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

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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.