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Computational Studies of Molecular Structure, Vibrational Frequencies and Equilibrium Constant for Lactam-Lactim Tautomerism by HF and DFT Methods in Gas Phase

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ABSTRACT

The geometries of various tautomers of different ring size lactams have been studied by ab initio Hatree–Fock and Density Functional Theory calculations at B3LYP level with different basis sets in the gas phase. Optimized geometries and total energies for 12 possible tautomers of studied lactams were determined. Thermodynamic properties and tautomeric equilibria between different tautomers were calculated using the frequency calculations. The results of calculations are applied to the bond lengths of β- lactam which showed a good agreement with experimentally determined data. In the gas phase, the amino tautomers are computed to be more stable than the lactim tautomers. Equilibrium constant results suggested that, the lactam form is a more dominant tautomer for the all cases and the lactim forms are not present in detectable amounts.

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, β-lactam 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 β-lactam 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.

Computational methods

Theoretical calculations were carried out at the Hartree–Fock (HF) level of theory [18] and Density Functional Theory (DFT) [19] with Becke's three parameter hybrid exchange functional of [20], Lee-Yang-Parr correlation functionals (B3LYP) [21,22] and different basis sets were chosen to optimize the structures of the molecules under investigation in gaseous phase. All these calculations were carried out on a desktop computer. The geometries of all tautomers investigated were completely optimized with the GAUSSIAN 09W program [23]. All tautomer's structures were drawn using Gaussview 5.08 program [24]. 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.

In the present research paper we have chosen the different ring size of lactams structures such β (four membered ring), γ (five membered ring) , δ (six membered ring) , and ε (seven membered ring) lactams as shown in scheme 1.

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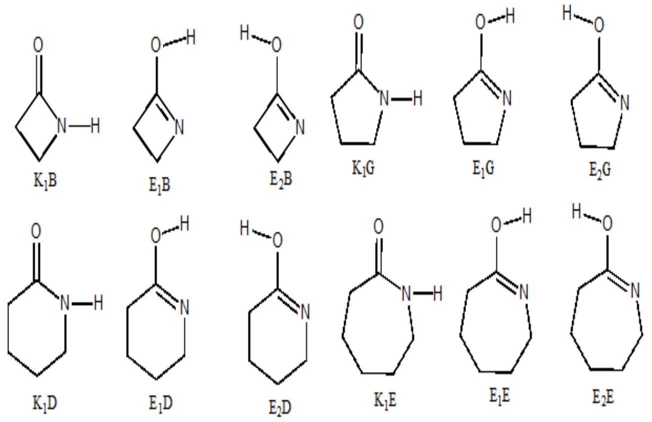

Scheme 1. Tautomeric forms of studied lactams.

Results and discussion

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 as given in the scheme 1.

The geometry optimizations structures (Fig.1) of all tautomers were computed by Hartree–Fock (HF) and density functional theory (DFT) with different basis set levels using the triple split valence basis set along with diffuse and polarization functions. The geometrical parameters (bond orders and bond angles) have also been calculated for all tautomers and presented in table 1,2 and 3.

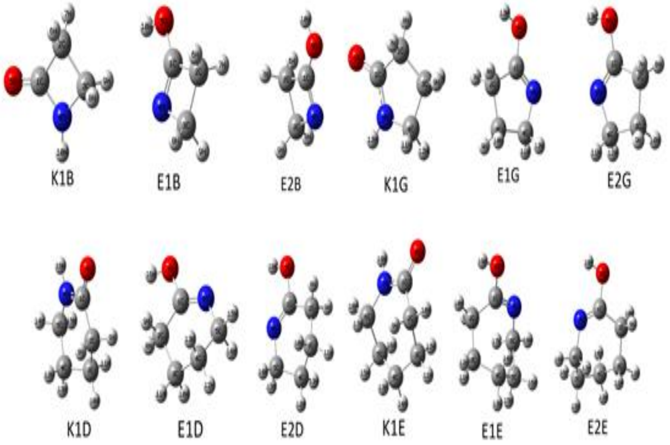

Figure 1. Optimized structures of different ring size lactam tautomers with DFT/B3LYP-6-311++G(d,p) method.

