Charles University
Faculty of Science

Study program: Organic Chemistry

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Využití *N*-fluoralkyl-1,2,3-triazolů v organické syntéze

Utilization of *N*-fluoroalkyl-1,2,3-triazoles in organic synthesis

Doctoral thesis

Supervisor: Ing. Petr Beier, Ph.D.

Prague, 2021

Prohlášení:

Prohlašuji, že jsem závěrečnou práci zpracoval samostatně a že jsem uvedl všechny použité informační zdroje a literaturu. Tato práce ani její podstatná část nebyla předložena k získání jiného nebo stejného akademického titulu.

V Praze, 14.6.2021

Podpis:

Acknowledgements

First, I would like to thank my supervisor Dr Petr Beier for allowing me to work in his group on the project dealing with transformations of *N*-fluoroalkyl-1,2,3-triazoles. Petře, it was my great pleasure to work under your supervision. I very much appreciate the trust and freedom you gave me during the last four years. I could never have thought of a better environment for my personal and academic development.

I would like to express my deep acknowledgement to all members of the Beier group, I had the opportunity to work with. Very special thanks go to Dr Svatava Voltrová. Sváťo, you have been the best colleague I could ever have. Thank you that you have been here whenever I needed advice, help or when I wanted to share both professional and personal accomplishments. I am also very happy that I could meet your family during barbecue parties you all organized. Thanks to Soňa, Zsofi, Javi, Viktor, Iveta and Jirka for welcoming me when I joined the group. You all were very kind to me, and you made an amazing atmosphere in the group.

Thanks to Vladimir for our amazing collaboration and friendship. Vladimir, I enjoyed time in the lab with you, our trip to Sněžka, the conference in Vienna and our regular Facebook calls. I am already looking forward to our next works! Thanks to Vojta, Dominik, Šarlota, Tomáš, Lukáš and Anežka for your hard work in our collaborative projects. My next big thanks go to other members of the group. Martin, Norbert, Olga, Nick, Vašek, Jožka and David, thank you for our chats and coffee breaks.

I would also thank Dr Václav Matoušek for our fruitful discussions and his advice.

I am grateful to Dr Blanka Klepetářová for X-ray analyses and to Dr Radek Pohl for measuring advanced NMR experiments. I also thanks to MS department at IOCB Prague for performing HMRS analyses, especially to Mrs Kertisová.

I cannot forget to thank IOCB Prague for the unique environment not only for work but also for social life. I am grateful for the opportunity to participate in Joint Prague-

Weizmann Winter School on Drug Discovery in Rehovot (Israel). I thank Dr Irena G. Stará for organizing IOCB Wednesday seminars and many other events I had the opportunity to participate in.

Last but not least, I would like to thank my family for their continuous support. Thank you, mom and dad for the support not only during my studies but also during my cycling career. Without you, I could not write these lines. The last sentence of this acknowledgement belongs to a special person in my life. Thank you, my love Anička, for all support you gave me during the last five years.

Abstract

This Thesis deals with denitrogenative transformations of *N*-fluoroalkyl-1,2,3-triazoles, easily available heterocycles via copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) of safe and stable *N*-fluoroalkyl azides and alkynes.

The introductory chapter describes general approaches towards *N*1-substituted 1,2,3-triazoles, methods of *N*1-α,α-difluoroalkyl-1,2,3-triazoles preparation and both, transition metal-catalyzed and transition metal-free transformations of *N*1-substituted 1,2,3-triazoles.

In the first part of the Thesis, rhodium-catalyzed reactions of *N*-fluoroalkyl-1,2,3-triazoles are described. Rhodium-catalyzed reactions of *N*-fluoroalkyl-1,2,3-triazoles in presence of suitable reagents provide access to five-membered *N*-fluoroalkyl heterocycles, 2-fluoroalkyl oxazoles and ketamides.

In the second part of the Thesis, both Brønsted and Lewis acid-mediated transformations of *N*-fluoroalkyl-1,2,3-triazoles leading to stereodefined *N*-alkenyl compounds, such as enamides, enimines, amidines and other are discussed. The robustness of the method is showcased on gram scale syntheses and preparation of a drug analogue. At last, thermally-induced rearrangement of *N*-fluoroalkyl-1,2,3-triazoles to 3-fluoroalkyl-2*H*-azirines and the proposed mechanism of the reaction are described.

Abstrakt

Tato práce se zabývá denitrogenativními transformacemi *N*-fluoralkyl-1,2,3-triazolů, snadno dostupných heterocyklů prostřednictvím azido-alkynové cykloadiční reakce katalyzované měďnými solemi bezpečných a stabilních *N*-fluoralkyl azidů a alkynů.

Úvodní kapitola popisuje obecné přístupy k 1,2,3-triazolům, známé metody přípravy *N*1-α,α-difluoralkyl-1,2,3-triazolů a reakce *N*1-substituovaných 1,2,3-triazolů, jednak katalyzované přechodnými kovy a jednak nekatalyzované.

V první části práce jsou popsány reakce *N*-fluoralkyl-1,2,3-triazolů katalyzované rhodiem. Tyto reakce poskytují v přítomnosti vhodných činidel přístup k pětičlenným *N*-fluoralkylovaným heterocyklům, 2-fluoralkyl oxazolům a ketamidům.

Ve druhé části práce jsou diskutovány transformace *N*-fluoralkyl-1,2,3-triazolů zprostředkované Brønstedovými a Lewisovými kyselinami vedoucí ke stereodefinovaným *N*-alkenylovým sloučeninám, jako jsou enamidy, eniminy, amidiny a další. Robustnost metody je předvedena na syntézách v gramovém měřítku a přípravě analogu léčiva. Závěrečná část práce popisuje tepelně indukovaný přesmyk *N*-fluoralkyl-1,2,3-triazolů na 3-fluoralkyl-2*H*-aziriny a uvádí předpokládaný mechanismus této reakce.

List of publications

Part of the work described in this thesis has been published.

The first authors are underlined

Markos, **A**.; Janecký, L.; Klepetářová, B.; Pohl, R.; Beier, P. Stereoselective Synthesis of (*Z*)-β-Enamido Fluorides from *N*-Fluoroalkyl- and *N*-Sulfonyl-1,2,3-Triazoles. *Org. Lett.* **2021**, *23* (11), 4224–4227. (IF = 6.1)

Markos, **A**.; Janecký, L.; Chvojka, T.; Martinek, T.; Martines-Seara, H.; Klepetářová, B.; Beier, P. Haloalkenyl Imidoyl Halides as Multifacial Substrates in the Stereoselective Synthesis of N-Alkenyl Compounds. *Adv. Synth. Catal.* **2021**, accepted, https://doi.org/10.1002/adsc.202100009. (IF = 5.9)

Motornov, V.; Košťál, V.; **Markos**, **A**.; Täffner, D.; Beier, P. General Approach to 2-Fluoroalkyl 1,3-Azoles via the Tandem Ring Opening and Defluorinative Annulation of N-Fluoroalkyl-1,2,3-Triazoles. *Org. Chem. Front.* **2019**, *6* (22), 3776–3780. (IF = 5.2)

Markos, **A**.; Voltrová, S.; Motornov, V.; Tichý, D.; Klepetářová, B.; Beier, P. Stereoselective Synthesis of (Z)-β-Enamido Triflates and Fluorosulfonates from N-Fluoroalkylated Triazoles. *Chem. Eur. J.* **2019**, *25* (32), 7640–7644. (IF = 5.2)

Motornov, V.; **Markos**, **A**.; Beier, P. A Rhodium-Catalyzed Transannulation of N-(per)Fluoroalkyl-1,2,3-Triazoles under Microwave Conditions - a General Route to N-(per)Fluoroalkyl-Substituted Five-Membered Heterocycles. *Chem. Commun.* **2018**, *54* (26), 3258–3261. (IF = 6.2)

Patents

Beier, P.; **Markos, A**. Process for Preparing Substituted Vinyl Sulfonates, CZ308450B6, August 26, **2020**.

Contributions in form of an oral presentation

2021	XX. Interdisciplinary Meeting of Young Life Scientists – (Online conference) – poster
2019	Advances in Organic, Bioorganic and Pharmaceutical Chemistry – Liblice (Špindlerův Mlýn, Czech Rep.) – lecture
	Chemistry at via Carolina (Erlangen, Germany) – lecture
	21st European Symposium on Organic Chemistry (Vienna, Austria) – poster
2018	Joint Prague-Weizmann Winter School on Drug Discovery (Rehovot, Israel) – poster

Abbreviations

Å	Ångström
An	anisyl
APT	attached proton test
Ar	aryl
Boc	*tert*-Butyloxycarbonyl
br	broad
Bn	benzyl
Bu	butyl
CCDC	Cambridge Crystallographic Data Centre
COSY	homonuclear correlation spectroscopy
CuAAC	copper-catalyzed azide-alkyne cycloaddition
CuMeSal	copper(I) 3-methylsalicylate
CuTC	copper(I) thiophene-2-carboxylate
DCE	1,2-dichloroethane
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DFT	density functional theory
DIPEA	*N,N*-diisopropylethylamine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DOSP	1-[[4-alkyl(C_{11}-C_{13})phenyl]sulfonyl]-(2*S*)-pyrrolidinecarboxylate
dr	diastereomeric ratio
EDG	electron donating group
ee	enantiomeric excess
EI	electron impact ionization
equiv	equivalent(s)
ESI	electrospray ionization

Esp	α,α,α′,α′-tetramethyl-1,3-benzenedipropionate
Et	ethyl
EtOAc	ethyl acetate
EWG	electron withdrawing group
FDA	Food and Drug Administration
Het	hetero
HMBC	heteronuclear multiple bond correlation spectroscopy
HMDS	bis(trimethylsilyl)amine
HRMS	high-resolution mass spectrometry
HSQC	heteronuclear single quantum correlation spectroscopy
GC-MS	gas chromatography-mass spectrometry
IOCB	Institute of Organic Chemistry and Biochemistry
Me	methyl
MW	microwave
Nf	nonafluorobutanesulfonyl, nonaflyl
NMR	nuclear magnetic resonance
NOE	Nuclear Overhauser effect
NTTL	*N*-(1,2-naphthaloyl)-(*S*)-*tert*-Leucinate
Oct	octanoate
ORTEP	Oak Ridge thermal ellipsoid plot
Ph	phenyl
Phth	phthalimido
PTAD	[(1-adamantyl)-(*N*-phthalimido)acetate]
Pr	propyl
R_F	perfluoroalkyl
ROESY	rotating frame overhause effect spectroscopy
RuAAC	ruthenium-catalyzed azide-alkyne cycloaddition
SSA	silica sulfuric acid
SPAAC	strain-promoted azide-alkyne cycloaddition
SuFEx	sulfur (VI) fluoride exchange

TBAA	tetrabutylammonium acetate
TBAF	tetrabutylammonium fluoride
TBS	*tert*-Butyldimethylsilyl
TBTA	tris(benzyltriazolylmethyl)amine
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl, tosyl
UV-Vis	ultraviolet-visible spectrophotometry

Contents

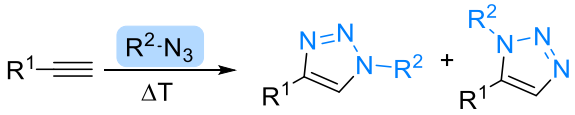
1. Introduction

1,2,3-Triazoles are aromatic five-membered heterocyclic compounds containing three adjacent nitrogen atoms.[1] The introduction of the click chemistry in 2001 by Sharpless[2] and subsequent discovery of the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) by Meldal[3] as a prototypical click reaction have made the *N*1-substituted-1,2,3-triazoles privileged heterocyclic scaffolds across life sciences. They find applications as bioisosteres in medicinal chemistry,[4] ligands in metal complexes,[5] linking units in bioconjugations[6] and in supramolecular chemistry,[7] or as valuable substrates for organic synthesis, among other.[8] In the first part of the introductory chapter are described the most common methods for the preparation of *N*1-substituted 1,2,3-triazoles and syntheses of *N*1-α,α-difluoroalkyl-1,2,3-triazoles. The second part of this chapter deals with known denitrogenative transformations of *N*1-substituted 1,2,3-triazoles to provide an introduction to the main theme of the thesis, which is the denitrogenative transformations of *N*1-fluoroalkyl-1,2,3-triazoles.

1.1. Synthesis of *N*1-substituted 1,2,3-triazoles

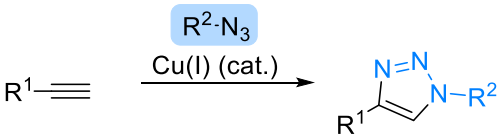
The first synthesis of *N*1-substituted 1,2,3-triazoles was the reaction of phenyl azide with dimethyl acetylenedicarboxylate published in the late 19th century by Arthur Michael.[9] Since then, many methods have been developed. The prevailing strategy in the 1,2,3-triazole synthesis involves the [3+2] cycloaddition of organic azides as 1,3-dipoles and appropriate dipolarophiles e.g., alkynes. In the following section, the most common methods for an effective synthesis of *N*1-substituted 1,2,3-triazoles based on [3+2] cycloadditions will be discussed.

In the 1960´s Prof. Rolf Huisgen published a seminal work describing the scope and the mechanism of 1,3-dipolar cycloadditions.[10] The [3+2] cycloaddition between azides and alkynes belongs to this category and for a long time served as a major approach towards 1,2,3-triazoles (Scheme 1). However, the reaction requires high temperatures, long reaction times, and in the case of non-symmetrical alkynes affords a mixture of regioisomers which are often difficult to separate.[10]



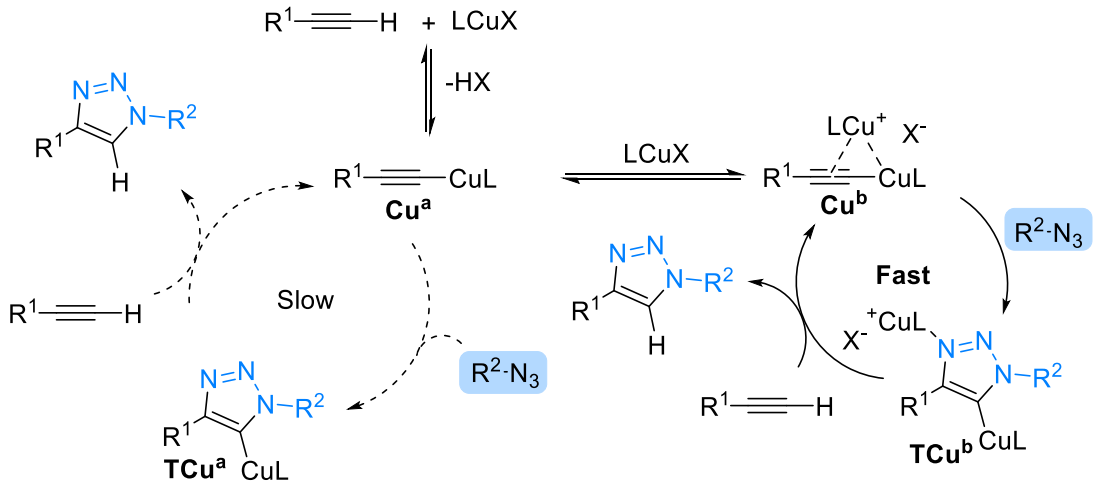
Scheme 1 Huisgen cycloaddition of organic azides and alkynes.

A breakthrough in the synthesis of 1,2,3-triazoles came at the beginning of the 2000´s when groups of Meldal and Sharpless independently described copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC), (Scheme 2).[3,11] The reaction leads to the selective formation of 1,4-disubstituted 1,2,3-triazoles and in most cases works at ambient temperature (Scheme 2).



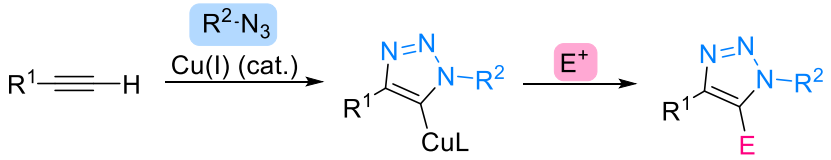
Scheme 2 Copper-catalyzed azide-alkyne cycloaddition.

The early accepted mechanism of the CuAAC involved the monomeric copper-acetylides **Cu^{a}** as active species reacting with azides to form the triazole complexes **TCu^{a}**, which upon the reaction with proton form the final triazoles (Scheme 3, left).[12] However, in 2013, a mechanistic study by the Fokin group revealed that monomeric copper acetylides are reactive towards organic azides only if an exogenous copper catalyst is added.[13] Based on this finding, the σ,π-bis(copper)acetylide complexes of type **Cu^{b}** were accepted as catalytically active species. Later in 2015, Bertrand and co-workers isolated complexes of type **Cu^{b}** and **TCu^{b}** serving as an evidence that these species are involved in the reaction mechanism.[14] Moreover, the stability of isolated **Cu^{b}** and **TCu^{b}** complexes enabled the comparison of the mono- and dinuclear mechanisms and revealed that, even though both mono- and dinuclear pathways are active, the latter mechanism is kinetically favored (Scheme 3, right).



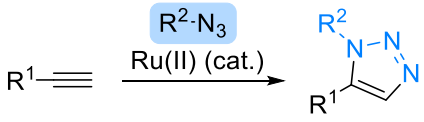
Scheme 3 Mechanisms of the CuAAC.

Although the CuAAC leads to 1,4-disubstituted 1,2,3-triazoles, the copper triazole complexes can be trapped by a variety of electrophiles to form 1,4,5-trisubstituted triazoles (Scheme 4). The detailed description of the interrupted CuAAC can be found in the review by Xu and co-workers.[15]



Scheme 4 The interrupted CuAAC providing 1,4,5-trisubstituted triazoles.

In 2005, the Fokin group discovered the ruthenium-catalyzed azide-alkyne cycloaddition (RuAAC) as a complementary reaction to CuAAC leading to 1,5-disubstituted 1,2,3-triazoles (Scheme 5).[16]

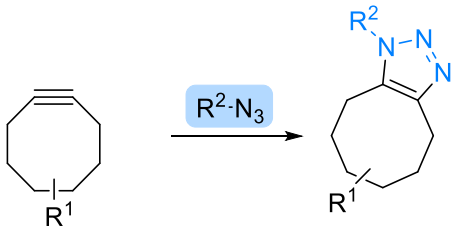


Scheme 5 Ruthenium-catalyzed azide-alkyne cycloaddition (RuAAC).

An extensive review dealing with RuAAC and other approaches towards 1,5-disubstituted 1,2,3-triazoles from organic azides and alkynes has been recently published by Kann and co-workers.[17]

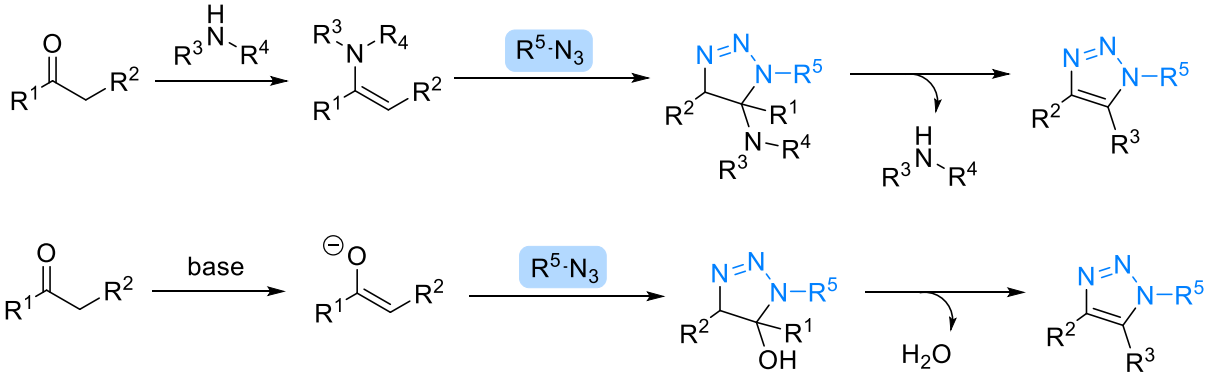
The strain promoted azide-alkyne cycloaddition (SPAAC) introduced by the Bertozzi group in 2004 represents another method for effective 1,2,3-triazole

synthesis (Scheme 6).[18] In SPAAC, organic azides react with cyclooctynes as reactive alkynes at ambient temperature, without metal-catalyst. The mild conditions make SPAAC highly useful as a bioorthogonal reaction. During the last two decades, the structure of the cyclooctynes has been optimized for effective SPAAC in biological systems.[19]



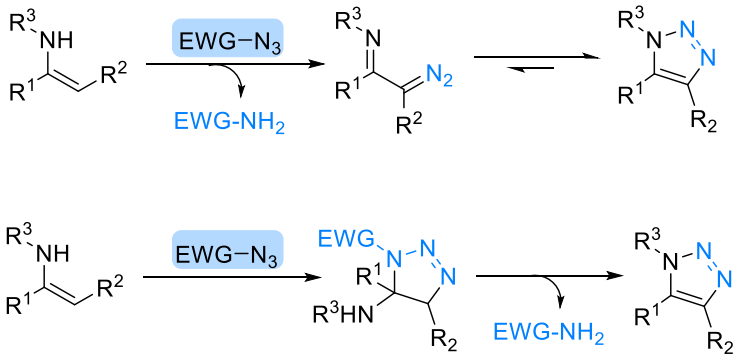
Scheme 6 Strain promoted azide-alkyne cycloaddition.

Alkynes are not the only dipolarophiles reacting with organic azides to 1,2,3-triazoles. Already at the beginning of the 19th century, Otto Dimroth described the base-mediated reaction of carbonyl compounds with phenyl azide.[20] This seminal work served as an inspiration for modern organocatalytic reactions of carbonyl compounds and organic azides. Enamines and enolates generated from carbonyl compounds react as dipolarophiles with organic azides to triazoline intermediates which upon elimination of the leaving group afford 1,2,3-triazoles (Scheme 7).[21] Also, olefines containing leaving groups such as the nitro group, halogens and other are appropriate dipolarophiles that can be used for 1,2,3-triazole synthesis in reactions with azides.[22] In the case of activated olefins without leaving group, an oxidant is required.



Scheme 7 Organocatalytic reaction between carbonyl compounds and organic azides.

Methods which do not utilize [3+2] cycloadditions are less common. For example, electron-deficient azides such as tosyl azide react with secondary enamines to form 1,2,3-triazoles. The reaction mechanism involves either the Regitz diazo transfer, formation of a diazoimine and subsequent cyclization to the final triazole or formal [3+2] cycloaddition to form a triazoline which eliminates amine derivatized from stronger acid (Scheme 8).[22]

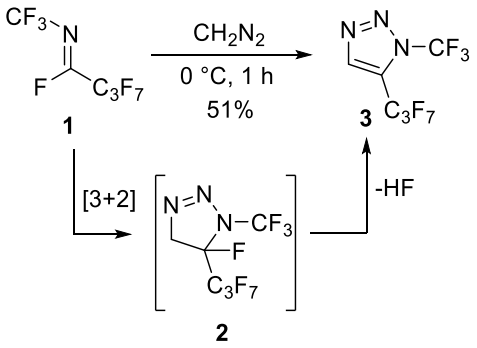


Scheme 8 Reactions between secondary enamines and organic azides.

During the last two decades, a great progress in the development of efficient [3+2] cycloadditions of organic azides has been made, providing powerful tools for effective syntheses of 1,2,3-triazoles. The next chapter deals with the synthesis of *N*1-α,α-difluoroalkyl-substituted 1,2,3-triazoles, compounds whose transformations are the main subject of this thesis.

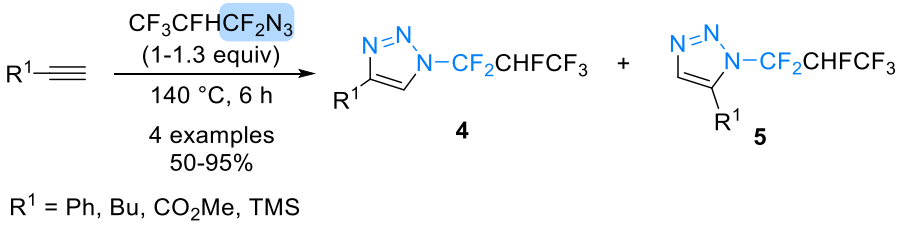
1.1.1. Synthesis of *N*1-fluoroalkyl-1,2,3-triazoles

The first synthesis of *N*1-α,α-difluoroalkyl-1,2,3-triazoles was published in 1977 by Holton and Coe (Scheme 9).[23] The cycloaddition reaction of imidoyl fluoride **1** with diazomethane afforded 1,5-disubstituted triazoline **2** which after elimination of HF formed triazole **3**.



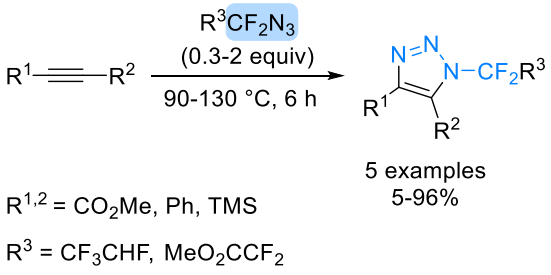
Scheme 9 The first reported synthesis of *N*-fluoroalkyl-1,2,3-triazole.

In 2000, Lermontov described the synthesis of *N*-fluoroalkyl triazoles using fluoroalkyl azides (Scheme 10).[24] The Huisgen [3+2] cycloaddition of terminal alkynes and $CF_3CFHCF_2N_3$ provided triazoles **4** and **5** as a mixture of regioisomers.



Scheme 10 Huisgen cycloaddition between terminal acetylenes and hexafluoropropyl azide.

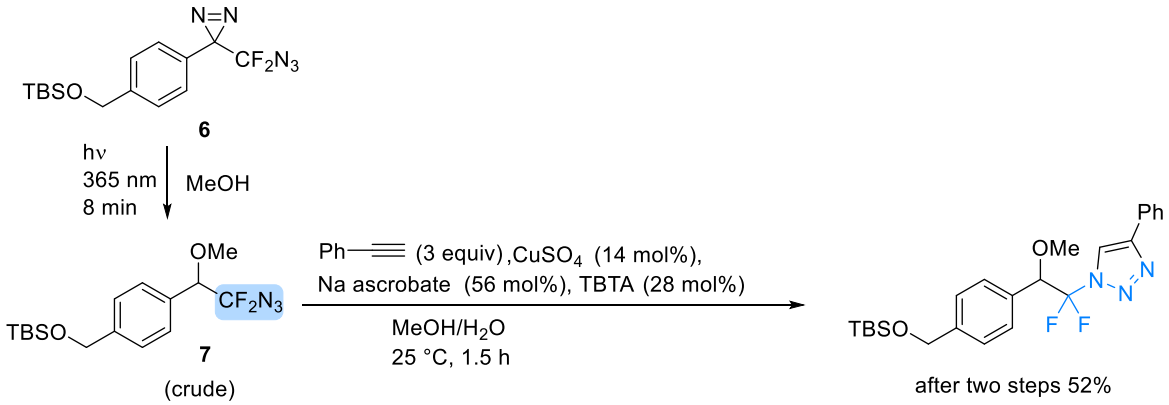
In the case of internal alkynes, *N*1-fluoroalkyl-4,5-disubstituted triazoles were formed (Scheme 11). Although the reaction provided final triazoles in good to excellent yields, the method suffers from the required high temperatures and poor regioselectivity.



Scheme 11 Huisgen cycloaddition of internal acetylenes and fluoroalkyl azides.

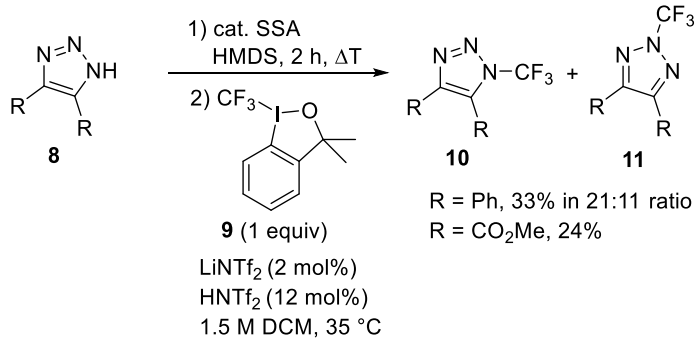
In 2007 the Hosoya group described the first CuAAC of *N*1-α,α-difluoroalkyl azides and terminal alkynes.[25] The α,α-difluoroalkyl azide **6** containing diazirine

group was initially irradiated in methanol to form the azide **7**, which was without purification used for CuAAC with phenylacetylene (Scheme 12).



Scheme 12 The first reported CuAAC of fluoroalkyl azides and terminal alkynes.

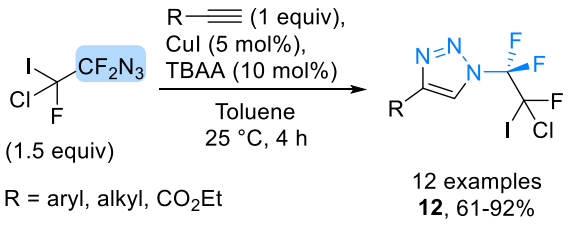
The next approach for the preparation of *N*-α,α-difluoroalkyl triazoles was published by the Togni group in 2012 (Scheme 13).[26] In this method, the 1*H*-1,2,3-triazole (**8**) was used for the direct *N*-trifluoromethylation by the Togni reagent **9**. The method provided a mixture of the *N*1- and *N*2-trifluoromethylated triazoles **10** and **11** in low yields.



Scheme 13 Togni direct trifluoromethylation of 1*H*-1,2,3-triazole.

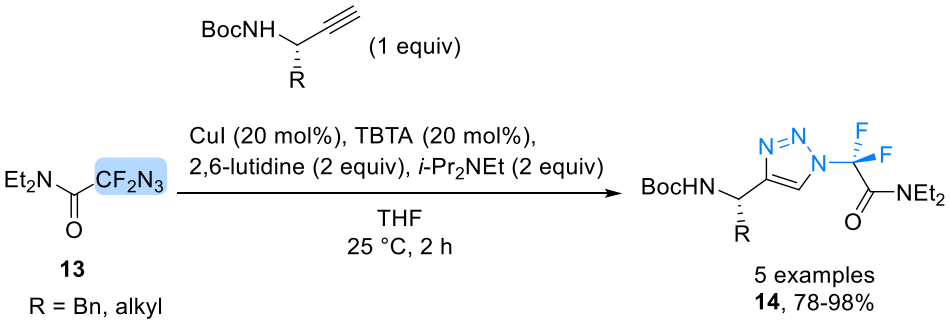
Recently, methods leading to a variety of new *N*-α,α-difluoroalkyl azides emerged, supplying ideal starting materials for *N*-α,α-difluoroalkyl triazoles constructions by CuAAC.[27]

In 2016 the Bai group employed 1-azido-2-chloro-1,1,2-trifluoro-2-iodoethane in CuAAC with terminal alkynes for the synthesis of triazoles **12** (Scheme 14).[28] The iodine can be further substituted using photochemical reactions.



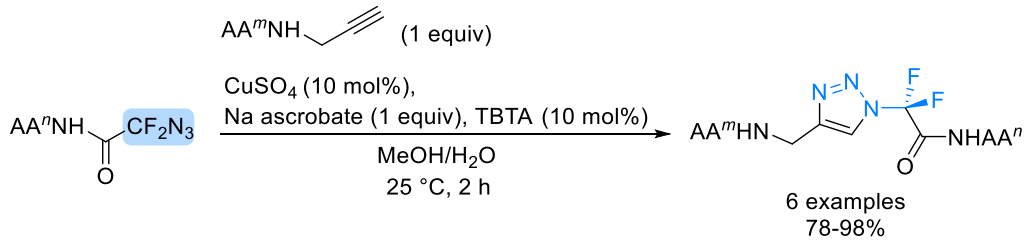
Scheme 14 CuAAC of 1-azido-2-chloro-1,1,2-trifluoro-2-iodoethane and terminal alkynes.

The Olsen group used azide **13** in CuAAC with terminal alkynes derived from amino acids for the preparation of triazoles **14** as peptidomimetics containing the difluoromethylene moiety (Scheme 15).[29]



Scheme 15 CuAAC of azide **13** with terminal alkynes.

Another synthesis of *N*-α,α-difluoroalkyl triazoles as peptidomimetics was published by Milcent, Crousee and co-workers, starting from 1-azido-1,1-difluoroacetamides which are derived from amino acids (Scheme 16).[30]

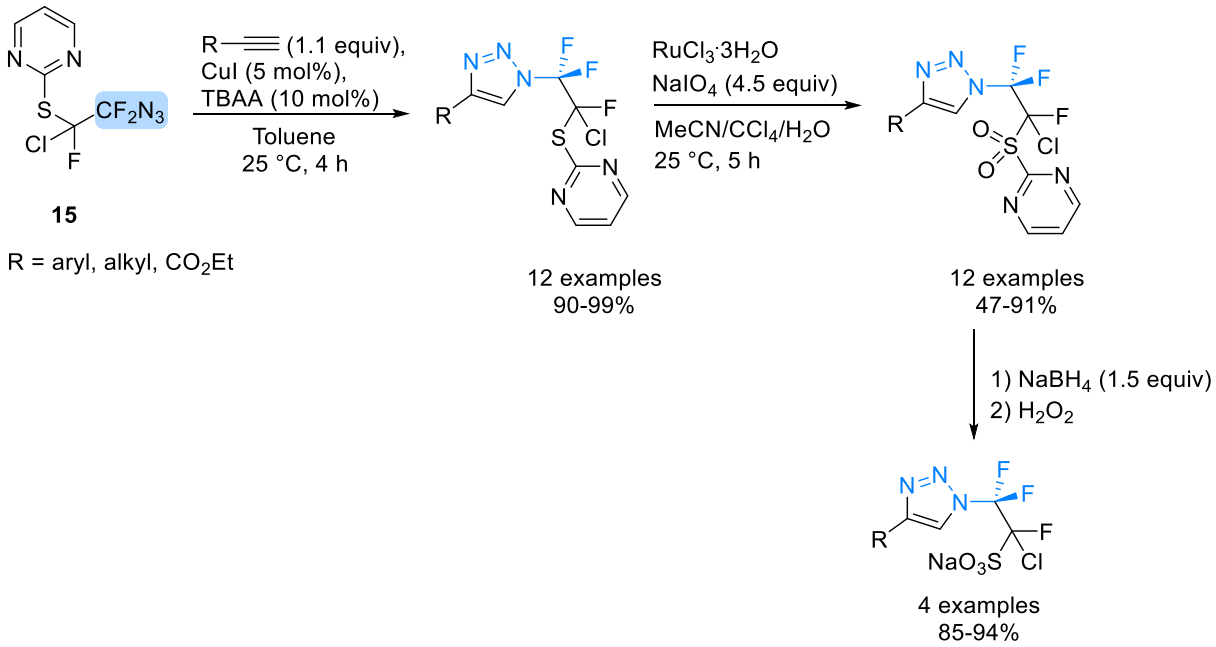


AA^n = MeO-Phe, MeO-Leu, MeO-Gly
AA^m = OBn-Ser-NHBoc, Thr-NHBoc, Gly-NHBoc

Scheme 16 CuAAC of 1-azido-1,1-difluoroacetamides and alkynes in the synthesis of peptidomimetics.

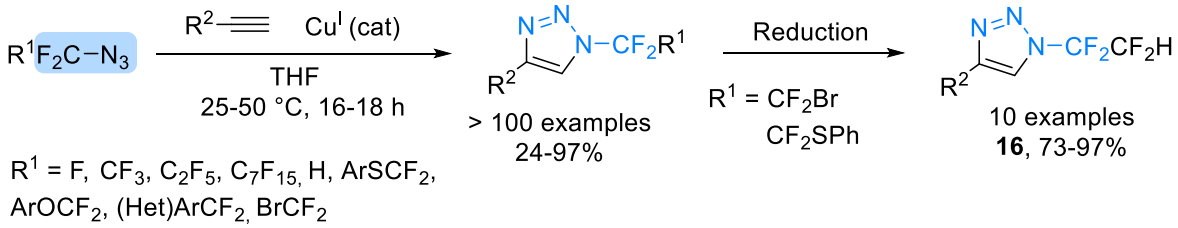
The next azide which was used for 1,2,3-triazoles formation is 2-((2-azido-1-chloro-1,2,2-trifluoroethyl)thio)-pyrimidine (**15**), described by the Bai group in

2017 (Scheme 17).[31] Triazoles formed by the CuAAC could be oxidized to the corresponding sulfones and eventually transformed to fluorinated sulfonates.



Scheme 17 Bai´s synthesis of fluoroalkyl triazoles.

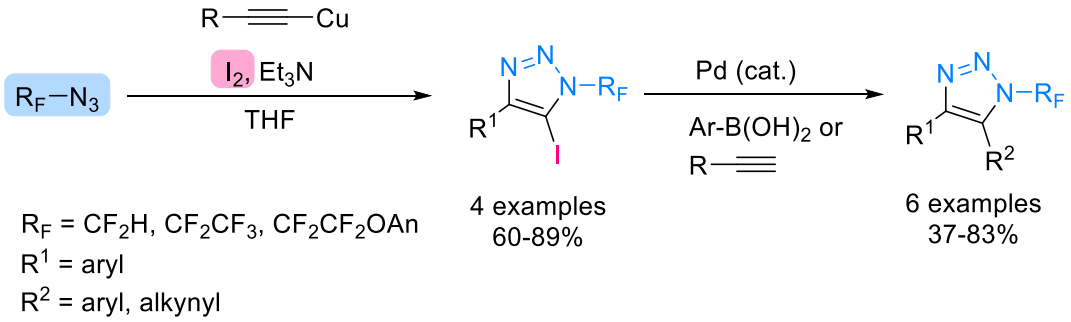
In the last five years, our group described several new fluoroalkyl azides including perfluoroethyl-, perfluoropropyl-, perfluorooctyl-,[32] difluoromethyl-[33] and tetrafluoroethylene-substituted azides.[34,35] Moreover, a method for effective synthesis of azidotrifluoromethane was developed.[32] All azides established in our group afford *N*1-substituted triazoles in CuAAC with terminal alkynes (Scheme 18). The *N*1-2-bromo-1,1,2,2-tetrafluro- and *N*1-CF_2CF_2SAr-substituted triazoles can be furthermore reduced to the tetrafluoroethyl-substituted triazoles **16**.



Scheme 18 CuAAC of fluoroalkyl azides developed in the Beier´s group.

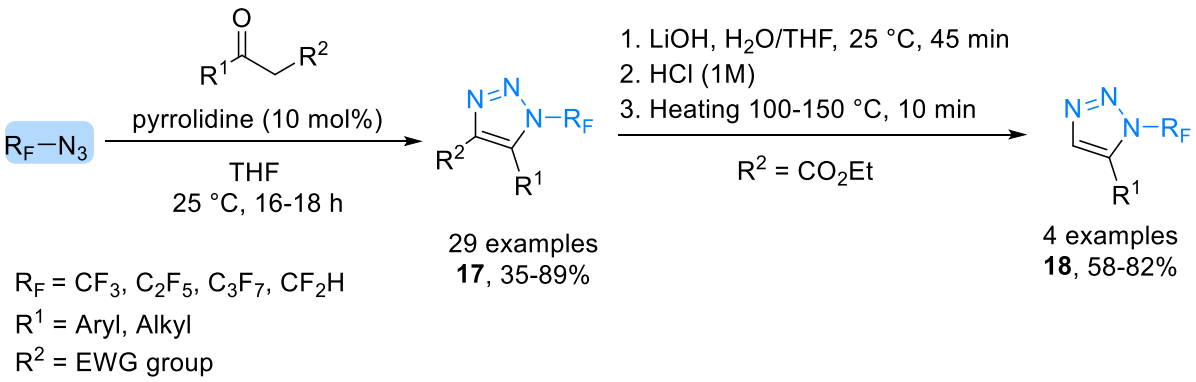
5-Iodo-substituted *N*-fluoroalkyl-1,2,3-triazoles were synthesized using copper(I) acetylides in the presence of iodine as a trapping reagent for the copper-triazole complexes (Scheme 19).[32–34] The prepared 5-iodo-substituted triazoles further

undergo cross-coupling reactions to afford 1-fluoroalkyl-4,5-disubstituted-1,2,3-triazoles.



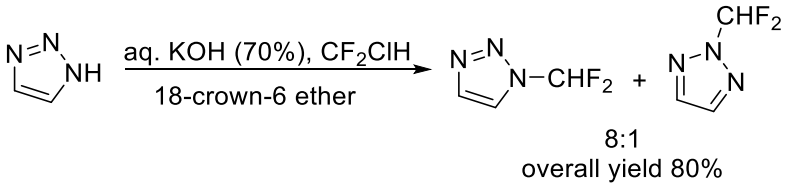
Scheme 19 Synthesis of 4-substituted 5-iodo-*N*-fluoroalkyl-1,2,3-triazoles and subsequent cross-coupling reactions.

Perfluoroalkyl azides and difluoromethyl azide were used in an organocatalytic reaction with carbonyl compounds to form the 4,5-disubstituted triazoles **17** (Scheme 20).[33,36] Additionally, *N*-perfluoroalkyl-1,2,3-triazoles containing ester group at position 4 were hydrolyzed under basic conditions and subsequently decarboxylated to 5-substituted triazoles **18**.



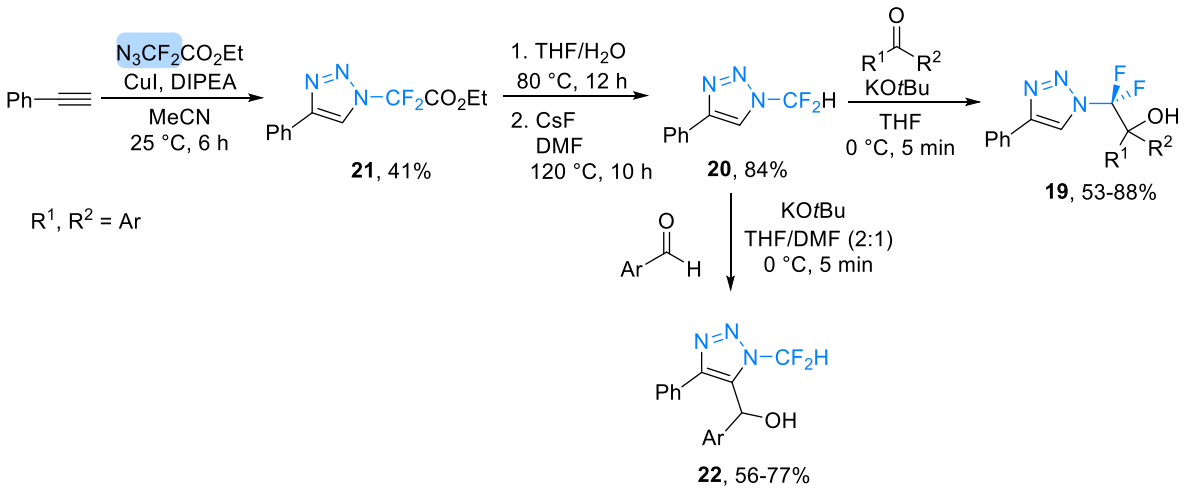
Scheme 20 Organocatalyzed [3+2] cycloaddition of *N*-fluoroalkyl azides and carbonyl compounds and subsequent hydrolysis of the resulting triazoles to 1-fluoroalkyl-5-substituted triazoles.

The direct difluoromethylation of 1*H*-1,2,3-triazole was described in 2018 by Petko (Scheme 21).[37] The method involves difluoromethylation of nitrogen by difluoromethyl carbene, which is generated from chlorodifluoromethane by KOH, and give a mixture of *N*1- and *N*2-substituted difluoromethyl triazoles.



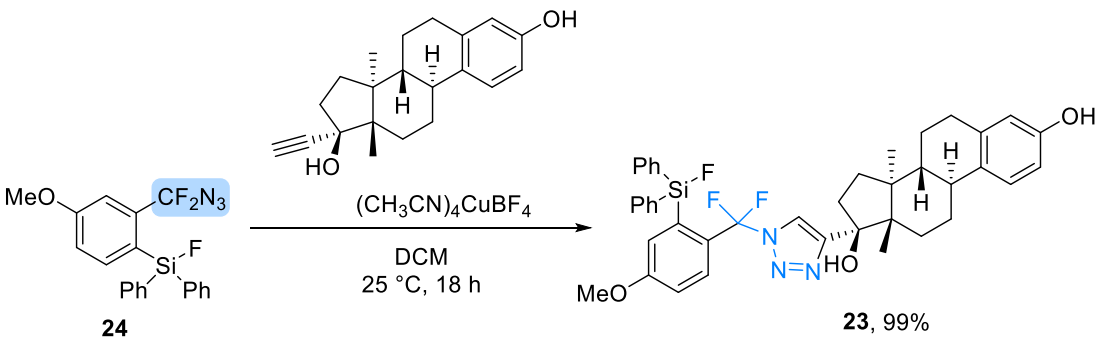
Scheme 21 Direct difluoromethylation of 1*H*-1,2,3-triazole.

Last year, the Chi group described the synthesis of *N*1-difluoromethylene-containing 1,2,3-triazoles **19** by deprotonation of difluoromethyl group to *N*1-difluoromethyl-1,2,3-triazole **20** and subsequent reaction with ketones as electrophiles (Scheme 22).[38] The starting triazoles **20** were prepared by decarboxylation of triazole **21**. In case the reaction was performed in a mixture of THF/DMF (2:1) as a solvent and using benzaldehydes, 4,5-disubstituted triazoles **22** were formed.



Scheme 22 Synthesis of 1-difluoromethyl-4-phenyl triazole **20** and its transformation to triazoles **19** and **22**.

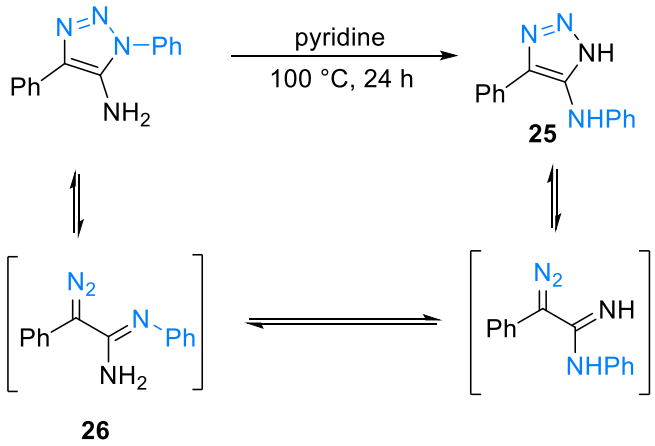
In the same year, the Yoshida group prepared *N*1-difluoromethylene-containing 1,2,3-triazole **23** by CuAAC of aryldifluoromethylazide **24** and the 17α-ethynylestradiol (Scheme 23).[39]



Scheme 23 Synthesis of estradiol derivative containing difluoromethyl triazole group.

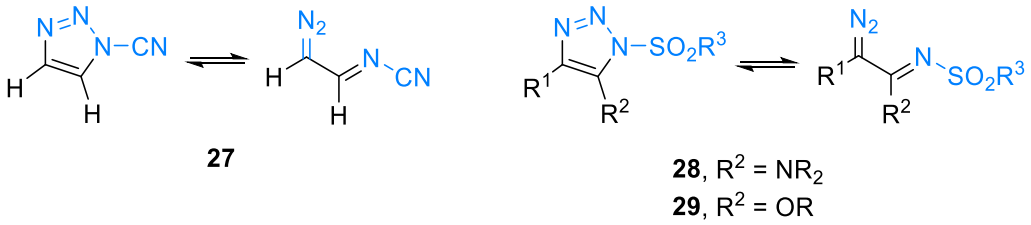
1.2. Denitrogenative transformations of 1,2,3-triazoles

As early as 1909, Otto Dimroth discovered that *N*1-substituted 1,2,3-triazole containing exocyclic amino group can undergo a rearrangement leading to isomeric triazole **25** (Scheme 24).[40] The reaction proceeds via ring-opening to the diazoimine **26**, which cyclizes to the triazole **25**, and is known as the Dimroth rearrangement.



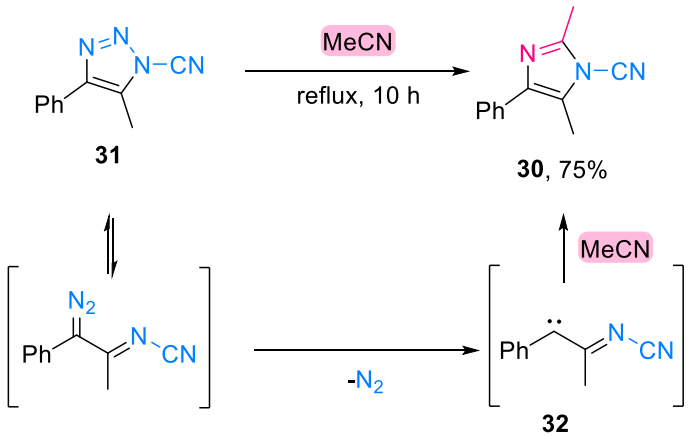
Scheme 24 Dimroth rearrangement.

In 1960-70´s, three articles describing the existence of 1-cyano-1,2,3-triazole **27**, *N*1-sulfonyl-5-alkoxy-1,2,3-triazoles **28** and *N*1-sulfonyl-5-amino-1,2,3-triazoles **29** as a tautomeric mixture of the triazoles and diazoimines were published (Scheme 25).[41–43]



Scheme 25 Triazole-diazoimine equilibrium.

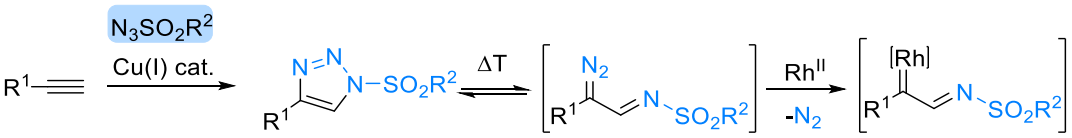
These reports revealed that although 1,2,3-triazoles exist in thermodynamically stable triazole form, the presence of a strongly electron-withdrawing group on *N*1 can shift the equilibrium towards the diazoimine form. Later in 1981, Regitz and co-workers found the synthetic application of the triazole-diazomine equilibrium in the synthesis of imidazole **30** (Scheme 26). In this often neglected work, the *N*1-cyano-1,2,3-triazole **31** undergoes heating induced tautomerization to diazoimine that loses nitrogen to form azavinyl carbene **32** and subsequent [3+2] cycloaddition with acetonitrile affords imidazole **30**.[44]



Scheme 26 Regitz synthesis of 1-cyano imidazole **30** from *N*1-cyano-1,2,3-triazole **31**.

The transformations of *N*1-substituted 1,2,3-triazoles had not received much attention until the groundbreaking work by the Gevorgyan and the Fokin groups in 2008, describing easily available *N*-sulfonyl-1,2,3-triazoles as precursors of rhodium(II) stabilized azavinyl carbenes (Scheme 27).[45] Since then, the rhodium-catalyzed reactions of *N*-sulfonyl-1,2,3-triazoles have become a valuable method for the construction of aza-heterocycles and stereoselective synthesis of nitrogen-containing compounds. In the last decade, five extensive reviews describing the recent development of metal-catalyzed transformations of *N*-

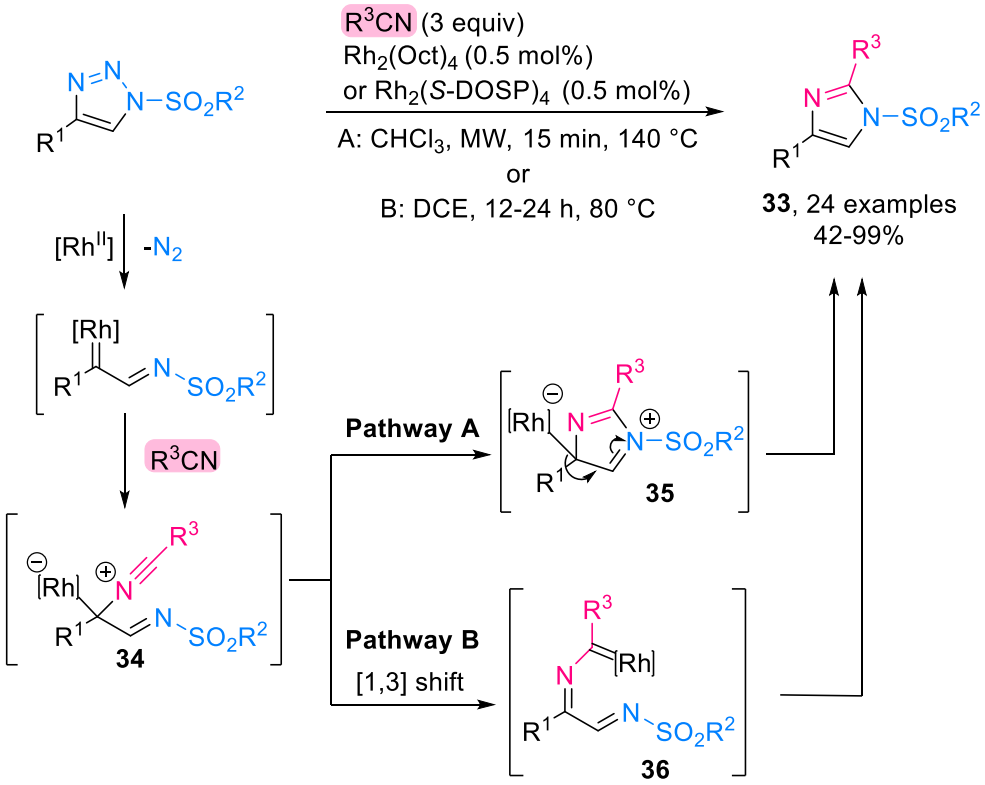
sulfonyl-1,2,3-triazoles have been published.[8,46–49] Thus, in this chapter, representative examples of metal-catalyzed and metal-free transformations of 1,2,3-triazoles will be described to provide a background for the next part of this thesis.



Scheme 27 CuAAC of sulfonyl azides and terminal alkynes followed by the formation of rhodium azavinyl carbene.

