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LETTERS

Synthesis of 1,4-disubstituted-1,2,3-Triazole derivatives for investigation of inhibition and molecular docking studies against Xanthine Oxidase

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Supporting Information

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Physical and spectroscopic data of compounds 9a-e

9a

1-(3-Fluorobenzyl)-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole. Solid, m.p: 145 ^{o}C[33], yield: 31%. IR vmax (cm^{-1}): 3105, 2916, 1617, 1501, 1458, 1027. ^{1}H-NMR (δ (ppm), $CDCl_3$): 7.73 (d, *J= 8.8 Hz*, 2H), 7.67 (s, 1H), 7.35 (m, 1H), 7.07 (m, 1H), 7.04 (m, 1H), 7.00 (m, 1H), 6.94 (d, *J*= 8.8 Hz, 2H), 5.55 (s, 2H), 3.82 (s, 3H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 163.1, 159.7, 148.6, 137.3, 130.8, 127.1, 123.6, 123, 119, 115.8, 115, 114.3, 55.4, 53.5. HRMS (TOF): m/*z* calcd for $C_{16}H_{14}FN_3O$: 283.3064 found: 284.12040 $[M+H]^+$

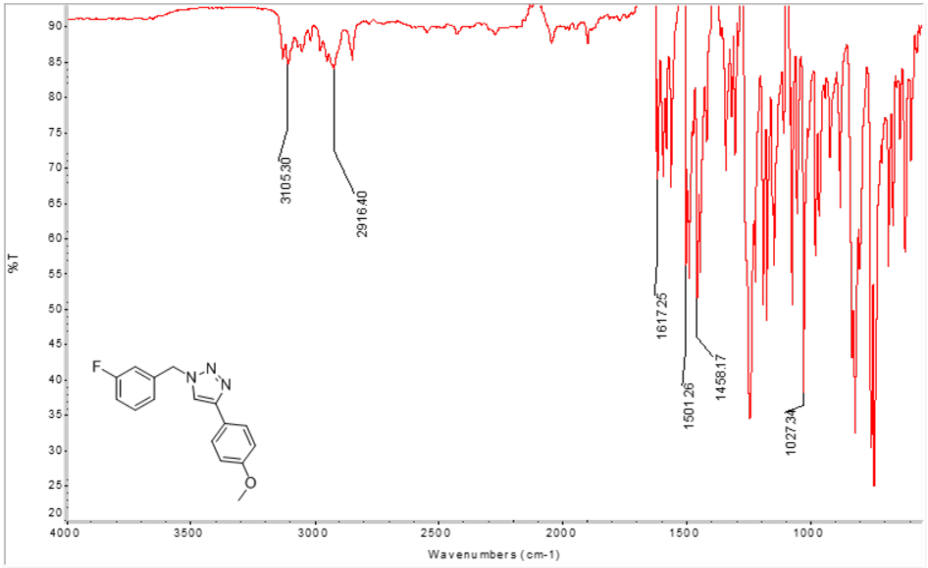

Figure S1. FTIR of 9a compound

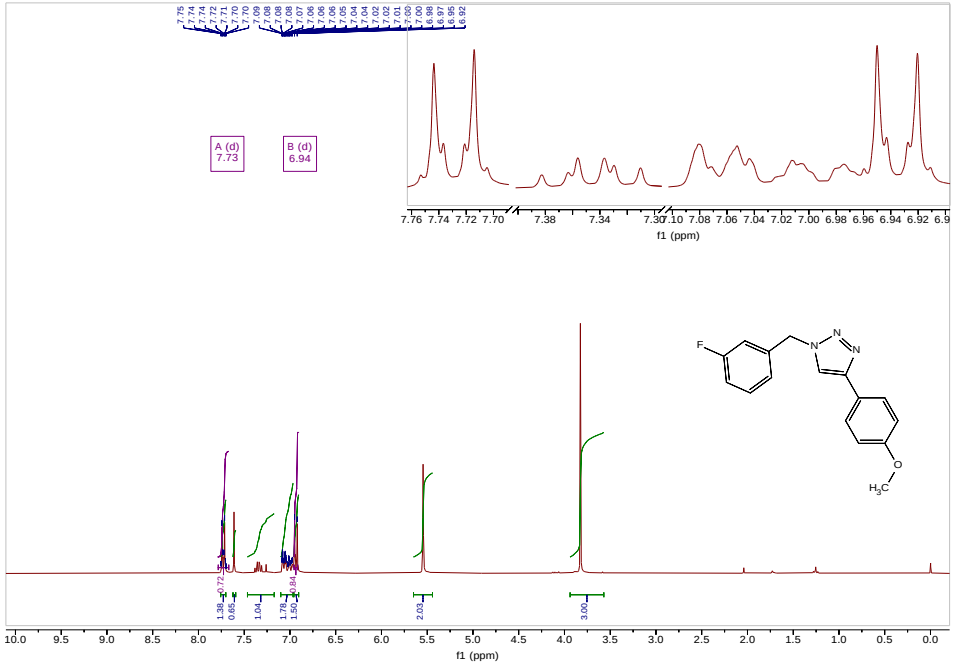

Figure S2. ^{1}H-NMR of 9a compound

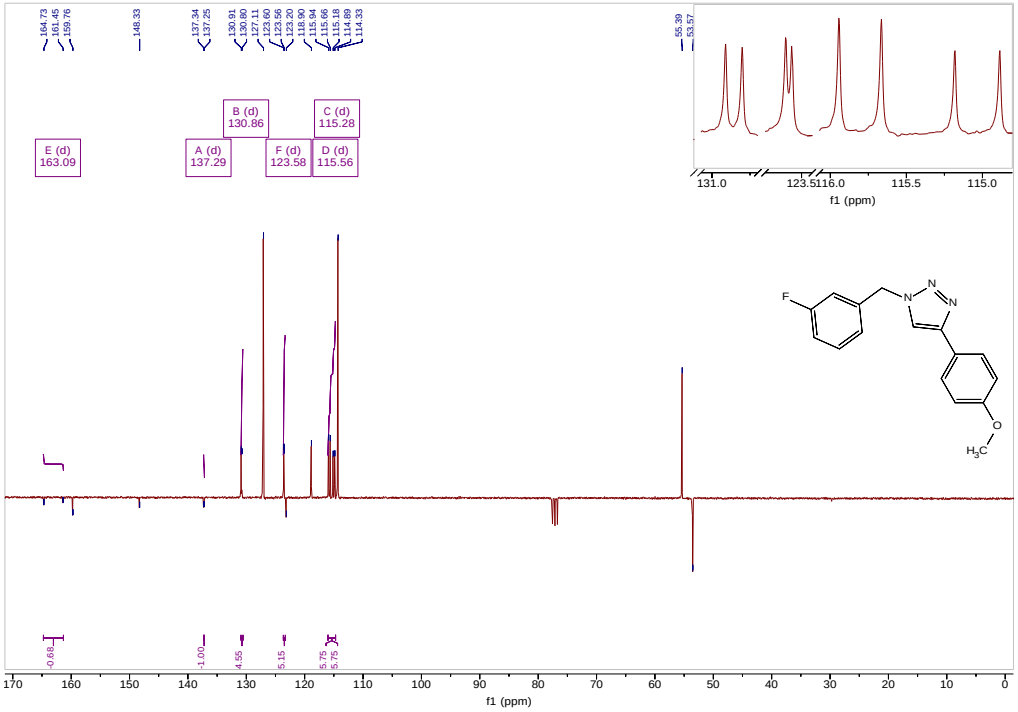

Figure S3. ^{13}C-APT NMR of 9a compound

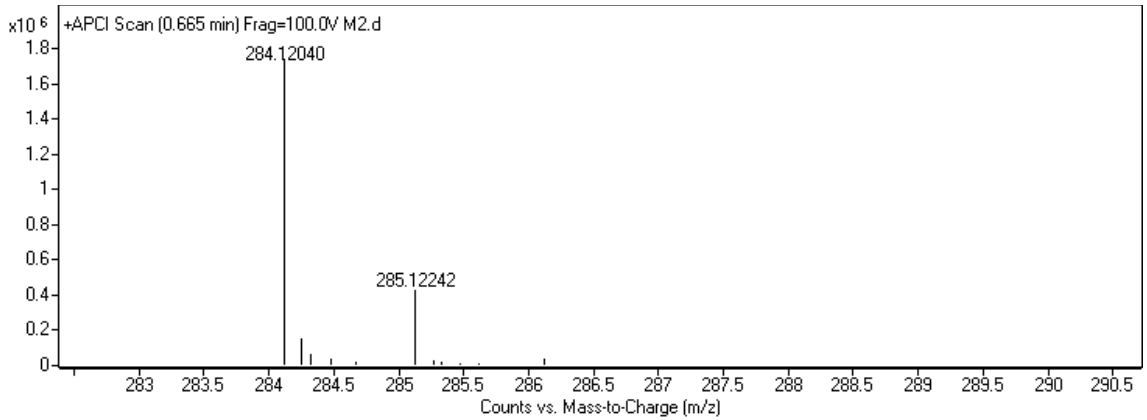

Figure S4. HRMS-TOF of 9a compound

9b

1-(4-Fluorobenzyl)-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole. Solid, m.p: 157 ^{o}C[34], yield: 93%. IR vmax (cm-1): 3135, 2926, 1607, 1502, 1458, 1222. ^{1}H-NMR (δ (ppm), $CDCl_3$): 7.72 (d, *J*= 8.8 Hz, 2H), 7.57 (s, 1H), 7.30 (dd, *J*= 8.6, 5.3 Hz, 2H), 7.08 (t, *J*= 8.6 Hz, 2H), 6.94 (d, *J*= 8.8 Hz, 2H), 5.65 (s, 2H), 3.82 (s, 3H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 163, 159.8, 148.2, 130.8, 130, 127, 123.3, 118.5, 116.3, 114, 55.5, 53.6. HRMS (TOF): m/*z* calcd for $C_{16}H_{14}FN_3O$: 283.3064 found: 284.12067 $[M+H]^+$

