

Article

Synthesis, Crystal Structure, and Biological Evaluation of Novel 5-Hydroxymethylpyrimidines

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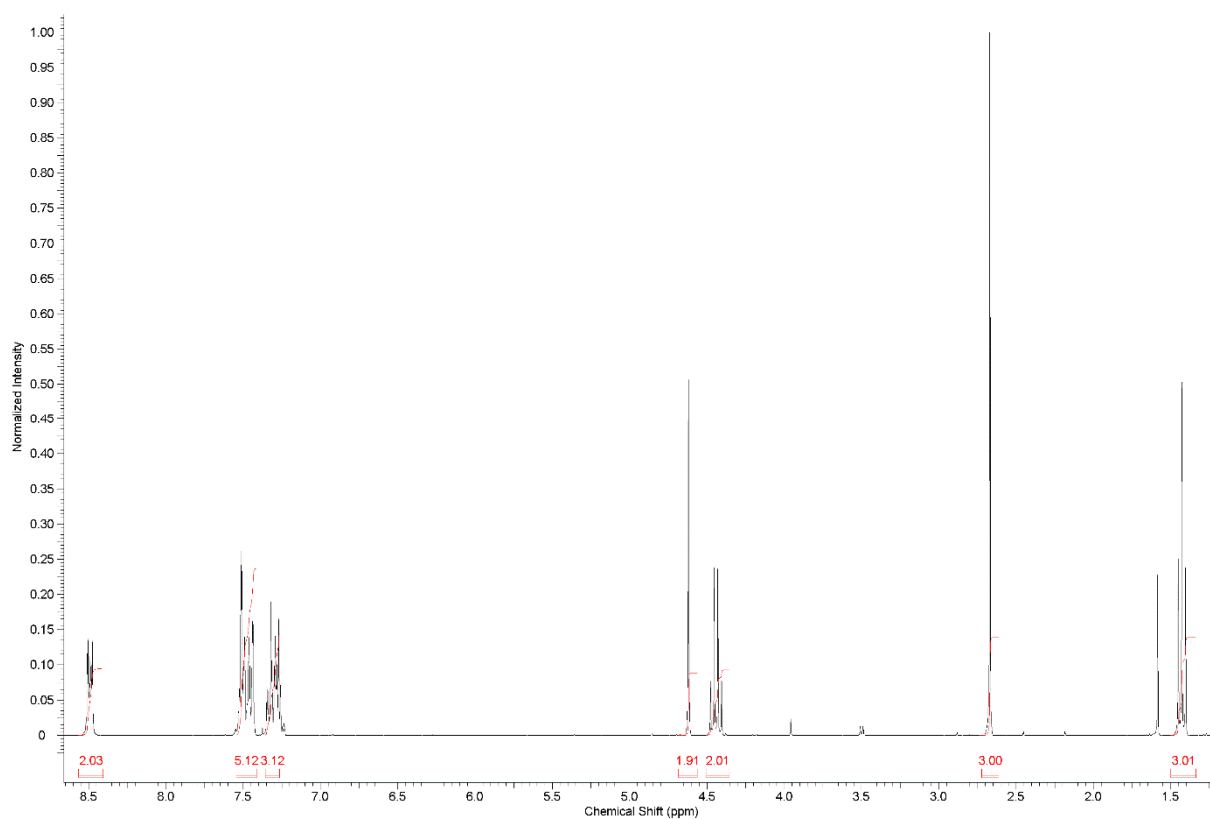


Figure S1. ¹H NMR spectrum of compound **2a** (300 MHz, CDCl₃).

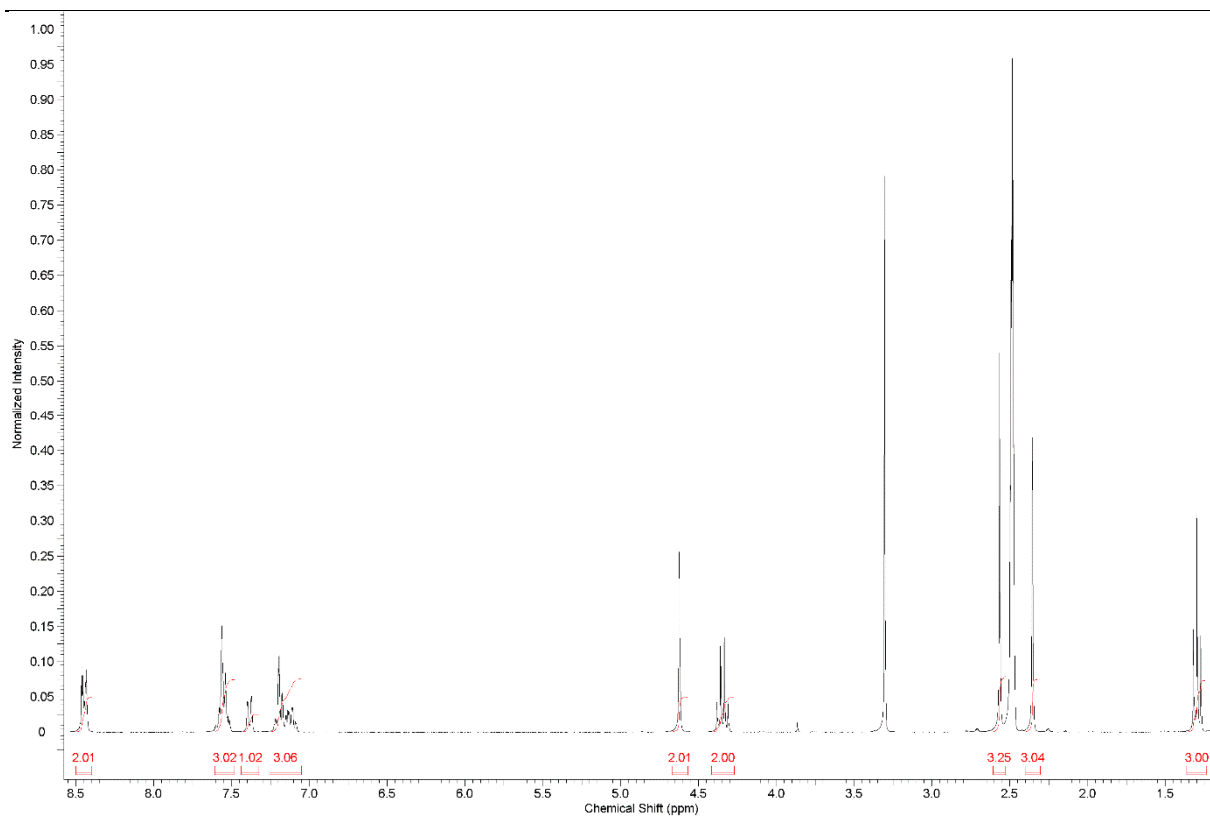


Figure S2. ^1H NMR spectrum of compound **2b** (300MHz, DMSO-d_6).

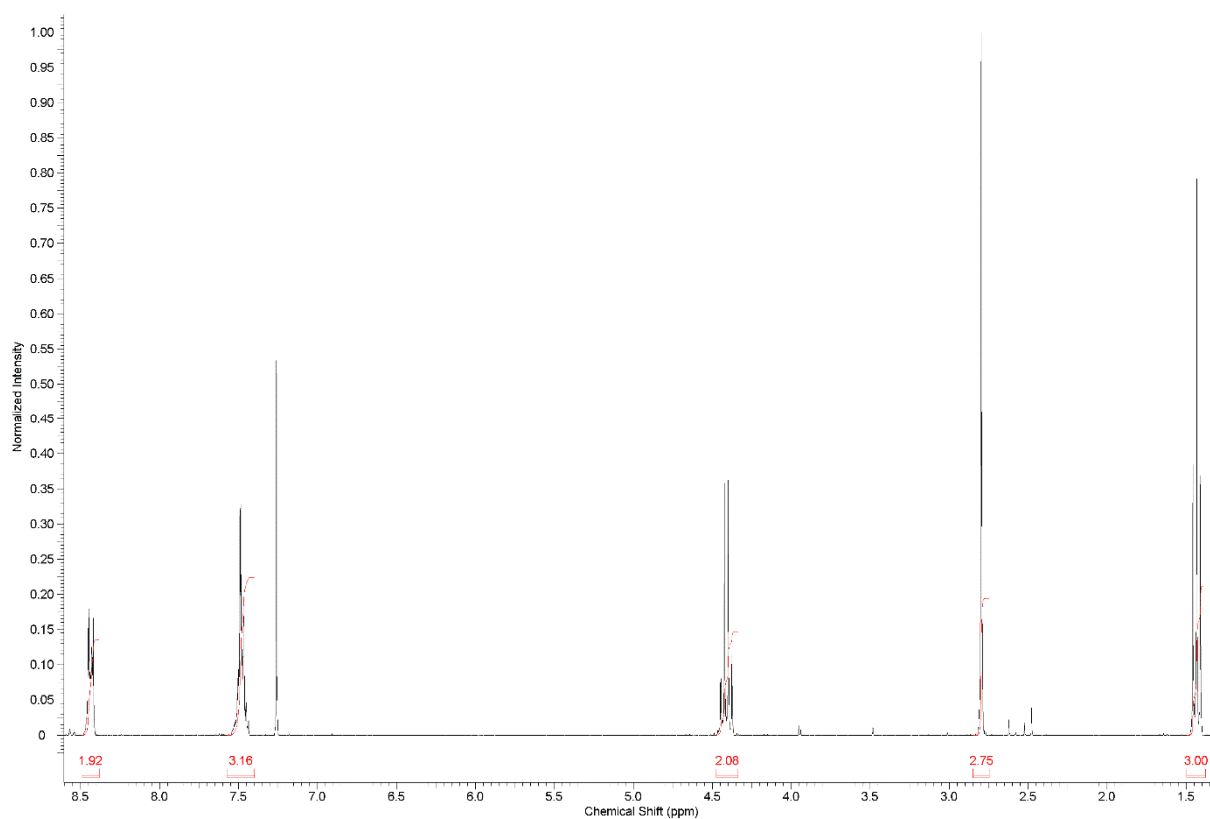


Figure S3. ^1H NMR spectrum of compound **2c** (300MHz, CDCl_3).

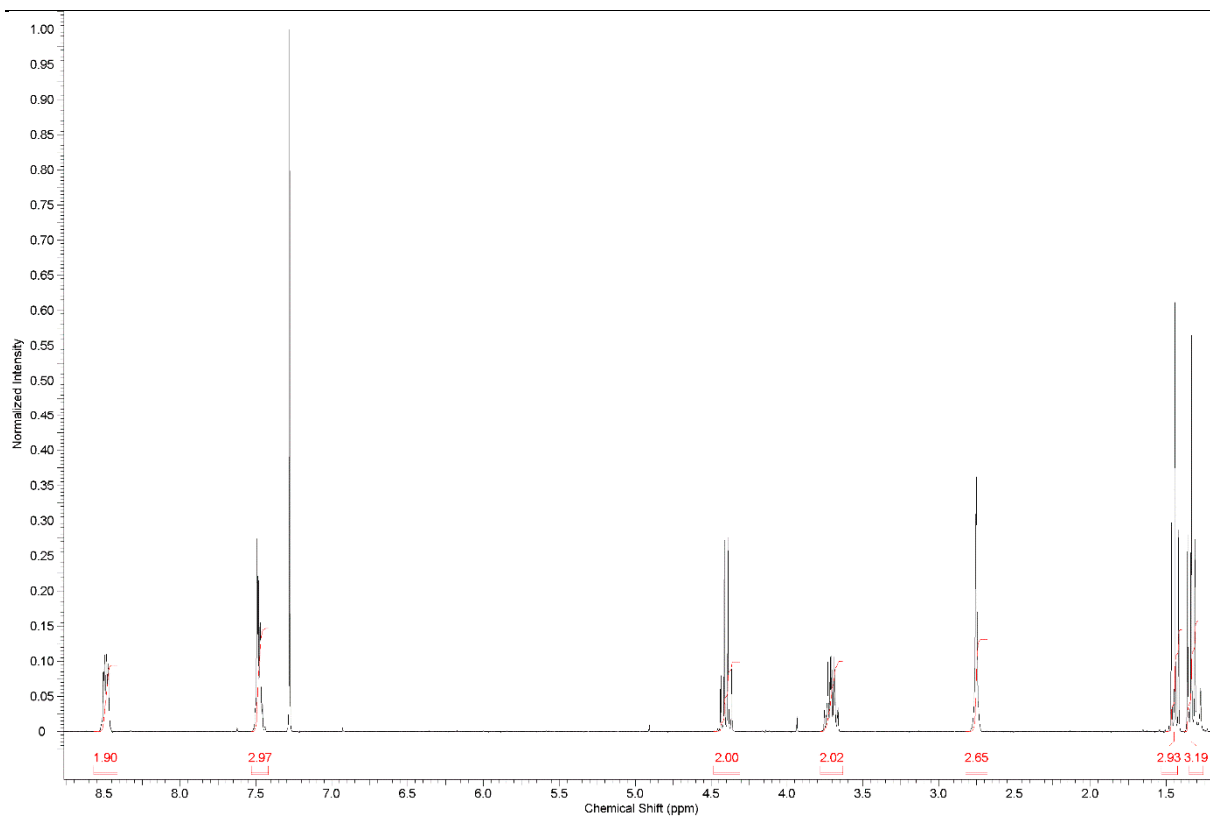


Figure S4. ¹H NMR spectrum of compound **2d** (300MHz, CDCl₃).

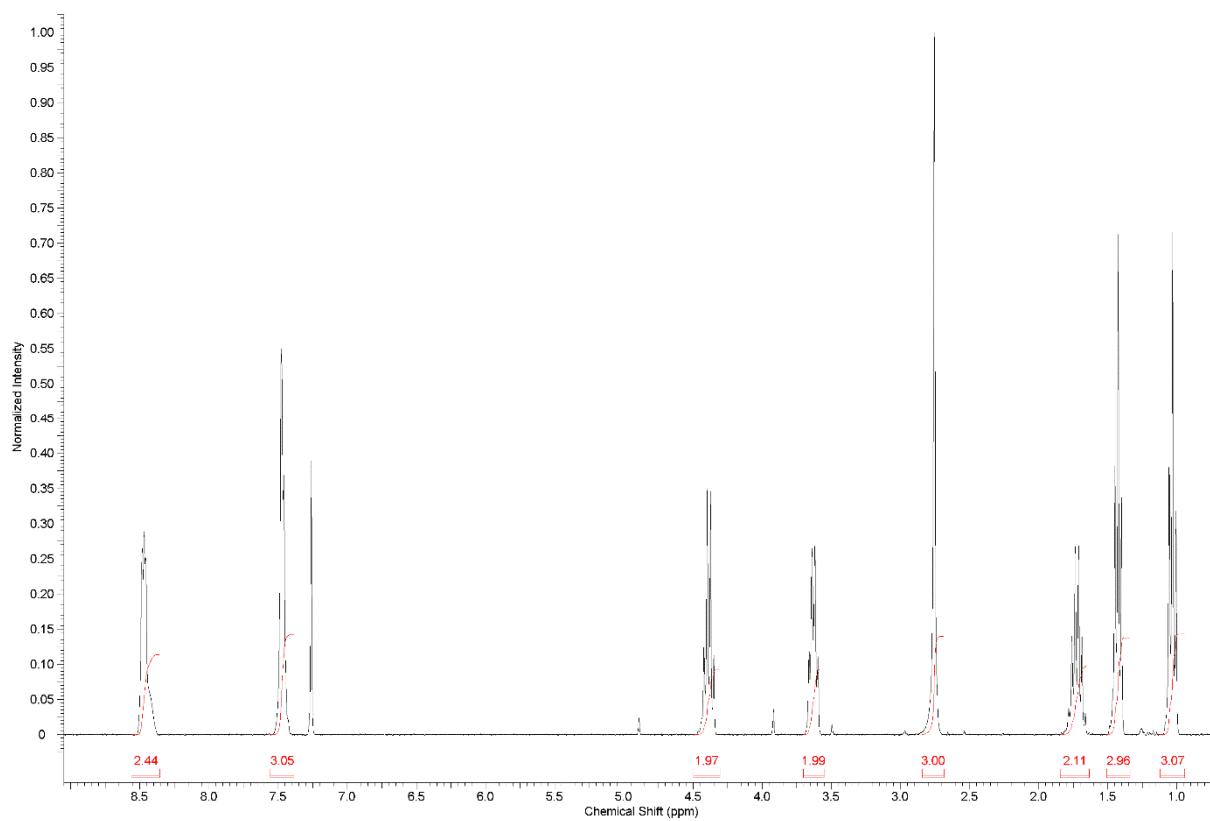


Figure S5. ¹H NMR spectrum of compound **2e** (300MHz, CDCl₃).

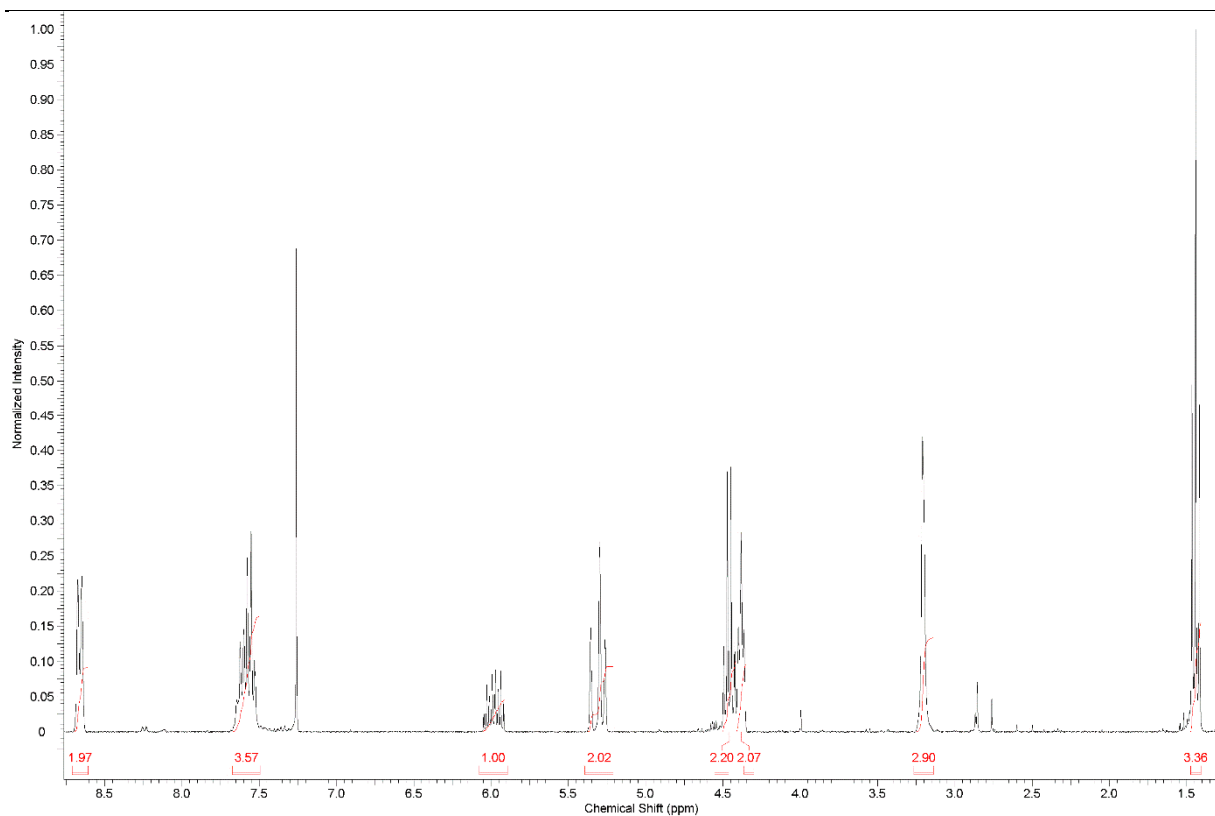


Figure S6. ^1H NMR spectrum of compound **2f** (300MHz, CDCl_3).

