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SwissADME

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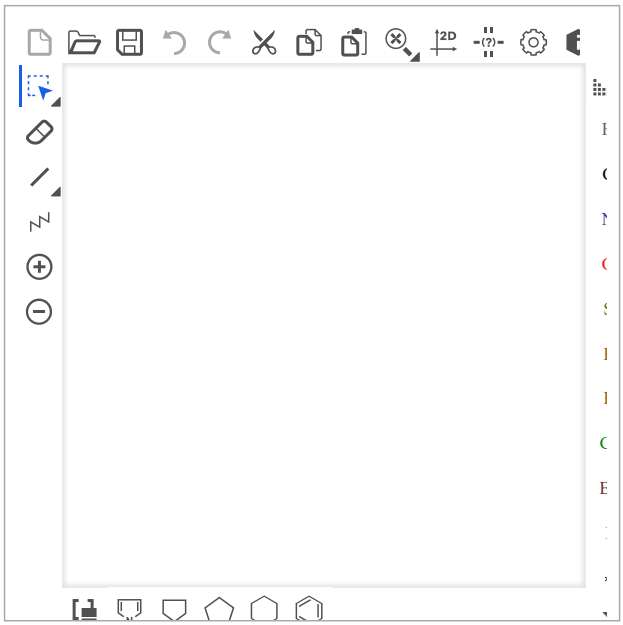
This website allows you to compute physicochemical descriptors as well as to predict ADME parameters, pharmacokinetic properties, druglike nature and medicinal chemistry friendliness of one or multiple small molecules to support drug discovery.

The main article describing the web service and its underlying methodologies is SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Sci. Rep.* (2017) 7:42717.
For details about development and validation of iLOG, please refer to this article: iLOGP: a simple, robust, and efficient description of *n*-octanol/water partition coefficient for drug design using the GB/SA approach. *J. Chem. Inf. Model.* (2014) 54(12):3284-3301.
For details about development and validation of the BOILED-Egg, please refer to this article: A BOILED-Egg to predict gastrointestinal absorption and brain penetration of small molecules. *ChemMedChem* (2016) 11(11):1117-1121.

Developed and maintained by the Molecular Modeling Group of the SIB | Swiss Institute of Bioinformatics.



Enter a list of SMILES here:

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CC(=O)NC[C@@H]1CN(C(=O)O1)C1=CC=C(N2CCOCC2)C(F)=C1
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CC(=O)NC[C@H]1CN(C(=O)O1)C1=CC=C(NCCO)C(F)=C1
NC[C@H]1CN(C(=O)O1)C1=CC=C(N2CCOCC2)C(F)=C1
O=CNC[C@H]1CN(C(=O)O1)C1=CC=C(C=C1)N1CCOCC1=O
CCOCC(=O)NC[C@H]1CN(C(=O)O1)C1=CC=C(F)C=C1
FC1=CC(=CC=C1N1CCOCC1)N1C[C@H](CN2C(=O)C3=CC=CC=C3C2=O)OC1=O
CCOCC(=O)NC[C@@H]1CN(C(=O)O1)C1=CC=C(F)C=C1
COCC(=O)NC[C@H]1CN(C(=O)O1)C1=CC=C(F)C=C1
COCC(=O)NC[C@@H]1CN(C(=O)O1)C1=CC=C(F)C=C1
CC(=O)NC[C@H]1CN(C(=O)O1)C1=CC=C(N2CCN(CC2)C(=O)CO)C(F)=C1
FC1=CC(=CC=C1N1CCOCC1)N1C[C@@H](CN2C(=O)C3=CC=CC=C3C2=O)OC1=O
CCOCC(=O)NC[C@H]1CN(C(=O)O1)C1=CC=CC=C1
CCOC(=O)NC1=CC=C(N2CCOCC2)C(F)=C1
COCC(=O)NC[C@@H]1CN(C(=O)O1)C1=CC=CC=C1
CCOCC(=O)NC[C@@H]1CN(C(=O)O1)C1=CC=CC=C1
CC(=O)NC[C@@H]1CN(C(=O)O1)C1=CC=C(N2CCN(CC2)C(=O)CO)C(F)=C1
C[C@@H]1CN(C[C@H]2CN(C(=O)O2)C2=CC=CC=C2)CC(C)(C)O1
```

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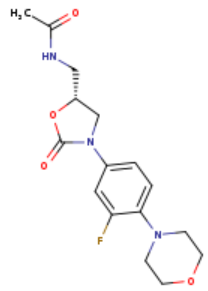
Retrieve data: CSV POWERED BY ChemAxon

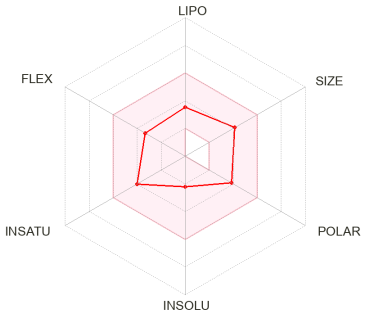
Molecule 1

Water Solubility

Log *S* (ESOL) -2.22

ESOL: Topological method implemented from





SMILES CC(=O)NC[C@H]1OC(=O)N(C1)c1ccc(c(c1)F)N1CCOCC1

Physicochemical Properties

Formula	C16H20FN3O4
Molecular weight	337.35 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	6
Fraction Csp3	0.50
Num. rotatable bonds	5
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	91.06
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	71.11 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.58
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	0.69
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.78
Log $P_{o/w}$ (MLOGP)	0.99
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull.	

Delaney JS. 2004 J. Chem. Inf. Model.	
