Journal of the Korean Chemical Society
2014, *Vol. 58, No. 5*
Printed in the Republic of Korea
http://dx.doi.org/10.5012/jkcs.2014.58.5.450

Synthesis and Characterization of Novel Oxadiazole Derivatives from Benzimidazole

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(Received April 8, 2014; Accepted July 18, 2014)

ABSTRACT. In the present study, a series of novel *N*-(1*H*-benzo[*d*]imidazol-2-yl)methyl-5-[(hetero)aryl-1,3,4-oxadiazol-2-yl]methanamine (**4a**–**4j**) were efficiently synthesized. Condensation of hydrazide derivative **3** with various carboxylic acid derivatives yielded *N*-[(1*H*-benzo[*d*]imidazol-2-yl)methy](5-substituted-1,3,4-oxadiazol-2-yl)methanamine **(4a**–**4j)** and compound 5-{[(1*H*-benzo[*d*]imidazol-2-yl)methylamino]methyl}-1,3,4-oxadiazole-2-thiol **(4k)** was obtained on treating hydrazide **3** with carbon disulfide. All the newly synthesized analogues were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data.

Key words: Benzimidazole, Oxadiazole

INTRODUCTION

The synthesis of heterocyclic systems containing nitrogen has attracted increasing interest in recent years because of their biological and pharmacological importance. As therapeutic agents, azoles are extensively manipulated and are deliberate class of antimicrobial agents due to their efficacy and safety profile.

Benzimidazole provides a scaffold on which pharmacophores can be arranged to yield potent and selective drugs.[1] A number of benzimidazole of clinical significance are in market for their therapeutic importance like thiabendazole and flubendazole (anthelmintic), omeprazole and lansoprazole (antiulcerative; proton pump inhibitor) and astemizole (antihistamines; H_1 antagonist) (*Figure* 1).

The synthesis of benzimidazole compounds has emerged as an essential need for development of new pharmaceutical entities. Benzimidazole derivatives impart their importance as antidiabetic,[2] antimicrobial,[3,4] antiviral,[5–9] antispasmodic,[10] anticancer[11] and antiasthmatic[12] agents. The outcome of numerous attempts to develop new structural prototypes in the search for effective antimicrobials indicates that the benzimidazoles still remain as one of the most versatile class of compounds against microbes.[13,14]

Similarly, oxadiazole derivatives are also recognized for their pharmacological importance and are reported to possess wide spectrum of activities. Studies highlights that substituted 1,3,4-oxadiazoles have revealed antibacterial,[15–17] antimycobacterial,[18] antifungal,[19,20] anti-inflammatory,[21,22] analgesic,[23] anticonvulsant,[24,25] hypoglycemic[26] and anticancer[27] properties. Furthermore, compounds derived from oxadiazole moiety also possess muscle relaxants activity[28] and tyrosinase inhibitory activity.[29] Thus oxadiazole, a physiologically active nucleus, an important pharmacophore in modern drug discovery and as a privileged structure in medicinal chemistry has attracted the attention of many researchers. In the present study a series of novel oxadiazoles were synthesized from benzimidazole and their structural characterization are reported.

