

Das Reagenz • The Reagent

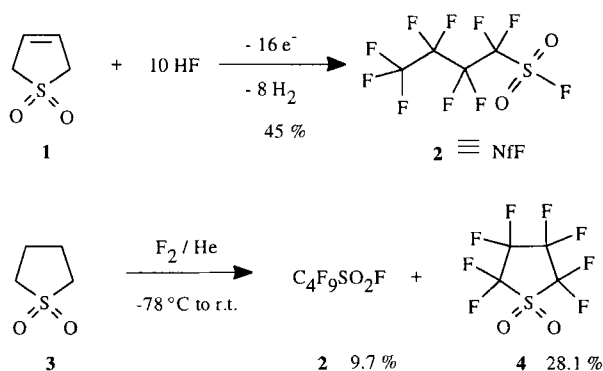
Nonafluoro-1-butanesulfonyl Fluoride: More than a Fluorinating Reagent

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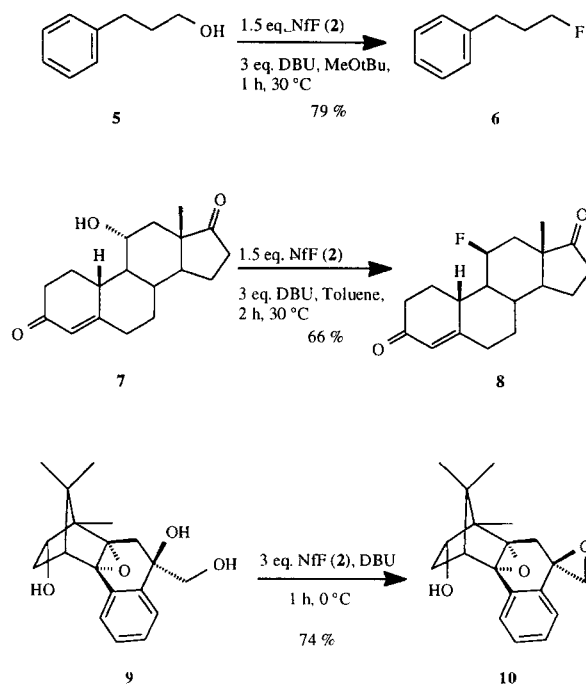
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The increasing importance of fluorine containing products has led to rapid progress in their syntheses and applications. Fluoroorganic compounds possess often unusual physical properties, specific chemical reactivities, and potential biological activities [1]. Herein we describe the utilization of nonafluoro-1-butanesulfonyl fluoride (**2**, abbreviated as NfF) as an attractive perfluorinated reagent in organic synthesis. NfF (**2**) is easily accessible in large quantities by anodic fluorination of sulfolene **1** [2]. The perfluorinated alkanesulfone **2** can also be prepared by direct fluorination of tetramethylene sulfone (**3**) but only in 9.7% yield [3]. In this reaction the major product is perfluorotetramethylene sulfone (**4**) (28.1% yield).



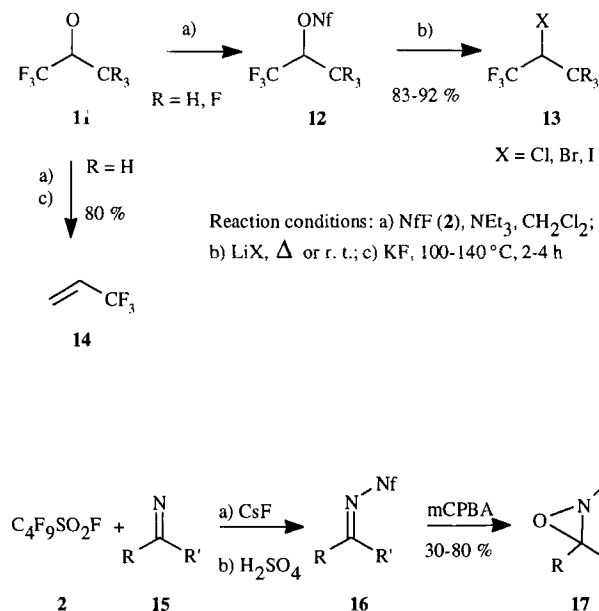
NfF (**2**) serves as a convenient reagent to introduce fluorine or the perfluorobutyl residue in a number of organic compounds. Vorbrüggen and Bennua-Skalmowski [4] have recently described a protocol for the conversion of aliphatic primary and secondary alcohols to the corresponding fluorides by treating the alcohols with NfF (**2**) and a strong organic base (e.g., 1,8-Diazabicyclo[5.4.0]undec-7-ene, DBU) in an inert organic solvent (e.g., **5** → **6** and **7** → **8**). On the other hand replacement of DBU by 4-dimethylaminopyridine (DMAP)

leads to a complex mixture of the expected fluorides, olefinic products and (4-dimethylamino-pyridinium) nonaflate [5]. The combination of **2** and DBU is also reported to be very effective in an epoxide forming reaction [6]. For example, the reaction of 1,2-diol **9** with NfF (**2**)/DBU gives epoxide **10** in 74% yield.



