Electronic Supplementary Material (ESI) for New Journal of Chemistry.

SUPPORTING INFORMATION

Ionic Liquid-assisted Synthesis of Dihydropyrimidin(thi)ones Biginelli adducts and investigation of their mechanism of urease inhibition

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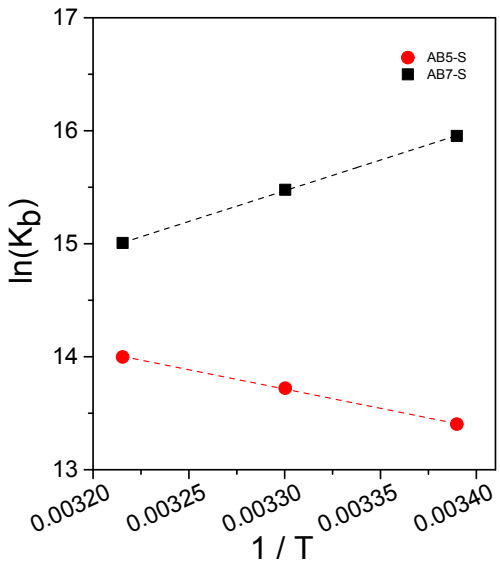

Figure S1. Van't Hoff plot for the Biginelli adducts **BA5-S** and **BA7-S** with urease.

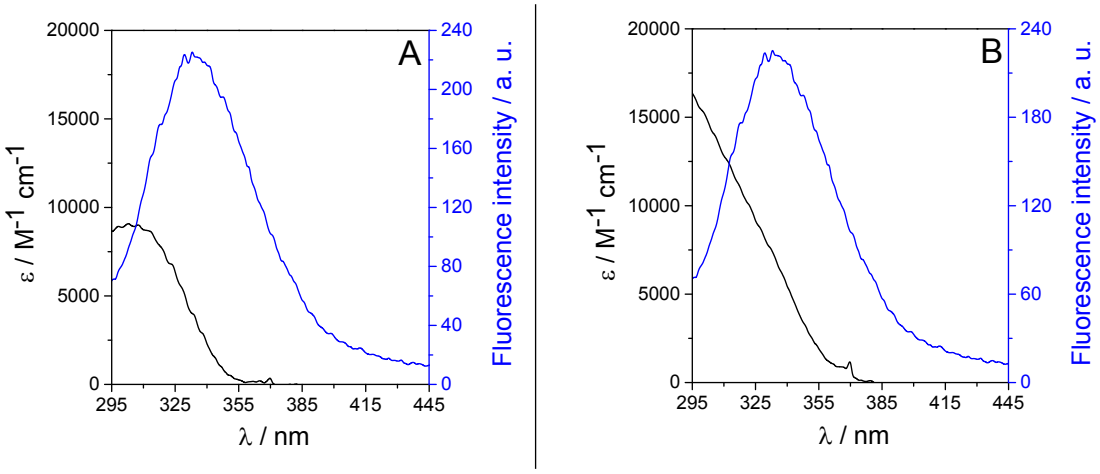

Figure S2. Overlap of the fluorescence emission of urease (blue, 5 μM) with the absorption spectrum of (A) **BA5-S** (black, 5 μM) and (B) **BA7-S** (black, 5 μM).

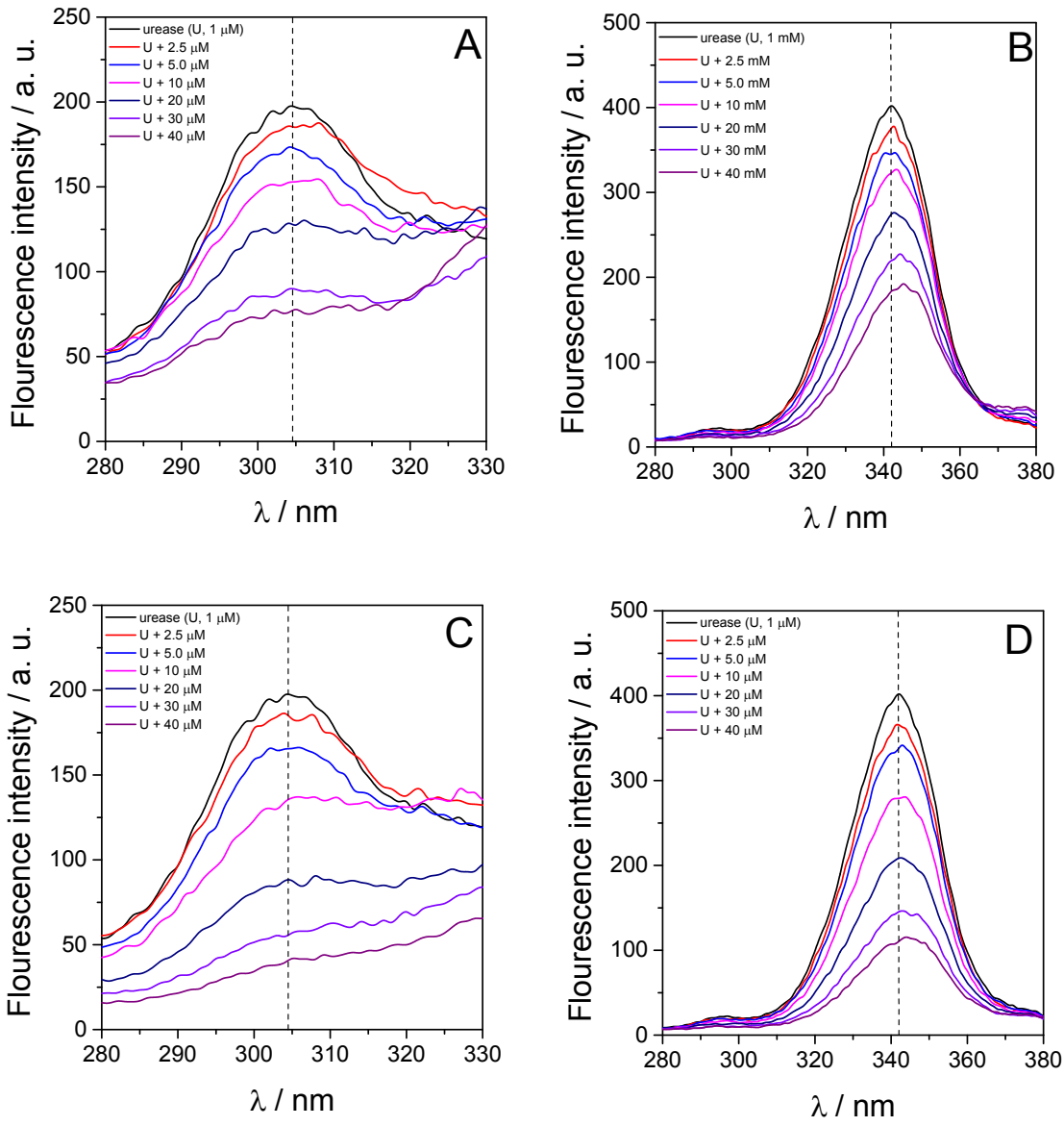

Figure S3. Urease (1.0 μM, pH 7.4) synchronous fluorescence spectra upon addition of increasing concentrations of **BA5-S**, monitoring (A) $\Delta\lambda$ = 15 nm (Tyr residues) and (B) $\Delta\lambda$ = 60 nm (Trp residues), and **BA7-S** monitoring (C) $\Delta\lambda$ = 15 nm (Tyr residues) and (D) $\Delta\lambda$ = 60 nm (Trp residues).

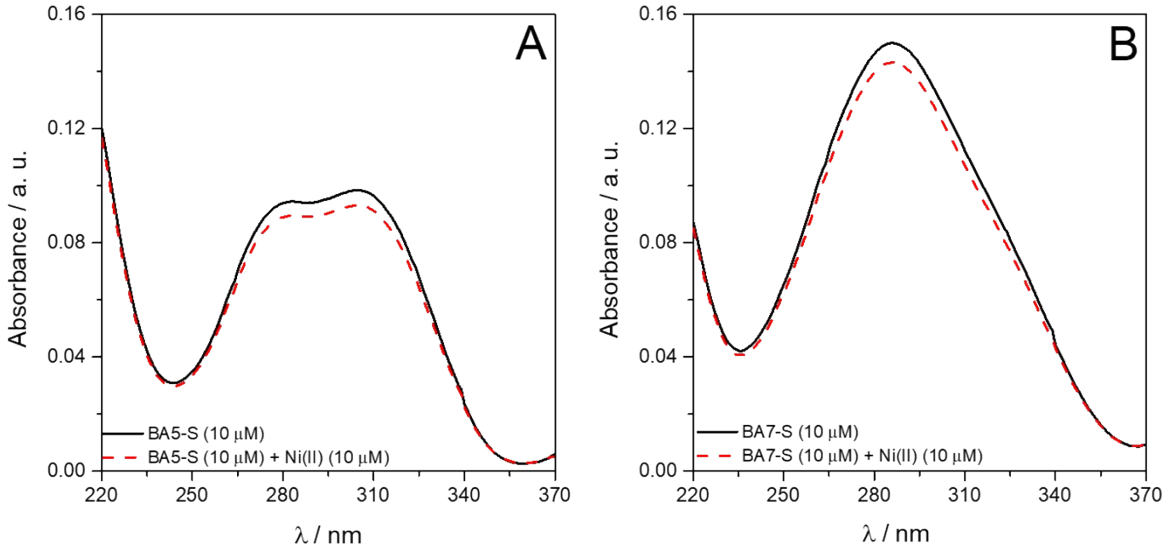

Figure S4. UV-vis spectra of the Biginelli adducts (A) **BA5-S** and (B) **BA7-S** in the presence and absence of Ni(II) ions with urease. All compounds and Ni(II) ions in, the same concentration at pH 7. The spectrum for Ni(II) solution was baseline.

Table S1.Tridimensional fluorescence parameters for free urease (pH 7.4) or in the presence of the Biginelli adducts **BA5-S** and **BA7-S**. Protein and ligands were used at 1.0 and 40 μM, respectively.

Peak	free urease			urease + **BA5-S**			urease + **BA7-S**		
	Position (λ_{ex} / λ_{em})	Stokes[1] $\Delta\lambda$ (nm)	F (a. u.)	Position (λ_{ex} / λ_{em})	Stokes $\Delta\lambda$ (nm)	F (a. u.)	Position (λ_{ex} / λ_{em})	Stokes $\Delta\lambda$ (nm)	F (a. u.)
1	$\lambda_{ex} = \lambda_{em}$	0	> 1000	$\lambda_{ex} = \lambda_{em}$	0	> 1000	$\lambda_{ex} = \lambda_{em}$	0	> 1000
2	285 / 339	54	408 (100%)[2]	285 / 350	65	194 (47%)	285 / 353	68	115 (28%)
3	238 / 348	110	53 (100%)	238 / 353	115	21 (40%)	238 / 355	117	11 (21%)

[1]Stokes shift ($\Delta\lambda = \lambda_{em} - \lambda_{ex}$)

[2]Numbers in parentheses represent the relative percentage of fluorescence signal. Lower values indicate greater variation in relation to control (urease by itself).

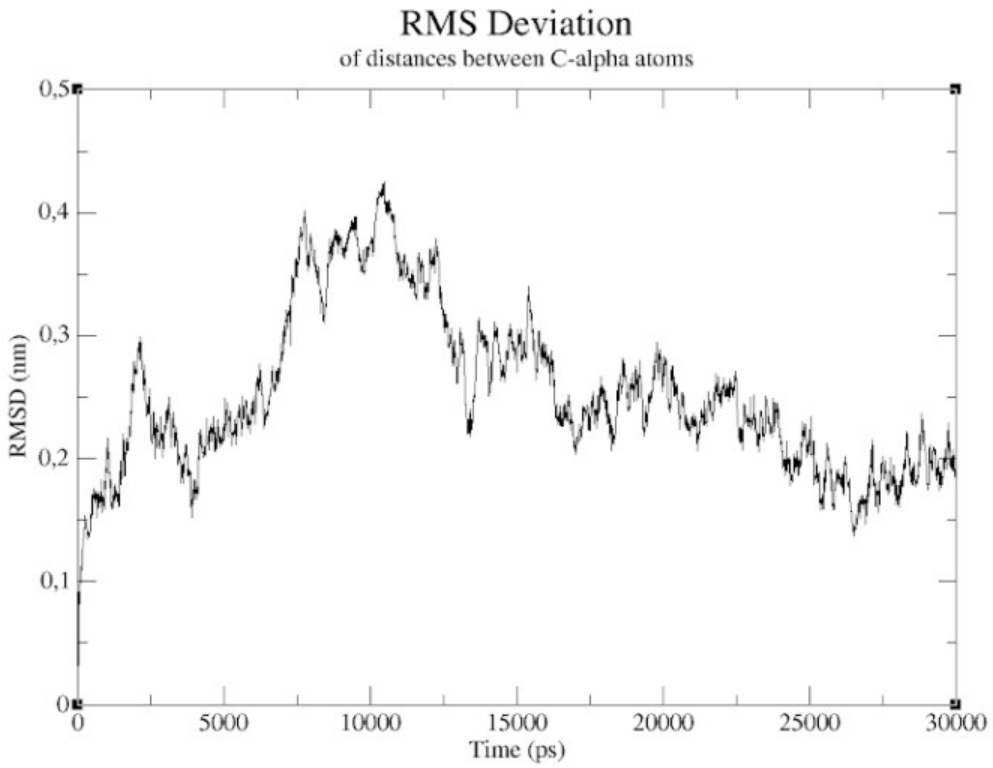

Figure S5. RMSD graphic generated for C_α atoms of the jack bean urease.

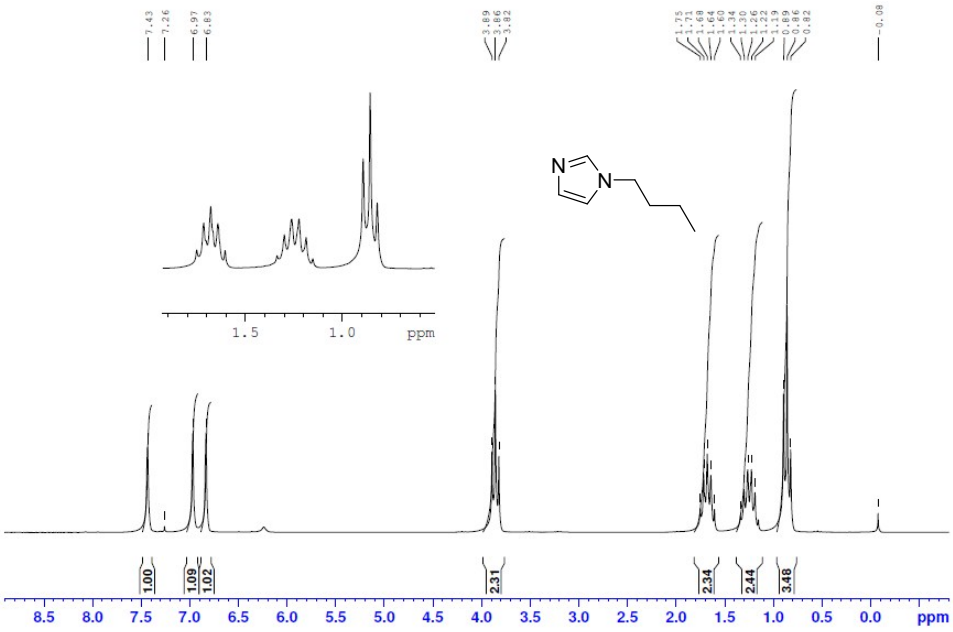

Figure S6. ^{1}H spectrum of compound 1-butyl-1*H*-imidazole (BIM) (200 MHz, $CDCl_3$).

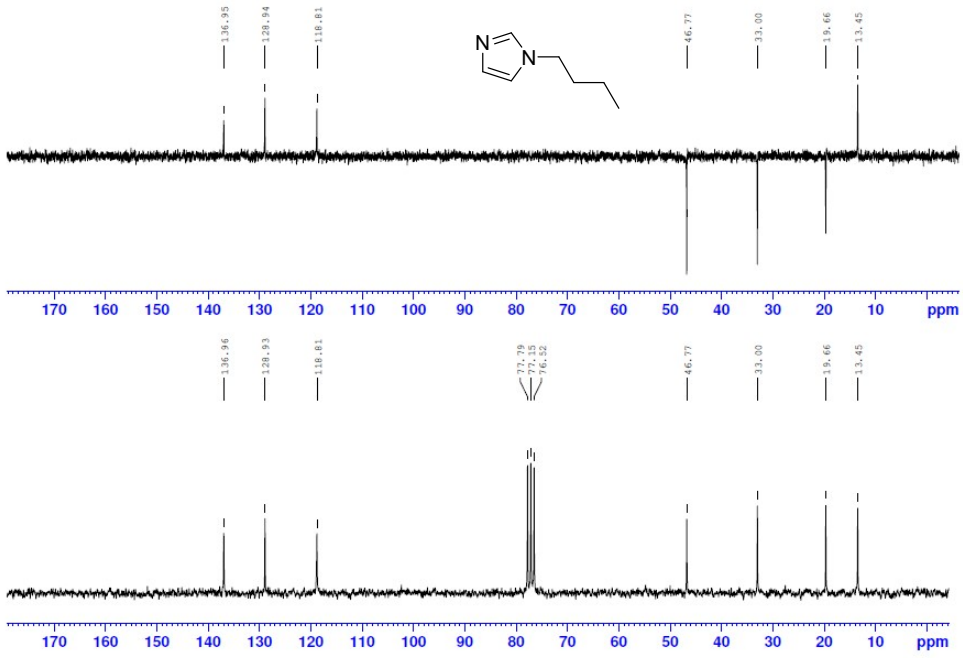

Figure S7. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound 1-butyl-1*H*-imidazole (**BIM**) (50 MHz, $CDCl_3$).

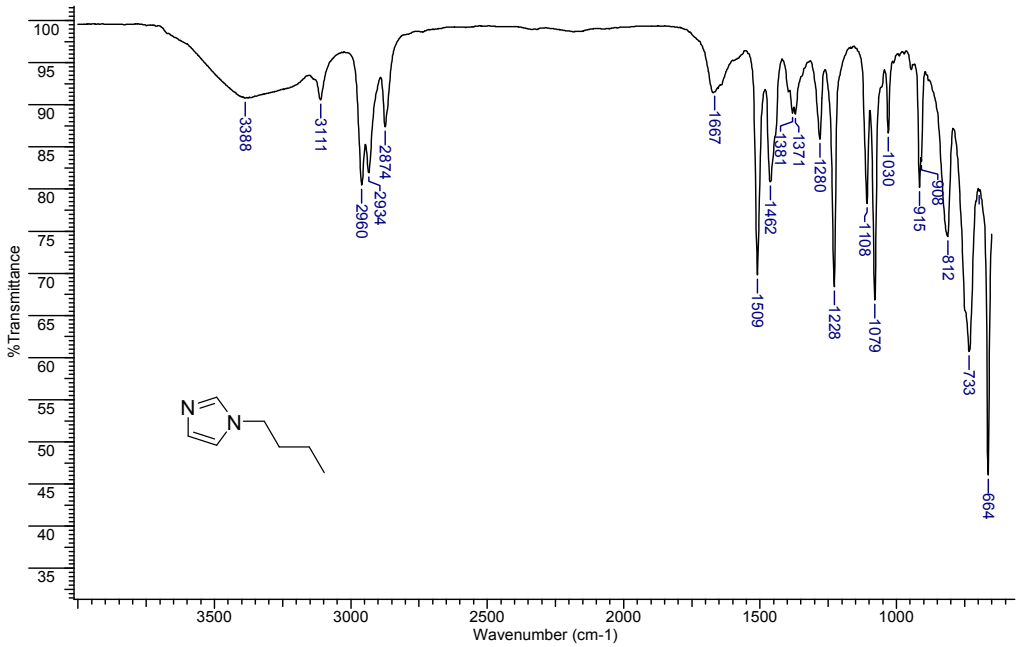

Figure S8. Infrared spectrum (ATR) of 1-butyl-1*H*-imidazole (**BIM**).

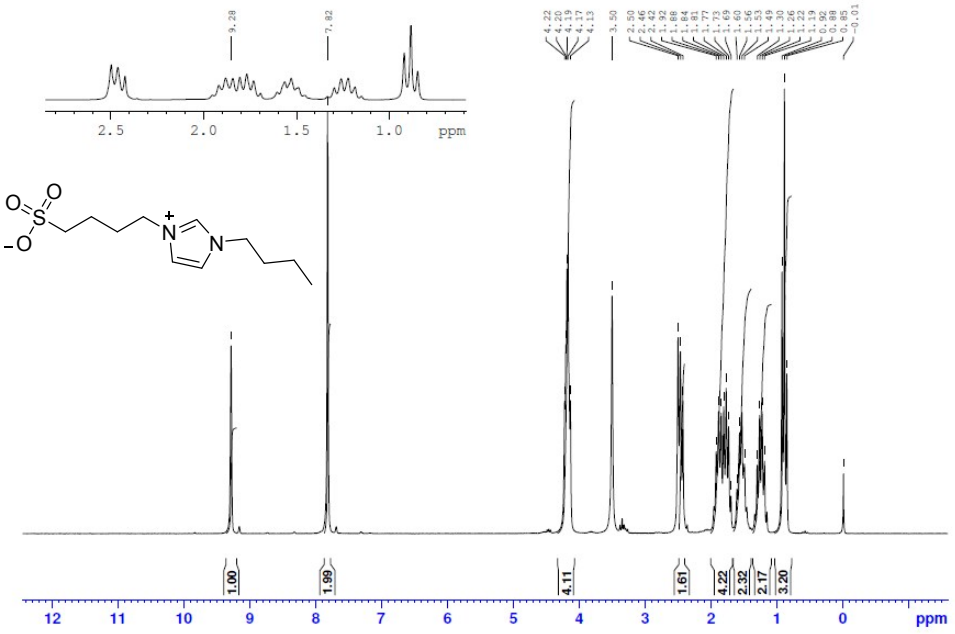

Figure S9. [1]H spectrum of compound 4-(1-butyl-1*H*-imidazol-3-ium-3-yl)butane-1-sulfonate (**BIMS**) (200 MHz, DMSO-d_6).

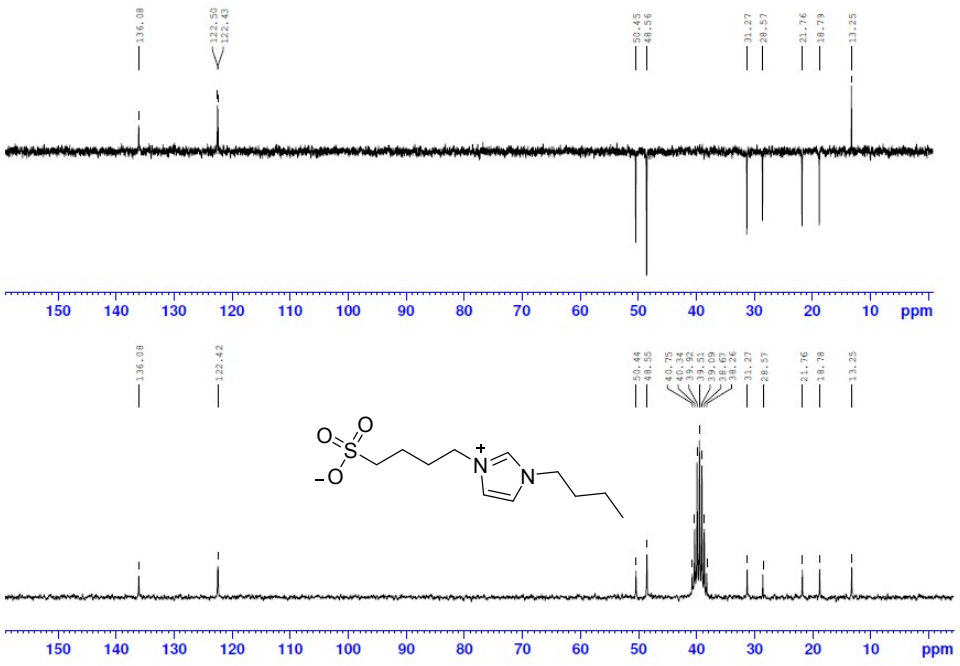

Figure S10. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound 4-(1-butyl-1*H*-imidazol-3-ium-3-yl)butane-1-sulfonate (**BIMS**) (50 MHz, DMSO-d_6).

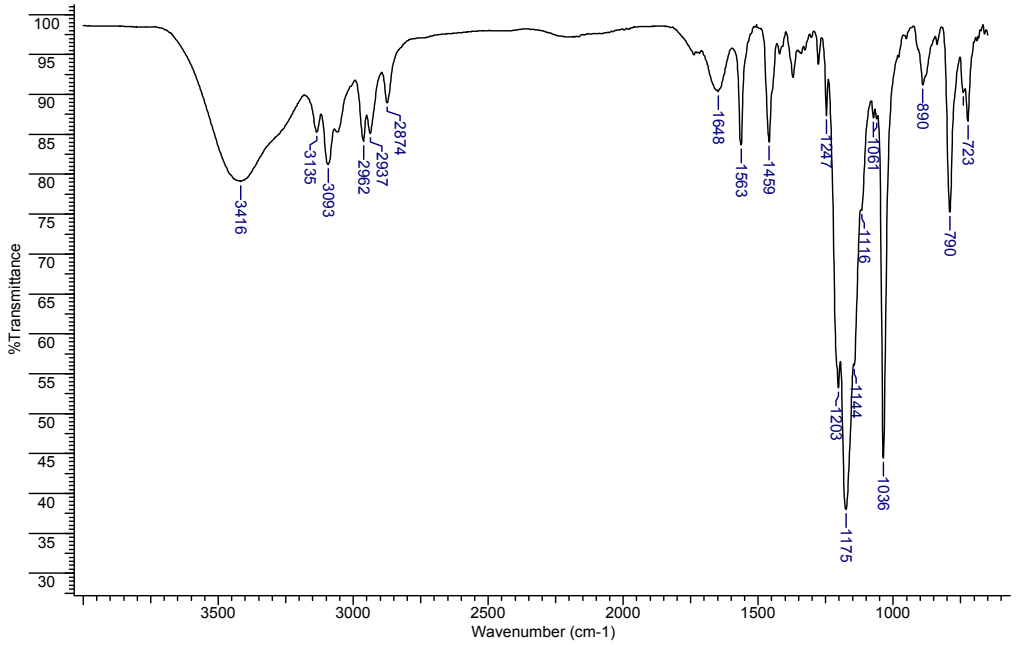

Figure S11. Infrared spectrum (ATR) of 4-(1-butyl-1*H*-imidazol-3-ium-3-yl)butane-1-sulfonate (**BIMS**) .

