Synthesis, crystal structure and spectroscopic study of (*E*)-2-methoxy-4-((1-phenylethylimino)methyl)phenol

ABSTRACT

A new unsymmetrical ligand (E)-2-methoxy-4-((1-phenylethylimino)methyl)phenol $C_{16}N_{17}NO_2$ (**I**), was synthetized by one-step condensation reaction. The structure of this new compound was confirmed by elemental analysis, FT-IR, UV-Visible and ^1H and ^{13}C NMR spectroscopy techniques.The compound (**I**) crystallizes in the orthorhombic space group $P2_12_12_1$ with the following unit cell parameters a = 11.7570 (6) Å, b = 10.0711 (6) Å, c = 23.4478(13) Å, V = 2776.4(3) $Å^3$, Z = 4, R_1 = 0.045 and wR_2 = 0.125. The title compound crystallizes with two enantiomers (A and B) in the asymmetric unit which are both in E-stereoisomers. In the crystal structure of the racemic compound, the most noticeable difference between these two molecules is the dihedral angle values between the phenyl rings: 61.61 (1)° and 60.96(1)°.

Keywords: *4-hydroxy-3-methoxybenzaldehyde, 1-phenylethanamine, NMR, UV-Visible, X-ray*

INTRODUCTION

Over the past two decades, vanillin has been widely used as a source of Schiff bases due to its ability to react rapidly with primary aliphatic amino and amino aromatic compounds. These compounds which can present donor sites such as O or N are ligands widely used in coordination chemistry to develop complex materials with original properties[1–3]. Depending on their topology and the nature of the substituents, they can interact with various metal ions such as bidentate[4, 5], tridentate[5, 6] or tetradentate[7, 8] ligands. These ligands can also act in their neutral or deprotonated forms because of the keto-enolic equilibrium which can be established in solution [9–11]. Several works in coordination chemistry involving ligands derived from vanillin have generated compounds with interesting properties. Antioxidant properties acting positively on the prevention and treatment of cancer[12, 13], inflammatory diseases[14], cardiovascular diseases[15], and neurodegenerative diseases[16] have been reported in the literature. In continuing our work in this area, we isolated the ligand (*E*)-2-methoxy-4-((1-phenylethylimino)methyl)phenol from the condensation reaction between p-vanillin and 1-phenylethanamine. The structure of the ligand was elucidated by elemental analyses, FT-IR and NMR spectroscopic studies and X-ray diffraction. The ligand crystallizes with two enantiomers (*A* and *B*) in the asymmetric unit.

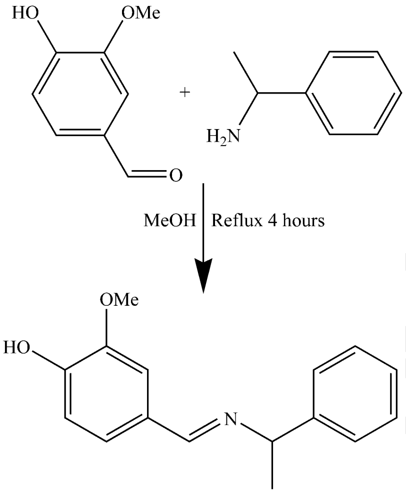
EXPERIMENTAL

Starting materials and instrumentations

4-hydroxy-3-methoxybenzadehyde and 1-phenylethanamine were purchased from Aldrich and used without any further purification. The solvents and reagents were of good quality and were purified by usual methods. Elementary analyzes were carried out in a Carlo-Erba EA microanalyzer. Infrared spectra were recorded with a Perkin Elmer Spectrum Two FT-IR spectrometer in the 4000-400 cm^{-1} region. The ^1H NMR spectrum was recorded in DMSO-d_6 on a Bruker 500 MHz spectrometer at room temperature using TMS as an internal reference. UV-Vis spectra were run on a Perkin-Elmer Lambda 365 UV/Visible spectrometer (1000-200 nm).

