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Encyclopedia of Reagents for Organic Synthesis

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

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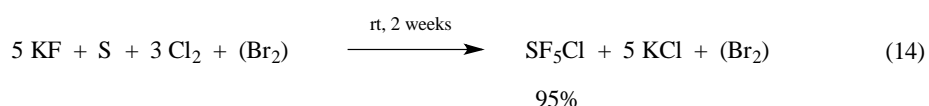
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Compounds featuring the SF₅ motif stand out through their remarkable chemical properties that include outstanding chemical and thermal stability, hydrolytic stability, high lipophilicity and hydrophobicity, low polarizability, high-density, low boiling 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

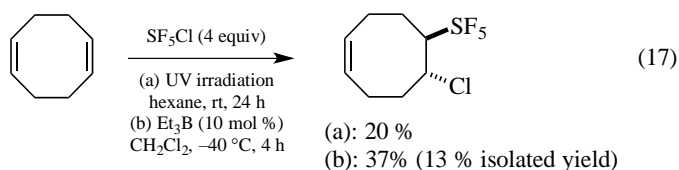
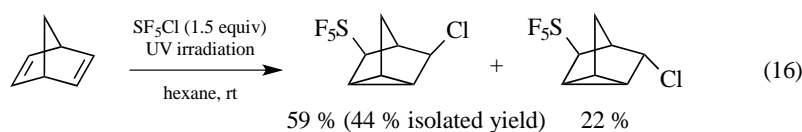
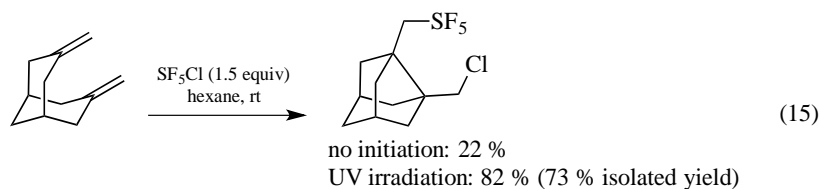


Reactions with C=C bonds

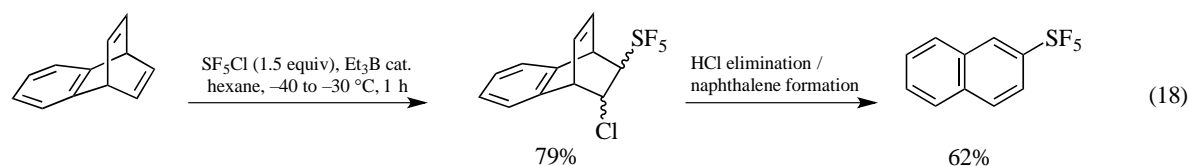
Addition to Unfunctionalized Alkenes.

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

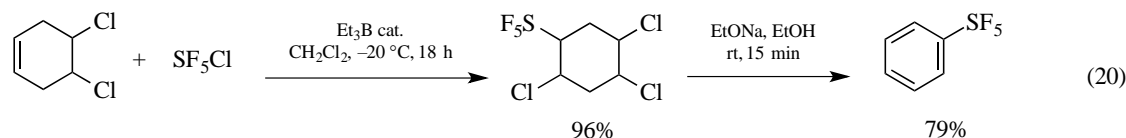
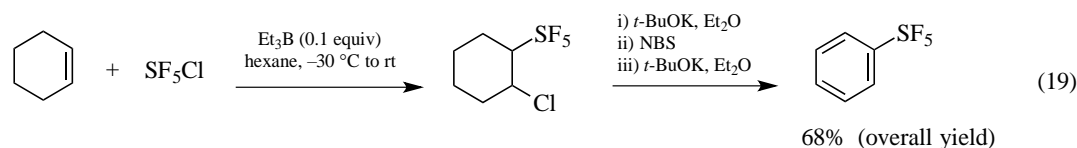
transannulation, but gave as major product the addition of SF₅Cl to only one double bond of the diene. Use of triethylborane as radical initiator improved slightly the yield, but no transannulation was observed (eq 17).²²



