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Synthesis, biopharmaceutical characterization, antimicrobial and antioxidant activities of 1-(4′-*O*-β-D-glucopyranosyloxy-2′-hydroxyphenyl)-3-aryl-propane-1,3-diones

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ABSTRACT

This research communication is toward the investigation of the antibacterial, antifungal and antioxidant activities of the synthesized compounds 1-(4′-*O*-β-D-glucopyranosyloxy-2′-hydroxyphenyl)-3-aryl-propane-1,3-diones (**5a**)–(**5h**). These compounds have been obtained by the interaction of α-aceto-bromoglucose with 1-(2′,4′-dihydroxyphenyl)-3-aryl-propane-1,3-diones (**3a**)–(**3h**) under anhydrous condition and at lower temperature. The structures of these newly synthesized *O*-β-D-glucopyranosides were established on the basis of chemical, elemental, and spectral analyses. Further, the compounds (**5b**), (**5c**), (**5d**) and (**5g**) showed potent antibacterial and antifungal activity. A good correlation was obtained between the theoretical predictions of bioavailability using Lipinski's rule-of-five and experimental verification.

1. Introduction

The clinical relevance of bacterial and fungal diseases has increased over the past 30 years due to an increasing population of immunocompromised patients who have cancer, AIDS or have received transplants. Actually the problems of multi-drug resistant microorganism have reached on alarming level in many countries around the world. A numbers of recent clinical reports describe the increasing occurrence of penicillin-resistant *Staphylococcus aureus* and other antibiotic-resistant human pathogenic microorganisms in United States of America and European countries. Infections caused by those microorganisms pose a serious challenge to the medical community and need for an effective therapy has led to a search for novel more selective and efficient antimicrobial agents.

In this work, we report the synthesis, antimicrobial and antioxidant activity of *O*-β-D-glucoside derivatives of β-diketones. The β-diketones and carbohydrate have broad spectrum of medicinal values. β-diketones shown to have anecdotal extent of pharmacological activities like antibacterial [1], antiviral [2], insecticidal [3], antioxidant [4] and potential prophylactic antitumor activity [5,6]. It has also been used as an anti-sunscreen agent [7]. In liquid solutions [8] as well as in the solid state [9] beta-diketones exists almost exclusively as the enol tautomer, which is stabilized by the intramolecular hydrogen bonding. Recently it is reported that β-ketoenols are important pharmacophores of HIV-1 integrase (IN) inhibitors [10].

The rational design of new HIV-1 Integrase (H-I) inhibitors, one validated target for chemotherapeutic intervention [11], is fundamentally based on intermolecular coordination between H-I/chemical inhibitor/metals (Mg^{2+} and Mn^{2+}, co-factors of the enzyme), leading in the formation of bimetallic complexes [12,13]. Thereby, several bimetallic metal complexes, in many cases exploring the well-known polydentate ligands, appear in this scenario as the most promising concept to employ in either enzyme/drug interaction or electron transfer process, in the last case involving the biological oxygen transfer [14–16]. Another exciting

