# Synthesis and structural characterisation of 2,4-bis(5-aryl-1,3,4-oxdiazol-2-yl) pyridine derivatives <br> XiaoQing Wang, ZhiGang Zhao*, XingLi Liu and WeiJie Li <br> College of Chemistry and Environmental Protection Engineering, Southwest University for Nationalities, Chengdu 610041, P.R. China 


#### Abstract

A convenient synthesis of 2,4-bis (5-aryl-1,3,4-oxdiazol-2-yl) derivatives of pyridine by the $\mathrm{POCl}_{3}$-mediated cyclodehydration of a variety of pyridine-2,4-dicarboxylic dihydrazides has been developed. The 20 novel intermediates and target molecules were characterised by IR, ${ }^{1} \mathrm{H}$ NMR, MS and elemental analysis.


Keywords: pyridine-2,4-dicarboxylic acid, pyridine-2,4-dicarboxylic dihydrazides, 2,4-bis(5-aryl-1,3,4-oxdiazol-2-yl)pyridine

1,3,4-Oxadiazoles are an important class of heterocyclic compounds possessing a wide range of biological activities. The interest in their synthesis stems from their anti-inflammatory, ${ }^{1}$ antimicrobial, ${ }^{2}$ antifungal, ${ }^{3}$ anticonvulsant, ${ }^{4}$ antihypertensive ${ }^{5}$ and anticancer, ${ }^{6}$ insecticide, ${ }^{7}$ enzyme inhibitory ${ }^{8}$ and kinase ${ }^{9}$ activities. Substituted 1,3,4-oxdiazole heterocycles are also useful intermediates in organic synthesis ${ }^{11}$ and an important scaffold in medicinal chemistry. ${ }^{12}$ Further, they have proved to be useful in material science for their fluorescence and electrochromic properties. ${ }^{13,14}$ Compounds with a 1,3,4-oxdiazole core have also been widely employed as electron transporting and hole-blocking materials. ${ }^{15}$

The present investigation describes many bisheterocyclic compounds endowed with potentially significant bioactivities. In studies by Holla et al. ${ }^{16}$, some bis-1,2,4-triazole compounds were found to be active against dozens of cancer cell lines. In addition, bisoxadiazoles show good electronic transmission performance and are widely used in organic electroluminesent materials. ${ }^{17}$ Furthermore, it has been reported that many biological active natural and synthetic products have interesting molecular symmetry. ${ }^{18}$ It is also observed that incorporation of more active structures into the same molecule augments the biological activities considerably. ${ }^{19}$

Prompted by these observations and in continuation of our attempt to prepare new heterocyclic compounds with anticipated biological activity, which can be used in the pharmaceutical field, we designed the synthesis of a series of novel pyridine-2,4-dicarboxylic dihydrazides and 2,4-bis(5-aryl-1,3,4-oxadiazol-2-yl)pyridines starting from a substituted benzoic acid and pyridine-2,4-dicarboxylic acid. The synthesis and characterisation of the newly synthesised compounds are now presented. These compounds were synthesised according to Scheme 1.

## Result and discussion

Formation of the intermediates $\mathbf{2}$ and $\mathbf{3}$ proceeded cleanly in nearly quantitative yields by microwave irradiation. ${ }^{19}$ The pyridine-2,4-dihydrazides were synthesised by acylation of substituted benzoylhydrazides with pyridine-2,4-dicarbonyl chloride in the presence of pyridine. The reaction proceeded in good yields ( $70-85 \%$ ) and was moderated by ice water cooling. Compared with the reported research ${ }^{20}$, which employed the reaction of a pyridine dihydrazide with a substituted benzoyl chloride in THF-pyridine solution, the reactants in this approach both possess good solubility. In addition, the solvent $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ is less toxic than THF and the amount of pyridine is significantly reduced.

