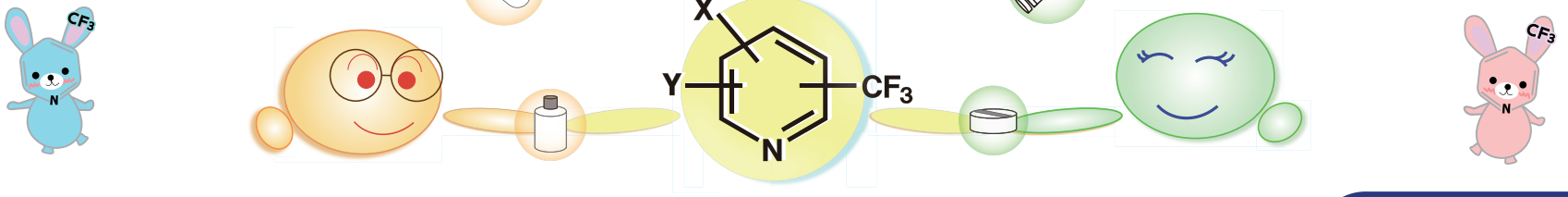
CF_3-Pyridine Compounds Enhance some Functions and/or Activities of Medicines

We have a variety of hands for creating new medicines



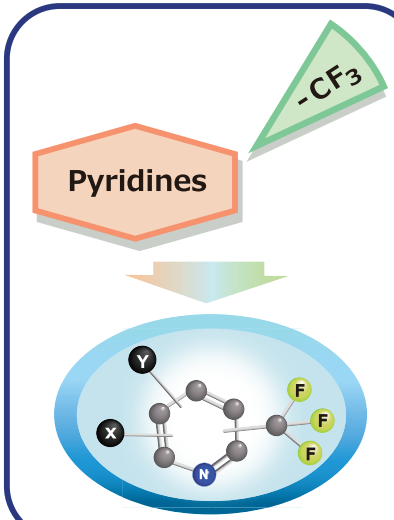
Both properties of CF_3-group & Pyridine ring can be combined to generate a variety of unique properties on CF_3 (trifluoromethyl)-Pyridine compounds.

CH_3-Mimic・Polarity・Blocking ・Hydrophobicity

N-Unshared electron pair ・Hydrophilicity・Basicity

+ Confidence & Technique +

- Biochemical stability to oxidative metabolism
- Interaction with intracellular protein and nucleic acid
- Enhancement of bioabsorbability and phamaceutical action
- Reduction of toxicity and side effect etc.



Since the early 1980's, we have been carrying out research and development on new pharmaceutical compounds and agrochemicals based on CF_3-pyridine chemical. Therefore, we can accommodate customer's needs in this field with confidence.

We aim for customer's ease and satisfaction in supplying. Your order, inquiry, and consultation are always welcome!

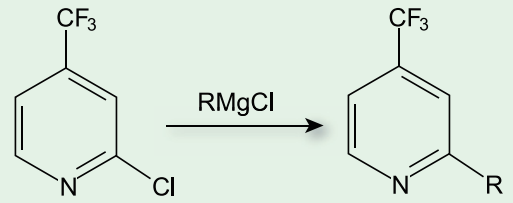
We can not only provide the cataloged compounds, but also consult for the compounds you propose.

