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## SwissADME

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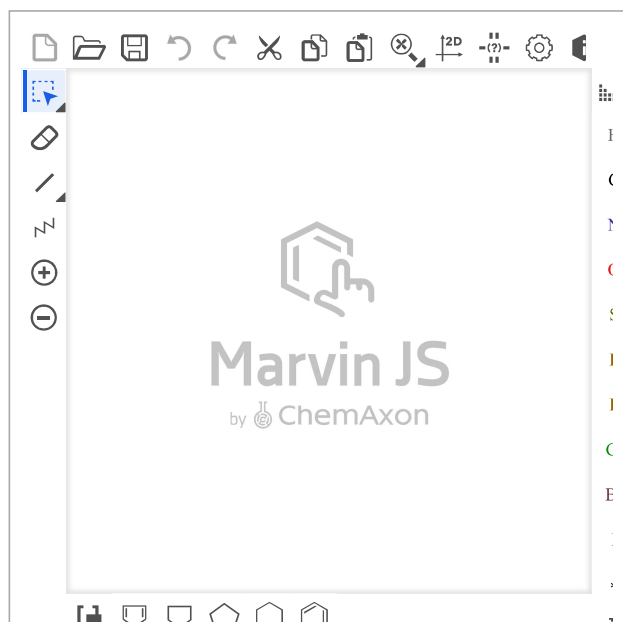
This website allows you to compute physicochemical descriptors as well as to predict ADME parameters, pharmacokinetic properties, druglike nature and medicinal chemistry friendliness of one or multiple small molecules to support drug discovery.

The main article describing the web service and its underlying methodologies is [SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules](#), *Sci. Rep.* (2017) 7:42717.

For details about development and validation of iLOG, please refer to this article: [iLOGP: a simple, robust, and efficient description of \*n\*-octanol/water partition coefficient for drug design using the GB/SA approach](#), *J. Chem. Inf. Model.* (2014) 54(12):3284-3301.

For details about development and validation of the BOILED-Egg, please refer to this article: [A BOILED-Egg to predict gastrointestinal absorption and brain penetration of small molecules](#), *ChemMedChem* (2016) 11(11):1117-1121.

Developed and maintained by the [Molecular Modeling Group](#) of the SIB | Swiss Institute of Bioinformatics.



Enter a list of SMILES here:

```
COC1=C(C=C2C(=C1)C(=O)C(=C2)C3=CC(=C4C(=C3OC)OC4)OC)OCC5=CC(=O)C(C#C)C1C(OCc2ccccc2)cc2OC=C(c3c(OC)c4OC0c4c(OC)c3)C(=O)c2c1  
O(Cc1ccccc1)c1c(OC)cc2C(=O)C(c3cc4OC0c4c3)=C0c2c1 S3  
O(Cc1ccccc1)c1c(OC)cc2C(=O)C(c3c(OC)c(OC)c(OC)c3)=C0c2c1  
O(Cc1ccccc1)c1c(OC)cc2C(=O)C(c3c(OC)c4OC(C)(C)Oc4c(OC)c3)=C0c2c1  
O(Cc1ccccc1)c1c(OC2OCCC2)cc2C(=O)C(c3c(OC)c4OC0c4c(OC)c3)=C0c2c1  
O(Cc1ccccc1)c1c(OC)cc2C(=O)C(c3c(OC)c4OC0c4c(OC)c3)=C0c2c1 S7  
O(Cc1ccccc1)c1c(OCc2ccccc2)cc2OC=C(c3c(OC)c4OC0c4c(OC)c3)C(=O)c2c1  
O(Cc1ccccc1)c1c(OC2OCCC2)cc2C(=O)C(c3c(OC)c4OC(C)(C)Oc4c(OC)c3)=C0c2c1  
O(Cc1ccccc1)c1c(OC)cc2C(=O)C(c3c(OC)c4OC(C)(C)Oc4c(OC)c3)=C0c2c1  
O(Cc1ccccc1)c1c(OCc2ccccc2)cc2OC=C(c3c(OC)c4OC(C)(C)Oc4c(OC)c3)C(=O)c2c1  
O(Cc1ccccc1)c1c(OCc2ccccc2)cc2OC=C(c3c(OC)c4OC(C)(C)Oc4c(OC)c3)C(=O)c2c1  
O(Cc1ccccc1)c1c(OCc2ccccc2)cc2OC=C(c3c(OC)c4OC(C)(C)Oc4c(OC)c3)C(=O)c2c1
```

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Retrieve data: POWERED BY ChemAxon

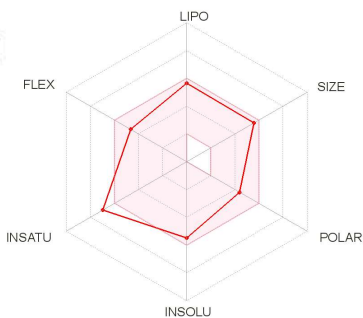
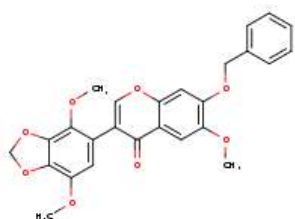
G1



Water Solubility

Log S (ESOL) -5.48

[ESOL: Topological method implemented](#)



SMILE COc1cc2c(cc1OCc1ccccc1)occ(c2=O)c1cc(OC)c2c(c1O)C)OCO2

#### Physicochemical Properties

Formula	C26H22O8
Molecular weight	462.45 g/mol
Num. heavy atoms	34
Num. arom. heavy atoms	22
Fraction Csp3	0.19
Num. rotatable bonds	7
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	124.44
TPSA	

#### Topological Polar Surface Area:

Calculated from [Ertl P. et al. 2000 J. Med. Chem.](#) 85.59 Å<sup>2</sup>

#### Lipophilicity

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

**iLOGP:** in-house physics-based method implemented from [Daina A et al. 2014 J. Chem. Inf. Model.](#) 4.24

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. 4.37

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

**WLOGP:** Atomistic method implemented from [Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.](#) 4.64

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

**MLOGP:** Topological method implemented from [Moriguchi I. et al. 1992 Chem. Pharm. Bull.](#) and [Moriguchi I. et al. 1994 Chem. Pharm. Bull.](#) 1.58

from [Delaney JS. 2004 J. Chem. Inf. Model.](#)

Solubility 1.54e-03 mg/ml ; 3.33e-06 mol/l  
Class

**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.](#) -5.88

Solubility 6.05e-04 mg/ml ; 1.31e-06 mol/l  
Class

**Solubility class:** Log  $S$  scale

Insoluble < -10 < Poorly < -6 < Moderately < -4 < 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](#) -8.79

Solubility 7.52e-07 mg/ml ; 1.63e-09 mol/l  
Class

**Solubility class:** Log  $S$  scale

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

#### Pharmacokinetics

GI absorption

**Gastrointestinal absorption:** according to the white of the BOILED-Egg High

BBB permeant

**BBB permeation:** according to the yolk of the BOILED-Egg No

P-gp substrate Yes

**P-glycoprotein substrate:** SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set). 10-fold CV: ACC=0.72 /

[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, 5.46  
version 1.0.2, courtesy  
of SILICOS-IT,  
[http://www.silicos-  
it.com](http://www.silicos-it.com)

Consensus Log  $P_{o/w}$

?

**Consensus Log  $P_{o/w}$ :** 4.06  
[Average of all five  
predictions](#)

[AUC=0.77](#)  
[External: ACC=0.88 /](#)  
[AUC=0.94](#)

CYP1A2 inhibitor

?

**Cytochrome P450 1A2  
inhibitor:** SVM model  
built on 9145 molecules  
(training set) No  
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) Yes  
and tested on 3000  
molecules (test set)  
10-fold CV: ACC=0.80 /  
[AUC=0.86](#)  
[External: ACC=0.80 /](#)  
[AUC=0.87](#)

CYP2C9 inhibitor

?

**Cytochrome P450 2C9  
inhibitor:** SVM model  
built on 5940 molecules  
(training set) Yes  
and tested on 2075  
molecules (test set)  
10-fold CV: ACC=0.78 /  
[AUC=0.85](#)  
[External: ACC=0.71 /](#)  
[AUC=0.81](#)

CYP2D6 inhibitor

?

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

CYP3A4 inhibitor

?

**Cytochrome P450 3A4  
inhibitor:** SVM model  
built on 7518 molecules  
(training set) Yes  
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)

-6.02 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.](#)

Yes; 0 violation

[MW < 500](#)[MLOGP < 4.15](#)[N or O < 10](#)[NH or OH < 5](#)

Ghose ?

**Ghose filter:**

implemented from

[Ghose AK. et al. 1999 J.](#)[Comb. Chem.](#)

Yes

[160 < MW < 480](#)[-0.4 < WLOGP < 5.6](#)[40 < MR < 130](#)[20 < atoms < 70](#)

Veber ?

**Veber (GSK) filter:**

implemented from

[Veber DF. et al. 2002 J.](#)[Med. Chem.](#)

Yes

[Rotatable bonds < 10](#)[TPSA < 140](#)

Egan ?

**Egan (Pharmacia)****filter:** implemented

from

[Egan WJ. et al. 2000 J.](#)[Med. Chem.](#)

Yes

[WLOGP < 5.88](#)[TPSA < 131.6](#)

Muegge ?

**Muegge (Bayer) filter:**

implemented from

[Muegge I. et al. 2001 J.](#)[Med. Chem.](#)[200 < MW < 600](#)[-2 < XLOGP < 5](#)[TPSA < 150](#)

Yes

[Num. rings < 7](#)[Num. carbon > 4](#)[Num. heteroatoms > 1](#)[Num. rotatable bonds <](#)[15](#)[H-bond acc. < 10](#)[H-bond don. < 5](#)

Bioavailability Score ?

