DFT AND HF STUDIES OF MOLECULAR STRUCTURE, EQUILIBRIUM CONSTANT AND VIBRATIONAL FREQUENCIES FOR LACTAM - LACTIM TAUTOMERISM IN DIFFERENT SOLVENTS

[1]Saidi Mohamedi Katundu, [2]John Joseph Makangara and [3]N.Surendra babu
[1]Assistant Lecturer, [2]Senior lecturer, and [3]Associate Professor
Department of Chemistry
College of Natural& Mathematical Sciences
The University of Dodoma, Dodoma,Tanzania

***Abstract*:** The geometries of different tautomers of various ring size lactams have been studied by ab initio Hatree– Fock(HF) and Density Functional Theory (DFT) computations at B3LYP level with6-311G++(d,p) basis set in different solvents. Optimized geometries and relative energies for 12 tautomers of lactams were calculated by using HF and DFT methods with 6-3611G(d,p) basis set in different solvents. Thermodynamic properties and tautomeric equilibria between different tautomers were calculated. The results of calculations are applied to the bond lengths of β- lactam which showed a good agreement with experimentally determined data. The amino tautomers are more stable than the lactim tautomers in all studied solvents. From the equilibrium constant results, the lactam form is a more dominant tautomer for the all cases and the lactim forms are not present in detectable amounts.

kEYWORDS: **lactams tautomers, Density Functional Theory, thermodynamic properties and equilibrium constants.**

1. Introduction

Lactams are one of the fundamental functional molecules in organic chemistry [1-3]. They serve as pharmacophores in antibiotics, antipsychotics, drug candidates, and intermediates in the synthesis of dopamine receptors [4-8]. Moreover, they can be used as the monomers of versatile synthetic polymers, such as poly(1-vinylpyrrolidin-2-one) derivatives [9,10].Conventional synthetic methods for lactam include the intramolecular condensation of amino acid derivatives /under extremely high temperature conditions and the use of activating reagents, such as Grignard reagents[11] and Brønsted acids.[12]. Lactams are cyclic amides of varying ring sizes, such as alpha (three membered ring), beta (four membered ring), gamma (five membered ring) lactams, delta (six membered ring) lactams, epsilon (seven membered ring) lactams. Since the discovery of penicillin by Fleming in 1928 and its clinical introduction as an antibacterial agent in the early 1950s, βlactam antibiotics have remained the most popular drugs for treating bacterial infections. The success of penicillin led to the discovery and development of various β-lactam antibiotics: penicillins, cephalosporins, monobactams and carbapenems [13] which all contain the four membered βlactam ring. β-lactams are the most known lactam as they are a notable antibiotics; however, lactam ring derivatives exhibit additional pharmacological effects. β-Lactam antibiotics are the most important class of antibacterial agents. They irreversibly inhibit the last step of the bacterial cell wall biosynthesis mediated by the serine transpeptidase activity of the penicillin binding proteins (PBPs)[14] β-Lactams are supposed to be reactive mimics of the D-alanyl-D-alanine dipeptide substrate of PBPs. Both a molecular shape mimicking the dipeptide (i.e., a carboxylic acid located at a given distance of the lactam C=O) and an acylating ability due to an enhanced reactivity compared to a normal lactam are the basic requirements for biological activity of inhibitors.[15-17] In the present research paper, we have investigated theoretically, the optimized geometries, vibrational spectra, thermodynamic properties, dipole movements and equilibrium constants of amide-imidol tautomers of different lactams, by performing HF and DFT calculations. Literature survey reveals that to the best of our knowledge, no ab initio HF/DFT quantum chemical calculations of lactams tautomers in different basis sets have been reported so far.

1.1 Implicit Solvent Models

Many molecules do not show most of their properties in gaseous phase and are instead found in solvents. The interaction between the solvent and the solute impacts the general chemistry of the molecule being studied. The interaction can alter energy, stability, and molecular orientation. Thus properties relating to energy (i.e. vibrational frequency, spectrum, etc.) will also change. Therefore we need a way to model the chemistry of these molecules in a solvent like state. This is accomplished using implicit solvation models. These models differ from the "explicit" models which attempt to deal with the solvent as individual molecules, and instead treat the solvent as a continuous medium that acts upon the solute. This leads to a significant reduction in complexity by describing the solvent as a uniform continuum than having to calculate multiple molecular interactions. In order to perform computations in aqueous solution phase, model chemistry, Self-Consistent Reaction Field – Polarizable Continuum Model (SCRF-PCM) was used[18]. SCRF models all the solvent as a continuum reaction field with uniform dielectric constant ε. Otherwise, if the solvent is treated as separate molecules, the computational cost will grow prohibitively high. The solute is placed in a cavity within the reaction field. There are several ways to define the cavity, such as Onsager model, PCM and isodensity PCM. In PCM model, the cavity is defined as a union of a series of interlocking atomic spheres.

1.2 Polarizable Continuum Model (PCM)

One of the more modern methods to deal with implicit solvation is the Polarizable Continuum Model (PCM) [19]. This model is based upon the idea of generating multiple overlapping spheres for each of the atoms within the molecule inside of a dielectric continuum. This differs from the Onsager methodology which uses a single sphere (or an ellipse) to surround the whole molecule and thus allows for a greater amount of accuracy in determining the solute-solvent interaction energy. This method treats the continuum as a polarizable dielectric and thus is sometimes referred to as dielectric PCM (DPCM). The PCM model calculates the free energy of solvation by attempting to sum over three different terms:

$G_{solvation} = G_{electrostatic} + G_{dispersion\ -\ repulsion} + G_{cavitation}$

The cavity used in the PCM is generated by a series of overlapping spheres normally defined by the van der Waals radii of the individual atoms; however there is no set way to define the radii of the spheres and it is possible in Gaussian to customize the spherical radii. The PCM method attempts to give a complete answer to the free energy of solvation but it fails to directly calculate the energy of cavitation which is the energy defined by the surface of the van der Waals-spheres and the dispersion-repulsion energy. The free energy of solvation for any PCM calculation is primarily the electrostatic energy. Advantage of the PCM model is provision of good electrostatic energy results and the disadvantage is computationally expensive (it needs a lot of gradients and derivatives). Another disadvantage is that it does not account for the cavitation or dispersion-repulsion energies and no set rules for the radii of the spheres in the cavity.

