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ORIGINAL PAPER

Solid State Structure and Intermolecular Interactions of two *N*-Benzylidenephenylethylamines

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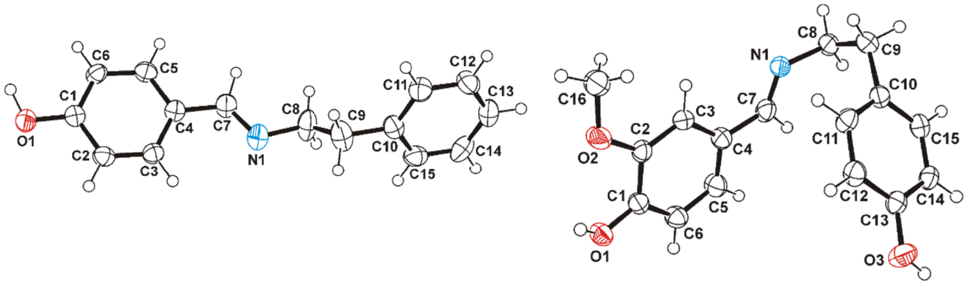
Abstract

This article describes single crystal X-ray diffraction studies of two Schiff bases containing hydroxyl groups in aromatic rings: *N*-(4-hydroxybenzylidene)phenylethylamine (**1**) and *N*-(4-hydroxy-3-methoxybenzylidene)tyramine (**2**). Molecules of compound **1**, with just one phenolic OH group, adopted an *anti* conformation, and were associated in zigzag chains with O–H···N hydrogen bonds between the azomethine fragment and the hydroxyl group. However, a gauche conformation was preferred by compound **2**, which contained two hydroxyl groups in aromatic rings. Molecules of **2** were arranged in a three-dimensional array through O–H···N and O–H···O hydrogen bonding interactions. The results highlighted the importance of OH positions in the aromatic ring for the structural behaviour of the Schiff bases derived from phenylethylamines.

Graphical Abstract

Molecules of Schiff bases containing the moiety ArCH=N–CH_2CH_2Ar with one or two hydroxyl groups in the *para* position in the aromatic rings are associated in zigzag chains in the solid state through O–H···N hydrogen bonding interactions.



Keywords Hydrogen bond · Benzylamine · Phenylethylamine · Schiff base · X-ray structure determination

Introduction

Phenolic Schiff bases have drawn attention due to their important role in biological systems and great ability to coordinate metals and form liquid crystals. The formation of metal complexes, the stability of liquid crystals and the photophysical properties of these compounds are consequences of hydrogen bonds or proton transfer between phenolic hydroxyls and the nitrogen of the azomethine group [1–3].

Structural studies of phenolic Schiff bases derived from tyramine (4-hydroxyphenylethylamine) have revealed intermolecular interactions through hydrogen bonds between the phenolic hydroxyl from one unit of *N*-benzylidenetyramine

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with the imine nitrogen from the other, thereby forming infinite zigzag chains [4]. Continuing our studies related to the β-phenylethylamines' chemical and structural behaviour [5], this article describes the single crystal X-ray diffraction (XRD) structural analysis of two *N*-benzylidenephenylethylamines having different degrees of hydroxylation: 4-hydroxybenzylidenephenylethylamine **1** and 4-hydroxy-3-methoxybenzylidenetyramine **2**.

Experimental Section

Materials

The reagents (tyramine, phenylethylamine and aldehydes) were purchased from Aldrich and used as received and the solvents (Merck, analytical grade methanol and ethanol) were also used without further purification. A Nicolet iS10 spectrometer (Thermo Fisher Scientific, 4000–400 cm^{-1}) was used for infrared (IR) analysis, using KBr disks. Nuclear magnetic resonance spectra were registered on a Bruker Avance 400 spectrometer with a direct probe (5 mm BBO BB-1H/2H) operating at 400.130 MHz for ^1H and 100.634 MHz for ^{13}C. DMSO-d_6 was acquired from Merck.

