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# **Graphical Abstract**

An effective and clean aerobic oxidative method for the synthesis of 2,6-disubstituted benzobisoxazole using the free radical catalysis was obtained. 2, 6-Di(pyridin-4-yl)-benzo[1,2-d:4,5-d']bisoxazole was synthesized and characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, elemental analysis, UV-vis and emission spectroscopy, as well as by single-crystal X-ray crystallography. In the crystal structure, a self-assembled two-dimensional (2-D) layer supramolecular frameworks is formed with the help of intermolecular hydrogen bonds and  $\pi \cdots \pi$ stacking interactions. On the basis of experimental results, a plausible reaction mechanism of 2,2'-disubstituted benzoxdiazoles with 4-methoxy-TEMPO as the catalyst is proposed. To obtain more insights into the structure and bonding, DFT calculations were performed. The obtained calculation results were compared with the X-ray diffraction data. The electronic transitions and spectral features of 5a and 5b were discussed by TD-DFT calculations. In addition, the noncovalent interactions among compounds have been also analyzed using Hirshfeld surface analysis.



# Synthesis, characterization, spectral property, Hirshfeld surface analysis and TD/DFT calculations of 2, 6-disubstituted benzobisoxazoles

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# ABSTRACT

An effective and clean aerobic oxidative method for the synthesis of 2,6-disubstituted benzobisoxazole radical catalysis obtained. using the free was 2. 6-Di(pyridin-4-yl)-benzo[1,2-d:4,5-d']bisoxazole was synthesized and characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, elemental analysis, UV-vis and emission spectroscopy, as well as by single-crystal X-ray crystallography. In the crystal structure, a self-assembled two-dimensional (2-D) layer supramolecular frameworks is formed with the help of intermolecular hydrogen bonds and  $\pi \cdots \pi$  stacking interactions. On the basis of experimental results, a plausible reaction mechanism of 2,2'-disubstituted benzoxdiazoles with 4-methoxy-TEMPO as the catalyst is proposed. To obtain more insights into the structure and bonding, DFT calculations were performed. The obtained calculation results were compared with the X-ray diffraction data. The electronic transitions and spectral features of 5a and 5b were discussed by TD-DFT calculations. In addition, the noncovalent interactions among compounds have been also analyzed using Hirshfeld surface analysis.

**Keywords**: 4-Methoxy-TEMPO Free Radical; Spectroscopic studies; Density functional theory; Hirshfeld surface analysis; 2,6-disubstituted benzobisoxazole; X-ray crystal structure

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#### 1. Introduction

Plane heterocycles define an important class of chemical entities in life science research. Benzoxazole are benzoheterocyclic compounds containing nitrogen and oxygen atoms in a molecular structure. Benzoxazole derivatives possess rigid backbone and high conjugated system. Such as this kind of five-membered heterocyclic ring compounds always show good biological and therapeutic activities, for example antiproliferative [1], anti-inflammatory, and the efficacy of kill the plant virus [2] and coordination properties [3]. Besides they also used widely in the field of medicine [4,5], pesticide, coordination catalysis and in synthetic pharmaceutical [6] and agrochemical compounds [7]. Benzoxazole structure also has significant influence on the fluorescence of conjugate system [8,9], is considered to be the potential materials of electron transfer in polymer light-emitting diode and hole conduction block [10].

Compared with benzoxazoles, 2, 6-disubstituted benzobisoxazoles have larger conjugated systems. Herein, an effective and more eco-friendly new aerobic approach for the synthesis of 2, 6-disubstituted benzobisoxazole using a one-pot reaction of an organic catalyst is reported (Scheme aminoxyl radical as the 1). Especially, 2, 6-di(pyridin-4-yl)-benzo[1, 2-d:4, 5-d']bisoxazole (5a) was characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, UV-visible and photoluminescence spectroscopy, as well as by single-crystal X-ray crystallography. On the basis of experimental results, a plausible reaction mechanism for 4-methoxy-2,2,6,6-tetramethyl-1-piperidinyloxy (4-methoxy-TEMPO) catalyzed aerobic oxidative synthesis of 2, 2'-disubstituted benzoxdiazoles is proposed. Moreover, DFT calculations have been also carried out to corroborate the experimental results. DFT coupled with TD-DFT calculations ascertain the nature of orbitals involved in transition processes and to correlate the structural parameters. In addition, by means of Hirshfeld surface analysis are useful for the understanding of the noncovalent forces and for rationalizing their influence in the crystal packing.

