

Hydrogen bonded complexes of oxazole family: electronic structure, stability, and reactivity aspects

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Abstract In the present study, five-membered heterocyclic ring systems containing oxygen with one, two, three, and four nitrogen atoms in the ring along with their isomeric forms and their corresponding 1:1 water complexes have been fully optimized at the ab initio molecular orbital theory and Density Functional Theory (DFT) using aug-cc-pVDZ basis set. The optimized geometric parameters and stabilization energies of the complexes are reported. The study suggests that nitrogen of heterocyclic ring is a stronger hydrogen bond acceptor in comparison to oxygen and ability of nitrogen to act as hydrogen bond acceptor increases in the order oxazole (OZ) > oxadiazole (ODZ) > oxatriazole (OTZ) > oxatetrazole (OTTZ). The results are corroborated by Natural Bond Orbital (NBO) analysis, Quantum Theory of Atoms in Molecules (QTAIM), Symmetry Adapted Perturbation Theory (SAPT), and Molecular Electrostatic Potential (MEP) studies. The blue- and red-shifts in the hydrogen bond donors X-H (X = O, C) stretching frequencies have also been analyzed. Hydrogen bond ability has also been governed in the presence of reactivity descriptors including chemical potential (μ), global hardness (η), and electrophilicity index (ω).

Keywords Hydrogen bond · Oxazoles · NBO · MEP · QTAIM · SAPT

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Introduction

Five-membered heterocycles with O and N heteroatoms are among the privileged structures that play pivotal role in many biologically natural products and useful pharmaceutical agents [1–4]. The oxazole moiety is a valuable precursor in many biological potent natural products such as phenoxan, pimprinetine, pimprinaphine, calyculins, pimprinine, and rhizoxin [5–8]. In nature, the oxazole ring is created by microorganisms in post-translational modifications from serine or threonine residues in peptides. Oxazole derivatives display anti-inflammatory [9], analgesic [10, 11], antibacterial [12], antifungal [13, 14], antimicrobial [15–17], antituberculosis [18, 19], antidiabetic [20], antiviral [21], antiproliferative [22–24], and anticancer [25–27] activities. Within the drug discovery and development, a number of compounds containing an oxadiazole moiety are in late stage clinical trials including zibotentan [28] as an anticancer agent, ataluren for the treatment of cystic fibrosis [29], and raltegravir [30] as an antiretroviral drug for the treatment of HIV infection. Attributing to these facts, heterocyclic ring systems with O and N heteroatoms have allured attention in the field of medicinal research.

The hydrogen bonding interactions are important because these interactions play an influential role in determining the shapes, properties, and functions of number of biomolecules. Heterocycles with O and N heteroatoms display interesting hydrogen bond (HB) acceptor properties. Studies have shown that hydrogen bonding ability of oxygen covalently bonded to sp^2 hybridized carbon atoms are weaker relative to nitrogen in the equivalent situation. This is in contrast to the common expectation, based exclusively on electronegativity, that both are good acceptors. In biological systems, the prevalence of N and O suggests that substituting an oxygen with a nitrogen acceptor in a ligand could retain the hydrogen bonding in the protein and yet produces a chemically distinct ligand.

This requires knowledge of the directionality and relative strengths of the HB acceptors. The water is known as an active constituent in biochemical processes [31, 32]. Thus, the intermolecular hydrogen bonding between the water and molecules of biological interest is significant in rationalizing the mechanism to regulate the biochemical processes. HB interactions involving oxygen and nitrogen (as HB acceptors) and C-H (as HB donors) of heterocyclic molecules with water play an important role in drug-receptor interactions, protein structure, crystal structure arrangement, and conformational preferences of drug molecules in the ligand pocket. The theoretical study of non-classical C-H...O HBs with C-H of heterocycles as hydrogen donors has significance in structures of biopolymers and in the living processes like enzyme catalysis or molecular recognition.

The aim of the present work is focused on studying hydrogen bonding ability of family of oxazole members with water through 1:1 complex formation. The HB donor and acceptor abilities of various sites of heterocycles have been studied. The energetic, topological, electronic, and structural factors affecting the stability of hydrogen bonded complexes of heterocycles with water have been analyzed and compared. By investigating HOMO-LUMO energy gap, the chemical stability against electronic excitation also has been studied. The global molecular descriptors including chemical potential (μ), hardness (η), and electrophilicity index (ω) have also been calculated from the optimized geometries of heterocycles with water.

Computational methods

The geometries of the monomers and the corresponding hydrogen bonded complexes were optimized using second-order Møller-Plesset perturbation theory (MP2) with aug-cc-pVDZ basis set using Gaussian 09 software [33]. The density functional theory calculations at B3LYP level were also performed using aug-cc-pVDZ basis set for comparison purposes. The stabilization energy (ΔE_{BSSE}) was estimated as the difference between the total energy of the complex and the sum total of the monomers. Calculated interaction energies (ΔE_{BSSE}) for the hydrogen bonded complexes were corrected for the basis set superposition error (BSSE) employing counterpoise (CP) method of Boys and Bernadi [34]. Natural Bond Orbital (NBO) analysis was performed at B3LYP/aug-cc-pVDZ level via the method incorporated within the Gaussian 09 package [35]. The topological and energetical properties at the bond critical points (BCP) were analyzed using the QTAIM program [36]. The Molecular Electrostatic Potential (MEP) was computed using WFA surface analysis suite [37], using 0.001 au (electrons/bohr³) contour on the molecule's electron density [38]. To analyze the electrostatic, induction, dispersion, and exchange contributions to the total stabilization energy, Symmetry Adapted Perturbation Theory (SAPT) analysis was

performed at the MP2/aug-cc-pVDZ level with the use of GAMESS package linked to the SAPT 2012.2 code [39–41].

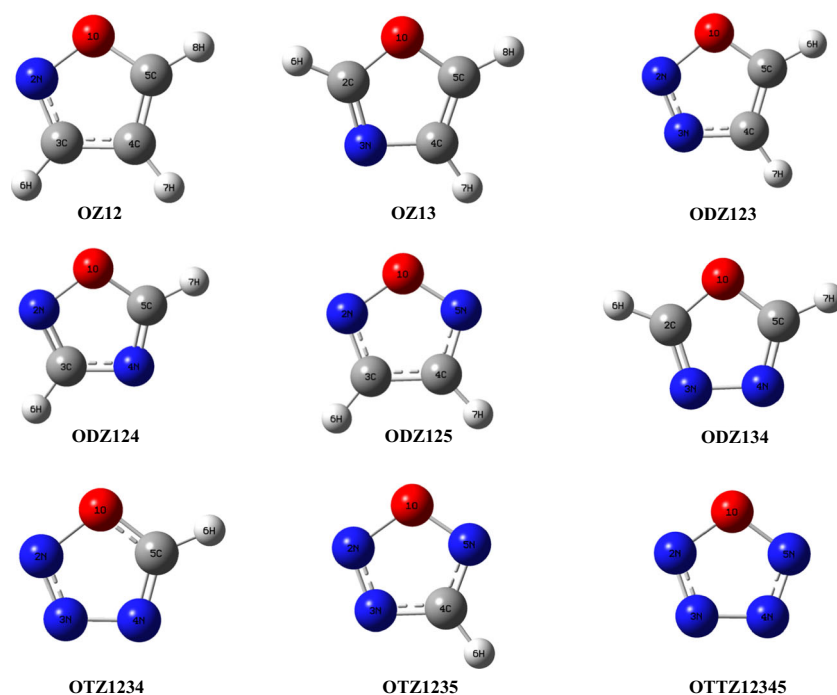
Results and discussion

Stabilization energies and geometrical parameters

The five-membered heterocycles oxazole (OZ), oxadiazole (ODZ), oxatriazole (OTZ), and oxatetrazole (OTTZ) along with their isomeric forms have been optimized at B3LYP/aug-cc-pVDZ (L1) and MP2/aug-cc-pVDZ (L2) theoretical levels (Fig. 1). The relative energy order of isomeric forms of OZ, ODZ, OTZ is as follows: OZ13 > OZ12, ODZ134 > ODZ124 > ODZ123 > ODZ125, and OTZ1234 > OTZ1235. The 1:1 complexes of these heterocycles with water have also been optimized at the abovementioned levels. The stabilization energy (ΔE_{BSSE}) of hydrogen bonded complex is an important criterion in diagnosing the presence of HBs. The presence of HBs in these complexes has been explored by analyzing the distances and respective angles between the probable HB donors and acceptors and is cited in Table 1. The Δr values that represent the difference in sum of van der Waals radii of atoms involved in hydrogen bonding and the distances computed between the atoms in the complex are also included in Table 1. The optimized geometrical parameters for the complexes are using L1, and L2 theoretical levels are summarized in Tables S1–S13. It is apparent from Table 1 that the stabilization energies of these complexes are computed with in a range of -1.56 to -5.72 kcal/mol at L2 theoretical level, while the range at L1 level falls in -1.30 to -5.42 kcal/mol. The IUPAC report agrees on important geometric feature that the angle D-H...A (D is HB donor and A is HB acceptor) should preferably be above 110° and close to 180° . The noncovalent bonded distance between H...A is usually observed to be lower than sum of van der Waals radii of H and A, but in some cases, it is found to be longer also. Furthermore, the length of D-H bond usually increases on HB formation. As can be seen from Table 1, the angle D-H...A in all these complexes is above 110° , i.e., they tend towards linearity except in case of C-H...O interactions. As can be seen from Table 1, the HB angles in the complexes range between 101.81° and 178.74° . Interestingly, the HB angles in the complexes that are stabilized by single HB are more linear while the presence of second HB leads to the formation of quasi five-membered ring structure along with heterocyclic ring forcing the HB angle to be less than 180° .

Table 1 displays the change in D-H bond length and shifts of stretching frequencies (Δ in cm^{-1}) of the HB donor group upon complex formation relative to monomers. Red-shift in the O-H stretching frequency has been traditionally considered as one of the main fingerprints of HBs, assuming that formation of a HB weakens an O-H single bond. Upon complex formation, the O-H bond of water (HB donor) in all the

Fig. 1 Optimized geometries of five-membered heterocycles along with their isomeric forms at MP2/aug-cc-pVDZ level



complexes is elongated and accompanied by a red-shift in the stretching frequency which spans over a range of -9.43 to -154.50 cm^{-1} for this bond. Blue-shift in C-H is reflected with a range of $+2.52$ to $+12.69$ cm^{-1} in complexes involving C-H as HB donor and O-H of water acting as HB acceptor. But it is worth emphasizing that the C-H stretching is found to be red-shifted for complexes involving single $\text{C-H}\cdots\text{O}_w$ interaction. For such complexes, the increase in C-H bond length ranges between 0.001 and 0.004 Å and stretching frequency shift for this bond lies in the range -8.49 to -49.54 cm^{-1} .

The 1,2 and 1,3 positioning of O and N in the heterocyclic ring represents the two isomeric forms of OZ. The complexation between the OZ12 and water resulted in three energy minimum structures, out of which OZ12-W1 is the highest in stabilization ($\Delta E_{\text{BSSE}} = -4.85$ kcal/mol) and is supported by single $\text{O10-H9}\cdots\text{N2}$ HB. The $\text{O9}\cdots\text{H10-O1}$ and $\text{C5-H8}\cdots\text{O9}$ HBs in OZ12-W2 stabilize the complex by -3.68 kcal/mol which is next to OZ12-W1. The HB distances and HB angles both suggest $\text{O9-H10}\cdots\text{O1}$ HB to be more stable relative to $\text{C5-H8}\cdots\text{O9}$. The stabilization energy of -2.29 kcal/mol associated with $\text{C4-H7}\cdots\text{O9}$ single HB in OZ12-W3 supports the importance of nonconventional HBs. The OZ13-W1 with N of heterocyclic ring as HB acceptor to water has stabilization -5.72 kcal/mol which is 0.87 kcal/mol higher relative to that of OZ12-W1 having similar HB. The $\text{C5-H8}\cdots\text{O9}$ hydrogen bonded OZ13-W2 (single HB) has ΔE_{BSSE} value of -2.46 kcal/mol which is higher relative to $\text{C4-H7}\cdots\text{O9}$ hydrogen bonded OZ12-W3 (single HB). The difference in HB strength can be rationalized in view of difference in HB strength.