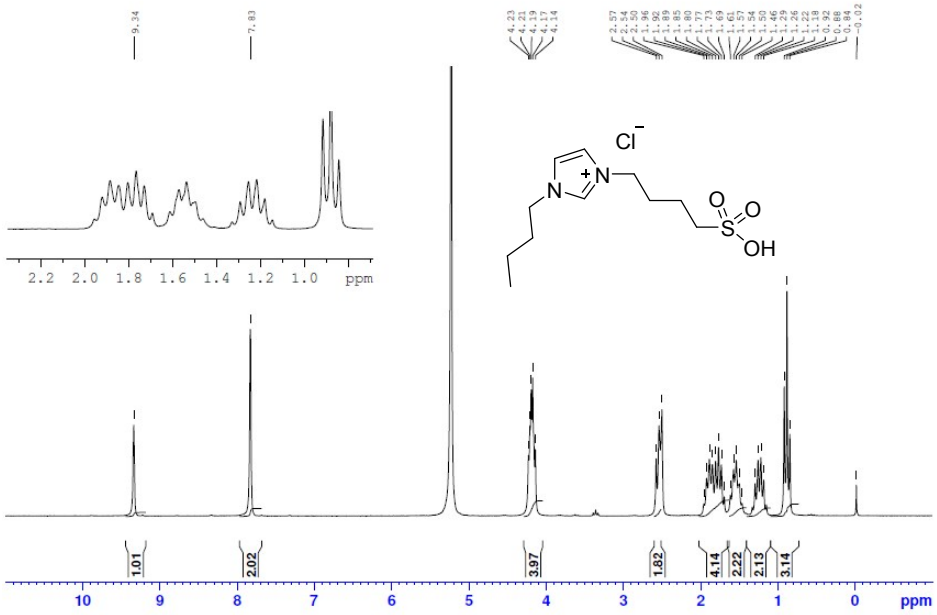

Figure S12. [1]H spectrum of compound 1-butyl-3-(4-solfobutyl)-1*H*-imidazol-3-ium chloride (**[BIMS][Cl]**) (200 MHz, DMSO-d_6).

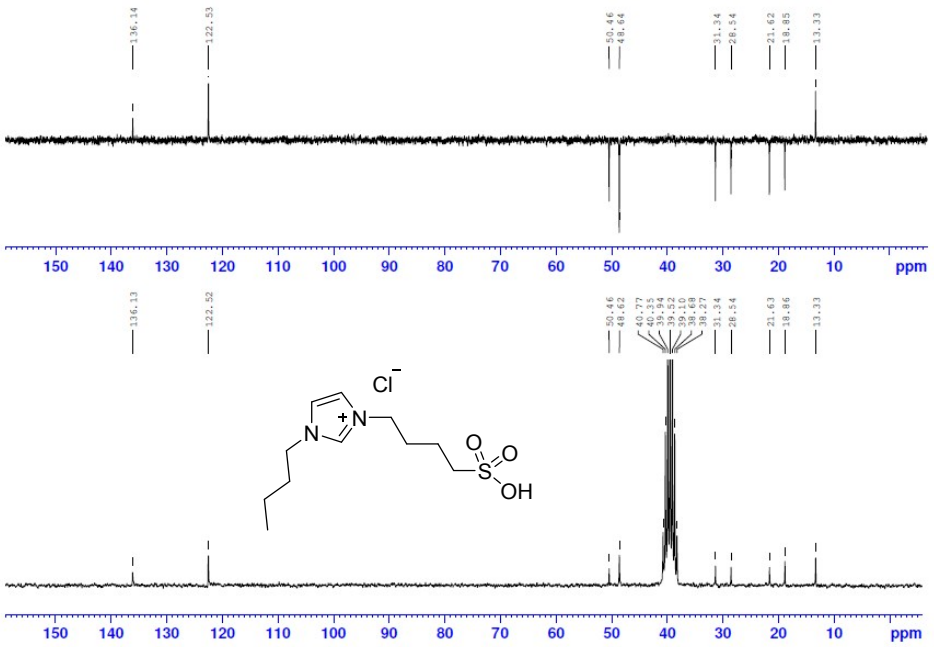

Figure S13. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound 1-butyl-3-(4-solfobutyl)-1*H*-imidazol-3-ium chloride (**[BIMS][Cl]**) (50 MHz, DMSO-d_6).

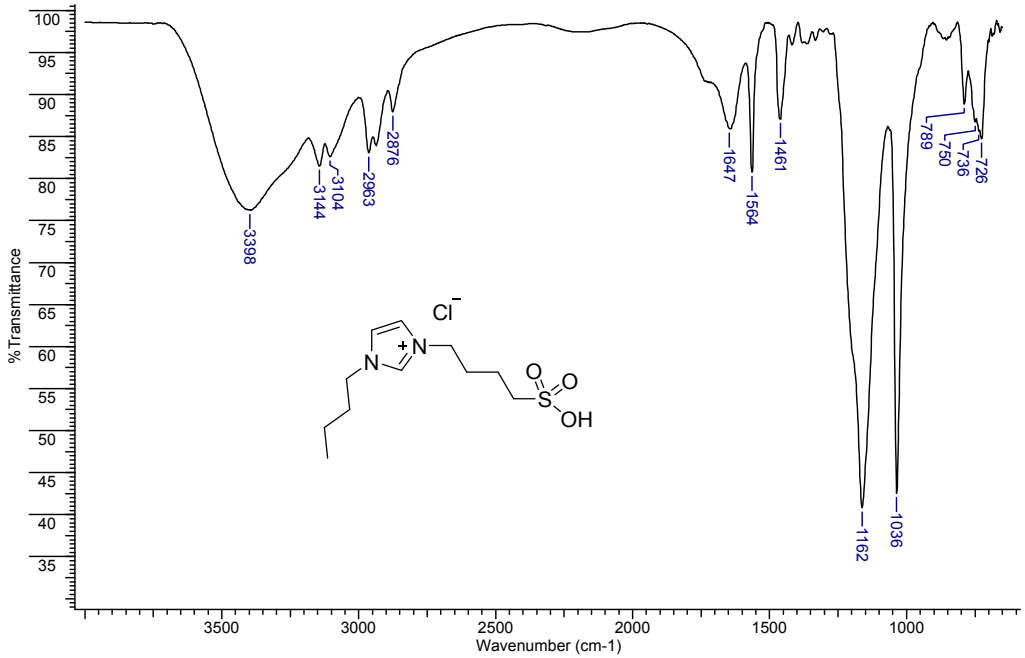

Figure S14. Infrared spectrum (ATR) of 1-butyl-3-(4-solfobutyl)-1*H*-imidazol-3-ium chloride (**[BIMS][Cl]**) .

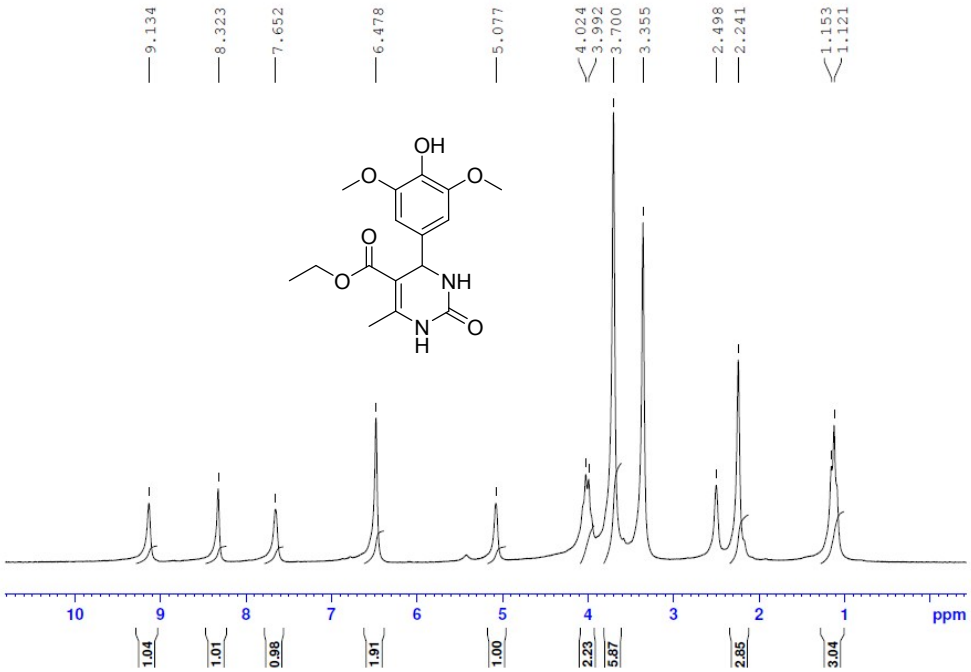

Figure S15. [1]H spectrum of compound **BA1-O** (200 MHz, DMSO-d_6).

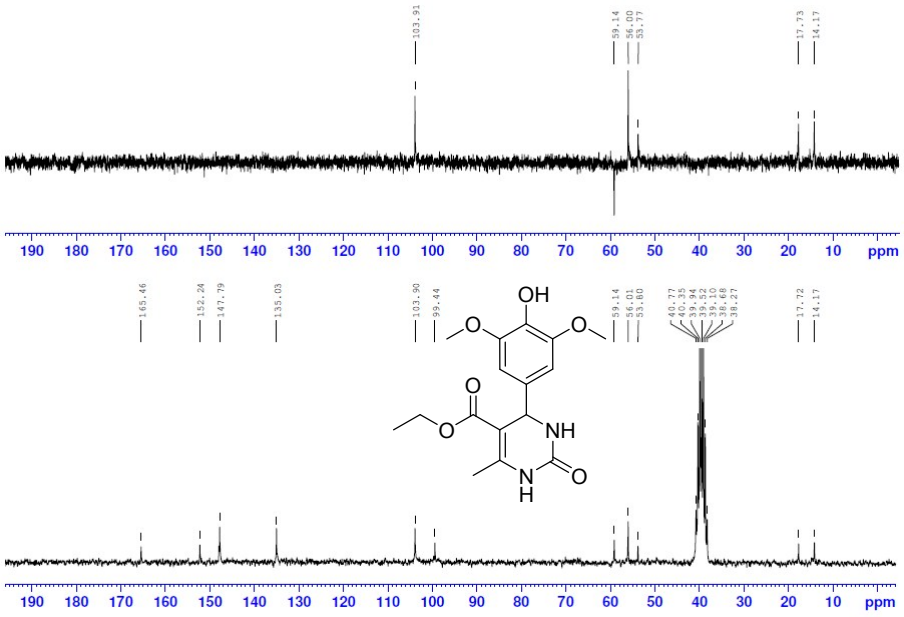

Figure S16. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA1-O** (50 MHz, DMSO-d_6)

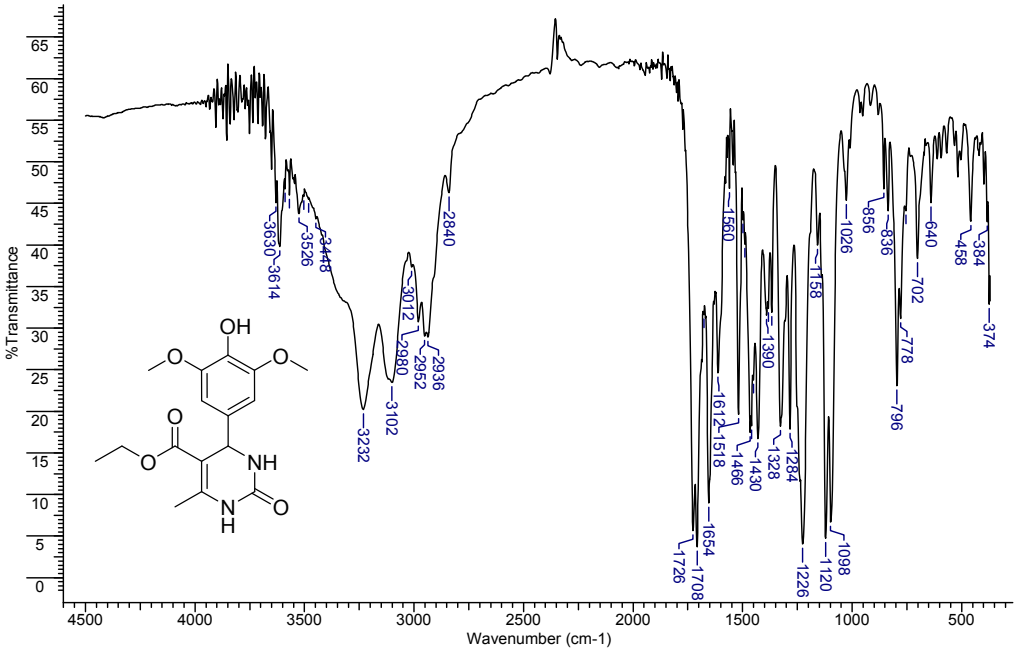

Figure S17. Infrared spectrum (KBr) of **BA1-O**.

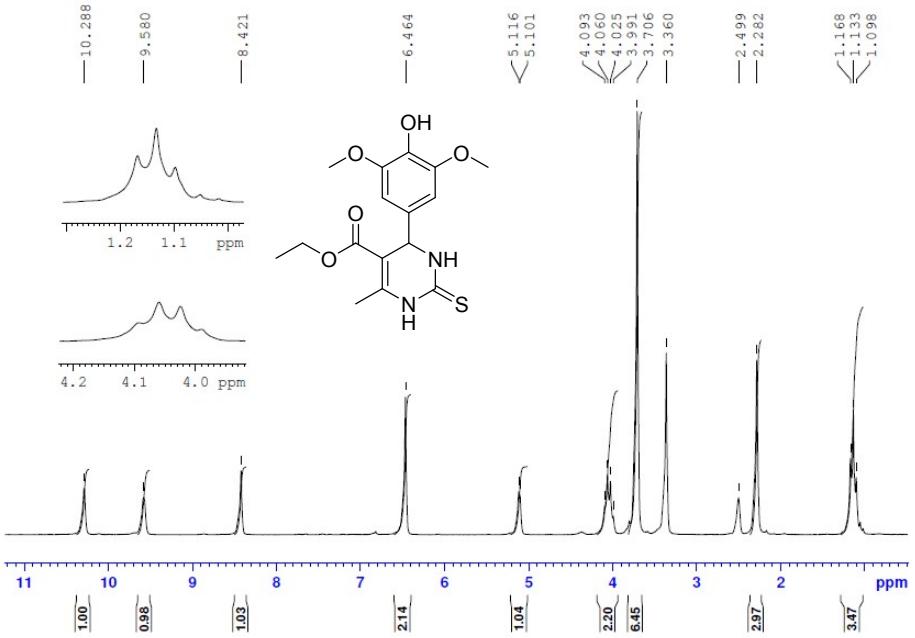

Figure S18. ^{1}H spectrum of compound **BA1-S** (200 MHz, DMSO-d_6).

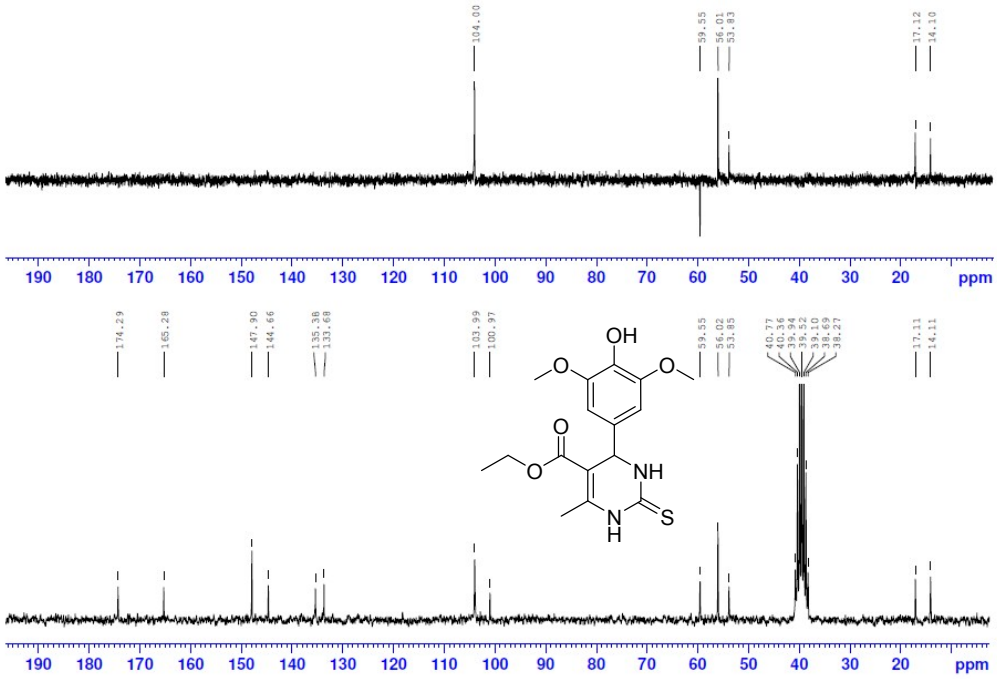

Figure S19. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA1-S** (50 MHz, DMSO-d_6).

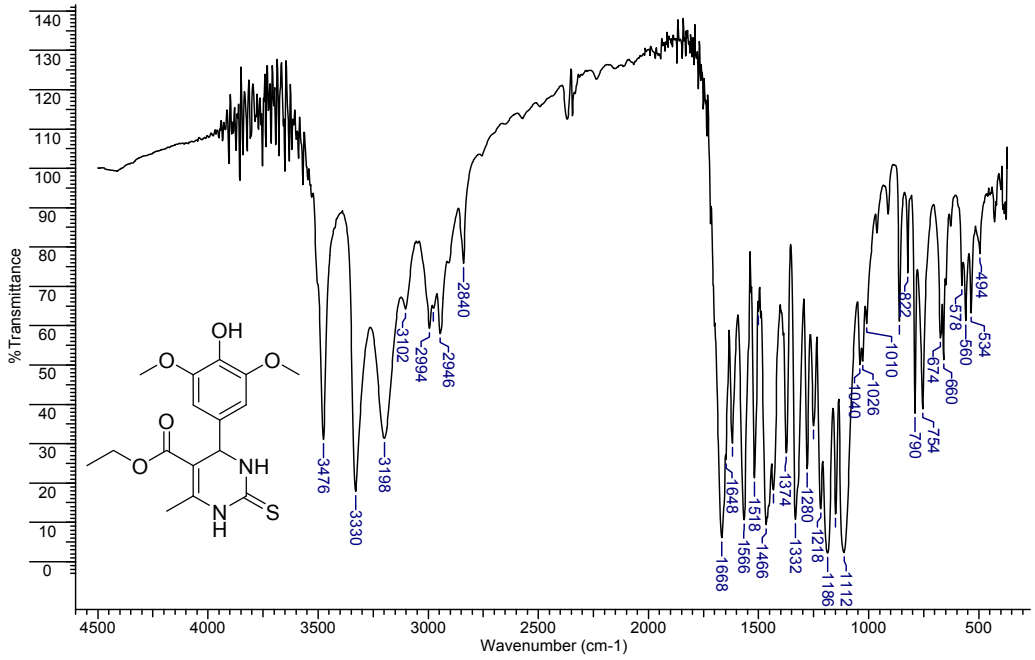

Figure S20. Infrared spectrum (KBr) of **BA1-S**.

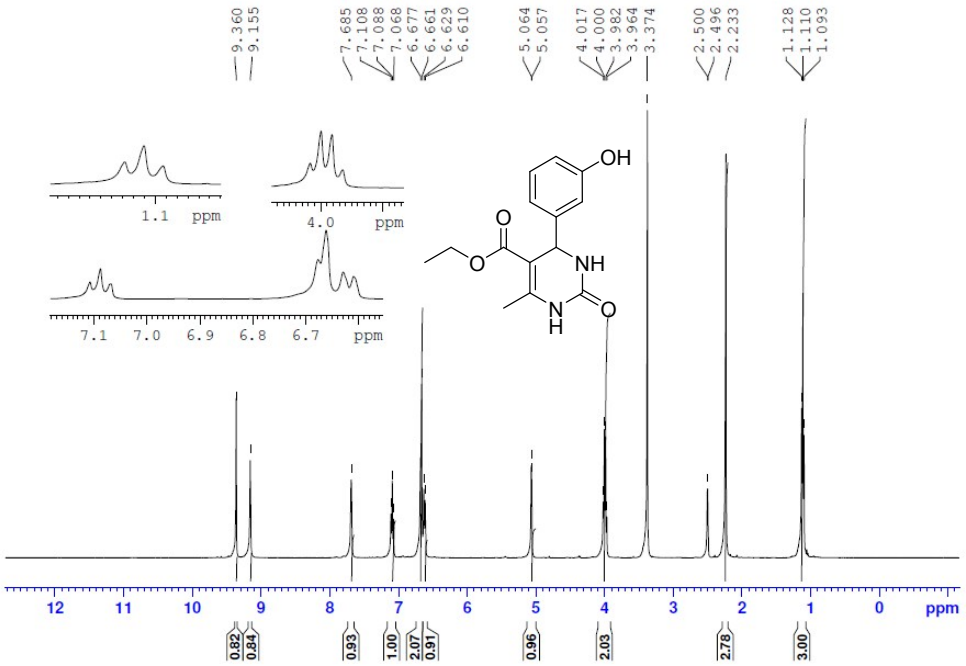

Figure S21. [1]H spectrum of compound **BA2-O** (400 MHz, DMSO-d_6).

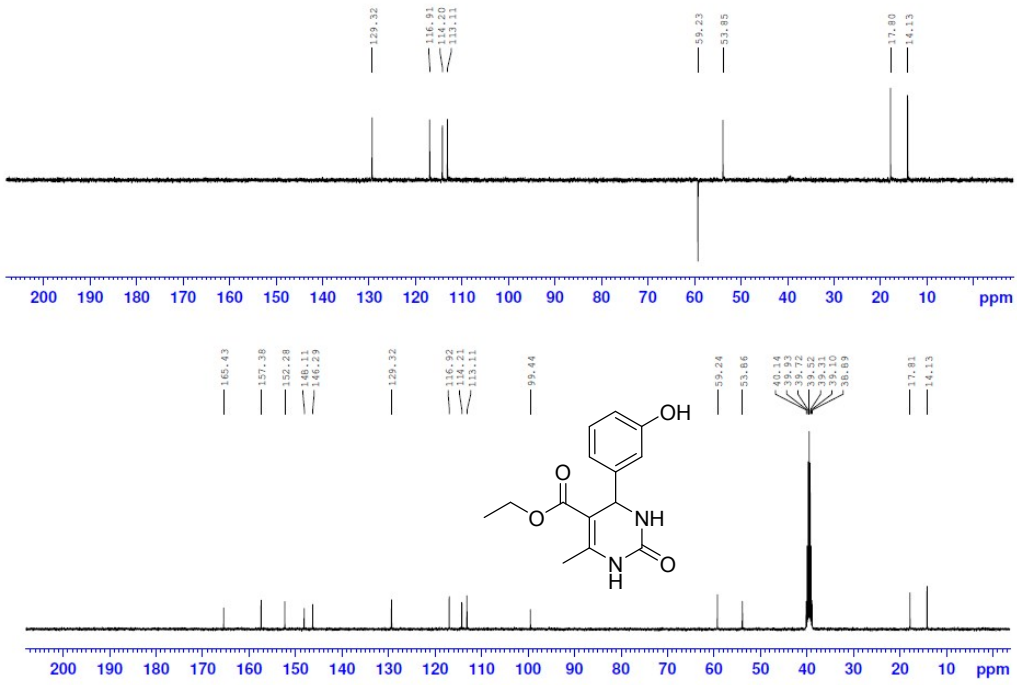

Figure S22. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA2-O** (100 MHz, DMSO-d_6).

