Synthesis of some novel benzimidazole derivatives and its biological evaluation

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ABSTRACT

A series of new benzimidazole derivatives have been synthesized by simple condensation reaction between benzimidazole derivatives and phenyl sulphonyl chloride derivatives. All these compounds were characterized by FT-IR, 1H NMR, MS and elemental analysis. These compounds were screened for antibacterial and antioxidant activities, respectively. The antibacterial activities were compared with the standard drug such as chlorophenicol and antioxidant activities were compared with the ascorbic acid.

1. Introduction

Heterocyclic compounds have occupied a prominent place among various classes of organic compounds by virtue of their diverse biological activities. Hence the design, synthesis and production of new molecules for crop health and human health have taken center stage in recent years. Among the wide variety of heterocyclics that have been explored for developing pharmaceutically important role in medicinal chemistry [1].

Benzimidazole and its derivatives are of great importance in medicinal chemistry because of their wide variety of biological and pharmacological activities [1,2]. The literature survey shows several examples of compounds having a benzimidazole ring which exhibit remarkable bioactivity that could make them potentially useful in the treatment of cancer, and cardiovascular diseases [3]. The benzimidazole unit and its derivatives possess anticancer [4], antiinflammatory [5], antibacterial [6], antifungal [7], antidiabetic [8], and anti-HIV activities [9]. On the basis of this observation we have synthesized benzimidazole derivatives as hitherto unreported analogues.

Literature survey has also revealed the importance of benzimidazoles as antimicrobial and antioxidant agents [10-14]. It has also been reported that certain substituted benzimidazole derivatives have a broad antimicrobial spectrum [11]. Motivated by this above-mentioned facts herein we reported the synthesis and antimicrobial, anti oxidant activities of new benzimidazole series.

2. Experimental

2.1. Instrumentation

All the reagents were purchased from Aldrich Chemicals Co., Loba Chemie. All the solvents and reagents used for the synthesis and analysis were of analytical grade. The progress of the reaction and the purity of the compounds were checked by thin layer chromatography (TLC). 1H NMR spectra were recorded on a BRUKER-AV-400 spectrometer in CDCl₃ and tetramethylsilane (TMS; δ = 0.00 ppm) served as internal standards. IR spectra were measured using a JASCO FT/IR-4100 spectrometer. Mass spectra were measured with Micromass Q-Tof. CHNS were measure by the Elementar Vario EL III (Germany). Thin-layer chromatography was carried out using SILICA GEL GF₂₅₄. The melting points (uncorrected) were measured on a SALACO apparatus.

2.2. Synthesis

2.2.1. General procedure for the synthesis of 1-(phenoxycarbonyloxy)ethyl 2-ethoxy-1-((2'-1-(phenylsulfonyl)-1H-tetrazol-5-yl) biphenyl-4-yl)methyl)-1H-benzo[d]imidazole-7-carboxylate derivatives

The compound 1-(phenoxycarbonyloxy)ethyl 1-((2'-1H-tetrazol-5-yl) biphenyl-4-yl)methyl)-2-ethoxy-1H-benzo[d] imidazole-7-carboxylate was purchased from Pure Chem. Scientific Limited, USA. Mixture of 1-(phenoxycarbonyloxy)ethyl 1-((2'-1H-tetrazol-5-yl) biphenyl-4-yl)methyl)-2-ethoxy-1H-benzo[d]imidazole-7-carboxylate (0.2 g, 0.33 mmol), substituted phenyl sulfonyl chloride (0.36 mmol) and triethyl amine (0.66 mmol) in 10 mL of dichloromethane was stirred for 2 h at room temperature. After the completion of the reaction, 5 mL water was poured; the organic layer was extracted and distilled off completely to get product in good yield (Scheme 1).