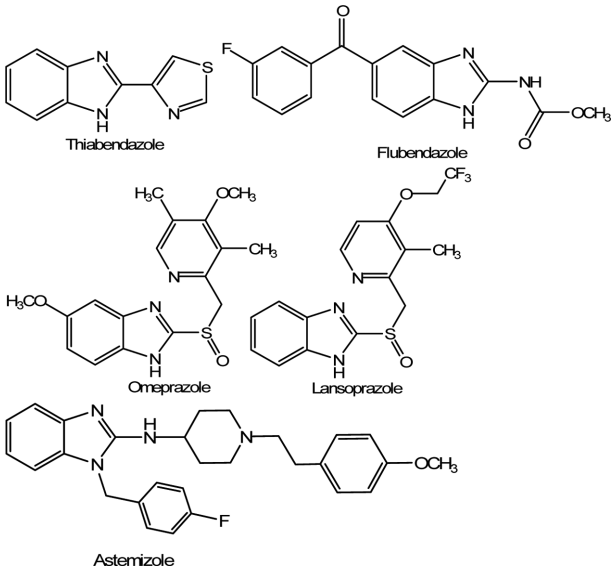


***Figure* 1.** Benzimidazole derivatives as therapeutic agents in clinical use.

EXPERIMENTAL

Material and Methods

Melting points were determined in an open capillary tube and are uncorrected. TLC was used to assess the progress/completion of the reactions and the purity of the synthesized compounds using ethyl acetate and hexane (8:2) as solvent system and iodine vapors as visualizing agent. The FTIR spectra were recorded using Shimadzu FTIR-8400 instrument by KBr disc pellet method and only noteworthy absorption levels (cm^{-1}) are listed, ^1H NMR and ^{13}C NMR spectra were recorded using Brucker AV400 high resolution multinuclear FT-NMR spectrometer at 400 MHz with deuteriated dimethyl sulfoxide (DMSO-d_6) as solvent and tetramethylsilane (TMS) as internal standard (chemical shifts in δ, ppm), and mass spectra were recorded using JEOL GCMATE II GC-MS. Elementary analyses of final compounds were recorded using Thermo Finnigan FLASH EA 1112 CHNS analyzer and all the compounds gave satisfactory data.

Synthesis of (1*H*-benzo[*d*]imidazol-2-yl)methanamine (1)

A solution of 1,2-phenylenediamine (13 g, 0.12 mol) and glycine (18 g, 0.24 mol) in 4 N hydrochloric acid (40 mL) was heated to reflux with stirring for 2 h. The progress of the reaction was monitored by TLC. On completion of the reaction, the reaction mixture was cooled to room temperature and the pH was adjusted to 7.2 using 1 N sodium hydroxide solution to obtain buff colored product **1**. The product was recrystallized using rectified sprit as solvent. Yield: 87%, mp 261–263 ºC, R_f: 0.72, IR (KBr) 3371 (NH_2), 3053 (=C–H), 1591 (C=N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.1 (s, 1H, NH), 7.2–6.9 (m, 4H), 5.2 (s, 2H, NH_2), 2.3 (d, J = 12.7 Hz, 2H, CH_2).

Synthesis of ethyl 2-[(1*H*-benzo[*d*]imidazol-2-yl)methylamino]acetate (2)

A solution of compound **1** (15 g, 0.10 mol), ethyl 2-chloroacetate (30 mL, 0.24 mol) and activated anhydrous potassium carbonate (12 g) in acetone (30 mL) were heated to reflux with stirring for 8 h. The progress of the reaction was monitored by TLC. On completion of the reaction, the reaction mixture was cooled to room temperature and filtered. The filtrate was concentrated and poured into the crushed ice to obtain the solid product **2**. The product was recrystallized using rectified sprit as solvent. Yield: 69%, mp 143–144 ºC, R_f: 0.68, IR (KBr) 3384 (NH), 3030 (C=C), 1737 (C=O), 1633 (C=N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6,) δ 12.5 (s, 1H, NH), 7.6–7.2 (m, 4H), 5.1 (s, 1H, $CH_2\underline{NH}$), 3.4 (d, J = 11.3 Hz, 2H, $\underline{CH_2}COO$), 3.2 (q, J = 6.4 Hz, 2H, $COO\underline{CH_2}$), 2.4 (d, J = 16.6 Hz, 2H, $\underline{CH_2}NH$), 1.3 (t, J = 14.8 Hz, 3H, CH_3).

Synthesis of 2-[(1*H*-benzo[*d*]imidazol-2-yl)methylamino]-acetohydrazide (3)

A solution of ester **2** (18 g, 0.08 mol) and hydrazine monohydrate (10 mL, 0.20 mol) in ethanol (30 mL) were heated to reflux for 12 h. The progress of the reaction was monitored by TLC. On completion of the reaction the reaction mixture was cooled to room temperature and allowed to cool in refrigerator overnight to precipitate the hydrazide **3**. Then product was recrystallized using rectified sprit as solvent. Yield: 56%, mp 262–264 ºC, R_f: 0.71, IR (KBr) 3398–3450 (NH_2, NH), 3045 (C=C), 1718 (C=O), 1627 (C=N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6,) δ 12.4 (s, 1H, NH), 11.7 (s, 1H, $CO\underline{NH}$), 7.6–7.1 (m, 4H), 5.2 (s, 1H, $CH_2\underline{NH}$), 4.2 (s, 2H, $NH\underline{NH_2}$), 3.3 (d, J = 12.5 Hz, 2H, $\underline{CH_2}CO$), 2.3 (d, J = 9.7 Hz, 2H, $\underline{CH_2}NH$).

