

SUPPORTING INFORMATION

Design, synthesis and biological evaluation of 4*H*-pyrido[1,2-*a*] pyrimidin-4-one derivatives as anticancer agents via ROR1 inhibition

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NMR spectra of intermediates and target compounds

8-(6-Aminopyridin-3-yl)-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (3)

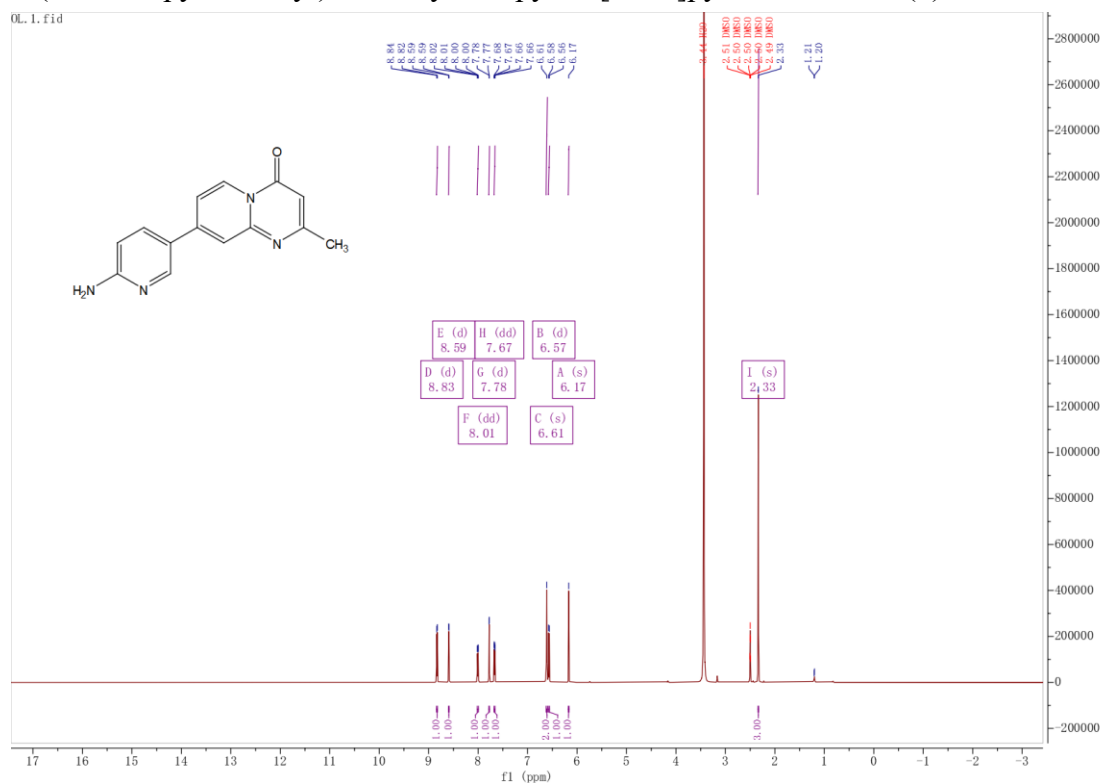


Figure S1. ¹H NMR Spectrum of intermediate 3

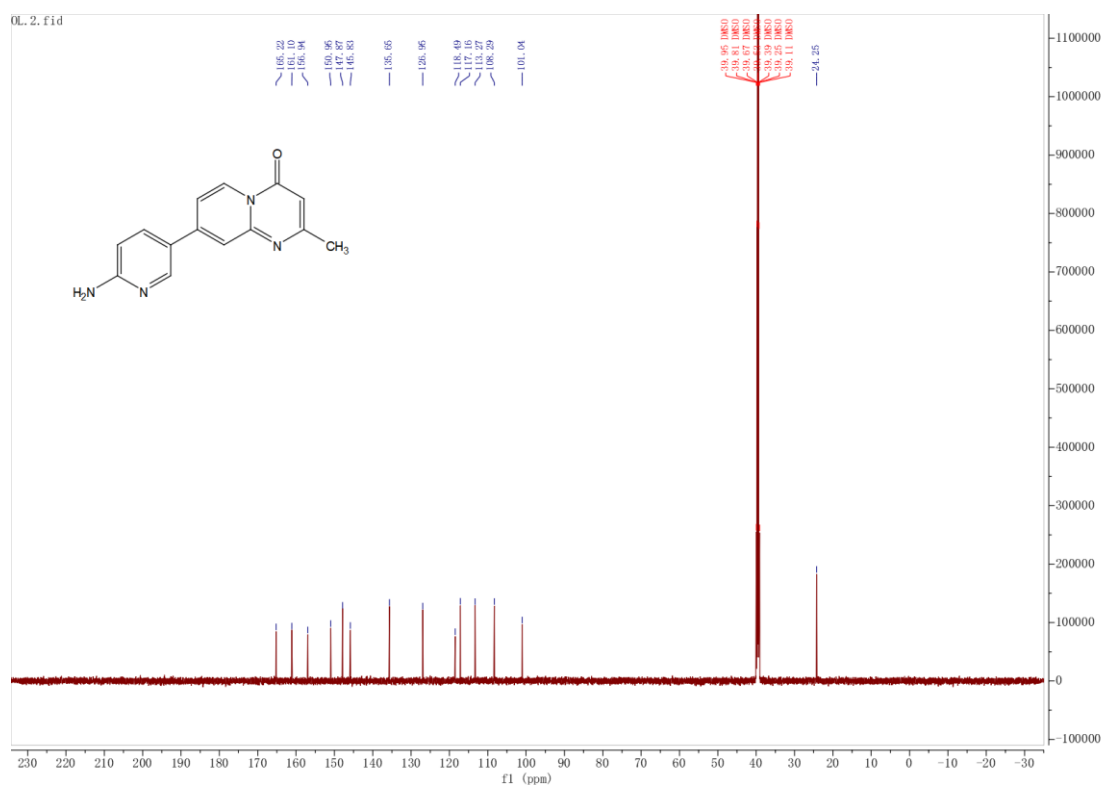


Figure S2. ¹³C NMR Spectrum of intermediate 3

8-(4-Amino-3-nitrophenyl)-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (7)

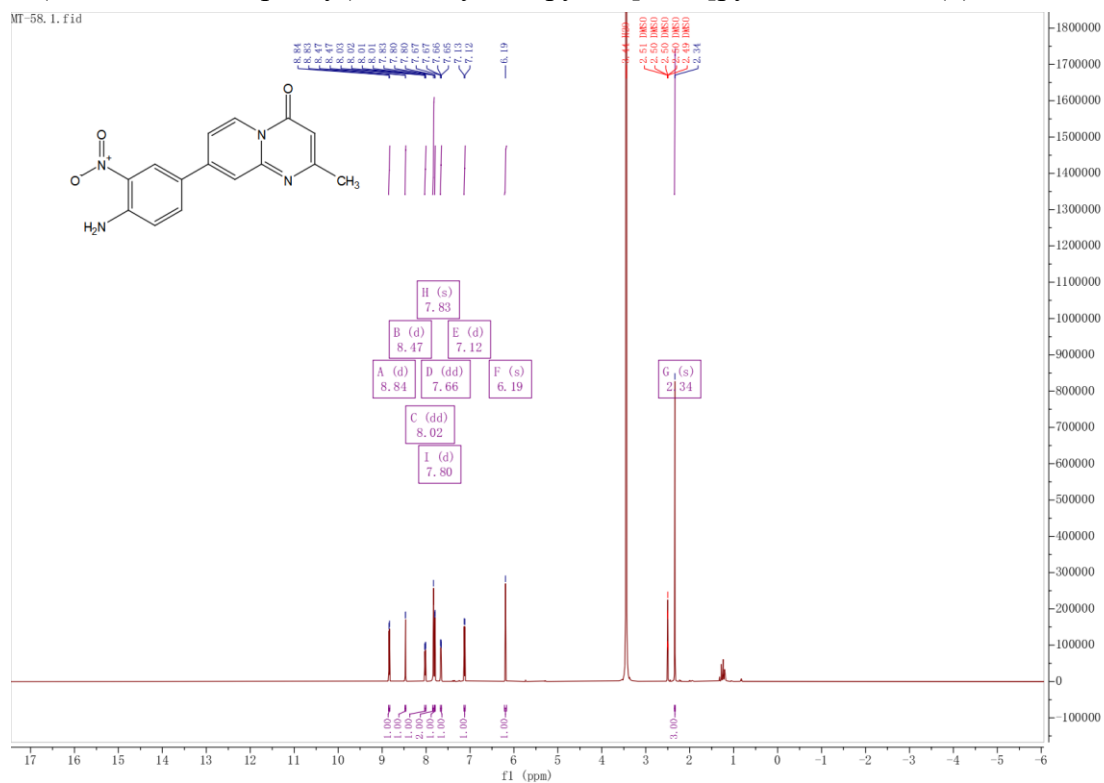


Figure S3. ¹H NMR Spectrum of intermediate 7

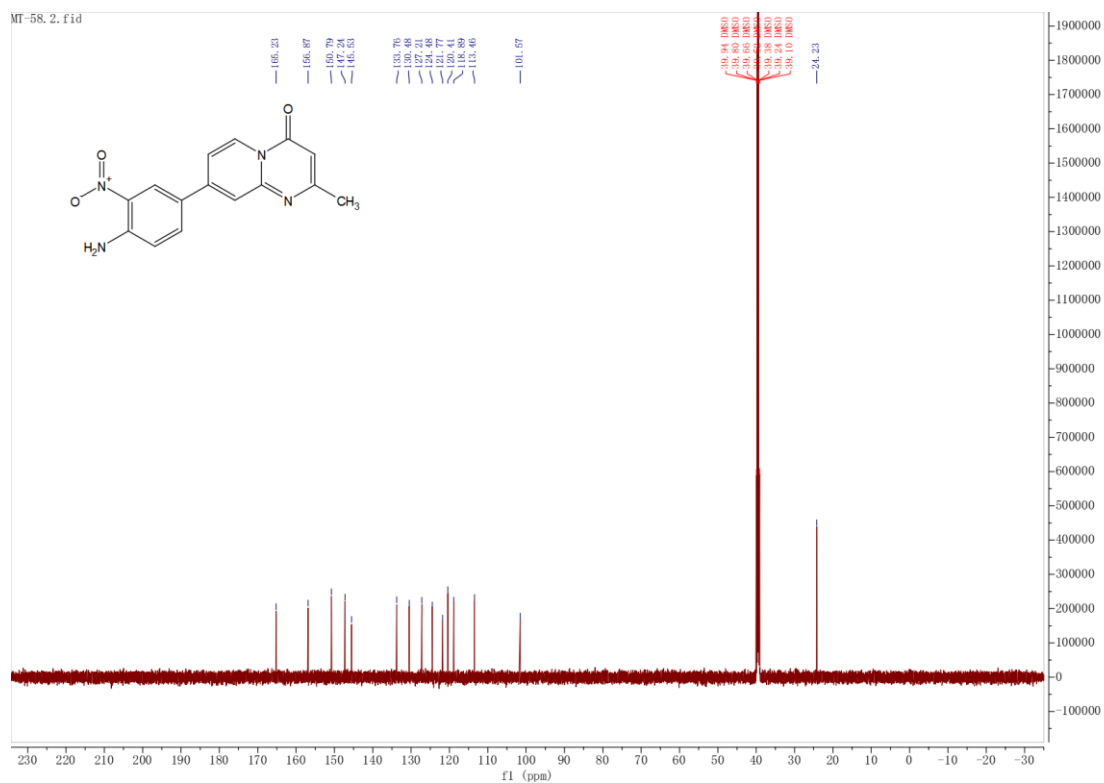


Figure S4. ¹³C NMR Spectrum of intermediate 7

8-(3,4-Diaminophenyl)-2-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8**)

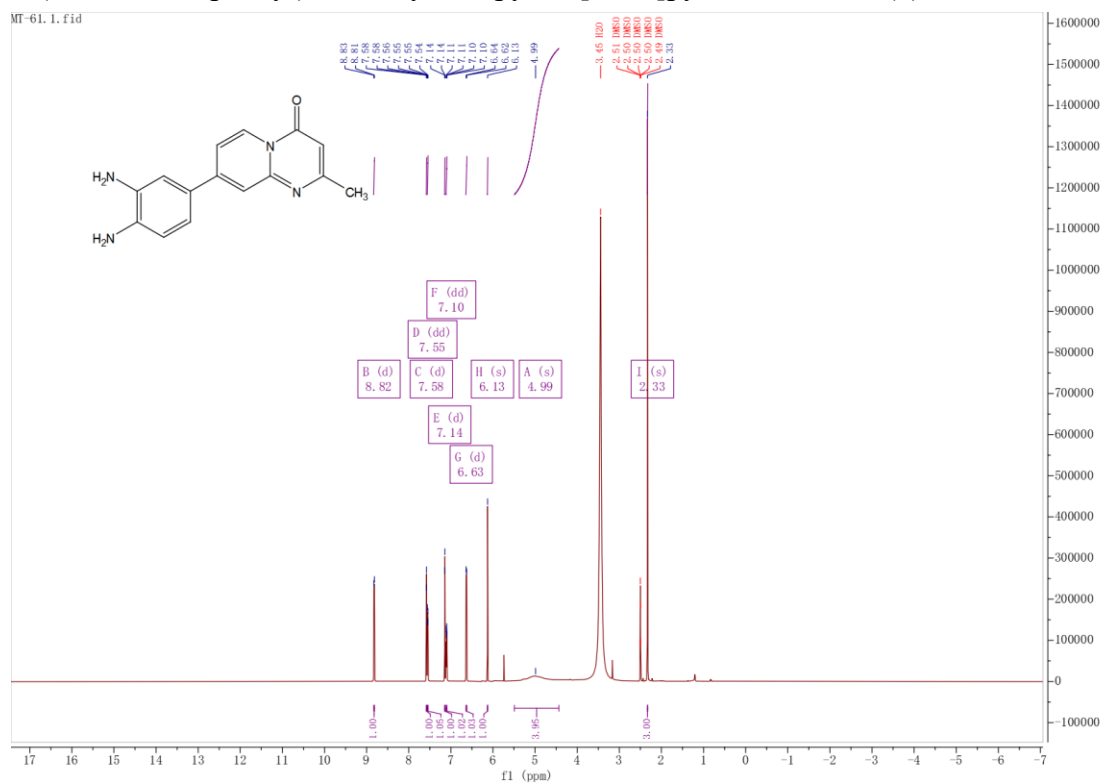


Figure S5. ¹H NMR Spectrum of intermediate **8**

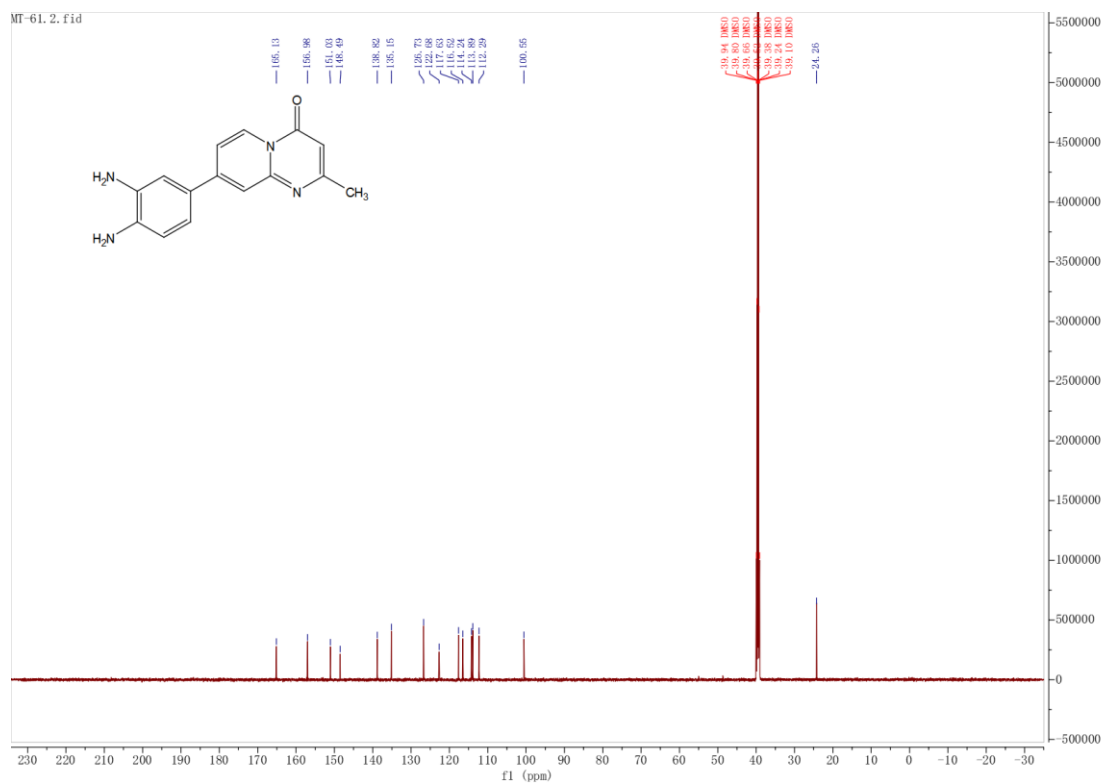


Figure S6. ¹³C NMR Spectrum of intermediate **8**

8-(2-Amino-1*H*-benzo[*d*]imidazol-5-yl)-2-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one
(9)

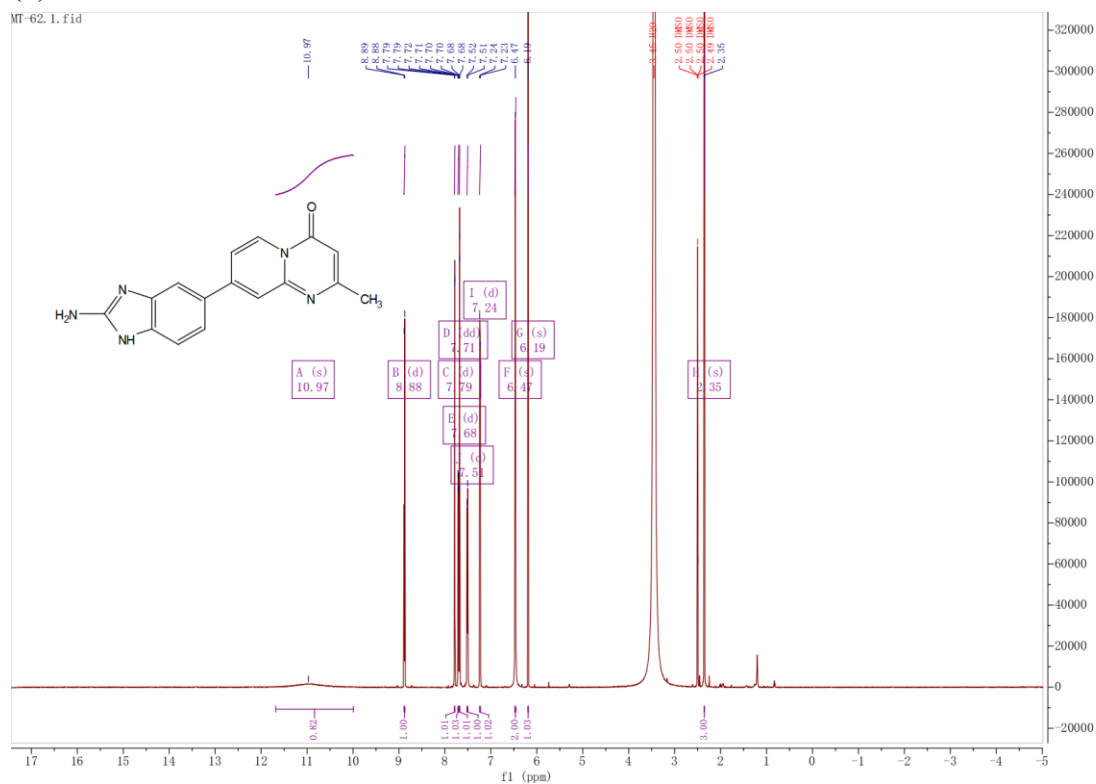


Figure S7. ¹H NMR Spectrum of intermediate 9

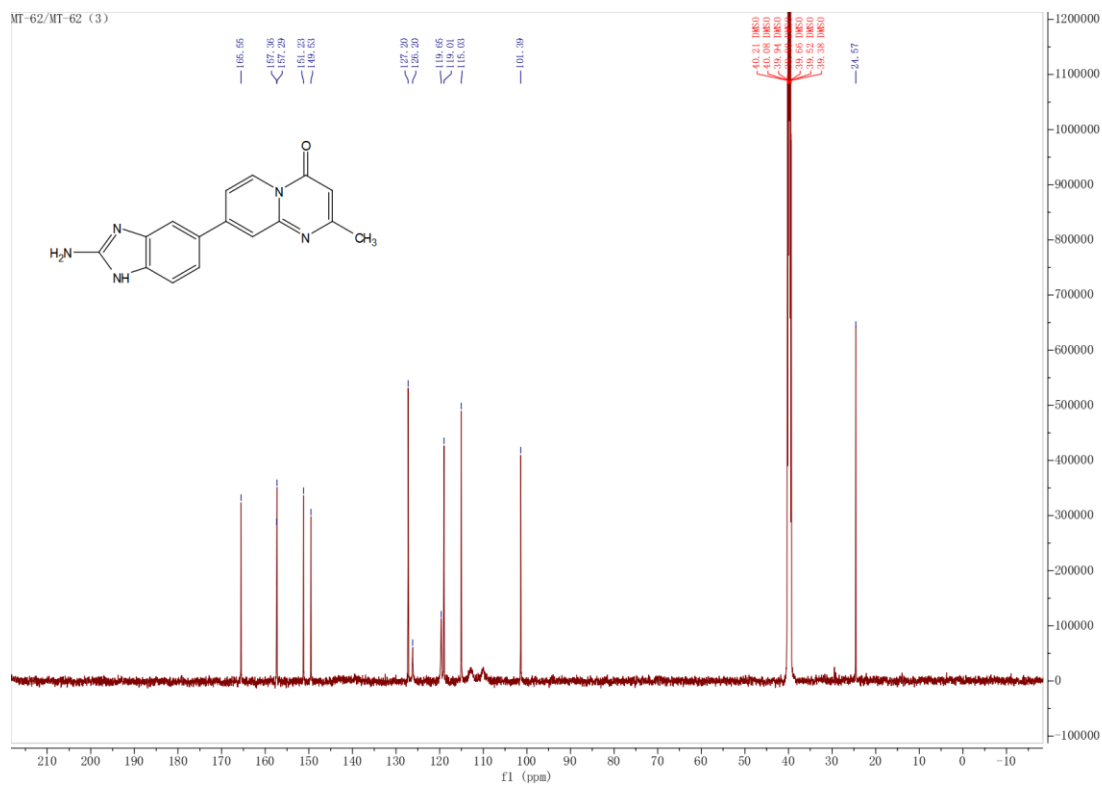


Figure S8. ¹³C NMR Spectrum of intermediate 9

1-(5-(2-Methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl) pyridin-2-yl)-3-(*p*-tolyl) urea
(4a)

