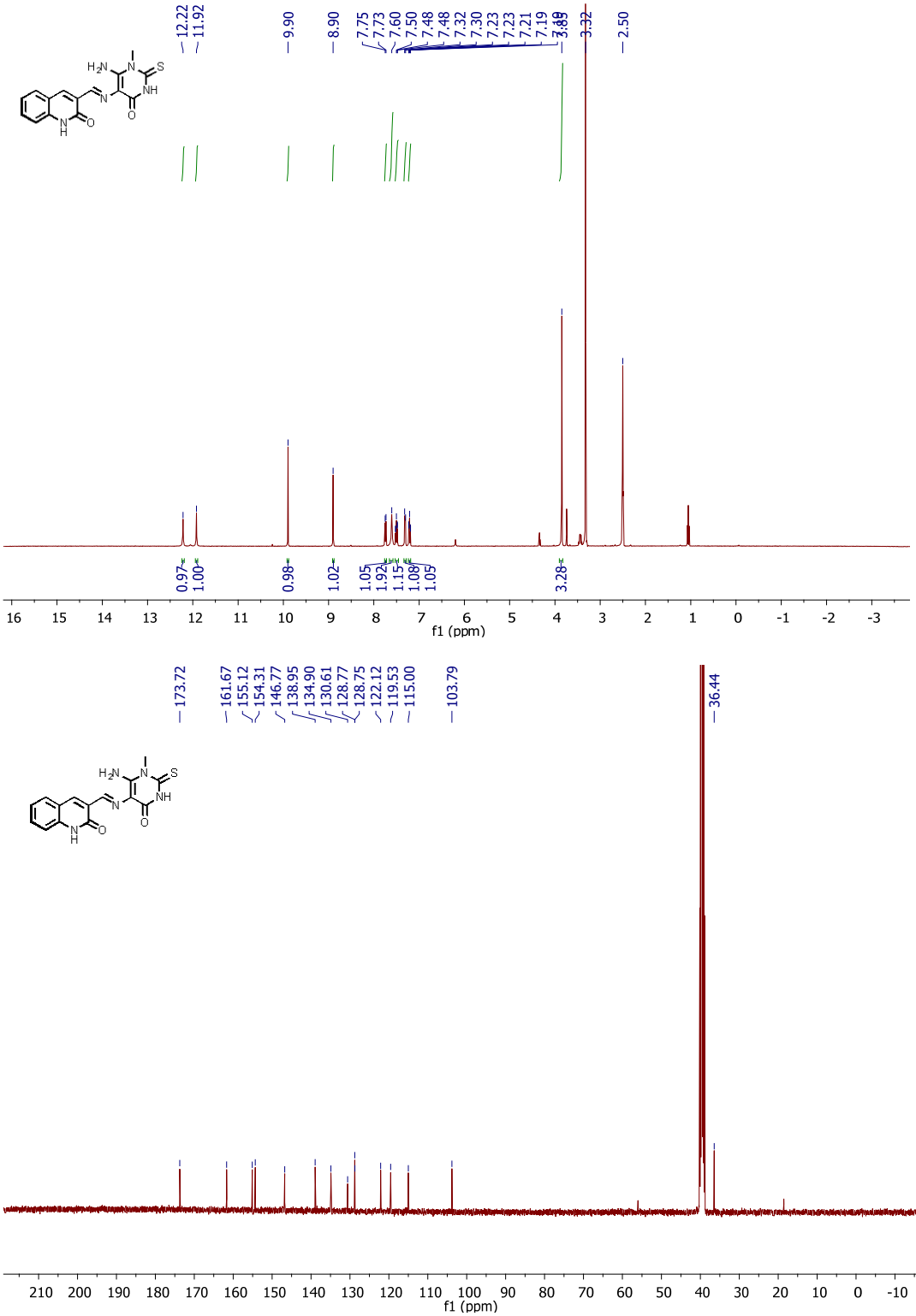


Figure S6: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-1-ethyl-5-(((8-methyl-2-oxo-1,2-dihydroquinolin-3-yl)methylene)amino) pyrimidine-2,4(1H,3H)-dione (10f)

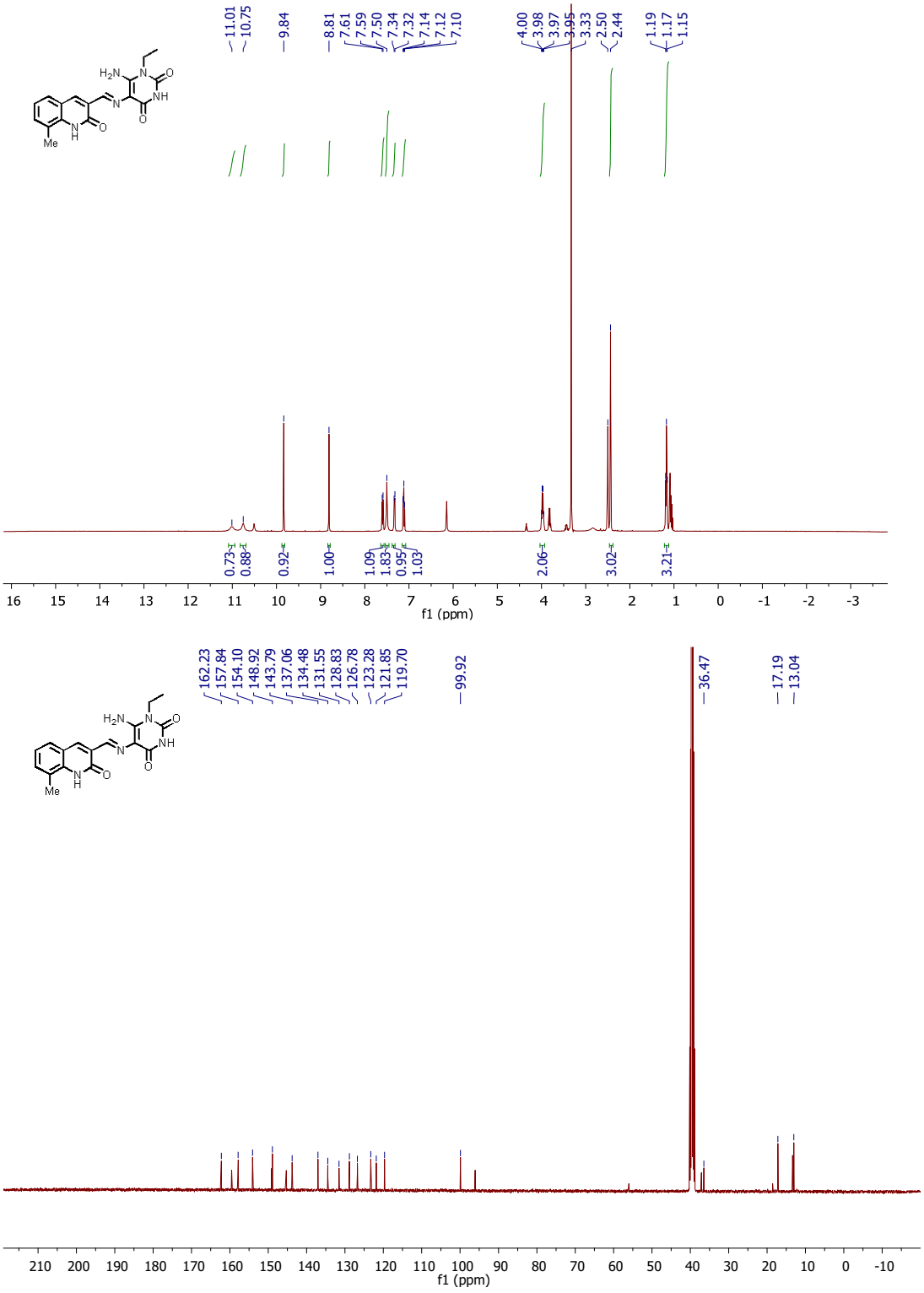
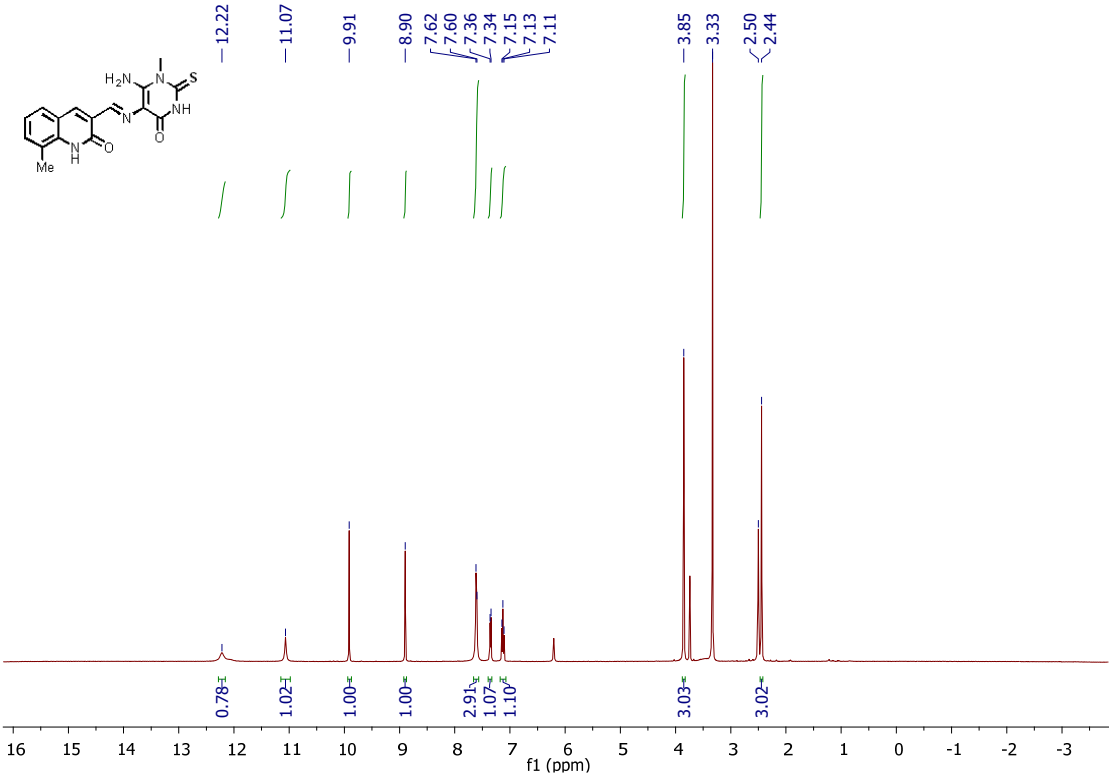


