

キシダオリジナル ビルディングブロック (K-BB)

- Scaffold別 -



KISHIDA

本製品は試験研究用途でのみご使用いただけます

2023年8月版

K-BB は、

創薬研究にご活用いただけるビルディングブロックを、
メディシナルケミストの目線からご提供します



キシダオリジナルビルディングブロック（K-BB）の特徴

K-BBのコンセプトは？

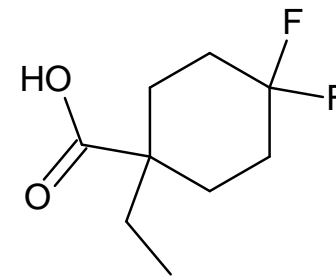
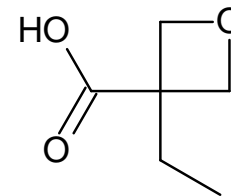
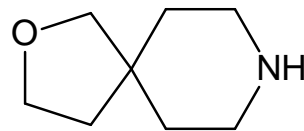
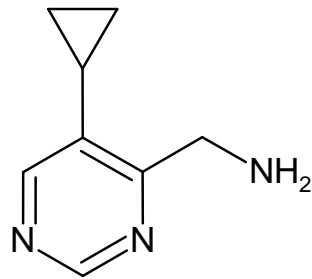
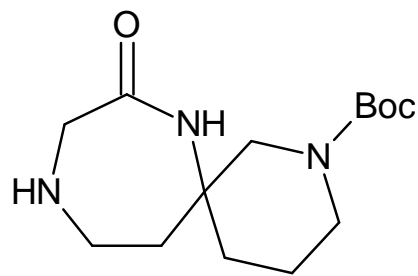
創薬研究に汎用されるScaffoldに加え、文献・特許情報からトレンドのBBをメディシナルケミストの視点でラインナップしています（2023年7月末：6,363品）

K-BBと他のサプライヤーBBの違いは？

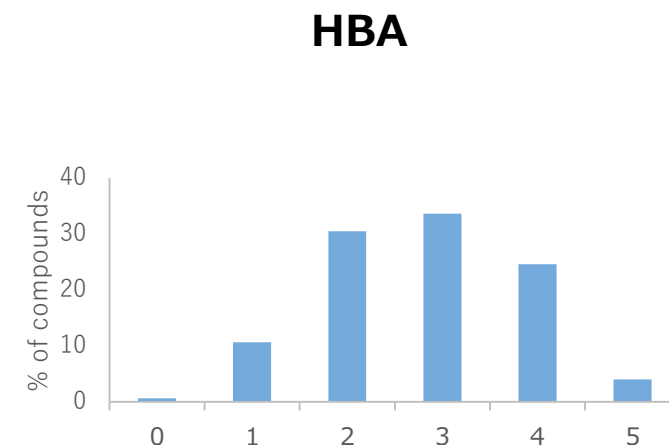
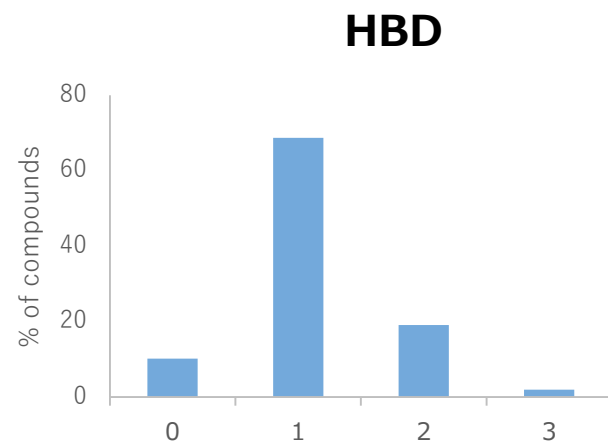
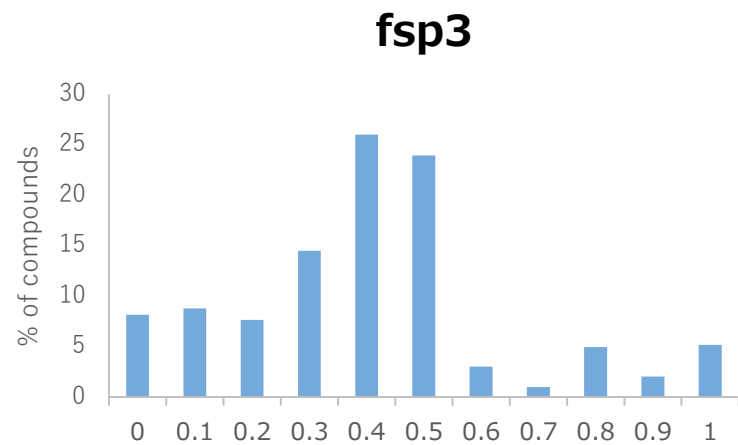
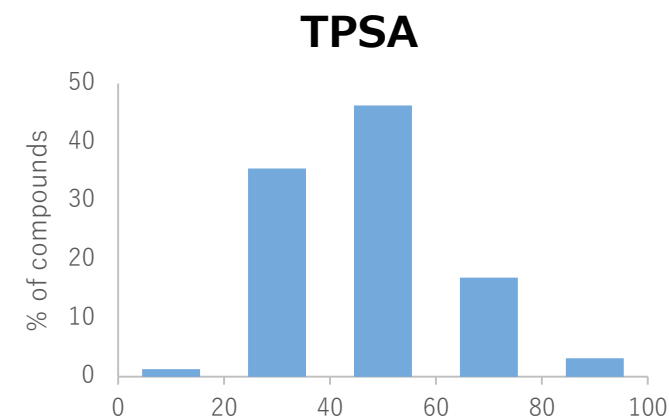
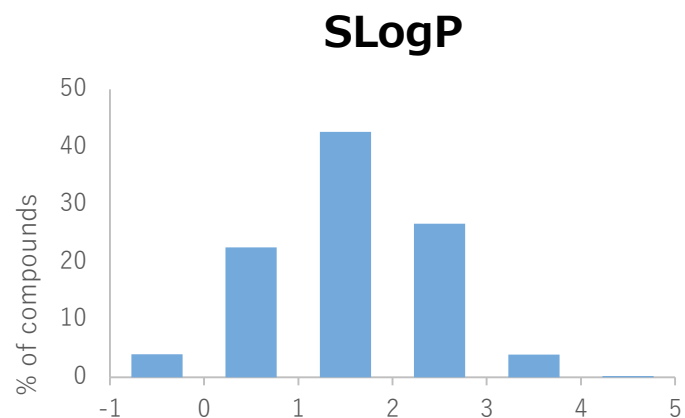
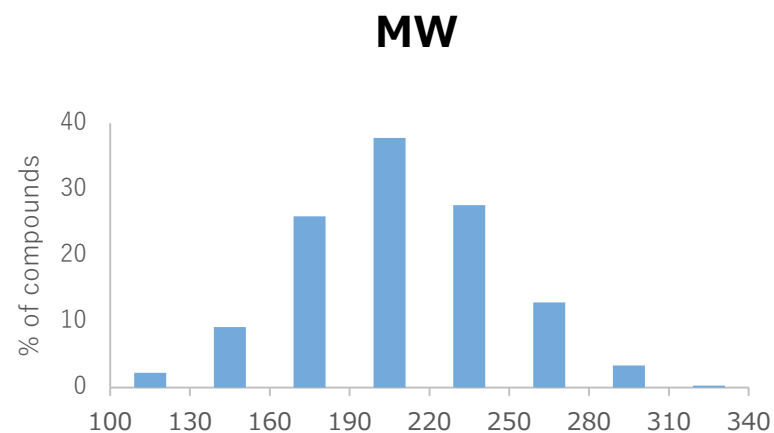
- 創薬の課題（活性・薬効の向上、物性や体内動態の改善など）に**効果が期待できる置換基**を積極的に導入しています。
- BBの主要な置換位置に多種の置換基を導入していますので、「**アナログ群**」として展開性が広く、幅広いSAR取得にご活用いただけます。
- 最適な合成法を精査し、**スケールアップ**にも対応可能です。
- **100mg, 250mg, 1g**の容量をラインナップしています。
- 国内研究者の皆様にタイムリーにお届けできるよう、多くのBBを**在庫化**しています。

キシダオリジナルビルディングブロック (K-BB) の特徴 ～構造・合成の観点から～

- **マルチファンクション**を有する化合物
- 取り扱いサプライヤー数が限られる化合物
- **スピロ化合物**、**Sp³リッチ**な化合物を多数取り扱い
- 取り扱い困難な**高極性化合物**を取り扱い
- 分子量の小さい化合物（揮発性の高い化合物）
- UV吸収が弱い、または持たない化合物

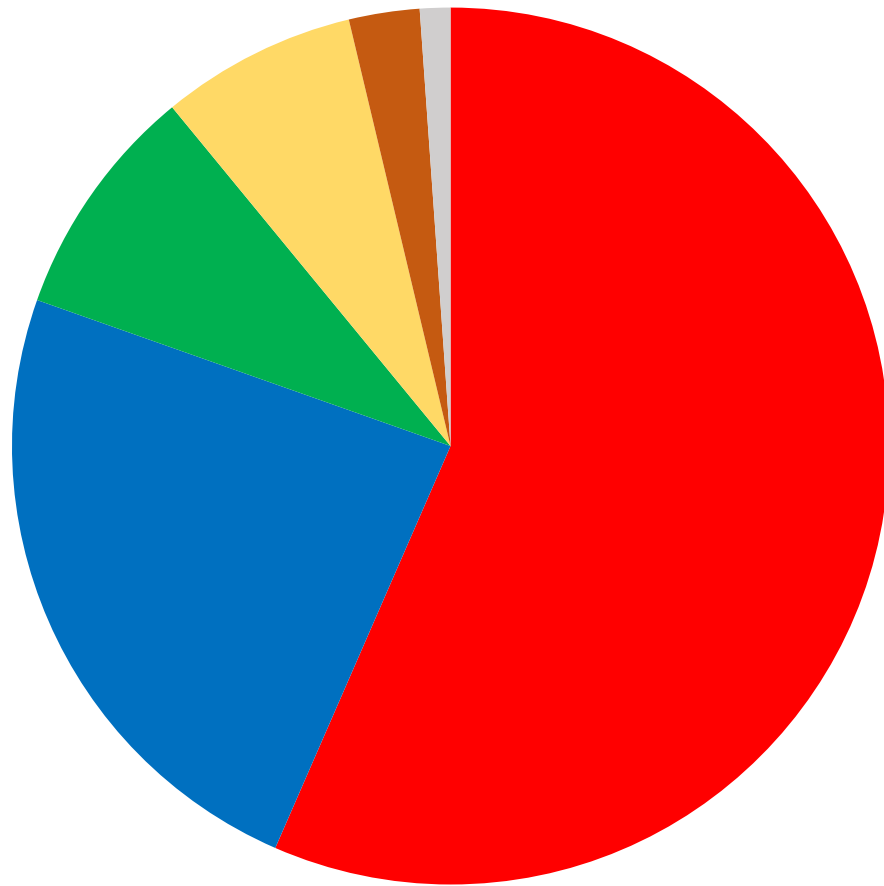


K-BBの計算物性値分布 (対象: 5093化合物)



※保護基のあるBBは脱保護した化合物を対象としています。

K-BBの構成（官能基別）

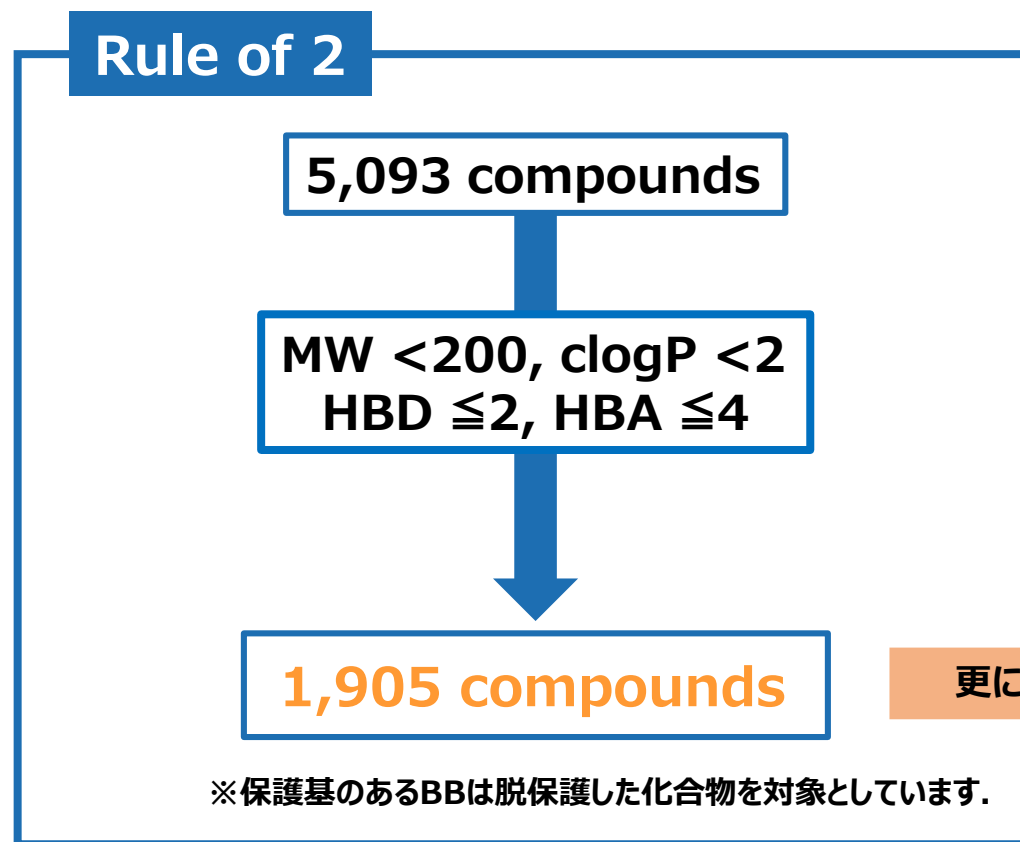


- Amine
- Carboxylic acid
- N-Boc
- Ar-Br
- NO2
- Ester

Product lineup

Homo-benzylamine
Imidazole
Benzylamine
Aryl carboxylic acid/ester
Pyrazole
Aniline
3-Hydroxypiperidine
4-Hydroxypiperidine
or 4-Alkoxy piperidine
4-Aminopiperidine
Piperazine
3-Aminopyrrolidine
3-Hydroxypyrrolidine
etc.

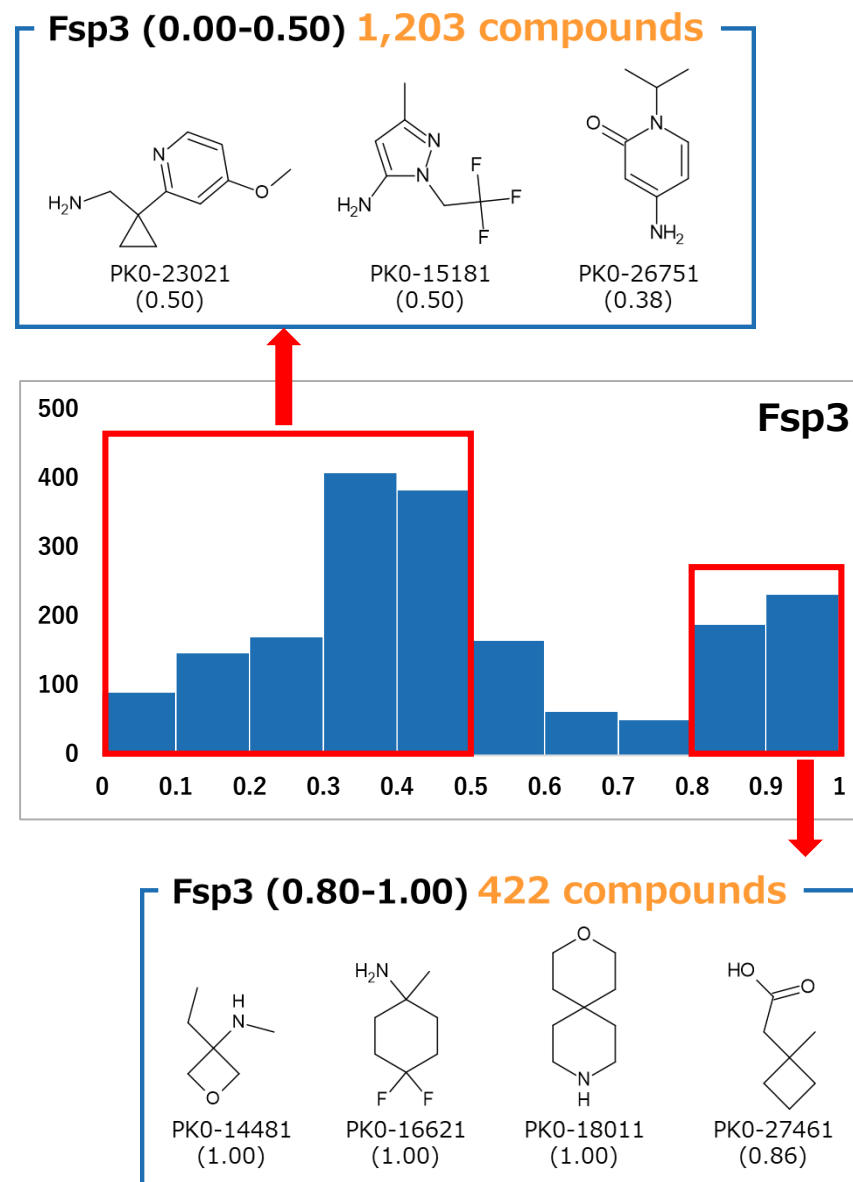
K-BBの計算物性値分布 (Rule of 2 : Ro2)



K-BBの約4割は「Rule of 2」のクライテリアを満たしています。

Designing novel building blocks is an overlooked strategy to improve compound quality
Drug Discov. Today, 2015, 20(1), 11-17.

更に、Fsp3で分類

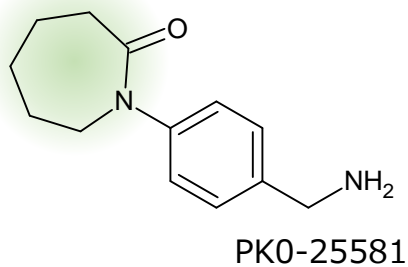
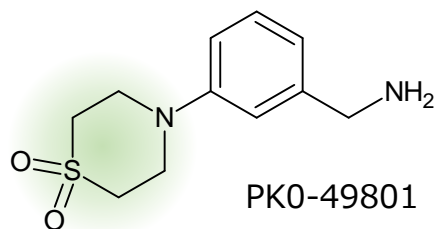
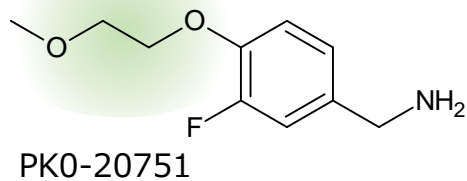
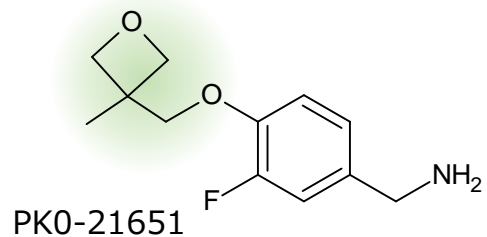


表記の構造式には塩を反映しておりません。

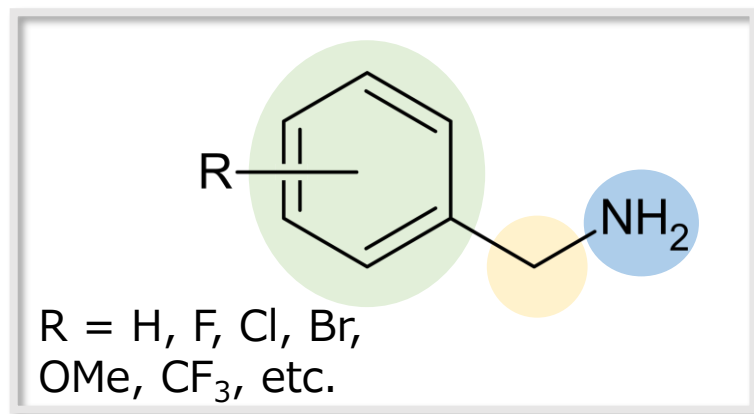
キシダオリジナル ビルディングブロック (K-BB)

-アミン-

Benzylamine analogs

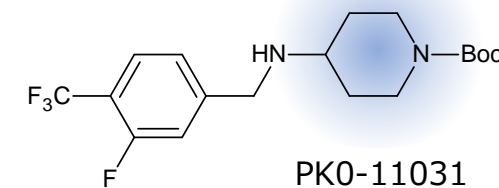
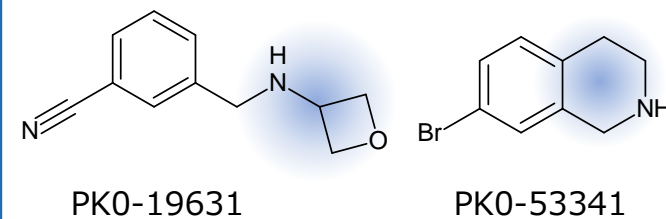


35
analogos



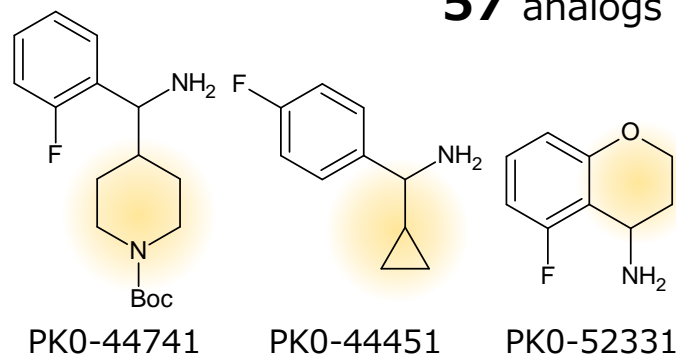
170
analogos

N-alkyl type



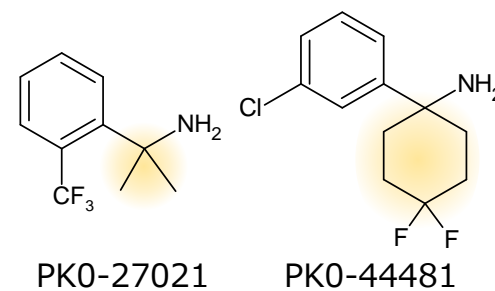
Mono-alkyl type

57 analogos



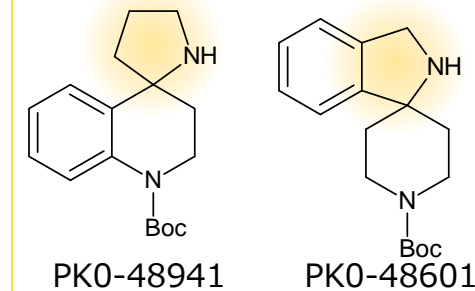
Di-alkyl type

114 analogos

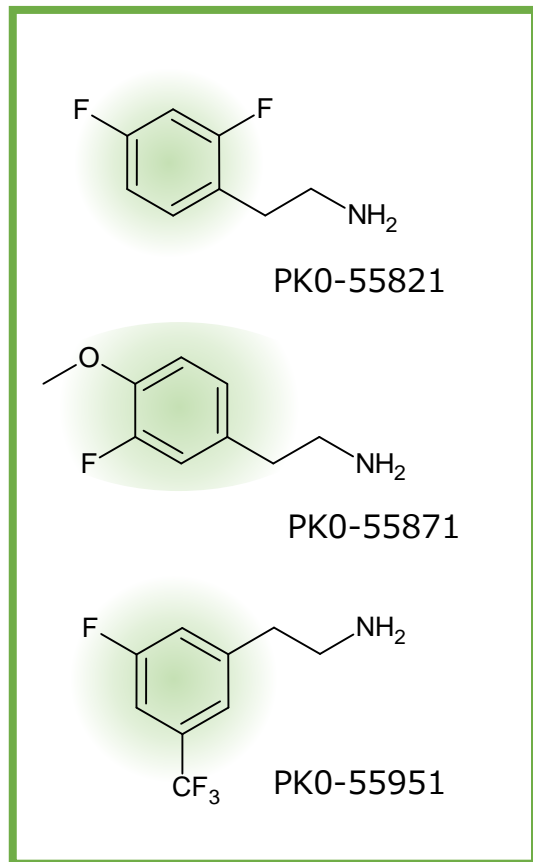


Cyclic type

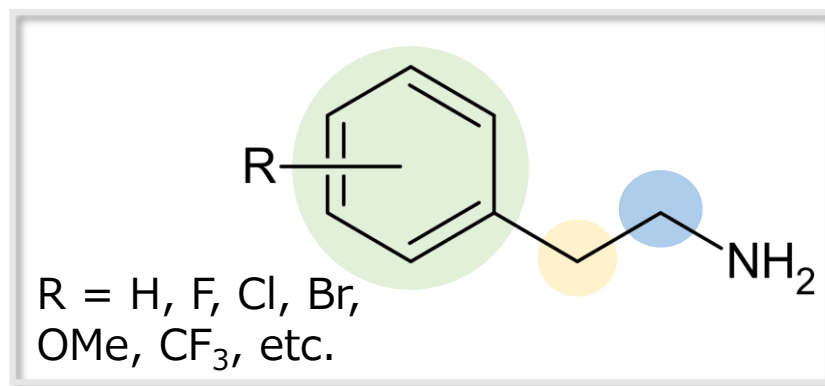
3 analogos



Homo-benzylamine analogs



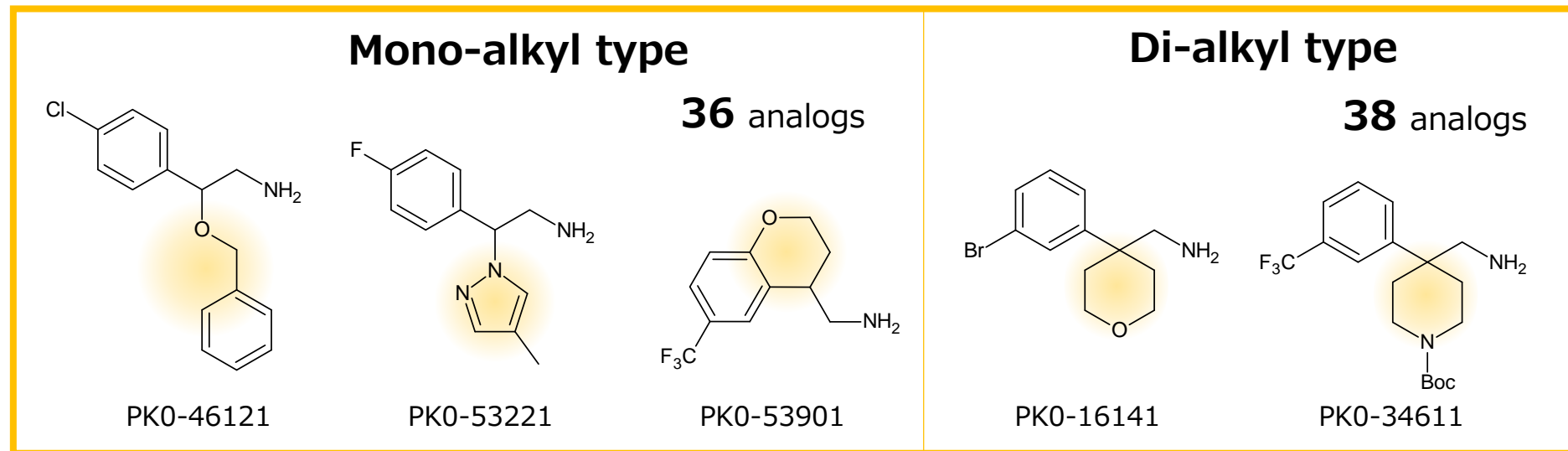
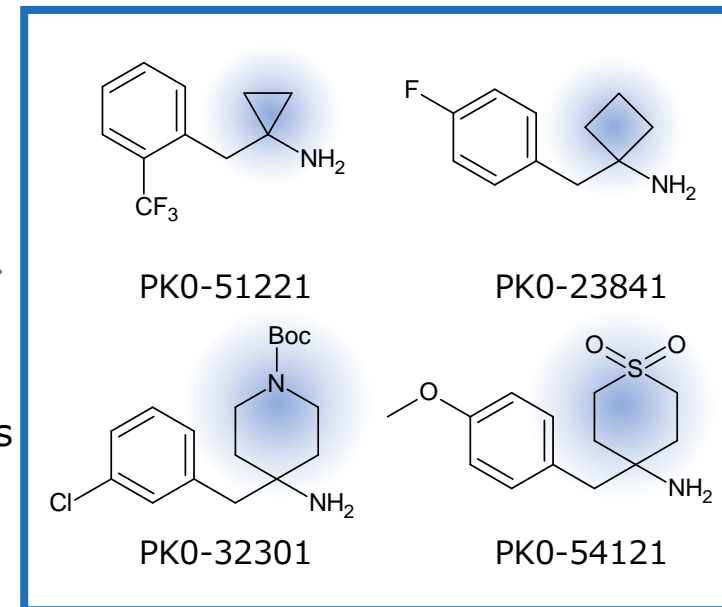
18
analogos



