**The hydroamination of TIPS-C ≡ C-SF₅ - A bench-top route to pentafluorosulfanylated enamines**

Jonas O. Wenzel†[a], Fabian Jester[a], David Rombach*[a]

---

**Abstract:** Synthetic access to a variety of aliphatic and vinylic pentafluorosulfanylated building blocks remains a major challenge in contemporary organofluorine chemistry hampering its investigation in the context of medicinal chemistry, agrochemistry and functional materials. Herein, we report a bench-top protocol to access the virtually unknown class of α-SF₅-enamines under rather benign reaction conditions. This reaction combines the protodesilylation of the commercially available precursor TASP with the in-situ hydroamination of HC≡C-SF₅. The on-site use of highly toxic gases is avoided, granting access to α-SF₅-enamines to conventional labs. Furthermore, employing a combined experimental and computational approach, we revealed a two-step cascade reaction. The excellent E-diastereoselectivity of the reaction is suggested to be the result of the convergence of the fast Z/E-isomerization of a vinyl anion as well as the isomerization of the iminium ion in the equilibrium. The remarkable thermal stability of these SF₅-enamines encourages further studies of their synthetic utility.

**Introduction**

Since its initial discovery in the 1950s, the pentafluorosulfanyl (SF₃) group has been proposed as a promising structural motif for applications in medicinal chemistry,[1] and functional materials.[2] For instance, the strongly lipophilic SF₃ moiety is suggested to act as a bioisosteric replacement of CF₃, tBu, NO₂, or halogen substituents and is therefore expected to have important indications for modern drug discovery.[18] Despite of the increasing interest in organic molecules bearing the SF₃ group,[3] the synthesis of small non-aromatic SF₅ building blocks remains challenging due to the lack of broadly applicable and robust synthetic methodology available. In 2012, Umemoto et al. reported the chlorofluorination of aromatic disulfides by C₅F₆ in the presence of KF to access the corresponding SF₅Cl compounds, advancing the chemical space of accessible aromatic SF₅ compounds. Later this protocol was expanded to the use of TCICA, employing gas-reagent free conditions.[4] Recently, a variety of innovative solutions have been developed to circumvent the problem of accessibility of vinyl- and alkyl SF₅ compounds, comprising the single electron activation of SF₅Cl,[3c, 3e, 5] or the in-situ generation of SF₅Cl from SF₅ by TCICA and KF or SF₅.[6] Despite these novel approaches, the general dependence on the use of the highly toxic mixed sulfur fluorides SF₅Cl or SF₅Br hampered non-aromatic SF₅ building blocks from being explored.

In this light, the increased inclusion of SF₅ arenes into routine screening processes in modern academic and industrial research programs seems to be largely attributable to commercial availability of prefunctionalized aromatic SF₅-building blocks.[7] The recent progress in fundamental methodology enabled the commercialization of these compounds, which ultimately relieved the experimentalist from the burden to employ hazardous or synthetically challenging fluorination or pentafluorosulfanylation chemistry on-site. However, this process so far is limited to SF₅-containing arenes, while alkyl- and vinyl analogs are still perceived as chemical curiosities due to the lack of commercially available pentafluorosulfanyl building blocks as well as missing methodology to avoid the use of highly toxic gaseous reagents.[8] This consideration inspired us to analyze the commercial availability of such reagents and to think about potential valorization.

In order to explore a commercially available, bench-stable SF₅-containing precursor in 2019 we found triisopropyl acetylene sulfur pentafluoride (TASP or 1) (air-stable, tolerates ambient conditions, liquid, bp: 35°C at 0.6 mmHg) to be a promising precursor for SF₅ chemistry. Despite observing temporarily delivery bottlenecks, the material generally was available in reasonable quantities from different suppliers (> 25 g), allowing for detailed reactivity studies of 1. We also have been in touch with commercial suppliers to improve its supply in the future. This reagent is reasonably cheap (30 €/mmol) and the liquid can routinely be handled under atmospheric conditions.

