



SYNTHESIS OF SOME BIOLOGICALLY POTENT NOVEL 5-(5-SUBSTITUTEDPHENYL)-4H-1,2,4-TRIAZOLE-3-YL-1,3-BENZOXAZOLES

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ABSTRACT

A series of some novel 5-(5-substitutedphenyl)-4H-1,2,4-triazole-3-yl-1,3-benzoxazoles 3a-o were synthesized from 2-substituted-5-carbomethoxy benzoxazole 1. 2-substituted-5-carbomethoxy benzoxazoles on reaction with hydrazine hydrate resulted in the formation of 2-substituted 1,3-benzoxazole-5-carbonhydrazides 2a-c. The subsequent treatment of compounds 2 with an appropriate aromatic aldehyde in presence of ammonium acetate leads to the synthesis of the target compounds in good yields. The chemical structures of the newly synthesized compounds were elucidated by their IR, ¹H NMR, ¹³C NMR and Mass spectral data analysis.

Key words: Benzoxazoles, Triazoles, Benzoxazolyl triazoles.

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INTRUDUCTION

Triazole, possess three nitrogens in five membered heterocyclic ring. Triazole is an important pharmacophore and shows various medicinal properties such as antimicrobial, antitubercular, anti-inflammatory, hypoglycemic, anticonvulsant and antidepressant activity¹. The triazole antifungal drugs include fluconazole, isavuconazole, itraconazole, viriconazole, posaconazole, and posaconazole. At high concentrations (micro molar) the triazoles are fungicidal and at low concentrations (nanomolar), they are fungistatic²⁻⁴. The Schiff's bases of triazoles show antibacterial as well as antifungal activity⁵. Triazolam is used as sedative and hypnotic⁶, and bittertanol is used as broad-spectrum fungicide⁷. Several methods were reported for the synthesis of triazoles and their derivatives⁸.

Benzoxazoles are used primarily in industry and being a heterocyclic compound, benzoxazole finds use in research as a starting material for the synthesis of larger, usually bioactive structures. It is found within the chemical structures of drugs such as flunoxapfen, and Zoxazolamine. Some novel benzoxazole derivatives were investigated for their inhibitory activity on both eukaryotic DNA topoisomerase in a cell free system⁹, antibacterial activity¹⁰ antitubercular activity¹¹, acts as 5-HT₃ receptor agonist for the treatment of diarrhoea predominant irritable bowel syndrome¹². However, several methods have been reported for the synthesis of various kinds of benzoxazole derivatives and their biological importance¹³. Hence, the synthesis and biological screening of benzoxazoles and triazoles attracted special attention. On the other hand, there is no report on the synthesis of 5-(5-substitutedphenyl)-4H-1,2,4-triazol-3-yl-1,3-benzoxazoles mentioned in the scheme of the present study. Despite their wide range of pharmacological, industrial and synthetic applications, synthesis of benzoxazolyl triazoles have received little attention. Keeping in view of the biological prominence of both benzoxazole and triazole moieties, it is planned to synthesize the new compounds as presented in scheme.

EXPERIMENTAL

General

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. The purity of the compounds was checked using precoated TLC plates (Merck, 60F-254). IR spectra were

obtained on a Perkin-Elmer FTIR 5000 spectrophotometer, using K Br pellets. NMR spectra were recorded on a Varian 300 MHz spectrometer for ^1H NMR and 100 MHz for ^{13}C NMR. The chemical shifts were reported as parts per millions (δ ppm) down field using TMS as an internal standard. Mass spectra were obtained on a VG micro mass 7070H spectrometer operating at 70 eV. All solvents and chemicals were purchased from Sigma Aldrich chemical company and used without further purification.

Synthesis of 2-substituted-1,3-benzoxazole-5-carbohydrazides (2a-c)

A mixture of 2-substituted-5-carbomethoxy benzoxazole **1** (0.01 mol) and hydrazine hydride (0.02 mol) in ethanol (15 ml) was refluxed for 4 h. The reaction mixture was cooled and the solvent was reduced to half of its volume. The product separated was filtered, washed with small portions of cold ethanol and water repeatedly and dried. The product was purified by recrystallization from suitable solvent. The synthesized compounds were confirmed by their IR, ^1H NMR, ^{13}C NMR, and Mass spectral data along with physical data.

