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# MOLECULAR STRUCTURE AND CONFORMATION STUDY OF *p*-[N,N-bis(2-CHLOROETHYL)AMINO]BENZALDEHYDE-4-PHENYL THIOSEMICARBAZONE

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The crystal structure of *p*-[N,N-bis(2-chloroethyl)amino]benzaldehyde-4-phenyl thiosemicarbazone(CEAB-4-PTSC) is described. The compound crystallizes in the monoclinic crystal system, $P2_1/c$ space group, $Z = 4$, calculated density = 1.327 Mg/m$^3$, $V = 1978.2(6)$ Å$^3$ with unit cell parameters $a = 16.240(3)$ Å, $b = 12.821(2)$ Å, $c = 9.8543(16)$ Å, $\beta = 105.382(6)°$. The crystal structure reveals that the compound exists in the thione form and S1 and N2 are at *trans*-conformation to each other with respect to the N3—C12 bond. The packing of molecules in the crystal lattice is stabilized by intramolecular hydrogen bonds.

**K e y w o r d s:** phenyl thiosemicarbazone, thiosemicarbazone, *p*-[N,N-bis(2-chloroethyl)amino]-benzaldehyde-4-phenyl thiosemicarbazone, spectral studies.

## INTRODUCTION

The chemistry of thiosemicarbazone have been of immense interest because these compounds provide intriguing chelating patterns, profound biomedical properties, structural diversity, chromogenic, ion-sensing and photoisomerism abilities [ 1—5 ]. Compounds of this type have been used as antibacterial, antifungal and antitumor agents [ 6, 7 ]. Due to their long chain structure, they are very flexible and form linkages with a variety of metal ions [ 8 ]. It was advocated that their flexibility and bioactivity arise because of the presence of the imino group (—N=CH—) in addition to thioamino moieties present in the skeleton of the molecule. The title thiosemicarbazone was synthesized and its crystal structure is reported here, is likely to have biomedical properties similar to other nitrogen-sulfur donor ligands studied. Hence the study of molecular geometry and stereochemistry of thiosemicarbazones have received much attention. The chemical structure of compound is shown in Fig. 1.

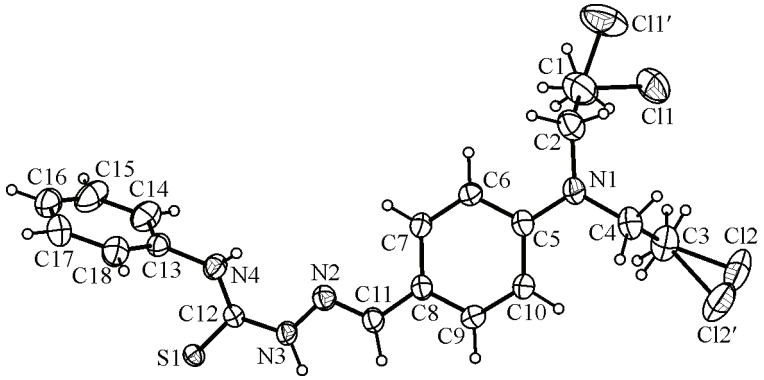
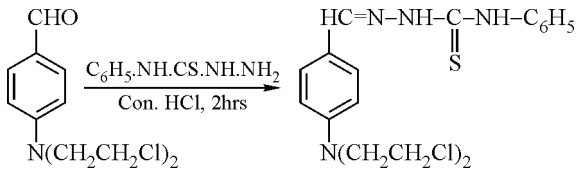