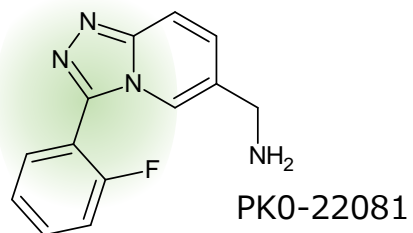
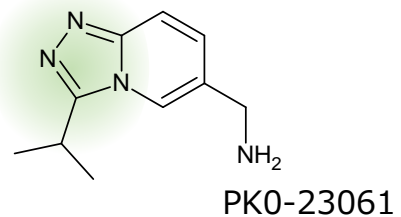
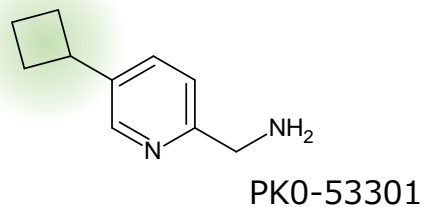
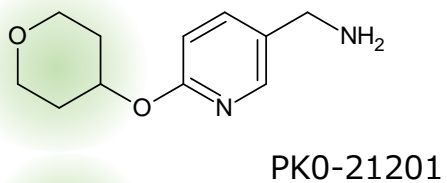
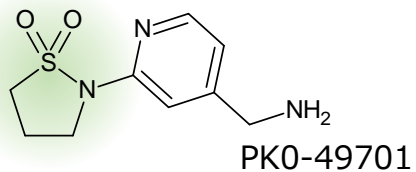
97
analogos



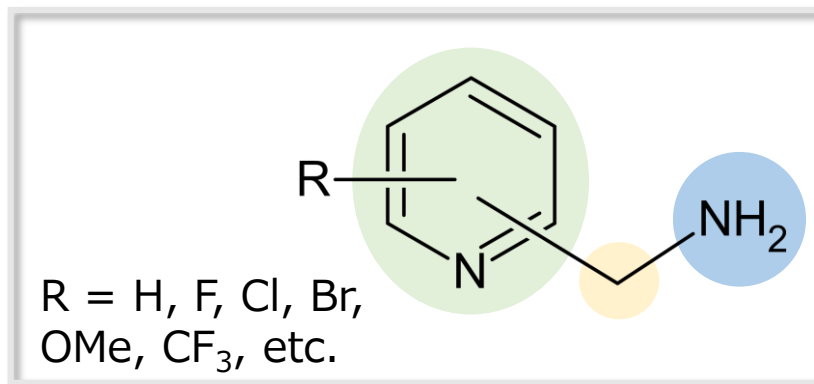
74
analogos



Picolylamine analogs

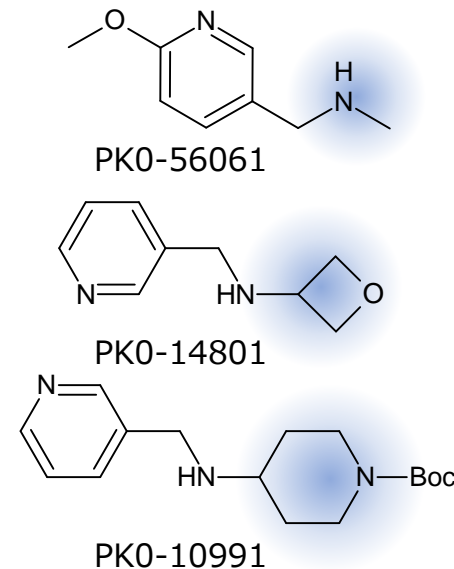


80
analogos

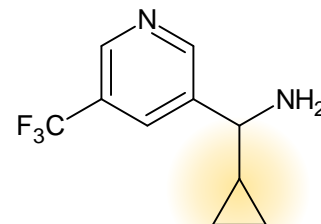
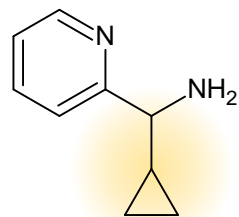


43
analogos

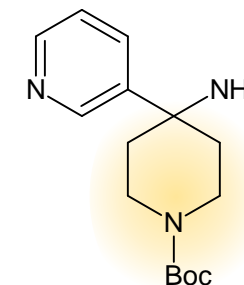
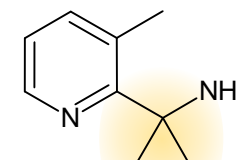
55
analogos



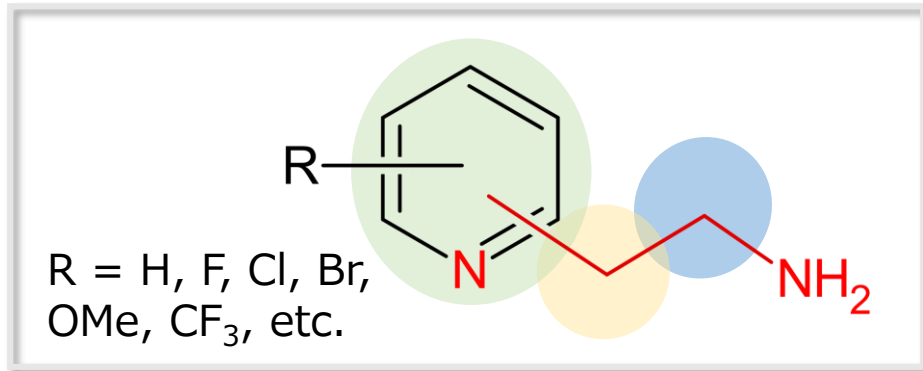
Mono-alkyl type 32 analogos



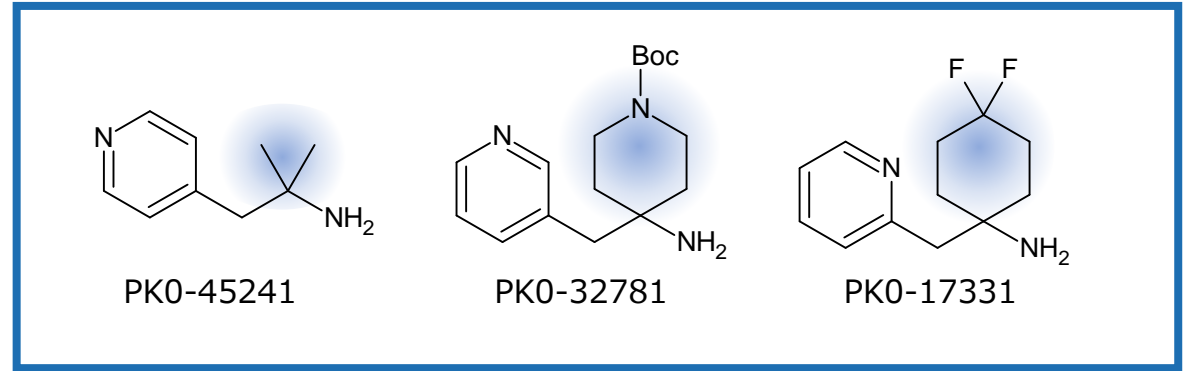
Di-alkyl type 11 analogos



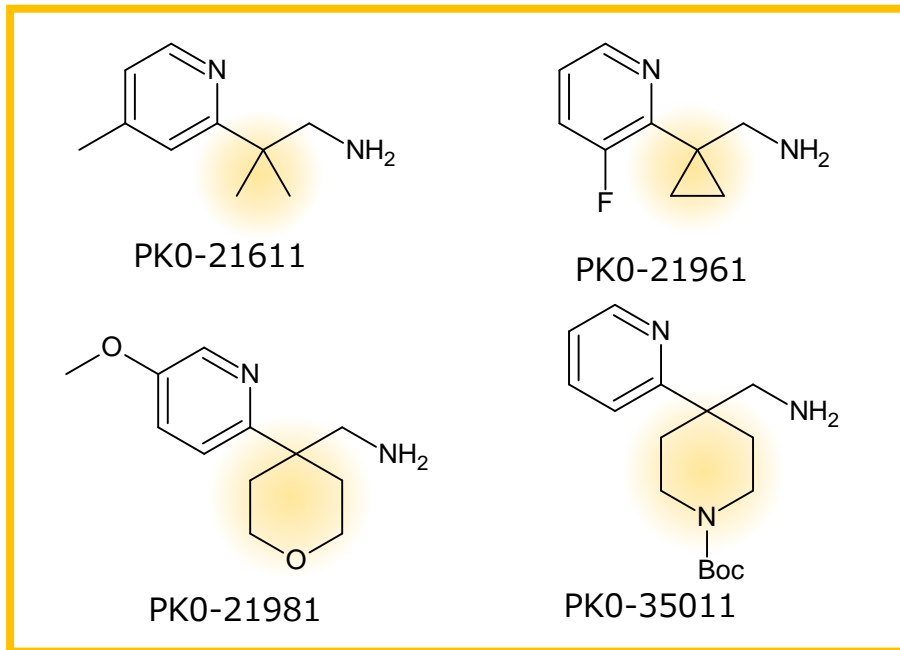
Aminoethylpyridine analogs



19
analogos



38
analogos

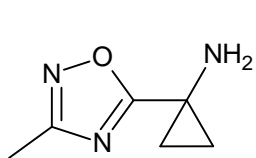


組み合わせにより、幅広いSARを取得できます。

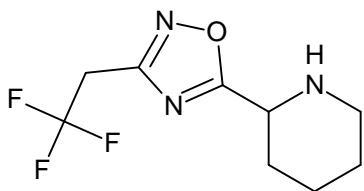
	PKO-21611	PKO-22011	PKO-22551
	PKO-21631	PKO-21591	PKO-21601
	PKO-23331	PKO-22501	PKO-38921

Azole-methylamine analogs

Oxadiazoles



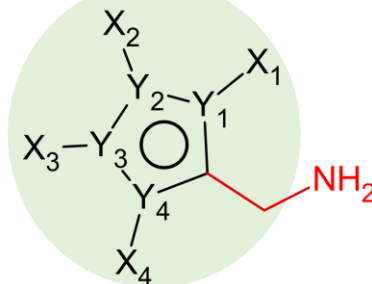
PKO-15321



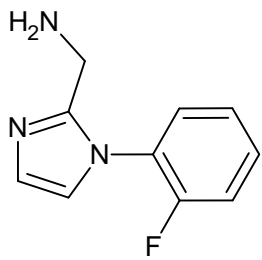
PKO-19971

16
analogos

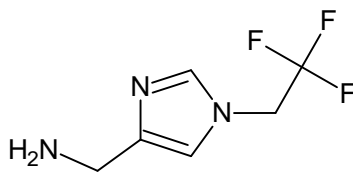
61
analogos



Imidazoles



PKO-54531

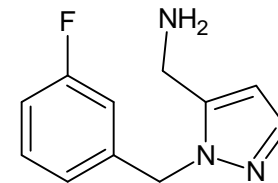


PKO-30751

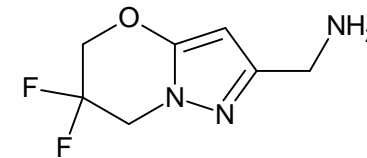
77
analogos

10
analogos

Pyrazoles

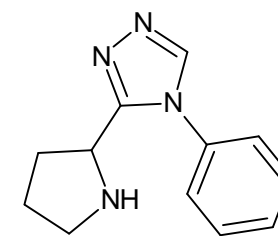


PKO-57831

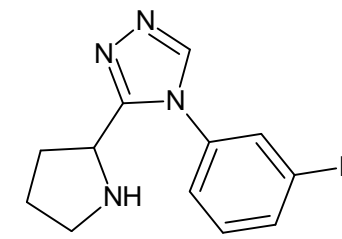


PKO-50441

Triazoles

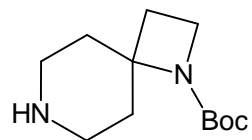


PKO-53601

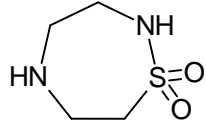


PKO-53801

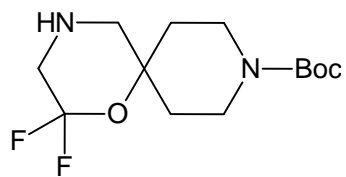
Aliphatic amine analogs



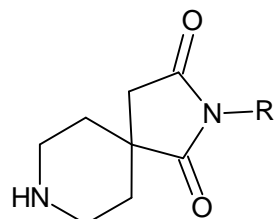
PK0-21751



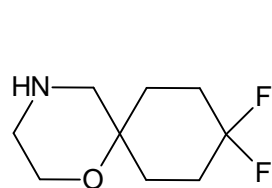
PK0-55131



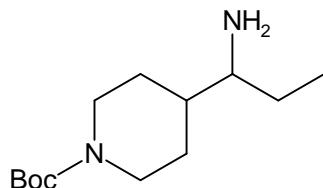
PK0-59081



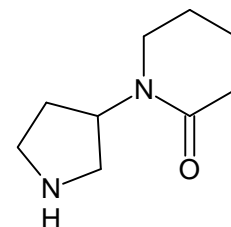
R = Me : PK0-59301
R = Et : PK0-59401



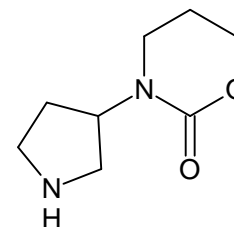
PK0-59481



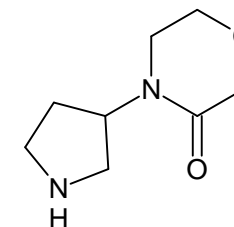
PK0-59521



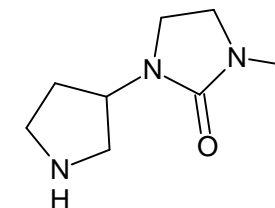
PK0-53811



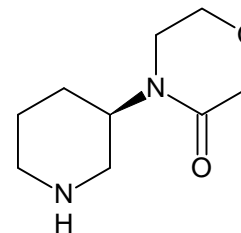
PK0-54131



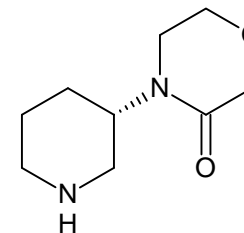
PK0-54011



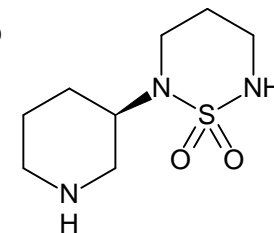
PK0-54151



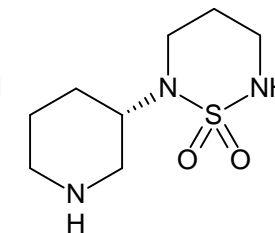
PK0-56801



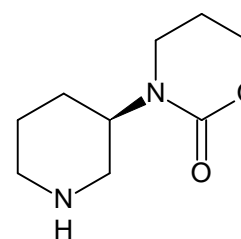
PK0-56581



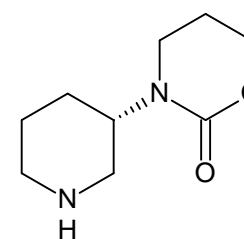
PK0-56831



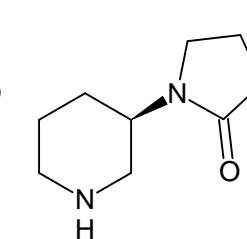
PK0-56851



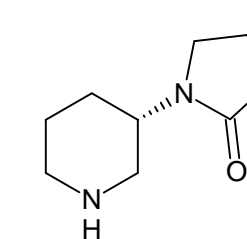
PK0-56811



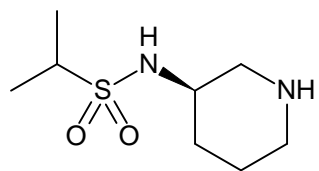
PK0-56591



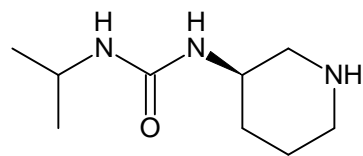
PK0-56841



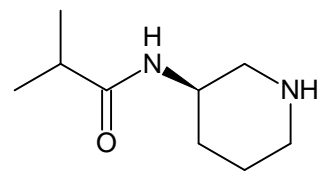
PK0-56611



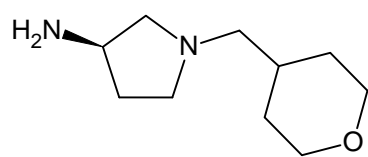
PK0-08771



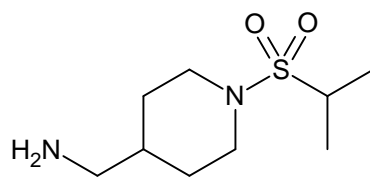
PK0-08961



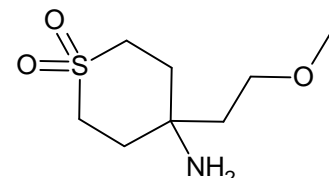
PK0-08101



PK0-07301



PK0-07761

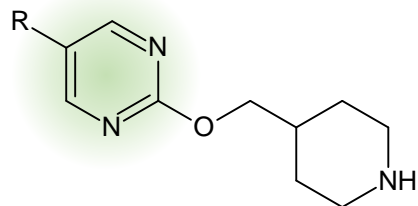


PK0-43521

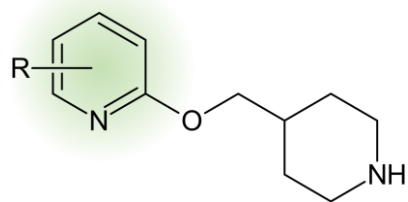


524
analogues

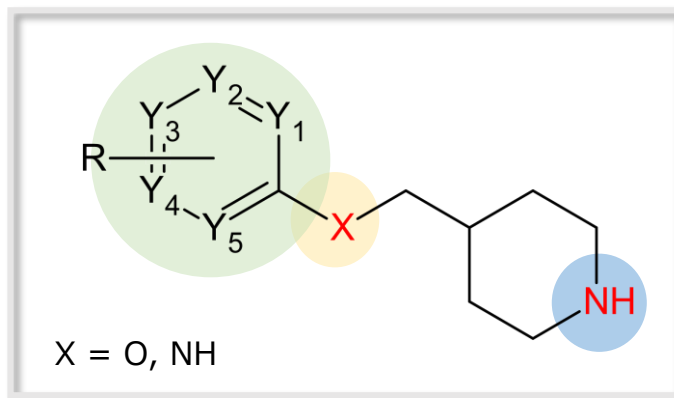
Piperidine analogs



R = H : PK0-55431
R = F : PK0-55621
R = Cl : PK0-55491
R = OMe : PK0-55731



R = 3-F : PK0-55591
R = 3-CF₃ : PK0-55471
R = 6-CF₃ : PK0-55451



X = O, NH



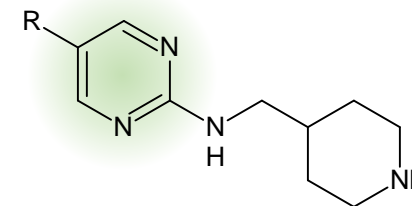
X = O

41
analogs
(Ph体含)

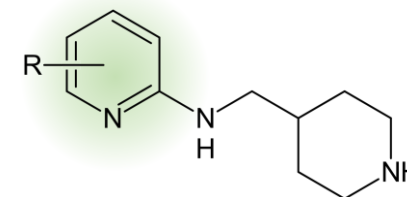


X = NH

38
analogs
(Ph体含)



R = H : PK0-55681
R = F : PK0-55581
R = Cl : PK0-55421
R = OMe : PK0-55701



R = H : PK0-55291
R = 3-F : PK0-55531
R = 3-CF₃ : PK0-55401
R = 6-CF₃ : PK0-55381

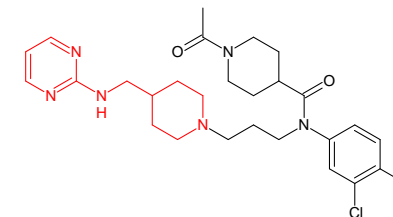
Piperidine analogs <参考情報>

1. 高い主活性を示し、細胞毒性との乖離がある、PK0-55681の構造が導入された化合物を報告 (comp.1)

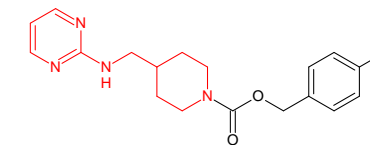
Design, synthesis, and biological activity of novel 1,4-disubstituted piperidine/piperazine derivatives as CCR5 antagonist-based HIV-1 entry inhibitors *Bioorg.Med.Chem.Lett.* **2012**, 22, 3284-3286.

2. 高い主活性、hERG活性との選択性を示す、PK0-55681、55291などの構造が導入された化合物を報告 (comp.2)

Identification and Characterization of 4-Methylbenzyl 4-[(Pyrimidin-2-ylamino)methyl]piperidine-1-carboxylate, an Orally Bioavailable, Brain Penetrant NR2B Selective N-Methyl-D-Aspartate Receptor Antagonist *J.Med.Chem.* **2007**, 50, 807-819.

