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Synthesis, Characterization, And Crystal Structure Of A New Compound 1,2-Bis(*N'*-Ethanoylthioureido)Benzene

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Abstract
The compound H_4L with the chemical formula $C_{12}H_{14}N_4O_2S_2$ (H_4L) obtained by reaction of 1,2-diaminobenzene, potassium thiocyanate and ethanoyl chloride in a 1/1/2 ratio is characterized by elemental analyses, IR, ^1H and ^{13}C NMR spectroscopy. The structure of the compound was confirmed by single crystal X-ray diffraction study. The compound crystallizes in the orthorhombic system with a Fdd2 space group with unit cell parameters: a = 32.7133 (13) Å, b = 13.4503 (8) Å, c = 13.3065 (6) Å, V = 5854.9 (5) Å^3, Z = 16, R_1 = 0.030 , wR_2 = 0.083. The asymmetric unit consisting of one molecule of the compound shows that ethanoyl groups of the thiourea subunits are in the trans position with respect to the sulfur atom S of the thione functions across the related C—N bonds. The bond distances S1—C7 [1.668 (2) Å], S2—C10 [1.6736 (17) Å], O1—C8 [1.226 (3) Å] and O2—C11 [1.230 (2) Å] indicate double bonds character. The crystal structure of the H_4L compound is stabilized by intramolecular and intermolecular N(thiourea)-H··· O(amide) hydrogen bonds .

Keywords*: 1,2-Diaminobenzene; Ethanoyl Chloride; Potassium Thiocyanate; Hydrochloric Acid.*

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I. Introduction

Thiourea-derived compounds are substructures in many pharmaceutical compounds with a wide range of therapeutic applications [1, 2]. It has been shown that compounds derived from thiourea possess biological activities such as antiviral, anti-antibacterial, antiviral, antimoral, anti-inflammatory, anticonvulsant [3–8] and antifungal [9]. Considering this great importance, various thiourea-derived compounds have already been approved for the treatment of different human diseases [10, 11]. Therefore, many promising drug candidates are currently in development [12]. For example, certain derivatives of thiourea have been used as active medical ingredients to treat mycobacterium tuberculosis infection *ca*. 4,4′-diisoamyloxydiphenylthiourea [13]. Thiourea derivatives are also known as an organic corrosion inhibitor [14, 15]. This property is due to the easy protonation of the sulfur atom in acid medium. Recently thiourea derivatives have been studied in coordination chemistry to form complexes with Ag(I) and Au(I) ions [16]. Currently the pharmaceutical field is in need of new sustainable, green, and safe synthetic method to prepare new derivatives of thiourea with biological activities. In this context we report the synthesis of a new thiourea derivative (H_4L) obtained under very mild synthesis conditions from accessible and less expensive reagents and solvents. Spectroscopic techniques and single crystal X-ray diffraction were used for characterization and structural study of the compound.

II. Experimental part

Materials and instruments

All chemicals and solvents were analytical grade and were used directly without further purification. Potassium thiocyanate and ethanoyl chloride are obtained from Sigma-Aldrich. Elemental analyzes of C, H, N and S were recorded on a VxRio EL instrument. Infrared spectra were obtained on a Perkin Elmer Spectrum Two FTIR spectrometer in the 4000-400 cm^{-1} region . NMR spectra were recorded in $CDCl_3$ solution with a Bruker 250 MHz spectrometer at room temperature using TMS as internal reference.

Synthesis of the compound H_4L

Potassium thiocyanate (5.832 g, 60 mmol) was dissolved in a 250 mL flask containing 60 mL of acetone. An acetone solution containing ethanoyl chloride (4.77 g, 60 mmol) was added dropwise. The formation of KCl salt and the simultaneous appearance of a yellow solution are observed. The mixture is refluxed for one hour and then cooled to room temperature. Acetone (30 mL) solution of 1,2–diaminobenzene (3.246 g, 30 mmol) was added