General procedure for the synthesis of *N*-[(1*H*-benzo[*d*]imidazol-2-yl)methyl](5-substituted-1,3,4-oxadiazol-2-yl)methanamine (4a–4j)

The hydrazide **3** was condensed with different carboxylic acid derivatives to afford the title oxadiazole derivatives.

To the solution of hydrazide **3** (2.2 g, 0.01 mol) in ethanol (25 mL), carboxylic acid derivatives (0.01 mol) and phosphorous oxychloride (1.6 mL, 0.01 mol) were added slowly in an exhaustion chamber and heated to reflux for 8–12 h. The progress of the reaction was monitored by TLC. On completion of the reaction the reaction mixture was cooled to room temperature and crushed ice was added to obtain oxadiazole derivative (**4a–4j**). The product was recrystallized using rectified sprit as solvent.

***N*-[(1*H*-benzo[*d*]imidazol-2-yl)methyl](5-phenyl-1,3,4-oxadiazol-2-yl)methanamine (4a):** Yield: 81%, mp 256–257 ºC, R_f: 0.75, IR (KBr) 3242 (NH), 3026 (C=C), 1662 (C=N), 1271 (C–O–C) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.4 (s, 1H, NH), 7.5–6.7 (m, 9H), 5.1 (s, 1H, $CH_2\underline{NH}$), 3.3 (d, J = 12.1 Hz, 2H, $NH\underline{CH_2}$), 3.1 (d, J = 14.6 Hz, 2H, $\underline{CH_2}NH$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 46.3, 56.7, 119.7, 121.1, 123.6, 123.7, 125.2, 126.3, 127.5, 137.4, 138.2, 146.9, 151.6, 167.5, 171.5; MS: m/z (%) 305 (15) [M^+], 159 (60) [$C_9H_7N_2O^+$], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{17}H_{15}N_5O$: C 66.87, H 4.95, N 22.94, Found C 66.74, H 4.89, N 22.79.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-(2-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl]methanamine (4b): Yield: 76%,

