

Synthesis, Structure, Hirshfeld surface analysis and Anti-oxidant studies on 2-(4-dimethylamino) benzyldene) hydrazine-1-carbothioamide

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Abstract: The crystallographic structure of the Schiff base, 2-(4-dimethylamino) benzyldene) hydrazine-1-carbothioamide (H₁L) is reported from X-ray single crystal data. The crystal structure is a triclinic crystal unit cell, space group P-1(2) with a = 8.529(3) Å, b = 9.387(4) Å, c = 15.538(6) Å, alpha = 73.926(12) °, beta = 79.730(12) °, gamma = 83.087(13) °, V = 1174.2(8) Å³ and Z = 4. The Hirshfeld surface analysis revealed the presence of $\pi \dots \pi$ stacking and N-H... π interactions. The title compound (H₁L) was synthesized by the condensation reaction of thiosemicarbazide, and p-dimethylaminobenzaldehyde and characterized using microanalysis, FT-IR, UV-Visible, ¹H-NMR, ¹³C-NMR, HMBC, COZY, NOESY and used to investigate their antioxidant potency. Antioxidant activity of H₁L shows that the potency of the Schiff base is comparable to that of vitamin C.

Keywords: Thiosemicarbazone, p-dimethylaminobenzaldehyde, Crystal structure, antioxidant activity, Spectroscopic methods.

1. Introduction

The design and elaboration of organic compounds for biological applications is an important area of synthetic chemistry. More precisely, Schiff bases are an important class of organic compounds due to their excellent coordination abilities and their wide range of industrial and biological applications. For example, recently Schiff bases have been shown to exhibit a broad range of biological properties (Boshaala *et al.*, 2020; Fitsum *et al.*, 2021). The presence of the imine group (RHC=NR', where R and R' are alkyl or aryl groups) in Schiff bases has been shown to account for the observed biological properties (Sunjuk *et al.*, 2022; Soroceanu *et al.*, 2022; Titi *et al.* 2020; Mainsah *et al.*, 2013). Schiff bases containing aryl substituents are easier to synthesize and are more stable than those involving alkyl substituents. Indeed, Schiff bases formed from aliphatic aldehydes are unstable and can easily polymerize (Udaysinha *et al.*, 2018). Schiff base compounds containing many donor atoms (N, O, S), are biologically active and are excellent chelators of metal ions and therefore, serve as important building blocks for new materials with promising electronic, mechanical or biological properties (Ceramella *et al.*, 2022), (Nasiri *et al.*, 2020), (Tanzeela *et al.*, 2022). Moreover, they have been shown

to exhibit antibacterial, antifungal, antimalarial, antiviral, and anticancer properties, which are often enhanced when they form metal complexes (Ceramella *et al.*, 2022).

Schiff bases have also attracted renewed interest in recent years as they form building blocks for the design of new biologically significant compounds. Thiosemicarbazone containing the azomethine group ($-C=N-$), are usually synthesized by the condensation of primary amines and carbonyl groups. Systematic studies have revealed that the S- and N-donor atoms of hydrazine are the active centres of thiosemicarbazone (Ram *et al.*, 2006), (Alonso *et al.*, 2022; Rayyan *et al.*, 2023). Extensive investigations have revealed that thiosemicarbazone derivatives show remarkable biological properties (Grieve *et al.*, 2021), (Castineiras *et al.*, 2000), (Swearingen *et al.*, 2001), (Murali *et al.*, 2013), (Shim *et al.*, 2013). Heterocyclic thiosemicarbazones, for example, are chelating ligands with the ability to form air-stable and less toxic complexes which have been extensively studied for their antimicrobial, anticancer, and antiviral properties (Abdul khaderJailani *et al.*, 2018; Ngoudjou *et al.*, 2022).

Within this framework, our group has recently reported on studies on the antimicrobial and antioxidant activities of complexes of heterocyclic Schiff bases, some of which are derived from thiosemicarbazone (Kuate *et al.*, 2020). They generally behave as bidentate or tridentate chelators, forming six-coordinate complexes.

In continuation of an ongoing studies on thiosemicarbazones, we hereby report on the synthesis, characterization, and antioxidant properties of p-dimethylaminobenzaldehyde thiosemicarbazone derived from the condensation reaction of thiosemicarbazide and p-dimethylaminobenzaldehyde. We also revisit the crystal structure of the titled compound, using Hirshfeld surface analysis to study the intermolecular interactions in the molecule.

2. Materials and Experimental Methods

2.1 Materials and instruments

All reagents (*p*-dimethylaminobenzaldehyde (97%), thiosemicarbazide (98%), ethanol (95%), and solvents) used in this work were obtained from commercial sources and used without any further purification. Microanalysis (C, H, N, and S) data were obtained using a Euro EA 3000 elemental analyzer. Infrared spectra were obtained using KBr pellets on a Genesis FTIR/TM spectrophotometer (ATI Mattson) equipped with a DTGS (Deuterated Tri Glycine sulfate) detector in the transmittance mode from 400-4000 cm^{-1} . Electronic spectra were obtained on an Ocean Insight FX-VIS-IRS-ES spectrophotometer at room temperature. NMR spectra were obtained on a Bruker Advance II 500MHz Spectrometer with 5mm BBO Probehead using d_6 -DMSO as solvent. Complete assignment of the NMR signals of the compounds was supported by two-dimensional spectral analysis (heteronuclear multiple bond correlation (HMBC) and heteronuclear single quantum correlation (HSQC)).

2.2 Synthesis and crystallization of 2-(4-dimethylamino) benzylidene)hydrazine-1-carbothioamide

2-(4-dimethylamino) benzylidene)hydrazine-1-carbothioamide (H_1L) was synthesized according to the general synthetic procedure reported elsewhere with some slight modifications (Murali *et al.*, 2013). The Schiff base was synthesized by the condensation reaction between *p*-dimethylaminobenzaldehyde (0.75 g; 5 mmol) and thiosemicarbazide (0.46 g; 5 mmol) dissolved in hot ethanol. The mixture was maintained under reflux for three hours, after which the volume of the resulting yellow solution was reduced to half by evaporation and the resulting yellow precipitate was filtered, washed several times with ethanol, and air-dried to obtain a yellow product. Suitable crystals of the Schiff base (H_1L) were grown by slow evaporation of a dilute ethanolic solution to produce crystals suitable for X-ray analysis. The reaction equation is represented in Scheme 1.

