

# **New quinoline-urea-benzothiazole hybrids as promising antitubercular agents: Synthesis, *in vitro* antitubercular activity, cytotoxicity studies, and *In in silico* ADME profiling**

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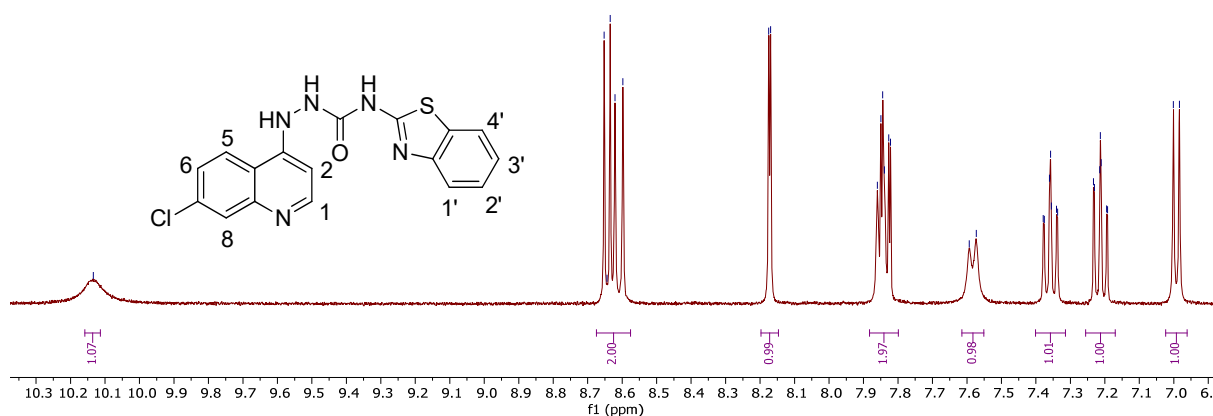
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Africa.

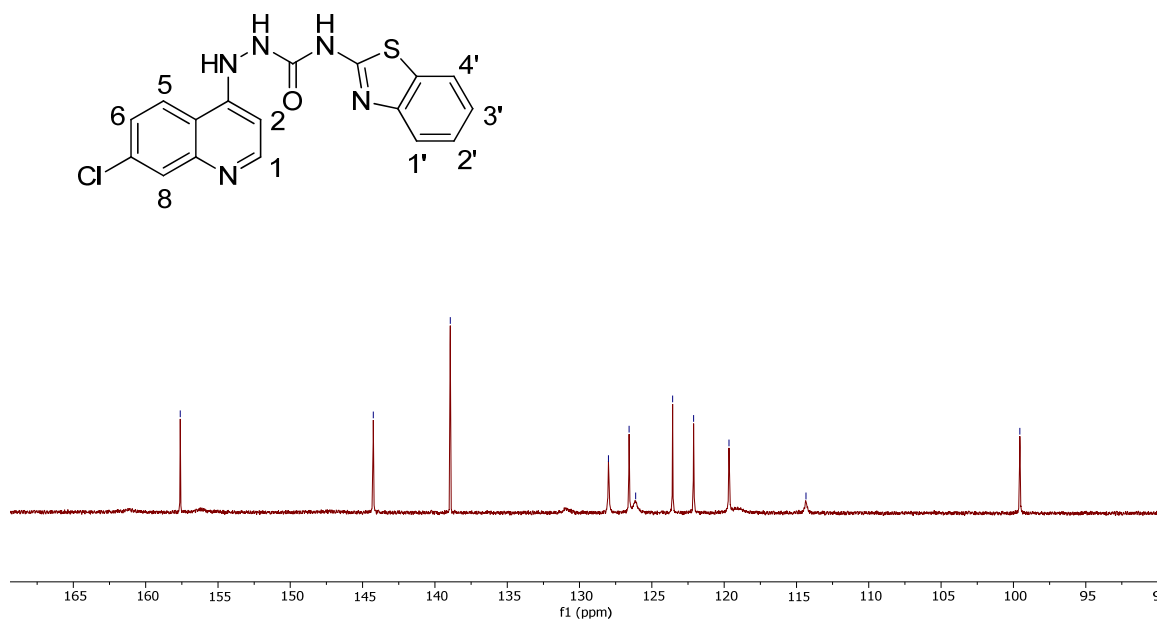
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#Equal contribution

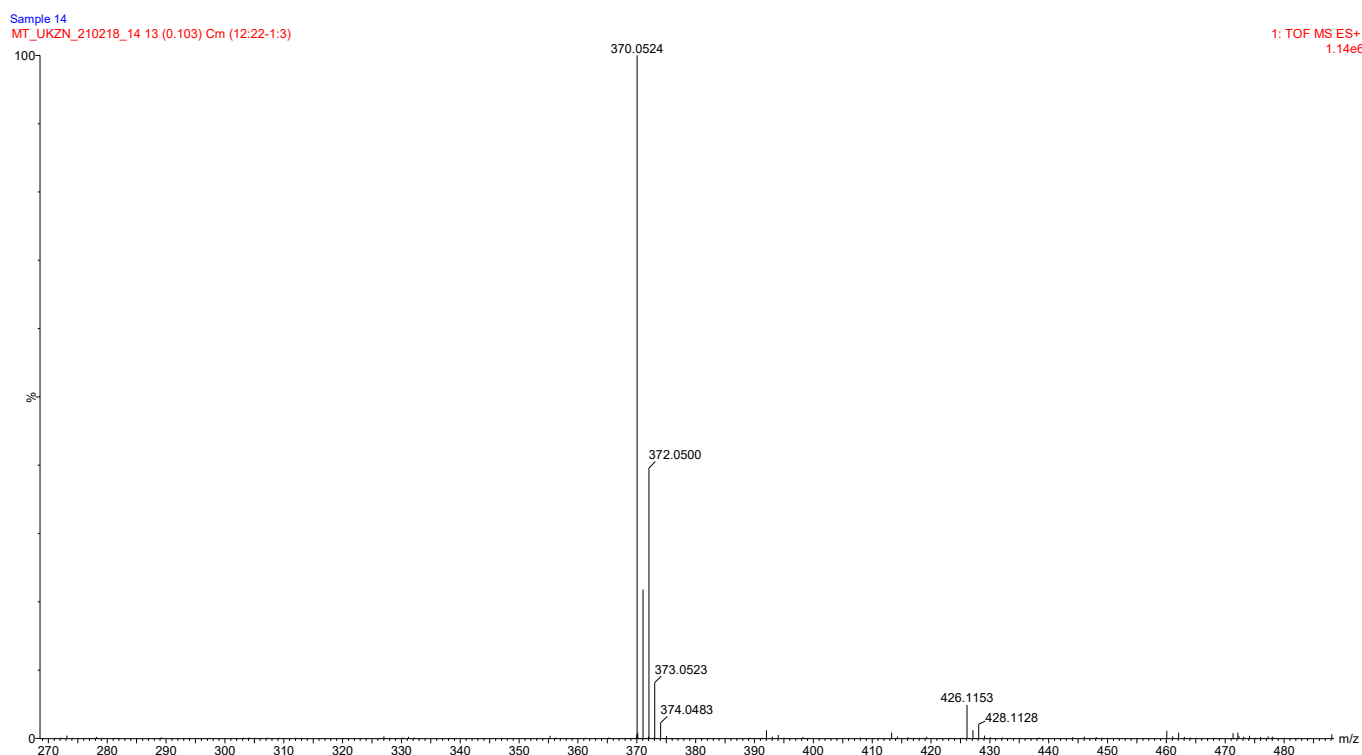
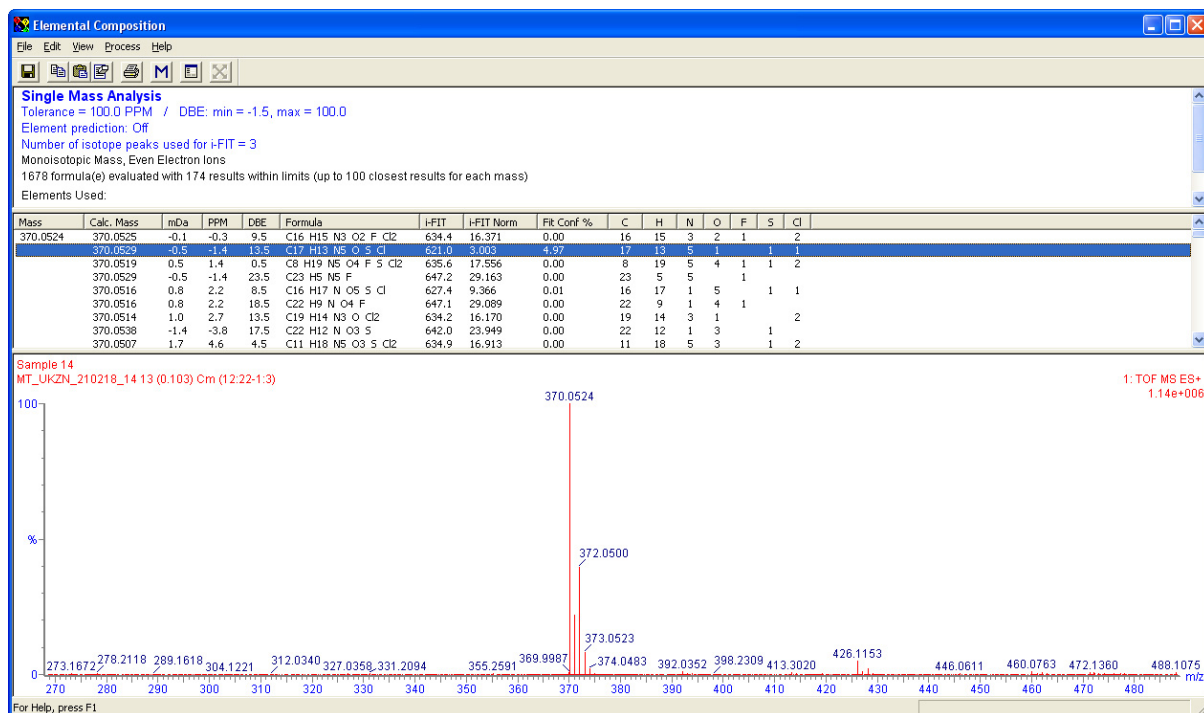
#### REPRESENTATIVE NMR AND HRMS SPECTRA OF FINAL COMPOUNDS



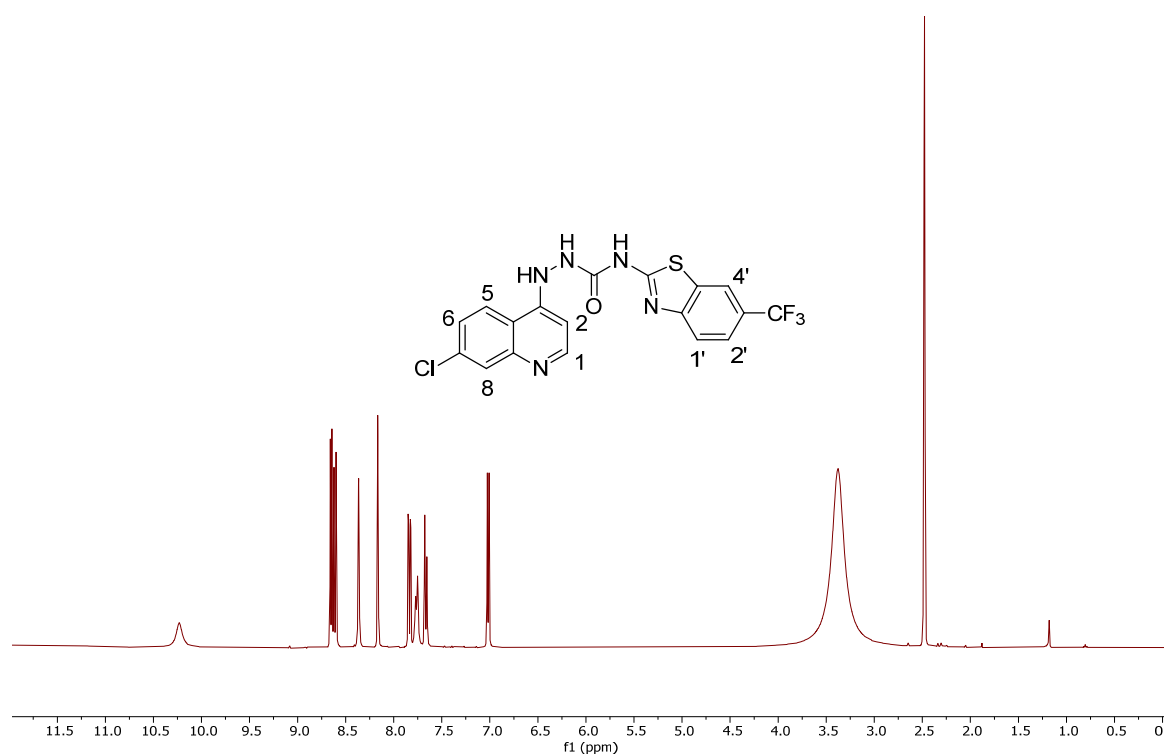
**Figure S1:** 400 MHz <sup>1</sup>H-NMR *N*-(benzo[d]thiazol-2-yl)-2-(7-chloroquinolin-4-yl)hydrazine-1-carboxamide in DMSO-*d*<sub>6</sub> (6a).



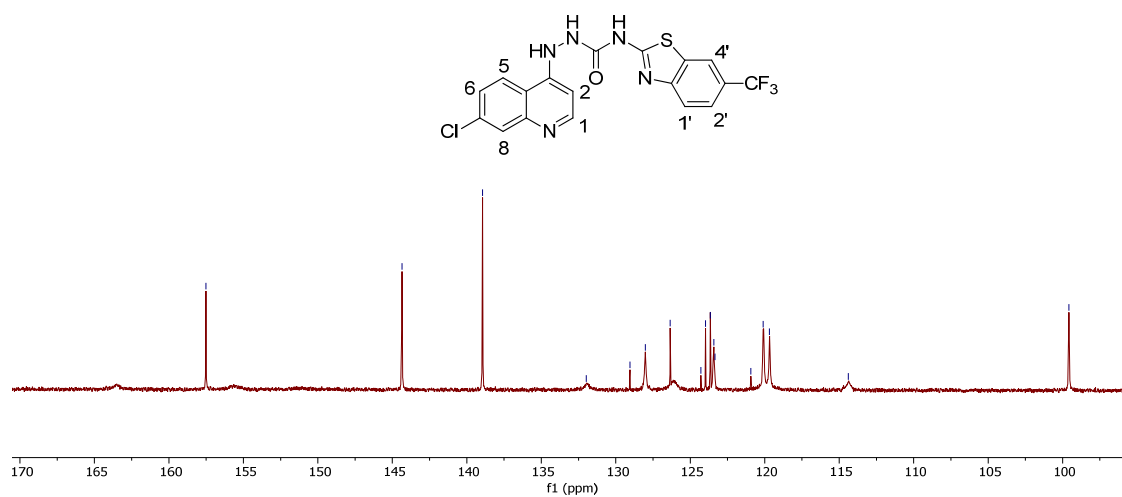
**Figure S2:** 101 MHz <sup>13</sup>C-NMR *N*-(benzo[d]thiazol-2-yl)-2-(7-chloroquinolin-4-yl)hydrazine-1-carboxamide in DMSO-*d*<sub>6</sub> (6a).



**Figure S3:** HRMS (ES<sup>+</sup>) for *N*-(benzo[d]thiazol-2-yl)-2-(7-chloroquinolin-4-yl)hydrazine-1-carboxamide (**6a**).

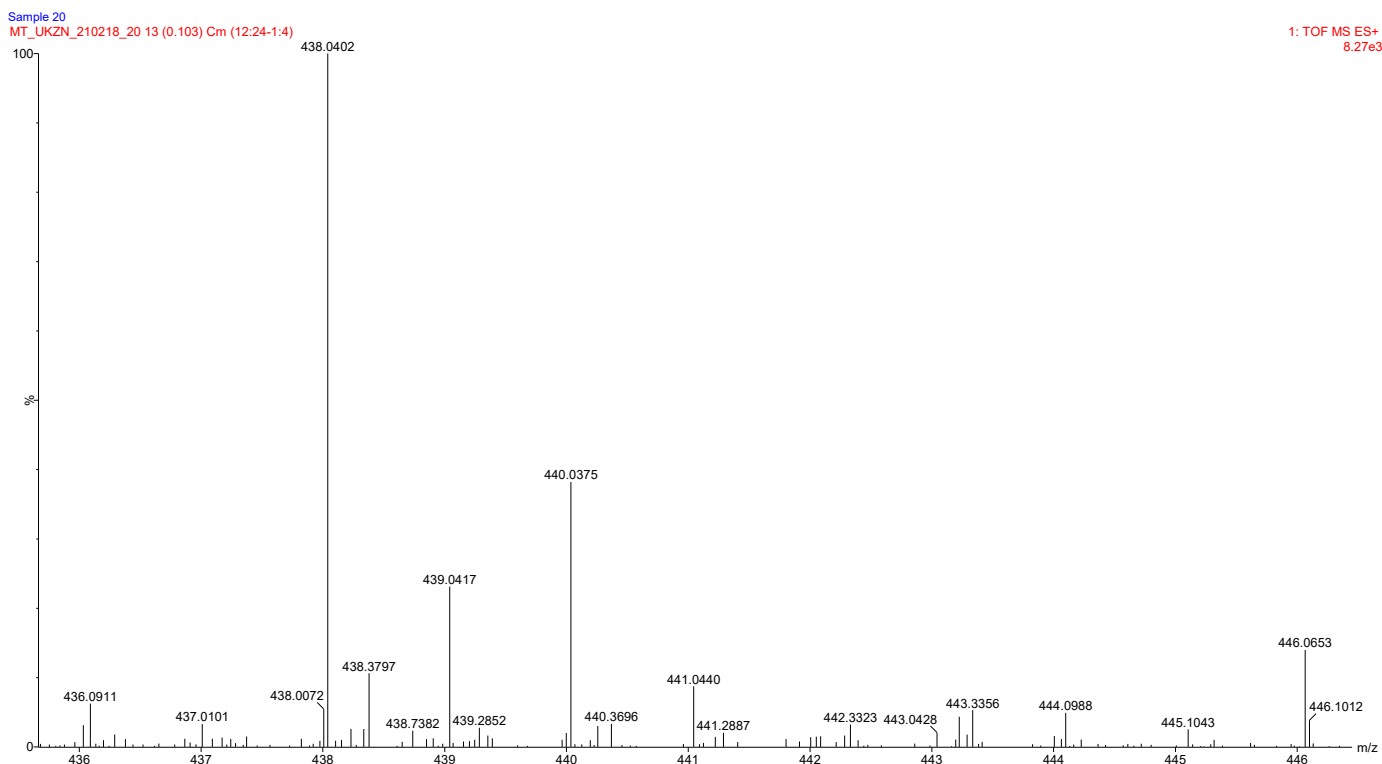
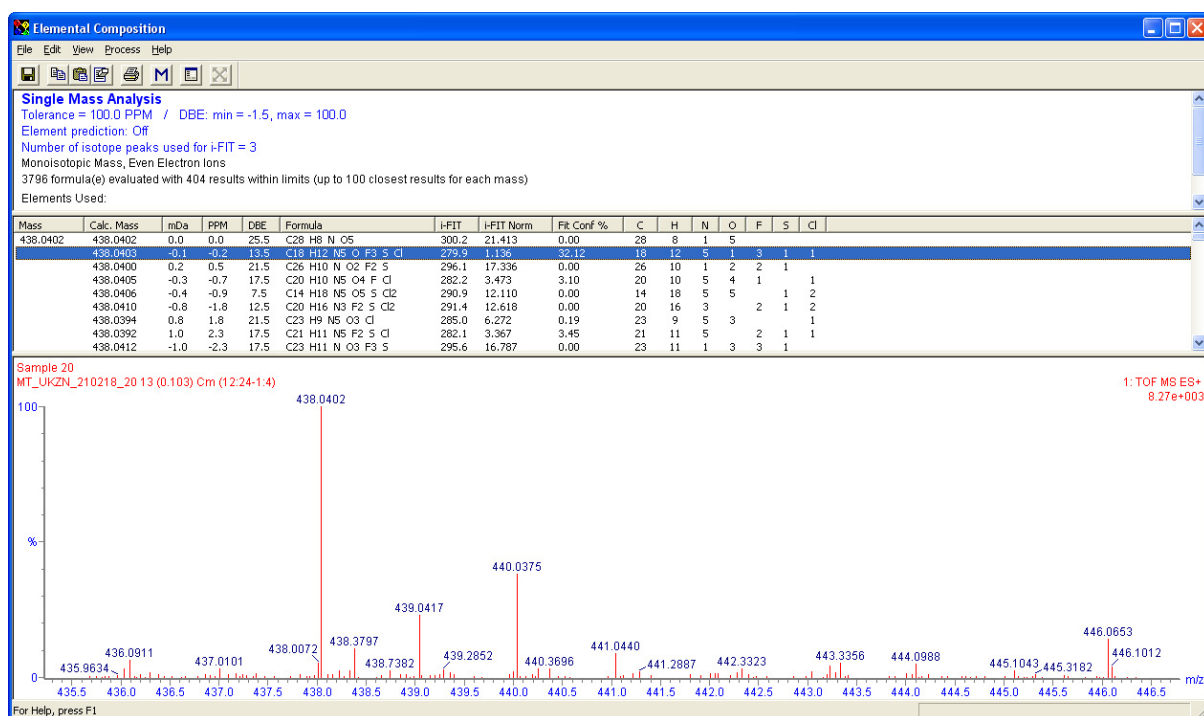


**Figure S4:** 400 MHz  $^1\text{H}$ -NMR of 2-(7-chloroquinolin-4-yl)-N-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)hydrazine-1-carboxamide in DMSO- $d_6$  (**6b**).

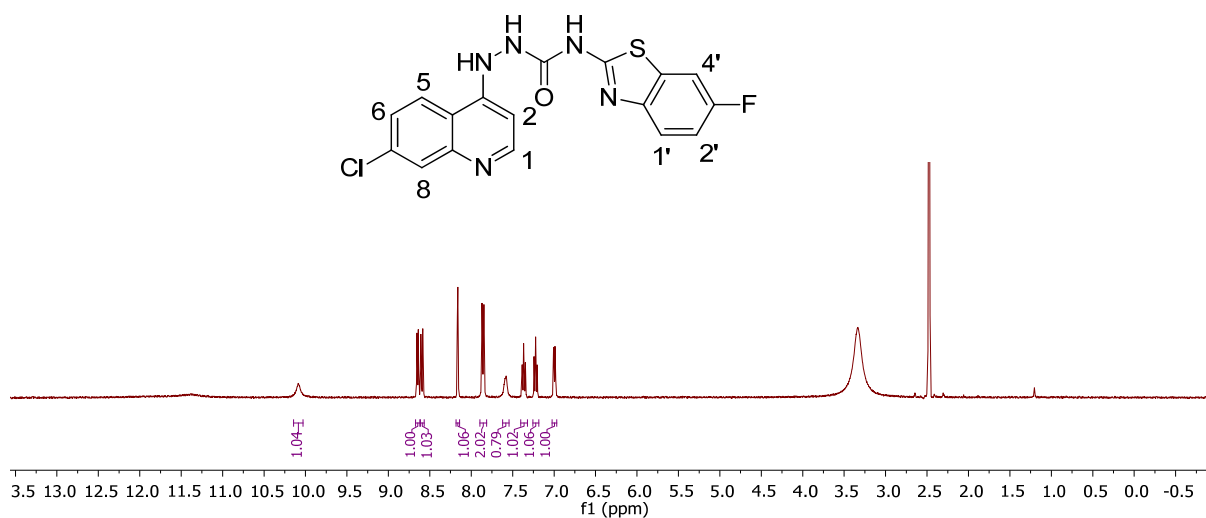


**Figure S5:** 101 MHz  $^{13}\text{C}$ -NMR of 2-(7-chloroquinolin-4-yl)-N-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)hydrazine-1-carboxamide in DMSO- $d_6$  (**6b**).

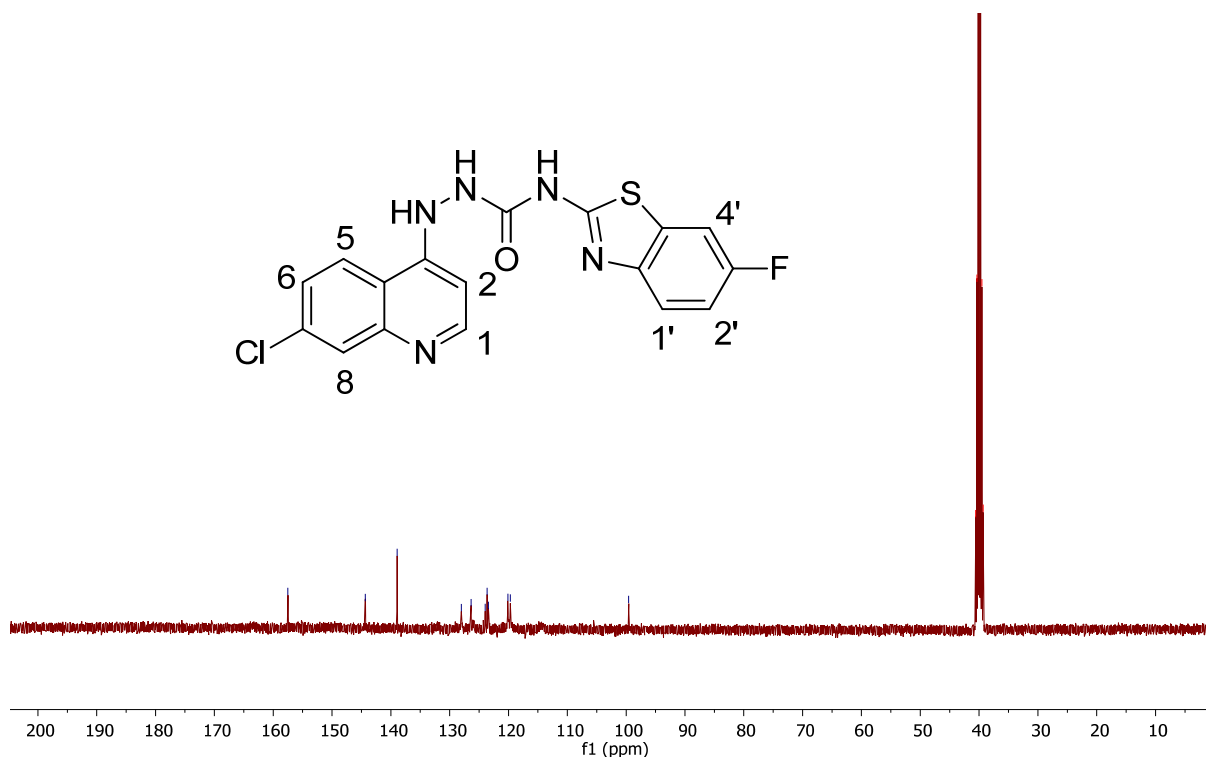




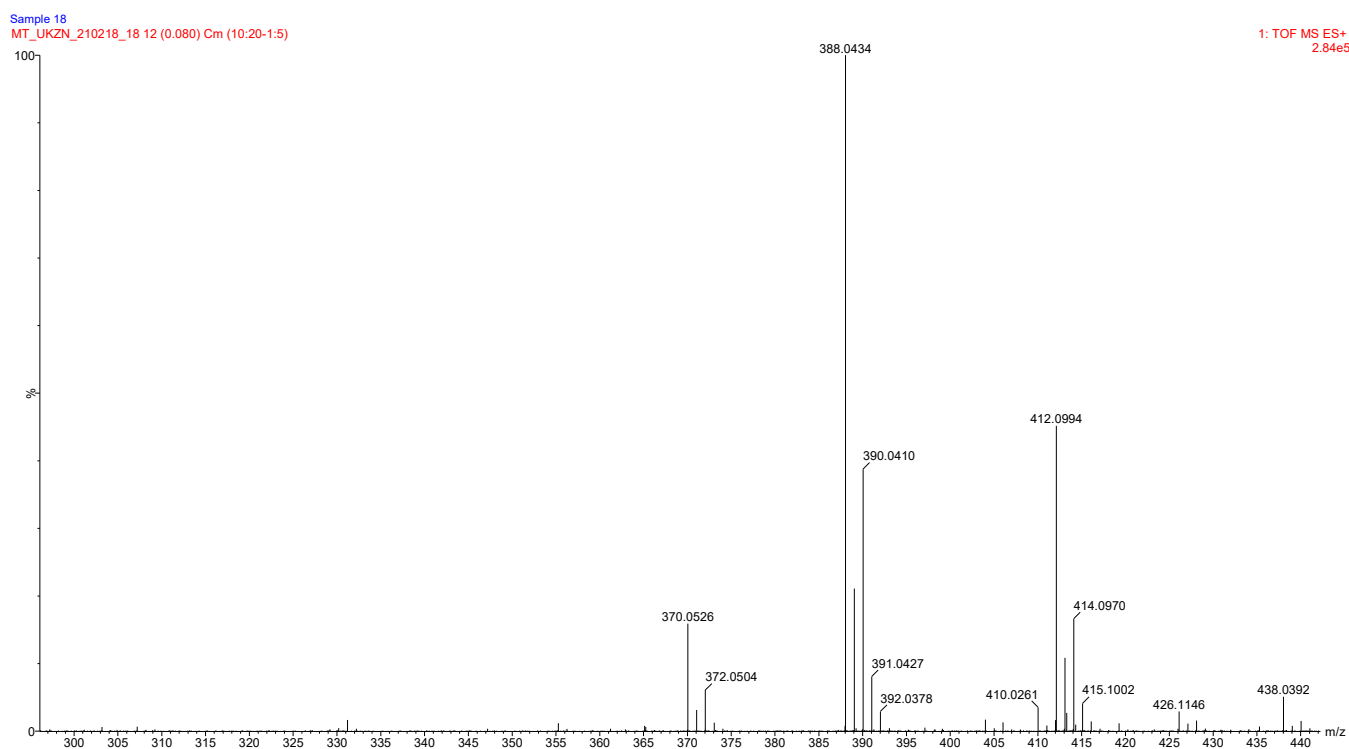
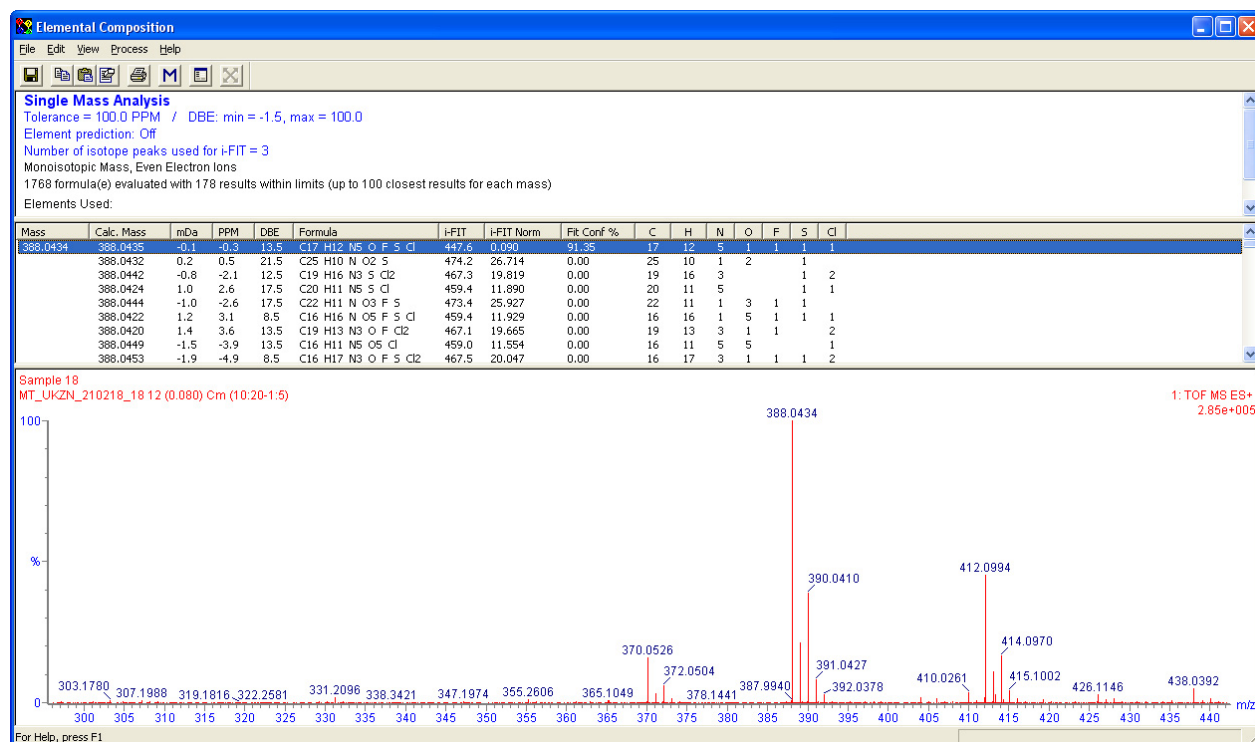
**Figure S6:** HRMS (ES<sup>+</sup>) for 2-(7-chloroquinolin-4-yl)-N-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)hydrazine-1-carboxamide (**6b**).



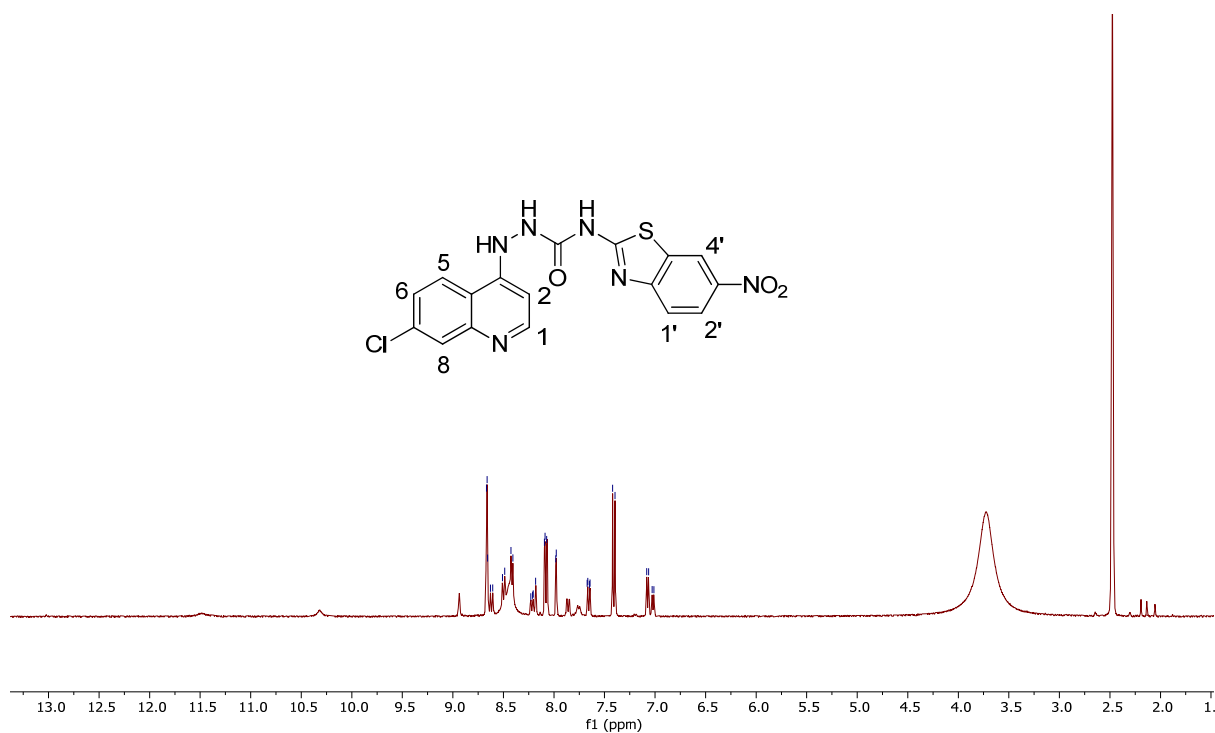
**Figure S7:** 400 MHz <sup>1</sup>H-NMR of 2-(7-chloroquinolin-4-yl)-N-(6-fluorobenzo[d]thiazol-2-yl)hydrazine-1-carboxamide in DMSO-d<sub>6</sub> (**6c**).



