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ORIGINAL ARTICLE

2nd Heterocyclic Update

Synthesis, characterization and antimicrobial screening of quinoline based quinazolinone-4-thiazolidinone heterocycles

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Thiazolidinone;
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Abstract In an attempt to find new pharmacologically active molecules, we report here the synthesis and *in vitro* antimicrobial activity of various 2-(2-chloro-6-methyl(3-quinolyl))-3-[2-(4-chlorophenyl)-4-oxo(3-hydroquinazolin-3-yl)]-5-[(aryl)methylene]-1,3-thiazolidin-4-ones. *In vitro* antimicrobial activity of the title compounds are screened against two Gram positive bacteria (*Staphylococcus aureus*, *Streptococcus pyogenes*), two Gram negative bacteria (*Escherichia coli, Pseudomonas aeruginosa*) and three strains of fungi (*Candida albicans, Aspergillus niger*, *Aspergillus clavatus*) using broth micro dilution method. Some derivatives bearing chloro or hydroxy group exhibited very good antimicrobial activity.

1. Introduction

Quinazoline derivatives represent one of the most active classes of compounds possessing a wide spectrum of biological activity (Apfel et al., 2001). They are widely used in pharmaceuticals and agrochemicals (Tobe et al., 2003); e.g. fluquinconazole fungicide for the control of agriculture diseases (Guang-Fang et al., 2007). Many reports have been published on the biological activity of quinazoline derivatives, including their bactericidal, herbal and antitumor activity (Raffa et al., 1999; Chenard et al., 2001). Thus, their synthesis has been of great interest in the elaboration of biologically active heterocyclic compounds. Recently, it was reported that some quinazolines exhibited very good antimicrobial activity (Alafeefy, 2008; Desai and Dodiya, 2010). Prompted by these findings, the present paper describes the synthesis of an extension series of 3-substituted-2-phenylquinazolin-4(3*H*)-one derivatives and testing of their antimicrobial activity.

Quinolines are known to inhibit DNA synthesis by promoting cleavage of bacterial DNA gyrase and type-IV topoisomer-

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ase, resulting in rapid bacterial death (Hooper and Wolfson, 1989; Hooper, 1995; Hardman et al., 2002). Certain drugs based on quinoline moiety such as doxorubicin and mitoxantrone have been established as one of the most effective classes of anticancer agents in clinical use today with broad application in the treatment of several leukemia and lymphomas as well as in combination chemotherapy of solid tumors (Wakelin and Waring, 1990). The potent anticancer activity as well as toxic effects described for these compounds are normally ascribed, at least, to two main mechanisms: one, which is associated with protein, involves trapping of a protein enzyme–DNA cleavable intermediate, whereas the other, a non-protein-associated mechanism, is related to redox cycling of the quinoline moiety, which produces damaging free-radical species (Murray, 2000).