Synthesis of 2-ethyl-5-substituted phenyl-4H-1,2,4-triazole-3-yl]-1,3-benzoxazoles(3a-o)

To a solution of 2-substituted-1,3-benzoxazole-5-carbohydrazide, **2** (0.01 mol) in ethanol (10 ml) was added a equimolar ratio of ammonium acetate followed by the addition of benzaldehyde and substituted benzaldehyde (0.01 mol) and the mixture was stirred for 24 h. The solution was then neutralized with liq. Ammonia solution and the product obtained was filtered, washed with water and recrystallized from ethanol.

1,3-Benzoxazol-5-carbohydrazide (2a)

Color: Orange solid. Yield: 87 %. M.p.98-99°C. IR (KBr) (ν) max: 3450, 3065, 3010, 1670, 1645, 1110, 890, 750 cm^{-1} . ^1H NMR (400MHz, CDCl_3): 5.64 (S, 2H), 7.40 (S, 1H), 7.60 (D, 1H), 7.72 (D, 1H), 8.35 (S, 1H), 8.81 (S, 1H). ^{13}C NMR (75MHz, CDCl_3): 111.3, 121.5, 124.7, 129.0, 142.0, 152.9, 154.1, 168.3. MS: m/z 177.2. Anal. Calcd. for $\text{C}_8\text{H}_7\text{N}_3\text{O}_2$: C, 54.24; H, 3.98; N, 23.72; O, 18.06. Found: C, 53.21; H, 2.99; N, 22.71; O 17.04%.

2-Methyl-1,3-benzoxazole-5-carbohydrazide (2b)

Color: Pale Brown solid. Yield: 80 %. M.p. 110-112°C .IR(KBr) (ν) max: 3460, 3070, 3020, 1675, 1640, 1115, 880, 755 cm^{-1} . ^1H NMR (400MHz, CDCl_3): 2.63 (S, 3H), 5.64, (S, 2H), 7.40 (S, 1H), 7.57 (D, 1H), 7.73 (D, 1H), 8.57 (S, 1H). ^{13}C NMR (75MHz, CDCl_3): 14.3, 111.3, 121.2, 124.7, 128.5, 141.6, 151.2, 166.7, 168.3. MS: m/z 191.2. Anal. Calcd. for $\text{C}_9\text{H}_9\text{N}_3\text{O}_2$: C, 56.54; H, 4.74; N, 21.98, O, 16.74. Found: C, 55.53; H, 3.78; N, 20.96; O. 15.78%.

2-Ethyl-1,3-benzoxazole-5-carbohydrazide(2c)

Color: Brown solid. Yield: 77 %. M.p.121-123°C. IR(KBr) (ν) max: 3455, 3060, 3013, 1674, 1642, 1117, 896, 752 cm^{-1} . ^1H NMR (400MHz, CDCl_3): 1.30 (D, 3H), 2.75 (Q, 2H), 5.62 (S, 2H), 7.40 (S, 1H), 7.62 (D, 1H), 7.70 (D, 1H), 8.43 (S, 1H). ^{13}C NMR (75MHz, CDCl_3): 11.0, 111.6, 121.0, 124.5, 128.6, 142.5, 168.3, 172.3. MS: m/z 205.0. Anal. Calcd. for $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_2$: C, 58.53; H, 5.40; N, 20.48, O, 15.59. Found: C, 57.52; H, 4.58; N, 19.68; O, 14.68%.