2.1 Synthesis of the ligand

p-Vanillin (2 g, 13.145 mmol) was dissolved in a vial containing 20 mL of methanol.1-phenylethanamine(1.6 g, 13.145 mmol) and two drops of glacial acetic acid were added successively. The reaction mixture is brought to reflux for 4 hours. The resulting pink solution was filtered hot. After cooling, the resulting clear solution was left to slowly evaporate. Pink crystals were isolated after few days. Yield: 80%. Tf: > 260°C. Anal. Calc. for [$C_{16}H_{17}NO_2$] (%): C, 75.27; H, 6.71; N, 5.49. Found: C, 75.22; H, 6.70; N, 5.90. IR (ν, cm^{-1}): 3200, 3080, 2980, 1628, 1577, 1513, 1396, 1262, 1026, 865, 826, 769, 699. ^{1}H NMR [DMSO-d_6; δ(ppm)]: 1.56 (d, 3H, –CH_3), 3.73 (s, 3H, –OC$\mathbf{H}_3$),4.59 (q, 1H, –C**H**–N), 8.11 (s, 1H, **H**–C=N),6.65-7.25 (8H, $\mathbf{H}_{Ar}$), 12 (s, 1H, **H**-phenol).



(I)

Scheme 1. Synthetic scheme for the compound (**I**)

2.2 Crystal structure determination

Crystals suitable for X-diffraction, of the reported compound, were grown by slow evaporation of MeOH solution of the complex. Details of the X-rays crystal structure solution and refinement are given in Table 1. Diffraction data were collected using an automatic XtaLAB AFC12 (RINC): Kappa single type diffractometer with graphite monochromatized MoKα radiation (λ = 0.70173 Å). All data were corrected for Lorentz and polarization effects. No absorption correction was applied. Complex scattering factors were taken from the program package SHELXTL[17]. The structures were solved by direct methods which revealed the position of all non-hydrogen atoms. All the structures were refined on F^2 by a full-matrix least-squares procedure using anisotropic displacement parameters for all non-hydrogen atoms [18]. The hydrogen atoms of OH groups were located in the Fourier difference maps and refined. Others H atoms (CH and CH_3 groups) were geometrically optimized and refined as riding model by AFIX instructions. Molecular graphics were generated using ORTEP-3 [19].

Table-1. Crystallographic data and refinement parameter for the compound(I)

Chemical formula	$C_{32}H_{34}N_2O_4$
*M*r	510.61
Crystal system, space group	Orthorhombic, $P2_12_12_1$

Crystal size (mm)	0.20 × 0.15 × 0.02
a (Å)	11.7570 (6)
b (Å)	10.0711 (6)
c (Å)	23.4478 (13)
V ($Å^3$)	2776.4 (3)
Z	4
D_{calc} ($g.cm^{-3}$)	1.222
l (Cu *K*α) (Å)	1.54187
T (K)	296
μ (mm^{-1})	0.64
F(000)	1088
□ range (°)	3.770-77.246
No. of measured reflections	19470
No. of independent reflections	5862
No. of observed [$I > 2\sigma(I)$] reflections	5001
*R*int	0.030
$R[F^2 > 2\sigma(F^2)]$	0.045
$wR(F^2)$	0.125
Goodness-of-fitt (Gof) on F^2	1.03
No. of reflections	5862
No. of parameters	359
No. of restraints	0
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.22, −0.19