The constitution of the pyridine-2,4-dihydrazides $\mathbf{6 a - j}$ was confirmed by their IR, ${ }^{1} \mathrm{H}$ NMR and mass spectra in addition to elemental analysis. The IR spectrum of compound 6a showed absorption bands at 3233 and $1694 \mathrm{~cm}^{-1}$ corresponding to the NH and $\mathrm{C}=\mathrm{O}$ groups, respectively. The IR spectra of other

[^0]bishydrazides of the series showed similar absorption bands. The ${ }^{1} \mathrm{H}$ NMR spectra of $\mathbf{6 a}$ showed four sharp singlets at $\delta$ $10.62,10.69,10.79$ and 11.08 corresponding to the four NH protons. The pyridine protons resonated at $\delta 9.38,8.53$ and 8.10 integrating for three protons. Two multiplets in the region $\delta 7.91-7.96$ and $\delta 7.52-7.67$ are attributed to the aromatic protons. The ${ }^{1} \mathrm{H}$ NMR spectra of the other compounds exhibited similar chemical shift ranges. The mass spectra and elemental analyses of compounds $\mathbf{6 a - j}$ were in full agreement with their structures.

The synthesis of target scaffolds 7a-i, (Scheme 1) was catalysed by $\mathrm{POCl}_{3}$ as dehydrating agent and gave the products in good yields ( $67-82 \%$ ). The IR spectrum of compound 7a showed absorption bands at 1539 and $1076 \mathrm{~cm}^{-1}$ corresponding to the $\mathrm{C}=\mathrm{N}$ and $\mathrm{C}-\mathrm{O}-\mathrm{C}$ groups respectively of the oxdiazole ring. The absence of absorption bands at 3233 and $1694 \mathrm{~cm}^{-1}$ due to the NH and $\mathrm{C}=\mathrm{O}$ groups of the starting dihydrazide clearly indicated the formation of cyclised products. In the ${ }^{1} \mathrm{H}$ NMR spectrum of compound $7 \mathbf{a}$, the the pyridine group resonated as three signals at $\delta 9.10,8.82$ and 8.34 , respectively. The aromatic protons appeared as two multiplets in the region $\delta 8.17-8.25$ and $\delta 7.68-7.69$ integrating for 10 protons. The structures of newly synthesised bisoxdiazoles were also confirmed by recording their mass spectra and elemental analysis.

The biological activities of $\mathbf{7 a} \mathbf{a} \mathbf{j}$ are currently under further investigation.

## Experimental

Melting points were determined on a micro-melting point apparatus and the thermometer was uncorrected. IR spectra were obtained on 1700 Perkin-Elmer FTIR using KBr disks. ${ }^{1} \mathrm{H}$ NMR spectra were recorded on a Varian INOVA 400 MHz spectrometer using DMSO- $d_{6}$ as solvent and TMS as internal standard. Mass spectra were determined on Finnigan LCQ ${ }^{\text {DECA }}$ instrument. Elemental analysis was performed on a Carlo-Erba-1106 autoanalyser. Microwave irradiation was carried out with a MCL-3 microwave oven (very safe, reliable) at full power ( 700 W ), which was modified from domestic microwave oven and tested to conform to the performance index before use. All solvents were purified before use. The ${ }^{1} \mathrm{H}$ NMR spectra of the hydrazides $\mathbf{6 a} \mathbf{-} \mathbf{j}$ and the 1,3,4-oxadiazoles 7a-j are given in the Electronic Supplementary Information.

Preparation of benzoylhydrazides (3a-j) ${ }^{19}$
The aromatic acid ( 5 mmol ), ethanol ( 15 mL ) and thionyl chloride $(0.2 \mathrm{~mL})$ were placed in a dried round-bottomed flask and the mixture was subjected to microwave irradition ( 75 W ) for 4 min . On completion of the reaction, the mixture was cooled to room temperature. The excess thionyl chloride was removed. Then the reaction mixture was added to $85 \%$ hydrazine hydrate ( 2 mL ) and subjected to microwave irradiation ( 75 W ) for 3 min . The mixture was evaporated to give the crude product. The crude product was recrystallised from ethanol to give a pure sample.