Analysis: Yield: 94 %; M.p.: 187 °C; Calcd. For C₁₀H₁₄N₄S: C, 54.03; H, 6.36; N, 25.20; S, 14.42. Found: C, 54.68.; H, 6.48; N, 25.48; S, 14.42%. FT-IR (KBr, ν , cm⁻¹): 3378-3413 (NH₂, thioamide), 3126 (NH, carbazid), 1586 (C=N) (Azomethine), 1169 (N-N) (Azid), 808 (C=S, thioamide); ¹H NMR (500 MHz, DMSO-d₆, δ , ppm): 11.17 (s, 1H, N-H), 7.99 (s, 1H, Ar-C=N), 7.75 (s, 2H, NH₂), 7.58 (d, 2H, Ar), 6.69 (d, 2H, Ar), 3.34 (m, 6H, CH₃). ¹³C NMR (125 MHz, CDCl₃, δ , ppm): 176.99 (1C, C=S), 143.34 (1C, C=N), 151.35 (1C, Ar-N), 121.38 (1C, Ar-C=N), 128.59 (1C, Ar-C), 111.66 (1C, Ar-C), 39.76 (1C, CH₃). UV/Vis (CHCl₃, λ_{max} , nm): 354, 400.

2.3 Crystallographic details of H₁L

A single crystal of 2-(4-dimethylamino) benzyldiene)hydrazine-1-carbothioamide (H₁L) ; C₁₀H₁₄N₄S (H₁L), measuring 0.80 x 0.60 x 0.50 mm³, was mounted on the goniometer head and X-ray data were collected on a Bruker APEXII QUAZAR CCD diffractometer using a monochromated I μ S Mo-K α radiation, λ = 0.71073 Å at a temperature of 293K. Crystal data, data collection and structure refinement details are summarized in Table 1. All non-hydrogen atoms were refined with anisotropic displacement parameters and the hydrogen atoms were included in the calculated positions and refined riding on their respective carbon atoms with isotropic displacement parameters. Supplementary crystallographic data have been deposited with Cambridge Crystallographic Data Centre with deposition number CCDC 2206249.

2.4 Antioxidant Study

The compound was tested for *in vitro* antioxidant activity at 37°C using both the free radical scavenging assay (DPPH) and Ferric Ion Reducing Antioxidant Power assay (FRAP). Ascorbic acid was used as a positive control and was treated in the same way as the DPPH assay. The assay was performed in triplicate.

2.4.1 DPPH Free Radical Trapping Assay

The principle is based on the capacity of compounds in the extracts to supply protons to 2-Diphenyl-1-picrylhydrazyl (DPPH) free radicals. DPPH is an unstable, violet-coloured molecule that absorbs light at 517 nm (Scherer *et al.*, 2009). In the presence of a free radical scavenger, it is reduced to a stable yellow compound whose colour intensity is proportional to the capacity of the antioxidants present in the medium. The extracts were prepared at 40mg/mL. In fact, 10mg of extracts were dissolved in 250 μ L of 100% DMSO to reduce the final DMSO concentration to 0.5% in the first well. A 0.02% DPPH solution was prepared with ethanol and stored in a tightly closed jar in the dark. Initially, the samples were diluted to give final concentrations of 200, 100, 50, 25, 12.5, and 6.25 μ g/mL. Ten microplate (10 μ L) from each dilution was introduced into a new microplate and 90 μ L of 0.02% DPPH solution was added to obtain final concentrations of 200, 100, 50, 25, 12.5, and 6.25 μ g/mL. Optical densities were read at 517 nm after 30 minutes incubation at room temperature in the dark. The positive control made of ascorbic acid was treated in the same way as the extracts and assays also performed in triplicate. The antioxidant activity related to the DPPH' radical scavenging effect is expressed in relative terms using the following formula in Eqn. 1:

$$(IP) = \frac{\text{Control Absorbance} - \text{Sample Absorbance}}{\text{Control absorbance}} \times 100 \quad \text{Eqn. 1}$$

where IP= Inhibition percentage

2.4.2 Ferric Ion Reducing Antioxidant Power Assay (FRAP)

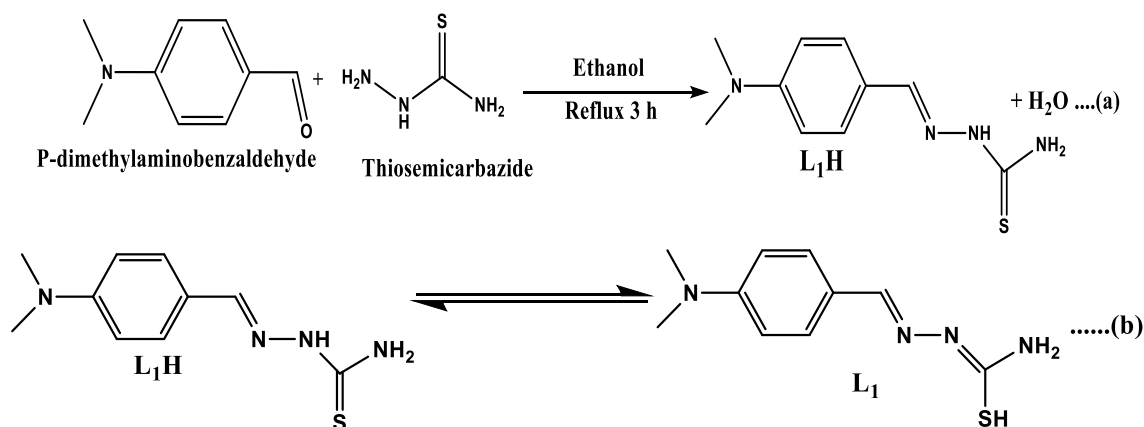
The Fe³⁺ reduction test was carried out according to the protocol described by Path Canada *et al.*, 1994 with some modifications. This method is based on the ability of a substance to reduce Fe³⁺ ions to Fe²⁺

ions which in the presence of 1,10-phenanthroline form a red-orange complex whose optical density can be measured at 505nm. The intensity of the coloration is proportional to the amount of Fe^{3+} ions converted by the extract. A solution of 1.2 mg/mL of Fe^{3+} was prepared in distilled water. The sample was diluted to various concentrations and 10 μl from each dilution was introduced into a new microplate. Orthophenanthroline solution prepared at 0.2% was used to determine the amount of Fe^{2+} formed and ascorbic acid was used as a positive control at a concentration of 10mg/ml. The plates were pre-incubated for 15 minutes at room temperature. The stock extract solution was concentrated to 40 mg/mL. 10mg of each extract was weighed and dissolved in 250 μl of 100 % DMSO. In a 96-well microplate, 190 μl of distilled water was introduced into the first column and 160 μl into all subsequent columns for dilution. After this, 10 μl of each extract prepared at 40mg/mL was then added and the dilution was carried out according to a dilution factor of 10 for a final volume of 160 μl . From the optical density of the products, the relative 50 % reducing concentrations of the samples were determined using ascorbic acid (positive control) as a 100 % reduction.

