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# A Research Article lentil Unexplored – Design, Synthesis, Development and Characterization of Newer Five Member Heterocyclic Compound for 1,2,4-oxadiazole.

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**ABSTRACT-** The combinations of five-membered hetero-aromatic compounds such as is 1,2,4-oxadiazoles are of interest to the pharmaceutical industry and scientific data for their applications. Although there are many ways to prepare these compounds, new variations are constantly emerging as they provide many recreational and therapeutic benefits. This article presents a new method for the synthesis of 1,2,4-oxadiazole.

The α,β-alkyne hydrazone was then treated with molecular iodine in the presence of $NaHCO_3$ to give 1,2,4-oxadiazole in good yield. Then, the same reaction with CuI in the presence of %yields the corresponding synthesis 1,2,4-oxadiazole. In this study, the reaction between propargyl aldehyde and amidoxime was evaluated. This reaction only produces more compounds.

***Keyword:*** 1,2,4-oxadiazole.

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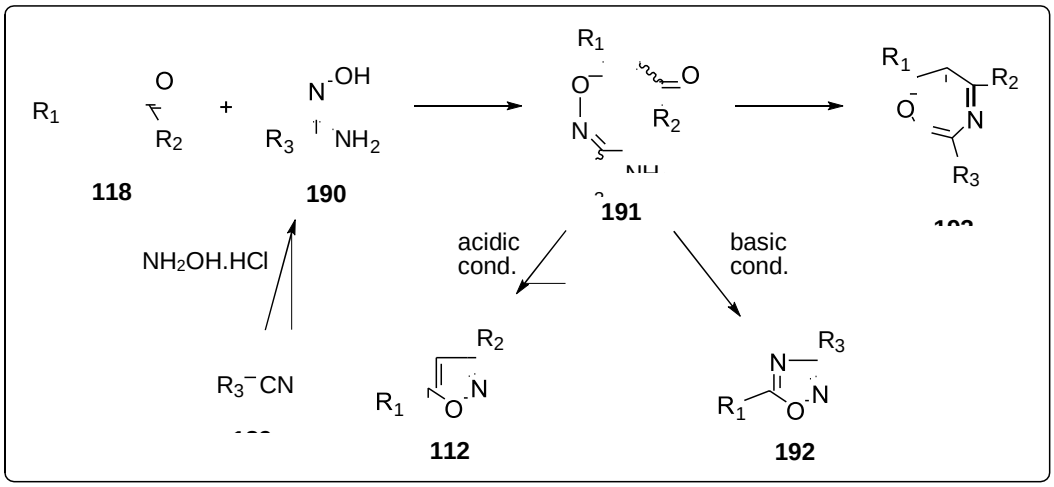
**Aim of the study**

we will investigate the reactions of amidoximes **190**with propargyl aldehydes and ketones **118** for the synthesis of 1,2,4-oxadiazepines**193** (Figure 69). Initially, these reactions could produce conjugate addition products**191** before cyclization reactions. If we will not obtain oxadiazepine




**193**, the cyclization would be carried out under basic or acidic conditions. We hyphothesize that conjugate addition products **191** may also give 1,2,4-oxadiazoles **192** or isoxazoles **112**. Interestingly, under basic conditions, conjugate addition products **191** could afford 1,2,4-oxadiazoles **192** along with methyl ketones. On the other hand, under acidic conditions, conjugate addition products **191** could furnish isoxazoles **112** (Figure 69). It should be mentioned that if these reactions produce isoxazoles and 1,2,4-oxadiazoles under acidic and basic conditions, respectively, they will be previously unknown reactions from the mechanistic point of view.

**Fig.-1** Synthesis of pyrazoles and 4-iodopyrazoles via electrophilic cyclization.

## INTRODUCTION

Heterocyclic compounds are organic compounds which have at least one element other than carbon, such as oxygen, nitrogen or sulfur, within a ring skeleton. Heterocyclic compounds are not only found in natural products, such as aflatoxin $B_1$, caffeine, reserpine and biotin [2], but also obtained synthetically. Heterocyclic compounds are generally classified according to the

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number of atoms on the ring. Some examples for the known heterocyclics include 3-membered oxiranes and aziridines, 4-membered oxetanes and azetidines, 5-membered furans, pyrroles and thiophenes, and 6-membered pyridines [3].

