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Synthesis and Antibacterial activity of some Novel 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs

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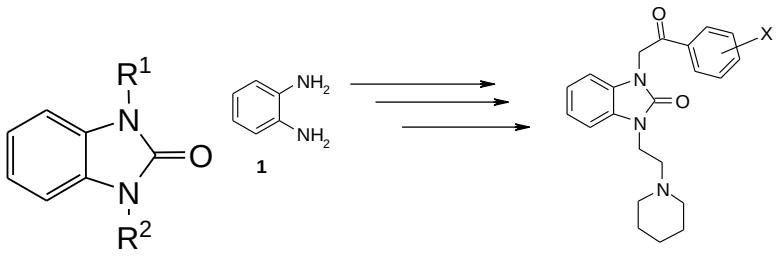
ABSTRACT

*Synthesis of some novel 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs (**10 -17**) were prepared from commercially available 1,2-phenylenediamine. Compounds (**10 -17**) were tested for Gram positive: Streptococcus pyogenes and Staphylococcus aureus. Gram negative: Escherichia coli, Pseudomonas arzenous, Proteus vulgaris, Salmonella typhii bacterial cultures. Compounds **10 – 13** were found to be highly active against Streptococcus pyogenes and Escherichia coli.*

Keywords: Antibacterial activity, 1,3-dihydro-2H-benzimidazol-2-one.

INTRODUCTION

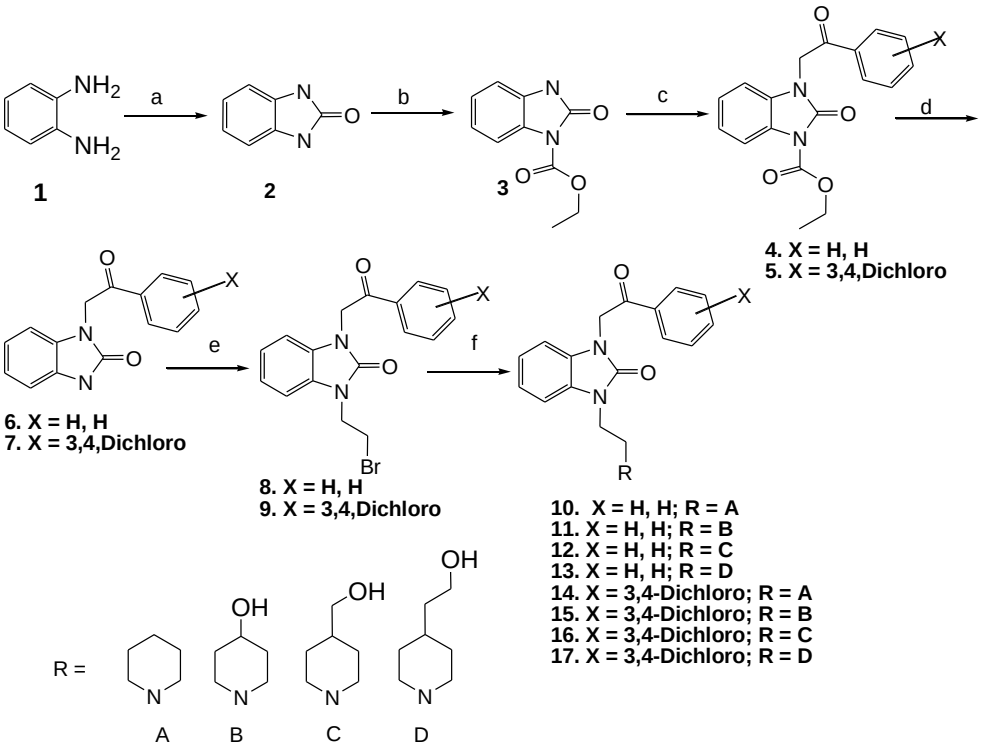
The emergence of bacterial resistance to β-lactam antibiotics, macrolides, quinolones, and vancomycin is becoming a major worldwide health problem [1-4]. In particular, antibiotic resistance among Gram-positive bacteria (staphylococci, enterococi, and streptococci) is becoming increasingly serious [5-10]. However, with the recent increased use of vancomycin in methicillin-resistance *Staphylococcus aureus* (MRSA) infections and colitis due to *Clostridium difficile*, multiple resistant *Entercoecus faecium* has been spreading [11]. As such, the last resort for anti-infective diseases, the Vancomycin family of antibiotics, has now been gravely challenged in recent years due to the emergence of Vancomycin resistance in clinical practice [7, 12]. In order to overcome these emerging resistance problems, there is an urgent need to discover novel antibacterial agents in structural classes distinct from existing antibiotics. In recent years, some of the 1,3-dihydro-2H-benzimidazole-2-one ring system **1** represents the core skeleton of a large number of biologically active, structurally intriguing compounds found in a multitude of pharmaceutically important compounds[13]. Both mono and disubstituted benzimidazol-2-one derivatives **1** have been identified as potent NK1 antagonists[14], CGRP receptor antagonists[15], farnesyl transfer inhibitors[16], p38 inhibitors[17], cathepsin S inhibitors[18], 5-HT4 agonists and antagonists[19], progesterone receptor antagonist[20], respiratory syncytial virus (RSU) inhibitors[21], vasopressin 1a receptor antagonists[22]. The development of efficient and practical methods for construction of this important heterocycle remains as an active area of synthetic research **(Fig 1).** Herein, we report on the synthesis and antibacterial activity of some novel 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs.