Figure S7: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-3-(((6-amino-1-methyl-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)imino)methyl)-8-methylquinolin-2(1H)-one (10g)



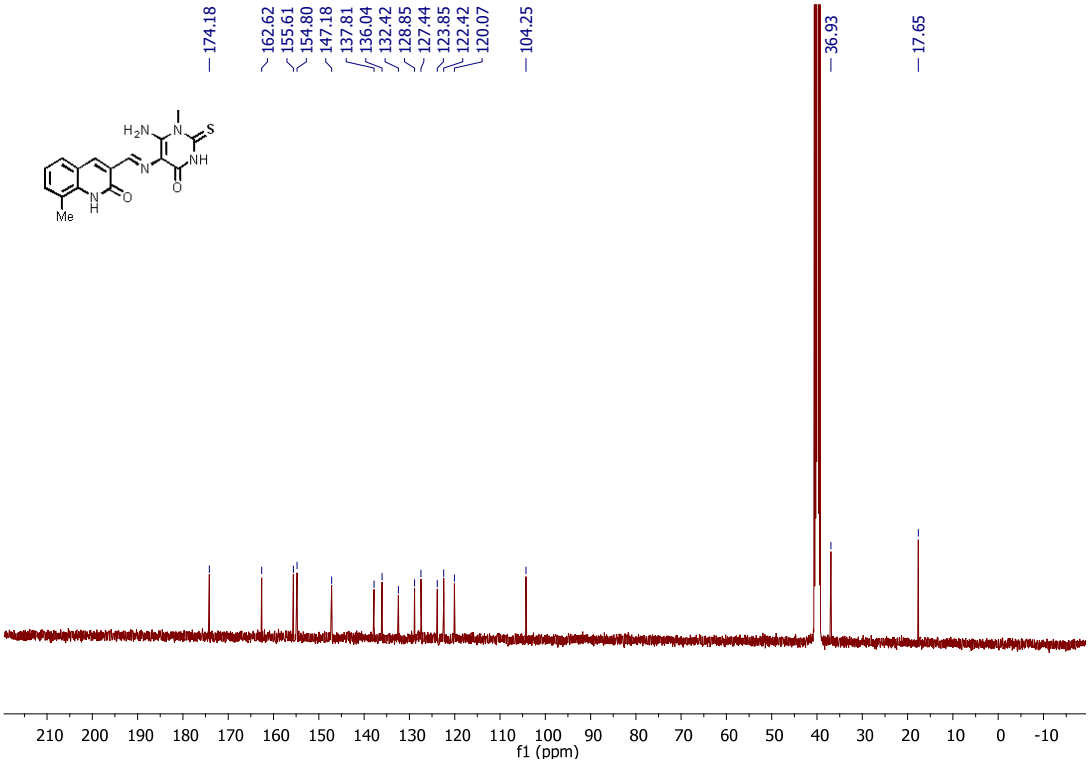


Figure S8: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-5-(((6-methoxy-2-oxo-1,2-dihydroquinolin-3-yl)methylene)amino)pyrimidine-2,4(1H,3H)-dione (10h)

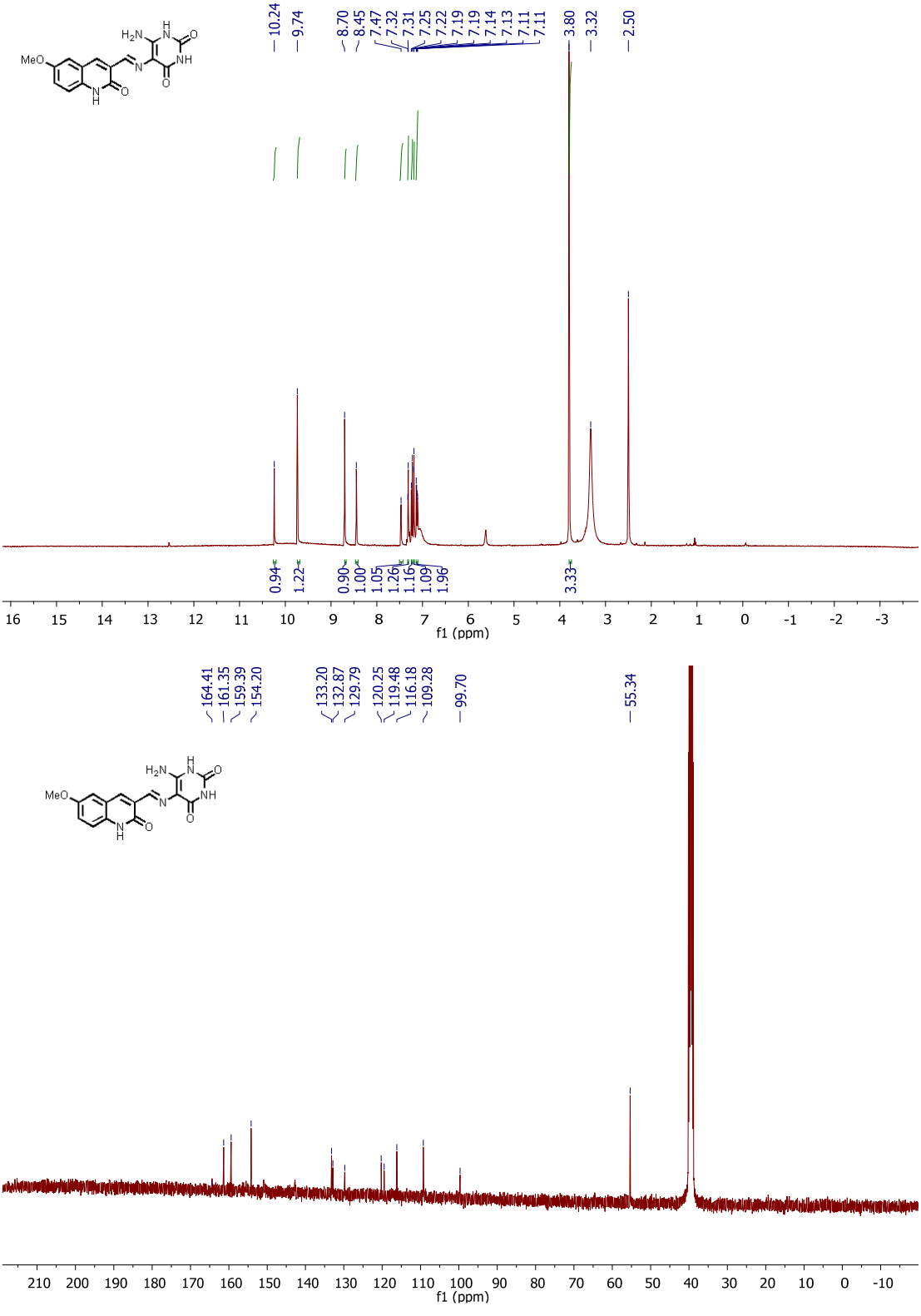


Figure S9: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-1-benzyl-5-(((6-methoxy-2-oxo-1,2-dihydroquinolin-3-yl)methylene)amino) pyrimidine-2,4(1H,3H)-dione (10i)

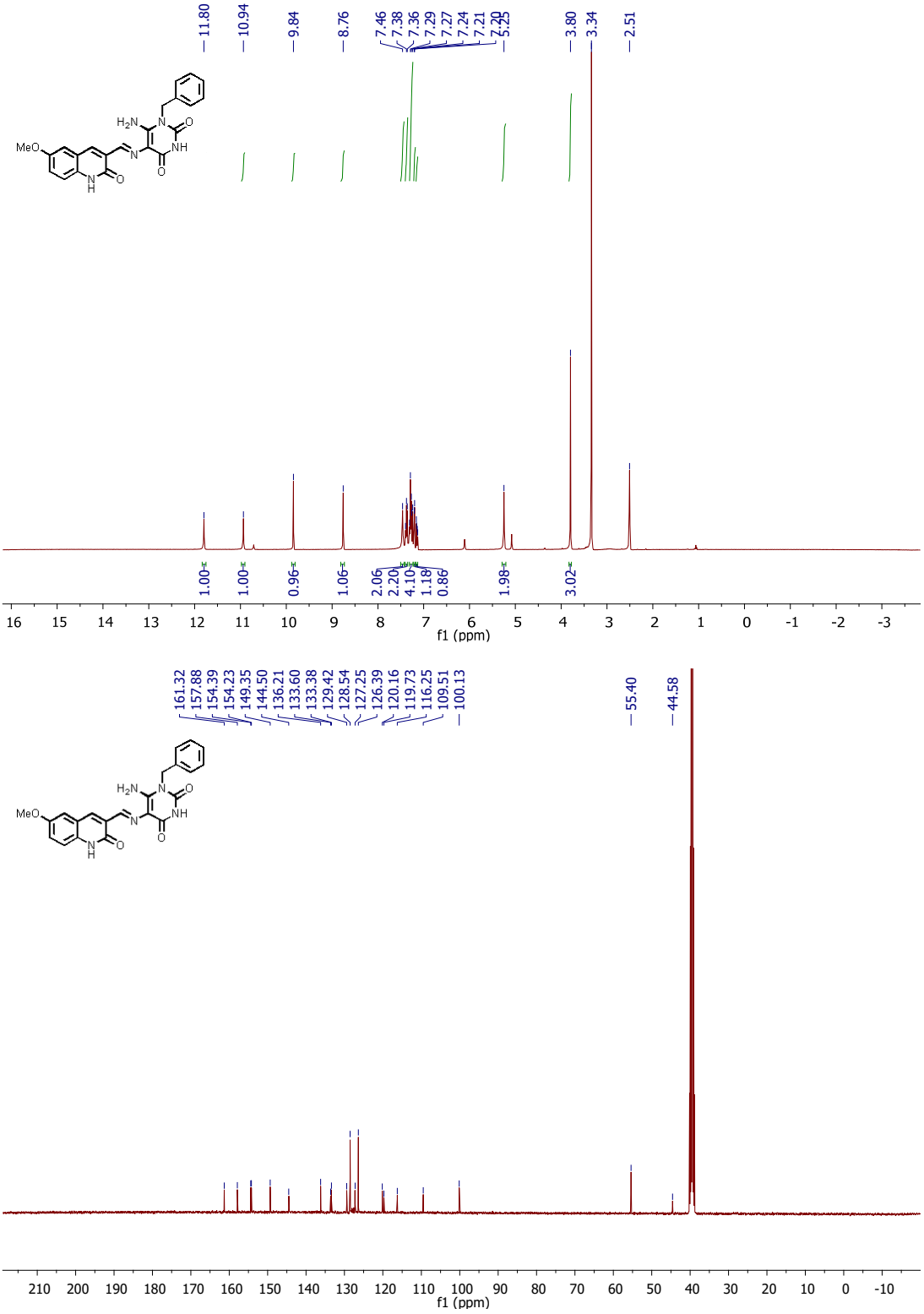
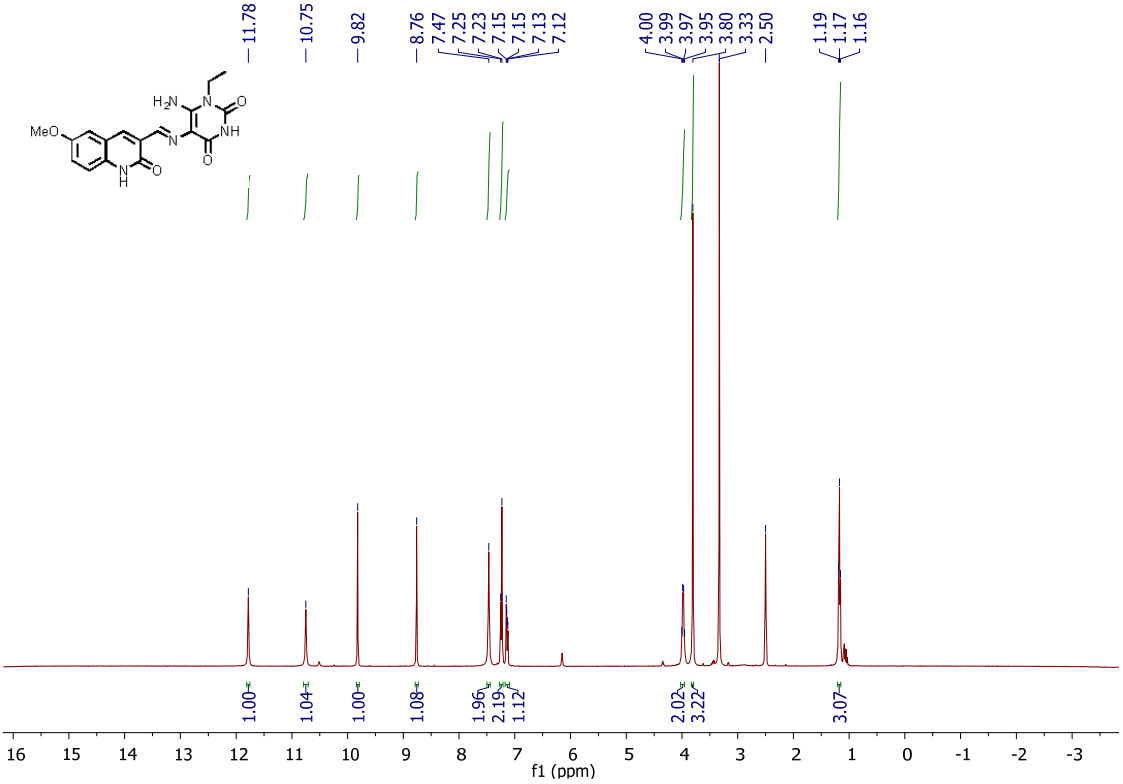