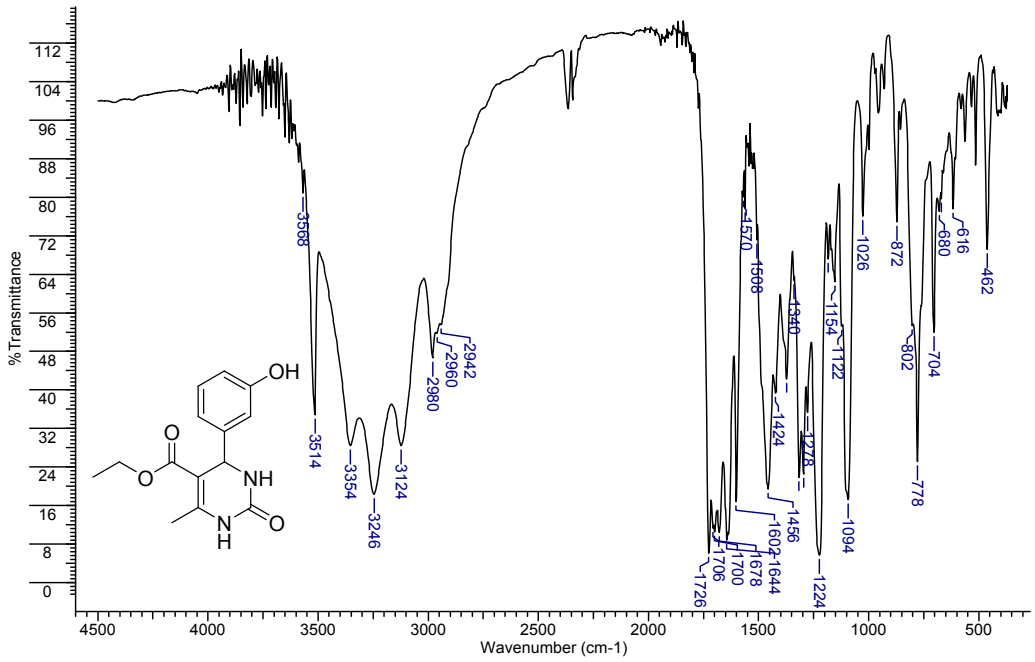

Figure S23. Infrared spectrum (KBr) of **BA2-O.**

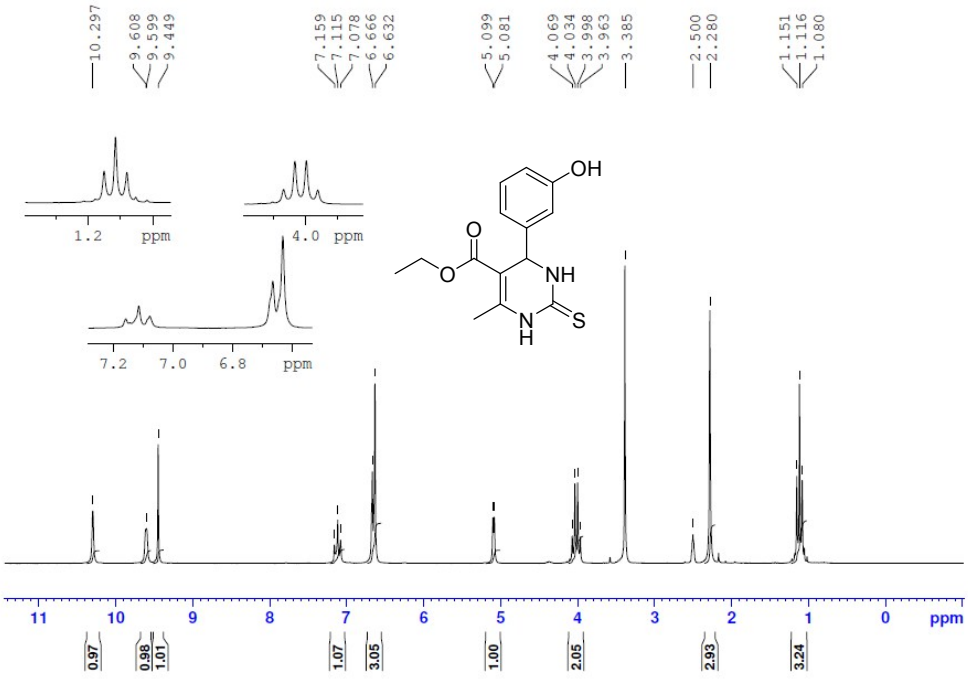

Figure S24. ^{1}H spectrum of compound **BA2-S** (200 MHz, DMSO-d_6).

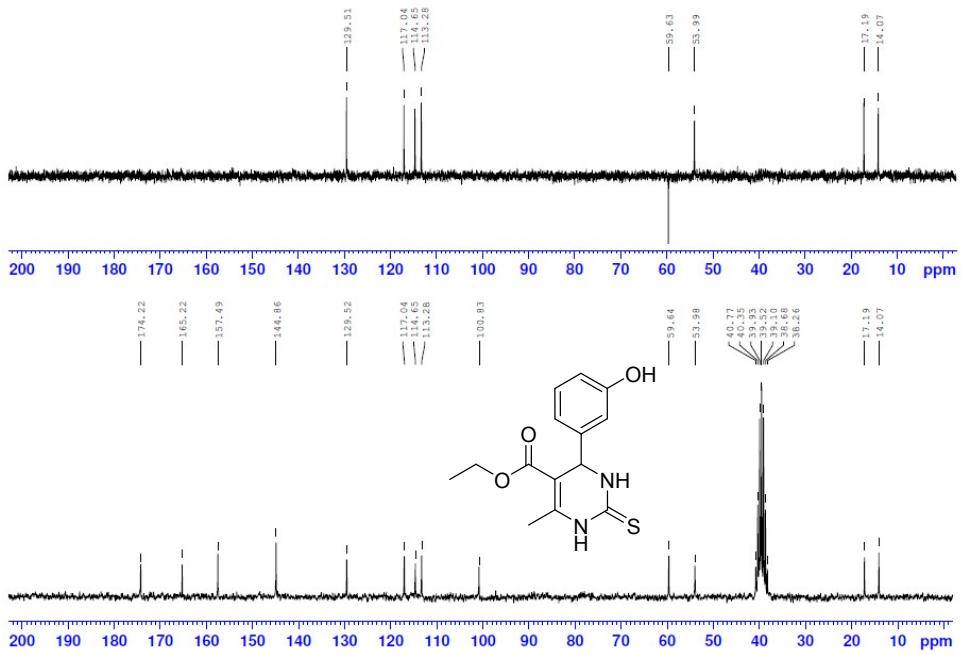

Figure S25. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA2-S** (50 MHz, DMSO-d_6).

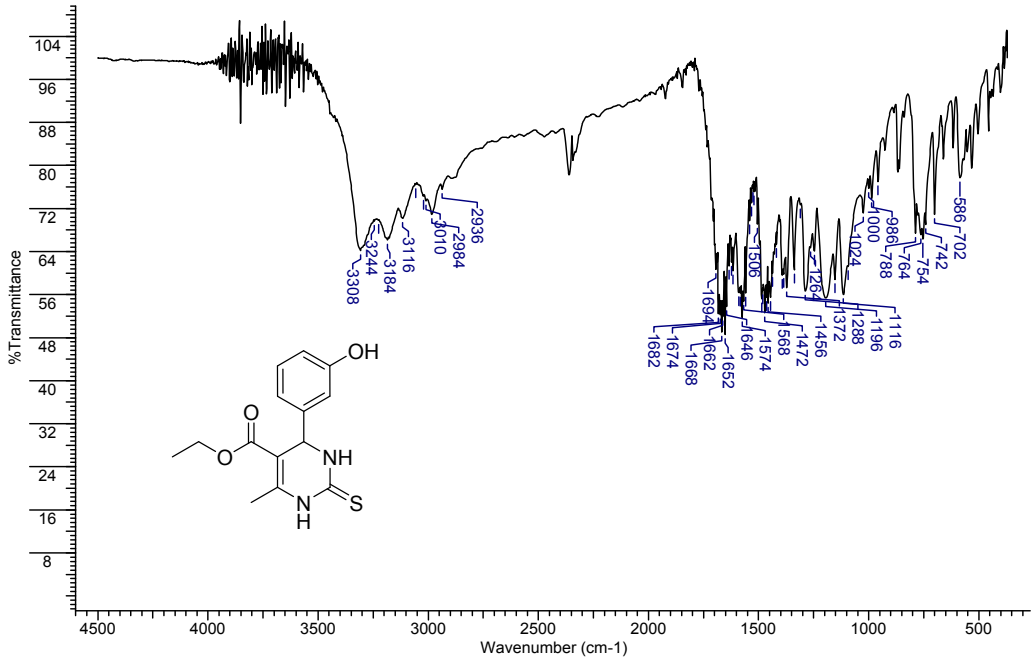

Figure S26. Infrared spectrum (KBr) of **BA2-S**.

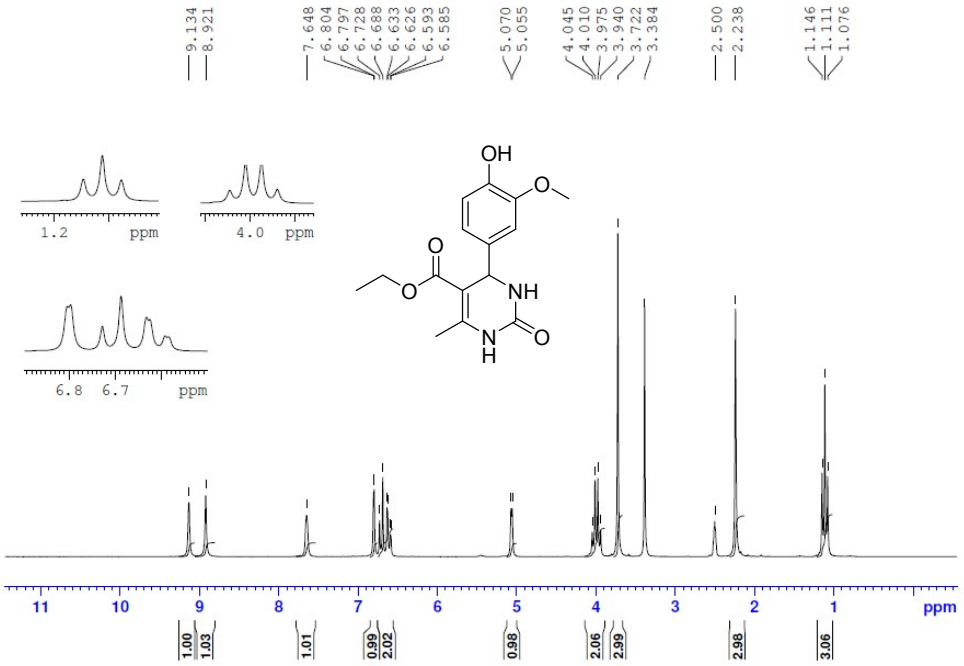

Figure S27. [1]H spectrum of compound **BA3-O** (200 MHz, DMSO-d_6).

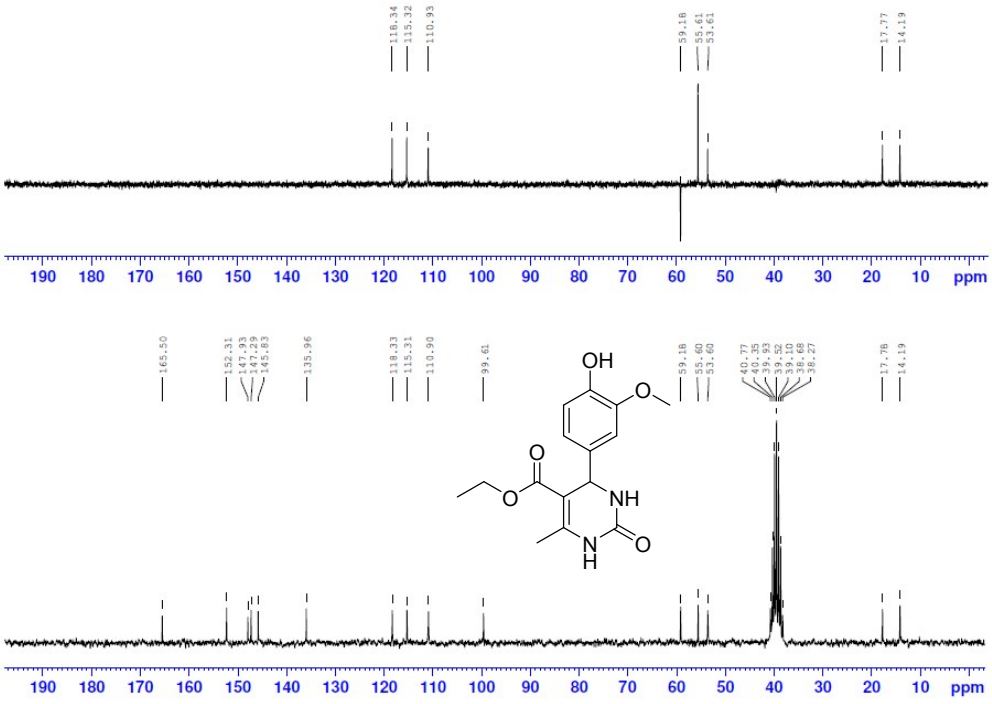

Figure S28. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA3-O** (50 MHz, DMSO-d_6).

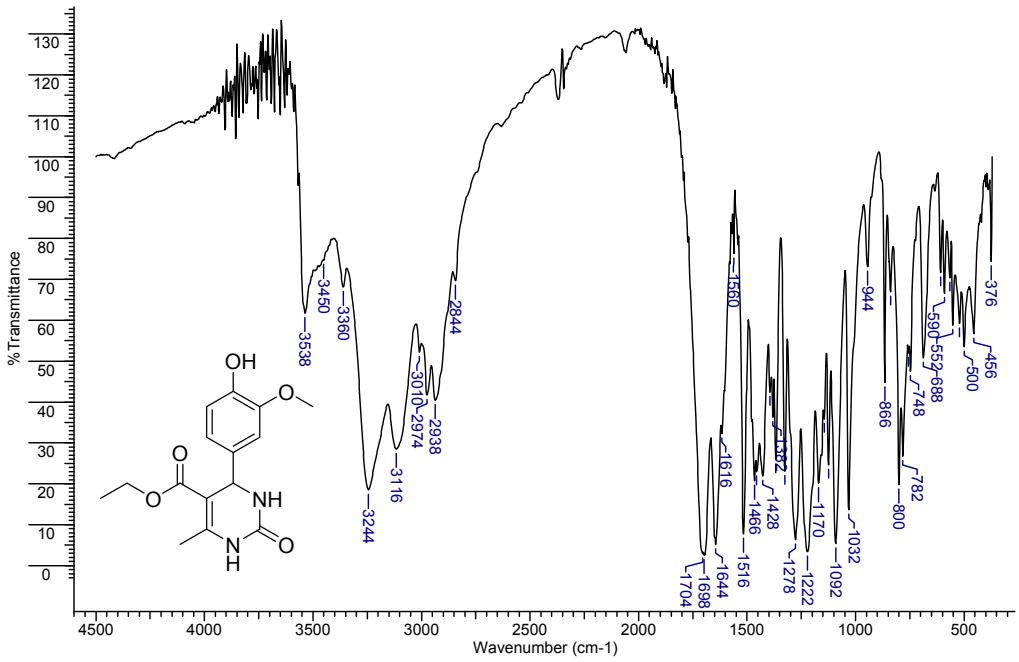

Figure S29. Infrared spectrum (KBr) of **BA3-O**.

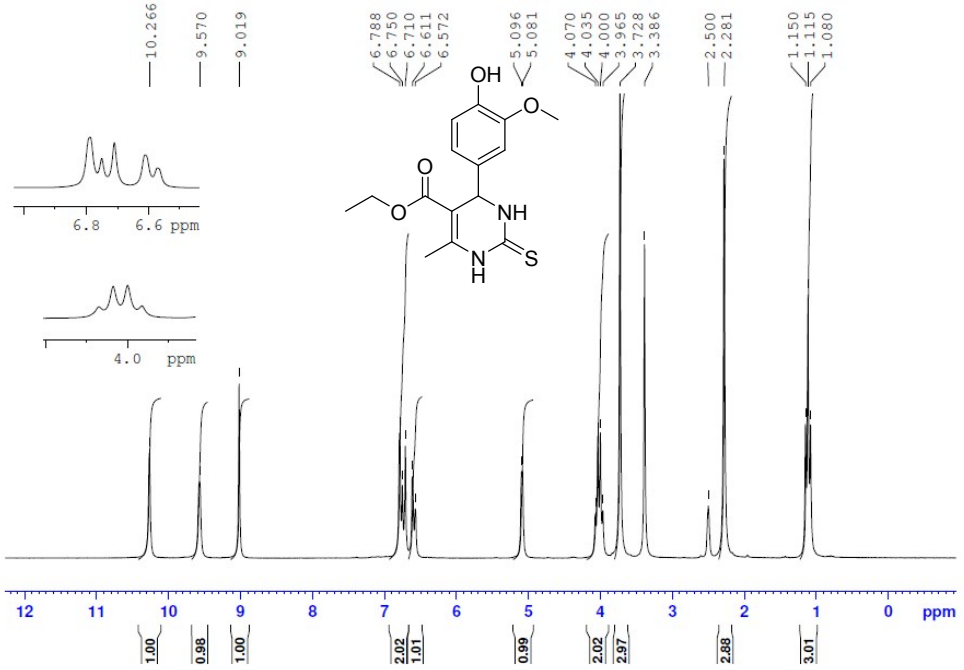

Figure S30. ^{1}H spectrum of compound **BA3-S** (200 MHz, DMSO-d_6).

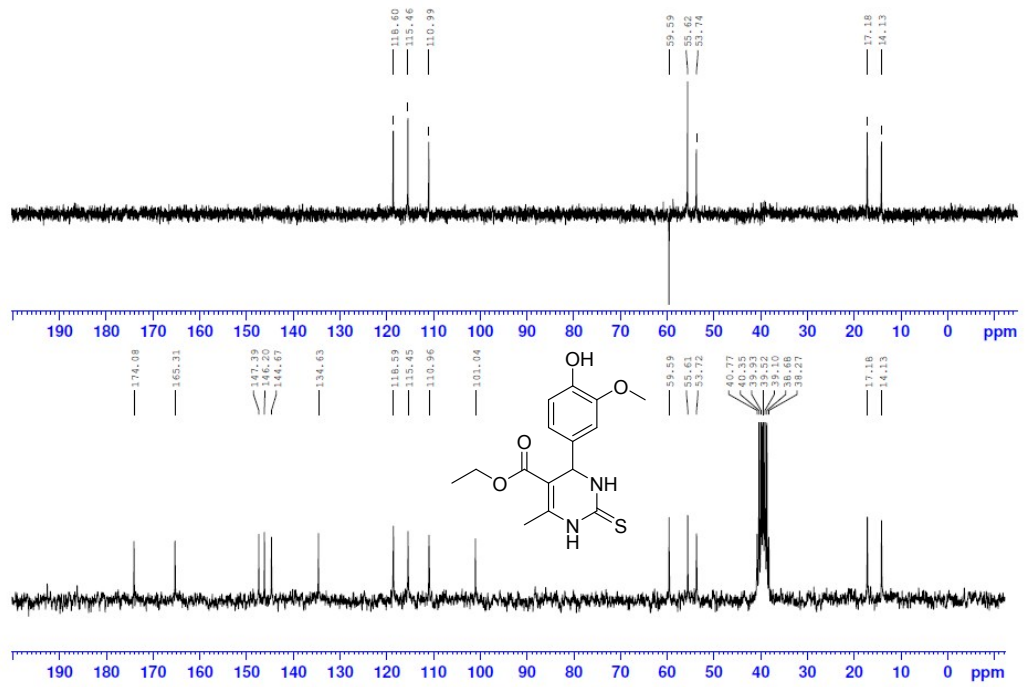

Figure S31. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA3-S** (50 MHz, DMSO-d_6).

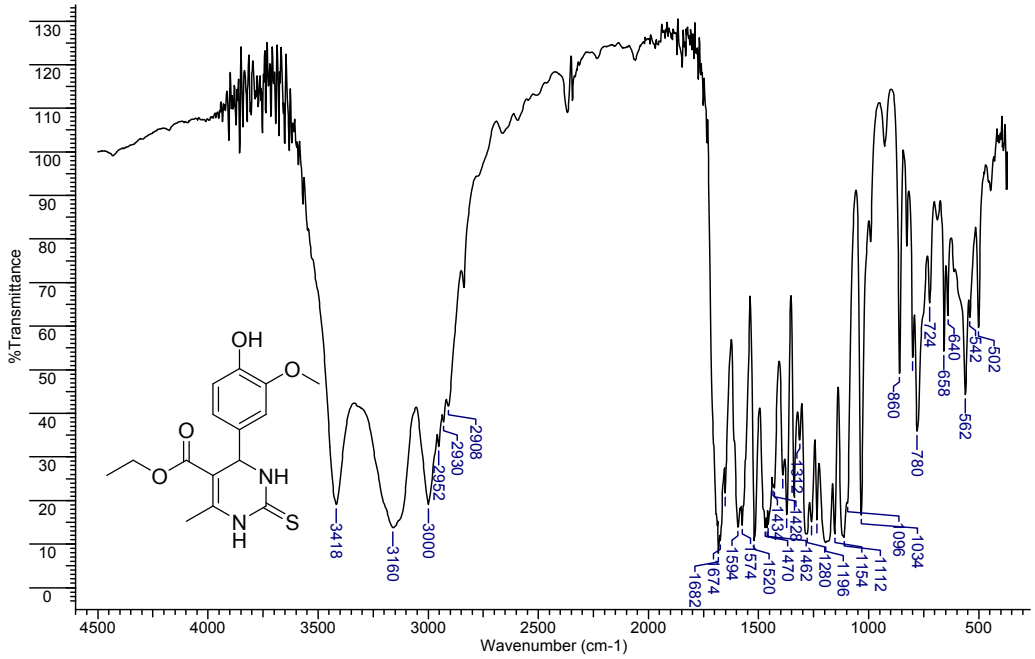

Figure S32. Infrared spectrum (KBr) of **BA3-S**.

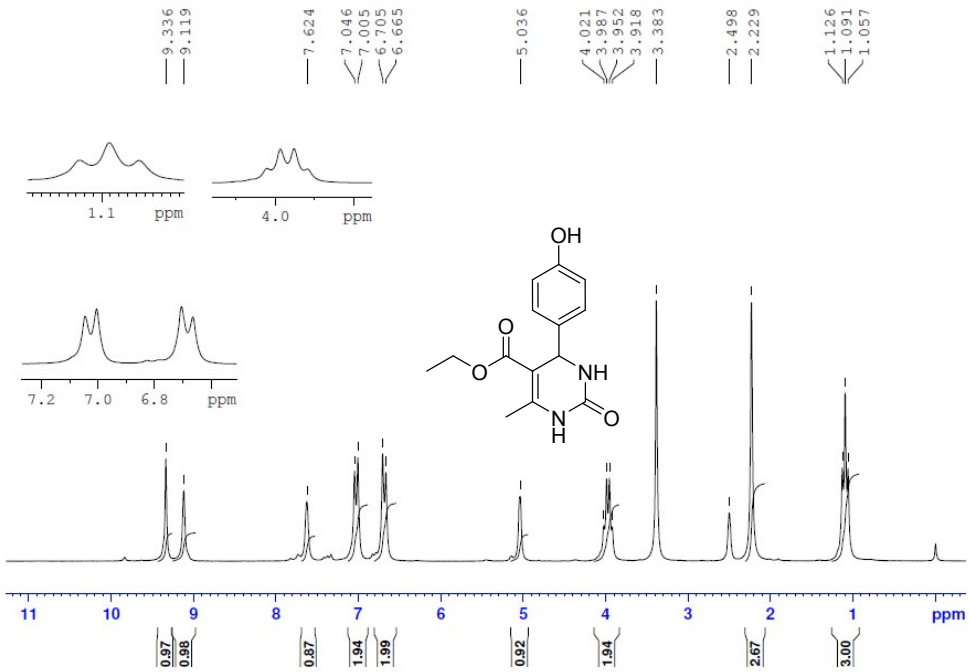

Figure S33. [1]H spectrum of compound **BA4-O** (200 MHz, DMSO-d_6).

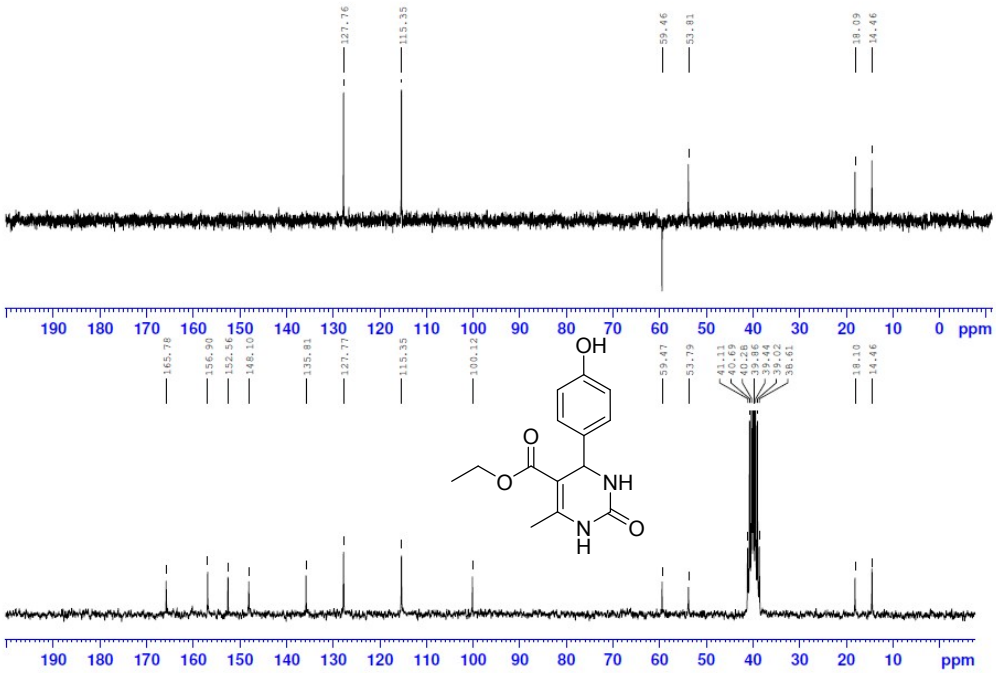

Figure S34. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA4-O** (50 MHz, DMSO-d_6).