---

Department of Chemistry and Applied Biosciences  
ETH Zürich  
Vladimir-Prelog-Weg 2, CH-8093 Zürich, Switzerland  
E-mail: david.rombach@kit.edu  
Supporting information for this article is given via a link at the end of the document.
A more detailed analysis of literature revealed that today TASP exclusively had been investigated in the context of cycloaddition reactions.\[9\] Interestingly, even reports on the parent compound HC \(\equiv\) C-SF\(_5\) (2) in the context of synthetic organic chemistry remain scarce mainly covering cycloaddition reactions\[9a, 10\] as well as its deprotonation.\[11\] Furthermore, the addition of SF\(_5\)Br\[12\]fluoride abstraction by Lewis acids to access sulfuranonium ions,\[13\]the formation of dicyclobutatetrahedran \[\text{as well as its}\] trimerization to 1,3,5-(pentafluorosulfanyl)benzene have been reported.\[14\] This situation is even more astonishing since preliminary studies by Hoover and Coffman on the parent acetylene sulfur pentafluoride, reported as early as in 1969, already hinted on a more widespread chemistry based on its electronic properties. In this work the authors showcased the addition of methanol to the free acetylene under strongly basic conditions.\[10c\]

Herein, we disclose the initial stage of our discovery of unexplored modes of reactivity of TASP (1). Our initial considerations were focused on the negative hyperconjugation of the SF\(_5\) group, which adds some \(\pi\)-accepting properties to the structural motif. While the low-lying \(\sigma\)\(_{SF}\) orbitals are responsible for the low stability of the corresponding enolates, we became curious in exploiting the reactivity enabled by this unique feature.\[15\] We therefore anticipated TASP (1) to be a precious precursor to access the corresponding enamines by an unprecedented \textit{in situ} deprotection/hydroamination sequence parallaling the reactivity of conventional \(\pi\)-acceptors. The spontaneous addition of secondary amines to alkynes trace back to 1899, when Ruhemann reported the violently exothermic reaction between diethylyamine and diethylacetylene dicarboxylate.\[16\] In the aftermath this approach has been generalized to a broad variety of \(\pi\)-acceptor substituted alkynes like carbonyls,\[17\]sulfonfylated functional groups\[17b, 18\], phosphonates\[19\] or phosphate oxides.\[20\] This mode of reactivity has been widely exploited in sequence-controlled synthesis of polymers.\[21\] In contrast, the uncatalyzed addition of amines to non-\(\pi\)-acceptor substituted alkynes at room temperature has been described scarcely and is only applicable to intramolecular cyclization reactions.\[22\] The general reactivity and use of SF\(_5\)-alkynes in organic synthesis has recently been reviewed by Bizet.\[23\] In 2021, the base catalyzed hydroamination of (2-aminoaryl)-substituted SF\(_5\)-acytlenes based on 5-endo-dig cyclization to access to corresponding 2-SF\(_5\) substituted indoles has been reported.\[24\] Further hydrofunctionalization reactions comprise the gold-catalyzed hydrofluorination and hydration of SF\(_5\)-acetylenes.\[25\] Fascinated by the so far out of reach \(\alpha\)-SF\(_5\)-amine motif and the potential impact of a method to access this class of molecules, we became interested in the hydroamination of 2 starting from 1. This elusive motif has not conclusively been described so far. To the best of our knowledge, the only reports of the putative existence of \(\alpha\)-SF\(_5\)-amines trace back to the reports of Welch investigating the stereochemical control by the SF\(_5\) group in 2013 and 2018. Herein, the formation of two putative enamine species were suggested, which were either not or only tentatively described NMR spectroscopically (see Fig. 1c).\[26\]

In general, \(\alpha\)-SF\(_5\)-carbonyl chemistry is hampered by the low stability of the corresponding enolates and their known derivatives. A limited number of reports are available on the chemistry of labile SF\(_5\) enolates by Seppelt, Carreira as well as Röschenthaler and Fokin, by harnessing the Ti- or B-enolates (see Fig. 1a).\[26-27\] While these methods represent precious and creative tools in synthetic chemistry, they are based on multistep downstream processing of the corresponding SF\(_5\)-Carbonyl compounds prepared from the on-site addition of SF\(_5\)Cl to vinyl ethers or esters. A general approach to unsubstituted SF\(_5\) carbonyl derivatives is therefore highly desirable to generally access the toolbox of carbonyl chemistry. Enamines are key to many synthetic strategies to access heterocycles or complex molecules, employing fundamental carbonyl chemistry. Furthermore, a wide variety of transformations is known for enamines including \(\alpha\)-alkylation, -acylation, -halogenation,\[28\]Robinson-type annelation\[29\] as well as oxidative coupling reactions.\[30\] Ultimately the use of chiral secondary amines paired with organocatalysis or photoexod catalytic SOMO-catalysis enables for their use in asymmetric synthesis.\[31\] Herein, we report a protocol for the hydroamination of commercially available 1 to access \(\alpha\)-SF\(_5\)-enamines under bench-top conditions with high diastereoselectivity, short reaction times and minimal preparative requirements.