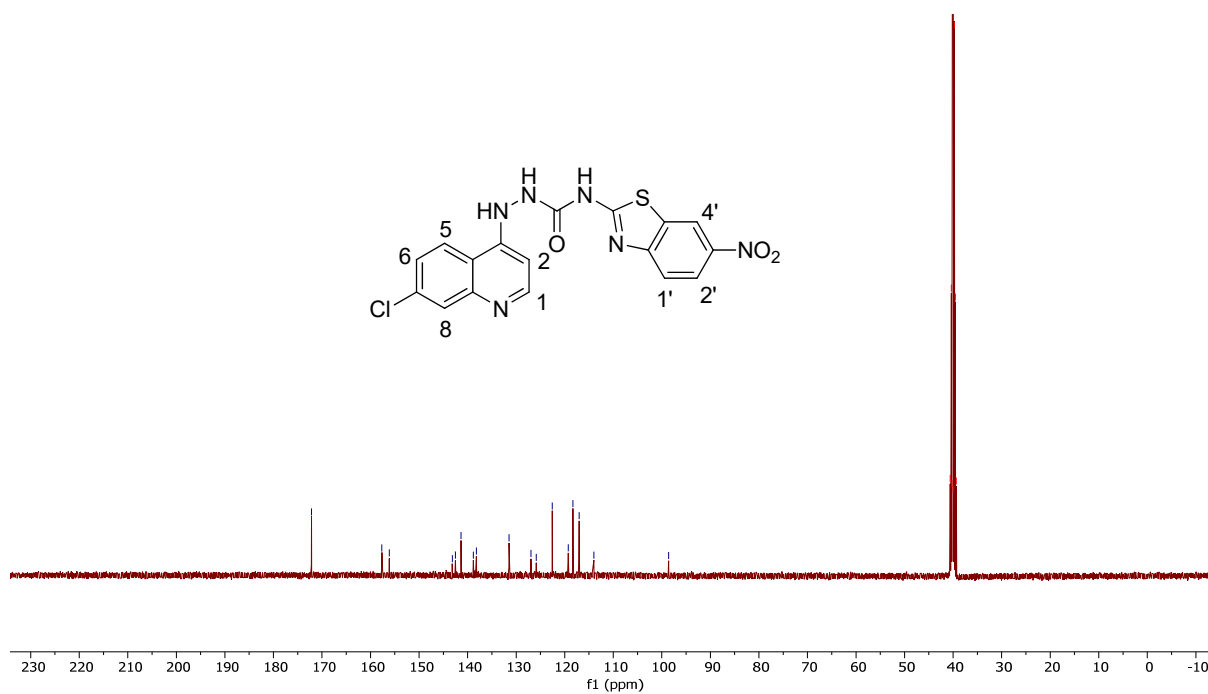
**Figure S8:** 101 MHz <sup>13</sup>C-NMR of 2-(7-chloroquinolin-4-yl)-N-(6-fluorobenzo[d]thiazol-2-yl)hydrazine-1-carboxamide in DMSO-d<sub>6</sub> (**6c**).



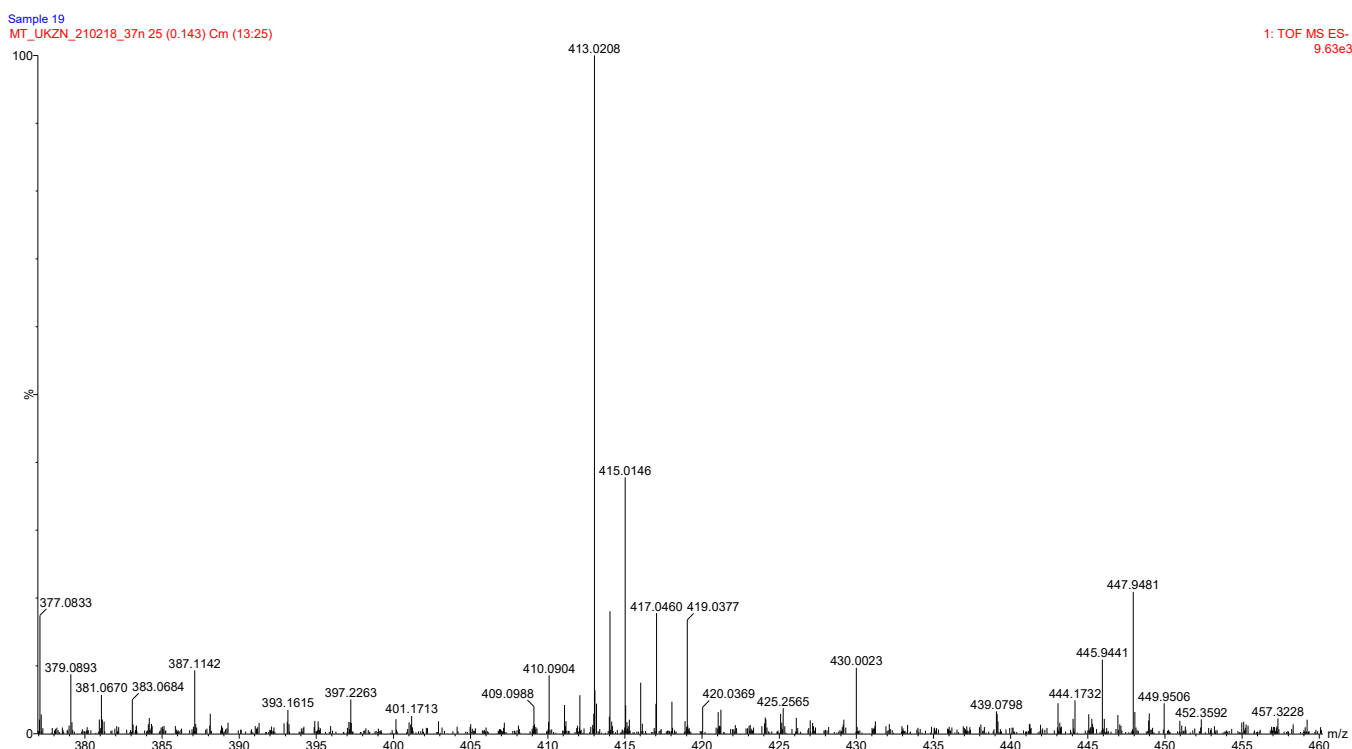
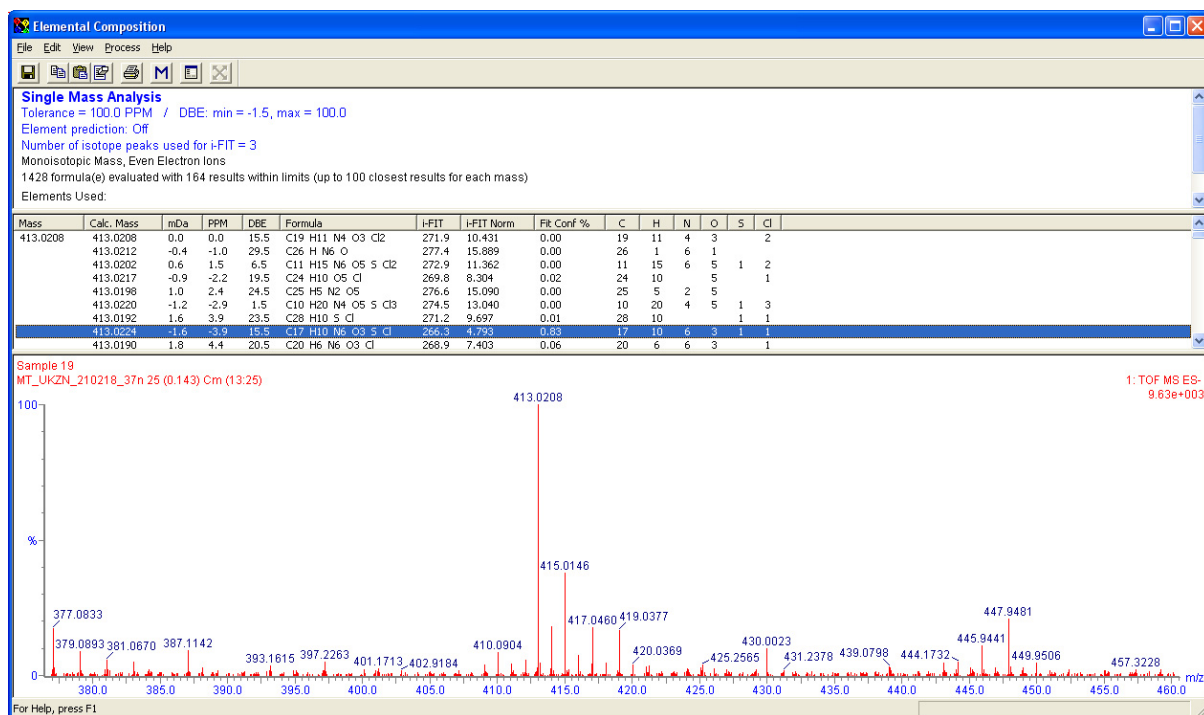
**Figure S9:** HRMS (ES<sup>+</sup>) for 2-(7-chloroquinolin-4-yl)-N-(6-fluorobenzo[d]thiazol-2-yl)hydrazine-1-carboxamide (**6c**).



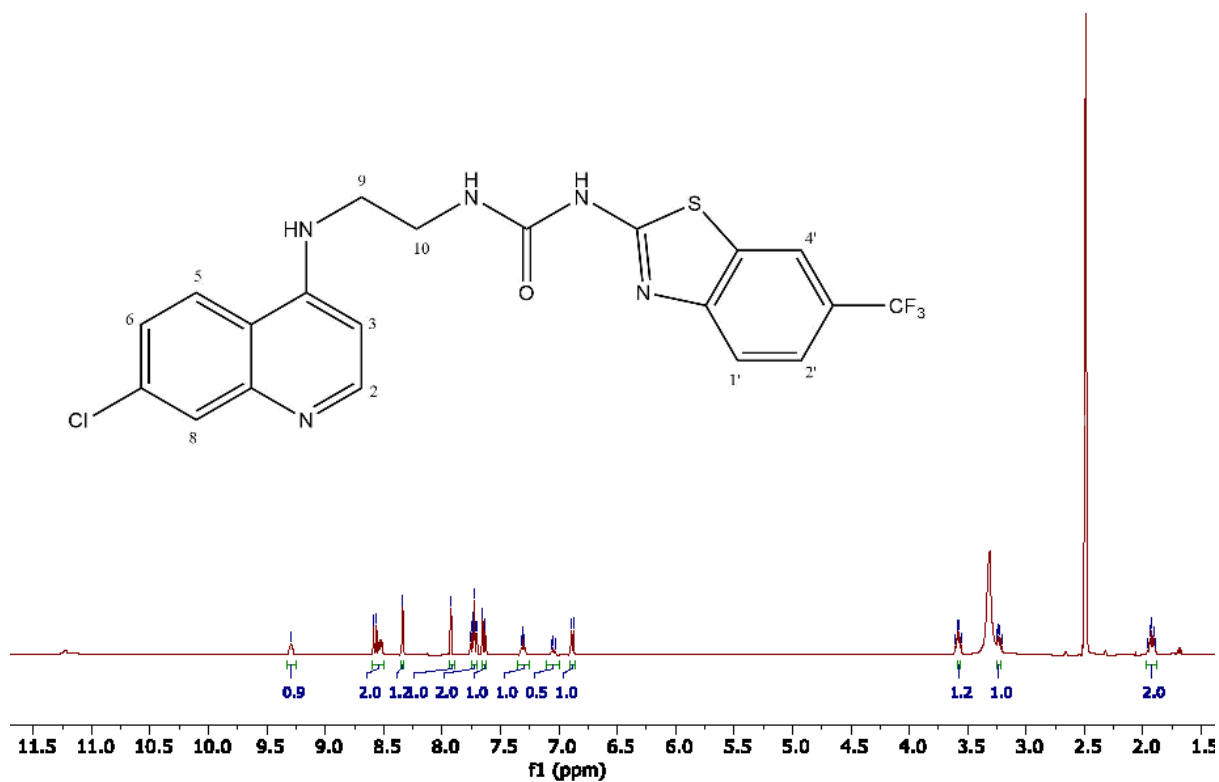
**Figure S10:** 400 MHz <sup>1</sup>H-NMR of 2-(7-chloroquinolin-4-yl)-N-(6-nitrobenzo[d]thiazol-2-yl)hydrazine-1-carboxamide in DMSO-d<sub>6</sub> (**6d**).



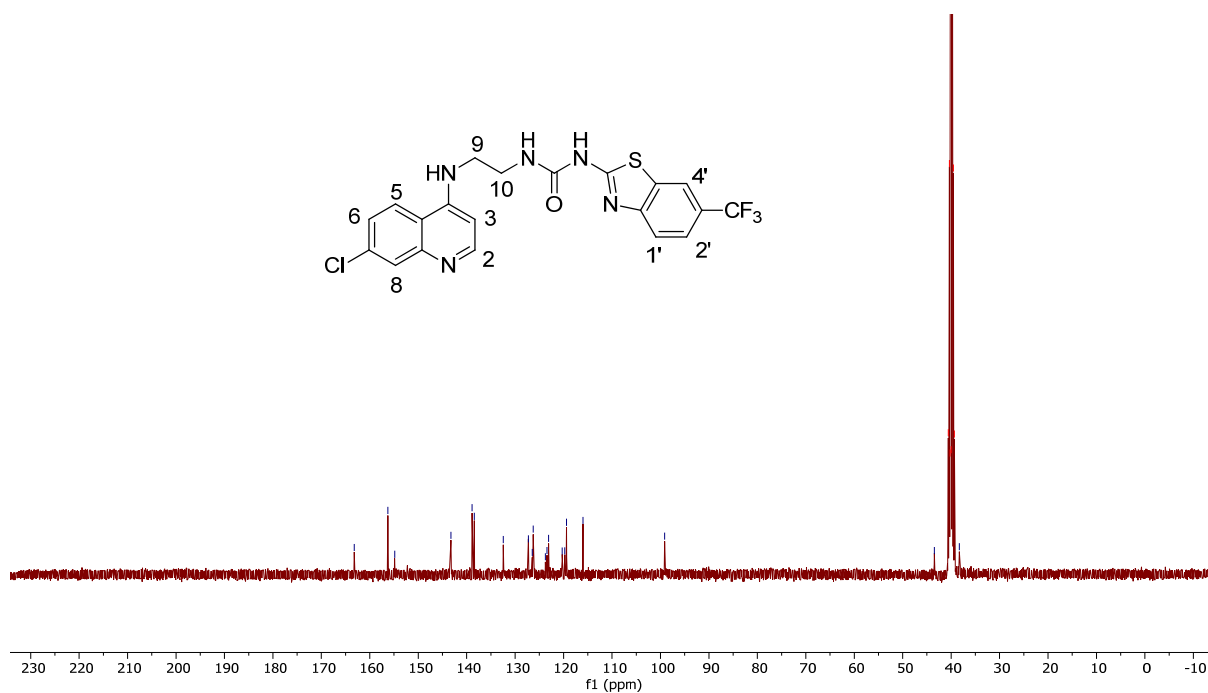
**Figure S11:** 101 MHz <sup>13</sup>C-NMR of 2-(7-chloroquinolin-4-yl)-N-(6-nitrobenzo[d]thiazol-2-yl)hydrazine-1-carboxamide in DMSO-d<sub>6</sub> (**6d**).



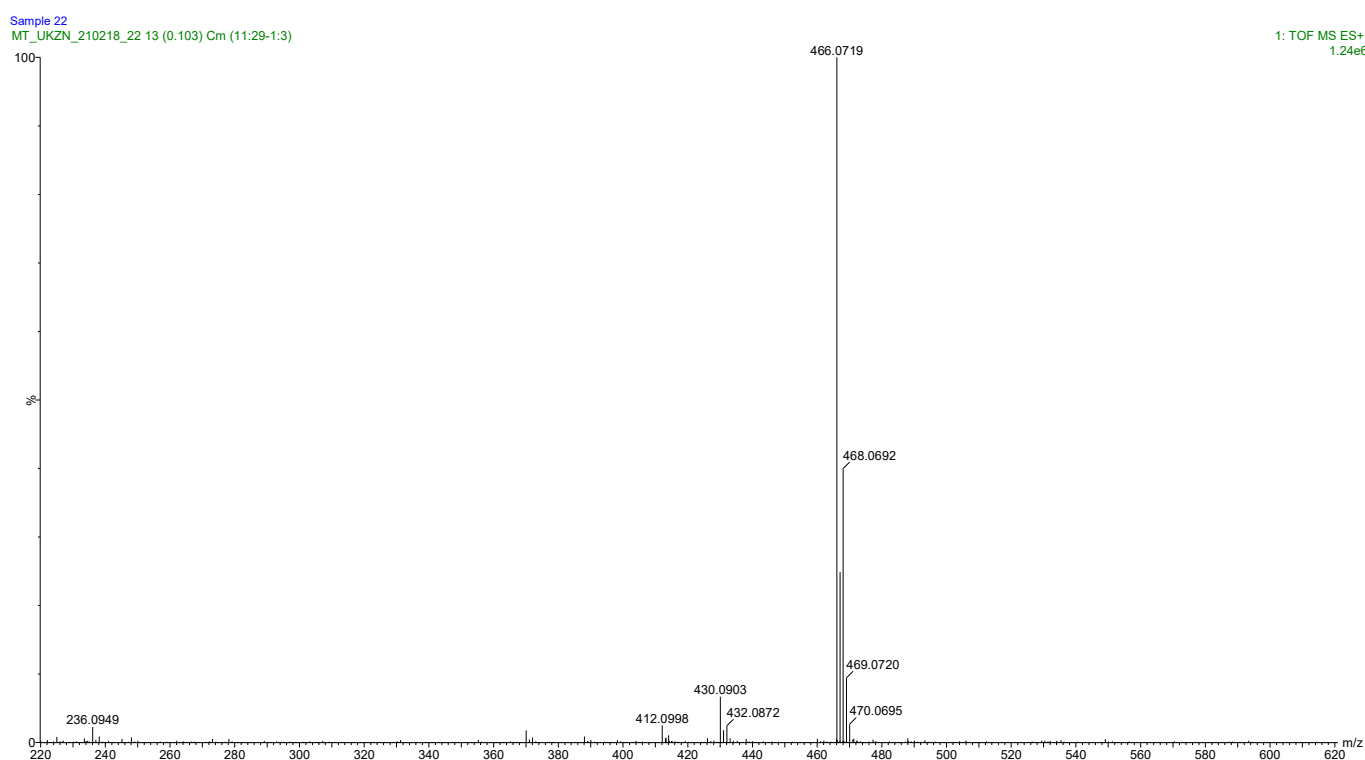
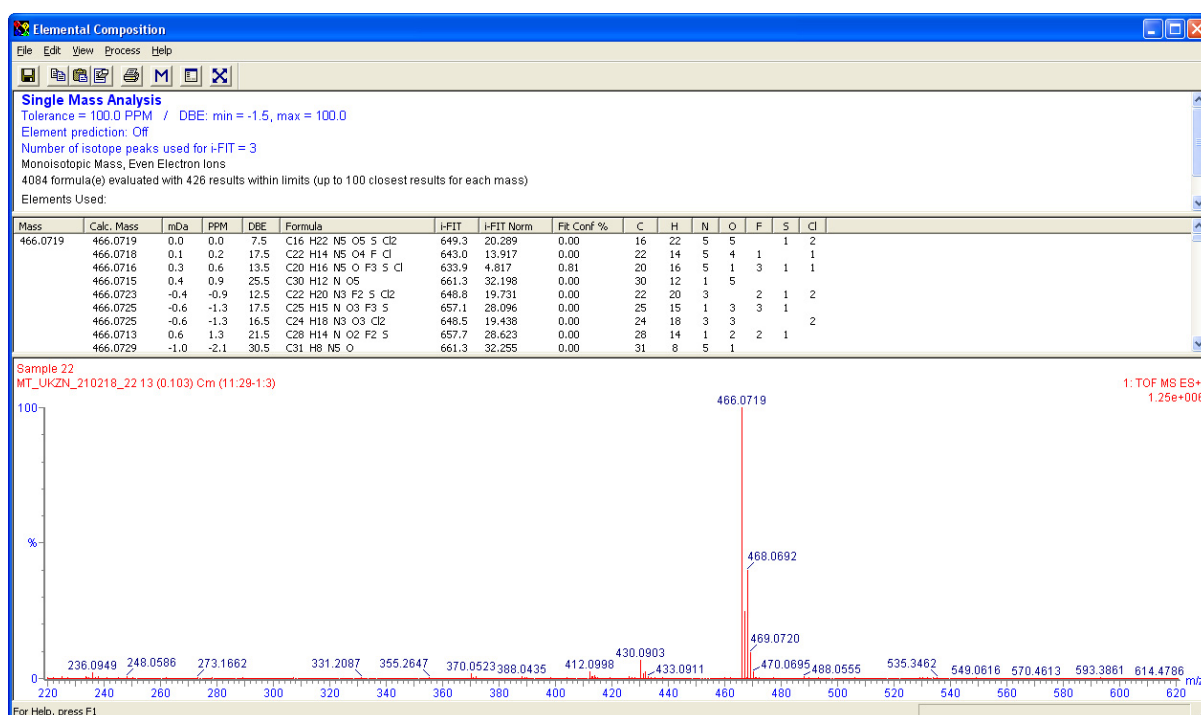
**Figure S12:** HRMS (ES<sup>-</sup>) for 2-(7-chloroquinolin-4-yl)-N-(6-nitrobenzo[d]thiazol-2-yl)hydrazine-1-carboxamide (**6d**) (negative ion mode).



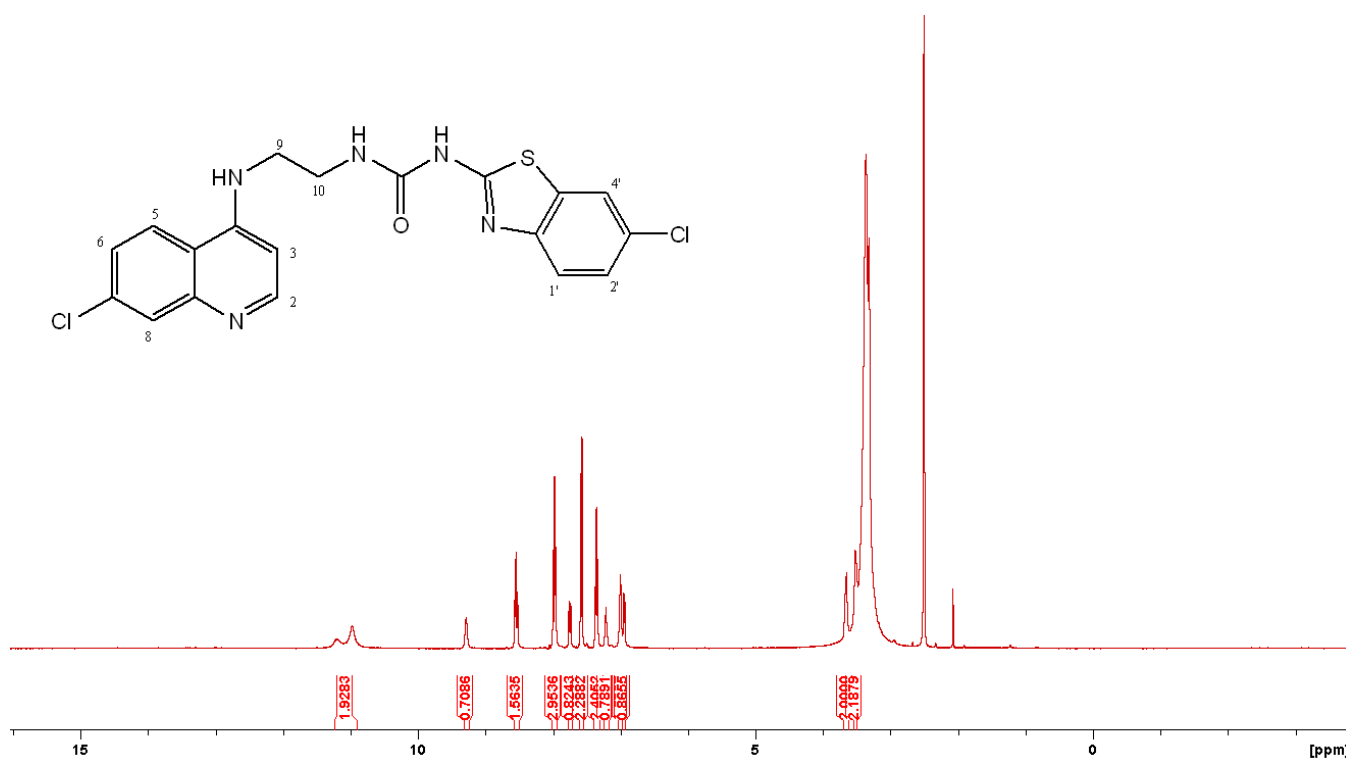
**Figure S13:** 400 MHz  $^1\text{H}$ -NMR of 1-(2-((7-chloroquinolin-4-yl)amino)ethyl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6e**).



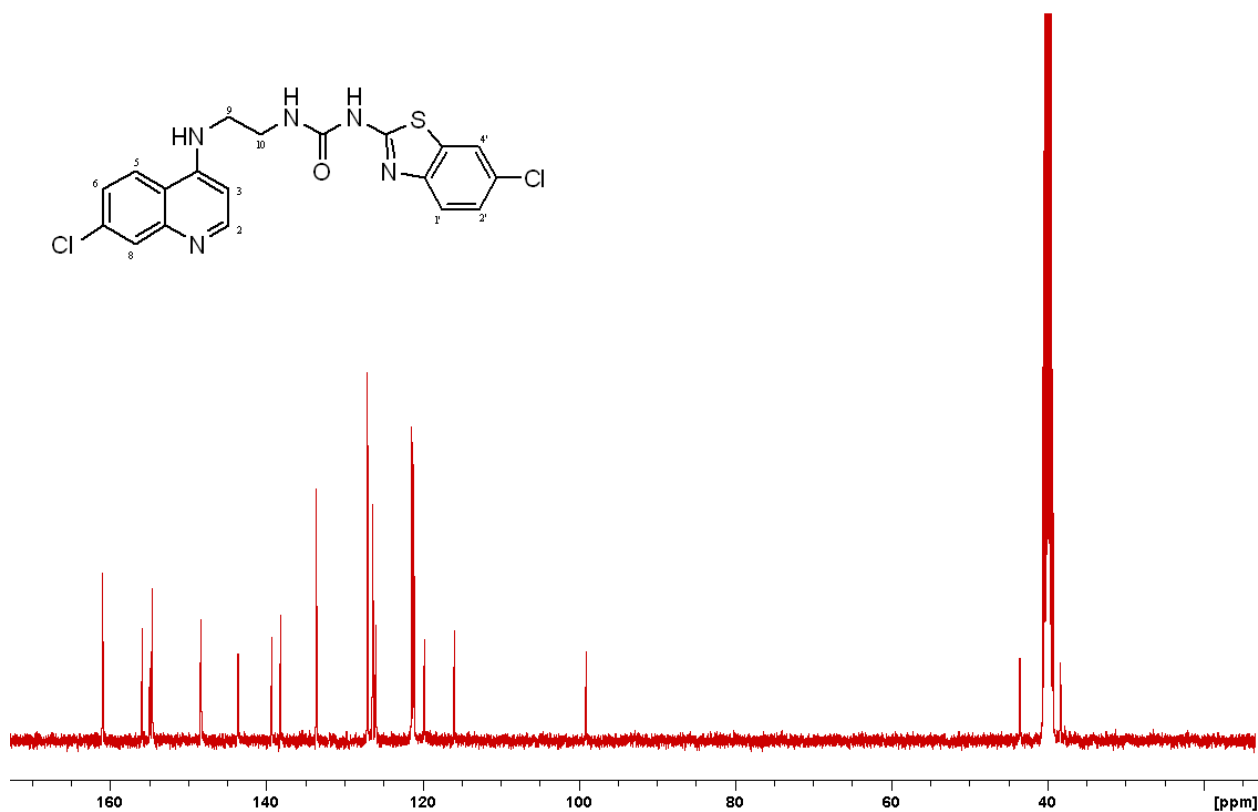
**Figure S14:** 101 MHz  $^{13}\text{C}$ -NMR of 1-(2-((7-chloroquinolin-4-yl)amino)ethyl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6e**).



**Figure S15:** HRMS (ES<sup>+</sup>) 1-(2-((7-chloroquinolin-4-yl)amino)ethyl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea (**6e**).

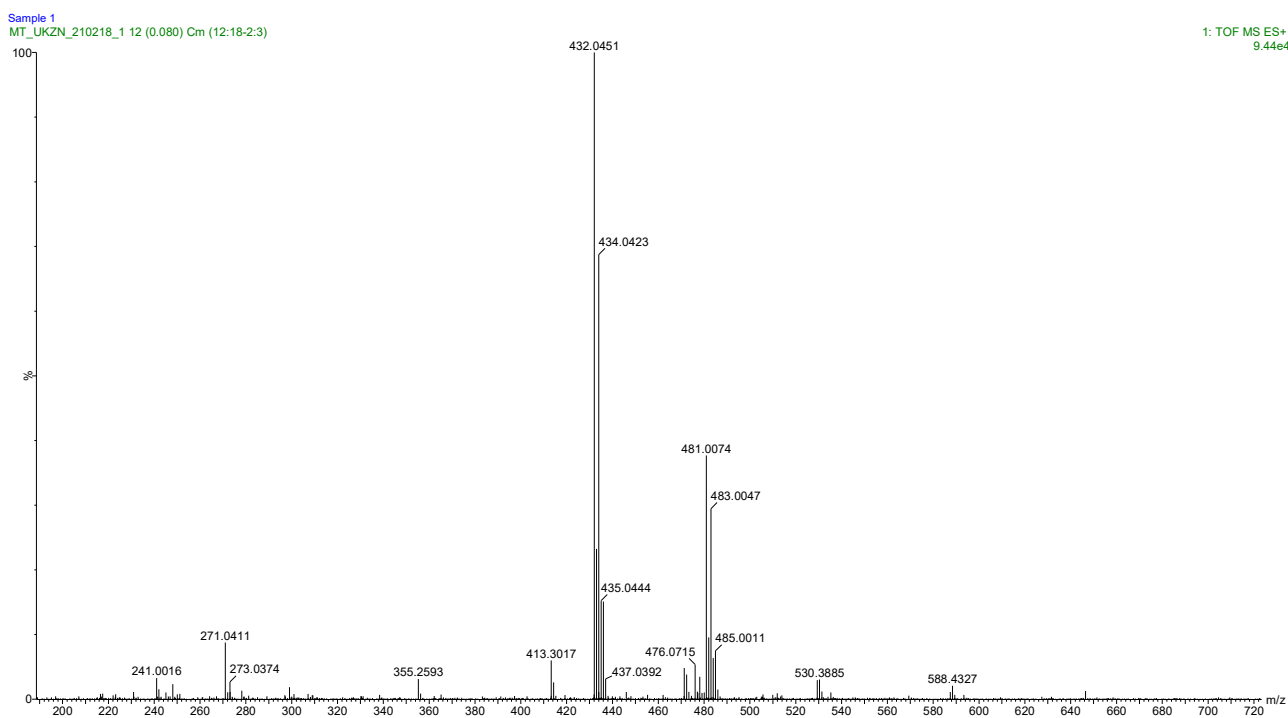
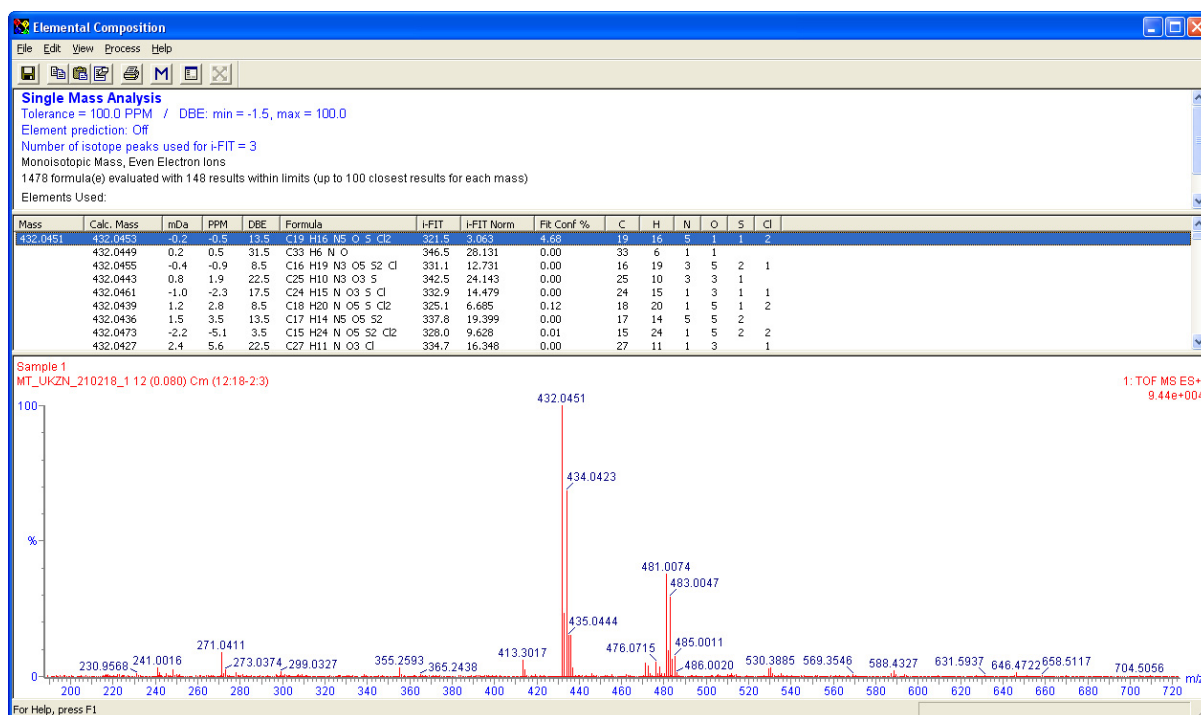


**Figure S16:** 400 MHz  $^1\text{H}$ -NMR of 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea in DMSO- $d_6$  (**6f**).

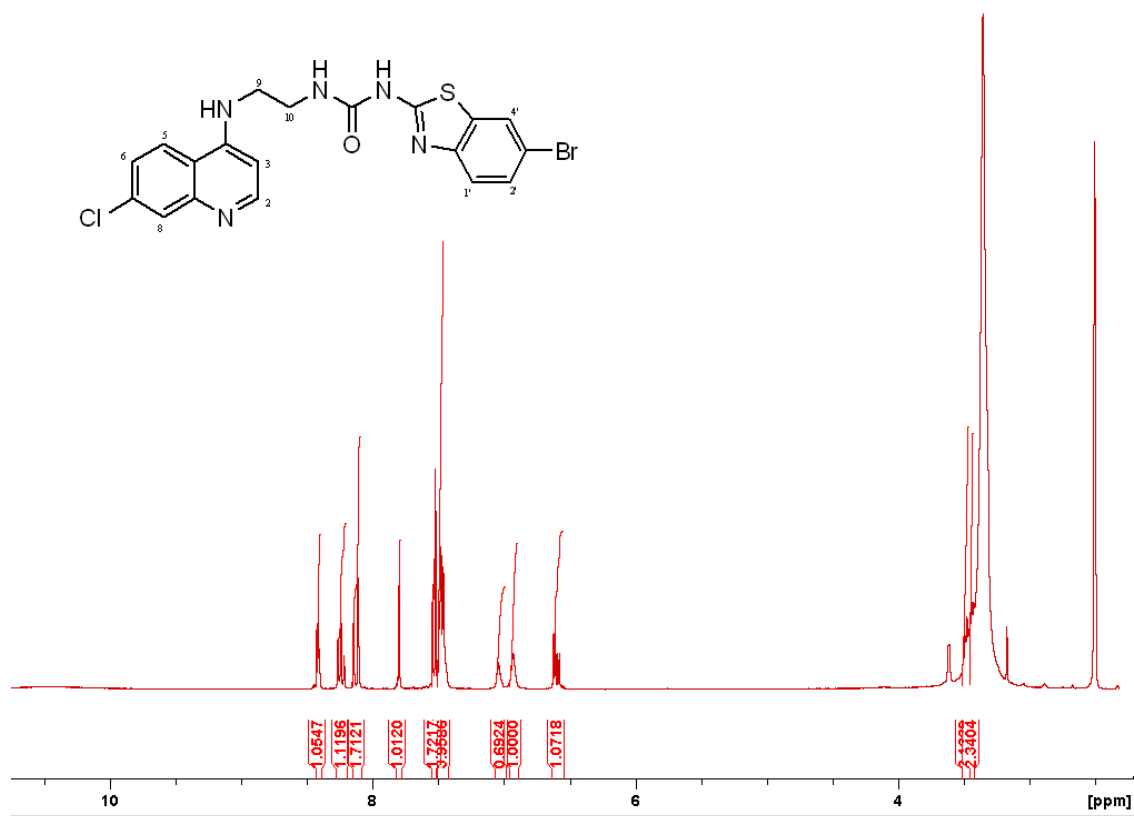


**Figure S17:** 101 MHz  $^{13}\text{C}$ -NMR of 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea in DMSO- $d_6$  (**6f**).

