A new class of multi-substituted oxazole derivatives: Synthesis and antimicrobial activity

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Abstract. A new and efficient method for the synthesis of multi-substituted oxazole derivatives from various aldehydes has been described. Twenty novel multi-substituted oxazoles containing a heterocyclic moiety were synthesized and evaluated for their antimicrobial activity. The prepared compounds are all reported for the first time and their structures were established by elemental analysis, IR, ¹H-NMR, and ¹³C-NMR and Mass spectra. All the synthesized compounds exhibited *in vitro* antimicrobial activity.

Keywords. Oxazoles; antimicrobial activity.

1. Introduction

Oxazoles are a common structural motif found in numerous molecules that display antiviral, antifungal, antibacterial, and antiproliferative activities.^{1,2} In particular, many efforts have been focused for synthesis of substituted oxazoles, due to their existence in substructures of many pharmaceuticals.^{3–5} The most common methods for the preparation of substituted oxazoles include Negishi cross-coupling,⁶ Ritter reactions of α -oxo tosylates,⁷ one-pot Van Leusen synthesis of 4,5-disubstituted oxazoles in ionic liquids,⁸ Nickel-catalysed synthesis of oxazoles,⁹ transformation of 4-bis(methylthio)methylene-2-phenyloxazol-5-one,¹⁰ one-pot Friedel–Crafts/Robinson–Gabriel synthesis of oxazoles,¹¹ reaction of β -(acyloxy)vinyl azides with (EtO)₃P,¹² reaction of benzoin carboxylates with formamide,¹³ and decarboxylation of *N*-acylisoxazol-5-ones by means of photolysis or pyrolysis.^{14,15} Direct conversion of ketones to the corresponding oxazoles has received little attention and there are only few studies published. For example, 2-alkyl-5-aryloxazoles were prepared by the direct reactions of aromatic methyl ketones and nitriles with Ti(OAc)₃¹⁶ or iodobenzene diacetate¹⁷ in the presence of trifluoromethanesulphonic acid (TfOH). Furthermore, very recently, an expedient method for the direct conversion of aldehydes to substituted oxazoles was presented,^{18,19}

but products were only disubstituted oxazoles. However, these methods have been applied only for few aromatic aldehydes, which limit their practical applications. We therefore, developed a new and efficient method for the synthesis of multi-substituted oxazoles at room temperature.

2. Experimental

All melting points were determined in open capillary tubes on Mel-Temp apparatus (Laboratory Devices, Cambridge, MA), and are uncorrected. IR spectra were recorded as KBr pellets on a Perkin-Elmer 283 double beam spectrophotometer in cm⁻¹. ¹H and ¹³C NMR spectra were recorded on Mercury-400 spectrophotometer operating at 400 MHz for ¹H, and 100 MHz for ¹³C using DMSO-d₆ and CDCl₃ as solvent; chemical shifts were referenced to TMS. All compounds were characterized by the above techniques.

2.1 Preparation of compound 2-benzo[d][1,3]dioxol-5-yl)-2-(tert-butyl dimethylsilyloxy)acetonitrile (2)

A solution of benzo[d][1,3]dioxole-5-carbaldehyde (**1**; 25 g, 166 mmol) in MeCN was added drop-wise to a stirring mixture of KCN (43.3 g, 666 mmol), TBSCl (25 g, 166 mmol) and ZnI₂ (0.8 g, 1.7 mmol) at room temperature and the mixture was stirred at this temperature for overnight. The mixture was diluted with H₂O

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and extracted with EtOAc (3 × 50 mL). The organic extract was washed with brine and dried over anhydrous Na₂SO₄. The solvent was removed *in vacuo* and the residue was purified by silica gel (100–200 mesh) column chromatography (CC) using EtOAc-petroleum ether (5:1) as eluent affording **2** as pale brown liquid in 85% yield. IR (KBr, cm⁻¹): 3184, 2812, 2157, 1975, 1254. ¹H NMR (CDCl₃, 400 MHz) δ: 0.24 (6H, s), 0.98 (9H, s), 5.42 (1H, s), 6.02 (2H, s), 6.86 (1H, d, *J* = 6.4 Hz), 7.03 (1H, d, *J* = 5.6 Hz), 7.27 (1H, s). ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 25.94 (CH₃), 30.54 (C), 69.25 (CH), 102.32 (CH₂), 112.74 (CH), 114.58 (CH), 119.53 (CN), 1223.17 (CH), 128.69 (C), 148.75 (C), 148.93 (C). MS (ESI, *m/z*): 292.5 [M⁺+1]. Anal. Calcd for C₁₅H₂₁NO₃Si (291.42): C, 61.84; H, 7.27; N, 4.85. Found: C, 61.82; H, 7.26; N, 4.83.

2.2 General procedure for synthesis of compounds (3a–t)

n-BuLi (1.6 M in hexane, 1.1 eq.) was added dropwise to a solution of DPA (1.1 eq.) in THF at –78°C under an inert atmosphere, the pale yellow solution was warmed to 0°C and stirred at this temperature for 30 min. The LDA solution thus prepared was again cooled to –78°C and a solution of compound **2** in THF was added dropwise over a period of 1.5 h under an inert atmosphere. The resulting mixture was stirred at –78°C temperature for 30 min, and then solution of the respective aldehydes (0.8 eq.) in THF was added at –78°C. The mixture was stirred at same temperature for 8–12 h under an inert atmosphere. The reaction was quenched by addition of ice-cold H₂O and extracted with EtOAc. The organic extract was washed with brine and dried over anhydrous Na₂SO₄, prior to concentration under reduced pressure. The residue was purified by CC over silica gel (60–120 mesh) adsorbent, using EtOAc–petroleum ether to get compound **3**.

2.2a 1-Benzo[d][1,3]dioxol-5-yl)-2-(*tert*butyldimethylsilyloxy)-2-(furan-3-yl)ethanone (**3a**): Yield: 85%, mp: 155–157°C. IR (KBr, cm⁻¹): 3433, 3141, 2262, 1724, 1254. ¹H NMR (CDCl₃) δ: 0.26 (6H, s), 0.96 (9H, s), 4.92 (1H, s), 6.03 (1H, s), 6.11 (2H, s), 6.58 (1H, d, *J* = 19.6 Hz), 7.16 (1H, d, *J* = 3.6 Hz), 7.27 (1H, d, *J* = 12 Hz), 7.46 (1H, d, *J* = 6.4 Hz), 7.59 (1H, s), 7.78 (1H, s). ¹³C NMR (CDCl₃) δ: –2.83 (CH₃), 26.02 (CH₃), 31.55 (C), 87.66 (CH), 101.02 (CH₂), 108.74 (CH), 110.41 (CH), 112.74 (CH), 121.14 (C), 123.79 (CH), 143.75 (CH), 148.43 (C), 153.37 (C), 194.63 (C=O). MS (ESI, *m/z*): 361.2 [M⁺+1]. Anal.

calcd for C₁₉H₂₄O₅Si (360.44): C 63.29, H 6.67; found C 63.32, H 6.74.

2.2b 1-Benzo[d][1,3]dioxol-5-yl)-2-(*tert*butyldimethylsilyloxy)-2-(furan-2-yl)ethanone (**3b**): Yield: 82%, mp: 147–148°C. IR (KBr, cm⁻¹): 3421, 3044, 2243, 1712, 1215. ¹H NMR (CDCl₃) δ: 0.26 (6H, s), 0.98 (9H, s), 4.86 (1H, s), 6.03 (2H, s), 6.83 (1H, d, *J* = 5.6 Hz), 7.05 (1H, d, *J* = 2.8 Hz), 7.35 (1H, t, *J* = 16.4 Hz), 7.56 (1H, d, *J* = 12.6 Hz), 7.78 (1H, d, *J* = 10.8 Hz). ¹³C NMR (CDCl₃) δ: –2.63 (CH₃), 25.91 (CH₃), 39.55 (C), 89.68 (CH), 102.32 (CH₂), 108.74 (CH), 111.41 (CH), 125.17 (CH), 126.69 (C), 148.75 (C), 153.97 (C), 196.66 (C=O). MS (ESI, *m/z*): 361.04 [M⁺+1]. Anal. Calcd for: C₂₁H₃₂O₅Si (360.54): C 66.89, H 8.57; found C 66.82, H 8.62.

2.2c 1-Benzo[d][1,3]dioxol-5-yl)-2-(*tert*butyldimethylsilyloxy)-2-(thiophen-2-yl)ethanone (**3c**): Yield: 88%, Semi solid. IR (KBr, cm⁻¹): 3341, 3120, 2255, 1755, 1288. ¹H NMR (CDCl₃) δ: 0.24 (6H, s), 0.99 (9H, s), 4.75 (1H, s), 6.03 (2H, s), 6.82 (1H, d, *J* = 5.6 Hz), 7.18 (1H, d, *J* = 3.2 Hz), 7.43 (1H, t, *J* = 3.2, 5.6 Hz), 7.52 (1H, s), 7.74 (1H, d, *J* = 8.0 Hz), 7.86 (1H, d, *J* = 12.4 Hz). ¹³C NMR (CDCl₃) δ: –2.81 (CH₃), 25.97 (CH₃), 26.01 (CH₂), 39.54 (C), 89.67 (CH), 102.34 (CH₂), 108.73 (CH), 111.42 (CH), 125.17 (CH), 126.64 (C), 148.71 (C), 153.93 (C), 196.55 (C=O). MS (ESI, *m/z*): 377.1 [M⁺+1]. Anal. calcd for C₁₉H₂₄O₄SSi (376.54): C 60.69, H 6.47, S 8.52; found C 60.82, H 6.45, S 8.55.

2.2d 1-Benzo[d][1,3]dioxol-5-yl)-2-(*tert*butyldimethylsilyloxy)-2-(pyridin-4-yl)-ethanone (**3d**): Yield: 87%, mp: 171–172°C. IR (KBr, cm⁻¹): 3427, 3014, 2214, 1711, 1657. ¹H NMR (CDCl₃) δ: 0.27 (6H, s), 0.97 (9H, s), 4.95 (1H, s), 6.07 (2H, s), 7.13 (1H, d, *J* = 8.0 Hz), 7.46 (1H, s), 7.49 (1H, d, *J* = 4.8 Hz), 7.65 (2H, d, *J* = 8.8 Hz), 8.52 (2H, d, *J* = 6.4 Hz). ¹³C NMR (CDCl₃) δ: –2.46 (CH₃), 25.91 (3CH₃), 30.19 (C), 91.54 (CH), 102.38 (CH₂), 109.72 (CH), 111.99 (CH), 124.55 (CH), 125.22 (CH), 148.75 (C), 149.99 (CH), 150.35 (CH), 153.91 (C), 195.84 (C=O). MS (ESI, *m/z*): 372.2 [M⁺+1]. Anal. calcd for C₂₀H₂₅NO₄Si (371.50): C 64.69, H 6.77, N 3.76; found C 64.62, H 6.75, N 3.79.

