Synthesis and Molecular Structures of 1-Hydroxyethyl-2-(*p*-Substituted) Phenoxymethyl Benzimidazoles

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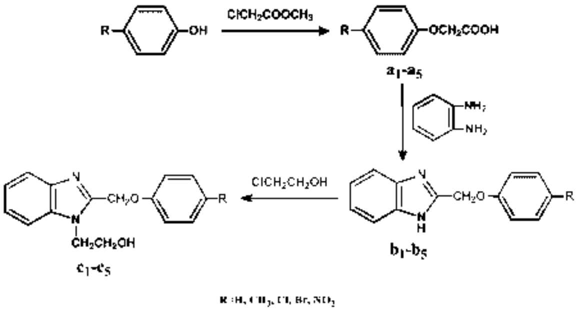
Summary: Five novel 1-hydroxyethyl-2-(*p*-substituted) phenoxymethyl benzimidazoles were synthesized by a three-step route. Under microwave irradiation, the *p*-substituted phenols were firstly O-carboxymethylated to prepare the corresponding *p*-substituted phenoxymethyl acids, which then reacted with *o*-phenylendiamine to get the key intermediates 2-(*p*-substituted) phenoxymethyl benzimidazole. Finally, the solid-liquid phase transfer catalysis method, where tetrabutyl ammonium bromide (TBAB) was used as the catalyst, was applied to synthesize the target compounds **c_1-c_5** by the N-hydroxyethylation reaction with 2-chloroethyl alcohol. The structures of the obtained compounds were well characterized and confirmed by elemental analysis, MS, IR, ^{1}H NMR, ^{13}C NMR and single-crystal X-ray diffraction analysis.

Keywords: Benzimidazole, *O*-carboxymethylation, *N*-hydroxyethylation, Synthesis, Crystal structures.

Introduction

Benzimidazole and its derivatives play an important role in the medicinal chemistry and drug discovery with many pharmacological activities which have made an indispensable anchor for discovery of novel therapeutic agents.[1-5] In recent years, the synthesis of benzimidazole derivatives has attracted the attention of many organic and medicinal chemists because of their diverse biological and clinical applications such as anticancer, antiviral, anti-inflammatory, anti-HIV, hormone antagonist, anthelmintic, antihypertensive, anxiolytic, antioxidant and antidiabetic activities.[6-10] In this respect, substitution of benzimidazole nucleus is an important and effective synthetic strategy in the drug discovery process. The substituent groups can be located on the phenyl ring or/and the imidazole ring. For the later, there are also two subtypes, namely, C (or 1)-substituted and N (or 2)-substitued. In this article, *p*-substituted phenoxymethyl structure was introduced to the 1(C)-position of the imidazole ring by the reaction between *o*-phenylendiamine and the corresponding *p*-substituted phenoxymethyl acid which have attracted much attention in agriculture, biochemistry and pharmacology due to their antiviral, antimicrobial activities and phytohormone activities.[11-13] Then, the hydroxyethyl group was connected to the 1(N)-position of the imidazole ring using the N-hydroxyethylation reaction with 2-chloroethyl alcohol. The five obtained 1-hydroxyethyl-2-(*p*-substituted) phenoxymethyl benzimidazoles were characterized by elementary analysis, MS, IR, ^{1}H and ^{13}C NMR. In order to obtain information about the stereochemistry of the molecules and to confirm the assigned structure, X-ray analyses were also undertaken.



Scheme-1: Synthesis route for 1-hydroxyethyl-2-(*p*-substituted) phenoxymethyl benzimidazoles

Experimental

All compounds used were research grade, commercially purchased and used as received. All the solvents used were dried and freshly distilled. Melting points were determined on a Shanghai Zhongguang WRS-2 melting point apparatus and

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uncorrected. Elemental analysis (C, H, N) were performed on a Carlo-Erba 1106 analyser. FT-IR spectra were obtained on a Magna.IR506 (Nicolet Ltd, USA) FT-IR spectrophotometer using KBr disk in the range 4000-400 cm^{-1}. ^1H and ^{13}C NMR spectra were recorded at 25 °C with a Bruker AV II-400 or 600 MHz spectrometer. All the chemical shifts are reported in parts per million (δ, ppm) with reference to tetramethylsilane (TMS). Mass spectra were measured on a GCMS-QP2010 Plus Model GC-MS spectrometer.