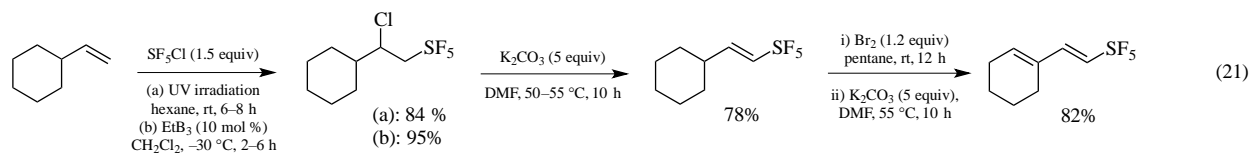
The addition of SF₅Cl to benzobarralene followed by a sequence of base-promoted HCl elimination / naphthalene formation gave access to 2-pentafluorosulfanyl naphthalene (eq 18).²³



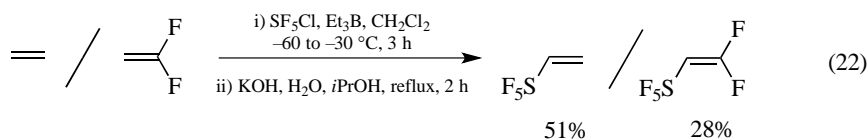
A route to pentafluorosulfanylbenzene (C₆H₅SF₅) was developed through addition of SF₅Cl to cyclohexene, followed by HCl elimination, dibromination with *N*-bromosuccinimide and dehydrobromination under basic conditions to afford the desired C₆H₅SF₅ in 68% overall yield (eq 19).²⁴ The two halogen atoms 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 SF₅ was performed from terminal olefins. Comparative radical addition of SF₅Cl 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 SF₅-substituted mono-olefins. Then, reaction with bromine led selectively to allylic bromination and consecutive elimination of HBr under basic conditions provided access to SF₅-substituted 1,3-dienes (eq 21).²⁶

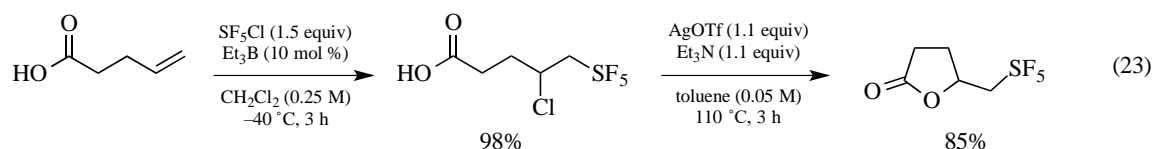


Using the Et₃B-initiation approach, SF₅Cl was added to ethylene and 1,1-difluoroethylene for the preparation of monomers intended for radical polymerization and production of original SF₅-containing copolymers (eq 22).²⁷



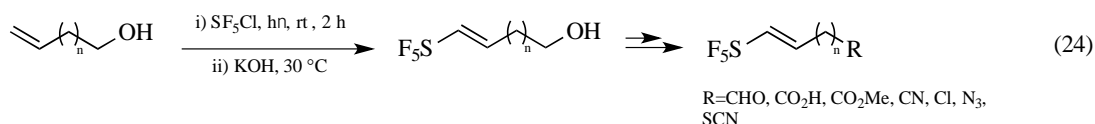
Unactivated alkenes with a distant functional group react almost identically to simple olefins; however, the distant function could participate in a subsequent reaction. The Et₃B-mediated addition of SF₅Cl to mono-substituted alkenes proved to be tolerant to the presence of an ω-

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

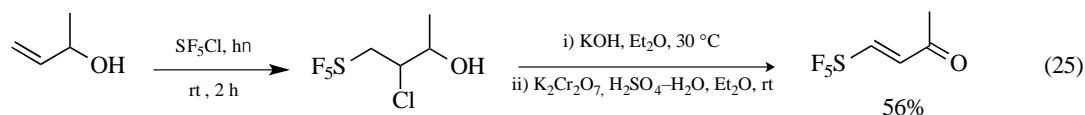


Addition to Allylic Alcohols and derivatives.