RESULTS AND DISCUSSIONS

3.1 General study

The ligand H*L* was prepared by a facile condensation of p-vanillin and 1-phenylethanamine in methanol in 1/1 ratio (**Scheme 1**). The resulting compound is quantitatively yielded (80 %). The elemental analyses results is in accordance with the chemical formulae obtained from X-ray diffraction study. The infrared spectrum of the compound (**I**)reveals bands which are in agreement with those of analogous compounds reported in the literature [20, 21]. In fact, the mainly interested band pointed at *ca*. 1628 $cm^{-1}$is characteristic of the $\nu_{C=N}$absorption, thus confirming the formation of the Schiff base. The $\nu_{O–H}$(3200 cm^{-1}) absorption of the phenolic group,which is expected in the range 3500 cm^{-1} and 3300 cm^{-1}, is shifted to low frequencies due to the intramolecular hydrogen bond established with the methoxy groupsituated on the ortho position of the hydroxy group[22]. Bands pointed at *ca.* 3080 cm^{-1} were attributed to C_{sp2}–H stretching of the phenyl groups while bandspointed in the range 2800–2900 $cm^{-1}$are due to C_{sp3}–H stretching of the aliphatic group. The band characteristic of the presence of aromatic ring are pointed in the range 1577–1450 cm^{-1}[23]. In addition, the characteristic bands of deformation vibrations of out-of-plane aromatic C–H bonds are pointed at 865 cm^{-1} and 769 cm^{-1}.The band which appears at 1262 $cm^{-1}$was assigned to the stretching vibration $\nu_{C–O}$ of the phenolic group. The ^1H spectrum of the H*L* ligand was recorded in DMSO (dmso–d_6). The signals at 12 ppm representing one proton is due to the –OH of the phenolic moiety. The –HC=N proton of the azomethinemoietyis pointed at 8.11 ppm. Signals at 1.56 ppm, 3.73 ppm and 4.59 ppm are, respectively, assigned to the protons of the methyl groups (CH_3–C and CH_3–O) and the proton of the methylidyne group (–CH–N) .The electronic spectrum of the organic molecule recorded in DMF solution shows an intense absorption at 307 nm attributed to the π→π* transitions of the aromatic rings and/or n→π* of the imine function of the ligand.

3.2 Structure description of the compound (I)

The title compound crystallizes in the orthorhombic system with space group $P2_12_12_1$. The asymmetric unit of the title compound (I), $C_{16}H_{17}NO_2$, contains two neutral molecules which are enantiomers (Figure 1). The selected bond lengths and angles are collected in Table 2. The predominant structural feature is the formation of the C=N bonds between the carbonyl carbon atom of the p-vanillin molecules C9/C26 with the amino nitrogen atom of the 1-phenylethanamine molecules N1/N2 [C9–N1 = 1.269(4) Å and C26–N2 = 1.268(4) Å]. These two distances are found to be quite equal and are comparable to those found for similar Schiff bases[24, 25].All other bond lengths and angles are of expected values with C7–N1 [1.480(4) Å], C13–O2 [1.350(3) Å], C14–O1[1.368(3) Å], C23–N2 [1.484(4) Å], C30–O4 [1.348(3) Å], C31–O3[1.361(3) Å]. In the isomer *A*, the methyl group on the asymmetric carbon atom is disordered with two sites having occupancies of 0.7(1) and 0.3(1) for C24 and C25 respectively. The title compound crystallizes with two enantiomers (*A* and *B*) in the asymmetric unit which are both *E*-stereoisomers. In the crystal structure of the racemic compound, the most noticeable difference in the structures of two enantiomers is the dihedral angle values between the phenyl rings: 61.61(1)° for *A*and 60.96(1)° for *B*. The 1-Hydroxy-2-methoxy units of the enantiomers *A* and *B*are planar (rms=0.0139 (A), rms=0.0070 (B))and are quite parallel with a dihedral angle value of 1.091(2)°. The two phenyl rings of the two units are slightly twisted each other with a dihedral angle value of 4.851(3)°. The crystal packing of compound (I) (Figure 2) is stabilized by intermolecular hydrogen bonds N(imino)–H···O(phenol). Intermolecular hydrogen bonds, N2(imino)–H2···$O2^i$(phenol) (i: 1/2-x, 1-y, -1/2+z), N1(imino)–H4···$O4^i$(phenol), (ii: 3/2-x, 1-y, 1/2+z),to the formation of layers parallel to *b* axis (Figure 2, Table 3).

