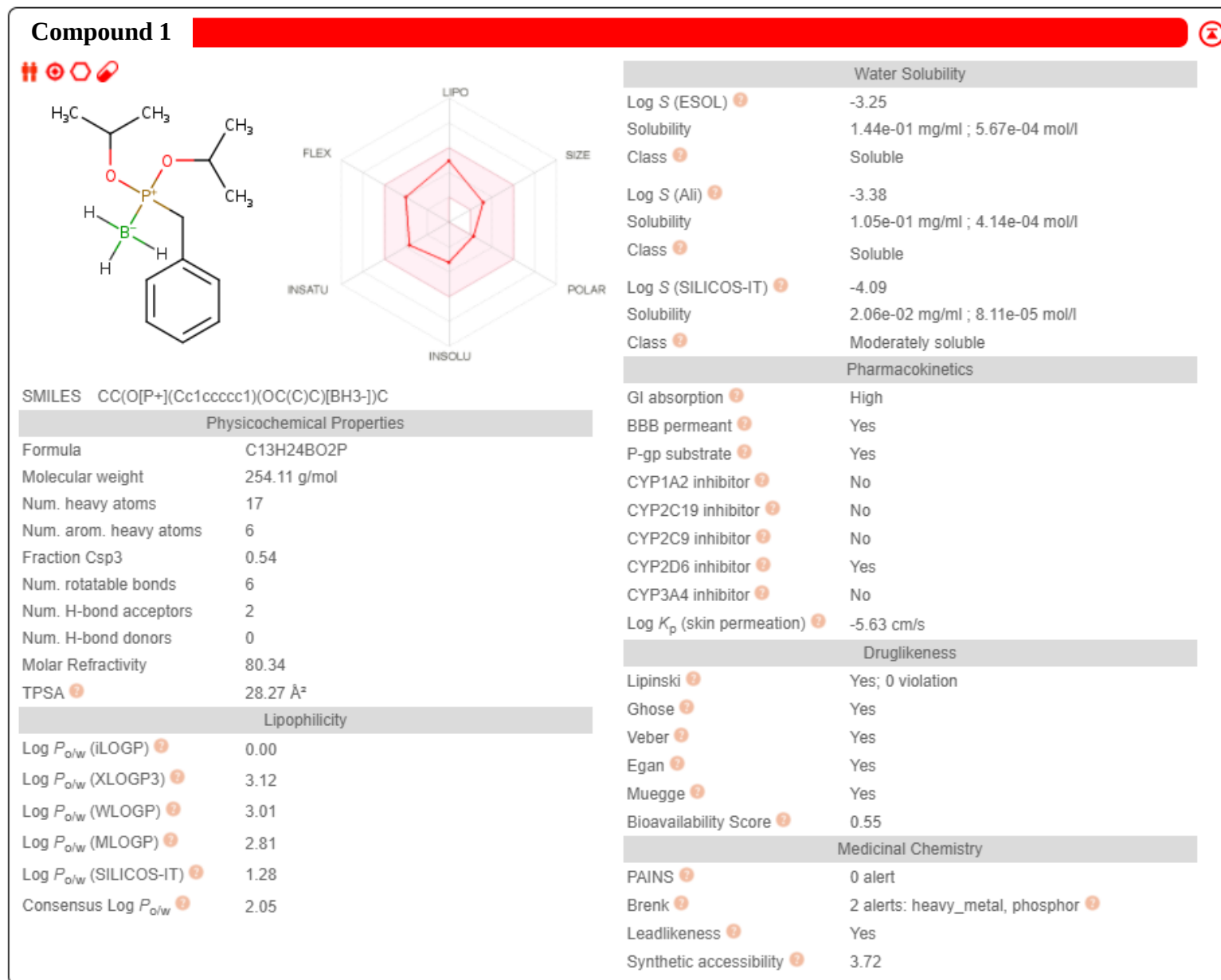
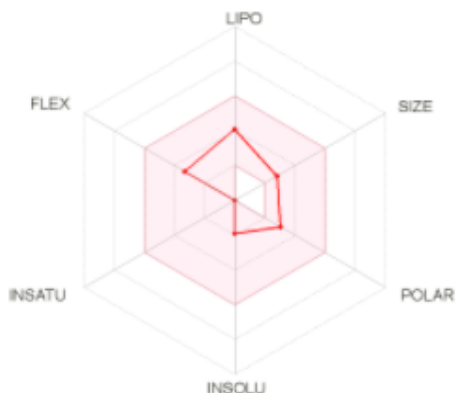
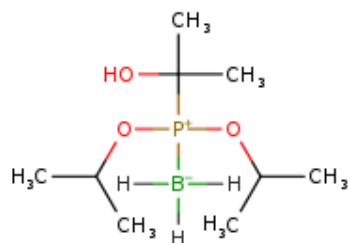


