Supporting Information related to the article

Inhibition of the replication of different strains of chikungunya virus by 3-aryl-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-ones

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Includes:

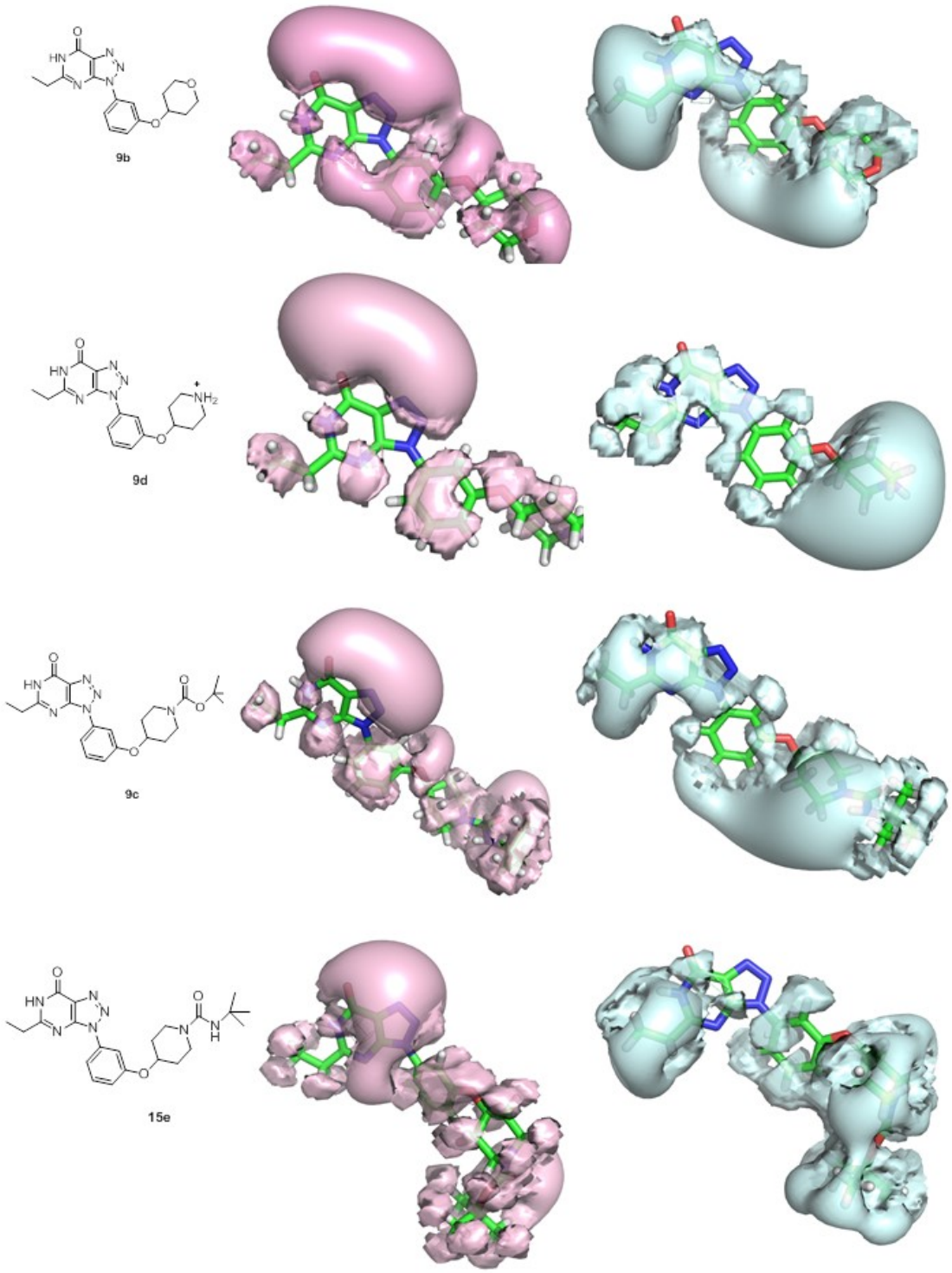

Figure S1: MEP maps of compounds **9a, 9c, 9d and 15e**. Positive and negative isopotential surfaces are colored in cyan and pink, respectively.

