

The versatility and synthetic utility of Gewald reaction

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Highly substituted thiophenes are important heterocycles found in numerous biologically active compounds. The 2-aminothiophenes has been exhibiting diverse applications in combinatorial and medicinal chemistry and its products are of great use in pharmaceutical industry.

The chemistry of 2-aminothiophenes has received much attention upon their convenient availability through the most versatile synthetic method developed by Gewald and his co-workers.

Many methods of synthesis of substituted 2-aminothiophenes published before the Gewald are generally unsuitable because they involve difficult preparation of the starting materials, multi step synthesis with low yields.

The availability of reagents and the mild reaction conditions all contribute to the versatility of this reaction. This abstract summarizes the synthetic strategies for 2-amino thiophenes with substitutions at 4- and 5-positions.

The Gewald reaction represents the multi component process to prepare numerous 2-aminothiophenes in generally high yields from α -substituted acetonitriles carrying electron-withdrawing groups and α -methylene carbonyl compounds (aldehydes or ketones) in the presence of the base - organic bases such as secondary or tertiary amines (diethylamine, morpholine, triethylamine, pyridine). Polar solvents, like DMF, alcohols, 1,4-dioxane enhance the condensation of intermediates - α,β -unsaturated nitriles with sulfur, which are either prepared in situ or externally.

Although this one-pot synthesis is well established, the two-step procedure in which an α,β -unsaturated nitrile is first prepared by a Knoevenagel-Cope condensation of ketone or aldehyde with an activated nitrile, followed by base-promoted reaction with sulfur has been also widely employed.

Recently, the improvements of the Gewald synthesis were announced. They are based in diminution of the reaction time by using microwave technology.

Biography

J.Saravanan is working as Professor and HOD, Department of Pharmaceutical Chemistry, PES College of Pharmacy, Bangalore, Karnataka, India. He has completed his Ph.D. from Bangalore University. He has published more than 60 research papers and presented over 65 research presentations in national & international conferences, seminars & workshops. He has received various research grants and seminars / conferences grants. He has organized four international conferences, two national seminars and a national workshop. He is also serving as a reviewer in reputed national & international journals.

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