In order to avoid security-related warning messages when switching to secured connection, you may want either to:

- confirm the exception on the next page, or
- import our CA key in your web browser

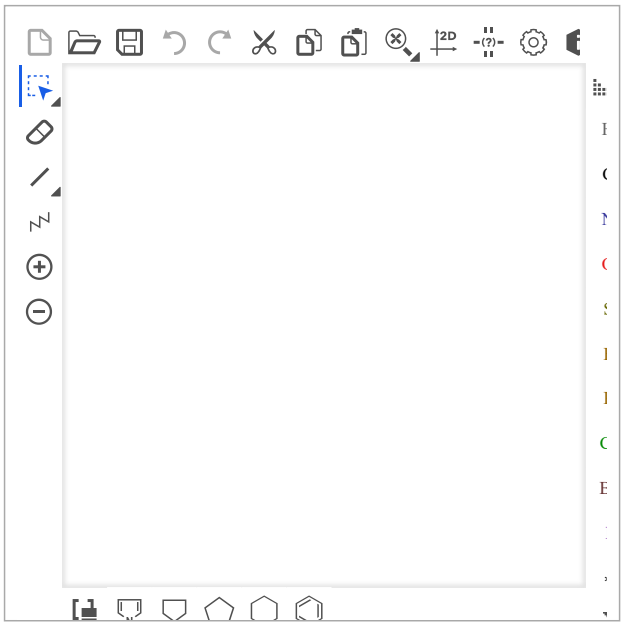
Click here to proceed.

SwissADME

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:

```
COC1=CC2=NC(OC)=C(CN3CCC(O)(CC3)C3=CC=CC=C3OC)C=C2C=C1
CN(C)CC[C@](O)(C1=CC=C(Br)C=C1)C1=CC=CN=C1
CCC1=C2NC=C([C@@H](CC(=O)NCCCOC)C3=CC=CC=C3OC)C2=CC=C1
COCCCNC(=O)C[C@H](C1=CNC2=CC=CC=C12)C1=CC=C(OC)C=C1OC
CN(C)CC[C@@](O)(C1=CC=C(Br)C=C1)C1=CC=CN=C1
COC1=NC=CC=C1C1(O)C[C@@H]2CC[C@H](C1)N2C(=O)C1=CC=C(OCC=C)C=(
COC1=CC=C(C=N1)[C@@H](NC(=O)CCC1=CC=CC=C1OC)[C@@H]1C[C@H](O)(
CCC1=C2NC=C([C@H](CC(=O)NCCCOC)C3=CC=C(OC)C=C3OC)C2=CC=C1
CCC1=C2NC=C([C@@H](CC(=O)NCCCOC)C3=CC=C(OC)C=C3OC)C2=CC=C1
CCC1=C2NC=C([C@H](CC(=O)NCCCOC)C3=CC=CC=C3OC)C2=CC=C1
COCCCNC(=O)C[C@@H](C1=CNC2=CC=CC=C12)C1=CC=C(OC)C=C1OC
COC1=NC=CC=C1C(=O)N1CCC(O)(CC1)C1=CC2=CC=C(C)N=C2C=C1
COC1=CC=C(C=N1)[C@H](NC(=O)CCC1=CC=CC=C1OC)[C@@H]1C[C@H](O)C1
C([C@@H]1COCCN(CC2=CC(OC3=NC=CC=N3)=CC=C2)C1)C1=CN=CC2=CC=CC=
COC1=NC=CC=C1C1(O)C[C@@H]2CC[C@H](C1)N2C(=O)C1=CC=CC(=C1)N1N=
COC1=NC=CC=C1C1(O)C[C@@H]2CC[C@H](C1)N2C(=O)C1=CC=C(OC2CSC2)(
CC1=CC2=CC3=C(OC(C)(C)[C@@H]4CC5(CCNCC5)CO[C@@H]34)N=C2C=C1
CCC1=C2NC=C([C@@H](CC(=O)NCCOC)C3=CC=C(OC)C=C3OC)C2=CC=C1
CN(C)CC[C@](O)(C1=CNC2=CC=CC=C12)C1=CC=CC=C1
OC1(CCN(C[C@@H]2CCOC3=CC=CC=C3C2)CC1)C1=CC=CN=C1
```

Fill with an example | Clear | Run!

