Electronic Supplementary Material (ESI) for RSC Advances.

SUPPLEMENTARY INFORMATION

Identification of Xanthine Oxidase Inhibitors through Hierarchical Virtual Screening

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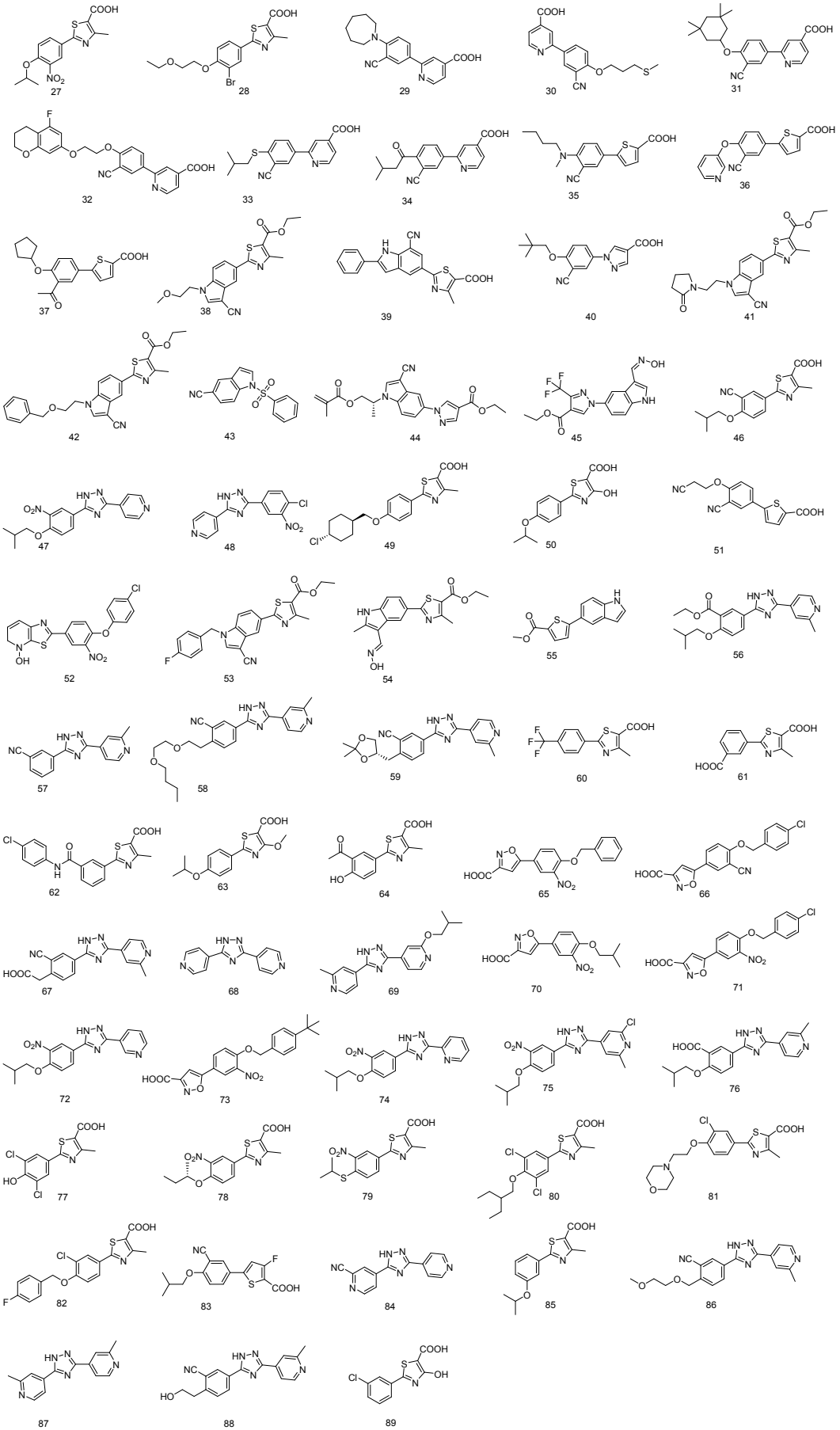
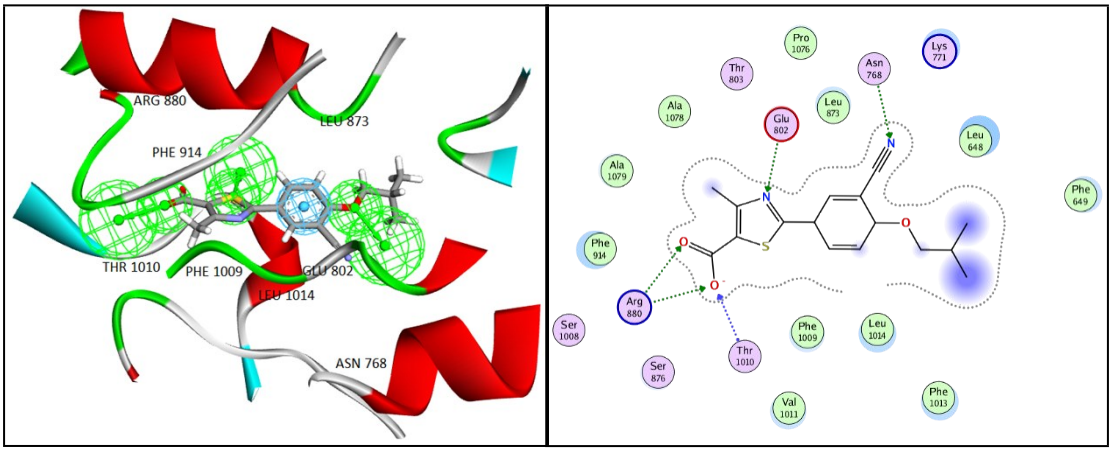
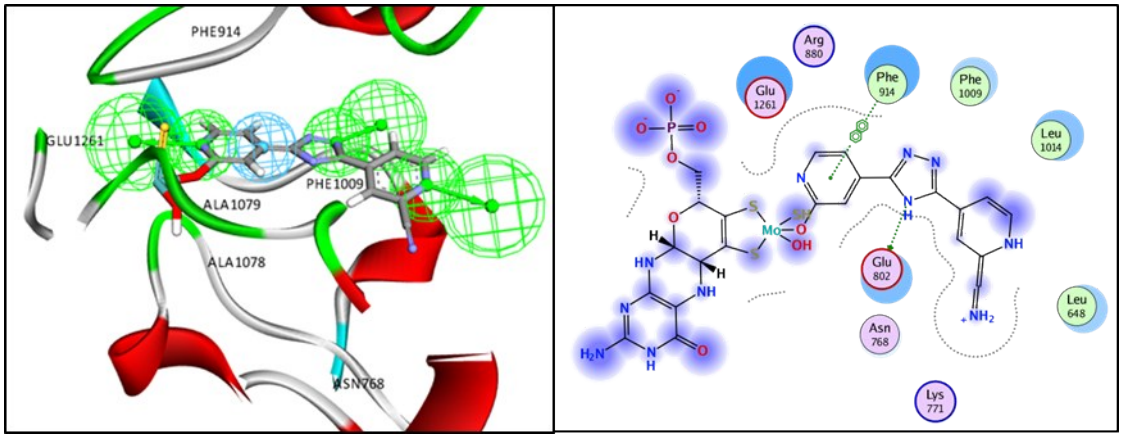