Measurements of the crystals were carried out on a CCD X-ray single crystal diffractometer (Xcalibur, Eos, UK) with a graphite-monochromated Mo*Kα* radiation. A single crystal of a compound was mounted on a glass fiber, and X-ray diffraction intensity data were collected using the ω-2θ scan technique. The Multi-scan/CrysAlisPro, Oxford Diffraction Ltd., was applied for the data reduction and absorption correction. All the structures were solved by direct method and refined by full matrix least squares method using SHELX-97 program[14]. The hydrogen atoms located in a difference Fourier map were limitedly refined with isotropic temperature factors and other hydrogen atoms that were added in their calculated positions were refined using a riding model.

General procedure for the Synthesis of **(b_1-b_5):** The prepared *p*-substituted phenoxymethyl acid **a_1-a_5** (0.011 mol) and 1,2-phenylenediamine (1.08 g, 0.01 mol) were dissolved in 120 mL of 4M HCl solution, and then 100 mL polyphosphoric acid was added and the mixture was stirred vigorously (1200 r/min) for 15 minutes under microwave irradiation condition (350 W). The reaction solution was cooled to room temperature (20 ^oC), added into 1000 mL cold distilled water, and neutralized to pH 7.5 by the 6M NaOH solution. The obtained flocculent precipitate was washed with water (3 × 15 mL), recrystallized from 75% (v/v) ethanol, and dried at 70 ^oC to yield 2-(*p*-substituted) phenoxymethyl benzimidazole **b_1-b_5**.

Synthesis of **c_1:** 2-Phenoxymethyl benzimidazole **b_1** (2.24 g, 0.01 mol) and 2-chloroethyl alcohol (1.61 g, 0.02 mol) were dissolved in 100 mL of acetone, and then tetrabutylammonium bromide (64.5 mg, 0.2 mmol) and NaOH (0.8 g, 0.02 mol) were added. The mixture was refluxed at 65 ^oC for 5h, added into 1000 mL cold distilled water, and cooled to room temperature. The obtained precipitate was filtered, washed with water (3 × 15 mL), recrystallized from 65% (v/v) ethanol, and dried to get **c_1** as a white solid. The synthesis of **c_2-c_5** also followed the similar procedure. Yield: 91.8%. m. p. 142 ^oC. Anal. calcd. (%) for $C_{16}H_{16}O_2N_2$: C, 71.64; H, 5.97; N, 10.45. Found (%): C,71.60; H, 5.87; N, 10.51. MS (ESI, *m/z*), calcd. for $C_{16}H_{16}O_2N_2$: 268.31; found: 269.14 ($M+H^+$). Selected IR (KBr, cm^{-1}): 3166.52 (ν_{OH}), 1599.71 ($\nu_{C=N}$), 1589.52, 1496.80 ($\nu_{C=C,\ Ar}$), 1333.24 (ν_{C-N}), 1236.51(ν_{Ar-O-C}). ^1H NMR (400 MHz, DMSO-d_6), δ_{ppm}: 7.67-6.97 (m, 9H, Ar-H), 5.44 (s, 2H, CH_2-O-Ar), 5.08 (t, 1H, OH), 4.39 (t, 2H, N-CH_2), 3.78-3.74 (q, 2H, C***H***$_2$OH). ^{13}C NMR (100 MHz, DMSO-d_6), δ_{ppm}: 158.3, 150.4 (N***C***N), 142.4, 136.0, 130.0, 123.1, 122.2 , 121.7, 119.7, 115.3 , 111.3 , 63.1 (***C***H_2O-Ar), 60.3 (***C***H_2OH), 46.7 (N***C***H_2).

c_2: white solid. Yield:85.9%. m. p. 137℃. Anal. calcd. (%) for $C_{17}H_{18}O_2N_2$: C, 72.34; H, 6.38; N, 9.93; Found (%): C, 72.43; H, 6.42; N, 9.99. MS (ESI, *m/z*), calcd. for $C_{17}H_{18}O_2N_2$: 283.34; found: 283.14 (M^+). Selected IR (KBr, cm^{-1}): 3196.55 (ν_{OH}), 1617.06 ($\nu_{C=N}$), 1589.48, 1511.73 ($\nu_{C=C,\ Ar}$), 1334.79 (ν_{C-N}), 1238.14 cm^{-1} (ν_{Ar-O-C}). ^1H NMR (400 MHz, DMSO-d_6), δ_{ppm}: 7.66-6.99 (m, 8H, Ar-H), 5.39 (s, 2H, CH_2-O-Ar), 5.06 (t, 1H, OH), 4.38 (t, 2H, N-CH_2), 3.77-3.74 (q, 2H, C*H*$_2$OH), 2.22 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6), δ_{ppm}: 155.7, 150.0 (N*C*N), 141.9, 135.5, 130.0, 129.8, 122.5, 121.6, 119.2, 114.7, 110.8, 62.8 (*C*H_2O-Ar), 59.8 (*C*H_2OH), 46.1 (N*C*H_2), 20.0 (*C*H_3).