Many alkaloids, vitamins, antibiotics and synthetic medicines as well as dyestuffs are heterocyclic compounds. The seven of the top 10 best selling prescription drugs include heterocyclic moieties in their structures, which emphasizes the importance of heterocyclic compounds for human life [4]. Therefore, the synthesis of heterocyclic compounds has attracted great attention in organic community for a long time because of their biological activities, properties and applications. Pyrazoles, isoxazoles and 1,2,4-oxadiazoles are important classes of heterocyclic chemistry due to the broad range of biological activities they possess, which will be discussed in the following sections.

## EXPERIMENTAL

$^{1}H$ and $^{13}C$ NMR spectra were recorded on a Bruker Spectrospin (400 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from an internal TMS (trimethylsilane) reference. Coupling constants (*J*) are reported in hertz (Hz), and spin multiplicities are presented by the following symbols: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet). DEPT $^{13}C$ NMR information is given in parentheses as C, CH, $CH_2$ and $CH_3$. Band positions are reported in reciprocal centimeters ($cm^{-1}$). Band intensities are indicated relative to most intense band, and are listed as: br (broad), vs (very strong), s (strong), m (medium), w (weak), vw (very weak). Flash chromatography was performed using thick-walled glass columns and ‘’flash grade’’ silica (Merck 230-400 mesh). Thin layer chromatography (TLC) was performed by using commercially prepared 0.25 mm silica gel plates and visualization was effected with short wavelength UV lamp. The relative proportions of solvents in chromatography solvent mixtures refer to the volume: volume ratio. All commercially available reagents were used directly without purification unless otherwise stated. All the solvents used in reactions distilled for purity. The inert atmosphere was created by slight positive pressure (ca. 0.1 psi) of argon. All glassware was dried in oven prior to use.

**General procedure for the synthesis of 1,2,4-oxadiazoles 192 fromconjugate addition**

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**products 191 in the presence of NaH.**

To a solution of **191** (0.25 mmol) in 10 mL of anhydrous acetonitrile was added 1.05 equiv. of sodium hydride (60% suspension in mineral oil). The mixture was stirred at ambient temperature for appropriate time. Then, the mixture was filtrated and washed two times with diethylether (2 x 25 mL). The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane as the eluent to afford the desired product.

**3,5-Diphenyl-1,2,4-oxadiazole (192a).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 85% of the indicated product. The spectral data were given the in previous section.

**3-Phenyl-5-(thiophen-3-yl)-1,2,4-oxadiazole (192d).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 83% of the indicated product. The spectral data were given the in previous section.

**5-Pentyl-3-phenyl-1,2,4-oxadiazole (192e) (Table 12, Entry 3).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 84% of the indicated product. The spectroscopic data were given the in previous section.

**3-(4-Methoxyphenyl)-5-phenyl-1,2,4-oxadiazole (192i) (Table 12, Entry 4).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 85% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.21 (d, $J$ = 6.9 Hz, 2H), 8.12 (d, $J$= 8.8 Hz, 2H), 7.55 (m, 3H), 7.01 (d, $J$ = 8.6 Hz, 2H), 3.87 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 175.4 (C), 168.7 (C), 161.9 (C), 132.6 (CH), 129.1 (CH), 129.0 (CH), 128.1 (CH), 124.5 (C), 119.5 (C), 114.3 (CH), 55.4 ($CH_3$). The spectral data were in agreement with those reported previously for this compound [201].

**3-(2-Chlorophenyl)-5-phenyl-1,2,4-oxadiazole (192j) (Table 12, Entry 5).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 93% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.22 (d, $J$ = 7.9 Hz, 2H), 8.03 (dd, $J$ = 7.2 Hz, $J$ = 1.7, 1H), 7.54 (m, 4H),

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7.42 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 175.3 (C), 167.8 (C), 133.6 (C), 132.9 (CH), 131.9 (CH), 131.6 (CH), 130.9 (CH), 129.1 (CH), 128.2 (CH), 126.9 (CH), 126.3 (C), 124.1 (C). The spectral data were in agreement with those reported previously for this compound [202].