Show BOILED-Egg

Retrieve data: CSV POWERED BY ChemAxon

Molecule 1

SMILES: COc1ccc2c(c1)nc(c(c2)CN1CCC(CC1)(O)c1ccccc1OC)OC

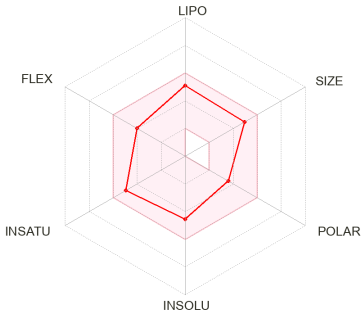
Physicochemical Properties

Formula: C24H28N2O4

Water Solubility

Log *S* (ESOL): -4.53

ESOL: Topological method implemented from



Molecular weight	408.49 g/mol
Num. heavy atoms	30
Num. arom. heavy atoms	16
Fraction Csp3	0.38
Num. rotatable bonds	6
Num. H-bond acceptors	6
Num. H-bond donors	1
Molar Refractivity	120.45
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	64.05 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	4.08
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	3.43
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	3.10
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.	2.24

Delaney JS. 2004 J. Chem. Inf. Model.	
Solubility	1.20e-02 mg/ml ; 2.94e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-4.46
Solubility	1.43e-02 mg/ml ; 3.50e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-7.06
Solubility	3.57e-05 mg/ml ; 8.75e-08 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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 (training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77	

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	4.12
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	3.40

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	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.	-6.36 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

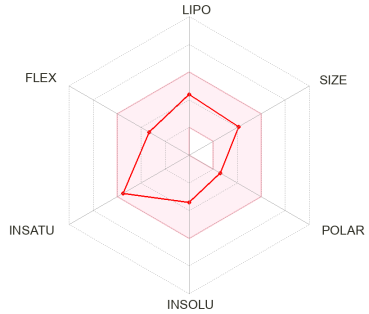
Leadlikeness

Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	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)	2.92

Molecule 2



SMILES CN(CC[C@@](c1cccnc1)(c1ccc(cc1)Br)O)C

Physicochemical Properties

Formula	C16H19BrN2O
Molecular weight	335.24 g/mol
Num. heavy atoms	20
Num. arom. heavy atoms	12
Fraction Csp3	0.31
Num. rotatable bonds	5
Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	84.56
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	36.36 Å²

Lipophilicity

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.41
Solubility	1.30e-01 mg/ml ; 3.87e-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.	-2.59
Solubility	8.67e-01 mg/ml ; 2.59e-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.	3.02
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	2.19
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	2.92
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.	2.28
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	3.27
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.74

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	-5.76
Solubility	5.85e-04 mg/ml ; 1.75e-06 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble

Pharmacokinetics

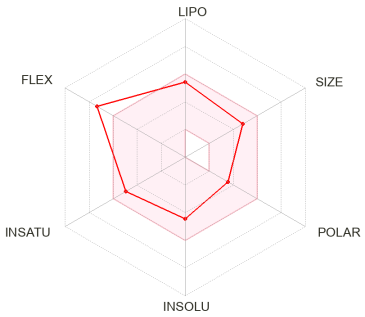
GI absorption	
Gatrointestinal absorption: according to the white of the BOILED-Egg	High
BBB permeant	
BBB permeation: according to the yolk of the BOILED-Egg	Yes
P-gp substrate	
P-glycoprotein substrate: SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) 10-fold 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.	-6.79 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	2.72
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 COCCCNC(=O)C[C@H](c1c[nH]c2c1cccc2CC)c1ccccc1OC

Physicochemical Properties

Formula	C24H30N2O3
Molecular weight	394.51 g/mol
Num. heavy atoms	29
Num. arom. heavy atoms	15
Fraction Csp3	0.38
Num. rotatable bonds	11
Num. H-bond acceptors	3
Num. H-bond donors	2
Molar Refractivity	116.95
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	63.35 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.64
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	3.99
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	4.41

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.46
Solubility	1.38e-02 mg/ml ; 3.50e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-5.02
Solubility	3.75e-03 mg/ml ; 9.51e-06 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-8.44
Solubility	1.43e-06 mg/ml ; 3.61e-09 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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.	2.48
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	5.83
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	4.07

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	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	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	Yes
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.	-5.87 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	No; 1 violation: Rotors>10
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

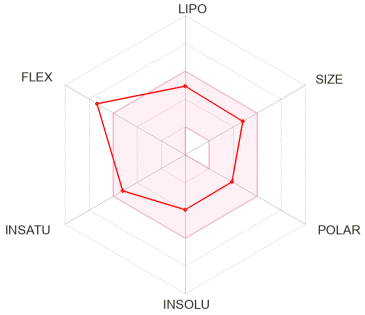
Leadlikeness

Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5

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)	3.48

Molecule 4



SMILES	COCCCNC(=O)C[C@H](c1c[nH]c2c1cccc2)c1ccc(cc1OC)OC

Physicochemical Properties

Formula	C23H28N2O4
Molecular weight	396.48 g/mol
Num. heavy atoms	29

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.95
Solubility	4.49e-02 mg/ml ; 1.13e-04 mol/l

