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SYNTHESIS AND ANTIMICROBIAL ACTIVITY SCREENING OF NEW CYCLIC IMIDES COMPRISING ANTIPYRINE AND OXAZOLE CYCLES

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ABSTRACT : In this work, a variety of new cyclic imides bearing both antipyrine and oxazole moieties were synthesized. Synthesis of the new imides was based on the key compound [2] 2-amino-4-(antipyrine-4-yl-amino) oxazole, which was prepared via reaction between 4-(2-chloro acetamido) antipyrine [1] and urea. The target imides were synthesized by two steps in the first one compound [2] was introduced in reaction with different cyclic anhydrides affording amic acids [3-6] and these inturn were dehydrated by fusion in the second step affording the target imides [7-10]. Naphthalimide [11] is the only imide that was synthesized by direct fusion of key compound [2] with napthalic anhydride.

Key words : Cyclic imides, antipyrine, oxazole, amic acids, key compound.

INTRODUCTION

Azoles are very important heterocycles that form the basis of different drugs, pharmaceuticals and agrochemical products due to their wide spectrum of biological activities such as antimicrobial, anti-inflammatory, anticancer and antiviral activities (Al-Azzawi and Hamd, 2014; Mahdi and AL-Azzawi, 2013). On the other hand, cyclic imides have been extensively investigated because of the wide range of biological activities (Latief and Al-Azzawi, 2018; Al-Azzawi and Raheem, 2017). They exert, as well as due to their importance as synthetic intermediates. Nowdays, focus has been placed on this important class of compound for their potential new applications especially in the area of pharmaceutical chemistry (Al-Azzawi and Hassan). Keeping in minal all these points, it seems worthwhile to combine these two biologically active components (cyclic imides and azoles) in one molecule, which may exhibit different biological activities (Alaa ***et al***, 2011).

Thus the present work involved synthesis a variety of new cyclic imide containing two azole moieties (antipyrine and oxazole).

The newly synthesized molecules are expected to exhibit biological activity since they are built from three biologically active segments.

MATERIALS AND METHODS

The used chemicals in this work were purchased by Aldrich, BDH, Fluka and Merk companies.

Synthesis of 4-(2-chloro acetamido) antipyrine[1] (Al-Azzawi, 2011)

A mixture of (0.01mol, 2.03g) of 4-aminoantipyrine and (0.01mol, 0.56gm) of chloro acetyl chloride in (25 mL) chloroform was refluxed in the presence of K_2CO_3 (0.01mol, 0.69gm) for about 12hrs. After removing excess solvent the residue was stirred with water (25 mL). The formed precipitate was filtered, washed with sodium bicarbonat solution (5%) and subsequently with distilled water, dried and purified by recrystallization from ethanol to afford Yellow crystals in (84%) Yield and m.p (139-141^{0}C).

Synthesis of 2-amino-4- (antipyrine-4-yl-amino) oxazole [2] (Singh *et al*, 2010)

To a methanolic solution of compound [1] (0.01mol, 2.79gm) in (25 mL) methanol, urea (0.01mol, 0.6gm) was added then the mixture was refluxed for (12 hrs). After distillation of methanol the residue was poured into crushed ice with stirring and the obtained solid was filtered, dried then recrystallized from methanol to affordeda yellow crystals. Yield (93%), m.p (125-126^{0}C).

Synthesis of N-[4-(antipyrine-4-yl- amino) oxazole-2-yl] amic acids [3-6] (Al-Azzawi and Raheem, 2017)

The titled amic acids [3-6] were synthesized via addition of (0.01mol, 2.85gm) of compound [2] dissolved in (30 mL) dry acetone to (0.01mol) of cyclic anhydride (maleic, phthalic, citraconic or tetrachlorophthalic anhydrides) dissolved in (20 mL) dry acetone with cooling and stirring. After completion of addition the mixture was