# 2. Experimental Section

### 2.1 Materials and physical measurements

Pyrocatechol and pyridine-4-carbaldehyde were purchased from Alfa Aesar. All chemicals were of analytical reagent grade and were used without further purification. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured on Mercury Plus (400 MHz) spectrometers. Chemical shifts

of <sup>1</sup>H NMR were expressed in parts per million relative to the singlet (d = 7.26) for CDCl<sub>3</sub>. Chemical shifts of <sup>13</sup>C NMR were expressed in parts per million relative to the central line of the triplet (d = 77.0 ppm) for CDCl<sub>3</sub> and TMS as internal standard. HRMS spectra were obtained with a Bruker APEX II FT-MS instrument using CD<sub>2</sub>Cl<sub>2</sub> as solvent. UV/Vis spectra were recorded on a Shimadzu UV-2550 spectrometer. The fluorescence spectra were taken on a 970 CRT spectrofluorometer (Spectro, Shanghai/China) with 370 nm excitation. Single-crystal X-ray structures were determined using an Agilent SuperNova Dual area detector diffractometer. Elemental analysis was performed on an Elementar Vario EL Elemental Analysis instrument.





Scheme 1 The detailed synthetic route of the target molecules 5a-5d.

**4, 5-dimethoxycyclohexa-3, 5-diene-1, 2-dione** (**1**). Lead(IV) oxide (19.12 g, 80 mmol) and sodium hydroxide (2.0 g, 50 mmol) were dissolved following the atmosphere was replaced with argon, and stirred rapidly in anhydrous methanol (100 mL) at room temperature. The solution of catechol (2.2 g, 20.0 mmol) added dropwise slowly into the reaction system and stirred for 15 min. After the reaction was stopped, the residual solid PbO<sub>2</sub> was removed by suction filtration under reduced pressure, then the pH of the filtrate was adjusted to 5.0 with 50 % H<sub>2</sub>SO<sub>4</sub>, and the solution was filtered again with suction to remove the precipitated Pb in the solution. The filtrate was extracted for three times with an appropriate amount of dichloromethane, the extracts were combined, and 90 % of the solvent was distilled off under reduced pressure, then acidified with glacial acetic acid under an argon atmosphere, and

cooled to 5 °C at the same time a large amount of crystals were formed. Yellow crystalline solids (1.61 g) were obtained by vacuum drying at 50 °C. Yield 48.0 %. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta = 5.77$  (s, 2H), 3.90 (s, 6H).

2, 5-dimethoxycyclohexa-2, 5-diene-1,4-dione (2). 1 (336.0 mg, 2.0 mmol) were stirred rapidly in anhydrous methanol (100 mL), then concentrated sulfuric acid (5 mL) was added dropwise to the solution slowly, and the resulting solution was further stirred for 4 h at room temperature. The insoluble solids were precipitated sufficiently resting 0.5 h, then filtered under normal pressure. The crude products were washed with a large amount of secondary distilled water and absolute ethanol. Yellow powdery solids (322.5 mg) were obtained by vacuum drying at 50 °C. Yield 96.0 %. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta = 5.87$  (s, 2H), 3.85 (s, 6H).

2, 5-diaminocyclohexa-2, 5-diene-1,4-dione (3). 2 (308.0 mg, 2.0 mmol) was placed in a three-necked flask (250 mL), and an argon atmosphere was used to replace completely the air with the purpose of ensuring the air was eliminated as much as possible. Strong ammonia solution (1.0 mL) and anhydrous ethanol (100 mL) in the system was maintained refluxing for 3 h meanwhile producing a large amount of ammonia gas. The color of the mixing solution turned light purple gradually from yellow. The precipitates were washed with distilled water and absolute ethanol after filtering and sheet purple crystals (148.7 mg) were obtained by vacuum drying at 50 °C. Yield 58.8 %. <sup>1</sup>H NMR (*d*-DMSO, 400 MHz):  $\delta = 6.12$  (s, 2H), 3.29 (s, 4H).

2, 5-diaminobenzene-1, 4-diol (4). 3 (276.0 mg, 2.0 mmol) and reducing agent sodium thiosulfate (1044.6 mg, 6.0 mmol) were added to distilled water (20 mL) in a two-necked flask (100 mL) under an argon atmosphere. The solution changed from pale purple to light yellow after the mixture was stirred for 1 h at 40 °C. The resulting solution was filtered under atmospheric pressure, and the precipitates were washed with distilled water and anhydrous ethanol several times. Powdery yellow solids (272.2 mg) were obtained by vacuum drying at 50 °C. Yield 97.2 %. <sup>1</sup>H NMR (*d*-DMSO, 400 MHz):  $\delta$  = 7.96 (s, 2H), 6.06 (s, 2H), 3.75 (s, 4H); <sup>13</sup>C NMR (*d*-DMSO, 400 MHz):  $\delta$  = 137.98, 126.58, 105.06.

**2, 6-disubstituted benzobisoxazoles** (5). To *o*-xylene solution (25 mL) of **4** (280.0 mg, 2.0 mmol), pyridine-4-carbaldehyde (**a**) (0.5 mL, 4.5 mmol) was added dropwise and refluxed for 5 h at 120  $^{\circ}$ C under argon atmosphere, then cooled at room temperature.