mp 312–313 °C, R_f: 0.64, IR (KBr) 3263 (NH), 3016 (C=C), 1653 (C=N), 1264 (C–O–C), 1526 (N–O, NO_2) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.6 (s, 1H, NH), 8.2–7.3 (m, 8H), 4.9 (s, 1H, CH_2NH), 3.2 (d, J = 11.8 Hz, 2H, NHCH_2), 2.8 (d, J = 13.7 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.3, 53.2,121.6, 121.9, 123.8, 124.2, 125.9, 126.4, 139.1, 142.5, 146.4, 148.4, 151.3, 162.5, 168.3; MS: m/z (%) 350 (14) [M^+], 204 (55) [$C_9H_6N_3O_3^+$], 146 (100); Anal. Calcd for $C_{17}H_{14}N_6O_3$: C 58.28, H 4.03, N 23.99, Found C 55.39, H 4.13, N 22.81.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-(3,5-dinitrophenyl)-1,3,4-oxadiazol-2-yl)methyl]methanamine (4c): Yield: 71%, mp 298–299 °C, R_f: 0.74, IR (KBr) 3253 (NH), 3019 (C=C), 1663 (C=N), 1256 (C–O–C), 1519, 1522 (NO_2) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.5 (s, 1H, NH), 8.7–7.2 (m, 7H), 5.3 (s, 1H, CH_2NH), 3.1 (d, J = 12.7 Hz, 2H, NHCH_2), 2.9 (d, J = 14.1 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 42.3, 54.1,123.9, 124.8, 125.2, 125.6, 129.7, 131.7, 133.7, 141.1, 146.5, 147.8, 149.2, 149.6, 163.7, 169.5; MS: m/z (%) 395 (20) [M^+], 249 (24) [$C_9H_9N_4O_5^+$], 167 (52) [$C_6H_3N_2O_4^+$], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{17}H_{13}N_7O_5$: C 51.65, H 3.31, N 24.80, Found C 51.61, H 3.39, N 24.81.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-(4-aminophenyl)-1,3,4-oxadiazol-2-yl)methyl]methanamine (4d): Yield: 68%, mp 257–259 °C, R_f: 0.65, IR (KBr) 3318 (NH_2), 3251 (NH), 3024 (C=C), 1659 (C=N), 1276 (C–O–C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.3 (s, 1H, NH), 8.6–7.4 (m, 8H), 5.2 (s, 1H, CH_2NH), 3.3 (d, J = 19.2 Hz, 2H, NHCH_2), 2.8 (d, J = 14.8 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 41.6, 56.2, 121.7, 121.8, 121.9, 122.8, 122.9, 123.2, 139.2, 145.4, 146.2, 147.6, 149.8, 164.8, 174.5; MS: m/z (%) 320 (12) [M^+], 174 (20) [$C_9H_8N_3O^+$], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{17}H_{16}N_6O$: C 63.74, H 5.03, N 26.23, Found C 63.46, H 4.89, N 26.17.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-(2-aminophenyl)-1,3,4-oxadiazol-2-yl)methyl]methanamine (4e): Yield: 46%, mp 215–215 °C, R_f: 0.72, IR (KBr) 3249 (NH), 3021 (C=C), 1652 (C=N), 1266 (C–O–C), 3324 (NH_2) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.6 (s, 1H), 8.9–7.6 (m, 8H), 6.6 (s, 2H, NH_2), 5.2 (s, 1H, CH_2NH), 3.4 (d, J = 12.6 Hz, 2H, NHCH_2), 3.1 (d, J = 9.4 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 47.3, 57.9, 119.3, 121.1, 121.7, 121.8, 122.9, 124.2, 127.3, 136.8, 138.5, 139.6, 143.2, 148.3, 149.1, 164.1, 167.2; MS: m/z (%) 320 (20) [M^+], 174 (35) [$C_9H_8N_3^+$], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{17}H_{16}N_6O$: C 63.74, H 5.03, N 26.23, Found C 63.98, H 5.29, N 26.41.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-(4-hydroxyphenyl)-1,3,4-oxadiazol-2-yl)methyl]methanamine (4f): Yield: 31%, mp 117–118 °C, R_f: 0.55, IR (KBr) 3321 (O–H), 3245 (NH), 3023 (C=C), 1663 (C=N), 1334 (C–O) 1278 (C–O–C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.4 (s, 1H, NH), 9.8 (s, 1H, OH), 8.4–7.5 (m, 8H), 5.2 (s, 1H, CH_2NH), 3.2 (d, J = 14.2 Hz, 2H, NHCH_2), 2.7 (d, J = 11.5 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.6, 56.2, 121.9, 122.8, 123.7, 124.8, 125.9, 142.2, 148.6, 149.2, 153.8, 155.4, 166.8, 169.5; MS: m/z (%) 324 (13) [M^+], 175 (21) [$C_9H_7N_2O_2^+$], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{17}H_{15}N_5O_2$: C 63.54, H 4.71, N 21.79, Found C 63.18, H 4.51, N 21.62.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-(2-hydroxyphenyl)-1,3,4-oxadiazol-2-yl)methyl]methanamine (4g): Yield: 56%, mp 152–154 °C, R_f: 0.68, IR (KBr) 3343 (O–H), 3239 (NH), 3027 (C=C), 1661 (C=N), 1331 (C–O) 1272 (C–O–C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.5 (s, 1H, NH), 10.2 (s, 1H, OH), 8.6–7.6 (m, 8H), 5.6 (s, 1H, CH_2NH), 3.4 (d, J = 13.9 Hz, 2H, NHCH_2), 2.8 (d, J = 9.4 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 43.2, 53.5, 121.9, 123.8, 124.3, 124.9, 125.6, 126.1, 126.8, 127.3, 138.3, 141.6, 147.1, 148.9, 156.3, 164.6, 169.1; MS: m/z (%) 321 (24) [M^+], 175 (43) [$C_9H_7N_2O_2^+$], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{17}H_{15}N_5O_2$: C 63.54, H 4.71, N 21.79, Found C 63.31, H 4.65, N 21.56.

