



## Computational study of the charge transfer molecular complexes of 3-methyl-2-thioxoimidazolidin-4-one with I<sub>2</sub>, IBr, and ICl

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### ABSTRACT

Imidazoline derivatives can be used to treat hyperthyroidism due to their ability to make complexes with iodine. DFT and ab initio theoretical methods were used to calculate the relative stability of the molecular complexes between 3-methyl-2-thioxoimidazolidin-4-one (T) and the dihalogens IY (Y = Cl, Br, I). Stereoisomeric energy minima have been studied for thioamide system. It presents a collinear S–I–Y geometry and was distinguished by the geometry of the dihalogen IY molecular axis located at either a planar or a perpendicular arrangement with respect to the 3-methyl-2-thioxoimidazolidin-4-one(T) plane. The results show that the planar complexes have more effective interaction than the perpendicular ones. Also, the results reveal interesting correlations of various structural and frequency features like the C–S and S–I bonding distances and the N–H stretching frequency shifts with the enthalpy of complexation, the electron donor–acceptor capacity of the dihalogen and the electronegativity of the Y atom and the strength of the interaction between the amidic hydrogen and the inner I. © 2015 Trade Science Inc. - INDIA

### KEYWORDS

3-methyl-2-thioxoimidazolidin-4-one;  
Charge transfer;  
DFT;  
NBO;  
Electronegativity.

### INTRODUCTION

Carbimazole, methimazole (MMI) 1 and propylthiouracil are anti-thyroid drugs which depress the formation of thyroid hormones by inhibiting the first step of the hormonal biosynthesis which is the incorporation of oxidized iodines into tyrosine residues in the large thyroid hormone precursor molecule, thyroglobulin. These anti-thyroid drugs could divert I<sub>2</sub> from the second oxidation step of iodides and consequently prevent the electrophilic substitution of IC on the tyrosine residues of thyroglobulin by forming a stable complex with I<sub>2</sub><sup>[1,2]</sup>.

The diverse properties of the imidazolethione

molecules have been attributed to the coordination ability of the heterocyclic RN-C(=S)-NR'/thioamide group to both metallic and non-metallic elements, leading to stable electron donor–acceptor complexes<sup>[3]</sup>. Indeed, because of the transfer of electron density from the nitrogen lone pair electrons to the thiocarbonyl group, the above thiourea pharmacophore possesses significant electron donor properties at the sulfur site<sup>[4]</sup>. The formation of stable molecular complexes from the interaction of derivativemethimazole with the dihalogens IY (Y = Cl, Br, I) belongs to the general reactions of the electron donor–acceptor systems<sup>[4–6]</sup> between species of the type LE (L: organic framework, E: S, Se), fea-

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turing a C=E double bond, and halogen molecules, I<sub>2</sub>, Br<sub>2</sub>, IBr, ICl<sup>[7]</sup>. They also present a great deal of interest from the purely scientific point of view as two electronic structures of different connectivity and stability are possible to be formed, the charge transfer (CT) complexes bearing a linear E–X–Y arrangement and the hypervalent T-shaped adducts presenting a X–E–Y geometry<sup>[7,8]</sup>. In the present work we have carried out the computational examination of the charge transfer (CT) molecular complexes of 3-methyl-2-thioxoimidazolidin-4-one (T) with the dihalogens IY (Y = I, Br, Cl). Structural, frequency and energy features are fully characterized. Our calculations demonstrate the significant influence of the electronegativity of the Y atom and the polarization of the IY bond on the structural parameters, the amidic stretching harmonic frequency values, the conformational stabilization and the complexation enthalpy of the adduct formed<sup>[8-16]</sup>.

## METHODS

All geometries were optimized with MP2 method in conjunction with 6-31G(d,p) basis set

(6-31+G(d) basis set for sulfur atom) using Gaussian03 program package<sup>[17]</sup>. Also, natural bond orbital (NBO) analysis was performed on optimized geometries using NBO.3 program implemented in the Gaussian03 software for both isolated T compound and T–IY, (Y = Cl, Br, and I) complexes<sup>[18-23]</sup>.