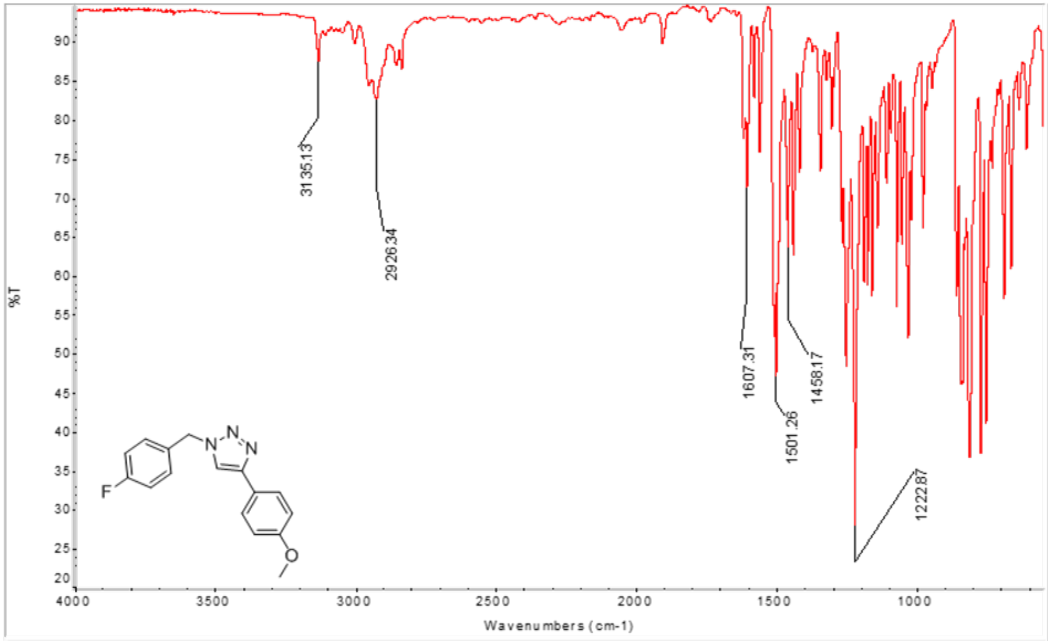

Figure S5. FTIR of 9b compound

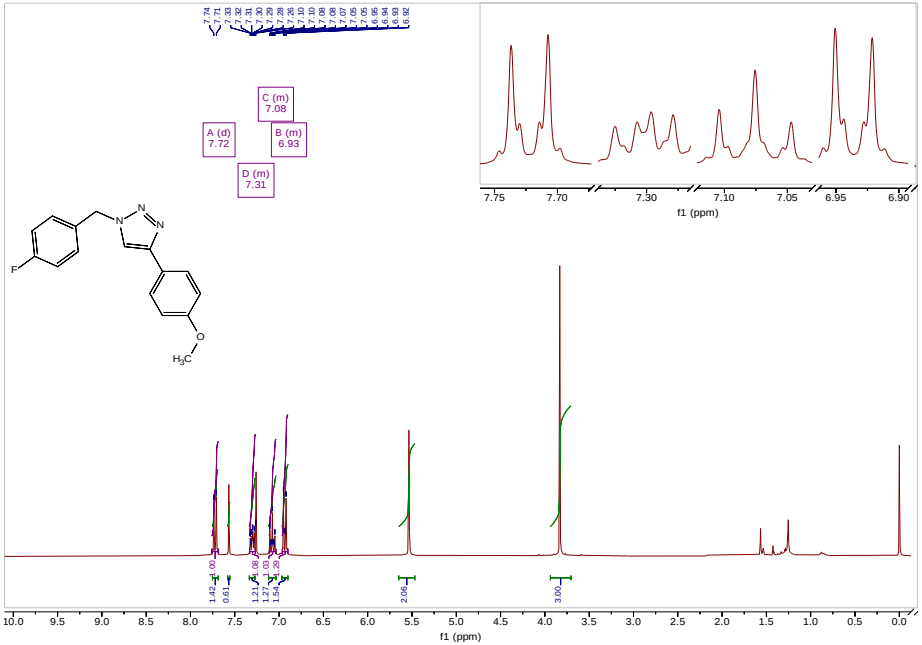

Figure S6. ^{1}H-NMR of 9b compound

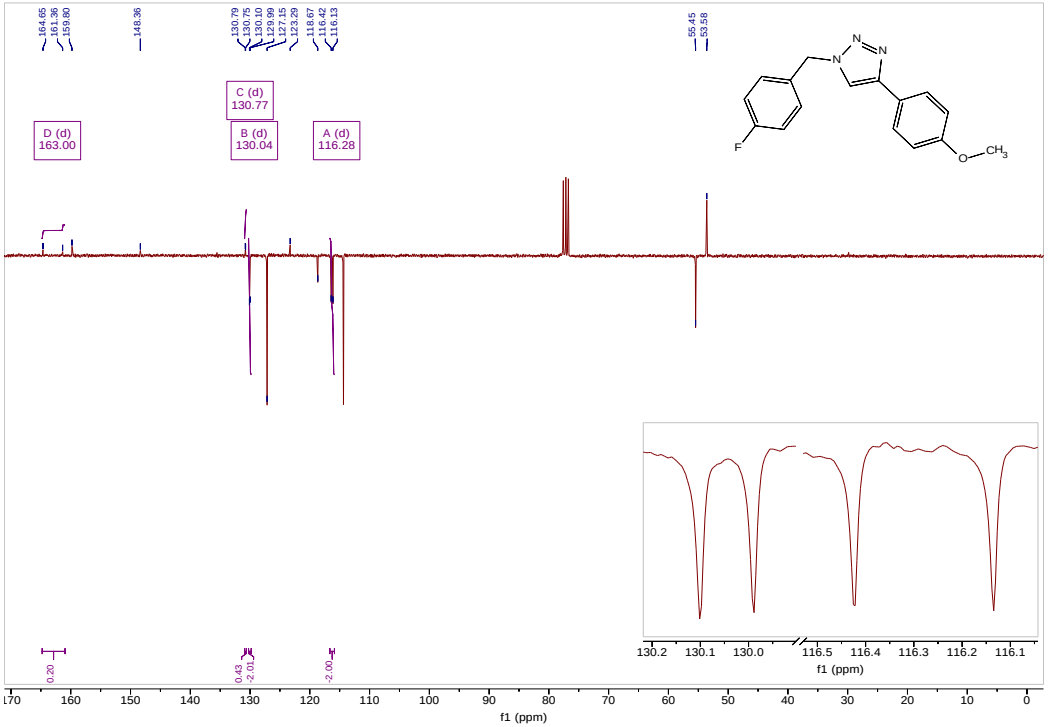

Figure S7. ^{13}C-APT NMR of 9b compound

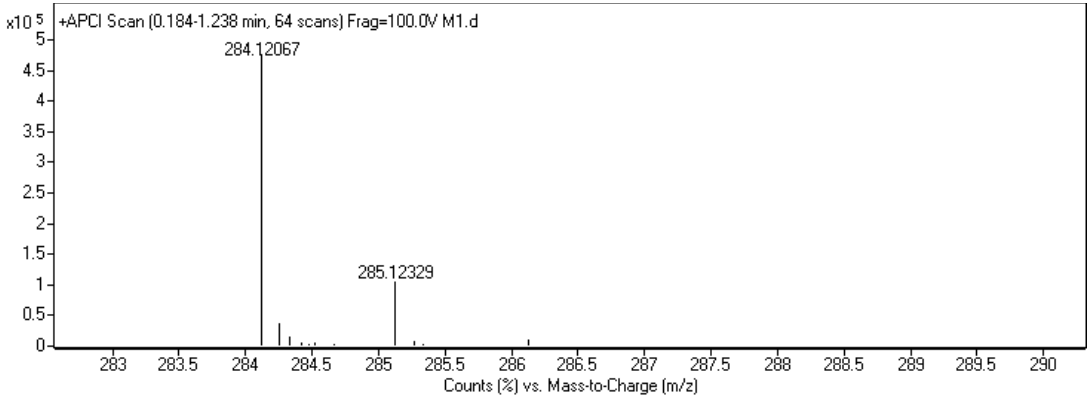

Figure S8. HRMS-TOF of 9b compound

9c

1-(3,4-Difluorobenzyl)-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole. Solid, m.p: 160 °C, yield: 37%. IR vmax (cm-1): 3128, 2962, 1610, 1501, 1434, 1030. ^{1}H-NMR (δ (ppm), $CDCl_3$): 7.73 (d, J= 8.6 Hz, 1H), 7.61 (s, 1H), 7.22 (m, 3H), 7.00 (m, 3H), 6.93 (d, J= 8.6 Hz, 1H), 5.65 (s, 2H), 3.82 (s, 3H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 159.9, 157.3, 150.8, 146.6, 132.7, 127.2, 126.3, 124.3, 123.1, 117.3, 114.4, 55.5, 53.2. HRMS (TOF): m/*z* calcd for $C_{16}H_{13}F_2N_3O$: 301.2968 found: 302.11147 $[M+H]^+$

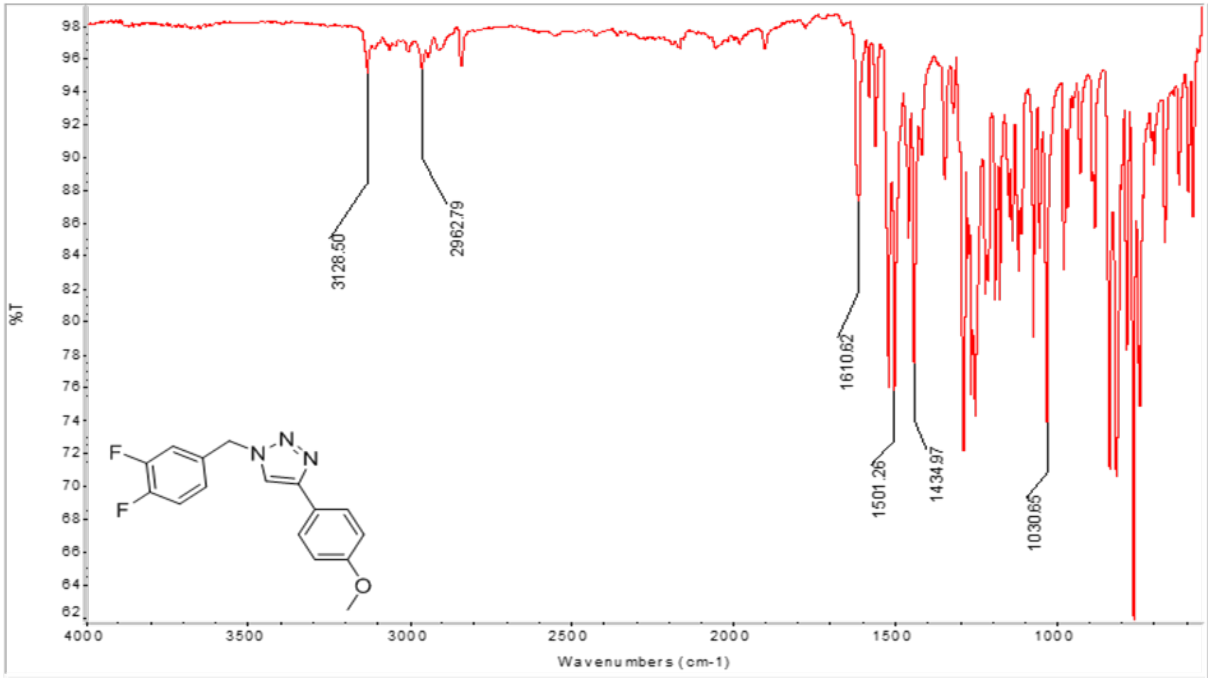

Figure S9. FTIR of 9c compound

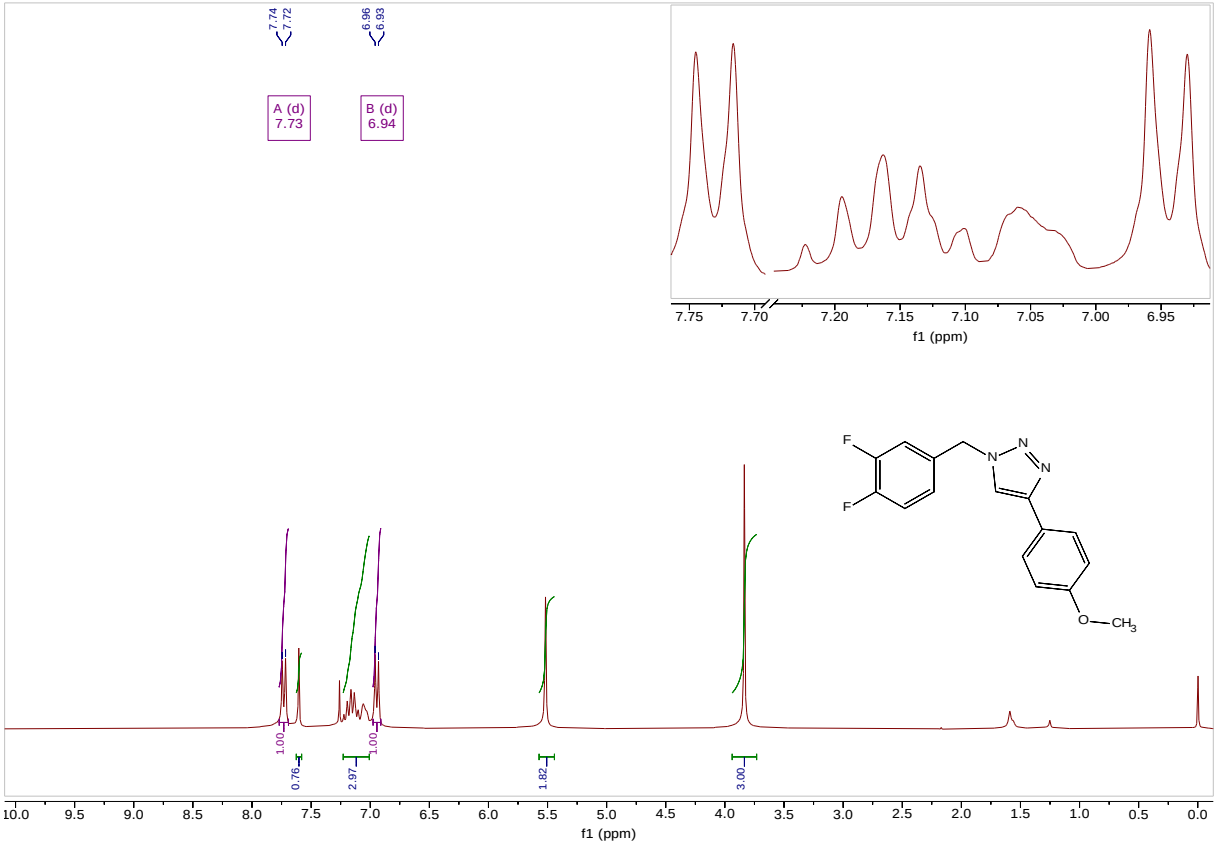

Figure S10. ^{1}H-NMR of 9c compound

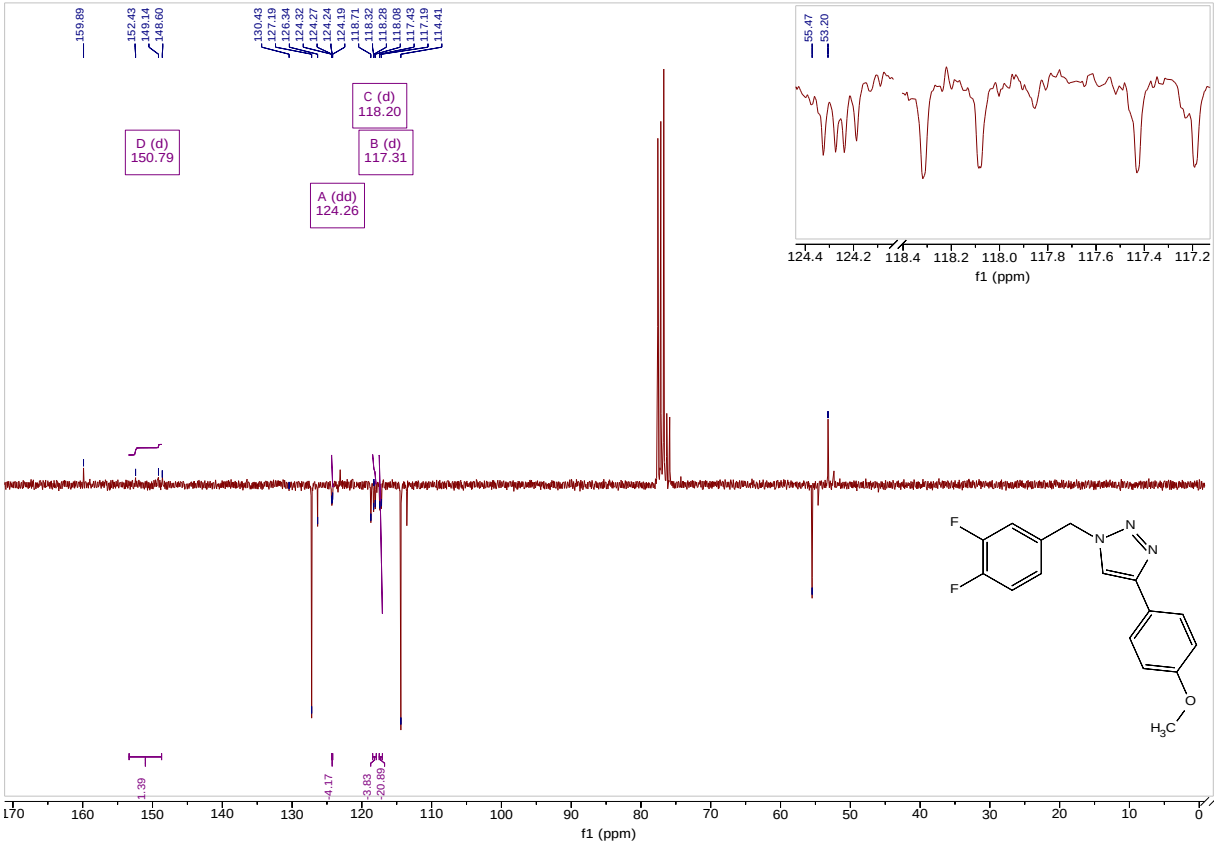

Figure S11. ^{13}C-APT NMR of 9c compound

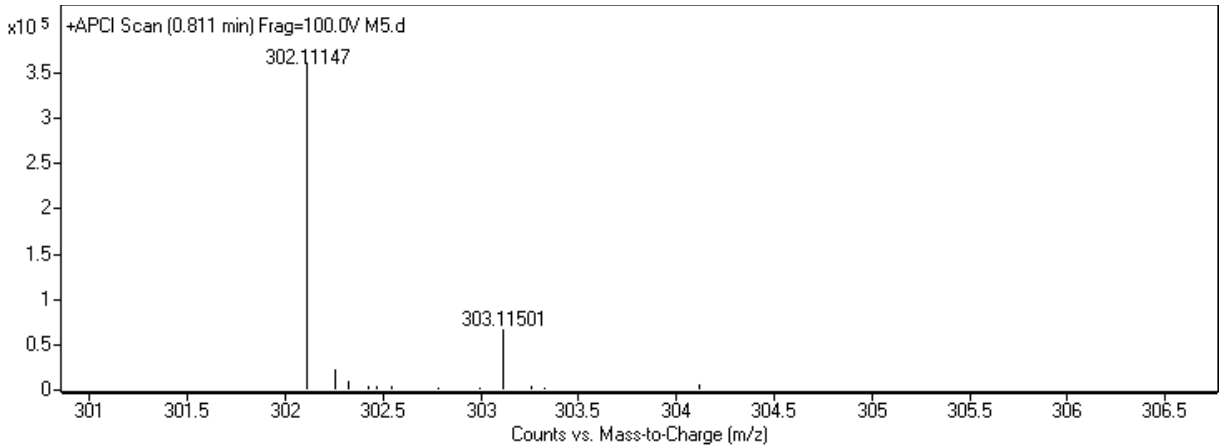

Figure S12. HRMS-TOF of 9c compound

9d

1-(4-Methoxyphenyl)-4-(4-nitrobenzyl)-1*H*-1,2,3-triazole. Solid, m.p: 140 ^{o}C[35], yield: 28%. IR vmax (cm-1): 3088, 2956, 1613, 1501, 1454, 1027. ^{1}H-NMR (δ (ppm), $CDCl_3$): 8.22 (d, *J*= 8.4 Hz, 2H), 7.73 (d, *J*= 8.4 Hz, 2H), 7.67 (s, 1H), 7.43 (d, *J*= 8.4 Hz, 2H), 6.94 (d, *J*= 8.5 Hz, 2H), 5.6 (s, 2H), 3.8 (s, 2H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 160, 148.7, 148.2, 142, 128.7, 127.2, 122.9, 119, 114.4, 55.5, 53.3. HRMS (TOF): m/*z* calcd for $C_{16}H_{14}N_4O_3$: 310.3130 found: 311.11560 $[M+H]^+$