ISK ISHIHARA SANGYO KAISHA, LTD.
https://www.iskweb.co.jp/products/organic.html

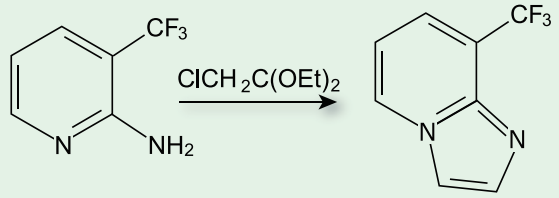
Application of CF_3-Pyridine

Modification of CF_3-Pyridine

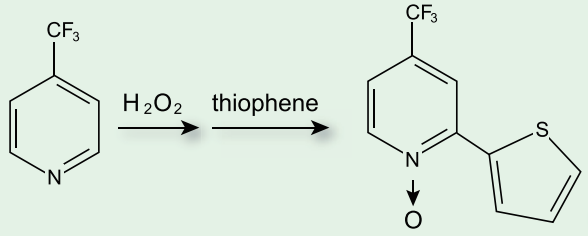
Alkylation



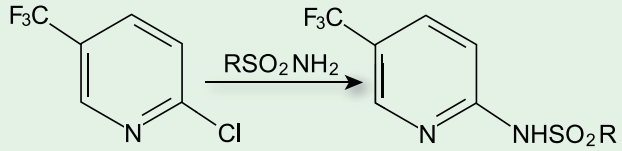
Cyclization



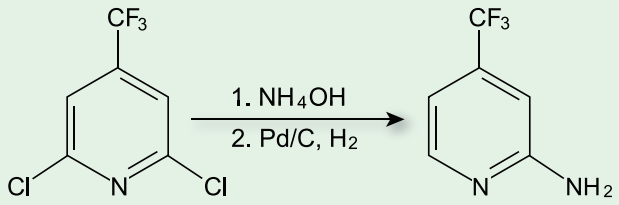
Arylation



Sulfonamidation



Amination

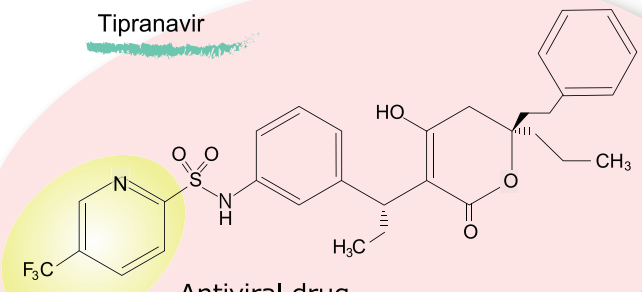


We have a lot of modification techniques other than discribed here.

There are not a few reports of the research on the compounds having partial CF_3-pyridine structures.

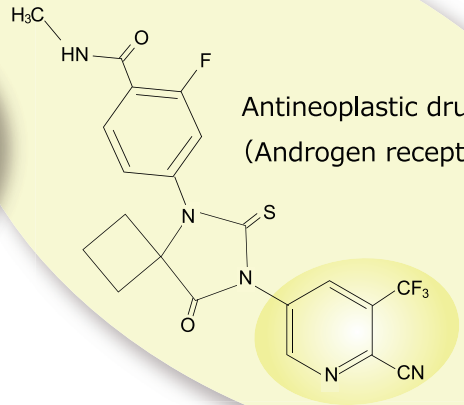
CF_3-Pyridine Introduced Medicine

Tipranavir



Antiviral drug
(HIV protease inhibitor)

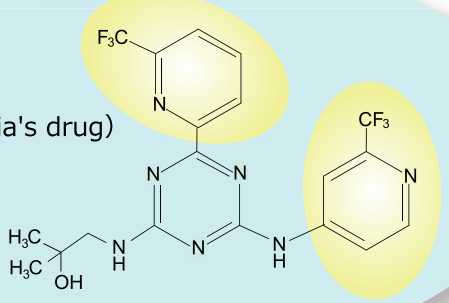
Apalutamide



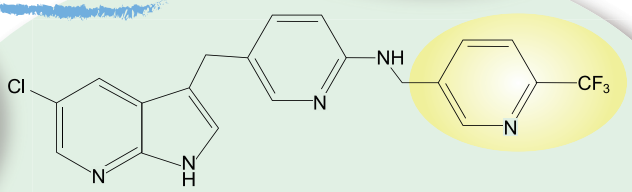
Antineoplastic drug
(Androgen receptor antagonist)

Enasidenib

Antineoplastic drug
(Acute myeloid leukemia's drug)



Pexidartinib



Antineoplastic drug for TGCT
(Tenosynoviral giant cell tumor)
(CSF1R inhibitor)

ISK ISHIHARA SANGYO KAISHA, LTD.

CF_3-Pyridine Structure Effect

Positional Effect of a CF_3 on Pyridine

Calculated pKa values of CF_3 -pyridyl nirogen

	Pyridine	*o*-CF_3	*m*-CF_3	*p*-CF_3
Cal pKa *)	5.2	0.6	2.8	2.9

*)ACD/Percepta, Build 2726, Advanced Chemistry Development, Inc.