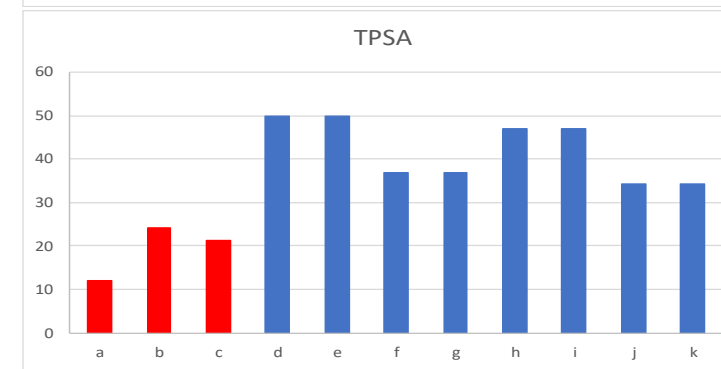
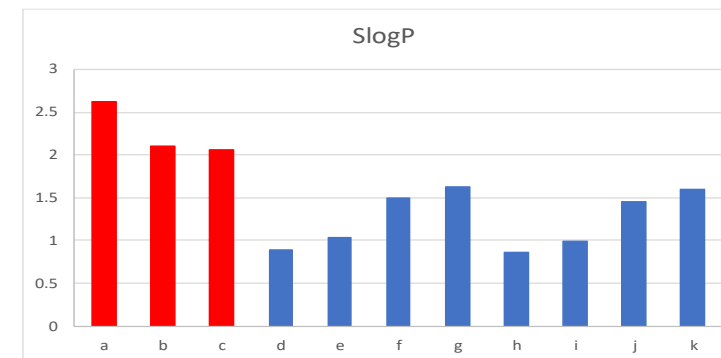
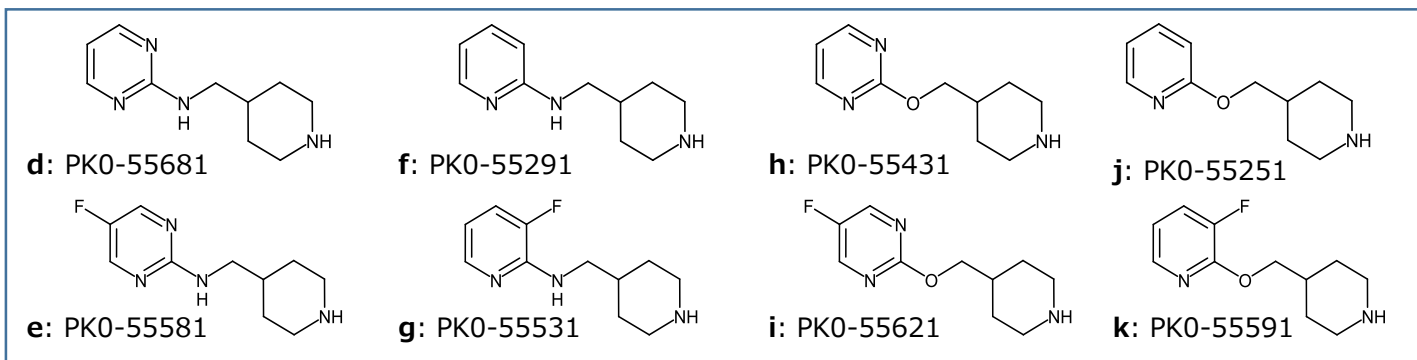
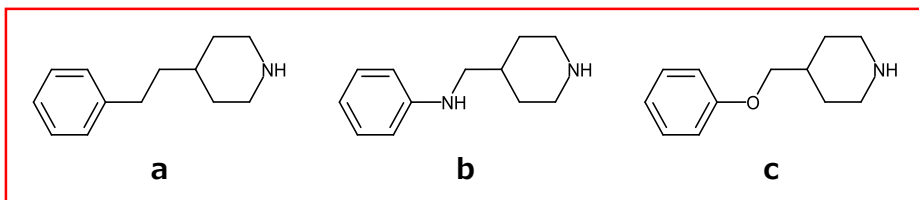


comp.1



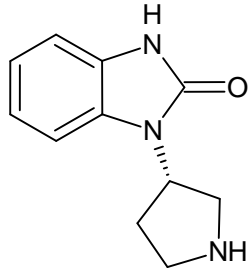
comp.2

ヘテロ環の導入した当社のPiperidine analogsの利用により、市販されている化合物a-cに比べ、SlogPの低減とTPSAの向上が期待できます

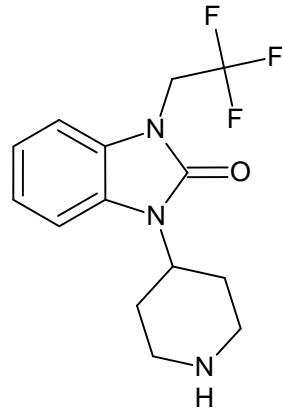


SlogP and TPSA of compd. a-k

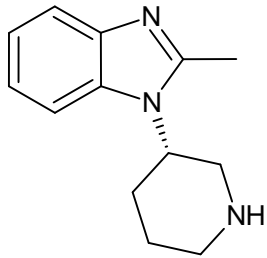
3/4-Aminoepiperidine & 3-Aminopyrrolidine Analogs



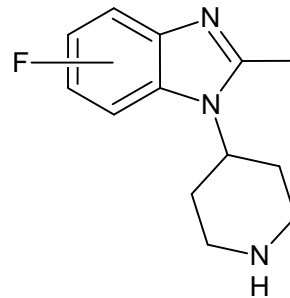
PKO-56661



PKO-55761



PKO-56531



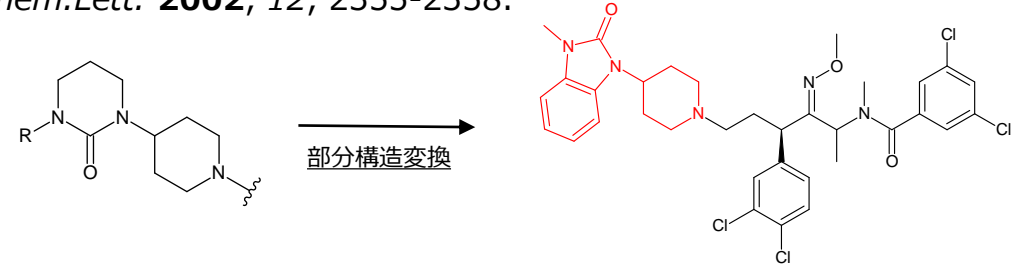
- 4- : PKO-57261
- 5- : PKO-57251
- 6- : PKO-57241
- 7- : PKO-57231



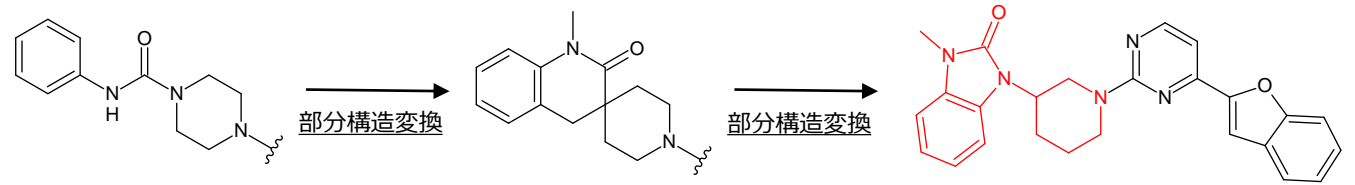
22
analogs

<参考情報 / K-BB構造が導入されている事例>

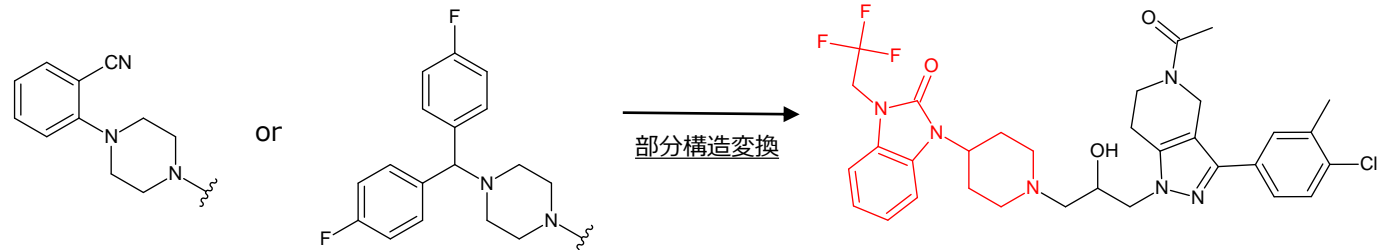
- 1. 1桁ナノモルのNK1/NK2親和性とNK3に対する選択性を有する化合物群の骨格として導入**
Preparation of oxime dual NK1/NK2 antagonists with reduced NK3 affinity
Bioorg.Med.Chem.Lett. **2002**, 12, 2355-2358.



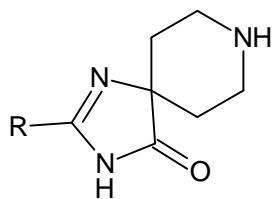
- 2. PKO-55741、56491などBB構造を含む複数化合物のFAAH阻害活性を報告**
Identification of potent, noncovalent fatty acid amide hydrolase (FAAH) inhibitors
Bioorg.Med.Chem.Lett. **2011**, 21, 2492-2496.



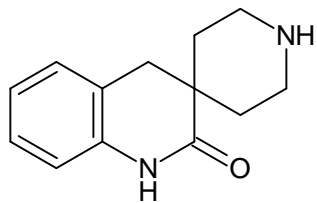
- 3. 4-arylpiperazine moietyの等価体としてPKO-55761などの導入結果が報告**
Discovery and SAR studies of a novel series of noncovalent cathepsin S inhibitors
Bioorg.Med.Chem.Lett. **2005**, 15, 1687-1691.



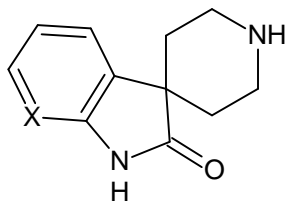
Spiro-piperidine analogs



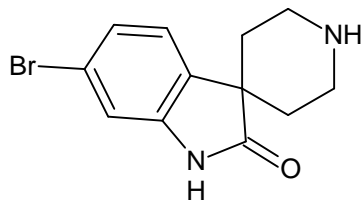
R = Me : PK0-30321
R = Ph : PK0-30261



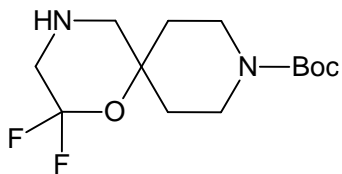
PK0-15451



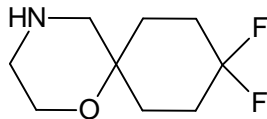
X = CH : PK0-31191
X = N : PK0-51511



PK0-31791



PK0-59081



PK0-59481

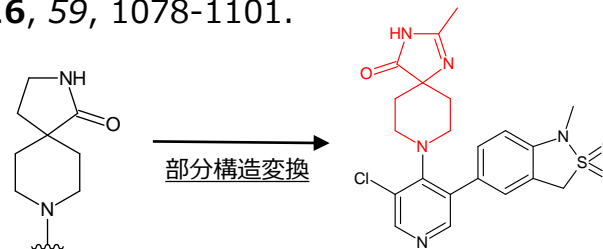


55
analogues

<参考情報 / K-BB構造が導入されている事例>

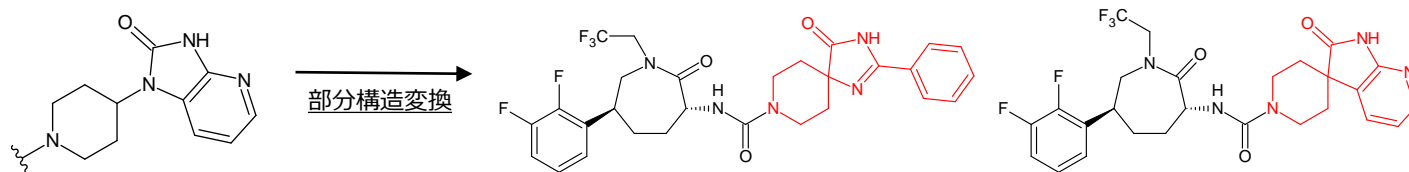
1. 2,8-diazaspiro[4.5]decan-1-one等価体の探索でPK0-30321の導入結果が報告

Discovery of Potent, Selective, and Orally Bioavailable Small-Molecule Modulators of the Mediator Complex-Associated Kinases CDK8 and CDK19
J. Med. Chem. **2016**, *59*, 1078-1101.



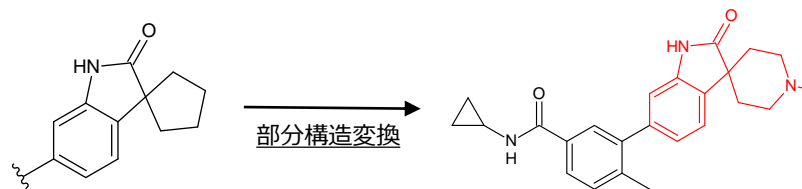
2. Piperidinyl-imidazopyridinone等価体の探索でPK0-30261, 51511などの導入結果が報告

Optimization of azepanone calcitonin gene-related peptide (CGRP) receptor antagonists: Development of novel spiropiperidines
Bioorg. Med. Chem. Lett. **2009**, *19*, 6368-6372.



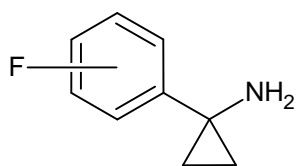
3. Spiroindolone部分の返還でPK0-31791を用いた代替構造の導入結果が報告

Indolin-2-one p38 α inhibitors II: Lead optimisation.
Bioorg. Med. Chem. Lett. **2011**, *21*, 5270-5273.

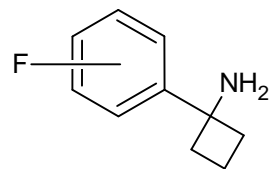


α,α -Disubstituted benzyl/picolylamine analogs

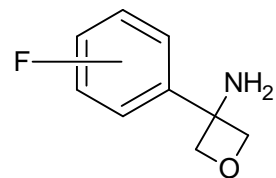
α,α -Disubstituted benzylamine analogs



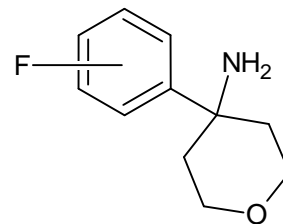
o- : PK0-09701
m- : PK0-09721
p- : PK0-09741



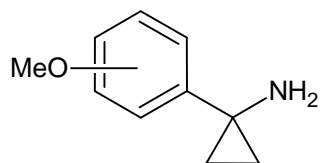
o- : PK0-09761
m- : PK0-09781
p- : PK0-09801



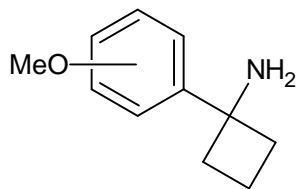
o- : PK0-11091
m- : PK0-11101
p- : PK0-11111



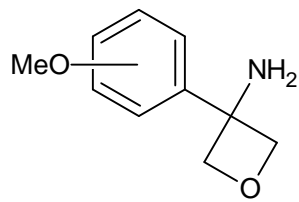
o- : PK0-17731
m- : PK0-16901
p- : PK0-18471



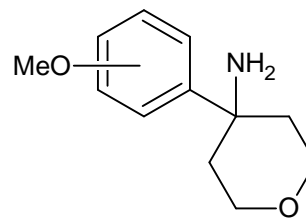
o- : PK0-10161
m- : PK0-10181
p- : PK0-10201



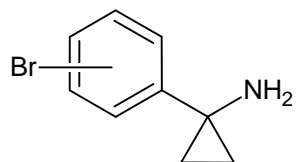
o- : PK0-10221
m- : PK0-10241
p- : PK0-10261



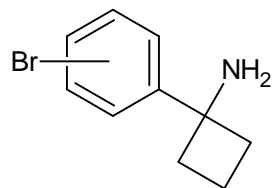
o- : PK0-11161
m- : PK0-11171
p- : PK0-11181



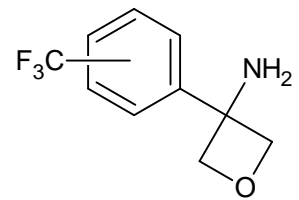
o- : PK0-17741
m- : PK0-16931
p- : PK0-16941



o- : PK0-09981
m- : PK0-10001
p- : PK0-10021



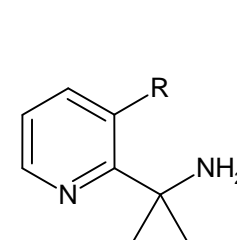
o- : PK0-10041
m- : PK0-10061
p- : PK0-10081



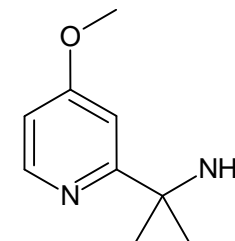
o- : PK0-13501
m- : PK0-13511
p- : PK0-12331

 **109**
analogs

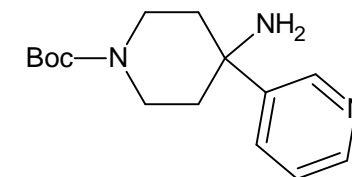
α,α -Disubstituted picolylamine analogs



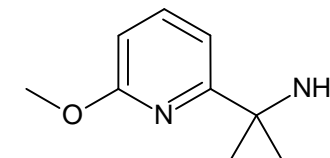
R = F : PK0-58971
R = Me : PK0-59041
R = OMe : PK0-59051



PK0-59181



PK0-34471



PK0-59031

 **11**
analogs

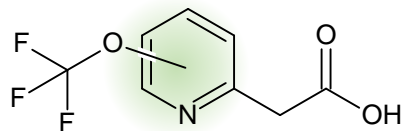
<参考情報 / K-BB構造及び類縁構造が使用されている事例>

α,α -ジ置換ベンジルアミンによる配座制御により阻害活性が向上
Discovery of isoxazole voltage gated sodium channel
blockers for treatment of chronic pain
Bioorg. Med. Chem. Lett. **2009**, *19*, 5334-5338.

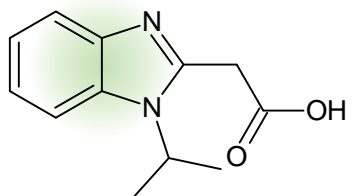
キシダオリジナル ビルディングブロック (K-BB)

-カルボン酸-

Phenylacetic acid analogs



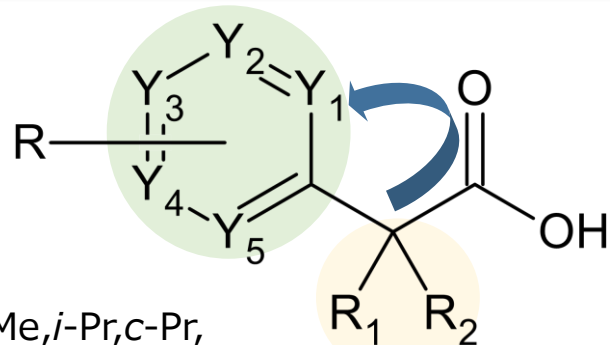
4- : PK0-40741
5- : PK0-40751
6- : PK0-40771



PK0-53931



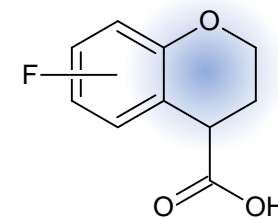
50
analog



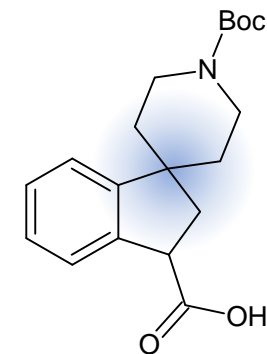
Y = C, N
R = F, Cl, Me, *i*-Pr, *c*-Pr,
c-Bu, CHF₂, CF₃, OMe, etc



14
analog



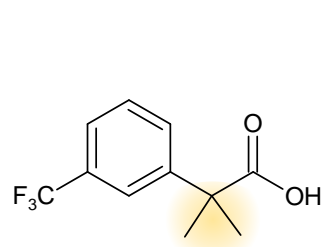
5- : PK0-52511
6- : PK0-52521
7- : PK0-52531
8- : PK0-52381



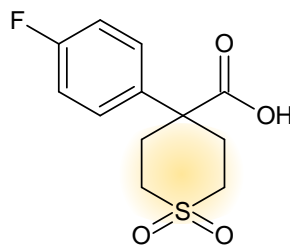
PK0-48101



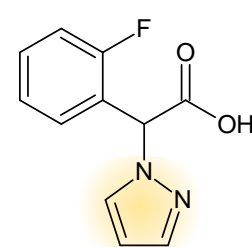
161
analog



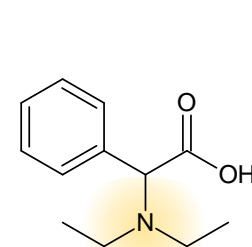
PK0-25631



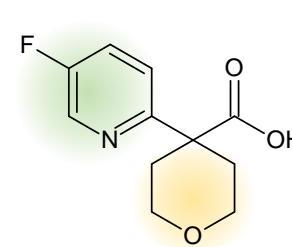
PK0-53761



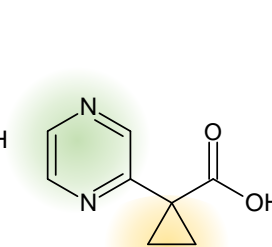
PK0-52691



PK0-51941

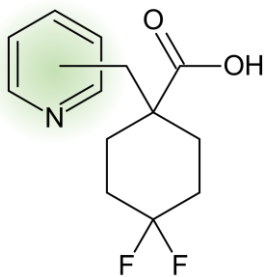


PK0-21701

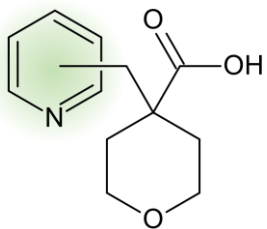


PK0-22151

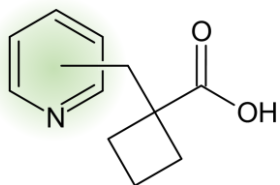
Phenylpropionic acid analogs



2-yl : PK0-17261
3-yl : PK0-17271
4-yl : PK0-17281



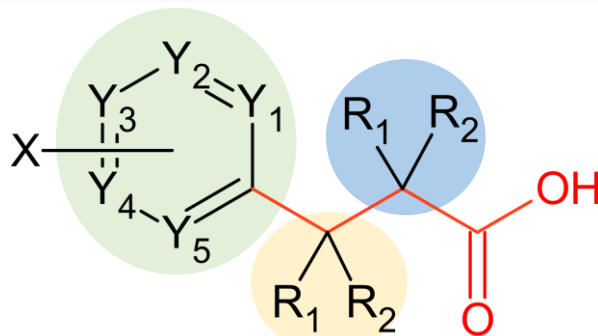
2-yl : PK0-20361
3-yl : PK0-19671
4-yl : PK0-19681



2-yl : PK0-25011
3-yl : PK0-45351
4-yl : PK0-44841



17
analog



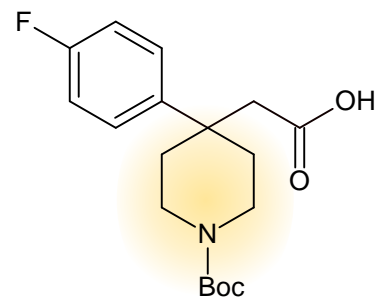
Y=C or N
R=H, F, Cl, Br, Me, OMe, CF₃



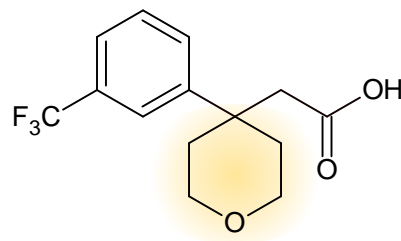
93
analog



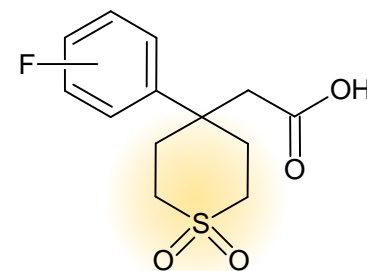
110
analog



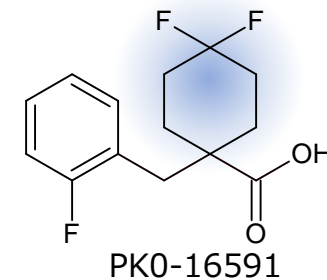
PK0-28321



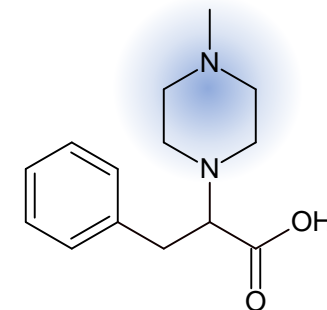
PK0-27591



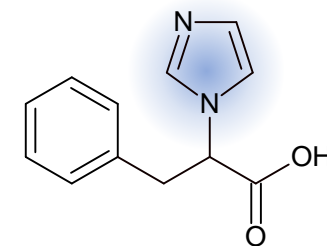
o- : PK0-59251
m- : PK0-59091
p- : PK0-59021



PK0-16591

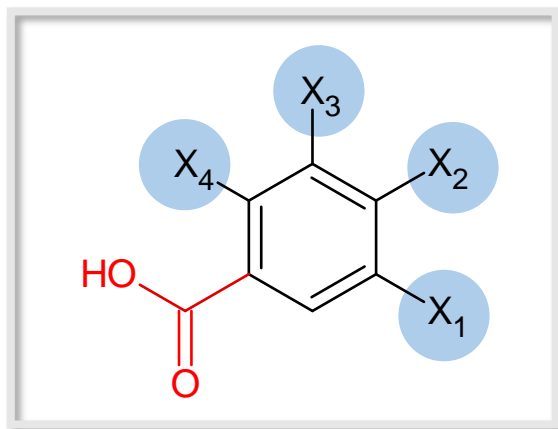


PK0-52211



PK0-57011

Benzoic acid analogs



Mono functional

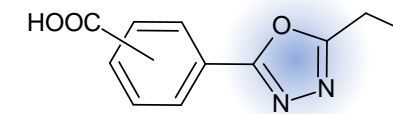
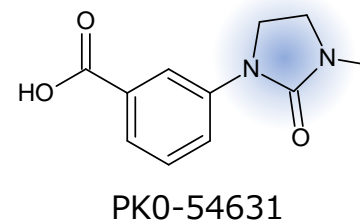
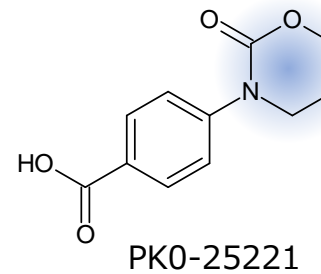
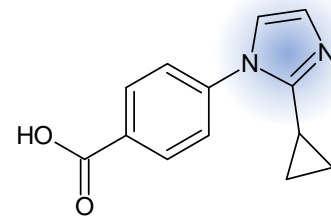