N-benzylidenephenylethylamines Synthesis (1, 2)

The *N*-benzylidenephenylethylamines were synthesized following the procedure previously described [6].

N-(4-hydroxybenzylidene)phenylethylamine 1 ($C_{15}H_{15}NO$)

White solid, yield 80%, m.p. 187–189 °C, FT-IR (KBr) (cm^{-1}): 3300–2200 and 1665. ^1H NMR (DMSO-d_6) (ppm): 2.88 (2H, t, J = 7.2 Hz), 3.71 (2H, t, J = 7.2 Hz), 6.76 (2H, d, J = 8.4 Hz), 7.19 (5H, m), 7.48 (2H, d, J = 8.4 Hz), 8.12 (1H, s). ^{13}C NMR (DMSO-d_6) (ppm): 37.6, 62.5, 62.5, 115.7, 126.2, 127.7, 128.4, 129.1, 129.8, 140.3, 160.1, 160.8.

N-(4-hydroxy-3-methoxybenzylidene)tyramine 2 ($C_{16}H_{17}NO_3$)

Yellow solid, yield 90%, m.p. 223–225 °C, FT-IR (KBr) (cm^{-1}): 3300–2200 and 1665. ^1H NMR (DMSO-d_6) (ppm): 2.76 (2H, t, J = 7.4 Hz), 3.66 (2H, t, J = 7.4 Hz), 3.78 (3H, s), 6.65 (2H, d, J = 8.4 Hz), 6.79 (1H, d, J = 8.0 Hz), 7.02 (2H, d, J = 8.4 Hz), 7.06 (1H, dd, J = 8.0 Hz, 1.7 Hz), 7.31 (1H, d, J = 1.7 Hz), 8.08 (1H, s). ^{13}C NMR (DMSO-d_6) (ppm): 36.4, 55.6, 62.4, 110.0, 115.1, 115.3, 122.7, 128.0, 129.8, 130.1, 148.0, 149.3, 155.6, 160.6 [6].

Table 1 Experimental data for the X-ray diffraction studies on **1** and **2**

	1	**2**
Formula	$C_{15}H_{15}NO$	$C_{16}H_{17}NO_3$
M_r	225.28	271.30
T (K)	200 (2)	200 (2)
λ (Å)	0.71073	0.71073
Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1/c$	$P2_12_12_1$
a (Å), α (°)	5.898 (1)	8.868 (1)
b (Å), β (°)	17.476 (1), 99.22 (1)	9.236 (1)
c (Å), γ (°)	11.884 (1)	17.568 (1)
V [$Å^3$]	1209.1 (1)	1439.0 (2)
Z	4	4
ρ_{calcd} (g cm^{-3})	1.238	1.252
$\mu_{MoK\alpha}$ (mm^{-1})	0.077	0.087
F(000)	480	576
Crystal size (mm^3)	0.28 × 0.28 × 0.22	0.29 × 0.26 × 0.18
θ Range (°)	3.47 to 27.50	3.18 to 27.49
Index ranges	− 7 to 7 − 22 to 22 − 15 to 15	− 11 to 10 − 11 to 11 − 22 to 22
Reflections collected	26,438	21,225
Unique data	2774 (R_{int} = 0.109)	3296 (R_{int} = 0.068)
Obsd data [I > 2σ(I)]	1582	2583
Goodness-of-fit on F^2	1.069	1.153
Final R^a indices [I > 2σ(I)]	R1 = 0.063 wR2 = 0.136	R1 = 0.054 wR2 = 0.100
R^a indices (all data)	R1 = 0.135 wR2 = 0.174	R1 = 0.082 wR2 = 0.111
Largest diff. peak/hole (e $Å^{-3}$)	0.229/− 0.292	0.340/− 0.308

[a] $R1 = \sum||F_0| - |F_c||/[\sum|F_0|]$; $wR2 = \{[\sum w(F_0^2 - F_c^2)^2]/[\sum w(F_0^2)^2]\}^{1/2}$