c_3: white solid. Yield: 85.7%. m. p. 164^oC. Anal. calcd. (%) for $C_{16}H_{15}O_2N_2Cl$: C, 63.47; H, 4.96; N, 9.26%. Found (%): C, 63.46; H, 4.89; N, 9.31. MS (ESI, *m/z*), calcd. for $C_{16}H_{15}O_2N_2Cl$: 302.78; found: 303.10 ($M+H^+$). Selected IR (KBr, cm^{-1}): 3198.19 (ν_{OH}), 1596.58 ($\nu_{C=N}$), 1583.79, 1492.47 ($\nu_{C=C,\ Ar}$), 1364.13 (ν_{C-N}), 1239.58 (ν_{Ar-O-C}). ^1H NMR (400 MHz, DMSO-d_6), δ_{ppm}: 7.67-7.14 (m, 8H, Ar-H), 5.46 (s, 2H, CH_2-O-Ar), 5.07 (s, 1H, OH), 4.39 (t, 2H, N-CH_2), 3.75 (t, 2H, C***H***$_2$OH). ^{13}C NMR (100 MHz, DMSO-d_6), δ_{ppm}: 156.7, 149.6 (N***C***N), 141.7, 135.5, 129.3, 125.0, 122.7, 121.8, 119.2, 116.6, 110.90, 63.0 (***C***H_2O-Ar), 59.8 (***C***H_2OH), 46.2 (N***C***H_2).

c_4: white solid. Yield: 87.0%. m. p. 171℃. Anal. calcd. (%) for $C_{16}H_{15}O_2N_2Br$: C, 55.33; H, 4.32; N, 8.07. Found (%): C, 55.36; H, 4.22; N, 8.14. MS (ESI, *m/z*), calcd. for $C_{16}H_{15}O_2N_2Br$: 347.23; found: 347.06 (M^+). Selected IR (KBr, cm^{-1}): 3193.26 (ν_{OH}), 1591.01 ($\nu_{C=N}$), 1578.77, 1488.01 ($\nu_{C=C,\ Ar}$), 1371.73 (ν_{C-N}), 1236.12 (ν_{Ar-O-C}). ^1H NMR (400M Hz, DMSO-d_6), δ_{ppm}: 7.67-7.09 (m, 8H, Ar-H), 5.45 (s, 2H, CH_2-O-Ar), 5.07 (s, 1H, OH), 4.38 (t, 2H, N-CH_2), 3.76-3.73 (q, 2H, C***H*₂**OH). ^{13}C NMR (100 MHz, DMSO-d_6), δ_{ppm}: 157.6, 150.1 (N***C***N), 142.3, 136.0, 132. 7, 123.1, 122.2, 119.7, 117.7, 113.2, 111.4, 63.4 (***C***H_2O-Ar), 60.3 (***C***H_2OH), 46.7 (N***C***H_2).

c_5: yellow solid. Yield: 56.2%. m. p. 193℃. Anal. calcd. (%) for $C_{16}H_{15}O_4N_3$: C, 61.34; H, 4.79; N, 13.42. Found (%): C, 61.43; H, 4.78; N, 13.52. MS (ESI, *m/z*), calcd. for $C_{16}H_{15}O_4N_3$: 313.34; found: 314.02 ($M+H^+$). Selected IR (KBr, cm^{-1}): 3157.52 (ν_{OH}), 1611.29 ($\nu_{C=N}$), 1594.42, 1512.17 ($\nu_{C=C,\ Ar}$), 1384.10 ($\nu_{C\text{-}N}$), 1264.31 ($\nu_{Ar\text{-}O\text{-}C}$). ^1H NMR (600 MHz, DMSO-d_6), δ_{ppm}: 8.25-7.23 (m, 8H, Ar-H), 5.64 (s, 2H, CH_2-O-Ar), 5.09 (s, 1H, OH), 4.41 (t, 2H, N-CH_2), 3.76 (t, 2H, C***H*₂**OH). ^{13}C NMR (150 MHz, DMSO-d_6), δ_{ppm}: 163.5, 149.5 (N***C***N), 142.3, 135.9, 126.3, 126.1, 123.3, 122.6, 122.3, 119.7, 116.0, 115.9, 111.4, 63.8 (***C***H_2O-Ar), 60.3 (***C***H_2OH), 46. 7 (N***C***H_2).

