A nature-inspired design yields a new class of steroids against tripanosomatids.

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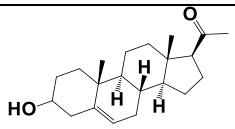
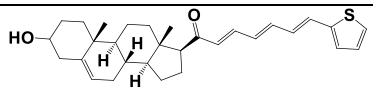
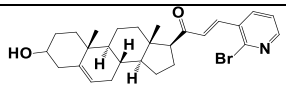
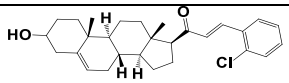
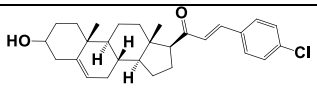
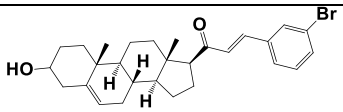
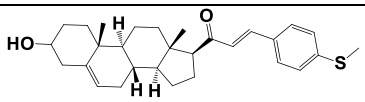
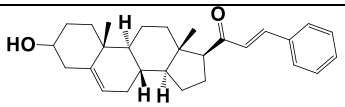
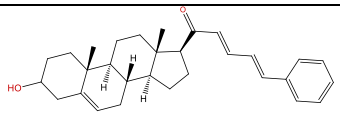
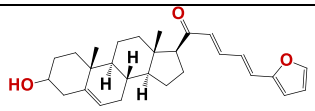
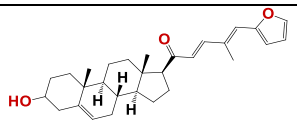
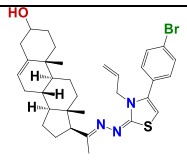
Table 1S. Total data from the in vitro assays with the parasites for 20 compounds

STRUCTURE	IDENTIFIER	IC_{50} ± %SD (µM) epimastigotes *T. cruzi*	IC_{50} ± %SD (µM) promastigotes *L. braziliensis*/ *L. amazonensis*	IC_{50}± %SD (µM) promastigotes *L. infantum*	IC_{50}± %SD (µM) promastigotes *L. infantum uy*p/c*
	Nifurtimox®	7±2	nd	6±2	10±2[c]
	Glucantime®	nd	18±2	20±9	nd
	Miltefosine®	8±2	nd	0.9±0.2	5±2
	**1054**	>25	>25	>25	>25
	**1319**	>25	>25	>25	>25
	**1257**	>25	>25	>25	>25
	**1259**	12±3	23±5	>25	>25
	**1256**	>25	>25	>25	>25
	**1417**	20±5	>25	>25	>25
	**1262**	>25	>25	>25	>25
	**1288**	>25	>25	>25	>25
	**1279**	>25	>25	>25	>25
	**1289**	>25	>25	>25	>25
	**1287**	>25	23±3	>25	>25
	**1272**	>25	16±3	>25	>25