Figure 1. a) Overview of commercially available reagents to access aromatic and aliphatic/vinyl SF\(_5\) containing motifs. b) Hydroamination of 1 to access the corresponding enamines (this work). c) Observation of the putative morpholine enamine by Welch.
Results and Discussion

We started our investigations by an initial addition of 1.50 eq. of pyrrolidine (3) to a solution of TIPS-C≡C-SF₅₂⁻ (TASP, 1) at ambient temperature in CDCl₃ which did not show any reactivity after 10 min according to ¹⁹F NMR spectroscopy. However, after 15.5 h at room temperature a new SF₅₂⁻-species was observed. Interestingly, the apical fluoride substituent was found to resonate in an untypical chemical shift range at δ = 96.7 ppm (p) respectively 75.3 ppm (dd) in ¹⁹F NMR spectroscopy. Both, the apical fluoride substituent (comp. alkynes ~80–87 ppm) as well as the equatorial in-plane fluoride substituents (comp. alkynes 59–66 ppm) were found to experience a strong deshielding effect of about 10–15 ppm indicating an unexpected low electron density at the position of the fluoride atoms.¹³¹ NMR spectroscopic analysis based on 1D and 2D correlation experiments indeed indicated the formation of the previously undescribed secondary enamine 4-E (see Fig. 1b). The debated spectroscopic signatures of the putative assignment of primary alkynes are partially aligned for the F₅⁺ but deviate for F₅⁻ from the NMR spectroscopic signatures of the secondary enamines isolated in this work. Thrilled by the unusual ability of the amine to deprotect the acetylene in situ, a careful analysis of the ¹⁹F NMR spectrum revealed the partial degradation of the SF₅₂⁻ moiety under formation of the very strong Si-F bond resulting in the formation of TIPS-F (5).

An initial screening of reaction conditions revealed the beneficial effect of polar aprotic solvents on the reaction times, shortening the reaction times to < 1 h. Based on the initially observed formation of TIPS-F (5), we started our screening considering the addition of an external fluoride source to suppress this side reaction. Mixing the alkyn with 1.00 eq. of tetra-n-butylammonium fluoride (TBAF) as well as 1.00 eq. of pyrrolidine 3 at -78 °C in CH₂Cl₂ showed immediately deep brown colorization of the reaction mixture and formation of 4-E in 37% ¹⁹F NMR yield after 50 min. An increase of the pyrrolidine concentration to 1.70 eq. finally revealed an increased yield of the putative assignment of primary enamines are partially indicated the formation of the previously undescribed secondary enamine 4-E (see Fig. 1b). The debated spectroscopic signatures of the putative assignment of primary enamines are partially aligned for the F₅⁺ but deviate for F₅⁻ from the NMR spectroscopic signatures of the secondary enamines isolated in this work. Thrilled by the unusual ability of the amine to deprotect the acetylene in situ, a careful analysis of the ¹⁹F NMR spectrum revealed the partial degradation of the SF₅₂⁻ moiety under formation of the very strong Si-F bond resulting in the formation of TIPS-F (5).