Table 1. The theoretical and experimental geometrical parameters (bond length and bond angles in Ǻ) of β- lactams with different basis sets in gas phase bond.

	HF				**DFT**				**EXP VALUES**
BOND	**6-311G**	**6-311G (d,p)**	**6-311G++**	**6-311G++ (d,p)**	**6-311G**	**6-311G (d,p)**	**6-311G++**	**6-311G++ (d,p)**	
C1-C2	1.5258	1.5324	1.5263	1.5313	1.5491	1.5505	1.5477	1.5475	1.53
C1-N4	1.3632	1.3579	1.3623	1.3577	1.3827	1.3749	1.3816	1.3744	1.38
C1-O5	1.2094	1.1802	1.2099	1.182	1.2293	1.2009	1.2307	1.2035	1.20
C2-C3	1.5541	1.5494	1.5545	1.5498	1.5638	1.5552	1.5644	1.5559	1.55
C2-H6	1.0772	1.082	1.0776	1.082	1.0874	1.09 00	1.0877	1.0900	1.10
C2-H7	1.0772	1.082	1.0775	1.082	1.0873	1.09 00	1.0876	1.0900	1.10
C3-N4	1.4711	1.4567	1.4722	1.4581	1.4856	1.4690	1.4877	1.4712	1.48
C3-H8	1.0779	1.0837	1.0781	1.0834	1.089	1.0928	1.0889	1.0923	1.10
C3-H9	1.0779	1.0837	1.0781	1.0836	1.0889	1.0928	1.0889	1.0923	1.10
N4-H10	0.9883	0.9944	0.9892	0.9949	1.0065	1.0106	1.0074	1.0111	0.99
C2-C1-N4	91.22	90.79	91.42	91.02	91.10	90.79	91.42	91.02	91.1
C2-C1-O5	136.12	136.17	136.04	136.06	136.60	136.17	136.04	136.06	136.6
C1-C2-C3	86.20	85.90	86.15	85.89	86.60	85.90	86.15	85.89	86.6
C1-C2-H7	114.02	114.01	114.02	113.93	115.10	114.01	114.02	113.93	115.1
C3-C2-H6	115.53	115.67	115.54	115.69	114.50	115.67	115.54	115.69	114.5
H6-C2-H7	109.88	109.92	109.92	109.99	110.00	109.92	109.92	109.99	110.0
C2-C3-N4	86.92	87.20	86.92	87.17	87.60	87.20	86.92	87.17	87.6
N4-C3-H8	113.99	114.10	113.83	113.95	114.40	114.10	113.83	113.95	114.4
C1-N4-C3	95.67	96.11	95.51	95.92	95.30	96.11	95.51	95.92	95.3
C3-N4-H10	132.76	132.63	132.84	132.75	131.00	132.63	132.84	132.75	131.0

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

Bond	**K1B**				**bond**	**E1B**				**E2B**			
	6-311	**6-311 G(d,p)**	**6-311 G++**	**6-311 G++ (d,p)**		**6-311**	**6-311 G(d,p)**	**6-311 G++**	**6-311 G++ (d,p)**	**6-311**	**6-311 G(d,p)**	**6-311 G++**	**6-311 G++ (d,p)**
Five membered ring													
C1-C2	1.51	1.5196	1.5108	1.5191	C1-C2	1.4967	1.5121	1.4969	1.5122	1.5097	1.5028	1.5099	1.5009
C1-N5	1.3538	1.3564	1.3522	1.3558	C1-N5	1.2573	1.244	1.2575	1.2445	1.2546	1.2475	1.2545	1.247
C1-O6	1.2228	1.1905	1.224	1.1925	C1-O6	1.3505	1.3355	1.3498	1.3351	1.3595	1.3282	1.358	1.3291
C2-C3	1.5361	1.5322	1.5367	1.5328	C2-C3	1.5444	1.5324	1.5447	1.5332	1.5399	1.5348	1.5404	1.5393
C2-H7	1.0825	1.0868	1.0829	1.0868	C2-H7	1.0805	1.0882	1.0813	1.0882	1.0837	1.087	1.0842	1.085
C2-H8	1.0771	1.0815	1.0777	1.0818	C2-H8	1.0803	1.0861	1.0808	1.0861	1.0818	1.0833	1.0823	1.0848
C3-C4	1.5429	1.537	1.5441	1.5373	C3-C4	1.5584	1.5448	1.5577	1.545	1.5513	1.5457	1.5514	1.5543
C3-H9	1.0784	1.0827	1.0789	1.0828	C3-H9	1.0794	1.0832	1.0799	1.0833	1.0788	1.0833	1.0795	1.0834