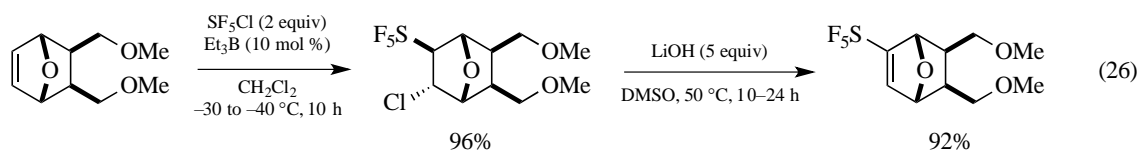
Primary allylic and homoallylic alcohols were subjected to the photo-induced radical addition of SF_5Cl to the $\text{C}=\text{C}$ bond followed by dehydrochlorination with potassium hydroxide (eq 24).^{29, 30} The resulting primary alcohols were further transformed (Cl , N_3 , SCN) or oxidized to higher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



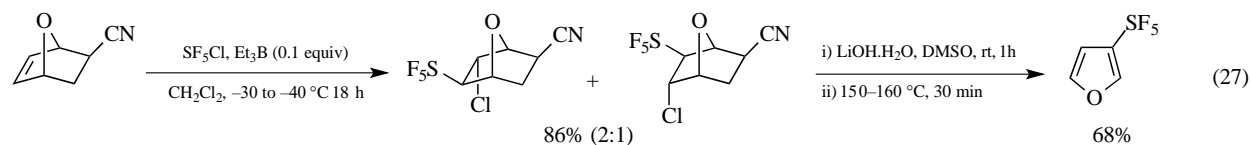
Secondary allylic alcohols reacted similarly and afforded β - SF_5 enones after an oxidation step (eq 25).³¹ The same intermediate treated with KOH and then dehydrated gave 1-pentafluorosulfanylbuta-1,3-diene.³²



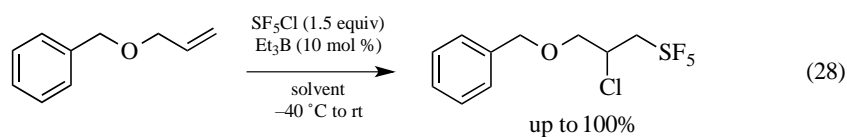
Allyl ethers are also suitable substrates for SF_5Cl addition. The *trans* addition of SF_5Cl to 7-oxanorbornene derivatives afforded exclusively the *endo* addition of the SF_5 moiety caused by the steric bulk of SF_5 (eq 26). The elimination step mediated by lithium hydroxide proceeded smoothly but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



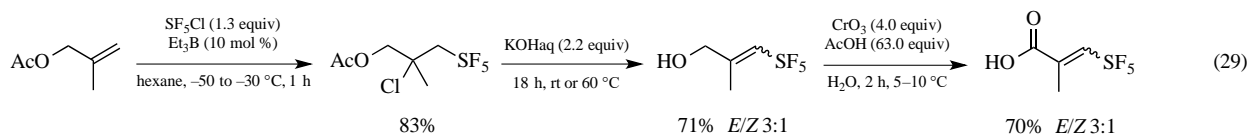
Using the low temperature Et₃B initiated free radical chain procedure, SF₅Cl underwent addition to 7-oxabicyclo[2.2.1]hept-5-ene-2-carbonitrile to give two regioisomeric adducts as precursor of the pentafluorosulfanyl furans via a retro-Diels-Alder approach (eq 27).³⁴



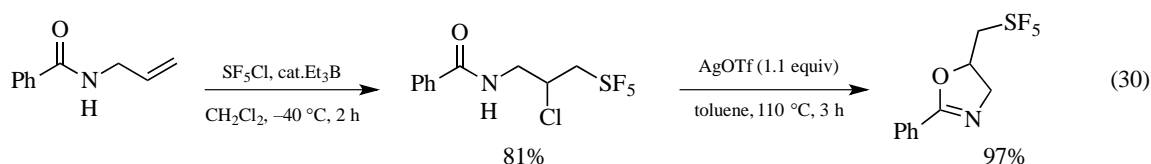
The Et₃B-mediated radical addition of SF₅Cl was initially reported in hexane and latter in dichloromethane at -40 °C. It was later showed that the chloropentafluorosulfanylation of ((allyloxy)methyl)benzene tolerated many solvents such as toluene, ethyl acetate, THF, acetone, methanol, acetonitrile, 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}

