Direct Synthesis of Fluorinated Heteroarylether Bioisosteres


Direct Difluoroethylation of Heteroaromatics, Michael Acceptors and Thiols

**Significance:** A novel protocol for direct difluoroethylation of a broad range of heterocycles, Michael acceptors and even thiols with sodium difluoroethylsulfinate (DFES-Na) has been described. DFES-Na is shown to be compatible with various sensitive functional groups, reacts site selectively in high conversion and is easy to handle.

**Comment:** Interestingly, performing the reaction with DFES-Na and *tert*-butylhydroperoxide (TBHP) solely results in only traces of the desired product. Only after addition of stoichiometric amounts of ZnCl₂ and TsOH·H₂O, the product is obtained in high yield.

R₁ = various substituted heteroaromatics, Michael acceptors and thiols
R₂ = Me, CH₂-4-BrC₆H₄, (CH₂)₆Cl

Selected examples:

![Chemical structures showing selected examples of difluoroethylation products.](image)

- CO₂Me: 92% yield
- Me: 58% yield
- 51% yield
- 83% yield
- 66% yield
- 83% yield
- 56% yield