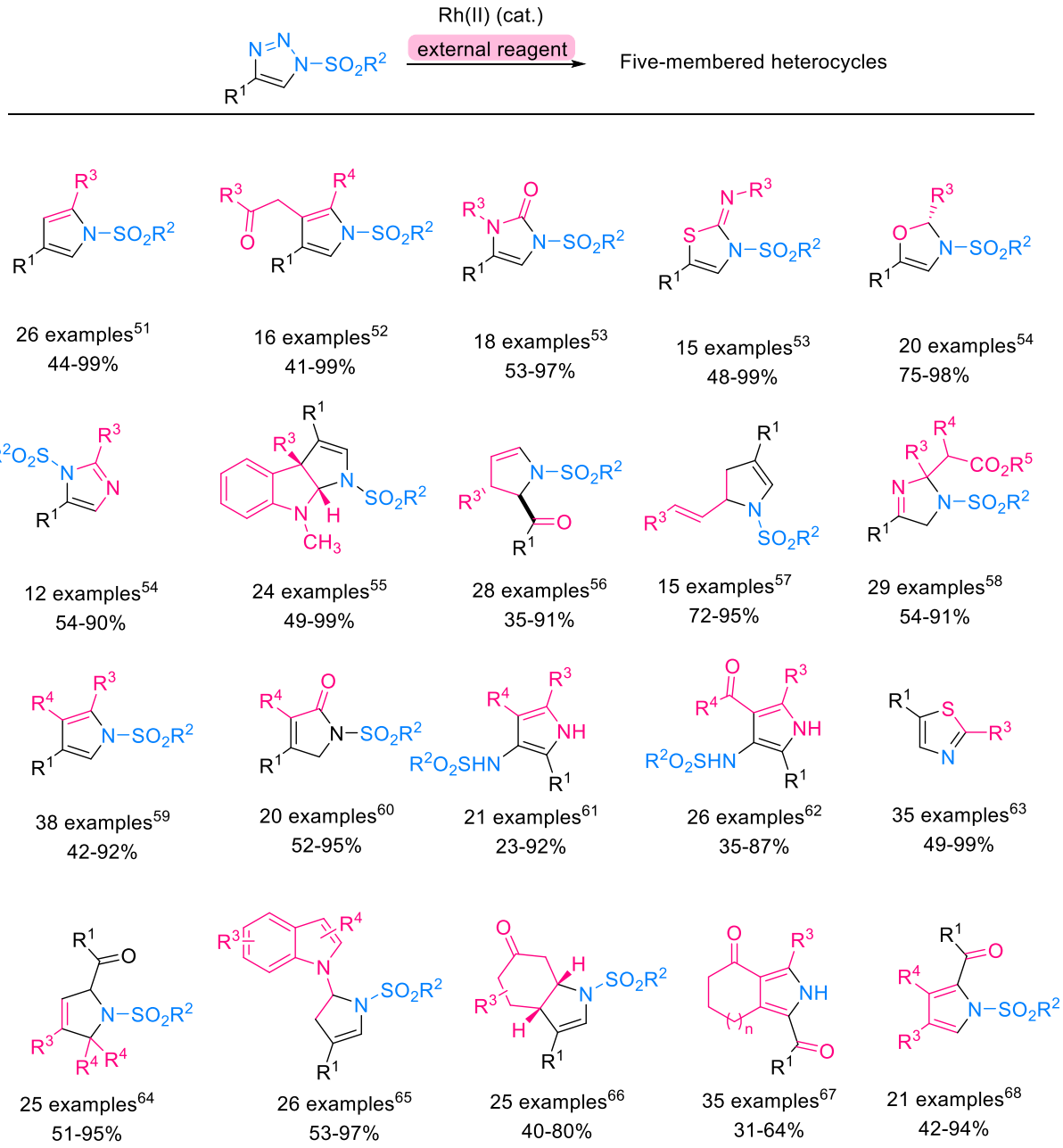
1.2.1. Transition metal-catalyzed transformations of 1,2,3-triazoles

The most widely utilized catalysts for the 1,2,3-triazoles denitrogenative transformation are rhodium(II) carboxylates. Rhodium carbenes are reactive intermediates with an immense synthetic application, which are conventionally formed from diazocompounds.[50] In 2008 Fokin, Gevorgyan and co-workers reported rhodium-catalyzed transannulation of *N*-sulfonyl triazoles with nitriles to form imidazoles **33** (Scheme 28).[45] The reaction can be performed under microwave-assisted or conventional heating conditions. Two possible mechanistic pathways were proposed for the reaction. In both cases, nucleophilic attack of the nitrile nitrogen to the rhodium carbene leads to zwitterionic intermediate **34**. In the Pathway A, intermediate **34** cyclizes to zwitterion **35** that subsequently loses rhodium catalyst (Scheme 28). In the Pathway B, intermediate **34** undergoes rhodium [1,3] shift to derivative **36** which cyclizes to the final imidazole **33**.

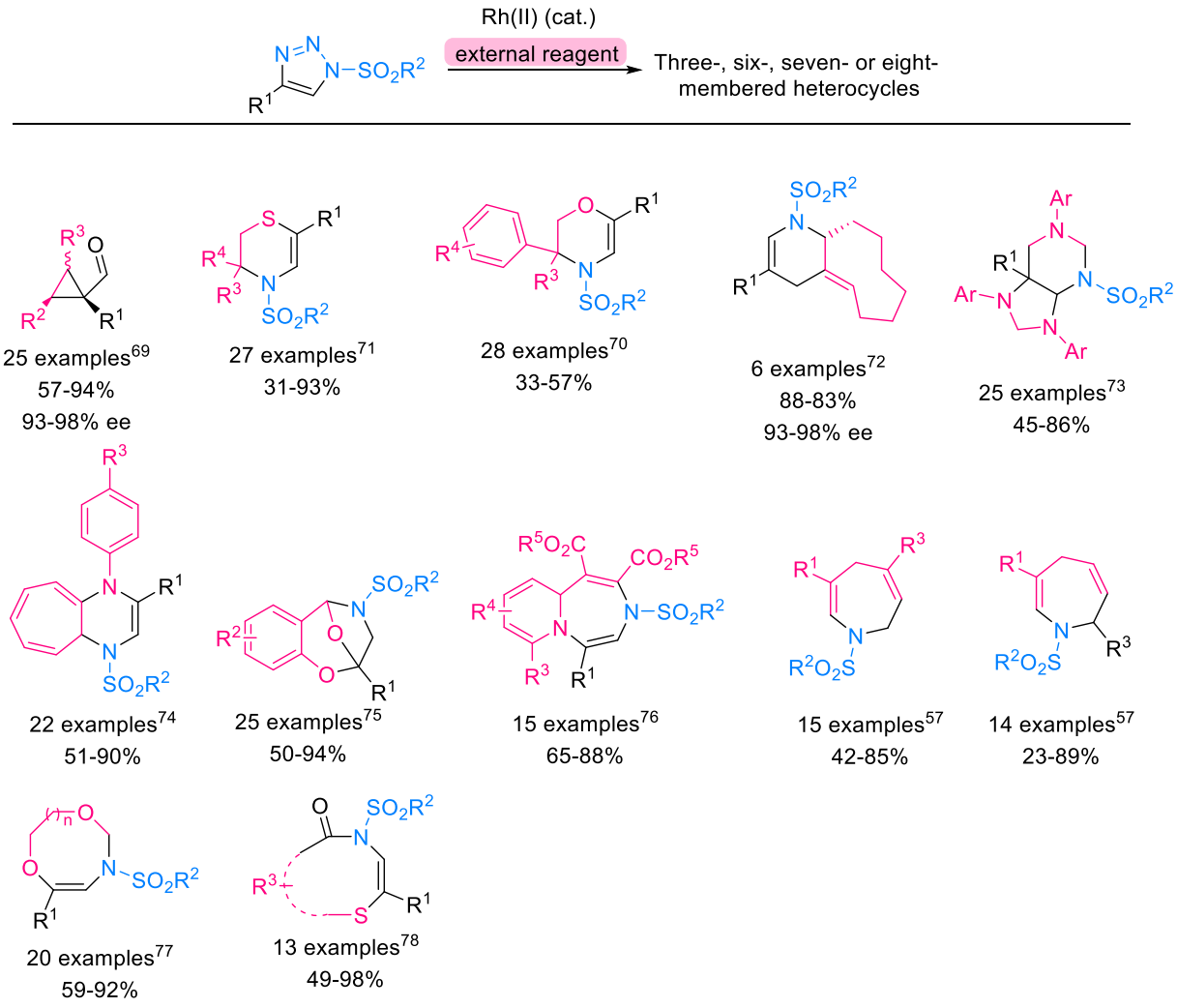


Scheme 28 Rhodium-catalyzed synthesis of *N*-sulfonyl imidazoles from *N*-sulfonyl-1,2,3-triazoles and proposed reaction mechanisms.

Following this work, groups of Fokin, Murakami, Gevorgyan, Davies and others described the synthesis of five-membered *N*-heterocycles by using rhodium-catalyzed reactions of *N*-sulfonyl-1,2,3-triazoles with external reagents, such as dipolarophiles (Scheme 29).[51,52,61–68,53–60] The synthesis of three-, six- seven- and eight-membered heterocycles with the utilization of external reagents has been also well established (Scheme 30).[57,69,78,70–77] Moreover, chiral rhodium catalysts such as Rh_2(*S*-NTTL)$_4$, Rh_2(*S*-PTAD)$_4$ were used for stereoselective transannulations to construct chiral heterocycles.

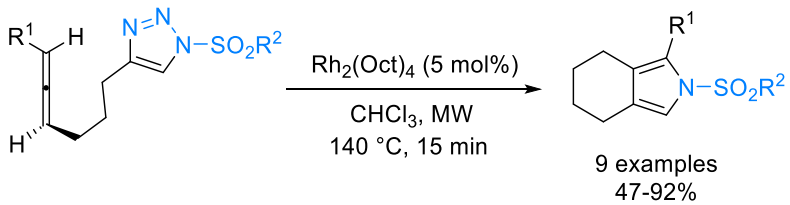


Scheme 29 Synthesis of five-membered heterocycles by rhodium-catalyzed reaction of *N*-sulfonyl triazoles and external reagents.



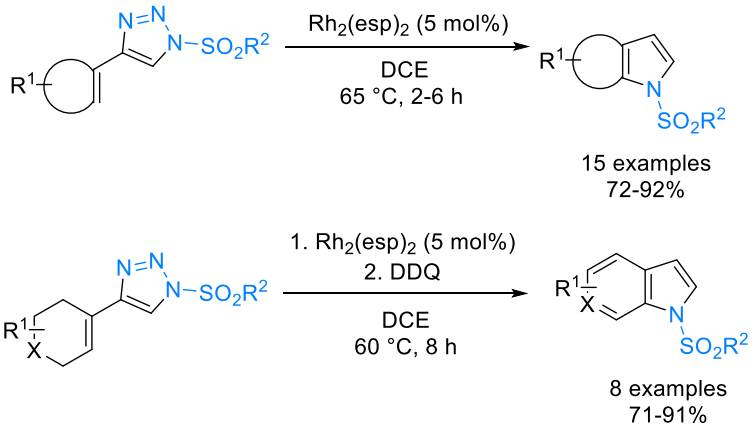
Scheme 30 Synthesis of three-, six- and seven-membered heterocycles by rhodium catalyzed reaction of *N*-sulfonyl triazoles and external reagents.

In 2013 Sarpong and Scholtz reported the rhodium-catalyzed intramolecular formation of *N*-heterocycles, starting from *N*-sulfonyl-1,2,3-triazoles containing an allene moiety (Scheme 31).[79]



Scheme 31 Rhodium-catalyzed intramolecular synthesis of pyrrole derivatives from *N*-sulfonyl triazoles.

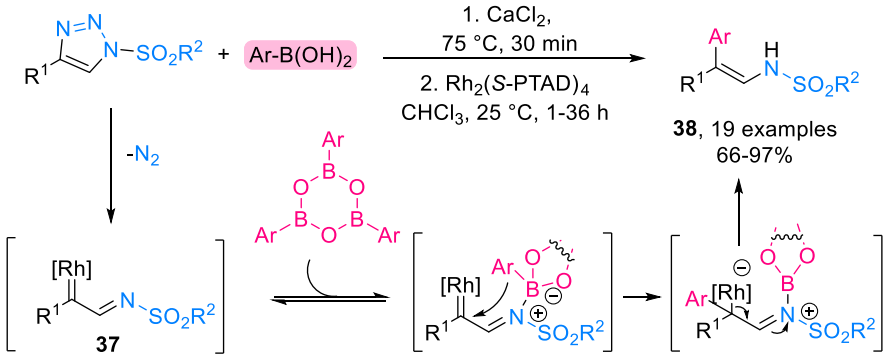
The next early example of intramolecular cyclization of *N*-sulfonyl triazoles is the rhodium-catalyzed 4π electrocyclization of 4-alkenyl-1-sulfonyl triazoles, providing 3,4-fused pyrroles which can be oxidized by DDQ to indoles (Scheme 32).[80]



Scheme 32 Intramolecular electrocyclization of 4-alkenyl-1-sulfonyl triazoles and the subsequent oxidation of the formed pyrroles to indoles.

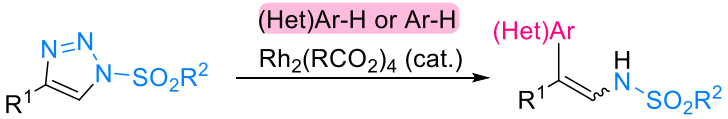
Since the above-mentioned reports, rhodium-catalyzed intramolecular cyclizations of *N*-sulfonyl-1,2,3-triazoles have been used for the synthesis of a variety of non-fused, fused, achiral and chiral nitrogen-containing heterocycles.[48,49]

N-Sulfonyl-1,2,3-triazoles do not undergo only rhodium-catalyzed cyclization reactions. In 2012 the Fokin group reported stereoselective arylation of *N*-sulfonyl-1,2,3-triazoles with boronic acids (Scheme 33).[81] The proposed reaction mechanism consists of the formation of rhodium azavinyl carbene **37**, which is coordinated by nitrogen atom to the boron of the boronic acid trimer, followed by selective aryl delivery to the rhodium carbene. In the last step, the rhodium catalyst is regenerated back to the reaction cycle to form enamide **38**. It is worth to mention, that $Rh_2(Oct)_4$ was found unsuitable for the reaction and the effect of the chiral rhodium catalyst on the stereoselective outcome of the reaction was not investigated.



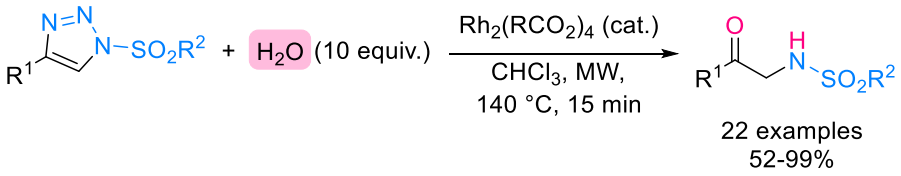
Scheme 33 Rhodium-catalyzed stereoselective synthesis of β,β-disubstituted enamides from *N*-sulfonyl-1,2,3-triazoles.

Subsequently, direct (hetero)arylation of rhodium carbenes by electron-rich (hetero)aryls were reported; however, the stereoselectivity of the reactions was mostly poor (Scheme 34).[82–86]



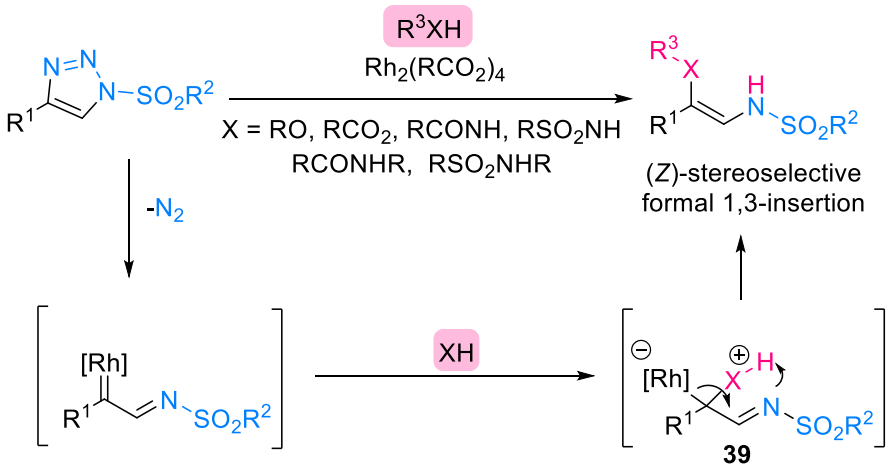
Scheme 34 Direct (hetero)arylation of rhodium azavinyl carbenes.

Murakami and co-workers reported the denitrogenative hydrolysis of *N*-sulfonyl triazoles in the presence of water and a rhodium catalyst.[87]



Scheme 35 The synthesis of ketamides by rhodium-catalyzed hydrolysis of *N*-sulfonyl triazoles.

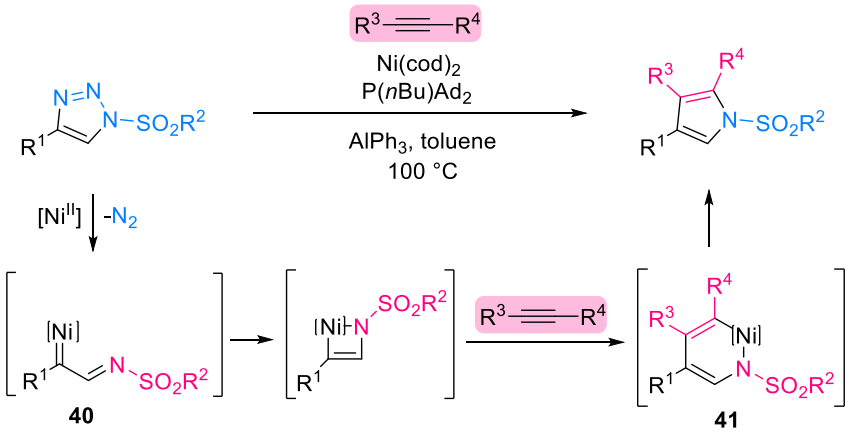
Following Murakami´s work, Fokin and co-workers reported the insertion of functional groups containing polar X-H (X = O, N) bonds to rhodium azavinyl carbenes (Scheme 36).[88] This work revealed the mechanism of the addition of polar X-H (X = O, N) bonds on the rhodium azavinyl carbenes, which proceeds via the formation of the ylide intermediate **39**. The proton on heteroatom X is eventually intramolecularly trapped by nitrogen lone pair which makes the reaction stereoselective.



Scheme 36 Reactions of rhodium azavinyl carbenes with alcohols, carboxylic acids, and amides.

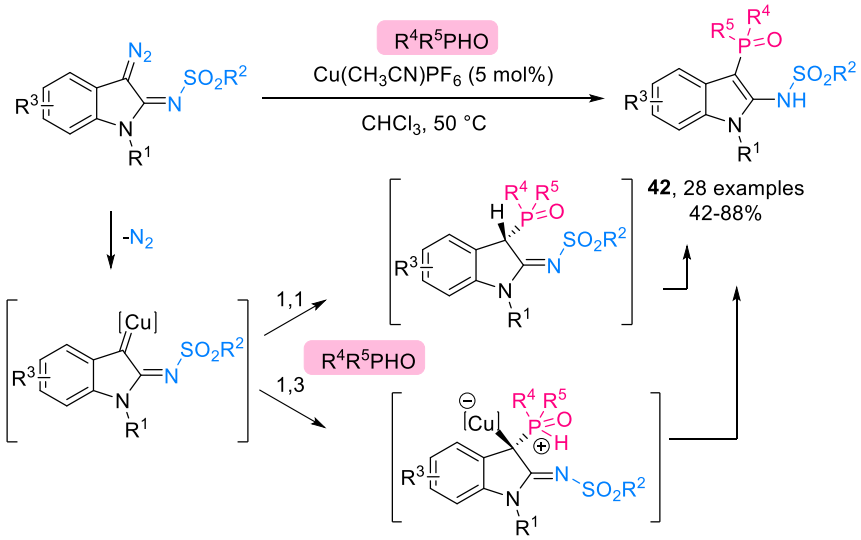
Apart from the above-mentioned examples, rhodium-catalyzed reactions of *N*-sulfonyl triazoles have been utilized in many more types of transformations such as stereoselective C-H functionalization of alkanes,[89] 1,2 migration reactions[90,91] or in natural product synthesis.[92]

Other well-established metallocarbenes derived from azavinyl diazocompounds are nickel azavinyl carbenes. Nickel-catalyzed denitrogenative transformations of *N*-sulfonyl triazoles were pioneered by Murakami and co-workers in the synthesis of pyrroles (Scheme 37).[93] The authors hypothesized a mechanism involving the formation of nickel carbene **40**, its cyclization to a four-membered ring which subsequently reacted with alkynes to form six-membered ring **41**. Finally, the nickel catalyst was regenerated back to the reaction cycle and the pyrrole was formed.



Scheme 37 Nickel-catalyzed synthesis of pyrroles from *N*-sulfonyl triazoles and internal alkynes.

In addition to rhodium and nickel azavinyl carbenes, the formation of copper and silver carbenes derived from azavinyl diazocompounds was proposed in the report by the Tang group.[94] In 2017 Jiang and co-workers described copper-catalyzed denitrogenative reaction of 3-diazoindolin-2-imine, which exists in a thermodynamically favored opened ring form (Scheme 38).[95] The authors proposed copper carbene as a reaction intermediate which reacts with H-phosphine oxide either by 1,1- or 1,3-type insertion providing 3-phosphinoyl indoles **42**.



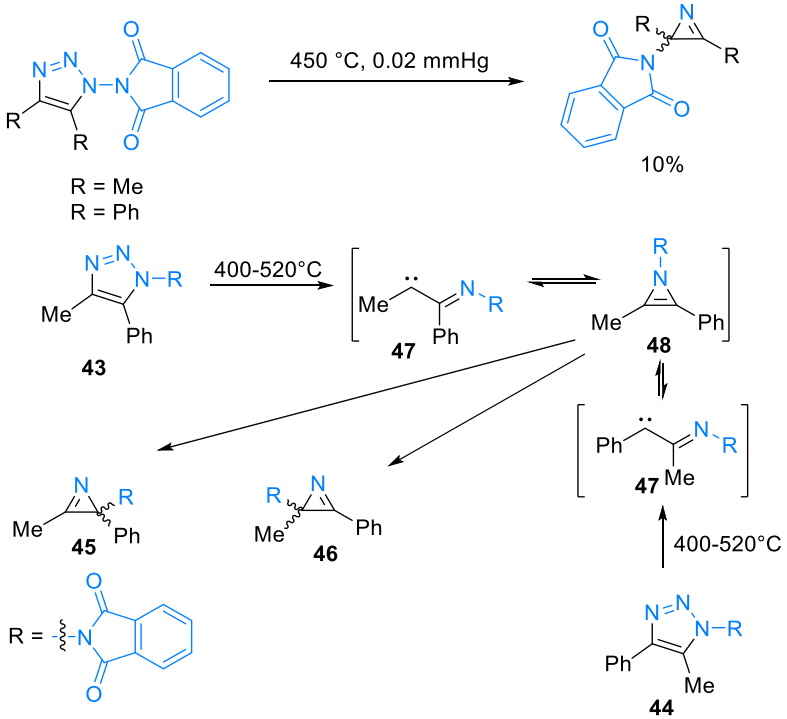
Scheme 38 Copper-catalyzed reaction of 3-diazoindolin-2-imine to 3-phosphinoyl indoles.

1.2.2. Transition metal-free transformations of 1,2,3-triazoles

Thermally induced denitrogenative transformations of 1,2,3-triazoles

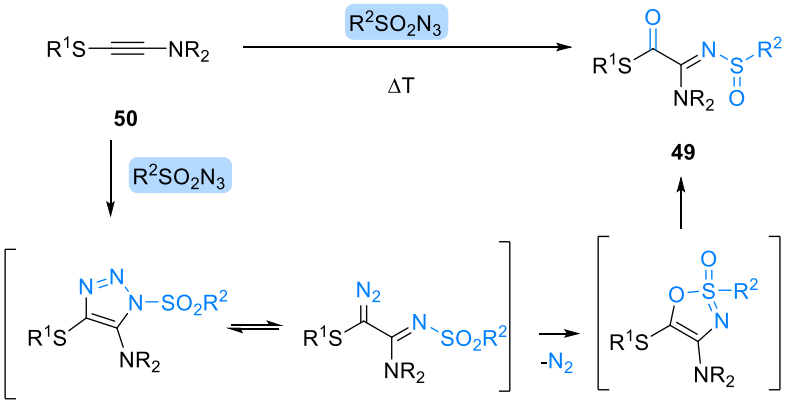
Transformations of 1,2,3-triazoles that do not bear at *N*1 strongly electron-withdrawing groups are rare and, in most cases, lack synthetic application. Additionally, these transformations often require high reaction temperatures (above 300 °C) to overcome the high aromatic stability of the triazole ring.

In the 1970s Rees and co-workers studied flash vacuum pyrolysis of *N*-phthalimido triazoles (Scheme 39).[96] The observed products were 2*H*-azirines. To investigate the mechanism of the reaction, the authors synthesized two isomeric *N*-phthalimido triazoles **43** and **44** which were subjected to vacuum pyrolysis.[97] Both triazoles were transformed to a mixture of 2*H*-azirines **45** and **46** in similar ratios. This observation suggested the formation of carbene **47** followed by its cyclization to unstable 1*H*-azirine **48** which quickly rearranges to the mixture of 2*H*-azirines **45** and **46**.



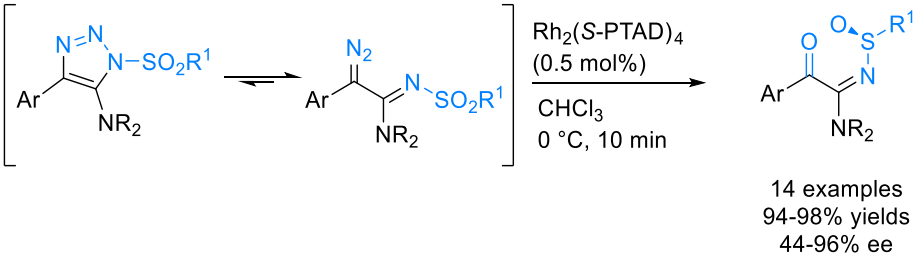
Scheme 39 Vacuum pyrolysis of *N*1-phthalimido-1,2,3-triazoles.

At the end of the same decade, Regitz and co-workers reported the synthesis of thiooxoaldimine esters **49** by heating induced transformation of ethyl/phenylthioethynyl amines **50** and sulfonyl azides (Scheme 40). The reaction proceeds through the formation of 1,2,3-triazoles which exist in both, ring-opened and cyclic forms.[98]



Scheme 40 Heat induced transformation of sulfonyl azides and activated alkynes providing thiooxoalidimine esters.

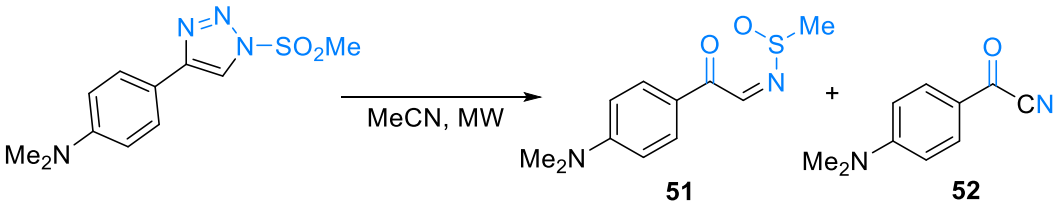
Almost 30 years later, He and Zhu described an analogous reaction using aryl ynamines and sulfonyl azides.[99] In 2012 the Fokin group used chiral rhodium catalyst to perform the same reaction in an enantioselective fashion (Scheme 41).[100] It is worth mentioning that 4-aryl-5-amino-*N*-sulfonyl triazoles exist in ring-opened form.



Scheme 41 The rhodium-catalyzed enantioselective synthesis of sulfinyl amidines from 4-amino-*N*-sulfonyl-1,2,3-triazoles.

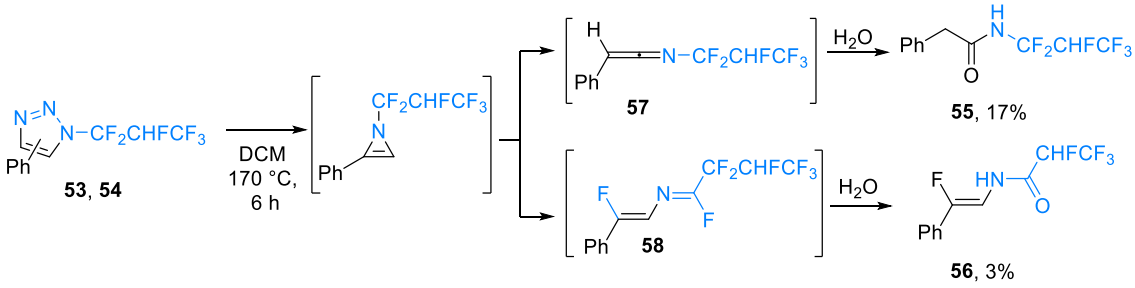
In addition to the transformations of 5-amino-substituted *N*-sulfonyl-1,2,3-triazoles, Murakami and co-workers reported a thermal reaction of 4-(*p*-aminophenyl)-1-sulfonyl triazoles providing aldimines **51** in good yields (Scheme

42). However, in the case of longer reaction times, benzoyl cyanides **52** were formed as products of Cope-type elimination of the sulfinyl group.[101]



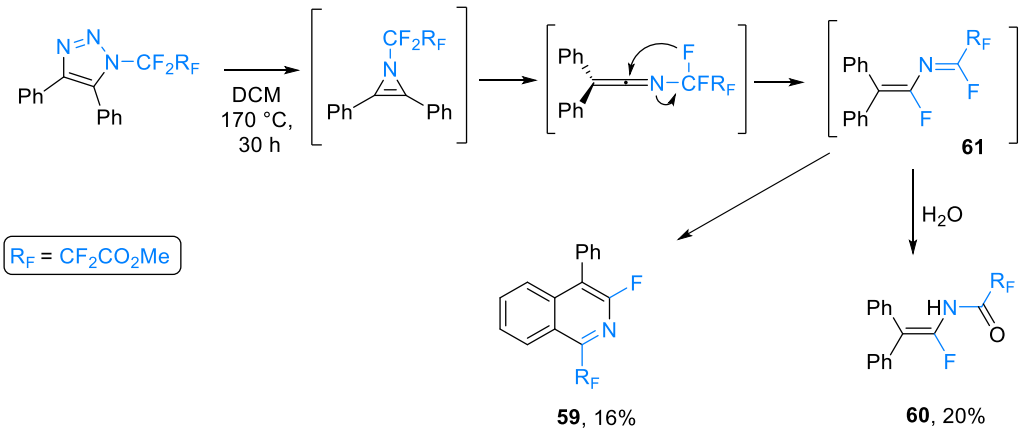
Scheme 42 Thermally induced transformation of 4-(*p*-aminophenyl)-1-sulfonyl triazole to sulfinyl amidines and benzoyl cyanides.

The first mention of a denitrogenative transformation of *N*-fluoroalkyl triazoles is from the year 2000 in the report by Lermontov and co-workers (Scheme 43).[24] Although the authors found a high thermal stability of 4,5-disubstituted triazoles containing *N*-CF_2CHFCF_3 moiety (180 °C, 10 h, no decomposition), thermolysis of the equimolar mixture of 1,4- and 1,5-disubstituted triazoles **53** and **54** afforded two products **55** and **56** in low yields. The proposed mechanism consists of the formation of 1*H*-azirine via cyclization of the formed iminocarbene intermediate and subsequent rearrangement to ketene imine **57** or imidoyl fluoride **58** which are in the final step hydrolyzed to isolated products **55** and **56**.



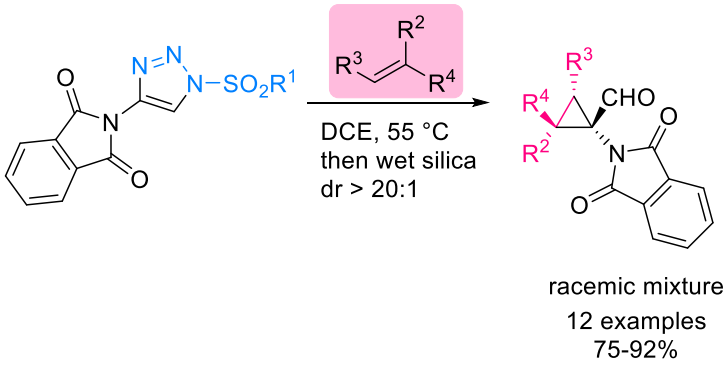
Scheme 43 Thermally induced transformation of hexafluoropropyl triazoles to amide **55** and enamido fluoride **56**.

In the following work, Lermontov and co-workers reported thermal decomposition of 4,5-diphenyl-substituted triazoles containing N-$CF_2CF_2CO_2Et$ group to isoquinoline **59** and enamidofluoride **60** (Scheme 44).[102] The products are formed either by hydrolysis or intramolecular cyclization of intermediate **61**.



Scheme 44 Thermally induced formation of isoquinoline **59** and enamidofluoride **60** from *N*-fluoroalkyl-1,2,3-triazole.

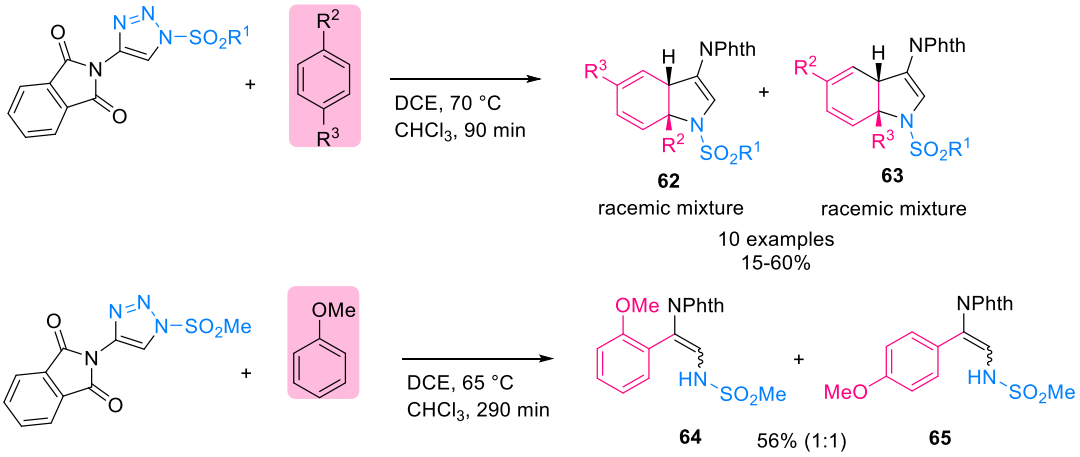
In 2012, Davies and co-workers described thermally induced diastereoselective cyclopropanation of 4-phthalimido-*N*-sulfonyl-1,2,3-triazoles (Scheme 45).[103] Authors initially envisioned the formation of rhodium azavinyl carbenes which would provide the cyclopropanes in an enantioselective fashion. However, the observed enantioselectivities were low and the control experiment without chiral rhodium catalyst revealed the formation of the product in high yield and in good diastereoselectivies.



Scheme 45 Metal-free cyclopropanation of 4-phthalimido-*N*-sulfonyl triazoles.

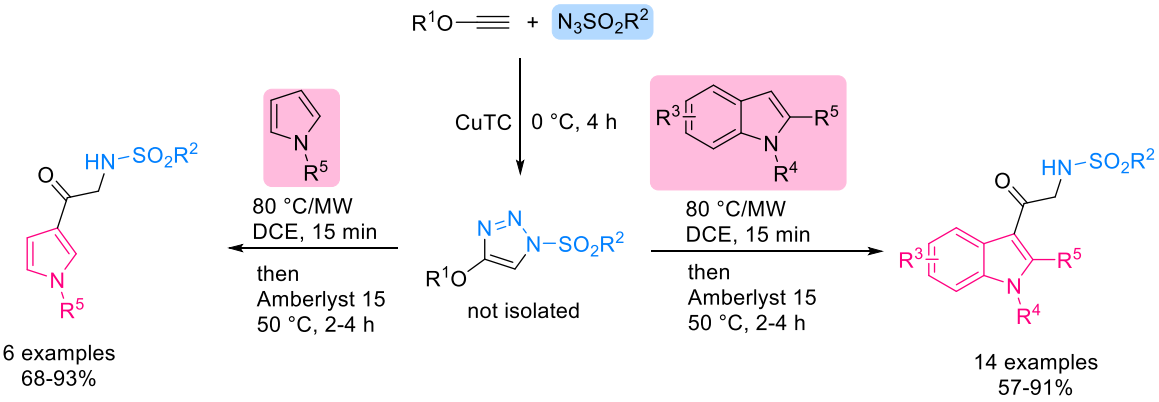
The same group subsequently used 4-phthalimido-*N*-sulfonyl-1,2,3-triazoles for the metal free synthesis of [3a,7a]-dihydroindoles **62** and **63** in the reaction with a variety of substituted benzenes (Scheme 46).[104] If electron rich aromatic ring such as anisole was used as an external reagent, the mixture of isomeric enamides **64** and **65** was observed as a major product. The mechanistic and

computational investigation revealed the formation of enamides **64** and **65** by thermal decomposition of [3a,7a]-dihydroindoles **62** and **63**.



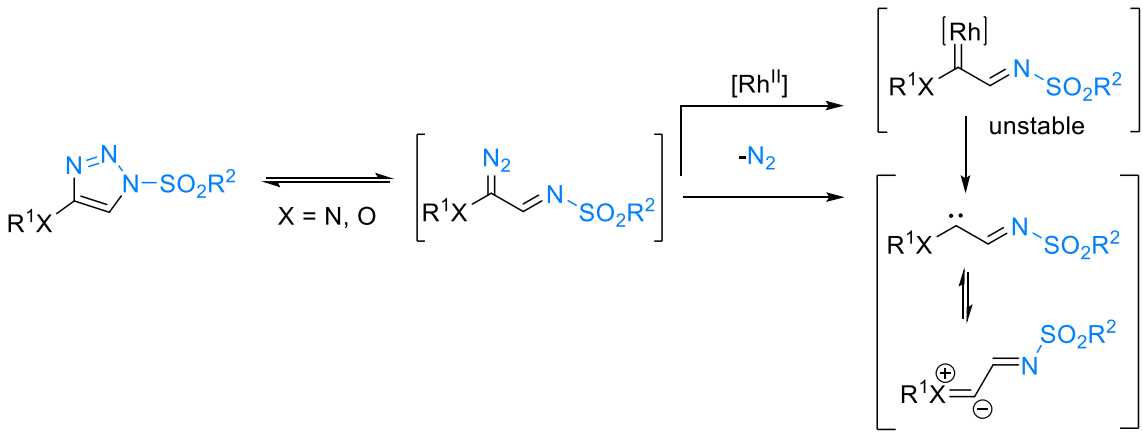
Scheme 46 Synthesis of [3a,7a]-dihydroindoles and enamides from 4-phthalimido-*N*-sulfonyl triazoles.

The Davies group also developed an effective method for aminoacylation of indoles and pyrroles by the multicomponent one-pot reaction between indoles or pyrroles, ynol ethers, and sulfonyl azides. The reaction involves the formation of *N*-sulfonyl triazole as a reaction intermediate (Scheme 47).[105]



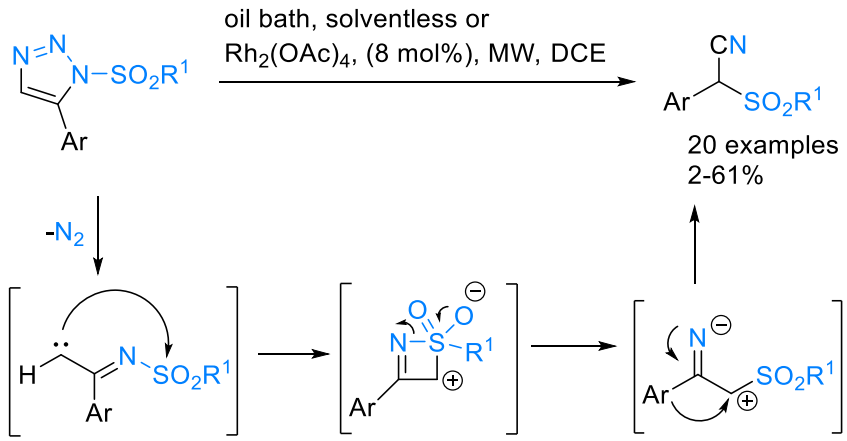
Scheme 47 Multicomponent reaction between indoles or pyrroles, ynol ethers, and sulfonyl azides.

The above-mentioned reports from the Davies group dealing with transformations of 4-alkoxy- or 4-amino-substituted triazoles point to instability of rhodium azavinyl carbenes with directly attached oxygen or nitrogen substituents, and therefore they are not appropriate reagents for enantioselective reactions (Scheme 48).



Scheme 48 Mechanism of denitrogenative reactions of 4-alkoxy- or 4-amino-substituted *N*-sulfonyl triazoles, showing instability of rhodium carbenes derived from these triazoles.

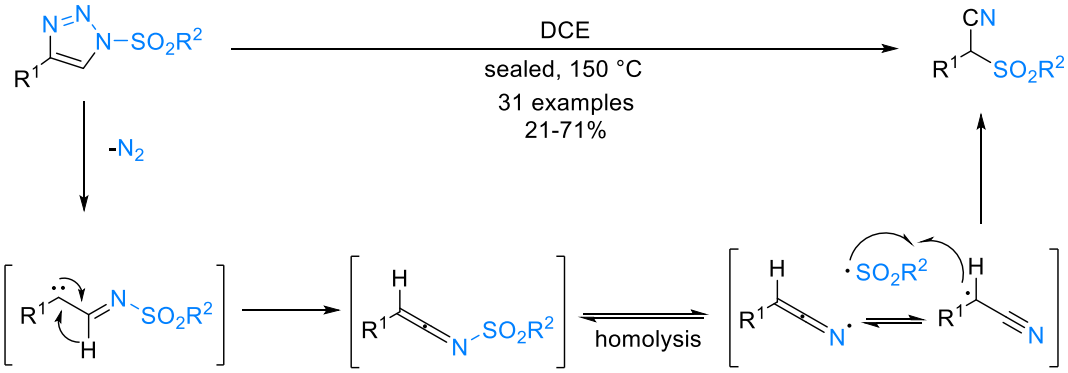
1,5-Disubstitued triazoles were found to undergo thermolysis providing α-sulfonyl nitriles (Scheme 49).[106] The reaction works under both rhodium-free and rhodium conditions. The proposed mechanism starts by denitrogenation of the triazole and subsequent formation of iminocarbene, which undergoes 1,3-sulfonyl shift and after aryl migration affords final nitrile. The authors also observed isomerization of the 1,5-disubstitued triazoles to 1,4-disubstituted triazoles.



Scheme 49 Thermally induced formation of α-sulfonyl nitriles from 5-aryl-1-sulfonyl triazoles and the proposed reaction mechanism.

Recently, Li and co-workers reported thermal-induced rearrangement of 1,4-disubstituted triazoles leading to the same α-sulfonyl nitriles as mentioned above (Scheme 50).[107] This report suggests that the thermolysis of 1,5-disubstituted triazoles does not work by the mechanism shown on Scheme 49,[106] but the first

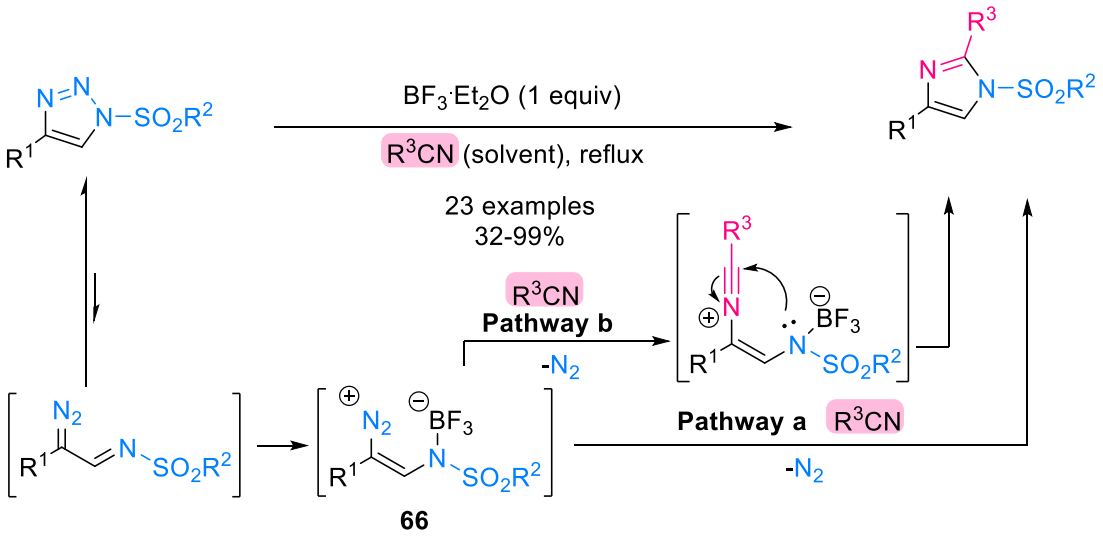
step involves the formation of *N*1-sulfonyl-4-aryl triazoles which subsequently react to α-sulfonyl nitriles. The detailed mechanistic investigation revealed a carbene and radical species as well as the formation of ketene imine as reactive intermediates in a thermal-induced, metal-free rearrangement of 1,4-disubstituted 1,2,3-triazoles.



Scheme 50 Transformation of 1-sulfonyl-4-substituted 1,2,3-triazoles to α-sulfonyl nitriles

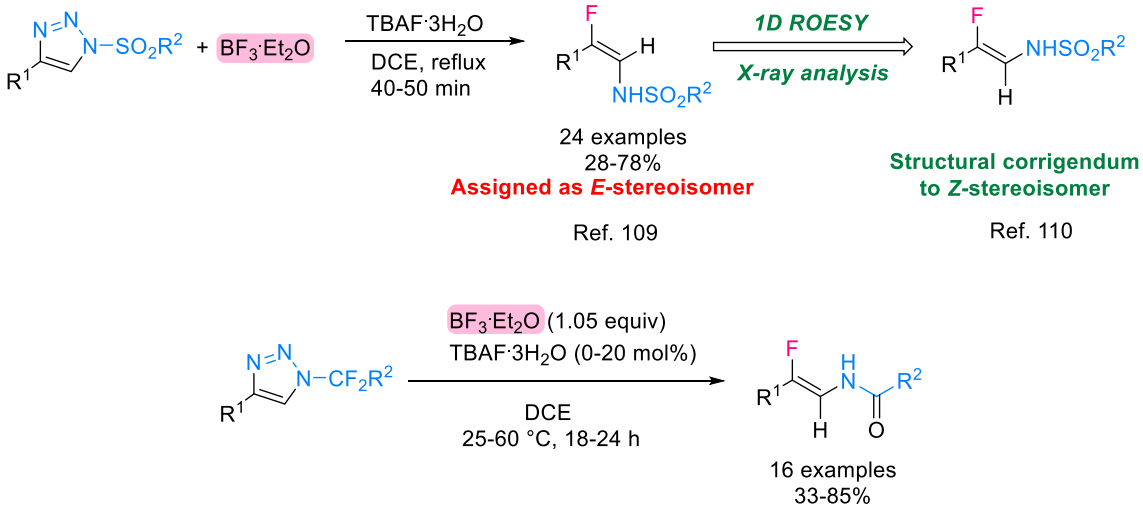
Acid-mediated transformations of N-1,2,3-sulfonyl triazoles

In 2018 Li and co-workers reported transannulation of *N*-sulfonyl-1,2,3-triazoles in presence of nitriles and an equimolar amount of $BF_3{\cdot}Et_2O$ as Lewis acid (Scheme 51).[108] The authors hypothesized reaction mechanism initiated by Dimroth ring-opening with subsequent coordination of BF_3 on imine nitrogen and formation of diazonium salt **66**. The intermediate **66** then reacts either by [3+2] cycloaddition (Pathway a) or by the stepwise annulation (Pathway b).



Scheme 51 Transition-metal free reaction of *N*-sulfonyl triazoles and nitriles affording imidazoles.

Simultaneously with above-mentioned work, the same group published stereospecific synthesis of (*E*)-enamidofluorides by a similar reaction between *N*-sulfonyl triazoles and BF_3; however, using DCE instead of nitrile as a solvent (Scheme 52).[109] The authors suggested three mechanistic pathways clarifying (*E*)-stereochemistry on the C-C double bond, nevertheless, none of them sufficiently explained claimed stereochemistry. This year (2021) we have reinvestigated the structure of formed enamido fluorides and with the utilization of ge-1D ROESY NMR and X-ray analysis corrected the stereochemistry to the (*Z*)-stereoisomers. Moreover, we extended the scope of the reaction to *N*-fluoroalkyl-1,2,3-triazoles.[110]



Scheme 52 Stereoselective synthesis of enamidofluorides from *N*-sulfonyl triazoles, structural corrigendum of the structure of (*E*)-enamidofluorides to (*Z*)-enamidofluorides and BF_3-mediated transformation of *N*-fluoroalkyl-1,2,3-triazole to enamidofluorides.

2. Aims of the Thesis

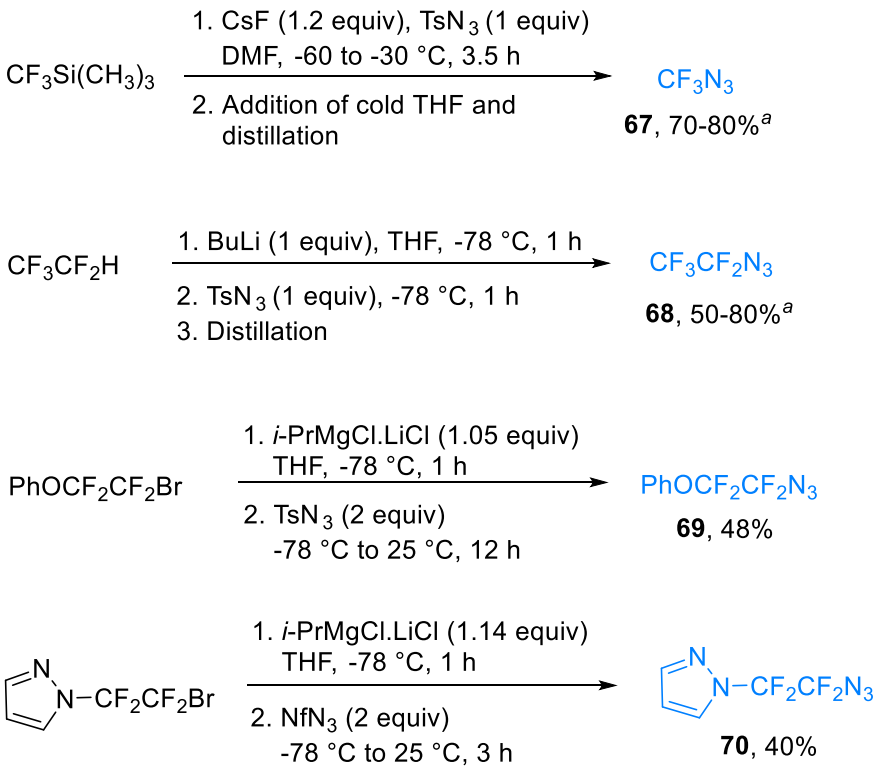
This Thesis aims at the exploration of *N*-fluoroalkyl-1,2,3-triazoles reactivity in an effort to develop novel synthetic methodologies which would provide access to a variety of *N*-fluoroalkyl substituted heterocycles as well as other fluorinated compounds. The specific aims of the Thesis are the following.

- Exploration of *N*-fluoroalkyl-1,2,3-triazoles reactivity in rhodium-catalyzed reactions to access *N*-fluoroalkyl-substituted imidazoles, pyrroles, pyrrolones and imidazolones and other fluorinated heterocycles.

- Investigating the reactivity of *N*-fluoroalkyl-1,2,3-triazoles in acid-mediated transformations to find new reacting modes in 1,2,3-triazoles.

3. Synthesis of *N*-fluoroalkyl azides and *N*-fluoroalkyl-1,2,3-triazoles

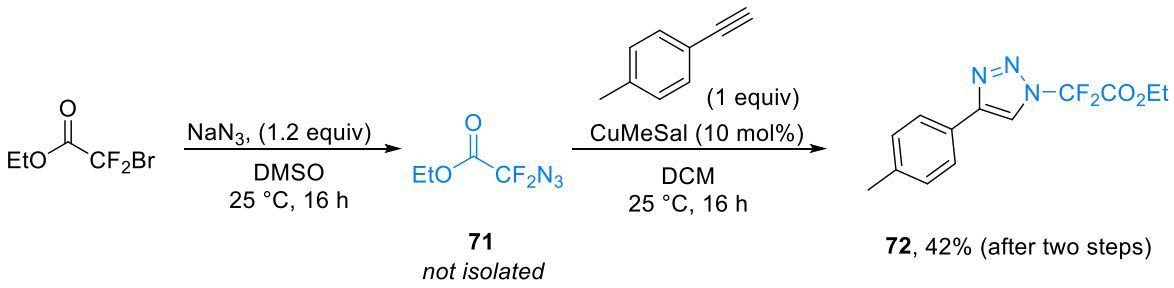
The synthesis of *N*-fluoroalkyl-1,2,3-triazoles started with the preparation of azidofluoroalkanes which were subsequently used in the CuAAC with terminal alkynes. Azidotrifluoromethane CF_3N_3 (**67**), azidoperfluoroethane $CF_3CF_2N_3$ (**68**) and tetrafluoroethyl azides **69** and **70** were prepared based on previously developed strategies in our group (Scheme 53).[32,34]



[a] Yields determined by ^{19}F NMR, using $PhCF_3$ as an internal standard.

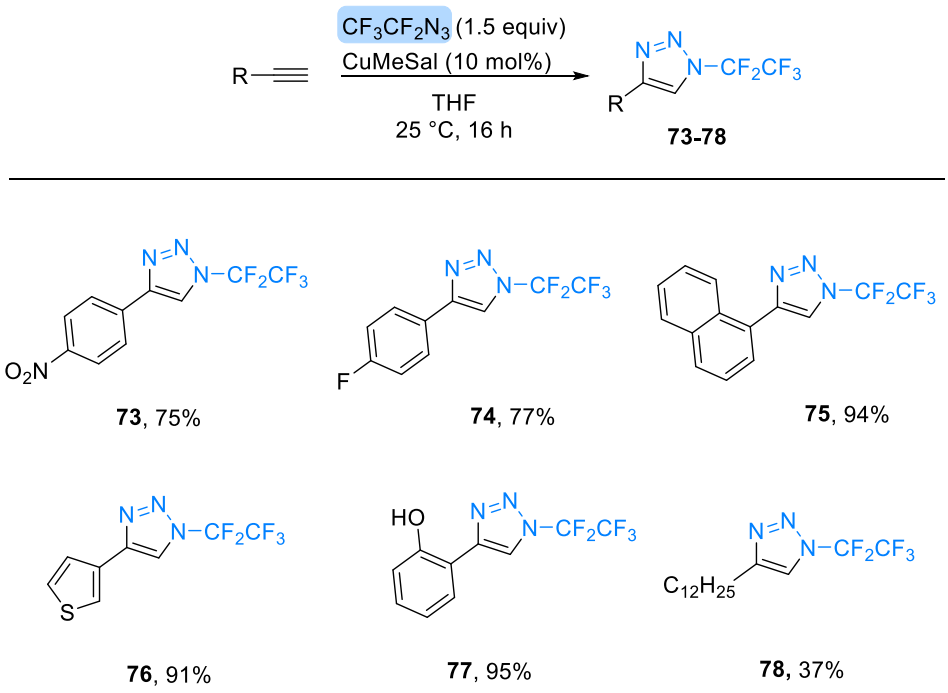
Scheme 53 Synthesis of starting azidofluoroalkanes.