Solubility Class	2.03e+00 mg/ml ; 6.01e-03 mol/l
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.76
Solubility Class	5.86e+00 mg/ml ; 1.74e-02 mol/l
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.19
Solubility Class	2.18e-01 mg/ml ; 6.47e-04 mol/l
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	Yes
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77	

Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.25
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.26

External: ACC=0.88 / AUC=0.94	
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.87 cm/s

Druglikeness

Lipinski

Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW ≤ 500 MLOGP ≤ 4.15 N or O ≤ 10 NH or OH ≤ 5	Yes; 0 violation

Ghose

Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes

Veber

Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes

Egan

Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA ≤ 131.6	Yes

Muegge

Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings < 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds < 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes

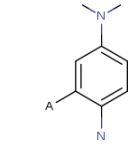
Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

1 alert: anil_di_alk_A

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

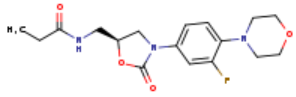
Leadlikeness

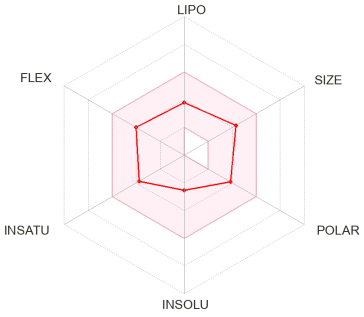
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	Yes

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.32

Molecule 2





SMILES CCC(=O)NC[C@@H]1OC(=O)N(C1)c1ccc(c(c1)F)N1CCOCC1

Physicochemical Properties

Formula	C17H22FN3O4
Molecular weight	351.37 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	6
Fraction Csp3	0.53
Num. rotatable bonds	6
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	95.87
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	71.11 Å²

Lipophilicity

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-2.53
Solubility	1.03e+00 mg/ml ; 2.95e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Log *S* (Ali)

Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.25
Solubility	1.98e+00 mg/ml ; 5.65e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

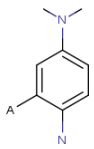
Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.39
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	1.16
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	1.17
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	1.23
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.63
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.52

Log S (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.58
Solubility	9.14e-02 mg/ml ; 2.60e-04 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

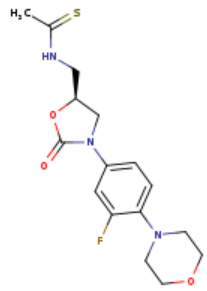
GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No

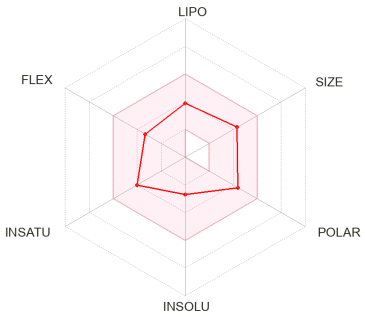
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.62 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW ≤ 500 MLOGP ≤ 4.15 N or O ≤ 10 NH or OH ≤ 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	Yes
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem.	

Rotatable bonds ≤ 10 TPSA ≤ 140	
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55
	Medicinal Chemistry
PAINS	1 alert: anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert
Leadlikeness	
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP ≤ 3.5 Num. rotatable bonds ≤ 7	No; 1 violation: MW>350
Synthetic accessibility	3.43
Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties,	

trained on 12’782’590 molecules and tested on 40 external molecules (r^2 = 0.94)

Molecule 3





SMILES CC(=S)NC[C@@H]1OC(=O)N(C1)c1ccc(c(c1)F)N1CCOCC1

Physicochemical Properties

Formula	C16H20FN3O3S
Molecular weight	353.41 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	6
Fraction Csp3	0.50
Num. rotatable bonds	5
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	98.65
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	86.13 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.80
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	1.29
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	1.58

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-2.70
Solubility	7.07e-01 mg/ml ; 2.00e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.70
Solubility	7.07e-01 mg/ml ; 2.00e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.38
Solubility	1.47e-01 mg/ml ; 4.15e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High

Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	1.38
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	2.71
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.95

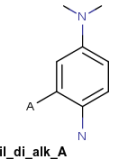
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	No
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set)	

and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.54 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings < 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds < 15 H-bond acc. < 10 H-bond don. < 5	Yes

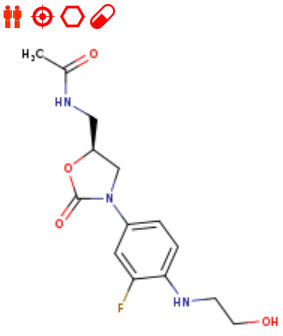
Bioavailability Score

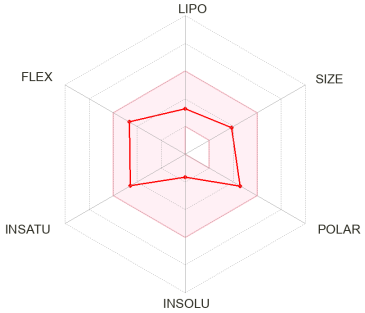
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS	1 alert: anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A
Brenk	1 alert: thiocarbonyl_group
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	thiocarbonyl_group
Leadlikeness	
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	No; 1 violation: MW>350
Synthetic accessibility	
Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.44

Molecule 4





SMILES	OCCNc1ccc(cc1F)N1C[C@@H](OC1=O)CNC(=O)C

Physicochemical Properties

Formula	C14H18FN3O4
Molecular weight	311.31 g/mol

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.66
Solubility	6.79e+00 mg/ml ; 2.18e-02 mol/l
Class	Very soluble
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	

Num. heavy atoms	22
Num. arom. heavy atoms	6
Fraction Csp3	0.43
Num. rotatable bonds	7
Num. H-bond acceptors	5
Num. H-bond donors	3
Molar Refractivity	80.61
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	90.90 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.05
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	0.24
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.54
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.49
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	0.79
Consensus Log $P_{o/w}$	0.82
Consensus Log $P_{o/w}$: Average of all five predictions	

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.71
Solubility	6.08e+00 mg/ml ; 1.95e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.31
Solubility	1.54e-01 mg/ml ; 4.95e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	No
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90	

External: ACC=0.84 / AUC=0.91	
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-8.03 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation

Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA ≤ 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. < 10 H-bond don. < 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

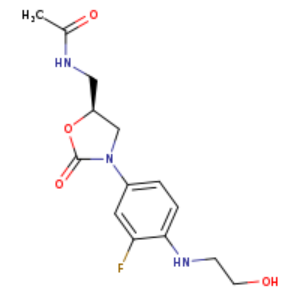
PAINS	
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert
Leadlikeness	Yes
Leadlikeness: implemented from	

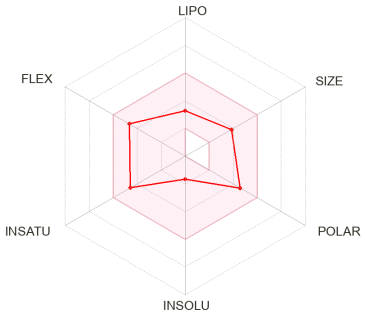
Teague SJ. 1999 Angew. Chem. Int. Ed.