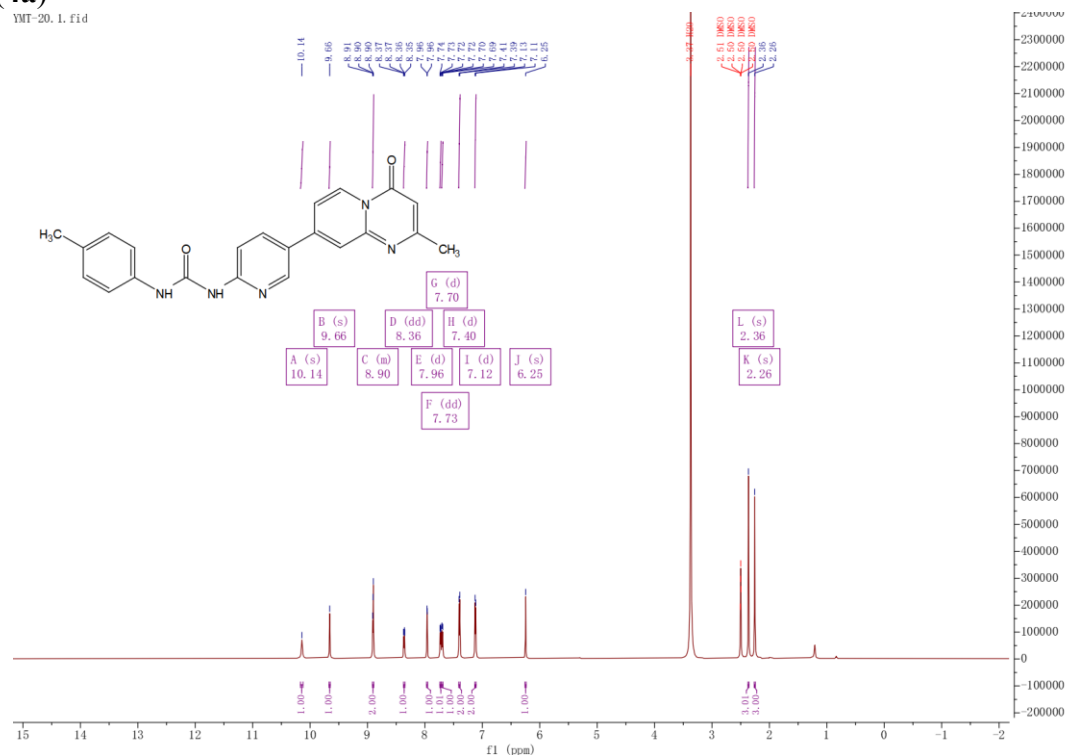


Figure S9. ^1H NMR Spectrum of compound **4a**

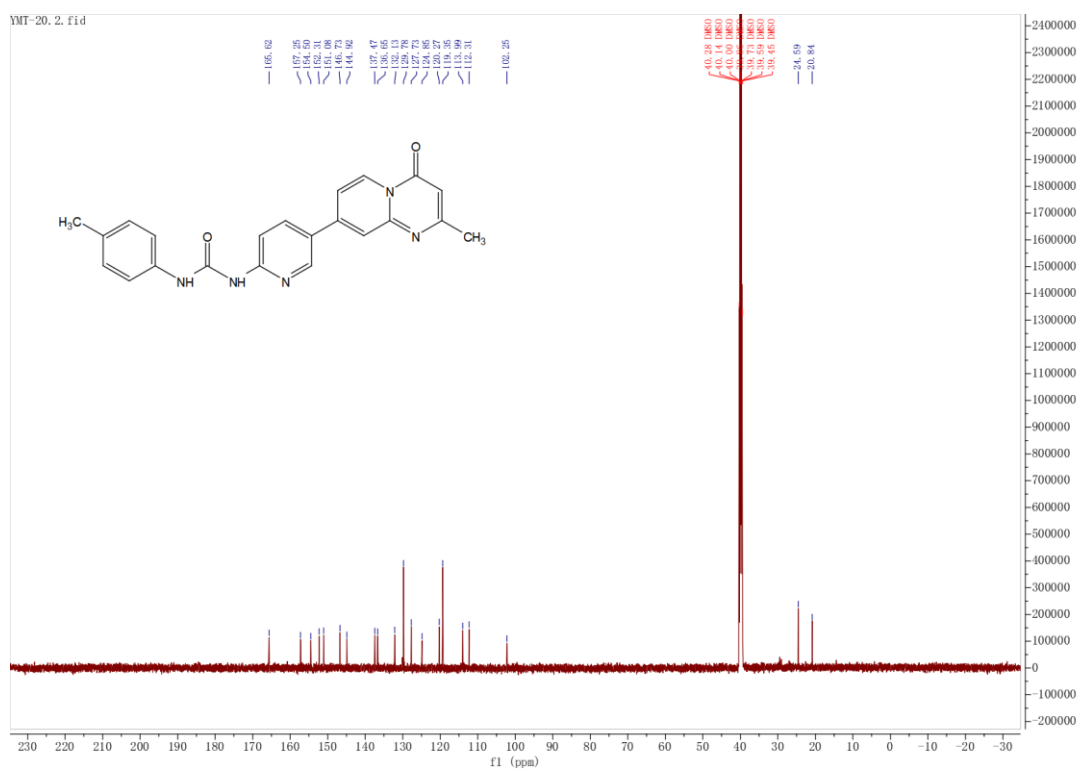


Figure S10. ^{13}C NMR Spectrum of compound **4a**

1-(5-(2-Methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl) pyridin-2-yl)-3-(*o*-tolyl) urea
(4b)

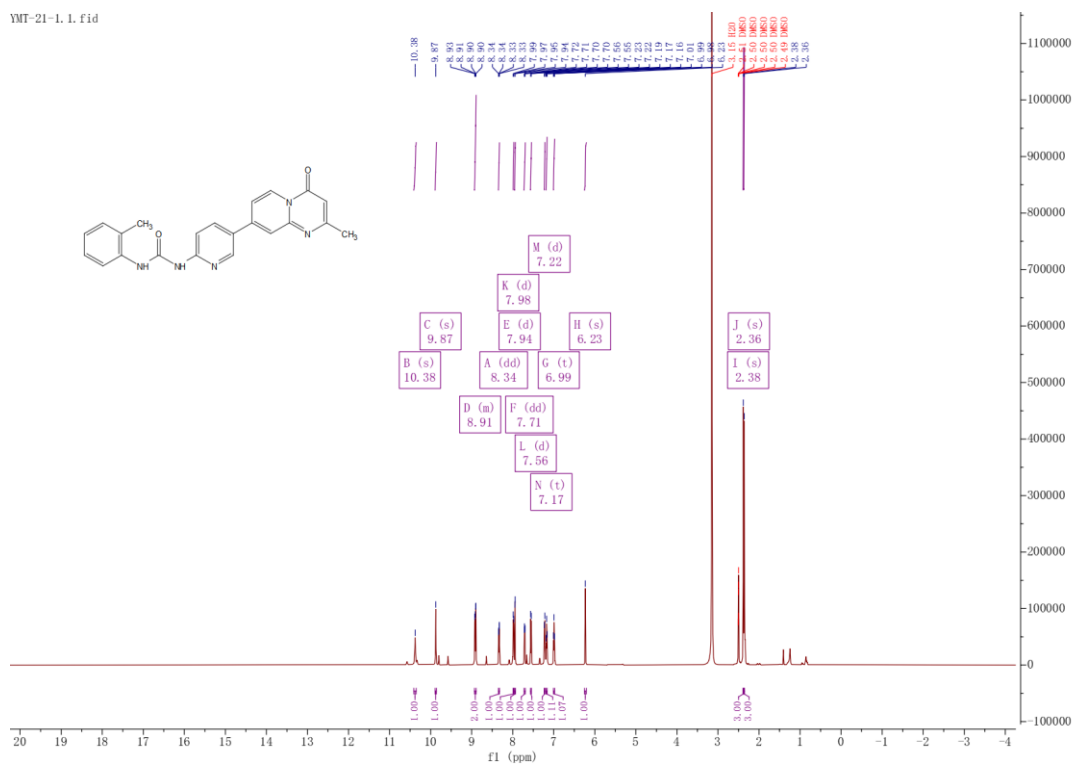


Figure S11. ¹H NMR Spectrum of compound 4b

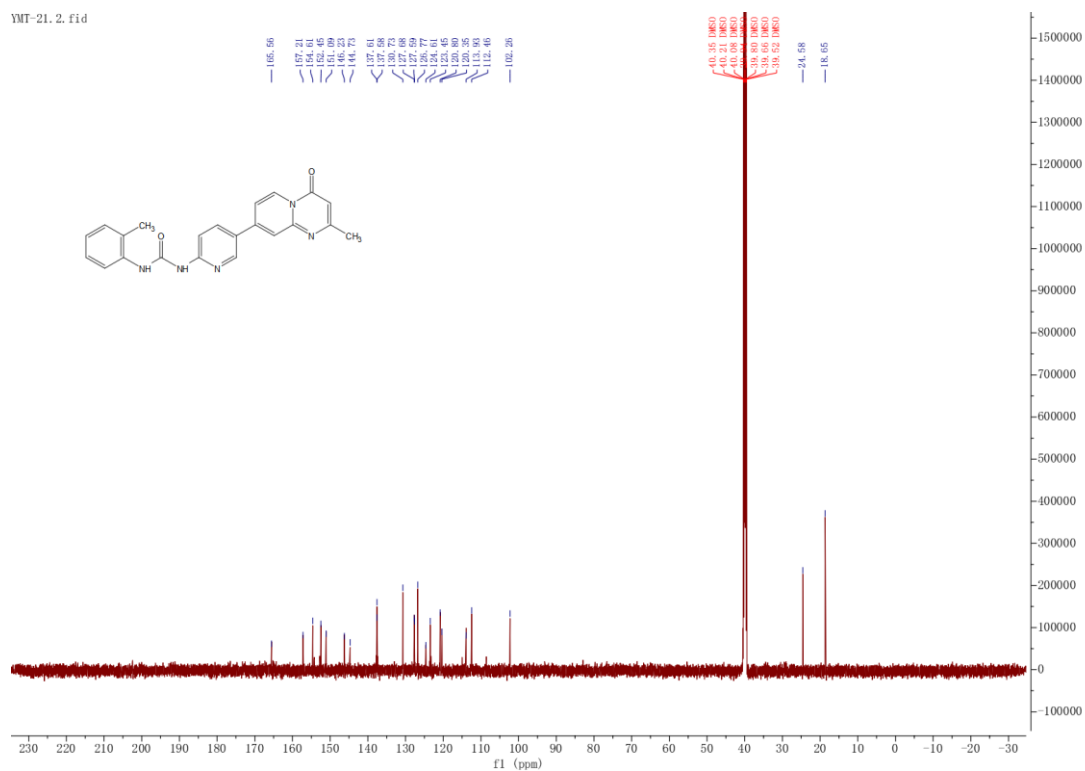


Figure S12. ¹³C NMR Spectrum of compound 4b

1-(5-(2-Methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl) pyridin-2-yl)-3-(*p*-tolyl) urea
(4c)

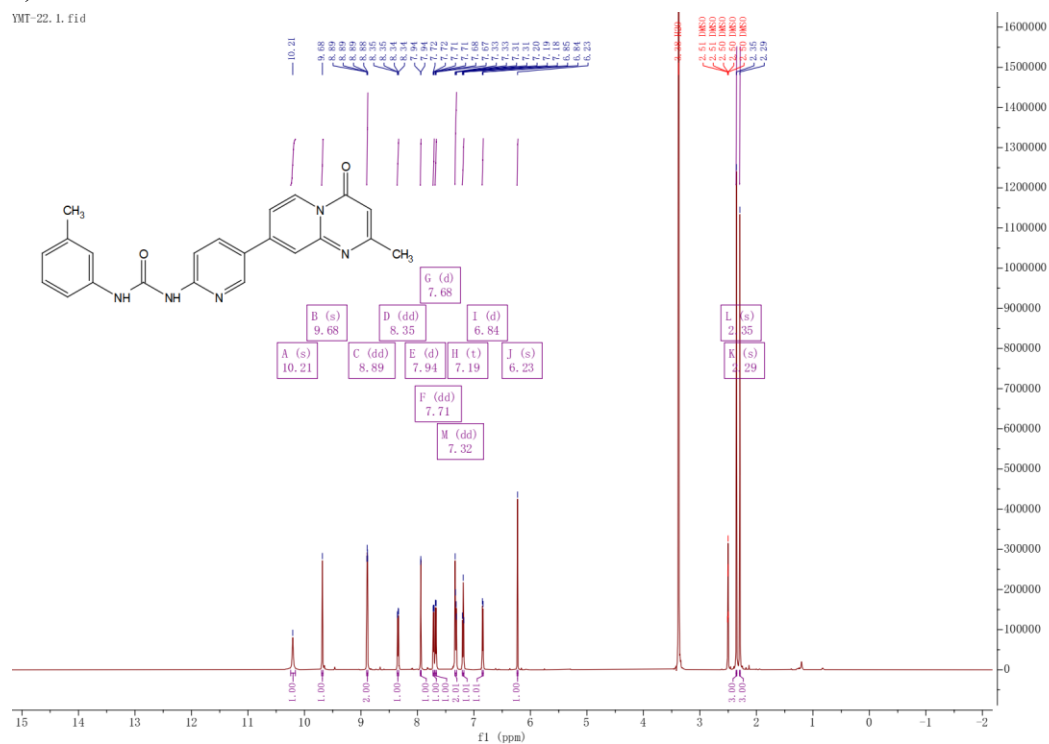


Figure S13. ¹H NMR Spectrum of compound 4c

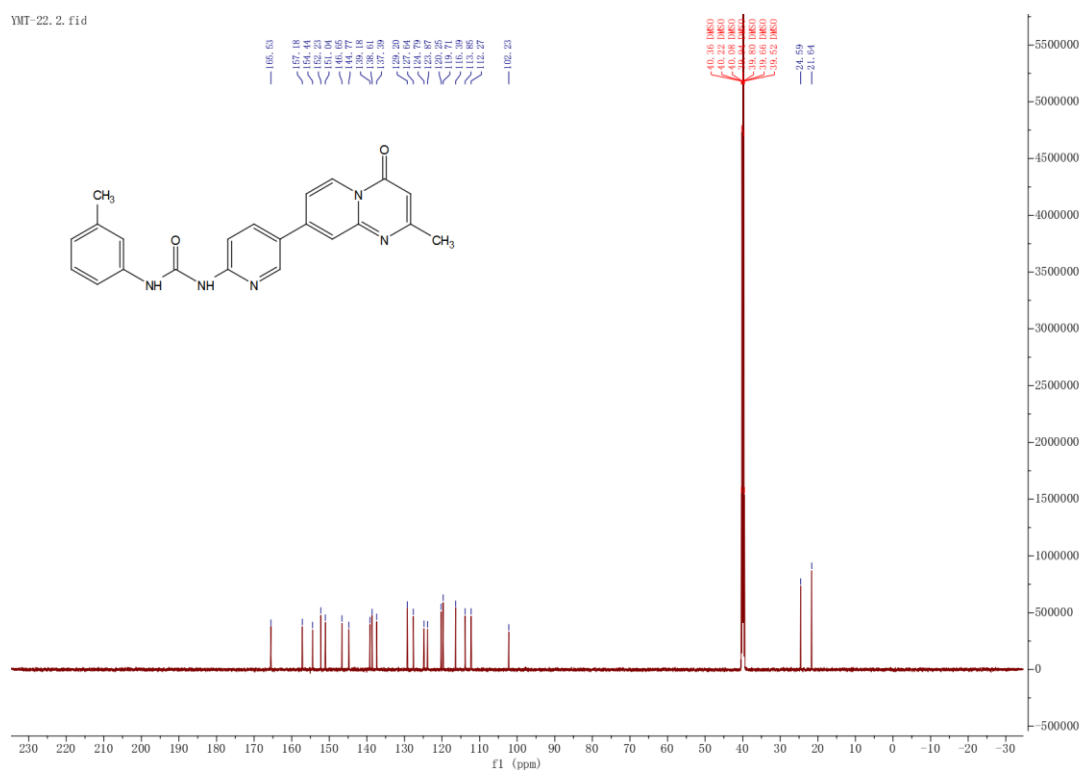


Figure S14. ¹³C NMR Spectrum of compound 4c

1-(3-Methoxyphenyl)-3-(5-(2-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-8-yl)pyridin-2-yl) urea (**4d**)

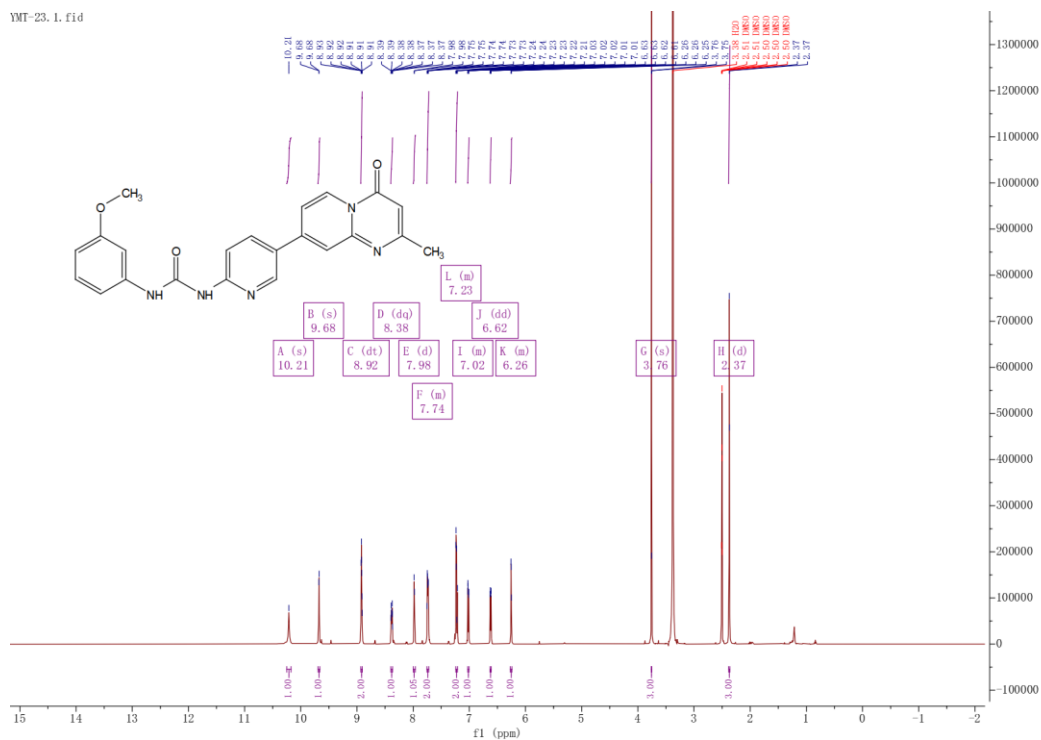


Figure S15. ¹H NMR Spectrum of compound **4d**

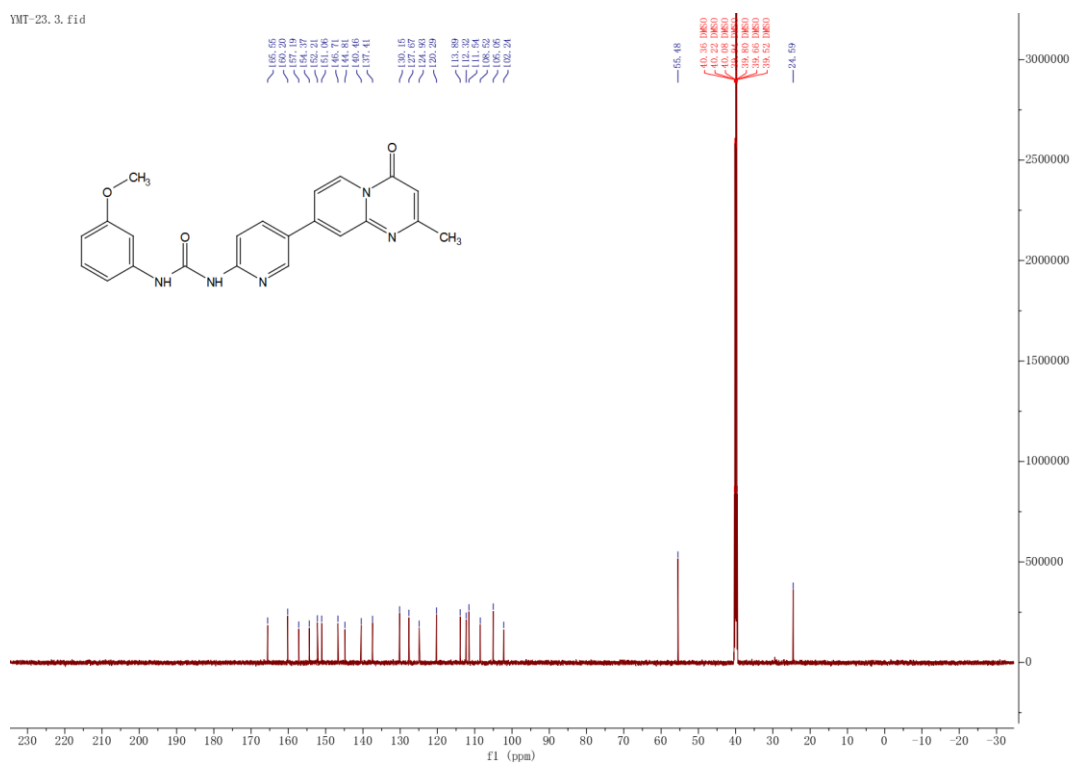


Figure S16. ¹³C NMR Spectrum of compound **4d**

1-(3-Fluorophenyl)-3-(5-(2-methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl) pyridin-2-yl) urea (**4f**)