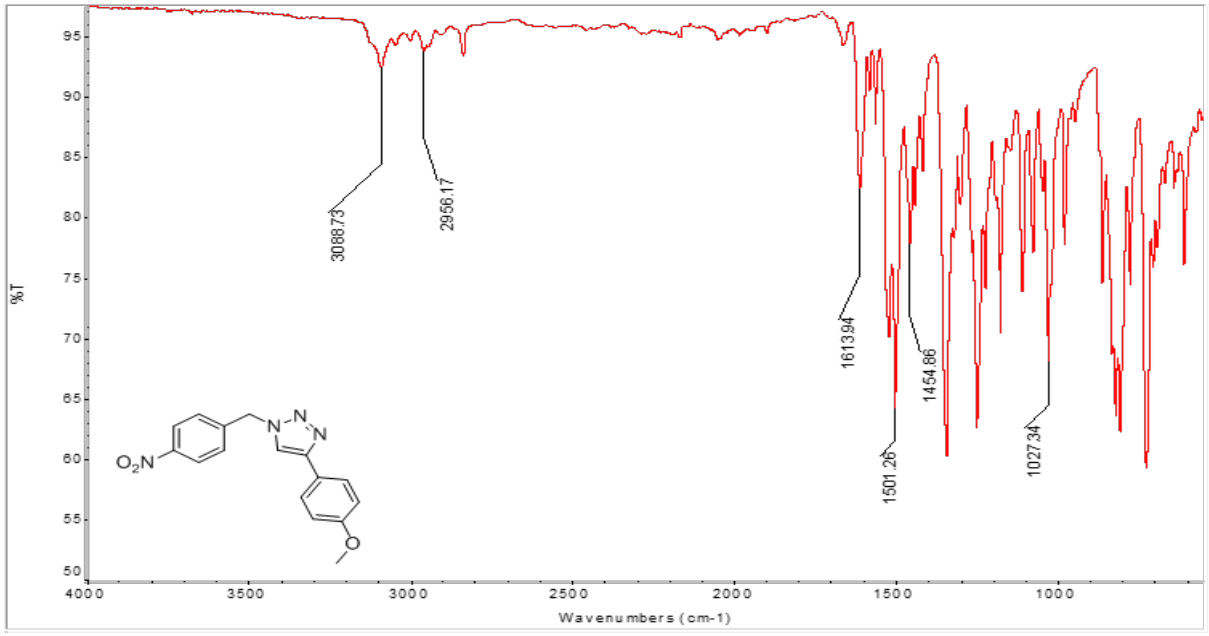

Figure S13. FTIR of 9d compound

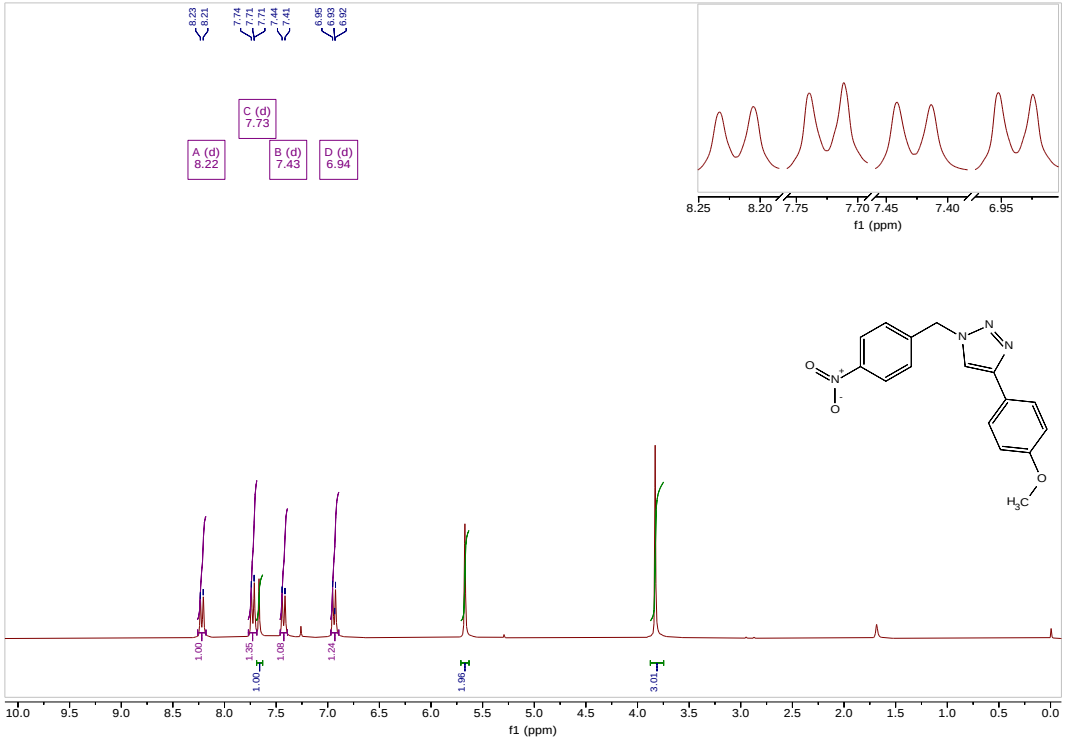

Figure S14. ^{1}H-NMR of 9d compound

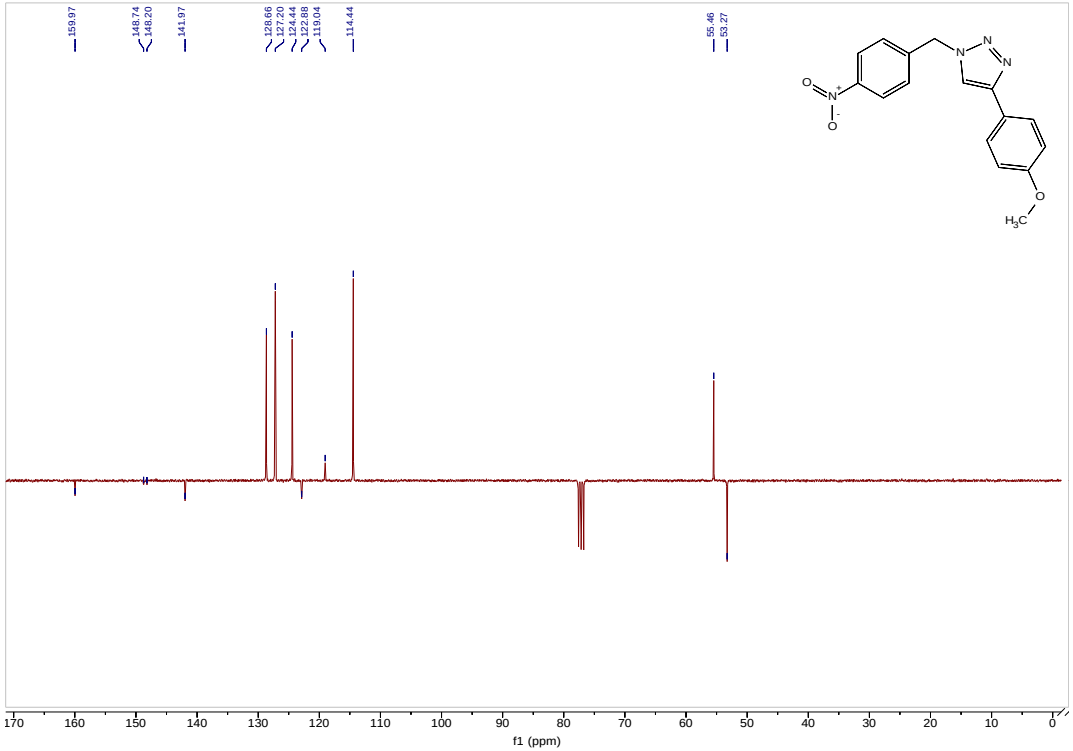

Figure S15. ^{13}C-APT NMR of 9d compound

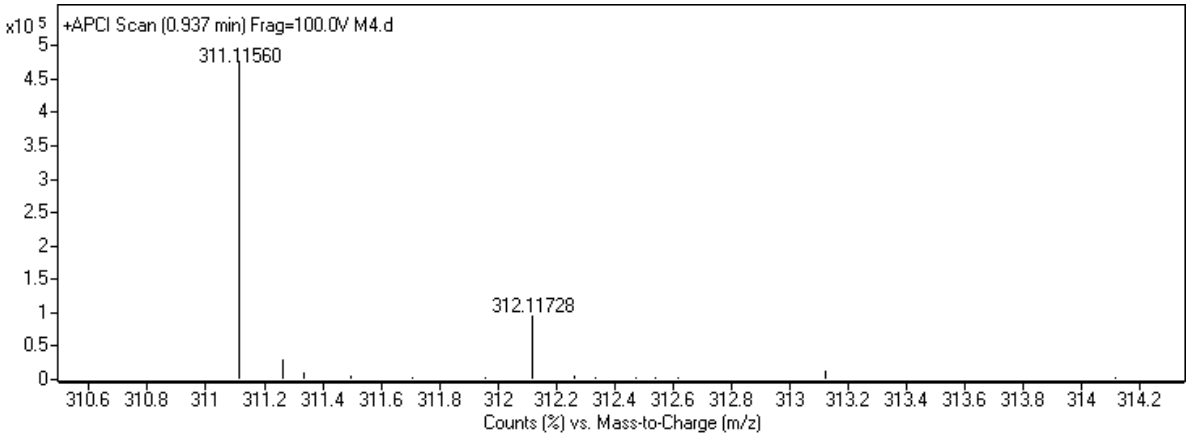

Figure S15. HRMS-TOF of 9d compound

9e

1-(3,5-Difluorobenzyl)-4-(thiophen-2-yl)-1*H*-1,2,3-triazole. Solid, m.p: 135-140 °C, yield: 71%. IR vmax (cm-1): 3125, 3068, 1600, 1511, 1461. 1H-NMR (δ (ppm), $CDCl_3$): 7.67 (s, 1H), 7.33 (d, 2H), 7.08 (dd, 1H), 6.8 (d, 3H), 5.6 (s, 2H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 163.5, 163.4, 138.3, 138.2, 138.1, 130.6, 127.9, 125.5, 124.6, 111.1, 104.6, 53.7. HRMS (TOF): m/*z* calcd for $C_{13}H_{9e2}N_3S$: 277.2928 found: 278.05701 $[M+H]^+$

