Hydrogen bonding of formamide, urea, urea monoxide and their thio-analogs with water and homodimers

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Abstract. Ab initio and DFT methods have been employed to study the hydrogen bonding ability of formamide, urea, urea monoxide, thioformamide, thiourea and thiourea monoxide with one water molecule and the homodimers of the selected molecules. The stabilization energies associated with the monohydrated adducts and homodimers' formation were evaluated at B3LYP/6-311++G** and MP2/6-311++G** levels. The energies were corrected for zero-point vibrational energies and basis set superposition error using counterpoise method. Atoms in molecules study has been carried out in order to characterize the hydrogen bonds through the changes in electron density and laplacian of electron density. A natural energy decomposition and natural bond orbital analysis was performed to understand the nature of hydrogen bonding.

Keywords. Hydrogen bonding; stabilization energy; AIM; NEDA; NBO.

1. Introduction

Intermolecular interactions like van der Waals or hydrogen bonding have drawn attention of many scientific groups due to their importance in physical, chemical and biological fields.[1–4] Formamide-water complex provides the simplest model for the hydration of proteins. Due to the simplicity of this model, it has been subjected to a large number of theoretical and experimental studies.[5–17] Formamide-water complex also plays an essential role in the properties of various materials such as synthetic polymers, biomolecules, molecular solids and fluids.[18–21] Urea and thiourea are widely used in the production of some pharmaceuticals (sulfothiazoles, barbiturates) and as an additive to some plastic materials.[22] Zhang *et al.* used radial distribution functions, statistics of hydrogen bonding networks and the viscosities to study the interactions and structures of urea-water system by an all-atom molecular dynamics simulation. They concluded that urea molecule shows the tendency to self-aggregate with increasing mole fraction of urea.[23] Many theoretical and experimental investigations performed on this urea-water system.[24–35] The stabilities of thiourea-water complexes were investigated theoretically as well.[36]

Thiourea and its oxides were extensively used in various industrial productions such as in photosensitive materials, medicine, spices and the recycle of precious metals.[37–41] The Jacobsen group made the most remarkable advances in the domain of urea and thiourea catalysts.[42] Thiourea and thiourea oxides are also valuable for fundamental scientific researches, especially in the study of non-linear reaction dynamics.[43] The studies on the kinetics and mechanisms of thiourea oxidation have attracted a great deal of attention.[44,45] These investigations have led to a general conclusion that the oxidation of thiourea goes through S-oxygenation to form sulfenyl, sulfinic and sulfonic acids and finally sulfate ions. The R-naphthylthiourea and phenylthiourea are pulmonary toxins to rats. Thiourea causes liver and thyroid tumors in rats.[46,47] Theoretical study on interactions between thiourea monoxide and water has been carried out to understand its stability in water.[48]

A variety of experimental and theoretical methods have been used to study the hydrogen bonding of homodimers. Formamide homodimers is important as a simple model for establishing the characteristics of N-H···O=C interaction present in a wide variety of biological systems.[49–51] These interactions have been studied by both theoretical and experimental methods.[52–60] For comparisons, the analysis of similar homodimers in case of thioformamide have also been studied.[60] Several groups have studied urea homodimer interactions theoretically.[61–64] The formation of urea homodimers and higher aggregates was confirmed from osmotic pressure measurements[65] and some evidence of urea homodimer pairing in solution emerged at higher concentrations emerged from X-ray study.[66] Present study systematically investigates the hydrogen bonding

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interactions that plays a significant role in stabilizing the monohydrated adducts of formamide, urea, urea monoxide, thioformamide, thiourea and thiourea monoxide with the aid of AIM, NEDA and NBO analysis. In this work, we have also conducted ab initio and DFT studies of the interaction in formamide, urea, urea monoxide, thioformamide, thiourea and thiourea monoxide homodimers.

2. Computational Details

All the calculations carried out with the Gaussian 09 package.[67] The theoretical methods employed were Density Functional Theory (DFT) and ab initio molecular orbital method.[68,69] The geometries of isolated formamide (**F**), urea (**U**), urea monoxide (**UO**), thioformamide (**TF**), thiourea (**TU**) and thiourea monoxide (**TUS**) and their corresponding 1:1 water adducts have been fully optimized at B3LYP/6-311++G** [**L1**] and MP2/6-311++G** [**L2**] levels (geometrical parameters are given in supplementary information TS1–TS22). The optimized orientations of the adducts of the molecule with water obtained at MP2/6-311++G** [**L2**] level are shown in figure 1. The homodimers of selected molecules were also optimized using above-mentioned theoretical methods. The geometrical parameters of optimized homodimers are reported in supplementary information TS23–TS38. The stabilization energy (ΔE) calculated as the difference of the total energy of the monohydrated adducts or homodimers and the sum of the isolated monomers in their minima configurations. The zero-point vibrational energy (ZPE) with basis set superposition error (BSSE) corrected stabilization energy (ΔE_{Corr}) for all of the monohydrated adducts and homodimers were calculated at B3LYP/6-311++G**[**L1**] and MP2/6-311++G** [**L2**] levels. The counterpoise method proposed by Boys and Bernardi used to estimate the BSSE.[70]

The scaling factor of 0.96 and 0.95 was used for ZPE at B3LYP/6-311++G**[**L1**] and MP2/6-311++G** [**L2**] levels respectively.[71] The atoms in molecules (AIM) calculations were performed using the AIM2000 program.[72,73] The natural energy decomposition analysis (NEDA)[74–76] calculations were performed with the NBO 5.9[77,78] program linked to the GAMESS[79] package. A natural bond orbital (NBO) analysis were carried out using the NBO package included in the Gaussian 09 suite of programs.[80,81] The geometrical parameters and ΔE_{Corr} values obtained at MP2/6-311++G** [**L2**] level are considered for discussion unless and otherwise mentioned.

3. Results and Discussion

3.1 *AIM analysis*

The analysis of topology of electron density using AIM has been used extensively to locate the hydrogen bonds. The values of electron density (ρ) at bond critical point (BCP) and its laplacian (∇_ρ^2) are important quantities to characterize hydrogen bond's strength and its nature. The value of topological properties at BCPs characterizing the hydrogen bonds in monohydrate adducts and homodimers are reported in supplementary information table TS39–TS40. The ρ values at BCP in monohydrate adducts for molecules containing oxygen are in the range 0.014–0.042 au and the similar range for the monohydrate adducts of thio-analogs is 0.008–0.035 au. Relatively lower range of ρ values point towards the comparatively weak nature of hydrogen interactions in latter adducts. The ∇_ρ^2 indicating whether the electron density is locally concentrated ($\nabla_\rho^2 < 0$) or depleted ($\nabla_\rho^2 > 0$) for all the hydrogen bonded monohydrate adducts shown in table TS39 range from 0.052–0.160 au and from 0.020–0.104 au for oxo- and thio-adducts, respectively. The values for ∇_ρ^2 are clearly positive, as expected for the hydrogen bond. For homodimers of molecules containing oxygen ρ values at BCPs falls in the range of 0.011–0.032 au, whereas homodimers of thio-analogs falls in the range of 0.010–0.028 au and the values of $\nabla^2\rho$ at the BCPs are positive and well within the range suggested for hydrogen bonds (table TS40). The ρ and ∇_ρ^2 at BCP are smaller for the H$\cdots$S bonds than that for H$\cdots$O bonds in monohydrated adducts and homodimers. These values of ρ and ∇_ρ^2 fall within the range specified for the existence of the hydrogen bond in terms of ρ (0.002–0.040 au) and its ∇_ρ^2 (0.024–0.139 au) as suggested by Koch and Popelier with a few exceptions.[82,83]