2.2e 1-Benzo[d][1,3]dioxol-5-yl)-2-(*tert*butyldimethylsilyloxy)-2-cyclohexyl-ethanone (**3e**): Yield: 82%, IR (KBr, cm⁻¹): 3335, 3010, 2231, 1700, 1612, 1125, 943. ¹H NMR (CDCl₃) δ: 0.23 (6H, s, CH₃), 0.98 (9H, s), 1.28–1.36 (4H, q), 1.46 (4H, q), 1.98 (2H, q), 2.54 (1H,

q), 4.35 (1H, d, $J = 8.4$ Hz), 6.03 (2H, s), 6.83 (1H, d, $J = 6.4$ Hz), 7.59 (1H, s), 7.78 (1H, d, $J = 6.8$ Hz). ^{13}C NMR (CDCl_3) δ : -2.38 (CH_3), 25.82 (2CH_2), 25.91 (CH_3), 26.07 (CH_2), 27.13 (2CH_2), 39.55 (C), 89.68 (CH), 102.32 (CH_2), 108.74 (CH), 111.41 (CH), 125.17 (CH), 126.69 (C), 148.75 (C), 153.97 (C), 196.66 ($\text{C}=\text{O}$). MS (ESI, m/z): 377.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{21}\text{H}_{32}\text{O}_3\text{Si}$ (376.54): C 66.89, H 8.57; found C 66.82, H 8.62.

2.2f *1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-phenylethanone (3f)*: Yield: 87%, mp: 122–124°C. IR (KBr, cm^{-1}): 3387, 3074, 2235, 1714, 1624. ^1H NMR (CDCl_3) δ : 0.22 (6H, s), 0.99 (9H, s), 5.96 (1H, s), 6.07 (2H, s), 7.09 (1H, s), 7.13 (1H, d, $J = 6.0$ Hz), 7.49 (1H, d, $J = 8.4$ Hz). ^{13}C NMR (CDCl_3) δ : -2.86 (CH_3), 25.94 (3CH_3), 30.25 (C), 90.55 (CH), 103.55 (CH_2), 109.77 (CH), 111.06 (CH), 127.08 (CH), 129.29 (2CH), 129.88 (2CH), 132.43 (C), 148.75 (C), 151.33 (CH), 153.94 (C), 196.83 ($\text{C}=\text{O}$). MS (ESI, m/z): 371.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{21}\text{H}_{26}\text{NO}_4\text{Si}$ (370.21): C 68.09, H 7.07; found C 68.02, H 7.15.

2.2g *1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(3-nitrophenyl)ethanone (3g)*: Yield: 80%, mp: 110–112°C. IR (KBr, cm^{-1}): 3342, 3032, 2247, 1715, 1601, 1542, 1367, 1208. ^1H NMR (CDCl_3) δ : 0.23 (6H, s), 0.97 (9H, s), 5.97 (1H, s), 6.07 (2H, s), 7.02 (1H, s), 7.13 (1H, d, $J = 4.0$ Hz), 7.29 (1H, d, $J = 8.0$ Hz), 7.42 (1H, t, $J = 8.4, 4.6$ Hz), 7.49 (1H, d, $J = 4.8$ Hz), 7.64 (1H, d, $J = 8.8$ Hz), 7.86 (1H, d, $J = 12.0$ Hz). ^{13}C NMR (CDCl_3) δ : -2.45 (CH_3), 25.86 (3CH_3), 30.22 (C), 90.57 (CH), 103.54 (CH_2), 109.77 (CH), 111.07 (CH), 127.05 (CH), 129.55 (2CH), 129.84 (CH), 132.47 (C), 143.44 (CH), 148.77 (C), 151.35 (C), 153.86 (C), 196.94 ($\text{C}=\text{O}$). MS (ESI, m/z): 416.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_6\text{Si}$ (415.16): C 60.74, H 6.07, N 3.35; found C 60.02, H 6.12, N 3.41.

2.2h *1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(2-nitrophenyl)ethanone (3h)*: Yield: 75%, IR (KBr, cm^{-1}): 3322, 3030, 2237, 1710, 1611, 1548, 1362, 1214. ^1H NMR (CDCl_3) δ : 0.22 (6H, s), 0.98 (9H, s), 5.96 (1H, s), 6.07 (2H, s), 7.12 (1H, s), 7.21 (1H, d, $J = 8.0$ Hz), 7.34 (1H, d, $J = 4.8$ Hz), 7.45 (1H, t, $J = 8.8, 8.0$ Hz), 7.56 (1H, d, $J = 6.4$ Hz), 7.69 (1H, d, $J = 8.0$ Hz), 7.82 (1H, d, $J = 6.8$ Hz). ^{13}C NMR (CDCl_3) δ : -2.54 (CH_3), 25.87 (3CH_3), 30.23 (C), 90.56 (CH), 103.57 (CH_2), 109.72 (CH), 111.17 (CH), 127.10 (CH), 129.54 (2CH), 129.78

(CH), 132.56 (C), 143.58 (CH), 148.77 (C), 151.15 (C), 153.42 (C), 196.87 ($\text{C}=\text{O}$). MS (ESI, m/z): 416.5 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_6\text{Si}$ (415.16): C 60.74, H 6.07, N 3.35; found C 60.06, H 6.11, N 3.42.

2.2i *1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(m-tolyl)ethanone (3i)*: Yield: 87%, mp 197–199°C. IR (KBr, cm^{-1}): 3341, 3124, 2252, 1713, 1602, 1214, 987. ^1H NMR (CDCl_3) δ : 0.20 (6H, s), 0.99 (9H, s), 3.45 (3H, s), 5.97 (1H, s), 6.07 (2H, s), 7.08 (1H, s), 7.16 (1H, d, $J = 8.8$ Hz), 7.23 (1H, d, $J = 6.4$ Hz), 7.48 (1H, t, $J = 8.0$ Hz), 7.62 (1H, d, $J = 4.8$ Hz), 7.73 (1H, d, $J = 2.8$ Hz), 7.84 (1H, d, $J = 4.8$ Hz). ^{13}C NMR (CDCl_3) δ : -2.47 (CH_3), 25.89 (3CH_3), 26.35 (CH_3), 30.24 (C), 89.43 (CH), 102.43 (CH_2), 108.99 (CH), 110.14 (CH), 126.97 (CH), 129.53 (2CH), 129.98 (CH), 133.05 (C), 144.11 (CH), 148.27 (C), 151.41 (C), 153.43 (C), 196.88 ($\text{C}=\text{O}$). MS (ESI, m/z): 385.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{22}\text{H}_{28}\text{O}_4\text{Si}$ (384.18): C 68.71, H 7.32; found C 68.72, H 7.24.

2.2j *1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(3-bromophenyl)ethanone (3j)*: Yield: 89%, mp: 210–212°C. IR (KBr, cm^{-1}): 3347, 3138, 2242, 1712, 1597, 1213, 867. ^1H NMR (CDCl_3) δ : 0.25 (6H, s), 0.99 (9H, s), 5.97 (1H, s), 6.07 (2H, s), 7.11 (1H, s), 7.19 (1H, d, $J = 8.8$ Hz), 7.32 (1H, d, $J = 6.4$ Hz), 7.46 (1H, t, $J = 8.8, 7.6$ Hz), 7.54 (1H, d, $J = 4.4$ Hz), 7.63 (1H, d, $J = 8.8$ Hz), 7.79 (1H, d, $J = 8.4$ Hz). ^{13}C NMR (CDCl_3) δ : -2.54 (CH_3), 25.85 (3CH_3), 29.95 (C), 90.44 (CH), 103.77 (CH_2), 109.64 (CH), 110.97 (CH), 127.15 (CH), 129.35 (2CH), 129.74 (CH), 132.81 (C), 143.41 (CH), 148.13 (C), 151.34 (C), 153.87 (C), 196.97 ($\text{C}=\text{O}$). MS (ESI, m/z): 450.0 [$\text{M}^+ + 1$], 451.2 [$\text{M}^+ + 2$]. Anal. calcd for $\text{C}_{21}\text{H}_{25}\text{BrO}_4\text{Si}$ (449.04): C 56.14, H 5.67; found C 56.07, H 5.12.

2.2k *1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(3-chlorophenyl)ethanone (3k)*: Yield: 85%, mp: 118–122°C. IR (KBr, cm^{-1}): 3338, 3122, 2257, 1710, 1601, 1214, 989. ^1H NMR ($\text{DMSO}-d_6$) δ : 0.24 (6H, s), 1.05 (9H, s), 5.99 (1H, s), 6.05 (2H, s), 7.10 (1H, s), 7.14 (1H, d, $J = 2.8$ Hz), 7.38 (1H, d, $J = 6.0$ Hz), 7.49 (1H, t, $J = 19.6$ Hz), 7.53 (1H, d, $J = 8.4$ Hz), 7.67 (1H, d, $J = 4.8$ Hz), 7.82 (1H, d, $J = 8.8$ Hz). ^{13}C NMR ($\text{DMSO}-d_6$) δ : -2.64 (CH_3), 25.99 (3CH_3), 29.84 (C), 90.64 (CH), 103.33 (CH_2), 108.69 (CH), 110.92 (CH), 127.14 (CH), 129.54 (2CH), 129.73 (CH), 132.82 (C), 143.47 (CH), 148.23 (C), 151.42 (C), 153.72 (C), 197.01 ($\text{C}=\text{O}$). MS (ESI, m/z): 404.9 [M^+], 405.2 [$\text{M}^+ + 1$]; Anal. calcd for

$C_{21}H_{25}ClO_4Si$ (404.92): C 62.28, H 6.24, Cl 8.73; found C 62.27, H 6.28, Cl 8.73.

