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Synthesis of mono and bis-substituted asymmetrical compounds, (1-(pyridin-2-yl)ethylidene)carbohydrazide and 1-(2-hydroxy-3-methoxybenzylidene)-5-(1-(pyridin-2-yl)ethylidene)carbohydrazide: Structural characterization andantioxidant activity study

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Abstract: *A new dissymmetrical ligand 1-(2-hydroxy-3-methoxybenzylidene)-5-(1-(pyridin-2-yl)ethylidene)carbohydrazide (**H_3L^2**) was synthetized from the precursor (1-(pyridin-2-yl)ethylidene)carbohydrazide (**H_5L^1**) which is obtained bya monocondensation reaction of carbohydrazide with 2-acetylpyridine.The two compounds were characterized by Physico-chemical analyses, elementalanalysis, FTIR, ^1H and ^{13}C NMR spectroscopy techniques. The structures of the two compoundswere determined by single-crystal X-ray diffraction study. The precursor H_5L^1 ($C_8H_{11}N_5O$) crystallizes in the monoclinic space group P21/c with the following unit cellparameters: a = 8.9329 (5) Å, b = 9.8728 (4) Å, c = 10.5538 (7) Å, β = 94.155 (7)°, V = 928.32 (9) Å3, Z = 4, R_1 = 0.0445, wR_2 = 0.112. The ligand H_3L^2 ($C_{17}H_{21}N_5O_4$) crystallizes in the triclinic space group P-1 with the following unit cell parameters: a = 7.2851 (3) Å, b = 10.4542 (6) Å, c = 12.0306 (5) Å, a = 87.973 (4)°, β = 79.372 (4)°, β = 69.850 (5)°, V = 845.02 (7) Å3, Z = 2, R_1 = 0.044, wR_2 = 0.1274. The crystal packing of compound H_5L^1 is stabilized by intermolecular N–H···O(carbohydrazide) hydrogen bonds which form layers parallel to b axis. The crystal packing of compound H_3L^2 is stabilized by intramolecular [(O(Phenol)–H···N(carbohydrazide) and EtO–H···N(pyridine)] and intermolecular hydrogen bonds which form layers parallel to b axis.Each of the two arms of the carbohydrazide is almost coplanar with his corresponding aromatic ring : C6=N2–N3–C8=O and pyridine [4.76°]; C9=N5–N4–C8=O and phenyl [5.29°]. The dihedral angle between the mean planes of the phenyl and the pyridine rings is 5.43°.The antioxidant activities of the two compounds were investigated.*

Keywords*: Carbohydrazide, o-vanillin, 2-acetylpyridine, X-ray.*

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I. Introduction

Carbohydrazide and thiocarbohydrazide ($H_2NNHC(X)NHNH_2$: X=O or S) aresymmetrical compounds with two identical fractions which are very reactive towards carbonyl compounds. The control of the ratio of hydrazide to carbonyl compound makes it possible to synthesize monosubstituted, disubstituted symmetrical or asymmetrical compounds by condensation reaction. Many compounds derived from carbohydrazide are used as precursors in the preparation of heterocyclic compounds with valuable biological properties[1–4]. Some of these compounds have made it possible to develop drugs with a broad spectrum of activities such as antimicrobial [5], anticonvulsant [6], antidepressant [7], antioxidant [8], analgesic [9], antifungal [10], antiplatelet [11], anti-tuberculosis [12], anti-HIV [13], inflammatory [14], anti-diabetic [15] and anti-cancer [16]. These molecules are also known as multitopic ligands for the controlled construction of complex architectures with particular properties such as magnetism [17,18].We have recently begun to examine the coordination behavior of a series of carbohydrazide and thiocarbohydrazide derivatives that possess a number of interesting properties and we have reported a carbohydrazide ligand in which the two arms are reacted with the same or two different carbonyl compounds [19,20]. In this paper, we report the synthesis and the characterization of two

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carbohydrazide derivatives ligand : a monosubstituted (H_5L^1) and a dissymmetrical disubstituted (H_3L^2) compounds. The antioxidant activities of the two compounds were examined.

II. Experimental

2.1. Starting materials and Instrumentations

2-acetylpyridine, 2-hydroxy-3-methoxybenzaldehyde, as well as carbohydrazide were commercial products (from Alfa and Aldrich) and were used without further purification. Solvents were of reagent grade and were purified by the usual methods. Elemental analyses of C, H and N were recorded on a VxRio EL Instrument. Infrared spectra were obtained on an FTIR Spectrum Two of Perkin Elmer spectrometer in the 4000-400 cm^{-1} region. The ^1H NMR spectra were recorded at 300 MHz and $^{13}C\{^1H\}$ NMR spectra at 75 MHz on a Bruker AC-300 instrument.

2.1.1. Preparation of the ligand1-(1-(pyridin-2-yl)ethylidene)carbohydrazide(H_5L^1).

To a solution of carbohydrazide (3.0 g, 0.333 mmol) in a mixture of 10 mL of distillated water and 30 mL of methanol was added dropwise a solution of 2-acetylpyridine (2.019 g, 0.165 mmol) in 10 mL of methanol. The mixture was stirred under reflux for 4 hours. A white precipitate appears gradually. On cooling, the precipitate was isolated by filtration and successively washed with 2 × 10 mL of hot methanol and dried under P_4O_{10}. M.P.: 222°C. Yield: 86.4%. Analytical for**H_5L^1** $C_8H_{11}N_5O$: Calc (found) %C = 49.73 (49.43); %H = 5.74 (5.78); %N = 36.25 (36.21). IR (ν, cm^{-1}): 3306; 3086; 1671; 1629; 1578; 1506; 1466, 1141. ^1H NMR (*dmso-d_6*, δ (ppm)): 2.36 (s, 3H, -CH_3); 4.12 (s, 2H, -NH_2); 7.32 - 8.51 (m, 4H, H_{Py}); 8.19 (s, 1H, -(C=O)-NH-NH_2); 9.64 (s, 1H, -(C=O)-NH-(C=N)-). ^{13}C NMR (*dmso-d_6*, δ (ppm)):157.32 (CH_3-C=N-); 155.30 (C=O); 148.37 (C_{ipso}); 145.45 (C_{Py}); 136.43 (C_{Py}); 123.47 (C_{Py}); 120.13 (C_{Py}); 11.03 (-CH_3).