MATERIALS AND METHODS

Synthesis of some novel 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs is outlined in (**Scheme I)**. Reaction of 1,2-phenylenediamine with CDI in DMF gave compound **2** in 98 % yield. Compound **3** was prepared by alkylation of compound **2** with ethylchloroformate in 85 % yield. Compounds **4** and **5** were prepared by alkylation of compound **3** with phenacyl bromide and 3,4-dichloro phenacyl bromide. Hydrolysis of compounds **4** and **5** with 5N NaOH at room temperature afforded compounds **6** and **7** in 90 % and 92 % yield respectively. Reaction of compounds **6** and **7** with 1,2-Dibromoethane in acetonitrile gave compounds **8** and **9** in 50 % and 62 % yield respectively. Reaction of Compounds **8** and **9** with piperidines **(A- D)** with K_2CO_3 in Acetonitrile afforded compounds **10 – 17**.

Reagents: a) CDI, DMF, RT; b) ethylchloroformate, K_2CO_3, Acetonitrile, Δ; c) 2-bromo-acetophenone, K_2CO_3, Acetonitrile, Δ; d) 5N NaOH, Ethanol, RT; e) 1,2-dibromoethane, K_2CO_3, Acetonitrile, Δ; f) RNH, K_2CO_3, Acetonitrile.



Scheme I

Measurement of Antibacterial activity: The 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs **10 – 17** were dissolved in dimethyl sulphoxide at 200 µg/mL concentration. The composition of

nutrient agar medium was 10 g Bactotryptone, 5g yeast extract, 10g NaCl, final pH 7.4. After 18 hrs the exponentially growing cultures of the six bacteria in nutrient broth at 37 ^{0}C were diluted in further sterile broth. From each of these diluted cultures, 1mL was added to 100 mL sterilized and cooled nutrient agar media to give a final bacterial count of 1 x 10^6 cell ml^{-1}. The plates were allowed to set at room temperature and later dried at 37 ^{0}C for 2hrs. Paper discs (6mm, punched from Whatman no 41 paper) were ultraviolet sterilized and were used for the assays. Discs were soaked in different concentration of the test solution and placed on the inoculated agar media at regular intervals of 6-7 cm, care was taken to ensure that excess solution was not on the discs. All the samples were taken in triplicates. The plates were incubated at 37 ^{o}C in an inverted fashion.