2.2l *1-Benzo[d][1,3]dioxol-5-yl*-2-(*tert*butyldimethylsilyloxy)-2-(3-hydroxyphenyl)ethanone (**3l**): Yield: 84%, mp: 174–175°C. IR (KBr, cm^{-1}): 3546, 3342, 3165, 2240, 1707, 1589, 1235. 1H NMR ($CDCl_3$) δ : 0.23 (6H, s), 0.99 (9H, s), 5.97 (1H, s), 6.07 (2H, s), 7.12 (1H, s), 7.25 (1H, d, $J = 6.4$ Hz), 7.37 (1H, d, $J = 6.8$ Hz), 7.46 (1H, t, $J = 4.8$ Hz), 7.58 (1H, d, $J = 7.6$ Hz), 7.74 (1H, d, $J = 8.8$ Hz), 7.88 (1H, d, $J = 8.8$ Hz), 10.54 (1H, s) ppm. ^{13}C NMR ($CDCl_3$) δ : -2.45 (CH_3), 25.89 ($3CH_3$), 30.88 (C), 90.45 (CH), 103.53 (CH_2), 109.77 (CH), 111.03 (CH), 127.18 (CH), 129.54 (2CH), 129.77 (CH), 132.59 (C), 143.53 (CH), 148.77 (C), 150.99 (C), 153.44 (C), 196.57 (C=O). MS (ESI, m/z): 387.2 [$M^+ + 1$]. Anal. calcd for $C_{21}H_{25}O_5Si$ (386.17): C 65.26, H 6.77; found C 65.16, H 6.71.

2.2m *1,2-Bis-benzo[d][1,3]dioxol-5-yl*-2-(*tert*butyldimethylsilyloxy)-ethanone (**3m**): Yield: 87%, mp: 125–129°C. IR (KBr, cm^{-1}): 3343, 3121, 2250, 1717, 1607, 1217; 1H NMR ($CDCl_3$) δ : 0.21 (6H, s), 1.11 (9H, s), 6.02 (1H, s), 6.09 (4H, s), 6.82 (1H, t, $J = 2.8, 3.2$ Hz), 6.89 (1H, d, $J = 4.0$ Hz), 6.99 (1H, d, $J = 4.8$ Hz), 7.19 (1H, d, $J = 6.8$ Hz), 7.38 (1H, d, $J = 8.4$ Hz), 7.49 (1H, s). ^{13}C NMR ($CDCl_3$) δ : -2.48 (CH_3), 25.94 ($3CH_3$), 30.55 (C), 86.24 (CH), 102.33 (CH_2), 102.99 (CH_2), 108.69 (CH), 110.92 (CH), 116.34 (CH), 125.14 (CH), 126.54 (2CH), 129.73 (C), 132.82 (C), 143.47 (C), 148.23 (C), 151.42 (C), 153.72 (C), 194.22 (C=O). MS (ESI, m/z): 415.5 [$M^+ + 1$]. Anal. calcd for $C_{22}H_{26}O_6Si$ (414.55): C 63.73, H 6.32; found C 63.77, H 6.33.

2.2n *1-Benzo[d][1,3]dioxol-5-yl*-2-(*tert*butyldimethylsilyloxy)-2-(quinolin-2-yl)ethanone (**3n**): Yield: 89%, mp: 224–227°C. IR (KBr, cm^{-1}): 3352, 3017, 2243, 1707, 1611, 1238. 1H NMR ($CDCl_3$) δ : 0.23 (6H, s), 1.01 (9H, s), 6.01 (1H, s), 6.07 (2H, s), 7.19 (1H, d, $J = 8.0$ Hz), 7.24 (1H, d, $J = 8.4$ Hz), 7.42 (1H, s), 7.45 (1H, d, $J = 8.4$ Hz), 7.62 (1H, t, $J = 6.4$ Hz), 7.83 (1H, t, $J = 6.0$ Hz), 7.98 (1H, d, $J = 8.8$ Hz), 8.14 (1H, d, $J = 8.8$ Hz), 8.38 (1H, d, $J = 12.4$ Hz). ^{13}C NMR ($CDCl_3$) δ : -2.54 (CH_3), 25.84 ($3CH_3$), 30.68 (C), 90.84 (CH), 102.03 (CH_2), 109.77 (CH), 110.68 (CH), 123.87 (CH), 125.44 (CH), 126.77 (C), 127.18 (CH), 129.54 (CH), 130.17 (CH), 132.55 (C), 142.59 (CH), 147.53 (C), 148.77 (C), 153.99 (C), 158.44 (C), 194.55 (C=O). MS (ESI, m/z): 422.1 [$M^+ + 1$]. Anal. calcd for $C_{24}H_{27}NO_4Si$ (421.17): C 68.36, H 6.47, N 3.33; found C 68.37, H 6.43, N 3.38.

2.2o *1-Benzo[d][1,3]dioxol-5-yl*-2-(*tert*butyldimethylsilyloxy)-2-(5-methyl-1*H*-indol-3-yl)ethanone (**3o**): Yield: 89%, mp: 224–227°C. IR (KBr, cm^{-1}): 3398, 3312, 3018, 2249, 1717, 1608, 1547, 1285. 1H NMR ($CDCl_3$) δ : 0.22 (6H, s), 1.05 (9H, s), 2.58 (3H, s), 4.87 (1H, brs), 5.99 (1H, s), 6.07 (2H, s), 7.15 (1H, d, $J = 8.4$ Hz), 7.22 (1H, s), 7.31 (1H, d, $J = 8.8$ Hz), 7.37 (1H, d, $J = 8.4$ Hz), 7.42 (1H, d, $J = 10.4$ Hz), 7.63 (1H, s), 7.82 (1H, d, $J = 8.4$ Hz). ^{13}C NMR ($CDCl_3$) δ : -2.47 (CH_3), 22.54 (CH_3), 25.84 ($3CH_3$), 30.37 (C), 90.44 (CH), 102.03 (CH_2), 108.11 (CH), 110.75 (CH), 111.68 (CH), 112.87 (C), 122.87 (CH), 123.44 (CH), 125.77 (CH), 127.18 (C), 129.54 (C), 131.88 (C), 134.57 (C), 148.77 (C), 153.99 (C), 194.52 (C=O). MS (ESI, m/z): 424.1 [$M^+ + 1$]. Anal. calcd for $C_{24}H_{29}NO_4Si$ (423.17): C 68.06, H 6.94, N 3.32; found C 68.07, H 6.37, N 3.35.

2.2p *1-Benzo[d][1,3]dioxol-5-yl*-2-(*tert*butyldimethylsilyloxy)-2-(1-methyl-1*H*-indol-3-yl)ethanone (**3p**): Yield: 81%, mp: 175–177°C. IR (KBr, cm^{-1}): 3308, 3023, 2257, 1707, 1612, 1215. 1H NMR ($CDCl_3$) δ : 0.24 (6H, s), 0.99 (9H, s), 3.86 (3H, s), 6.01 (1H, s), 6.07 (2H, s), 6.88 (1H, s), 7.12 (1H, d, $J = 8.8$ Hz), 7.22 (1H, d, $J = 8.4$ Hz), 7.37 (1H, d, $J = 8.0$ Hz), 7.38 (1H, d, $J = 4.8$ Hz), 7.39 (1H, s), 7.52 (1H, d, $J = 8.8$ Hz), 7.58 (1H, d, $J = 8.0$ Hz). ^{13}C NMR ($CDCl_3$) δ : -2.46 (CH_3), 25.43 ($3CH_3$), 29.99 (C), 34.54 (CH_3), 90.67 (CH), 102.08 (CH_2), 108.11 (CH), 109.45 (CH), 110.75 (CH), 111.63 (CH), 112.54 (C), 122.87 (CH), 123.44 (CH), 125.77 (CH), 127.18 (C), 131.55 (C), 141.54 (C), 148.72 (C), 153.28 (C), 194.77 (C=O). MS (ESI, m/z): 424.2 [$M^+ + 1$]. Anal. calcd for $C_{24}H_{29}NO_4Si$ (423.17): C 68.06, H 6.94, N 3.32; found C 68.07, H 6.37, N 3.35.

2.2q *1-Benzo[d][1,3]dioxol-5-yl*-2-(*tert*butyldimethylsilyloxy)-2-(1-methyl-1*H*-benzo[d]imidazole-2-yl)ethanone (**3q**): Yield: 83%, mp: 189–191°C. IR (KBr, cm^{-1}): 3272, 3002, 2258, 1711, 1604, 1228. 1H NMR ($CDCl_3$) δ : 0.23 (6H, s), 1.01 (9H, s), 3.94 (3H, s), 6.01 (1H, s), 6.07 (2H, s), 7.07 (1H, d, $J = 2.8$ Hz), 7.12 (1H, s), 7.24 (1H, d, $J = 8.4$ Hz), 7.32 (1H, d, $J = 6.4$ Hz), 7.39 (1H, d, $J = 6.8$ Hz), 7.41 (1H, t, $J = 8.8, 7.6$ Hz), 7.52 (1H, t, $J = 6.0$ Hz). ^{13}C NMR ($CDCl_3$) δ : -2.46 (CH_3), 25.75 ($3CH_3$), 30.11 (C), 33.31 (CH_3), 90.47 (CH), 102.08 (CH_2), 108.18 (CH), 109.55 (CH), 110.44 (CH), 119.55 (CH), 122.54 (CH), 123.46 (2CH), 131.88 (C), 135.66 (C), 142.05 (C), 143.54 (C), 148.74 (C), 153.27 (C), 194.44 (C=O). MS (ESI, m/z): 425.21 [$M^+ + 1$]. Anal. calcd for $C_{23}H_{28}N_2O_4Si$

(424.17): C 65.06, H 6.64, N 6.62; found C 65.07, H 6.68, N 6.65.

2.2r 1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(1-acetyl-1H-indol-3-yl)ethanone (3r): Yield: 77%, mp: 238–240°C. IR (KBr, cm^{-1}): 3356, 3122, 2255, 1702, 1728, 1612, 1232. ^1H NMR ($\text{DMSO}-d_6$) δ : 0.26 (6H, s), 0.99 (9H, s), 4.08 (3H, s), 6.01 (1H, s), 6.07 (2H, s), 6.94 (1H, s), 7.17 (1H, d, $J = 8.4$ Hz), 7.22 (1H, s), 7.28 (1H, d, $J = 8.4$ Hz), 7.38 (1H, d, $J = 5.6$ Hz), 7.41 (1H, t, $J = 12.4$ Hz), 7.43 (1H, t, $J = 4.4, 3.6$ Hz), 7.54 (1H, d, $J = 8.4$ Hz). ^{13}C NMR ($\text{DMSO}-d_6$) δ : -2.46 (CH_3), 24.87 (CH_3), 25.87 (3CH_3), 30.22 (C), 90.67 (CH), 102.07 (CH_2), 108.13 (CH), 109.44 (CH), 110.76 (CH), 111.67 (CH), 112.34 (C), 122.84 (CH), 123.24 (CH), 125.22 (CH), 127.13 (C), 131.57 (C), 141.58 (C), 148.71 (C), 153.27 (C), 168.44 (C=O), 194.55 (C=O). MS (ESI, $2m/z$): 451.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{25}\text{H}_{29}\text{NO}_5\text{Si}$ (451.42): C 66.46, H 6.44, N 3.12; found C 66.57, H 6.37, N 3.15.