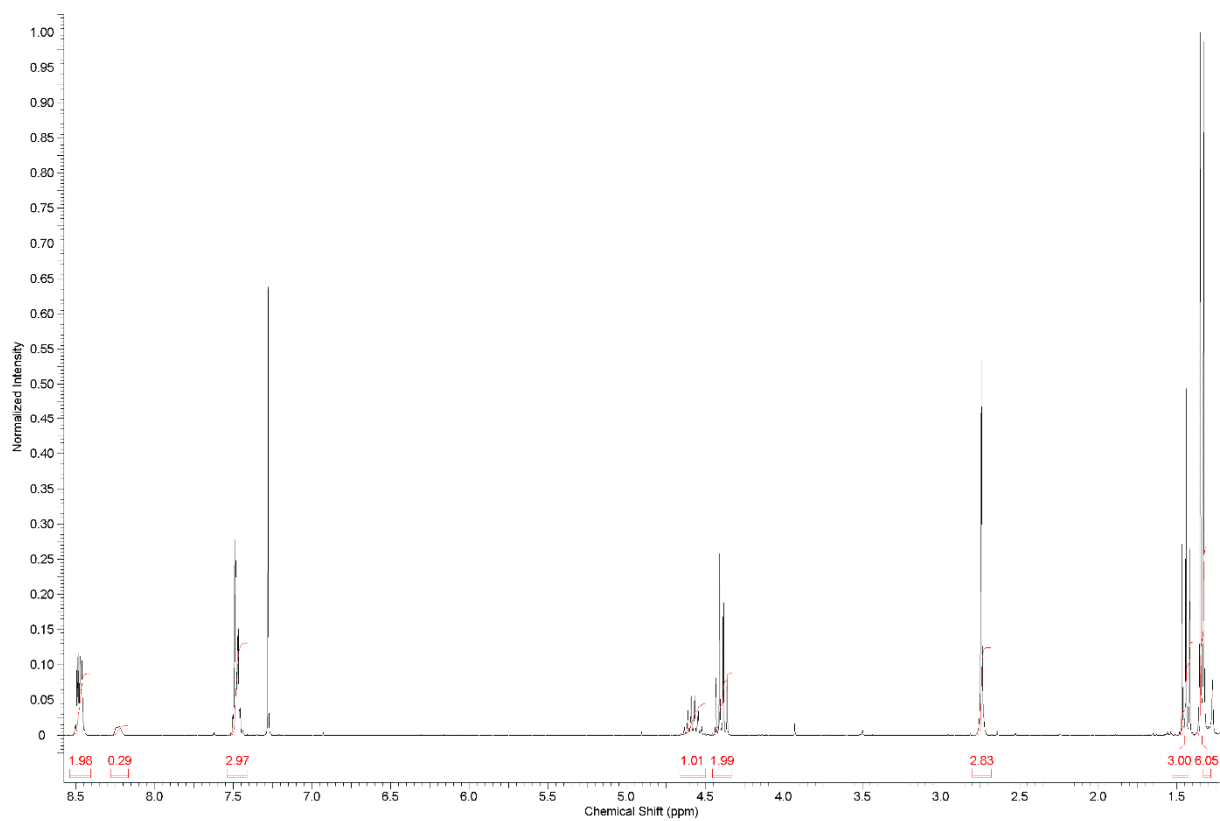


Figure S7. ^1H NMR spectrum of compound **2g** (300MHz, CDCl_3).

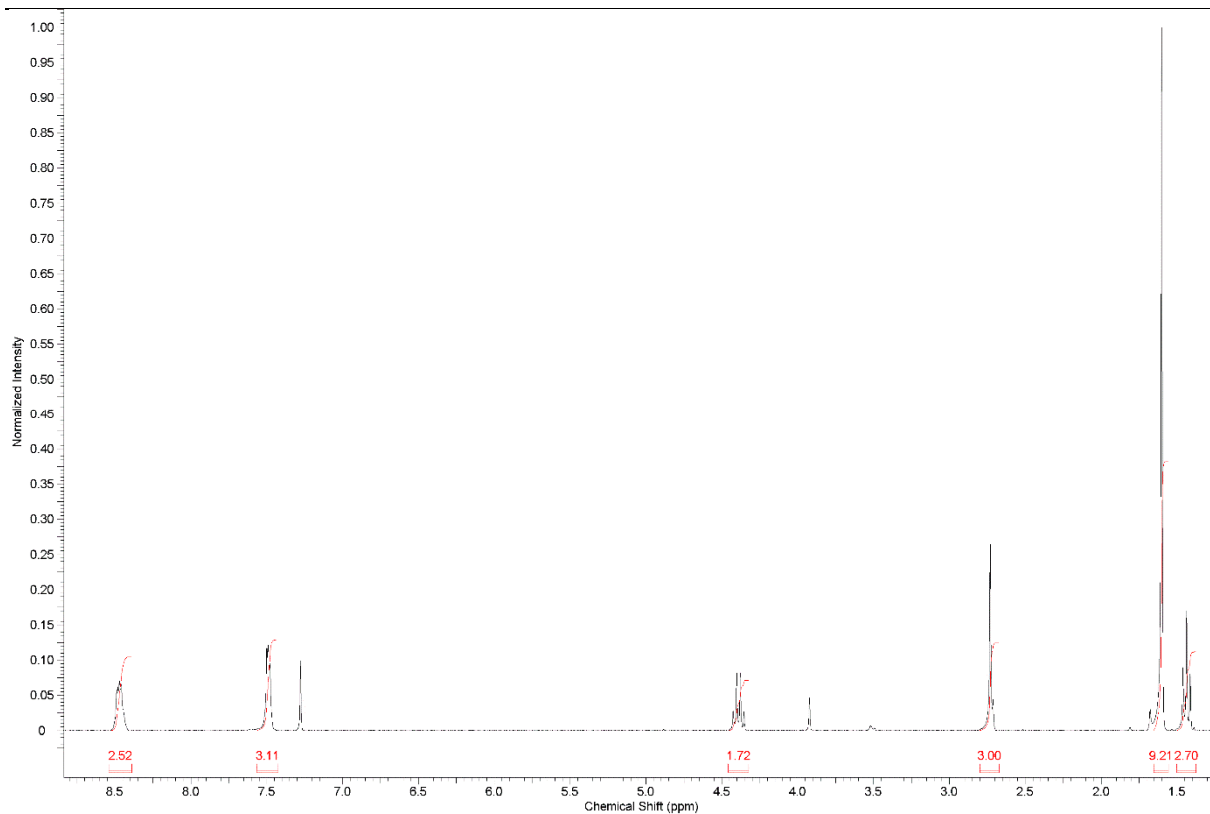


Figure S8. ¹H NMR spectrum of compound **2h** (300MHz, CDCl₃).

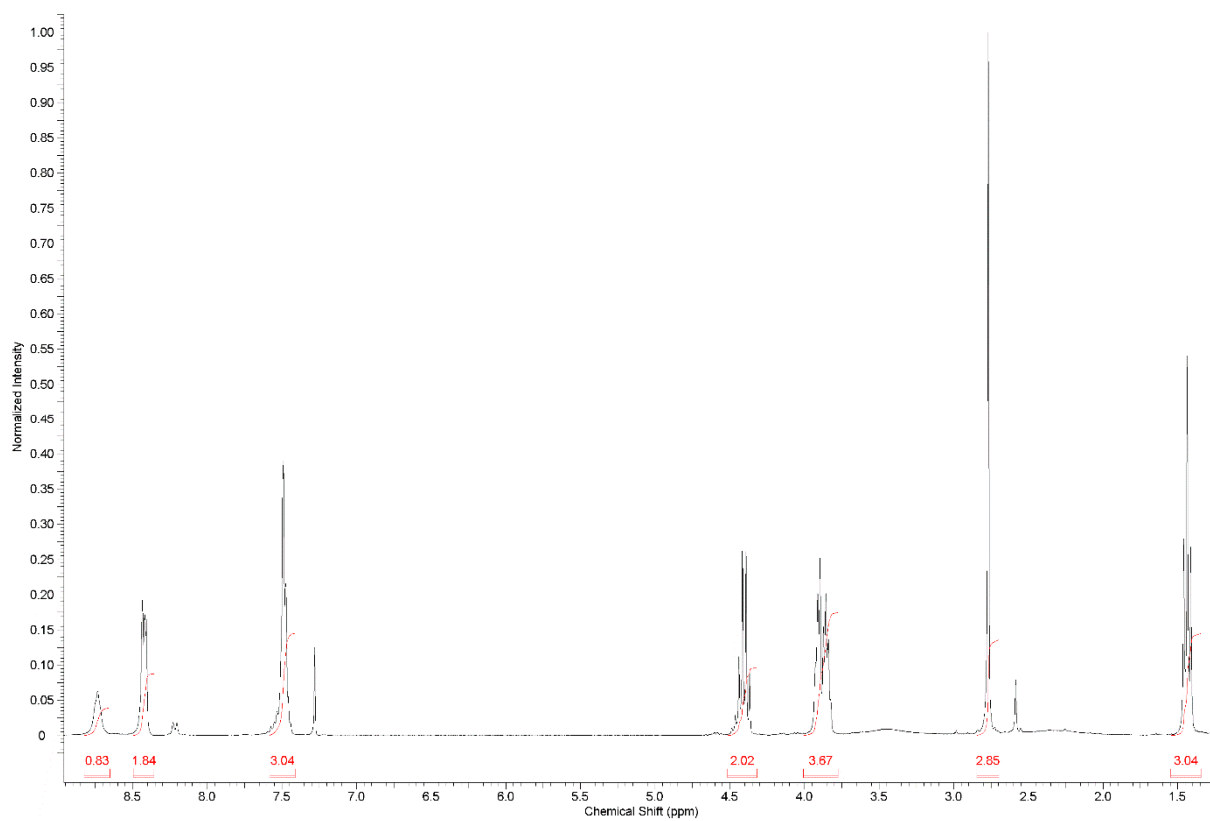
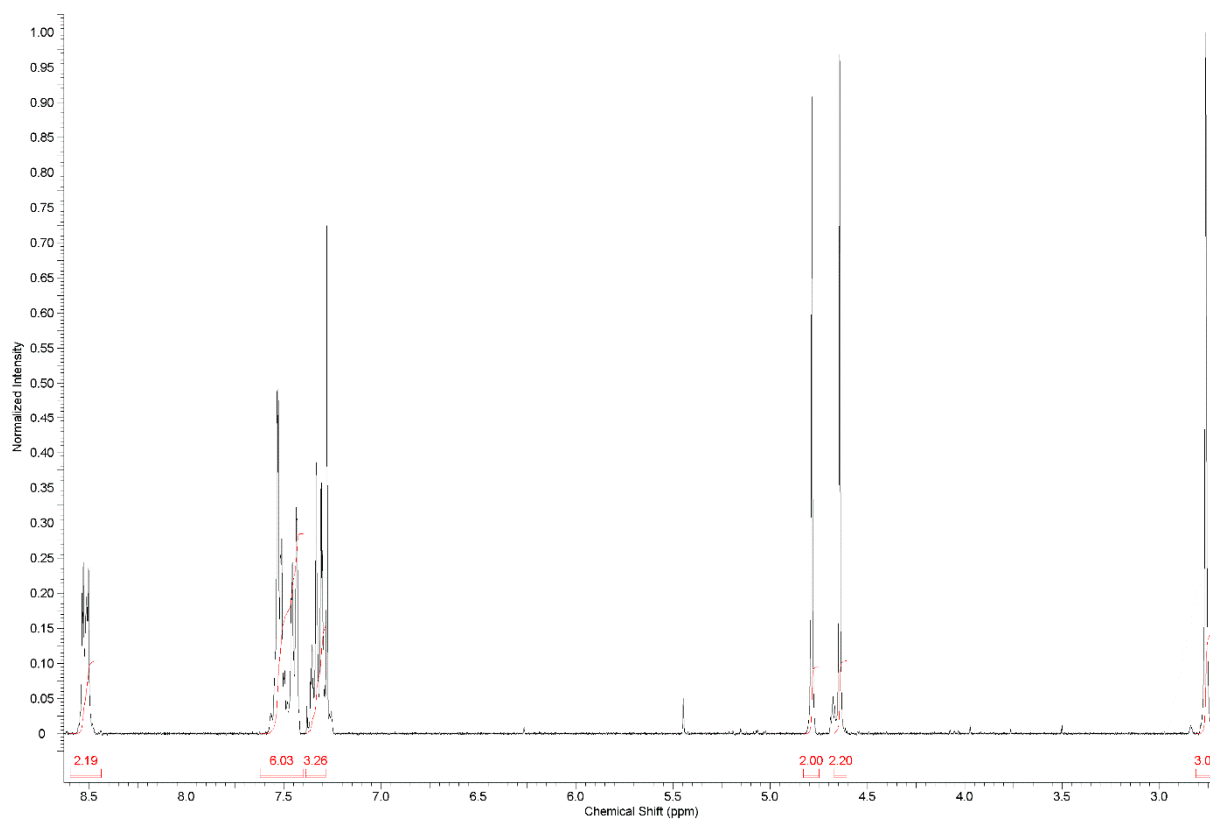
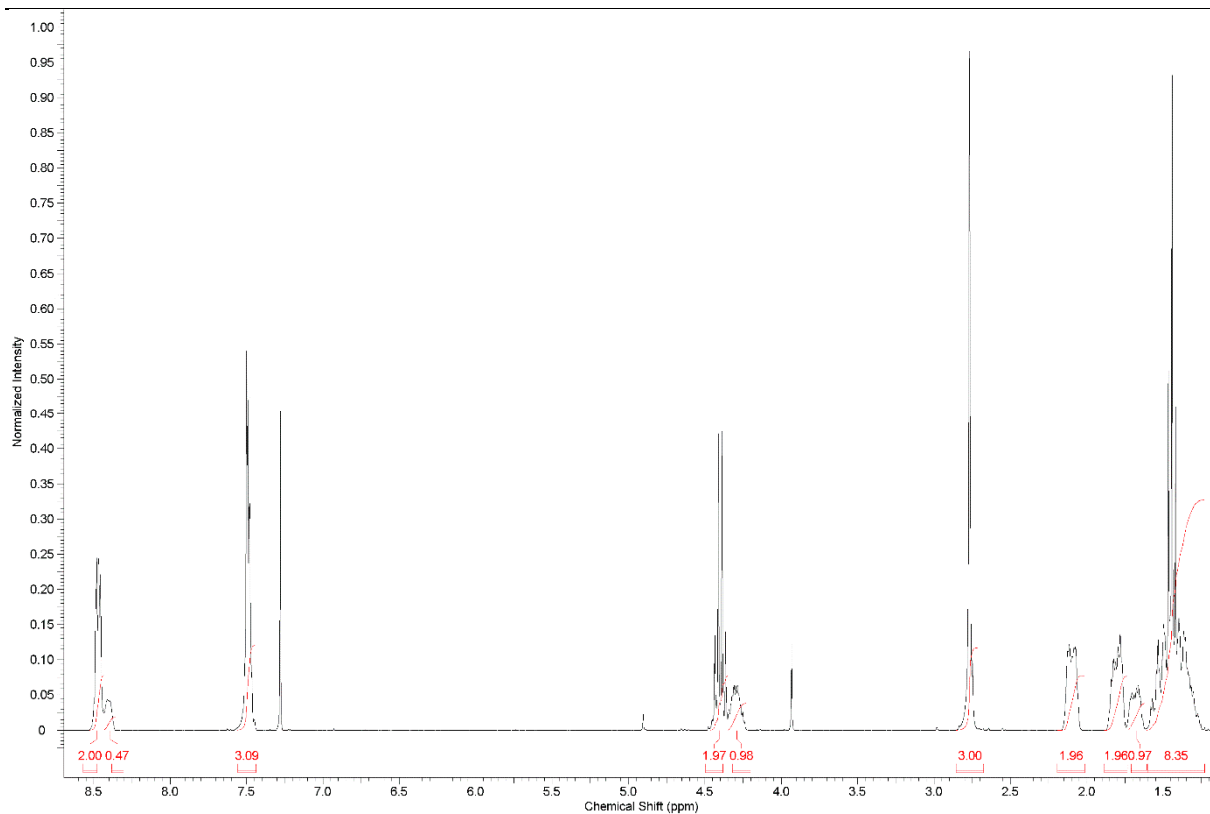


Figure S9. ¹H NMR spectrum of compound **2i** (300MHz, CDCl₃).



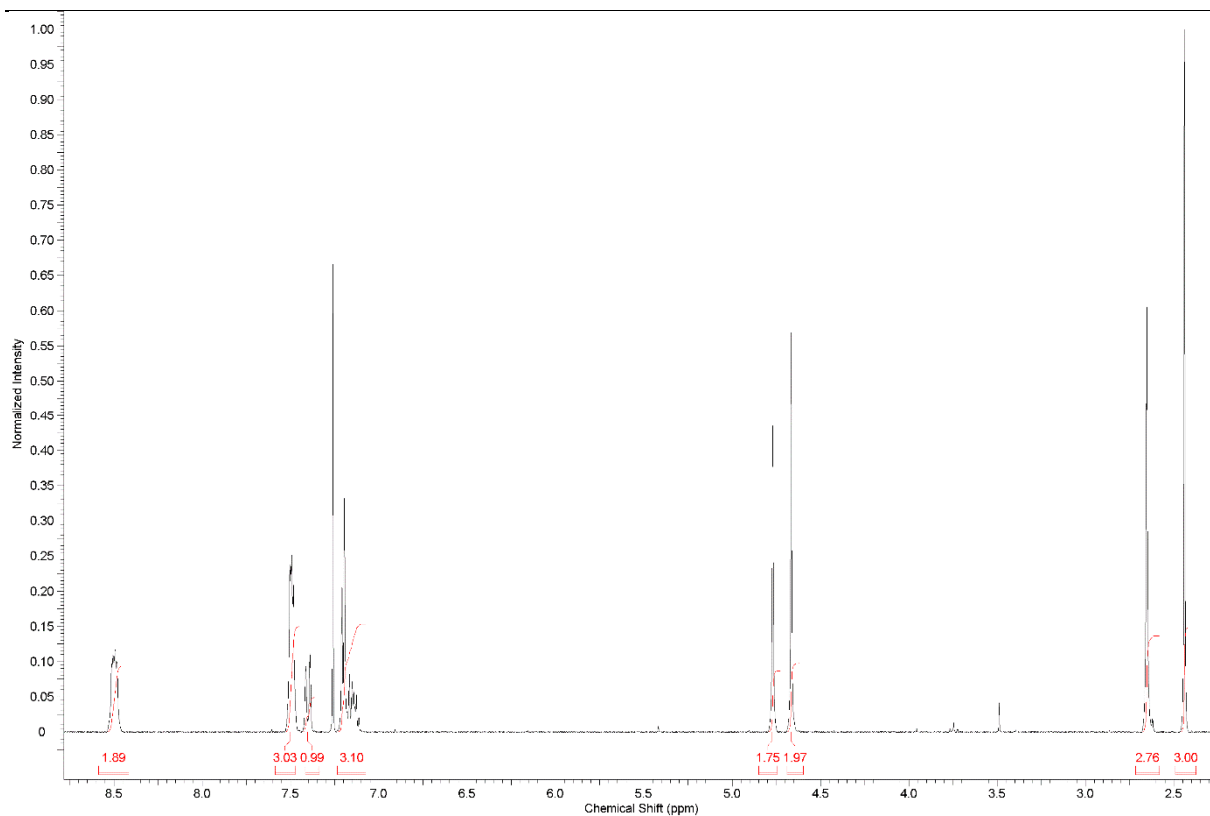


Figure S12. ^1H NMR spectrum of compound **3b** (300MHz, CDCl_3).