Supplementary Figure S1 The ADME analysis of compounds (1 – 7), esters of phosphonous acid-borane (1), α -hydroxy phosphonite-boranes (2 and 3) and α -amino phosphonite-boranes (4, 5, 6, and 7). [http://www.swissadme.ch/]



Compound 2



SMILES CC(O[P+](C(O)(C)C)(OC(C)C)[BH3-])C

Physicochemical Properties

Formula	C ₉ H ₂₄ BO ₃ P
Molecular weight	222.07 g/mol
Num. heavy atoms	14
Num. arom. heavy atoms	0
Fraction Csp ³	1.00
Num. rotatable bonds	5
Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	66.66
TPSA [?]	48.50 Å ²

Lipophilicity

Log <i>P</i> _{o/w} (iLOGP) [?]	0.00
Log <i>P</i> _{o/w} (XLOGP3) [?]	1.66
Log <i>P</i> _{o/w} (WLOGP) [?]	1.69
Log <i>P</i> _{o/w} (MLOGP) [?]	1.14
Log <i>P</i> _{o/w} (SILICOS-IT) [?]	-0.62
Consensus Log <i>P</i> _{o/w} [?]	0.77

Water Solubility

Log S (ESOL) [?]	-1.93
Solubility	2.59e+00 mg/ml ; 1.17e-02 mol/l
Class [?]	Very soluble
Log S (Ali) [?]	-2.29
Solubility	1.13e+00 mg/ml ; 5.10e-03 mol/l
Class [?]	Soluble
Log S (SILICOS-IT) [?]	-1.42
Solubility	8.42e+00 mg/ml ; 3.79e-02 mol/l
Class [?]	Soluble

Pharmacokinetics

GI absorption [?]	High
BBB permeant [?]	Yes
P-gp substrate [?]	No
CYP1A2 inhibitor [?]	No
CYP2C19 inhibitor [?]	No
CYP2C9 inhibitor [?]	No
CYP2D6 inhibitor [?]	No
CYP3A4 inhibitor [?]	Yes
Log <i>K</i> _p (skin permeation) [?]	-6.48 cm/s

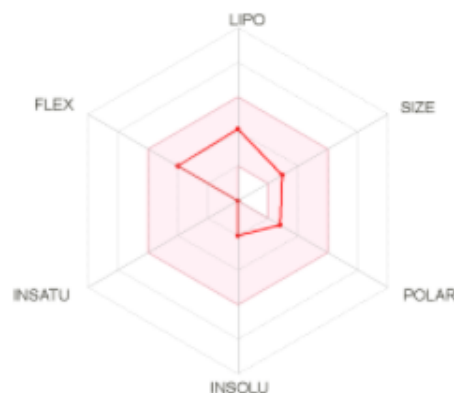
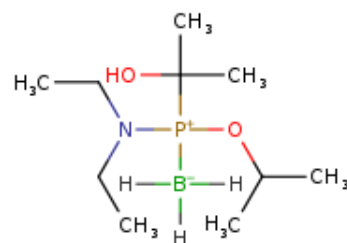
Druglikeness

Lipinski [?]	Yes; 0 violation
Ghose [?]	Yes
Veber [?]	Yes
Egan [?]	Yes
Muegge [?]	Yes
Bioavailability Score [?]	0.55

Medicinal Chemistry

PAINS [?]	0 alert
Brenk [?]	2 alerts: heavy_metal, phosphor [?]
Leadlikeness [?]	No; 1 violation: MW<250
Synthetic accessibility [?]	4.27

Compound 3



SMILES CCN([P+](C(O)(C)C)(OC(C)C)[BH3-])CC

Physicochemical Properties

Formula	C10H27BNO2P
Molecular weight	235.11 g/mol
Num. heavy atoms	15
Num. arom. heavy atoms	0
Fraction Csp3	1.00
Num. rotatable bonds	6
Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	73.28
TPSA ¹	42.51 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP) ²	0.00
Log $P_{o/w}$ (XLOGP3) ²	1.78
Log $P_{o/w}$ (WLOGP) ²	1.61
Log $P_{o/w}$ (MLOGP) ²	1.44
Log $P_{o/w}$ (SILICOS-IT) ²	-0.80
Consensus Log $P_{o/w}$ ³	0.81