3.2 *Important structural changes and stabilization energies*

Full geometrical optimizations of formamide, urea, urea monoxide, thioformamide, thiourea and thiourea monoxide and their adducts with single water have been carried out at B3LYP/6-311++G** [**L1**] and MP2/6-311++G** [**L2**] theoretical levels. The hydrogen bond distances and angles at the bridging hydrogen along with the stabilization energies are recorded in table 1. It was observed that the stabilization energies evaluated at MP2/6-311++G** [**L2**] level fall in the range of 2.73–9.29 kcal/mol and are consistently lower than the values obtained at B3LYP/6-311++G** [**L1**] which fall in the range of 3.64–10.54 kcal/mol theoretical level.
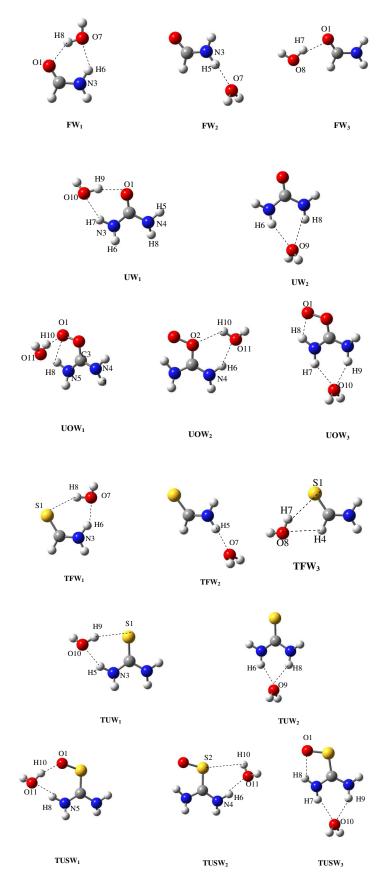
Figure 1. The optimized hydrogen bonded adducts with water at MP2/6-311++G** **[L2]** level.

Table 1. Hydrogen bond distances (r) in (Å), angles in (°) important for hydrogen bonding interactions, difference of hydrogen bond distances from sum of vander Waals radii (Δr) at MP2/6-311++G** **[L2]** level and stabilization energies (ΔE_{Corr}) in (kcal/mol) for monohydrated adducts at B3LYP/6-311++G** **[L1]** and MP2/6-311++G** **[L2]** levels are obtained. r_{VW}* (sum of van der Waals radii) = r_O+ r_H = 2.6Å, r_H+ r_S = 3.05 Å.

Adducts	Hydrogen bond distances(r)		$\Delta r = r_{VW*}- r$	Hydrogen bonding angles		ΔE_{Corr} L1	L2
FW$_1$	O1$\cdots$H8	1.947	0.653	O1-H8-O7	145.30	7.21	6.34
	O7$\cdots$H6	2.060	0.540	N3-H6-O7	136.40		
TFW$_1$	S1$\cdots$H8	2.394	0.206	S1-H8-O7	146.70	6.81	5.23
	O7$\cdots$H6	1.940	0.660	H6-O7-H9	135.85		
FW$_2$	O7$\cdots$H5	1.995	0.605	H5-O7-H8	177.61	3.83	3.54
TFW$_2$	O7$\cdots$H5	1.961	0.639	O7-H5-N3	176.57	4.52	3.85
FW$_3$	O1$\cdots$H7	1.900	0.700	O1-H7-O8	156.63	4.73	3.67
TFW$_3$	S1$\cdots$H7	2.390	0.660	S1-H7-O8	153.00	3.64	2.73
	O8$\cdots$H4	2.520	0.080	H4-O7-H8	145.74		
UW$_1$	O1$\cdots$H9	1.906	0.694	O1-H9-O10	149.94	7.51	6.68
	O10$\cdots$H7	2.060	0.540	O10-H7-N3	142.70		
TUW$_1$	S1$\cdots$H9	2.368	0.682	S1-H9-O10	148.47	7.28	5.67
	O10$\cdots$H5	1.940	0.660	O10-H5-N3	155.02		
UW$_2$	O9$\cdots$H8	2.240	0.355	O9-H8-N4	142.00	5.10	4.68
	O9$\cdots$H6	2.200	0.400	O9-H6-N4	145.78		
TUW$_2$	O9$\cdots$H8	2.164	0.436	O9-H8-N4	151.38	6.05	5.35
	O9$\cdots$H6	2.164	0.436	O9-H6-N4	151.38		
UOW$_1$	O1$\cdots$H10	1.730	0.870	O1-H10-O11	158.01	8.74	8.59
	O1$\cdots$H8	1.930	0.670	O1-H8-N5	111.98		
TUSW$_1$	O1$\cdots$H10	1.710	0.890	O1-H12-O10	158.13	10.54	9.29
	O11$\cdots$H8	1.839	0.761	O10-H8-N5	173.24		
UOW$_2$	O2$\cdots$H10	2.200	0.400	O2-H10-O11	122.95	7.09	6.67
	O11$\cdots$H6	1.960	0.640	O11-H6-N4	151.40		
TUSW$_2$	S2$\cdots$H10	3.128	-0.922	S2-H10-O11	100.62	7.78	4.28
	O11$\cdots$H6	1.970	0.630	O11-H6-N4	167.15		
UOW$_3$	O1$\cdots$H8	1.789	0.811	O1-H8-N5	116.49	6.60	6.50
	O10$\cdots$H7	2.154	0.446	O10-H7-N4	145.71		
	O10$\cdots$H9	2.180	0.420	O10-H9-N5	142.18		
TUSW$_3$	O1$\cdots$H8	2.031	0.569	O1-H8-N5	117.40	9.11	5.58
	O10$\cdots$H7	2.185	0.415	O10-H7-N4	142.40		
	O10$\cdots$H9	2.220	0.380	O10-H9-N5	137.70		

Three different conformations **FW$_1$**, **FW$_2$** and **FW$_3$** for the formamide-water adduct have been optimized and are shown in figure 1. **FW$_1$** is the most stabilized adduct with oxygen of formamide as the hydrogen bond acceptor and N-H as hydrogen bond donor to water. It is perceived that the adduct **FW$_1$** has two hydrogen bonds with lengths (O1$\cdots$H8) and (O7$\cdots$H6) of 1.947 Å and 2.060 Å and angles of 145.30° and 136.40° respectively with ΔE_{Corr} of 6.34 kcal/mol. The difference in hydrogen bond distances from the respective sum of van der Waals radii and the ρ values at the BCP of two hydrogen bonds suggest both the hydrogen bonds play significant role in stabilizing the adduct. Experimental results reported by Langley *et al.*,[84] include the hydrogen bond distance and angles in the formamide-water adduct in **FW$_1$** conformation as (O$\cdots$H-O = 1.902 Å, $\angle$O-H-O= 151.1°, O$\cdots$H-N= 2.002 Å, $\angle$O-H-N= 141.5°) which matches with the values obtained at MP2/6-311++G** **[L2]** levels with small variations. The other two adducts of formamide with water **FW$_2$**

and FW_3 are stabilized through single hydrogen bond as reflected by the geometrical parameters in table 1 and AIM analysis (table TS39) and thereby, their stabilization energies are relatively lower. The hydrogen bond distances in FW_2 and FW_3 are $O7\cdots H5$ and $O1\cdots H7$ are 1.995 Å and 1.900 Å and angles of 177.61° and 156.63°, respectively with difference of 0.13 kcal/mol in ΔE_{Corr}. The geometrical parameters for the hydrogen bond have an agreement with the experimentally reported values for similar adducts FW_2 (O$\cdots$H-O = 1.981 Å, ∠O-H-O= 173.9°) and FW_3 (O$\cdots$H-O = 1.907 Å, ∠O-H-O= 156.1°).[84]

The particulars of three adducts of thioformamide with water listed in table 1 also suggest that the most stabilized structure TFW_1 out of three is analogous to the most stable formamide-water adduct. The adduct TFW_1 is stabilized by two hydrogen bonds; $S1\cdots H8$ (2.394 Å) and $O7\cdots H6$ (1.940 Å) with ΔE_{Corr} of 5.23 kcal/mol. The S and N-H of thioformamide act as hydrogen bond acceptor and hydrogen bond donor towards water molecule respectively and the ΔE_{Corr} is 1.11 kcal/mol lower in comparison to that of FW_1. The $O7\cdots H5$ hydrogen bonded adduct TFW_2, has hydrogen bond distance of 1.961 Å and angle of 176.57°. Interestingly both TFW_2 and FW_2 involve single hydrogen bond N-H$\cdots O_{water}$ interactions but the ΔE_{Corr} of stabilization energy of TFW_2 is relatively higher (0.31 kcal/mol) supported by shorter hydrogen bond distance. During the MP2 and B3LYP calculations with the same basis set, the maximum stability difference among three conformation of formamide and thioformamide water adduct is for FW_1 and TFW_1 is 0.87 and 1.58 kcal/mol respectively.

