CONTRIBUTION FOR:**ELECTRONIC ENCYCLOPEDIA OF REAGENTS FOR ORGANIC SYNTHESIS****Pentafluorosulfanyl chloride (13780-57-9)****(First Update)**

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Compounds featuring the SF₅ motif stand out through their remarkable chemical properties that include outstanding chemical and thermal stability, hydrolytic stability, high lipophilicity and hydrophobicity, low polarizability, high-density, low boiling point, and low surface tension as well as potentially great biological activity.^{17,18,19} Before 2002, the production of pentafluorosulfanyl compounds with the aid of SF₅Cl relied on the use of excessive temperatures, high-pressure autoclaves, photochemical procedures, hazardous reactants to end up with low or variable yields together with the generation of toxic side-products. In 2002, the use of triethylborane (Et₃B) as a catalytic initiator for the free radical chain addition of SF₅Cl to alkenes and alkynes provided a major breakthrough.^{11, 20} This is currently the method of choice for pentafluorosulfanylation serving as starting point for several synthetic applications.

Preparative Methods

A method of producing SF₅Cl without the use of SF₄ includes admixing potassium fluoride, sulfur powder, chlorine and bromine (possibly acting as a solvent) at room temperature for two weeks (eq 14).²¹

Reactions with C=C bonds

Addition to Unfunctionalized Alkenes.

Transannular cyclization of 3,7-dimethylenebicyclo[3.3.1]nonane has been developed for the synthesis of SF₅-substituted noradamantane. The reaction proceeds without initiation in low yield, but light irradiation improves greatly the yield and selectivity (eq 15). Transannular cyclization of norbornadiene works equally well and SF₅-nortricyclanes were obtained as a 2.7:1 isomeric product ratio (eq 16). In contrast, reaction of SF₅Cl with *cis,cis*-1,5-cyclooctadiene didn't yield

transannulation, but gave as major product the addition of SF_5Cl to only one double bond of the diene. Use of triethylborane as radical initiator improved slightly the yield, but no transannulation was observed (eq 17).²²

The addition of SF_5Cl to benzobarralene followed by a sequence of base-promoted HCl elimination / naphthalene formation gave access to 2-pentafluorosulfanylnaphthalene (eq 18).²³

A route to pentafluorosulfanylbenzene ($\text{C}_6\text{H}_5\text{SF}_5$) was developed through addition of SF_5Cl to cyclohexene, followed by HCl elimination, dibromination with *N*-bromosuccinimide and dehydrobromination under basic conditions to afford the desired $\text{C}_6\text{H}_5\text{SF}_5$ in 68% overall yield (eq 19).²⁴ The two halogen atoms required for the dehydrohalogenation step can be initially present on the cyclohexene (eq 20).²⁵

The synthesis of conjugated 1,3-dienes substituted with a terminal SF_5 was performed from terminal olefins. Comparative radical addition of SF_5Cl to olefins under UV irradiation or with a catalytic amount of triethylborane showed that the second method gave higher yields. Elimination of HCl under basic conditions afforded the SF_5 -substituted mono-olefins. Then, reaction with bromine led selectively to allylic bromination and consecutive elimination of HBr under basic conditions provided access to SF_5 -substituted 1,3-dienes (eq 21).²⁶

Using the Et_3B -initiation approach, SF_5Cl was added to ethylene and 1,1-difluoroethylene for the preparation of monomers intended for radical polymerization and production of original SF_5 -containing copolymers (eq 22).²⁷

Unactivated alkenes with a distant functional group react almost identically to simple olefins; however, the distant function could participate in a subsequent reaction. The Et_3B -mediated addition of SF_5Cl to mono-substituted alkenes proved to be tolerant to the presence of an ω -

carboxylic acid function, which then served for the cyclization into γ -butyrolactone in the presence of silver triflate and triethylamine (eq 23).²⁸

Addition to Allylic Alcohols and derivatives.

Primary allylic and homoallylic alcohols were subjected to the photo-induced radical addition of SF_5Cl to the $\text{C}=\text{C}$ bond followed by dehydrochlorination with potassium hydroxide (eq 24).^{29, 30} The resulting primary alcohols were further transformed (Cl , N_3 , SCN) or oxidized to higher oxidation state functional groups (aldehyde, acid, ester, nitrile) and engaged, for example, as dienophiles in Diels–Alder cycloadditions.

Secondary allylic alcohols reacted similarly and afforded β - SF_5 enones after an oxidation step (eq 25).³¹ The same intermediate treated with KOH and then dehydrated gave 1-pentafluorosulfanylbuta-1,3-diene.³²

Allyl ethers are also suitable substrates for SF_5Cl addition. The *trans* addition of SF_5Cl to 7-oxanorbornene derivatives afforded exclusively the *endo* addition of the SF_5 moiety caused by the steric bulk of SF_5 (eq 26). The elimination step mediated by lithium hydroxide proceeded smoothly but depends on the lateral substituents.³³

Using the low temperature Et₃B initiated free radical chain procedure, SF₅Cl underwent addition to 7-oxabicyclo[2.2.1]hept-5-ene-2-carbonitrile to give two regioisomeric adducts as precursor of the pentafluorosulfanylfurans via a retro-Diels-Alder approach (eq 27).³⁴

The Et₃B-mediated radical addition of SF₅Cl was initially reported in hexane and latter in dichloromethane at –40 °C. It was later showed that the chloropentafluorosulfanylation of ((allyloxy)methyl)benzene tolerated many solvents such as toluene, ethyl acetate, THF, acetone, methanol, acetonitrile, acetic acid or even water . In contrast, DMF and DMSO completely inhibit the SF₅ addition. Noteworthy, the temperature seems to remain the main limitation since the highest yields were obtained at –40 °C (eq 28).³⁵