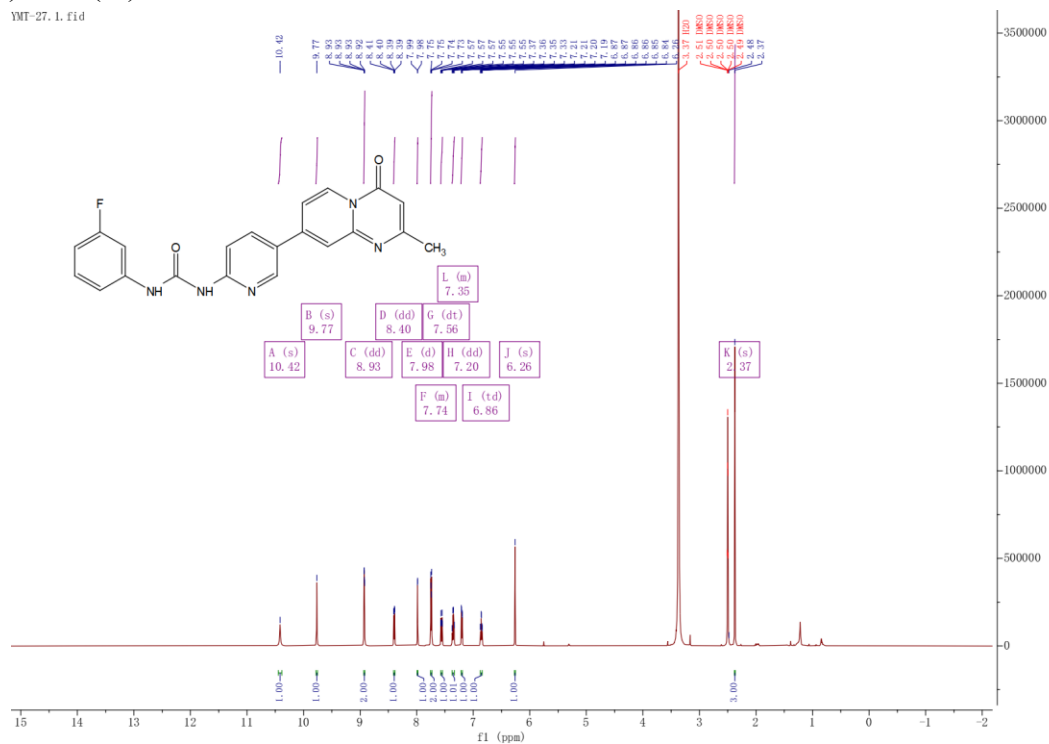


Figure S19. ¹H NMR Spectrum of compound **4f**

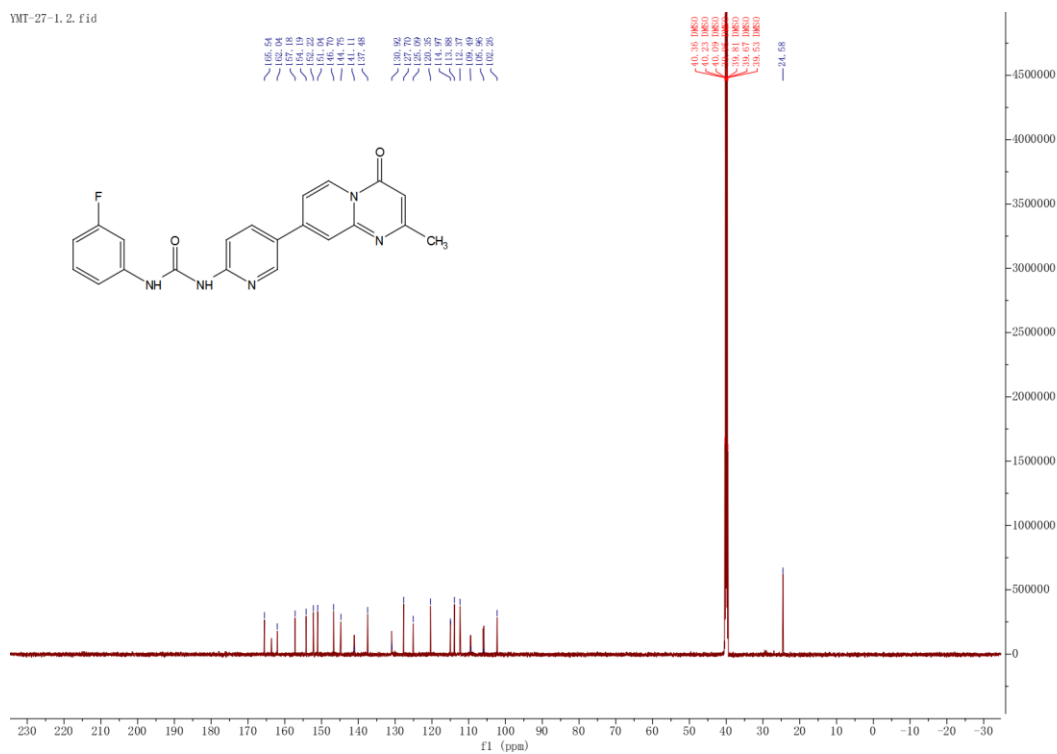
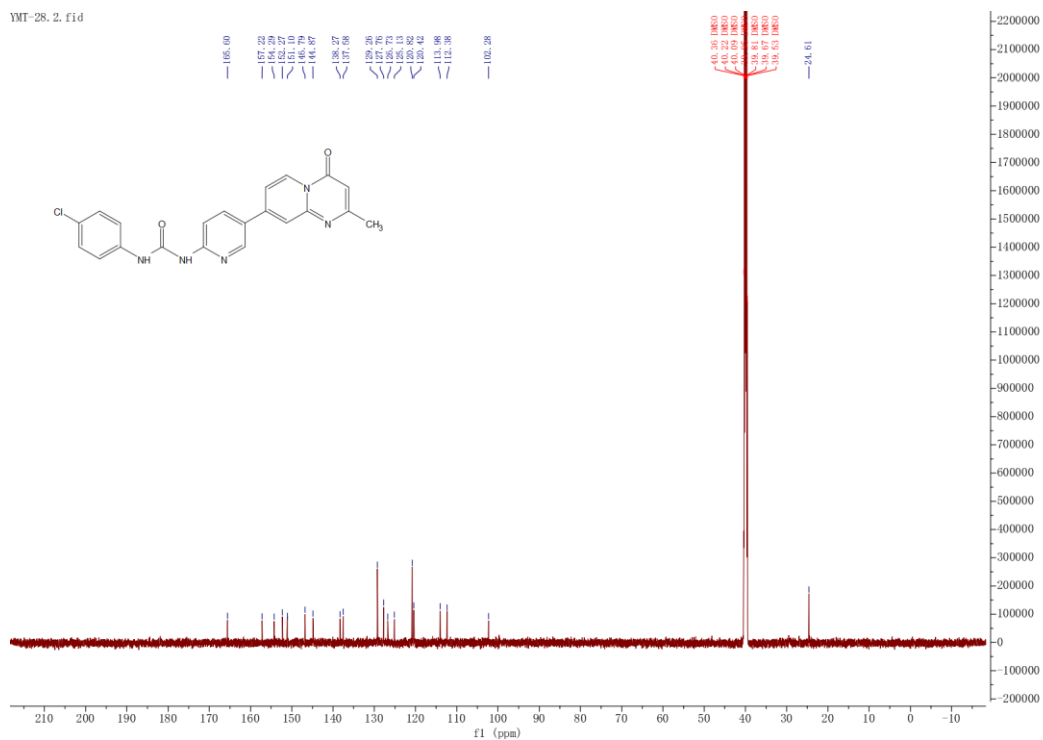
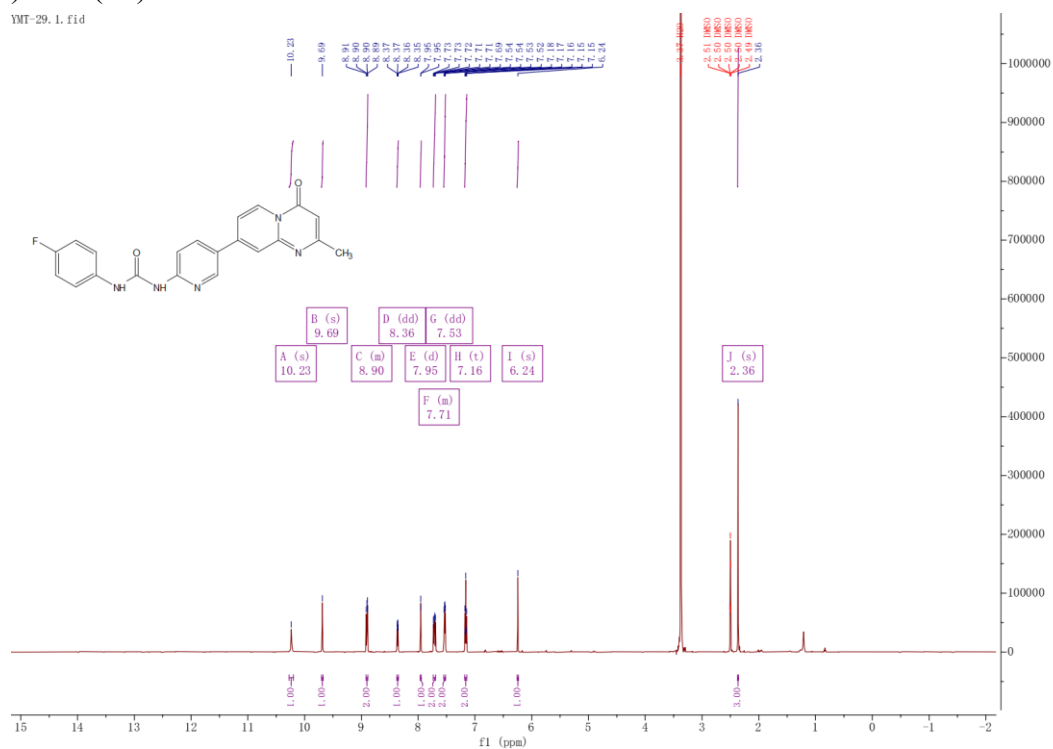


Figure S20. ¹³C NMR Spectrum of compound **4f**



1-(4-Fluorophenyl)-3-(5-(2-methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl) pyridin-2-yl) urea (**4h**)



YMT-29. 2. fid

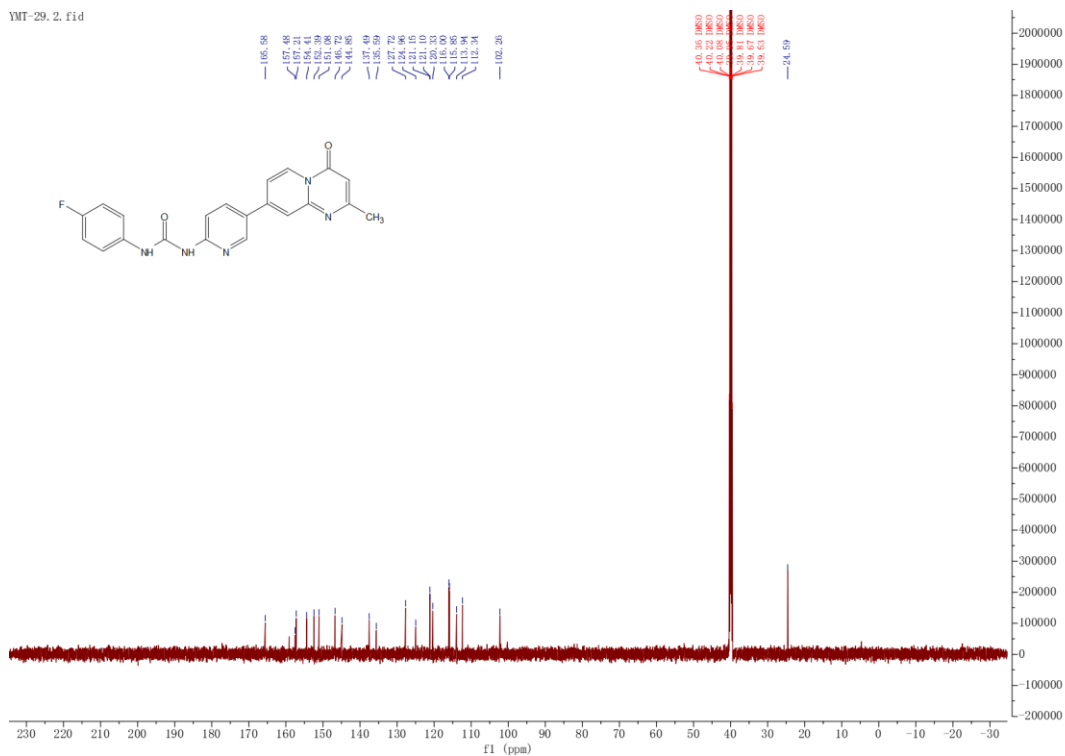


Figure S25. ¹³C NMR Spectrum of compound 4h

YMT-29. 3. fid



Figure S26. ¹⁹F NMR Spectrum of compound 4h

1-(5-(2-Methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl) pyridin-2-yl)-3-(4-(trifluoromethyl) phenyl) urea (**4i**)



Figure S27. ¹H NMR Spectrum of compound **4i**

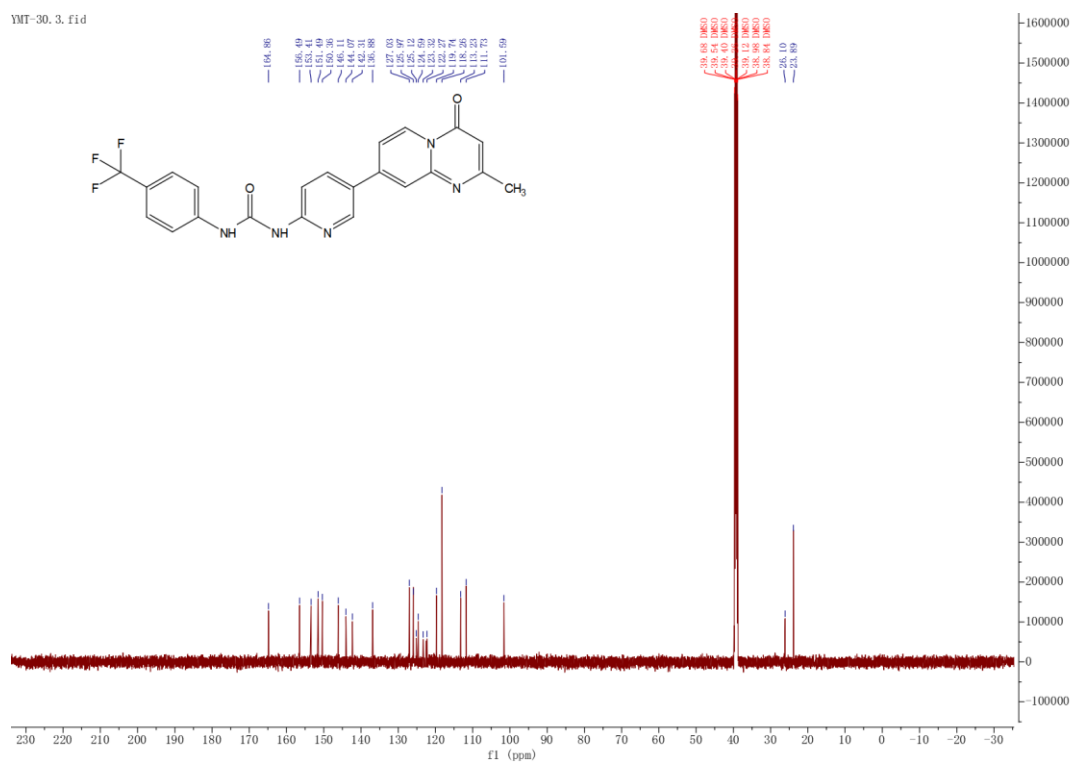
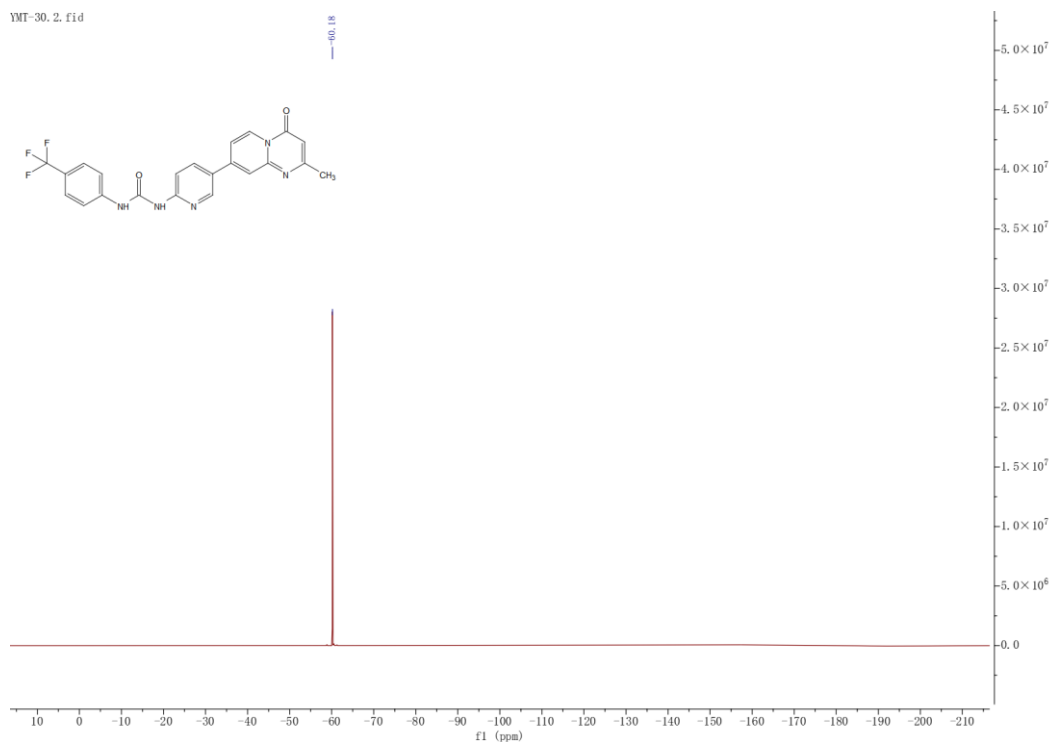
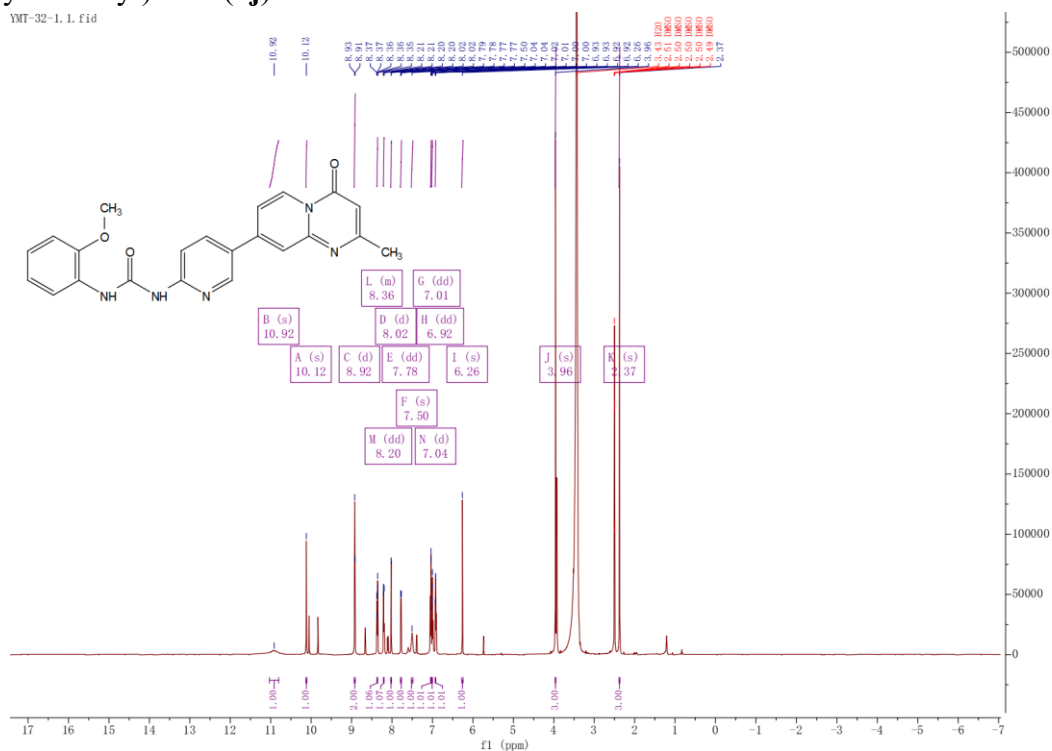
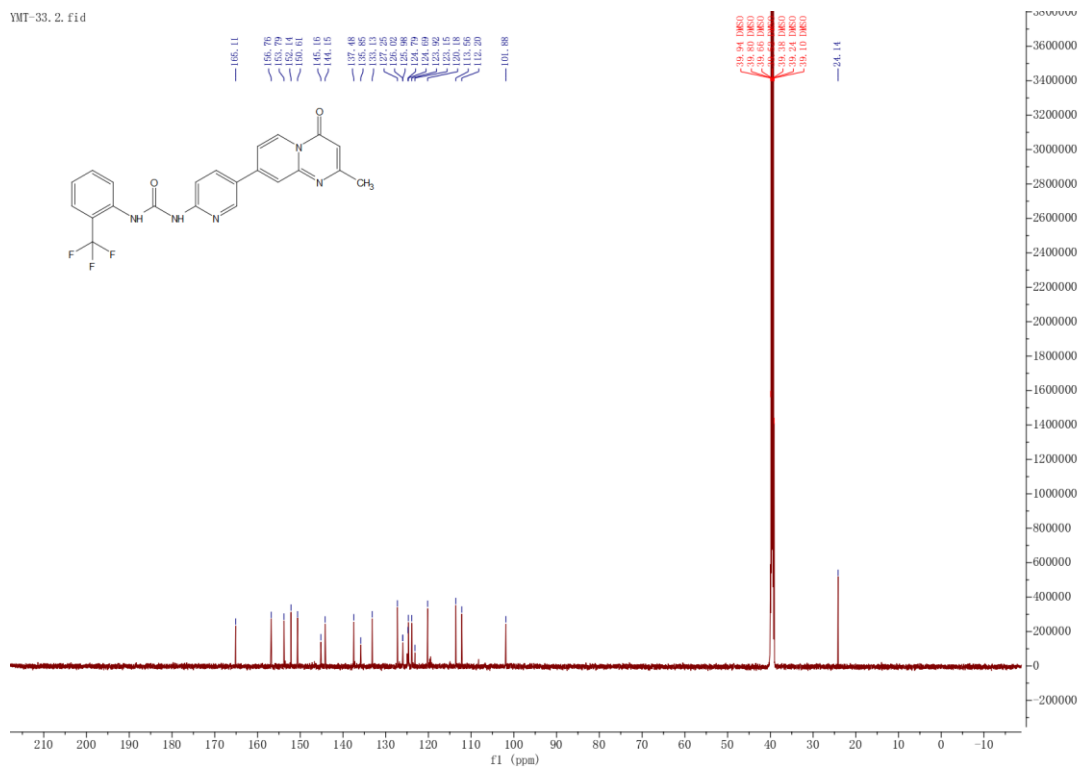


Figure S28. ¹³C NMR Spectrum of compound **4i**



1-(2-Methoxyphenyl)-3-(5-(2-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-8-yl)pyridin-2-yl) urea (4j)





1-(2-Fluorophenyl)-3-(5-(2-methyl-4-oxo-4H-pyrido[1,2-a] pyrimidin-8-yl) pyridin-2-yl) urea (**4I**)

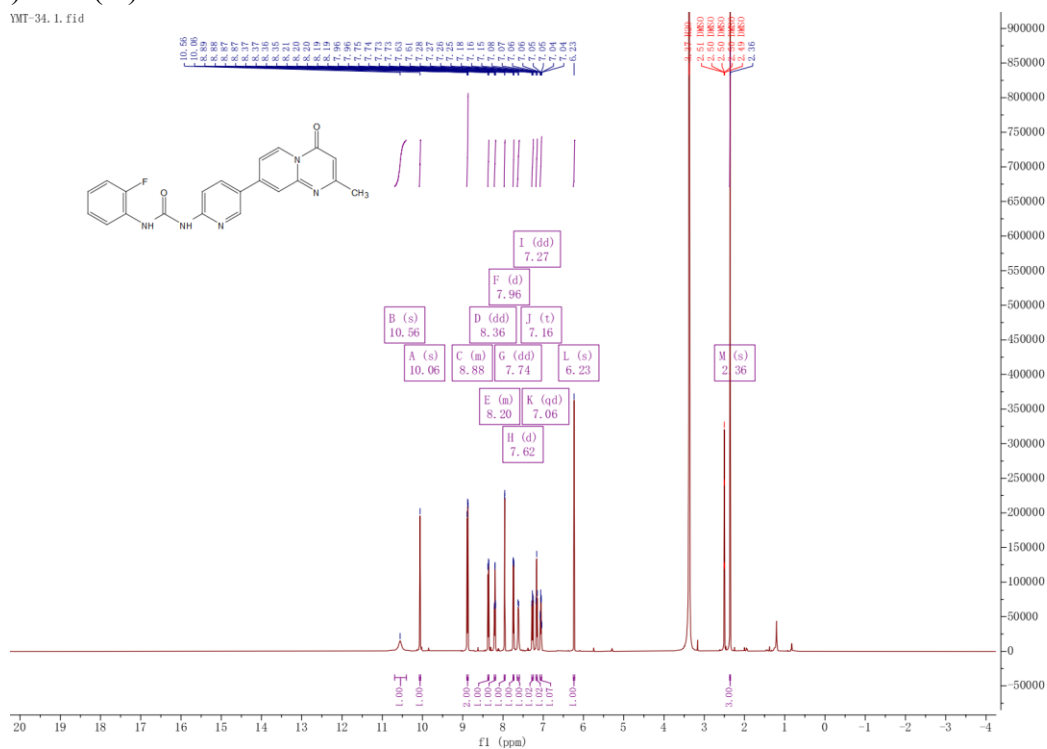


Figure S35. ¹H NMR Spectrum of compound **4I**

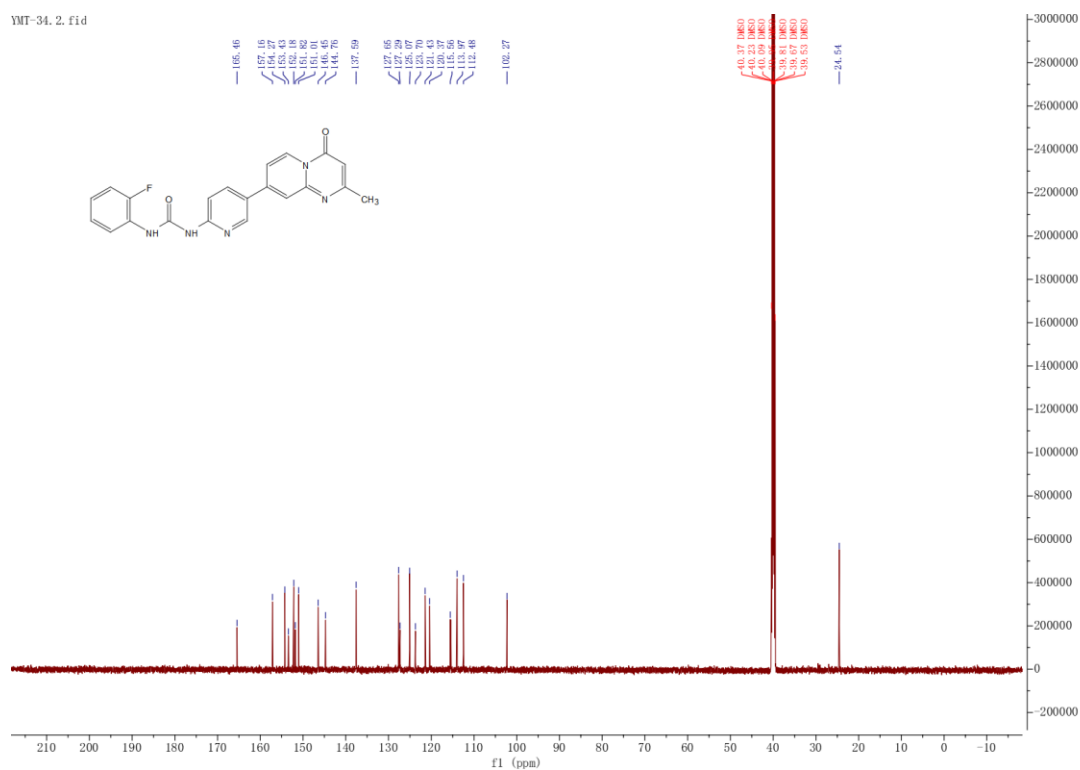
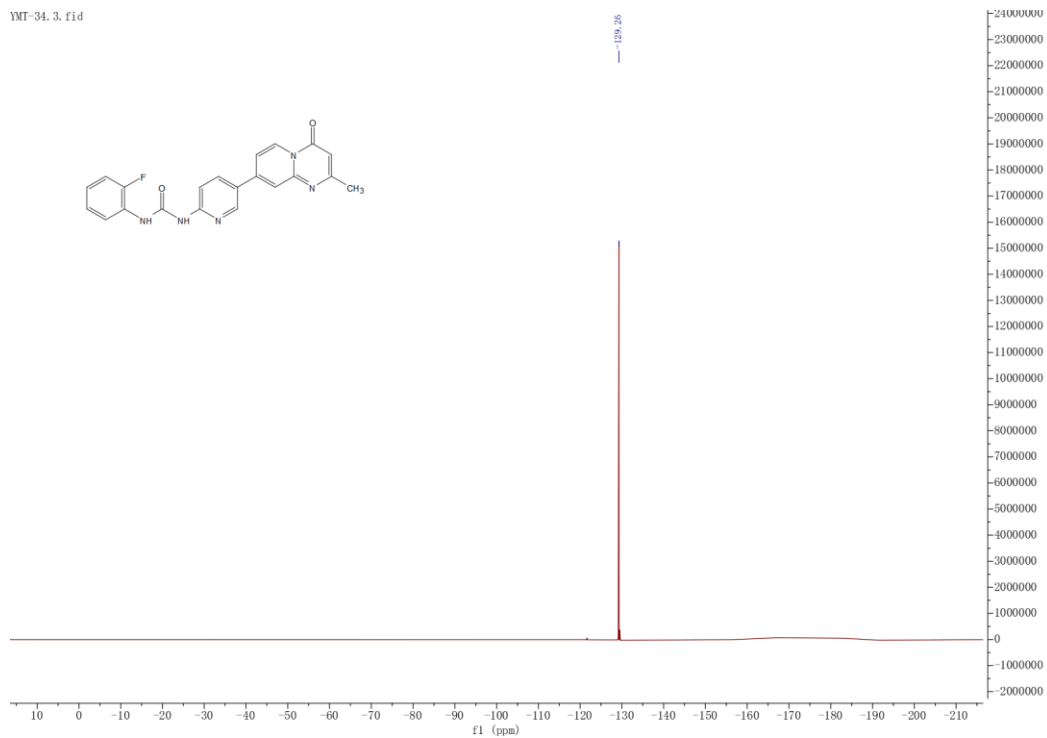


