



Counterpoise Correction on the Geometries and Vibrational Frequencies of Acetazolamide Dimers

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Acetazolamide (m.f. $C_4H_6N_4O_3S_2$) (*N*-(5-sulfamoyl-1,3,4-thiadiazol-2-yl)acetamide), is a sulfonamide derivative and carbonic anhydrase inhibitor. It is often used in the treatment of various diseases. In this study, the effect of the counterpoise correction of the basis set superposition errors (BSSE) on the geometries, interaction energies and vibrational wavenumbers of four more stable acetazolamide dimers have been analyzed at the DFT/B3LYP level of theory, using 6-31++G(d,p) basis set. The difference in the basis set superposition error corrected (-72.39 kJ/mol) and uncorrected (-77.72 kJ/mol) interaction energy of the most stable acetazolamide dimer (dimer I) indicates the magnitude of error caused due to the basis set superposition. The counterpoise correction increases the H-bond distance and decreases the wavenumbers of the intermolecular modes compared to the results of calculations without the basis set superposition error-correction.

Key Words: Acetazolamide, Basis set superposition errors, Counterpoise correction, Dimer, DFT calculations, Vibrational spectra.

INTRODUCTION

Acetazolamide (m.f. $C_4H_6N_4O_3S_2$) (*N*-(5-sulfamoyl-1,3,4-thiadiazol-2-yl)acetamide), belongs to a group of medicines called carbonic anhydrase inhibitors. It is effective in the control of fluid secretion, in the treatment of certain convulsive disorders and in the promotion of diuresis in instances of abnormal fluid retention. For these reasons it is used to treat glaucoma and to treat and to prevent acute mountain sickness (altitude sickness). It is also used as a part of some treatment plans for congestive heart failure and seizure disorders¹⁻³. Acetazolamide is used as a modulator in anticancer therapies mixing with different cytotoxic agents^{4,5} and is found to be a good choice for treatment of benign intracranial hypertension⁶.

The quantum chemical calculation of intermolecular interaction energies of the hydrogen bonded systems, is of great interest because of their chemical and biological significance. However, calculations generally use finite basis sets in the calculation of different properties, thus leading to the so-called basis set superposition error (BSSE). This error is derived from the effective larger basis set used to compute the monomers within the complexes than the one used in the isolated monomers. Thus, the energy of the complex is over estimated with respect to the isolated monomers. The effect of the BSSE, particularly in the hydrogen bonded systems are very important. Therefore, several approaches have been improved to correct this error^{7,8}, the counterpoise (CP) correction is the most popular

one⁷. In our previous work, conformational analysis on acetazolamide monomer was performed and vibrational modes and wavenumbers of the most stable conformation of acetazolamide monomer and dimer were calculated⁹. In the present work, we have extended this investigation and the BSSEs corrected structures and vibrational frequencies of four energetically favourable dimers of acetazolamide were investigated. The effect of counterpoise correction on the geometries of the acetazolamide dimers has been taken into account and the correction is applied to recalculate the binding energies of the H-bonded dimers. The aims of this study are to elucidate the BSSEs for acetazolamide dimers and calculate the effect of counterpoise correction on the interaction energy, structure and vibrational spectra of the most stable acetazolamide dimer.

COMPUTATIONAL METHOD

All of the calculations were carried out by using the Gaussian03© program suite¹⁰. Due to success in calculating the electronic structure and energy, the calculations were carried out by using the hybrid density functional theory (DFT/B3LYP) method. For the calculations of monomer, dimer forms of acetazolamide 6-31++G(d,p) basis set was used. The X-ray crystallographic results¹¹ of acetazolamide molecule were used as initial input geometrical data. The minimum energy conformers of the acetazolamide were identified by the potential energy surface scan studies by varying D1 (1S-2C-6S-9N),

D2 (4N-5C-12N-14C) and D3 (5C-12N-14C-16C) dihedral angles. The final geometrical parameters for the obtained stable conformers were determined by means of geometry optimization carried out at DFT/B3LYP/6-31G++(d,p) level of theory. Furthermore acetazolamide dimers were constructed by bringing together two identical acetazolamide monomers in possible configurations and energetically preferred conformations of dimers were investigated using the same method and the same level of theory. In this work the original counterpoise (CP) method of Boys and Bernardi⁷ is used. The effect of counterpoise correction on the geometries has been taken into account and the correction is applied to recalculate the binding energy of the H-bonded dimer.

The harmonic vibrational wavenumbers, IR intensities of the four more stable dimers were calculated by using both counterpoise corrected and uncorrected geometries. The simulated spectra were plotted using a Lorentzian band shape with a full-width at half-height (FWHM) of 14 cm⁻¹.