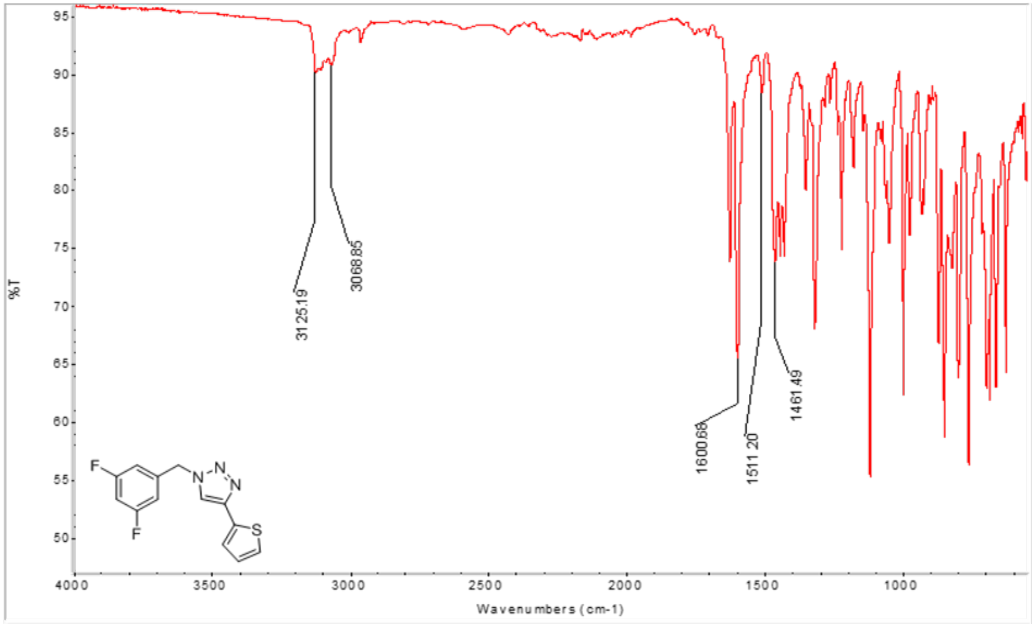

Figure S16. FTIR of 9e compound

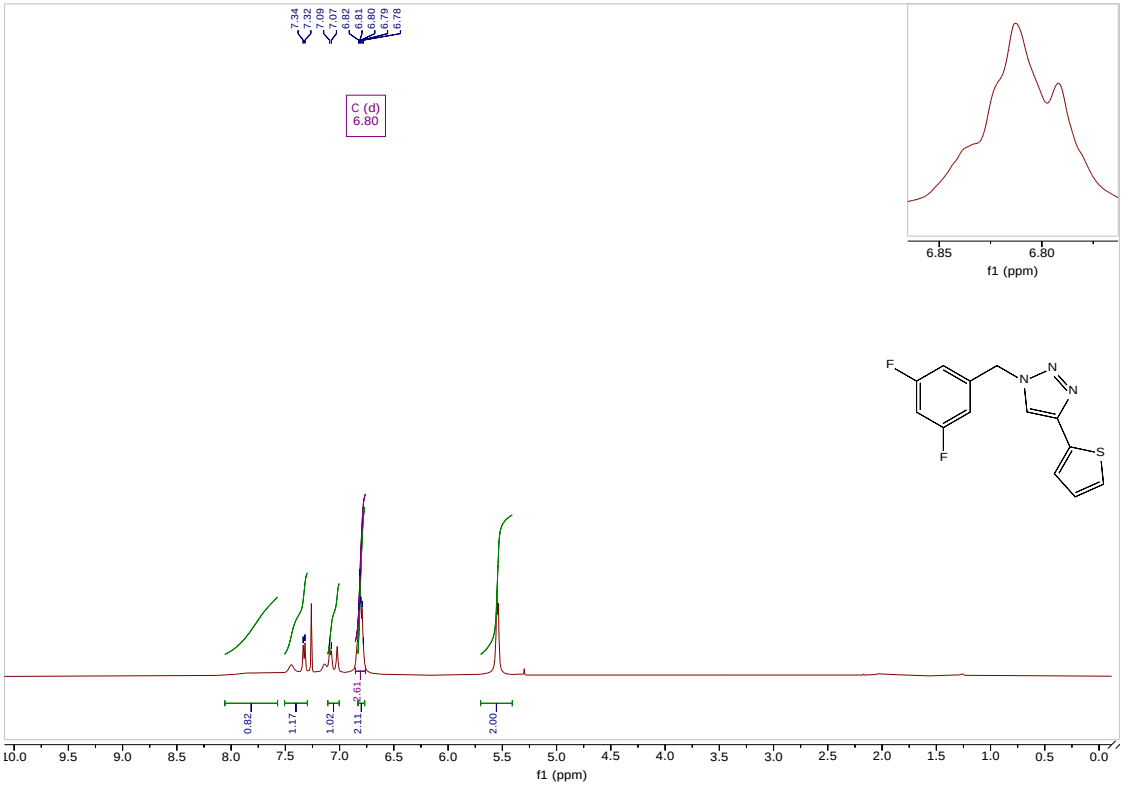

Figure S18. ^{1}H-NMR of 9e compound

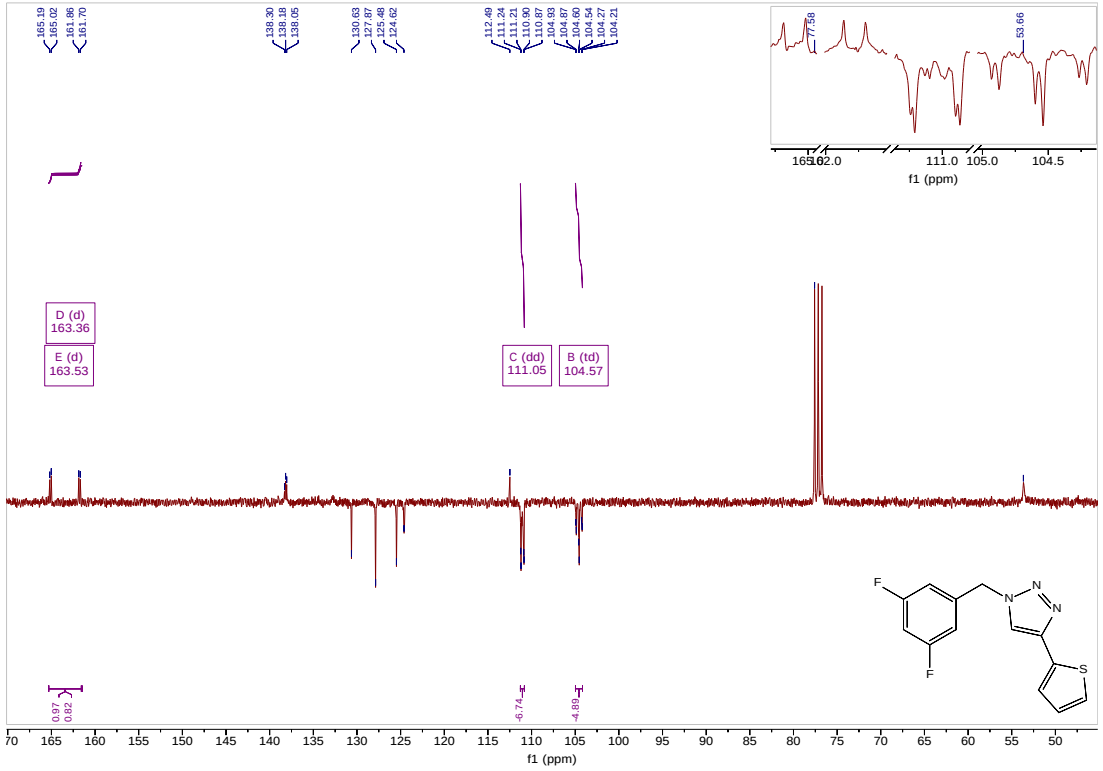

Figure S19. ^{13}C-APT NMR of 9e compound

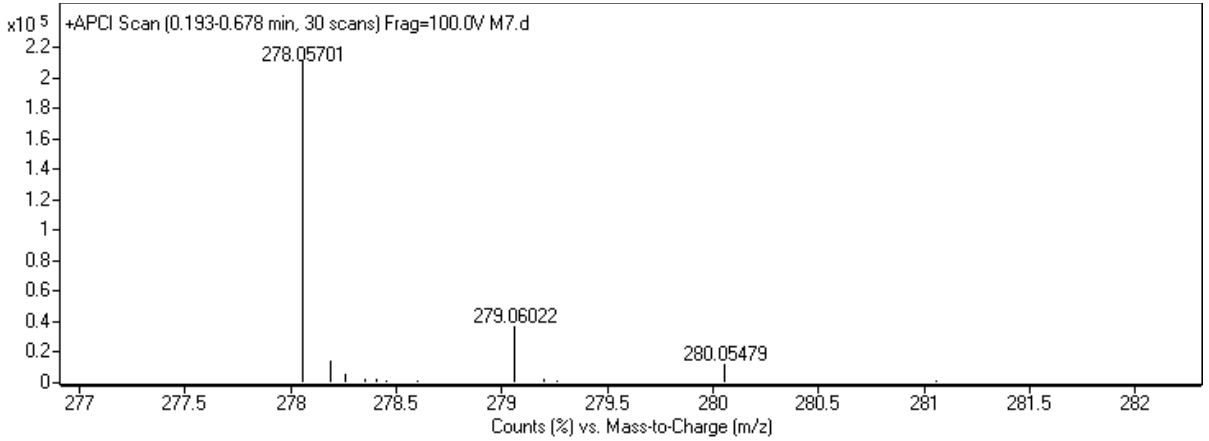

Figure S20. HRMS-TOF of 9e compound

Some physical and spectroscopic data of compounds 9f-i

9f

(5-Bromothiophen-2-yl)(1-(3-fluorobenzyl)-1*H*-1,2,3-triazole-4-yl)methanone. Solid, m.p: 150 °C, yield: 31. IR vmax (cm^{-1}): 3111, 2952, 2853, 170, 1613, 1527, 1451. ^{1}H-NMR (δ (ppm), $CDCl_3$): 8.37 (d, 1H), 8.09 (s, 1H), 7.37 (td, 1H), 7.10 (d, 1H), 7.01 (dd, 2H), 6.93 (d, 1H), 5.6 (s, 2H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 175.8, 163.2, 147.8, 145, 136.7, 136.0, 131.7, 131.3, 127.8, 124.8, 124.0, 116.5, 115.5. HRMS (TOF): m/z calcd for $C_{14}H_{19e}BrN_3OS$: 366.2084 found: 365.97295 $[M-H]^+$

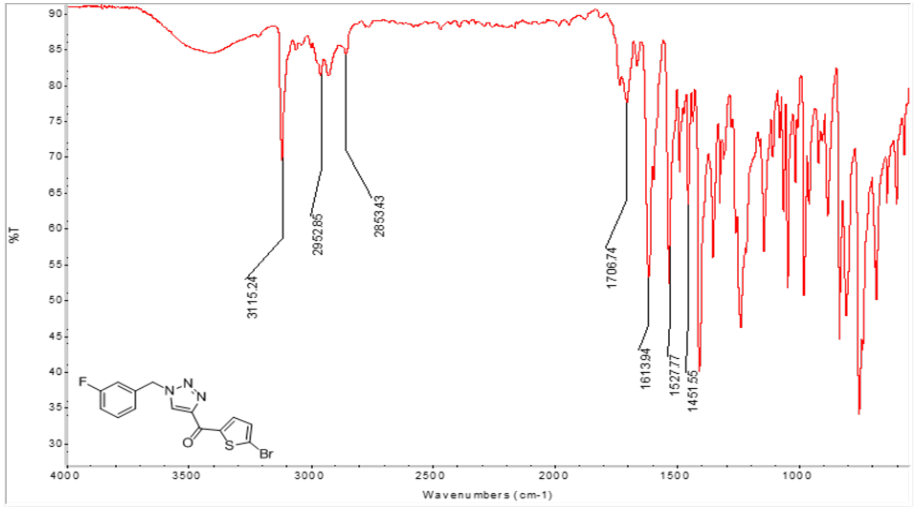

Figure S21. FTIR of 9f compound

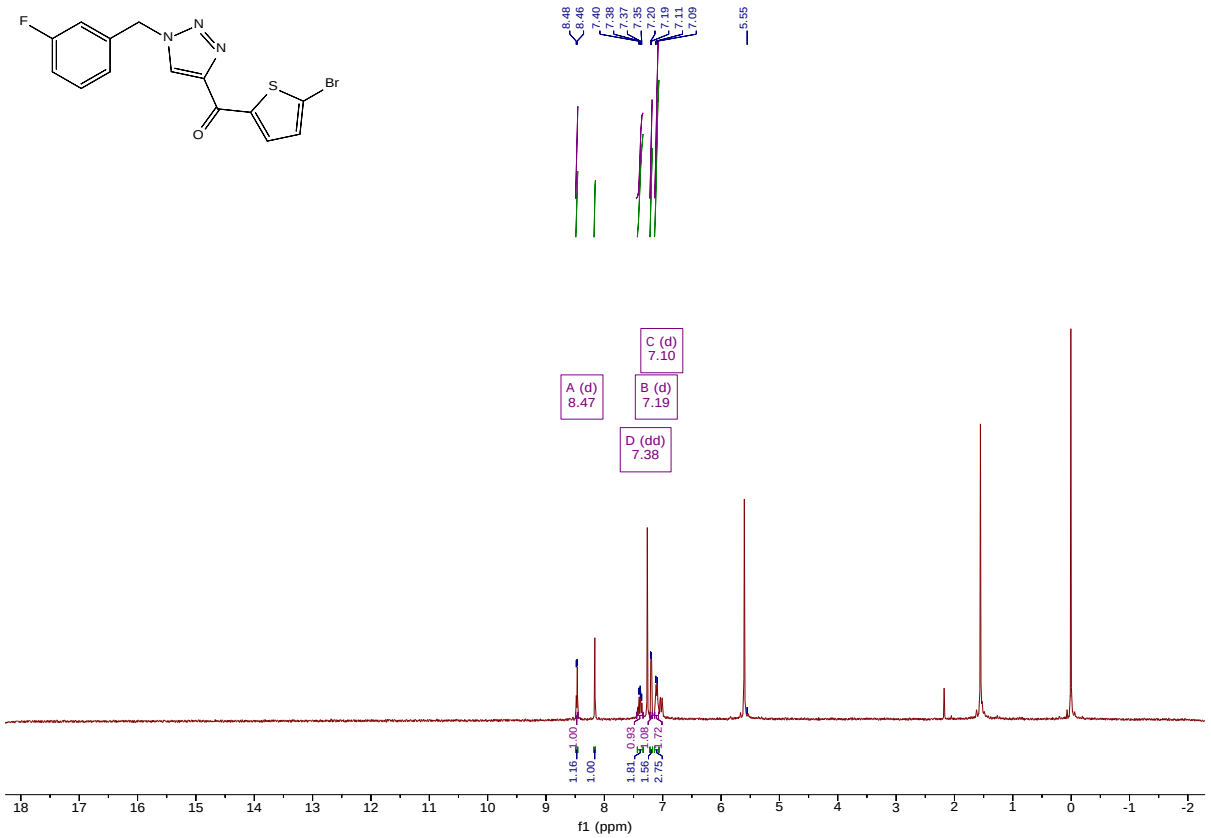

Figure S22. ^{1}H-NMR of 9f compound

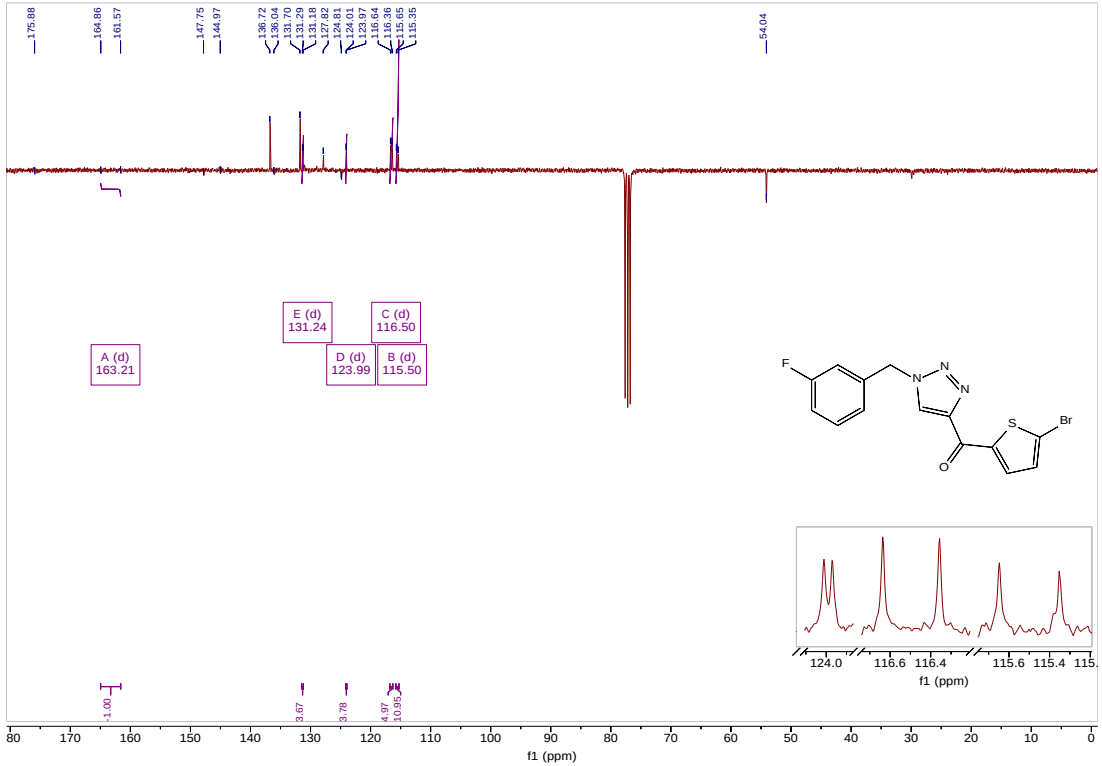

Figure S23. ^{13}C-APT NMR of 9f compound

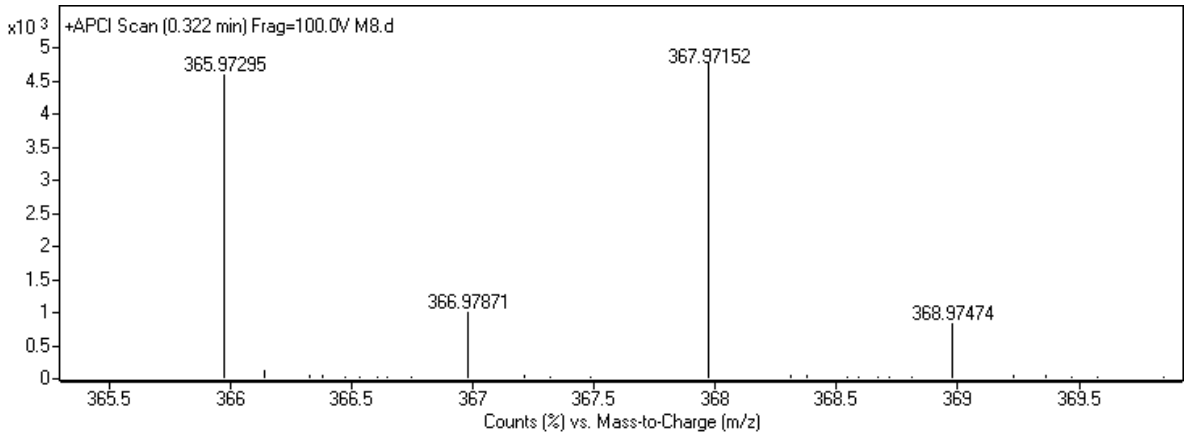

Figure S24. HRMS-TOF of 9f compound

9g

(1-(3-Fluorobenzyl)-1*H*-1,2,3-triazole-4-yl)(5-methylthiophen-2-yl)methanone. Solid, m.p: 155 °C, yield: 34%. IR vmax (cm^{-1}): 3121, 3068, 1604, 1531, 1491, 1438. ^{1}H-NMR (δ (ppm), $CDCl_3$): 8.56 (d, 1H), 8.17 (s, 1H), 7.37 (td, 1H), 7.09 (dd, 1H), 7.02 (dt, 2H), 6.89 (d, 1H), 5.6 (s, 2H), 2.37 (s, 3H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 176.7, 163.2, 151.6, 148.4, 140, 137.3, 136.2, 131.1, 127.6, 127.5, 123.9, 116.4, 115.4, 53.9, 14.6. HRMS (TOF): m/z calcd for $C_{15}H_{12}FN_3OSNa^+$: 324.06003 found: 324.05773 $[M+Na]^+$