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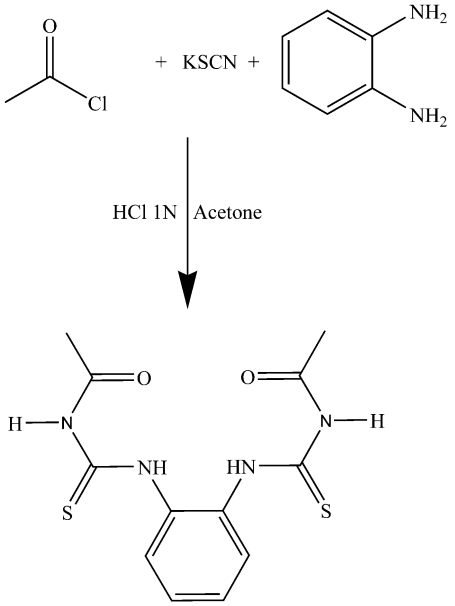
at room temperature. After three hours under stirring, 100 mL of 1N HCl aqueous solution was added. The KCl was dissolved, and a white precipitate was observed. The precipitate is recovered by filtration and then washed several times with acetone and ether before being dried under P_2O_5. Yield: 89.37%. M.P. 230°C. Anal. Calc. for $C_{12}H_{14}N_4O_2S_2$: C, 46.43; H, 4.55; N, 18.05; S; 20.66. Found: C, 46.41; H, 4.52; N, 18.01; S; 20.64. IR (cm^{-1}) : 3210 ν(NH); 1675 ν(C=O); 1465-1595 ν(C_{Ar}=C_{Ar}); 1265 cm^{-1} ν_{as}(C=S); 1149 ν□C–N); 780 cm^{-1} δ(C_{Ar}–H). ^{1}H NMR ($CDCl_3$, δ (ppm)): 2.78 (s, 6H, C**H**$_3$–), 7.4–7.9 (m, 4H, Ph–**H**); 9.37 (s, 2H, –C(S)–N**H**–C) ; 12.4 (s, 2H, –CO–N**H**–). ^{13}C NMR ($CDCl_3$, δ (ppm)): 166.8 (**C**=O); 179.6 (**C**=S); 126.8 (**C**$_{Ar}$) ; 127.9 (**C**$_{Ar}$) ; 133.3 (**C**$_{Ar}$) ; 23.5 (**C**H$_3$–).



Scheme 1. Synthetic scheme of the compound H_4L.

Crystal structure determination

Crystals suitable for X-ray diffraction on single crystal of compound H_4L were grown by slow evaporation in a mixture of methanol and chloroform solvent. Crystallographic data and structure refinement parameters are given in Table 1. Diffraction data were collected using a Rigaku XtaLAB Pro: Kappa single diffractometer with graphite monochromatized MoKα radiation (□ = 0.71073 Å). All data have been corrected for Lorentz and polarization effects. The diffusion factors were taken from the *SHELXTL* software package [17]. The structures were solved by direct methods, which revealed the position of all atoms other than hydrogen. All structures were refined over F^2 by a full matrix least squares procedure using anisotropic shift parameters for all non-hydrogen atoms [18]. The hydrogen atoms of the NH group were located in the Fourier difference maps and refined. Other H atoms (CH and CH_3) have been geometrically optimized and refined as a driving model by the AFIX instructions. Molecular graphs were generated using *ORTEP* [19].

Table 1. Crystal data and structure refinement for compound (H_4L).

Formula	$C_{12}H_{14}N_4O_2S_2$
M_r	310.39
Crystal shape/color	prism/colorless
Temperature (K)	290
Crystal system	Orthorhombic
Space group	*Fdd*2
a (Å)	32.7133 (13)
b (Å)	13.4503 (8)
c (Å)	13.3065 (6)
V (Å^3)	5854.9 (5)
Z	16
*D*calc (mg. m^{-3})	1.409
F(000)	2592
Radiation (Mo *K*α) Å	0.71073
μ (mm^{-1})	0.37
θ_{max} ; θ_{min} (°)	30.6 ; 3.8
Crystal size (mm)	0.20 × 0.18 × 0.12
T_{min} ; T_{max}	0.388 ; 1.000