Figure S1. Chemical structures of the sixty-three test set compounds.



A



B

Figure S2. Alignments of Hypo 1 with co-crystallized structures of (**A**) febuxostat (PDB code: 1N5X) and (**B**) topiroxostat (PDB code: 1V97). The ligand-receptor interactions were shown in 2D plots on the right.

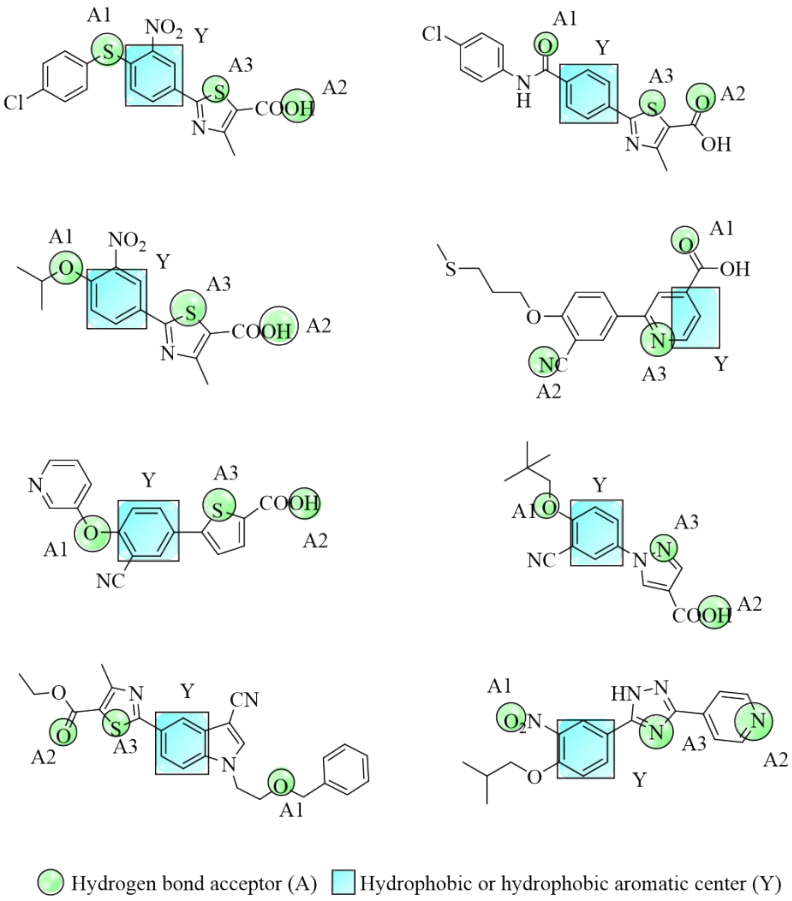


Figure S3. Mapping Hypo 1 to different inhibitor structures. Each feature of Hypo 1 could perfectly match to the corresponding molecular areas.

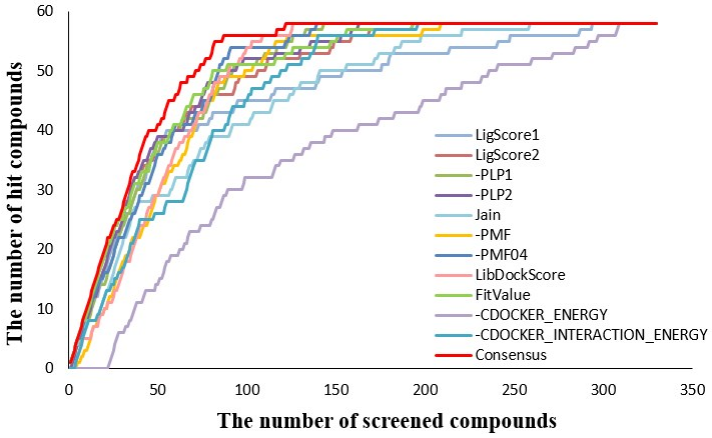


Figure S4. Comparison of different scoring functions by their capability to distinguish the active from the inactive ones in the decoy set. Ten scoring functions were initially evaluated and the five performed best (-PLP2, -PMF04, LibDockScore, LigScore2 and -CDOCKER_INTERACTION_ENERGY) were combined with the fit value based on Hypo 1 to generate the consensus score, which had the AUC of 0.96 and exceeded any of the individual scoring function.

