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New and Convenient Method for Incorporation of Pentafluorosulfanyl (SF_5) Substituents Into Aliphatic Organic Compounds

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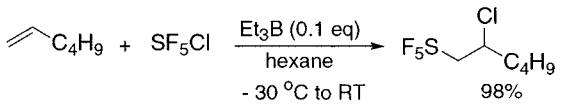
ABSTRACT



Use of Et_3B as a catalytic initiator allows the convenient, regiospecific, and highly stereoselective addition of SF_5Cl in high yield to a variety of alkenes and alkynes.

There is currently great interest in methods for the preparation of selectively fluorinated organic compounds, in no small part because of the profound influence that fluorine incorporation can have on the physical and chemical properties and biological activity of molecules. Thus, for example, methods for putting the bulky, highly electronegative, and generally inert trifluoromethyl group into organic compounds have received much research attention during recent years. Another fluorinated substituent that could attract at least as much interest among synthetic organic chemists in the future is the pentafluorosulfanyl (SF_5) group,[1−3] which bears much similarity to the trifluoromethyl group but is more electronegative ($\sigma_p = +0.68$ versus $+0.54$ for CF_3)[4] and more sterically demanding. The SF_5 substituent should emulate the CF_3 group in altering molecular properties such as density, refractive index, dipole moment, lipophilicity, and thermal and chemical stability, and it should have a similar but intriguingly distinct impact on biological activity, as foreshadowed by its demonstrated effect on insecticidal properties.[5,6]

However, until now the methods required to put an SF_5 substituent onto a benzene ring (elemental F_2 or oxidative fluorination by AgF_2)[7−10] or to incorporate an SF_5 group into aliphatic compounds (high-pressure autoclave or specialized photochemical procedures)[11−14] have not encouraged utility by synthetic organic chemists.

SF_5Cl is presently the only commercially available "reagent" that can be used to introduce the SF_5 substituent into aliphatic compounds. As a gaseous pseudo-halogen, this reagent cannot be used as an electrophilic source of SF_5, but ever since Roberts' pioneering work in 1961,[11] it has

(1) Winter, R.; Gard, G. L. In *Inorganic Fluorine Chemistry—Toward the 21st Century*; Thrasher, J. S., Strauss, S. H., Eds.; American Chemical Society: Washington, DC, 1994; Vol. 555, pp 128−147.
(2) Lentz, D.; Seppelt, K. In *Chemistry of Hypervalent Compounds*; Akiba, K., Ed.; Wiley-VCH: New York, 1999; pp 295−326.
(3) Verma, R. D.; Kirchmeier, R. L.; Shreeve, J. M. In *Advances in Inorganic Chemistry*; Sykes, A. G., Ed.; Academic Press: San Diego, 1994; Vol. 41, pp 125−169.
(4) Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 3072−3076.
(5) Salmon, R. Preparation of *N*-(4-pentafluorosulfenylphenyl)-pyrazoles as insecticides and acaricides. Patent WO 9306089, 1993.
(6) Howard, M. H., Jr.; Stevenson, T. M. Arthropodicidal pentafluorothiosubstituted anilides. Patent WO 9516676, 1995.
(7) Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 3064−3072.
(8) Chambers, R. D.; Spink, R. C. H. *Chem. Commun.* **1999**, 883−884.
(9) Bowden, R. D.; Comina, P. J.; Greenhall, M. P.; Kariuki, B. M.; Loveday, A.; Philp, D. *Tetrahedron* **2000**, *56*, 3399−3408.
(10) Sipyagin, A. M.; Bateman, C. P.; Tan, Y.-T.; Thrasher, J. S. *J. Fluorine Chem.* **2001**, *112*, 287−295.
(11) Case, J. R.; Ray, N. H.; Roberts, H. L. *J. Chem. Soc.* **1961**, 2066−2070.
(12) Wessel, J.; Kleemann, G.; Seppelt, K. *Chem. Ber.* **1983**, *116*, 2399−2407.
(13) Winter, R.; Gard, G. L. *J. Fluorine Chem.* **1994**, *66*, 109−116.
(14) Fokin, A. V.; Studnev, Y. N.; Stolyarov, V. P.; Chilikin, V. G.; Prigorelov, G. A. *Russ. Chem. Bull.* **1996**, *45*, 2804−2806.