Fig. 4 in order to correct overestimation between unscaled and observed wavenumbers dual scaling factors were used. We scaled all the computed harmonic wavenumbers under 1800 cm⁻¹ with the scale factor 0.977 and wavenumbers greater than 1800 cm⁻¹ with the scale factor 0.955¹². The potential energy distribution (PED) of the vibrational modes of the molecules was calculated with Gar2ped program¹³ and the fundamental vibrational modes were characterized by their PED.

RESULTS AND DISCUSSION

Basis set superposition error (BSSE) correction: The binding energy is calculated by the eqn. 1, for the dimers of acetazolamide molecule.

$$\Delta E = E_{AB} - (E_A + E_B) \quad (1)$$

where E_{AB} is the total energy of the dimer and E_A , E_B are the total energies of the two monomers of acetazolamide.

The corrected binding energies ($\Delta E'$) for the dimers are calculated by the eqn. 2.

$$\Delta E' = E_{AB} - (E_A' + E_B') \quad (2)$$

The energies of the monomer constituents A and B are calculated separately within the basis set of the whole dimer. A and B is taken a 'ghost' molecule respectively and the calculated monomer energies are E_A' and E_B' .

The basis set superposition error (BSSE) for the dimer I of acetazolamide molecule is calculated as the difference between corrected ($\Delta E'$) and uncorrected (ΔE) dissociation energies.

$$BSSE = \Delta E' - \Delta E$$

The optimized values of binding energies of the acetazolamide dimers have been calculated at DFT/B3LYP/6-31++G(d,p) level of theory. Table-1 shows calculated BSSE corrected total energies of four more stable dimers (I-IV) of acetazolamide in comparison with those uncorrected energies and monomer energy. Table-1 also includes BSSE uncorrected and corrected interatomic distances and binding energies of dimers. Dimer I is the most stable structure characterized in this study and it has no imaginary frequencies at the same time. Its binding energy is -77.72 kJ/mol. The binding energy of the second most stable dimer is -65.66 kJ/mol. After BSSE correction the binding energies of acetazolamide dimers are changed properly. The BSSE values of the four more stable dimers (I-IV) are 5.33, 17.29, 7.38 and 1.15 kJ/mol, respectively and the BSSE/ $\Delta E_{\text{uncorrected}}$ ratio are 6.85, 26.33, 21.14, 4.26 %, respectively. These results it should be concluded that BSSE is large and should be considered in calculations of the binding energies.

Comparison between structural parameters of the most stable acetazolamide dimers (I-IV) before and after BSSE correction are tabulated in Table-2. The energy minimized structures of four low energy conformers (I-IV) of dimeric forms of the acetazolamide before or after applying the counterpoise correction is given Figs. 1 and 2, respectively. The inter-molecular hydrogen bond distance N12-H13...N25 was found to be 1.88901 and 1.90641 Å, before and after BSSE correction respectively at the same level of theory. Due to dimer formation the elongation of intermolecular N12-H13...N25 hydrogen bond and the contraction of intramolecular N12-H13 bond are 0.0174 and 0.00109 Å, respectively, after the BSSE correction.

The shape of the potential energy surface is not the same before or after applying the counterpoise correction. Several authors have studied the effect of basis set superposition error on the surfaces of several H-bonded systems¹⁴⁻²⁷ such as (H₂O)₂^{15,17,18,21-26}, (HF)₂^{17,20,21,26}, HF-H₂O^{14,17,19,26}, HF-HCN^{14,16,19}, HCCH-H₂O¹⁹, formamide and formic acid dimers²¹ at different

TABLE-1
(a) THE CALCULATED ENERGIES OF MONOMERIC, DIMERIC (I-IV) (b) THE COUNTERPOISE CORRECTED AND UNCORRECTED INTERATOMIC DISTANCE (Å) AND BINDING ENERGY (kJ/mol) OF DIMERS OF ACETAZOLAMIDE

(a) DFT/RB3LYP/6-31++G(d,p)				
	Uncorrected (Hartree)	Corrected (Hartree)	Relative energy differences (kJ/mol)	
Monomer		-1397.04486477		
Dimer I	-2794.11744494	-2794.11541296	0	
Dimer II	-2794.10266315	-2794.09997379	38.80	
Dimer III	-2794.10016490	-2794.10060403	45.36	
Dimer IV	-2794.10601076	-2794.09685269	30.02	
(b) DFT-RB3LYP /6-31++G(d,p)				
	BSSE uncorrected		BSSE corrected	
	R(4N-20H) (Å)	ΔE (kJ/mol)	R(4N-20H) (Å)	$\Delta(E + BSSE)$ (kJ/mol)
Dimer I	1.88908	-77.72	1.90651	-72.39
Dimer IV	6.53615	-65.66	8.36371	-48.37
Dimer II	8.47920	-34.91	8.63147	-27.53
DimerIII	6.20265	-26.96	5.63760	-28.11