Table I-Antibacterial activity of compounds **10-17**

	Antibacterial activity					
Compd (200µg /ml in dmso)	Streptococous pyrogenes	Stapylococcus aureus	Escherechia coli	Pseudomonas arzenosa	Proteus vulgaris	samonella typhii
10	++	++	++	+++	-	-
11	+++	-	++	-	-	++
12	++	-	++	-	+	-
13	++	++	++	++	+	+
14	-	-	+	-	-	-
15	-	-	+	-	-	-
16	+	+	+	+	-	+
17	+	+	+	+	+	+

Zone of inhibition (dmso as solvent), +++ = 15-20 mm, 8-14 mm, + = 5-7mm, - = No inhibition

Antibacterial activity of 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs (10 - 17): The following bacterial cultures were tested for their susceptibility to 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs (**10 - 17**) by the disc diffusion method in nutrient agar media. Gram positive: *Streptococcus pyogenes* and *Staphylococcus aureus*. Gram negative: *Escherichia coli*,*Pseudomonas arzenous*, *Proteus vulgaris*, *Salmonella typhii*. The results obtained are shown in **Table I**.

Compound 10 is highly active against all the bacterial cultures and inactive against *Proteus vulgaris and Salmonella typhii*. Compound **11** is highly active against *Streptococcus Pyogenes*, *Escherechia coli* and *Salmonella typhii* and inactive against the other bacterial cultures. Compound **12** is highly active against *Streptococcus Pyogenes*, *Escherechia coli* and moderately active against *Proteus vulgaris*. Compound **13** is highly against all the bacterial cultures and moderately active against *Proteus vulgaris* and *Salmonella typhii*. Compound **14** and **15** are moderately active against *Escherichia coli* and inactive against all other bacterial cultures. Compound **16** is moderately active against all the bacterial cultures and inactive against *Proteus vulgaris*. Compound **17** is moderately active against all the bacterial cultures. Novel 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs (**10-17**) were prepared from commercially available 1,2-phenylenediamine and tested for Gram positive and Gram Negative bacterial cultures. Among the 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs (**10-17**), compounds **10 -13** were found to be higly active against *Streptococcus pyogenes* and *Escherichia coli.*

General Methods

Melting points were determined in open glass capillaries on a Mel-temp apparatus and are uncorrected. The homogeneity of the compounds was checked by TLC (silicagel H, BDH, ethylacetate/hexane, 1:3). The IR spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wave numbers were given in cm^{-1}. The ^1H NMR spectra were recorded in $CDCl_3$/DMSO-*d* on a Varian EM-360 spectrometer (300MHz).The ^{13}C NMR spectra recorded in $CDCl_3$/DMSO-*d* on a Varian VXR spectrometer operating at 75.5 MHz. All chemical shifts were reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer. The mass spectra were recorded on Jeol JMS-D 300 and Finnigan Mat b at 70 eV with an emission current of 100µA

RESULTS AND DISCUSSION

1H-benzo[α]imidazol-2(3H)-2-one 2 To a stirred solution of 1,2-phenylenediamine(10g, 0.092 mole) in DMF (150ml) was added 1,1'-carbonyldiimidazole (14.99g, 0.092 mole). The resulting solution was stirred at rt for 22 hr. The solvent was concentrated under reduced pressure, filtered, and recrystallized from dichloromethane to afford compound **2** (12.1g, 98%), m.p : 100-102 ^0C; ^1H NMR ($CDCl_3$): δ 6.92 (m, 4H), 10.6 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 121, 124.6, 129.9, 155.2; IR (KBr): 3199, 2806, 1739, 1627, 1481 cm^{-1}; FAB MS: *m/z* 134.0 $(M+H)^+$.

Ethyl 2,3-dihydro-2-oxobenzo[α]imidazole-1-carboxylate 3 To a stirred suspension of 1H-benzo[α]imidazol-2(3H)-2-one **2** (15g, 0.111 mole) and K_2CO_3 (18.53g, 0.134 mole) in Acetonitrile (240 ml) was added Ethylchloroformate (12g ,0.111 mole) dropwise over 30min at room temperature. The reaction mixture was stirried at 90^{0}C for 10 hr. The mixture was concentrated in *vacuo* and the residue diluted with water. The solid filtered, washed with water, dried in air to afford a compound **3**. Crude solid recrystallized from a mixture Dichloromethane and Hexane, m.p. 149-15^{0}C. ^1H NMR ($CDCl_3$): δ 1.48 (t, *J* = 7 Hz, 3H), 4.53 (q, *J* = 7 Hz, 2H), 7.0-7.20 (m, 3H), 7.77 (d, *J* = 7.5 Hz, 1H), 10.27 (s, 1H), ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.8, 58.3, 121.8, 124.6, 127.3, 129.9, 150.2, 151.4; IR (KBr): 3270, 1780 ,1480 cm^{-1}; FAB MS: *m/z* 206.0 $(M+H)^+$.

