Supplementary Materials

Indole-acrylonitrile derivatives as potential antitumor and antimicrobial agents – synthesis, *in vitro* and *in silico* studies

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Table S1. FRED Chemgauss4 scores of the docked ligands **1**, **2a-x**, **3**, **4a-c**, **5a-d**, **6a-b** and **7**.

Compd	FRED Chemgauss4 score				
	caspase-3 (2xyp)	caspase-9 (2ar9)	tubulin (5eyp)	penicillin-binding protein 4 (2ex8)	β-lactamase (1fqg)
1	-5.23302	-5.08912	-8.9825	-5.27782	-6.51337
2a	-5.90363	-3.884	-10.8717	-5.17229	-8.23318
2b	-5.08525	-3.37537	-11.6776	-5.77427	-8.2824
2c	-5.60849	-3.65052	-11.4421	-5.0086	-8.18364
2d	-4.94597	-3.66019	-11.2076	-4.86242	-8.06483
2e	-6.27092	-3.58057	-10.6082	-5.30321	-8.12786
2f	-5.47292	-4.32452	-11.6918	-4.40842	-7.48552
2g	-5.51387	-3.34911	-11.1683	-5.73747	-7.95726
2h	-5.67204	-3.7449	-11.1333	-5.90206	-9.63335
2i	-5.67204	-3.7449	-11.1333	-5.90206	-9.63335
2j	-5.34182	-3.86886	-11.1676	-5.44939	-7.9373
2k	-5.11492	-3.82303	-10.779	-5.61474	-8.12498
2l	-5.54945	-3.57143	-11.4581	-5.12205	-8.33456
2m	-5.85053	-3.3784	-10.0974	-4.70873	-7.88071
2n	-4.71896	-3.80598	-10.2373	-4.84896	-7.80353
2o	-6.20214	-3.50577	-13.2754	-5.65625	-9.23724
2p	-6.61627	-3.47568	-12.2016	-5.56695	-8.22868
2q	-5.96685	-3.61183	-11.7359	-5.3542	-9.61483
2r	-6.7915	-4.39583	-11.7718	-5.20843	-7.84654
2s	-5.65366	-3.97643	-11.2263	-5.48613	-8.53547
2t	-5.86027	-3.8612	-10.9212	-5.38187	-8.18399
2u	-6.16928	-4.19446	-11.1868	-5.13292	-8.16696
2v	-5.27053	-3.8119	-11.1987	-4.94718	-8.15649
2w	-6.21192	-4.00936	-11.1138	-4.90712	-8.22966
2x	-6.20929	-6.6242	-10.2871	-5.99989	-7.75472
3	-6.48325	-3.37125	-9.97834	-4.45381	-8.18494
4a	-5.6432	-4.20064	-12.4149	-6.23501	-8.78394
4b	-5.85867	-3.97765	-11.548	-6.40248	-8.57117
4c	-6.31567	-4.53341	-12.3295	-6.87913	-8.76742
5a	-4.98728	-2.59772	-12.4227	-4.76406	-7.88166
5b	-4.92247	-2.4134	-12.3072	-4.77243	-7.60658
5c	-5.32272	-2.35997	-11.5326	-4.13846	-8.25605
5d	-6.09417	-3.05058	-13.3035	-5.41821	-8.54794
6a	-5.55541	-2.59091	-11.8886	-4.51006	-8.18193
6b	-5.98233	-3.47475	-11.6401	-4.3311	-7.96514
7	-4.87739	-2.1102	-12.0286	-4.53795	-7.71406
original ligand*	-5.14153	-7.50372	-17.5854	-5.65605	-9.54773

*Phenylmethyl *N*-[(2S)-4-chloro-3-okso-1-phenyl-butan-2-yl]carbamate, D-maleate and colchicine (*N*-[(7S)-1,2,3,10-tetramethoxy-9-oxo-6,7-dihydro-5*H*-benzo[*d*]heptalen-7-yl]-ethanamide) were used as original ligands for 2xyp, 2ar9 and 5eyp, respectively, whereas penicillin G was used as the original ligand for 2ex8 and 1fqg.