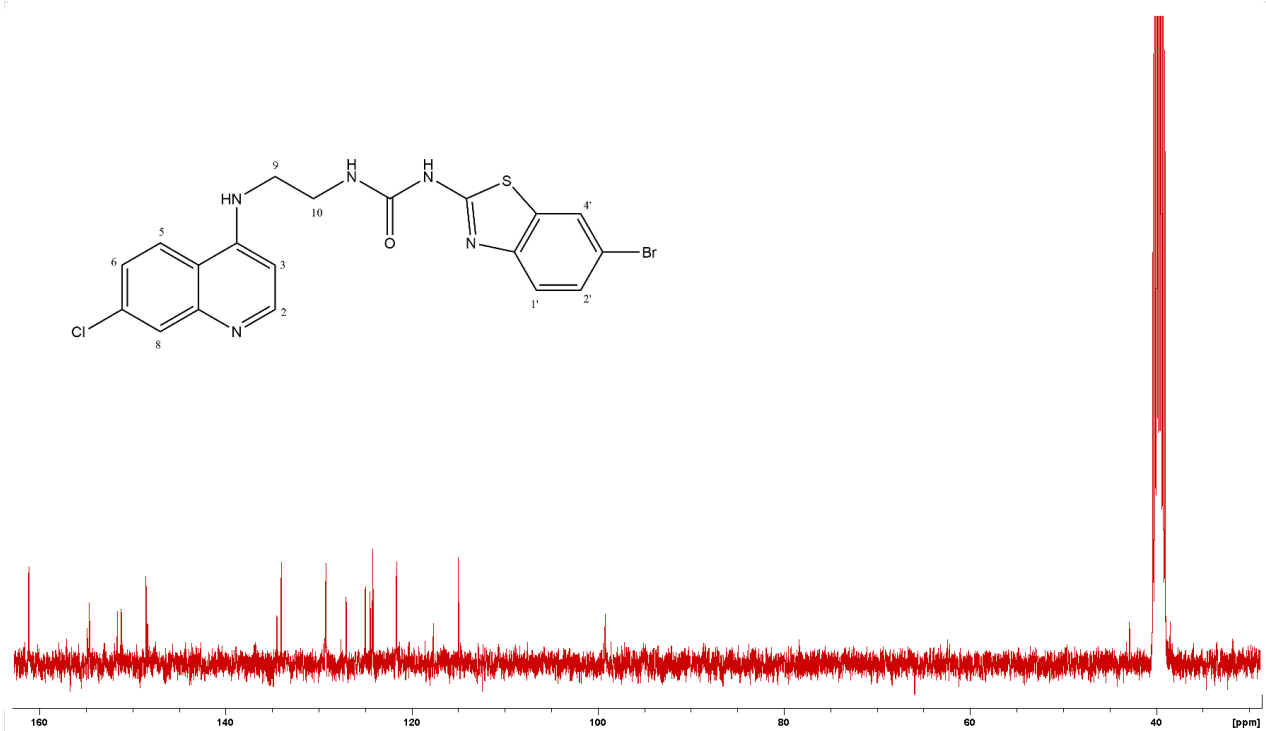




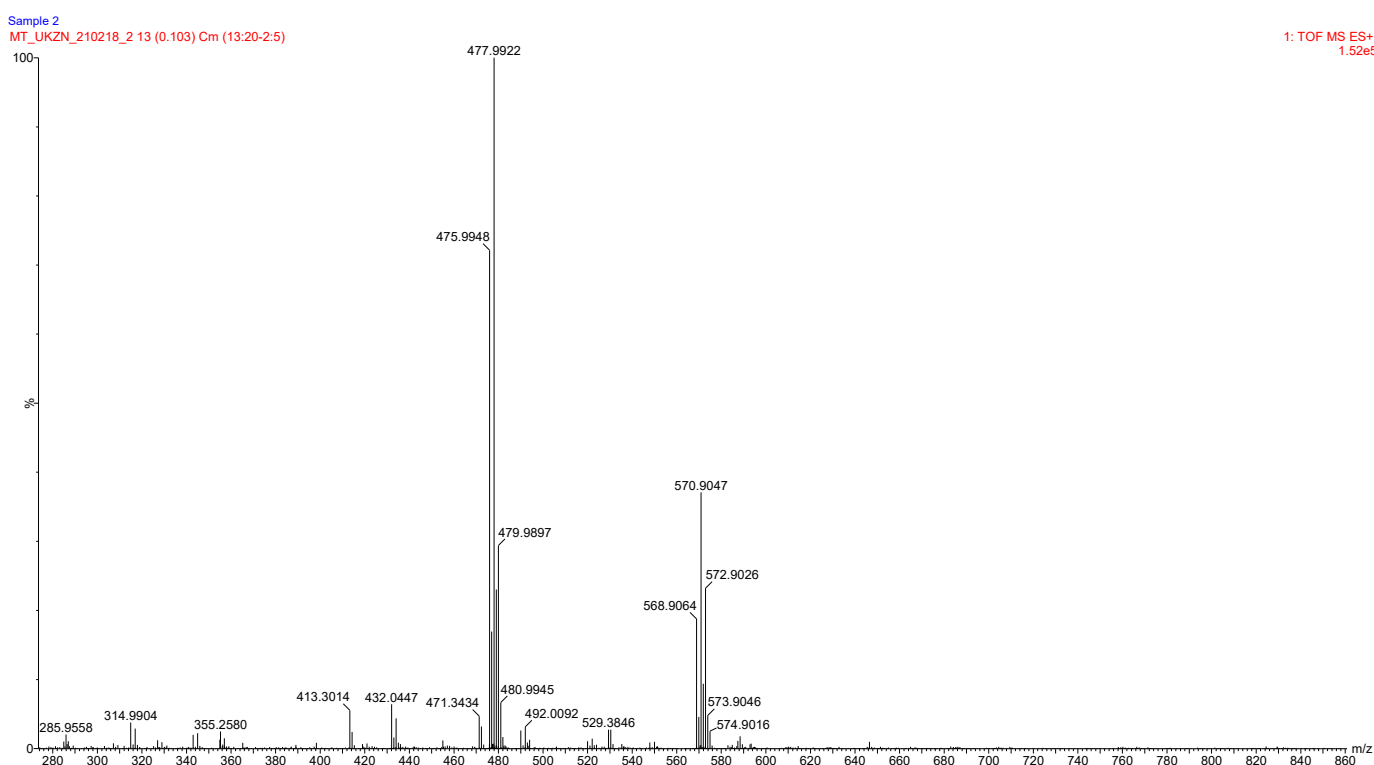
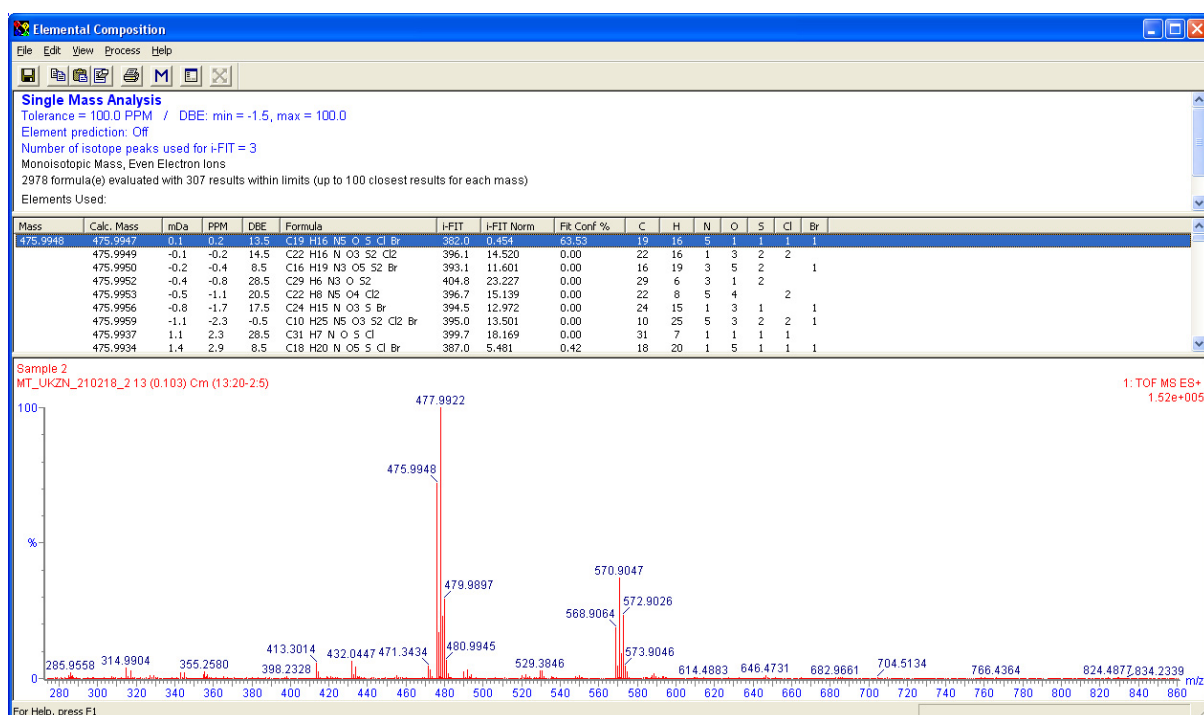
**Figure S18:** HRMS (ES<sup>+</sup>) for 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea (**6f**).



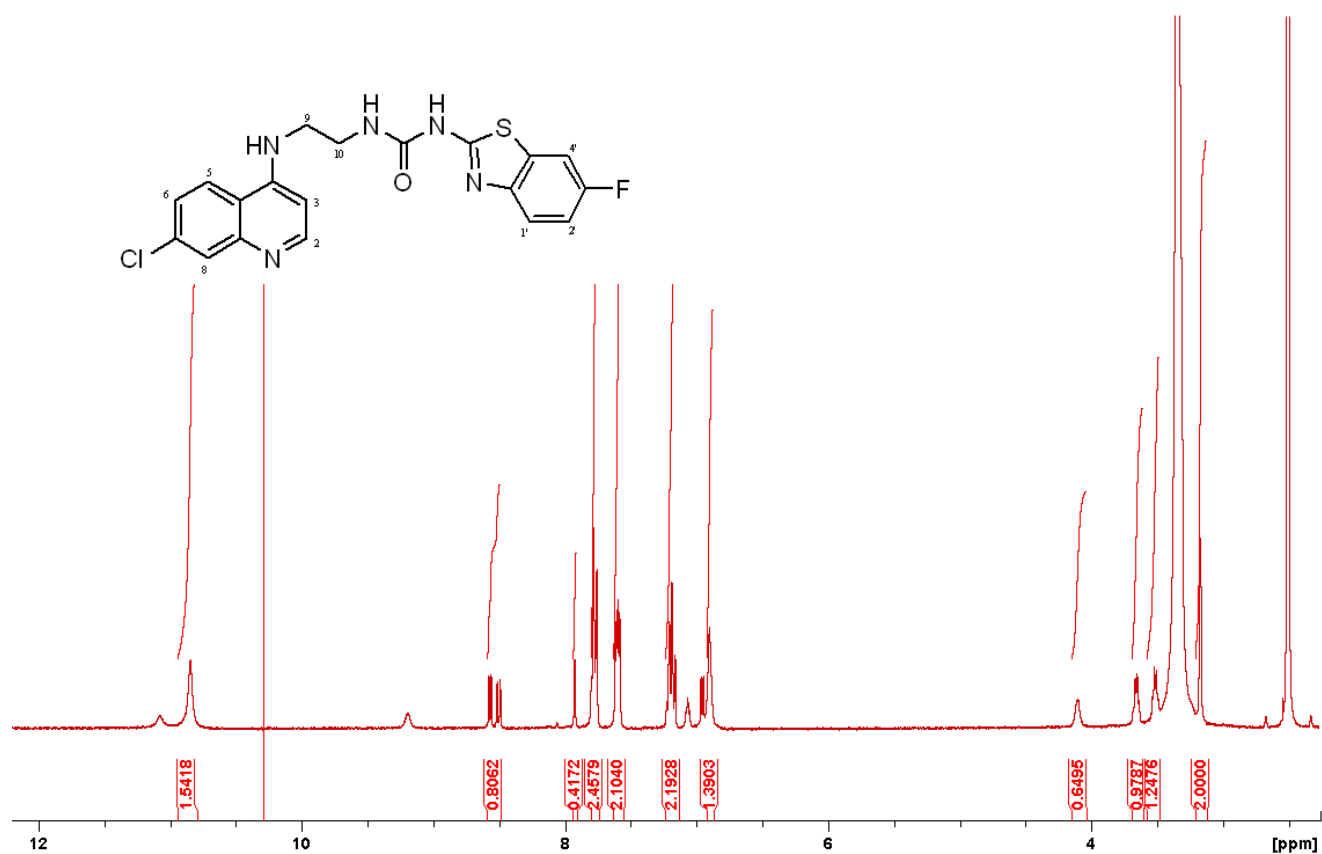
**Figure S19:**  $^1\text{H}$ -NMR of 1-(6-bromobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea in DMSO- $d_6$  (**6g**).



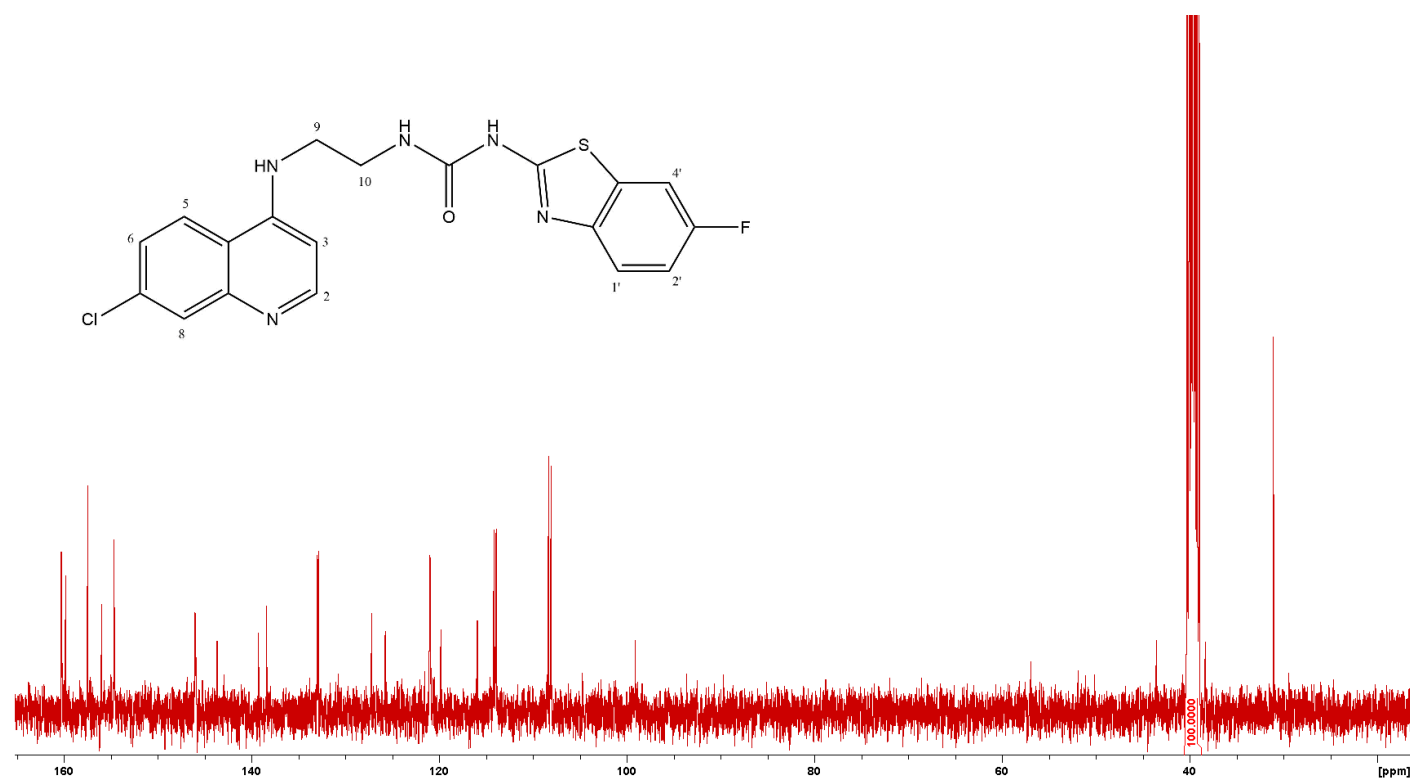
**Figure S20:**  $^{13}\text{C}$  NMR (APT) of 1-(6-bromobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea in DMSO- $d_6$  (**6g**).



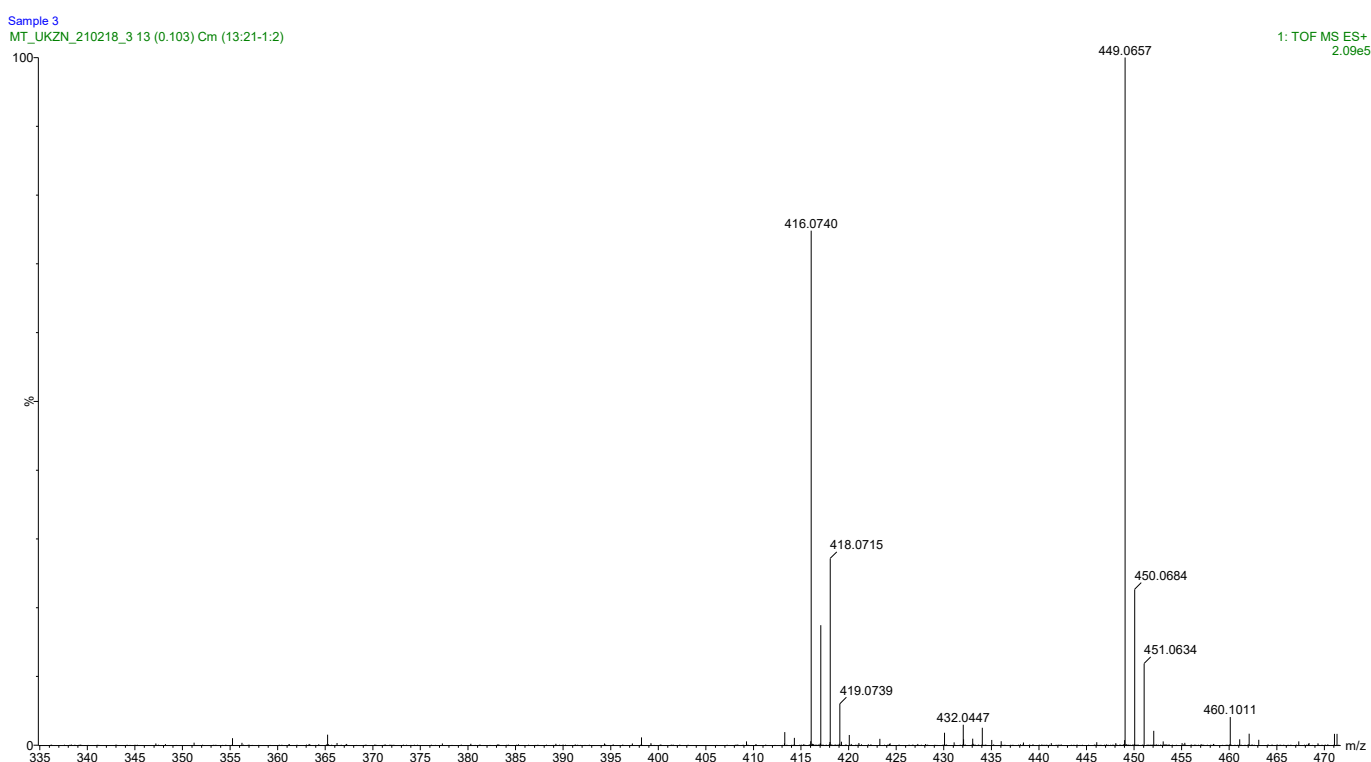
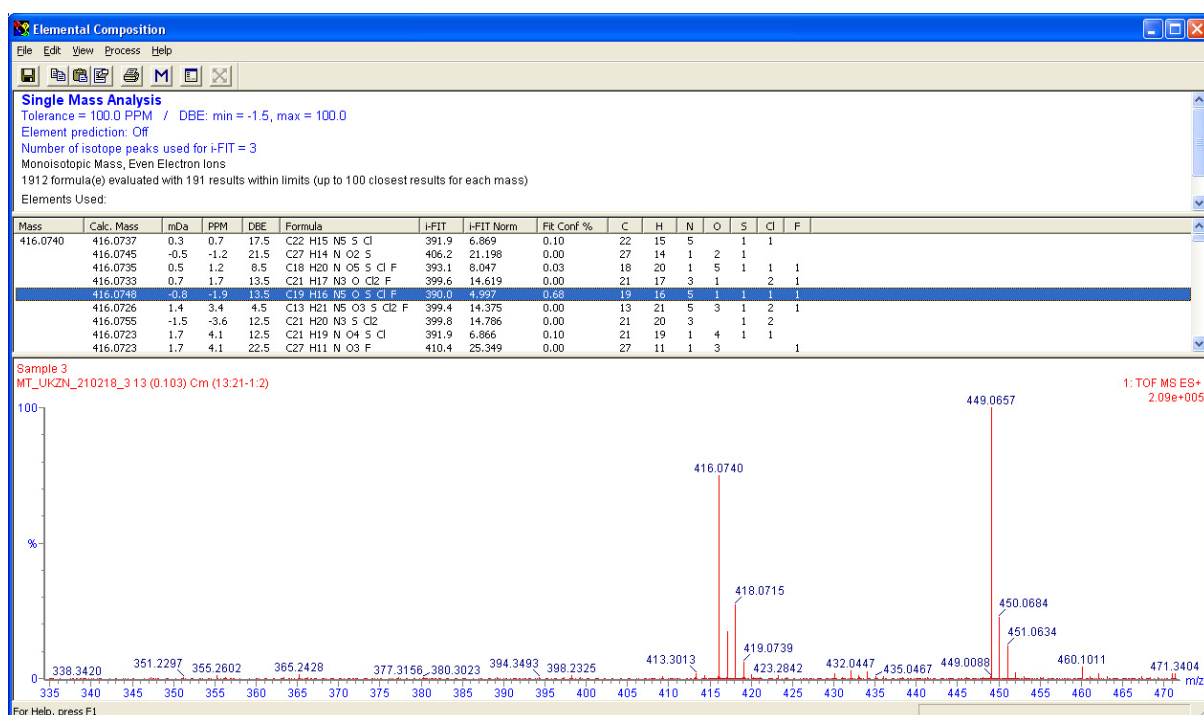
**Figure S21:** HRMS (ES<sup>+</sup>) for 1-(6-bromobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea (**6g**).



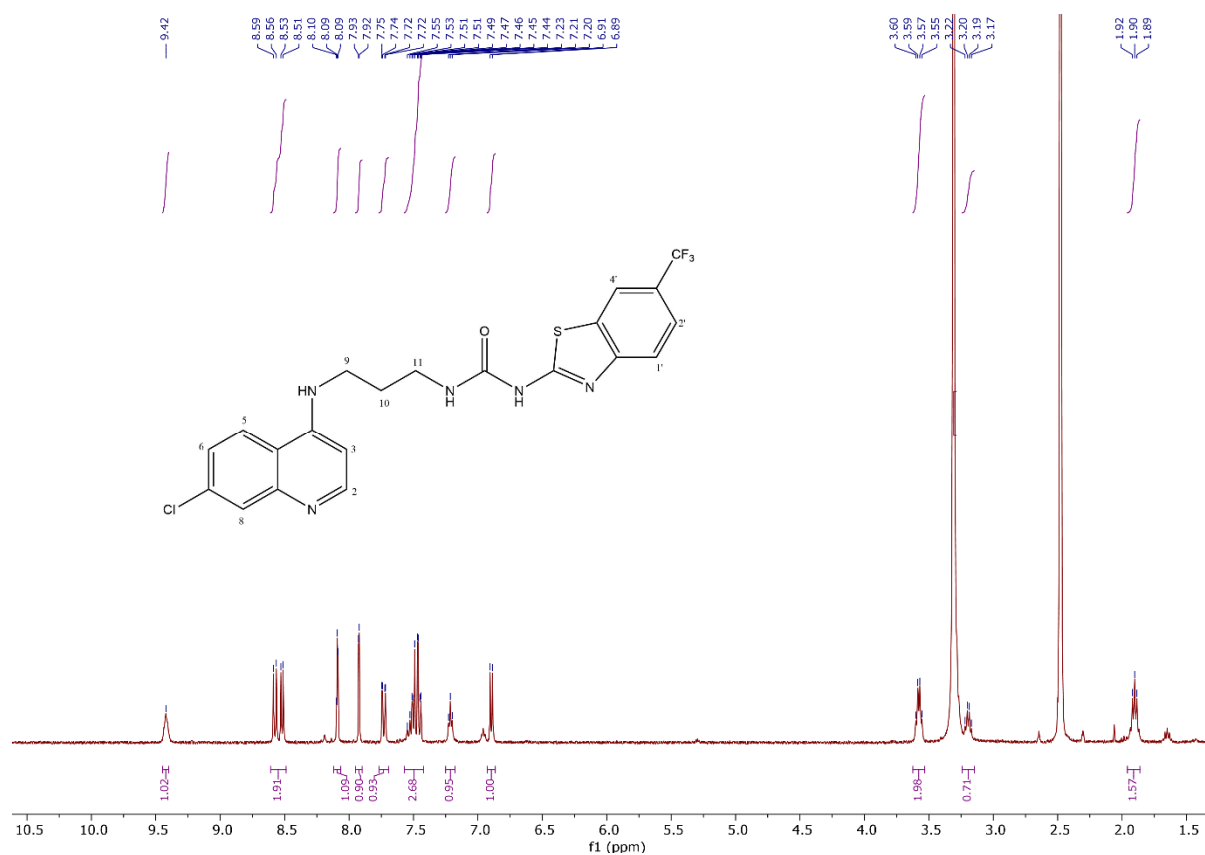
**Figure S22:** 400 MHz <sup>1</sup>H-NMR of 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea in DMSO-d<sub>6</sub> (**6h**).



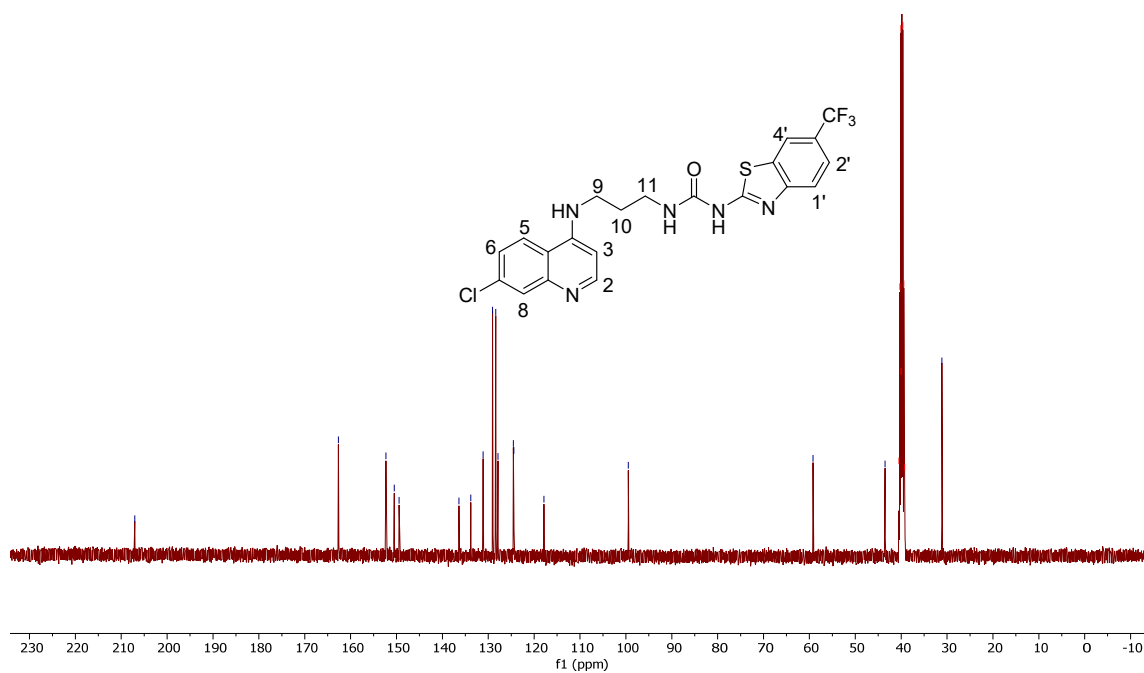
**Figure S23:** 101 MHz <sup>13</sup>C-NMR of 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea in DMSO-d<sub>6</sub> (**6h**).



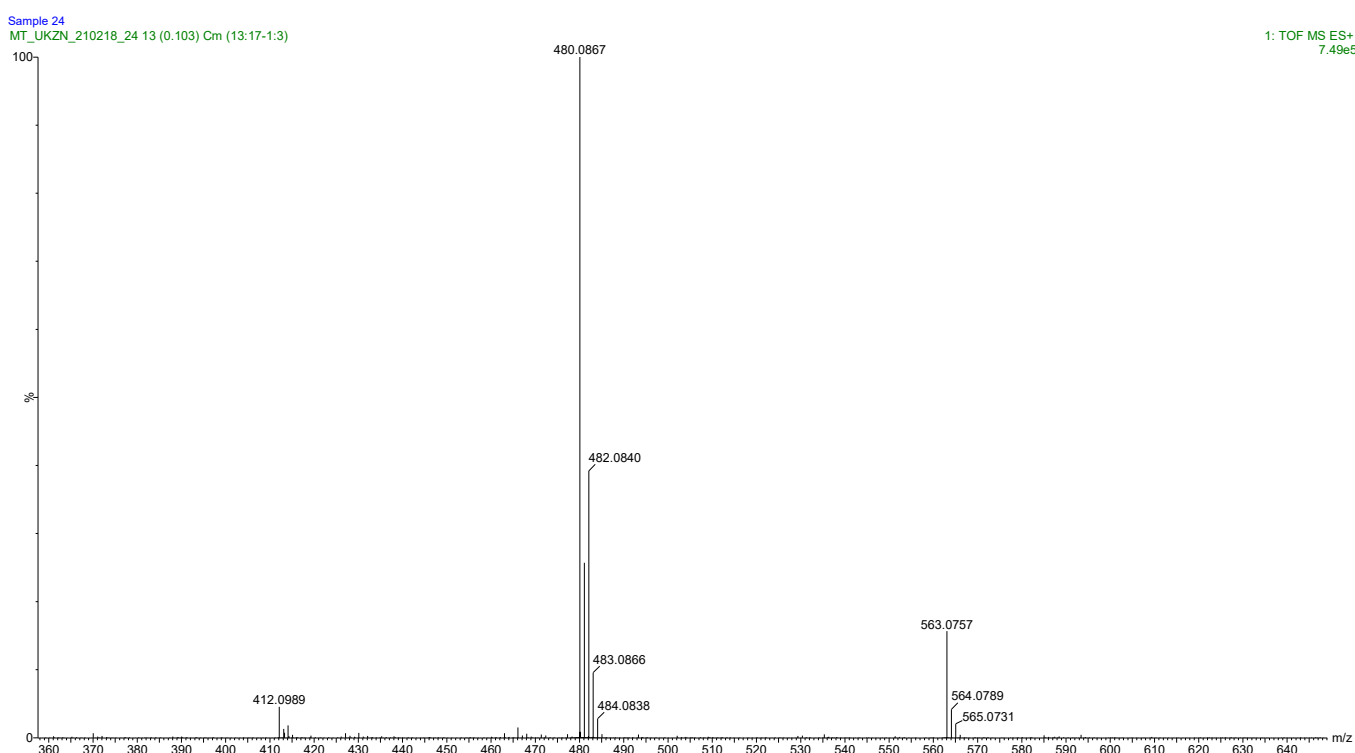
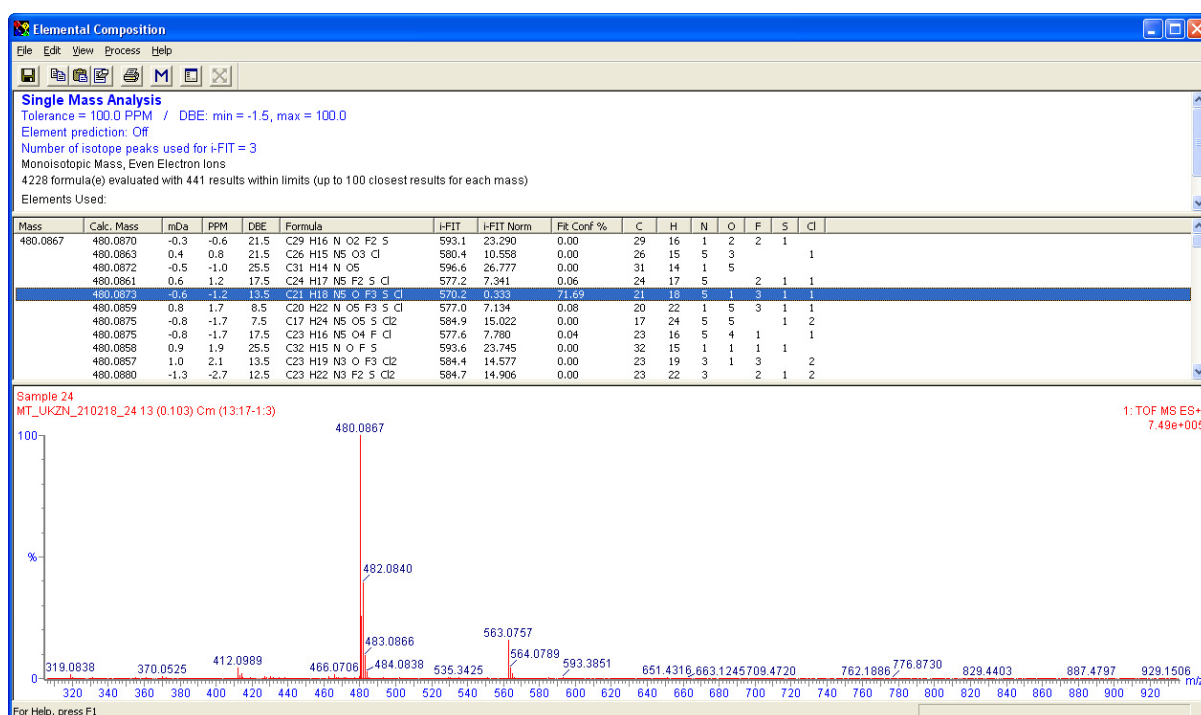
**Figure S24:** HRMS (ES<sup>+</sup>) for 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(2-((7-chloroquinolin-4-yl)amino)ethyl)urea (**6h**).



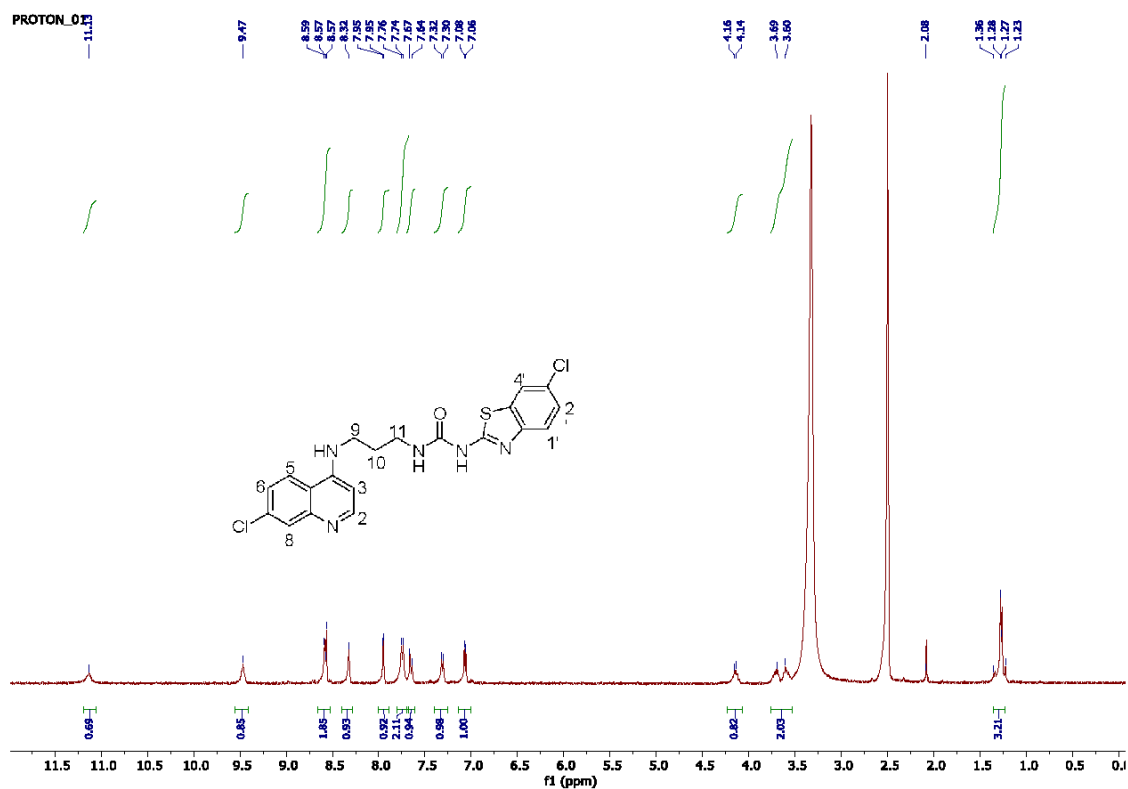
**Figure S25:** 400 MHz <sup>1</sup>H-NMR of 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (6i).