TABLE-2
AN OPTIMIZED MOLECULAR STRUCTURE FOR MONOMER AND DIMER I, DIMER II, DIMER III AND DIMER IV
(UNCORRECTED AND CORRECTED) ACETAZOLAMIDE WERE OBTAINED AS PART OF THE DFT CALCULATIONS

Bond	Mono	Dimer I uncorrect	Dimer I correct	Dimer II correct	Dimer III correct	Dimer IV correct	Calc. ³²	Calc. ³³	Exp. ³⁴	Exp. ¹¹	Exp. ³⁵
S1-C2	1.7523	1.7538	1.7537	1.7532	1.7518	1.7549	1.761	1.750	1.728	1.730	1.725
S1-C5	1.7492	1.7498	1.7498	1.7472	1.7523	1.7441	1.760	1.749	1.737	1.724	1.727
C2-N3	1.2985	1.2968	1.2968	1.2969	1.2982	1.2973	1.291	1.292	1.283	1.294	1.293
C2-S6	1.8092	1.8086	1.8086	1.8084	1.8072	1.810	1.791	1.811	1.767	1.774	1.779
N3-N4	1.3667	1.3655	1.3653	1.3649	1.3663	1.3636	1.361	1.365	1.375	1.372	1.375
N4-C5	1.3115	1.322	1.322	1.312	1.3167	1.3121	1.317	1.306	1.317	1.311	1.311
C5-N12	1.3804	1.3681	1.3684	1.3817	1.3744	1.3855	1.364	1.379	1.333	1.369	1.363
S6-N9	1.662	1.6634	1.6632	1.6494	1.6649	1.6553	1.683	1.658	1.569	1.594	1.570
N9-H10	1.0165	1.0159	1.0158	1.0232	1.0163	1.0249	1.017	–	0.86	0.82	–
N9-H11	1.0169	1.0162	1.0161	1.0163	1.0169	1.0148	1.017	–	0.81	0.78	–
N12-H13	1.0127	1.0371	1.03601	1.0127	1.0248	1.0133	–	–	–	0.69	–
N12-C14	1.3862	1.3874	1.3877	1.3845	1.3858	1.3770	–	1.386	–	1.355	1.375
C14-O15	1.2228	1.2253	1.2252	1.2233	1.2250	1.2301	–	1.215	–	1.222	1.212
C14-C16	1.5108	1.5088	1.5087	1.5116	1.5097	1.5085	–	1.509	–	1.492	1.492
Angle											
C2-S1-C5	84.454	84.8783	84.8697	84.4183	84.6167	84.5443	84.69	–	85.9	85.0	85.2
S1-C2-N3	115.5648	115.7151	115.7039	115.5660	115.660	115.3862	115.01	–	115.5	116.4	116.2
C2-N3-N4	112.6178	112.2786	112.3118	112.6459	112.5661	112.6067	113.49	–	112.5	111.3	111.6
N3-N4-C5	111.8012	112.5522	112.5144	111.7938	112.0359	111.9834	112.13	–	112.1	112.1	111.8
S1-C5-N4	115.5616	114.5739	114.5985	115.5720	115.1194	115.4707	114.67	–	114	115.3	115.2
N4-C5-N12	120.3435	121.0589	121.0679	120.0359	120.9569	119.7654	122.54	120.4	123.3	119.6	121.5
C5-N12-H13	114.6399	115.9732	116.0020	114.4349	115.9251	114.2979	–	–	–	115	–
H13-N12-C14	120.6841	120.9988	120.9432	120.6216	120.5092	120.3013	–	–	–	120	–
Dihedral angle											
S1-C2-N3-N4	0.0061	-0.1875	-0.2098	-0.1489	-0.0572	-0.9839	–	–	–	–	–
S6-C2-N3-N4	178.2686	177.2392	177.3307	177.0587	177.0659	-177.1630	–	–	–	–	–
C2-N3-N4-C5	-0.1802	-0.1519	-0.1029	-0.3047	-0.2391	0.9509	–	–	–	–	–
N3-N4-C5-S1	0.2799	0.4251	0.37048	0.6337	0.4346	-0.5201	–	–	–	–	–
N3-N4-C5-N12	-179.944	-179.961	179.988	-179.7824	-179.9608	-178.6296	–	–	–	–	–
S1-C5-N12-H13	-179.993	179.0355	178.5583	-179.9412	179.2438	-172.0987	–	–	–	–	–
N4-C5-N12-H13	0.2512	-0.5394	-1.02062	0.5136	-0.3246	5.8244	–	–	–	–	–

Dimer parameters found to be altered in comparison to those of monomer, due to formation of hydrogen bonding, are marked as bold.