2-Oxo-3-(2-oxo-2-phenyl-ethyl)-2,3-dihydro-benzoimidazole-1-carboxylic acid ethyl ester 4 A mixture of compound **3** (10g, 0.0308 mole), 2-bromoacetophenone (6.09g, 0.0308 mole), K_2CO_3 (13.385g, 0.0969 mole) in acetonitrile (100 ml) was refluxed at 90 ^{0}C for 4.5 hr. The reaction mixture was cooled to room temperature, diluted with water and extracted with ethyl acetate, organic layer dried over $MgSO_4$,filtered and evaporated in *vacuo* to give **4** as crude solid (12g, 76.33%) and was taken to next step without further purification, m.p. 124-127 ^{0}C. ^1H NMR ($CDCl_3$): δ 1.48 (t, *J* = 7 Hz, 3H), 4.53 (q, *J* = 7 Hz, 2H), 5.2 (s, 2H) 7.05-7.20 (m, 3H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.2-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.8, 49.7, 58.3, 121.8, 124.6, 127.3, 128.7, 128.8, 133.2, 136.8, 151.4, 156.2, 195.4; IR (KBr) 3414, 1711, 1417, 1265 cm^{-1}; FAB MS: *m/z* 324.1 $(M+H)^+$.

3-[2-(3,4-Dichloro-phenyl)-2-oxo-ethyl]-2-oxo-2,3-dihydro-benzoimidazole-1-carboxylic acid ethyl ester 5 : m.p. 149-151^{0}C. ^1H NMR ($CDCl_3$): δ 1.48 (t, *J* = 7.2 Hz, 3H), 4.54 (q, *J* = 7.1 Hz, 2H), 5.27 (s, 2H), 7.05-7.20 (m, 2H), 7.77 (d, *J* = 7.5 Hz, 1H), 6.8 (t, *J* = 8.7 Hz, 1H), 8.1 (s, 1H), 7.92 (t, *J* = 10, 2H), 7.77 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.8, 58.3, 49.7, 121.8, 124.6, 128.3, 130.2, 133.3, 136.3, 137.8, 195.4; IR(KBr) 3410, 2927, 1711, 1417, 1198 cm^{-1}; FAB MS: *m/z* 392.0 $(M+H)^+$.

2-Oxo-3-(2-oxo-2-phenyl-ethyl)-1,3-dihydro-benzoimidazol-2 -one 6 : To a stirred solution of Compound **4** (12 g, 0.037 mole) in EtOH (28ml) was added NaOH (5N, 100 ml). The reaction mixture was stirred for 2 hr at rt. The reaction mixture was concentrated under reduced pressure and extracted with ethyl acetate. The organic layer was washed with water and saturated NaCl solution, dried over Na_2SO_4 filtered and evaporated to afford compound **6** (8.5 g , 91%), m.p. 233-235^{0}C. ^1H NMR ($CDCl_3$): δ 5.2 (s,

2H), 7.05-7.20 (m, 3H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.21-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 49.7, 121.8, 129.9, 128.7, 128.8, 133.2, 136.8, 151.7, 195.1; IR (KBr): 3414, 2690, 1700, 1488, 1213 cm^{-1}; FAB MS: *m/z* 252.2 $(M+H)^+$.