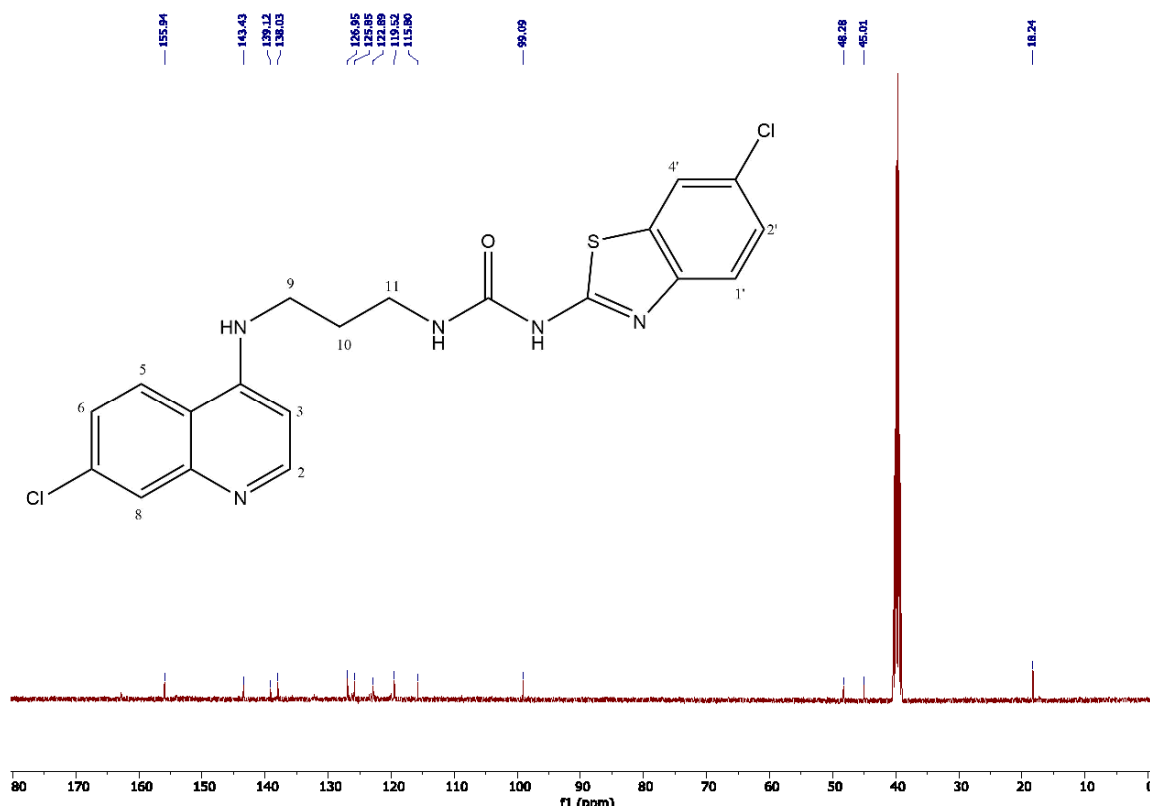
**Figure S26:** 101 MHz <sup>13</sup>C-NMR of 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (6i).



**Figure S27:** HRMS (ES+) for 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6i**).

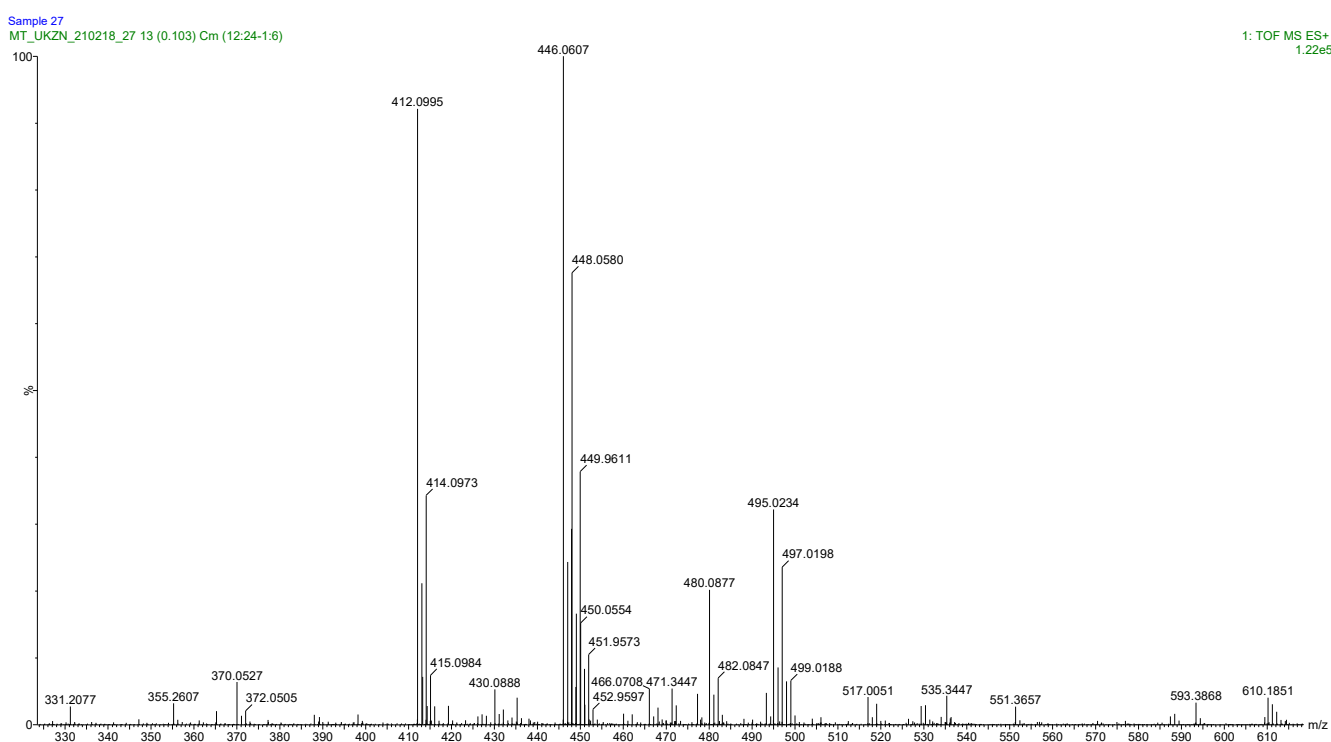
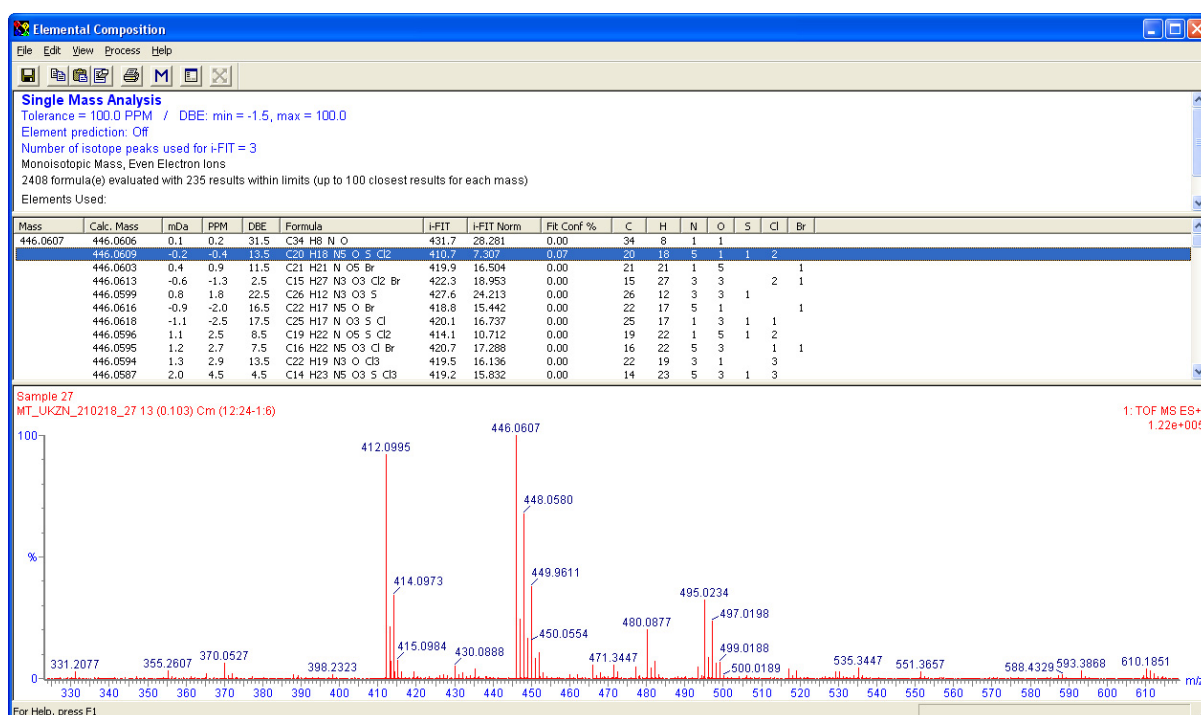


**Figure S28:** 400 MHz <sup>1</sup>H-NMR of 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(3-((7-chloroquinolin-4-yl)amino)propyl)urea in DMSO-d<sub>6</sub> (6j).

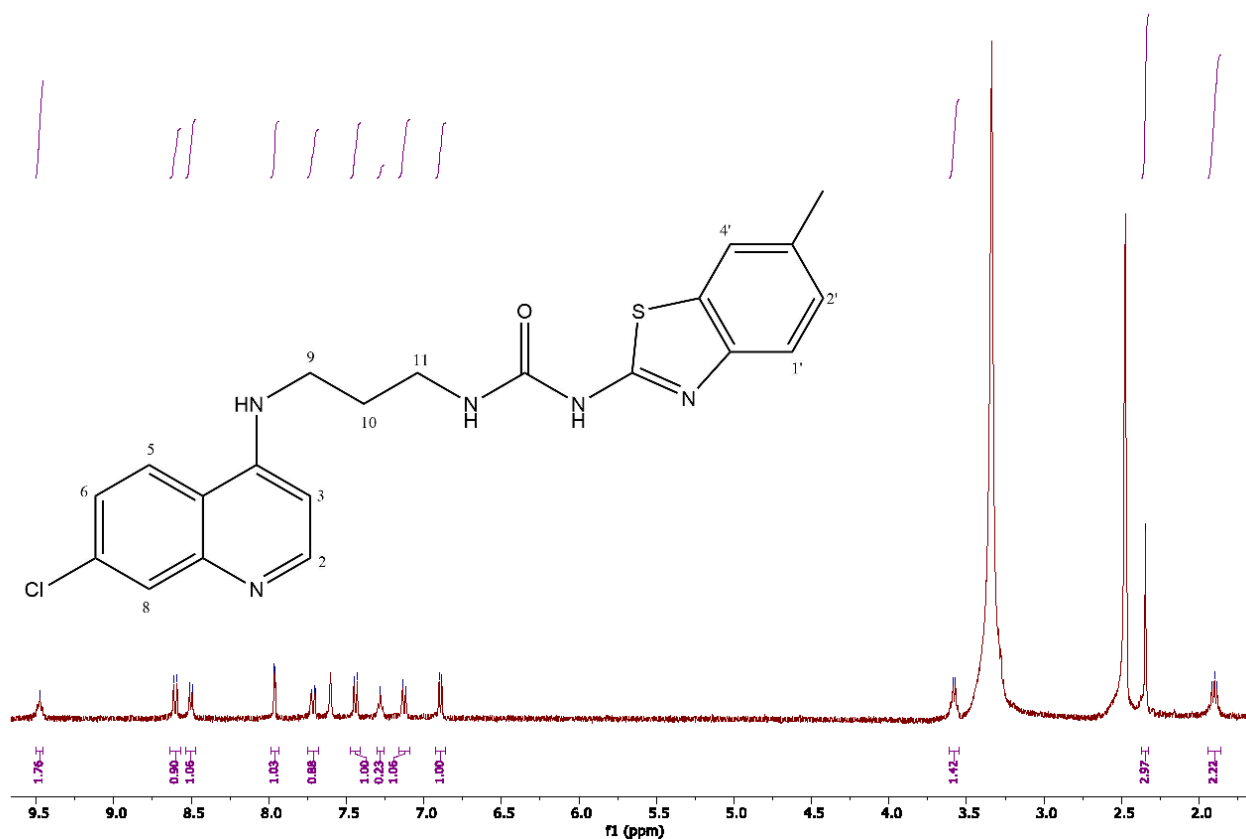


**Figure S29:** 101 MHz <sup>13</sup>C-NMR of 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(3-((7-chloroquinolin-4-yl)amino)propyl)urea in DMSO-d<sub>6</sub> (6j).

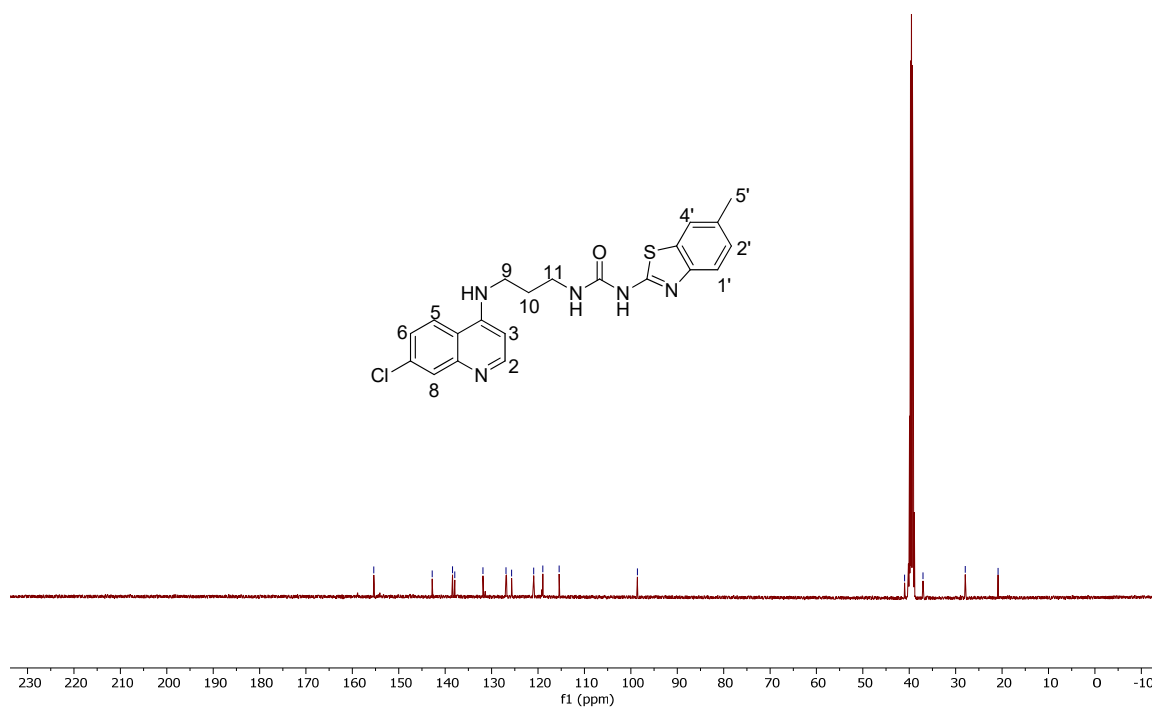




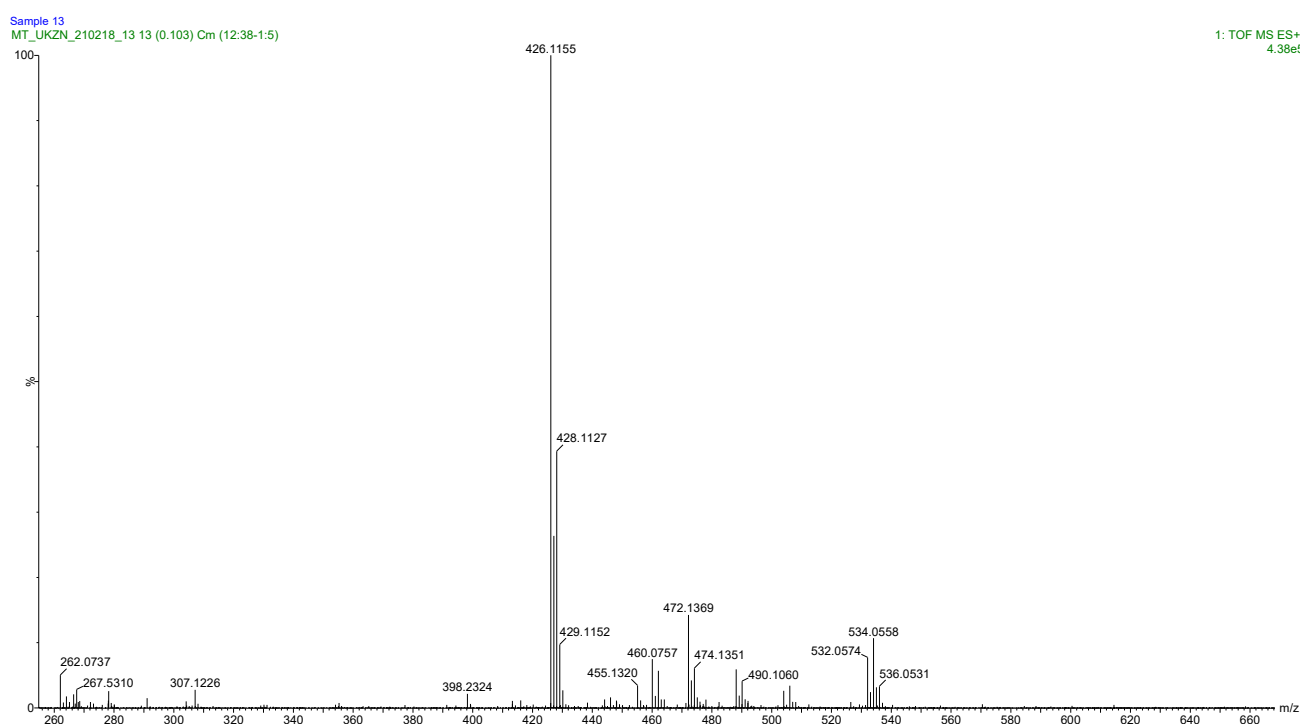
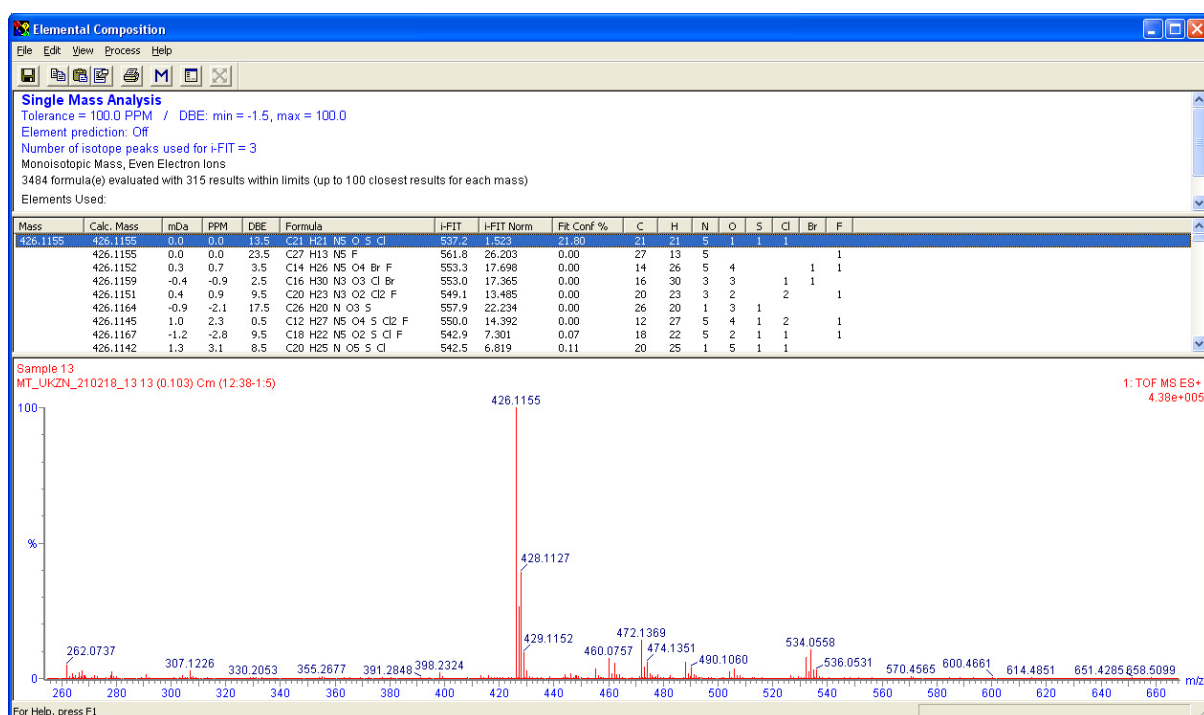
**Figure S30:** HRMS (ES+) for 1-(1-(7-chloroquinolin-4-ylamino)propan-2-yl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea (**6j**).



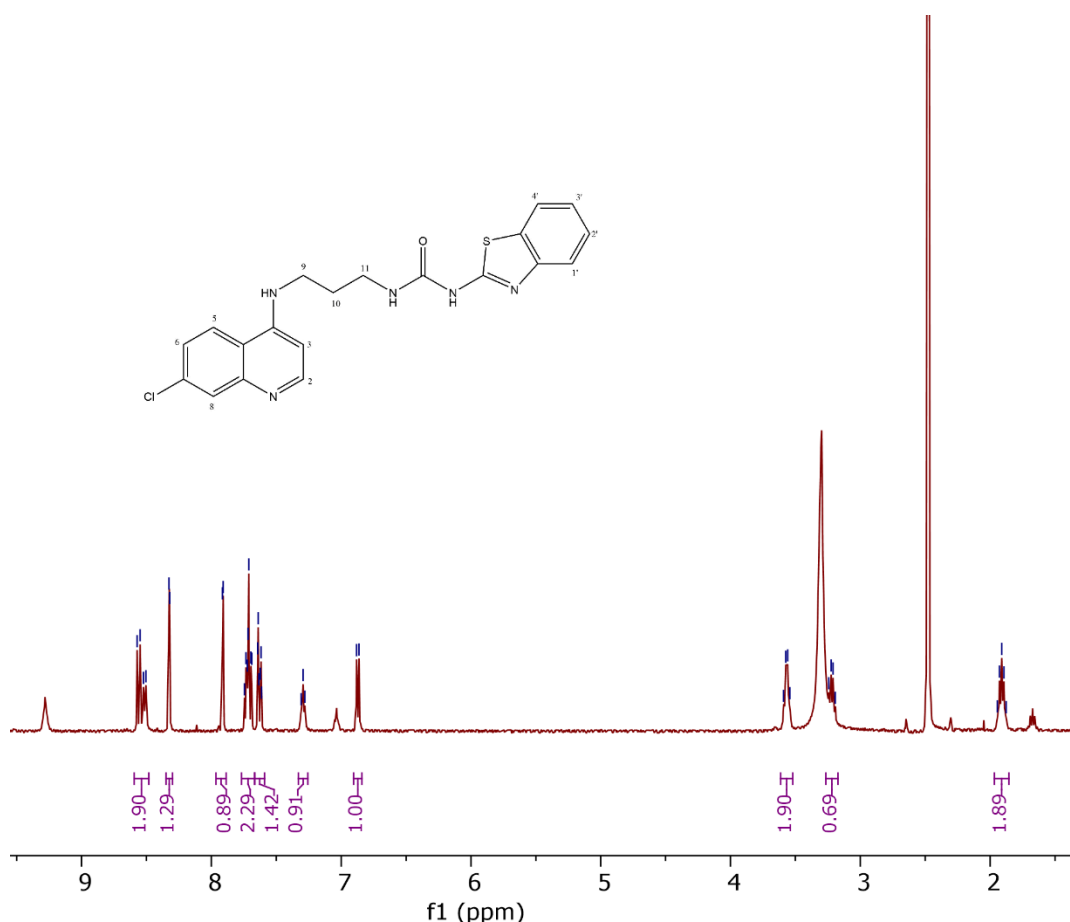
**Figure S31:** 400 MHz  $^1\text{H}$ -NMR of 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(6-methylbenzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6k**).



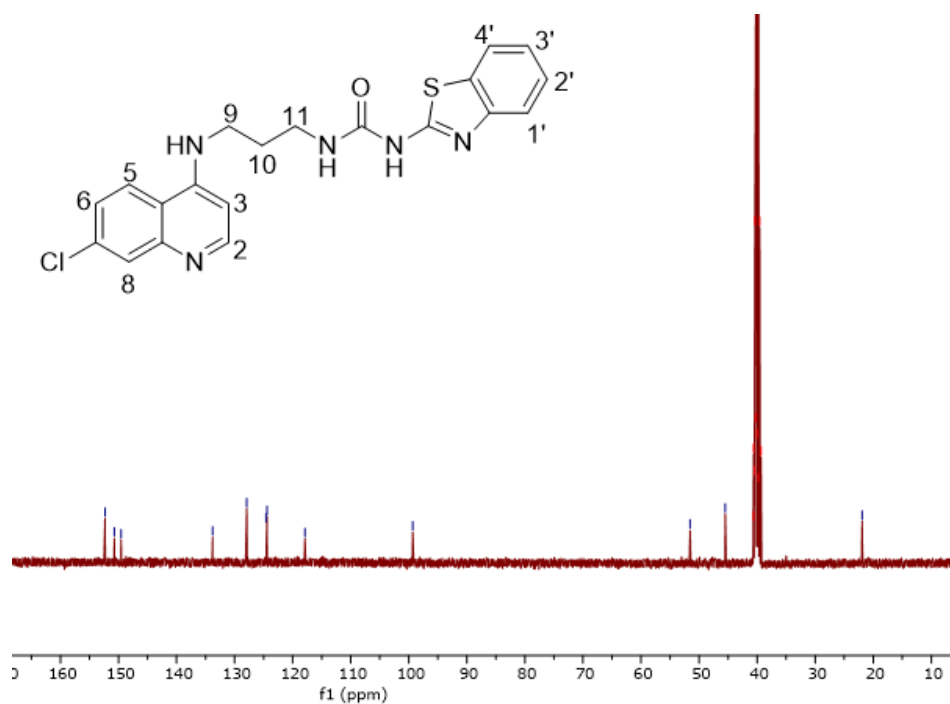
**Figure S32:** 101 MHz  $^{13}\text{C}$ -NMR of 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(6-methylbenzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6k**).



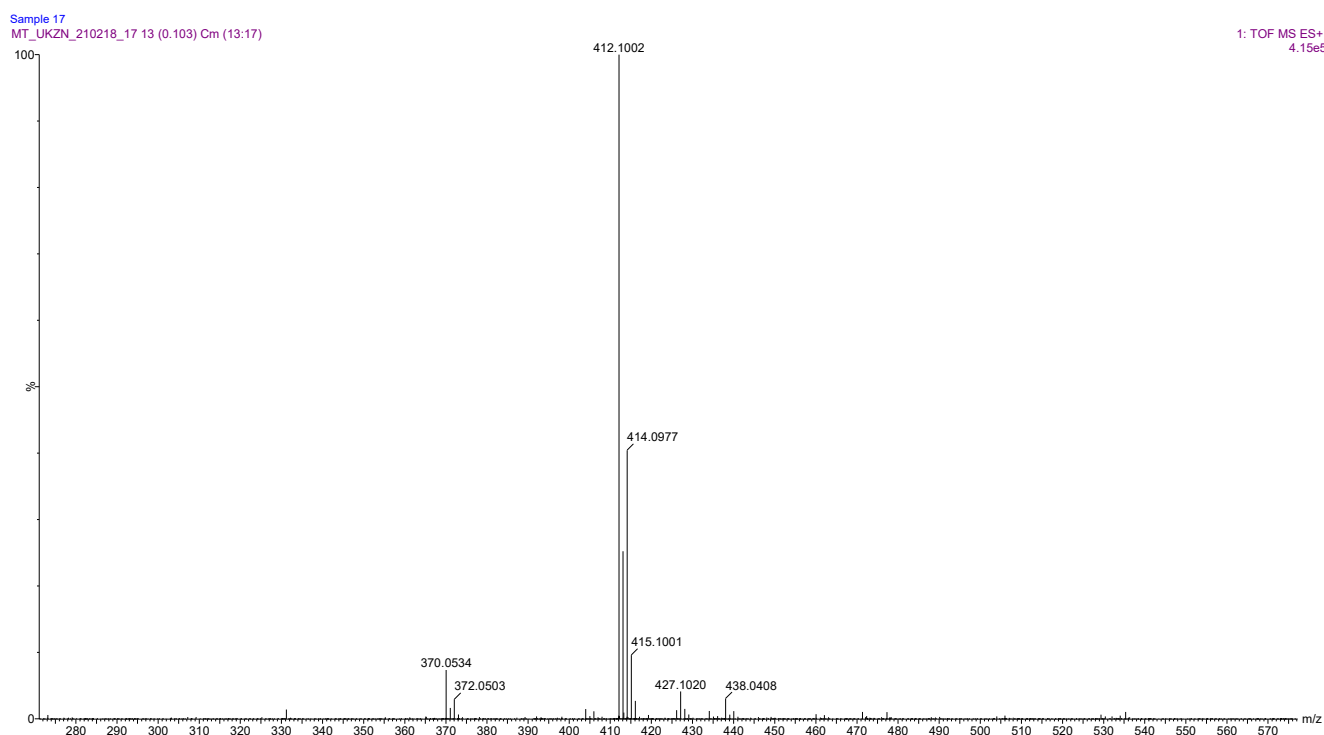
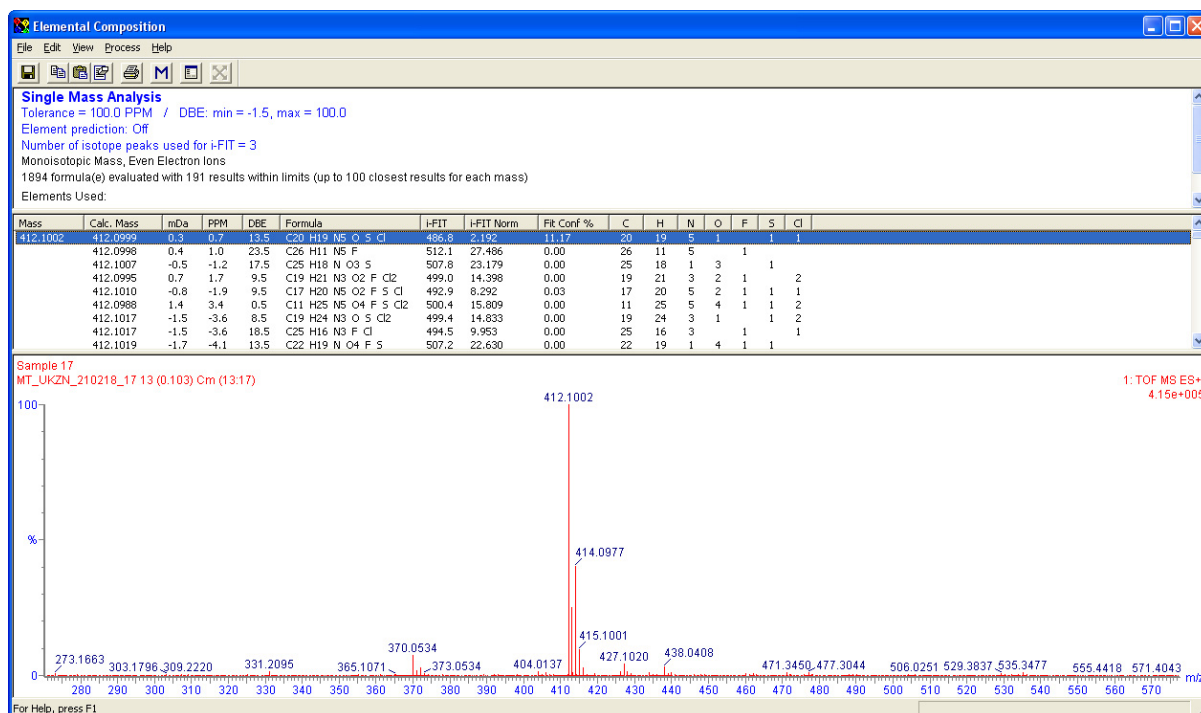
**Figure S33:** HRMS (ES<sup>+</sup>) for 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(6-methylbenzo[d]thiazol-2-yl)urea (**6k**).



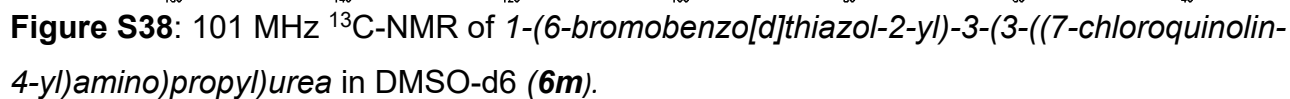
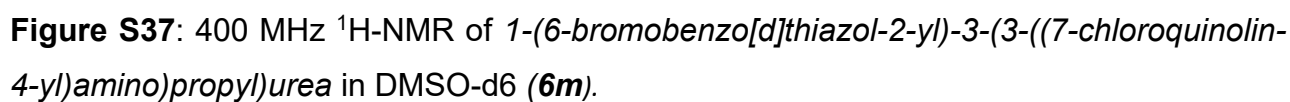
**Figure S34:** 400 MHz <sup>1</sup>H-NMR of 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(benzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6l**).

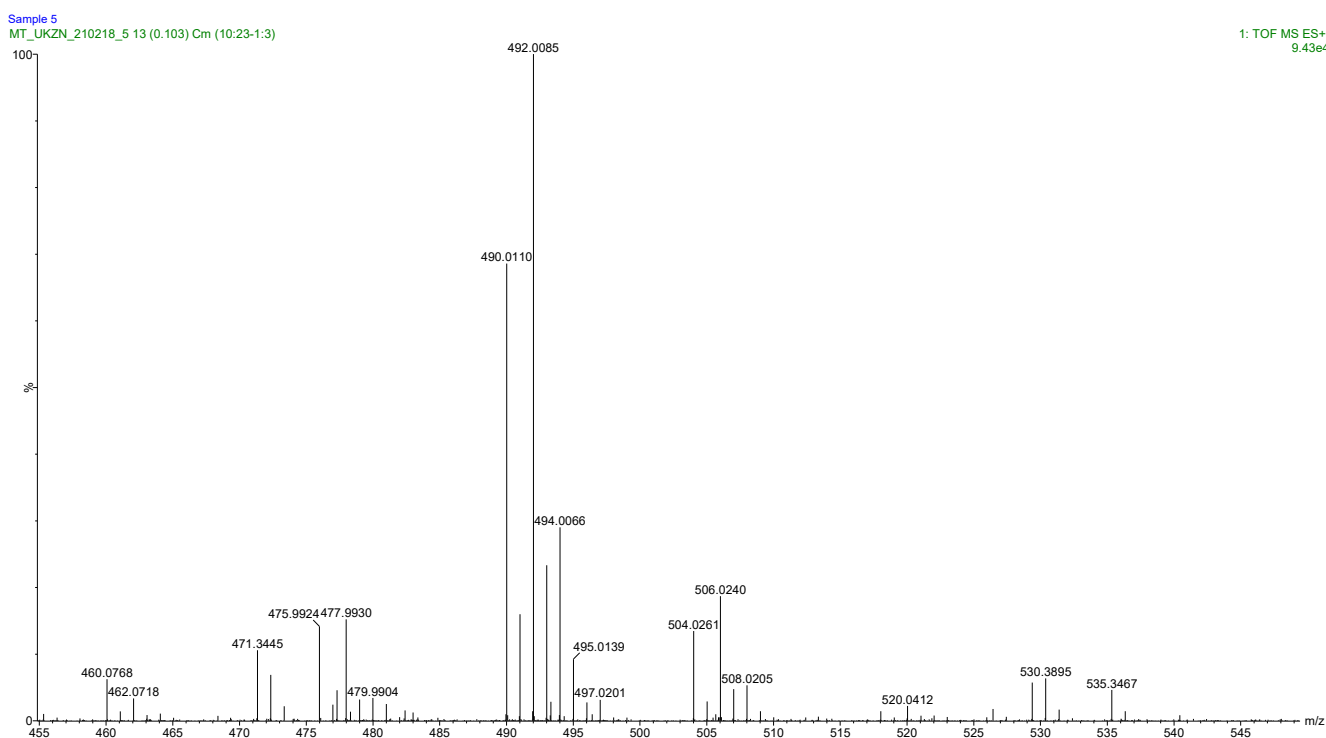
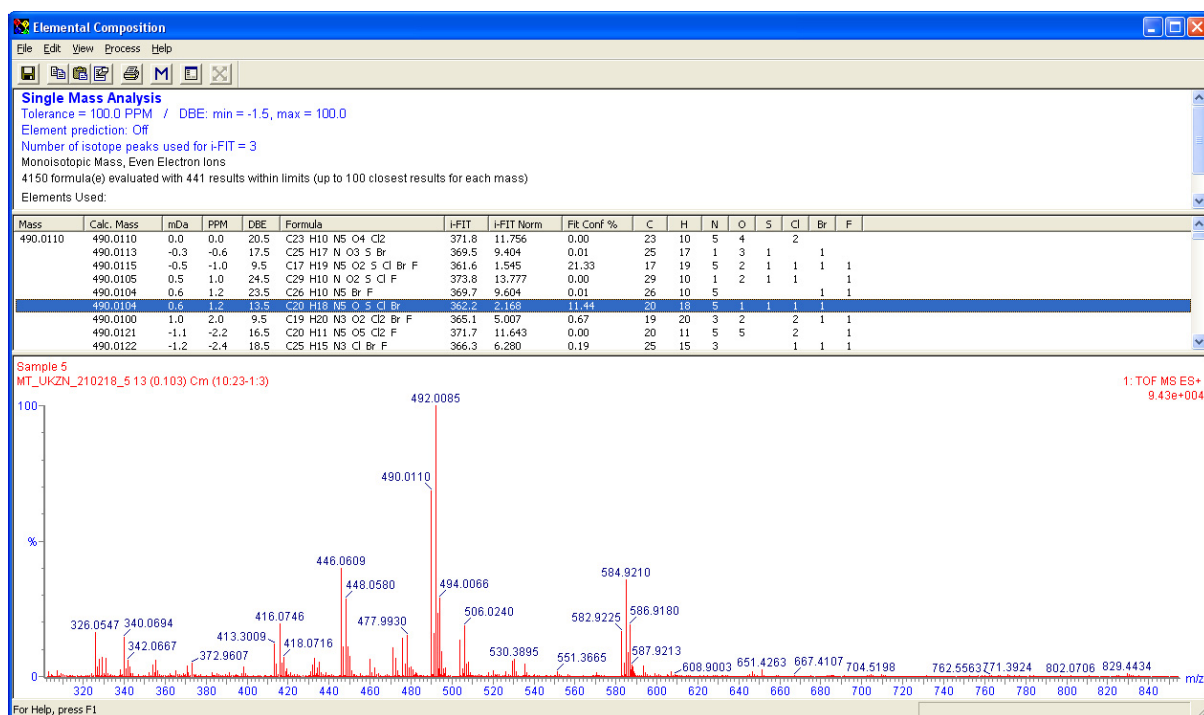


**Figure S35:** 101 MHz <sup>13</sup>C-NMR of 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(benzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6l**).