Two conformations have been optimized for the adduct between urea and water in 1:1 ratio. Both UW_1 and UW_2 are stabilized by the two hydrogen bonds each. However, UW_1 with oxygen and N-H of urea as hydrogen bond acceptor and donor respectively towards water is 2 kcal/mol more stable relative to UW_2 wherein two N-H bonds of two amino groups act as hydrogen bond donor to oxygen of water. The two hydrogen bond distances in UW_1 are $O1\cdots H9$ and $O10\cdots H7$ are 1.906 Å and 2.060 Å with angles 149.94° and 142.70° respectively. For UW_2 adduct, oxygen of water acts as hydrogen bond acceptor to N4-H8 and N3-H6 of urea with the hydrogen bond distances $O9\cdots H8$ (2.240 Å) and $O9\cdots H6$ (2.200Å) and angles of 142.00° and 145.78°. The TUW_1 being analogous to UW_1 has ΔE_{Corr} of 5.67 kcal/mol while TUW_2 has ΔE_{Corr} of 5.35 kcal/mol. The maximum difference for ΔE_{Corr} for both selected theoretical methods for UW_1 and TUW_1 is 0.83 and 1.61 kcal/mol respectively.

In case of urea monoxide, the attempt to optimize the adduct with hydrogen bonding to O1 reveals adduct UOW_1, wherein there is intramolecular N5-H8$\cdots$O1 hydrogen bond along with O1$\cdots$H10-O11 intermolecular hydrogen bond which exhibits the ΔE_{Corr} of 8.59 kcal/mol. The hydrogen bond distances in the two hydrogen bonds are 1.730 Å and 1.930 Å respectively with angles of 158.01° and 111.98° respectively. The order of stability for most stable adducts of formamide, urea and urea monoxide is $UOW_1 > UW_1 > FW_1$. The thio-analog $TUSW_1$ reflects six-membered cyclic structure with the presence of two intermolecular O1$\cdots$H10 and O11$\cdots$H8 hydrogen bonds with bond distances 1.710 Å and 1.839 Å. Both the bonds are relatively stronger, as suggested by geometrical parameters and ΔE_{Corr}. The $TUSW_1$ adduct is 0.70 kcal/mol more stabilized than UOW_1.

The O2 and H6-N4 bond of urea monoxide acts as hydrogen acceptor, and hydrogen bond donor respectively toward water in UOW_2 with hydrogen bond distances of 2.200 Å and 1.960 Å and angles of 122.95° and 151.40° respectively. The N4-H6$\cdots$O11 hydrogen bond in $TUSW_2$ has a bond distance of 1.970 Å with an angle of 167.15° and ΔE_{Corr} of 4.28 kcal/mol. Though the hydrogen bond distance for S2$\cdots$H10 is longer than the sum of van der Waals radii of the two participating atoms, the presence of hydrogen bond is indicated by the BCP (table TS39). Three hydrogen bond interactions are located in the adducts UOW_3 and $TUSW_3$ with the bifurcated hydrogen bonding N-H$\cdots$O$\cdots$H-N interaction in which the water acts as hydrogen bond acceptor and urea monoxide or thiourea monoxide acts as hydrogen bond donor and one intramolecular hydrogen bond. The UOW_3 adduct with bond distance (O1$\cdots$H8) 1.789 Å, (O10$\cdots$H7) 2.154 Å and (O10$\cdots$H9) 2.180 Å and angles of 116.49°, 145.71° and 142.18° respectively has ΔE_{Corr} of 6.50 kcal/mol. $TUSW_3$ O1$\cdots$H8, O10$\cdots$H7 and O10$\cdots$H9 are 2.031 Å, 2.185 Å and 2.220 Å with angles of 117.40°, 142.40° and 137.70°, respectively. The adduct UOW_3 is 0.92 kcal/mol more stabilized than $TUSW_3$. The order of stabilization for urea monoxide-water adducts is $UOW_1 > UOW_2 > UOW_3$ whereas for thiourea monoxide-water adduct is $TUSW_1 > TUSW_3 > TUSW_2$. In the adducts of urea monoxide and their thio-analogs, the B3LYP calculations show a tendency to give a larger value for the ΔE_{Corr} compared to the MP2 values with difference falls in range 0.10–3.5 kcal/mol.

For comparing the hydrogen bond strength and hydrogen bonding ability of the molecules with themselves, the homodimers of the molecules have also been studied. The optimization of homodimers of the

selected molecules have been carried out at B3LYP/6-311++G** **[L1]** and MP2/6-311++G** **[L2]** theoretical levels. The presence of hydrogen bonds in the homodimers is confirmed through location of BCP with AIM studies (table TS40). The results depict that the stabilization energies for optimized homodimers calculated at MP2/6-311++G** **[L2]** method are higher than those obtained using B3LYP/6-311++G** **[L1]** method. The optimization of homodimers of formamide revealed the presence of five minima. Figure 2 shows the minima for formamide homodimer and table 2 summarizes their structural parameters important for hydrogen bonding. The most stable **DF$_1$**, which correspond to planar cyclic structure involving two hydrogen bonds N-H$\cdots$O=C with hydrogen bond distance 1.890 Å and 1.880 Å and nearly same hydrogen bond angle 172.8° with ΔE_{Corr} 12.34 kcal/mol. The planar **DF$_2$** comprise of hydrogen bonds N-H$\cdots$O=C and C-H$\cdots$O=C with bonding distance of 2.316 Å and 1.924 Å and angles of 141.23° and 167.20° respectively result in relatively lower ΔE_{Corr} value of 8.54 kcal/mol while the homodimers **DF$_3$** and **DF$_4$** are non-planar. The presence of single hydrogen bond in **DF$_4$** and the two hydrogen bonds in **DF$_3$** show larger deviation from linearity and the stabilization associated with these homodimers are comparatively lower. The planar homodimer **DF$_5$** with ΔE_{Corr} of 5.01 kcal/mol is stabilized by O1$\cdots$H9 and H6$\cdots$O7 where the hydrogen bond distances and angles are (2.389 Å and 2.387 Å) and (138.68° and 138.75°) respectively. The stability order for formamide dimer is **DF$_1$** > **DF$_2$** > **DF$_3$** > **DF$_4$** > **DF$_5$**.