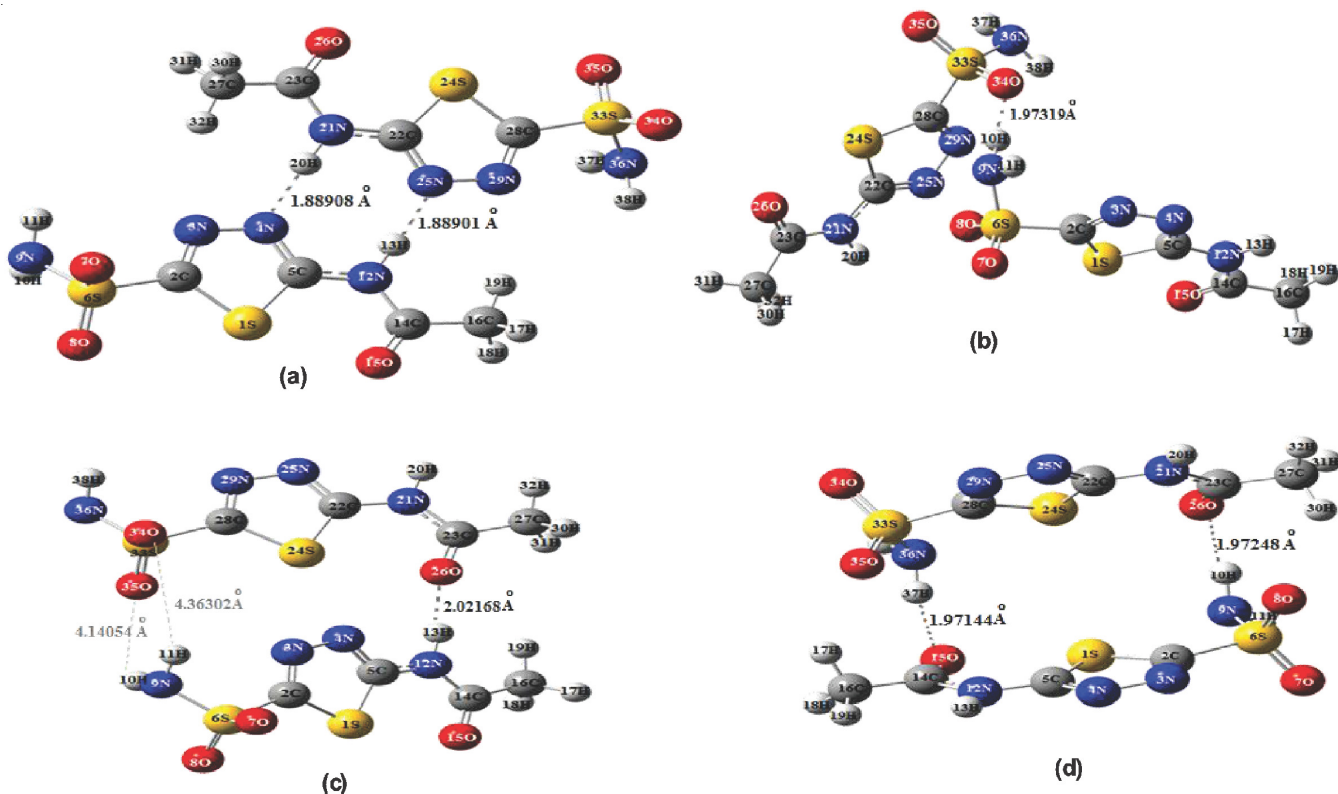


Fig. 1. Energy minimized structures of four low energy conformers (I-IV) of dimeric forms of the acetazolamide, (a), (b), (c), (d) respectively

