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Microwave assisted synthesis and *in silico* screening of steroidal pyrazolines

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Abstract

The present manuscript describes solid-state synthesis of some reported steroidal pyrazolines by a novel eco-friendly route. The synthesized pyrazolines were compared with those obtained from conventional methods in terms of reaction time and overall yield. A substantial enhancement in reaction rate and yield was observed. The antimicrobial activity and the subsequent molecular docking studies of the steroidal pyrazolines have also been carried out.

Keywords: Solid state synthesis; Pyrazolines; *In silico* study; Antimicrobial study

Studies pertaining to the synthesis of steroidal pyrazolines using microwave-induced heating are scarce [1–3]. Hence, we explored the green synthetic procedure to validate the synthesis of reported steroidal pyrazolines. The identity of the synthesized compounds has been ascertained by their physical, analytical and spectral data [4]. The *in silico* studies of the synthesized compounds have also been carried out to predict pathogenic protein (3H2X pdb) behavior.

1. Experimental

1.1. Preparation of steroidal pyrazolines: general procedure

A mixture of α,β-unsaturated steroidal ketone (**1**, **2** or **3**) (1 mmol), thiosemicarbazide (1.2 mmol) and basic alumina (2.0 g) were grounded thoroughly in a mortar. This reaction mixture in 100 ml flask was heated in a microwave oven (CEM Discover apparatus) in time interval 30 s to 2.0 min, respectively, and monitored by tlc. After completion of the reaction, the beaker was cooled and the organic matter was diluted with water and filtered. The

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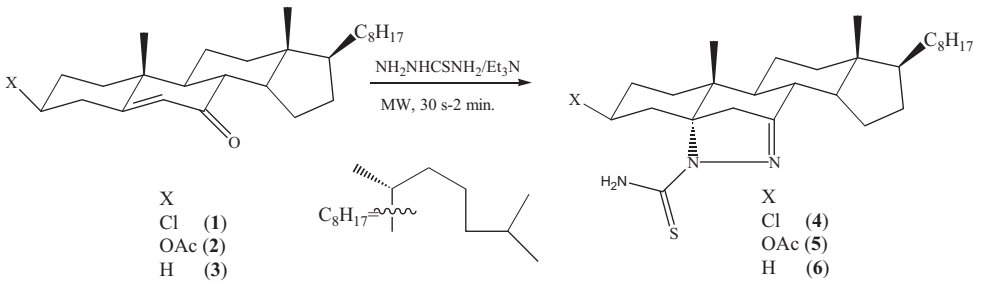

Scheme 1. Synthesis of title compounds (**4–6**).

precipitate was dissolved in ether and washed with water and dried over anhydrous sodium sulfate; evaporation of solvent and crystallization from dry methanol afforded compound **4**, **5** or **6**, respectively (Scheme 1).

A comparative study in terms of yield and reaction period is given. All the spectral and analytical data for compounds **4**, **5** and **6** are identical to those previously reported [4,5].

Comparison of conventional and microwave synthesis for **4–6**: (1) conventional procedure; compound **4**, yield: 65%, time: 6 h, compound **5**, yield: 85%, time: 5 h, compound **6**, yield: 70%, time: 6 h, (2) microwave procedure; compound **4**, yield: 78%, time: 3.0 min, compound **5**, yield: 90%, time: 2.5 min, compound **6**, yield: 85%, time: 3.0 min, respectively.

The *in vitro* antimicrobial activity of compounds **4–6** were tested against pathogenic strains *i.e*. *Bacillus subtilis*, *Streptococcus pyogenes*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli* by disc diffusion [4].

1.2. In silico study

The retrieved protein 3H2X (Pdb) was improved by using import and preparation option of MVD software, and missing bond order, hybridization state, angel and flexibility for achieving reliable potential binding site in receptor. The energy minimized ligands (synthesized compounds) were drawn with ChemDraw Ultra (2D and 3D) and LigandScout, respectively. Discovery studio [6], MVD [7] and Ligand scout [8] were used to perform molecular docking, energy profile of ligand–receptor interaction and structure activity relationship, independently.

2. Result and discussion

The steroidal α,β-unsaturated ketones, 3β-chlorocholest-5-en-7-one (**1**) [9], 3β-acetoxycholest-5-en-7-one (**2**) [10,11] and cholest-5-en-7-one (**3**) [9], on treatment with thiosemicarbazide under microwave radiation furnished the desired products (**4–6**), respectively (Scheme 1).

The nature of each carbon in the compound **6** was deduced through Distortionless Enhancement by Polarization Transfer (DEPT) experiment using polarization pulses of 135°, obtaining positive (up) signals for CH, CH_3 and negative (down) signals for CH_2 groups. Its DEPT (135) (Fig. 1) revealed the presence of five methyl, twelve sp^3 methylene and six sp^3 methine carbons.

2.1. Antimicrobial test

The growth inhibiting potential of compound **6** was compared with the standard drug, chloramphenicol [12]. The compounds were found to restrain pathogens *B. subtilis*, *S. pyogenes*, *S. aureus*, *P. aeruginosa*, *K. pneumoniae* and *E. coli*. The antimicrobial activity of compound **6** was found to be the highest [4]. In order to verify the above results we performed the *in silico* screening of compounds **4–6**.