We therefore hypothesized that a fast trapping of an initially formed acetylide anion 6 might be critical to avoid detrimental polymerization of the said acetylide 6. Indeed, a second screening showed the beneficial effect of the addition of a proton source to scavenge primarily formed acetylide anion 6. The addition of 2.00 eq. of acetic acid (10) caused a dramatic increase of the yield of the enamine from 33% to 83%. Further increase of the acidity of the proton source, employing formic acid, TFA, HBF₄·EtO or H₂SO₄ turned out to be detrimental to the yield of the reaction. Next, screening of TBAF equivalents showed optimized reaction conditions using 1.00 eq. of an external fluoride source. Remarkably, a screening of fluoride sources revealed that TBAF, CsF or even KF was tolerated without any significant reduction of the yield of the reaction (see ESI). In contrast, we found a strong dependence on the temperature of the addition aligned with reduced yields on upscaling of the reaction. When upscaling the reaction by a factor of 10 the strong heat formation of the vigorous reaction resulted in a significant decrease of the yield of 4-E under standard conditions (36%). These findings indicated a strong dependence on the effectiveness of heat dissipation on the course of the reaction. To proof this hypothesis, we carried out the same reaction under cooling at -11°C. To our surprise a tremendous increase of yield of 4-E to up to 91% was observed. However, initially the method suffered from severe reproducibility issues. While investigating these issues, we found a strong influence of the elapsed time between deprotection of the alkyn and addition of the secondary amine. While product 4-E was afforded in 90% yield adding the amine immediately after the deprotection, its yield dropped rapidly to 67% after 10 min incubation and after 15h only 32% of product formation was observed. This background reaction of 2 in the absence of the amine was also confirmed by IR-spectroscopy (see ESI).

Furthermore, we realized a pronounced influence of the quality of TBAF employed in the reaction, showing a reduction of the yield of 4-E if fresh TBAF solution (1M in THF) was employed. A screening of the influence of tributylamine and water to the reaction, which were anticipated to be the main contaminants of altered TBAF solutions revealed that the presence of 5% tributylamine or water increased the yield significantly and suppressed the formation of side products. This is suggested to be caused by the role of water as acid catalyst during the scavenging of the acetylide. Interestingly, a control reaction to reveal a potential catalytic role of trialkylamines, confirmed that preformed putative vinylc triethylammonium salt 11 (NEt₃·3HF and 1) was converted to 4-E after addition of pyrrolidine. Finally, we found optimized reaction conditions by subjecting a solution of 1 to deprotection by the fluoride source (1.00 eq.) in the presence of 2.00 eq. of acetic acid and fast addition of the amine (1.70 eq.) at about -20 °C. Under these conditions the formation of the colorful side product was strongly suppressed, and 4-E was formed in up to 91% ¹⁹F NMR yield in 5 min.

Next, we turned to an investigation of the substrate scope of the reaction. A broad variety of functionalized secondary amines including alkynes (30, 31), alkynes (27), sulfur (25), oxygen (18) and nitrogen (16,17,32) containing heterocycles, acetal and ethers (33) could be subjected to the reaction conditions (see Fig. 2). Furthermore, several approved drugs and drug-like molecules, namely amoxapine, paroxetine, nortripylamine and sertralin (34-37, yellow) were confirmed to deliver the corresponding enamines in moderate to good yields (25% - 73%). Limitations of the method have been found using primary amines,
which formed a complex mixture of products under the reaction conditions. Furthermore, anilines did not undergo reaction due to their low nucleophilicity. In case of sterically demanding secondary amines, the use of 4.00 eq. of amine turned out to be beneficial to improve the yield of the reaction.

With optimal reaction conditions in hands, we aimed to develop a suited purification protocol. While the products did not tolerate conventional column chromatography purification on Silica, eventually we found conditions to purify the sensitive aldehyde enamines by column chromatography using pre-incubated aluminum oxide (EtOH:cyclohexane = 1:1 (1% NEt₃)) to protect the enamines from decomposition. If the deactivation of the column material had been neglected, the partial formation of the corresponding sulfonyl fluoride was observed due to hydrolysis of the pentafluorosulfanyl group. Remarkably, we found the SF₅-enamines to be surprisingly stable under storage even in MeCN or CDCl₃ solution under ambient conditions in the dark. For most of the compounds no significant decomposition was observed after storage for 7 months at -20 °C in the NMR solvent.