Preparation of pyridine-2,4-dicarboxylic dihydrazides (6a-j)
Compound 3 ( 3 mmol ), dichloromethane ( 10 mL ) and pyridine $(0.2 \mathrm{~mL})$ were placed in a dried round-bottomed flask and the mixture was put in a beaker which was filled with ice water. A solution of $\mathbf{5}$


Scheme 1
$(1 \mathrm{mmol})$ in dichloromethane $(5 \mathrm{~mL})$ was added slowly to the mixture and a solid was obtained. After the addition was complete, the reaction mixture was kept for 2 h . The solid was collected by suction filtration and washed with cold ethanol. The crude product was recrystallised to give a pure sample. The progress of the reaction was monitored by TLC. The physical and spectra data of the compounds $\mathbf{6 a - j}$ are as follows.

6a: White solid, yield $85 \%$, m.p. $114-116{ }^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.08(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.79(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.69(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.62(1 \mathrm{H}$, s, NH), $8.93(1 \mathrm{H}, \mathrm{d}, J=5.2 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.53(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.10(1 \mathrm{H}, \mathrm{dd}, J=1.6,4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.91-7.96(4 \mathrm{H}, \mathrm{m}$, $\mathrm{ArH}), 7.52-7.67(6 \mathrm{H}, \mathrm{m}, \mathrm{ArH})$; IR (KBr, $\left.\mathrm{cm}^{-1}\right): 3233,3046,1694$, 1651, 1569, 1523, 872; ESI-MS m/z (\%): 829 [(2M+23) ${ }^{+}$, 100]. Anal. Calcd for $\mathrm{C}_{21} \mathrm{H}_{17} \mathrm{~N}_{5} \mathrm{O}_{4}$; C, 62.53; H, 4.25; N, 17.36. Found; C, 62.37; H, 4.26; N, 17.22\%.

6b: White solid, yield $77 \%$, m.p. $136-138{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.36(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.81(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.21(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.17(1 \mathrm{H}$, $\mathrm{s}, \mathrm{NH}), 8.90(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.51(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.07(1 \mathrm{H}$, dd, $J=1.6,4.8 \mathrm{~Hz}$, pyridine H-5), $7.79-7.83(2 \mathrm{H}, \mathrm{m}$, ArH), 7.57-7.63 (2H, m, ArH), 7.10-7.19 (4H, m, ArH), 3.90 ( $6 \mathrm{H}, \mathrm{s}$, $\mathrm{OCH}_{3}$ ); IR (KBr, cm ${ }^{-1}$ ): 3269, 2977, 1696, 1648, 1598, 1479, 1242, 758; ESI-MS m/z (\%): 462 [(M-1) $\left.{ }^{-}, 100\right]$. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{6}$; C, 59.61; H, 4.57; N, 15.11. Found; C, 59.38; H, 4.56; N, $15.15 \%$.
6c: White solid, yield $74 \%$, m.p. $117-119{ }^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.09(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.80(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.65(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.57(1 \mathrm{H}$, s, NH), $8.94(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.52(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.09(1 \mathrm{H}$, dd, $J=1.6,4.8 \mathrm{~Hz}$, pyridine H-5), $7.73-7.76(4 \mathrm{H}, \mathrm{m}$, $\mathrm{ArH}), 7.41-7.43(4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 2.39\left(6 \mathrm{H}, \mathrm{s}, \mathrm{CH}_{3}\right)$; IR $\left(\mathrm{KBr}, \mathrm{cm}^{-1}\right)$ : 3237, 3036, 1693, 1651, 1518, 816, 737, 682; ESI-MS m/z (\%): 430 [(M-1)-, 100]. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{4} ; \mathrm{C}, 64.03 ; \mathrm{H}, 4.91$; N, 16.23. Found; C, 63.85 ; H, 4.90 ; N, $16.18 \%$.

