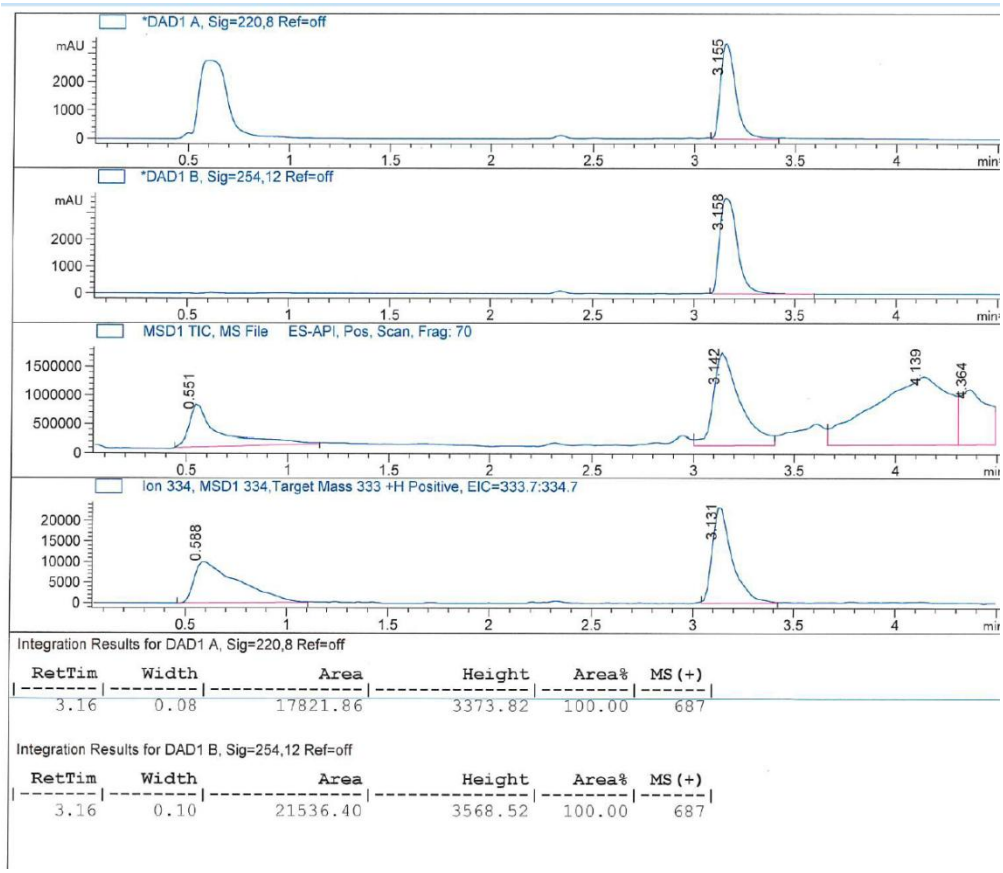
Chemical characterization of compounds (Figures S1–16, and Table S1):



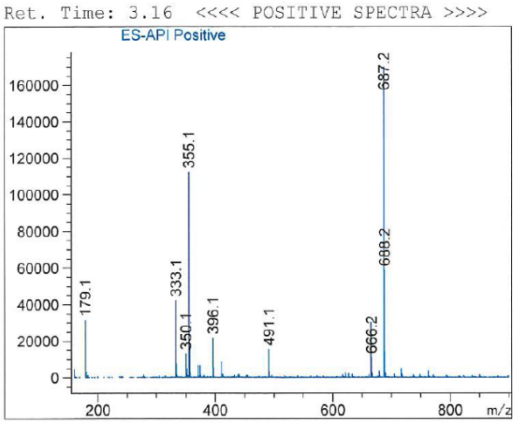
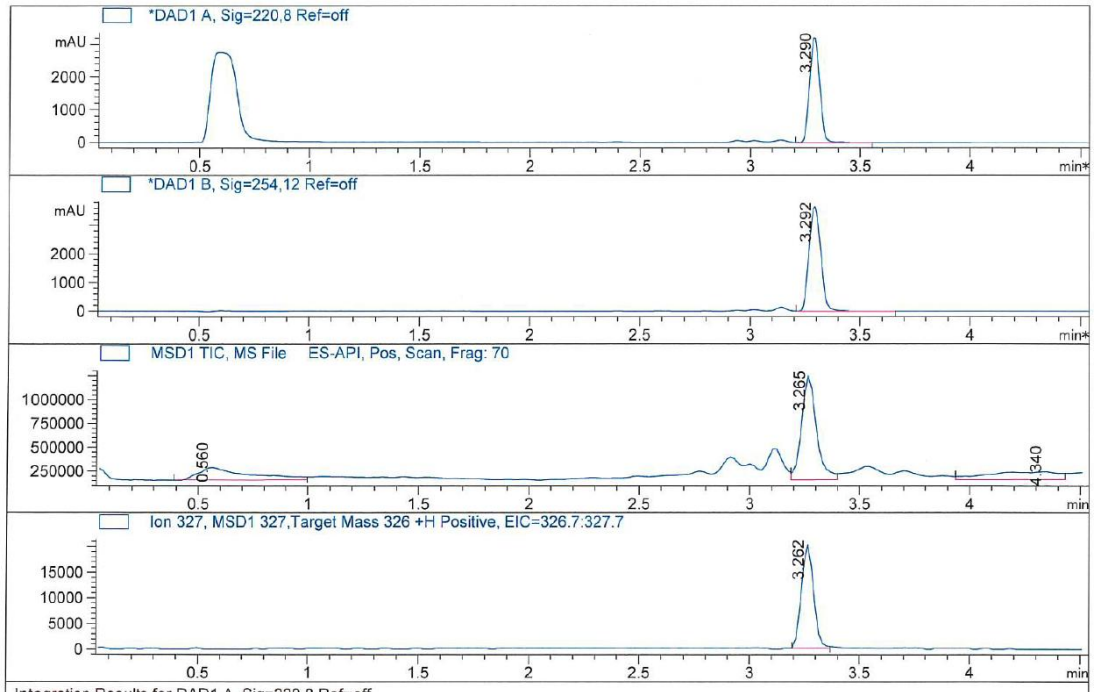


Figure S1. Comp. 4e. *N*-(2-methoxy-4-nitrophenyl)-*N*-(2-nitrophenyl)urea. Yellow, crystalline solid (180 mg, 88.9%). MP 219.50°C; LC/MS-ESI (*m/z*): 333 ($M+H^+$); 355 ($M+Na^+$); dimer 687 ($M+Na^+$); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 9.42 (s, 1H), 8.96 (d, J = 2.2 Hz, 1H), 7.98 (ddd, J = 8.3, 3.5, 1.4 Hz, 2H), 7.92 (dd, J = 9.0, 2.9 Hz, 1H), 7.66 (dt J = 7.6, 1.3 Hz, 1H), 7.28–7.18 (m, 2H), 4.00 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6); δ 152.58, 151.42, 142.65, 135.68, 134.94, 134. 45, 130.26, 125.47, 118.23, 117.51, 117.28, 114.25, 114.09. Anal. Calcd for C14H12N4O6, 332.27, found 333.21; IR (cm^{-1}): 1,717.70 (C=O).



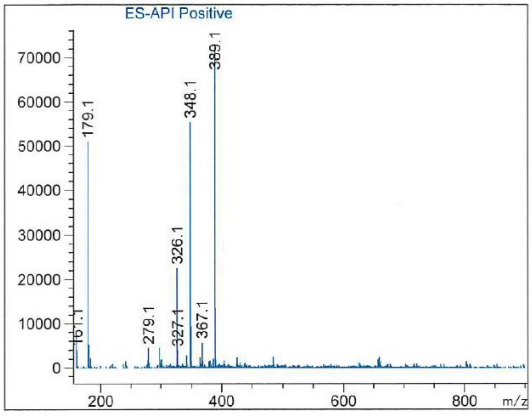
Integration Results for DAD1 A, Sig=220,8 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.29	0.05	10334.83	3240.43	100.00	389

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.29	0.06	13675.01	3654.32	100.00	389

Ret. Time: 3.29 <<<< POSITIVE SPECTRA >>>>



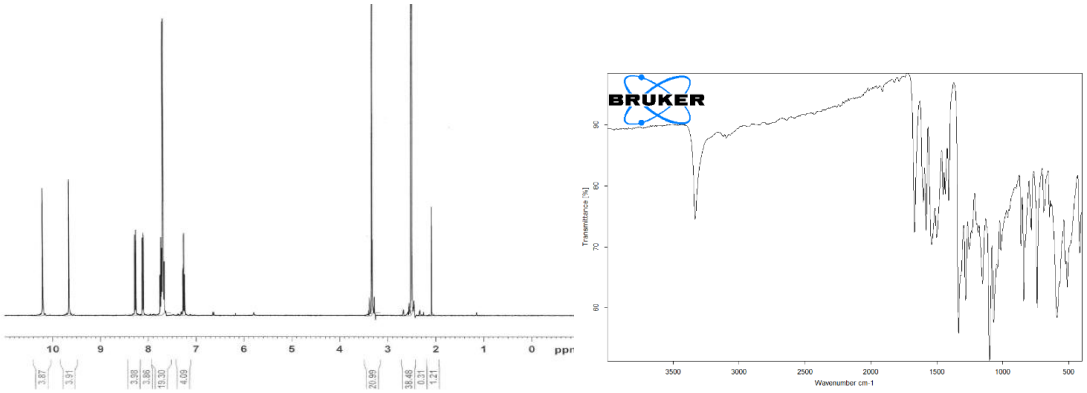
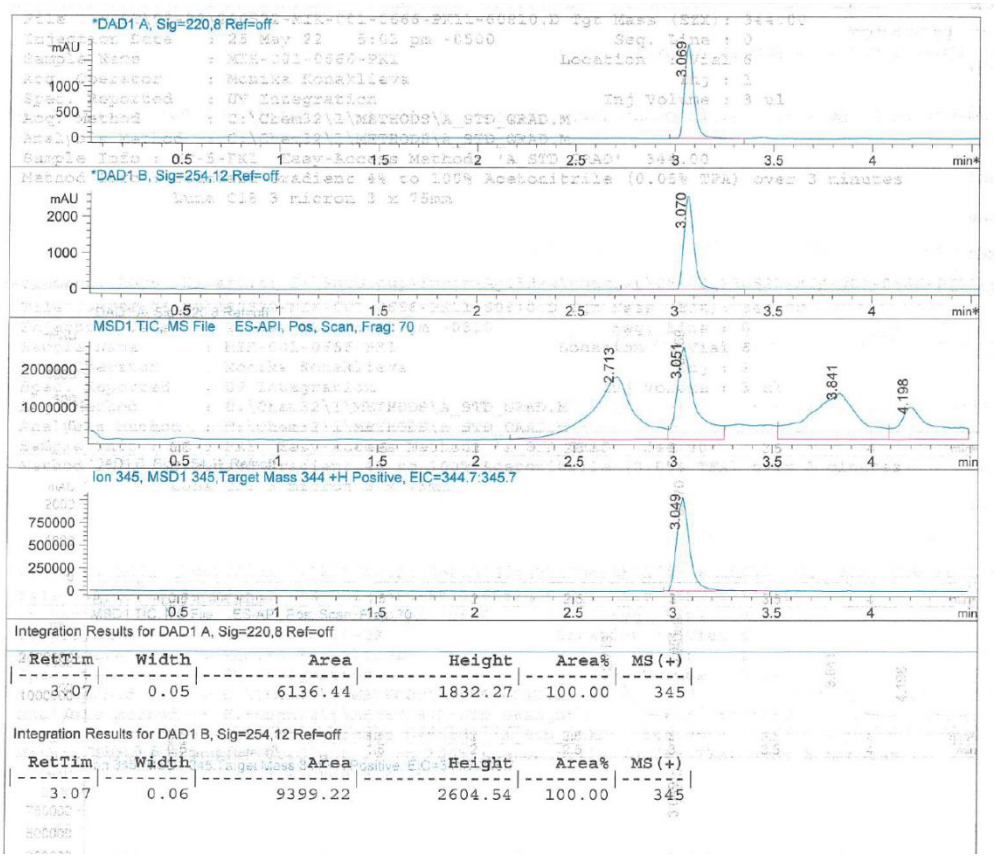


Figure S2. Comp. 4g. *N*-(2-nitrophenyl)-*N*-4-(trifluoromethyl)phenyl]-urea. Bright, yellow crystalline solid (122.8 mg, 62.0%). MP 215.4–217.7°C; LC/MS-ESI (*m/z*): 326 ($M+H^+$); 348.1 ($M+Na^+$); 389 ($M+ACN+Na^+$); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.3 (s, 1H), 9.6 (s, 1H), 8.3 (dd, J = 8.7, 1.5 Hz, 1H), 8.1 (dd, J = 8.7, 1.5 Hz, 1H), 7.75–7.61 (m, 1H), 7.3 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.29, 150.48, 143.44, 138.67, 135.48, 134.69, 126.70, 126.65, 125.92, 123.34, 118.76, 40.25, 39.14, 31.17; Anal. Calcd for $C_{14}H_{10}F_3N_3O_3$, 325.24; found, 325.1; IR (cm^{-1}): 1,666.10 (C=O).