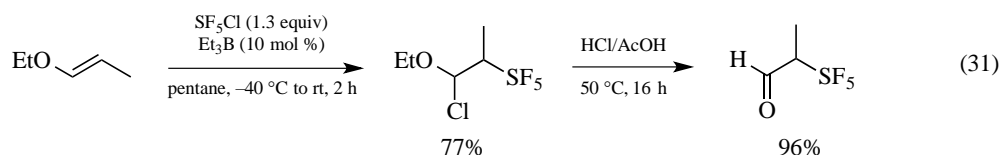


Addition to *N*-Allylamides. The addition of SF₅Cl to *N*-allylbenzamides under standard conditions was employed in the first step towards 5-[(pentafluorosulfanyl)methyl]-2-oxazolines (eq 30). The subsequent cyclization in the presence of silver triflate proceeded through chlorine substitution rather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

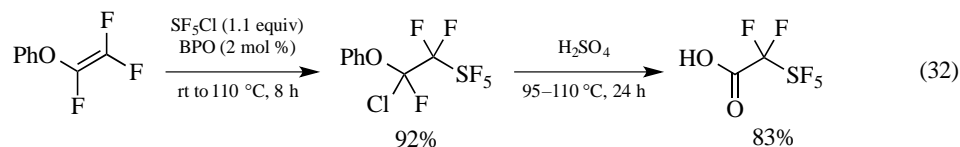


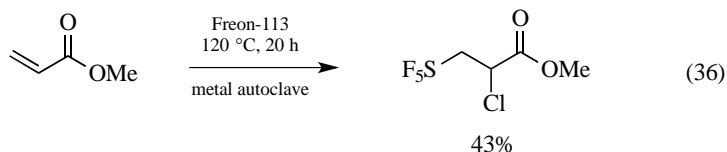
Additions to Enol Ethers.

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.



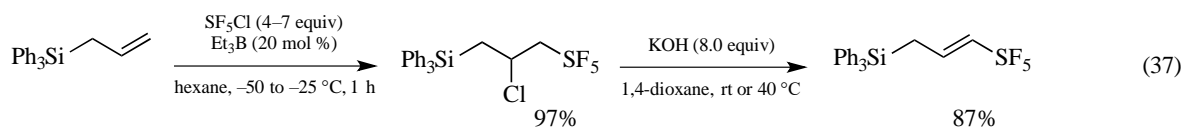
Addition of SF₅Cl to phenyl trifluorovinyl ether was performed in the presence of a catalytic amount of benzoyl peroxide (BPO) at 110 °C; then, treatment with sulfuric acid at the same temperature afforded the pentafluorosulfanyldifluoroacetic acid (eq 32). The latter can be converted to the corresponding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





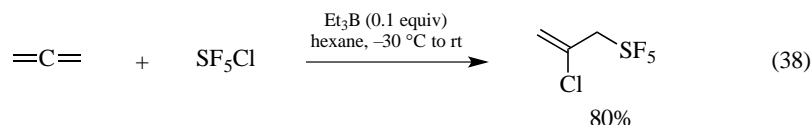
Addition to Allyl Silanes.

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.