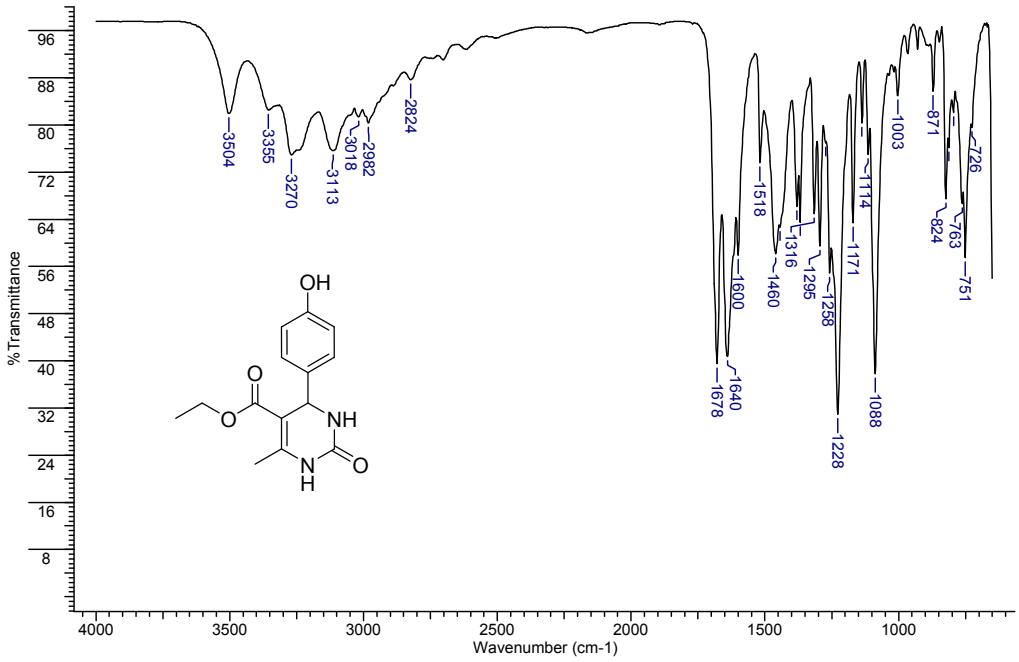

Figure S35. Infrared spectrum (ATR) of **BA4-O**.

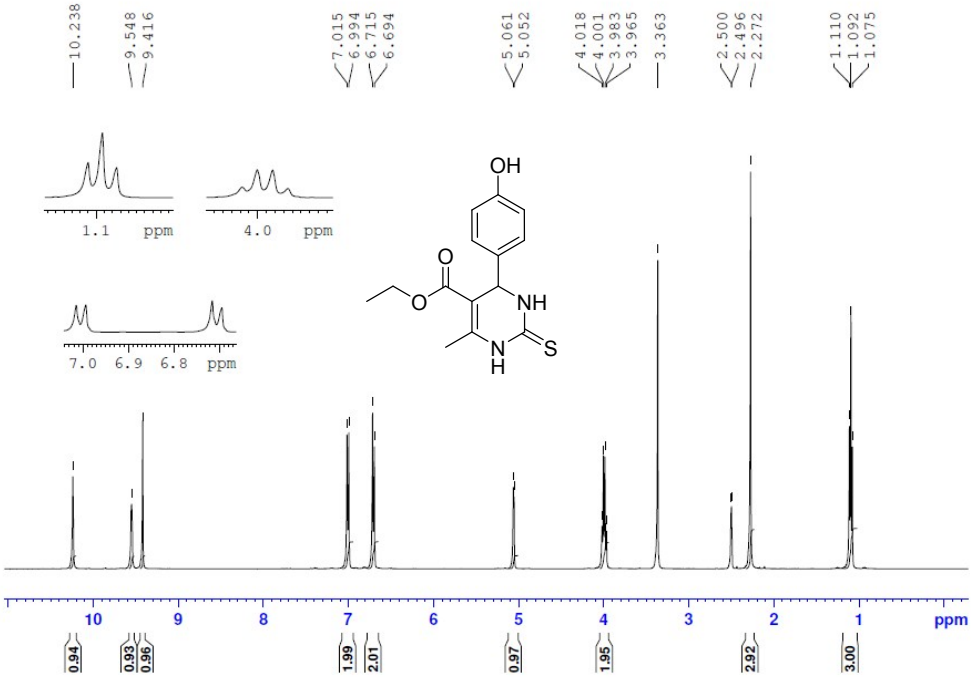

Figure S36. ^{1}H spectrum of compound **BA4-S** (200 MHz, DMSO-d_6).

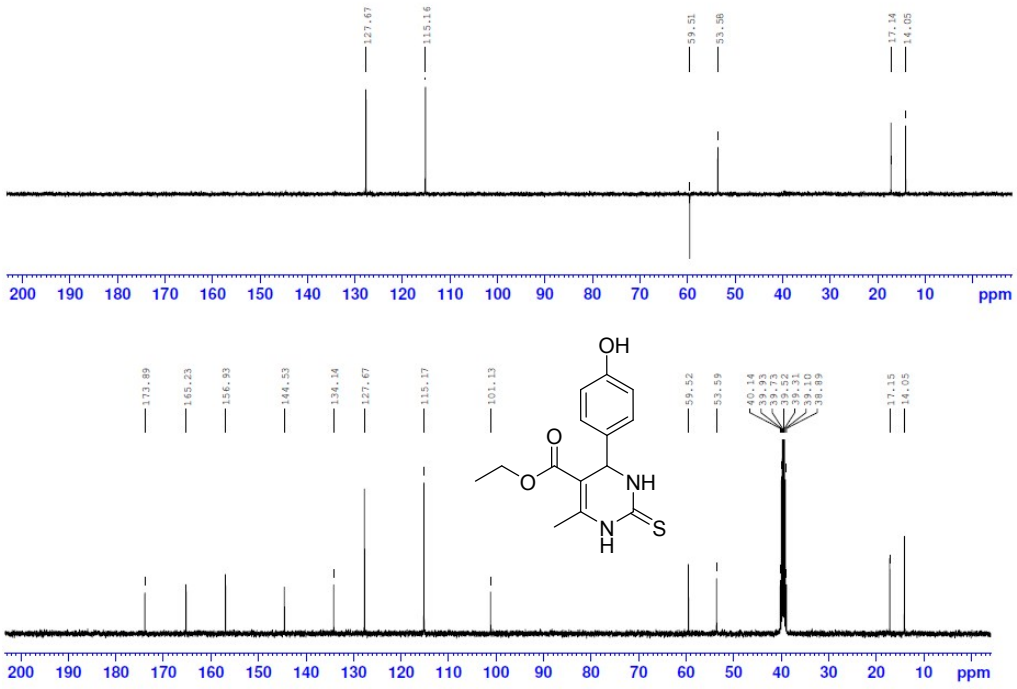

Figure S37. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA4-S** (50 MHz, DMSO-d_6).

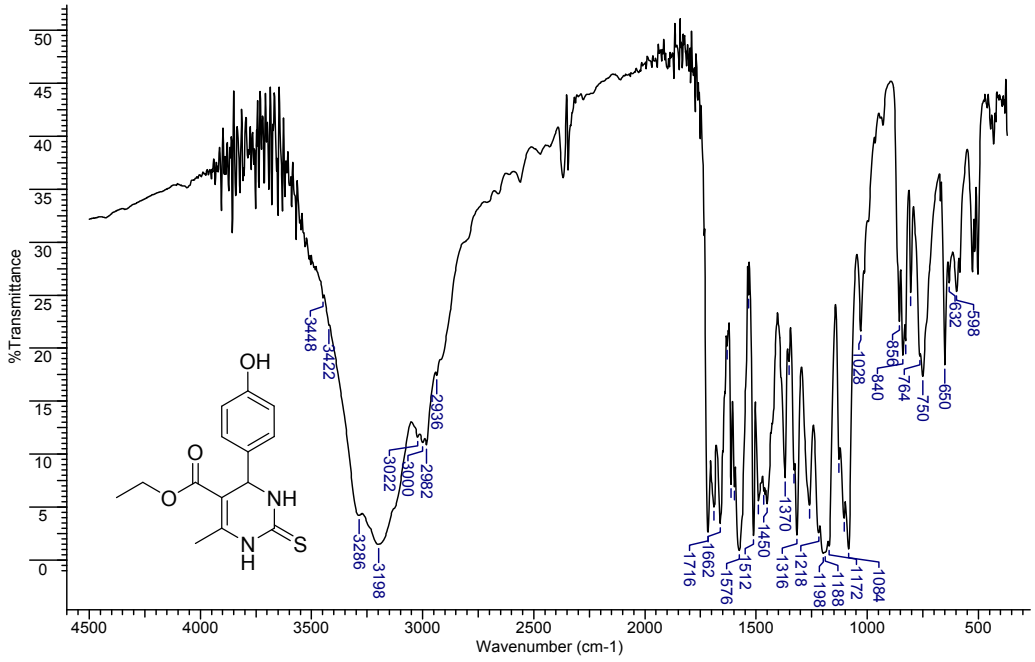

Figure S38. Infrared spectrum (KBr) of **BA4-S.**

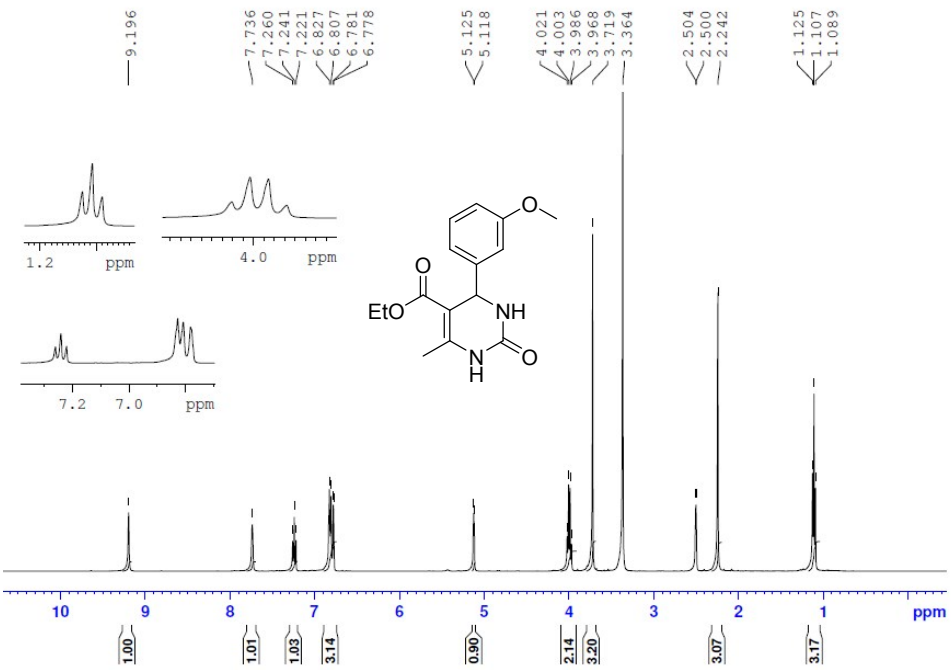

Figure S39. [1]H spectrum of compound **BA5-O** (200 MHz, DMSO-d_6).

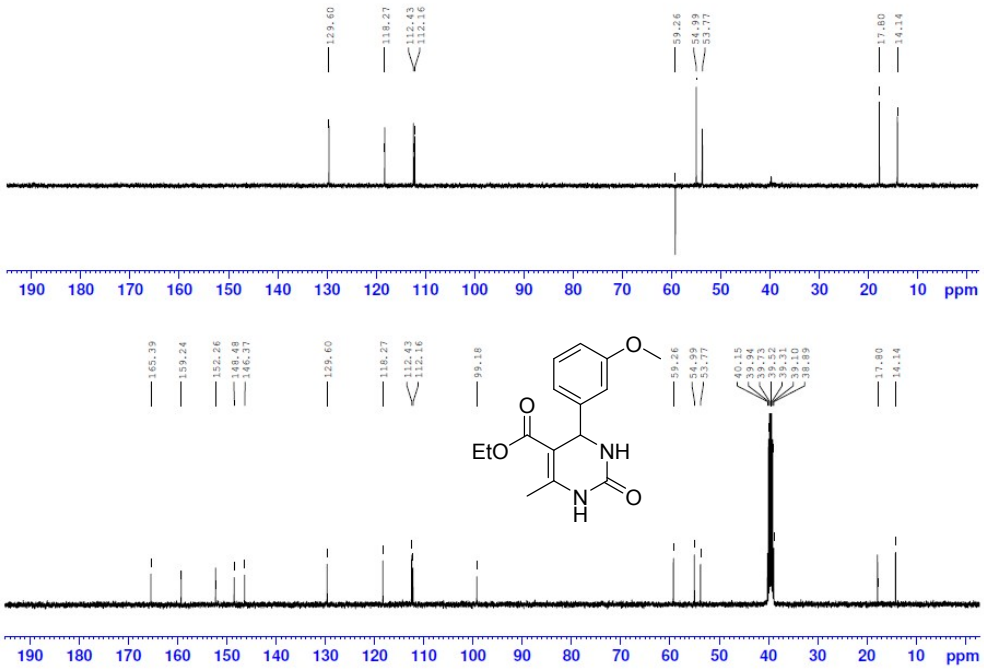

Figure S40. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA5-O** (50 MHz, DMSO-d_6).

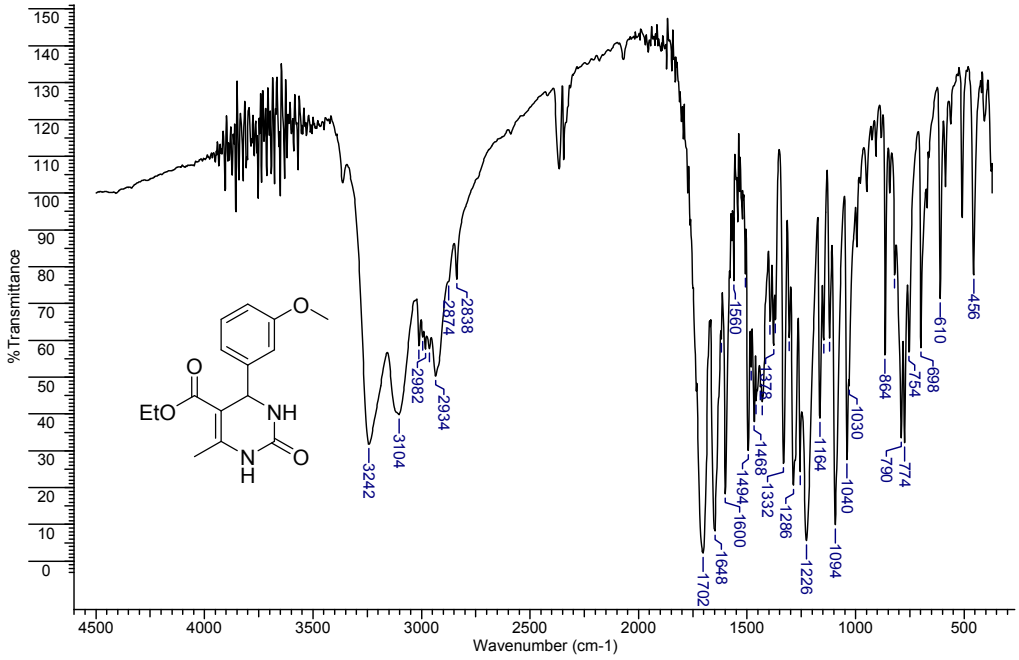

Figure S41. Infrared spectrum (KBr) of **BA5-O**.

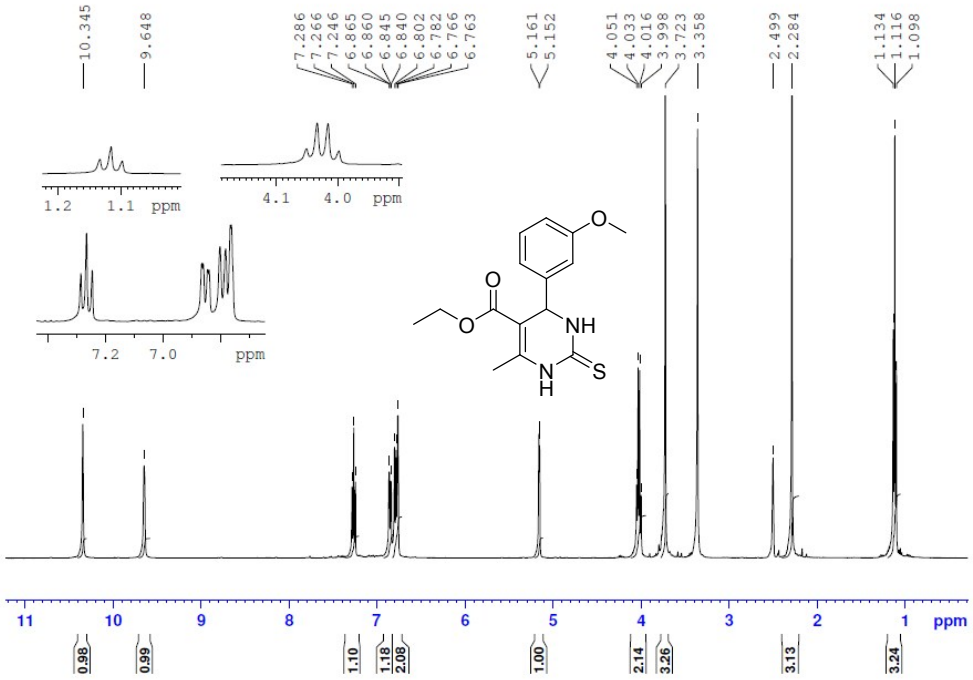

Figure S42. ^{1}H spectrum of compound **BA5-S** (200 MHz, DMSO-d_6).

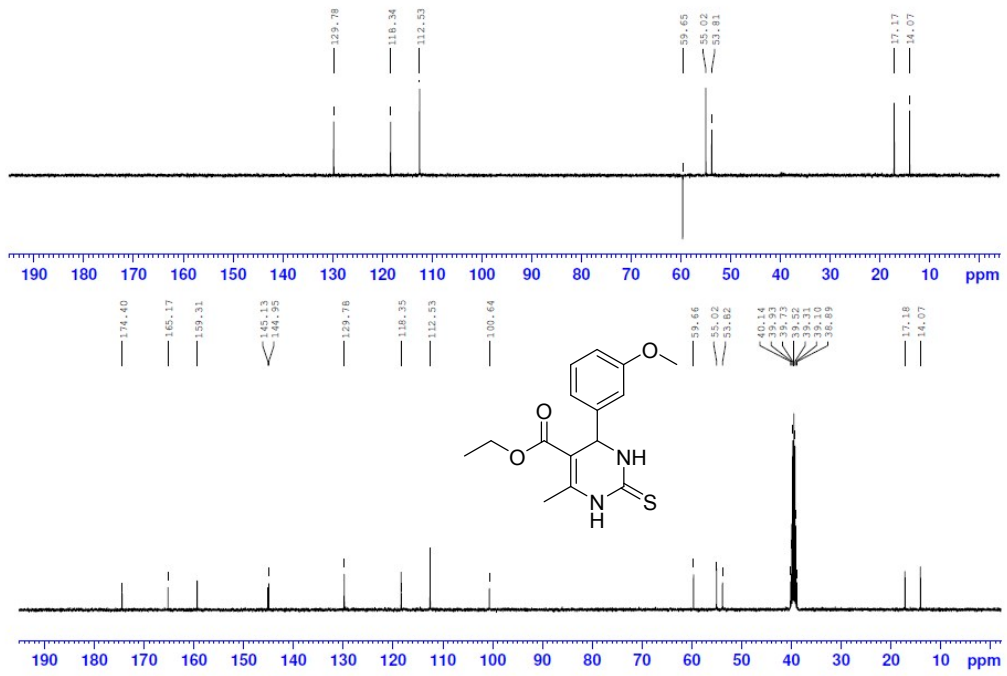

Figure S43. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA5-S** (50 MHz, DMSO-d_6).

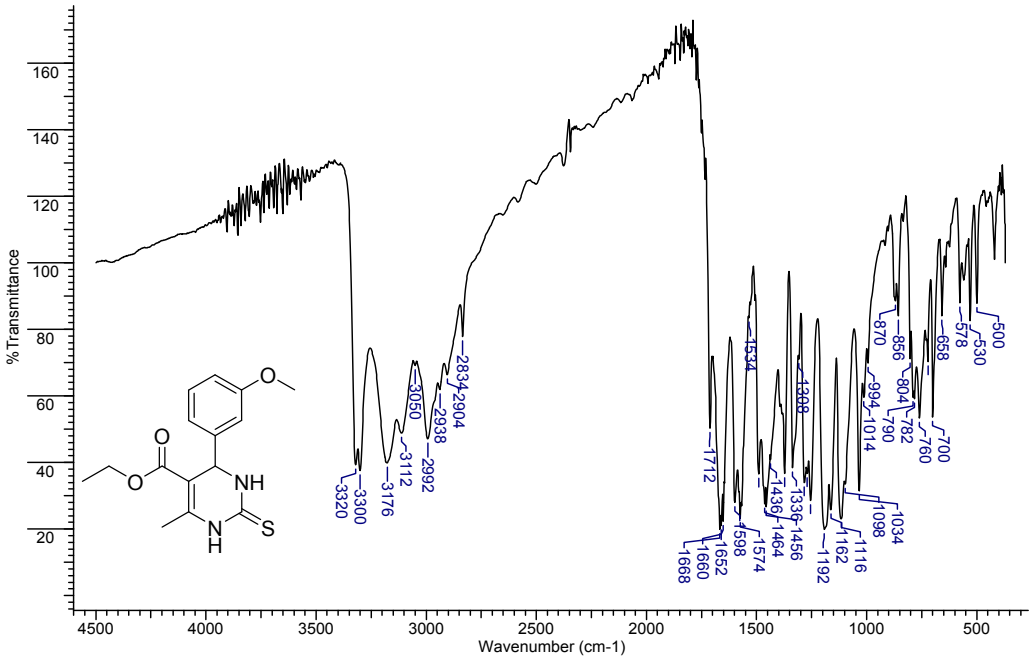

Figure S44. Infrared spectrum (KBr) of **BA5-S**.

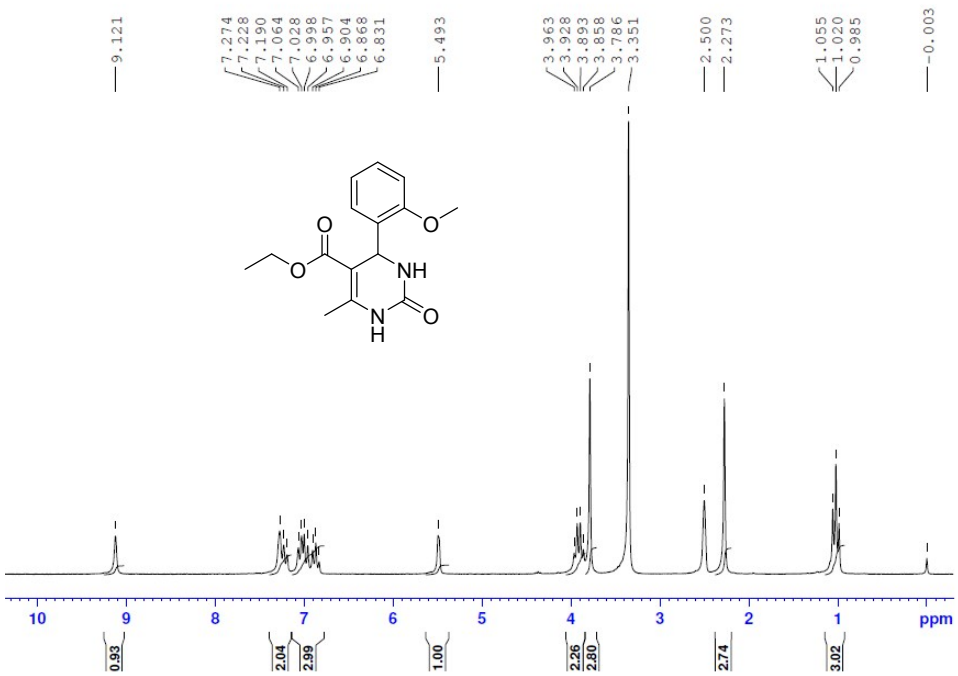

Figure S45. [1]H spectrum of compound **BA6-O** (200 MHz, DMSO-d_6).

