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CONTRIBUTION FOR:

ELECTRONIC ENCYCLOPEDIA OF REAGENTS FOR ORGANIC SYNTHESIS

2,2,2-Trifluoroethyltrichloromethanesulfonate

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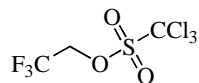
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2,2,2-Trifluoroethyltrichloromethanesulfonate

[23199-56-6] C₃H₂Cl₃F₃O₃S (MW 281.47)

(Trifluoroethylation agent for heteroatom nucleophiles, alkylating agent)¹

Alternate Names: 2,2,2-trifluoroethyltrichloromethanesulphonate; methanesulfonic acid trichloro-2,2,2-trifluoroethyl ester; trichloromethanesulfonic acid 2,2,2-trifluoroethyl ester; trichloromethanesulfonic acid 2,2,2-trifluoroethyl ester.

Physical Data: colorless liquid, mp -70 °C, bp 84-86 °C / 20 mmHg, d. 1.714.

Solubility: sol in all common organic solvents.

Form Supplied in: commercially available.

Preparative Methods: the reagent is prepared in one step from trichloromethanesulfonyl chloride and 2,2,2-trifluoroethanol.

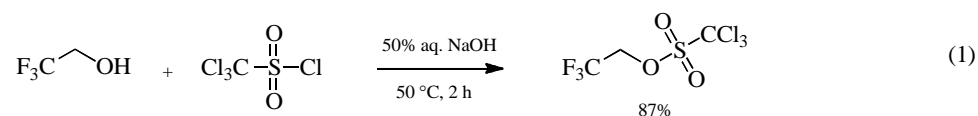
Analysis of Reagent Purity: bp

Handling, Storage, and Precautions: It is an extremely toxic, corrosive and a moisture sensitive liquid that may cause severe injuries, such as burns and irritations of the skin and eyes. Also, in aqueous media, it liberates highly toxic gases. Suitable protective clothing, gloves and eye/face protection should be worn upon its manipulation.

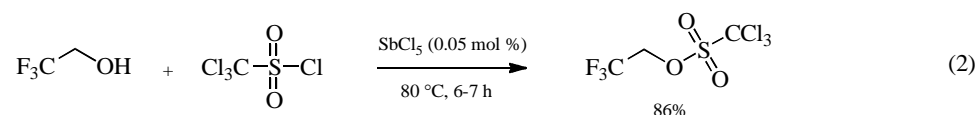
Purification: distillation under reduced pressure.

Preparation

2,2,2-Trifluoroethyltrichloromethanesulfonate ($\text{CF}_3\text{CH}_2\text{OSO}_2\text{CCl}_3$) can be readily prepared in the laboratory on a large scale.² A typical procedure involves the treatment of a mixture of 2,2,2-trifluoroethanol (TFE) (5 g, 0.05 mol) and trichloromethanesulfonyl chloride (11.3 g, 0.052 mol) in 15 mL of H_2O at 50 °C, with an aqueous solution of NaOH (2.2 g in 9 mL of H_2O). After 2 h at the same temperature, the reaction mixture was allowed to warm to room temperature (~20 °C). Petroleum ether was used to extract the sulfonate ester, and this solution was then washed several times with concentrated NH_4OH and H_2O . Filtration, drying over Na_2SO_4 and evaporation of the organic phase by rotary evaporation afforded the title compound as an oily residue, which could be further purified by distillation under reduced pressure. 2,2,2-Trifluoroethyltrichloromethanesulfonate was obtained in 87% yield (eq 1).