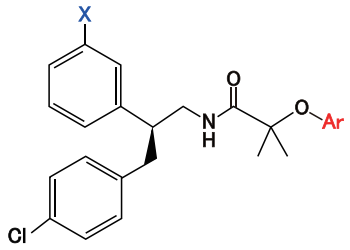
*Pest Manag Sci 2018, **74**, 1228-1238*

There are some reports compering CF_3-Pyridine in some labs. And we have also studied about it.

The Effect of CF_3-Pyridine structure on Fluazifop-butyl, **16**, is shown in the Table below. This compound has a selectivity of killing grass weeds without damaging broad-leaf crops.

Substituent effect of Bioactive Compound

Inhibition of CB1R for the Treatment of Obesity

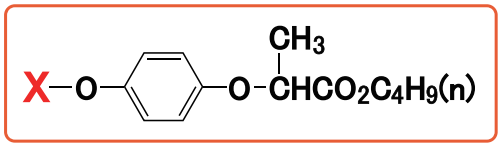


No.	X	Ar	CB1RIC$_{50}$, nM
1	H	4-Cl-Ph	3.0 ± 1.2
2	H	3-Cl-Ph	1.5 ± 0.5
3	H	2-Cl-Ph	18 ± 4
4	H	Ph	2.0 ± 1.4
5	H	3-F-Ph	1.6 ± 0.8
6	H	3,5-F_2-Ph	1.1 ± 1.0
7	H	2-Pyr	1.8 ± 1.4
8	H	3-Pyr	19 ± 3
9	H	4-Pyr	17 ± 1
10	H	5-Cl-2-Pyr	1.3 ± 0.3
11	H	5-CF_3-2-Pyr	0.5 ± 0.2
12*)	CN	5-CF_3-2-Pyr	0.3 ± 0.1

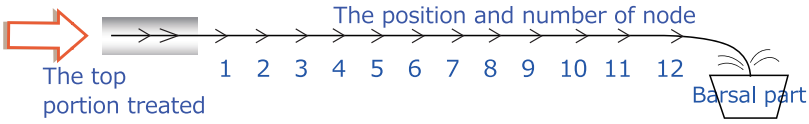
*) **12** is dropped out at phase lll of clinical trial.

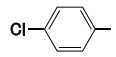
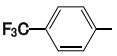
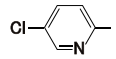
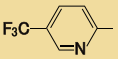
*J. Med. Chem. 2006, **49**, 7584-7587*

Translocation Test of Fluazifop-butyl Analogs by Top Treatment on *C. dactylon*



Method of treatment:



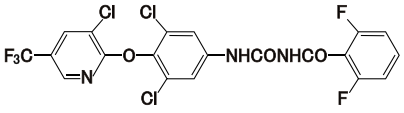
No.	X	Top kill[a]	Sprout inhibition[b] (Nodes of stolon) 1	2	3	4	5	6	7	8	9	10	11	12	Barsal part
13		8	I	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV
14		10	I	II	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV
15		8	I	I	I	II	II	II	II	II	III	III	III	III	III
16		10	I	I	I	I	I	I	I	I	I	I	I	I	II

a) Top kill: 1 = no effect - 10 = complete kill

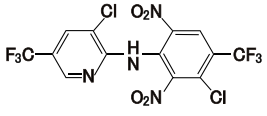
b) Sprout inhibition: IV= no inhibition - I = complete inhibition.

We have also produced unique Insecticide and Fungicide having CF_3-Pyridine structures.

This structure has a wide field of application.



Chlorfluazuron
(Insecticide)



Fluazinam
(Fungicide)

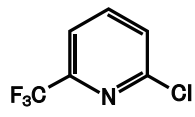
*Japanese Journal of Pesticide Science **12**, 311-325*

ISK ISHIHARA SANGYO KAISHA, LTD.

