

A New Synthesis of
Pentafluorosulfanylbenzene

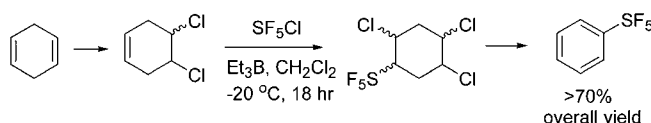
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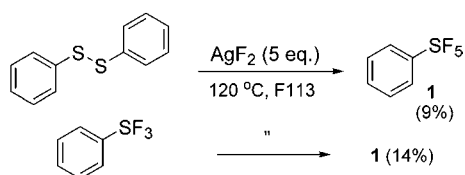
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ABSTRACT



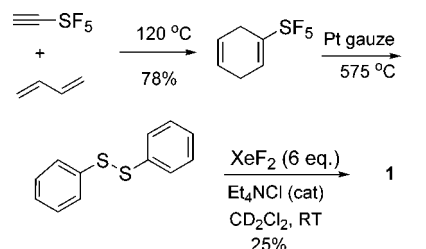
A new and convenient three-step synthesis of pentafluorosulfanylbenzene from 1,4-cyclohexadiene with an overall yield of >70% is reported along with a number of derivatization reactions.

Interest in the chemistry of aromatic pentafluorosulfanyl compounds was briefly ignited in 1960 when Sheppard reported the first low yield synthesis of pentafluorosulfanylbenzene (**1**) via the reaction of aryl disulfides or aryl sulfur trifluorides with silver difluoride at 120 °C.¹ Sheppard's process was better suited for preparation of 3- and 4-nitropentafluorosulfanylbenzenes, which were prepared in 30% yield. In this initial report, the first examples of reactions of



1 were provided, including electrophilic aromatic substitution reactions, Sandmeyer chemistry, and Grignard chemistry. After a brief flurry of activity, mostly involving the reporting of physical and spectroscopic properties of **1** and some of its derivatives,^{2–6} there ensued a period of little activity related to pentafluorosulfanylbenzene and its derivatives until

the 1990s, when Sheppard's AgF_2 method was elaborated and improved upon by Thrasher to prepare ortho-substituted pentafluorosulfanylbenzenes⁷ and a new direct fluorination method was developed by Bowden and Greenhall of F2 Chemicals for conversion of 3- and 4-nitrophenyl disulfides to the respective SF_5 nitrobenzenes.^{8–10} However, since Sheppard's original report, there have been only two other methods reported for the preparation of the parent compound **1**. Hoover and Coffman were able to take advantage of the addition of pentafluorosulfanylacetylene (itself a challenging compound to make) to butadiene to make **1**,¹¹ whereas Ou and Janzen found that XeF_2 was a sufficiently strong fluorinating agent to convert phenyl disulfide to pentafluorosulfanylbenzene, although again in but a modest, 25% yield.¹²



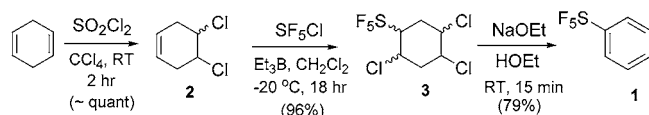
Thus, until the present work, there existed no satisfactory general procedure for synthesis of pentafluorosulfanyl-

- (1) Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 3064–3072.
- (2) Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 3072–3076.
- (3) Brownlee, R. T. C.; Hutchinson, R. E. J.; Katritzky, A. R.; Tidwell, T. T.; Topsom, R. D. *J. Am. Chem. Soc.* **1968**, *90*, 1757–1767.
- (4) Brownlee, R. T. C.; English, P. J. Q.; Katritzky, A. R.; Topsom, R. D. *J. Phys. Chem.* **1969**, *73*, 557–564.
- (5) Chawla, B.; Pollack, S. K.; Lebrilla, C. B.; Kamlet, M. J.; Taft, R. W. *J. Am. Chem. Soc.* **1981**, *103*, 6924–6930.
- (6) Eaton, D. R.; Sheppard, W. A. *J. Am. Chem. Soc.* **1963**, *85*, 1310–1313.

- (7) Sipyagin, A. M.; Bateman, C. P.; Tan, Y.-T.; Thrasher, J. S. *J. Fluorine Chem.* **2001**, *112*, 287–295.

benzene in decent yield from readily available starting materials, in particular, without the use of highly energetic reagents. In the meantime, considerable interest in pentafluorosulfanyl aromatics emerged during the 1990s within the agrochemical and pharmaceutical industries,^{13,14} as witnessed by a surge in related patent applications. The Bowden/Greenhill work particularly served to bolster this interest.^{8,10}

After our recent discovery of a simple, benchtop procedure for carrying out the addition of SF₅Cl to alkenes and alkynes,¹⁵ we sought to find a way to utilize this chemistry in the synthesis of pentafluorosulfanylbenzene. In the end, our successful strategy involved the three step conversion of readily available 1,4-cyclohexadiene to pentafluorosulfanylbenzene in an overall yield of >70%.^{16,17} Experimental details for all three steps may be found in the Supporting Information.

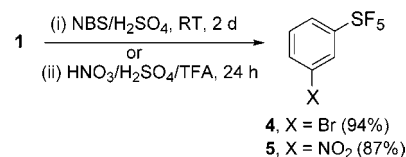


1,4-Cyclohexadiene was easily transformed into 4,5-dichlorocyclohexene, **2**,¹⁸ via its essentially quantitative reaction with SO₂Cl₂ in CCl₄ at room temperature. This was followed by the key step in the synthesis, which was the introduction of the SF₅ group via the high yield, Et₃B-catalyzed addition of SF₅Cl to **2** at -20 °C. To obtain the reported high yield, it was essential that a longer reaction time and larger (3.5-fold) excess of SF₅Cl be used for this addition, in comparison to the conditions that were necessary for SF₅Cl additions to simple alkenes. The product, **3**, was obtained as a mixture of stereoisomers that were not readily separated, but which could be used directly in the subsequent elimination reaction.