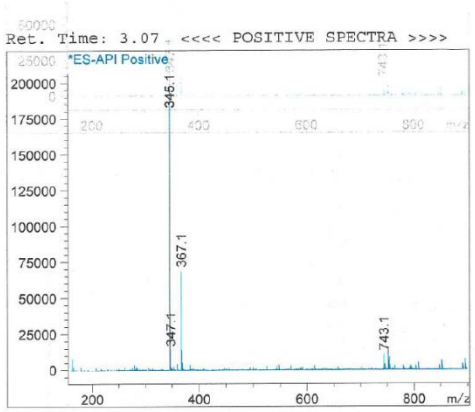
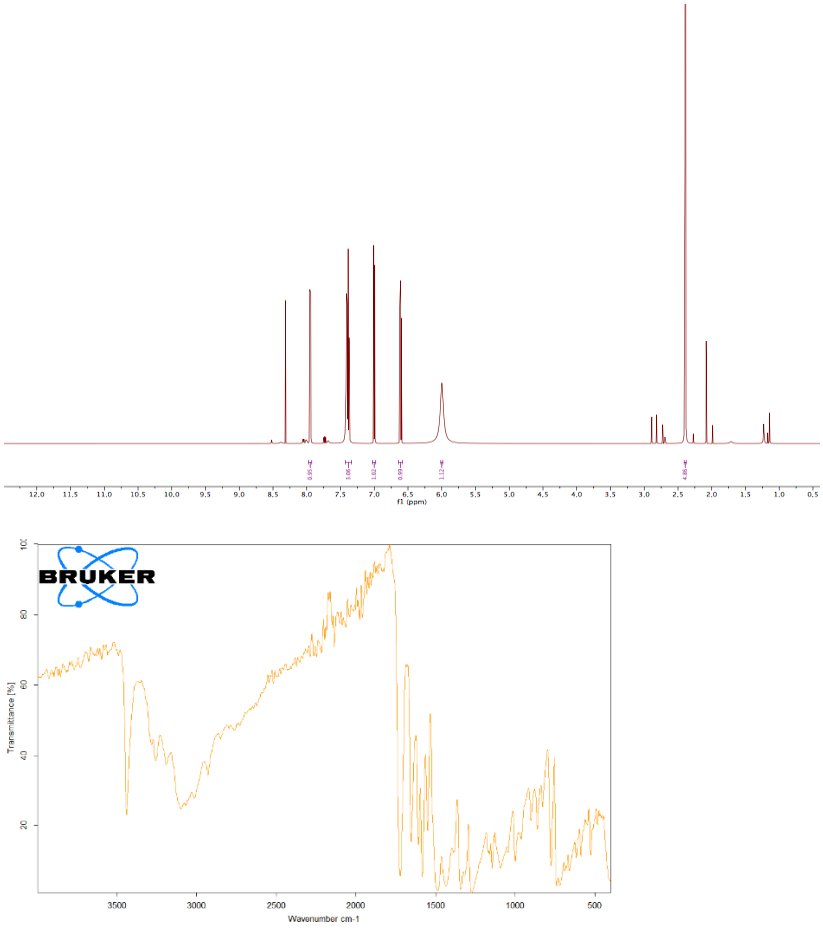
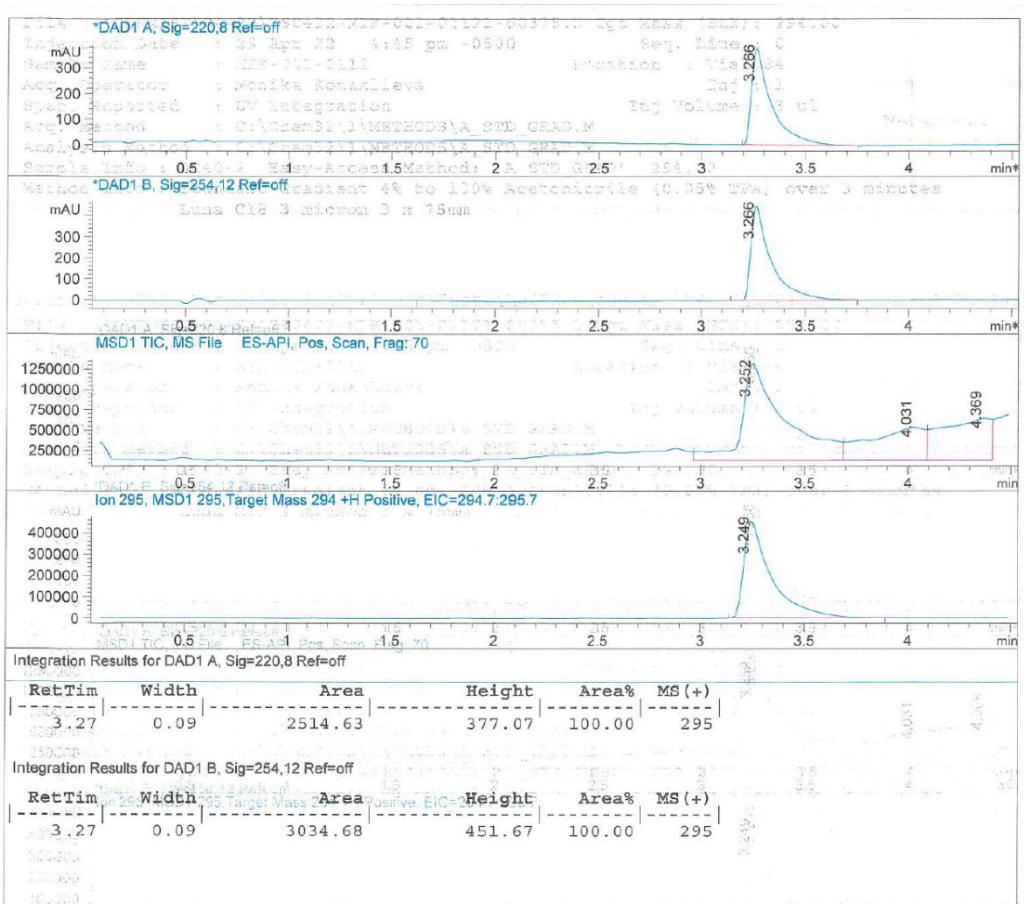


Figure S3. Comp. 5a. *N*-(2-hydroxy-6-nitrophenyl)-4-(pyrimidin-2-yl)piperazine-1-carboxamide. White solid (100 mg, 70%). LC/MS-ESI (*m/z*): 345 ($M+H^+$); 367 ($M+Na^+$).





Integration Results for DAD1 A, Sig=220,8 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.27	0.09	2514.63	377.07	100.00	295

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.27	0.09	3034.68	451.67	100.00	295

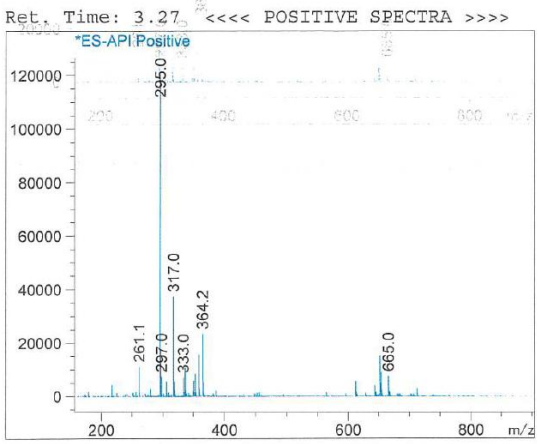
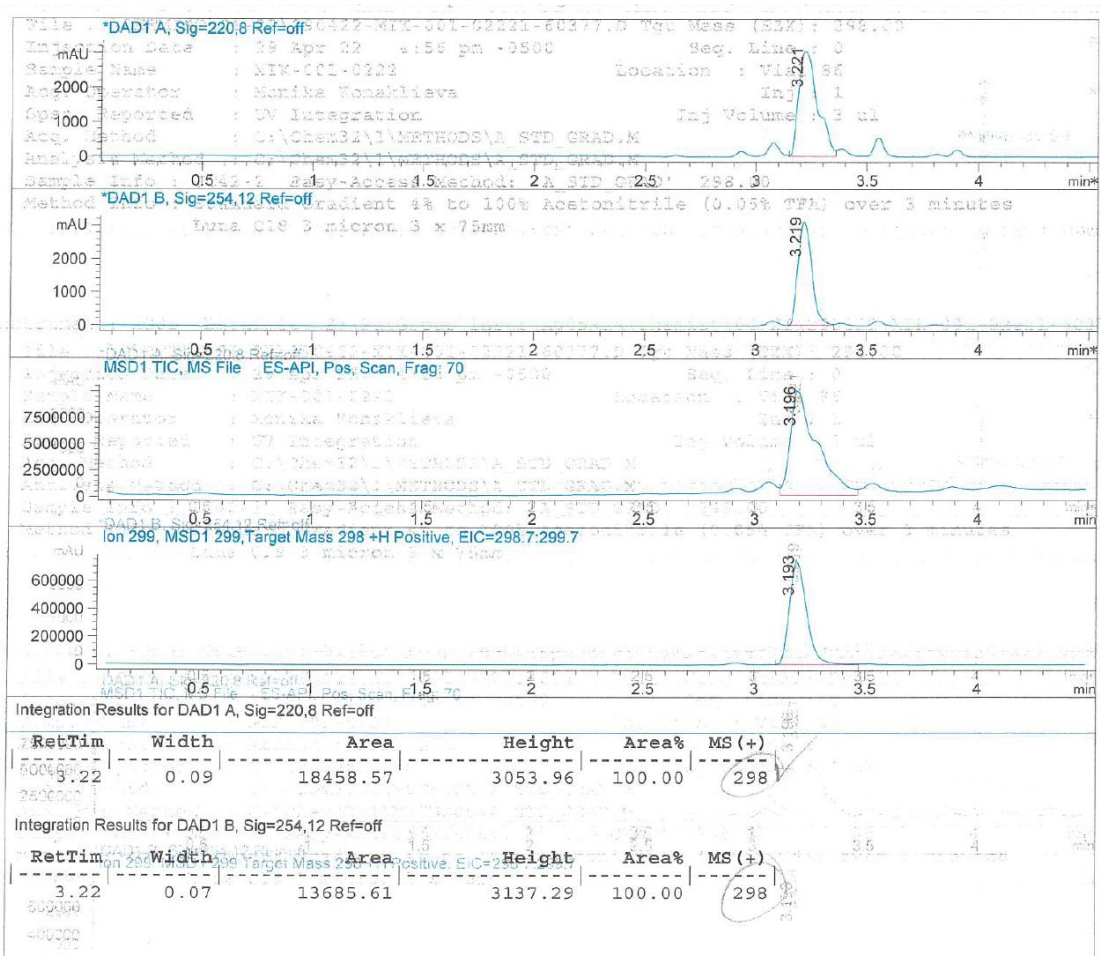


Figure S4. Comp. 6a. 3-amino-5-(methylsulfanyl)-*N*-(2-nitrophenyl)-1*H*-1,2,4-triazole-1-carboxamide. Yellow, crystalline solid (144 mg, 28.9%). MP 216.14°C; LC/MS-ESI (*m/z*): 294.29; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.31 (s, 1H), δ 7.95 (dd, J = 8.7, 1.6 Hz, 1H), 7.43–7.34 (dt, 1H), 7.00 (dd, J = 8.5, 1.3 Hz, 1H), 6.64–6.58 (dt, 2H), 6.00 (bs, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.44, 148.00, 141.16, 135.99, 125.98, 125.14, 124.52, 120.76, 116.78, 16.40; Anal. Calcd for $C_{10}H_{10}N_6O_3S$, 294.29; found, 295.01; IR (cm^{-1}): 1,727.08 (C=O).



