



CF PLUS CHEMICALS

Your specialist in fluoroalkylation

CF Plus Chemicals is an ETH Zurich spin-off founded in 2014 in Brno focusing on life science applications of fluoroorganic chemistry.

Our mission is to make fluoroalkylation a widely used tool for effective modification of a complete scope of molecular targets, spanning from small molecules to large molecules - unlocking the full potential of drug candidates and enabling effective bioconjugation of biologically relevant entities.

In small molecule research, the company envisions to help their customers open new, hitherto unexplored chemical space in medicinal chemistry with reagents that are easy to use.

Our goal is to deliver, and help to deliver, better and cost-effective solutions for development of cures of devastating human diseases.

Dr. Václav Matoušek, CEO and founder

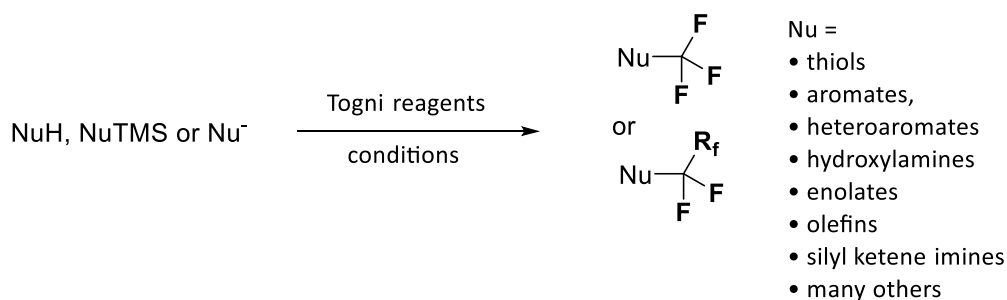
Table of contents

Fluoroalkylation portfolio.....	3
Togni perfluoroalkyl reagents	3
Other hypervalent iodine reagents	4
Togni - CF ₂ CF ₂ R reagents	5
Fluoroalkyl bromides.....	8
Fluoroalkyl silanes	10
Fluoroalkyl carboxylates.....	12
Fluoroalkyl sulfonylfluorides	14
Fluoroalkyl azides	15
Fluoroalkyl triazoles	16
Difluoromethylation reagents.....	17
Trifluoromethoxylation reagents	17
Bioconjugation portfolio	18
Protein crosslinkers	18
Speciality chemicals.....	21
Dihydroisoquinolines.....	21
Azide building blocks	22

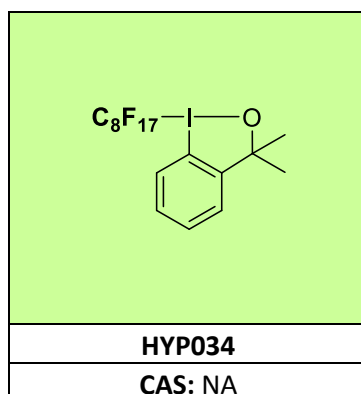
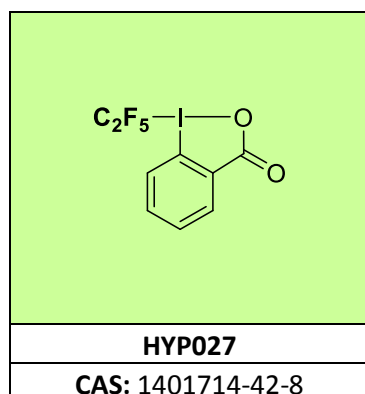
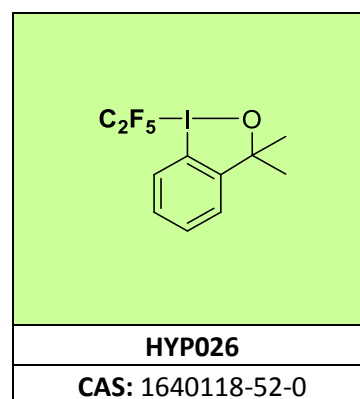
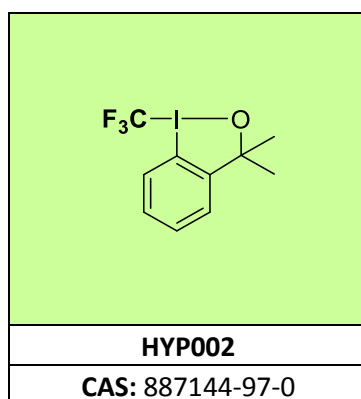
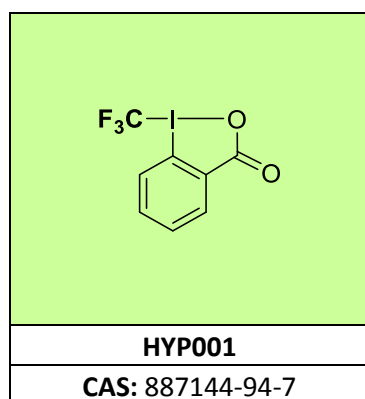
Fluoroalkylation portfolio

Togni perfluoroalkyl reagents

The so-called Togni reagents have over the last years become a standard tool that provides expedient access to trifluoromethylated and perfluoroalkylated compounds important for drug and pesticide discovery programs. In many cases, these reagents operate via trifluoromethyl or perfluoroalkyl radicals as the key reactive intermediates.

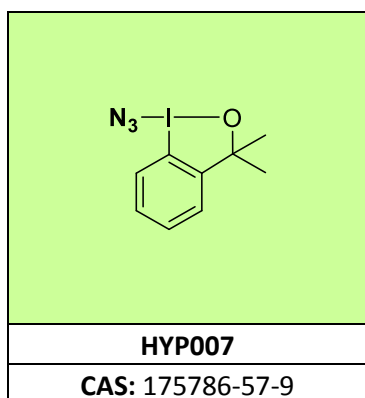
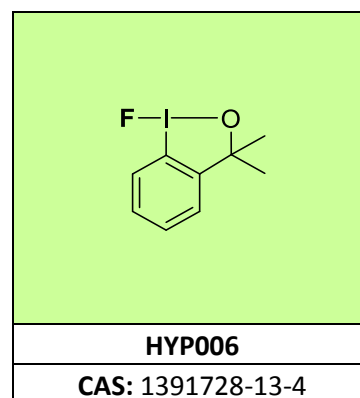
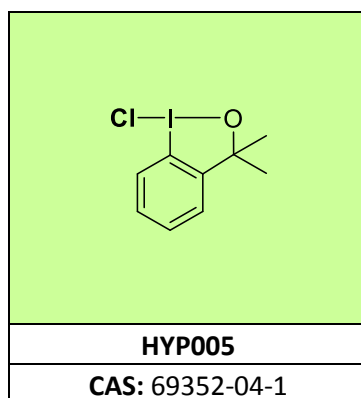
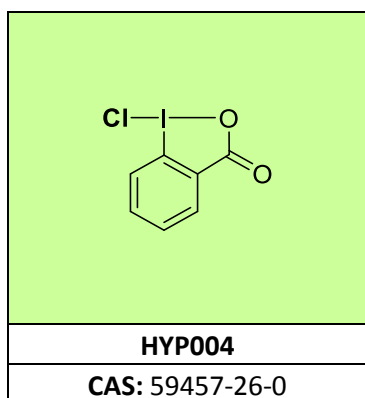
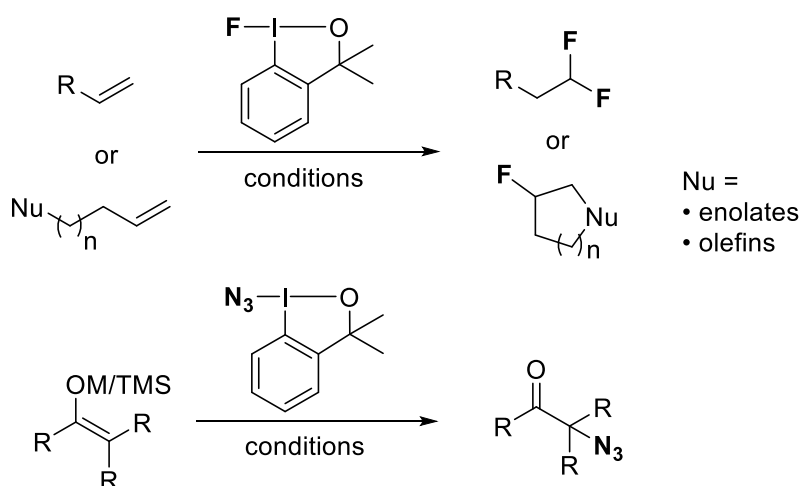


For a review, see: J. Charpentier, N. Früh, A. Togni, Chem. Rev. 2015, 115, 650-682.