Index ranges	$-43 \leq h \leq 46$, $-15 \leq k \leq 17$, $-18 \leq l \leq 17$
Measured reflections	10731
Independent reflections	3871
Reflections with $I > 2\sigma(I)$	3612
R_{int}	0.030
$R[F^2 > 2\sigma(F^2)]$ =	0.030
$wR(F^2)$	0.083
Parameters/restraints	195/5
Goodness-of-fit on F^2	1.05
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (eA^{-3})	0.22, −0.24

III. Results and discussion

General study

The results of the elemental analysis are in accordance with the molecular formula $C_{12}H_{14}N_4O_2S_2$. The IR spectrum of the compound shows a band centered at 3213 cm^{-1} assigned to the N—H stretching of the thiourea and the amide fragments [20]. The band appearing at 1675 cm^{-1} is attributed to the $\nu_{C=O}$ vibration of the amide function [21, 22]. The absorptions observed at 1265 cm^{-1} and 780 cm^{-1} correspond respectively to the vibration bands $\nu_{as(C=S)}$ and $\nu_{s(C=S)}$ [23]. The antisymmetric vibrations $\nu_{as(C-N)}$ and symmetric $\nu_{s(C-N)}$ are respectively pointed at 1149 cm^{-1} and 1100 cm^{-1}. The ^1H NMR spectrum of compound H_4L shows that the ligand is in its amide form in solution in $CDCl_3$. The appearance of two signals at 9.37 ppm and 12.40 ppm confirms the presence of the amidic form. These signals are attributed, respectively, to the NH protons of (C_{Ar}-N**H**-C(S) and (-C(S)-N**H**-C(O)) groups. The signals of the aromatic protons are located between 7.4 ppm and 7.9 ppm. The ^{13}C NMR spectrum of the compound H_4L reveals two signals at 166.8 ppm and 179.6 ppm corresponding to the signals of the carbon atoms of the amide function (**C**=O) and of the thione function (**C**=S). Aromatic carbon atom signals are pointed between 126.8-133.3 ppm. The signal of the carbon atoms of the methyl groups (-CH_3) is spotted at 23.5 ppm.