4-Methoxy-2,2,6,6-tetramethyl-1-piperidinyloxy (4-methoxy-TEMPO) (47.0 mg, 5.0 mmol) as a free radical catalyst was added carefully and stirred for 15 h at 120  $\Box$  under oxygen atmosphere. The resulting solution was evaporated under vacuum to remove the solvent, and the excess *o*-xylene was extracted by chloroform (3 × 20 mL). The crude product was washed with distilled water (3 × 20 mL) and dried over anhydrous sodium sulfate. The residue was purified by chromatography using petroleum ether-ethyl acetate (3:2) to give white crystalline. The identidy and purity of the product was confirmed by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopic analysis.

**5b**, **5c** and **5d** were prepared using similar procedure as for **5a** except for using thiophene-2-carbaldehyde (**b**), furan-2-carbaldehyde (**c**) or picolinaldehyde (**d**) instead of pyridine-4-carbaldehyde.

**2, 6-di(pyridin-4-yl)-benzo[1, 2-d:4, 5-d']bisoxazole** (5a). Yield 81 % (508.7 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 25°C, TMS):  $\delta = 8.87$  (d, 4H), 8.14 (d, 4H), 8.04 (s, 2H) ppm. <sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 163.32$ , 149.88, 142.41, 136.25, 133.26, 121.53, 116.19 ppm. MS (EI): m/z = 314. Analysis for C<sub>18</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub> (332.32): calcd. C, 65.06; H, 3.64; N, 16.86. Found, C, 65.13; H, 3.76; N, 16.94.

**2, 6-di(thiophene-2-yl)-benzo[1, 2-d:4, 5-d']bisoxazole** (**5b**). Yield 87.2 % (535.9 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 25°C, TMS): δ = 7.97 (q, J<sub>1</sub> = 4.8 Hz, J<sub>2</sub> = 3.2 Hz, 2H), 7.86 (s, 2H), 7.61 (q, J<sub>1</sub> = 6.4 Hz, J<sub>2</sub> = 1.6 Hz, 2H), 7.23 (q, J<sub>1</sub> = 10.18 Hz, J<sub>2</sub> = 3.6 Hz, 2H) ppm. <sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>): δ = 160.22, 148.32, 140.28, 136.25, 130.61, 130.17, 129.47, 128.40, 100.66 ppm. MS (EI): m/z = 324.

**2, 6-di(furan-2-yl)-benzo[1, 2-d:4, 5-d']bisoxazole** (5c). Yield 67.1 % (391.9 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 25°C, TMS):  $\delta$  = 7.89 (s, 2H), 7.71 (t, *J* = 0.8 Hz, 2H), 7.33 (t, *J* = 1.6 Hz, 2H), 6.66 (t, J=1.8 Hz, 2H) ppm. <sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 156.46, 148.08, 146.07, 142.35, 140.06, 114.76, 112.44, 101.11 ppm. MS (EI): m/z = 292.

**2, 6-di(pyridin-2-yl)benzo[1, 2-d:4, 5-d']bisoxazole** (**5d**). Yield 81.0 % (508.7 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 25 °C, TMS):  $\delta = 8.55$  (t, J = 1.2 Hz, 2H), 7.93 (m, 2H), 7.38 (t, J = 1.8 Hz, 2H), 7.19 (m, 2H) ppm. <sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 165.24$ , 155.80, 151.46, 137.93, 133.61, 126.35, 121.48, 118.26 ppm. MS (EI): m/z = 314.

#### 2.3 Computational method.

In order to understand the electronic structure of compounds 5a and 5b further, Density

Functional Theory (DFT) calculation of the target 2,6-disubstituted benzobisoxazoles has been carried out using Gaussian 09 program package [11], such as optimized geometries and corresponding molecule orbitals (MOs) energy for **5a** and **5b** performed with the aid of the Gauss View 5.0 visualisation software at the B3LYP level [12,13]. The 6-31G(d) basis set for C, H, O, N and S atoms were employed. Vertical electronic excitations based on the DFT-B3LYP optimised geometry were calculated using the Time-Dependent Density Functional Theory (TD-DFT) formalism [14,15] in CH<sub>2</sub>Cl<sub>2</sub> using conductor-like polarisable continuum model (CPCM) [16]. Molecular Hirshfeld surface calculations were generated using a high surface resolution[17].

# 2.4 X-ray Crystallography

Suitable colorless needle-like crystals of **5a** were obtained by vapour diffusion of ethyl acetate and methanol solution for two weeks. X-ray diffraction measurement for **5a** was collected on Agilent SuperNova diffractometer equipped with graphite monochromated Mo-K $\alpha$  radiation ( $\lambda = 0.71073$  Å). Data reduction and cell parameter refinement were performed using OLEX2 [18]. The structures were solved using Fourier difference techniques and refined by full-matrix least-squares methods on  $F^2$  data [19,20]. All hydrogen atoms were added in calculated positions except for the hydrogen atoms of the water molecule. Relevant crystallographic data together with refinement details are listed in Table 1.