The hydrogen bonding between ODZ and water resulted in 12 optimized complexes, considering the four isomeric forms

of ODZ. The optimized structures are shown in Fig. 2. In all the isomeric forms of ODZ, the most stable 1:1 complex with water is named with W1 at the suffix. As can be viewed from Fig. 2, in all these four complexes, water acts as an HB acceptor towards C-H of heterocyclic ring and HB donor towards the N of the ring, resulting in quasi-five-membered ring. The stabilization energy of these four complexes increases in the order $\text{ODZ125-W1} < \text{ODZ123-W1} < \text{ODZ124-W1} < \text{ODZ134-W1}$. The $\text{O-H}\cdots\text{N}$ is the major contributing interaction in ΔE_{BSSE} in comparison to $\text{C-H}\cdots\text{O}_w$ as suggested by geometrical parameters. The geometrical parameters reflect that the $\text{O-H}\cdots\text{N}$ HB distance increases in the order of decreasing stabilization energy. The complex ODZ125-W2 is unique in the sense that both the lone pairs present on oxygen of water act as an HB acceptor towards two C-H bonds of heterocyclic ring. The complexes ODZ123-W2, ODZ124-W2, and ODZ134-W2 have ΔE_{BSSE} values -3.74 , -3.66 , and -3.08 kcal/mol, respectively, and have similar HB donors and acceptors. The ΔE_{BSSE} values for ODZ123-W3 complex are -1.38 kcal/mol lower than that of ODZ124-W3 though both are stabilized through $\text{O-H}\cdots\text{N}$ HB. The $\text{C-H}\cdots\text{O}_w$ hydrogen bonded ODZ123-W4 complex with ΔE_{BSSE} of -2.84 kcal/mol highlights the importance of such interaction in drug target binding. The geometrical parameters of ODZ134-W2 also reflect $\text{C-H}\cdots\text{O}_w$ strong HB interactions along with weak support from $\text{O-H}\cdots\text{O}_w$ HB. The weakly bound ODZ125-W2 complex with two unconventional $\text{C-H}\cdots\text{O}_w$ interactions where C-H bonds of heterocyclic ring are donor to oxygen of the water has $\text{O}\cdots\text{H}$ distance exceeding over 2.6 Å. The $\Delta r_{\text{H}\cdots\text{A}}$ values for these weak interactions are negative with $\text{C-H}\cdots\text{O}_w$ angles nearly equal to 108° , and the

Table 1 Hydrogen bond (HB) distances $r_{H\cdots A}$ (in Å), angles θ (D-H \cdots A) (in °), difference of HB distances from sum of van der Waals radii of interacting atoms $\Delta r_{H\cdots A}$; change in bond length Δd (in Å) and shifts of stretching frequencies $\Delta\nu$ (in cm^{-1}) of the HB donor group (D-H) of

complexes of five-membered heterocycles with water upon complexation at MP2/aug-cc-pVDZ (L2) level and BSSE-corrected stabilization energies (ΔE_{BSSE} in kcal/mol) of complexes at B3LYP/aug-cc-pVDZ (L1) and MP2/aug-cc-pVDZ (L2) levels

Complexes	HB distances	$r_{H\cdots A}$ (Å)	$\Delta r_{H\cdots A}$ (Å)	HB angles	(D-H \cdots A) θ (°)	$\Delta\nu$	Δd	ΔE_{BSSE}	
								L1	L2
OZ12-W1	H9 \cdots N2	2.044	0.698	O10-H9 \cdots N2	143.00	-100.37	0.007	-4.74	-4.85
OZ12-W2	H10 \cdots O1	2.202	0.398	O9-H10 \cdots O1	125.71	-23.67	0.002	-3.11	-3.68
	H8 \cdots O9	2.509	0.091	C5-H8 \cdots O9	113.65	0.00	0.000		
OZ12-W3	H7 \cdots O9	2.272	0.328	C4-H7 \cdots O9	178.74	-8.49	0.001	-2.02	-2.29
OZ13-W1	H9 \cdots N3	1.994	0.746	O10-H9 \cdots N3	152.63	-154.50	0.010	-5.42	-5.72
OZ13-W2	H8 \cdots O9	2.241	0.359	C5-H8 \cdots O9	177.90	-12.86	0.002	-1.98	-2.46
ODZ123-W1	H8 \cdots N3	2.103	0.639	O9-H8 \cdots N3	136.95	-77.50	0.006	-4.56	-4.96
	H7 \cdots O9	2.590	0.010	C4-H7 \cdots O9	107.29	0.00	0.000		
ODZ123-W2	H8 \cdots O1	2.367	0.233	O9-H8 \cdots O1	115.53	-16.15	0.002	-3.39	-3.74
	H6 \cdots O9	2.415	0.185	C5-H6 \cdots O9	116.26	0.00	0.000		
ODZ123-W3	H8 \cdots N2	2.114	0.626	O9-H8 \cdots N2	176.41	-57.04	0.004	-2.64	-3.38
ODZ123-W4	H7 \cdots O8	2.236	0.364	C4-H7 \cdots O8	174.88	-8.99	0.002	-3.06	-2.84
ODZ124-W1	H9 \cdots N4	2.102	0.636	O8-H9 \cdots N4	136.98	-85.68	0.005	-4.89	-5.06
	H7 \cdots O8	2.567	0.052	C5-H7 \cdots O8	103.26	+9.01	0.000		
ODZ124-W2	H9 \cdots O1	2.395	0.205	O8-H9 \cdots O1	111.25	-13.18	0.010	-3.79	-3.66
	H6 \cdots O8	2.414	0.188	C5-H6 \cdots O8	115.55	+4.75	-0.005		
ODZ124-W3	H8 \cdots N4	2.073	0.667	O9-H8 \cdots N4	140.39	-86.75	0.006	-4.16	-4.76
ODZ124-W4	H9 \cdots N2	2.127	0.613	O8-H9 \cdots N2	133.57	-60.05	0.001	-4.41	-4.14
	H7 \cdots O8	2.654	0.054	C3-H7 \cdots O8	106.59	0.00	0.000		
ODZ125-W1	H9 \cdots N2	2.150	0.590	O8-H9 \cdots N2	131.37	-57.89	0.004	-3.67	-4.48
	H6 \cdots O8	2.568	0.034	C3-H6 \cdots O8	109.24	0.00	0.000		
ODZ125-W2	H6 \cdots O8	2.652	-0.052	C3-H6 \cdots O8	108.29	+12.69	-0.001	-2.52	-3.26
	H7 \cdots O8	2.659	-0.059	C4-H7 \cdots O8	108.04	+12.69	-0.001		
ODZ134-W1	H9 \cdots N4	2.070	0.713	O8-H9 \cdots N4	136.96	-104.20	0.009	-5.04	-5.70
	H7 \cdots O8	2.606	-0.006	C5-H7 \cdots O8	101.81	0.00	0.000		
ODZ134-W2	H9 \cdots O1	2.516	0.084	O8-H9 \cdots O1	109.27	-9.43	0.001	-3.10	-3.08
	H7 \cdots O8	2.372	0.228	C2-H7 \cdots O8	118.66	+2.52	0.000		
OTZ1234-W1	H8 \cdots N4	2.212	0.528	O7-H8 \cdots N4	125.52	-53.10	0.001	-4.49	-5.35
	H6 \cdots O7	2.451	0.149	C5-H6 \cdots O7	106.43	+3.95	-0.001		
OTZ1234-W2	H7 \cdots N2	2.169	0.571	O8-H7 \cdots N2	160.54	-30.93	0.003	-2.13	-2.46
OTZ1234-W3	H6 \cdots O7	2.103	0.497	C5-H6 \cdots O7	172.11	-49.54	0.004	-4.65	-4.33
OTZ1234-W4	H6 \cdots O7	2.287	0.313	C5-H6 \cdots O7	124.07	0.00	0.000	-4.49	-4.07
OTZ1235-W1	H7 \cdots N5	2.312	0.428	O8-H7 \cdots N5	118.86	-29.02	0.003	-3.33	-4.17
	H6 \cdots O8	2.465	0.135	C4-H6 \cdots O8	110.15	0.00	0.000		
OTZ1235-W2	H7 \cdots N2	2.164	0.576	O8-H7 \cdots N2	170.24	-34.24	0.003	-1.86	-2.37
OTZ1235-W3	H6 \cdots O7	2.152	0.448	C4-H6 \cdots O7	174.08	-35.59	0.003	-3.18	-3.69
OTZ1235-W4	H7 \cdots N3	2.255	0.485	O8-H7 \cdots N3	123.59	-37.06	0.003	-3.60	-4.60
	H6 \cdots O8	2.460	0.140	C4-H6 \cdots O8	109.14	0.00	0.000		
OTTZ12345-W1	H6 \cdots N5	2.324	0.416	O7-H6 \cdots N5	130.00	-10.43	0.002	-1.30	-1.56

hydrogen-donating bonds are shortened by 0.001 Å as shown by Δd values in Table 1.

The two isomers of OTZ are OTZ1234 and OTZ1235, each containing one oxygen and three nitrogens at 1,2,3,4 and 1,2,3,5 positions, respectively. Four complexes each of the two isomers with single water have been optimized and are shown in Figs. 2 and 3. The most stabilized complex in the two isomeric forms (OTZ1234-W1 and OTZ1235-W4) have stabilization energy of -5.35 and -4.60 kcal/mol, respectively.