250 < MW < 350
XLOGP < 3.5
Num. rotatable bonds < 7

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94) 3.14

Molecule 5





SMILES OCCNc1ccc(cc1F)N1C[C@@H](OC1=O)CNC(=O)C

Physicochemical Properties

Formula	C14H18FN3O4
Molecular weight	311.31 g/mol
Num. heavy atoms	22
Num. arom. heavy atoms	6
Fraction Csp3	0.43
Num. rotatable bonds	7
Num. H-bond acceptors	5
Num. H-bond donors	3
Molar Refractivity	80.61
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	90.90 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.05
Log $P_{o/w}$ (XLOGP3)	0.24
XLOGP3: Atomistic and knowledge-based	

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.66
Solubility	6.79e+00 mg/ml ; 2.18e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.71
Solubility	6.08e+00 mg/ml ; 1.95e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.31
Solubility	1.54e-01 mg/ml ; 4.95e-04 mol/l

method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.54
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.49
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	0.79
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	0.82

Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No

CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-8.03 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes

Muegge

Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 ≤ XLOGP ≤ 5 TPSA ≤ 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

Leadlikeness

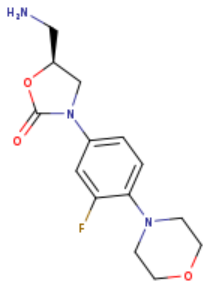
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds ≤ 7	Yes

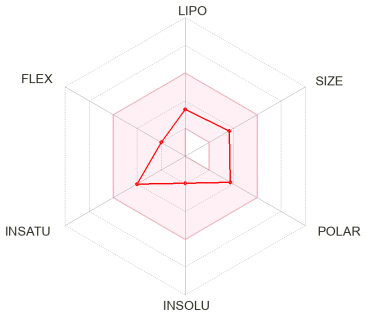
Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.14

Molecule 6

Water Solubility





SMILES NC[C@@H]1OC(=O)N(C1)c1ccc(c(c1)F)N1CCOCC1

Physicochemical Properties

Formula	C14H18FN3O3
Molecular weight	295.31 g/mol
Num. heavy atoms	21
Num. arom. heavy atoms	6
Fraction Csp3	0.50
Num. rotatable bonds	3
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	81.15
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	68.03 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.25
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	0.43
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.60
Log $P_{o/w}$ (MLOGP)	0.97
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull.	

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.96
Solubility	3.27e+00 mg/ml ; 1.11e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.43
Solubility	1.11e+01 mg/ml ; 3.75e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-2.46
Solubility	1.01e+00 mg/ml ; 3.43e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	Yes
P-glycoprotein substrate: SVM model built on 1033 molecules	

Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.

Log $P_{o/w}$ (SILICOS-IT)

SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com — 0.91

Consensus Log $P_{o/w}$

Consensus Log $P_{o/w}$: Average of all five predictions — 1.03

(training set)
and tested on 415 molecules (test set)
10-fold CV: ACC=0.72 / AUC=0.77
External: ACC=0.88 / AUC=0.94

CYP1A2 inhibitor

Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set)
and tested on 3000 molecules (test set)
10-fold CV: ACC=0.83 / AUC=0.90
External: ACC=0.84 / AUC=0.91 — No

CYP2C19 inhibitor

Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set)
and tested on 3000 molecules (test set)
10-fold CV: ACC=0.80 / AUC=0.86
External: ACC=0.80 / AUC=0.87 — No

CYP2C9 inhibitor

Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set)
and tested on 2075 molecules (test set)
10-fold CV: ACC=0.78 / AUC=0.85
External: ACC=0.71 / AUC=0.81 — No

CYP2D6 inhibitor

Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set)
and tested on 1068 molecules (test set)
10-fold CV: ACC=0.79 / AUC=0.85
External: ACC=0.81 / AUC=0.87 — No

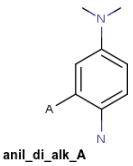
CYP3A4 inhibitor

Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set)
and tested on 2579 molecules (test set)
10-fold CV: ACC=0.77 / AUC=0.85
External: ACC=0.78 / AUC=0.86 — No

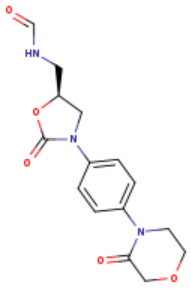
Log K_p (skin permeation) — -7.80 cm/s

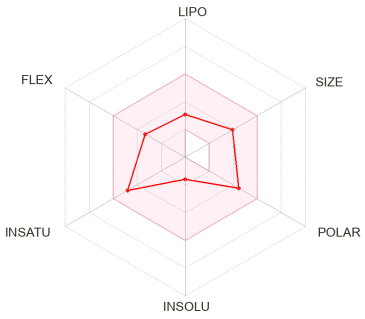
Skin permeation: QSPR model

implemented from Potts RO and Guy RH. 1992 Pharm. Res.	