Water Solubility

Log S (ESOL) ²	-2.02
Solubility	2.23e+00 mg/ml ; 9.48e-03 mol/l
Class ²	Soluble
Log S (Ali) ²	-2.29
Solubility	1.20e+00 mg/ml ; 5.12e-03 mol/l
Class ²	Soluble
Log S (SILICOS-IT) ²	-1.78
Solubility	3.92e+00 mg/ml ; 1.67e-02 mol/l
Class ²	Soluble

Pharmacokinetics

GI absorption ²	High
BBB permeant ²	Yes
P-gp substrate ²	No
CYP1A2 inhibitor ²	No
CYP2C19 inhibitor ²	No
CYP2C9 inhibitor ²	No
CYP2D6 inhibitor ²	No
CYP3A4 inhibitor ²	No
Log K_p (skin permeation) ²	-6.47 cm/s

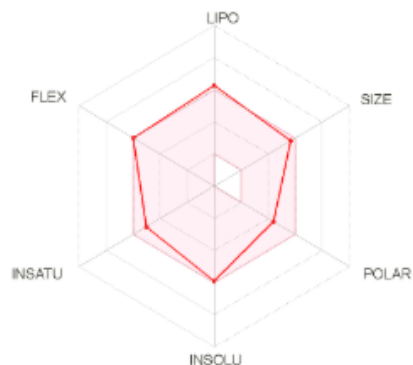
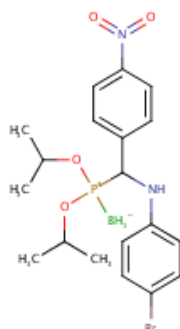
Druglikeness

Lipinski ²	Yes; 0 violation
Ghose ²	Yes
Veber ²	Yes
Egan ²	Yes
Muegge ²	Yes
Bioavailability Score ²	0.55

Medicinal Chemistry

PAINS ²	0 alert
Brenk ²	2 alerts: heavy_metal, phosphor ²
Leadlikeness ²	No; 1 violation: MW<250
Synthetic accessibility ²	4.93

Compound 4



SMILES CC(O[P+](C(c1ccc(cc1)N(=O)=O)Nc1ccc(cc1)Br)(OC(C)C)[BH3-])C

Physicochemical Properties

Formula	C ₁₉ H ₂₇ BrN ₂ O ₄ P
Molecular weight	469.12 g/mol
Num. heavy atoms	28
Num. arom. heavy atoms	12
Fraction Csp ³	0.37
Num. rotatable bonds	9
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	125.68
TPSA [?]	86.12 Å ²

Lipophilicity

Log <i>P</i> _{o/w} (iLOGP) [?]	0.00
Log <i>P</i> _{o/w} (XLOGP3) [?]	5.45
Log <i>P</i> _{o/w} (WLOGP) [?]	5.45
Log <i>P</i> _{o/w} (MLOGP) [?]	2.94
Log <i>P</i> _{o/w} (SILICOS-IT) [?]	0.95
Consensus Log <i>P</i> _{o/w} [?]	2.96

Water Solubility

Log <i>S</i> (ESOL) [?]	-5.91
Solubility	5.84e-04 mg/ml ; 1.24e-06 mol/l
Class [?]	Moderately soluble
Log <i>S</i> (Ali) [?]	-7.02
Solubility	4.53e-05 mg/ml ; 9.66e-08 mol/l
Class [?]	Poorly soluble
Log <i>S</i> (SILICOS-IT) [?]	-6.87
Solubility	6.39e-05 mg/ml ; 1.36e-07 mol/l
Class [?]	Poorly soluble

Pharmacokinetics

GI absorption [?]	High
BBB permeant [?]	No
P-gp substrate [?]	Yes
CYP1A2 inhibitor [?]	No
CYP2C19 inhibitor [?]	Yes
CYP2C9 inhibitor [?]	Yes
CYP2D6 inhibitor [?]	Yes
CYP3A4 inhibitor [?]	Yes
Log <i>K</i> _p (skin permeation) [?]	-5.29 cm/s