2. Computational methods

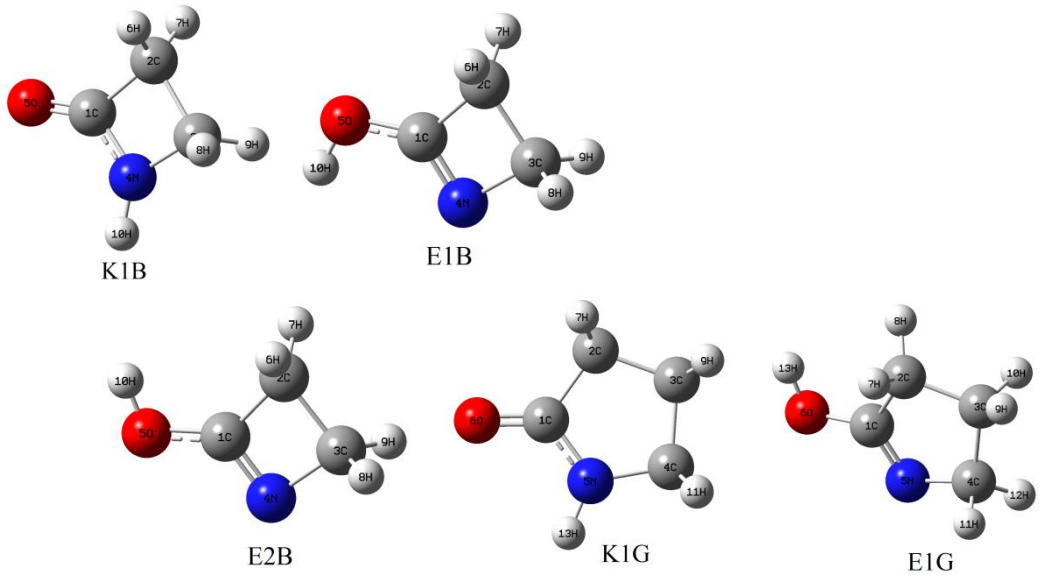
Theoretical calculations were carried out at the Hartree– Fock (HF) level of theory [20] and Density Functional Theory (DFT) [21] with Becke's three parameter hybrid exchange functional of [22], Lee-Yang-Parr correlation functionals (B3LYP) [23] and different basis sets were chosen to optimize the structures of the molecules under investigation indifferent solvents. The solvent effect was accounted for by using the polarizable continuum model (PCM) [24] which treats the solvent as a homogeneous dielectric medium. All these calculations were carried out on a desktop computer. The geometries of all tautomers investigated were completely optimized with the GAUSSIAN 09W program [25]. All tautomer's structures were drawn using Gaussview 5.08 program [26]. Positive values of all the calculated vibrational wave numbers confirmed the geometry to be located at true local minima on the potential energy surface. The stationary structures are confirmed by ascertaining that all ground states have only real frequencies. Thermodynamic quantities were obtained through standard harmonic oscillator-rigidrotator treatments.

3. Results and discussion

3.1 Geometries

All studied lactams have amide (lactam) and iminol(lactim) tautomeric forms, and iminol tautomers are further classified in to two types depending on the orientation of hydroxyl hydrogen (whether it's in the same or opposite direction with C=N bond of imidol tautomer). Considering all the possible geometric isomers totally 12 structures in each of three tautomers were considered in the present study. Four solvents were selected basing on their different dielectric constants (ε) starting from DMSO (46.7), Acetonitrile (37.5), 1,2-Dichloroethane (10.36) to Toluene (2.38). All calculations were done by using HF and DFT /B3LYP with 6-311G++(d,p) basis set.

The calculated geometric parameters of β-lactam were compared to experimental values obtained from literature. The correlation between theoretical values and experimental values are given in Table 1 below as well as in the figure 2. The calculated values are very consistent to experimental data (with exception to few cases) but they showed an interesting trend. The less polar bonds (eg C1-C2) are decreasing in lengths as moving from less polar solvents (eg. toluene) to highly polar solvents (eg. DMSO). On the other hand the polar bonds (eg. C1-O5) showed an opposite trend of increasing in their lengths moving from less polar to highly polar solvents. This indicates that, there is high interaction between solvent molecules with solute (β-lactam) bonds of similar polarities. This trend was exactly the same for the rest of lactam molecules in both HF and DFT methods. Tables 2 and 3 contain the bond lengths for all lactam tautomers in HF and DFT methods respectively.



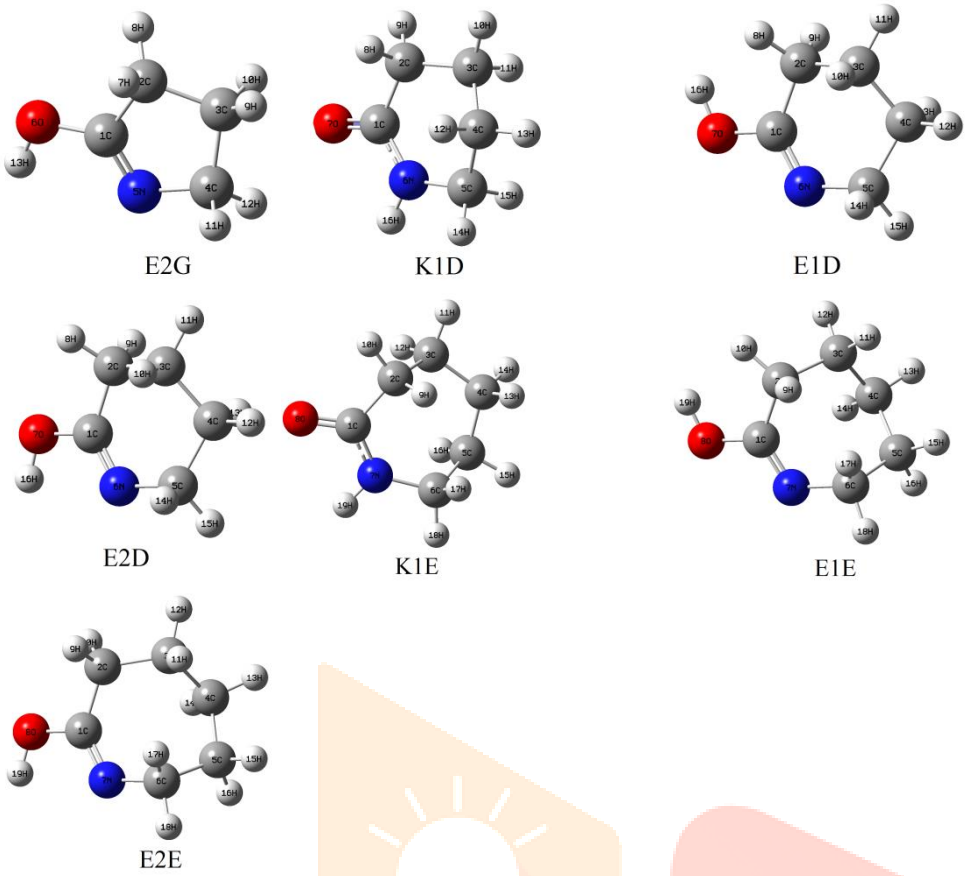


Fig.1. The optimized geometry structures of β-lactams determined by DFT method in Acetonitrile solvent at 6-311G++ (d,p) basis.

Table. 1. Theoretical and experimental geometric parameters (bond length in Å) of β-lactams in different solvents.

bond	HF/6-311G(d,p)				DFT/B3LYP//6-311G(d,p)				Experimental (Cyclobutane)
	Toluene	1,2-Dichloroethane	Aceto nitrile	DMSO	toluene	1,2-Dichloroethane	Aceto nitrile	DMSO	
C1-C2	1.5284	1.5262	1.5257	1.5256	1.5438	1.5409	1.5401	1.5400	1.53
C1-N4	1.3501	1.3440	1.3423	1.3421	1.3674	1.3613	1.3596	1.3595	1.38
C1-O5	1.1891	1.1951	1.1969	1.1970	1.2100	1.2159	1.2176	1.2178	1.20
C2-C3	1.5496	1.5494	1.5493	1.5493	1.5560	1.5561	1.5561	1.5561	1.55
C2-H6	1.0818	1.0817	1.0817	1.0817	1.0899	1.0899	1.0899	1.0899	1.10
C2-H7	1.0818	1.0817	1.0817	1.0817	1.0899	1.0899	1.0899	1.0899	1.10
C3-N4	1.4601	1.4619	1.4624	1.4624	1.4728	1.4743	1.4748	1.4748	1.48
C3-H8	1.0826	1.0819	1.0817	1.0817	1.0915	1.0908	1.0906	1.0906	1.10
C3-H9	1.0827	1.0819	1.0817	1.0817	1.0915	1.0908	1.0906	1.0906	1.10
N4-H10	0.9956	0.9961	0.9962	0.9963	1.0116	1.0121	1.0122	1.0122	0.99

Table 2. The bond lengths for HF method for different basis sets in gas phase (bond length in Å).