Class

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

Num. arom. heavy atoms	15
Fraction Csp3	0.35
Num. rotatable bonds	11
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	113.66
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	72.58 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.95
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	3.16
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	3.86
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.	1.73
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	4.97
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	3.33

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-4.35
Solubility	1.75e-02 mg/ml ; 4.42e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-7.78
Solubility	6.64e-06 mg/ml ; 1.67e-08 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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	Yes
CYP1A2 inhibitor	Yes
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.	-6.47 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	No; 1 violation: Rotors>10

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 — No; 2 violations: MW>350, Rotors>7

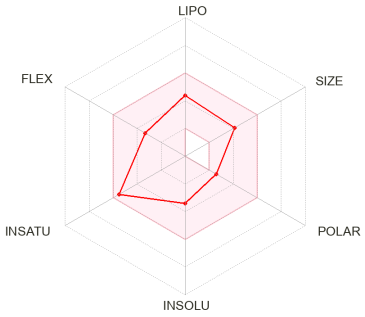
Leadlikeness: implemented from	

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) 3.46

Molecule 5



SMILES CN(CC[C@](c1cccnc1)(c1ccc(cc1)Br)O)C

Physicochemical Properties

Formula	C16H19BrN2O
Molecular weight	335.24 g/mol
Num. heavy atoms	20
Num. arom. heavy atoms	12
Fraction Csp3	0.31
Num. rotatable bonds	5
Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	84.56
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	36.36 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)

iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model. 2.98

Log $P_{o/w}$ (XLOGP3) 2.19

XLOGP3: Atomistic and knowledge-based

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model. -3.41

Solubility 1.30e-01 mg/ml ; 3.87e-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. -2.59

Solubility 8.67e-01 mg/ml ; 2.59e-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 -5.76

Solubility 5.85e-04 mg/ml ; 1.75e-06 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.	2.92
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.	2.28
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	3.27
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.73

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	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.	-6.79 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

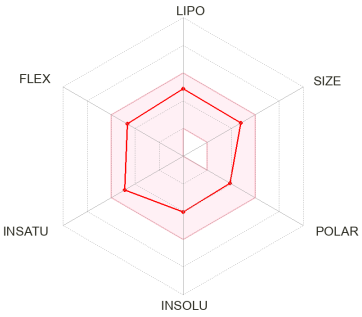
Synthetic accessibility

Synthetic accessibility score: from 1 (very easy) to 10 (very difficult) based on 1024 fragmental contributions (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules (r^2 = 0.94)	2.72

Molecule 6

Water Solubility

SMILES C=CCOc1ccc(cc1)C(=O)N1[C@@H]2CC[C@H]1CC(C2)(O)c1cccnc1OC



Physicochemical Properties

Formula	C23H26N2O4
Molecular weight	394.46 g/mol
Num. heavy atoms	29
Num. arom. heavy atoms	12
Fraction Csp3	0.39
Num. rotatable bonds	7
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	113.51
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	71.89 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.33
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	3.01
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	2.82
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.	2.21

Log S (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.03
Solubility	3.71e-02 mg/ml ; 9.41e-05 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble
Log S (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-4.18
Solubility	2.58e-02 mg/ml ; 6.54e-05 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-5.36
Solubility	1.71e-03 mg/ml ; 4.33e-06 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	Yes
P-gp substrate	Yes
P-glycoprotein substrate: SVM model built on 1033 molecules	

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	3.41
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.96

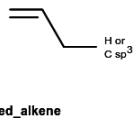
(training set) and tested on 415 molecules (test set) 10-fold CV: ACC=0.72 / AUC=0.77 External: ACC=0.88 / AUC=0.94	
CYP1A2 inhibitor	
Cytochrome P450 1A2 inhibitor: SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.83 / AUC=0.90 External: ACC=0.84 / 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	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)	-6.57 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 1 alert: isolated_alkene

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



isolated_alkene

Leadlikeness

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

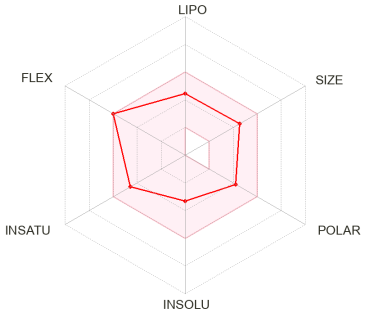
No; 1 violation: MW>350

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)