Results and Discussion

Synthesis

As shown in Scheme 1, *p*-substituted phenols were used as the starting reagents to prepare the target compounds. Firstly, following the reported procedure[15], these phenols reacted with methyl chloroacetate under microwave irradiation and phase-transfer catalysis conditions to synthesize *p*-substituted phenoxyacetates that was then hydrolyzed to get corresponding phenoxyacetic acid compounds (**a_1-a_5**). Secondly, *o*-phenylendiamine was taken to react with the obtained compounds to achieve the key intermediates - 2-(*p*-substituted) phenoxymethyl benzimidazoles (**b_1-b_5**). As a consequence of the solid-liquid phase transfer catalysis method, the intermediates reacts with 2-chloroethyl alcohol to form the final new products 1-hydroxyethyl-2-(*p*-substituted) phenoxymethyl benzimidazoles (**c_1-c_5**) in high yield. Notably, all these compounds, which are white or light-yellow solid, were purified by the simple recrystallization technique, and no complex purification process like column chromatography was adopted.

NMR Spectra

^1H NMR spectra of all the obtained compounds **c_1-c_5** were recorded in DMDO-d_6. There is no speak at 12.20-12.90 ppm or so which is assigned to the N-H proton of benzimidazole structure. Instead, peaks arising from the protons of hydroxyethyl group appeared. For instance, in the ^1H NMR spectrum of compound **c_1**, the triple peak at 4.39 ppm corresponded to the methylene protons close to the nitrogen atom of imidazole ring, and the multiple peaks at 3.78-3.74 ppm were assigned to the methylene protons close to hydroxy group, while the triple peak at 5.08 ppm originated from the active proton of hydroxy group. These results confirmed the successful formation of the target compound by the N-hydroxyethylation reaction. Similarly, these peaks can also be found in the ^1H NMR spectra of other four 1-hydroxyethyl-2-(*p*-substituted) phenoxymethyl benzimidazoles (**c_2-c_5**). It should be pointed out that the locations of these peaks were hardly influenced by electron-attracting or electron-repulsing properties of substituent groups on the phenoxymethyl structure. Furthermore, the single peak corresponding to the methylene protons of the phenoxymethyl unit were found at 5.39-5.64 ppm, which varied its location with the properties of substituent groups. All the other peaks were clearly assigned and matched well with the structures of target compounds.

^{13}C NMR spectra can further demonstrate their structures. The two carbons of hydroxyethyl group was located at 46 and 60 ppm or so, respectively. The peaks at approximately 63 ppm were assigned to the methylene cabons of phenoxymethyl moieties, while the peaks at about 150 ppm corresponded to the carbons of imidazole rings. Other peaks originated from the carbons of benzene rings.

FT-IR Spectra

All the target compounds showed similar FT-IR spectra. The broad absorption bands at 3200 cm^{-1} or so were appropriated to the stretching vibration of O-H group, which further indicated the successful N-hydroxyethylation of the intermediates **b_1-b_5**. The peaks observed at about 1600 cm^{-1} corresponded to the stretching vibration of C=N groups of imidazole rings, while the absorption bands found in the range of 1333-1384 cm^{-1} were assigned to the C-N bond. The peaks due to the presence of ether bond (Ar-O-C) were found at 1236-1239 cm^{-1}, except for 1264.31 cm^{-1} for **c_5** that contains the strong nucleophilic NO_2 group. Furthermore, the several absorption peaks at 1600-1450 cm^{-1} were the characteristic skeletal vibration of benzene rings.

Single Crystal X-ray Analysis

For the intermediate $\mathbf{b_1}$, single crystal suitable for the X-ray diffraction study was obtained by slow evaporation of its hydrous ethanol solution. The crystal molecular structure is shown in Fig. 1, while crystal data and structure refinements are given in Table 1. Selected bond lengths and angles are listed in Table 2, and hydrogen bond lengths bond and angles were shown in Table 3.

