



A cost-effective strategy for artificial siderophores with potential biological applications using a fragment-based approach for targeted antimicrobial therapy

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BACKGROUND AND MOTIVATION

The study addresses the escalating threat of antimicrobial resistance (AMR) by exploring two approaches: discovering new antimicrobial agents and enhancing existing ones. Focusing on the latter, the study employs the Trojan-horse strategy, centering on siderophores and fragments. Siderophores, organic chelators, facilitate iron uptake in bacteria, crucial for growth. By covalently linking antibiotics to siderophores, the Trojan-horse approach exploits bacterial ferri-

siderophore uptake pathways, enabling antibiotics to penetrate bacterial cells. Unlike prior studies, this research pioneers a fragment-based synthesis of siderophores, constructing a library for testing synthetic analogues. The study integrates various assays for identification and characterization, offering potential breakthroughs in combating AMR.

MATERIALS AND METHODS

PROPOSED METHODOLOGY

1. Synthesis of fragments

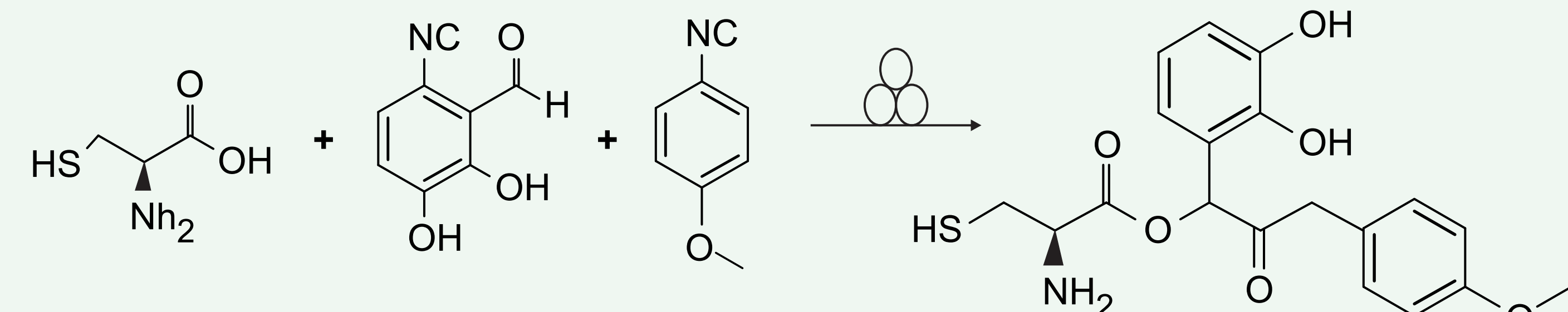


Figure 1 : Mechanochemical assisted passerini reaction

2. Synthesis of siderophores

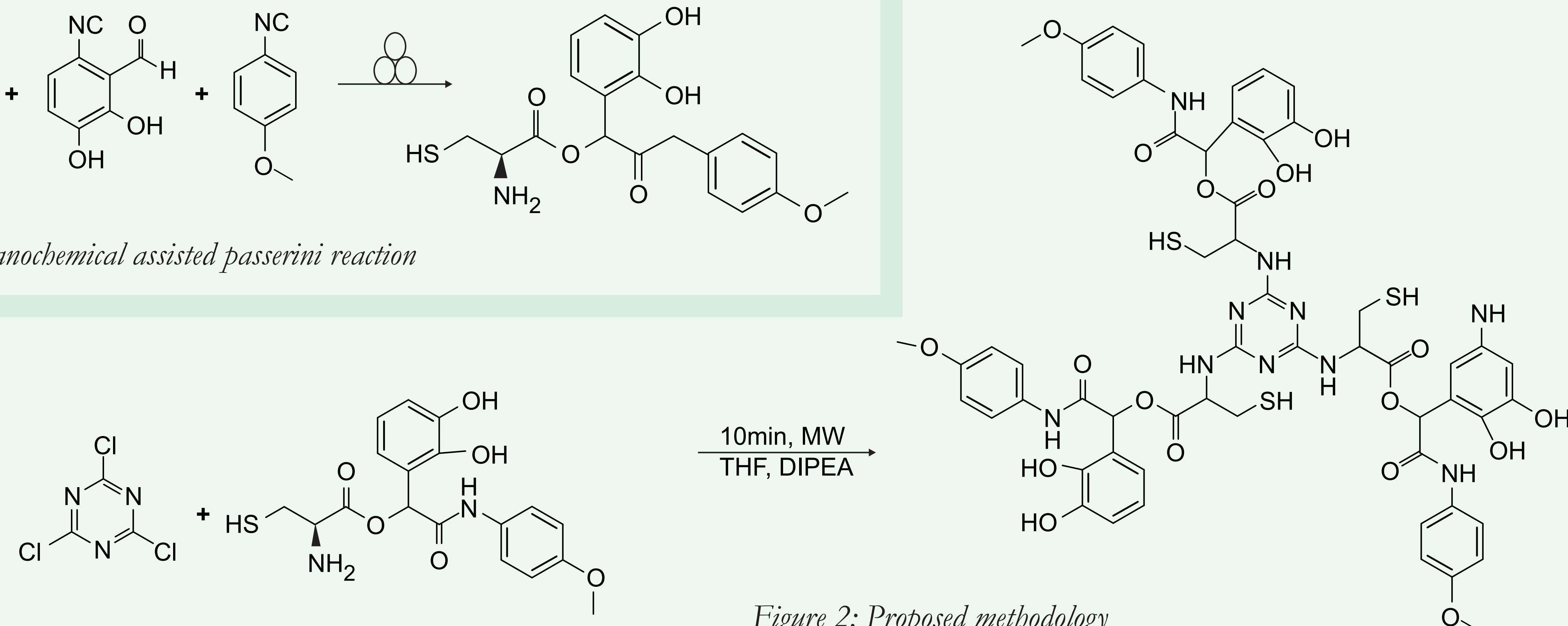


Figure 2: Proposed methodology

RESULTS

Cyanuric chloride (1.03g, 5.6mmol) was combined with an amine (16.76mmol) in a reaction vessel and dissolved in tetrahydrofuran (5mL) and Diisopropylethylamine (0.2mL) was added. This reaction was conducted in a microwave with 200W and a temperature of 60 °C for 30 minutes (**Figure 1**). This reaction was monitored using

TLC (**Figure 2**). The products were tested using a Fujiwara test (**Figure 3**). The following step is to do structure elucidation of the compounds using Mass spectroscopy (HRMS), Infrared Spectroscopy, 1D and 2D Nuclear Magnetic Resonance (NMR).