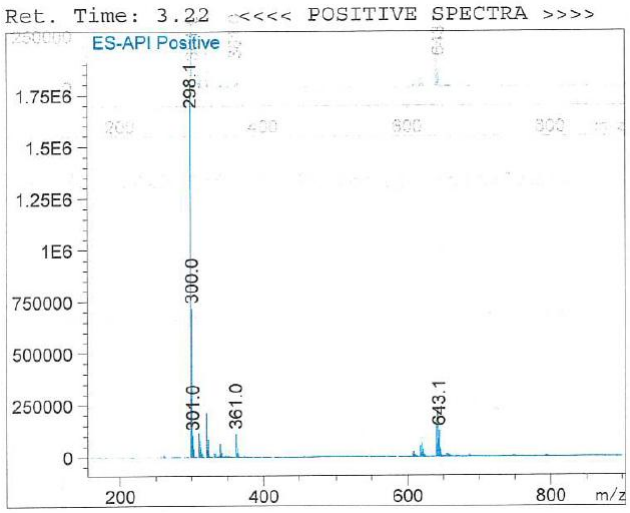
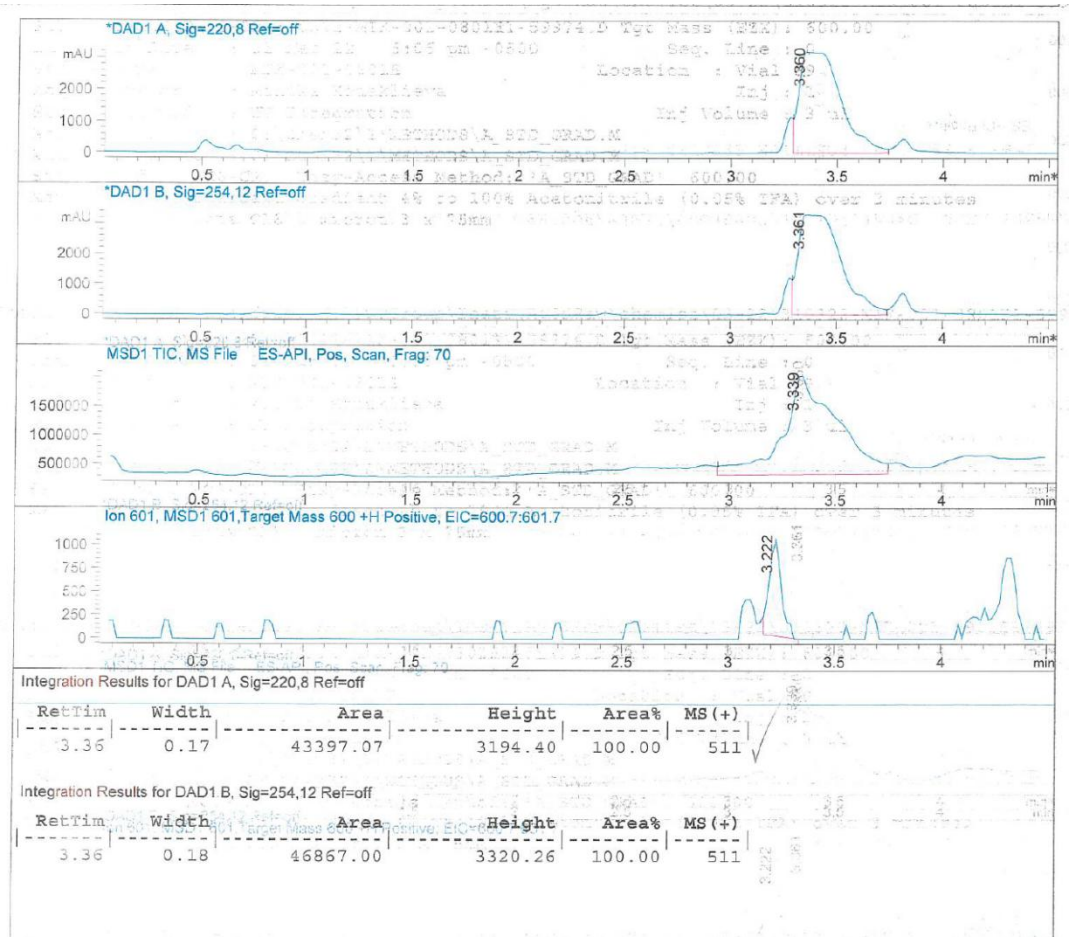


Figure S5. Comp. 6b. 3-amino-*N*-[(2-chlorophenyl)methyl]-5-(methylsulfanyl)-4*H*-1,2,4-triazole-4-carboxamide. Tan, crystalline solid (933 mg, 81.5%). MP 120.98°C; LC/MS-ESI (*m/z*): 298 ($M+H^+$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.64 (t, J = 6.2 Hz, 2H), 7.45 (d, J = 1.0 Hz, 2H), 7.45–7.39 (m, 2H), 6.03 (s, 1H), 4.29 (d, J = 6.0 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.35, 151.22, 136.25, 132.19, 129.53, 129.06, 128.79, 127.62, 41.21, 13.66; Anal. Calcd for $C_{11}H_{12}ClN_5OS$, 297.76; found, 299.21; IR (cm^{-1}): 1,722.38 (C=O).



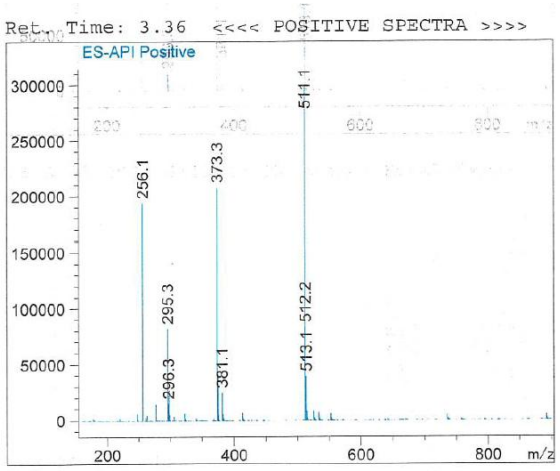
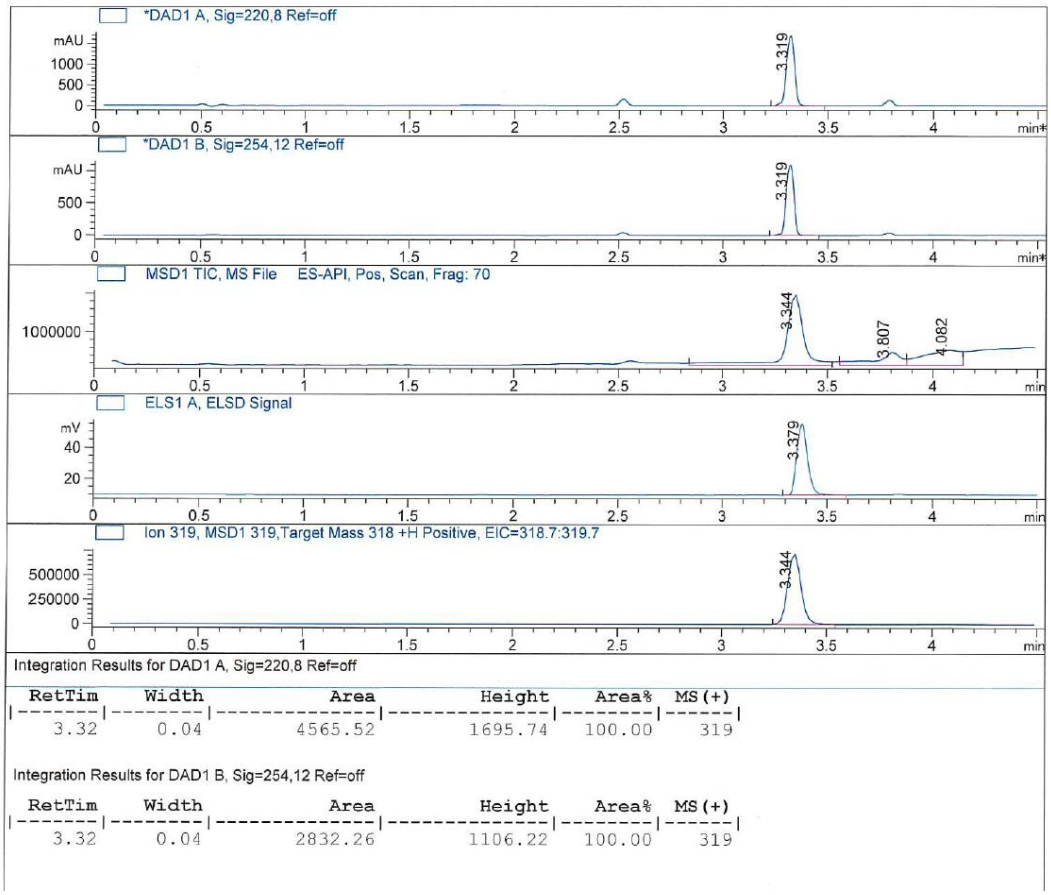


Figure S6. Comp. 6c. 5-amino-*N*-(3-(4-(5-amino-3-(methylthio)-1*H*-1,2,4-triazole-1-carboxamido)benzyl)phenyl)-3-(methylthio)-1*H*-1,2,4-triazole-1-carboxamide. Very light yellow solid (100 mg, 55%). LC/MS-ESI (*m/z*): 511 ($M+H^+$); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.11 (s, 1H), 7.49–7.43 (m, 2H), 7.15 (dt, J = 7.6, 0.9 Hz, 2H), 7.04 (s, 2H), 3.84 (p, J = 0.9 Hz, 1H), 2.63 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.99, 159.97, 150.27, 138.41, 134.62, 130.29, 120.08, 42.07, 13.26.