Other hypervalent iodine reagents

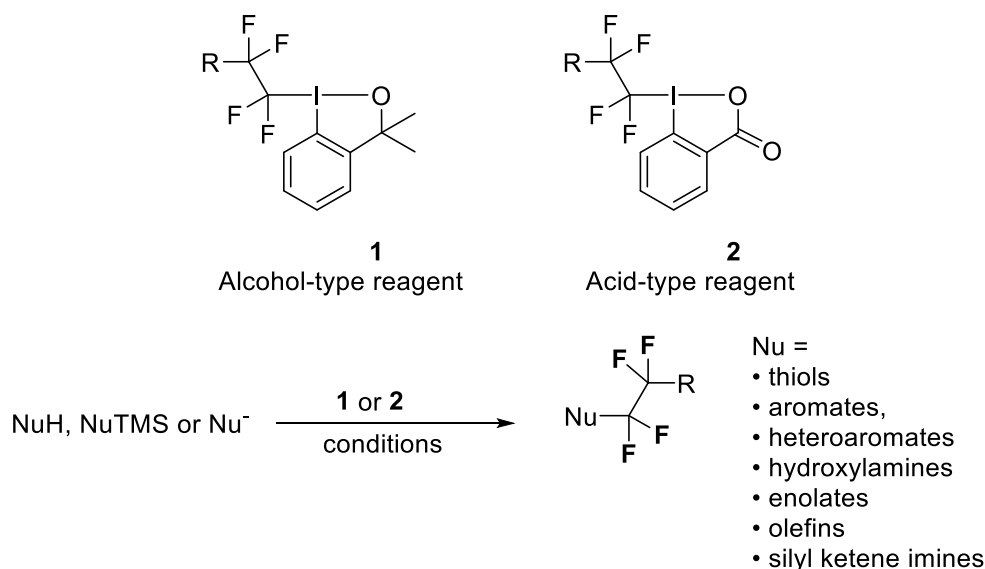
Cyclic hypervalent iodine reagents with increased hydrolytical and thermal stability have been described as mild and conveniently handled electrophilic chlorination, fluorination and azidation reagents. The shelf-stable fluoroiodane reagent allows to perform elegant fluorinative functionalizations and fluorocyclizations of olefins under mild conditions, while the azidoiodane reagent can be used to as a formally electrophilic azidation reagent for azidation of enolates.



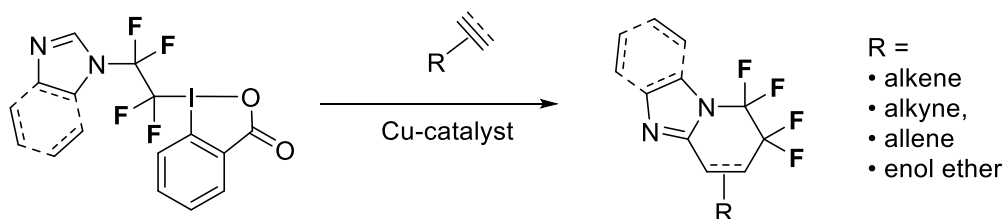
Togni - CF₂CF₂R reagents

The second generation of Togni reagents („extended Togni reagents“) incorporate substituted tetrafluoroethyl groups instead of plain perfluoroalkyls. With essentially similar reactivity patterns as the original CF₃-analogues, many types of transformations that work well with CF₃-Togni reagents can be done with these reagents as well, providing access to rare and potentially attractive fluorinated chemical space. With a set of „extended Togni reagents“ in hand, the lead compound can be diversified in the last stage of the synthesis to afford the hard-to-access fluoroalkyl-decorated derivatives.

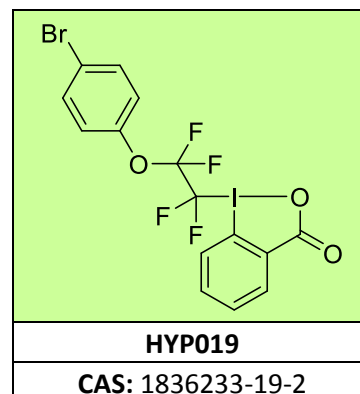
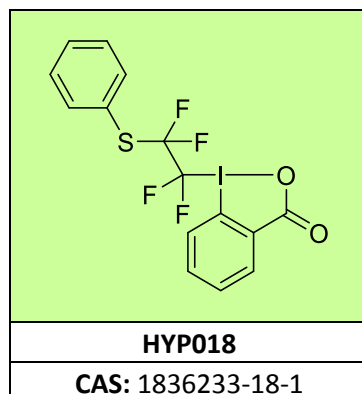
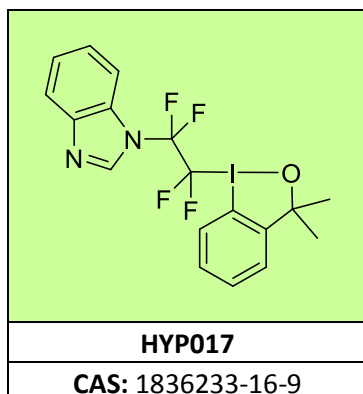
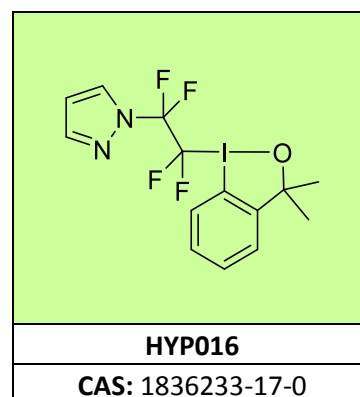
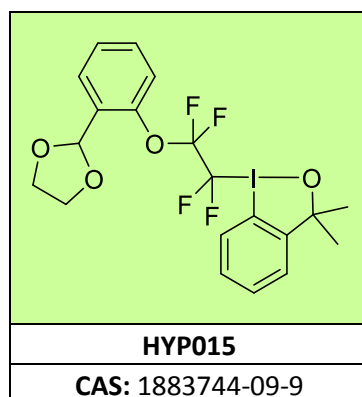
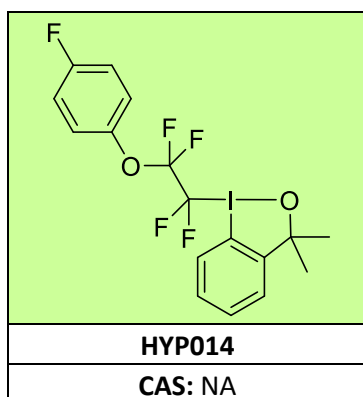
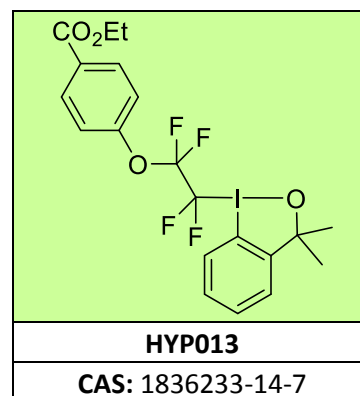
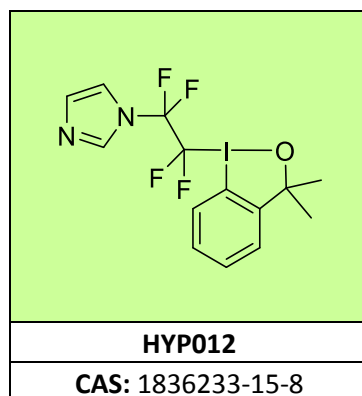
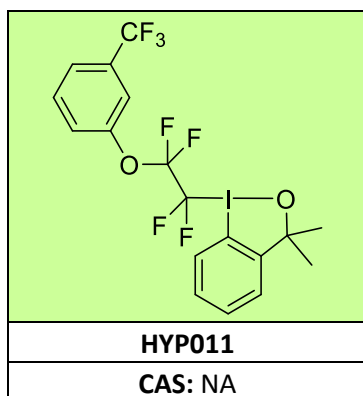
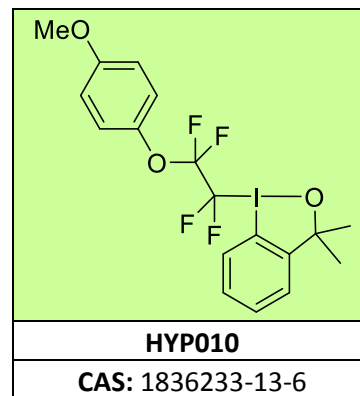
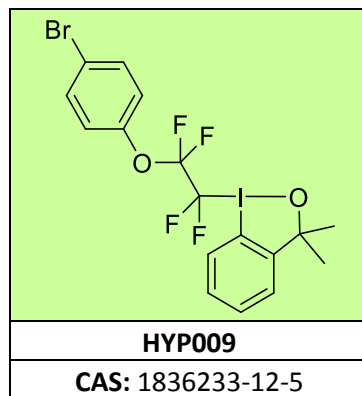
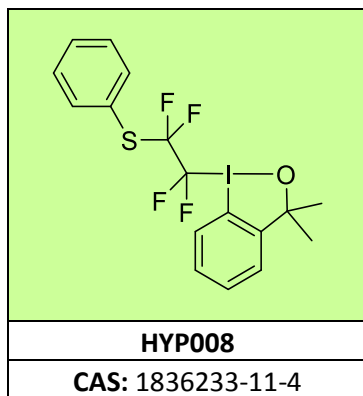
The azole-substituted —CF₂CF₂— „extended Togni reagents“ engage in a radical cyclisation reaction with olefins and acetylenes giving access to rare tetrafluorinated heterocycles. The incorporation of a —CF₂CF₂— moiety into a cyclic structure imparts the molecule a unique combination of properties called „polar hydrophobicity“ – a permanent dipole combined with the solvophobic behaviour of the tetrafluoroethylene unit.