**Abbott Bioavailability****Score:** Probability of F[≥ 10% in rat](#)

0.55

implemented from

[Martin YC. 2005 J.](#)[Med. Chem.](#)

## 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

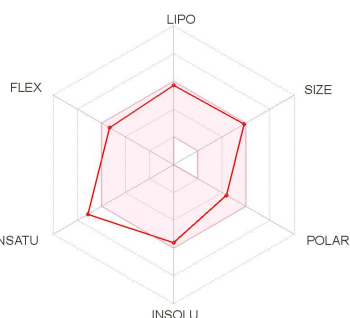
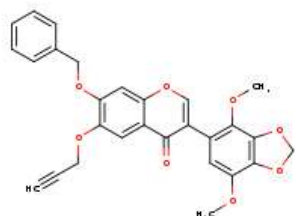
Leadlikeness

**Leadlikeness:**  
[implemented from Teague S.J. 1999 Angew. Chem. Int. Ed.](#)  
[250 < MW < 350](#)  
[XLOGP < 3.5](#)  
[Num. rotatable bonds < 7](#)  
 No; 2 violations: MW>350, 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](#)  
[\(r<sup>2</sup> = 0.94\)](#)

G2



SMILE C#CCOCc1cc2c(cc1OCc1cccc1)occ(c2=O)c1cc(OC)c2c(c1OC)OCO2

#### Physicochemical Properties

Formula	C28H22O8
Molecular weight	486.47 g/mol
Num. heavy atoms	36
Num. arom. heavy atoms	22
Fraction Csp3	0.18
Num. rotatable bonds	8
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	132.21
TPSA	

**Topological Polar Surface Area:**  
[Calculated from Ertl P. et al. 2000 J. Med. Chem.](#)  
 85.59 Å<sup>2</sup>

#### Lipophilicity

Log P<sub>o/w</sub> (iLOGP) 4.69

#### Water Solubility

Log S (ESOL)

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

-5.61

Solubility 1.20e-03 mg/ml ; 2.46e-06 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.**

-6.01

Solubility 4.78e-04 mg/ml ; 9.82e-07 mol/l  
 Class

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

Log S (SILICOS-IT) -8.86

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

Log  $P_{o/w}$  (XLOGP3) <sup>2</sup>

**XLOGP3:** Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry

4.49

Log  $P_{o/w}$  (WLOGP) <sup>2</sup>

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

4.72

Log  $P_{o/w}$  (MLOGP) <sup>2</sup>

**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.

1.91

Log  $P_{o/w}$  (SILICOS-IT) <sup>2</sup>

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

6.09

Consensus Log  $P_{o/w}$  <sup>2</sup>

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

4.38

**SILICOS-IT:** Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <http://www.silicos-it.com>

Solubility 6.65e-07 mg/ml ; 1.37e-09 mol/l

Class <sup>2</sup>

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

## Pharmacokinetics

GI absorption <sup>2</sup>

**Gastrointestinal absorption:** according to the white of the BOILED-Egg High

BBB permeant <sup>2</sup>

**BBB permeation:** according to the yolk of the BOILED-Egg No

P-gp substrate <sup>2</sup>

**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 Yes  
External: ACC=0.88 / AUC=0.94

CYP1A2 inhibitor <sup>2</sup>

**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 No  
External: ACC=0.84 / AUC=0.91

CYP2C19 inhibitor <sup>2</sup>

**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 Yes  
External: ACC=0.80 / AUC=0.87

CYP2C9 inhibitor <sup>2</sup> Yes

**Cytochrome P450 2C9 inhibitor:** SVM model built on 5940 molecules

(training set)  
and tested on 2075  
molecules (test set)  
10-fold CV: ACC=0.78 /  
AUC=0.85  
External: ACC=0.71 /  
AUC=0.81

CYP2D6 inhibitor ?

**Cytochrome P450 2D6  
inhibitor:** SVM model  
built on 3664 molecules  
(training set)  
and tested on 1068 molecules (test set)  
10-fold CV: ACC=0.79 /  
AUC=0.85  
External: ACC=0.81 /  
AUC=0.87

No

CYP3A4 inhibitor ?

**Cytochrome P450 3A4  
inhibitor:** SVM model  
built on 7518 molecules  
(training set)  
and tested on 2579 molecules (test set)  
10-fold CV: ACC=0.77 /  
AUC=0.85  
External: ACC=0.78 /  
AUC=0.86

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

No; 2 violations: MW>480, MR>130

Veber ?

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

Yes

Egan ?

Yes

**Egan (Pharmacia)**

**filter:** [implemented from](#)

[Egan WJ. et al. 2000 J.](#)

[Med. Chem.](#)

[WLOGP < 5.88](#)

[TPSA < 131.6](#)

Muegge 

**Muegge (Bayer) filter:**

[implemented from](#)

[Muegge I. et al. 2001 J.](#)

[Med. Chem.](#)

[200 < MW < 600](#)

[-2 < XLOGP < 5](#)

[TPSA < 150](#)

Yes

[Num. rings < 7](#)

[Num. carbon > 4](#)


[Num. heteroatoms > 1](#)

[Num. rotatable bonds <](#)

[15](#)

[H-bond acc. < 10](#)

[H-bond don. < 5](#)

Bioavailability Score 

**Abbott Bioavailability**

**Score:** [Probability of F](#)

[≥ 10% in rat](#)

0.55

[implemented from](#)

[Martin YC. 2005 J.](#)

[Med. Chem.](#)

**Medicinal Chemistry**

PAINS 

**Pan Assay Interference**

**Structures:**

[implemented from](#)


0 alert

[Baell JB. & Holloway](#)

[GA. 2010 J. Med.](#)

[Chem.](#)

Brenk 

1 alert: triple\_bond 

**Structural Alert:**

[implemented from](#)

[Brenk R. et al. 2008](#)

[ChemMedChem](#)



triple\_bond

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  4.29

**Synthetic accessibility.**

**score:** [from 1 \(very](#)

[easy\) to 10 \(very](#)

[difficult\)](#)

[based on 1024](#)

[fragmental contributions](#)

[\(FP2\) modulated by size](#)

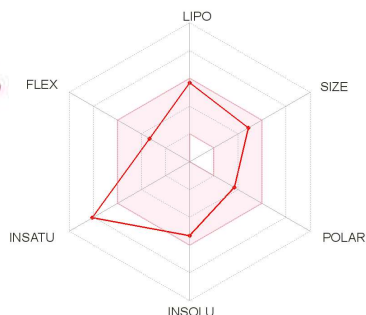
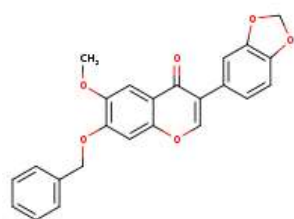
[and complexity penalties,](#)

[trained on 12'782'590](#)

[molecules and tested on](#)

[40 external molecules](#)

[\(r<sup>2</sup> = 0.94\).](#)



SMILE COc1cc2c(cc1OCc1ccccc1)occ(c2=O)c1ccc2c(c1)OCO  
S 2

#### Physicochemical Properties

Formula	C <sub>24</sub> H <sub>18</sub> O <sub>6</sub>
Molecular weight	402.40 g/mol
Num. heavy atoms	30
Num. arom. heavy atoms	22
Fraction Csp <sup>3</sup>	0.12
Num. rotatable bonds	5
Num. H-bond acceptors	6
Num. H-bond donors	0
Molar Refractivity	111.45
TPSA	

#### Topological Polar Surface Area:

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

67.13 Å<sup>2</sup>

#### Lipophilicity

Log *P*<sub>o/w</sub> (iLOGP)

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

3.93

Log *P*<sub>o/w</sub> (XLOGP3)

**XLOGP3:** Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry.

4.43

Log *P*<sub>o/w</sub> (WLOGP)

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

4.62

Log *P*<sub>o/w</sub> (MLOGP)

2.22

**MLOGP:** Topological method implemented from  
Moriguchi I. et al. 1992

#### Water Solubility

Log *S* (ESOL)

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

-5.34

Solubility

1.85e-03 mg/ml ; 4.59e-06 mol/l

Class

**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.

-5.56

Solubility

1.11e-03 mg/ml ; 2.77e-06 mol/l

Class

**Solubility class:** Log *S* scale

Insoluble < -10 < Poorly  
< -6 < Moderately < -4  
< 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>

-8.59

Solubility

1.03e-06 mg/ml ; 2.56e-09 mol/l

Class

**Solubility class:** Log *S* scale

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

#### Pharmacokinetics

GI absorption

**Gastrointestinal absorption:** according to the white of the BOILED-Egg

High

BBB permeant

**BBB permeation:** according to the yolk of the BOILED-Egg

Yes

[Chem. Pharm. Bull.](#)  
[Moriguchi I. et al. 1994](#)  
[Chem. Pharm. Bull.](#)  
[Lipinski PA. et al. 2001](#)  
[Adv. Drug. Deliv. Rev.](#)

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

5.33  
**SILICOS-IT:** Hybrid  
fragmental/topological  
method calculated by  
FILTER-IT program,  
version 1.0.2, courtesy  
of SILICOS-IT,  
[http://www.silicos-  
it.com](http://www.silicos-it.com)

Consensus Log  $P_{o/w}$

4.11  
**Consensus Log  $P_{o/w}$ :**  
Average of all five  
predictions

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  
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

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

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

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

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. -5.61 cm/s

Druglikeness

Lipinski ?

**Lipinski (Pfizer) filter:**

implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. Yes; 0 violation  
MW < 500  
MLOGP < 4.15  
N or O < 10  
NH or OH < 5

Ghose ?

**Ghose filter:**

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

Veber ?

**Veber (GSK) filter:**

implemented from Veber DF. et al. 2002 J. Med. Chem. Yes  
Rotatable bonds < 10  
TPSA < 140

Egan ?

**Egan (Pharmacia) filter:**

implemented from Egan WJ. et al. 2000 J. Med. Chem. Yes  
WLOGP < 5.88  
TPSA < 131.6

Muegge ?

**Muegge (Bayer) filter:**

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

Bioavailability Score ?

**Abbott Bioavailability Score:**

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

## PAINS ?

**Pan Assay Interference****Structures:**

implemented from 0 alert  
[Baell JB. & Holloway](#)  
[GA. 2010 J. Med.](#)  
[Chem.](#)

## Brenk ?

**Structural Alert:**

implemented from 0 alert  
[Brenk R. et al. 2008](#)  
[ChemMedChem](#)

## Leadlikeness ?

**Leadlikeness:**

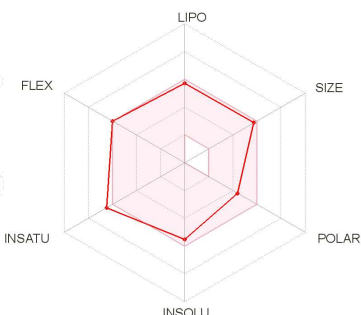
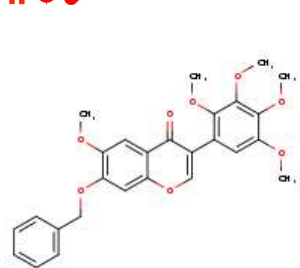
implemented from  
[Teague SJ. 1999 Angew.](#)  
[Chem. Int. Ed.](#) No; 2 violations: MW>350,  
 250 < MW < 350 XLOGP3>3.5  
 XLOGP < 3.5  
 Num. rotatable bonds <  
 7

## Synthetic accessibility ?

**Synthetic accessibility**

**score:** from 1 (very  
 easy) to 10 (very  
 difficult)  
 based on 1024  
 fragmental contributions 3.76  
 (FP2) modulated by size  
 and complexity penalties,  
 trained on 12'782'590  
 molecules and tested on  
 40 external molecules  
 ( $r^2 = 0.94$ )

S4



SMILE COc1cc2c(cc1OCc1ccccc1)occ(c2=O)c1cc(OC)c(c(c1O  
 S C)OC)OC

**Physicochemical Properties**

Formula	C27H26O8
Molecular weight	478.49 g/mol
Num. heavy atoms	35
Num. arom. heavy atoms	22
Fraction Csp3	0.22
Num. rotatable bonds	9
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	131.36

**Water Solubility**

## Log S (ESOL) ?

**ESOL:** Topological  
 method implemented  
 from -5.51  
[Delaney JS. 2004 J.](#)  
[Chem. Inf. Model.](#)

Solubility 1.47e-03 mg/ml ; 3.07e-06 mol/l  
 Class ?