C3-H10	1.0808	1.0848	1.0813	1.0849	C3-H10	1.0795	1.0848	1.0801	1.0849	1.0805	1.085	1.0811	1.0835
C4-N5	1.4561	1.448	1.4567	1.449	C4-N5	1.4725	1.4565	1.473	1.4565	1.4725	1.4592	1.4728	1.4565
C4-H11	1.0828	1.0887	1.083	1.0884	C4-H11	1.0792	1.0873	1.0797	1.0872	1.0808	1.0873	1.0812	1.0849
C4-H12	1.0788	1.0833	1.0793	1.0832	C4-H12	1.0789	1.0835	1.0793	1.0835	1.0774	1.0836	1.0779	1.0848
N5-H13	0.989	0.9938	0.9899	0.9944	O6-H13	0.9486	0.94	0.9495	0.9403	0.9454	0.9449	0.946	0.945
Six membered ring													
C1-C2	1.5073	1.5172	1.5082	1.5171	C1-C2	1.508	1.5136	1.5084	1.5139	1.4977	1.5051	1.4978	1.5052
C1-N6	1.3543	1.3581	1.3523	1.3569	C1-N6	1.2499	1.2408	1.2497	1.2411	1.2553	1.2455	1.2553	1.2461
C1-O7	1.2298	1.1958	1.2316	1.1981	C1-O7	1.3751	1.3481	1.3743	1.3483	1.363	1.3393	1.3632	1.3399
C2-C3	1.5285	1.5279	1.5285	1.528	C2-C3	1.5308	1.527	1.5307	1.5273	1.5308	1.5274	1.5308	1.5274
C2-H8	1.0842	1.088	1.0848	1.0881	C2-H8	1.0839	1.0878	1.0843	1.0878	1.0801	1.0844	1.0806	1.0845
C2-H9	1.0786	1.0824	1.0792	1.0825	C2-H9	1.0853	1.0891	1.0858	1.0891	1.0837	1.0876	1.0843	1.0877
C3-C4	1.5285	1.5255	1.5283	1.5253	C3-C4	1.5298	1.5245	1.5293	1.5241	1.5313	1.5257	1.5307	1.5255
C3-H10	1.0812	1.0852	1.0819	1.0854	C3-H10	1.0839	1.0876	1.0846	1.0878	1.0843	1.0879	1.085	1.0881
C3-H11	1.0846	1.0885	1.0852	1.0887	C3-H11	1.0811	1.0851	1.0817	1.0853	1.0811	1.0851	1.0817	1.0853
C4-C5	1.5241	1.5218	1.5244	1.5217	C4-C5	1.5282	1.5262	1.5277	1.526	1.5294	1.527	1.529	1.5267
C4-H12	1.0839	1.0877	1.0845	1.0879	C4-H12	1.082	1.086	1.0825	1.0863	1.0821	1.0862	1.0827	1.0863
C4-H13	1.0816	1.0856	1.0822	1.0857	C4-H13	1.0848	1.0887	1.0854	1.0891	1.0848	1.0888	1.0855	1.089
C5-N6	1.4598	1.4533	1.4604	1.4543	C5-N6	1.4644	1.4512	1.4647	1.4511	1.4655	1.453	1.4661	1.4535
C5-H14	1.0803	1.0843	1.0807	1.0843	C5-H14	1.0832	1.0885	1.0837	1.0885	1.0832	1.0884	1.0837	1.0884
C5-H15	1.0846	1.0896	1.0849	1.0894	C5-H15	1.0785	1.0844	1.0791	1.0844	1.0788	1.0845	1.0793	1.0845