To get a more detailed insight into the operating reaction mechanism we relied on a combined experimental and in-silico approach. Incubation of 1 with CH₃COOH (10) in MeCN-d₅ did not show any reaction after 15 h at room temperature, excluding the acid as the primary desilylation agent. As expected, IR and NMR spectroscopic analysis revealed the deprotection of 1 by TBAF to be completed within few seconds. A combined ¹⁹F NMR as well as IR spectroscopic study employing dibenzylamine 39 as the nucleophile in the absence of fluoride, confirmed a stepwise reaction mechanism first protodesilylating 1 under formation of 2, followed by hydroamination of 2 by the amine (see Fig. 3b & 3c). An initial induction period of the deprotection of the starting material by dibenzylamine hinted on an autocatalytic reaction. The length of this induction period was found to be a function of the amine concentration, confirming an involvement of the amine in the deprotection step. While silylamines experience a strong increase in nucleophilicity, the steric bulk of the TIPS group let us exclude any involvement of initially formed TIPS-pyrrolidine (42) as nucleophile. Due to the presence of TIPS-F (5) formed by decomposition of 1, we considered an interaction of the SF₅-group of 1 with 3-TIPS leading to TIPS-F (5) and a strongly nucleophilic pyrrolidinide anion 40. Both hypotheses have been excluded by the lack of any reactivity incubating 1 with TIPS-pyrdinoline (42). These results left us with two plausible mechanistic proposals causing the observed autocatalytic behavior. First, the...
fragmentation of methylene tetrafluorosulfanyl compound 7 to SF₄ in the presence of small amounts of water might form several fluoride anion equivalents accelerating the deprotection of 1. Secondly, the overall consumption of protons by protonation of the acetylide anion reduces the pH of the solution, shifting the pyrrolidinium/pyrrolidine equilibrium towards the free base which is suggested to be the critical species for the deprotection process in the absence of fluoride. To challenge this hypothesis, a potential participation of the pyrrolidinium salt has been investigated by a control reaction subjecting 3 (2.00 eq.) to HNTf₂ (2.00 eq.). After addition of 1 (1.00 eq.) no reactivity was observed over a period of 15 h. Furthermore, TIPS-OAc (41) has been shown to be formed by silyl transfer from TIPS-pyrrrolidine (42) in the presence of CH₃COOH (10). These data indicate a catalytic deprotection mechanism under formation of 42 which is discharged by acetic acid in the reaction mixture to reform the free amine and TIPS-OAc (41) which is suggested to act as sink of the TIPS group in the absence of fluoride anions (Fig. 4 Top). Secondly, enamine formation only ramps up after a significant build-up of the free alkyne, excluding a mechanism initiated by the direct addition of 3 to the terminal carbon center of the acetylene 1 (see Fig. 3C). Another remarkable conclusion was drawn studying the deprotection step in the presence of an external fluoride source. When HF was quantitatively generated in-situ by subjecting CsF with HNTf₂ or triflic acid, no deprotection of 1 was observed at all after 1 h, once more highlighting the necessity of free fluoride anions in the reaction mixture which is intrinsically compromised by the essential requirement of a proton source to trap the reactive intermediates. These findings indicate the thin line of reaction conditions suitable for this cascade reaction to proceed efficiently.

Next, we turned our attention to the source of the transferred α-proton of 4-E and the role of TBAF in the deprotection step by a series of ¹³C NMR experiments including ¹H-²D-permutations of acetonitrile and acetic acid. Surprisingly, in the all-deutero experiment still a large amount of ¹H-acetylene was observed, indicating a Hofmann elimination of the tetrabutyl ammonium (TBA) cation 43. Substitution of TBA to tetramethyl ammonium fluoride in the presence of acetic acid-d₃ caused almost full formation of deuterated acetylene as monitored by ¹³C NMR spectroscopy showcasing CD₃COOD to be the predominant proton source (see Fig. 3A).

