Supplementary file 1

Synthesis and initial *in vitro* evaluation of olmutinib derivatives as prospective imaging probe for non-small cell lung cancer

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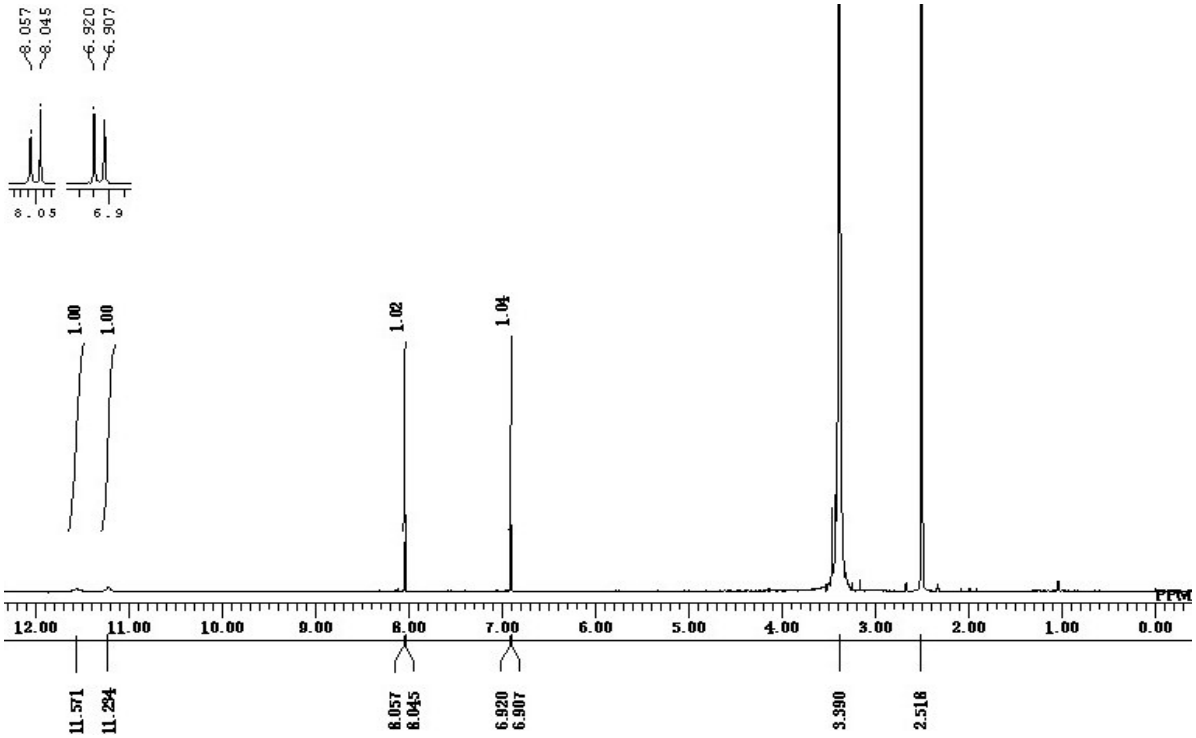

Figure S1. The 1H NMR spectrum of thieno(3,2-d)pyrimidine-2,4(1H,3H)-dione **(1)**. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 6.91 (1H, d, *J* = 5.2 Hz), 8.04 (1H, d, *J* = 4.8 Hz), 11.23 (1H, s), 11.57 (1H, s).