*Fig. 1.* Chemical structure of CEAB-4-PTSC

## EXPERIMENTAL

### *Synthesis and Characterization of* CEAB-4-PTSC

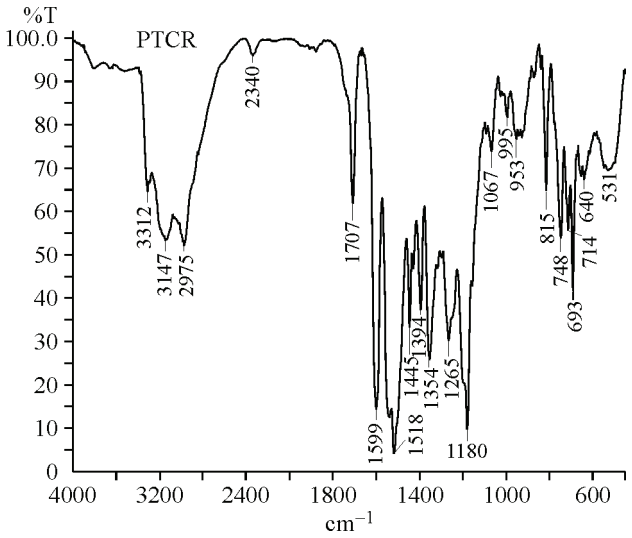



The starting material *p*-[N,N-bis(2-chloroethyl)amino]benzaldehyde was prepared by the reported procedure [ 9 ]. The purity of the compound was checked by the elemental analysis and the melting point. The title compound was prepared by a simple condensation reaction of the ethanolic solution of *p*-[N,N-bis(2-chloroethyl)amino]benzaldehyde (2 $cm^3$) with 4-phenyl thiosemicarbazide (20 $cm^3$) with hydrochloric acid (35 %, 0.5 $cm^3$) taken into a 250 ml round bottom flask, which was refluxed using a steam bath for around 2 h. The yellow powder precipitated after cooling to 5 °C. The resulting precipitate were collected by filtration and then washed with ethanol followed by ether, and small quantities of the product were recrystallized from ethanol to get pure shiny yellow crystals suitable for X-ray crystallography.

### *UV Spectral Studies*

The UV-Visible studies of the compound CEAB-4-PTSC were performed in the DMSO solvent. The Schiff bases show absorption in between 320 nm and 380 nm. The maximum absorption takes place at a wavelength of 360 nm. This absorbance maximum at 360 nm (27 777 $cm^{-1}$) was assigned to the *n*—π* transition of the thione function of the thiosemicarbazone moiety [ 19 ].

**IR spectral studies.** The Fourier transform infrared (FTIR) analysis of CEAB-4-PTSC was carried out in the range 400—4000 $cm^{-1}$. The spectrum is shown in Fig. 2. Infrared spectroscopy is effectively used to identify the functional groups to determine the molecular structure of the synthesized compounds. Various functional groups present in the compound CEAB-4-PTSC were identified and the chemical structure was confirmed by recording the IR spectrum. The characteristic IR absorption bands observed are consistent with the functional groups present in the compound and the assigned values are as recorded in the table. The N—H stretching vibrations generally occur in the region 3500—3000 $cm^{-1}$ [ 10 ]. The IR band appeared at 3312 $cm^{-1}$ has been assigned to the N—H stretching vibration. In phenyl hydrazones, the possibility of obtaining charge transfer interactions is related to the absence of even a minor amount of strain in the hydrazono group, which must be perfectly planar




| IR ($cm^{-1}$) | Mode assignments |
|---|---|
| 3312 | —NH Stretching |
| 2975 | $\nu_{C—H}$, Ar—H) |
| 1599 | —C=N Stretching |
| 1180 | N—N Stretching |
| 995 | —C—Cl |
| 815 | —C=S Stretching |