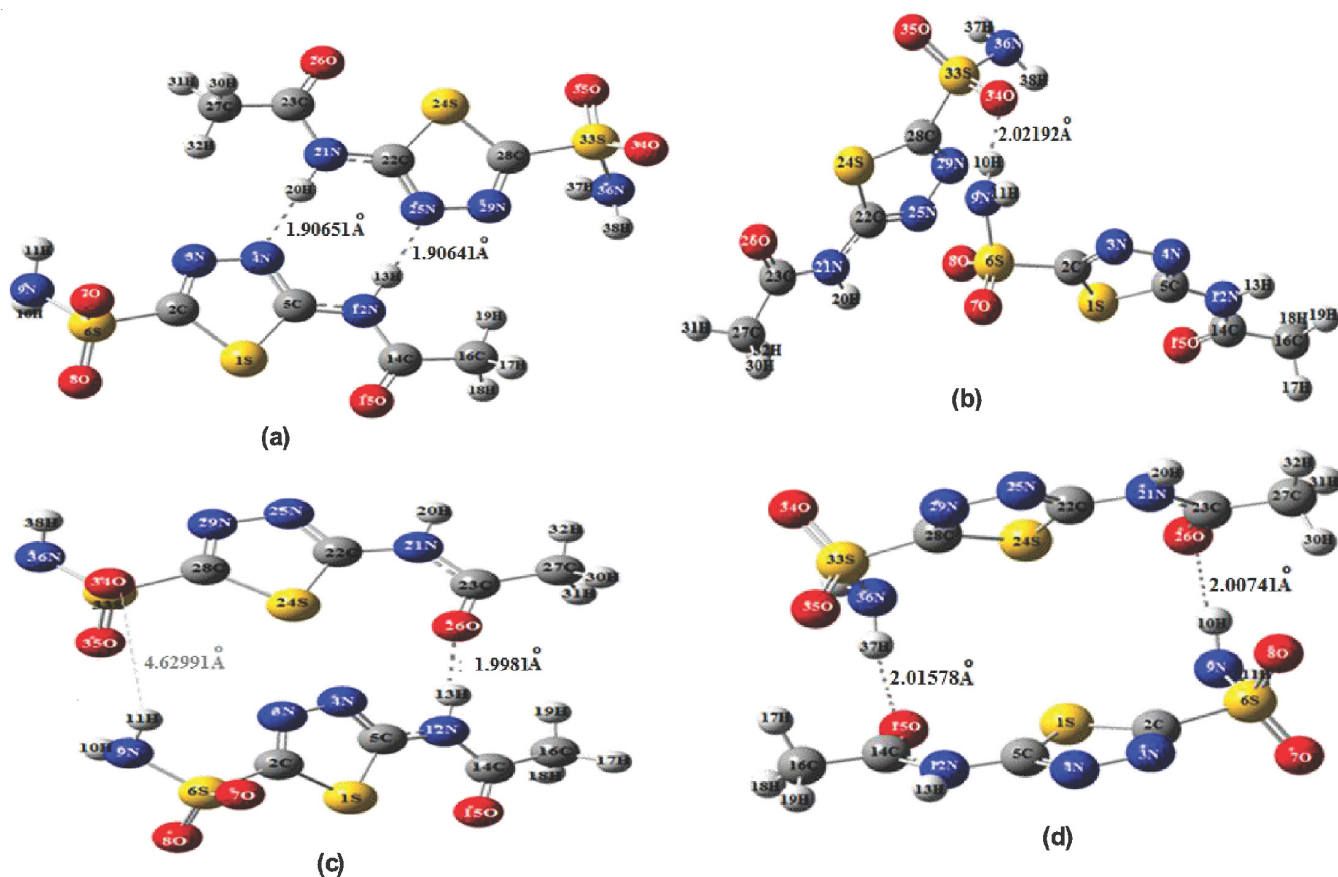


Fig. 2. Energy minimized structures of four low energy conformers (I-IV) of dimeric forms of the acetazolamide with counterpoise Correction, (a), (b), (c), (d) respectively

levels of theory. Fig. 3 shows a posteriori BSSE correction of binding energy with stretching the H-bond length (4N-20H) at the DFT/631++G(d,p) level. The uncorrected and BSSE corrected binding energies are plotted in the blue and red line, respectively. The results shows the difference between a priori and posteriori correction of the BSSE with the error in the dissociation energy is 3.5 cm^{-1} ($6051.7\text{-}6048.23 \text{ cm}^{-1} = 3.5 \text{ cm}^{-1}$) and the equilibrium distances between intermolecular H-bonding is almost 0.018 \AA .

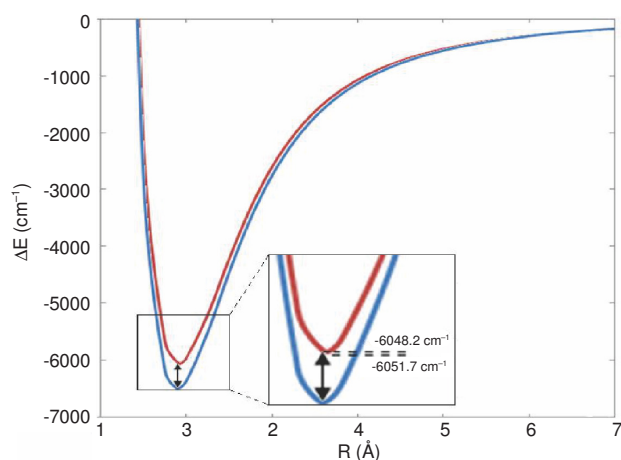


Fig. 3. Intermolecular potential energies curves of BSSE-corrected and uncorrected dimer I (ΔE , cm^{-1}) along the intermolecular coordinate R obtained with DFT method and using 6-31++G(d,p) basis set. The uncorrected and BSSE corrected binding energies are plotted in the blue and red line, respectively