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. < 10 H-bond don. < 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55
	Medicinal Chemistry

PAINS	1 alert: anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert
Leadlikeness	
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 ≤ MW ≤ 350 XLOGP ≤ 3.5 Num. rotatable bonds ≤ 7	Yes
Synthetic accessibility	
Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.12

Molecule 7





SMILES O=CNC[C@@H]1OC(=O)N(C1)c1ccc(cc1)N1CCOCC1=O

Physicochemical Properties

Formula	C15H17N3O5
Molecular weight	319.31 g/mol
Num. heavy atoms	23
Num. arom. heavy atoms	6
Fraction Csp3	0.40
Num. rotatable bonds	5
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	86.88

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.60
Solubility	8.00e+00 mg/ml ; 2.51e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble

Log *S* (Ali)

Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.27
Solubility	1.72e+01 mg/ml ; 5.39e-02 mol/l

TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	88.18 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	1.59
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	-0.13
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	-0.64
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.29
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	0.31
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	0.28

Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-2.42
Solubility	1.21e+00 mg/ml ; 3.78e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	No
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set)	

and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-8.34 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 < MR < 130 20 < atoms < 70	No; 1 violation: WLOGP<-0.4

Veber

Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds ≤ 10 TPSA ≤ 140	Yes

Egan

Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes

Muegge

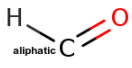
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 < XLOGP < 5 TPSA < 150 Num. rings < 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert
Brenk	1 alert: aldehyde
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	 aldehyde

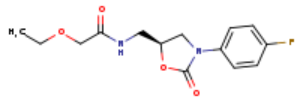
Leadlikeness

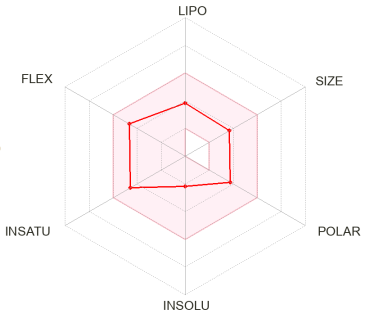
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds ≤ 7	Yes

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.08

Molecule 8





SMILES CCOCC(=O)NC[C@H]1CN(C(=O)O1)c1ccc(cc1)F

Physicochemical Properties

Formula	C14H17FN2O4
Molecular weight	296.29 g/mol
Num. heavy atoms	21
Num. arom. heavy atoms	6
Fraction Csp3	0.43
Num. rotatable bonds	7
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	76.03
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	67.87 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.06
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	1.19

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-2.18
Solubility	1.98e+00 mg/ml ; 6.67e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.21
Solubility	1.82e+00 mg/ml ; 6.15e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.58
Solubility	7.88e-02 mg/ml ; 2.66e-04 mol/l
Class	Soluble
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	

Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	1.34
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	1.02
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.57
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.44

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	Yes
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	No
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	No
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85	

External: ACC=0.81 / AUC=0.87	
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.26 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW ≤ 500 MLOGP ≤ 4.15 N or O ≤ 10 NH or OH ≤ 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds ≤ 10 TPSA ≤ 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes
Muegge	Yes
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 ≤ XLOGP ≤ 5 TPSA ≤ 150 Num. rings ≤ 7	

Num. carbon > 4
Num. heteroatoms > 1
Num. rotatable bonds < 15
H-bond acc. < 10
H-bond don. < 5

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem. — 0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem. — 0 alert

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem — 0 alert

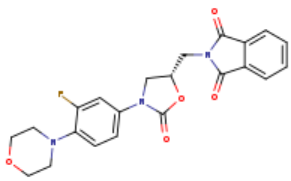
Leadlikeness

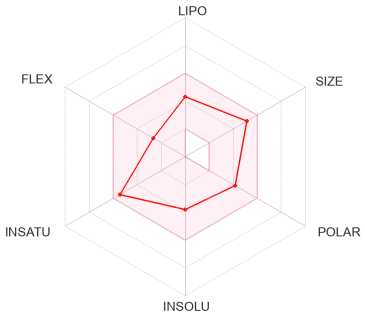
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. — Yes
250 < MW < 350
XLOGP < 3.5
Num. rotatable bonds < 7

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94) — 3.02

Molecule 9





Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model. — -3.79

Solubility — 6.88e-02 mg/ml ; 1.62e-04 mol/l
Class — Soluble

Solubility class: Log *S* scale

SMILES O=C1O[C@H](CN1c1ccc(c(c1)F)N1CCOCC1)CN1C(=O)c2c(C1=O)cccc2

Physicochemical Properties

Formula	C22H20FN3O5
Molecular weight	425.41 g/mol
Num. heavy atoms	31
Num. arom. heavy atoms	12
Fraction Csp3	0.32
Num. rotatable bonds	4
Num. H-bond acceptors	6
Num. H-bond donors	0
Molar Refractivity	118.24
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	79.39 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.84
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	2.05
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	1.56
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	1.92
Log $P_{o/w}$ (SILICOS-IT)	2.10

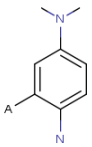
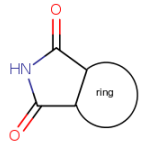
Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-3.35
Solubility	1.92e-01 mg/ml ; 4.51e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-4.91
Solubility	5.19e-03 mg/ml ; 1.22e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	No
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set)	

SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.10
and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	Yes
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	Yes
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	Yes
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	Yes
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.44 cm/s
	Druglikeness
Lipinski	Yes; 0 violation
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15	

N or O ≤ 10 NH or OH ≤ 5	
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds ≤ 10 TPSA ≤ 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 ≤ XLOGP ≤ 5 TPSA ≤ 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55