The elimination of HCl from SF₅Cl adducts of simple alkenes has been achieved previously using various eliminative procedures.^{11,19–22} Thus, straight chain, SF₅-substituted

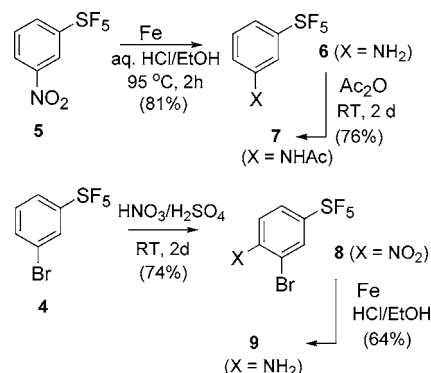
alkenes have been prepared by 1,2-elimination of hydrogen chloride using K₂CO₃ in acetone, KOH in aqueous or H₂O/*i*-PrOH media, or a KOH–diethyl ether system. In our particular case, treatment of the compound **3** with a large (up to 12–15-fold) excess of potassium hydroxide in ether did lead to **1**, but in only a modest, 45–50% yield, even after a prolonged reaction time (up to 3 days). The best results were achieved using sodium ethoxide. Treatment of **3** with 1.5 M sodium ethoxide (7.5 equiv) led to formation of **1** in a yield of 79%. Initially, the reaction was carried out overnight, but it was found that only a few minutes at room temperature were sufficient for the reaction to be complete. The pentafluorosulfanylbenzene obtained in this manner is sufficiently pure to be used directly in the following reactions to prepare derivatives.

The pentafluorosulfanyl substituent is a powerful deactivating and thus meta-directing group with respect to electrophilic aromatic substitution, as was demonstrated by Sheppard in 1960. Indeed, we found that our earlier method for bromination of highly deactivated benzenes²³ was also effective for conversion of **1** to its 3-bromo derivative.



Nitration could also be readily carried out in very good yield. 3-Nitropentafluorosulfanylbenzene, **5**, had been obtained earlier by direct fluorination of bis(3-nitrophenyl)-disulfide in yields of 39–75%,^{9,10} whereas Sheppard had reported the preparation of both **4** and **5** in his original 1962 paper.¹

To facilitate the synthetic use of the parent **1**, an improved method for the conversion of **5** to 3-pentafluorosulfanyl-aniline (**6**) is also reported in this paper, as is a procedure for regioselective nitration of **4**²⁴ and its subsequent reduction to aniline derivative **9**.



In conclusion, using SF₅Cl as the source of the SF₅ group, we have reported a new and convenient three-step synthesis

(8) Bowden, R. D.; Greenhill, M. P. F2 Chemicals Ltd. PCT Int. Appl., 2002.

(9) Chambers, R. D.; Spink, R. C. H. *Chem. Commun.* **1999**, 883–884.

(10) Bowden, R. D.; Comina, P. J.; Greenhill, M. P.; Kariuki, B. M.; Loveday, A.; Philp, D. *Tetrahedron* **2000**, 56, 3399–3408.

(11) Hoover, F. W.; Coffman, D. D. *J. Org. Chem.* **1964**, 29, 3567–3570.

(12) Ou, X.; Janzen, A. F. *J. Fluorine Chem.* **2000**, 101, 279–283.

(13) Carlini, F. M. *Chim. Oggi* **2003**, 21, 14–16.

(14) Dolbier, W. R., Jr. *Chim. Oggi* **2003**, 21, 66–69.

(15) Ait-Mohand, S.; Dolbier, W. R., Jr. *Org. Lett.* **2002**, 4, 3013–3015.

(16) A paper reporting some additional, related approaches to the synthesis of pentafluorosulfanylbenzene, using cyclohexene derivatives as starting materials, appeared as this paper was going to press.¹⁷

(17) Winter, R. W.; Gard, G. L. *J. Fluorine Chem.* **2004**, 125, 549–552.

(18) Riemschneider, R.; Triebel, W. *Chem. Ber.* **1955**, 88, 1442–1450.

(19) Klauback, A.; Seppelt, K. *Angew. Chem., Int. Ed. Engl.* **1994**, 33, 93–95.

(20) Case, J. R.; Ray, N. H.; Roberts, H. L. *J. Chem. Soc.* **1961**, 2066–2070.

(21) Fokin, A. V.; Studnev, Y. N.; Stolyarov, V. P.; Chilikin, V. G.; Prigorelov, G. A. *Russ. Chem. Bull.* **1996**, 45, 2804–2806.

(22) 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, p 128–147.

(23) Duan, J.-X.; Zhang, L.-H.; Dolbier, W. R., Jr. *Synlett* **1999**, 1245–1246.

(24) NMR spectra of crude **8** indicated the presence of ~10% of a minor product, most likely the 6-nitro isomer. Because the spectra of **9** (in the Supporting Information) were of a sample prepared from crude **8**, one can see the respective 6-amino product as a ~10% impurity in product **9**.

of pentafluorosulfanylbenzene in an overall yield of >70%. This synthesis provides a viable technological alternative to the direct fluorination method for the preparation of SF₅-containing aromatic derivatives.

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Supporting Information Available: Experimental procedures for all reactions and NMR spectra of compounds **4**, **8**, and **9**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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