6d: White solid, yield $83 \%$, m.p. $244-245^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.02(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.72(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.59(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.53(1 \mathrm{H}$, $\mathrm{s}, \mathrm{NH}), 8.93(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.51(1 \mathrm{H}, \mathrm{s}$, pyridine
$\mathrm{H}-3), 8.09(1 \mathrm{H}, \mathrm{dd}, J=1.6,4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.83-7.86(4 \mathrm{H}, \mathrm{m}$, ArH), $7.34(4 \mathrm{H}, \mathrm{d}, J=8.0 \mathrm{~Hz}, \mathrm{ArH}), 2.39\left(6 \mathrm{H}, \mathrm{s}, \mathrm{CH}_{3}\right)$; IR $\left(\mathrm{KBr}, \mathrm{cm}^{-1}\right.$ ): 3238, 3033, 1695, 1653, 1499, 839, 744, ESI-MS m/z (\%): 430 [(M-1)-, 100]. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{4} ; \mathrm{C}, 64.03$; H, 4.91; N, 16.23. Found; C, 63.88; H, 4.89; N, $16.28 \%$.

6e: White solid, yield $79 \%$, m.p. $261-262{ }^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.12(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.83(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.81(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.73(1 \mathrm{H}$, $\mathrm{s}, \mathrm{NH}), 8.94(1 \mathrm{H}, \mathrm{d}, J=5.2 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.52(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.10(1 \mathrm{H}, \mathrm{dd}, J=1.6,4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.94-7.97(4 \mathrm{H}, \mathrm{m}$, $\mathrm{ArH}), 7.61-7.64(4 \mathrm{H}, \mathrm{m}, \mathrm{ArH})$; $\mathrm{IR}\left(\mathrm{KBr}, \mathrm{cm}^{-1}\right): 3234,3024,1692$, 1651, 1599, 1564, 1487, 1453, 741; ESI-MS m/z (\%): 470[(M-1) ${ }^{-}$, 100]. Anal. Calcd for $\mathrm{C}_{21} \mathrm{H}_{15} \mathrm{Cl}_{2} \mathrm{~N}_{5} \mathrm{O}_{4} ; \mathrm{C}, 53.41 ; \mathrm{H}, 3.20 ; \mathrm{N}, 14.83$. Found; C, 53.25; H, 3.21; N, $14.90 \%$.

6f: White solid, yield $81 \%$, m.p. $228-230{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.01(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.73(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.54(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.47(1 \mathrm{H}$, $\mathrm{s}, \mathrm{NH}), 8.93(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.51(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.08(1 \mathrm{H}$, dd, $J=1.6,4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.91-7.94(4 \mathrm{H}, \mathrm{m}$, ArH), 7.05-7.08 (4H, m, ArH), 3.84( $6 \mathrm{H}, \mathrm{s}, \mathrm{OCH}_{3}$ ); IR ( $\mathrm{KBr}, \mathrm{cm}^{-1}$ ): 3226, 2976, 1693, 1648, 1571, 1519, 1252, 741; ESI-MS m/z (\%): $949\left[(2 \mathrm{M}+23)^{+}, 100\right]$. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{6} ; \mathrm{C}, 59.61 ; \mathrm{H}, 4.57$; N, 15.11. Found; C, 59.48 ; H, 4.58; N, $15.15 \%$.

6g: White solid, yield $72 \%$, m.p. $230-232{ }^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.21(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.91(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.67(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.58(1 \mathrm{H}$, $\mathrm{s}, \mathrm{NH}), 8.98(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.65(1 \mathrm{H}, \mathrm{s}$, pyridine H-3), 8.41-8.47 (2H, m, ArH, pyridine H-5), 8.01-8.17 (5H, m, ArH), $7.59-7.76(8 \mathrm{H}, \mathrm{m}, \mathrm{ArH})$; IR (KBr, $\left.\mathrm{cm}^{-1}\right): 3344,3190,3047,1703$, 1602, 1478, 778, 659; ESI-MS m/z (\%): 502 [(M-1)- 100]. Anal. Calcd for $\mathrm{C}_{29} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{4} ; \mathrm{C}, 69.18 ; \mathrm{H}, 4.20 ; \mathrm{N}, 13.91$. Found; C, 69.38; H, 4.21; N, 13.87\%.