N6-H16	0.9922	0.9956	0.9928	0.9959	O7-H16	0.9459	0.9397	0.9463	0.94	0.9491	0.9449	0.9499	0.9452
Seven membered ring													
C1-C2	1.5056	1.5164	1.5063	1.5164	C1-C2	1.514	1.5223	1.5148	1.5226	1.5038	1.5134	1.5041	1.5135
C1-N7	1.3553	1.3564	1.3534	1.3554	C1-N7	1.2486	1.2405	1.2485	1.2407	1.2548	1.2457	1.2547	1.2461
C1-O8	1.2299	1.1968	1.2316	1.1991	C1-O8	1.3805	1.3511	1.3797	1.3515	1.368	1.3423	1.3684	1.3432
C2-C3	1.5399	1.5376	1.5398	1.5377	C2-C3	1.5367	1.5371	1.5378	1.5374	1.5365	1.5372	1.5369	1.537
C2-H9	1.0845	1.0883	1.0851	1.0885	C2-H9	1.0854	1.0887	1.0856	1.0887	1.0838	1.0874	1.0842	1.0875
C2-H10	1.0768	1.0808	1.0774	1.081	C2-H10	1.0859	1.0889	1.0862	1.089	1.0815	1.0849	1.0821	1.0851
C3-C4	1.5324	1.5305	1.5323	1.5303	C3-C4	1.535	1.5315	1.5347	1.5313	1.5358	1.5323	1.5354	1.532
C3-H11	1.0825	1.0859	1.0831	1.0861	C3-H11	1.0816	1.0849	1.0822	1.0851	1.0824	1.0856	1.083	1.0857
C3-H12	1.0841	1.0879	1.0847	1.0881	C3-H12	1.0826	1.0859	1.0831	1.086	1.0825	1.0857	1.083	1.0859
C4-C5	1.5317	1.5296	1.5317	1.5296	C4-C5	1.5415	1.5389	1.5408	1.5386	1.5419	1.5393	1.5416	1.5392
C4-C13	1.0866	1.0898	1.0871	1.0899	C4-H13	1.0825	1.0859	1.083	1.086	1.0825	1.086	1.0831	1.0861
C4-C14	1.0835	1.0869	1.084	1.0871	C4-H14	1.0839	1.0874	1.0845	1.0876	1.0839	1.0874	1.0845	1.0876
C5-C6	1.5298	1.5287	1.5299	1.5286	C5-C6	1.5314	1.5296	1.5316	1.5297	1.5323	1.5301	1.5323	1.5301
C5-H15	1.0845	1.0879	1.0851	1.088	C5-H15	1.0847	1.0884	1.0853	1.0885	1.0848	1.0884	1.0854	1.0885
C5-H16	1.0836	1.0875	1.0842	1.0877	C5-H16	1.082	1.0859	1.0826	1.086	1.0823	1.0862	1.0829	1.0864
C6-N7	1.4567	1.4509	1.4572	1.4519	C6-N7	1.461	1.4491	1.4609	1.4491	1.4616	1.4507	1.4619	1.4508
C6-H17	1.0844	1.0884	1.0848	1.0883	C6-H17	1.0835	1.0879	1.084	1.0878	1.0835	1.0877	1.0839	1.0876
C6-H18	1.0793	1.0829	1.0798	1.083	C6-H18	1.077	1.0832	1.0776	1.0833	1.0774	1.0833	1.0778	1.0834
N7-H19	0.9915	0.994	0.9921	0.9944	O8-H19	0.9456	0.9392	0.946	0.9395	0.949	0.9448	0.9498	0.945