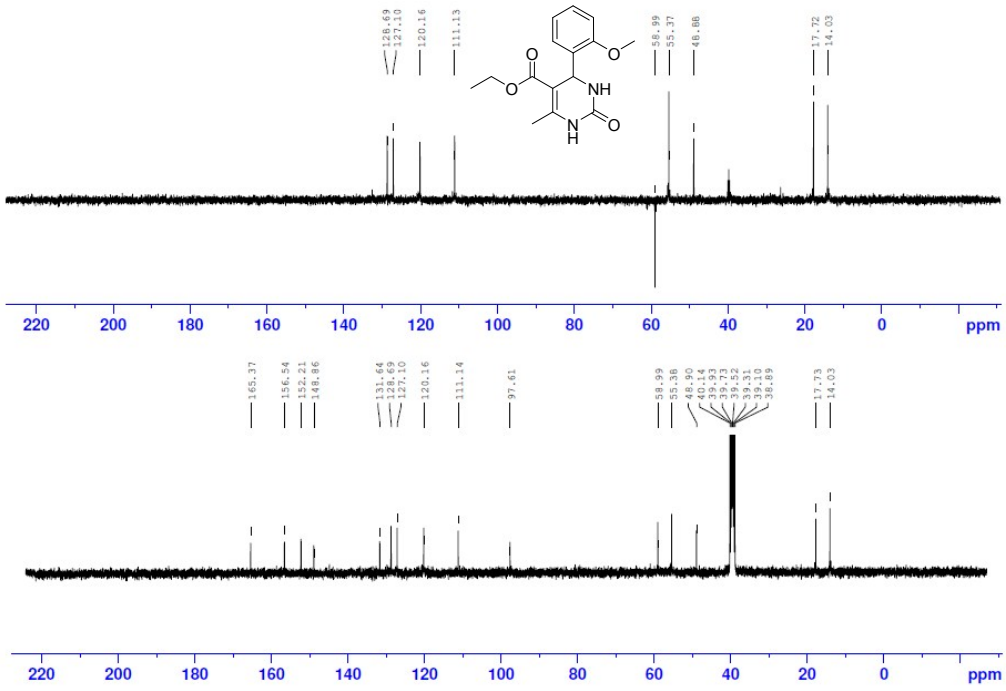

Figure S46. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA6-O** (50 MHz, DMSO-d_6)

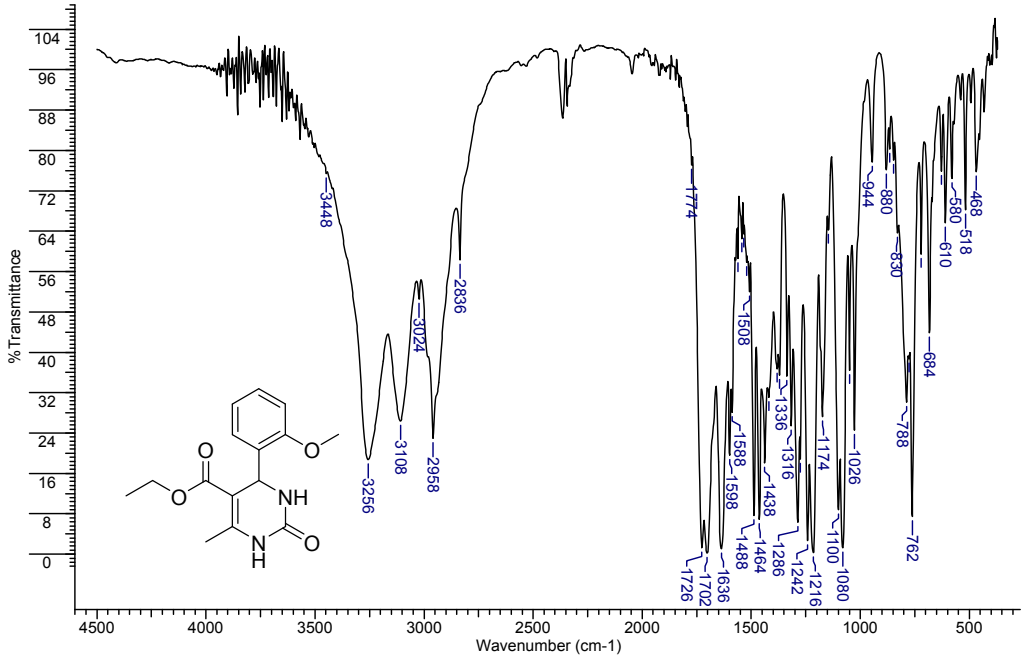

Figure S47. Infrared spectrum (KBr) of **BA6-O**.

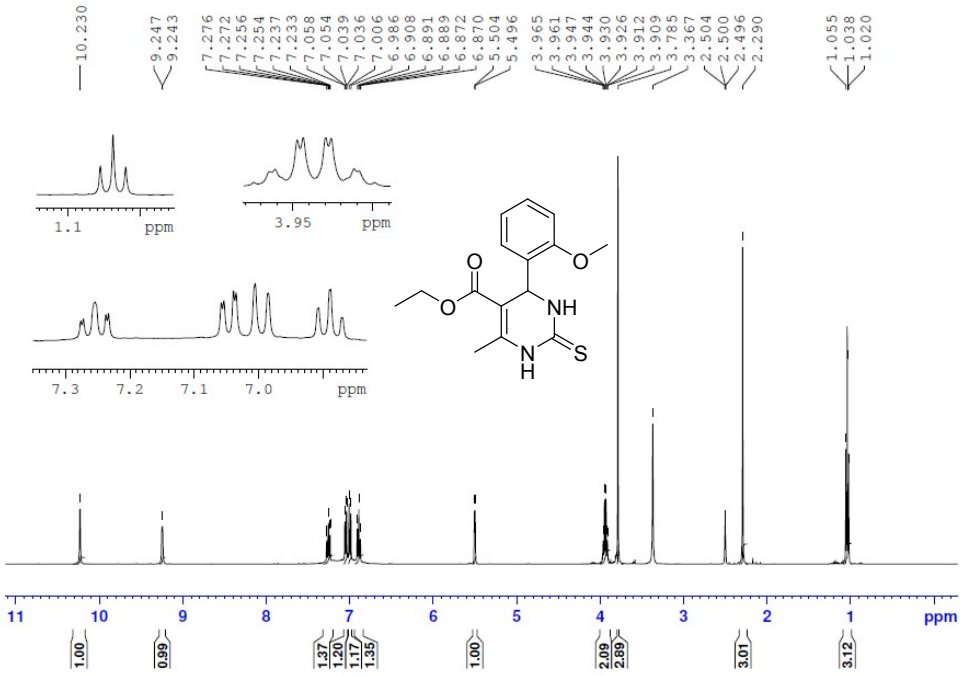

Figure S48. ^{1}H spectrum of compound **BA6-S** (400 MHz, DMSO-d_6).

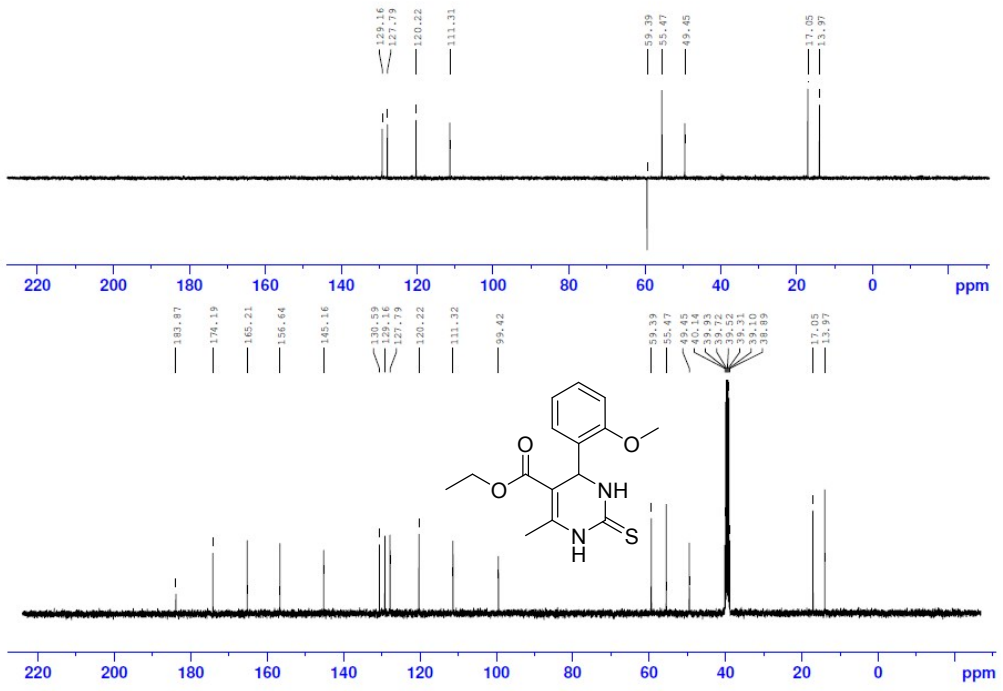

Figure S49. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA6-S** (100 MHz, DMSO-d_6).

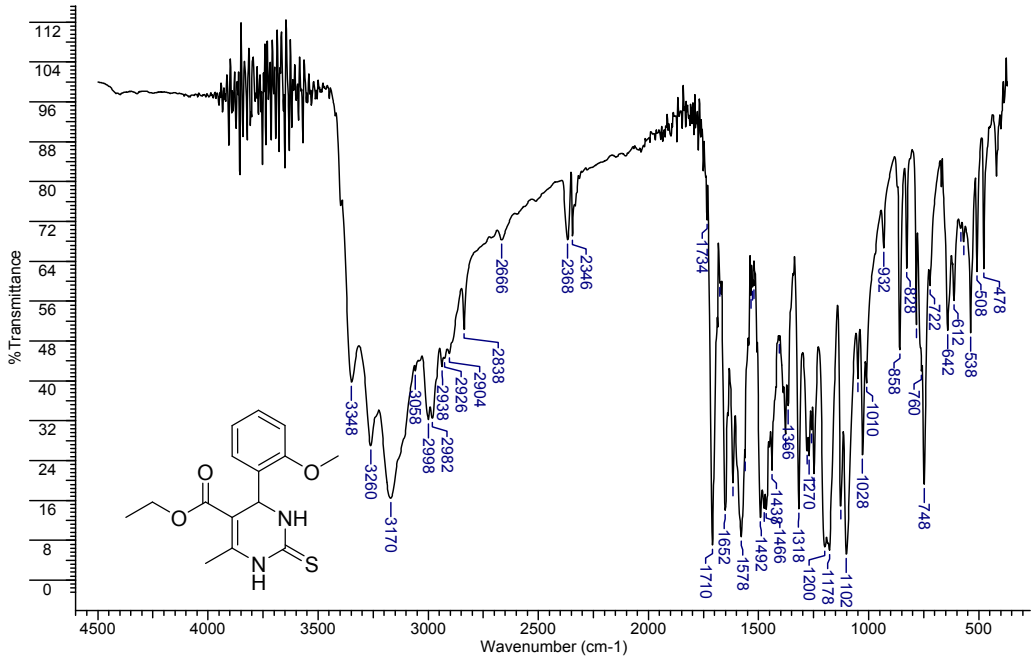

Figure S50. Infrared spectrum (KBr) of **BA6-S**.

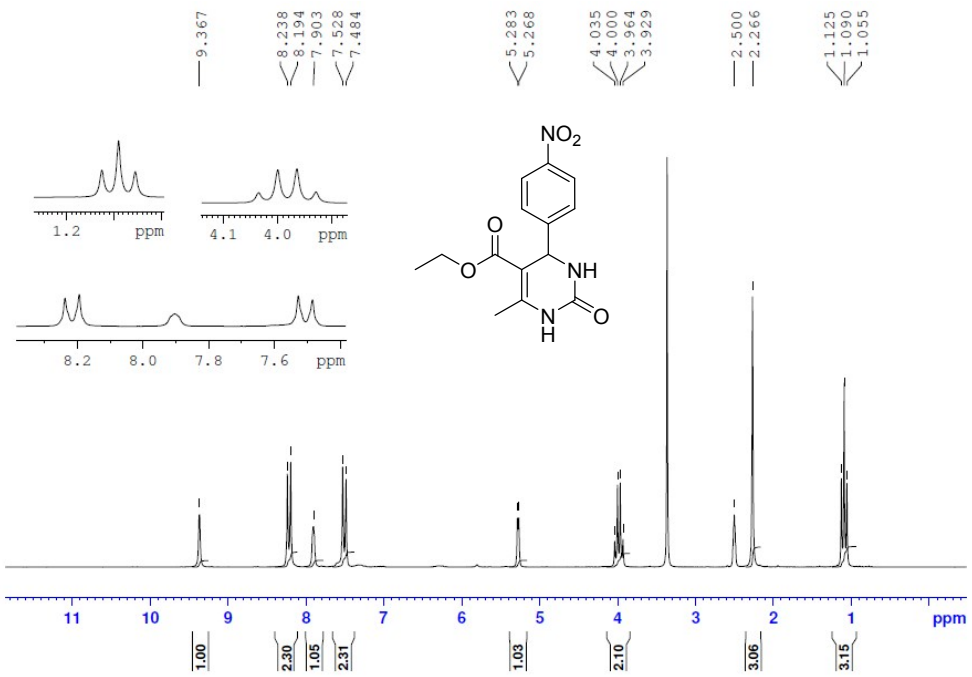

Figure S51. [1]H spectrum of compound **BA7-O** (200 MHz, DMSO-d_6).

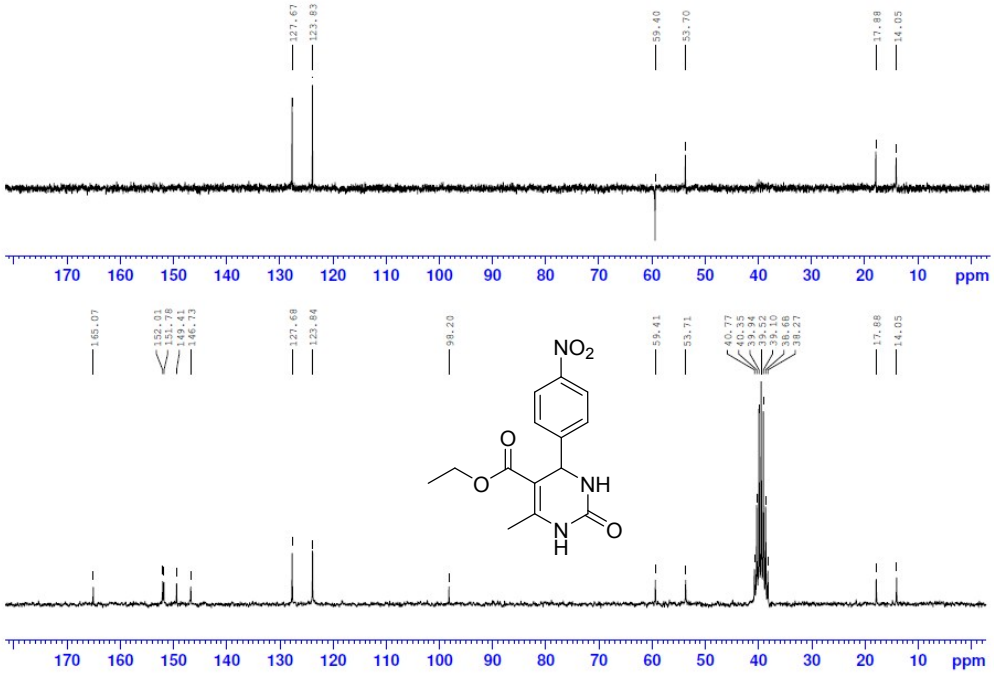

Figure S52. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA7-O** (50 MHz, DMSO-d_6).

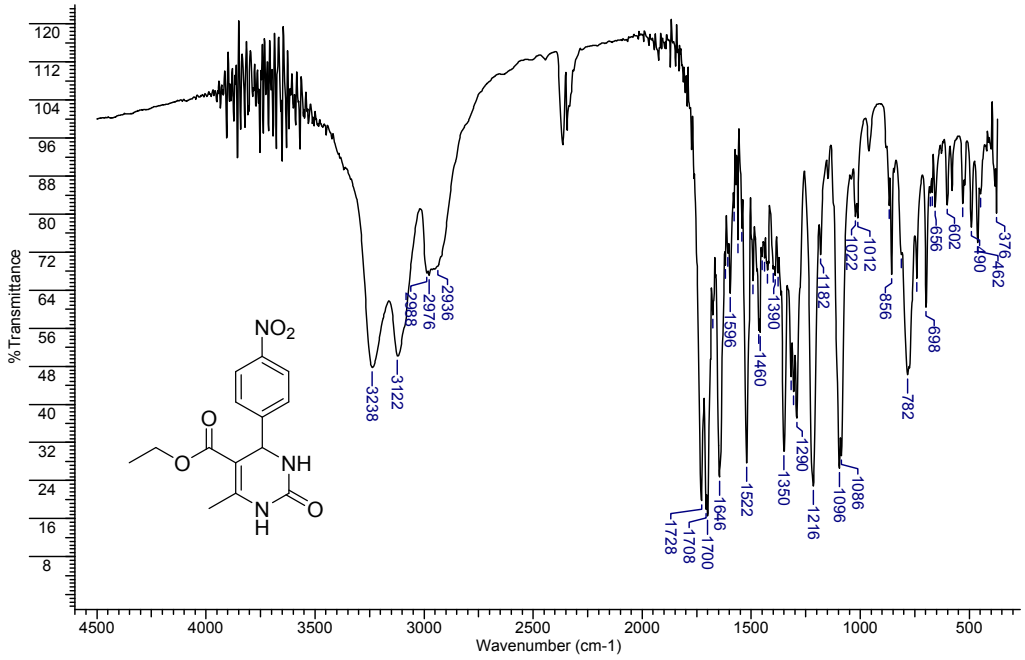

Figure S53. Infrared spectrum (KBr) of **BA7-O**.

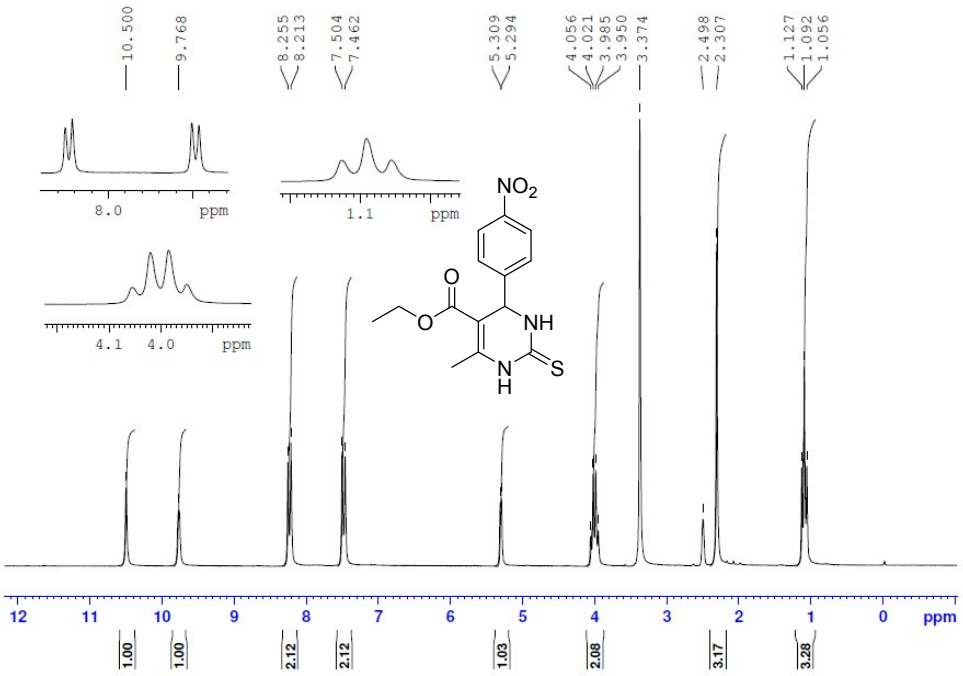

Figure S54. ^{1}H spectrum of compound **BA7-S** (200 MHz, DMSO-d_6).

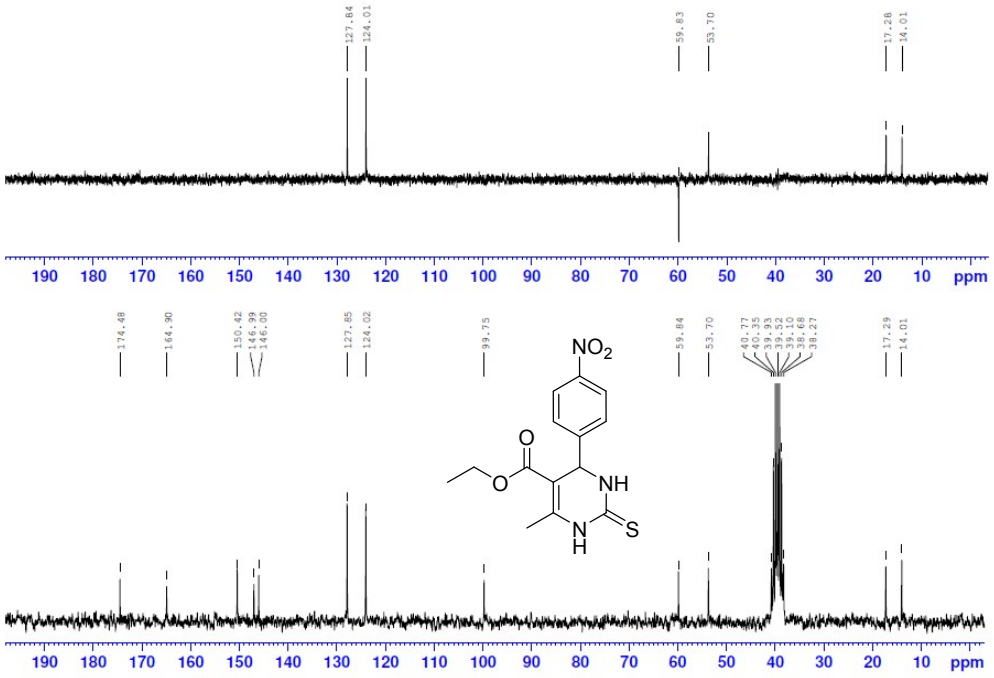

Figure S55. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA7-S** (50 MHz, DMSO-d_6).

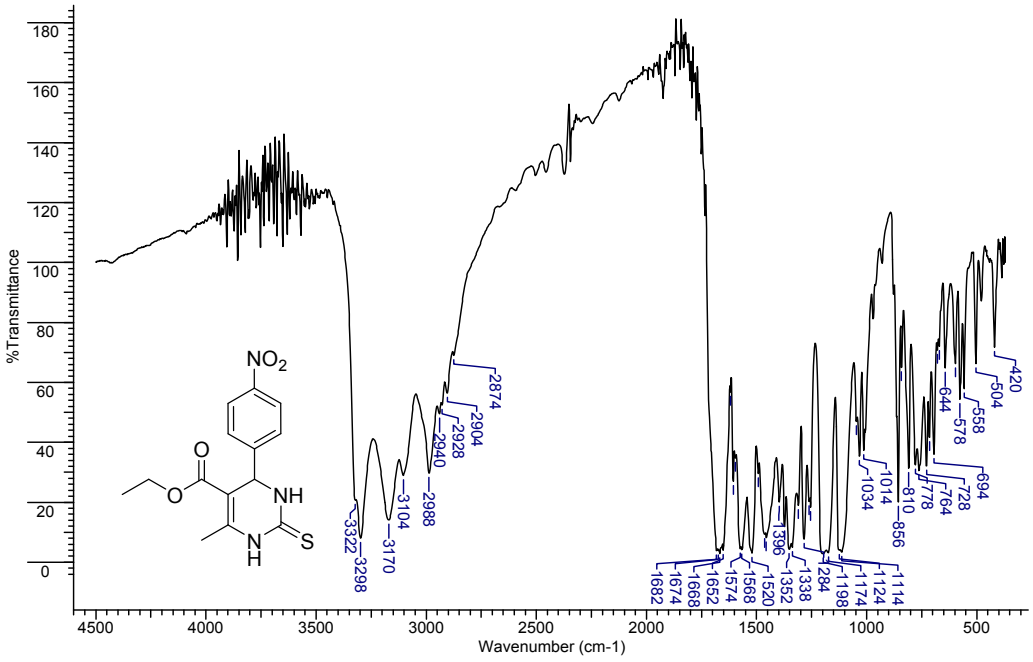

Figure S56. Infrared spectrum (KBr) of **BA7-S**.

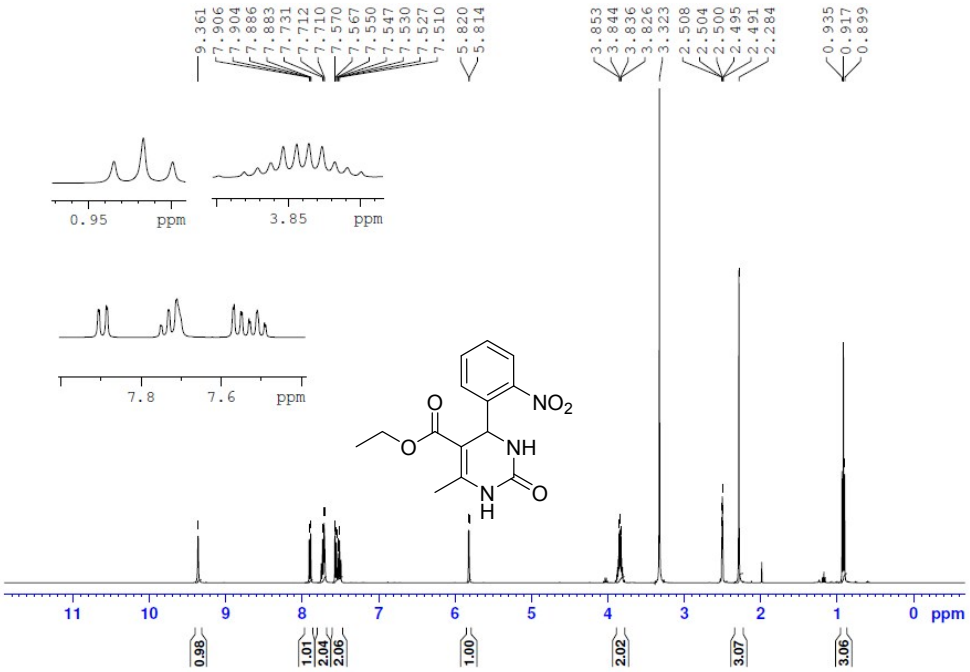

Figure S57. [1]H spectrum of compound **BA8-O** (400 MHz, DMSO-d_6).