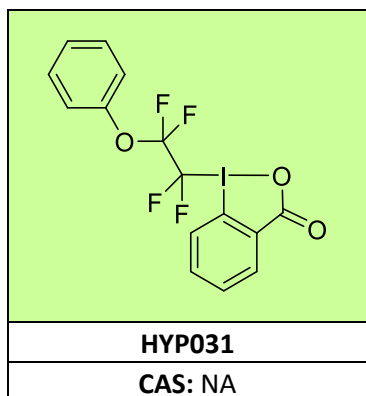
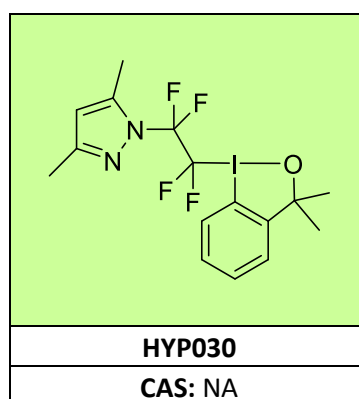
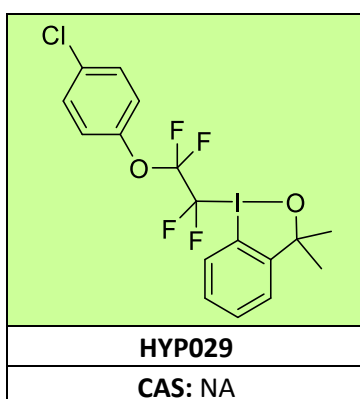
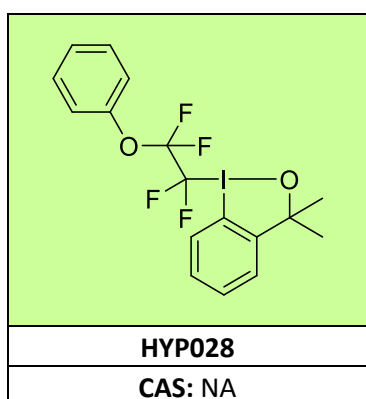
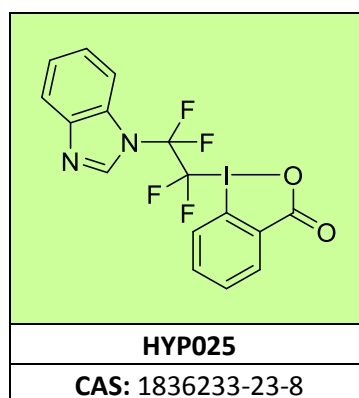
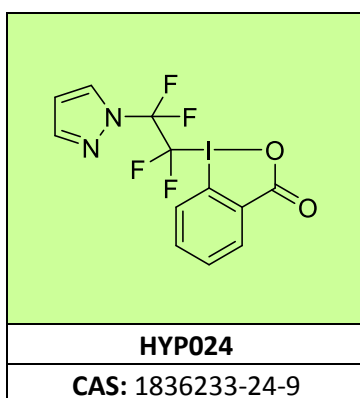
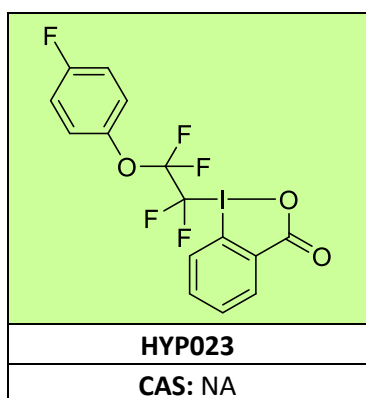
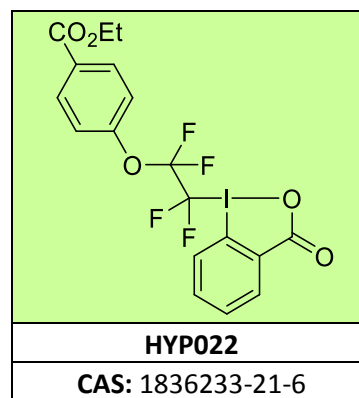
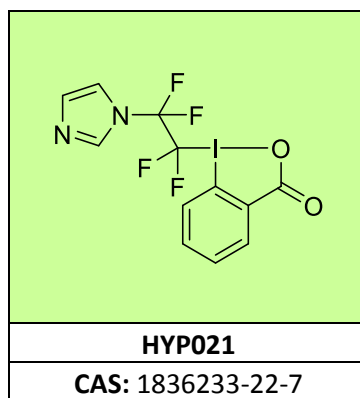
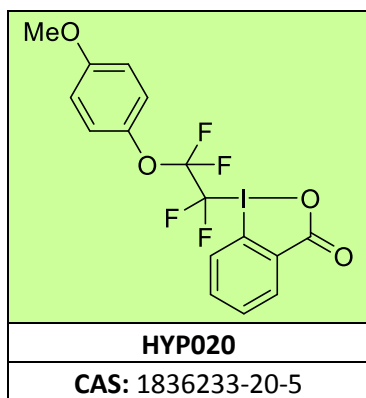