***N*,*N*-Dimethyl-4-(5-pentyl-1,2,4-oxadiazol-3-yl)aniline(192k).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 85% of the indicated product. $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.93 (d, $J$ = 8.8 Hz, 2H), 6.75 (d, $J$ = 8.8 Hz, 2H), 3.02 (s, 6H), 2.90 (t, $J$ = 7.6 Hz, 2H), 1.86 (m, 2H), 1.40 (m, 4H), 0.92 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.3 (C), 168.3 (C), 152.0 (C), 128.6 (CH), 111.8 (CH), 40.2 ($CH_3$), 31.2 ($CH_2$), 26.6 ($CH_2$), 26.4 ($CH_2$), , 22.2 ($CH_2$), 13.8 ($CH_3$).

**General procedure for the one-pot synthesis of 1,2,4-oxadiazoles 192.**

To a stirred solution of propargyl aldehyde **118** (0.25 mmol) and amidoxime **190** (0.325 mmol) in dioxane (7 mL) was added KOH flakes (0.25 mmol), and the solution was allowed to stir at 100 $^o$C under argon for appropriate time. After the reaction was over, the dioxane was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane as the eluent to afford the desired product.

**3,5-Diphenyl-1,2,4-oxadiazole (192a).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 61% of the indicated product. The spectral data were given the in previous section.

**3-Phenyl-5-(*p*-tolyl)-1,2,4-oxadiazole (192b)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 55% of the indicated product. The spectral data were given the in previous section..

**5-(4-Methoxyphenyl)-3-phenyl-1,2,4-oxadiazole (192c)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 76% of the indicated product. The spectral data were given the in previous section.

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**5-Pentyl-3-phenyl-1,2,4-oxadiazole (192e)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 72% of the indicated product. The spectral data were given the in previous section.

**5-Phenyl-3-(*p*-tolyl)-1,2,4-oxadiazole (192g)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 59% of the indicated product. The spectral data were given the in previous section.

**3-(4-Chlorophenyl)-5-phenyl-1,2,4-oxadiazole (192h)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 42% of the indicated product. The spectral data were given the in previous section.

**3-(4-Methoxyphenyl)-5-phenyl-1,2,4-oxadiazole (192i)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 60% of the indicated product. The spectral data were given the in previous section.

**3-(2-Chlorophenyl)-5-phenyl-1,2,4-oxadiazole (192j)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 49% of the indicated product. The spectral data were given the in previous section.

**3-(Naphthalen-1-yl)-5-phenyl-1,2,4-oxadiazole (192l)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 48% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.10 (d, $J$ = 8.4 Hz, 1H), 8.42 (d, $J$ = 7.1 Hz, 1H), 8.30 (d, $J$ = 7.5 Hz, 2H), 8.03 (d, $J$ = 8.2 Hz, 1H), 7.56 (d, $J$ = 8.1 Hz, 1H), 7.70 (t, $J$ = 7.1 Hz, 1H), 7.58 (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 176.3 (C), 170.8 (C), 135.4 (C), 134.7 (CH), 133.3 (CH), 132.2 (C), 130,9 (CH), 130.6(CH), 130.1 (CH), 129.7 (CH), 129.0 (CH), 127.85 (CH), 127.8 (CH), 126.6 (CH), 125.7 (C), 125.5 (C); MS (ESI, *m/z*): 295.08 $[M+Na]^+$; HRMS (ESI): calcd. for $C_{18}H_{12}N_2NaO$: 295.0847 $[M+Na]^+$; Found: 298.0842.

**5-Pentyl-3-(*p*-tolyl)-1,2,4-oxadiazole (192m)**Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 80% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.87(d, $J$ = 7.9 Hz, 2H), 7.17 (d, J=7.9 Hz, 2H), 2.82 (t, J=7.5 Hz, 2H), 2.30 (s, 3H), 1.77 (m,

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2H), 1.29 (m, 4H), 0.82 (t, *J* = 6.8 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.9 (C), 168.2 (C), 141.3 (C), 129.5 (CH), 127.3 (CH), 124.2 (C), 31.2 ($CH_2$), 26.6 ($CH_2$), 26.4 ($CH_2$), 22.2 ($CH_3$), 21.5 ($CH_2$), 13.8 ($CH_3$); IR (neat): 2956, 2929, 1589, 1568, 1411, 1363, 1180, 116, 902, 829, 740 $cm^{-1}$. MS (ESI, *m/z*): 253.13 $[M+Na]^+$; HRMS (ESI): calcd. for $C_{14}H_{18}N_2NaO$: 253.1317$[M+Na]^+$; Found: 253.1311.