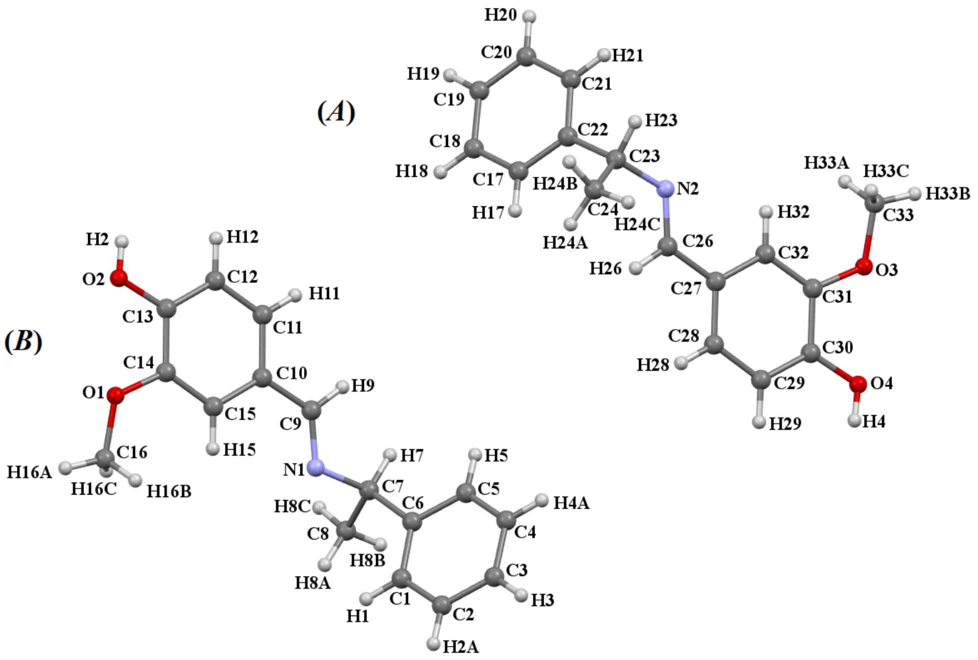


Figure 1. Molecular structures of both enantiomers (*A*) and (*B*) of the title compound with

displacement ellipsoids drawn at the 30% probability.

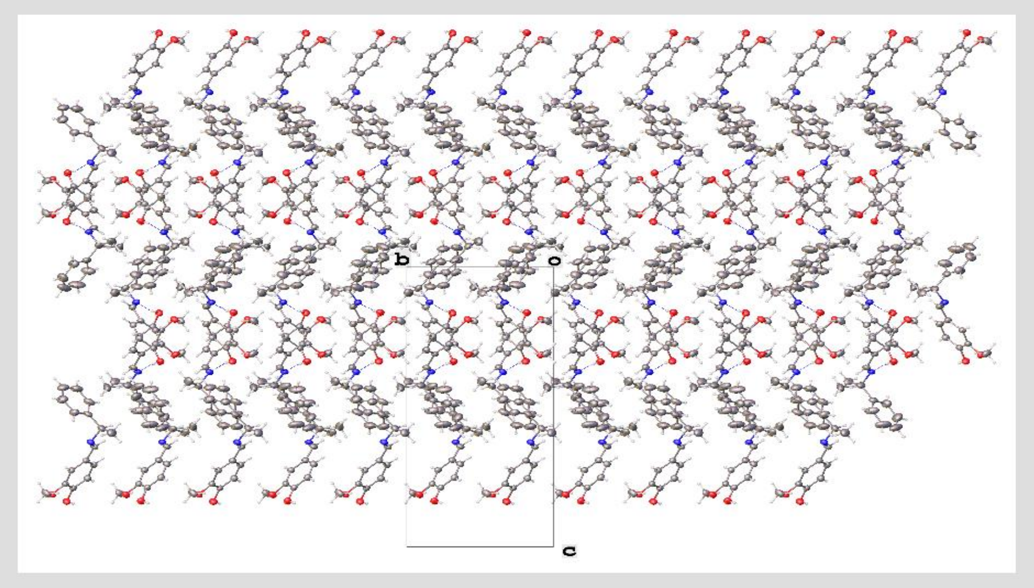


Figure 2. View along the a axis of the crystal packing of molecule of compound and hydrogen bond