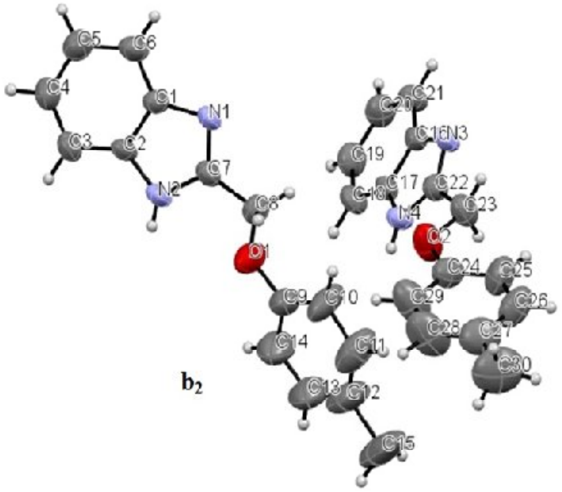

Fig. 1: Crystal molecular structure of $\mathbf{b_2}$.

In the molecular structure of $\mathbf{b_2}$, there are two 2-(*p*-CH_3) phenoxymethyl benzimidazole molecules due to the strong hydrogen bonds between the hydroxyl of ethanol solvent and the N or O atom in $\mathbf{b_2}$ molecule[16]. The angle between the imidazole ring and phenyl ring in the $\mathbf{b_2}$ molecule on the left is 46.64°, while it is 42.82° in the right $\mathbf{b_2}$ molecule. The angle between the two planes of imidazole rings is 59.39°, and the angle between the two planes of the phenyl rings is 16.63°. Meanwhile, as shown in Table 2, a little difference can be found at the bond lengths and angles in the imidazole rings of the two $\mathbf{b_2}$ molecules. For instance, in the left molecule, the bond lengths of N1-C1, N1-C7, N2-C1 and N2-C7 are 1.408(5), 1.315(5), 1.383(5) and 1.361(5) Å, respectively, while in the right unit, the corresponding lengths of N3-C16, N3-C22, N4-C17 and N4-C22 are 1.372(5), 1.321(5), 1.359(6) and 1.341(5) Å, respectively. The angle of C7-N2-C2 (106.8(3)°) is also different from that of C22-N4-C17 (107.6(3)°) . In addition, there is a strong intermolecular hydrogen bond between N2 and the N1 of another $\mathbf{b_2}$ molecule, N2-H2...N1^1 (2.181 Å). Similarly, another hydrogen bond N4-H4...N3^2 (2.181Å) exists between the N4 and N3 in another molecule.

For the target compounds $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$, single crystals suitable for the X-ray diffraction study were also obtained by slow evaporation of the hydrous ethanol solution of the respective compounds. Their crystal molecular structures, structure refinements details, selected bond lengths and angles, hydrogen bond lengths and angles are shown in Fig. 2, Tables 1, 2, and 3, respectively. All the crystal molecular structures of $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$ belong to orthorhombic systems, and only one molecular unit was observed. In these three crystals, the planes between imidazole ring and the substituted benzene ring are not co-plane and the intersection angles are 65.78°($\mathbf{c_1}$), 72.00°($\mathbf{c_2}$), 68.40°($\mathbf{c_3}$), respectively. As shown in Fig. 2, in the molecules of $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$, all the hydroxyethyl groups were found to be connected to the N atoms of imidazole rings, which further proved the success of the N-hydroxyethylation synthesis route for the target compounds. The bond lengths between the N and C atoms are 1.463 (3), 1.456 (4) and 1.466 (4) Å for $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$, respectively. The bond angles of C1-N1-C8 ($\mathbf{c_1}$), C1-N1-C16 ($\mathbf{c_2}$) and C1-N1-C8 ($\mathbf{c_3}$) are 126.60(17)°, 126.4(3)° and 126.6(2)°, respectively. And the bond angles of C7-N1-C8 ($\mathbf{c_1}$), C7-N1-C16 ($\mathbf{c_2}$) and C7-N1-C8 ($\mathbf{c_3}$) areare 127.05(18)°, 127.5(4)° and 127.0(3)°, respectively.

Furthermore, there are a large number of hydrogen bonds in the three crystal molecular structures. For example, in the crystal molecular structure of $\mathbf{c_1}$, there are intermolecular hydrogen bond between the H2 atom in hydroxyl and the N2 atom of another $\mathbf{c_1}$ molecule (O2-H2 ... N2^1, 1.964 Å), The hydrogen bonds, in the crystal molecular structure of $\mathbf{c_2}$, exist between the H2 atom in hydroxyl and the N2 atom of another $\mathbf{c_2}$ molecule (O2-H2...N2, 2.010 Å). However, in the crystal molecular structure of $\mathbf{c_3}$, the hydrogen bond was found only between the H2 atom in hydroxyl and the N2 atom of another $\mathbf{c_3}$ molecule (O2-H2...N2^1, 2.019Å). So, these results indicate clearly that the properties of substituent groups can influence the type and number of hydrogen bonds in the crystal structures of the obtained target compounds $\mathbf{c}$.

