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SHORT COMMUNICATION

"Green synthesis" of benzothiazepine library of indeno analogues and their in vitro antimicrobial activity

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A novel series of indeno-benzothiazepine derivatives was synthesised via a "green" route. Synthesis of these compounds involves the treatment of dinucleophiles such as 2-aminobenzenethiols with α,β-unsaturated ketones in poly(oxyethylene) (poly(ethylene glycol), PEG-400) catalysed by acetic acid. The synthone α,β-unsaturated ketones were obtained by Claisen–Schmidt condensation of indan-1-one with substituted pyrazole-2-carbaldehydes prompted by bleaching earth (pH 12.5) as catalyst and PEG-400 as "green" reaction solvent. Screening of all the synthesised compounds for antimicrobial activity revealed that most of these compounds exhibited moderate to significant antimicrobial activity.

Keywords: indeno-benzothiazepine, PEG-400, bleaching earth, antimicrobial activity

The seven-membered heterocycle 1,5-benzothiazepine is a versatile scaffold and it features in a number of well-known life-saving drugs such as CGP37157, Clonazepam and Diltiazem (Cox & Matlib, 1993) which have gained recognition for their multi-faceted pharmacological and medicinal applications. 1,5-Benzothiazepines are currently used as coronary vasodilators and as antidepressants. In addition, the 1,5-benzothiazepine moiety is a remarkable class of pharmacophore, as compounds bearing this structural unit possess a broad spectrum of biological activities such as antitubercular (Upadhyay et al., 2012), anticonvulsant (De Sarro et al., 1995), Ca^{2+} channel antagonist (Kurokawa et al., 1997), antianginal (Miyata et al., 1997), anti-HIV (Grandolini et al., 1999), squalene synthase inhibitor (Yang et al., 2000), V_2-arginine vasopressin receptor antagonist (Urbanski et al., 2003), and HIV-1 reverse transcriptase inhibitor (Di Santo & Costi, 2005).

The importance of 1,5-benzothiazepine derivatives in the field of pharmacological and medicinal chemistry has stimulated interest in developing new methodologies for their synthesis. In this respect, numerous strategies have been reported including one-pot to multi-step approaches using various catalysts (Baag et al., 2007; El-Bayouki, 2013; Jain et al., 2011; Prakash et al., 2005; Rao et al., 1995; Sindler-Kulyk & Neckers, 1982; Yadav et al., 2002; Zhong et al., 2000). However, some of these methods have one or more drawbacks such as long reaction time, use of expensive reagents, low yields, harsh reaction conditions, effluent pollution, and tedious preparation procedure. The most convenient method for the synthesis of these compounds involves the treatment of dinucleophiles such as 2-aminobenzenethiols with α,β-unsaturated ketones in PEG-400.

Liquid polymers or low melting polymers have recently emerged as alternative "green" solvent systems with unique properties such as thermal stability, commercial availability, non-volatility, immiscibil-

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