ALPHA-FLUORONITROALKENES: USEFUL BUILDING BLOCKS FOR THE CONSTRUCTION OF NOVEL FLUORINATED HETEROCYCLES

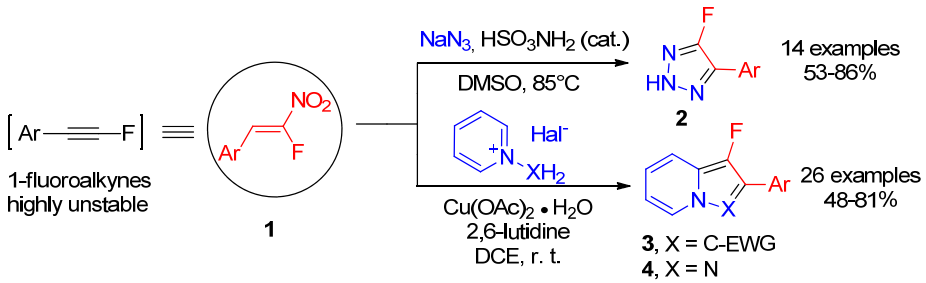
Vladimir Motornov, Andrey A. Tabolin, Sema L. Ioffe

N. D. Zelinsky Institute of Organic Chemistry, Leninsky pr. 47, 119991, Moscow, Russia

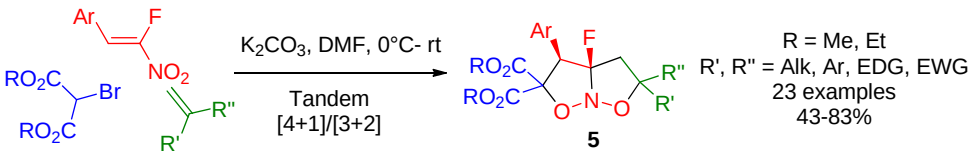
Fluorine-containing molecules are widely used as important pharmaceuticals and agrochemicals. Among them fluorinated heterocycles are the compounds of special interest, possessing different types of biological activity.[1]

We have reported the efficient method for the two-step synthesis of α-fluoronitroalkenes from aromatic aldehydes.[2] In the present work a number of routes to previously inaccessible fluorinated heterocycles from fluoronitroalkenes was developed.

First, the reactivity of α-fluoronitroalkenes in [3+2]-cycloadditions as 2π-components was studied. While synthesis of different fluorinated heterocycles via [3+2]-cycloaddition was limited due to extreme instability of 1-fluoroalkynes,[3] α-fluoronitroalkenes 1 were found to act as their suitable synthetic equivalents. Thus, a route to previously inaccessible 4-fluoro-1,2,3-NH-triazoles 2 by cycloaddition with sodium azide was developed. Sulfamic acid was found to be the optimal catalyst for this transformation. Oxidative [3+2]-annulation of α-fluoronitroalkenes with pyridinium ylides and imines mediated by copper (II) acetate provides a direct route to novel fluorinated indolizines 3 and pyrazolo[1,5-a]pyridines 4.



Next, the reactivity of nitroalkenes as 4π-components was explored. The one-pot reaction of α-fluoronitroalkenes, bromomalonic ester and different dipolarophiles in basic conditions resulted in formation of bicyclic 5,5-annulated nitroso acetals 5. The mechanism involving tandem [4+1]/[3+2]-cycloaddition was discussed. Nitroso acetals formed with complete regioselectitity and high diastereoselectivity, and both electron-rich and electron-deficient dipolaropiles were suitable substrates for cycloaddition.



This work was supported by the Russian Foundation for Basic Research (grant № 18-03-00810).

[1] Fluorine in Heterocyclic Chemistry, Vols. 1-2, Ed. V. G. Nenajdenko, Springer International Publishing: Switzerland, **2014**.

[2] V. A. Motornov, V. M. Muzalevskiy, A. A. Tabolin, R. A. Novikov, Yu. V. Nelyubina, V. G. Nenajdenko, S. L. Ioffe, J. Org. Chem. **2017**, 82, 5274-5284.

[3] H. G. Viehe, R. Merenyi, J. F. M. Oth, P. Valange, Angew. Chem., Int. Ed., **1964**, 3, 746-746.