SYNTHESIS OF IMIDAZO(2,1-b)(1,3)THIAZINES VIA ELECTROPHILE-PROMOTED CYCLIZATION OF 2-ALKENYLTHIOIMIDAZOLES

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Compounds containing an imidazo[2,1-*b*][1,3]thiazine fragment exhibit a wide range of biological properties, including anti-tuberculosis [1], anti-inflammatory [2], antifungal [3], and amyloid aggregation inhibitory [4] activities. These diverse biological activities highlight the importance of this heterocyclic system in medicinal chemistry, as imidazo[2,1-*b*][1,3]thiazine derivatives display structure–activity trends that enable targeted modification of the core structure to improve biological efficacy. This system's high chemical stability and ability to interact with biomolecules selectively further support its importance in synthetic and medicinal chemistry. Due to the biological significance of this heterocyclic system, developing efficient synthetic strategies is important. Conventional approaches to constructing the imidazo[2,1-*b*][1,3]thiazine framework typically involve nucleophilic substitution or condensation reactions. These methods often require multiple synthetic steps and are associated with limited overall efficiency. In recent years, electrophile-promoted nucleophilic cyclization reactions have emerged as an effective strategy for the one-step formation of complex heterocyclic systems [5]. This approach not only enables efficient formation of the imidazo[2,1-*b*][1,3]thiazine core but also ensures good selectivity and high yields, making it a promising tool for the synthesis of structurally diverse derivatives.

In this study, electrophile-initiated cyclization reactions of 2-alkenylthioimidazoles were investigated. 2-Cinnamylthiobenzimidazole was selected as a model substrate for the optimization of cyclization reaction conditions. The optimized reaction conditions were applied to the cyclization of other 2-alkenylthioimidazole analogues. The resulting compounds underwent base-promoted elimination to efficiently yield the corresponding imidazo[2,1-*b*][1,3]thiazine derivatives (Fig. 1).

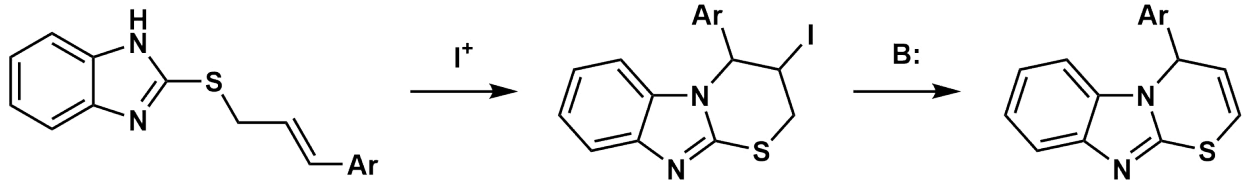

Fig. 1. Synthesis of benzimidazo[2,1-*b*][1,3]thiazine frameworks

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