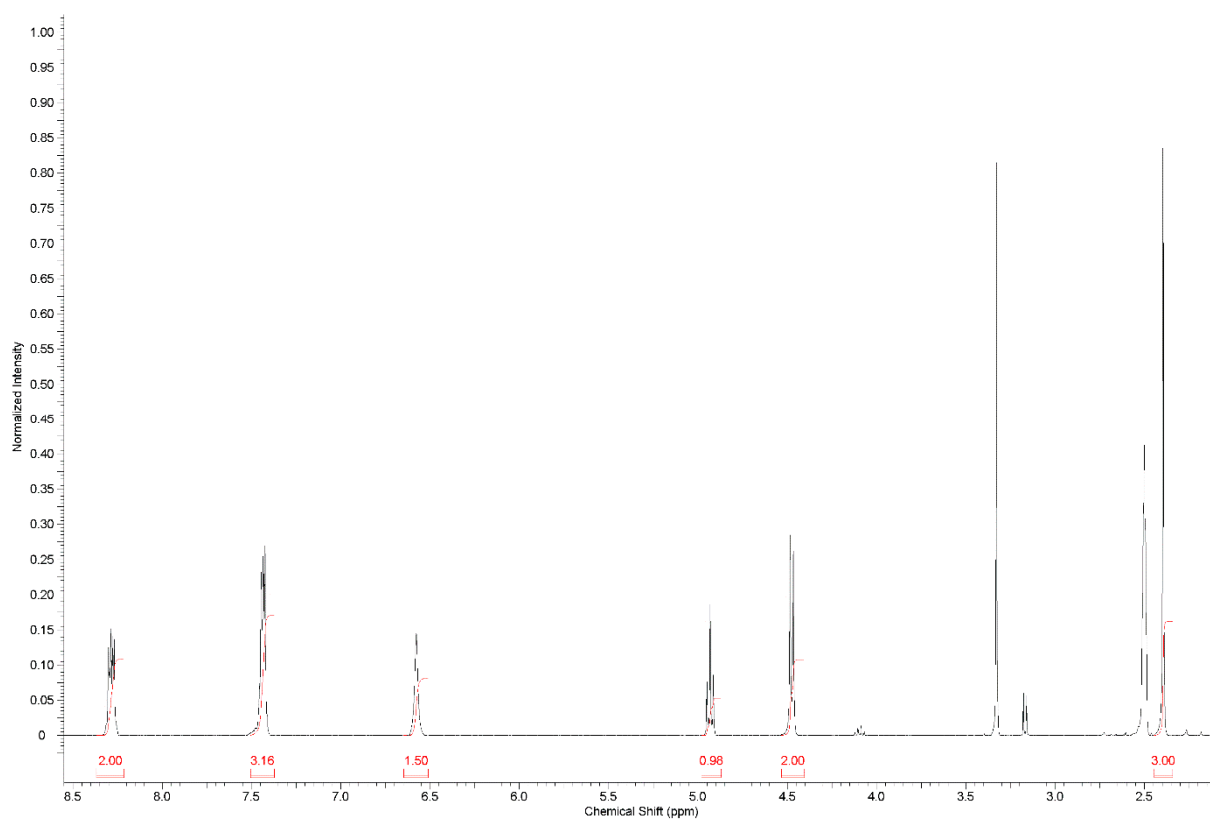


Figure S13. ^1H NMR spectrum of compound **3c** (300MHz, DMSO-d_6).

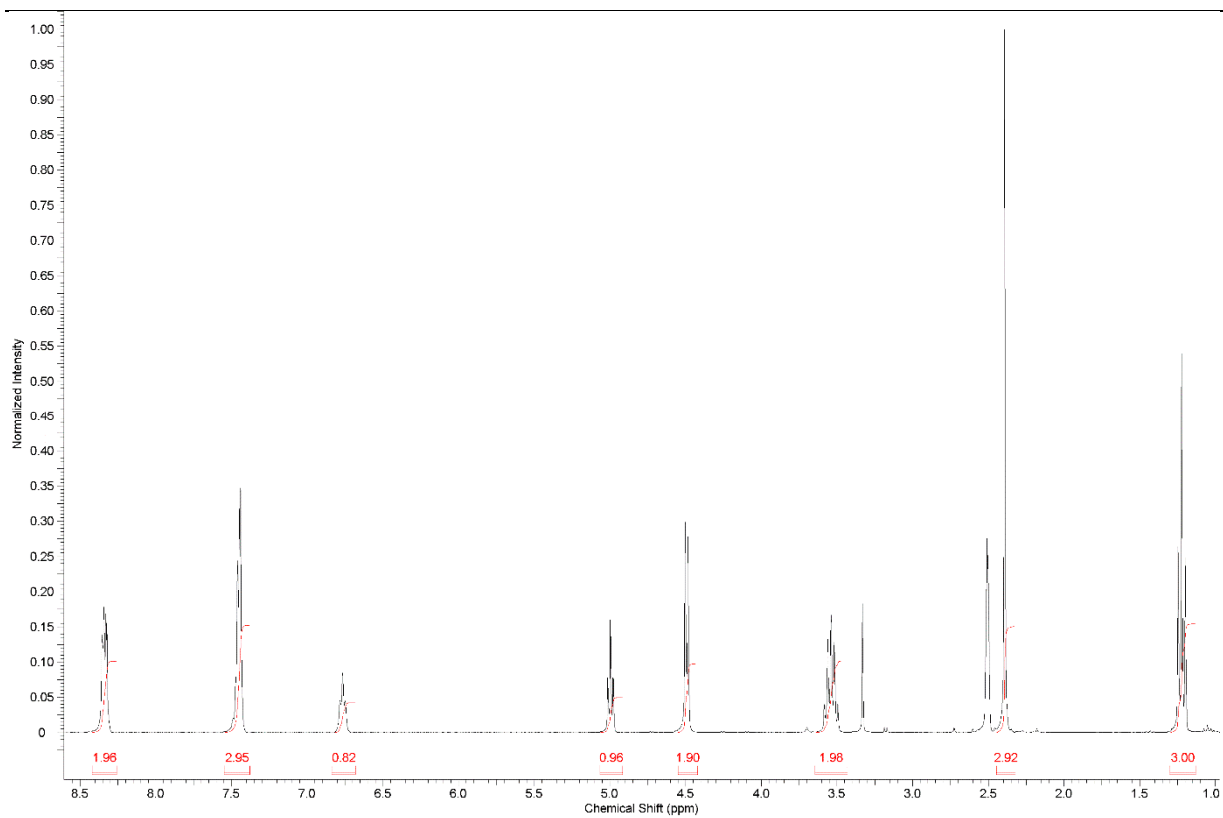


Figure S14. ^1H NMR spectrum of compound **3d** (300MHz, DMSO- d_6).

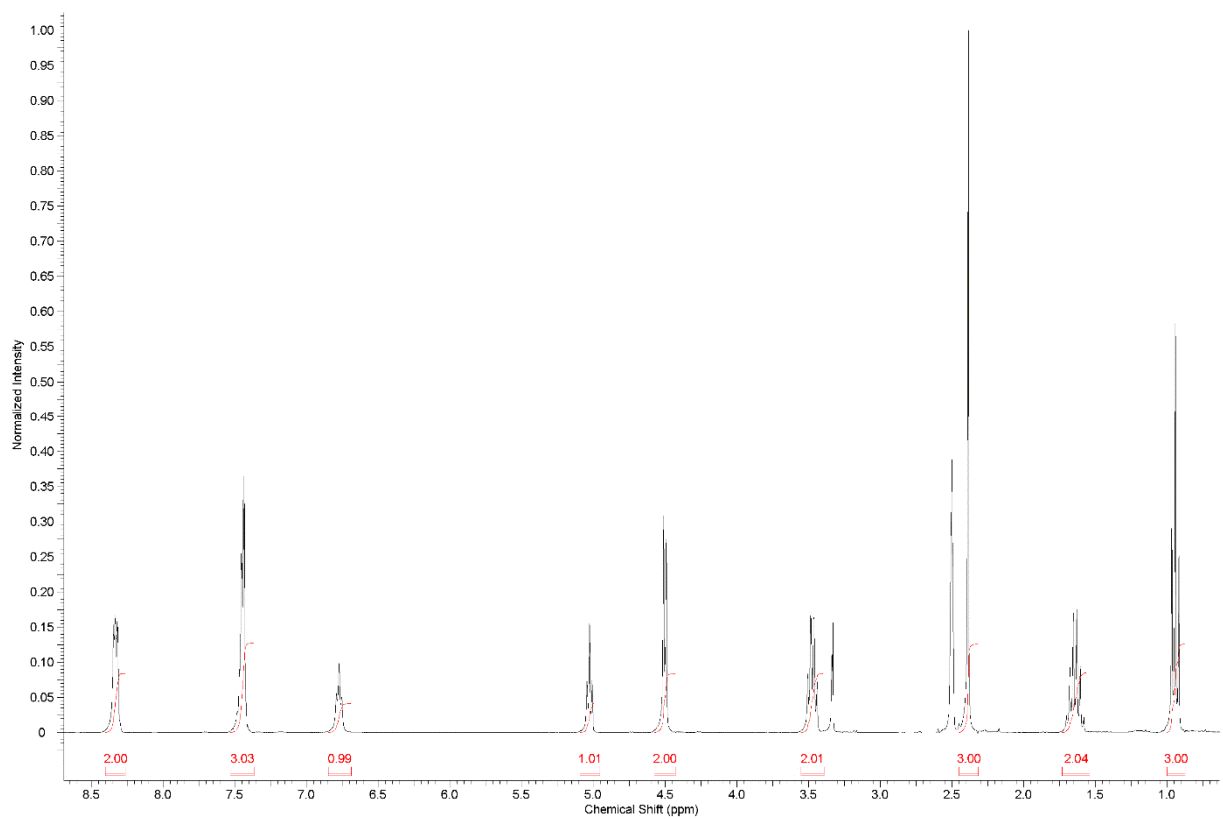


Figure S15. ^1H NMR spectrum of compound **3e** (300MHz, DMSO- d_6).

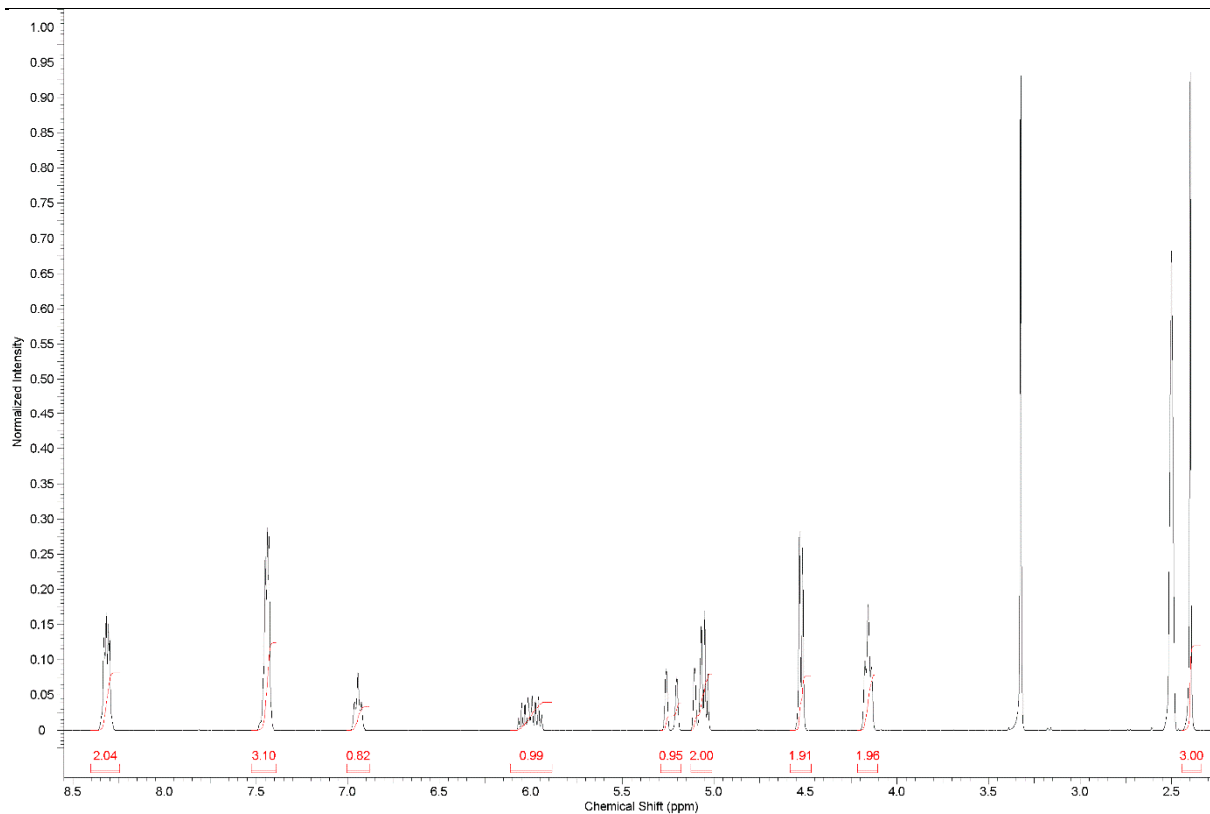


Figure S16. ^1H NMR spectrum of compound **3f** (300MHz, DMSO- d_6).

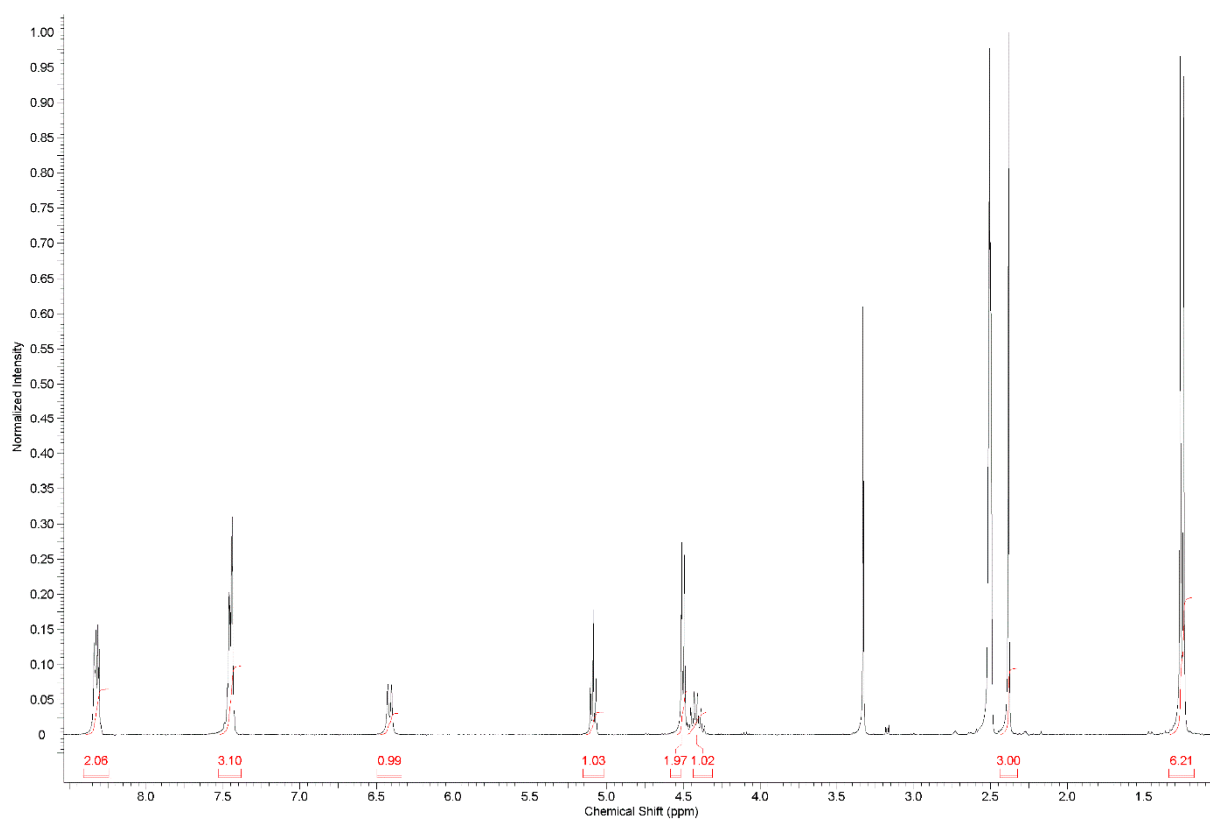


Figure S17. ^1H NMR spectrum of compound **3g** (300MHz, DMSO- d_6).

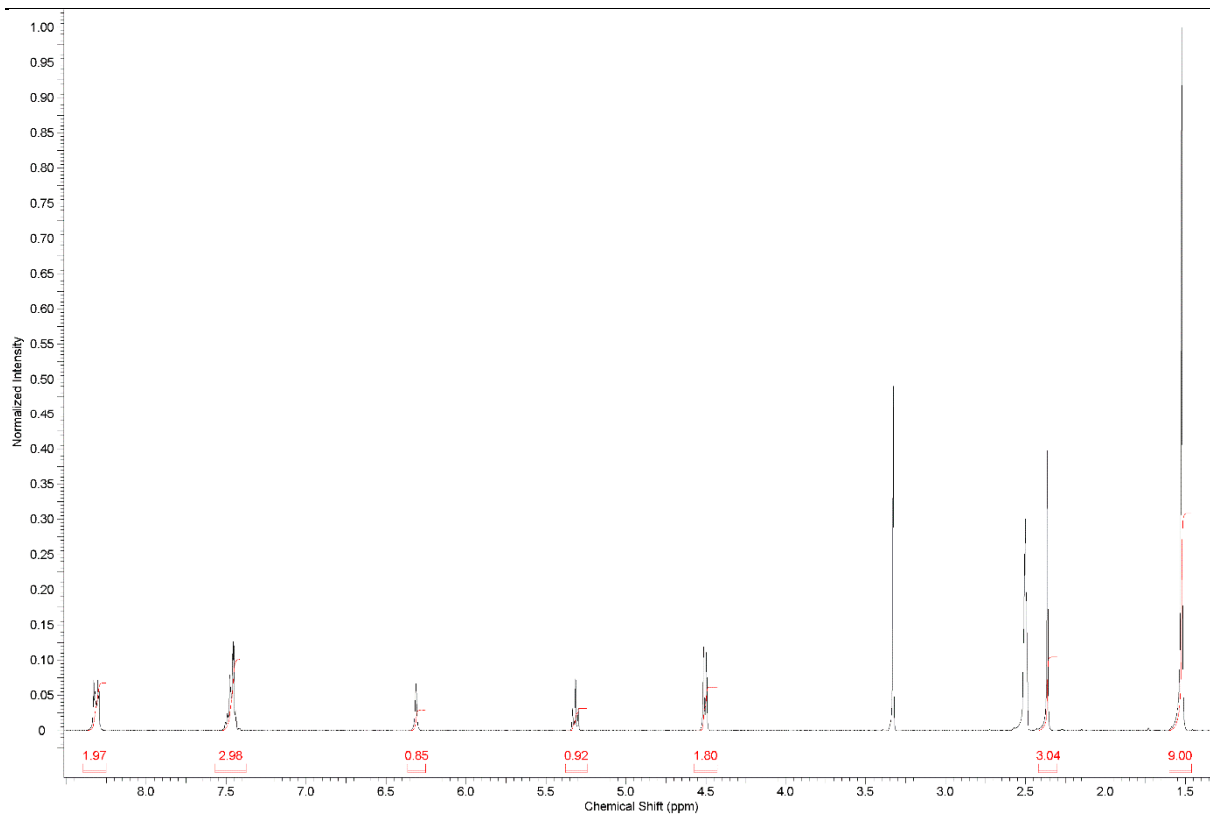


Figure S18. ^1H NMR spectrum of compound **3h** (300MHz, DMSO- d_6).