*Fig. 2.* FT-IR spectra of CEAB-4-PTSC

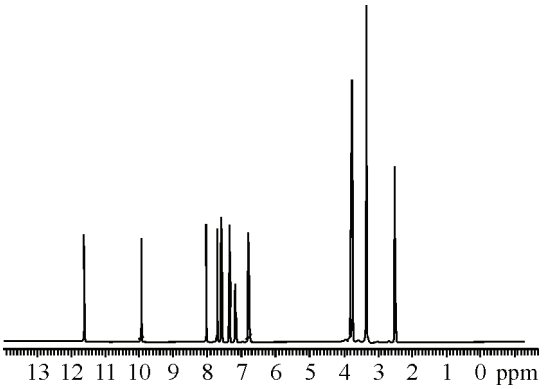



*Fig. 3.* $H^1$-NMR spectrum of CEAB-4-PTSC

to allow conjugation of the group. The C=N stretching mode can be used as a good probe for evaluating the bonding configuration around the amino N atom and the electronic distribution of aromatic amine compounds [ 11, 12 ]. The C=N stretching appears in the region 1670—1600 $cm^{-1}$. In CEAB-4-PTSC, the C=N stretching wavenumber is observed as a strong intense band in IR at 1599 $cm^{-1}$. The slight downshift of the C=N stretching frequency is due to the charge transfer interaction between phenyl rings through the —C=N—N— skeleton. The charge transfer interaction is related to the presence of at least one H atom bonded to the atoms of the phenyl hydrazone skeleton. The N—N stretching vibration is observed as a medium intense band at 1180 $cm^{-1}$.

**$H^1$ NMR spectral studies.** The $H^1$ NMR studies of the compound CEAB-4-PTSC were performed in the DMSO solvent. The spectrum is shown in Fig. 3. The $H^1$ NMR data for the compound show that azomethine(—CH=N—) protons are observed as a 8.04 ppm singlet. Two sharper singlets at 9.953 ppm and 11.63 ppm in the spectra of the free ligands are assigned to Ph—NH— (9.953 ppm) and $^3$NH protons (11.63 ppm) next to C=S, deshielded as expected [ 13 ], while the phenyl protons of the compound gave multiplets at δ = 7.8—7.1. The absence of a signal from thiol —SH, which would be expected around 4 ppm [ 14 ], strongly confirms the thione form.

### *Unit Cell Determination*

An X-ray diffraction study was carried out using a Bruker AXS Kappa APEX II single crystal CCD diffractometer equipped with Mo$K_\alpha$ (λ = 0.7107 Å) radiation. A crystal specimen of the size 0.30×0.25×0.25 mm was cut and mounted on a glass fiber using cyanoacrylate. The unit cell parame-

T a b l e 1

*Crystal data and structure refinement for* CEAB-4-PTSC

| Parameters | CEAB-4-PTSC |
|---|---|
| CCDC | CCDC 804440 |
| Empirical formula | $C_{18}H_{20}Cl_2N_4S$ |
| Formula weight | 395.34 |
| Temperature, K | 293(2) |
| Wavelength, Å | 0.71073 |
| Crystal system, space group | Monoclinic, *P*21/*c* |
| Unit cell dimensions *a*, *b*, *c*, Å; α, β, γ, deg. | 16.240(3), 12.821(2), 9.8543(16); 90, 105.382(6), 90 |
| *Z*, Calculated density, $Mg/m^3$ | 4, 1.327 |
| Crystal size, mm | 0.30×0.25×0.20 |
| *F*(000) | 824 |
| θ range for data collection, deg. | 1.30 to 23.80 |
| Limiting indices | $-18 \le h \le 18$, $-14 \le k \le 13$, $-11 \le l \le 11$ |
| Reflections collected / unique | 17084 / 3034 [*R*(int) = 0.0800] |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3034 / 6 / 260 |
| Goodness-of-fit on $F^2$ | 1.049 |
| Final *R* indices [$I > 2\sigma(I)$] | *R*1 = 0.0523, *wR*2 = 0.1434 |
| *R*-indices (all data) | *R*1 = 0.0734, *wR*2 = 0.1633 |
| Largest diff. peak and hole, $e \cdot Å^{-3}$ | 0.357 and –0.242 |