## RESULTS AND DISCUSSION

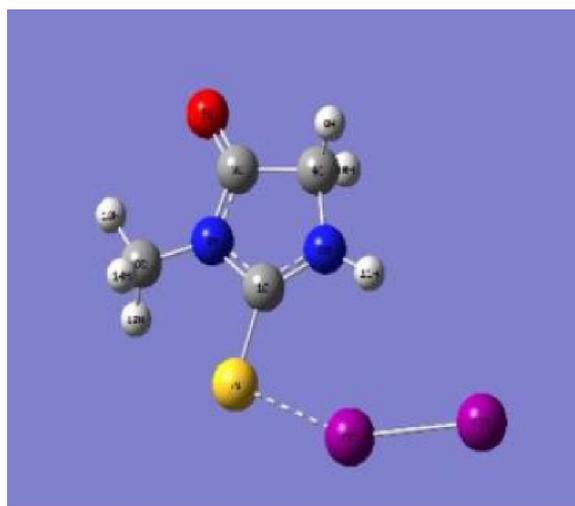
### Structural, frequency, and NBO analysis

Optimized structures of the complexes studied in this work are presented in Figure 1. As can be seen, there are charge transfer interactions between molecule T and di-halogenes I<sub>2</sub>, IBr, and ICl. Indeed, on the basis of direction of interaction there are two types of complexes. Dihedral angles  $\alpha$ NCSI are 180° and 96-99° in the planar and perpendicular complexes, respectively.

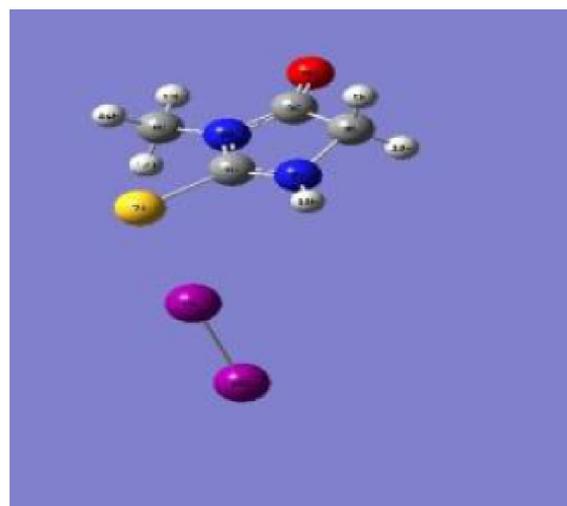
Structural parameters, results of NBO analysis, and vibrational frequencies are gathered in TABLE 1. As can be observed, formation of complexes leads to increment of C-S bond lengths by 0.024 Å. The  $\alpha$ N-H bond lengths are larger in the planar complexes than those in the perpendicular ones because of existence of an additive interaction between amide Hydrogen and Iodine atom in the later complexes. Results of vibrational frequencies are also verified existence of this interaction.

The S-I bond lengths are larger in the perpendicular complexes than those in the planar ones and largest S-I bond length corresponds to complex T-I-I which shows lower charge transfer from Sulfur atom to Iodine. In fact, increase of electronegativity of halogens is accompanied by decrease of S-I bond lengths in these complexes.

Formation of the complexes leads to increase of I-Y (Y=I, Br, and Cl) bond lengths. The I-bond



T-IY(Plan)



T-IY(Perp)

Figure 1 : Manifestation of the planar and perpendicular complexes T–IY

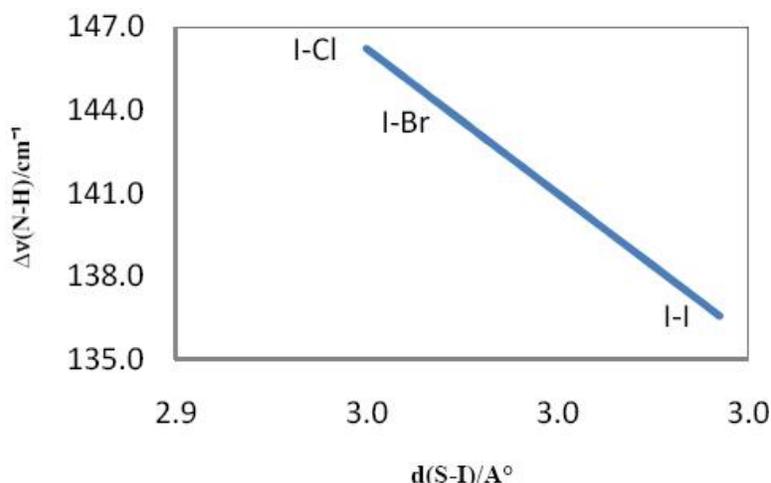


Figure 2 : Variations of  $\Delta\nu$  (N-H) with respect to the S-I bonding distances in the complexes T-IY

TABLE 1 : Selected structural parameters (in Å and degree), and amidic stretching frequencies (in  $\text{cm}^{-1}$ )

Complexes	T	T-I <sub>2</sub> (plan)	T-I <sub>2</sub> (Perp)	T-IBr(plan)	T-IBr(Perp)	T-ICl(plan)	T-ICl(Perp)
C-S	1.657	1.678	1.677	1.681	1.680	1.682	1.681
S-I	-	3.034	3.156	2.98	3.105	2.96	3.09
I-Y	-	2.802	2.774	2.601	2.591	2.523	2.429
N-H	1.008	1.015	1.008	1.015	1.009	1.015	1.009
S-I-Y	-	177.7	177.1	177.8	177.4	177.9	177.5
C-S-I	-	97.7	86.8	98.1	87.7	98.3	89.0
N-C-S-I	-	180.0	77.4	180.0	78.4	180.0	78.9

