

# SYNLETT Spotlight 219

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

## *N*-Fluorobenzenesulfonimide [(PhSO<sub>2</sub>)<sub>2</sub>NF] – A Neutral N–F- Containing Electrophilic Fluorinating Agent

Compiled by Amin Rostami

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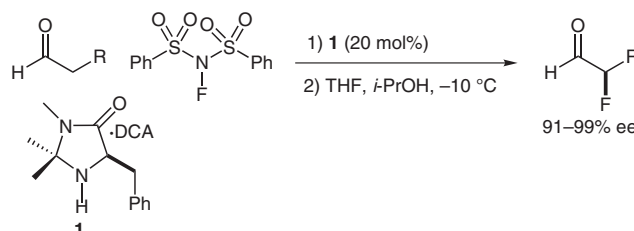


### Introduction

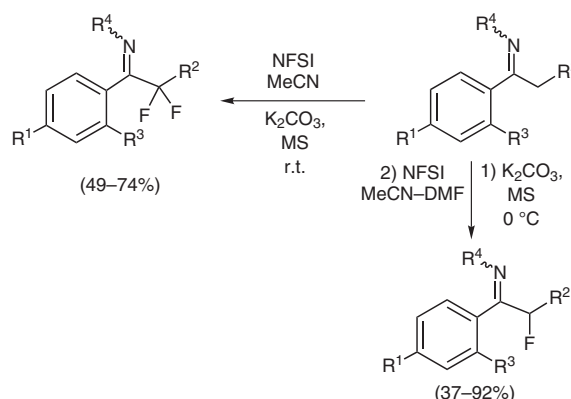
*N*-Fluorobenzenesulfonimide [NFSI] is a stable crystalline solid that is easy to handle, non-hygroscopic, soluble in most common ethereal and chlorinated solvents, and commercially available. It is a neutral N–F-containing electrophilic fluorinating agent that permits the incorporation of fluorine into neutral and carbanionic nucleophiles ranging from very reactive organometallic species to slightly activated aromatic compounds.<sup>1</sup>

### Abstracts

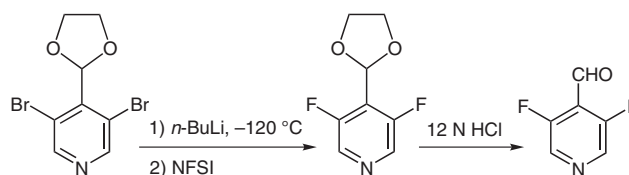
The use of imidazolidinone **1** as the asymmetric catalyst has been found to mediate the fluorination of aldehyde substrates with *N*-fluorobenzenesulfonimide serving as the electrophilic source of fluorine. A wide range of functional groups, including olefins, esters, amines, carbamates, and aryl rings, can be readily tolerated on the aldehydic substrate.<sup>9</sup>



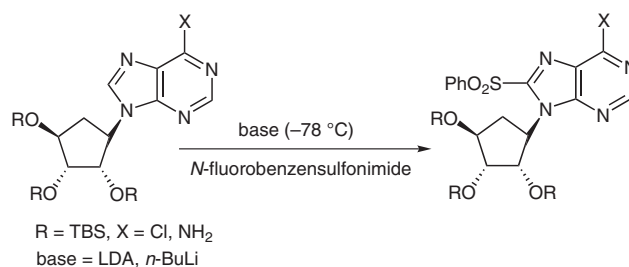
Various *N*-alkylimines derived from acetophenones were successfully monofluorinated using *N*-fluorobenzenesulfonimide (NFSI) in a mixture of acetonitrile and DMF at 0 °C. Alternatively the same procedure without DMF gave rise to difluorinated imines when performed at room temperature. The obtained  $\alpha$ - and  $\alpha,\alpha$ -difluorinated imines were subsequently reduced to give the corresponding  $\beta$ -fluoro- and  $\beta,\beta$ -difluoroamines in good yield.<sup>10</sup>



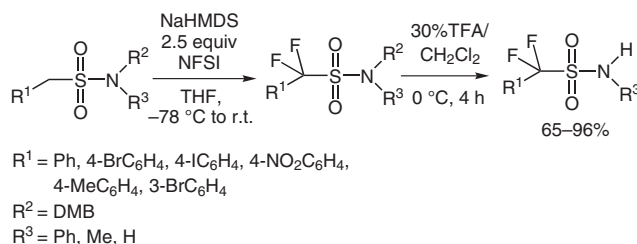
NFSI was used for synthesis of novel 3,5-difluoropyridine-4-carboxaldehyde. Difluorination was achieved through the reaction of 3,5-dibromo-1,3-dioxolane pyridine with *n*-butyllithium followed by *N*-fluorobenzenesulfonimide at  $-120\text{ }^{\circ}\text{C}$  in good yield.<sup>11</sup>



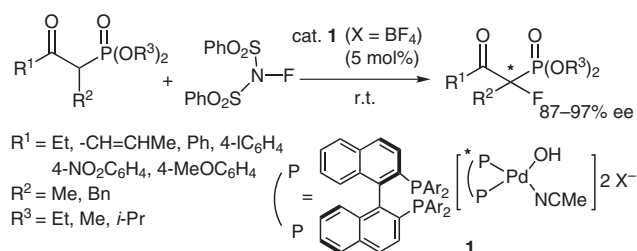
Reaction of the in situ generated purine C-8 carbanion of a protected 5'-noraristeromycin derivative with *N*-fluorobenzenesulfonimide gave 8-phenylsulfonyl-5'-noraristeromycin rather than the expected 8-fluoro derivative. A single electron transfer (SET) mechanism is proposed for this occurrence. The phenylsulfonyl product offers a structural feature common to some anti-HIV agents.<sup>12</sup>



$\alpha$ -Fluorosulfonamides were prepared by electrophilic fluorination of tertiary sulfonamides using *N*-fluorobenzenesulfonimide as fluorinating agent and utilizing the dimethoxybenzyl group (DMB) as a new sulfonamide protecting group. Removal of the DMB group with TFA/ $\text{CH}_2\text{Cl}_2$  gave primary and secondary  $\alpha$ -fluorosulfonamides.<sup>13</sup>



D. Y. Kim and coworkers reported the catalytic enantioselective fluorination of  $\beta$ -keto phosphonates catalyzed by a chiral palladium complex. Reaction of  $\beta$ -keto phosphonates with *N*-fluorobenzenesulfonimide (NFSI) as electrophilic fluorinating reagent under mild reaction conditions afforded the corresponding  $\alpha$ -fluorinated  $\beta$ -keto phosphonates in moderate to excellent yields with excellent enantiomeric excesses.<sup>14</sup>



## References

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