BOND	K1B				BOND	E1B				E2B			
	TOLUENE	DCE	ACETONITRILE	DMSO		TOLUENE	DCE	ACETONITRILE	DMSO	TOLUENE	DCE	ACETONITRILE	DMSO
Four membered ring													
C1-C2	1.5284	1.5262	1.5257	1.5256	C1-C2	1.4936	1.4934	1.4933	1.4933	1.5009	1.4995	1.499	1.4989
C1-N4	1.3501	1.344	1.3423	1.3421	C1-N4	1.2595	1.261	1.2614	1.2614	1.2573	1.2594	1.2601	1.2602
C1-O5	1.1891	1.1951	1.1969	1.197	C1-O5	1.3174	1.3165	1.3162	1.3162	1.3222	1.3201	1.3195	1.3194
C2-C3	1.5496	1.5494	1.5493	1.5493	C2-C3	1.5526	1.5516	1.5513	1.5512	1.5509	1.5501	1.5498	1.5498
C2-H6	1.0818	1.0817	1.0817	1.0817	C2-H6	1.0828	1.0825	1.0824	1.0824	1.0837	1.083	1.0828	1.0827
C2-H7	1.0818	1.0817	1.0817	1.0817	C2-H7	1.0828	1.0825	1.0824	1.0824	1.0837	1.083	1.0828	1.0828
C3-N4	1.4601	1.4619	1.4624	1.4624	C3-N4	1.4855	1.4875	1.488	1.4881	1.4824	1.4852	1.486	1.4861
C3-H8	1.0826	1.0819	1.0817	1.0817	C3-H8	1.0828	1.0826	1.0826	1.0825	1.0829	1.0827	1.0827	1.0827
C3-H9	1.0827	1.0819	1.0817	1.0817	C3-H9	1.0828	1.0826	1.0826	1.0826	1.0829	1.0827	1.0827	1.0827
N4-H10	0.9956	0.9961	0.9962	0.9963	O5-H10	0.947	0.9477	0.9478	0.9478	0.9425	0.9439	0.9443	0.9443
Five membered ring													
C1-C2	1.5173	1.5157	1.5152	1.5151	C1-C2	1.5103	1.5086	1.5081	1.508	1.5023	1.5019	1.5018	1.5017
C1-N5	1.3479	1.3412	1.3394	1.3392	C1-N5	1.2467	1.249	1.2498	1.2498	1.2496	1.2508	1.2512	1.2511
C1-O6	1.1996	1.2061	1.2079	1.2081	C1-O6	1.334	1.3327	1.3323	1.3322	1.3283	1.3281	1.3279	1.3278
C2-C3	1.5328	1.5328	1.5328	1.5328	C2-C3	1.5332	1.5332	1.5331	1.5331	1.535	1.5346	1.5346	1.5346
C2-H7	1.0868	1.0868	1.0868	1.0868	C2-H7	1.0877	1.0872	1.0871	1.0871	1.0869	1.0867	1.0867	1.0866
C2-H8	1.0816	1.0817	1.0818	1.0818	C2-H8	1.0854	1.0845	1.0843	1.0842	1.0832	1.0831	1.0831	1.0831
C3-C4	1.5368	1.5364	1.5363	1.5362	C3-C4	1.5441	1.543	1.5427	1.5427	1.5451	1.5442	1.5439	1.5439
C3-H9	1.0823	1.0819	1.0818	1.0818	C3-H9	1.083	1.0826	1.0825	1.0825	1.083	1.0827	1.0826	1.0826
C3-H10	1.0847	1.0844	1.0844	1.0844	C3-H10	1.0847	1.0845	1.0845	1.0845	1.0848	1.0846	1.0846	1.0846
C4-N5	1.4516	1.454	1.4547	1.4547	C4-N5	1.4595	1.4623	1.4631	1.4631	1.4616	1.4638	1.4643	1.4643
C4-H11	1.0873	1.0864	1.0861	1.0861	C4-H11	1.087	1.0869	1.0869	1.0869	1.0869	1.0868	1.0868	1.0868