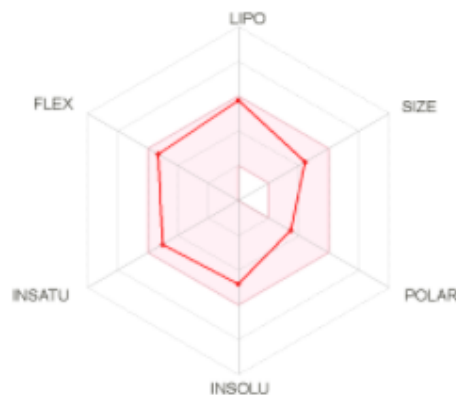
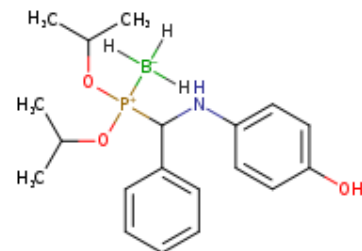
Druglikeness

Lipinski [?]	Yes; 0 violation
Ghose [?]	Yes
Veber [?]	Yes
Egan [?]	Yes
Muegge [?]	No; 1 violation: XLOGP3>5
Bioavailability Score [?]	0.55

Medicinal Chemistry

PAINS [?]	0 alert
Brenk [?]	3 alerts: heavy_metal, nitro_group, phosphor [?]
Leadlikeness [?]	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility [?]	4.43

Compound 5



SMILES CC(O[P+](C(c1ccccc1)Nc1ccc(cc1)O)(OC(C)C)[BH3-])C

Physicochemical Properties

Formula	C ₁₉ H ₂₉ BN ₃ O ₃ P
Molecular weight	361.22 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	12
Fraction Csp ³	0.37
Num. rotatable bonds	8
Num. H-bond acceptors	3
Num. H-bond donors	2
Molar Refractivity	111.19
TPSA ¹	60.53 Å ²

Lipophilicity

Log <i>P</i> _{o/w} (iLOGP) ²	0.00
Log <i>P</i> _{o/w} (XLOGP3) ²	4.58
Log <i>P</i> _{o/w} (WLOGP) ²	3.97
Log <i>P</i> _{o/w} (MLOGP) ²	2.84
Log <i>P</i> _{o/w} (SILICOS-IT) ²	1.51
Consensus Log <i>P</i> _{o/w} ²	2.58

Water Solubility

Log <i>S</i> (ESOL) ²	-4.79
Solubility	5.83e-03 mg/ml ; 1.61e-05 mol/l
Class ²	Moderately soluble
Log <i>S</i> (Ali) ²	-5.57
Solubility	9.61e-04 mg/ml ; 2.66e-06 mol/l
Class ²	Moderately soluble
Log <i>S</i> (SILICOS-IT) ²	-5.68
Solubility	7.60e-04 mg/ml ; 2.10e-06 mol/l
Class ²	Moderately soluble

Pharmacokinetics

GI absorption ²	High
BBB permeant ²	Yes
P-gp substrate ²	Yes
CYP1A2 inhibitor ²	No
CYP2C19 inhibitor ²	No
CYP2C9 inhibitor ²	No
CYP2D6 inhibitor ²	Yes
CYP3A4 inhibitor ²	Yes
Log <i>K</i> _p (skin permeation) ²	-5.25 cm/s

Druglikeness

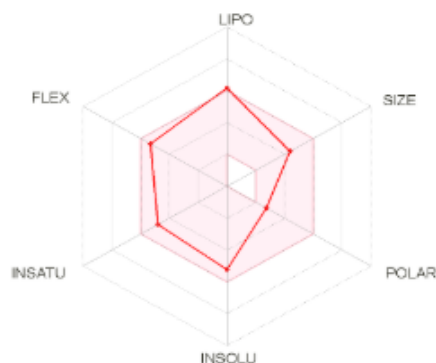
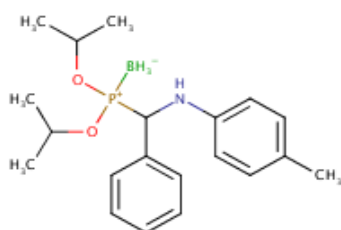
Lipinski ²	Yes; 0 violation
Ghose ²	Yes
Veber ²	Yes
Egan ²	Yes
Muegge ²	Yes
Bioavailability Score ²	0.55

Medicinal Chemistry

PAINS ²	0 alert
Brenk ²	3 alerts: heavy_metal, hydroquinone, phosphor ²
Leadlikeness ²	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility ²	4.27