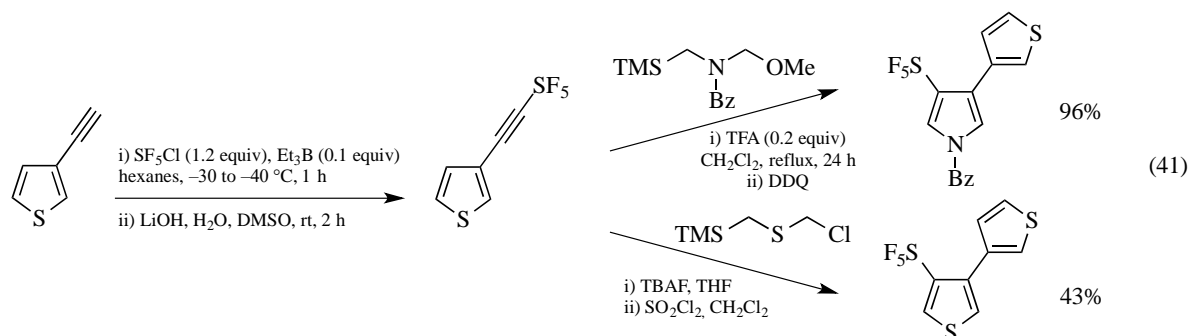
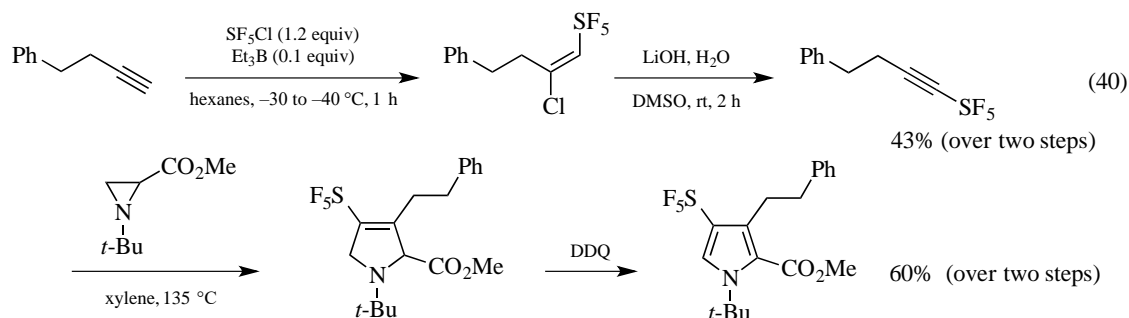
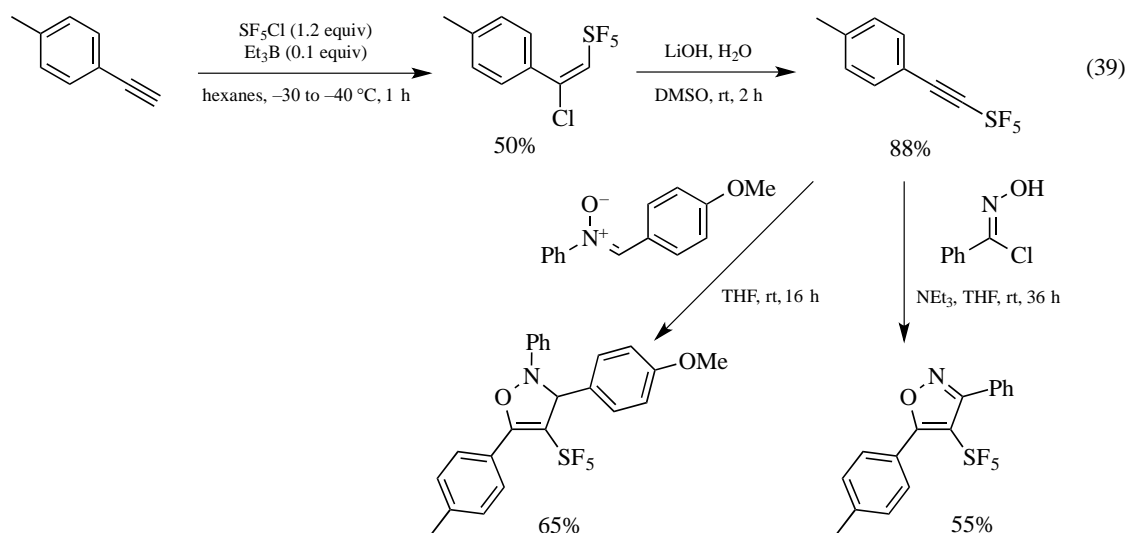
A single case of addition of SF₅Cl to allene mediated by triethylborane gave access to (2-chloro-2-propen-1-yl) pentafluorosulfur (eq 38).⁴⁴