C4-H12	1.0826	1.082	1.0818	1.0818	C4-H12	1.0834	1.0835	1.0835	1.0835	1.0835	1.0835	1.0835	1.0835
N5-H13	0.9948	0.9952	0.9954	0.9954	O6-H13	0.9415	0.9427	0.9431	0.9431	0.9458	0.9463	0.9464	0.9463
Six membered ring													
C1-C2	1.5159	1.5148	1.5145	1.5145	C1-C2	1.5123	1.5108	1.5103	1.5103	1.5049	1.5046	1.5045	1.5045
C1-N6	1.3484	1.3413	1.3393	1.3391	C1-N6	1.2432	1.2455	1.2462	1.2463	1.2471	1.248	1.2483	1.2483
C1-O7	1.2056	1.2124	1.2143	1.2145	C1-O7	1.3484	1.348	1.3477	1.3477	1.3409	1.3415	1.3416	1.3417
C2-C3	1.5277	1.5275	1.5275	1.5275	C2-C3	1.5272	1.527	1.527	1.527	1.5272	1.5272	1.5271	1.5271
C2-H8	1.0879	1.0879	1.0879	1.0879	C2-H8	1.087	1.0863	1.0861	1.0861	1.0844	1.0844	1.0844	1.0844
C2-H9	1.0827	1.0829	1.083	1.083	C2-H9	1.0887	1.0882	1.0881	1.0881	1.0876	1.0875	1.0875	1.0875
C3-C4	1.5249	1.5247	1.5246	1.5246	C3-C4	1.524	1.5238	1.5238	1.5238	1.5251	1.5249	1.5248	1.5248
C3-H10	1.085	1.0847	1.0846	1.0846	C3-H10	1.0876	1.0875	1.0874	1.0874	1.0879	1.0877	1.0877	1.0877
C3-H11	1.0883	1.088	1.0879	1.0878	C3-H11	1.0849	1.0846	1.0844	1.0844	1.0849	1.0847	1.0846	1.0846
C4-C5	1.5213	1.5208	1.5207	1.5207	C4-C5	1.5254	1.5249	1.5247	1.5247	1.5262	1.5257	1.5256	1.5255
C4-H12	1.0878	1.0877	1.0877	1.0877	C4-H12	1.086	1.0858	1.0857	1.0857	1.0861	1.0858	1.0858	1.0858
C4-H13	1.0853	1.0849	1.0848	1.0848	C4-H13	1.0888	1.0887	1.0887	1.0887	1.0889	1.0887	1.0887	1.0887
C5-N6	1.4569	1.4594	1.4601	1.4601	C5-N6	1.4543	1.4569	1.4577	1.4577	1.4557	1.4581	1.4587	1.4587
C5-H14	1.0837	1.0831	1.0829	1.0829	C5-H14	1.0883	1.0882	1.0882	1.0881	1.0882	1.0881	1.088	1.088
C5-H15	1.0882	1.0872	1.087	1.0869	C5-H15	1.0844	1.0845	1.0845	1.0845	1.0845	1.0844	1.0845	1.0845
N6-H16	0.9961	0.9964	0.9965	0.9965	O7-H16	0.9412	0.9424	0.9428	0.9428	0.9457	0.946	0.9461	0.9462
Seven membered ring													
C1-C2	1.5152	1.5142	1.514	1.5139	C1-C2	1.5212	1.5195	1.519	1.5189	1.5132	1.513	1.5129	1.5129
C1-N7	1.3484	1.3423	1.3406	1.3404	C1-N7	1.2429	1.2454	1.2461	1.2462	1.2472	1.2482	1.2485	1.2485
C1-O8	1.2059	1.2122	1.214	1.2141	C1-O8	1.3514	1.3509	1.3507	1.3507	1.3441	1.3447	1.3449	1.3449
C2-C3	1.5382	1.5386	1.5387	1.5387	C2-C3	1.5379	1.5377	1.5375	1.5375	1.537	1.5372	1.5373	1.5373
C2-H9	1.088	1.0875	1.0874	1.0874	C2-H9	1.0882	1.0878	1.0877	1.0877	1.0874	1.0873	1.0873	1.0873
C2-H10	1.081	1.0811	1.0812	1.0812	C2-H10	1.0881	1.0873	1.0871	1.0871	1.085	1.0849	1.0849	1.0849
C3-C4	1.5301	1.53	1.5299	1.5299	C3-C4	1.5311	1.531	1.5309	1.5309	1.5318	1.5316	1.5316	1.5316
C3-H11	1.0858	1.0856	1.0855	1.0855	C3-H11	1.085	1.0848	1.0848	1.0848	1.0855	1.0853	1.0853	1.0852
C3-H12	1.0881	1.0882	1.0883	1.0883	C3-H12	1.0856	1.0852	1.0851	1.0851	1.0856	1.0853	1.0853	1.0852
C4-C5	1.5295	1.5294	1.5293	1.5293	C4-C5	1.5384	1.5384	1.5385	1.5385	1.5392	1.539	1.539	1.5389
C4-C13	1.0897	1.0894	1.0893	1.0893	C4-H13	1.0859	1.0857	1.0857	1.0856	1.0859	1.0858	1.0858	1.0857
C4-C14	1.0869	1.0868	1.0868	1.0868	C4-H14	1.0876	1.0876	1.0877	1.0877	1.0876	1.0877	1.0877	1.0878
C5-C6	1.5282	1.5278	1.5276	1.5276	C5-C6	1.5295	1.5293	1.5293	1.5293	1.5299	1.5297	1.5296	1.5296
C5-H15	1.0876	1.0873	1.0872	1.0871	C5-H15	1.0883	1.088	1.0879	1.0879	1.0883	1.088	1.0879	1.0879
C5-H16	1.0878	1.0878	1.0878	1.0878	C5-H16	1.0862	1.0866	1.0867	1.0867	1.0865	1.0867	1.0868	1.0868
C6-N7	1.4547	1.4572	1.4579	1.458	C6-N7	1.4517	1.4541	1.4548	1.4549	1.453	1.455	1.4555	1.4556
C6-H17	1.0875	1.0867	1.0865	1.0865	C6-H17	1.0873	1.0866	1.0864	1.0863	1.087	1.0866	1.0864	1.0864
C6-H18	1.0824	1.0818	1.0817	1.0817	C6-H18	1.0833	1.0835	1.0836	1.0836	1.0834	1.0835	1.0835	1.0835
N7-H19	0.9948	0.9952	0.9953	0.9953	O8-H19	0.9406	0.9418	0.9422	0.9423	0.9455	0.9459	0.946	0.946

Table.3.The bond lengths for lactam tautomers determined by DFT method in different solvents at 6-311G++(d,p) basis set

BOND	K1B				BOND	E1B				E2B			
	Toluene	DCE	Aceto nitrile	DMSO		Toluene	Dce	Aceto nitrile	Dmso	Toluene	DCE	Aceto nitrile	DMSO
Four membered ring													
C1-C2	1.5438	1.5409	1.5401	1.54	C1-C2	1.4967	1.4963	1.4961	1.4961	1.5048	1.5031	1.5025	1.5025
C1-N4	1.3674	1.3613	1.3596	1.3595	C1-N4	1.2836	1.2847	1.2852	1.2852	1.2816	1.2834	1.284	1.284
C1-O5	1.21	1.2159	1.2176	1.2178	C1-O5	1.3368	1.3361	1.3354	1.3354	1.3428	1.3408	1.3402	1.3401
C2-C3	1.556	1.5561	1.5561	1.5561	C2-C3	1.5605	1.5595	1.5591	1.5591	1.5589	1.5579	1.5577	1.5576
C2-H6	1.0899	1.0899	1.0899	1.0899	C2-H6	1.0912	1.091	1.0909	1.0909	1.0921	1.0914	1.0913	1.0913
C2-H7	1.0899	1.0899	1.0899	1.0899	C2-H7	1.0912	1.091	1.0909	1.0909	1.092	1.0915	1.0913	1.0913
C3-N4	1.4728	1.4743	1.4748	1.4748	C3-N4	1.5081	1.5097	1.5107	1.5108	1.5045	1.5071	1.5079	1.508
C3-H8	1.0915	1.0908	1.0906	1.0906	C3-H8	1.0911	1.0909	1.0909	1.0909	1.0913	1.0911	1.091	1.091
C3-H9	1.0915	1.0908	1.0906	1.0906	C3-H9	1.0911	1.0909	1.0909	1.0909	1.0913	1.0911	1.091	1.091
N4-H10	1.0116	1.0121	1.0122	1.0122	O5-H10	0.9697	0.9702	0.9702	0.9702	0.9641	0.9653	0.9656	0.9657
Five membered ring													
C1-C2	1.5253	1.5232	1.5226	1.5225	C1-C2	1.5164	1.5139	1.5132	1.5131	1.5067	1.5062	1.506	1.506
C1-N5	1.3581	1.3519	1.3502	1.35	C1-N5	1.267	1.2691	1.2698	1.2699	1.27	1.271	1.2713	1.2713
C1-O6	1.2229	1.2291	1.231	1.2311	C1-O6	1.3548	1.3537	1.3533	1.3532	1.3482	1.3481	1.348	1.348
C2-C3	1.5431	1.5432	1.5433	1.5433	C2-C3	1.5403	1.5402	1.5402	1.5402	1.5421	1.5418	1.5417	1.5417
C2-H7	1.092	1.0922	1.0923	1.0923	C2-H7	1.0965	1.0961	1.0959	1.0959	1.0956	1.0955	1.0955	1.0955
C2-H8	1.092	1.0922	1.0922	1.0922	C2-H8	1.0938	1.0931	1.0929	1.0928	1.0918	1.0917	1.0917	1.0917
C3-C4	1.557	1.5559	1.5556	1.5556	C3-C4	1.5542	1.5528	1.5524	1.5524	1.5551	1.5537	1.5533	1.5533
C3-H9	1.0902	1.0899	1.0898	1.0898	C3-H9	1.0908	1.0905	1.0904	1.0904	1.0908	1.0905	1.0904	1.0904
C3-H10	1.0902	1.0899	1.0898	1.0898	C3-H10	1.0925	1.0923	1.0923	1.0923	1.0925	1.0924	1.0923	1.0923
C4-N5	1.4571	1.4593	1.4599	1.46	C4-N5	1.4705	1.4735	1.4744	1.4744	1.473	1.4757	1.4764	1.4764
C4-H11	1.0936	1.0929	1.0927	1.0927	C4-H11	1.0962	1.096	1.096	1.096	1.096	1.0958	1.0958	1.0958
C4-H12	1.0936	1.0929	1.0927	1.0927	C4-H12	1.0925	1.0924	1.0924	1.0924	1.0925	1.0924	1.0924	1.0924
N5-H13	1.0096	1.0101	1.0102	1.0102	O6-H13	0.9634	0.9644	0.9647	0.9647	0.9687	0.969	0.9691	0.9691
Six membered ring													
C1-C2	1.5227	1.5213	1.5209	1.5208	C1-C2	1.5153	1.5131	1.5124	1.5123	1.507	1.5064	1.5062	1.5062
C1-N6	1.3612	1.3547	1.3528	1.3527	C1-N6	1.2621	1.2641	1.2648	1.2649	1.2663	1.267	1.2672	1.2672
C1-O7	1.229	1.2353	1.2372	1.2374	C1-O7	1.372	1.3719	1.3717	1.3717	1.3629	1.364	1.3643	1.3643
C2-C3	1.533	1.5329	1.5329	1.5329	C2-C3	1.5343	1.5341	1.534	1.534	1.5337	1.5337	1.5336	1.5336
C2-H8	1.0966	1.0966	1.0966	1.0966	C2-H8	1.0958	1.0952	1.0951	1.0951	1.0933	1.0933	1.0933	1.0933
C2-H9	1.0917	1.0919	1.092	1.092	C2-H9	1.0973	1.097	1.0969	1.0969	1.0964	1.0964	1.0964	1.0964
C3-C4	1.53	1.5297	1.5296	1.5296	C3-C4	1.5297	1.5294	1.5294	1.5294	1.5307	1.5304	1.5303	1.5303
C3-H10	1.0932	1.0929	1.0928	1.0928	C3-H10	1.0957	1.0955	1.0955	1.0955	1.096	1.0957	1.0957	1.0957
C3-H11	1.0964	1.0961	1.096	1.0959	C3-H11	1.0928	1.0925	1.0924	1.0924	1.0928	1.0926	1.0925	1.0925
C4-C5	1.526	1.5253	1.5252	1.5251	C4-C5	1.5319	1.5311	1.5308	1.5308	1.5324	1.5317	1.5315	1.5315
C4-H12	1.0959	1.0958	1.0958	1.0958	C4-H12	1.0939	1.0937	1.0937	1.0936	1.094	1.0938	1.0937	1.0937
C4-H13	1.0932	1.0929	1.0928	1.0928	C4-H13	1.0967	1.0966	1.0965	1.0965	1.0967	1.0966	1.0965	1.0965
C5-N6	1.467	1.4692	1.4699	1.4699	C5-N6	1.4633	1.4662	1.4671	1.4671	1.465	1.4676	1.4683	1.4684
C5-H14	1.0929	1.0923	1.0921	1.0921	C5-H14	1.0978	1.0977	1.0977	1.0976	1.0978	1.0976	1.0975	1.0975
C5-H15	1.0979	1.0969	1.0966	1.0966	C5-H15	1.094	1.0939	1.0939	1.0939	1.0939	1.0938	1.0938	1.0938
N6-H16	1.0116	1.012	1.0121	1.0121	O7-H16	0.9637	0.9646	0.9649	0.9649	0.9693	0.9695	0.9695	0.9695
Seven membered ring													