Medicinal Chemistry	
PAINS	1 alert: anil_di_alk_A  anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	
Brenk	1 alert: phthalimide  phthalimide
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	

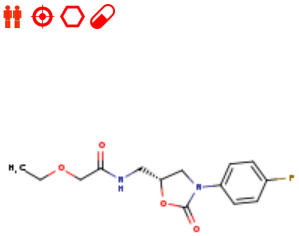
Leadlikeness

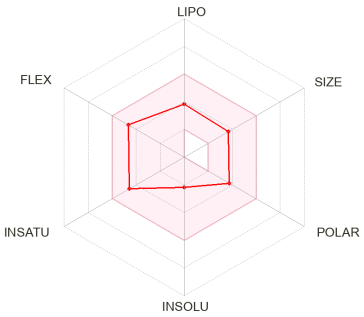
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 ≤ MW ≤ 350 XLOGP ≤ 3.5 Num. rotatable bonds ≤ 7	No; 1 violation: MW>350

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.48

Molecule 10





SMILES	CCOCC(=O)NC[C@@H]1CN(C(=O)O1)c1ccc(cc1)F

Physicochemical Properties

Formula	C14H17FN2O4
Molecular weight	296.29 g/mol
Num. heavy atoms	21
Num. arom. heavy atoms	6
Fraction Csp3	0.43
Num. rotatable bonds	7
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	76.03
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	67.87 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.39

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-2.18
Solubility	1.98e+00 mg/ml ; 6.67e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.21
Solubility	1.82e+00 mg/ml ; 6.15e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	-3.58
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT,	

Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	1.19
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	1.34
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	1.02
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.57
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.50

http://www.silicos-it.com	
Solubility	7.88e-02 mg/ml ; 2.66e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	Yes
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	No
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	No
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	

CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.26 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	Yes
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	

Muegge

Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings < 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds < 15 H-bond acc. < 10 H-bond don. < 5	Yes

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

Leadlikeness

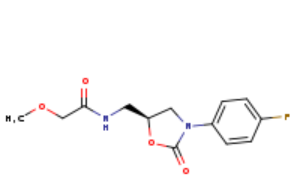
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	Yes

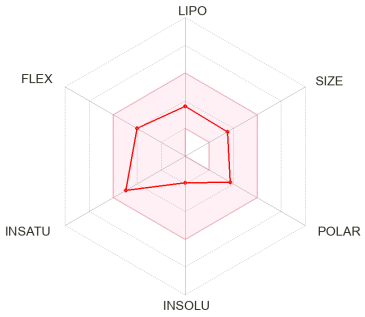
Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.02

Molecule 11

Water Solubility





SMILES COCC(=O)NC[C@H]1CN(C(=O)O1)c1ccc(cc1)F

Physicochemical Properties

Formula	C13H15FN2O4
Molecular weight	282.27 g/mol
Num. heavy atoms	20
Num. arom. heavy atoms	6
Fraction Csp3	0.38
Num. rotatable bonds	6
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	71.22
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	67.87 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	1.55
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	0.82
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.95
Log $P_{o/w}$ (MLOGP)	0.76
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull.	

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.93
Solubility	3.30e+00 mg/ml ; 1.17e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.83
Solubility	4.20e+00 mg/ml ; 1.49e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble

Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.18
Solubility	1.88e-01 mg/ml ; 6.67e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	No
P-glycoprotein substrate: SVM model built on 1033 molecules	

Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.

Log $P_{o/w}$ (SILICOS-IT)

SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com — 1.20

Consensus Log $P_{o/w}$

Consensus Log $P_{o/w}$: Average of all five predictions — 1.06

(training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94

CYP1A2 inhibitor

Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91 — No

CYP2C19 inhibitor

Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87 — No

CYP2C9 inhibitor

Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81 — No

CYP2D6 inhibitor

Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87 — No

CYP3A4 inhibitor

Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86 — No

Log K_p (skin permeation) — -7.44 cm/s

Skin permeation: QSPR model

implemented from Potts RO and Guy RH. 1992 Pharm. Res.	
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. < 10 H-bond don. < 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55
	Medicinal Chemistry
PAINS	0 alert
Pan Assay Interference Structures:	

implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem — 0 alert

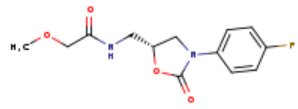
Leadlikeness

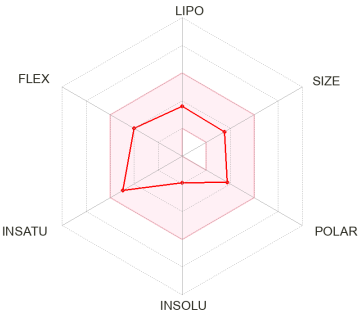
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7 — Yes

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94) — 2.89

Molecule 12





SMILES: COCC(=O)NC[C@@H]1CN(C(=O)O1)c1ccc(cc1)F

Physicochemical Properties

Formula	C13H15FN2O4
Molecular weight	282.27 g/mol
Num. heavy atoms	20
Num. arom. heavy atoms	6
Fraction Csp3	0.38
Num. rotatable bonds	6
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	71.22
TPSA	67.87 Å²

Topological Polar Surface Area: Calculated from

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model. — -1.93

Solubility — 3.30e+00 mg/ml ; 1.17e-02 mol/l

Class

Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly — Very soluble

Log *S* (Ali)

Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model. — -1.83

Solubility — 4.20e+00 mg/ml ; 1.49e-02 mol/l

Class — Very soluble

Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4

Ertl P. et al. 2000 J. Med. Chem.

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	1.86
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	0.82
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.95
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.76
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.20
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.12

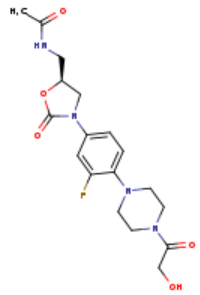
< Soluble < -2 Very < 0 < Highly	
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.18
Solubility	1.88e-01 mg/ml ; 6.67e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Pharmacokinetics	
GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	No
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No

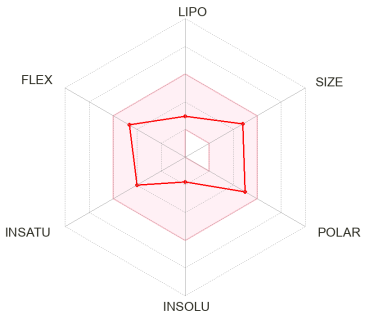
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.44 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW ≤ 500 MLOGP ≤ 4.15 N or O ≤ 10 NH or OH ≤ 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	Yes
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem.	