Table-1: Crystal data and structure refinement details for $\mathbf{b_2}$, $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$.

Compounds	b_2	c_1	c_2	c_3
Formula	$C_{15}H_{14}N_2O$	$C_{16}H_{16}N_2O_2$	$C_{17}H_{18}N_2O_2$	$C_{16}H_{15}ClN_2O_2$
Molecular weight	238.28	268.31	282.33	302.75
Temperature/K	293.15	296.15	293.15	296.15
Crystal system	orthorhombic	orthorhombic	orthorhombic	orthorhombic
Space group	$Pn2_1a$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a/Å	10.1845(5)	4.3074(8)	4.4469(4)	4.3906(17)
b/Å	31.422(2)	14.133(3)	14.2061(11)	14.324(5)
c/Å	8.1289(6)	22.807(4)	23.7756(19)	23.559(9)
α/°, β/°, γ/°	90, 90, 90	90, 90, 90	90, 90, 90	90, 90, 90
Volume/Å^3	8, 2601.4(3)	1388.4(5)	1502.0(2)	1481.7(10)
Z, ρ_{calc}(mg/mm^3)	1.217	4, 1.284	4, 1.249	4, 1.357
μ/mm^{-1}, F(000)	0.078, 1008.0	0.086, 568.0	0.083, 600.0	0.263, 632.0
Crystal size/mm^3	0.3 × 0.2 × 0.2	0.3 × 0.25 × 0.25	0.25 × 0.25 × 0.2	0.4 × 0.2 × 0.13
2θ range for data collection	6.344° to 52.736°	3.39° to 57.046°	5.886 to 52.724°	3.328 to 50.688°
Index ranges	$-6 \leq h \leq 12$, $-39 \leq k \leq 20$, $-10 \leq l \leq 4$	$-5\leq h\leq 5$, $18\leq k\leq 18$, $-30\leq l \leq 30$	$-5\leq h\leq 3$, $-17 \leq k\leq 14$, $-29\leq l\leq 24$	$-5\leq h\leq 5$, $-17\leq k\leq 17$, $-28 \leq l \leq 28$
Reflections collected	6589	18514	4447	15570
Independent reflections (R_{int})	3345 (0.0202)	3493(0.0253)	2818 (0.0174)	2719(0.0301)
Data/restraints/ parameters	3345/1/351	3493/0/182	2818/0/200	2719/0/199
Goodness-of-fit on F^2	1.029	1.031	0.993	1.044
Final R indexes [I≥2σ (I)]	R_1=0.0544, wR_2=0.1429	R_1= 0.0414, wR_2= 0.1077	R_1 = 0.0522, wR_2 = 0.0927	R_1 = 0.0361, wR_2 = 0.0890
Final R indexes (all data)	R_1=0.0675, wR_2=0.1531	R_1= 0.0497 wR_2= 0.1136	R_1= 0.1101 wR_2= 0.1161	R_1 = 0.0409 wR_2 = 0.0925
Largestdiff.peak/ hole/eÅ^{-3}	0.22/-0.17	0.16/-0.15	0.10/-0.14	0.25/-0.23
Flack parameter	0.8(10)			

Table-2: Selected bond lengths (Å) and angles (°) for $\mathbf{b_2}$, $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$.