**Solubility class: Log S**

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

## Log S (Ali) ?

**Ali:** Topological method  
 implemented from -6.02  
[Ali J. et al. 2012 J.](#)  
[Chem. Inf. Model.](#)

Solubility 4.59e-04 mg/ml ; 9.59e-07 mol/l  
 Class ? Poorly soluble

TPSA <sup>2</sup> 85.59 Å<sup>2</sup>

### Topological Polar Surface Area:

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

### Lipophilicity

Log *P*<sub>o/w</sub> (iLOGP) <sup>2</sup>

**iLOGP:** in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model. 4.83

Log *P*<sub>o/w</sub> (XLOGP3) <sup>2</sup>

**XLOGP3:** Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry. 4.50

Log *P*<sub>o/w</sub> (WLOGP) <sup>2</sup>

**WLOGP:** Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model. 4.93

Log *P*<sub>o/w</sub> (MLOGP) <sup>2</sup>

**MLOGP:** Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. Moriguchi I. et al. 1994 Chem. Pharm. Bull. Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev. 1.38

Log *P*<sub>o/w</sub> (SILICOS-IT) <sup>2</sup>

**SILICOS-IT:** Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com 5.76

Consensus Log *P*<sub>o/w</sub> <sup>2</sup>

**Consensus Log *P*<sub>o/w</sub>:** Average of all five predictions 4.28

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

Log *S* (SILICOS-IT) <sup>2</sup>

**SILICOS-IT:** Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com -9.28

Solubility 2.54e-07 mg/ml ; 5.31e-10 mol/l  
Class <sup>2</sup>

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

### Pharmacokinetics

GI absorption <sup>2</sup>

**Gastrointestinal absorption:** according to the white of the BOILED-Egg High

BBB permeant <sup>2</sup>

**BBB permeation:** according to the yolk of the BOILED-Egg No

P-gp substrate <sup>2</sup>

**P-glycoprotein substrate:** SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set). Yes  
10-fold CV: ACC=0.72 / AUC=0.77  
External: ACC=0.88 / AUC=0.94


CYP1A2 inhibitor <sup>2</sup>

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

CYP2C19 inhibitor <sup>2</sup> Yes


**Cytochrome P450 2C19 inhibitor:** SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set).

[10-fold CV: ACC=0.80 /](#)  
[AUC=0.86](#)  
[External: ACC=0.80 /](#)  
[AUC=0.87](#)

CYP2C9 inhibitor 


**Cytochrome P450 2C9**

**inhibitor:** [SVM model](#)  
[built on 5940 molecules](#)  
[\(training set\)](#)  
[and tested on 2075](#) Yes  
[molecules \(test set\).](#)  
[10-fold CV: ACC=0.78 /](#)  
[AUC=0.85](#)  
[External: ACC=0.71 /](#)  
[AUC=0.81](#)

CYP2D6 inhibitor 


**Cytochrome P450 2D6**

**inhibitor:** [SVM model](#)  
[built on 3664 molecules](#)  
[\(training set\)](#)  
[and tested on 1068](#) No  
[molecules \(test set\).](#)  
[10-fold CV: ACC=0.79 /](#)  
[AUC=0.85](#)  
[External: ACC=0.81 /](#)  
[AUC=0.87](#)

CYP3A4 inhibitor 

**Cytochrome P450 3A4**

**inhibitor:** [SVM model](#)  
[built on 7518 molecules](#)  
[\(training set\)](#)  
[and tested on 2579](#) Yes  
[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](#) -6.02 cm/s  
[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.](#) Yes; 0 violation  
[MW < 500](#)  
[MLOGP < 4.15](#)  
[N or O < 10](#)  
[NH or OH < 5](#)

Ghose 

**Ghose filter:**  
[implemented from](#)  
[Ghose AK, et al. 1999 J.](#)  
[Comb. Chem.](#) No; 1 violation: MR>130  
[160 < MW < 480](#)  
[-0.4 < WLOGP < 5.6](#)  
[40 < MR < 130](#)  
[20 < atoms < 70](#)

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. Yes  
Med. Chem.  
WLOGP < 5.88  
TPSA < 131.6

Muegge ?

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

Bioavailability Score ?

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

## Medicinal Chemistry

PAINS ?

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

Brenk ?

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

Leadlikeness ?

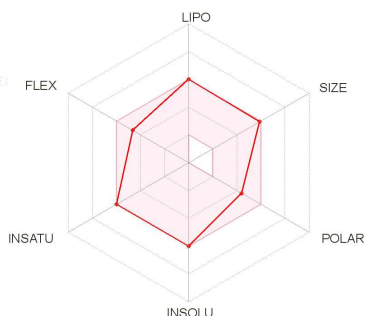
**Leadlikeness:**  
implemented from  
Teague SJ. 1999 Angew. No; 3 violations: MW>350, Rotors>7,  
Chem. Int. Ed. XLOGP3>3.5  
250 < MW < 350  
XLOGP < 3.5  
Num. rotatable bonds <  
7

Synthetic accessibility ? 4.20

**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  
( $r^2 = 0.94$ )

S5



SMILE COc1cc2c(cc1OCc1ccccc1)occ(c2=O)c1cc(OC)c2c(c1OC)OC(O2)(C)C

#### Physicochemical Properties

Formula	C28H26O8
Molecular weight	490.50 g/mol
Num. heavy atoms	36
Num. arom. heavy atoms	22
Fraction Csp3	0.25
Num. rotatable bonds	7
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	134.09
TPSA	

#### Topological Polar Surface Area:

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

85.59 Å<sup>2</sup>

#### Lipophilicity

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

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

5.01

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.

4.99

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

5.42

**WLOGP:** Atomistic  
method implemented  
from  
Wildman SA and

#### Water Solubility

Log  $S$  (ESOL)

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

-6.02

Solubility  
Class

4.74e-04 mg/ml ; 9.66e-07 mol/l

**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.

-6.53

Solubility  
Class

1.46e-04 mg/ml ; 2.97e-07 mol/l

**Solubility class:** Log  $S$   
scale

Insoluble < -10 < Poorly  
< -6 < Moderately < -4  
< 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>

-9.52

Solubility  
Class

1.47e-07 mg/ml ; 3.01e-10 mol/l

**Solubility class:** Log  $S$   
scale


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

#### Pharmacokinetics

GI absorption


High

[Crippen GM. 1999 J. Chem. Inf. Model.](#)


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

**MLOGP:** Topological method implemented from

[Moriguchi I. et al. 1992 Chem. Pharm. Bull.](#) 1.98  
[Moriguchi I. et al. 1994 Chem. Pharm. Bull.](#)  
[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> 6.09


Consensus Log  $P_{o/w}$  

**Consensus Log  $P_{o/w}$ :** 4.70  
[Average of all five predictions](#)


**Gastrointestinal absorption:** according to the white of the BOILED-Egg

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) Yes  
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) No  
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) Yes  
10-fold CV: ACC=0.80 / AUC=0.86  
External: ACC=0.80 / AUC=0.87

CYP2C9 inhibitor 

**Cytochrome P450 2C9 inhibitor:** SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) Yes  
10-fold CV: ACC=0.78 / AUC=0.85  
External: ACC=0.71 / AUC=0.81

CYP2D6 inhibitor 

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

CYP3A4 inhibitor  No

**Cytochrome P450 3A4 inhibitor:** [SVM model built on 7518 molecules \(training set\) and tested on 2579 molecules \(test set\)](#)  
[10-fold CV: ACC=0.77 / AUC=0.85](#)  
[External: ACC=0.78 / AUC=0.86](#)

Log  $K_p$  (skin permeation) ?

**Skin permeation:** [QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.](#) -5.75 cm/s

#### Druglikeness

Lipinski ?

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

Ghose ?

**Ghose filter:** [implemented from Ghose AK. et al. 1999 J. Comb. Chem.](#) No; 2 violations: MW>480, MR>130  
[160 < MW < 480](#)  
[-0.4 < WLOGP < 5.6](#)  
[40 < MR < 130](#)  
[20 < atoms < 70](#)

Veber ?

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

Egan ?

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

Muegge ? Yes

**Muegge (Bayer) filter:** [implemented from Muegge I. et al. 2001 J. Med. Chem.](#)  
[200 < MW < 600](#)  
[-2 < XLOGP < 5](#)  
[TPSA < 150](#)  
[Num. rings < 7](#)  
[Num. carbon > 4](#)  
[Num. heteroatoms > 1](#)  
[Num. rotatable bonds < 15](#)

H-bond acc. < 10

H-bond don. < 5

Bioavailability Score

**Abbott Bioavailability**

**Score:** Probability of F  
≥ 10% in rat 0.55  
implemented from  
Martin YC. 2005 J.  
Med. Chem.

#### Medicinal Chemistry

PAINS

**Pan Assay Interference**

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

Brenk

**Structural Alert:**

implemented from 0 alert  
Brenk R. et al. 2008  
ChemMedChem

Leadlikeness

**Leadlikeness:**

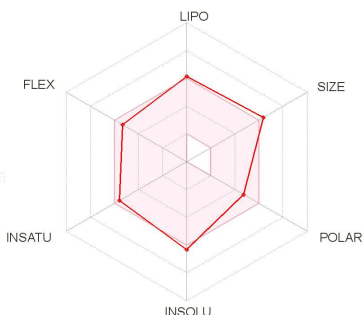
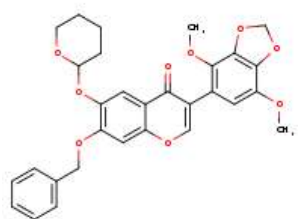
implemented from  
Teague SJ. 1999 Angew.  
Chem. Int. Ed. No; 2 violations: MW>350,  
250 < MW < 350 XLOGP3>3.5  
XLOGP < 3.5  
Num. rotatable bonds <  
7

Synthetic accessibility

**Synthetic accessibility**

**score:** from 1 (very  
easy) to 10 (very  
difficult)  
based on 1024  
fragmental contributions 4.36  
(FP2) modulated by size  
and complexity penalties,  
trained on 12'782'590  
molecules and tested on  
40 external molecules  
( $r^2 = 0.94$ ).