C1-C2	1.5217	1.5202	1.5198	1.5197	C1-C2	1.5194	1.5172	1.5164	1.5194	1.5155	1.515	1.5149	1.5148
C1-N7	1.3615	1.3557	1.354	1.3538	C1-N7	1.2656	1.2678	1.2685	1.2656	1.2663	1.2671	1.2673	1.2673
C1-O8	1.2296	1.2355	1.2373	1.2374	C1-O8	1.3685	1.3679	1.3676	1.3685	1.3668	1.3678	1.368	1.3681
C2-C3	1.5431	1.5437	1.5438	1.5438	C2-C3	1.5614	1.5612	1.561	1.5614	1.5434	1.5436	1.5438	1.5438
C2-H9	1.0972	1.0968	1.0967	1.0967	C2-H9	1.0943	1.0941	1.094	1.0943	1.0963	1.0962	1.0962	1.0962
C2-H10	1.0898	1.09	1.09	1.09	C2-H10	1.0931	1.0923	1.092	1.0931	1.094	1.0939	1.0939	1.0939
C3-C4	1.5346	1.5344	1.5344	1.5344	C3-C4	1.5376	1.5373	1.5372	1.5376	1.5364	1.5362	1.5362	1.5362
C3-H11	1.0942	1.094	1.094	1.094	C3-H11	1.0944	1.0941	1.094	1.0944	1.094	1.0938	1.0938	1.0937
C3-H12	1.0961	1.0962	1.0962	1.0962	C3-H12	1.0933	1.093	1.0929	1.0933	1.0936	1.0933	1.0933	1.0933
C4-C5	1.5335	1.5334	1.5334	1.5334	C4-C5	1.5375	1.5375	1.5376	1.5375	1.5445	1.5444	1.5443	1.5443
C4-C13	1.098	1.0977	1.0977	1.0976	C4-H13	1.0946	1.0944	1.0944	1.0946	1.0939	1.0938	1.0937	1.0937
C4-C14	1.095	1.0949	1.0949	1.0949	C4-H14	1.0946	1.0948	1.095	1.0946	1.0956	1.0957	1.0957	1.0957
C5-C6	1.534	1.5334	1.5332	1.5332	C5-C6	1.5432	1.5432	1.5434	1.5432	1.5362	1.5359	1.5358	1.5358
C5-H15	1.0956	1.0953	1.0952	1.0952	C5-H15	1.0959	1.0957	1.0955	1.0959	1.0961	1.0959	1.0958	1.0958
C5-H16	1.096	1.096	1.096	1.096	C5-H16	1.0944	1.0946	1.0947	1.0944	1.0944	1.0946	1.0946	1.0947
C6-N7	1.4638	1.4663	1.4669	1.467	C6-N7	1.4607	1.4633	1.464	1.4607	1.4621	1.4642	1.4649	1.4649
C6-H17	1.097	1.0962	1.096	1.096	C6-H17	1.0994	1.0985	1.0982	1.0994	1.0967	1.0962	1.0961	1.096
C6-H18	1.0912	1.0906	1.0904	1.0904	C6-H18	1.0921	1.0922	1.0922	1.0921	1.0926	1.0926	1.0926	1.0926
N7-H19	1.0104	1.0108	1.0109	1.0109	O8-H19	0.9629	0.9639	0.9642	0.9629	0.9691	0.9694	0.9694	0.9694

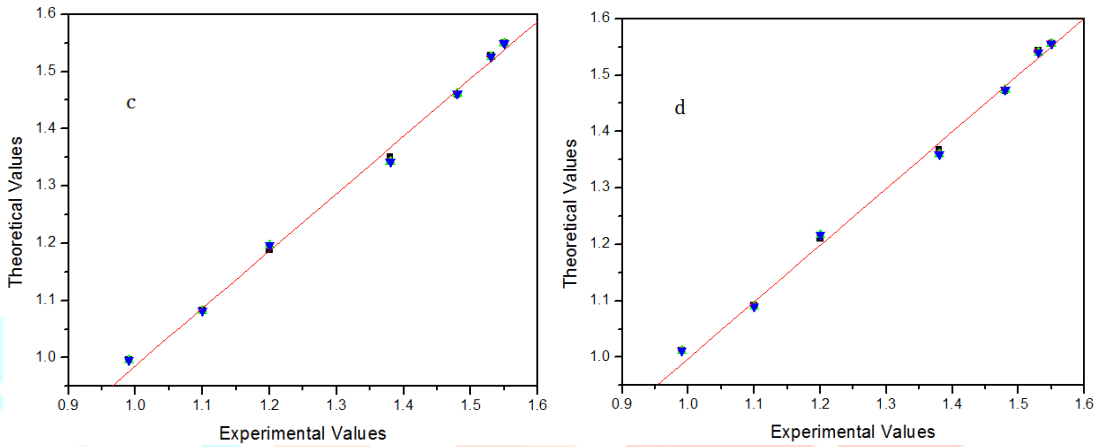


Fig.2. The calculated bond lengths vs experimental bond lengths in different solvents by HF (c) and DFT (d) methods for β lactam.

