Microwave Assisted One Pot Synthesis of N-Substituted Phenyl-4-Thiophenyl-2-Azetidinones as Potent Antimicrobial Agents

D H More, N S Pawar and P P Mahulikar*

School of Chemical Sciences, North Maharashtra University, Jalgaon 425 001

Received: 25 March 2003; accepted: 05 June 2003

Simple, rapid, clean and environmentally friendly methods for the synthesis of Schiiff’s bases and their cycladition with acetyl chloride to N-substituted phenyl-4-thiophenyl-2-azetidinones under microwave irradiation are reported.

Keywords: Microwave, Phenyl-4-thiophenyl-2-azetidone, Antimicrobial agents

Introduction

Azetidinones have occupied a unique place in medicinal and biological chemistry due to their diverse pharmacological display as antiflammatory, sedative, hypnotic, and anticonvulsant properties. The β-lactum ring of azetidinones mainly possesses the antibiotic activity. The application of microwaves (MW) in organic synthesis is now a well known practice. The practical utility of MW assisted solvent-free protocols has now been realized in several synthetic operations such as, protection and deprotection, condensation, oxidation, reduction, cyclization, rearrangement reactions, and rapid synthesis of heterocyclic system on solid supports.

Furthermore, MW assisted solvent-free organic synthesis is an important aspect of the today’s green or clean or environmentally benign chemistry approach.

In continuation of our work on the application of MW assisted synthesis of biologically active compounds and pest management agents, we report simple, rapid, clean and eco-friendly MW assisted synthesis of Schiiff’s bases and N-substituted phenyl-4-thiophenyl-2-azetidinones (Scheme 1). The method involves the microwave irradiation of thiophenyl-2-carbaldehyde and aromatic amines in ethanol for 4 min at power level 3 which resulted in the formation of corresponding Schiff’s bases without using dehydrating agent followed by their cyclization with acetyl chloride in the presence of triethyl amine using benzene-ethanol mixture (1:1) as solvent by irradiation for 6 min at power level 3 to afford azetidinones in good yields (Table 1).

Experimental Procedure

The completion of reaction and purity of products were checked using silica gel TLC. The products were characterized by comparing their physical constants and spectral data with authentic samples. Melting points were determined by open capillary method and were uncorrected.

I One Pot Synthesis of N-substituted Phenyl-4-thiophenyl-2-azetidinones (2, a-g)

A mixture of thiophene-2-carbaldehyde (1, 0.01 M) and aromatic amine (2, 0.01 M) was taken in 100 mL beaker and dissolved in ethanol (50 mL) and then irradiated under MW for 4 min at power level 3. Then a mixture of acetyl chloride (0.012 M) and triethyl amine (5 mL) in benzene (10 mL) was added to reaction content in small lots with stirring and again irradiated under MW for 6 min at power level 2. The crude sticky product
In one pot synthesis, 5-6 per cent less yields of products (4, a-g) were obtained. A two-step synthesis of same products has also been attempted to achieve higher yields, as summarized in Table 1.

### 2 General Procedure for Preparation of Schiff’s bases of Thiophene-2-carboxaldehyde (3, a-g)

A mixture of thiophene-2-carboxaldehyde (1, 0.01 M) and amine (2, 0.01 M) was taken in a 100 mL beaker and dissolved in ethanol (50 mL) and then irradiated under MW for 4 min at power level 3. The content was poured in ice-water (50 mL) to give solid, which was then recrystallised from 40 per cent ethanol.

### 3 General Procedure for Preparation of N-substituted Phenyl-4-thiophenyl-2-azetidinones (4, a-g)

A mixture of Schiff base (3, 0.01 M), acetyl chloride (0.01 M) and triethyl amine (5 mL) in benzene-ethanol solvent mixture (1:1) was then irradiated under MW for 6 min at power level 2. The removal of solvent afforded sticky viscous mass, which was washed with petroleum ether and the obtained solid was then recrystallized from 40 per cent ethanol.

---

![Scheme 1 — Synthesis of Schiff’s bases and azetidinones](image-url)
References