Figure S10: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-1-ethyl-5-(((6-methoxy-2-oxo-1,2-dihydroquinolin-3-yl)methylene)amino) pyrimidine-2,4(1H,3H)-dione (10j)



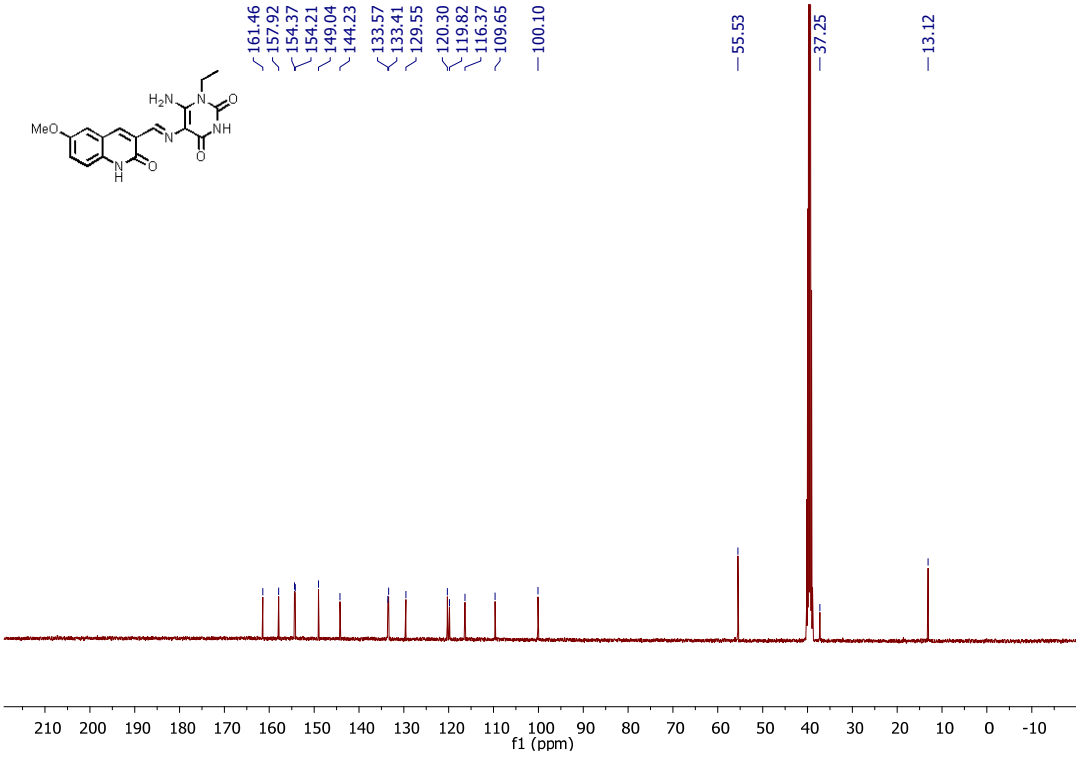


Figure S11: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-6-amino-5-(((6-methoxy-2-oxo-1,2-dihydro-quinolin-3-yl)methylene)amino)-1-methyl pyrimidine-2,4(1H,3H)-dione (10k)

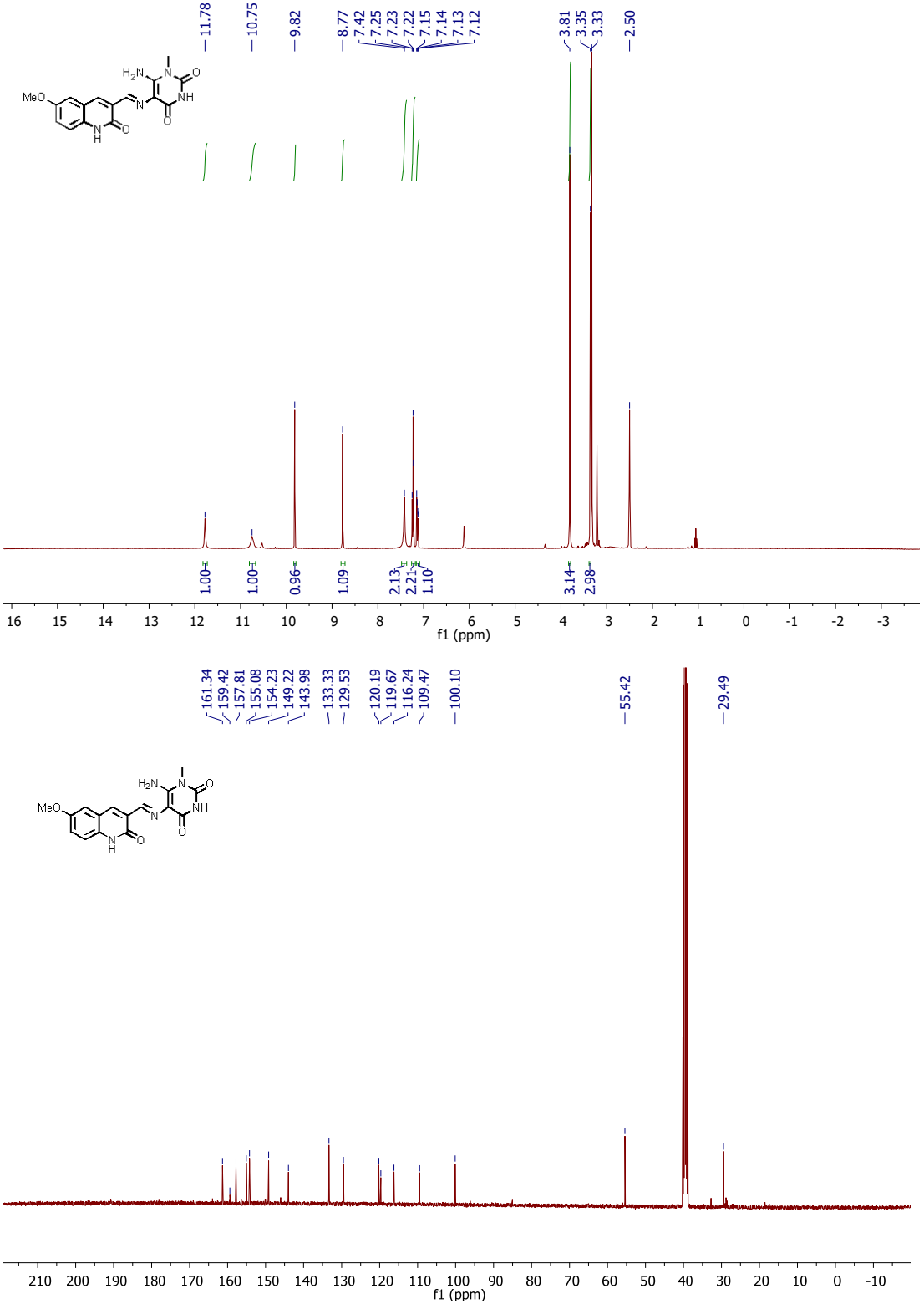
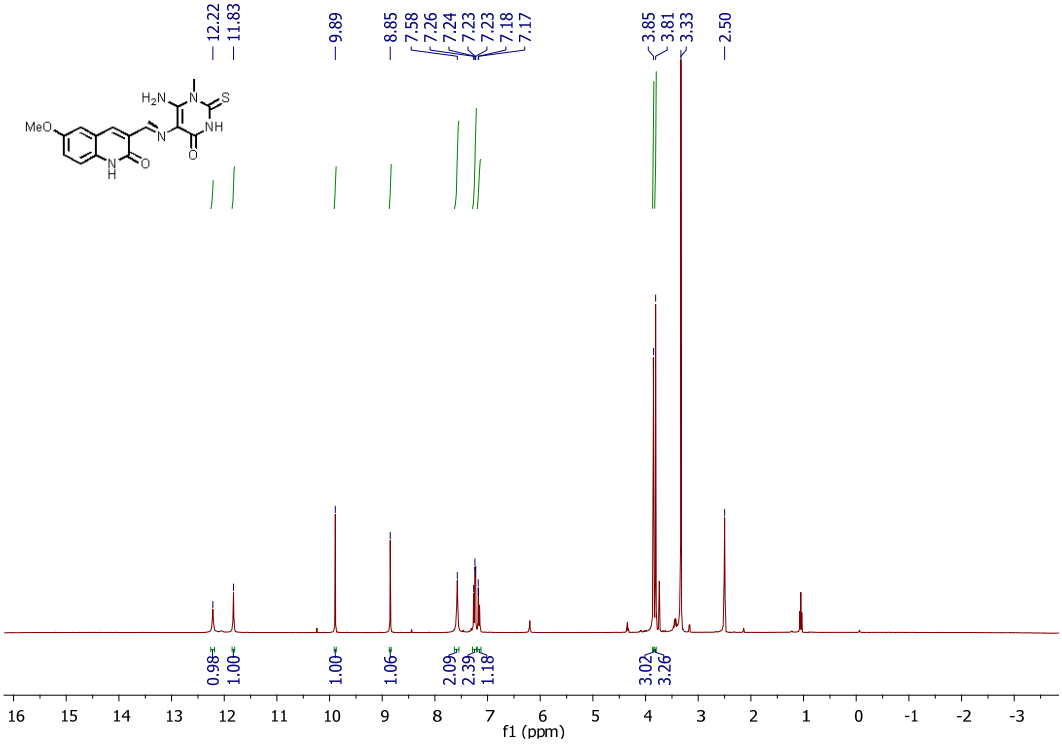