To get more insights into the operating reaction and to explain the excellent diastereoselectivity, we supplemented our experimental work with an in-silico study (see Fig. 4). We started our investigation with a thermodynamic analysis of the influence of the more bulky SF₅ group on the relative stability between Z- vs. E-isomers (4-Z and 4-E) by 1.4 kcal/mol compared to the carboxylic ester homologues (see ESI) investigated by Tang.[21b] This effect is suggested to be due to higher steric repulsion between the SF₅ group and residues of the amine. A detailed
analysis of the proposed reaction mechanism indicated a very low barrier for the attack of pyrrolidine on \( \pi \)-acceptor of \( \Delta G^\ddagger = 8.1 \text{ kcal/mol} \) via TS-1 to form the twitter ion 44-Z (\( \Delta G^\ddagger_{\text{trans}} = 0.3 \text{ kcal/mol} \)) compared to 44-E via TS-2 (\( \Delta G^\ddagger = 8.4 \text{ kcal/mol} \)). This indicates a 1.7-fold faster formation of the Z-configured twitter ion 44-Z. The distinct E-diastereoselectivity of the reaction therefore cannot be explained by the difference in transition state energies of the primary attack on the free alkyne. Astonishingly, we found a remarkable stability of the primarily formed twitter-ions 44-Z and 44-E, rendering the primary attack of the amine virtually irreversible. A potential interconversion of 44-Z to the thermodynamically more stable trans-twitter ion (44-E) via TS-3 (\( \Delta G^\ddagger = 23.1 \text{ kcal/mol} \), \( t_{1/2} = 2.7 \text{ h} \)) was found to be too high to be overcome under the reaction conditions even if local overheating is considered a throughout E-selectivity cannot be justified. Similarly, the interconversion of the putative primary reaction product 4-Z by a twist-mechanism (see Fig. 4; T5S) turned out to be inaccessible (\( \Delta G^\ddagger = 27.0 \text{ kcal/mol} \), \( t_{1/2} = 81 \text{ days} \)) under the reaction conditions.

We therefore considered two more mechanistic proposals to reveal the origin of stereoselectivity of the reaction. An investigation of the acidity of twitter-ion (44-Z) revealed a slightly lower pKa than \( \text{CH}_3\text{COOH} \) resulting in an equilibrium constant of \( K = 3.8 \times 10^3 \) with acetate to form the corresponding anion (45-Z) and acetic acid. However, this anion formation was found to be too high to be accessible (\( \Delta G^\ddagger = 26.4 \text{ kcal/mol} \)). After reprotonation, 4-E is suggested to be consequently formed as the observed net reaction product.

Additionally, we considered the enamine/iminium equilibrium and a consecutive rotation of the N-C-C-single bond of the iminium ion a suitable reaction pathway for configurational exchange. Enamine 4-Z was found to be in low concentrations in equilibrium with a pre-assembled acetic-acid complex 52 with \( K = 1.2 \times 10^5 \text{ mol}^{-1} \text{L}. \) The barrier for proton transfer of this assembly via TS-6 was found to be easily overcome at room temperature (\( \Delta G^\ddagger = 8.1 \text{ kcal/mol} \), \( t_{1/2} = 97 \text{ ns} \)) to form iminium ion 46 (\( \Delta G^\ddagger_0 = 8.7 \text{ kcal/mol} \)) with \( K_0 = 4.2 \times 10^7 \) opening a window for bond rotation and loss of a proton to form 4-E.

An intramolecular proton transfer of 44-E, previously suggested for the propiolic ester, was found to require the passage of an unreasonably high barrier via TS-10 (\( \Delta G^\ddagger = 26.4 \text{ kcal/mol} \)) due to strong solvent stabilization of 44-E/44-Z. We therefore suggest a main protonation pathway based on an intermolecular pathway and exclude a significant contribution of an intramolecular proton transfer. (see Fig. 4 Top)

However, as described above our experimental data also suggest an involvement of the acetate anion after liberation of free acetylene 2 under formation of an enol acetate 47-Z/47-E. Indeed, acetate anion 48 was found to be able to slowly undergo direct addition to the acetylene at room temperature via TS-6 (\( \Delta G^\ddagger = 17.1 \text{ kcal/mol} \)) to form vinyl anion 49-Z while the corresponding TS-7 (\( \Delta G^\ddagger = 22.4 \text{ kcal/mol} \)) connected to 49-E was found to be significantly higher in energy. While these data clearly show that the acetate anion 48 can form the vinyl acetate over 1 h as observed experimentally, due to the very different rate constants compared to the attack of 3, a significant contribution of the two-step mechanism via a vinyl and consecutive substitution by 3 only seems to be important during the initial phase of the deprotection period in the presence of a significant amount of protonated pyrrolidine 3-H. This is also aligned with a \(^{19}\text{F} \) NMR spectroscopic investigation proving that the formation of side products exclusively happens during the initial phase of the reaction, namely during the deprotection step. Furthermore, a control experiment in the absence of a secondary amine revealed the addition of TIPS-OAc 41 being capable of suppressing the formation of acetyl fluoride 50, a central loss channel of the starting material. However, incubating this reaction mixture for 13 h at room temperature showed decomposition of the vinyl acetate and the build-up of acetyl fluoride. We therefore suggest that the decomposition of the SF₅ group is mainly induced by two mechanisms: (I) the direct decomposition of the acetylide anion 46 and (II) by the nucleophilic deacylation of a transiently formed vinyl enol acetates 47-Z/47-E liberating an enolate anion 51, which decomposes under formation of a deoxygenating species.