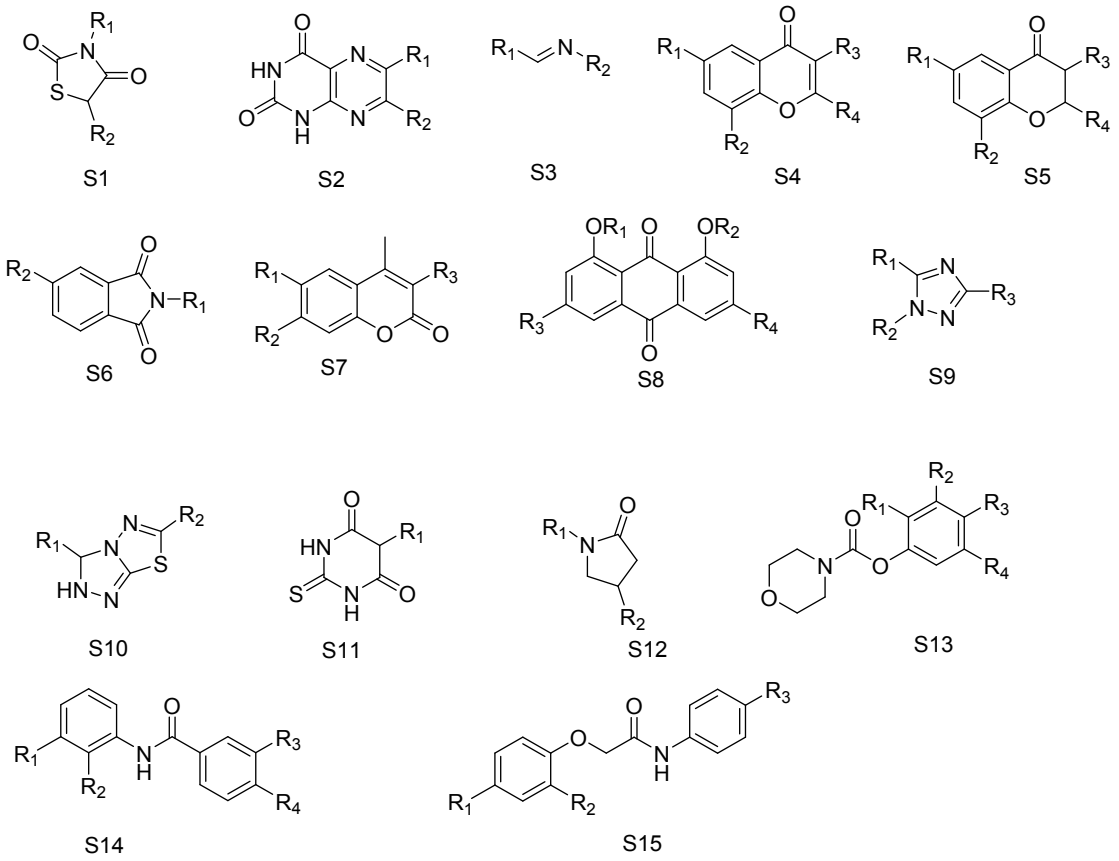
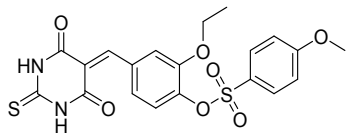


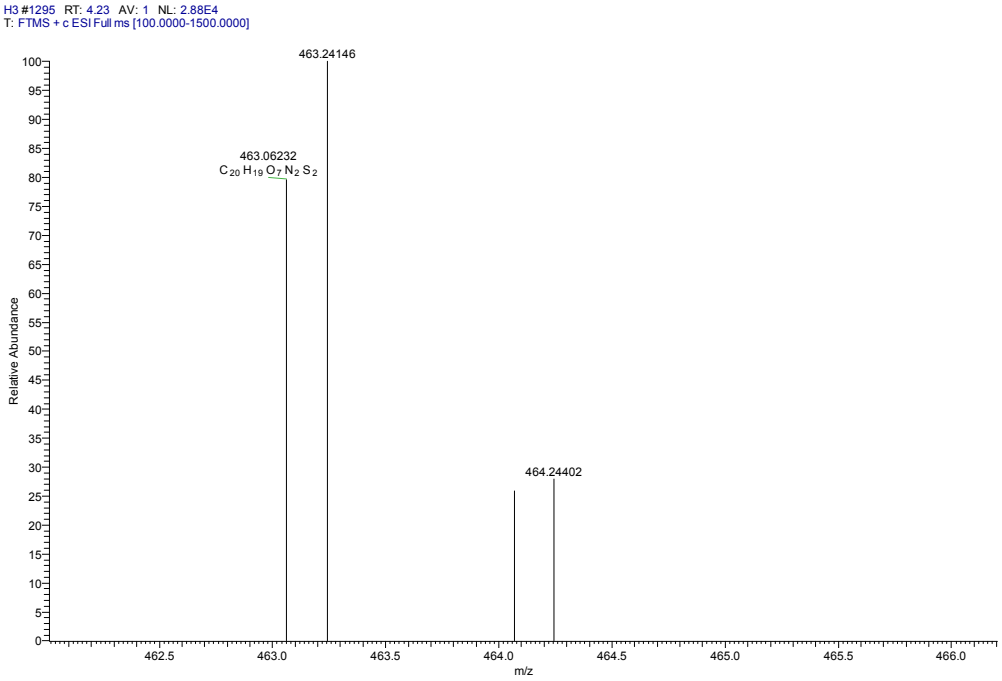
Figure S5. The 74 potential hits were classified into sixteen subgroups. The eighteen compounds in S16 have no common scaffold.