3. Results and Discussion

3.1 Synthesis

2-(4-dimethylamino) benzyldene)hydrazine-1-carbothioamide (H_1L) was prepared by the condensation reaction between *p*-dimethylaminobenzaldehyde and thiosemicarbazide in hot ethanol under reflux as shown in [scheme 1](#).



Scheme 1. Synthesis of 2-(4-dimethylamino)benzyldene)hydrazine-1-carbothioamide (H_1L) (a) and resonance forms was also shown in (b).

The yellow colour of the product was evidence of the formation of 2-(4-dimethylamino) benzyldene)hydrazine-1-carbothioamide (H_1L) Schiff base. Microanalysis results confirmed the purity of the Schiff base which was obtained with a yield at 94 % indicating that the method is quantitative ([Scherer et al., 2009](#)). The melting point of *p*-dimethylaminobenzaldehydethiosemi carbazone (H_1L) is 187°C.

3.2 Infrared study

In the IR spectrum of the H_1L ([Figure S1](#)), the strong and broad band in the 3378– 3413 cm^{-1} range are attributed to $-\text{NH}_2$ group while the band at 3126 cm^{-1} is attributed to N-H of N-NH-N group. The strong band at 1586 cm^{-1} is assigned to the $\nu(\text{C}=\text{N})$ of azomethine group of the Schiff base (H_1L) ([Alim et al., 2015](#)) and the strong band which appear at 1169 cm^{-1} corresponds to (N-N) of the azide group in thiosemicarbazone. The strong band at 808 cm^{-1} is assigned to the $\nu(\text{C}=\text{S})$ in thiosemicarbazone. It is important to note that (H_1L) may exhibit thione-thiol tautomerism, as it contains a thioamide function

($-\text{NH}-\text{C}=\text{S}$) \leftrightarrow ($-\text{N}=\text{C}-\text{S}-\text{H}$). Thus, the absence of the (SH) moiety in the H_1L spectrum around 2570 cm^{-1} indicates the thione nature of the Schiff base. The presence of ($-\text{NH}$) and (NH_2) bands in the spectrum of H_1L suggests that in the solids state, it retains the thione tautomer (Refat *et al.*, 2009).

3.3 NMR Spectral Analysis

3.3.1 ^1H -NMR & ^{13}C -NMR of 2-(4-dimethylamino)benzylidene)hydrazine-1-carbothioamide (H_1L)

The ^1H NMR spectrum (Figures S2) of H_1L is consistent with the expected structure and shows a singlet at δ 11.17 ppm corresponding to the azide N-H proton (Reddy *et al.*, 2016). The spectrum exhibits resonance at δ 7.75 ppm assignable to the thioamide protons. These results are similar to the chemical shifts reported for Phenyl-N4-[ent-kauren-16 β -methyl-19-oic acid]-thiosemicarbazone, which exist in the E isomeric form (Tiwari *et al.*, 2016). NMR spectrum also shows the presence of two doublets, the first at δ 7.58 ppm attributed to the H-4 proton and the second at δ 6.67 ppm attributed to the proton H-3 of the aromatic ring respectively. In addition, this spectrum also contains a signal in the form of a singlet at δ 7.99 ppm assignable to the H-6 proton at position C-6, in agreement with the chemical shifts found for other compounds derived from benzaldehyde thiosemicarbazone (Aziz El-Hashash *et al.*, 2012). The resonances of the protons in the multiplet corresponding to the methyl group were observed at δ 3.34 ppm. NMR spectra of H_1L confirm the presence of the characteristic functional groups and confirm the proposed molecular structure. It was possible to assign almost all resonance signals in the ^{13}C NMR spectrum (Figure S3). The primary assignments correspond to the two signals at δ 176.99 ppm and δ 143.34 ppm assigned to thioamide ($\text{C}=\text{S}$) and azomethine carbon ($\text{C}=\text{N}$), respectively. The aromatic ring signals are observed at the usual place (δ 111- 128 ppm). The ^{13}C NMR spectrum showed 10 carbons signals expected for the structure with chemical shifts similar to those described in the literature (Figure S2) (Haraguchi *et al.*, 2011).

3.3.2 COSY, NOESY and HMBC Spectra Analysis

An examination of the COSY spectrum in (Figure S4 (a)), we show the correlation between H-3 (δ =7.6 ppm) and H-4 protons (δ =6.7 ppm) of the aromatic group. All protons and carbons were assigned after analysis of HMBC. HMBC spectrum (Figure S4(c)) shows correlation of the N-H proton with the quaternary carbon of the thioamide group ($\text{C}=\text{S}$) at δ = 176.99 ppm, which allows the attribution of the latter to the C-7 carbon. The same spectrum also shows the correlations of protons H-3 and H-4 with carbons C-2 and C-5 at δ = 151.35 and 121.38 ppm, respectively. Dimensional experiments (COSY, HSQC, and HMBC) confirmed the structure.

3.4 Electronic Spectra

The UV-Visible spectrum of 2-(4-dimethylamino)benzylidene)hydrazine-1-carbothioamide (H_1L) is presented in Figure S4 and shows two absorption bands at 353 nm (28571 cm^{-1}) and 400 nm (25000 cm^{-1}), assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions respectively. The large red shift of the absorption wavelength demonstrates that the benzene ring in the molecule is conjugated with the azomethine ($-\text{C}=\text{N}-$) group of the Schiff base as depicted by its planar crystal structure (Figure S5). A similar effect was also observed in quinoline-2-carboxaldehyde and 4-methyl-3-thiosemicarbazone (Lavanya *et al.*, 2021).