b_2					
Bond	Length (Å)	Bond	Length (Å)	Bond	Length (Å)
O1-C8	1.400(6)	N2-C2	1.383(5)	N4-C22	1.341(5)
O1-C9	1.376(6)	N2-C7	1.361(5)	C7-C8	1.485(7)
O2-C23	1.405(6)	N3-C16	1.372(5)	C12-C15	1.527(9)
O2-C24	1.384(6)	N3-C22	1.312(5)	C22-C23	1.493(7)
N1-C1	1.408(5)	N4-C17	1.359(6)	C27-C30	1.506(8)
N1-C7	1.315(5)				
Angle	(°)	Angle	(°)	Angle	(°)
C9-O1-C8	118.3(4)	N2-C7-C8	122.6(4)	N3-C22-N4	113.1(4)
C24-O2-C23	117.2(4)	O1-C8-C7	107.5(4)	N3-C22-C23	124.0(4)
C7-N1-C1	104.7(3)	O1-C9-C14	115.1(5)	N4-C22-C23	122.5(4)
C7-N2-C2	106.8(3)	C10-C9-O1	125.4(5)	N1-C7-N2	113.2(4)
C22-N3-C16	104.4(3)	N2-C2-C1	105.9(3)	N1-C7-C8	124.0(3)
C22-N4-C17	107.6(3)	C3-C2-N2	131.8(3)	O2-C23-C22	108.1(4)
C2-C1-N1	109.4(3)	C29-C24-O2	115.6(5)	C25-C24-O2	125.4(5)
C6-C1-N1	130.0(4)	N3-C16-C17	110.2(3)	N4-C17-C16	104.8(3)
N4-C17-C18	133.0(3)	N3-C16-C21	130.2(3)		
c_1					
Bond	Length (Å)	Bond	Length (Å)	Bond	Length(Å)
O1-C10	1.431(3)	N1-C1	1.375(3)	C8-C9	1.504(3)
O1-C11	1.373(3)	N1-C7	1.361(2)	C7-C10	1.487(3)
O2-C9	1.404(3)	N1-C8	1.463(3)	N2-C2	1.385(3)
N2-C7	1.313(3)				
Angle	(°)	Angle	(°)	Angle	(°)
C11-O1-C10	117.33(16)	N1-C1-C2	105.87(16)	N1-C7-C10	123.37(18)
C1-N1-C8	126.60(17)	N1-C1-C6	131.9(2)	N2-C7-N1	113.43(18)
C7-N1-C1	106.26(17)	C6-C1-C2	122.2(2)	N2-C7-C10	123.18(18)
C7-N1-C8	127.05(18)	N2-C2-C1	109.64(18)	N1-C8-C9	113.79(18)
C7-N2-C2	104.81(17)	N2-C2-C3	130.1(2)	O2-C9-C8	108.800(2)
O1-C10-C7	106.96(16)	O1-C11-C16	115.6(2)	C12-C11-O1	124.700(2)
c_2					
Bond	Length (Å)	Bond	Length (Å)	Bond	Length (Å)
O1-C8	1.434(5)	N1-C1	1.375(4)	N2-C2	1.376(5)
O1-C9	1.383(4)	N1-C7	1.369(4)	N2-C7	1.316(4)
O2-C17	1.402(4)	N1-C16	1.456(4)	C7-C8	1.478(6)
C12-C15	1.513(5)	C16-C17	1.511(5)		
Angle	(°)	Angle	(°)	Angle	(°)
C9-O1-C8	116.8(3)	N1-C1-C2	105.8(4)	N2-C7-N1	113.3(4)
C1-N1-C16	126.4(3)	N1-C1-C6	132.1(4)	N2-C7-C8	123.2(4)

Table continue..

C7-N1-C1	**106.0(3)**	**N2-C2-C1**	**110.2(4)**	**O1-C8-C7**	**106.4(3)**
C7-N1-C16	**127.5(4)**	**N2-C2-C3**	**130.0(4)**	**C10-C9-O1**	**125.9(4)**
C7-N2-C2	**104.7(3)**	**N1-C7-C8**	**123.5(4)**	**C14-C9-O1**	**115.0(4)**
C11-C12-C15	**122.3(5)**	**C13-C12-C15**	**121.6(5)**	**N1-C16-C17**	**114.0(3)**
O2-C17-C16	**108.5(3)**				
			c_3		
Bond	**Length (Å)**	**Bond**	**Length (Å)**	**Bond**	**Length (Å)**
***Cl* 1-C14**	**1.742(3)**	**N2-C7**	**1.319(3)**	**C8-C9**	**1.511(4)**
O1-C10	**1.433(3)**	**N1-C1**	**1.377(4)**	**N2-C2**	**1.387(4)**
O1-C11	**1.380(3)**	**N1-C7**	**1.364(3)**	**C7-C10**	**1.484(4)**
O2-C9	**1.400(4)**	**N1-C8**	**1.466(4)**		
Angle	**(°)**	**Angle**	**(°)**	**Angle**	**(°)**
C11-O1-C10	**117.6(2)**	**N1-C1-C6**	**132.3(3)**	**N1-C8-C9**	**114.0(3)**
C1-N1-C8	**126.6(2)**	**N2-C2-C1**	**109.2(2)**	**O2-C9-C8**	**109.3(3)**
C7-N1-C1	**106.3(2)**	**N2-C2-C3**	**130.4(3)**	**O1-C10-C7**	**106.4(2)**
C7-N1-C8	**127.0(3)**	**N1-C7-C10**	**123.8(3)**	**C12-C11-O1**	**125.1(3)**
C7-N2-C2	**105.2(2)**	**N2-C7-N1**	**113.1(2)**	**C16-C11-O1**	**114.9(2)**
N1-C1-C2	**106.1(2)**	**N2-C7-C10**	**123.0(2)**	**C13-C14-*Cl*1**	**120.2(2)**
C15-C14-*Cl*1	**119.5(3)**				