S6



SMILE COc1c2OCOc2c(cc1c1coc2c(c1=O)cc(c2)OCc1ccccc1)OC1CCCCO1)OC  
S

Physicochemical Properties

#### Water Solubility

Log S (ESOL)

**ESOL:** Topological  
method implemented  
from -6.33  
Delaney JS. 2004 J.  
Chem. Inf. Model.

Solubility 2.51e-04 mg/ml ; 4.72e-07 mol/l  
Class Poorly soluble

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

Formula	C30H28O9	< Soluble < -2 Very < 0
Molecular weight	532.54 g/mol	< Highly
Num. heavy atoms	39	
Num. arom. heavy atoms	22	Log <i>S</i> (Ali) ?
Fraction Csp3	0.30	<b>Ali:</b> Topological method implemented from <a href="#">Ali J. et al. 2012 J. Chem. Inf. Model.</a> -6.97
Num. rotatable bonds	8	
Num. H-bond acceptors	9	
Num. H-bond donors	0	
Molar Refractivity	142.64	Solubility 5.71e-05 mg/ml ; 1.07e-07 mol/l
TPSA ?		Class ?

**Topological Polar Surface Area:** 94.82 Å<sup>2</sup>  
 Calculated from [Ertl P. et al. 2000 J. Med. Chem.](#)

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

#### Lipophilicity


Log <i>P</i> <sub>o/w</sub> (iLOGP) ?		Log <i>S</i> (SILICOS-IT) ?	
<b>iLOGP:</b> in-house physics-based method implemented from <a href="#">Daina A et al. 2014 J. Chem. Inf. Model.</a> 4.88		<b>SILICOS-IT:</b> Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <a href="http://www.silicos-it.com">http://www.silicos-it.com</a> -9.22	
Log <i>P</i> <sub>o/w</sub> (XLOGP3) ?			
<b>XLOGP3:</b> Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry. 5.23		Solubility 3.20e-07 mg/ml ; 6.01e-10 mol/l	
		Class ?	
Log <i>P</i> <sub>o/w</sub> (WLOGP) ?		<b>Solubility class:</b> Log <i>S</i> scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	
<b>WLOGP:</b> Atomistic method implemented from <a href="#">Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.</a> 5.54			
Log <i>P</i> <sub>o/w</sub> (MLOGP) ?			
<b>MLOGP:</b> Topological method implemented from <a href="#">Moriguchi I. et al. 1992 Chem. Pharm. Bull.</a> <a href="#">Moriguchi I. et al. 1994 Chem. Pharm. Bull.</a> <a href="#">Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.</a> 2.00			
Log <i>P</i> <sub>o/w</sub> (SILICOS-IT) ?			
<b>SILICOS-IT:</b> Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <a href="http://www.silicos-it.com">http://www.silicos-it.com</a> 5.93			
Consensus Log <i>P</i> <sub>o/w</sub> ?	4.72		

#### Pharmacokinetics


GI absorption ?	
<b>Gastrointestinal absorption:</b> according to the white of the BOILED-Egg High	
BBB permeant ?	
<b>BBB permeation:</b> according to the yolk of the BOILED-Egg No	
P-gp substrate ?	
<b>P-glycoprotein substrate:</b> 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
<b>Cytochrome P450 1A2 inhibitor:</b> SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set)	

Consensus Log  $P_{ow}$ :  
Average of all five  
predictions


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 Yes  
molecules (test set).  
10-fold CV: ACC=0.80 /  
AUC=0.86  
External: ACC=0.80 /  
AUC=0.87

CYP2C9 inhibitor 


**Cytochrome P450 2C9**  
**inhibitor:** SVM model  
built on 5940 molecules  
(training set)  
and tested on 2075 Yes  
molecules (test set).  
10-fold CV: ACC=0.78 /  
AUC=0.85  
External: ACC=0.71 /  
AUC=0.81

CYP2D6 inhibitor 

**Cytochrome P450 2D6**  
**inhibitor:** SVM model  
built on 3664 molecules  
(training set)  
and tested on 1068 Yes  
molecules (test set).  
10-fold CV: ACC=0.79 /  
AUC=0.85  
External: ACC=0.81 /  
AUC=0.87

CYP3A4 inhibitor 

**Cytochrome P450 3A4**  
**inhibitor:** SVM model  
built on 7518 molecules  
(training set)  
and tested on 2579 Yes  
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 -5.84 cm/s  
implemented from  
Potts RO and Guy RH.  
1992 Pharm. Res.

Druglikeness

Lipinski  Yes; 1 violation: MW>500

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

Ghose ?

**Ghose filter:**

implemented from  
Ghose AK. et al. 1999 J.  
Comb. Chem.  
 $160 < MW < 480$   
 $-0.4 < WLOGP < 5.6$   
 $40 < MR < 130$   
 $20 < \text{atoms} < 70$

No; 2 violations: MW>480, MR>130

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.  $< 5$

No; 1 violation: XLOGP3>5

Bioavailability Score ?

**Abbott Bioavailability**

**Score:** Probability of F  
 $\geq 10\%$  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; 3 violations: MW>350, Rotors>7,  
XLOGP3>3.5

**Leadlikeness:**

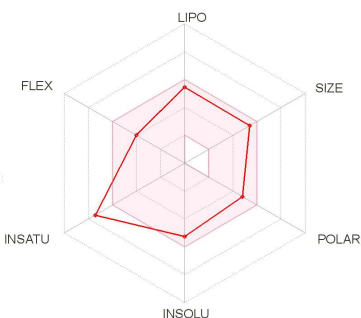
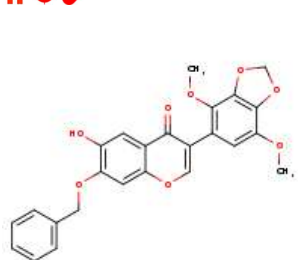
implemented from

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 5.05  
(FP2) modulated by size  
and complexity penalties,  
trained on 12'782'590  
molecules and tested on  
40 external molecules  
( $r^2 = 0.94$ ).

S7



SMILE COc1c2OCOc2c(cc1c1coc2c(c1=O)cc(c(c2)OCc1ccccc1)O)OC

#### Physicochemical Properties

Formula	C25H20O8
Molecular weight	448.42 g/mol
Num. heavy atoms	33
Num. arom. heavy atoms	22
Fraction Csp3	0.16
Num. rotatable bonds	6
Num. H-bond acceptors	8
Num. H-bond donors	1
Molar Refractivity	119.97
TPSA	

**Topological Polar Surface Area:** 96.59 Å<sup>2</sup>  
Calculated from  
Ertl P. et al. 2000 J.  
Med. Chem.

#### Lipophilicity

Log $P_{o/w}$ (iLOGP)	
<b>iLOGP:</b> in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.	4.08
Log $P_{o/w}$ (XLOGP3)	4.05

**XLOGP3:** Atomistic  
and knowledge-based

#### Water Solubility

Log  $S$  (ESOL)

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

-5.27

Solubility 2.41e-03 mg/ml ; 5.38e-06 mol/l  
Class

**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.

-5.78

Solubility 7.40e-04 mg/ml ; 1.65e-06 mol/l  
Class

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

-8.10

Solubility 3.55e-06 mg/ml ; 7.93e-09 mol/l  
Class Poorly soluble

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 4.34  
Wildman SA and  
Crippen GM. 1999 J.  
Chem. Inf. Model.

Log  $P_{o/w}$  (MLOGP) ?

**MLOGP:** Topological  
method implemented  
from 1.38  
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.

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

**SILICOS-IT:** Hybrid  
fragmental/topological  
method calculated by  
FILTER-IT program, 4.91  
version 1.0.2, courtesy  
of SILICOS-IT,  
[http://www.silicos-  
it.com](http://www.silicos-it.com)

Consensus Log  $P_{o/w}$  ?

**Consensus Log  $P_{o/w}$ :** 3.75  
Average of all five  
predictions

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

## Pharmacokinetics

GI absorption ?

**Gastrointestinal  
absorption:** according High  
to the white of the  
BOILED-Egg

BBB permeant ?

**BBB permeation:** No  
according to the yolk of  
the BOILED-Egg

P-gp substrate ?

**P-glycoprotein  
substrate:** SVM model  
built on 1033 molecules  
(training set) Yes  
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) No  
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) Yes  
and tested on 3000  
molecules (test set)  
10-fold CV: ACC=0.80 /  
AUC=0.86  
External: ACC=0.80 /  
AUC=0.87


CYP2C9 inhibitor ?

**Cytochrome P450 2C9  
inhibitor:** SVM model  
built on 5940 molecules  
(training set) Yes  
and tested on 2075  
molecules (test set)  
10-fold CV: ACC=0.78 /  
AUC=0.85  
External: ACC=0.71 /  
AUC=0.81

CYP2D6 inhibitor ? Yes


**Cytochrome P450 2D6  
inhibitor:** SVM model

[built on 3664 molecules](#)  
[\(training set\)](#)  
[and tested on 1068](#)  
[molecules \(test set\)](#)  
[10-fold CV: ACC=0.79 /](#)  
[AUC=0.85](#)  
[External: ACC=0.81 /](#)  
[AUC=0.87](#)

CYP3A4 inhibitor 

**Cytochrome P450 3A4**  
**inhibitor:** [SVM model](#)  
[built on 7518 molecules](#)  
[\(training set\)](#)  
[and tested on 2579](#)  
[molecules \(test set\)](#)  
[10-fold CV: ACC=0.77 /](#)  
[AUC=0.85](#)  
[External: ACC=0.78 /](#)  
[AUC=0.86](#)

Yes

Log  $K_p$  (skin  
permeation) 

**Skin permeation:**  
[QSPR model](#)  
[implemented from](#)  
[Potts RO and Guy RH.](#)  
[1992 Pharm. Res.](#)

-6.16 cm/s

#### Druglikeness

Lipinski 

**Lipinski (Pfizer) filter:**  
[implemented from](#)  
[Lipinski CA. et al. 2001](#)  
[Adv. Drug Deliv. Rev.](#)  
[MW < 500](#)  
[MLOGP < 4.15](#)  
[N or O < 10](#)  
[NH or OH < 5](#)

Yes; 0 violation

Ghose 

**Ghose filter:**  
[implemented from](#)  
[Ghose AK. et al. 1999 J.](#)  
[Comb. Chem.](#)  
[160 < MW < 480](#)  
[-0.4 < WLOGP < 5.6](#)  
[40 < MR < 130](#)  
[20 < atoms < 70](#)

Yes

Veber 


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

Yes

Egan 

**Egan (Pharmacia)**  
**filter:** [implemented](#)  
[from](#)  
[Egan WJ. et al. 2000 J.](#)  
[Med. Chem.](#)  
[WLOGP < 5.88](#)  
[TPSA < 131.6](#)


Yes

Muegge 

Yes

**Muegge (Bayer) filter:**  
[implemented from](#)

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

Bioavailability Score 

**Abbott Bioavailability Score:** [Probability of F ≥ 10% in rat implemented from Martin YC. 2005 J. Med. Chem.](#) 0.55

#### Medicinal Chemistry

PAINS 


**Pan Assay Interference Structures:**  
[implemented from Baell JB. & Holloway GA. 2010 J. Med. Chem.](#) 0 alert

Brenk 

**Structural Alert:**  
[implemented from Brenk R. et al. 2008 ChemMedChem](#) 0 alert

Leadlikeness 

**Leadlikeness:**  
[implemented from Teague S.J. 1999 Angew. Chem. Int. Ed.](#) No; 2 violations: MW>350, XLOGP3>3.5  
[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 \(r<sup>2</sup> = 0.94\)](#) 3.99