Table S2. The 2D diagrams of interactions created by compounds 2l and **5a-d** in the active site of caspase-3 (2xyp) generated by BIOVA Discovery Studio Visualizer and Pose View.

Compd	Discovery Studio	PoseView
2l		
5a		No interactions found by the PoseView interaction model
5b		

Table S2. Continued

Compd	Discovery Studio	PoseView
5c		
5d		No interactions found by the PoseView interaction model

Table S3. The 2D diagrams of interactions created by compounds **2l** and **5a-d** in the active site of caspase-9 (2ar9) generated by BIOVA Discovery Studio Visualizer and Pose View.

Compd	Discovery Studio	PoseView
2l		
5a		
5b		
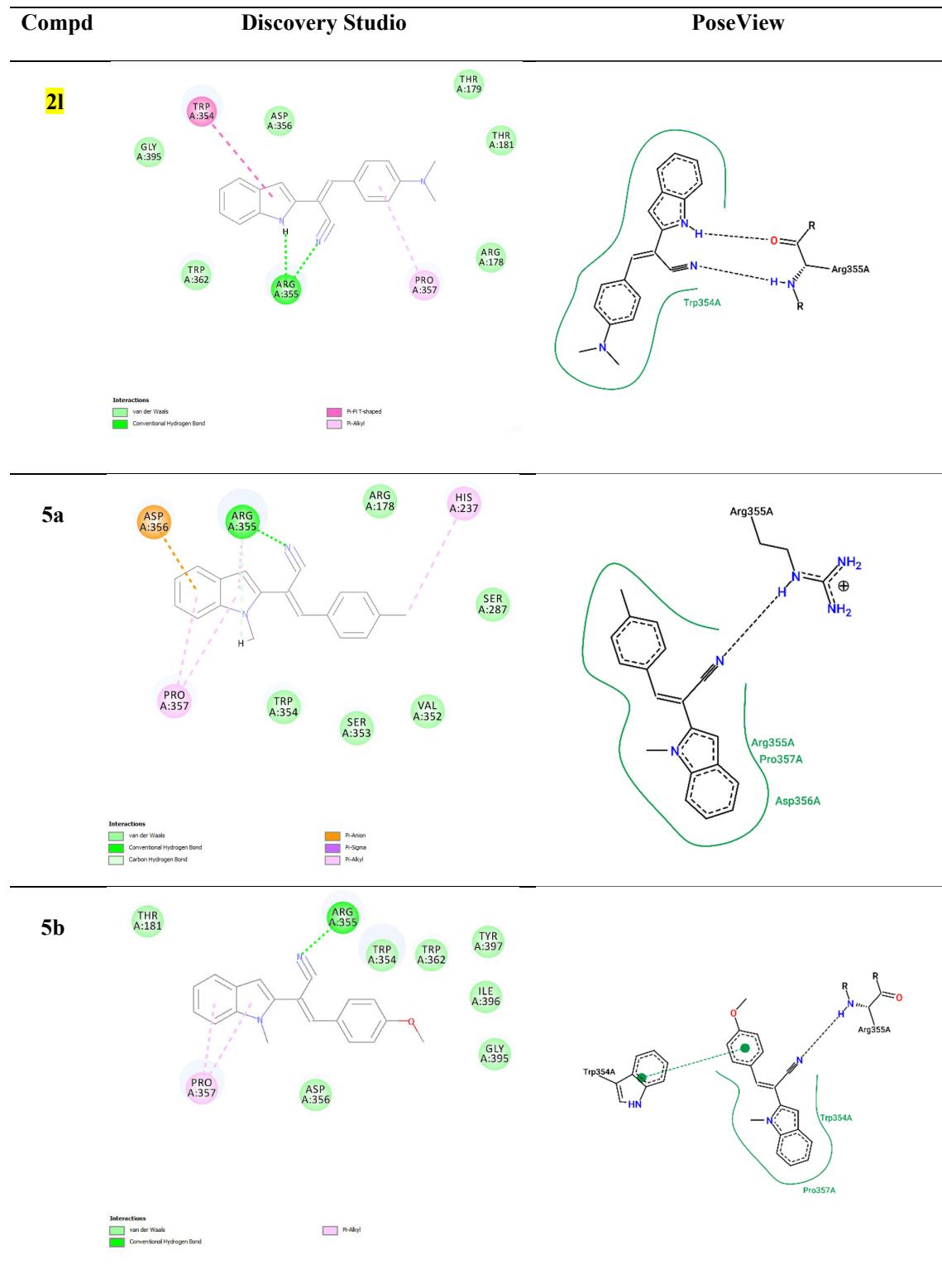
Table S3. Continued