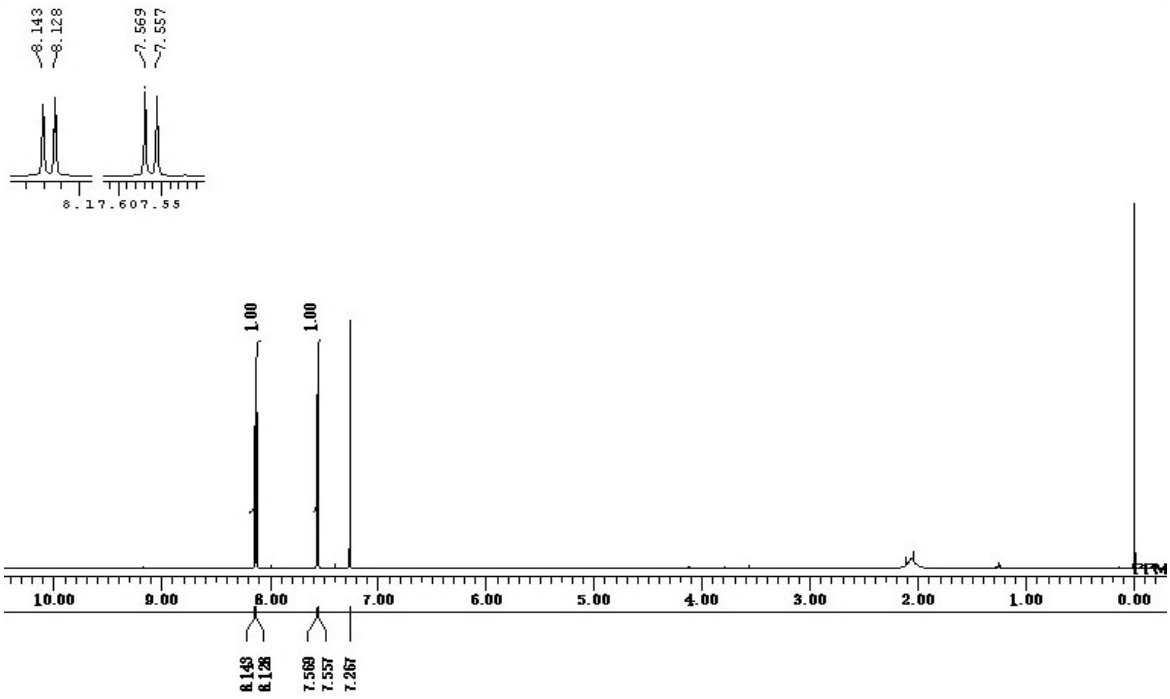

Figure S2. The 1H NMR spectrum of 2,4-dichlorothieno(3,2-d)pyrimidine **(2)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (1H, d, *J* = 5.2 Hz), 8.13 (1H, d, *J* = 6.0 Hz).

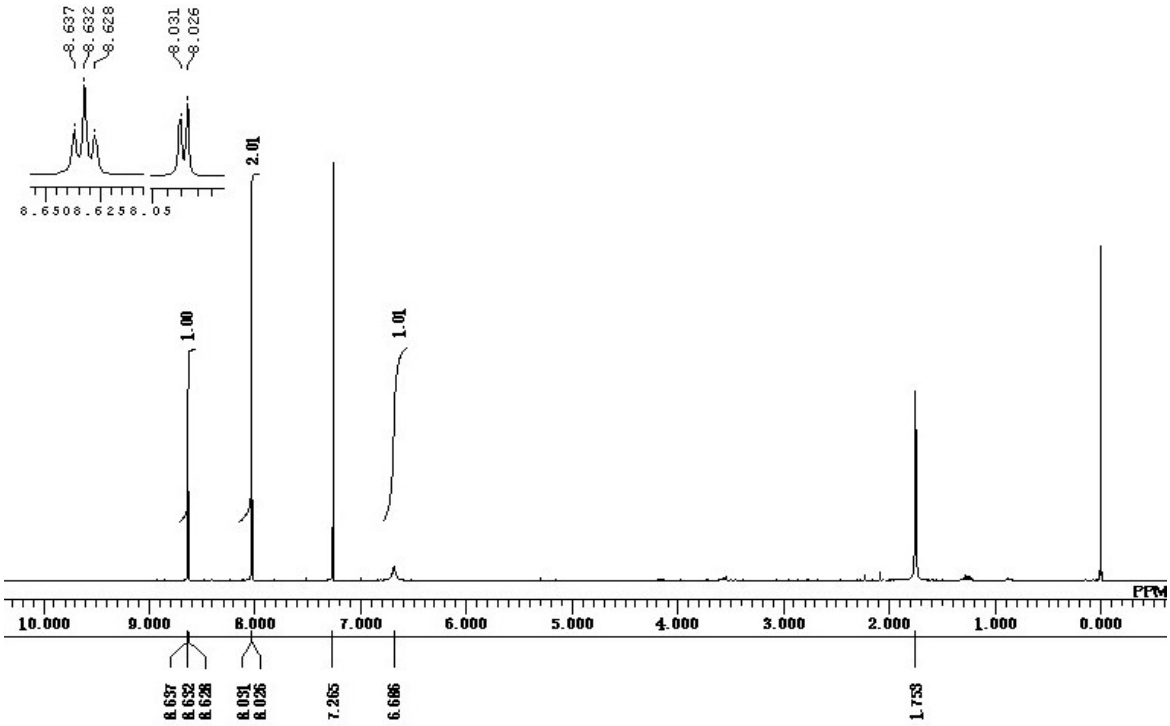

Figure S3. The 1H NMR spectrum of 3,5-dinitrophenol (**3**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69 (1H, s), 8.02 (2H, d, *J* = 2.0 Hz), 8.63 (1H, t, *J* = 2.0 Hz).