2.1.2. Preparation of the ligand (1*E*,5*E*)1-(2-hydroxy-3-methoxybenzylidene)-5-(1-(pyridin-2-yl)ethylidene)carbohydrazide methanol monosolvate (H_3L^2).

To a suspension of **H_5L^1**in 20 mL of methanol 1 g (5.18 mmol) was added a solution of 10 mL methanol containing 1.1822 g (7.77 mol) of ortho-vanillin. The mixture is brought to reflux for 30 minutes. The suspension remains and disappears when a drop of glacial acetic acid is added. Reflux is continued for four hours. A clear yellow solution is obtained. After cooling, the solution was stored at 4°C until precipitate appears. The precipitate is collected by filtration, washed with cold methanol (2 x 10 mL) to remove the excess of ortho-vanillin before being dried under P_2O_5. The filtrate which was stored for two weeks at 4°C gave white crystals suitable for X-ray diffraction. The crystals and the precipitate obtained have the same melting point.M.P.: 195-200°C.Yield 74 %. Analytical for **H_3L^2** $C_{17}H_{21}N_5O_4$: Calc (found) % C = 56.82 (56.78) ; % H = 5.89 (5.87) ; % N = 19.49 (19.41). IR (ν, cm^{-1}): 3245; 3198; 3094; 1671; 1616; 1573; 1532; 1468; 1374 ; 1249 ; 1201 ; 1132.NMR^{1}H (*dmso-d_6*, δ(ppm)) : 2.36 (s, 3H, CH_3) ; 3.82 (s, 3H, O-CH_3) ; 6.86 – 7.1 (m, 3H, Har) ; 7.38 – 8.64 (m, 4H, H_{PY}) ; 8.5 (s, 1H, N=C-H) ; 10.86 (s, 2H, N-H) ; 10.09 (s, 1H, O-H_{phenol}). NMR^{13}C (*dmso-d_6*, δen ppm) : 155.22 (CH_3-**C**=N-); 152.55 (**C**=O); 148.87 ($\mathbf{C}_{Ar}$); 148.40 (C_{Ar}); 147.24 (C_{Ar}); 136.96 (C_{Ar}); 119.4-136.6 (C_{Ar}); 56.28 (—O**C**H_3) ; 12.08 (**C**H_3—C=N).

2.2. Free radical scavenging antioxidant assay

Antioxidant capacities of compounds **H_5L^1**and **H_3L^2**are measuredaccording to Akhtar *et al*. [21] method with some modifications. 3.8 mL of themethanol solution of DPPH• (40 mg/L) was added to testcompounds (200 µL) at different concentrations. The mixturewas shaken vigorously and incubated in dark for 30 min atroom temperature. After the incubation time, the absorbance ofthe solution was measured at 517 nm by using UV-visspectrophotometer Perkin two. The DPPH• radical scavengereffect was calculated using the Equation (1):

$$\text{Scavenging activity (\% control)} = \frac{A_{control} - A_{sample}}{A_{control}} \times 100 \quad (1)$$

where $A_{control}$ is the absorbance of the control reaction andA_{sample} is the absorbance of the test compound. The tests werecarried out in triplicate. Trolox was used as positive control.

2.3. X-ray crystallography

Crystals suitable for X-ray-diffraction, of the reported compounds, were grown by slow evaporation of their MeOH solution. Details of the X-rays crystal structure solution and refinement are given in Table 1. Diffraction data were collected using an ENRAF NONIUS Kappa CCD diffractometer with graphite monochromatized MoKα radiation (λ = 0.71073 A). All data were corrected for Lorentz and polarization effects. No absorption correction was applied. Complex scattering factors were taken from the program package SHELXTL[22]. 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 nonhydrogen atoms[23]. The hydrogen atoms of OH and NH groups were

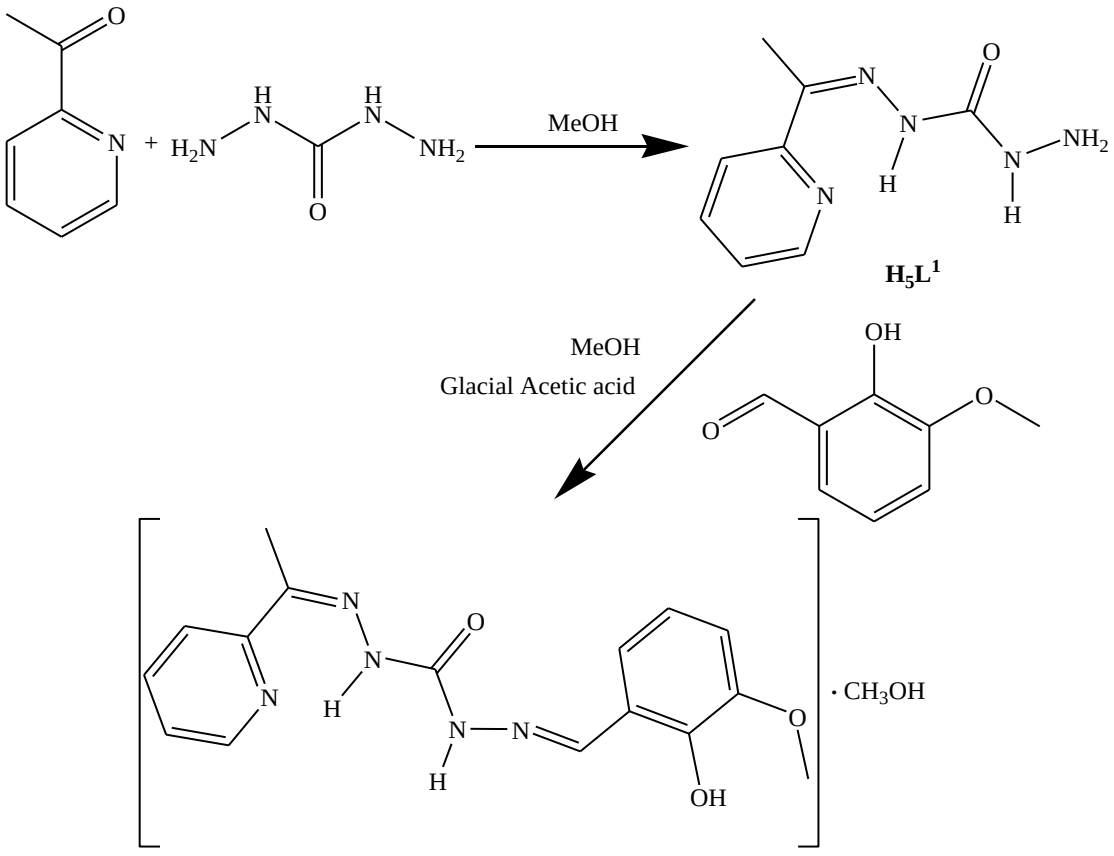
located in the Fourier difference maps and refined. Others H atoms (CH and CH_3 groups) were geometrically optimized and refined as riding model byAFIX instructions. Molecular graphics were generated using ORTEP-3[24].

