

## Supplementary Material

### Synthesis and biochemical evaluation of 5-(pyridin-4-yl)-3-(alkylsulfanyl)-4H-1,2,4-triazol-4-amine-based inhibitors of tyrosinase from *Agaricus bisporus*

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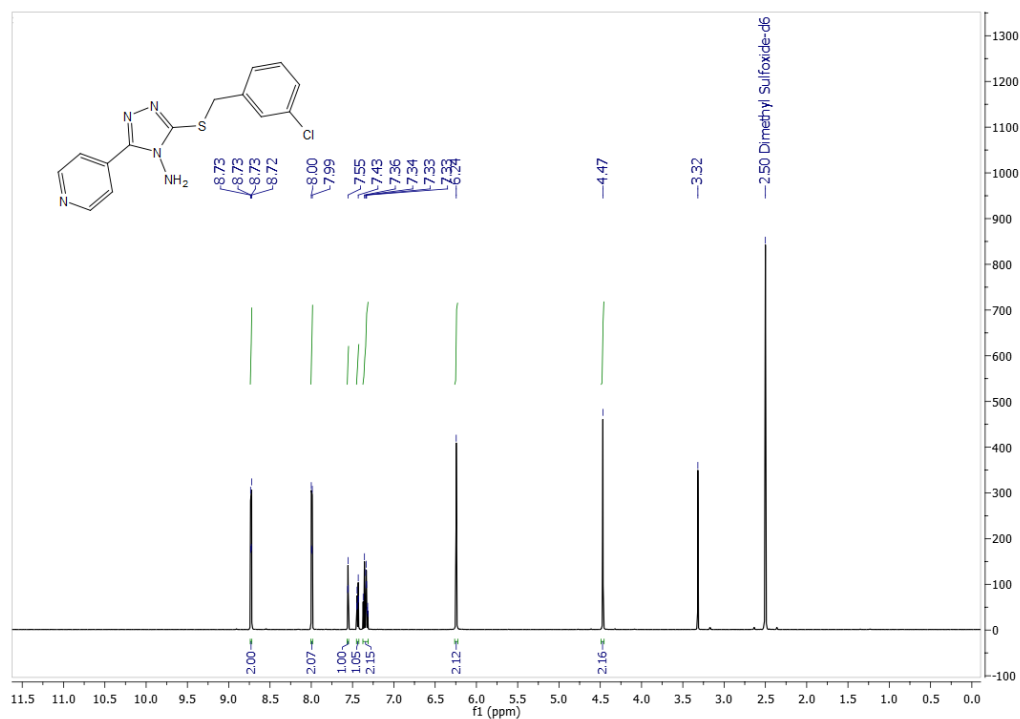
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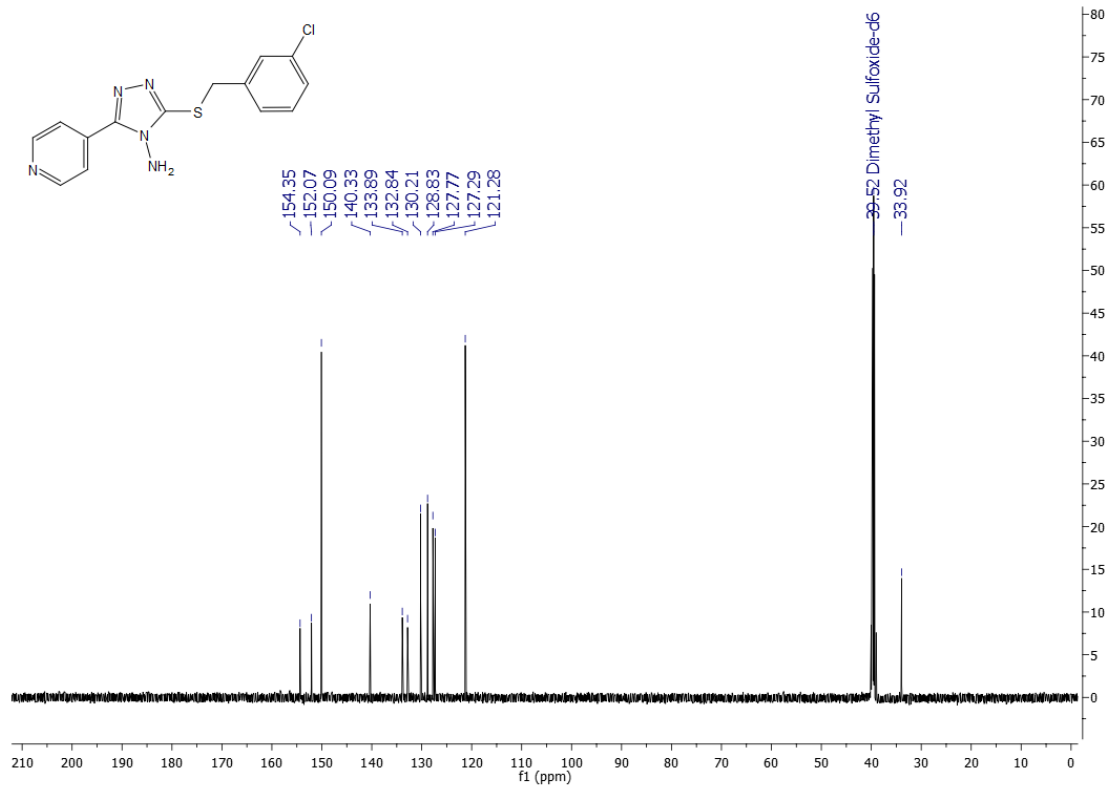
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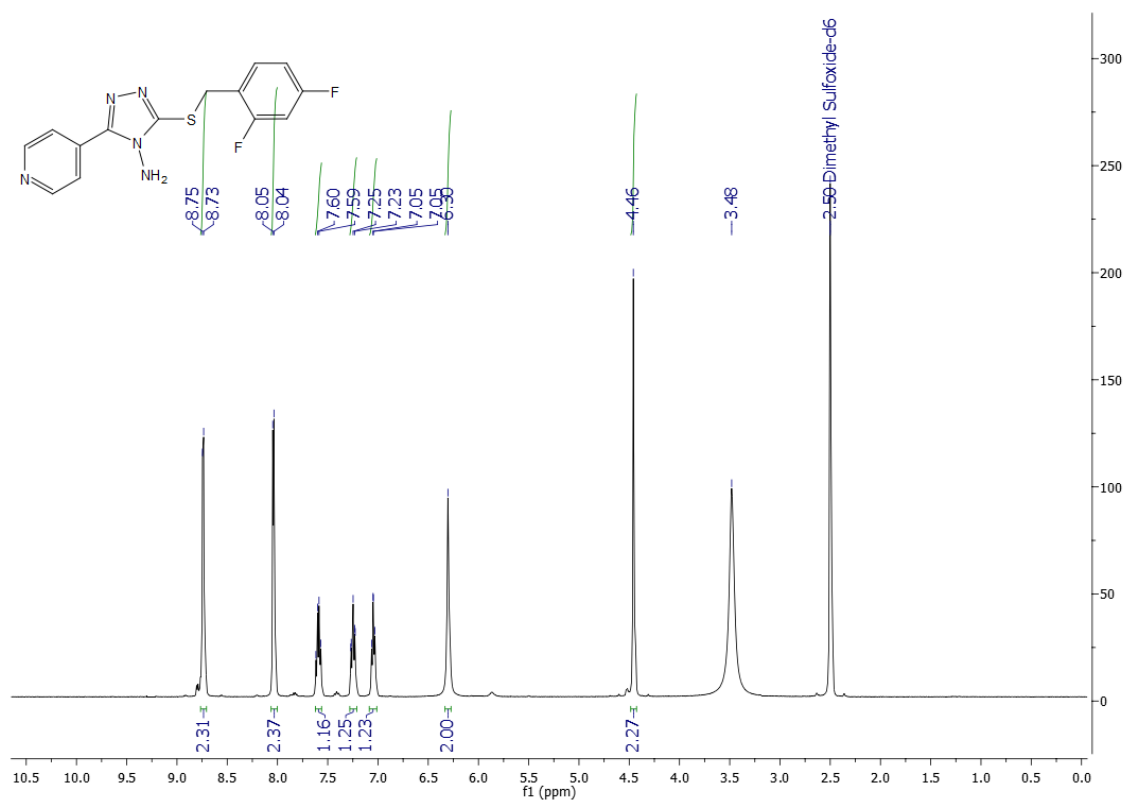
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Selected  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectra

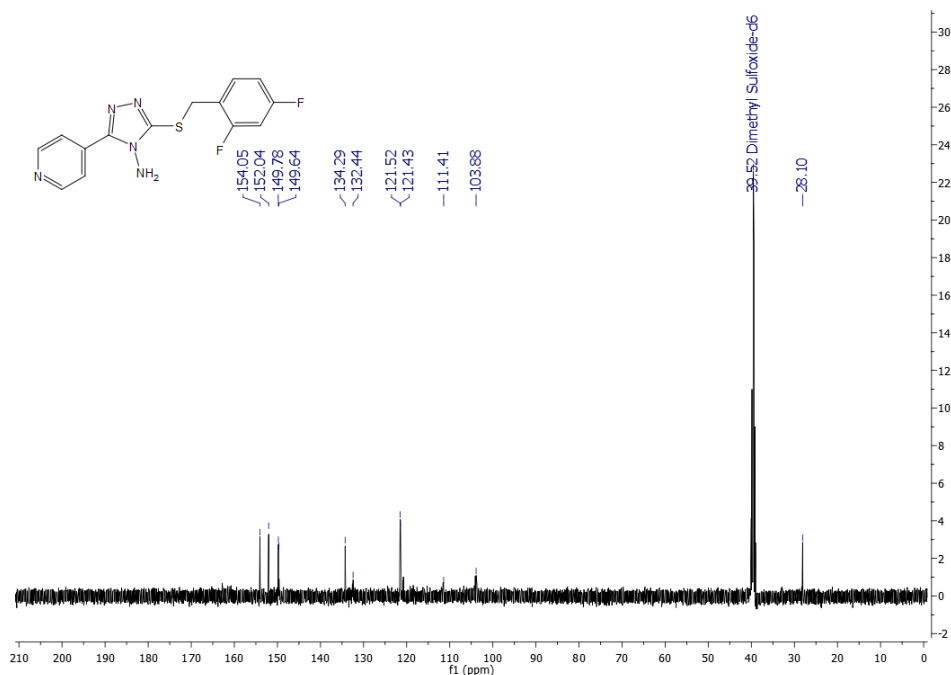
**Figure S1:**  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((3-chlorobenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (9).