**Conclusion**

In conclusion, we report a robust and facile bench-top protocol that allows reliable access to the so far elusive class of \( \alpha \)-pentafluorosulfanylated enamines in moderate to excellent yields from commercially available trisopropylsilyl acetylene sulfur pentafluoride (TASP or 1) under bench-top conditions in very short reaction times. This very versatile motif in organic chemistry has so far only been described as a putative side product relying on the necessity to employ SF₅Cl on-site.
Figure 4. Top: Scheme of potential reaction pathways investigated and suggested viable reaction pathways. Bottom: Calculated energies along the reaction coordinate from 1 and pyrrolidine to cis and trans configured enamine 4. Energies have been calculated on the DLPNO-CCSD(T)/M062X/6-311++G(d,p)/CPCM level of theory. All energies are given in kcal/mol.
We want to highlight that the commercially available trisopropylsilyl acetylene sulfur pentafluoride (TASP) can be used as a precious precursor to access unprecedented pentaffluorosulfanylated motifs, playing a central role in synthetic organic chemistry, under bench-top conditions. We predict this reagent being capable of opening-up a more widespread use of vinyl and aliphatic SF$_5$ containing molecules in the future. This method tolerates a variety of functionalized secondary amines and is highly robust towards ambient conditions. The yielded enamines are surprisingly stable and have been isolated and characterized. Furthermore, we shone light on the operating reaction mechanism revealing a cascade of a protodesilylation and hydromamination on the edge of decomposition of the primarily formed acetylide anion. The observed excellent E-diastereoselectivity could be attributed to the convergence of two alternative pathways starting from an initially Z-configured twitter ion, the isomerization of the vinyl anion or the formation of an iminium ion. This work complements the reported cycloaddition reactivity of TASP by its ability to parallel the reactivity of classical n-acceptors. This method adds to the toolbox of modern pentaffluorosulfanyl chemistry by allowing the downstream processing of a commercially available non-aromatic building block to access the central structural motif of enamines. The separation of the addition step of SF$_5$Cl to industrial suppliers will significantly broaden the accessibility of small SF$_5$-containing motifs to conventional chemistry or even biochemistry laboratories in the future, rendering the on-site use of highly toxic gaseous sulfur fluorides reagents or the employment of strictly inert conditions superfluous. We are hopeful that this work will catch-up with the broader use of commercially aromatic building blocks.

**Acknowledgements**

Financial support by the Swiss National Science Foundation (SNSF grant number: CRSK2_198683) and ETH Zürich is gratefully acknowledged. We thank Prof. Dr. Antonio Togni for continuous support of this work, financial support and for fruitful scientific discussions. D.R. thanks Prof. Dr. Hans-Achim Wagenknecht for his continuous and generous support. D.R. furthermore thanks Prof. Erick M. Carreira for generous support as well as hosting and financial support. J.O.W. thanks the FCI for generous financial support by a Kekulé scholarship. We thank Prof. Dr. Frank Breher for kindly sharing his glovebox infrastructure as well as his continuous support of this work. We thank Prof. Dr. Hans-Jörg Grützmacher for his kind support and for sharing his IR spectroscopy infrastructure. Furthermore, we thank Prof. Bill Morandi for kindly sharing his infrastructure and for granting glovebox access. We want to thank the mass spectrometric department of ETH Zürich, namely Luis Bertschi and Michael Meier. We thank Nils Trapp and Michael Solar for their kind support with SC-XRD measurements and Luis Santos Correa for GPC measurements. We thank Manuel Schupp and Dr. Tim Schober for fruitful discussions and support during preparation of this manuscript.

**Keywords:** pentaffluorosulfanyl group • hydromamination • organofluorine chemistry • enamines • acetylene.