X-Ray Structure Determination of 1 and 2

Colourless single crystals were grown from ethanolic solutions of the *N*-benzylidenephenylethylamines **1** and **2** by slow evaporation at room temperature. Suitable crystals were selected with the aid of a microscope, mounted on a cryoloop with a layer of a viscous perfluoropolyether (Fomblin®Y) and placed in the low temperature nitrogen stream of the diffractometer. The intensity data sets were collected on a Bruker-Nonius KappaCCD diffractometer equipped with an Oxford Cryostream 700 unit. The molybdenum radiation was used, graphite monochromated and enhanced with a MIRACOL collimator. Table 1 shows the crystallographic data.

The WinGX package [7] was employed for solving structures by using intrinsic phasing methods (**1**) (SHELXT) or direct methods (**5**) (SHELXS-2013) [8] and refined by least-squares against F^2 (SHELXL-2014/7) [9]. In both

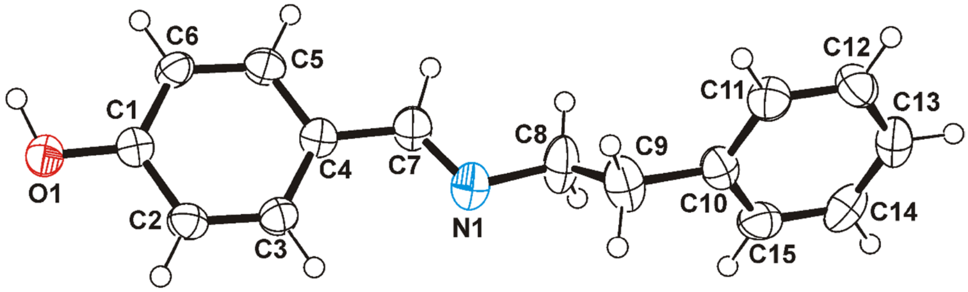

Fig. 1 ORTEP diagram of *N*-(4-hydroxybenzylidene)phenylethylamine **1**. Ellipsoids are drawn at the 50% probability level

crystallographic studies all non-hydrogen atoms were anisotropically refined. The hydrogen atoms were positioned geometrically and refined using a riding model, except those of the imine groups [H(7) in **1** and **2**] and the hydroxylic hydrogens [H(1) in **1**, and H(3) in **2**] which were located in the difference Fourier map and isotropically refined. Hydrogen H(1) of the hydroxyl group next to the methoxy fragment in structure of **2** was also found in the difference Fourier map. Unfortunately the isotropic displacement parameter obtained for H(1) was not appropriate, so the U_{iso} was forced to be 0.05 $Å^2$. Moreover DFIX instruction was applied to constrain the distance O(1)–H(1).

Results and Discussion

Two benzylidenephenylethylamines were synthesized for the present study. The first, with a phenolic hydroxyl in its structure [*N*-(4-hydroxybenzylidene)phenylethylamine **1**] was obtained by reaction of phenylethylamine with 4-hydroxybenzaldehyde. The second, with two hydroxyl groups in its structure (one on each aromatic ring) [*N*-(4-hydroxy-3-methoxybenzylidene)tyramine **2**] was obtained by reaction of tyramine with vanillin [6].

Crystal structures of **1** and **2** were determined by single crystal XRD and analysed to gain information about the influence of phenolic hydroxyl groups on the crystal packing of Schiff bases with the moiety ArCH=N–CH_2CH_2Ar.

In the crystallographic study of the Schiff base *N*-(4-hydroxybenzylidene)phenylethylamine (**1**), the azomethine group presents an *E* configuration between the phenylethylamine and the 4-hydroxyphenyl fragments, with a torsion angle C(4)–C(7)–N(1)–C(8) of 179.6 (2)° (Fig. 1). Additionally, structure of **1** shows a torsion angle N(1)–C(8)–C(9)–C(10) of 176.1 (2)°, which is consistent with an *anti*-staggered conformation regarding rotation around C(8)–C(9) bond.