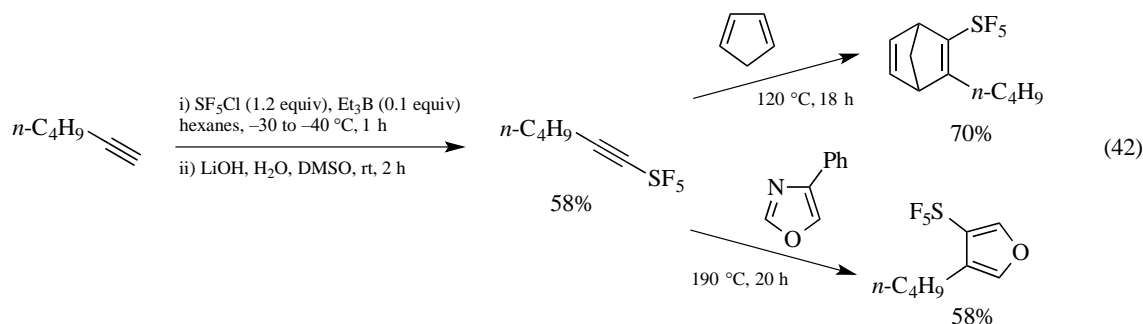
Additions to Alkynes

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

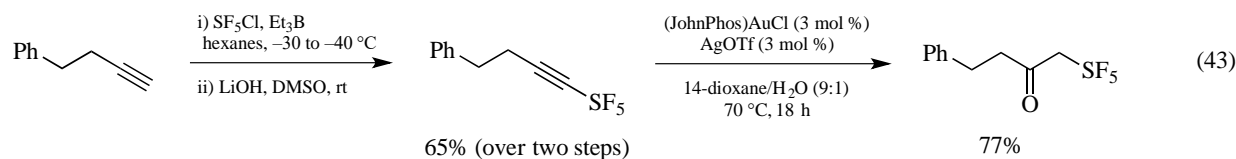
SF₅-pyrroles (eq 41)⁵¹, and with thiocarbonyl ylide obtained from chloromethyl trimethylsilylmethyl sulfide to provide 3-pentafluorosulfanyl-4-(3'-thienyl)thiophene (eq 41).⁵²



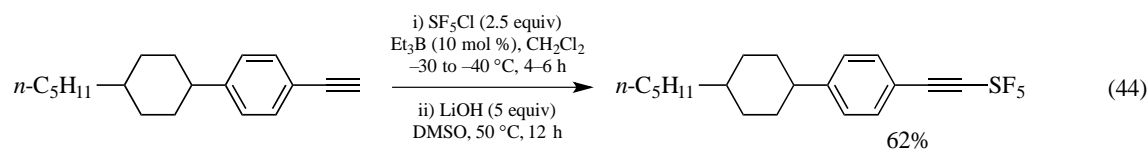
SF₅-Substituted alkynes were also subjected to Diels–Alder reactions or a sequence Diels–Alder / retro-Diels–Alder reactions for the synthesis of SF₅-bicyclo[2.2.1]hepta-2,5-diene derivatives and SF₅-furans, respectively (eq 42).^{53, 34}



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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References

17. Winter, R. W.; Dodean, R. A.; Gard, G. L., *ACS Symp. Ser.* **2005**, *911*, 87.
18. Savoie, P. R.; Welch, J. T., *Chem. Rev.* **2015**, *115*, 1130.
19. Altomonte, S.; Zanda, M., *J. Fluorine Chem.* **2012**, *143*, 57.
20. Dolbier, W. R., Jr.; Ait-Mohand, S., University of Florida, USA. **2004**, WO2004011422A1.
21. Winter, R., Avantbio Corporation, USA. **2009**, WO2009152385A2.
22. Ponomarenko, M. V.; Serguchev, Y. A.; Roeschenthaler, G.-V., *J. Fluorine Chem.* **2010**, *131*, 270.
23. Dolbier, W. R.; Mitani, A.; Warren, R. D., *Tetrahedron Lett.* **2007**, *48*, 1325.
24. Winter, R. W.; Gard, G. L., *J. Fluorine Chem.* **2004**, *125*, 549.
25. Sergeeva, T. A.; Dolbier, W. R., Jr., *Org. Lett.* **2004**, *6*, 2417.
26. Ponomarenko, M. V.; Serguchev, Y. A.; Roschenthaler, G.-V., *Synthesis* **2010**, 3906.
Erratum in *Synthesis* **2011**, 827.
27. Kostov, G.; Ameduri, B.; Sergeeva, T.; Dolbier, W. R., Jr.; Winter, R.; Gard, G. L., *Macromolecules* **2005**, *38*, 8316.
28. Roudias, M.; Gilbert, A.; Paquin, J.-F. *Eur. J. Org. Chem.* **2019**, 6655.
29. Brel, V. K., *Phosphorus, Sulfur Silicon Relat. Elem.* **2011**, *186*, 1284.
30. Trushkov, I. V.; Brel, V. K., *Tetrahedron Lett.* **2005**, *46*, 4777.
31. Brel, V. K., *Synthesis* **2006**, 339.
32. Brel, V. K., *Synthesis* **2005**, 1245.