Similarly to (homo)allylic alcohols and allyl ethers, the addition of SF₅Cl to allylic esters under standard radical conditions worked efficiently (eq 29). SF₅-Containing allylic alcohols can then be obtained by elimination/deprotection with KOH. Consecutive oxidation with CrO₃ affords β-SF₅ acrylic acid (eq 29),³⁶ while oxidation with PCC yields β-SF₅ enal.^{37, 38}

Addition to *N*-Allylamides. The addition of SF₅Cl to *N*-allylbenzamides under standard conditions was employed in the first step towards 5-[(pentafluorosulfanyl)methyl]-2-oxazolines (eq 30). The subsequent cyclization in the presence of silver triflate proceeded through chlorine substitution rather than leading to elimination products typically obtained with the aid of various bases.³⁹

Additions to Enol Ethers.

α -SF₅ Substituted aldehydes can be synthesized by radical addition of SF₅Cl to enol ethers in the presence of Et₃B followed by acidic hydrolysis. The chloropentafluorosulfanyl intermediates were typically 9:1 diastereomeric mixtures (eq 31).⁴⁰ High purity of enol ethers proved to be crucial to reach satisfactory yields. α -SF₅ Aldehydes were further transformed into α -SF₅-substituted aldimines and used in cycloaddition reactions.

Addition of SF₅Cl to phenyl trifluorovinyl ether was performed in the presence of a catalytic amount of benzoyl peroxide (BPO) at 110 °C; then, treatment with sulfuric acid at the same temperature afforded the pentafluorosulfanyldifluoroacetic acid (eq 32). The latter can be converted to the corresponding acyl chloride in reaction with PCl₅ for reactions with various nucleophiles (alcohols, amines, Grignard reagents).⁴¹

Additions to Enol Acetates.

The first addition of SF₅Cl to vinyl acetate was performed under thermal conditions in an iron-nickel-molybdenum pressure reactor (eq 33).⁴² The resulting adduct was used to access α-SF₅ methyl ester by forming an acetal in hot methanol and then oxidation with *m*-CPBA (eq 33).⁴³ The SF₅ addition was improved thanks to the use of triethylborane as radical initiator (eq 34) whereas the conversion into methyl ester followed basically the same process.⁴⁴ A modified strategy was later proposed that include a reduction into primary alcohol, oxidation to the acid and esterification.⁴⁵

The preparation of α-SF₅ ketones was achieved by reaction of SF₅Cl with enol acetates such as isopropenyl acetate at 100 °C for 1 h in a Ni-Fe-Mo alloy at autogenous pressure.⁴² More conveniently, the enol acetate of acetophenone reacts with SF₅Cl and Et₃B in hexane at −30 °C (eq 35).⁴⁶

Additions to α,β-Unsaturated Esters.

Methyl acrylate (also methyl methacrylate) reacted with the SF₅ radical generated from SF₅Cl under thermal conditions in an autoclave at 120 °C (Eq 36).^{47, 48}

Addition to Allyl Silanes.

Addition of SF₅ to allyl silanes required 4 to 7 equivalents of SF₅Cl to reach full conversions; then, HCl elimination with the aid of KOH gave the corresponding (*E*)-3-SF₅ allyl silanes in high yields, except in the case of the volatile trimethylallylsilane (eq 37).³⁶

Addition to Allene.

A single case of addition of SF₅Cl to allene mediated by triethylborane gave access to (2-chloro-2-propen-1-yl) pentafluorosulfur (eq 38).⁴⁴

Additions to Alkynes

Aryl-, hetaryl-, and alkyl-acetylenes react with SF₅Cl in the presence of triethylborane at -40 °C to give regioselectively the corresponding pentafluorosulfanyl alkenyl chlorides. Aryls featuring electron-donating substituents afforded higher yields. Dehydrochlorination was then achieved with lithium hydroxide in DMSO to produce the SF₅-substituted alkynes, which utility as building blocks was demonstrated in many 1,3-dipolar cycloadditions for the synthesis of SF₅-isoxazole and -isoxazolines (eq 39),⁴⁹ with azomethine ylides generated in situ from aziridine esters for the synthesis of SF₅-dihydropyrroles and SF₅-pyrroles (eq 40),⁵⁰ with azomethine ylides generated in situ from *N*-benzyl-*N*-(methoxymethyl)-*N*-[(trimethylsilyl)-methyl]amine for the preparation of

SF₅-pyrroles (eq 41)⁵¹, and with thiocarbonyl ylide obtained from chloromethyl trimethylsilylmethyl sulfide to provide 3-pentafluorosulfanyl-4-(3'-thienyl)thiophene (eq 41).⁵²

SF₅-Substituted alkynes were also subjected to Diels–Alder reactions or a sequence Diels–Alder / retro-Diels–Alder reactions for the synthesis of SF₅-bicyclo[2.2.1]hepta-2,5-diene derivatives and SF₅-furans, respectively (eq 42).^{53, 34}

Hydration of SF₅-alkynes has been delineated. The study revealed that SF₅ acts as an efficient directing group in gold-catalyzed regioselective hydration of SF₅-alkynes with the aid of (JohnPhos)AuCl (eq 43).⁵⁴

Toward the synthesis of liquid crystals, the radical addition of SF₅Cl onto alkynes (alkenes also reacted but less efficiently) followed by standard elimination with LiOH/DMSO combination gave SF₅-acetylene structures (eq 44). The compounds showed low birefringences (Δn), but high dielectric anisotropies ($\Delta\epsilon$) which are interesting properties for polar liquid crystals.⁵⁵

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