2.2s 1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(4-(piperidin-1-yl)phenyl)ethanone (3s): Yield: 82%, mp: 186–188°C. IR (KBr, cm^{-1}): 3344, 3027, 2244, 1712, 1604, 1229. ^1H NMR (CDCl_3) δ : 0.23 (6H, s), 0.97 (9H, s), 1.53 (6H, m), 3.58 (4H, d, $J = 8.4$ Hz), 6.01 (1H, s), 6.07 (2H, s), 7.04 (1H, d, $J = 4.4$ Hz), 7.18 (1H, s), 7.24 (1H, d, $J = 4.8$ Hz), 7.33 (1H, d, $J = 2.4$ Hz), 7.44 (1H, d, $J = 8.4$ Hz), 7.52 (1H, d, $J = 8.4$ Hz), 7.64 (1H, d, $J = 4.4$ Hz), 7.86 (1H, d, $J = 8.8$ Hz). ^{13}C NMR (CDCl_3) δ : -2.46 (CH_3), 24.22 (CH_2), 25.54 (2CH_2), 25.99 (3CH_3), 30.25 (C), 54.89 (2CH_2), 90.44 (CH), 101.57 (CH_2), 109.77 (CH), 110.12 (CH), 113.55 (2CH), 123.77 (CH), 127.05 (C), 129.84 (CH), 132.47 (C), 148.25 (C), 151.37 (C), 153.83 (C), 196.22 (C=O). MS (ESI, m/z): 454.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{26}\text{H}_{35}\text{NO}_4\text{Si}$ (453.56): C 68.84, H 7.77, N 3.05; found C 68.82, H 7.72, N 3.09.

2.2t 1-Benzo[d][1,3]dioxol-5-yl)-2-(tertbutyldimethylsilyloxy)-2-(4-morpholinophenyl)ethanone (3t): Yield: 86%, mp: 201–203°C. IR (KBr, cm^{-1}): 3425, 3212, 3033, 2248, 1702, 1608, 1357, 1217. ^1H NMR (CDCl_3) δ : 0.23 (6H, s, CH_3), 0.97 (9H, s), 3.13–3.22 (4H, d), 3.61 (4H, d), 6.01 (1H, s), 6.07 (2H, s), 6.88 (1H, d, $J = 2.8$ Hz), 6.92 (1H, d, $J = 4.8$ Hz), 7.14 (1H, d, $J = 8.0$ Hz), 7.28 (1H, d, $J = 4.8$ Hz), 7.32 (1H, d, $J = 4.0$ Hz), 7.51 (1H, d, $J = 8.4$ Hz), 7.64 (1H, s) ppm. ^{13}C NMR (CDCl_3) δ : -2.39 (CH_3), 25.43 (3CH_3), 30.44 (C), 55.42 (2CH_2), 68.34 (2CH_2), 90.55

(CH), 101.54 (CH_2), 108.55 (CH), 110.8 (CH), 114.26 (CH), 125.11 (CH), 129.55 (CH), 130.84 (C), 132.47 (CH), 147.99 (C), 148.86 (C), 153.88 (C), 196.94 (C=O). MS (ESI, m/z): 456.0 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{25}\text{H}_{33}\text{NO}_5\text{Si}$ (455.23): C 65.91, H 7.34, N 3.05; found C 65.91, H 7.32, N 3.01.

2.3 General procedure for the synthesis of compounds (4a–t)

To a solution of **3** (1 eq.) in THF was added 10% HCl (25 mL/g of starting material) at room temperature and stirring was continued for 16–28 h. The mixture was diluted with H_2O and extracted with EtOAc. The organic extract was washed with brine dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue obtained was purified by CC silica gel (60–120 mesh) EtOAc–petroleum ether (5:1) to give compound **4a–4t** in 78–89% yield.

2.3a 1-(Benzo[d][1,3]dioxol-5-yl)-2-cyclohexyl-2-hydroxyethanone (4e): Yield: 88%, mp: 231–232°C. IR (KBr cm^{-1}): 3508, 3307, 3034, 2254, 1708, 1607, 1120, 947. ^1H NMR (CDCl_3) δ : 1.43–1.58 (11H, m), 1.99 (1H, m), 4.98 (1H, s), 5.98 (1H, brs), 6.05 (2H, s), 6.94 (1H, d, $J = 4.4$ Hz), 7.42 (1H, s), 7.58 (1H, d, $J = 8.8$ Hz) ppm. ^{13}C NMR (CDCl_3) δ : 25.88 (2CH_2), 26.97 (CH_2), 27.08 (2CH_2), 38.51 (CH), 86.61 (CH), 102.34 (CH_2), 108.72 (CH), 111.46 (CH), 124.12 (CH), 126.05 (C), 148.73 (C), 153.90 (C), 196.45 (C=O). MS (ESI, m/z): 263.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{15}\text{H}_{18}\text{O}_4$ (262.34): C 68.64, H 6.93; found C 68.80, H 6.96.

2.4 General procedure for the synthesis of compound (5a–t)

A mixture of compound **4** (1 eq.), EDCI (1 eq.) and DMAP (1 eq.) was stirred in dry CH_2Cl_2 at room temperature under N_2 atmosphere. *N*-acetyl-4-piperidinecarboxylic acid (1 eq.) was added to the mixture and stirring was continued at room temperature for 18–37 h. The mixture was diluted with H_2O and extracted with CH_2Cl_2 . The organic extract was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue obtained was purified by CC [silica gel (60–120 mesh), MeOH/ CH_2Cl_2 (1:15)] to get **5a–t** in 68–82% yield.

2.4a 2-(Benzo[d][1,3]dioxol-5-yl)-2-oxo-1-cyclohexylethyl-1-acetyl-piperidine-4-carboxylate (5e): Yield: 88%, mp: 231–232°C. IR (KBr, cm^{-1}): 3284, 3057,

1728, 1712, 1699, 1600, 1354, 1219, 1122, 1054. ^1H NMR (CDCl_3) δ : 1.26–1.34 (10H, m), 1.79–1.99 (4H, t, $J = 12.8, 1.6$ Hz), 2.36 (3H, s), 2.52 (1H, m), (1H, s), 3.31 (4H, m), 5.36 (1H, d, $J = 2.8$ Hz), 6.07 (2H, s), 6.98 (1H, d, $J = 8.4$ Hz), 7.45 (1H, s), 7.68 (1H, d, $J = 8.8$ Hz) ppm. ^{13}C NMR (CDCl_3) δ : 22.99 (CH_3), 25.66 (2CH_2), 26.07 (CH_2), 27.16 (2CH_2), 29.44 (2CH_2), 34.55 (CH), 41.75 (CH), 45.89 (2CH_2), 91.05 (CH), 102.44 (CH_2), 107.77 (CH), 112.41 (CH), 124.34 (CH), 126.15 (C), 149.01 (C), 153.84 (C), 172.55 ($\text{C}=\text{O}$), 174.26 ($\text{C}=\text{O}$), 196.43 ($\text{C}=\text{O}$). MS (ESI, m/z): 410.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{23}\text{H}_{23}\text{NO}_6$ (409.45): C 67.54, H 5.63, N 3.45; found C 67.57, H 5.64, N 3.45.

2.5 General procedure for the synthesis of compound (6a–t)

To a solution of **5** (10 eq.) in AcOH was added NH_4OAc (20 eq.) at room temperature and mixture was heated to 90°C for 30 h. The mixture was cooled to room temperature, quenched with saturated NaHCO_3 solution and extracted with EtOAc. The organic extract was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by CC [silica gel (60–120 mesh) MeOH/ CH_2Cl_2 ; table 1)].

2.5a 4-(Benzo[d][1,3]dioxol-5-yl)-5-(furon-3-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6a**): Mp: 124–126°C. IR (KBr, cm^{-1}): 3057, 1712, 1678, 1652, 1612, 1353, 1207, 1143, 1023, 974. ^1H NMR (CDCl_3) δ : 1.52 (4H, t), 2.38 (3H, s), 2.84 (1H, m), 3.25 (4H, t, $J = 9.6$ Hz), 6.08 (2H, s), 6.76 (1H, d, $J = 7.6$ Hz), 6.99 (1H, d, $J = 8.4$ Hz), 7.13 (1H, d, $J = 12.8$ Hz), 7.21 (1H, d, $J = 8.0$ Hz), 7.33 (1H, s), 7.78 (1H, s). ^{13}C NMR (CDCl_3) δ : 22.57 (CH_3), 30.44 (2CH_2), 38.44 (CH), 47.34 (2CH_2), 101.51 (CH_2), 108.88 (CH), 109.23 (CH), 110.41 (CH), 121.22 (CH), 129.32 (C), 131.25 (C), 140.15 (CH), 146.43 (CH), 148.43 (C), 149.09 (C), 150.21 (C), 171.34 (C), 175.36 ($\text{C}=\text{O}$). MS (ESI, m/z): 381.0 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_5$ (380.36): C 66.31, H 5.32, N 7.35; found C 66.37, H 5.34, N 7.24.

2.5b 4-(Benzo[d][1,3]dioxol-5-yl)-5-(furon-2-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6b**): Mp: 147–149°C. IR (KBr, cm^{-1}): 3105, 1717, 1656, 1641, 1603, 1341, 1212, 1152, 1011, 955. ^1H NMR (CDCl_3) δ : 1.54 (4H, t, $J = 2.8, 3.6$ Hz), 2.42 (3H, s), 2.87 (1H, m), 3.24 (4H, t, $J = 4.0, 4.8$ Hz), 6.09 (2H, s), 6.89 (1H, d, $J = 8.8$ Hz), 6.93 (1H, t, $J = 19.6$ Hz), 7.17 (1H, d, $J = 6.0$ Hz), 7.28 (1H, d, $J = 4.8$ Hz), 7.37 (1H, s), 7.72 (1H, s). ^{13}C NMR (CDCl_3) δ : 21.99 (CH_3), 29.41

(2CH_2), 38.47 (CH), 47.77 (2CH_2), 102.08 (CH_2), 108.28 (CH), 109.45 (CH), 110.47 (CH), 122.27 (CH), 129.11 (C), 131.35 (C), 139.71 (CH), 146.13 (CH), 147.47 (C), 149.02 (C), 150.77 (C), 171.87 (C), 174.98 ($\text{C}=\text{O}$). MS (ESI, m/z): 381.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_5$ (380.36): C 66.37, H 5.38, N 7.27; found C 66.37, H 5.38, N 7.22.