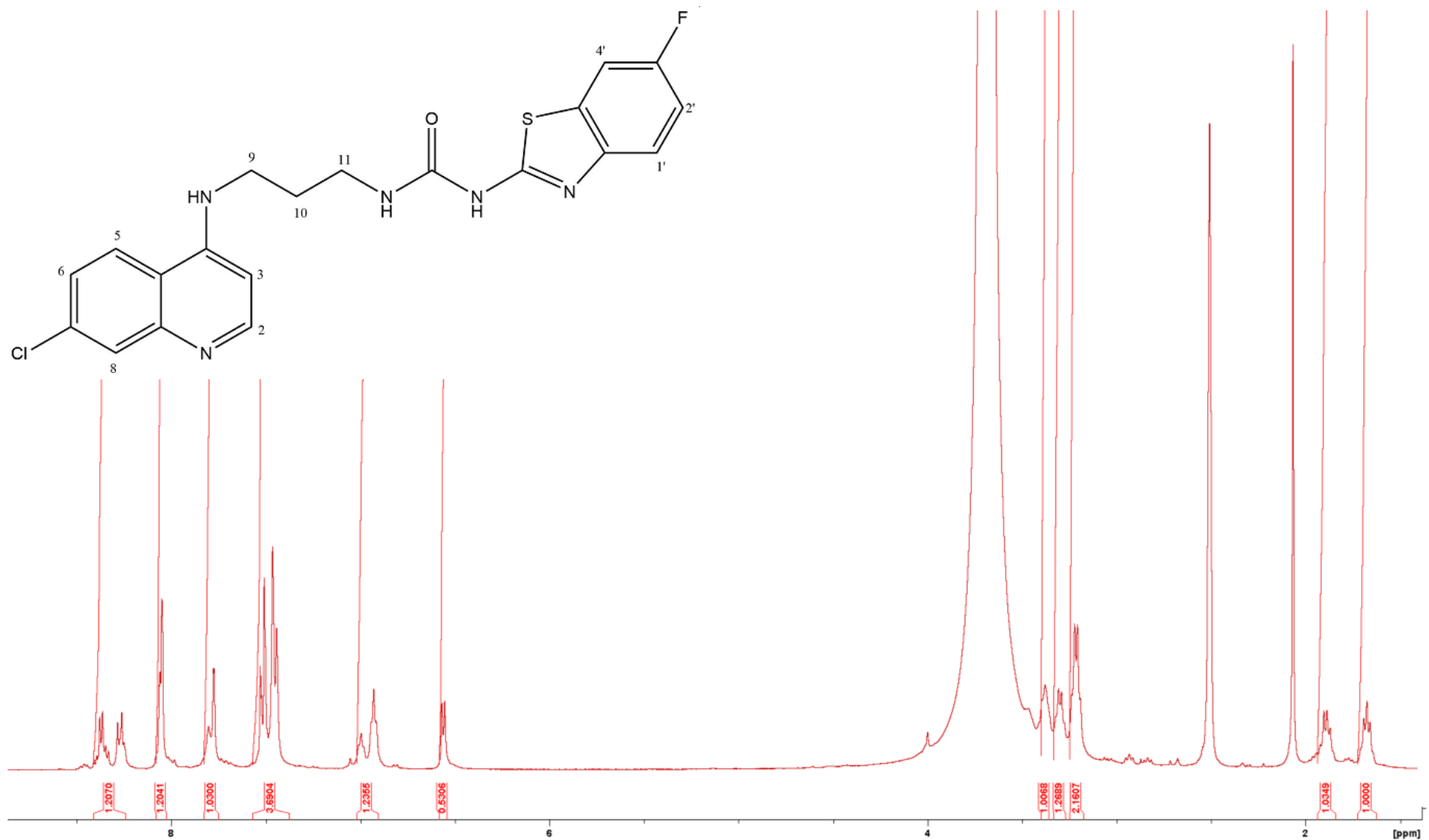


**Figure S36:** HRMS (ES<sup>+</sup>) for 1-(3-((7-chloroquinolin-4-yl)amino)propyl)-3-(benzo[d]thiazol-2-yl)urea (**6l**).



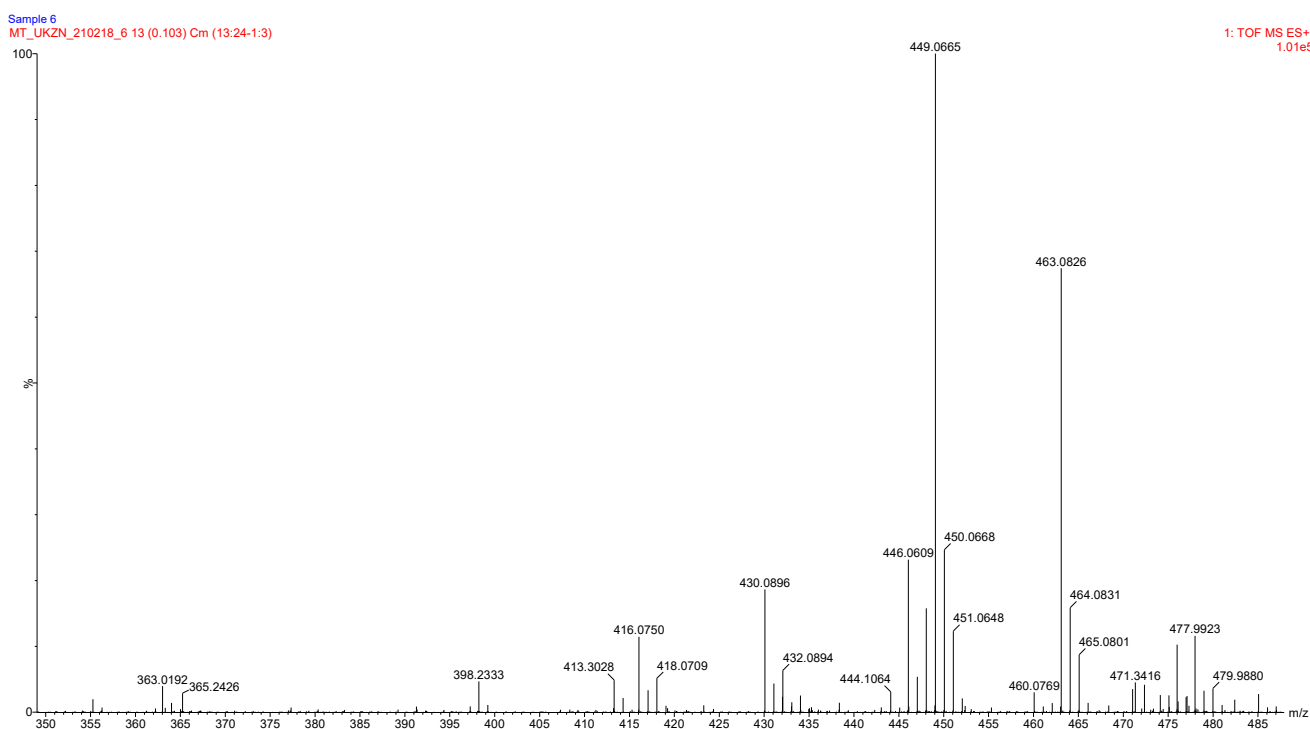
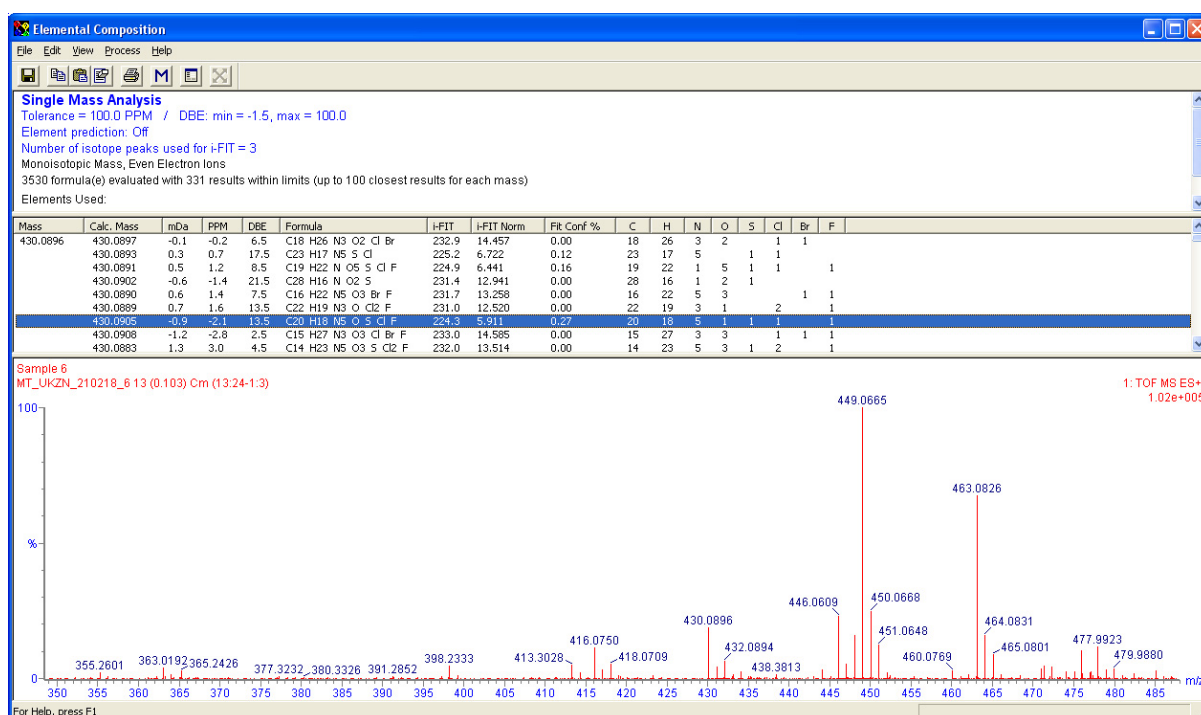


**Figure S39:** HRMS (ES<sup>+</sup>) for 1-(6-bromobenzo[d]thiazol-2-yl)-3-(3-((7-chloroquinolin-4-yl)amino)propyl)urea (**6m**).

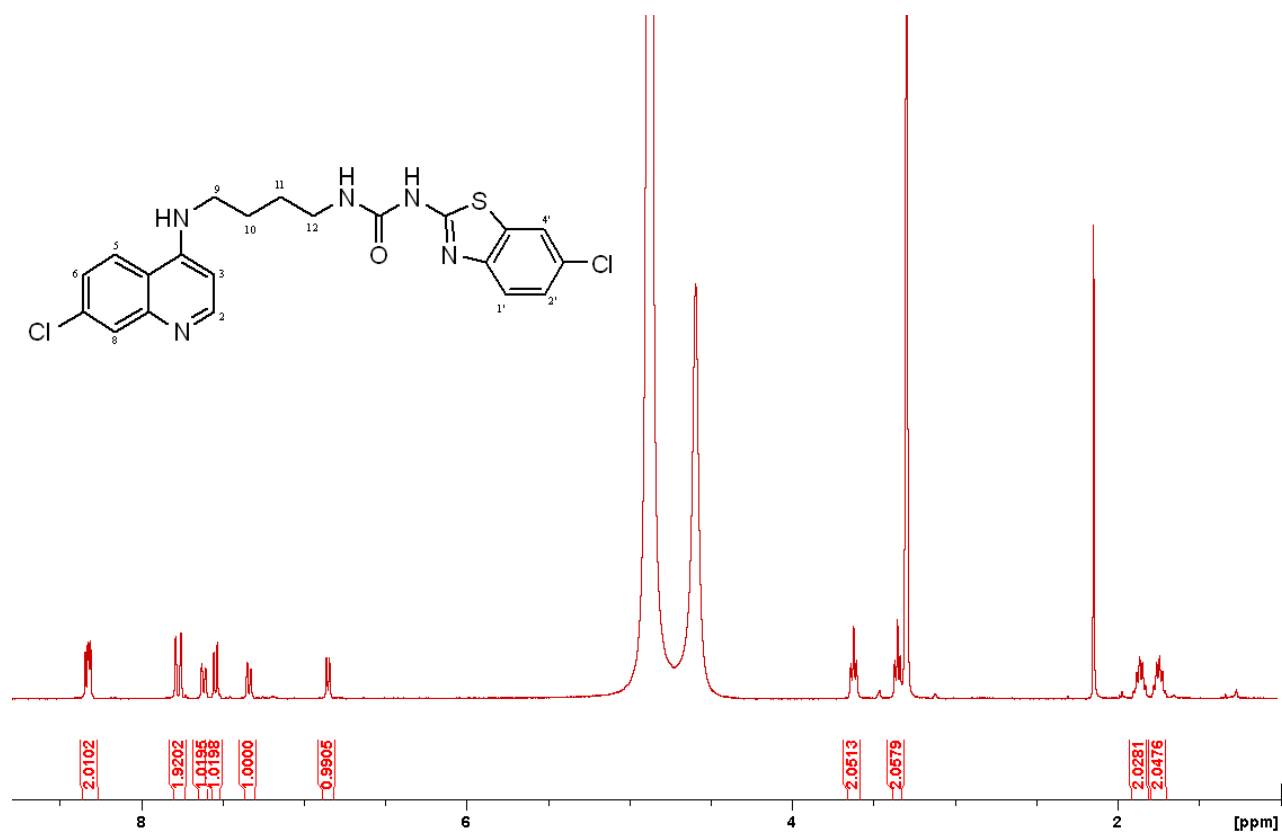


**Figure S40:** 400 MHz  $^1\text{H}$ -NMR of 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(3-((7-chloroquinolin-4-yl)amino)propyl)urea in  $\text{DMSO-d}_6$  (**6n**).

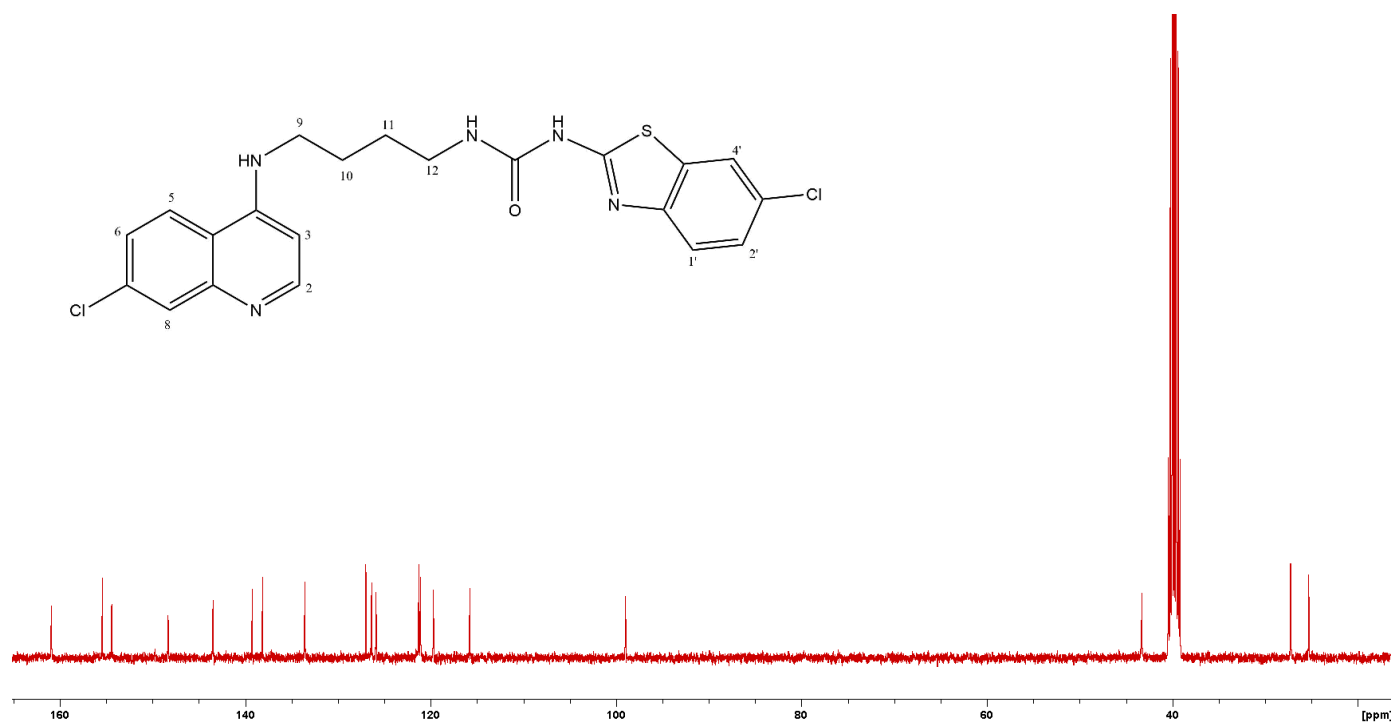




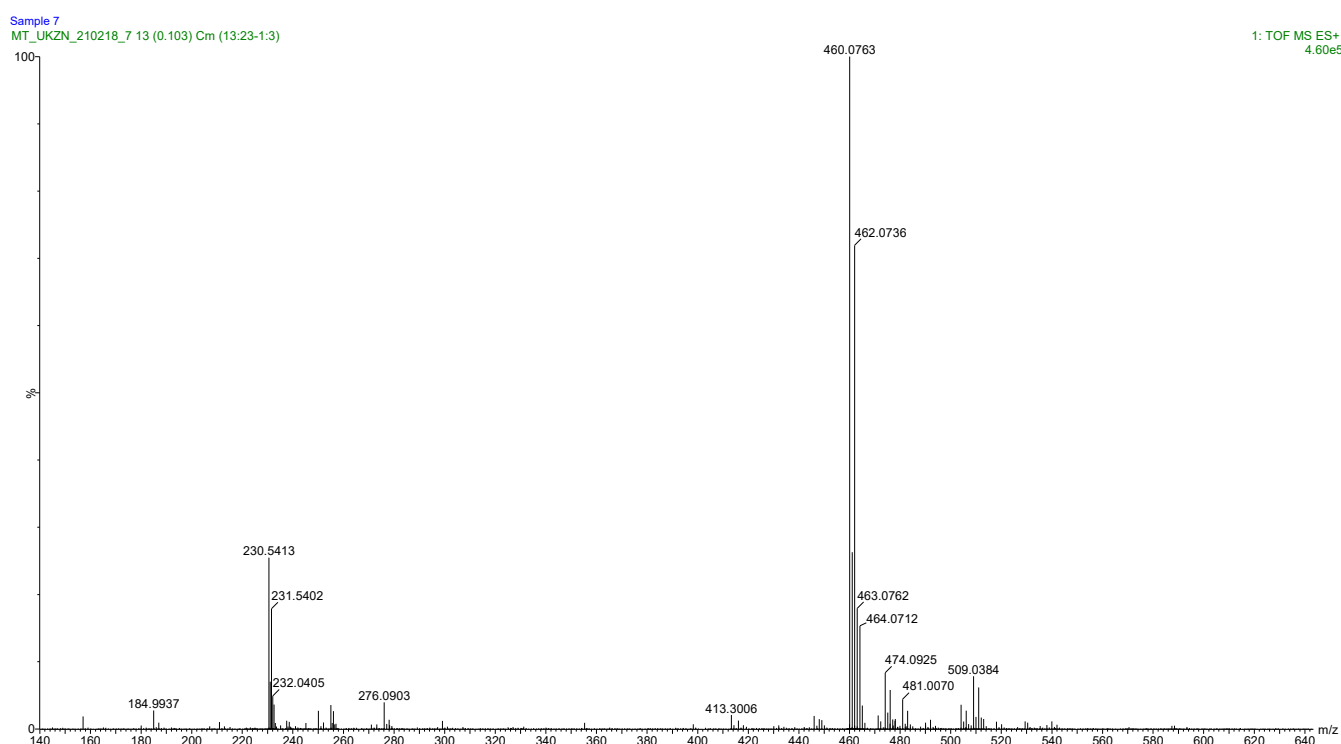
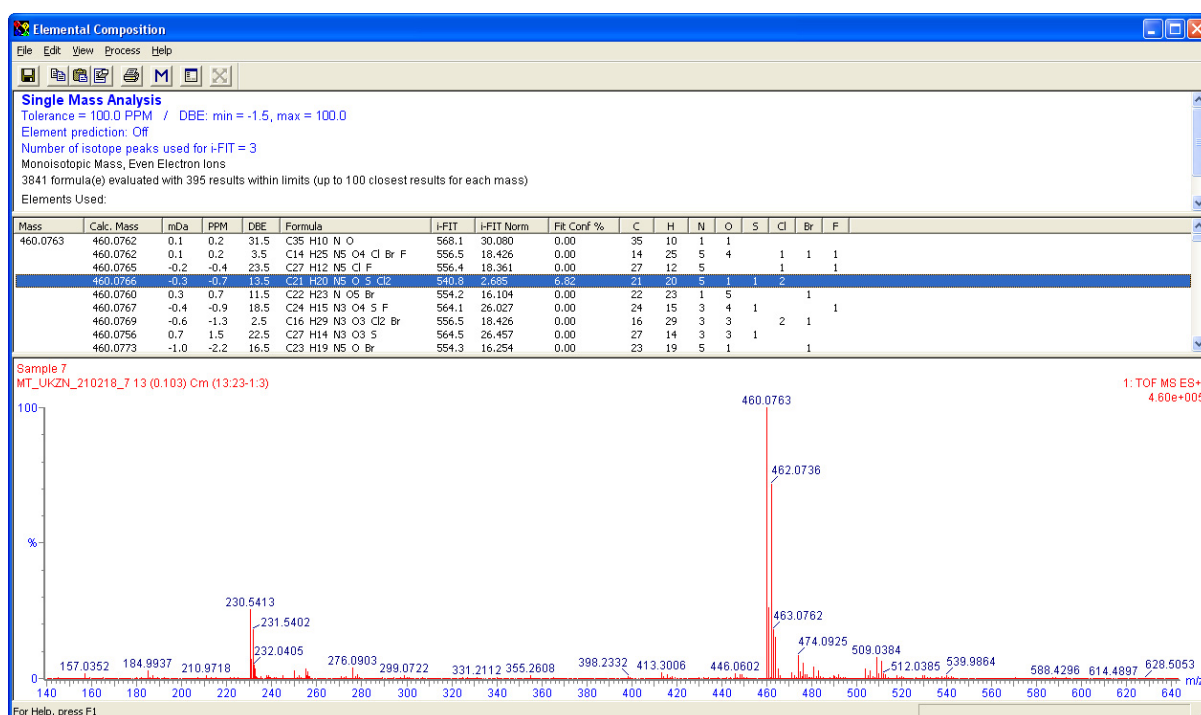
**Figure S41:** HRMS (ES+) for 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(3-((7-chloroquinolin-4-yl)amino)propyl)urea (**6n**).



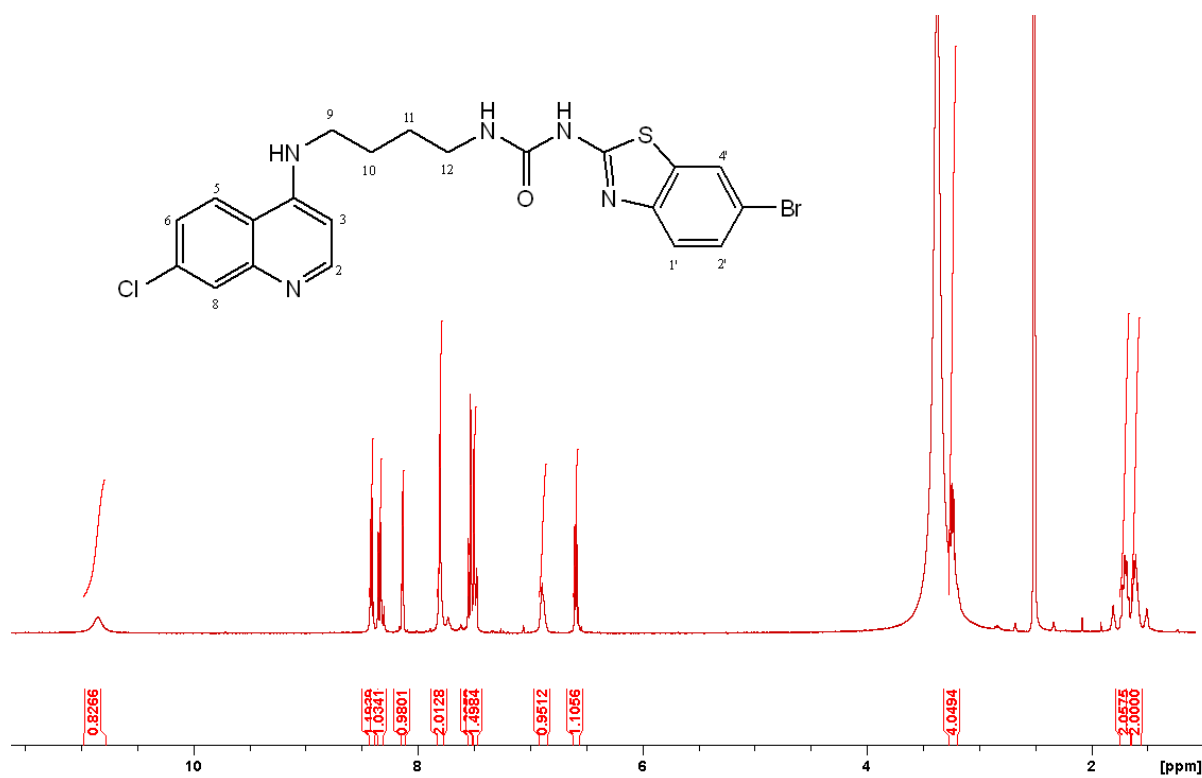
**Figure S42:** 400 MHz <sup>1</sup>H NMR for 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea in MeOH-d<sub>4</sub> (**6o**).



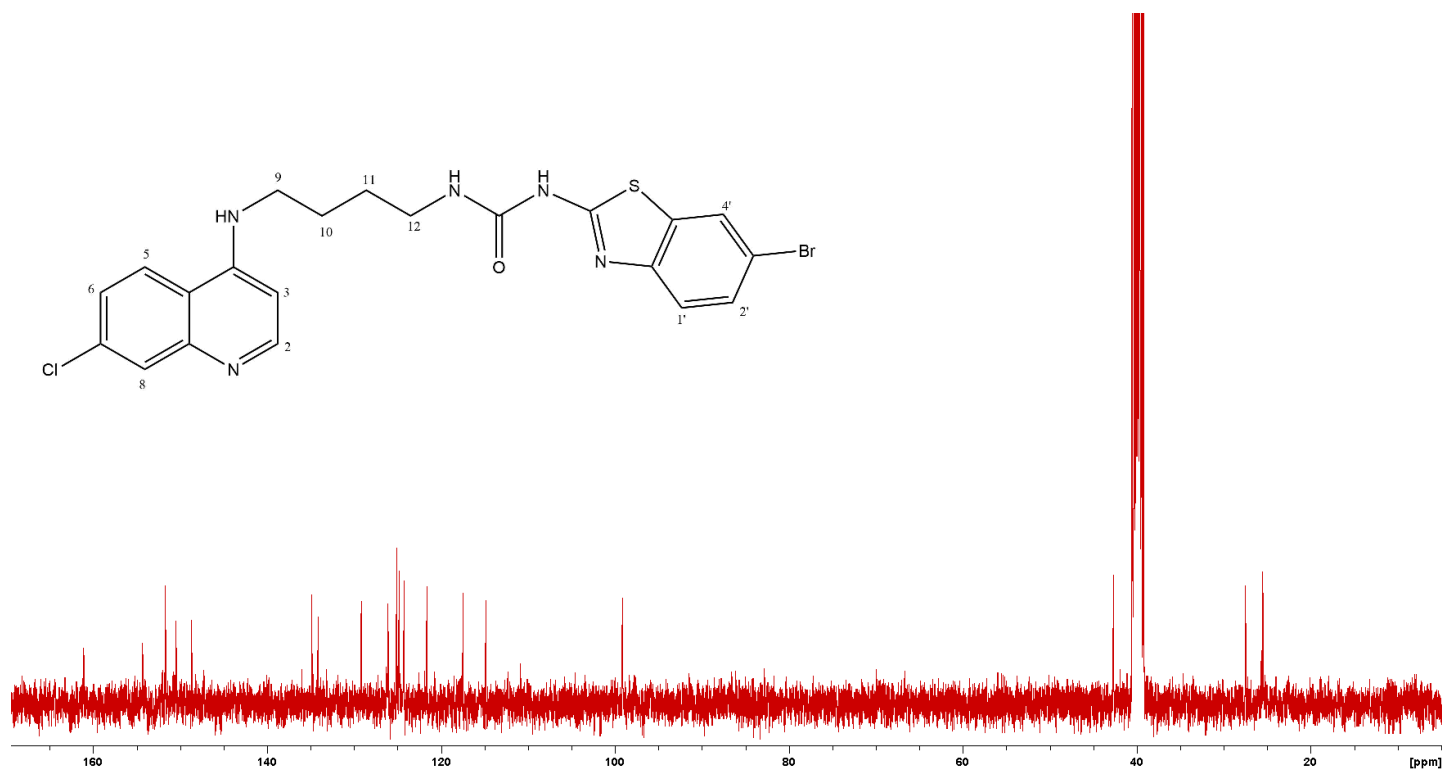
**Figure S43:** 101 MHz <sup>13</sup>C NMR for 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea in DMSO-d<sub>6</sub> (**6o**).



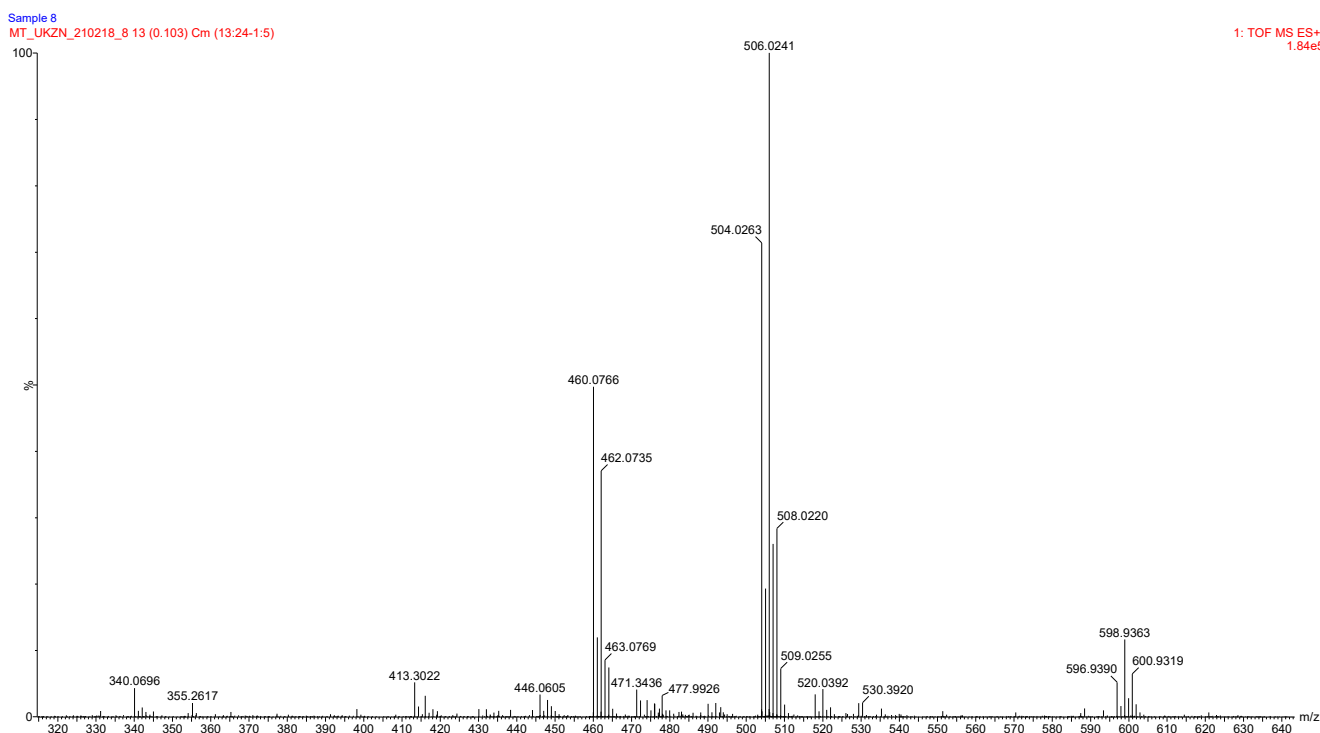
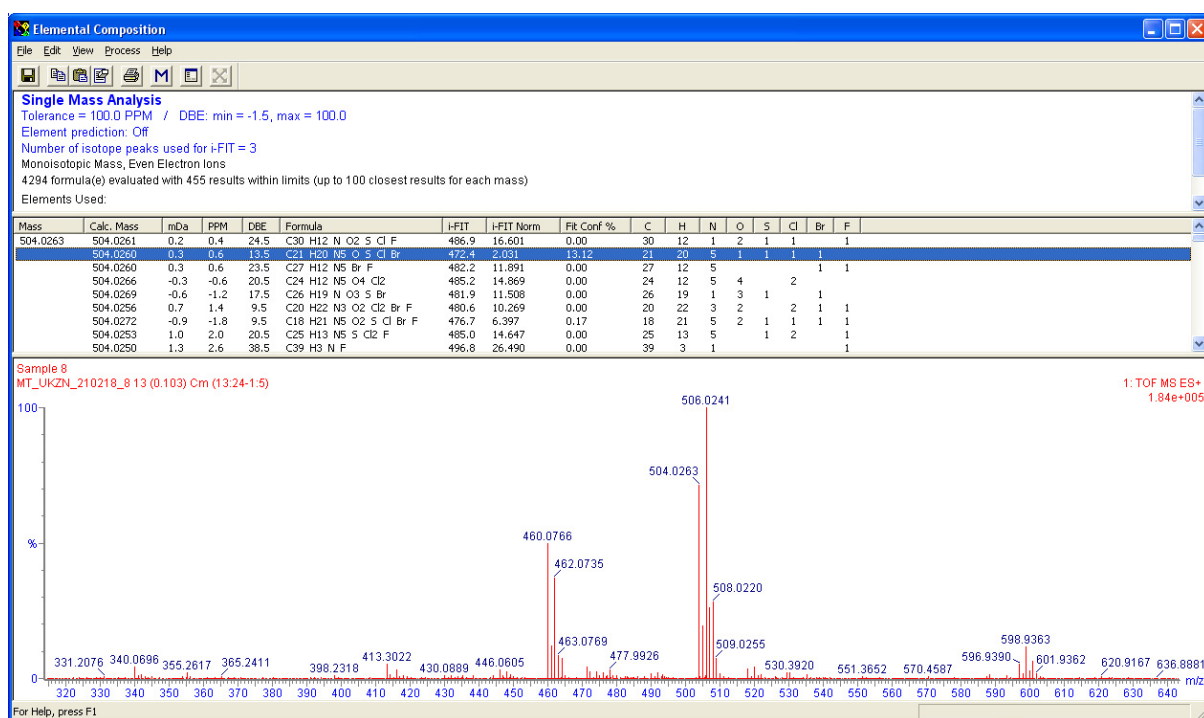
**Figure S44:** HRMS (ES+) for 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea (**60**).