4.57

Molecule 7



SMILES COc1ccc(cn1)[C@H]([C@@H]1C[C@@H](C1)O)NC(=O)CCc1ccccc1OC

Physicochemical Properties

Formula	C21H26N2O4
Molecular weight	370.44 g/mol
Num. heavy atoms	27
Num. arom. heavy atoms	12
Fraction Csp3	0.43
Num. rotatable bonds	9
Num. H-bond acceptors	5
Num. H-bond donors	2
Molar Refractivity	102.37
TPSA	80.68 Å²

Topological Polar Surface Area: Calculated from

Water Solubility

Log *S* (ESOL)

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

-3.31

Solubility	1.80e-01 mg/ml ; 4.85e-04 mol/l
Class	Soluble

Solubility class: Log *S* scale
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.

-3.62

Solubility	8.85e-02 mg/ml ; 2.39e-04 mol/l
Class	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.	3.23
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	2.29
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	2.34
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.	1.58
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	3.31
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.55

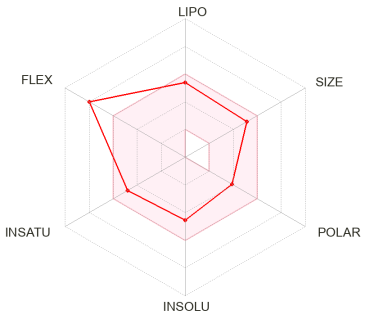
< Soluble < -2 Very < 0 < Highly	
Log S (SILICOS-IT)	
SILICOS-IT: Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com	-5.67
Solubility	7.83e-04 mg/ml ; 2.11e-06 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -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	
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	Yes
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-6.93 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	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	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	3.75
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 8



SMILES COCCCNC(=O)C[C@@H](c1c[nH]c2c1cccc2CC)c1ccc(cc1OC)OC

Physicochemical Properties

Formula	C25H32N2O4
Molecular weight	424.53 g/mol
Num. heavy atoms	31
Num. arom. heavy atoms	15
Fraction Csp3	0.40
Num. rotatable bonds	12
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	123.44
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	72.58 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.62
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	3.96
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	4.42

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.53
Solubility	1.24e-02 mg/ml ; 2.93e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-5.18
Solubility	2.77e-03 mg/ml ; 6.54e-06 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-8.54
Solubility	1.22e-06 mg/ml ; 2.86e-09 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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.	2.15
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	5.92
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	4.01

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	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	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	Yes
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.	-6.08 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	No; 1 violation: Rotors>10
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

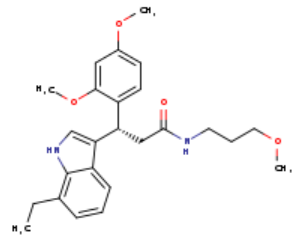
Leadlikeness

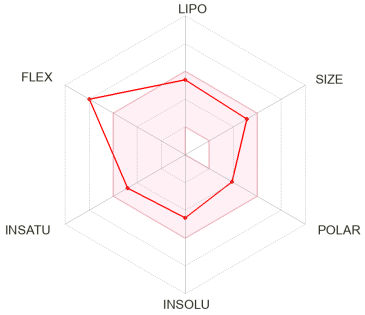
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5

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)	3.71

Molecule 9





SMILES COCCCNC(=O)C[C@H](c1c[nH]c2c1cccc2CC)c1ccc(cc1OC)OC

Physicochemical Properties

Formula	C25H32N2O4
Molecular weight	424.53 g/mol
Num. heavy atoms	31

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.53
Solubility	1.24e-02 mg/ml ; 2.93e-05 mol/l
Class	Moderately soluble

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

Num. arom. heavy atoms	15
Fraction Csp3	0.40
Num. rotatable bonds	12
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	123.44
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	72.58 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.39
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	3.96
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	4.42
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.	2.15
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	5.92
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	3.97

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-5.18
Solubility	2.77e-03 mg/ml ; 6.54e-06 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-8.54
Solubility	1.22e-06 mg/ml ; 2.86e-09 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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	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.	-6.08 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	No; 1 violation: Rotors>10

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

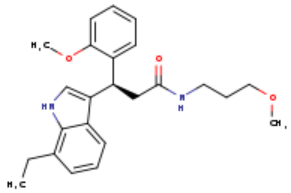
Leadlikeness **Leadlikeness:** implemented from	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5