Table 3. The bond lengths for DFT/B3LYP method for different basis sets in gas phase.

Bond	**K1B**				**bond**	**E1B**				**E2B**			
	6-311	**6-311 G(d,p)**	**6-311 G++**	**6-311G++ (d,p)**		**6-311**	**6-311 G(d,p)**	**6-311 G++**	**6-311 G++ (d,p)**	**6-311**	**6-311 G(d,p)**	**6-311 G++**	**6-311 G++ (d,p)**
Five membered ring													
C1-C2	1.5274	1.5326	1.5263	1.5278	C1-C2	1.5194	1.5199	1.5185	1.5189	1.5051	1.5082	1.505	1.5074
C1-N5	1.3722	1.3712	1.3705	1.3653	C1-N5	1.2759	1.2648	1.2754	1.2650	1.2798	1.2685	1.2805	1.2689
C1-O6	1.2434	1.2122	1.2457	1.216	C1-O6	1.3825	1.3546	1.3826	1.3558	1.371	1.3462	1.3716	1.3479
C2-C3	1.5442	1.5366	1.5451	1.5428	C2-C3	1.5519	1.539	1.5524	1.5401	1.5545	1.5416	1.5528	1.5425
C2-H7	1.0931	1.0952	1.0933	1.0919	C2-H7	1.0934	1.097	1.0939	1.0969	1.0912	1.0959	1.0932	1.0957
C2-H8	1.0876	1.0899	1.0881	1.0918	C2-H8	1.0934	1.0945	1.0935	1.0944	1.0911	1.0918	1.0902	1.0919
C3-C4	1.5539	1.5457	1.5546	1.5582	C3-C4	1.5707	1.5556	1.5682	1.5557	1.5704	1.5556	1.5649	1.556
C3-H9	1.0885	1.0907	1.0889	1.0905	C3-H9	1.0894	1.0911	1.0897	1.0911	1.0895	1.0911	1.0895	1.0911
C3-H10	1.0908	1.0927	1.0911	1.0905	C3-H10	1.0894	1.0927	1.09	1.0927	1.0895	1.0929	1.0909	1.0927
C4-N5	1.467	1.4561	1.4685	1.4545	C4-N5	1.4865	1.4672	1.4875	1.4673	1.4892	1.4708	1.4928	1.471
C4-H11	1.0947	1.0983	1.0945	1.0945	C4-H11	1.0903	1.0967	1.0908	1.0964	1.0904	1.0966	1.0922	1.0962
C4-H12	1.0901	1.0926	1.0902	1.0945	C4-H12	1.0903	1.0927	1.0902	1.0926	1.0904	1.0927	1.0891	1.0925
N5-H13	1.0059	1.0086	1.0069	1.0089	O6-H13	0.9717	0.962	0.9724	0.9624	0.976	0.9681	0.9768	0.9682
Six membered ring													
C1-C2	1.5199	1.5259	1.5193	1.5244	C1-C2	1.5164	1.5183	1.5157	1.5176	1.5044	1.5076	1.5036	1.5076
C1-N6	1.371	1.3702	1.3689	1.3688	C1-N6	1.2701	1.2602	1.2694	1.2602	1.276	1.2656	1.2757	1.2656
C1-O7	1.2516	1.2188	1.2544	1.2221	C1-O7	1.4005	1.3695	1.4023	1.3716	1.3858	1.3616	1.3885	1.3616
C2-C3	1.537	1.5329	1.5372	1.5332	C2-C3	1.5412	1.534	1.5412	1.5345	1.5403	1.5339	1.5403	1.5339
C2-H8	1.0951	1.0965	1.0955	1.0966	C2-H8	1.0947	1.0966	1.095	1.0966	1.091	1.0934	1.0915	1.0934
C2-H9	1.0897	1.0913	1.0901	1.0914	C2-H9	1.096	1.0977	1.0963	1.0976	1.0946	1.0965	1.0951	1.0965
C3-C4	1.5363	1.5304	1.5362	1.5303	C3-C4	1.5375	1.5304	1.5371	1.5299	1.539	1.531	1.5384	1.5310
C3-H10	1.0917	1.0935	1.0922	1.0936	C3-H10	1.0943	1.0958	1.0948	1.096	1.0946	1.0961	1.095	1.0961
C3-H11	1.0949	1.0966	1.0954	1.0967	C3-H11	1.0911	1.093	1.0916	1.0932	1.0912	1.0931	1.0916	1.0931