Table S1. Predicted properties physicochemical parameters cLogP, tPSA and water solubility

Comp	MW[a]	clogP CD[b]	clogP SA[c]	tPSA CD[d]	tPSA SA[e]	Solubility CD[f]	Solubility SA[g]
2	299.33	2.32	2.13	78.65	85.69	-3.24	-3.22
9b	341.37	1.11	1.91	87.88	94.92	-3.23	-3.16
9c	440.50	3.03	2.68	108.19	115.23	-4.73	-4.14
9d	340.38	1.09	1.66	90.68	97.72	-3.24	-2.98
13	453.50	2.17	1.73	119.27	126.31	-4.11	-3.39
15e	439.52	1.93	2.36	110.99	118.03	-4.49	-3.77

[a] MW: Molecular weight

[b] cLogP CD: calculated octanol/water partition coefficient using ChemDraw 15.0

[c] cLogP CD: concensus calculated octanol/water partition coefficient using SwissADME[h]

[d] tPSA: topological surface area calculated using ChemDraw 15.0

[e] tPSA: topological surface area calculated using SwissADME[h]

[f] Calculated water solubility using LogS in ChemDraw 15.0

[g] Calculated water solubility by LogS (ESOL) using SwissADME[h]

[h] http://www.swissadme.ch/

Table S2. *In silico* rapid ADME predictions performed for compounds **9b and 15e** using QikProp (version 3.5, Schrödinger Release 2015-4, Schrödinger, LLC, New York, NY, 2015) and range of recommended values for oral drugs.

Parameter	**QikProp prediction**		**Range of QikProp recommended values[a]**
Compound	**9b**	**15e**	
QPPCaco[b]	324.2	120.9	<25 poor; > 500 excellent
QPPMDCK[c]	146.4	74.3	<25 poor; > 500 excellent
QPlogKhsa[d]	-0.11	0.32	-1.5-1.5
Percent of Human Oral Absorption[e]	82	81	<25% poor, >80% high

[a] Range predicted by QikProp for 95% of known oral drugs. [b] Predicted apparent Caco-2 cell permeability (nm/s). [c] Predicted apparent MDCK cell permeability in nm/sec, as a mimic of blood-brain barrier. [d] Prediction of binding to human serum albumin. [e]Predicted human oral absorption on 0 to 100% scale.

Table S3. *In vitro* microsomal stability in mouse liver microsomes[a]

Comp	$t_{1/2}$ [b] (min)	CL_{int} [c] (µL/min/mg)
2	8.14	680.8
9b	23.57	235.2
Diclofenac	>120	<46.2
Imipramine	10.15	564.4

[a] Data from Anthem Biosciences; [b] $t_{½}$: half-life; [c] CL_{int}: microsomal intrinsic clearance

Table S4. Mean PK parameters after single dose intraperitoneal and subcutaneous administration of **9b** in male BALB/c mice at 10 mg/kg body weight[a]

Parameters	Intraperitoneal	Subcutaneous
Dose (mg/kg b.w.)	10.00	10.00
Cmax (ng/mL)	1168.01	806.61
Tmax (hr)	0.16	0.16
AUC last (hr*ng/mL)[b]	619.57	1002.94
AUC inf (hr*ng/mL)[c]	629.48	1007.03
AUC % extrap(%)	1.58	0.41
T1/2 (hr)	0.34	0.47
MRT last (hr)[d]	0.43	0.93

a Data from Anthem Biosciences [b]AUC last: AUC to the last measured timepoint. [c] AUC inf: AUC extrapolated to infinity. [d]MRT: mean residence time