**3-(4-Methoxyphenyl)-5-pentyl-1,2,4-oxadiazole (192n)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 67% of the indicated product. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03 (d, *J* = 8.7 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 3.85 (s, 3H), 2.91 (td, *J* = 2.9 Hz, *J* = 7.5 Hz, 2H), 1.88 (m, 2H), 1.40 (m, 4H), 0.93 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.7 (C), 167.9 (C), 161.8 (C), 128.9 (CH), 119.5 (C), 114.2 (CH), 55.3 ($CH_3$), 31.2 ($CH_2$), 26.6 ($CH_2$), 26.3 ($CH_2$), 22.2 ($CH_2$), 13.8 ($CH_3$); IR (neat): 2956, 2933, 1614, 1591, 1569, 1483, 1423, 1363, 1301, 1251, 1172, 1107, 1029, 900, 839, 752 $cm^{-1}$; MS (ESI, *m/z*): 269.13 $[M+Na]^+$; HRMS (ESI): calcd. for $C_{14}H_{18}N_2NaO_2$: 269.1266 $[M+Na]^+$; Found: 269.1260.

**3-(4-Chlorophenyl)-5-pentyl-1,2,4-oxadiazole (192o)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 76% of the indicated product. $^1$H NMR (400MHz, $CDCl_3$): $\delta$ 7.99 (d, *J* = 8.5 Hz, 1H), 7.98 (d, *J* = 8.6 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 2.90 (m, 2H), 1.85(m, 2H), 1.39 (m, 4H), 0.90 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 180.2 (C),167.4 (C), 137.1 (C), 129.1 (CH), 128.7 (CH), 125.6 (C), 31.1 ($CH_2$), 26.5 ($CH_2$), 26.3 ($CH_2$), 22.2 ($CH_2$), 13.8 ($CH_3$); IR (neat): 2954, 2927, 1591, 1562, 1465, 1407, 1365, 1085, 1008, 904, 839, 785, 744 $cm^{-1}$; MS (ESI, *m/z*): 273.07 $[M+Na]^+$; HRMS (ESI): calcd. for $C_{13}H_{15}N_2ClNaO$: 273.0771 $[M+Na]^+$; Found: 273.0767.

***N,N*-Dimethyl-4-(5-pentyl-1,2,4-oxadiazol-3-yl)aniline (192p)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 79% of the indicated product. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.93 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), 3.02 (s, 3H), 2.90 (t, *J* = 7.6 Hz, 2H), 1.86 (m, 2H), 1.40 (m, 4H), 0.92 (t, *J* = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.3 (C), 168.3 (C), 152.0 (C), 128.6 (CH), 111.8 (CH), 40.2 ($CH_3$), 31.2 ($CH_2$), 26.6 ($CH_2$), 26.4 ($CH_2$), 22.2 ($CH_2$), 13.8 ($CH_3$); MS (ESI, *m/z*): 282.16 $[M+Na]^+$; HRMS (ESI): calcd. for $C_{15}H_{21}N_3NaO$: 282.1582 $[M+Na]^+$; Found: 282.1577.

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**3-(Naphthalen-1-yl)-5-pentyl-1,2,4-oxadiazole (192q)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 52% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.01 (d, $J$ = 9.0 Hz, 1H), 8.30 (d, $J$ = 7.25 Hz, 1H), 8.00 (d, $J$ = 8.2 Hz, 1H), 7.93 (d, $J$ = 8.1 Hz, 1H), 7.67 (t, $J$ = 7.1 Hz, 1H), 7.60 (M, 2H), 3.01 (t, $J$ = 7.9 Hz, 2H), 1.95 (p, 2H), 1.44 (m, 4H), 0.97 (t, $J$ = 6.7 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.1 (C), 168.7 (C), 134.0 (C), 131.7 (CH), 130.7 (C), 129.3 (CH), 128.6 (CH), 127.5 (CH), 126.4 (CH), 126.3 (CH), 125.0 (CH), 124.1 (C), 31.3 (CH2), 26.5 (CH2), 26.4 (CH2), 22.2 (CH2), 13.9(CH3); IR (neat): 2954, 2929, 1579, 1514, 1456, 1352, 1307, 1261, 1145, 1020, 900, 806, 775 cm$^{-1}$; MS (ESI, *m/z*): 289.13 $[M+Na]^+$; HRMS (ESI): calcd. for $C_{17}H_{18}N_2NaO$: 289.1317 $[M+Na]^+$; Found: 289.1311.