The synthesis of ethyl 2-azido-2,2-difluoroacetate (**71**) was performed according to the reported procedure from ethyl 2-bromo-2,2-difluoroacetate and sodium azide (Scheme 54).[111] Ethyl 2-azido-2,2-difluoroacetate (**71**) was directly used for the synthesis of triazole **72** without characterization.



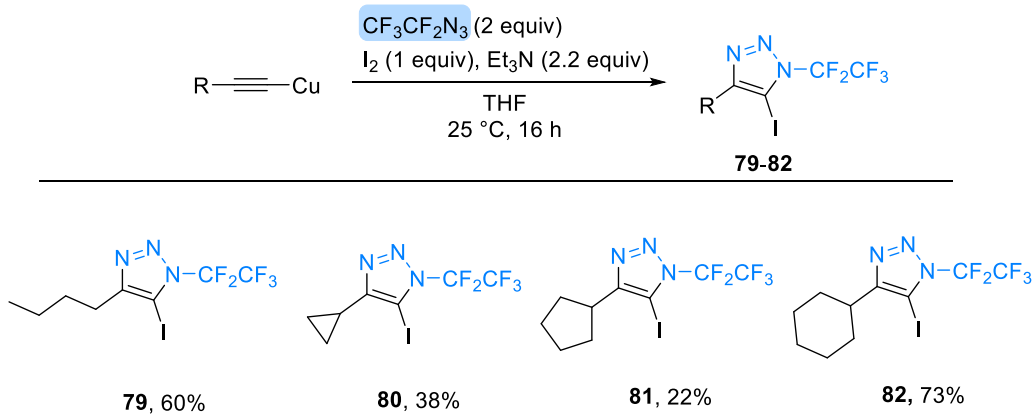
Scheme 54 Two-step synthesis of triazole **72**.

1-Perfluoroethyl-4-substituted triazoles **73-78** which were prepared for the first time are summarized in Scheme 55. All other 1-fluoroalkyl-4-substituted triazoles used in this thesis were prepared according to published procedures.[32–35,112]



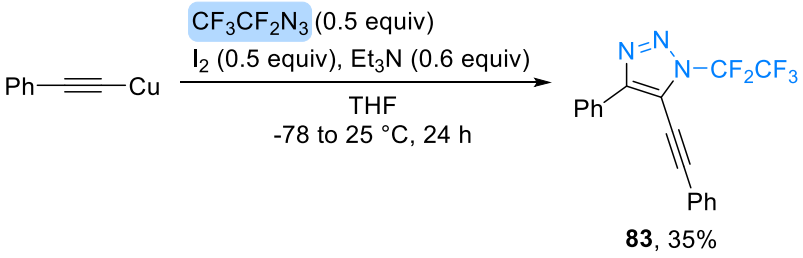
Scheme 55 Synthesis of novel 4-substituted-*N*1-perfluoroethyl 1,2,3-triazoles.

1-Perfluoroethyl-4,5-disubstituted triazoles were synthesized by interrupted CuAAC, using copper(I) acetylides and perfluoroethyl azide as starting materials. In the case of the synthesis of 5-iodosubstituted triazoles **79-82**, iodine was used as a trapping reagent (Scheme 56).



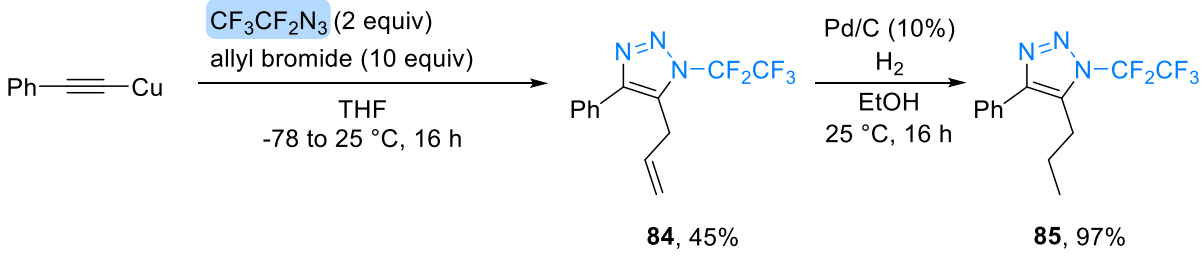
Scheme 56 The scope of previously unreported 4-substituted 5-iodo-*N*-fluoroalkyl-1,2,3-triazoles.

When excess of copper(I) acetylide was used, triazole **83** was formed in moderate yield (Scheme 57). The formation of triazole **83** can be explained either by the Glaser coupling of the formed 5-copper(I) triazolide complex and copper(I) acetylide or by the Cadiot-Chodkiewitz cross-coupling of 5-iodo triazole and copper(I) acetylide.[113]



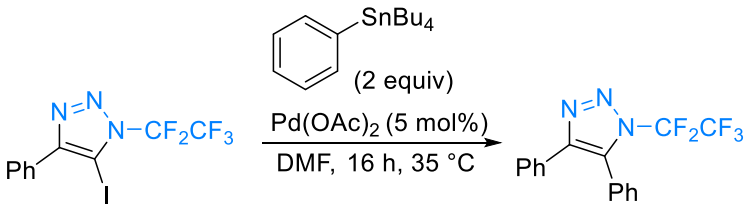
Scheme 57 Synthesis of the triazole **83**.

Changing from iodine to allyl bromide, 5-allyl triazole **84** was prepared in moderate yield and its palladium-catalyzed hydrogenation afforded 5-propyl-substituted 1,2,3-triazole **85** in excellent yield (Scheme 58).



Scheme 58 Synthesis of triazoles **84** and **85**.

The synthesis of 1-perfluoroethyl-4,5-diphenyl-1,2,3-triazole (**86**) was achieved by the Stille cross-coupling of 5-iodo triazole **87** and tributylphenylstannane (Scheme 59). It is worth to mention, that the cross-coupling reactions of 1-perfluroethyl-5-iodo-substituted triazoles are highly challenging due to the thermal instability of these triazoles.



Scheme 59 Stille cross-coupling of triazole **87** providing 4,5-diphenyl-*N*-perfluoroethyl-1,2,3-triazole (**86**).

4. Rhodium-catalyzed transformations of *N*-fluoroalkyl-1,2,3-triazoles

The introduction of fluorine atom and fluorinated groups into organic molecules is a highly valuable approach to modify the properties of many bioactive molecules as well as materials.[114–116] For example, 13 of 35 small molecules drugs approved by the FDA in 2020 contain at least one fluorine atom.[117] Fluorine is the most electronegative element in the periodic table, is small in size, and forms very stable bonds with carbon.[118–120] These features confer the organofluorine compounds a unique position in organic chemistry.

Substituted five-membered heterocycles such as pyrroles, imidazoles, thiazoles or oxazoles are heterocycles occurring in many biologically active molecules and have immense utilization ranging from drug discovery to application in medicine or agrochemistry.[121] However, nitrogen heterocycles containing *N*-fluoroalkyl groups are rare and to the best of our knowledge, there is no general method for their synthesis.

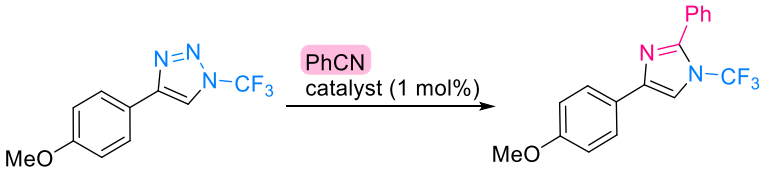
As described in the theoretical part of this Thesis, rhodium-catalyzed reactions of *N*-sulfonyl triazoles are transformations providing access to a wide array of

nitrogen-containing heterocycles. We envisioned the utilization of *N*-fluoroalkyl triazoles, which bear electron-withdrawing N*1*-fluoroalkyl group, as starting materials capable to undergo rhodium-catalyzed reactions and providing straightforward access to a wide range of *N*-fluoroalkylated heterocycles and other organofluorinated compounds.

4.1. Transannulations into *N*-(per)fluoroalkyl-substituted heterocycles

Inspired by the rhodium-catalyzed transannulation of *N*-sulfonyl triazoles and nitriles,[45] we initiated our investigation by the reaction of 4-substituted 1-trifluoromethyl triazole **88** with benzonitrile in DCE, using rhodium(II) acetate dimer as a catalyst. Stirring the triazole **88** with benzonitrile at 80 °C for 17 h afforded only traces of the product (Table 1, entry 1). Changing from conventional heating to microwave irradiation at 150 °C for 1 h led to full conversion to the product and imidazole **89a** was isolated in 40% yield (Table 1, entry 2). When 2 equivalents of the nitrile were used, the yield improved to 51% (Table 1, entry 3). Decreasing the temperature from 150 to 100 °C led to lower conversion (Table 1, entry 4); however, reduced reaction time to 20 min did not affect the reaction efficiency (Table 1, entry 5). In chloroform as the solvent, the yield improved to 59% (Table 1, entry 6). Furthermore, applying rhodium(II) octanoate dimer eventually increased the isolated yield of the reaction to 72% (Table 1, entry 7). It is worth to mention, that the presence of rhodium(II) carboxylate was found essential for the transformation (Table 1, entry 8).

Table 1 Optimization of the reaction conditions for rhodium-catalyzed transannulation of *N*-fluoroalkyl-1,2,3-triazoles and isonitriles.[a]



88 **89a**

Entry	catalyst	PhCN[b]	Solvent, temp, time	Yield (%)[c]
1	$Rh_2(OAc)_4$	1.3	DCE, 80 °C, 17 h	3
2	$Rh_2(OAc)_4$	1.3	DCE, 150 °C MW, 1 h	100 (40)
3	$Rh_2(OAc)_4$	2	DCE, 150 °C MW, 1 h	100 (51)
4	$Rh_2(OAc)_4$	2	DCE, 100 °C MW, 20 min	40 (24)
5	$Rh_2(OAc)_4$	2	DCE, 140 °C MW, 20 min	100 (44)
6	$Rh_2(OAc)_4$	2	$CHCl_3$, 140 °C MW, 20 min	100 (59)
7	$Rh_2(Oct)_4$	2	$CHCl_3$, 140 °C MW, 20 min	100 (**72**)
8	none or CuTC	2	$CHCl_3$, 140 °C MW, 20 min	0

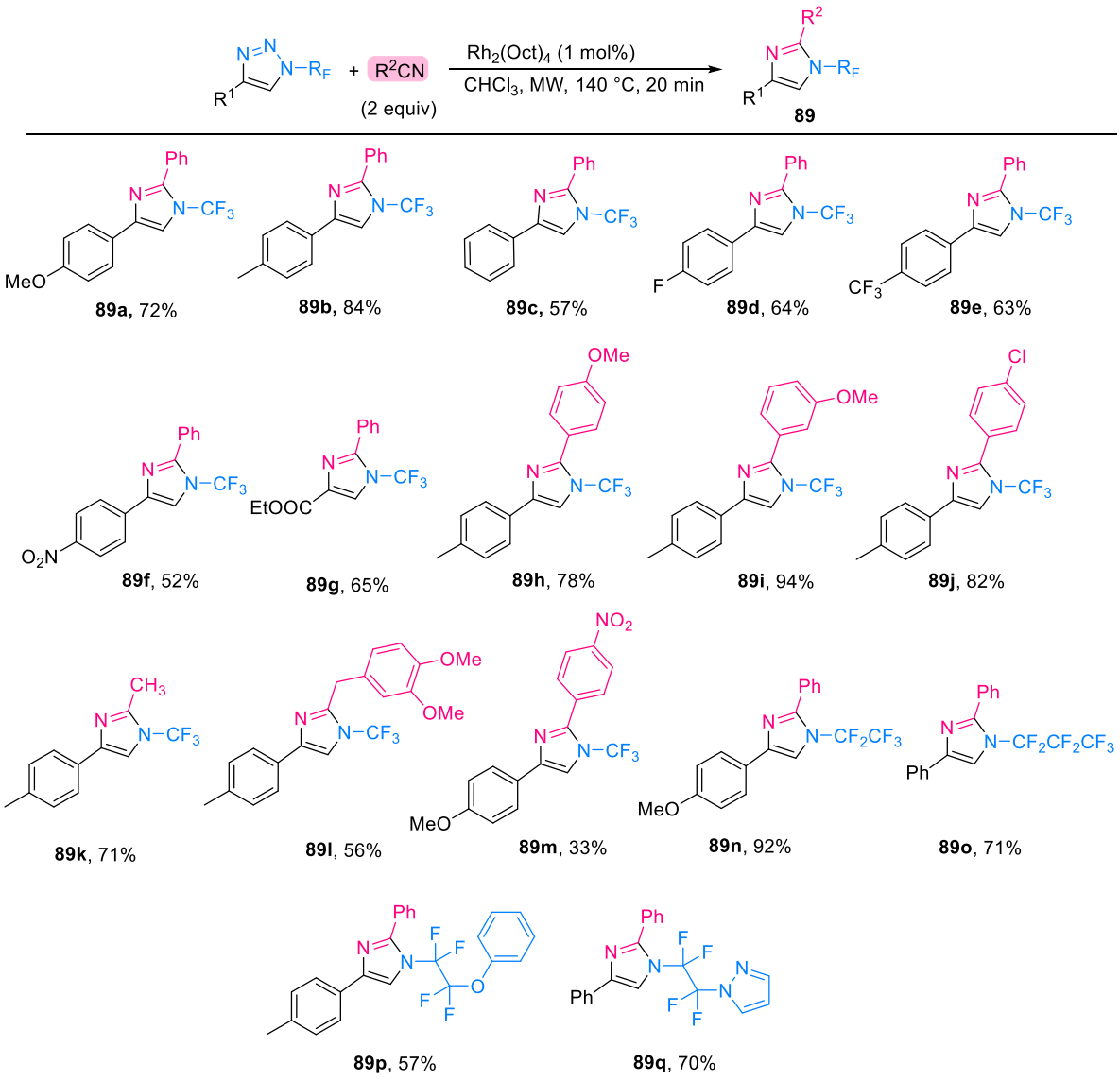
[a] Reaction conditions: **88** (0.10 mmol), PhCN (0.13-0.20 mmol), [Rh^{II}] (1 mol%), solvent (2 mL). [b] equiv. [c] Conversion of **88** was determined by ^{19}F NMR, in brackets isolated yields of **89a**.

Having the optimized conditions in hands, we investigated the scope of the reaction. Firstly, the reactivity of *N*-trifluoromethyl triazoles bearing different 4-aryl groups was investigated in the reaction with benzonitrile (Scheme 60). Triazoles with EDG on 4-aryl substituent provided imidazoles **89a** and **89b** in better yields than *N*-trifluoromethyl triazoles bearing EWG or neutral groups **89c-89g**. Both aromatic and aliphatic nitriles afforded imidazoles in good to excellent yields **89h-89l**. The reaction worked even with electron-poor *p*-nitrobenzonitrile; however, imidazole **89m** was formed in moderate yield. Triazoles containing longer perfluoroalkyl chain, such as *N*-perfluoroethyl and *N*-perfluoropropyl, formed final imidazoles **89n** and **89o** in excellent and good yield, respectively. In addition to the perfluoroalkylated triazoles, rhodium-catalyzed reaction of *N*-tetrafluoroethylene triazoles gave imidazoles **89p** and **89q** in good yields.

Encouraged by the successful formation of *N*-fluoroalkyl imidazoles, we investigated rhodium-catalyzed transannulations of *N*-fluoroalkyl-1,2,3-triazoles in synthesis of previously unknown *N*-(per)fluoroalkyl-substituted pyrroles **90** (Scheme 61). In the case of the *N*-(per)fluoroalkylpyrrole synthesis, we used vinyl

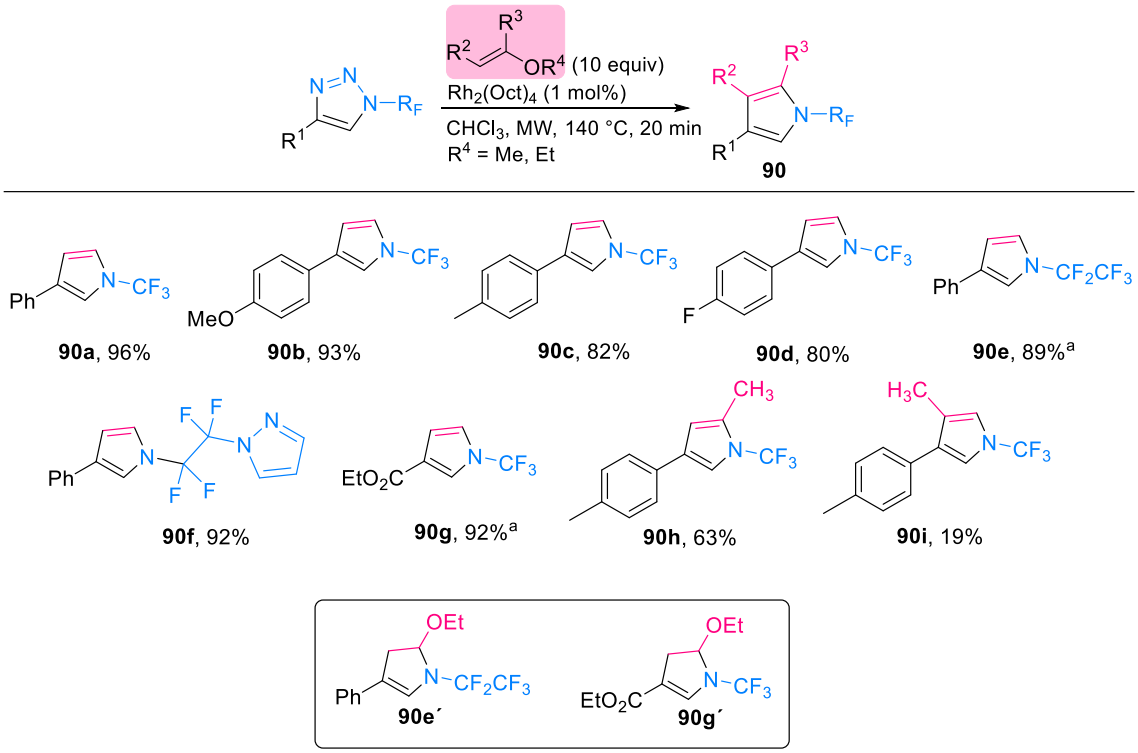
ethers as reacting partners. The reaction of *N*-fluoroalkyl-1,2,3-triazoles with ethyl vinyl ether provided 1,3-disubstituted pyrroles **90a**-**90g** in good to excellent yields. Interestingly, the transformation of 1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole led to a mixture of 2,3-dihydropyrrole **90e´** and pyrrole **90e** and the transformation of ethyl 1-(trifluoromethyl)-1*H*-1,2,3-triazole-4-carboxylate provided exclusive formation of 2,3-dihydropyrrole **90g´**. Nevertheless, treatment of 2,3-dihydropyrroles with *p*-toluenesulfonic acid afforded final pyrroles **90a** and **90g** in excellent yields. Using 2-methoxypropene as an external reagent resulted in the formation of *N*-trifluoromethyl-2,4-disubstituted pyrrole **90h** in good yield, whereas the reaction with 1-ethoxypropene afforded isomeric *N*-trifluoromethyl-3,4-disubstituted pyrrole **90i** in low yield.

In order to find an ideal reagent for pyrrole synthesis, transannulation of the 4-phenyl-1-(trifluoromethyl)-1*H*-1,2,3-triazole and both ethyl vinyl ether and vinyl acetate was performed by my colleague Vladimir Motornov (Scheme 62). The reaction with ethyl vinyl ether showed the exclusive formation of pyrrole **90a**, whereas, in the case of vinyl acetate, the mixture of 2-hydroxypyrroline **91** and pyrrole **90a** was formed. The formation of 2-hydroxypyrroline **91** can be explained by hydrolysis of acetoxy intermediate **90a´´**.



Scheme 60 Substrate scope of the prepared *N*-fluoroalkyl imidazoles.

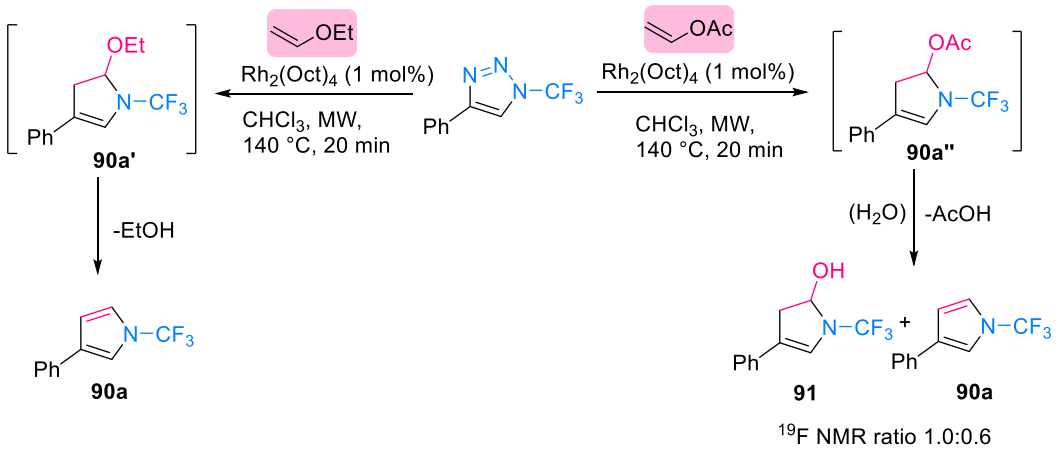
After successful synthesis of *N*-fluoroalkyl imidazoles and pyrroles, we turned our attention to the preparation of *N*-fluoroalkyl imidazolones and pyrrolones (Scheme 63). The rhodium-catalyzed reaction of 4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole and phenyl isocyanate provided *N*-trifluoromethyl-substituted imidazole **92** in very good yield. Pyrrolone **93** was prepared in good yield by one-pot two-step synthesis with silyl ketene acetal.



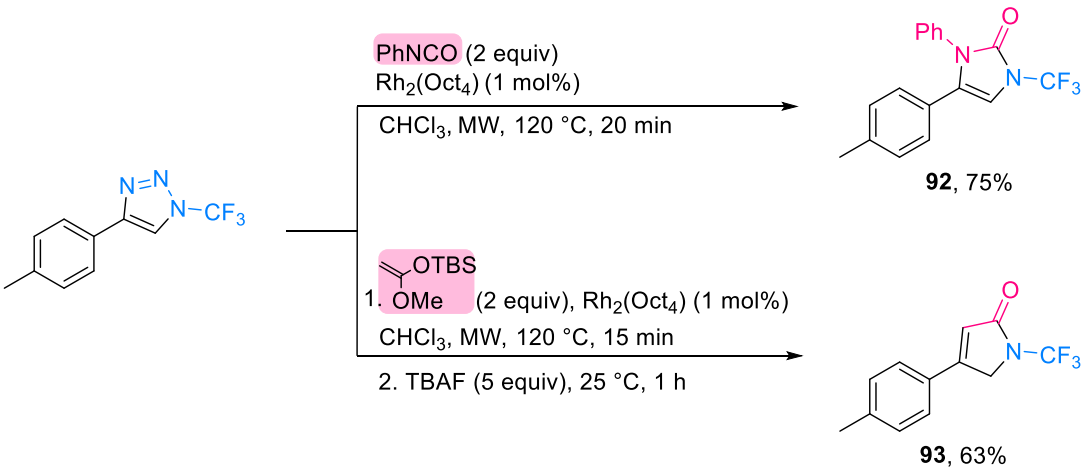
[a] After treatment of intermediates **90e´** and **90g´** with TsOH (2 equiv), 25 °C, 2 h.

Scheme 61 Substrate scope of prepared *N*-fluoroalkyl pyrroles.

We were also interested to compare the reactivity of *N*-sulfonyl triazoles and the corresponding *N*-fluoroalkyl triazoles in the rhodium-catalyzed transformations. The competition experiment revealed that although *N*-sulfonyl triazole **94** is slightly more reactive towards rhodium-catalyzed reaction with benzonitrile than its trifluoromethylated analogue **95**, the reactivity difference is small (Scheme 64).

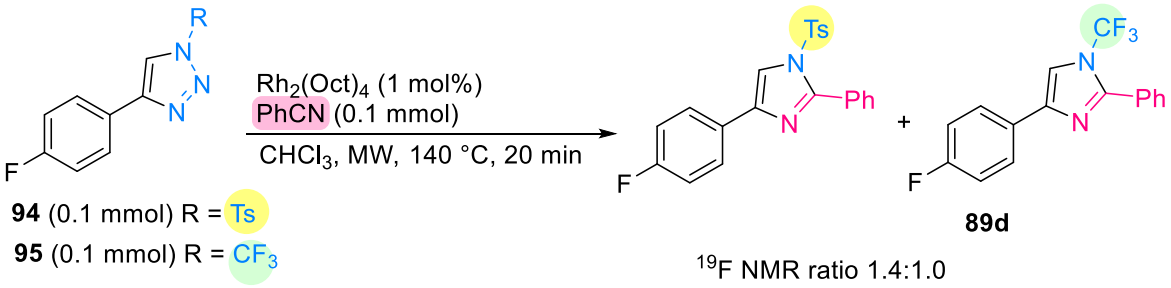


Scheme 62 Seeking for the ideal dipolarophile for *N*-fluoroalkyl pyrrole synthesis.

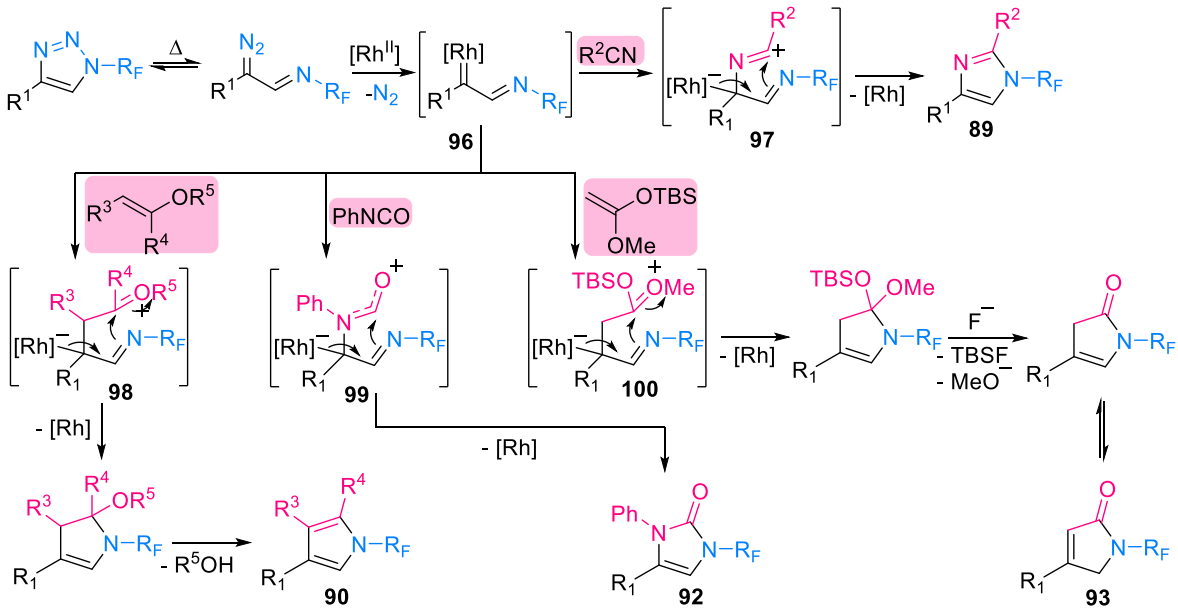


Scheme 63 Rhodium-catalyzed synthesis of *N*-fluoroalkyl imidazolone **92** and *N*-fluoroalkyl pyrrolone **93**.

A plausible mechanism for the rhodium-catalyzed reactions of *N*-fluoroalkyl-1,2,3-triazoles involves the triazole ring-opening, followed by the formation of rhodium azavinyl carbene **96** (Scheme 65). This reactive intermediate reacts in formal [3+2] cycloaddition with a variety of reagents (dipolarophiles) to zwitterionic intermediates **97-100**. These intermediates eventually cyclize to final heterocycles simultaneously with rhodium elimination.



Scheme 64 Competitive experiment of *N*-sulfonyl **94** and *N*-fluoroalkyl **95** triazoles in rhodium-catalyzed reaction with benzonitrile.



Scheme 65 Plausible mechanisms of rhodium-catalyzed transannulations of *N*-fluoroalkyl-1,2,3-triazoles.

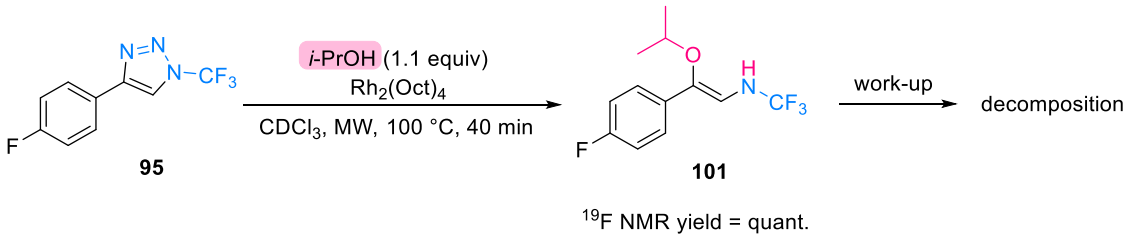
It is worth mentioning that *N*-difluoromethyl- and *N*-fluoromethyl-substituted triazoles did not work in rhodium-catalyzed reactions even at 160 °C. Moreover, 1-fluoroalkyl-4,5-disubstituted triazoles, easily accessible by organocatalytic [3+2] cycloaddition of azidofluoroalkanes and carbonyl compounds,[36] were found also unreactive.

Further studies in our group revealed that *N*-2-bromo-1,1,2,2-tetrafluoroethyl and 1,1,2,2-tetrafluoroethyl-substituted triazoles are capable to undergo rhodium-catalyzed transannulation to *N*-fluoroalkyl imidazoles.[35] Furthermore, rhodium-catalyzed reactions of *N*-fluoroalkyl-1,2,3-triazoles with dienes in chemoselective [3+4] cycloaddition to azepines[122] and in [3+2] cycloaddition with alkynes to form pyrroles were found to be succesfull.[123]

The utilization of *N*-fluoroalkyl heterocycles in drug discovery was showcased by Schiesser and co-workers in 2020.[124] The authors discovered, that whereas *N*-trifluoromethyl amines are prone to hydrolysis, *N*-trifluoromethyl imidazoles and pyrazoles are hydrolytically stable. Moreover, a comparison with *N*-methylated analogues showed higher lipophilicity, metabolic stability, and Coco-2-permeability of *N*-trifluoromethyl heterocycles.

4.2. Synthesis of 2-fluoroalkyl 1,3-azoles

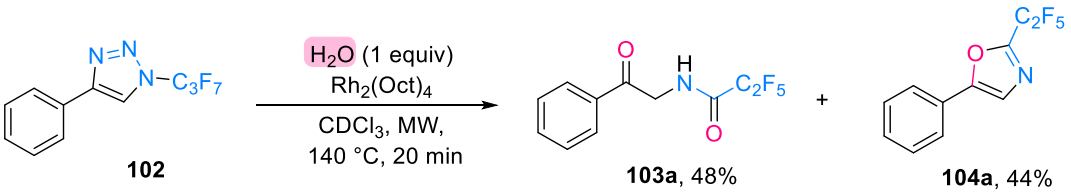
As a next goal, we decided to explore rhodium-catalyzed reactions of *N*-fluoroalkyl triazoles with reagents containing polar X-H bonds (X = RO, R_2N). We envisioned the stereoselective formation of enamines, similarly to the case of *N*-sulfonyl triazoles. Our investigation started with microwave-assisted reaction of triazole **95** with isopropanol in $CDCl_3$, using $Rh_2(Oct)_4$ dimer as a catalyst. Indeed, 40 minutes of heating led to the formation of the enamine **101** in almost quantitative ^{19}F NMR yield (Scheme 66). However, attempts to isolate the product failed due to the high instability of NH-CF_3 group.



Scheme 66 Rhodium-catalyzed reaction of *N*-trifluoromethyl triazole **95** and isopropyl alcohol.

Secondary *N*-trifluoromethyl amines are well known to be unstable compounds which readily eliminate HF molecule.[125] The tendency to eliminate HF together with the decreased nucleophilicity of nitrogen lone pair make further transformations highly challenging and to the best of our knowledge, there exists only one example of substitution of secondary trifluoromethyl amines in the literature.[126]

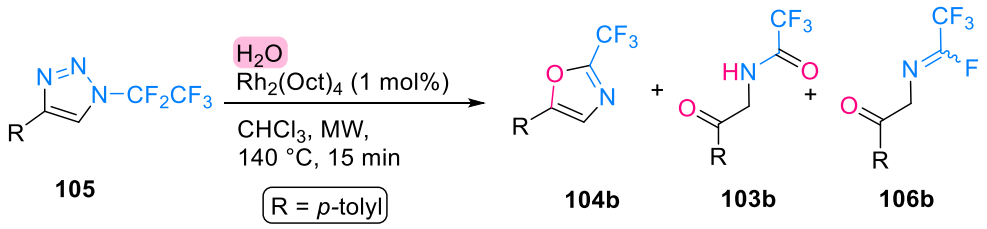
To avoid the formation of the *N*-trifluoromethyl amines which always decompose to a complex mixture of products in low yields, e.g., benzoyl esters, we decided to use triazoles bearing longer *N*-fluoroalkyl chains. We subjected *N*-perfluoropropyl triazole **102** to the reaction with an equivalent of water in the presence of $Rh_2(Oct)_4$ in $CDCl_3$ at 140 °C (Scheme 67). To our surprise, along with 48% of ketamide **103a** as the expected product of double hydrolysis, oxazole **104a** bearing perfluoroethyl group at position 2 was formed in a significant yield.



Scheme 67 Rhodium-catalyzed reaction of *N*-perfluoropropyl triazole **102** with water.

For a detailed investigation of the oxazole formation, we selected *N*-perfluoroethyl triazole **105** as a model substrate. A reaction with an equimolar amount of water furnished imidoyl fluoride **106b** as the main product (Table 2, entry 1). Optimization revealed that applying 2-3 equivalents of water provides oxazole **104b** as a major product (Table 2, entries 2,3), while more than 5 equivalents lead to the formation of ketamide **103b** (Table 2, entries 4,5). In the absence of water, the starting material decomposed, and no product was observed (Table 2, entry 6). Surprisingly, the scale-up of the reaction as well as the change of the amount of the catalyst affected the ratio of the formed products in favor of ketamide **103b** (Table 2, entries 7-9).

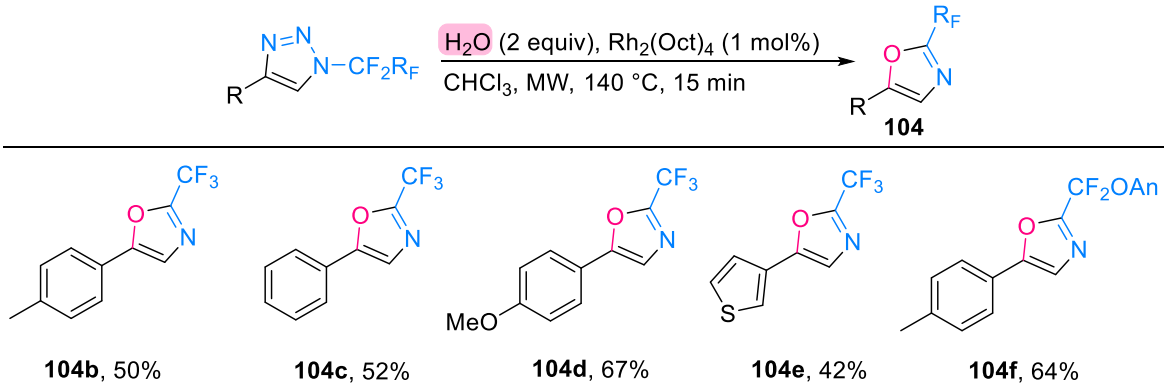
Table 2 Optimization of the reaction conditions for rhodium-catalyzed transannulation of *N*-fluoroalkyl-1,2,3-triazoles and water to form oxazoles.



Entry	H_2O (equiv)	Yield (%)		
		104b	**103b**	**106b**
1[a]	1	<5	<5	37
2[a]	**2**	**65**	**25**	**<5**
3[a]	3	59	28	<5
4[a]	5	32	44	n. d.
5[a]	10	n. d.	**98**	n. d.
6[a]	0	<5	n. d.	<5
7[b]	2	32	30	<5
8[c]	2	38	28	<5
9[d]	3	12	74	<5

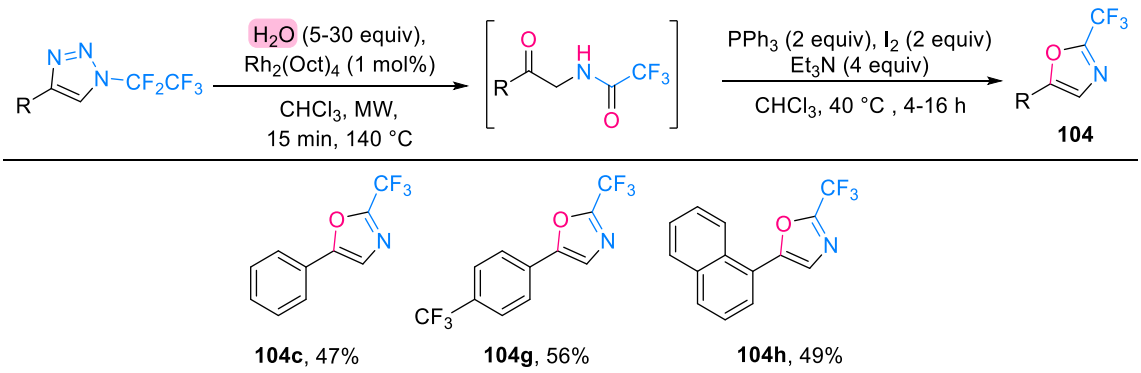
[a] **105** (0.15 mmol), $Rh_2(Oct)_4$ (1 mol%), $CHCl_3$ (2.5 mL), [b] $Rh_2(Oct)_4$ (0.5 mol%), [c] $Rh_2(Oct)_4$ (2 mol%), [d] **105** (0.2 mmol), $CHCl_3$ (3.3 mL).

Next the scope of the oxazole formation in the reaction of *N*-fluoroalkyl triazoles with 2 equivalents of water in 0.15 mmol scale was investigated. *N*-Fluoroalkyl triazoles with EDG or neutral groups on 4-aryl substituent provided oxazoles **104b-f** in moderate to good yields (Scheme 68). In addition to *N*-perfluoroethyl-1,2,3-triazoles, the triazole bearing N-CF_2CF_2OAn (An = anisyl) group furnished oxazole **104g** in good yield. Unfortunately, triazoles bearing electron-deficient (*p*-trifluoromethyl)phenyl group or sterically hindered *o*-bromophenyl group, were found to be unsuitable for the reaction.



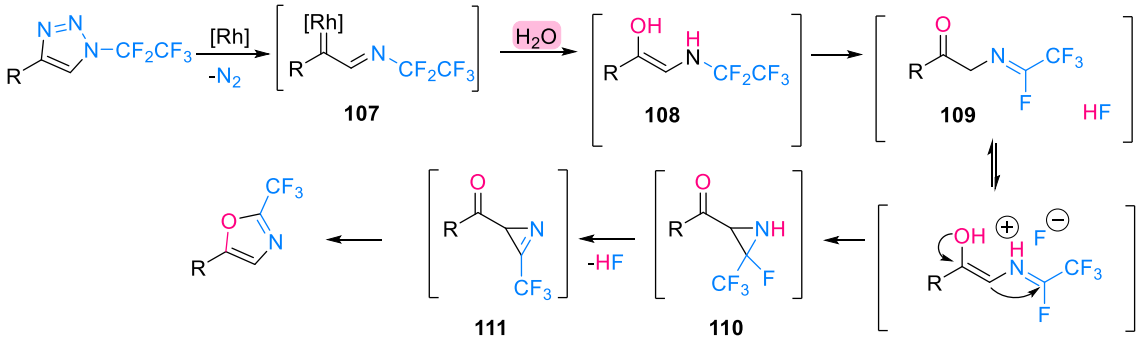
Scheme 68 Substrate scope for rhodium-catalyzed transannulation of *N*-fluoroalkyl-1,2,3-triazoles to 2-fluoroalkyl oxazoles.

To provide alternative access to the 2-fluoroalkyl oxazoles, which would extend the substrate scope, we developed a one-pot two-step synthesis through ketamide formation. The triazoles were first hydrolyzed in the excess of water to the corresponding ketamides and subsequently dehydrated by $PPh_3/I_2/Et_3N$ system to final oxazoles **104c**, **104g** and **104h** (Scheme 69).



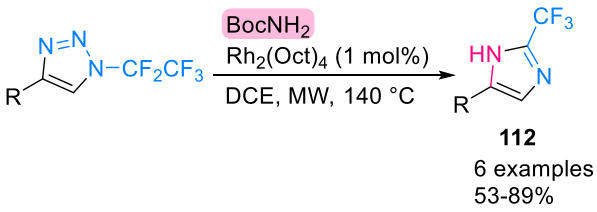
Scheme 69 One-pot two-step approach towards 2-trifluoromethyl oxazoles.

A plausible mechanism for the direct oxazole formation is shown in Scheme 70. The formed rhodium iminocarbene **107** is attacked by water via formal 1,3 insertion to generate enol **108**. Elimination of HF provides compound **109** which under acidic conditions undergoes keto-enol tautomerism resulting in intramolecular cyclization to form aziridine **110**. Subsequent second HF elimination leads to the formation of acyl azirine **111**, which is known to undergo cyclization into oxazoles.[127]



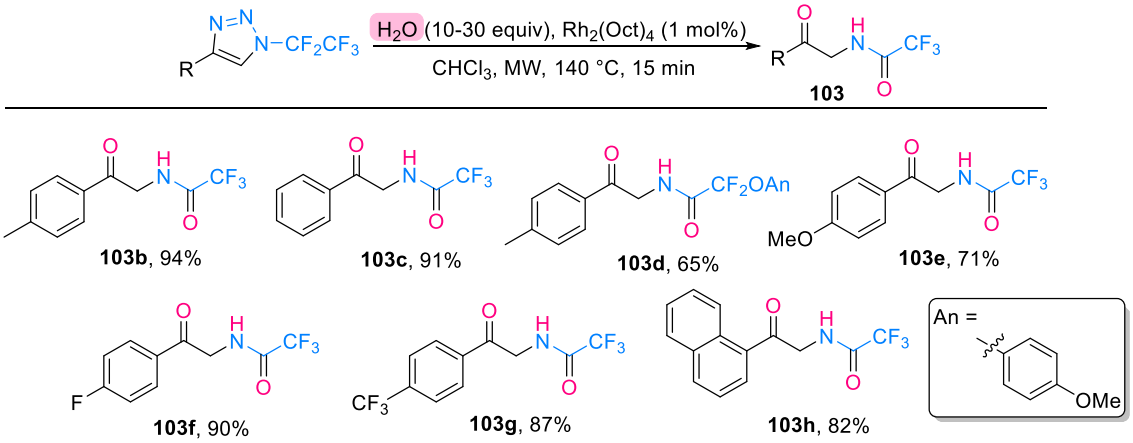
Scheme 70 Plausible mechanism of rhodium-catalyzed transannulation of *N*-fluoroalkyl triazoles to 2-fluoroalkyl oxazoles.

Having developed an effective route to 2-fluoroalkyl oxazoles, we examined the synthesis of 2-fluoroalkyl imidazoles **112** by rhodium-catalyzed reaction of *N*-perfluoroethyl triazoles with *tert*-butyl carbamate. The reaction provided imidazoles **112** in good to excellent yields (Scheme 71). The experimental work was done under my supervision by a former bachelor student from our group, BSc. Vojtěch Košťál. The details of the transformation are summarized in Vojtěch Košťál´s bachelor thesis.[128]



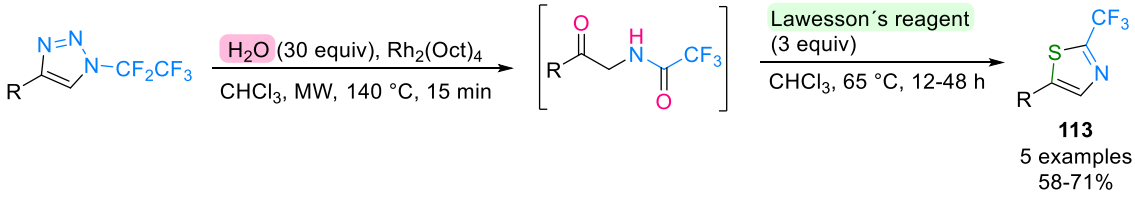
Scheme 71 Synthesis of 2-fluoroalkyl-imidazoles **112** through the transannulation of *N*-perfluoroethyl triazoles with *tert*-butyl carbamate.

Next, we investigated the scope of the triazole hydrolysis to ketamides **103** (Scheme 72). Triazoles bearing EDG and neutral group on aryl ring formed ketamides in excellent yields, using 10 equivalents of water. For the triazoles with electron-poor aryl groups, 30 equivalents of water were necessary to achieve full conversion.



Scheme 72 Synthesis of ketamides **103** via rhodium-catalyzed reaction of *N*-perfluoroethyl triazoles with water.

My colleague Vladimir Motornov further studied the cyclization of *in situ* formed ketamides to 2-fluoroalkyl thiazoles **113** as another example of 2-fluoroalkyl-1,3-azoles available by rhodium-catalyzed reaction of *N*-fluroalkyl-1,2,3-triazoles (Scheme 73). Applying a one-pot two-step approach, thiazoles **113** were formed in moderate to good yields by intramolecular cyclization of the formed ketamides by Lawesson´s reagent.



Scheme 73 One-pot two-step approach towards 2-trifluoromethyl thiazoles.

Similarly to the rhodium-catalyzed reactions with nitriles, rhodium-catalyzed reactions leading to 2-fluoroalkyl oxazoles and ketamides are effective even in the transformations of *N*-2-bromo-1,1,2,2-tetrafluoroethyl and *N*-1,1,2,2-tetrafluoroethyl triazoles.[35]

In summary, *N*-fluoroalkyl triazoles react in rhodium-catalyzed reactions with reagents containing polar XH groups (X = RO, R_2N) in the same way as *N*-sulfonyl triazoles. However, the products contain unstable secondary aminofluoroalkyl groups which easily eliminate HF molecule. Providing that starting triazoles contain longer than CF_3 chain, *N*-fluoroalkyl triazoles react to 2-fluoroalkyl-1,3-azoles (oxazoles, imidazoles, thiazoles) and ketamides.

5. Acid-mediated transformations of *N*-fluoroalkyl-1,2,3-triazoles

The denitrogenative transformations based on thermal-induced Dimroth equilibrium and the formation of azavinyl carbenes have provided the extensive synthetic application of 1,2,3-triazoles. However, the reactivity through the Dimroth equilibrium is not the only possible reactive mode of 1,2,3-triazoles. Structural similarity with triazenes (Figure 1) raises the question of whether the triazoles bearing at N1 electron-withdrawing groups can be used in acid-mediated transformations which are typical for triazenes.

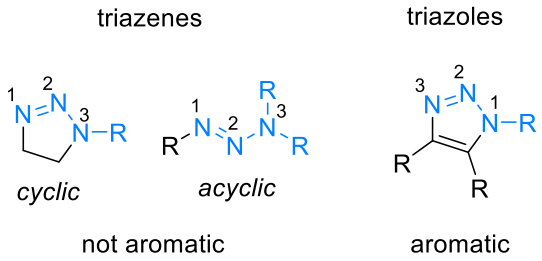
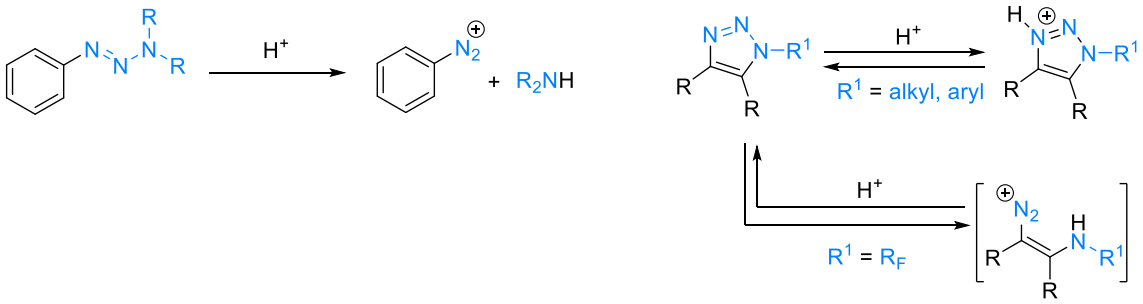


Figure 1 Structure of triazenes (left) and triazoles (right).

Triazenes are a non-aromatic class of compounds with immense synthetic and medical application. In the presence of acids, they are cleaved to diazonium salts and amines (Scheme 74).[129] Although 1,2,3-triazoles are protonated on N3 atom providing stable triazolium salts,[5] we speculated that *N*-fluoroalkyl-1,2,3-triazoles could behave similarly to the triazenes and in the presence of strong acid could open to α-diazo amines. This novel mode of triazole ring-opening would extend the synthetic utility of 1,2,3-triazoles.



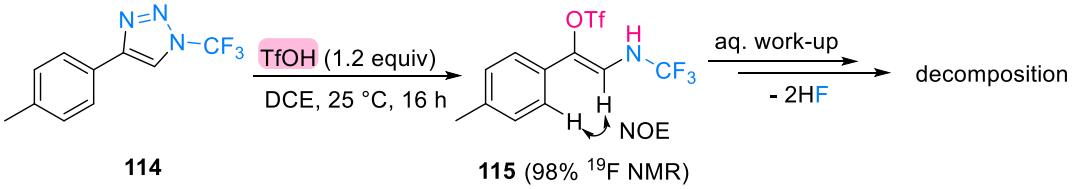
Scheme 74 Acid-mediated transformations of triazenes (left) and the proposed triazole ring-opening in the presence of strong acids (right).

5.1. Stereoselective synthesis of (*Z*)-β-enamido sulfonates

To explore the reactivity of *N*-fluoroalkyl-1,2,3-triazoles in acid-mediated reactions, we selected trifluoromethanesulfonic (triflic) acid as one of the strongest Brønsted acids, capable to protonate the electron-deficient *N*-fluoroalkyl triazole ring. Moreover, we expected that after ring-opening and nitrogen elimination, the triflic anion could serve as a trapping agent for generated vinyl cation, which would lead to the formation of vinyl triflate.

Vinyl triflates are highly valuable synthons in organic synthesis. For example, they are used in cross-coupling reactions[130–134] and serve as a valuable source of vinyl cation reactive intermediates.[135,136]

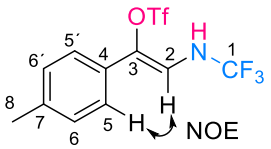
Our investigation started with the reaction of triazole **114** and triflic acid in DCE as a solvent (Scheme 75). Mixing of all components resulted in precipitation of a white solid, which slowly dissolved, with distinct gas elimination from the reaction mixture. The 1D NMR analysis showed triflate **115** as the product of the reaction in almost quantitative ^{19}F NMR yield. To our surprise, ge-1D ROESY NMR analysis proved (*Z*)-stereoisomer as the only product (Figure 2). As expected, the separation of the triflate **115** containing liable NH-CF_3 moiety failed.



114 **115** (98% ^{19}F NMR)

Scheme 75 Triflic acid-mediated reaction of *N*-trifluoromethyl triazole **114**.

Hence, in our effort to obtain stable products, we selected *N*-perfluoroethyl triazoles as starting materials which would after HF elimination and subsequent hydrolysis of the formed imidoyl fluorides provide trifluoroacetamides. Indeed, treating triazole **116** with 1.2 equivalent of triflic acid furnished enamidotriflate **117a** in 88% isolated yield (Scheme 76). Hydrolysis of imidoyl fluoride **118** to trifluoroacetamide **117a** was achieved either by elevated temperatures in the presence of solvent moisture or by hydrolysis on silica gel.



115

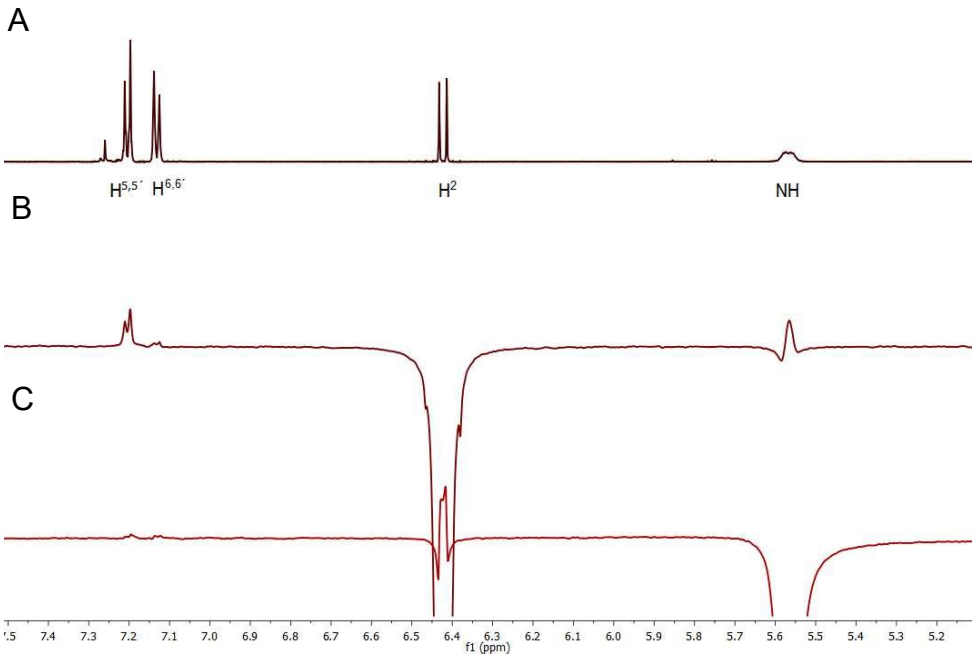
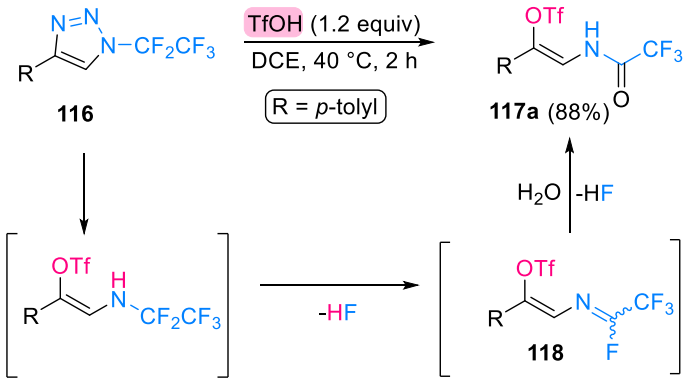


Figure 2 A) ^{1}H NMR spectrum of **115** in $CDCl_3$ B) ge-1D ROESY spectrum of vinyl triflate **115** in $CDCl_3$ with selective irradiation of H2 at 6.4 ppm C) ge-1D ROESY spectrum of vinyl triflate **115** in $CDCl_3$ with selective irradiation of NH at 5.6 ppm.