3.2 Relative Stabilities

The most stable tautomer is considered as reference to obtain the relative energetic values of the other tautomers as it was done in different solvent phase. The lactam form of all lactams had the lowest energy values (most stable in each lactam). Only β lactam showed a peculiar trend of having E1 tautomer more stable than E2 tautomer in all four solvents. The rest lactam molecules had their E2 tautomers more stable (less energy values than) than E1 tautomers. The reason behind this observation is that after optimization of molecules, E1 tautomer of β lactam had its hydrogen atom oriented on the same side with C=N double bond of the ring. But other lactams had their E1 tautomers having hydrogen atom on the opposite side to C=N bond. Therefore, there is a possibility of forming intramolecular H-bonding in E1 tautomer of β lactam and E2 tautomers of γ, δ and ε lactams. The intramolecular hydrogen bond increase stability of these molecules. The overall order of relative stabilities for all tautomers in solvent phases with respect to stable tautomer is the same as in gas phase and given as: K1E > E2E > E1E > K1D > E2D > E1D > K1G > E2G > E1G > K1B > E1B > E2B. The total and relative energies (Kcal/mol) at HF and DFT in different solvents of 12 tautomers are presented in Table below.

Table 4. The energies of tautomers (a.u) at HF and DFT/B3LYP with different basis sets and the relative energies compared to the most stable tautomer. The relative energies in brackets in kcal mol^{-1} (in brackets Kcal/mole).

MOL	HF				DFT			
	DMSO	ACETONITRILE	DICHLOROETHANE	TOLUENE	DMSO	ACETONITRILE	DICHLOROETHANE	TOLUENE
K1B	-245.891665 (0.000)	-245.890334 (0.000)	-245.891796 (0.000)	-245.885435 (0.000)	-247.375042 (0.000)	-247.374923 (0.000)	-247.373722 (0.000)	-247.369344 (0.000)
E1B	-245.859506 (20.18)	-245.858563 (20.96)	-245.859599 (20.20)	-245.855089 (19.04)	-247.342474 (20.44)	-247.342387 (20.42)	-247.341514 (20.21)	-247.338304 (19.48)
E2B	-245.857366 (21.52)	-245.855613 (21.79)	-245.857542 (21.49)	-245.849583 (22.50)	-247.340687 (21.56)	-247.340526 (21.58)	-247.338922 (21.84)	-247.333416 (22.54)
K1G	-284.970367 (0.000)	-284.968953 (0.000)	-284.970507 (0.000)	-284.963807 (0.000)	-286.729457 (0.000)	-286.729327 (0.000)	-286.728016 (0.000)	-286.723277 (0.000)
E1G	-284.939116 (19.61)	-284.937380 (19.81)	-284.939291 (19.59)	-284.931449 (20.30)	-286.700387 (18.24)	-286.700230 (18.26)	-286.698668 (18.42)	-286.693368 (18.77)
E2G	-284.942981 (17.18)	-284.942157 (16.81)	-284.943063 (17.22)	-284.939148 (15.47)	-286.703731 (16.14)	-286.703657 (16.11)	-286.702912 (15.75)	-286.700201 (14.48)
K1D	-324.015879 (0.000)	-324.014456 (0.000)	-324.016020 (0.000)	-324.009305 (0.000)	-326.056984 (0.000)	-326.056853 (0.000)	-326.055539 (0.000)	-326.050824 (0.000)
E1D	-323.985052 (19.34)	-323.983328 (19.53)	-323.985225 (19.32)	-323.977441 (19.99)	-326.027744 (18.35)	-326.027588 (18.36)	-326.026035 (18.51)	-326.020770 (18.86)
E2D	-323.990455 (15.95)	-323.989701 (15.53)	-323.990530 (16.00)	-323.986969 (14.02)	-326.032498 (15.36)	-326.032430 (15.33)	-326.031748 (14.93)	-326.029283 (13.52)
K1E	-363.055075 (0.000)	-363.053689 (0.000)	-363.055213 (0.000)	-363.048695 (0.000)	-365.377600 (0.000)	-365.377472 (0.000)	-365.376188 (0.000)	-365.371606 (0.000)
E1E	-363.015660 (24.73)	-363.013874 (24.98)	-363.015840 (24.71)	-363.007895 (25.60)	-365.333257 (27.82)	-365.340152 (23.42)	-365.338555 (23.61)	-365.333257 (24.06)

E2E	-363.021678 (20.96)	-363.020915 (20.57)	-363.021754 (21.00)	-363.018202 (19.13)	-365.345783 (19.96)	-365.345715 (19.93)	-365.345027 (19.55)	-365.342593 (18.21)

3.3 Themodynamic properties

The change in enthalpy (ΔH) and change in Gibbs free energy (ΔG) have positive values in all equilibrium equations except E1G-E2G, E1D-E2D and E1E-E2E in all solvents and both HF and DFT methods. Change in entropy (ΔS) values were negative except for E1B-E2B, K1G-E1G, K1E-E1E and K1E-E2E equilibria in all solvents and both HF and DFT methods. The positive values of ΔH and ΔG indicated endothermic processes and non-spontaneous equilibria while the negative values of ΔH and ΔG indicated exothermic and spontaneous processes.

Table 5. The enthalpy (ΔH),Gibbs free energy(ΔG) and entropy(ΔS) in kcal/molK, for the tautomers at HF and DFT/B3LYP with different basis sets in gas phase.