H3 (SPECS product ID: AN-698/40748954)

A. The MS spectrum for **H3**.

HR-ESI-MS: *m/z* calcd for $C_{20}H_{19}O_7N_2S_2$ 463.06282, found 463.06232



B. The ^{1}H NMR spectrum for **H3** (300 MHz, DMSO-d_6).

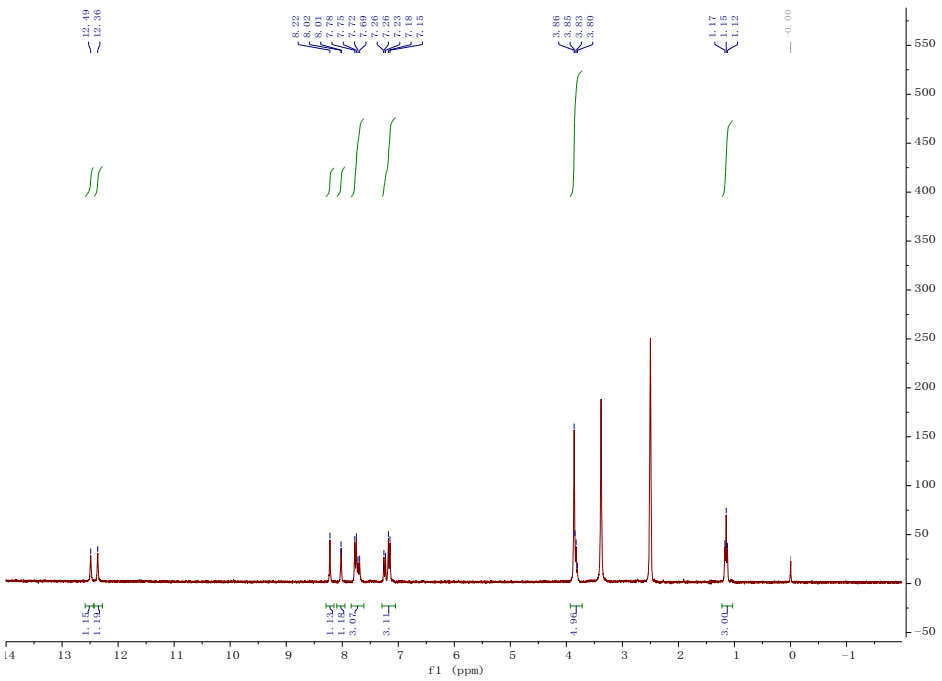


Figure S6. The chemical characterization of compound **H3**.

Table S1. Experimental and estimated XO inhibitory activities of the training set and test set compounds.

Compound Number	Experimental IC_{50} (nM)	Estimated activity (nM)	Compound Number	Experimental IC_{50} (nM)	Estimated activity (nM)
1	0.02	0.16	46	1.40	2.59
2	0.32	0.27	47	3.70	35.73
3	0.38	0.41	48	4.70	37.71
4	0.5	9.9	49	17.00	9.13
5	0.7	0.69	50	45.00	67.83
6	0.94	0.41	51	13.00	14.66
7	2.2	10	52	20.20	22.11
8	2.4	2.2	53	60.00	665.23
9	3.2	3.2	54	13.00	7.08
10	4.2	8.2	55	40.00	39.68
11	5.7	2.6	56	20.00	34.68
12	6	11	57	43.00	203.58
13	6	0.29	58	26.00	3.22
14	6.2	7.7	59	60.00	206.77
15	7	5.5	60	310.00	741.46
16	9.3	5.5	61	320.00	432.04
17	10	15	62	150.00	268.98
18	10	8.1	63	130.00	71.69
19	24	41	64	300.00	294.88
20	30	40	65	970.00	960.49
21	37	74	66	630.00	654.48
22	53	74	67	110.00	79.74
23	160	120	68	170.00	220.09
24	3940	940	69	170.00	99.75
25	29200	23000	70	1000.00	957.16
26	32640	2400	71	2830.00	2885.26
27	0.57	0.29	72	5900.00	8885.02
28	2.90	4.16	73	12750.00	1112.61
29	1.20	8.87	74	10000.00	7547.12
30	5.00	7.10	75	10000.00	11798.90
31	4.30	3.20	76	10000.00	11181.20
32	7.30	5.16	77	26.00	36.62
33	2.50	8.18	78	2.40	4.17
34	3.10	9.10	79	0.30	0.16
35	4.10	7.96	80	0.80	0.42
36	2.80	9.32	81	1.50	2.22
37	5.90	6.18	82	3.40	2.40
38	3.50	5.83	83	2.20	8.67
39	4.00	3.21	84	5.30	77.46

40	4.30	9.17	85	67.00	24.57
41	4.40	2.93	86	24.00	26.82
42	4.60	2.00	87	310.00	133.41
43	4.20	69.85	88	40.00	12.78
44	6.90	7.83	89	720.00	781.54
45	4.60	76.86			