Table 2

*Selected Bond Lengths* (Å) *and Angles* (deg.) *in* CEAB-4-PTSC

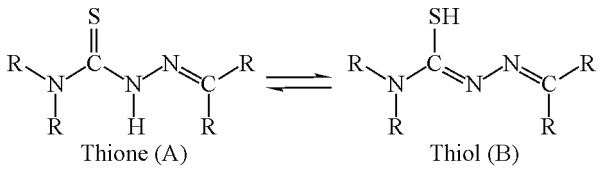
| Bond length | | | | | |
|---|---|---|---|---|---|
| C(1)—Cl(1′) | 1.625(7) | C(6)—C(7) | 1.373(4) | C(13)—N(4) | 1.429(4) |
| C(1)—Cl(1) | 1.746(5) | C(7)—C(8) | 1.388(4) | C(13)—C(14) | 1.362(5) |
| C(1)—C(2) | 1.495(6) | C(8)—C(9) | 1.391(4) | C(14)—C(15) | 1.383(5) |
| C(2)—N(1) | 1.460(4) | C(9)—C(10) | 1.368(4) | C(15)—C(16) | 1.345(7) |
| Cl(2)—C(3) | 1.730(6) | C(8)—C(11) | 1.445(4) | C(16)—C(17) | 1.362(7) |
| Cl(2′)—C(3) | 1.841(5) | C(11)—N(2) | 1.273(4) | C(17)—C(18) | 1.390(6) |
| C(3)—C(4) | 1.500(5) | N(2)—N(3) | 1.378(3) | C(13)—C(18) | 1.366(5) |
| C(4)—N(1) | 1.454(4) | C(12)—N(3) | 1.346(4) | N(3)—H(3) | 1.00(3) |
| C(5)—N(1) | 1.384(4) | C(12)—S(1) | 1.683(3) | N(4)—H(4C) | 0.80(3) |
| C(5)—C(6) | 1.398(4) | C(12)—N(4) | 1.339(4) | C(11)—H(11) | 0.96(3) |
| C(5)—C(10) | 1.400(4) | | | | |
| **Bond angles** | | | | | |
| Cl(1′)—C(1)—Cl(1) | 74.5(3) | C(4)—N(1)—C(2) | 117.7(3) | N(4)—C(12)—N(3) | 116.1(3) |
| Cl(2)—C(3)—Cl(2′) | 27.05(16) | N(3)—C(12)—S(1) | 119.5(2) | N(4)—C(12)—S(1) | 124.4(2) |
| C(5)—N(1)—C(4) | 120.2(3) | N(2)—C(11)—C(8) | 123.3(3) | C(14)—C(13)—C(18) | 120.4(3) |
| C(5)—N(1)—C(2) | 121.0(3) | | | | |

ters were determined by collecting the diffracted intensities from 36 frames measured in three different crystallographic zones and using the method of difference vectors followed by data collection at 293 K using ω—φ scan modes.

**Structure solution and refinement.** The structure was solved by direct methods using the SHELXS-97 program [ 15 ], which revealed the positions of all non-hydrogen atoms, and refined on $F^2$ by a full matrix least squares procedure using SHELXL-97. The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were allowed to ride over their parent atoms. Both chlorine atoms are disodered over two positions. The final cycle of the refinement converged to $R_1 = 0.0523$ and $wR_2 = 0.1434$ for the observed reflections. The maximum and minimum heights in the final difference Fourier map were found to be 0.357 e·Å$^{-3}$ and –0.242 e·Å$^{-3}$ respectively. Least squares planes and asymmetry calculations were made using the PARST 97 program. The thermal ellipsoid plot and packing were done using ORTEP and PLATON respectively [ 16, 17 ]. Non-bonded interaction graphics were created using the PLATON program. The crystallographic data and methods of data collection, solution and refinement are shown in Table 1 and selected bond distances and angles in Table 2. The atomic coordinates and equivalent isotropic displacement coefficients are included in the deposited material (CCDC 804440) as a complete list of bond distances and angles.