33. Ponomarenko, M. V.; Lummer, K.; Fokin, A. A.; Serguchev, Y. A.; Bassil, B. S.; Roeschenthaler, G.-V., *Org. Biomol. Chem.* **2013**, *11*, 8103.
34. Dolbier, W. R., Jr.; Mitani, A.; Xu, W.; Ghiviriga, I., *Org. Lett.* **2006**, *8*, 5573.
35. Gilbert, A.; Paquin, J.-F., *J. Fluorine Chem.* **2019**, *221*, 70.
36. Falkowska, E.; Suzenet, F.; Jubault, P.; Bouillon, J.-P.; Pannecoucke, X., *Tetrahedron Lett.* **2014**, *55*, 4833.
37. Dreier, A.-L.; Matsnev, A. V.; Thrasher, J. S.; Haufe, G., *J. Fluorine Chem.* **2014**, *167*, 84.
38. Husstedt, W. S.; Thrasher, J. S.; Haufe, G., *Synlett* **2011**, 1683.
39. Gilbert, A.; Bertrand, X.; Paquin, J.-F., *Org. Lett.* **2018**, *20*, 7257.
40. Penger, A.; von Hahmann, C. N.; Filatov, A. S.; Welch, J. T., *Beilstein J. Org. Chem.* **2013**, *9*, 2675.
41. Matsnev, A. V.; Qing, S.-Y.; Stanton, M. A.; Berger, K. A.; Haufe, G.; Thrasher, J. S., *Org. Lett.* **2014**, *16*, 2402.
42. Coffman, D. D.; Tullock, C. W., E. I. du Pont de Nemours & Co., 1963, US3102903.
43. Winter, R.; Gard, G. L. *J. Fluorine Chem.* **1994**, *66*, 109.
44. Dolbier, W. R.; Ait-Mohand, S.; Schertz, T. D.; Sergeeva, T. A.; Cradlebaugh, J. A.; Mitani, A.; Gard, G. L.; Winter, R. W.; Thrasher, J. S., *J. Fluorine Chem.* **2006**, *127*, 1302.
45. Joliton, A.; Plancher, J.-M.; Carreira, E. M., *Angew. Chem. Int. Ed.* **2016**, *55*, 2113.
46. Welch, J.; Ngo, S.; Lim, D., The Research Foundation of State University of New York, USA . **2009**, WO2009026191A1.
47. Studnev, Y. N.; Stolyarov, V. P.; Prigorelov, G. A.; Fokin, A. V., *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 197.

48. Fokin, A. V.; Studnev, Y. N.; Stolyarov, V. P.; Chilikin, V. G.; Prigorelov, G. A., *Izv. Akad. Nauk, Ser. Khim.* **1996**, 2952 & *Russ. Chem. Bull.* **1997**, 45, 2804.
49. Lopez, S. E.; Mitani, A.; Pena, P.; Ghiviriga, I.; Dolbier, W. R., *J. Fluorine Chem.* **2015**, 176, 121.
50. Dolbier, W. R., Jr.; Zheng, Z., *J. Org. Chem.* **2009**, 74, 5626.
51. Dolbier, W. R., Jr.; Zheng, Z.-Y., *J. Fluorine Chem.* **2011**, 132, 389.
52. Zheng, Z.; Dolbier, J. W. R., University of Florida Research Foundation Inc., **2010**, US2011040103 (A1).
53. Mitani, A.; Dolbier, W. R., University of Florida Research Foundation, Inc., USA . **2007**, WO2007106818A1.
54. Cloutier, M.; Roudias, M.; Paquin, J.-F., *Org. Lett.* **2019**, 21, 3866.
55. Ponomarenko, M. V.; Kalinovich, N.; Serguchev, Y. A.; Bremer, M.; Roeschenthaler, G.-V., *J. Fluorine Chem.* **2012**, 135, 68.