38
analog

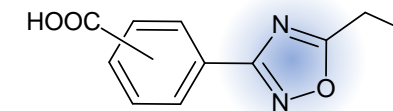
Multi functional



26
analog



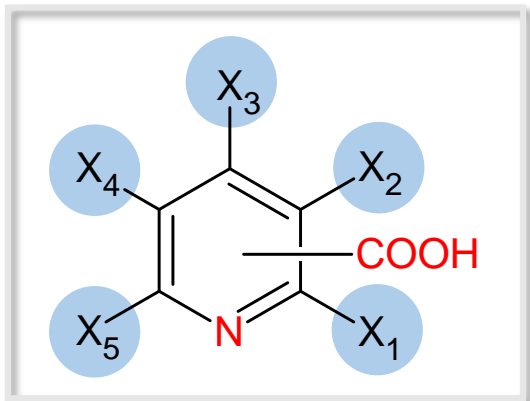
o- : PK0-57331
m- : PK0-57441
p- : PK0-57321



o- : PK0-57311
m- : PK0-57301
p- : PK0-57161

ID	X ₁	X ₂	X ₃	X ₄
PK0-17461	F		F	H
PK0-18161	F		F	H
PK0-20571	F		H	H
PK0-20141	H		H	H

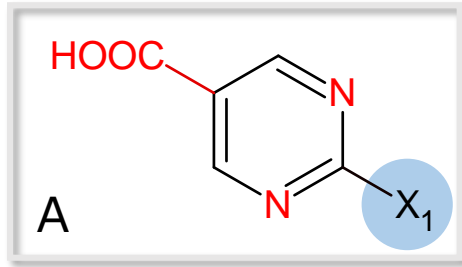
Pyridine-carboxylic acid analogs



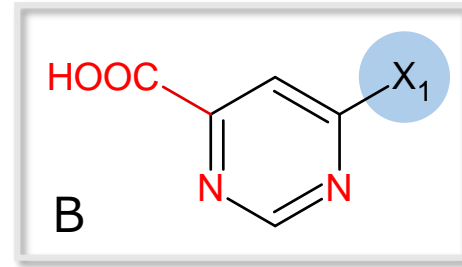
189
analogues

Scaffold	置換基	X1	X2	X3	X4	X5
 84 ~analogues		-	PK0-30991	PK0-30631	PK0-30081	PK0-29681
		-	PK0-21091	PK0-16731	PK0-20241	PK0-20161
		-	PK0-29181	PK0-29171	PK0-28981	PK0-29161
 62 ~analogues		PK0-30111	-	PK0-30641	PK0-49181	PK0-29691
		PK0-20201	-	PK0-22381	PK0-18341	PK0-19511
		PK0-29191	-	PK0-29201	PK0-29001	PK0-28991
 43 ~analogues		PK0-30101	PK0-30091	-	-	-
		PK0-18181	PK0-38431	-	-	-
		PK0-18261	PK0-38811	-	-	-

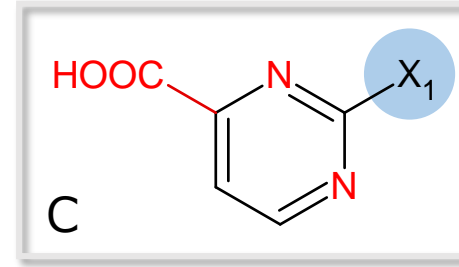
Pyrimidine-carboxylic acid analogs



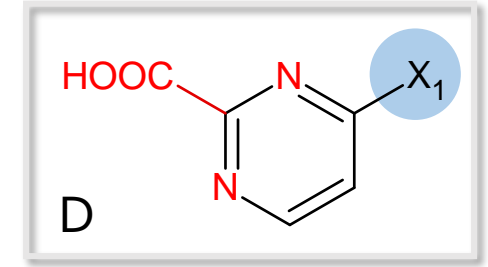
24
analog



21
analog



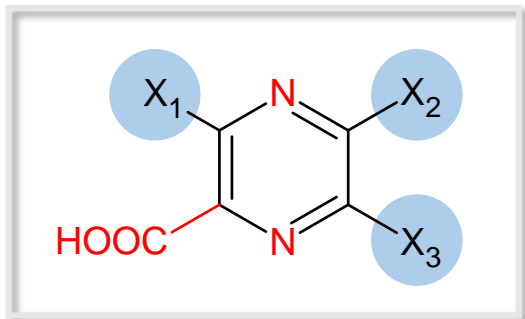
12
analog



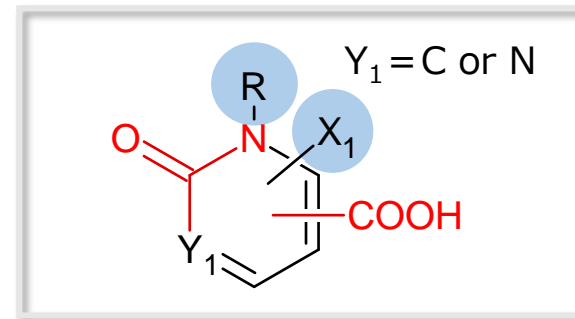
11
analog

X ₁	A型	B型	C型	D型
	PK0-19471	PK0-21481	PK0-43091	PK0-43421
	PK0-21021	PK0-22321	PK0-43741	PK0-49771
	PK0-20651	PK0-22891	PK0-43101	PK0-43781
	PK0-21031	PK0-24841	PK0-43761	PK0-42701
	PK0-21891	PK0-24831	PK0-43731	PK0-43151

Pyrazine/Pyridone/Pyrimidone-carboxylic acid analogs

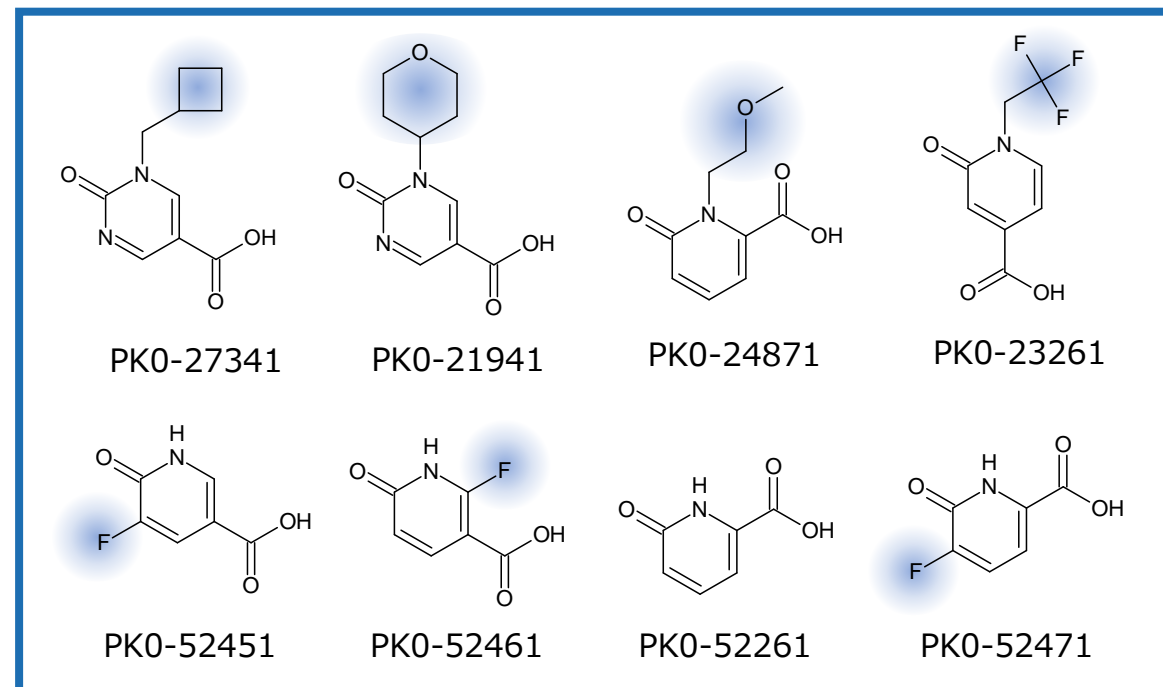


36
analog

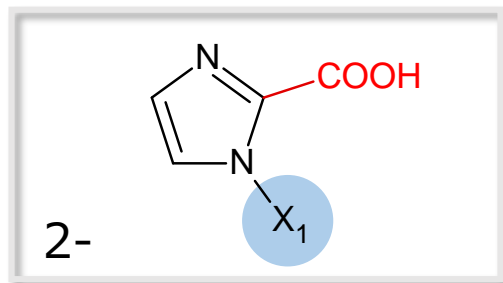


38
analog

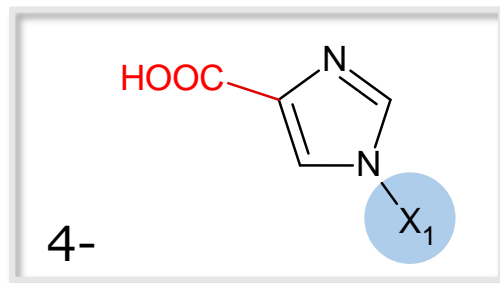
	X_1	X_2	X_3
	PK0-39601	PK0-38061	PK0-39581
	PK0-43181	PK0-39261	PK0-39591
	PK0-41621	PK0-38441	PK0-45001
	PK0-41651	PK0-38841	PK0-40931
	PK0-40951	PK0-38451	PK0-39271



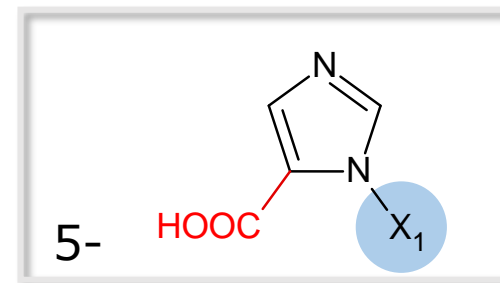
Imidazole-carboxylic acid analogs



33
analog



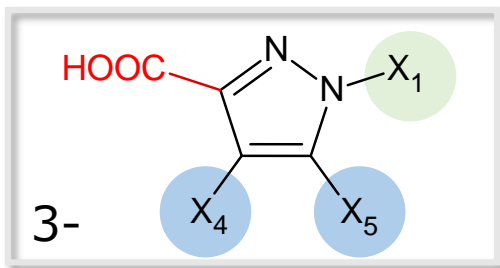
48
analog



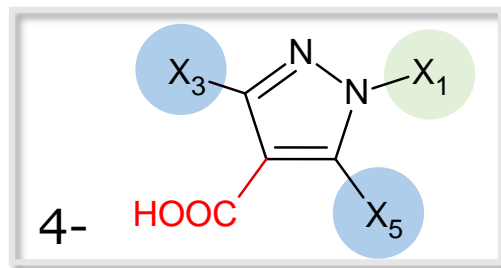
48
analog

X ₁	2-COOH	4-COOH	5-COOH
	PK0-59431	PK0-37421	PK0-37431
	PK0-25481	PK0-26181	PK0-37801
	PK0-27001	PK0-26991	PK0-35551
	PK0-25491	PK0-24471	PK0-26391
	PK0-27401	PK0-26241	PK0-30191

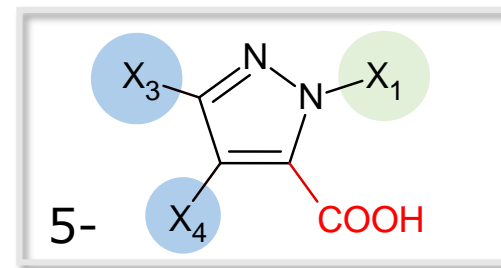
Pyrazole-carboxylic acid analogs



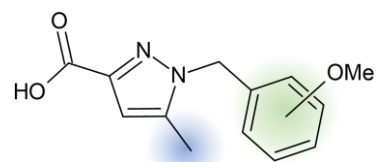
62
analog



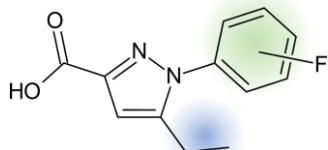
70
analog



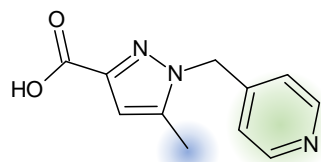
53
analog



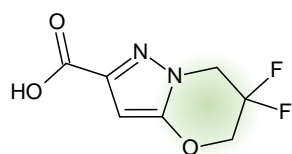
o- : PK0-59271
m- : PK0-59121
p- : PK0-59131



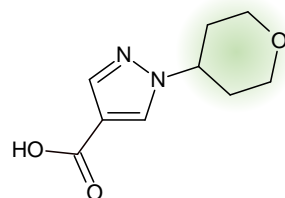
o- : PK0-59411
m- : PK0-59321
p- : PK0-59331



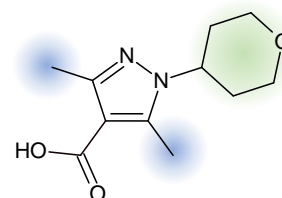
PK0-37691



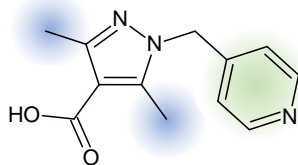
PK0-38871



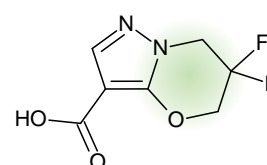
PK0-13341



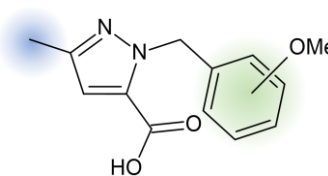
PK0-26151



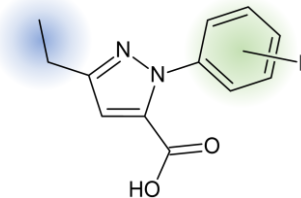
PK0-26761



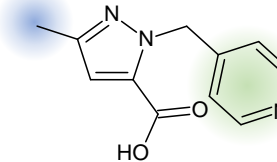
PK0-49321



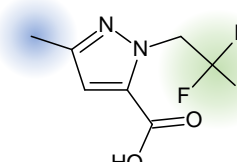
o- : PK0-59281
m- : PK0-59141
p- : PK0-59151



o- : PK0-59421
m- : PK0-59341
p- : PK0-59351



PK0-38131

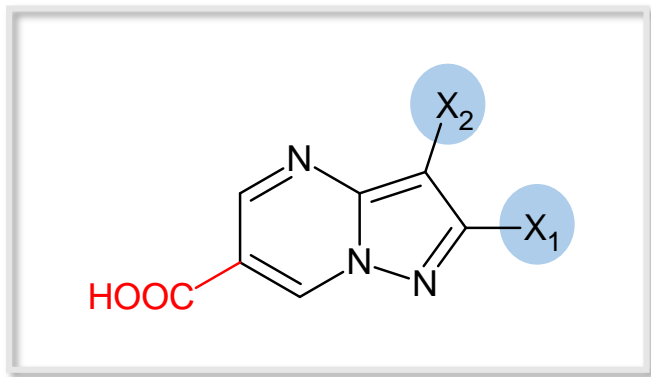


PK0-15191

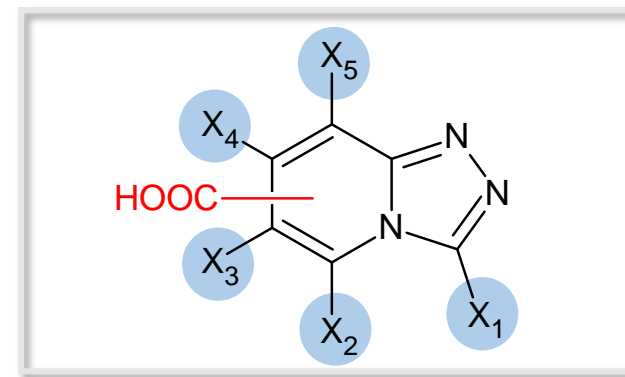
<参考情報 / K-BB構造が導入されている事例>

- Preparation of heteroaryl-substituted indole derivatives for restoring mutant p53 function, WO2021231474.
- Preparation of bicyclic heterocyclyl compounds as SOS1 modulators, WO2020180770.

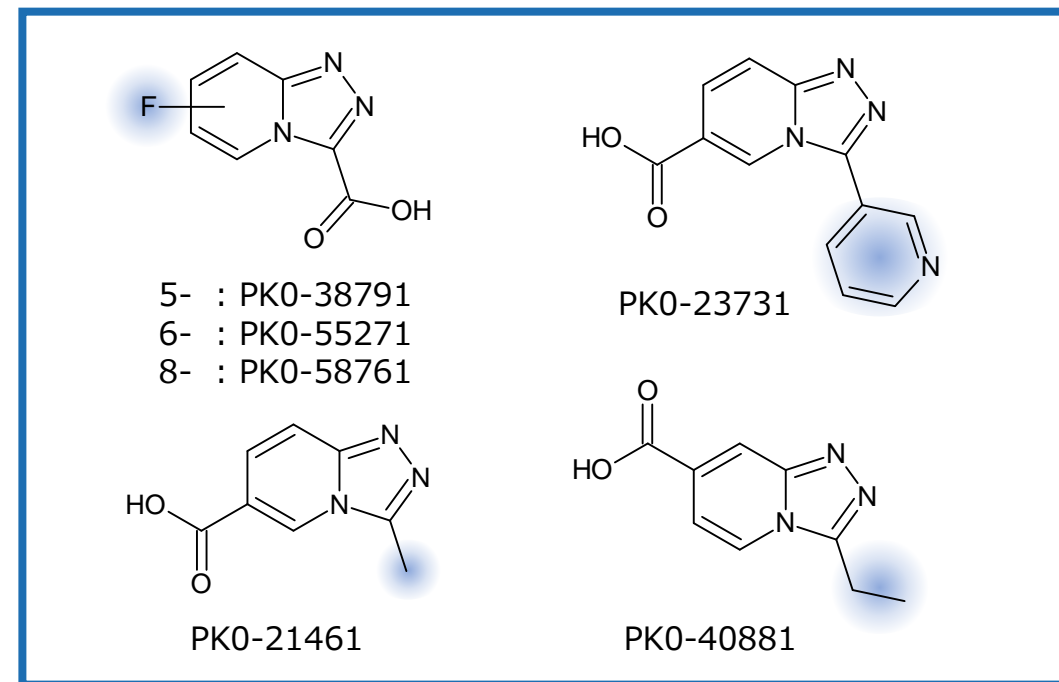
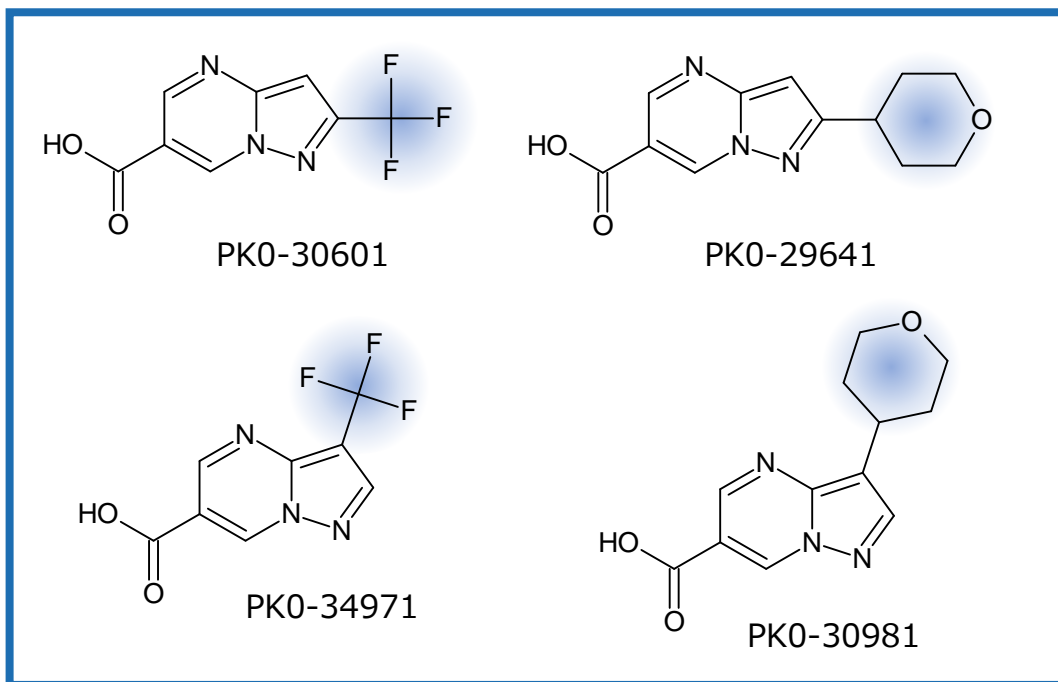
Fused heterocyclic-carboxylic acid analogs (1)



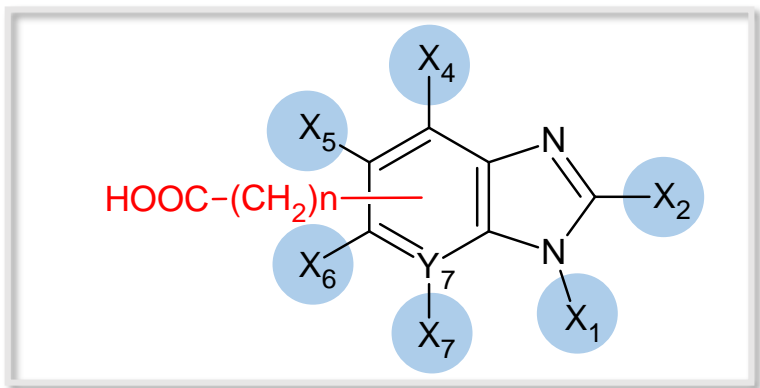
16
analog



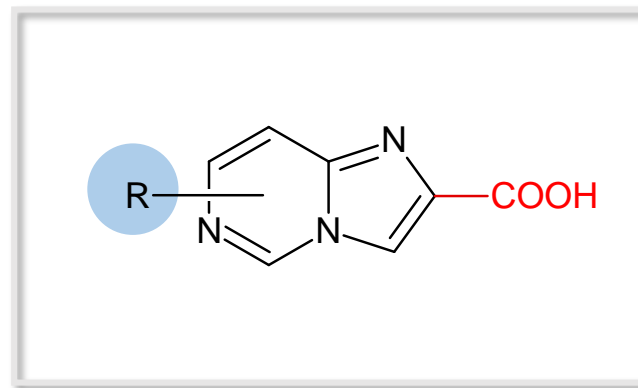
57
analog



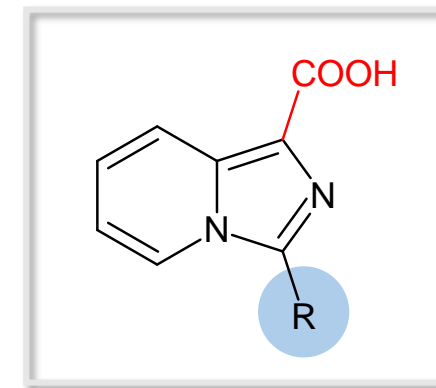
Fused heterocyclic-carboxylic acid analogs (2)



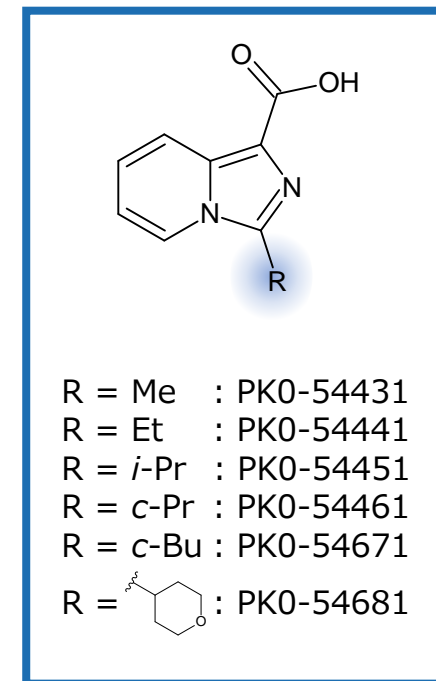
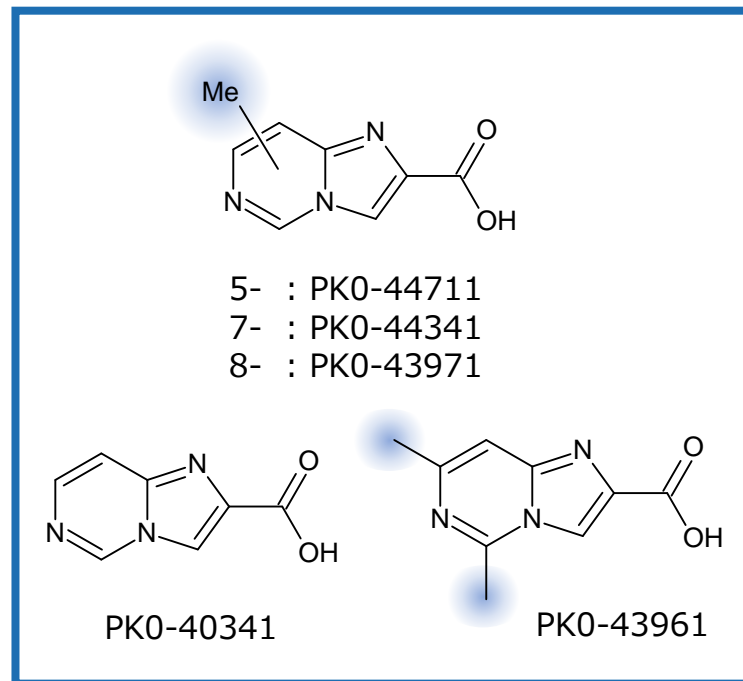
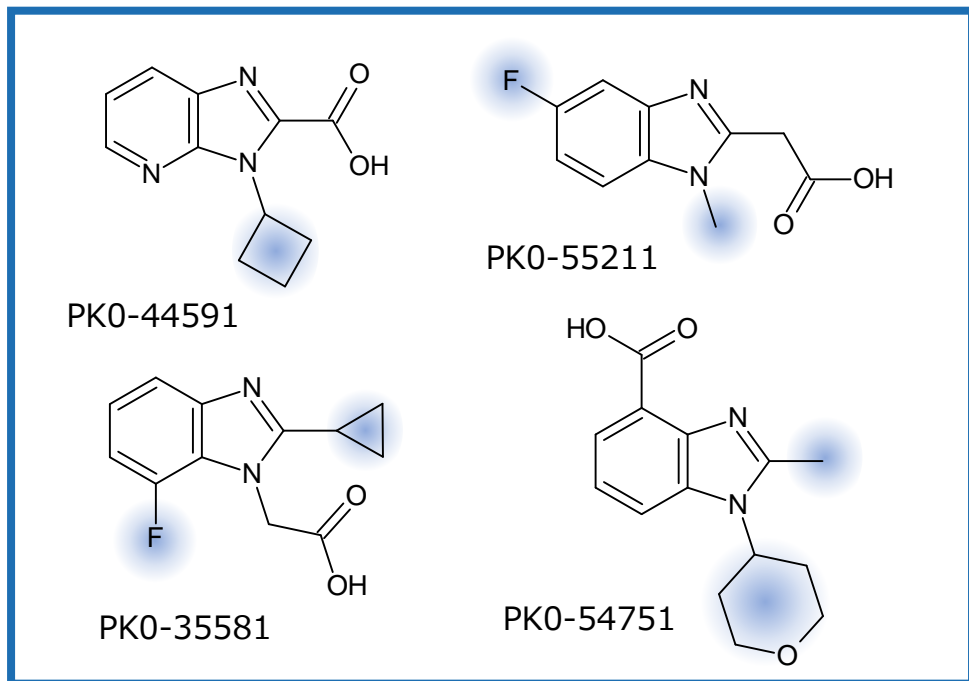
109
analog