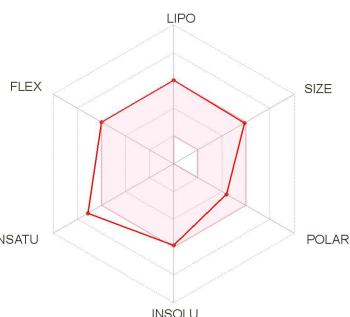
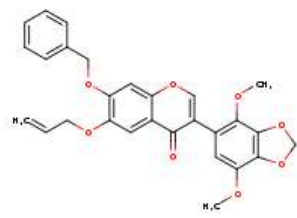
S8



#### Water Solubility

Log S (ESOL)  -5.89

**ESOL:** [Topological method implemented from](#)



SMILE C=CCOc1cc2c(cc1OCc1cccc1)occ(c2=O)c1cc(OC)c2c(c1OC)OCO2

#### Physicochemical Properties

Formula	C28H24O8
Molecular weight	488.49 g/mol
Num. heavy atoms	36
Num. arom. heavy atoms	22
Fraction Csp3	0.18
Num. rotatable bonds	9
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	133.58
TPSA	

**Topological Polar Surface Area:** 85.59 Å<sup>2</sup>  
Calculated from  
Ertl P. et al. 2000 J. Med. Chem.

#### Lipophilicity

Log *P*<sub>o/w</sub> (iLOGP) 4.77  
**iLOGP:** in-house physics-based method implemented from  
Daina A et al. 2014 J. Chem. Inf. Model.

Log *P*<sub>o/w</sub> (XLOGP3) 5.02  
**XLOGP3:** Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry.

Log *P*<sub>o/w</sub> (WLOGP) 5.20  
**WLOGP:** Atomistic method implemented from  
Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.

Log *P*<sub>o/w</sub> (MLOGP) 1.91  
**MLOGP:** Topological method implemented from  
Moriguchi I. et al. 1992 Chem. Pharm. Bull.  
Moriguchi I. et al. 1994 Chem. Pharm. Bull.

Delaney JS. 2004 J. Chem. Inf. Model.

Solubility 6.30e-04 mg/ml ; 1.29e-06 mol/l  
Class

**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.

Solubility 1.35e-04 mg/ml ; 2.77e-07 mol/l  
Class

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

Solubility 2.91e-07 mg/ml ; 5.96e-10 mol/l  
Class

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

#### Pharmacokinetics

GI absorption

**Gastrointestinal absorption:** according to the white of the BOILED-Egg High

BBB permeant

**BBB permeation:** according to the yolk of the BOILED-Egg No

P-gp substrate Yes

**P-glycoprotein substrate:** SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set). 10-fold CV: ACC=0.72 / AUC=0.77

[Lipinski PA. et al. 2001](#)  
[Adv. Drug. Deliv. Rev.](#)

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

?

**SILICOS-IT:** Hybrid  
fragmental/topological  
method calculated by  
FILTER-IT program,  
version 1.0.2, courtesy  
of SILICOS-IT,  
[http://www.silicos-  
it.com](http://www.silicos-it.com) 6.25

Consensus Log  $P_{o/w}$

?

**Consensus Log  $P_{o/w}$ :** 4.63  
[Average of all five  
predictions](#)

[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 No  
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 Yes  
molecules (test set).  
10-fold CV: ACC=0.80 /  
AUC=0.86  
External: ACC=0.80 /  
AUC=0.87

CYP2C9 inhibitor

?

**Cytochrome P450 2C9  
inhibitor:** SVM model  
built on 5940 molecules  
(training set)  
and tested on 2075 Yes  
molecules (test set).  
10-fold CV: ACC=0.78 /  
AUC=0.85  
External: ACC=0.71 /  
AUC=0.81

CYP2D6 inhibitor

?

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

CYP3A4 inhibitor

?

**Cytochrome P450 3A4  
inhibitor:** SVM model  
built on 7518 molecules  
(training set)  
and tested on 2579 Yes  
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 -5.72 cm/s  
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](#)

No; 2 violations: MW>480, MR>130

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](#)

No; 1 violation: XLOGP3>5

Bioavailability Score ?

**Abbott Bioavailability Score:** [Probability of F](#)  
[≥ 10% in rat](#)  
[implemented from](#)  
[Martin YC. 2005 J.](#)  
[Med. Chem.](#)

0.55

## Medicinal Chemistry

PAINS ?

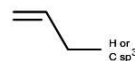
0 alert

**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

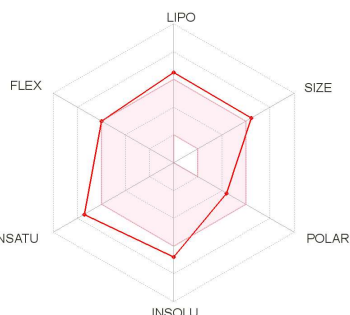
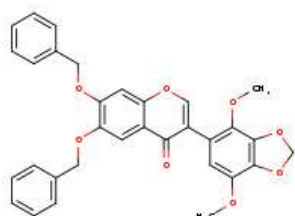
**Leadlikeness:**  
 implemented from  
 Teague SJ. 1999 Angew.  
 Chem. Int. Ed.  
 250 < MW < 350  
 XLOGP < 3.5  
 Num. rotatable bonds <  
 7

No; 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 4.28  
 (FP2) modulated by size  
 and complexity penalties,  
 trained on 12'782'590  
 molecules and tested on  
 40 external molecules  
 ( $r^2 = 0.94$ )

S10



SMILE COc1c2OCOc2c(cc1c1coc2c(c1=O)cc(c(c2)OCc1cccc1)OCc1cccc1)OC

## Physicochemical Properties

Formula	C32H26O8
Molecular weight	538.54 g/mol
Num. heavy atoms	40
Num. arom. heavy atoms	28
Fraction Csp3	0.16
Num. rotatable bonds	9
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	148.92
TPSA	

**Topological Polar Surface Area:**  
 Calculated from  
 Ertl P. et al. 2000 J.  
 Med. Chem.  
 85.59 Å<sup>2</sup>

## Lipophilicity

## Water Solubility

Log S (ESOL)

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

-6.80

Solubility 8.51e-05 mg/ml ; 1.58e-07 mol/l  
 Class

**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.

-7.44

Solubility 1.96e-05 mg/ml ; 3.63e-08 mol/l  
 Class

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

Log S (SILICOS-IT) -11.24

Log $P_{o/w}$ (iLOGP) <sup>?</sup>	4.87		
<b>iLOGP:</b> in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model.			<b>SILICOS-IT:</b> Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <a href="http://www.silicos-it.com">http://www.silicos-it.com</a>
Log $P_{o/w}$ (XLOGP3) <sup>?</sup>		Solubility	3.12e-09 mg/ml ; 5.79e-12 mol/l
<b>XLOGP3:</b> Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry	5.87	Class <sup>?</sup>	
		<b>Solubility class:</b> Log $S$ scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 < Very < 0 < Highly	
Log $P_{o/w}$ (WLOGP) <sup>?</sup>		Pharmacokinetics	
<b>WLOGP:</b> Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.	6.06	GI absorption <sup>?</sup>	
		<b>Gastrointestinal absorption:</b> according to the white of the BOILED-Egg	High
Log $P_{o/w}$ (MLOGP) <sup>?</sup>		BBB permeant <sup>?</sup>	
<b>MLOGP:</b> 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.	2.54	<b>BBB permeation:</b> according to the yolk of the BOILED-Egg	No
Log $P_{o/w}$ (SILICOS-IT) <sup>?</sup>		P-gp substrate <sup>?</sup>	
<b>SILICOS-IT:</b> Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <a href="http://www.silicos-it.com">http://www.silicos-it.com</a>	6.89	<b>P-glycoprotein substrate:</b> 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
Consensus Log $P_{o/w}$ <sup>?</sup>		CYP1A2 inhibitor <sup>?</sup>	
<b>Consensus Log <math>P_{o/w}</math>:</b> Average of all five predictions	5.24	<b>Cytochrome P450 1A2 inhibitor:</b> 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 <sup>?</sup>	
		<b>Cytochrome P450 2C19 inhibitor:</b> 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 <sup>?</sup>	Yes
		<b>Cytochrome P450 2C9 inhibitor:</b> SVM model built on 5940 molecules	

(training set)  
and tested on 2075  
molecules (test set)  
10-fold CV: ACC=0.78 /  
AUC=0.85  
External: ACC=0.71 /  
AUC=0.81

CYP2D6 inhibitor ?

**Cytochrome P450 2D6  
inhibitor:** SVM model  
built on 3664 molecules  
(training set)  
and tested on 1068 molecules (test set)  
10-fold CV: ACC=0.79 /  
AUC=0.85  
External: ACC=0.81 /  
AUC=0.87

No

CYP3A4 inhibitor ?

**Cytochrome P450 3A4  
inhibitor:** SVM model  
built on 7518 molecules  
(training set)  
and tested on 2579 molecules (test set)  
10-fold CV: ACC=0.77 /  
AUC=0.85  
External: ACC=0.78 /  
AUC=0.86

Yes

Log  $K_p$  (skin  
permeation) ?

**Skin permeation:**  
QSPR model  
implemented from  
Potts RO and Guy RH.  
1992 Pharm. Res.

-5.42 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; 1 violation: MW>500

Ghose ?

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

No; 3 violations: MW>480,  
WLOGP>5.6, MR>130


Veber ?

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


Yes

Egan ?