Integration Results for DAD1 A, Sig=220,8 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.32	0.04	4565.52	1695.74	100.00	319

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.32	0.04	2832.26	1106.22	100.00	319

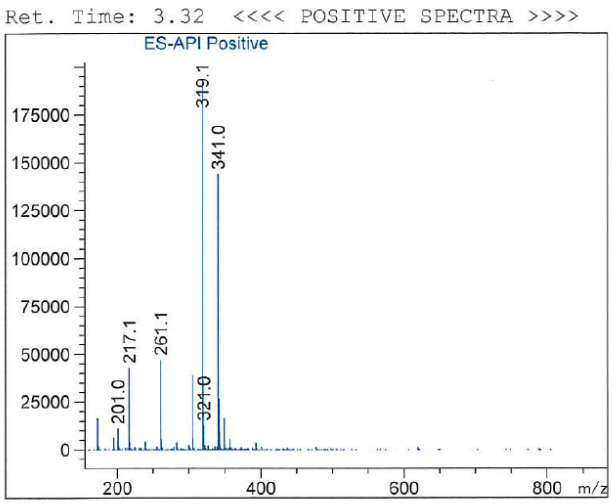
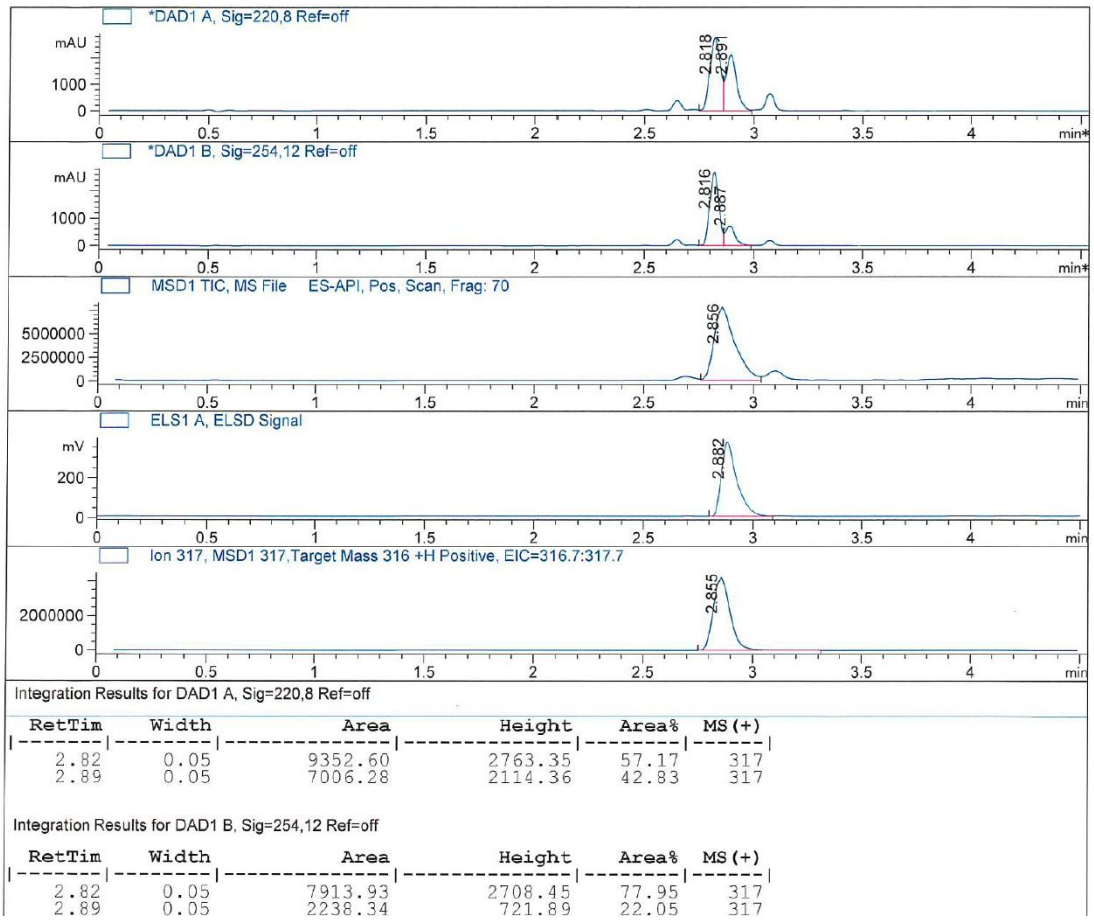


Figure S7. Comp. 7d. *N*-(2-cyanophenyl)-3-((2,4-difluorophenyl)thio)propenamide. White solid (100 mg, 30%). LC/MS-ESI (*m/z*): 319 ($M+H^+$); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.39 (s, 1H), 7.72 (dd, J = 6.6, 1.4 Hz, 1H), 7.66 (dd, J = 7.9, 1.4 Hz, 1H), 7.45 (ddd, J = 7.9, 6.8, 1.3 Hz, 1H), 7.28–7.20 (m, 2H), 6.99–6.89 (m, 2H), 3.26 (t, J = 5.9 Hz, 2H), 2.69 (t, J = 5.9 Hz, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.77, 163.45, 163.34, 162.21, 162.11, 161.48, 161.37, 160.22, 160.12, 141.60, 133.24, 131.58, 131.53, 131.51, 131.46, 131.42, 122.53, 121.48, 121.20, 121.17, 121.10, 121.07, 117.61, 113.17, 113.13, 112.99, 112.95, 105.34, 105.14, 105.13, 104.93, 100.00, 36.52, 29.22, 29.19.



Integration Results for DAD1 A, Sig=220,8 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
2.82	0.05	9352.60	2763.35	57.17	317
2.89	0.05	7006.28	2114.36	42.83	317

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
2.82	0.05	7913.93	2708.45	77.95	317
2.89	0.05	2238.34	721.89	22.05	317

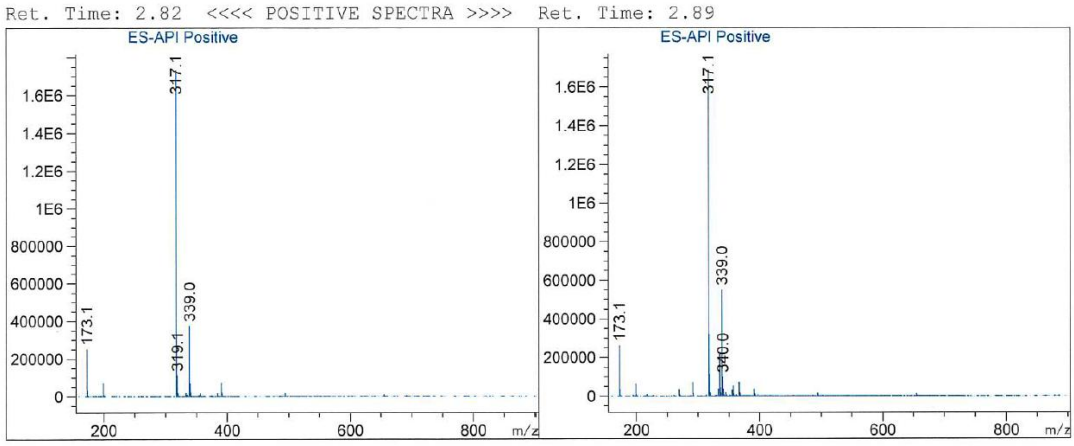
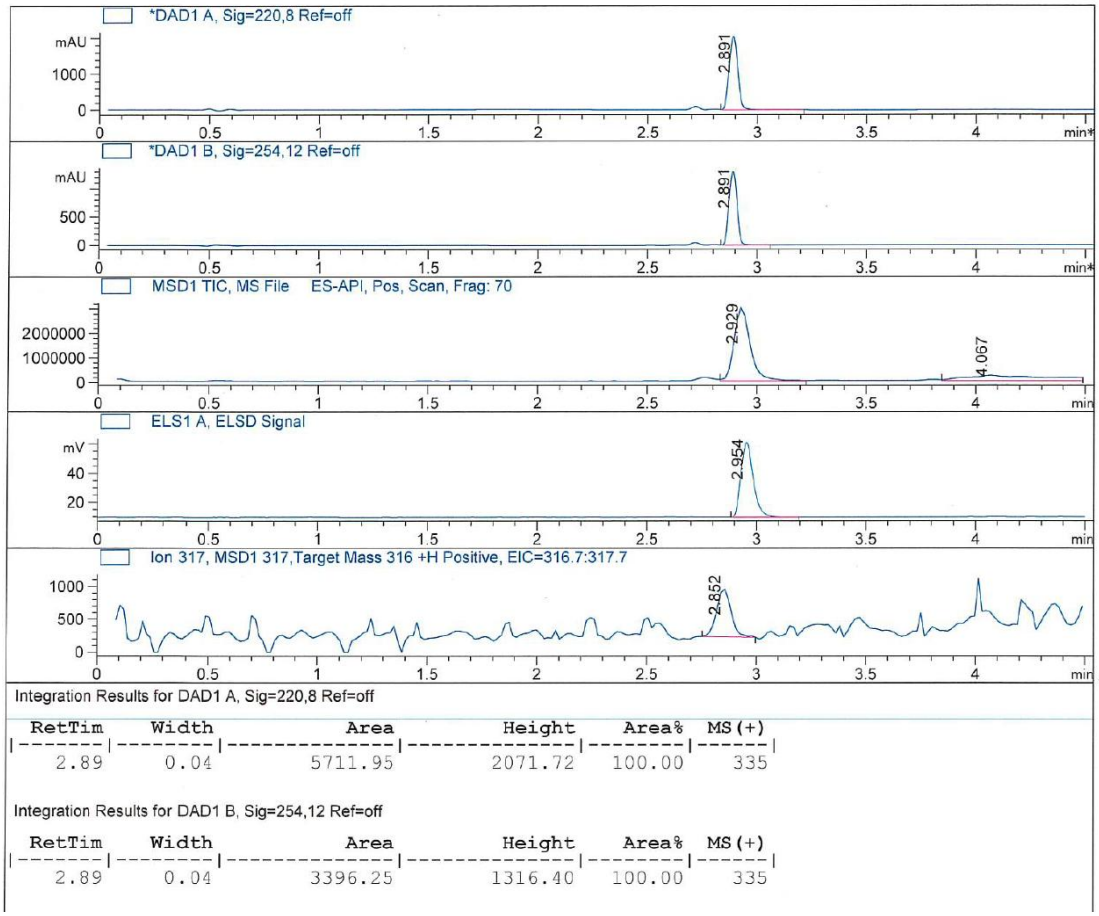


Figure S8. Comp. 7i. *N*-(2-cyanophenyl)-3-((2-fluorophenyl)sulfinyl)propenamide. White solid (55 mg, 35%) LC/MS-ESI (*m/z*): 317 ($M+H^+$).



Integration Results for DAD1 A, Sig=220,8 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
2.89	0.04	5711.95	2071.72	100.00	335

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
2.89	0.04	3396.25	1316.40	100.00	335

Ret. Time: 2.89 <<<< POSITIVE SPECTRA >>>>

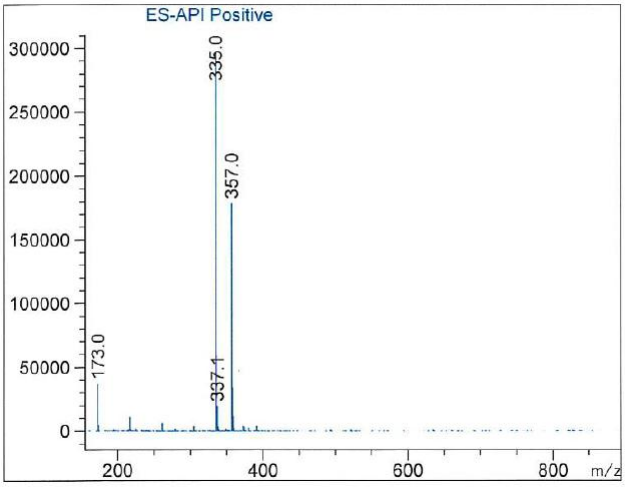
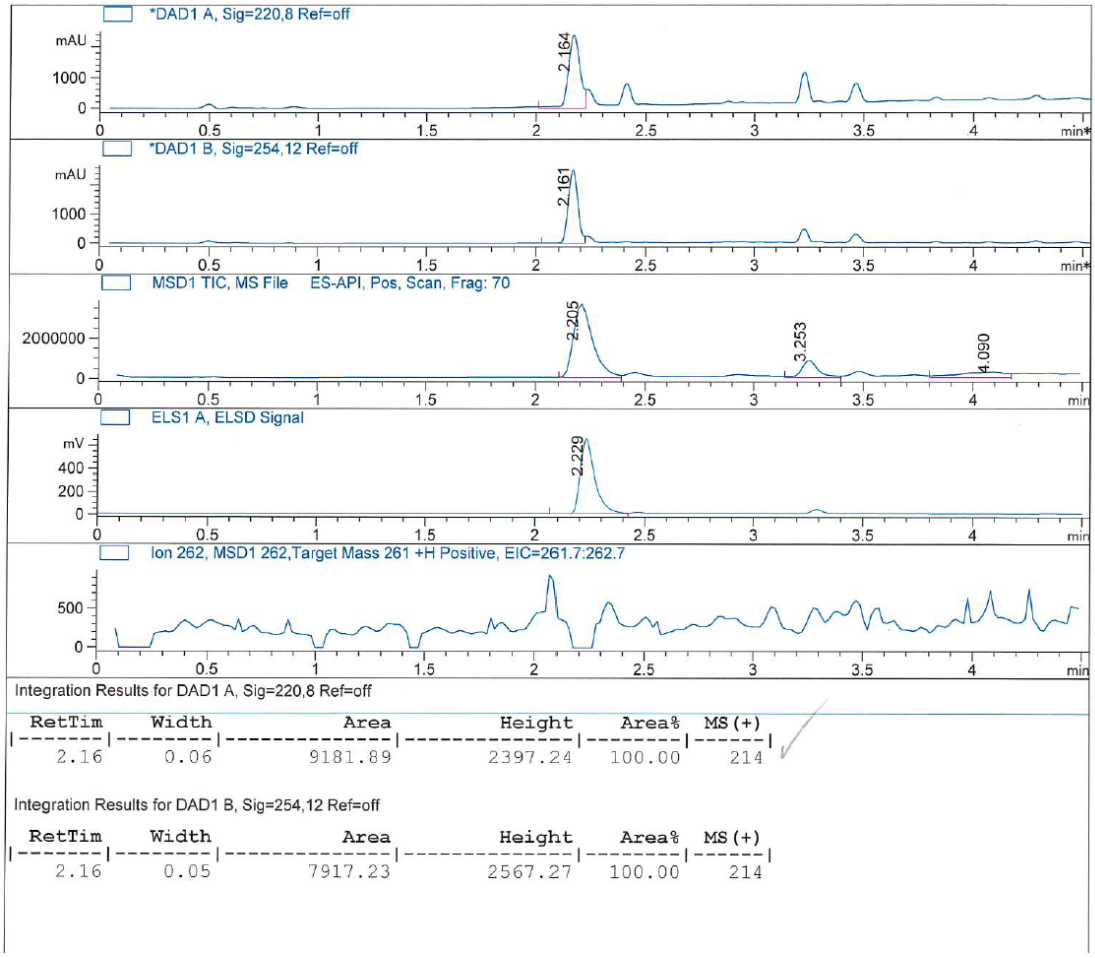