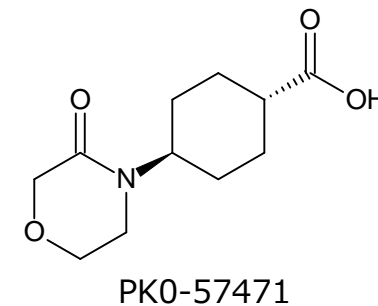
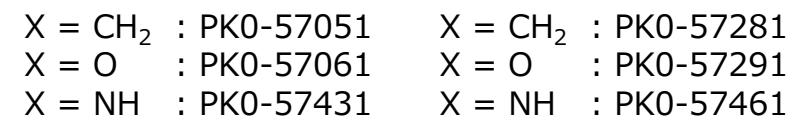
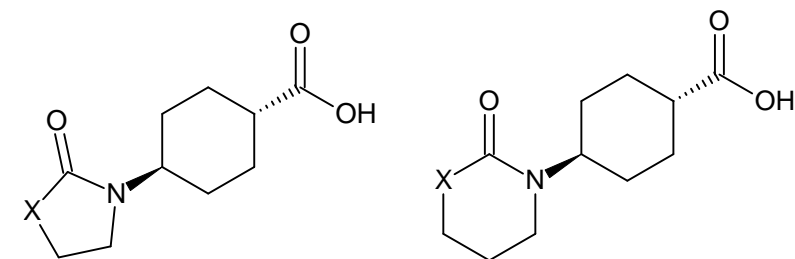
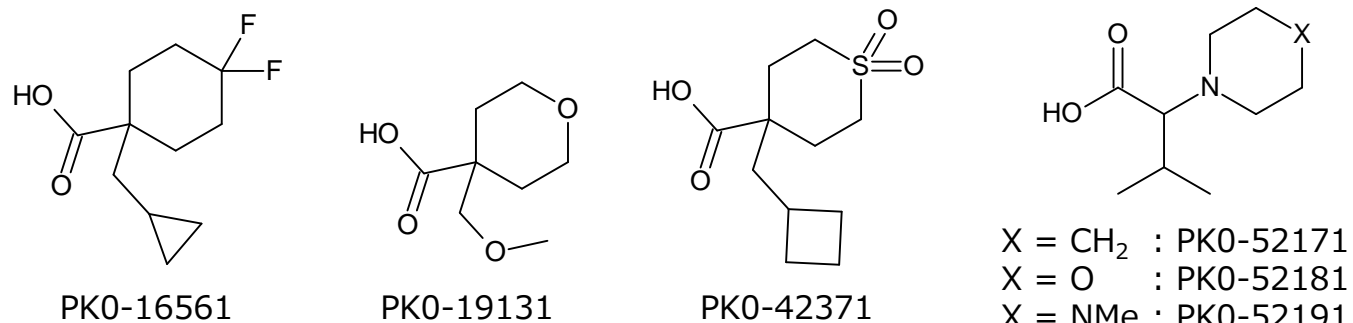
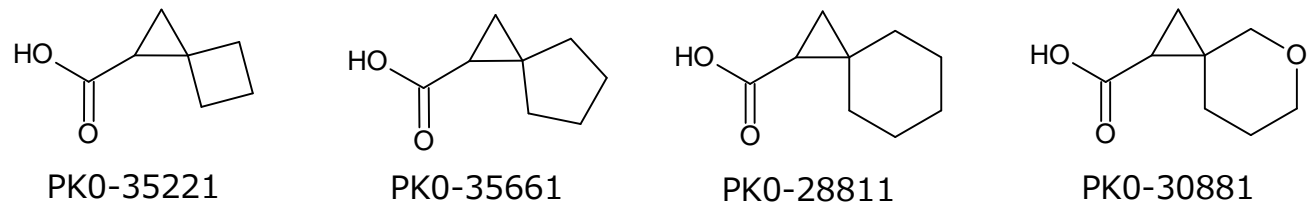
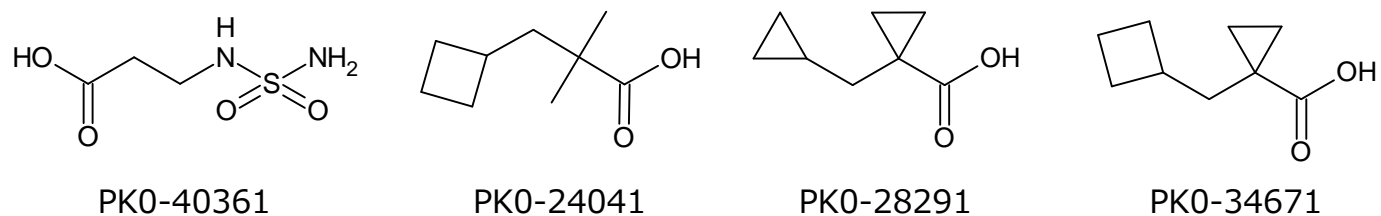
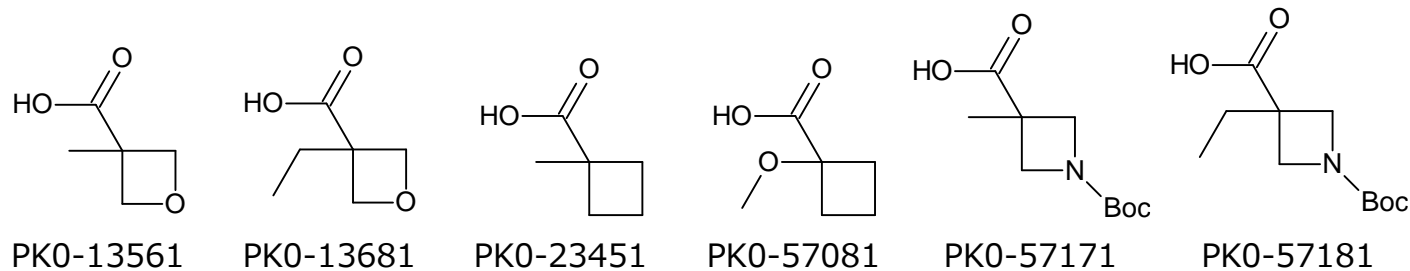
5
analog



6
analog



Aliphatic acid analogs



97
analog

<参考情報>

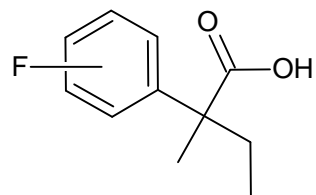
PK0-57051の構造が活用された報告

cis-1-Oxo-heterocyclcyl-4-amido cyclohexane derivatives
as NPY5 receptor antagonists

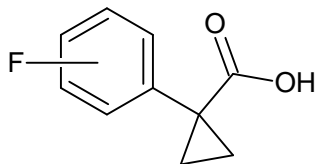
Bioorg. Med. Chem. Lett. **2014**, *24*, 1458-1461.

α,α -Disubstituted phenyl/pyridinylacetic acid analogs

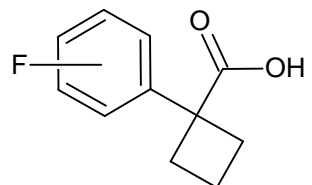
α,α -Disubstituted phenylacetic acid analogs



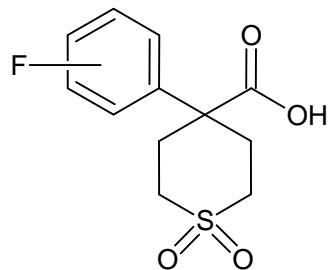
o- : PK0-55501
m- : PK0-55631
p- : PK0-55641



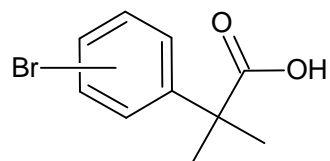
o- : PK0-10461
m- : PK0-10471
p- : PK0-10481



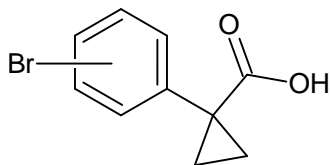
o- : PK0-10491
m- : PK0-10501
p- : PK0-10511



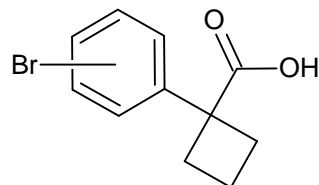
o- : PK0-53951
m- : PK0-53961
p- : PK0-53761



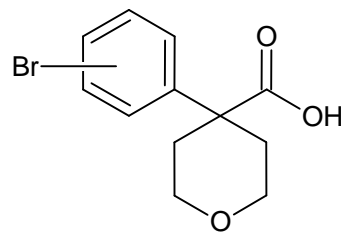
o- : PK0-10561
m- : PK0-08511
p- : PK0-08521



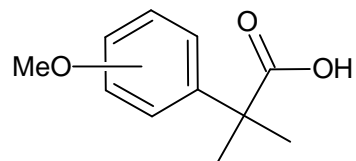
o- : PK0-10571
m- : PK0-10581
p- : PK0-10591



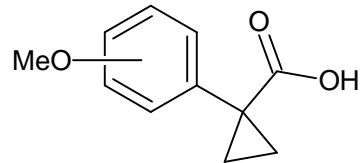
o- : PK0-10601
m- : PK0-10611
p- : PK0-10621



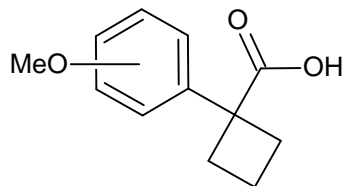
o- : PK0-18391
m- : PK0-16271
p- : PK0-16281



o- : PK0-10631
m- : PK0-10641
p- : PK0-10651



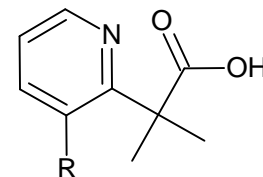
o- : PK0-10661
m- : PK0-10671
p- : PK0-10681



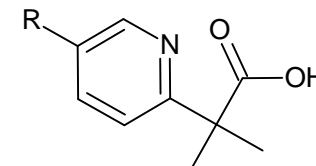
o- : PK0-10691
m- : PK0-10701
p- : PK0-10711

 **79**
analog

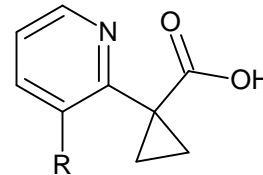
α,α -Disubstituted pyridinylacetic acid analogs



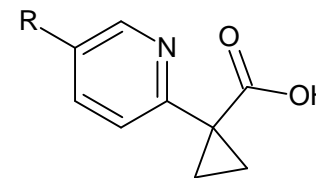
R = F : PK0-21371
R = OMe : PK0-23691



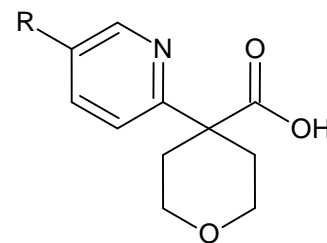
R = F : PK0-22241
R = OMe : PK0-22851



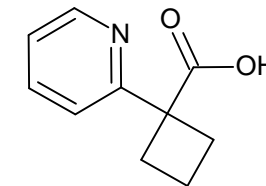
R = F : PK0-21681
R = Cl : PK0-40621
R = Me : PK0-21691
R = OMe : PK0-24051
R = CF₃ : PK0-40631



R = F : PK0-21671
R = Me : PK0-16681
R = OMe : PK0-23161



R = F : PK0-21701
R = OMe : PK0-22731



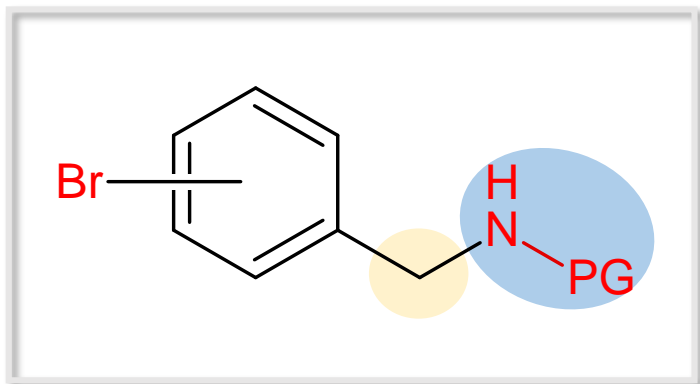
PK0-40601

 **22**
analog

キシダオリジナル ビルディングブロック (K-BB)

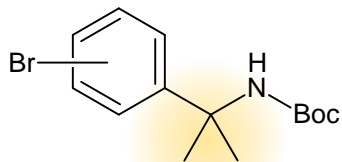
-Br化合物-

Br-benzene analogs (1)

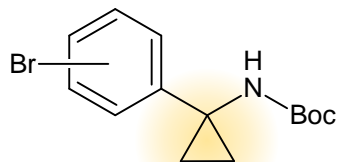


33
analog

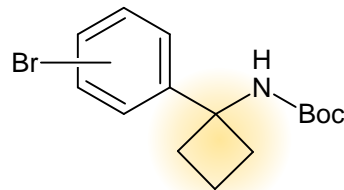
9
analog



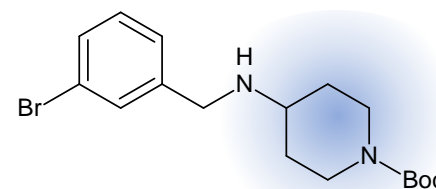
o- : PK0-09931
m- : PK0-09951
p- : PK0-08481



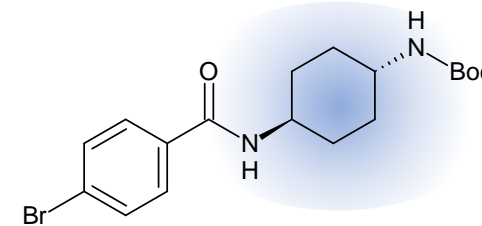
o- : PK0-09971
m- : PK0-09991
p- : PK0-10011



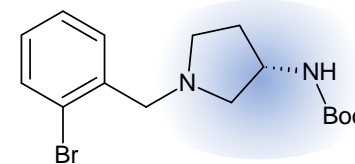
o- : PK0-10031
m- : PK0-10051
p- : PK0-10071



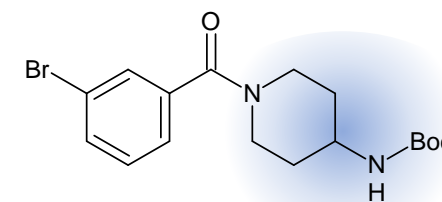
PK0-00571



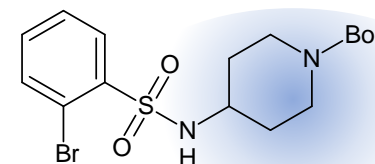
PK0-04571



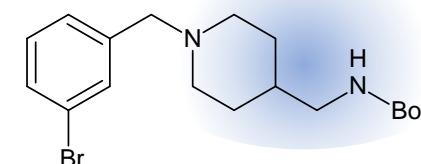
PK0-06021



PK0-03041

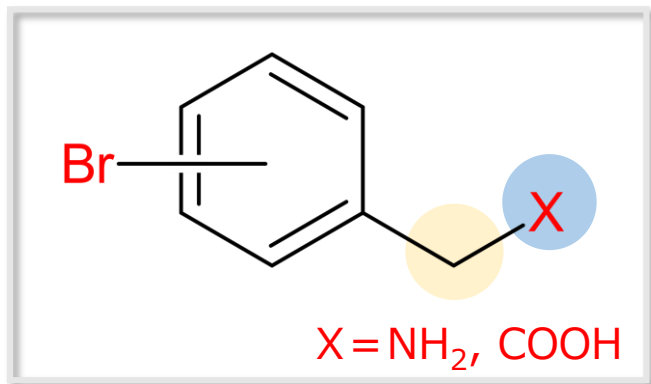


PK0-01971



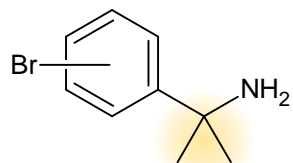
PK0-07061

Br-benzene analogs (2)

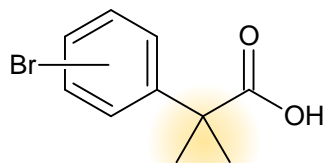


84
analog

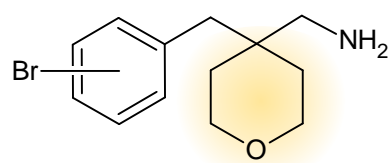
53
analog



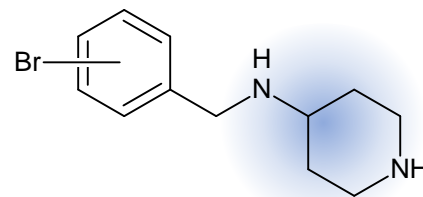
o- : PK0-09941
m- : PK0-09961
p- : PK0-08491



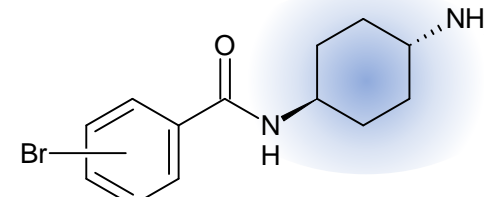
o- : PK0-10561
m- : PK0-08511
p- : PK0-08521



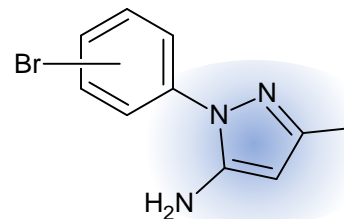
o- : PK0-19201
m- : PK0-17861
p- : PK0-17871



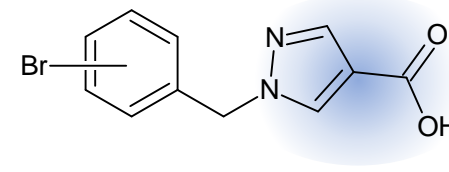
o- : PK0-00561
m- : PK0-00581
p- : PK0-00591



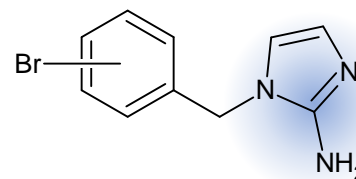
o- : PK0-05391
m- : PK0-04321
p- : PK0-04331



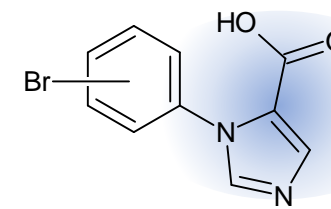
o- : PK0-11611
m- : PK0-11621
p- : PK0-11631



o- : PK0-12171
m- : PK0-12181
p- : PK0-12191

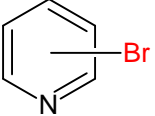
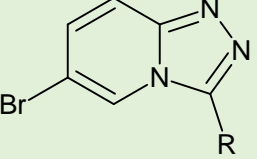
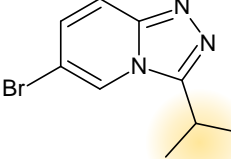
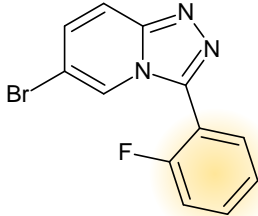
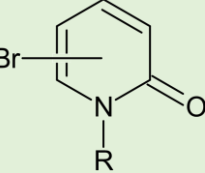
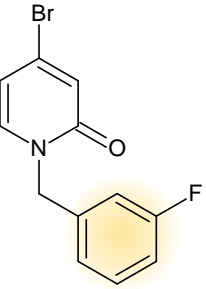
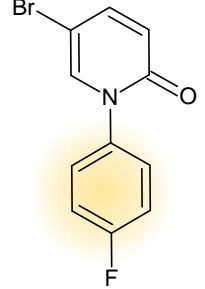
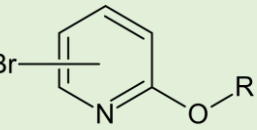
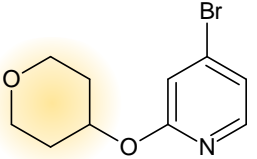
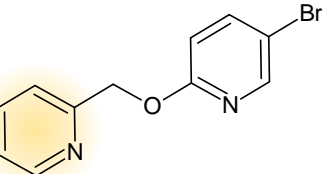


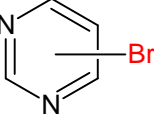
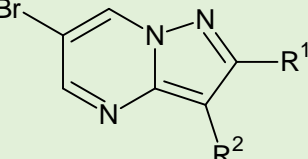
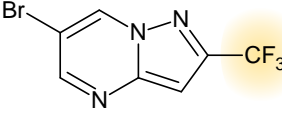
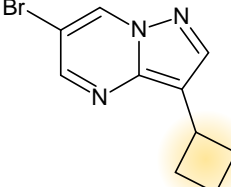
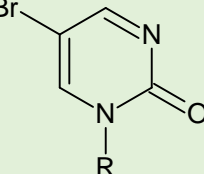
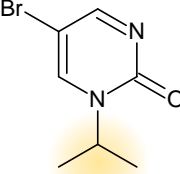
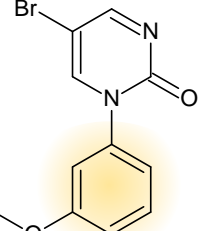
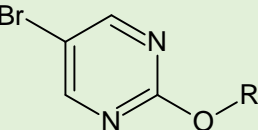
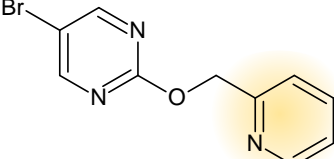
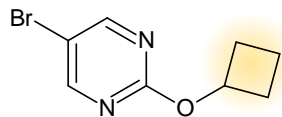
o- : PK0-32591
m- : PK0-32601
p- : PK0-31661



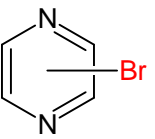
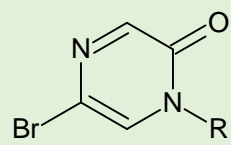
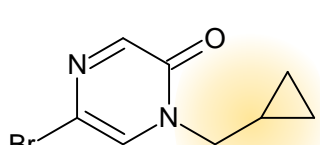
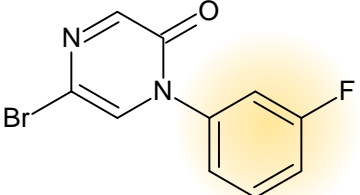
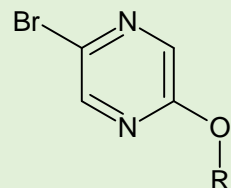
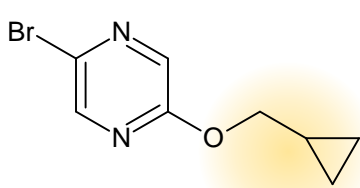
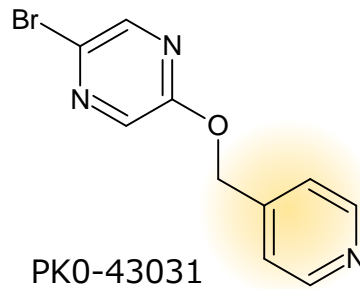
o- : PK0-24951
m- : PK0-24571
p- : PK0-24581

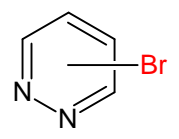
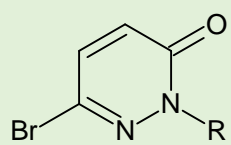
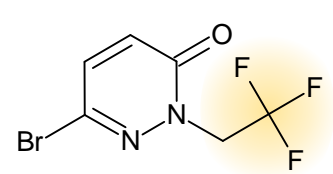
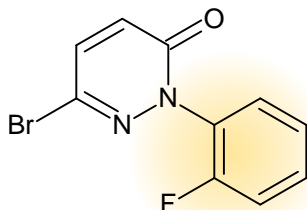
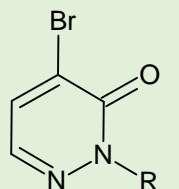
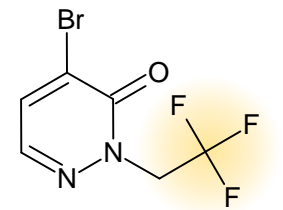
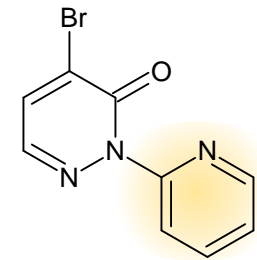
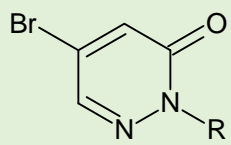
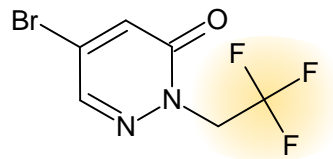
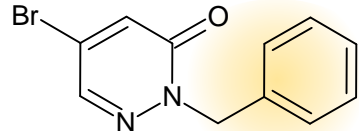
Br-heteroring analogs (1)