Scheme 76 Triflic acid mediated synthesis of enamidotriflate **117a** from *N*-perfluoroethyl triazoles **116**.

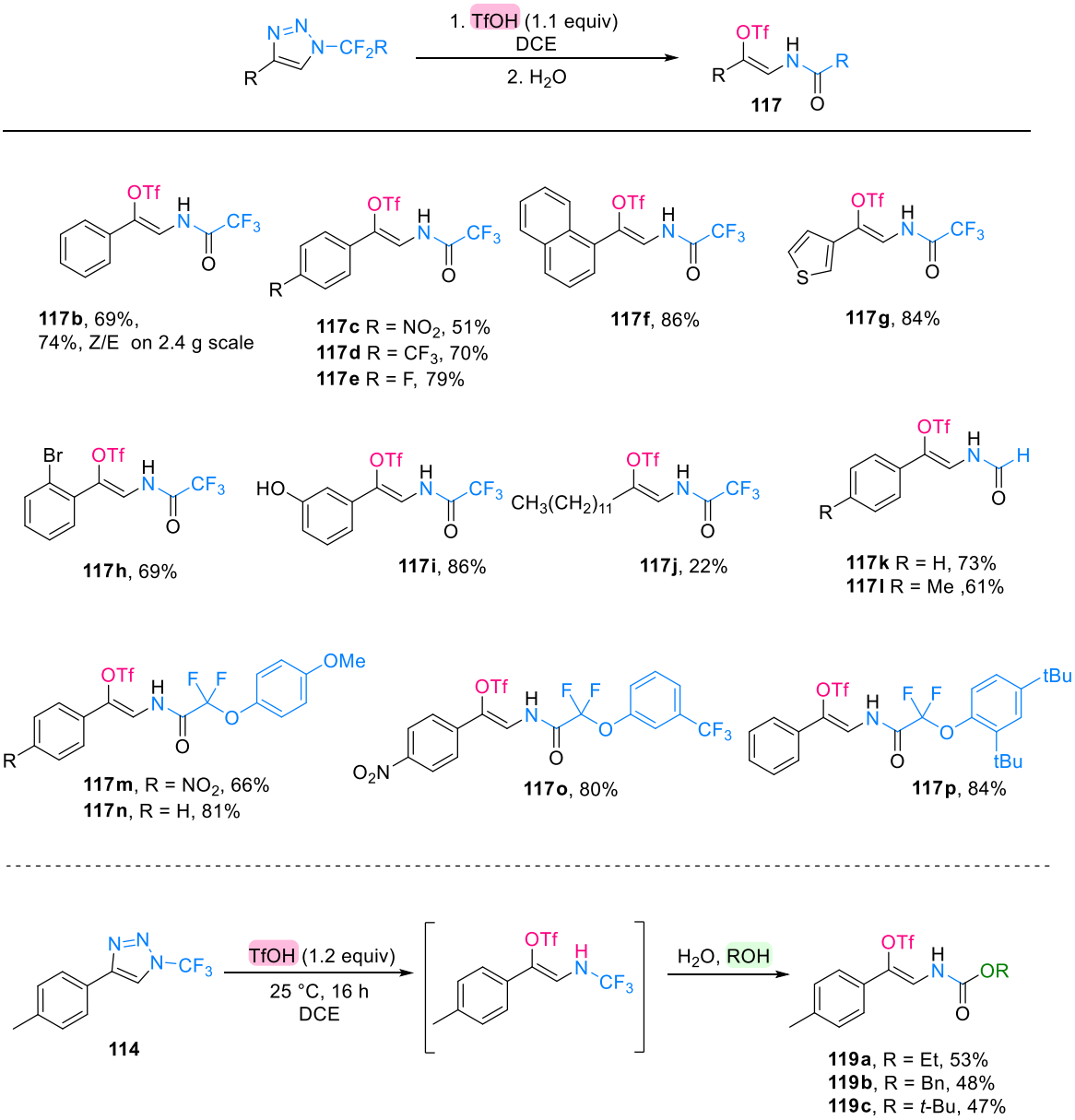
While exploring the scope of the reaction, we found out that triazoles bearing both electron-poor and electron-rich 4-aryl groups give enamido triflates **117b-f** in good to excellent yields and excellent stereoselectivies ($Z/E_{c\text{-}c}$ >20:1), (Scheme 77). The scalability of the method was demonstrated on 2.4 g scale synthesis of derivative **117b**. In the case of triazoles bearing electron-poor 4-aryl groups **117c-d**, prolonged reaction time to several hours was necessary to achieve full conversion. Furthermore, 4-(3-thienyl)-, 4-(2-bromophenyl)- and 4-(3-hydroxyphenyl)-substituted *N*-perfluoroethyl triazoles gave enamido triflates **117g-i** in good to excellent yields. The addition of acetonitrile or 2-methyl-2-butene in 10-fold excess as additives did not affect the efficiency of the reaction, showing the difference to rhodium-catalyzed reactions. 4-Dodecyl-1-perfluroethyl triazole was found less effective and gave enamidotriflate **117j** in 22% yield. My colleague Dr. Svatava Voltrová extended the scope of the reaction with the preparation of two formamides **117k-l** (they are not included in the experimental part of the Thesis), starting from *N*-difluoromethyl triazoles. However, the *N*-difluoromethyl triazoles were found less reactive and required longer reaction times. Importantly, 4-aryl-*N*-fluoromethyl triazoles were stable even upon 3 days of stirring at 70 °C, showing the unique effect of N-CF_2 moiety on the triazole ring-opening. Reactivity of the triazoles with *N*-CF_2CF_2OAr group was investigated by my colleague Vladimir Motornov. Enamido triflates **117m-p** (they are not included in the experimental part of the Thesis) formed from good to very good yields. Moreover, 4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**114**) can be transformed to stable vinyl triflates, when alcohols are added, giving enamidocarbamates **119a-c** in moderate yields. The exclusive stereoselectivity

of the reaction (*Z*/*E* > 20:1) was observed in all cases except of enamido triflates **117g** (*Z*/*E* = 8:1) and **117n** (*Z*/*E* = 5:1).

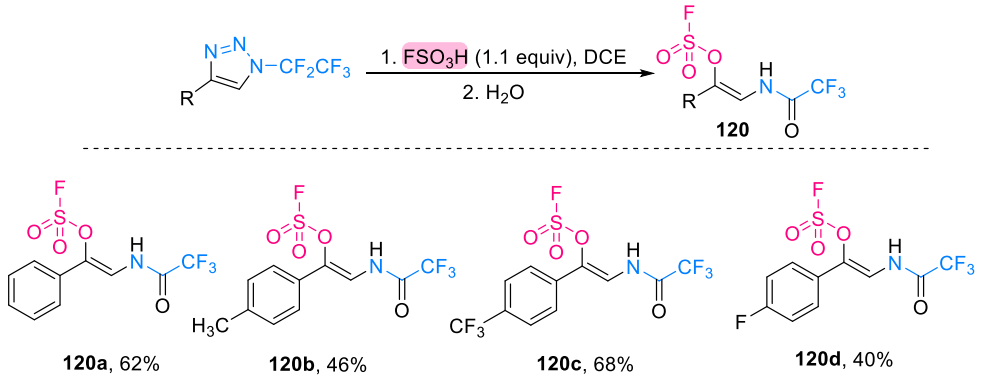
From the observed reactivity of *N*-fluoroalkyl triazoles with triflic acid, the effect of *N*-fluoroalkyl group on reactivity was the following: C_2F_5 > CF_3 > CF_2CF_2OAr > CF_2H >> CFH_2 where N-CFH_2 triazoles were unreactive. In the case of 4-substituent on the triazole ring, the reactivity decreased with EDG property of the 4-aryl groups.

Fluorosulfonic acid-mediated transformation of *N*-flurooalkyl-1,2,3-triazoles was examined next. Fluorosulfonates has been recently revealed as effective reagents for novel click reaction, so-called sulfur (IV) fluoride exchange (SuFEx) reaction.[137] *N*-Perfluoroethyl triazoles reacted with fluorosulfonic acid in an analogous way to the triflic acid-mediated reaction, providing enamido fluorosulfonates **120a-d** in moderate to good yields (Scheme 78). Other strong Brønsted acids, such as nitric and chlorosulfonic acids were found unreactive with *N*-fluoroalkyl-1,2,3-triazoles.

Along with the formation of enamido triflates and enamido fluorosulfonates we observed the formation of enamido fluorides **121** in yields up to 20%. The formation of enamidofluorides can be explained either by the fluorination reaction of vinyl triflates and vinyl fluorosulfonates[138,139] or by the addition of fluoride anion to vinyl cation, which as shown later, is a plausible reactive intermediate of the reaction. The (*Z*)-stereochemistry on the C-C double bond was confirmed by ge-1D ROESY NMR analysis of enamido fluoride **121a** as a representative example (Figure 3).



Scheme 77 Substrate scope for triflic acid-mediated transformation of *N*-fluoroalkyl triazoles.



Scheme 78 Synthesis of enamido fluorosulfonates **112**.

In comparison to most vinyl triflates which are oily compounds sensitive to hydrolysis,[140] enamido triflates and fluorosulfonates are bench stable, crystalline solids. The stereochemistry of the enamido triflates and enamido fluorosulfonates was verified by X-ray analysis of compounds **117a** and **120a** (Figure 4), and 2D ROESY NMR spectroscopy of selected derivatives.

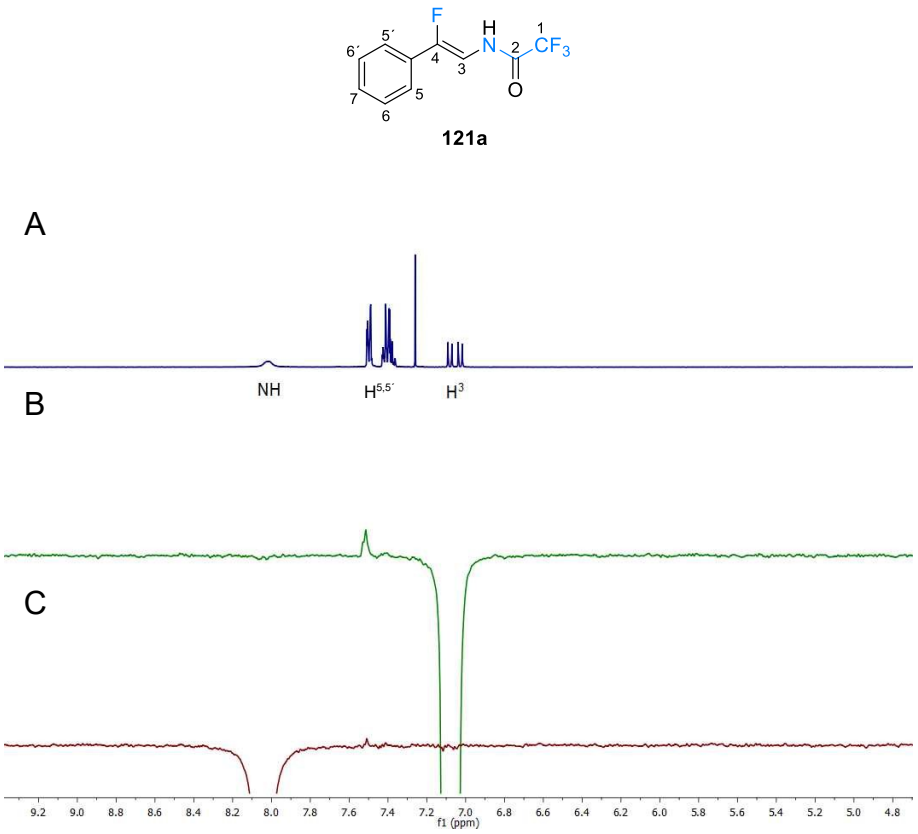


Figure 3 A) ^{1}H NMR spectrum of **121a** in $CDCl_3$ B) ge-1D ROESY spectrum of vinyl triflate **121a** in $CDCl_3$ with selective irradiation of H3 at 7.1 ppm C) ge-1D ROESY spectrum of vinyl triflate **121a** in $CDCl_3$ with selective irradiation of NH at 8.1 ppm.

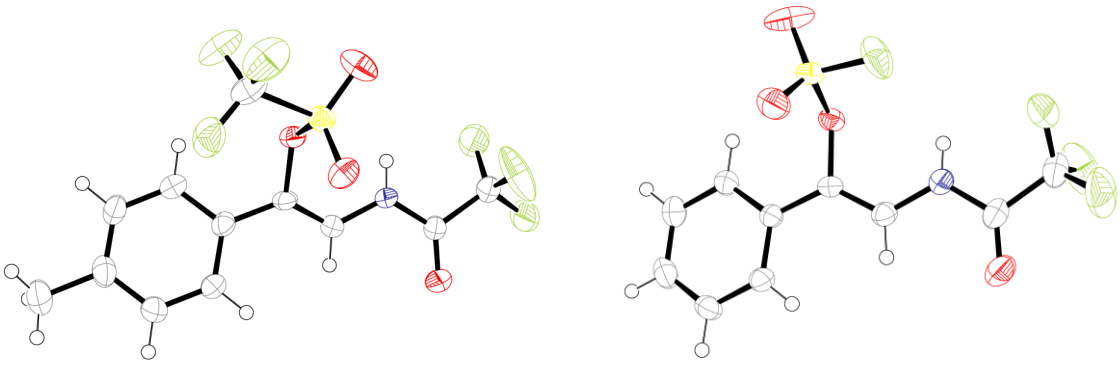
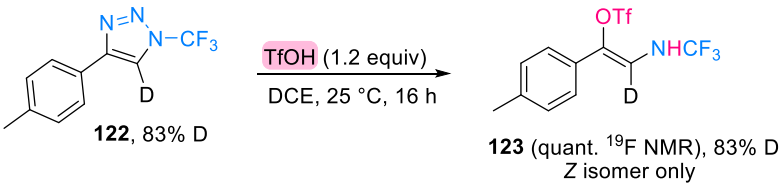


Figure 4 ORTEP[160] representation of the X-ray structures of **117a** and **120a**, displacement ellipsoids are shown with 50% probability.

To investigate the mechanism of the reaction, we synthesized deuterated triazole **122** (Scheme 79). The labelling experiment did not show any D/H exchange in triflic acid-mediated reaction suggesting that the ring-opening takes place by protonation on one of the nitrogen atoms.



Scheme 79 Triflic acid-mediated reaction of deuterium labelled triazole **122**.

In order to gain more insight in the mechanism, we have in collaboration with Tomáš Martinek and Hector Martinez-Seara from IOCB Prague performed DFT calculations. Inspired by a recent work by Severin and co-workers,[141] showing that the protonation of N1 in triazenes leads to shortening of the N2-N3 bond and thus does not lead to the N2-N3 bond cleavage, we were interested in bond lengths of protonated triazolium salts (*note: triazenes have opposite numbering than triazoles, see Figure 1*). Based on DFT calculations, protonation on both N3 and N2 led to shortening of the N1-N2 bond in comparison with unprotonated triazoles and thus should not lead to N1-N2 bond cleavage, similarly as in the case of triazenes (Figure 5). In the other hand, when N1 was protonated, the N1-N2 bond brakes and the triazole ring opens to diazonium amine.

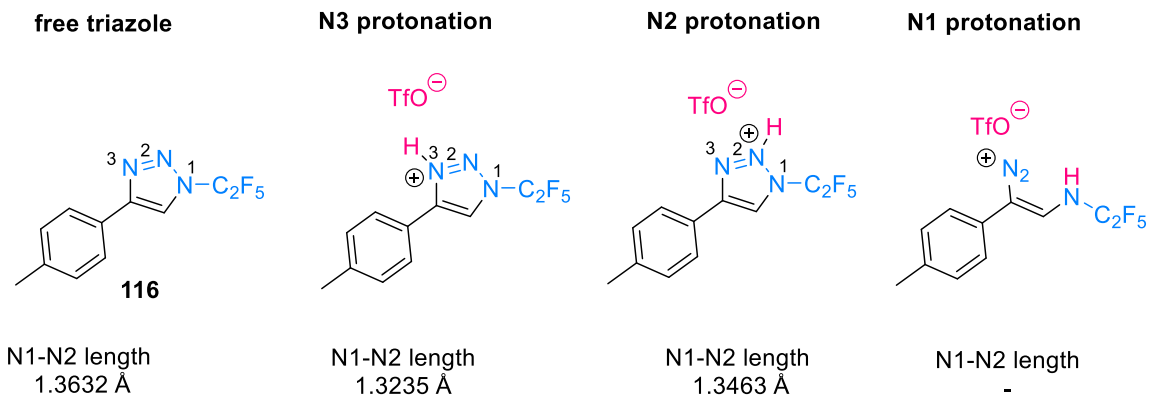


Figure 5 Calculated lengths for N1-N2 bonds of unprotonated and protonated forms of 1-(perfluoroethyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole.

Figure 6 shows calculated energies of 1-(perfluoroethyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole (**116**) in both unprotonated and protonated states. Protonation on N3 (structure **A**) provided stable triazolium salt which was assumed to be the observed precipitate. In the case of N2 protonation (structure **B**) in the presence of triflic anion, the salt was not stable and reverted to the triflic acid and triazole **109a**. The calculated energy of the N2 protonation was anticipated as a sum of energies of the N2 protonated triazole and the triflate anion, which were independently simulated. When the triazole was protonated on N1 (structure **C**), the ring is always opened affording diazonium amine (structure **D**). Following the loss of the nitrogen and the formation of vinyl cation (structure **E**), hydrogen-bonded triflate anion was stereoselectivelly delivered to the vinyl cation and vinyl triflate formed (structure **F**).

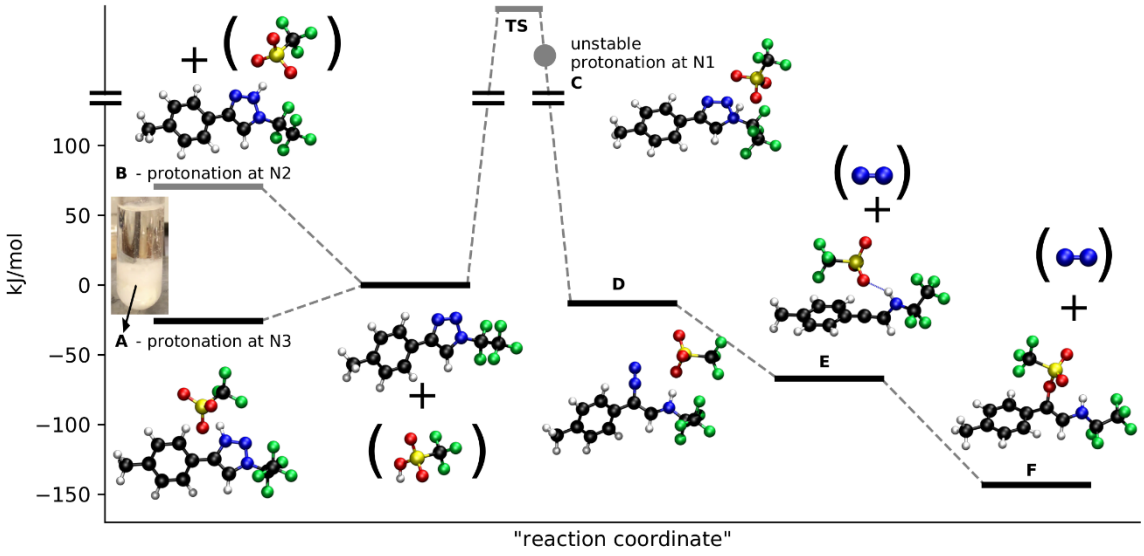
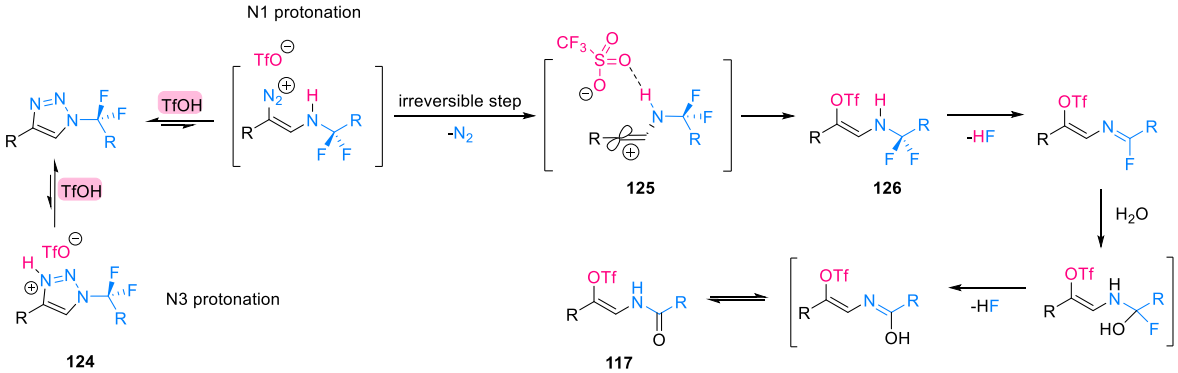


Figure 6 DFT calculations of triflic acid-mediated ring opening of the 1-(perfluoroethyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole (**116**).

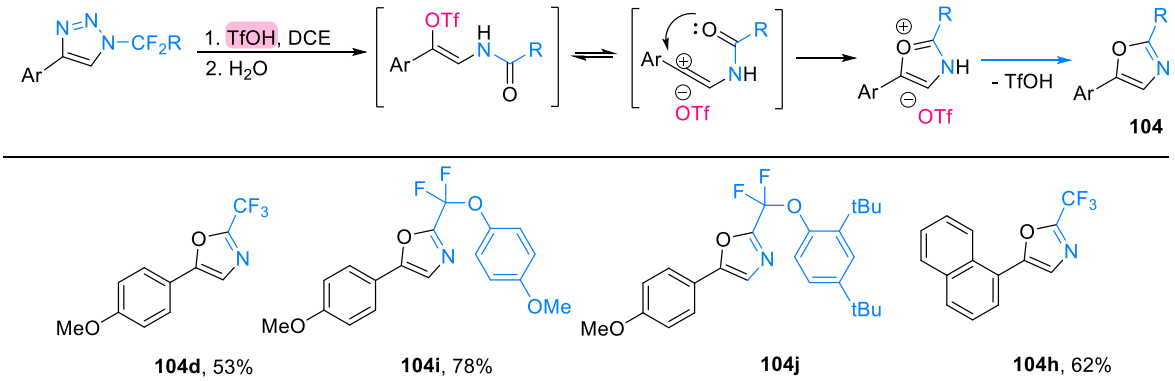
The summarized plausible mechanism of the transformation is shown in Scheme 80. The protonation takes place on N3 providing thermodynamically the most stable triazolium salt **124**. However, proton scrambling from N3 to N1 led to the ring-opening and upon irreversible nitrogen elimination, vinyl cation **125** was formed. Hydrogen bonding of the triflate anion to the hydrogen of amino group resulted in stereoselective addition of the triflate anion to the vinyl cation, affording enamine **126** in (*Z*)-configuration. Following a series of HF eliminations and H_2O addition eventually led to the formation of enamido triflate **117**.



Scheme 80 Proposed mechanism of triflic acid-mediated triazole ring opening.

When triazoles bearing *p*-methoxyphenyl group were used in triflic acid-mediated reactions, we observed an unexpected formation of 2-fluoroalkyl-1,3-oxazoles

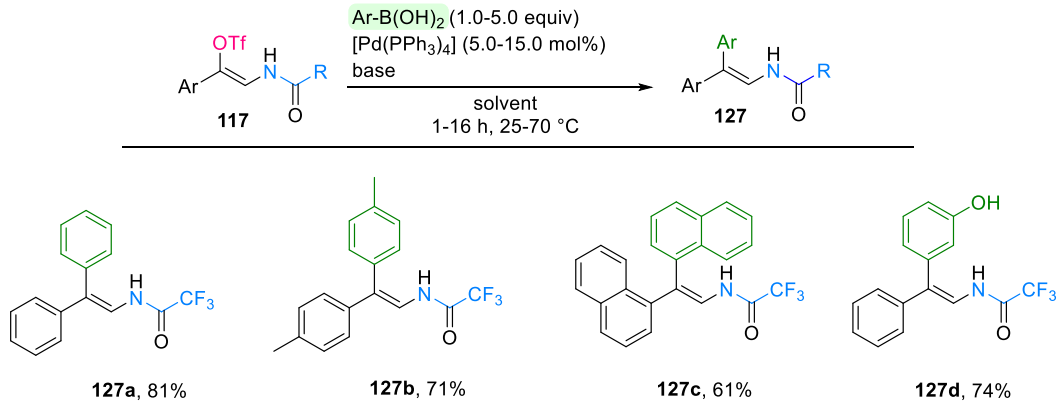
104 in moderate to very good yields (Scheme 81). Based on the observed formation of enamido triflates (via ^{19}F NMR of the crude reaction mixture), which over a longer reaction period or isolation converted to oxazoles, we suggested the following mechanism. *p*-Methoxphenyl group facilitated the formation of vinyl cation, which was intramolecularly attacked by amide oxygen atom to form oxazole (Scheme 81). Likewise, the formation of 2-trifluoromethyl-1,3-oxazole **104h** was observed in the reaction of 4-naphthyl-*N*-perfluoroethyl triazole (**75**), but in this case, the isolation and full characterization of the enamino triflate was achieved (Scheme 77).



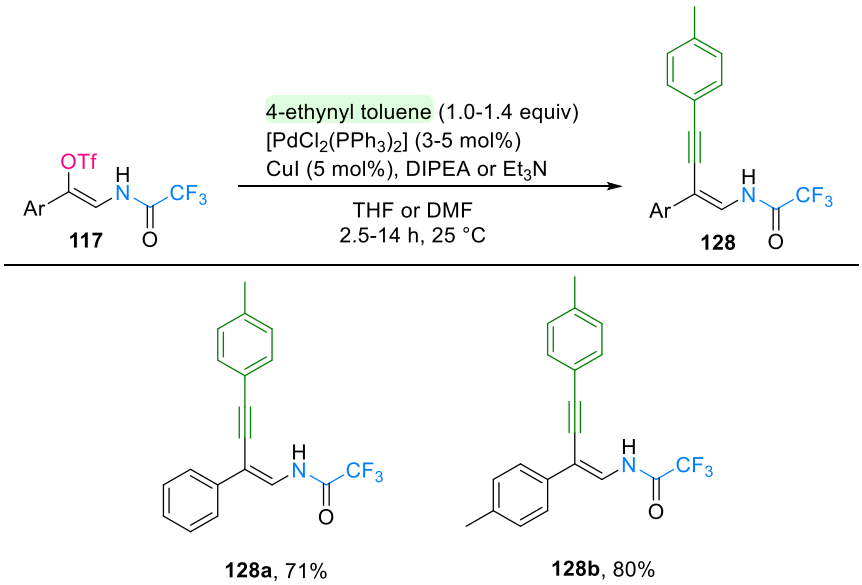
Scheme 81 Mechanism and reaction scope of 2-fluoroalkyl oxazoles through triflic acid-mediated reaction of *N*-fluoroalkyl-1,2,3-triazoles.

5.1.1. Cross-coupling reactions of (*Z*)-β-enamidotriflates

To demonstrate the synthetic potential of enamido triflates in stereoselective synthesis of β,β-disubstituted enamides, we performed a series of palladium-catalyzed cross-coupling reactions. Suzuki cross-coupling of aryl boronic acids and enamido triflates provided β,β-diaryl-substituted enamides **127a-d** in good to excellent yields using tetrakis(triphenylphosphine)palladium as a catalyst (Scheme 82). Furthermore, Sonogashira coupling of aryl acetylenes gave β-aryl-β-alkynyl-substituted enamides **128a** and **128b** in good and excellent yields, respectively (Scheme 83). In addition, Negishi cross-coupling of enamide **117b** with diethyl zinc resulted in 62% yield of β-phenyl-β-ethyl enamide **129** in a stereoselective way (Scheme 84). The stereoselective outcome of the cross-coupling reactions was evaluated by 2D ROESY NMR analysis of representative examples.

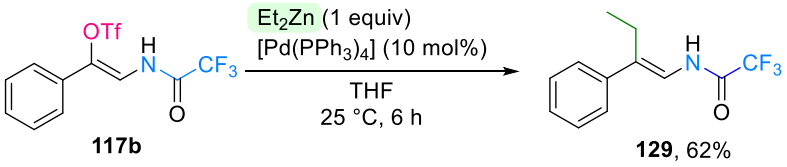


Scheme 82 Suzuki cross-coupling reactions of enamido triflates.



Scheme 83 Sonogashira cross-coupling reactions of enamido triflates.

When we investigated the Suzuki cross-coupling in a more detail, surprisingly, we observed the formation of both (*Z*)- and (*E*)-stereoisomers on the C-C double bond. A comprehensive investigation of the stereoselectivity in Suzuki cross-coupling of enamido triflates was performed under my supervision by a former high-school student from our group, Tomáš Chvojka. We found the catalyst influence as well as solvent and base effect on the stereoselectivity of the reaction. The detailed description of the optimization and the scope of the reaction can be found in Tomáš Chvojka´s high-school thesis (*Středoškolská odborná činnost*).[142] The results are currently being summarized for a publication.



Scheme 84 Negishi cross-coupling of enamido triflates.

In summary, acid-mediated ring-opening of *N*-fluoroalkyl-1,2,3-triazoles was achieved using triflic and fluorosulfonic acids providing β-enamido triflates and β-enamido fluorosulfonates in a stereoselective fashion. Based on deuterium labelled experiment and DFT calculations, the mechanism comprising of protonation on N1 atom, followed by diazonium amine formation, nitrogen elimination, sulfonate addition and hydrolysis of the secondary fluoroalkyl amine was proposed. Triflic acid mediated reaction of *N*-perfluoroethyl-1,2,3-triazoles bearing electron-rich 4-aryl substituents afforded 2-trifluoromethyl oxazoles. The formed vinyl triflates have been shown to undergo stereoselective cross-coupling reactions giving β,β-disubstituted enamides.

5.2. Stereoselective synthesis of functionalized *N*-alkenyl imidoyl halides

N-Alkenyl compounds, such as enamides, enimines and 2-azadienes are compounds, with great utility in organic synthesis,[143–148] or drug discovery, and represent essential structural patterns in many biologically active compounds.[149–152] Their stereoselective synthesis is in many cases very challenging and specific for a narrow group of compounds. In the last decade, stereoselective synthesis of enamides has received extensive attention from the synthetic community, due to the immense utilization in asymmetric synthesis.[153–157] However, to the best of our knowledge, stereoselective synthesis of other *N*-alkenyl compounds such as enimines, enamidines or *N*-alkenyl-substituted heterocycles remain challenging and there is no general method for the synthesis of *N*-alkenyl compounds.

Imidoyl halides (chlorides, bromides, iodides) are compounds with immense utilization in the synthesis of nitrogen-containing compounds.[158] In particular, trifluoroacetimidoyl halides are valuable for the synthesis of medicinally relevant trifluoromethylated compounds, including heterocycles.[159] We envisioned applying acid-mediated reaction of *N*-fluoroalkyl-1,2,3-triazoles for the synthesis

of haloalkenyl imidoyl halides as building blocks providing stereoselective access to a wide array of *N*-alkenyl compounds (Figure 7).

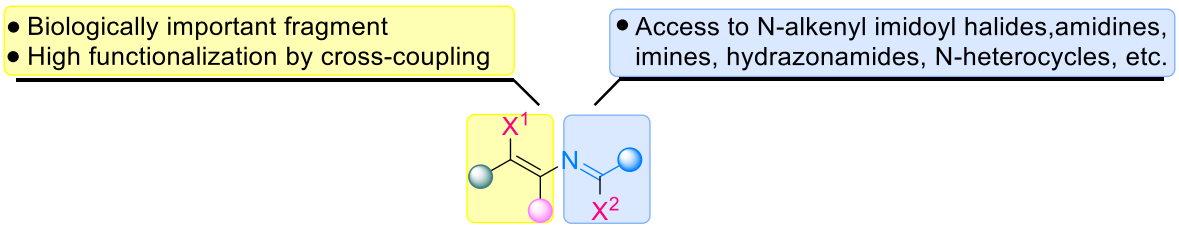
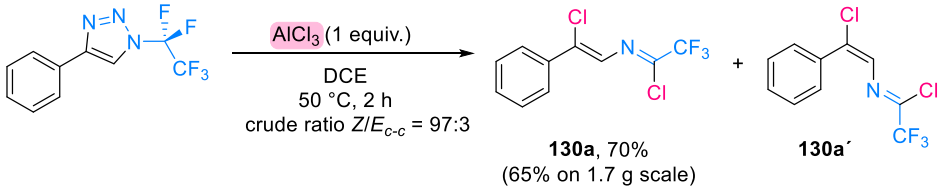


Figure 7 Structure of halovinylimidoyl halide.

As described in the previous chapter, triflic acid-mediated transformations of *N*-fluoroalkyl triazoles afforded *N*-alkenyl imidoyl fluorides as intermediates; however, they easily hydrolyzed to enamides. We intended to use $AlCl_3$ as a strong Lewis acid, capable to facilitate triazole ring-opening followed by chloride addition, and at the same time undergoing the C-F/Cl exchange on the imidoyl fluoride to hydrolytically more stable imidoyl chloride. The formed imidoyl chloride would enable the formation of a variety of nitrogen-containing functional groups as well as high diversification of the double bond by cross-coupling reactions (Figure 7).

Our exploration started with the reaction of the 1-perfluoroethyl-4-phenyl-1,2,3-triazole and $AlCl_3$ in DCE. Similarly to the reaction with triflic acid, a significant gas evolution was observed.^{19}F NMR analysis of a crude mixture revealed the formation of two new compounds in a 93:7 ratio. Subsequent separation by column chromatography showed chloroalkenyl imidoyl chloride **130a** as a major product of the reaction, which was isolated in 70% yield (Scheme 85). X-Ray analysis revealed (*Z*)-configuration on the C-C double bond (Figure 8). Subsequent scale-up reaction afforded imidoyl chloride **130a** in 1.7 g scale. Moreover, the scale-up reaction enabled us to isolate the minor product of the reaction, which was based on 2D HOESY and 2D ROESY NMR identified as the (*E*)-stereoisomer **130a´** on the C-C double bond.



Scheme 85 $AlCl_3$ mediated reaction of 1-perfluoroethyl-4-phenyl-1,2,3-triazoles to imidoyl halides **130a** and **130a´**.

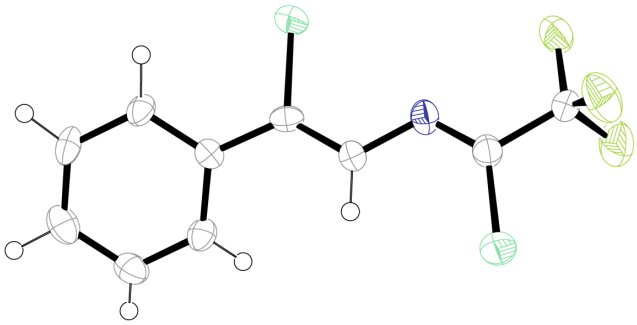
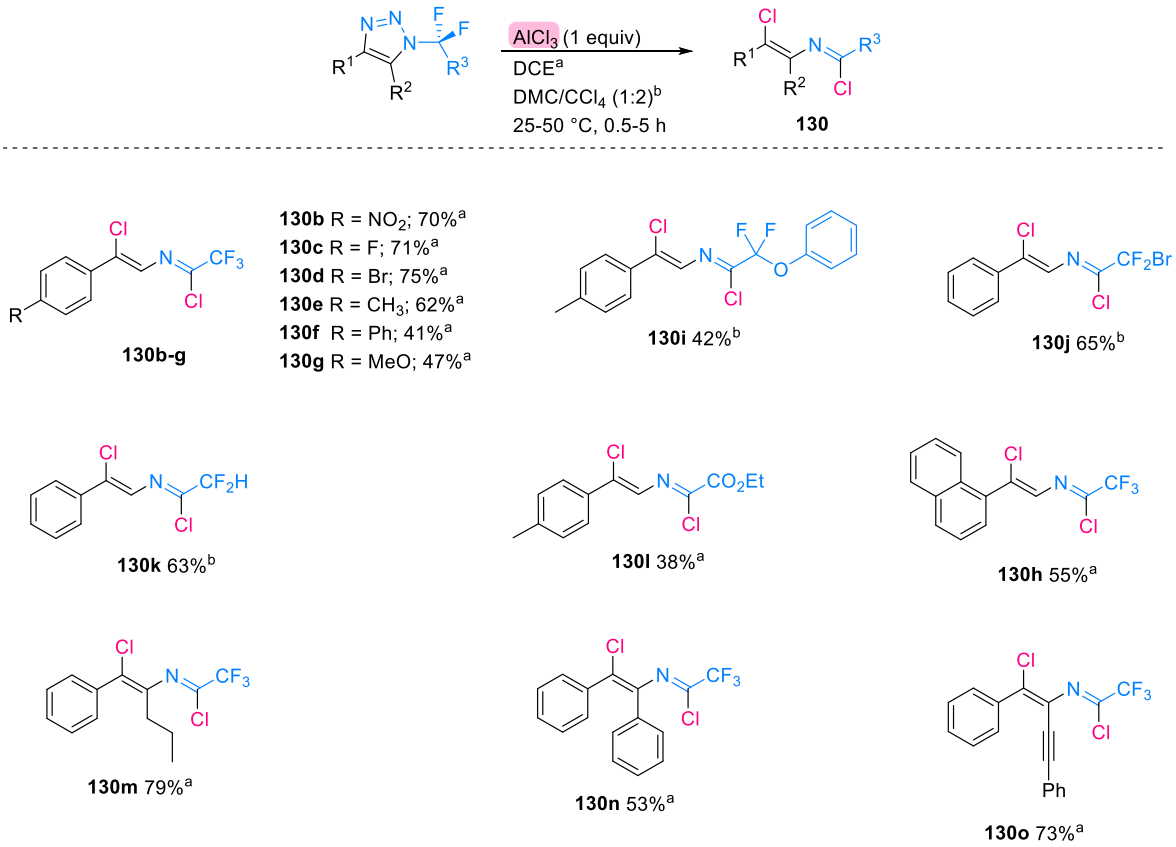


Figure 8 ORTEP[160] representation of the X-ray structure of **130a**, displacement ellipsoids shown with 50% probability.

Next, we investigated the scope of the reaction (Scheme 86). We tested $AlCl_3$-mediated transformation on substituted *N*-fluoroalkyl-1,2,3-triazoles. *N*-Perfluoroethyl-substituted triazoles bearing electron-poor and neutral aryl groups **130b-e** provided imidoyl halides in better yields than triazoles with electron-rich 4-aryl groups **130f-g**. When N-tetrafluoroethyl, N-CF_2CF_2Br and NCF_2CF_2OAr triazoles were examined, we found that the fluorine-chlorine atom exchange took place on the formed difluoromethylene imidoyl chloride group. To overcome this side-reaction, we changed DCE to DCM/CCl_4 solvent system which led to the formation of imidoyl chlorides **130i-k** in moderate to good yields. Additionally, $AlCl_3$-mediated reaction of N-CF_2CO_2Et substituted triazole **72** provided the formation of non-fluorinated imidoyl chloride **130l** in moderate yield. *N*-Perfluoroethyl triazole with 4-(4-trifluoromethylphenyl) group was found unsuitable for the reaction, due to the preferential F/Cl exchange on the trifluoromethylphenyl group. Moreover, *N*-difluoromethyl and *N*-trifluoromethyl triazoles did not give isolable products.

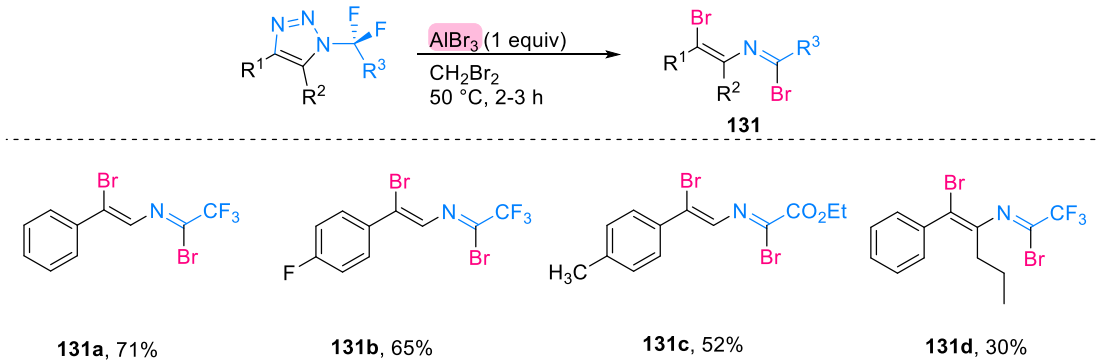
Having demonstrated the scope of various *N*-fluoroalkyl as well as 4-aryl substitutions we set our attention to the transformation of 1-fluoroalkyl-4,5-

disubstituted triazoles. 4-Phenyl-1-perfluoroethyl-substituted triazoles bearing propyl, phenyl and alkynyl substituents in position 5 afforded fully substituted imidoyl chlorides **130m-o** in moderate to very high yields.

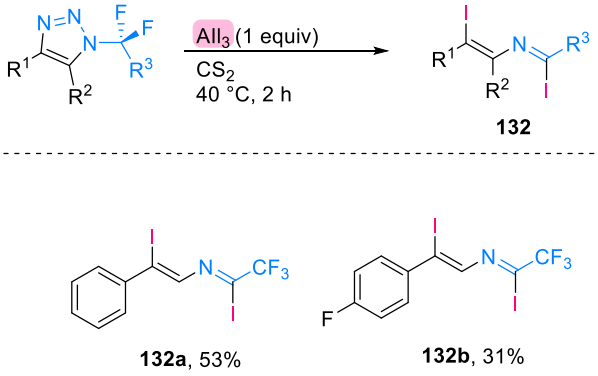


Scheme 86 Substrate scope of $AlCl_3$-mediated reaction of *N*-fluoroalkyl-1,2,3-triazoles.

Next, we investigated the reactivity of *N*-fluoroalkyl-1,2,3-triazoles with $AlBr_3$ (Scheme 87). To avoid the side reaction of $AlBr_3$ with chlorinated solvents, we replaced DCE with CH_2Br_2. To our delight, haloalkenylimidoyl bromides **131a-d** were formed in moderate to good yields. In addition to $AlCl_3$ and $AlBr_3$ we investigated the reactivity of *N*-fluoroalkyl triazoles with AlI_3 (Scheme 88). In this case, we used CS_2 as the solvent and imidoyl iodides **132a-b** were formed in moderate yields.



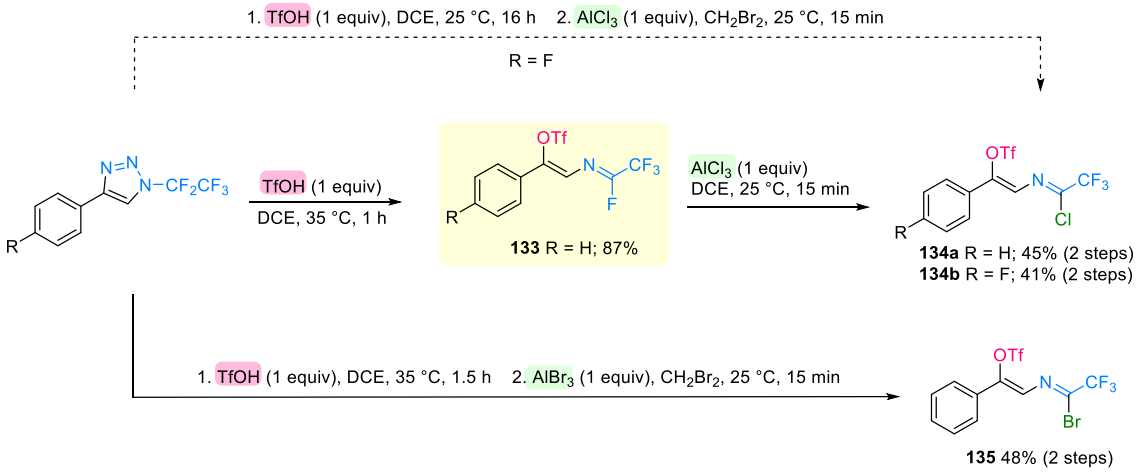
Scheme 87 Substrate scope of $AlBr_3$-mediated reaction of *N*-fluoroalkyl-1,2,3-triazoles.



Scheme 88 AlI_3-mediated reaction of *N*-fluoroalkyl-1,2,3-triazoles.

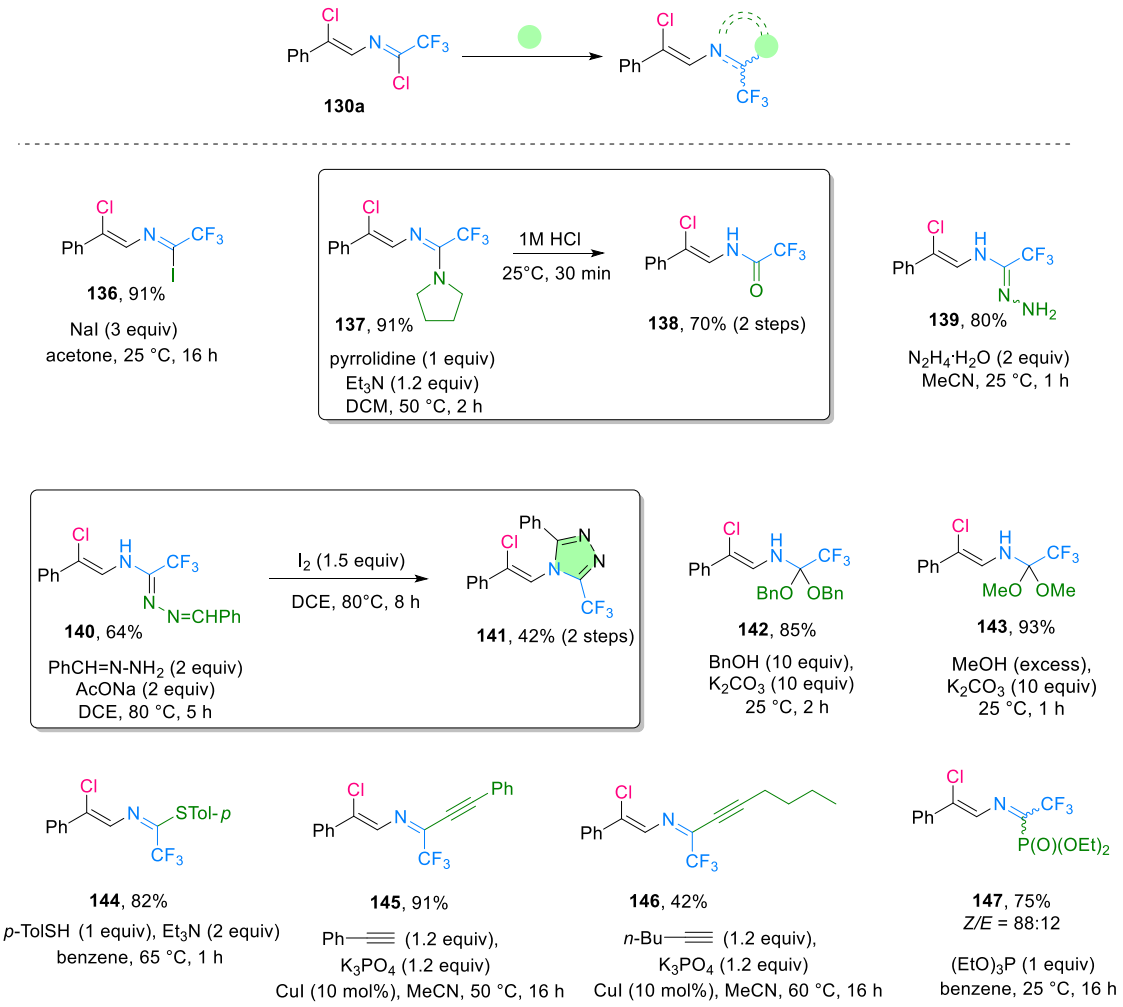
Reactivity of 1-pentafluoroalkyl-4-phenyl-5-halo-1,2,3-triazoles (halogen = Cl, Br, I) was investigated under my supervision by undergraduate student from our group, Lukáš Janecký. The results are summarized in MSc. Lukáš Janecký´s Master thesis.[161]

We were interested if triflic acid-mediated reactions could be used for the preparation of vinyl triflates with imidoyl chloride or bromide group. Thus, we tried to turn hydrolytically unstable imidoyl fluorides to imidoyl chlorides by the reaction with $AlCl_3$. We started with the preparation and isolation of imidoyl fluoride **133**. Mixing of 1-perfluoroethyl-4-phenyl triazoles with one equivalent of triflic acid led to the formation of imidoyl fluoride **133** which was purified by a quick short plug silica gel chromatography. As we expected, the following addition of $AlCl_3$ provided imidoyl chloride **134a** in moderate yield. The process can be achieved in a one-pot two-step settings employing both triflic acid and AlX_3 (X = Cl, Br).



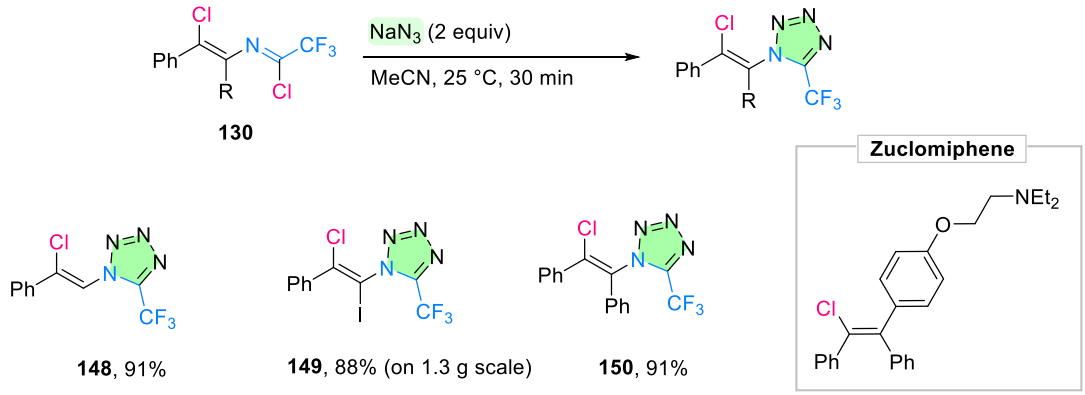
Scheme 89 Triflic acid-mediated synthesis of alkenyl triflate imidoyl fluoride and its conversion to imidoyl chloride and imidoyl bromide.

Having demonstrated the efficiency and substrate scope of aluminium halide mediated transformations of *N*-fluoroalkyl-1,2,3-triazoles we investigated their synthetic utility in the synthesis of a variety of different nitrogen functional groups (Scheme 90). We selected imidoyl chloride **130a** as a model example. The Finkelstein reaction with NaI provided imidoyl iodide **136** in excellent yield. Reaction with pyrrolidine afforded amidine **137** in good yield and its hydrolysis gave enamide **138**. Reaction with hydrazines led to the formation of hydrazones **139** and **140**. Cyclization of hydrazone **140** provided 1,2,4-triazole **141** in moderate yield. Reaction with alcohols afforded acetals **142** and **143** in excellent yields. Moreover, the reaction with *p*-methylbenzenethiol furnished trifluoroethanimidothioate **144** in a very good yield; however, in 2D NOE NMR analysis showed the (*Z*)-configuration on the C-N double bond. The same stereoselective outcome was observed in copper-catalyzed alkynylation affording 2-aza-1,3-dienes **145** and **146**. Finally, the reaction with triethyl phosphine gave imino phosphonates **147** as a mixture of *Z*/*E* isomers on the C-N double bond.



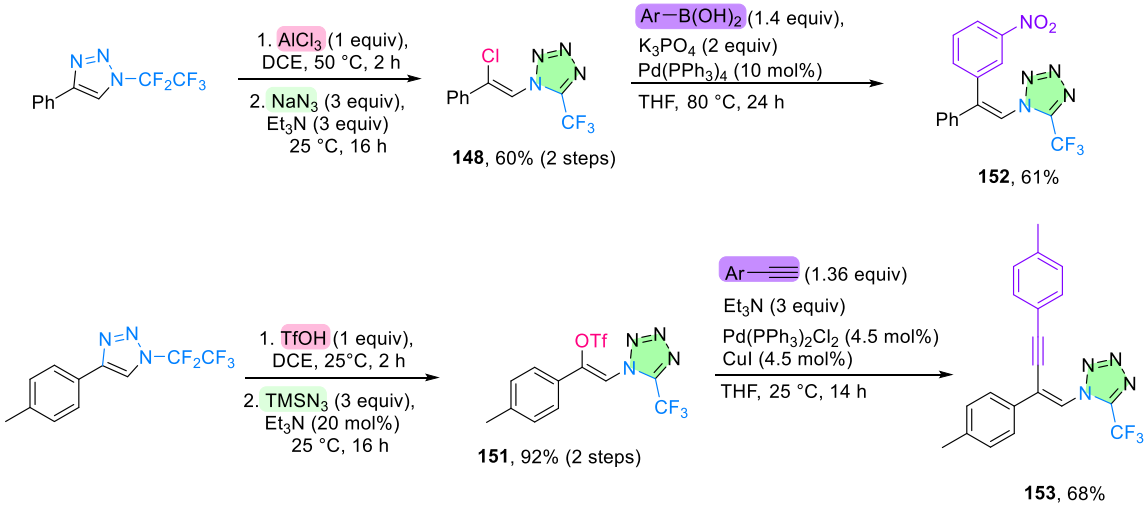
Scheme 90 Synthesis of a variety of nitrogen functional groups from halovinyl imidoyl halide **130a**.