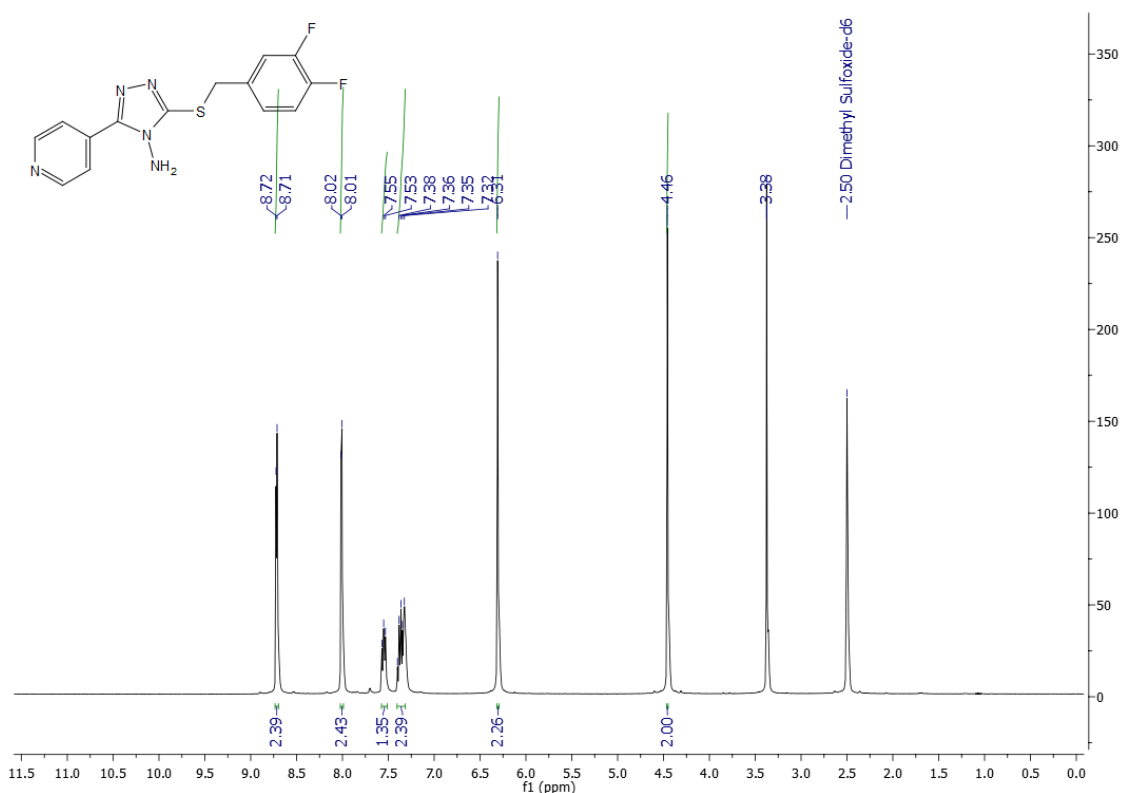
**Figure S2:**  $^{13}\text{C-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((3-chlorobenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (9).