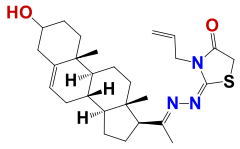
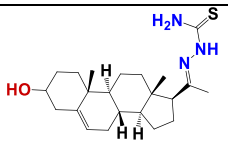
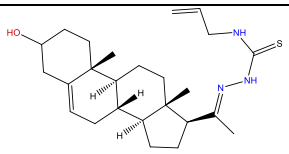
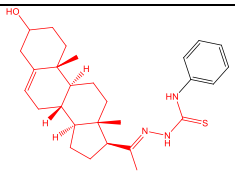
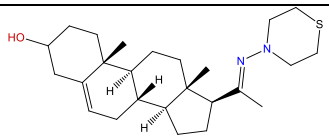
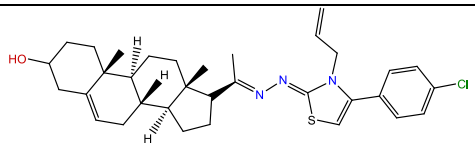
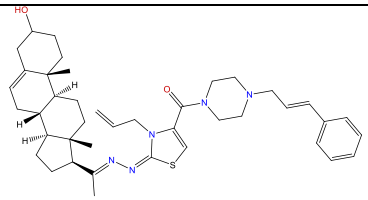
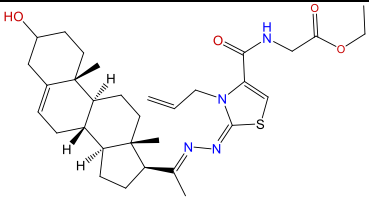
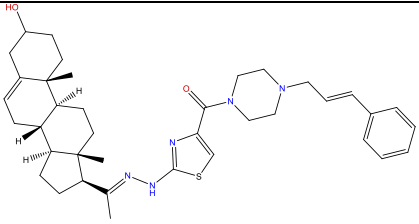
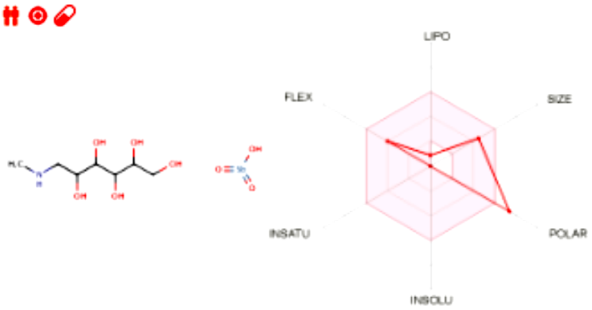
	**1125**	>25	<20	>25	25/>25
	**1260**	1.2	<22	0.2±0.1	0.2
	**1154**	7,8	nd	>25	>25
	**1291**	25	nd	>25	>25
	**1087**	>25	>25	>25	nd
	**1144**	>25	>25	>25	nd
	**1261**	>25	>25	>25	>25
	**1263**	8	>25	>25	>25
	**1317**	>25	>25	>25	>25

Figure 1S. Pharmacokinetic r profiles data output from SwissADME.

A) Glucantime

Molecule 1



SMILES O[Sb](=O)=O.CNCC(C(C(C(CO)O)O)O)O

Physicochemical Properties	
Formula	C7H18NO8Sb
Molecular weight	365.98 g/mol
Num. heavy atoms	17
Num. arom. heavy atoms	0
Fraction Csp3	1.00
Num. rotatable bonds	6
Num. H-bond acceptors	9
Num. H-bond donors	7
Molar Refractivity	47.68
TPSA	167.55 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.00
Log $P_{o/w}$ (XLOGP3)	-3.96
Log $P_{o/w}$ (WLOGP)	-3.77
Log $P_{o/w}$ (MLOGP)	-5.03
Log $P_{o/w}$ (SILICOS-IT)	-1.72
Consensus Log $P_{o/w}$	-2.90

Water Solubility	
Log *S* (ESOL)	0.78
Solubility	2.21e+03 mg/ml ; 6.05e+00 mol/l
Class	Highly soluble
Log *S* (Ali)	1.04
Solubility	4.01e+03 mg/ml ; 1.10e+01 mol/l
Class	Highly soluble
Log *S* (SILICOS-IT)	1.55
Solubility	1.29e+04 mg/ml ; 3.53e+01 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-11.34 cm/s

Druglikeness	
Lipinski	Yes; 1 violation: NHorOH>5
Ghose	No; 1 violation: WLOGP<-0.4
Veber	No; 1 violation: TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 3 violations: XLOGP3<-2, TPSA>150, H-don>5
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	1 alert: heavy_metal
Leadlikeness	No; 1 violation: MW>350
Synthetic accessibility	3.51