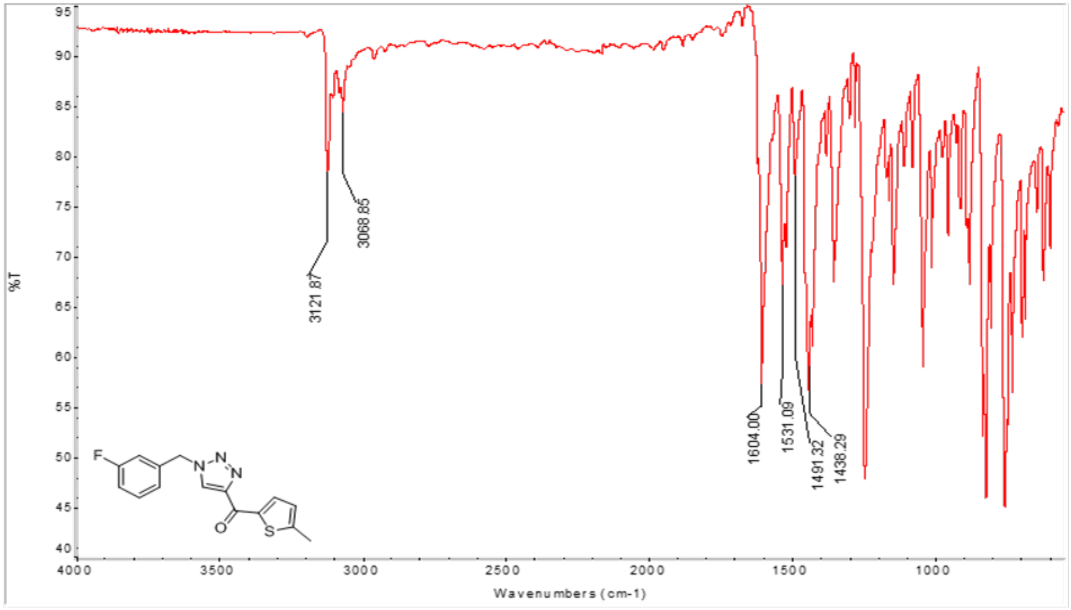

Figure S25. FTIR of 9g compound

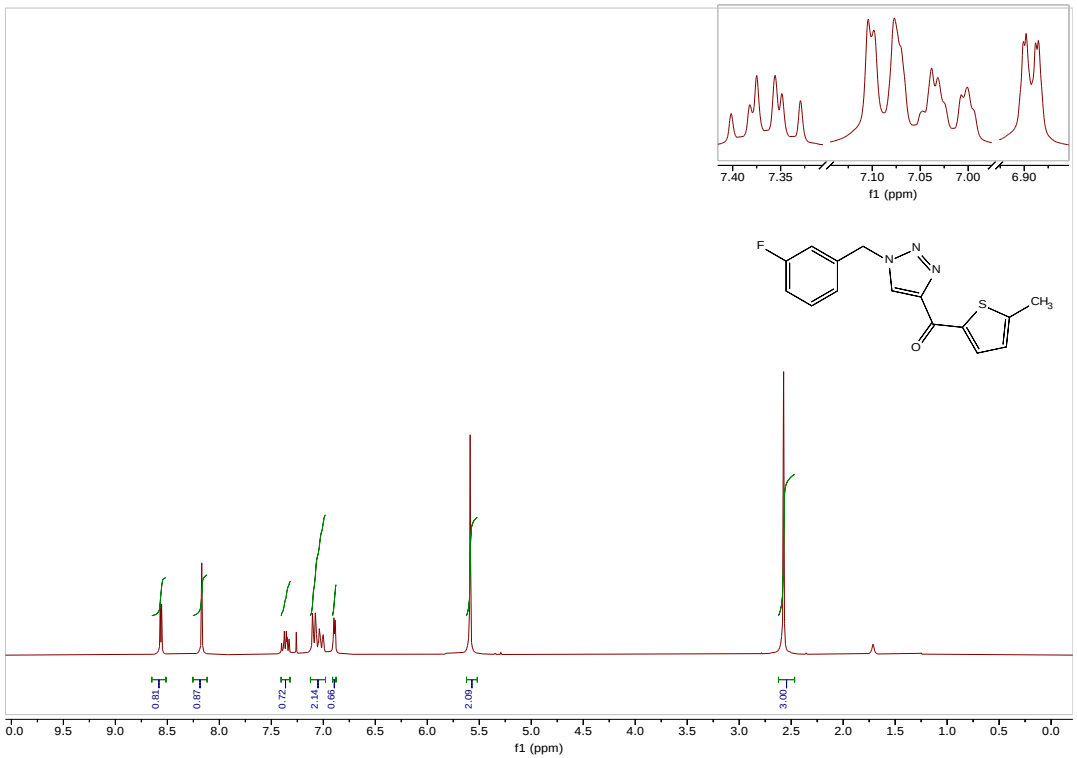

Figure S26. ^{1}H-NMR of 9g compound

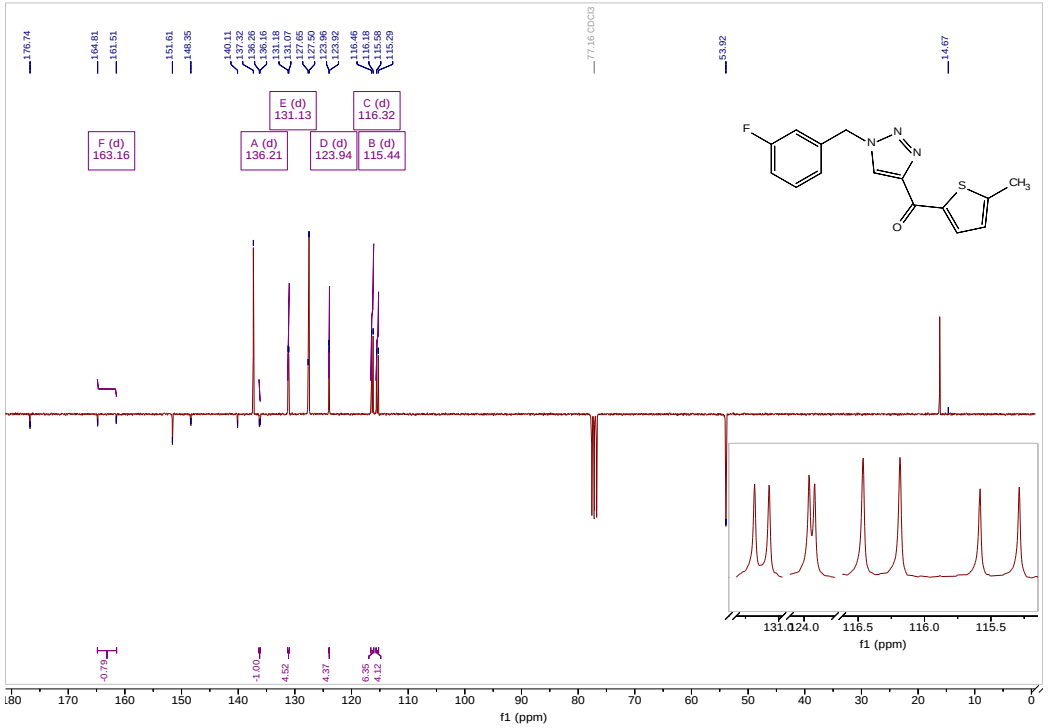

Figure S27. ^{13}C-APT NMR of 9g compound

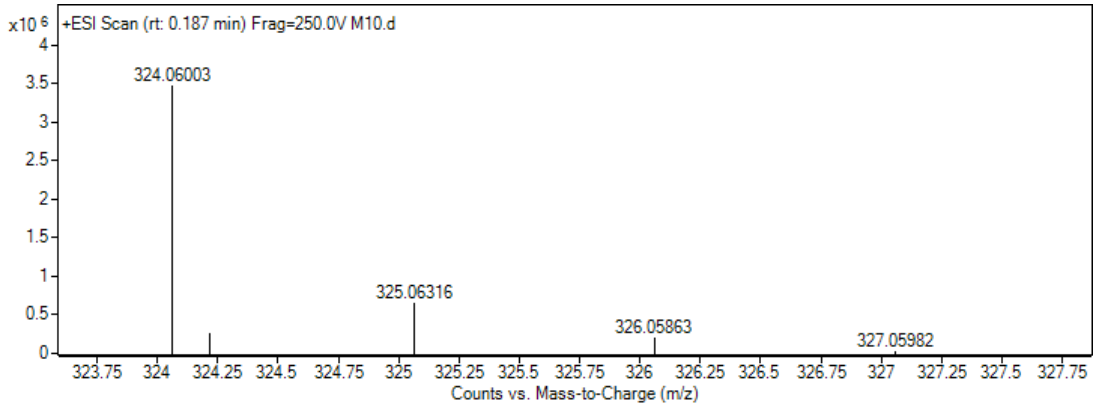

Figure S28. HRMS-TOF of 9g compound

9h

(5-Bromothiophen-2-yl(1-(4-methoxybenzyl)-1*H*-1,2,3-triazole-4-yl)methanone. Solid, m.p: 168 °C, yield:82%. IR vmax (cm^{-1}): 3125, 2938, 2841, 1700, 1634, 1534, 1406, 1046. ^{1}H-NMR (δ (ppm), $CDCl_3$): 8.45 (d, 1H), 8.08 (s, 1H), 7.28 (d, *J*= 8.7 Hz, 2H), 7.18 (d, 1H), 6.92 (d, *J*= 8.7 Hz, 2H), 5.6 (s, 2H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 176, 160.4, 149.7, 147.5, 136.6, 131.6, 130.2, 127.5, 125.6, 124.6, 114.9, 55.5, 54.3. HRMS (TOF): m/*z* calcd for $C_{15}H_{12}BrN_3O_2SNa^+$: 399.9726 found: 399.9753 $[M+Na]^+$

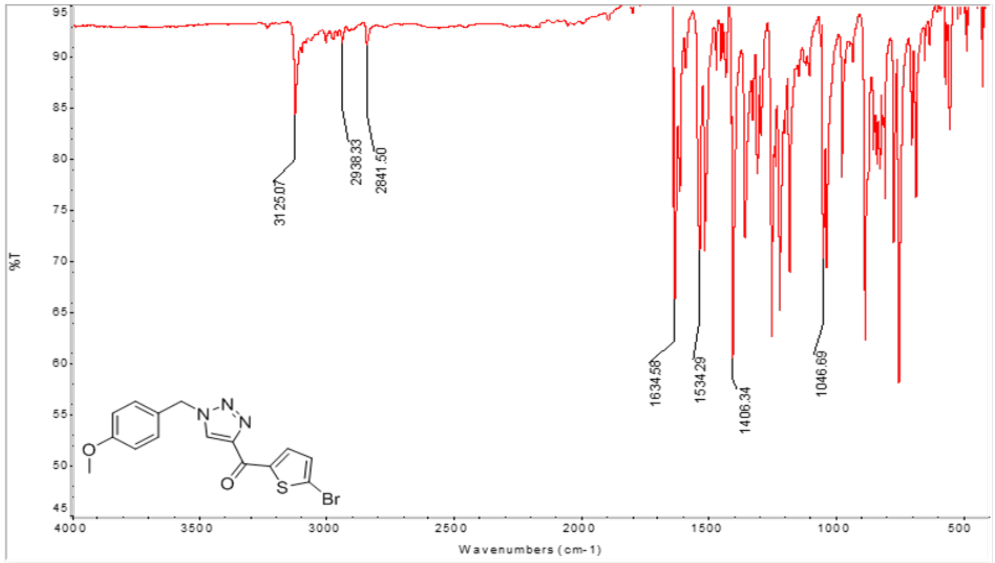

Figure S29. FTIR of 9h compound

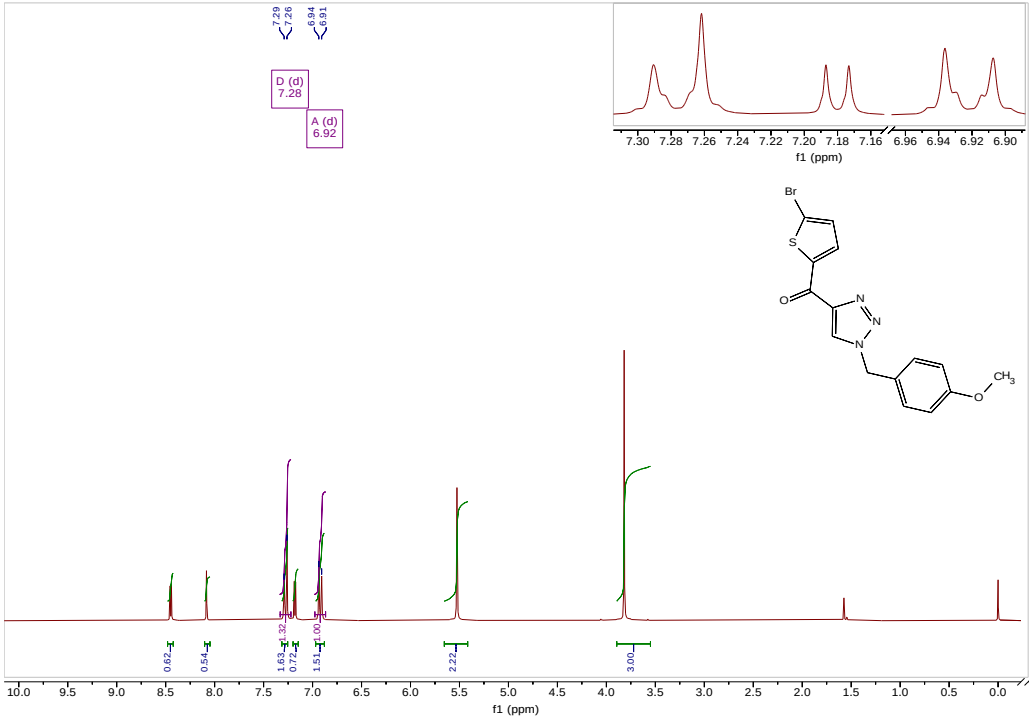

Figure S30. ^{1}H-NMR of 9h compound

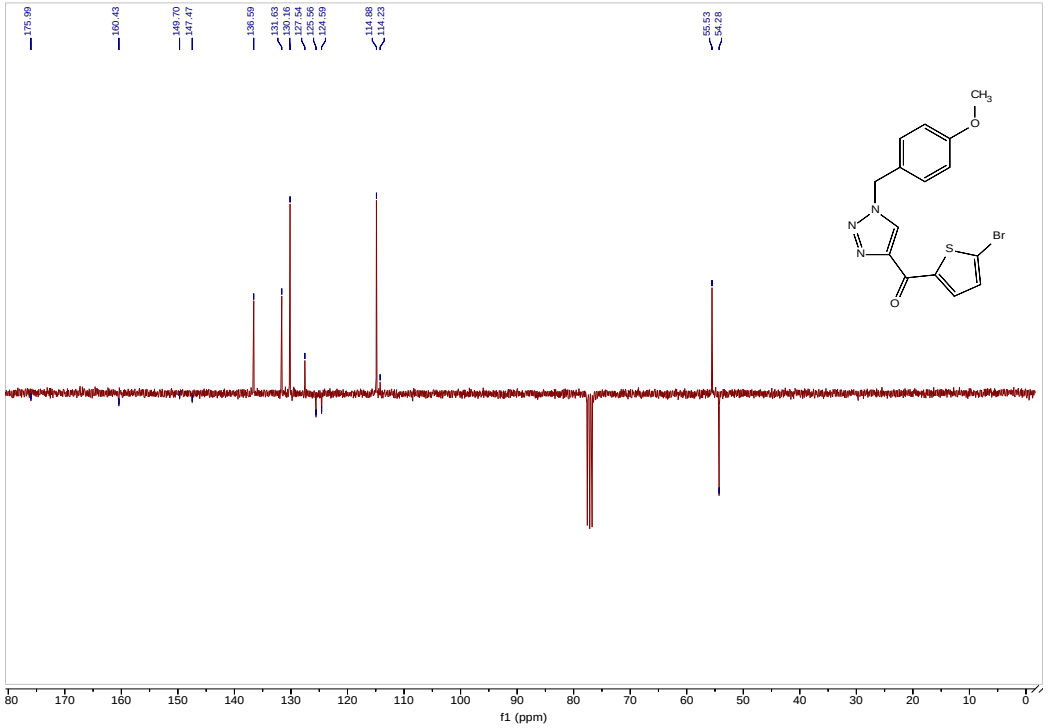

Figure S31. ^{13}C-APT NMR of 9h compound

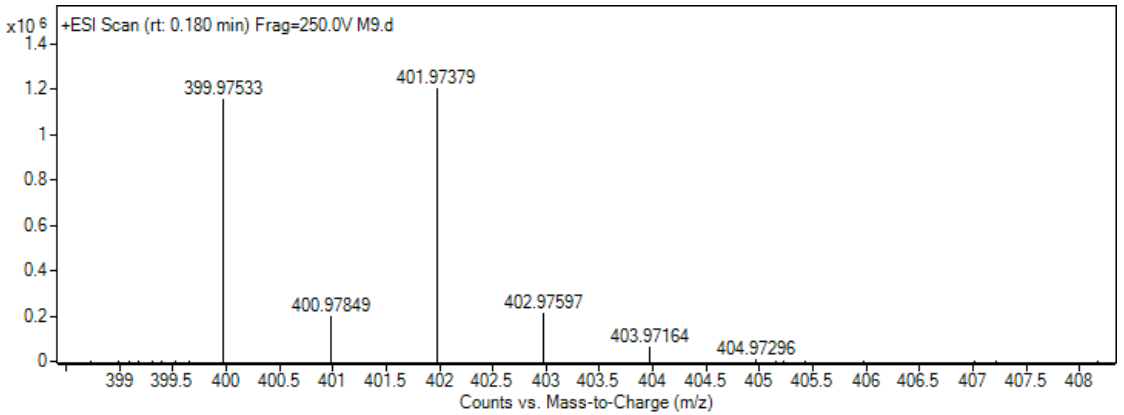

Figure S32. HRMS-TOF of 9h compound

9i

(1-(3,5-Difluorobenzyl)-1*H*-1,2,3-triazole-4-yl)(5-methylthiophen-2-yl)methanone. Solid, m.p: 168-171 °C, yield: 69%. IR vmax (cm^{-1}): 3121, 3068, 2926, 2853, 1736, 1600, 1531, 1438. ^{1}H-NMR (δ (ppm), $CDCl_3$): 8.48 (s, 1H), 8.11 (s, 1H), 7.17 (s, 1H), 6.77 (s, 3H), 5.6 (s, 2H), 2.37 (s, 3H). ^{13}C-NMR (δ (ppm), $CDCl_3$): 176.6, 163.6, 163.4, 151.8, 148.6, 140.1, 138.1, 137.4, 127.6, 124.9, 111.3, 104.8, 53.5, 16.4. HRMS (TOF): m/z calcd for $C_{15}H_{11}F_2N_3OSNa^+$: 342.04831 found: 342.05078 $[M+Na]^+$