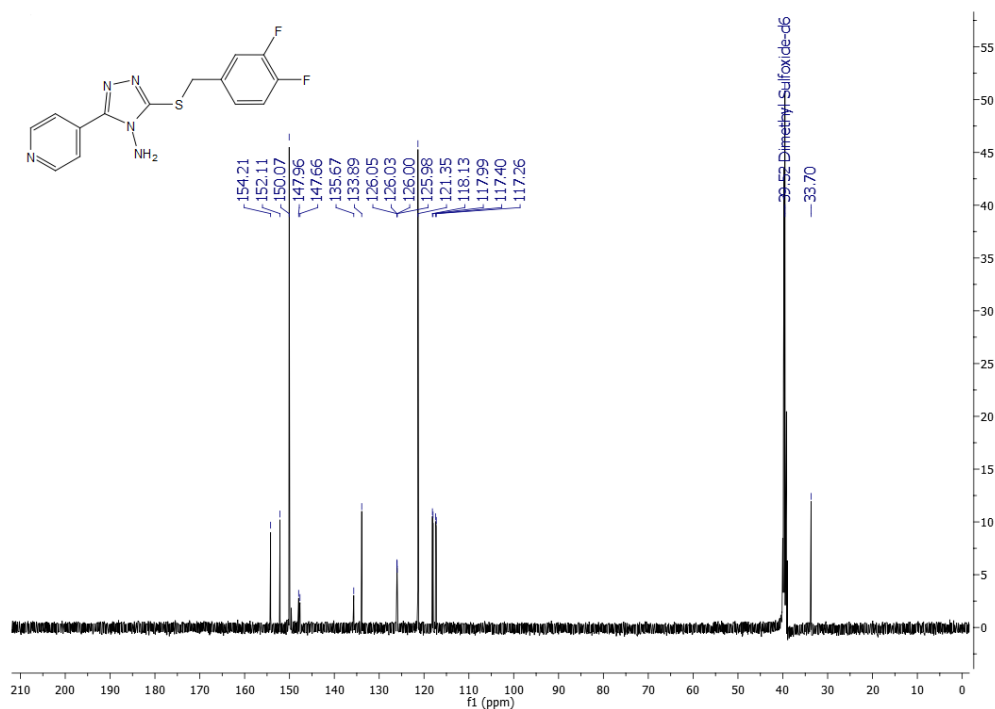
**Figure S3:**  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((2,4-difluorobenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (**13**).



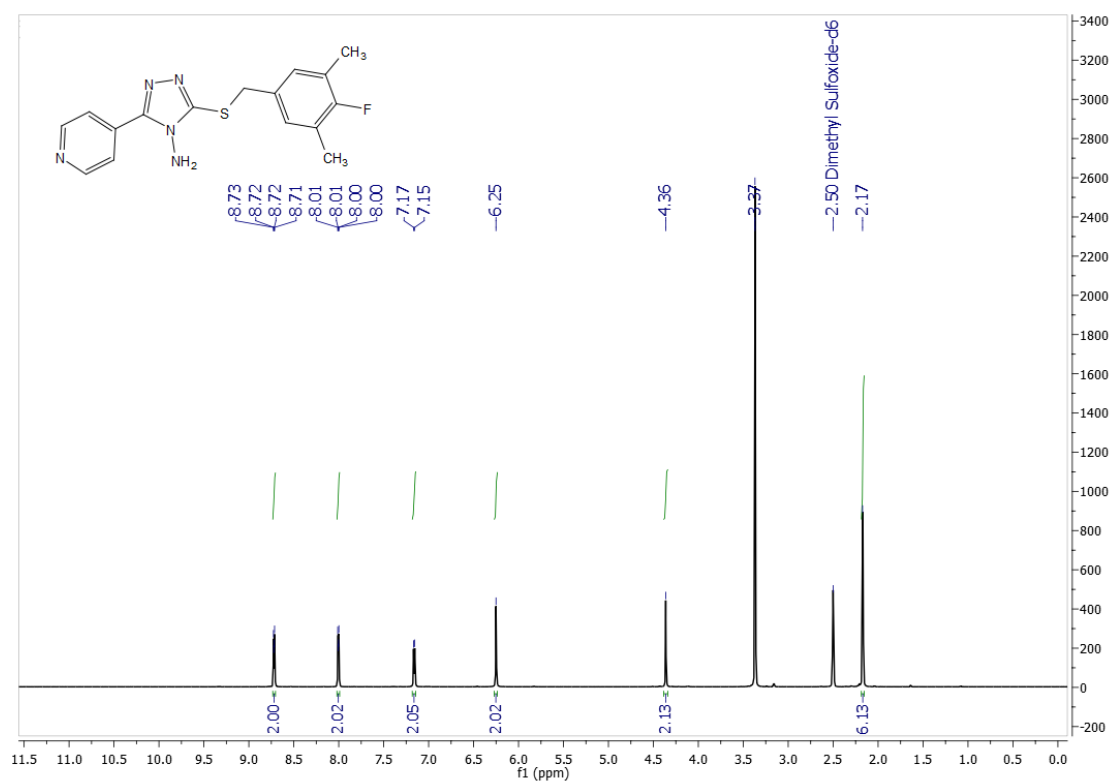
**Figure S4:**  $^{13}\text{C-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((2,4-difluorobenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (**13**).