Molecules of **1** are associated by O–H···N hydrogen bonding interactions between the hydroxyl group and the imine nitrogen atom, with O(1)···N(1)^{i} and H(1)···N(1)^{i}

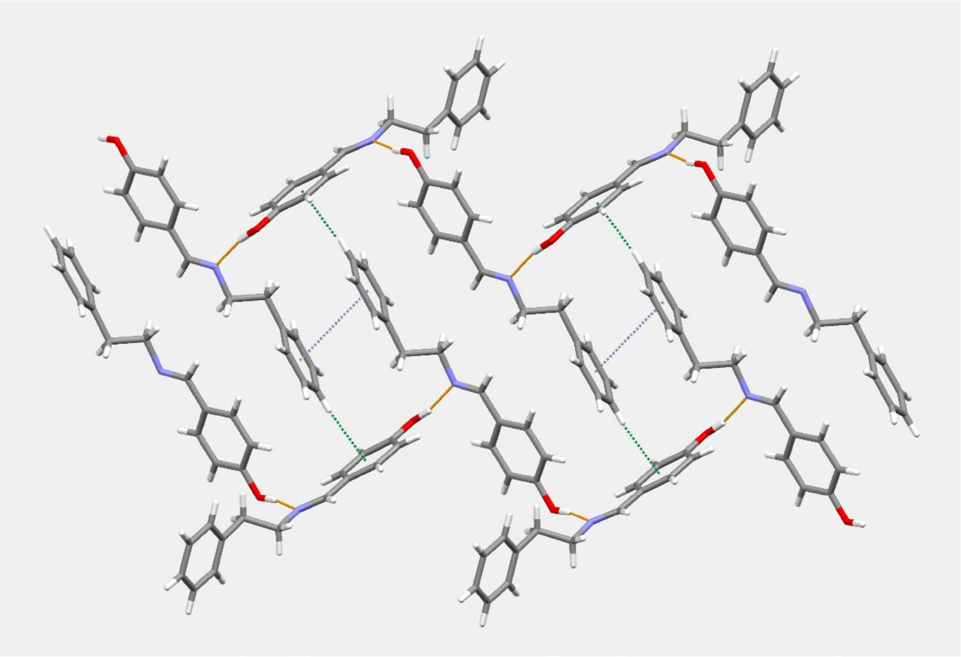

Fig. 2 Perspective view of zigzag chains in **1**. O–H···N hydrogen bonds are drawn in orange, C–H···π interactions in green, and π···π interactions in purple (Color figure online)

Table 2 Bond parameters for relevant π···π and C–H···π interactions in **1**

π···π interaction^a		C–H···π interaction^b	
Cg(2)···Cg(2)^i	3.962 Å	C(13)–H(13)···Cg(1)^{ii}	167°
α	0.0°	H(13)···Cg(1)^{ii}	2.713 Å
β	23.5°	C(13)···Cg(1)^{ii}	3.645 Å
d_p	3.634 Å	δ	6.3°

Symmetry transformation: (i) $-x+1$, $-y+1$, $-z+2$; (ii) $-x+1$, $y-1/2$, $-z+3/2$. Cg(1) and Cg(2) are the geometrical centers of the rings C(1)–C(6) and C(10)–C(15) respectively

[a] Cg(A)···Cg(B) indicates the distance between the centroids of the aromatic rings, α is the dihedral angle between the planes A and B through the carbon atoms of the rings, β is the angle between the Cg(A)···Cg(B) vector and the normal to plane A, and d_p is the perpendicular distance of Cg(A) on plane B

[b] δ is the angle between the H···Cg(A) vector and the normal vector of plane A formed by the aromatic ring