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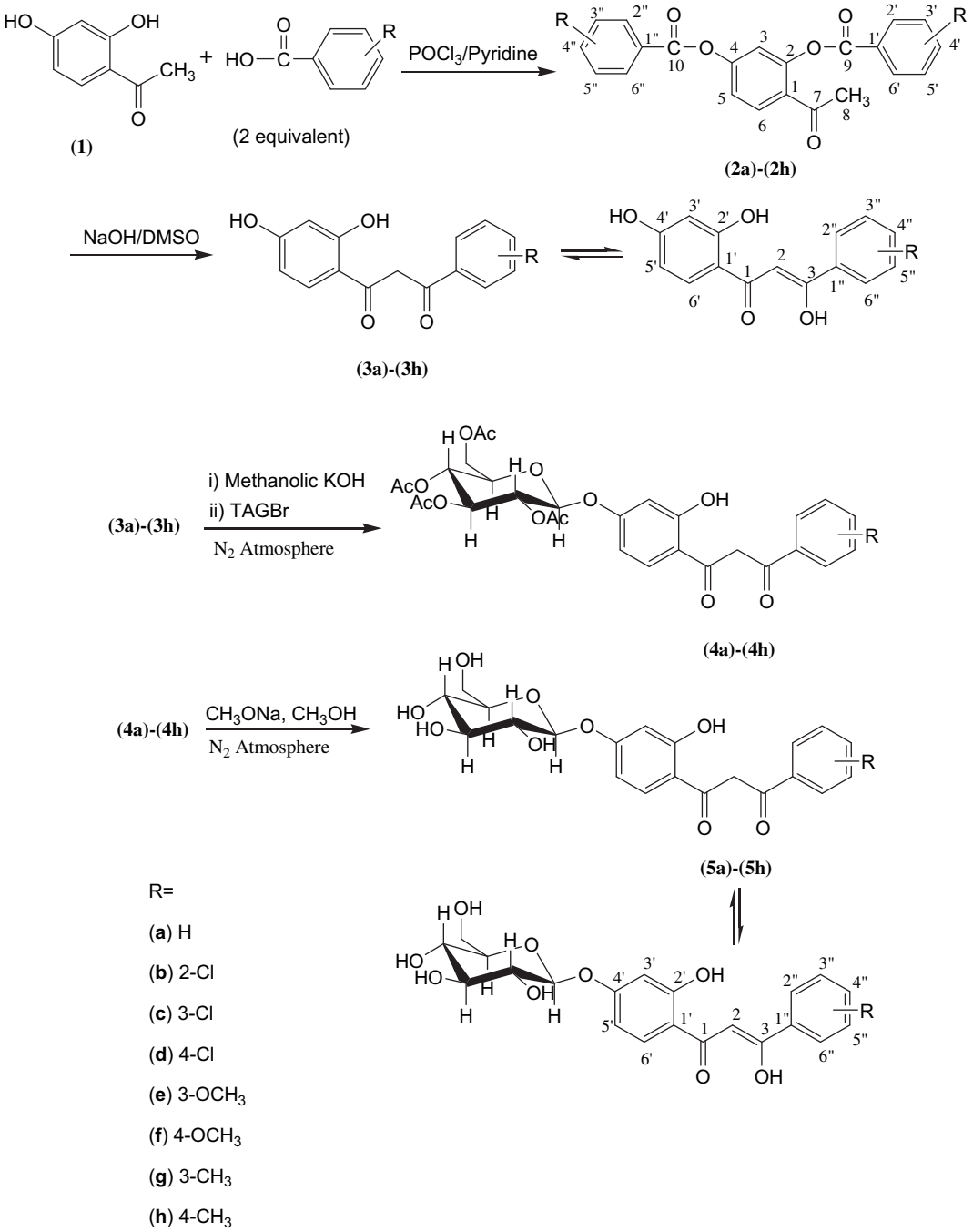
example of application for such polydentate ligand involves the synergic water activation, which occurs via the so-called "remote metallic atoms". Such organometallic compounds are structurally deemed to promote or block the H-I activity [17]. These explanations above detailed clearly demonstrate that polydentate ligands are of special interest in the bioorganometallic chemistry field [18]. Looking for the design of new bimetallic coordinating ligands to further explore in the building of intermolecular system involving H-I/inhibitor/metal complexation, we have targeted to study the synthesis and structural biology of diketo O,O,O-ligands (**5a**)–(**5h**).

Correspondingly, carbohydrates play important structural and functional roles in numerous physiological processes, including various disease states [19,20]. The relatively recent recognition of carbohydrates as a medicinally relevant class of biomolecules has led to the investigation of therapeutic agents based on either glycan structure or mimics thereof [21]. For example, cancer cell metastasis [22] and cell–cell adhesion in the inflammatory response [23] are dependent on cell surface presentation of specific glycans. Synthetic carbohydrates-based cancer vaccines [24] and small molecules selective inhibitors [25] are thereof being pursued as potential medicinal agents, respectively. Likewise, the initial stages of bacterial or viral infection often rely on the recognition of host cell glycoconjugates by the invading organism [26].

The enormous significance of β-diketones and carbohydrate-based drugs caught our attention for the synthesis of *O*-β-D-glucosyl derivatives of β-diketones and to study their pharmacological



Scheme 1. Synthesis of 1-(4′-*O*-β-D-glucopyranosyloxy-2′-hydroxyphenyl)-3-arylpropane-1,3-diones (**5a**)–(**5h**).