III. Results and Discussion

3.1. General Study

The IR spectrum of the H_5L^2 precursor shows main bands at 3450 cm^{-1}, 3200 cm^{-1}, 1618 cm^{-1} attributable respectively to ν(–NH_2), ν(–NH–)and ν(C=O)[25]. Upon condensation of the H_5L^1 ligand with o-vanillin additional bands appear in the IR spectrum of the resulting H_3L^2 at 3245 cm^{-1} and 1143 cm^{-1} attributed respectively to ν(O–H) and ν(O–C) stretching vibrations of the 2-methoxyphenolic moiety. The band which was pointed at 3450 cm^{-1} in the spectrum of H_5L^1 is not present, confirming the occurring of the condensation. Both spectra show bands due to the aromatic rings in the range 1458 cm^{-1}–1573 cm^{-1}. The bands which are pointed at *ca*. 1670 cm^{-1} and at *ca*. 1615 cm^{-1} are respectively attributed to ν(C=O) and ν(C=N)[26].

The ^{1}H NMR spectrum of the H_5L^1 ligand was recorded in DMSO (*dmso–d_6*). The signals at 8.19 ppm and 9.64 ppm representing one proton each, are respectively due to the two N**H** which are in different environments. The –N$\mathbf{H}_2$ protons of the hydrazonic moiety are revealed at 4.12 ppm. Signals at 2.36 ppm is assigned to the methyl group protons (C$\mathbf{H}_3$–C=N). The ^{13}C NMR spectrum of the H_5L^1 ligand shows signals at 155.30 ppm (**C**=O), 157.32 ppm (**C**=N), and 11.03 ppm (**C**H_3–C=N). The ^{1}H NMR spectrum of the H_3L^2 shows a broad signal at 10.09 ppm representing one proton and a broad singlet representing two protons at 10.86 ppm which are respectively due to the phenolic proton O–**H** and –N**H**–protons of the hydrazonic moiety. The signal at 8.5 ppm attributed to the **H**C=N is indicative of the occurring of the condensation. Signals at 3.82 ppm and 2.36 ppm are assigned respectively to the methoxy group protons (C$\mathbf{H}_3$–O) and those of the methyl group (C$\mathbf{H}_3$–C=N). The ^{13}C NMR spectrum of the H_3L^2 ligand recorded in DMSO (*dmso–d_6*) shows signals at 152.55 ppm (**C**=O), 155.22 ppm (**C**=N), 56.28 ppm (–O**C**H_3) and 12.08 ppm (**C**H_3–C=N). In both NMR spectra, aromatic protons show signal in the range 7.32–8.64 ppm whilearomatic carbon atoms show signal in range 119.4–148.78 ppm.



H_5L^1

H_3L^2

Scheme 1. Synthesis procedure of the ligands.

Table-1. Crystal data and details of the structure determination of $\mathbf{H_5L^1}$and $\mathbf{H_3L^2}$.

Chemical formula	$C_8H_{11}N_5O$	$C_{17}H_{21}N_5O_4$
M (g/mol)	193.21	359.39
Temperature (K)	293(2)	293(2)
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/c$	P-1
a (Å)	8.9329 (5)	7.2851(3)
b (Å)	9.8728 (4)	10.4542(6)
c (Å)	10.5538 (7)	12.0306(5)
α(°)	90.000 (0)	87.973(4)
β(°)	94.155 (7)	79.372(4)
γ (°)	90.000 (0)	69.850(5)
V ($Å^3$)	928.32 (9)	845.02(7)
Z	4	2
Radiation type	Cu *K*α	Cu *K*α
μ (mm^{-1})	0.80	0.858
Crystal size (mm)	0.15 × 0.05 × 0.03	0.21 × 0.18 × 0.12
T_{min}, T_{max}		0.729, 1.000
No. of measured reflections	1665	13196
Independent reflections	1665	2924
Observed reflections [$I > 2\sigma(I)$]	702	2770
R_{int}	0.036	0.0246
R_1, wR_2 ($I \geq 2\sigma(I)$)	0.0445, 0.112	R_1 = 0.044, wR_2 = 0.1274
R_1, wR_2 indices (all data)	0.0615, 0.127	R_1 = 0.0451, wR_2 = 0.1288
Data/parameters/restraints	1665/140/0	2924/254/0
GOF	0.95	1.097
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.17, -0.17	0.28, -0.30
ρ_{calc}(g /cm^3)	1.375	1.412
Indices h, k, l	$-9 \leq h \leq 6$, $-11 \leq k \leq 6$, $-114 \leq l \leq 10$	$-8 \leq h \leq 8$, $-12 \leq k \leq 12$, $-14 \leq l \leq 14$

Table-2. Selected bond distances [Å] and angles [°] for the compounds.