***N*-[(1,3,4-oxadiazol-2-yl)methyl](1*H*-benzo[*d*]imidazol-2-yl)methanamine (4h):** Yield: 87%, mp 197–198 °C, R_f: 0.57, IR (KBr) 3248 (NH), 3028 (C=C), 1661 (C=N), 1274 (C–O–C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.1 (s, 1H, NH), 8.1–7.6 (m, 4H), 8.6 (s, 1H, CH oxadiazole), 5.2 (s, 1H, CH_2NH), 3.1 (d, J = 13.6 Hz, 2H, NHCH_2), 2.7 (d, J = 10.6 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 44.6, 52.6, 122.7, 123.4, 124.4, 125.6, 136.9, 141.8, 147.1, 161.3, 165.1; MS: m/z (%) 229 (32) [M^+], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{11}H_{11}N_5O$: C 57.63, H 4.84, N 30.55, Found C 57.58, H 4.69, N 30.47.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]methanamine (4i): Yield: 78%, mp 211–212 °C, R_f: 0.68, IR (KBr) 3245 (NH), 3023 (C=C), 1663 (C=N), 1278 (C–O–C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.3 (s, 1H, NH), 7.8–7.3 (m, 4H), 5.4 (s, 1H, CH_2NH), 3.2 (d, J = 12.5 Hz, 2H, NHCH_2), 2.8 (d, J = 14.1 Hz, 2H, CH_2NH), 1.9 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-

d_6) δ 27.6, 41.6, 57.8, 121.2, 123.4, 123.6, 126.1, 139.7, 147.2, 149.1, 166.4, 171.8; MS: m/z (%) 243 (45) [M^+], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{12}H_{13}N_5O$): C 59.25, H 5.39, N 28.79, Found C 59.52, H 5.66, N 28.96.

(1*H*-benzo[*d*]imidazol-2-yl)-*N*-[(5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)methyl]methanamine (4j): Yield: 42%, mp 231–232 °C, R_f: 0.74, IR (KBr) 3245, 3215 (NH), 3023 (C=C), 1663 (C=N), 1278 (C–O–C) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.7 (s, 1H, NH), 8.9–8.1 (m, 8H), 4.9 (s, 1H, CH_2NH), 3.1 (d, J = 14.4 Hz, 2H, NHCH_2), 2.9 (d, J = 11.2 Hz, 2H, CH_2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 46.1, 52.9, 121.3, 122.4, 123.7, 124.1, 131.3, 138.3, 143.6, 146.9, 147.3, 147.5, 164.6, 169.1, 172.4, 178.3; MS: m/z (%) 306 (41) [M^+], 160 (22) [$C_8H_6N_3O^+$], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{16}H_{14}N_6O$: C 62.74, H 4.61, N 27.44, Found C 62.42, H 4.56, N 27.11.

Synthesis of 2-mercapto 1,3,4-oxadiazole 5-{[(1*H*-benzo[*d*]imidazol-2-yl)methylamino]methyl}-1,3,4-oxadiazole-2-thiol (4k)

2-(Benzo[*d*]thiazol-2-yl amino) acetohydrazide (**3**) (2.2 g, 0.01 mol) was dissolved in ethanol (30 mL) and equimolar quantities of carbon disulphide (3.8 mL, 0.05 mol) and potassium hydroxide (2.8 g, 0.05 mol) were added to the solution. The contents were heated to reflux for 4 h. Distilled water was added followed by neutralization with dilute HCl, to obtain a solid mass product **4k**. The product separated out, was filtered and recrystallized using methanol as solvent. Yield: 52%, mp 146–147 °C, R_f: 0.53, IR (KBr) 3342 (NH), 3087 (C=C), 1620 (C=N), 1283 (C–O–C), 2587 (SH) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.2 (s, 1H, SH), 12.3 (s, 1H, NH), 8.2–7.6 (m, 4H), 5.2 (s, 1H, CH_2NH), 3.4 (d, J = 14.7 Hz, 2H, NHCH_2), 3.1 (d, J = 12.8 Hz, 2H, CH_2NH); ^{13}C NMR (400 MHz, DMSO-d_6) δ 47.2, 56.3, 122.4, 124.8, 125.7, 126.7, 143.8, 147.3, 156.9, 169.2, 179.7; MS: m/z (%) 261 (30) [M^+], 146 (100) [$C_8H_8N_3^+$]; Anal. Calcd for $C_{11}H_{11}N_5OS$: C 50.56, H 4.24, N 26.80, S 12.27, Found C 50.72, H 4.33, N 27.13, S 12.49.