	Example-1	Example-2
 19 analogs	 PK0-18111	 PK0-20011
 77 analogs	 PK0-39411	 PK0-39431
 30 analogs	 PK0-42641	 PK0-39881

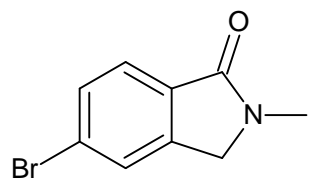
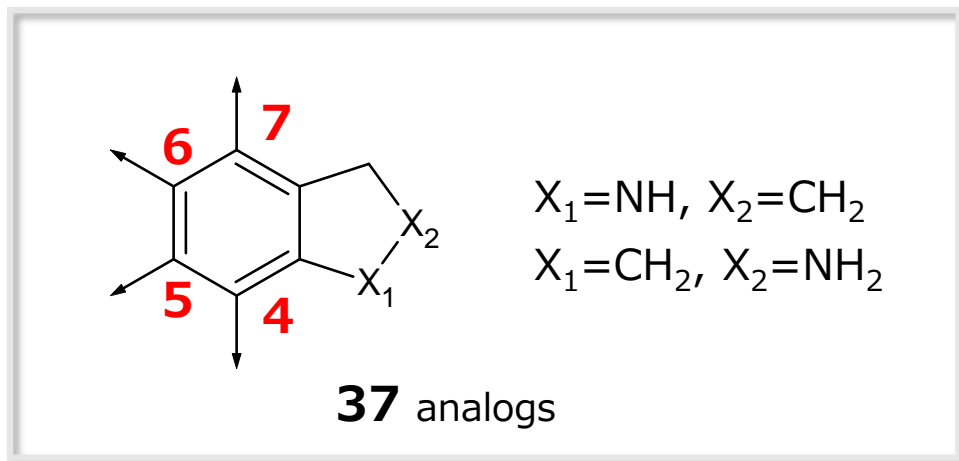
	Example-1	Example-2
 17 analogs	 PK0-30201	 PK0-30221
 23 analogs	 PK0-41161	 PK0-39491
 12 analogs	 PK0-41591	 PK0-41191

Br-heteroring analogs (2)

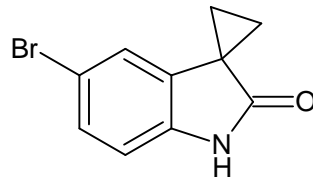
	Example-1	Example-2
 <p>23 analogs</p>	 <p>PK0-42151</p>	 <p>PK0-42471</p>
 <p>17 analogs</p>	 <p>PK0-42291</p>	 <p>PK0-43031</p>

	Example-1	Example-2
 <p>25 analogs</p>	 <p>PK0-41551</p>	 <p>PK0-49731</p>
 <p>25 analogs</p>	 <p>PK0-50161</p>	 <p>PK0-50401</p>
 <p>27 analogs</p>	 <p>PK0-42551</p>	 <p>PK0-41531</p>

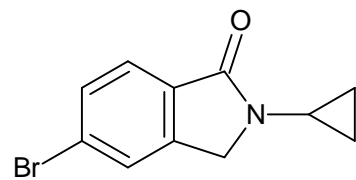
Br-bicyclic analogs (1)



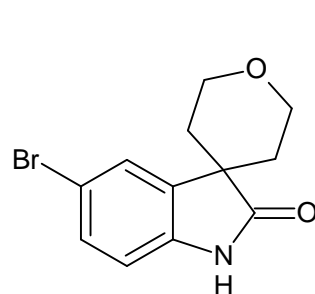
PK0-27621



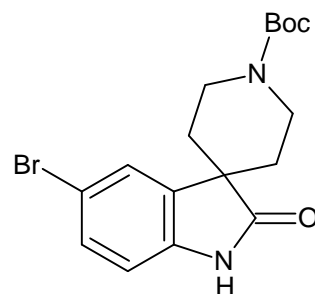
PK0-45911



PK0-27641



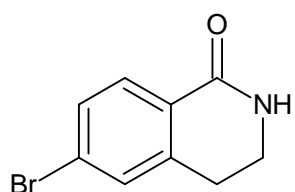
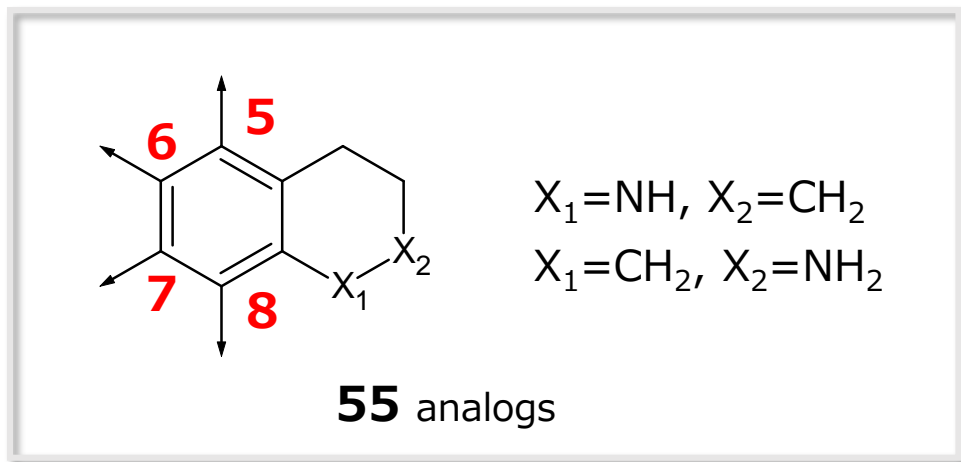
PK0-46271



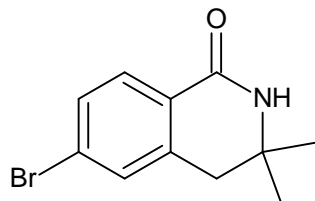
PK0-31741

	4-Br	5-Br	6-Br	7-Br
	PK0-27631	PK0-27621	PK0-27891	PK0-32711
	PK0-46571	PK0-45911	PK0-46771	PK0-47161
	PK0-27651	PK0-27641	PK0-27901	PK0-32721
	PK0-46921	PK0-46271	PK0-46931	PK0-47221
	PK0-33081	PK0-31741	PK0-31751	PK0-32641

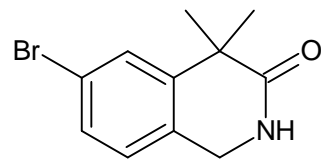
Br-bicyclic analogs (2)



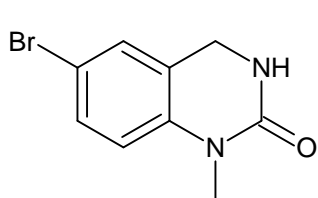
PKO-36311



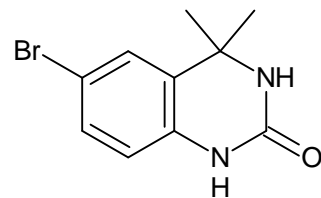
PKO-49051



PKO-37901



PKO-37081



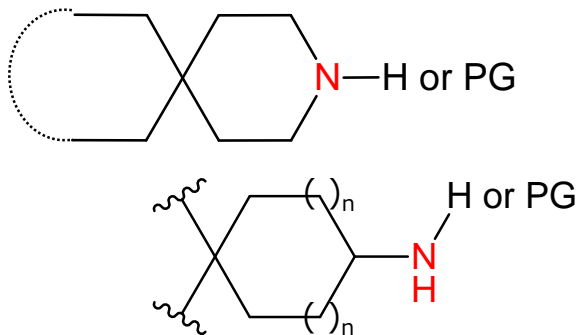
PKO-43461

	5-Br	6-Br	7-Br	8-Br
	PKO-36321	PKO-36311	PKO-36301	PKO-38961
	PKO-49711	PKO-49051	PKO-49041	PKO-49261
	PKO-43471	PKO-37901	PKO-37101	PKO-37911
	PKO-37091	PKO-37081	PKO-37071	PKO-37881
	PKO-49851	PKO-43461	PKO-38491	PKO-45971

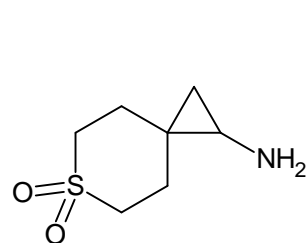
キシダオリジナル ビルディングブロック (K-BB)

-スピロ骨格化合物-

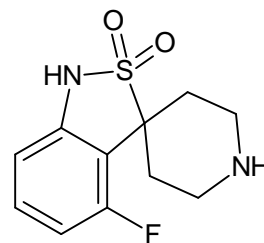
Spiro compounds (1)



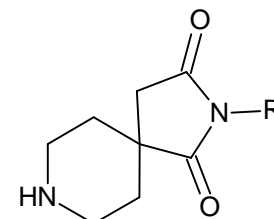
224
analogs



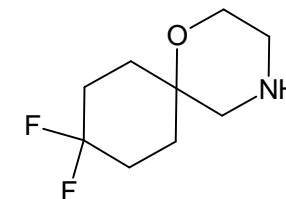
PK0-49961



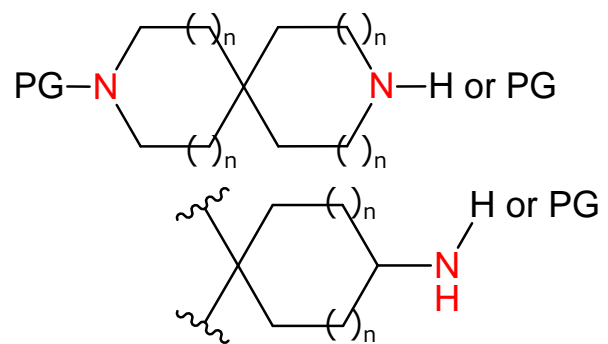
PK0-54241



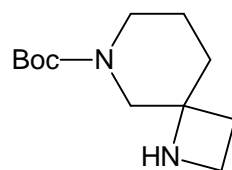
R = Me : PK0-59301
R = Et : PK0-59401



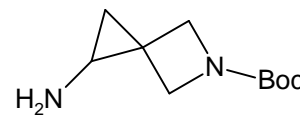
PK0-59481



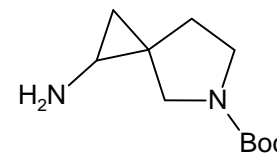
151
analogs



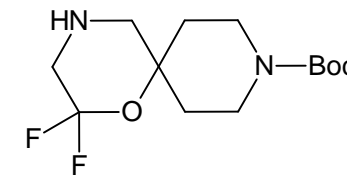
PK0-50091



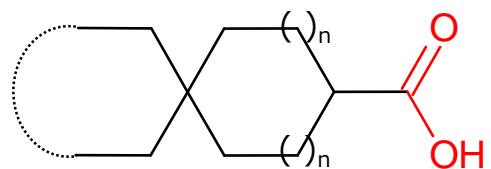
PK0-50371



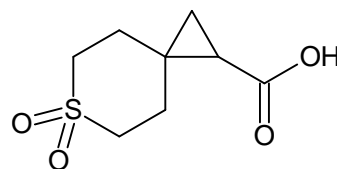
PK0-50381



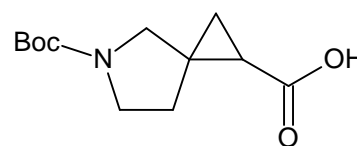
PK0-59081



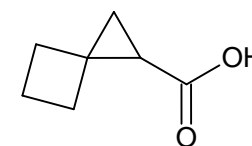
19
analogs



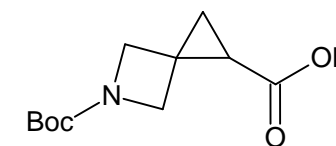
PK0-45981



PK0-33151

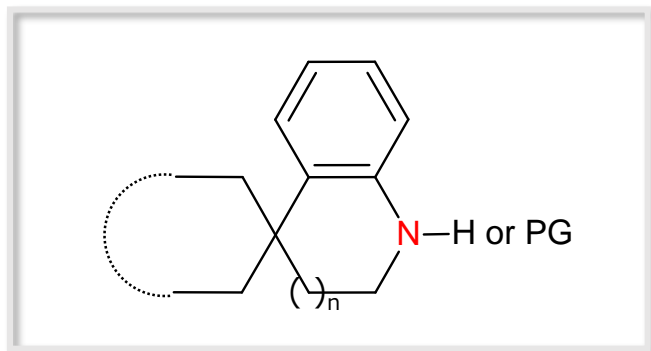


PK0-35221

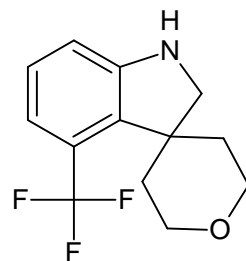


PK0-44561

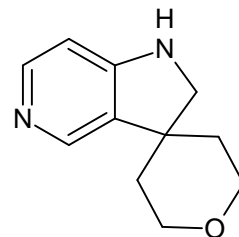
Spiro compounds (2)



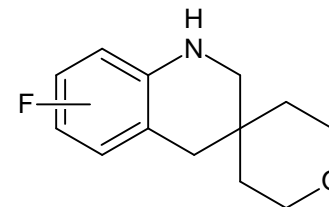
110
analog



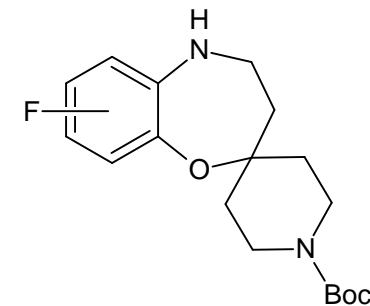
PK0-47041



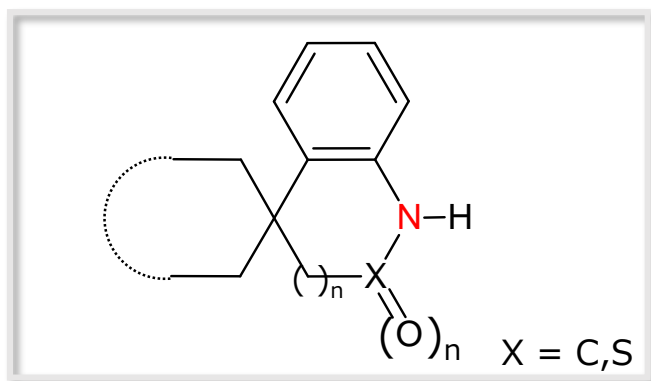
PK0-51881



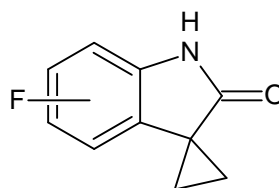
5- : PK0-22181
6- : PK0-23591
7- : PK0-22791
8- : PK0-22801



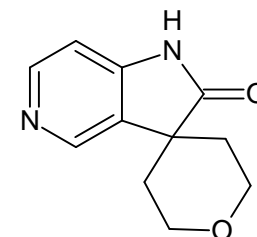
6- : PK0-48471
7- : PK0-48481
8- : PK0-48491
9- : PK0-48501



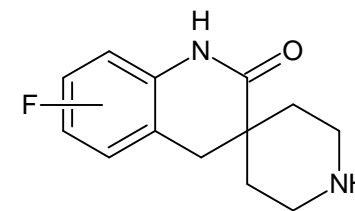
115
analog



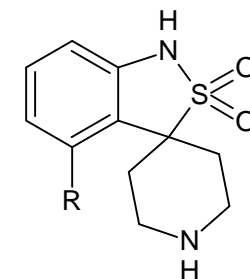
4- : PK0-46541
5- : PK0-45891
6- : PK0-45901
7- : PK0-47351



PK0-51781

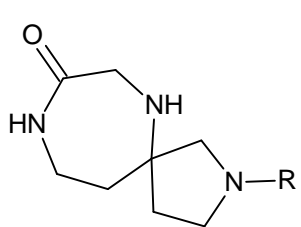


5- : PK0-21291
6- : PK0-23581
7- : PK0-20871
8- : PK0-23211

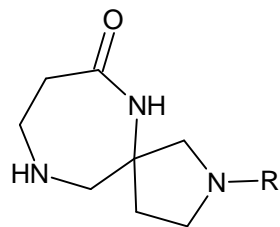


R = H : PK0-53941
R = F : PK0-54241

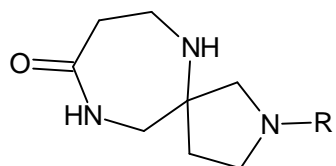
Spiro compounds – オリジナリティが高いBB –



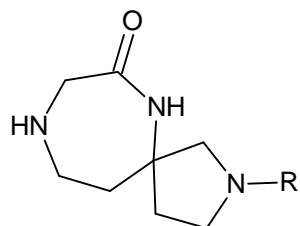
R = H : PK0-52701
R = Boc : PK0-52721



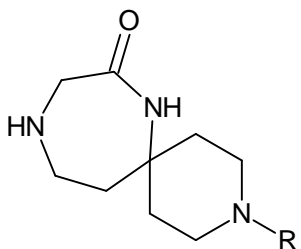
R = H : PK0-52411
R = Boc : PK0-52431



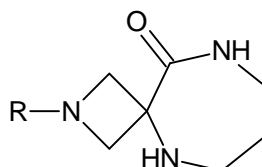
R = H : PK0-52861
R = Boc : PK0-52921



R = H : PK0-52661
R = Boc : PK0-52561

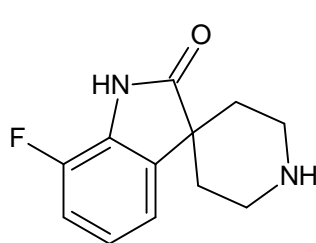


R = H : PK0-52671
R = Boc : PK0-52571

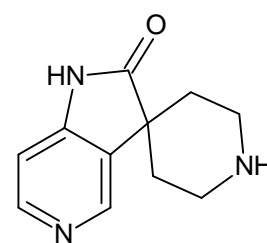


R = H : PK0-52851
R = Boc : PK0-52911

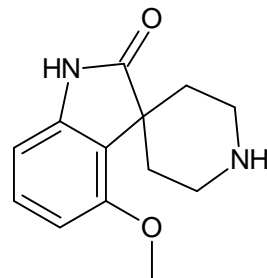
etc.



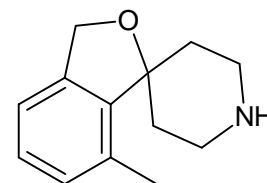
PK0-55261



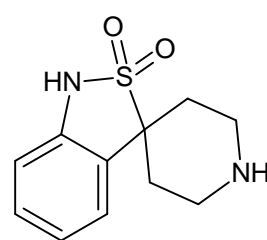
PK0-51771



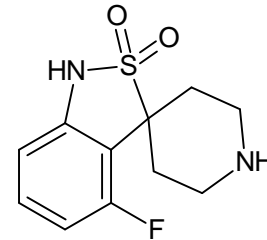
PK0-51651



PK0-50541

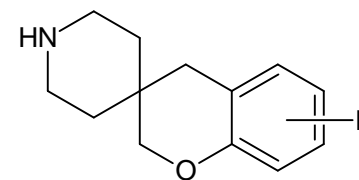


PK0-53941

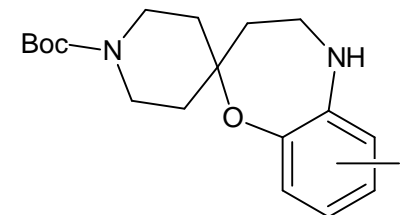


PK0-54241

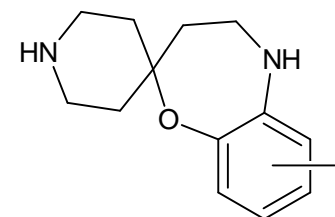
etc.



5- : PK0-53391
6- : PK0-53131
7- : PK0-53121
8- : PK0-53111

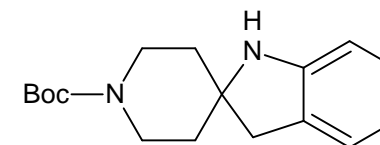


6- : PK0-48471
7- : PK0-48481
8- : PK0-48491
9- : PK0-48501



6- : PK0-48571
7- : PK0-48251
8- : PK0-48581
9- : PK0-48591

etc.



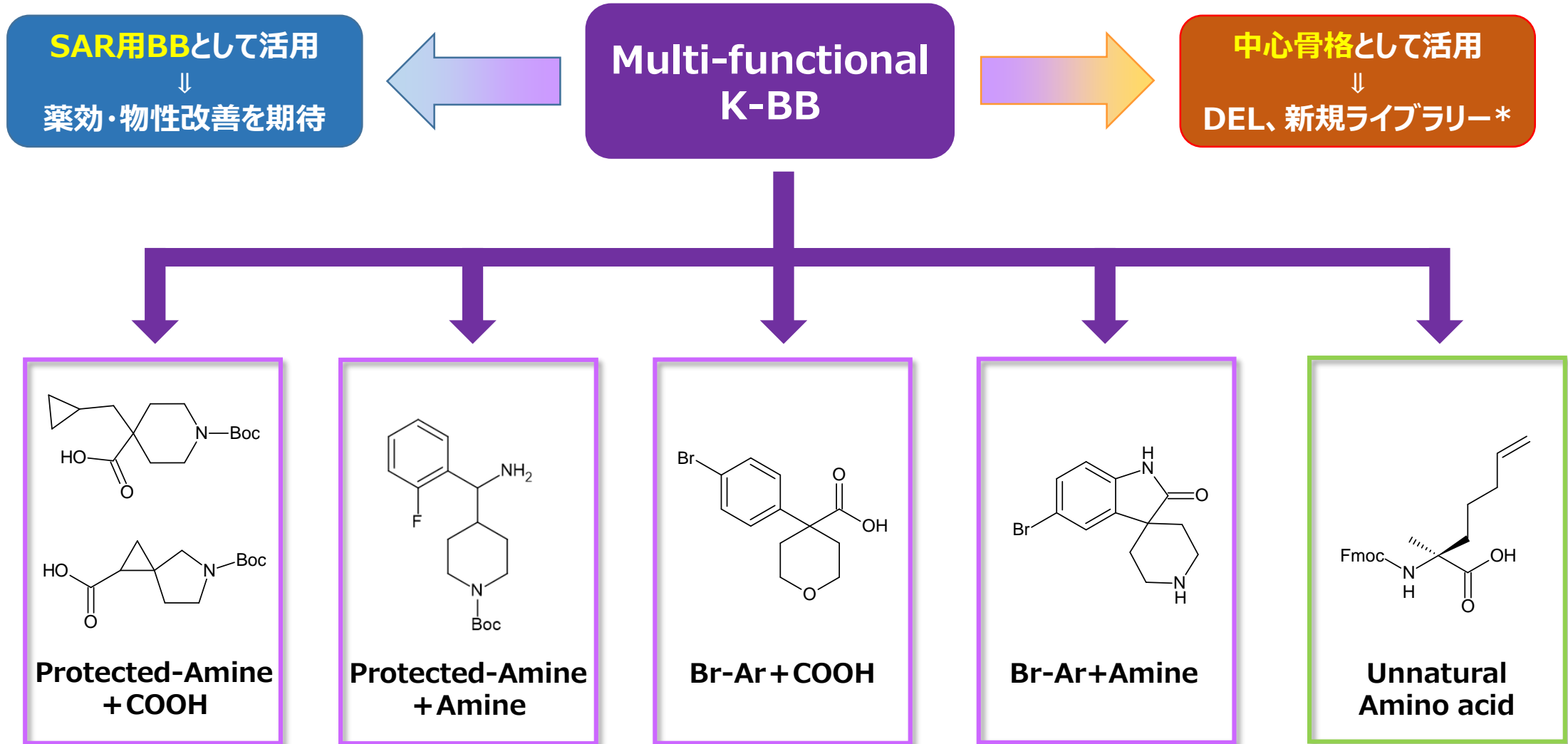
R = H : PK0-48341
R = Boc : PK0-48331

etc.