Figure 2 also depicts the structure corresponding to the minima on the potential surface of thioformamide dimers and table 2 lists their structural parameters important for hydrogen bonding. The structures are similar to those of formamide homodimer and follow the same stability sequence. Again, the most stable structure occurs in a conformation **DTF$_1$** where the two molecules form two equivalent N-H$\cdots$S=C hydrogen bonds that results in ΔE_{Corr} of 10.50 kcal/mol with each bond distance 2.382 Å and angle 171.0° nearly same. **DTF$_2$** forms two hydrogen bonds N-H$\cdots$S=C and C-H$\cdots$S=C with ΔE_{Corr} of 8.35 kcal/mol defined by the hydrogen bond distance H4$\cdots$S7 of 2.400 Å and angle 159.66° in the former bond. The position of S1 and H9 does not fall within their sum of van der Waals radii with angle of 106.35°, but the presence of the BCP (table TS40) reflects presence of electrostatic interactions between the two atoms. The homodimer **DTF$_3$** and **DTF$_4$** are stabilized with ΔE_{Corr} of 6.25 and 5.63 kcal/mol respectively. The hydrogen bond distances in **DTF$_3$**, H5$\cdot\cdot$S7 and N3$\cdots$H12 are 2.492 Å and

2.319 Å with angles of 148.06° and 146.54° respectively. Whereas **DTF$_4$** is stabilized with single hydrogen bond with bond distance 2.449 Å and angle 151.24°. **DTF$_5$** and **DF$_5$** have symmetrically hydrogen bonded cyclic structure involving S$\cdots$H-C in the former and O$\cdots$H-C hydrogen bonds in the latter but the former dimer is 0.23 kcal/mol more stabilized. The formamide homodimers are more stabilized than thioformamide with two exceptions (**DF$_3$**, **DTF$_3$**) and (**DF$_5$**, **DTF$_5$**). The homodimers of formamide and thioformamide are more stable than their monohydrated adducts respectively. The most stable **DF$_1$** is 6.0 kcal/mol more stabilized as compared to **FW$_1$** adduct whereas formation of **DTF$_1$** is 5.27 kcal/mol more strengthened in contrast to **TFW$_1$**. In the homodimers of formamide and their thio-analogs, the B3LYP calculations often produce a lower value for the ΔE_{Corr} on comparing to the MP2 values.

Two conformations for the energy minimum structure have been obtained in case of urea homodimer, and these structures are reported in figure 2. These structures adorn two hydrogen bonds each. In **DU$_1$**, one of the N-H of each monomer unit acts as hydrogen bond donor towards the carbonyl oxygen as hydrogen bond acceptor. The distances and angles of each hydrogen bonds O1$\cdots$H15 and H5$\cdots$O9 are 1.864 Å and angles 176.22° nearly same. The **DU$_2$** dimer involves two N-H$\cdots$O=C and N-H$\cdots$N-C hydrogen bonds with distances 1.994 Å and 2.129 Å and angles 150.97° and 155.24° respectively. The differences in ΔE_{Corr} of homodimers **DU$_1$** and **DU$_2$** is 2.06 kcal/mol with the stability order **DU$_1$** > **DU$_2$**. The homodimers of thiourea labeled as **DTU$_1$** and **DTU$_2$** that have conformation orientation similar to **DU$_1$** and **DU$_2$** respectively are also placed in figure 2. The **DTU$_1$** has two equivalent hydrogen bonds (N-H$\cdots$S) with hydrogen bond distance and angle of 2.365 Å and 169.26° respectively nearly same. However, the **DTU$_1$** is 0.59 kcal/mol more stabilized than the **DU$_1$**. The **DU$_1$** is 4.72 kcal/mol more stabilized as compared to **UW$_1$** whereas **DTU$_1$** is 5.81kcal/mol more stabilized as compared to **TUW$_1$** adduct.

The **DUO$_1$** with single N-H$\cdots$O bond distance and angle of 1.889 Å and 169.56° stabilized by ΔE_{Corr} of 11.05 kcal/mol. Similar conformation of homodimer **DTUS$_1$** is obtained for thiourea monoxide with ΔE_{Corr} of 10.25 kcal/mol with hydrogen bond distance of 1.933 Å and angle of 150.05°. The stability order is as follows **DUO$_1$** > **DTUS$_1$**. It is found that stability difference for homodimer of urea monoxide and thiourea monoxide is about 2.55–2.75 kcal/mol for two selected methods. The **DUO$_1$** is 2.46 kcal/mol more stabilized as compared to most stable **UOW$_1$** adduct while other
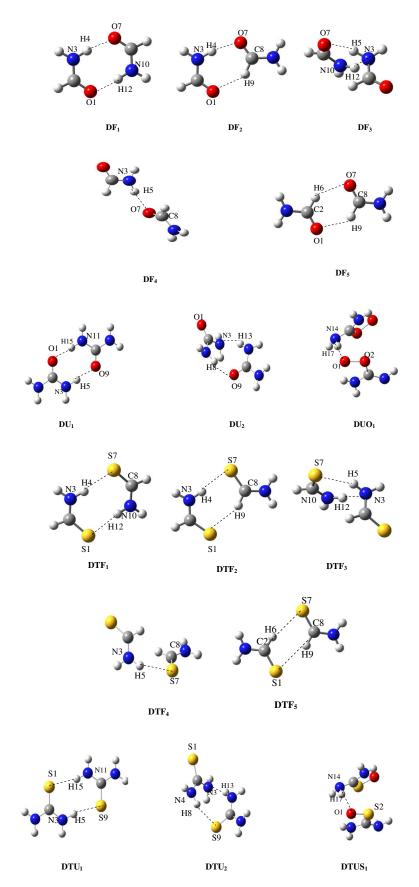
Figure 2. The optimized hydrogen bonded homodimers of selected molecules at MP2/6-311++G** **[L2]** level.

Table 2. Hydrogen bond distances (r) in (Å), angles in (°) important for hydrogen bonding interactions, difference of hydrogen bond distances from sum of vander Waals radii (Δr) at MP2/6-311++G** **[L2]** level and stabilization energies (ΔE_{Corr}) in (kcal/mol) for homodimers under investigation at B3LYP/6-311++G** **[L1]** and MP2/6-311++G** **[L2]** levels are obtained.

Homodimers	Hydrogen bond distances(r)		$\Delta r = r_{VW_*}$- r	Hydrogen bonding angles		ΔE_{Corr} L1	L2
DF$_1$	O1···H12	1.890	0.710	O1-H12-N10	172.80	12.05	12.34
	H4···O7	1.880	0.720	N3-H4-O7	172.85		
DTF$_1$	S1···H12	2.382	0.668	S1-H12-N10	171.35	10.09	10.50
	H4···S7	2.382	0.668	N3-H4-S7	171.40		
DF$_2$	O1···H9	2.316	0.284	O1-H9-C8	141.23	8.22	8.54
	H4···O7	1.924	0.676	N3-H5-O7	167.20		
DTF$_2$	S1···H9	3.953	−0.903	S1-H9-C8	106.35	8.11	8.35
	H4···S7	2.400	0.650	N3-H5-S7	159.66		
DF$_3$	H5···O7	2.025	0.575	O7-H5-N3	154.12	5.80	6.01
	N3···H12	2.416	0.324	N3-H12-H11	116.58		
DTF$_3$	H5···S7	2.492	0.558	O7-H5-N3	148.06	6.05	6.25
	N3···H12	2.319	0.731	N3-H12-N10	146.54		
DF$_4$	H5···O7	1.976	0.624	N3-H5-O7	166.50	5.46	5.80
DTF$_4$	H5···S7	2.449	0.601	N3-H5-S7	151.24	5.30	5.63
DF$_5$	O1···H9	2.389	0.211	O1-H9-C8	138.68	4.50	5.01
	H6···O7	2.387	0.213	C2-H6-O7	138.75		
DTF$_5$	S1···H9	2.724	0.326	S1-H9-C8	159.50	4.66	5.24
	H6···S7	2.723	0.327	C2-H6-S7	159.36		
DU$_1$	O1···H15	1.864	0.736	O1-H15-N11	176.22	10.34	10.89
	H5···O9	1.864	0.736	O9-H5-N3	176.20		
DTU$_1$	S1···H15	2.365	0.685	S1-H15-N11	169.26	8.45	11.48
	H5···S9	2.366	0.684	S9-H5-N3	169.49		
DU$_2$	H8···O9	1.994	0.606	O9-H8-N4	150.97	8.11	8.83
	N3···H13	2.129	0.611	N3-H13-N10	155.24		
DTU$_2$	H8···S9	2.411	0.639	S9-H8-N4	161.76	8.12	9.08
	N3···H13	2.047	1.453	N3-H13-N10	162.41		
DUO$_1$	O1···H17	1.889	0.711	O1-H17-N14	169.56	8.50	11.05
DTUS$_1$	O1···H17	1.933	0.667	O1-H17-N14	150.05	7.50	10.25

adducts, **UOW$_2$** and **UOW$_3$** are 4.38–4.55 kcal/mol less stabilized. The **DTUS$_1$** is 0.96 kcal/mol more stabilized as compared to most stable **TUSW$_1$** adduct while other adducts, **TUSW$_2$** and **TUSW$_3$** are 4.67–5.97 kcal/mol less stabilized.