Compd	Discovery Studio	PoseView
5c		
5d		

Table S4. The 2D diagrams of interactions created by compounds **2l** and **5a-d** in the active site of tubulin (5eyp) generated by BIOVA Discovery Studio Visualizer and Pose View.

Compd	Discovery Studio	PoseView
2l		No interactions found by the PoseView interaction model
5a		No interactions found by the PoseView interaction model
5b		No interactions found by the PoseView interaction model

Table S4. Continued

Compd	Discovery Studio	PoseView
5c		No interactions found by the PoseView interaction model
5d		No interactions found by the PoseView interaction model

Table S5. The 2D diagrams of interactions created by compounds **2x** in the active site of penicillin-binding protein 4 (2ex8) generated by BIOVA Discovery Studio Visualizer and Pose View.

Comp d	Discovery Studio	PoseView
2x		
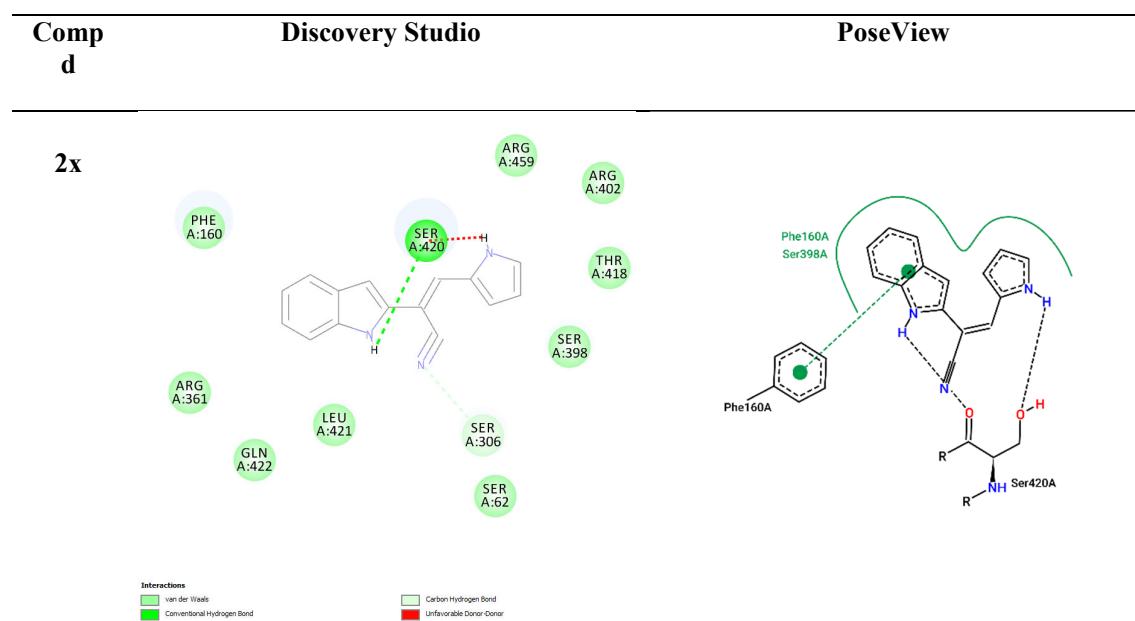
Table S6. The 2D diagrams of interactions created by compounds **2x** in the active site of β-lactamase (1fqg) generated by BIOVA Discovery Studio Visualizer and Pose View.