キシダオリジナル ビルディングブロック (K-BB)

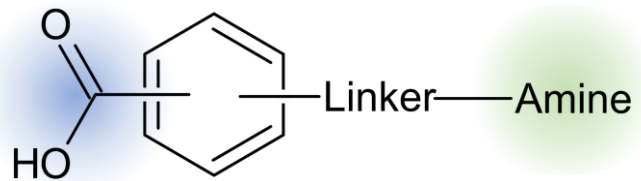
-中心骨格化合物-

Multi-functional building blocks

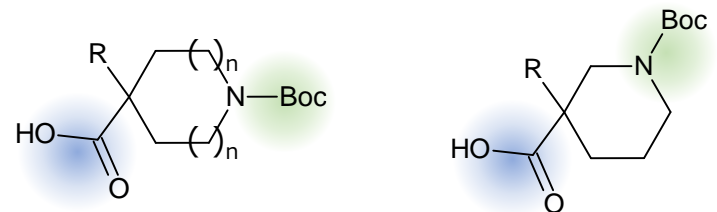


*お客様がお持ちのBBと組み合わせることで、オリジナルライブラリーの作製が可能です。
当社の平行合成サービスもご利用いただけます。

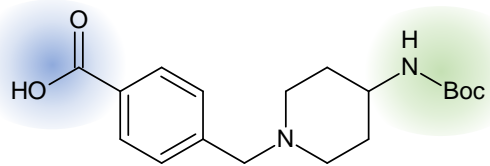
"Protected amine + COOH" analogs



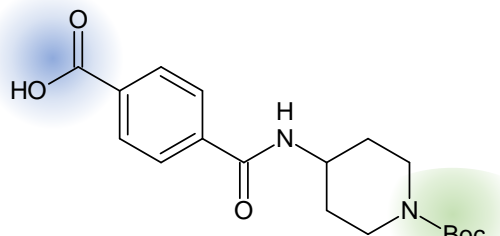
10
analog



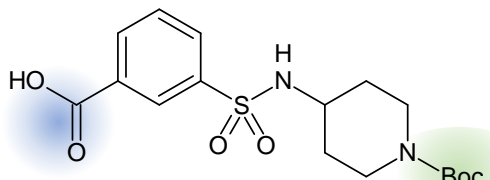
40
analog



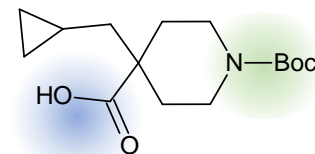
PK0-03641



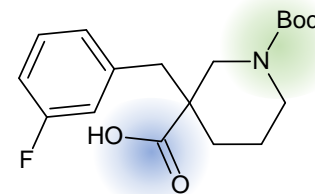
PK0-02081



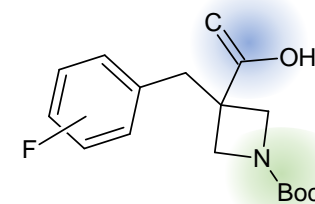
PK0-02011



PK0-31981

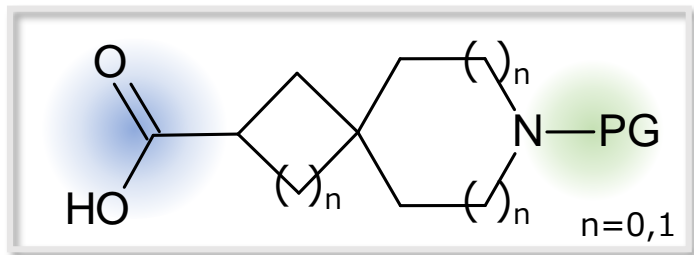


PK0-53681

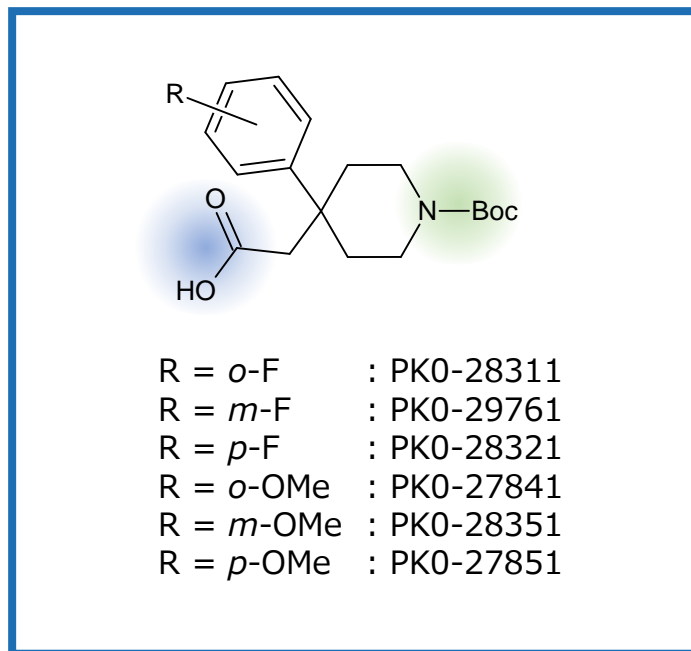
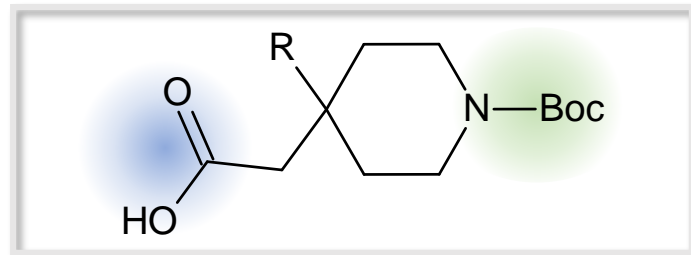
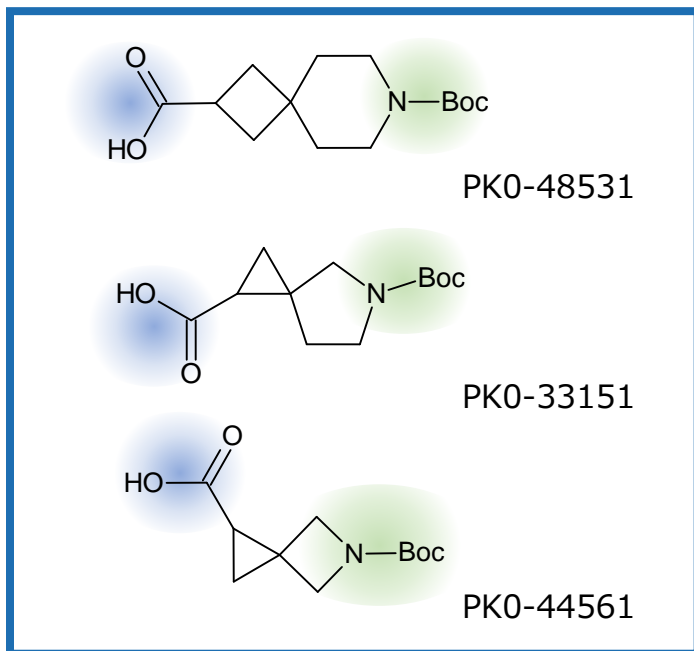


2- : PK0-55171
3- : PK0-55181
4- : PK0-55191

"Protected amine + COOH" analogs



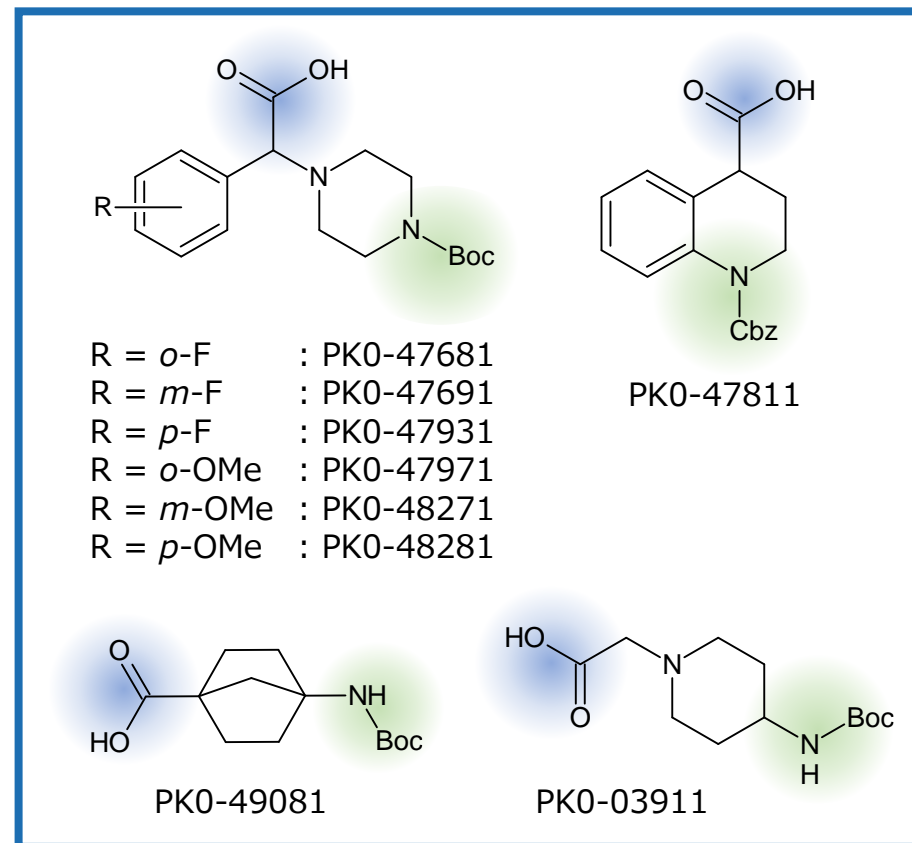
8
analog



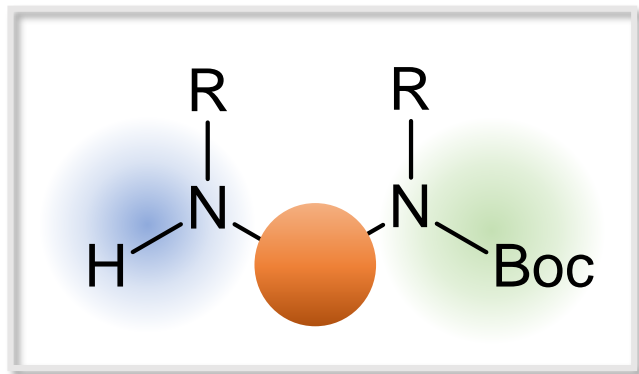
Others



11
analog



“Protected amine + Amine” analogs



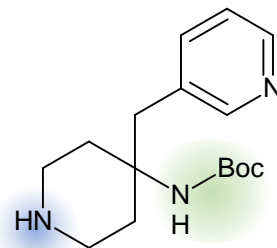
448
analog

<参考情報 / K-BB構造及び類縁構造が使用されている事例>

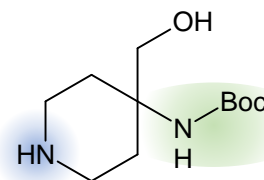
N-Boc-ジアミン化合物をPROTACリンカーとして利用

Direct-to-Biology Accelerates PROTAC Synthesis and the Evaluation of Linker Effects on Permeability and Degradation

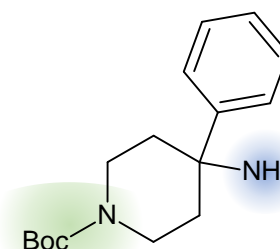
ACS Med. Chem. Lett. 2022, 13, 1182-1190.



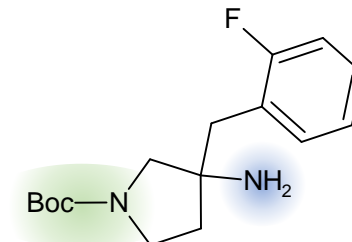
PK0-32781



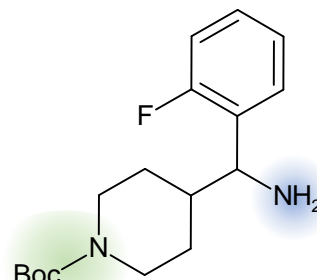
PK0-24211



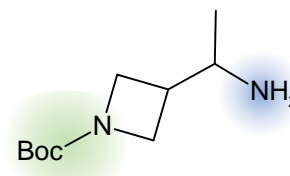
PK0-31841



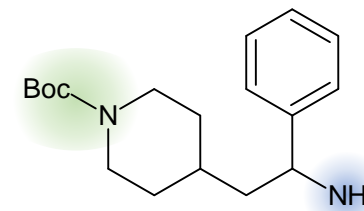
PK0-31841



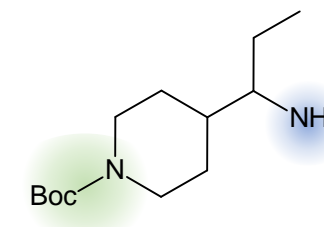
PK0-44741



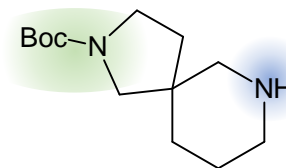
PK0-48211



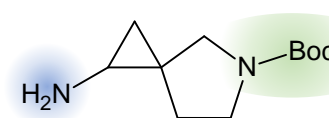
PK0-45731



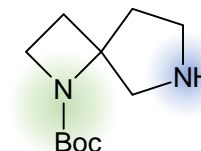
PK0-59521



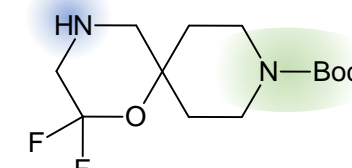
PK0-48551



PK0-50381



PK0-52621



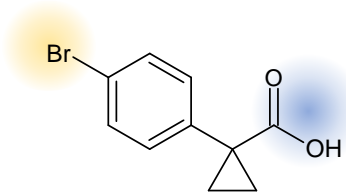
PK0-59081

"Bromide + COOH" analogs

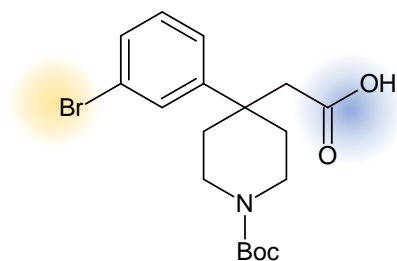
Br + Alkyl-COOH



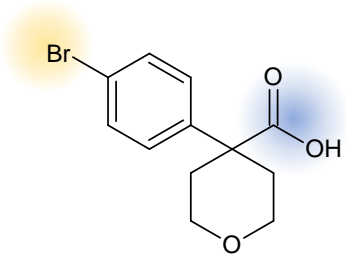
26
analogos



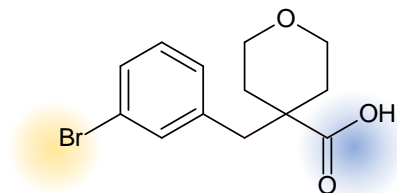
PKO-10591



PKO-28341



PKO-16281

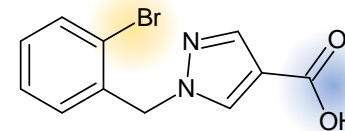


PKO-18511

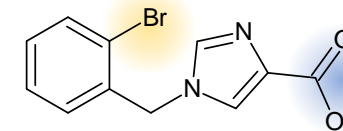
Br + Heteroaryl-COOH



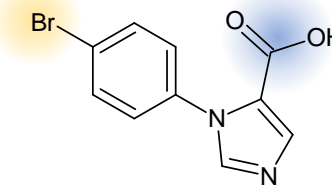
26
analogos



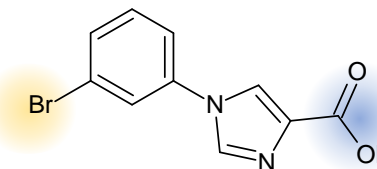
PKO-12171



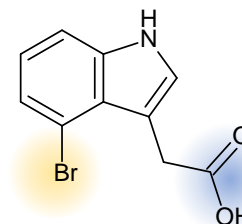
PKO-26201



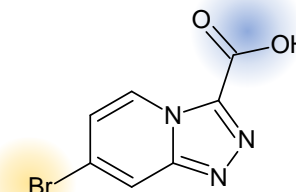
PKO-24581



PKO-26281



PKO-38221



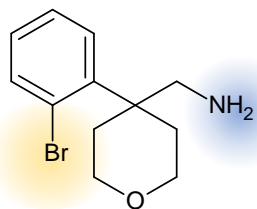
PKO-58771

"Bromide + Amine" analogs

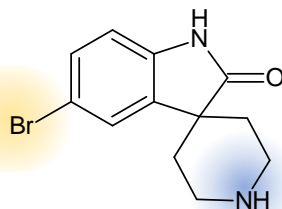
Br + Free-Amine



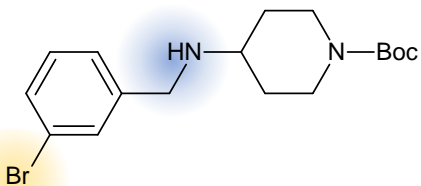
112
analogs



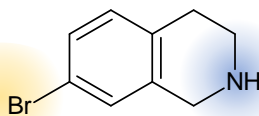
PKO-16851



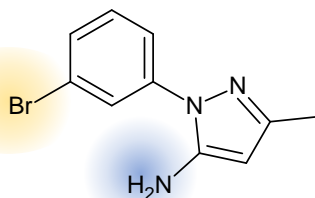
PKO-31781



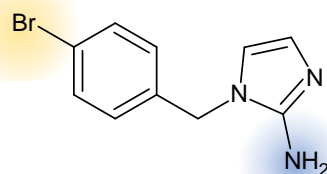
PKO-00571



PKO-53341



PKO-11621

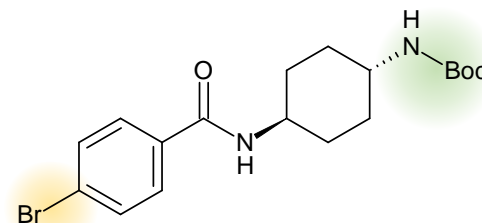


PKO-31661

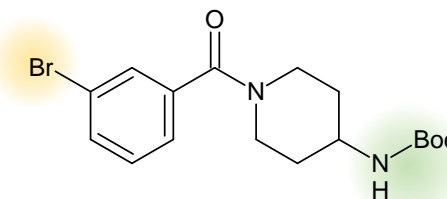
Br + Protected-Amine



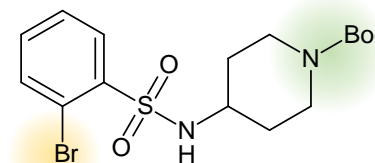
40
analogs



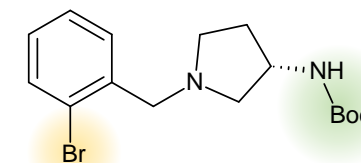
PKO-04571



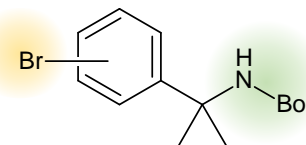
PKO-03041



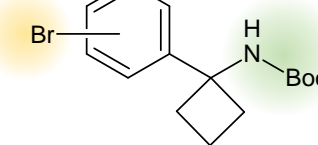
PKO-01971



PKO-06021



o- : PKO-09931
m- : PKO-09951
p- : PKO-08481



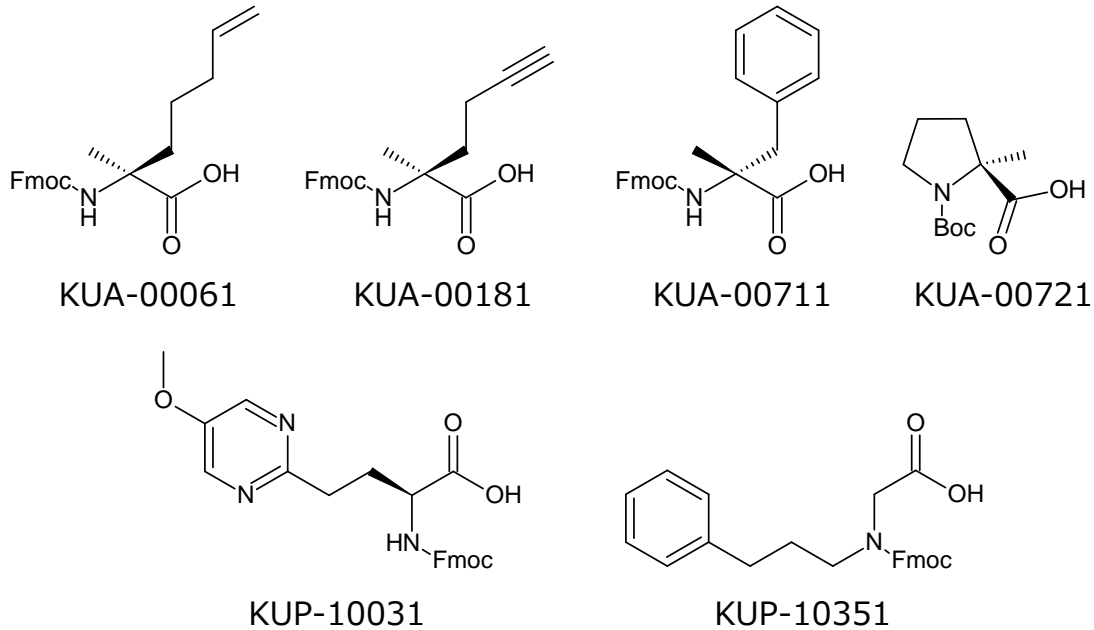
o- : PKO-10031
m- : PKO-10051
p- : PKO-10071

Unnatural amino acid

N-Protected Unnatural Amino Acid



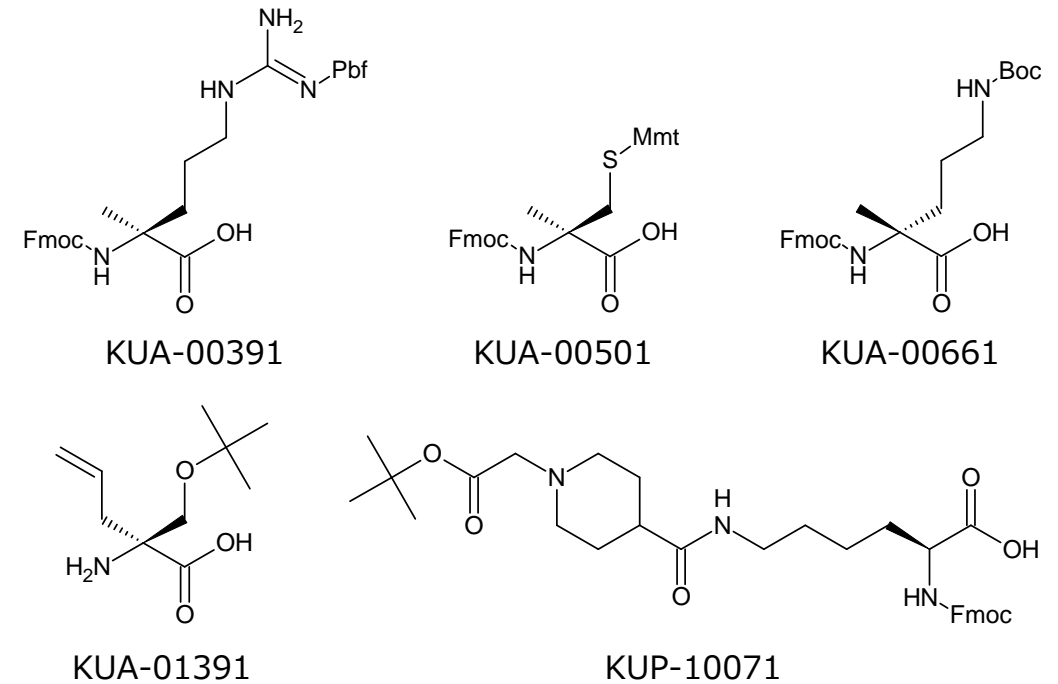
55
analog



Side Chain & N-Protected Unnatural Amino Acid



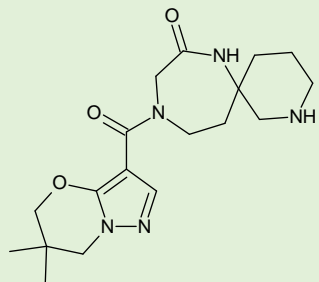
25
analog



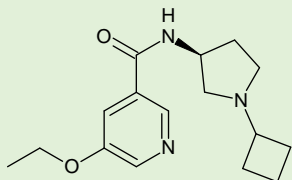
当社のアミノ酸事業での取り扱っているユニークな非天然型アミノ酸です
KUA化合物は、当社が特許使用権を有する丸岡触媒を用いて合成しています

Kishida original virtual library (K-LB)

