SYNLETT
# Spotlight 273

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

# 2-(Trimethylsilyl)ethanesulfonamide ($TMS(CH_2)_2SO_2NH_2$ or SES-$NH_2$) – A Sulfonamidation Agent With Multiple Qualities

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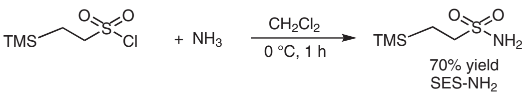
## Introduction

Sulfonamides act as protecting and activating groups in the synthesis of amines[1] and they are among the most stable amine protecting groups under a wide range of conditions.[2] SES-$NH_2$ plays this role in synthesis and can be used alternatively to introduce a SES-protected amine functionality directly into a molecule.[2]

Weinreb and co-workers prepared sulfonamides from a primary or secondary amine using the previously unknown β-(trimethylsilyl)ethanesulfonyl chloride (SES-Cl).[3]

In 1996, Griffith and Danishefsky synthesized 2-(trimethylsilyl)ethanesulfonamide (SES-$NH_2$) by bubbling ammonia gas through a stirred solution of SES-Cl in dichloromethane at 0 °C. The reaction occurs with good yield of 70% over a period of one hour (Scheme 1).[4]




**Scheme 1**

Nosyl, tosyl and mesyl groups would perform the same role as the SES group, however, tosyl and mesyl groups are usually troublesome to deprotect.[1,2] Although SES-protected amines are stable compounds, they can be readily cleaved under mild conditions using fluoride sources (CsF or TBAF) to generate the parent amine.[2,5]

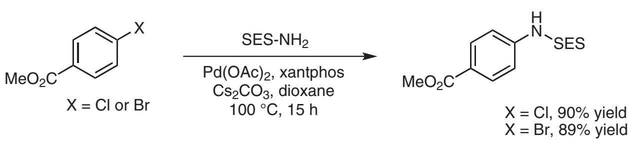
On deprotection, the fluoride ion attacks the silicon atom leading to the free amine and to volatile products such as ethylene, fluorotrimethylsilane and sulfur dioxide through β-elimination.[6]

SES-$NH_2$ is considered as an ammonia surrogate for the palladium-catalyzed amination of aryl bromides and aryl chlorides.[6] Moreover, this reagent can be used in iminations reaction,[7] synthesis of azamacrocycles,[8] aza-Baylis–Hillman reaction,[9,10] synthesis of the aziridines[11,12] and important biologically compounds.[12,13]

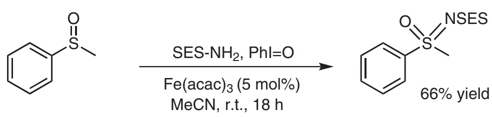
The reagent is commercially available as a white solid (mp 86–89 °C).[4] It should be used with carefull precaution, because it can be irritating to the eyes, the skin and the respiratory system.

## Abstracts

(A) The SES-$NH_2$ can be used as an ammonia substitute in the palladium-catalyzed synthesis of primary arylamines from aryl halides. This reaction, known by Buchwald–Hartwig method, works well with aryl bromides, aryl chlorides and heterocyclic chlorides to produce high yields of the adducts with different substituents such as cyano, ester, keto, nitro and aldehyde.[6]




(B) The stereospecific imination of various sulfoxides has been achieved under mild conditions (room temperature) using the inexpensive $Fe(acac)_3$ as a catalyst. Sulfonamide in combination with iodosylbenzene is a nonhazardous nitrogen source for this reaction in substitution of potentially explosive azides.[7]

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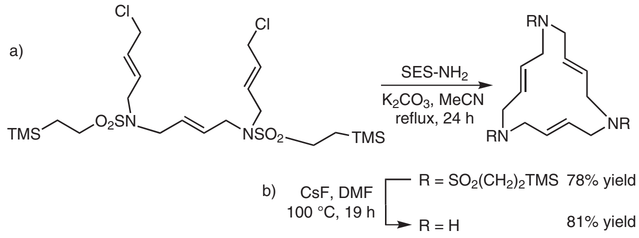
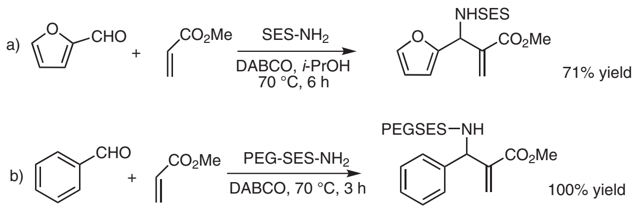
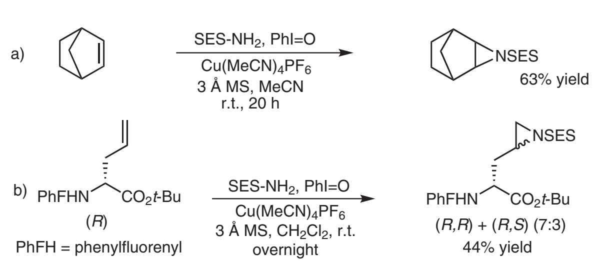
(C) $SES-NH_2$ offers a convenient access to the synthesis of linear and cyclic triamines with control over the carbon-bridge architecture. Masllorens et al. proposed the synthesis of 15-membered triolefinic azamacrocycles using $SES-NH_2$ as an amine protecting group [example a)]. An example of removal of the protecting group by fluoride can be verified on second stage of the reaction supplying a good yield of 81% [example b)].[8]



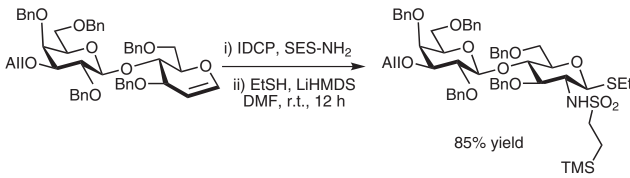

(D) An attractive method for the synthesis of β-aminoesters is the 3-component aza version of Baylis–Hillman reaction. Reaction of furfural at 70 °C and 6 h have showed high selectivity, yielding 71% (example a).[9] Ribière et al. reported the first nitrogen-anchored polymer-supported aza-Baylis–Hillman reaction, by means of PEG-$SES-NH_2$.[10] This support allows the use of large excess of reactants that is easily removed after precipitation by filtration and washing. In the case of benzaldehyde a quantitative conversion was achieved in 3 h and in the absence of solvent (example b).[10]




(E) A series of olefins reacts to afford N-sulfonylated aziridines in moderate yields. This reaction is a direct copper-catalyzed nitrogen transfer mediated by the iodosylbenzene, a powerful oxygen atom donor (example a).[11] Example b) shows an diastereoselective aziridination which provided a 7:3 ratio of the (2*R*,4*R*) and (2*R*,4*S*) isomers, with yield 40% of the major diastereomer. This reaction was an important stage on the synthesis of enduracididine, an α-amino acid isolated from *Streptomyces fungicidicus* in 1968.[12] Moreover, the comercial availability of easy-to-handle copper(II) complexes as catalyst makes this reaction highly practical.[11–13]




(F) Wang et al. used $SES-NH_2$ in a stage to the synthesis of an N-linked glycopeptide presenting the H-type 2 human blood group determinant. The iodosulfonamidation was followed by thiolysis and release of iodide, providing a thioglycoside at room temperature in 85% yield.[14]

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