3.5 Crystal Structure

The molecular structure of the Schiff base is shown in Figure 1 and the crystal structure and refinement data are listed in (Table 1), while the selected bond distances and bond angles are summarized in Tables 2 and 3 respectively. The structure is Centro-symmetric, V-shaped molecule (Figure 1) which crystallizes in the triclinic crystal system, space group $P\bar{1}(2)$. The C00C-S001 and C00B-S002 at

1.685(2) Å and 1.697(2) Å bond distances in the H₁L are longer than of C-S single bonds (1.338(2) Å and 1.343(3) Å (Table 2), which are intermediate between those of single and double bonds, indicating that the thiosemicarbazones adopt the thiol tautomeric form, suggesting that there is considerable electron delocalisation within the C, N, N, C, S framework of the H₁L (Yang *et al.*, 2013). The azometine (C=N) bonds are 1.279(3) Å, 1.277(2) Å and the N–N bonds are shorter than 1.44 Å, which agrees well with those of similar thiosemicarbazones (Antonov *et al.*, 2000), (West *et al.*, 1993). As a general rule, the S and hydrazinic N atoms lie in a trans configuration in thiosemicarbazides and thiosemicarbazones in their unprotonated and uncomplexed forms (Sampath *et al.*, 2006). The S atom and the hydrazinic (N003) atom are *trans* with respect to C00C–N005 bond. A similar type of *trans* configuration is noted in many structures of thiosemicarbazide, 3-Methyl, 6-bis (4-chlorophenyl) piperidin-4-one thiosemicarbazone and Benzaldehyde thiosemicarbazone (Hernández *et al.*, 2008). The reaction product of *p*-dimethylamino benzaldehyde and thiosemicarbazide shows the bond length variation (Table 2) C00D–C00E/C009–C00F (1.445(3) Å and 1.447(3) Å) indicates the influence of conjugation on the phenyl ring, this bond is shorter in the present molecule when compared to the C(phenyl)–C(keto) at (1.468(5)) Å (Figure 1) (Sampath *et al.*, 2010). Similar effect is also observed in other structures, such as 2, 3-Dihydroxybenzaldehyde thiosemicarbazone where the bond lengths in the thiosemicarbazone moiety show an electron delocalization effect (Scheme 2) and this is extended even up to the imine nitrogen group (Abdurazag *et al.*, 2006).



Scheme 2. Resonance structures of thiosemicarbazone moiety (Sampath *et al.*, 2010).

The thiosemicarbazone moiety and phenyl ring almost lie in the same plane, which is confirmed by the orientation angle of 119°. Table 4 shows selected bond angles of the title compound and C00Q–C00L–C00M (117.3(2) Å is comparatively much shorter than for similar structures with bond angles ranging from 120° to 121° respectively (Sampath *et al.*, 2010). This may be due to the effect of H short contacts between the atoms (H00T to H00M 1.89 Å and H00Q to H00E 1.89 Å). These short contacts create electron–electron repulsion between the hydrogens, pushing the atoms C00Q and C00M in opposite directions. The bond lengths of C00L–C00Q, C00L–C00M, C00K–C00E, C00E–C00I in the H₁L molecules (Table 2) vary from 1.406(3), 1.400 (3), 1.394 (3) to 1.390 (3) and are attributed to the resonance character of the dimethylamine, phenyl ring and that of imine nitrogen as shown in scheme 2. Similar dimeric structures of the title compound were reported by Chattopadhyay *et al.*, 1988. Yu *et al.*, 2006 and Sampath *et al.*, 2010. The structures obtained from this work clearly shows strong H-bonding resulting in the observed V-shaped dimeric molecule.

Table 1. Crystal data and other relevant details of the Schiff base

Parameters	H ₁ L
CCDC	2206249
Empirical formula	C ₁₀ H ₁₄ N ₄ S
Formula weight	222.31 g/mol
Temperature	293(2) K
Wavelength	354–400 nm

Cristal system, Space group	Triclinic, P-1(2)
Unit cell dimensions	
a (Å) ; α (°)	8.529(3) ; 73.926(12)
b (Å) ; β (°)	9.387(4) ; 79.730(12)
c (Å) ; γ (°)	15.538(6) ; 83.087(13)
Cell ratio	a/b = 0.9085 ; b/c = 0.6041 ; c/a = 1.8217
Volume Å ³	1174.2(8)
Z	4
Calc.density	1.258 g/cm ³
Absorption coefficient(mm ⁻¹)	0.250
F(000)	472.0
2Theta range for data collection	4.528/56.182
Limiting indices	-11 ≤ h ≤ 11, -12 ≤ k ≤ 12, -20 ≤ l ≤ 20
Reflections collected/independent	30165/5672
Data/restraints/parameters	5672/0/275
Goodness-of-fit on F ²	1.021
Final R-indices [I>2 σ (I)]	R1 = 0.0427, wR2 = 0.1089
R-indices (all data)	R1 = 0.0667, wR2 = 0.1233
Largest diff.peak/ hole /eÅ ⁻³	0.20 / -0.19

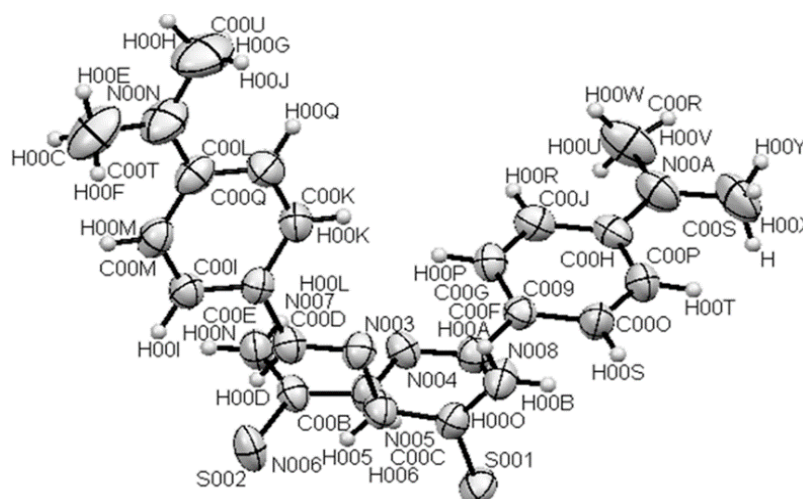


Figure 1. Crystal structure of 2-(4-dimethylamino)benzylidene)hydrazine-1-carbothioamide (H₁L), viewed with 50% probability ellipsoids