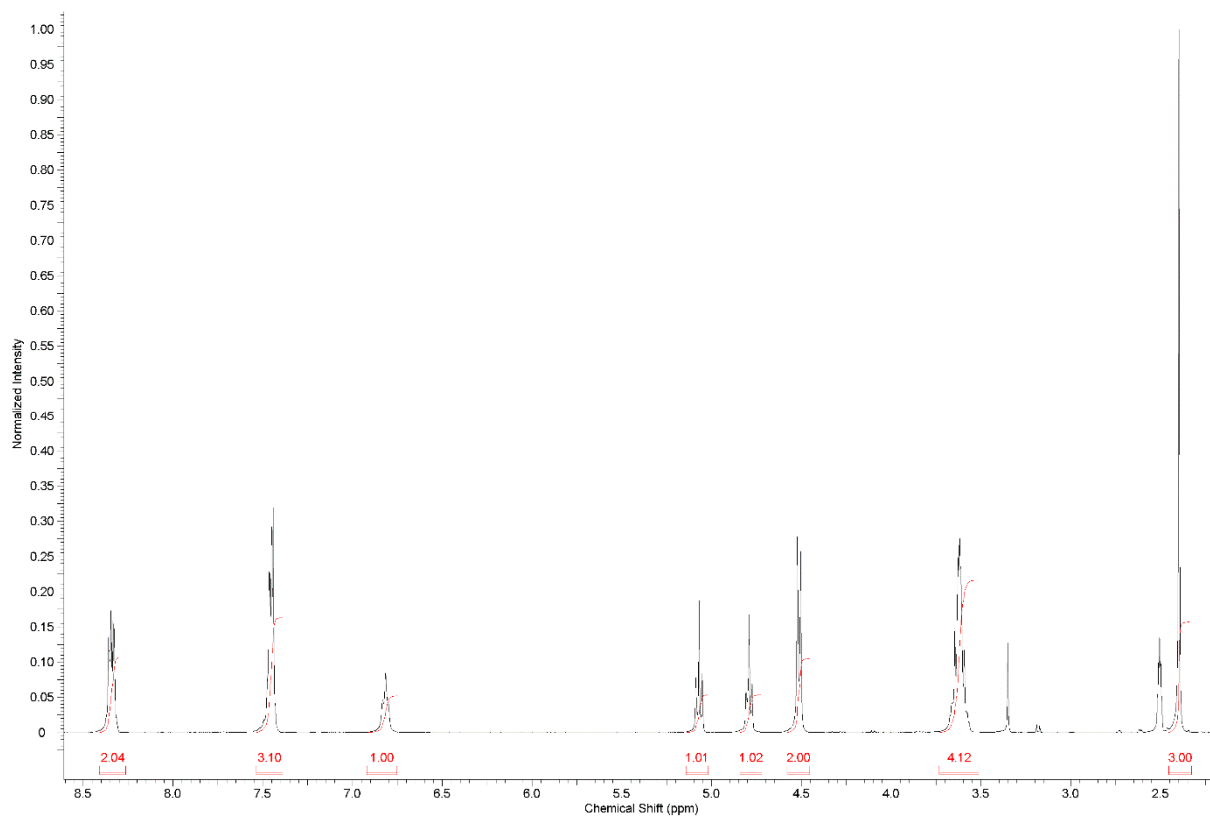


Figure S19. ^1H NMR spectrum of compound **3i** (300MHz, DMSO- d_6).

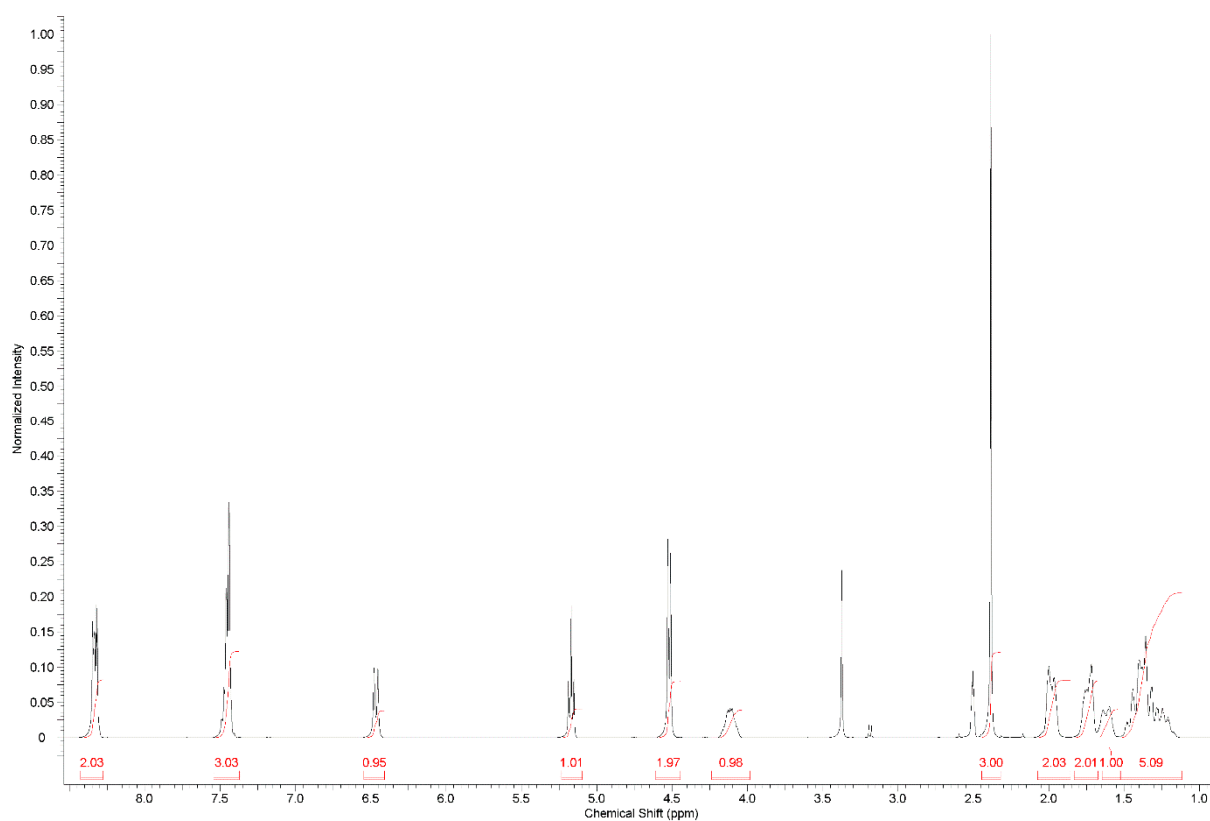


Figure S20. ¹H NMR spectrum of compound **3j** (300 MHz, DMSO-d₆).

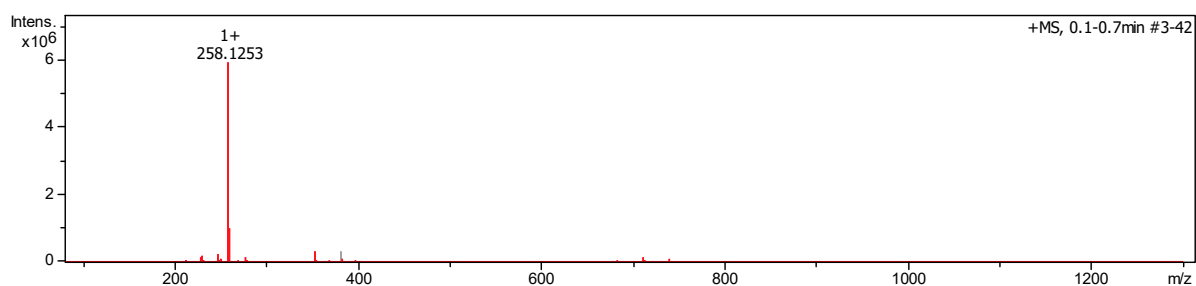


Figure S21. ESI-MS spectrum of compound **2a**.

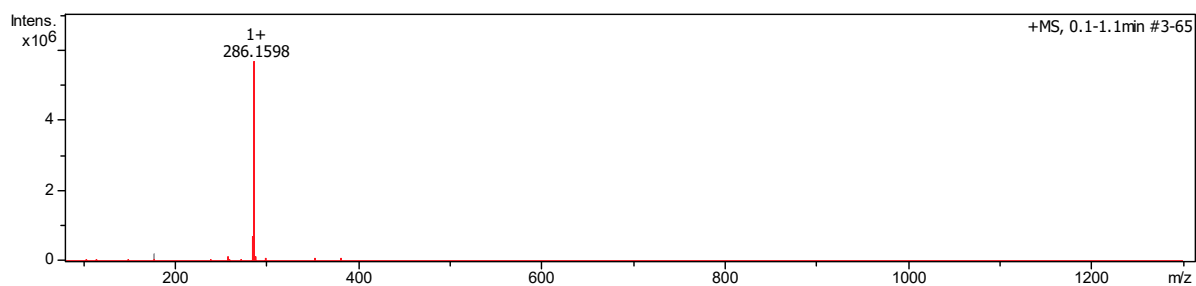


Figure S22. ESI-MS spectrum of compound **2b**.

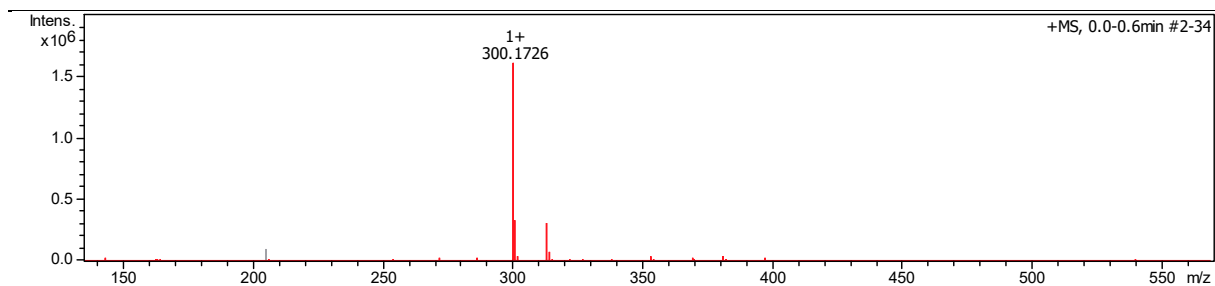


Figure S23. ESI-MS spectrum of compound **2c**.

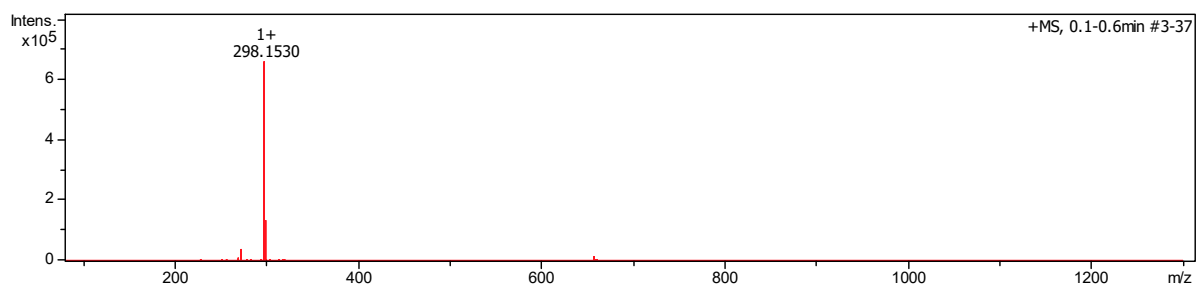


Figure S24. ESI-MS spectrum of compound **2d**.

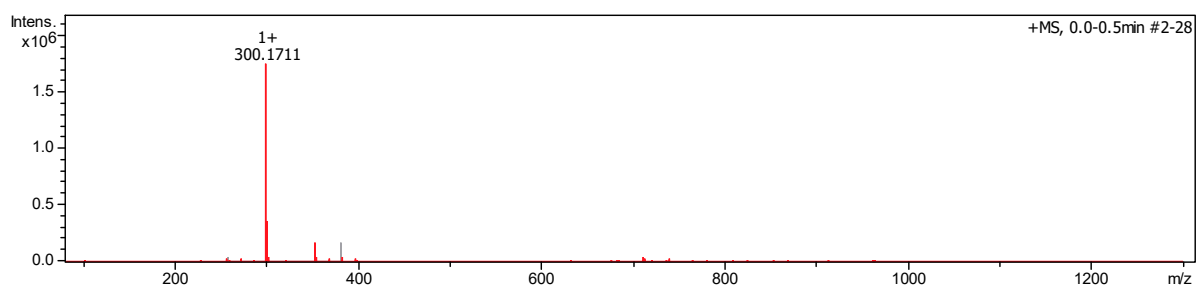


Figure S25. ESI-MS spectrum of compound **2e**.

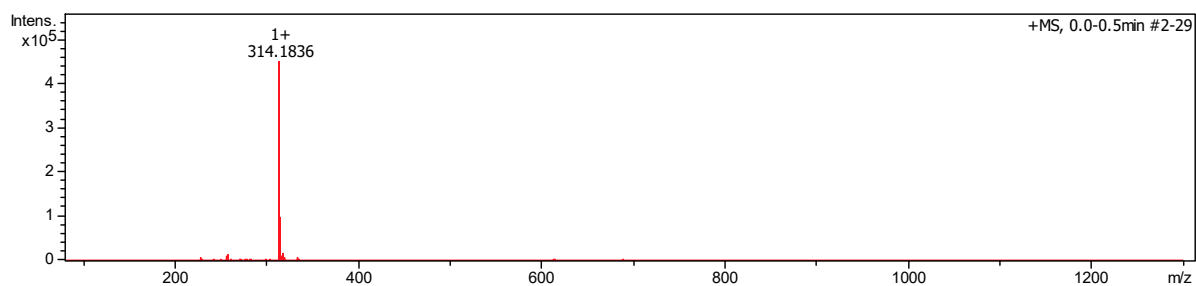


Figure S26. ESI-MS spectrum of compound **2f**.

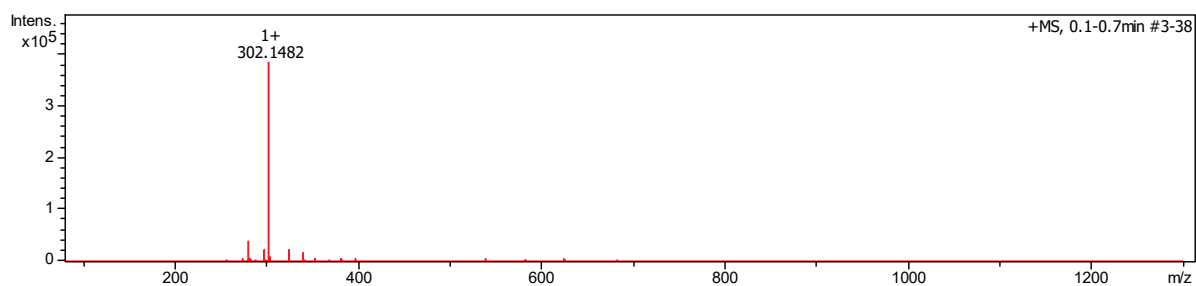


Figure S27. ESI-MS spectrum of compound **2g**.

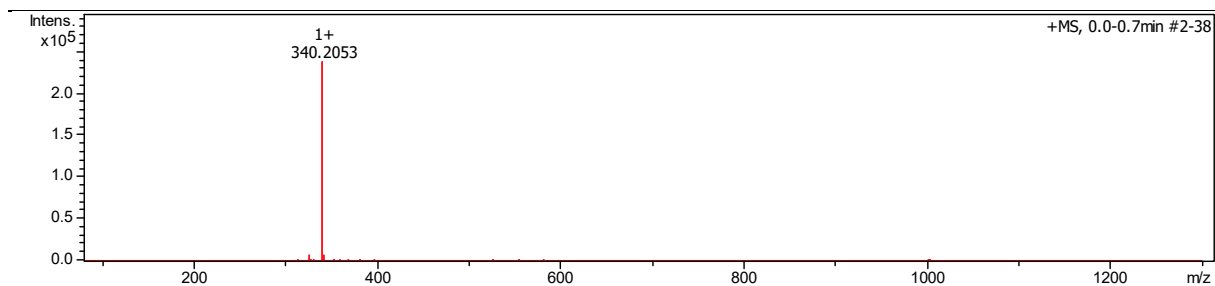


Figure S28. ESI-MS spectrum of compound 2h.

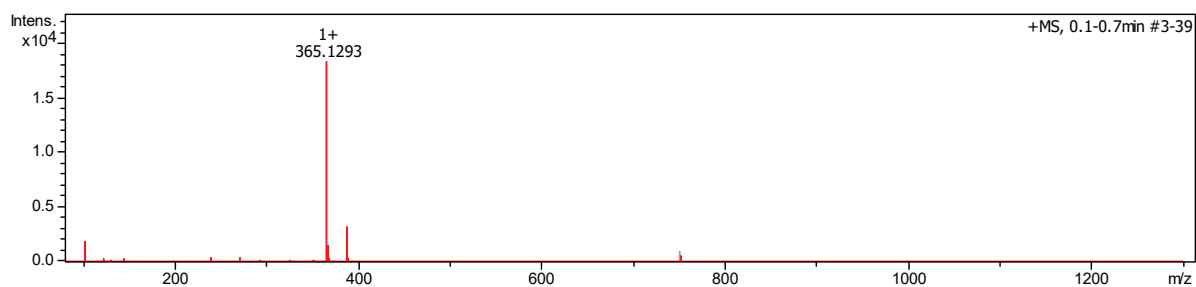


Figure S29. ESI-MS spectrum of compound 2i.

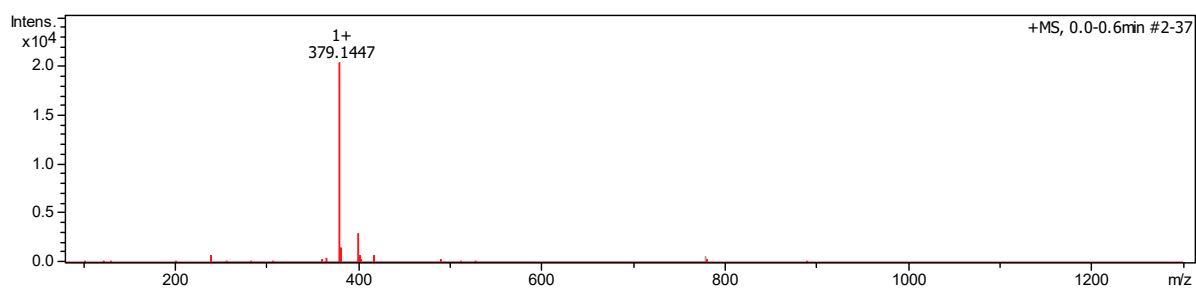


Figure S30. ESI-MS spectrum of compound 2j.