1[2-(3,4-Dichloro-phenyl)-2-oxo-ethyl]-4-ethylidene-imidazolidin-2-one 7 ; m.p. 175-177^{0}C. ^{1}H NMR ($CDCl_3$): δ 5.21 (s, 2H), 7.05-7.2 (m, 3H), 7.77 (d, *J* = 7.5, 1H), 6.8 (t, *J* = 8.7 Hz, 1H), 8.1(s, 1H), 7.92 (t, *J* = 10.8, 1H), 8.91 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 49.7, 121.8, 124.6, 128.3, 130.2, 130.3, 133.3, 136.3, 154.6, 195.4; IR (KBr): 3179, 3022, 1700, 1488, 1213; FAB MS: *m/z* 321.1 $(M+H)^+$**.**

1-(2-Bromo-ethyl)-3-(2-oxo-2-phenyl-ethyl)-1, 3-dihydro-benzoimidazol-2-one 8 : To a stirred mixture of compound **4** (8.5 g, 0.0337 mole) and K_2CO_3 (9.3g, 0.0674 mole) in ACN (42.5ml) was added dropwise 1,2-Dibromoethane (18.92g, 0.101 mole) over 10 min. The reaction mixture was refluxed at 90^{0}C for 6 hr. The reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with water and saturated NaCl, dried over Na_2SO_4, filtered and evaporated in *vacuo.* The product **4, 5** were purified by flash column chromatography using silicagel with hexane-ethyl acetate as eluant to afford compounds **4, 5** (6g , 49.71%), m.p. 184-185^{0}C. ^{1}H NMR ($CDCl_3$): δ 2.79 (t, *J* = 6.75 Hz, 2H), 3.8 (t, *J* = 6.6 Hz, 2H), 5.2 (s, 2H), 7.05-7.20 (m, 3H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.21-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 27.9, 55.8, 124.6, 121.8, 128.7, 128.8, 133.3, 136.8, 154.6, 195.4; IR (KBr): 3414, 2690, 1700, 1488, 1213 cm^{-1}; FAB MS: *m/z* 359.2 M+H)$^+$.

1-(2-Bromo-ethyl)-3-[2-(3,4-dichloro-phenyl)-2-oxo-ethyl]-1,3-dihydro-benzoimidazol-2-one 9 : m.p. 156-158^{0}C. ^{1}H NMR($CDCl_3$): δ 3.68 (t, *J* = 6.9 Hz, 2H), 4.318 (t, *J* = 7.05 Hz, 2H), 5.21 (s, 2H), 7.05-7.21 (m, 3H), 7.77 (d, *J* = 7.5,1H), 6.8 (t, *J* = 8.7 Hz, 1H), 8.1 (s, 1H), 7.92 (t, *J* = 10.8, 1H), 8.91 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 27.9, 49.7, 55.8, 121.8, 124.6, 121.8, 124.6, 128.3, 130.2, 130.3,133.3, 136.3, 154.6, 195.4; IR (KBr): 3401.8, 2920, 1716, 1695, 1496, 1227, 1137; FAB: MS: *m/z* 425.9 (M+H)$^+$.

1-(2-oxo-2-phenyl-ethyl)-3-(2-piperidin-1-yl-ethyl)-1,3-dihydro-benzoimidazol-2-one 10 : A mixture of compound **8** (0.15g, 0.00041 mole), piperdin (0.052g, 0.000615 mole), K_2CO_3 (0.113g, 0.00082 mole) in ACN (1.5ml) was refluxed for 8 h. The mixture was concentrated in *vacuo* and the residue diluted with H_2O and extracted with EtOAc. The residue was chromatographed on a column of silicagel using a mixture of Methanol and Dichloromethane(3-4%) as eluent to furnish compound **10 (**0.070g, 87.5 %), m.p. 136-138^{0}C. ^{1}H NMR($CDCl_3$): δ 1.72 (m, 6H), 2.28 (m, 4H), 3.68 (t, J = 6.95, 2H), 4.31 (t, *J* = 7.05, 2H), 5.21 (s, 2H), 7.72 (d, *J* = 7.5, 1H), 7.05-7.2 (m, 3H), 7.2-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.9, 49.0, 50.0, 50.2, 54.3, 121.8, 124.6, 128.8, 128.7, 133.2, 133.3, 136.8, 154.6, 195.4; IR (KBr): 2992, 2690, 1700, 1488, 1213 cm^{-1}; FAB: MS: *m/z* 363.1 (M+H)$^+$.