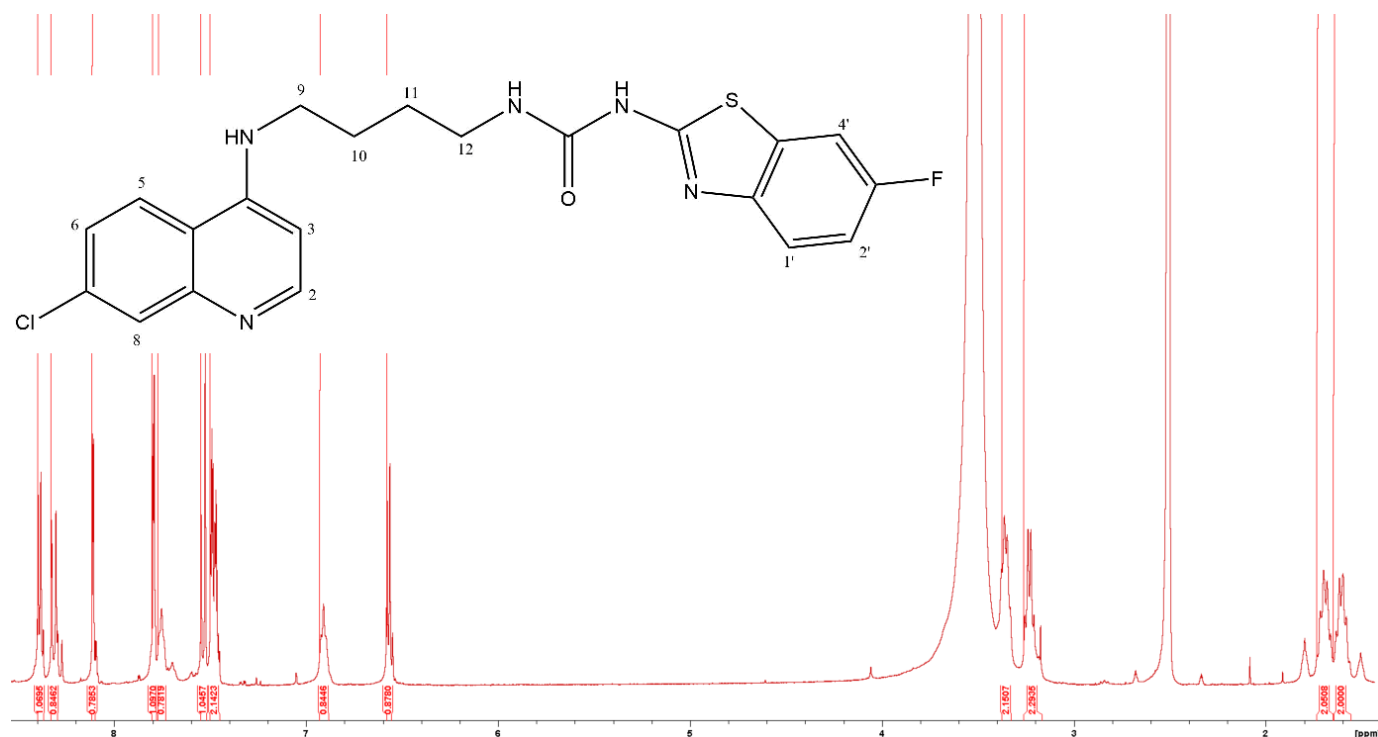
**Figure S45:** 400 MHz  $^1\text{H}$  NMR for 1-(6-bromobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea in DMSO- $d_6$  (**6p**).



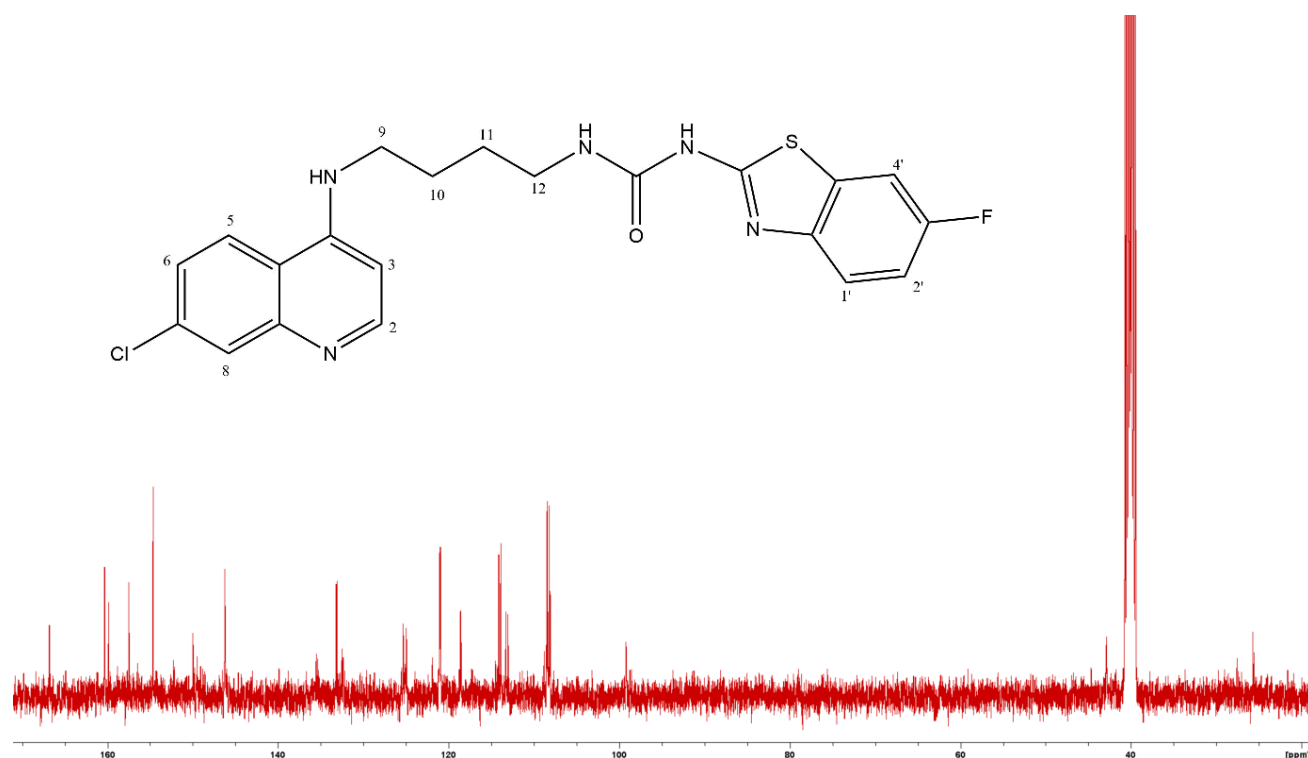
**Figure S46:** 101 MHz  $^{13}\text{C}$  NMR for 1-(6-bromobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea in DMSO- $d_6$  (**6p**).



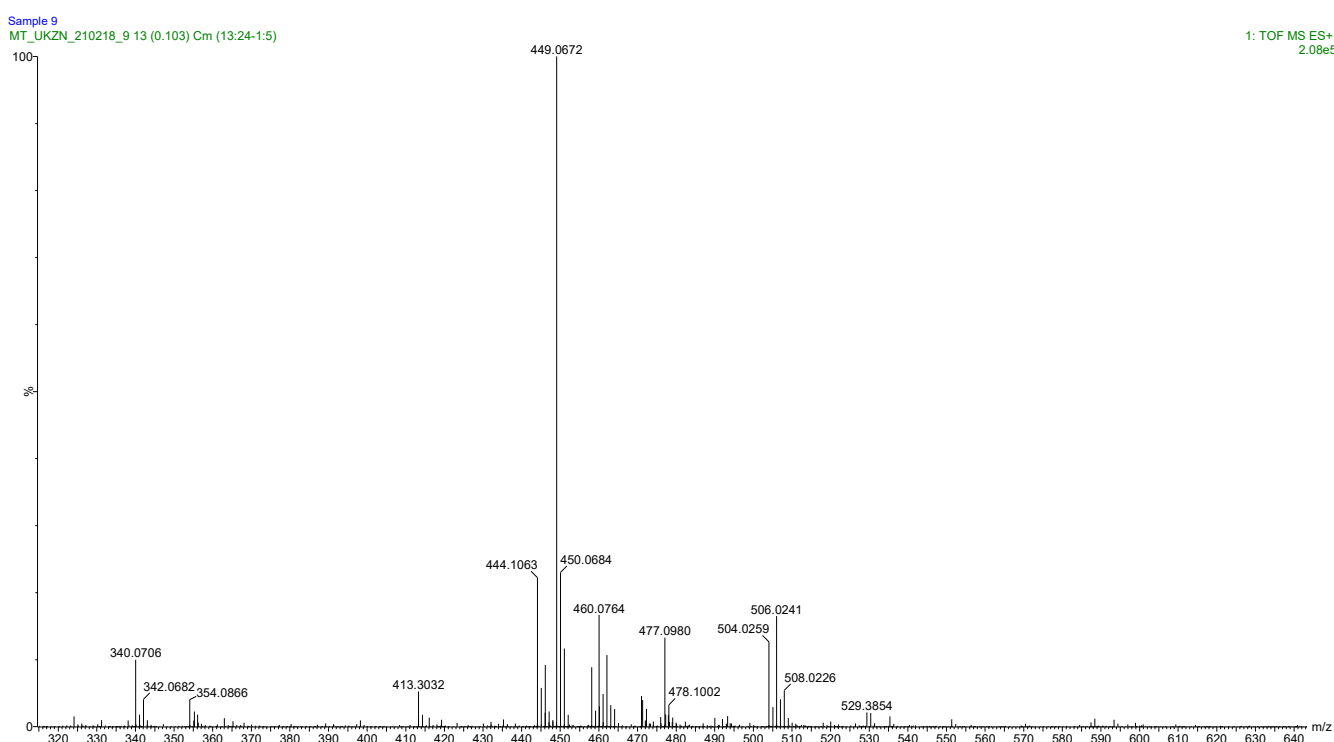
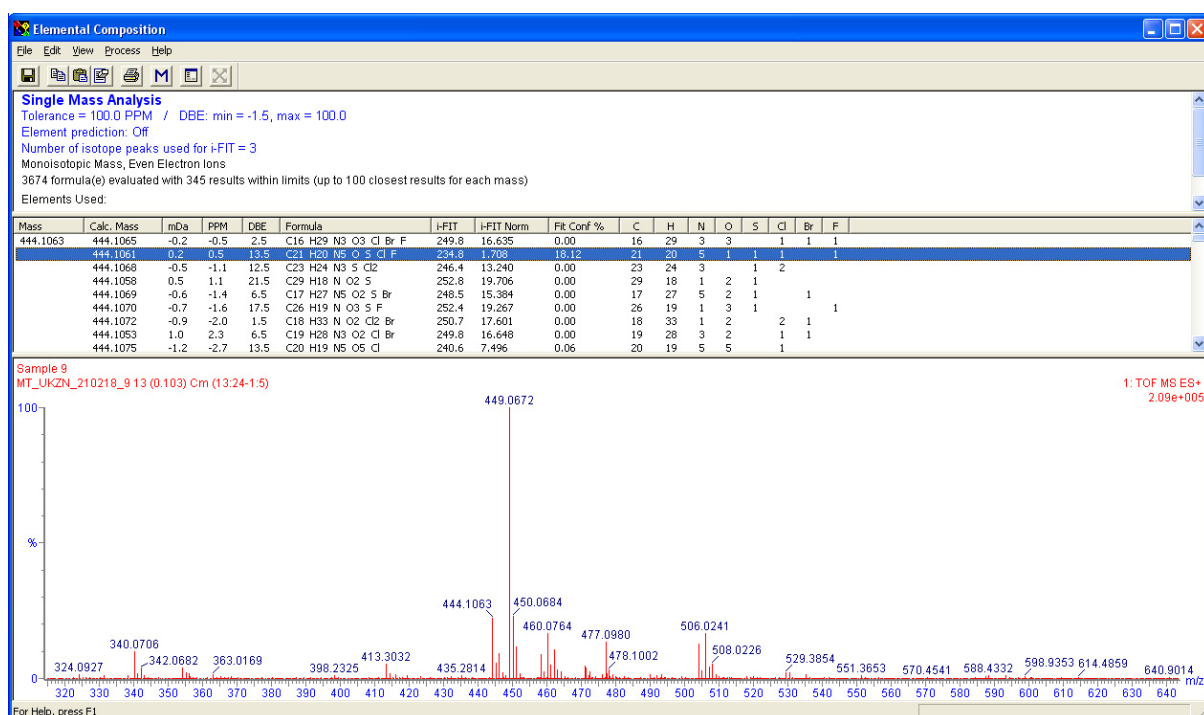
**Figure S47:** HRMS (ES+) for 1-(6-bromobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea (**6p**).



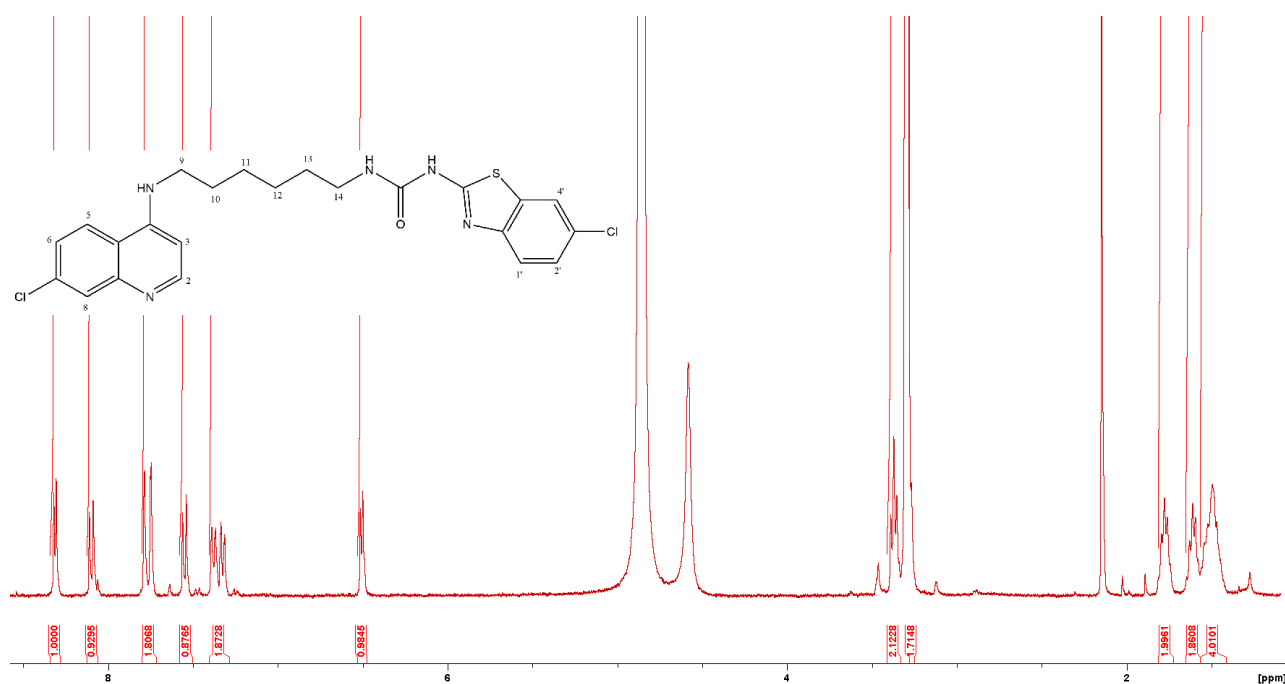
**Figure S48:** 400 MHz  $^1\text{H}$  NMR for 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea in DMSO- $\text{d}_6$  (**6q**).



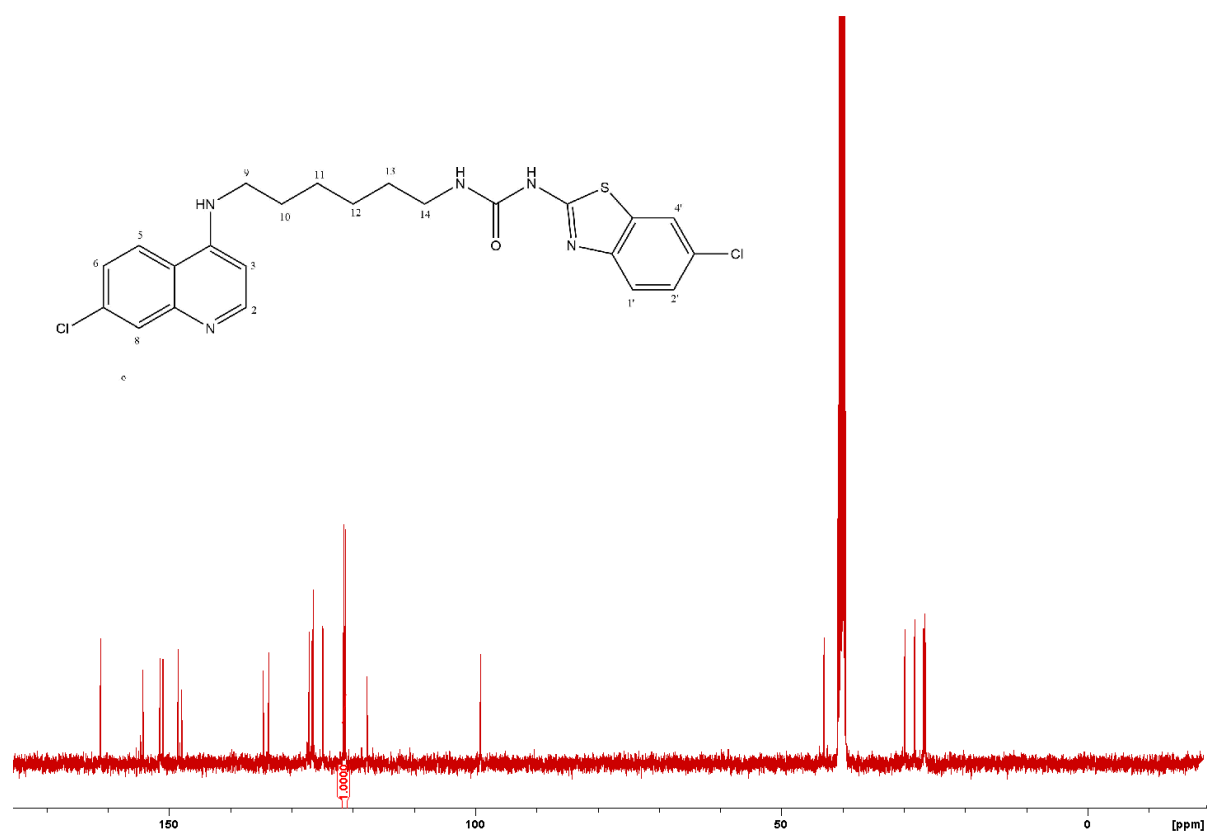
**Figure S49:** 101 MHz  $^{13}\text{C}$  NMR for 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea in DMSO- $\text{d}_6$  (**6q**).



**Figure S50:** HRMS (ES+) for 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(4-((7-chloroquinolin-4-yl)amino)butyl)urea (**6q**).

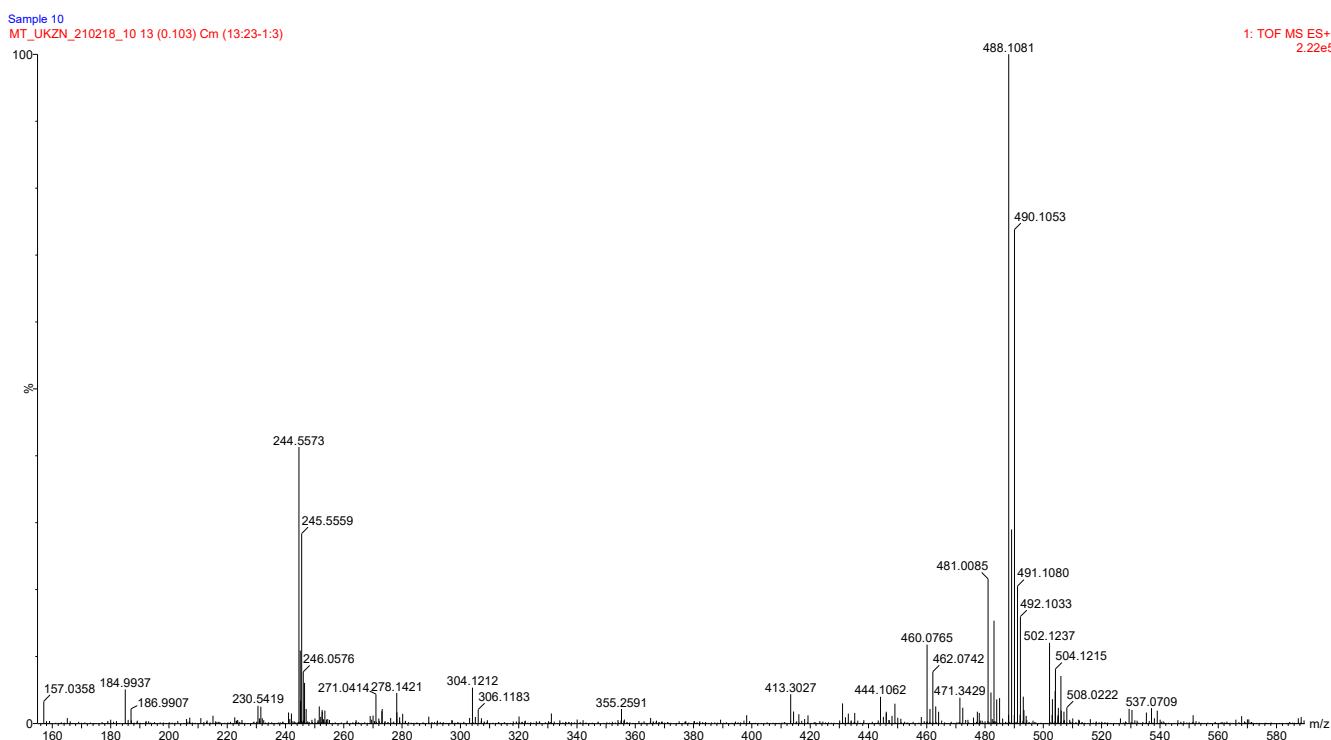
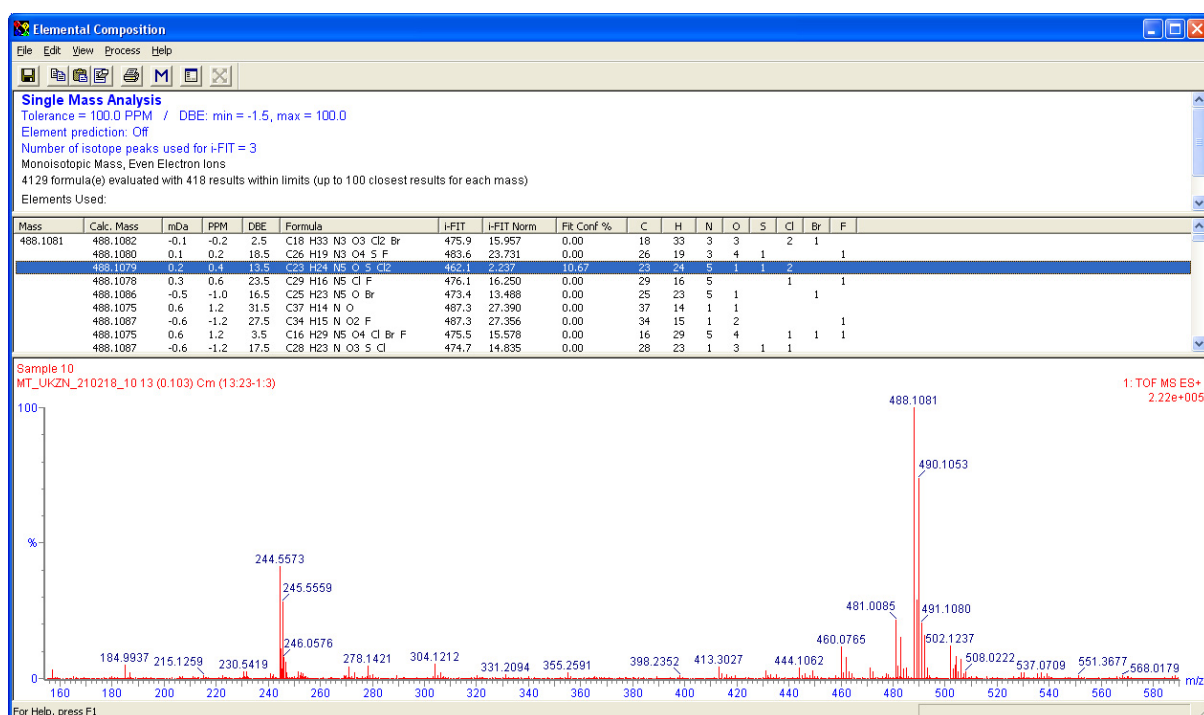


**Figure S51:** 400 MHz <sup>1</sup>H-NMR of 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea in MeOH-d<sub>4</sub> (6r).

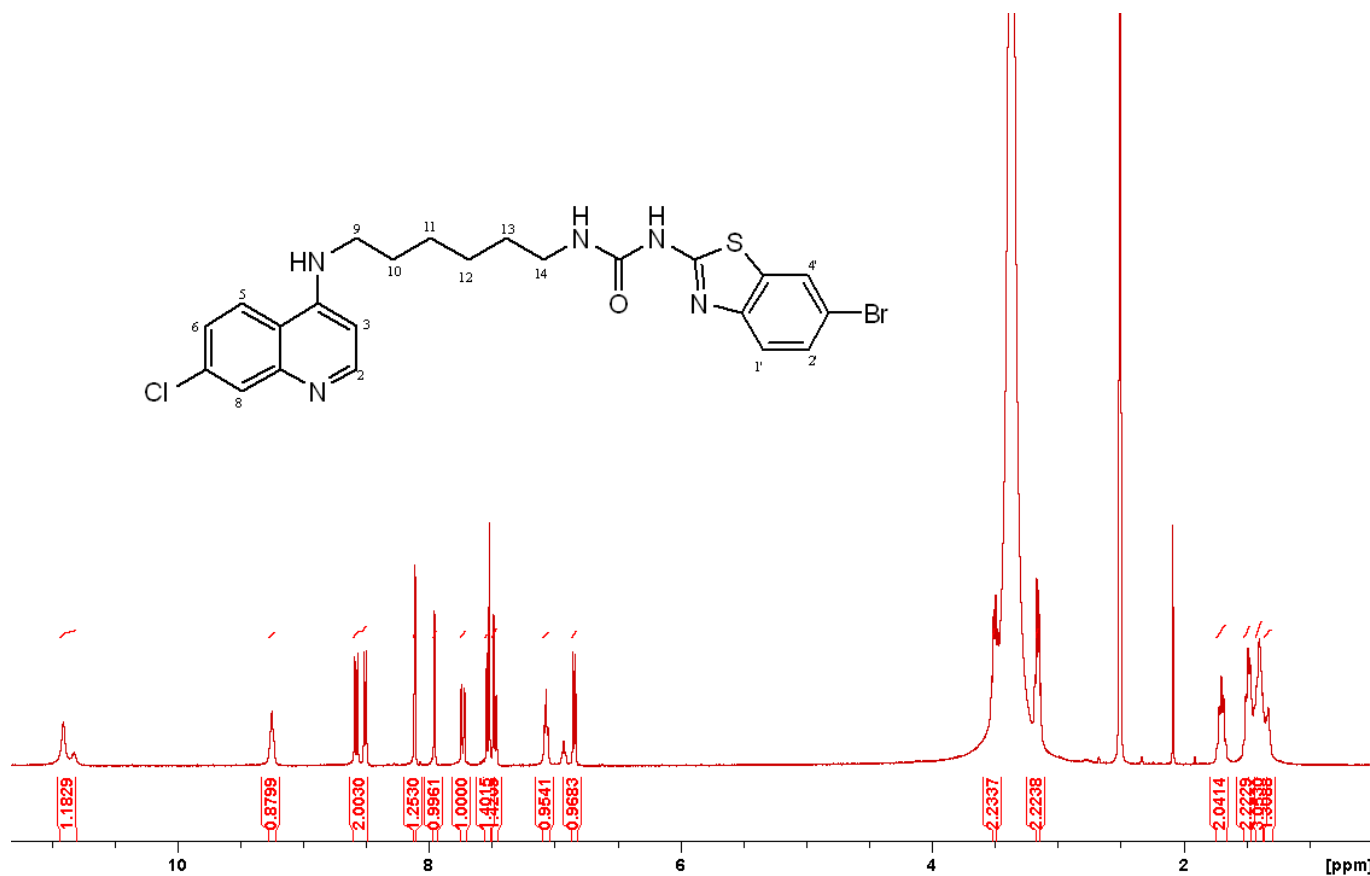


**Figure S52:** 101 MHz <sup>13</sup>C-NMR of 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea in DMSO-d<sub>6</sub> (6r).

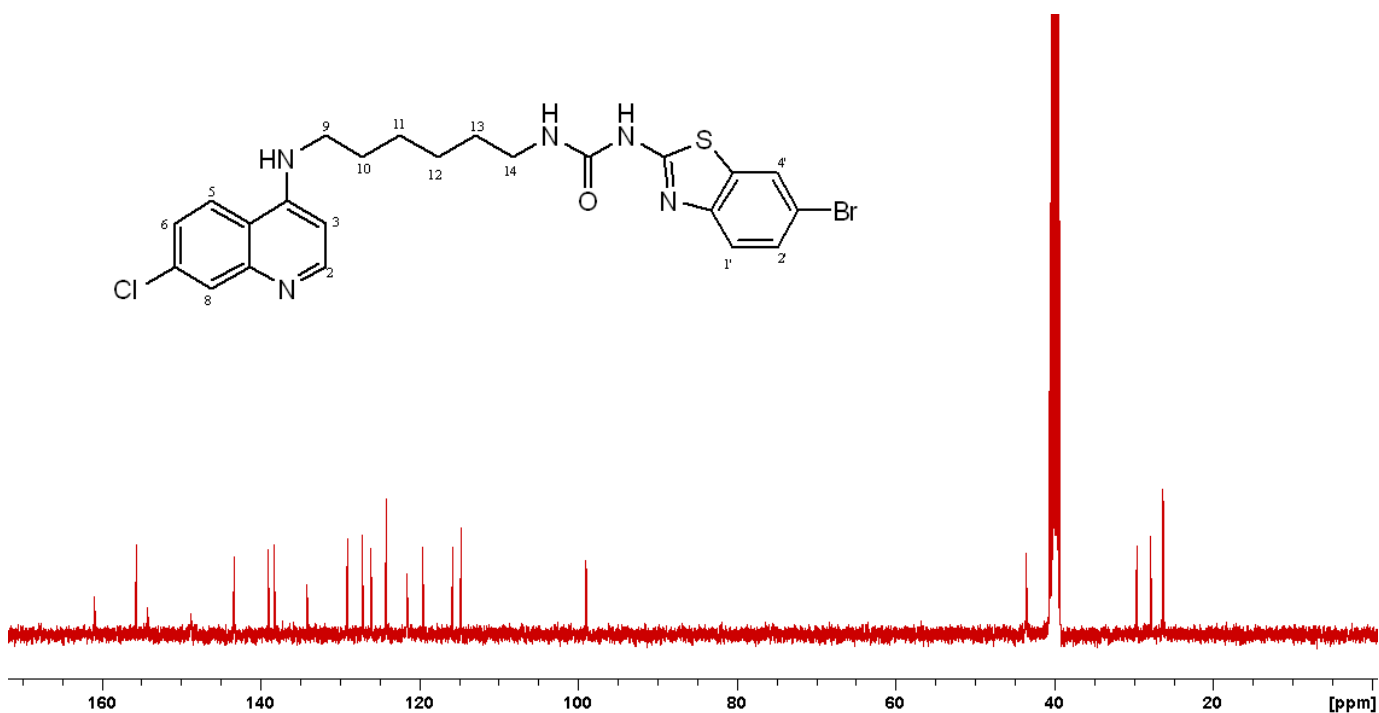




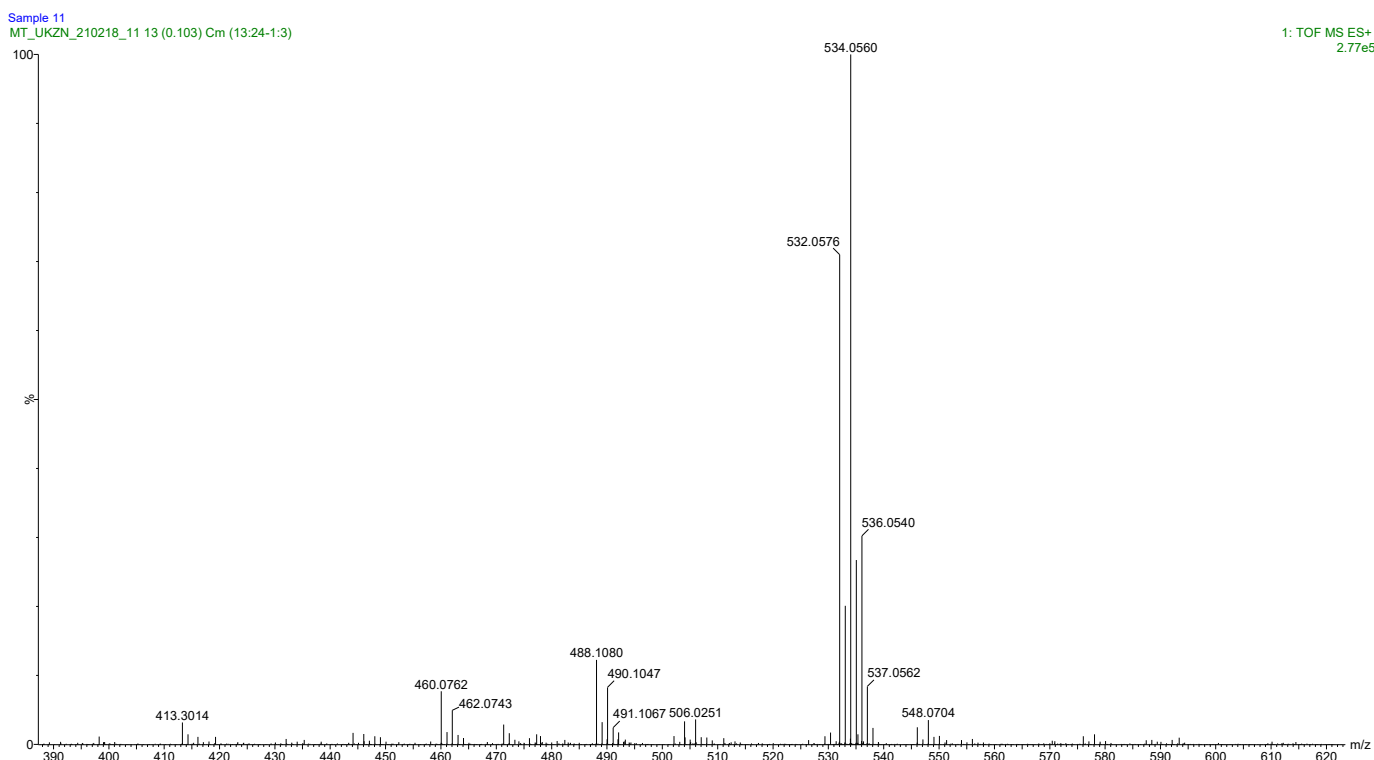
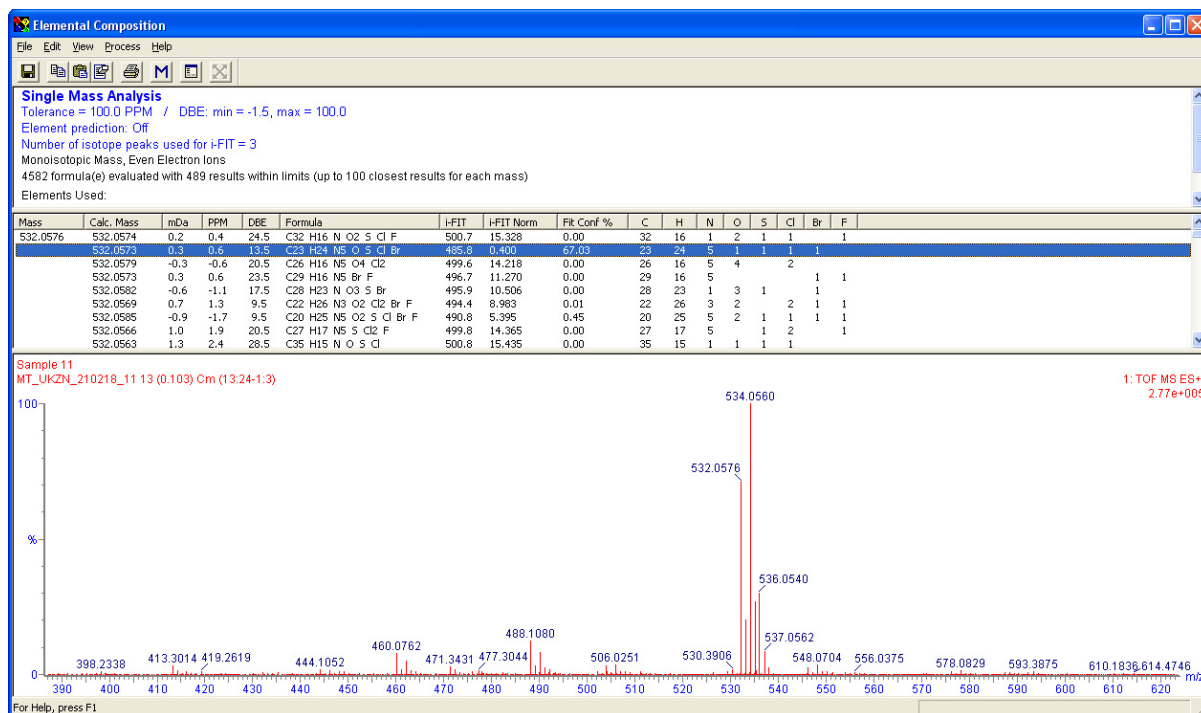
**Figure S53:** HRMS (ES+) for 1-(6-chlorobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea (**6r**).