$\mathbf{H_5L^1}$		$\mathbf{H_3L^2}$	
O1—C2	1.231 (3)	C6—N2	1.2895 (17)
C1—N2	1.270 (4)	C8—N3	1.3704 (17)
N1—C3	1.336 (4)	C8—N4	1.3593 (17)
N2—N3	1.374 (3)	C8—O1	1.2299 (17)
C2—N4	1.339 (3)	C9—N5	1.2862 (17)
C2—N3	1.374 (4)	N2—N3	1.3690 (16)
N4—N5	1.395 (4)	N4—N5	1.3695 (15)
C1—N2—N3	118.4 (2)	N4—C8—N3	116.37 (12)
O1—C2—N4	122.9 (4)	O1—C8—N3	120.47 (11)
O1—C2—N3	120.7 (3)	N2—N3—C8	119.89 (11)
N4—C2—N3	116.4 (3)	N5—N4—C8	116.50 (11)
C2—N4—N5	121.3 (3)		

Table-3. Hydrogen-bond geometry (Å, °) H_5L^1.

D—H···*A*	*D*—H	H···*A*	D···*A*	D—H···*A*
N4—H4···O1i	0.86(3)	2.31(3)	3.009(3)	140(3)
N4—H4···N2	0.86(3)	2.21(3)	2.641(5)	111(2)
C4—H4A···O1i	0.93	2.51	3.406(4)	161.8
N3—H3···N5ii	0.93(3)	2.07(3)	2.991(3)	170(2)
N5—H5A···O1iii	0.90(3)	2.50(3)	3.340(4)	156(3)
C8—H8A···N1	0.96	2.34	2.819(4)	110.3

C8—H8C···O1iv	0.96	2.61	3.551(4)	165.9
C6—H6···N1v	0.93	2.62	3.525(5)	166.3

Symmetrycodes: (i) −x+1, y−1/2, −z+1/2; (ii) −x+1, y+1/2, −z+1/2; (iii) −x+1, −y+1, −z; (iv) x, −y+3/2, z+1/2; (v) −x, y−1/2, −z+3/2.

Table-4: Hydrogen-bond geometry (Å, °) H_3L^2.

D—H···*A*	*D*—H	H···*A*	D···*A*	D—H···*A*
N3—H3a···O1^{i}	0.97(2)	1.86(2)	2.8218(15)	170.9(18)
N4—H4a···O21	0.795(18)	2.063(19)	2.8476(16)	168.7(16)
O2—H2a···N5	0.89(2)	1.78(2)	2.6136(15)	154(2)
O21—H21···N1	0.92(2)	1.85(2)	2.7740(15)	175.4(19)

Symmetry code: (i) −x+1, −y+1, −z+2.

3.2. Structure of H_5L^1

The H_5L^1ligand crystallizes in the monoclinic space group $P2_1/c$. The asymmetric unit contains one ligand molecule. The molecular structure with the atomic-labelling scheme is shown in figure 1. The molecule adopts an *E* configuration with respect to C1=N2 bond. In the structure of the H_5L^1 ligand, the O1 atom of the carbonyl group and the azomethine nitrogen atom N2 are in *trans* with respect to the C2—N3 bond [O1—C2—N3—N2 = 178.9(3)°]. The O1 and N5 atoms are in *syn*conformation with respect to C2—N4 link [O1—C2—N4—N5 = 3.9(5)°]. The pyridine ring is almost coplanar with the carbohydrazide moiety C1=N2–N3–C2=O1 with an angle of 8.02° between their means planes. The C2–O1 bond length of 1.231(3) Å, which has double-bond character, shows that the compound is only in the keto-form in solid state[27]. This forms is confirmed by C2–N3 [1.374(4) Å], and N2–N3 [1.374(3) Å] bond distances, which indicate that these are single bonds[28] and by C1–N2 [1.270(4) Å] which is double bond[29].The crystal packing of compound **H_5L^1** is stabilized by intramolecular and intermolecular hydrogen bonds. The intramolecular hydrogen bond $N4_{(hydrazinyl)}$—$H4\cdots N2_{(azomethine)}$ forms a five membered ring. The numerous intermolecular hydrogen bonds $N4_{(hydrazinyl)}$—$H4\cdots O1^{i}_{(carbonyl)}$(*i*: −x+1, y−1/2, −z+1/2), $N3_{(hydrazinyl)}$—$H3\cdots N5^{ii}_{(carbohydrazide)}$(*ii*: −x+1, y+1/2, −z+1/2), $N5_{(carbohydrazide)}$—$H5A\cdots O1^{iii}_{(carbonyl)}$(*iii*: −x+1, −y+1, −z)lead to the formation of layers parallel to *b* axis (Figure 2, Table 3). Additional weak hydrogen bonds C8—H8C···O1^{iv}(*iv*: x, −y+3/2, z+1/2)and C6—H6···N1^{v} (*v*: −x, y−1/2, −z+3/2) connect the layers and consolidate the structure.