1-[2-(4-Hydroxy-piperdin-1-yl)-ethyl]-3-(2-oxo-2-phenyl-ethyl)-1,3-dihydro-benzoimidazol-2-one 11 m.p. 179-181^{0}C. ^{1}H NMR($CDCl_3$): δ 1.78 (m, 4H), 2.28 (m, 4H), 3.38 (m, 1H), 2.79 (t, *J* = 6.75 Hz, 2H), 3.8 (t, *J* = 6.6 Hz, 2H), 5.2 (s, 2H), 7.05-7.20 (m, 3H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.2-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 48.1, 33.8,67.8, 50.2, 50.0, 49.0, 121.8, 124.6, 128.7, 133.2, 136.8, 154.6, 195.4; IR(KBr): 3414, 2690, 1700, 1488, cm^{-1}; FAB: MS: *m/z* 379.1 (M+H)$^+$.

1-[2-(4-Hydroxymehyl-piperdin-1-yl)-ethyl]-3-(2-oxo-2-phenyl-ethyl)-1,3-dihydro-benzoimidazol-2-one 12 : m.p. 202-205^{0}C. ^{1}H NMR($CDCl_3$): δ 1.59 (q, 4H), 2.29 (t, 4H), 1.58 (m, 1H), 3.49 (d, 2H), 2.79 (t, *J* = 6.75 Hz, 2H), 3.8 (t, *J* = 6.6 Hz, 2H), 5.2 (s, 2H), 7.05-7.20 (m, 3H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.2-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 34.3, 52.1, 67.8, 50.2, 50.0, 49.0, 121.8, 124.6, 128.7, 133.2 , 136.8, 154.6, 195.4; IR (KBr): 3416, 2690, 1700, 1488, 1213 cm^{-1}; FAB: MS: *m/z* 393.2 (M+H)$^+$.

1-{2-[4-(2-Hydroxy-ethyl)-piperdin-1-yl)-ethyl]-ethyl}-3-(2-oxo-2-phenyl-ethyl)-1,3-dihydro-benzoimidazol-2-one 13 : m.p. 242-245^{0}C. ^{1}H NMR($CDCl_3$): δ 1.45 (m, 1H), 1.46 (m, 2H), 3.54 (t, *J* = 8.2 Hz, 2H), 1H), 3.68 (t, *J* = 6.91 Hz, 2H), 4.31 (t, *J* = 9.3 Hz, 2H), 5.21 (s, 2H), 7.05-7.20 (m, 3H), 7.77

(d, *J* = 7.5 Hz, 1H), 7.2-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.8, 30.3, 37.1, 49.0, 50.0, 50.2, 52.1, 34.3, 52.1, 121.8, 124.6, 128.7, 133.2, 136.8, 154.6, 195.4; IR (KBr): 3414, 2690, 1700, 1488 cm^{-1}; FAB: MS: *m/z* 407.2 (M+H)$^+$.

1-[2-(3,4-Dichloro-phenyl)-2-oxo-ethyl]-3-(2--piperidin-1-yl)-ethyl)-1,3-dihydro-benzoimidazol-2-one 14 : m.p. 139-141^{0}C. ^{1}H NMR($CDCl_3$): δ 1.72 (m, 6H), 2.28 (m, 4H), 3.68 (t, *J* = 6.91 Hz, 2H), 4.31 (t, *J* = 9.3 Hz, 2H), 5.21 (s, 2H), 6.83 (d, *J* = 9.3 Hz, 1H), 7.05-7.2 (m, 3H), 7.72 (d, *J* = 7.5, 1H), 7.9 (d, 1H, *J* = 10.5), 8.13 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.9, 33.8, 48.1, 49.0, 54.3, 67.8, 50.2, 121.8, 124.6, 128.3, 130.2, 130.3, 133.2, 133.2, 136.3, 137.8, 154.6, 195.4; IR(KBr): 2920, 1716, 1695.12, 1496, 1227, 1137 cm^{-1}; FAB: MS: *m/z* 431.1 (M+H)$^+$.