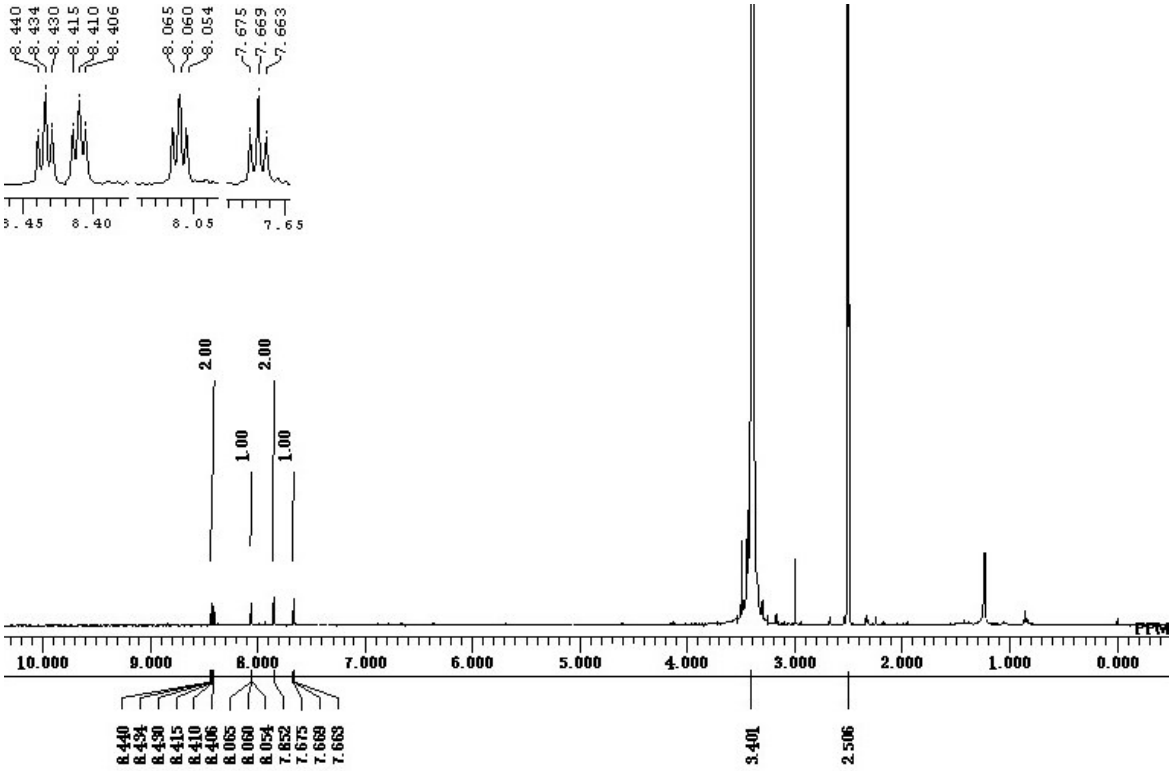

Figure S4. The 1H NMR spectrum of 3-amino-5-nitrophenol **(4)**. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 7.67 (1H, t, *J* = 2.4 Hz), 7.85 (2H, s), 8.06 (1H, t, *J* = 2.4 Hz), 8.42 (2H, td, *J* = 7.6, 1.6 Hz).

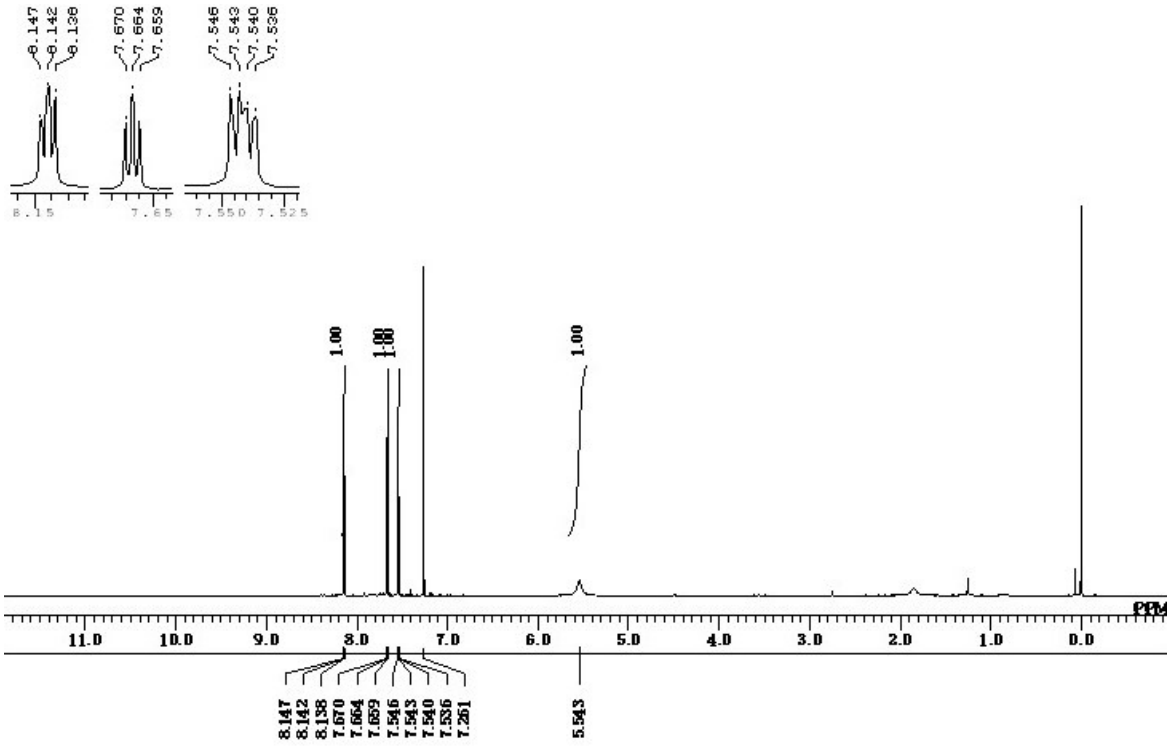

Figure S5. The 1H NMR spectrum of 3-iodo-5-nitrophenol **(5)**. ^{1}H NMR (400 MHz, ($CDCl_3$): δ 5.54 (1H, s), 7.54 (1H, dd, *J* = 2.4, 1.2 Hz), 7.66 (1H, t, *J* = 2.4 Hz), 8.14 (1H, t, *J* = 2.0 Hz).