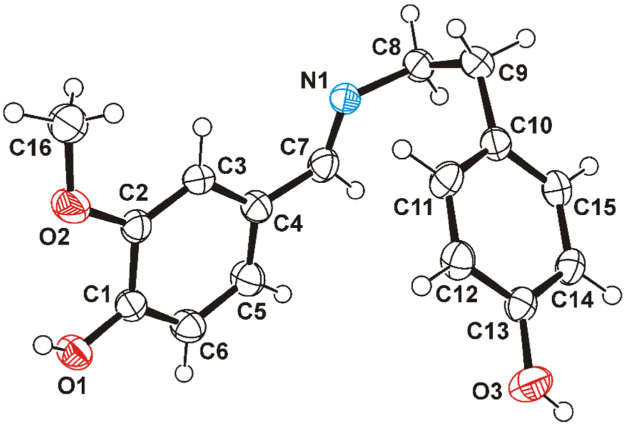

Fig. 4 ORTEP diagram of *N*-(4-hydroxy-3-methoxybenzylidene) tyramine **2**. Ellipsoids are drawn at the 50% probability level

distances of 2.747 (3) and 1.80 (3) Å respectively, and O(1)–H(1)···N(1)^i angle of 169(3)° (symmetry transformation: (i) $-x+1$, $-y+1$, $-z+2$). These hydrogen bonds lead to the formation of zigzag chains along the *c* axis, which are held together through C–H···π and π···π interactions (Fig. 2; Table 2) to generate corrugated layers. The zigzag arrangement in **1** is similar to those found for other Schiff bases with the moiety ArCH=N–CH_2CH_2Ar containing just one hydroxyl group in *para* position, as *N*-(4-nitrobenzylidene) tyramine and *N*-(4-methylbenzylidene)tyramine (Fig. 3) [4, 10]. Interestingly, Schiff bases containing an aromatic ring with just one hydroxyl group in *ortho* position do not show zigzag chains in the crystal packing [11–14].

Comparing with the structure of **1**, the crystallographic analysis of the Schiff base *N*-(4-hydroxy-3-methoxybenzylidene)tyramine (**2**), with two hydroxyl groups in *para* positions, also reveals an *E* configuration for the azomethine group between the tyramine and the 4-hydroxy-3-methoxyphenyl units, with a torsion angle C(4)–C(7)–N(1)–C(8) of 173.4 (3)° (Fig. 4). However, a *gauche* conformation is adopted with a torsion angle around C(8)–C(9) bond quite different [torsion angle N(1)–C(8)–C(9)–C(10) of 60.4 (3)°], which is caused by the crystal packing.