5-[(5-Phenyl)-4H-1,2,4-triazol-3-yl]-1,3-benzoxazole(3a)

Color: Pale yellow solid. Yield: 87 %. M.p.97-99°C. IR (KBr) (ν) max: 3452, 3048, 3022, 1668, 1637, 1109, 910, 775 cm^{-1} . ^1H NMR (400MHz, CDCl_3): 7.50 (M, 2H), 7.51 (S, 1H), 7.69 (S, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.49 (M., 2H), 8.82 (D, 1H), 9.88 (S, 1H). ^{13}C NMR (75 MHz, CDCl_3): 110.0, 122.7, 124.0, 124.7, 128.6, 128.7, 129.3, 131.3, 132.0, 145.5, 151.0, 154.1, 156.6, 159.3. MS: m/z 262.2. Anal. Calcd. for $\text{C}_{15}\text{H}_{10}\text{N}_4\text{O}$: C, 68.69; H, 3.84; N, 21.36, O, 6.10. Found: C, 67.75; H, 2.98; N, 20.58; O, 5.26%.

2-[5-(5-1,3-Benzoxazol-5-yl)-4H-1,2,4-triazole-3yl]phenylmethyl ether (3b)

Color: Yellow solid. Yield: 88 %. M.p. 80-82°C. IR (KBr) (ν) max: 3446, 3072, 3021, 1688, 1630, 1120, 884, 735 cm^{-1} . ^1H NMR (400MHz, CDCl_3): 3.87 (S, 3H), 6.87 (D, 1H), 7.30 (DD, 1H), 7.27 (DD, 1H), 7.69 (S, 1H), 8.83 (D, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.87 (S, 1H), 8.92 (S, 1H). ^{13}C NMR(75 MHz, CDCl_3): 55.2, 110.5, 116.1, 118.8, 122.7, 123.1, 123.9, 126.9, 127.4, 132.7, 145.5, 151.4, 154.2, 158.6, 159.8, 161.7. MS: m/z 292.2. Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_4\text{O}_2$: C, 65.75; H, 4.14; N, 19.17, O, 10.95. Found: C, 64.76; H, 3.58; N, 18.67; O, 9.58%.

5-[5-(4-Chlorophenyl)-4H-1,2,4-triazole-3-yl]-1,3-benzoxazole(3c)

Color: Pale brown solid. Yield: 85 %. M.p.85-87°C. IR (KBr) (ν) max: 3472, 3073, 3045, 1645, 1630, 1130, 975, 897, 746 cm⁻¹. ¹HNMR (400MHz, CDC1₃): 7.50 (D, 2H), 7.69 (S, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.51(D, 2H), 8.82 (S, 1H), 8.86 (S, 1H). ¹³CNMR (75MHz, CDC1₃): 110.3, 122.7, 124.3, 127.4, 128.3, 130.2, 131.4, 135.4, 145.5, 151.0, 151.4, 156.6, 159.3. MS: m/z 296.2. Anal. Calcd. for C₁₅H₉ClN₄O: C, 60.72; H, 3.06; Cl, 11.95, N, 18.88; O, 5.39, Found: C, 59.58; H, 2.56; Cl, 10.59, N, 17.67; O, 4.89%.

N-{3-[5-(1,3-Benzoxazol-5-yl)-4H-1,2,4-triazole-3yl]phenyl}-N,N-dimethylamine(3d)

Color: Yellow Brown solid. Yield: 87 %. M.p.112-114°C. IR(KBr) (ν) max: 3465, 3080, 3062, 1635, 1625, 1142, 973, 894, 735 cm⁻¹. ¹HNMR (400MHz, CDC1₃): 2.87 (S, 6H), 6.65 (M, 2H), 7.69 (S, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.82 (S, 1H), 8.87 (S, 1H), 8.92 (D, 2H). ¹³CNMR (75MHz, CDC1₃): 39.9, 110.5, 112.9, 122.7, 124.0, 124.7, 124.9, 130.8, 145.5, 151.0, 151.1, 151.4, 156.6, 159.3. MS: m/z 305.6. Anal. Calcd. for C₁₇H₁₅N₅O: C, 66.87; H, 4.95; N, 22.94; O, 5.24, Found: C, 65.56; H, 3.59; N, 21.49; O, 4.42%.