C4-C5	1.5318	1.5268	1.5317	1.5266	C4-C5	1.5376	1.5331	1.5368	1.533	1.5384	1.533	1.5374	1.533
C4-H12	1.0941	1.0959	1.0946	1.096	C4-H12	1.0924	1.094	1.0928	1.0941	1.0924	1.0942	1.0928	1.0942
C4-H13	1.0918	1.0935	1.0922	1.0936	C4-H13	1.095	1.0967	1.0954	1.0968	1.0949	1.0968	1.0954	1.0968
C5-N6	1.4721	1.4628	1.4736	1.4644	C5-N6	1.4781	1.4597	1.479	1.46	1.4798	1.4629	1.4811	1.4629
C5-H14	1.0917	1.0939	1.0918	1.0936	C5-H14	1.0949	1.0983	1.0951	1.0981	1.0948	1.098	1.095	1.098
C5-H15	1.0966	1.0995	1.0966	1.099	C5-H15	1.0903	1.0942	1.0906	1.0941	1.0905	1.094	1.0907	1.094
N6-H16	1.0097	1.011	1.0104	1.0114	O7-H16	0.9728	0.9623	0.9735	0.9628	0.9773	0.9689	0.9779	0.9689
Seven membered ring													
C1-C2	1.5178	1.5247	1.5172	1.5233	C1-C2	1.5208	1.5233	1.5195	1.5216	1.5116	1.5168	1.511	1.5161
C1-N7	1.3711	1.3693	1.3691	1.3681	C1-N7	1.2739	1.2637	1.273	1.2635	1.2753	1.2655	1.2748	1.2655
C1-O8	1.2525	1.2199	1.2552	1.2232	C1-O8	1.3975	1.3664	1.3991	1.3687	1.3915	1.3626	1.3944	1.3655
C2-C3	1.5476	1.5421	1.5477	1.5425	C2-C3	1.567	1.5617	1.5667	1.5615	1.5462	1.5432	1.5469	1.5434
C2-H9	1.0959	1.0974	1.0963	1.0975	C2-H9	1.0938	1.0945	1.0941	1.0944	1.0947	1.0962	1.0951	1.0964
C2-H10	1.0878	1.0897	1.0883	1.0898	C2-H10	1.0922	1.0941	1.0925	1.0941	1.0925	1.0939	1.0928	1.094
C3-C4	1.5397	1.535	1.5396	1.5349	C3-C4	1.5437	1.5381	1.5435	1.538	1.543	1.5369	1.5427	1.5367
C3-H11	1.0932	1.0945	1.0936	1.0945	C3-H11	1.0933	1.0946	1.0937	1.0947	1.093	1.0942	1.0934	1.0942
C3-H12	1.0944	1.0961	1.0948	1.0961	C3-H12	1.0924	1.0936	1.0928	1.0937	1.0927	1.0938	1.093	1.0938
C4-C5	1.5385	1.5337	1.5385	1.5337	C4-C5	1.5427	1.5376	1.5425	1.5375	1.5503	1.5447	1.5497	1.5446
C4-C13	1.0972	1.0982	1.0975	1.0982	C4-H13	1.0934	1.0946	1.0938	1.0947	1.0928	1.094	1.0932	1.0941
C4-C14	1.0939	1.0951	1.0943	1.0952	C4-H14	1.0927	1.0942	1.0932	1.0944	1.0941	1.0954	1.0945	1.0955
C5-C6	1.5386	1.5352	1.5383	1.5346	C5-C6	1.5459	1.5427	1.5462	1.5433	1.5409	1.5366	1.5407	1.5365
C5-H15	1.0948	1.096	1.0952	1.096	C5-H15	1.0947	1.0961	1.0952	1.0962	1.0949	1.0963	1.0954	1.0964
C5-H16	1.0941	1.0959	1.0945	1.096	C5-H16	1.0924	1.0942	1.0928	1.0943	1.0925	1.0942	1.093	1.0943
C6-N7	1.4686	1.4595	1.4700	1.4613	C6-N7	1.4757	1.4574	1.4768	1.4579	1.4747	1.4594	1.4758	1.4598
C6-H17	1.0957	1.098	1.0959	1.0977	C6-H17	1.0987	1.1008	1.0986	1.1003	1.0953	1.0976	1.0954	1.0973
C6-H18	1.0901	1.0918	1.0904	1.0917	C6-H18	1.0882	1.0923	1.0883	1.0922	1.0891	1.0928	1.0892	1.0927
N7-H19	1.0089	1.0095	1.0096	1.0100	O8-H19	0.9714	0.9612	0.9723	0.9618	0.9771	0.9687	0.9779	0.9688