TABLE 2 : The calculated NH stretching wave numbers ( $\text{cm}^{-1}$ ) of the T and T-IY complexes

-	$\nu$ (N-H)(plan)	$\Delta\nu$ (N-H)	$\nu$ (N-H)(perp)	$\Delta\nu$ (N-H)
-	3681.33		3681.33	
I	3544.76	136.57	3668.30	13.02
Br	3537.72	143.61	3667.01	14.32
Cl	3535.13	146.23	3666.12	15.21

TABLE 3 : The occupation numbers of NBOs (in atomic units)

	T	T-I <sub>2</sub> (plan)	T-I <sub>2</sub> (Perp)	T-IBr(plan)	T-IBr(Perp)	T-ICl(plan)	T-ICl(perp)
$\delta$ (I-Y)	-	1.9972	1.9977	1.9982	1.9989	1.9991	1.996
$\delta$ C-S	1.9877	1.9895	1.9867	1.9892	1.9867	1.9893	1.9867
LP <sub>1</sub> S	1.9907	1.9865	1.9852	1.9859	1.9837	1.9855	1.9830
LP <sub>2</sub> S	1.8710	1.9848	1.8761	1.9924	1.9850	1.9945	1.9854
LP <sub>3</sub> S	-	1.7173	1.6259	1.6852	1.6174	1.6820	1.6197
LP <sub>1</sub> (I)	-	1.9983	1.9986	1.9980	1.9985	1.9976	1.9983
LP <sub>2</sub> (I)	-	1.9939	1.9948	1.7801	1.9020	1.7814	1.9024
LP <sub>3</sub> (I)	-	1.9653	1.9881	1.9632	1.9867	1.9852	1.9858
LPN	1.6806	1.6393	1.6495	-	-	-	-
LPaN	1.5886	1.5875	1.5749	1.5844	1.5715	1.5834	1.5701
N-H	1.9896	1.9875	1.9884	1.9887	1.9883	1.9886	1.9883
$\delta^*$ (I-Y)	-	0.2176	0.1543	0.2385	0.1752	0.2409	0.1819
$\delta^*$ (N-H)	0.0143	0.0392	0.0144	0.0402	0.0144	0.0409	0.0144

TABLE 4 : The natural charges on the atoms (in atomic units)

Atome	T	T-II(plan)	T-II(perp)	T-IBr(plan)	T-IBr(perp)	T-ICl(plan)	T-ICl(perp)
S	-0.1729	-0.0901	-0.1516	-0.8867	-0.8923	-0.8854	-0.9172
C	0.2334	0.2676	0.2700	0.2350	0.2283	-0.2356	-0.1385
aN	-0.4846	-0.4832	-0.4780	-0.4823	-0.4745	-0.4820	-0.4813
I	-	-0.1685	-0.1264	-0.2768	-0.2708	-0.3687	-0.3721
Y	-	-0.0206	-0.0229	-0.1604	-0.1456	-0.2559	-0.2679
C(Me)	-0.4693	-0.4740	-0.4715	-0.4698	-0.4708	-0.4698	-0.4518
aH	0.4417	0.4471	0.4491	0.4501	0.4456	0.4501	-0.4453
N	-0.6205	-0.6017	-0.6001	-0.6002	-0.5930	-0.6000	-0.5923

TABLE 5 : The second order perturbation energies  $E^{(2)}$  (kcal/mol) corresponding to the maincharge transfer interactions for the T-IY complexes

Donor	Acceptor	T-I <sub>2</sub> (plan.)	T-I <sub>2</sub> (perp.)
LP3(S)	N-C	16.9	79.5
LP3(S)	aN-C	6.8	0.8
LP3(S)	I-I	65.6	54.4
LP3(I)	N-H	7.85	-
		T-IBr (plan.)	T-IBr (perp.)
LP3(S)	N-C	14.6	74.8
LP3(S)	aN-C	7.8	0.7
LP3(S)	I-Br	77.9	63.4
LP3(I)	N-H	7.98	-
		T-ICl(plan.)	T-ICl (perp.)
LP3(S)	N-C	13.7	72.3
LP3(S)	aN-C	8.0	0.9
LP3(S)	I-Cl	85.6	69.4
LP3(I)	N-H	7.99	-

length in free molecule, planar and perpendicular complexes is 2.653, 2.771, and 2.766 Å, respectively. Also, C-S-I angle increases from Y=I to Y=Cl.