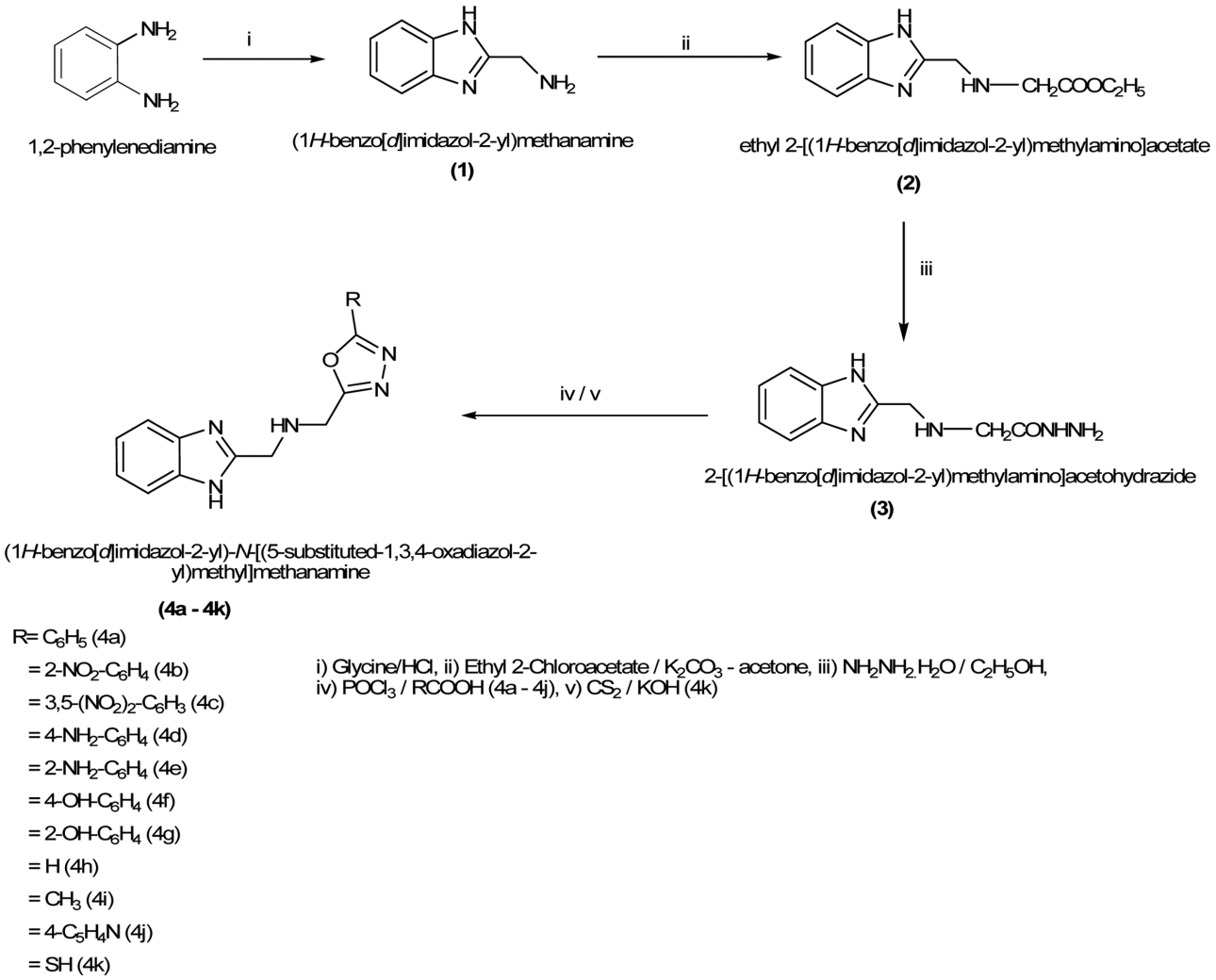
RESULTS AND DISCUSSION

The target compounds **4a**–**4k** were synthesized by multiple step procedure as depicted in the *Scheme* 1. The synthesis of title compounds, started from condensation of (1*H*-benzo[*d*]imidazol-2-yl)methanamine (**1**) with ethyl 2-chloroacetate in the presence of anhydrous potassium carbonate to yield ethyl 2-[(1*H*-benzo[*d*]imidazol-2-yl)methylamino]acetate (**2**), the ester derivative **2** was taken for nucleophilic addition with hydrazine monohydrate in ethanol to afford 2-[(1*H*-benzo[*d*]imidazol-2-yl)methylamino]acetohydrazide (**3**). The hydrazide derivatives **3** when condensed with carboxylic acid derivatives yielded *N*-[(1*H*-benzo[*d*]imidazol-2-yl)methyl](5-substituted-1,3,4-oxadiazol-2-yl)methanamine (**4a–4j**) and when condensed with carbon disulphide and potassium hydroxide afforded 5-{[(1*H*-benzo[*d*]imidazol-2-yl)methylamino]methyl}-1,3,4-oxadiazole-2-thiol (**4k**).

Absence of the characteristic absorption peak corresponding to the carbonyl group stretching at 1650–1750 cm^{-1} in the IR spectrum of compound **4a** suggests the cyclization of the acetohydrazide into oxadiazole derivative. In the ^{1}H NMR spectra of compound **4a**, the methylene protons bridge between amino group and oxadiazole moiety has resonated at 3.3 ppm and this down field value can be attributed to electronegative nitrogen of the amino linkage and due to the oxadiazole moiety. Similarly the methylene protons bridge between benzimidazole moiety and amino group has resonated at 3.1 ppm. Furthermore, the ^{1}H NMR spectrum accounts for 15 protons out of which nine aromatic protons of benzimidazole and phenyl moiety appears at 7.5–6.7 ppm as multiplet. The oxadiazole ring formation is confirmed by the absence of hydrazide protons at 11.7 and 4.2 ppm. The ^{13}C NMR spectra of compound **4a** indicated that C2 and C5 carbons of oxadiazole moiety have resonated at 151 and 167 ppm, respectively, indicating the formation of the oxadiazole molecule. The mass spectra characterization of the compound **4a**, exhibits a molecular ion peak at 305 m/z confirming the formation of the oxadiazole derivative.