5-[5-(4-Nitrophenyl)-4H-1,2,4-triazole-3yl]-1,3-benzoxazole(3e)

Color: Yellow solid. Yield: 79 %. M.p.80-82 °C. IR (KBr) (ν) max: 3468, 3066, 3038, 1655, 1642, 1138, 973, 886, 748 cm⁻¹. ¹HNMR (400MHz, CDC1₃): 8.08 (D, 1H), 8.10 (D, 1H), 8.33 (D, 2H), 8.82 (S, 1H), 8.86 (S, 1H), 8.98 (D, 2H). ¹³CNMR(75MHz, CDC1₃): 110.5, 122.7, 124.0, 124.7, 125.8, 131.0, 134.8, 145.5, 147.8, 151.4, 154.1, 156.6, 159.7. MS: m/z 321.3. Anal. Calcd. for C₁₅H₉N₅O₃: C, 58.63; H, 2.95; N, 22.79; O, 15.62, Found: C, 57.36; H, 1.59; N, 21.97; O, 14.26%.

2-Methyl-{5-(5-phenyl)-4H-1,2,4-triazole-3-yl}-1,3-benzoxazole(3f)

Color: Red solid. Yield: 77 %. M.p.117-119°C. IR (KBr) (ν) max: 3350, 2930, 2233, 1605, 1505, 1460, 1275, 1030, 975, 897, 746 cm⁻¹. ¹HNMR (400MHz, CDC1₃): 2.60 (S, 3H), 7.50 (DD, 2H), 7.51 (DD, 1H), 7.69 (S, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.49 (D, 2H), 8.82 (S, 1H). ¹³CNMR (75MHz, CDC1₃): 14.3, 110.5, 122.7, 123.7, 124.7, 128.7, 129.7, 131.3, 132.3, 145.1, 150.1, 156.6, 159.3, 166.7. MS: m/z 276.3. Anal. Calcd. for C₁₆H₁₂N₄O: C, 69.55; H, 4.38; N, 20.28; O, 5.79, Found: C, 68.55; H, 3.83; N, 19.82; O, 4.97%.

5-[5-(2-Methoxyphenyl)-4H-1,2,4-triazole-3-yl]-2-methyl-1,3-benzoxazole(3g)

Color: Pale yellow solid. Yield: 88 %. M.p.92-94°C. IR(KBr) (ν) max: 3468, 3078, 3049, 1638, 1642, 1138, 980, 892, 748 cm⁻¹. ¹HNMR (400MHz, CDC1₃): 2.60 (S, 3H), 3.87 (S, 3H), 6.81 (D, 2H), 7.24 (DD, 2H), 8.08 (D, 1H), 8.10 (D, 1H), 8.77 (S, 1H), 8.80 (D, 1H), 8.90 (S, 1H). ¹³CNMR (75MHz, CDC1₃): 14.3, 55.2, 110.5, 118.5, 116.1, 122.7, 123.1, 123.7, 124.7, 126.9, 132.7, 145.1, 150.1, 156.6, 158.9, 159.3, 166.7. MS: m/z 306.3. Anal. Calcd. for C₁₇H₁₄N₄O₂: C, 66.66; H, 4.61; N, 18.29; O, 10.45, Found: C, 65.64; H, 3.16; N, 17.92; O, 9.54%.

5-[5-(4-Chlorophenyl)-4H-1,2,4-triazole-3-yl]-2-methyl-1,3-benzoxazole(3h)

Color: Yellow solid. Yield: 88 %. M.p.113-115 °C. IR (KBr) (ν) max: 3472, 3073, 3045, 1645, 1630, 1130, 975, 897, 746 cm⁻¹. ¹HNMR (400MHz, CDC1₃): 2.60 (S, 3H), 7.50 (D, 2H), 7.69 (S, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.51 (D, 2H), 8.77 (S, 1H). ¹³CNMR (75MHz, CDC1₃): 14.3, 110.5, 122.7, 123.7, 124/7, 128.3, 130.2, 131.4, 135.3, 145.1, 150.1, 156.6, 159.3, 166.7. MS: m/z 306.3. Anal. Calcd. for C₁₆H₁₁N₄O: C, 61.84; H, 3.57; Cl, 11.41 N, 18.03; O, 5.15, Found: C, 77.71; H, 5.27; Anal. Calcd. for C₁₆H₁₁ClN₄O: C, 61.84; H, 3.57; Cl, 11.41 N, 18.03; O, 5.15, Found: C, 60.46; H, 2.75; Cl, 10.14; N, 17.02; O, 4.51%.