Rotatable bonds ≤ 10 TPSA ≤ 140	
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55
Medicinal Chemistry	
PAINS	
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert
Leadlikeness	
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP ≤ 3.5 Num. rotatable bonds ≤ 7	Yes
Synthetic accessibility	2.89
Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties,	

trained on 12’782’590 molecules and tested on 40 external molecules (r^2 = 0.94)

Molecule 13





SMILES OCC(=O)N1CCN(CC1)c1ccc(cc1F)N1C[C@@H](OC1=O)CNC(=O)C

Physicochemical Properties

Formula	C18H23FN4O5
Molecular weight	394.40 g/mol
Num. heavy atoms	28
Num. arom. heavy atoms	6
Fraction Csp3	0.50
Num. rotatable bonds	7
Num. H-bond acceptors	6
Num. H-bond donors	2
Molar Refractivity	107.76
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	102.42 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	1.73
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	-0.32
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	-0.79

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.78
Solubility	6.54e+00 mg/ml ; 1.66e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.37
Solubility	1.68e+01 mg/ml ; 4.27e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-2.52
Solubility	1.19e+00 mg/ml ; 3.01e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High

Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.22
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	0.20
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	0.21

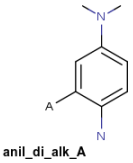
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	No
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set)	

and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-8.93 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	No; 1 violation: WLOGP<-0.4
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings < 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds < 15 H-bond acc. < 10 H-bond don. < 5	Yes

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS	1 alert: anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

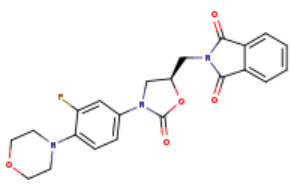
Leadlikeness

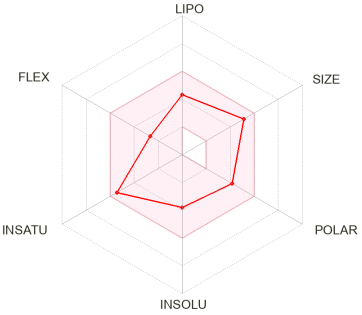
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	No; 1 violation: MW>350

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.58

Molecule 14





Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.79
Solubility	6.88e-02 mg/ml ; 1.62e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

SMILES	O=C1O[C@@H](CN1c1ccc(c(c1)F)N1CCOCC1)CN1C(=O)c2c(C1=O)cccc2

Physicochemical Properties

Formula	C22H20FN3O5
Molecular weight	425.41 g/mol

Num. heavy atoms	31
Num. arom. heavy atoms	12
Fraction Csp3	0.32
Num. rotatable bonds	4
Num. H-bond acceptors	6
Num. H-bond donors	0
Molar Refractivity	118.24
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	79.39 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.81
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	2.05
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	1.56
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	1.92
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	2.10
Consensus Log $P_{o/w}$	2.09
Consensus Log $P_{o/w}$: Average of all five predictions	

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-3.35
Solubility	1.92e-01 mg/ml ; 4.51e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-4.91
Solubility	5.19e-03 mg/ml ; 1.22e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble

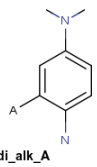
Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	No
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90	

External: ACC=0.84 / AUC=0.91	
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	Yes
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	Yes
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	Yes
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	Yes
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.44 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation

Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds ≤ 10 TPSA ≤ 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 ≤ XLOGP ≤ 5 TPSA ≤ 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS	1 alert: anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A
Brenk	1 alert: phthalimide
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	 phthalimide

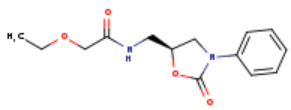
Leadlikeness

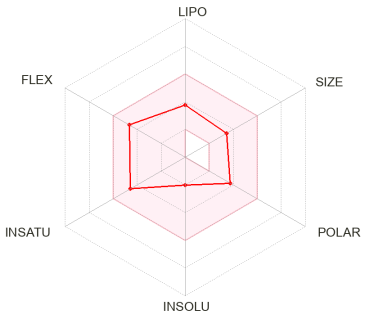
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 ≤ MW ≤ 350 XLOGP ≤ 3.5 Num. rotatable bonds ≤ 7	No; 1 violation: MW>350

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.48

Molecule 15





SMILES CCOCC(=O)NC[C@@H]1OC(=O)N(C1)c1ccccc1

Physicochemical Properties

Formula	C14H18N2O4
Molecular weight	278.30 g/mol
Num. heavy atoms	20
Num. arom. heavy atoms	6
Fraction Csp3	0.43
Num. rotatable bonds	7
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	76.07
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	67.87 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.37

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-2.01
Solubility	2.71e+00 mg/ml ; 9.72e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.11
Solubility	2.17e+00 mg/ml ; 7.81e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	-3.30
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT,	

Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	1.09
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.78
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.62
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.14
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.20

http://www.silicos-it.com	
Solubility	1.39e-01 mg/ml ; 4.98e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics	
GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	No
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	No
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	

CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.22 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	Yes
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	

Muegge

Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings < 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds < 15 H-bond acc. < 10 H-bond don. < 5	Yes

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

Leadlikeness

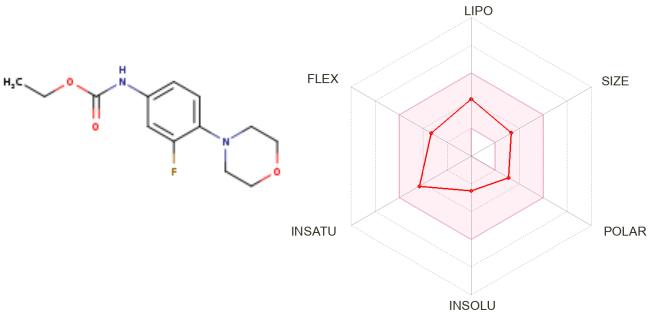
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	Yes

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	2.99

Molecule 16

Water Solubility



SMILES CCOC(=O)Nc1ccc(c(c1)F)N1CCOCC1

Physicochemical Properties

Formula	C13H17FN2O3
Molecular weight	268.28 g/mol
Num. heavy atoms	19
Num. arom. heavy atoms	6
Fraction Csp3	0.46
Num. rotatable bonds	5
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	72.72
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	50.80 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.62
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	1.72
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	2.08
Log $P_{o/w}$ (MLOGP)	1.52
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull.	