Figure S9. Comp. 7j. *N*-(2-cyanophenyl)-3-((2,4-difluorophenyl)sulfinyl)propenamide. White solid (60 mg, 35%). LC/MS-ESI (*m/z*): 335 ($M+H^+$), 357 ($M+Na^+$).



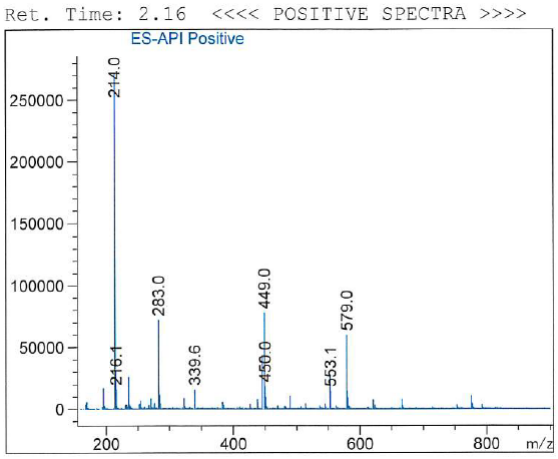


Figure S10. Comp. 8c. 4-((2-fluorophenyl)(methylidyne)(l1-oxidaneyl)-l6-sulfaneyl)azetidin-2-one. White solid (50 mg, 33%). LC/MS-ESI (*m/z*): 214 ($M+H^+$); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (ddd, *J* = 8.7, 3.6, 1.4 Hz, 1H), 7.56 (tdd, *J* = 7.5, 3.9, 1.4 Hz, 1H), 7.40 (ddd, *J* = 9.0, 7.9, 1.4 Hz, 1H), 7.23–7.12 (m, 1H), 4.52 (dt, *J* = 7.3, 5.5 Hz, 1H), 3.36 (dd, *J* = 14.7, 5.4 Hz, 1H), 3.11 (dd, *J* = 14.7, 5.4 Hz, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.60, 160.12, 158.09, 133.63, 133.57, 131.21, 131.10, 128.52, 128.48, 125.48, 125.45, 117.39, 117.22, 74.22, 74.16, 36.88.

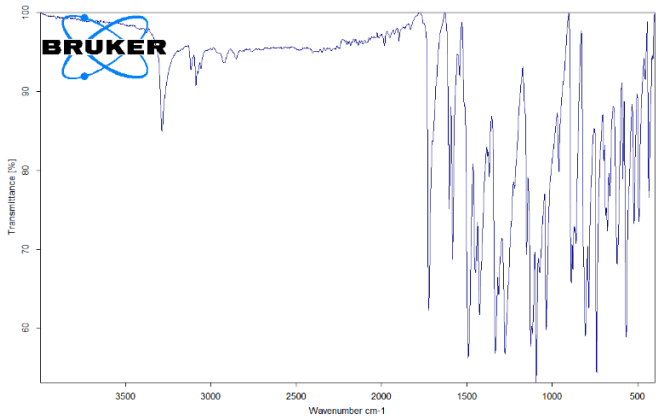


Figure S11. Comp. 9c. *S*-(2,5-Dichlorophenyl)-(2-nitrophenyl)-carbamothioate. Light-yellow crystals (175 mg, 30.4%). MP 154.6-156.8°C; MS *(m/z)*: 341.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98–7.89 (m, 1H), 7.76–7.63 (m, 1H), 7.27 (ddd, J = 8.4, 7.3, 1.3 Hz, 1H), 7.19 (s, 2H), 6.98 (dd, J = 8.5, 1.3 Hz, 1H), 6.59 (ddd, J = 8.7, 6.8, 1.3 Hz, 1H), 2.57–2.51 (m, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.69, 143.25, 140.35, 137.28, 136.13, 134.94, 132.20, 130.66, 127.94, 126.76, 125.81, 124.33, 119.62; Anal. Calcd for $C_{13}H_8Cl_2N_6O_3S$, 343.19; found, 341.2; IR (cm^{-1}): 1,717.69 (C=O).

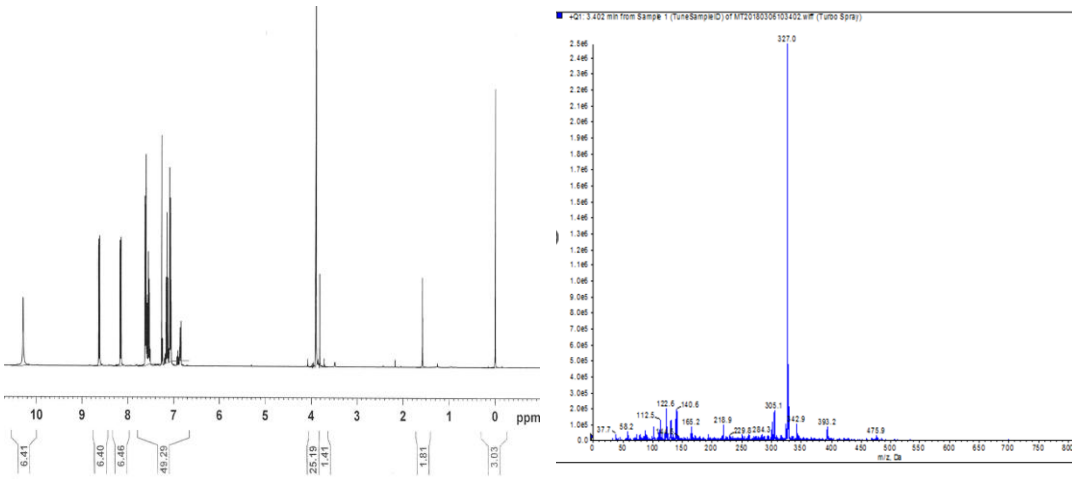
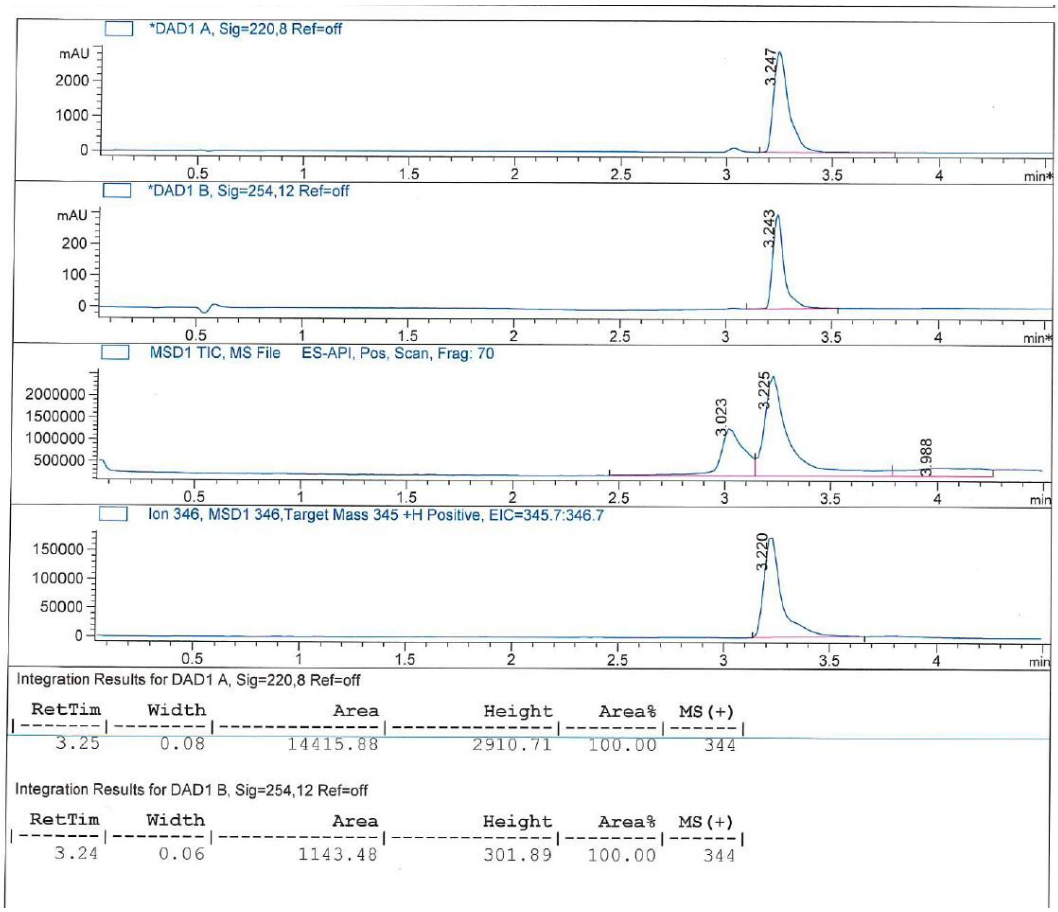


Figure S12. Comp. 9f. *S*-(2-Methoxyphenyl)-(2-nitrophenyl)-carbamothioate (7). Light-yellow crystalline solid (72.6 mg, 39.2%). MP 149.7-152.0°C; MS-ESI (*m/z*): 327.0 (M+Na$^+$); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.44 (s, 1H), 7.71 (dd, J = 8.2, 1.6 Hz, 1H), 7.52–7.44 (m, 1H), 7.44–7.37 (m, 1H), 7.29–7.20 (m, 2H), 7.17 (s, 1H), 7.18–6.97 (m, 1H), 6.93–6.68 (m, 2H), 2.26 (p, J = 1.8 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.58, 159.85, 142.39, 137.71, 134.71, 132.50, 131.39, 125.98, 125.61, 125.40, 121.35, 112.54, 56.37, 31.14; Anal. Calcd for $C_{14}H_{12}N_2O_4S$, 304.32; found, 303.0.