5-[5-(4-N,N-Dimethylamine)-phenyl-4H-1,2,4-triazole-3-yl]-2-methyl-1,3-benzoxazole (3i)

Color: Brown solid. Yield: 83 %. M.p.99-101 °C. IR (KBr) (ν) max: 3477, 3084, 3032, 1648, 1632, 1144, 970, 893, 742 cm⁻¹. ¹HNMR (400MHz, CDC1₃): 2.60 (S, 3H), 2.85 (S, 6H), 6.65 (D, 2H), 7.69 (S, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.77 (S, 1H), 8.92 (D, 2H). ¹³CNMR (75MHz, CDC1₃): 14.3, 39.9, 110.5, 112.9, 122.7, 123.7, 124.7, 124.9, 130.8, 145.1, 150.1, 151.0, 156.6, 159.3, 166.7. MS: m/z 319.3. Anal. Calcd. for C₁₈H₁₇N₅O: C, 67.70; H, 5.37; N, 21.93; O, 5.01, Found: C, 66.68; H, 4.73; N, 20.39; O, 4.28%.

5-[5-(4-Nitrophenyl)-4H-1,2,4-triazole-3-yl]-2-methyl-1,3-benzoxazole(3j)

Color: Red solid. Yield: 77 %. M.p. 125-127 °C. IR (KBr) (ν) max: 3466, 3070, 3036, 1638, 1622, 1141, 968, 875, 766 cm⁻¹. ¹HNMR (400MHz, CDCl₃): 2.60 (S, 3H), 7.69 (S, 1H), 8.08 (D, 1H), 8.10 (D, 1H), 8.33 (D, 2H), 8.77 (S, 1H), 8.98 (D, 2H). ¹³CNMR (75MHz, CDCl₃): 14.3, 110.5, 122.7, 123.7, 124.7, 125.8, 131.0, 134.8, 145.1, 147.8, 150.1, 156.6, 159.3, 166.7. MS: m/z 321.8. Anal. Calcd. for C₁₆H₁₁N₃O₃: C, 59.81; H, 3.45; N, 21.80; O, 14.94. Found: C, 58.18; H, 2.78; N, 20.47; O, 13.49%.

2-Ethyl-5-phenyl-4H-1,2,4-triazole-3-yl-1,3-benzoxazole(3k)

Color: Orange solid. Yield: 79 %. M.p. 144-146°C. IR (KBr) (ν) max: 3468, 3077, 3038, 1668, 1656, 1145, 968, 889, 738 cm⁻¹. ¹HNMR (400MHz, CDCl₃): 1.30 (T, 3H), 2.75 (Q, 2H), 7.50 (DD, 2H), 7.51 (m, 1H), 7.69 (S, 1H), 7.98 (D, 1H), 8.25 (D, 1H), 8.45 (S, 1H), 8.49 (DD, 2H). ¹³CNMR(75MHz, CDCl₃): 11.0, 18.3, 110.4, 122.5, 128.7, 129.4, 131.3, 132.0, 132.4, 124.5, 146.4, 150.2, 156.7, 159.3, 172.5. MS: m/z 290.3. Anal. Calcd. for C₁₇H₁₄N₄O: C, 70.33; H, 4.86; N, 19.30; O, 5.51. Found: C, 69.67; H, 3.85; N, 18.86; O, 4.59%.

2-Ethyl-5-[5-(2-methoxyphenyl)-4H-1,2,4-triazole-3-yl]-1,3-benzoxazole(3l)

Color: Yellow solid. Yield: 83 %. M.p.84-86 °C. IR (KBr) (ν) max: 3470, 3066, 3044, 1662, 1641, 1156, 968, 878, 765 cm⁻¹. ¹HNMR (400MHz, CDCl₃): 1.30 (T, 3H), 2.75 (Q, 2H), 3.87 (S, 3H), 6.87 (D, 1H), 7.27 (DD, 1H), 7.30 (DD, 1H), 7.69, (S, 1H), 7.98 (D, 1H), 8.25 (D, 1H), 8.45 (S, 1H), 8.83 (D, 1H). ¹³CNMR (75MHz, CDCl₃): 11.0, 18.3, 55.2, 110.4, 116.2, 118.8, 122.5, 123.2, 124.5, 132.4, 132.8, 136.1, 146.4, 150.2, 156.7, 158.6, 159.3, 172.5. MS: m/z 320.4. Anal. Calcd. for C₁₈H₁₆N₄O₂: C, 67.49; H, 5.03; N, 17.49; O, 9.99. Found: C, 66.48; H, 4.72; N, 16.67, O, 8.76%.

