

SYNLETT Spotlight 273

2-(Trimethylsilyl)ethanesulfonamide (TMS(CH₂)₂SO₂NH₂ or SES-NH₂) – A Sulfonamidation Agent With Multiple Qualities



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

Compiled by Carmelita Gomes da Silva

Carmelita Gomes da Silva was born in 1978 in Rio de Janeiro, Brazil. She received her Pharmacy degree from Universidade Estácio de Sá (UNESA) in 2005 and her M.Sc. in Biochemistry from Universidade Federal do Rio de Janeiro (UFRJ) in 2007. Nowadays, she studies towards her Ph.D. under the supervision of Dr. Cláudia Moraes de Rezende and Dr. Elis Cristina Araújo Eleutherio with a CNPQ scholarship at the UFRJ. Her research is focused on isolation, structure elucidation and transformation of biologically active natural products.

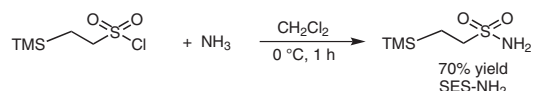
Departamento de Química Orgânica, Instituto de Química, Universidade Federal do Rio de Janeiro (UFRJ), Avenida Athos da Silveira Ramos, Centro de Tecnologia, Bloco A, 6º andar, Ilha do Fundão, Cidade Universitária, Rio de Janeiro; RJ, CEP 21941-909, Brazil.
E-mail: carmelita@iq.ufrj.br

Introduction

Sulfonamides act as protecting and activating groups in the synthesis of amines¹ and they are among the most stable amine protecting groups under a wide range of conditions.² SES-NH₂ 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

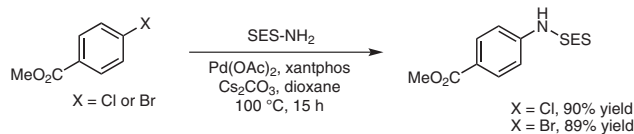
In 1996, Griffith and Danishefsky synthesized 2-(trimethylsilyl)ethanesulfonamide (SES-NH₂) by bubbling ammonia gas through a stirred solution of SES-Cl in dichloromethane at 0 °C. The reaction occurs with good yield of 70% over a period of one hour (Scheme 1).⁴



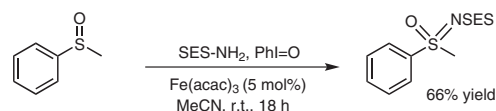
Scheme 1

Abstracts

(A) The SES-NH₂ 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



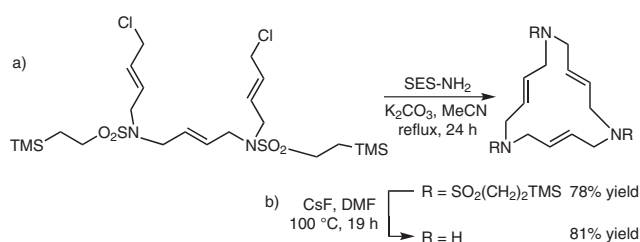
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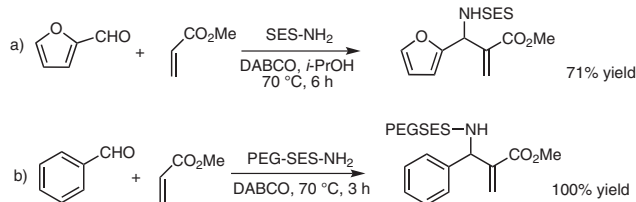
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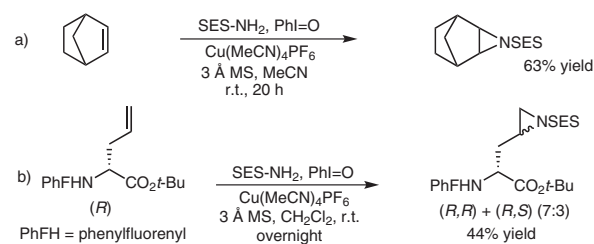
(C) SES-NH₂ offers a convenient access to the synthesis of linear and cyclic triamines with control over the carbon-bridge architecture. Masllorens et al. proposed the synthesis of 15-membered triolefinic azamacrocycles using SES-NH₂ as an amine protecting group [example a]. An example of removal of 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-NH₂.¹⁰ 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 a 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 commercial availability of easy-to-handle copper(II) complexes as catalyst makes this reaction highly practical.^{11–13}



(F) Wang et al. used SES-NH₂ 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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