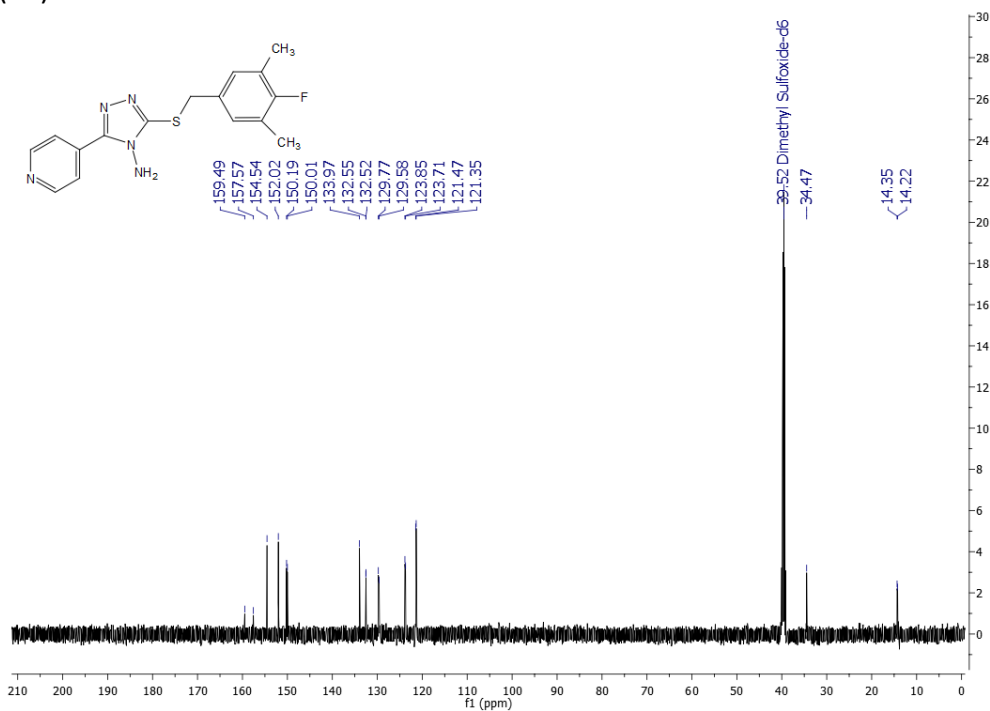
**Figure S5:**  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((3,4-difluorobenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (14).