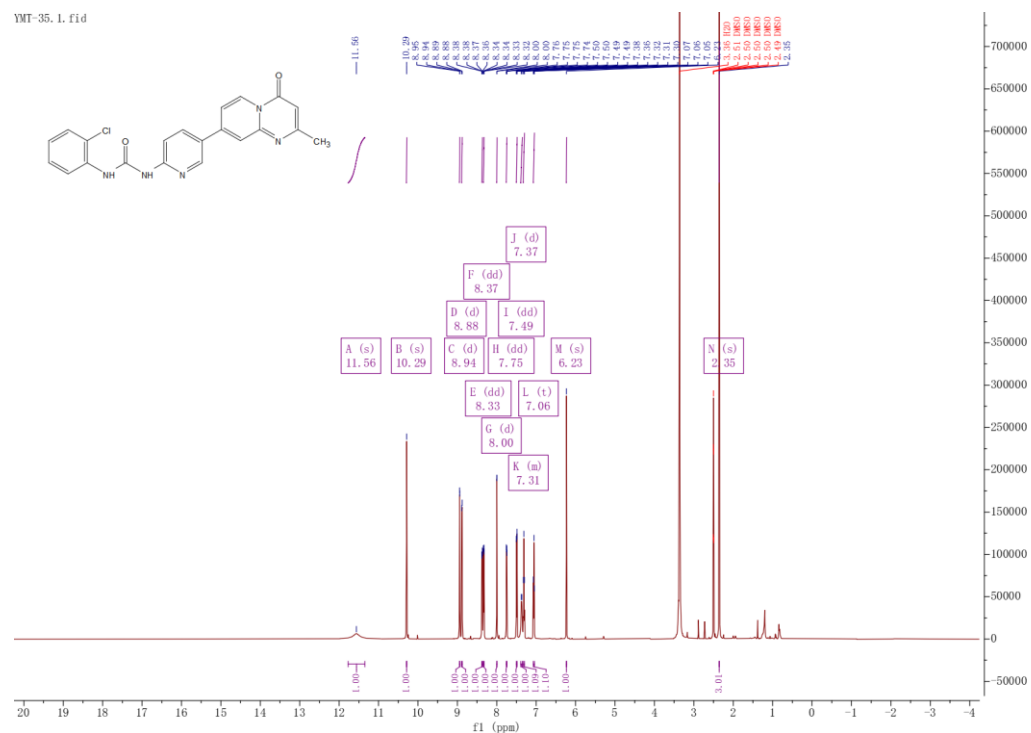
Figure S36. ¹³C NMR Spectrum of compound **4I**

YMT-34. 3. fid



1-(2-Chlorophenyl)-3-(5-(2-methyl-4-oxo-4H-pyrido[1,2-a] pyrimidin-8-yl) pyridin-2-yl) urea (**4m**)

YMT-35. 1. fid



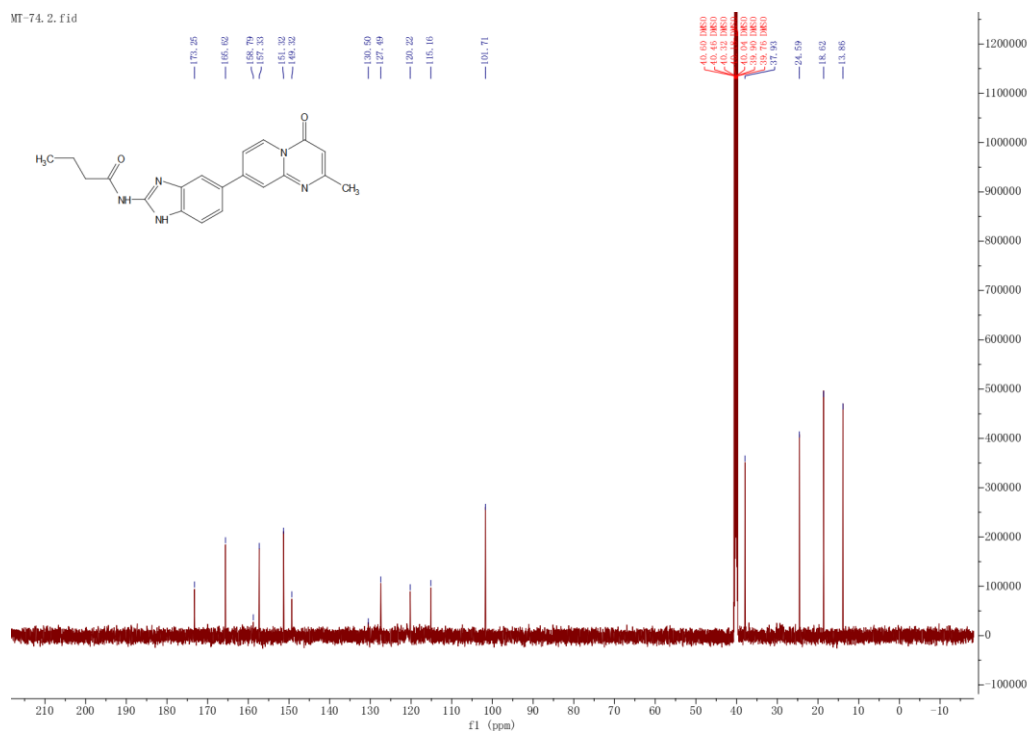


Figure S43. ^{13}C NMR Spectrum of compound 10a

O-(5-(2-Methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl)-1*H*-benzo[*d*]imidazol-2-yl) pivalamide (10b)

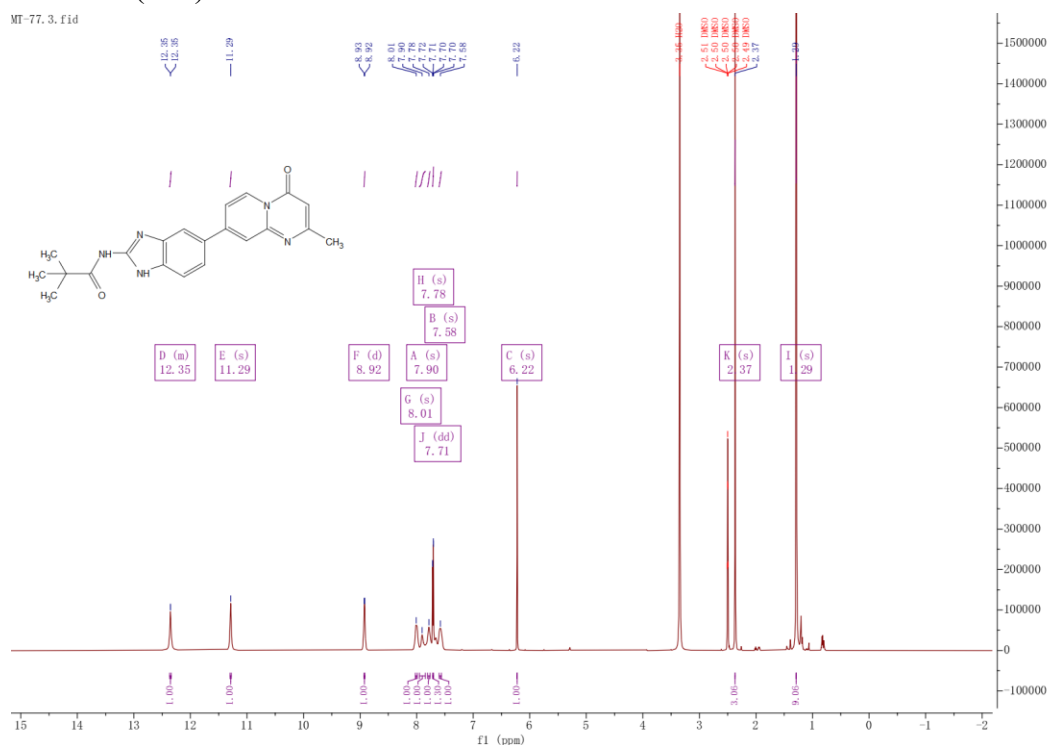


Figure S44. ^1H NMR Spectrum of compound 10b

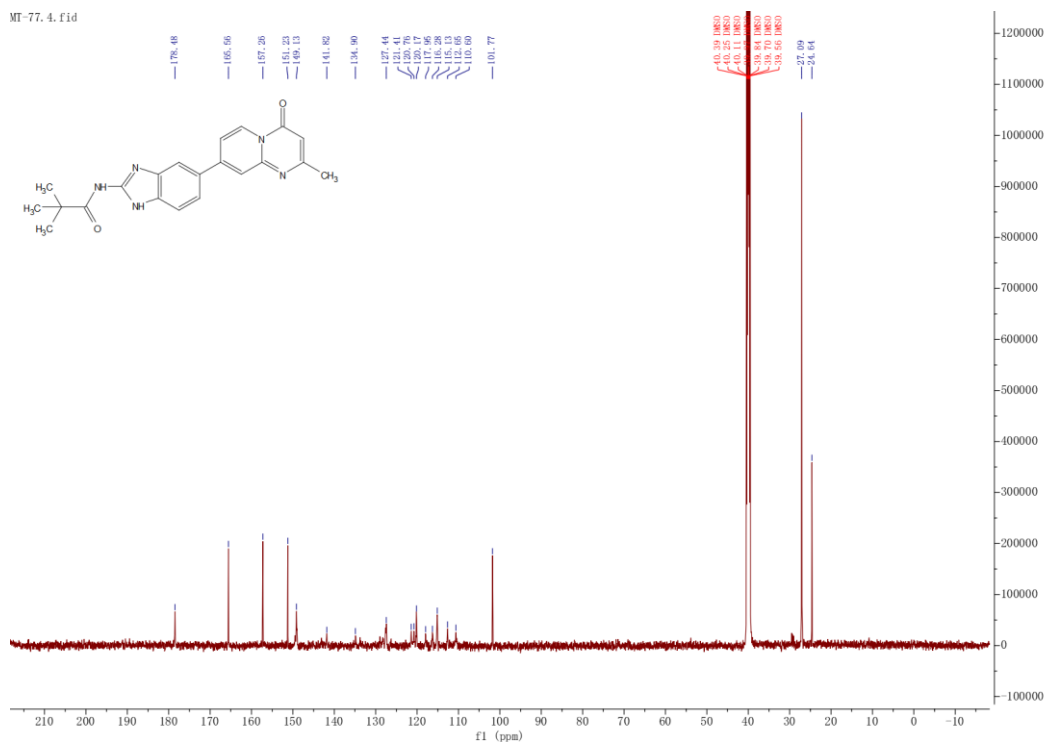


Figure S45. ¹³C NMR Spectrum of compound **10b**

4-(*Tert*-Butyl)-*N*-(5-(2-methyl-4-oxo-4*H*-pyrido[1,2-*a*] pyrimidin-8-yl)-1*H*-benzo[*d*]imidazol-2-yl) benzamide (**10c**)

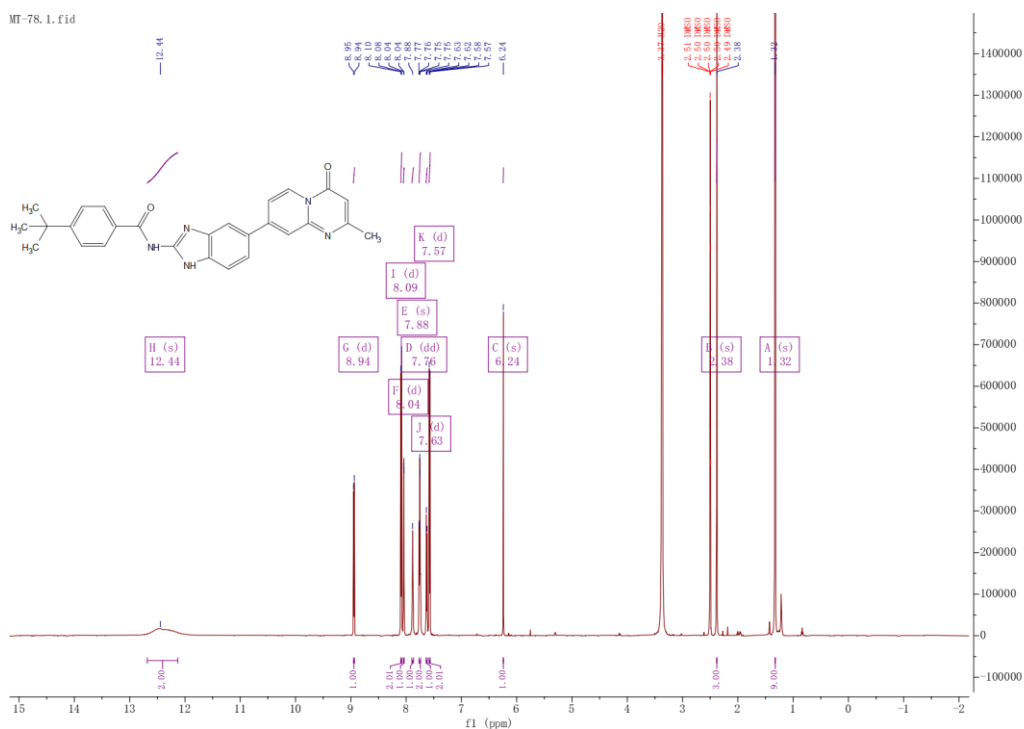


Figure S46. ¹H NMR Spectrum of compound **10c**

MT-78 (碳谱). 2.fid

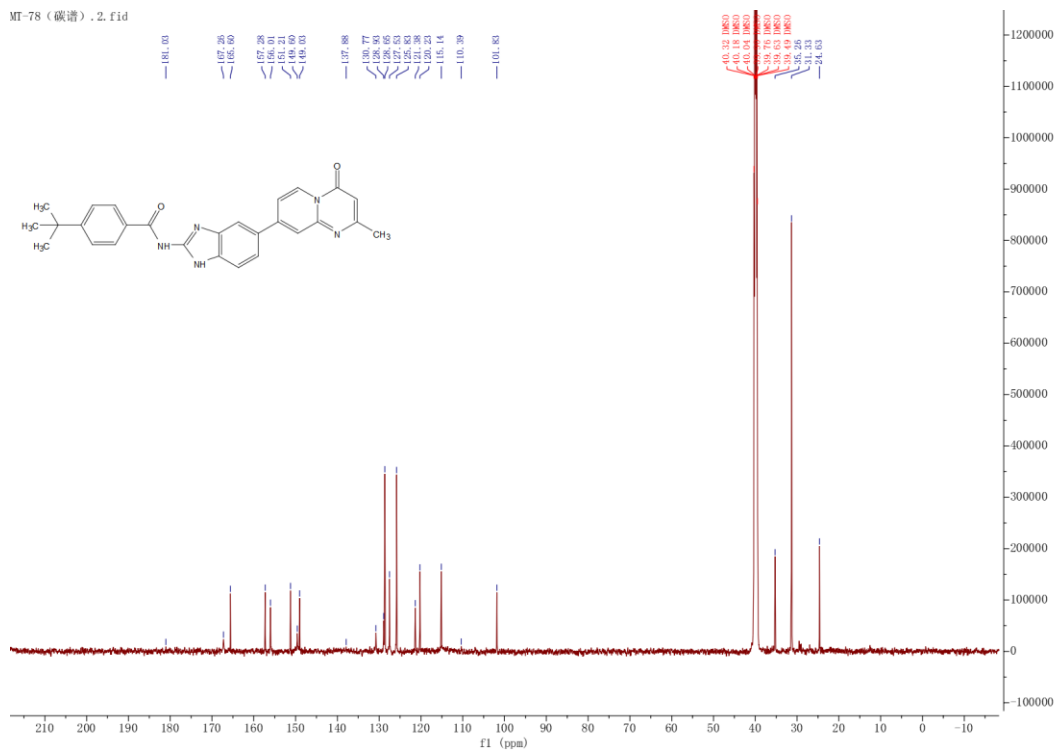


Figure S47. ^{13}C NMR Spectrum of compound 10c

HRMS spectra of intermediates and target compounds

OL #29 RT: 0.13 AV: 1 NL: 7.71E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

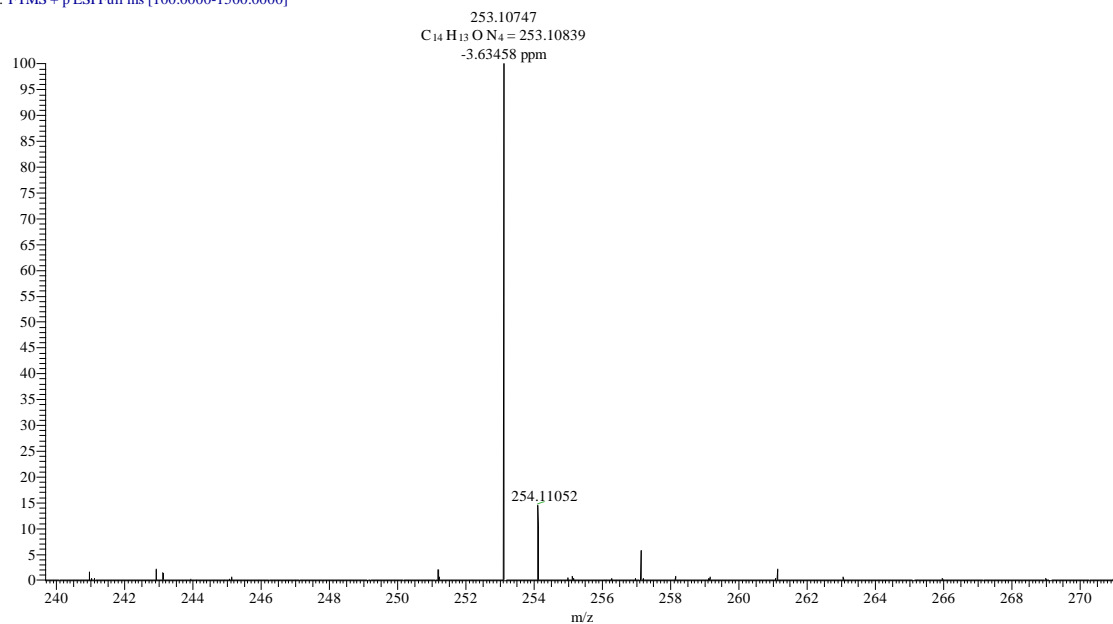


Figure S48. HRMS Spectrum of intermediate 3

MF-58 #29 RT: 0.13 AV: 1 NL: 2.24E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]

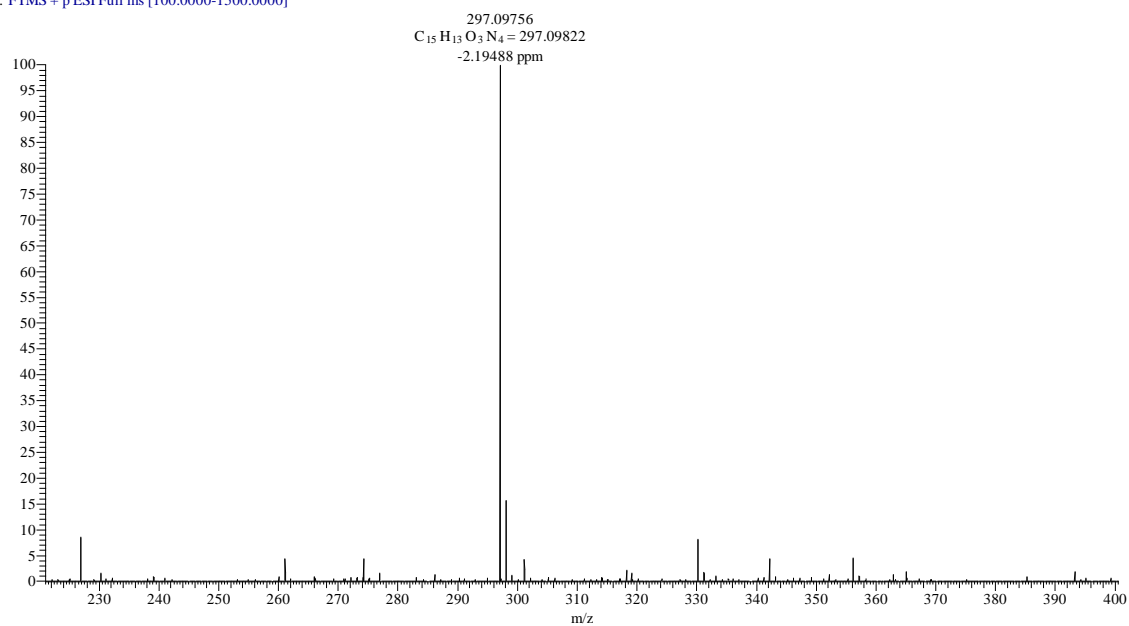


Figure S49. HRMS Spectrum of intermediate 7

MT-61_230613160207 #30 RT: 0.13 AV: 1 NL: 7.73E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