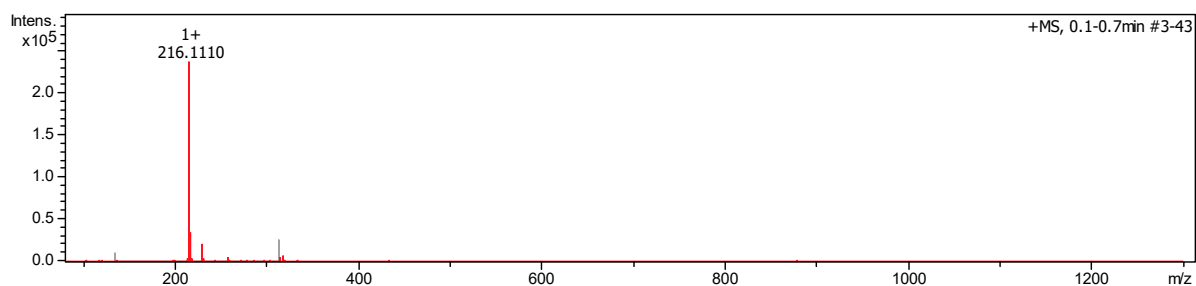


Figure S31. ESI-MS spectrum of compound 3a.

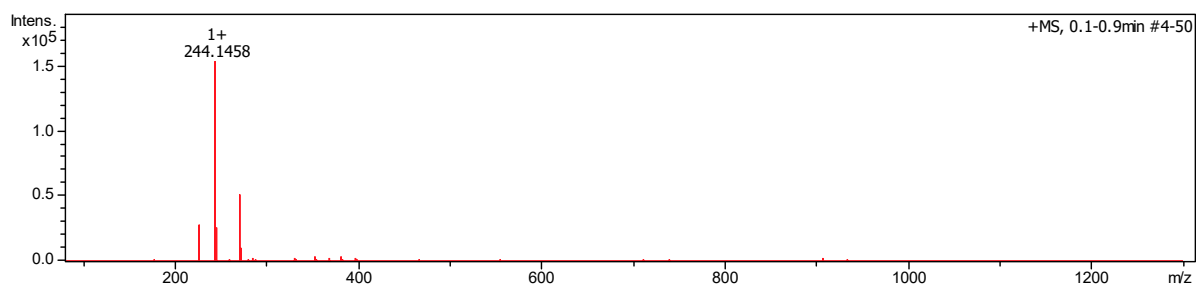


Figure S32. ESI-MS spectrum of compound 3b.

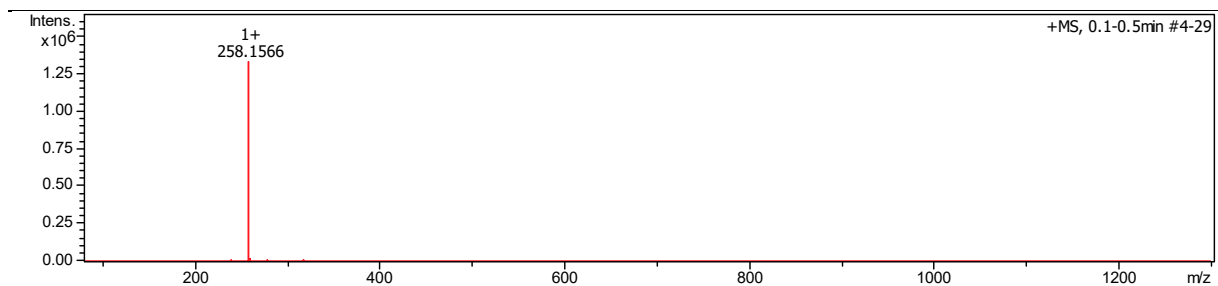


Figure S33. ESI-MS spectrum of compound **3c**.

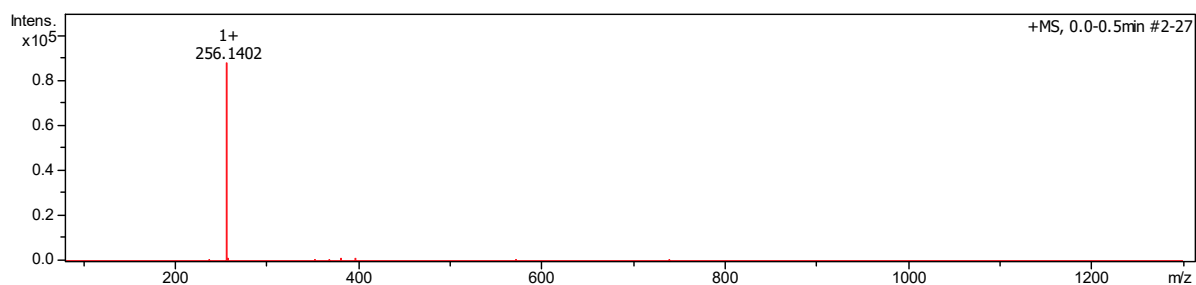


Figure S34. ESI-MS spectrum of compound **3d**.

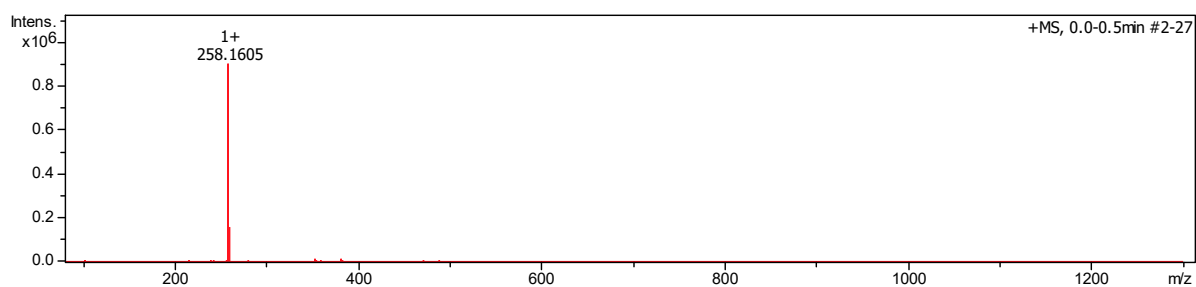


Figure S35. ESI-MS spectrum of compound **3e**.

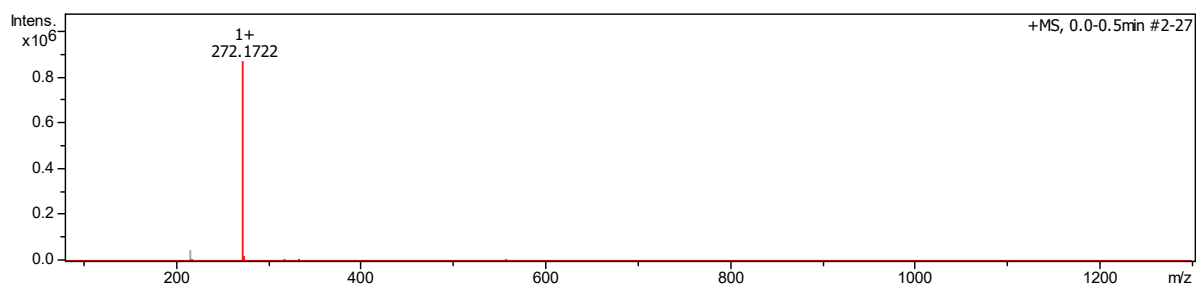


Figure S36. ESI-MS spectrum of compound **3f**.

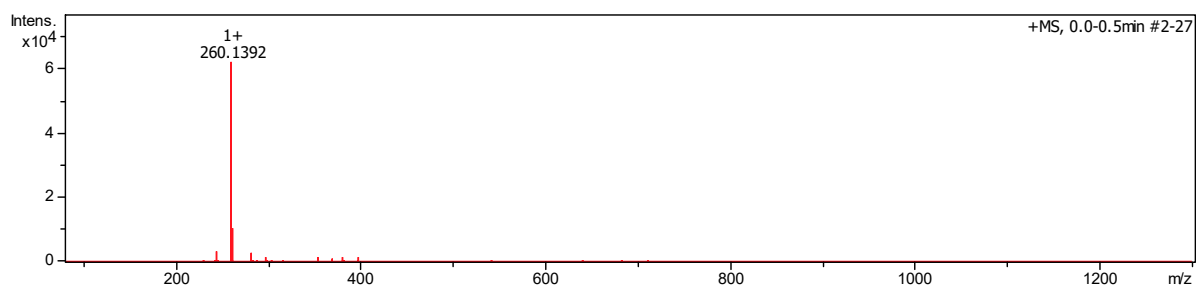


Figure S37. ESI-MS spectrum of compound **3g**.

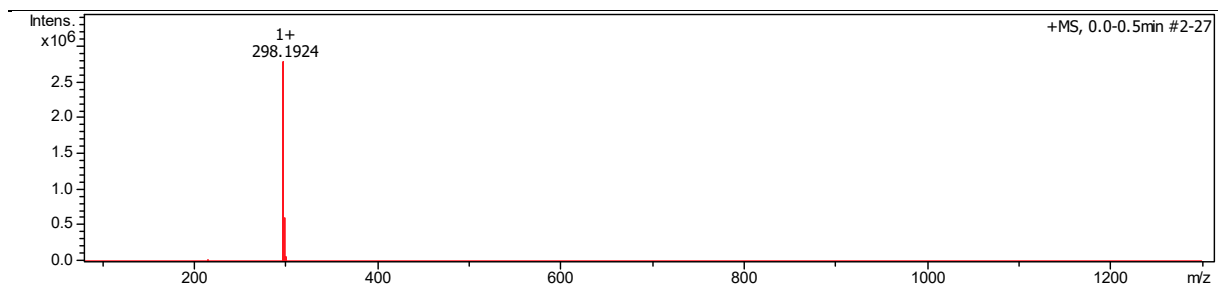


Figure S38. ESI-MS spectrum of compound 3h.

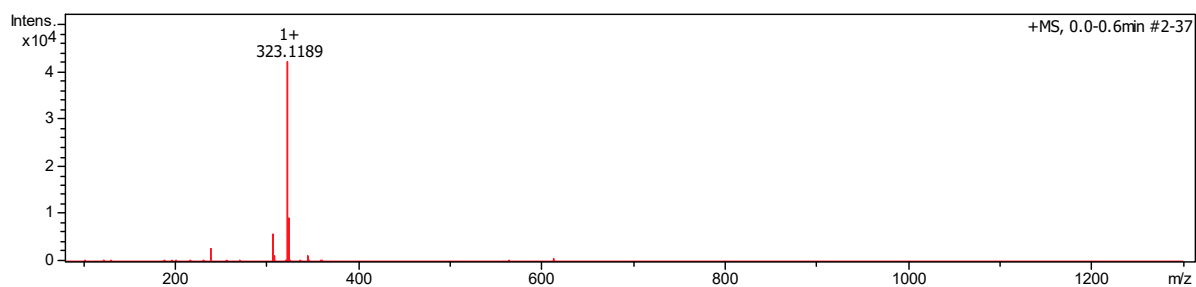


Figure S39. ESI-MS spectrum of compound 3i.

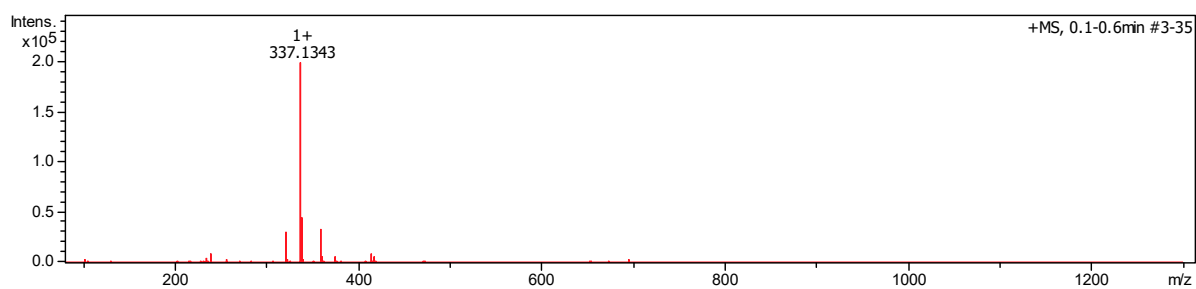


Figure S40. ESI-MS spectrum of compound 3j.

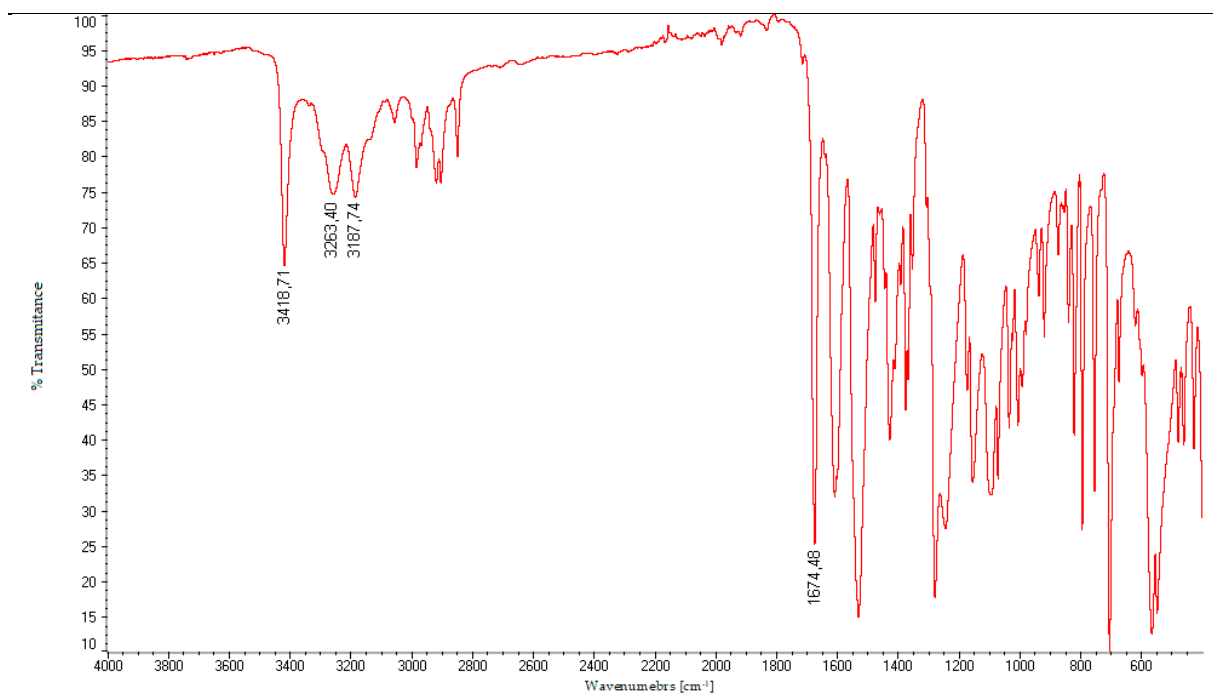


Figure S41. IR spectrum of compound 2a.

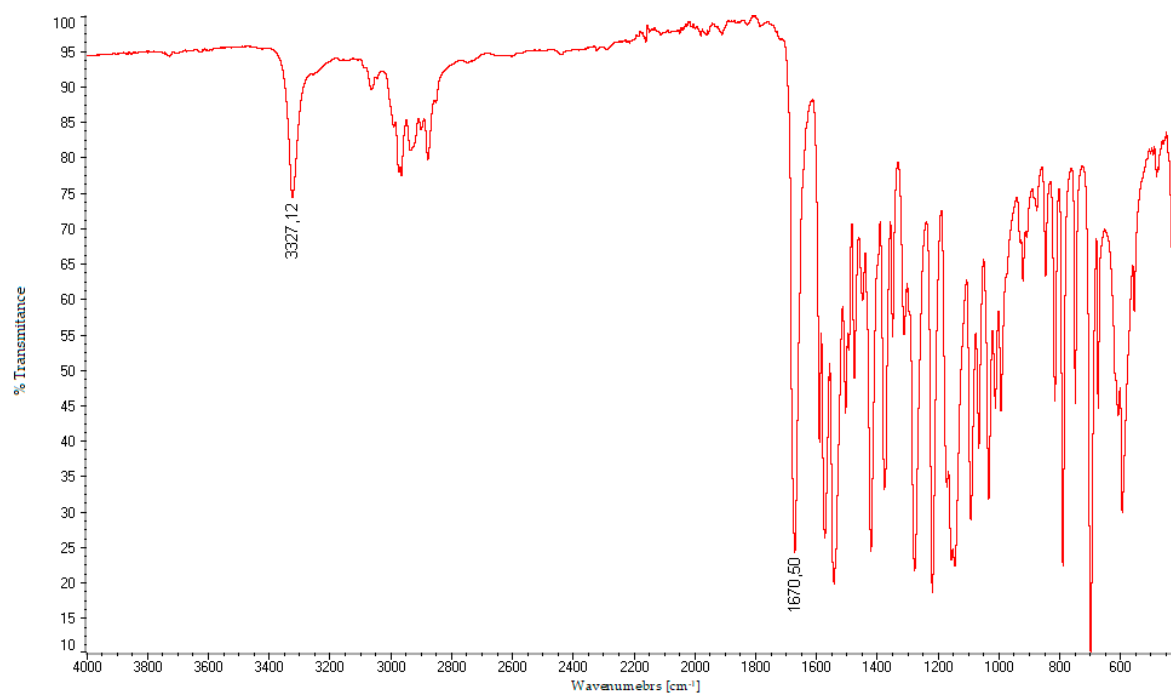


Figure S42. IR spectrum of compound 2b.

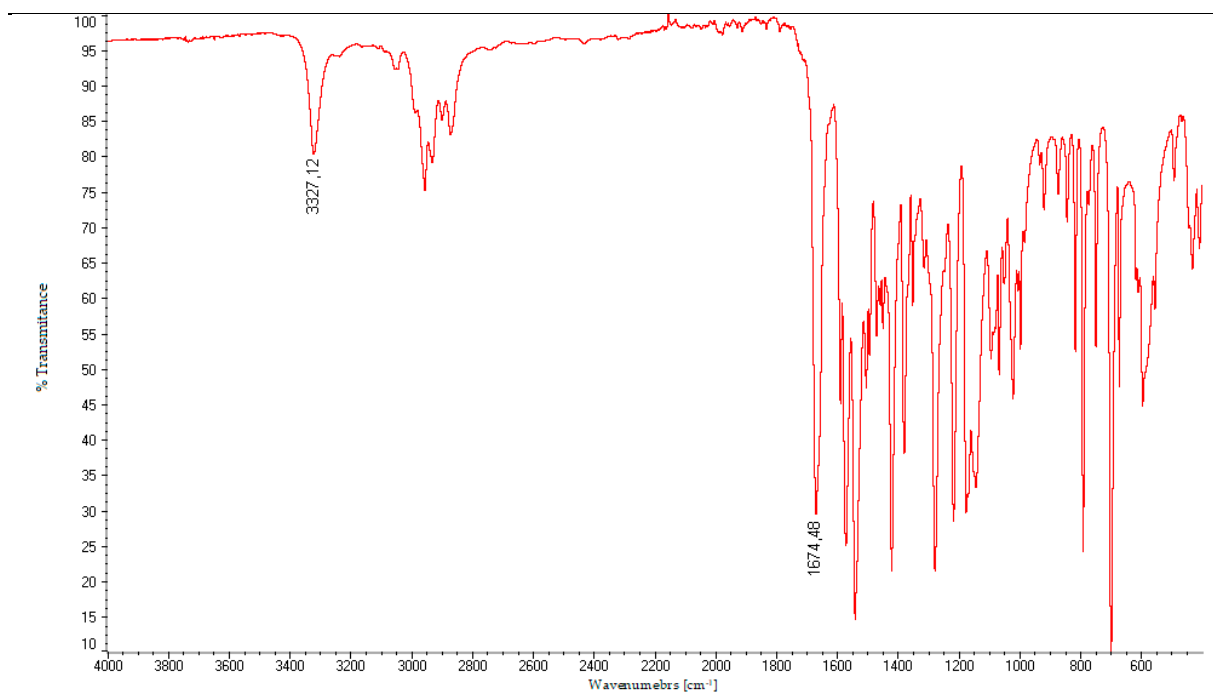


Figure S43. IR spectrum of compound 2c.