Empirical formula	$C_{18}H_{12}N_4O_3$
Formula weight	332.32
Temperature (K)	273.4(6)
Wavelength (Å)	0.71073
Crystal system	monoclinic
Space group	C2/c
Unit cell dimensions (Å, °)	
a	12.7875(17)
b	3.7629(6)
С	30.418(4)
β	94.125(13)
Volume (Å <sup>3</sup> ), Z	1459.9(4), 4
Calculated density(Mg /m <sup>3</sup> )	1.512
Absorption coefficient $(mm^{-1})$	0.107
<i>F</i> (000)	688
Crystal size (mm <sup>3</sup> )	$0.19 \times 0.05 \times 0.04$

Table 1 Crystallographic data and structure refinement parameters of 5a.

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$\theta$ Range for data collection (°)	4.0240-24.9920
Index ranges	$-15 \le h \le 9; -4 \le k \le 2; -35 \le l \le 37$
Reflections collected	2524
Independent reflections	1440 [ $R(int) = 0.0336$ ]
Completeness to $\theta = 26.32$ (%)	99.54
Data/restraints/parameters	1440/0/118
Goodness-of-fit on $F^2$	1.055
Final <i>R</i> indices $[I > 2\sigma(I)]$	$R_1 = 0.0448, wR_2 = 0.1163$
<i>R</i> indices (all data)	$R_1 = 0.0574, wR_2 = 0.1231$
Largest difference peak and hole(e $Å^{-3}$ )	0.191 and – 0.302
$w = 1/[s^2(F_0^2) + (0.0697P)^2 + 1.6634P],$ WI	here $P = (F_0^2 + 2F_c^2)/3.$

#### 3. Results and discussion

As shown in Scheme 1, compounds **5a-5d** were synthesized with 4-methoxy-TEMPO as a free radical catalyst using a one-pot reaction and **5b** only reported previously [21]. 4-Methoxy-TEMPO radical is widely used for the selective oxidation of primary or secondary alcohols [22,23]. 4-Methoxy-2, 2, 6, 6-tetramethyl-1-piperidinyloxy (4-methoxy-TEMPOH) can be slowly oxidized to 4-methoxy-TEMPO radical in air at room temperature, so a strategy for the aerobic catalytic oxidative synthesis of benzoxazole using 4-methoxy-TEMPO as the catalyst was developed [4].

# 3.1 Benzodioxazole synthesis mechanism

As shown in Scheme 2, the synthesis of mono-benzoxazole catalyzed aerobicly by 4-methoxy-TEMPOH oxygen free radical was proposed [24]. The catalytic reaction begins with the reaction of 4-methoxy-TEMPO with 2-aminophenol [25,26]. In the first step, 2-aminophenol reacts with of the aromatic aldehyde through Schiff base reaction. The 4-methoxy-TEMPO catalyst attack the H atom on the phenolic hydroxyl group to generate active phenoxy radicals and 4-methoxy-TEMPOH [27,28]. At the same time, the generated 4-methoxy-TEMPOH can be reoxidized by air  $O_2$  to 4-methoxy-TEMPO and reused [29]. In the third step, the phenoxy free radical attack molecules within the imine double bond, a five-membered ring addition reaction takes place and generates reactive amine radical. In the fourth step, 4-methoxy-TEMPO catalyst offensive activity amino radical on the tertiary carbon atoms in the H atom, regenerate the imine double bond, and yield the final product of the target mono-benzoxazole molecule.



Scheme 2 A proposed mechanism for 4-methoxy-TEMPO-catalyzed aerobic oxidative synthesis of 2-substituted benzoxazoles.



Scheme 3 A proposed mechanism for 4-methoxy-TEMPO-catalyzed aerobic oxidative synthesis of 2, 2'-disubstituted benzoxdiazoles.

The synthesis mechanism of benzobisoxazole derivatives containing heteroaromatic ring substituents catalyzed by 4-methoxy-TEMPO was further studied as shown in Scheme 3. Firstly, the 2, 5-diaminohydroquinone reacts with twice the equivalent of aromatic aldehyde to generate a Schiff-base containing two symmetrical imine double bonds [30]. 4-Methoxy-TEMPO catalyst then attacks the H atom on the two phenolic hydroxyl groups on the benzene ring to form two active phenoxy radicals and 4-methoxy-TEMPOH [31]. At the same time, the generated 4-methoxy-TEMPOH can be re-oxidized by O<sub>2</sub> in the air to

4-methoxy-TEMPO for reuse; and then two phenoxy oxygen free base respectively attack the molecule within its adjacent imine double bond, five-membered cycloaddition reaction, while generating two active amine free radicals. Finally, 4-methoxy-TEMPO catalyst attacks the H atom on the tertiary carbon atom in the molecule and regenerates the imine double bond to finally obtain the target benzoxobioxazole derivative [32].