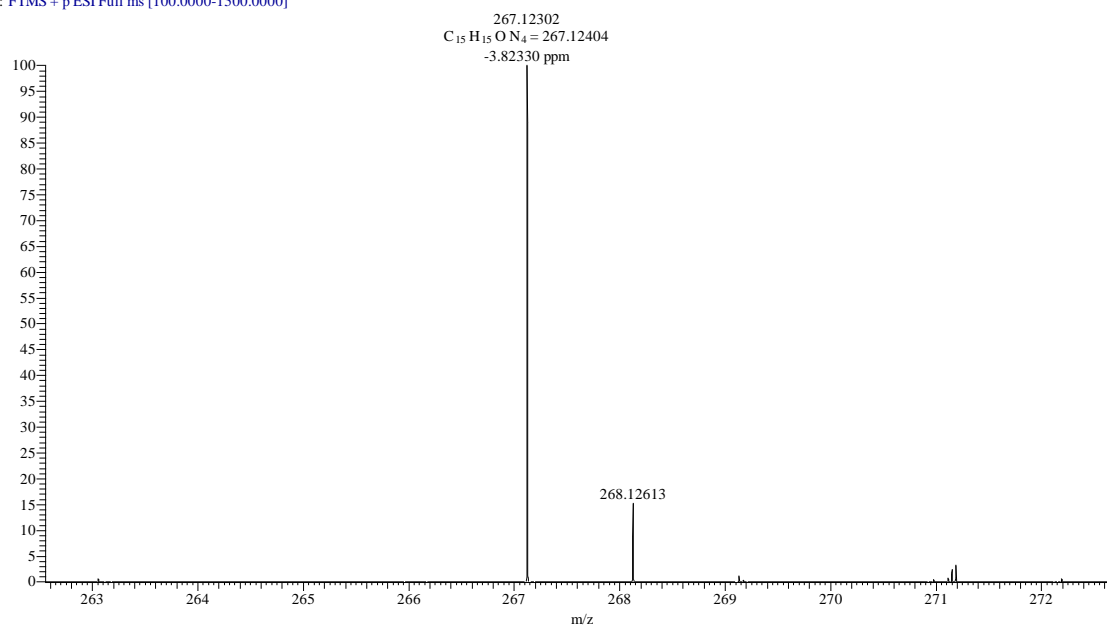


Figure S50. HRMS Spectrum of intermediate **8**

MT-62 #26 RT: 0.11 AV: 1 NL: 9.99E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

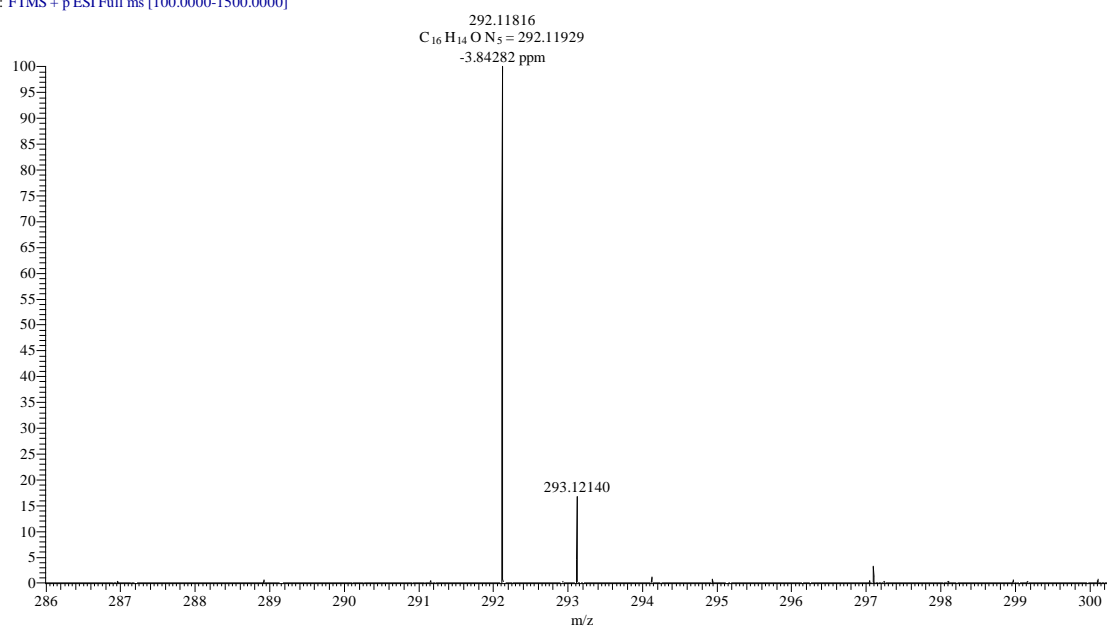


Figure S51. HRMS Spectrum of intermediate **9**

YMT-20 #25 RT: 0.12 AV: 1 NL: 5.96E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

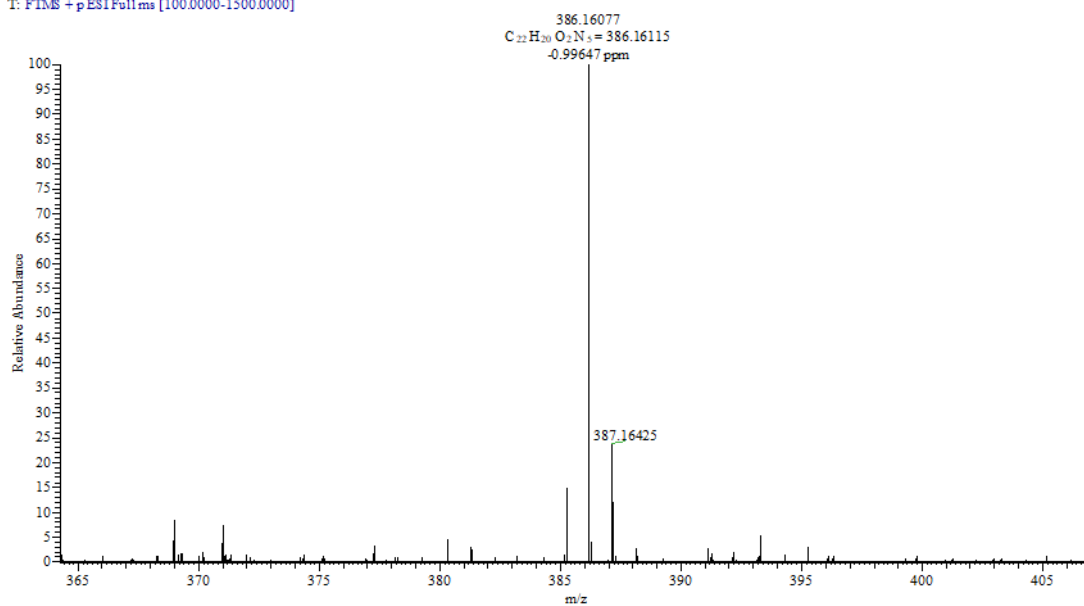


Figure S52. HRMS Spectrum of compound **4a**

YMT-21 #23 RT: 0.10 AV: 1 NL: 1.26E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

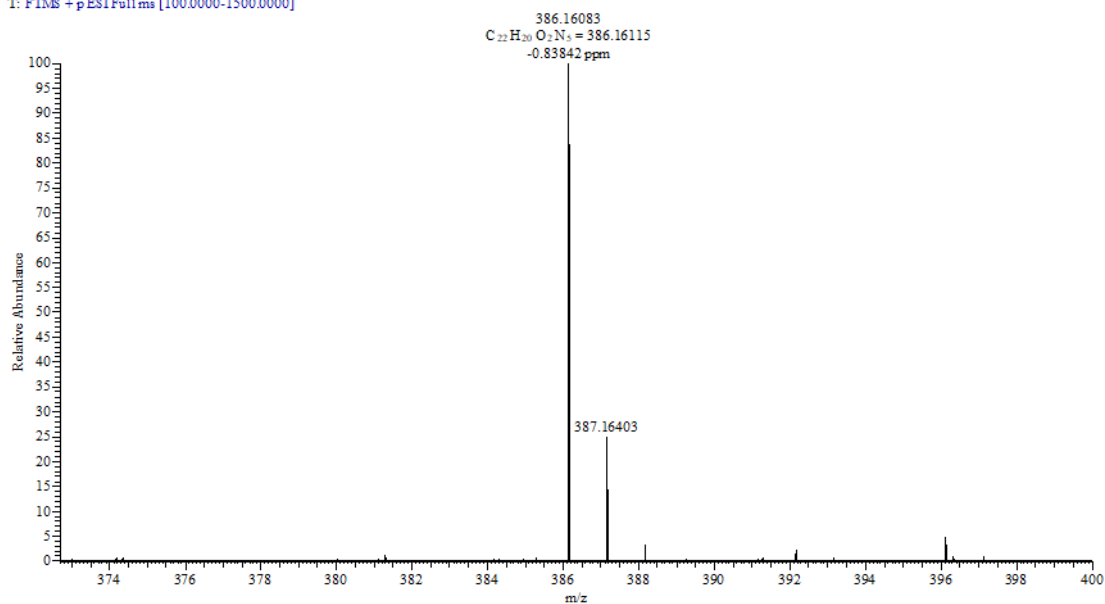


Figure S53. HRMS Spectrum of compound **4b**

YMT-22 #22 RT: 0.10 AV: 1 NL: 1.64E7
T: FTMS + p ESI Fullms [100.0000-1500.0000]

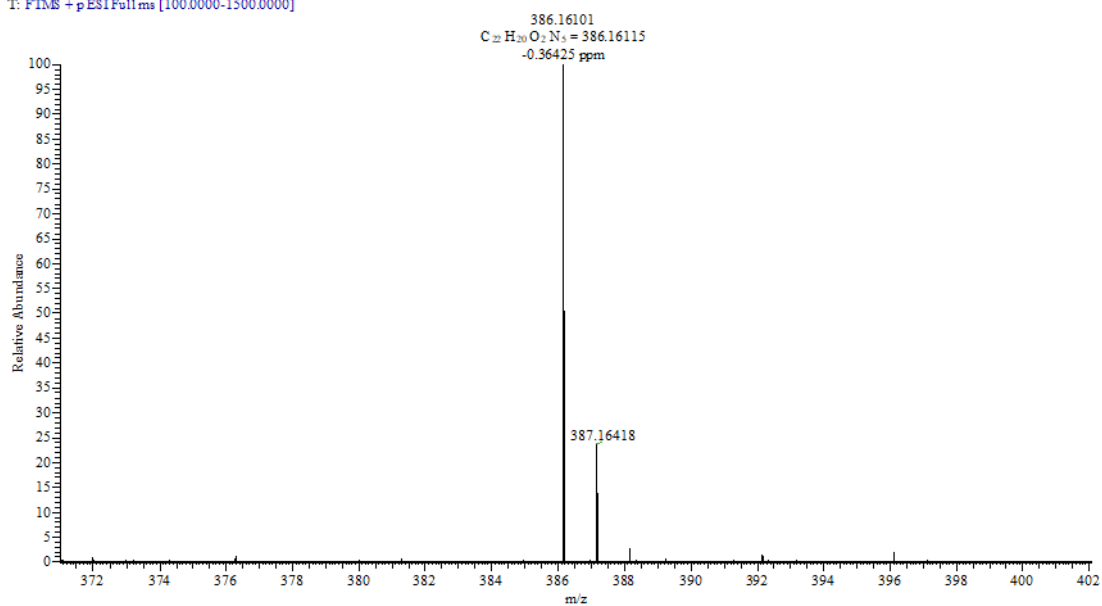


Figure S54. HRMS Spectrum of compound **4c**

YMT-23 #24 RT: 0.11 AV: 1 NL: 1.08E7
T: FTMS + p ESI Fullms [100.0000-1500.0000]

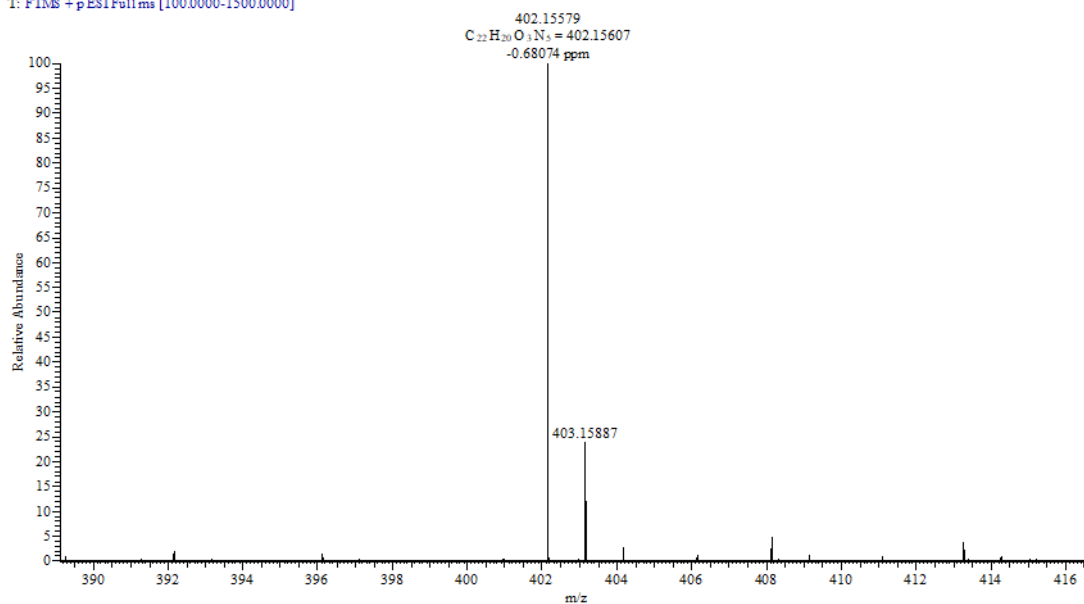


Figure S55. HRMS Spectrum of compound **4d**

YMT-24 #23 RT: 0.10 AV: 1 NL: 1.25E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

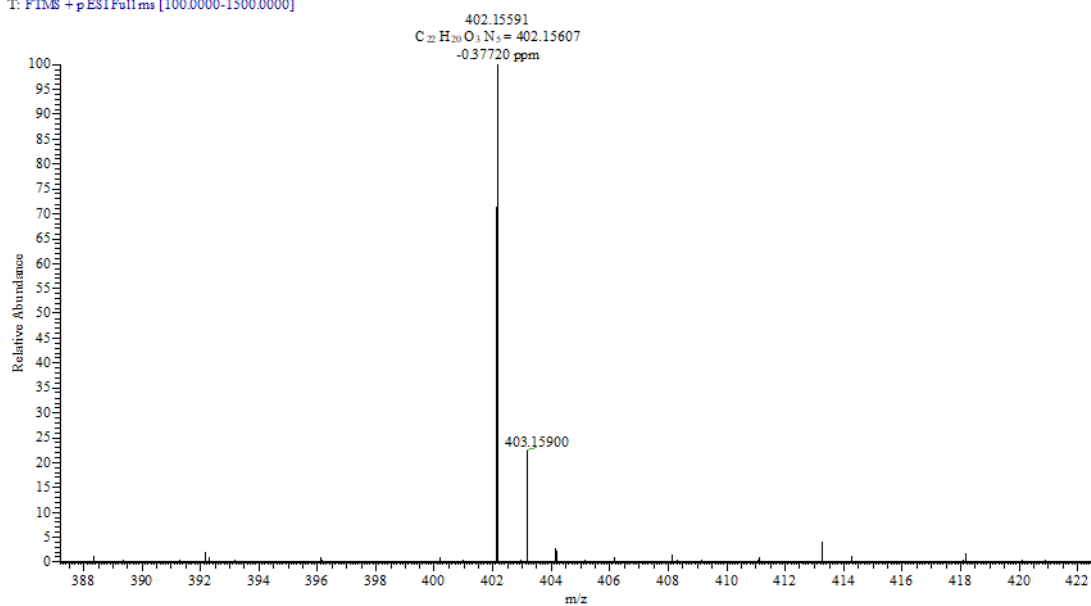


Figure S56. HRMS Spectrum of compound 4e

YMT-27 #24 RT: 0.11 AV: 1 NL: 2.81E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

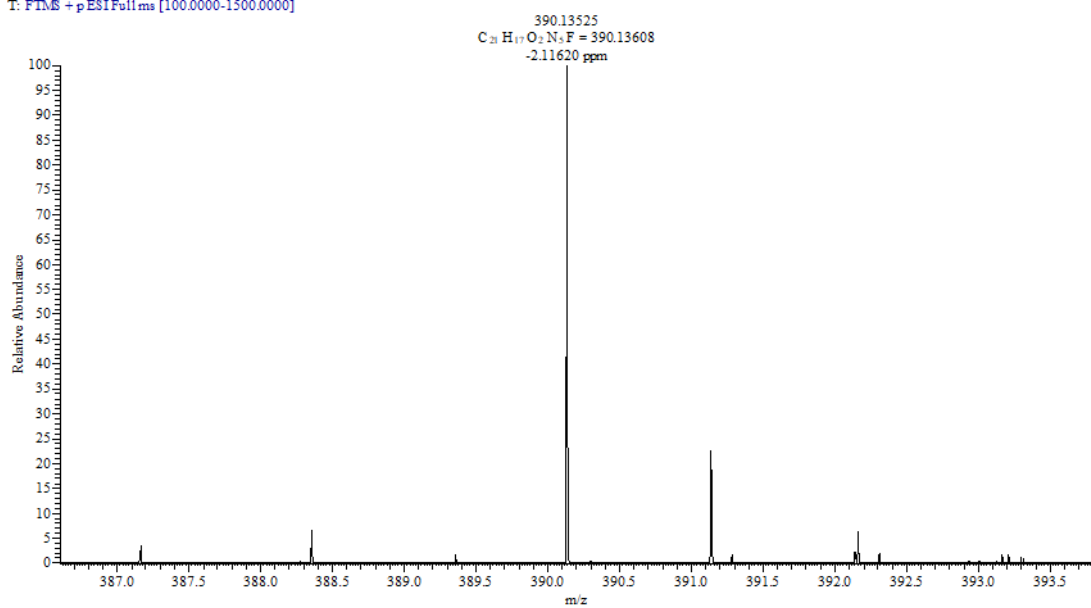


Figure S57. HRMS Spectrum of compound 4f

YMT-28 #22 RT: 0.10 AV: 1 NL: 1.09E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

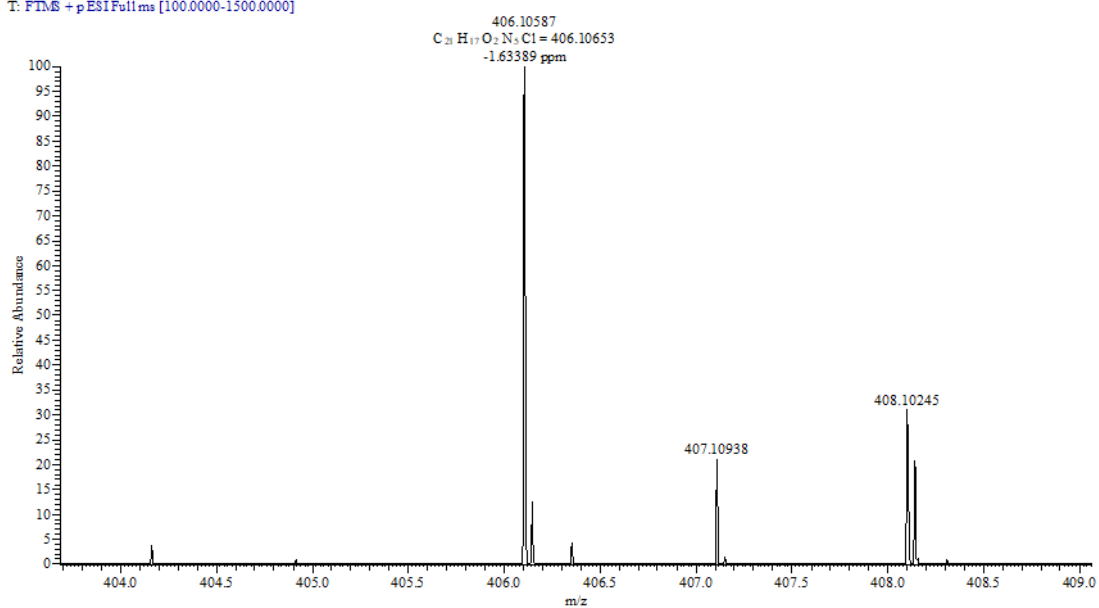


Figure S58. HRMS Spectrum of compound **4g**

YMT-29 #21 RT: 0.09 AV: 1 NL: 6.37E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

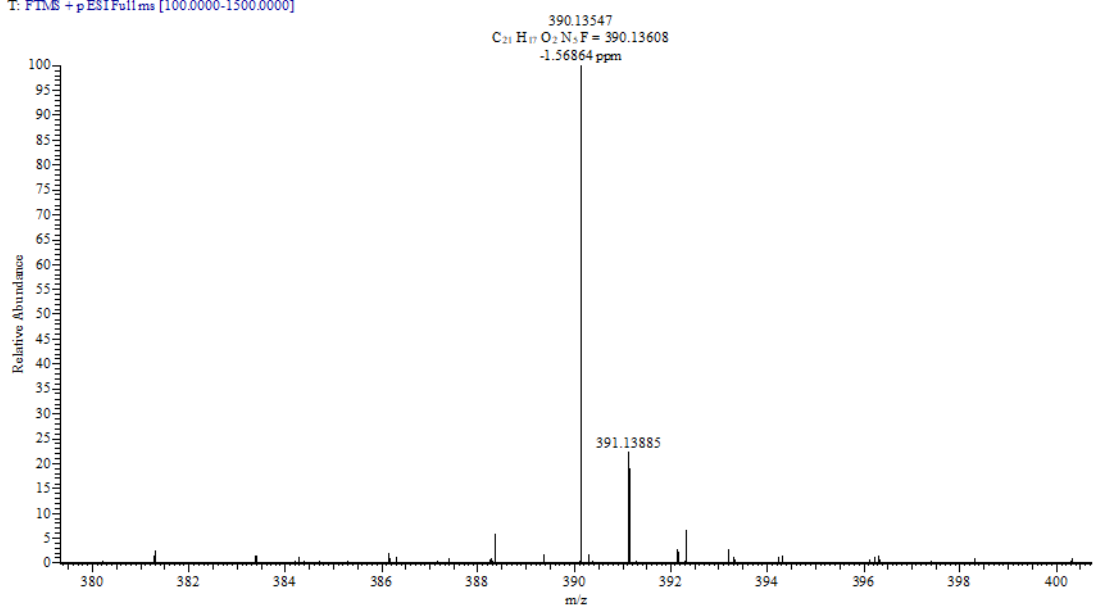


Figure S59. HRMS Spectrum of compound **4h**

YMT-30 #22 RT: 0.10 AV: 1 NL: 3.19E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

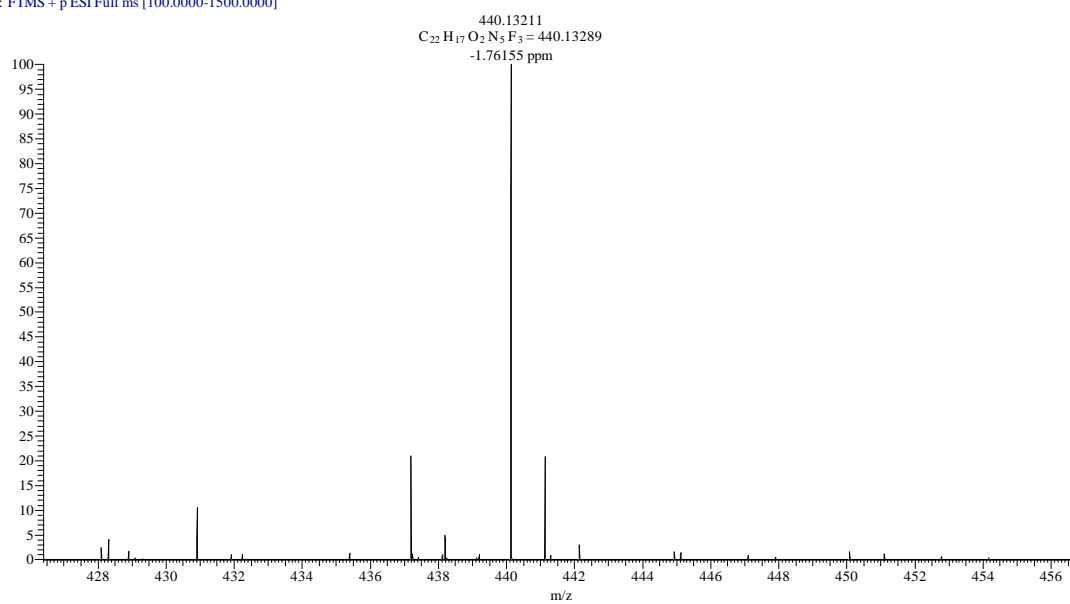


Figure S60. HRMS Spectrum of compound **4i**

YMT-32 #25 RT: 0.11 AV: 1 NL: 2.66E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