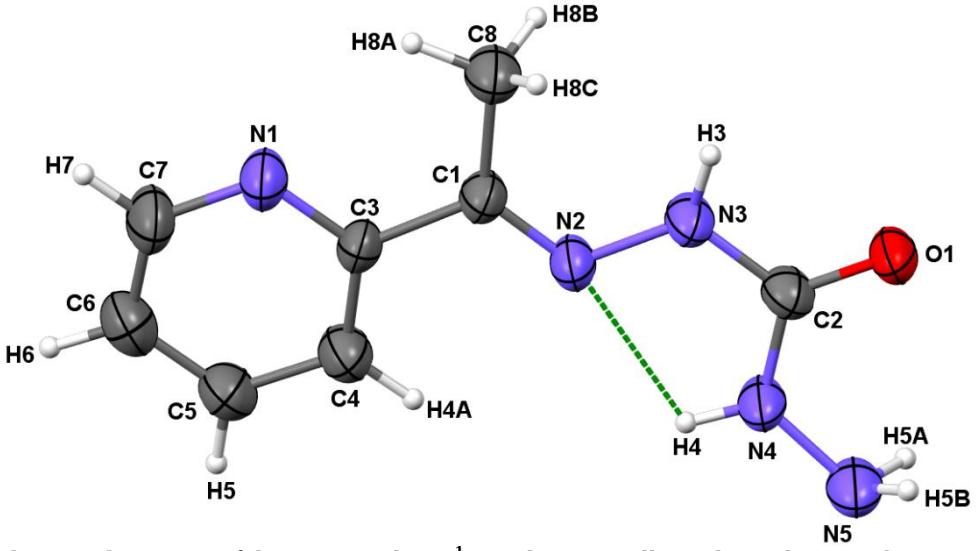


Figure 1: The crystal structure of the compound **H_5L^1**. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small sphere.

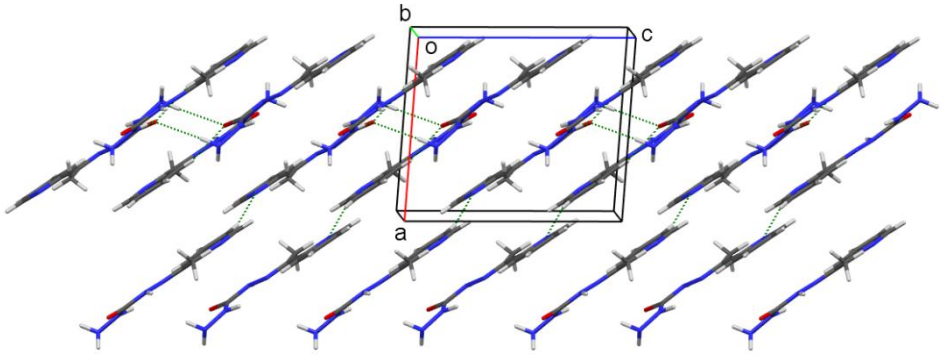


Figure 2: Layers of the title compound $\mathbf{H_5L^1}$viewed along the *b* axis.

3.3. Structure of H_3L^2

The H_3L^2ligand crystallizes in the triclinic space group P-1. The asymmetric unit contains one ligand molecule and one methanol molecule. The molecular structure with the atomic-labelling scheme is shown in figure 3. The two arms of the carbohydrazide are almost coplanar with their corresponding aromatic ring C6=N2–N3–C8=O and pyridine [4.76°]; C9=N5–N4–C8=O and phenyl [5.29°]. The phenyl and the pyridine rings are also almost coplanar [5.43°]. The pyridine ring and the phenol subunit are *trans* with respect to the hydrazino across the C6=N2 and C9=N5 respectively. The C8–O1 bond length of 1.2299(17) Å, which has double-bond character, shows that the compound did not undergo enolization as observed in hydrazides derivatives [30].The bond lengths values of C6–N2 [1.2895(17) Å] and C9–N5 [1.2862(17) Å] are indicative of double bond character. These bond lengths are in the range reported for similar compounds [31].This form is confirmed by C8–N4 [1.3593(17) Å], C8–N3 [1.3704(17) Å] which are typical of an amide. The N2–N3 [1.3690(16) Å] andN4–N5 [1.3695(15) Å] bond distances are shorter than the expected value of 1.40 Å typical for a nominal N(sp^2)—N(sp^2). These observations are indicative of an electronic conjugation over C6=N2–N3–C8=O and C9=N5–N4–C8=O.The atoms O1 and N2 are in a *trans* conformation with respect toC8—N3 with torsion angle O1—C8—N3—N2 = 177.0 (1)°, while O1 and N5 are in a *syn* conformation with respect to C8—N4 with torsion angle O1—C8—N4—N5 = -6.7 (2)°[27].

The crystal packing of compound $\mathbf{H_3L^2}$ is stabilized by hydrogen bonds. The intramolecular hydrogen bonds $O2_{(phenol)}$–H···$N5_{(azomethine)}$forms a six-membered ring. Additional intramolecular hydrogen bonds are observed with the methanol solvate : $O21_{(methanol)}$–H···$N1_{(pyridine)}$, $N4_{(hydrazinyl)}$—H4···$O21_{(methanol)}$, C9—H9···$O21_{(methanol)}$.

Intermolecular hydrogen bonds $N3_{(hydrazinyl)}$—H3···$O1^{i}_{(carbonyl)}$(*i*: −*x*+1, −*y*+1, −*z*+2)lead to the formation of layers parallel to *b* axis (Figure 3-4, Table 4).

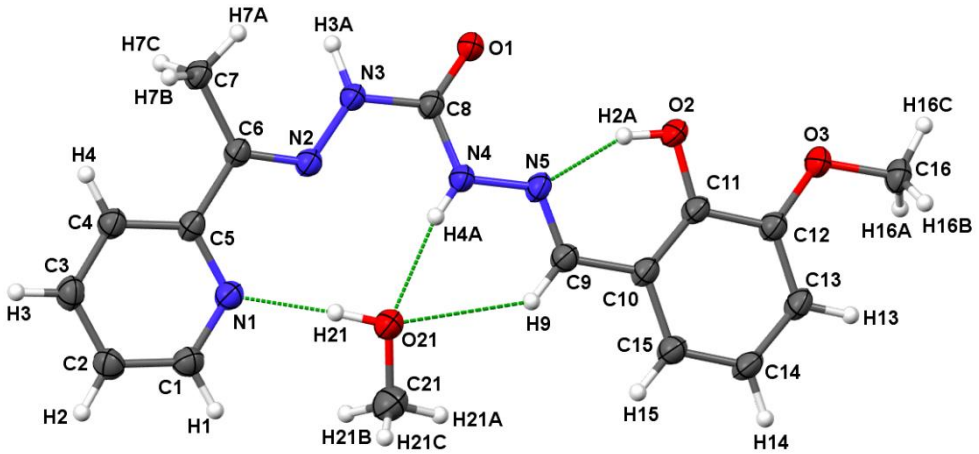


Figure 3: The crystal structure of the compound $\mathbf{H_3L^2}$. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small sphere.