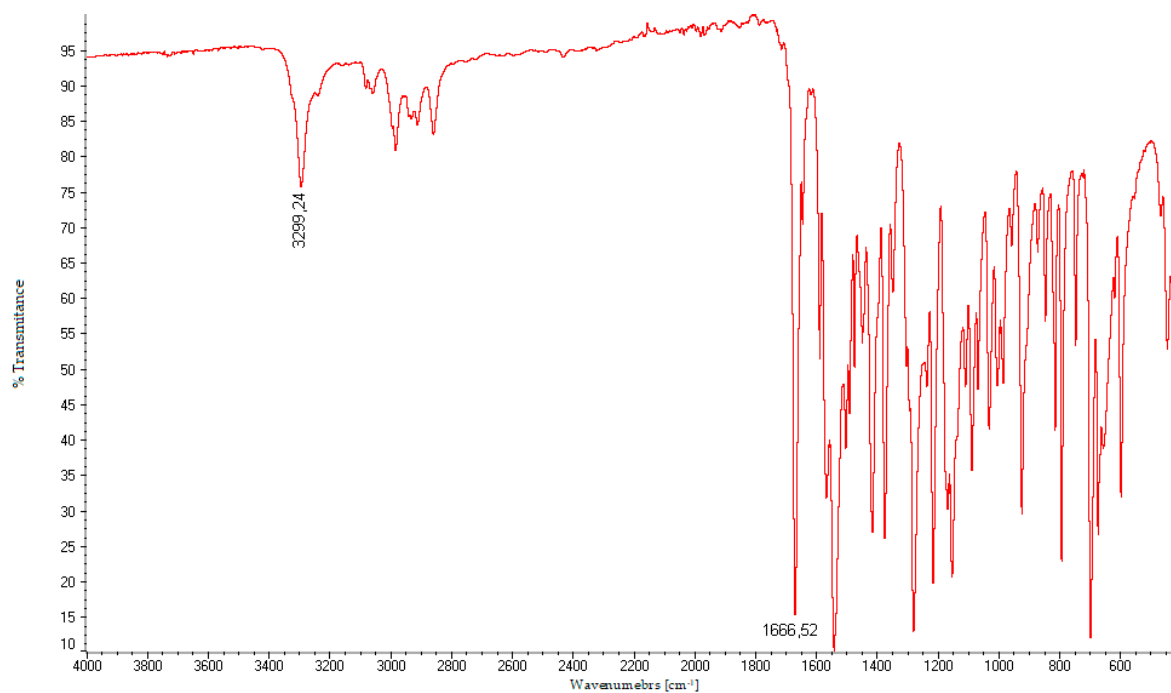


Figure S44. IR spectrum of compound 2d.

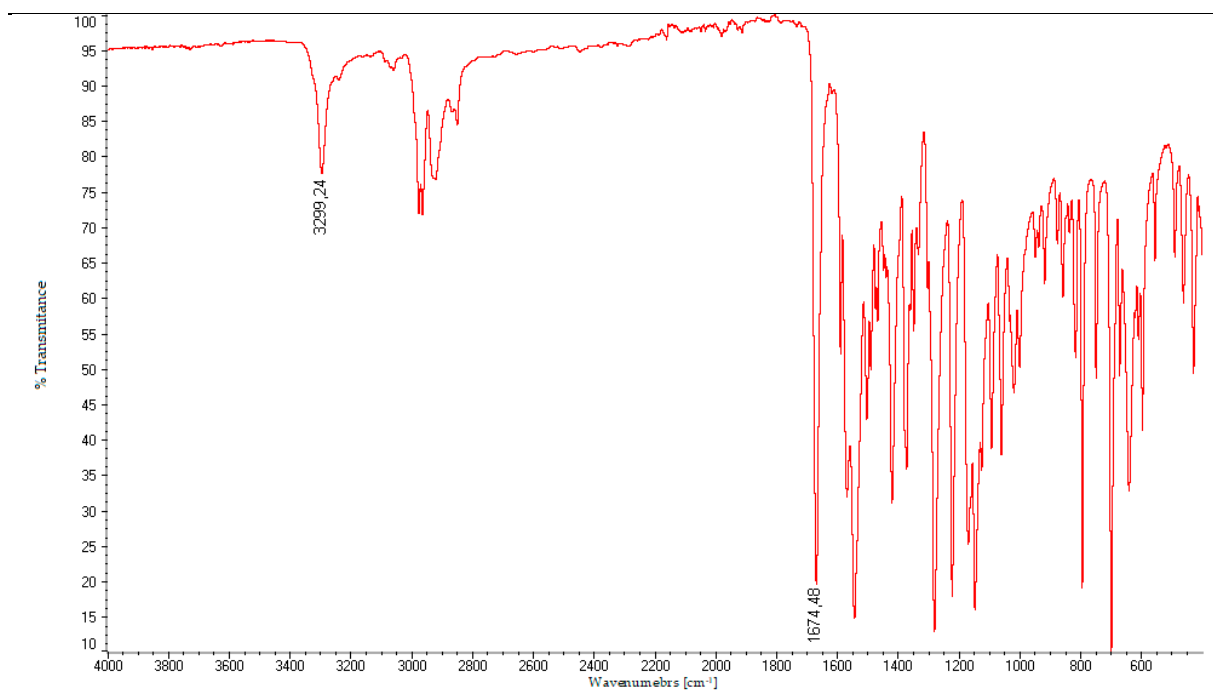


Figure S45. IR spectrum of compound 2e.

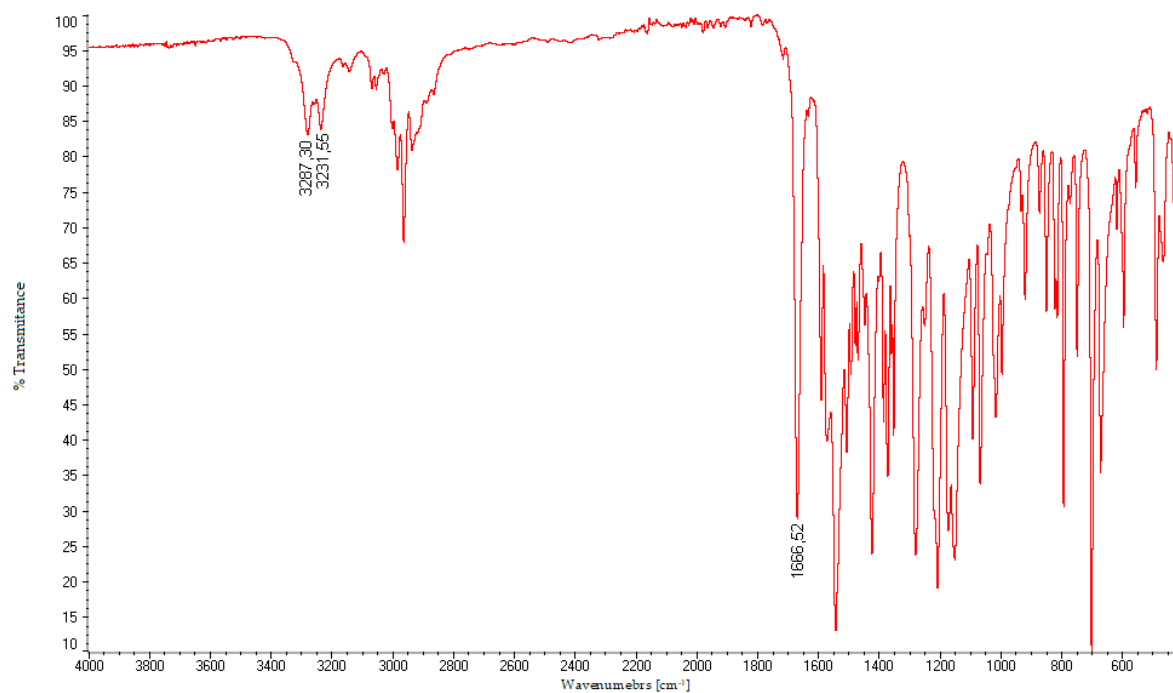


Figure S46. IR spectrum of compound 2f.

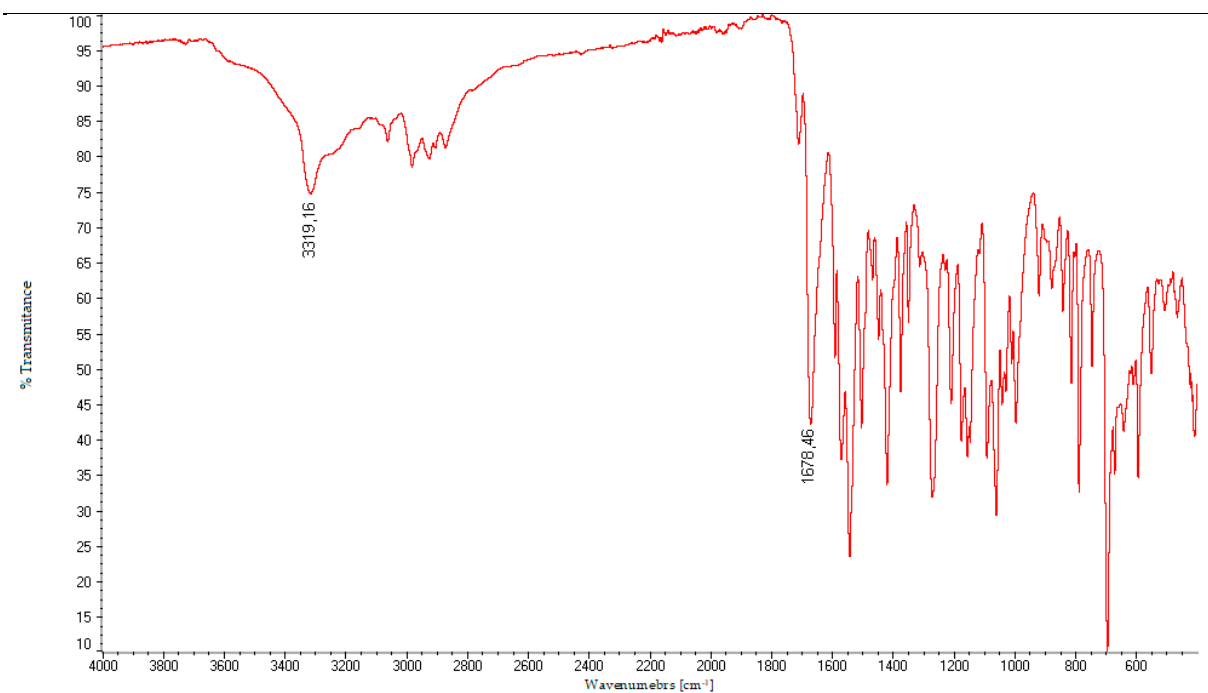


Figure S47. IR spectrum of compound 2g.

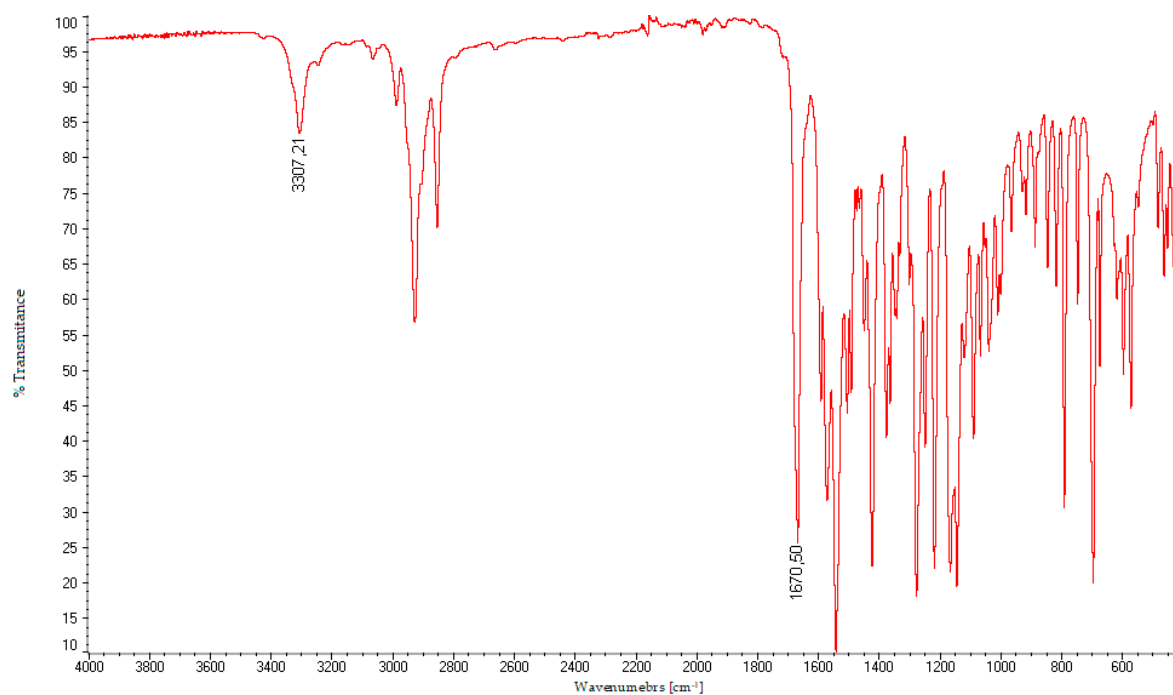


Figure S48. IR spectrum of compound 2h.

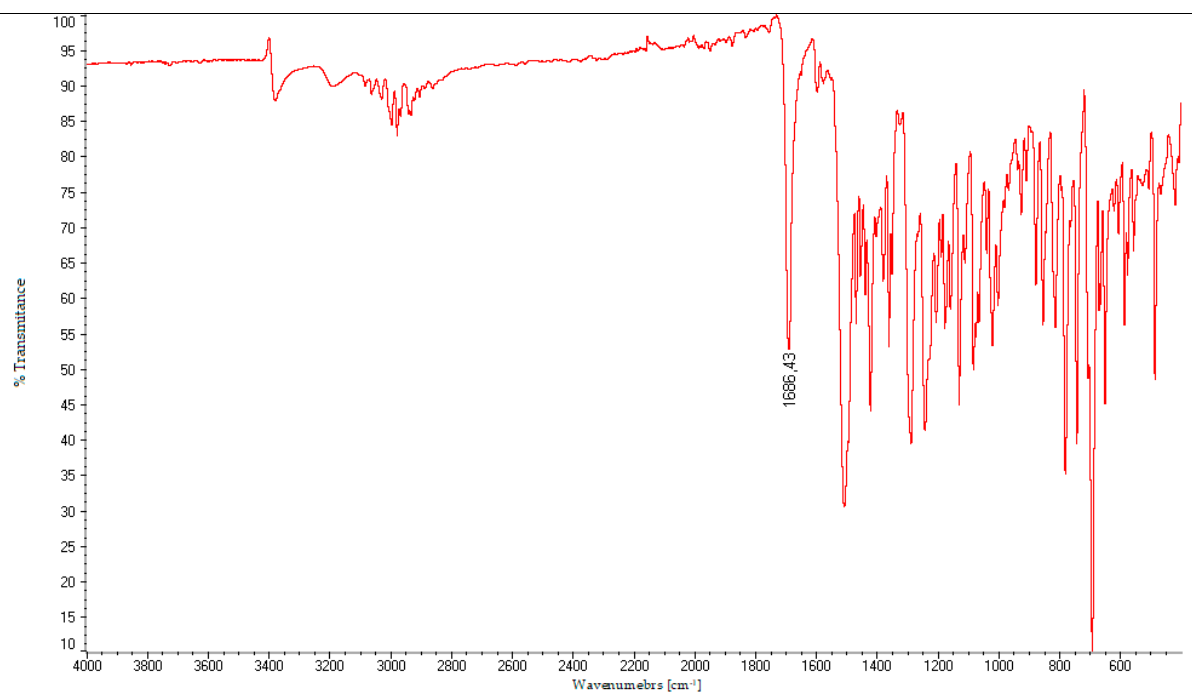


Figure S49. IR spectrum of compound 2i.

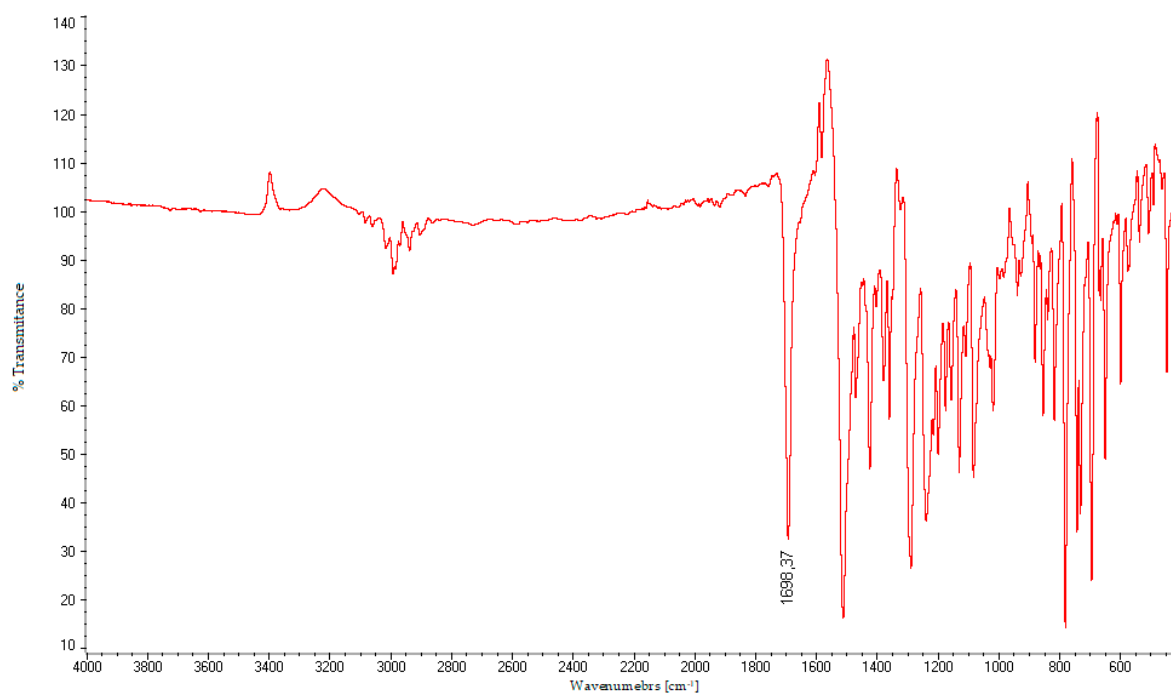


Figure S50. IR spectrum of compound 2j.