Figure S12: ^{1}H NMR and ^{13}C NMR spectra of (*E*)-3-(((6-amino-1-methyl-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)imino)methyl)-6-methoxyquinolin-2(1H)-one (10l)



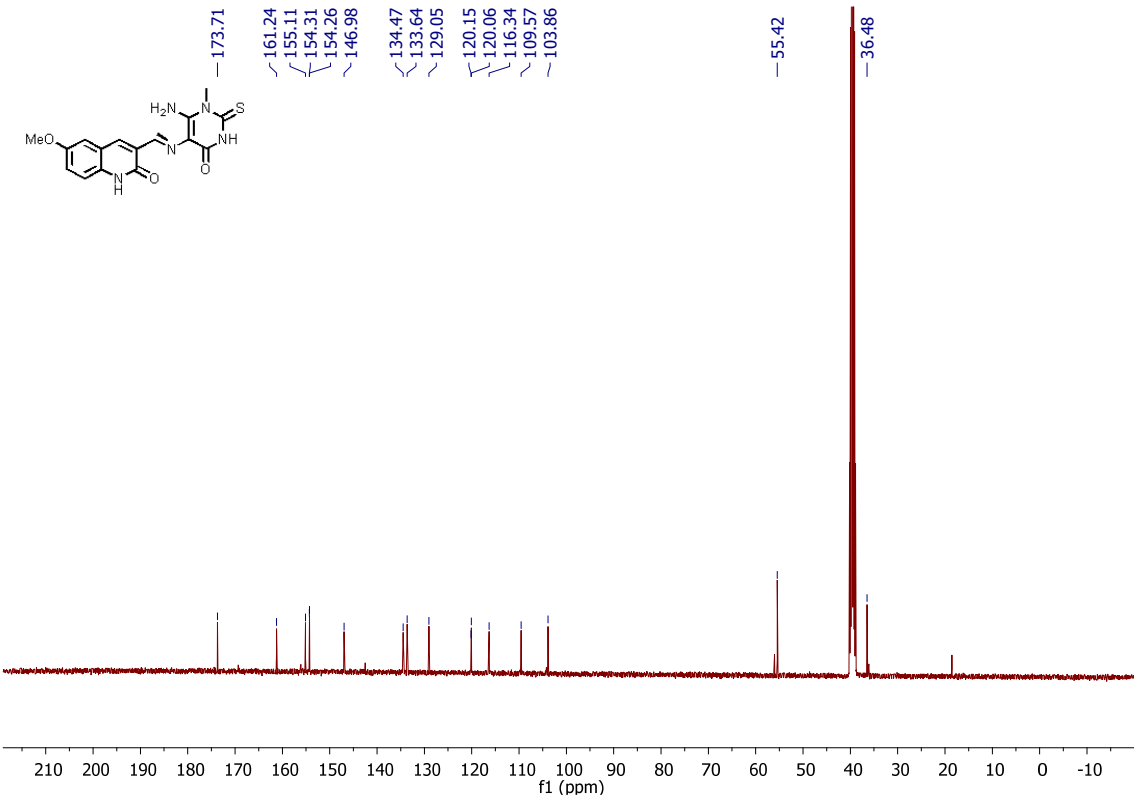
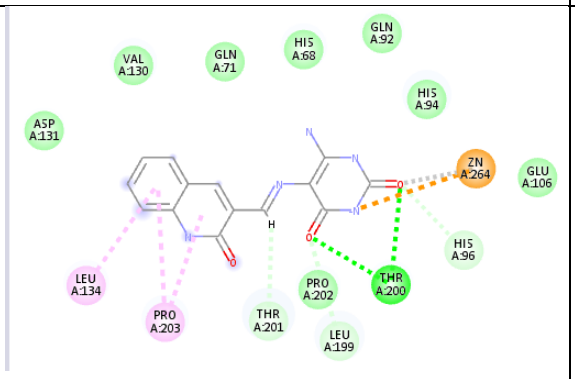
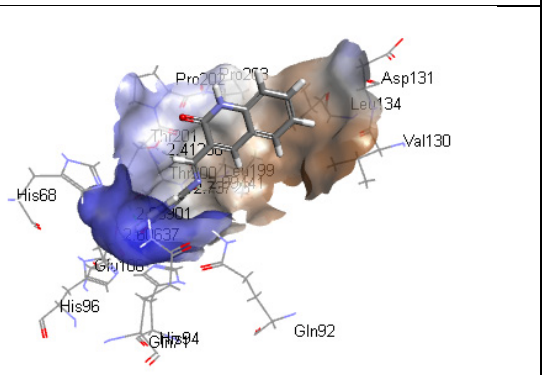
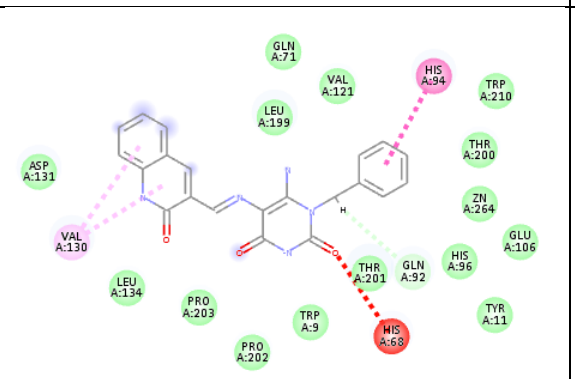
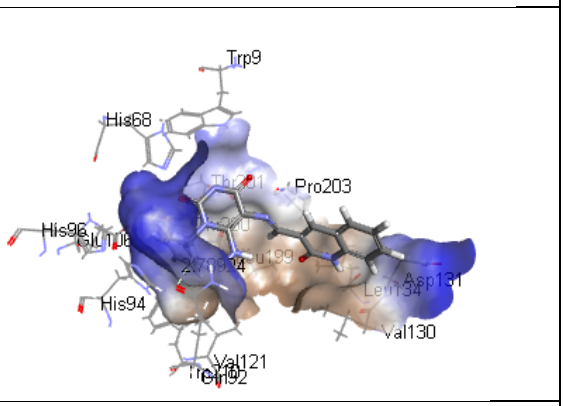
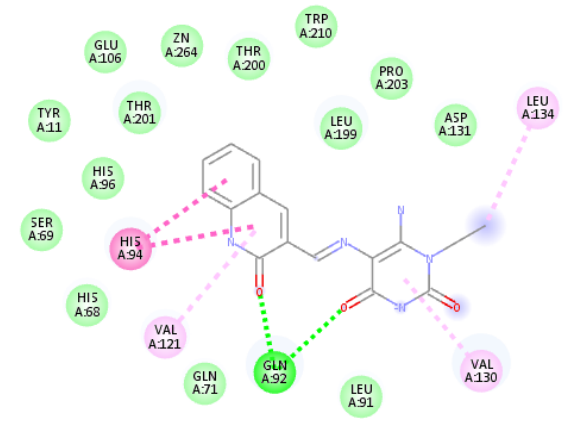
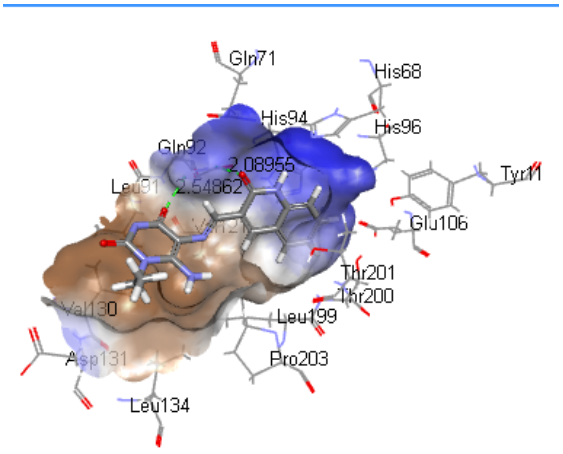
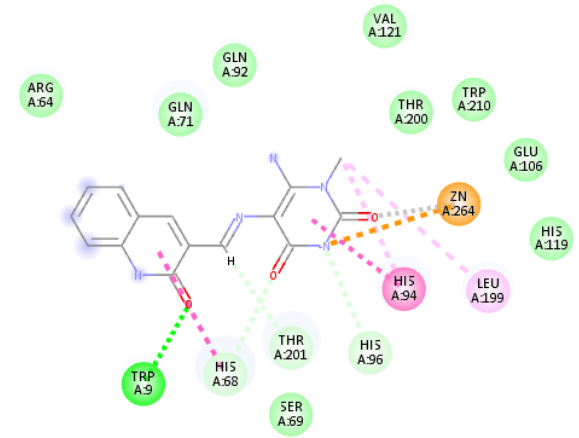
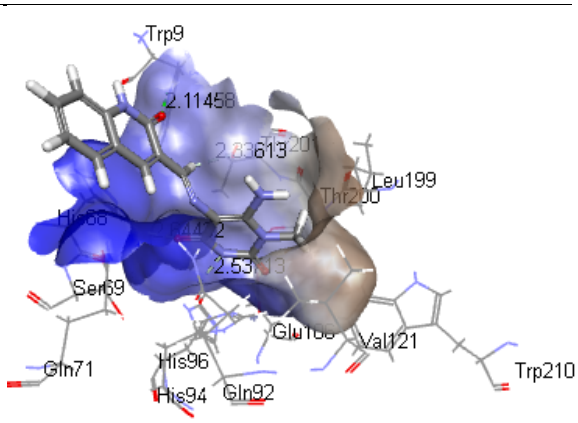
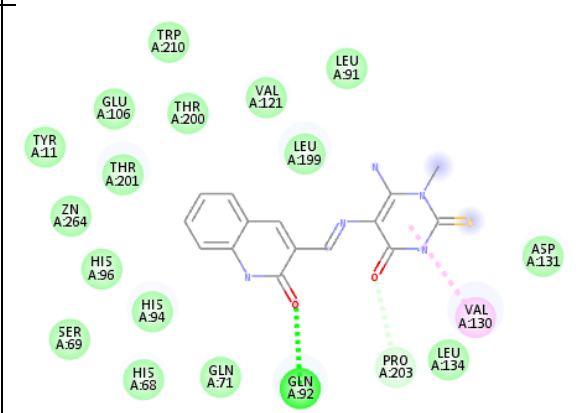