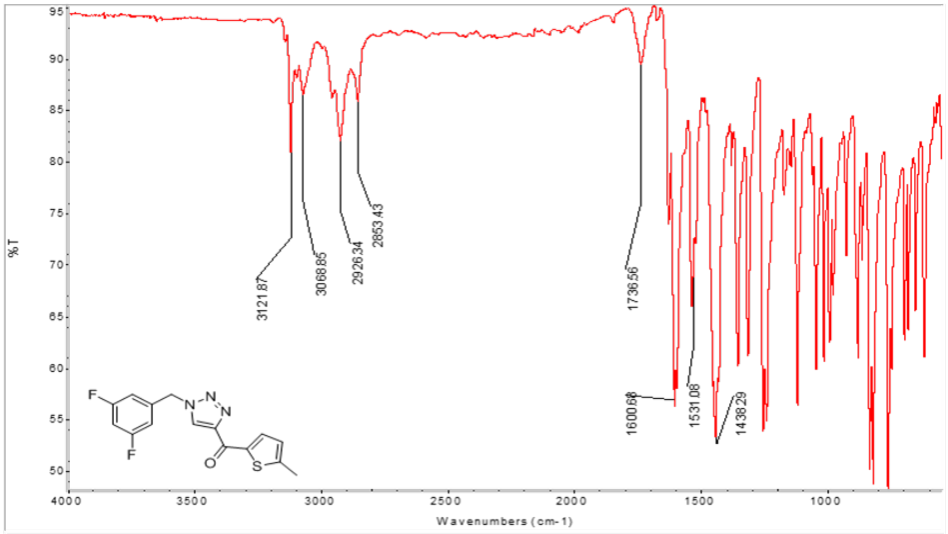

Figure S33. FTIR of 9i compound

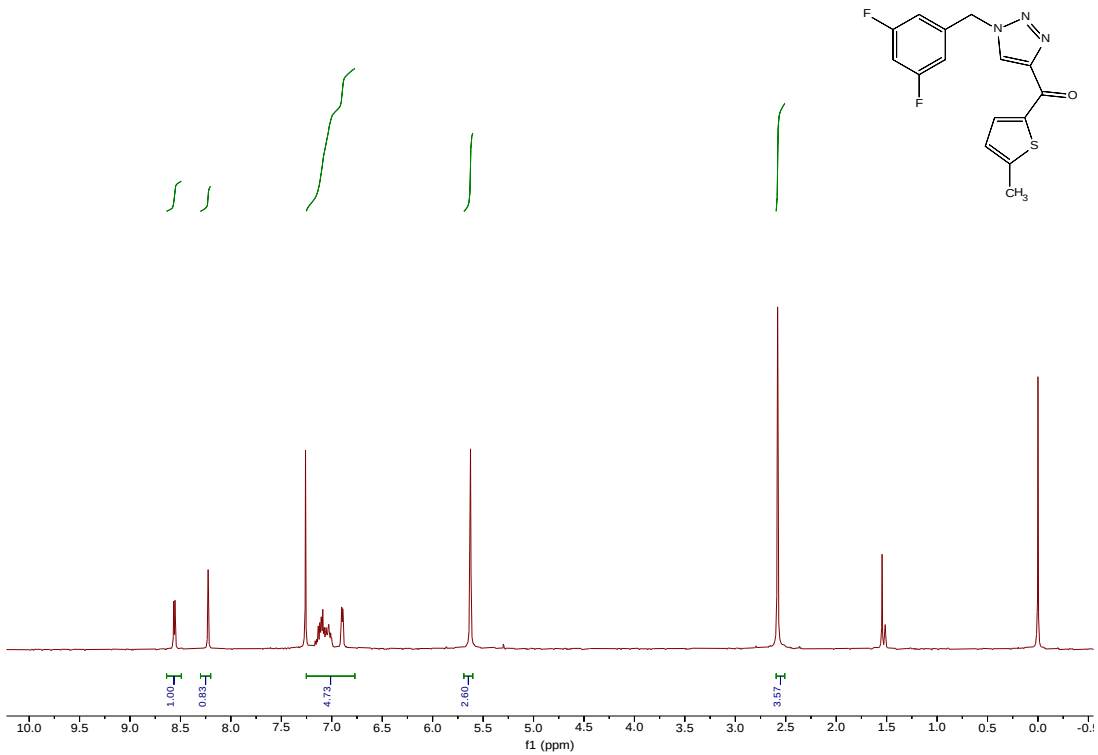

Figure S34. ^{1}H-NMR of 9i compound

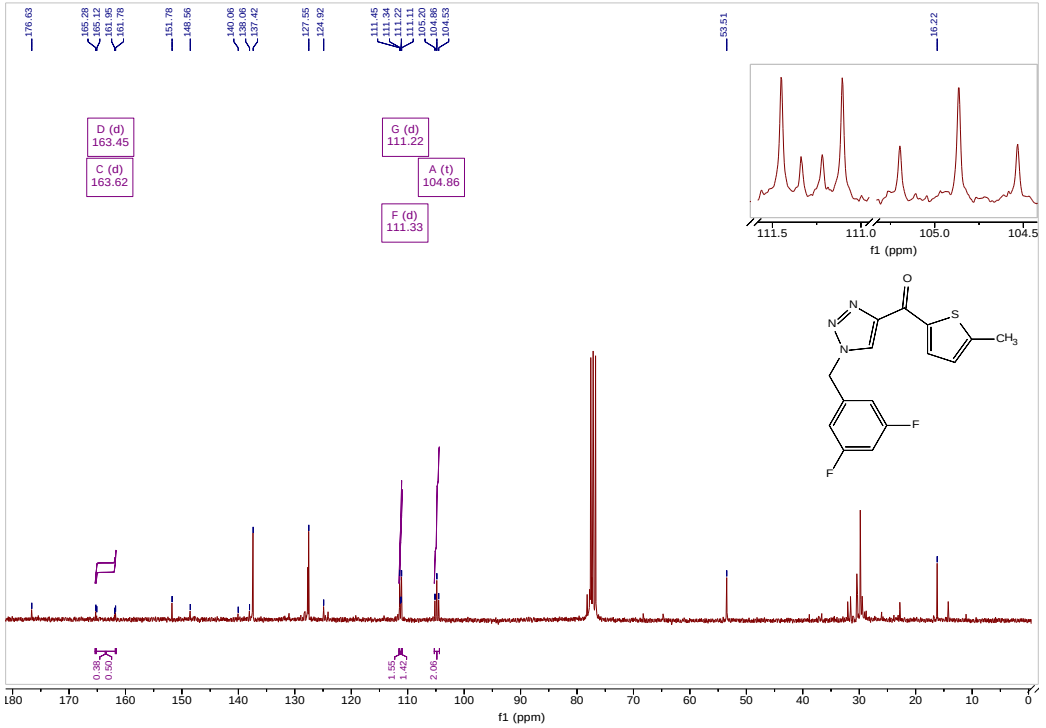

Figure S35. ^{13}C-APT NMR of 9i compound

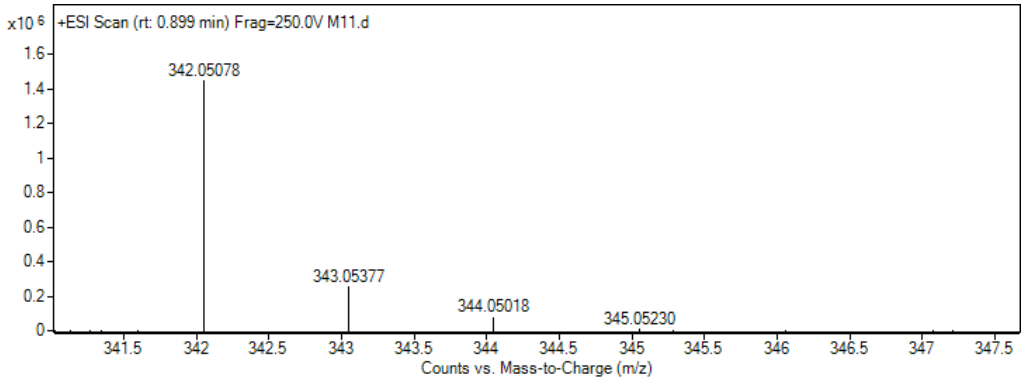

Figure S36. HRMS-TOF of 9i compound

Table S1. The stationary orientations of the compound (9a) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	1.306653	-1.483713	-0.600318
2	6	0	0.282354	-0.658929	-0.933336
3	6	0	-0.763622	-1.046454	-0.112778
4	7	0	-0.310536	-2.077300	0.670967
5	7	0	0.931548	-2.338091	0.380450
6	6	0	2.674751	-1.514476	-1.105683
7	6	0	3.512476	-0.335032	-0.648021
8	6	0	-2.135371	-0.537042	-0.010996
9	6	0	4.201217	0.449251	-1.578296
10	6	0	4.994718	1.517679	-1.151661
11	6	0	5.103899	1.818032	0.204579
12	6	0	4.407366	1.026936	1.114308
13	6	0	3.617052	-0.042253	0.717553
14	6	0	-3.045136	-1.128540	0.885716
15	6	0	-4.345595	-0.661509	0.994648

16	6	0	-4.781259	0.415827	0.207791
17	6	0	-3.890026	1.017416	-0.688311
18	6	0	-2.583191	0.537752	-0.787783
19	9	0	4.507887	1.308992	2.428785
20	8	0	-6.079197	0.797809	0.388719
21	6	0	-6.575577	1.878005	-0.384453
22	1	0	0.381958	0.102895	-1.690720
23	1	0	3.089121	-2.458329	-0.739364
24	1	0	2.645029	-1.561580	-2.198904
25	1	0	4.120767	0.224618	-2.638859
26	1	0	5.526778	2.122342	-1.880507
27	1	0	5.709093	2.643252	0.564795
28	1	0	3.089980	-0.630480	1.462487
29	1	0	-2.711601	-1.961933	1.494905
30	1	0	-5.049287	-1.116421	1.684879
31	1	0	-4.196898	1.852411	-1.307588
32	1	0	-1.906749	1.021353	-1.488206
33	1	0	-7.617607	2.006345	-0.085712
34	1	0	-6.024567	2.806583	-0.183555
35	1	0	-6.531413	1.659295	-1.459821

Table S2. The stationary orientations of the compound (9b) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-1.184787	-1.602583	0.553271
2	6	0	-0.205143	-0.719626	0.869992
3	6	0	0.876506	-1.098488	0.092494
4	7	0	0.487115	-2.182748	-0.652122
5	7	0	-0.749899	-2.483554	-0.377567
6	6	0	-2.566408	-1.665894	1.022964
7	6	0	-3.433233	-0.542691	0.488435
8	6	0	2.226955	-0.533830	-0.003112
9	6	0	-4.123792	0.303055	1.361581
10	6	0	-4.939049	1.327044	0.875404
11	6	0	-5.045840	1.492612	-0.499110

12	6	0	-4.369798	0.670507	-1.396459
13	6	0	-3.565273	-0.348646	-0.894101
14	6	0	3.177851	-1.115705	-0.862732
15	6	0	4.458505	-0.595824	-0.967045
16	6	0	4.832561	0.526804	-0.212488
17	6	0	3.900078	1.119089	0.647066
18	6	0	2.613807	0.585884	0.742360
19	9	0	-5.826961	2.480730	-0.980614
20	8	0	6.115562	0.959494	-0.385877
21	6	0	6.549447	2.088335	0.354759
22	1	0	-0.355899	0.072235	1.586984
23	1	0	-2.929142	-2.643107	0.691392
24	1	0	-2.564528	-1.662594	2.117791
25	1	0	-4.030182	0.163589	2.436092
26	1	0	-5.480993	1.990471	1.541143
27	1	0	-4.481364	0.835181	-2.463044
28	1	0	-3.026745	-0.997928	-1.579414
29	1	0	2.892103	-1.984018	-1.446960

30	1	0	5.193646	-1.043245	-1.628814
31	1	0	4.159195	1.987652	1.241571
32	1	0	1.905036	1.062774	1.414869
33	1	0	7.589957	2.252633	0.068591
34	1	0	5.961359	2.983201	0.110595
35	1	0	6.495652	1.907065	1.436619

Table S3. The stationary orientations of the compound (9c) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-0.894694	-1.705800	0.522892
2	6	0	0.102561	-0.881160	0.930550
3	6	0	1.136675	-1.110200	0.038356
4	7	0	0.703100	-2.052727	-0.859323

5	7	0	-0.515686	-2.408143	-0.570551
6	6	0	-2.246661	-1.859753	1.048531
7	6	0	-3.169482	-0.712061	0.684910
8	6	0	2.481134	-0.528227	-0.034163
9	6	0	-3.891657	-0.038372	1.672675
10	6	0	-4.766482	0.999075	1.336500
11	6	0	-4.908339	1.361239	0.006368
12	6	0	-4.185519	0.694589	-0.986099
13	6	0	-3.322143	-0.337178	-0.658063
14	6	0	3.386531	-0.961191	-1.021425
15	6	0	4.661032	-0.423229	-1.105926
16	6	0	5.074277	0.568708	-0.203178
17	6	0	4.187101	1.012122	0.784655
18	6	0	2.906426	0.462442	0.858445
19	9	0	-4.345952	1.069984	-2.264809
20	9	0	-5.736766	2.356415	-0.349174
21	8	0	6.347037	1.031787	-0.370456
22	6	0	6.818053	2.036110	0.513144

23	1	0	-0.003764	-0.230095	1.784153
24	1	0	-2.607432	-2.804037	0.630213
25	1	0	-2.188507	-1.973973	2.135403
26	1	0	-3.778838	-0.321737	2.715714
27	1	0	-5.334808	1.533010	2.090944
28	1	0	-2.770196	-0.837958	-1.447835
29	1	0	3.070544	-1.727827	-1.720948
30	1	0	5.361247	-0.755515	-1.866044
31	1	0	4.477060	1.778179	1.494749
32	1	0	2.232688	0.823776	1.631518
33	1	0	7.841249	2.253633	0.201322
34	1	0	6.215669	2.951647	0.442664
35	1	0	6.823167	1.688217	1.554833

Table S4. The stationary orientations of the compound (9d) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-0.410910	-1.951010	0.381711
2	6	0	0.520967	-1.079395	0.845299
3	6	0	1.567822	-1.169796	-0.056603
4	7	0	1.205640	-2.082470	-1.015340
5	7	0	0.019101	-2.549140	-0.754869
6	6	0	-1.746728	-2.236547	0.887009
7	6	0	-2.763414	-1.162391	0.542621
8	6	0	2.864084	-0.484173	-0.087065
9	6	0	-3.615234	-0.654662	1.530168
10	6	0	-4.573497	0.307696	1.219077
11	6	0	-4.661031	0.757141	-0.095261

12	6	0	-3.824443	0.271929	-1.100148
13	6	0	-2.876247	-0.691610	-0.773678
14	6	0	3.790003	-0.769307	-1.108374
15	6	0	5.019995	-0.132465	-1.153572
16	6	0	5.366064	0.813397	-0.175940
17	6	0	4.457311	1.109893	0.846972
18	6	0	3.221914	0.461803	0.880590
19	8	0	6.598712	1.381862	-0.310228
20	6	0	7.003099	2.346526	0.647992
21	7	0	-5.667607	1.777426	-0.433535
22	8	0	-6.389996	2.189180	0.473764
23	8	0	-5.725455	2.156088	-1.602469
24	1	0	0.367748	-0.496123	1.739893
25	1	0	-2.028154	-3.193139	0.435992
26	1	0	-1.689808	-2.380270	1.970284
27	1	0	-3.532356	-1.012671	2.553211
28	1	0	-5.240360	0.713148	1.969819
29	1	0	-3.927741	0.648833	-2.110151