Three complexes OTZ1234-W1, OTZ1235-W1, and OTZ1235-W4 are adorned by two ${}_{\text{w}}\text{O-H}\cdots\text{N}$ and $\text{C-H}\cdots\text{O}_{\text{w}}$ HBs. The difference in ΔE_{BSSE} values results from difference in HB donor and acceptor sites in the presence of three nitrogens and one oxygen in the heterocyclic ring. The W2 complexes of OTZ1234 and OTZ1235 involve single HB in which water is acting as HB donor towards N of heterocyclic ring and ΔE_{BSSE} values are -2.46 and -2.37 kcal/mol, respectively. The lower ΔE_{BSSE} values for these two complexes indicate

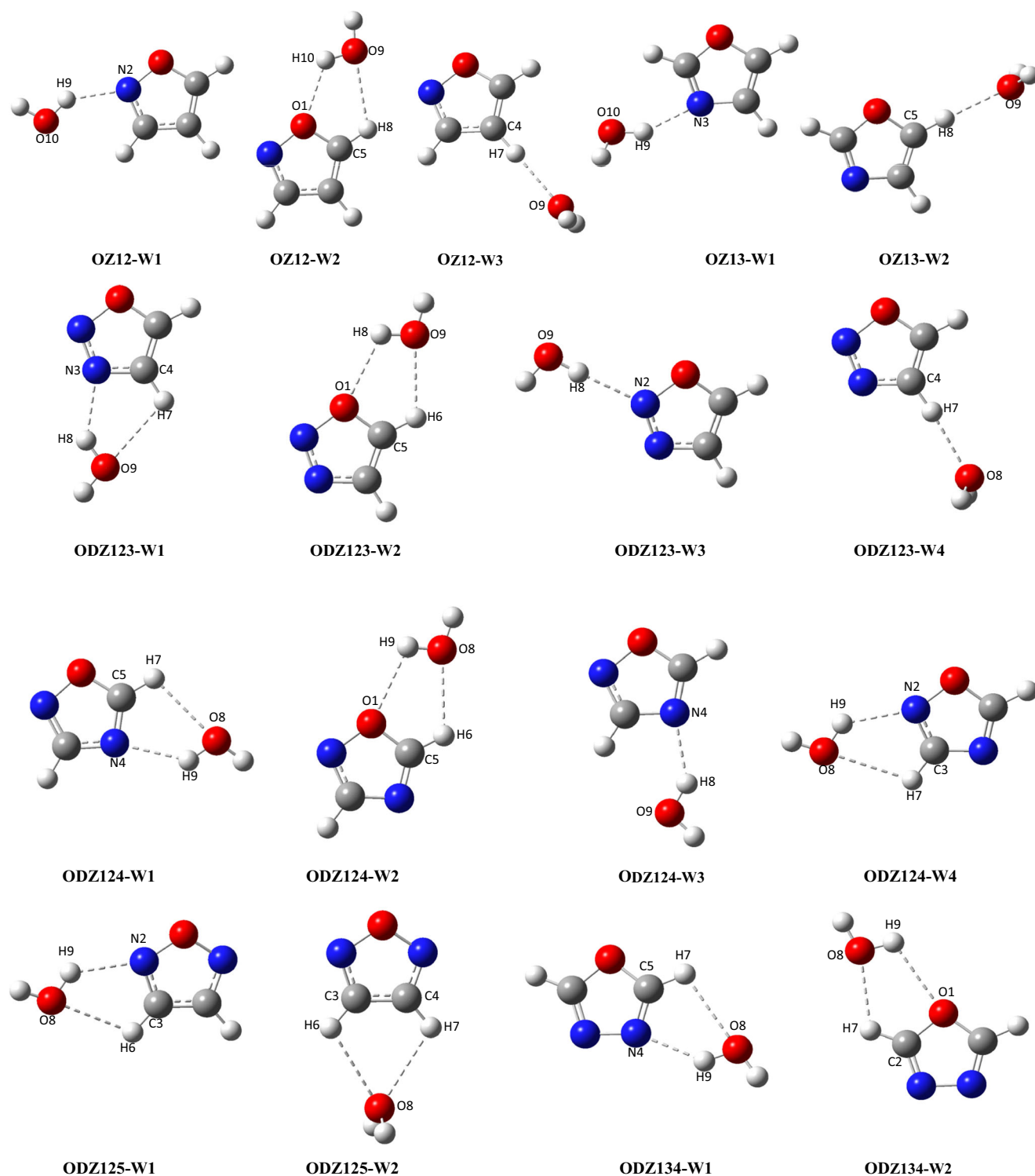


Fig. 2 Optimized geometries of 1:1 hydrogen-bonded complexes of five-membered heterocycles with water at MP2/aug-cc-pVDZ level

that electronegativity of N atom involved in HB is decreased significantly by the electronegative atoms in adjacent position to it and the linear approach being hindered.

Complexes which involve single HB formation with $wO-H \cdots N$ interaction are OZ12-W1 (2.044 Å), OZ13-W1 (1.994 Å), ODZ123-W3 (2.114 Å), ODZ124-W3 (2.073 Å),

OTZ1234-W2 (2.169 Å), OTZ1235-W2 (2.164 Å), and OTTZ12345-W1 (2.324 Å). The order of stabilization energies in these complexes is OZ13-W1 (−5.72 kcal/mol) > OZ12-W1 (−4.85 kcal/mol) > ODZ124-W3 (−4.76 kcal/mol) > ODZ123-W3 (−3.38 kcal/mol) > OTZ1234-W2 (−2.46 kcal/mol) > OTZ1235-W2 (−2.37 kcal/mol) >

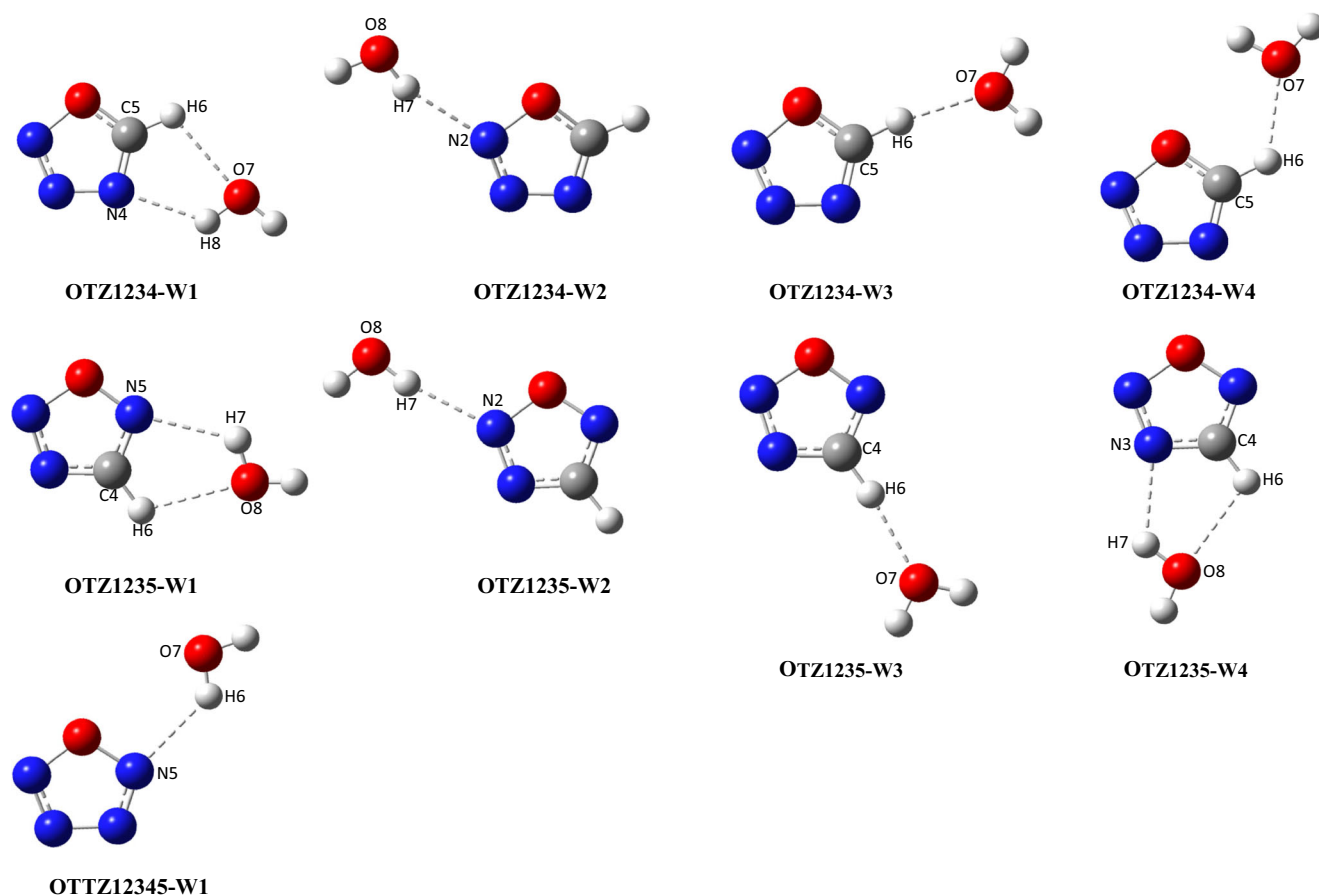


Fig. 2 continued.

OTTZ12345-W1 (−1.56 kcal/mol) which support the fact that N of heterocyclic ring act as strong HB acceptor and the ability increases in the order OZ > ODZ > OTZ > OTTZ. Complexes which involve single HB formation with C-H \cdots O_w interactions are OZ12-W3 (2.272 Å), OZ13-W2 (2.241 Å), ODZ123-W4 (2.236 Å), OTZ1234-W3 (2.103 Å), and OTZ1235-W3 (2.152 Å). The order of stabilization energy in these complexes is OTZ1234-W3 (−4.33 kcal/mol) > OTZ1235-W3 (−3.69 kcal/mol) > ODZ123-W4 (−2.84 kcal/mol) > OZ13-W2 (−2.46 kcal/mol) > OZ12-W3 (−2.29 kcal/mol) which support the fact that C-H HB donor ability decreases in the order OTZ > ODZ > OZ.

NBO analysis

Charge analysis

NBO has been used to determine the extent of charge transfer and predict the HB acceptor ability of various sites in a molecule. Table 2 illustrates the values of charge transfer from heterocyclic unit to water (CT_{H-W}) for the complexes under study at B3LYP/aug-cc-pVDZ level. The complexes OZ12-W2, ODZ123-W1, ODZ124-W1, ODZ124-W4, ODZ125-W1, ODZ134-W1, OTZ1234-W1, OTZ1235-W1, and

OTZ1235-W4 involve HBs with both heterocyclic ring and water acting as donor as well as acceptor; therefore, charge transfer occurs from heterocyclic unit to water and vice versa. The CT_{H-W} values of these complexes being positive indicate that charge transfer from the heterocyclic unit to water is higher than that from water to heterocyclic unit, so the direction of net charge transfer is from heterocyclic ring to water.

The CT_{H-W} values of complexes that are stabilized through single HB with ${}_{w}O-H\cdots N$ interaction fall in the order OZ13-W1 > OZ12-W1 > ODZ123-W3 ~ ODZ124-W3 > OTZ1234-W2 ~ OTZ1235-W2 > OTTZ12345-W1. The CT_{H-W} values of these complexes being positive indicate that charge transfer occurs from heterocyclic unit to water and indicates that N of heterocyclic ring acts as better HB acceptor in the order OZ > ODZ > OTZ > OTTZ. The C-H \cdots O_w single hydrogen bonded complexes OZ12-W3, OZ13-W2, ODZ123-W4, OTZ1234-W3, and OTZ1235-W3 have negative values of CT_{H-W} , as net charge transfer occurs from water to heterocyclic ring. The order of CT_{H-W} values suggest that C-H HB donor ability increases in the order OTZ > ODZ > OZ.