CF_3-Pyridine Compounds

α-CF_3-Pyridine

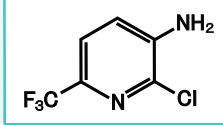
2,6-CTF
2-Chloro-6-(trifluoromethyl)pyridine



CAS No.39890-95-4

mp 33℃

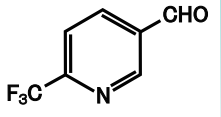
3,2,6-ACTF
3-Amino-2-chloro-6-(trifluoromethyl)pyridine



CAS No.117519-09-2

mp 96-97℃

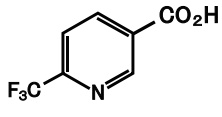
6-TF-3-CHO
6-(Trifluoromethyl)pyridine-3-carboxaldehyde



CAS No.386704-12-7

mp 52-56℃

6-TFNA
6-(Trifluoromethyl)nicotinic acid



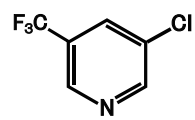
CAS No.231291-22-8

mp 195℃

We have a lot of other compounds. Please see the catalog arranged below.

β-CF_3-Pyridine

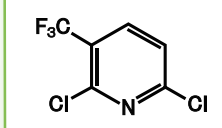
3,5-CTF
3-Chloro-5-(trifluoromethyl)pyridine



CAS No.85148-26-1

mp 23-24℃

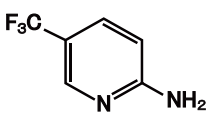
2,6,3-DCTF
2,6-Dichloro-3-(trifluoromethyl)pyridine



CAS No.55304-75-1

oil (mp 6℃)

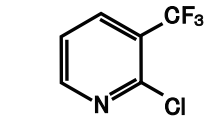
2,5-ATF
2-Amino-5-(trifluoromethyl)pyridine



CAS No.74784-70-6

mp 42℃

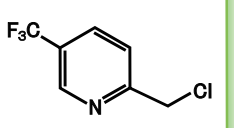
2,3-CTF
2-Chloro-3-(trifluoromethyl)pyridine



CAS No.65753-47-1

mp 38℃

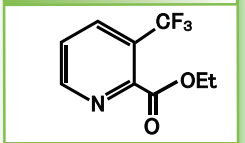
2,5-CmTF
2-Chloromethyl-5-(trifluoromethyl)pyridine



CAS No.128790-14-7

oil

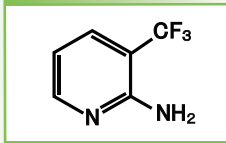
3-TF-2-CO_2Et
Ethyl 3-(trifluoromethyl)picolinate



CAS No.952182-76-2

oil

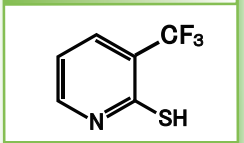
2,3-ATF
2-Amino-3-(trifluoromethyl)pyridine



CAS No.183610-70-0

mp 67-69℃

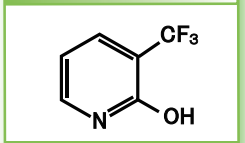
2,3-MTF
2-Mercapto-5-(trifluoromethyl)pyridine



CAS No.104040-74-6

mp 170-176℃

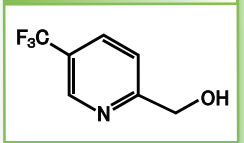
2,3-HTF
2-Hydroxy-3-(trifluoromethyl)pyridine



CAS No.22245-83-6

mp 152℃

2,5-HmTF
5-(Trifluoromethyl)pyridine-2-methanol

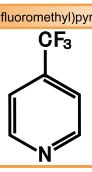


CAS No.31181-84-7

oil

γ-CF_3-Pyridine

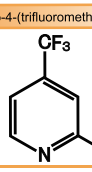
4-TF
4-(Trifluoromethyl)pyridine



CAS No.3796-24-5

oil

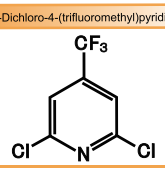
2,4-CTF
2-Chloro-4-(trifluoromethyl)pyridine



CAS No.81565-18-6

oil

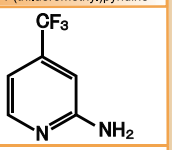
2,6,4-DCTF
2,6-Dichloro-4-(trifluoromethyl)pyridine