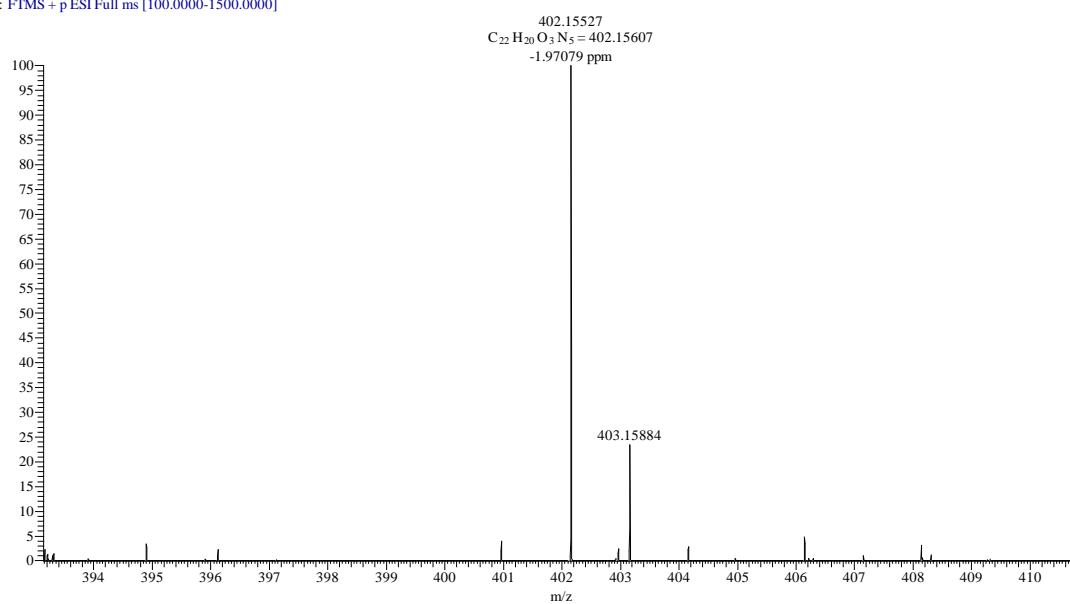


Figure S61. HRMS Spectrum of compound **4j**

YMT-33 #23 RT: 0.10 AV: 1 NL: 4.48E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

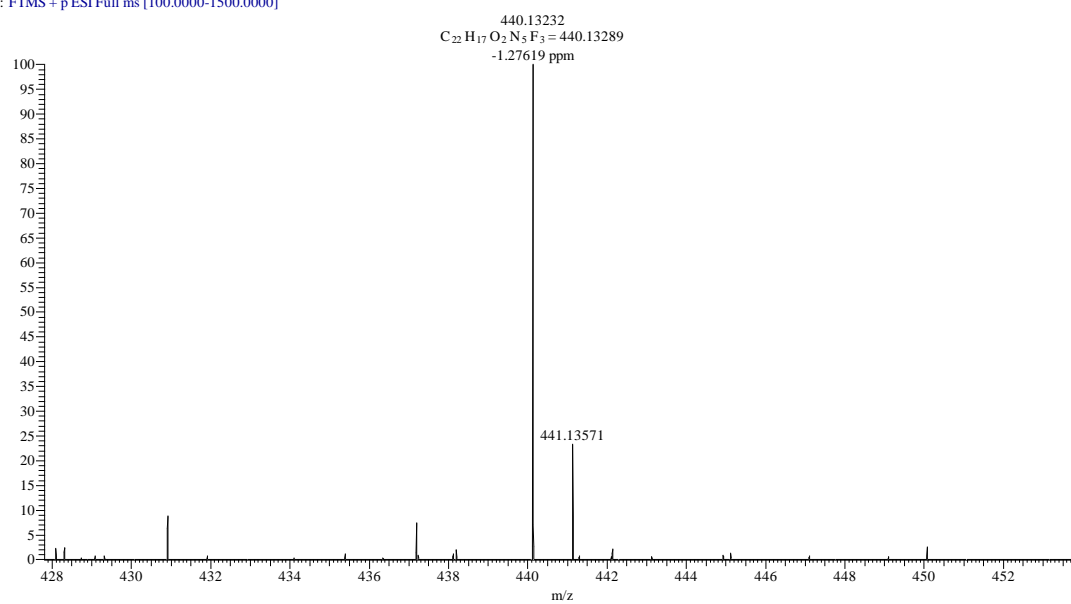


Figure S62. HRMS Spectrum of compound **4k**

YMT-34 #24 RT: 0.11 AV: 1 NL: 4.13E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

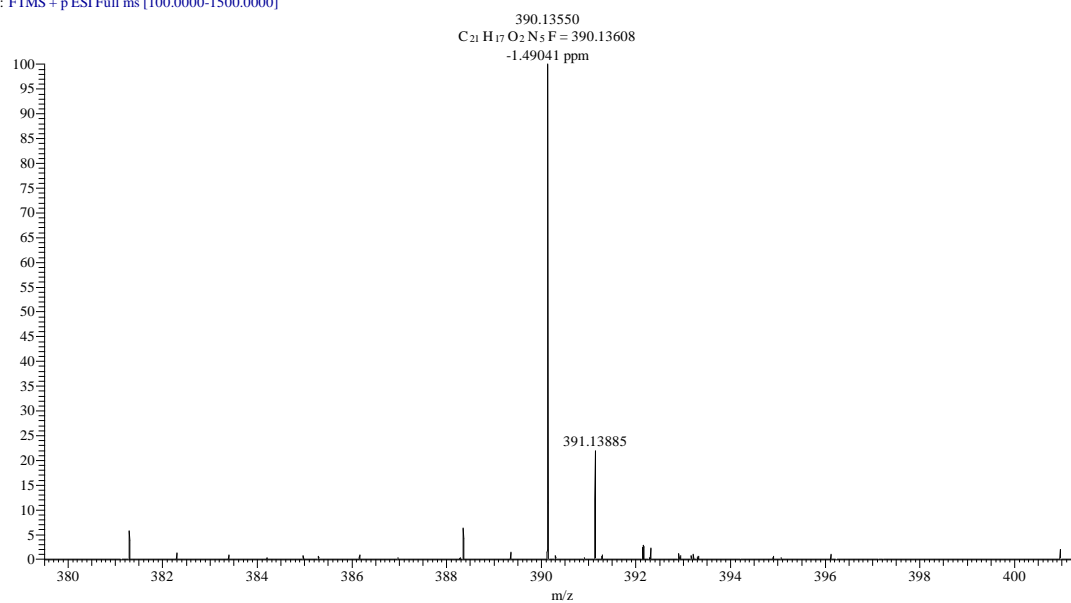


Figure S63. HRMS Spectrum of compound **4l**

YMT-35 #25 RT: 0.11 AV: 1 NL: 1.06E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

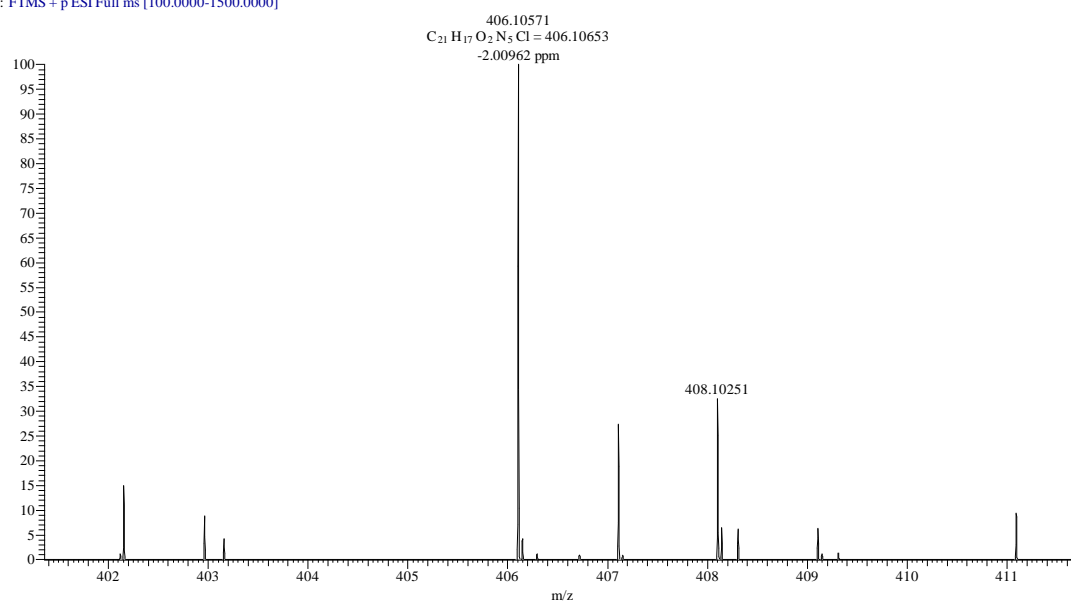


Figure S64. HRMS Spectrum of compound **4m**

YMT-31 #24 RT: 0.11 AV: 1 NL: 3.78E5
T: FTMS + p ESI Full ms [100.0000-1500.0000]

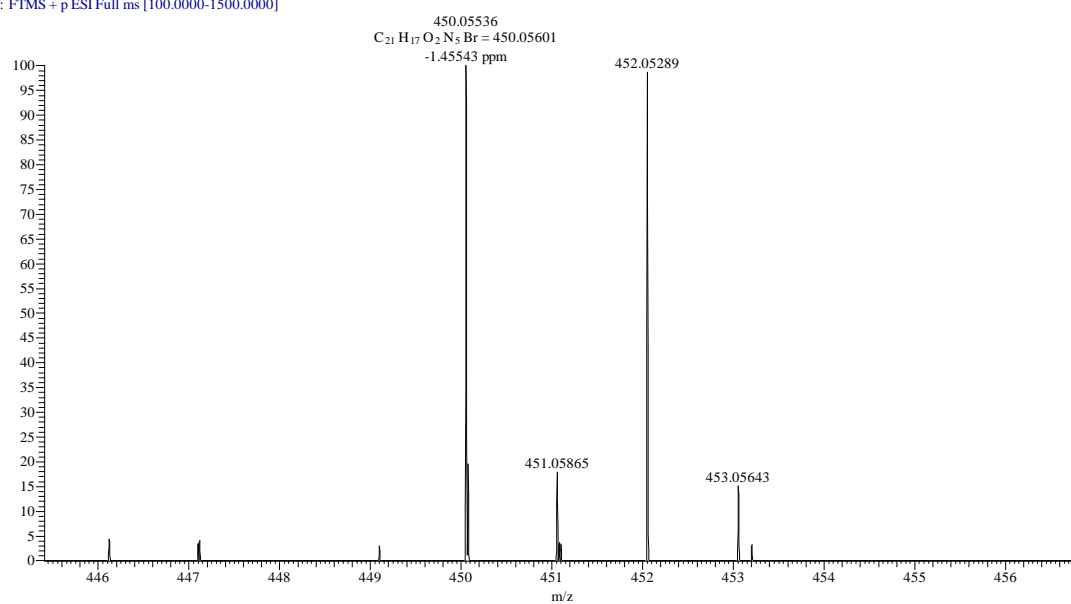


Figure S65. HRMS Spectrum of compound **4n**

MT-74 #22 RT: 0.10 AV: 1 NL: 3.02E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]

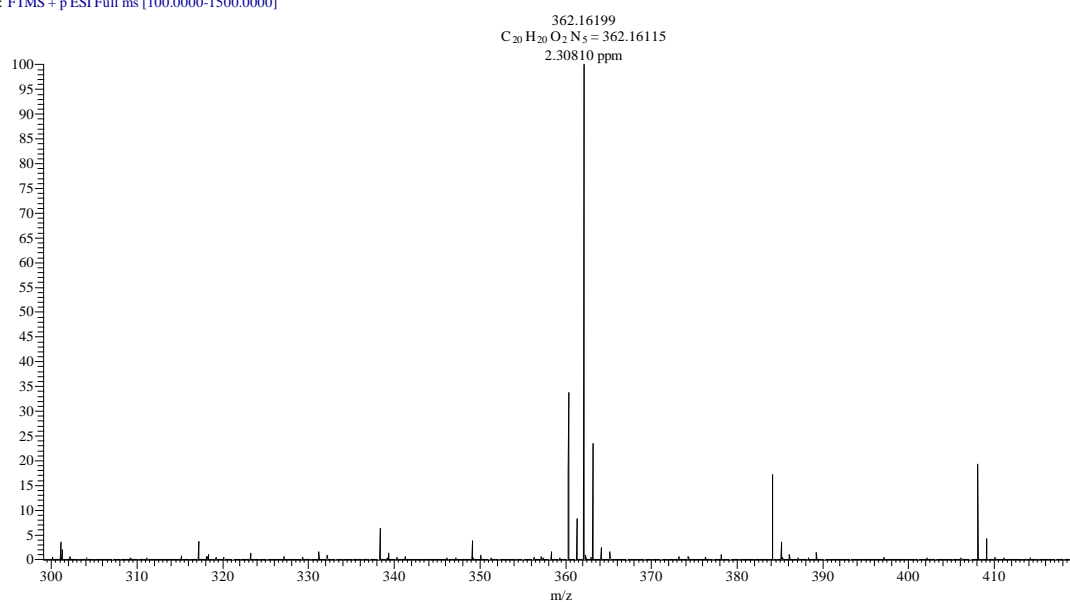


Figure S66. HRMS Spectrum of compound 10a

MT-77 #20 RT: 0.09 AV: 1 NL: 2.54E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]

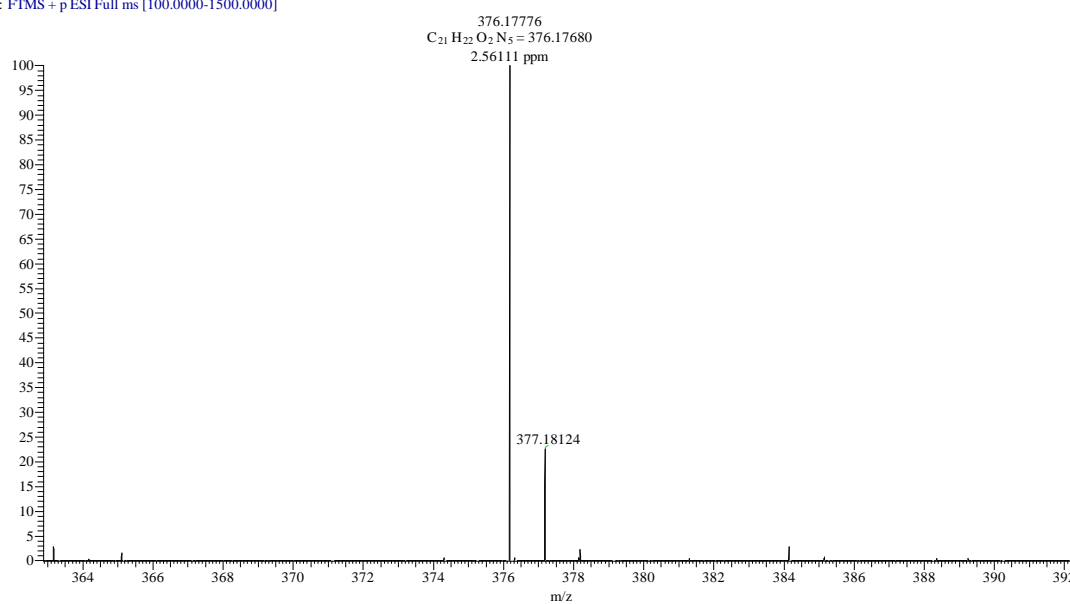


Figure S67. HRMS Spectrum of compound 10b

MT-78 #37 RT: 0.16 AV: 1 NL: 3.16E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