2-Ethyl-5-[5-(4-chlorophenyl)-4H-1,2,4-triazole-3-yl]-1,3-benzoxazole(3m)

Color: Red solid. Yield: 84 %. M.p.81-83 °C. IR (KBr) (ν) max: 3487, 3076, 3038, 1665, 1644, 1145, 988, 887, 766 cm⁻¹. ¹HNMR (400MHz, CDCl₃): 1.30 (T, 3H), 2.75 (Q, 2H), 7.50 (D, 2H), 7.69 (S, 1H), 7.98 (D, 1H), 8.25 (D, 1H), 8.45 (S, 1H), 8.51(D, 2H). ¹³CNMR (75MHz, CDCl₃): 11.0, 18.3, 110.4, 122.5, 124.5, 128.3, 130.2, 131.4, 130.2, 132.4, 135.3, 146.4, 150.2, 156.7, 159.3, 172.5. MS: m/z 324.3. Anal. Calcd. for C₁₇H₁₃ClN₄O: C, 62.87; H, 4.03; Cl, 10.92; N, 17.25; O, 4.93. Found: C, 61.78; H, 3.28; Cl, 9.29; N, 16.52; O, 3.39%.

2-Ethyl-5-[5-(4-N,N-dimethylaminophenyl)-4H-1,2,4-triazole-3-yl]-1,3-benzoxazole (3n)

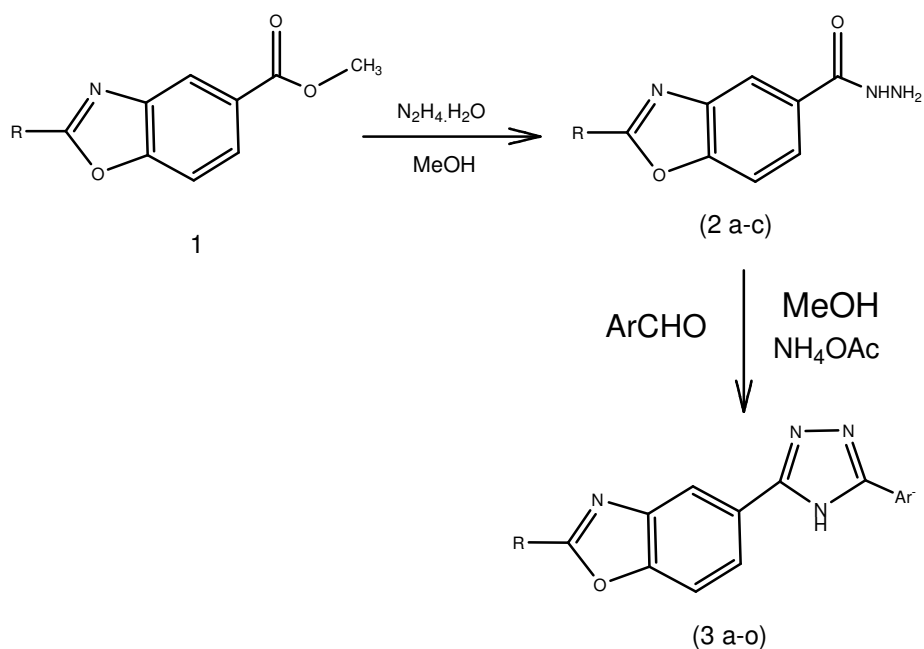
Color: Brown solid. Yield: 82 %. M.p.121-123 °C. IR (KBr) (ν) max: 3466, 3072, 3065, 1655, 1642, 1136, 978, 892, 766 cm⁻¹. ¹HNMR (400MHz, CDCl₃): 1.30 (T, 3H), 2.75 (Q, 2H), 2.85 (S, 6H), 6.65 (D, 2H), 7.69 (S, 1H), 7.98 (D, 1H), 8.25 (D, 1H), 8.45 (S, 1H), 8.92 (D, 2H). ¹³CNMR (75MHz, CDCl₃): 11.0, 18.3, 39.3, 110.4, 112.9, 122.5, 124.9, 130.8, 132.4, 124.5, 146.4, 150.2, 151.0, 156.7, 159.3, 172.5. MS: m/z 333.4. Anal. Calcd. for C₁₉H₁₉N₅O: C, 68.45; H, 5.74; N, 21.01; O, 4.80. Found: C, 67.54; H, 4.68; N, 20.28; O, 3.67%.