Late stage introduction of —CF₂CF₂R moieties into molecules
 Ref: Chem. Eur. J., 22: 417–424; Patent WO2016019475A1



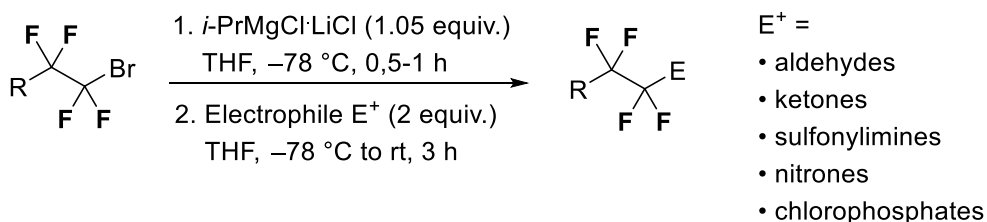
Access to tetrafluorinated di- and tetrahydro(benz)imidazopyridines
 Ref: Org. Lett., 2016, 18 (4), pp 756–759



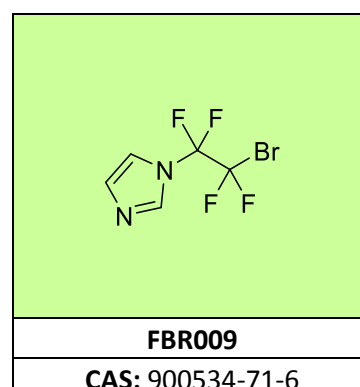
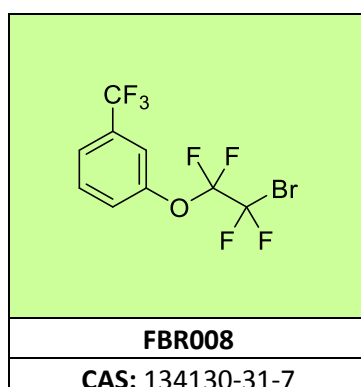
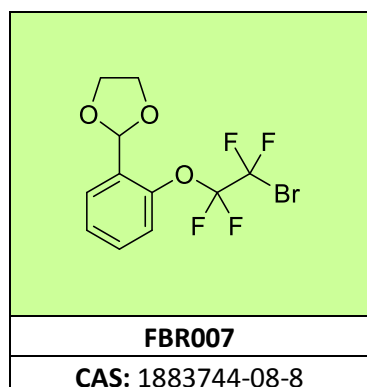
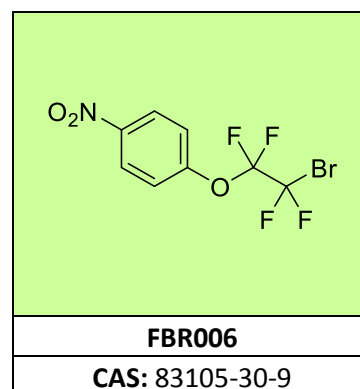
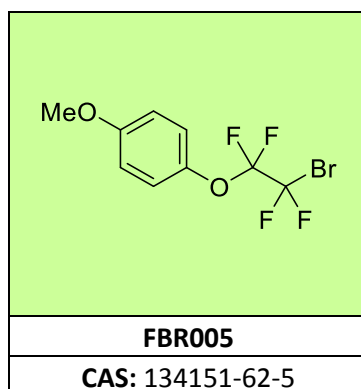
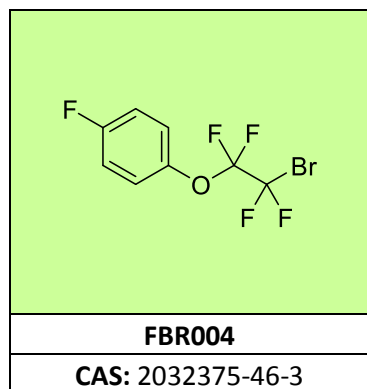
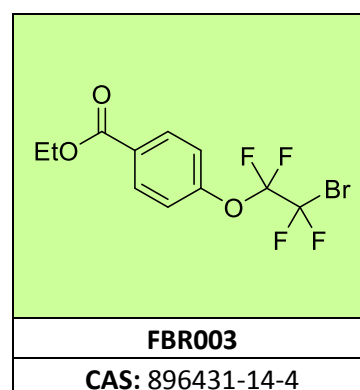
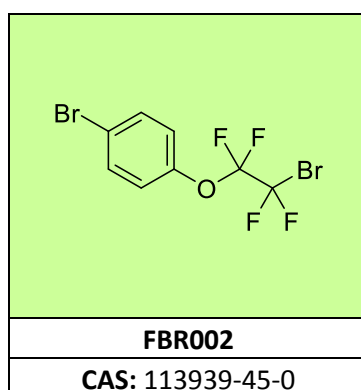
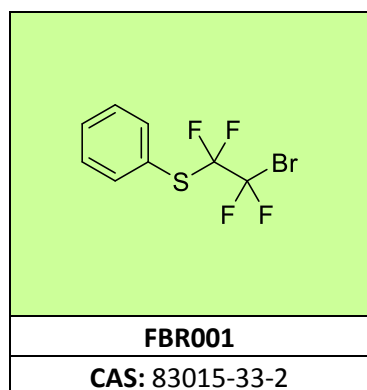


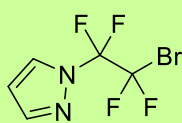
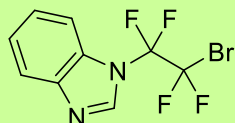
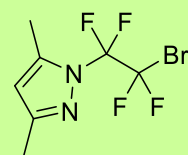
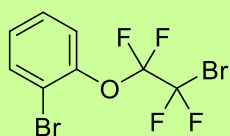
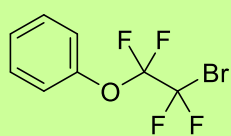
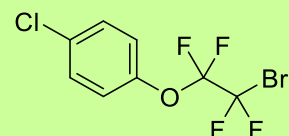
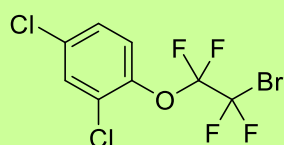
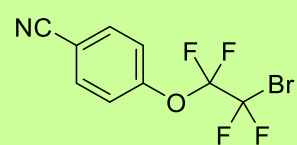
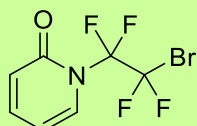
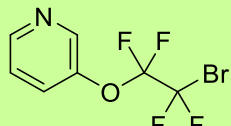
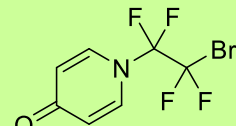
Fluoroalkyl bromides

Substituted fluoroalkyl bromides turn into powerful nucleophilic fluoroalkylation reagents after being metallated with isopropyl magnesium chloride-lithium chloride complex (Turbo-Grignard). The in-situ generated fluoroalkyl magnesium chloride intermediate is moderately stable up to $-40\text{ }^{\circ}\text{C}$ and can be efficiently trapped with various electrophiles to afford the $-\text{CF}_2\text{CF}_2-$ linked products.