2.5c 4-(Benzo[d][1,3]dioxol-5-yl)-5-(thiophen-2-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6c**): IR (KBr, cm^{-1}): 3112, 1708, 1646, 1627, 1600, 1354, 1223, 1153, 1087. ^1H NMR (CDCl_3) δ : 1.53 (4H, t), 2.44 (3H, s), 2.82 (1H, m), 3.24 (4H, t, $J = 2.2$ Hz), 6.11 (2H, s), 6.82 (1H, d, $J = 7.2$ Hz), 6.96 (1H, t, $J = 8.4$ Hz), 7.08 (1H, d, $J = 6.4$ Hz), 7.17 (1H, d, $J = 8.8$ Hz), 7.38 (1H, s), 7.74 (1H, s). ^{13}C NMR (CDCl_3) δ : 22.07 (CH_3), 29.88 (2CH_2), 37.55 (CH), 48.24 (2CH_2), 102.11 (CH_2), 108.27 (CH), 109.46 (CH), 110.42 (CH), 122.24 (CH), 128.23 (C), 130.39 (C), 139.77 (CH), 146.18 (CH), 147.88 (C), 149.35 (C), 151.48 (C), 172.02 (C), 175.28 ($\text{C}=\text{O}$). MS (ESI, m/z): 397.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_4\text{S}$ (396.38): C 63.67, H 5.09, N 7.08; found C 63.66, H 5.14, N 7.06.

2.5d 4-(Benzo[d][1,3]dioxol-5-yl)-5-(pyridin-4-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6d**): Mp: 187–190°C. IR (KBr, cm^{-1}): 3124, 1720, 1653, 1638, 1612, 1547, 1483, 1348, 1202, 1146, 1018, 921. ^1H NMR (CDCl_3) δ : 1.49 (4H, t, $J = 2.4, 3.2$ Hz), 2.41 (3H, s), 2.85 (1H, m), 3.18 (4H, t, $J = 2.0, 1.6$ Hz), 6.08 (2H, s), 6.98 (1H, d, $J = 4.4$ Hz), 7.14 (1H, d, $J = 8.4$ Hz), 7.34 (1H, s), 7.84 (2H, d, $J = 8.8$ Hz), 8.62 (2H, d, $J = 12.4$ Hz). ^{13}C NMR (CDCl_3) δ : 21.88 (CH_3), 29.13 (2CH_2), 36.24 (CH), 47.76 (2CH_2), 101.87 (CH_2), 108.44 (CH), 108.98 (CH), 119.87 (CH), 122.55 (CH), 127.77 (CH), 128.47 (C), 138.44 (C), 143.33 (C), 147.54 (C), 147.88 (C), 149.88 (C), 150.24 (C), 151.42 (C), 171.22 (C), 173.34 ($\text{C}=\text{O}$). MS (ESI, m/z): 392.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_4$ (391.42): C 67.48, H 5.39, N 10.75; found C 67.60, H 5.44, N 10.76.

2.5e 4-(Benzo[d][1,3]dioxol-5-yl)-5-cyclohexyl-2-(1-acetylpiperidin-4-yl)oxazole (**6e**): IR (KBr, cm^{-1}): 3142, 1700, 1647, 1633, 1645, 1532, 1302, 1247, 1136, 1011. ^1H NMR (CDCl_3) δ : 1.28 (10H, m), 1. (4H, t, $J = 4.0, 4.8$ Hz), 2.38 (3H, s), 2.75 (1H, m), 2.83 (1H, m), 3.37 (4H, m), 6.05 (2H, s), 6.99 (1H, d, $J = 8.4$ Hz), 7.35 (1H, s), 7.48 (1H, d, $J = 8.4$ Hz). ^{13}C NMR (CDCl_3) δ : 21.56 (CH_3), 25.44 (2CH_2), 26.12 (CH_2), 29.22 (2CH_2), 33.56 (2CH_2), 35.87 (CH), 44.55

Table 1. Synthesis of novel multi-substituted oxazole derivatives.

S. No.	Aldehyde	Product ^a	Time (min)	Yield(%) ^b
1	(a)	(6a)	40	38
2	(b)	(6b)	34	35
3	(c)	(6c)	42	45
4	(d)	(6d)	38	69
5	(e)	(6e)	30	63
6	(f)	(6f)	46	86
7	(g)	(6g)	35	90
8	(h)	(6h)	48	84

Table 1. (continued)

S. No.	Aldehyde	Product ^a	Time (min)	Yield(%) ^b
9	<p>(i)</p>	<p>(6i)</p>	50	84
10	<p>(j)</p>	<p>(6j)</p>	45	83
11	<p>(k)</p>	<p>(6k)</p>	45	87
12	<p>(l)</p>	<p>(6l)</p>	50	84
13	<p>(m)</p>	<p>(6m)</p>	38	26
14	<p>(n)</p>	<p>(6n)</p>	50	84
15	<p>(o)</p>	<p>(6o)</p>	55	87

Table 1. (continued)

S. No.	Aldehyde	Product ^a	Time (min)	Yield(%) ^b
16	(p)	(6p)	63	84
17	(q)	(6q)	40	34
18	(r)	(6r)	43	32
19	(s)	(6s)	30	59
20	(t)	(6t)	35	63

^aAll products were characterized by elemental analysis IR, ¹H MR and ¹³C NMR data^bYield refers to pure products after purification by column chromatography

(2CH₂), 47.75 (CH), 102.77 (CH₂), 107.54 (CH), 108.56 (CH), 122.35 (CH), 125.65 (C), 126.34 (C), 138.15 (C), 148.12 (C), 149.05 (C), 170.55 (C), 172.35 (C=O). MS (ESI, *m/z*): 397.4 [M⁺+1]. Anal. calcd for C₂₃H₂₈N₂O₄ (396.47): C 69.67, H 7.12, N 7.05; found C 69.59, H 7.14, N 7.05.

2.5f 4-(Benzo[d][1,3]dioxol-5-yl)-5-phenyl-2-(1-acetylpiperidin-4-yl)oxazole (**6f**): IR (KBr, cm⁻¹): 3131, 1704, 1642, 1620, 1607, 1543, 1387, 1228, 1150, 1042. ¹H NMR (CDCl₃) δ: 1.32 (4H, t, *J* = 7.6 Hz), 2.32 (3H, s), 2.80 (1H, m), 3.22 (4H, t, *J* = 4.0 Hz), 6.07 (2H, s), 6.99 (1H, d, *J* = 6.0 Hz), 7.11 (1H, d, *J*

= 8.4 Hz), 7.31 (1H, s), 7.44 (1H, t, J = 8.0, 8.8 Hz), 7.55 (2H, t, J = 6.4, 3.2 Hz), 8.14 (2H, d, J = 8.4 Hz). ^{13}C NMR (CDCl_3) δ : 21.22 (CH_3), 29.84 (2CH_2), 35.35 (CH), 45.84 (2CH_2), 101.22 (CH_2), 108.44 (CH), 109.56 (CH), 121.16 (CH), 126.36 (C), 127.44 (2CH), 128.09 (C), 128.88 (CH), 129.34 (2CH), 137.22 (C), 146.08 (C), 148.34 (C), 149.09 (C), 171.48 (C), 173.68 ($\text{C}=\text{O}$). MS (ESI, m/z): 391.0 [M^++1]. Anal. calcd for $\text{C}_{23}\text{H}_{22}\text{N}_2\text{O}_4$ (390.34): C 70.74, H 5.69, N 7.21; found C 70.67, H 5.72, N 7.26.

2.5g 4-(Benzo[d][1,3]dioxol-5-yl)-5-(3-nitrophenyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6g**): Mp: 243–245°C. IR (KBr, cm^{-1}): 3010, 2254, 1712, 1608, 1545, 1322, 1207, 1155, 1002, 985. ^1H NMR (CDCl_3) δ : 1.48 (4H, t, J = 1.6, 3.2 Hz), 2.37 (3H, s), 2.82 (1H, m), 3.23 (4H, t, J = 2.8, 9.6 Hz), 6.09 (2H, s), 6.96 (1H, d, J = 8.4 Hz), 7.14 (1H, d, J = 6.8 Hz), 7.33 (1H, s), 7.82 (1H, t, J = 6.4 Hz), 8.22 (1H, d, J = 8.8 Hz), 8.49 (1H, d, J = 8.4 Hz), 8.65 (1H, s). ^{13}C NMR (CDCl_3) δ : 21.85 (CH_3), 29.34 (2CH_2), 34.34 (CH), 44.87 (2CH_2), 101.08 (CH_2), 108.22 (CH), 109.02 (CH), 120.77 (CH), 123.44 (CH), 124.52 (C), 127.09 (C), 129.99 (CH), 130.81 (CH), 132.56 (C), 137.34 (C), 146.22 (C), 148.52 (C), 148.99 (C), 149.18 (C), 171.33 (C), 173.47 ($\text{C}=\text{O}$). MS (ESI, m/z): 436.1 [M^++1]. Anal. calcd for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_6$ (435.12): C 63.44, H 4.89, N 9.64; found C 63.42, H 4.91, N 9.66.