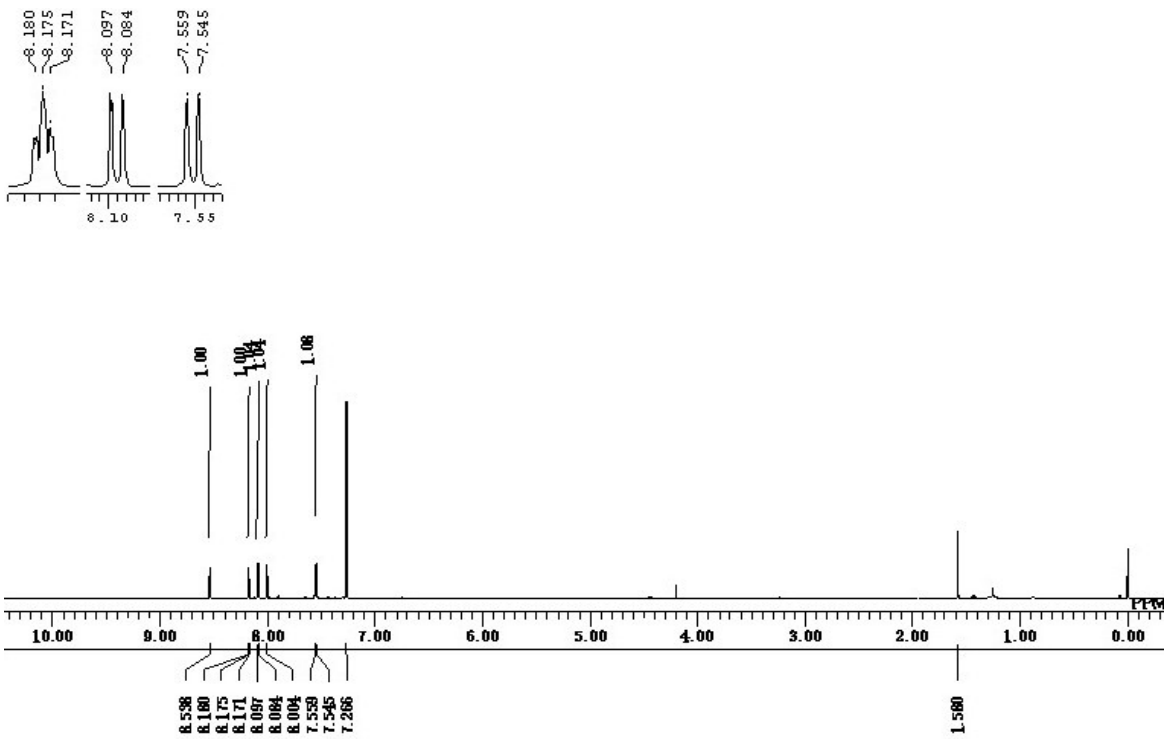

Figure S6. The 1H NMR spectrum of 2-chloro-4-(3-iodo-5-nitrophenoxy)thieno(3,2-d)pyrimidine **(6)**. ^{1}H NMR (400 MHz, ($CDCl_3$): δ 7.55 (1H, d, *J* = 5.6 Hz), 8.00 (1H, s), 8.08 (1H, d, *J* = 4.0 Hz), 8.17 (1H, t, *J* = 1.6 Hz), 8.54 (1H, s).