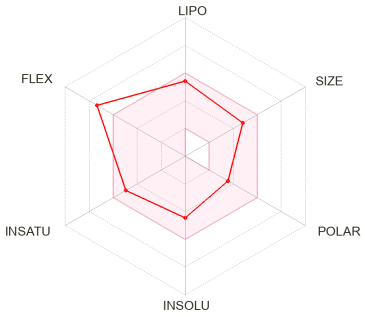
Teague SJ. 1999 Angew. Chem. Int. Ed.
250 < MW < 350
XLOGP < 3.5
Num. rotatable bonds < 7

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) 3.71

Molecule 10





SMILES COCCCNC(=O)C[C@@H](c1c[nH]c2c1cccc2CC)c1ccccc1OC

Physicochemical Properties

Formula	C24H30N2O3
Molecular weight	394.51 g/mol
Num. heavy atoms	29
Num. arom. heavy atoms	15
Fraction Csp3	0.38
Num. rotatable bonds	11
Num. H-bond acceptors	3
Num. H-bond donors	2
Molar Refractivity	116.95
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	63.35 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.18
Log $P_{o/w}$ (XLOGP3)	3.99
XLOGP3: Atomistic and knowledge-based	

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.46
Solubility	1.38e-02 mg/ml ; 3.50e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-5.02
Solubility	3.75e-03 mg/ml ; 9.51e-06 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-8.44
Solubility	1.43e-06 mg/ml ; 3.61e-09 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.	4.41
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.	2.48
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	5.83
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	3.98

Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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	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	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.	-5.87 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	No; 1 violation: Rotors>10
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

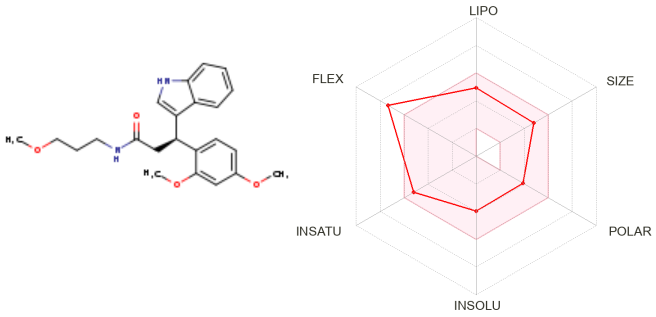
Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds ≤ 7	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5

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)	3.48

Molecule 11

Water Solubility



SMILES COCCCNC(=O)C[C@@H](c1c[nH]c2c1cccc2)c1ccc(cc1OC)OC

Physicochemical Properties

Formula	C23H28N2O4
Molecular weight	396.48 g/mol
Num. heavy atoms	29
Num. arom. heavy atoms	15
Fraction Csp3	0.35
Num. rotatable bonds	11
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	113.66
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	72.58 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.14
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	3.16
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	3.86
Log $P_{o/w}$ (MLOGP)	1.73
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.	-3.95
Solubility	4.49e-02 mg/ml ; 1.13e-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.	-4.35
Solubility	1.75e-02 mg/ml ; 4.42e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-7.78
Solubility	6.64e-06 mg/ml ; 1.67e-08 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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 — 4.97

Consensus Log $P_{o/w}$

Consensus Log $P_{o/w}$: Average of all five predictions — 3.37

(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 — 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) — -6.47 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	No; 1 violation: Rotors>10
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

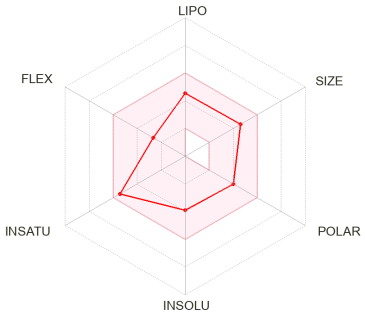
Leadlikeness

Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	No; 2 violations: MW>350, Rotors>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)	3.46

Molecule 12



SMILES COc1ncccc1C(=O)N1CCC(CC1)(O)c1ccc2c(c1)ccc(n2)C

Physicochemical Properties

Formula	C22H23N3O3
Molecular weight	377.44 g/mol
Num. heavy atoms	28
Num. arom. heavy atoms	16
Fraction Csp3	0.32
Num. rotatable bonds	4
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	110.65
TPSA	75.55 Å²

Topological Polar Surface Area: Calculated from

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.88
Solubility	5.02e-02 mg/ml ; 1.33e-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.	-3.67
Solubility	8.07e-02 mg/ml ; 2.14e-04 mol/l
Class	Soluble
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4	