The CT_{H-W} values of complexes ODZ123-W1, ODZ124-W1, ODZ124-W4, ODZ125-W1, ODZ134-W1, OTZ1234-W1, OTZ1235-W1, and OTZ1235-W4 (${}_{w}O-H\cdots N$ as much stabilizing HB interactions along with weak C-H \cdots O_w

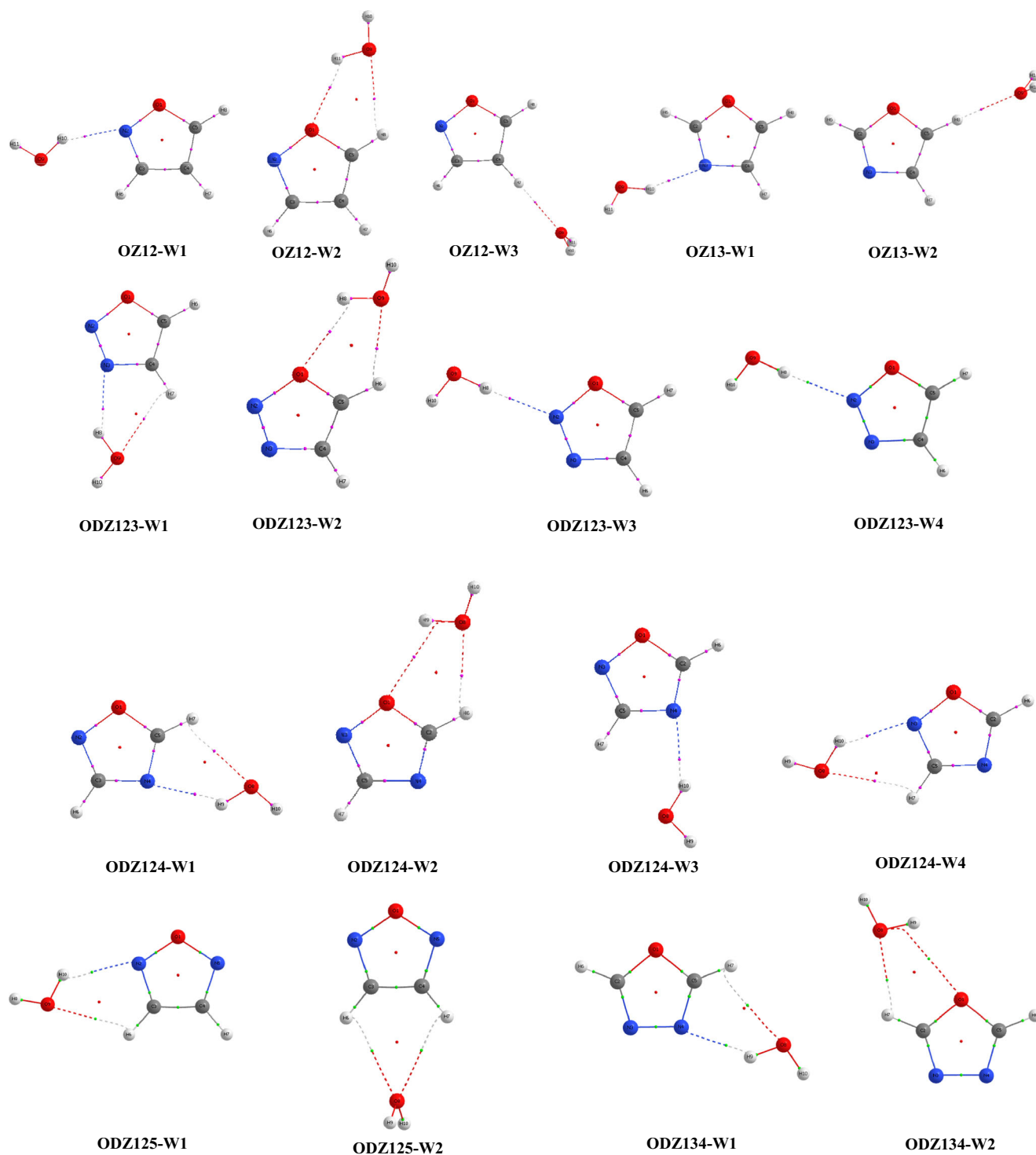


Fig. 3 Molecular graphs of complexes of five-membered heterocycles with water at the MP2/aug-cc-pVDZ level. Small green balls indicate bond critical points and small red balls indicate ring critical points

interactions) being positive and the CT_{H-W} values for complexes OZ12-W2, ODZ123-W2, ODZ124-W2, and ODZ134-W2 (with ${}_{w}O-H\cdots O$ as main stabilizing interactions along with weak $C-H\cdots O_w$ interactions) being negative indicate that N of ring act as better HB acceptor as compared to O of ring.

The largest charge transfer with CT_{H-W} value of +0.011 and -0.011 is reflected for OZ13-W1 and OTZ1235-W3. Both the complexes are bonded through single HB. The former has charge transfer associated with in $n_{N3} \rightarrow \sigma^*_{O-H}$, while the latter reflects $n_{O7} \rightarrow \sigma^*_{C4-H6}$. Both the charge transfers are in opposite directions and clearly indicate that charge transfer

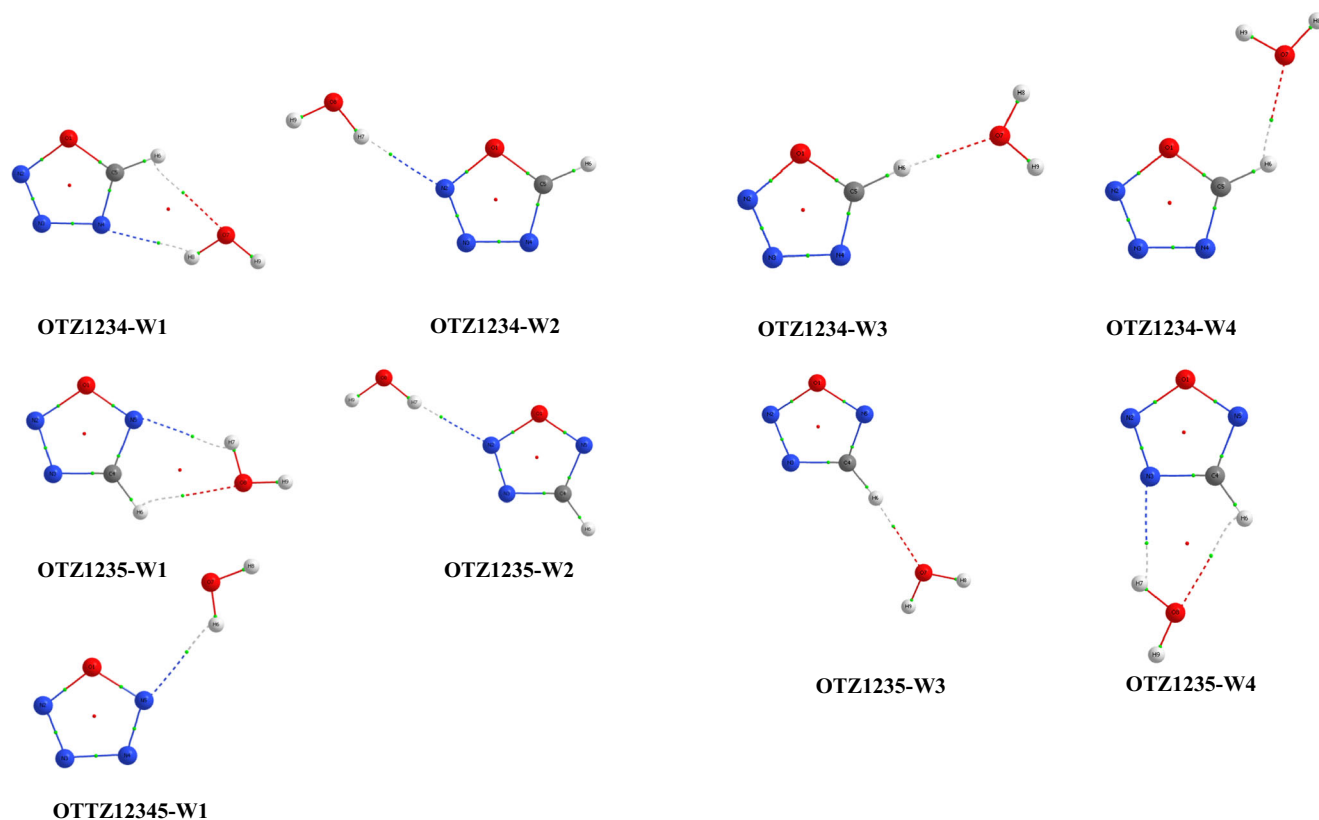


Fig. 3 continued.

away from heterocyclic ring contributes more towards stability.

Analysis based on second-order delocalization energy [$E^{(2)}$]

The information about the electron delocalization is reflected by the $E^{(2)}$ values, second-order perturbation energies associated with the orbital interaction. The complexes OZ13-W1, OZ12-W1, ODZ123-W3, ODZ124-W3, OTZ1234-W2, OTZ1235-W2, and OTTZ12345-W1 possess $n_N \rightarrow \sigma_{O-H}^*$ charge transfer interactions only. The order of $E^{(2)}$ values in the complexes OZ13-W1 (8.38 kcal/mol) > OZ12-W1 (6.01 kcal/mol) > ODZ124-W3 (5.43 kcal/mol) > ODZ123-W3 (5.38 kcal/mol) > OTZ1234-W2 (4.11 kcal/mol) > OTZ1235-W2 (4.03 kcal/mol) > OTTZ12345-W1 (1.36 kcal/mol) again strengthens the fact that N of heterocyclic ring acts as strong HB acceptor in the order OZ > ODZ > OTZ > OTTZ and the HB acceptor ability of N decreases with increasing number of N atoms in the ring. This order matches with ΔE_{BSSSE} and charge transfer values.

Complexes OZ12-W3, OZ13-W2, ODZ123-W4, OTZ1234-W3, and OTZ1235-W3 possess $n_O \rightarrow \sigma_{C-H}^*$ charge transfer interactions only. The $E^{(2)}$ values in these complexes OTZ1234-W3 (8.37 kcal/mol), OTZ1235-W3 (7.15 kcal/mol), ODZ123-W4 (6.16 kcal/mol), OZ13-W2 (5.68 kcal/mol), and OZ12-W3 (4.82 kcal/mol) which strengthens the

fact that the C-H of heterocyclic ring act as HB donor in the order OTZ > ODZ > OZ and this ability increases with increasing number of heteroatoms in the ring. This order matches with ΔE_{BSSSE} and charge transfer values.

The $E^{(2)}$ values of orbital interaction $n_N \rightarrow \sigma_{O-H}^*$ for complexes ODZ123-W1 (4.36 kcal/mol), ODZ124-W1 (3.28 kcal/mol), ODZ124-W4 (3.61 kcal/mol), ODZ125-W1 (3.07 kcal/mol), ODZ134-W1 (5.20 kcal/mol), OTZ1234-W1 (2.28 kcal/mol), OTZ1235-W1 (1.18 kcal/mol), and OTZ1235-W4 (1.81 kcal/mol) with N of ring as HB acceptor are comparatively higher than bond orbital interaction $n_O \rightarrow \sigma_{C-H}^*$ for complexes OZ12-W2 (1.29 kcal/mol), ODZ123-W2 (0.42 kcal/mol), ODZ124-W2 (0.34 kcal/mol), and ODZ134-W2 (0.16 kcal/mol). Thus, the strength of N \cdots H HB has edge over O \cdots H because of stronger covalent component inspite of the fact that O being more electronegative than N favors stronger electrostatic interactions with HB donors. The $n_O \rightarrow \sigma_{C-H}^*$ orbital interaction in complexes OZ12-W2 (0.76 kcal/mol), ODZ123-W1 (0.38 kcal/mol), ODZ124-W1 (0.37 kcal/mol), ODZ124-W4 (0.32 kcal/mol), ODZ125-W1 (0.49 kcal/mol), ODZ125-W2 (0.29 kcal/mol), ODZ134-W1 (0.36 kcal/mol), OTZ1234-W1 (0.81 kcal/mol), OTZ1235-W1 (0.87 kcal/mol), and OTZ1235-W4 (0.82 kcal/mol) have $E^{(2)}$ values with negligible to small magnitude only as the angle at bridging hydrogen disfavors the CT.