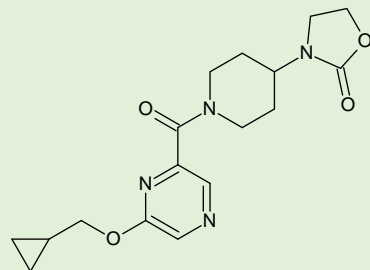
2-component Library



MW 361.45
Fsp3 0.72

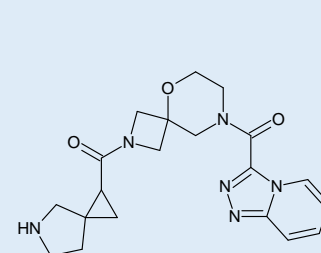


MW 289.38
Fsp3 0.63

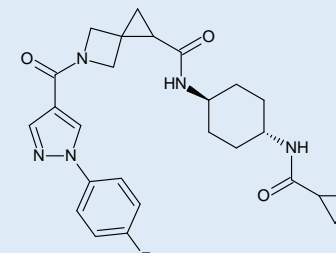


MW 346.39
Fsp3 0.65

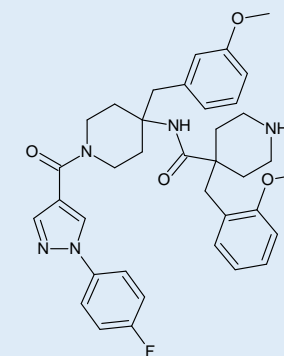
3-component Library



MW 396.45
Fsp3 0.60



MW 479.56
Fsp3 0.54



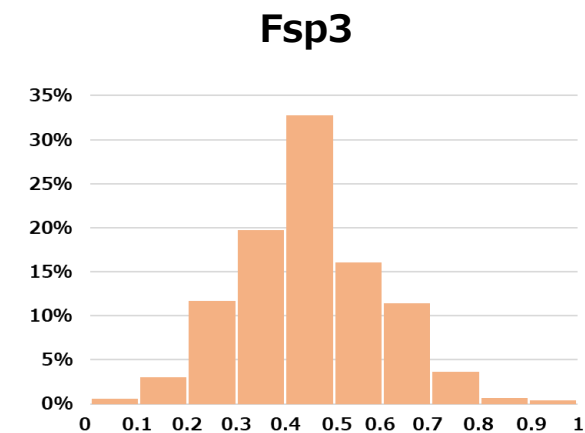
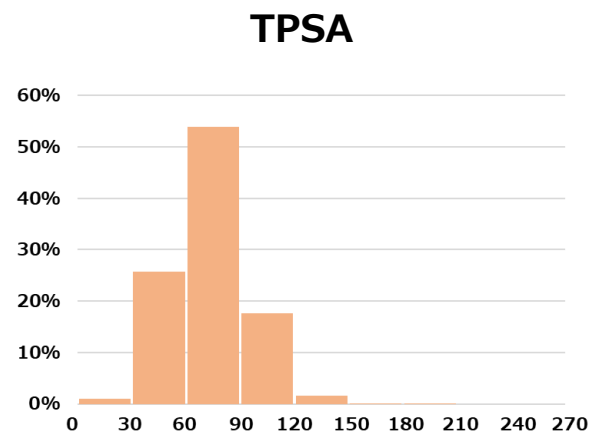
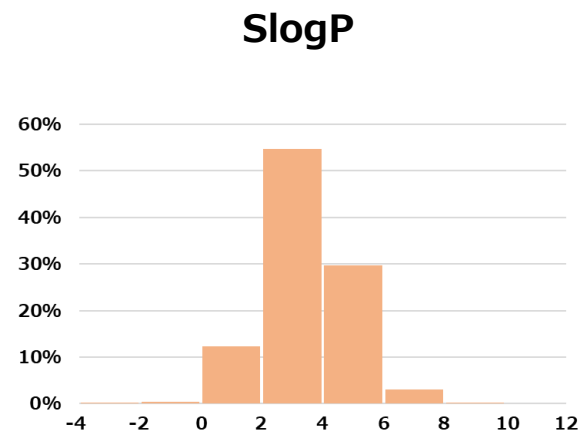
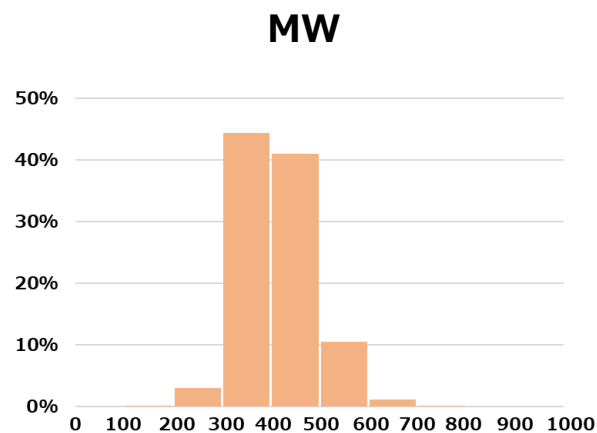
MW 639.77
Fsp3 0.38

K-LBの特徴

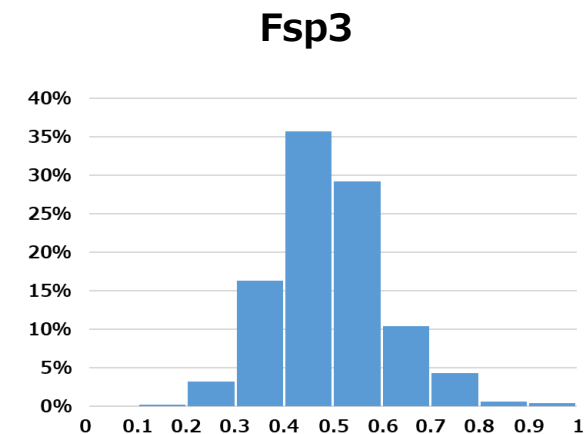
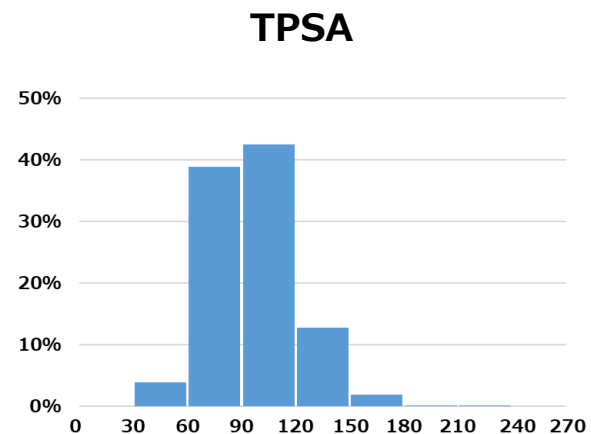
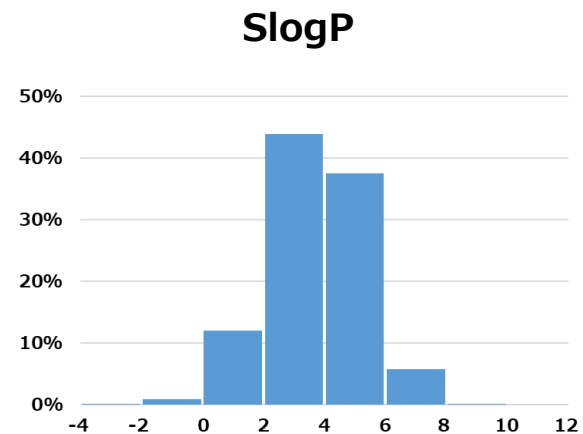
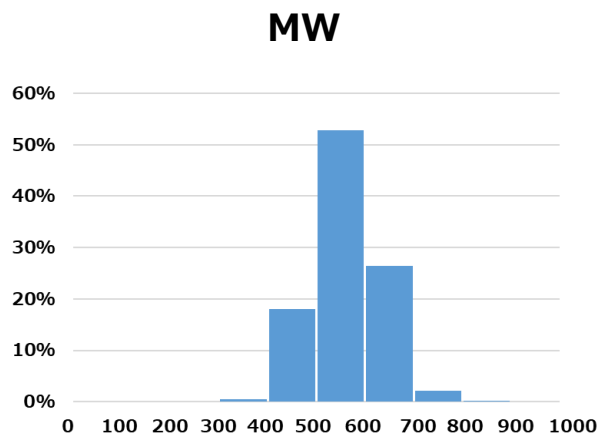
- 2成分結合ライブラリー：約500万化合物
- 3成分結合ライブラリー：約30万化合物
- 構成素子：キシダオリジナルビルディングブロック (K-BB)
- 反応形式：縮合反応 (アミド化)
- ファイル形式：SD file

Kishida original virtual library (K-LB) の物理化学的特性分布

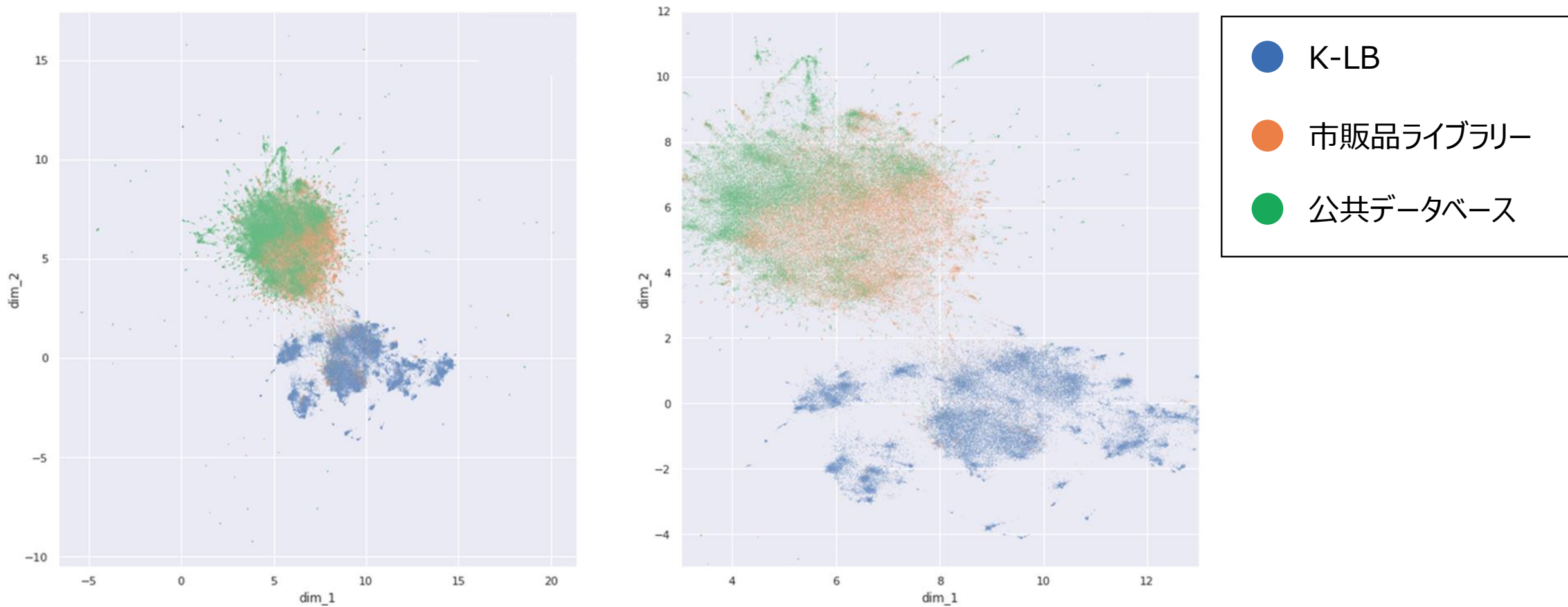
2-Component Library



3-Component Library

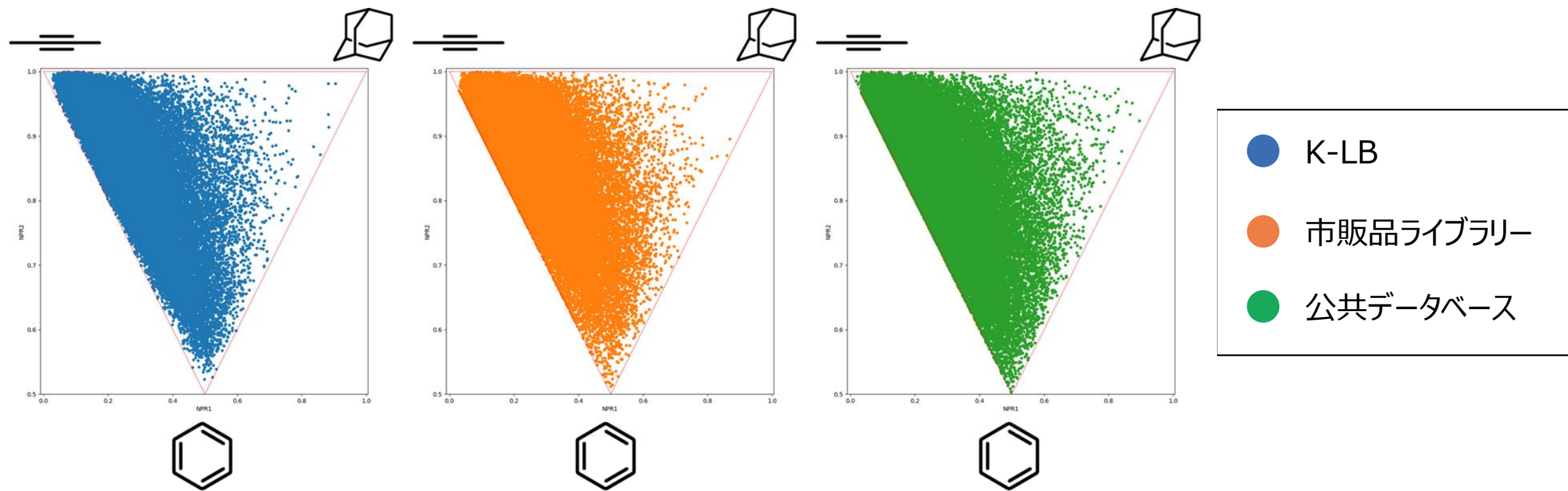


Chemical space



市販品ライブラリー及び公共データベースとの比較より、K-LBは異なるケミカルスペースを保有している

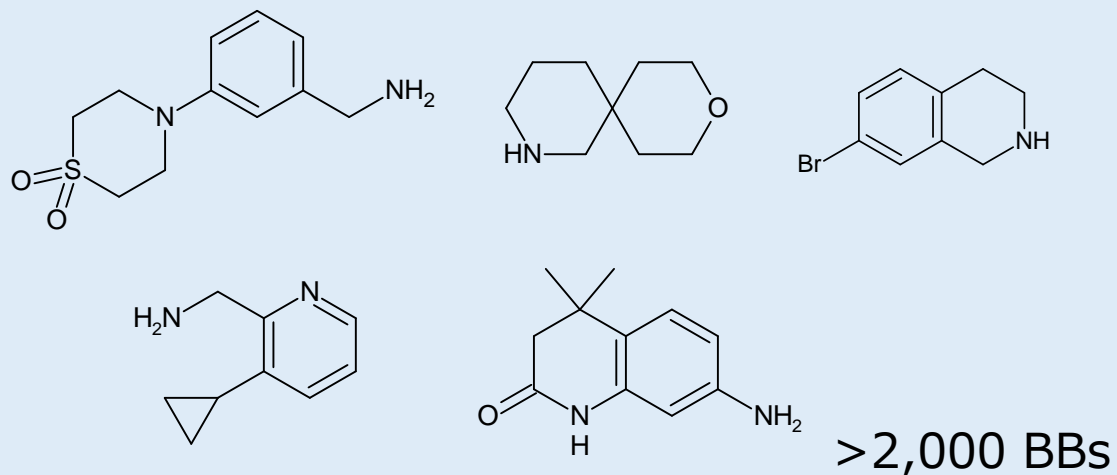
PMI plot



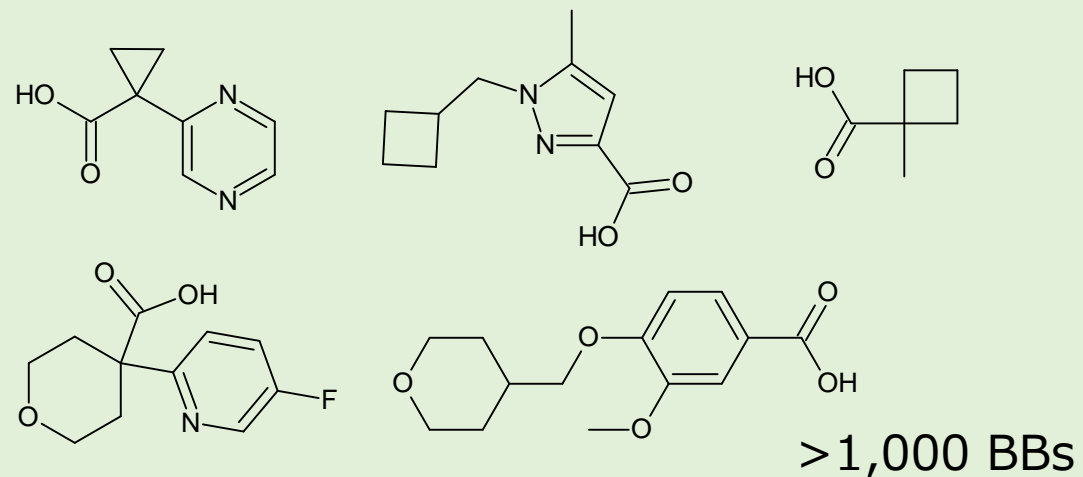
3次元構造の分布に大きな差はなし

2-Component library

Amines



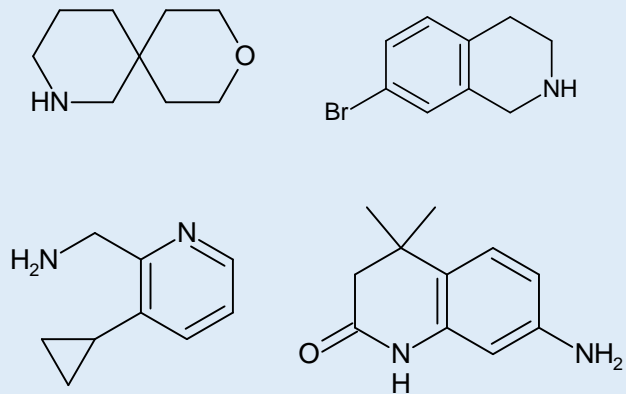
Carboxylic acids



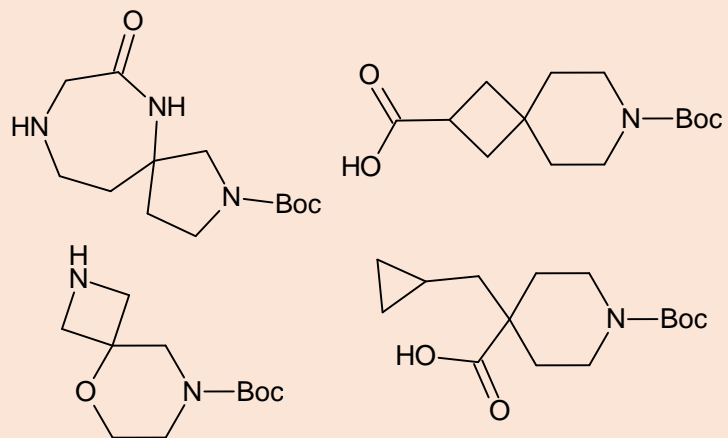
2-component Library

3-Component library

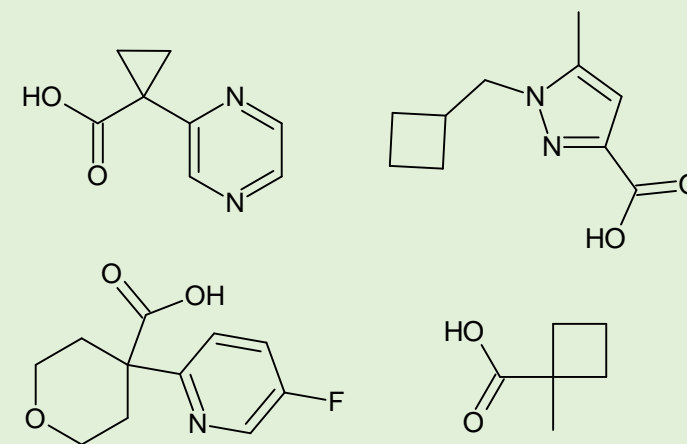
Amines



Bi-functional BBs



Carboxylic acids

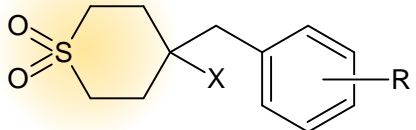


3-component Library

キシダオリジナル ビルディングブロック (K-BB)

-その他-

Tetrahydrothiopyran dioxide analogs

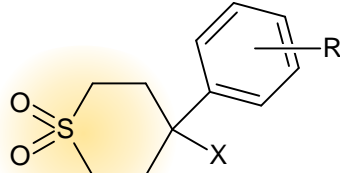
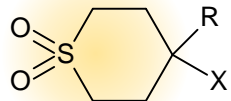
Structure	R	X=NH ₂	X=COOH
	H	PK0-39661	PK0-32691
	<i>o</i> -OMe	PK0-43231	PK0-43211
	<i>m</i> -OMe	PK0-54111	PK0-41781
	<i>p</i> -OMe	PK0-54121	PK0-41331
	<i>o</i> -Cl	PK0-41811	PK0-41771
	<i>m</i> -Cl	PK0-53991	PK0-42001
	<i>p</i> -Cl	PK0-43531	PK0-43481
	<i>o</i> -F	PK0-41791	PK0-41751
	<i>m</i> -F	PK0-42021	PK0-41991
	<i>p</i> -F	PK0-41801	PK0-41761
	<i>o</i> -CF ₃	PK0-43541	PK0-42011
	<i>m</i> -CF ₃	PK0-45381	PK0-43491
<i>p</i> -CF ₃	PK0-45391	PK0-43501	

 **65**
analogues

<参考情報>

Tetrahydrothiopyran dioxide骨格の導入が、薬効・非薬効に効果的だった事例

5-Chloroindoloyl glycine inhibitors of glycogen phosphorylase: synthesis, in vitro, in vivo, and X-ray crystallographic characterization.
Bioorg. Med. Chem. Lett. **2005**, *15*, 459-465.

Structure	R	X=NH ₂	X=COOH
	H	PK0-49861	PK0-49721
	<i>o</i> -Cl	PK0-53781	PK0-53971
	<i>m</i> -Cl	PK0-53581	PK0-53981
	<i>p</i> -Cl	PK0-53541	PK0-53771
	<i>o</i> -F	PK0-53561	PK0-53951
	<i>m</i> -F	PK0-53571	PK0-53961
	<i>p</i> -F	PK0-53401	PK0-53761
	Me	PK0-39651	PK0-32681
	Et	PK0-42381	PK0-41981
	iBu	PK0-42781	PK0-42351
	CH ₂ -cPr	PK0-43221	PK0-42361
	CH ₂ -cBu	PK0-42391	PK0-42371
	CH ₂ CH ₂ OCH ₃	PK0-43521	PK0-42761
	2-Py-CH ₂	PK0-42791	PK0-42771
3-Py-CH ₂	PK0-53531	PK0-43511	

青字はScifinderで提供サプライヤーが限られた製品です。

Fluorinated building blocks

各種のScaffoldに対して、
フッ素原子を積極的に導入



1912
analogs

種類	構造例
モノフルオロ	<p>4- : PK0-47851 5- : PK0-32651 6- : PK0-31761 7- : PK0-55261</p> <p><i>o</i>- : PK0-59201 <i>m</i>- : PK0-59211 <i>p</i>- : PK0-59221</p> <p><i>o</i>- : PK0-59411 <i>m</i>- : PK0-59321 <i>p</i>- : PK0-59331</p>
ジフルオロ	<p>PK0-38871 PK0-28881 PK0-59081 PK0-59481</p>
トリフルオロ	<p>PK0-29161 PK0-59551 PK0-59601 PK0-59751</p>

当社のBBを活用したFBDDにより、ヒット化合物を取得した論文

Comprehensive approach of ^{19}F nuclear magnetic resonance, enzymatic, and In Silico methods for site-specific hit selection and validation of fragment molecules that inhibit Methionine γ -Lyase activity. Kazuyoshi Ikeda, Yuichiro Kezuka, Takamasa Nonaka, Tomoki Yonezawa, Masanori Osawa, and Etsuko Katoh *J.Med.Chem.* **2021**, *64*, 14299-14310.

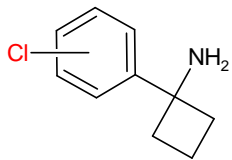
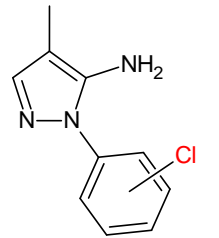
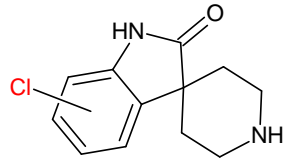
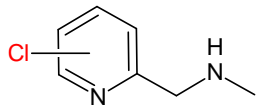
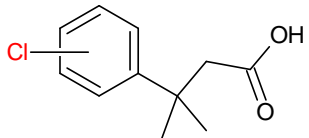
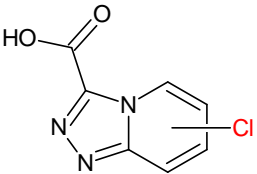
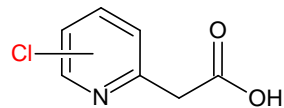
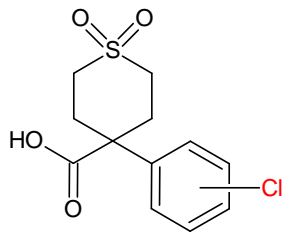
Chlorinated building blocks

クロル基導入の効果

- 酸性度の上昇 (塩基性度の低下)
- Me基と近いファンデルワールス半径
- “acceptor”または“donor”として機能
- 配座制御
- 疎水性相互作用の増大



313
analogues

種類	構造例			
アミン	 <i>o</i> - : PK0-09901 <i>m</i> - : PK0-09921	 <i>o</i> - : PK0-14681 <i>m</i> - : PK0-14311 <i>p</i> - : PK0-14321	 4- : PK0-31771 5- : PK0-32191 6- : PK0-31231 7- : PK0-41011	 3- : PK0-55991 4- : PK0-58791 5- : PK0-54771 6- : PK0-54571
カルボン酸	 <i>o</i> - : PK0-27091 <i>m</i> - : PK0-27101 <i>p</i> - : PK0-27111	 5- : PK0-36701 6- : PK0-37651 8- : PK0-37671	 3- : PK0-47471 5- : PK0-47311 6- : PK0-46101	 <i>o</i> - : PK0-53971 <i>m</i> - : PK0-53981 <i>p</i> - : PK0-53771

<参考情報>

創薬研究における塩素原子の効果 (Magic Chloro)

“Magic Chloro”: Profound Effects of the Chlorine Atom in Drug Discovery

J. Med. Chem. 2023, 66, 5305-5331.

参考情報

K-BB・K-LBをご活用いただいた研究論文

K-BB

1. A combination of ^{19}F NMR and surface plasmon resonance for site-specific hit selection and validation of fragment molecules that bind to the ATP-binding site of a kinase. *Bioorg.Med.Chem.* **2018**, 26, 1929-1938.
2. Comprehensive approach of ^{19}F nuclear magnetic resonance, enzymatic, and In Silico methods for site-specific hit selection and validation of fragment molecules that inhibit Methionine γ -Lyase activity. *J.Med.Chem.* **2021**, 64, 14299-14310.

K-LB

1. Identification of novel inhibitors of Keap1/Nrf2 by a promising method combining protein-protein interaction-oriented library and machine learning. *Scientific Reports*, **2021**, 11, 7420.
2. DLiP-PPI library: An integrated chemical database of small-to-medium-sized molecules targeting protein-protein interactions. *Front. Chem.*, **2023**, 10, 1090643.
3. Applying deep learning to iterative screening of medium-sized molecules for protein-protein interaction-targeted drug discovery. *Chem. Commun.*, **2023**, 59, 6722.