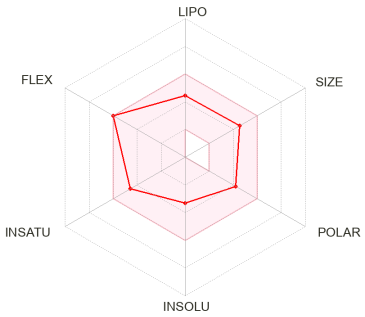
Ertl P. et al. 2000 J. Med. Chem.	
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.16
Log $P_{o/w}$ (XLOGP3)	
XLOGP3: Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	2.44
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	2.58
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.	1.88
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	3.50
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.71
< 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	-6.39
Solubility	1.55e-04 mg/ml ; 4.10e-07 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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	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	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	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.	-6.87 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	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	No; 1 violation: MW>350
Synthetic accessibility	2.60
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 13



SMILES COc1ccc(cn1)[C@@H]([C@@H]1C[C@@H](C1)O)NC(=O)CCc1ccccc1OC

Physicochemical Properties

Formula	C21H26N2O4
Molecular weight	370.44 g/mol
Num. heavy atoms	27
Num. arom. heavy atoms	12
Fraction Csp3	0.43
Num. rotatable bonds	9
Num. H-bond acceptors	5
Num. H-bond donors	2
Molar Refractivity	102.37
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	80.68 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.25
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	2.29
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	2.34

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.31
Solubility	1.80e-01 mg/ml ; 4.85e-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.	-3.62
Solubility	8.85e-02 mg/ml ; 2.39e-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	-5.67
Solubility	7.83e-04 mg/ml ; 2.11e-06 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

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.	1.58
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	3.31
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.55

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	Yes
CYP3A4 inhibitor	Yes
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.	-6.93 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	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

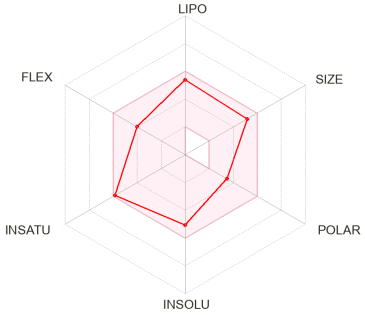
Leadlikeness

Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	No; 2 violations: MW>350, Rotors>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)	3.75

Molecule 14



SMILES	c1cnc(nc1)Oc1cccc(c1)CN1CCOC[C@H](C1)Cc1cncc2c1cccc2

Physicochemical Properties

Formula	C26H26N4O2
Molecular weight	426.51 g/mol
Num. heavy atoms	32

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-5.07
Solubility	3.66e-03 mg/ml ; 8.58e-06 mol/l

Class

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

Num. arom. heavy atoms	22
Fraction Csp3	0.27
Num. rotatable bonds	6
Num. H-bond acceptors	6
Num. H-bond donors	0
Molar Refractivity	127.93
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	60.37 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.80
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	3.92
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	3.98
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.	2.31
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	4.38
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	3.68

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-4.89
Solubility	5.54e-03 mg/ml ; 1.30e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-8.67
Solubility	9.08e-07 mg/ml ; 2.13e-09 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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	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	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.	-6.12 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

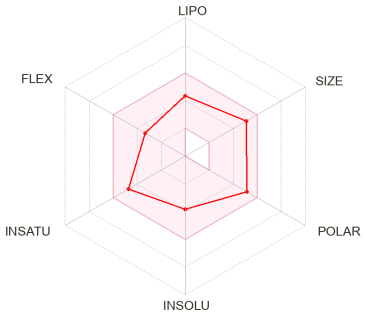
Ghose	
Ghose filter: implemented from Ghose AK. et al. 1999 J. Comb. Chem. 160 ≤ MW ≤ 480 -0.4 ≤ WLOGP ≤ 5.6 40 ≤ MR ≤ 130 20 ≤ atoms ≤ 70	Yes
Veber	
Veber (GSK) filter: implemented from Veber DF. et al. 2002 J. Med. Chem. Rotatable bonds < 10 TPSA < 140	Yes
Egan	
Egan (Pharmacia) filter: implemented 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	No; 2 violations: MW>350, XLOGP3>3.5
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) 3.64

Molecule 15



SMILES COc1ncccc1C1(O)C[C@@H]2CC[C@H](C1)N2C(=O)c1cccc(c1)n1nnnc1C

Physicochemical Properties

Formula	C22H24N6O3
Molecular weight	420.46 g/mol
Num. heavy atoms	31
Num. arom. heavy atoms	17
Fraction Csp3	0.41
Num. rotatable bonds	5
Num. H-bond acceptors	7
Num. H-bond donors	1
Molar Refractivity	115.56
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	106.26 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.06
Log $P_{o/w}$ (XLOGP3)	2.09
XLOGP3: Atomistic and knowledge-based	