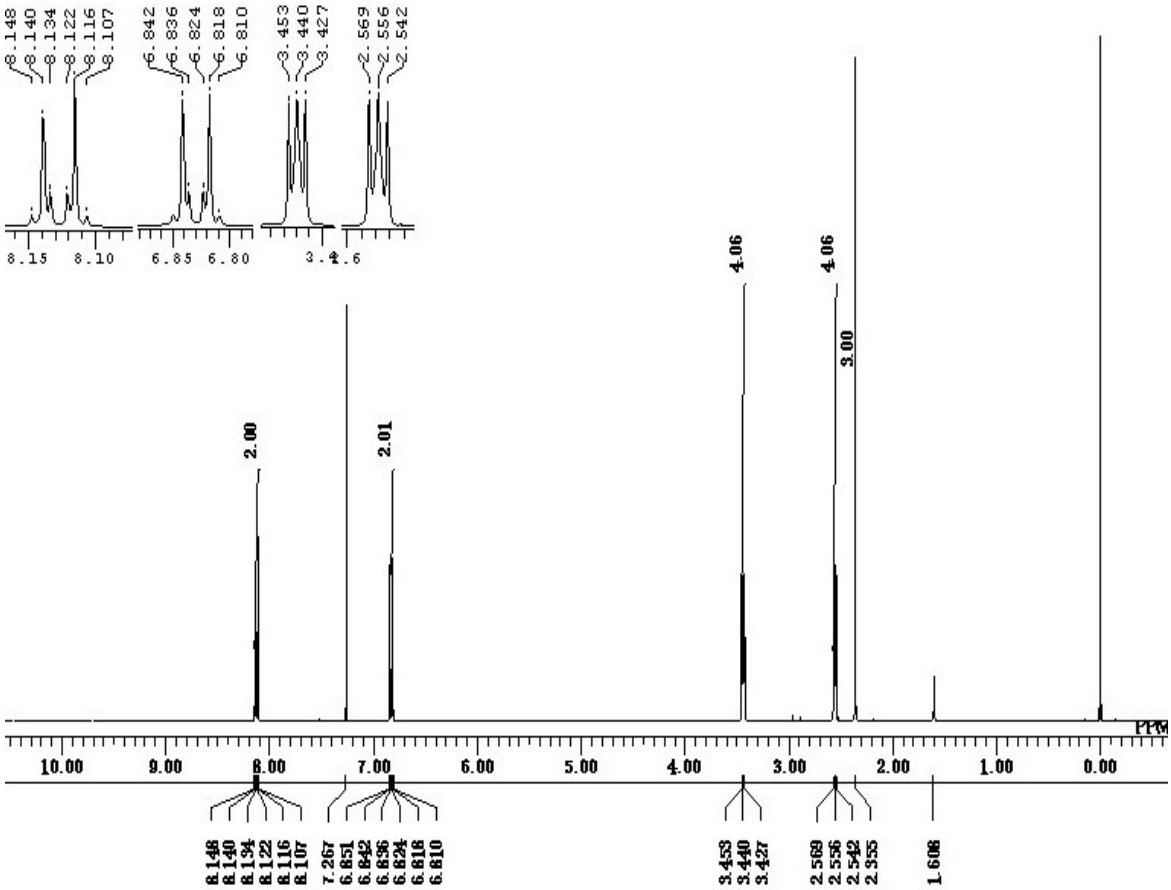

Figure S7. The 1H NMR spectrum of 1-methyl-4-(4-nitrophenyl)piperazine **(7).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (3H, s), 2.56 (4H, t, *J* = 5.6 Hz), 3.44 (4H, t, *J* = 5.6 Hz), 6.82 (2H, dt, *J* = 9.6, 2.4 Hz), 8.12 (2H, dt, *J* = 9.6, 2.4 Hz).

