

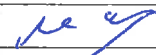
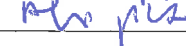
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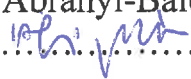
„Continuous-Flow Synthesis of Thioureas, Enabled by Aqueous Polysulfide Solution”

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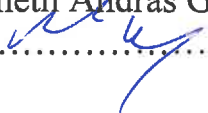
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Article

Continuous-Flow Synthesis of Thioureas, Enabled by Aqueous Polysulfide Solution

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Abstract: We have developed the continuous-flow synthesis of thioureas in a multicomponent reaction starting from isocyanides, amidines, or amines and sulfur. The aqueous polysulfide solution enabled the application of sulfur under homogeneous and mild conditions. The crystallized products were isolated by simple filtration after the removal of the co-solvent, and the sulfur retained in the mother liquid. Presenting a wide range of thioureas synthesized by this procedure confirms the utility of the convenient continuous-flow application of sulfur.

Keywords: continuous flow; sulfur; aqueous polysulfide solution; thiourea; multicomponent reaction



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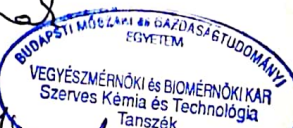
1. Introduction

In the last two decades, continuous-flow (CF) synthesis has become a powerful and versatile tool in synthetic organic chemistry. The enhanced mixing properties, heat, and mass transfer of CF systems lead to more precise regulation of the reaction conditions, and thus, better reproducibility and selectivity can be realized than in batch processes [1,2]. Notably, CF chemistry has been used in hazardous reactions (nitration, halogenation, reaction with organolithium reagents and azides, etc.) [3,4] and in synthetic methods requiring a high temperature and pressure [5–7], as well. In addition, it enables cleaner reaction profiles with better product–side-product ratios, and reaction pathways that could hardly be realized in batch processes (e.g., use of highly reactive peptidyl donors) [8–10]. Moreover, CF techniques are suitable for multistep [11–14] and automated synthetic processes, which is a rapidly growing field in modern organic chemistry [15–17].

Sulfur-containing compounds are widely known as biologically active molecules [18] and functional organic materials [19,20]. Thioureas, in particular, are used as pharmaceutical and agrochemical intermediates or active ingredients represented by the marketed drug thiocarbide [21], and by algicides [22], fungicides [23], and the insecticide chloromethiuron [24]. In addition, they are key intermediates of nitrogen- and sulfur-containing compounds, especially pharmacologically relevant heterocycles [25–29]. Notably, in the last two decades, thioureas were also applied as highly selective and efficient organocatalysts [30–34] (Scheme 1). Given the wide utility of thioureas, their clean and efficient synthesis is of high interest.

A közlemény kivonatának hitelességét igazolom.

Kupai József
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