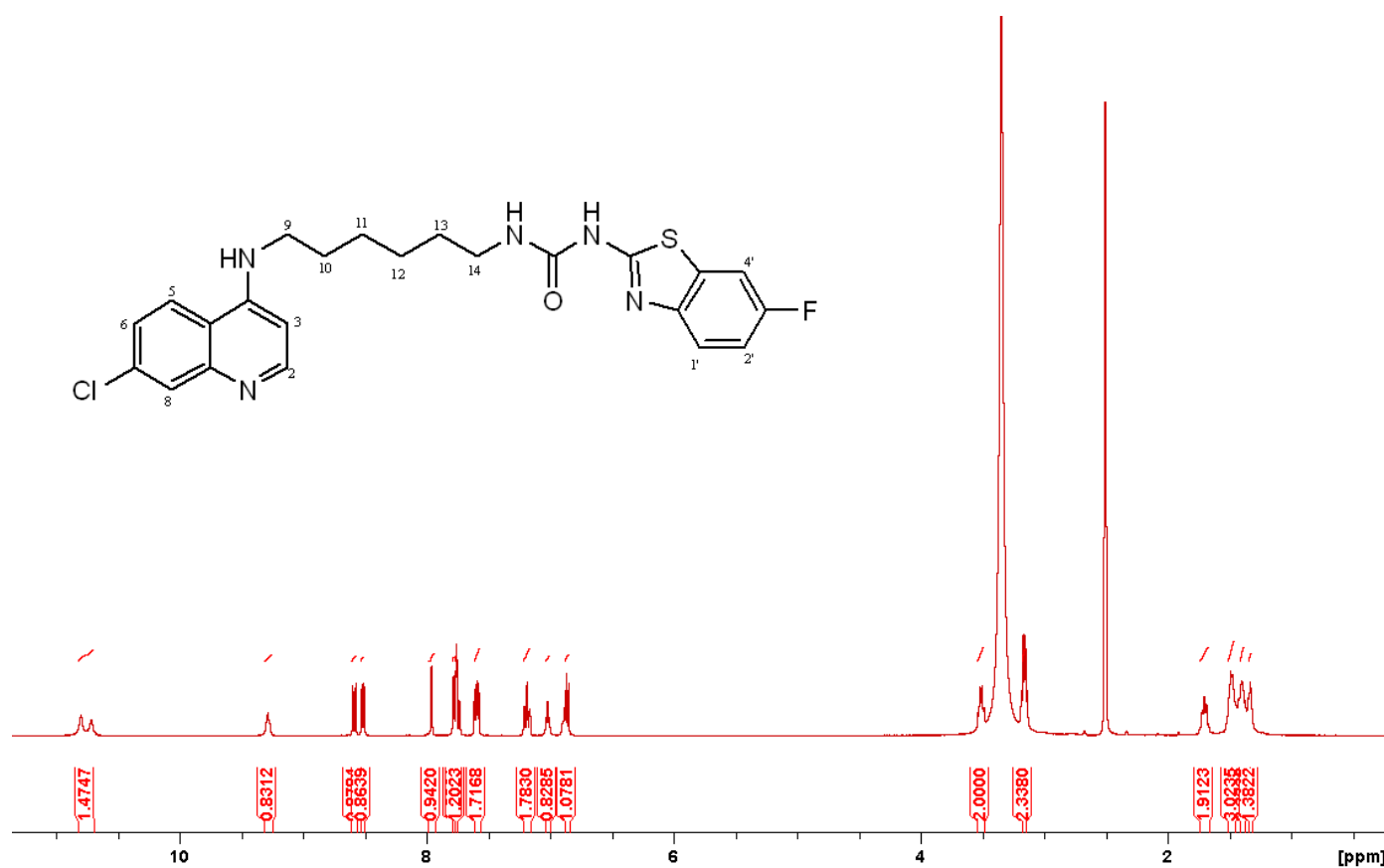
**Figure S54:** 400 MHz  $^1\text{H}$ -NMR of 1-(6-bromobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea in  $\text{DMSO}-d_6$  (6s).



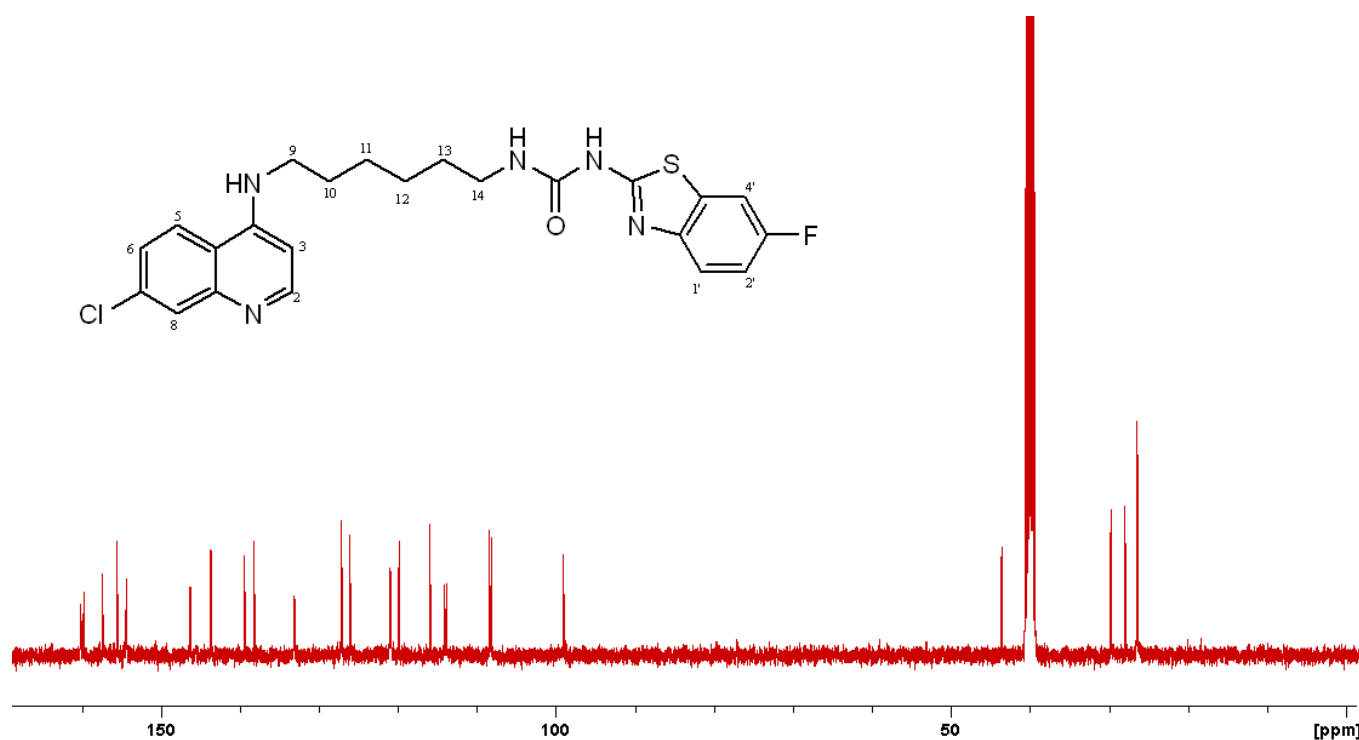
**Figure S55:** 101 MHz  $^{13}\text{C}$ -NMR of 1-(6-bromobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea (6s).



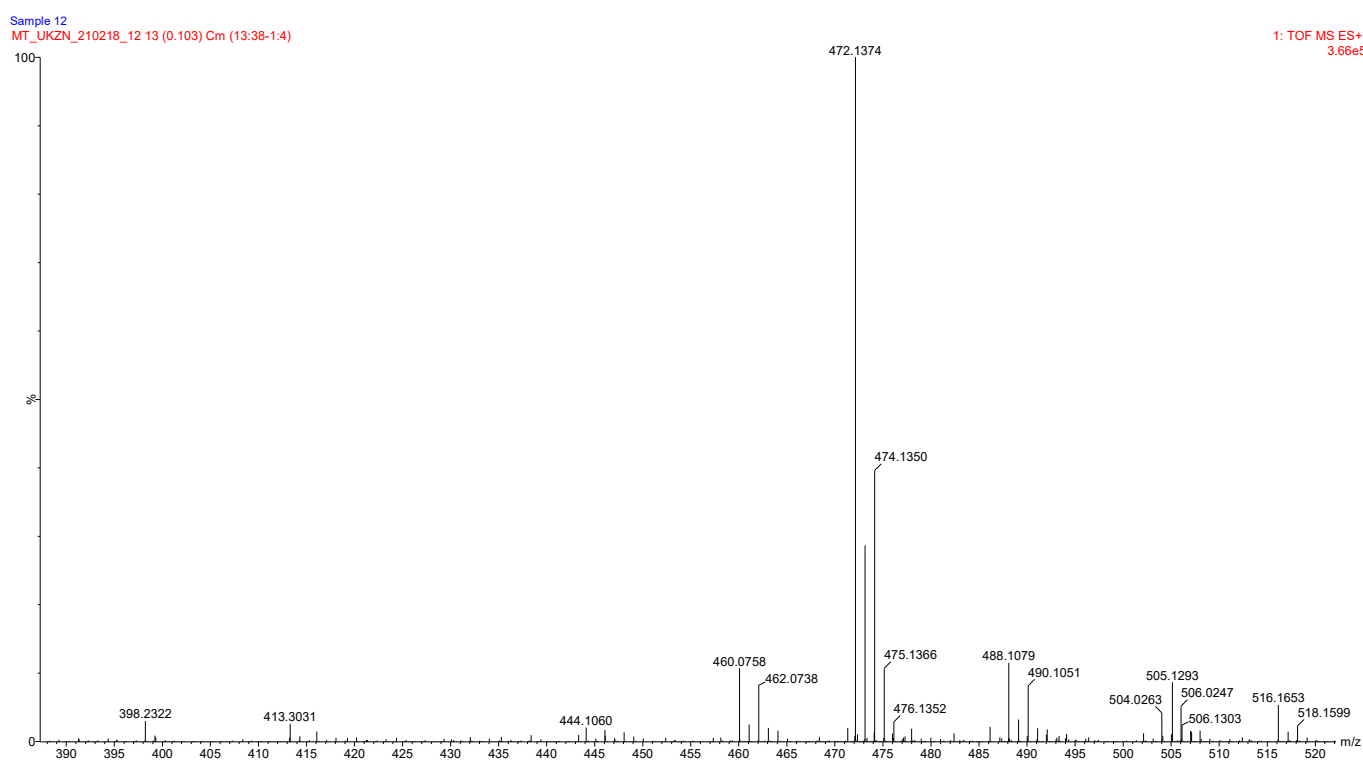
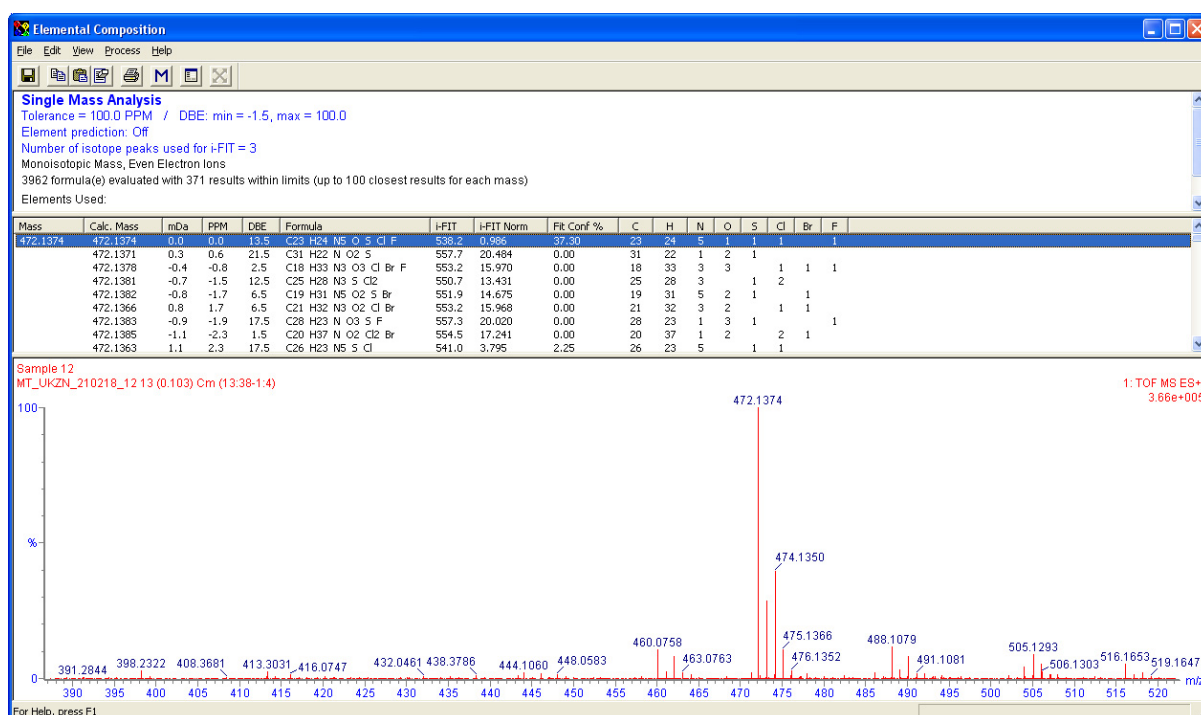
**Figure S56:** HRMS (ES<sup>+</sup>) for 1-(6-bromobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea (**6s**).



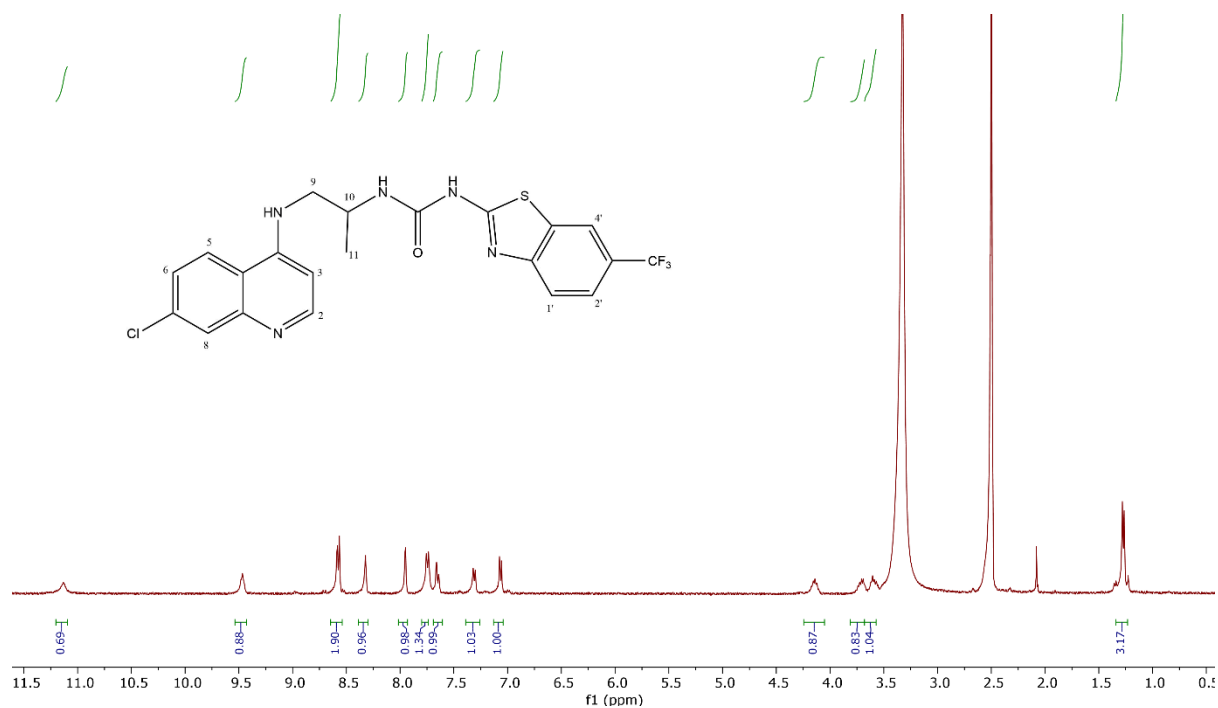
**Figure S57:** 400 MHz <sup>1</sup>H-NMR of 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea in DMSO-d<sub>6</sub> (**6t**).



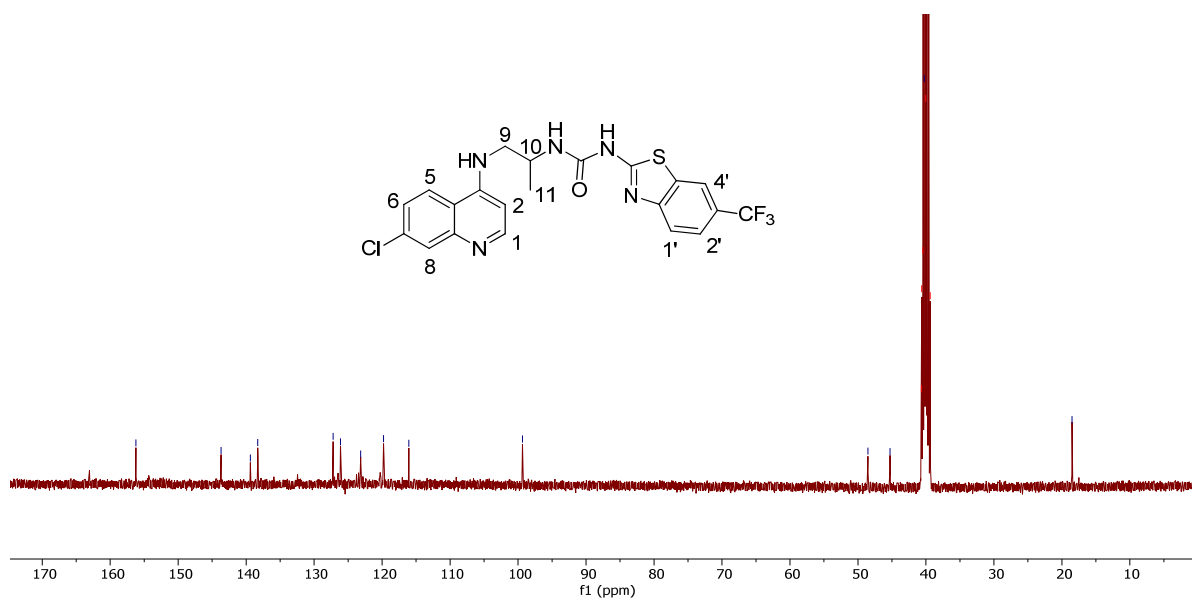
**Figure S58:** 101 MHz <sup>13</sup>C-NMR of 1-(6-fluorobenzo[d]thiazol-2-yl)-3-(6-((7-chloroquinolin-4-yl)amino)hexyl)urea in DMSO-d<sub>6</sub> (**6t**).



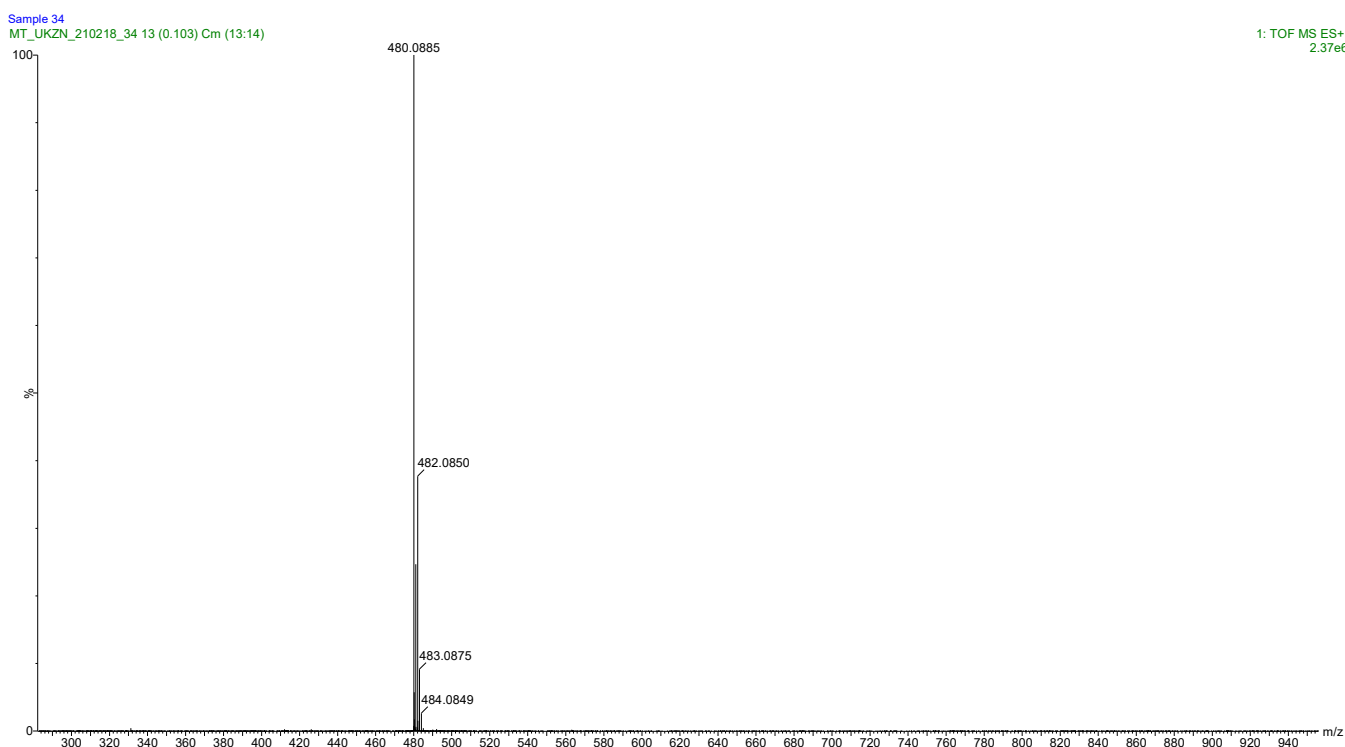
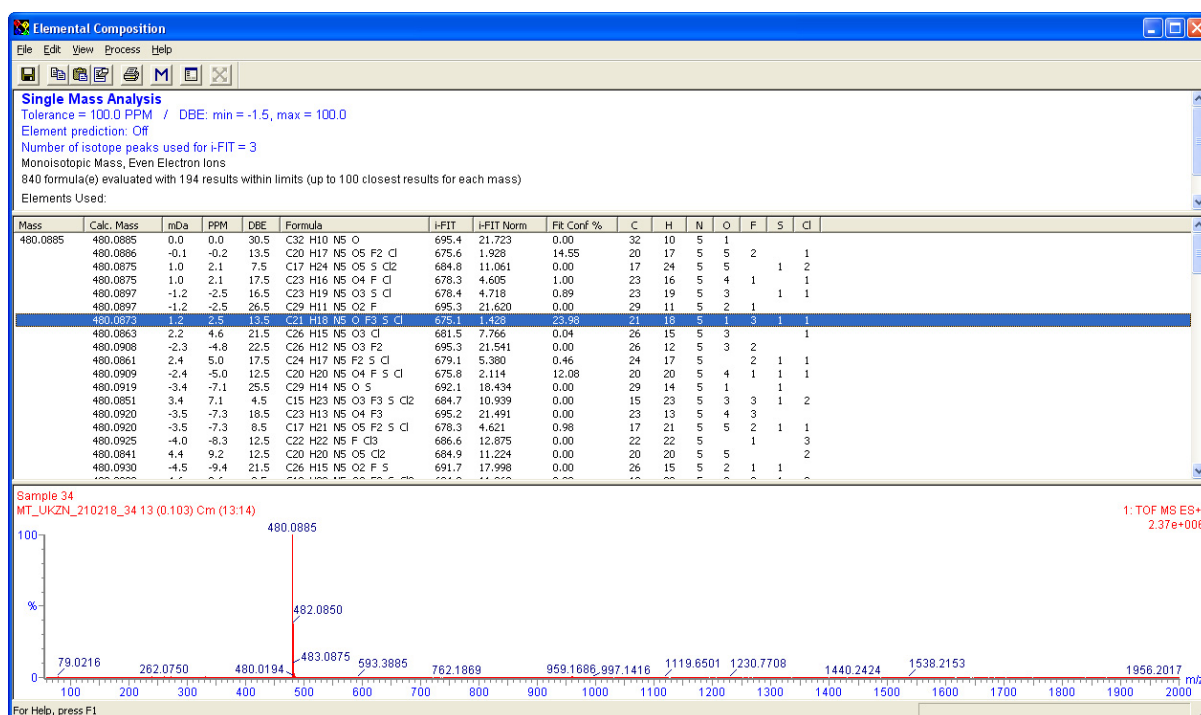
**Figure S59:** HRMS (ES<sup>+</sup>) for 1-(6-((7-chloroquinolin-4-yl)amino)hexyl)-3-(6-fluorobenzo[d]thiazol-2-yl)urea (**6t**).



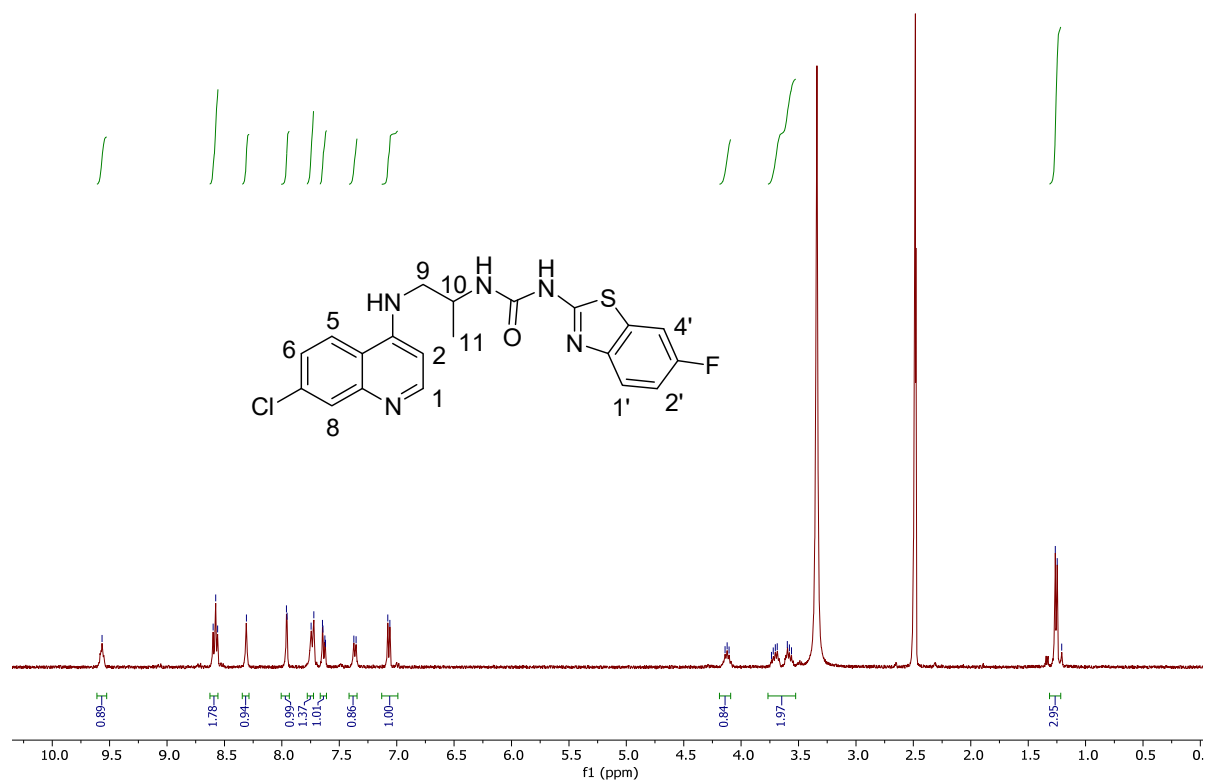
**Figure S60:** 400 MHz <sup>1</sup>H-NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6u**).



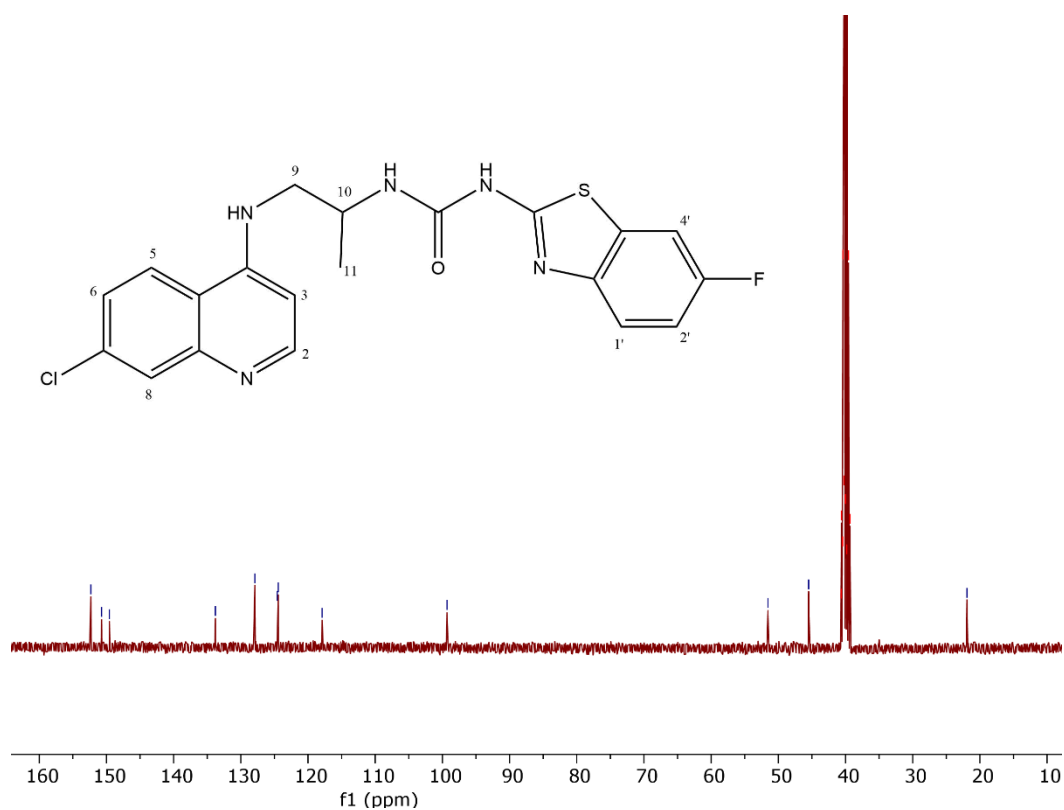
**Figure S61:** 101 MHz <sup>13</sup>C-NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6u**).



**Figure S62:** HRMS (ES<sup>+</sup>) for 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-(trifluoromethyl)benzo[d]thiazol-2-yl)urea (**6u**).

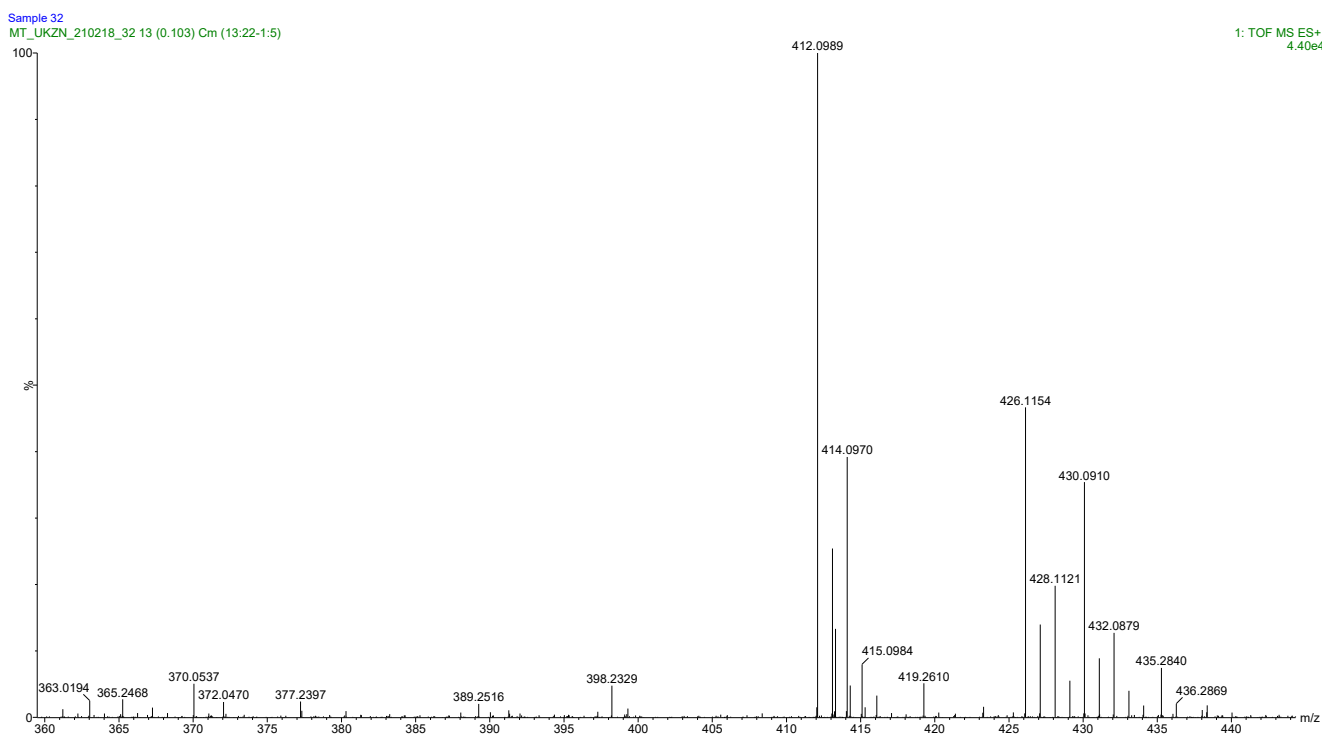
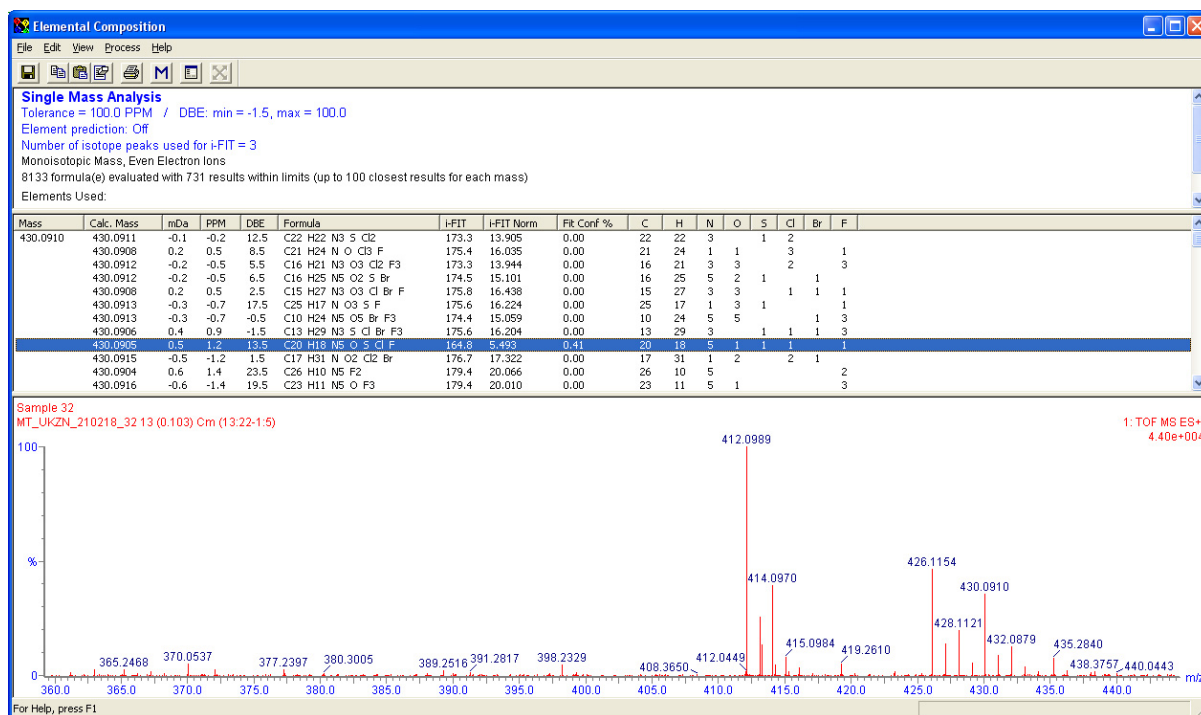


**Figure S63:** 400 MHz  $^1\text{H}$ -NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-fluorobenzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6v**).