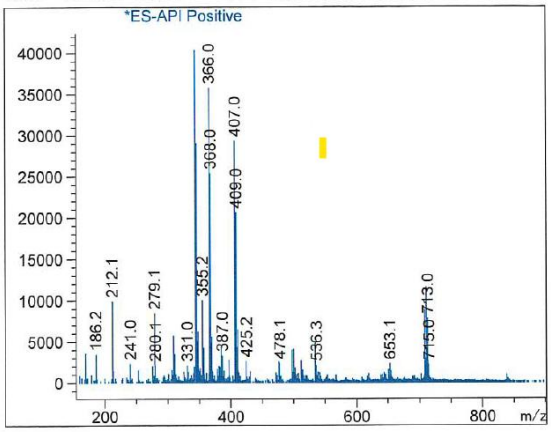
Integration Results for DAD1 A, Sig=220,8 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.25	0.08	14415.88	2910.71	100.00	344

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
3.24	0.06	1143.48	301.89	100.00	344

Ret. Time: 3.25 <<<< POSITIVE SPECTRA >>>>



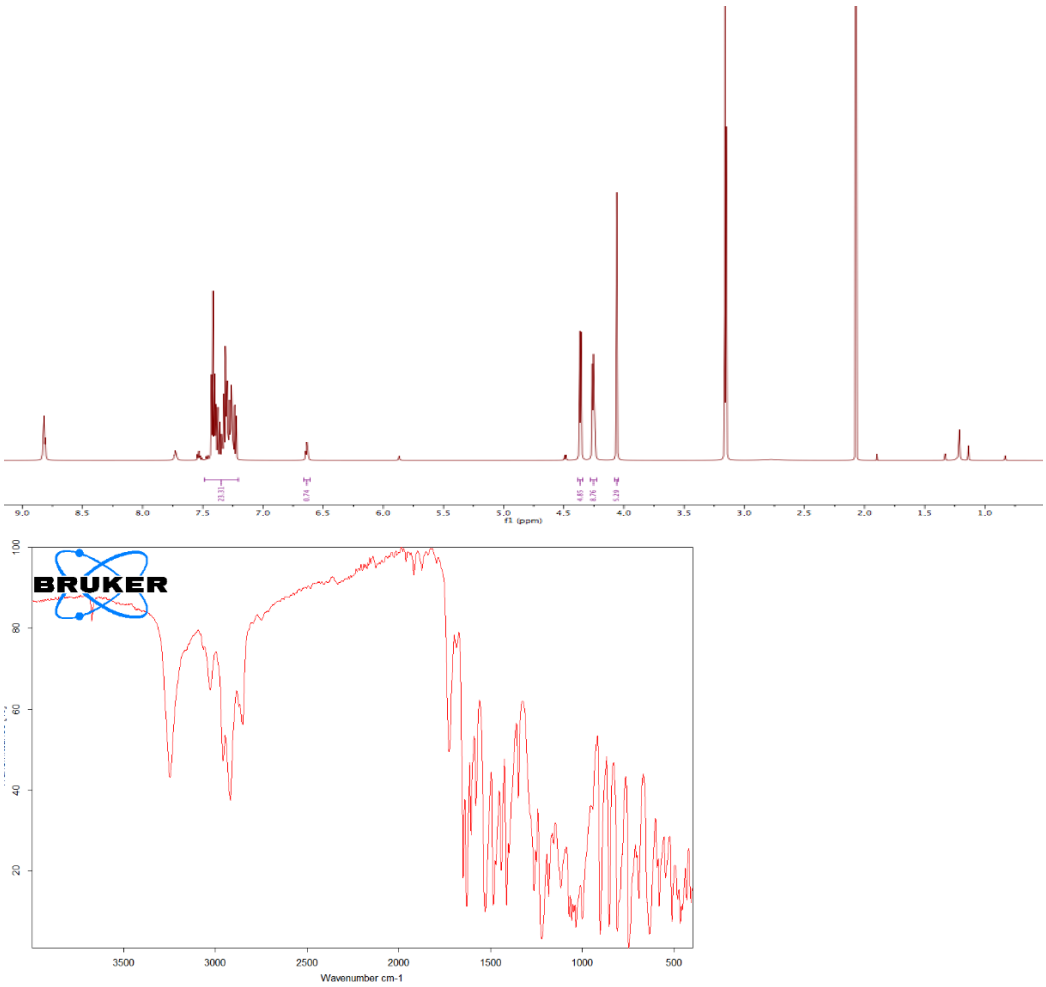
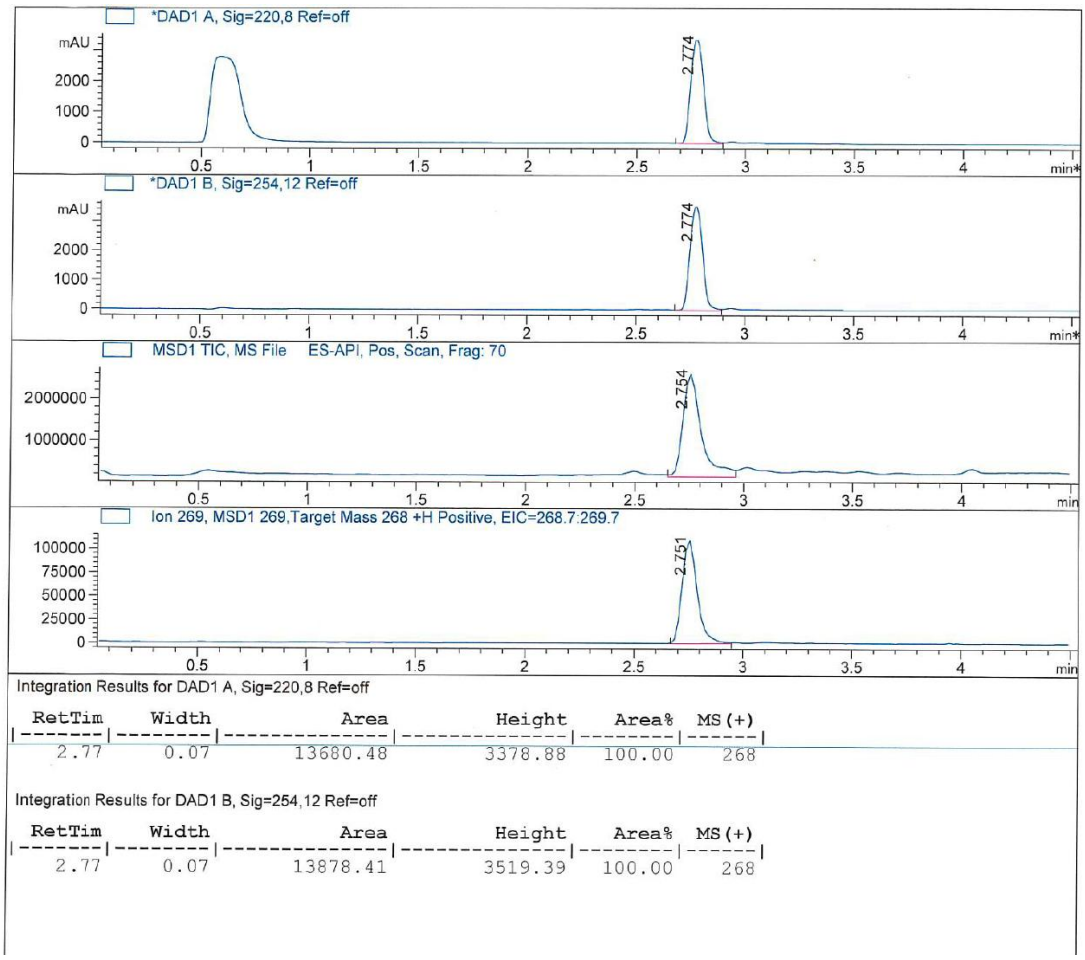


Figure S13. Comp. 9g. *S*-[(4-chloro-2-fluorophenyl)methyl]-[(2-chlorophenyl)methyl]carbamothioate. Orange, crystalline solid (17 mg, 4.1%). MP 198.65°C; LC/MS-ESI (*m/z*): 344.2; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.49–7.21 (m, 8H), 6.64 (t, J = 6.1 Hz, 1H), 4.36 (d, J = 5.7 Hz, 2H), 4.06 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.78, 161.78, 159.26, 137.24, 135.52, 135.44, 133.67, 130.14, 129.47, 129.21, 127.45, 125.60, 122.72, 116.05, 115.85; Anal. Calcd for $C_{15}H_{12}Cl_2FNOS$, 344.23; IR (cm^{-1}): 1,727.08 (C=O).



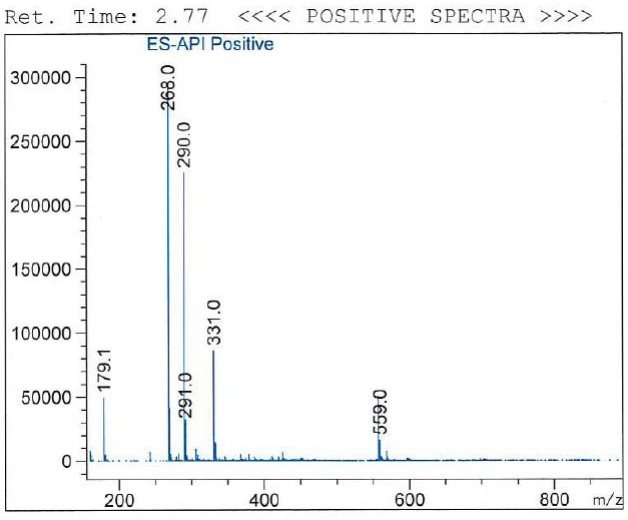


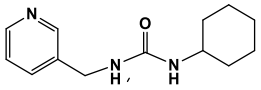
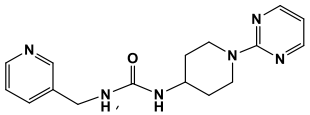
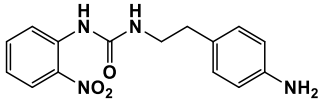
Figure S14. Comp. 11. Compound A-analog 3-((5-(methylthio)-1,3,4-thiadiazol-2-yl)thio)pyrazine-2-carbonitrile. Pale yellow crystals (200 mg, 55%). MP 198.65°C; LC/MS-ESI (*m/z*): 268 ($M+H^+$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 2.0 Hz, 1H), 8.53 (d, J = 2.0 Hz, 1H), 3.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.15, 136.25, 133.00, 129.66, 127.70, 16.18.

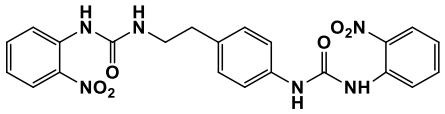
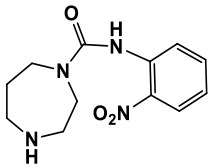
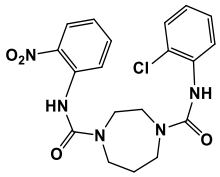
Table S1. Summary of physicochemical characterization data for compounds 7a, 7b, and 9a–d.