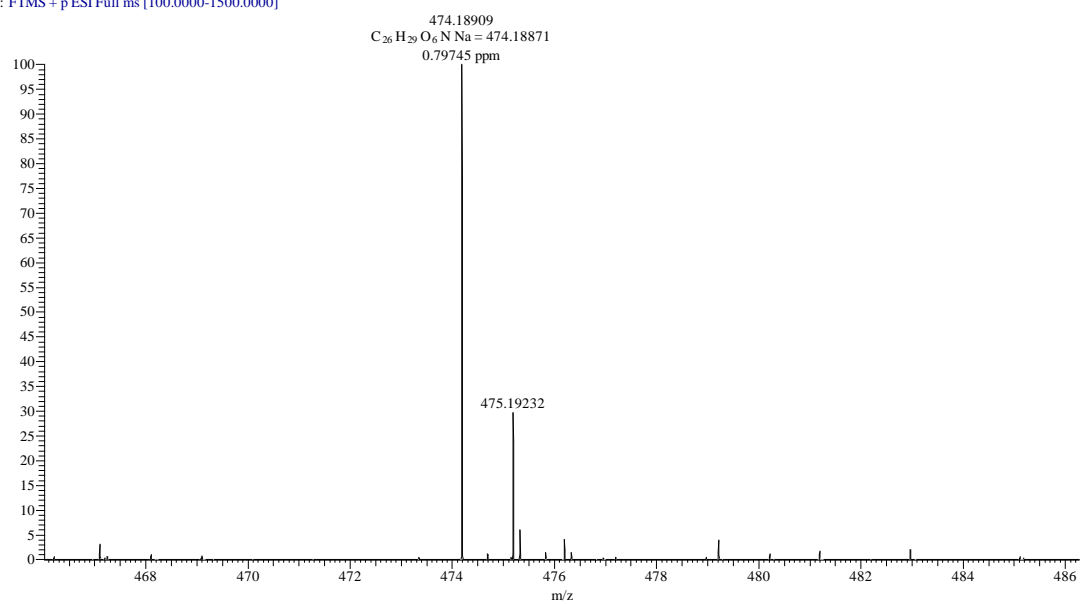


Figure S68. HRMS Spectrum of compound **10c**

IR spectra of intermediates 3, 7-9

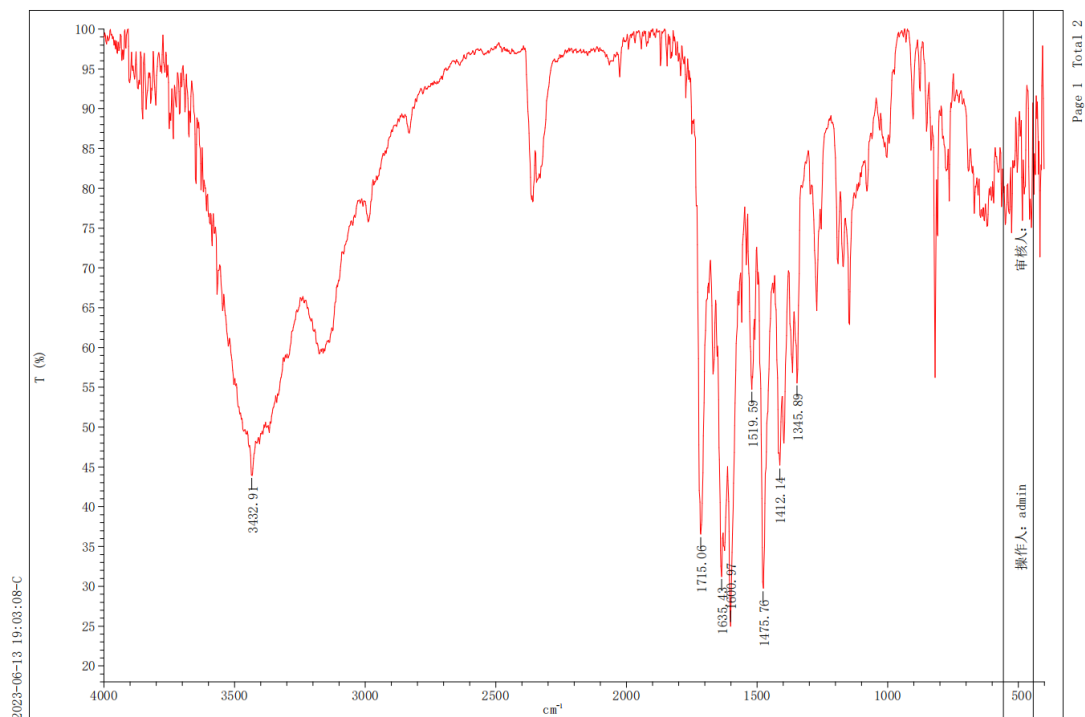


Figure S69. IR spectra of intermediate 3

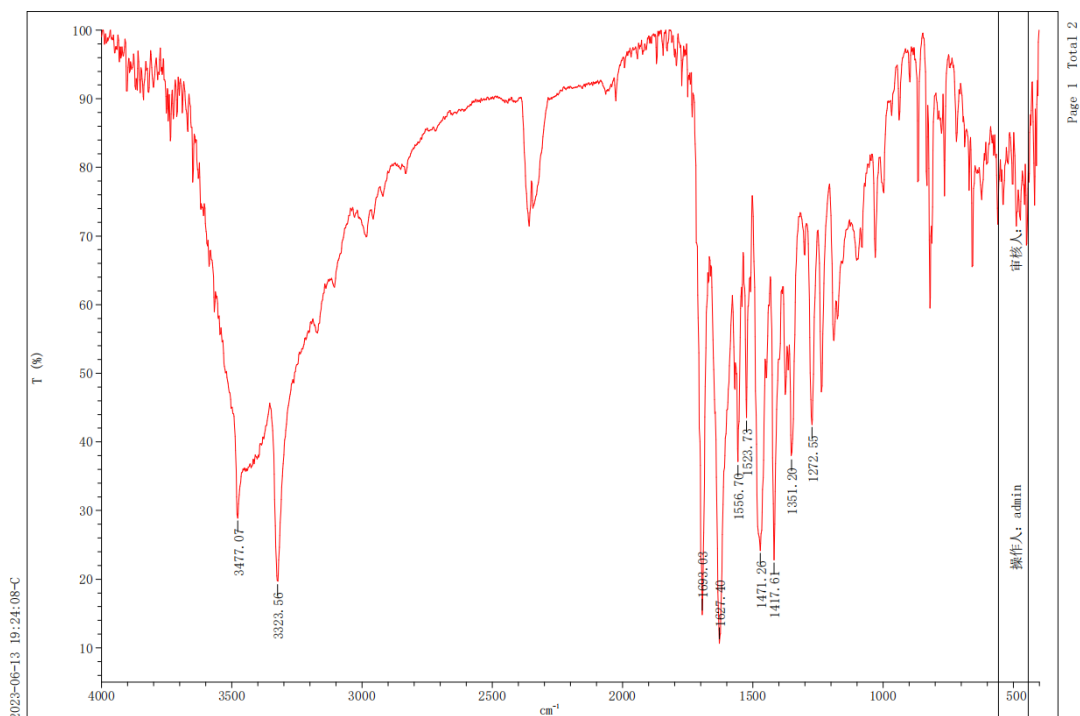


Figure S70. IR spectra of intermediate 7

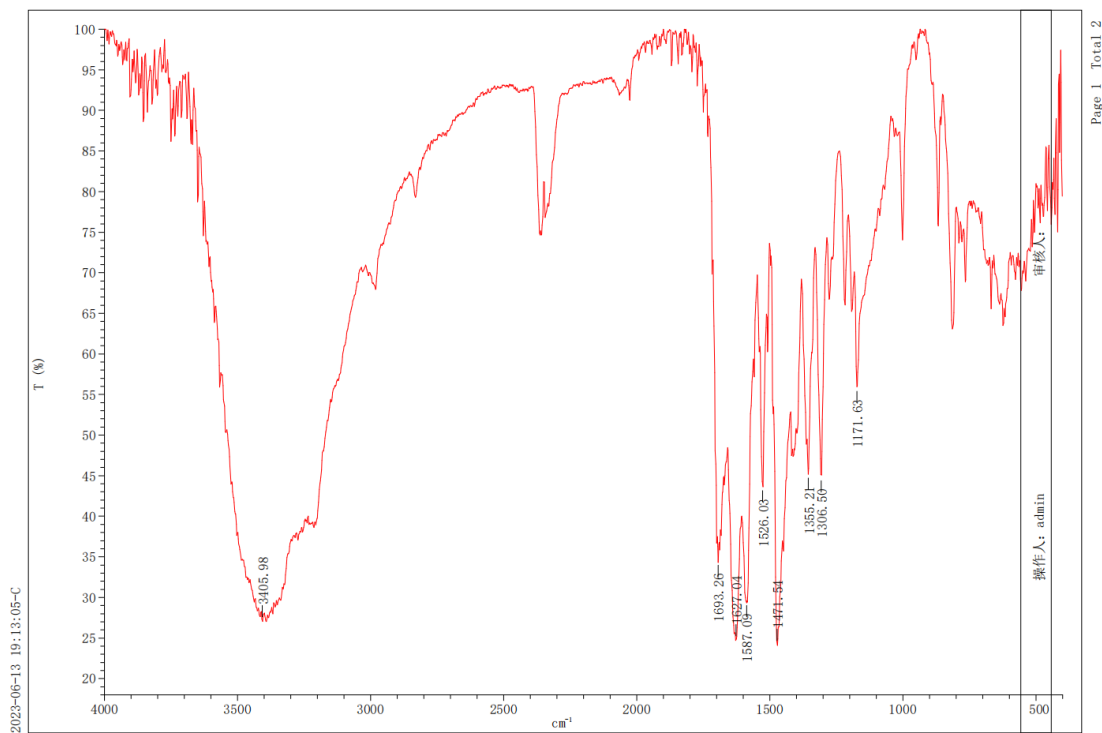


Figure S71. IR spectra of intermediate 8

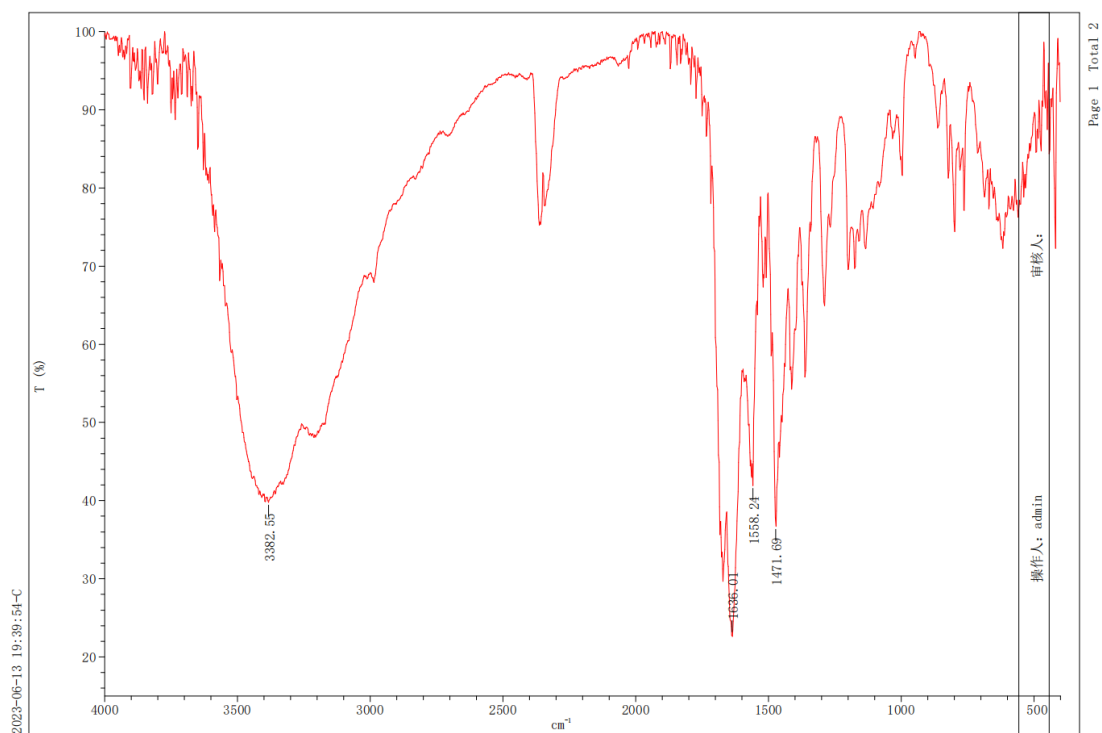


Figure S72. IR spectra of intermediate 9

IR spectra of compounds 4a-n, 10a-c

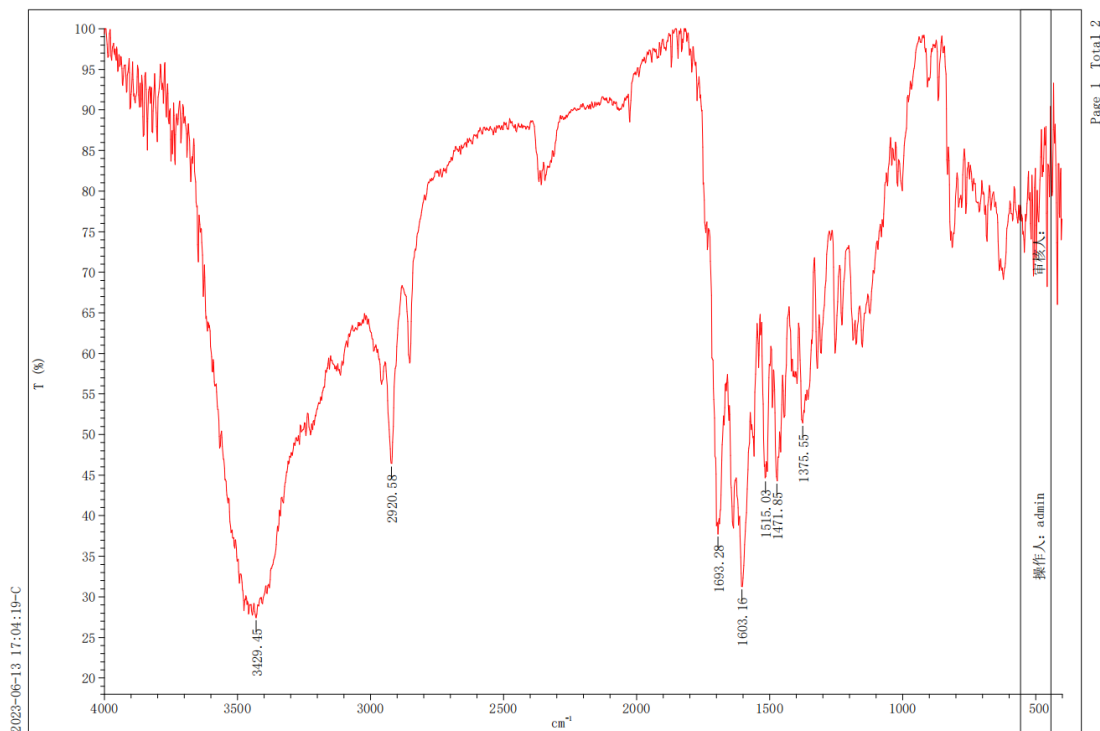


Figure S73. IR spectra of compound 4a

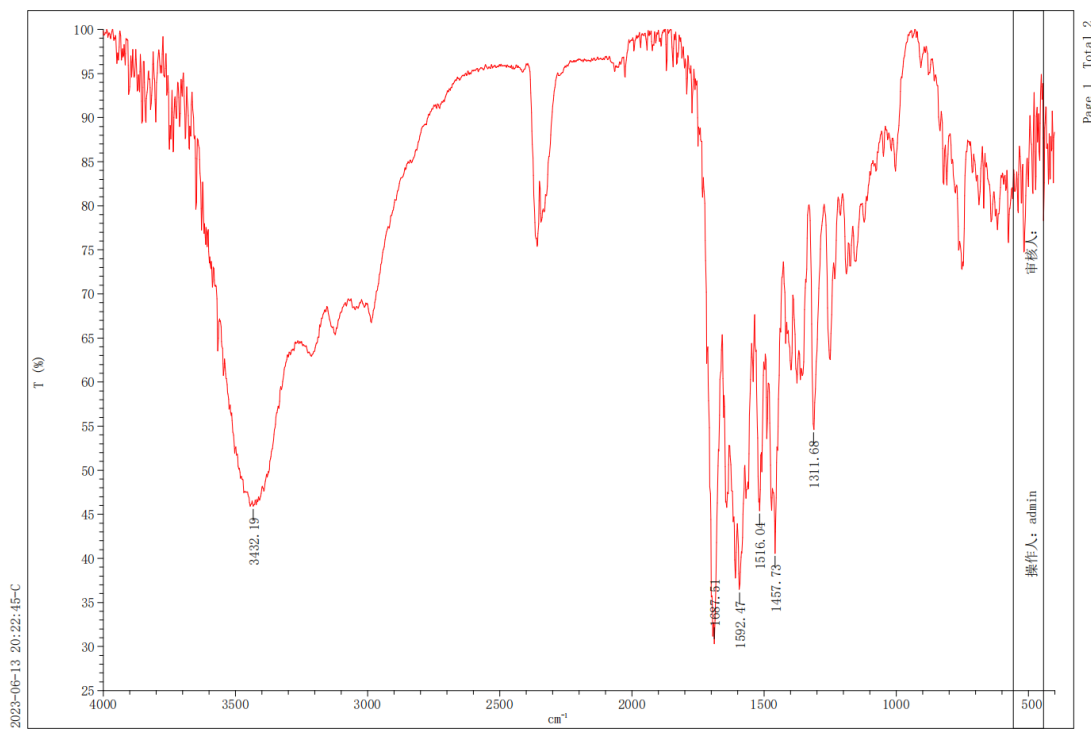


Figure S74. IR spectra of compound 4b

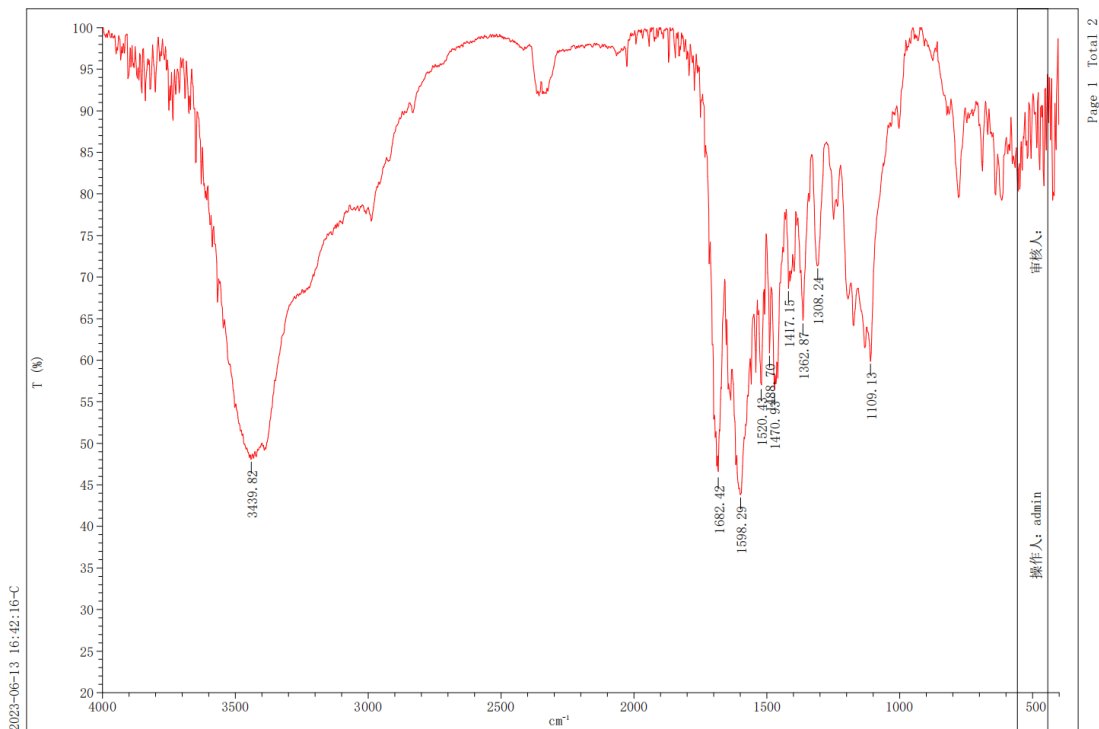


Figure S75. IR spectra of compound 4c



Figure S76. IR spectra of compound 4d

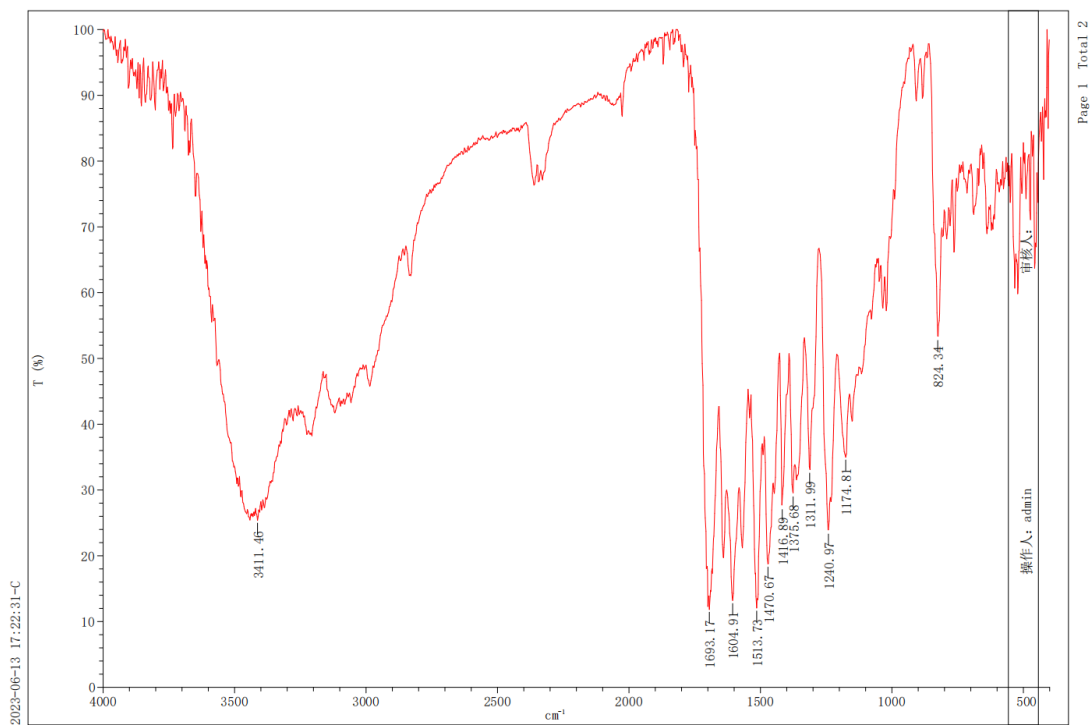


Figure S77. IR spectra of compound 4e

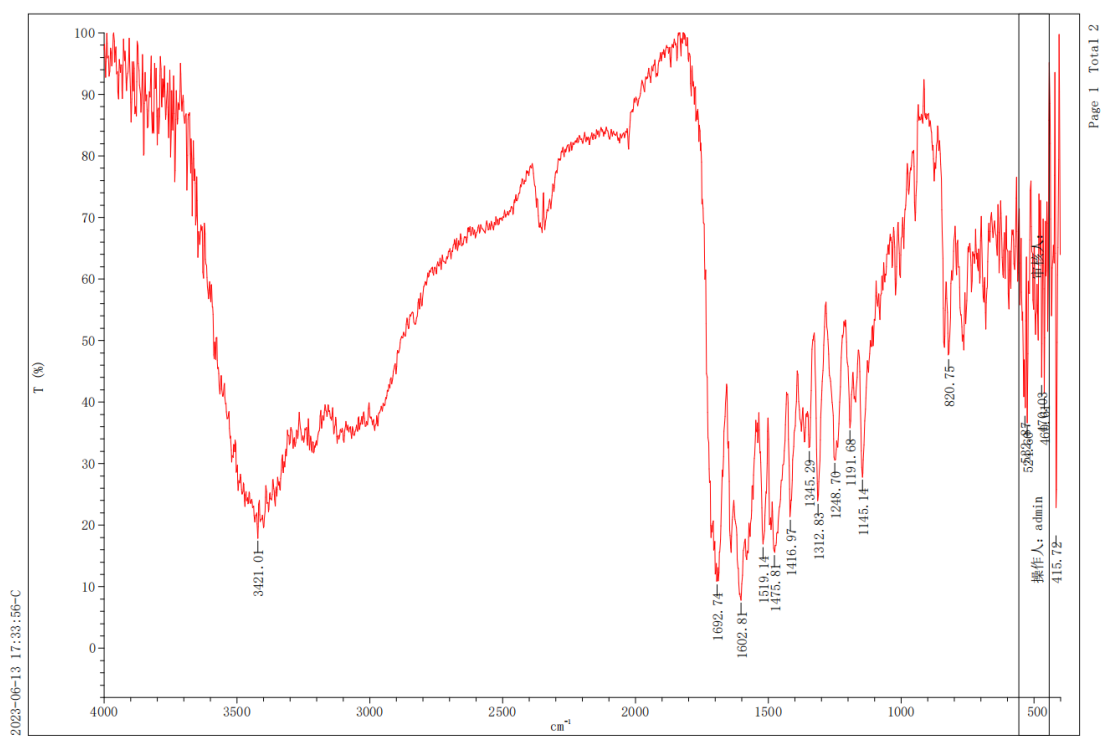


Figure S78. IR spectra of compound 4f

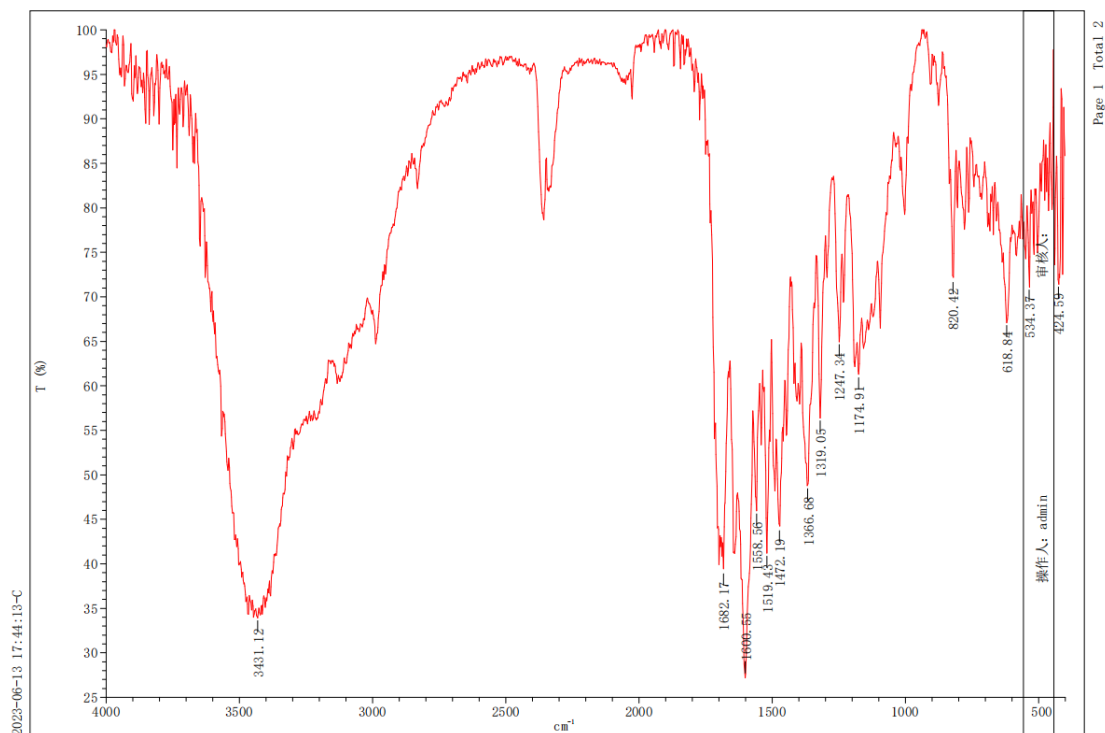


Figure S79. IR spectra of compound 4g

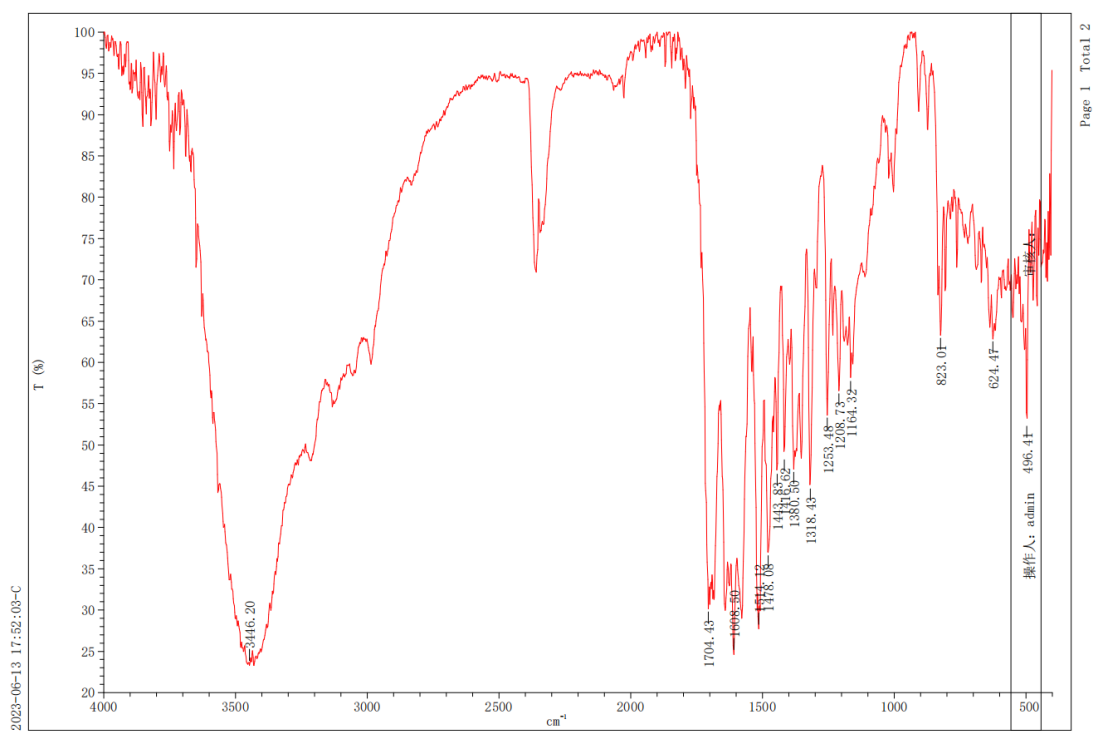


Figure S80. IR spectra of compound 4h

