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 [(PhSO₂)₂NF] – A Neutral N–F- Containing Electrophilic Fluorinating Agent

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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.¹

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.⁹

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 α - and α,α -difluorinated imines were subsequently reduced to give the corresponding β -fluoro- and β,β -difluoroamines in good yield.¹⁰

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.¹¹

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.¹²

α -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/ CH_2Cl_2 gave primary and secondary α -fluorosulfonamides.¹³

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

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