Compound

6



SMILES CC(O[P+](C(c1ccccc1)Nc1ccc(cc1)C)(OC(C)C)[BH3-])C

Physicochemical Properties

Formula	C20H31BNO2P
Molecular weight	359.25 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	12
Fraction Csp3	0.40
Num. rotatable bonds	8
Num. H-bond acceptors	2
Num. H-bond donors	1
Molar Refractivity	114.13
TPSA [?]	40.30 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP) [?]	0.00
Log $P_{o/w}$ (XLOGP3) [?]	5.30
Log $P_{o/w}$ (WLOGP) [?]	4.57
Log $P_{o/w}$ (MLOGP) [?]	3.65
Log $P_{o/w}$ (SILICOS-IT) [?]	2.51
Consensus Log $P_{o/w}$ [?]	3.21

Water Solubility

Log S (ESOL) [?]	-5.23
Solubility	2.10e-03 mg/ml ; 5.84e-06 mol/l
Class [?]	Moderately soluble
Log S (Ali) [?]	-5.90
Solubility	4.55e-04 mg/ml ; 1.27e-06 mol/l
Class [?]	Moderately soluble
Log S (SILICOS-IT) [?]	-6.64
Solubility	8.21e-05 mg/ml ; 2.29e-07 mol/l
Class [?]	Poorly soluble

Pharmacokinetics

GI absorption [?]	High
BBB permeant [?]	Yes
P-gp substrate [?]	Yes
CYP1A2 inhibitor [?]	No
CYP2C19 inhibitor [?]	No
CYP2C9 inhibitor [?]	No
CYP2D6 inhibitor [?]	Yes
CYP3A4 inhibitor [?]	Yes
Log K_p (skin permeation) [?]	-4.73 cm/s

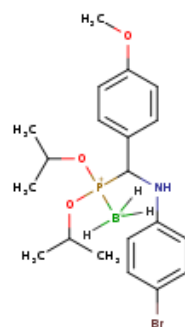
Druglikeness

Lipinski [?]	Yes; 0 violation
Ghose [?]	Yes
Veber [?]	Yes
Egan [?]	Yes
Muegge [?]	No; 1 violation: XLOGP3>5
Bioavailability Score [?]	0.55

Medicinal Chemistry

PAINS [?]	0 alert
Brenk [?]	2 alerts: heavy_metal, phosphor [?]
Leadlikeness [?]	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility [?]	4.41

Compound 7



SMILES COC1ccc(cc1)C([P+](OC(C)C)(OC(C)C)[BH3-])Nc1ccc(cc1)Br

Physicochemical Properties

Formula	C20H30BBBrNO3P
Molecular weight	454.15 g/mol
Num. heavy atoms	27
Num. arom. heavy atoms	12
Fraction Csp3	0.40
Num. rotatable bonds	9
Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	123.35
TPSA ²	49.53 Å²

Lipophilicity

Log $P_{o/w}$ (iLOGP) ²	0.00
Log $P_{o/w}$ (XLOGP3) ²	5.60
Log $P_{o/w}$ (WLOGP) ²	5.03
Log $P_{o/w}$ (MLOGP) ²	3.67
Log $P_{o/w}$ (SILICOS-IT) ²	2.75
Consensus Log $P_{o/w}$ ²	3.41

Water Solubility

Log S (ESOL) ²	-5.92
Solubility	5.48e-04 mg/ml ; 1.21e-06 mol/l
Class ²	Moderately soluble
Log S (Ali) ²	-6.40
Solubility	1.80e-04 mg/ml ; 3.96e-07 mol/l
Class ²	Poorly soluble
Log S (SILICOS-IT) ²	-7.15
Solubility	3.22e-05 mg/ml ; 7.08e-08 mol/l
Class ²	Poorly soluble

Pharmacokinetics

GI absorption ²	High
BBB permeant ²	Yes
P-gp substrate ²	Yes
CYP1A2 inhibitor ²	No
CYP2C19 inhibitor ²	No
CYP2C9 inhibitor ²	Yes
CYP2D6 inhibitor ²	Yes
CYP3A4 inhibitor ²	Yes
Log K_p (skin permeation) ²	-5.09 cm/s

Druglikeness

Lipinski ²	Yes; 0 violation
Ghose ²	Yes
Veber ²	Yes
Egan ²	Yes
Muegge ²	No; 1 violation: XLOGP3>5
Bioavailability Score ²	0.55

Medicinal Chemistry

PAINS ²	0 alert
Brenk ²	2 alerts: heavy_metal, phosphor ²
Leadlikeness ²	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility ²	4.39