2.5h 4-(Benzo[d][1,3]dioxol-5-yl)-5-(2-nitrophenyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6h**): Mp: >300°C. IR (KBr, cm^{-1}): 3124, 3017, 2174, 1708, 1611, 1575, 1338, 1242, 1133, 985, 756. ^1H NMR ($\text{DMSO}-d_6$) δ : 1.52 (4H, t, J = 1.2, 2.4 Hz), 2.39 (3H, s), 2.88 (1H, m), 3.42 (4H, t, J = 4.4, 4.8 Hz), 6.07 (2H, s), 6.99 (1H, d, J = 8.4 Hz), 7.11 (1H, d, J = 8.0 Hz), 7.36 (1H, s), 7.71 (1H, t, J = 8.4, 8.8 Hz), 7.85 (1H, t, J = 8.0, 8.4 Hz), 8.13 (1H, d, J = 6.4 Hz), 8.21 (1H, d, J = 8.8 Hz). ^{13}C NMR ($\text{DMSO}-d_6$) δ : 21.89 (CH_3), 29.37 (2CH_2), 34.33 (CH), 44.82 (2CH_2), 101.12 (CH_2), 108.21 (CH), 109.01 (CH), 120.12 (CH), 123.22 (CH), 124.56 (C), 127.29 (C), 129.76 (CH), 130.83 (CH), 132.57 (C), 137.32 (C), 146.24 (C), 148.53 (C), 148.91 (C), 149.17 (C), 171.17 (C), 173.85 ($\text{C}=\text{O}$). MS (ESI, m/z): 436.1 [M^++1]. Anal. calcd for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_6$ (435.12): C 63.45, H 4.87, N 9.62; found C 63.47, H 4.98, N 9.62.

2.5i 4-(Benzo[d][1,3]dioxol-5-yl)-5-(*m*-tolyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6i**): Mp: 245–247°C. IR (KBr, cm^{-1}): 3254, 3032, 2161, 1713, 1619, 1544,

1325, 1254, 1130, 984, 845. ^1H NMR (CDCl_3) δ : 1.54 (4H, t, J = 3.6, 4.0 Hz), 2.34 (3H, s), 2.42 (3H, s), 2.80 (1H, m), 3.32–3.73 (4H, t, J = 2.8, 3.6 Hz), 6.09 (2H, s), 6.94 (1H, d, J = 6.4 Hz), 7.08 (1H, d, J = 8.4 Hz), 7.24 (1H, d, J = 8.0 Hz), 7.32 (1H, s), 7.48 (1H, t, J = 8.0, 8.4 Hz), 7.74 (1H, s), 7.92 (2H, d, J = 8.8 Hz). ^{13}C NMR (CDCl_3) δ : 21.22 (CH_3), 21.99 (CH_3), 29.74 (2CH_2), 35.44 (CH), 45.24 (2CH_2), 101.20 (CH_2), 108.47 (CH), 109.74 (CH), 120.55 (CH), 122.68 (CH), 126.42 (C), 129.23 (CH), 129.76 (CH), 131.24 (C), 136.34 (C), 146.18 (C), 148.34 (C), 149.14 (C), 172.24 (C), 173.55 ($\text{C}=\text{O}$). MS (ESI, m/z): 404.3 [M^+], 405.1 [M^++1]. Anal. calcd for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_4$ (404.32): C 71.24, H 5.96, N 6.93; found C 71.27, H 5.92, N 6.93.

2.5j 4-(Benzo[d][1,3]dioxol-5-yl)-5-(3-bromophenyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6j**): Mp: 198–199°C. IR (KBr, cm^{-1}): 3147, 3008, 2036, 1725, 1654, 1562, 1308, 1235, 1131, 1047, 974. ^1H NMR (CDCl_3) δ : 1.55 (4H, t, J = 2.8 Hz), 2.47 (3H, s), 2.82 (1H, m), 3.24 (4H, t, J = 6.4, 6.8 Hz), 6.11 (2H, s), 6.98 (1H, d, J = 8.4 Hz), 7.11 (1H, d, J = 8.4 Hz), 7.26 (1H, s), 7.41 (1H, t, J = 8.0, 6.4 Hz), 7.44 (1H, s), 7.62 (1H, d, J = 4.8 Hz), 8.06 (1H, d, J = 8.8 Hz). ^{13}C NMR (CDCl_3) δ : 21.88 (CH_3), 29.33 (2CH_2), 35.27 (CH), 45.74 (2CH_2), 101.08 (CH_2), 108.12 (CH), 109.73 (CH), 120.75 (CH), 122.62 (CH), 126.44 (C), 129.22 (CH), 129.44 (CH), 131.22 (C), 136.55 (C), 146.17 (C), 148.33 (C), 149.17 (C), 172.21 (C), 173.57 ($\text{C}=\text{O}$). MS (ESI, m/z): 469.2 [M^+], 471.1 [M^++2]. Anal. calcd for $\text{C}_{23}\text{H}_{21}\text{BrN}_2\text{O}_4$ (469.22): C 58.87, H 4.54, N 5.96; found C 58.87, H 4.42, N 5.98.

2.5k 4-(Benzo[d][1,3]dioxol-5-yl)-5-(3-chlorophenyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6k**): Mp: 153–155°C. IR (KBr, cm^{-1}): 3138, 3095, 2022, 1764, 1624, 1575, 1311, 1233, 1137, 1045, 909, 856. ^1H NMR (CDCl_3) δ : 1.52 (4H, t, J = 3.6, 1.6 Hz), 2.41 (3H, s), 2.83 (1H, m), 3.24 (4H, t, J = 2.8, 2.4 Hz), 6.07 (2H, s), 6.97 (1H, d, J = 8.4 Hz), 7.14 (1H, d, J = 8.4 Hz), 7.27 (1H, s), 7.45 (1H, t, J = 8.4, 7.6 Hz), 7.58 (1H, s), 7.72 (1H, d, J = 8.0 Hz), 7.89 (1H, d, J = 8.8 Hz). ^{13}C NMR (CDCl_3) δ : 22.08 (CH_3), 29.24 (2CH_2), 35.77 (CH), 45.22 (2CH_2), 101.08 (CH_2), 108.14 (CH), 109.54 (CH), 121.34 (CH), 123.52 (CH), 127.74 (C), 129.24 (CH), 129.44 (CH), 132.54 (C), 136.74 (C), 145.23 (C), 148.38 (C), 149.17 (C), 172.22 (C), 173.55 ($\text{C}=\text{O}$). MS (ESI, m/z): 424.2 [M^+], 425.1 [M^++1]. Anal. calcd for $\text{C}_{23}\text{H}_{21}\text{ClN}_2\text{O}_4$ (424.22): C 65.08, H 4.96, Cl 8.35, N 6.56; found C 65.07, H 4.91, Cl 8.35, N 6.68.

2.5l 4-(Benzo[d][1,3]dioxol-5-yl)-5-(3-hydroxyphenyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6l**): Mp: 178–179°C. IR (KBr, cm^{-1}): 3542, 3328, 3077, 2152, 1709, 1645, 1531, 1344, 1220, 1187, 1045. ^1H NMR (CDCl_3) δ : 1.53 (4H, t, $J = 3.2, 3.6$ Hz), 2.44 (3H, s), 2.80 (1H, m), 3.24 (4H, t, $J = 2.8, 3.6$ Hz), 6.01 (2H, s), 6.98 (1H, d, $J = 8.4$ Hz), 7.11 (1H, d, $J = 6.0$ Hz), 7.29 (1H, s), 7.44 (1H, t, $J = 6.8, 12.4$ Hz), 7.59 (1H, s), 7.77 (1H, d, $J = 8.0$ Hz), 7.92 (1H, d, $J = 8.4$ Hz) 8.64 (1H, brs). ^{13}C NMR (CDCl_3) δ : 22.07 (CH_3), 29.24 (2CH_2), 35.77 (CH), 45.22 (2CH_2), 101.11 (CH_2), 108.25 (CH), 110.24 (CH), 121.56 (CH), 123.53 (CH), 128.08 (C), 129.09 (CH), 129.87 (CH), 131.24 (C), 136.75 (C), 145.33 (C), 148.37 (C), 149.22 (C), 172.74 (C), 173.01 (C=O). MS (ESI, m/z): 407.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{23}\text{H}_{22}\text{N}_2\text{O}_5$ (406.23): C 67.96, H 5.46, N 6.88; found C 67.97, H 4.51, N 6.89.

2.5m 4,5-di(Benzo[d][1,3]dioxol-5-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6m**): Mp: 108–110°C. IR (KBr, cm^{-1}): 3144, 3063, 2147, 1707, 1600, 1570, 1307, 1234, 1131, 1009. ^1H NMR (CDCl_3) δ : 1.35 (4H, t, $J = 3.6, 1.6$ Hz), 2.39 (3H, s), 2.82 (1H, m), 3.25 (4H, t, $J = 2.8, 3.2$ Hz), 6.07 (2H, s), 6.18 (2H, s), 6.94 (2H, d, $J = 8.8$ Hz), 7.12 (2H, d, $J = 8.4$ Hz), 7.22 (1H, s), 7.43 (1H, t, $J = 8.8$ Hz), 7.65 (1H, d, $J = 8.4$ Hz), 7.28 (1H, d, $J = 8.4$ Hz). ^{13}C NMR (CDCl_3) δ : 22.14 (CH_3), 29.55 (2CH_2), 35.32 (CH), 44.76 (2CH_2), 101.08 (CH_2), 102.84 (CH_2), 108.89 (2CH), 111.38 (2CH), 122.36 (2CH), 128.28 (C), 129.87 (CH), 131.44 (C), 136.64 (C), 142.68 (C), 148.36 (2C), 149.34 (2C), 172.55 (C), 173.85 (C=O). MS (ESI, m/z): 435.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_6$ (434.15): C 66.36, H 5.13, N 6.46; found C 66.37, H 5.11, N 6.39.

2.5n 4-(Benzo[d][1,3]dioxol-5-yl)-5-(quinolin-2-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6n**): Mp: 223–224°C. IR (KBr, cm^{-1}): 3185, 3005, 2053, 1715, 1638, 1574, 1328, 1222, 1154, 1024. ^1H NMR (CDCl_3) δ : 1.34 (4H, t, $J = 2.4, 1.6$ Hz), 2.43 (3H, s), 2.82 (1H, m), 3.22 (4H, t, $J = 2.4, 2.8$ Hz), 6.04 (2H, s), 6.96 (1H, d, $J = 8.4$ Hz), 7.11 (1H, d, $J = 6.8$ Hz), 7.24 (1H, s), 7.48 (1H, d, $J = 6.0$ Hz), 7.66 (1H, t, $J = 8.4, 8.0$ Hz), 7.81 (2H, t, $J = 6.4, 7.6$ Hz), 7.98 (1H, d, $J = 8.8$ Hz), 8.12 (1H, d, $J = 10.4$ Hz), 8.46 (2H, d, $J = 8.8$ Hz). ^{13}C NMR (CDCl_3) δ : 21.25 (CH_3), 29.84 (2CH_2), 35.44 (CH), 46.87 (2CH_2), 101.07 (CH_2), 108.11 (CH), 108.99 (CH), 119.22 (CH), 120.22 (CH), 122.61 (CH), 125.42 (C), 126.24 (C), 127.46 (CH), 128.47 (CH), 129.48 (CH), 137.42 (C), 138.76 (CH), 139.48 (C), 145.22 (C), 148.46 (C), 149.847 (C), 157.24 (C), 171.42 (C), 173.39 (C=O). MS (ESI, m/z):

442.1 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{26}\text{H}_{23}\text{N}_3\text{O}_4$ (441.47): C 70.72, H 5.29, N 9.55; found C 70.67, H 5.34, N 9.56.