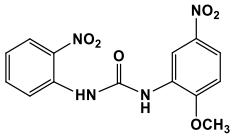
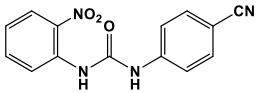
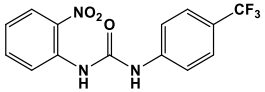
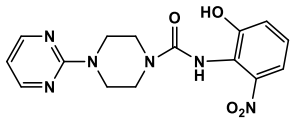
Compounds	Chemical name	Characterization data
7a	4-bromo-*N*-(2-cyanophenyl) benzamide	Bright, yellow crystalline solid (28 mg, 11%). MP 206.2-207.8°C; MS-ESI (*m/z*): 301.0; ^{1}H NMR (400 MHz, DMSO-d_6) 7.88–7.82 (m, 2H), 7.79 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.70 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.67–7.60 (m, 2H), 7.53 (td, *J* = 7.4, 1.5 Hz, 1H), 7.28 (td, *J* = 7.4, 1.5 Hz, 1H), 6.05 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.97, 141.75, 133.06 (d, *J* = 19.4 Hz), 131.86, 130.07, 129.21, 124.32, 123.51, 120.82, 117.32, 100.98; Anal. Calcd for $C_{14}H_9BrN_2O$, 301.14; found, 301.0; IR (cm^{-1}): 1,676.03 (C=O).
7b	*N*-(2-cyanophenyl)-4-(methylamino)benzamide	Tan, crystalline solid (13 mg, 6.1%). MP 145.7-146.9°C; 249.0; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.32 (s, 1H), 7.81 (dd, *J* = 7.5, 1.3 Hz, 3H), 7.70 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.55 (td, *J* = 7.4, 1.5 Hz, 1H), 7.28 (td, *J* = 7.4, 1.5 Hz, 1H), 6.74–6.67 (m, 2H), 5.52 (q, *J* = 2.6 Hz, 1H), 2.91 (d, *J* = 2.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.07, 152.06, 142.11, 133.05, 129.94, 129.74, 129.25, 129.12, 128.10, 123.41, 120.81, 117.12, 112.34, 100.98, 30.27; Anal. Calcd for C15H13N3O, 251.28; found, 249.0; IR (cm^{-1}): 1,713.0 (C=O).
9a	*S*-(2-Chloro-4-fluorophenyl) -[2-(trifluoromethyl)phenyl]-carbamothioate	White, flaky crystals (110 mg, 37.9%). MP 111.5–114.0°C; MS-ESI (*m/z*): 349.1; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.33 (s, 1H), 7.79–7.64 (m, 1H), 7.55–7.43 (m, 1H), 7.32–7.20 (m, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.63–6.55 (m, 1H), 5.80 (s, 1H), 3.40 (d, *J* = 0.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.78, 159.51, 157.03, 137.25, 136.48, 136.41, 135.12, 133.76, 131.26, 128.33, 125.95, 122.46, 120.24, 118.01; Anal. Calcd for $C_{14}H_8ClF_4NOS$, 349.73; found, 349.1.
9b	*S*-[4-(methylsulfanyl)phenyl]-(2-nitrophenyl)-carbamothioate	Bright, yellow crystalline solid (133 mg, 68.2%). MP 105.0-105.8°C; MS-ESI (*m/z*): 342.9 (M+Na^{+}); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.44 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.85 (ddt, *J* = 7.6, 4.9, 2.4 Hz, 1H), 7.70 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.58 (dt, *J* = 9.0, 1.7 Hz, 1H), 7.44 (ddd, *J* = 7.9, 7.2, 1.5 Hz, 1H), 7.43–7.34 (m, 2H), 7.33–7.15 (m, 1H), 7.12 (ddd, *J* = 8.2, 7.3, 1.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-

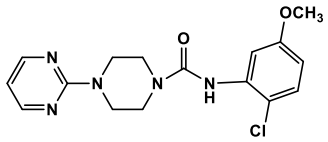
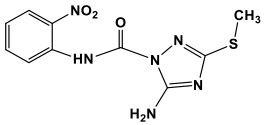
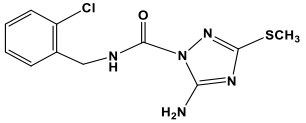
		d_6): NT; Anal. Calcd for $C_{14}H_{12}N_2O_3S_2$, 320.39; found, 319.9.
9c	*S*-(2,5-Dichlorophenyl)-(2-nitrophenyl)-carbamothioate	Light-yellow crystals (175 mg, 30.4%). MP 154.6–156.8°C; MS-ESI (*m/z*): 341.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98–7.89 (m, 1H), 7.76–7.63 (m, 1H), 7.27 (ddd, J = 8.4, 7.3, 1.3 Hz, 1H), 7.19 (s, 2H), 6.98 (dd, J = 8.5, 1.3 Hz, 1H), 6.59 (ddd, J = 8.7, 6.8, 1.3 Hz, 1H), 2.57–2.51 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.69, 143.25, 140.35, 137.28, 136.13, 134.94, 132.20, 130.66, 127.94, 126.76, 125.81, 124.33, 119.62; Anal. Calcd for $C_{13}H_8Cl_2N_6O_3S$, 343.19; found, 341.2; IR (cm^{-1})*:* 1,717.69 (C=O).
9d	*S*-Pyrimidin-2-yl (2-nitrophenyl)-carbamothioate	Yellow crystalline solid (97 mg, 57.7%). MP 111.3–112.5°C; MS-ESI (*m/z*): 287.0; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.02 (s, 1H), 8.25 (s, 1H), 7.92 (dd, J = 8.6, 1.6 Hz, 1H), 7.37 (s, 1H), 7.36 (ddd, J = 8.5, 6.8, 1.6 Hz, 1H), 6.98 (dd, J = 8.6, 1.3 Hz, 1H), 6.81 (t, J = 5.3 Hz, 1H), 6.59 (ddd, J = 8.6, 6.9, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.34, 159.51, 152.91, 140.88, 136.69, 134.00, 131.26, 126.35, 124.87, 120.14, 116.47; Anal. Calcd for $C_{11}H_8N_4O_3S$, 276.27; found, 277.0.

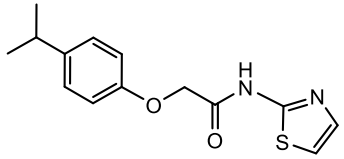
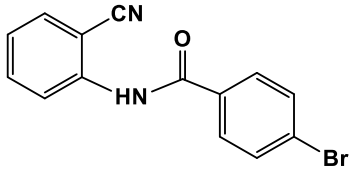
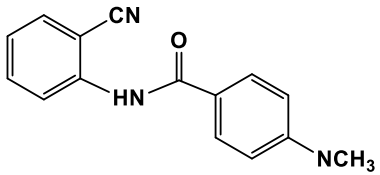
Table S2. Compounds from our library lacking activity, regardless of similarity to referenced active fragments/compounds.

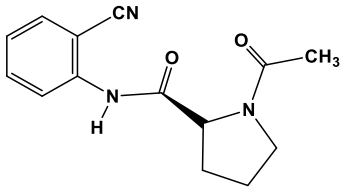
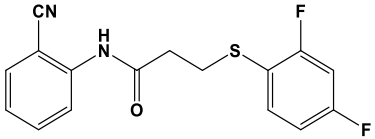
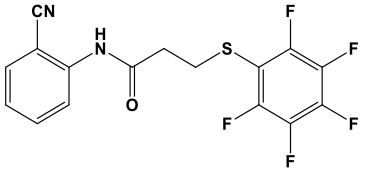
Structure **Name(#)MW/Log P**	***M. marinum*** **(µg/mL)** **Day 7**		**Mtb (µg/mL)** **Day 14**				
	GAST-Fe	**7H9**	**GAST-Fe**	**7H9 Control**	**7H9[a] Media A**	**7H9[b] Media B**	**7H9[c] Media C**
Ureas							
  3-(pyridin-3-yl methyl) ureas as InhA inhibitors [51]							
4a.  1-(4-aminophenethyl)-3-(2-nitrophenyl)urea *MW* = 300.3 Log*P* = 1.8	nd	nd	> 50	> 50	> 50	> 50	37

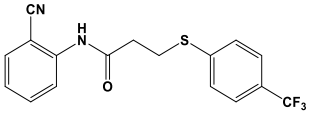
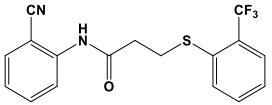
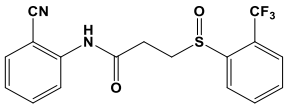
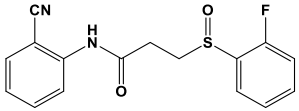
4b.  1-(2-nitrophenyl)-3-(4-(3-(2-nitrophenyl)ureido)phenethyl)urea *MW* = 464.44 Log*P* = 3.24	nd	nd	> 50	> 50	> 50	> 50	> 50
4c.  N-(2-nitrophenyl)-1,4-diazepane-1-carboxamide *MW* = 264.29 Log*P* = 0.73	nd	nd	> 50	> 50	> 50	> 50	> 50
4d.  N1-(2-chlorophenyl)-N4-(2-nitrophenyl)-1,4-diazepane-1,4-dicarboxamide *MW* = 417.85 Log*P* = 2.88	nd	nd	> 50	> 50	> 50	> 50	> 50

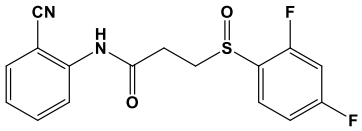
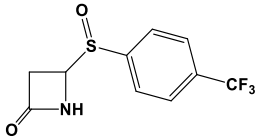
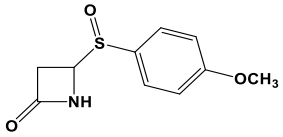
4e.  1-(2-methoxy-5-nitrophenyl)-3-(2-nitrophenyl)urea *MW* = 332.27 Log*P* = 2.58	nd	nd	nd	> 50	> 50	> 50	37
4f.  N-(4-cyanophenyl)-N'-(2-nitrophenyl) urea *MW* = 298.30 Log*P* = 3.04	> 50	> 50	> 50	> 50	nd	nd	nd
4g.  N-(2-nitrophenyl)-N'-[4-(trifluoromethyl)phenyl] urea *MW* = 325.25 Log*P* = 3.47	> 50	> 50	> 50	> 50	nd	nd	nd
5a. 	nd	nd	nd	> 50	> 50	> 50	> 50

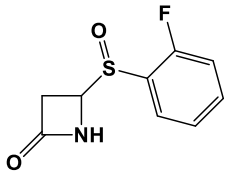
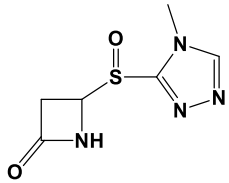
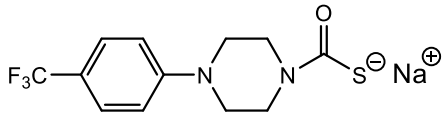
N-(2-hydroxy-6-nitrophenyl)-4-(pyrimidin-2-yl)piperazine-1-carboxamide *MW* = 344.33 Log*P* = 0.36							
5b.	> 50	> 50	> 50	> 50	> 50	> 50	> 50
 N-(2-chloro-5-methoxyphenyl)-4-(pyrimidin-2-yl)piperazine-1-carboxamide *MW* = 347.80 Log*P* = 1.92							
6a.	> 50	> 50	> 50	> 50	> 50	> 50	> 50
 3-amino-5-(methylsulfanyl)-N-(2-nitrophenyl)-1H-1,2,4-triazole-1-carboxamide *MW* = 294.29 Log*P* = 1.12							
6b.	nd	nd	nd	nd	> 50	> 50	25
 5-amino-N-(2-chlorobenzyl)-3-(methylthio)-1H-1,2,4-triazole-1-carboxamide							

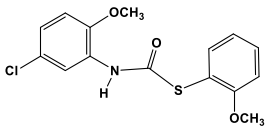
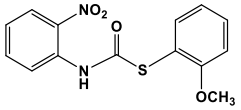
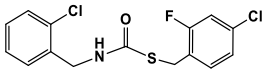
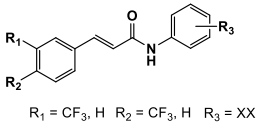
MW = 297.76 CLog*P* = 2.24 **Amides**  [51]							
7a.  4-bromo-N-(2-cyanophenyl)benzamide *MW* = 301.14 Log*P* = 3.7	> 50	> 50	> 50	> 50	nd	nd	nd
7b.  N-(2-cyanophenyl)-4-(methylamino)benzamide *MW* = 250.28 Log*P* = 2.37	> 50	> 50	> 50	> 50	nd	nd	nd

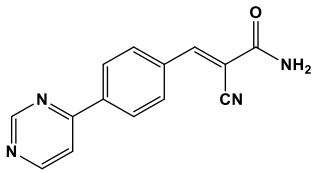
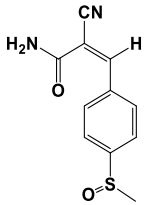
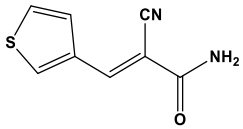
7c.  (R)-1-acetyl-N-(2-cyanophenyl)pyrrolidine-2-carboxamide *MW* = 257.29 Log*P* = 0.53	> 50	> 50	25	> 50	nd	nd	nd
7d.  N-(2-cyanophenyl)-3-((2,4-difluorophenyl)thio)propanamide *MW* = 318.06 Log*P* = 3.63	> 50	> 50	> 50	> 50	> 50	> 50	> 50
7e.  N-(2-cyanophenyl)-3-((perfluorophenyl)thio)propanamide *MW* = 372.31 Log*P* = 4.1	> 50	> 50	> 50	> 50	nd	nd	nd