HF method												
EQUILIBRIUM	**DMSO**			**ACETONITRILE**			**DCE**			**TOLUENE**		
	ΔH	**ΔG**	ΔS	**ΔH**	**ΔG**	**ΔS**	**ΔH**	**ΔG**	**ΔS**	**ΔH**	**ΔG**	**ΔS**
K1B ⇌ E1B	20.22	20.61	-1.29	19.99	20.40	-1.37	20.25	20.63	-1.28	19.13	19.64	-1.71
K1B ⇌ E2B	21.56	21.85	-0.97	21.82	22.12	-1.01	21.53	21.82	-0.97	22.51	22.85	-1.17
E1B ⇌ E2B	1.33	1.24	0.32	1.83	1.72	0.36	1.28	1.19	0.31	3.37	3.21	0.54
K1G ⇌ E1G	19.50	19.46	0.15	19.69	19.65	0.15	19.48	19.44	0.15	20.13	20.05	0.27
K1G ⇌ E2G	17.08	17.11	-0.08	16.72	16.75	-0.10	17.12	17.14	-0.07	15.42	15.47	-0.18
E1G ⇌ E2G	-2.42	-2.35	-0.22	-2.97	-2.90	-0.25	-2.36	-2.30	-0.22	-4.71	-4.58	-0.46
K1D ⇌ E1D	19.03	19.12	-0.30	19.21	19.29	-0.27	19.01	19.10	-0.30	19.64	19.70	-0.23
K1D ⇌ E2D	15.68	15.91	-0.76	15.28	15.51	-0.79	15.72	15.95	-0.75	13.81	14.09	-0.95
E1D ⇌ E2D	-3.35	-3.21	-0.46	-3.94	-3.78	-0.52	-3.29	-3.16	-0.46	-5.83	-5.61	-0.72
K1E ⇌ E1E	24.59	24.45	0.45	24.81	24.66	0.51	24.57	24.44	0.44	25.37	25.20	0.57
K1E ⇌ E2E	20.83	20.79	0.14	20.46	20.44	0.07	20.87	20.83	0.14	19.09	19.14	-0.18
E1E ⇌ E2E	-3.76	-3.66	-0.32	-4.35	-4.22	-0.44	-3.70	-3.61	-0.30	-6.29	-6.06	-0.75
DFT method												
K1B ⇌ E1B	20.29	20.51	-0.763	20.27	20.49	-0.768	20.07	20.31	-0.824	19.37	19.68	-1.032
K1B ⇌ E2B	21.41	21.53	-0.419	21.44	21.56	-0.422	21.69	21.82	-0.444	22.38	22.53	-0.511
E1B ⇌ E2B	1.12	1.02	0.344	1.17	1.07	0.346	1.62	1.50	0.38	3.01	2.85	0.521
K1G ⇌ E1G	18.36	17.57	2.65	18.38	17.59	2.645	18.53	17.75	2.611	18.84	18.07	2.604
K1G ⇌ E2G	16.27	15.55	2.428	16.24	15.52	2.424	15.90	15.19	2.377	14.68	14.02	2.206
E1G ⇌ E2G	-2.09	-2.02	-0.222	-2.14	-2.07	-0.221	-2.63	-2.56	-0.234	-4.17	-4.05	-0.398
K1D ⇌ E1D	17.83	17.85	-0.073	17.85	17.87	-0.072	17.99	18.01	-0.061	18.31	18.33	-0.05
K1D ⇌ E2D	14.86	15.01	-0.48	14.83	14.97	-0.483	14.45	14.60	-0.511	13.10	13.30	-0.668
E1D ⇌ E2D	-2.97	-2.85	-0.407	-3.02	-2.90	-0.411	-3.55	-3.41	-0.45	-5.22	-5.03	-0.618
K1E ⇌ E1E	27.56	27.11	1.504	23.12	22.79	1.121	23.31	22.97	1.166	23.75	23.36	1.297
K1E ⇌ E2E	19.64	19.52	0.425	19.61	19.48	0.424	19.25	19.13	0.398	17.96	17.90	0.217
E1E ⇌ E2E	-7.91	-7.59	-1.079	-3.51	-3.30	-0.697	-4.06	-3.84	-0.768	-5.78	-5.46	-1.08

3.4 Tautomeric equilibria

The calculated tautomeric equilibrium constants at HF and DFT method with different basis sets are listed in Table 6. The tautomeric equilibrium between tautomers a and b is described as

$$a \overset{K_T}{\leftrightarrow} b \quad (1)$$

Equilibrium constants and the pKT values of the studied molecules were calculated by means of the following equations:

$$K_T = e^{-(\Delta G/RT)} \quad (2)$$

$$pK_T = \Delta G / 2.303RT \quad (3)$$

Where K_T is the tautomeric equilibrium constant between the tautomers, the gas constant R is 1.987×10^{-3} kcal/mol; and the temperature T is 298.15 K.

In order to determine the kinetic parameters of the transformations, we calculated their tautomeric equilibrium constants by using the relation equations 3 & 4 . The constants were calculated by considering that all the tautomers can be in the equilibrium with the most stable tautomer. Table 5 contains the equilibrium constants (K) and the pKT values in different basis sets. All pKT values in gas phase are presented in table. The amide form is a more dominant tautomer for the all cases and the imidol forms are not present in detectable amounts. The imidol tautomers are transformed from one form to another. The pKT were negative that determines the privileged direction of equilibrium. If the pK_T was positive, equilibrium moved from right towards the left and when it was negative, equilibrium moved from left towards the right.

Table .6. The equilibrium constants (K) and pK_Tvalues for the tautomers at HF and DFT/B3LYP level with different basis sets in different solvent phase.

Equilibrium	DMSO		ACETONITRILE		DCE		TOLUENE	
	K_T	pK_T	K_T	pK_T	K_T	pK_T	K_T	pK_T
HF								
K1B ⇌ E1B	$4.9835x10^{-6}$	15.11	$5.6437 x10^{-6}$	14.95	$4.9248 x10^{-6}$	15.12	$8.8531 x10^{-6}$	14.40
K1B ⇌ E2B	$2.3906x10^{-6}$	16.02	$2.0372 x10^{-6}$	16.21	$2.4335 x10^{-6}$	15.99	$1.3220 x10^{-6}$	16.75
E1B ⇌ E2B	0.47970	0.91	0.3609	1.26	0.4941	0.87	0.1493	2.35
K1G ⇌ E1G	$9.8493x10^{-6}$	14.26	$8.8008 x10^{-6}$	14.40	$9.9667 x10^{-6}$	14.25	$6.9440 x10^{-6}$	14.70
K1G ⇌ E2G	$3.9628x10^{-5}$	12.54	$4.9048 x10^{-5}$	12.28	$3.8930 x10^{-5}$	12.56	0.0001	11.34
E1G ⇌ E2G	4.0234	-1.72	5.5731	-2.13	3.9060	-1.69	15.0773	-3.36
K1D ⇌ E1D	1.2047x10-5	14.01	$1.0892 x10^{-5}$	14.14	$1.2190 x10^{-5}$	14.00	$8.5440 x10^{-6}$	14.44
K1D ⇌ E2D	$8.0674x10^{-5}$	11.66	0.0001	11.37	$7.8785 x10^{-5}$	11.69	0.0002	10.33
E1D ⇌ E2D	6.6966	-2.35	9.3864	-2.77	6.5011	-2.32	27.7535	-4.11
K1E ⇌ E1E	$5.1239x10^{-7}$	17.92	$4.5245 x10^{-7}$	18.08	$5.1543 x10^{-7}$	17.91	$3.2858 x10^{-7}$	18.47
K1E ⇌ E2E	$4.4795x10^{-6}$	15.24	$5.5116 x10^{-6}$	14.98	$4.3746 x10^{-6}$	15.27	$1.1905 x10^{-5}$	14.03
E1E ⇌ E2E	8.7423	-2.68	12.1816	-3.09	8.4872	-2.65	36.2320	-4.44
DFT								
K1B ⇌ E1B	$5.2877 x10^{-6}$	15.03	$5.3507 x10^{-6}$	15.02	$5.9528 x10^{-6}$	14.89	$8.6458 x10^{-6}$	14.43
K1B ⇌ E2B	$2.8897 x10^{-6}$	15.78	$2.8388 x10^{-6}$	15.80	$2.4335 x10^{-6}$	15.99	$1.5980 x10^{-6}$	16.51
E1B ⇌ E2B	0.54649	0.75	0.53054	0.78	0.41123	1.10	0.18483	2.09
K1G ⇌ E1G	$3.0176 x10^{-5}$	12.88	$2.9820 x10^{-5}$	12.89	$2.7124 x10^{-5}$	13.01	$2.2440 x10^{-5}$	13.24
K1G ⇌ E2G	$9.9852 x10^{-5}$	11.40	$1.0164 x10^{-4}$	11.38	$1.2359 x10^{-4}$	11.13	$2.4717 x10^{-4}$	10.28
E1G ⇌ E2G	3.3090	-1.48	3.4085	-1.52	4.5565	-1.88	11.015	-2.97
K1D ⇌ E1D	$2.5564 x10^{-5}$	13.08	$2.5263 x10^{-5}$	13.10	$2.3252 x10^{-5}$	13.20	$1.9237 x10^{-5}$	13.44
K1D ⇌ E2D	$1.3749 x10^{-4}$	11.00	$1.4079 x10^{-4}$	10.97	$1.7530 x10^{-4}$	10.70	$3.7864 x10^{-4}$	9.75
E1D ⇌ E2D	5.4105	-2.09	5.5731	-2.13	7.5390	-2.50	19.683	-3.69
K1E ⇌ E1E	$1.0599 x10^{-7}$	19.87	$1.3699 x10^{-6}$	16.70	$1.2313 x10^{-6}$	16.84	$9.7731 x10^{-7}$	17.12
K1E ⇌ E2E	$9.5054 x10^{-6}$	14.31	$9.7334 x10^{-6}$	14.28	$1.1976 x10^{-5}$	14.02	$2.4818 x10^{-5}$	13.12
E1E ⇌ E2E	89.6860	-5.56	7.0634	-2.42	9.7261	-2.81	25.3940	-4.00