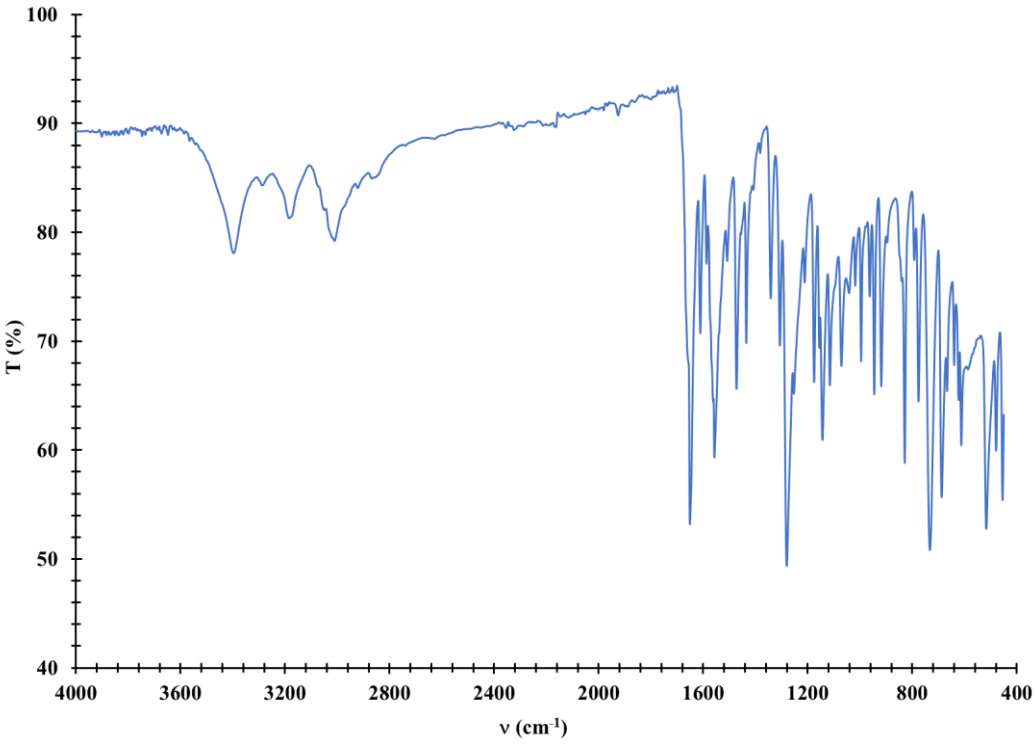


Figure 2.

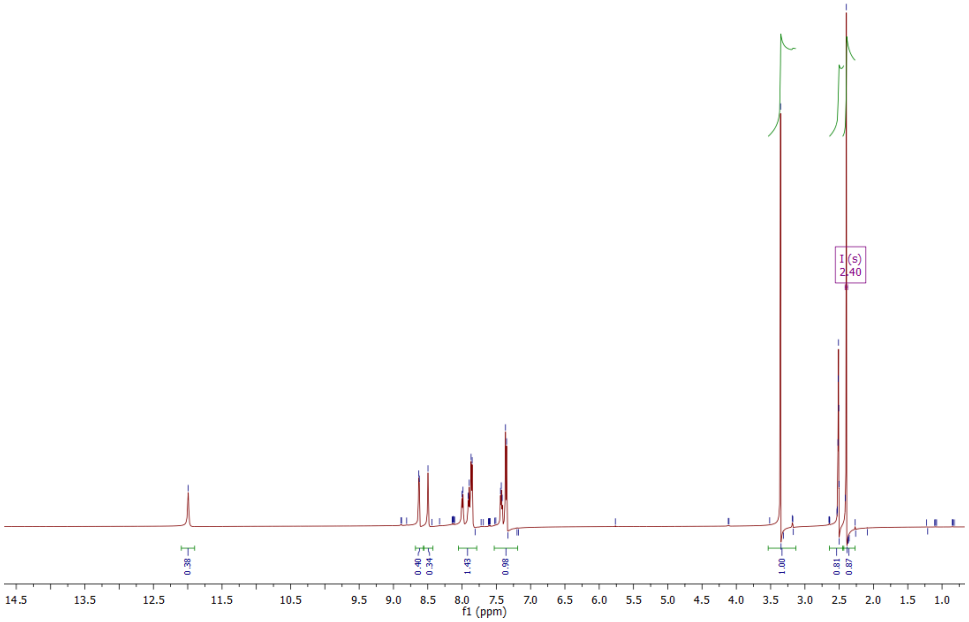


Figure 3.