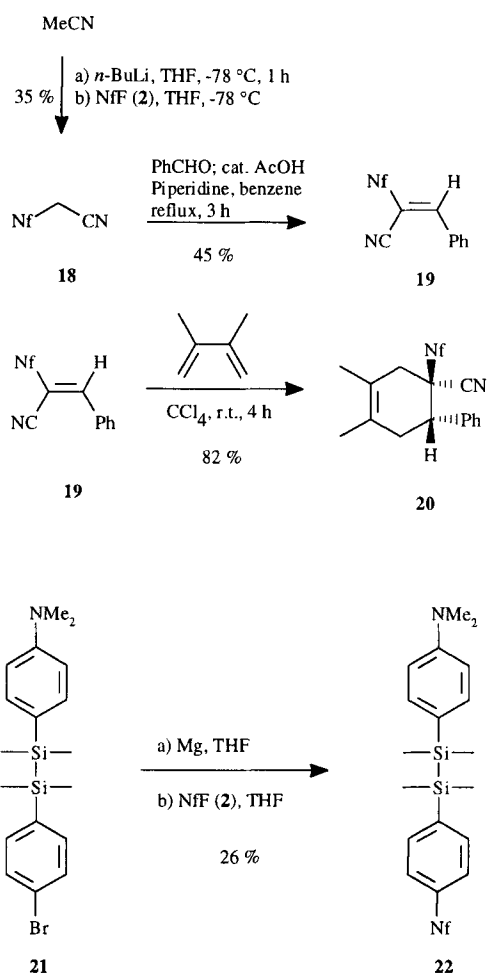
In 1989 investigations of Hanack and Ullmann [7] illustrated the synthetic utility of **2** in the preparation of trifluoro- and hexafluoroisopropyl halides **13** by nucleophilic substitution of nonafllyl precursor **12** with lithium salts (LiCl, LiBr, or LiI). However, the corresponding tri- (or hexa)fluoroisopropyl fluorides could not be observed by the treatment of

12 (R = H) with KF under same reaction conditions. Instead, elimination product **14** was isolated in high yield [7]. A further remarkable application of NfF (**2**) is demonstrated by the synthesis of the well-known perfluorinated oxidizing reagents such as oxaziridines **17** [8]. Polyfluoro-*N*-butanesulfonamides **16** are prepared by the reaction of imines **15** with NfF (**2**) in the presence of CsF followed by reaction with sulfuric acid [9]. In the next step the oxidation of intermediates **16** with *m*-CPBA gives polyfluoro-2-butanefluoronyl-3,3-dialkyloxaziridines **17** in wide ranging yields (30–80%) [9].



Hanack *et al.* also demonstrated the application of functionalized perfluoroalkanesulfonyl alkenes, especially nonafllyl substituted olefins, as highly reactive dienophiles in Diels–Alder reactions [10]. For example, [4+2] cycloaddition of 2-phenyl-1-(nonafluorobutanesulfonyl) acrylonitrile (**19**) and 2,3-dimethylbutadiene takes place under mild reaction conditions to form the highly substituted cyclohexene derivative **20** in good yield. The required starting material **18** in the preceding Knoevenagel reaction is easily prepared in a one-pot procedure by the deprotonation of acetonitrile with *n*-BuLi followed by treatment with NfF (**2**) at -78°C (35% yield) [10]. When the *in situ* generated Grignard compound of **21** reacts with NfF (**2**) the donor–acceptor-substituted diphenylsilane derivative **22** is produced which is an interesting product because of its nonlinear optical properties [11].