3.3 *NEDA analysis*

To better understand the nature and relative stability arising from components contributing to the intermolecular attraction in these monohydrated adducts, individual energy components {static polarization (ES), induced polarization (PL), self energy correction at each polarizing centre (SE)}, collectively referred as electrical components (EL) were obtained using NEDA procedures, where EL = ES + PL + SE. The EL component describes both static and induced interactions between monomer charge densities, generally compared favourably with estimates from classical point multipole/polarizability approximations. The charge transfer (CT) component describes delocalizing, donor-acceptor interactions. CORE accounts for the quantum mechanical effects (Pauli repulsions and exchange) of filled orbital (σ-σ) interactions that arise from the required antisymmetry of the wave function for the interacting monomers.[85] The evaluated components at

B3LYP/6-311++G** **[L1]** theoretical level are listed in table 3.

As can be seen from table 3, the ES components of most of the adducts are higher than CT component with the exception of four monohydrated adducts **TFW₁**, **TUW₁**, **UOW₁** and **TUSW₁**. The adduct **TUSW₁** shows a difference of 5.57 kcal/mol between ES and CT while in other three cases the difference is less than 1.22 kcal/mol. The highest ES component is observed for **TUSW₁** amongst all the adducts under study. The adduct **FW₁**, the most stable of formamide-water adducts has highest ES component amongst the three, while in case of its thio-analogs **TFW₁**, though the ES is relatively highest amongst the three conformation, CT component is larger than ES. Results in table reflect that in addition to attractive interactions, EL and CT add significantly to stability and CORE component. This plays an important role in overall stabilization energy. The CT component is more favourable in **TFW₁**, but high CORE component makes it overall less stabilized in comparison to **FW₁**. The ES component for **FW₁** is 27.3% of total attractive interactions. In spite of low polarity of C-S bond in **TFW₁**, in comparison to C-O bond in **FW₁**, the comparable ES component in the two cases indicates favourable placement of other dipoles. The lowest ES component is indicated for the adduct **FW₂**. Though both **FW₂** and **TFW₂** have N3-H5···O7 hydrogen bond, the hydrogen bond angles and the atomic charges on the hydrogen bond donor and acceptor in the two cases also show

negligible difference, the higher ES associated with **TFW₂** relative to **FW₂** results from closer proximity of hydrogen bond donor and acceptor in case of **TFW₂**. It is interesting to note that in spite of low magnitude of atomic charge on S, the EL component in case of thio-analogs is comparable to that observed for oxocarbonyl compounds with the exception of two adducts.

The EL and CT component explains higher stability of **UW₁** and **TUW₁** as compared to **FW₁** and **TFW₁** respectively. In fact, in case of **UOW₁** and **TUSW₁** pair, the ES component is higher in the latter and the huge difference can be traced to the presence of highly electronegative oxygen in thiourea monoxide. In case of **TUSW₁**, S does not act as hydrogen bond acceptor but favours in the electron delocalization through polarization of S-O bond as well comparatively larger CT component. In spite of the higher polarizability of sulfur relative to oxygen, the PL component is higher in oxygen adducts (**FW₁**, **FW₃**, **UW₁**, **UOW₂** and **UOW₃**) and the high electronegative nature of oxygen enhances EL component in these adducts relative to the adducts of sulfur. The order of stability for most stable adducts of formamide, urea and urea monoxide is **UOW₁** > **UW₁** > **FW₁** is supported by CT and EL from NEDA analysis.

3.4 *Atomic charge analysis*

The atomic charges are reflective of the electrostatic component. The values of atomic charges of hydrogen

Table 3. NEDA Analyses[a] of Electrical (EL) {Static (ES) and Induced Polarization (PL)}, Charge Transfer (CT), and Core repulsions (CORE) components in the monohydrated adducts under investigation at B3LYP/6-311++G** **[L1]** level. All the energy components are in kcal/mol.

Adducts	ES	PL	EL[b]	CT	CORE	ΔE_{INT}^{c}
FW₁	−17.38	−9.32	−21.97	−14.86	29.03	−7.79
TFW₁	−18.49	−4.99	−20.99	−19.01	33.41	−6.58
FW₂	−8.43	−4.70	−10.75	−7.97	14.06	−4.66
TFW₂	−9.53	−4.98	−11.97	−9.02	15.54	−5.44
FW₃	−11.36	−4.89	−13.80	−10.06	18.13	−5.72
TFW₃	−9.55	−3.74	−11.43	−8.54	15.69	−4.29
UW₁	−18.75	−8.13	−22.78	−16.2	31.08	−7.91
TUW₁	−19.22	−4.38	−21.44	−20.44	35.07	−6.82
UW₂	−9.96	−6.00	−12.91	−6.70	14.01	−5.59
TUW₂	−11.70	−6.74	−14.99	−8.22	16.36	−6.85
UOW₁	−19.45	−4.37	−21.69	−19.84	32.34	−9.19
TUSW₁	−30.56	−11.06	−35.92	−36.13	58.57	−13.48
UOW₂	−15.95	−8.48	−20.13	−12.32	24.23	−8.23
TUSW₂	−12.44	−6.26	−15.52	−10.91	20.23	−6.20
UOW₃	−12.68	−6.74	−15.98	−7.62	15.79	−7.81
TUSW₃	−12.28	−6.28	−15.36	−6.80	15.72	−7.44

In NEDA scheme[b]EL = ES + PL +SE, [c]ΔE_{INT} = EL + CORE +CT

bond acceptor and hydrogen bond donor are analyzed from NBO obtained at B3LYP/6-311++G** [L1] theoretical level. The atomic charges for all the sixteen monohydrated adduct with water are reported in tables TS41–TS42. Atomic charge analysis indicates that the charge on S1 is comparatively much smaller in magnitude than on O1 in the adducts of thioformamide and formamide respectively. Hence, the contribution of electrostatic interactions in adducts involving sulfur of thioformamide as hydrogen bond acceptor is expected to be smaller in comparison to oxygen of formamide. In monohydrated adducts, the oxygen of water is more electron dense than the oxygen of formamide but polarity of O-H of water favours the carbonyl oxygen to act as hydrogen bond acceptor.

The decrease in electron density on hydrogen atom of water involved in hydrogen bonding has been accepted as one of the criteria for hydrogen bond and clearly shows that the hydrogen nuclei are deshielded upon hydrogen bond formation. The analysis of atomic charges on atoms involved in hydrogen bond formation in table TS41–TS42 reflects that the hydrogen atoms of the hydrogen bond donors have charge in the range 0.203–0.509 au. In addition, the charge density on the atom acting as hydrogen bond acceptor is increased. The NEDA study indicated that ES components of thio-analogs of formamide, urea and urea monoxide have comparative value with few exceptions.