CAS No.39890-98-7

oil

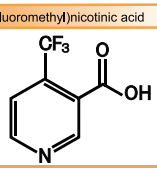
2,4-ATF
2-Amino-4-(trifluoromethyl)pyridine



CAS No.106447-97-6

mp 67-70℃

4-TFNA
4-(Trifluoromethyl)nicotinic acid

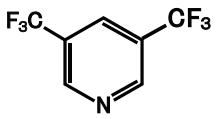


CAS No.158063-66-2

mp 147-149℃

Bis-CF_3-Pyridine

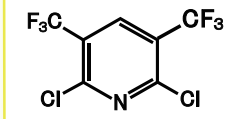
3,5-BiTF
3,5-Bis(trifluoromethyl)pyridine



CAS No.20857-47-0

mp 30℃

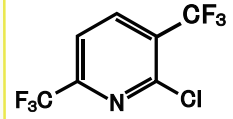
2,6,3,5-DCBiTF
2,6-Dichloro-3,5-bis(trifluoromethyl)pyridine



CAS No.142889-02-9

mp 75-76℃

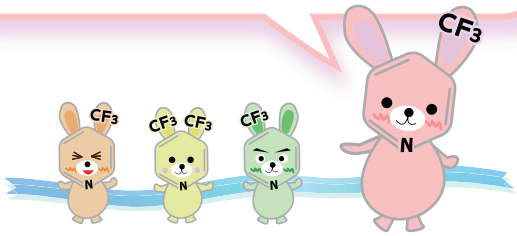
2,3,6-CBiTF
2-Chloro-3,6-bis(trifluoromethyl)pyridine



CAS No.70158-60-0

oil

The contact number and the homepage address are provided in the catalog and the flier arranged below. Please feel free to browse them and ask us more.



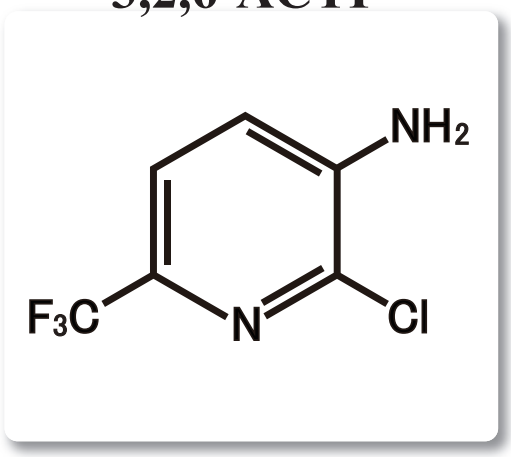
カタログ中で※のついた 25g 以下の製品は、富士フイルム和光純薬株式会社の取扱製品となります。
100g 以上のバルク製品につきましては、当社まで直接お問合せください。（【お問合せ先】ご参照）

ISK ISHIHARA SANGYO KAISHA, LTD.

Features of α-& β-CF_3-Pyridine Compounds

α-CF_3-Pyridine

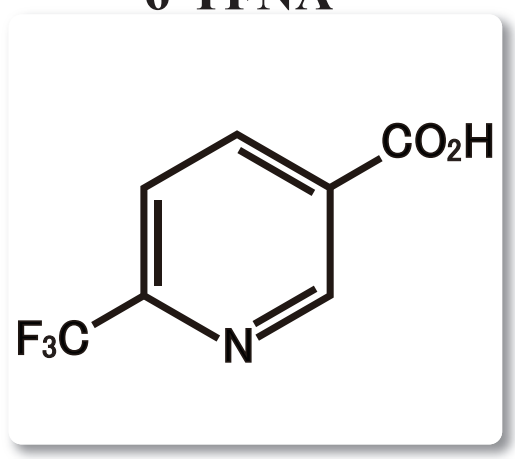
3,2,6-ACTF



CAS：117519-09-2

3 ,2,6-ACTF [3-Amino-2-chloro-6-(trifluoromethyl)pyridine] is pale yellow solid of mp 96-97˚C and over 98% purity. The Cl-group at 2-position can be displaced by nucleophilic substitution reaction such as alkylation, etherification, cyanation, etc. The NH_2-group at 3-position can form amide linkage and react as nucleophile. These possible variety of reactions are very useful to insert CF_3-pyridine structure into your compounds.