Formation of the complexes leads to decrease of the stretching vibrational frequencies of N-H bonds which these decreases in planar complexes are higher than those in perpendicular ones. The lowest stretching vibrational frequency of aN-H bond corresponds to the planar complex with dihalogenI-Cl. In fact, formation of aN...H-I hydrogen bonds in the planar complexes lead to decrease of stretching vibrational frequencies of N-H bonds in comparison with perpendicular complexes. The inner Iodine atom in planar complexes acts at the same time as an electron-acceptor from sulfur atom and as an electron-donor to acidic Hydrogen. The magnitude of change in stretching vibrational frequency of N-H bond can be considered as a factor for interplay be-

tween N-H and Iodine. Increase of  $\Delta\nu(\text{N-H})$  from Y=I to Y=Cl indicates higher polarization of I-Cl compared to I-I which arises from high electronegative atom Cl.

Results of NBO analysis are also confirmed the above mentioned discussions. Formation of the complexes leads to decrease of occupation number  $\sigma_1(\text{C-S})$  which this decrease is more outstanding in perpendicular complexes than those in planar ones. On the other hand, formation of the complexes is accompanied by excellent increase of occupation number  $\sigma^*(\text{N-H})$  which indicates charge transfer from Iodine to N-H bond (the most charge transfer corresponds to planar complex(T-I-Cl)). The occupation numbers  $\sigma^*(\text{I-Y})$  are larger in the planar complexes than those in perpendicular ones which highlights higher charge transfer in the planar complexes. As a result of charge transfer inter-

**TABLE 6 : Complexation enthalpies,  $\Delta H^\circ_{298}$ , relative stabilities,  ${}^2E$  (including ZPE corrections) and BSSE (in kJ mol<sup>-1</sup>) for the molecular complexes T-IY**

Planar	BSSE	$\Delta H^\circ_{298}$	Perp	BSSE	$\Delta H^\circ_{298}$	${}^2E$
T-I <sub>2</sub>	8.23	-43.83	T-I <sub>2</sub>	7.98	-29.68	1.8
T-IBr	10.32	-61.51	T-IBr	8.76	-30.62	3.6
T-ICl	10.91	-67.30	T-ICl	9.48	-33.29	4.8

actions between electron-acceptor and electron-donor orbitals, interaction between sulfur and Iodine, formation of the complexes leads to decrease of negative charge on sulfur atom which is more exceptional in planar complexes. Increment of electronegativity of atom Y is accompanied by decrease of negative charge on sulfur atom. Results show that the negative charge on sulfur atom in T-I-I, T-I-Br, and T-I-Cl is -0.0901, -0.8867, and -0.8854 e, respectively. All of these results indicate higher stability of planar complexes in comparison with perpendicular ones. In fact, sulfur atom can give its lone pair  $lp_{(s)}$  to anti-bonding orbital  $\sigma^*(I-Y)$  and makes  $lp_{(s)}-\sigma^*(I-Y)$  interaction. Moreover, donor-acceptor  ${}^2E$  interaction energy values correspond to the above mentioned charge transfers are presented in the TABLE 1. Results indicate that the planar complexes have more  ${}^2E$  interaction energy values compared to the perpendicular ones. The  ${}^2E$  interaction energy for the planar complexes T-I-I, T-I-Br, and T-I-Cl is 65.60, 77.90, and 85.60 kcal mol<sup>-1</sup>, respectively.

Results of changes of thermodynamic quantities  $\Delta H$  and  $\Delta E$  in 298 K are gathered in TABLE 6. As can be observed, changes of standard enthalpy of formation for the planar complexes T-I-I,

T-I-Br, and T-I-Cl is -43.83, -61.51, and -67.30 kcal mol<sup>-1</sup>, respectively. Consequently, electronegative nature of atoms Y leads to polarization of I-Y bonds which makes better interactions between Sulfur and Iodine in the above mentioned complexes. Decrement of S-I distance in the planar complex T-I-Cl is accompanied by less  $\Delta H$  for this complex. Moreover, additional NH-I interactions in the planar complexes lead to high stability for these complexes and polarization of the I-Y bond in planar complex T-I-Cl is higher than those other planar complexes.

## CONCLUSIONS

In the present work interactions between molecule T and dihalogenes I-Y (Y=I, Br, and Cl) have been studied using computational quantum chemistry methods.

Results show that the planar complexes T-I-Y are more stable than the perpendicular ones. The dihedral angles NCSI are close to 180° in the planar complexes. Also, there are additive NH-I interactions in these complexes.

There is potent donor-acceptor interaction between  $lp_{(s)}$  and  $\sigma^*(I-Y)$  in the planar complex

T-I-Cl which arises from more polarization of the I-Cl bond

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