Comp d	Discovery Studio	PoseView
2x		
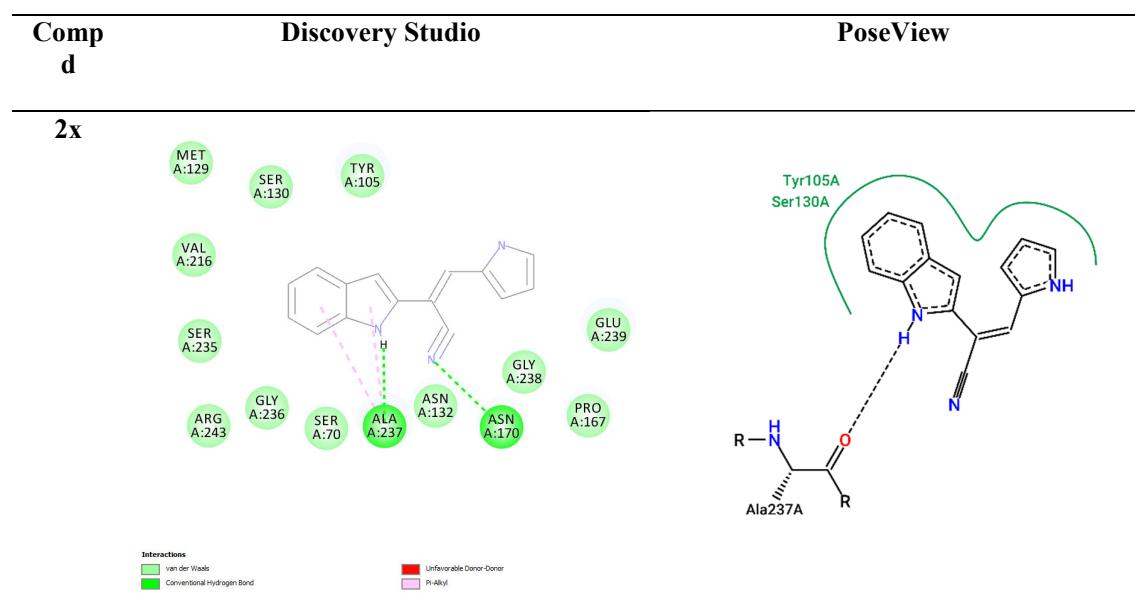
Tables S7. Predicted physicochemical, pharmacokinetic and drug-likeness properties of compounds **2l**, **2x**, **5a-d.**