Next, we were interested in the synthesis of *N*-alkenyl-substituted 5-trifluoromethyl tetrazoles. 5-Trifluoromethyl tetrazole group is an important motif in drug discovery and thus, compounds containing this motif could exhibit interesting biological activities.[162] Reactions of imidoyl halides **130** and sodium azide resulted in the formation of tetrazoles **148**-**150** in high yields (Scheme 91). Tetrazole **149** was prepared on a 1.3 g scale starting from (dihalogenalkenyl)imidoyl halide which was prepared by MSc student Lukáš Janecký. It is worth mentioning that tetrazole **150** is a tetrazole structural analogue of Zuclomiphene, (*Z*)-stereoisomer of infertility treatment drug Clomiphene.



Scheme 91 Synthesis of *N*-alkenyl-substituted tetrazoles from imidoyl chlorides **130**.

Moreover, tetrazoles **148** and **151** were prepared in a one-pot two-step procedure starting from *N*-fluoroalkyl triazoles. Cross-coupling of vinyl (pseudo)halide allowed further functionalization on the double bond, as shown by Suzuki and Sonoghasira cross-couplings affording *N*-alkenyl tetrazoles **152** and **153**.



Scheme 92 One-pot two-step synthesis of *N*-alkenyl tetrazoles and subsequent cross-coupling reactions.

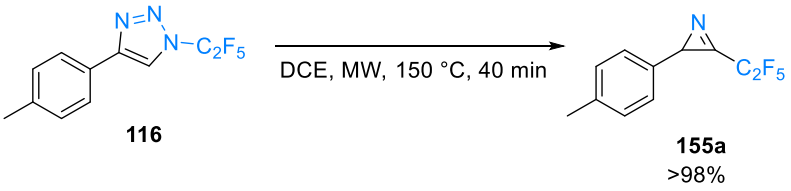
In summary, *N*-fluoroalkyl-1,2,3-triazoles underwent aluminium halide-mediated reactions affording halovinylimidoyl halides (chlorides, bromides and iodides). The reaction is scalable, stereoselective, with broad functional group tolerance, and the formed imidoyl halides are bench stable compounds. We showcased the halovinylimidoyl halides as general building blocks for the synthesis of geometrically defined *N*-alkenyl compounds, including enamides, enamidines,

enimines and other. Moreover, palladium-catalyzed cross-coupling reactions enable high functionalization on the double bond.

6. Thermally induced transformation of *N*-fluoroalkyl-1,2,3-triazoles

Organic azides with the azido group connected directly to the difluoromethylene group (RCF_2N_3) are extraordinarily stable compounds. For example, azidotrifluoromethane CF_3N_3 (**67**), azidoperfluoroethane $C_2F_5N_3$ (**68**) or azidodifluoromethane (HCF_2N_3) have been demonstrated to be stable in the solution of chloroform at 150 °C for 90 min.[32,33] Moreover, GC-MS analyses (inlet at 250 °C) clearly show molecular ion M^+ of these azides, indicating their thermal stability at temperatures even higher than 200 °C. However, when *N*-fluoroalkyl-1,2,3-triazoles are measured by GC-MS analysis, instead of the molecular ion M^+, only compound with mass lost 28 (N_2 molecule) were detected. Hence, our next goal was the exploration of the thermal degradation of *N*-fluoroalkyl-1,2,3-triazoles.

To our surprise, microwave heating of *N*-perfluoroethyl-1,2,3-triazole **116** at 150 °C for 40 min afforded 2*H*-azirine **155a** in quantitative yield (Scheme 93). The structure was evaluated by 2D HMBC and HSQC NMR analyses, and HMRS analysis (Figure 9).



116 **155a** >98%

Scheme 93 Synthesis of 3-fluoroalkyl-2*H*-azirine **155a** from *N*-perfluoroethyl-1,2,3-triazole **116**.

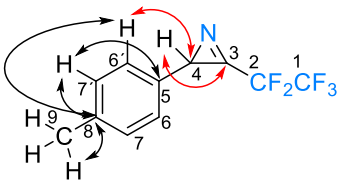


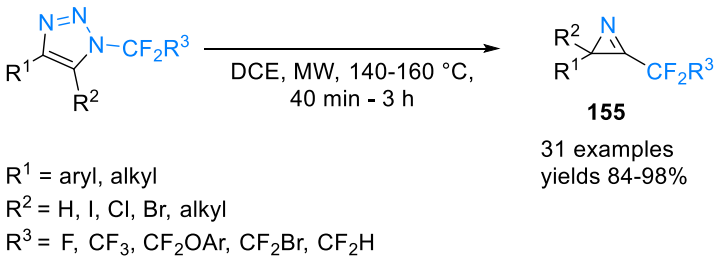
Figure 9 Selected ^{1}H-^{13}C interactions in the HMBC spectra of **155a** supporting a structure of the 3-fluoroalkyl-2*H*-azirine.

2*H*-Azirines are three-membered heterocyclic compounds with an immense application in organic synthesis[163] and chemical biology.[164,165] For example, they serve as 3 atom (CCN) synthons in the synthesis of three-, five-, six- and seven-membered heterocycles, amino acids and many other valuable compounds.[166] They are also broadly present in numerous natural products of pharmacological importance such as antifungal dysidazirine[167] and antazirine or in the structure of aziridomycine.[168]

2-Fluoroalkyl-2*H*-azirines have been recently reported as building blocks with a great potential for the synthesis of pharmaceutically relevant fluoroalkyl containing compounds.[169–172] The methods of their preparation are based either on Neber reaction of trifluoromethyl ketoximes[170] or thermally or photochemically induced rearrangement of 1-azido-2-fluoroalkyl olefins, whose efficient synthesis has been recently discovered: Liu and Liang groups independently reported copper-catalyzed trifluoromethylazidation of alkynes[171,172] and Bao and co-workers described iron-catalyzed azidofluoroalkylation of alkynes.[173] However, an effective synthesis of isomeric 3-fluoroalkyl-2*H*-azirines is to the best of our knowledge unknown. The Neber reaction is not suitable for their synthesis, because the formed R_F-C=N group in the three-membered ring is prone to react with nucleophilic species which are required for the Neber reaction,[174] while cyclization of 1-azido-1-fluoroalkyl olefins have not been reported due to difficulties in the in their synthesis.

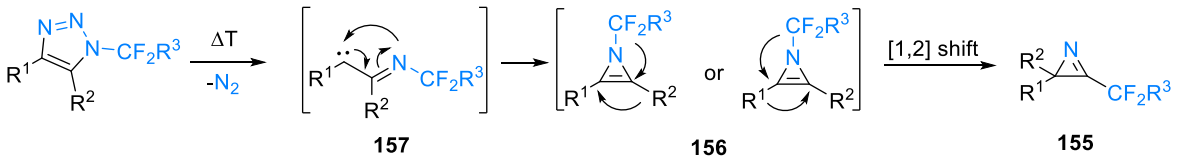
The substrate scope of the thermal transformations of *N*-fluoroalkyl-1,2,3-triazoles to 3-fluoroalkyl-2*H*-azirines was investigated under my supervision by a former bachelor student from our group, BSc. Anežka Marková. The results are summarized in BSc. Anežka Marková´s bachelor thesis.[175] Moreover, my

colleague Dr. Svatova Voltrová extended the scope of another 4-substituted *N*-fluoroalkyl triazoles and 4,5-disubstituted *N*-fluoroalkyl triazoles (Scheme 94).



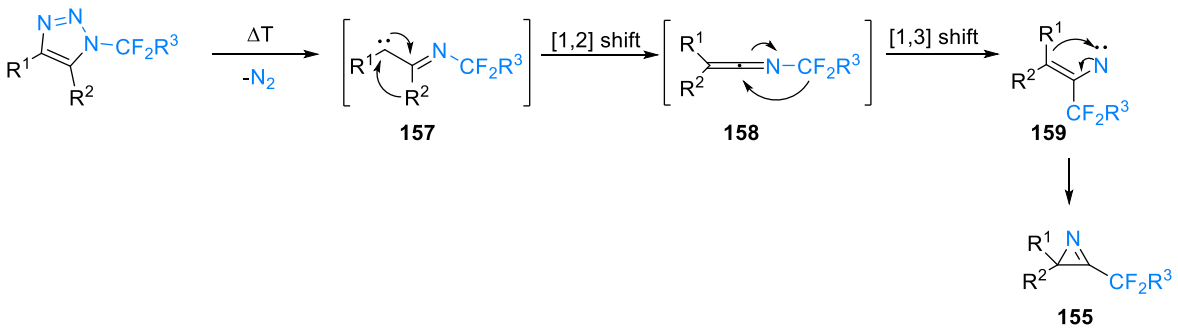
Scheme 94 Synthesis of 3-fluoroalkyl-2*H*-azirines **155** from *N*-fluoroalkyl-1,2,3-triazoles.

We hypothesized two possible reaction mechanisms. The first was based on the formation of antiaromatic 1*H*-azirine **156** via azavinyl carbene **157** as proposed by Lermontov and co-workers[24,102], followed by either simultaneous CF_2R^3 and R^1 [1,2] or CF_2R^3 and R^2 [1,2] shifts (Scheme 95).



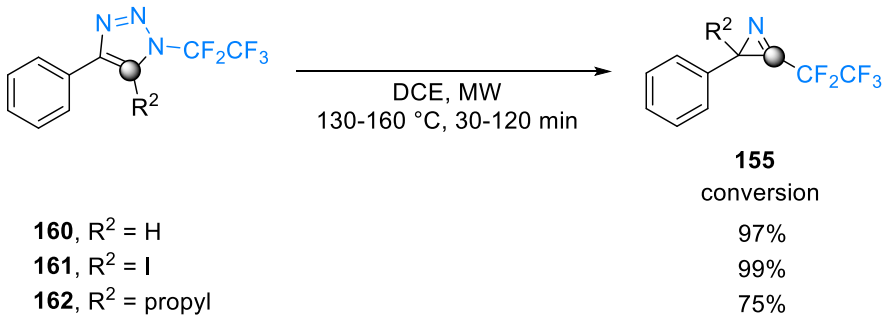
Scheme 95 Proposed mechanism for the formation of 3-fluoroalkyl-2*H*-azirines via 1*H*-azirine intermediate.

The second possible mechanism involved the formation of azavinyl carbene **157**, [1,2] shift of R^2 group to form keteneimine **158** followed by [1,3] shift to afford vinyl nitrene **159**. In the last step, nitrile imine cyclized to the final 3-fluoroalkyl-2*H*-azirine **155** (Scheme 96).



Scheme 96 Proposed mechanism for the formation of 3-fluoroalkyl-2*H*-azirines **155** via ketene imine intermediate.

To investigate the mechanism in detail, Dr. Svatava Voltrová synthesized 4-phenyl-*N*-perfluoroethyl-substituted triazoles **160, 161** and **162**, which were labelled by ^{13}C in the position five of the triazole ring. The labelled triazoles were subjected to the thermal reaction in a microwave reactor. In all cases only the 3-^{13}C labelled 2*H*-azirine formed (Scheme 97).

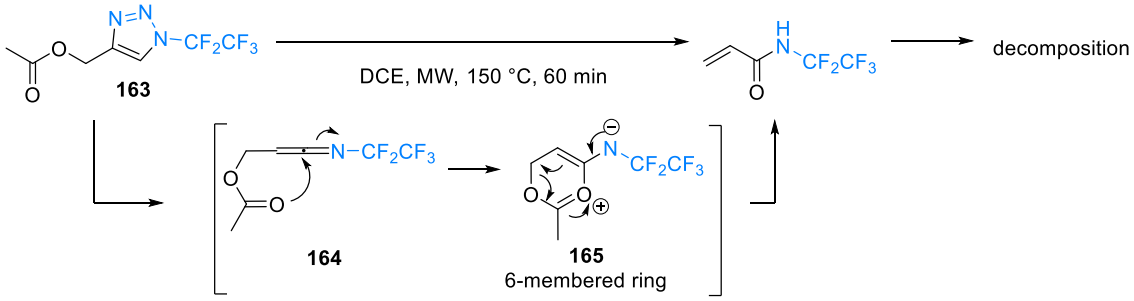


	155 conversion
160, R^2 = H	97%
161, R^2 = I	99%
162, R^2 = propyl	75%

Scheme 97 Synthesis of 3-^{13}C labelled 3-fluoroalkyl-2*H*-azirines **155**.

Even in the case of 4-phenyl-5-propyl-*N*-perfluoroethyl-substituted triazole **162** no 2-^{13}C labelled 2*H*-azirine was observed, serving as an evidence that the reaction via 1*H*-azirine is not proceeding.

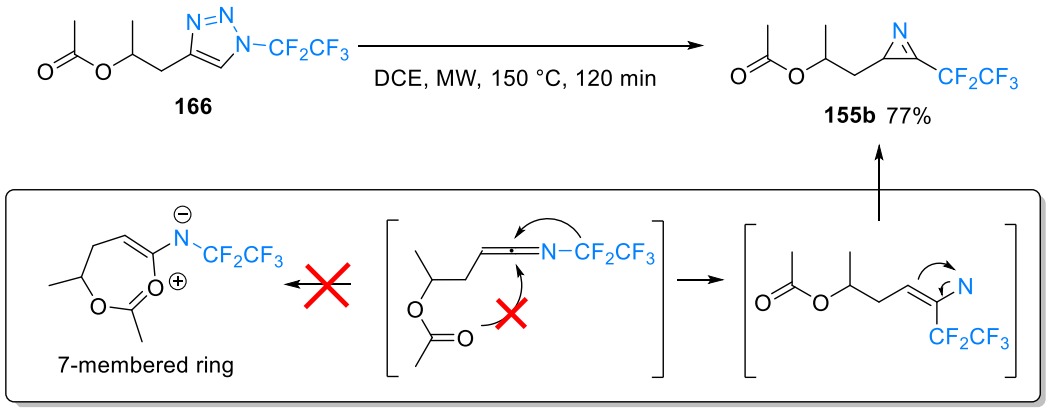
Moreover, inspired by the recent work of Li and co-workers[107], we synthesized triazole **163** in order to trap the potentially formed ketene imine **164** via 6-membered intermediate **165** which would prevent the formation of the azirine. Indeed, when triazole **163** was heated in the microwave reactor, full decomposition of the starting material was observed with no 2*H*-azirine formation (Scheme 98).



Scheme 98 Heating induced transformation of triazole **163**.

When we performed heat-induced transformation of triazole **166**, 3-fluoroalkyl-2*H*-azirine was formed **155b** in good yield. This observation indicated that the [1,3] shift of the fluoroalkyl group at the stage of ketene imine

is favored over intramolecular attack of the acetoxy group which would require the formation of the less stable 7-membered intermediate (Scheme 99).



Scheme 99 Synthesis of azirine **155b** from triazole **166**.

In summary, we have discovered novel, highly efficient, waste- and reagent-free synthesis of 3-fluoroalkyl-2*H*-azirines from *N*-fluoroalkyl-1,2,3-triazoles. The mechanistic investigation suggests the mechanism of the reaction via azavinyl carbene, formation of ketene imine, fluoroalkyl [1,3] shift and cyclization of the formed vinyl nitrene. Synthetic application of 3-fluoroalkyl-2*H*-azirines is currently investigated in our laboratory.

7. General conclusions and outlook

The main purpose of this Thesis was to investigate *N*-fluoroalkyl-1,2,3-triazoles reactivity in the effort to develop novel synthetic methodologies providing access to rare *N*-fluoroalkyl substituted heterocycles as well as other fluorinated compounds.

First, we investigated rhodium-catalyzed reactions of *N*-fluoroalkyl-1,2,3-triazoles. *N*-Fluoroalkyl-1,2,3-triazoles underwent in the presence of suitable dipolarophiles (vinyl ethers, silyl ketene acetals, nitriles or isocyanates) rhodium-catalyzed transannulations to five-membered heterocycles, such as hitherto unreported *N*-(per)fluoroalkyl-substituted pyrroles, pyrrolones, imidazoles and imidazolones, respectively. These reactions were found to be applicable to the synthesis of a variety of 5-membered heterocycles bearing different (per)fluoroalkyl substituents as well as both electron-donating and electron-

withdrawing groups attached to the heterocyclic core. Additionally, in the presence of water, *N*-fluoroalkyl-1,2,3-triazoles underwent rhodium-catalyzed tandem ring-opening and defluorinative annulation to form 2-fluoroalkyl-substituted oxazoles. When excess of water was used, ketamides were obtained in excellent yields.

The second part of the Thesis focused on acid-mediated transformations of *N*-fluoroalkyl-1,2,3-triazoles. In the presence of triflic acid or fluorosulfonic acid, *N*-fluoroalkyl-1,2,3-triazoles underwent a cascade reaction consisting of triazole protonation, ring-opening, nitrogen elimination, sulfonate addition, HF elimination, and hydrolysis to furnish novel trifluoromethanesulfonyloxy- or fluorosulfonyloxy-substituted enamides (*N*-alkenyl amides), respectively, in a highly stereoselective fashion. The alkenyl triflates underwent cross-coupling reactions to a variety of stereodefined substituted β,β-disubstituted enamides. In addition, aluminium halide-mediated transformations of *N*-fluoroalkyl-1,2,3-triazoles led to the stereoselective formation of haloalkenyl imidoyl halides, bench stable building blocks for the synthesis of highly functionalized, stereodefined *N*-alkenyl amides, amidines, imines, hydrazonoamides, imidothioates, iminophosphonates, 1,2,4-triazoles and tetrazoles. Both, sulfonic acid- and aluminium halide mediated transformations have been shown to be scalable, with a broad functional group tolerance and used inexpensive reagents. Furthermore, their synthetic application was demonstrated on the synthesis of tetrazole structural analog of (*Z*)-isomer of infertility treatment drug Clomiphene.

At last, the thermal stability o *N*-fluoroalkyl-1,2,3-triazoles was investigated. *N*-fluoroalkyl-1,2,3-triazole underwent high yielding thermal-induced rearrangement to 3-fluoroalkyl-2*H*-azirine. Mechanistic investigation supported a mechanism involving the formation of azavinyl carbene, ketene imine and vinyl nitrene intermediates.

In summary, this work introduced *N*-fluoroalkyl-1,2,3-triazoles as powerful building blocks for effective syntheses of a variety of fluoroalkyl-substituted heterocycles as well as stereodefined *N*-alkenyl compounds. Moreover it was demonstrated that *N*-fluoroalkyl-1,2,3-triazoles served as precursors of three

different reactive intermediates, rhodium azavinyl carbenoids, aminovinyl cations and azavinyl carbenes.

8. Experimental part

8.1. General remarks

All commercially available chemicals were used as received unless stated otherwise. All starting *N*-fluoroalkyl-1,2,3-triazoles which are not included in the experimental part of this thesis were prepared according to procedures published in the literature or supplied by CF Plus Chemicals (www.cfplus.cz).[32–35] Reactions with air-sensitive materials were carried out under argon or nitrogen atmosphere using standard Schlenk techniques. Chloroform stabilized with ethanol (~1%), 1,2-dichloroethane or 1,1-dichloromethane were dried by activated molecular sieves (3 and 4 Å) and stored under argon. Rhodium catalysts $Rh_2(Oct)_4$ and $Rh_2(esp)_2$ were used as 0.01 M solutions in dry chloroform or DCE unless specified otherwise.

Flash column chromatography was performed using silica gel 60 (0.040–0.063 mm). Automated flash column chromatography was performed on Teledyne ISCO CombiFlash Rf+ Lumen Automated Flash Chromatography System with UV/Vis detection using standard manufacturer's RediSep Rf columns. The TLC analyses were done using TLC silica gel 60 F254 aluminum sheets from Merck, which were visualized under UV (254/366 nm).

^{1}H, ^{13}C, and ^{19}F NMR spectra were measured on Bruker Avance III 400 MHz, Bruker Avance III 400 MHz Prodigy or Bruker Avance III 500 MHz spectrometers, at ambient temperature using 5 mm diameter NMR tubes. ^{1}H-^{1}H ROESY NMR spectra were recorded on Bruker Avance III 500 MHz spectrometer. ^{13}C NMR spectra were proton decoupled. The chemical shift values (δ) are reported in ppm relative to internal Me_4Si (0 ppm for ^{1}H and ^{13}C NMR) or residual solvents and internal $CFCl_3$ (0 ppm for ^{19}F NMR). Coupling constants (J) are reported in Hertz. Structural elucidation was aided by additional acquisition of ^{13}C APT, ge-1D ROESY spectra and/or various 2D spectra (^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{13}C-^{19}F HMBC, ^{1}H-^{1}H ROESY, ^{1}H-^{19}F HOESY). Multiplicity is described

by abbreviations (s - singlet, d - doublet, t - triplet, q - quartet, br s - broad singlet, dd - doublet of doublets, etc.).

High resolution mass spectra (HRMS) were recorded on a Waters Micromass AutoSpec Ultima or Agilent 7890A GC coupled with Waters GCT Premier orthogonal acceleration time-of-flight detector using electron impact (EI) or chemical ionization (CI), on an LTQ Orbitrap XL using electrospray ionization (ESI), and on Q-Tof micro (Waters) quadrupole orthogonal acceleration time-of-flight tandem mass spectrometer using atmospheric-pressure chemical ionization (APCI). UPLC-MS analyses were performed on Acquity UPLC Instrument (Waters Corporation).

Reactions under microwave conditions were performed in Biotage Initiator EXP EU (300 W power) microwave reactor or CEM Focused Microwave TM Synthesis System, Discover R® SP with continuous microwave power delivery (150 W).

8.2. Synthesis and characterization of azidofluoroalkanes

Azidotrifluoromethane (**67**): Prepared according to the previously published procedure.[32] CsF (4.38 g; 28.8 mmol) was dried overnight at 120 °C under a high vacuum in a two-neck round-bottom flask. The flask was cooled to room temperature, backfilled with nitrogen, dry DMF (44 mL) was added and the mixture was cooled to -60 °C. A cold solution of CF_3TMS (3.55 mL; 24 mmol) and TsN_3 (3.68 mL; 24 mmol) in dry DMF (6 mL) was added dropwise over 30 min, and then the reaction mixture was stirred at -60 °C to -30 °C for 3.5 h. Cold dry THF (40 mL) was added and the product was distilled (heating up to 120 °C, ambient pressure) together with THF to a cooled (-78 °C) receiving flask containing $PhCF_3$ as an internal standard. The product was obtained as a solution in THF containing TMSF as a side-product and traces of CF_3H. Yield 70–80% (determined by ^{19}F NMR); ^{19}F NMR (376 MHz, $CDCl_3$) δ = -56.3 (s, 3F).

1-Azido-1,1,2,2,2-pentafluoroethane (**68**): Prepared according previously published procedure.[32] An oven-dried Schlenk flask was evacuated, backfilled with nitrogen and then charged with dry THF (50 mL). C_2F_5H (3 g; 25.0 mmol) was bubbled into the THF, followed by cooling the solution to -78 °C and slow

addition of *n*-BuLi (1.6 M in hexanes; 10.0 mL; 25.0 mmol). Stirring was continued for 1 h at -78 °C while the color changed from transparent to deep yellow. A solution of the TsN_3 (3.8 mL; 25.0 mmol) in THF (20 mL) was slowly added, resulting in the formation of a peach-colored precipitate. The stirring was continued for another 60 min at -78 °C and then the product was distilled together with THF (heating up to 120 °C, ambient pressure) to a cooled (-78 °C) receiving flask containing $PhCF_3$ as an internal standard. Yield: 50-80%; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -85.9 (s, 3F), -93.6 (s, 2F).

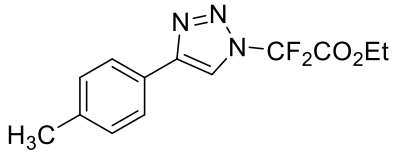
(2-Azido-1,1,2,2-tetrafluoroethoxy)benzene (**69**): Prepared according to the previously published procedure.[34] (2-Bromo-1,1,2,2-tetrafluoroethoxy)benzene (8.2 g; 28.6 mmol) was dissolved in anhydrous THF (100 mL) and cooled to –78 °C. A solution of *i*-PrMgCl·LiCl in THF (1.3 M, 23 mL, 30.0 mmol), was added dropwise. After 1 h, a solution of TsN_3 (11.3 g; 57.1 mmol) in THF (50 mL) was introduced dropwise at –78 °C, and the mixture was stirred for 12 h while warming up to room temperature. Saturated aqueous NH_4Cl (300 mL) was added, the product was extracted with Et_2O, dried ($MgSO_4$), and concentrated. The crude product was purified by flash column chromatography (hexane), affording a colorless liquid. Yield 48%. colorless oil; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.29-7.25 (m, 2H), 7.19-7.15 (m, 1H), 7.12-7.10 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) *δ* -87.0 (t, *J* = 3.8 Hz, 2F), -94.2 (t, *J* = 3.8 Hz, 2F).

1-(2-Azido-1,1,2,2-tetrafluoroethoxy)-1*H*-pyrazole (**70**): Prepared according to the previously published procedure.[34] 1-(2-bromo-1,1,2,2-tetrafluoroethoxy)-1*H*-pyrazole (1.12 g; 4.6 mmol) was dissolved in anhydrous THF (16 mL) and cooled to –78 °C. A solution of *i*-PrMgCl·LiCl in THF (1.3 M, 4 mL, 5.20 mmol), was added dropwise. After 60 min, a solution of NfN_3 (1.69 mL; 9.1 mmol) in THF (8 mL) was introduced dropwise at –78 °C, and the mixture was stirred for 3 h while warming up to room temperature. Saturated aqueous NH_4Cl (50 mL) was added, the product was extracted with Et_2O, dried ($MgSO_4$), and concentrated. The crude product was purified by flash column chromatography (pentane/DCM, 2:1), affording a colorless liquid. Yield 40%. colorless oil; ^1H NMR (400 MHz, $CDCl_3$)

δ 7.83 – 7.77 (m, 4H), 6.52 – 6.46 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -91.5 (t, *J* = 5.4 Hz, 2F), -98.8 (t, *J* = 5.2 Hz, 2F).

8.3. Synthesis and characterization of *N*-fluoroalkyl-1,2,3-triazoles

Ethyl 2,2-difluoro-2-(4-(*p*-tolyl)-1H-1,2,3-triazol-1-yl)acetate (**72**): Sodium azide

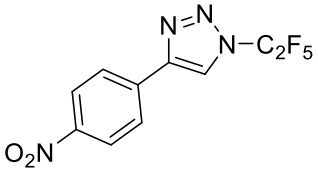


(384 mg; 5.9 mmol) was added into a 50 mL round bottom flask with solution of ethyl 2-bromo-2,2-difluoroacetate (1 g, 4.9 mmol) in dry DMSO (13 mL). The reaction mixture was stirred 16 h at 25 °C. Water was added and reaction mixture was extracted with DCM (3x). DCM layer was washed with water (2x) and concentrated. Solution of the formed ethyl 2-azido-2,2-difluoroacetate **71** in DCM was directly used for the CuAAC reaction. Under air atmosphere, a solution of ethyl 2-azido-2,2-difluoroacetate **71** in DCM (~2.5 mmol, 10 mL) was placed into 25 mL round bottom flask. Subsequently copper(I) 3-methylsalicylate (105.8 mg; 0.49 mmol) and 1-ethynyl-4-methylbenzene (317 μL; 2.5 mmol) were added. Reaction mixture was stirred for 16 h at 25 °C. DCM was removed under reduced pressure, Et_2O (40 mL) was added and the organic phase was washed with aqueous $NaHCO_3$ solution (5%, 2 × 20 mL), water (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (cyclohexane/EtOAc, from 100:0 to 80:20). Yield: 42%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.12 (s, 1H), 7.78 – 7.73 (m, 2H), 7.29 – 7.25 (m, 2H), 4.51 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.42 (td, *J* = 7.1, 0.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5 (t, *J* = 34.5 Hz), 148.7, 139.3, 129.8, 126.2, 126.1, 116.7, 109.6 (t, *J* = 266.7 Hz), 65.1, 21.5, 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -87.0 (s, 2F); HRMS (ESI) *m/z* calcd for $C_{13}H_{14}F_2N_3O_2$ $[M+H]^+$: 282.10486, found 282.10496.

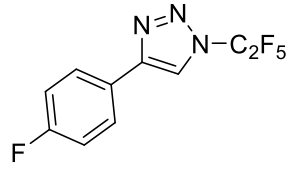
Procedure for the synthesis of previously unreported 4-substituted *N*1-perfluoroethyl-1,2,3-triazoles **73**-**78**

Copper(I) 3-methylsalicylate (2.1–10.7 mg; 0.01–0.05 mmol) was placed in a 10 mL screw-cap glass tube and a cold solution of $C_2F_5N_3$ in THF (~1.5 mmol, 3–4 mL) was added. Subsequently alkyne (1.0 mmol) in THF (0.5 mL) was added, the tube was closed and stirred at 25 °C for 16 h. THF was removed under reduced pressure, Et_2O (20 mL) was added and the organic phase was washed with aqueous $NaHCO_3$ solution (5%, 2 × 10 mL), water (10 mL), aqueous LiCl solution (1M, 10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (cyclohexane/EtOAc, from 100:0 to 80:20).

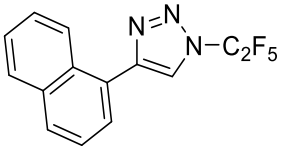
4-(4-Nitrophenyl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**73**): Yield: 75%; yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.38–8.33 (m, 2H), 8.31 (s, 1H), 8.12–8.05 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 146.7, 134.7, 127.0, 124.7, 119.6, 117.0 (qt, *J* = 287.6 Hz, *J* = 40.7 Hz), 110.3 (tq, *J* = 272.5 Hz, *J* = 43.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -84.3 (s, 3F), -99.2 (s, 2F); HRMS (CI) *m/z* calcd for $C_{10}H_6F_5N_4O_2$ $[M+H]^+$: 309.0405, found 309.0412.



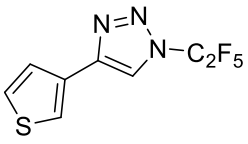
4-(4-Fluorophenyl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**74**): Yield: 77%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.91–7.82 (m, 2H), 7.22–7.12 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5 (d, *J* = 249.4 Hz), 148.0, 128.2 (d, *J* = 8.1 Hz), 124.9 (d, *J* = 3.3 Hz), 117.7, 117.1 (qt, *J* = 287.5 Hz, *J* = 41.3 Hz), 116.4 (d, *J* = 22.0 Hz), 110.3 (tq, *J* = 271.1 Hz, *J* = 42.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.4 (s, 3F), -99.2 (s, 2F), -111.8 (tt, *J* = 8.0, 5.2 Hz); HRMS (CI) *m/z* calcd for $C_{10}H_6F_6N_3$ $[M+H]^+$: 282.0460, found 282.0468.



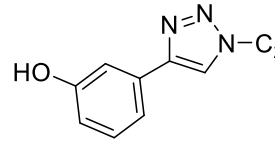
4-(Naphthalen-1-yl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**75**): Yield: 94%; light yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.26–8.23 (m, 1H), 8.20 (s, 1H), 7.99–7.91 (m, 2H), 7.76 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.59–7.55 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0, 134.0, 131.1, 130.3, 128.8, 128.1, 127.4, 126.5, 125.9, 125.4, 124.9, 120.9, 117.2 (qt, *J* = 287.3, *J* = 41.1 Hz), 110.5 (tq, *J* = 270.7 Hz, *J* = 42.9 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -84.2 (s, 3F), -98.9 (s, 2F); HRMS (ESI) *m/z* calcd for $C_{14}H_9N_3F_5$ $[M+H]^+$: 314.07111, found 314.07095.



1-(Perfluoroethyl)-4-(thiophen-3-yl)-1*H*-1,2,3-triazole (**76**): Yield: 91%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.83 (dd, *J* = 2.9, 1.3 Hz, 1H), 7.48 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.44 (dd, *J* = 5.0, 2.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 129.7, 127.2, 125.8, 123.3, 117.5, 117.1 (qt, *J* = 287.6 Hz, *J* = 41.3 Hz), 110.3 (tq, *J* = 271.1 Hz, *J* = 42.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.4 (s, 3F), -99.2 (s, 2F); HRMS (ESI) *m/z* calcd for $C_8H_5F_5N_3S$ $[M+H]^+$: 270.01189, found 270.01184.



4-(3-Hydroxyphenyl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**77**): Yield: 95%; white solid; ^{1}H NMR (401 MHz, Acetone-d_6) δ 9.06 (s, 1H), 8.60 (s, 1H), 7.56–7.49 (m, 1H), 7.47 (ddd, *J* = 7.7, 1.6, 1.0 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 6.92 (ddd, *J* = 8.1, 2.5, 1.0 Hz, 1H); ^{13}C NMR (101 MHz, Acetone-d_6) δ 158.9, 149.4, 131.1 (2C), 120.6, 118.2, 118.1 (qt, *J* = 286.8 Hz, *J* = 41.7 Hz), 117.2, 113.8, 111.2 (tq, *J* = 268.8 Hz, *J* = 42.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.4 (s, 3F), -99.2 (s, 2F); HRMS (CI) *m/z* calcd for $C_{10}H_7N_3OF_5$ $[M+H]^+$: 280.0509, found 280.0515.



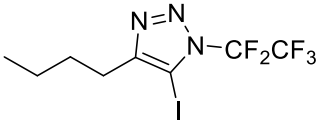
4-Dodecyl-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**78**): Yield: 37%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.65 (s, 1H), 2.78 (t, *J* = 7.5 Hz, 2H), 1.71 (p, *J* = 7.9 Hz, 2H), 1.40 –1.21 (m 18H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.7, 119.2, 117.2 (qt, *J* = 287.3

Hz, *J* = 41.5 Hz), 110.3 (tq, *J* = 270.1 Hz, *J* = 42.8 Hz), 32.1, 29.8 (3C), 29.6, 29.5, 29.4, 29.3, 29.1, 25.4, 22.8, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.5 (s, 3F), -99.1 (s, 2F); HRMS (CI) *m/z* calcd for $C_{16}H_{27}F_5N_3$ $[M+H]^+$: 356.2120, found 356.2125.

Procedure for the synthesis of previously unreported 4-substituted 5-iodo-*N*-perfluoroethyl-1,2,3-triazoles **79-82**

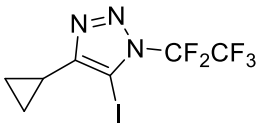
Under air atmosphere, a solution of $C_2F_5N_3$ in THF (~6 mmol, 15 mL) in 50 mL round bottom flask was cooled to -78 °C, followed by the addition of copper(I) acetylide (3 mmol) and iodine (761 mg; 3 mmol). Triethylamine (934 μL; 6.72 mmol) was added dropwise and the reaction mixture was slowly warmed to 25 °C and stirred for 16 h. Et_2O (50 mL) was added and reaction mixture was filtered through silica gel. The filtrate was evaporated with silica gel and the product was purified by column flash chromatography (pentane/DCM, from 100:0 to 20:80).

4-Butyl-5-iodo-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**79**): Yield: 60%; white solid;



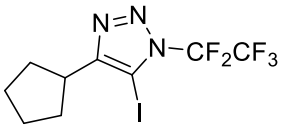
^{1}H NMR (401 MHz, $CDCl_3$) δ 2.76 – 2.70 (m, 2H), 1.76 – 1.66 (m, 2H), 1.48 – 1.34 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 117.2 (qt, *J* = 287.9, 39.4 Hz), 111.1 (tq, *J* = 270.7, 42.9 Hz), 73.3, 30.8, 25.5, 22.4, 13.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.9 (s, 3F), -94.2 (s, 2F); HRMS (ESI) *m/z* calcd for $C_8H_{10}F_5IN_3$ $[M+H]^+$: 369.9834, found 369.98332.

4-Cyclopropyl-5-iodo-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**80**): Yield: 38%; white

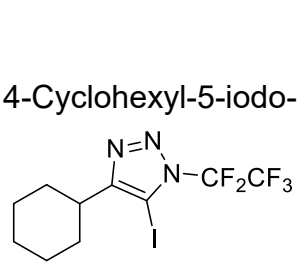


solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92 – 1.83 (m, 1H), 1.15 – 1.03 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 117.1 (qt, *J* = 288.0, 39.4 Hz), 111.0 (tq, *J* = 271,9, 43.3 Hz), 72.4, 8.2, 7.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -82.0 (s, 3F), -94.1 (s, 2F); HRMS (ESI) *m/z* calcd for $C_7H_6F_5IN_3$ $[M+H]^+$: 353.95211, found 353.95213.

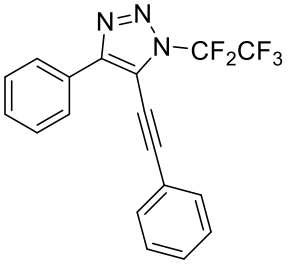
4-Cyclopentyl-5-iodo-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**81**): Yield: 22%; pale-yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.18 – 3.07 (m, 1H), 2.13 – 1.98 (m, 2H), 1.97 – 1.82 (m, 4H), 1.78 – 1.65 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 117.2 (qt, *J* = 287.7, 39.2 Hz), 111.1 (tq, *J* = 270.6, 42.9 Hz), 72.9, 36.5, 32.6, 25.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.8 (s, 3F), -93.8 (s, 2F); HRMS (ESI) *m/z* calcd for $C_9H_{10}F_5IN_3$ $[M+H]^+$: 381.98341, found 381.98361.



4-Cyclohexyl-5-iodo-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**82**): Yield: 73%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 2.70 (tt, *J* = 11.8, 3.6 Hz, 1H), 1.94 – 1.80 (m, 4H), 1.79 – 1.66 (m, 3H), 1.48 – 1.26 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 117.2 (qt, *J* = 287.8, 39.3 Hz), 111.2 (tq, *J* = 270.8, 43.1 Hz), 72.2, 35.7, 31.8, 26.4, 25.8. ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.8 (3F), -93.7 (s, 2F); HRMS (ESI) *m/z* calcd for $C_{10}H_{12}F_5IN_3$ $[M+H]^+$: 395.99906, found 395.99936.

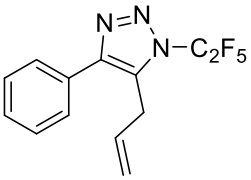


1-(Perfluoroethyl)-4-phenyl-5-(phenylethynyl)-1*H*-1,2,3-triazole (**83**): Under air atmosphere, a solution of $C_2F_5N_3$ in THF (~10 mmol, 25 mL) in 100 mL round bottom flask was cooled to -78 °C followed by addition of copper(I) phenylacetylide (1.61 g; 20 mmol) and iodine (2.54 g; 10 mmol). Triethylamine (1.7 mL; 12 mmol) was added dropwise and the reaction mixture was slowly warmed to 25 °C and stirred for 24 h. Diethyl ether (100 mL) was added and the reaction mixture was filtered through silica gel. The filtrate was concentrated, potassium *tert*-butoxide (561 mg; 5 mmol) was added and the mixture was stirred for 30 min at 25 °C. (*Note: Potassium* tert-*butoxide is added for decomposition of 5-iodo-1-(perfluoroethyl)-4-phenyl-1H-1,2,3-triazole which is a side-product of the reaction and is difficult to separate by column chromatography*). Et_2O (100 mL) was added into the reaction mixture and organic layer was washed with water (100 mL) and brine (20 mL), dried over $MgSO_4$, filtrated and evaporated on silica gel and product was purified by column chromatography (cyclohexane/EtOAc, from 100:0 to 20:80). Yield: 35%;



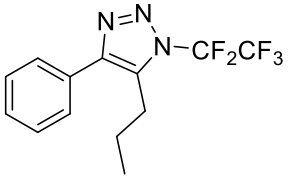
white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.26 – 8.21 (m, 2H), 7.61 – 7.56 (m, 2H), 7.54 – 7.49 (m, 2H), 7.48 – 7.41 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.1, 131.9, 130.5, 129.8, 129.0, 128.9, 128.7, 126.9, 120.9, 117.4 (qt, *J* = 288.1, 40.3 Hz), 116.9, 111.0 (tq, *J* = 272.0, 43.1 Hz), 104.5, 73.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -83.0 (s, 3F), -97.4 (s, 2F); HRMS (EI) *m/z* calcd for $C_{18}H_{10}F_5N_3$ [M]$^+$: 363.0795, found 363.0798.

5-Allyl-1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole (**84**): Under air atmosphere,



a solution of $C_2F_5N_3$ in THF (~10 mmol, 25 mL) in 100 mL round bottom flask was cooled to -78 °C, followed by the addition of copper(I) phenylacetylide (1.1 g; 6.68 mmol). Allyl bromide (5.8 mL; 66.8 mmol) was added dropwise and the reaction mixture was slowly warmed to 25 °C and stirred for 16 h. Diethyl ether (50 mL) was added and the reaction mixture was filtered through silica gel. The filtrate was evaporated with silica gel and the product was purified by column flash chromatography (cyclohexane/EtOAc, from 100:0 to 20:80). Yield: 45%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.74 – 7.66 (m, 2H), 7.53 – 7.39 (m, 3H), 5.96 (ddt, *J* = 17.2, 10.5, 5.4 Hz, 1H), 5.25 (dtd, *J* = 10.3, 1.8, 0.8 Hz, 1H), 5.02 (dqd, *J* = 17.2, 1.3, 0.6 Hz, 1H), 3.74 (dtt, *J* = 5.0, 2.0, 1.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.0, 132.3 (t, *J* = 2.2 Hz), 132.2, 129.4, 129.1, 129.0, 128.0, 118.4, 117.4 (qt, *J* = 287.6, 39.8 Hz), 111.3 (tq, *J* = 271.4, 42.7 Hz), 27.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -82.2 (s, 3F), -96.0 (s, 2F); HRMS (EI) *m/z* calcd for $C_{13}H_{10}F_5N_3$ [M]$^+$: 303.0795, found 303.0793.

1-(Perfluoroethyl)-4-phenyl-5-propyl-1*H*-1,2,3-triazole (**85**): Triazole **84** (493 mg;



1.62 mmol) was dissolved in EtOH (20 mL), Pd/C (10%) was added and the reaction mixture was stirred for 16 h under hydrogen atmosphere at 25 °C. The reaction mixture was filtered and purified by column flash chromatography (pentane/EtOAc, 95/5). Yield: 97%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.63 (m, 2H), 7.53 – 7.44 (m, 2H), 7.47 – 7.38 (m, 2H), 3.00 – 2.91 (m, 2H), 1.77 – 1.62 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101

MHz, $CDCl_3$) δ 146.1, 135.5 (t, *J* = 2.2 Hz), 129.9, 129.0, 128.9, 127.9, 117.4 (qt, *J* = 287.9, 40.0 Hz), 111.6 (tq, *J* = 267.8, 42.9 Hz), 25.3 (t, *J* = 3.1 Hz), 22.9 (t, *J* = 1.3 Hz), 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -82.1 (s, 3F), -95.8 (s, 2F); HRMS (EI) *m/z* calcd for $C_{13}H_{12}F_5N_3$ $[M]^+$: 305.0951, found 305.0949.

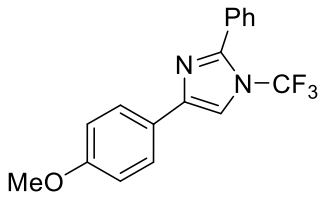
1-(Perfluoroethyl)-4,5-diphenyl-1*H*-1,2,3-triazole (**86**): The starting 4-phenyl-5-iodo-1-(perfluoroethyl)-1*H*-1,2,3-triazole (389 mg; 1 mmol) and tributylphenylstannane (653 μL; 2 mmol) were dissolved in DMF (4 mL) and the reaction mixture was cooled to -100 °C. The reaction flask was evacuated and back filled with argon 3 times, warmed to room temperature and palladium(II) acetate (11.2 mg; 0.05 mmol) was added. The reaction mixture was stirred for 16 h at 35 °C. Potassium *tert*-butoxide (224 mg; 2 mmol) was added and reaction mixture was stirred for 1 h at 40 °C (*Note: Potassium* tert-*butoxide is added for decomposition of 1-(perfluoroethyl)-4-phenyl-1*H-*1,2,3-triazole which is a side-product of the reaction and is difficult to separate by column chromatography*). Et_2O was added into the reaction mixture and organic layer was washed with water (4 × 20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and evaporated to give crude brown oil, which was purified by column chromatography (pentane/EtOAc, 3/1). The obtained brown solid was washed with pentane to give a white solid. Yield: 10%; white solid; ^1H NMR (401 MHz, $CDCl_3$) δ 7.59 – 7.48 (m, 5H), 7.41 – 7.36 (m, 2H), 7.31 – 7.25 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.0, 134.2 (t, *J* = 1.5 Hz), 130.6, 130.3 (t, *J* = 1.3 Hz), 129.2, 129.1, 128.9, 128.8, 127.3, 125.7 (t, *J* = 1.3 Hz), 117.2 (qt, *J* = 287.6, 39.6 Hz), 111.3 (tq, *J* = 270.3, 42.7 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -82.2 (s, 3F), -93.4 (s, 2F); HRMS (EI) *m/z* calcd for $C_{16}H_{10}F_5N_3$ $[M]^+$: 339.0795, found 339.0797.

8.4. Synthesis and characterization of *N*-(per)fluoroalkyl imidazoles, pyrroles, pyrrolones and imidazolones

General procedure A for the synthesis of *N*-(per)fluoroalkyl imidazoles **89**

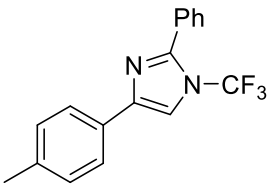
Initial *N*-(per)fluoroalkyl-triazole (0.20 mmol) was dissolved in dry $CHCl_3$ (2 mL) in a 5 mL microwave tube. Nitrile (2 equiv., 0.40 mmol) and a solution of rhodium (II) octanoate (2 μmol; 0.01 M in dry $CHCl_3$), (0.2 mL) were added. The vial was capped and heated at 140°C for 20 min in a microwave reactor. The resulting mixture was evaporated on silica gel (100 mg) and purified either by filtration through silica gel (washing with DCM) and further evaporation (55°C, 3 Torr) to remove the nitrile or by CombiFlash automatic column chromatography (EtOAc/cyclohexane, 0:100 to 10:90).

4-(4-Methoxyphenyl)-2-phenyl-1-(trifluoromethyl)-1*H*-imidazole (**89a**): Prepared



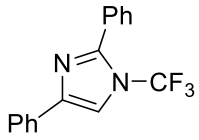
according to the **general procedure A**. Yield: 72%; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.70–7.65 (m, 2H), 7.53–7.43 (m, 4H), 6.99–6.91 (m, 2H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 147.0, 142.0, 130.2, 129.7, 129.3 (q, *J* = 1.5 Hz), 128.6, 126.9, 125.1, 118.4 (q, *J* = 265.1 Hz), 114.3, 111.4, 55.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.7 (s, 3F); HRMS (EI) *m/z* calcd for $C_{17}H_{13}F_3N_2O$ $[M]^+$: 318.0980, found 318.0981.

2-Phenyl-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-imidazole (**89b**): Prepared according

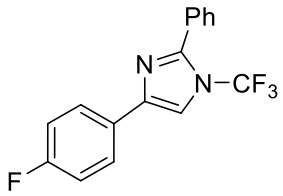


to the **general procedure A**. Yield: 84%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.72 (m, 2H), 7.72–7.67 (m, 2H), 7.54–7.52 (m, 1H), 7.51–7.44 (m, 3H), 7.25–7.21 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 142.2, 137.8, 130.0, 129.7, 129.5, 129.4, 129.2 (q, *J* = 1.5 Hz), 128.4, 125.3, 118.3 (q, *J* = 265.1 Hz), 111.9, 21.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.7 (s, 3F); HRMS (EI) *m/z* calcd for $C_{17}H_{13}F_3N_2$ $[M]^+$: 302.1031 , found 302.1032.

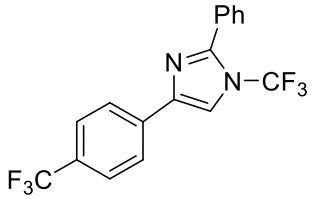
2,4-Diphenyl-1-(trifluoromethyl)-1*H*-imidazole (**89c**): Prepared according to the **general procedure A**. Yield: 57%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.85 (m, 1H), 7.85–7.83 (m, 1H), 7.71–7.67 (m, 2H), 7.57 (q, *J* = 0.9 Hz, 1H), 7.52–7.46 (m, 3H), 7.45–7.39 (m, 2H), 7.36–7.30 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 142.2, 132.4, 130.2, 129.7, 129.3 (q, *J* = 1.5 Hz), 128.9, 128.6, 128.1, 125.6, 118.4 (q, *J* = 265.1 Hz), 112.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.7 (s, 3F); HRMS (EI) *m/z* calcd for $C_{16}H_{11}F_3N_2$ $[M]^+$: 288.0874, found 288.0875.



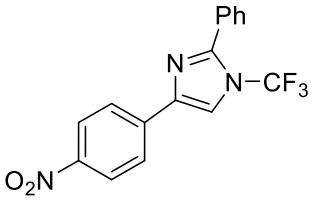
4-(4-Fluorophenyl)-2-phenyl-1-(trifluoromethyl)-1*H*-imidazole (**89d**): Prepared according to the **general procedure A**. Yield: 64%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.78 (m, 2H), 7.72–7.63 (m, 2H), 7.54–7.44 (m, 4H), 7.15–7.06 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8 (d, *J* = 246.9 Hz), 147.3, 141.4, 130.3, 129.6, 129.3 (q, *J* = 1.4 Hz), 128.7 (d, *J* = 3.2 Hz), 128.6, 127.3 (d, *J* =8.1 Hz), 118.3 (q, *J* = 265.5 Hz), 115.8 (d, *J* = 21.7 Hz), 112.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.7 (s, 3F), -114.5 (s, 1F); HRMS (EI) *m/z* calcd for $C_{16}H_{10}F_4N_2$ $[M]^+$: 306.0780, found 306.0778.



2-Phenyl-1-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-imidazole (**89e**): Prepared according to the **general procedure A**. Yield: 63%; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.93 (m, 2H), 7.74–7.63 (m, 5H), 7.55–7.45 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 140.8, 135.9 (q, *J* = 1.4 Hz), 130.4, 130.0 (q, *J* = 32.48 Hz), 129.4, 129.3 (q, *J* = 1.4), 128.7, 125.9, (q, *J* = 3.8 Hz), 125.7, (q, *J* = 272.07 Hz), 125.7, 118.3 (q, *J* = 265.7 Hz), 113.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.7 (s, 3F), -63.0 (s, 3F); HRMS (EI) *m/z* calcd for $C_{17}H_{10}F_6N_2$ $[M]^+$: 356.0748, found 356.0746.

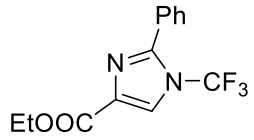


4-(4-Nitrophenyl)-2-phenyl-1-(trifluoromethyl)-1H-imidazole (**89f**): Prepared



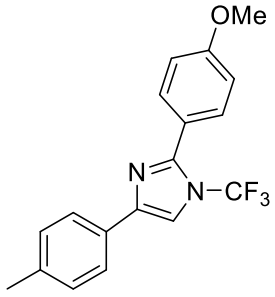
according to the **general procedure A**. Yield: 52%; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33–8.25 (m, 2H), 8.05–7.99 (m, 2H), 7.76–7.73 (m, 1H), 7.71–7.67 (m, 2H), 7.57–7.46 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0, 147.4, 140.0, 138.7, 130.6, 129.3 (q, *J* = 1.5 Hz), 129.1, 128.7, 126.0, 124.4, 118.2 (q, *J* = 266.2 Hz) 114.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.8 (s, 3F); HRMS (EI) *m/z* calcd for $C_{16}H_{10}F_3N_3O_2$ $[M]^+$: 333.0725, found 333.0726.

Ethyl 2-phenyl-1-(trifluoromethyl)-1*H*-imidazole-4-carboxylate (**89g**): Prepared



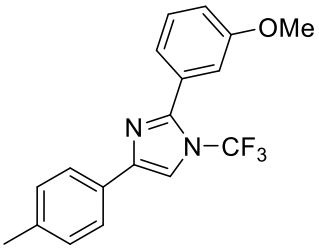
according to the **general procedure A**. Yield: 65%, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (q, *J* = 0.9 Hz, 1H), 7.67–7.59 (m, 2H), 7.55–7.41 (m, 3H), 4.42 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 147.6, 134.2, 130.7, 129.4 (q, *J* = 1.3 Hz), 128.6, 128.5, 122.9 (q, *J* = 1.2 Hz), 117.9 (q, *J* = 267.1 Hz), 61.4, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -53.1 (s, 3F); HRMS (EI) *m/z* calcd for $C_{13}H_{11}F_3N_2O_2$ $[M]^+$: 284.0773, found 284.0770.

2-(4-Methoxyphenyl)-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-imidazole (**89h**): Prepared

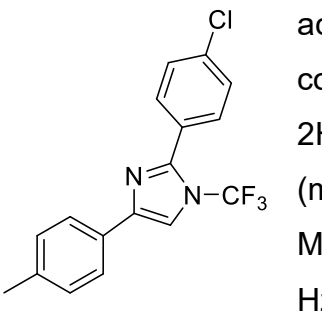


according to the **general procedure A**. Yield: 78%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.69 (m, 2H), 7.67–7.58 (m, 2H), 7.49 (q, *J* = 0.8 Hz, 1H), 7.24–7.20 (m, 2H), 7.05–6.94 (m, 2H), 3.87 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 147.0, 142.0, 137.8, 130.8 (q, *J* = 1.5 Hz), 129.7, 129.5, 125.4, 122.2, 118.4 (q, *J* = 264.9 Hz), 114.0, 111.8, 55.5, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.7 (s, 3F); HRMS (EI) *m/z* calcd for $C_{18}H_{15}F_3N_2O$ $[M]^+$: 332.1136, found 332.1134.