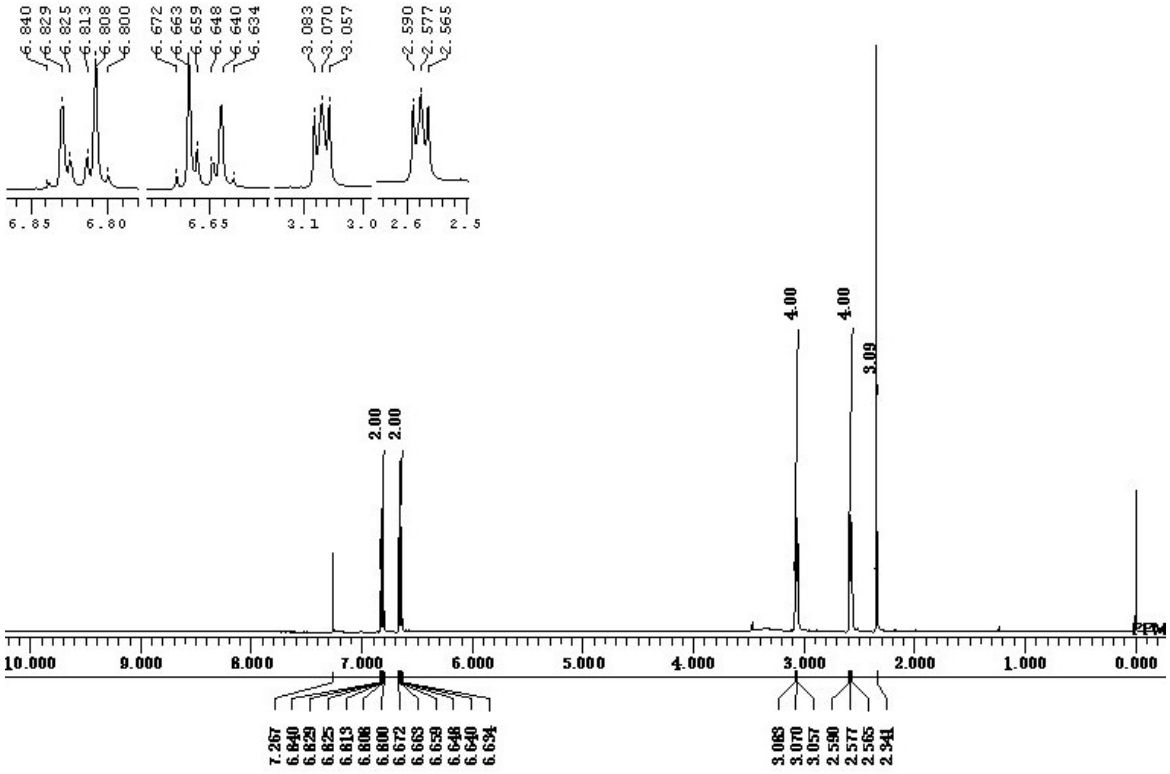

Figure S8. The 1H NMR spectrum of 4-(4-methylpiperazin-1-yl)aniline **(8).** ^{1}H NMR (400 MHz, ($CDCl_3$): δ 2.34 (3H, s), 2.58 (4H, t, *J* = 4.8 Hz), 3.07 (4H, t, *J* = 4.8 Hz), 6.65 (2H, dt, *J* = 9.2, 2.4 Hz), 6.81 (2H, dt, *J* = 8.4, 1.6 Hz).

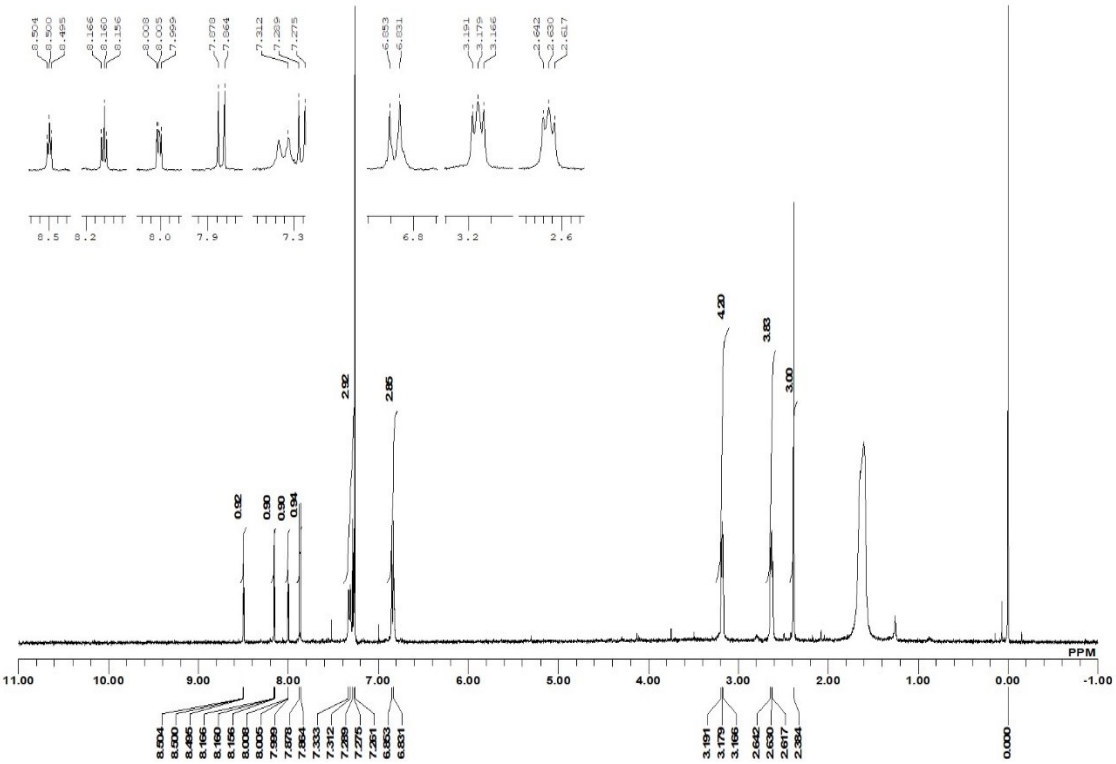

Figure S9. The 1H NMR spectrum of *4-(3-nitro-5-iodophenoxy)-N-[4-(4-methylpiperazin-1-yl)phenyl]thieno(3,2-d)pyrimidin-2-amine* **(9).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (3H, s), 2.63 (4H, t, *J* = 5.0 Hz), 3.18 (4H, t, *J* = 5.0 Hz), 6.80–6.85 (3H, m), 7.28 (1H, d, *J* = 5.6 Hz), 7.33 (1H, d, *J* = 8.8 Hz), 7.87 (1H, d, *J* = 5.6 Hz), 8.01 (1H, t, *J* = 1.8 Hz), 8.16 (1H, t, *J* = 2.0 Hz), 8.50 (1H, t, *J* = 1.8 Hz).