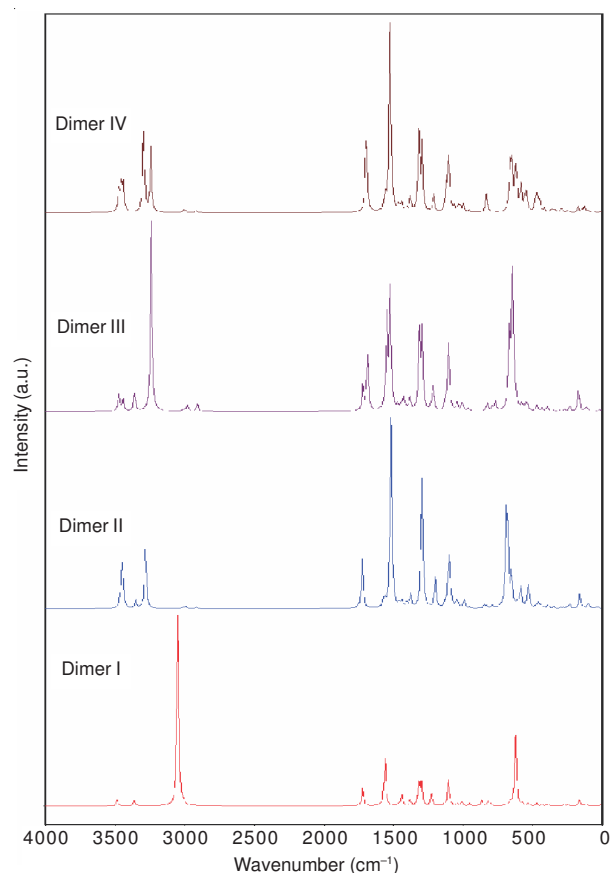


Fig. 4. Calculated IR spectra of dimers (I-IV) of acetazolamide

The calculated wavenumbers of monomer and four more stable acetazolamide dimers (dimer I-IV) are given in Table-3.

Each acetazolamide dimer has 108 vibrational normal modes from which 51 vibrations are characteristic to monomer-type vibrational motion and the several normal modes with frequency values have purely intermolecular character in Table-3. The dimer frequency shift related with several effects like, BSSE effects and intermolecular effects. BSSE influences fairly significant for the intermolecular normal modes, so removing this effect is very important.

Table-3 showed that the NH₂ asymmetric and symmetric bond stretching vibrations where the H atoms do not contribute intermolecular dimer formations, the N12-H13 and N21-H20 bond stretching vibrations located at intermolecular region and contribute intermolecular dimer form (Figs. 1 and 2).

The frequency of $\nu(\text{NH})$ stretching mode, δ_{CNH} bending mode, $\delta_{\text{CNH}} + \nu_{\text{CN}}$ bending and stretching mode and $\gamma(\text{N-H})$ out of plane mode are more impressed by the BSSE than $\nu(\text{C=N})_{\text{ring}}$, $\nu_{\text{s}}(\text{N-N})_{\text{ring}}$ and $\delta_{\text{ring}} + \nu_{\text{ring}}$ stretching vibrations.

Those normal modes which is contribute intermolecular region are altered more than the vibration motion which is located far from the intermolecular region.

However, NH stretching vibrations have anharmonic behavior²⁸⁻³⁰. Thus in harmonic approximation procedure, NH₂ stretching wavenumbers are over estimated due to neglect of anharmonicity³¹. The calculated values of $\nu(\text{NH})$ stretching wavenumbers were 3452, 3035 and 3051 cm⁻¹ for monomer, dimer I and BSSE correction for dimer I, respectively. As seen from Table-3, due to the participation of the -NH group in hydrogen bonds, $\nu(\text{NH})$ in dimer I and BSSE corrected dimer I (with two N...H bonds; Fig. 1) showed negative shifts 417 and 401 cm⁻¹ ($\Delta\nu = \nu_{\text{dimer I}} - \nu_{\text{monomer}} = -417$ cm⁻¹ and $\Delta = \nu_{\text{BSSE corrected-dimer I}} - \nu_{\text{dimer I}} = +16$ cm⁻¹), respectively. The BSSE effect is smaller but not negligible for positively shifted frequency values.