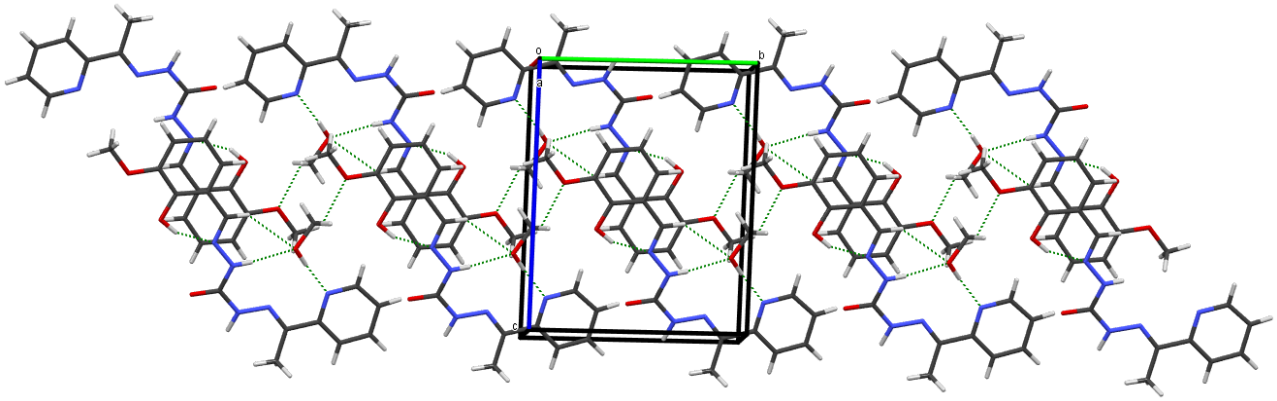


Figure 4: Layers of the title compound $\mathbf{H_3L^2}$viewed along the *b* axis.

3.4. Antioxidant activities

The method of scavenging the DPPH$^{\bullet}$ radical is largely used to evaluate the antioxidant activity of organic or inorganic compounds [32,33]. The antioxidant activities of the two organic compounds $\mathbf{H_5L^1}$and $\mathbf{H_3L^2}$have been substantially investigated. Figure 5shows the plots of DPPH$^{\bullet}$ free radical scavenging activity (%) for Trolox, compounds $\mathbf{H_5L^1}$and $\mathbf{H_3L^2}$. The DPPH$^{\bullet}$ is a stable free radical and becomes a stable molecule when it accepts an electron or hydrogen radical.The antioxidant activity of TROLOX as well as those of the two compounds increase with the concentration. At low concentration (50-200 µM) the antioxidant activity of $\mathbf{H_5L^1}$is comparable to those of TROLOX. When the concentration increases from 300 to 500 µM, the activity of $\mathbf{H_5L^1}$deviates from 25 % to 50 % comparatively to the TROLOX antioxidant activity which present the best results. From 50 to 500 µM, H_3L_2 shows low antioxidant activity which increases slowly from 4% to 15% inhibition.

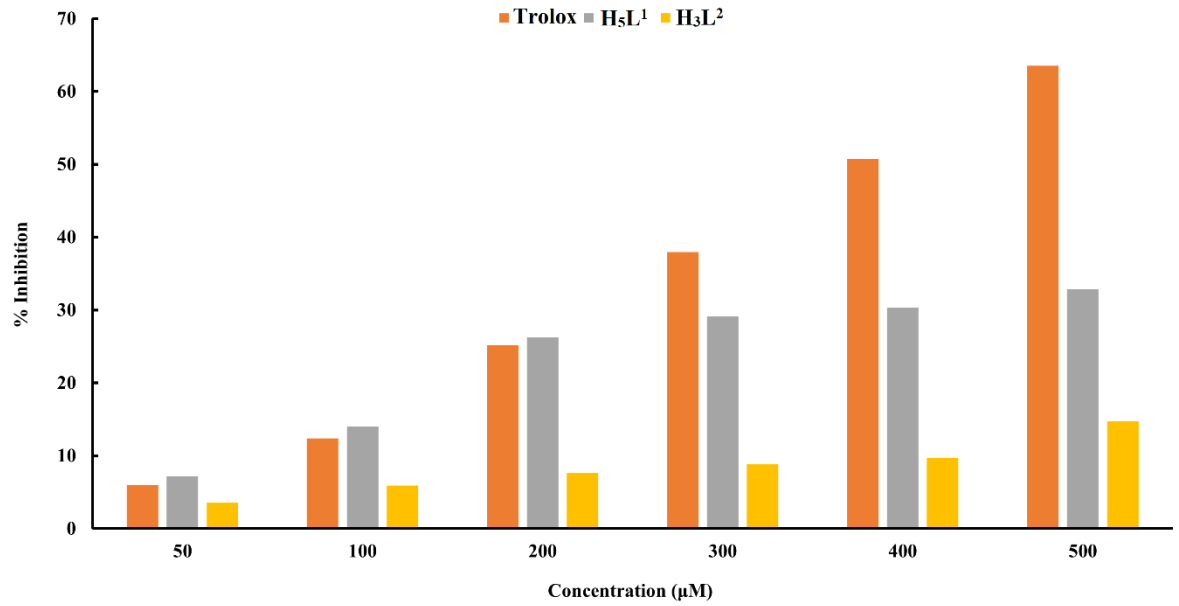


Figure 5: Antioxidant activity of H_5L^1, H_3L^2 and TROLOX.