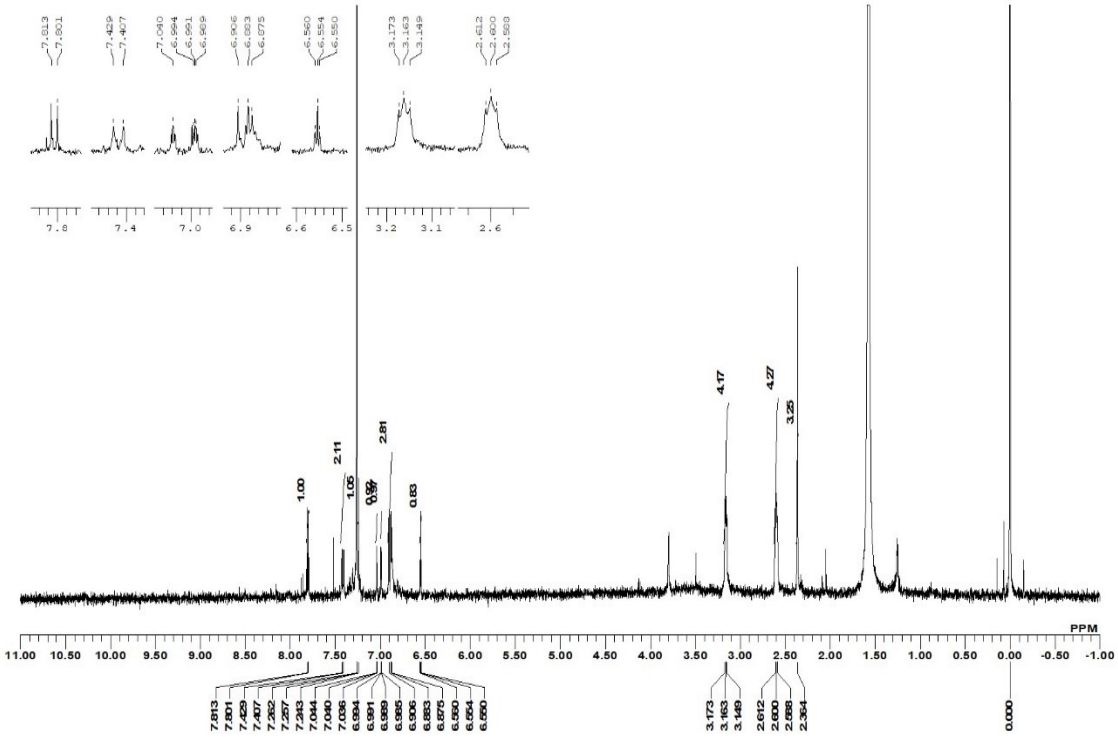

Figure S10. The 1H NMR spectrum of *4-(3-amino-5-iodophenoxy)-N-[4-(4-methylpiperazin-1-yl)phenyl]thieno(3,2-d)pyrimidin-2-amine* **(10)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (3H, s), 2.59 (4H, t, *J* = 4.4 Hz), 3.16 (4H, t, *J* = 4.8), 6.55 (1H, t, *J* = 1.6 Hz), 6.88 (1H, s), 6.89 (1H, d, *J* = 9.2 Hz), 6.99 (1H, td, *J* = 1.6, 2.0 Hz), 7.04 (1H, t, *J* = 1.6 Hz), 7.25 (1H, d, 5.6 Hz), 7.42 (1H, d, *J* = 8.8 Hz), 7.81 (1H, t, *J* = 4.8 Hz).