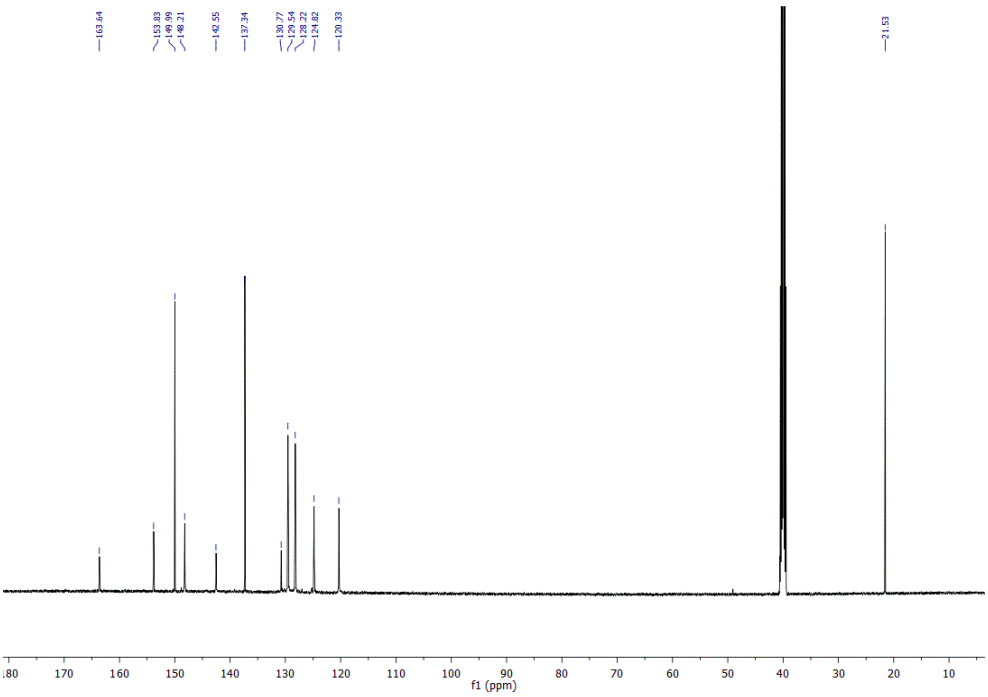


Figure 4.

Description of the structure of the compound

X-ray structure determination reveals that the compound H_4L crystallizes in the orthorhombic system with a space group *Fdd2*. The unit cell parameters are listed in Table 1. The asymmetric unit consisting of a single molecule of the compound is shown in Figure 2. Selected bond lengths and angles are listed in Table 2 . The ethanoyl groups of each thiourea subunits are *trans* with respect to the thiono S atoms across the respective C—N bonds [S1/C7—N2 and S2/C10—N4]. The bond lengths S1—C7 [1.668 (2) Å], S2—C10 [1.6736 (17) Å], O1—C8 [1.226 (3) Å] and O2—C11 [1.230 (2) Å] are characteristics of a double bond character and are comparable to those observed for 1,2-Bis(*N*'-benzoylthioureido)benzene compounds [1.660 (2) Å for C—S, and 1.222 (2) Å for C—O respectively] [24], 1-(2-Benzamidophenyl)-3-benzoylthiourea Hemihydrate [1.661 (4) Å for C—S, and 1.236 (5) Å for C—O respectively] [25] and 1-(4-Methylbenzoyl)-3-{2-[3-(4-methylbenzoyl)thioureido]phenyl}thiourea [1.656-1.665 (3) Å for C—S, and 1.213-1.225 (3) Å for C—O respectively] [26]. The C—N bond lengths[1.340 (2)– 1.391 (3) Å] are in the normal range observed for a single C—N bond. The thiourea fragments S1/N1/N2/C7/C1 and S2/N3/N4/C10/C6 are planar, with a maximum

deviation from the least-squares plane of 0.0183(2) Å for the N1 atom and 0.0599(1) Å for the N3 atom, respectively. The mean planes S1/N1/N2/C7/C1 and S2/N3/N4/C10/C6 form a dihedral angle of 63.191(5)° and are twisted with respect of the benzene ring C1-C6 with dihedral angle values of 27.593(5)° and 69.113(7)°, respectively. In the crystal structure of the compound, intramolecular hydrogen bonds of the type N–H···O [N1–H1···O1 and N3–H3···O2] which are established between the H atom of the thiourea nitrogen atoms as donor and the carbonyl oxygen atoms as acceptor result in *S*(6) rings. The different molecules in the crystal are connected by intermolecular hydrogen bonds of type N–H···S [N2–H2···S2^{i} : i = −x+1/2, −y+1, z−1/2] and N–H···O [N4–H4···O2^{ii} : ii = −x+3/4, y+1/4, z−1/4] and C–H···O [C12–H12A···O2^{ii}] (Table 3). All these intramolecular and intermolecular hydrogen bonds ensure the stability of the structure and its development in a three-dimensional network (Figure 2).