IV. Conclusion

The monosubstituted carbohydrazide derivative 1-(1-(pyridin-2-yl)ethylidene)carbohydrazide (H_5L^1) firstly prepared was used to prepare the asymmetrical disubstituted 1-(2-hydroxy-3-methoxybenzylidene)-5-(1-(pyridin-2-yl)ethylidene)carbohydrazide (H_3L^2). The structures of the two derivatives were confirmed by elemental analysis andspectroscopic techniques (FT-IR, ^{1}H and ^{13}C NMR).The molecular structure of the two molecules are determined by X-ray diffraction technique. The monosubstituted H_5L^1shows good antioxidant activity at low concentration (50-300 mM) comparatively to the antioxidant activity of TROLOX. The

disubstituted H_3L^2 show low antioxidant activity in the concentration range 50-500 ppm comparatively to those of $H_5L^1$and TROLOX.

Supplementary Materials:
CCDC-2036802(H_5L^1) and 2031061 (H_3L^2)contain 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 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(0)1223-336033.

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References

[1]. Z. Moussa, M. Al-Mamary, S. Al-Juhani, S.A. Ahmed, Preparation and biological assessment of some aromatic hydrazones derived from hydrazides of phenolic acids and aromatic aldehydes, *Heliyon*, *2020*, 6, e05019.
[2]. I.A. Khodja, H. Boulebd, C. Bensouici, A. Belfaitah, Design, synthesis, biological evaluation, molecular docking, DFT calculations and in silico ADME analysis of (benz)imidazole-hydrazone derivatives as promising antioxidant, antifungal, and anti-acetylcholinesterase agents, *J. Mol. Struct., 2020*, 1218, 128527.
[3]. B.S.K. Aktar, Y. Sıcak, T.T. Tok, E.E. Oruç-Emre, A.Ş. Yağlıoğlu, A.K. Iyidoğan, M. Öztürk, I. Demirtaş, Designing heterocyclic chalcones, benzoyl/sulfonyl hydrazones: An insight into their biological activities and molecular docking study, *J. Mol. Struct., 2020*, 1211, 128059.
[4]. Y. Han, Y. Tian, R. Wang, S. Fu, J. Jiang, J. Dong, M. Qin, Y. Hou, Y. Zhao, Design, synthesis and biological evaluation of thieno[3,2-d]pyrimidine derivatives containing aroyl hydrazone or aryl hydrazide moieties for PI3K and mTOR dual inhibition, *Bioorg. Chem., 2020*, 104, 104197.
[5]. K.D. Katariya, S.R. Shah, D. Reddy, Anticancer, antimicrobial activities of quinoline based hydrazone analogues: Synthesis, characterization and molecular docking, *Bioorg. Chem., 2020*, 94, 103406.
[6]. L. Dehestani, N. Ahangar, S.M. Hashemi, H. Irannejad, P.H. Masihi, A. Shakiba, S. Emami, Design, synthesis, in vivo and in silico evaluation of phenacyl triazole hydrazones as new anticonvulsant agents, *Bioorg. Chem., 2018*,78, 119–129.
[7]. A.B. Thomas, R.K. Nanda, L.P. Kothapalli, S.C. Hamane, Synthesis and biological evaluation of Schiff's bases and 2-azetidinones of isonocotinyl hydrazone as potential antidepressant and nootropic agents, *Arabian J. Chem., 2016*, 9, S79–S90.
[8]. M. Demurtas, A. Baldisserotto, I. Lampronti, D. Moi, G. Balboni, S. Pacifico, S. Vertuani, S. Manfredini, V. Onnis, Indole derivatives as multifunctional drugs: Synthesis and evaluation of antioxidant, photoprotective and antiproliferative activity of indole hydrazones, *Bioorg. Chem., 2019*, 85, 568–576.
[9]. A.T. Taher, M.T.M. Sarg, N.R.E.-S. Ali, N.H. Elnagdi, Design, synthesis, modeling studies and biological screening of novel pyrazole derivatives as potential analgesic and anti-inflammatory agents, *Bioorg. Chem., 2019*,89, 103023.
[10]. A.-E. Dascalu, A. Ghinet, E. Lipka, C. Furman, B. Rigo, A. Fayeulle, M. Billamboz, Design, synthesis and evaluation of hydrazine and acyl hydrazone derivatives of 5-pyrrolidin-2-one as antifungal agents, *Bioorg. Med. Chem. Lett*., *2020*, 30, 127220.
[11]. A.K. Jordão, V.F. Ferreira, E.S. Lima, M.C.B.V. de Souza, E.C.L. Carlos, H.C. Castro, R.B. Geraldo, C.R. Rodrigues, M.C.B. Almeida, A.C. Cunha, Synthesis, antiplatelet and in silico evaluations of novel N-substituted-phenylamino-5-methyl-1H-1,2,3-triazole-4-carbohydrazides, *Bioorg. Med. Chem*., *2019*, 17, 3713–3719.
[12]. P. Rawat, R.N. Singh, P. Niranjan, A. Ranjan, N.R.F. Holguín, Evaluation of antituberculosis activity and DFT study on dipyrromethane-derived hydrazone derivatives, *J. Mol. Struct*., *2017*, 1149, 539–548.
[13]. P. Vicini, M. Incerti, P.L. Colla, R. Loddo, Anti-HIV evaluation of benzo[d]isothiazole hydrazones, *Eur. J. Med. Chem*., *2009*, 44, 1801–1807.
[14]. S.M. Sondhi, M. Dinodia, A. Kumar, Synthesis, anti-inflammatory and analgesic activity evaluation of some amidine and hydrazone derivatives, *Bioorg. Med. Chem*., *2006*, 14, 4657–4663.
[15]. K. Karrouchi, S. Fettach, M.M. Jotani, A. Sagaama, S. Radi, H.A. Ghabbour, Y.N. Mabkhot, B. Himmi, M.E.A. Faouzi, N. Issaoui, Synthesis, crystal structure, hirshfeld surface analysis, DFT calculations, anti-diabetic activity and molecular docking studies of (E)-N'-(5-bromo-2-hydroxybenzylidene) isonicotinohydrazide, *J. Mol. Struct*., *2020*, 1221, 128800.
[16]. S. Narayanan, P. Gupta, U. Nazim, M. Ali, N. Karadkhelkar, M. Ahmad, Z.-S. Chen, Anti-cancer effect of Indanone-based thiazolyl hydrazone derivative on colon cancer cell lines, *Int. J. Biochem. Cell Biol*., *2019*, 110, 21–28.
[17]. B. Čobeljić, I. Turel, A. Pevec, Z. Jagličić, D. Radanović, K. Anđelković, M.R. Milenković, Synthesis, structures and magnetic properties of octahedral Co(III) complexes of heteroaromatic hydrazones with tetraisothiocyanato Co(II) anions, *Polyhedron*, *2018*, 155, 425–432.
[18]. M. El-Behery, H. El-Twigry, Synthesis, magnetic, spectral, and antimicrobial studies of Cu(II), Ni(II) Co(II), Fe(III), and UO_2(II) complexes of a new Schiff base hydrazone derived from 7-chloro-4-hydrazinoquinoline, *Spectrochim. Acta, Part A, 2007*, 66, 28–36.
[19]. T.M. Seck, M. Diop, D. Diouf, O. Diouf, A.H. Barry, M. Gaye, Synthesis, spectroscopic studies and crystal structure determination of a tetranuclearZn(II) [2x2] square grid structure of 1,5-bis(1-(pyridin-2-yl)ethylidene)carbonohydrazide, *IOSJR J. Appl. Chem*., *2018*, 11, 06–14.
[20]. T.M. Seck, F.D. Faye, A.A. Gaye, E.I. Thiam, O. Diouf, M. Gaye, P. Retailleau, Synthesis of mono and bis-substituted asymmetrical compounds, (1-(pyridin- 2-yl)ethylidene)carbonohydrazide and 1-(2'-hydroxybenzylidene)-5-(1'-pyridylethylidene)carbonohydrazone: Structural characterization and antioxidant activity study, *Eur. J. Chem*., *2020*, 11, 285–290.
[21]. P. Akhtar, Z. Yaakob, Y. Ahmed, M. Shahinuzzaman, M.K.M. Hyder, Total Phenolic Contents and Free Radical Scavenging Activity of Different Parts of Jatropha Species, *Asian J. Chem*., *2018*, 30, 365–370.
[22]. G.M. Sheldrick, ıt SHELXT – Integrated space-group and crystal-structure determination, *Acta Crystallogr. Sect.A: Found. Adv*.,*2015*, 71, 3–8.
[23]. G.M. Sheldrick, Crystal structure refinement with ıt SHELXL, *Acta Crystallogr*., *Sect. C*: *Struct. Chem*., *2015*, 71, 3–8.
[24]. L.J. Farrugia, ıt WinGX and ıt ORTEP for Windows: an update, *J. Appl. Crystallogr*., *2012*, 45, 849–854.