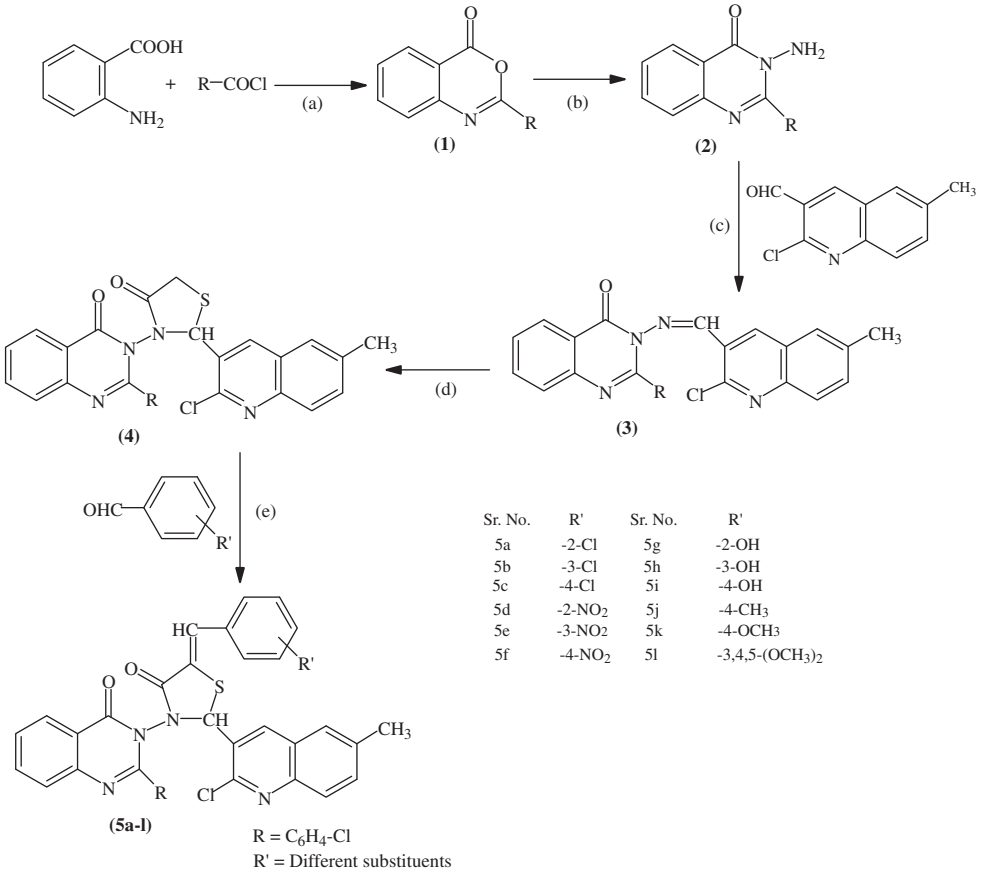
Similarly, various 4-thiazolidinones (Pan et al., 2010; Youssef et al., 2010) have attracted considerable attention as they are also endowed with a wide range of pharmaceutical activities including anesthetic (Surrey, 1949), anticonvulsant (Troutman and Long, 1948), antibacterial (Sayyed and Mokle, 2006) and antiviral (Rao and Zappala, 2004). Furthermore, drug research and development have led to the discovery of new pharmacologically active agents, including imidoxy compounds such as succinimidoxy (Farror et al., 1993). They also possess a strong anti-convulsant activity (Edafiogho et al., 1991). 4-Thiazolidinones may be considered as phosphate bioisosteres and therefore inhibit the bacterial enzyme MurB which is involved in the biosynthesis of peptidoglycan layer of the cell wall (Gursoy et al., 2005). In addition, some thiazolidinones were recently reported as novel inhibitors of mycobacterial rhamnose synthetic enzymes (Gursoy et al., 2005). This new approach is believed to be selective, as rhamnose is not found in humans, but is essential for mycobacterial cell wall synthesis in animals (Andres et al., 2000).

Looking to the medicinal importance of 4(*3H*)-quinazolinone, 4-thiazolidinone and quinoline, we report here the synthesis of a new class of heterocyclic molecules in which all of these moieties are present and try to develop potential bioactive molecules. The structures of compounds synthesized are assigned on the basis of IR, ^{1}H NMR, ^{13}C NMR and Mass spectral data. These compounds are evaluated for their antimicrobial screening on different strains of bacteria and fungi Scheme 1.

2. Experimental

2.1. Materials and methods

All chemicals are of analytical grade and used directly. Melting points are determined in PMP-DM scientific melting point apparatus and are uncorrected. IR spectra are recorded on a Perkin-Elmer RX 1 FTIR spectrophotometer, using potassium bromide pellets and the frequencies are expressed in cm^{-1}. The ^{1}H NMR and ^{13}C NMR spectra are recorded with a Bruker



Sr. No.	R'	Sr. No.	R'
5a	-2-Cl	5g	-2-OH
5b	-3-Cl	5h	-3-OH
5c	-4-Cl	5i	-4-OH
5d	-2-NO_2	5j	-4-CH_3
5e	-3-NO_2	5k	-4-OCH_3
5f	-4-NO_2	5l	-3,4,5-$(OCH_3)_2$

Reagents : (a) Pyridine, 0-5°C, (b) Pyridine, $NH_2NH_2.H_2O$, (c) Ethanol, acetic acid, (d) 1,4-dioxane, thioglycolic acid, anhydrous $ZnCl_2$, (e) Ethanol, sodium ethoxide

Scheme 1 Preparation of compounds **5a–l**.