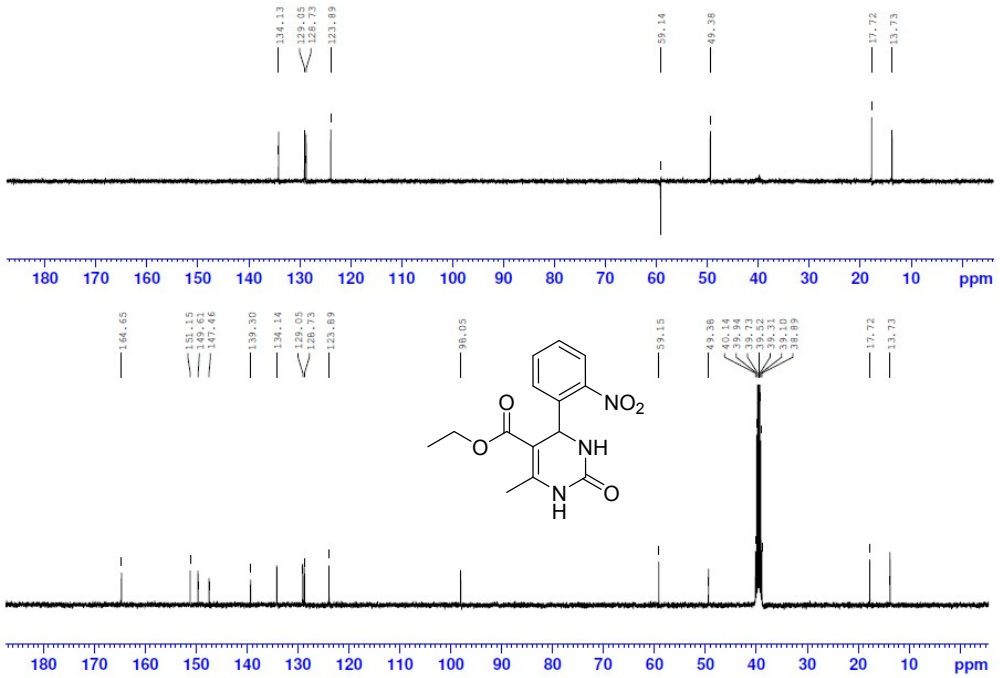

Figure S58. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA8-O** (100 MHz, DMSO-d_6).

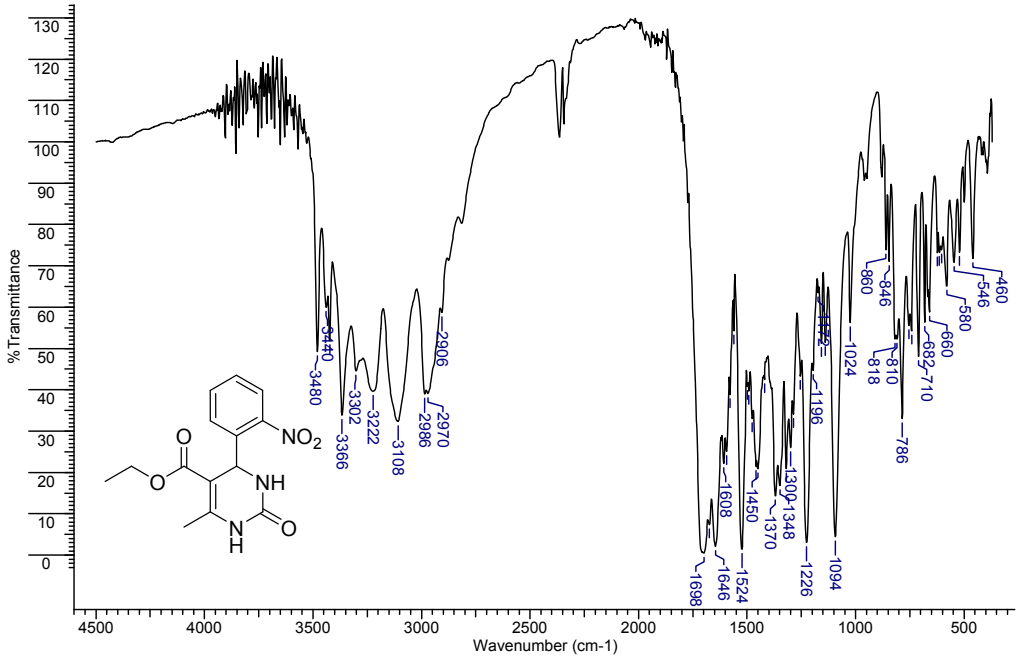

Figure S59. Infrared spectrum (KBr) of **BA8-O**.

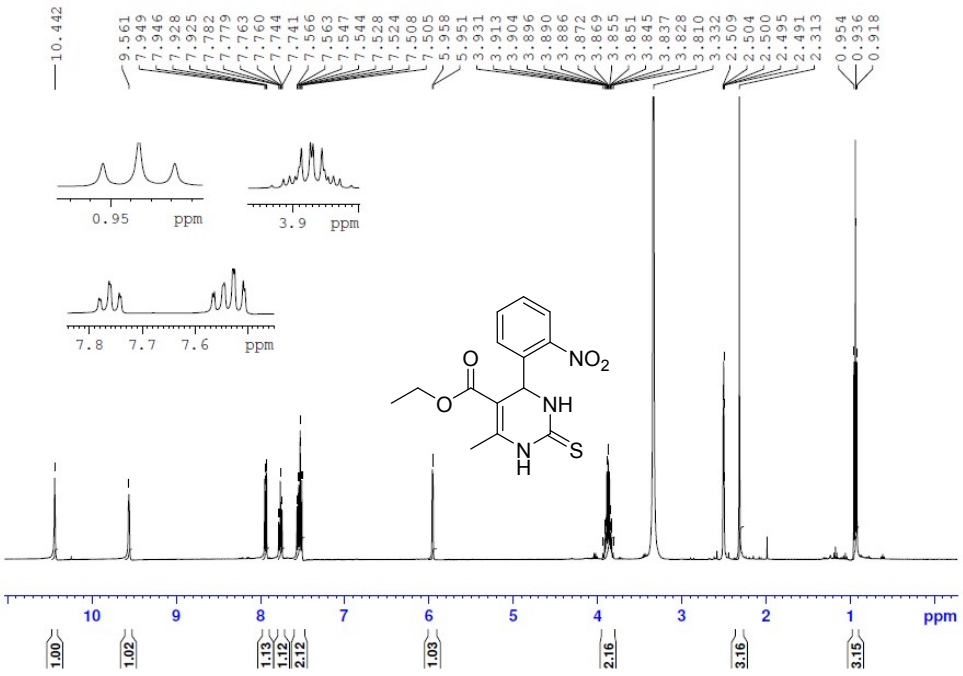

Figure S60. ^{1}H spectrum of compound **BA8-S** (400 MHz, DMSO-d_6).

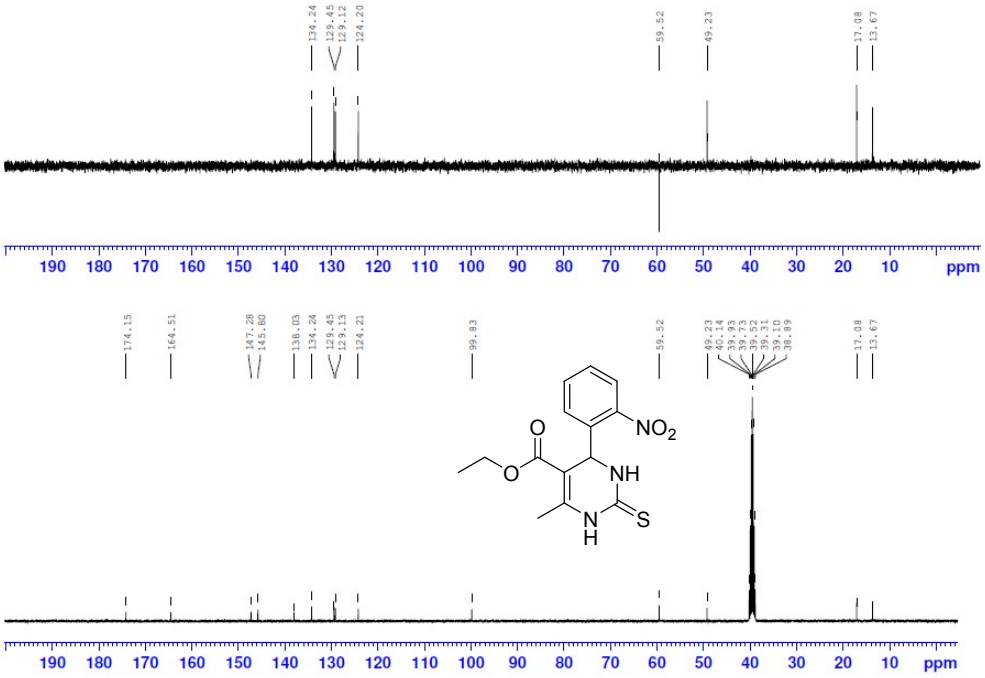

Figure S61. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA8-S** (100 MHz, DMSO-d_6).

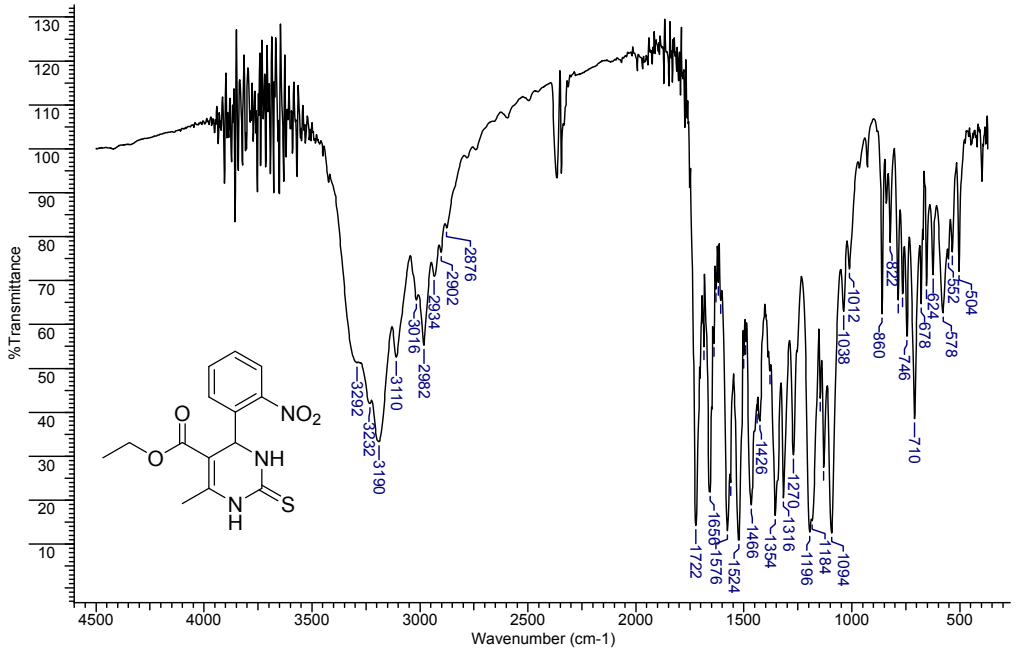

Figure S62. Infrared spectrum (KBr) of **BA8-S**.

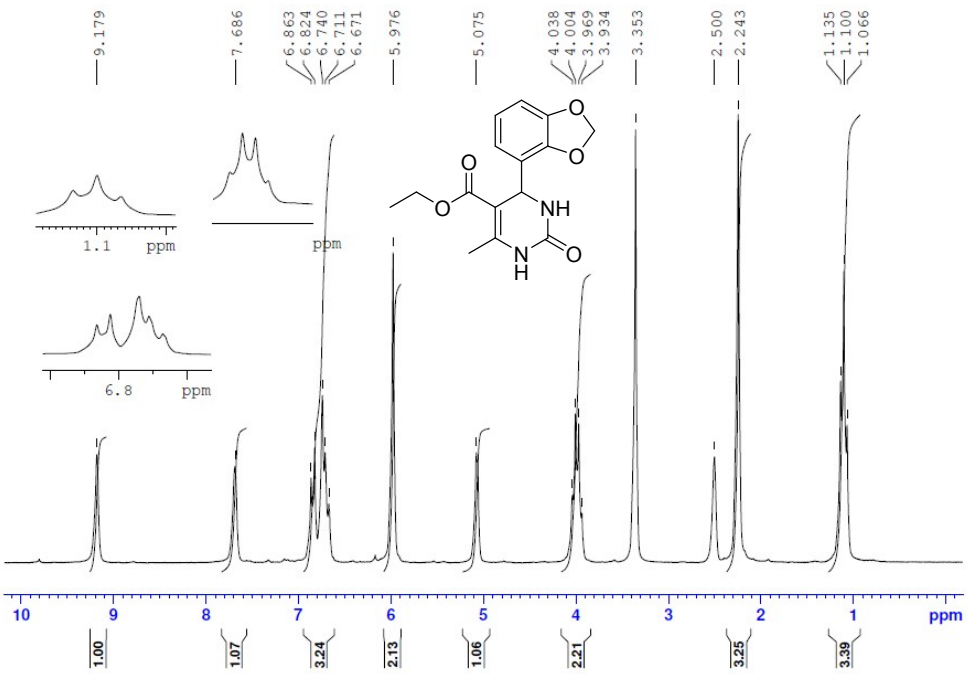

Figure S63. [1]H spectrum of compound **BA9-O** (200 MHz, DMSO-d_6).

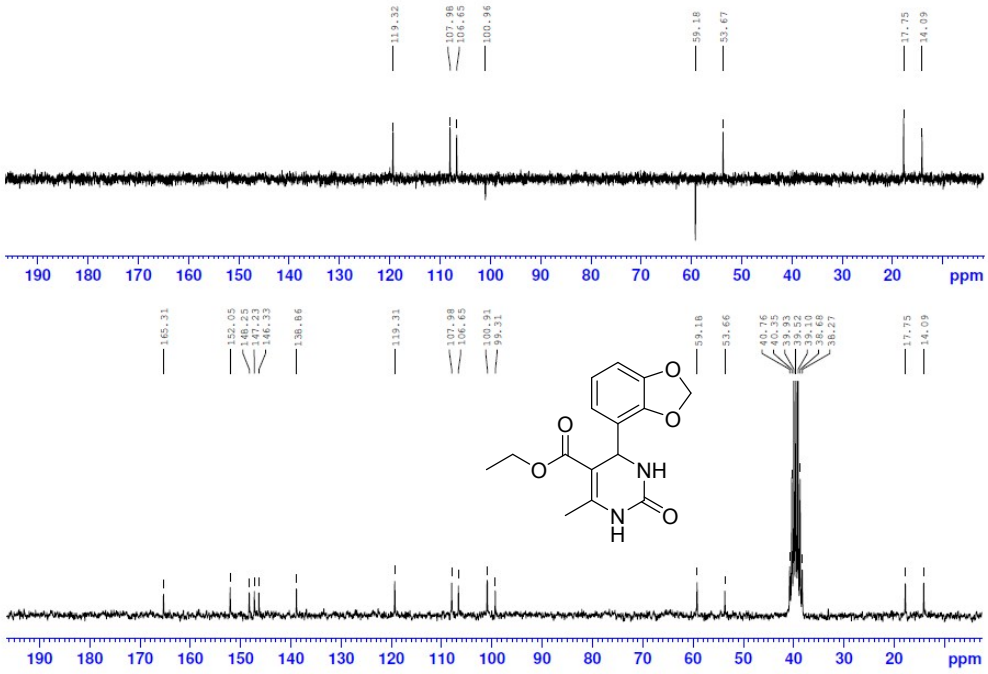

Figure S64. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA9-O** (50 MHz, DMSO-d_6)

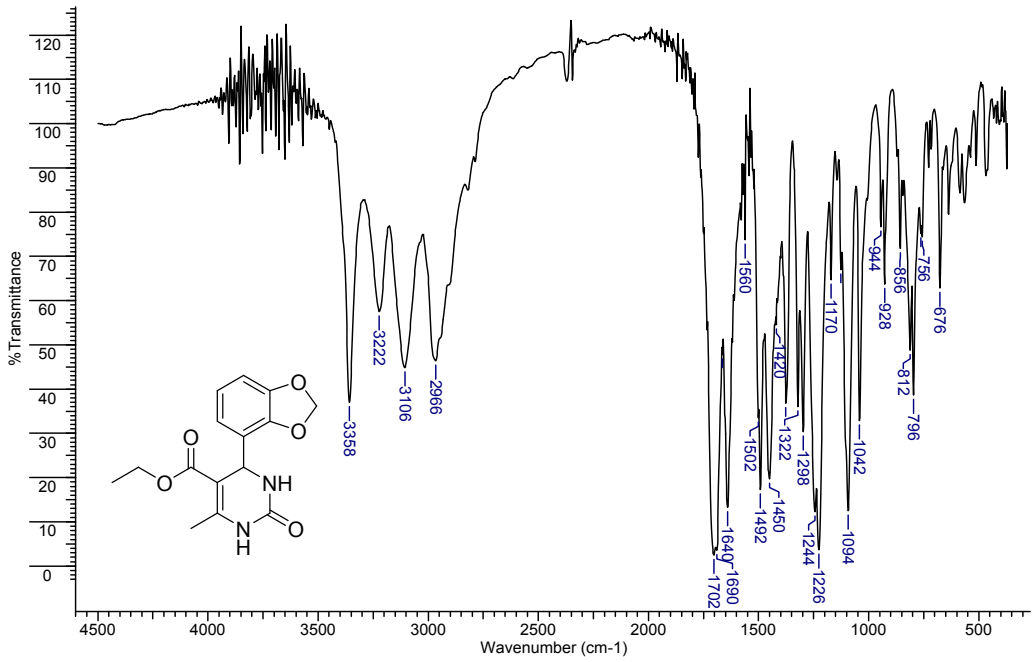

Figure S65. Infrared spectrum (KBr) of **BA9-O**.

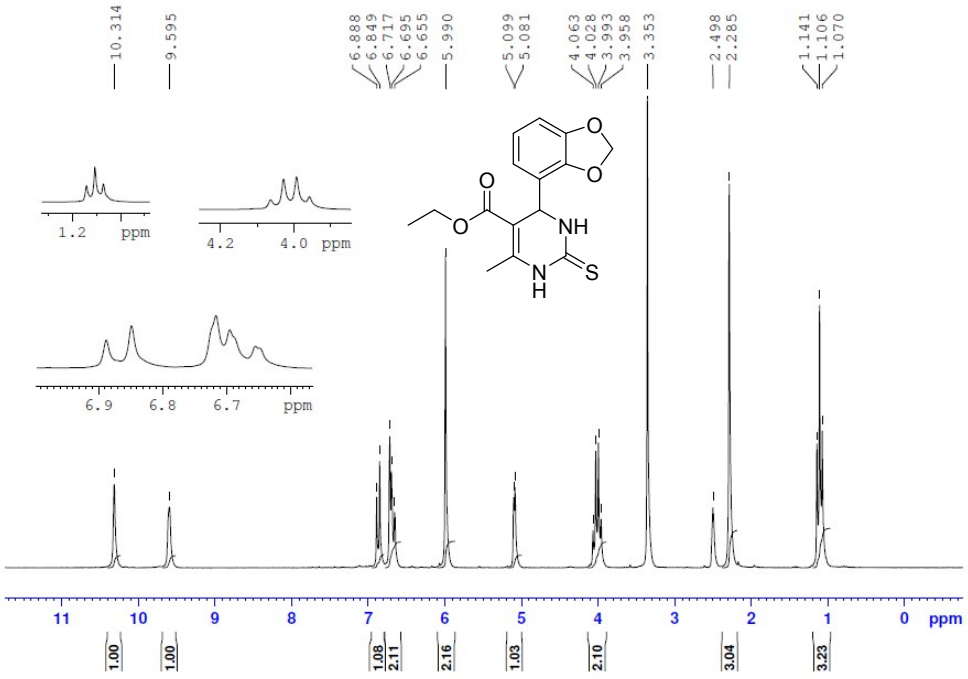

Figure S66. ^{1}H spectrum of compound **BA9-S** (200 MHz, DMSO-d_6).

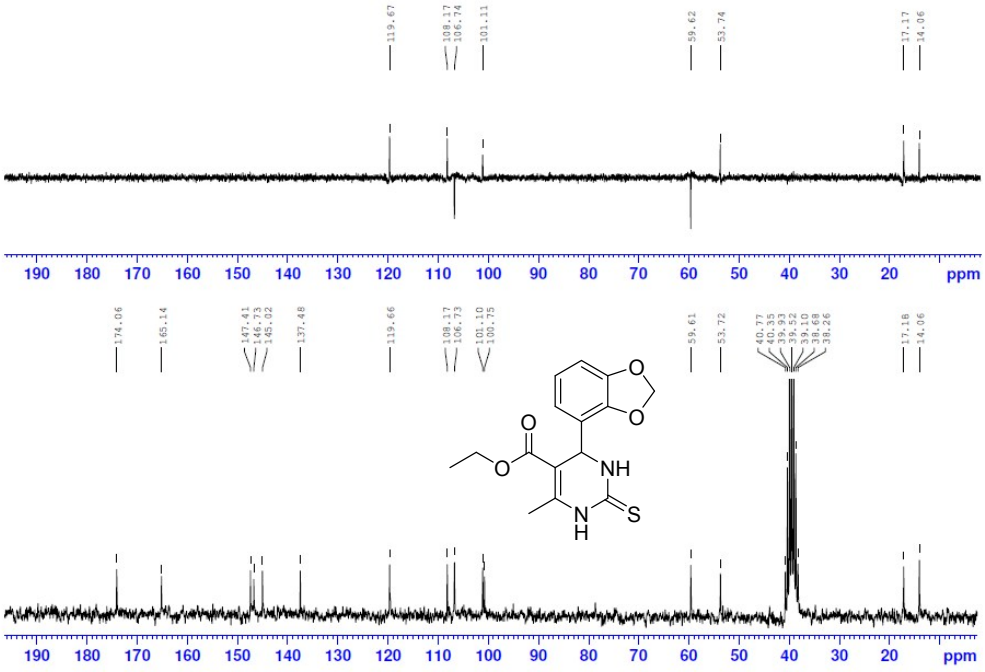

Figure S67. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA9-S** (50 MHz, DMSO-d_6)

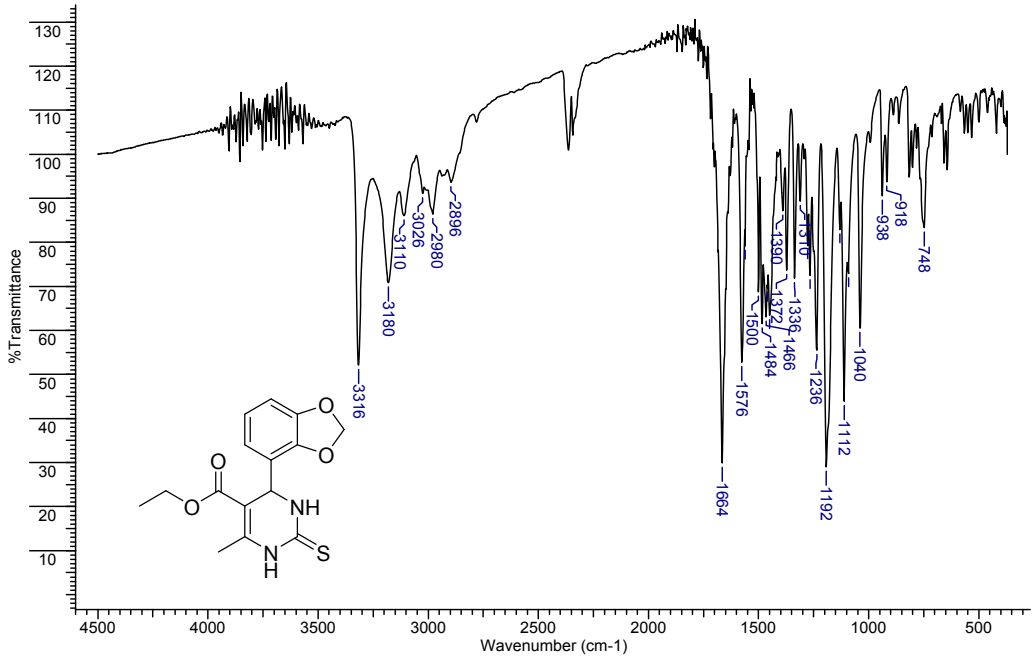

Figure S68. Infrared spectrum (KBr) of **BA9-S**.

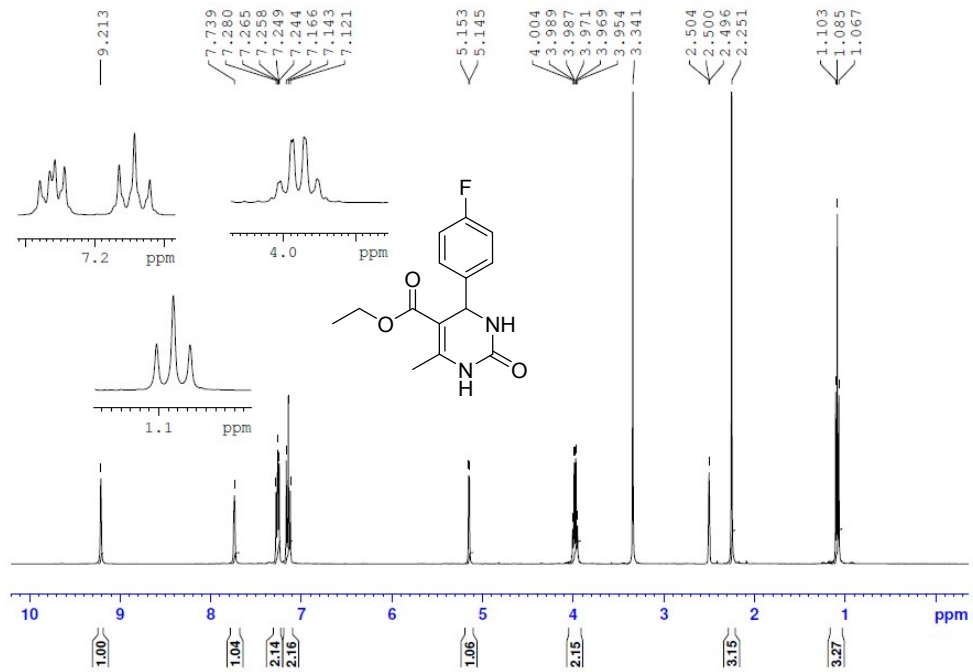

Figure S69. [1]H spectrum of compound **BA10-O** (200 MHz, DMSO-d_6).