6-TFNA

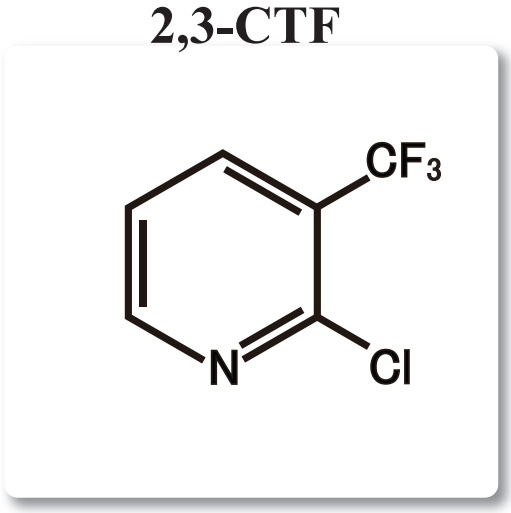


CAS：231291-22-8

6-TFNA [6-(Trifluoromethyl)nicotinic acid] is white to pale yellow powder of mp 195˚C and over 95% purity. The -CO_2H at 3-position can react with nucleophilic amine led to some linkages or heterocycles. This compound is found as raw materials in some patent of bioactive researches.

β-CF_3-Pyridine

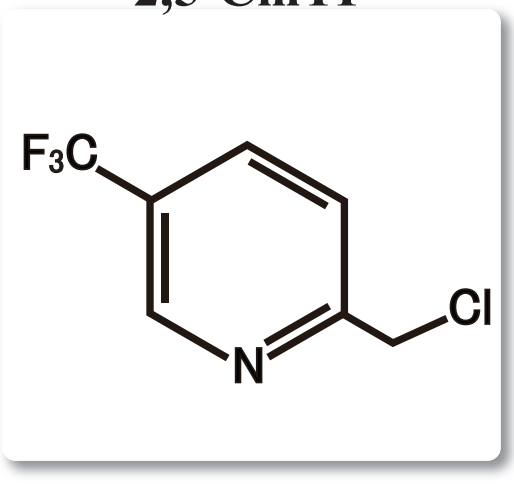
2,3-CTF



CAS：65753-47-1

2,3-CTF [2-Chloro-3-(trifluoromethyl)pyridine] is white solid of mp 38˚C and over 98% purity. The -Cl at 2-position can be displaced by nucleophilic substitution reaction such as alkylation, amination, etherification, cyanation, hydroxylation, etc. and its 5-position can be actively substituted via hydroxylation at 2-position. Actually, this compound is found as raw materials in some syntheses of available pharmaceuticals.

2,5-CmTF



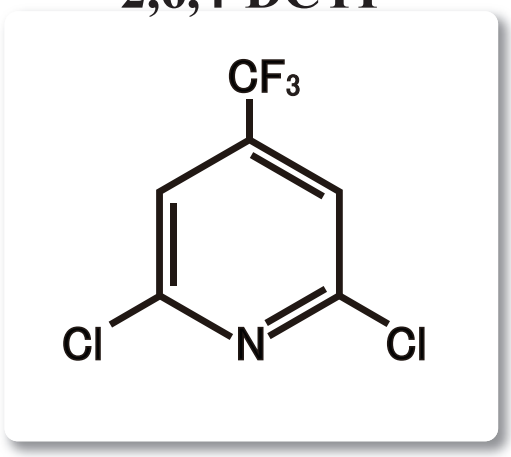
CAS：128790-14-7

2,5-CmTF [2-Chloromethyl-5-(trifluoromethyl)pyridine] is pale yellow oil and over 98% purity. The -Cl on methyl-group can be easily replaced by nucleophilic substitution reaction such as hydroxylation, amination, etherification, etc. to form variety of -CH_2-linkages and thus compounds having CF_3-pyridylmethylene structure. This compound was actually used on a past research.