[25]. A.K. Singh, O.P. Pandey, S.K. Sengupta, Synthesis, spectral and antimicrobial activity of Zn(II) complexes with Schiff bases derived from 2-hydrazino-5-[substituted phenyl]-1,3,4-thiadiazole and benzaldehyde/2-hydroxyacetophenone/indoline-2,3-dione, *Spectrochim. Acta, Part A, 2013*, 113, 393–399.
[26]. F.B. Tamboura, O. Diouf, A.H. Barry, M. Gaye, A.S. Sall, Dinuclear lanthanide(III) complexes with large-bite Schiff bases derived from 2,6-diformyl-4-chlorophenol and hydrazides: Synthesis, structural characterization and spectroscopic studies, *Polyhedron, 2012*, 43, 97–103.
[27]. R. Karimian, H. Hosseini-Monfared, R. Bikas, N.B. Arslan, C. Kazak, A. Koroglu, (*E, E*)-*N*′-{4-[(2-Benzoylhydrazin-1-ylidene)methyl]benzylidene]}benzohydrazide, *Acta Crystallogr*., *Sect. E*: *Struct. Chem*., 2012, 68, o1433.
[28]. H.H. Monfared, R. Bikas, P. Mayer, (*E*)-3-Hydroxy-*N*′-(2-hydroxybenzylidene)-2-naphthohydrazide, *Acta Crystallogr*., *Sect. E*: *Struct. Chem*., *2010*, 66, o236–o237.
[29]. R. Bikas, P.M. Anarjan, S.W. Ng, E.R.T. Tiekink, 2-[((*E*)-2-{2-[(*E*)-2-Hydroxybenzylidene]hydrazinecarbonyl]}hydrazinylidene)methyl]phenol, *Acta Crystallogr*., *Sect. E*: *Struct. Chem*., *2012*, 68, o193.
[30]. M.C. Rodríguez-Argüelles, R. Cao, A.M. García-Deibe, C. Pelizzi, J. Sanmartín-Matalobos, F. Zani, Antibacterial and antifungal activity of metal(II) complexes of acylhydrazones of 3-isatin and 3-(N-methyl)isatin, *Polyhedron*, *2009*, 28, 2187–2195.
[31]. E.I. Thiam, M. Diop, M. Gaye, A.S. Sall, A.H. Barry, 1,2-Bis(*N*'-benzoylthioureido)benzene, *Acta Crystallogr*., *Sect. E*: *Struct. Chem*., *2008*, 64, o776.
[32]. Z.A. Taha, A.M. Ajlouni, W.A. Momani, A.A. Al-Ghzawi, Syntheses, characterization, biological activities and photophysical properties of lanthanides complexes with a tetradentate Schiff base ligand, *Spectrochim. Acta, Part A, 2011*, 81, 570–577.
[33]. M.C. Foti, C. Daquino, C. Geraci, Electron-Transfer Reaction of Cinnamic Acids and Their Methyl Esters with the DPPH• Radical in Alcoholic Solutions, *J. Org. Chem*., *2004*, 69, 2309–2314.

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