30	1	0	-2.214393	-1.082171	-1.541293
31	1	0	3.525860	-1.500449	-1.864991
32	1	0	5.736372	-0.350217	-1.939567
33	1	0	4.696565	1.836556	1.614746
34	1	0	2.530359	0.708036	1.682567
35	1	0	8.004676	2.662290	0.350595
36	1	0	6.334533	3.217690	0.651081
37	1	0	7.043060	1.919566	1.658980

Table S5. The stationary orientations of the compound (9e) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	7	0	0.006007	-0.915698	1.245539

2	6	0	0.887543	0.077539	0.967812
3	6	0	1.983830	-0.572077	0.427493
4	7	0	1.703588	-1.916313	0.401858
5	7	0	0.515403	-2.119591	0.890924
6	6	0	-1.348607	-0.830363	1.778017
7	6	0	-2.363677	-0.334432	0.763535
8	6	0	3.253035	-0.056122	-0.055667
9	6	0	-3.229840	0.709800	1.098232
10	6	0	-4.174356	1.126093	0.164141
11	6	0	-4.285683	0.547765	-1.092728
12	6	0	-3.404246	-0.487218	-1.392459
13	6	0	-2.448250	-0.943175	-0.494530
14	9	0	-3.489827	-1.067620	-2.602934
15	9	0	-5.007190	2.132716	0.489323
16	6	0	4.300095	-0.776531	-0.578911
17	6	0	5.405374	0.037350	-0.962186
18	6	0	5.195176	1.368310	-0.729579
19	16	0	3.630015	1.653541	-0.032563

20	1	0	0.674666	1.116935	1.165446
21	1	0	-1.590958	-1.844898	2.107614
22	1	0	-1.337906	-0.182781	2.659794
23	1	0	-3.185325	1.201509	2.064680
24	1	0	-5.023501	0.887302	-1.809671
25	1	0	-1.782796	-1.752533	-0.775967
26	1	0	4.263183	-1.854786	-0.678984
27	1	0	6.320038	-0.354372	-1.393924
28	1	0	5.858165	2.200678	-0.922739

Table S6. The stationary orientations of the compound (9f) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	7	0	2.538412	-1.217466	0.905005
2	6	0	1.722899	-1.421115	-0.147759
3	6	0	0.495161	-0.933205	0.265903
4	7	0	0.636015	-0.455930	1.540541
5	7	0	1.863734	-0.622996	1.929470
6	6	0	3.969297	-1.490538	1.045475
7	6	0	4.840638	-0.522412	0.268941
8	6	0	-1.990760	-0.396665	-0.019782
9	6	0	5.752448	-0.994662	-0.679786
10	6	0	6.569842	-0.101367	-1.377816
11	6	0	6.481315	1.268770	-1.141162
12	6	0	5.564598	1.718502	-0.194564
13	6	0	4.745229	0.852929	0.515940
14	9	0	5.472794	3.041590	0.042984
15	6	0	-2.304966	0.184251	1.192917
16	6	0	-3.662839	0.583062	1.287374
17	6	0	-4.355930	0.295034	0.137661
18	16	0	-3.387268	-0.461993	-1.080820

19	1	0	2.036985	-1.870563	-1.076297
20	1	0	4.164266	-1.428211	2.119702
21	1	0	4.156076	-2.519746	0.726003
22	1	0	5.828029	-2.061524	-0.873577
23	1	0	7.100259	1.985367	-1.670593
24	1	0	4.044080	1.250292	1.243468
25	1	0	-1.571382	0.311837	1.978994
26	1	0	-4.109171	1.056749	2.153305
27	35	0	-6.177340	0.647602	-0.180910
28	1	0	7.275858	-0.475246	-2.113555
29	6	0	-0.740492	-0.945774	-0.551486
30	8	0	-0.695343	-1.425445	-1.685698

Table S7. The stationary orientations of the compound (9g) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	1.420813	-1.065043	1.039590
2	6	0	0.604087	-1.369371	0.011790
3	6	0	-0.595625	-0.755644	0.327928
4	7	0	-0.437944	-0.108998	1.523425
5	7	0	0.773722	-0.290217	1.955440
6	6	0	2.830516	-1.397192	1.242651
7	6	0	3.768682	-0.583022	0.372232
8	6	0	-3.042718	-0.131531	-0.090114
9	6	0	4.675972	-1.219919	-0.479512
10	6	0	5.555139	-0.467359	-1.263104
11	6	0	5.533913	0.924706	-1.208816
12	6	0	4.620553	1.539209	-0.356373

13	6	0	3.740232	0.815800	0.435516
14	9	0	4.593438	2.885214	-0.295506
15	6	0	-3.335457	0.636537	1.018841
16	6	0	-4.670043	1.115085	1.020343
17	6	0	-5.398098	0.718131	-0.078863
18	16	0	-4.438017	-0.263717	-1.146168
19	1	0	0.898523	-1.965836	-0.836883
20	1	0	3.014877	-1.213362	2.304875
21	1	0	2.962021	-2.466863	1.056075
22	1	0	4.698997	-2.305381	-0.531042
23	1	0	6.201816	1.534371	-1.808092
24	1	0	3.043024	1.338251	1.083364
25	1	0	-2.605199	0.837309	1.792486
26	1	0	-5.086786	1.735198	1.807790
27	1	0	6.256924	-0.968780	-1.923184
28	6	0	-1.820849	-0.818376	-0.508024
29	8	0	-1.777677	-1.462393	-1.558559
30	6	0	-6.828554	1.041261	-0.393126

31	1	0	-6.923810	1.583848	-1.341420
32	1	0	-7.441715	0.135450	-0.472468
33	1	0	-7.252563	1.667391	0.397822

Table S8. The stationary orientations of the compound (9h) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-1.982795	-1.773973	0.353727
2	6	0	-1.305212	-0.799177	0.989189
3	6	0	-0.023059	-0.874191	0.471548
4	7	0	0.003406	-1.884791	-0.450766
5	7	0	-1.173736	-2.429093	-0.525365
6	6	0	-3.389536	-2.174723	0.483890

7	6	0	-4.357840	-1.072708	0.119879
8	6	0	2.426397	-0.167196	0.254540
9	6	0	-5.213651	-0.525686	1.075229
10	6	0	-6.118886	0.488884	0.748322
11	6	0	-6.166074	0.971614	-0.563646
12	6	0	-5.306684	0.428947	-1.534874
13	6	0	-4.418941	-0.579177	-1.194605
14	6	0	2.900855	-1.044609	-0.699858
15	6	0	4.273528	-0.853405	-1.003161
16	6	0	4.816057	0.171508	-0.268537
17	16	0	3.685127	0.926304	0.802959
18	1	0	-1.743811	-0.140150	1.721153
19	1	0	-3.487176	-3.041547	-0.175476
20	1	0	-3.557087	-2.512501	1.511693
21	1	0	-5.186031	-0.894385	2.098460
22	1	0	-3.757494	-0.989446	-1.953936
23	1	0	2.269186	-1.795988	-1.156855
24	1	0	4.834660	-1.437336	-1.722578

25	1	0	-6.770417	0.888723	1.516501
26	6	0	1.104306	0.000231	0.866494
27	8	0	0.913398	0.869685	1.718870
28	1	0	-5.360231	0.816221	-2.547348
29	8	0	-7.000787	1.953979	-1.000702
30	6	0	-7.888886	2.550698	-0.066650
31	1	0	-7.343754	3.037678	0.752329
32	1	0	-8.448047	3.302775	-0.625578
33	1	0	-8.588011	1.814445	0.350998
34	35	0	6.598655	0.772294	-0.344908

Table S9. The stationary orientations of the compound (9i) using the DFT/B3LYP/6-31G* level by using Gaussian 09.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	7	0	0.998564	-1.835519	-0.719093
2	6	0	-0.130238	-1.101142	-0.838563
3	6	0	-1.065805	-1.772640	-0.071403
4	7	0	-0.455217	-2.872790	0.475107
5	7	0	0.784768	-2.904470	0.098833
6	6	0	2.326840	-1.605275	-1.279196
7	6	0	3.078628	-0.479383	-0.593041
8	6	0	-2.982812	-0.117517	0.089428
9	6	0	3.630985	0.554578	-1.353623
10	6	0	4.341702	1.561046	-0.705257
11	6	0	4.517666	1.581637	0.671400
12	6	0	3.950848	0.537500	1.397204
13	6	0	3.237354	-0.492473	0.798306
14	9	0	4.106622	0.530834	2.732768
15	6	0	-2.293062	1.070792	0.212427
16	6	0	-3.137833	2.211037	0.187470
17	6	0	-4.471069	1.898703	0.051815
18	16	0	-4.703910	0.176094	-0.033409

19	1	0	-0.190623	-0.218165	-1.455303
20	1	0	2.853584	-2.556661	-1.161815
21	1	0	2.225481	-1.405647	-2.349943
22	1	0	3.522967	0.590697	-2.432870
23	1	0	5.070590	2.374673	1.160368
24	1	0	2.815064	-1.284223	1.408387
25	1	0	-1.219468	1.122313	0.352805
26	1	0	-2.778306	3.231549	0.273559
27	6	0	-2.520251	-1.514454	0.118658
28	8	0	-3.305017	-2.441670	0.275609
29	9	0	4.871700	2.556098	-1.440378
30	6	0	-5.631921	2.846029	-0.015841
31	1	0	-6.178511	2.751475	-0.961850
32	1	0	-6.348556	2.668403	0.794777
33	1	0	-5.277419	3.877888	0.067418

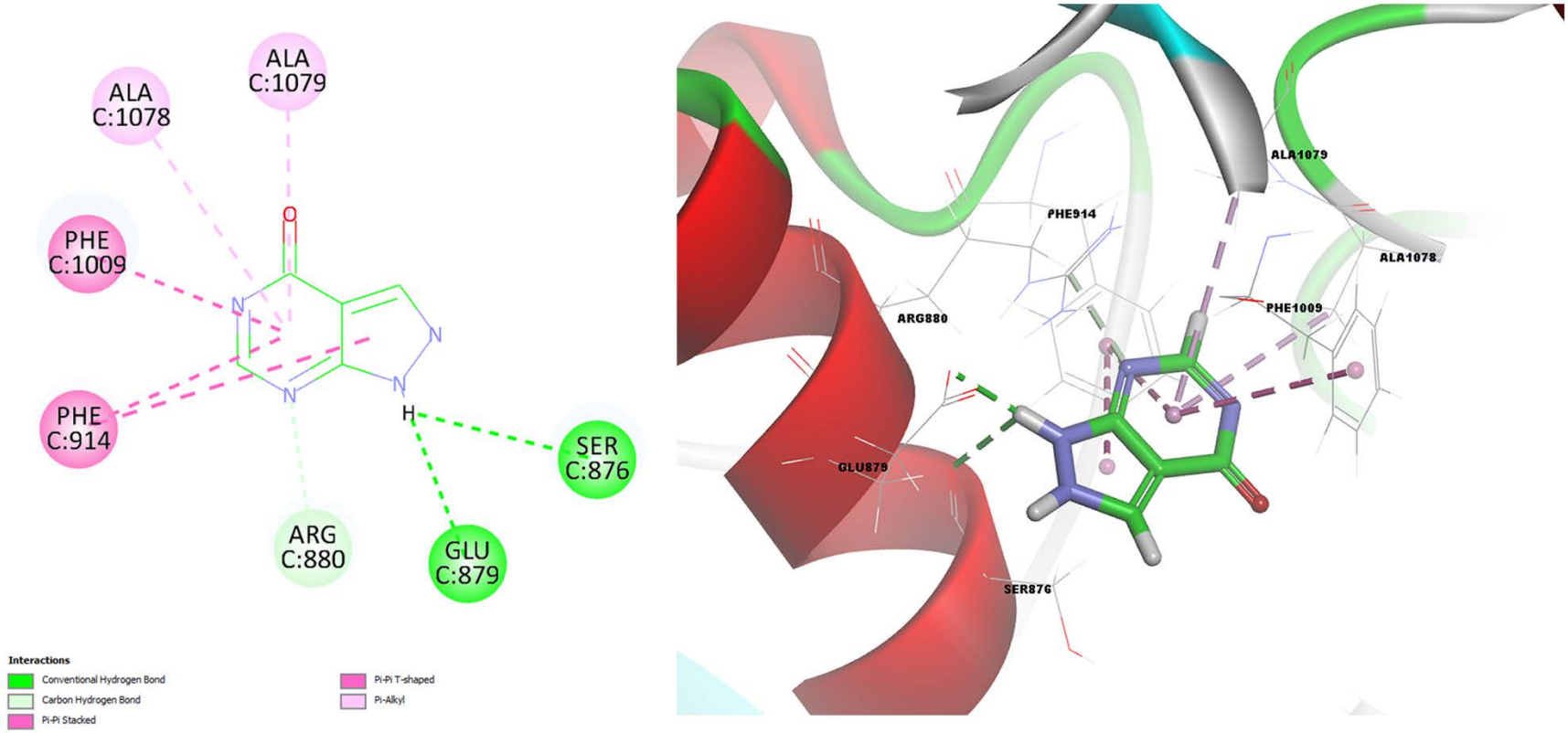

Figure S41. 2D and 3D interactions of allopurinol with active site in XO.

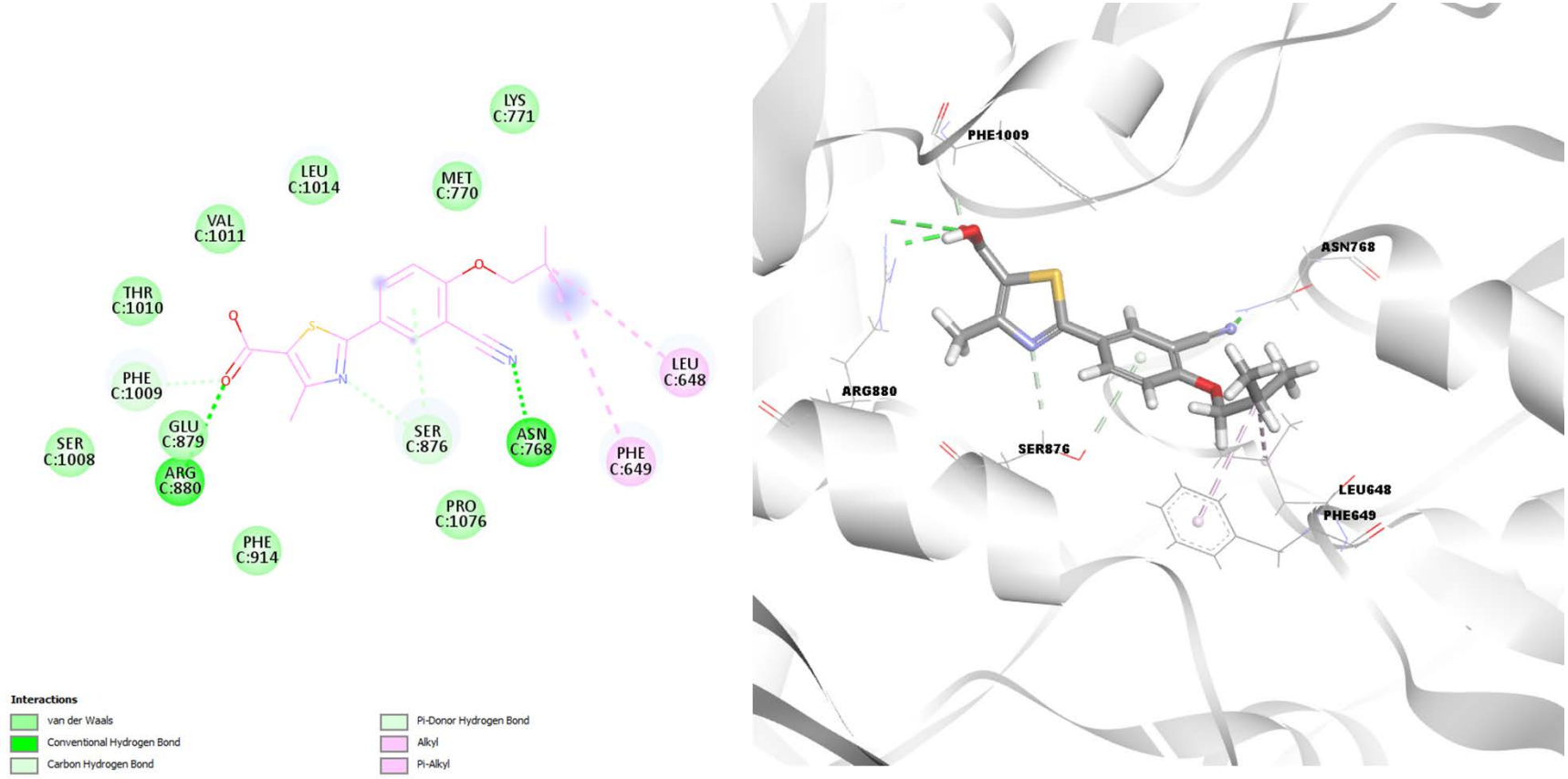

Figure S42. 2D and 3D interactions of febuxostat with active site in XO.

