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A Facile Conversion of Aliphatic Aldehydes to 1,1-Difluoroalkanes

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Abstract: *Aliphatic aldehydes can be easily converted to 1,1-difluoroalkanes by reaction of the corresponding gem-bistriflates with tetrabutylammonium difluorotriphenylstannate.*

Organofluorine compounds are of demonstrated importance in organic chemistry because of their applications in the areas of biological chemistry, agrochemicals, pharmaceuticals and fluoropolymers[1]. Numerous fluorinating reagents[2] have been developed for the transformation of aldehydes to the difluoromethyl group like NH_2-NH_2/IF[3], SF_4[4] or DAST[5]. However, most of these reagents present disadvantages because of their toxicity and handling difficulties or require special equipment and/or vigorous reaction conditions[2-5]. In order to find an easy procedure for the synthesis of the -CHF_2 moiety, in the present work we have studied the reaction of *gem*-bistriflates, which are obtained by reaction of the corresponding aliphatic aldehydes with triflic anhydride (Tf_2O)[6], with $[n\text{-}Bu_4N]^+F^-$[7], CsF/18-crown-6[8] and the recently reported[9] tetrabutylammonium difluorotriphenylstannate ($[n\text{-}Bu_4N]^+[Ph_3SnF_2]^-$).

$$\text{R-CHO} \longrightarrow \text{R-CH(OTf)}_2 \xrightarrow{\qquad} \text{R-CHF}_2$$

The reaction of *gem*-bistriflates with n-Bu_4NF and CsF/18-crown-6 affords mixtures in which the aldehyde is the main product. These results can be explained by residual moisture in the reagents[7] or by fission of the S-O bond. In contrast to this, the reaction with the non-hygroscopic $[n\text{-}Bu_4N]^+[Ph_3SnF_2]^-$ affords the corresponding *gem*-difluorides in good yield Table 1)[10]. Therefore, our procedure is a viable alternative for the transformation of aliphatic aldehydes into the difluoromethyl group.

Table 1. Yields of conversion of aldehydes to *gem*-bistriflates and 1,1-difluoroalkanes.

Aldehyde	Yield of *gem*-bistriflate(%)	Yield of 1,1-difluoroalkane(%)[a]
Tridecanal	85	75
Octanal	81	77
3-Phenylpropionaldehyde	74	70
Phenylacetaldehyde	62	68[b]
2-Phenylpropionaldehyde	63	59
2-Ethylhexanal	68	63[b]
Cyclohexanecarboxaldehyde	76	72[b]
Cyclooctanecarboxaldehyde	72	72[b]

[a] All compounds were characterized by IR, MS, ^{1}H-NMR, and ^{13}C-NMR spectroscopy.
[b] Determined by GLC using internal standard.

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References and Notes

1)*Fluorine-containing Molecules. Structure, Reactivity, Synthesis and Applications*; Liebman, J. F.; Greenberg, A.; Dolbier, W. R. Jr. Eds.; VCH; New York. 1988. 2)Welch, J. T. *Tetrahedron* **1987**, *43*, 3123. 3)Rozen, S.; Zamir, D. *J. Org. Chem.* **1991**, *56*, 4695.4)Boswell, G. A.; Ripka, W. C.; Schribner, R. M.; Tullock, C. W. *Org. React.* **1974**, *21*, 1. 5)Middleton, W. J. *J. Org. Chem.* **1975**, *40*, 574. 6)García Martínez, A.; Martínez Alvarez, R.; García Fraile, A.; Subramanian, L. R.; Hanack, M. *Synthesis* **1987**, 49. *Gem*-bistriflates were prepared according to ref. 6 using N,N-diisobutyl-2,4-dimethyl-3-pentylamine(Fluka) as base. 7)Chi, D. Y.; Kilbourn, M. R.; Katzenellenbogen, J. A.; Welch, M. J. *J. Org. Chem.* **1987**, *52*, 658. 8)Gingras, M.; Harpp, D. N. *Tetrahedron Lett.* **1988**, *29*, 4669. 9)Gingras, M. *Tetrahedron Lett.* **1991**, *32*, 7381. 10) In a typical procedure, 3.7g (6 mmol) of tetrabutylammonium difluorotriphenylstannate are added, at room temperature, to a solution of 2 mmol of *gem*-bistriflate in 25 ml of dry methylene chloride. After stirring for 2 h (8 h in the case of α-branched *gem*-bistriflates), 50 ml of *n*-pentane are slowly added to the reaction mixture. After separation of the inorganic salts, the solvent is distilled using a 20 cm Vigreux column and the *gem*-difluoride is purified by chromatography (silica gel, *n*-pentane). The results are summarized in Table 1.

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