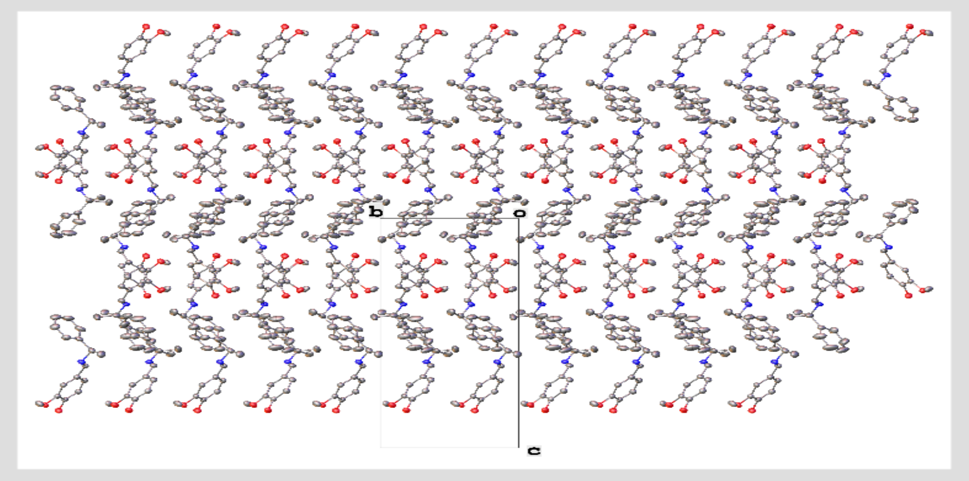


Figure 3. View along the a axis of the crystal packing of molecule of compound without hydrogen atom

Table-2. Selected bond distances [Å] and angles [deg] for the compound (I)

O2—C13	1.350 (3)	O1—C16	1.413 (4)
O4—C30	1.348 (3)	N2—C26	1.268 (4)
O3—C31	1.361 (3)	N2—C23	1.484 (4)

O3—C33	1.419 (4)	N1—C9	1.269 (4)
O1—C14	1.368 (3)	N1—C7	1.480 (4)
N1—C7—C6	109.7 (3)	C24—C23—N2	117.9 (4)
N1—C7—C8	108.4 (3)	C25—C23—C22	125.8 (6)
C6—C7—C8	113.9 (3)	C24—C23—C22	115.6 (4)
N1—C7—H7	108.2	N2—C23—C22	109.5 (3)
C6—C7—H7	108.2	C24—C23—H23	104.0
C8—C7—H7	108.2	N2—C23—H23	104.0
C25—C23—N2	116.7 (6)	C22—C23—H23	104.0

Table-3. Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···N2^{i}	0.82	1.88	2.689(3)	168.3
O4—H4···N1^{ii}	0.82	1.93	2.738(3)	166.2

Symmetry code : (i) 1/2-x,1-y,-1/2+z;(ii) 3/2-x,1-y,1/2+z

CONCLUSION

In this present work we reported the synthesize of anunsymmetrical (*E*)-2-methoxy-4-((1-phenylethylimino)methyl)phenol $C_{16}N_{17}NO_2$ (**I**). The structure of the new Schiff base was discussed by elemental analysis and spectroscopic techniques (FT-IR, UV-visible, ^{1}H NMR). X-rays diffraction technique was used to determine the molecular structure of (**I**).

SUPPLEMENTARY MATERIALS

CCDC-2310613 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/ or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

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