1-(Phenoxycarbonyloxy)ethyl-2-ethoxy-1-((2'-1-(phenyl sulfonyl)-1H-tetrazol-5-yl) biphenyl-4-yl)methyl)-1H-benzo[d] imidazole-7-carboxylate (3a): Color: White. Yield: 80% (0.2 g). M.p.: 78-80 °C. FT-IR (KBr, cm⁻¹): 1690 (ketone CO stretch.), 1700 (ester CO stretch.), 3030 (aromatic CH stretch.). 1H NMR (400 MHz, CDCl₃, 8 ppm): 1.25-1.32 (t, 3H, CH₃), 1.43-1.45 (d,
3H, CH₃), 2.9-3.0 (q, 2H, OCH₃), 4.66 (s, 2H, NCH₂), 5.59-5.67 (m, 1H, CH), 6.81-7.10 (m, J = 7.5 Hz, 2H, ArH), 7.12-7.46 (m, 9H, ArH), 7.58-7.88 (m, J = 8 Hz, 10H, ArH). Anal. calcld. for C₃₉H₃₂N₆O₈S: C, 62.89; H, 4.33; N, 11.28; S, 4.31. Found: C, 62.89; H, 4.33; N, 11.28; S, 4.31. Found: C, 62.80; H, 4.29; N, 11.26; S, 4.30%. MS (m/z): (M+1) 745.79.

1-(Phenoxycarbonyloxy)ethyl 2-ethoxy-1-((2'-[1-(2-nitrophenyl)sulfonyl]-1H-tetrazol-5-yl)-phenylsulfonyl)-1H-benzof[d]imidazole-7-carboxylate (3a): Color: Yellow. Yield: 76% (0.19 g). M.p.: 323-344 °C. FT-IR (KBr, cm⁻¹): 3420 (OH stretch.), 1620 (C=O stretch.), 1545 (NO₂ stretch.).

1H NMR (400 MHz, CDCl₃, δ, ppm): 1.19-1.20 (t, 3H, CH₃), 1.90-2.01 (d, 3H, CH₃), 3.14-3.15 (q, 2H, OCH₂), 4.79 (s, 2H, NCH₂), 5.18-5.20 (m, 1H, CH), 7.07-7.12 (m, J = 7.4 Hz, 3H, ArH), 8.15-8.20 (m, 8H, ArH), 8.20-8.27 (m, 9H, ArH). Anal. calcld. for C₄₀H₃₁F₃N₆O₈S: C, 64.49; H, 5.03; N, 10.49; S, 3.87%. MS (m/z): (M+1) 801.73.

1-(Phenoxycarbonyloxy)ethyl 2-ethoxy-1-((2'-[1-(1-tosyl-1H-tetrazol-5-yl)-phenylsulfonyl]-1H-benzof[d]imidazole-7-carboxylate (3b): Color: Yellow. Yield: 78% (0.19 g). M.p. 87-90 °C. FT-IR (KBr, cm⁻¹): 1695 (ketone CO stretch.), 1712 (acid CO stretch.). 1H NMR (400 MHz, CDCl₃, δ, ppm): 1.13-1.18 (s, 9H, CH₃), 1.19-1.20 (t, 3H, CH₃), 1.90-2.01 (d, 3H, CH₃), 3.14-3.15 (q, 2H, OCH₂), 4.79 (s, 2H, NCH₂), 5.18-5.20 (m, 1H, CH), 7.10-7.12 (m, J = 7.4 Hz, 3H, ArH), 8.15-8.20 (m, 8H, ArH), 8.20-8.27 (m, 9H, ArH). Anal. calcld. for C₃₉H₃₉F₃N₆O₈S: C, 64.49; H, 5.03; N, 10.49; S, 3.87%. MS (m/z): (M+1) 759.80.