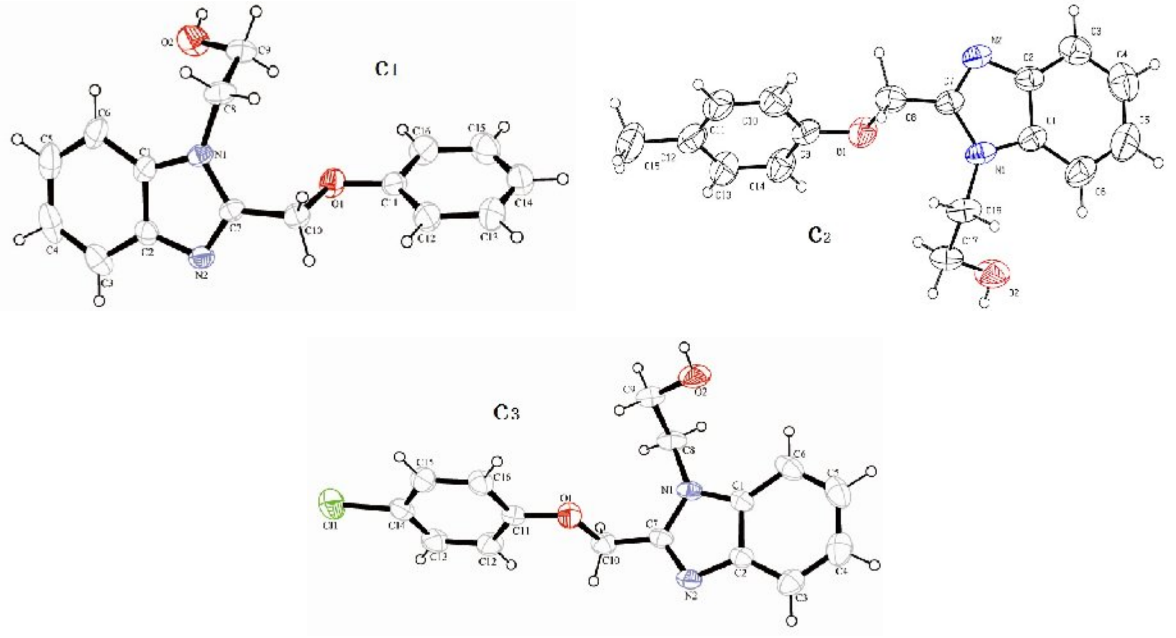

Fig. 2 Crystal molecular structures of $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$

Table-3: Hydrogen bond lengths (Å) and bond angles (°) for $\mathbf{b_2}$, $\mathbf{c_1}$, $\mathbf{c_2}$ and $\mathbf{c_3}$.

D - H ... A	D-H(Å)	H…A(Å)	D…A(Å)	<(DHA)(°)
		b_2		
N2-H2...N1^1	0.761	2.181	2.893	156.01
N4-H4...N3^2	0.794	2.184	2.922	154.55
		c_1		
O2-H2 ... N21	0.820	1.964	2.759	163.34
		c_2		
O2-H2...N2^1	0.820	2.010	2.809	164.71
		c_3		
O2-H2...N2^1	0.820	2.019	2.819	165.26

Symmetry code: (for $\mathbf{b_2}$) ^{1}[x+1/2, y, -z+3/2], ^{2}[x+1/2, y, -z+3/2]; (for $\mathbf{c_1}$) ^{1}[-x, y+1/2, -z+1/2]; (for $\mathbf{c_2}$) ^{1}[-x+1, y-1/2, -z+1/2], ^{2}[-x+1, y+1/2, -z+1/2]; (for $\mathbf{c_3}$) ^{1}[-x-2, y+1/2, -z-1/2].

Supplementary Material

Crystallographic data for the compound $\mathbf{b_1}$, $\mathbf{c_1}$, $\mathbf{c_2}$, and $\mathbf{c_3}$ have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. The deposition numbers are CCDC 1058718, CCDC 1058719, CCDC 1058720, CCDC 1058721, for the structure of $\mathbf{b_1}$, $\mathbf{c_1}$, $\mathbf{c_2}$, and $\mathbf{c_3}$, respectively. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data request/cif, by e-mailing data request@ccdc.cam.ac.uk or by contacting the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033.

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