6h: White solid, yield $81 \%$, m.p. $285-287{ }^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.12(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.84(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.81(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.73(1 \mathrm{H}$, $\mathrm{s}, \mathrm{NH}), 8.94(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.51(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.09(1 \mathrm{H}, \mathrm{dd}, J=1.6,4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5)$, $7.86-7.89(4 \mathrm{H}, \mathrm{m}$, ArH), 7.75-7.78 (4H, m, ArH); IR (KBr, $\mathrm{cm}^{-1}$ ): 3205, 2980, 1690,

1635, 1599, 1554, 1463, 1073, 742; ESI-MS m/z (\%): 560 [(M-1)-, 100]. Anal. Calcd for $\mathrm{C}_{21} \mathrm{H}_{15} \mathrm{Br}_{2} \mathrm{~N}_{5} \mathrm{O}_{4}$; C, 44.95; H, 2.69; N, 12.48. Found; C, 44.80; H, 2.68; N, 12.45\%.
6i: White solid, yield $78 \%$, m.p. $202-203{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.41(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.86(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.26(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.23(1 \mathrm{H}$, $\mathrm{s}, \mathrm{NH}), 8.91(1 \mathrm{H}, \mathrm{d}, J=5.2 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.54(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.10(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.78-7.84(2 \mathrm{H}, \mathrm{m}, \mathrm{ArH})$, 7.51-7.55 ( $2 \mathrm{H}, \mathrm{m}, \mathrm{ArH}$ ), 7.08-7.22 (4H, m, ArH), 4.21-4.28 (4H, m, $\mathrm{OCH}_{2}$ ), 1.42-1.47 ( $6 \mathrm{H}, \mathrm{m}, \mathrm{CH}_{3}$ ); IR ( $\mathrm{KBr}, \mathrm{cm}^{-1}$ ): 3221, 2981, 2893, 1654, 1604, 1540, 1392, 760; ESI-MS m/z (\%): 983 [(2M+1)+, 100]. Anal. Calcd for $\mathrm{C}_{25} \mathrm{H}_{25} \mathrm{~N}_{5} \mathrm{O}_{6} ; \mathrm{C}, 61.09 ; \mathrm{H}, 5.13 ; \mathrm{N}, 14.25$. Found; C, 61.32; H, 5.12; N, 14.22\%.

6j: White solid, yield $70 \%$, m.p. $270-271^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $11.09(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.79 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.74(1 \mathrm{H}, \mathrm{s}, \mathrm{NH}), 10.67(1 \mathrm{H}, \mathrm{s}$, $\mathrm{NH}), 8.95(1 \mathrm{H}, \mathrm{d}, J=5.2 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.55(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.11(1 \mathrm{H}, \mathrm{dd}, J=1.6,4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.99-8.06(4 \mathrm{H}, \mathrm{m}$, ArH ), 7.74-7.86 ( $8 \mathrm{H}, \mathrm{m}, \mathrm{ArH}$ ), 7.41-7.54 (6H, m, ArH); IR (KBr, $\left.\mathrm{cm}^{-1}\right): 3225,3034,1692,1649,1562,1523,854,739,686$; ESI-MS $\mathrm{m} / \mathrm{z}(\%): 1133\left[(2 \mathrm{M}+23)^{+}, 100\right]$. Anal. Calcd for $\mathrm{C}_{33} \mathrm{H}_{25} \mathrm{~N}_{5} \mathrm{O}_{4} ; \mathrm{C}, 71.34$; H, 4.54; N, 12.61. Found; C, 71.11; H, 4.55; N, $12.58 \%$.

