

SYNLETT Spotlight 360

Elemental Sulfur: A Simple, Economic, and Versatile Reagent

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

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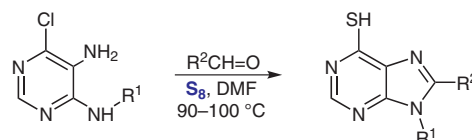
Introduction

Elemental sulfur is a pale yellow, odorless and brittle solid, which is insoluble in water, but soluble in CS₂.¹ It is very inexpensive and easily available, because of its abundance in many natural sources (petroleum crude, minerals, etc.).² Elemental sulfur appears in several allotropic forms: octahedral, rhombic or α-sulfur, monoclinic, pris-

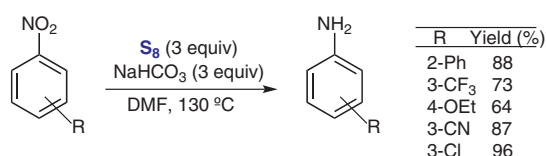
matic or β-sulfur.¹ Both the rhombic and monoclinic forms are made up of eight sulfur atoms arranged in a puckered structure. Literature reveals that S₈ has been extensively used in numerous organic transformations, including synthesis of mercaptopurines,³ oxazolidinones,⁴ aminothiophenes,⁵ reduction of nitroarenes,⁶ and as oxidation agents.⁷ These and some other applications are described below.

Abstracts

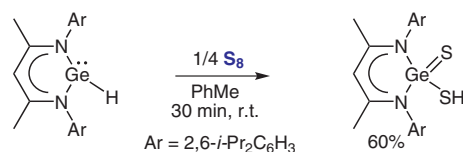
(A) A one-pot conversion of 4,5-diamino-6-chloropyrimidines into 6-mercaptapurines was presented by Tandel et al.³ The reaction is easy to perform by simply heating of a mixture of pyrimidine, aldehydes and an equimolar amount of elemental sulfur in DMF. All reactions were carried out in 17 hours with good to high yields (18–93%) and the method uses an in situ generated H₂S for the conversion of the chloro into the mercapto group.



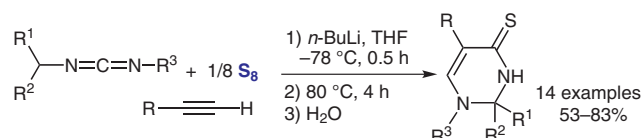
(B) McLaughlin and Barnes reported an efficient method for the transformation of functionalized nitroarenes to the corresponding anilines with elemental sulfur and base in good yields.⁶ The process takes advantage of the capacity of sulfur to be an inexpensive 2-electron reductant. The reaction conditions are also notable for their compatibility with a range of functional groups and use of a mild base.



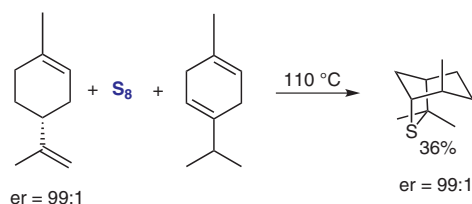
(C) Recent efforts have been directed to study the use of germanium(II) hydrides in hydrogenation reactions.⁸ The rapid simultaneous insertion of elemental sulfur into the germylene hydrogen bond and oxidative addition of sulfur to the germylene atom has been reported. The product is the first representative example of a dithiocarboxylic acid analogue with a heavier group 14 element and a terminal S–H bond, and constitute a new precursor for many metal complexes.



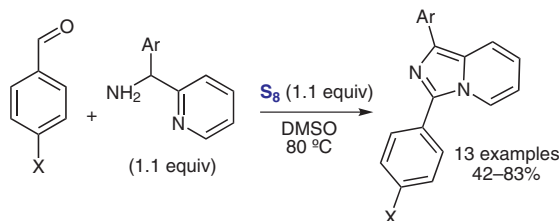
(D) Elemental sulfur has proved to be an efficient component in the one-pot synthesis of 2,3-dihydropyrimidinethiones via multicomponent coupling with terminal alkynes and carbodiimides.⁹



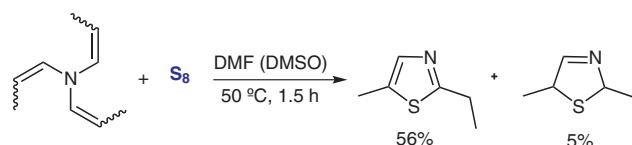
(E) The solvent-free reaction between elemental sulfur and limonene in the presence of γ -terpinene afforded the isothiocieneole in 36% yield, useful in the asymmetric epoxidation and aziridination reactions. Moreover, the sulfide product was used in the synthesis of the cinchona alkaloids, quinine and quinidine, interesting molecules with a relevant history in medicine, synthesis, and catalysis.¹⁰



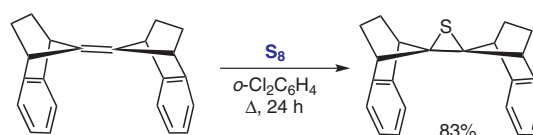
(F) Elemental sulfur catalyzed the oxidative condensation–cyclization of aromatic aldehydes and aryl-2-pyridylmethyl amines afforded an elegant access to appropriate 1,3-diarylated imidazo[1,5-*a*]pyridines. The products show a wide variety of fluorescent emissions at 454–524 nm.⁷



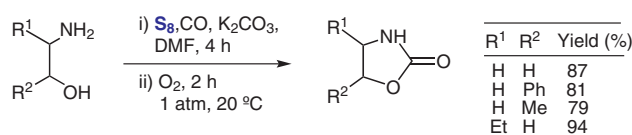
(G) The reaction of tri(1-propenyl)-amine with elemental sulfur can be realized to the synthesis of thiazoles in good yield.¹¹



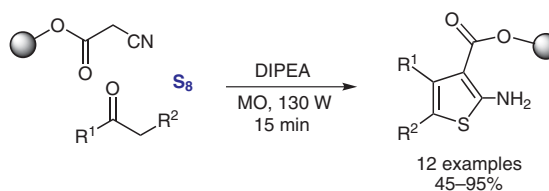
(H) An interesting strategy to mono-sulfuration of alkenes has been reported by Sugihara and co-workers.¹² The reaction of *syn*-bibenzonorbonylidene with elemental sulfur furnished the episulfide exclusively in 83% yield with retention of the original stereochemistry.



(I) A series of 2-oxazolidinones were synthesized by thiocarboxylation of 2-aminoethanols with carbon monoxide using elemental sulfur, followed by the oxidative cyclization by molecular oxygen.⁴



(J) The most convergent and well-established classical approach for the synthesis of 2-aminothiophenes is Gewald's protocol, which involves the multicomponent reaction of a ketone with an activated nitrile and elemental sulfur in the presence of an organic base.⁵ Recently, Zhang et al. reported that the PEG-bound cyanoacetic ester also undergoes the Gewald reaction under microwave irradiation.



References

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