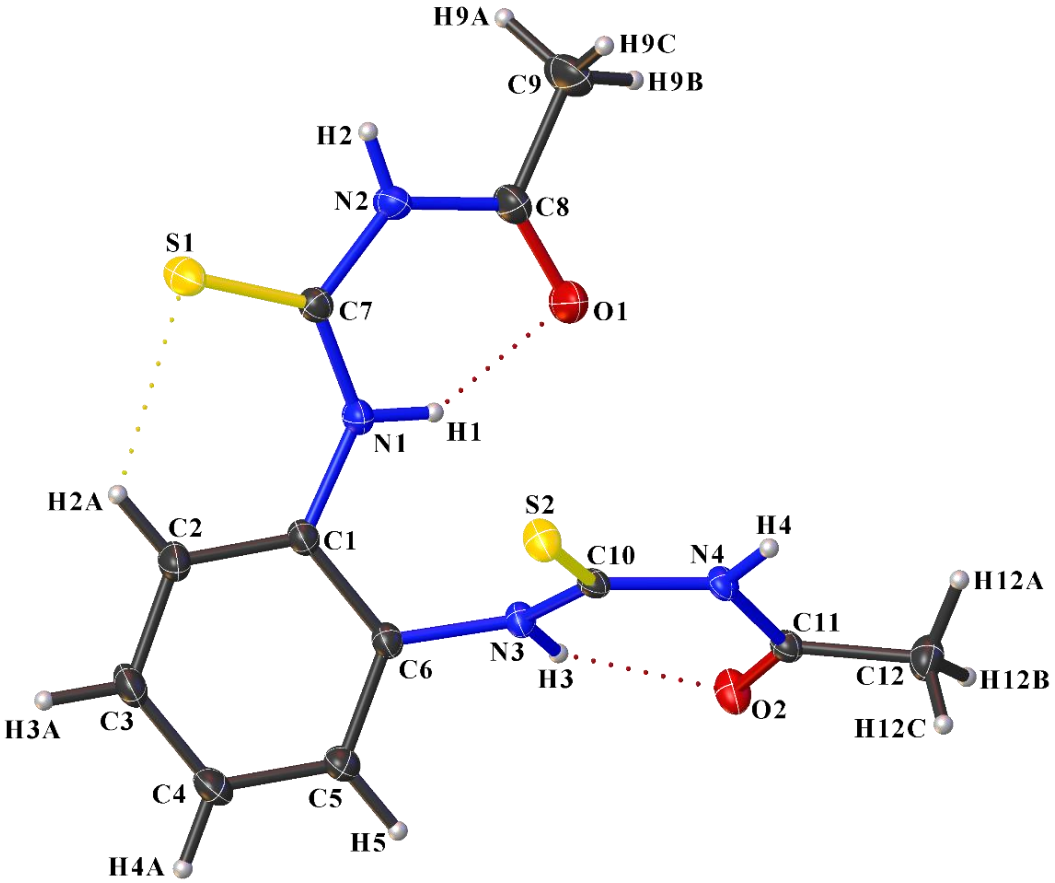


Figure 1. ORTEP plot (30% probability ellipsoids) showing the molecule structure.

Table 2. Bond lengths [Å] and angles [°] for H_4L.

S1—C7	1.668 (2)	S2—C10	1.6736 (17)
O1—C8	1.226 (3)	O2—C11	1.230 (2)
N1—C7	1.341 (3)	N3—C10	1.340 (2)
N2—C7	1.391 (3)	N4—C10	1.391 (2)
N2—C8	1.377 (3)	N4—C11	1.372 (2)
N1—C7—S1	127.41 (16)	N1—C7—N2	114.62 (18)
N2—C7—S1	117.98 (17)	O1—C8—N2	122.8 (2)
N3—C10—S2	125.38 (13)	N3—C10—N4	116.01 (15)
N4—C10—S2	118.60 (13)	O2—C11—N4	122.21 (16)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O1	0.87 (2)	1.89 (3)	2.636 (3)	144 (3)
N2—H2···S2^{i}	0.83 (2)	2.79 (2)	3.610 (2)	174 (3)
N3—H3···O2	0.87 (2)	1.95 (2)	2.658 (2)	136 (2)
N4—H4···O2^{ii}	0.82 (2)	2.09 (2)	2.874 (2)	160 (3)
C2—H2A···S1	0.93	2.65	3.227 (2)	120.4
C12—H12A···O2^{ii}	0.96	2.59	3.352 (3)	136.8

Symmetry codes: (i) −x+1/2, −y+1, z−1/2; (ii) −x+3/4, y+1/4, z−1/4.