Table 2 Second-order delocalization energies $E^{(2)}$ (in kcal/mol) associated with orbital interactions, amount of charge transfer from five-membered heterocycles to water (CT_{H-W} in e), MEP parameters V_{min} and ΔV_{min} (in kcal/mol) in complexes of five-membered heterocycles with water at L1 level

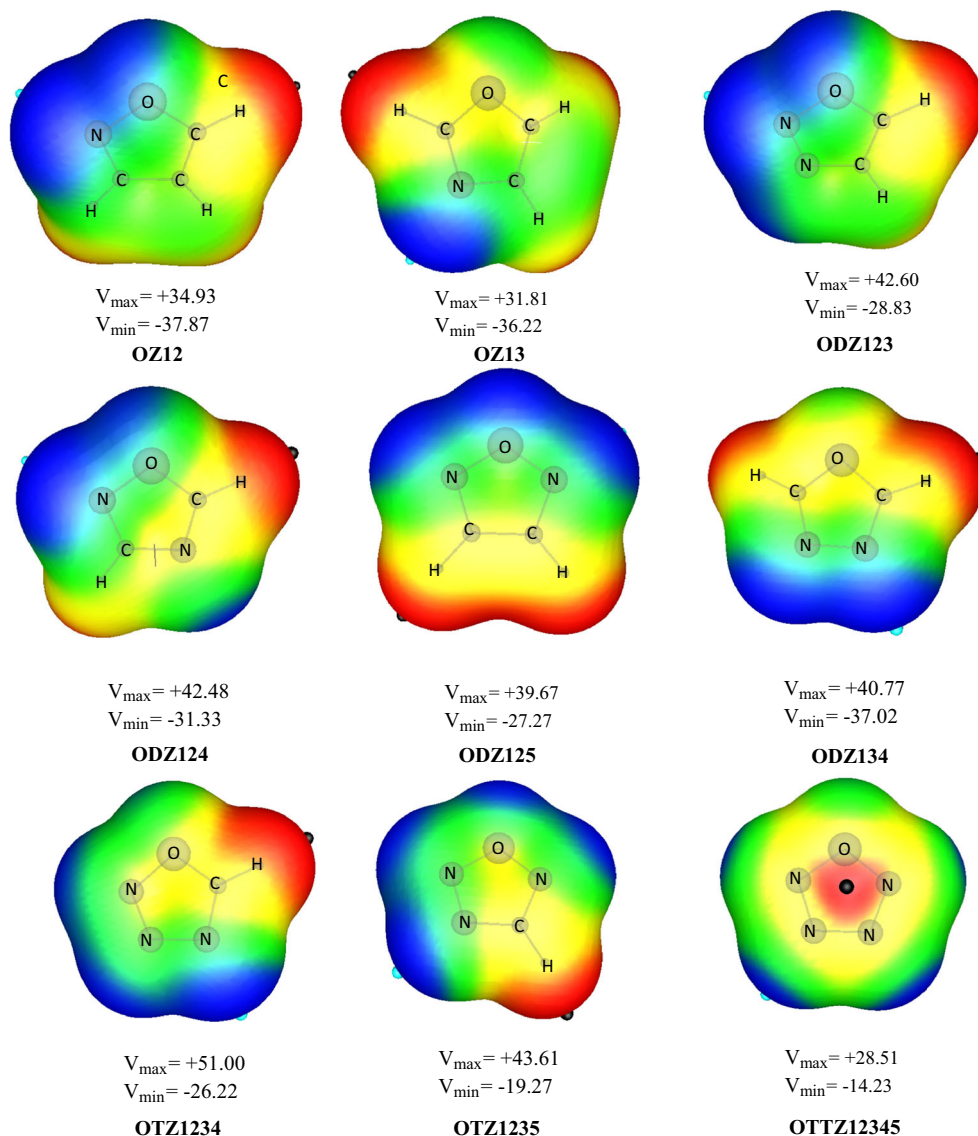
Complexes	Orbital interactions	$E^{(2)}$	CT_{H-W}	V_{min}	$^*\Delta V_{min}$
OZ12-W1	$n_{N2} \rightarrow \sigma_{H9-O10}^*$	6.01	+0.008	-21.76	+16.11
OZ12-W2	$n_{O1} \rightarrow \sigma_{H10-O9}^*$	1.29	+0.001	-35.41	+2.46
	$n_{O9} \rightarrow \sigma_{C5-H8}^*$	0.76			
OZ12-W3	$n_{O9} \rightarrow \sigma_{C4-H7}^*$	4.82	-0.008	-42.26	-4.39
OZ13-W1	$n_{N3} \rightarrow \sigma_{H9-O10}^*$	8.38	+0.011	-18.20	+18.02
OZ13-W2	$n_{O9} \rightarrow \sigma_{C5-H8}^*$	5.68	-0.008	-40.95	-4.73
ODZ123-W1	$n_{N3} \rightarrow \sigma_{H8-O9}^*$	4.36	+0.003	-25.74	+3.09
	$n_{O9} \rightarrow \sigma_{C4-H7}^*$	0.38			
ODZ123-W2	$n_{O1} \rightarrow \sigma_{H8-O9}^*$	0.42	-0.001	-28.99	-0.16
	$n_{O9} \rightarrow \sigma_{C5-H6}^*$	1.29			
ODZ123-W3	$n_{N2} \rightarrow \sigma_{H8-O9}^*$	5.38	+0.007	-20.50	+8.33
ODZ123-W4	$n_{O8} \rightarrow \sigma_{C4-H7}^*$	6.16	-0.009	-32.40	-3.57
ODZ124-W1	$n_{N4} \rightarrow \sigma_{O8-H9}^*$	3.28	+0.002	-30.08	+1.25
	$n_{O8} \rightarrow \sigma_{C5-H7}^*$	0.37			
ODZ124-W2	$n_{O1} \rightarrow \sigma_{O8-H9}^*$	0.34	-0.002	-31.93	-0.60
	$n_{O8} \rightarrow \sigma_{C5-H6}^*$	1.37			
ODZ124-W3	$n_{N4} \rightarrow \sigma_{H8-O9}^*$	5.43	+0.007	-28.23	+3.10
ODZ124-W4	$n_{N2} \rightarrow \sigma_{O8-H9}^*$	3.61	+0.004	-27.66	+3.67
	$n_{O8} \rightarrow \sigma_{C3-H7}^*$	0.32			
ODZ125-W1	$n_{N2} \rightarrow \sigma_{O8-H9}^*$	3.07	+0.002	-25.51	+1.76
	$n_{O8} \rightarrow \sigma_{C3-H6}^*$	0.49			
ODZ125-W2	$n_{O8} \rightarrow \sigma_{C3-H6}^*$	0.29	-0.003	-34.77	-7.50
	$n_{O8} \rightarrow \sigma_{C4-H7}^*$	0.26			
ODZ134-W1	$n_{N4} \rightarrow \sigma_{O8-H9}^*$	5.20	+0.005	-33.63	+3.39
	$n_{O8} \rightarrow \sigma_{C5-H7}^*$	0.36			
ODZ134-W2	$n_{O1} \rightarrow \sigma_{O8-H9}^*$	0.16	-0.004	-40.70	-3.68
	$n_{O8} \rightarrow \sigma_{C2-H7}^*$	1.78			
OTZ1234-W1	$n_{N4} \rightarrow \sigma_{O7-H8}^*$	2.28	+0.001	-23.09	+3.13
	$n_{O7} \rightarrow \sigma_{C5-H6}^*$	0.81			
OTZ1234-W2	$n_{N2} \rightarrow \sigma_{H7-O8}^*$	4.11	+0.006	-22.71	+3.51
OTZ1234-W3	$n_{O7} \rightarrow \sigma_{C5-H6}^*$	8.37	-0.012	-31.57	-5.35
OTZ1234-W4	$n_{O7} \rightarrow \sigma_{C5-H6}^*$	2.75	-0.005	-31.38	-5.16
OTZ1235-W1	$n_{N5} \rightarrow \sigma_{H7-O8}^*$	1.18	+0.001	-19.09	+0.18
	$n_{O8} \rightarrow \sigma_{C4-H6}^*$	0.87			
OTZ1235-W2	$n_{N2} \rightarrow \sigma_{H7-O8}^*$	4.03	+0.006	-16.03	+3.24
OTZ1235-W3	$n_{O7} \rightarrow \sigma_{C4-H6}^*$	7.15	-0.011	-25.37	-6.10
OTZ1235-W4	$n_{N3} \rightarrow \sigma_{H7-O8}^*$	1.81	+0.0005	-19.16	+0.11
	$n_{O8} \rightarrow \sigma_{C4-H6}^*$	0.82			
OTTZ12345-W1	$n_{N5} \rightarrow \sigma_{H6-O7}^*$	1.36	+0.002	-13.59	+0.64

Molecular electrostatic potential

MEP is useful in understanding the interactive behavior as well as determining sites for electrophilic and nucleophilic attack. Electrostatic potential is increasingly becoming a regularly used tool in the basic research of molecular behavior in the design and synthesis of potent and safer molecules of medicinal interest. The importance of electrostatic potential in the research of molecular reactivity is assumed to grow. Figures 4 and 5 depict the contour maps of MEP of heterocyclic molecules on the 0.001-au electron density isosurface

where red and blue regions indicate positive and negative MEP regions, respectively. As evident, the MEP of these monomers exhibit positive region on the outermost portion of hydrogen atom, along the C-H bond vector and large region of negative MEP can be observed on the outer surface of oxygen and nitrogen atoms. The most negative-valued points in the MEP topography usually indicated with the notation V_{min} is widely used to gauge the electron rich site of the molecule, while the most positive-valued denoted by V_{max} is used to indicate the electron-deficient site of the molecule.

Fig. 4 Molecular electrostatic potentials on the 0.001 au contour of molecular electron density of five-membered heterocycles. The black dot represents the location of V_{\max} and blue dot represents the location of V_{\min}



The electronic changes that accompany the bond formation can be clearly understood by comparing V_{\min} values of isolated heterocyclic molecules with V_{\min} values of heterocyclic molecules in the complex (designated as V'_{\min}). Hence, the electronic reorganization during the bond formation can be quantified as $\Delta V_{\min} = V'_{\min} - V_{\min}$ and these MEP parameters are summarized in Table 2. For the complexes OZ12-W1, OZ13-W1, ODZ123-W3, ODZ124-W3, OTZ1234-W2, OTZ1235-W2, and OTT12345-W1, involving single N-H \cdots O_W interaction, ΔV_{\min} is positive indicating that amount of electron density from heterocyclic ring has been transferred to water during the formation of complex. The complex OZ12-W3, OZ13-W2, ODZ123-W4, OTZ1234-W3, and OTZ1235-W3, involving single C-H \cdots O_W interaction, value of ΔV_{\min} comes out to be negative indicating the gain in electron density by heterocyclic ring at the expense of water molecule upon complexation with it. In complex ODZ125-

W2, ΔV_{\min} is more negative which indicate a greater shift of electron density towards heterocyclic ring from water. The $E^{(2)}$ and charge transfer values also corroborate the same as evident from Table 2.