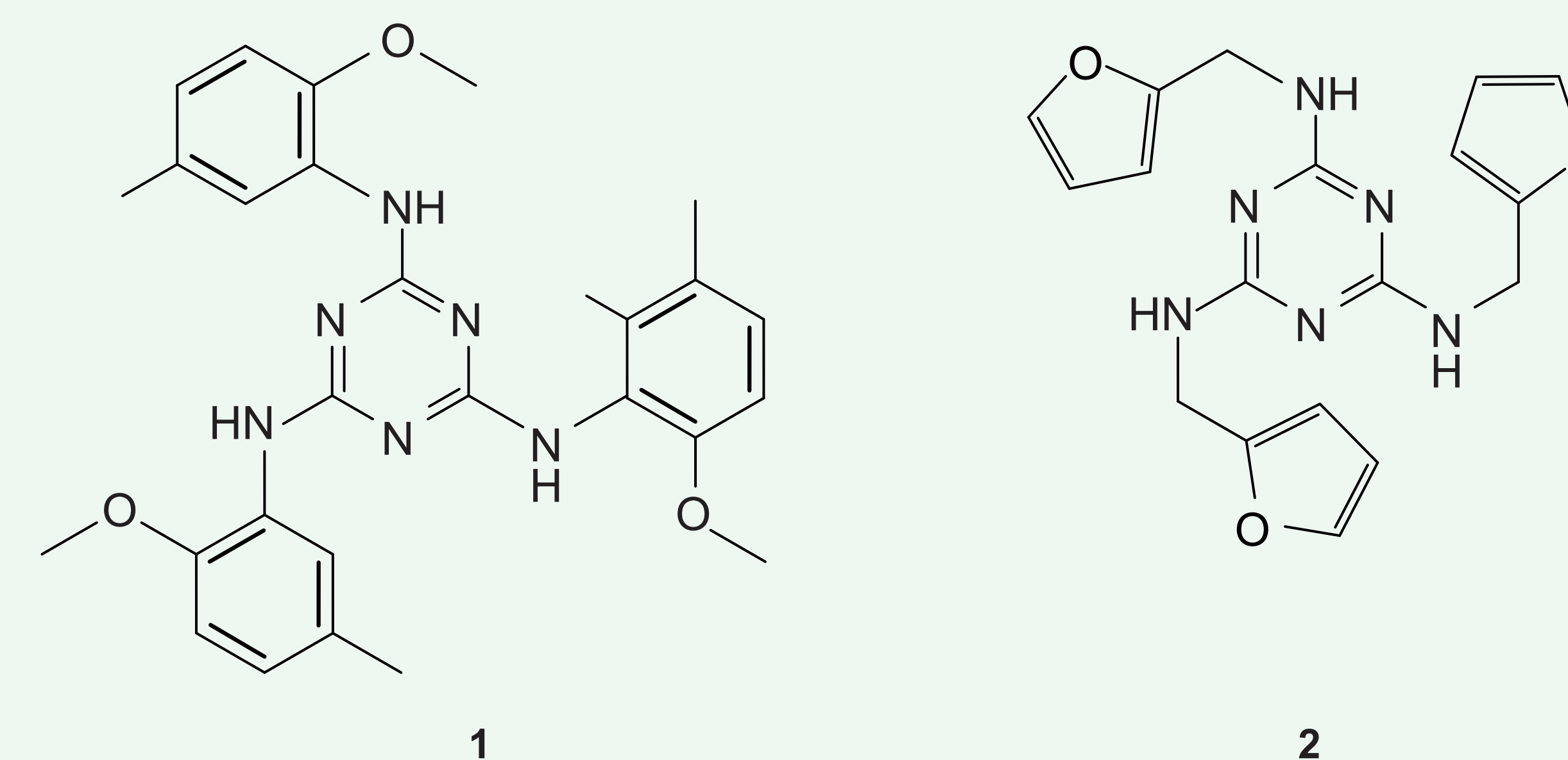
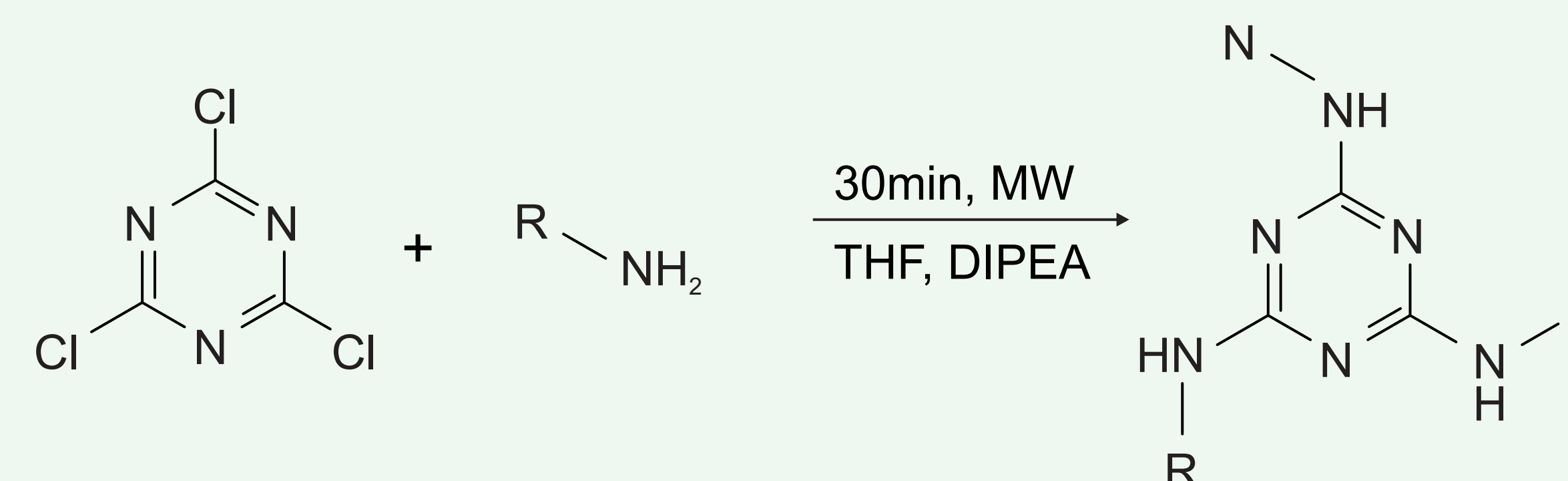