No; 1 violation: WLOGP>5.88

**Egan (Pharmacia)****filter:** [implemented](#)[from](#)[Egan WJ. et al. 2000 J.](#)[Med. Chem.](#)[WLOGP < 5.88](#)[TPSA < 131.6](#)Muegge **Muegge (Bayer) filter:**[implemented from](#)[Muegge I. et al. 2001 J.](#)[Med. Chem.](#)[200 < MW < 600](#)[-2 < XLOGP < 5](#)[TPSA < 150](#)

No; 1 violation: XLOGP3&gt;5

[Num. rings < 7](#)[Num. carbon > 4](#)[Num. heteroatoms > 1](#)[Num. rotatable bonds <](#)[15](#)[H-bond acc. < 10](#)[H-bond don. < 5](#)Bioavailability Score **Abbott Bioavailability****Score:** [Probability of F](#)[≥ 10% in rat](#)

0.55

[implemented from](#)[Martin YC. 2005 J.](#)[Med. Chem.](#)


## Medicinal Chemistry

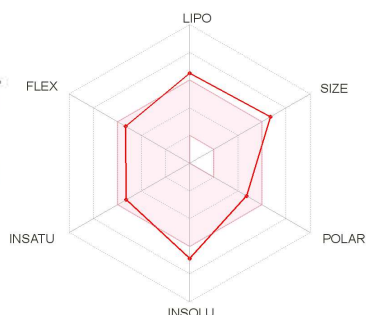
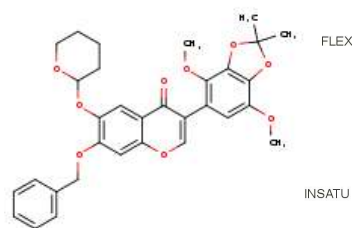
PAINS **Pan Assay Interference****Structures:**[implemented from](#)

0 alert

[Baell JB. & Holloway](#)[GA. 2010 J. Med.](#)[Chem.](#)Brenk **Structural Alert:**[implemented from](#)

0 alert

[Brenk R. et al. 2008](#)[ChemMedChem](#)Leadlikeness **Leadlikeness:**[implemented from](#)[Teague SJ. 1999 Angew.](#)[Chem. Int. Ed.](#)[250 < MW < 350](#)[XLOGP < 3.5](#)[Num. rotatable bonds <](#)[7](#)No; 3 violations: MW>350, Rotors>7,  
XLOGP3>3.5Synthetic accessibility **Synthetic accessibility****score:** [from 1 \(very](#)[easy\) to 10 \(very](#)[difficult\)](#)[based on 1024](#)[fragmental contributions](#) 4.52[\(FP2\) modulated by size](#)[and complexity penalties,](#)[trained on 12'782'590](#)[molecules and tested on](#)[40 external molecules](#)[\( \$r^2 = 0.94\$ \).](#)



SMILE COc1c2OC(Oc2c(cc1c1coc2c(c1=O)cc(c2)OCc1cccc1)OC1CCCCO1)OC)(C)C

#### Physicochemical Properties

Formula	C32H32O9
Molecular weight	560.59 g/mol
Num. heavy atoms	41
Num. arom. heavy atoms	22
Fraction Csp3	0.34
Num. rotatable bonds	8
Num. H-bond acceptors	9
Num. H-bond donors	0
Molar Refractivity	152.29
TPSA	

#### Topological Polar Surface Area:

Calculated from 94.82 Å<sup>2</sup>  
 Ertl P. et al. 2000 J. Med. Chem.

#### Lipophilicity

Log *P*<sub>o/w</sub> (iLOGP)

**iLOGP:** in-house physics-based method implemented from 5.44  
 Daina A et al. 2014 J. Chem. Inf. Model.

Log *P*<sub>o/w</sub> (XLOGP3)

**XLOGP3:** Atomistic and knowledge-based method calculated by XLOGP program, 5.85  
 version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry.

Log *P*<sub>o/w</sub> (WLOGP)

**WLOGP:** Atomistic method implemented from 6.32  
 Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model.

Log *P*<sub>o/w</sub> (MLOGP) 2.38

**MLOGP:** Topological method implemented from   
 Moriguchi I. et al. 1992

#### Water Solubility

Log *S* (ESOL)

**ESOL:** Topological method implemented from -6.87  
 Delaney JS. 2004 J. Chem. Inf. Model.

Solubility 7.56e-05 mg/ml ; 1.35e-07 mol/l  
 Class

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

Log *S* (Ali)

**Ali:** Topological method implemented from -7.61  
 Ali J. et al. 2012 J. Chem. Inf. Model.

Solubility 1.37e-05 mg/ml ; 2.44e-08 mol/l  
 Class

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

Log *S* (SILICOS-IT)

**SILICOS-IT:** Fragmental method calculated by FILTER-IT program, -9.95  
 version 1.0.2, courtesy of SILICOS-IT,  
<http://www.silicos-it.com>

Solubility 6.30e-08 mg/ml ; 1.12e-10 mol/l  
 Class

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

#### Pharmacokinetics

GI absorption

**Gastrointestinal absorption:** according to the white of the BOILED-Egg Low

BBB permeant

**BBB permeation:** according to the yolk of the BOILED-Egg No

[Chem. Pharm. Bull.](#)  
[Moriguchi I. et al. 1994](#)  
[Chem. Pharm. Bull.](#)  
[Lipinski PA. et al. 2001](#)  
[Adv. Drug. Deliv. Rev.](#)

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

6.57  
**SILICOS-IT:** Hybrid  
fragmental/topological  
method calculated by  
FILTER-IT program,  
version 1.0.2, courtesy  
of SILICOS-IT,  
[http://www.silicos-  
it.com](http://www.silicos-it.com)

Consensus Log  $P_{o/w}$

5.31  
**Consensus Log  $P_{o/w}$ :**  
Average of all five  
predictions

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  
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 No

**Cytochrome P450 3A4  
inhibitor:** SVM model  
built on 7518 molecules  
(training set)  
and tested on 2579  
molecules (test set).  
10-fold CV: ACC=0.77 /  
AUC=0.85  
External: ACC=0.78 /  
AUC=0.86

Log  $K_p$  (skin permeation) <sup>?</sup>

**Skin permeation:**

QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res. -5.57 cm/s

Druglikeness

Lipinski <sup>?</sup>

**Lipinski (Pfizer) filter:**

implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev. Yes; 1 violation: MW>500  
MW < 500  
MLOGP < 4.15  
N or O < 10  
NH or OH < 5

Ghose <sup>?</sup>

**Ghose filter:**

implemented from Ghose AK. et al. 1999 J. Comb. Chem. No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70  
160 < MW < 480  
-0.4 < WLOGP < 5.6  
40 < MR < 130  
20 < atoms < 70

Veber <sup>?</sup>

**Veber (GSK) filter:**

implemented from Veber DF. et al. 2002 J. Med. Chem. Yes  
Rotatable bonds < 10  
TPSA < 140

Egan <sup>?</sup>

**Egan (Pharmacia) filter:**

implemented from Egan WJ. et al. 2000 J. Med. Chem. No; 1 violation: WLOGP>5.88  
WLOGP < 5.88  
TPSA < 131.6

Muegge <sup>?</sup>

**Muegge (Bayer) filter:**

implemented from Muegge I. et al. 2001 J. Med. Chem. No; 1 violation: XLOGP3>5  
200 < MW < 600  
-2 < XLOGP < 5  
TPSA < 150  
Num. rings < 7  
Num. carbon > 4  
Num. heteroatoms > 1  
Num. rotatable bonds < 15  
H-bond acc. < 10  
H-bond don. < 5

Bioavailability Score <sup>?</sup>

**Abbott Bioavailability Score:**

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

## PAINS ?

**Pan Assay Interference****Structures:**

implemented from 0 alert  
[Baell JB. & Holloway GA. 2010 J. Med. Chem.](#)

## Brenk ?

**Structural Alert:**

implemented from 0 alert  
[Brenk R. et al. 2008 ChemMedChem](#)

## Leadlikeness ?

**Leadlikeness:**

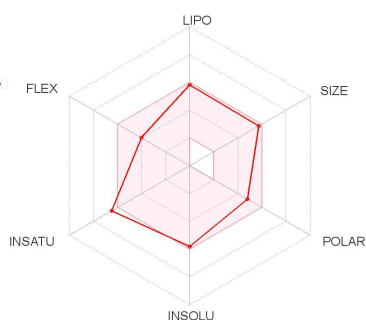
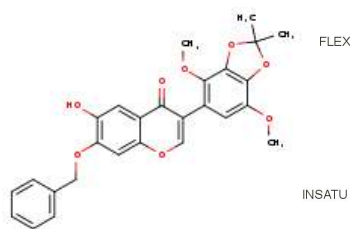
implemented from  
[Teague SJ. 1999 Angew. Chem. Int. Ed.](#) No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5  
 $250 < MW < 350$   
 $XLOGP < 3.5$   
 Num. rotatable bonds < 7

## Synthetic accessibility ?

**Synthetic accessibility**

**score:** from 1 (very easy) to 10 (very difficult)  
 based on 1024 fragmental contributions 5.31  
 (FP2) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules  
 ( $r^2 = 0.94$ )

S12



SMILE COc1c2OC(Oc2c(cc1c1coc2c(c1=O)cc(c(c2)OCc1ccccc1)O)OC)(C)C

**Physicochemical Properties**

Formula	C27H24O8
Molecular weight	476.47 g/mol
Num. heavy atoms	35
Num. arom. heavy atoms	22
Fraction Csp3	0.22
Num. rotatable bonds	6
Num. H-bond acceptors	8
Num. H-bond donors	1
Molar Refractivity	129.62

**Water Solubility**

## Log S (ESOL) ?

**ESOL:** Topological method implemented from  
[Delaney JS. 2004 J. Chem. Inf. Model.](#)

-5.80

Solubility 7.57e-04 mg/ml ; 1.59e-06 mol/l  
 Class ?

**Solubility class: Log S scale**

[Insoluble < -10 < Poorly](#) Moderately soluble  
 $< -6 < \text{Moderately} < -4$   
 $< \text{Soluble} < -2 \text{ Very} < 0$   
 $< \text{Highly}$

## Log S (Ali) ?

**Ali:** Topological method implemented from  
[Ali J. et al. 2012 J. Chem. Inf. Model.](#)

-6.42

Solubility 1.83e-04 mg/ml ; 3.84e-07 mol/l  
 Class ? Poorly soluble

TPSA <sup>?</sup> 96.59 Å<sup>2</sup>

### Topological Polar Surface Area:

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

### Lipophilicity

Log  $P_{o/w}$  (iLOGP) <sup>?</sup>

**iLOGP:** in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model. 4.52

Log  $P_{o/w}$  (XLOGP3) <sup>?</sup>

**XLOGP3:** Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry. 4.66

Log  $P_{o/w}$  (WLOGP) <sup>?</sup>

**WLOGP:** Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model. 5.12

Log  $P_{o/w}$  (MLOGP) <sup>?</sup>

**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. 1.78

Log  $P_{o/w}$  (SILICOS-IT) <sup>?</sup>

**SILICOS-IT:** Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com 5.54

Consensus Log  $P_{o/w}$  <sup>?</sup>

**Consensus Log  $P_{o/w}$ :** Average of all five predictions 4.32

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

Log  $S$  (SILICOS-IT) <sup>?</sup>

**SILICOS-IT:** Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, http://www.silicos-it.com -8.84

Solubility 6.97e-07 mg/ml ; 1.46e-09 mol/l  
Class <sup>?</sup>

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

### Pharmacokinetics

GI absorption <sup>?</sup>

**Gastrointestinal absorption:** according to the white of the BOILED-Egg High

BBB permeant <sup>?</sup>

**BBB permeation:** according to the yolk of the BOILED-Egg No

P-gp substrate <sup>?</sup>

**P-glycoprotein substrate:** SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set). Yes  
10-fold CV: ACC=0.72 / AUC=0.77  
External: ACC=0.88 / AUC=0.94