Nearly all the atoms in the urea and thiourea undergo variation in atomic charge density upon adduct formation with water in UW_1 and TUW_1 orientations. Relatively high variation in atomic charge on atoms H5, H6 and H8 is observed. The most stable adduct of urea monoxide with water UOW_1, reflects large atomic charge variations on O1, C3 and both the N atoms. The addition of water molecule to thiourea monoxide increases charge on C atom and decreases that on S atom, which indicates that with the addition of water molecule, the polarity of C-S bond becomes larger. These results are supported by the molecular electrostatic potential (MEP maps) calculated using Molekel 4.3 version on molecules and their adducts with water under study at B3LYP/6-311++G** [L1] theoretical level shown in figure S1. The red region indicates the most negative potential V_{min} while blue region indicates the positive potential V_{max}. As can be seen from the figure, sulfur and oxygen involved in adducts under study exhibits negative electrostatic potential and hydrogen exhibits positive electrostatic potential. The electrostatic potential on oxygen is 62.75 kcal/mol while for sulfur is 53.33 kcal/mol reflects higher stability of adducts of formamide with water relative to thioformamide adducts.

The atomic charges for all the sixteen homodimers are reported in tables TS43–TS45. Atomic charge analysis indicates that the charge on S1 is relatively −0.427 to −0.515 au lower in magnitude than on O1 in homodimers of thioformamide and formamide respectively. This shows large electrostatic contribution to the total energy in formamide homodimers under study, which dominates over all other stabilizing interactions. However, in case of formamide and thioformamide homodimers, the small difference in stabilization energies is indicated in the results. Polarizations of all the bonds are increased in DF_1 and DTF_1. However, variations in DF_1 are larger at the hydrogen bond acceptor and hydrogen bond donor group. Atomic charge variations in DU_1 also suggest change in polarization of bonds on dimer formation. However, high atomic charge values caused by the presence of the two –NH$_2$ group, the electrostatic interactions are anticipated to be higher in DU_1 relative to DF_1. The thio-analogs of urea, also reflects change in bond polarities upon dimer formation. However, the variations are relatively smaller in comparison to DU_1 formation.

3.5 *NBO analysis*

The second order interactions energies ($E^{(2)}$) of relevant orbital interactions associated with hydrogen bond donor and acceptor from NBO analysis obtained at B3LYP/6-311++G** [L1] theoretical level are reflective of the charge transfer between the monomeric units in monohydrated adducts and are recorded in table 4. The occupancies of the acceptor orbitals are indicative of extent of charge transfer and are also included in the table 4. As can be seen in case of FW_1, the orbital interactions $n_{O1} \rightarrow \sigma^*_{H8\text{-}O7}$ and $n_{Ow} \rightarrow \sigma^*_{N\text{-}H}$ stabilize the adduct with $E^{(2)}$ values of 6.91 and 3.58 kcal/mol. The $E^{(2)}$ values also suggest that former interactions are larger in comparison to latter. Hence, strength of O1$\cdots$H8-O7 is relatively stronger, which is also reflected by the ρ value of the BCP and the hydrogen bond length. The hydrogen bonded FW_2 and FW_3 have $n_{O7} \rightarrow \sigma^*_{N3\text{-}H5}$ and $n_{O1} \rightarrow \sigma^*_{O8-H7}$ with $E^{(2)}$ values 6.65 and 7.43 kcal/mol. The $E^{(2)}$ values for both the hydrogen bonds in TFW_1 are higher in comparison to the respective values present in FW_1 which suggests CT component to be relatively higher which indeed is reflected in NEDA analysis as well.

The CT in case of UW_1 is indicated to be higher in relation to that in FW_1 by the $E^{(2)}$ values. The NEDA also suggests similar results where EL and CT components favour UW_1. The orbital interactions $n_{O1} \rightarrow \sigma^*_{H10\text{-}O11}$ with $E^{(2)}$ value of 17.85 kcal/mol strengthen the O1$\cdots$H10 bond in UOW_1 while $n_{O1} \rightarrow$

Table 4. Important second order stabilization energies $E^{(2)}$ (kcal/mol) and occupancies of acceptor orbitals for the orbital interactions strengthening adduct with water at B3LYP/6-311++G** **[L1]** level.

	D	A		D	A		Occupancies			
Adducts	Molecule	H_2O	$E^{(2)}$	H_2O	Molecule	$E^{(2)}$	Acceptor	H_2O	Acceptor	Molecule
FW$_1$	$n_{O1} \rightarrow \sigma^*_{H8\text{-}O7}$		6.91	$n_{O7} \rightarrow \sigma^*_{N3\text{-}H6}$		3.58	$\sigma^*_{H8\text{-}O7}$	0.023	$\sigma^*_{N3\text{-}H6}$	0.019
TFW$_1$	$n_{S1} \rightarrow \sigma^*_{H8\text{-}O7}$		7.75	$n_{O7} \rightarrow \sigma^*_{N3\text{-}H6}$		9.02	$\sigma^*_{H8\text{-}O7}$	0.034	$\sigma^*_{N3\text{-}H6}$	0.033
FW$_2$				$n_{O7} \rightarrow \sigma^*_{H5\text{-}N3}$		6.65	$\sigma^*_{H5\text{-}N3}$	0.019		
TFW$_2$				$n_{O7} \rightarrow \sigma^*_{H5\text{-}N3}$		7.74	$\sigma^*_{H5\text{-}N3}$	0.026		
FW$_3$	$n_{O1} \rightarrow \sigma^*_{H7\text{-}O8}$		7.43				$\sigma^*_{H8\text{-}O7}$	0.021		
TFW$_3$	$n_{S1} \rightarrow \sigma^*_{H7\text{-}O8}$		5.32	$n_{O8} \rightarrow \sigma^*_{H4\text{-}C2}$		0.58	$\sigma^*_{H7\text{-}O8}$	0.021	$\sigma^*_{H4\text{-}C2}$	0.043
UW$_1$	$n_{O1} \rightarrow \sigma^*_{H9\text{-}O10}$		8.32	$n_{O10} \rightarrow \sigma^*_{H7\text{-}N3}$		4.94	$\sigma^*_{H9\text{-}O10}$	0.026	$\sigma^*_{H7\text{-}N4}$	0.016
TUW$_1$	$n_{s1} \rightarrow \sigma^*_{H9\text{-}O10}$		9.06	$n_{O10} \rightarrow \sigma^*_{H7\text{-}N3}$		9.74	$\sigma^*_{H9\text{-}O10}$	0.036	$\sigma^*_{H7\text{-}N4}$	0.028
UW$_2$				$n_{O10} \rightarrow \sigma^*_{H8\text{-}N4}$		1.76	$\sigma^*_{H8\text{-}N4}$	0.013		
				$n_{O10} \rightarrow \sigma^*_{H6\text{-}N3}$		1.84	$\sigma^*_{H6\text{-}N3}$	0.013		
TUW$_2$				$n_{O10} \rightarrow \sigma^*_{H8\text{-}N4}$		2.43	$\sigma^*_{H8\text{-}N4}$	0.021		
				$n_{O10} \rightarrow \sigma^*_{H6\text{-}N3}$		2.37	$\sigma^*_{H6\text{-}N3}$	0.021		
UOW$_1$	$n_{O1} \rightarrow \sigma^*_{H10\text{-}O11}$		17.85				$\sigma^*_{H12\text{-}O10}$	0.046		
TUSW$_1$	$n_{O1} \rightarrow \sigma^*_{H10\text{-}O11}$		10.21	$n_{O11} \rightarrow \sigma^*_{H8\text{-}N5}$		15.77	$\sigma^*_{H12\text{-}O10}$	0.030	$\sigma^*_{H8\text{-}N5}$	0.043
UOW$_2$	$n_{O2} \rightarrow \sigma^*_{H10\text{-}O11}$		1.40	$n_{O10} \rightarrow \sigma^*_{H6\text{-}N4}$		8.02	$\sigma^*_{H10\text{-}O11}$	0.006	$\sigma^*_{H6\text{-}N4}$	0.024
TUSW$_2$				$n_{O11} \rightarrow \sigma^*_{H6\text{-}N4}$		8.83	$\sigma^*_{H6\text{-}N4}$	0.014		
UOW$_3$				$n_{O10} \rightarrow \sigma^*_{H7\text{-}N4}$		2.98	$\sigma^*_{H7\text{-}N4}$	0.012		
				$n_{O10} \rightarrow \sigma^*_{H9\text{-}N5}$		1.20			$\sigma^*_{H9\text{-}N5}$	0.014
TUSW$_3$				$n_{O10} \rightarrow \sigma^*_{H7\text{-}N4}$		2.47	$\sigma^*_{H7\text{-}N4}$	0.017		
				$n_{O10} \rightarrow \sigma^*_{H9\text{-}N5}$		1.86			$\sigma^*_{H9\text{-}N5}$	0.017