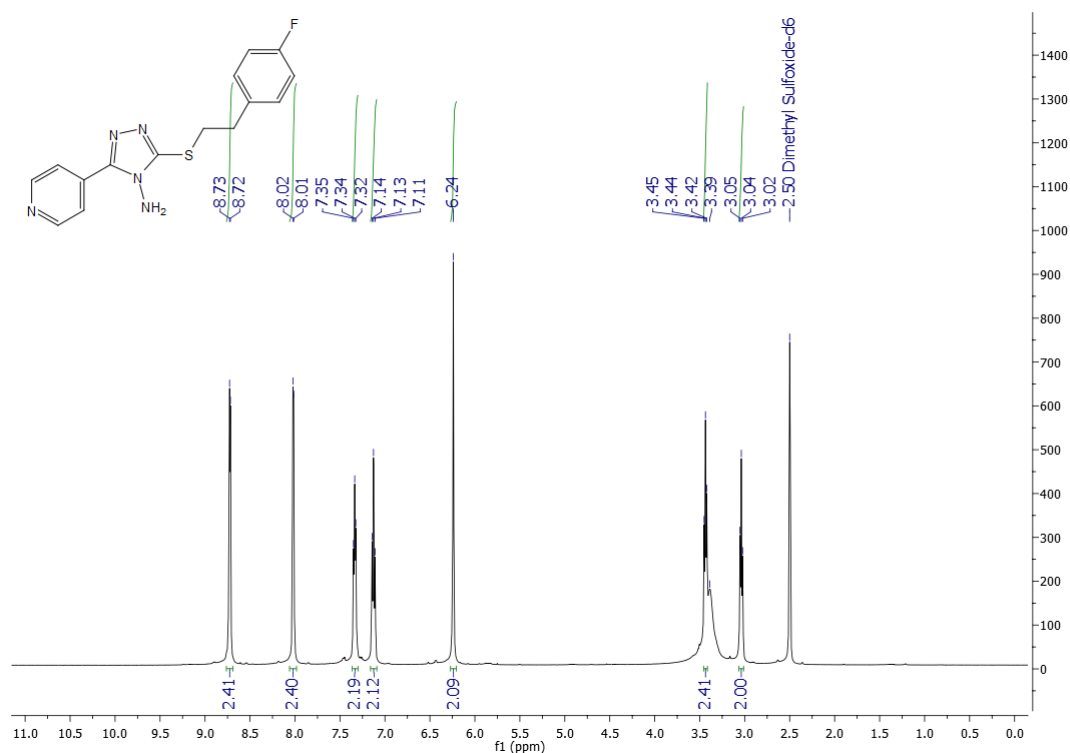
**Figure S6:**  $^{13}\text{C-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((3,4-difluorobenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (14).



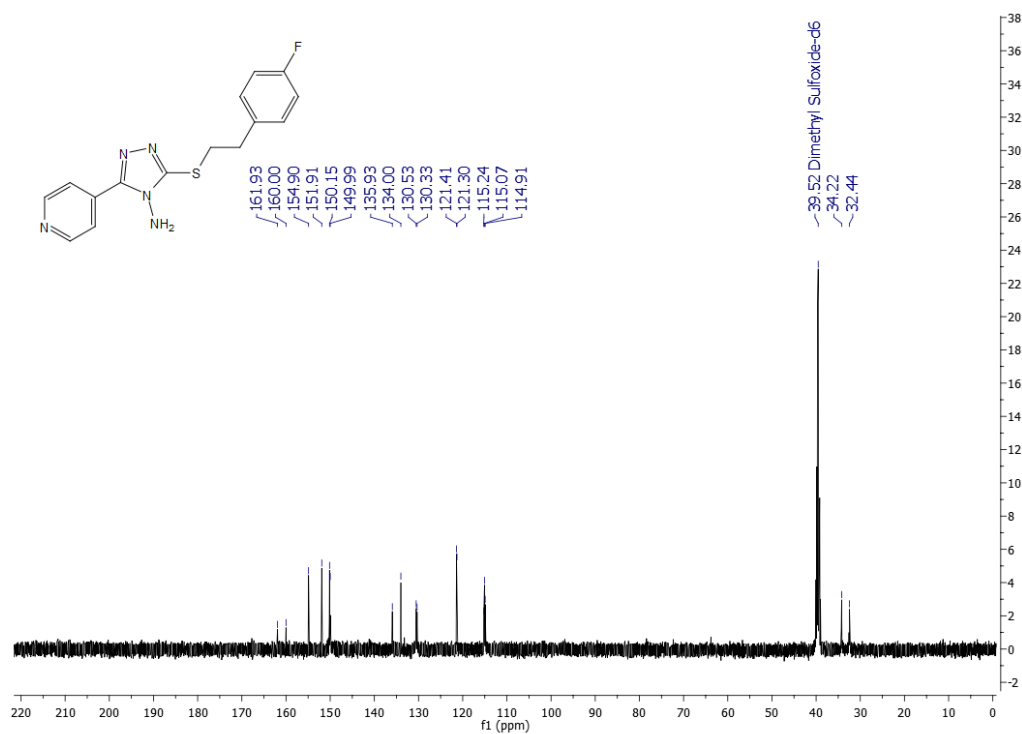
**Figure S7:**  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((4-fluoro-3,5-dimethylbenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (**15**).