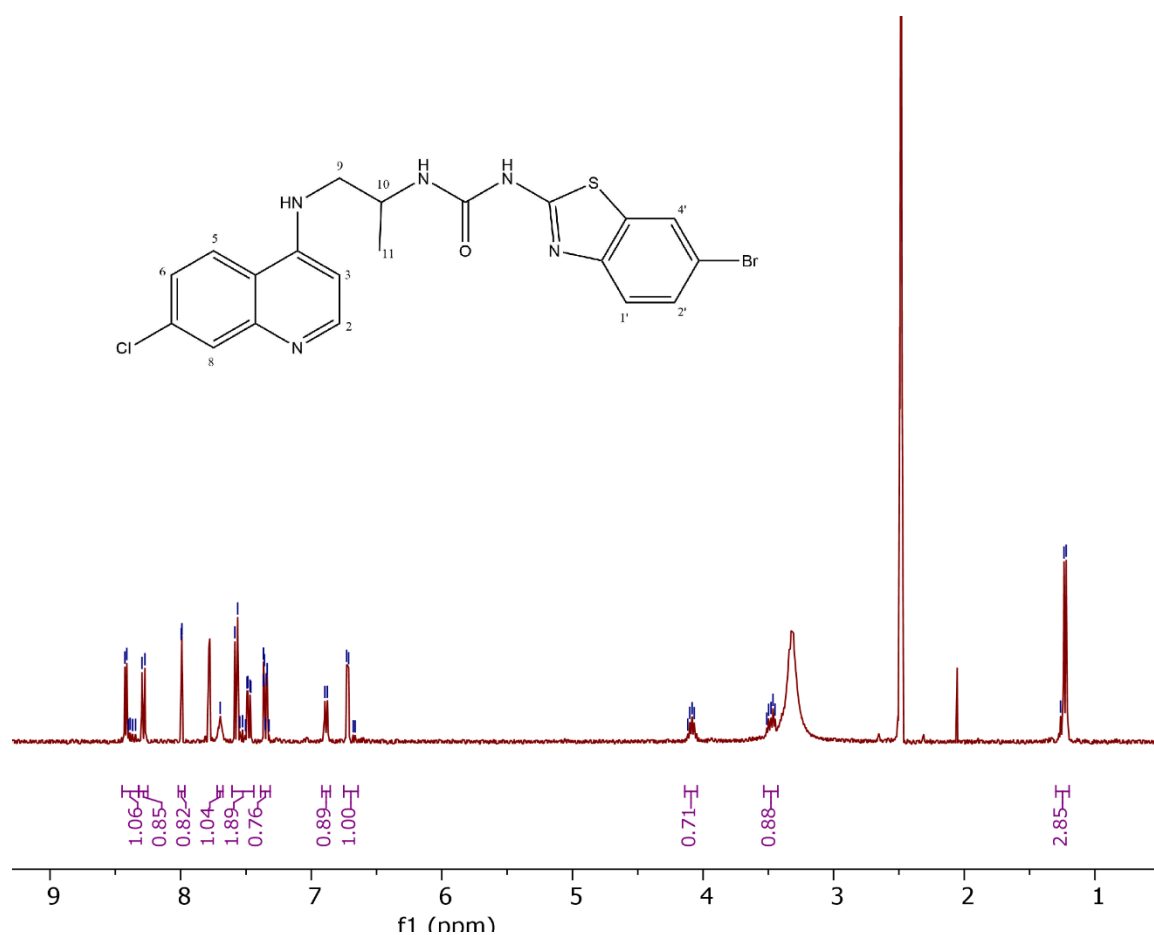


**Figure S64:** 101 MHz  $^{13}\text{C}$ -NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-fluorobenzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6v**).

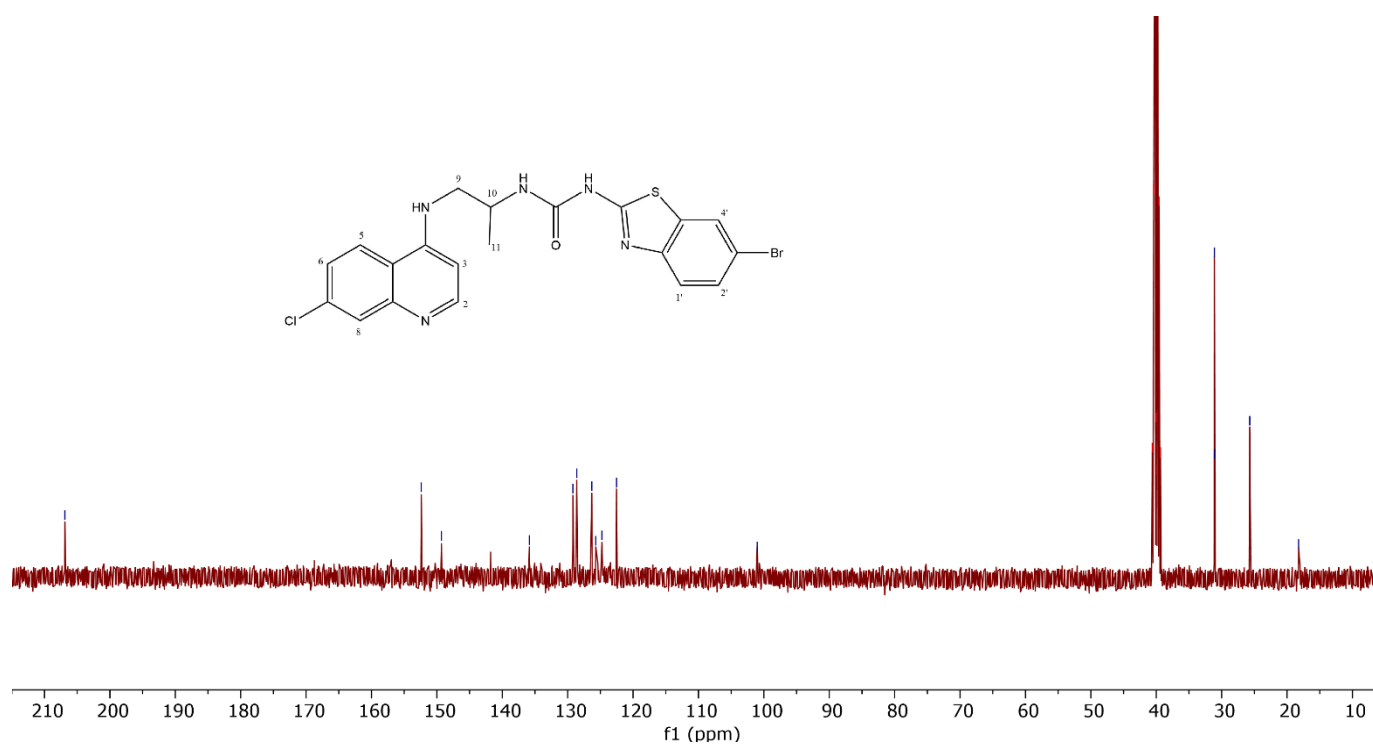




**Figure S65:** HRMS (ES<sup>+</sup>) for 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-fluorobenzo[d]thiazol-2-yl)urea (**6v**).

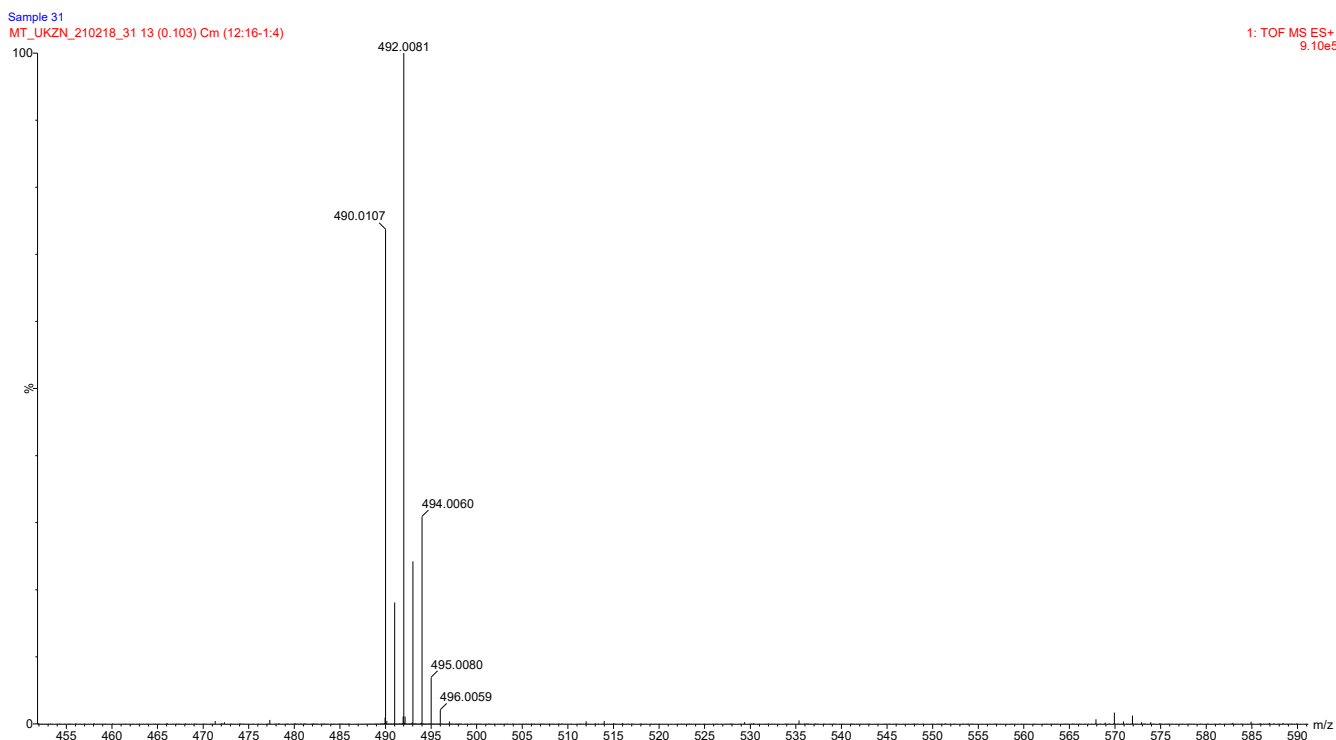
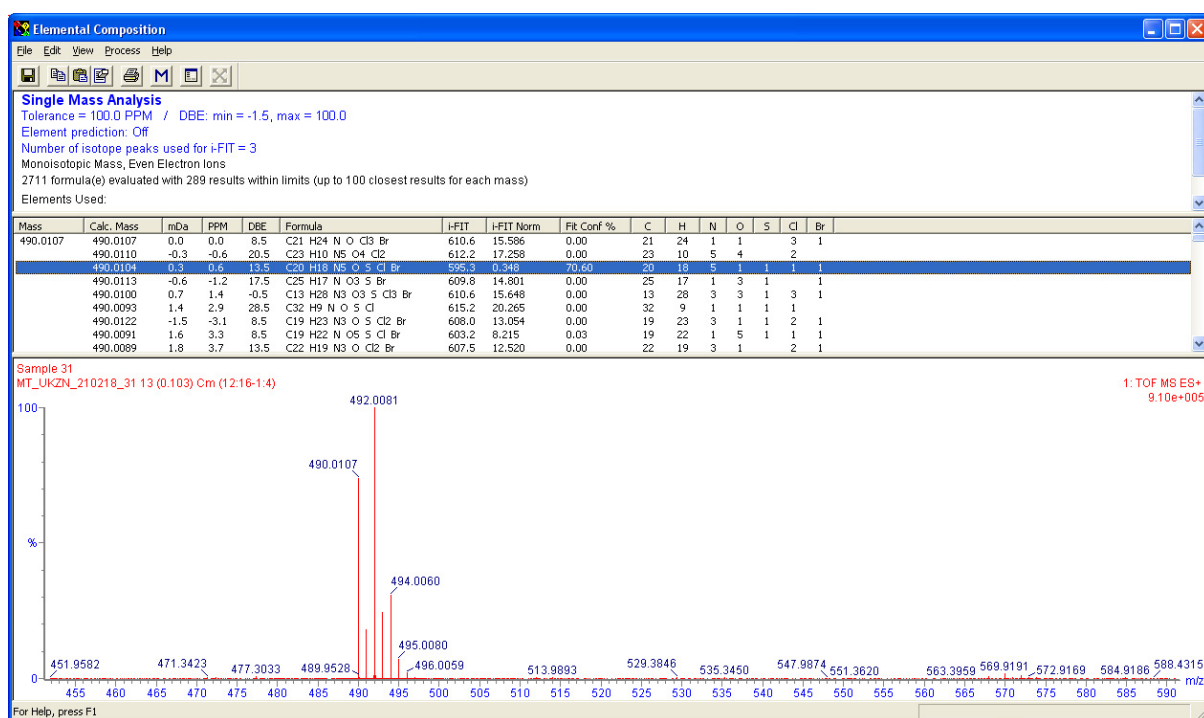


**Figure S66:** 400 MHz <sup>1</sup>H-NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-bromobenzo[d]thiazol-2-yl)urea (**6w**).

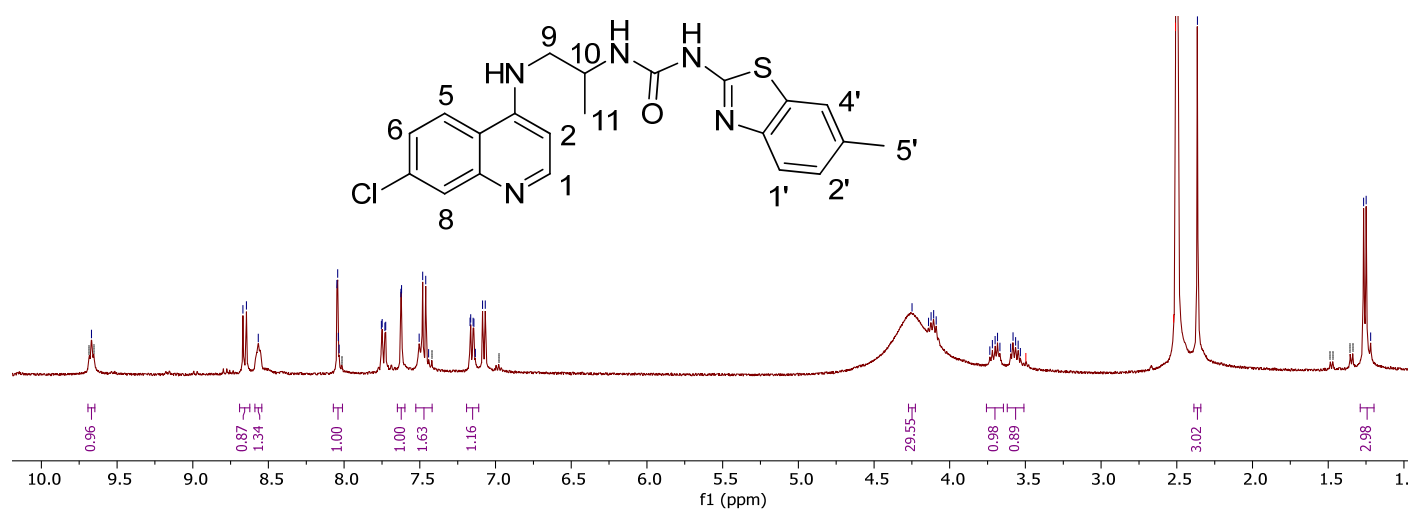


**Figure S67:** 101 MHz <sup>13</sup>C-NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-bromobenzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6w**).

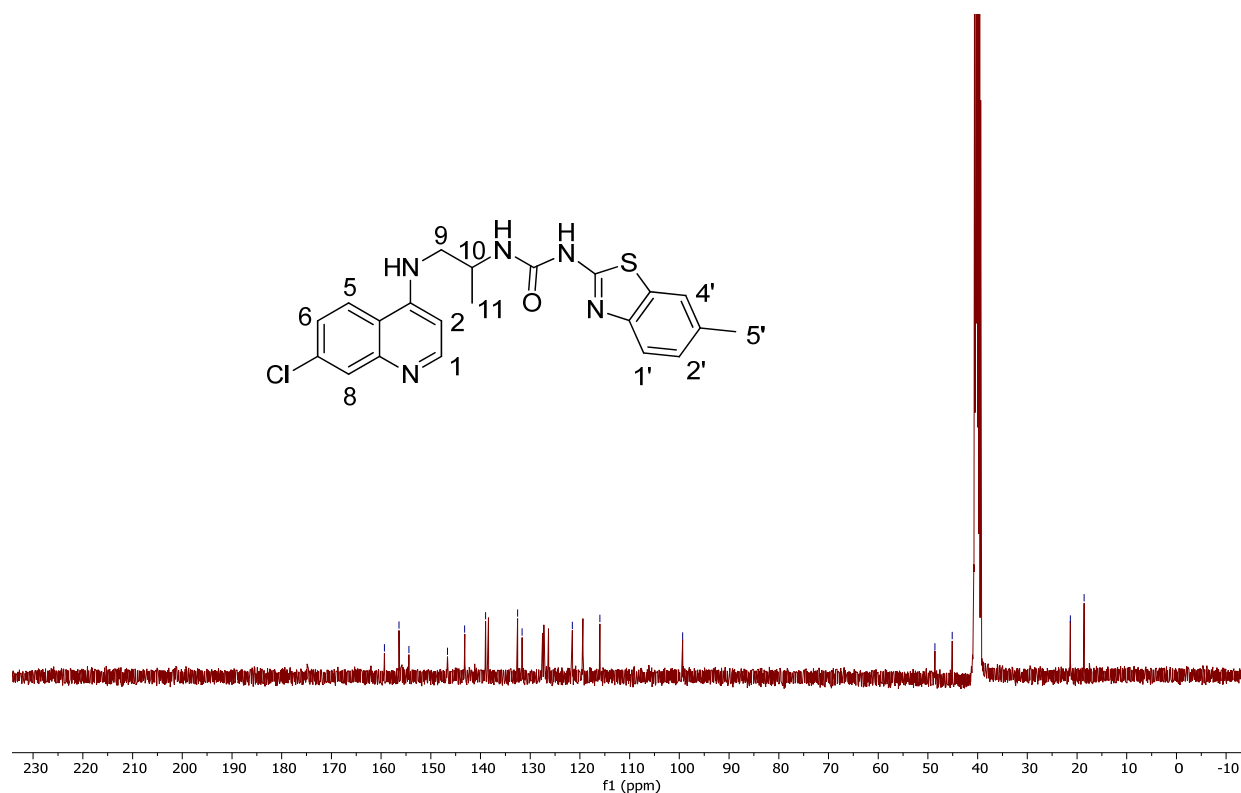
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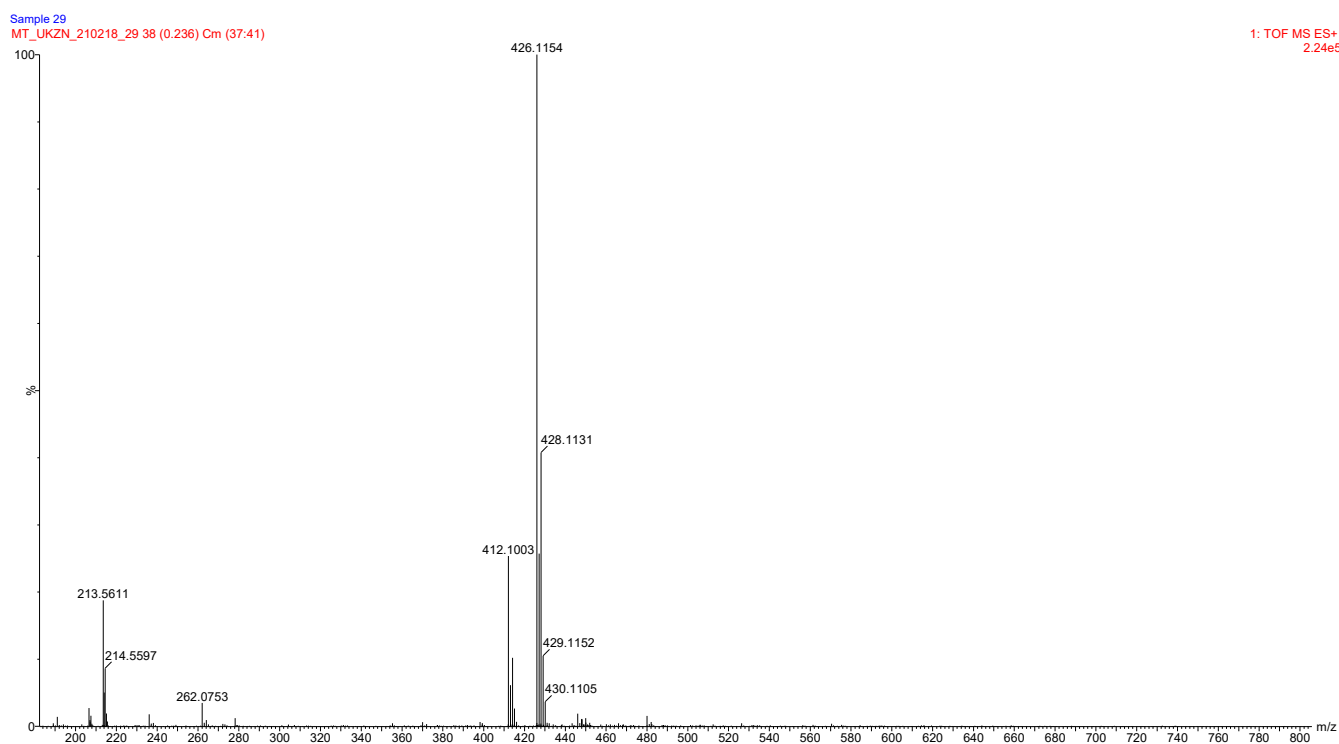
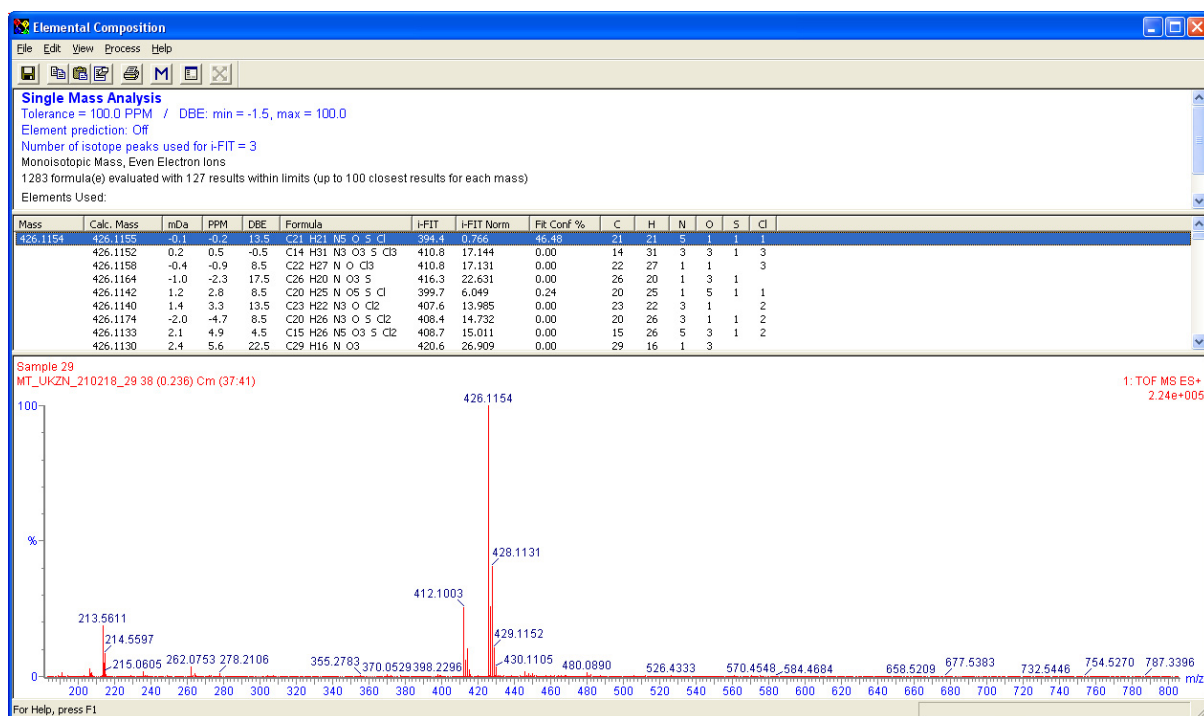
**Figure S68:** HRMS (ES<sup>+</sup>) for 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-bromobenzo[d]thiazol-2-yl)urea (**6w**).



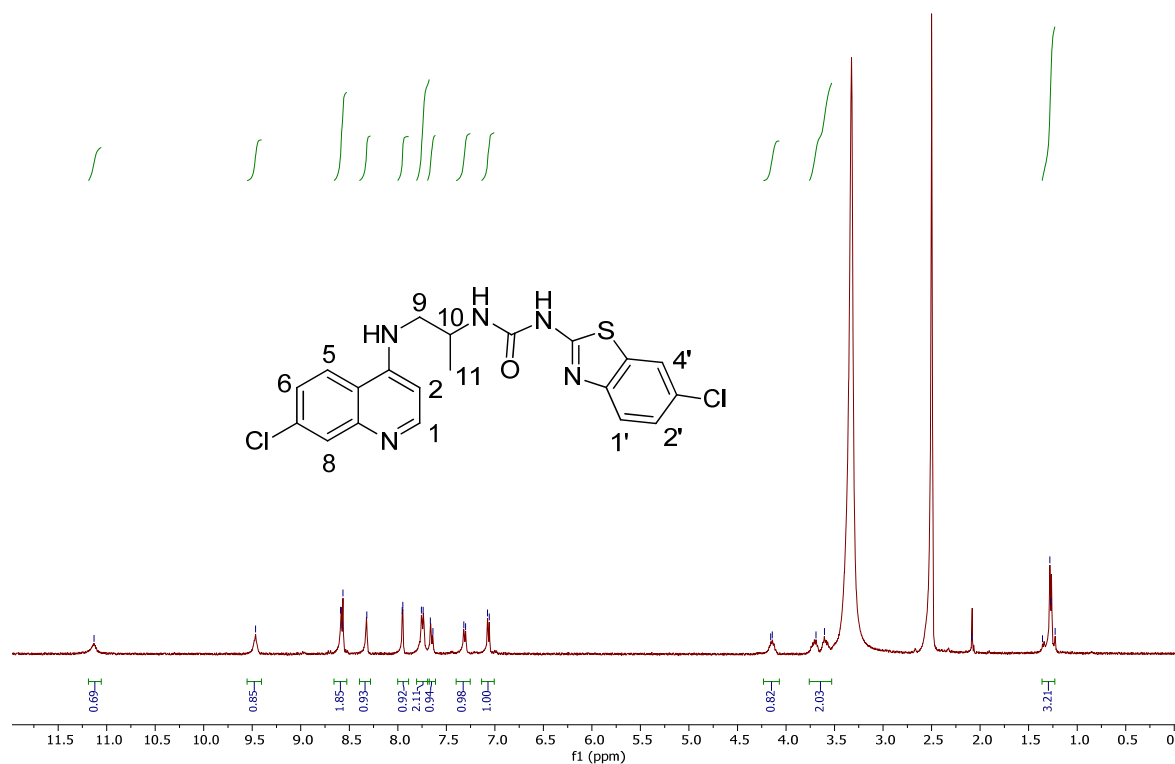
**Figure S69:** 400 MHz  $^1\text{H}$ -NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-methylbenzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6x**).



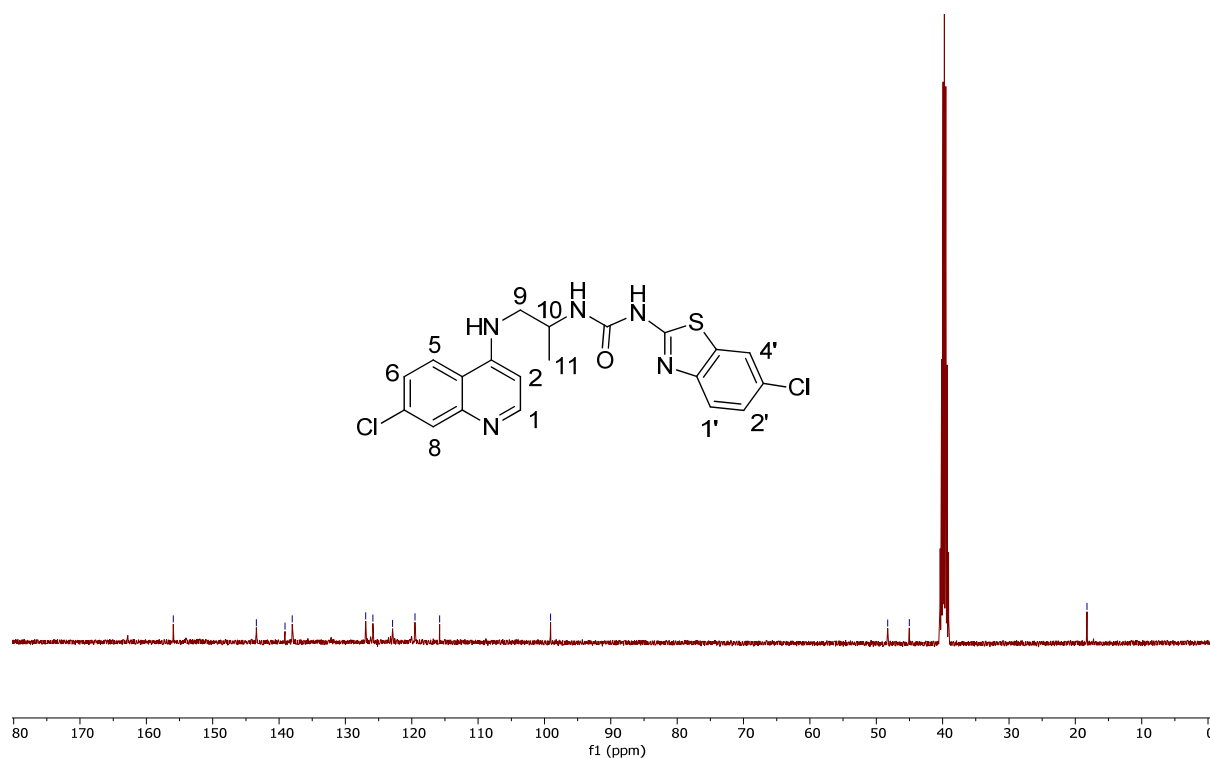
**Figure S70:** 101 MHz  $^{13}\text{C}$ -NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-methylbenzo[d]thiazol-2-yl)urea in DMSO- $d_6$  (**6x**).



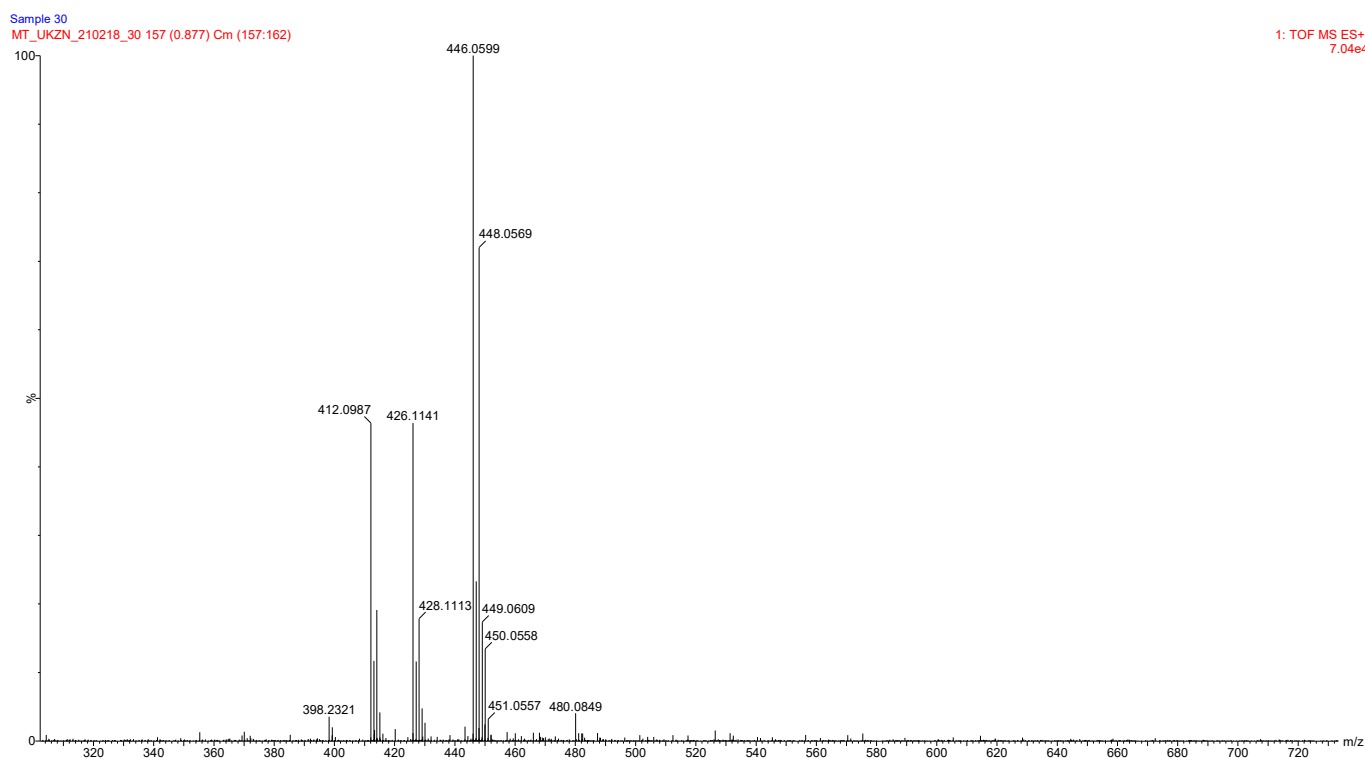
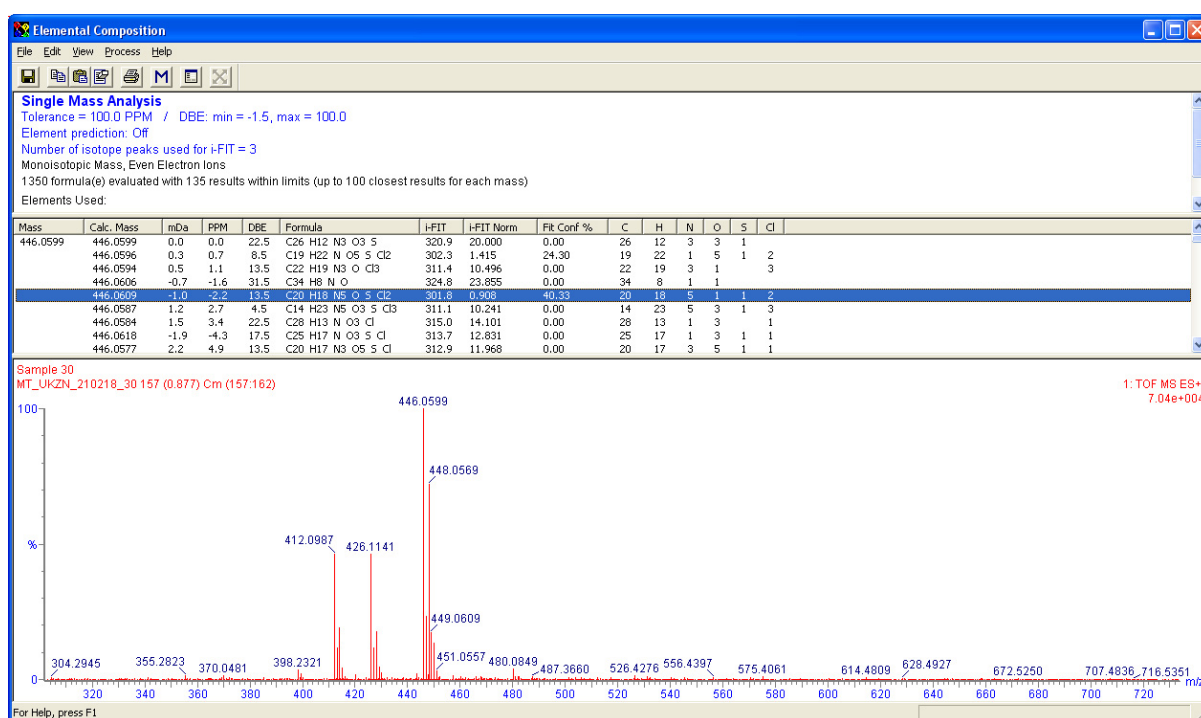
**Figure S71:** HRMS (ES<sup>+</sup>) for 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-methylbenzo[d]thiazol-2-yl)urea (**6x**).



**Figure S72:** 400 MHz <sup>1</sup>H-NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-chlorobenzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6y**).



**Figure S73:** 101 MHz <sup>13</sup>C-NMR of 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-chlorobenzo[d]thiazol-2-yl)urea in DMSO-d<sub>6</sub> (**6y**).



**Figure S74:** HRMS (ES<sup>+</sup>) for 1-(1-((7-chloroquinolin-4-yl)amino)propan-2-yl)-3-(6-chlorobenzo[d]thiazol-2-yl)urea (**6y**).