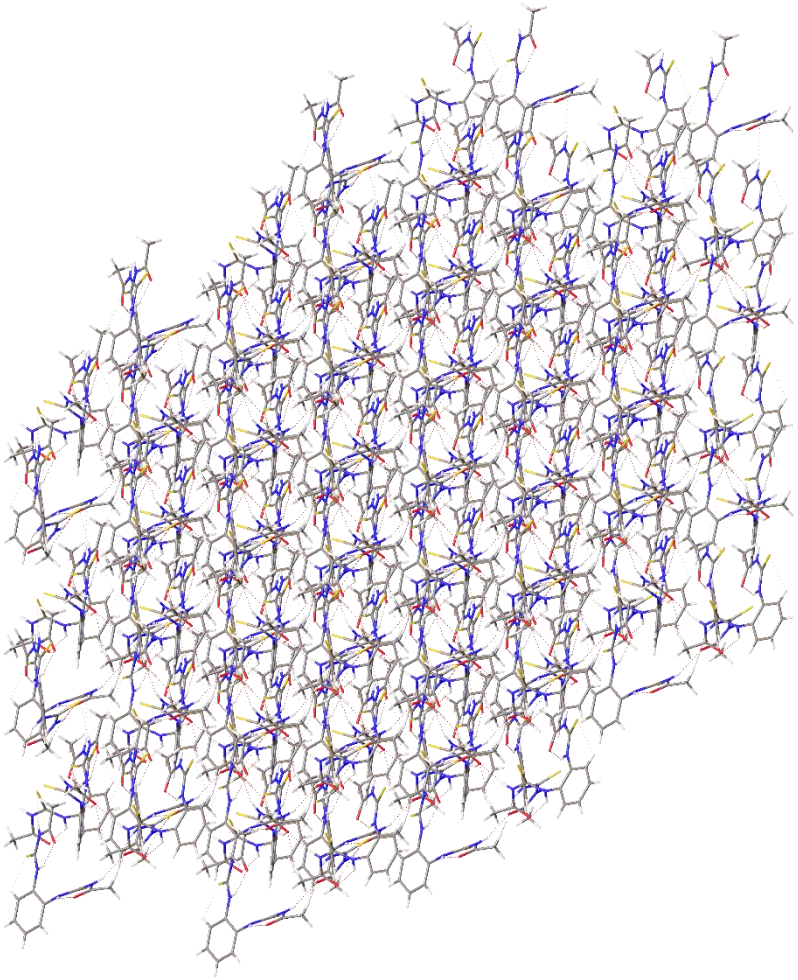


Figure 2. View of the packing diagram of the structure.

IV. Conclusion

A new compound based on thiourea H_4L was synthesized from 1,2-diaminobenzene with potassium thiocyanate and ethanoyl chloride under very mild conditions with a high yield of 89.37%. The structure of the isolated compound is characterized by elemental analysis and IR, ^{1}H and ^{13}C NMR spectroscopic techniques . Single crystal X-ray diffraction confirmed the structure. The crystal structure of the compound reveals that the two ethanoyl groups of the thiourea subunits are in the trans position with respect to the sulfur atom S1 of the thione function through the C7—N2 bond and to the S2 atom through the C10—N4 bond. The bond lengths S1—C7 [1.668 (2) Å], S2—C10 [1.6736 (17) Å], O1—C8 [1.226 (3) Å] and O2—C11 [1.230 (2) Å] are characteristics of a double bond. The stability and development of the crystal structure was ensured by intramolecular N1-H1 ··· O1 and N3-H3 ··· O2 and intermolecular N4-H4 ··· O2 hydrogen bonds .

V. Supplementary Materials

CCDC-2285385 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 e-mailing data_request@ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Center 12 Union Road Cambridge CB2 1EZ UK; fax: +44(0)1223-336033.

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