## Design, Synthesis, Crystal Structure and Anti-plasmodial Evaluation of Tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidine Derivatives

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Figure S1. <sup>1</sup>H NMR spectrum of compound F1 in  $CDCl_3$ 



Figure S2. <sup>1</sup>H NMR spectrum of compound F2 in CDCl<sub>3</sub>.



Figure S3. <sup>1</sup>H NMR spectrum of compound F3 in CDCl<sub>3</sub>.



Figure S4. <sup>1</sup>H NMR spectrum of compound F4 in CDCl<sub>3</sub>.



Figure S5. <sup>1</sup>H NMR spectrum of compound F5 in CDCl<sub>3</sub>.



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Figure S7. <sup>1</sup>H NMR spectrum of compound F7 in CDCl<sub>3</sub>.



Figure S8. <sup>1</sup>H NMR spectrum of compound F8 in CDCl<sub>3</sub>.



Figure S9. <sup>1</sup>H NMR spectrum of compound F9 in CDCl<sub>3</sub>.



Figure S10. <sup>1</sup>H NMR spectrum of compound F10 in CDCl<sub>3</sub>.



Figure S11. <sup>1</sup>H NMR spectrum of compound F11 in CDCl<sub>3</sub>.



Figure S12. <sup>1</sup>H NMR spectrum of compound F12 in CDCl<sub>3</sub>.



Figure S13. <sup>1</sup>H NMR spectrum of compound F13 in CDCl<sub>3</sub>.



Figure S14. <sup>1</sup>H NMR spectrum of compound F14 in CDCl<sub>3</sub>.



Figure S15. <sup>1</sup>H NMR spectrum of compound F15 in CDCl<sub>3</sub>.



Figure S16. <sup>1</sup>H NMR spectrum of compound F16 in CDCl<sub>3</sub>.



Figure S17. <sup>13</sup>C NMR spectrum of compound F1 in CDCl<sub>3</sub>.



Figure S18. <sup>13</sup>C NMR spectrum of compound F2 in CDCl<sub>3</sub>.



Figure S19. <sup>13</sup>C NMR spectrum of compound F3 in CDCl<sub>3</sub>.



Figure S20. <sup>13</sup>C NMR spectrum of compound F4 in CDCl<sub>3</sub>.



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Figure S30. <sup>13</sup>C NMR spectrum of compound F14 in CDCl<sub>3</sub>.



Figure S31. <sup>13</sup>C NMR spectrum of compound F15 in CDCl<sub>3</sub>.



Figure S32. <sup>13</sup>C NMR spectrum of compound F16 in CDCl<sub>3</sub>.



Figure S33. Mass spectrum of compound F1 in MeOH.



Figure S34. Mass spectrum of compound F2 in MeOH.



Figure S35. Mass spectrum of compound F3 in MeOH.



Figure S36. Mass spectrum of compound F4 in MeOH.



Figure S37. Mass spectrum of compound F5 in MeOH.



Figure S38. Mass spectrum of compound F6 in MeOH.



Figure S39. Mass spectrum of compound F7 in MeOH.



Figure S40. Mass spectrum of compound F8 in MeOH.



Figure S41. Mass spectrum of compound F9 in MeOH.



Figure S42. Mass spectrum of compound F10 in MeOH.



Figure S43. Mass spectrum of compound F11 in MeOH.



Figure S44. Mass spectrum of compound F12 in MeOH.



Figure S45. Mass spectrum of compound F13 in MeOH.



Figure S46. Mass spectrum of compound F14 in MeOH.



Figure S47 Mass spectrum of compound F`15 in MeOH.



Figure S48. Mass spectrum of compound F16 in MeOH.

Sample code	Calculated Mass	Observed Mass	Difference in calculated mass and observed mass	Mass variation in ppm
F1	487.2168	487.2164.	0.0004	0.820990
F2	471.2219	471.2216	0.0003	0.636643
<b>F3</b>	493.1899	493.1870	0.0029	5.880088
<b>F</b> 4	525.1283	525.1278	0.0005	0.952148
F5	541.1885	541.0176	0.1709	315.78645
F6	509.1578	509.1583	-0.0005	0.982014
<b>F7</b>	475.1968	475.1973	-0.0005	1.052196
F8	525.1936	525.1935	0.0001	0.190406
<b>F9</b>	517.2273	517.2271	0.0002	0.386677
F10	501.2324	501.2321	0.0003	0.598525
F11	523.1979	523.1975	0.0004	0.764529
F12	556.5259	556.5251	0.0008	1.437489
F13	571.1991	571.1981	0.0010	1.750703
F14	540.0713	540.0712	0.0001	0.185161
F15	505.2074	505.2070	0.0004	0.791754
F16	555.2042	555.2045	-0.0003	0.791754

Figure S49. Table showing Mass variation in ppm of Compounds F1 – F16



Figure S50. Unit cell packing diagram of compound F1, Color code: S, yellow; N, blue; C, black; O, red.



Figure S51. Unit cell packing diagram of compound F1, showing hydrogen bonding. Color code: S, yellow; N, blue; C, black; O, red.



**Figure S52.** Unit cell packing diagram of compound **F1**, showing short contact bonding. Color code: S, yellow; N, blue; C, black; O, red.



Figure S53. Unit cell packing diagram of compound F2, Color code: S, yellow; N, blue; C, black; O, red.



**Figure S54.** Unit cell packing diagram of compound **F2**, showing Hydrogen-Bonding, Color code: S, yellow; N, blue; C, black; O, red.



**Figure S55.** Unit cell packing diagram of compound **F2**, showing short contact bonding, Color code: S, yellow; N, blue; C, black; O, red.



(a) Cytotoxicity assay against human A549 (Lung) cancer cells



(b) Cytotoxicity assay against HeLa (Cervical) cancer cells

Figure S56. Graph showing cytotoxicity assay of selected compounds

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