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Musa Özil, Cansu Parlak, Nimet Baltaş

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A Simple and Efficient Synthesis of Benzimidazoles Containing Piperazine or Morpholine Skeleton at C-6 Position as Glucosidase Inhibitors with Antioxidant Activity

Musa Özil*, Cansu Parlak, and Nimet Baltaş

Department of Chemistry, Recep Tayyip Erdogan University, 53100, Rize, Turkey

Abstract

A novel 2-(aryl)-6-morpholin-4-yl(or 4-methylpiperazin-1-yl)-1*H*-benzimidazole derivatives were designed and expeditiously synthesized starting from 5-morpholin-4-yl(or 4-methylpiperazin-1-yl)-2-nitroaniline with various aldehydes which were preliminarily screened for *in vitro* antioxidant activities and glucosidase inhibitors. The benzimidazoles were effectively synthesized by a rapid ‘onepot’ nitro reductive cyclization reaction using sodium hydrosulfite as a reagent. All reactions were conducted using both the microwave and conventional methods to compare yields and reaction times. Antioxidant activities of the synthesized compounds were clarified using various *in vitro* antioxidant assays including Cupric Reducing Antioxidant Capacity (CUPRAC, ranging from 5.511 to 19.703 mM Trolox / mg compound) and Ferric Reducing Antioxidant Power (FRAP) (1.141-12.943 mM FeSO₄.7H₂O / mg compound) assays. Also, the radical scavenging activities of these compounds were assayed using ABTS^{•+} and DPPH[•] methods. The results showed that all compounds exhibited very high scavenging activity. These synthesized compounds were then evaluated for their α -glucosidase inhibitory potential and seven compounds demonstrated an inhibitory potential much better than the standard acarbose. Herein, we will provide details of the structure activity relationship of the benzimidazole analog for the potency.

Keywords: Benzimidazole, Microwave, α -Glucosidase, Antioxidant, Structure–activity relationship (SAR), Synthesis

*Corresponding Author. Tel: +90 464 223 61 26; fax: +90 464 223 40 19.

E-mail: musa.ozil@erdogan.edu.tr

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