**General procedure for the one-pot synthesis of 3-aryl-5-ferrocenyl-1,2,4-oxadiazoles221.**
To a stirred solution of 3-ferrocenylpropynal (**45**) (0.25 mmol) and amidoxime **190** (0.325 mmol) in dioxane (7 mL) was added KOH flakes (0.25 mmol), and the solution was allowed to stir at 100 $^{o}$C under argon for appropriate time. After the reaction was over, the dioxane was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane as the eluent to afford the desired product.

**5-Ferrocenyl-3-phenyl-1,2,4-oxadiazole (221a).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 84% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.16 (m, 2H), 7.52 (m, 3H), 5.08 (s, 2H), 4.56 (s, 2H), 4.22 (s, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.3 (C), 168.7 (CH), 131.0 (CH) 128.8 (CH), 127.6 (CH), 127.2 (C), 71.5 (CH), 70.1 (CH), 69.1 (CH), 66.2 (C); IR (neat): 1595, 1583, 1477, 1444, 1352, 1274, 1139, 1109, 1024, 999, 904, 881, 819, 752 cm$^{-1}$.

**5-Ferrocenyl-3-(*p*-tolyl)-1,2,4-oxadiazole (221b).** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 95% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.04 (d, $J$ = 7.9 Hz, 2H), 7.31 (d, $J$ = 7.9 Hz, 2H), 5.07 (s, 2H), 4.54 (s, 2H), 4.21 (s, 5H), 2.34 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.1 (C), 168.7 (C), 141.3 (C), 129.5 (CH), 127.5 (CH), 124.4 (C), 71.5 (CH), 70.1 (CH), 69.1 (CH), 66.3 (C), 21.6 ($CH_3$); IR (neat): 1595, 1575, 1409, 1346, 1278, 1143, 1103, 1029, 908, 881, 821, 759 cm$^{-1}$; MS (ESI, *m/z*): 344.06 $[M]^+$;HRMS (ESI): calcd. for $C_{19}H_{16}FeN_2O$: 364.0612 $[M]^+$; Found: 364.0607.

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**5-Ferrocenyl-3-(4-methoxyphenyl)-1,2,4-oxadiazole (221c).**Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 85% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.09(d, $J$ = 8.7 Hz, 2H), 7.01(d, $J$ = 8.7 Hz, 2H), 5.06 (s, 2H), 4.53 (s, 2H), 4.20 (s, 5H), 3.87 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 178.9 (C), 168.4 (C), 161.9 (C), 133.9 (CH), 119.7 (C), 114.2 (CH), 71.5 (CH), 70.1 (CH), 69.1 (CH), 66.4 (C), 55.4 ($CH_3$); IR (neat): 1595, 1485, 1417, 1352, 1251, 1172, 1107, 1026, 1002, 900, 877, 817, 765 cm$^{-1}$; MS (ESI, *m/z*): 360.06 $[M]^+$; HRMS (ESI): calcd. for $C_{19}H_{16}FeN_2O_2$: 360.0561 $[M]^+$; Found: 360.0558.

**3-(4-Chlorophenyl)-5-ferrocenyl-1,2,4-oxadiazole (221d** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 90% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.08 (d, $J$ = 8.2 Hz, 2H), 7.47 (d, $J$ = 8.2 Hz, 2H), 5.05 (s, 2H), 4.55 (s, 2H), 4.20 (s, 5H); $^{13}$C NMR (100MHz, $CDCl_3$): $\delta$ 179.6 (C), 167.9 (C), 137.1 (C), 129.1 (CH), 128.9 (CH), 125.7 (C), 71.7 (CH), 70.2 (CH), 69.1 (CH), 65.9 (C); IR (neat): 1591, 1571, 1473, 1404, 1348, 1278, 1143, 108, 1004, 910, 823, 761 cm$^{-1}$; MS (ESI, *m/z*): 364.01 $[M]^+$; HRMS (ESI): calcd. for $C_{18}H_{13}ClFeN_2O$: 364.0065 $[M]^+$; Found: 364.0061.