Preparation of 2,4-bis(5-aryl-1,3,4-oxadiazol-2-yl)pyridines (7a-j) A mixture of compound $6(1 \mathrm{mmol})$ and phosphorus oxychloride ( 10 mL ) was heated under reflux for 15 h . Excess phosphorus oxychloride was then distilled off and the residue was poured onto crushed ice with vigorous stirring. The resulting solid was washed with cold water, dilute $\mathrm{NaHCO}_{3}$ solution and then recrystallised from a mixture of dimethylformamide and water. The characterisation data of title compounds $\mathbf{7 a}-\mathbf{j}$ are as follows.
2,4-Bis[5-phenyl-1,3,4-oxadiazol-2-yl]pyridine (7a): Green solid, yield $80 \%$, m.p. $220-222{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $9.10(1 \mathrm{H}, \mathrm{d}$, $J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.82(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.34(1 \mathrm{H}, \mathrm{d}$, $J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 8.17-8.25(4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 7.68-7.69(6 \mathrm{H}, \mathrm{m}$, ArH); IR (KBr, $\mathrm{cm}^{-1}$ ): 3060, 1604, 1539, 1442, 1076, 775, 701; ESI-MS $m / z(\%): 368\left[(M+1)^{+}, 70\right]$. Anal. Calcd for $\mathrm{C}_{21} \mathrm{H}_{13} \mathrm{~N}_{5} \mathrm{O}_{2} ; \mathrm{C}$, 68.66; H, 3.57; N, 19.06. Found; C, 68.45; H, 3.56; N, $19.11 \%$.

2,4-Bis[5-(2-methoxyphenyl)-1,3,4-oxadiazol-2-yl]pyridine (7b): Brown solid, yield $70 \%$, m.p. $166-168{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): 9.08 $(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.73(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.26$ ( $1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine H-5), 8.04-8.08 ( $2 \mathrm{H}, \mathrm{m}, \mathrm{ArH}$ ), 7.61-7.63 $(2 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 7.33-7.36(4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 3.97\left(6 \mathrm{H}, \mathrm{s}, \mathrm{OCH}_{3}\right)$; IR (KBr, $\left.\mathrm{cm}^{-1}\right): 3072,2933,1599,1533,1467,1380,1257,1014,756 ;$ ESI-MS $m / z(\%): 428\left[(M+1)^{+}, 50\right]$. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{17} \mathrm{~N}_{5} \mathrm{O}_{4} ;$ C, 64.63; H, 4.01; N, 16.39. Found; C, 64.82; H, 4.02; N, $16.36 \%$.

2,4-Bis[5-(3-methylphenyl)-1,3,4-oxadiazol-2-yl]pyridine (7c): Green solid, yield $75 \%$, m.p. $155-156{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): 9.00 $(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.81$ ( 1 H , s, pyridine $\mathrm{H}-3$ ), 8.35 ( $1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5$ ), $8.02-8.05$ ( $4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}$ ), $7.39-7.43$ $(4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 2.50\left(6 \mathrm{H}, \mathrm{s}, \mathrm{CH}_{3}\right)$; IR ( $\mathrm{KBr}, \mathrm{cm}^{-1}$ ): 3058, 2921, 1601, 1541, 1471, 1377, 1201, 1082, 731; ESI-MS m/z (\%): $791\left[(2 \mathrm{M}+1)^{+}\right.$, 60]. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{17} \mathrm{~N}_{5} \mathrm{O}_{2} ; \mathrm{C}, 69.86 ; \mathrm{H}, 4.33 ; \mathrm{N}, 17.71$. Found; C, 70.08; H, 4.34; N, 17.68\%.
2,4-Bis[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]pyridine (7d): Brown solid, yield $80 \%$, m.p. $178-179^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): 9.08 $(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.80(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.32$ ( $1 \mathrm{H}, \mathrm{d}, J=4.8$, pyridine $\mathrm{H}-5$ ), 8.06-8.14 ( $4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}$ ), 7.49 ( $4 \mathrm{H}, \mathrm{d}$, $J=8.0, \mathrm{ArH}), 2.38\left(6 \mathrm{H}, \mathrm{s}, \mathrm{CH}_{3}\right) ; \mathrm{IR}\left(\mathrm{KBr}, \mathrm{cm}^{-1}\right): 3033,2921,1608$, 1533, 1492, 1379, 1081, 737; ESI-MS $m / z(\%): 813$ [(2M+23)+ 65$]$. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{17} \mathrm{~N}_{5} \mathrm{O}_{2} ; \mathrm{C}, 69.86 ; \mathrm{H}, 4.33 ; \mathrm{N}, 17.71$. Found; C, 70.05; H, 4.30; N, 17.66\%.