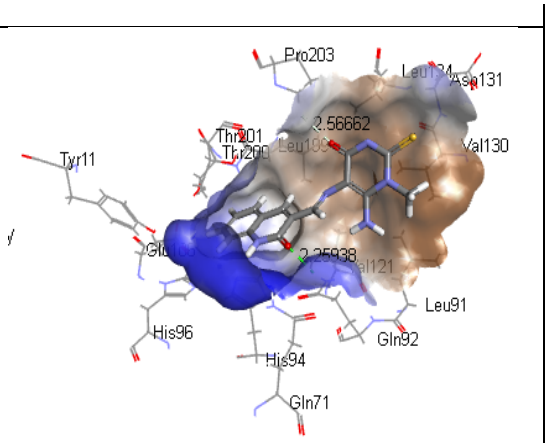
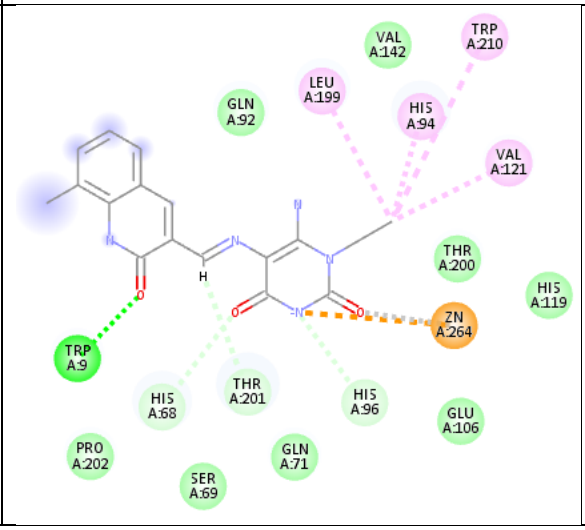
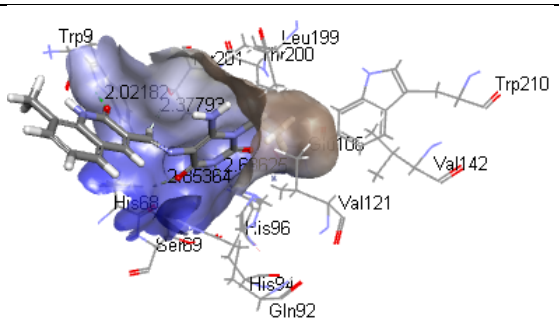
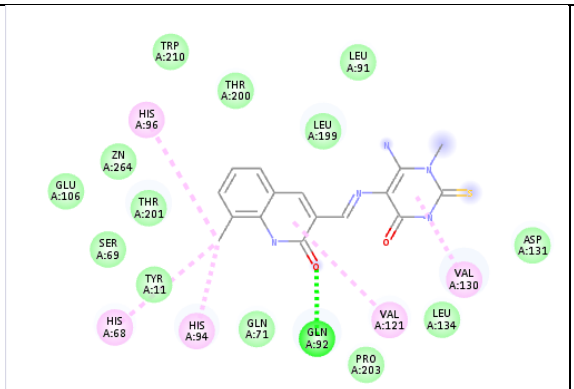
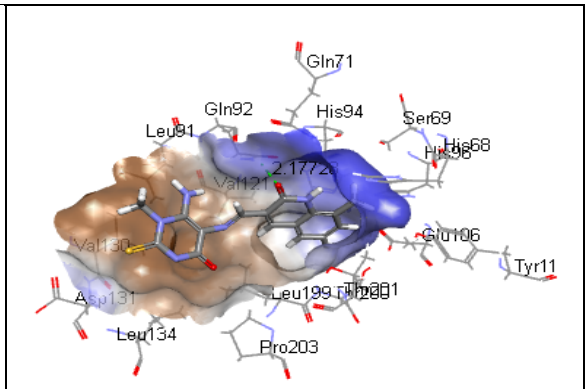
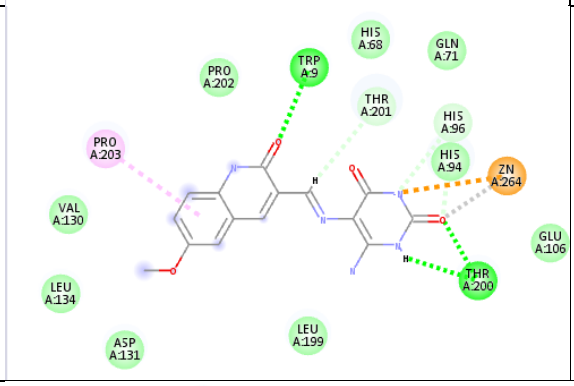
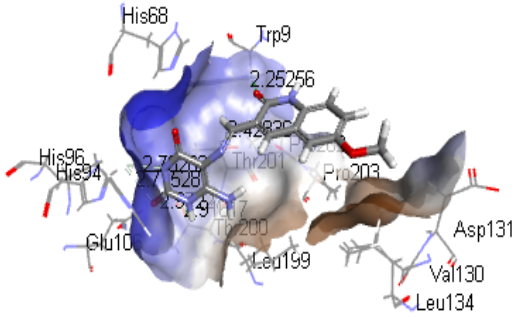
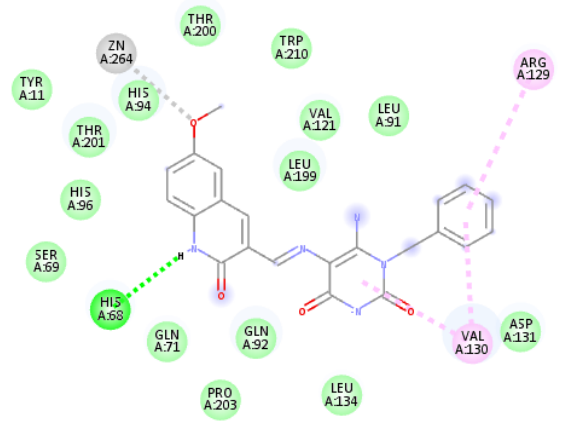
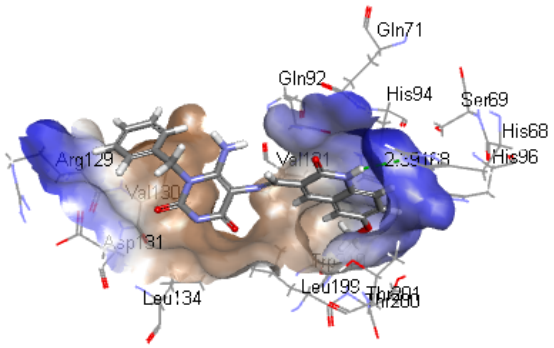
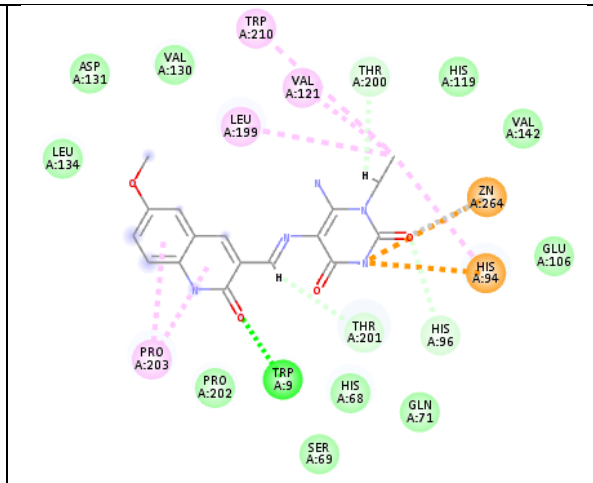
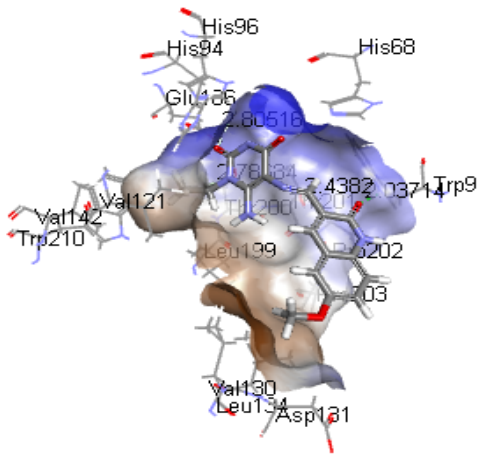
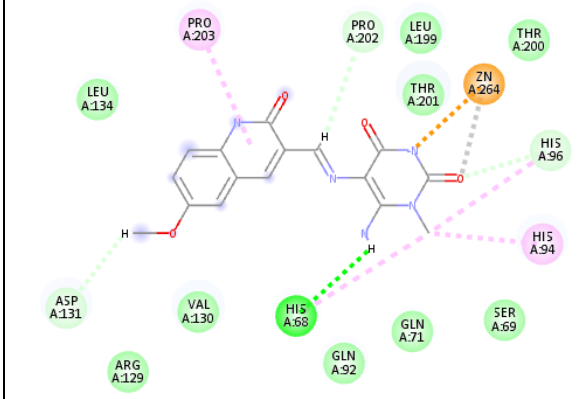
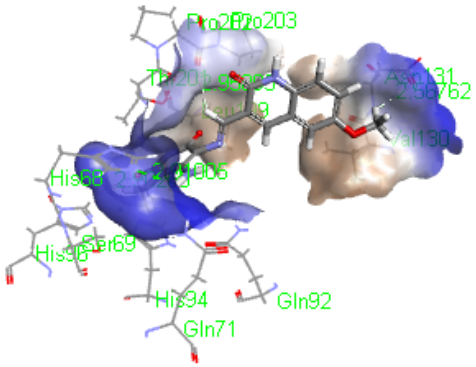
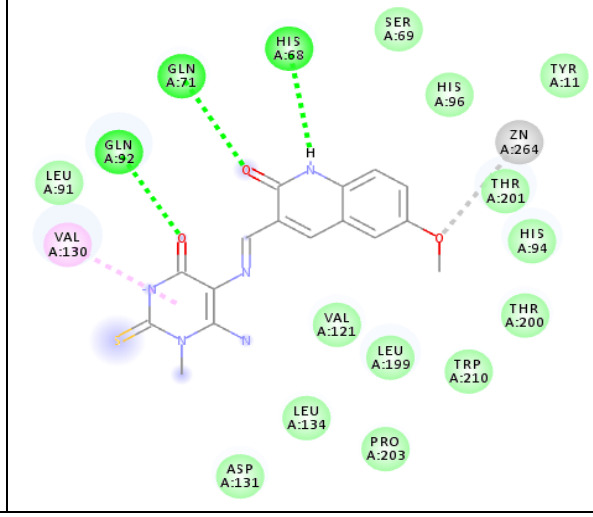
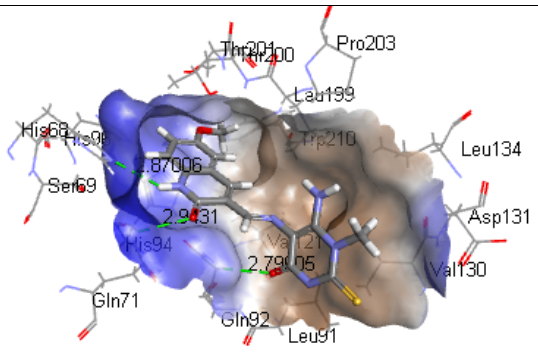