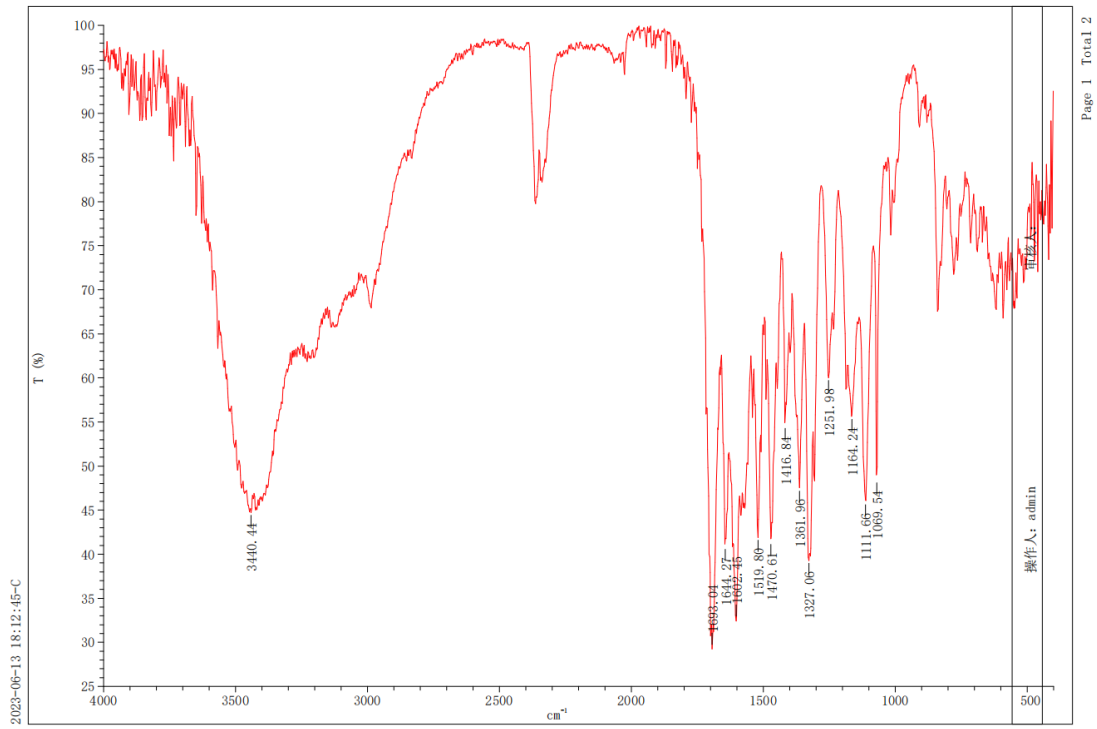


Figure S81. IR spectra of compound 4i

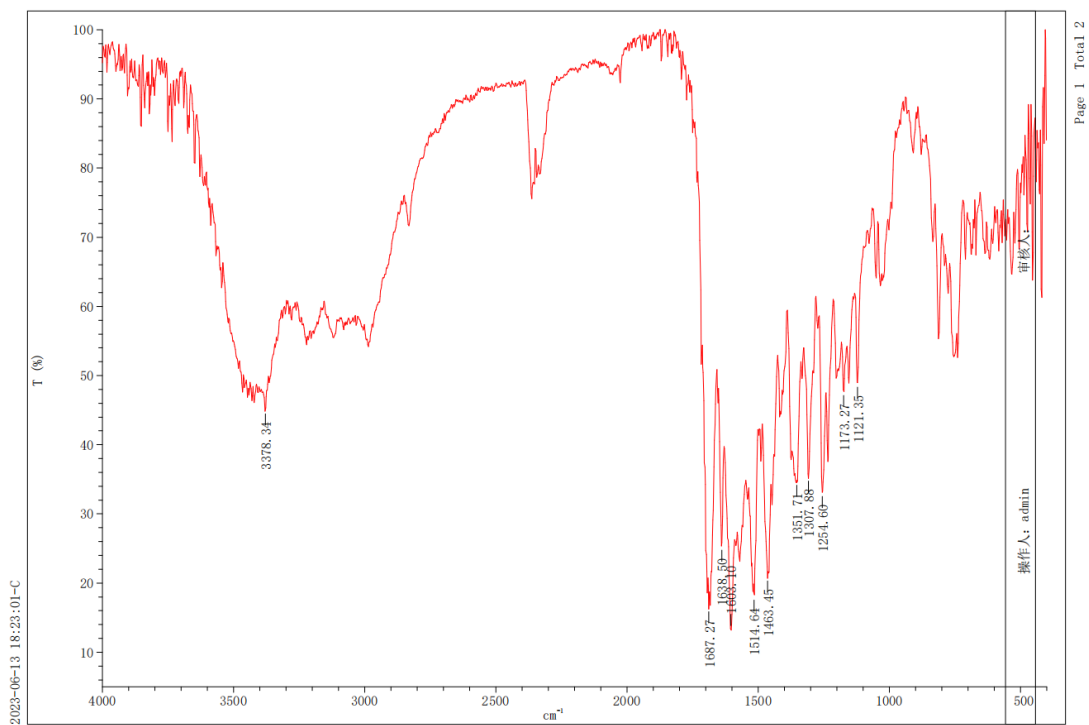


Figure S82. IR spectra of compound 4j

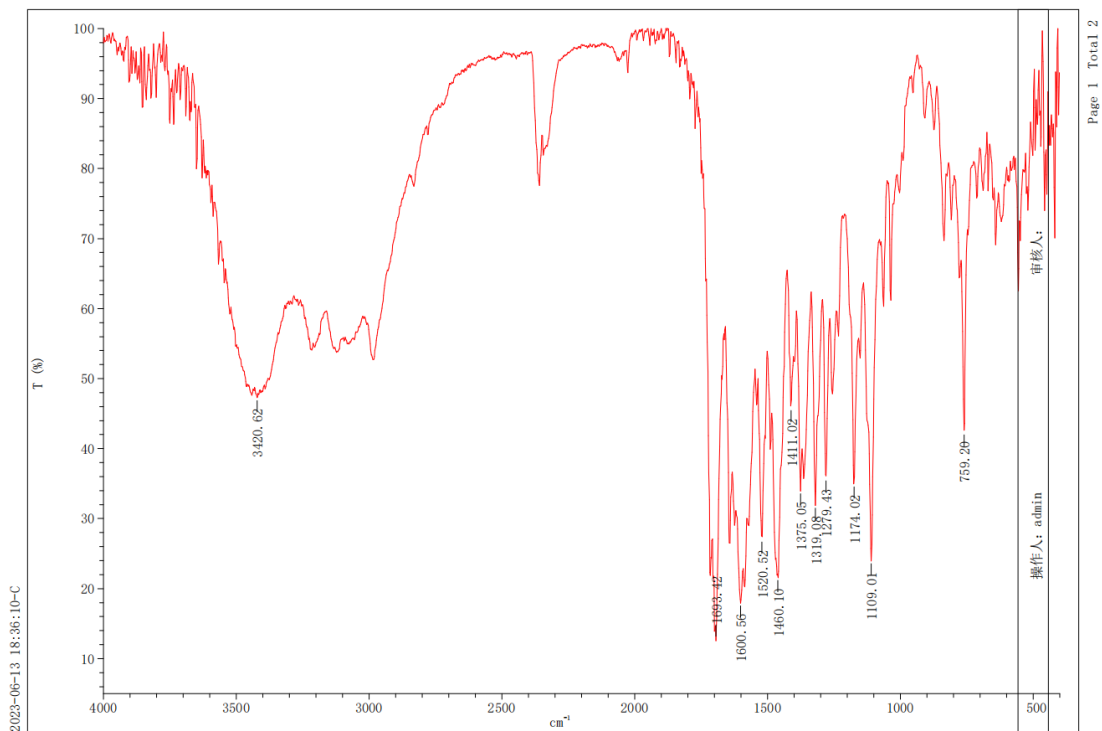


Figure S83. IR spectra of compound 4k

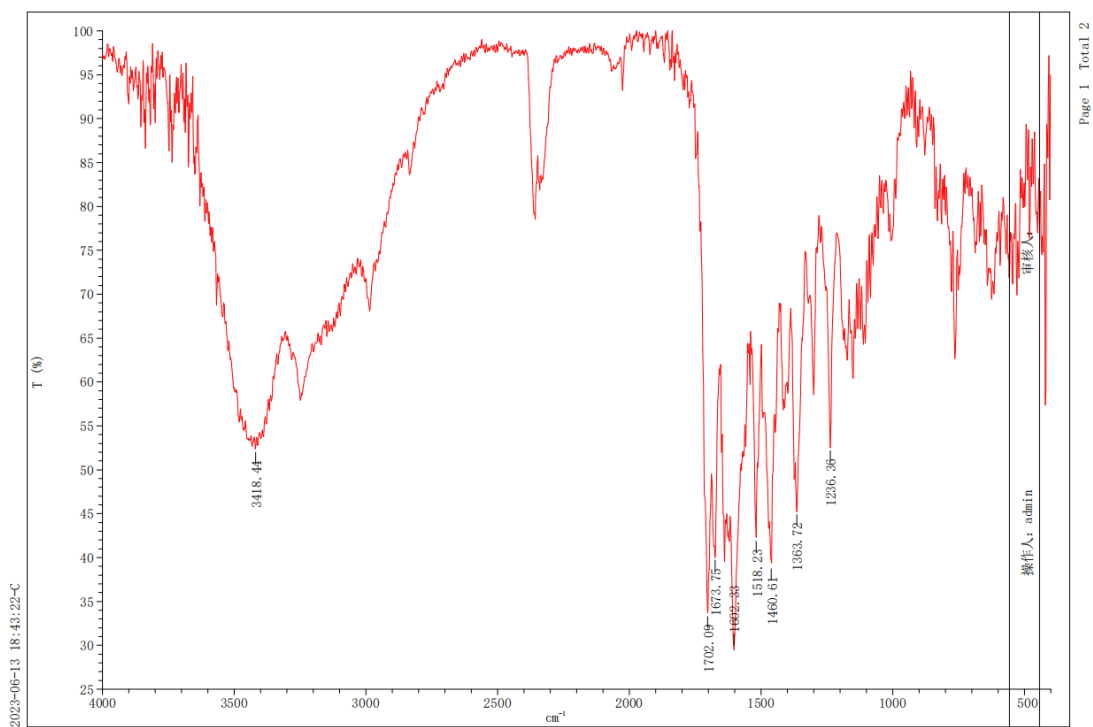


Figure S84. IR spectra of compound 4l

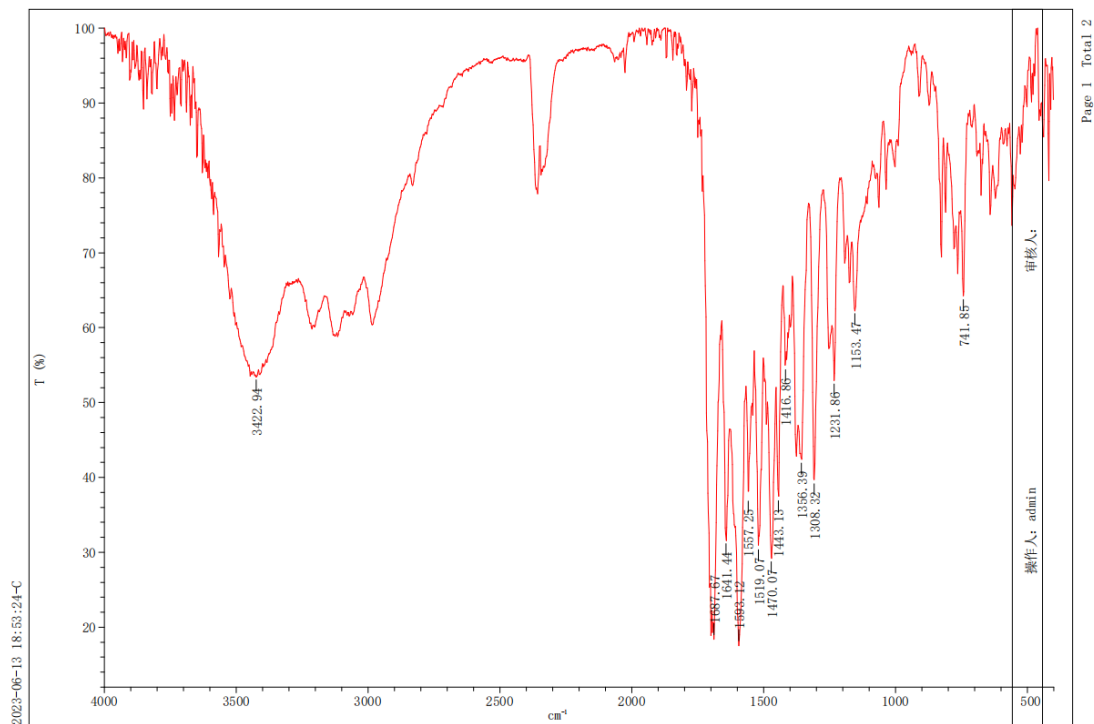


Figure S85. IR spectra of compound 4m

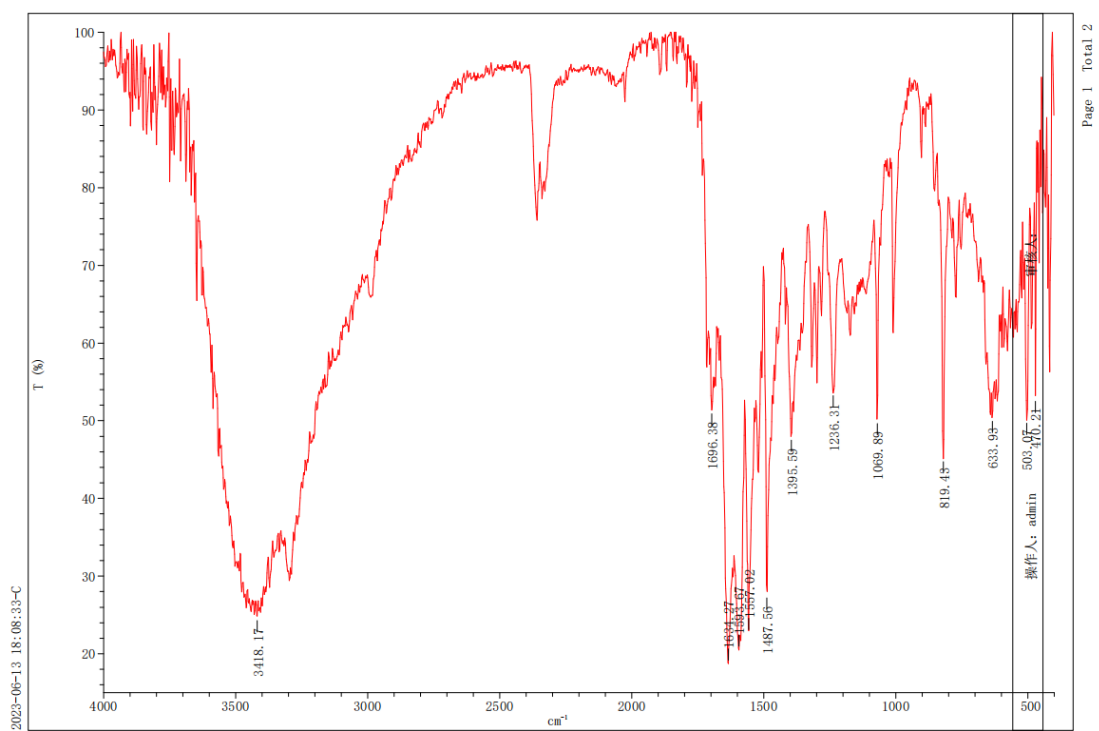


Figure S86. IR spectra of compound 4n

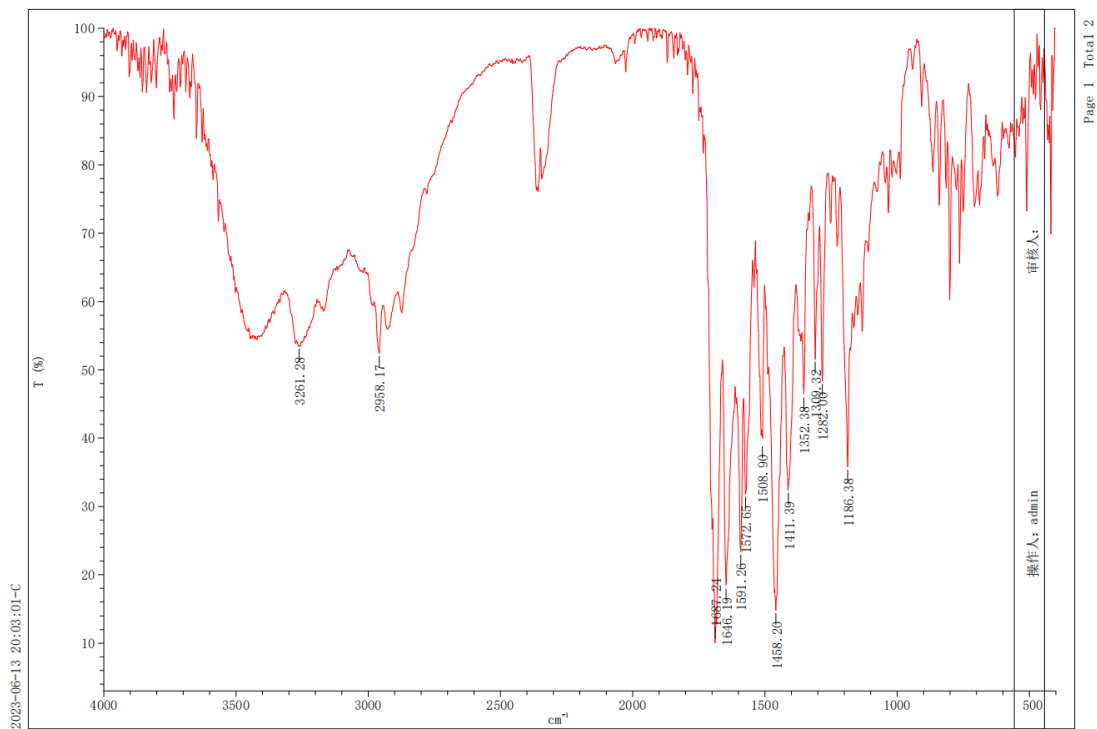


Figure S87. IR spectra of compound 10a

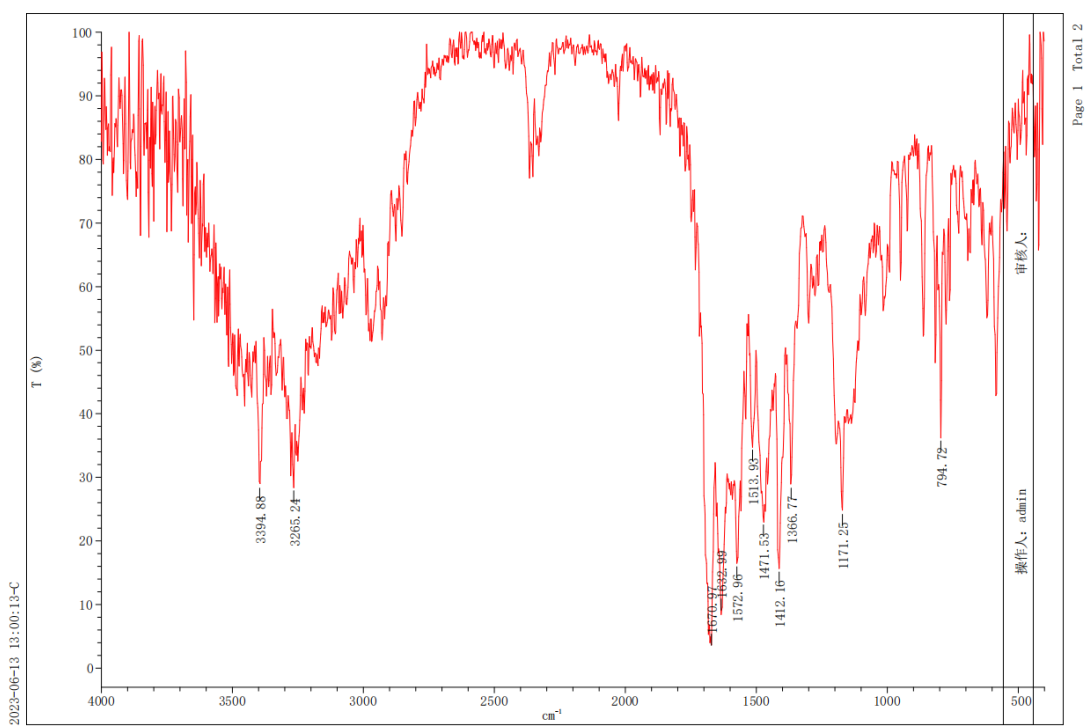


Figure S88. IR spectra of compound 10b

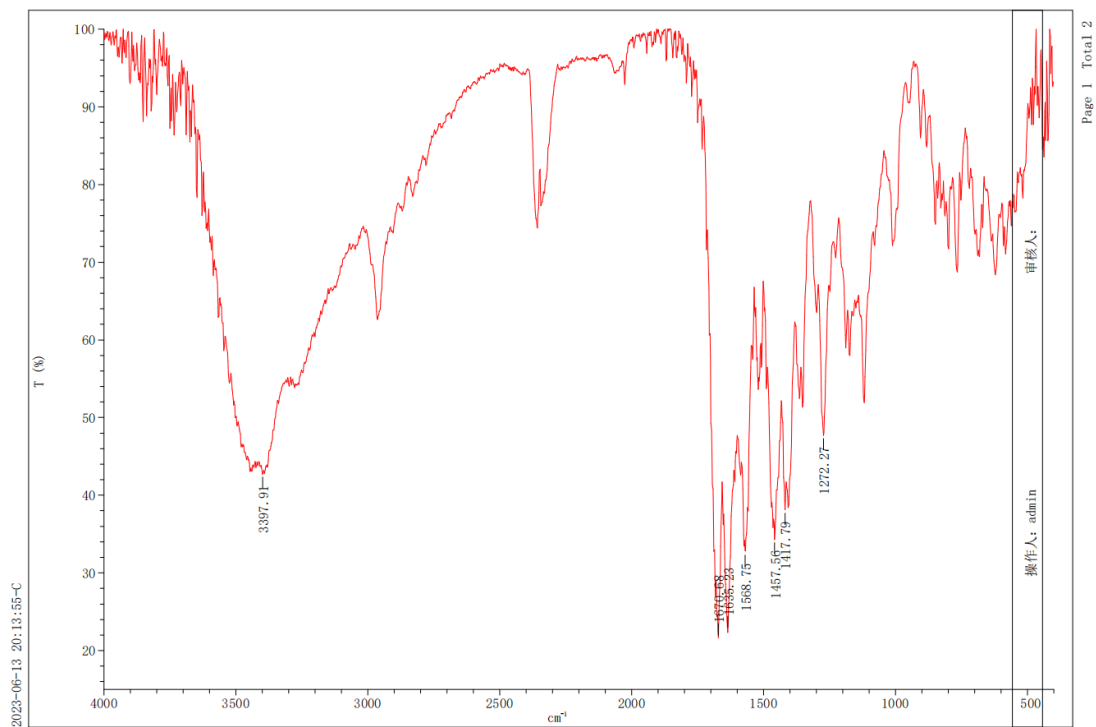
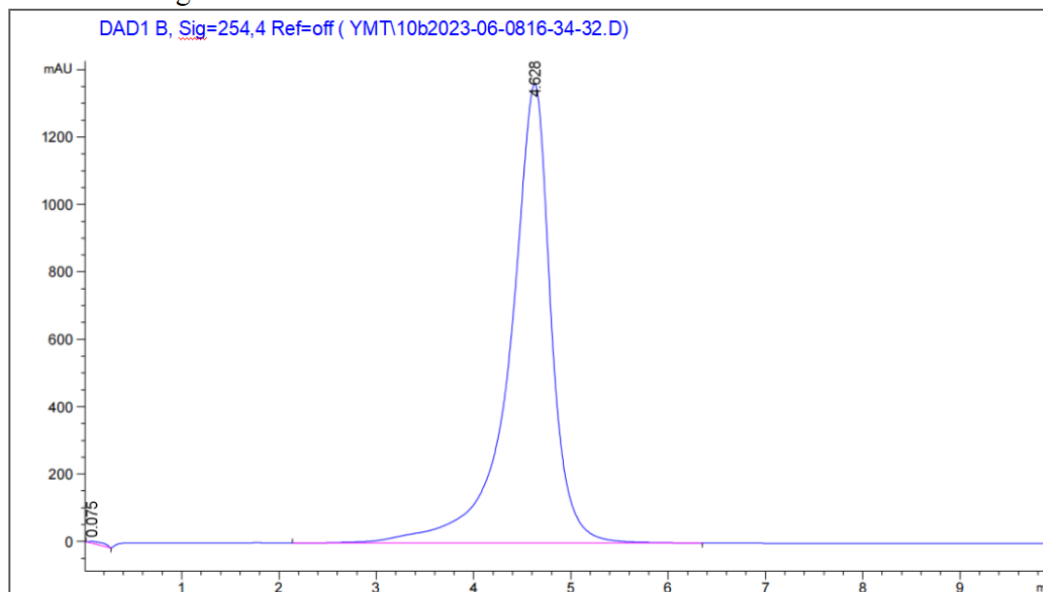


Figure S89. IR spectra of compound **10c**

Purity report of active compound 10b by HPLC

Instrument: AgilentLC1260



Area Percentage

Peak	Retention Time (min)	Type	Width (min)	Area (mAU*s)	Height (mAU)	Area (%)
1	0.075	BB	0.2071	79.23689	4.99298	0.1966
2	4.628	BB	0.4245	4.02201e4	1362.21777	99.8034

Figure S90. Purity analysis of the active compound 10b