Table S10. Interactions types and distances of allopurinol and febuxostat with XO.

Interactions- Allopurinol	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
Allopurinol: H14 - C: SER876: O	2.949	Hydrogen Bond	Conventional Hydrogen Bond	C: SER876: O	Allopurinol:H14
Allopurinol:H14 - C:GLU879:OE2	2.224	Hydrogen Bond	Conventional Hydrogen Bond	C:GLU879:OE2	Allopurinol:H14
C:ARG880:HD2 - Allopurinol:N2	2.706	Hydrogen Bond	Carbon Hydrogen Bond	C:ARG880:HD2	Allopurinol:N2
C:PHE914 - Allopurinol	4.447	Hydrophobic	Pi-Pi Stacked	C:PHE914	Allopurinol
Allopurinol - C:PHE914	5.633	Hydrophobic	Pi-Pi Stacked	C:PHE914	Allopurinol
C:PHE1009 - Allopurinol	4.797	Hydrophobic	Pi-Pi T-shaped	C:PHE1009	Allopurinol
Allopurinol - C:ALA1078	5.097	Hydrophobic	Pi-Alkyl	C:ALA1078	Allopurinol
Allopurinol - C:ALA1079	5.209	Hydrophobic	Pi-Alkyl	C:ALA1079	Allopurinol
Interactions-Febuxostat	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
C:ASN768:HD21 - :Febuxostat:N6	1.6909	Hydrogen Bond	Conventional Hydrogen Bond	C:ASN768:HD21	:Febuxostat:N6
C:ARG880:HH12 - :Febuxostat:O4	2.9192	Hydrogen Bond	Conventional Hydrogen Bond	C:ARG880:HH12	:Febuxostat:O4
C:ARG880:HH21 - :Febuxostat:O4	2.3001	Hydrogen Bond	Conventional Hydrogen Bond	C:ARG880:HH21	:Febuxostat:O4
C:SER876:HB1 - :Febuxostat:N5	2.4496	Hydrogen Bond	Carbon Hydrogen Bond	C:SER876:HB1	:Febuxostat:N5
C:PHE1009:HA - :Febuxostat:O4	1.7801	Hydrogen Bond	Carbon Hydrogen Bond	C:PHE1009:HA	:Febuxostat:O4
C:SER876:HG - :Febuxostat	3.2248	Hydrogen Bond	Pi-Donor Hydrogen Bond	C:SER876:HG	:Febuxostat
:Febuxostat:C7 - C:LEU648	4.3666	Hydrophobic	Alkyl	C:LEU648	:Febuxostat:C7
C:PHE649 - :Febuxostat:C7	4.5641	Hydrophobic	Pi-Alkyl	C:PHE649	:Febuxostat:C7

Table S11. Interactions types and distances of the ligands (**9a-9i**) with XO.

Interactions-9a	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
C:VAL1011:HN - :9a:F19	2.567	Hydrogen Bond;Halogen	Conventional Hydrogen Bond;Halogen (Fluorine)	C:VAL1011:HN	:9a:F19

C:PHE1009:HA - :9a:F19	2.114	Hydrogen Bond;Halogen	Carbon Hydrogen Bond;Halogen (Fluorine)	C:PHE1009:HA	:9a:F19
:9a:H13 - C:THR772:OG1	2.428	Hydrogen Bond	Carbon Hydrogen Bond	C:THR772:OG1	:9a:H13
C:PHE1009:C - :9a:F19	3.288	Halogen	Halogen (Fluorine)	C:PHE1009:C	:9a:F19
C:VAL1011:O - :9a:F19	3.632	Halogen	Halogen (Fluorine)	C:VAL1011:O	:9a:F19
C:ARG880:NH2 - :9a	3.152	Electrostatic	Pi-Cation	C:ARG880:NH2	:9a
C:GLU879:OE2 - :9a	4.174	Electrostatic	Pi-Anion	C:GLU879:OE2	:9a
C:PHE1009 - :9a	4.998	Hydrophobic	Pi-Pi T-shaped	C:PHE1009	:9a
:9a - C:ALA1078	3.650	Hydrophobic	Pi-Alkyl	C:ALA1078	:9a
:9a - C:VAL1011	5.472	Hydrophobic	Pi-Alkyl	C:VAL1011	:9a
:9a - C:LEU648	5.107	Hydrophobic	Pi-Alkyl	C:LEU648	:9a
:9a - C:LEU873	5.001	Hydrophobic	Pi-Alkyl	C:LEU873	:9a
Interactions-9b	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
:9b:H13 - C:THR772:OG1	2.426	Hydrogen Bond	Carbon Hydrogen Bond	C:THR772:OG1	:9b:H13
C:GLU879:OE1 - :9b:F19	3.063	Halogen	Halogen (Fluorine)	C:GLU879:OE1	:9b:F19
C:ARG880:NH2 - :9b	3.100	Electrostatic	Pi-Cation	C:ARG880:NH2	:9b
C:GLU879:OE2 - :9b	4.115	Electrostatic	Pi-Anion	C:GLU879:OE2	:9b
C:PHE1009 - :9b	5.0316	Hydrophobic	Pi-Pi T-shaped	C:PHE1009	:9b
:9b - C:ALA1078	3.639	Hydrophobic	Pi-Alkyl	C:ALA1078	:9b
:9b - C:LEU648	5.104	Hydrophobic	Pi-Alkyl	C:LEU648	:9b
:9b - C:LEU873	4.997	Hydrophobic	Pi-Alkyl	C:LEU873	:9b
Interactions-9c	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
C:VAL1011:HN - :9c:F19	2.578	Hydrogen Bond;Halogen	Conventional Hydrogen Bond;Halogen (Fluorine)	C:VAL1011:HN	:9c:F19

C:PHE1009:HA - :9c:F19	2.122	Hydrogen Bond;Halogen	Carbon Hydrogen Bond;Halogen (Fluorine)	C:PHE1009:HA	:9c:F19
:9c:H12 - C:THR772:OG1	2.425	Hydrogen Bond	Carbon Hydrogen Bond	C:THR772:OG1	:9c:H12
C:GLU879:OE1 - :9c:F20	3.0688	Halogen	Halogen (Fluorine)	C:GLU879:OE1	:9c:F20
C:PHE1009:C - :9c:F19	3.309	Halogen	Halogen (Fluorine)	C:PHE1009:C	:9c:F19
C:VAL1011:O - :9c:F19	3.661	Halogen	Halogen (Fluorine)	C:VAL1011:O	:9c:F19
C:ARG880:NH2 - :9c	3.110	Electrostatic	Pi-Cation	C:ARG880:NH2	:9c
C:GLU879:OE2 - :9c	4.144	Electrostatic	Pi-Anion	C:GLU879:OE2	:9c
C:PHE1009 - :9c	5.000	Hydrophobic	Pi-Pi T-shaped	C:PHE1009	:9c
:9c - C:ALA1078	3.622	Hydrophobic	Pi-Alkyl	C:ALA1078	:9c
:9c - C:LEU648	5.119	Hydrophobic	Pi-Alkyl	C:LEU648	:9c
:9c - C:LEU873	5.0174	Hydrophobic	Pi-Alkyl	C:LEU873	:9c
Interactions-9d	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
9d:H6 - C:THR772:OG1	2.580	Hydrogen Bond	Carbon Hydrogen Bond	C:THR772:OG1	9d:H6
C:ARG880:NH2 - 9d	3.527	Electrostatic	Pi-Cation	C:ARG880:NH2	9d
C:GLU879:OE2 - 9d	3.779	Electrostatic	Pi-Anion	C:GLU879:OE2	9d
C:PHE1009 - 9d	5.904	Hydrophobic	Pi-Pi T-shaped	C:PHE1009	9d
9d - C:ALA1078	3.700	Hydrophobic	Pi-Alkyl	C:ALA1078	9d
9d - C:LEU648	5.215	Hydrophobic	Pi-Alkyl	C:LEU648	9d
9d - C:LEU873	4.970	Hydrophobic	Pi-Alkyl	C:LEU873	9d
Interactions-9e	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
C:VAL1011:HN - :9e:F15	2.569	Hydrogen Bond;Halogen	Conventional Hydrogen Bond;Halogen (Fluorine)	C:VAL1011:HN	:9e:F15
C:SER876:HA - :9e:F14	2.563	Hydrogen Bond;Halogen	Carbon Hydrogen Bond;Halogen (Fluorine)	C:SER876:HA	:9e:F14

C:PHE1009:HA - :9e:F15	2.185	Hydrogen Bond;Halogen	Carbon Hydrogen Bond;Halogen (Fluorine)	C:PHE1009:HA	:9e:F15
C:SER876:O - :9e:F14	3.360	Halogen	Halogen (Fluorine)	C:SER876:O	:9e:F14
C:GLU879:CD - :9e:F14	3.322	Halogen	Halogen (Fluorine)	C:GLU879:CD	:9e:F14
C:PHE1009:C - :9e:F15	3.428	Halogen	Halogen (Fluorine)	C:PHE1009:C	:9e:F15
C:ARG880:NH2 - :9e	3.144	Electrostatic	Pi-Cation	C:ARG880:NH2	:9e
C:GLU879:OE2 - :9e	4.108	Electrostatic	Pi-Anion	C:GLU879:OE2	:9e
:9e - C:ALA1078	3.658	Hydrophobic	Pi-Alkyl	C:ALA1078	:9e
:9e - C:LEU648	5.0587	Hydrophobic	Pi-Alkyl	C:LEU648	:9e
:9e - C:LEU873	5.0327	Hydrophobic	Pi-Alkyl	C:LEU873	:9e
Interactions-9f	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
C:VAL1011:HN - :9f:O14	2.250	Hydrogen Bond	Conventional Hydrogen Bond	C:VAL1011:HN	:9f:O14
C:PHE1009:HA - :9f:N3	2.403	Hydrogen Bond	Carbon Hydrogen Bond	C:PHE1009:HA	:9f:N3
C:PHE1009:HA - :9f:O14	2.387	Hydrogen Bond	Carbon Hydrogen Bond	C:PHE1009:HA	:9f:O14
C:GLU879:OE1 - :9f	3.485	Electrostatic	Pi-Anion	C:GLU879:OE1	:9f
:9f - C:PHE1009	3.675	Hydrophobic	Pi-Pi Stacked	C:PHE1009	:9f
:9f - C:PHE914	5.837	Hydrophobic	Pi-Pi T-shaped	C:PHE914	:9f
:9f - C:ALA1079	4.430	Hydrophobic	Pi-Alkyl	C:ALA1079	:9f
:9f - C:PRO1076	5.413	Hydrophobic	Pi-Alkyl	C:PRO1076	:9f
:9f - C:ALA1078	4.482	Hydrophobic	Pi-Alkyl	C:ALA1078	:9f
:9f - C:VAL1011	4.230	Hydrophobic	Pi-Alkyl	C:VAL1011	:9f
Interactions-9g	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
C:VAL1011:HN - :9g:O	2.3200	Hydrogen Bond	Conventional Hydrogen Bond	C:VAL1011:HN	:9g:O

C:PHE1009:HA - :9g:N	2.4122	Hydrogen Bond	Carbon Hydrogen Bond	C:PHE1009:HA	:9g:N
C:PHE1009:HA - :9g:O	2.3350	Hydrogen Bond	Carbon Hydrogen Bond	C:PHE1009:HA	:9g:O
C:GLU879:OE1 - :9g	3.3855	Electrostatic	Pi-Anion	C:GLU879:OE1	:9g
:9g - C:PHE1009	3.5771	Hydrophobic	Pi-Pi Stacked	C:PHE1009	:9g
:9g - C:ALA1079	4.3475	Hydrophobic	Pi-Alkyl	C:ALA1079	:9g
:9g - C:PRO1076	5.3595	Hydrophobic	Pi-Alkyl	C:PRO1076	:9g
:9g - C:ALA1078	4.5113	Hydrophobic	Pi-Alkyl	C:ALA1078	:9g
:9g - C:VAL1011	4.3612	Hydrophobic	Pi-Alkyl	C:VAL1011	:9g
Interactions-9h	**Distance Å**	**Bonding**	**Bonding Types**	**Binding site of enzyme**	**Binding site of ligand**
C:ARG880:HH12 - :9h:O	2.8392	Hydrogen Bond	Conventional Hydrogen Bond	C:ARG880:HH12	:9h:O
C:ARG880:HH21 - :9h:O	2.4824	Hydrogen Bond	Conventional Hydrogen Bond	C:ARG880:HH21	:9h:O
C:PHE1009:HA - :9h:O	1.8778	Hydrogen Bond	Carbon Hydrogen Bond	C:PHE1009:HA	:9h:O
C:ARG880:NH2 - :9h	3.6331	Electrostatic	Pi-Cation	C:ARG880:NH2	:9h
C:GLU879:OE1 - :9h	3.5129	Electrostatic	Pi-Anion	C:GLU879:OE1	:9h
:9h- C:PHE1009	4.2078	Hydrophobic	Pi-Pi Stacked	C:PHE1009	:9h
:9h:C - C:LEU648	4.2371	Hydrophobic	Alkyl	C:LEU648	:9h:C
:9h:C - C:MET770	5.1518	Hydrophobic	Alkyl	C:MET770	:9h:C
:9h - C:ALA1078	3.8971	Hydrophobic	Pi-Alkyl	C:ALA1078	:9h
:9h - C:ALA1079	4.2056	Hydrophobic	Pi-Alkyl	C:ALA1079	:9h
:9h - C:PRO1076	4.6897	Hydrophobic	Pi-Alkyl	C:PRO1076	:9h
:9h - C:ALA1078	5.3331	Hydrophobic	Pi-Alkyl	C:ALA1078	:9h
:9h - C:VAL1011	4.7429	Hydrophobic	Pi-Alkyl	C:VAL1011	:9h

Interactions-9i	Distance Å	Bonding	Bonding Types	Binding site of enzyme	Binding site of ligand
C:SER876:HG - :9i:F	2.6998	Hydrogen Bond;Halogen	Conventional Hydrogen Bond;Halogen (Fluorine)	C:SER876:HG	:9i:F
C:ARG880:HH12 - :9i:O	2.8489	Hydrogen Bond	Conventional Hydrogen Bond	C:ARG880:HH12	:9i:O
C:ARG880:HH21 - :9i:O	2.5730	Hydrogen Bond	Conventional Hydrogen Bond	C:ARG880:HH21	:9i:O
C:PHE1009:HA - :9i:O	1.9824	Hydrogen Bond	Carbon Hydrogen Bond	C:PHE1009:HA	:9i:O
:9i:H3 - C:GLU802:OE1	3.0829	Hydrogen Bond	Carbon Hydrogen Bond	C:GLU802:OE1	:9i:H3
C:ARG880:NH2 - :9i	3.5764	Electrostatic	Pi-Cation	C:ARG880:NH2	:9i
C:GLU879:OE1 - :9i	3.4809	Electrostatic	Pi-Anion	C:GLU879:OE1	:9i
:9i - C:PHE1009	4.1919	Hydrophobic	Pi-Pi Stacked	C:PHE1009	:9i
:9i - C:ALA1078	3.8454	Hydrophobic	Pi-Alkyl	C:ALA1078	:9i
:9i - C:ALA1079	4.3946	Hydrophobic	Pi-Alkyl	C:ALA1079	:9i
:9i - C:PRO1076	5.3412	Hydrophobic	Pi-Alkyl	C:PRO1076	:9i
:9i - C:VAL1011	4.8093	Hydrophobic	Pi-Alkyl	C:VAL1011	:9i