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Synthesis and biological activity of phenylglycosides containing fragments of imidazoles and triazoles

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Abstract

2- and 4-(1*H*-azolyl-1-ylmethyl)phenols were synthesized by fusing 2- and 4-hydroxybenzyl alcohols with imidazole, 2-methylimidazole, 1,2,4-triazole, benzimidazole, 2-methylbenzimiazole, 2-benzylbenzimidazole, benzotriazole. The main intermediate in this kind of reaction is *o*- or *p*-methylenquinones. For the glycosylation of 4-(1*H*-azolyl-1-ylmethyl) phenols, the Gelfherich method was used using $BF_3 \cdot (C_2H_5)_2O$ as a catalyst. Because of the high affinity of $BF_3 \cdot (C_2H_5)_2O$ to the pyridinium nitrogen atom of heterocyclic residues, it is possible to form sufficiently strong coordination compounds in which the catalyst loses its catalytic activity. Therefore, in the glycosylation reaction, it must be used in excess. The high stereospecificity of this reaction is that when a β-pentaacetate monosaccharide is used as the glycosylation reagent, its β-stereoisomer is predominantly formed. To remove the acetyl protection, sodium methoxide was used in absolute methanol. Genotoxicity of 2- and 4-(1*H*-azolyl-1-ylmethyl)phenols was studied using biotests of onion seeds *Allium fistulosum* and *Allium cepa*. It is proved that they are weak mutagens. It was found that 4-(1*H*-azol-1-ylmethyl)phenols are more toxic than 2-(1*H*-azole-1-ylmethyl)phenols. The introduction of a methyl group into imidazole and benzimidazole fragments turns phenols into more toxic compounds. A study of hemolytic properties using whole venous human blood showed that 4-(2-methyl-1*H*-benzimidazol-1-ylmethyl)phenol does not increase the number of hemolysed cells, and 4-(1*H*-benzimidazol-1-ylmethyl)-phenol has a membrane-stabilizing property. At reduced concentrations, 4-(1*H*-benzimidazol-1-ylmethyl)-phenyl-β-*D*-glucopyranoside and 4-(1*H*-2-methyl-benzimidazol-1-ylmethyl)phenyl-β-*D*-glucopyranoside also do not increase the number of hemolysed cells. To study the antifungal properties, 4-(2-methyl-1*H*-benzimidazol-1-ylmethyl)phenol was chosen which does not show a hemolytic effect, which indicates its low toxicity with respect to human erythrocytes. As biotests, *Aspergillus niger* strains isolated from soil suspension were used, and *Cladosporium herbarum* – from the air of the bathroom. They are capable of causing diseases of three types: mycosis, mycotoxicosis and allergies. It was found that 4-(2-methyl-1*H*-benzimidazol-1-ylmethyl)phenol had an effective fungiostatic property, retarding the growth of these opportunistic fungi by an average of 50%.

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