Intramolecular hydrogen transfer (**UOW$_1$**) $n_{O1} \rightarrow \sigma^*_{H8\text{-}N5(6.56 kcal/mol)}$, (**UOW$_3$**) $n_{O1} \rightarrow \sigma^*_{H8\text{-}N5(10.41 kcal/mol)}$, (**TUS$_3$**) $n_{O1} \rightarrow \sigma^*_{H8\text{-}N5(4.78 kcal/mol)}$

$\sigma^*_{H10\text{-}O11}$ and $n_{O11} \rightarrow \sigma^*_{H8\text{-}N5}$ orbital interactions with $E^{(2)}$ values of 10.21 and 15.77 kcal/mol strengthen the **TUSW$_1$** adduct. The orbital interactions $n_{O11} \rightarrow \sigma^*_{H6\text{-}N4}$ in **TUSW$_2$**, $n_{O2} \rightarrow \sigma^*_{H10\text{-}O11}$ and $n_{O10} \rightarrow \sigma^*_{H6\text{-}N4}$ in **UOW$_2$** have $E^{(2)}$ values of 8.83, 1.40 and 8.02 kcal/mol respectively suggesting higher stabilization of **UOW$_2$** adduct. The $E^{(2)}$ values in the adducts **UOW$_2$**, **UOW$_3$**, **TUSW$_2$**, and **TUSW$_3$** indicate that CT components are relatively lower than the respective values for **UOW$_1$** and **TUSW$_1$**. The $E^{(2)}$ values indicate that the covalent character of the hydrogen bonds in urea monoxide-water adducts follow the same order **UOW$_1$** > **UOW$_2$** > **UOW$_3$** as that of stabilization energies. The order of stability for adducts **UOW$_1$** > **UW$_1$** > **FW$_1$** is supported by CT.

Important second order stabilization energies for the orbital interactions strengthening the formation of homodimers at B3LYP/6-311++G** **[L1]** level are reported in table 5. In the most stable homodimer of formamide, **DF$_1$** that have two N-H$\cdots$O=C as hydrogen bonds, $E^{(2)}$ values for the orbital interactions $n_{O1} \rightarrow \sigma^*_{H12\text{-}N10}$ and $n_{O7} \rightarrow \sigma^*_{H4\text{-}N3}$ is 12.02 kcal/mol each

which are higher in comparison to the $E^{(2)}$ values in **FW$_1$**. Thus the larger stability of **DF$_1$** can be assigned to better CT between the monomeric units. The $E^{(2)}$ values associated with orbital interactions among N-H$\cdots$S=C in most stable **DTF$_1$** is 11.63 kcal/mol nearly each which explains its higher stability in comparison to **TFW$_1$**. The $E^{(2)}$ values for the orbital interactions in **DF$_2$** are $n_{O1} \rightarrow \sigma^*_{H9\text{-}C8}$ (3.56 kcal/mol) and $n_{O7} \rightarrow \sigma^*_{H4\text{-}N3}$ (11.88 kcal/mol) indicating higher contribution of H4$\cdots$O7 hydrogen bond as well supported by geometrical parameters for the hydrogen bond reported in table 2. In **DTF$_2$**, the small $E^{(2)}$ values for $n_{S1} \rightarrow \sigma^*_{H9\text{-}C8}$ (4.98 kcal/mol) supporting the weak hydrogen bond S1$\cdots$H9 also supported by geometrical parameters. However, the second hydrogen bond has $n_{S7} \rightarrow \sigma^*_{H4\text{-}N3}$ orbital interaction that gives rise to $E^{(2)}$ value of 11.12 kcal/mol. The stability of **DF$_3$** is more supported by orbital interaction H5$\cdots$O7 as suggested by $E^{(2)}$ value of $n_{O7} \rightarrow \sigma^*_{H5\text{-}N3}$ (7.75 kcal/mol) and favoured by short hydrogen bond distance and more linearity as compared to N3$\cdots$H12 hydrogen bond which possesses small $E^{(2)}$ value of

Table 5. Second order stabilization energies $E^{(2)}$ (kcal/mol) and occupancies of acceptor orbitals for the orbital interactions strengthening the formation of homodimers at B3LYP/6-311++G** **[L1]** level.

Homodimers	D Monomer 1	A Monomer 2	$E^{(2)}$	D Monomer 2	A Monomer 1	$E^{(2)}$	Acceptor	Monomer 2	Acceptor	Monomer 1
DF$_1$	$n_{O1} \rightarrow$	$\sigma^*_{H12\text{-}N10}$	12.02	$n_{O7} \rightarrow$	$\sigma^*_{H4\text{-}N3}$	12.02	$\sigma^*_{H12\text{-}N10}$	0.050	$\sigma^*_{H4\text{-}N3}$	0.049
DTF$_1$	$n_{S1} \rightarrow$	$\sigma^*_{H12\text{-}N10}$	11.63	$n_{S7} \rightarrow$	$\sigma^*_{H4\text{-}N3}$	11.66	$\sigma^*_{H12\text{-}N10}$	0.047	$\sigma^*_{H4\text{-}N3}$	0.047
DF$_2$	$n_{O1} \rightarrow$	$\sigma^*_{H9\text{-}C8}$	3.56	$n_{O7} \rightarrow$	$\sigma^*_{H4\text{-}N3}$	11.88	$\sigma^*_{H9\text{-}C8}$	0.062	$\sigma^*_{H4\text{-}N3}$	0.044
DTF$_2$	$n_{S1} \rightarrow$	$\sigma^*_{H9\text{-}C8}$	4.98	$n_{S7} \rightarrow$	$\sigma^*_{H4\text{-}N3}$	11.12	$\sigma^*_{H9\text{-}C8}$	0.054	$\sigma^*_{H4\text{-}N3}$	0.055
DF$_3$	$n_{N3} \rightarrow$	$\sigma^*_{H12\text{-}N10}$	1.72	$n_{O7} \rightarrow$	$\sigma^*_{H5\text{-}N3}$	7.75	$\sigma^*_{H12\text{-}N10}$	0.018	$\sigma^*_{H5\text{-}N3}$	0.035
DTF$_3$	$n_{N3} \rightarrow$	$\sigma^*_{H12\text{-}N10}$	2.30	$n_{S7} \rightarrow$	$\sigma^*_{H5\text{-}N3}$	9.70	$\sigma^*_{H12\text{-}N10}$	0.022	$\sigma^*_{H5\text{-}N3}$	0.050
DF$_4$				$n_{O7} \rightarrow$	$\sigma^*_{H5\text{-}N3}$	11.32			$\sigma^*_{H5\text{-}N3}$	0.62
DTF$_4$				$n_{S7} \rightarrow$	$\sigma^*_{H5\text{-}N3}$	10.37			$\sigma^*_{H5\text{-}N3}$	0.044
DF$_5$	$n_{O1} \rightarrow$	$\sigma^*_{H9\text{-}C8}$	2.24	$n_{O7} \rightarrow$	$\sigma^*_{H6\text{-}C2}$	2.26	$\sigma^*_{H9\text{-}C8}$	0.060	$\sigma^*_{H6\text{-}C2}$	0.060
DTF$_5$	$n_{S1} \rightarrow$	$\sigma^*_{H9\text{-}C8}$	3.84	$n_{S7} \rightarrow$	$\sigma^*_{H6\text{-}C2}$	3.82	$\sigma^*_{H9\text{-}C8}$	0.050	$\sigma^*_{H6\text{-}C2}$	0.050
DU$_1$	$n_{O1} \rightarrow$	$\sigma^*_{H15\text{-}N11}$	13.33	$n_{O9} \rightarrow$	$\sigma^*_{H5\text{-}N3}$	13.43	$\sigma^*_{H15\text{-}N11}$	0.044	$\sigma^*_{H5\text{-}N3}$	0.045
DTU$_1$	$n_{S1} \rightarrow$	$\sigma^*_{H15\text{-}N11}$	17.79	$n_{S9} \rightarrow$	$\sigma^*_{H5\text{-}N3}$	17.75	$\sigma^*_{H15\text{-}N11}$	0.040	$\sigma^*_{H5\text{-}N3}$	0.040
DU$_2$	$n_{N3} \rightarrow$	$\sigma^*_{H13\text{-}N10}$	8.90	$n_{O9} \rightarrow$	$\sigma^*_{H8\text{-}N4}$	4.27	$\sigma^*_{H13\text{-}N10}$	0.030	$\sigma^*_{H8\text{-}N4}$	0.029
DTU$_2$	$n_{N3} \rightarrow$	$\sigma^*_{H13\text{-}N10}$	10.25	$n_{S9} \rightarrow$	$\sigma^*_{H8\text{-}N4}$	6.32	$\sigma^*_{H13\text{-}N10}$	0.030	$\sigma^*_{H8\text{-}N4}$	0.038
DUO$_1$	$n_{O1} \rightarrow$	$\sigma^*_{H17\text{-}N14}$	18.39						$\sigma^*_{H17\text{-}N14}$	0.063
DTUS$_1$	$n_{O1} \rightarrow$	$\sigma^*_{H17\text{-}N14}$	9.05						$\sigma^*_{H17\text{-}N14}$	0.045