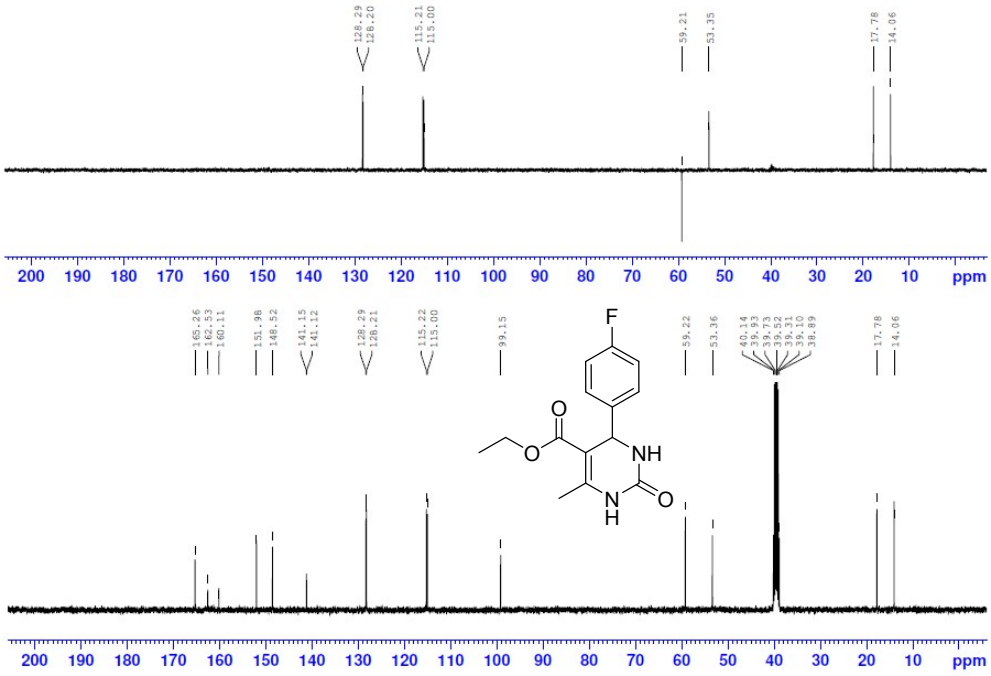

Figure S70. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA10-O** (50 MHz, DMSO-d_6).

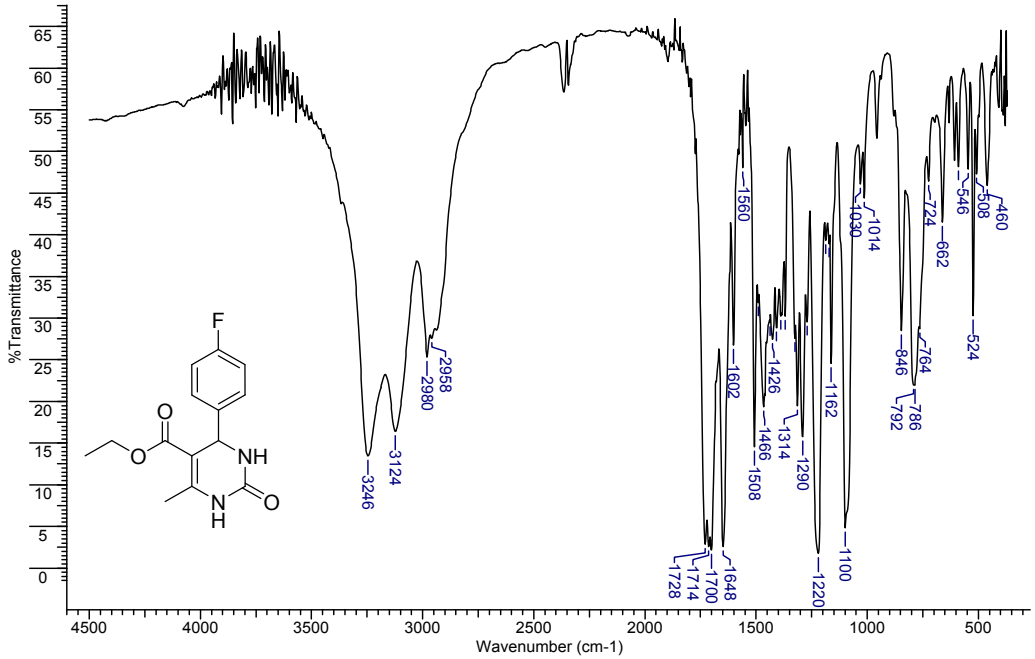

Figure S71. Infrared spectrum (KBr) of **BA10-O**.

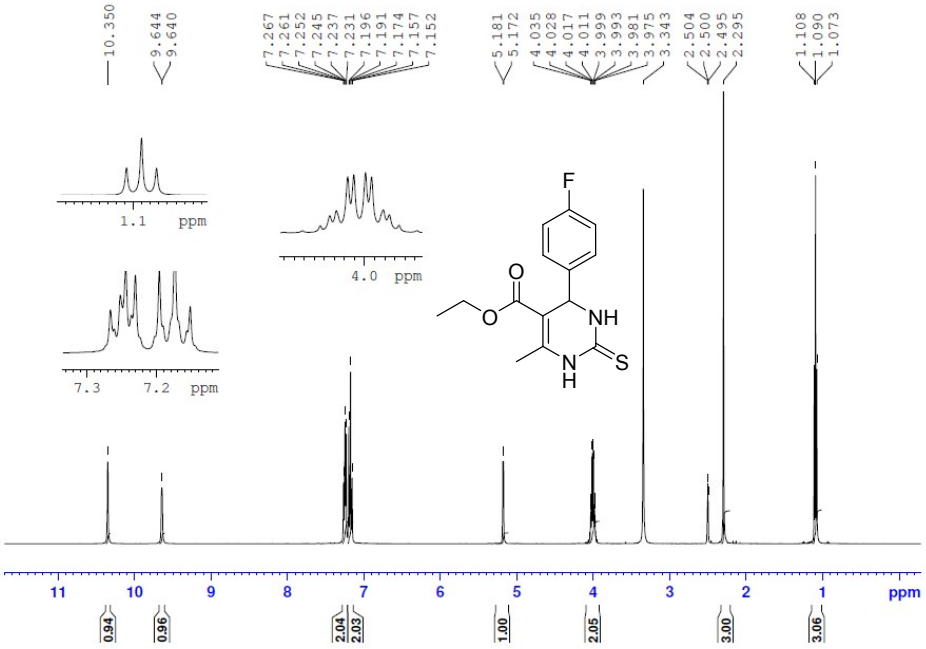

Figure S72. ^{1}H spectrum of compound **BA10-S** (400 MHz, DMSO-d_6).

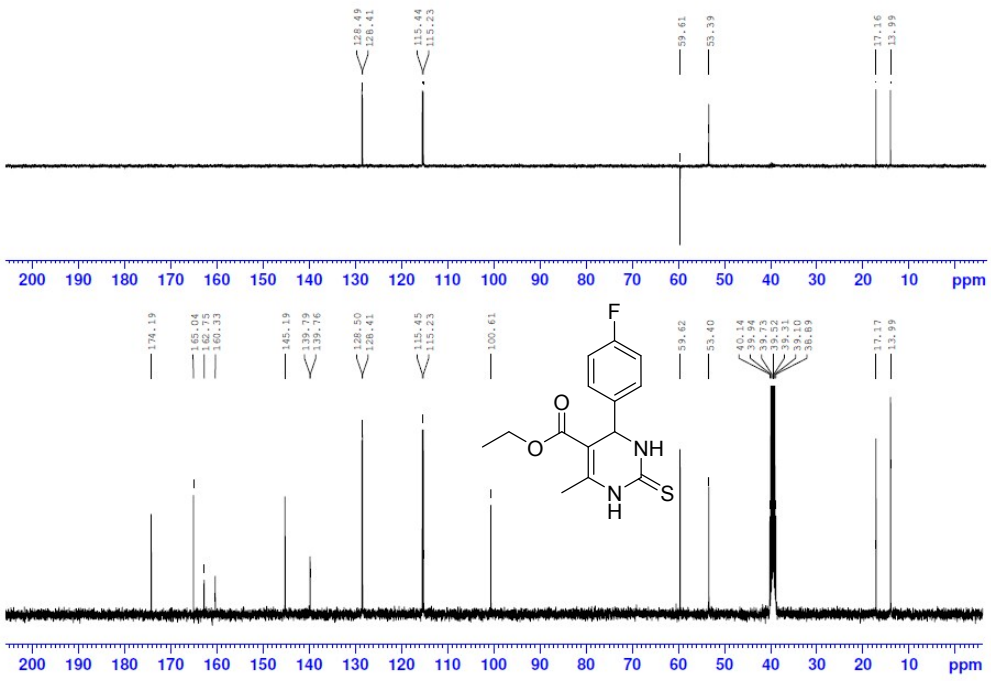

Figure S73. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA10-S** (100 MHz, DMSO-d_6).

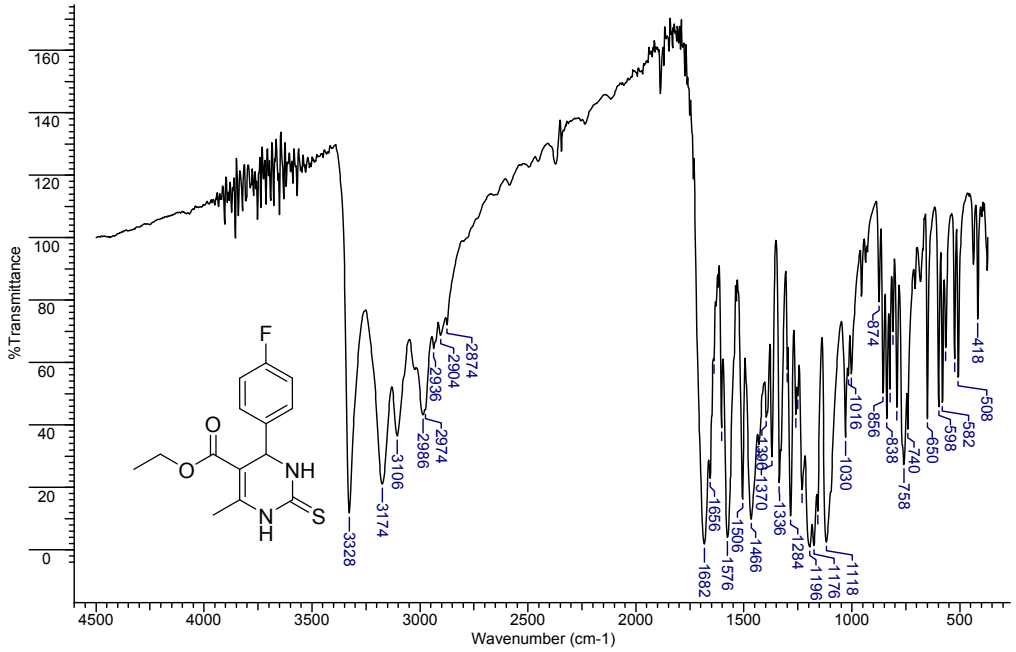

Figure S74. Infrared spectrum (KBr) of **BA10-S**.

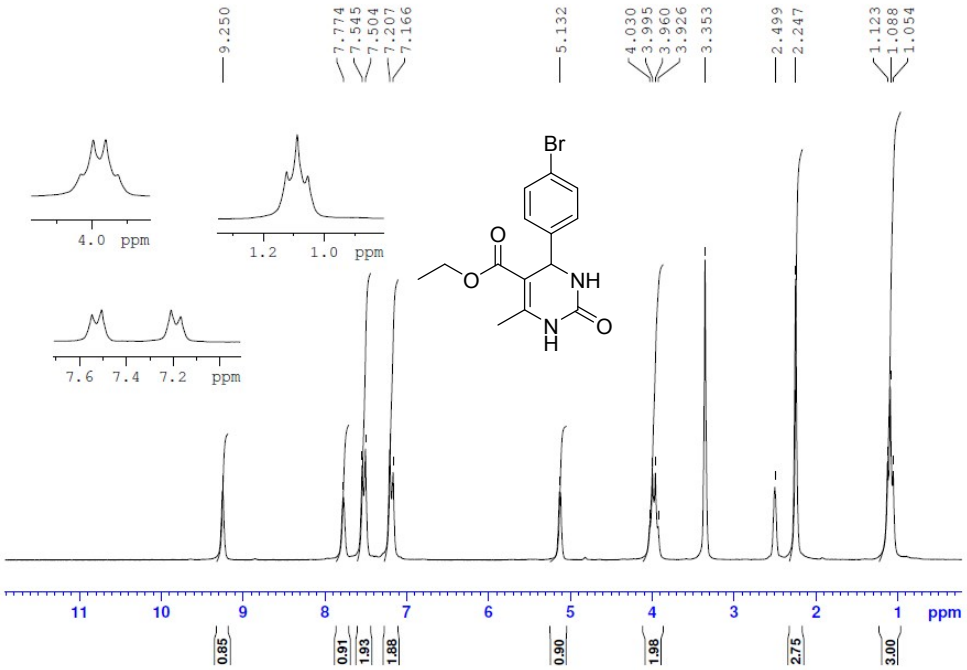

Figure S75. [1]H spectrum of compound **BA11-O** (200 MHz, DMSO-d_6).

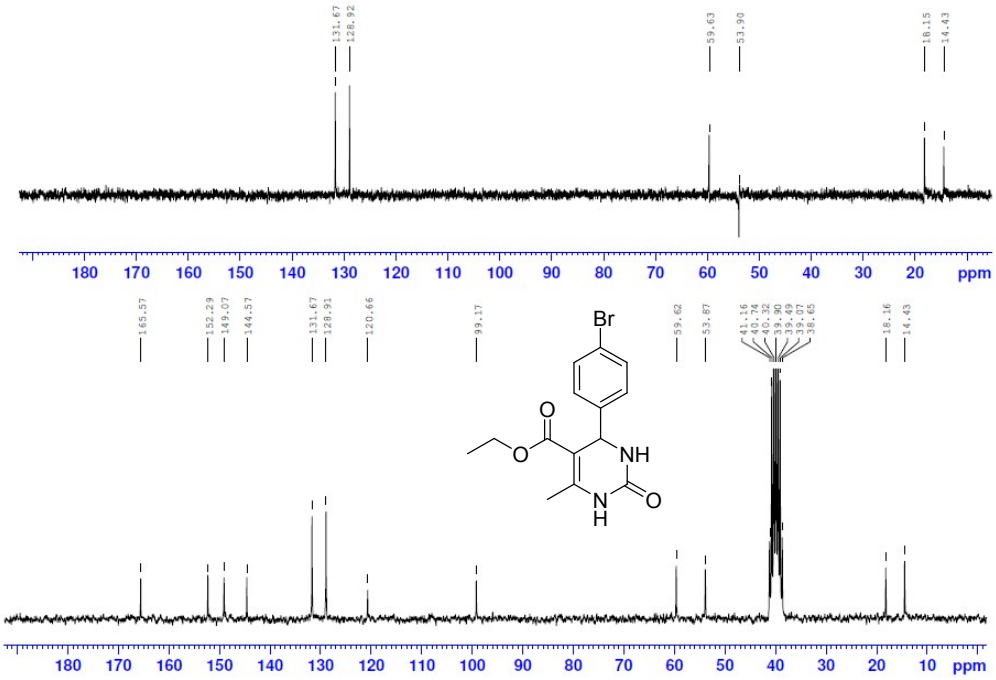

Figure S76. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA11-O** (50 MHz, DMSO-d_6).

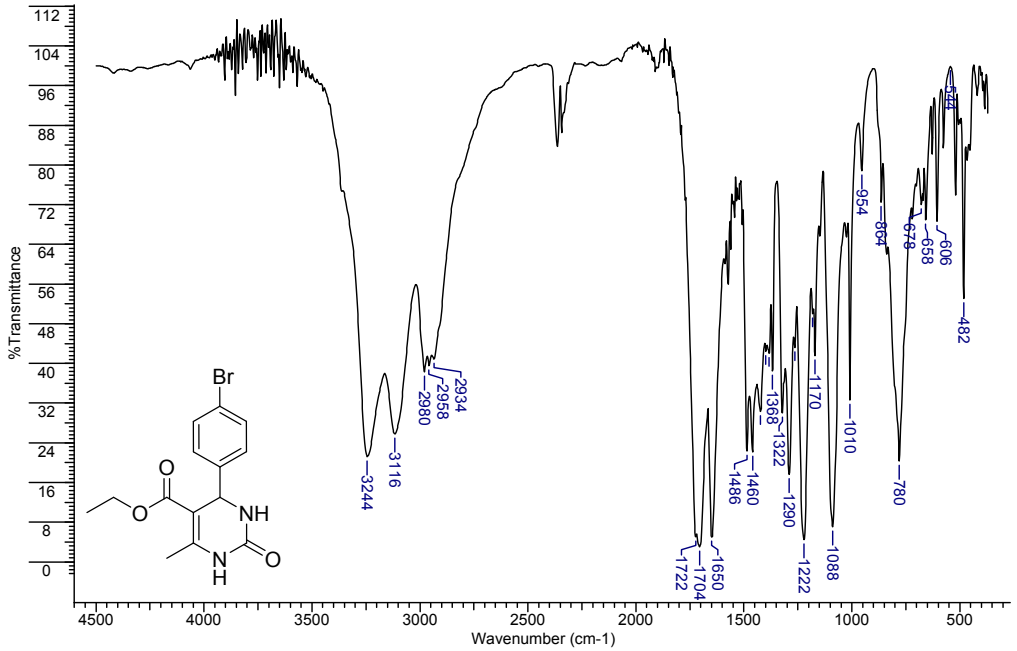

Figure S77. Infrared spectrum (KBr) of **BA11-O**.

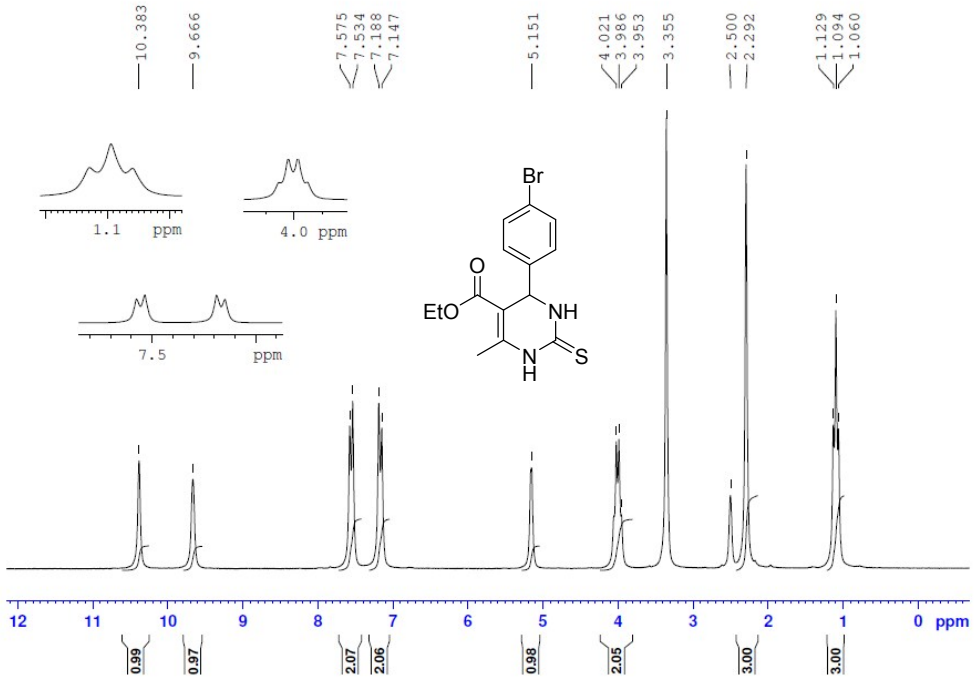

Figure S78. ^{1}H spectrum of compound **BA11-S** (200 MHz, DMSO-d_6).

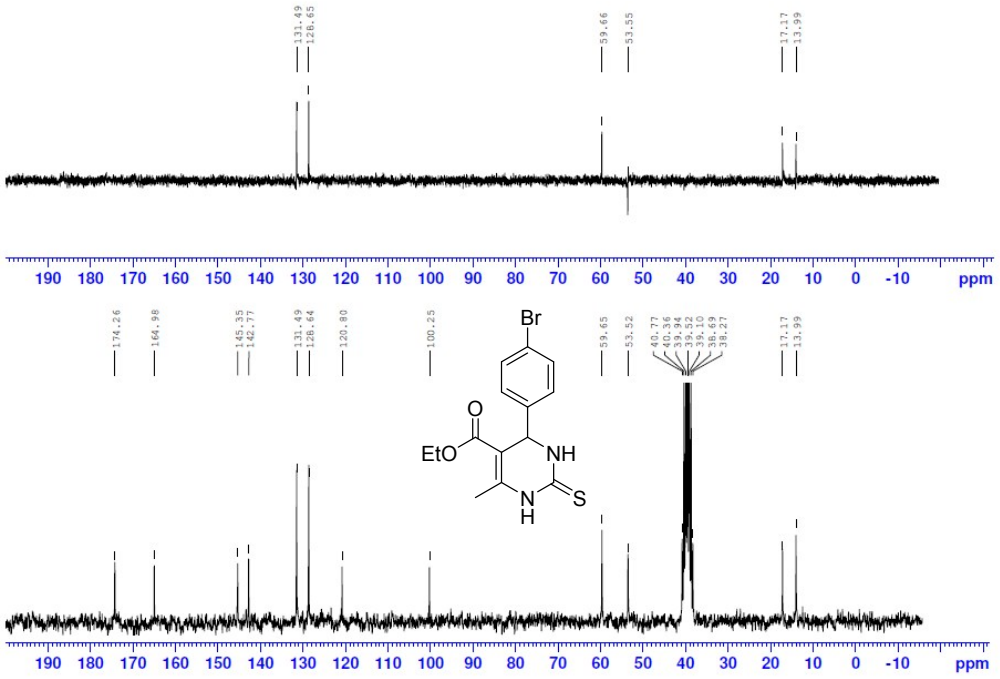

Figure S79. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA11-S** (50 MHz, DMSO-d_6).

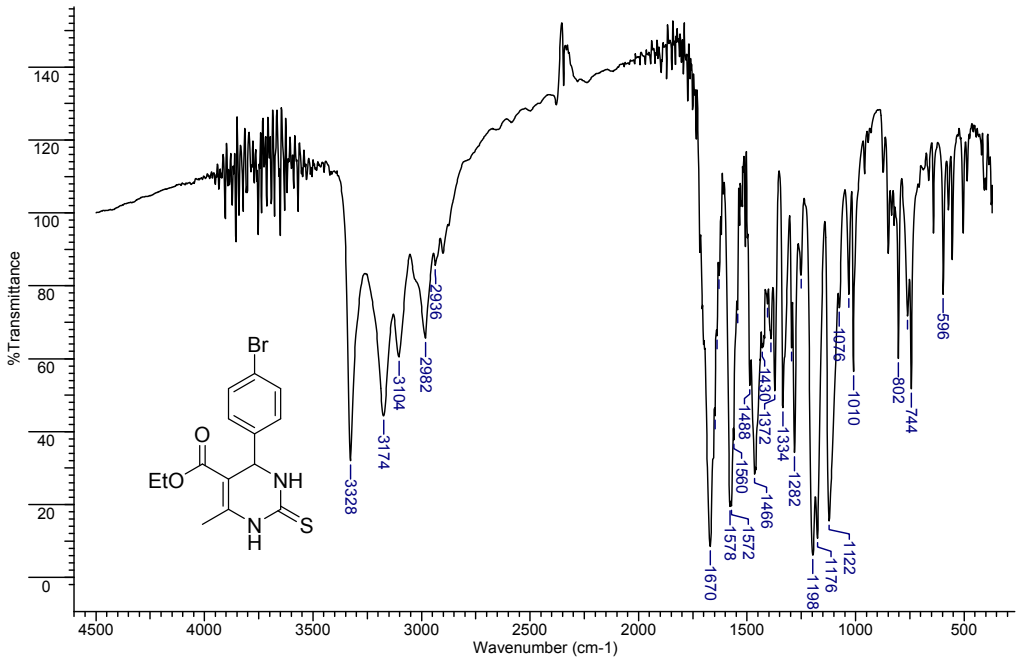

Figure S80. Infrared spectrum (KBr) of **BA11-S**.