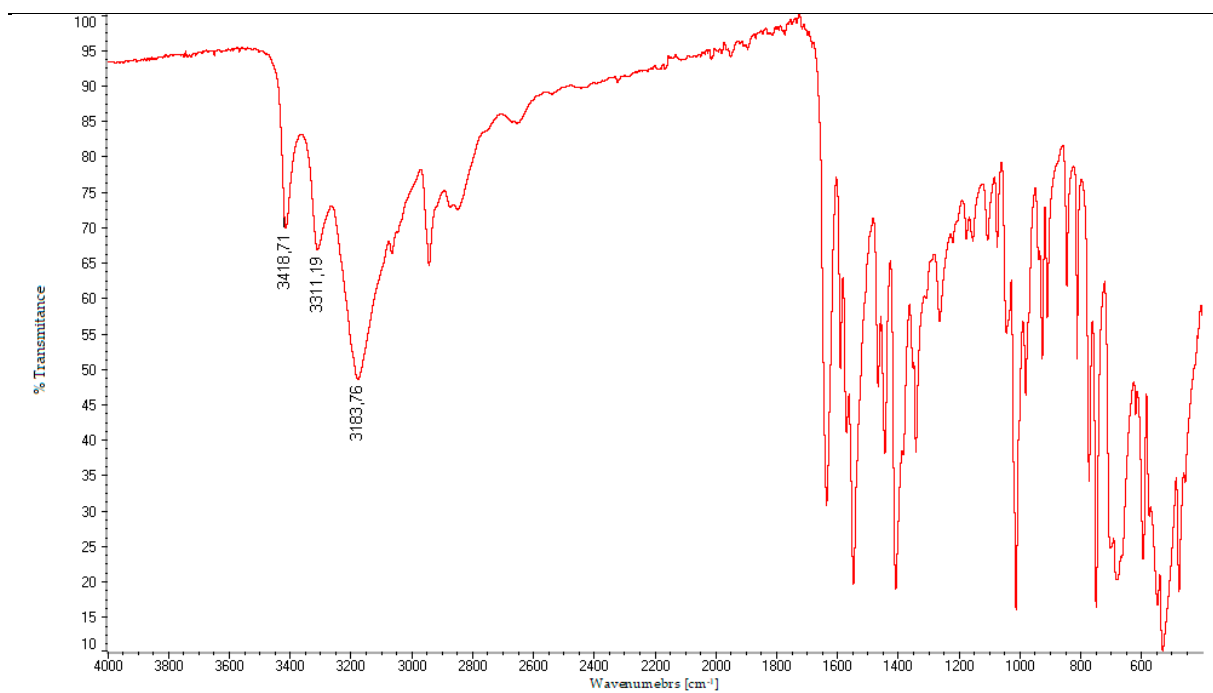


Figure S51. IR spectrum of compound 3a.

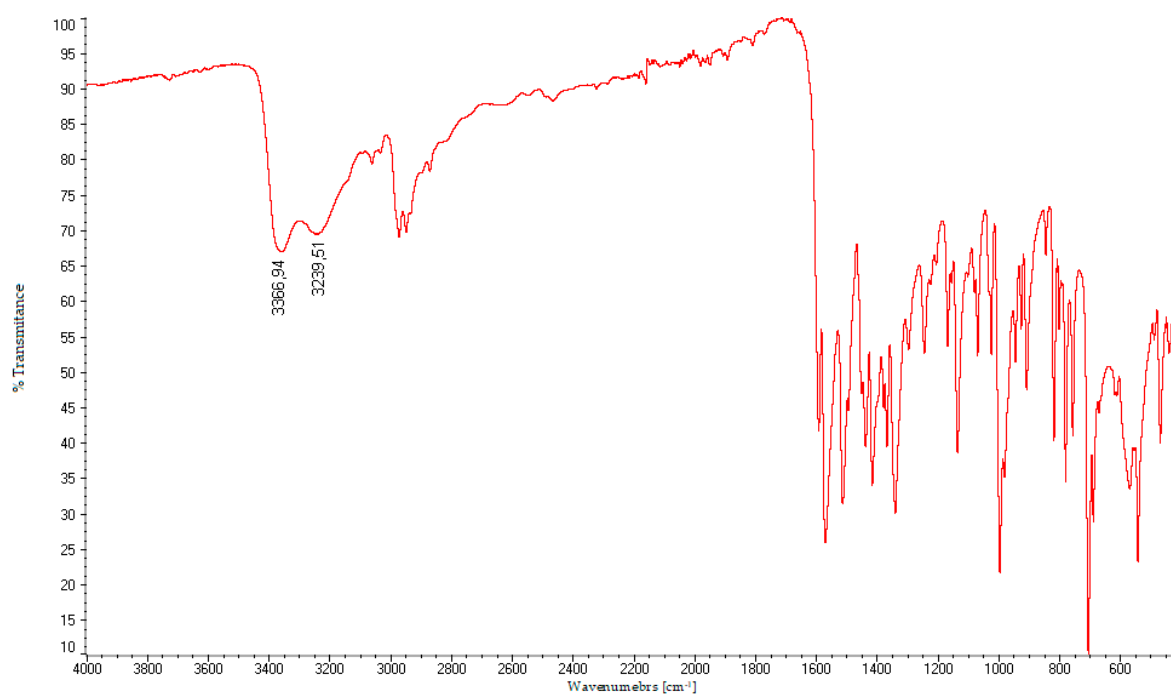


Figure S52. IR spectrum of compound 3b.

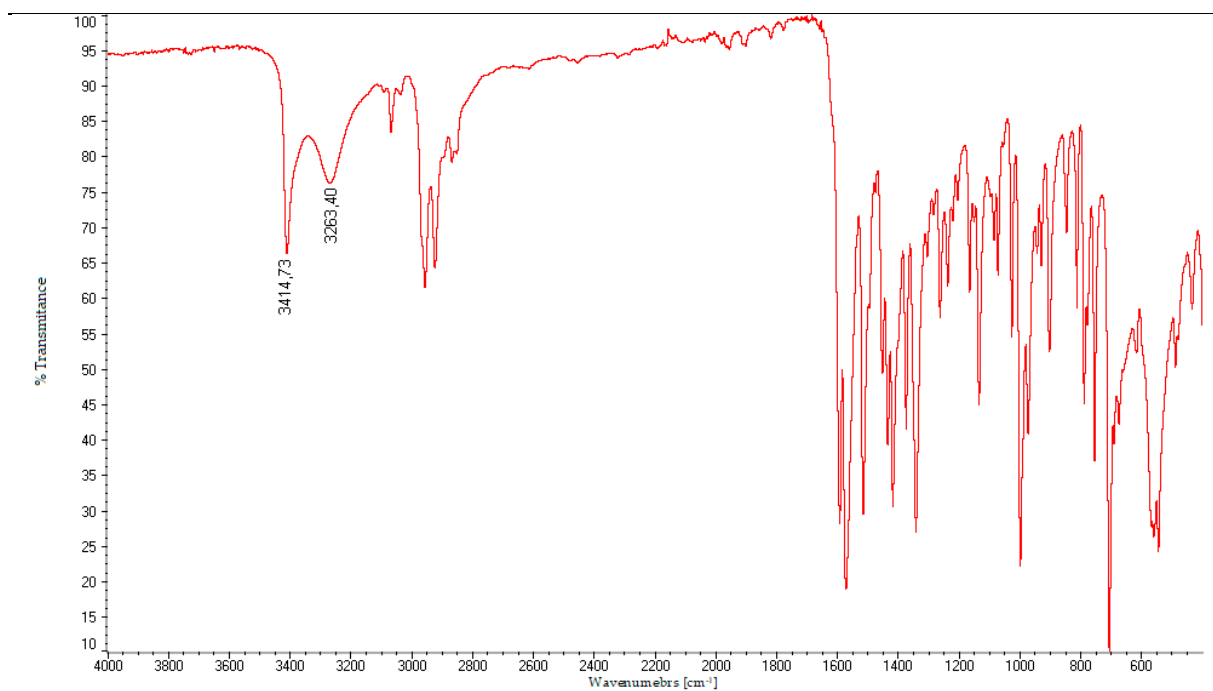


Figure S53. IR spectrum of compound 3c.

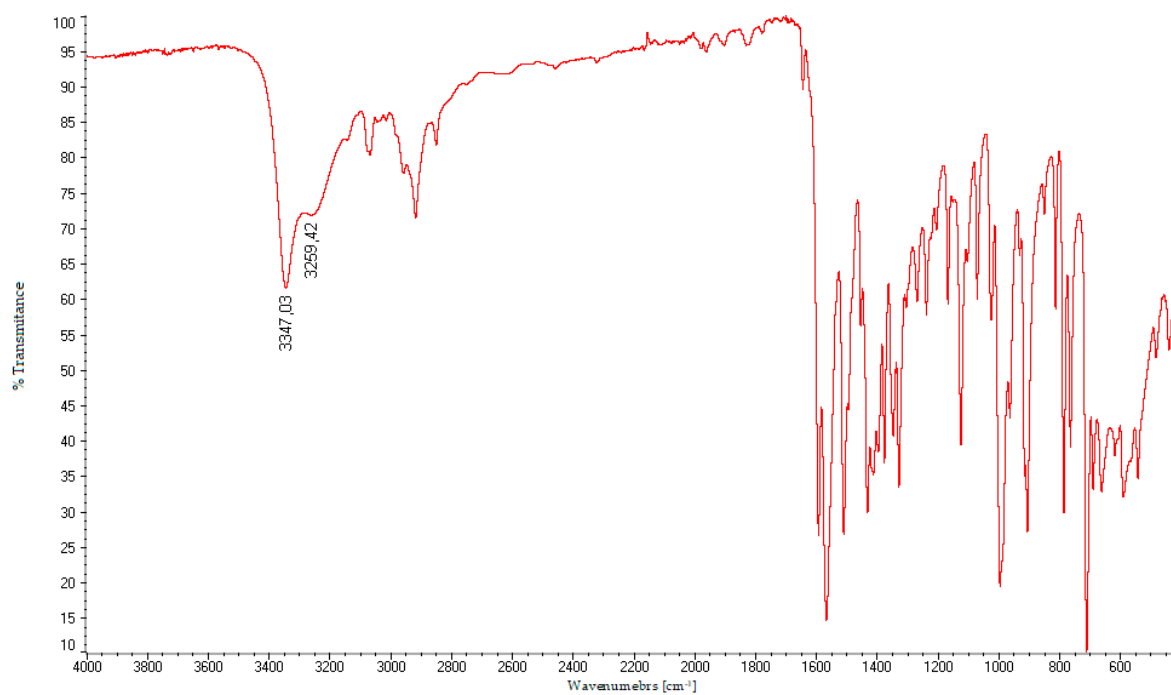


Figure S54. IR spectrum of compound 3d.

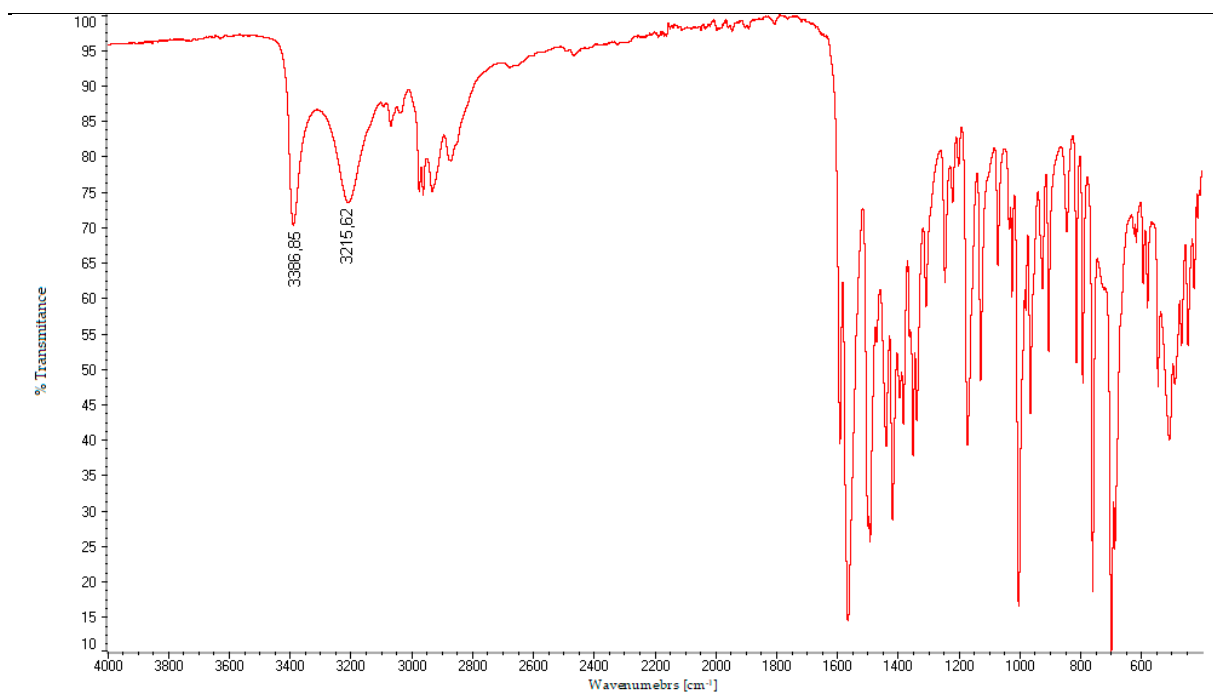


Figure S55. IR spectrum of compound 3e.

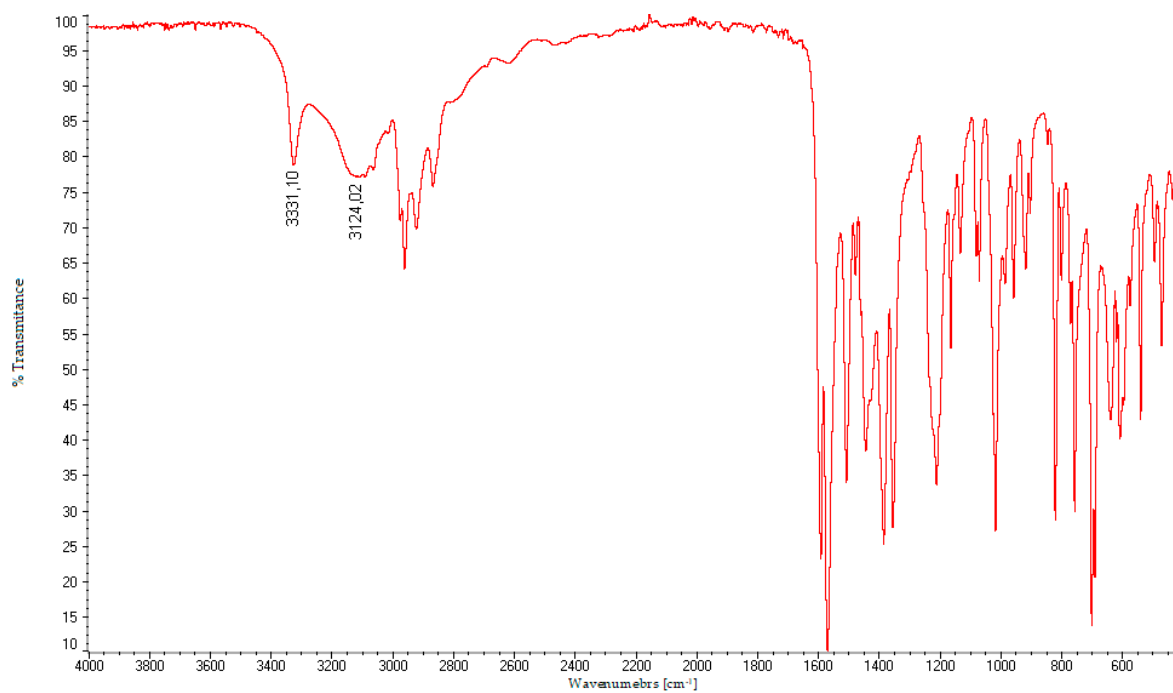


Figure S56. IR spectrum of compound 3f.

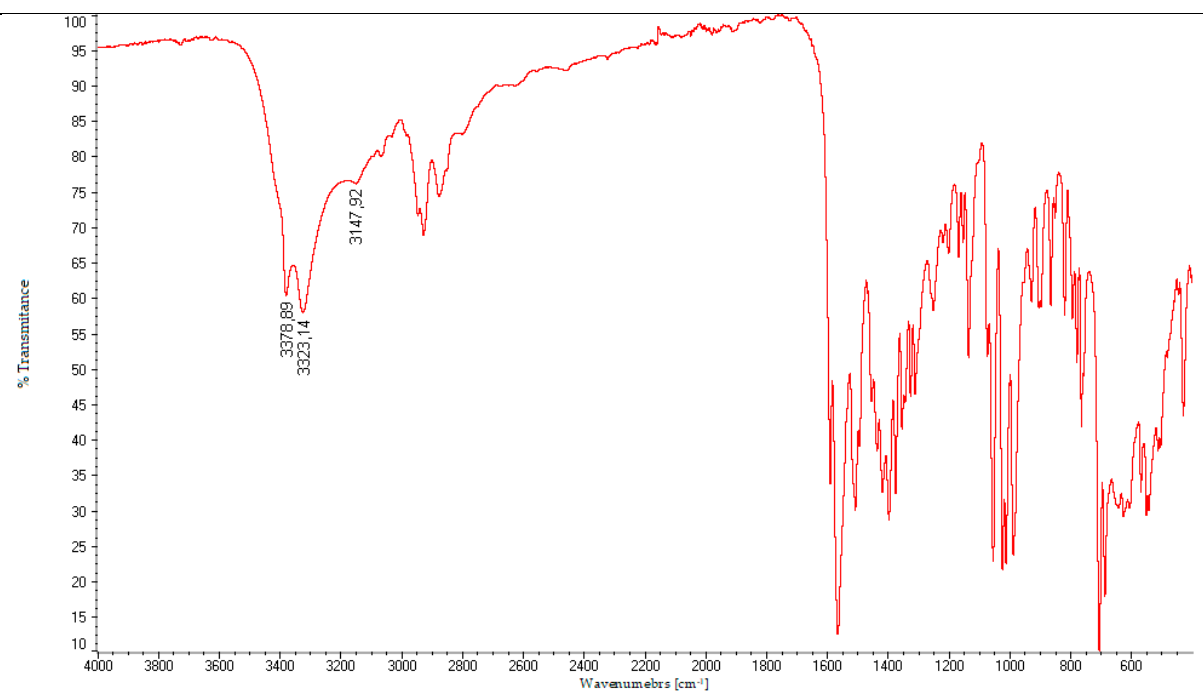


Figure S57. IR spectrum of compound 3g.