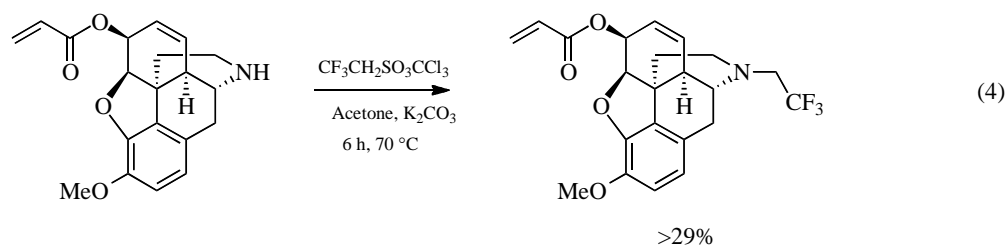
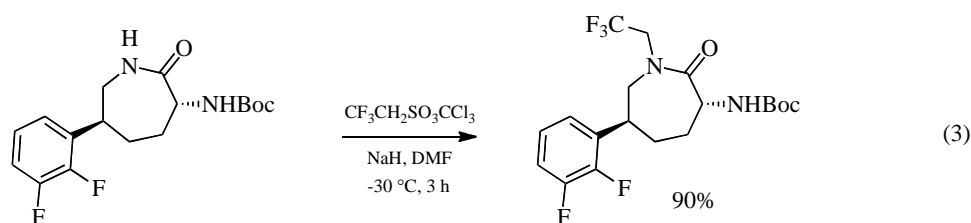


An improved procedure involving a Lewis acid-catalyzed mesylation of TFE in the absence of solvents at 80 °C was reported.³ In this way, 2,2,2-trifluoroethyltrichloromethanesulfonate was synthesized and isolated in an excellent chemical yield of 86% (eq 2). In comparison with the previously mentioned method, the latter (*i.e.* the SbCl_5 -catalyzed process) presents several advantages including, among others, (i) a maximum productivity because no solvent or base is used, and (ii) a possibility of catalyst recycling. Indeed, $\text{CF}_3\text{CH}_2\text{OSO}_2\text{CCl}_3$ is distilled directly from the reaction mixture, with hydrochloric acid being the only side product of the reaction.



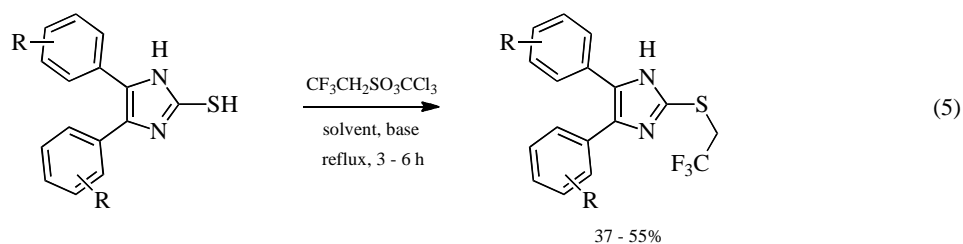
Trifluoroethylation of Nitrogen Derivatives

2,2,2-trifluoroethyltrichloromethanesulfonate is one of the most reactive reagents for trifluoroethylation of heteroatom nucleophiles. However, depending on pK_a values of the substrates, the addition of an equivalent of base is needed to avoid deactivation of the nucleophilic residues by protonation (*e.g.* CCl_3SO_3H generated along the reaction). Therefore, $Cl_3CSO_3CH_2CF_3$ has been used in the *N*-alkylation of anilines, amides (eq 3)⁴ and free amines (eq 4).⁵



Trifluoroethylation of Thiols

Thioimidazoles undergo S-trifluoroethylation upon treatment with $Cl_3CSO_3CH_2CF_3$. Typical examples are depicted below (eq 5).



R = H, *p*-OMe, *p*-Cl
 solvent = EtOH, toluene
 base = NaOMe, Et₃N

Trifluoroethylation of Phenols

Phenols have also been trifluoroethylated using this reagent and sodium hydroxide as the base, but representative examples can only be found in the patent literature.

Related reagents

2,2,2-trifluoroethyl benzenesulfonate; 2,2,2-trifluoroethyl chloride; 2,2,2-trifluoroethyl iodide; 2,2,2-trifluoroethyl methanesulfonate; trifluoroethyl phenyliodonium bis-((trifluoromethyl)sulfonyl)imide; 2,2,2-trifluoroethyl *p*-toluenesulfonate and perfluoroalkanesulfonate esters such as 2,2,2-trifluoroethyl trifluoromethanesulfonate.

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