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.84
Solubility	6.09e-02 mg/ml ; 1.45e-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.	-3.95
Solubility	4.70e-02 mg/ml ; 1.12e-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	-4.92
Solubility	5.03e-03 mg/ml ; 1.20e-05 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.	1.54
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.	2.36
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	1.43
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.10

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	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	Yes
Log K_p (skin permeation)	
Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-7.38 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	No; 1 violation: MW>350

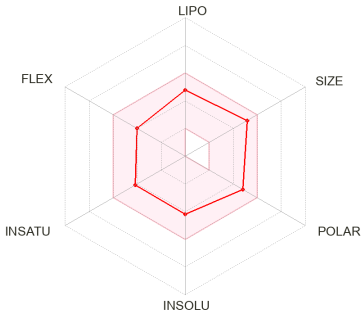
Synthetic accessibility

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)	4.81

Molecule 16

Water Solubility

SMILES COc1ncccc1C1(O)C[C@@H]2CC[C@H](C1)N2C(=O)c1ccc(cc1)OC1CSC1



Physicochemical Properties

Formula	C23H26N2O4S
Molecular weight	426.53 g/mol
Num. heavy atoms	30
Num. arom. heavy atoms	12
Fraction Csp3	0.48
Num. rotatable bonds	6
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	119.46
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	97.19 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.23
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	2.85
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	2.75
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.	2.29

Log S (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.18
Solubility	2.82e-02 mg/ml ; 6.61e-05 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble
Log S (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-4.55
Solubility	1.20e-02 mg/ml ; 2.82e-05 mol/l
Class	
Solubility class: Log S scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-5.20
Solubility	2.72e-03 mg/ml ; 6.38e-06 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	Yes
P-glycoprotein substrate: SVM model built on 1033 molecules	

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	3.23
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.87

(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	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)	-6.88 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

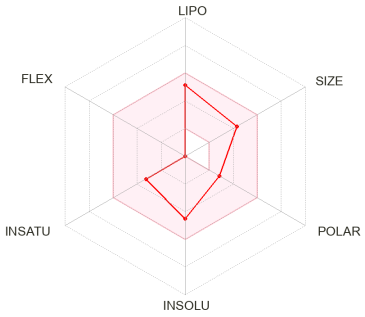
Leadlikeness

Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	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)	4.71

Molecule 17



SMILES Cc1ccc2c(c1)cc1c(n2)OC([C@H]2[C@H]1OCC1(C2)CCNCC1)(C)C

Physicochemical Properties

Formula	C22H28N2O2
Molecular weight	352.47 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	10
Fraction Csp3	0.59
Num. rotatable bonds	0
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	107.47
TPSA	43.38 Å²

Topological Polar Surface Area: Calculated from

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.51
Solubility	1.08e-02 mg/ml ; 3.06e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble

Log *S* (Ali)

Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-4.09
Solubility	2.84e-02 mg/ml ; 8.05e-05 mol/l
Class	Moderately 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. 3.52

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 3.50

Log $P_{o/w}$ (WLOGP)

WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model. 3.46

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. 3.16

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 4.33

Consensus Log $P_{o/w}$

Consensus Log $P_{o/w}$: Average of all five predictions 3.59

< 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 -6.64

Solubility 8.09e-05 mg/ml ; 2.30e-07 mol/l

Class

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

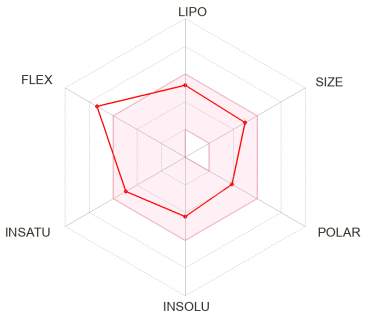
Cytochrome P450 2C19 inhibitor: SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) 10-fold CV: ACC=0.80 / AUC=0.86 External: ACC=0.80 / AUC=0.87 No

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	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.	-5.97 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	No; 1 violation: MW>350
Synthetic accessibility	4.49
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 18



SMILES COCCNC(=O)C[C@H](c1c[nH]c2c1cccc2CC)c1ccc(cc1OC)OC

Physicochemical Properties

Formula	C24H30N2O4
Molecular weight	410.51 g/mol
Num. heavy atoms	30
Num. arom. heavy atoms	15
Fraction Csp3	0.38
Num. rotatable bonds	11
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	118.63
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	72.58 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	3.54
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	3.60
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	4.03