The δ_{CNH} bending and $\delta_{\text{CNH}} + \nu_{(\text{C-N})}$ mixture modes was calculated at 1519 cm⁻¹ for monomer, 1581 and 1565 cm⁻¹ for dimer I and 1578 and 1564 cm⁻¹ for BSSE corrected dimer I. We found $\Delta\nu = \nu_{\text{dimer I}} - \nu_{\text{monomer}} = +62$ and 46 cm⁻¹, $\Delta = \nu_{\text{BSSE corrected-dimer I}} - \nu_{\text{dimer I}} = -3$ and -1 cm⁻¹.

TABLE-3
CALCULATED WAVENUMBERS (cm⁻¹) AND THE TOTAL ENERGY DISTRIBUTION OF THE VIBRATIONAL MODES OF THE MONOMER AND FOUR DIMERS (BSSE CORRECTED AND UNCORRECTED) OF ACETAZOLAMIDE

Assignment	Dimer I		Dimer II		Dimer III		Dimer IV		Acetazolamide Dimer I PED (≥5%) Gar2ped	
	Monomer	BSSE correct ν_{scal}	Uncorr ν_{scal}	BSSE correct ν_{scal}	Uncorr ν_{scal}	BSSE correct ν_{scal}	Uncorr ν_{scal}	BSSE correct ν_{scal}		Uncorr ν_{scal}
$\nu_{\text{as}}(\text{NH})$	3473	3486	3484	3466	3463	3477	3474	3476	3444	$\nu_{\text{NH(asym.)}}(100)$
$\nu_{\text{s}}(\text{NH})$		3485	3484	3447	3442	3473	3464	3460	3444	$\nu_{\text{NH(sym.)}}(100)$
$\nu_{\text{as}}(\text{NH})$	3361	3365	3364	3354	3352	3363	3361	3296	3254	$\nu_{\text{NH(sym.)}}(100)$
$\nu_{\text{s}}(\text{NH})$		3365	3364	3284	3272	3360	3354	3246	3251	$\nu_{\text{NH(sym.)}}(100)$
$\nu(\text{NH})$	3452	3051	3035	3450	3450	3446	3447	3445	3443	$\nu_{\text{NH}}(93)$
$\nu_{\text{as}}(\text{CH}_3)$	3007	3017	3015	3020	3020	3017	3011	3016	3014	$\nu_{\text{CH}_3(\text{asym.})}(93)$
$\nu_{\text{s}}(\text{CH}_3)$		3015	3014	3008	3008	3003	3008	3010	3014	$\nu_{\text{CH}_3(\text{asym.})}(93)$
$\nu(\text{NH})$		3012	2995	3450	3449	3242	3351	3445	3442	$\nu_{\text{NH}}(90)$
$\nu(\text{C=O})$	1725	1722	1721	1727	1726	1720	1720	1699	1690	$\nu_{\text{CO}}(67)$
$\nu(\text{C=O})$		1721	1720	1723	1723	1685	1699	1690	1690	$\nu_{\text{CO}}(67)$
δ_{CNH}	1519	1578	1581	1518	1517	1545	1534	1524	1520	$\delta_{\text{CNH}}(44)+\delta_{\text{NH}}(16)+\gamma_{\text{NCNH}}(17)$
$\delta_{\text{CNH}}+\nu_{\text{CN}}$		1564	1565	1517	1517	1522	1524	1517	1514	$\delta_{\text{CNH}}(20)+\nu_{\text{CN}}(20)+\delta_{\text{NH}}(19)+\gamma_{\text{NCNH}}(19)$
$\delta\text{NH}_2(\text{scis.})$	1562	1553	1554	1574	1576	1561	1563	1564	1564	$\delta_{\text{NH}}(97)$
$\delta\text{NH}_2(\text{scis.})$		1553	1554	1564	1564	1560	1561	1556	1563	$\delta_{\text{NH}}(97)$
$\delta_{\text{as}}(\text{CH}_3)$	1460	1463	1463	1460	1460	1471	1461	1463	1464	$\delta_{\text{HCH}}(38)+\delta_{\text{CCH}}(38)$
$\delta_{\text{s}}(\text{CH}_3)$		1462	1462	1458	1458	1460	1460	1460	1464	$\delta_{\text{HCH}}(38)+\delta_{\text{CCH}}(38)$
$\nu_{\text{as}}(\text{C=N})_{\text{ring}}$	1442	1456	1456	1447	1447	1445	1445	1448	1449	$\nu_{\text{CN}}(85)$
$\nu_{\text{s}}(\text{C=N})_{\text{ring}}$		1456	1456	1435	1435	1445	1436	1442	1448	$\nu_{\text{CN}}(81)$
$\delta_{\text{as}}(\text{CH}_3)$	1440	1448	1449	1441	1441	1446	1446	1441	1440	$\delta_{\text{HCH}}(54)+\delta_{\text{CCH}}(36)$
$\delta_{\text{s}}(\text{CH}_3)$		1448	1448	1435	1440	1440	1441	1439	1440	$\delta_{\text{CCH}}(54)+\delta_{\text{HCH}}(36)$
$\nu_{\text{s}}(\text{C=N})_{\text{ring}}$	1409	1438	1439	1407	1406	1429	1422	1412	1407	$\nu_{\text{CN}}(60)+\delta_{\text{NH}}(6)+\gamma_{\text{NCNH}}(6)$
$\nu_{\text{s}}(\text{C=N})_{\text{ring}}$		1435	1435	1405	1405	1412	1407	1406	1407	$\nu_{\text{CN}}(74)$
$\delta_{\text{s}}(\text{CH}_3)$	1376	1379	1379	1377	1377	1386	1378	1380	1375	$\delta_{\text{CCH}}(43)+\delta_{\text{HCH}}(41)$
$\delta_{\text{s}}(\text{CH}_3)$		1379	1379	1375	1375	1377	1375	1376	1375	$\delta_{\text{CCH}}(41)+\delta_{\text{HCH}}(43)$
$\nu_{\text{as}}(\text{SO}_2)$	1312	1319	1319	1302	1302	1315	1313	1319	1300	$\nu_{\text{SO}}(89)$
$\nu_{\text{s}}(\text{SO}_2)$		1319	1319	1297	1296	1313	1310	1318	1298	$\nu_{\text{SO}}(89)$
$\gamma(\text{N-H})$	531	867	881	610	533	767	712	617	615	$\Gamma_{\text{NCNH}}(25)+\Gamma_{\text{CCNH}}(20)+\gamma_{\text{NCNH}}(21)+\gamma_{\text{CCNH}}(10)+\delta_{\text{NH}}(21)$
$\gamma(\text{N-H})$		842	864	601	525	618	618	616	614	$\Gamma_{\text{CCNH}}(26)+\gamma_{\text{NCNH}}(28)+\gamma_{\text{CCNH}}(12)+\delta_{\text{NH}}(28)$