The Schiff base molecule therefore lies almost in the same plane due to the presence of hetero π -electron delocalization in the entire molecule (Scheme 2). The torsion angle and mean plane calculations confirm that the Schiff base adopts a v-shaped conformation and almost lies in the same plane as the benzene ring (Brameld *et al.*, 2008). This is supported by the corresponding torsional angles of Thiosemicarbazone as shown in Table 4. The corresponding torsion angles of [C00D-N003-N005-C00C] (-178.3(3) °), [N003-N005-C00C-N008] (8.2(3) °), and [N003-N006-C00B-S001] (172,3(1)°)] are comparable to similar reported by Sampath (Sampath *et al.*, 2010).

Table 2. Selected bond distances (Å°) for the Schiff base

twisted arm	d [Å°]	on twisted arm	d [Å°]
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S001-C00C	1.685(2)	S002-C00B	1.697(2)
N003-C00D	1.279(3)	N004-C00F	1.277(2)
N003-N005	1.381(3)	N004-N006	1.387(2)
N005-C00C	1.343(3)	N006-C00B	1.338(2)
N008-C00C	1.325(2)	N007-C00B	1.325(2)
C00D-C00E	1.445(3)	C00F-C009	1.447(3)
C00E-C00I	1.390(3)	C009-C00O	1.390(3)
C00E-C00K	1.394(3)	C009-C00G	1.398(2)
C00K-C00Q	1.366(4)	C00O-C00P	1.375(3)
C00I-C00M	1.366(3)	C00G-C00J	1.370(3)
C00L-N00N	1.368(4)	C00H-N00A	1.370(3)
C00L-C00Q	1.406(3)	C00H-C00J	1.408(3)
C00L-C00M	1.400(3)	C00H-C00P	1.406(3)

Table 3. Selected bond angles (Å°) for H₁L

twisted arm	d [Å°]	on twisted arm	d [Å°]
C00D-N003-N005	115.6(2)	C00F-N004-N006	115.1(2)
C00C-N003-N005	119.4(2)	C00B-N004-N006	119.7(2)
N003-N005-H005	120.3(2)	N004-N006-H006	120.1(2)
C00C-N008-H00A	120.0(2)	C00B-N007-H00A	120.2(2)
C00C-N008-H00B	120.0(2)	C00B-N007-H00B	120.2(2)
N008-C00C-N005	116.9(2)	N007-C00B-N006	116.9(2)
N008-C00C-S001	123.9(1)	N007-C00B-S002	122.9(1)
N005-C00C-S001	119.2(1)	N006-C00B-S002	119.7(2)
N003-C00D-C00E	122.2(2)	N004-C00F-C009	122.8(2)
N003-C00D-H00D	118.9(2)	C00O-C009-C00G	122.7(2)
C00I-C00E-C00K	117.2(2)	C00O-C009-C00F	120.1(2)
C00E-C00D-H00D	119.6(2)	C00S-N00A-C00R	117.4(2)
C00I-C00E-C00D	119.0(2)		
C00T-N00N-C00U	121.7(3)		
C00I-C00M-C00L	120.9(2)		

Table 4. Torsion angle (Å°) for Schiff base

Conformational bonds	Schiff base angle (°)	
	twisted arm	on twisted arm
C00D-N003-N005-C00C	-178.3(2)	-179.6(2)
N003-N005-C00C-N008	8.2(3)	-0.9
N003-N006-C00B-S001	-172.3(1)	178.6(1)

Crystallographic analysis reveals that the asymmetric unit of H₁L (C₁₀H₁₄N₄S)₂ contains two thiosemicarbazone arms, with one of them “twisted” with a torsional angle of 17.83° along C00K, C00E, C00D and CN003 atoms. The arenes are responsible for the $\pi\cdots\pi$ interactions observed in the compound. The interactions arise between parallel adjacent arenes in a face-to-face stacking pattern. The interaction distances vary according to the type of arenes which come into contact. For instance, the $\pi\cdots\pi$ interaction between the “twisted” arene arms are longer (4.298 Å) than those of the normal arene arms (3.786 Å) (Figure 2) N-H... π interactions arise between the adjacent benzyl moieties and the amine H-atoms of the thiosemicarbazone group in a perpendicular stacking pattern as shown in Figure 3. The perpendicular π stacking is observed between the centroid defined by atoms C00L–C00Q and atom H00L with a distance of 3.025 Å and an angle of 128.94 ° and between the centroid defined

by C00H–C00P and atom H00A with a distance of 2.954 Å and an angle of 130.38 °. This shows that π stacking is the primary contact connecting adjacent chains of molecules along the c axis, and the compound appears to be packed in a zig-zag form as shown in Figure 4.

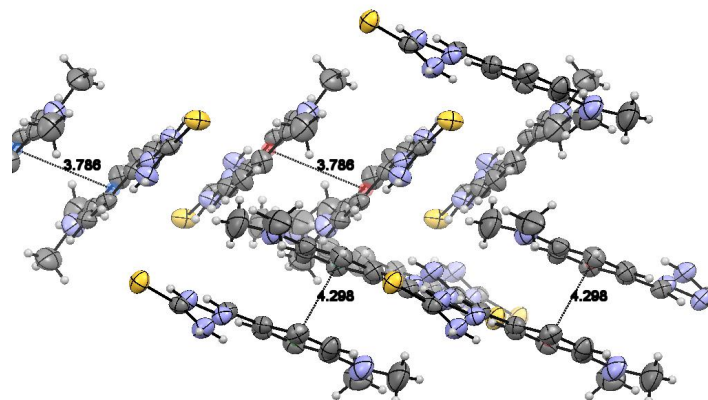


Figure 2. View of $(C_{10}H_{14}N_4S)_2$ drawn with 50% probability displacement ellipsoids, highlighting the face-to-face stacking. Distances are in Å