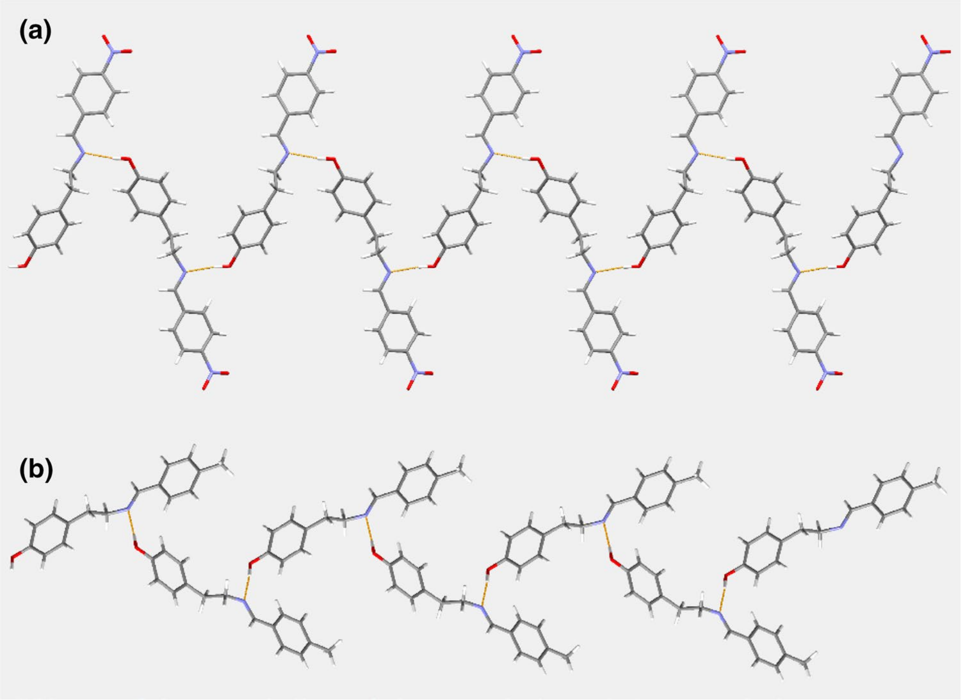

Fig. 3 Perspective view of zigzag chains in the crystal packing of **a** *N*-(4-nitrobenzylidene) tyramine and **b** *N*-(4-methylbenzylidene)tyramine. O–H···N hydrogen bonds are drawn in orange (Color figure online)

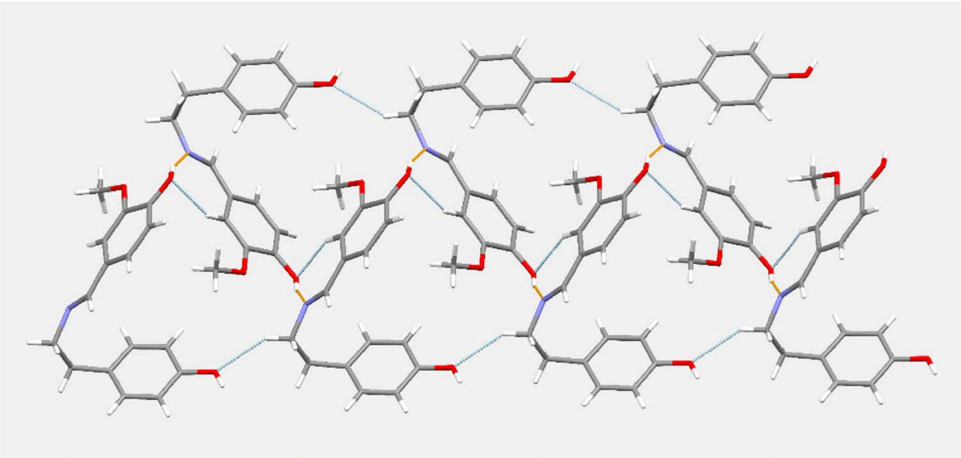

Fig. 5 Perspective view of zigzag motif in **2**. O–H···N hydrogen bonds are drawn in orange, and C–H···O interactions in light blue (Color figure online)

Table 3 Bond parameters for relevant hydrogen bonding interactions in **2**

D–H···A	D···A (Å)	H···A (Å)	D–H···A (°)
O(1)–H(1)···N(1)^{i}	2.792 (4)	2.02 (3)	161 (3)
O(3)–H(3)···O(1)^{iv}	2.589 (3)	1.72 (4)	169 (4)
C(3)–H(3a)···O(1)^{ii}	3.383 (4)		
C(8)–H(8a)···O(3)^{iii}	3.302 (4)		
C(7)–H(7)···O(3)^{v}	3.635 (4)		

Symmetry transformations: (i) $-x+1$, $y+1/2$, $-z+1/2$; (ii) $-x+1$, $y-1/2$, $-z+1/2$; (iii) x, $y-1$, z; (iv) $-x+1/2$, $-y+1$, $z+1/2$; (v) $x-1/2$, $-y+1/2$, $-z+1$