## RESULTS AND DISCUSSION

Thiosemicarbazones exist in two tautomeric forms: thione (A) and thiol (B) (Scheme 1). Thione functions as a bidentate neutral ligand and thiol can be deprotonated and act as an anionic ligand [ 18 ]. Due to the presence of C=N, thiosemicarbazones exist as E and Z isomers. Considering the thermodynamic stability, the E isomer will predominate in the mixture [ 19 ]. The crystal structure reveals that




Scheme 1. Tautomeric forms of thiosemicarbazone

Table 3

*Torsion angles of the selected bonds*

| Conformational Bonds | CEAB-4-PTSC angle, deg. |
|---|---|
| S(1)—C(12)—N(3)—N(2) | 172.0(2) |
| C(11)—N(2)—N(3)—C(12) | 173.4(3) |
| N(4)—C(12)—N(3)—N(2) | –9.2(4) |

Table 4

*Hydrogen bonding interactions* [Å and deg.]

| D—H…A | *d*(D—H) | *d*(H…A) | *d*(D…A) | ∠(DHA) |
|---|---|---|---|---|
| N(3)—H(3)…S(1)$^{\#1}$ | 1.00(3) | 2.48(4) | 3.463(3) | 168(3) |
| N(4)—H(4C)…S(1)$^{\#2}$ | 0.80(3) | 2.95(3) | 3.670(3) | 151(3) |

Symmetry transformations used to generate equivalent atoms: $^{\#1}$ $-x+1, -y, -z+1$; $^{\#2}$ $x, -y+1/2, z-1/2$.

the compound exists in the thione form and S1 and N2 are at *trans*-conformation to each other with respect to the N3—C12 bond. This is confirmed by the torsion angle of 172.0(2)° of the S1—C12—N3—N2 moiety [ 20—22 ]. The thione form in the solid state is strongly confirmed by the observed bond lengths: C12—S1 [1.683(3) Å] and C12—N3 [1.346(4) Å]. The C12—S1 distance of 1.683(3) Å is closer to the C=S bond length [1.62 Å] than to the C—S bond length [1.81 Å], and the C12—N3 distance of 1.346(4) Å is in the range of 1.349(6)—1.386(4) Å for other thiosemicarbazones having the C—N single bond reported earlier [ 23, 24 ]. The shorter than usual length of C—N and longer than usual length of C=S points out the extended conjugation in the molecule, However, the N(2)—N(3) [1.378(3) Å] and N(3)—C(12) [1.346(4) Å] bond distances observed are intermediate between the ideal values of the corresponding single [N—N, 1.45 Å; C—N, 1.47 Å] and double bonds [N=N, 1.25 Å; C=N, 1.28 Å], which are in support of the extended π delocalization along the thiosemicarbazone chain [ 25—28 ]. The dihedral angle between the benzene ring and the thiosemicarbazide group is 26.84(11)°. The torsion angles and mean plane calculations confirm that the whole thiosemicarbazone moiety adopts an extended conformation and almost lies in the same plane of the benzene ring. The corresponding torsion angles are given in Table 3.

**Packing features.** In the crystal, the molecules are linked through intermolecular N—H…S hydrogen bonds to form chains [ 29 ]. There are two polar hydrogen atoms on the title thiosemicarbazone fragment: one on N3 and another on N4, participating in the hydrogen bond. The dimensions of the hydrogen bonds are listed in Table 4. The conformation of the thiosemicarbazone fragment is such that the imine N atom is oriented in a way to form an intramolecular hydrogen bond (N(3)—H(3)…S(1), resulting in the formation of a four-membered ring. The intramolecular hydrogen bond in the molecule forces it to exist in such a conformation that S1 and N2 are *trans* to each other with respect to the N3—C12 bond [ 30 ].

**Supplementary material.** All crystallographic data for this paper are deposited with the Cambridge Crystallographic Data Centre (CCDC-804440). The data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44 (0) 1223-336033, e-mail:deposit@ccdc.cam.ac.uk.]

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