Topological analysis

QTAIM specifies an atom as an open system and provides a substantial method for the study of hydrogen bonding using the electron density distribution $\rho(r)$. The critical points can be recognized in the electron density distribution where $\rho(r) = 0$ and classified according to the properties of the Hessian matrix. There are two types of topologically stable critical points in three dimensions, which are designated as (3, -1) and (3, +1) called bond critical points (bcps) and ring critical points (rcps), respectively. Figure 3 shows the molecular graphs of complexes of five-membered heterocycles with water. The

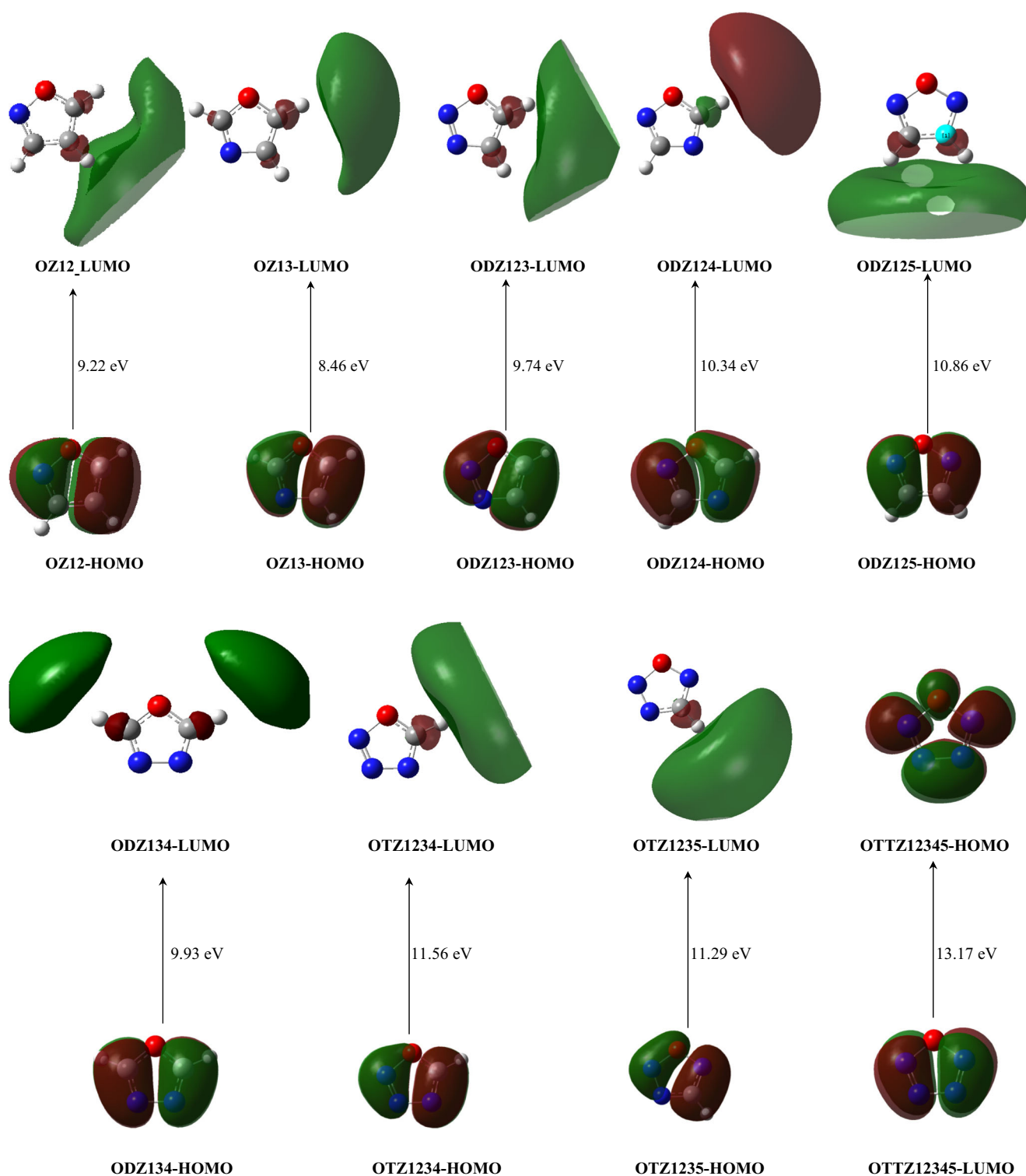


Fig. 5 HOMO-LUMO of five-membered heterocycles and their energy gap calculated at the MP2/aug-cc-pVDZ level

most studied topological properties at the critical points are the electron density (ρ_c), its Laplacian ($\nabla^2 \rho_c$), the total electron energy density (H_c), and its two components potential electron energy density (V_c) and kinetic electron energy density (G_c). The QTAIM has been broadly and successfully applied to the

study of the properties of HBs. The main topological properties at the $(3, -1)$, $(3, +1)$ critical points were computed and displayed in Table 3. The values of the Laplacian $\nabla^2 \rho_c$, the energy density H_c , and the balance between the kinetic electron energy density and the potential electron energy density

Table 3 The topological and energy properties at the bond critical points (bcps) and the ring critical points (rcps) for the complexes of five-membered heterocycles with water evaluated at MP2/aug-cc-pVDZ theoretical level using QTAIM analysis (all the values are in au)

Complexes	HB distances	CP	ρ_c	$\nabla^2_{\rho_c}$	G_c	V_c	H_c	$-G_c/V_c$	
OZ12-W1	H9...N2	(3, -1)	0.0199	0.0773	0.0166	-0.0139	0.0027	1.19	
		(3, +1) ^a	0.0527	0.4058	0.0937	-0.0860	0.0077	1.09	
OZ12-W2	H10...O1	(3, -1)	0.0131	0.0528	0.0123	-0.0113	0.0010	1.09	
		(3, -1)	0.0079	0.0345	0.0074	-0.0062	0.0012	1.19	
	H8...O9	(3, +1) ^a	0.0525	0.4032	0.0931	-0.0853	0.0078	1.09	
		(3, +1)	0.0066	0.0408	0.0080	-0.0058	0.0022	1.38	
OZ12-W3	H7...O9	(3, -1)	0.0116	0.0420	0.0095	-0.0085	0.0010	1.12	
		(3, +1) ^a	0.0527	0.4033	0.0933	-0.0858	0.0075	1.09	
OZ13-W1	H9...N3	(3, -1)	0.0231	0.0884	0.0189	-0.0156	0.0033	1.21	
		(3, +1) ^a	0.0565	0.4102	0.0977	-0.0928	0.0049	1.05	
OZ13-W2	H8...O9	(3, -1)	0.0124	0.0446	0.0101	-0.0091	0.0010	1.11	
		(3, +1) ^a	0.0566	0.4076	0.0974	-0.0929	0.0045	1.05	
ODZ123-W1	H7...O9	(3, -1)	0.0070	0.0343	0.0070	-0.0054	0.0016	1.30	
		(3, -1)	0.0183	0.0690	0.0152	-0.0131	0.0021	1.16	
	H8...N3	(3, +1) ^a	0.0540	0.4486	0.1013	-0.0905	0.0108	1.12	
		(3, +1)	0.0068	0.0399	0.0078	-0.0056	0.0022	1.39	
ODZ123-W2	H8...O1	(3, -1)	0.0097	0.0418	0.0095	-0.0086	0.0009	1.10	
		(3, -1)	0.0097	0.0399	0.0088	-0.0077	0.0011	1.14	
	H6...O9	(3, +1) ^a	0.0537	0.0418	0.1003	-0.0895	0.0108	1.12	
		(3, +1)	0.0068	0.0399	0.0081	-0.0061	0.0020	1.33	
ODZ123-W3	H8...N2	(3, -1)	0.0172	0.0651	0.0131	-0.0100	0.0031	1.31	
		(3, +1) ^a	0.0543	0.4490	0.1016	-0.0909	0.0107	1.12	
ODZ123-W4	H7...O8	(3, -1)	0.0133	0.0456	0.0105	-0.0097	0.0008	1.08	
		(3, +1) ^a	0.0538	0.4441	0.1004	-0.0898	0.0106	1.12	
ODZ124-W1	H9...N4	(3, -1)	0.0088	0.0389	0.0081	-0.0066	0.0015	1.23	
		(3, -1)	0.0163	0.0589	0.0133	-0.0119	0.0014	1.12	
	H7...O8	(3, +1) ^a	0.0596	0.4594	0.1078	-0.1008	0.0070	1.07	
		(3, +1)	0.0077	0.0460	0.0090	-0.0066	0.0024	1.36	
ODZ124-W2	H9...O1	(3, -1)	0.0095	0.0425	0.0096	-0.0085	0.0011	1.13	
		(3, -1)	0.0099	0.0405	0.0089	-0.0077	0.0012	1.16	
	H6...O8	(3, +1) ^a	0.0589	0.4510	0.1058	-0.0988	0.0070	1.07	
		(3, +1)	0.0068	0.0408	0.0082	-0.0062	0.0020	1.32	
ODZ124-W3	H8...N4	(3, -1)	0.0194	0.0735	0.0160	-0.3013	0.0023	1.17	
		(3, +1) ^a	0.0588	0.4515	0.1058	-0.0987	0.0071	1.07	
	ODZ124-W4	H9...N2	(3, -1)	0.0167	0.0632	0.0140	-0.0123	0.0017	1.14
			(3, -1)	0.0060	0.0305	0.0061	-0.0046	0.0015	1.33
ODZ125-W1	H9...N2	(3, +1) ^a	0.0590	0.4534	0.1064	-0.0994	0.0070	1.07	
		(3, +1)	0.0059	0.0344	0.0067	-0.0048	0.0019	1.40	
	H6...O8	(3, -1)	0.0141	0.0519	0.0119	-0.0108	0.0011	1.10	
		(3, -1)	0.0081	0.0356	0.0076	-0.0063	0.0013	1.21	
ODZ125-W2	H6...O8	(3, +1) ^a	0.0542	0.4533	0.1023	-0.0912	0.0111	1.12	
		(3, +1)	0.0069	0.0414	0.0082	-0.0060	0.0022	1.37	
	H7...O8	(3, -1)	0.0070	0.0302	0.0062	-0.0049	0.0013	1.27	
		(3, -1)	0.0069	0.0300	0.0063	-0.0049	0.0014	1.29	
ODZ134-W1	H9...N4	(3, +1) ^a	0.0535	0.4455	0.1005	-0.0896	0.0109	1.12	
		(3, +1)	0.0054	0.0270	0.0052	-0.0036	0.0016	1.44	
	H7...O8	(3, -1)	0.0196	0.0740	0.0163	-0.0141	0.0022	1.16	
		(3, -1)	0.0069	0.0369	0.0074	-0.0055	0.0019	1.34	
		(3, +1) ^a	0.0594	0.4463	0.1054	-0.0993	0.0061	1.06	

Table 3 (continued)