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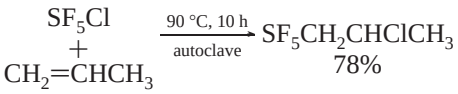
been used in free radical chain alkene/alkyne addition processes,[15] generally done thermally, in an autoclave, with or without an initiator, or using room-temperature gas-phase or low-temperature solution-phase photochemical processes. For example:[11]

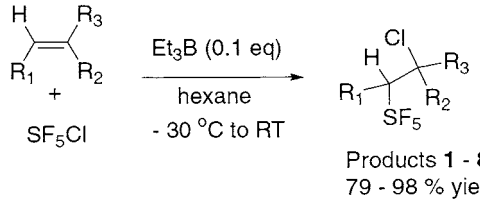


In order for SF_5 derivatives to become incorporated into the day-to-day strategic planning of working synthetic organic chemists, a convenient, benchtop procedure needs to be developed for introduction of SF_5 substituents into organic substrates. In this Letter, we provide such a method, one that will allow convenient addition of SF_5Cl to a large variety of alkenes and alkynes in excellent yield. The method is based upon our discovery that Et_3B could readily initiate the free radical chain addition of SF_5Cl to unsaturated compounds at the low temperatures required for convenient use of SF_5Cl in solution at atmospheric pressure. Triethylborane has been recognized for more than a decade to be a unique low-temperature initiator of free radical reactions.[16] Although other potential initiators were examined, thus far Et_3B is the only one that has been found to successfully initiate the SF_5Cl addition reactions.

With a boiling point of −21 °C, SF_5Cl is readily condensed into hexane, which contains the alkene or alkyne substrate, at −40 °C. When the Et_3B initiator is added by syringe at ca. −30 °C, an immediate reaction is evident, and for most substrates, the reaction is effectively complete after 30 min.[17] The reaction can be worked up by simple evaporation of the hexane to give, in most cases, essentially pure product. (No significant impurities are observed by ^1H, ^{19}F, or ^{13}C NMR, but passage through a short column is recommended before further use, to eliminate possible traces of Et_3B.) Table 1 gives the yields for addition of SF_5Cl to a variety of alkenes, whereas Table 2 gives the results for addition to three typical alkynes.[18]

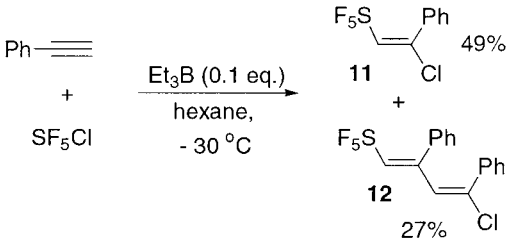
In the reaction with phenyl acetylene, a 2:1 adduct was also obtained in 27% yield. In this case, addition of the propagating radical intermediate to a second phenyl acetylene is obviously competing with the chain transfer step. Using a larger excess of SF_5Cl in the reaction can minimize this 2:1 product.

Table 1. Yields for Addition of SF_5Cl to Alkenes[a]



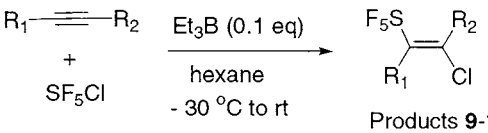
R_1	R_2	R_3	product, % yield
H	n-C_6H_{13}	H	**1**, 95
H	n-C_4H_9	H	**2**, 98[19]
H	t-C_4H_9	H	**3**, 96
H	C_2H_5	C_2H_5	**4**, 89
n-C_3H_7	H	n-C_3H_7	**5**, 95[b]
$(CH_2)_4$		H	**6**, 98[b,11]
H	p-tolyl	H	**7**, 79
H	OAc	H	**8**, 98[20]

[a] In hexane, at −30 °C, 0.1 equiv of Et_3B, 30 min. [b] One major diastereomer (>90% by NMR).