In synthetic experiments, we found that when 2-aldehyde-based imidazole and 2, 5-diaminohydroquinone were reacted under the same experimental conditions, the target molecule could not be obtained. One of the reasons is that the solubility of 2-allyl imidazole in the solvent *o*-xylene is very small. Therefore, the reaction between the 2-aldehyde imidazole and 2, 5-diamino-p-phenol did not occur. The second reason is that due to the presence of active H atoms on the amine groups in the 2-aldehyde-based imidazole molecules, they are readily linked to 4-methoxy-TEMPO thereby reducing the free radical catalyst and 2, 5-diaminohydroquinone phenolic hydroxyl reaction efficiency, and ultimately lead to the failure of free-radical catalyst. On the other hand, this further confirms the rationality of the proposed mechanism of using the free radical catalysis.

#### 3.2 Crystal structure determination

X-ray crystallographic analysis reveals that **5a** crystallizes in the form of a hydrate and in the monoclinic system with space group C2/c. The molecular structure and intermolecular hydrogen bonds of **5a** are depicted in Fig. 1. Selected bond lengths and angles from X-ray diffraction as well as DFT optimization geometric parameters of **5a** are compared in Table 2.



Fig. 1 Crystal structure and intermolecular hydrogen bond of 5a with 30 % thermal ellipsoids probability.

The dihedral angles defined by the central benzo[1, 2-d:4, 5-d']bisoxazole ring plane both left and right side planes have the same value, which is only  $6.32^{\circ}$ . The distance between the center of both sides pyridine ring is about 0.198 Å, showing that **5a** has a good coplanar property owing to the absence of steric hindrance of alkyl chains [33]. There are two pyridine rings and two oxazole rings in the crystal structure of **5a**. The dihedral angles between the

ACCEPTED MANUSCRIPT middle benzene ring and each side oxazole rings are equal 0.22°. The distance between the middle benzene ring and each side pyridine ring are equal 6.04 Å. The two torsion angles C4–C3–C6–O1 and C2–C3–C6–N1 are practically the same (the mean angle is 180°). Thus it can be seen that the molecule is center symmetrical structure on the benzene ring centroid as the center of symmetry.

Bond lengths	Experimental	Theoretical	Bond lengths Experimental		Theoretical
O1–C6	1.351(4)	1.3750	01–C7 1.389(4)		1.3736
N1–C6	1.306(4)	1.3016	N1–C8	1.392(3)	1.3893
N2C1	1.336(5)	1.3422	N2-C5	1.342(5)	1.3443
C1–C2	1.383(5)	1.3935	C2–C3	1.392(4)	1.4023
C3–C4	1.385(5)	1.4032	C3–C6	1.452(4)	1.4606
C4–C5	1.379(5)	1.3914	C7–C8	1.402(4)	1.4168
C7–C17	1.371(4)	1.3844	C8–C9	1.386(4)	1.4009
Bond angles	Experimental	Theoretical	Bond angles	Experimental	Theoretical
C6–O1–C7	104.4(2)	104.6674	C6–N1–C8	105.3(3)	104.9958
C1-N2-C5	116.7(3)	117.8061	N2C1C2	123.6(3)	123.3547
C1–C2–C3	118.9(3)	118.5496	C2C3C4	118.0(3)	118.3592
C2–C3–C6	121.8(3)	121.5872	C4-C3-C6	120.2(3)	120.0536
C3–C4–C5	118.8(3)	118.6088	N2-C5-C4	124.0(3)	123.3216
O1-C6-N1	115.2(3)	114.9381	01C6C3	1-C6-C3 119.9(3)	
N1-C6-C3	124.9(3)	127.5594	O1–C7–C8	107.4(2)	106.9689
O1–C7–C17	128.4(2)	127.5685	C8–C7–C17	124.2(3)	125.4626
N1-C8-C7	107.8(2)	108.4299	N1-C8-C9	129.3(2)	130.0651
С8–С7–С9	122.9(2)	121.5050	C8–C9–C7	113.0(2)	113.0282
Torsion angles	Experimental	Theoretical	Torsion angles	Experimental	Theoretical
O1-C7-C8-N1	-0.2(3)	0.0042	01–C7–C8–C9	-179.9(3)	180.0035
C8-N1-C6-C3	-178.6(3)	180.0012	N2-C1-C2-C3	-0.5(5)	0.0004
C1-N2-C5-C4	0.5(5)	0.0007	C1–C2–C3–C4	0.9(5)	0.0011
C1–C2–C3–C6	-179.7(3)	-180.0	C2C3C4C5	-0.7(5)	-0.0016
C2-C3-C6-O1	6.4(5)	0.0002	C2-C3-C6-N1	-175.7(3)	-180.001
C3-C4-C5-N2	-0.1(5)	0.0007	C4-C3-C6-O1	-174.3(3)	-179.9
C4-C3-C6-N1	3.7(5)	0.0019	C5-N2-C1-C2	-0.2(5)	-0.0013
C601C7C8	-0.1(3)	-0.0038	C8-N1-C6-O1	-0.5(4)	0.0002
C6-N1-C8-C7	0.4(3)	-0.0027	C6-N1-C8-C9	-179.9(3)	-180.002
C6-C3-C4-C5	180.0(3)	180.0	C7-O1-C6-N1	0.4(4)	0.0024
C701C6C3	178.5(3)	-180.0			

Table 3 Hydrogen-bonding distances (Å) and angles (°) of 5a.