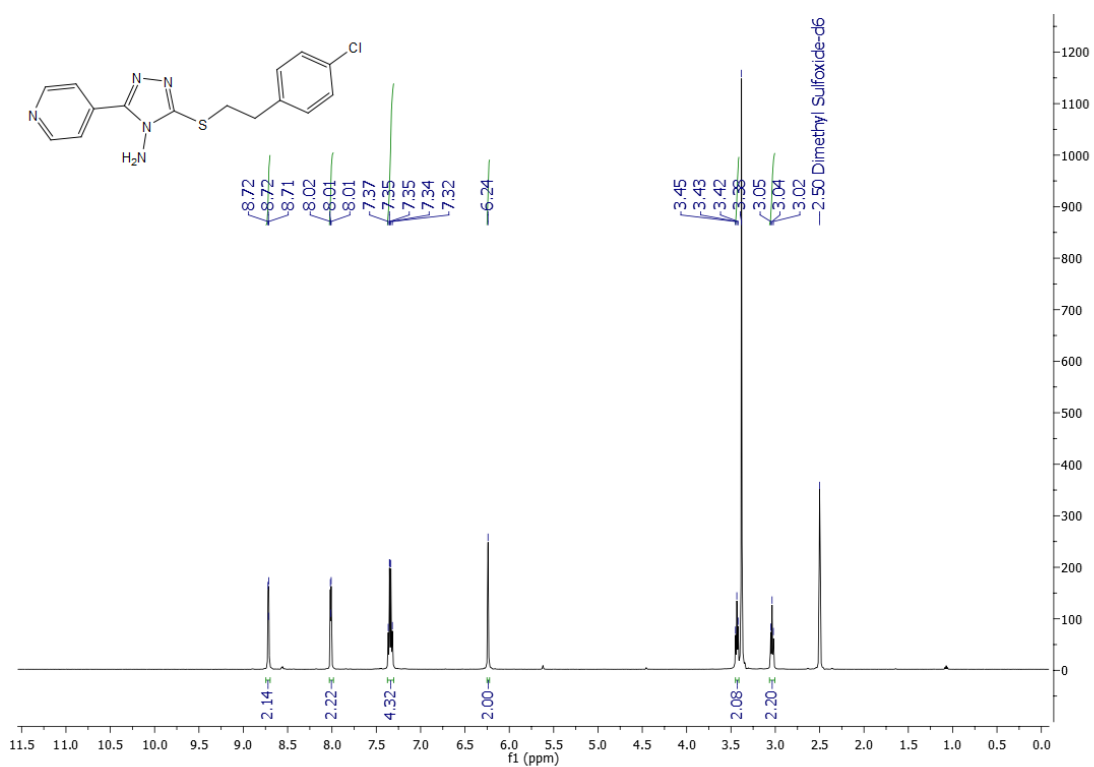
**Figure S8:**  $^{13}\text{C-NMR}$  (DMSO- $d_6$ ) spectrum of 3-((4-fluoro-3,5-dimethylbenzyl)sulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (**15**).



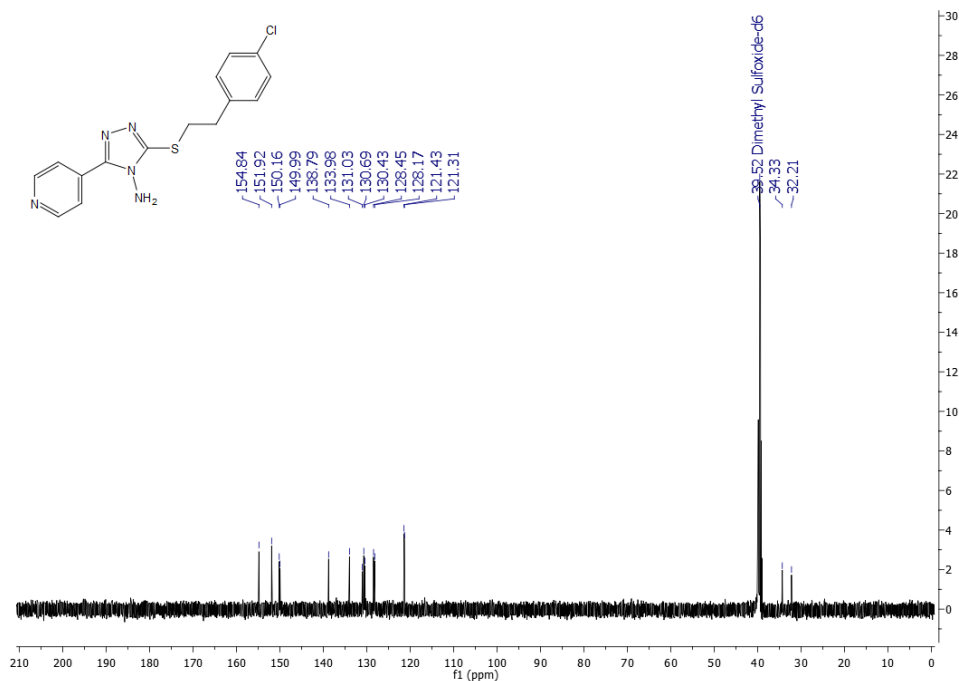
**Figure S9:** <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>) spectrum of 3-(4-fluorophenethylsulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (17).