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-2.49
Solubility	8.67e-01 mg/ml ; 3.23e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.40
Solubility	1.06e+00 mg/ml ; 3.96e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.40
Solubility	1.08e-01 mg/ml ; 4.01e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

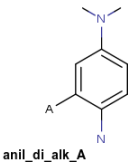
Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	Yes
P-gp substrate	Yes
P-glycoprotein substrate: SVM model built on 1033 molecules	

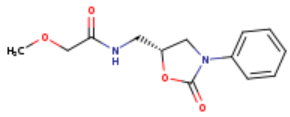
Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.79
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.94

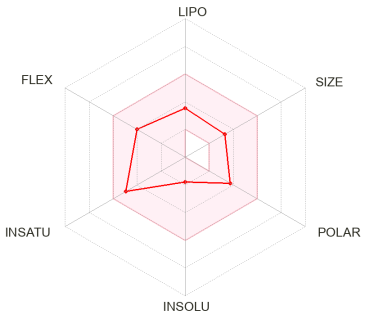
(training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	Yes
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	-6.72 cm/s
Skin permeation: QSPR model	

implemented from Potts RO and Guy RH. 1992 Pharm. Res.	
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. < 10 H-bond don. < 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55
	Medicinal Chemistry

PAINS	1 alert: anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert
Leadlikeness	
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 ≤ MW ≤ 350 XLOGP ≤ 3.5 Num. rotatable bonds ≤ 7	Yes
Synthetic accessibility	
Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	2.49

Molecule 17





SMILES	COCC(=O)NC[C@@H]1CN(C(=O)O1)c1ccccc1

Physicochemical Properties

Formula	C13H16N2O4
Molecular weight	264.28 g/mol
Num. heavy atoms	19
Num. arom. heavy atoms	6
Fraction Csp3	0.38
Num. rotatable bonds	6
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	71.27

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.77
Solubility	4.49e+00 mg/ml ; 1.70e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.72
Solubility	4.99e+00 mg/ml ; 1.89e-02 mol/l

TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	67.87 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	1.66
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	0.72
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	0.39
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.36
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	0.77
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	0.78

Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-2.90
Solubility	3.31e-01 mg/ml ; 1.25e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	No
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	No
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set)	

and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.40 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 < MR < 130 20 < atoms < 70	Yes

Veber

Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds ≤ 10 TPSA ≤ 140	Yes

Egan

Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes

Muegge

Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 ≤ XLOGP ≤ 5 TPSA ≤ 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

Leadlikeness

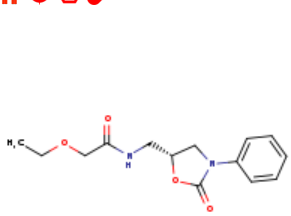
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 ≤ MW ≤ 350 XLOGP ≤ 3.5 Num. rotatable bonds ≤ 7	Yes

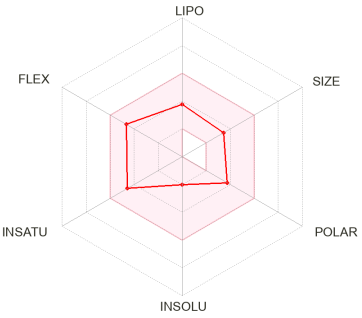
Synthetic accessibility 2.86

Synthetic accessibility score: from 1 (very

easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)

Molecule 18





SMILES CCOCC(=O)NC[C@H]1OC(=O)N(C1)c1ccccc1

Physicochemical Properties

Formula	C14H18N2O4
Molecular weight	278.30 g/mol
Num. heavy atoms	20
Num. arom. heavy atoms	6
Fraction Csp3	0.43
Num. rotatable bonds	7
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	76.07
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	67.87 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	1.94
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	1.09
Log $P_{o/w}$ (WLOGP)	0.78
WLOGP: Atomistic method implemented	

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-2.01
Solubility	2.71e+00 mg/ml ; 9.72e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.11
Solubility	2.17e+00 mg/ml ; 7.81e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.30
Solubility	1.39e-01 mg/ml ; 4.98e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.62
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.14
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	1.12

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	No
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	No
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	

CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.22 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes
Muegge	Yes
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 < MW < 600 -2 < XLOGP < 5 TPSA < 150 Num. rings < 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds <	

15
H-bond acc. < 10
H-bond don. < 5

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

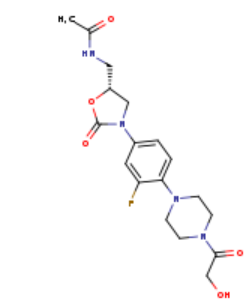
Leadlikeness

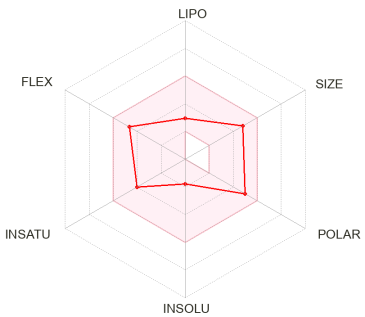
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	Yes

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	2.99

Molecule 19





SMILES OCC(=O)N1CCN(CC1)c1ccc(cc1F)N1C[C@H](OC1=O)CNC(=O)C

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-1.78
Solubility	6.54e+00 mg/ml ; 1.66e-02 mol/l
Class	Very soluble

Solubility class: Log *S* scale
Insoluble < -10 < Poorly < -6 < Moderately < -4

Physicochemical Properties	
Formula	C18H23FN4O5
Molecular weight	394.40 g/mol
Num. heavy atoms	28
Num. arom. heavy atoms	6
Fraction Csp3	0.50
Num. rotatable bonds	7
Num. H-bond acceptors	6
Num. H-bond donors	2
Molar Refractivity	107.76
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	102.42 Å²