Table S1. 2D & 3D interactions of new compounds with the binding site of the human carbonic anhydrases IX (PDB file 5FL4)

Compound	2D Interaction	3D Interaction
10a		
10b		
10c		

10d	 VAL A:121 GLN A:92 ARG A:64 GLN A:71 THR A:200 TRP A:210 GLU A:106 ZN A:264 HIS A:119 HIS A:94 LEU A:199 THR A:201 HIS A:96 TRP A:9 HIS A:68 SER A:69	 Trp9 2.11458 Leu199 Thr200 Ser69 Gln71 His96 His94 Gln92 Val121 Trp210
10e	 TRP A:210 LEU A:91 GLU A:106 THR A:200 VAL A:121 TYR A:11 LEU A:199 THR A:201 ZN A:264 HIS A:96 ASP A:131 HIS A:94 VAL A:130 SER A:69 PRO A:203 LEU A:134 HIS A:68 GLN A:71 GLN A:92	 Pro203 Asp131 2.56662 Thr201 Val130 Tyr11 Leu91 His96 Gln92 His94 Gln71
10f	 VAL A:142 TRP A:210 LEU A:199 GLN A:92 HIS A:94 VAL A:121 THR A:200 HIS A:119 ZN A:264 TRP A:9 HIS A:68 THR A:201 HIS A:96 GLU A:106 PRO A:202 GLN A:71 SER A:69	 Trp9 Leu199 Thr200 Trp210 2.02182 Val142 Val121 His96 Ser69 His94 Gln92

10g	 TRP A:210 LEU A:91 THR A:200 HIS A:96 LEU A:199 ZN A:264 GLU A:106 THR A:201 SER A:69 ASP A:131 TYR A:11 VAL A:130 HIS A:68 HIS A:94 GLN A:71 GLN A:92 VAL A:121 LEU A:134 PRO A:203	 Gln71 Gln92 His94 Ser69 Leu91 His68 Val121 Val130 Glu106 Tyr11 Asp131 Leu199 Leu134 Pro203
10h	 HIS A:68 GLN A:71 TRP A:9 PRO A:202 THR A:201 HIS A:96 PRO A:203 HIS A:94 ZN A:264 VAL A:130 GLU A:106 THR A:200 LEU A:134 ASP A:131 LEU A:199	 His68 Trp9 2.25256 His96 His94 Thr201 Pro203 Glu10 Leu199 Asp131 Val130 Leu134
10i	 THR A:200 ZN A:264 TRP A:210 ARG A:129 TYR A:11 HIS A:94 VAL A:121 LEU A:91 THR A:201 LEU A:199 HIS A:96 SER A:69 HIS A:68 GLN A:71 GLN A:92 VAL A:130 ASP A:131 PRO A:203 LEU A:134	 Gln71 Gln92 His94 Ser69 His68 His96 Arg129 Val131 Val130 Asp131 Leu134 Leu199

10j	 TRP A:210 ASP A:131 VAL A:130 VAL A:121 THR A:200 HIS A:119 LEU A:199 VAL A:142 LEU A:134 ZN A:264 GLU A:106 HIS A:94 THR A:201 HIS A:96 PRO A:203 PRO A:202 TRP A:9 HIS A:68 GLN A:71 SER A:69	 His96 His94 His68 Val121 Val142 Trp210 Leu199 Trp9 Val130 Leu134 Asp131
10k	 PRO A:203 PRO A:202 LEU A:199 THR A:200 LEU A:134 THR A:201 ZN A:264 HIS A:96 HIS A:94 ASP A:131 VAL A:130 HIS A:68 GLN A:71 SER A:69 GLN A:92 ARG A:129	 Pro203 Asp131 Val130 His68 Ser69 His94 Gln92 Gln71
10l	 SER A:69 HIS A:68 GLN A:71 TYR A:11 HIS A:96 ZN A:264 GLN A:92 LEU A:91 THR A:201 VAL A:130 HIS A:94 THR A:200 VAL A:121 LEU A:199 TRP A:210 LEU A:134 PRO A:203 ASP A:131	 Pro203 Leu199 Trp210 Leu134 Ser69 Asp131 His94 Val130 Gln71 Gln92 Leu91