1-[2-(3,4-Dichloro-phenyl)-2-oxo-ethyl]-3-[2-(4-hydroxy-piperidin-1-yl)-ethyl]-1,3-dihydro-benzoimidazol-2-one 15 : m.p. 167-169^{0}C. ^{1}H NMR($CDCl_3$): δ 1.72 (m, 4H), 2.28 (m, 4H), 3.38 (m, 1H), 3.68 (t, *J* = 6.91 Hz, 2H), 4.31 (t, *J* = 9.3 Hz, 2H), 5.21 (s, 2H), 6.83 (d, *J* = 9.3 Hz, 1H), 7.05-7.20 (m, 3H), 7.72 (d, *J* = 7.5, 1H), 7.9 (d, J=10.5, 1H), 8.13 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 33.8, 48.1, 49.1, 50.0, 50.2 , 67.8, 121.8, 124.6, 128.3, 130.2, 130.3, 133.2, 133.2, 136.3, 137.8, 154.6, 195.4; IR(KBr): 3401, 2920, 1716, 1695, 1496, 1227, 1137 cm^{-1}; FAB: MS: *m/z* 447.1 (M+H)$^+$.

1-[2-(3,4-Dichloro-phenyl)-2-oxo-ethyl]-3-[2-(4-hydroxymethyl-piperidin-1-yl)-ethyl]-1,3-dihydro-benzoimidazol-2-one 16: m.p. 197-199^{0}C. ^{1}H NMR($CDCl_3$): δ 1.72 (m, 4H), 2.28 (m, 4H), 1.62 (m, 1H), 3.46 (m, 2H), 3.68 (t, *J* = 6.91 Hz, 2H), 4.31 (t, *J* = 9.3 Hz, 2H), 5.21 (s, 2H), 6.83 (d, *J* = 9.3 Hz, 1H), 7.05-7.20 (m, 3H), 7.72 (d, *J* = 7.5,1H), 7.9 (d, *J* = 10.5, 1H), 8.13 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 34.3, 49.0, 50.0, 50.2, 50.2, 67.6, 121.8, 124.6, 128.3, 130.2, 130.3, 133.2, 133.2, 136.3, 137.8, 154.6, 195.4; IR(KBr): 3401, 2920, 1716, 1695, 1496, 1227, 1137 cm^{-1}; FAB: MS: *m/z* 461.1 (M+H)$^+$.

1-[2-(3,4-Dichloro-phenyl)-2-oxo-ethyl]-3-{2-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-ethyl}-1,3-dihydro-benzoimidazol-2-one 17 : m.p. 209-211^{0}C. ^{1}H NMR($CDCl_3$): δ 1.45 (m, 1H), 1.46 (m, 2H), 3.54 (t, 2H, *J* = 8.2), 1H), 3.68 (t, *J* = 6.91 Hz, 2H), 4.31 (t, *J* = 9.3 Hz, 2H), 5.21 (s, 2H), 6.83 (d, *J* = 9.3 Hz, 1H), 7.05-7.2 (m, 3H), 7.72 (d, J=7.5,1H), 7.9 (d, *J* = 10.5, 1H), 8.13 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.8, 30.3, 30.3, 37.1, 49.0, 50.2, 52., 60.7, 121.8, 124.6, 128.3, 130.2, 130.3, 133.2, 133.2, 136.3, 137.8, 154.6, 195.4; IR(KBr): 3412, 2920, 1716, 1695, 1496, 1227, 1137 cm^{-1}; FAB: MS: *m/z* 475.1 (M+H)$^+$.

APPLICATIONS

Some of the Synthesized novel 1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one analogs are found to be highly active against Streptococcus pyogenes and Escherichia coli.

CONCLUSIONS

In conclusion, the PPG has been employed as a novel, mild and highly efficient solvent system for the convenient preparation of benzimidazoles in excellent yields from o-phenyldiamine and a wide variety of aryl aldehydes using $ZnCl_2$ as catalyst. In addition low cost, recyclable solvent system and ready availability of catalyst, an environmentally benign procedure makes this methodology a useful contribution to the existing procedures available for the synthesis of benzimidazole derivatives.

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