***N,N*-Dimethyl-4-(5-ferrocenyl-1,2,4-oxadiazol-3-yl)aniline (221e)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 61% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.00 (d, $J$ = 8.8 Hz, 2H), 6.78 (d, $J$ = 8.8 Hz, 2H), 5.06 (s, 2H), 4.53 (s, 2H), 4.21 (s, 5H), 3.05 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 178.4 (C), 169.8 (C), 152.2 (C), 128.7 (CH), 114.5 (C), 111.8 (CH), 71.3 (CH), 70.1 (CH), 69.0 (CH), 66.7 (C), 40.2 ($CH_3$); IR (neat): 1598, 1564, 1487, 1431, 1355, 1280, 1193, 1145, 1103, 1024, 1001, 89, 877, 819, 765 cm$^{-1}$; MS (ESI, *m/z*): 373.09 $[M]^+$; HRMS (ESI): calcd. for $C_{20}H_{19}FeN_3O$: 373.0877 $[M]^+$; Found: 373.0872.

**5-Ferrocenyl-3-(naphthalen-1-yl)-1,2,4-oxadiazole (221f)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 54% of the indicated product. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.99 (d, $J$ = 8.5 Hz, 1H), 8.34 (d, $J$ = 7.1 Hz, 1H), 8.03 (d, $J$ = 8.2 Hz, 1H), 7.95 (d, $J$ = 8.1 Hz, 1H), 7.62 (m, 3H), 5.14 (s, 2H), 4.57 (s, 2H), 4.25 (s, 5H); $^{13}$C NMR (100

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MHz, $CDCl_3$): $\delta$ 178.5 (C), 169.1 (C), 133.9 (C), 131.7 (CH), 130.8 (C), 129.3 (CH), 128.7 (CH), 127.5 (CH), 126.4 (CH), 126.3 (CH), 125.1 (CH), 124.2 (C), 71.7 (CH), 70.2 (CH), 69.2 (CH), 66.2 (C); IR (neat): 1600, 1595, 1577, 1353, 1305, 1261, 1149, 1028, 1002, 904, 879, 808, 777 $cm^{-1}$; MS (ESI, *m/z*): 403.05 $[M+Na]^+$; HRMS (ESI): calcd. for $C_{22}H_{16}FeN_2ONa$: 403.0509 $[M+Na]^+$; Found: 403.0504.

**3-(2-Chlorophenyl)-5-ferrocenyl-1,2,4-oxadiazole (221g).**

Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 79% of the indicated product. $^1H$ NMR (400MHz, $CDCl_3$): $\delta$ 7.95 (dd, *J* = 1.9 Hz, *J* = 7.4 Hz, 1H), 7.56 (dd, *J* = 1.5 Hz, *J* = 7.9 Hz, 1H), 7.43 (m, 2H), 5.09 (s, 2H), 4.57 (s, 2H), 4.23 (s, 5H); $^{13}C$ NMR (100MHz, $CDCl_3$): $\delta$ 177.2 (C), 165.7 (C), 131.7 (C), 129.9 (CH), 129.7 (CH), 128.9 (CH), 125.0 (CH), 124.7 (C), 69.9 (CH), 68.4 (CH), 67.3 (CH), 63.9 (C); IR (neat): 1591, 1566, 1473, 1328, 1274, 1143, 1107, 1026, 1002, 908, 879, 823, 758 $cm^{-1}$; MS (ESI, *m/z*): 364.01 $[M]^+$; HRMS (ESI): calcd. For $C_{18}H_{13}ClFeN_2O$: 364.0065 $[M]^+$; Found: 364.0061.