**Figure S10:** <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>) spectrum of 3-(4-fluorophenethylsulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (17).



**Figure S11:** <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>) spectrum of 3-(4-chlorophenethylsulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (18).



**Figure S12:** <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>) spectrum of 3-(4-chlorophenethylsulfanyl)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (18).

**Table S1.** Selected physicochemical parameters, lipophilicity, solubility, pharmacokinetics and drug-likeness properties for compound **6-18** predicted by SwissADME (<http://swissadme.ch/>)

entry	MW (g/mol)	iLogP	Water solubility*	GI absorption	BBB permeant	Lipinski	Ghose	PAINS
<b>6</b>	283.35	2.16	Soluble	High	No	Yes 0 violation	Yes	0 alert
<b>7</b>	301.34	2.04	Soluble	High	No	Yes 0 violation	Yes	0 alert
<b>8</b>	301.34	2.33	Soluble	High	No	Yes 0 violation	Yes	0 alert
<b>9</b>	317.80	2.24	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert
<b>10</b>	317.80	2.55	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert
<b>11</b>	297.38	2.21	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert
<b>12</b>	297.38	2.26	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert
<b>13</b>	319.33	2.55	Soluble	High	No	Yes 0 violation	Yes	0 alert
<b>14</b>	319.33	2.25	Soluble	High	No	Yes 0 violation	Yes	0 alert
<b>15</b>	329.40	2.22	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert
<b>16</b>	297.38	2.30	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert
<b>17</b>	315.37	2.29	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert
<b>18</b>	331.82	2.61	Moderately soluble	High	No	Yes 0 violation	Yes	0 alert

\*Water solubility: Soluble= Log S (Ali) values between -4 and -2; Moderately soluble= Log S (Ali) values between -6 and -4.



**Table S2.** Smiles strings for compounds **6-18**

Compound	Smiles string
<b>6</b>	<chem>Nn1c(SCc2ccccc2)nnc1c3ccncc3</chem>
<b>7</b>	<chem>Nn1c(SCc2cccc(F)c2)nnc1c3ccncc3</chem>
<b>8</b>	<chem>Nn1c(SCc2ccc(F)cc2)nnc1c3ccncc3</chem>
<b>9</b>	<chem>Nn1c(SCc2cccc(Cl)c2)nnc1c3ccncc3</chem>
<b>10</b>	<chem>Nn1c(SCc2ccc(Cl)cc2)nnc1c3ccncc3</chem>
<b>11</b>	<chem>Cc1cccc(CSc2nnc(c3ccncc3)n2N)c1</chem>
<b>12</b>	<chem>Cc1ccc(CSc2nnc(c3ccncc3)n2N)cc1</chem>
<b>13</b>	<chem>Nn1c(SCc2ccc(F)cc2F)nnc1c3ccncc3</chem>
<b>14</b>	<chem>Nn1c(SCc2ccc(F)c(F)c2)nnc1c3ccncc3</chem>
<b>15</b>	<chem>Cc1cc(CSc2nnc(c3ccncc3)n2N)cc(C)c1F</chem>
<b>16</b>	<chem>Nn1c(SCCc2ccccc2)nnc1c3ccncc3</chem>
<b>17</b>	<chem>Nn1c(SCCc2ccc(F)cc2)nnc1c3ccncc3</chem>
<b>18</b>	<chem>Nn1c(SCCc2ccc(Cl)cc2)nnc1c3ccncc3</chem>