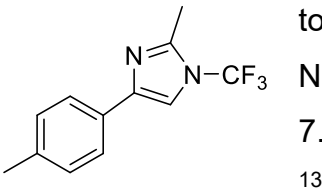
2-(3-Methoxyphenyl)-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-imidazole (**89i**): Prepared according to the **general procedure A**. Yield: 94%; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.70 (m, 2H), 7.51 (q, *J* = 0.9 Hz, 1H), 7.41–7.35 (m, 1H), 7.28–7.21 (m, 4H, *signal is overlapped with solvent*), 7.04 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 3.86 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 146.9, 142.2, 137.9, 130.9, 129.6 (3C), 125.4, 121.7 (q, *J* = 1.5 Hz), 118.4 (q, *J* = 265.2), 116.3, 114.6 (q, *J* = 1.2 Hz), 112.0 (q, *J* = 1.2 Hz), 55.5, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.6 (s, 3F); HRMS (EI) *m/z* calcd for $C_{18}H_{15}F_3N_2O$ $[M]^+$: 332.1136, found 332.1133.



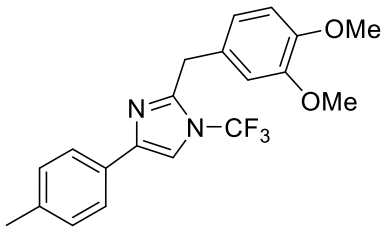
2-(4-Chlorophenyl)-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-imidazole (**89j**): Prepared according to the **general procedure A**. Yield: 82%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.68 (m, 2H), 7.67–7.59 (m, 2H), 7.52 (q, *J* = 0.9 Hz, 1H), 7.50–7.42 (m, 2H), 7.25–7.21 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 142.5, 138.1, 136.5, 130.7 (q, *J* = 1.4 Hz), 129.6, 129.4, 128.9, 128.2, 125.4, 118.3 (q, *J* = 265.1 Hz), 112.2, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.7 (s, 3F); HRMS (EI) *m/z* calcd for $C_{17}H_{12}ClF_3N_2$ $[M]^+$: 336.0641, found 336.0642.



2-Methyl-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-imidazole (**89k**): Prepared according to the **general procedure A**. Yield: 71%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.57 (m, 2H), 7.33 (s, 1H), 7.23–7.16 (m, 2H), 2.59 (q, *J* = 1.4 Hz, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 141.4, 137.7, 129.7, 129.5, 125.2, 118.5 (q, *J* = 263.8 Hz), 110.8, 21.4, 14.4 (q, *J* = 2.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -56.2 (s, 3F); HRMS (EI) *m/z* calcd for $C_{12}H_{11}F_3N_2$ $[M]^+$: 240.0874, found 240.0876.

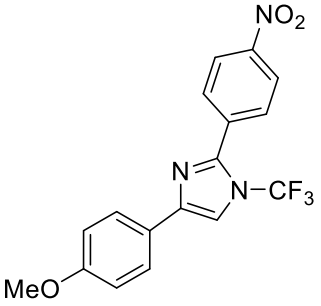


2-(3,4-Dimethoxybenzyl)-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-imidazole (**89l**):



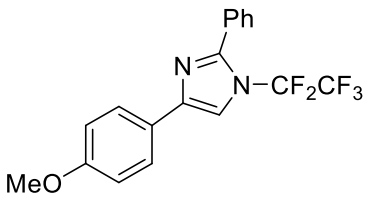
Prepared according to the **general procedure A**. Yield: 56%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.65 (m, 2H), 7.35 (d, *J* = 0.8 Hz, 1H), 7.23–7.19 (m, 2H), 6.86 (s, 1H), 6.79 (d, *J* = 1.0 Hz, 2H), 4.20 (d, *J* = 1.1 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.0, 148.1, 146.6, 141.7, 137.8, 129.8, 129.6, 129.5,128.5, 125.3, 120.9–120.5 (m), 118.4 (q, *J* = 264.6 Hz), 111.9 (m), 111.2 (m), 56.0 (q, *J* = 11.2 Hz), 34.5–33.8 (m), 21.4 (q, *J* = 7.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -55.1 (s, 3F); HRMS (EI) *m/z* calcd for $C_{20}H_{19}F_3N_2O_2$ $[M]^+$: 376.1399, found 376.1397.

4-(4-Methoxyphenyl)-2-(4-nitrophenyl)-1-(trifluoromethyl)-1*H*-imidazole (**89m**):



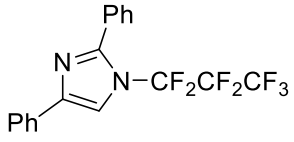
Prepared according to the **general procedure A**. Yield: 33%; purification by column chromatographny on C18 reverse-phase silica (H_2O/MeCN, 80:20 to 20:80); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37–8.32 (m, 2H), 7.95–7.88 (m, 2H), 7.81–7.73 (m, 2H), 7.53 (q, *J* = 0.9 Hz, 1H), 7.03–6.92 (m, 2H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 148.7, 144.4, 142.9, 135.7, 130.3, 126.9, 124.6, 123.8 (m), 118.3 (q, *J* = 265.6 Hz), 114.4 (m), 112.4, 55.5 (q, *J* = 10.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.4 (s, 3F); HRMS (EI) *m/z* calcd for $C_{17}H_{12}F_3N_3O_3$ $[M]^+$: 363.0831, found 363.0828.

4-(4-Methoxyphenyl)-1-(perfluoroethyl)-2-phenyl-1*H*-imidazole (**89n**): Prepared according to the **general procedure A**. Yield: 92%; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.73 (m, 2H), 7.62–7.54 (m, 2H), 7.52–7.41 (m, 3H), 7.39–7.35 (m, 1H), 7.01–6.90 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 148.2, 142.8, 130.5, 130.0 (2C), 128.2, 126.9, 125.0, 117.6 (qt, *J* = 288.0 Hz, *J* = 44.9 Hz), 114.3, 111.6, 110.6 (tq, *J* =

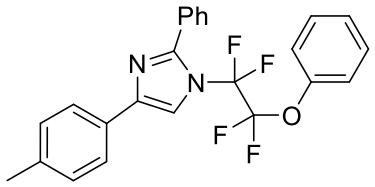


269.2 Hz, *J* = 44.9 Hz), 55.5; ^{19}FNMR (376 MHz, $CDCl_3$) δ -84.8 (s, 3F), -93.9 (s, 2F); HRMS (EI) *m/z* calcd for $C_{18}H_{13}F_5N_2O$ $[M]^+$: 368.0948, found 368.0954.

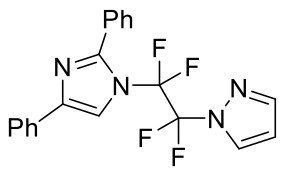
1-(Perfluoropropyl)-2,4-diphenyl-1*H*-imidazole (**89o**): Prepared according to the **general procedure A**. Yield: 71%,white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91–7.84 (m, 2H), 7.61–7.55 (m, 2H), 7.51–7.39 (m, 6H), 7.37–7.31 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 142.7, 132.2, 130.4, 130.1, 128.9, 122.2 (2C), 125.6, 117.4 (qtt, *J* = 287.7 Hz, *J* = 33.3 Hz, *J* = 2.1 Hz), 112.9, 112.4 (tt, *J* = 269.8 Hz, *J* = 32.1 Hz), 110.2–105.6 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.6 (t, *J* = 9.7 Hz, 3F), -89.8 (q, *J* = 9.7 Hz, 2F), -126.1 (s, 2F); HRMS (EI) *m/z* calcd for $C_{18}H_{11}F_7N_2$ $[M]^+$: 388.0810, found 388.0809.



2-Phenyl-1-(1,1,2,2-tetrafluoro-2-phenoxyethyl)-4-(*p*-tolyl)-1*H*-imidazole (**89p**): Prepared according to the **general procedure A**. Yield: 57%; brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.73 (m, 2H), 7.68–7.62 (m, 2H), 7.56 (s, 1H), 7.52–7.38 (m, 3H), 7.40–7.30 (m, 2H), 7.30–7.19 (m, 3H, *signal is overlapped with solvent*), 7.10–7.02 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 148.4, 142.3, 137.7, 131.2, 130.1, 129.9 (2C), 129.7, 129.5, 128.0, 127.0, 125.4, 121.5, 116.3 (tt, *J* = 277.3 Hz, *J* = 40.8 Hz), 113.2, 111.9 (tt, *J* = 268.8 Hz, *J* = 40.8 Hz), 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -86.3 (t, *J* = 4.2 Hz, 2F), -93.7 (t, *J* = 4.2 Hz, 2F); HRMS (EI) *m/z* calcd for $C_{24}H_{18}F_4N_2O$ $[M]^+$: 426.1355, found 426.1356.



1-(2-(2,4-Diphenyl-1*H*-imidazol-1-yl)-1,1,2,2-tetrafluoroethyl)-1*H*-pyrazole (**89q**): Prepared according to the **general procedure A**. Yield: 70%; red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.76 (m, 2H), 7.72 (qd, *J* = 1.5, 0.6 Hz, 1H), 7.64–7.58 (m, 1H), 7.54–7.35 (m, 7H), 7.35–7.26 (m, 1H), 7.25 (s, 1H, *signal is overlapped with the solvent*), 6.42 (dd, *J* = 2.7, 1.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3,

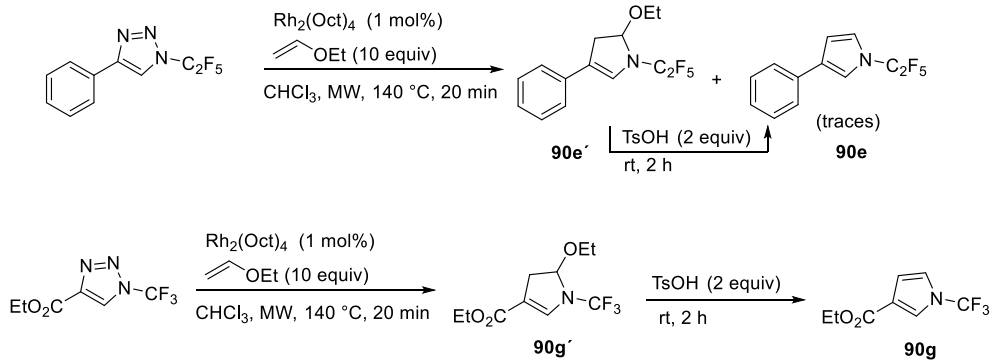


143.9, 142.4, 132.4, 130.5, 130.0, 129.8, 129.1, 128.8, 128.0 (2C), 125.5, 113.1, 112.6 (tt, *J* = 271.3 Hz, *J* = 42.1 Hz), 112.5 (tt, *J* = 269.2 Hz, *J* = 42.1 Hz), 108.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -92.1 (t, *J* = 4.7 Hz, 2F), -98.2 (t, *J* = 4.7 Hz, 2F); HRMS (EI) *m/z* calcd for $C_{20}H_{14}F_4N_4$ $[M]^+$: 386.1155, found 386.1156.

General procedure B for the synthesis of *N*-(per)fluoroalkyl pyrroles **90**

N-(per)fluoroalkyl-triazole (0.20 mmol) was dissolved in dry $CHCl_3$ (2 mL) in a 5 mL microwave tube. Vinyl ether (10 equiv., 2.0 mmol) and a solution of rhodium (II) octanoate (2 μmol; 0.01 M in dry $CHCl_3$), (0.2 mL) were added. The vial was capped and heated at 140°C for 20 min in a microwave reactor. The resulting mixture was evaporated on silica gel (100 mg) and purified by CombiFlash automatic column chromatography (cyclohexane). In the case of derivatives **90e** and **90g** the non-eliminated products were observed. For the preparation of the desired pyrroles a one-pot two-step procedure was used.

One-pot two-step procedure for the preparation of pyrroles **90e** and **90g**

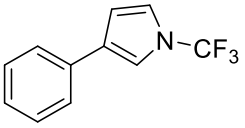


Scheme 100 One-pot two-step procedure for the synthesis of pyrroles **90e** and **90g**.

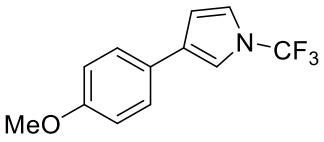
N-Perfluoroalkyl-triazole (0.20 mmol) was dissolved in dry $CHCl_3$ (2 mL) in a 5 mL microwave tube. Vinyl ether (10 equiv., 2.0 mmol) and a solution of rhodium (II) octanoate (2 μmol; 0.01 M in dry $CHCl_3$) were added. The vial was capped

and heated at 140°C for 20 min in microwave reactor. Then $TsOH \cdot H_2O$ (0.40 mmol; 76.1 mg) was added. The resulting suspension was stirred at 20 °C for 2 h, filtered, evaporated on silica gel (100 mg), and purified by CombiFlash automatic column chromatography (cyclohexane).

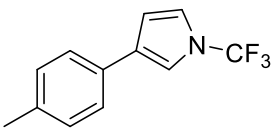
3-Phenyl-1-(trifluoromethyl)-1*H*-pyrrole (**90a**): Prepared according to the **general procedure B**. Yield: 96%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.48 (m, 2H), 7.41–7.34 (m, 2H), 7.30–7.21 (m, 2H), 7.03 (dd, *J* = 3.3, 2.3 Hz, 1H), 6.63 (ddq, *J* = 3.3, 1.6, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9, 128.9, 128.4, 127.0, 125.8, 119.5 (q, *J* = 260.1 Hz), 118.8, 113.9, 110.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.5 (s, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_8F_3N$ $[M]^+$: 211.0609, found 211.0611.



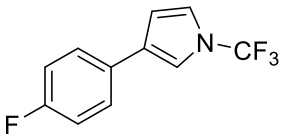
3-(4-Methoxyphenyl)-1-(trifluoromethyl)-1*H*-pyrrole (**90b**): Prepared according to the **general procedure B**. Yield: 93%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.40 (m, 2H), 7.16 (t, *J* = 2.0 Hz, 1H), 7.01 (dd, *J* = 3.3, 2.3 Hz, 1H), 6.96–6.88 (m, 2H), 6.57 (ddq, *J* = 3.2, 1.7, 0.7 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 128.1, 126.9, 126.7, 119.1 (q, *J* = 260.2 Hz), 118.7, 114.4, 113.1, 110.5, 55.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.5 (s, 3F); HRMS (EI) *m/z* calcd for $C_{12}H_{10}F_3NO$ $[M]^+$: 241.0714, found 241.0712.



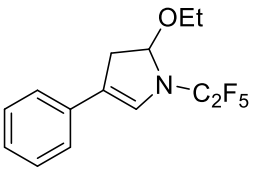
3-(*p*-Tolyl)-1-(trifluoromethyl)-1*H*-pyrrole (**90c**): Prepared according to the **general procedure B**. Yield: 82%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.39 (m, 2H), 7.25–7.16 (m, 3H), 7.02 (dd, *J* = 3.2, 2.3 Hz, 1H), 6.60 (ddq, *J* = 3.2, 1.5, 0.7 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.7, 131.1, 129.6, 128.4, 125.6, 119.1 (q, *J* = 260.2 Hz), 118.7, 113.5, 110.6, 21.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.5 (s, 3F); HRMS (EI) *m/z* calcd for $C_{12}H_{10}F_3N$ $[M]^+$: 225.0765, found 225.0762.



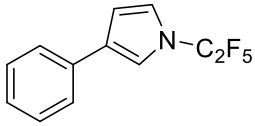
3-(4-Fluorophenyl)-1-(trifluoromethyl)-1*H*-pyrrole (**90d**): Prepared according to the **general procedure B**. Yield: 80%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.42 (m, 2H), 7.19 (t, *J* = 2.0 Hz, 1H), 7.10–7.04 (m, 2H), 7.03 (dd, *J* = 3.2, 2.3 Hz, 1H), 6.57 (ddq, *J* = 3.3, 1.5, 0.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (d, *J* = 245.7 Hz), 130.1 (d, *J* = 3.3 Hz), 127.5, 127.3 (d, *J* = 8.0 Hz), 119.2 (q, *J* = 260.8 Hz), 118.9, 115.8 (d, *J* = 21.6 Hz), 113.7, 110.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.5 (s, 3F), -116.2 (s, 1F); HRMS (EI) *m/z* calcd for $C_{11}H_7F_4N$ [M]$^+$: 229.0515, found 229.0514.



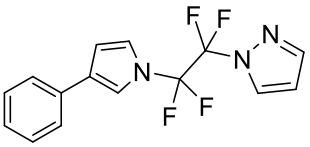
2-Ethoxy-1-(perfluoroethyl)-4-phenyl-2,3-dihydro-1*H*-pyrrole (**90e'**): not isolated; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.28 (m, 4H), 7.24–7.18 (m, 1H) ,6.56 (s, 1H), 5.45 (d, *J* = 7.6 Hz, 1H), 3.62 (dq, *J* = 9.2, 7.0 Hz, 1H), 3.52 (dq, *J* = 9.2, 7.0 Hz, 1H), 3.32–3.20 (m, 1H), 2.85 (m, 1H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.3 (s, 3F), -93.4 (d, *J* = 212.9 Hz, 1F), -95.8 (d, *J* = 212.9 Hz, 1F).



1-(Perfluoroethyl)-3-phenyl-1*H*-pyrrole (**90e**): Yield: 89%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.48 (m, 2H), 7.42–7.34 (m, 2H), 7.31–7.22 (m, 1H), 7.20 (tt, *J* = 1.7, 0.8 Hz, 1H), 7.02–6.95 (m, 1H), 6.67 (ddt, *J* = 3.4, 1.7, 0.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9, 129.0, 128.6, 127.0, 125.8, 119.3, 117.8 (qt, *J* = 287.6 Hz, *J* = 47.0 Hz), 114.4 110.9, 110.8 (tq, *J* = 263.8 Hz, *J* = 41.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.9 (s, 3F), -99.1 (s, 2F); HRMS (EI) *m/z* calcd for $C_{12}H_8F_5N$ [M]$^+$: 261.0577, found 261.0578.

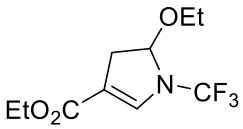


1-(1,1,2,2-Tetrafluoro-2-(3-phenyl-1*H*-pyrrol-1-yl)ethyl)-1*H*-pyrazole (**90f**): Prepared according to the **general procedure B**. Yield: 92%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (tq, *J* = 1.5, 0.7 Hz, 1H), 7.58–7.51 (m, 1H), 7.48–7.43 (m,



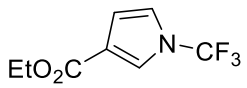
2H), 7.39–7.32 (m, 2H), 7.28–7.19 (m, 1H), 6.96 (ddt, *J* = 2.3, 1.6, 0.7 Hz, 1H), 6.77 (ddd, *J* = 3.3, 1.9, 0.6 Hz, 1H), 6.57 (ddt, *J* = 3.2, 1.8, 1.0 Hz, 1H), 6.41 (ddt, *J* = 2.8, 1.7, 0.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 134.0, 129.1, 128.9, 128.1, 126.8, 125.6, 119.3, 114.4, 112.8 (tt, *J* = 268.1 Hz, *J* = 40.9 Hz), 112.7 (tt, *J* = 269.2 Hz, *J* = 43.5 Hz), 110.3, 108.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -97.8 (t, *J* = 5.6 Hz, 2F), -100.1 (t, *J* = 5.6 Hz, 2F); HRMS (EI) *m/z* calcd for $C_{15}H_{11}F_4N_3$ $[M]^+$: 309.0889, found 309.0888.

Ethyl 5-ethoxy-1-(trifluoromethyl)-4,5-dihydro-1*H*-pyrrole-3-carboxylate (**90g'**):



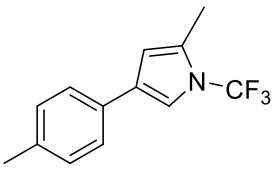
not isolated; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12–7.08 (m, 1H), 5.41 (ddq, *J* = 8.1, 2.3, 0.9 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.68–3.56 (m, 1H), 3.54–3.44 (m, 1H), 3.11–2.99 (m, 1H), 2.83–2.74 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (s, 3F).

Ethyl 1-(trifluoromethyl)-1*H*-pyrrole-3-carboxylate (**90g**): Yield: 92%; colorless oil;



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 2.3, 1.6 Hz, 1H), 6.96 (dd, *J* = 3.3, 2.3 Hz, 1H), 6.72 (ddq, *J* = 3.3, 1.7, 0.9 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 122.5, 120.2, 118.5, 118.5 (q, *J* = 262.6 Hz), 112.6, 60.6, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (s, 3F); HRMS (EI) *m/z* calcd for $C_8H_8F_3NO_2$ $[M]^+$: 207.0507, found 207.0506.

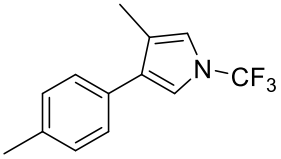
2-Methyl-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-pyrrole (**90h**): Prepared according to



the **general procedure B**. Yield: 63%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.33 (m, 2H), 7.17 (dddd, *J* = 7.6, 2.0, 1.2, 0.6 Hz, 2H), 7.13 (dt, *J* = 1.9, 0.6 Hz, 1H), 6.34–6.28 (m, 1H), 2.38 (dq, *J* = 2.0, 1.4 Hz, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.4, 131.3, 129.7, 129.6, 125.4, 119.5 (q, *J* = 261.0 Hz), 113.5 (q, *J* = 2.1 Hz), 110.4 (q, *J* = 1.6 Hz), 21.3, 12.7 (q, *J* = 2.4 Hz); ^{19}F NMR (376 MHz,

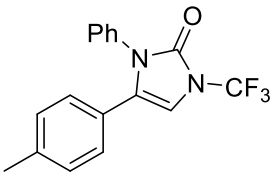
$CDCl_3$) δ -55.7 (s, 3F); HRMS (EI) *m/z* calcd for $C_{13}H_{12}F_3N$ $[M]^+$: 239.0922, found 239.0921.

3-Methyl-4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-pyrrole (**90i**): Prepared according to the **general procedure B**. Yield: 19%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.24–7.17 (m, 2H), 6.98 (d, *J* = 2.5 Hz, 1H), 6.84–6.78 (m, 1H), 2.38 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.6, 131.6, 129.4, 128.6, 128.0, 121.2, 119.1 (q, *J* = 259.5 Hz), 116.3, 115.2, 21.3, 11.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.6 (s, 3F); HRMS (EI) *m/z* calcd for $C_{13}H_{12}F_3N$ $[M]^+$: 239.0922, found 239.0924.



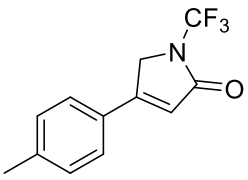
Synthesis of 3-phenyl-4-(*p*-tolyl)-1-(trifluoromethyl)-1,3-dihydro-2*H*-imidazol-2-one (**92**)

3-Phenyl-4-(*p*-tolyl)-1-(trifluoromethyl)-1,3-dihydro-2*H*-imidazol-2-one (**92**): 4-(*p*-Tolyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**114**) (0.20 mmol) was dissolved in dry $CHCl_3$ (2 mL) in a 5 mL microwave tube. Phenyl isocyanate (2 equiv., 0.4 mmol) and a solution of rhodium (II) octanoate (2 μmol; 0.01 M in dry $CHCl_3$) were added. The vial was capped and heated at 120°C for 20 min in a microwave reactor. The resulting mixture was evaporated on silica gel (100 mg) and purified by CombiFlash automatic column chromatography using the (EtOAc/cyclohexane). Yield: 75%; brown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.28 (m, 3H), 7.21–7.15 (m, 2H), 7.08–7.02 (m, 2H), 6.98–6.92 (m, 2H), 6.56 (s, 1H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.6, 138.9, 134.2, 129.5, 129.2, 128.0, 127.7, 127.4, 127.1, 125.0, 118.5 (q, *J* = 263.0 Hz), 103.3 (q, *J* = 1.4 Hz), 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.1 (s, 3F); HRMS (EI) *m/z* calcd for $C_{17}H_{13}F_3N_2O$ $[M]^+$: 318.0980, found 318.0979.



Synthesis of 4-(*p*-tolyl)-1-(trifluoromethyl)-1,5-dihydro-2*H*-pyrrol-2-one (**93**)

4-(*p*-Tolyl)-1-(trifluoromethyl)-1,5-dihydro-2H-pyrrol-2-one (**93**): 4-(*p*-Tolyl)-1-



(trifluoromethyl)-1*H*-1,2,3-triazole (**114**) (0.20 mmol) was dissolved in dry $CHCl_3$ (2 mL) in a 5 mL microwave tube. Ketene *t*-butyldimethylsilyl methyl acetal (2 equiv., 0.40 mmol) and a solution of rhodium (II) octanoate (2 μmol; 0.01 M in dry $CHCl_3$) were added. The vial was capped and heated at 120°C for 15 min in microwave reactor. Then 1M solution of TBAF (5 equiv., 1 mmol) in THF was added and resulting solution was stirred for 1 h, evaporated on silica gel (100 mg) and purified by CombiFlash automatic column chromatography (EtOAc/cyclohexane). Yield: 63%; slightly yellow crystals; ^{1}H NMR (400 MHz, CDCl3) δ 7.46–7.39 (m, 2H), 7.30–7.22 (m, 2H, *signal is overlapped with solvent*), 6.39–6.33 (m, 1H), 4.64–4.59 (m, 2H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 169.5, 157.2, 142.2, 130.0, 127.7, 126.1, 119.6 (q, *J* = 261.3 Hz), 118.0 (q, *J* = 2.0 Hz), 49.5, 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.7 (s, 3F); HRMS (EI) m/z calcd for C12H10F3NO [M]+: 241.0714, found 241.0711.

Competitive experiment of *N*-sulfonyl and *N*-fluoroalkyl triazoles in rhodium-catalyzed reaction with benzonitrile

4-(4-Fluorophenyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**95**) (0.1 mmol; 1 equiv.), 4-(4-Fluorophenyl)-1-tosyl-1*H*-1,2,3-triazole (**94**) (0.1 mmol; 1 equiv.) and benzonitrile (0.1 mmol; 1 equiv.) were dissolved in dry $CHCl_3$ (2 mL) and a solution of rhodium (II) octanoate (1 μmol; 0.01 M in dry $CHCl_3$) was added. The vial was capped and the mixture was heated at 140°C for 20 min in microwave reactor, followed by the measurement of ^{19}F {1H} NMR spectra.

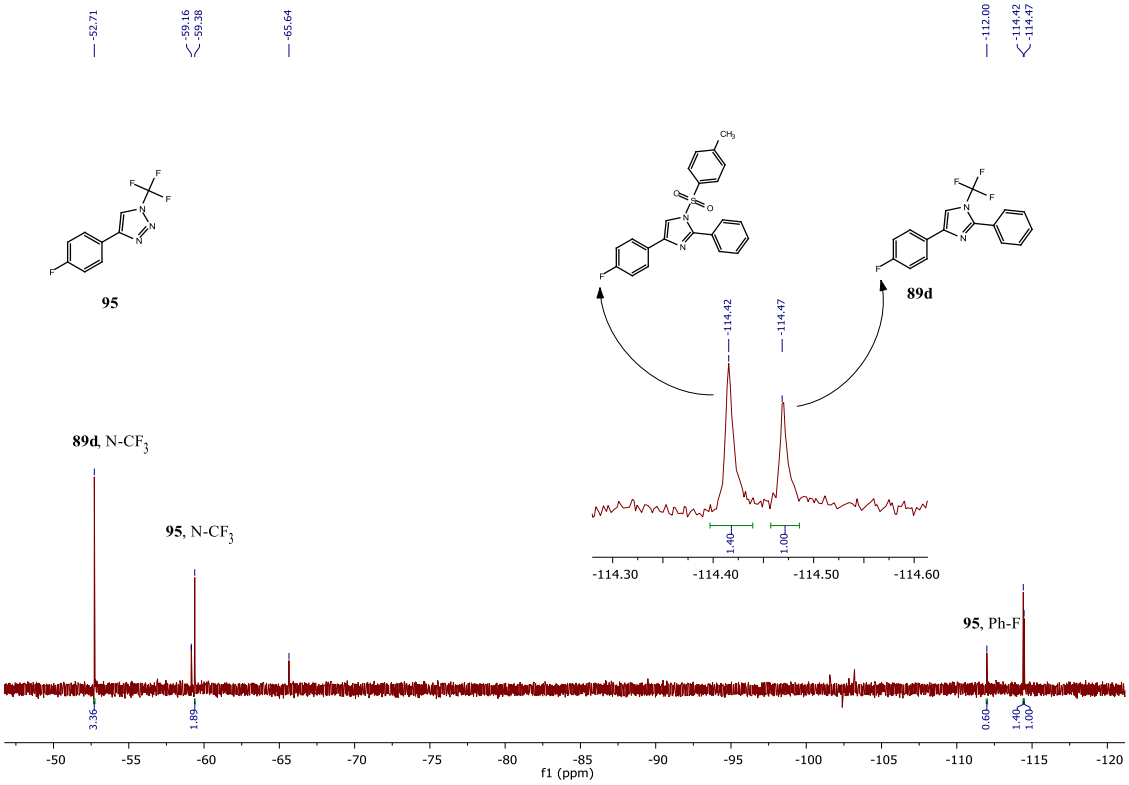
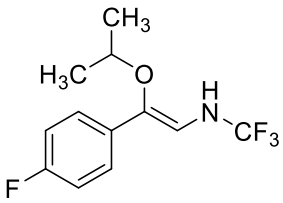


Figure 10 ^{19}F {^{1}H} NMR spectra (376 MHz, $CDCl_3$) - competition experiment between triazoles **94** and **95** in rhodium-catalyzed reaction with benzonitrile.

8.5. Rhodium-catalyzed reaction of *N*-fluoroalkyl-1,2,3-triazoles and external reagents containing polar X-H (X = N, O) bonds

Synthesis and characterization of enamine **101**

(*Z*)-2-(4-fluorophenyl)-2-isopropoxy-*N*-(trifluoromethyl)ethen-1-amine (**101**):

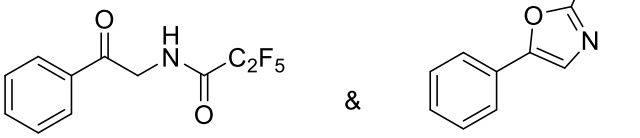


4-(4-fluorophenyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**95**) (0.20 mmol) was dissolved in dry $CDCl_3$ (2 mL) in a 5 mL microwave tube. Isopropyl alcohol (1.1 equiv., 0.22 mmol) and a solution of rhodium (II) octanoate (2 μmol; 0.01 M in dry $CHCl_3$) were added. The vial was capped and heated at 100°C for 40 min in microwave reactor. Then the standard ($PhCF_3$) was added to the reaction mixture and 600 μL of the solution was transferred into an NMR tube and ^{1}H and ^{19}F NMRs were measured. ^{19}F NMR yield >95%. Further work-up failed due to the instability of $NHCF_3$ group. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H),

7.07 – 6.99 (m, 2H), 5.95 (d, *J* = 11.0 Hz, 1H), 5.35 – 5.20 (m, 1H), 3.98 (hept, *J* = 6.1 Hz, 1H), 1.23 (d, *J* = 6.1 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -50.5 (d, *J* = 5.7 Hz, 3F), -107.5 (tt, *J* = 8.6, 5.4 Hz, 1F).

Synthesis and characterization of ketamide **103a** and oxazole **104a**

2,2,3,3,3-Pentafluoro-N-(2-oxo-2-phenylethyl)propenamide (**103a**) and 2-(Perfluoroethyl)-5-phenyloxazole (**104a**): 1-Perfluoroethyl-4-phenyl-1*H*-1,2,3-triazole **102** (0.1 mmol) was dissolved in $CDCl_3$ (2 mL) in a 5 mL microwave tube, followed by water (0.1 mmol) and $Rh_2(Oct)_4$ (2 μmol; 0.01 M in dry $CHCl_3$) addition. The vial was capped and heated at 140°C for 20 min in microwave reactor. The resulting mixture was evaporated on silica gel (100 mg) and purified by CombiFlash automatic column chromatography using the (EtOAc/cyclohexane) giving compounds **103a** and **104a**. **103a** Yield: 48%, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.96 (m, 2H), 7.70 – 7.65 (m, 1H), 7.60 (br s, 1H), 7.57 – 7.51 (m, 2H), 4.84 (dt, *J* = 4.3, 0.9 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.3 (t, *J* = 1.5 Hz, 3F), -123.3 (s, 2F). HRMS (ESI) *m/z* calcd for $C_{11}H_8NO_2F_5Na$ $[M+Na]^+$: 304.03674, found 304.03668. **104a** Yield: 44%, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.71 (m, 2H), 7.55 – 7.43 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.7 (t, *J* = 2.9 Hz), -108.2 (q, *J* = 2.9 Hz). HRMS (EI) *m/z* calcd for $C_{11}H_{16}F_5NO$ [M]+: 263.0370, found 263.0366.



103a **104a**

General procedure C for the synthesis of ketamides **103**

To a solution of *N*-fluoroalkyl-1,2,3-triazole (0.2 mmol) in dry chloroform (2 mL), water (10-30 equiv.) and a solution of $Rh_2(Oct)_4$ (2 μmol; 0.01 M in dry $CHCl_3$) in dry chloroform (0.2 mL) were added. The mixture was heated under microwave conditions (140 °C, 15 min, power 150 W), then evaporated with silica gel and

the crude product was purified by column chromatography (cyclohexane/EtOAc, 7:1 to 4:1) to give target ketamides **103**.

2,2,2-Trifluoro-*N*-(2-oxo-2-(*p*-tolyl)ethyl)acetamide (**103b**): Prepared according to the **general procedure C**. Yield 94%; pale brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.53 (bs, 1H), 7.37 – 7.29 (m, 2H), 4.79 (d, *J* = 4.2 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 157.3 (q, *J* = 37.8 Hz), 146.1, 131.3, 129.9, 128.3, 115.9 (q, *J* = 287.4 Hz), 46.2, 21.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.2 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{11}H_{10}F_3O_2NNa$ [M+Na]$^+$: 268.05558, found 268.05579.

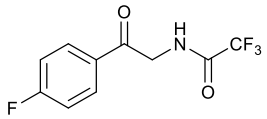
2,2,2-Trifluoro-*N*-(2-oxo-2-phenylethyl)acetamide (**103c**): Prepared according to the **general procedure C**. Yield 91%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.02 – 7.96 (m, 2H), 7.72 – 7.63 (m, 1H), 7.57 – 7.46 (m, 3H), 4.83 (dd, *J* = 4.3, 0.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 157.3 (q, *J* = 37.6 Hz), 134.9, 133.8, 129.3, 128.2, 115.8 (q, *J* = 287.6 Hz), 46.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.2 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{10}H_8F_3O_2NNa$ [M+Na]$^+$: 254.03993, found 254.04012.

2,2-Difluoro-2-(4-methoxyphenyl)-*N*-(2-oxo-2-(*p*-tolyl)ethyl)acetamide (**103d**): Prepared according to the **general procedure C**. Yield 65%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.95 – 7.86 (m, 2H), 7.74 – 7.67 (m, 1H), 7.37 – 7.30 (m, 2H), 7.24 – 7.17 (m, 2H), 6.99 – 6.83 (m, 2H), 4.82 (d, *J* = 4.4 Hz, 2H), 3.82 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 160.0 (t, *J* = 37.1 Hz), 158.0, 145.9, 142.7 (t, *J* = 2.1 Hz), 131.6, 129.9, 128.3, 123.4, 114.7 (t, *J* = 272.2 Hz), 114.7, 55.7, 46.3, 22.0; ^{19}F NMR (377 MHz, $CDCl_3$) δ -77.7 (s, 2F); HRMS (ESI) *m/z* calcd for $C_{18}H_{17}F_2O_4NNa$ [M+Na]$^+$: 372.10179, found 372.10214.

2,2,2-Trifluoro-*N*-(2-(4-methoxyphenyl)-2-oxoethyl)acetamide (**103e**): Prepared according to the **general procedure C**. Yield 71%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.99 – 7.92 (m, 2H),

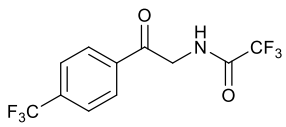
7.55 (br s, 1H), 7.04 – 6.95 (m, 2H), 4.76 (d, *J* = 4.2 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.4, 164.9, 157.3 (q, *J* = 37.8 Hz), 130.6, 126.8, 115.9 (q, *J* = 287.4 Hz), 114.5, 55.8, 46.0; ^{19}F NMR (377 Hz, $CDCl_3$) δ -76.2 (s, 3F); HRMS (APCI) *m/z* calcd for $C_{11}H_{11}F_3O_3N$ $[M+H]^+$: 262.06855, found 262.06864.

2,2,2-Trifluoro-*N*-(2-(4-fluorophenyl)-2-oxoethyl)acetamide (**103f**): Prepared



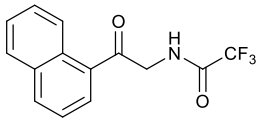
according to the **general procedure C**. Yield 90%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.97 (m, 2H), 7.50 (br s, 1H), 7.26 – 7.15 (m, 2H), 4.80 (d, *J* = 4.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 166.8 (d, *J* = 257.9 Hz), 157.4 (q, *J* = 38.0 Hz), 131.0 (d, *J* = 9.5 Hz), 130.3 (d, *J* = 2.9 Hz), 116.6 (d, *J* = 22.0 Hz), 115.8 (q, *J* = 287.3 Hz), 46.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (s, 3F), -101.4 – -102.1 (m, 1F); HRMS (ESI) *m/z* calcd for $C_{10}H_7F_4NO_2Na$ $[M+Na]^+$: 272.03051, found 272.03072.

2,2,2-Trifluoro-*N*-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)acetamide (**103g**):



Prepared according to the **general procedure C**. Yield 87%, white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.17 – 8.03 (m, 2H), 7.85 – 7.77 (m, 2H), 7.42 (br s, 1H), 4.86 (d, *J* = 4.3 Hz, 2H); ^{13}C NMR (101 MHz $CDCl_3$) δ 191.4, 157.4 (q, *J* = 37.8 Hz), 136.4 (q, *J* = 1.3 Hz), 136.2 (q, *J* = 32.9 Hz), 128.6, 126.4 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 273.3 Hz), 115.8 (q, *J* = 287.6 Hz), 46.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.9 (s, 3F), -76.2 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{11}H_8F_6NO_2$ $[M+H]^+$: 300.04537, found 300.04635.

2,2,2-Trifluoro-*N*-(2-(naphthalen-1-yl)-2-oxoethyl)acetamide (**103h**): Prepared



according to the **general procedure C**. Yield 82%; pale brown solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.87 (dq, *J* = 8.7, 1.0 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.2 Hz, 1H), 8.00 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.92 (ddt, *J* = 8.2, 1.5, 0.7 Hz, 1H), 7.71 – 7.64 (m, 1H), 7 7.63 – 7.55 (m, 2H), 7.54 (dd, *J* = 8.3, 7.3 Hz, 1H), 4.88 (dd, *J* = 4.4, 0.7 Hz, 2H); ^{13}C NMR (101 MHz,

$CDCl_3$) δ 194.8, 157.3 (q, *J* = 37.8 Hz), 135.3, 134.2, 130.9, 130.5, 129.3, 129.2, 128.9, 127.2, 125.6, 124.5, 115.9 (q, *J* = 287.5 Hz), 47.8; ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.2 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{14}H_{10}F_3NO_2Na$ $[M+Na]^+$: 304.05558, found 304.05570.

General procedure D for the synthesis of oxazoles **104** by the direct method of transannulation with water

To a solution of *N*-fluoroalkyl-1,2,3-triazole (0.15 mmol) in dry chloroform (2.5 mL) water (5.4 µl, 0.30 mmol, 2 equiv.) and a solution of $Rh_2(Oct)_4$ (1.5 µmol; 0.01 M in dry $CHCl_3$), (0.15 mL) were added. The mixture was heated under microwave conditions (140 °C, 15 min, power 150 W), then evaporated with silica gel under reduced pressure (300-400 Torr). The crude product was purified by column chromatography (pentane/DCM, 5:1 to 1:1) with subsequent evaporation at 300-400 Torr to give target oxazoles **104**.

General procedure E for the synthesis of oxazoles **104** by the one-pot two step method with dehydration of ketamide

To a solution of *N*-fluoroalkyl-1,2,3-triazole (0.2 mmol) in dry chloroform (2 mL) water (5-30 equiv.) and a solution of $Rh_2(Oct)_4$ (2 µmol; 0.01 M in dry $CHCl_3$), (0.2 mL) was added. The mixture was heated under microwave conditions (140 °C, 15 min, power 150 W) then dried by excess of anhydrous $MgSO_4$ to remove unreacted water. Triphenylphosphine (105 mg, 0.4 mmol, 2 equiv.) and iodine (102 mg, 0.4 mmol, 2 equiv.) were dissolved in dry chloroform (1 mL) and the resulting suspension was stirred for 5 min. Triethylamine (81 mg, 0.8 mmol, 4 equiv.) was added with vigorous stirring to the mixture containing ketamide, followed by slow addition of PPh_3/I_2 mixture. The resulting mixture was heated at 40 °C for 4-16 h (monitored by TLC or ^{19}F NMR), then evaporated with silica gel under reduced pressure (300-400 Torr). The crude product was purified by column chromatography (pentane/DCM, 5:1 to 1:1) with subsequent evaporation at 300-400 Torr to give target oxazoles **104**.

5-(*p*-Tolyl)-2-(trifluoromethyl)oxazole (**104b**): Prepared according to the **general procedure D**. Yield: 50%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 2H), 7.40 (s, 1H), 7.31 – 7.25 (m, 2H, *signal is overlapped with the solvent*), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3, 149.6 (q, *J* = 43.9 Hz), 140.4, 130.0, 125.0, 123.7, 121.9, 116.7 (q, *J* = 270.3 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.1 (s, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_8F_3NO$ $[M]^+$: 227.0558, found 227.0559.

5-Phenyl-2-(trifluoromethyl)oxazole (**104c**): Prepared according to the **general procedures D** and **E**. (10 equiv. of water was used for the first step). Yield by direct method (general procedure C): 52%. Yield by one-pot two step method (general procedure D): 47%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.72 – 7.68 (m, 2H), 7.51 – 7.39 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 150.0 (q, *J* = 44.0 Hz), 130.1, 129.3, 126.4, 125.1, 122.5 (q, *J* = 2.6 Hz), 116.7 (q, *J* = 270.7 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -66.2 (s, 3F); HRMS (CI) *m/z* calcd for $C_{10}H_7F_3NO$ $[M+H]^+$: 214.0480, found 214.0482.

5-(4-Methoxyphenyl)-2-(trifluoromethyl)oxazol (**104d**): Prepared according to the **general procedure D**. Yield: 67%; yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.58 (m, 2H), 7.32 (s, 1H), 7.02 – 6.94 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 154.2, 149.3 (q, *J* = 43.9 Hz), 126.7, 121.0, 119.1, 116.8 (q, *J* = 270.2 Hz), 114.8, 55.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.1 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{11}H_9F_3NO_2$ $[M+H]^+$: 244.05799, found 244.05821.

5-(Thiophen-3-yl)-2-(trifluoromethyl)oxazole (**104e**): Prepared according to the **general procedure D**. Yield: 42%; yellowish oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 2.8, 1.1 Hz, 1H), 7.44 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.35 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.30 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.7, 149.3 (q, *J* = 44.0 Hz), 127.7, 127.5, 124.7, 123.3, 122.1, 116.7 (q, *J* = 270.1 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -66.1 (s, 3F); HRMS (EI) *m/z* calcd for $C_8H_4F_3NOS$ $[M]^+$: 218.9966, found 218.9968.

2-(Difluoro(4-methoxyphenoxy)methyl)-5-(*p*-tolyl)oxazole (**104f**): Prepared according to the **general procedure D**. Yield: 64%; pale yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 2H), 7.36 (s, 1H), 7.31 – 7.20 (m, 4H), 6.97 – 6.83 (m, 2H), 3.80 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 153.6, 152.5 (t, *J* = 43.1 Hz), 143.0 (t, *J* = 2.0 Hz), 139.8, 129.9, 124.9, 124.1, 123.4, 121.7, 115.5 (t, *J* = 258.5 Hz), 114.6, 55.7, 21.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -67.9 (s, 2F); HRMS (ESI) *m/z* calcd for $C_{18}H_{16}F_2NO_3$ $[M+H]^+$: 332.10928, found 332.10939.

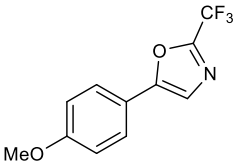
2-(Trifluoromethyl)-5-(4-(trifluoromethyl)phenyl)oxazole (**104g**): Prepared according to the **general procedure E**. (30 equiv. of water was used in the first step). Yield: 56%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 2H), 7.77 – 7.71 (m, 2H), 7.57 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.6, 150.7 (q, *J* = 44.0 Hz), 131.8 (q, *J* = 33.0 Hz), 129.6 (q, *J* = 1.3 Hz), 126.4 (q, *J* = 4.0 Hz), 125.3, 124.1, 123.8 (q, *J* = 272.3 Hz), 116.5 (q, *J* = 270.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ ^{19}F NMR (377 MHz, Methanol-d_4) δ -61.3 – -62.4 (m, 3F), -62.6 (s, 3F) ; HRMS (EI) *m/z* calcd for $C_{11}H_5F_6NO$ $[M]^+$: 281.0275, found 281.0276.

5-(Naphthalen-1-yl)-2-(trifluoromethyl)oxazole (**104h**): Prepared according to the **general procedure E**. (5 equiv. of water was used in the first step). Yield: 49%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.3 Hz, 1H), 7.99–7.92 (m, 3H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.66–7.52 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 150.4 (q, *J* = 43.8 Hz), 133.9, 131.1, 130.2, 129.1, 127.8, 127.6, 126.7, 126.0, 125.3, 124.4, 123.6, 116.8 (q, *J* = 270.3 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -66.1 (s, 3F); HRMS (CI) *m/z* calcd for $C_{14}H_9F_3NO$ $[M+H]^+$: 264.0631, found 264.0635.

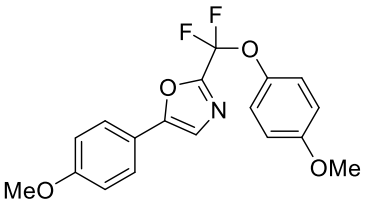
8.6. Sulfonic acid-mediated transformations of *N*-fluoroalkyl-1,2,3-triazoles

Preparation of oxazoles **104** by triflic acid-mediated transformation of *N*-fluoroalkyl-1,2,3-triazoles

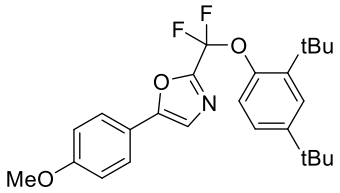
5-(4-Methoxyphenyl)-2-(trifluoromethyl)oxazole (**104d**): Starting 4-(4-methoxyphenyl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (0.1 mmol) was dissolved in DCE (1 mL) and cooled to -20 °C. Triflic acid (9.6 μL; 0.11 mmol) was added and reaction mixture was stirred for 16 h at 25 °C. The reaction mixture was evaporated on silica gel (cca 200 mg) and column chromatography was performed (cyclohexane/EtOAc). Yield: 53%; colorless oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.65–7.60 (m, 2H), 7.32 (s, 1H), 7.01–6.95 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 154.2, 149.3 (q, *J* = 43.9 Hz), 126.7, 121.0, 119.1, 116.8 (q, *J* = 270.2 Hz), 114.8, 55.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.1 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{11}H_9F_3NO_2$ $[M+H]^+$: 244.05799, found 244.05821.



2-(Difluoro(4-methoxyphenoxy)methyl)-5-(4-methoxyphenyl)oxazole (**104i**): The starting 4-(4-methoxyphenyl)-1-(1,1,2,2-tetrafluoro-2-(4-methoxyphenoxy)ethyl)-1*H*-1,2,3-triazole (0.1 mmol) was dissolved in DCE (1 mL). Triflic acid (9.6 μL; 0.11 mmol) was added and the reaction mixture was stirred for 10 h at 25 °C. The reaction mixture was evaporated on silica gel (cca 200 mg) and column chromatography was performed (cyclohexane/EtOAc). Yield: 78%; white-yellow solid. ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.67–7.61 (m, 2H), 7.29 (s, 1H), 7.25–7.20 (m, 2H), 7.00–6.95 (m, 2H), 6.91–6.85 (m, 2H), 3.85 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 157.9, 153.4, 152.3 (t, *J* = 43.1 Hz), 143.0 (t, *J* = 2.0 Hz), 126.5, 123.4, 120.9 (2C), 119.6, 115.5 (t, *J* = 258.4 Hz), 114.6, 55.7 (q, *J* = 6.6 Hz), 55.5 (q, *J* = 7.0 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -67.9 (s, 2F); HRMS (ESI) *m/z* calcd for $C_{18}H_{15}F_2NO_4Na$ $[M+Na]^+$: 370.08614, found 370.08586.

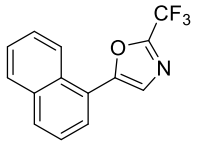


2-((2,4-Di-*tert*-butylphenoxy)difluoromethyl)-5-(4-methoxyphenyl)oxazole (**104j**):



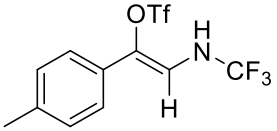
Starting 1-(2-(2,4-di-*tert*-butylphenoxy)-1,1,2,2-tetrafluoroethyl)-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole (0.1 mmol) was dissolved in DCE (1 mL). Triflic acid (9.6 μL; 0.11 mmol) was added and the reaction mixture was stirred for 10 h at 25 °C. The reaction mixture was evaporated on silica gel (cca 200 mg) and column chromatography was performed (cyclohexane/EtOAc). Yield: 81%; white-yellow solid. ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.63–7.59 (m, 2H), 7.42 (d, *J* = 2.6 Hz, 1H), 7.35 (dt, *J* = 8.7, 1.7 Hz, 1H), 7.32 (s, 1H), 7.20 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.01–6.95 (m, 2H), 3.86 (s, 3H), 1.46 (s, 9H), 1.32 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 153.3, 152.5 (t, *J* = 43.8 Hz), 147.7, 147.1, 139.8, 126.5, 124.7, 123.9, 121.0, 119.8, 119.2, 115.8 (t, *J* = 260.2 Hz), 114.7, 55.6, 35.2, 34.7, 31.6, 30.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -64.9 (s, 2F); HRMS (ESI) *m/z* calcd for $C_{25}H_{29}F_2NO_3Na$ $[M+Na]^+$: 452.20077, found 452.20019.

5-(Naphthalen-1-yl)-2-(trifluoromethyl)oxazole (**104h**): A solution of



trifluoromethanesulfonic acid (21 μL; 0.24 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 4-(naphthalen-1-yl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (62.6 mg; 0.2 mmol) in DCE (2 mL). The reaction mixture was stirred for 12 h at 50 °C. The reaction mixture was evaporated on silica gel (cca 300 mg) and column chromatography was performed (cyclohexane/EtOAc). Yield: 62%; pale red oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.3 Hz, 1H), 7.99–7.92 (m, 3H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.66–7.52 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 150.4 (q, *J* = 43.8 Hz), 133.9, 131.1, 130.2, 129.1, 127.8, 127.6, 126.7, 126.0, 125.3, 124.4, 123.6, 116.8 (q, *J* = 270.3 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -66.1 (s, 3F); HRMS (CI) *m/z* calcd for $C_{14}H_9F_3NO$ $[M+H]^+$: 264.0631, found 264.0635.

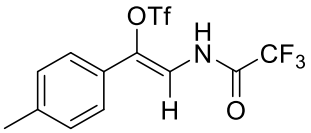
Synthesis and characterization of (*Z*)-1-(*p*-tolyl)-2-((trifluoromethyl)amino)vinyl trifluoromethanesulfonate (**115**)

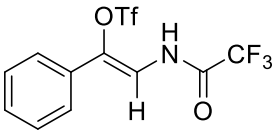
(*Z*)-1-(*p*-Tolyl)-2-((trifluoromethyl)amino)vinyl trifluoromethanesulfonate (**115**): A 

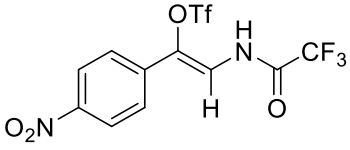
solution of trifluoromethanesulfonic acid (10.6 μL; 0.12 mmol) in DCE (0.5 mL) was added dropwise to a screw-cap glass tube containing a solution of triazole 4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**114**) (22.7 mg; 0.1 mmol) in DCE (1.5 mL). During the addition a suspension was formed. The reaction mixture was stirred for 16 h at 25 °C. $PhCF_3$ was added as a standard and ^{19}F NMR was measured. NMR yield: 98%. Stereochemistry was proved by NOE experiment. The reaction for characterization was performed in $CDCl_3$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.29–7.25 (m, 2H, *signal overlap the with solvent*), 7.22–7.17 (m, 2H), 6.44 (d, *J* = 11.2 Hz, 1H), 5.70–5.33 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.5, 132.3, 129.8, 128.6, 124.9, 120.9 (q, *J* = 257.1 Hz), 118.5 (q, *J* = 320.6 Hz), 115.7 (q, *J* = 2.2 Hz), 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.6 (d, *J* = 4.0 Hz, 3F), -74.2 (s, 3F); HRMS (CI) *m/z* calcd for $C_{11}H_{10}F_6NO_3S$ $[M+H]^+$: 349.0207, found 349.0204.

General procedure F for the synthesis of vinyl triflates **117**

A solution of trifluoromethanesulfonic acid (19.3 μL; 0.22 mmol) in DCE (1 mL) was added dropwise to screw-cap glass tube containing solution of triazole (0.2 mmol) in DCE (3 mL). During the addition a suspension was formed. The reaction mixture was stirred for 15 min - 18 h at 25-60 °C. Conversion to the product was monitored by LC-MS analysis or ^{19}F NMR spectroscopy. After full conversion, the reaction mixture was evaporated on silica gel (400 mg, 40 °C, 1 h) and purified by CombiFlash automatic or manual column chromatography (EtOAc/cyclohexane, 0:100 to 10:90 or DCM/cyclohexane).

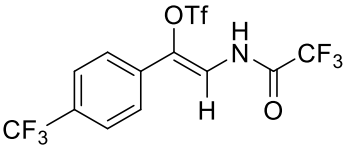
(*Z*)-1-(*p*-Tolyl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117a**):  Prepared according to the **general procedure F** using (21.1 μL; 0.24 mmol) of trifluoromethanesulfonic acid with stirring at 40 °C for 2 h. Yield: 88%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.25 (d, *J* = 9.9 Hz, 1H), 7.39–7.34 (m, 2H), 7.30–7.22 (m, 3H, *signal overlap the with solvent*), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4 (q, *J* = 39.2 Hz), 141.0, 137.0, 130.0, 127.6, 125.3, 118.5 (q, *J* = 320.3 Hz), 115.4 (q, *J* = 287.2 Hz), 111.8, 21.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -73.9 (s, 3F), -76.3 (s, 3F); HRMS (EI) *m/z* calcd for $C_{12}H_9F_6NO_4S$ [M]$^+$: 377.0156, found 377.0157.