2-Ethyl-5-[5-(4-nitrophenyl)-4H-1,2,4-triazole-3-yl]-1,3-benzoxazole(3o)

Color: Yellow solid. Yield: 79 %. M.p .95-97°C. IR (KBr) (ν) max: 3466, 3081, 3065, 1643, 1632, 1142, 969, 887, 742 cm⁻¹. ¹HNMR (400MHz, CDCl₃): 1.30 (T, 3H), 2.75 (Q, 2H), 7.69 (S, 1H), 7.98 (D, 1H), 8.25 (D, 1H), 8.33 (D, 2H), 8.45 (S, 1H), 8.98 (D, 2H). ¹³CNMR (75MHz, CDCl₃): 11.0, 18.3, 110.4, 122.5, 124.5, 125.8, 131.0, 132.4, 134.8, 146.4, 147.8, 150.2, 156.7, 159.3, 172.5. MS: m/z 335.8. Anal. Calcd. for C₁₇H₁₃N₅O₃: C, 60.89; H, 3.91; N, 20.89; O, 14.31. Found: C, 59.98; H, 2.89; N,19.98; O, 13.46%.

RESULTS AND DISCUSSION

For the synthesis of the target compounds (3a-o), a solution of 2-substituted-5-carbomethoxy benzoxazole **1** and hydrazine hydride in ethanol was refluxed for 4 h. To a solution of 2-substituted-1,3-benzoxazole-5-carbohydrazide **2** in ethanol was added ammonium acetate followed by the addition of benzaldehyde and substituted benzaldehyde and the mixture was stirred for 24h. In all cases the reaction mixture was worked-up in the usual manner. The products were purified by column chromatography and characterized by their IR, ¹H NMR, ¹³C NMR and Mass spectral data. In conclusion, the operational simplicity of this cost-benefit method makes it attractive for preparative applications as well as for the synthesis of screening libraries for drug discovery.



Scheme-1

2. R = (a)-H, (b)-CH₃, (c)-C₂H₅

3. R = (a)-H, Ar = (a)-C₆H₅, (b)-2-MeO-C₆H₄, (c)-4-Cl-C₆H₄, (d)-N,N-dimethylamino-C₆H₄, (e)-4-NO₂-C₆H₄, (b)-CH₃, Ar = (f)-C₆H₅, (g)-2-MeO-C₆H₄, (h)-4-Cl-C₆H₄, (i)-4-N,N-dimethylamino-C₆H₄, (j)-4-NO₂-C₆H₄, (c)-C₂H₅, Ar = (k)-C₆H₅, (l)-2-MeO-C₆H₄, (m)-4-Cl-C₆H₄, (n)-4-N,N-dimethylamino-C₆H₄, (o)-4-NO₂-C₆H₄.