CYP1A2 inhibitor <sup>?</sup>

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

CYP2C19 inhibitor <sup>?</sup> Yes

**Cytochrome P450 2C19 inhibitor:** SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set).

[10-fold CV: ACC=0.80 /](#)  
[AUC=0.86](#)  
[External: ACC=0.80 /](#)  
[AUC=0.87](#)

CYP2C9 inhibitor ⓘ

**Cytochrome P450 2C9 inhibitor:** [SVM model built on 5940 molecules \(training set\)](#)

[and tested on 2075 molecules \(test set\).](#) Yes  
[10-fold CV: ACC=0.78 /](#)  
[AUC=0.85](#)  
[External: ACC=0.71 /](#)  
[AUC=0.81](#)

CYP2D6 inhibitor ⓘ

**Cytochrome P450 2D6 inhibitor:** [SVM model built on 3664 molecules \(training set\)](#)

[and tested on 1068 molecules \(test set\).](#) No  
[10-fold CV: ACC=0.79 /](#)  
[AUC=0.85](#)  
[External: ACC=0.81 /](#)  
[AUC=0.87](#)

CYP3A4 inhibitor ⓘ

**Cytochrome P450 3A4 inhibitor:** [SVM model built on 7518 molecules \(training set\)](#)

[and tested on 2579 molecules \(test set\).](#) No  
[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.](#) -5.90 cm/s

Druglikeness

Lipinski ⓘ

**Lipinski (Pfizer) filter:** [implemented from Lipinski CA, et al. 2001](#)

[Adv. Drug Deliv. Rev.](#) Yes; 0 violation  
[MW < 500](#)  
[MLOGP < 4.15](#)  
[N or O < 10](#)  
[NH or OH < 5](#)

Ghose ⓘ

**Ghose filter:** [implemented from Ghose AK, et al. 1999 J. Comb. Chem.](#)

Yes  
[160 < MW < 480](#)  
[-0.4 < WLOGP < 5.6](#)  
[40 < MR < 130](#)  
[20 < atoms < 70](#)

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.](#) Yes  
[WLOGP < 5.88](#)  
[TPSA < 131.6](#)

Muegge ?

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

Bioavailability Score ?

**Abbott Bioavailability Score:** [Probability of F > 10% in rat](#) 0.55  
[implemented from](#)  
[Martin YC. 2005 J. Med. Chem.](#)

## Medicinal Chemistry

PAINS ?

**Pan Assay Interference Structures:**  
[implemented from](#) 0 alert  
[Baell JB. & Holloway GA. 2010 J. Med. Chem.](#)

Brenk ?

**Structural Alert:**  
[implemented from](#) 0 alert  
[Brenk R. et al. 2008 ChemMedChem](#)

Leadlikeness ?

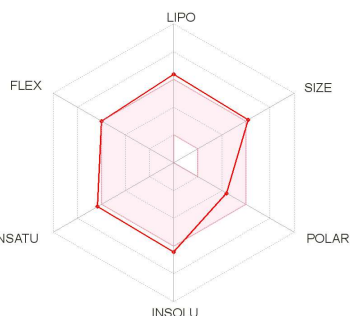
**Leadlikeness:**  
[implemented from](#)  
[Teague SJ. 1999 Angew. Chem. Int. Ed.](#) No; 2 violations: MW>350, XLOGP3>3.5  
[250 < MW < 350](#)  
[XLOGP < 3.5](#)  
[Num. rotatable bonds < 7](#)

Synthetic accessibility ? 4.21

**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  
 ( $r^2 = 0.94$ )

S13



SMILE C=CCOc1cc2c(cc1OCc1ccccc1)occ(c2=O)c1cc(OC)c2c(c1OC)OC(O2)(C)C

#### Physicochemical Properties

Formula	C30H28O8
Molecular weight	516.54 g/mol
Num. heavy atoms	38
Num. arom. heavy atoms	22
Fraction Csp3	0.23
Num. rotatable bonds	9
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	143.23
TPSA	

#### Topological Polar Surface Area:

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

85.59 Å<sup>2</sup>

#### Lipophilicity

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

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

5.34

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.

5.63

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

5.98

**WLOGP:** Atomistic  
 method implemented  
 from  
 Wildman SA and

#### Water Solubility

Log  $S$  (ESOL)

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

-6.42

Solubility  
 Class

1.95e-04 mg/ml ; 3.77e-07 mol/l

**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.

-7.19

Solubility  
 Class

3.33e-05 mg/ml ; 6.44e-08 mol/l

**Solubility class:** Log  $S$   
 scale

Insoluble < -10 < Poorly  
 < -6 < Moderately < -4  
 < 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>

-9.96

Solubility  
 Class

5.72e-08 mg/ml ; 1.11e-10 mol/l

**Solubility class:** Log  $S$   
 scale


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

#### Pharmacokinetics

GI absorption


High

[Crippen GM. 1999 J. Chem. Inf. Model.](#)


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

**MLOGP:** Topological method implemented from

[Moriguchi I. et al. 1992 Chem. Pharm. Bull.](#) 2.30  
[Moriguchi I. et al. 1994 Chem. Pharm. Bull.](#)  
[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> 6.89


Consensus Log  $P_{o/w}$  

**Consensus Log  $P_{o/w}$ :** 5.23  
[Average of all five predictions](#)


**Gastrointestinal absorption:** according to the white of the BOILED-Egg

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) Yes  
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) No  
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) Yes  
10-fold CV: ACC=0.80 / AUC=0.86  
External: ACC=0.80 / AUC=0.87

CYP2C9 inhibitor 

**Cytochrome P450 2C9 inhibitor:** SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) Yes  
10-fold CV: ACC=0.78 / AUC=0.85  
External: ACC=0.71 / AUC=0.81

CYP2D6 inhibitor 

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

CYP3A4 inhibitor  No

**Cytochrome P450 3A4 inhibitor:** [SVM model built on 7518 molecules \(training set\) and tested on 2579 molecules \(test set\)](#)  
10-fold CV: ACC=0.77 / AUC=0.85  
External: ACC=0.78 / AUC=0.86

Log  $K_p$  (skin permeation) ?

**Skin permeation:** [QSPR model implemented from Potts RO and Guy RH. 1992 Pharm. Res.](#) -5.45 cm/s

#### Druglikeness

Lipinski ?

**Lipinski (Pfizer) filter:** [implemented from Lipinski CA. et al. 2001 Adv. Drug Deliv. Rev.](#) Yes; 1 violation: MW>500  
[MW < 500](#)  
[MLOGP < 4.15](#)  
[N or O < 10](#)  
[NH or OH < 5](#)

Ghose ?

**Ghose filter:** [implemented from Ghose AK. et al. 1999 J. Comb. Chem.](#) No; 3 violations: MW>480, WLOGP>5.6, MR>130  
[160 < MW < 480](#)  
[-0.4 < WLOGP < 5.6](#)  
[40 < MR < 130](#)  
[20 < atoms < 70](#)

Veber ?

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

Egan ?

**Egan (Pharmacia) filter:** [implemented from Egan WJ. et al. 2000 J. Med. Chem.](#) No; 1 violation: WLOGP>5.88  
[WLOGP < 5.88](#)  
[TPSA < 131.6](#)

Muegge ? No; 1 violation: XLOGP3>5

**Muegge (Bayer) filter:** [implemented from Muegge I. et al. 2001 J. Med. Chem.](#)  
[200 < MW < 600](#)  
[-2 < XLOGP < 5](#)  
[TPSA < 150](#)  
[Num. rings < 7](#)  
[Num. carbon > 4](#)  
[Num. heteroatoms > 1](#)  
[Num. rotatable bonds < 15](#)

H-bond acc. < 10

H-bond don. < 5

Bioavailability Score

**Abbott Bioavailability**

**Score:** Probability of F  
≥ 10% in rat 0.55  
implemented from  
Martin YC. 2005 J.  
Med. Chem.

Medicinal Chemistry

PAINS

**Pan Assay Interference**

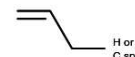
**Structures:**  
implemented from 0 alert  
Baell JB. & Holloway  
GA. 2010 J. Med.  
Chem.

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

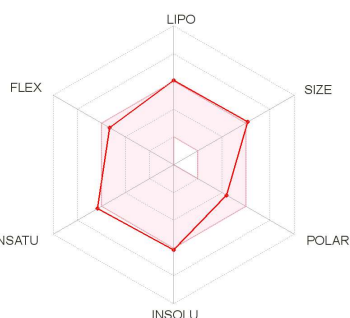
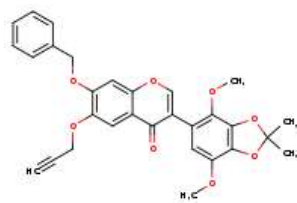
No; 3 violations: MW>350, Rotors>7,  
XLOGP3>3.5

Synthetic accessibility

**Synthetic accessibility**

**score:** from 1 (very  
easy) to 10 (very  
difficult)  
based on 1024  
fragmental contributions 4.51  
(FP2) modulated by size  
and complexity penalties,  
trained on 12'782'590  
molecules and tested on  
40 external molecules  
( $r^2 = 0.94$ )

S14



SMILE C#CCOc1cc2c(cc1OCc1cccc1)oc(c2=O)c1cc(OC)c2c  
S (c1OC)OC(O2)(C)C

Physicochemical Properties

Water Solubility

Log S (ESOL)

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

-6.14

Solubility

3.70e-04 mg/ml ; 7.19e-07 mol/l

Class

Poorly soluble

**Solubility class:** Log S

scale  
Insoluble < -10 < Poorly  
< -6 < Moderately < -4

Formula	C30H26O8	< Soluble < -2 Very < 0
Molecular weight	514.52 g/mol	< Highly
Num. heavy atoms	38	
Num. arom. heavy atoms	22	Log <i>S</i> (Ali) ?
Fraction Csp3	0.23	<b>Ali:</b> Topological method implemented from Ali J. et al. 2012 J. Chem. Inf. Model. -6.64
Num. rotatable bonds	8	
Num. H-bond acceptors	8	
Num. H-bond donors	0	
Molar Refractivity	141.87	Solubility 1.18e-04 mg/ml ; 2.29e-07 mol/l
TPSA ?		Class ?