2,4-Bis[5-(4-chlorphenyl)-1,3,4-oxadiazol-2-yl]pyridine (7e): Brown solid, yield $82 \%$, m.p. $267-268{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $9.00(1 \mathrm{H}, \mathrm{d}$, $J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.63(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.36(1 \mathrm{H}, \mathrm{dd}$, $J=1.6,4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.75(4 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}, \mathrm{ArH}), 7.63$ $(4 \mathrm{H}, \mathrm{d}, J=8.8 \mathrm{~Hz}, \mathrm{ArH})$; IR ( $\mathrm{KBr}, \mathrm{cm}^{-1}$ ): $3004,1600,1534,1476$, 1274, 1090, 835, 732; ESI-MS m/z (\%): $436\left[(\mathrm{M}+1)^{+}, 40\right]$. Anal. Calcd for $\mathrm{C}_{21} \mathrm{H}_{11} \mathrm{Cl}_{2} \mathrm{~N}_{5} \mathrm{O}_{2}$; C, 57.82; H, 2.54; N, 16.05. Found; C, $57.68 ; \mathrm{H}, 2.53 ; \mathrm{N}, 16.01 \%$.
2,4-Bis[5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl]pyridine (7f): Brown solid, yield $76 \%$, m.p. $210-212{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): 8.98 $(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.79(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.32$ $(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-5), 7.82(4 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}, \mathrm{ArH}), 7.03$ $(4 \mathrm{H}, \mathrm{d}, J=8.8 \mathrm{~Hz}, \mathrm{ArH}), 3.85\left(6 \mathrm{H}, \mathrm{s}, \mathrm{OCH}_{3}\right)$; IR $\left(\mathrm{KBr}, \mathrm{cm}^{-1}\right): 3066$, 2932, 1605, 1492, 1428, 1379, 1255, 1172, 1021, 838; ESI-MS m/z (\%): $428\left[(\mathrm{M}+1)^{+}, 58\right]$. Anal. Calcd for $\mathrm{C}_{23} \mathrm{H}_{17} \mathrm{~N}_{5} \mathrm{O}_{4} ; \mathrm{C}, 64.63 ; \mathrm{H}, 4.01$; N, 16.39. Found; C, 64.75; H, 4.00; N, 16.42\%.

2,4-Bis/5-(1-naphthyl)-1,3,4-oxadiazol-2-yllpyridine (7g): Brown solid, yield $74 \%$, m.p. $190-192{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $9.00(1 \mathrm{H}, \mathrm{d}$, $J=4.8 \mathrm{~Hz}$, pyridine H-6), 8.79-8.83 ( $2 \mathrm{H}, \mathrm{m}, \mathrm{ArH}$, pyridine H-5), 8.57 $(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.04-8.26(7 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 7.65-7.76(6 \mathrm{H}, \mathrm{m}$, ArH ); IR (KBr, $\mathrm{cm}^{-1}$ ): 3054, 1666, 1568, 1520, 1451, 1197, 769; ESI-MS m/z (\%): $468\left[(\mathrm{M}+1)^{+}, 50\right]$. Anal. Calcd for $\mathrm{C}_{29} \mathrm{H}_{17} \mathrm{~N}_{5} \mathrm{O}_{2} ; \mathrm{C}$, 74.51; H, 3.67; N, 14.98. Found; C, 74.72; H, 3.68; N, 14.94\%.