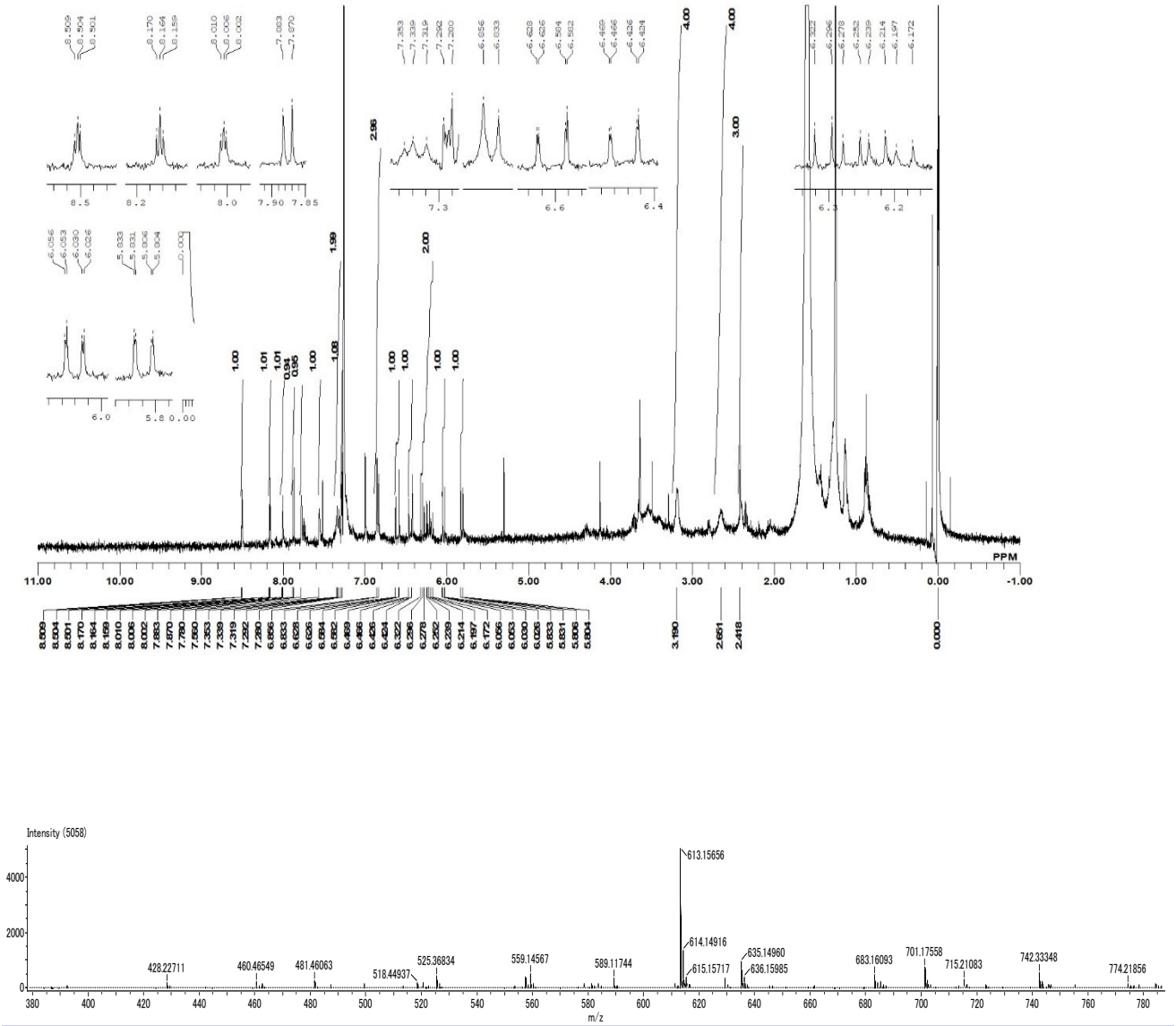

Figure S11. The NMR and MS spectra of *N-{3-iodo-5-[(2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}thieno{3,2-d}pyrimidin-4-yl)oxy]phenyl}* **(11)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (3H, s), 2.65 (4H, br, s), 3.19 (4H, br, s), 5.80–6.70 (3H, m), 6.80–6.85 (3H, m)[a], 7.29 (1H, d, *J* = 4.8 Hz), 7.33 (2H, d, *J* = 8.0 Hz), 7.56 or 7.78 (1H, s)[b], 7.88 (1H, d, *J* = 5.2 Hz), 8.01 (1H, t, *J* = 1.6 Hz), 8.16 (1H, t, *J* = 2.0 Hz), 8.50 (1H, t, *J* = 2.0 Hz). MS (ESI+) calculated for $C_{26}H_{25}IN_6O_2S$ $[M+H]^+$: *m/z* = 613.1, found 613.2. [a]Three protons derived from an impurity are also observed in this area. [b]One of these two singlet signals is derived from an impurity.

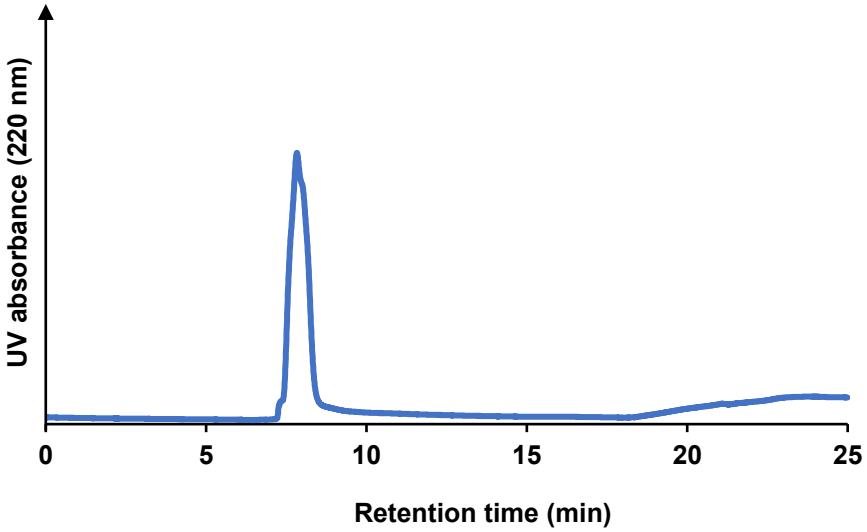

Figure S12. HPLC chromatogram of *N-{3-iodo-5-[(2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}thieno{3,2-d}pyrimidin-4-yl)oxy]phenyl}* **(11).** HPLC condition: An isocratic mobile phase of chloroform/methanol = 9/1, Cosmosil® 5SL-II (20 ID × 250 mm) column, flow rate 9.5 mL/min.