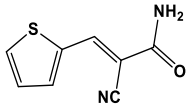
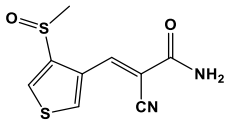
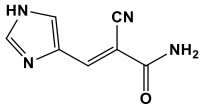
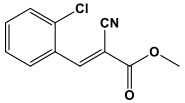
7f.  N-(2-cyanophenyl)-3-((4-(trifluoromethyl)phenyl)thio)propanamide *MW* = 350.36 Log*P* = 4.24	> 50	> 50	> 50	> 50	nd	nd	nd
7g.  N-(2-cyanophenyl)-3-((2-(trifluoromethyl)phenyl)thio)propenamide *MW* = 350.36 Log*P* = 4.24	> 50	> 50	> 50	> 50	> 50	> 50	> 50
7h.  N-(2-cyanophenyl)-3-((2-(trifluoromethyl)phenyl)sulfinyl)propenamide *MW* = 366.36 Log*P* = 2.63	nd	nd	nd	nd	> 50	> 50	> 50
7i.  N-(2-cyanophenyl)-3-((2-fluorophenyl)sulfinyl)propenamide	> 50	> 50	50	> 50	nd	nd	nd

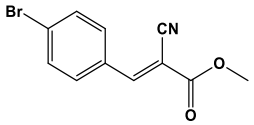
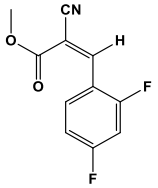
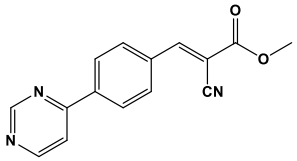
MW = 316 CLog*P* = 1.87							
7j. 	> 50	> 50	> 50	> 50	nd	nd	nd
N-(2-cyanophenyl)-3-((2,4-difluorophenyl)sulfinyl)propenamide *MW* = 334 CLog*P* = 2.02							
8a. 	nd	nd	nd	nd	> 50	> 50	> 50
4-((1-oxidaneyl)(4-(trifluoromethyl)phenyl)-3-sulfaneyl)azetidin-2-one MW = 263.23 CLog*P* = 1.08							
8b. 	nd	nd	nd	nd	> 50	> 50	> 50
4-((4-methoxyphenyl)sulfinyl)azetidin-2-one *MW* = 225.26 Log*P* = 0.5							

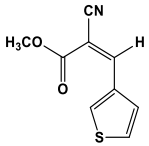
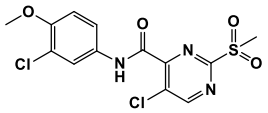
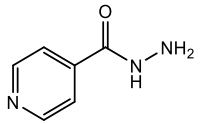
8c.  4-((2-fluorophenyl)(methylidyne)(l1-oxidaneyl)-l6-sulfaneyl)azetidin-2-one *MW* = 247.6 Log*P* = 1.09	> 50	> 50	50	> 50	nd	nd	nd
8d.  4-((4-methyl-4H-1,2,4-triazol-3-yl)(methylidyne)(l1-oxidaneyl)-l6-sulfaneyl)azetidin-2-one *MW* = 213.24 Log*P* = –2.27	> 50	> 50	> 50	> 50	nd	nd	nd
Carbamothioates  [41, 42]							

9e.  S-(2-methoxyphenyl) (5-chloro-2-methoxyphenyl)carbamothioate *MW* = 323.79 Log*P* = 4.06	> 50	> 50	> 50	50	nd	nd	nd
9f.  S-(2-methoxyphenyl) (2-nitrophenyl) carbamothioate *MW* = 304.32 Log*P* = 3.85	> 50	> 50	> 50	> 50	nd	nd	nd
9g.  S-(4-chloro-2-fluorobenzyl) (2-chlorobenzyl)carbamothioate *MW* = 344.23 Log*P* = 5.17	nd	nd	nd	nd	> 50	> 50	19
Michael acceptors  R_1 = CF_3, H R_2 = CF_3, H R_3 = XX [39]							

10a.  (E)-2-methyl-3-(4-(pyrimidin-4-yl)phenyl)acrylamide *MW* = 250.26 Log*P* = 1.24	> 50	> 50	> 50	> 50	nd	nd	nd
10b.  (Z)-2-cyano-3-(4-(methylsulfinyl)phenyl)acrylamide *MW* = 234.28 Log*P* = –0.16	> 50	> 50	> 50	> 50	nd	nd	nd
10c.  (E)-2-cyano-3-(thiophen-3-yl)acrylamide *MW* = 178.21 Log*P* = 1.1	> 50	> 50	> 50	> 50	nd	nd	nd

10d.  (E)-2-cyano-3-(thiophen-2-yl)acrylamide *MW* = 178.21 Log*P* = 1.16	> 50	> 50	> 50	> 50	nd	nd	nd
10e.  (E)-2-methyl--(4-(methylsulfinyl)thiophen-3-yl)acrylamide *MW* = 240.30 Log*P* = –0.24	> 50	> 50	> 50	> 50	nd	nd	nd
10f.  (E)-3-(1H-imidazol-4-yl)-2-methylacrylamide *MW* = 162.15 Log*P* = –1.1	> 50	> 50	> 50	> 50	nd	nd	nd
10g.  methyl (E)-3-(2-chlorophenyl)-2-methylacrylate	> 50	> 50	50	> 50	nd	nd	nd

MW = 221.64 Log*P* = 2.65							
10h.	> 50	> 50	50	> 50	nd	nd	nd
 methyl (E)-3-(4-bromophenyl)-2-cyanoacrylate *MW* = 266.09 Log*P* = 2.92							
10i.	> 50	> 50	50	> 50	nd	nd	nd
 methyl (Z)-2-cyano-3-(2,4-difluorophenyl)acrylate *MW* = 223.18 Log*P* = 2.41							
10j.	> 50	> 50	> 50	> 50	nd	nd	nd
 methyl (E)-2-cyano-3-(4-(pyrimidin-4-yl)phenyl)acrylate *MW* = 265.27 Log*P* = 2.26							

10k.  methyl (Z)-2-cyano-3-(thiophen-3-yl)acrylate *MW* = 193.22 Log*P* = 2.02	> 50	> 50	> 50	> 50	nd	nd	nd
12.  AC2P36 [50]	nd	nd	nd	nd	nd	nd	nd
Positive controls							
Rifampicin	1.5	1.5	0.002	0.01	nd	nd	nd
Isoniazid  *MW* = 137.17 Log*P* = –0.64	nd	nd	nd	nd	0.02	0.03	0.07

nd = not determined

Table S3. Bacterial strains referenced herein.

Bacterium	OD_{600} at the time of setup	Medium
Staphylococcus aureus 13801	0.255	MHB
Enterococcus faecium 19581	0.178	MHB
Proteus vulgaris	0.138	MHB
Pseudomonas aeruginosa PA01	0.183	MHB
Corynebacterium glutamicum	0.147	MHB
Mycobacterium marinum	~0.2*	7H9 and GAST/Fe
Mycobacterium tuberculosis H37Rv	~0.2*	7H9 and GAST/Fe

*Exact OD_{600} not available

Table S4. **Activity of novel fragments on *M. marinum* and Mtb under various growth conditions.**

S No	Compound name	*Mycobacterium marinum* (µg/ml)				*Mycobacterium tuberculosis* (µg/ml)			
		Day 3/GAST-Fe	Day 7/GAST-Fe	Day 3/7H9	Day 7/7H9	Day 7/GAST-Fe	Day 14/GAST-Fe	Day 7/7H9	Day 14/7H9
1	MK11	50	> 50	> 50	> 50	50	> 50	50	> 50
2	MMK6	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
3	MK12	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
4	MK13	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
5	MK14	> 50	> 50	50	> 50	> 50	> 50	> 50	> 50
6	MK5	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
7	MK7	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
8	MC71	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
9	MK3	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
10	MK10	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
11	JC04	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
12	JC02	6.25	9.375	≥ 50	> 50	1.5	6.25	25	50

13	JC12	25	37.5	50	50	3.12	6.25	25	25
14	JC13	≥ 50	≥ 50	> 50	> 50	25	50	50	≥ 50
15	JC19	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
16	JC40	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
17	JC20	37.5	> 50	> 50	> 50	12.5	12.5	37.5	50
18	JC32	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
19	JC27	25	> 50	> 50	> 50	> 50	> 50	> 50	> 50
20	JC28	50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
21	JC11	25	25	50	≥ 50	1.5	6.25	25	25
22	JC16	50	50	> 50	> 50	25	50	50	≥ 50
23	JC10	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
24	JC05	50	> 50	> 50	> 50	12.5	25	> 50	> 50
25	JC39	> 50	> 50	> 50	> 50	25	25	> 50	> 50
26	JC18	12.5	12.5	25	> 50	12.5	12.5	25	25
27	JC15	> 50	> 50	> 50	> 50	12.5	12.5	≥ 50	> 50
28	JC31	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50

29	MC73	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
30	SM6	50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
31	SM9	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
32	SM8-4	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
33	SM7-3	50	> 50	> 50	> 50	25	50	> 50	> 50
34	KE22	> 50	> 50	> 50	> 50	50	> 50	> 50	> 50
35	MC62	50	50	> 50	> 50	25	25	> 50	> 50
36	KE24	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
37	MC70	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
38	SM7-4	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
39	MC63	> 50	> 50	> 50	> 50	> 50	> 50	> 50	> 50
Positive control									
40	Rif (uM)	1.5	1.5	1.5	1.5	0.002	0.002	0.01	0.01

The letter abbreviations of the compounds are the original chem lab numbers (raw MIC data).

Table S5. Data from compounds tested in Mtb in cholesterol-containing media (DPPC and DPPC-Cas).

Compound	7H9		GASTFe		DPPC		DPPC-Cas		Glu-Cas	
	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14
DL11	> 50	> 50	12.5	12.5	50.0	50.0	6.3	6.3	6.3	9.4
DL12	≥ 50	> 50	12.5	12.5	50.0	50.0	6.3	12.5	6.3	12.5
DL13	> 50	> 50	12.5	18.8	50.0	50.0	6.3	12.5	6.3	12.5
DL14	> 50	> 50	12.5	18.8	25.0	50.0	3.1	6.3	3.1	6.3
RK5/MC60	25.0	50.0	6.3	12.5	12.5	25.0	1.5	3.1	1.5	4.6
DL35/MC61	> 50	> 50	6.3	9.4	25.0	25.0	3.1	3.1	3.1	4.6
CR04/MC62	18.8	25.0	3.1	12.5	6.3	25.0	0.8	2.3	0.8	2.3
CONTROL-INH	0.4	0.8	0.1	0.4	0.4	0.4	0.1	0.2	0.2	0.2

	DPPC		DPPC-Cas		Glu-Cas	
	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14
RK3	12.5	25.0	3.1	6.3	3.1	9.4
D2	50.0	≥ 50	6.3	12.5	6.3	12.5
RK16	25.0	50.0	3.1	3.1	3.1	6.3
RK5	12.5	25.0	1.5	3.1	1.5	3.1
DL35	25.0	37.5	3.1	4.6	2.3	4.6
CR04	12.5	25.0	1.5	2.3	0.8	2.3

BSA-containing media; casitone-containing media (no BSA).

Table S6. MIC of select compounds in the presence and absence of cholesterol.

	7H9		Glu		Chol		DPPC		Glu-Cas		DPPC-Cas	
	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14
DL06	1.5	12.5	3.1	6.25	6.25	25	6.25	25	0.39	0.585	0.78	0.78
8b(KL03)	25	50	50	50	25	50	25	37.5	6.25	9.35	0.78	3.12
DL46	12.5	25	12.5	25	12.5	18.75	12.5	12.5	0.78	1.5	0.39	0.78
RK3	25	25	12.5	25	6.25	12.5	6.25	12.5	3.1	12.5	0.39	0.78
RK6	6.25	25	12.5	25	6.25	25	6.25	25	1.5	1.5	0.39	0.78
D2	50	100	50	100	12.5	50	25	50	6.25	50	0.78	4.675
MK102	12.5	25	25	25	12.5	25	25	12.5	3.1	6.25	0.78	1.5
RK16	25	50	25	100	12.5	100	12.5	100	1.5	12.5	0.78	1.5

BSA-containing media; casitone-containing media (no BSA).