2,4-Bis[5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl]pyridine (7h): Green solid, yield $78 \%$, m.p. $226-228^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $9.00(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.63(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3)$, $8.36(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine H-5), $8.24(2 \mathrm{H}, \mathrm{d}, J=8.0 \mathrm{~Hz}, \mathrm{ArH})$, 8.16 ( $2 \mathrm{H}, \mathrm{d}, J=8.0 \mathrm{~Hz}, \mathrm{ArH}$ ), $7.67(4 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}, \mathrm{ArH})$; IR (KBr, $\mathrm{cm}^{-1}$ ): 3066, 1597, 1534, 1474, 1267, 1076, 834; ESI-MS m/z (\%): $524\left[(\mathrm{M}+1)^{+}, 40\right]$. Anal. Calcd for $\mathrm{C}_{21} \mathrm{H}_{11} \mathrm{Br}_{2} \mathrm{~N}_{5} \mathrm{O}_{2} ; \mathrm{C}, 48.03 ; \mathrm{H}, 2.11$; N, 13.34. Found; C, 47.91 ; H, 2.12; N, $13.31 \%$.

2,4-Bis[5-(2-ethoxyphenyl)-1,3,4-oxadiazol-2-yl]pyridine (7i): Brown solid, yield $67 \%$, m.p. $172-174{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): 9.00 $(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.50(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 7.94$ ( 1 H , dd, $J=1.6,4.8 \mathrm{~Hz}$, pyridine H-5), $7.85-7.90(2 \mathrm{H}, \mathrm{m}, \mathrm{ArH})$, 7.63-7.69 ( $2 \mathrm{H}, \mathrm{m}, \mathrm{ArH}$ ), 7.16-7.26 (4H, m, ArH), 4.17-4.25 (4H, m, $\mathrm{OCH}_{2}$ ), 1.23-1.31 ( $6 \mathrm{H}, \mathrm{m}, \mathrm{CH}_{3}$ ); IR (KBr, cm ${ }^{-1}$ ): 3067, 2982, 1604, 1535, 1467, 1398, 1240, 1039, 756; ESI-MS m/z (\%): $456\left[(\mathrm{M}+1)^{+}\right.$, 100]. Anal. Calcd for $\mathrm{C}_{25} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{4} ; \mathrm{C}, 65.93 ; \mathrm{H}, 4.65 ; \mathrm{N}, 15.38$. Found; C, 66.12; H, 4.64; N, 15.33\%.
2,4-Bis[5-(4-biphenyl)-1,3,4-oxadiazol-2-yl]pyridine (7j): Green solid, yield $70 \%$, m.p. $204-205{ }^{\circ} \mathrm{C}$; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz ): $9.02(1 \mathrm{H}, \mathrm{d}$, $J=4.8 \mathrm{~Hz}$, pyridine $\mathrm{H}-6), 8.81(1 \mathrm{H}, \mathrm{s}$, pyridine $\mathrm{H}-3), 8.32(1 \mathrm{H}, \mathrm{d}$, $J=4.8 \mathrm{~Hz}$, pyridine H-5), $7.95-8.01(4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 7.83(4 \mathrm{H}, \mathrm{d}$, $J=8.0 \mathrm{~Hz}, \mathrm{ArH}), 7.69-7.76(4 \mathrm{H}, \mathrm{m}, \mathrm{ArH}), 7.46-7.56(6 \mathrm{H}, \mathrm{m}, \mathrm{ArH})$; IR (KBr, $\mathrm{cm}^{-1}$ ): 3059, 1602, 1476, 1272, 1081, 848, 735; ESI-MS $\mathrm{m} / \mathrm{z}(\%): 520\left[(\mathrm{M}+1)^{+}, 45\right]$. Anal. Calcd for $\mathrm{C}_{33} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{2} ; \mathrm{C}, 76.29 ; \mathrm{H}$, 4.07; N, 13.48. Found; C, 76.50; H, 4.09; N, 13.44\%.

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