B) Compound 1260

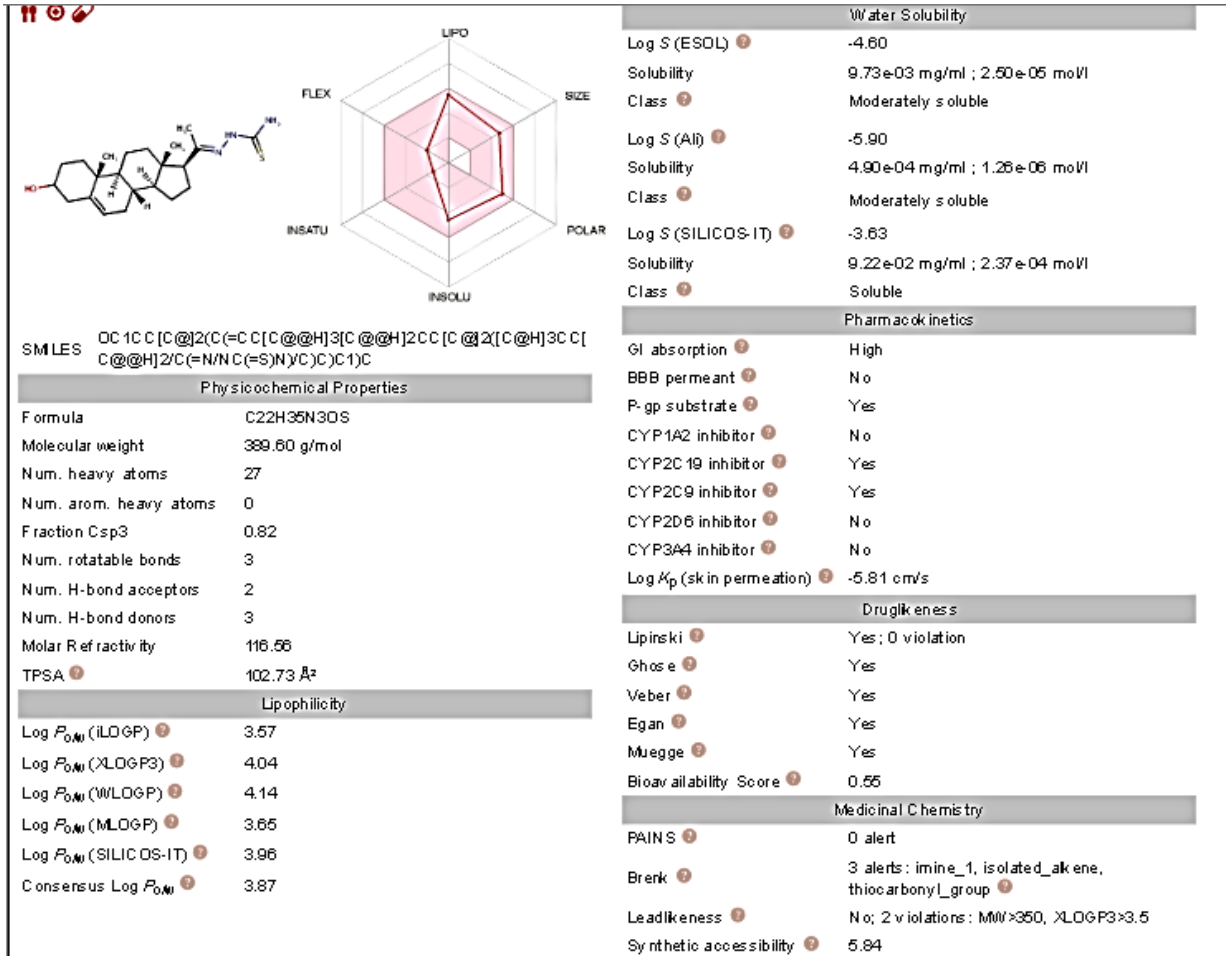
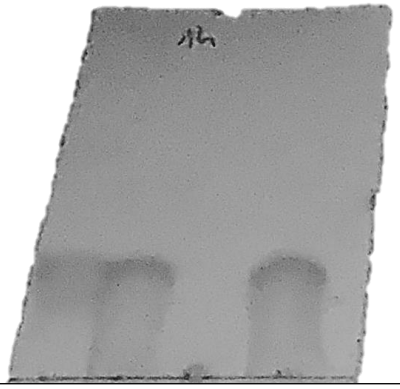
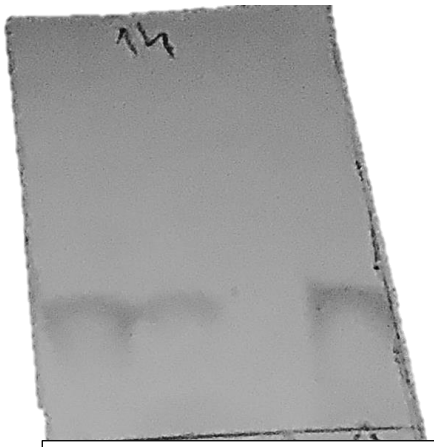


Figure 2S. TLC from the hepatic metabolic stability assay in vitro. FM (Microsomal fraction) FC (cytosolic Fraction).



1260 FM FM_only 1260+FM



1260 FC FC_only 1260+FM