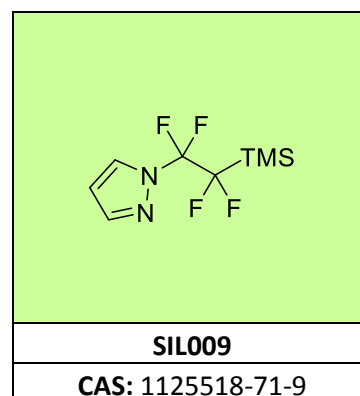
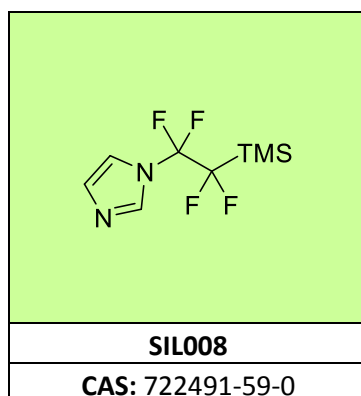
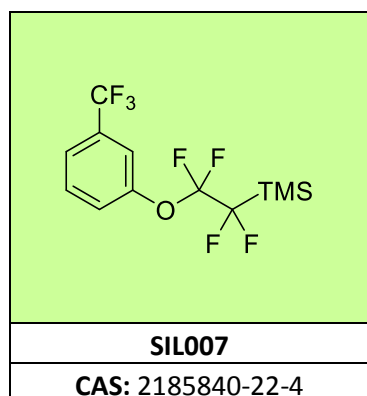
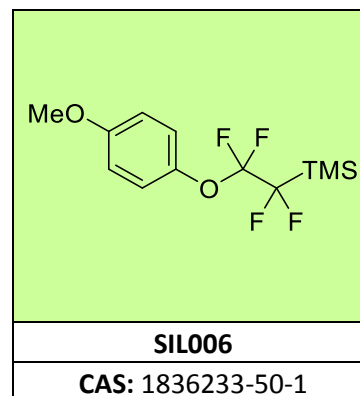
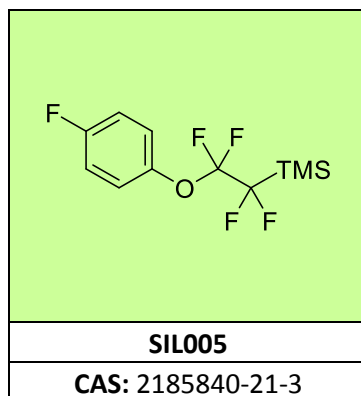
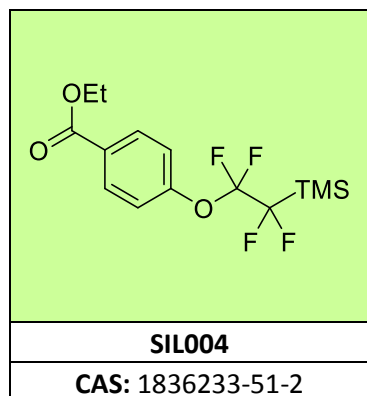
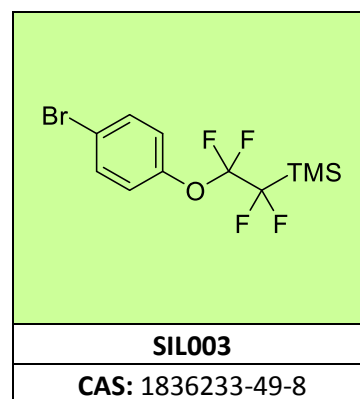
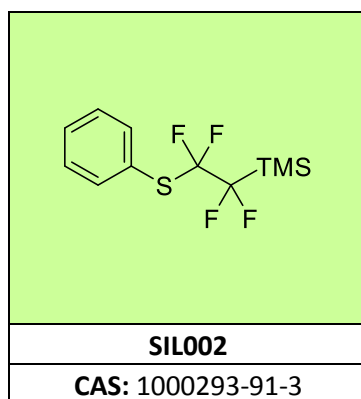
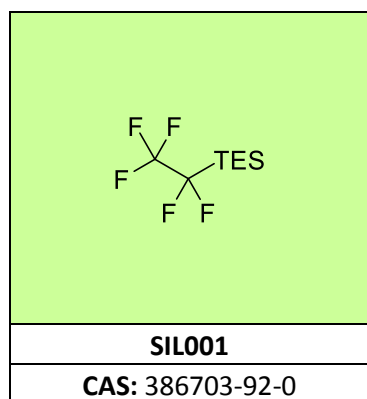
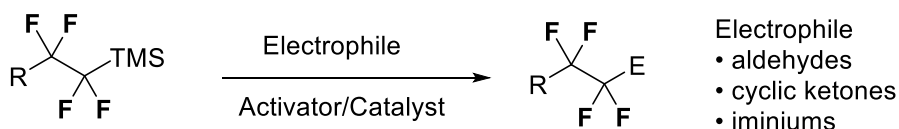
Ref: Org. Lett., 2016, 18 (22), pp 5844–5847

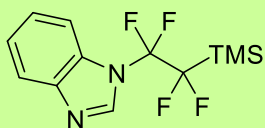
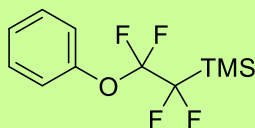
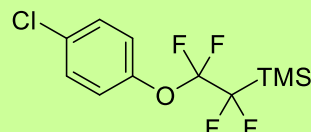
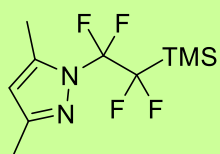
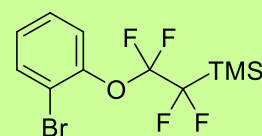
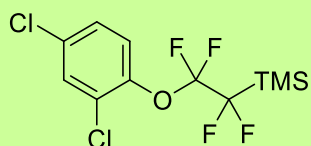


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Fluoroalkyl silanes

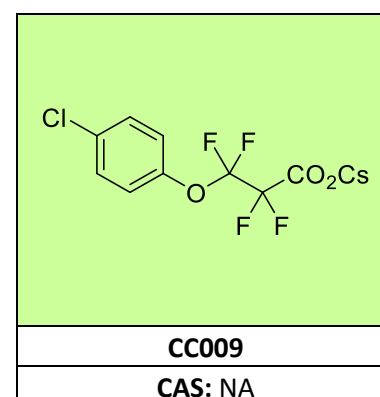
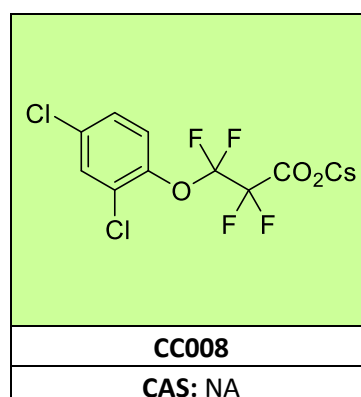
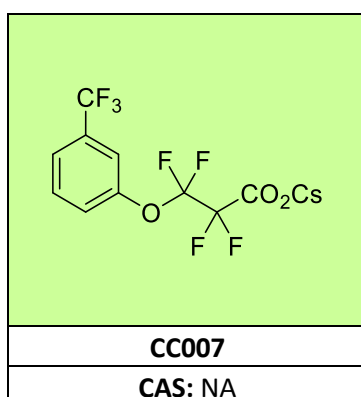
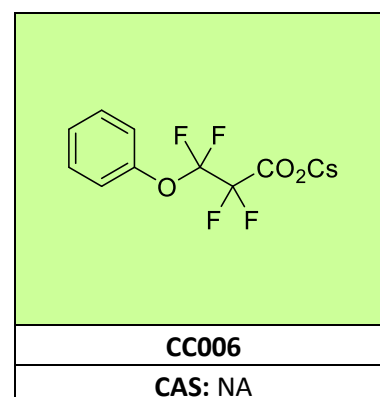
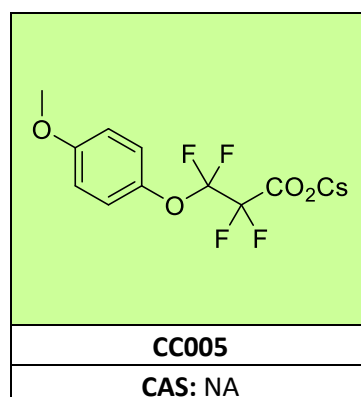
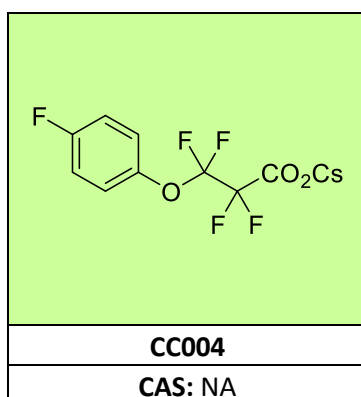
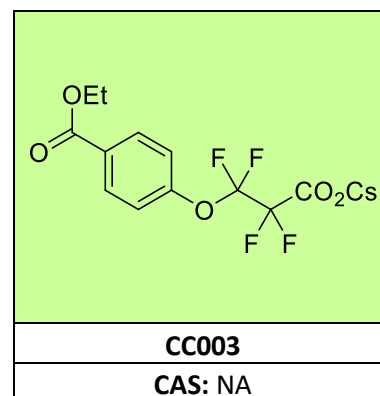
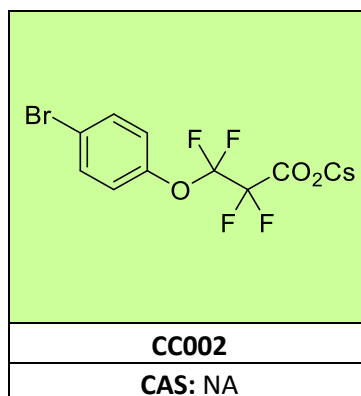
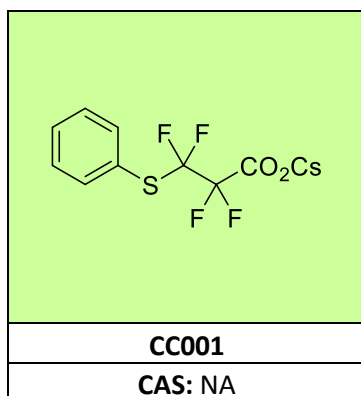
Substituted fluoroalkyl silanes serve as traditional nucleophilic sources of the fluoroalkyl synthon. Upon activation with catalytic fluoride or alkoxide, they can fluoroalkylate a range of aldehydes, reactive ketones or iminiums. The silanes can also engage in transition-metal catalyzed formation of R-CF₂CF₂-substituted aromatics.