1-(Phenoxycarbonyloxy)ethyl 2-ethoxy-1-((2'-[1-(4-chlorophenyl)sulfonyl]-1H-tetrazol-5-yl)-phenylsulfonyl)-1H-benzof[d]imidazole-7-carboxylate (3c): Color: Yellow. Yield: 78% (0.19 g). M.p. 87-90 °C. FT-IR (KBr, cm⁻¹): 1695 (ketone CO stretch.), 1712 (acid CO stretch.). 1H NMR (400 MHz, CDCl₃, δ, ppm): 1.13-1.18 (s, 9H, CH₃), 1.19-1.20 (t, 3H, CH₃), 1.90-2.01 (d, 3H, CH₃), 3.14-3.15 (q, 2H, OCH₂), 4.79 (s, 2H, NCH₂), 5.18-5.20 (m, 1H, CH), 7.10-7.12 (m, J = 7.4 Hz, 3H, ArH), 8.15-8.20 (m, 8H, ArH), 8.20-8.27 (m, 9H, ArH). Anal. calcld. for C₄₀H₃₁F₃N₆O₈S: C, 64.49; H, 5.03; N, 10.49; S, 3.87%. MS (m/z): (M+1) 759.80.

1-(Phenoxycarbonyloxy)ethyl 2-ethoxy-1-((2'-[1-(3-trifluoromethyl)phenyl)sulfonyl]-1H-tetrazol-5-yl)-phenylsulfonyl)-1H-benzof[d]imidazole-7-carboxylate (3d): Color: White. Yield: 78% (0.15 g). M.p. 63-65 °C. FT-IR (KBr, cm⁻¹): 1695 (ketone CO stretch.), 1725 (acid CO stretch.). 1H NMR (400 MHz, CDCl₃, δ, ppm): 1.21-1.23 (t, 3H, CH₃), 1.37-1.39 (q, 2H, OCH₂), 4.66 (s, 2H, NCH₂), 5.27-5.31 (m, 1H, CH), 7.01-7.12 (m, J = 7.2 Hz, 3H, ArH), 8.01-8.11 (m, 7H, ArH), 8.18-8.29 (m, 9H, ArH). Anal. calcld. for C₃₉H₃₉F₃N₆O₈S: C, 65.31; H, 4.52; N, 11.08; S, 4.23. Found: C, 65.31; H, 4.22; N, 10.87; S, 3.99%. MS (m/z): (M+1) 780.80.
We have synthesized a series of 1-(phenoxy carbonyloxy)ethyl 2-ethoxy-1-(2’-(1-(phenylsulfonyl)-1H-tetrazol-5-yl) biphenyl-4-yl) methyl)-1H-benz[de]imidazole-7-carboxylate derivatives using a known procedure and obtained products with good yield.

The structures of all the synthesized compounds were characterized by spectroscopic data, and allowed these molecules for study of antibacterial and antioxidant activities (Table 1 and 2). Benzimidazole derivatives shows a very good anti bacterial activities [10-14], we are comparing the synthesized new benzimidazole derivatives to the marketed chlorphenicol [15] which shows very good anti bacterial activity, here we are synthesizing the newly substituted benzimidazole derivatives for the studies of antibacterial activities by comparison with the drug molecule. In this studies compound 3f shows good bacterial activity, in which the tertiary butyl group is the electron releasing group, which is attached to the para position. The compound 3i shows least antibacterial activity, in which the fluoro group is attached to the para position, which is the electron withdrawing group. The remaining molecules showing the moderate activity.

The synthesized compounds were tested for anti oxidant activities by evaluation with ascorbic acid [16,17]. In antioxidant studies the compound 3h shows the good antioxidant activity, in which the trifluoro methyl group is attached to the meta position which is highly electron withdrawing. Compound 3a shows the least antioxidant activity, which does not having any substitution.

### Table 2. Antioxidant activity of synthesized compounds.

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### 4. Conclusion

The structure proposed of the synthesized compound is well supported by spectroscopic data. From the data of antibacterial activity and antioxidant activity, it may be concluded that all the synthesized compounds possess good to moderate activity.

### Acknowledgements

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References