(*Z*)-1-Phenyl-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117b**):  Prepared according to the **general procedure F** with stirring at 40 °C for 4 h. Yield: 69%. Scale-up reaction: 1-(Perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole (2.236 g; 8.5 mmol) was dissolved in DCE (85 mL) and trifluoromethanesulfonic acid (1.4 g; 9.35 mmol) was added dropwise. The reaction mixture was stirred for 12 h in an open flask at 25 °C. The reaction mixture was evaporated on silica gel and column chromatography was performed (cyclohexane/EtOAc). Final solid compound was recrystallized from pentane. Yield 74%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.28 (d, *J* = 9.4 Hz, 1H), 7.57–7.40 (m, 5H), 7.32 (d, *J* = 10.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5 (q, *J* = 39.4 Hz), 136.7, 130.5 (2C), 129.3, 125.3, 118.5 (q, *J* = 320.4 Hz), 115.4 (q, *J* = 287.2 Hz), 112.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.9 (s, 3F), -76.3 (s, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_7F_6NO_4S$ [M]$^+$: 363.0000, found 362.9999.

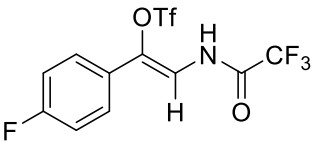
(*Z*)-1-(4-Nitrophenyl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117c**):  Prepared according to the **general procedure F** with stirring at 50 °C for 16 h followed by the addition of trifluoromethanesulfonic acid (0.1 mmol; 8.8 μL) and heating for the next 2 h at 50 °C. Yield: 51%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.40 (d, *J* = 10.3 Hz, 1H), 8.35–8.27 (m, 2H), 7.75–7.60 (m, 2H), 7.53

(d, *J* = 10.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6 (q, *J* = 39.8 Hz), 148.6, 136.6, 133.8, 125.7, 124.7, 118.5 (q, *J* = 320.6 Hz), 115.9, 115.2 (q, *J* = 287.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.5 (s, 3F), -76.2 (s, 3F); HRMS (ESI^-) *m/z* calcd for $C_{11}H_5F_6N_2O_6S$ $[M-H]^-$: 406.97780, found 406.97699.

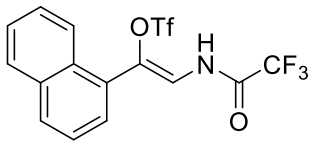
(*Z*)-2-(2,2,2-Trifluoroacetamido)-1-(4-(trifluoromethyl)phenyl)vinyl trifluoromethanesulfonate (**117d**): Prepared according to the **general procedure F** with stirring at 50 °C for 4 h. Yield: 70%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.34 (d, *J* = 10.1 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6 (q, *J* = 39.6 Hz), 134.8, 134.0 (q, *J* = 1.5 Hz), 132.2 (q, *J* = 33.0 Hz), 126.4 (q, *J* = 3.9 Hz), 125.4, 123.7 (q, *J* = 272.4 Hz), 118.5 (q, *J* = 320.4 Hz), 115.3 (q, *J* = 287.1 Hz), 114.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.5 (s, 3F), -73.6 (s, 3F), -76.2 (s, 3F); HRMS (EI) *m/z* calcd for $C_{12}H_6F_9NO_4S$ $[M]^+$: 430.9874, found 430.9877.



(*Z*)-1-(4-Fluorophenyl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117e**): Prepared according to **general procedure F** with stirring at 40 °C for 4 h. Yield: 79%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.8 Hz, 1H), 7.54–7.41 (m, 2H), 7.25 (d, *J* = 10.7 Hz, 1H, *signal overlap the with solvent*), 7.18–7.08 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9 (d, *J* = 252.0 Hz), 154.5 (q, *J* = 39.4 Hz), 135.7, 127.6 (d, *J* = 8.8 Hz), 126.7 (d, *J* = 3.7 Hz), 118.5 (q, *J* = 320.4 Hz), 116.6 (d, *J* = 22.4 Hz), 115.4 (q, *J* = 287.2 Hz), 112.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -73.9 (s, 3F), -76.3 (s, 3F), -109.1 – -110.0 (m, 1F); HRMS (EI) *m/z* calcd for $C_{11}H_6F_7NO_4S$ $[M]^+$: 380.9906, found 380.9903.

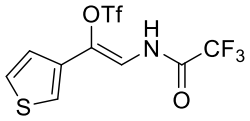


(*Z*)-1-(Naphthalen-1-yl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117f**): A solution of trifluoromethanesulfonic acid (21 μL; 0.24 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube

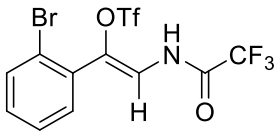


containing solution of 4-(naphthalen-1-yl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**75**) (62.6 mg; 0.2 mmol) in DCE (2 mL). The reaction mixture was stirred for 30 min at 50 °C. $PhCF_3$ was added as a standard and ^{19}F NMR was measured. The reaction for characterization was performed in $CDCl_3$. NMR yield: 86%. ^1H NMR (401 MHz, $CDCl_3$) δ 8.27 (d, *J* = 10.5 Hz, 1H), 8.02–7.97 (m, 2H), 7.94–7.90 (m, 1H), 7.66–7.53 (m, 3H), 7.51 (dd, *J* = 8.3, 7.1 Hz, 1H), 7.23 (d, *J* = 10.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5 (q, *J* = 39.4 Hz), 136.5, 133.7, 132.0, 131.2, 129.4, 129.0, 127.8, 127.3, 126.9, 125.2, 124.4, 118.2 (q, *J* = 320.7 Hz), 115.4 (q, *J* = 287.3 Hz), 116.2; ^{19}F NMR (377 MHz, $CDCl_3$) δ -74.4 (s, 3F), -76.2 (s, 3F).

(*Z*)-1-(Thiophen-3-yl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117g**): A solution of trifluoromethanesulfonic acid (21 μL; 0.24 mmol) in DCE (1 mL) was dropwise added to screw-cap glass tube containing a solution of 1-(perfluoroethyl)-4-(thiophen-3-yl)-1*H*-1,2,3-triazole **76** (53.8 mg; 0.2 mmol) in DCE (2 mL). The reaction mixture was stirred for 15 min at 55 °C. The reaction mixture was evaporated and a mixture of (*Z*/*E* = 8:1) isomers was obtained in 84% yield. Finally manual column chromatography on silica gel (cyclohexane/DCM, 80:20) was performed to give pure (*Z*)-isomer in 70% yield; white solid; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 10.2 Hz, 1H), 7.48 (dd, *J* = 3.1, 1.3 Hz, 1H), 7.45–7.38 (m, 1H), 7.28 (d, *J* = 10.8 Hz, 1H), 7.18 (dd, *J* = 5.1, 1.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4 (q, *J* = 39.4 Hz), 132.9, 131.7, 128.1, 124.0, 124.0, 118.5 (q, *J* = 320.2 Hz), 115.4 (q, *J* = 287.2 Hz), 111.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ -73.9 (s, 3F), -76.3 (s, 3F); HRMS (CI) *m/z* calcd for $C_9H_6F_6NO_4S_2$ $[M+H]^+$: 369.9637, found 369.9640.

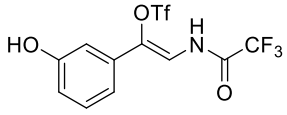


(*Z*)-1-(2-Bromophenyl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117h**): Prepared according to the **general procedure F** with stirring at 40 °C for 4 h. Yield: 69%; white solid; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 10.1 Hz, 1H), 7.69–7.65 (m, 1H), 7.48–7.31 (m, 3H), 7.16 (d, *J* = 10.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5 (q, *J* = 39.6 Hz), 135.2, 133.8, 132.4 (d,

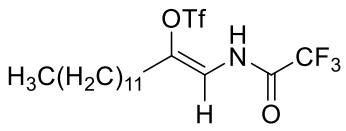


J = 2.2 Hz), 131.2, 127.9, 127.9, 123.6, 118.3 (q, *J* = 320.7 Hz), 116.9, 115.3 (q, *J* = 287.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.3 (s, 3F), -76.2.(s, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_6BrF_6NO_4S$ $[M]^+$: 440.9105, found 440.9106.

(*Z*)-1-(3-Hydroxyphenyl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117i**): Prepared according to the **general procedure F** with stirring at 50 °C for 2 h. Yield: 86%, colorless crystalline solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.27 (d, *J* = 12.5 Hz, 1H), 7.33–7.28 (m, 2H), 7.05 (d, *J* = 8.5 Hz, 1H), 6.96–6.93 (m, 1H), 6.90 (dd, *J* = 7.9, 2.2 Hz, 1H), 5.05 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 154.6 (q, *J* = 39.5 Hz), 136.3, 132.0, 130.7, 117.8, 118.5 (q, *J* = 320.4 Hz), 117.7, 115.4 (q, *J* = 287.3 Hz), 112.8, 112.1; ^{19}F NMR (377 MHz, $CDCl_3$) δ -73.8 (s, 3F), -76.3 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{11}H_7O_5NF_6NaS$ $[M+Na]^+$: 401.98413, found 401.98396.

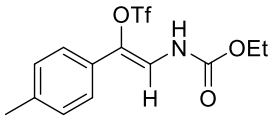


(*Z*)-1-(2,2,2-Trifluoroacetamido)tetradec-1-en-2-yl trifluoromethanesulfonate (**117j**): Prepared according to the **general procedure F** with stirring at 50 °C for 16 h. Yield: 22%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 10.5 Hz, 1H), 6.75 (d, *J* = 10.5 Hz, 1H), 2.50–2.38 (m, 2H), 1.55 (p, *J* = 7.6 Hz, 2H), 1.37–1.24 (m, 18H), 0.93–0.78 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2 (q, *J* = 39.1 Hz), 139.7, 118.5 (q, *J* = 320.6 Hz), 115.4 (q, *J* = 287.1 Hz), 112.2, 32.1, 31.8, 29.8, 29.7, 29.5 (2C), 29.3, 28.8, 26.1, 22.8, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.6 (s, 3F), -76.4 (s, 3F); HRMS (ESI^-) *m/z* calcd for $C_{17}H_{26}F_6NO_4S$ $[M-H]^-$: 454.14922, found 454.14854.



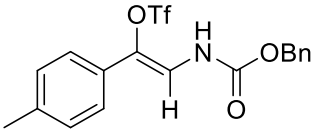
Synthesis and characterization of vinyl triflates with carbamoyl group **119**

(*Z*)-2-((Ethoxycarbonyl)amino)-1-(*p*-tolyl)vinyl trifluoromethanesulfonate (**119a**): A solution of trifluoromethanesulfonic acid (21 μL; 0.24 mmol) in DCE (1 mL) was dropwise added to a screw-cap



glass tube containing a solution of 4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**114**) (45.4 mg; 0.2 mmol) in DCE (2 mL). During the addition a suspension was formed. The reaction mixture was stirred for 16 h at 25 °C to form vinyl triflate **115**. In separate flask, a suspension of EtONa (272 mg; 4 mmol) in EtOH (4 mL) was prepared and the mixture of vinyl triflate **115** in DCE was added dropwise. The reaction mixture was stirred at 25 °C for 15 min (^{19}F NMR control). DCE was added (20 mL) and the solution was extracted with water (2 × 10 mL). The organic phase was separated, dried over $MgSO_4$, filtered, evaporated on silica gel and the product was isolated by column chromatography (cyclohexane/EtOAc). Yield: 53%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.27 (m, 2H), 7.20–7.17 (m, 2H), 7.11 (d, *J* = 11.2 Hz, 1H), 6.82 (d, *J* = 11.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 2.36 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 139.2, 131.8, 129.7, 128.9, 124.7, 118.5 (q, *J* = 320.2 Hz), 116.6, 62.8, 21.4, 14.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.2 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{13}H_{14}F_3NO_5NaS$ $[M+Na]^+$: 376.04370, found 376.04337.

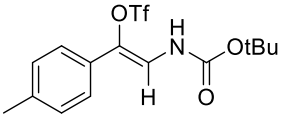
(*Z*)-2-(((Benzyloxy)carbonyl)amino)-1-(*p*-tolyl)vinyl trifluoromethanesulfonate



(**119b**): A solution of trifluoromethanesulfonic acid (21 μL; 0.24 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**114**) (45.4 mg; 0.2 mmol) in DCE (2 mL). During the addition a suspension was formed. The reaction mixture was stirred for 16 h at 25 °C to form vinyl triflate **115**. Benzyl alcohol (30 μL; 0.29 mmol) and Cs_2CO_3 (70 mg; 0.21 mmol) were added and the reaction mixture was stirred at 25 °C for 2 h. A mixture of trifluoromethansulfonic acid (15 μL; 0.17 mmol) in DCE (600 μL) was subsequently added and the reaction mixture was stirred next 30 min. Finally, DCE was added (20 mL) and the mixture was extracted with water (2 × 10 mL). The organic phase was separated, dried over $MgSO_4$, filtered, evaporated on silica gel and the product was isolated by column chromatography (cyclohexane/DCM). Yield: 48%; white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.33 (m, 5H), 7.32–7.27 (m, 2H), 7.23–7.15 (m, 2H), 7.11 (d, *J* = 11.2 Hz, 1H), 6.90 (d, *J* = 10.6 Hz, 1H), 5.23 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 139.3, 135.3, 132.0, 129.7, 128.8 (2C), 128.6, 124.7, 118.5 (q, *J* = 320.2

Hz), 116.4, 68.4, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.1 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{18}H_{16}F_3NO_5NaS$ $[M+Na]^+$: 438.05935, found 438.05893.

(*Z*)-2-((*tert*-Butoxycarbonyl)amino)-1-(*p*-tolyl)vinyl trifluoromethanesulfonate

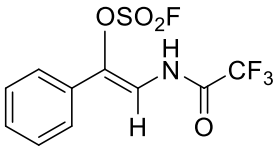


(**119c**): A solution of trifluoromethanesulfonic acid (21 μL; 0.24 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 4-(*p*-tolyl)-1-(trifluoromethyl)-1*H*-1,2,3-triazole (**114**) (45.4 mg; 0.2 mmol) in DCE (2 mL). During the addition a suspension was formed. The reaction mixture was stirred for 16 h at 25 °C to form vinyl triflate **115**. *t*-BuOH (3 mL) was added followed by a dropwise addition of Et_3N (82.5 μL, 0.59 mmol) in *t*-BuOH (3 mL). The reaction mixture was stirred at 25 °C for 30 min (^{19}F NMR control). DCE was added (20 mL) and the solution was extracted with water (2 × 10 mL). The organic phase was separated, dried over $MgSO_4$, filtered, evaporated on silica gel and the product was isolated by column chromatography (cyclohexane/DCM). Yield: 47%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.31–7.26 (m, 2H), 7.21–7.14 (m, 2H), 7.08 (d, *J* = 11.2 Hz, 1H), 6.71 (d, *J* = 10.7 Hz, 1H), 2.35 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.9, 138.9, 131.3, 129.7, 129.2, 124.6, 118.5 (q, *J* = 320.2 Hz), 116.8, 82.5, 28.3, 21.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -74.2 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{15}H_{18}F_3NO_5NaS$ $[M+Na]^+$: 404.07500, found 404.07471.

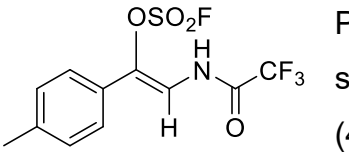
General procedure G for the synthesis of vinyl fluorosulfonates **120**

Solution of fluorosulfonic acid (12.8 μL; 0.22 mmol) in DCE (1 mL) was added dropwise to screw-cap glass tube containing solution of triazole (0.2 mmol) in DCE (3 mL). During the addition a suspension was formed. The reaction mixture was stirred for 2-16 h at 25-50 °C. Conversion to the product was monitored by LC-MS analysis or ^{19}F NMR spectroscopy. After full conversion, the reaction mixture was evaporated on silica gel (400 mg, 40 °C, 1 h) and purified by CombiFlash automatic or manual column chromatography (EtOAc/cyclohexane, 0:100 to 10:90 or DCM/cyclohexane).

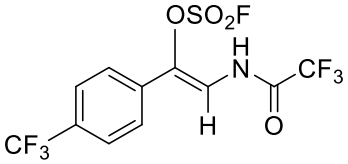
(*Z*)-1-Phenyl-2-(2,2,2-trifluoroacetamido)vinyl sulfurofluoridate (**120a**): Prepared according to the **general procedure G** with stirring at 25 °C for 16 h. Yield: 62%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 10.1 Hz, 1H), 7.53–7.41 (m, 5H), 7.32 (dq, *J* = 10.8, 0.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5 (q, *J* = 39.4 Hz), 138.0, 130.5, 129.7, 129.4, 125.2, 115.4 (q, *J* = 287.2 Hz), 112.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ 43.0 (s, 1F), -76.0 (s, 3F); HRMS (EI) *m/z* calcd for $C_{10}H_7F_4NO_4S$ [M]$^+$: 313.0032, found 313.0030.



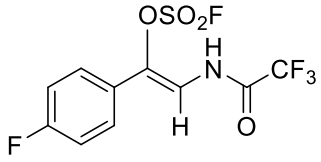
(*Z*)-1-(*p*-Tolyl)-2-(2,2,2-trifluoroacetamido)vinyl sulfurofluoridate (**120b**): Prepared according to the **general procedure G** with stirring at 50 °C for 2 h. Yield: 46%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 9.5 Hz, 1H), 7.40–7.35 (m, 2H), 7.28–7.23 (m, 3H, *signal overlap with the solvent*), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8 (q, *J* = 39.4 Hz), 141.4, 138.7, 130.4, 127.1, 125.5, 115.7 (q, *J* = 287.2 Hz), 111.9, 21.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ 42.9 (s, 1F), -76.0 (s, 3F); HRMS (CI) *m/z* calcd for $C_{11}H_{10}F_4NO_4S$ [M+H]$^+$: 328.0261, found 328.0269.



(*Z*)-2-(2,2,2-Trifluoroacetamido)-1-(4-(trifluoromethyl)phenyl)vinyl sulfurofluoridate (**120c**): Prepared according to the **general procedure G** with stirring at 40 °C for 16 h. Yield: 68%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.33 (d, *J* = 10.0 Hz, 1H), 7.87–7.67 (m, 2H), 7.66–7.58 (m, 2H), 7.44 (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7 (q, *J* = 40.1 Hz), 136.2, 133.3 (q, *J* = 1.1 Hz), 132.3 (q, *J* = 33.2 Hz), 126.5 (q, *J* = 3.9 Hz), 125.3, 123.6 (d, *J* = 272.4 Hz), 115.3 (q, *J* = 287.1 Hz), 114.2; ^{19}F NMR (377 MHz, $CDCl_3$) δ 42.5 (s, 1F), -63.5 (s, 3F), -75.9 (s, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_6F_7NO_4S$ [M]$^+$: 380.9906, found 380.9907.



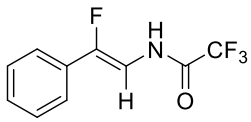
(*Z*)-1-(4-Fluorophenyl)-2-(2,2,2-trifluoroacetamido)vinyl sulfurofluoridate (**120d**):



Prepared according to **general procedure G** with stirring at 40 °C for 2 h. Yield: 40%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.24 (d, *J* = 10.0 Hz, 1H), 7.54–7.44 (m, 2H), 7.25 (d, *J* = 10.7 Hz, 1H, *signal overlap the with the solvent*), 7.19–7.12 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0 (d, *J* = 252.0 Hz), 154.6 (q, *J* = 39.8 Hz), 137.1, 127.5 (d, *J* = 8.8 Hz), 125.9 (d, *J* = 3.7 Hz), 116.7 (d, *J* = 22.4 Hz), 115.3 (q, *J* = 287.1 Hz), 112.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ 42.6 (s, 1F), -76.0 (s, 3F), -109.3 to -109.4 (m, 1F); HRMS (EI) *m/z* calcd for $C_{10}H_6F_5NO_4S$ $[M]^+$: 330.9938, found 330.9940.

Characterization of isolated side product **121a**

(*Z*)-2,2,2-Trifluoro-N-(2-fluoro-2-phenylvinyl)acetamide (**121a**): Isolated as a side



product of the reaction to **117b** and **120a**. White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.53–7.47 (m, 2H), 7.44–7.35 (m, 3H), 7.05 (dd, *J* = 26.5, 10.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8 (q, *J* = 38.3 Hz), 150.3 (d, *J* = 246.5 Hz), 129.7, 129.5 (d, *J* = 24.6 Hz), 129.0 (d, *J* = 2.2 Hz), 123.6 (d, *J* = 6.6 Hz), 115.7 (q, *J* = 287.0 Hz), 101.1 (d, *J* = 12.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.9 (s, 3F), -123.0 (dd, *J* = 26.3, 2.9 Hz, 1F); HRMS (EI) *m/z* calcd for $C_{10}H_7F_4NO$ $[M]^+$: 233.0464, found 233.0468.

Synthesis and characterization of deuterated triazole **122** and triflate **123**

*Preparation of deuterated triazole **122***

A solution of CF_3N_3 in THF (~0.6 mmol in 4 mL) was cooled to -100 °C and 1-(ethynyl-*d*)-4-methylbenzene (4.25 mmol; 500 mg), CuMeSal (0.2 mmol; 42.9 mg) and water (0.5 mL) were added. The reaction mixture was stirred at room temperature for 24 h and then evaporated on silica gel. Finally, flash column chromatography was performed (Cyclohexane/EtOAc) affording deuterated product as a pale brown solid. Yield 44 % (D/H = 83:17 by ^{1}H NMR). ^{1}H NMR

(400 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 2H), 7.39 – 7.20 (m, 2H), 2.41 (s, 3H); HRMS (CI) *m/z* calcd for $C_{10}H_7DF_3N_3$ $[M+H]^+$: 229.0811, found 229.0809.

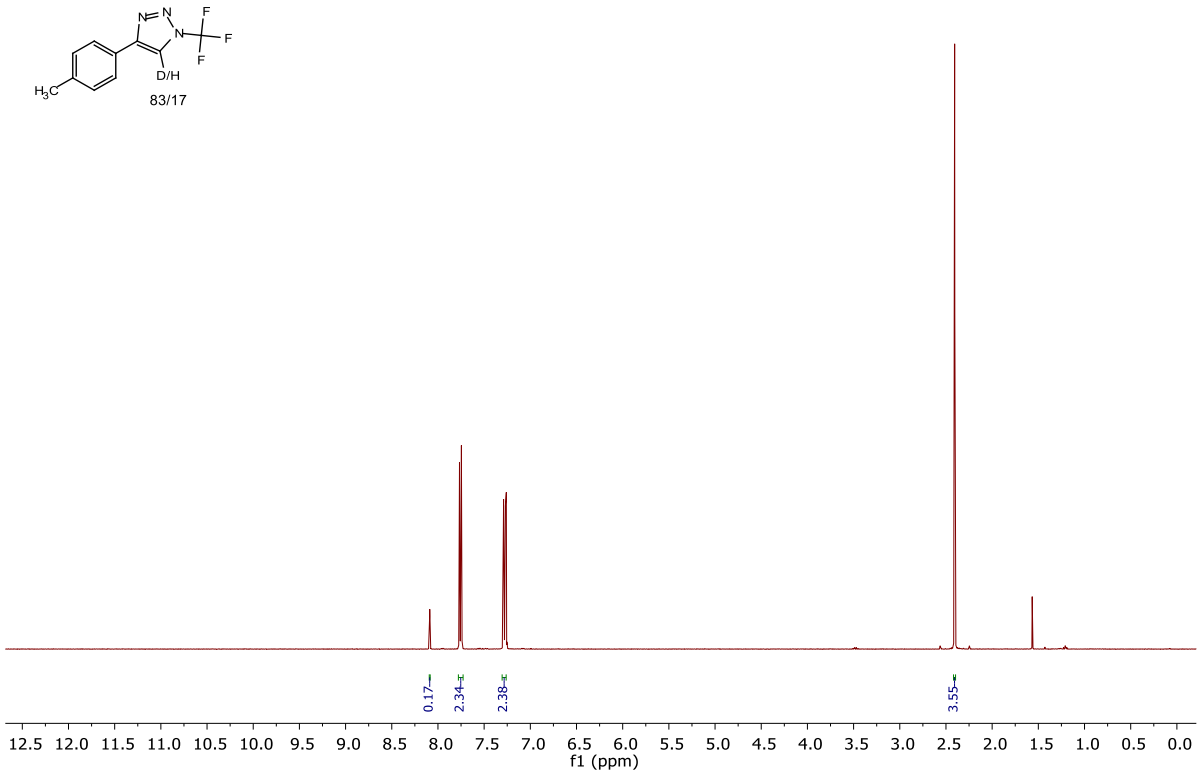


Figure 11 ^1H NMR spectrum of **122** ($CDCl_3$, 401 MHz).

*Preparation of deuterated vinyl triflate **123***

A solution of trifluoromethanesulfonic acid (10.6 μL; 0.12 mmol) in DCE (0.5 mL) was added dropwise to a screw-cap glass tube containing a solution of triazole **122** (22.8 mg; 0.1 mmol) in DCE (1.5 mL). During the addition a suspension was formed. The reaction mixture was stirred at 25 °C for 16 h. Finally, ^1H NMR was measured.

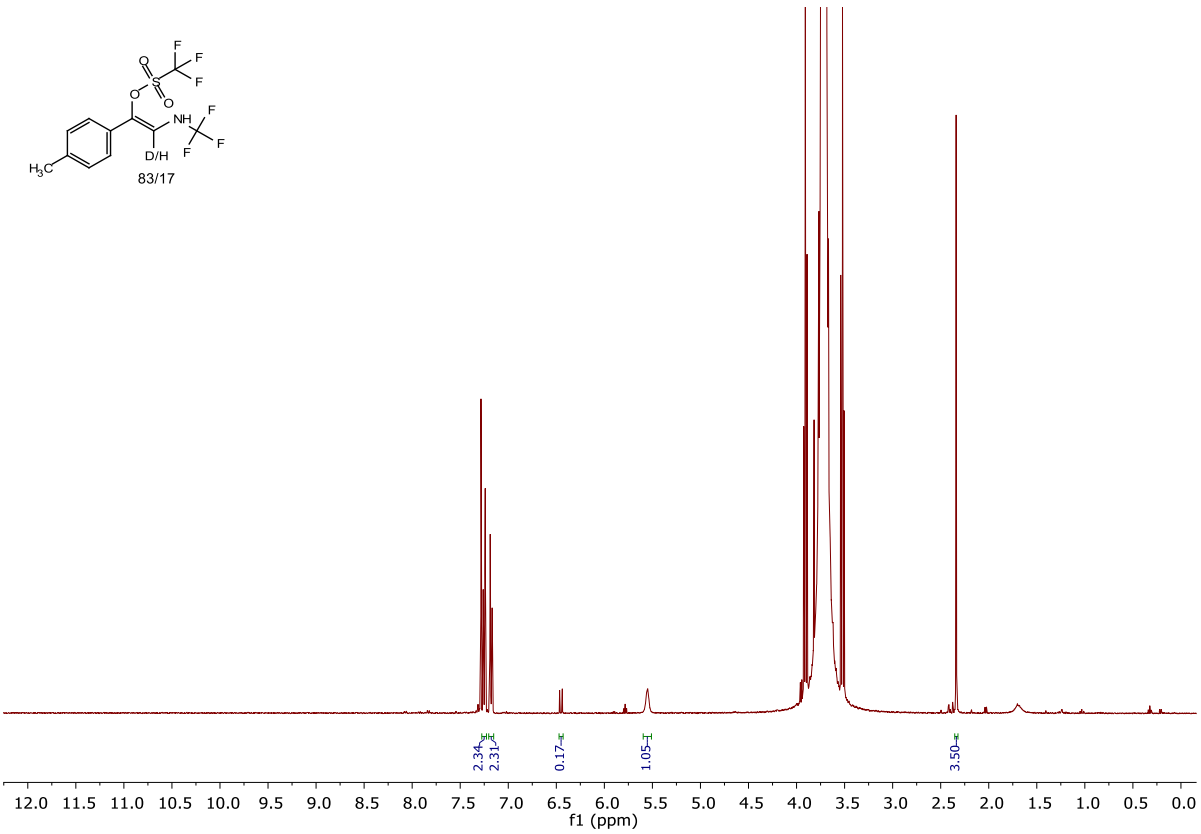
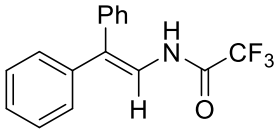


Figure 12 ^{1}H NMR spectrum of **123** ($CDCl_3$, 401 MHz).

8.7. Cross coupling reactions of vinyl triflates **117**

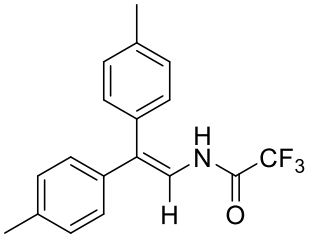
N-(2,2-Diphenylvinyl)-2,2,2-trifluoroacetamide (**127a**): Starting vinyl triflate **117b**



(181.5 mg; 0.5 mmol), phenylboronic acid (122 mg; 1 mmol) and KF (63.8 mg; 1.1 mmol) were suspended in DCE (5 mL) and the reaction mixture was cooled to -100 °C. The reaction flask was evacuated and back filled with argon 3 times, heated to room temperature and tetrakis(triphenylphosphine)palladium (2 mg; 2 μmol) was added. The reaction mixture was stirred for 2 h at 40 °C. Then Et_2O and brine were added. Aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was combined, dried over $MgSO_4$, filtered and evaporated on silica gel. Column chromatography was performed (cyclohexane/EtOAc). Yield: 81%; colorless oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.85 (d, J = 10.8 Hz, 1H), 7.56–7.46 (m, 2H), 7.49–7.40 (m, 1H), 7.36 (d, *J* = 11.0 Hz, 1H), 7.37–7.20 (m, 7H); ^{13}C

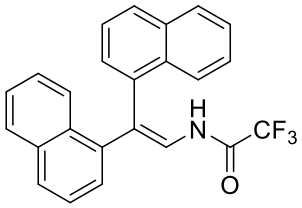
NMR (101 MHz, $CDCl_3$) δ 154.2 (q, *J* = 38.3 Hz), 138.9, 136.1, 130.2, 129.8, 129.6, 129.0, 128.7, 128.1, 127.3, 116,8, 115.7 (q, *J* = 287.4 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.3 (s, 3F); HRMS (CI) m/z calcd for $C_{16}H_{13}F_3NO$ $[M+H]^+$: 292.0994, found 292.0944.

N-(2,2-Di-*p*-tolylvinyl)-2,2,2-trifluoroacetamide (**127b**): Starting vinyl triflate **117a**



(15 mg; 0.04 mmol), *p*-tolylboronic acid (27 mg; 0.2 mmol), K_3PO_4 (42 mg; 0.2 mmol) and KBr (24 mg; 0.2 mmol) were dissolved in dioxane (1.5 mL) and reaction mixture was cooled to -100 °C. The reaction flask was evacuated and back filled with argon 3 times, heated to room temperature and tetrakis-(triphenylphosphine)palladium (4.6 mg; 0.004 mmol) was added. The reaction mixture was stirred for 2 h at 70 °C. Et_2O and 5% HCl were added into the reaction mixture and the organic phase was separated, dried over $MgSO_4$, filtered and evaporated on silica gel. Column chromatography was performed (cyclohexane/EtOAc). Yield: 71%; white solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 10.0 Hz, 1H), 7.32–7.28 (m, 3H), 7.17–7.07 (m, 6H), 2.42 (s, 3H), 2.34 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9 (q, *J* = 38.1 Hz), 138.7, 137.9, 136.2, 133.1, 130.3, 130.1, 129.3, 129.2, 127.1, 115.8, 115.3 (q, *J* = 287.2 Hz), 21.3, 21.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.3 (s, 3F); HRMS (ESI) m/z calcd for $C_{18}H_{16}F_3NONa$ $[M+Na]^+$: 342.10762, found 342.10734.

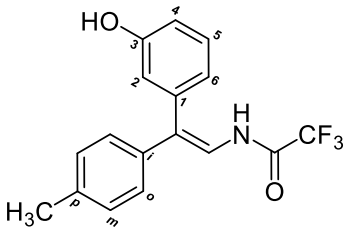
N-(2,2-Di(naphthalen-1-yl)vinyl)-2,2,2-trifluoroacetamide (**127c**): A solution of



trifluoromethanesulfonic acid (21 μL; 0.24 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 4-(naphthalen-1-yl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole (**75**) (0.2 mmol) in DCE (2 mL). The reaction mixture was stirred for 1 h at 50 °C (the formation of **117f** was monitored by ^{19}F NMR) and then cooled to room temperature. 1-Naphthylboronic acid (36 mg; 0.21 mmol) and K_2CO_3 (82.8 mg; 0.6 mmol) were added and the reaction mixture was cooled to -100 °C. The tube was evacuated and back filled with argon 3 times, heated to room temperature and

tetrakis(triphenylphosphine)palladium (0.005 mmol; 2 mg) was added. The reaction mixture was stirred at 25 °C for 16 h. Et_2O and 5% HCl were added and the organic phase was separated, dried over $MgSO_4$, filtered, evaporated on silica gel and the product was isolated by flash chromatography (cyclohexane/DCM). Yield: 61%; yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 1H), 8.08–8.01 (m, 1H), 8.01–7.93 (m, 1H), 7.96–7.85 (m, 2H), 7.87–7.80 (m, 1H), 7.71 (br d, *J* = 11.2 Hz, 1H), 7.62–7.52 (m, 2H), 7.55–7.36 (m, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2 (q, *J* = 38.1 Hz), 137.8, 134.4, 134.4, 134.3, 131.7, 130.1, 129.5, 129.4, 128.8, 128.8, 128.1, 127.8, 127.6, 126.8, 126.7, 126.6, 126.0, 125.9, 125.4, 125.3, 125.0, 121.3, 115.6 (q, *J* = 287.6, 287.0 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.4 (s, 3F); HRMS (ESI) m/z calcd for $C_{24}H_{16}F_3NONa$ $[M+Na]^+$: 414.10762, found 414.10756.

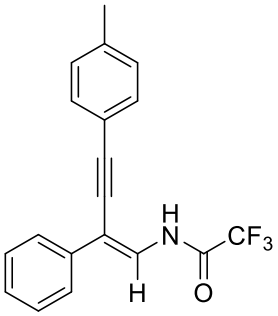
(*Z*)-2,2,2-Trifluoro-*N*-(2-(3-hydroxyphenyl)-2-(*p*-tolyl)vinyl)acetamide (**127d**)



Vinyl triflate **117a** (188.6 mg; 0.5 mmol), 3-hydroxyphenylboronic acid (69.5 mg; 0.505 mmol), and K_3PO_4 (174 mg; 0.82 mmol) were suspended in THF (2 mL) and water (0.2 mL). The reaction mixture was cooled to -30 °C. The tube was evacuated and back-filled with argon 3 times, heated to room temperature and tetrakis(triphenylphosphine)palladium (17 mg; 0.015 mmol) was added. The reaction mixture was stirred at 30 °C for 1 h (^{19}F NMR control). Et_2O and brine were added and the organic phase was separated, dried over $MgSO_4$, filtered, evaporated on silica gel and the product was isolated by flash chromatography (cyclohexane/DCM). Yield: 119 mg (74%); white solid; ^{1}H NMR (500 MHz, $CDCl_3$): 7.89 (br d, 1H, *J* = 11.0 Hz, NH), 7.38, (dd, 1H, $J_{5,4}$ = 8.2 Hz, $J_{5,6}$ = 7.5 Hz, H-5), 7.30 (d, 1H, *J* = 11.0, =CH), 7.09–7.17 (m, 4H, H-*o*,*m*-Tol), 6.90 (ddd, 1H, $J_{4,5}$ = 8.2 Hz, $J_{4,2}$ = 2.6 Hz, $J_{4,6}$ = 1.0 Hz, H-4), 6.85 (ddd, 1H, $J_{6,5}$ = 7.5 Hz, $J_{6,2}$ = 1.5 Hz, $J_{6,4}$ = 1.0 Hz, H-6), 6.69 (dd, 1H, $J_{2,4}$ = 2.6 Hz, $J_{2,6}$ = 1.5 Hz, H-2), 4.98 (m, 1H, OH), 2.34 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): 156.5 (C-3), 153.9 (q, $J_{C,F}$ = 38.1 Hz, CO), 137.7 (C-1); 138.0 (C-*p*-Tol), 135.6 (C-*i*-Tol), 130.9 (CH-5), 129.6 (=C), 129.3 (CH-*o*-Tol), 127.0 (CH-*m*-Tol), 121.5 (CH-6), 116.2 (CH-2), 115.9 (=CH), 115.8, 115.5 (q, $J_{C,F}$ = 287.2 Hz, CF_3), 21.1 (CH_3); ^{19}F NMR

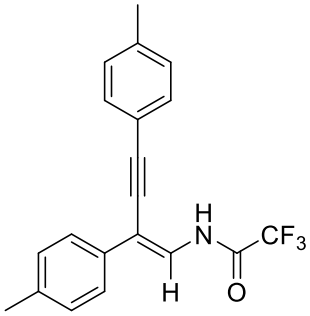
(377 MHz, $CDCl_3$) δ -76.2 (s, 3F); HRMS (ESI) m/z calcd for $C_{17}H_{14}F_3NO_2Na$ $[M+Na]^+$: 344.08688, found 344.08658.

(*Z*)-2,2,2-Trifluoro-N-(2-phenyl-4-(*p*-tolyl)but-1-en-3-yn-1-yl)acetamide (**128a**):



Starting vinyl triflate **117b** (72.6 mg; 0.2 mmol), 4-ethynyltoluene (24.4 mg; 0.21 mmol) and N,N-diisopropylethylamine (27.3 mg; 0.21 mmol) were dissolved in dry DMF (0.6 mL) and the reaction mixture was cooled to -100 °C. The tube was evacuated and back filled with argon 3 times, heated to room temperature and bis(triphenylphosphine)-palladium(II) dichloride (1.1 mg; 6 μmol) and CuI (1.9 mg; 0.01 mmol) were added. The reaction mixture was stirred for 2.5 h at 25 °C. Then Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on silica gel. The product was isolated by column chromatography (cyclohexane/EtOAc). Yield: 51%; white solid; ^1H NMR (401 MHz, $CDCl_3$) δ 8.65 (d, *J* = 10.4 Hz, 1H), 7.69–7.61 (m, 3H), 7.46–7.37 (m, 4H), 7.36–7.31 (m, 1H), 7.24–7.19 (m, 2H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1 (q, *J* = 38.5 Hz), 139.9, 134.5, 131.6, 129.6, 129.0, 128.6, 126.0, 123.6, 118.9, 115.8 (q, *J* = 287.6 Hz), 111.6, 101.8, 81.8, 21.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.2 (s, 3F); HRMS (ESI) m/z calcd for $C_{19}H_{14}F_3NONa$ $[M+Na]^+$: 352.09197, found 352.09180.

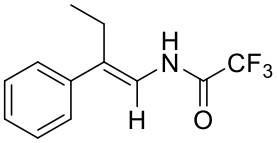
(*Z*)-*N*-(2,4-di-*p*-tolylbut-1-en-3-yn-1-yl)-2,2,2-trifluoroacetamide (**128b**): Starting



vinyl triflate **117a** (75.4 mg; 0.2 mmol), 4-ethynyltoluene (31.7 mg; 0.27 mmol) and triethylamine (83 μL; 0.6 mmol) were dissolved in dry THF (1.5 mL). The tube was evacuated and back filled with argon 3 times and bis(triphenylphosphine)-palladium(II) dichloride (7 mg; 0.01 mmol) and CuI (1.9 mg; 0.01 mmol) were added. The reaction mixture was stirred for 14 h at 25 °C. Then Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on silica gel. The product

was isolated by column chromatography (cyclohexane/EtOAc). Yield 80%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.64 (d, *J* = 11.2 Hz, 1H), 7.63 (d, *J* = 11.0 Hz, 1H), 7.57–7.51 (m, 2H), 7.46–7.41 (m, 2H), 7.25–7.18 (m, 4H), 2.41 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0 (q, *J* = 38.6 Hz), 139.8, 138.6, 131.6, 131.5, 129.6 (2C), 125.8, 122.9, 118.9, 115.8 (q, *J* = 287.3 Hz), 111.5, 101.6, 81.9, 21.7, 21.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.1 (s, 3F); HRMS (CI) m/z calcd for $C_{20}H_{17}F_3NO$ $[M+H]^+$: 344.1257, found 344.1260.

(*E*)-2,2,2-Trifluoro-*N*-(2-phenylbut-1-en-1-yl)acetamide (**129**): Starting vinyl triflate **117b** (72.6 mg; 0.2 mmol) was dissolved in THF (1 mL) and the reaction mixture was cooled to -100 °C. The tube was evacuated and back filled with argon 3 times, heated to room temperature and tetrakis(triphenylphosphine)palladium (23 mg; 0.02 mmol) and 1.1 M solution of diethyl zinc in hexanes (187 μL; 0.2 mmol) were added. The reaction mixture was stirred for 6 h at 25 °C. Then Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on silica gel. The product was isolated by column chromatography (cyclohexane/EtOAc). Yield: 66%; colorless oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.77–7.70 (br s, 1H), 7.41–7.26 (m, 5H), 6.96 (d, *J* = 10.7 Hz, 1H), 2.53 (qd, *J* = 7.6, 0.8 Hz, 2H), 1.10 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3 (q, *J* = 37.9 Hz), 138.8, 130.5, 128.8, 127.9, 126.4, 116.3, 115.9 (q, *J* = 287.2 Hz), 22.3, 12.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.0 (s, 3F); HRMS (CI) m/z calcd for $C_{12}H_{13}F_3NO$ $[M+H]^+$: 244.0949, found 244.0945.



8.8. Preparation and characterization of imidoyl halides

General procedure H for the synthesis of imidoyl chlorides **130**

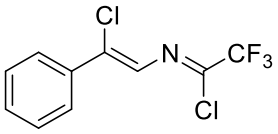
Under air atmosphere, a solution of triazole (0.2 mmol) in DCE (2 mL) was added dropwise to a 10 mL screw-cap glass tube containing anhydrous aluminum chloride (26.7 mg; 0.2 mmol) and DCE (1 mL). The reaction mixture was stirred

for 0.5-5 h at 25-50 °C. The conversion was monitored by TLC analysis or ^{19}F NMR spectroscopy. Then, Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated giving a crude oil. The product was isolated by column chromatography (pentane/dichloromethane, 95/5).

General procedure I for the synthesis of imidoyl chlorides **130**

Under air atmosphere, a solution of triazole (0.2 mmol) in DCM (1 mL) and CCl_4 (1 mL) was added dropwise to a 10 mL screw-cap glass tube containing anhydrous aluminum chloride (26.7 mg; 0.2 mmol) and CCl_4 (1 mL). The reaction mixture was stirred for 1-2 h at 25-50 °C. The conversion was monitored by TLC analysis or ^{19}F NMR spectroscopy. Then, Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated giving a crude oil. The product was isolated by column chromatography (pentane/dichloromethane, 95/5).

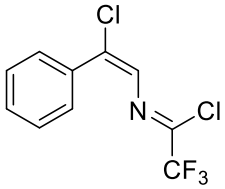
(*Z*)-*N*-((*Z*)-2-Chloro-2-phenylvinyl)-2,2,2-trifluoroacetimidoyl chloride (**130a**):



Prepared according to the **general procedure H** with stirring at 50 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 93:7; Yield: 70%. Scale-up reaction: A solution of 1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole (10 mmol; 2.632 g) in DCE (45 mL) was added dropwise to 100 mL round bottom flask containing anhydrous aluminum chloride (10 mmol; 1.33 g) and DCE (5 mL). The reaction mixture was stirred for 2 h at 50 °C. Then Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 200 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated giving a crude oil. The product was isolated by column chromatography (pentane/dichloromethane, 95/5). Yield 65%; white solid; ^1H NMR (401 MHz, $CDCl_3$) δ 7.76 – 7.72 (m, 2H), 7.60 (q, *J* = 0.9 Hz, 1H), 7.48 – 7.40 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7, 135.5, 132.4 (q, *J* = 43.6 Hz), 131.0, 129.0, 127.5, 127.0, 117.3 (q, *J* = 275.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$)

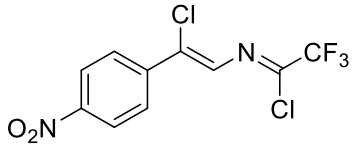
δ -71.0 (s, 3F); HRMS (CI) *m/z* calcd for $C_{10}H_7Cl_2F_3N$ $[M+H]^+$: 267.9908, found 267.9906.

(*Z*)-*N*-((*E*)-2-Chloro-2-phenylvinyl)-2,2,2-trifluoroacetimidoyl chloride (**130a´**):



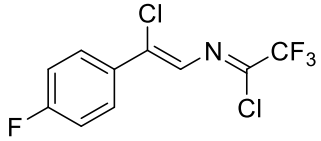
Isolated as a minor isomer from the reaction of 1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole with $AlCl_3$. Colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.82 – 7.74 (m, 2H), 7.45 (q, *J* = 0.9 Hz, 1H), 7.44 – 7.39 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 134.2, 130.6, 130.2, 130.2 (q, *J* = 43.4 Hz), 128.7, 128.2, 117.3 (q, *J* = 275.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.2 (s, 3F).

(*Z*)-*N*-((*Z*)-2-Chloro-2-(4-nitrophenyl)vinyl)-2,2,2-trifluoroacetimidoyl chloride



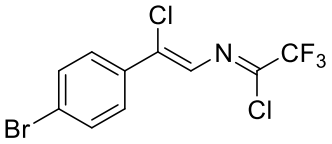
(**130b**): Prepared according to the **general procedure H** with stirring at 25 °C for 1 h. Crude ratio *Z*/*E*$_{(C=C)}$ 90:10; Yield: 70%; yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.34 – 8.26 (m, 2H), 7.95 – 7.87 (m, 2H), 7.68 (q, *J* = 0.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 141.2, 139.5, 135.1 (q, *J* = 43.6 Hz), 129.4, 128.3, 124.2, 117.1 (q, *J* = 276.4 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.2 (s, 3F); HRMS (CI) *m/z* calcd for $C_{10}H_6Cl_2F_3N_2O_2$ $[M+H]^+$: 312.9758, found 312.9755.

(*Z*)-*N*-((*Z*)-2-Chloro-2-(4-fluorophenyl)vinyl)-2,2,2-trifluoroacetimidoyl chloride



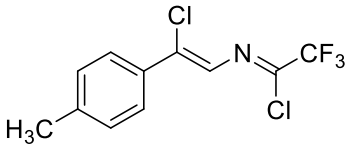
(**2c**): Prepared according to the **general procedure H** with stirring at 25 °C for 4 h. Crude ratio *Z*/*E*$_{(C=C)}$ 95:5; Yield: 71%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.70 (m, 2H), 7.56 – 7.51 (m, 1H), 7.19 – 7.10 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3 (d, *J* = 252.7 Hz), 141.5, 132.6 (q, *J* = 43.3 Hz), 131.6 (d, *J* = 3.7 Hz), 129.5 (d, *J* = 8.8 Hz), 126.8 (d, *J* = 1.8 Hz), 117.3 (q, *J* = 275.8 Hz), 116.1 (d, *J* = 22.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.0 (s, 3F), -109.3 (tt, *J* = 8.0, 5.2 Hz, 1F); HRMS (CI) *m/z* calcd for $C_{10}H_6Cl_2F_4N$ $[M+H]^+$: 285.9813, found 285.9811.

(*Z*)-*N*-((*Z*)-2-(4-Bromophenyl)-2-chlorovinyl)-2,2,2-trifluoroacetimidoyl chloride



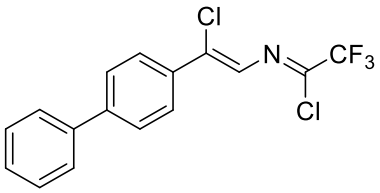
(**130d**): Prepared according to the **general procedure H** with stirring at 50 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 94:6; Yield: 75%; pale-yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.68 – 7.52 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.4, 134.3, 133.0 (q, *J* = 43.5 Hz), 132.2, 128.9, 127.2, 125.5, 117.6 (q, *J* = 275.8 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.1 (s, 3F); HRMS (EI) *m/z* calcd for $C_{10}H_5BrCl_2F_3N$ $[M]^+$: 344.8935, found 344.8937.

(*Z*)-*N*-((*Z*)-2-Chloro-2-(*p*-tolyl)vinyl)-2,2,2-trifluoroacetimidoyl chloride (**130e**):



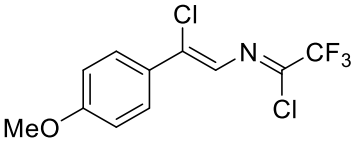
Prepared according to the **general procedure H** with stirring at 25 °C for 0.5 h. Crude ratio *Z*/*E*$_{(C=C)}$ 97:3; Yield: 62%; pale-yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.62 (m, 2H), 7.58 (q, *J* = 0.9 Hz, 1H), 7.27 – 7.23 (m, 2H, *signal is overlapped with solvent*), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.9, 141.6, 132.6, 131.7 (q, *J* = 43.5 Hz), 129.6, 127.4, 126.2, 117.3 (q, *J* = 275.6 Hz), 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.0 (s, 3F); HRMS (CI) *m/z* calcd for $C_{11}H_9Cl_2F_3N$ $[M+H]^+$: 282.0064, found 282.0065.

(*Z*)-*N*-((*Z*)-2-([1,1'-Biphenyl]-4-yl)-2-chlorovinyl)-2,2,2-trifluoroacetimidoyl

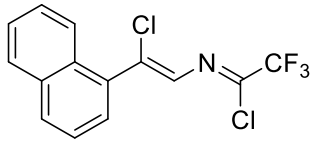


chloride (**130f**): Prepared according to the **general procedure H** with stirring at 25 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 98:2; Yield: 41%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.86 – 7.80 (m, 2H), 7.71 – 7.66 (m, 3H), 7.65 – 7.61 (m, 2H), 7.52 – 7.46 (m, 2H), 7.44 – 7.38 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 142.4, 139.9, 134.2, 132.2 (q, *J* = 43.5 Hz), 129.1, 128.3, 127.9, 127.5, 127.3, 126.8, 117.3 (q, *J* = 275.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.0 (s, 3F); HRMS (CI) *m/z* calcd for $C_{16}H_{11}Cl_2F_3N$ $[M+H]^+$: 344.0221, found 344.0218.

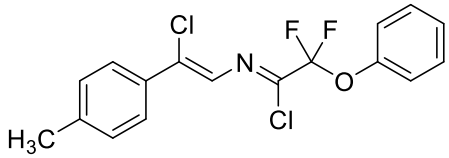
(*Z*)-*N*-((*Z*)-2-Chloro-2-(4-methoxyphenyl)vinyl)-2,2,2-trifluoroacetimidoyl chloride (**130g**): Prepared according to the **general procedure H** with stirring at 25 °C for 0.5 h. Crude ratio *Z*/*E*$_{(C=C)}$ 96:4; Yield: 47%; yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.72 – 7.68 (m, 2H), 7.53 (q, *J* = 0.8 Hz, 1H), 6.98 – 6.93 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 142.7, 131.0 (q, *J* = 43.3 Hz), 129.1, 127.8, 125.3, 117.4 (q, *J* = 275.5 Hz), 114.3, 55.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.9 (s, 3F), HRMS (CI) *m/z* calcd for $C_{11}H_9Cl_2F_3NO$ $[M+H]^+$: 298.0013, found 298.0011.



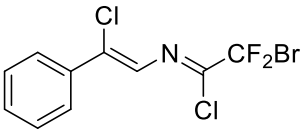
(*Z*)-*N*-((*Z*)-2-Chloro-2-(naphthalen-1-yl)vinyl)-2,2,2-trifluoroacetimidoyl chloride (**130h**): Prepared according to the **general procedure H** with stirring at 25 °C for 0.5 h. Crude ratio *Z*/*E*$_{(C=C)}$ 97:3; Yield: 55%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.11 (m, 1H), 7.97 – 7.94 (m, 1H), 7.94 – 7.90 (m, 1H), 7.63 – 7.49 (m, 4H), 7.40 (q, *J* = 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.1, 134.1, 133.8, 133.2 (q, *J* = 43.4 Hz), 131.0, 130.9, 130.8, 128.8, 127.7, 127.3, 126.7, 125.1, 117.3 (q, *J* = 276.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.6 (s, 3F); HRMS (CI) *m/z* calcd for $C_{14}H_9Cl_2F_3N$ $[M+H]^+$: 318.0064, found 318.0063.



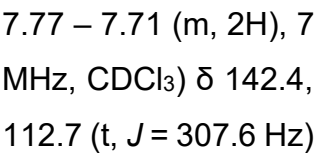
(*E*)-*N*-((*Z*)-2-Chloro-2-(*p*-tolyl)vinyl)-2,2-difluoro-2-phenoxyacetimidoyl chloride (**130i**): Prepared according to the **general procedure I** with stirring at 25 °C for 80 min. Crude ratio *Z*/*E*$_{(C=C)}$ 98:2; Yield: 42%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.59 (m, 2H), 7.59 (t, *J* = 0.9 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.32 – 7.27 (m, 2H), 7.27 – 7.22 (m, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0 (t, *J* = 1.6 Hz), 141.2, 141.1, 135.5 (t, *J* = 42.7 Hz), 132.9, 129.7, 129.6, 127.3, 126.8, 126.3, 121.9, 116.5 (t, *J* = 264.8 Hz), 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.0 (s, 2F); HRMS (CI) *m/z* calcd for $C_{17}H_{14}Cl_2F_2NO$ $[M+H]^+$: 356.0421, found 356.0421.



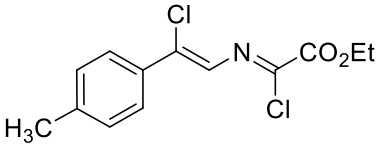
(*Z*)-2-Bromo-*N*-((*Z*)-2-chloro-2-phenylvinyl)-2,2-difluoroacetimidoyl chloride (**130j**): Prepared according to the **general procedure I** with stirring at 25 °C for 1 h. Crude ratio *Z*/*E*$_{(C=C)}$ 96:4; Yield: 65%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.57 (t, *J* = 1.0 Hz, 1H), 7.48 – 7.41 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4, 137.0 (t, *J* = 31.2 Hz), 135.6, 130.9, 128.9, 127.4, 127.2, 112.7 (t, *J* = 307.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -53.1 (s, 2F); HRMS (APCI) *m/z* calcd for $C_{10}H_6BrCl_2F_2N$ $[M]^+$: 326.90233, found 326.90182.