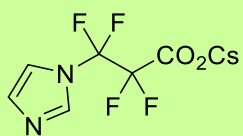


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Fluoroalkyl carboxylates

β -Substituted caesium tetrafluoropropionates are convenient starting materials for construction of fluoroalkyl carboxamides. The pK_a values of such amide groups are significantly lower than their non-fluorinated counterparts, offering potential to modulate the behaviour of drug candidates. The caesium salts can be easily handled on air due to their reduced hygroscopicity compared to the highly hygroscopic free carboxylic acids.

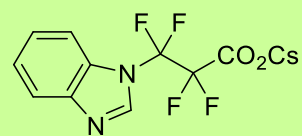


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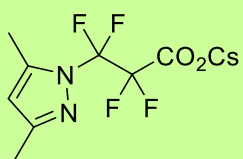
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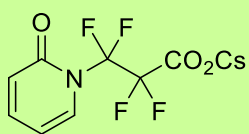
CAS: NA

**CC012**

CAS: NA

**CC013**

CAS: NA

**CC014**

CAS: NA

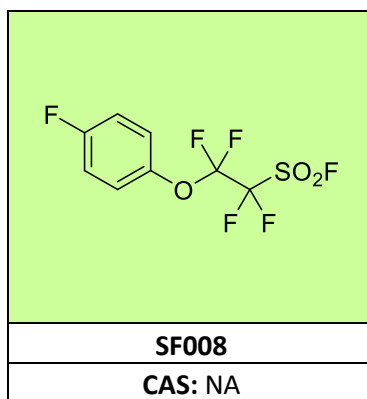
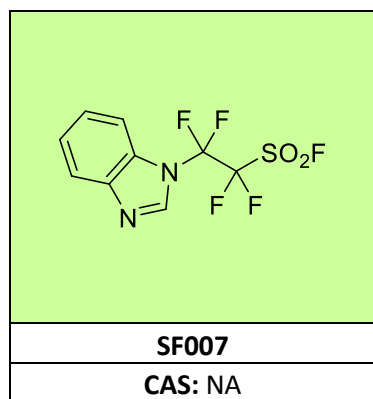
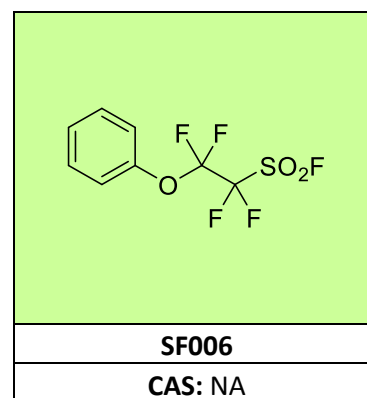
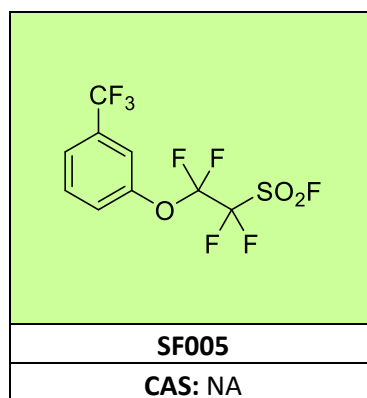
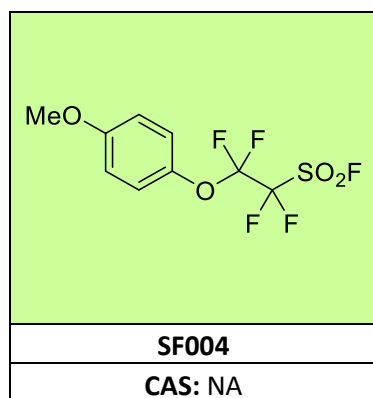
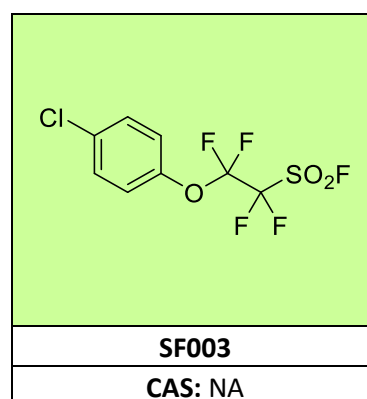
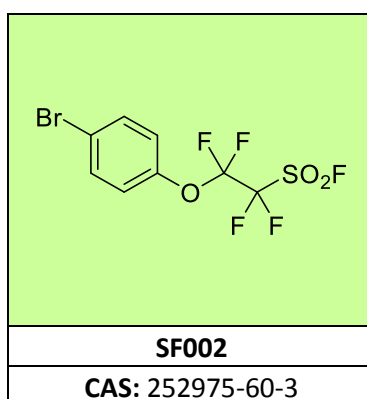
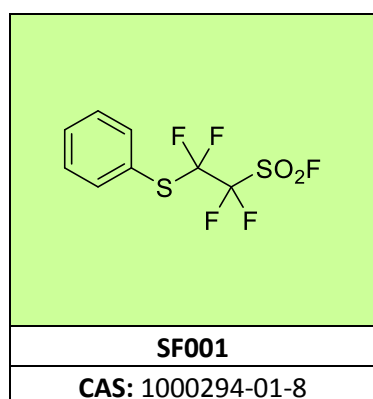
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CAS: NA

Fluoroalkyl sulfonylfluorides

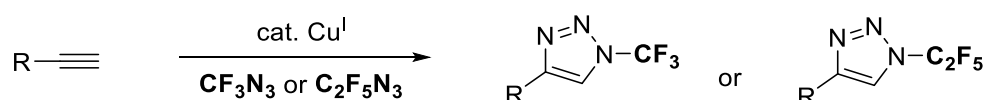
Fluoroalkyl sulfonylfluorides can be used as moderately reactive electrophilic fluoroalkyl sulfonylation reagents. Whereas the related fluoroalkyl sulfonylchlorides can also behave as electrophilic chlorination reagents towards amines affording undesirable *N*-chloroamines, the fluoroalkyl sulfonylfluorides give slower, yet very clean nitrogen sulfonylation to give the corresponding sulfonamides.

