1,1,2,2,3,3,4,4,4-Nonafluorobutane-1-sulfonyl fluoride (NfF)

Timon Kurzawa
Institut für Chemie und Biochemie, Freie Universität Berlin, Takustr. 3, 14195 Berlin, Germany
kurzimon@chemie.fu-berlin.de

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Introduction

1,1,2,2,3,3,4,4,4-Nonafluorobutane-1-sulfonyl fluoride (NfF) is a versatile compound in organic synthesis. It can be used as a fluoride source for the nucleophilic introduction of fluorine, but it is also frequently applied as sulfonylation reagent generating intermediates with strong electron-withdrawing perfluorinated alkyl substituents.

NfF is produced on industrial scale by anodic fluorination of sulfolene (1, Scheme 1), therefore it is a fairly cheap reagent and commercially available from several suppliers. The compound is bench-stable and storable for years, non-toxic and easy to handle.

Table 1 Use of 1,1,2,2,3,3,4,4,4-Nonafluorobutane-1-sulfonyl fluoride (NfF)

(A) NfF can be used as a convenient fluoride source for the nucleophilic introduction of fluorine via the corresponding O-nonaflate as demonstrated by Vorbrüggen. The application of this method on industrial scale was demonstrated for the synthesis of iodenosine by Takamatsu et al.

(B) NfF is also a common sulfonylating agent that allows the conversion of carbonyl compounds 2, their corresponding trimethylsilyl enol ethers or phenol derivatives 3 into nonaflates. These alkenyl and aryl nonaflates are efficient precursors for all kinds of cross-coupling reactions, in which they often show a better reactivity and a superior stability during transformations than the related tosylates or triflates.
(C) The elimination of in situ formed alkenyl nonaflates derived from aldehydes or ketones in the presence of P-base gives terminal alkyne intermediates 4, as reported by Lyapkalo and Vogel in their one-pot synthesis of enynes 5. This synthetically useful method was later successfully applied by Huwyler and Carreira in their total synthesis of the chlorinated sesquiterpene (±)-gomerone C 9 by Nicolaou et al. for the preparation of the cytotoxic polypeptides myceliothermophins E, C and D. 10

(D) Furthermore, NfF is also a powerful reagent in numerous nucleophilic displacement reactions under very mild reaction conditions. The intermediate nonaflates undergo intramolecular substitutions leading to useful compounds such as epoxides 6 (X = O), 11 aziridines 6 (X = NTs) or thiazolines 7. 12

(E) Another interesting application of NfF involves its reaction with sodium azide, smoothly forming nonafluorobutane sulfonyl azide 8. 13 This azide is a stable liquid at room temperature and therefore easier and safer to handle than the corresponding trifluoromethane sulfonyl azide. The compound was used for Cu(II)-catalyzed diazo transfer reactions furnishing organic azides (R = alkyl or aryl). 14

References