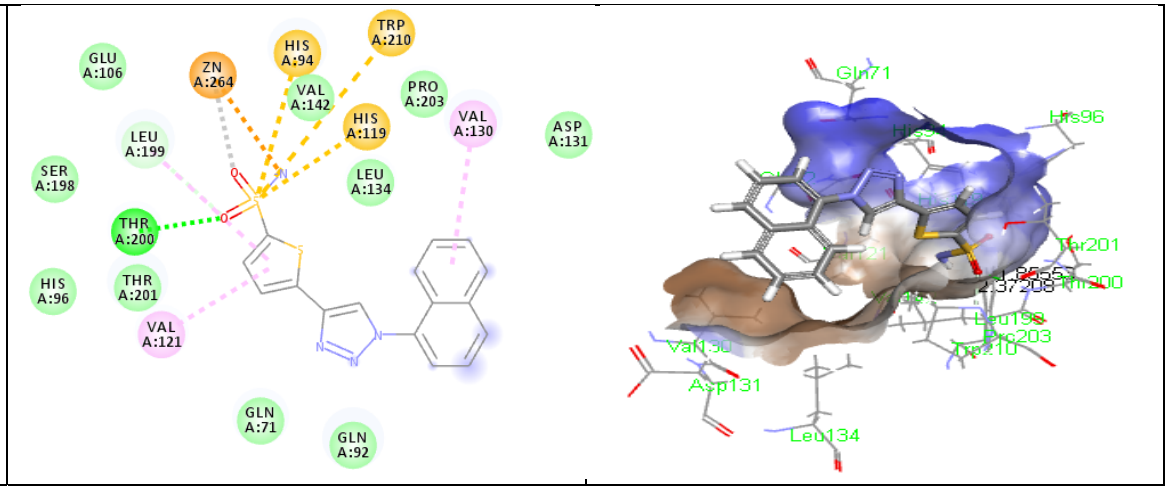
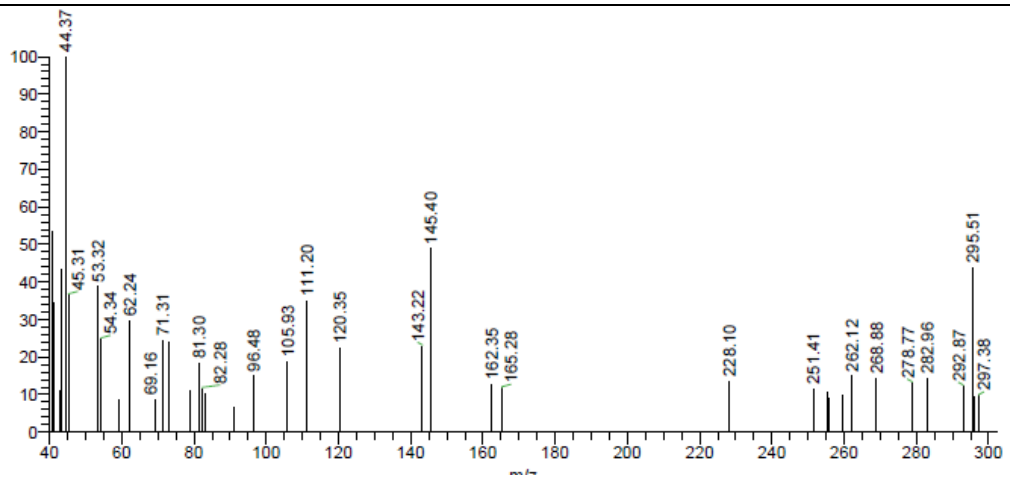
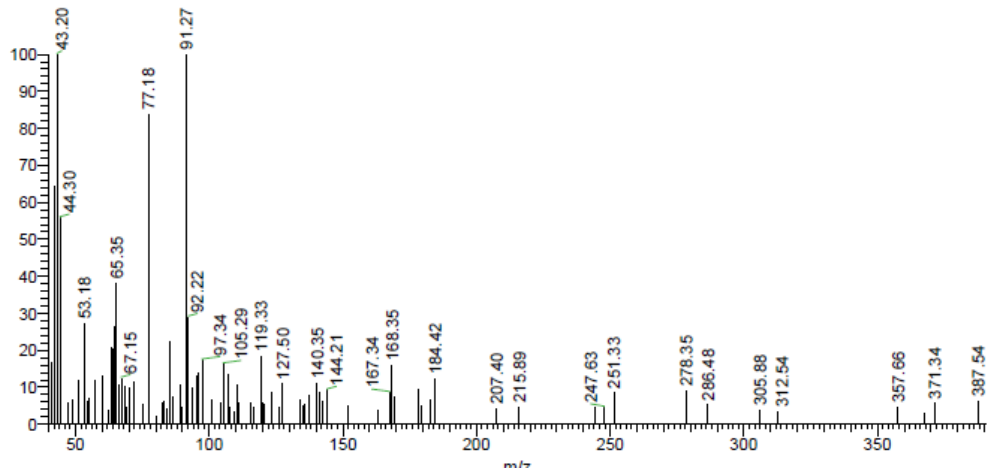
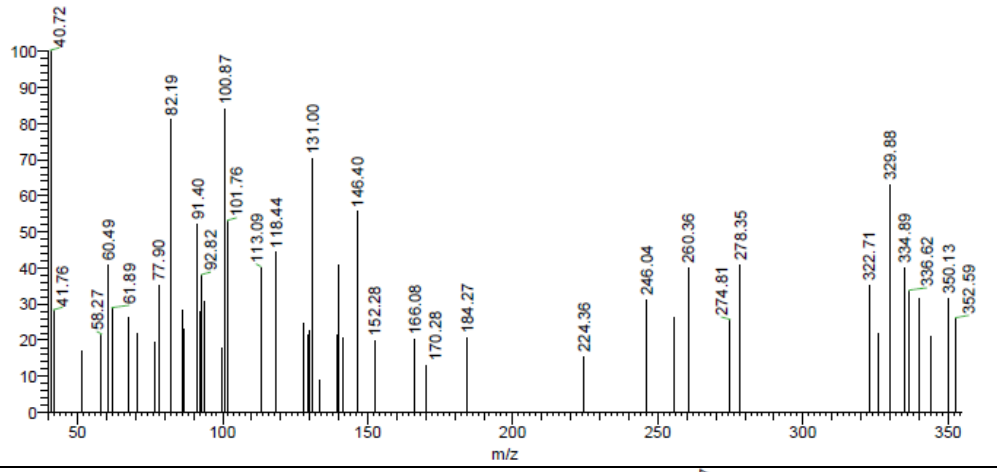
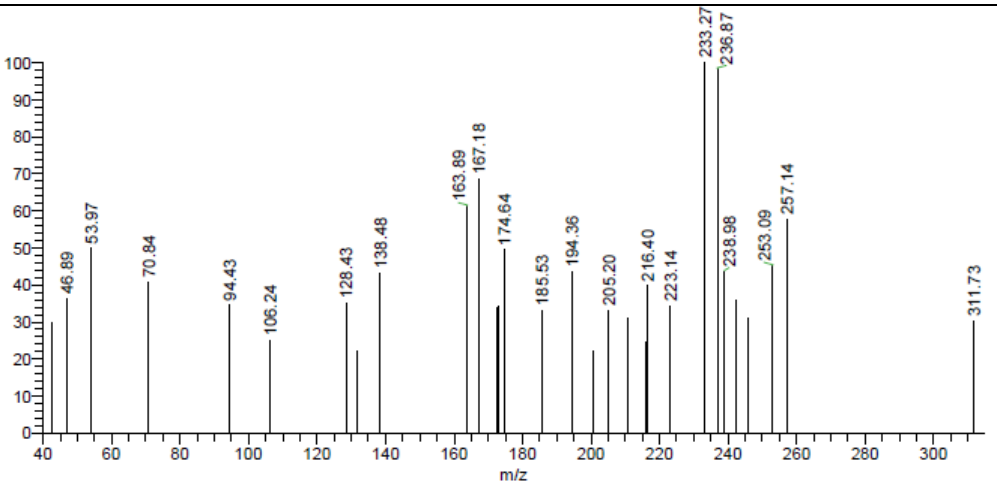
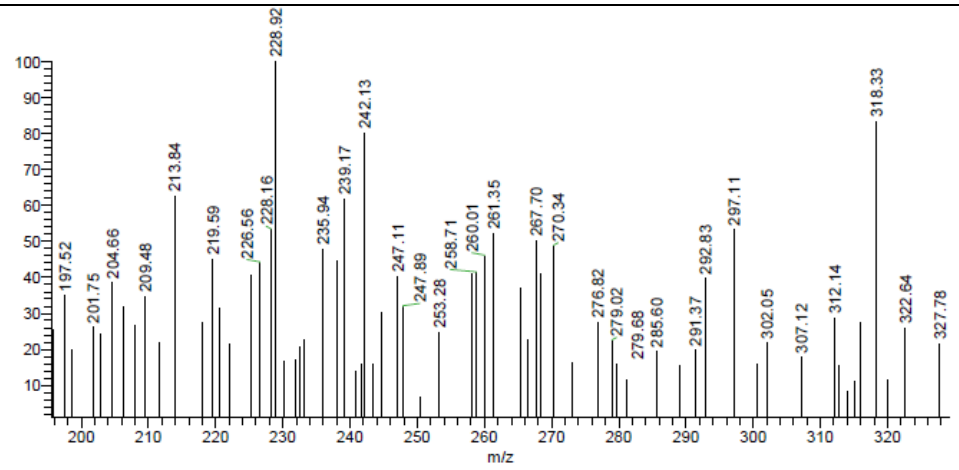
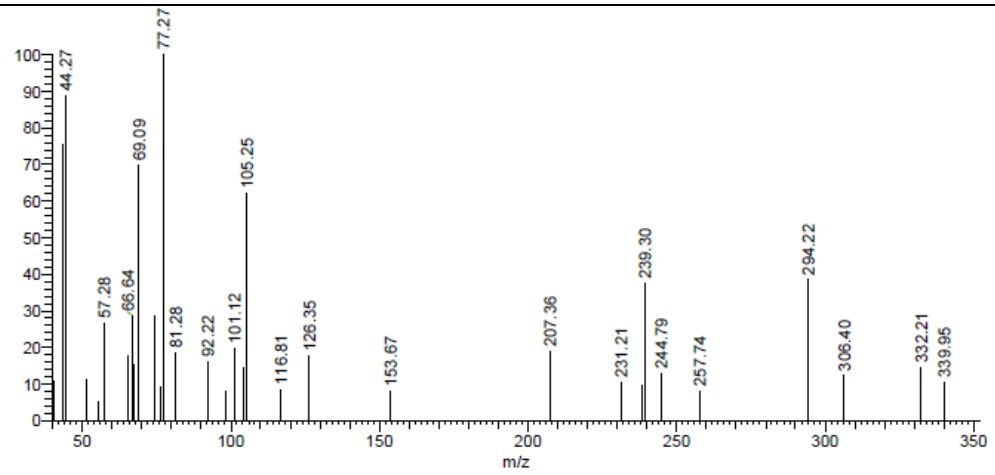
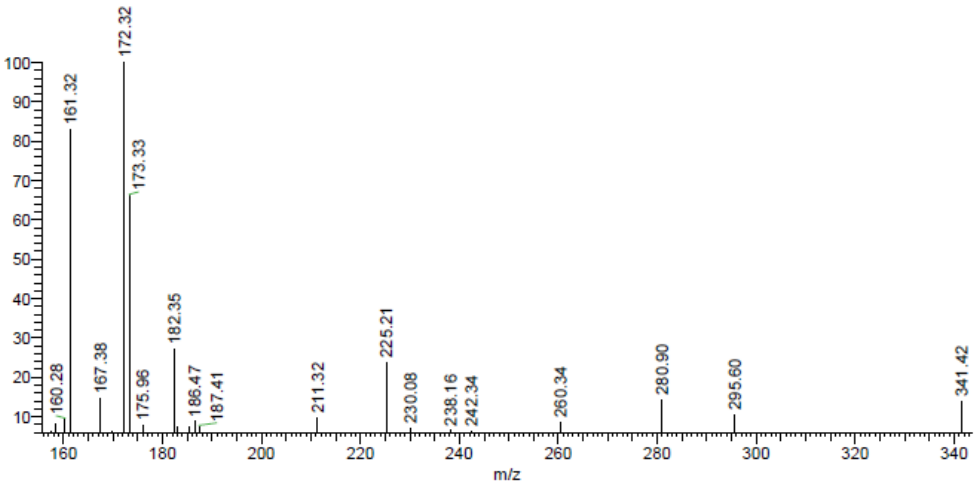
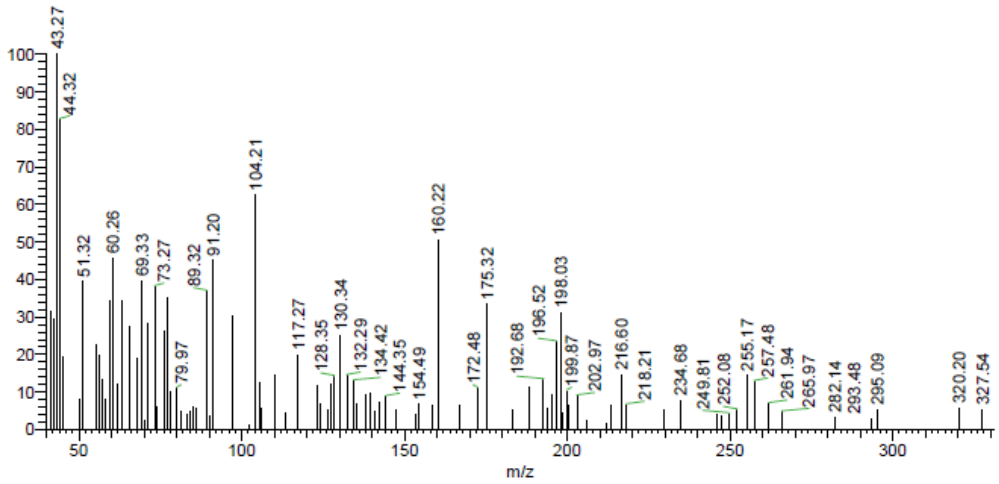
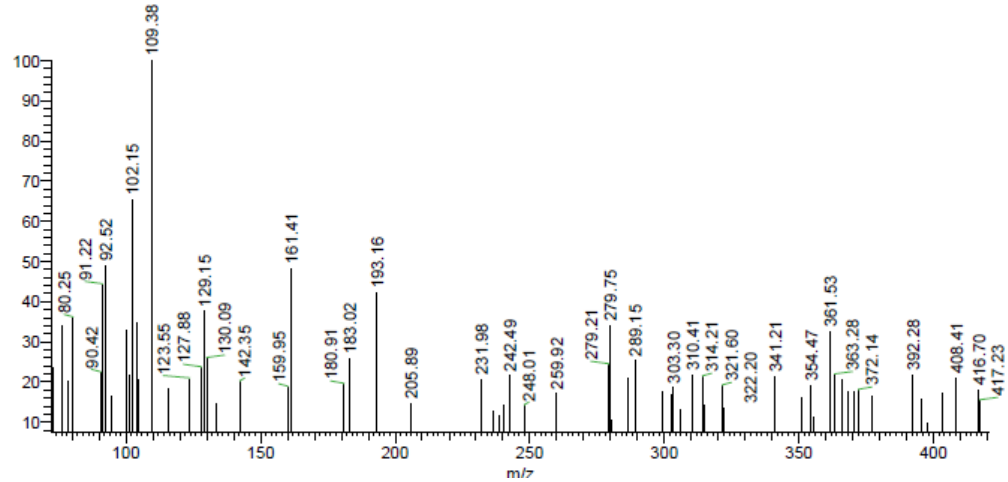
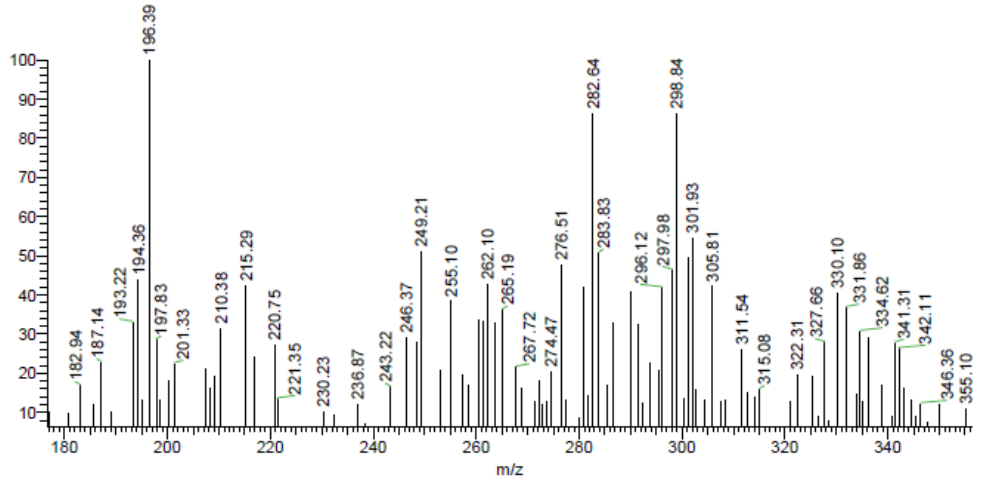
Ligand	