Features of γ- & Bis-CF_3-Pyridine Compounds

γ-CF_3-Pyridine

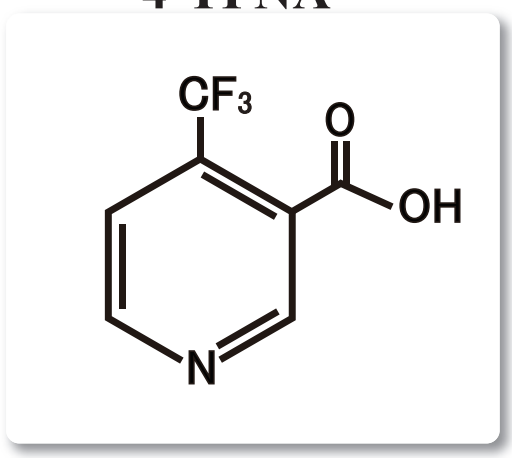
2,6,4-DCTF



CAS：39890-98-7

2,6,4-DCTF [2,6-Dichloro-4-(trifluoromethyl)pyridine] is colorless oil and over 95% purity. Both -Cls can be replaced by substitution reaction such as alkylation, arylation, carbonylaiton, amination, etc. simultaneously or separately. This compound is found as raw materials in some patents of bioactive researchers.

4-TFNA

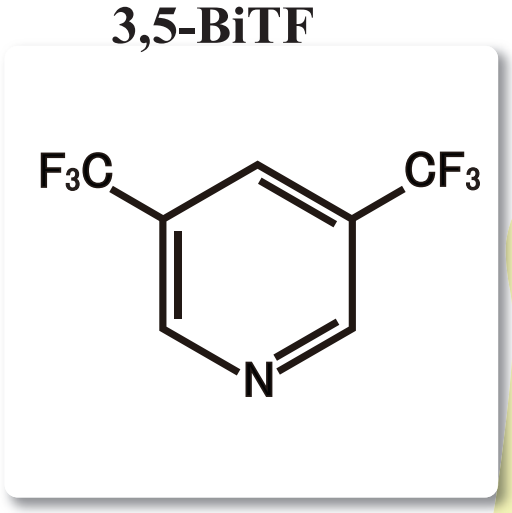


CAS：158063-66-2

4-TFNA [4-(Trifluoromethyl)nicotinic acid] is whitish powder of mp 147-149˚C and over 98% purity. The -CO_2H at 3-position can be reacted to form ester and amide to form essential partial structures of biologically active compounds. Actually, this compound is used as raw materials for some active products such as ISK's pesticide.

Bis-CF_3-Pyridine

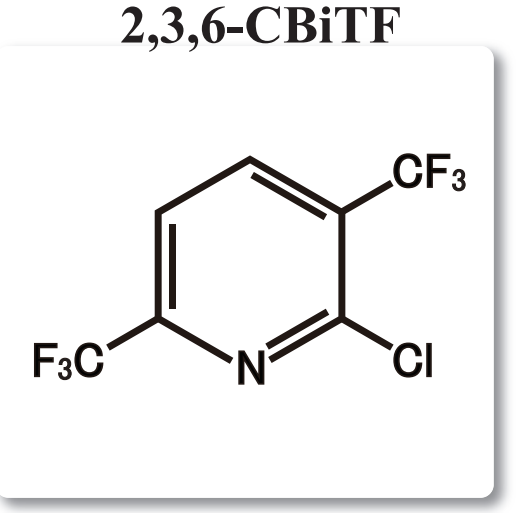
3,5-BiTF



CAS：20857-47-0

3,5-BiTF [3,5-Bis(trifluoromethyl)pyridine] is categorized into Bis–CF_3-Pyridine by the number of CF_3-group on pyridine ring. This product is white solid of mp 30˚C and over 95% purity. The 2-position can be replaced by –CO_2H via Lithiation which could be applied to other functional groups.

2,3,6-CBiTF



CAS：175136-26-2

2,3,6-CBiTF [2-Chloro-3,6-bis(trifluoromethyl)pyridine] is clear and colorless oil and over 95% purity. Bis-CF_3-pyridyl-group is rare, and the -Cl at 2-position is highly activated by two CF_3-groups to react with nucleophiles. Therefore you can try the insertion of bis-CF_3-pyridyl-group for new unique active pharmaceuticals and so on with this product.

ISK ISHIHARA SANGYO KAISHA, LTD.