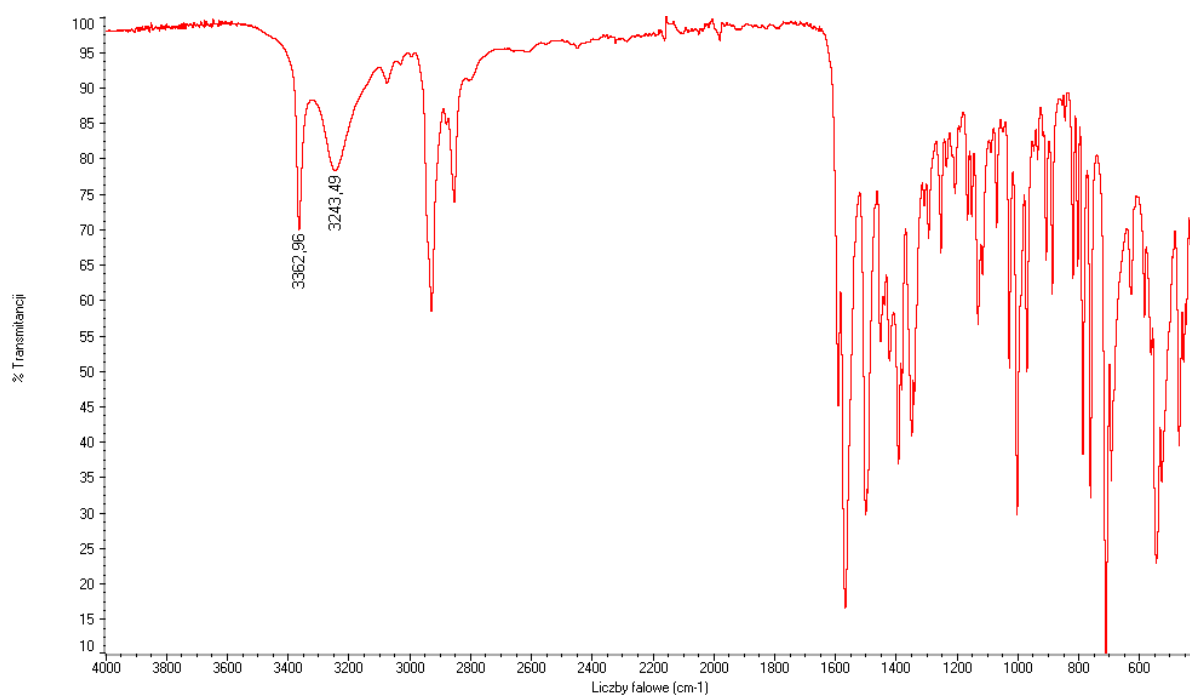


Figure S58. IR spectrum of compound 3h.

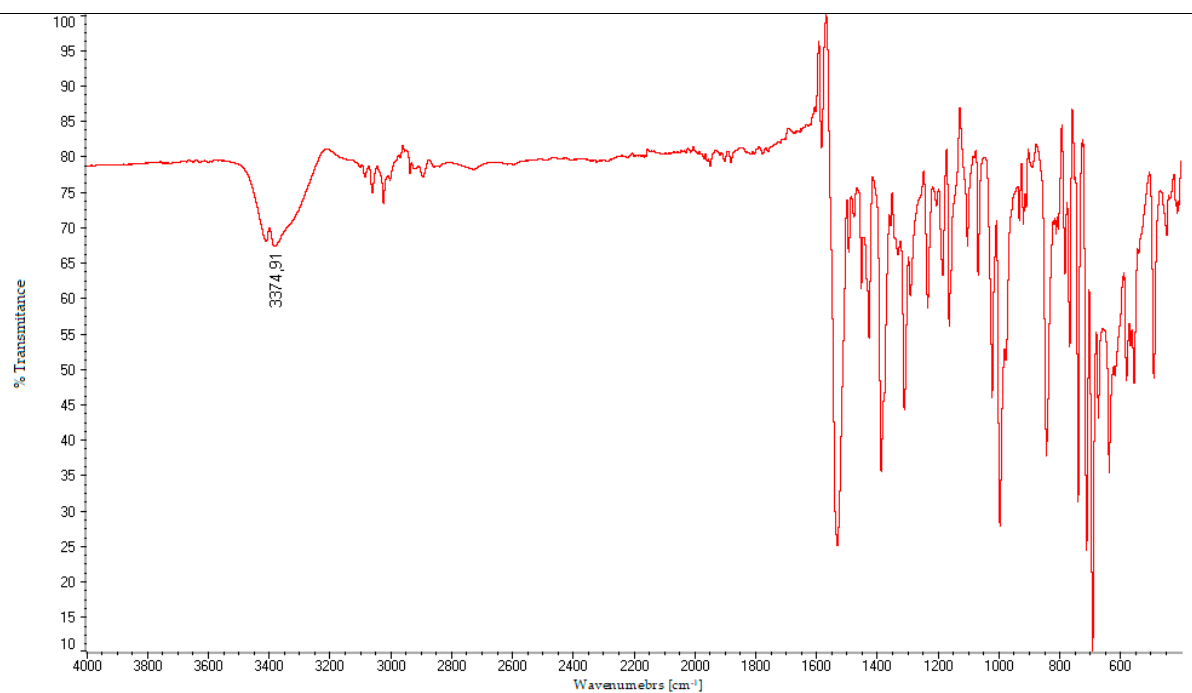


Figure S59. IR spectrum of compound 3i.

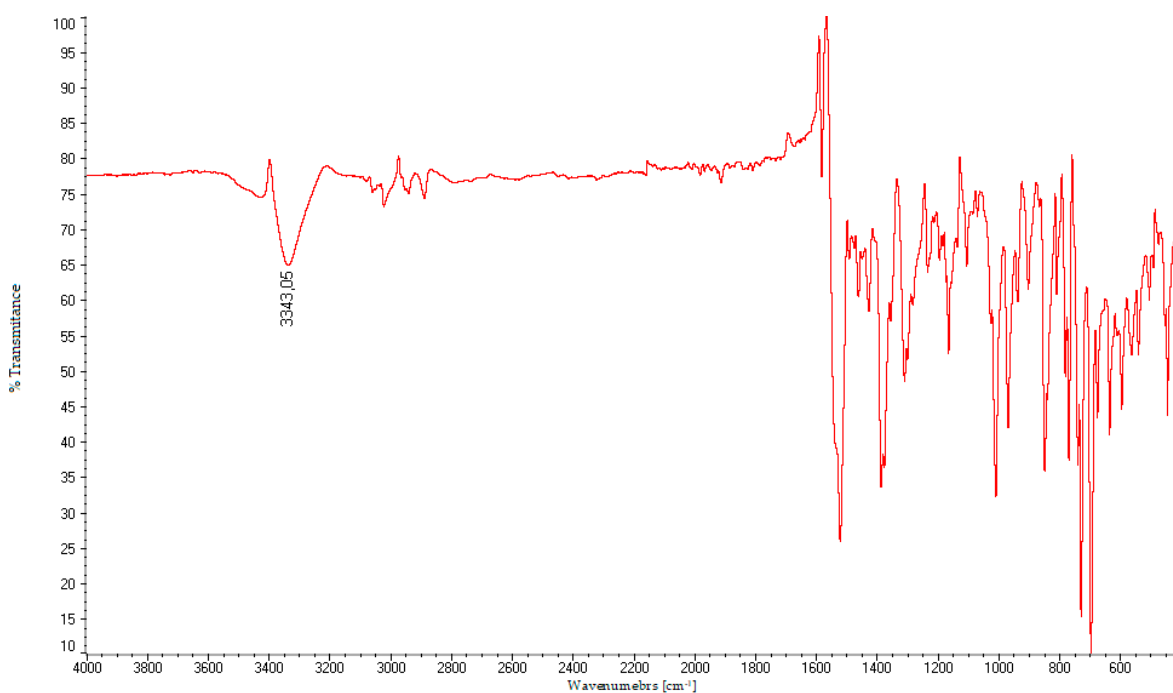


Figure S60. IR spectrum of compound 3j.

Table S1. Selected crystallographic data and structure refinements for **3c** and **3e–3h**.

	3c	3e	3f	3g	3h
Chemical formula	C ₁₂ H ₁₃ N ₃ O	C ₁₅ H ₁₉ N ₃ O	C ₁₅ H ₁₇ N ₃ O	C ₁₅ H ₁₉ N ₃ O	C ₁₆ H ₂₁ N ₃ O
<i>M_r</i> (g/mol)	215.25	257.33	255.31	257.33	271.36
Crystal system, space group	monoclinic, <i>P2₁/c</i>	monoclinic, <i>P2₁/c</i>	monoclinic, <i>P2₁/c</i>	monoclinic, <i>P2₁/c</i>	orthorhombic, <i>Pca2₁</i>
Temperature (K)	200	100	100	100	100
<i>a</i> , <i>b</i> , <i>c</i> (Å)	8.837 (2), 13.526 (3), 9.167 (2)	7.8736 (19), 18.819 (4), 9.437 (2)	7.9441 (10), 19.061 (2), 8.8572 (10)	8.9456(16), 17.818 (4), 8.4892 (19)	9.653 (3), 27.393 (10), 11.240 (3)
α , β , γ (°)	90, 102.95 (4), 90	90, 109.14 (3), 90	90, 103.78 (2), 90	90, 101.08 (2), 90	90, 90, 90
<i>V</i> (Å ³)	347.46 (17)	1321.0 (6)	1302.6 (3)	1327.9 (5)	2972.1 (16)
<i>Z</i>	4	4	4	4	8
λ (Å)	0.71073	0.71073	1.5418	0.71073	0.71073
Crystal size (mm)	0.52 × 0.36 × 0.16	0.45 × 0.24 × 0.08	0.50 × 0.36 × 0.25	0.42 × 0.22 × 0.05	0.42 × 0.31 × 0.11
<i>D_{calc}</i> (g/cm ³)	1.339	1.294	1.302	1.287	1.213
μ (mm ^{−1})	0.09	0.08	0.67	0.08	0.08
<i>F</i> (000)	456	552	544	552	1168
2 θ range (°)	3.3–28.8	2.7–30.8	5.6–68.4	3.2–28.5	2.9–28.8
No of measured, independent and observed [<i>I</i> > 2 σ (<i>I</i>)] reflections	5853, 2490, 1894	8814, 3737, 3082	6399, 2383, 2212	18751, 3362, 2928	14870, 6343, 4519
<i>R_{int}</i>	0.042	0.024	0.040	0.028	0.068
Parameters, restraints	147, 0	175, 0	174, 0	176, 0	552, 154
Goof on <i>F</i> ²	1.06	1.04	1.02	1.07	1.03
<i>R</i> ₁ [<i>I</i> > 2 σ (<i>I</i>)]	0.066	0.042	0.056	0.039	0.095
<i>wR</i> ₂ (all data)	0.196	0.109	0.153	0.108	0.285
<i>T_{min}</i> , <i>T_{max}</i>	–	–	0.782, 0.876	–	–
Extinction coefficient	–	–	–	–	0.018 (5)
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ^{−3})	0.31, −0.28	0.40, −0.22	0.34, −0.37	0.40, −0.22	0.55, −0.44
CCDC No	2102842	2102843	2102844	2102845	2102846

Table S2. Comparison of selected geometrical parameters of compounds **3c** and **3e-3h**.

	3c	3e	3f	3g	3h
Bond lengths (Å)	molecules A/B/C				
O1—C51	1.425 (2)	1.4338 (13)	1.4405 (18)	1.4318 (13)	1.425 (5)/1.418 (14)/1.426 (14)
N1—C2	1.340 (2)	1.3391 (14)	1.3419 (18)	1.3424 (13)	1.341 (6)/1.319 (14)/1.331 (13)
N1—C6	1.366 (2)	1.3646 (13)	1.3600 (18)	1.3663 (13)	1.370 (5)/1.380 (14)/1.357 (14)
N3—C2	1.339 (2)	1.3356 (13)	1.3322 (18)	1.3348 (13)	1.339 (6)/1.342 (14)/1.339 (14)
N3—C4	1.344 (2)	1.3462 (13)	1.3454 (18)	1.3439 (13)	1.345 (5)/1.342 (14)/1.358 (13)
N4—C4	1.350 (2)	1.3449 (13)	1.3491 (18)	1.3514 (13)	1.355 (6)/ 1.342 (14)/1.360 (18)
N4—C41	-	1.4557 (14)	1.4569 (18)	1.4673 (13)	1.467 (6)/ 1.502 (14)/1.488 (17)
C2—C21	1.483 (3)	1.4906 (14)	1.4925 (18)	1.4924 (14)	1.480 (6)/1.484 (13)/1.474 (13)
C4—C5	1.421 (2)	1.4275 (15)	1.423 (2)	1.4246 (14)	1.434 (6)/1.429 (14)/1.412 (15)
C5—C6	1.379 (3)	1.3806 (14)	1.382 (2)	1.3863 (15)	1.377 (6)/ 1.366 (16)/1.365 (15)
C5—C51	1.503 (2)	1.5066 (15)	1.5053 (18)	1.5093 (14)	1.502 (5)/1.535 (14)/1.524 (14)
C6—C61	1.503 (3)	1.5045 (15)	1.5046 (19)	1.5084 (14)	1.501 (6)/1.515 (18)/1.516 (19)
C41—C42	-	1.5200 (18)	1.499 (2)	1.5253 (16)	1.509 (7)/1.50 (2)/1.512 (17)
Bond angles (°)					
O1—C51—C5	112.28 (15)	112.42 (9)	112.17 (11)	112.88 (8)	114.5 (3)/ 113.8 (10)/ 115.6 (10)
N1—C2—N3	126.13 (16)	126.78 (9)	126.60 (12)	126.23 (9)	125.5 (4)/ 127.2 (11)/ 126.5 (11)
N3—C4—N4	117.66 (16)	117.68 (10)	117.35 (13)	116.34 (9)	119.3 (4)/ 119.6 (11)/ 117.4 (13)
N3—C4—C5	122.24 (17)	121.27 (9)	121.48 (12)	121.38 (9)	121.3 (4)/120.8 (11)/ 121.1 (11)
N4—C4—C5	120.10 (16)	121.04 (9)	121.18 (12)	122.28 (9)	119.3 (4)/119.6 (11)/ 121.3 (13)
N4—C41—C42	-	113.33 (9)	111.01 (12)	110.98 (9)	111.9 (4)/ 106.5 (12)/ 110.2 (15)
C2—N1—C6	116.93 (15)	115.99 (9)	116.20 (12)	115.94 (9)	117.3 (4)/117.3 (12)/ 116.6 (12)
C2—N3—C4	116.51 (15)	116.95 (9)	116.92 (12)	117.59 (9)	117.5 (4)/116.1 (10)/ 116.2 (10)
Torsion angles (°)					
O1—C51—C5—C4	-53.9 (2)	63.31 (12)	64.47 (17)	-62.94 (12)	49.0 (6)/-50.0 (19)/46 (2)
O1—C51—C5—C6	125.68 (19)	-116.12 (11)	-112.34 (15)	117.49 (11)	-133.5 (5)/136.8 (17)/-137.6 (18)
N1—C2—N3—C4	2.6 (3)	-1.31 (15)	0.9 (2)	2.80 (15)	0.1 (7)/1 (2)/-2 (2)
N1—C2—C21—C22	-25.2 (2)	-10.80 (15)	-12.00 (19)	-15.50 (14)	-22.9 (7)/16 (2)/-15 (2)

N1—C2—C21—C26	158.12 (17)	169.55 (9)	168.84 (13)	167.84 (9)	159.6 (5)/−161.7 (19)/160.0 (16)
N3—C2—N1—C6	−2.3 (3)	−2.50 (15)	−3.3 (2)	−3.78 (14)	−1.8 (7)/3 (3)/−3 (2)
N3—C4—C5—C6	−1.7 (2)	−2.02 (15)	−2.1 (2)	−2.19 (14)	−1.3 (7)/−3 (2)/0 (3)
N3—C2—C21—C22	151.94 (18)	169.71 (9)	168.15 (12)	163.56 (9)	158.2 (5)/ −161.5 (15)/166.3 (15)
N3—C2—C21—C26	−24.7 (2)	−9.93 (14)	−11.00 (19)	−13.11 (13)	−19.3 (7)/21 (2)/ −19 (2)
N3—C4—N4—C41	-	−6.83 (15)	17.1 (2)	0.42 (14)	10.7 (7)/−12 (3)/11 (4)
N4—C4—N3—C2	179.89 (16)	−177.36 (9)	−178.39 (12)	−179.33 (9)	−180.0 (4)/−180.0 (15)/178 (2)
N4—C4—C5—C6	177.95 (16)	178.95 (9)	178.24 (13)	177.52 (9)	−179.8 (5)/175.8 (17)/−175 (2)
N4—C4—C5—C51	−2.4 (2)	−0.52 (15)	1.2 (2)	−2.09 (14)	−2.2 (7)/2 (2)/ 1 (3)
C2—N1—C6—C61	−179.07 (15)	−174.33 (9)	−176.38 (11)	−178.88 (8)	−177.0 (4)/−176.6 (17)/−176 (2)
C4—N4—C41—C42	-	105.57 (12)	79.14 (17)	77.54 (12)	−63.0 (7)/63 (3)/−66 (3)
C5—C4—N4—C41	-	172.23 (10)	−163.30 (13)	−179.31 (9)	−170.7 (4)/ 168.5 (15)/−173 (2)
C51—C5—C6—C61	1.2 (3)	−4.23 (16)	−4.2 (2)	1.25 (15)	0.7 (8)/−11 (3)/1 (3)

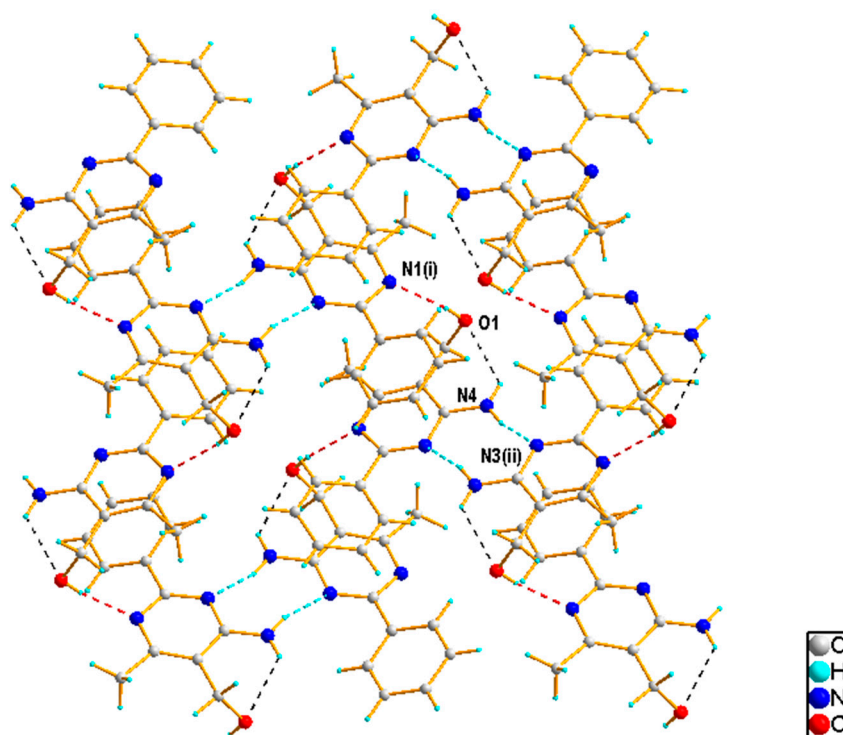


Figure S61. A packing diagram of **3c** viewed along the *a*-axis, showing the formation of 2D hydrogen-bonded network through intermolecular interactions, with O—H···N in red and N—H···N in cyan. Dashed lines in black indicate intramolecular N—H···O hydrogen bonds. Symmetry codes: (i) $x, -y+3/2, z-1/2$ and (ii) $-x+1, -y+1, -z$.