Complexes	HB distances	CP	ρ_c	$\nabla^2_{\rho_c}$	G_c	V_c	H_c	$-G_c/V_c$
ODZ134-W2	H9...O1	(3, +1)	0.0069	0.0398	0.0078	-0.0056	0.0022	1.39
		(3, -1)	0.0073	0.0353	0.0077	-0.0055	0.0022	1.40
	H7...O8	(3, -1)	0.0107	0.0425	0.0095	-0.0084	0.0011	1.13
		(3, +1) ^a	0.0590	0.4421	0.1044	-0.0983	0.0061	1.06
OTZ1234-W1	H8...N4	(3, +1)	0.0062	0.0367	0.0074	-0.0056	0.0018	1.32
		(3, -1)	0.0149	0.0551	0.0126	-0.0114	0.0012	1.10
	H6...O7	(3, -1)	0.0095	0.0426	0.0091	-0.0076	0.0015	1.20
		(3, +1) ^a	0.0576	0.4929	0.1110	-0.0987	0.0123	1.12
OTZ1234-W2	H7...N2	(3, +1)	0.0080	0.0485	0.0096	-0.0070	0.0026	1.37
		(3, -1)	0.0148	0.0559	0.0115	-0.0090	0.0025	1.28
OTZ1234-W3	H6...O7	(3, +1) ^a	0.0580	0.4953	0.1117	-0.0996	0.0121	1.12
		(3, -1)	0.0163	0.0613	0.0136	-0.0118	0.0018	1.15
OTZ1234-W4	H6...O7	(3, +1) ^a	0.0576	0.4917	0.1108	-0.0988	0.0120	1.12
		(3, -1)	0.0126	0.0481	0.0109	-0.0099	0.0019	1.10
OTZ1235-W1	H7...N5	(3, +1) ^a	0.0576	0.4914	0.1107	-0.0985	0.0122	1.12
		(3, -1)	0.0121	0.0462	0.0106	-0.0096	0.0010	1.10
	H6...O8	(3, -1)	0.0090	0.0392	0.0085	-0.7134	0.0014	1.20
		(3, +1) ^a	0.0558	0.4955	0.1102	-0.0965	0.0137	1.14
OTZ1235-W2	H7...N2	(3, +1)	0.0070	0.0423	0.0084	-0.0061	0.0023	1.38
		(3, -1)	0.0149	0.0568	0.0115	-0.0088	0.0027	1.31
	H6...O7	(3, +1) ^a	0.0563	0.4983	0.1111	-0.0976	0.0135	1.14
		(3, -1)	0.0147	0.0545	0.0121	-0.0107	0.0014	1.13
OTZ1235-W3	H6...O7	(3, +1) ^a	0.0559	0.4948	0.1102	-0.0968	0.0134	1.14
		(3, -1)	0.0139	0.0513	0.0118	-0.0107	0.0011	1.10
	H7...N3	(3, -1)	0.0139	0.0513	0.0118	-0.0107	0.0011	1.10
		(3, +1) ^a	0.0561	0.4974	0.1107	-0.9710	0.0136	1.14
OTZ1235-W4	H6...O8	(3, +1)	0.0075	0.0449	0.0088	-0.0064	0.0024	1.38
		(3, -1)	0.0093	0.0406	0.0087	-0.0073	0.0014	1.19
	H6...N5	(3, +1) ^a	0.0561	0.4974	0.1107	-0.9710	0.0136	1.14
		(3, -1)	0.0113	0.0419	0.0094	-0.0082	0.0012	1.15
OTTZ12345-W1	H6...N5	(3, +1) ^a	0.0559	0.5492	0.1186	-0.0999	0.0187	1.19
		(3, -1)	0.0113	0.0419	0.0094	-0.0082	0.0012	1.15

(3, -1) bcps, (3, +1)^a rcps in five-membered heterocycles, (3, +1) rcps in quasi five-membered ring

$-G_c/V_c$ display the nature of the interaction. $\nabla^2_{\rho_c}$ provides information about either the charge concentration ($\nabla^2_{\rho_c} < 0$) or the charge depletion ($\nabla^2_{\rho_c} > 0$) of the electron distribution. The negative $\nabla^2_{\rho_c}$ indicates that there is a shared interaction as in a covalent bond. The positive $\nabla^2_{\rho_c}$ concerns the interaction of closed-shell systems: ionic interaction, van der Waals forces or HBs. The positive $\nabla^2_{\rho_c}$ and the negative H_c mean that the interaction is partly covalent in nature. If the ratio $-G_c/V_c$ is greater than 1, then the interaction is noncovalent. If the ratio is between 0.5 and 1, then the interaction is partly covalent in nature, and when $-G_c/V_c$ is less than 0.5, the interaction is a shared covalent one.

In the present work, the wave functions of hydrogen bonded molecular geometries obtained from MP2/aug-cc-pVDZ have been employed to characterize the topological properties. As seen in Table 3, all the HBs in complexes under study satisfy Koch and Popelier's criteria with ρ_c and $\nabla^2_{\rho_c}$ of (3, -1) values well within the respective ranges 0.0060–

0.0231 au and 0.0300–0.0884 au. The ρ_c and $\nabla^2_{\rho_c}$ of (3, -1) values for the HBs involving N of ring as HB acceptor in complexes OZ13-W1, OZ12-W1, OTZ123-W3, OTZ1234-W2 ~ OTZ1235-W2 > OTTZ12345-W1 reflect N as a remarkable HB acceptor. The ρ_c and $\nabla^2_{\rho_c}$ of (3, -1) values of these complexes lie in range 0.0113–0.0231 and 0.0419–0.0884 au, respectively. The values of ρ_c and $\nabla^2_{\rho_c}$ in these complexes follow the order OZ13-W1 > OZ12-W1 > ODZ124-W3 > ODZ123-W3 > OTZ1234-W2 ~ OTZ1235-W2 > OTTZ12345-W1 which is same as stabilization energy, second-order delocalization energy, and charge transfer order. The ρ_c and $\nabla^2_{\rho_c}$ of (3, -1) values for HBs involving C-H of heterocyclic ring as HB donor lie in the ranges 0.0116–0.0163 and 0.0420–0.0613 au, respectively. The order of ρ_c and $\nabla^2_{\rho_c}$ of (3, -1) values in these complexes follow the order OTZ1234-W3 > OTZ1235-W3 > ODZ123-W4 > OZ13-W2 > OZ12-W3 which is same as stabilization energy, second-order delocalization, and charge transfer order. Complex

ODZ125-W2 shows the smallest values for the sum of ρ_c and $\nabla^2_{\rho_c}$ of (3, -1) bcps among all complexes. Though lower the value of sum of ρ_c and $\nabla^2_{\rho_c}$ of (3, -1) bcps, these values are large enough to state that HBs in ODZ125-W2 complex fulfill the Koch and Popelier criteria. The ρ and $\nabla^2_{\rho_c}$ values for C-H \cdots O_W interactions in quasi-five-membered ring structure are seen to be relatively smaller which indicates them to be weak HBs. Figure 6 depicts good correlation between the sum of ρ_c values and ΔE_{BSSE} for complexes under study. Also, there exists linear relationship between sum of $\nabla^2_{\rho_c}$ values and ΔE_{BSSE} (Fig. 7).

SAPT analysis

Decomposition of the stabilization energy by means of the SAPT method is useful for unveiling the nature of noncovalent interactions stabilizing the complexes. The method decomposes the stabilization energy arising from the intermolecular interactions into physically meaningful components like electrostatic (E_{els}), induced (E_{ind}), dispersion (E_{disp}), and exchange (E_{exch}) interactions. The SAPT components for the complexes of five-membered heterocycles with water at MP2/aug-cc-pVDZ basis set are reported in Table 4. The E_{els} , E_{ind} , and E_{disp} components are stabilizing and the E_{exch} component is destabilizing. The E_{exch} component arises mainly from the antisymmetry requirement of the wave function and the large magnitude of this component is due to the shorter binding distance. In all the complexes, E_{els} , E_{ind} , and E_{disp} contributions are 54.26–68.73, 13.79–27.05, and 14.94–20.96%, respectively, towards stabilization. The comparison highlights the importance of increasing electrostatic interactions involving permanent dipoles and interactions of the induced moments. Electrostatic component accounts for 67.11–68.73% of the total attractive interactions in complexes involving single C-H \cdots O_W interaction, while it accounts for 53.58–59.68% in complexes involving single _WO-H \cdots N interaction. The complexes involving single C-H \cdots O_W interaction have E_{els} , E_{ind} , and E_{disp} components in the range of -4.04 to -6.95, -0.83 to -1.70, and -1.15 to -1.48 kcal/mol,

respectively, while the ranges evaluated for the respective components are -2.87 to -11.89, -1.35 to -4.85, and -1.03 to -3.57 kcal/mol for the complexes involving single _WO-H \cdots N interaction. It is observed that the percentage stability due to electrostatic component is higher in complexes involving single C-H \cdots O_W interaction (67.11–68.93%) relative to that in complexes involving single _WO-H \cdots N interaction (53.38–59.68%). The percentage contribution of the E_{ind} (24.05–27.05%) and E_{disp} (14.47–19.62%) components in complexes involving single _WO-H \cdots N interaction suggests the relative importance of the E_{ind} term over the E_{disp} term, whereas the percentage contribution of the E_{ind} (13.79–16.91%) and E_{disp} (14.36–19.10%) components in complexes involving single C-H \cdots O_W interaction are nearly the same.

HOMO-LUMO analysis

In molecular interaction perspective, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) interact with each other and they are accepted as the most significant energy levels since they are considered for the determination of reactivity and nature of molecule. For heterocycles and their complexes, the HOMO and LUMO energies and their energy difference ($\Delta E = E_{\text{LUMO}} - E_{\text{HOMO}}$) are elucidated and the band gap energies are summarized in Tables 5 and 6. It is well known that the energy of HOMO characterizes the ionization potential, whereas the energy of LUMO is related to the electron affinity. The energy gap reflects the chemical reactivity of molecules. Global molecular descriptors including chemical potential (μ), hardness (η), and electrophilicity index (ω) are calculated from the optimized geometries obtained in gas phase. The chemical potential μ , which measures the escape tendency of an electron from equilibrium, is defined as $\mu = (E_{\text{HOMO}} + E_{\text{LUMO}}) / 2$. The global hardness η , that outlines important properties to measure the stability and reactivity of molecules is defined as $\eta = (E_{\text{LUMO}} - E_{\text{HOMO}}) / 2$. The electrophilicity index (ω) that outlines the capacity of a species to accept electrons is defined as $\omega = \mu^2 / 2\eta$. A hard molecule has a large energy gap and a

Fig. 6 A plot of the relation between stabilization energy (ΔE_{BSSE} in kcal/mol) and ρ_c (au) at MP2/aug-cc-pVDZ level

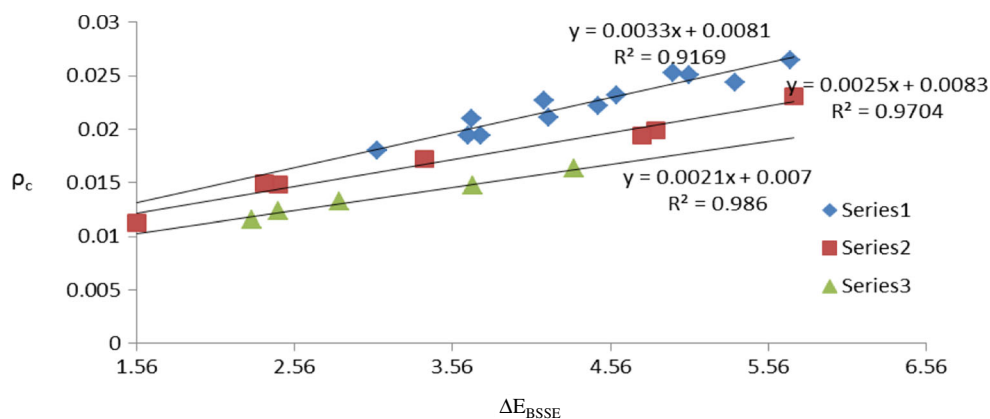
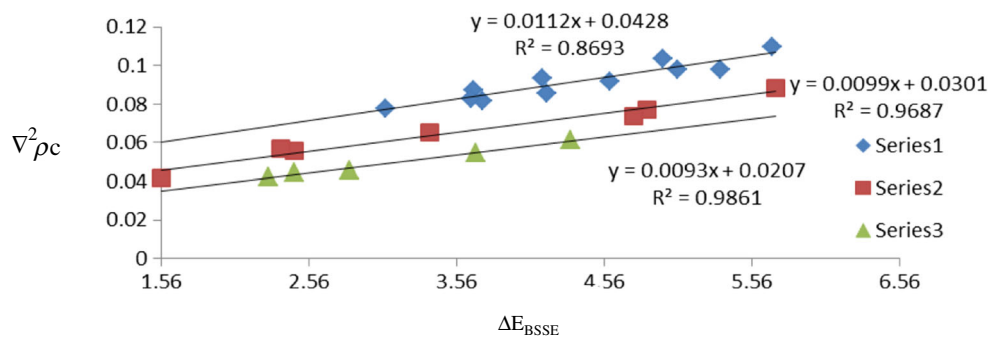