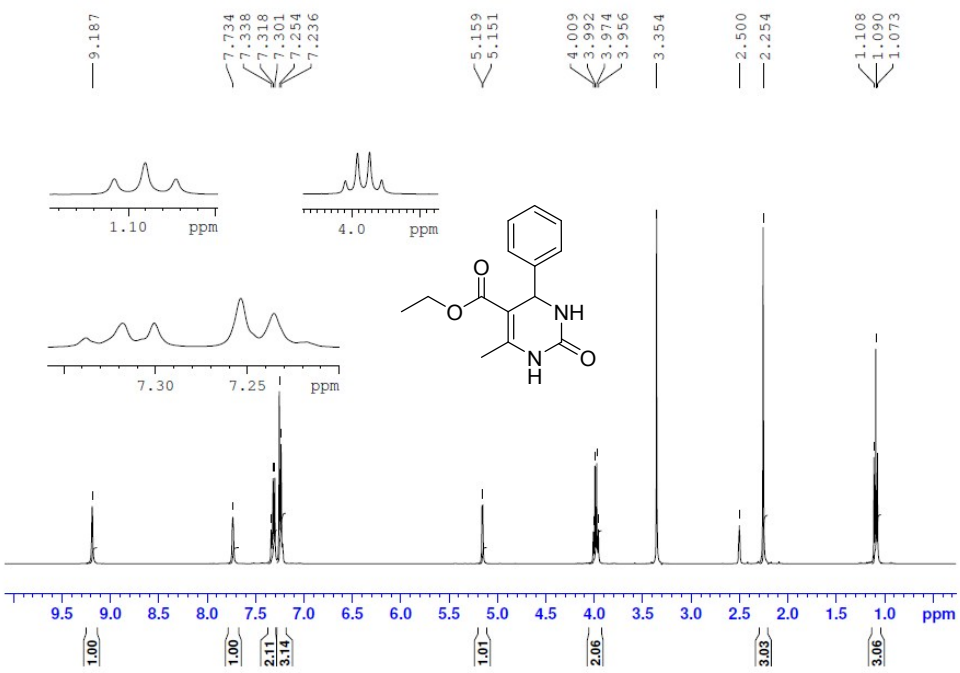

Figure S81. [1]H spectrum of compound **BA12-O** (400 MHz, DMSO-d_6).

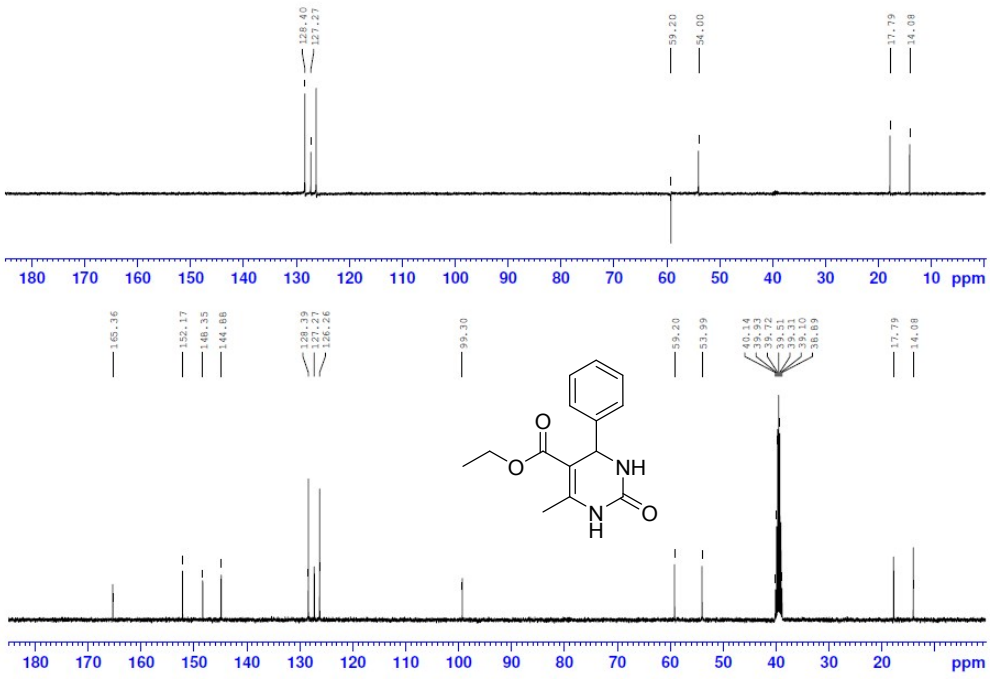

Figure S82. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA12-O** (100 MHz, DMSO-d_6)

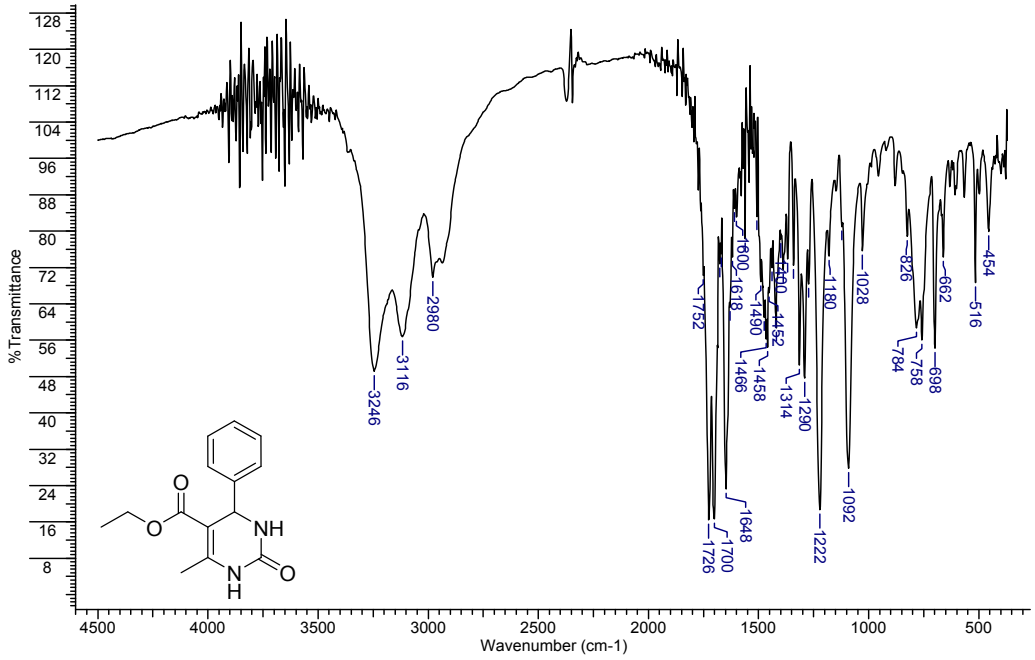

Figure S83. Infrared spectrum (KBr) of compound **BA12-O**.

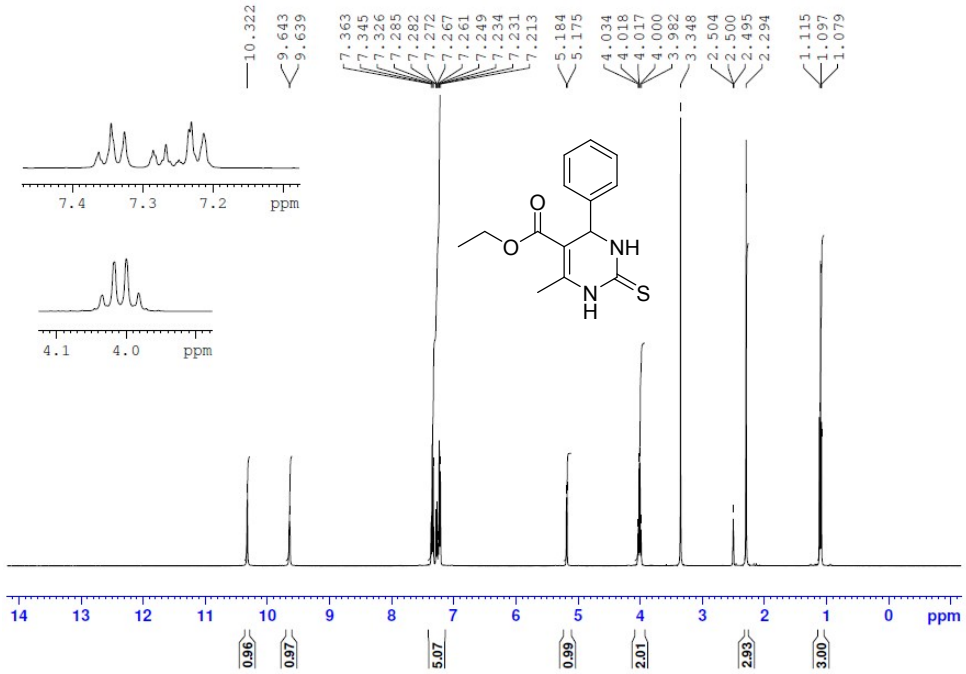

Figure S84. ^{1}H spectrum of compound **BA12-S** (400 MHz, DMSO-d_6).

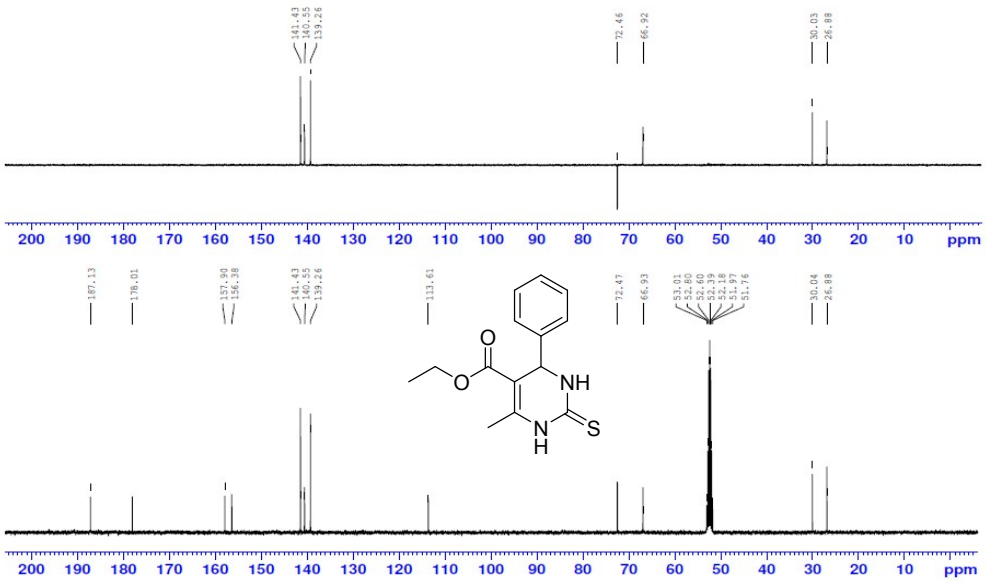

Figure S85. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA12-S** (100 MHz, DMSO-d_6).

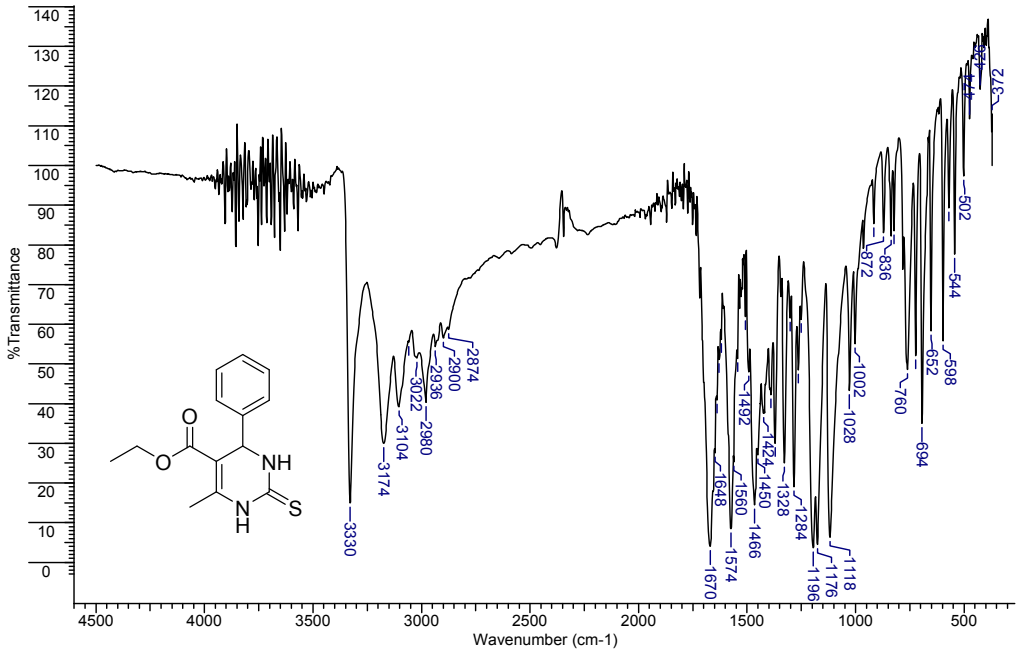

Figure S86. Infrared spectrum (KBr) of compound **BA12-S**.

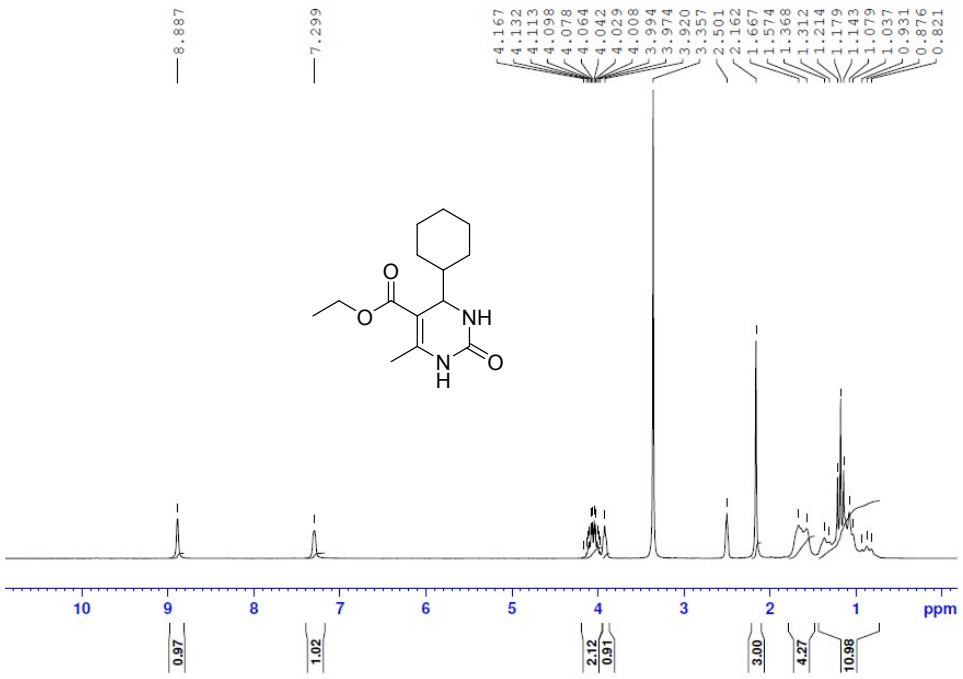

Figure S87. [1]H spectrum of compound **BA13-O** (200 MHz, DMSO-d_6)

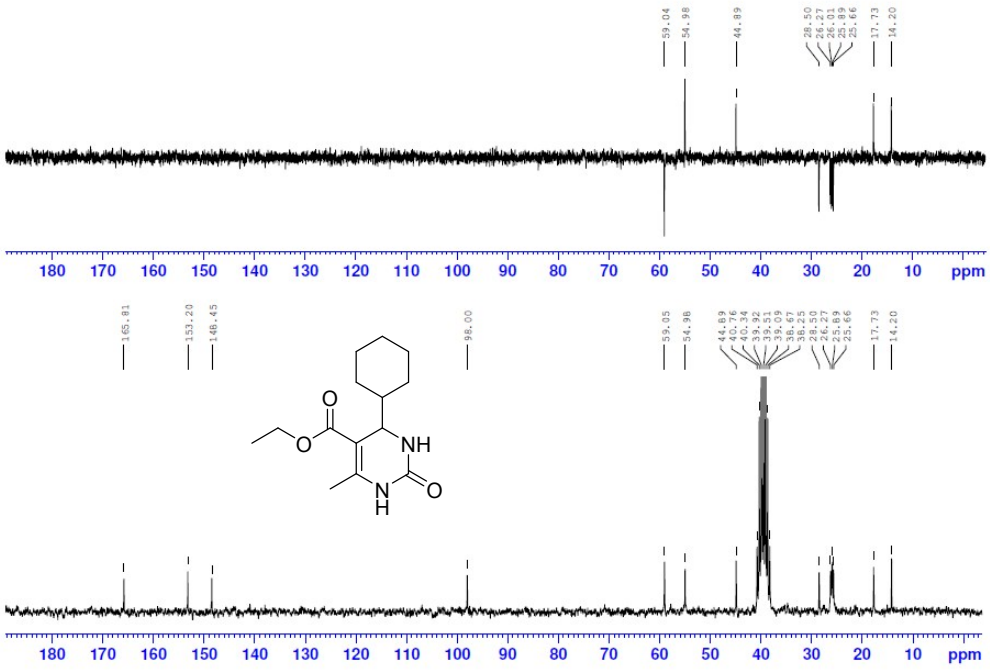

Figure S88. [13]C spectrum (bottom) and DEPT 135 subspectrum of compound **BA13-O** (50 MHz, DMSO-d_6

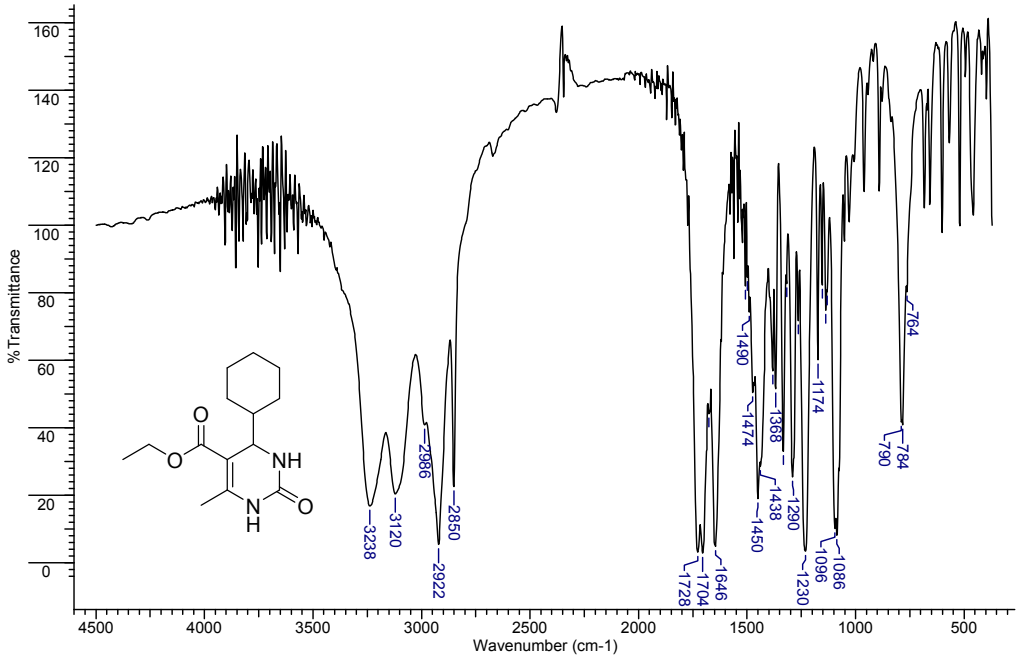

Figure S89. Infrared spectrum (KBr) of **BA13-O**.

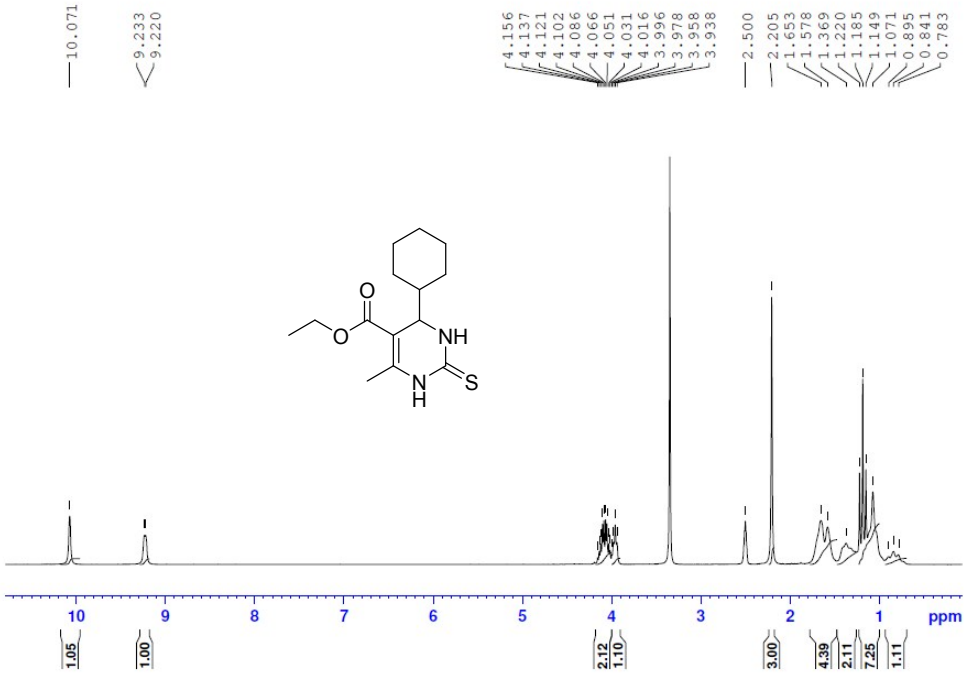

Figure S90. ^{1}H spectrum of compound **BA13-S** (200 MHz, DMSO-d_6).

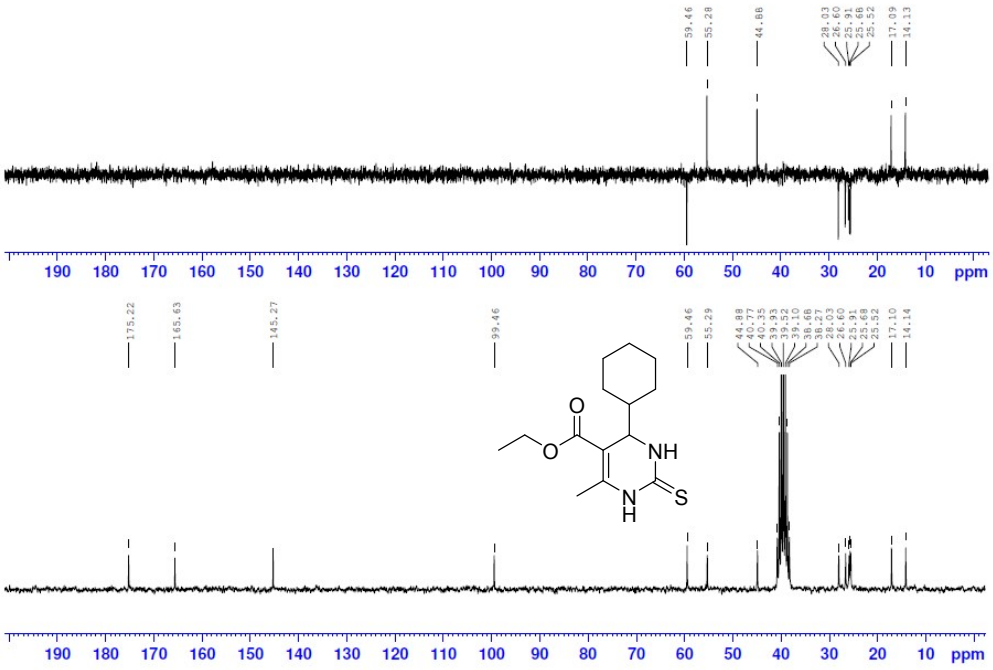

Figure S91. ^{13}C spectrum (bottom) and DEPT 135 subspectrum of compound **BA13-S** (50 MHz, DMSO-d_6

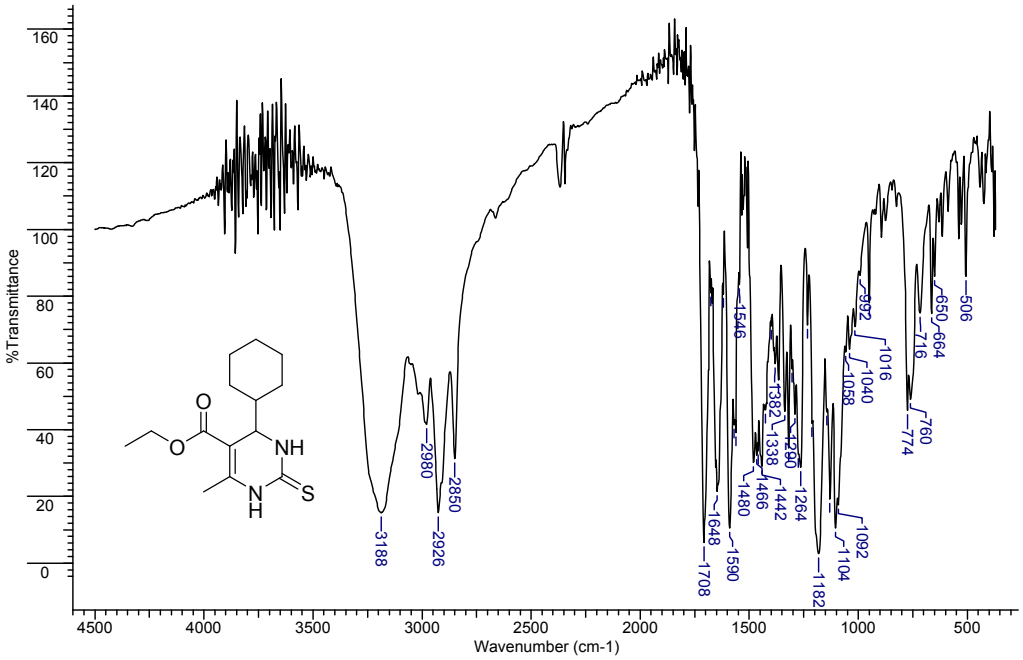

Figure S92. Infrared spectrum (KBr) of **BA13-S**.