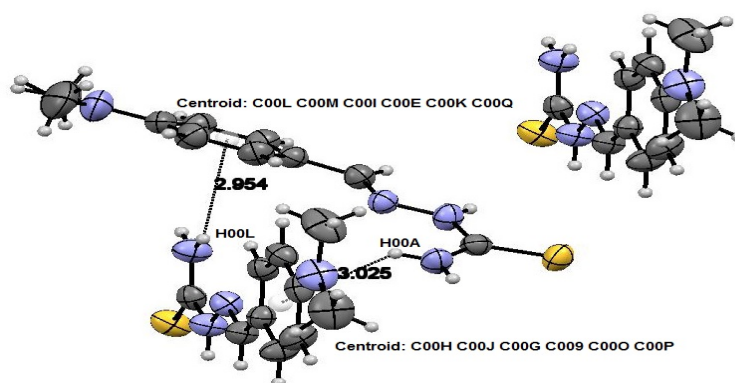


Figure 3. View of two molecules of $(C_{10}H_{14}N_4S)_2$, drawn with 50% probability displacement ellipsoids, highlighting the perpendicular π stacking. The distance is Å.

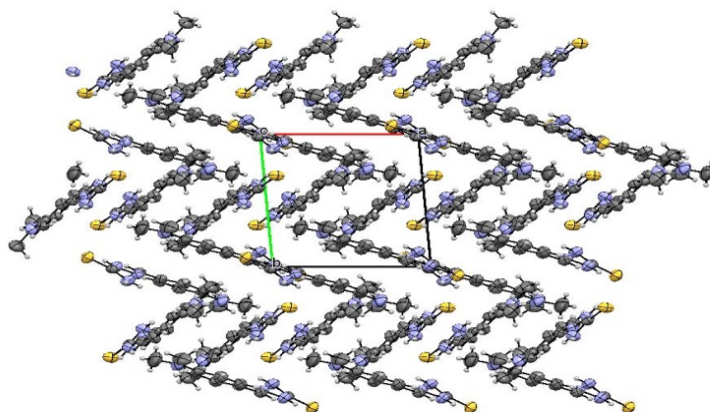


Figure 4. View of the macromolecular packing of $(C_{10}H_{14}N_4S)_2$ with 50% probability ellipsoids, as viewed along the c-axis.

The thiosemicarbazone groups are located at the base of the V-shaped molecule in the asymmetric unit. As a result, each arm donates and accepts a hydrogen bond with the neighbouring group to form intramolecular bonding (Figure 5).

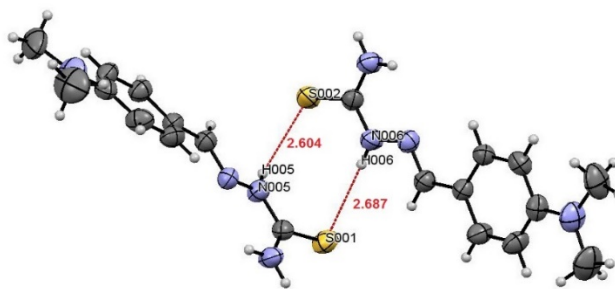


Figure 5. View of $(C_{10}H_{14}N_4S)_2$, drawn with 50% probability displacement ellipsoids,

highlighting the intramolecular hydrogen bonding (shown in red dots). The distance is in Å. The H-bonding between H- and S-atoms extends in the a-axis as shown in Figure 6 (dotted line) to form intermolecular H-bonding. Here, the bond distances vary from 2.604 to 2.666 Å, with bond angles ranging from 148.88° for N008–H00B...S001 to 158.52° for N007–H00N...S002. Similar structures of the title compound were reported by Chattopadhyay *et al.*, 1988, Yu *et al.*, 2006, and Sampath *et al.*, 2010, respectively. The structure obtained from this work clearly shows strong H-bonding resulting in the observed dimeric V-shaped molecule and probably accounts for the differences observed in the bond parameters (Chattopadhyay *et al.*, 1988), (Sampath *et al.*, 2010). Table 5 summarizes the distances and angles for the different bonding.

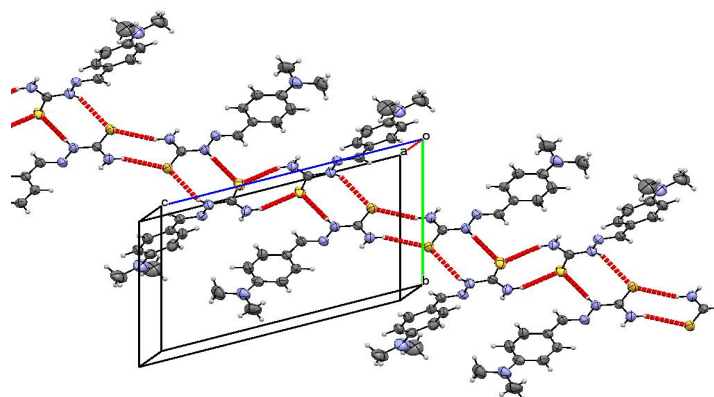


Figure 6. View of $(C_{10}H_{14}N_4S)_2$, drawn with 50% probability displacement ellipsoids, highlighting the hydrogen bonding (shown in red dots) along the a-axis.

Table 5. Hydrogen Bonds (Å and $^\circ$) for $(C_{10}H_{14}N_4S)_2$

D–H...A	Nature	d(D–H)	d(H...A)	d(D–A)	$\theta(DHA)$
N006–H006...S001	Intramolecular	0.86	2.604(9)	3.464(9)	171.23(117)
N008–H00B...S001	Intermolecular	0.86	2.604(11)	3.464(11)	148.88(116)
N005–H005...S002#	Intramolecular	0.86	2.687(10)	3.547(10)	139.33(113)
N007–H00N...S002#	Intermolecular	0.86	2.666(10)	3.526(10)	158.52(115)

3.6 Hirshfeld surface analysis

The Hirshfeld surface of the compound has been calculated from its X-ray structure using Crystal Explorer 17.5 (Spackman *et al.*, 2009) software and mapped over d_{norm} , shape index and curvedness (Figures 7 and 8). The intermolecular interactions that dominate in the structure are viewed by the bright red area of d_{norm} surface (Figure 8). The Hirshfeld surfaces mapped with properties such as shape-index and curvedness are employed to describe the effect of weak intermolecular interactions in a crystal structure (Camila *et al.*, 2019).