$n_{N3} \rightarrow \sigma^*_{H12\text{-}N10}$ (1.72 kcal/mol). The $E^{(2)}$ values for $n_{S7} \rightarrow \sigma^*_{H5\text{-}N3}$ orbital interactions (9.70 kcal/mol) strengthen the S7$\cdots$H5-N3 hydrogen bond in **DTF$_3$** in comparison to small $E^{(2)}$ stabilization for N3$\cdots$H12.

The strongly bound homodimers **DU$_1$** and **DTU$_1$** are supported by strong $E^{(2)}$ values for the two hydrogen bonds and can be seen in table 5. In **DU$_1$**, CT contribution arising from $n_{O1} \rightarrow \sigma^*_{H15\text{-}N11}$ and $n_{O9} \rightarrow \sigma^*_{H5\text{-}N3}$ orbital interactions with $E^{(2)}$ values of 13.33 and 13.43 kcal/mol respectively. Similarly for $n_{S1} \rightarrow \sigma^*_{H15\text{-}N11}$ and $n_{S9} \rightarrow \sigma^*_{H5\text{-}N3}$ orbital interactions in **DTU$_1$**, the $E^{(2)}$ values are 17.79 and 17.75 kcal/mol respectively indicating higher stability of **DTU$_1$** in comparison to the **DU$_1$**. Relatively weaker strengthening of hydrogen bond from the CT interactions occur in monohydrated adducts of urea and thiourea. As can be seen from table 5 in **DUO$_1$**, the $E^{(2)}$ value of orbital interactions $n_{O1} \rightarrow \sigma^*_{H17\text{-}N14}$ for the hydrogen bond O1$\cdots$H17 is 18.39 kcal/mol suggesting its high stability as compared to **DTUS$_1$** with $E^{(2)}$ value of 9.05 kcal/mol. From the analysis of $E^{(2)}$ values, it is reflected that homodimer **DUO$_1$** is 2.46 kcal/mol more stable as compared to the most stable monohydrated adduct **UOW$_1$** also supported by geometrical parameters in tables 1 and 2 whereas for other conformation of monohydrate adducts is 4.38–4.55 kcal/mol less stable.

The NBO analysis clearly states that better CT occurs between the monomers in homodimers, in comparison to the adducts with water. Important $E^{(2)}$ values for the orbital interactions that are explaining conjugation in adducts with water relative to monomer evaluated at B3LYP/6-311++G** **[L1]** level are reported in table TS46. It is reflected that conjugation in adducts is being enhanced on adduct formation suggesting their high stability. Similar enhancement in conjugation has been observed upon homodimeric formation reported in supporting information table TS47. The increment in $E^{(2)}$ values for conjugation is higher for homodimers relative to monohydrated adducts.

4. Conclusions

The hydrogen bonding ability of formamide, urea, urea monoxide and their thio-analogs have been analyzed by studying their adducts with water and the homodimers. The stabilization energies for the adduct between formamide, urea and urea monoxide with single water, range between 3.67–8.59 kcal/mol. While similar adducts with thio-analogs have the stabilization energy in the range 2.73–4.29 kcal/mol. Relatively stronger hydrogen bonds result in homodimers as

reflected by range of stabilization energy 5.01–12.54 kcal/mol for formamide, urea and urea monoxide and 5.63–11.48 kcal/mol for thio-analogs. The most stable adduct of formamide and urea with water has two hydrogen bonds with carbonyl oxygen and N-H as hydrogen bond acceptor and donor respectively towards water, the most stable homodimer also adorn two hydrogen bonds with similar sites as hydrogen bond donor and hydrogen bond acceptor in each monomeric unit. But the difference in stability of the two can be assigned to better CT in the homodimers assisted by resonance interactions in the monomeric units as reflected by NBO analysis.

In case of thioformamide and thiourea, it is thiocarbonyl sulfur and N-H as hydrogen bond acceptor and donor respectively. Thus, when both the sites (thiocarbonyl sulfur and N-H) are simultaneously involved in hydrogen bonding, it results in most stable conformation observed from the study of hydrated molecules and homodimers. The CT in the most stable conformation of homodimer is high as compared to monohydrated adducts. However in case of urea monoxide and thiourea monoxide, the most stable adducts with water involve additional oxygen and N-H as hydrogen bond acceptor and donor, respectively. In this case, stability of the latter is higher in comparison to former, which has been rationalized in terms of two hydrogen bonds involving resonance in the six-membered cyclic structure, due to high charge density of oxygen arising from the presence of sulfur. Whereas, in their homodimer, only single hydrogen bond with additional oxygen of one monomer and N-H of other monomer. Oxo-analog of homodimer is more stabilized relative to its thio-analog.

Supplementary Information

The optimized geometrical parameters for the adducts and corresponding monomeric units using the B3LYP and MP2 method are accessible through the supporting information tables TS1–TS22. The optimized geometrical parameters for the dimers are reported in tables TS23–TS38. The values of topological properties at BCPs characterizing the hydrogen bonds in monohydrate adducts and homodimers are reported in tables TS39–S40. The atomic charges have been evaluated using NBO analysis for all the thirty-two mono-hydrated adducts and homodimers reported in tables TS41–TS45. Important second order stabilization energies $E^{(2)}$ (kcal/mol) for the orbital interactions strengthening the formation of adduct with water and their homodimers reported in TS46–TS47. Molecular electrostatic potential (MEP) maps of the molecules and their adducts with water under investigation along with the V_{max} and V_{min} values from blue to red regions respectively are reported in figure S1. Supplementary information is available at www.ias.ac.in/chemsci.

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