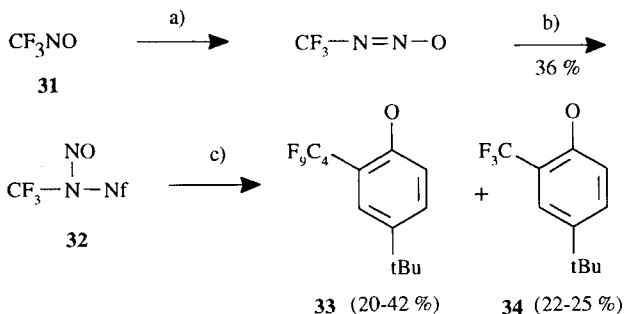
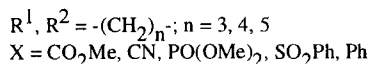
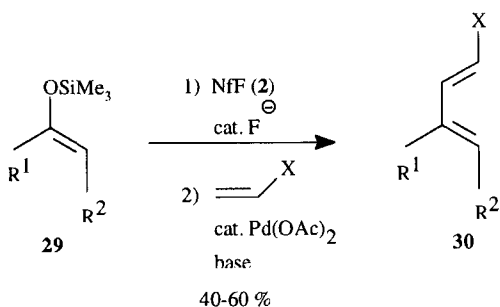
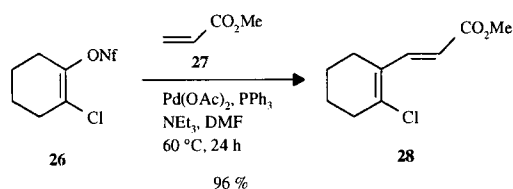
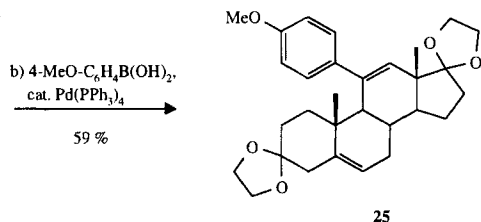
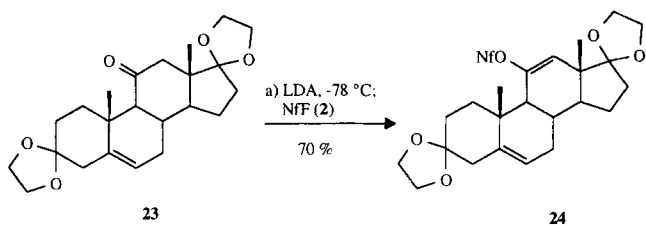
A relatively recent stimulus for the utilization of NfF (**2**) stems from the synthesis of alkenyl nonaflates and their application in palladium catalyzed reactions. An advantage of such nonaflates compared to the corresponding alkenyl triflates is the better quality of C₄F₉SO₃ as a leaving group which reflects in their greater reactivity [12]. Therefore it is possible to perform coupling reactions under slightly milder conditions than usually. However, the most important reason for the use of nonaflates instead of triflates is the considerably



lower price of the nonaflating agent NfF (**2**) compared with similar triflating compounds, such as (CF₃SO₂)O or Tf₂NPh. Treatment of nonaflate **24** with (4-methoxyphenyl)boronic acid and catalytic amounts of Pd(PPh₃)₄ resulted in a Suzuki coupling under formation of the arylsubstituted steroid derivative **25** in 59% yield [13]. The desired precursor **24** can be prepared by the deprotonation of ketone **23** followed by *O*-sulfonylation of the generated enolate with NfF (**2**). Nonaflates can also conveniently be used in Heck reactions. For example, the addition of methyl acrylate (**27**) to the cyclic nonaflate **26** leads to diene ester **28** in almost quantitative yield [14].

Our group recently developed a simple one-pot procedure for the Heck-coupling furnishing 1,3-dienes from silyl enol ethers [15]. The method works with a great variety of olefinic components, but mostly with electron-poor olefins. Using silyl enol ethers as starting material, which are easily available in very well-known syntheses in high regio- and stereoselective purity, the first step consists in the conversion into the nonaflates [16]. In a second step the nonaflates **29** are Heck-coupled without previous isolation with palladium(II)-acetate as catalyst, a mixture of potassium acetate and -carbonate as base, in DMF. Thus the corresponding 1,3-dienes **30** could be generated in satisfactory yields.

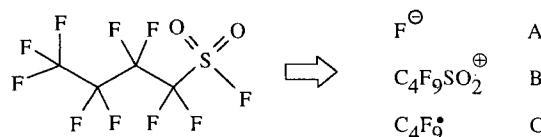
Finally, Umemoto and Ando described a radical perfluoroalkylation reaction of aromatic compounds [17]. The examination of the reactivity of **32** indicated that this type of *N*-



Reaction conditions: a) NH₂OH, -65 °C; b) NfF (2), NaH;
c) *p*-tert-Butylphenol, hv or 100 °C

nitroso sulfonamides are sources of nonafluorobutyl and trifluoromethyl radicals, respectively. Starting from nitroso compound **31** the preparation of perfluorobutyl substituted phenol **33** has been accomplished in 20–42% yield by reaction of **31** with hydroxylamine and NfF (2)/NaH followed by treatment with *p*-tert-butylphenol. The corresponding CF₃-substituted side-product **34** was also isolated in 22–25% yield.

In summary, the versatile compound nonafluoro-1-butanefluoride (2, NfF) can be used as reagent in different manner. It serves as fluorinating agent (A), nonafluorobutylsulfonylating agent (B) as well as nonafluorobutylating agent (C). New applications of this attractive compound NfF (2) are currently being investigated [18].



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