Fig. 7 A plot of the relation between stabilization energy (ΔE_{BSSE} in kcal/mol) and $\nabla^2\rho_{\text{C}}$ (au) at MP2/aug-cc-pVDZ level



soft molecule has small energy gap. The pictorial representation of HOMO and LUMO orbitals of five-membered heterocycles is shown in Fig. 5. Since energy gap between HOMO and LUMO orbitals ($\Delta E = E_{\text{LUMO}} - E_{\text{HOMO}}$) is believed to be index of kinetic stability, a large HOMO-LUMO gap implies high kinetic stability and low chemical reactivity. The order of ΔE in the selected five-membered heterocycles is as follows: OTTZ (13.17 eV) > OTZ (11.29–11.56 eV) > ODZ (9.74–10.86 eV) > OZ (8.46–9.22 eV). This order reflects that with

Table 4 SAPT components (kcal/mol) of the stabilization energy for complexes of five-membered heterocycles with water evaluated at MP2/aug-cc-pVDZ level

Complexes	E_{els}	E_{ind}	E_{disp}	E_{exc}	$\delta E_{\text{int,r}}^{\text{HF}}$	E_{int}
OZ12-W1	-11.89	-4.85	-3.57	16.36	-1.76	-5.71
OZ12-W2	-6.20	-1.59	-1.89	5.89	-0.29	-4.08
OZ12-W3	-4.04	-0.83	-1.15	4.12	-0.32	-2.22
OZ13-W1	-10.86	-4.69	-2.73	14.16	-1.12	-5.24
OZ13-W2	-4.88	-1.10	-1.20	4.60	-0.36	-2.95
ODZ123-W1	-8.48	-2.95	-2.72	9.83	-0.46	-4.78
ODZ123-W2	-6.14	-1.57	-1.80	5.52	-0.27	-4.26
ODZ123-W3	-7.50	-3.80	-2.68	11.05	-0.72	-3.65
ODZ123-W4	-5.07	-1.28	-1.23	4.99	-0.39	-2.98
ODZ124-W1	-8.98	-2.99	-2.82	10.36	-0.76	-5.19
ODZ124-W2	-6.12	-1.51	-1.71	5.34	-0.27	-4.27
ODZ124-W3	-10.60	-4.59	-2.57	14.50	-1.09	-4.35
ODZ124-W4	-7.28	-2.67	-2.21	8.70	-0.56	-4.02
ODZ125-W1	-7.58	-2.96	-2.10	9.01	-0.92	-4.55
ODZ125-W2	-6.15	-1.59	-1.98	6.98	-0.56	-3.30
ODZ134-W1	-10.11	-3.72	-2.58	11.66	-0.86	-5.61
ODZ134-W2	-6.50	-1.56	-1.88	5.88	-0.36	-4.42
OTZ1234-W1	-9.89	-3.40	-2.40	11.34	-0.80	-5.15
OTZ1234-W2	-3.50	-1.60	-1.35	8.95	-0.28	-2.22
OTZ1234-W3	-6.95	-1.70	-1.48	6.45	-0.59	-4.27
OTZ1234-W4	-6.20	-1.20	-1.38	5.50	-0.54	-3.82
OTZ1235-W1	-7.48	-2.86	-2.20	8.89	-0.72	-4.37
OTZ1235-W2	-3.20	-1.40	-1.22	8.20	-0.25	-2.13
OTZ1235-W3	-6.22	-1.53	-1.30	5.42	-0.49	-4.12
OTZ1235-W4	-7.68	-2.98	-2.38	9.16	-0.76	-4.64
OTTZ12345-W1	-2.87	-1.35	-1.03	3.86	-0.18	-1.57

an increase in number of heteroatoms, energy gap increases and stability decreases. The calculated μ , ω , and η values of five-membered heterocycles in gas phase range from -5.16 to -7.40, 3.15 to 4.15, and 4.23 to 6.59 eV, respectively. The values of μ , ω , and η for monomers decrease in the order OTTZ12345 > OTZ1234 > OTZ1235 > ODZ125 > ODZ124 > ODZ134 > ODZ123 > OZ12 > OZ13 in gas phase which show that OTTZ has the highest and OZ has the lowest escape tendency of electrons, capacity to accept electrons, and stability. In the complexes involving single $\text{wO-H}\cdots\text{N}$ interaction, μ , ω , and η values increase upon complexation except OTTZ12345-W1 which show that escape tendency of electrons, capacity to accept electrons, and stability of these complexes increase whereas these features decrease in complexes involving single $\text{C-H}\cdots\text{O}_{\text{w}}$ interaction as indicated by the decrease in the values of μ , ω , and η upon complexation.

The HOMO-LUMO gap of water is higher than that of OZ, ODZ, and OTZ but lower than that of OTTZ indicating its lesser reactivity than OZ, ODZ, and OTZ but higher reactivity than OTTZ and hence predicting its hydrogen bonding ability to be lower than OZ, ODZ, and OTZ but higher than OTTZ. The lower HB acceptor ability of OTTZ than that of water is evidenced through the ΔE_{BSSE} value of OTTZ12345-W1 predicting its HB acceptor ability to be lower than that of water.

Table 5 Quantum molecular descriptors for optimized geometries of five-membered heterocycles and water in gas phase at L2 level

Monomers	E_{HOMO}	E_{LUMO}	ΔE (au)	ΔE (eV)	η	μ	ω
OZ12	-0.369	-0.030	0.339	9.22	4.61	-5.43	3.20
OZ13	-0.345	-0.034	0.311	8.46	4.23	-5.16	3.15
ODZ123	-0.386	-0.028	0.358	9.74	4.87	-5.63	3.25
ODZ124	-0.413	-0.033	0.380	10.34	5.17	-6.07	3.48
ODZ125	-0.426	-0.027	0.399	10.86	5.43	-6.16	3.56
ODZ134	-0.396	-0.031	0.365	9.93	4.97	-5.81	3.40
OTZ1234	-0.453	-0.028	0.425	11.56	5.78	-6.54	3.69
OTZ1235	-0.447	-0.032	0.415	11.29	5.65	-6.51	3.75
OTTZ12345	-0.514	-0.030	0.484	13.17	6.59	-7.40	4.15
H ₂ O	-0.509	-0.035	0.474	12.89	6.45	-7.40	4.24

Table 6 Quantum molecular descriptors for optimized geometries of complexes of five-membered heterocycles with water in gas phase at L2 level

Complexes	E_{HOMO}	E_{LUMO}	ΔE (au)	ΔE (eV)	η	μ	ω
OZ12-W1	-0.376	-0.030	0.346	9.41	4.71	-5.52	3.23
OZ12-W2	-0.368	-0.033	0.335	9.11	4.56	-5.46	3.27
OZ12-W3	-0.355	-0.022	0.333	9.06	4.53	-5.13	2.90
OZ13-W1	-0.354	-0.032	0.322	8.76	4.38	-5.25	3.15
OZ13-W2	-0.330	-0.026	0.304	8.27	4.14	-4.84	2.83
ODZ123-W1	-0.388	-0.031	0.357	9.71	4.86	-5.70	3.34
ODZ123-W2	-0.381	-0.030	0.351	9.55	4.78	-5.59	3.27
ODZ123-W3	-0.399	-0.024	0.375	10.20	5.10	-5.75	3.24
ODZ123-W4	-0.373	-0.026	0.347	9.44	4.72	-5.43	3.12
ODZ124-W1	-0.416	-0.032	0.384	10.45	5.23	-6.10	3.56
ODZ124-W2	-0.408	-0.032	0.376	10.23	5.12	-5.99	3.50
ODZ124-W3	-0.418	-0.029	0.389	10.58	5.29	-6.08	3.49
ODZ124-W4	-0.417	-0.032	0.385	10.48	5.24	-6.11	3.56
ODZ125-W1	-0.429	-0.031	0.398	10.83	5.41	-6.26	3.62
ODZ125-W2	-0.411	-0.019	0.392	10.66	5.33	-5.85	3.21
ODZ 134-W1	-0.399	-0.032	0.367	9.99	4.99	-5.86	3.44
ODZ134-W2	-0.389	-0.024	0.365	9.93	4.96	-5.62	3.18
OTZ1234-W1	-0.452	-0.033	0.419	11.40	5.70	-6.60	3.82
OTZ1234-W2	-0.463	-0.027	0.436	11.86	5.93	-6.66	3.74
OTZ1234-W3	-0.436	-0.020	0.416	11.32	5.66	-6.20	3.40
OTZ1234-W4	-0.441	-0.024	0.417	11.35	5.67	-6.33	3.53
OTZ1235-W1	-0.443	-0.033	0.410	11.16	5.58	-6.48	3.76
OTZ1235-W2	-0.459	-0.028	0.431	11.73	5.86	-6.63	3.75
OTZ1235-W3	-0.430	-0.023	0.407	11.07	5.54	-6.16	3.42
OTZ1235-W4	-0.444	-0.032	0.412	11.21	5.60	-6.47	3.73
OTTZ12345-W1	-0.506	-0.027	0.479	13.03	6.52	-7.25	4.03

Conclusions

The hydrogen bonding ability of five-membered heterocyclic oxygen containing molecules with one, two, three, and four N atoms has been studied. The stabilization energies for all complexes under study fall in the range -1.56 to -5.72 kcal/mol. By selecting the most stable complex of each isomeric form of the five-membered heterocyclic ring system, the range of stabilization energies display is -4.17 to -5.72 kcal/mol. All these complexes have at least one HB with N of heterocyclic molecule as an HB acceptor. The study also reflects that nitrogen is a significantly better HB acceptor than oxygen. The ${}_{\text{w}}\text{O}-\text{H}\cdots\text{N}$ noncovalent distances are markedly shorter by 0.192–0.208 Å relative to the values for ${}_{\text{w}}\text{O}-\text{H}\cdots\text{O}$ noncovalent distance. The study also suggests that N at position β to O in the heterocyclic ring is a better HB acceptor relative to that in case of α -positioned N. Comparing stabilization energies associated with ODZ123-W1, ODZ124-W1, ODZ125-W1, and ODZ134-W1 highlights the important relative position of multiple heteroatoms leading to highest stabilization in ODZ134-W1. The stabilization energy indicates that in complexes which involve single HB formation with

${}_{\text{w}}\text{O}-\text{H}\cdots\text{N}$ interaction, N of heterocyclic ring acts as a strong HB acceptor in the order OZ > ODZ > OTZ > OTTZ, whereas in complexes which involve single HB formation with C-H \cdots O_w interactions, HB donor ability of C-H decreases in the order OTZ > ODZ > OZ as indicated by ΔE_{BSSE} values, NBO, AIM, and SAPT analysis. Significant frequency red-shifts for the O-H bond (-9.43 to -154.50 cm^{-1}) are predicted. The C-H stretching is found to be blue-shifted in the complexes involving C-H \cdots O_w interaction along with ${}_{\text{w}}\text{O}-\text{H}\cdots\text{N}$ interaction, whereas in the complexes involving single HB formation with C-H \cdots O_w interaction, C-H stretching is found to be red-shifted. MEP analysis indicates that in complexes involving single ${}_{\text{w}}\text{O}-\text{H}\cdots\text{N}$ interaction, ΔV_{min} is positive indicating that the amount of electron density from five-membered heterocyclic ring has been transferred to water during the formation of complex, and in complexes involving single C-H \cdots O_w interaction, the value of ΔV_{min} is negative indicating the gain in electron density by heterocyclic ring at the expense of water molecule upon complexation with it. The HOMO-LUMO analysis indicates that upon complexation, escape tendency of electron, capacity to accept electrons, and stability increase in complexes involving single ${}_{\text{w}}\text{O}-\text{H}\cdots$

N interaction, whereas these features decrease in the complexes involving single C-H \cdots O_W interaction.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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