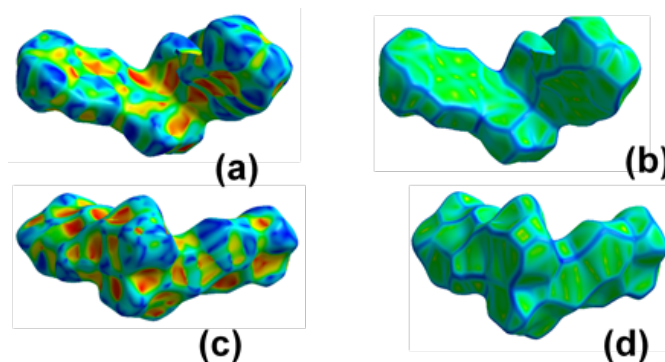


Figure 7. 3D Hirshfeld surface mapped with shape index of $(C_{10}H_{14}N_4S)_2$ ((a) front view and (c) back view) and curvedness ((b) front view and (d) back view).

The shape index property of the compound reveals the presence of $\pi \dots \pi$ stacking between the rings, and this is indicated by the appearance of small blue regions surrounding bright red spots within the six-membered rings (Figure 7 (a)). The presence of $\pi \dots \pi$ stacking is also evidenced by the flat regions around the front view of the benzene rings on the Hirshfeld surface mapped over the curvedness (Figure 7 (b)). The back view of the compound is however characterized by low curvedness (Figure 7 (d)), which is an indication of the absence of π - π interaction (Tan *et al.*, 2019). However, the Hirshfeld surfaces mapped over shape index and curvedness of the compound reveal the presence of N-H... π interactions (red spot at the center of the phenyl ring at the back view of the compound).

The blue and white areas on the Hirshfeld surfaces of the compound indicate the existence of weak intermolecular interactions in the crystal (Figure 8). Significant intermolecular interactions are mapped in Figure 8, which indicates the percentage contribution of the intermolecular contacts to the Hirshfeld surface. Significant contacts include 51.7% H...H, 20.9% H...C/C...H, 7.6% H...S/S...H, and 9.8% H...N/N...H. The largest contribution of 51.7% H...H interactions has a high concentration at $d_e = d_i$ 1.2 Å, as indicated by the sky-blue region (Figure 8(b)). Two sharp spikes at $d_e + d_i \sim 2.7$ Å were observed for H...C/C...H interactions and indicates the presence of weak N-H... π bonds (Figure 8 (c)). For H...S/S...H contacts, two spikes appear at $d_e + d_i \sim 2.4$ Å, while the H...N/N...H contacts have a $d_e + d_i \sim 2.6$ Å. Additional interactions representing C...C (2.0%), N...N (0.6%), C...N/N...C (0.1%), S...C/C...S (0.3%), and S...N/N...S (0.3%) are insignificant to the packing arrangement of the molecule.

4. Antioxidant Activities of 2-(4-dimethylamino)benzylidene)hydrazine-1-carbothioamide.

The total antioxidant potential of 2-(4-dimethylamino)benzylidene)hydrazine-1-carbothioamide was evaluated using free radical scavenging activity by both the DPPH and FRAP method using

4.1. DPPH Free Scavenging Test

In the present study, p-dimethylaminobenzaldehydethiosemicarbazone was investigated for antioxidant activity using ascorbic acid as standard. The results of the free radical scavenging activity of the Schiff base at different concentrations are shown in Figure 9. From the investigation it was clearly observed that Schiff base is significant, this observation could be due to free electron mobility and deprotonation of compound. DPPH radical shows that the Schiff base (H_1L) is capable of donating electrons to reduce free radicals (Tetteh *et al.*, 2014).

