New Method for the Synthesis of 1,1-fluoronitroalkenes by Radical Substitution in Fluorobromostyrenes

Motornov, Vladimir

Conjugated nitroalkenes are very useful substrates for the synthesis of biologically active compounds by different routes. Thus, fluoronitroalkenes may be used as precursors for fluorine-containing amines (that are important enzyme inhibitors) and other medicinally relevant compounds. But present method of the fluoronitroalkene synthesis by Horner-Wadsworth-Emmons reaction is laborious and it has limited use. In this work new method for the 1,1-fluoronitroalkene synthesis by radical substitution was investigated. 1,1-fluoronitroalkenes were synthesized by substituting nitration of corresponding 1,1-fluorobromoalkenes with NO2 generated in situ by thermal decomposition of different transition metal nitrates or by nitrite oxidation. Different conditions (nitrating agents and solvents) were checked. TEMPO and N-hydroxyphthalimide were checked as catalysts for radical substitution. The best yields (from 68 to 92% depending on substituents) were obtained using iron (III) nitrate, 0.2 eq. TEMPO as a catalyst and 1,2-dichloroethane as a solvent. Substrate scope was determined on series of substituted styrenes. The reaction was proceeded stereospecifically producing only (Z)-isomers of products. The structures of obtained products were confirmed by 1H, 13C, 19F-NMR spectroscopy and mass spectrometry. Also some chemical transformations with obtained fluoronitroalkenes (e.g. Michael addition, cycloadditions) were performed.

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