|	Molecule	2l	2x	5a	5b	5c	5d
Physicochemical Properties	Formula	$C_{19}H_{17}N_3$	$C_{15}H_{11}N_3$	$C_{19}H_{16}N2$	$C_{19}H_{16}N_2O$	$C_{20}H_{19}N3$	$C_{22}H_{16}N_2$
	MW	287.36	233.27	272.34	288.34	301.38	308.38
	Heavy atoms	22	18	21	22	23	24
	Aromatic heavy atoms	15	14	15	15	15	19
	Fraction Csp3	0.11	0.00	0.11	0.11	0.15	0.05
	Rotatable bonds	3	2	2	3	3	2
	H-bond acceptors	1	1	1	2	1	1
	H-bond donors	1	2	0	0	0	0
	MR	92.43	72.58	88.09	89.62	97.33	100.63
	TPSA	42.82	55.37	28.72	37.95	31.96	28.72
Lipophilicity	iLOGP	2.71	1.67	3.11	3.14	3.15	3.16
	XLOGP3	3.99	2.69	4.18	3.79	3.94	5.07
	WLOGP	4.19	3.45	4.44	4.14	4.20	5.29
	MLOGP	2.59	1.39	3.20	2.59	2.82	3.69
	Silicos-IT Log P	3.99	3.86	4.31	3.84	3.47	4.86
	Consensus Log P	3.49	2.61	3.83	3.50	3.51	4.41
Water Solubility	ESOL Log S	-4.44	-3.42	-4.56	-4.32	-4.48	-5.40
	ESOL Solubility (mg/ml)	1.04e-02	8.78e-02	7.53e-03	1.37e-02	1.01e-02	1.23e-03
	ESOL Solubility (mol/l)	3.62e-05	3.76e-04	2.76e-05	4.76e-05	3.35e-05	3.98e-06
	ESOL Class	Moderately soluble	Soluble	Moderately soluble	Moderately soluble	Moderately soluble	Moderately soluble
	Ali Log S	-4.59	-3.51	-4.49	-4.28	-4.31	-5.42
	Ali Solubility (mg/ml)	7.37e-03	7.29e-02	8.77e-03	1.51e-02	1.47e-02	1.18e-03
	Ali Solubility (mol/l)	2.57e-05	3.12e-04	3.22e-05	5.24e-05	4.89e-05	3.84e-06
	Ali Class	Moderately soluble	Soluble	Moderately soluble	Moderately soluble	Moderately soluble	Moderately soluble
	Silicos-IT LogSw	-6.08	-5.19	-5.92	-5.66	-5.64	-7.20

	Silicos-IT Solubility (mg/ml)	2.38e-04	1.49e-03	3.24e-04	6.31e-04	6.94e-04	1.95e-05
	Silicos-IT Solubility (mol/l)	8.28e-07	6.40e-06	1.19e-06	2.19e-06	2.30e-06	6.32e-08
	Silicos-IT class	Poorly soluble	Moderately soluble	Moderately soluble	Moderately soluble	Moderately soluble	Poorly soluble
Pharmacokinetics	GI absorption	High	High	High	High	High	High
	BBB permeant	Yes	Yes	Yes	Yes	Yes	Yes
	Pgp substrate	No	No	No	No	No	No
	CYP1A2 inhibitor	Yes	Yes	Yes	Yes	Yes	Yes
	CYP2C19 inhibitor	Yes	Yes	Yes	Yes	Yes	Yes
	CYP2C9 inhibitor	Yes	Yes	Yes	Yes	Yes	Yes
	CYP2D6 inhibitor	Yes	Yes	No	No	Yes	No
	CYP3A4 inhibitor	Yes	Yes	No	Yes	Yes	No
	log Kp (cm/s)	-5.22	-5.81	-4.99	-5.37	-5.34	-4.58
Drug-likeness	Lipinski violations	0	0	0	0	0	0
	Ghose violations	0	0	0	0	0	0
	Veber violations	0	0	0	0	0	0
	Egan violations	0	0	0	0	0	0
	Muegge violations	0	0	0	0	0	1
	Bioavailability Score	0.55	0.55	0.55	0.55	0.55	0.55
Medicinal Chemistry	PAINS alerts	1	0	0	0	1	0
	Brenk alerts	1	1	1	1	1	1
	Leadlikeness violations	1	1	1	1	1	1
	Synthetic Accessibility	2.52	2.32	2.57	2.51	2.70	2.66

Tables S8. Predicted human intestinal absorption, Caco-2 cell and MDCK cell permeabilities for compounds **2l**, **2x**, **5a-d.**

Compunds	Human intestinal absorption (%)	In vitro Caco-2 cell permeability (nm/s)	In vitro MDCK cell permeability (nm/s)
Rule	0 - 20 (poor) 20 – 70 (moderate) 70 – 100 (well)	<4 (low) 4-70 (moderate) >70 (high)	<25 (low) 25-500 (moderate) >500 (high)
2l	93.69	57.59	0.09
2x	90.15	12.20	48.88
5a	100.00	55.86	46.73
5b	98.27	55.43	14.80
5c	99.83	57.65	0.16
5d	100.00	55.74	54.34