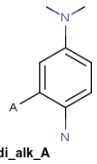
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	1.99
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	-0.32
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	-0.79
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	0.22
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	0.20

< Soluble < -2 Very < 0 < Highly	
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-1.37
Solubility	1.68e+01 mg/ml ; 4.27e-02 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Very soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-2.52
Solubility	1.19e+00 mg/ml ; 3.01e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics	
GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	No
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	Yes
CYP1A2 inhibitor	No
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set)	

Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	0.26

10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No
CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	No
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-8.93 cm/s
	Druglikeness
Lipinski	Yes; 0 violation
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW ≤ 500 MLOGP ≤ 4.15 N or O ≤ 10 NH or OH ≤ 5	

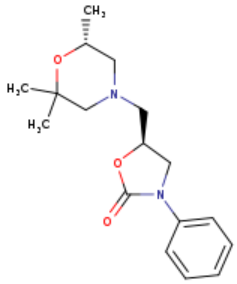
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	No; 1 violation: WLOGP<-0.4
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds ≤ 10 TPSA ≤ 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP ≤ 5.88 TPSA ≤ 131.6	Yes
Muegge	
Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 ≤ XLOGP ≤ 5 TPSA ≤ 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. ≤ 10 H-bond don. ≤ 5	Yes
Bioavailability Score	
Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55
Medicinal Chemistry	
PAINS	1 alert: anil_di_alk_A
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	 anil_di_alk_A
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert
Leadlikeness	No; 1 violation: MW>350
Leadlikeness: implemented from	

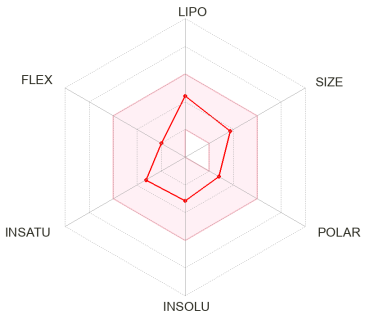
Teague SJ. 1999 Angew. Chem. Int. Ed.
250 < MW < 350
XLOGP < 3.5
Num. rotatable bonds < 7

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94) 3.58

Molecule 20





SMILES C[C@@H]1CN(C[C@@H]2OC(=O)N(C2)c2ccccc2)CC(O1)(C)C

Physicochemical Properties

Formula	C17H24N2O3
Molecular weight	304.38 g/mol
Num. heavy atoms	22
Num. arom. heavy atoms	6
Fraction Csp3	0.59
Num. rotatable bonds	3
Num. H-bond acceptors	4
Num. H-bond donors	0
Molar Refractivity	92.23
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	42.01 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.16
Log $P_{o/w}$ (XLOGP3)	2.24
XLOGP3: Atomistic and knowledge-based	

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.14
Solubility	2.19e-01 mg/ml ; 7.21e-04 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-2.76
Solubility	5.32e-01 mg/ml ; 1.75e-03 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble
Log *S* (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-3.46
Solubility	1.06e-01 mg/ml ; 3.47e-04 mol/l

method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	1.75
Log $P_{o/w}$ (MLOGP)	
MLOGP: Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.	1.86
Log $P_{o/w}$ (SILICOS-IT)	
SILICOS-IT: Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	1.87
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.18

Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Soluble

Pharmacokinetics

GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	Yes
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	No
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / AUC=0.91	No
CYP2C19 inhibitor	
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87	No
CYP2C9 inhibitor	
Cytochrome P450 2C9 inhibitor: SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) 10-fold CV: ACC=0.78 / AUC=0.85 External: ACC=0.71 / AUC=0.81	No

CYP2D6 inhibitor	
Cytochrome P450 2D6 inhibitor: SVM model built on 3664 molecules (training set) and tested on 1068 molecules (test set) 10-fold CV: ACC=0.79 / AUC=0.85 External: ACC=0.81 / AUC=0.87	Yes
CYP3A4 inhibitor	
Cytochrome P450 3A4 inhibitor: SVM model built on 7518 molecules (training set) and tested on 2579 molecules (test set) 10-fold CV: ACC=0.77 / AUC=0.85 External: ACC=0.78 / AUC=0.86	No
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-6.57 cm/s
	Druglikeness
Lipinski	
Lipinski (Pfizer) filter: implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. MW < 500 MLOGP < 4.15 N or O < 10 NH or OH < 5	Yes; 0 violation
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 < MW < 480 -0.4 < WLOGP < 5.6 40 < MR < 130 20 < atoms < 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented from Egan WJ. et al. 2000 J. Med. Chem. WLOGP < 5.88 TPSA < 131.6	Yes

Muegge

Muegge (Bayer) filter: implemented from Muegge I. et al. 2001 J. Med. Chem. 200 ≤ MW ≤ 600 -2 ≤ XLOGP ≤ 5 TPSA ≤ 150 Num. rings ≤ 7 Num. carbon > 4 Num. heteroatoms > 1 Num. rotatable bonds ≤ 15 H-bond acc. < 10 H-bond don. < 5	Yes

Bioavailability Score

Abbott Bioavailability Score: Probability of F > 10% in rat implemented from Martin YC. 2005 J. Med. Chem.	0.55

Medicinal Chemistry

PAINS

Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert

Brenk

Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert

Leadlikeness

Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds ≤ 7	Yes

Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penaties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	3.55

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