Fluoroalkyl sulfonylation of the amine nitrogen greatly lowers the pK_a value of NH and can be used to modulate the behaviour of the drug candidate or build additional molecular complexity around the highly acidic fluoroalkyl sulfonamide nitrogen.



Fluoroalkyl azides

Trifluoromethyl azide, pentafluoroethyl azide, difluoromethyl azide and trifluoroethyl azide represent four examples of exotic fluoroalkyl azides that are potentially very attractive for medicinal chemistry and agrochemistry discovery programmes. Generally, fluoroalkyl azides show much higher thermal stability than their alkyl counterparts, resulting in a good safety profile. Using the well-established copper catalyzed alkyne-azide cycloaddition, various alkynes can be reacted with trifluoromethyl azide or pentafluoroethyl azide affording regioselectively the 1,4-disubstituted *N*-CF₃ or *N*-C₂F₅ triazoles that would be otherwise very hard to access. *N*-trifluoromethylated azoles have been shown to be robust alternatives to potentially metabolically weak *N*-methyl analogues.

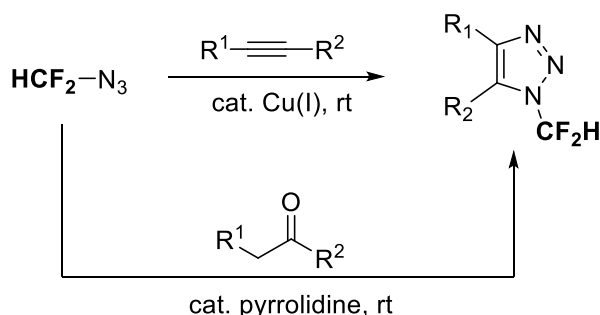


Straightforward and regioselective access to rare *N*-CF₃ and *N*-C₂F₅-1,4-disubstituted triazoles

Ref: Angew. Chem. Int. Ed. 2017, 56, 346

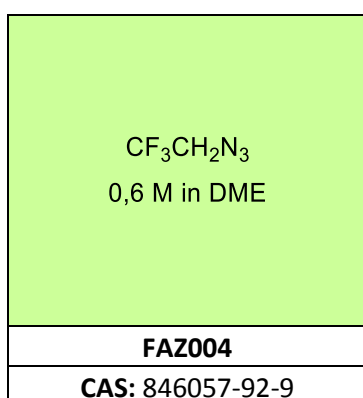
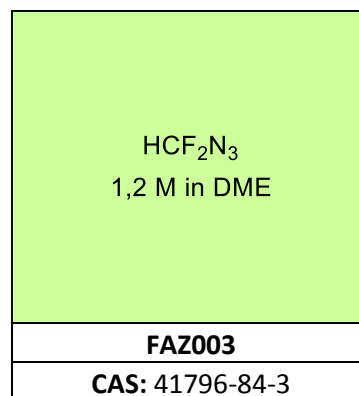
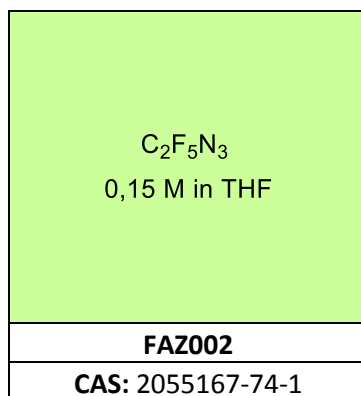
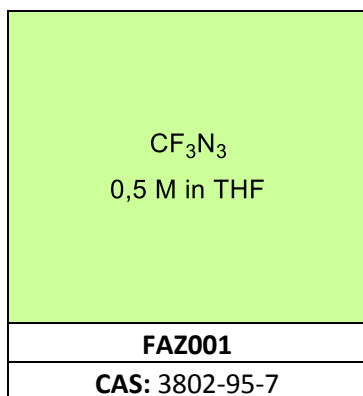
Difluoromethyl azide shares practically the same reactivity as trifluoromethyl azide in copper catalyzed alkyne-azide cycloadditions, providing expedient access to five-membered *N*-CF₂H heterocycles. Difluoromethyl azide provides similar synthetic benefits as other fluoroalkyl azides – a broad substrate scope of regiochemically defined *N*-difluoromethyl azoles can be accessed in a much simpler manner than with other synthetic routes.

Besides the established copper catalyzed alkyne-azide cycloaddition, difluoromethyl azide was shown to undergo an enamine mediated azide-ketone [3+2] cycloadditions, affording the corresponding *N*-CF₂H triazoles.



Ref: Eur. J. Org. Chem 2018 doi:10.1002/ejoc.201800650

3,3-Trifluoroethylazide represents a complementary fluorinated azide that can be used to access *N*-trifluoroethylated triazoles in a regioselective fashion using the established copper catalyzed azide-alkyne cycloaddition.

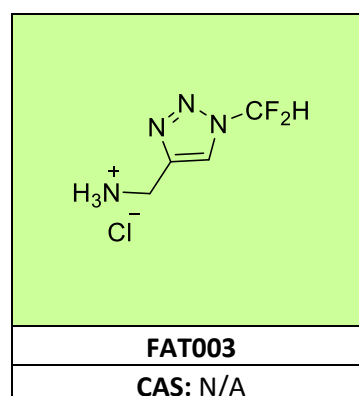
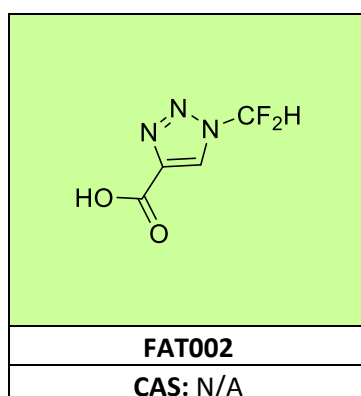
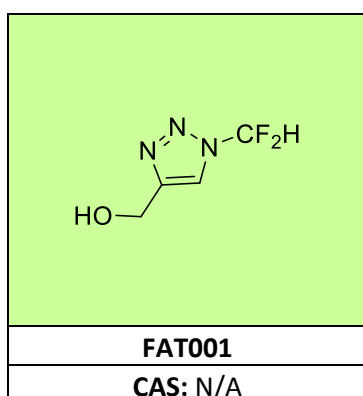


Fluoroalkyl triazoles

So far, *N*-fluoroalkyl triazoles have been very rare motifs in medicinal chemistry due to their limited synthetic availability, but thanks to the robust click chemistry based on *N*-fluoroalkyl azides, the attractive chemical space of *N*-fluoroalkyl triazoles is now unlocked.

N-fluoroalkyl triazoles can serve various purposes in drug design, depending on the nature of the fluoroalkyl, spanning from improved metabolic stability, use as hydrophobic amide bioisosteres or lipophilic hydrogen bond donors.

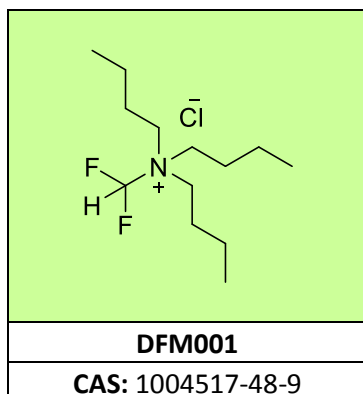
1,4-disubstituted *N*-fluoroalkyl triazoles with three different reactive handles (alcohol, amine and carboxylic acid) can be easily incorporated into synthesis routes, generating novel and potentially promising drug and pesticide candidates.