D–H···A	<i>d</i> (D–H)	$d(\mathbf{H}\cdots\mathbf{A})$	$d(\mathbf{D}\cdots\mathbf{A})$	∠D–H…A	Symmetry code
O2−H2A…N2	1.00(5)	2.09(6)	2.970(4)	146(5)	x, y, z

There is only one intermolecular O2–H2A····N2 hydrogen bond, which between the pyridine ring and non-coordinated water molecule (Fig. 1, Table 3). Molecules of **5a** are connected by extensive  $\pi \cdots \pi$  stacking interactions, which play significant roles in the crystal packing modes, face-to-face  $\pi \cdots \pi$  stacking interactions between neighboring benzene rings and oxazole rings with distances between the centroids of 3.763 Å and 3.764 Å [34] (Fig. 2, Table 4). Overall, with the help of intermolecular hydrogen bonds and  $\pi \cdots \pi$  stacking interactions, adjacent molecules also can be linked together into an infinite two-dimensional (2-D) layer supramolecular structure along the bc-plane (Fig. 3).



**Fig. 2.** Face-to-face  $\pi \cdots \pi$  stacking of **5a**.

RingI	RingJ	CgI····CgJ	CgI-Perp	Cg–J <sub>Perp</sub>	Slippage
Cg1	Cg1	3.7631(18)	3.3916(12)	-3.3917(12)	1.630
Cg1	Cg3	3.7638(18)	3.3880(12)	3.3943(12)	_
Cg2	Cg2	3.763(2)	3.4589(13)	-3.4588(13)	1.482
Cg3	Cg1	3.7640(18)	3.3943(12)	3.3882(12)	-
Cg3	Cg3	3.7629(18)	3.3915(12)	3.3915(12)	1.630

Table 4  $\pi$ - $\pi$  stacking interactions (Å, °) in the crystalline state of 5a.

Cg1, Cg2 and Cg3 are the centroids for O1–C6–N1–C8–C7, N2–C1–C2–C3–C4–C5 and C7–C8–C9–C7A–C8A–C9A, respectively. CgI···CgJ is the distance between ring centroids. CgI-<sub>Perp</sub> is the perpendicular distance of CgI on ring J. CgJ-<sub>Perp</sub> is the perpendicular distance of CgJ on ring I. Slippage is the distance between CgI and perpendicular projection of CgJ on ring I.



Fig. 3 View of an infinite 2-D layer supramolecular structure of **5a** (hydrogen atoms are omitted for clarity except those forming hydrogen bonds).

### 3.3 UV-Vis absorption spectra and TDDFT calculations

UV–Vis absorption spectra of **5a** and **5b** were determined in  $5.0 \times 10^{-5}$  mol L<sup>-1</sup> CH<sub>2</sub>Cl<sub>2</sub> solution at room temperature. As shown in Fig. 4 and Fig.S1, there were very similar triple absorption peak appeared between 320 and 400 nm of two compounds. Compared with **5b**, three peaks were observed at 328, 341 and 357 nm ( $\varepsilon = 1,4860, 1,9998, 1,5720 \text{ mol}^{-1} \text{ L cm}^{-1}$ ), respectively in the spectrum of **5a**, while three peaks centered at 344, 360 and 381 nm ( $\varepsilon = 1,9040, 2,3962, 1,8864 \text{ mol}^{-1} \text{ L cm}^{-1}$ ), respectively in **5b**. The maximum UV absorption peaks of two compounds produce a blue shift, mainly because the pyridine ring substituent is an electron-withdrawing group, which can reduce the charge density on the benzoxazole skeleton and reduce the degree of conjugation. In contrast, the thiophene ring substituent is an electron-donating group, which leads to an increase in the charge density on the benzoxazole skeleton and an increase in the degree of conjugation, so that the maximum UV-absorbing peak will undergo a significant red shift [21, 35]. The absorption edge ( $\lambda_{edge}$ ) of **5a** and **5b** are at 370 and 385 nm, corresponding to an optical band gap ( $E_g^{opt}$ ) of 3.351 and 3.221 eV [36].