The wavenumbers under 1800 cm⁻¹, were scaled with 0.977 and for over 1800 cm⁻¹ the scale factor 0.955 was used.

We have also indicated that the $\gamma(\text{N-H})$ out of plane modes were changed before and after BSSE correction for dimer I. Their shifted values are 14 and 22 cm^{-1} . The calculated values are 531, 881, 864, 867 and 842 cm^{-1} for monomer, dimer I and BSSE corrected dimer I. $\Delta v = v_{\text{dimer I}} - v_{\text{monomer}} = +350$ and 333 cm^{-1} , $\Delta = v_{\text{BSSE corrected-dimer I}} - v_{\text{dimer I}} = -14$ and -22 cm^{-1} .

This fundamental vibrational analysis shows that the most shifted frequencies of the monomer-type vibrations are the covalent N-H bond stretching and CNH bending vibrations (the H atom is involved in the formation of dimer I) as well as H-N out-of-plane vibrations. These shifting values of dimer I form between before and after BSSE correction are 16, 3 and 22 cm^{-1} , respectively.

Conclusion

In this paper the structures and vibrational wavenumber shifts of acetazolamide and its dimers have been studied using density functional theory. The possible dimer forms of the molecule were formed and their energetically preferred conformations were investigated using the same method and the same level of theory. The results show that the structure dimer I is the most stable conformer of the title molecule.

After BSSE correction, the binding energies of acetazolamide dimers changed properly and should be considered in calculations of the binding energies. It is known that the basis set superposition error (BSSE) effect is rather significant on the structure and energy of dimer forms, so removing this effect is very important. Therefore optimization of the dimer I was also carried out along with the counterpoise correction scheme proposed by Boys and Bernardi. The BSSE uncorrected and corrected distances between two acetazolamide units $\{R(4\text{N-20H}) (\text{\AA})\}$ and binding energy (ΔE) of acetazolamide dimer $\{\Delta E = 2 * E_{\text{monomer}} - E_{\text{dimer}}\}$ are given. The energy of dimer I is found to be 5.33 kJ/mol lower than total energy of the two monomer ($2 * E_{\text{monomer}}$) units, indicating that inter-molecular hydrogen bonding play an important role in stabilization of the molecule. The results show that the normal modes, where the vibration motion is far from the intermolecular interaction region are less altered than the normal modes which are the essential part of the intermolecular interaction region of dimer forms.

The aims of this study are to elucidate the importance of the BSSE using the counterpoise correction calculations and indicate the effect of hydrogen bonding in the formation of the dimer structures of acetazolamide.

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