**Topological Polar Surface Area:** 85.59 Å<sup>2</sup>  
 Calculated from Ertl P. et al. 2000 J. Med. Chem.

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

#### Lipophilicity


Log <i>P</i> <sub>o/w</sub> (iLOGP) ?		Log <i>S</i> (SILICOS-IT) ?	
<b>iLOGP:</b> in-house physics-based method implemented from Daina A et al. 2014 J. Chem. Inf. Model. 5.23		<b>SILICOS-IT:</b> Fragmental method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <a href="http://www.silicos-it.com">http://www.silicos-it.com</a> -9.60	
Log <i>P</i> <sub>o/w</sub> (XLOGP3) ?			
<b>XLOGP3:</b> Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry. 5.10		Solubility 1.31e-07 mg/ml ; 2.54e-10 mol/l	
Log <i>P</i> <sub>o/w</sub> (WLOGP) ?		Class ?	
<b>WLOGP:</b> Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model. 5.50		<b>Solubility class:</b> Log <i>S</i> scale Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 Very < 0 < Highly	
Log <i>P</i> <sub>o/w</sub> (MLOGP) ?			
<b>MLOGP:</b> 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. 2.30			
Log <i>P</i> <sub>o/w</sub> (SILICOS-IT) ?			
<b>SILICOS-IT:</b> Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <a href="http://www.silicos-it.com">http://www.silicos-it.com</a> 6.73			
Consensus Log <i>P</i> <sub>o/w</sub> ?	4.97		

#### Pharmacokinetics


GI absorption ?	
<b>Gastrointestinal absorption:</b> according to the white of the BOILED-Egg High	
BBB permeant ?	
<b>BBB permeation:</b> according to the yolk of the BOILED-Egg No	
P-gp substrate ?	
<b>P-glycoprotein substrate:</b> 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
<b>Cytochrome P450 1A2 inhibitor:</b> SVM model built on 9145 molecules (training set) and tested on 3000 molecules (test set)	

Consensus Log  $P_{0/w}$ :  
Average of all five  
predictions


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 Yes  
molecules (test set).  
10-fold CV: ACC=0.80 /  
AUC=0.86  
External: ACC=0.80 /  
AUC=0.87

CYP2C9 inhibitor 


**Cytochrome P450 2C9**  
**inhibitor:** SVM model  
built on 5940 molecules  
(training set)  
and tested on 2075 Yes  
molecules (test set).  
10-fold CV: ACC=0.78 /  
AUC=0.85  
External: ACC=0.71 /  
AUC=0.81

CYP2D6 inhibitor 

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

CYP3A4 inhibitor 

**Cytochrome P450 3A4**  
**inhibitor:** SVM model  
built on 7518 molecules  
(training set)  
and tested on 2579 No  
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 -5.82 cm/s  
implemented from  
Potts RO and Guy RH.  
1992 Pharm. Res.

Druglikeness

Lipinski  Yes; 1 violation: MW>500

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

Ghose ?

**Ghose filter:**

implemented from  
Ghose AK. et al. 1999 J.  
Comb. Chem.  
 $160 < MW < 480$   
 $-0.4 < WLOGP < 5.6$   
 $40 < MR < 130$   
 $20 < \text{atoms} < 70$

No; 2 violations: MW>480, MR>130

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.  $< 5$

No; 1 violation: XLOGP3>5

Bioavailability Score ?

**Abbott Bioavailability**

**Score:** Probability of F  
 $\geq 10\%$  in rat  
implemented from  
Martin YC. 2005 J.  
Med. Chem.

0.55

Medicinal Chemistry

PAINS ?

**Pan Assay Interference**

**Structures:**

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

0 alert

Brenk ?

1 alert: triple\_bond ?

**Structural Alert:**

implemented from  
Brenk R. et al. 2008  
ChemMedChem



triple\_bond

Leadlikeness ?

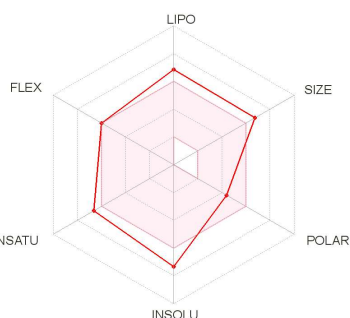
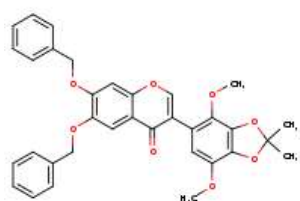
No; 3 violations: MW>350, Rotors>7,  
XLOGP3>3.5

**Leadlikeness:**  
 implemented from  
[Teague S.J. 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 4.51  
 (FP2) modulated by size  
 and complexity penalties,  
 trained on 12'782'590  
 molecules and tested on  
 40 external molecules  
 ( $r^2 = 0.94$ )

S15



SMILE COc1c2OC(Oc2c(cc1c1coc2c(c1=O)cc(c(c2)OCc1ccccc1)OCc1ccccc1)OC(C)C

#### Physicochemical Properties

Formula	C34H30O8
Molecular weight	566.60 g/mol
Num. heavy atoms	42
Num. arom. heavy atoms	28
Fraction Csp3	0.21
Num. rotatable bonds	9
Num. H-bond acceptors	8
Num. H-bond donors	0
Molar Refractivity	158.58
TPSA	

**Topological Polar Surface Area:**  
 Calculated from 85.59 Å<sup>2</sup>  
[Ertl P. et al. 2000 J. Med. Chem.](#)

#### Lipophilicity

Log $P_{o/w}$ (iLOGP)	
<b>iLOGP:</b> in-house physics-based method implemented from <a href="#">Daina A et al. 2014 J. Chem. Inf. Model.</a>	5.35
Log $P_{o/w}$ (XLOGP3)	6.48

#### Water Solubility

Log  $S$  (ESOL)

**ESOL:** Topological  
method implemented  
from  
[Delaney J.S. 2004 J. Chem. Inf. Model.](#)

-7.33

Solubility 2.62e-05 mg/ml ; 4.63e-08 mol/l  
 Class

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

Log  $S$  (Ali)

**Ali:** Topological method  
implemented from  
[Ali J. et al. 2012 J. Chem. Inf. Model.](#)

-8.07

Solubility 4.79e-06 mg/ml ; 8.46e-09 mol/l  
 Class

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

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>

-11.96

**XLOGP3:** Atomistic and knowledge-based method calculated by XLOGP program, version 3.2.2, courtesy of CCBG, Shanghai Institute of Organic Chemistry.

Log  $P_{o/w}$  (WLOGP) <sup>?</sup>

**WLOGP:** Atomistic method implemented from Wildman SA and Crippen GM. 1999 J. Chem. Inf. Model. 6.84

Log  $P_{o/w}$  (MLOGP) <sup>?</sup>

**MLOGP:** Topological method implemented from Moriguchi I. et al. 1992 Chem. Pharm. Bull. 2.91  
Moriguchi I. et al. 1994 Chem. Pharm. Bull.  
Lipinski PA. et al. 2001 Adv. Drug. Deliv. Rev.

Log  $P_{o/w}$  (SILICOS-IT) <sup>?</sup>

**SILICOS-IT:** Hybrid fragmental/topological method calculated by FILTER-IT program, version 1.0.2, courtesy of SILICOS-IT, <http://www.silicos-it.com> 7.53

Consensus Log  $P_{o/w}$  <sup>?</sup>

**Consensus Log  $P_{o/w}$ :** Average of all five predictions 5.82

Solubility 6.14e-10 mg/ml ; 1.08e-12 mol/l

Class <sup>?</sup>

**Solubility class:** Log  $S$  scale

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

#### Pharmacokinetics

GI absorption <sup>?</sup>

**Gastrointestinal absorption:** according to the white of the BOILED-Egg Low

BBB permeant <sup>?</sup>

**BBB permeation:** according to the yolk of the BOILED-Egg No

P-gp substrate <sup>?</sup>

**P-glycoprotein substrate:** SVM model built on 1033 molecules (training set) and tested on 415 molecules (test set) No  
10-fold CV: ACC=0.72 / AUC=0.77  
External: ACC=0.88 / AUC=0.94

CYP1A2 inhibitor <sup>?</sup>

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

CYP2C19 inhibitor <sup>?</sup>

**Cytochrome P450 2C19 inhibitor:** SVM model built on 9272 molecules (training set) and tested on 3000 molecules (test set) Yes  
10-fold CV: ACC=0.80 / AUC=0.86  
External: ACC=0.80 / AUC=0.87

CYP2C9 inhibitor <sup>?</sup>

**Cytochrome P450 2C9 inhibitor:** SVM model built on 5940 molecules (training set) and tested on 2075 molecules (test set) Yes  
10-fold CV: ACC=0.78 / AUC=0.85  
External: ACC=0.71 / AUC=0.81

CYP2D6 inhibitor <sup>?</sup> No

**Cytochrome P450 2D6**  
**inhibitor:** [SVM model](#)  
[built on 3664 molecules](#)  
[\(training set\)](#)  
[and tested on 1068](#)  
[molecules \(test set\)](#)  
[10-fold CV: ACC=0.79 /](#)  
[AUC=0.85](#)  
[External: ACC=0.81 /](#)  
[AUC=0.87](#)

CYP3A4 inhibitor ?

**Cytochrome P450 3A4**  
**inhibitor:** [SVM model](#)  
[built on 7518 molecules](#)  
[\(training set\)](#)  
[and tested on 2579](#) No  
[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](#) -5.16 cm/s  
[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.](#) Yes; 1 violation: MW>500  
[MW < 500](#)  
[MLOGP < 4.15](#)  
[N or O < 10](#)  
[NH or OH < 5](#)

Ghose ?

**Ghose filter:**  
[implemented from](#)  
[Ghose AK. et al. 1999 J.](#) No; 4 violations: MW>480,  
[Comb. Chem.](#) WLOGP>5.6, MR>130, #atoms>70  
[160 < MW < 480](#)  
[-0.4 < WLOGP < 5.6](#)  
[40 < MR < 130](#)  
[20 < atoms < 70](#)

Veber ?

**Veber (GSK) filter:**  
[implemented from](#)  
[Veber DE. et al. 2002 J.](#) Yes  
[Med. Chem.](#)  
[Rotatable bonds < 10](#)  
[TPSA < 140](#)


Egan ?

**Egan (Pharmacia)**  
**filter:** [implemented](#)  
[from](#)  
[Egan WJ. et al. 2000 J.](#) No; 1 violation: WLOGP>5.88  
[Med. Chem.](#)  
[WLOGP < 5.88](#)  
[TPSA < 131.6](#)

Muegge ? No; 1 violation: XLOGP3>5

**Muegge (Bayer) filter:**

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

Bioavailability Score **Abbott Bioavailability**

**Score:** [Probability of F](#) 0.55  
[≥ 10% in rat](#)  
[implemented from](#)  
[Martin YC. 2005 J. Med. Chem.](#)

## Medicinal Chemistry

PAINS **Pan Assay Interference**


**Structures:**  
[implemented from](#) 0 alert  
[Baell JB. & Holloway GA. 2010 J. Med. Chem.](#)

Brenk **Structural Alert:**

[implemented from](#) 0 alert  
[Brenk R. et al. 2008 ChemMedChem](#)

Leadlikeness **Leadlikeness:**

[implemented from](#)  
[Teague SJ. 1999 Angew. Chem. Int. Ed.](#) No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5  
[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](#) 4.75  
[\(FP2\) modulated by size and complexity penalties, trained on 12'782'590 molecules and tested on 40 external molecules](#)  
[\(r<sup>2</sup> = 0.94\)](#)