Time dependent DFT calculations have been done on the optimised geometry to further understand the electronic transitions in UV–Vis spectra of compounds in  $CH_2Cl_2$  and compared with experimentally observed absorption bands. The UV–Vis spectral analysis of **5a** and **5b** are calculated by TDDFT/B3LYP method and the calculated vertical electronic excitation energy (eV) and oscillator strength (f) are summarised in Table 5. The experimental absorption bands of **5a** and **5b** have been explained with help of TD-DFT calculations. The peak observed at 357 nm is identified to intra-ligand charge transfer (ILCT) character corresponds to (70 %) HOMO  $\rightarrow$  LUMO transitions respectively in **5a**. The peaks observed at

341 and 328 nm by experimentally are also attributable to ILCT character amounts to (69 %) HOMO-1  $\rightarrow$  LUMO and (70 %) HOMO  $\rightarrow$  LUMO+1 transitions in **5a**. The simulated broad peak at 388.12 nm whereas experimental peak at 380 nm in **5b** corresponds to (70 %) HOMO  $\rightarrow$  LUMO transitions [37]. Conclusively, theoretical simulation shows good agreement with the experimental phenomenon.



**Fig. 4** UV–Vis absorption spectra in  $CH_2Cl_2$  (5 × 10<sup>-5</sup> mol L<sup>-1</sup>): **5a** (a). Theoretical simulation of UV–vis absorption spectra: **5a** (b) and **5b** (c), and the oscillator strength of main excited states shown in the red color.

Excitation (eV)	λexcitation (nm)	Osc.strength (f)	Key transitions	Character	λexpt
5a					
3.3951 eV	365.18	1.5199	(70%) HOMO $\rightarrow$ LUMO	$L_1(\pi) \to L_1 \; (\pi^*)$	357
3.8761 eV	319.87	0.0373	(69%) HOMO–1 $\rightarrow$ LUMO	$L_1(\pi) \to L_1 \; (\pi^*)$	341
4.0753 eV	304.24	0.0090	(70%) HOMO $\rightarrow$ LUMO+1	$L_1(\pi) \to L_1 \; (\pi^*)$	328
5b					
3.1945	388.12	1.5685	(70%) HOMO $\rightarrow$ LUMO	$L_1(\pi) \to L_1 \; (\pi^*)$	380
4.0672	304.84	0.0211	(68%) HOMO–2 $\rightarrow$ LUMO	$L_1(\pi) \to L_1 \; (\pi^*)$	361
4.6072	269.11	0.0604	(64%) HOMO–4 $\rightarrow$ LUMO	$L_1(\pi) \to L_1 \; (\pi^*)$	344

Table 5 TD-DFT calculated electronic excitations of 5a and 5b in CH<sub>2</sub>Cl<sub>2</sub>.

#### 3.4 Fluorescence spectra

Fluorescent behaviors of compounds were recorded in  $5.0 \times 10^{-5}$  mol L<sup>-1</sup> CH<sub>2</sub>Cl<sub>2</sub> solution at ambient temperature (Fig. S2). Both of **5a** and **5b** showed broad emission bands indicating charge transfer nature of the transitions. The fluorescence spectrum of **5a** shows a maximum peak at 413 nm, a shoulder peak at 436 nm and another peak at 392 nm upon excitation at 360 nm. Similarly, **5b** shows a maximum peak at 408 nm, a shoulder peak at 428 nm and another peak at 387 nm. The Stokes shift between the maximum wavelength of the absorbance and fluorescence spectrum is 72 nm of **5a** while 47 nm of **5b** [21, 34]. Due to the benzoxazole ring participates in the conjugate molecule, it enhances the degree of conjugation and promotes the enhancement of the fluorescence intensity [38].

## 3.5 Theoretical investigations

To gain deeper insight into the frontier molecular orbital energies of the compounds, the structures were optimized by the Gaussian 09 package using density functional theory (DFT) method with the basis set of B3LYP/6-31G(d) based on the single-crystal X-ray diffraction structure data of **5a** and **5b**. The selected geometrical parameters are presented in Table 2 and the data are well replicated with the experimental data having minor deviations in bond lengths and angles. The optimized geometry of two planar symmetric compounds are shown in Fig. 5. As shown in Fig. 6, the lowest unoccupied molecular orbitals (LUMO) and the highest occupied molecular orbitals (HOMO) of the compounds are not significantly influenced by the substituents, and these molecular orbitals are clearly not different between 5a and 5b [39,40]. The energies of some selected molecular orbits for 5a and 5b are shown in Table 6, from LUMO-1 to HOMO+1 principally. According to Table 6, the frontier molecular orbital energies of the HOMO-1, HOMO, LUMO, and LUMO+1 for 5a are -7.138, -6.515, -2.693, and -2.011 eV, respectively. The mentioned energy HOMO-LUMO gap is 3.822 eV, which implies high kinetic stability and low chemical reactivity [41]. The HOMO energy level of 5b is -5.922 eV while the LUMO energy level of 5b is -2.342 eV. The HOMO-LUMO gap of **5b** is 3.580 eV. In other words, it is energetically disadvantageous to add electron to the high-lying LUMO (-2.693, -2.342 eV), or to extract electron from the low-lying HOMO (-6.515, -5.922 eV) [42-44]. The occupied molecular orbital energies are all negative, demonstrating the chemical stability of the structure [45]. A theoretical investigation utilizing DFT allows rationalization of experimental findings [46].