2.5o 4-(Benzo[d][1,3]dioxol-5-yl)-5-(5-methyl-1H-indol-3-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6o**): Mp: 192–195°C. IR (KBr, cm^{-1}): 3343, 3012, 2245, 2146, 1874, 1719, 1608, 1547, 1335, 1225, 1104, 1034. ^1H NMR (CDCl_3) δ : 1.54 (4H, t, $J = 2.4, 1.6$ Hz), 2.41 (3H, s), 2.52 (3H, s), 2.84 (1H, m), 3.42 (4H, t, $J = 2.8, 3.2$ Hz), 6.08 (2H, s), 6.99 (1H, d, $J = 6.4$ Hz), 7.14 (2H, d, $J = 8.4$ Hz), 7.33 (1H, s), 7.46 (1H, d, $J = 6.4$ Hz), 7.89 (1H, s), 8.65 (1H, s), 10.34 (1H, brs). ^{13}C NMR (CDCl_3) δ : 21.32 (CH_3), 22.02 (CH_3), 29.47 (2CH_2), 34.65 (CH), 44.84 (2CH_2), 99.87 (C), 101.08 (CH_2), 108.64 (CH), 109.85 (CH), 112.36 (CH), 121.56 (CH), 122.31 (CH), 123.44 (CH), 126.23 (C), 127.59 (CH), 129.21 (C), 130.46 (C), 134.77 (C), 136.42 (C), 146.62 (C), 148.95 (C), 149.12 (C), 170.49 (C), 172.55 (C=O). MS (ESI, m/z): 444.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{26}\text{H}_{25}\text{N}_3\text{O}_4$ (443.48): C 70.41, H 5.67, N 9.44; found C 70.43, H 5.68, N 9.42.

2.5p 4-(Benzo[d][1,3]dioxol-5-yl)-5-(1-methyl-1H-indol-3-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6p**): Mp: 245–247°C. IR (KBr, cm^{-1}): 3085, 2232, 2141, 1872, 1714, 1603, 1546, 1324, 1232, 1114. ^1H NMR (CDCl_3) δ : 1.52 (4H, t, $J = 3.6, 1.6$ Hz), 2.43 (3H, s), 2.84 (1H, m), 3.24 (4H, t, $J = 6.4, 6.8$ Hz), 3.76 (3H, s), 6.07 (2H, s), 6.96 (1H, d, $J = 7.6$ Hz), 7.11 (2H, d, $J = 6.8$ Hz), 7.28 (1H, s), 7.48 (2H, t, $J = 8.0, 7.6$ Hz), 7.69 (1H, d, $J = 8.4$ Hz), 8.25 (1H, d, $J = 8.8$ Hz). ^{13}C NMR (CDCl_3) δ : 21.87 (CH_3), 29.47 (2CH_2), 34.65 (CH), 35.97 (CH_3), 44.24 (2CH_2), 99.86 (C), 101.11 (CH_2), 108.84 (CH), 109.24 (CH), 110.31 (CH), 120.45 (CH), 121.38 (CH), 122.64 (CH), 123.80 (CH), 126.08 (C), 128.11 (C), 129.56 (CH), 136.23 (C), 137.46 (C), 146.33 (C), 148.47 (C), 149.36 (C), 170.49 (C), 172.64 (C=O). MS (ESI, m/z): 444.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{26}\text{H}_{25}\text{N}_3\text{O}_4$ (443.48): C 70.41, H 5.67, N 9.44; found C 70.43, H 5.68, N 9.42.

2.5q 4-(Benzo[d][1,3]dioxol-5-yl)-5-(1-methyl-1H-imidazol-2-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6q**): Mp: >300°C. IR (KBr, cm^{-1}): 3055, 2267, 2136, 1804, 1708, 1611, 1534, 1397, 1222, 1117. ^1H NMR (CDCl_3) δ : 1.35 (4H, t, $J = 2.0, 1.2$ Hz), 2.43 (3H, s), 2.82 (1H, m), 3.29 (4H, t, $J = 4.4, 4.8$ Hz), 4.08 (3H, s), 6.08 (2H, s), 6.99 (1H, d, $J = 6.0$ Hz), 7.07 (1H, d, $J = 6.8$ Hz), 7.22 (1H, t, $J = 8.0, 8.4$ Hz), 7.63 (1H, d, $J = 8.4$ Hz), 7.78 (1H, d, $J = 6.4$ Hz), 7.77 (1H, d, $J = 8.4$ Hz), 7.92 (1H, t, $J = 8.0, 8.8$ Hz). ^{13}C NMR (CDCl_3) δ :

20.44 (CH₃), 22.08 (CH₃), 29.09 (2CH₂), 35.71 (CH), 45.27 (2CH₂), 101.03 (CH₂), 108.24 (CH), 109.64 (CH), 111.21 (CH), 118.66 (CH), 121.22 (CH), 123.86 (2CH), 127.22 (C), 136.33 (C), 137.67 (C), 139.77 (C), 140.44 (C), 141.42 (C), 148.44 (C), 149.09 (C), 172.11 (C), 173.62 (C=O). MS (ESI, m/z): 445.2 [M⁺+1]. Anal. calcd for C₂₅H₂₄N₄O₄ (444.28): C 67.55, H 5.44, N 12.62; found C 67.57, H 4.41, N 12.63.

2.5r 4-(Benzo[d][1,3]dioxol-5-yl)-5-(1-acetyl-1H-indol-3-yl)-2-(1-acetylpiperidin-4-yl)oxazole (**6r**): Mp: 135–137°C. IR (KBr): 3038, 2108, 1831, 1728, 1635, 1528, 1333, 1244, 1143, 1058. ¹H NMR (CDCl₃) δ : 1.45 (4H, t, J = 2.8, 1.2 Hz), 2.42 (3H, s), 2.73 (3H, s), 2.81 (1H, m), 3.29 (4H, t, J = 4.0, 4.4 Hz), 6.09 (2H, s), 6.98 (1H, d, J = 8.0 Hz), 7.10 (2H, d, J = 6.0 Hz), 7.22 (1H, s), 7.44 (2H, t, J = 6.8, 8.8 Hz), 7.61 (1H, d, J = 8.0 Hz), 8.45 (1H, d, J = 8.8 Hz). ¹³C NMR (CDCl₃) δ : 21.87 (CH₃), 25.94 (CH₃), 29.33 (2CH₂), 34.47 (CH), 44.64 (2CH₂), 100.24 (C), 101.98 (CH₂), 108.99 (CH), 109.15 (CH), 111.47 (CH), 119.22 (CH), 121.74 (CH), 122.33 (CH), 123.82 (CH), 126.35 (C), 128.63 (C), 129.43 (CH), 135.23 (C), 138.41 (C), 145.32 (C), 148.47 (C), 149.36 (C), 170.49 (C=O), 170.58 (C), 172.94 (C=O). MS (ESI, m/z): 472.1 [M⁺+1]. Anal. calcd for C₂₆H₂₅N₃O₄ (471.27): C 68.76, H 5.36, N 8.92; found C 68.459, H 5.38, N 8.92.

2.5s 4-(Benzo[d][1,3]dioxol-5-yl)-5-(4-(piperidin-1-yl)phenyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6s**): IR (KBr, cm⁻¹): 3248, 3039, 2278, 2133, 1889, 1724, 1612, 1574, 1425, 1333, 1245, 1144, 1032, 985. ¹H NMR (CDCl₃) δ : 1.28 (4H, m), 1.32 (4H, t, J = 3.6, 2.8 Hz), 1.52 (2H, q), 2.34 (3H, s), 2.82 (1H, m), 3.18 (4H, t, J = 2.4, 2.8 Hz), 3.57 (4H, t, J = 2.8, 3.2 Hz), 6.09 (2H, s), 6.88 (2H, d, J = 8.4 Hz), 6.94 (1H, d, J = 7.2 Hz), 7.17 (1H, d, J = 8.0 Hz), 7.30 (1H, s), 7.74 (2H, d, J = 8.8 Hz). ¹³C NMR (CDCl₃) δ : 21.76 (CH₃), 24.54 (2CH₂), 25.88 (CH₂), 29.36 (2CH₂), 35.87 (CH), 45.66 (2CH₂), 55.28 (CH₂), 101.09 (CH₂), 108.55 (CH), 109.66 (CH), 113.33 (2CH), 119.78 (C), 121.36 (CH), 127.44 (2CH), 128.09 (C), 137.22 (C), 146.08 (C), 148.22 (C), 149.19 (C), 150.77 (C), 171.22 (C), 173.66 (C=O). MS (ESI, m/z): 474.2 [M⁺+1]. Anal. calcd for C₂₈H₃₁N₃O₄ (473.56): C 71.04, H 6.69, N 8.81; found C 71.07, H 6.72, N 8.86.

2.5t 4-(Benzo[d][1,3]dioxol-5-yl)-5-(4-morpholino-phenyl)-2-(1-acetylpiperidin-4-yl)oxazole (**6t**): IR (KBr, cm⁻¹): 3305, 3007, 2225, 2143, 1851, 1733, 1645, 1534, 1338, 1284, 1112, 963, 854. ¹H NMR (CDCl₃)

δ : 1.42 (4H, t, J = 2.8, 2.0 Hz), 2.37 (3H, s), 2.81 (1H, m), 3.14 (4H, t, J = 4.8, 1.6 Hz), 3.35 (4 H, t, J = 2.0, 2.4 Hz), 3.68 (4H, t, J = 4.4, 4.8 Hz), 6.11 (2H, s), 6.86 (2H, d, J = 6.4 Hz), 6.98 (1H, d, J = 8.8 Hz), 7.19 (1H, d, J = 8.8 Hz), 7.32 (1H, s), 7.65 (2H, d, J = 8.0 Hz). ¹³C NMR (CDCl₃) δ : 21.88 (CH₃), 29.74 (2CH₂), 35.16 (CH), 45.12 (2CH₂), 55.99 (CH₂), 66.38 (2CH₂), 101.12 (CH₂), 108.24 (CH), 109.62 (CH), 113.12 (2CH), 119.52 (C), 121.74 (CH), 127.63 (2CH), 128.12 (C), 137.27 (C), 146.18 (C), 148.78 (C), 149.34 (C), 150.54 (C), 171.24 (C), 173.67 (C=O). MS (ESI, m/z): 476.1 [M⁺+1]. Anal. calcd for C₂₇H₂₉N₃O₅ (475.54): C 68.17, H 6.17, N 8.80; found C 68.17, H 6.12, N 8.83.