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-4.30
Solubility	2.07e-02 mg/ml ; 5.05e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately soluble
Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-4.81
Solubility	6.34e-03 mg/ml ; 1.54e-05 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Moderately 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	-8.15
Solubility	2.89e-06 mg/ml ; 7.05e-09 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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.	1.94
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	5.51
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	3.72

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	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	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	Yes
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.	-6.25 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	No; 1 violation: Rotors>10
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

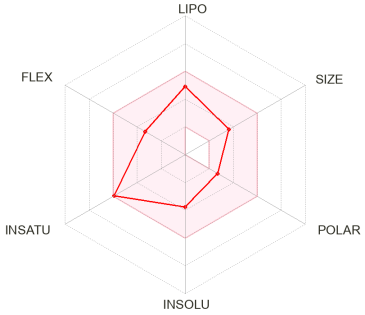
Leadlikeness

Leadlikeness: implemented from Teague SJ. 1999 Angew. Chem. Int. Ed. 250 < MW < 350 XLOGP < 3.5 Num. rotatable bonds < 7	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5

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)	3.59

Molecule 19



SMILES	CN(CC[C@](c1c[nH]c2c1cccc2)(c1ccccc1)O)C

Physicochemical Properties

Formula	C19H22N2O
Molecular weight	294.39 g/mol
Num. heavy atoms	22

Water Solubility

Log *S* (ESOL)

ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.78
Solubility	4.88e-02 mg/ml ; 1.66e-04 mol/l

Class

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

Num. arom. heavy atoms	15
Fraction Csp3	0.26
Num. rotatable bonds	5
Num. H-bond acceptors	2
Num. H-bond donors	2
Molar Refractivity	90.92
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	39.26 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.78
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	3.08
Log $P_{o/w}$ (WLOGP)	
WLOGP: Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	3.25
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.	2.47
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	3.74
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	3.06

Log *S* (Ali)	
Ali: Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model.	-3.57
Solubility	7.89e-02 mg/ml ; 2.68e-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	-6.19
Solubility	1.92e-04 mg/ml ; 6.52e-07 mol/l
Class	
Solubility class: Log *S* scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	Poorly 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	Yes
CYP1A2 inhibitor	Yes
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	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.	-5.91 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

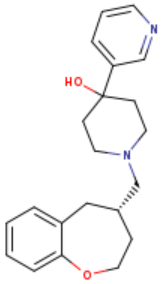
PAINS	
Pan Assay Interference Structures: implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.	0 alert
Brenk	
Structural Alert: implemented from Brenk R. et al. 2008 ChemMedChem	0 alert
Leadlikeness	Yes
Leadlikeness: implemented from	

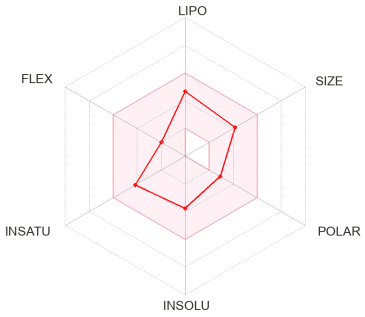
Teague SJ. 1999 Angew. Chem. Int. Ed.
250 < MW < 350
XLOGP < 3.5
Num. rotatable bonds < 7

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) 2.77

Molecule 20





SMILES OC1(CCN(CC1)C[C@@H]1CCOc2c(C1)cccc2)c1cccnc1

Physicochemical Properties

Formula	C21H26N2O2
Molecular weight	338.44 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	12
Fraction Csp3	0.48
Num. rotatable bonds	3
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	102.27
TPSA	
Topological Polar Surface Area: Calculated from Ertl P. et al. 2000 J. Med. Chem.	45.59 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP)	
iLOGP: in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	2.91
Log $P_{o/w}$ (XLOGP3)	2.66
XLOGP3: Atomistic and knowledge-based	

Water Solubility

Log *S* (ESOL)	
ESOL: Topological method implemented from Delaney JS. 2004 J. Chem. Inf. Model.	-3.77
Solubility	5.73e-02 mg/ml ; 1.69e-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.	-3.27
Solubility	1.82e-01 mg/ml ; 5.38e-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	-5.67
Solubility	7.20e-04 mg/ml ; 2.13e-06 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.	2.52
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.	2.23
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	3.50
Consensus Log $P_{o/w}$	
Consensus Log $P_{o/w}$: Average of all five predictions	2.76

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	Yes
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Skin permeation: QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.	-6.48 cm/s
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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

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