In the ^{1}H NMR spectrum of compound **4e**, the amino group protons at ortho position in the phenyl moiety at position 5 of the oxadiazole nucleus has resonated at 6.6 ppm. This down field value can be attributed to intramolecular hydrogen bonding between hydrogen of the amino group and electronegative oxygen of the oxadiazole moiety. The ^{13}C NMR spectra of compound **4e**, peak at 148 ppm accounts for the carbon, C2 substituted with amino group of the phenyl moiety. Moreover the mass spectra of the compound **4e**, confirms the formation of the derivative by the presence of molecular ion peak at 320 m/z, and a major ion peak at 174 m/z can be attributed to the oxadiazole fragment.

In the IR spectrum of compound **4k**, the absorption band corresponding to the carbonyl group stretching was shifted from 1718 to 1283 cm^{-1}, which can be attributed to the ring stretching of oxadiazole nucleus, and absorption band at 2587 cm^{-1} corresponding to mercapto group stretching confirms cyclization. In proton NMR spectra of the compound



***Scheme* 1.** Synthesis of title compounds.

4k, the mercapto proton has resonated at 13.2 ppm, which confirms the formation of the molecule.

CONCLUSION

A new class of benzimidazole encompassing oxadiazole derivatives were synthesized. Result of present study highlights the synthesis of oxadiazole derivatives and their characterization, which may be a possible hit as therapeutic agents. A further study to acquire information concerning the pharmacological activity is in progress.

Acknowledgments. We express our gratitude to the JSS College of Pharmacy, Mysore and JSS University for providing us all necessary facilities. We sincerely offer our gratitude to Chairman and Staff, NMR research Center, IISc, Bangalore for providing NMR and to the Chairman and staff, USIC, Karnataka University, Dharwad for providing mass spectra. And the publication cost of this paper was supported by the Korean Chemical Society.

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