2.6 Synthesis of compound (7)

A well-stirred solution of compound **1** (1 eq.) in AcOH was treated with 1,3-propanedithiol (2 eq.) and BF₃OEt₂ (2.5 eq.) at 0°C. The mixture was warmed to room temperature and stirred for 2 h. The solid that precipitated was filtered, washed with cold H₂O and dried under reduced pressure to give compound **7** in 87% yield. Mp: 98–101°C. IR (KBr, cm⁻¹): 3012, 2142, 1618, 1506, 1341, 1207, 1122. ¹H NMR (CDCl₃) δ : 1.82 (2H, q, CH₂), 2.85 (2H, t, J = 4.8, 4.0 Hz), 3.03 (2H, t, J = 4.8 Hz), 5.13 (1H, s), 5.98 (2H, s), 6.76 (1H, d, J = 8.8 Hz), 6.98 (1H, d, J = 8.0 Hz), 7.24 (1H, s). ¹³C NMR (CDCl₃) δ : 25.05 (CH₂), 27.55 (2CH₂), 51.75 (CH), 102.45 (CH₂), 103.77 (CH), 104.41 (CH), 122.34 (CH), 132.15 (C), 147.92 (C), 148.01 (C). MS (ESI, m/z): 241.2 [M⁺+1]. Anal. calcd for C₁₁H₁₂O₂S₂ (240.05): C 54.96, H 5.03, S 26.65; found C 54.97, H 5.04, S 26.65.

2.7 General procedure for the synthesis of compound (8)

Freshly titrated *n*-BuLi (1 M in hexane, 1.2 eq.) was added drop-wise to a solution of **7** (1 eq.) in THF at –78°C under inert atmosphere. After stirring at –78°C temperature for 30 min respective aldehydes (1 eq.) was added to the above reaction mixture at –78°C. The resulting mass was warmed to room temperature and stirred for further 2–3 h. The reaction was quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc. The organic extract was washed with brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue obtained was purified by CC [silica gel (60–120) EtOAc-petroleum] to get pure compound **8** in 79–88% yield.

2.7a 2-(Benzo[d][1,3]dioxol-5-yl)-1,3-dithian-2-yl)furon-2-yl)methanol (**8b**): Yield: 85%. mp: 173–175°C. IR (KBr, cm^{-1}): 3321, 3124, 2105, 1709, 1654, 1536, 1375, 1200, 1112, 1005. ^1H NMR (CDCl_3) δ : 1.24 (2H, q), 1.52 (1H, s), 1.98 (2H, t, $J = 4.4, 4.8$ Hz), 2.62 (2H, t, $J = 2.4, 2.0$ Hz), 5.01 (1H, s), 5.94 (2H, s), 6.15 (1H, d, $J = 8.8$ Hz), 6.24 (1H, d, $J = 6.4$ Hz), 6.74 (1H, d, $J = 8.0$ Hz), 6.99 (1H, d, $J = 8.4$ Hz), 7.24 (1H, s), 7.32 (1H, t, $J = 4.0, 4.4$ Hz). ^{13}C NMR (CDCl_3) δ : 25.35 (CH_2), 26.58 (2CH_2), 69.75 (C), 90.55 (CH), 102.55 (CH_2), 109.82 (CH), 111.70 (CH), 112.44 (CH), 113.05 (CH), 123.08 (CH), 132.45 (C), 141.86 (CH), 147.84 (C), 148.26 (C), 153.75 (C). MS (ESI, m/z): 337.2 [$\text{M}^+ + 1$]. Anal. calcd for $\text{C}_{16}\text{H}_{16}\text{O}_4\text{S}_2$ (336.13): C 57.16, H 4.78, S 19.05; found C 57.17, H 4.74, S 19.05.

2.8 General procedure for the synthesis of compound (**4**)

A suspension of compound **8** (1 eq.) in 90% aqueous MeOH was treated with HgCl_2 (2.1 eq.) and HgO (1.3 eq, red form) at room temperature. The reaction mixture was refluxed for 3–4 h. The reaction mixture was cooled to room temperature, filtered the salts and washed with CH_2Cl_2 . The combined filtrate was concentrated under reduced pressure to give a residue. The residue was

diluted with CH_2Cl_2 , washed with water and brine solution. After drying over anhydrous Na_2SO_4 and concentrated under reduced pressure to give crude compound **4** in 78–82% yields.

3. Results and discussion

The sequence leading to the formation of the title compounds is outlined in scheme 1. A solution of benzo[d][1,3]dioxole-5-carbaldehyde (**1**) in MeCN was added drop-wise to a stirring mixture of KCN, TBSCl and ZnI_2 at room temperature for overnight to afford compound **2**,^{20–22} as pale brown solid in 85% yield, which on treatment with aldehydes in the presence of lithiumdiisopropylamide (LDA) to yielded **3**²³ with good yields. The structure of these products was deduced from their elemental analysis, IR ^1H - and ^{13}C -NMR and MS data. These compounds were allowed to react with 10% HCl in THF to afford the intermediates **4**. The subsequent coupling of **4** with 1-acetyl-piperidine-4-carboxylic acid yielded **5**, which on treatment with NH_4OAc , in AcOH gave multi-substituted oxazole derivatives **6a–6t**. The intermediate **4** was also obtained via the synthesis of compound **7** and **8** (scheme 1).²⁴ The structures of the isolated products **6a – 6t** were

Scheme 1. Synthesis of a new class of multi-substituted oxazole derivatives.

Table 2. *In vitro* antibacterial activity data of multi-substituted oxazoles (6a-t).

Compound	Zone of Inhibition (MIC in μ g / mL)							
	<i>B.s</i>	<i>S.a</i>	<i>E.c</i>	<i>K.p</i>	<i>C.a</i>	<i>A.n</i>		
6a	+	(532)	*	++ (449)	+	(412)	*	
6b	*	+++ (387)	++ (418)	+	(554)	+++ (331)	++ (423)	
6c	++ (431)	+	*	+	(547)	+	(412)	*
6d	+++ (345)	+++ (376)	++ (447)	+++ (412)	+++ (362)	+++ (362)	++ (387)	
6e	*	*	+++ (364)	+++ (325)	*	*	+++ (344)	
6f	++++ (310)	++++ (285)	++++ (289)	++++ (273)	+++ (211)	+++ (211)	+++ (234)	
6g	++ (478)	++ (432)	+++ (315)	+	(564)	++ (477)	+++ (375)	
6h	++ (455)	+	+++ (351)	+++ (461)	+	(501)	+++ (320)	
6i	++++ (255)	++++ (312)	+++ (284)	++++ (291)	++++ (343)	++++ (343)	+++ (282)	
6j	++++ (264)	++++ (298)	+++ (254)	++ (277)	++++ (277)	++++ (277)	+++ (237)	
6k	+++ (258)	++++ (294)	+++ (276)	+++ (266)	++++ (241)	++++ (241)	+++ (234)	
6l	*	+	+++ (299)	++++ (347)	+	(514)	+++ (210)	
6m	++ (476)	+++ (395)	*	+	(524)	+++ (342)	*	
6n	+	(547)	+++ (408)	+++ (345)	+	(425)	+	(454)
6o	+++ (422)	++ (397)	+++ (345)	++ (419)	+++ (394)	+++ (394)	++ (324)	
6p	++++ (294)	++ (487)	*	+++ (386)	++++ (232)	++++ (232)	++ (484)	
6q	+++ (315)	++ (398)	+	+++ (394)	+++ (317)	+++ (317)	++ (417)	
6r	+	(512)	+++ (366)	+++ (457)	+	(400)	++++ (354)	
6s	*	+++ (398)	+++ (444)	++++ (298)	*	*	++ (335)	
6t	+	(507)	++ (427)	++++ (312)	+	(344)	++ (461)	
Ampicillin	+++++ (3.28)	+++++ (3.36)	+++++ (3.88)	+++++ (4.00)	+++++ (3.28)	+++++ (3.28)	+++++ (3.36)	

+: Less than 15 mm; ++: 15–20 mm; +++: 20–25 mm; ++++: 25–30 mm; +++++: > 30 mm; - : control; B.s: *Bacillus subtilis*; E.c: *Escherichia coli*; S.a: *Staphylococcus aureus*; K.p: *Klebsiella pneumoniae*; C.a: *Candida albicans*; A.n: *Aspergillus niger*

*: Not found

deduced from their elemental analyses, IR, ^1H , ^{13}C NMR and MS spectra.

4. Biological activity

It is reported^{25,26} that oxazoles showed antimicrobial activity against (*Staphylococcus aureus*; *Escherichia coli*; *Bacillus subtilis*; *Klebsiella pneumonia*). In view of that, in order to search for new antimicrobial agents, all the twenty compounds were evaluated for their antimicrobial activity against the above four bacteria and two fungi. The investigation of antimicrobial activity (tables 2) revealed that all the newly synthesized compounds showed good to moderate minimum inhibitory concentration at 258–564 $\mu\text{g/mL}$ in 20% water in dimethyl sulphoxide. Out of the twenty compounds, **6f**, **6j**, **6i** and **6k** exhibited pronounced antibacterial activity, and the inhibitory activity among these four compounds followed the increasing order: **6k** > **6j** > **6i** > **6f**. Compounds **6g**, **6h**, **6o** and **6r** showed good activity against *Escherichia coli*. Compounds **6s** and **6t** showed good activity against *Klebsiella pneumonia*. Compounds **6p** and **6q** moderate activity against *Bacillus subtilis*. The compounds were also screened for their antifungal activity against *Candida albicans* and *Aspergillus niger* using the fungicide clotrimazole in DMF as a standard.²⁷

5. Conclusion

In this work, we have reported a new class of multi-substituted oxazole derivatives which are characterized by FT-IR, PMR and ^{13}C NMR spectral analysis. Synthesized compounds are screened for their antifungal and antibacterial activity. These compounds show good activity against Gram +ve and Gram -ve bacteria and fungal species.

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