Figure 3: Triazine reaction

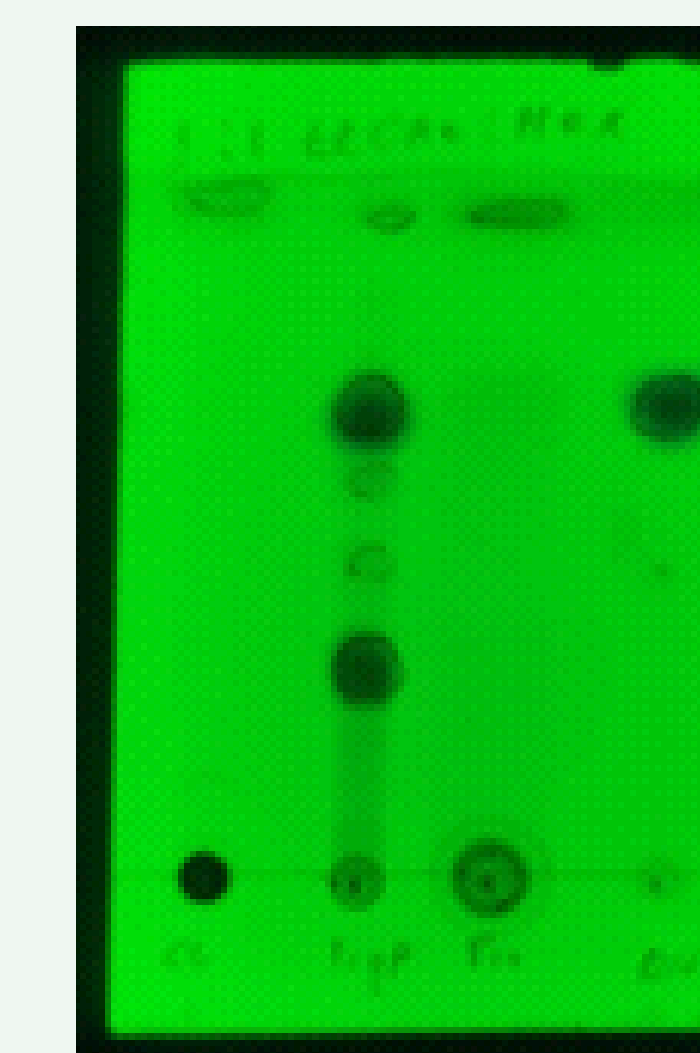


Figure 4: TLC plate of compound 1



Figure 5: Fujiwara test on compound 1