Fig. 5 Optimized molecular structure of 5a (left) and 5b (right).



Fig. 6 Surface plots of some selected HOMO-LUMO structures molecular orbitals of 5a (left) and 5b (right).

Table 6 Absorption spect	a and HOMO-LUMO structures	orbital energies of <b>5a</b> and <b>5b</b>
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Compound	$\lambda_{edge} (nm)$	$E_g^{opt}$ (eV) <sup>a</sup>	E <sub>HOMO-1</sub> (eV)	E <sub>HOMO</sub> (eV)	E <sub>LUMO</sub> (eV)	$E_{LUMO+1} (eV)$	$\Delta E_{gap} \left( eV \right)$
5a	370	3.351	-7.138	-6.515	-2.693	-2.011	3.822
5b	385	3.221	-6.929	-5.922	-2.342	-1.698	3.580

<sup>a</sup> E<sub>g</sub><sup>opt</sup> estimated from the UV–vis absorption spectrum.

# 3.6 Hirshfeld surfaces analysis (HSA)

Intermolecular forces between molecules packed in lattice were computed using the CIF under HSA condition to figure out the surface spots (Figs. 7 and 8). Fig. 7 indicates surfaces which have been mapped over  $d_{norm}$ , shape index and curvedness. To visualize the molecular moiety, around which they were calculated, the surfaces are shown as transparent. The detected of H-bonds types and number such as H…H, C…H/H…C, O…H/H…O, N…H/H…N and S…H/H…S surfaces of **5a** and **5b** were recorded as main H–bond type [47]. Fig. 8 shows the two-dimensional fingerprint plots generated correspond to the H…H, C…H,

O···H, N···H and S···H interactions appearing as distinct spikes of **5a** and **5b**. Additionally, the H···H contacts are discovered to be the largest contribute with 34.9 % and 23.7 % of **5a** and **5b**, respectively. Comparatively, the proportion of O···H/H···O, N···H/H···N, C···C and C···H/H···C interactions comprising 15.4 %, 15.0 %, 12.3 % and 11.4 % of the entire HSA surface for each molecule of **5a**, respectively. Simultaneously, **5b** also has the extents of S···H/H···S, C···H/H···C, N···H/H···N and O···H/H···O interactions cover 15.8 %, 13.4 %, 12.3 % and 10.2 %, respectively. Due to the existence of these hydrogen bonding contacts, the structures of both compounds can be stabilized [48].



Fig. 7. Hirshfeld surfaces mapped with  $d_{norm}$  and shape index of 5a and 5b.



Fig. 8. 2D fingerprint plots of 5a and 5b showing the percentages of contacts contributed on the total HSA surface.

# 4. Conclusion

In summary, we have successfully synthesized and characterized 2, 6-disubstituted benzobisoxazole by using an effective and clean aerobic oxidative approach with 4-methoxy-TEMPO as the catalyst. Especially, 2, 6-di(pyridin-4-yl)-benzo[1, 2-d:4, 5-d']bisoxazole (**5a**) was confirmed by single-crystal X-ray diffraction analyses. On the basis

of experimental results, a plausible reaction mechanism of 4-methoxy-TEMPO catalyzed aerobic oxidation to 2,2'-disubstituted benzoxdiazoles was proposed. DFT and TD-DFT calculations have also been performed to determine the origin of the spectral behavior of compound **5a** and **5b**. Experimental XRD-crystal packing and Hirshfeld surface computed analysis agreed on several hydrogen-bonds formation in compounds lattice. We will focus on the synthesis of other useful heterocycles based on this material, as well as device construction and evaluation of the electronic, photoluminescence and thermostability properties of oligomers and polymers containing the benzobisoxazole moiety.

## Appendix A. Supplementary data

CCDC 1442771 contains the supplementary crystallographic data for compound **a**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data\_request/cif., or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, B2 1EZ, UK; fax +44 1223 336033; or E-mail: deposit@ccdc.cam.ac.uk.

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# HIGHLIGHTS

- 2, 6-Disubstituted benzobisoxazole using an effective and clean aerobic oxidative approach were synthesized and structural characterized by spectroscopic methods and single-crystal X-ray diffraction.
- A plausible reaction mechanism for 4-methoxy-TEMPO-catalyzed aerobic oxidative synthesis of 2, 2'-disubstituted benzoxdiazoles is proposed.
- The structures of compounds are interesting and Hirshfeld surface analyses of
   5a and 5b were also measured and discussed.
- Time dependent DFT calculations on the optimized structure of compounds 5a and 5b allowed for the assignment of specific electronic transitions in the UV–Vis spectra.

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