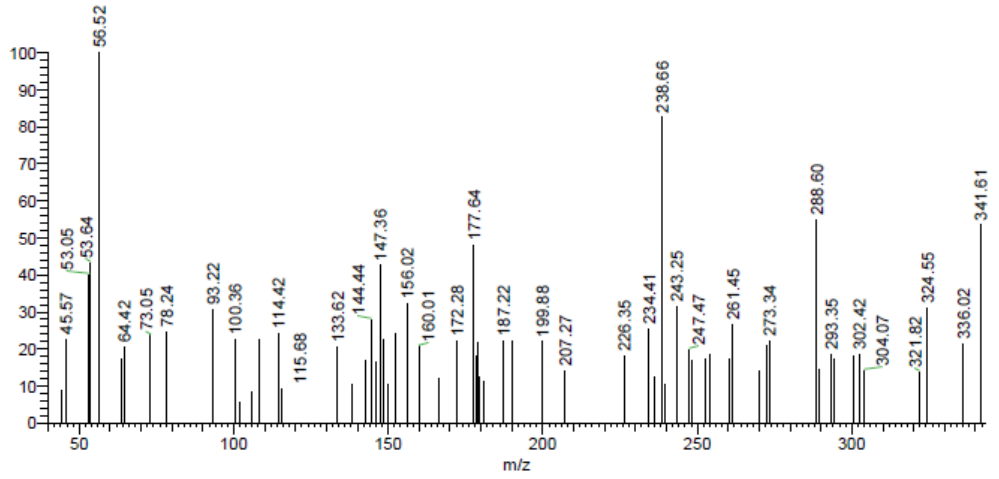
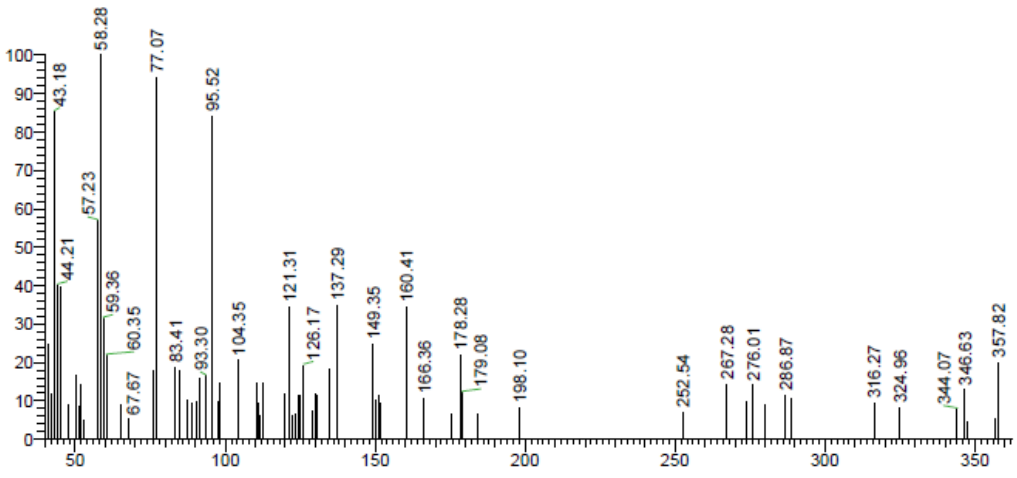
Table S2: Mass spectra for compounds 10a-l

Compound	Mass spectrum
10a	

10b	 43.20 91.27 77.18 44.30 65.35 53.18 92.22 97.34 105.29 119.33 67.15 127.50 140.35 144.21 167.34 168.35 184.42 207.40 215.89 247.63 251.33 278.35 286.48 305.88 312.54 357.66 371.34 387.54 m/z
10c	 40.72 82.19 100.87 131.00 91.40 146.40 101.76 92.82 118.44 113.09 60.49 77.90 61.89 41.76 58.27 152.28 166.08 170.28 184.27 224.36 246.04 260.36 274.81 278.35 322.71 329.88 334.89 336.62 350.13 352.59 m/z
10d	 233.27 236.87 163.89 167.18 174.64 257.14 53.97 46.89 70.84 138.48 94.43 128.43 106.24 185.53 194.36 205.20 216.40 223.14 238.98 253.09 311.73 m/z

10e	 228.92 242.13 318.33 213.84 239.17 228.16 219.59 226.56 235.94 247.11 261.35 267.70 270.34 197.52 204.66 209.48 247.89 253.28 258.71 260.01 276.82 279.02 279.68 285.60 291.37 292.83 297.11 302.05 307.12 312.14 322.64 327.78 201.75 100 90 80 70 60 50 40 30 20 10 200 210 220 230 240 250 260 270 280 290 300 310 320 m/z
10f	 77.27 44.27 69.09 105.25 57.28 66.64 81.28 92.22 101.12 116.81 126.35 153.67 207.36 231.21 239.30 244.79 257.74 294.22 306.40 332.21 339.95 100 90 80 70 60 50 40 30 20 10 0 50 100 150 200 250 300 350 m/z
10g	 172.32 161.32 173.33 182.35 225.21 160.28 167.38 175.96 186.47 187.41 211.32 230.08 238.16 242.34 260.34 280.90 295.60 341.42 100 90 80 70 60 50 40 30 20 10 160 180 200 220 240 260 280 300 320 340 m/z

10h	 43.27 44.32 51.32 60.26 69.33 73.27 79.97 89.32 91.20 104.21 117.27 128.35 130.34 132.29 134.42 144.35 154.49 160.22 172.48 175.32 192.68 196.52 198.03 199.87 202.97 216.60 218.21 234.68 249.81 252.08 255.17 257.48 261.94 265.97 282.14 293.48 295.09 320.20 327.54 m/z
10i	 80.25 90.42 91.22 92.52 102.15 109.38 123.55 127.88 129.15 130.09 142.35 159.95 161.41 180.91 183.02 193.16 205.89 231.98 242.49 248.01 259.92 279.21 279.75 289.15 303.30 310.41 314.21 321.60 322.20 341.21 354.47 361.53 363.28 372.14 392.28 408.41 416.70 417.23 m/z
10j	 182.94 187.14 193.22 194.36 196.39 197.83 201.33 210.38 215.29 220.75 221.35 230.23 236.87 243.22 246.37 249.21 255.10 262.10 265.19 267.72 274.47 276.51 282.64 283.83 296.12 297.98 298.84 301.93 305.81 311.54 315.08 322.31 327.66 330.10 331.86 334.62 341.31 342.11 346.36 355.10 m/z

10k	 56.52 53.05 53.64 45.57 64.42 73.05 78.24 93.22 100.36 114.42 115.68 133.62 144.44 147.36 156.02 160.01 172.28 177.64 187.22 199.88 207.27 226.35 234.41 238.66 243.25 247.47 261.45 273.34 288.60 293.35 302.42 304.07 321.82 324.55 336.02 341.61 m/z
10l	 58.28 43.18 77.07 95.52 57.23 44.21 59.36 60.35 67.67 83.41 93.30 104.35 121.31 126.17 137.29 149.35 160.41 166.36 178.28 179.08 198.10 252.54 267.28 276.01 286.87 316.27 324.96 344.07 346.63 357.82