The addition reactions are regiospecific and highly diastereoselective, with essentially one product being formed from the additions to cyclohexene, *trans*-4-octene, and the alkynes. Although confirmation of the specific stereochemistries of products **5**, **6**, **9**, **10**, and **11** is not possible at this time, one can be almost certain that the stereochemical outcomes of these reactions are sterically controlled, that the

Table 2. Addition of SF_5Cl to Alkynes[a]



R_1	R_2	product,[b] % yield
n-C_3H_7	n-C_3H_7	**9**, 93
H	n-C_6H_{13}	**10**, 94
H	Ph	**11**, 94 + **12**, 27

[a] In hexane, at −30 °C, 0.1 equiv of Et_3B, 30 min. [b] Single diastereomer in each case.

(15) Sidebottom, H. W.; Tedder, J. M.; Walton, J. C. *Trans. Faraday Soc.* **1969**, *65*, 2103−2109.

(16) Takeyama, Y.; Ichinose, Y.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1989**, *30*, 3159−3162.

(17) **Typical Procedure.** Into a three-necked flask equipped with a dry ice reflux condenser and a nitrogen inlet were added at −40 °C 15 mL of anhydrous hexane, alkene (3−4 mmol), and SF_5Cl (1.2 equiv). The solution was stirred at this temperature for 5 min, and then Et_3B (0.1 equiv, 1 M in hexane) was added slowly using a syringe. The solution was vigorously stirred for 1 h at −30 to −20 °C, and then the mixture was allowed to warm to room temperature. The mixture was hydrolyzed with aqueous $NaHCO_3$ (10%), and the organic layer was dried over $MgSO_4$. The solvent was removed, and the crude product was passed through a short column of silica gel, eluting with CH_2Cl_2. Removal of solvent in most cases provided the products in essentially pure form without the need for additional purification.

(18) Products containing the SF_5 substituent are readily confirmed by the presence of the characteristic AB_4 pair of pentuplet and doublet signals in their ^{19}F NMR spectra, which along with their ^1H and ^{13}C spectra allowed unambiguous characterization of all of the products (see Supporting Information).

alkyne and cyclohexene products are *E*-isomers, and that the product (**5**) from *trans*-4-octene is *erythro*. All of the alkyne adducts are new, although the SF_5Cl adduct of propyne has been reported.[11] Although many of the alkene adducts have been reported previously,[11,19] styrenes, 2,2-disubstituted alkenes, and nonterminal alkenes had not previously proved to be good substrates for SF_5Cl addition. The mildness of the Et_3B-catalyzed reaction conditions obviously contributes to the apparent broad applicability of this new method.

Regarding the scope of the present procedure, at least one limitation has already been observed. Although additions to enol ethers or enol esters should be fine, as exemplified by the almost quantitative addition to vinyl acetate, attempted additions to α,β-unsaturated carbonyl compounds, such as ethyl acrylate or ethyl methacrylate, were not successful, presumably because of a combination of reduced chain transfer rate to the electrophilic propagating radical and the problem of the ester tying up the Et_3B catalyst,[21] thus inhibiting free radical initiation and allowing polymerizing chain propagation to dominate the reaction.

We believe that the simplicity of our new method, combined with the generally excellent yields that are obtained, constitutes a breakthrough in SF_5 synthetic methodology that should open the door to the convenient, benchtop preparation of a multitude of SF_5-containing aliphatics by synthetic organic chemists. Future work will provide insight regarding the reaction's tolerance of functional groups, which appears to be good.

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Supporting Information Available: ^1H, ^{19}F, and ^{13}C NMR spectra for all products are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) Winter, R.; Nixon, P. G.; Gard, G. L.; Radford, D. H.; Holcomb, N. R.; Grainger, D. W. *J. Fluorine Chem.* **2001**, *107*, 23−30.

(20) E. I. duPont de Nemours & Co., U.S. Patent 3102903, 1961.

(21) Beraud, V.; Gnanou, Y.; Walton, J. C.; Maillard, B. *Tetrahedron Lett.* **2000**, *41*, 1195−1198.