REFERENCES

1. A.R. Karritzky, *Hand Book of Het. Chem*, 1st edn., Pergamon Press, Oxford, 87, (1985).
2. J.A. Joule, K. Mills, *Heterocyclic Chem*, 4th Edn, Blackwell Science Ltd, 1-14 (1995).
3. W.O. Foye, *Principles of Medicinal Chemistry*, 4th Edn, B. J. Waverly Pvt. Ltd., New Delhi, 1-7, (1996)
4. Z.N. Delgado, A. Remers, Williams, Wilson & Gisvold's, *Text Book of Organic, Med. and Pharma. Chem*, 10th edn., Zippincott Raven Publishers, Philadelphia, 189, (1998).
5. (a) G.K. Rao, S. Rajasekran, M. Attimarad, *Indian J. Pharm. Sci*, 475, (2000); (b) K.D. Patel, B.D. Mistry, K.R. Desai, *J. Indian Chem. Soc*, **79**, 964 (2000); (c) N.F. Eweiss, A.A. Bahajaj, E.A. Elsherbimi, *J. Heterocyclic Chem*, **23**, 1451 (1986); (d) R.H. Udipi, A. Kushnoor, A.R. Bhatt, *J. Indian Chem, Soc*, **76**, 461 (1999).
6. J.N. Delgado, W.A. Remers, *Text Book of Org. Med. Pharma. Chem*, 10th Edn., J. B. Lippincott Company, Philadelphia, 189 (1998).
7. The Merck Index, 'An Encyclopedia of chemicals, drugs and. biological', 12th Edn, Merck & Co, Inc. 1634 (1996).
8. (a) Z.Y. Yan, Y-B. Zhao, M-J Fan, W-M. Liu, Y-M. Liang, *Tetrahedron*, **61**, 9331 (2005); (b) D. Amantini, F. Fringuelli, O. Piermatti, F. Pizzo, E. Zunino, L. Vaccaro, *J. Org. Chem*, **70**, 652 (2005); (c) J. Barluenga, C. Valdes, G. Beltran, M. Escribano, F. Aznar, *Angew. Chem. Int. Ed*, **45**, 6893 (2006); (d) V.O. Rodionov, S.I. Presolski, S. Gardinier, Y-H. Lim, M.G. Finn, *J. Am. Chem. Soc*, **129**, 12696 (2007); (e) D. Luvino, C. Amalric, M. Smietana, J-J. Vasseur, *Synlett*, 3037 (2007); (f) I.S. Park, M.S. Kwon, Y. Kim, J.S. Lee, L. Park, *J. Org. Lett*, **10**, 497, (2008); (g) T. Miaoa, L. Wang, *Synthesis*, 363 (2008).
9. E. Oksuzoglu, B. Tekiner-Gulbas, S. Alper, O. Temiz-Arpaci, T. Ertan, I. Yildiz, N. Diri, E. Sener-Aki, I. Yalcin, *J. Enzyme Inhibition and Med Chem*, **23**, 37 (2008).
10. V. Jarmila, H. Vaclav, B. Vladimír, K. Jarmila, *Molecules*, **10**, 783 (2005).

11. V. Klimesova, J. Koci, K. Waisser, J. Kaustova, U. Mollmann, *Eur. J. Med. Chem*, **44**, 2286 (2009).
12. S. Yoshida, S. Shiokawa, K. Kawano, T. Ito, H. Murakami, H. Suzuki, Y. Sato, *J. Med.Chem*, **48**, 7075,(2005).
13. (a) V.I. Kelarev, V.N. Koshelev, *Chem. Heterocyclic Compd*, **32**, 762 (1996);(b) G. Evindar, R.A. Batey, *J. Org. Chem*, **71**,1802, (2006); (c) D.V. Russell, E. Ghotas, B. Robert, *J. Org. Chem*, **73**, 3452 (2008);(d) S. Hekmat, H.S. Rahim, H. Maryam, F. Maryam, M. Reihaneh, *Synth. Comm*, **39**,1742 (2009); (e) G.W. Stewart, C.A. Baxter, E. Cleator, F.J. Sheen, *J. Org. Chem*, **17**, 3229 (2009);(f) H.R.J. Yajnanarayana, H.W. Gibson, *J. Heterocyclic Chem*, **29**,1365 (2009); (g) A.J. Blacker, M.M. Farah, M.I. Hall, S.P. Marsden, O. Saidi, J.M. Williams, *J. Org.Lett*, **11**, 2039 (2009).
14. B.Gopala Krishna, N.Raghunandhan,J.V. Rao, M. Sarangapani, *Indian Drugs*, **42**, 369 (2005).

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