Difluoromethylation reagents

N-Difluoromethyltributylammonium chloride is an effective source of difluorocarbene for difluoromethylation of O-,S-,N-,C- centred nucleophiles under mild conditions. Using only 1.2 equivalent of this reagent, difluoromethylated products can be obtained in moderate to excellent yields under mild conditions.

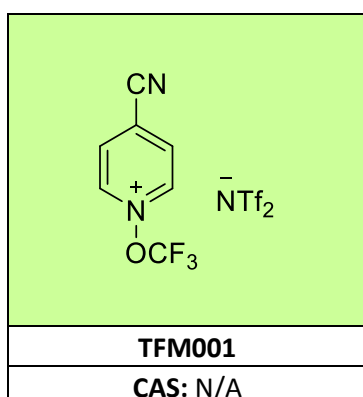
Ref: *Chin. J. Chem.*, 2011, 29, 2717-1721



Trifluoromethoxylation reagents

4-Cyano-N-trifluoromethoxypyridinium bis(trifluoromethanesulfonyl)imide acts as a formally electrophilic trifluoromethoxylation reagents operating via trifluoromethoxy radical as the key intermediate, enabling for example direct C-H trifluoromethoxylation of aromatics and heteroaromatics.

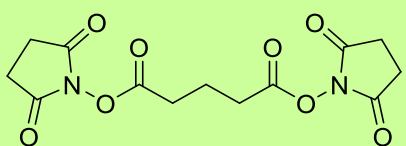
Ref: *Angew. Chem. Int. Ed.* **2018**, 57, 13784



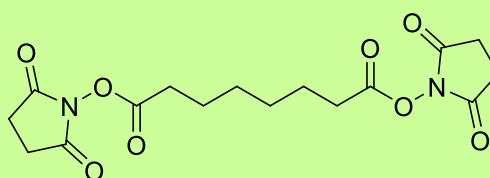
Bioconjugation portfolio

Protein crosslinkers

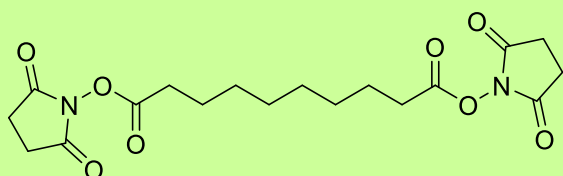
Protein cross-linkers are chemical reagents that play an important role in immunotechnology, structural biochemistry and biology. Protein cross-linking agents can be used to elucidate protein structure and study various protein-protein interactions. Formation of stable covalent bonds between reactive groups contained in protein framework allows easy identification of spatially close domains. The cross-linked conjugates can be identified for example by mass-spectroscopy.

**PCL001**

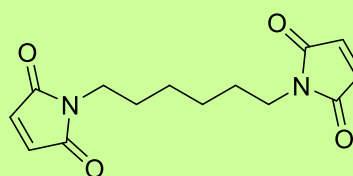
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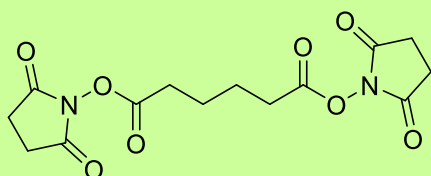
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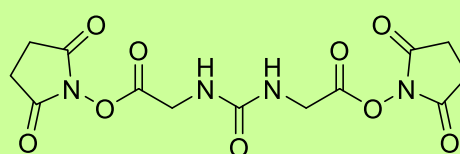
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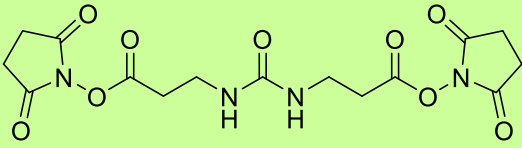
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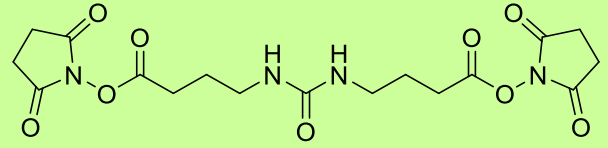
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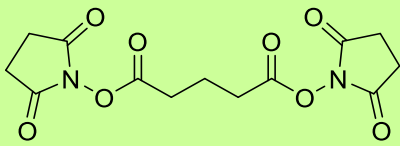
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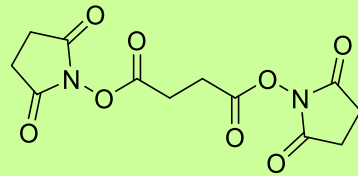
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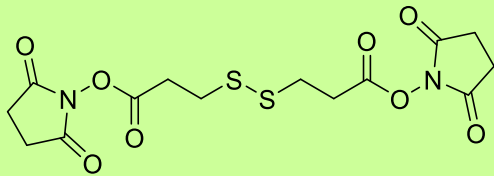
PCL009

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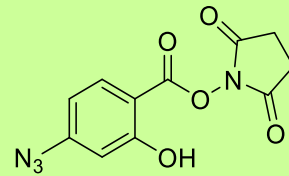
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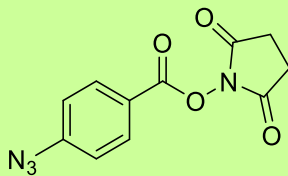
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CAS: 57757-57-0



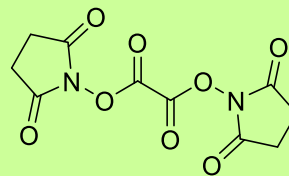
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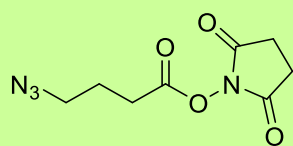
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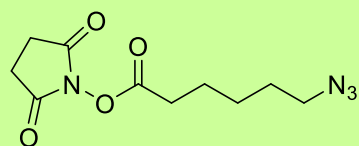
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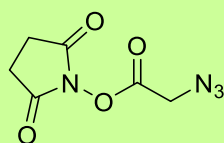
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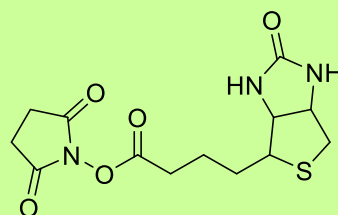
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PCL022

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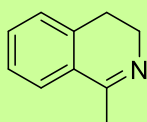
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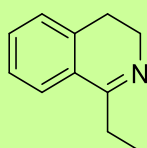
Speciality chemicals

Dihydroisoquinolines

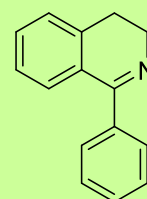
Substituted dihydroisoquinolines serve as useful entry points to synthesis of enantiopure tetrahydroisoquinolines by asymmetric hydrogenation, for example by the established enantioselective Ru-catalyzed transfer hydrogenation pioneered by Noyori *et. al.* Furthermore, the imine moiety of the dihydroisoquinolines can be oxidized to the corresponding nitrones which undergo a (3+2) cycloaddition with a range of olefins and acetylenes.

**DHIQ001**

CAS: 2412-58-0

**DHIQ002**

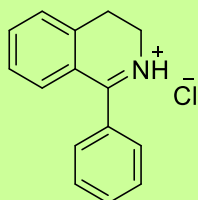
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**DHIQ003**

CAS: 52250-50-7

**DHIQ004**

CAS: 26323-31-9

**DHIQ005**

CAS: 52250-51-8

Azide building blocks

We offer a selection of azide building blocks for synthesis.