**5-Ferrocenyl-3-(3-fluorophenyl)-1,2,4-oxadiazole (221h).**

Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 78% of the indicated product. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, *J* = 7.7 Hz, 1H), 7.86 (d, *J* = 9.3 Hz, 1H), 7.48 (q, *J* = 7.8 Hz, 1H), 7.21 (td, *J* = 8.4 Hz, *J* = 2.1 Hz, 1H), 5.07 (s, 2H), 4.55 (s, 2H), 4.21 (s, 5H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 179.7 (C), 167.9 (C),162.9 (d, *J* = 244.5 Hz, C), 130.5 (d, *J* = 33 Hz, CH), 129.3 (d, *J* = 8 Hz, C), 123.2 (d, *J* = 2.7 Hz, CH), 117.9 (d, *J* = 21.3 Hz, CH), 114.6 (d, *J* = 23 Hz, CH), 71.7 (CH), 70.2 (CH), 69.1 (CH), 65.9 (C); IR (neat): 1600, 1585, 1523, 1488, 1415, 1357, 1267, 1201, 1132, 1026, 1001, 877, 858, 821, 798, 763 $cm^{-1}$; MS (ESI, *m/z*): 348.04 $[M]^+$; HRMS (ESI): calcd. for $C_{18}H_{13}FFeN_2O$: 348.0361 $[M]^+$; Found:348.0358.

**3-(Benzo[d][1,3]dioxol-5-yl)-5-ferrocenyl-1,2,4-oxadiazole (221i).**

Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 82% of the indicated product. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.71 (d, *J* = 8.0 Hz, 1H), 7.59 (s, 1H), 6.93 (d, *J* =

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8.0 Hz, 1H), 6.05 (s, 2H), 5.05 (s, 2H), 4.55 (s, 2H), 4.21 (s, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 179.0 (C), 168.3 (C), 149.9 (C), 148.1 (C), 122.4 (CH), 121.1 (C), 108.6 (CH), 107.6 (CH), 101.5 ($CH_2$), 71.5 (CH), 70.1 (CH), 69.1 (CH), 66.2 (C); IR (neat): 1591, 1456, 1325, 1238, 1134, 1103, 1035, 1008, 933, 881, 817, 761 cm$^{-1}$; MS (ESI, *m/z*): 397.03 $[M+Na]^+$; HRMS (ESI): calcd. For $C_{19}H_{14}FeN_2O_3Na$: 397.0251 $[M+Na]^+$; Found: 397.0246.

**5-Ferrocenyl-3-(1H-indol-4-yl)-1,2,4-oxadiazole (221j).**

Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 44% of the indicated product. $^1$H NMR (400 MHz, *d*-DMSO): $\delta$ 11.48 (S, 1H), 7.88-7.10 (m, 5H), 5.1 2(s, 2H), 4.68 (s, 2H), 4.25 (s, 5H); $^{13}$C NMR (100 MHz, *d*-DMSO): $\delta$ 177.8 (C), 168.5 (C), 136.4 (C), 127.0 (CH), 124.9 (C), 120.6 (CH), 120.0 (CH), 117.1 (C), 114.7 (CH), 102.3 (CH), 71.6 (CH), 69.8 (CH), 68.7 (CH), 65.6 (C); IR (neat): 3325, 3101, 1591, 1575, 1523, 1487, 1429, 1346, 1313, 1274, 1191, 1029, 1002, 893, 823, 761 cm$^{-1}$; MS (ESI, *m/z*): 369.06 $[M]^+$; HRMS (ESI): calcd. for $C_{20}H_{15}FeN_3O$: 369.0564 $[M]^+$; Found: 369.0559.

**3,5-Diferrocenyl-1,2,4-oxadiazole (221k)** Purification by flash chromatography (1:9 EtOAc/Hexane) afforded 22% of the indicated product. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 5.07 (s, 2H), 4.98 (s, 2H), 4.54 (s, 2H), 4.44 (s, 2H), 4.21 (s, 5H), 4.17 (s, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 178.4 (C), 170.4 (C), 71.4(CH), 70.4 (C), 70.2 (CH), 70.1 (CH), 69.8 (CH), 69.1 (CH), 68.4 (CH), 66.4 (C); IR (neat):1593, 1556, 1458, 1380, 1315, 1276, 1159, 1105, 1024, 999, 881, 813, 769 cm$^{-1}$; MS (ESI, *m/z*): 438.01 $[M]^+$; HRMS (ESI): calcd. for $C_{22}H_{18}Fe_2N_2O$: 438.0118 $[M]^+$; Found: 438.0113.

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