A acceptor, *D* donor, symmetry operators apply to acceptor atoms

Molecules of **2** are arranged in a zigzag motif (Fig. 5) by O–H···N hydrogen bonds between one hydroxyl group and the imine nitrogen atom, with O(1)···N(1)^{i} and H(1)···N(1)^{i} lengths of 2.792 (4) and 2.02 (3) Å respectively, and O(1)–H(1)···N(1)^{i} angle of 161 (3)° [symmetry transformation: (i) $-x+1$, $y+1/2$, $-z+1/2$]. Two non-classical C–H···O hydrogen bonding interactions contribute to maintain the zigzag pattern: C(3)–H(3a)···O(1)^{ii} and C(8)–H(8a)···O(1)^{iii} [Table 3, symmetry transformations: (ii) $-x+1$, $y-1/2$, $-z+1/2$, and (iii) x, $y-1$, z]. Furthermore, C(8)–H(8a)···O(1)^{iii} interactions probably prompt to molecule of **2** to adopt the *gauche* conformation in solid state.

Additionally, the mentioned zigzag motifs are hold together in a three-dimensional arrangement by O–H···O and C–H···O hydrogen bonding interactions (Fig. 6; Table 3), with O(3)···O(1)^{iv} and C(7)···O(3)^{v} distances of 2.589 (3) and 3.635 (4) Å, respectively [symmetry transformations: (iv) $-x+1/2$, $-y+1$, $z+1/2$, and (v) $x-1/2$, $-y+1/2$, $-z+1$].

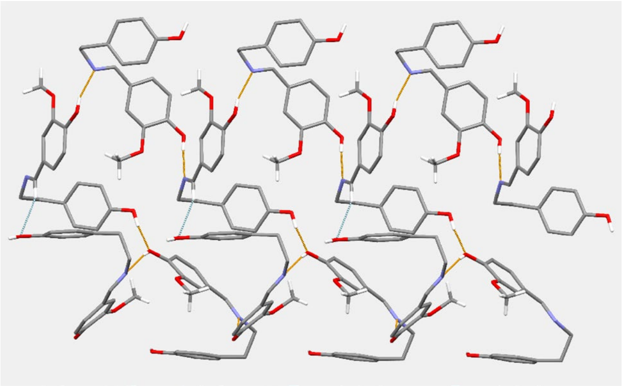

Fig. 6 Perspective view of two zigzag motifs in **2**. Most of hydrogen atoms are omitted for clarity. O–H···N and O–H···O hydrogen bonds are drawn in orange, and C–H···O interactions in light blue (Color figure online)

To the best of our knowledge, there are no examples of Schiff bases crystal structures containing the moiety ArCH=N–CH$_2$CH$_2$Ar with two hydroxyl functions in *para* positions. However, a few crystal structures were described with –OH groups bound to carbon atoms in *para* and *ortho* positions of different rings. In those Schiff bases, the imine nitrogen atoms were implied in O–H···N hydrogen bonding interactions with the hydroxyl groups in *ortho*, and the crystal packing revealed an array in zigzag chains which were built by O–H···O hydrogen bonds between both *ortho* and *para* OH groups [15–18]. The analysis of the crystal packing of **2** shows that the imine nitrogen atom and one of the hydroxyl function in *para* position are building a zigzag pattern, whereas the second hydroxyl group in *para* is implied in the construction of the three-dimensional arrangement.

Conclusion

Molecules of Schiff bases containing the moiety ArCH=N–CH$_2$CH$_2$Ar with one hydroxyl group in *para* position in an aromatic ring are associated in zigzag chains in the solid state through O–H···N hydrogen bonding interactions. The zigzag chains also appeared in Schiff bases crystal structures with one hydroxyl function in *ortho* position and a second OH group in *para* in the other aromatic ring, by forming O–H···O hydrogen bonds. Although a zigzag pattern could also discern in the XRD analysis of Schiff bases with two hydroxyl functions in *para* position, the crystal packing could be better described as a three-dimensional arrangement stabilised by O–H···N and O–H···O hydrogen bonds. The results confirmed that position of OH groups in phenylethylamine derivatives affects the structural behaviour of these compounds.

Supplementary Data

CCDC 1883771–1883772 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via.

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