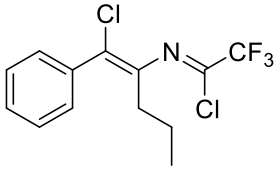
(*Z*)-*N*-((*Z*)-2-Chloro-2-phenylvinyl)-2,2-difluoroacetimidoyl chloride (**130k**): Prepared according to the **general procedure I** with stirring at 50 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 96:4; Yield: 63%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.75 – 7.70 (m, 2H), 7.63 (t, *J* = 0.9 Hz, 1H), 7.47 – 7.40 (m, 3H), 6.28 (t, *J* = 54.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 139.2 (t, *J* = 33.0 Hz), 135.6, 130.7, 128.9, 127.6, 127.4, 110.8 (t, *J* = 245.0 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -118.3 (d, *J* = 54.4 Hz, 2F); HRMS (CI) *m/z* calcd for $C_{10}H_8Cl_2F_2N$ $[M+H]^+$: 248.9924, found 248.9926.



Ethyl (*Z*)-2-chloro-2-(((*Z*)-2-chloro-2-(*p*-tolyl)vinyl)imino)acetate (**130l**): Prepared according to the **general procedure H** with stirring at 50 °C for 1 h. Crude ratio *Z*/*E*$_{(C=C)}$ >99:1; Yield: 38%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.69 – 7.62 (m, 2H), 7.28 – 7.20 (m, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 142.3, 141.4, 135.6, 132.9, 129.6, 128.6, 127.4, 64.0, 21.5, 14.2; HRMS (ESI) *m/z* calcd for $C_{13}H_{14}Cl_2NO_2$ $[M+H]^+$: 286.03961, found 286.03982.

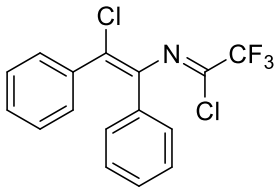


(*Z*)-*N*-((*Z*)-1-Chloro-1-phenylpent-1-en-2-yl)-2,2,2-trifluoroacetimidoyl chloride



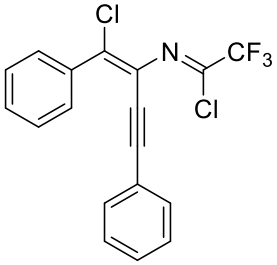
(**130m**): Prepared according to the **general procedure H** with stirring at 50 °C for 3 h. Crude ratio *Z*/*E*$_{(C=C)}$ >99:1; Yield: 79%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.47 – 7.34 (m, 5H), 2.31 – 2.26 (m, 2H), 1.52 – 1.38 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 136.7, 134.8 (q, *J* = 42.9 Hz), 129.6, 129.0, 128.7, 116.7 (q, *J* = 277.5 Hz), 115.0, 34.0, 20.8, 13.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -72.0 (s, 3F); HRMS (EI) *m/z* calcd for $C_{13}H_{12}Cl_2F_3N$ [M]$^+$: 309.0299, found 309.0297.

(*Z*)-*N*-((*Z*)-2-Chloro-1,2-diphenylvinyl)-2,2,2-trifluoroacetimidoyl chloride (**130n**):



Prepared according to the **general procedure H** with stirring at 50 °C for 5 h. Crude ratio *Z*/*E*$_{(C=C)}$ >99:1; Yield: 53%; pale- yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 2H), 7.26 – 7.18 (m, 6H), 7.16 – 7.12 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 136.4, 136.3 (q, *J* = 43.0 Hz), 133.7, 130.2, 129.3, 129.0, 128.8, 128.6, 128.4, 118.3, 116.8 (q, *J* = 277.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -72.0 (s, 3F); HRMS (EI) *m/z* calcd for $C_{16}H_{10}Cl_2F_3N$ [M]$^+$: 343.0142, found 343.0143.

(*Z*)-*N*-((*Z*)-1-chloro-1,4-diphenylbut-1-en-3-yn-2-yl)-2,2,2-trifluoroacetimidoyl

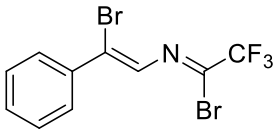


chloride (**130o**): Prepared according to the **general procedure H** with stirring at 50 °C for 5 h. Crude ratio *Z*/*E*$_{(C=C)}$ 95:5; Yield: 73%; green oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 2H), 7.48 – 7.42 (m, 3H), 7.36 – 7.28 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.7 (q; *J* = 43.3 Hz), 135.6, 133.5, 131.5, 130.1, 129.5, 129.4, 128.6, 128.2, 122.5, 121.9, 117.0 (q, *J* = 277.3 Hz), 96.8, 81.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.8 (s, 3F); HRMS (EI) *m/z* calcd for $C_{18}H_{10}Cl_2F_3N$ [M]$^+$: 367.0142, found 367.0149.

General procedure J for the synthesis of imidoyl bromides **131**

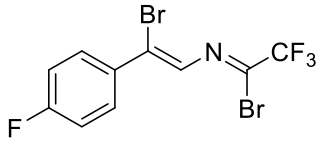
Under air atmosphere, a solution of triazole (0.2 mmol) in CH_2Br_2 (2.5 mL) was added dropwise to a 10 mL screw-cap glass tube containing anhydrous aluminium bromide (58.7 mg; 0.22 mmol) and CH_2Br_2 (0.5 mL). The reaction mixture was stirred for 2-3 h at 50 °C. The conversion was monitored by TLC analysis or ^{19}F NMR spectroscopy. Then, Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated giving a crude oil. The product was isolated by column chromatography (pentane/dichloromethane, 95/5).

(*Z*)-*N*-((*Z*)-2-Bromo-2-phenylvinyl)-2,2,2-trifluoroacetimidoyl bromide (**131a**):



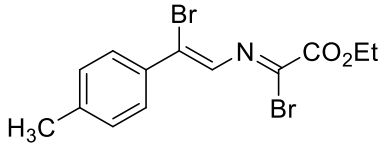
Prepared according to the **general procedure J** with stirring at 50 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 93:7; Yield: 71%; colorless oil; ^1H NMR (401 MHz, $CDCl_3$) δ 7.73 – 7.68 (m, 2H), 7.47 (q, *J* = 0.8 Hz, 1H), 7.46 – 7.41 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.0, 136.2, 132.7, 130.9, 128.9, 128.5, 126.7 (q, *J* = 43.8 Hz), 117.2 (q, *J* = 276.2 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -69.9 (s, 3F); HRMS (EI) *m/z* calcd for $C_{10}H_6Br_2F_3N$ $[M]^+$: 354.8819, found 354.8817.

(*Z*)-*N*-((*Z*)-2-Bromo-2-(4-fluorophenyl)vinyl)-2,2,2-trifluoroacetimidoyl bromide



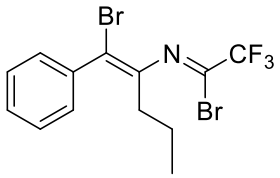
(**131b**): Prepared according to the **general procedure J** with stirring at 50 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 92:8; Yield: 65%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.66 (m, 2H), 7.42 – 7.41 (m, 1H), 7.18 – 7.08 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3 (d, *J* = 252.7 Hz), 134.9, 133.2 (d, *J* = 3.3 Hz), 132.5 (d, *J* = 1.8 Hz), 130.5 (d, *J* = 8.8 Hz), 126.9 (q, *J* = 43.7 Hz), 117.2 (q, *J* = 276.2 Hz), 116.1 (d, *J* = 22.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.0 (s, 3F), -109.42 to -109.52 (m, 1F); HRMS (EI) *m/z* calcd for $C_{10}H_5Br_2F_4N$ $[M]^+$: 372.8725, found 372.8726.

Ethyl (*Z*)-2-bromo-2-(((*Z*)-2-bromo-2-(*p*-tolyl)vinyl)imino)acetate (**131c**):



Prepared according to the **general procedure J** with stirring at 50 °C for 2 h. Crude ratio $Z/E_{(C=C)}$ >99:1; Yield: 52%; yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 2H), 7.58 (s, 1H), 7.25 – 7.20 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 141.3, 135.9, 134.4, 134.3, 131.0, 129.6, 128.4, 64.2, 21.5, 14.2; HRMS (APCI) *m/z* calcd for $C_{13}H_{14}Br_2NO_2$ $[M+H]^+$: 373.93858, found 373.93869.

(Z)-*N*-((*Z*)-1-Bromo-1-phenylpent-1-en-2-yl)-2,2,2-trifluoroacetimidoyl bromide (**131d**):

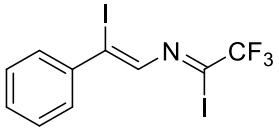


Prepared according to the **general procedure J** with stirring at 50 °C for 3 h. Crude ratio $Z/E_{(C=C)}$ 88:12; Yield: 30%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 5H), 2.31 – 2.22 (m, 2H), 1.51 – 1.41 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 138.2, 129.7, 128.9, 128.7, 127.8 (q, *J* = 43.3 Hz), 116.6 (q, *J* = 277.8 Hz), 105.4, 34.3, 20.8, 13.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.1 (s, 3F); HRMS (EI) *m/z* calcd for $C_{13}H_{12}Br_2F_3N$ $[M]^+$: 396.9289, found 396.9290.

General procedure K for the synthesis of imidoyl iodides **132**

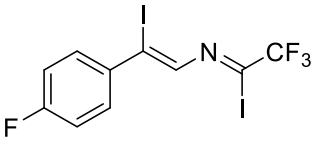
Under air atmosphere, a solution of triazole (0.2 mmol) in CS_2 (2.5 mL) was added dropwise to a 10 mL screw-cap glass tube containing aluminium iodide (81.5 mg; 0.2 mmol) and CS_2 (0.5 mL). The reaction mixture was stirred for 2 h at 40 °C. The conversion was monitored by TLC analysis or ^{19}F NMR spectroscopy. Then, Et_2O and brine were added. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated giving a crude oil. The product was isolated by column chromatography (pentane/dichloromethane, 95/5).

(*Z*)-2,2,2-Trifluoro-*N*-((*Z*)-2-iodo-2-phenylvinyl)acetimidoyl iodide (**132a**):



Prepared according to the **general procedure K** with stirring at 40 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 85:15; Yield: 53%; yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.66 – 7.62 (m, 2H), 7.43 – 7.38 (m, 3H), 6.83 (q, *J* = 1.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3, 140.0, 130.6, 129.4, 128.9, 117.4, 116.3 (q, *J* = 276.8 Hz), 114.6 (q, *J* = 42.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -67.99 to -71.18 (m, 3F); HRMS (EI) *m/z* calcd for $C_{10}H_6F_3I_2N$ $[M]^+$: 450.8542, found 450.8546.

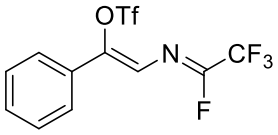
(*Z*)-2,2,2-Trifluoro-*N*-((*Z*)-2-(4-fluorophenyl)-2-iodovinyl)acetimidoyl iodide



(**132b**): Prepared according to the **general procedure K** with stirring at 40 °C for 2 h. Crude ratio *Z*/*E*$_{(C=C)}$ 93:7; Yield: 31%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.69 – 7.60 (m, 2H), 7.15 – 7.06 (m, 2H), 6.78 (q, *J* = 1.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0 (d, *J* = 252.4 Hz), 144.2 (d, *J* = 1.8 Hz), 136.2 (d, *J* = 3.7 Hz), 131.3 (d, *J* = 8.8 Hz), 116.3 (q, *J* = 277.0 Hz), 116.0 (d, *J* = 22.0 Hz), 115.5, 114.8 (q, *J* = 42.8 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -69.21 to -69.22 (m, 3F), -110.17 to -110.27 (m, 1F); HRMS (EI) *m/z* calcd for $C_{10}H_5F_4I_2N$ $[M]^+$: 468.8448, found 468.8445.

8.9. Preparation and characterization of vinyl triflates **133** and **135**

(*Z*)-2-(((*Z*)-Perfluoroethylidene)amino)-1-phenylvinyl trifluoromethanesulfonate



(**133**): A solution of trifluoromethanesulfonic acid (17.6 μL; 0.2 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole (52.6 mg; 0.2 mmol) in DCE (2 mL). During the addition a suspension was formed. The reaction mixture was stirred for 1 h at 35 °C. The reaction mixture was concentrated and applied on column as liquid (*Note: evaporation on silicagel led to hydrolysis of imidoyl fluoride*). A fast filtration was performed using DCM as the eluent. Yield: 87%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 2H), 7.53 – 7.43 (m, 3H), 7.38 – 7.35 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1 (d, *J* = 3.3 Hz), 139.0 (dq, *J* = 363.9, 45.7 Hz),

131.8, 130.6, 129.4, 126.2, 118.6 (d, *J* = 320.6 Hz), 116.0 (d, *J* = 17.2 Hz), 115.3 (qd, *J* = 275.04, 62.82 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -50.1 (q, *J* = 5.0 Hz, 1F), -72.3 (d, *J* = 5.0 Hz, 3F), -73.2 (s, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_6F_7NO_3S$ $[M]^+$: 364.9957, found 364.9959.

(Z)-2-(((Z)-1-Chloro-2,2,2-trifluoroethylidene)amino)-1-phenylvinyl trifluoromethanesulfonate (**134a**): A solution of trifluoromethanesulfonic acid (17.6 mL; 0.2 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole (52.6 mg; 0.2 mmol) in DCE (2 mL). During the addition a suspension was formed. The reaction mixture was stirred for 1 h at 35 °C. $AlCl_3$ (26.7 mg; 0.2 mmol) was added and the reaction mixture was stirred for 15 min at 25 °C, diluted with Et_2O, filtered, dried over $MgSO_4$ and evaporated. The product was purified by column flash chromatography (pentane/DCM, 4:1). Yield: 45%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 2H), 7.59 – 7.45 (m, 3H), 7.43 (d, J = 0.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3, 134.3 (q, *J* = 44.2 Hz), 132.1, 130.7, 129.5, 126.4, 121.1, 118.6 (q, *J* = 320.5 Hz), 117.1 (q, *J* = 276.3 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.3 (q, *J* = 1.7 Hz, 3F), -73.7 (q, *J* = 1.8 Hz, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_6ClF_6NO_3S$ $[M]^+$: 380.9661, found 380.9664.

(*Z*)-2-(((*Z*)-1-Chloro-2,2,2-trifluoroethylidene)amino)-1-(4-fluorophenyl)vinyl trifluoromethanesulfonate (**134b**): A solution of trifluoromethanesulfonic acid (17.6 mL; 0.2 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 4-(4-fluorophenyl)-1-(perfluoroethyl)-1*H*-1,2,3-triazole **74** (56.2 mg; 0.2 mmol) in DCE (2 mL). During the addition a suspension was formed. The reaction mixture was stirred for 16 h at 25 °C. $AlCl_3$ (26.7 mg; 0.2 mmol) was added and the reaction mixture was stirred for 15 min at 25 °C, diluted with Et_2O, filtered, dried over $MgSO_4$ and evaporated. The product was purified by column flash chromatography (pentane/DCM, 4:1). Yield: 41%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.72 – 7.63 (m, 2H), 7.37 (s, 1H), 7.25 – 7.14

(m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9 (d, *J* = 254.6 Hz), 150.2, 134.5 (q, *J* = 45.2 Hz), 128.7 (d, *J* = 9.2 Hz), 127.0 (d, *J* = 3.7 Hz), 121.0 (d, *J* = 1.8 Hz), 118.6 (q, *J* = 320.5 Hz), 117.1 (q, *J* = 276.4 Hz), 116.9 (d, *J* = 22.4 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.3 (q, *J* = 1.7 Hz, 3F), -73.6 (q, *J* = 1.7 Hz, 3F), -106.53 to -106.61 (m, 1F); HRMS (EI) *m/z* calcd for $C_{11}H_5ClF_7NO_3S$ $[M]^+$: 398.9567, found 398.9568.

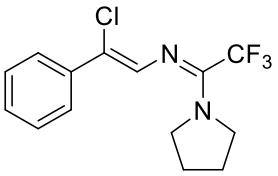
(*Z*)-2-(((*Z*)-1-Bromo-2,2,2-trifluoroethylidene)amino)-1-phenylvinyl trifluoromethanesulfonate (**135**): A solution of trifluoromethanesulfonic acid (17.6 mL; 0.2 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of 1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole (52.6 mg ; 0.2 mmol) in DCE (2 mL). During the addition, a suspension was formed. The reaction mixture was stirred for 1.5 h at 35 °C. CH_2Br_2 was added (1 mL) and the mixture was concentrated to ca. 1 mL of volume. The procedure with addition and subsequent evaporation of CH_2Br_2 was repeated 2 times and finally CH_2Br_2 (2 mL) was added. $AlBr_3$ (53.3 mg; 0.2 mmol) was added and reaction mixture was stirred for 15 min at 25 °C, diluted with Et_2O, filtered, dried over $MgSO_4$ and evaporated. The product was purified by column flash chromatography (pentane/DCM, 85:15). Yield: 48%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.72 – 7.66 (m, 2H), 7.58 – 7.48 (m, 3H), 7.28 (q, *J* = 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.1, 132.1, 130.7, 129.5, 128.7 (q, *J* = 44.4 Hz), 126.4, 123.9, 118.6 (q, *J* = 320.6 Hz), 117.1 (q, *J* = 276.5 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.2 (q, *J* = 1.8 Hz, 3F), -73.7 (q, *J* = 1.8 Hz, 3F); HRMS (EI) *m/z* calcd for $C_{11}H_6BrF_6NO_3S$ $[M]^+$: 424.9156, found 424.9157.

8.10. Preparation and characterization of *N*-alkenyl compounds **136-150**

(*Z*)-*N*-((*Z*)-2-Chloro-2-phenylvinyl)-2,2,2-trifluoroacetimidoyl iodide (**136**): Under air atmosphere, imidoyl chloride **130a** (160 mg; 0.6 mmol) was dissolved in acetone (1.5 mL) and NaI (268.4 mg; 1.8 mmol) was added. The reaction mixture stirred for 16 h at

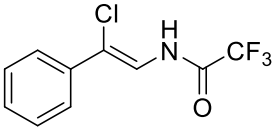
25 °C. The mixture was diluted by 5% solution of $Na_2S_2O_3$ (20 mL), Et_2O (50 mL) was added and two phases were separated. The organic phase was back-extracted with brine (2 × 20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 9:1). Yield: 91%; pale orange oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 2H), 7.50 – 7.43 (m, 3H), 7.07 (q, *J* = 1.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.1, 136.0, 135.4, 131.0, 129.0, 127.5, 116.2 (q, *J* = 276.7 Hz), 115.0 (q, *J* = 42.5 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -69.1 (d, *J* = 1.1 Hz, 3F); HRMS (EI) *m/z* calcd for $C_{10}H_6ClF_3IN$ $[M]^+$: 358.9186, found 358.9189

(*Z*)-*N*-((*Z*)-2-Chloro-2-phenylvinyl)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-imine



(**137**): Under air atmosphere, imidoyl chloride **130a** (107.2 mg; 0.4 mmol) was dissolved in DCM (2 mL) and pyrrolidine (33 μL; 0.4 mmol) followed by triethylamine (728 μL; 0.48 mmol) were added. The reaction mixture turned green/yellow and was heated for 2 h at 50 °C. The mixture was diluted by DCM (20 mL), brine was added and two phases were separated. The organic phase was back-extracted with brine (2 × 20 mL), dried over $MgSO_4$, filtered and evaporated to give a yellow solid. Yield: 91%; yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.63 – 7.57 (m, 3H), 7.38 – 7.32 (m, 2H), 7.30 – 7.24 (m, 1H), 3.69 – 3.62 (m, 4H), 2.04 – 1.90 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5 (q, *J* = 31.2 Hz), 137.8, 129.3, 128.4, 127.7, 126.2, 123.4, 118.4 (q, *J* = 287.9 Hz), 49.3, 25.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -55.7 (br s, 3F); HRMS (EI) *m/z* calcd for $C_{14}H_{14}ClF_3N_2$ $[M]^+$: 302.0798, found 302.0800.

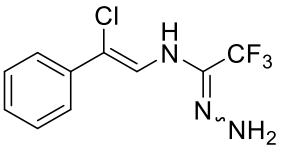
(*Z*)-*N*-(2-Chloro-2-phenylvinyl)-2,2,2-trifluoroacetamide (**138**):



Under air atmosphere, imidoyl chloride **130a** (107.2 mg; 0.4 mmol) was dissolved in DCM (2 mL) and pyrrolidine (33 μL; 0.4 mmol) followed by triethylamine (728 μL; 0.48 mmol) were added. The reaction mixture turned to green/yellow and was heated for 2 h at 50 °C. The mixture was diluted by DCM (10 mL), 1M HCl was added and the mixture was stirred for 30 min at 25 °C. Two phases were separated, the water phase was back-extracted with DCM (2 × 20 mL). The organic phase was collected,

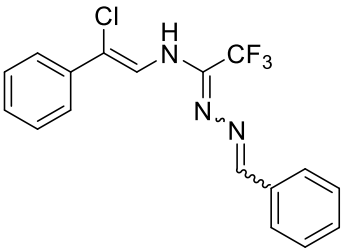
dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 1:1). Yield: 70%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.24 (br d, *J* = 10.7 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.52 (dq, *J* = 10.6, 0.5 Hz, 1H), 7.44 – 7.34 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3 (q, *J* = 38.9 Hz), 134.4, 129.4, 128.9, 126.1, 121.7, 116.4, 115.6 (q, *J* = 287.2 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.0 (s, 3F); HRMS (CI) *m/z* calcd for $C_{10}H_8ClF_3NO$ $[M+H]^+$: 250.0247, found 250.0247.

N-((*Z*)-2-chloro-2-phenylvinyl)-2,2,2-trifluoroacetohydrazonamide (**139**): Under



air atmosphere, imidoyl chloride **130a** (107.2 mg; 0.4 mmol) was dissolved in MeCN (1 mL) and hydrazine hydrate (39 μL, 0.8 mmol) was added. The reaction mixture was stirred 1 h at 25 °C. The mixture was diluted with Et_2O (40 mL), brine (20 mL) was added and the two phases were separated. The organic layer was back-extracted with brine (20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column chromatography (pentane/EtOAc, 7:3). Yield: 80%; white crystalline compound; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.46 (m, 2H), 7.40 – 7.33 (m, 2H), 7.31 – 7.26 (m, 1H), 7.12 (d, *J* = 10.5 Hz, 1H), 6.44 (d, *J* = 9.2 Hz, 1H), 5.04 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 133.7 (q, *J* = 35.6 Hz), 128.8, 128.0, 125.4, 120.5 (q, *J* = 2.6 Hz), 118.9 (q, *J* = 273.9 Hz), 113.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.9 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{10}H_{10}ClF_3N_3$ $[M+H]^+$: 264.05099, found 264.05075.

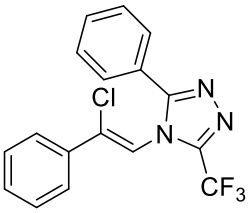
N'-Benzylidene-*N*-((*Z*)-2-chloro-2-phenylvinyl)-2,2,2-



trifluoroacetohydrazonamide (**140**): Under air atmosphere, imidoyl chloride **130a** (107.2 mg; 0.4 mmol) was dissolved in DCE (4 mL) followed by benzylidenehydrazine (96.1 mg; 0.8 mmol) and sodium acetate (65.6 mg; 0.8 mmol) addition. The reaction mixture was stirred for 5 h at 80 °C. The mixture was diluted with Et_2O (40 mL), brine (20 mL) was added and the two phases were separated. The organic layer was back-extracted with brine (20 mL),

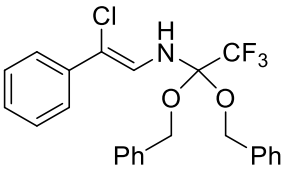
dried over $MgSO_4$, filtered and evaporated. The product was purified by column chromatography (pentane/EtOAc, 97/3). Yield: 64%; yellow crystalline compound; mixture of isomers, major trifluoroacetohydrazonamide form 96%, minor trifluoroacetimidohydrazide form 4%;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 11.9 Hz, 1H), 8.60 (s, 1H), 7.88 – 7.83 (m, 2H), 7.57 – 7.45 (m, 5H), 7.43 – 7.30 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 144.4 (q, *J* = 34.1 Hz), 135.6, 133.7, 132.0, 129.1, 128.9, 128.8, 128.3, 125.7, 119.4 (q, *J* = 3.3 Hz), 118.9 (q, *J* = 275.8 Hz), 115.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.9 (s, 3F, minor trifluoroacetimidohydrazide form 4%), -68.7 (s, 3F, major trifluoroacetohydrazonamide form 96%); HRMS (EI) *m/z* calcd for $C_{17}H_{13}ClF_3N_3$ $[M]^+$: 351.0750, found 351.0752.

(*Z*)-4-(2-Chloro-2-phenylvinyl)-3-phenyl-5-(trifluoromethyl)-4*H*-1,2,4-triazole



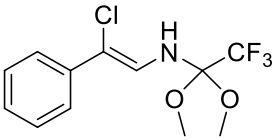
(**141**): Under air atmosphere, imidoyl chloride **130a** (107.2 mg; 0.4 mmol) was dissolved in DCE (4 mL) followed by benzylidenehydrazine (96.1 mg; 0.8 mmol) and sodium acetate (65.6 mg; 0.8 mmol) addition. The reaction mixture was stirred for 5 h at 80 °C. The reaction mixture was cooled to 25 °C, iodine (152.3 mg; 0.6 mmol) was added and the mixture was stirred for next 8 h at 80 °C. The mixture was diluted with Et_2O (50 mL), brine (20 mL) was added and the two phases were separated. The organic phase was back-extracted with brine (20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 75:25). Yield: 42%; yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 2H), 7.61 – 7.57 (m, 2H), 7.54 – 7.43 (m, 6H), 7.20 (q, *J* = 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 145.1 (q, *J* = 39.2 Hz), 142.6, 133.6, 131.4, 131.2, 129.2, 129.1, 128.4, 127.3, 125.6, 118.2 (d, *J* = 271.4 Hz), 115.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.6 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{17}H_{11}ClF_3N_3Na$ $[M+Na]^+$: 372.04858, found 372.04819.

(*Z*)-*N*-(1,1-Bis(benzyloxy)-2,2,2-trifluoroethyl)-2-chloro-2-phenylethen-1-amine



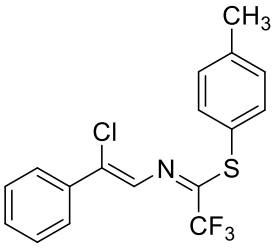
(**142**): Under air atmosphere, imidoyl chloride **130a** (53 mg; 0.20 mmol) was dissolved in benzyl alcohol (205 μL; 1.98 mmol) and K_2CO_3 (273 mg; 1.98 mmol) was added. The reaction mixture was stirred for 2 h at 25 °C, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 70:30). Yield: 85%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.34 (m, 12H), 7.33 – 7.27 (m, 2H), 7.23 – 7.18 (m, 1H), 6.93 (dq, *J* = 11.7, 1.2 Hz, 1H), 4.97 (d, *J* = 11.7 Hz, 1H), 4.87 (d, *J* = 11.9 Hz, 2H), 4.79 (d, *J* = 11.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.7, 136.4, 128.8, 128.5, 128.3, 127.6, 126.8, 124.7, 123.6, 121.8 (q, *J* = 293.3 Hz), 108.7, 101.7 (q, *J* = 33.0 Hz), 65.4 (dd, *J* = 2.7, 1.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.3 (s, 3F); HRMS (ESI^-) *m/z* calcd for $C_{24}H_{20}ClF_3NO_2$ $[M-H]^-$: 446.11401, found 446.11374.

(*Z*)-2-Chloro-2-phenyl-*N*-(2,2,2-trifluoro-1,1-dimethoxyethyl)ethen-1-amine



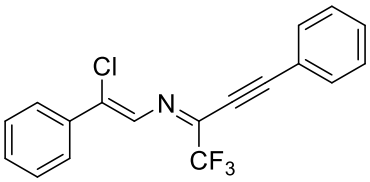
(**143**): Under air atmosphere, imidoyl chloride **130a** (53 mg; 0.20 mmol) was dissolved in methanol (1 mL) and K_2CO_3 (276 mg; 2.0 mmol) was added. The reaction mixture was stirred for 1 h at 25 °C, diluted with Et_2O (10 mL), filtered and evaporated. Yield: 93%; pale yellow oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 2H), 7.35 – 7.28 (m, 2H), 7.23 – 7.18 (m, 1H), 6.86 (dq, *J* = 11.7, 1.2 Hz, 1H), 4.76 (d, *J* = 11.9 Hz, 1H), 3.46 (q, *J* = 1.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8, 128.5, 126.7, 124.7, 123.7, 121.6 (q, *J* = 293.1 Hz), 108.4, 101.4 (q, *J* = 32.6 Hz), 50.5 (q, *J* = 1.5 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -80.48 to -80.54 (m, 3F); HRMS (ESI^-) *m/z* calcd for $C_{12}H_{12}ClF_3NO_2$ $[M-H]^-$: 294.05141, found 294.05090.

p-Tolyl (*E*)-*N*-((*Z*)-2-chloro-2-phenylvinyl)-2,2,2-trifluoroethanimidothioate (**144**):



Under air atmosphere, 4-methylbenzenethiol (54 mg; 0.44 mmol) was dissolved in benzene (0.5 mL) and imidoyl chloride **130a** (116.5 mg; 0.435 mmol), followed by Et_3N (121 μL; 0.87 mmol) addition. During Et_3N addition a precipitate formed and the reaction mixture was stirred for 1 h at 65 °C. The mixture was diluted by Et_2O (40 mL), brine (20 mL) was added and the two phases were separated. The organic phase was back-extracted with brine (20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 75:25). Yield: 82%; yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.53 (q, *J* = 1.1 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.43 – 7.39 (m, 2H), 7.39 – 7.33 (m, 3H), 7.22 – 7.16 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.6 (q, *J* = 37.8 Hz), 140.4, 137.1, 136.1, 134.1, 130.5, 129.9, 129.4, 128.6, 127.0, 124.0, 119.1 (q, *J* = 279.1 Hz), 21.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -66.9 (s, 3F); HRMS (CI) *m/z* calcd for $C_{17}H_{14}ClF_3NS$ $[M+H]^+$: 356.0488, found 356.0488.

(*Z*)-*N*-((*Z*)-2-Chloro-2-phenylvinyl)-1,1,1-trifluoro-4-phenylbut-3-yn-2-imine



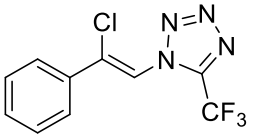
(**145**): The 10 mL screw-cap glass tube, containing imidoyl chloride **130a** (107.2 mg; 0.4 mmol) in dry MeCN (2 mL), was evacuated and back-filled with N_2 three times. Under nitrogen atmosphere, K_3PO_4 (102 mg; 0.48 mmol), phenylacetylene (53 μL; 0.48 mmol) and CuI (7.6 mg; 0.04 mmol) were added. The reaction mixture was stirred for 16 h at 50 °C, diluted with Et_2O (50 mL), brine (20 mL) was added and the two phases were separated. The organic phase was back-extracted with brine (20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 70:30). Yield: 91%; yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.07 (q, *J* = 0.9 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.63 – 7.57 (m, 2H), 7.54 – 7.39 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 138.9 (q, *J* = 38.9 Hz), 136.2, 132.7 (2C), 131.2, 130.6, 128.9 (2C), 127.5, 120.1, 119.3 (q, *J* = 275.8 Hz), 105.1, 78.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.4 (s, 3F); HRMS (CI) *m/z* calcd for $C_{18}H_{12}ClF_3N$ $[M+H]^+$: 334.0604, found 334.0610.

(*Z*)-*N*-((*Z*)-2-Chloro-2-phenylvinyl)-1,1,1-trifluorooct-3-yn-2-imine (**146**): The 10 mL screw-cap glass tube, containing imidoyl chloride **130a** (107.2 mg; 0.4 mmol) in dry MeCN (2 mL), was evacuated and back-filled with N_2 three times. Under nitrogen atmosphere, K_3PO_4 (102 mg; 0.48 mmol), hex-1-yne (55 μL; 0.48 mmol) and CuI (7.6 mg; 0.04 mmol) were added. The reaction mixture was stirred for 16 h at 60 °C, diluted with Et_2O (50 mL), brine (20 mL) was added and the two formed phases were separated. The organic phase was back-extracted with brine (20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 7:3). Yield: 42%; orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (q, *J* = 0.9 Hz, 1H), 7.79 – 7.70 (m, 2H), 7.46 – 7.41 (m, 3H), 2.55 (t, *J* = 7.0 Hz, 2H), 1.71 – 1.60 (m, 2H), 1.57 – 1.45 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 139.4 (q, *J* = 38.3 Hz), 136.1, 132.6, 130.3, 128.7, 127.3, 119.0 (q, *J* = 275.5 Hz), 108.5, 71.4, 29.8, 22.0, 19.5, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.0 (s, 3F); HRMS (CI) *m/z* calcd for $C_{16}H_{16}ClF_3N$ $[M+H]^+$: 314.0929, found 314.0923.

Diethyl (1-(((*Z*)-2-chloro-2-phenylvinyl)imino)-2,2,2-trifluoroethyl)phosphonate (**147**): Under air atmosphere, imidoyl chloride **130a** (107.2 mg; 0.4 mmol) was dissolved in benzene (2 mL) and triethyl phosphite (69 μL; 0.4 mmol) was added. The reaction mixture was stirred for 16 h at 25 °C. The solvents were removed and the product was purified by column flash chromatography (pentane/EtOAc, 75:25). Yield: 75%; yellow oil; Major (*Z*)-isomer form 88%: ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.79 (dq, *J* = 1.8, 0.9 Hz, 1H), 7.81 – 7.76 (m, 2H), 7.48 – 7.39 (m, 3H); (*signal is overlapped with signals from* E *isomer*), 4.31 – 4.15 (m, 4H), 1.38 (td, *J* = 7.0, 0.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.4 (dq, *J* = 158.5, 35.4 Hz), 145.1, 135.7, 131.0, 130.5 (d, *J* = 13.9 Hz), 128.9, 127.7, 120.1 (qd, *J* = 278.2, 44.6 Hz), 64.0 (d, *J* = 6.2 Hz), 16.4 (d, *J* = 5.9 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -68.0 (s, 3F); ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.71 (p, *J* = 8.8, 8.3 Hz); Minor *E* isomer form 12% : ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.91 (qd, *J* = 2.7, 1.5 Hz, 1H), 7.74 – 7.70 (m, 2H), 7.49 – 7.40 (m, 3H); (*signal*

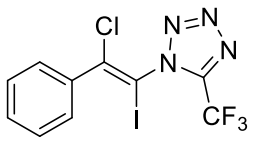
is overlapped with signals from Z isomer), 4.44 – 4.32 (m, 4H), 1.42 (td, *J* = 7.1, 1.0 Hz, 6H); ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.1 (dd, *J* = 8.6, 2.9 Hz, 3F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 2.66 (h, *J* = 7.8 Hz); HRMS (ESI) *m/z* calcd for $C_{14}H_{16}ClF_3NO_3PNa$ $[M+Na]^+$: 392.04006, found 392.03955.

(*Z*)-1-(2-Chloro-2-phenylvinyl)-5-(trifluoromethyl)-1*H*-tetrazole (**148**): Under air



atmosphere, imidoyl chloride **130a** (107.2 mg; 0.4 mmol) was dissolved in MeCN (2 mL) and sodium azide (52 mg, 0.8 mmol) was added. The reaction mixture was stirred for 0.5 h at 25 °C, diluted with Et_2O (20 mL) and water (5 mL). Two phases were separated and the organic phase back-extracted with brine (2 × 40 mL), dried over $MgSO_4$, filtered and evaporated. Yield; 91%. <u>One-pot two steps synthesis</u>: Under air atmosphere, a solution of triazole 1-(perfluoroethyl)-4-phenyl-1*H*-1,2,3-triazole (263 mg; 1 mmol) in DCE (10 mL) was added dropwise into 50 mL round bottom flask containing anhydrous aluminum chloride (1 mmol; 133 mg) and DCE (5 mL). The reaction mixture was stirred for 2 h at 50 °C. The mixture was cooled to 25 °C, NaN_3 (195 mg; 3 mmol) followed by Et_3N (416 μL; 3 mmol) were added and the reaction mixture was stirred for 16 h at 25 °C. The mixture was diluted with Et_2O (150 mL), water (60 mL) was added and the two formed phases were separated. The organic phase was back-extracted with water (2 × 40 mL), brine (40 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (cyclohexane/EtOAc, 8:1). Yield after two steps: 60%; brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.70 (m, 2H), 7.59 – 7.49 (m, 3H), 7.39 (q, *J* = 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.7 (d, *J* = 41.8 Hz), 143.5, 133.2, 132.0, 129.3, 127.5, 117.9 (q, *J* = 272.2 Hz), 114.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4 (s, 3F); HRMS (EI) *m/z* calcd for $C_{10}H_6ClF_3N_4$ $[M]^+$: 274.0233, found 274.0231.

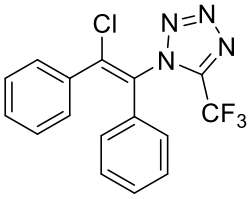
(*E*)-1-(2-Chloro-1-iodo-2-phenylvinyl)-5-(trifluoromethyl)-1*H*-tetrazole (**149**):



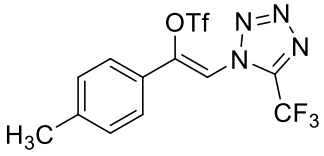
Under air atmosphere, imidoyl chloride (*E*)-(2-chloro-1-iodo-2-phenylvinyl)carbonimidic dichloride (1.45 g; 3.68 mmol) was dissolved in MeCN (12 mL) and sodium azide (479 mg,

7.36 mmol) was added. The reaction mixture was stirred for 0.5 h at 25 °C, diluted with Et_2O (80 mL) and water (30 mL). The two phases were separated and the organic phase was back-extracted with brine (2 × 40 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (pentane/DCM, 1:1). Yield: 88%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.41 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7 (q, *J* = 42.9 Hz), 138.5, 130.7, 129.1, 128.4, 117.6 (q, *J* = 273.3 Hz), 116.9, 105.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.1 (s, 3F); HRMS (APCI) *m/z* calcd for $C_{10}H_6ClF_3IN_4$ $[M+H]^+$: 400.92723, found 400.92716.

(*Z*)-1-(2-Chloro-1,2-diphenylvinyl)-5-(trifluoromethyl)-1*H*-tetrazole (**150**): Under air atmosphere, imidoyl chloride **130n** (13 mg; 0.038 mmol) was dissolved in MeCN (0.5 mL) and sodium azide (4.9 mg, 0.076 mmol) was added. The reaction mixture was stirred for 0.5 h at 25 °C, diluted with Et_2O (20 mL) and water (5 mL). The two phases were separated and the organic phase was back-extracted with brine (2 × 5 mL), dried over $MgSO_4$, filtered and evaporated. Yield: 92%; colorless oil; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.41 – 7.36 (m, 1H), 7.36 – 7.26 (m, 3H), 7.24 – 7.18 (m, 2H), 7.04 – 6.99 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5 (q, *J* = 42.3 Hz), 138.5, 134.7, 132.5, 130.8, 130.1, 129.8, 129.5 (2C), 129.1, 128.9, 117.9 (q, *J* = 272.2 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.3 (s, 3F); HRMS (APCI) *m/z* calcd for $C_{16}H_{11}ClF_3N_4$ $[M+H]^+$: 351.06189, found 351.06152.

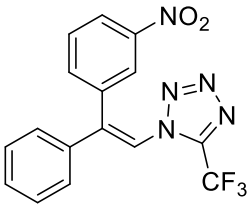


(*Z*)-1-(*p*-tolyl)-2-(5-(trifluoromethyl)-1*H*-tetrazol-1-yl)vinyl trifluoromethanesulfonate (**151**): A *s*olution of trifluoromethanesulfonic acid (17.6 μL; 0.2 mmol) in DCE (1 mL) was added dropwise to a screw-cap glass tube containing a solution of triazole 1-(perfluoroethyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole (**116**) (55.4 mg; 0.2 mmol) in DCE (1 mL). During the addition a suspension was formed. The reaction mixture was stirred for 2 h at 25 °C. $TMSN_3$ (69 mg; 0.6 mmol) and Et_3N (5.5 μL, 0.04 mmol) were added and the mixture was



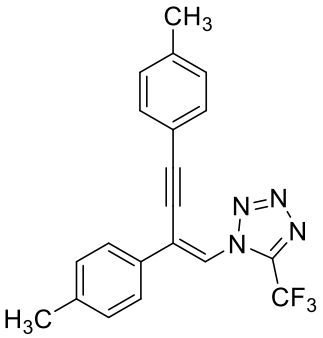
stirred for the next 16 h at 25 °C. Solvents were evaporated and the product was purified by column flash chromatography (cyclohexane/EtOAc, from 9:1 to 5:1). Yield: 92%; white solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 2H), 7.38 – 7.32 (m, 2H), 7.15 (q, *J* = 1.0 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.8, 146.4 (q, *J* = 42.5 Hz), 143.9, 130.4, 127.0, 126.3, 118.1 (q, *J* = 320.8 Hz), 117.9 (q, *J* = 272.4 Hz), 108.6, 21.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.0 (s, 3F), -74.3 (s, 3F); HRMS (EI) *m/z* calcd for $C_{12}H_8F_6N_4O_3S$ $[M]^+$: 402.0221, found 402.0218.

(*Z*)-1-(2-(3-Nitrophenyl)-2-phenylvinyl)-5-(trifluoromethyl)-1*H*-tetrazole (**152**):



Under nitrogen atmosphere, tetrazole **151** (99 mg; 0.36 mmol) was dissolved in THF (1.8 mL) followed by the addition of 3-nitrophenylboronic acid (85 mg; 0.51 mmol) and K_3PO_4 (153 mg; 0.72 mmol). The mixture was cooled down to -100 °C, evacuated and back-filled with nitrogen (3×) and warmed to 25 °C. $Pd(PPh_3)_4$ (41 mg; 0.036 mmol) was added and the reaction mixture was stirred for 24 h at 80 °C. The mixture was diluted with Et_2O (50 mL) and water (20 mL). The two phases were separated, and the organic phase was back-extracted with brine (2 × 20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (cyclohexane/DCM, 55:45). Yield: 61%; brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1H), 7.97 (t, *J* = 2.0 Hz, 1H), 7.56 – 7.44 (m, 4H), 7.39 (ddd, *J* = 7.7, 1.7, 1.1 Hz, 1H), 7.37 – 7.30 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 147.7, 146.3 (q, *J* = 41.8 Hz), 136.8, 136.3, 135.0, 131.1, 130.1, 129.5, 128.5, 124.5, 124.4, 117.9 (q, *J* = 272.2 Hz), 115.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.0 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{16}H_{10}F_3N_5O_2Na$ $[M+Na]^+$: 384.06788, found 384.06812.

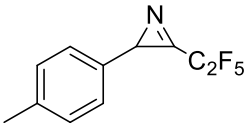
(*Z*)-1-(2,4-Di-*p*-tolylbut-1-en-3-yn-1-yl)-5-(trifluoromethyl)-1*H*-tetrazole (**153**):



Under nitrogen atmosphere, tetrazole **151** (89 mg; 0.22 mmol) was dissolved in THF (1.6 mL) followed by the addition of 4-ethynyltoluene (35 mg; 0.30 mmol) and Et_3N (91.5 μL; 0.66 mmol). The mixture was cooled down to -100 °C, evacuated, back-filled with nitrogen (3×) and warmed to 25 °C. $Pd(PPh_3)_2Cl_2$ (7 mg; 0.01 mmol) and CuI (1.9 mg; 0.01 mmol) were added and the reaction mixture was stirred for 14 h at 25 °C. The mixture was diluted with Et_2O (50 mL) and water (20 mL). The two phases were separated, and the organic phase was back-extracted with brine (2 × 20 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by column flash chromatography (cyclohexane/EtOAc, from 100:0 to 80:20). Yield: 68%; yellow solid; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 2H), 7.41 (q, *J* = 0.9 Hz, 1H), 7.32 – 7.25 (m, 4H), 7.16 – 7.11 (m, 2H), 2.43 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3 (q, *J* = 41.8 Hz), 141.2, 140.5, 132.0, 131.2, 130.8, 129.9, 129.4, 127.2, 118.3, 118.1, 118.1 (d, *J* = 272.1 Hz), 102.7, 81.8, 21.8, 21.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.1 (s, 3F); HRMS (ESI) *m/z* calcd for $C_{20}H_{15}F_3N_4Na$ $[M+Na]^+$: 391.11410, found 391.11387.

8.11. Synthesis and characterization of 3-(perfluoroethyl)-2-(*p*-tolyl)-2*H*-azirine (**155a**)

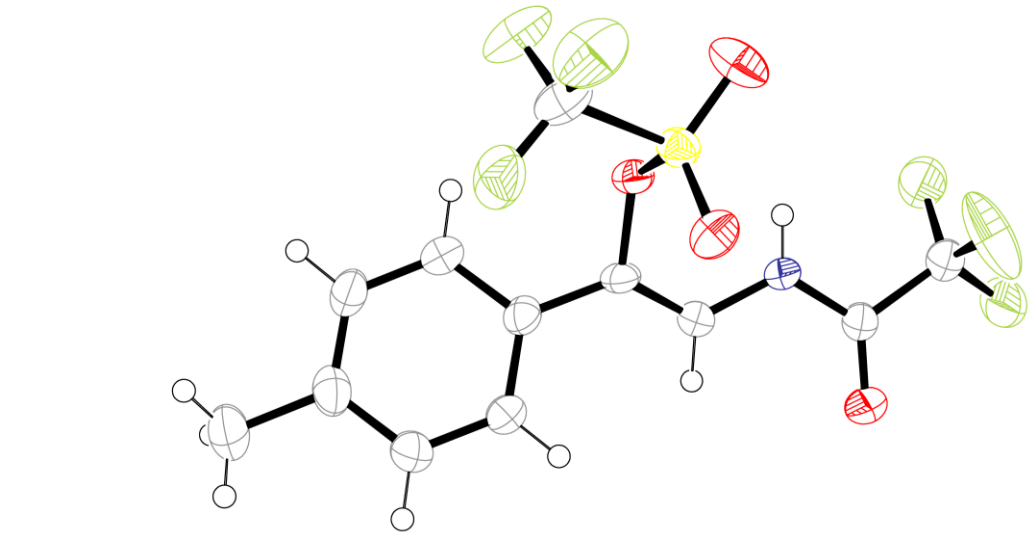
3-(Perfluoroethyl)-2-(*p*-tolyl)-2*H*-azirine (**155a**): The solution of 1-(perfluoroethyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole (**116**) (63.7 mg; 0.23 mmol) in dry DCE (3 mL) was heated under microwave conditions at 150 °C for 40 min (power 150 W). Then DCE was evaporated to give azirine **155a**. Pale yellow oil; yield >98%; ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.19 – 7.13 (m, 2H), 7.08 – 7.03 (m, 2H), 5.68 (t, *J* = 2.6 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.0 (t, *J* = 11.4 Hz), 137.6, 130.1, 126.8, 124.4, 117.7 (qt, *J* = 286.4, 41.5 Hz), 111.6 (tq, *J* =265.6, 39.4 Hz), 64.9, 21.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.8 (s, 3F), -96.7 (d, *J* = 2.6 Hz, 2F); HRMS (CI) *m/z* calcd for $C_{11}H_9F_5N$ $[M+H]^+$: 250.0655, found 250.0654.



8.12. Crystallographic data

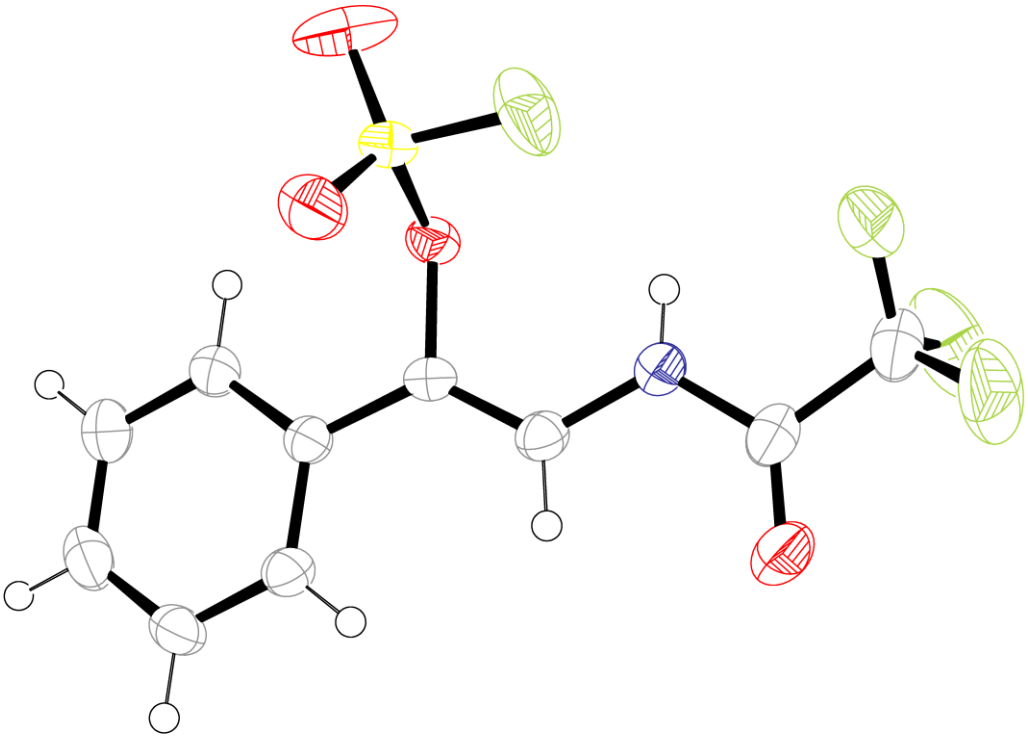
Single-crystal diffraction data of **117a**, **120a** and **130a** were collected on Xcalibur PX diffractometr with monochromatized $Cu_{K\alpha}$ radiation (λ=1.54180 Å) at 180K. CrysAlisProCCD[176] was used for data collection, cell refinement and data reduction. The structure was solved by direct methods with SIR92[177] and refined by full-matrix least-squares on F with CRYSTALS.[178] The positional and anisotropical thermal parameters of all non-hydrogen atoms were refined. All hydrogen atoms were located in a difference Fourier map, but those attached to carbon atoms were repositioned geometrically and then refined with riding constraints.

(*Z*)-1-(*p*-Tolyl)-2-(2,2,2-trifluoroacetamido)vinyl trifluoromethanesulfonate (**117a**) (0.10 x 0.12 x 0.40 mm)**:**



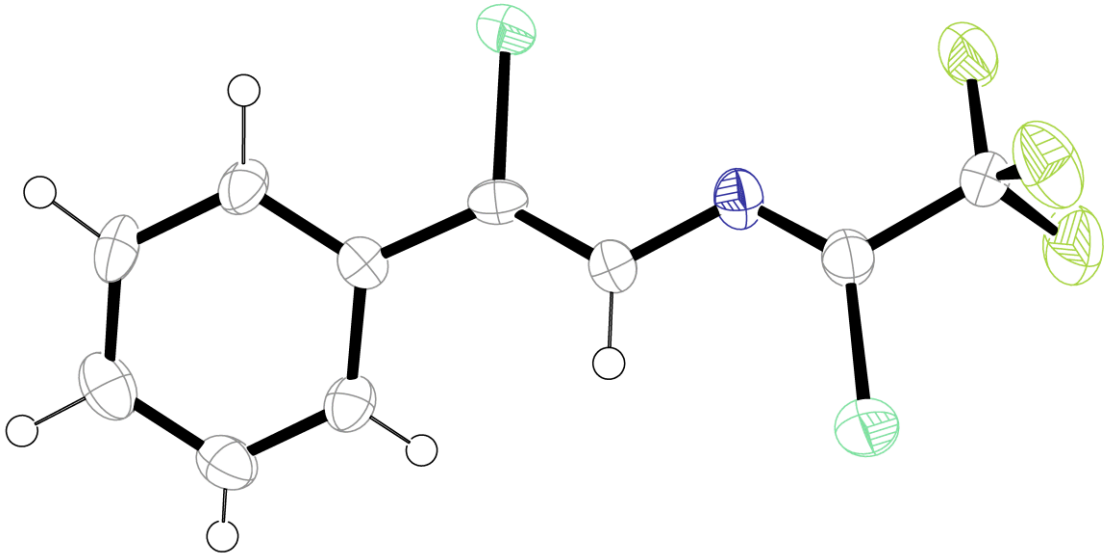
$C_{12}H_9F_6N_1O_4S_1$, monoclinic, space group $P2_1/c$, a = 4.7550(3) Å, b = 17.4603(12) Å, c = 17.8004(12) Å, β = 90.058(4)°, V = 1477.85(17) Å^3, Z = 4, M = 377.26, 13588 reflections measured, 2592 independent reflections. Final R = 0.049, wR = 0.036, GoF = 1.120 for 2063 reflections with $I > 2\sigma(I)$ and 245 parameters. One of the trifluoromethyl groups was found to be disordered over two positions (site occupation factors being 0.827 and 0.173). In consequence, several restraints were used to regularize the thermal motion of the disordered fluorine atoms. CCDC 1899950.

(*Z*)-1-Phenyl-2-(2,2,2-trifluoroacetamido)vinyl sulfurofluoridate (**120a**) (0.25 x 0.30 x 0.31 mm)**:**



$C_{10}H_7F_4N_1O_4S_1$, monoclinic, space group $P2_1/n$, a = 7.2020(5) Å, b = 7.2010(5) Å, c = 23.3184(15) Å, β = 90.2113(13)°, V = 1209.32(14) Å^3, Z = 4, M = 313.23, 10864 reflections measured, 2079 independent reflections. Final R = 0.044, wR = 0.049, GoF = 1.105 for 2079 reflections with $I > 2\sigma(I)$ and 182 parameters. CCDC 1899949.

(*Z*)-*N*-((*Z*)-2-Chloro-2-phenylvinyl)-2,2,2-trifluoroacetimidoyl chloride (**130a**) (0.048 × 0.058 × 0.544 mm)**:**



$C_{10}H_6Cl_2F_3N_1$, orthorhombic, space group $Pca2_1$, a = 6.4038(3) Å, b = 7.2700(3) Å, c = 23.6287(9) Å, V = 1100.05(4) Å^3, Z = 4, M = 268.06, 11440 reflections measured, 1852 independent reflections. Final R = 0.054, wR = 0.043, GoF = 1.084 for 1596 reflections with $I > 2\sigma(I)$ and 146 parameters. Flack parameter x = 0.12(2). CCDC 2042463.

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