3.6 IR Frequencies and Intensities

The final step of frequency calculations involved the analysis of IR frequencies and intensities of the selected lactam tautomers in solvent state by using DFT method only. Although this calculation gave almost all vibrations of each molecule but few fundamental vibrations were selected for discussion. These included **C=O** and **N-H** stretching vibrations of lactam tautomers and; **C=N** and **O-H** stretching vibrations of lactim tautomers.

3.6.1 C=O vibrations:

The experimental available value of **C=O** stretching vibration of β lactam analyzed in ethanol (dielectric constant equals to 24.5) is 1780 cm^{-1} (Jarrahpour A. A., 2004). The calculated **C=O** stretching vibrations of β lactam were 1765.75 cm^{-1}, 1766.78 cm^{-1}, 1777.07 cm^{-1}, 1813.74 cm^{-1} for DMSO, Acetonitrile, 1,2-Dichloroethane and toluene respectively. It can be noted from the above results that, dichloroethane gave a best consistency to experimental results. The experimental values of **C=O** stretching vibrations of γ, δ and ε lactams were also obtained (Guisheng Yang and Housheng Xia, 2013). The IR frequencies of γ, δ and ε were 1688 cm^{-1}, 1671 cm^{-1} and 1663 cm^{-1} respectively which gave a close correlation to our theoretical values in different solvents.

There are two other important observations to note from the **C=O** stretching frequencies of all studied lactams. The first one is the decrease in IR frequencies from small to large rings. This support the fact that as ring strain increases (for example in β lactam), the exocyclic bonds' (in this case **C=O** bond) strengths increases and thus the IR frequency becomes high.

Increasing ring size reduces ring strain; exocyclic bonds become weaker and therefore low IR frequencies. The second observation is the increase in IR frequencies moving from more to less polar solvents. This supports the fact which was discussed in section 4.4.1 (geometry optimization). Interaction between solvent molecules and certain bonds in lactam tautomers with similar polarity (to those solvents) increases bond lengths lowering bond strengths and therefore IR frequencies become low. **C=O** is a polar bond, it has greater interaction with more polar solvents (DMSO and Acetonitrile) thus having lower IR frequencies than in less polar solvents (Dichloroethane and Toluene).

3.6.2 N-H Stretching

N-H stretching vibrations showed a slight variation as moving from polar to non polar solvents. They had slightly higher values in non polar solvents than in polar solvents. Like in the above observation concerning C=O stretching; the N-H bond is polar, it has higher interaction in polar solvents which reduces bond strength and thus low IR vibration frequencies.

3.6.3 C=N stretching

The vibration frequencies of C=N bond increases from small to larger lactams. C=N bond is an endocylic double bond which has the tendency to increase in bond strength as moving from smaller rings (highly strained) to larger ones (less strained). This supports the observed increase in IR frequencies from β lactam to ε lactam. Between the two lactim forms; the tautomers with H on the same side with C=N bond had lower IR frequencies than the other forms with H on the opposite side to C=N bond. This observation was due to possibility of forming H-bond between nitrogen atom of C=N and hydrogen atom at –OH.

This reduces contribution of N onto C=N bond and thus the strength of C=N bond decreases as well as IR frequencies. The lactim tautomers which resulted into formation of H-bond were E1B, E2G, E2D and E2E (Refer scheme 2).

3.6.4 O-H vibrations:

The O-H bond is not directly attached to the atoms of the ring and thus, ring size has no greater influence on the observed variations of O-H stretching vibrations. Instead between the two lactim forms of each lactam it was observed that the one with the ability to form intramolecular H-bond has low IR frequencies. Reason behind this observation has been discussed in the previous section concerning C=N stretching vibrations.

Table.7. Selected frequencies (in cm-1) of studied tautomers DFT/B3LYP method with different basis set in the gas phase.

C=O								
	DMSO		**ACETONITRILE**		**DCE**		**TOLUENE**	
	Freq	**Inten**	**Freq**	**Inten**	**Freq**	**Inten**	**Freq**	**Inten**
K1B	1766	1224	1767	1217	1777	1146	1814	910
K1G	1700	1029	1701	1023	1711	961	1744	757
K1D	1666	880	1667	875	1675	824	1707	648
K1E	1665	893	1665	887	1674	831	1704	648
N-H								
K1B	3591	59	3591	59	3592	54	3596	39
K1G	3614	65	3615	64	3616	61	3623	48
K1D	3581	45	3581	44	3582	42	3587	33
K1E	3596	48	3596	48	3597	45	3602	37
C=N								
E1B	1674	456	1675	454	1678	429	1688	356
E2B	1700	311	1701	309	1704	291	1713	235
E1G	1726	331	1726	329	1730	310	1740	248
E2G	1704	443	1705	441	1707	417	1717	340
E1D	1674	456	1675	454	1678	429	1688	356
E2D	1700	311	1701	309	1704	291	1713	235
E1E	1726	331	1726	329	1730	310	1740	248
E2E	1704	443	1705	441	1707	417	1717	340
O-H								
E1B	3742	112	3742	111	3742	106	3748	86
E2B	3812	203	3813	202	3817	186	3831	138
E1G	3818	158	3819	157	3822	144	3834	105
E2G	3755	93	3755	93	3756	89	3760	74
E1D	3742	112	3742	111	3742	106	3748	86
E2D	3812	203	3813	202	3817	186	3831	138
E1E	3818	158	3819	157	3822	144	3834	105
E2E	3755	93	3755	93	3756	89	3760	74

4. Conclusions

The theoretical calculations in this work show that in the gas phase; optimized geometries, vibrational frequencies, thermodynamic properties, and equilibrium constants of amide-imidol tautomers of different lactams, were performed by HF and DFT calculations. The calculated geometrical parameters are in good agreement with experimental data. The change of enthalpy (ΔH) and the free energy (ΔG) change are positive in all equilibrium sates expect E1D-E2D and E1E and E2E. From equilibrium constants, the amide form is a more dominant tautomer for the all cases and the imidol forms are not present in detectable amounts. The imodol tautomers are formed one form to another. The pKT were negative that determinate the privileged direction of equilibrium. The vibrational frequencies and infrared intensities were calculated with the DFT/B3LYP and HF methods.

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