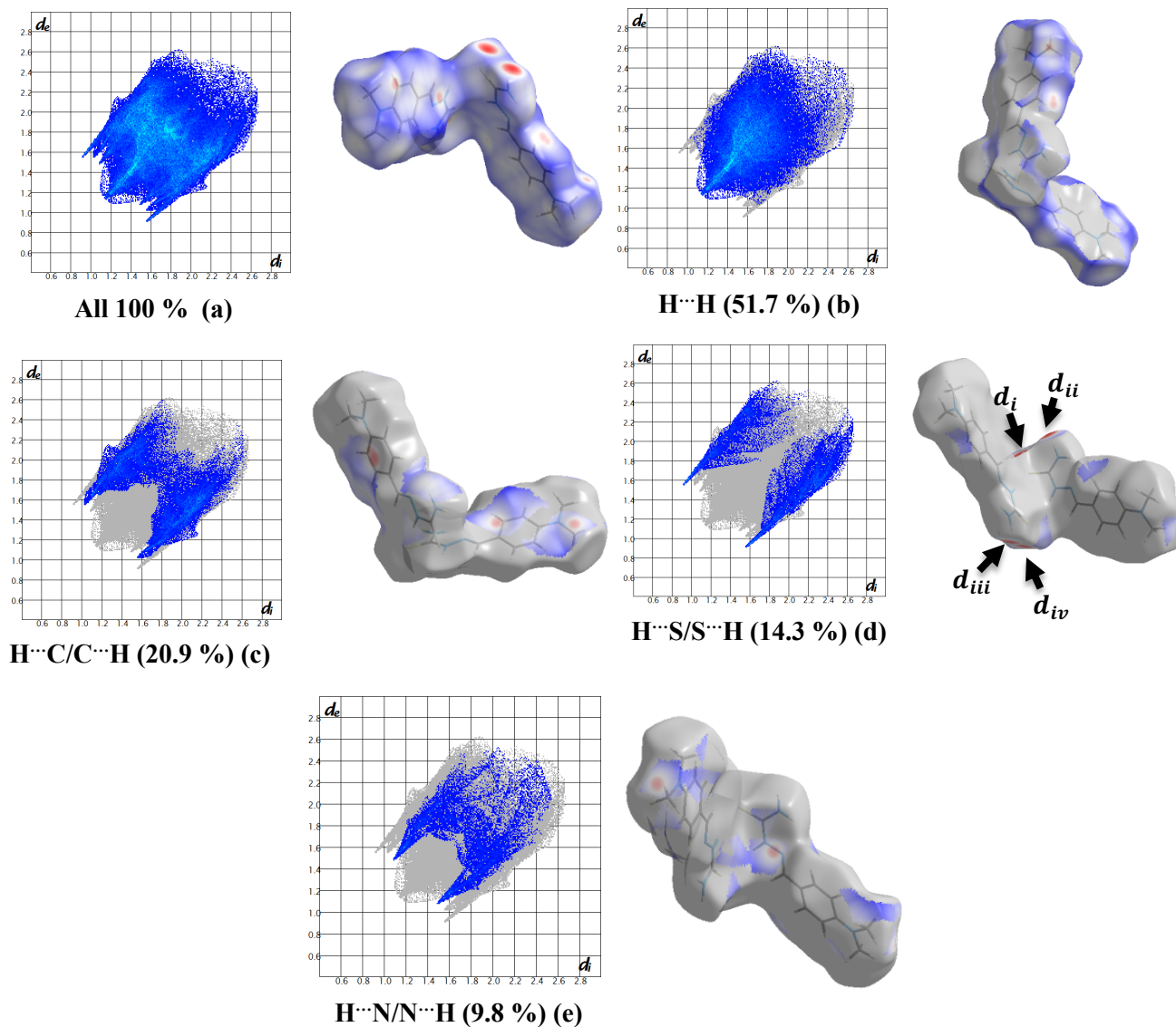


Figure 8. Hirshfeld fingerprint plots for $(C_{10}H_{14}N_4S)_2$ with highlighted contributions

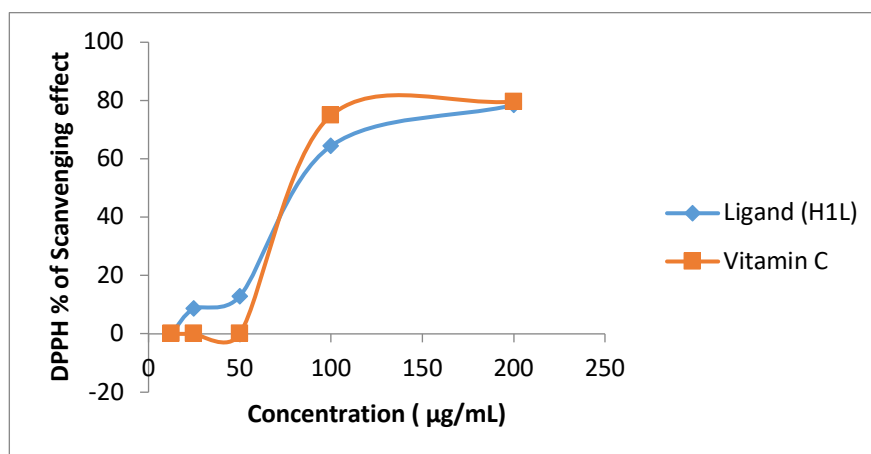


Figure 9. DPPH free radical scavenging activity of the Schiff base.

Antioxidant activity of Schiff base was also investigated by determining the concentration of the substance necessary to reduce 50 % of the DPPH• radical (IC_{50} values) of compounds. The results of the determination of IC_{50} values of the compound are shown in Table 6. The increased antioxidant activity of the Schiff base can be attributed to the electron withdrawing effect which facilitates the

release of hydrogen to reduce the DPPH radical (Soroceanu *et al.*, 2022). The IC₅₀ value of 46.93 µg/mL shows that this proton release is very pronounced.

Table 6. IC₅₀ values of Schiff base and its complexes against DPPH radicals

Compounds	DPPH radical scavenging activity
	IC ₅₀ (µg/mL) ± SD ₂
H ₁ L	46.93 ± 7.40
Vitamin C	30.50 ± 0.98

4.2. Ferric Ion Reducing Antioxidant Power Assay (FRAP) Test

The reducing powers of the compounds are associated with their antiradical power. The reducing powers of the synthesized compounds were determined using the FRAP method. This technique determines the ability of the tested compounds to reduce ferric iron (Fe³⁺). The results are shown in Figure 10 and the data are shown in Table 7. From the results, we observe that H₁L has the capacity to reduce iron. From all above results, it can be confirmed that H₁L exhibits good antiradical properties.

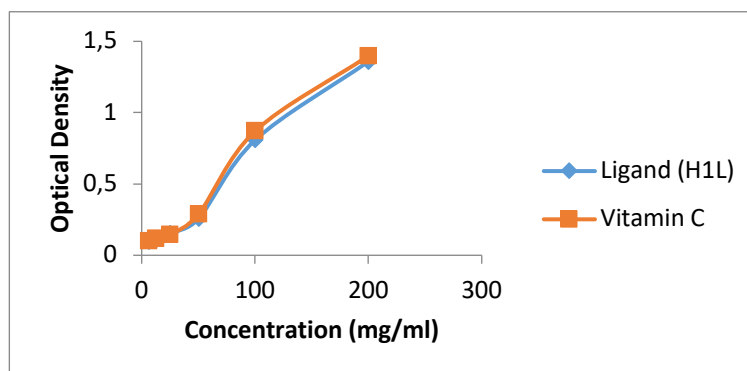


Figure 10. Ferric ion reducing power of H₁L and Vitamin C at different concentration,

Table 7. EC₅₀ data of Schiff base.

Compounds	FRAP ion reducing antioxidant
	IC ₅₀ (µg/mL) ± SD ₂
H ₁ L	36.84 ± 0.38
Vitamin C	29.99 ± 0.70

Conclusion

In this study, *p*-dimethylamino benzaldehyde thiosemicarbazone was synthesized and characterized by elemental analysis, NMR, and single crystal X-ray experiment. Both the NMR spectra confirmed that *p*-dimethylaminobenzaldehyde thiosemicarbazone existed in the Trans conformation. The crystal structure is Centro-symmetric and contains two arms, with one of them “twisted”. The Hirshfeld surfaces mapped reveal the presence of π...π stacking and N-H...π interactions. Antioxidant evaluation results revealed that H₁L is moderately potent as an antioxidant compared to the reference antioxidant (vitamin C).

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Disclosure statement: *Conflict of Interest:* The authors declare that there are no conflicts of interest.

Appendix A. Supplementary data: CCDC 2206249 contains the supplementary crystallographic data for C₁₀H₁₄N₄S. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

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