All the values are consistent. From the theoretical values we observed that most of the optimized bond lengths slightly varied from experimental value at HF and DFT levels, due to the fact that theoretical values being obtained from gas phase molecules and the experimental values belong to molecule in solution state. Comparing to the bond lengths and bond angles of HF and DFT methods with experimental values in table 1,(For four membered ring) they show very good agreement with the experimental results in figure.2 [25]. As it can be seen in Table 1; the C-O bond lengths in amide tautomers are shorter than the C-O bond in iminol tautomers. The reason is that, in amide the bond is C=O (double bond) and in iminol the bond is C-O (single bond). The same trend was observed to C=N to C-N bonds for imidol and amide tautomers respectively.

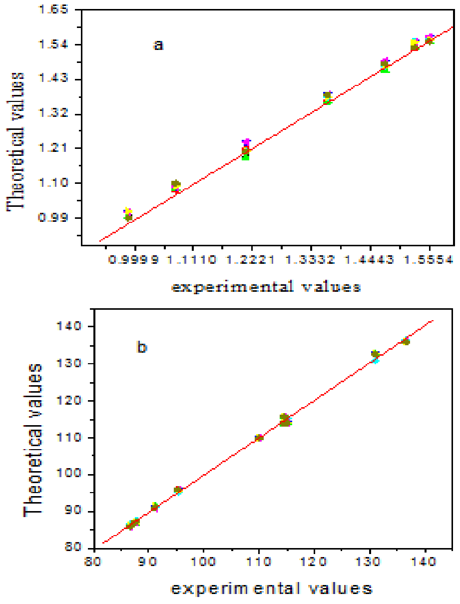

Fig 2. the Calculated band lengths Vs experimental bond lengths at different basis sets (a) HF and (b) DFT method for β lactam.

Relative stabilities

The total and relative energies (in brackets in Kcal/mol) at HF and DFT with different basis sets of 12 tautomers of are presented in Table 4, among the 12 tautomers, three are β-lactams (K1B, E1B and E2B) , three are γ-lactams (K1G, E1G and E2G), three are δ-lactams (K1D, E1D and E2D), three are ε-lactams (K1E, E1E and E2E).The most stable tautomer is taken in each category of lactms as reference to obtain the relative energetic stability of other tautomers. K1 tautomers of all lactams had the lowest energy values (highest stable in each lactam). Of the two possible lactim (E1 and E2) tautomers of all lactams, the (E2) tautomers had the highest energy in case of β lactam (all basis sets) and γ lactam (6-311G and 6-311G++) analyzed by HF. In case of γ lactam (6-311G(d,p) and 6-311G++(d,p) basis sets); δ and ε lactams had E1 tautomers with highest energy values. DFT calculations showed that E2 tautomers of β lactam had the highest energy values. For the remained lactams (γ, δ and ε); E1 tautomers had the highest values of energy. The trend in DFT was the same in all basis sets.

The overall order of relative stabilities for all tautomers in gas phase with respect to stable tautomer: K1E > E2E > E1E > K1D > E2D > E1D > K1G > E2G > E1G > K1B > E1B > E2B.

Themodynamic properties

Thermodynamic properties such as: enthalpy, Gibbs free energy and entropy were given according to the formulas [21]

$$H = E + RT \qquad (1)$$

$$G = H - TS \qquad (2)$$

E is the thermal energy; H is the enthalpy; G is the Gibbs free energy.

The thermodynamic parameters of the conversion processes, ΔH, ΔG, and ΔS were calculated from the results of quantum mechanical calculations of electronic, vibrational, rotational, and translational energy components. The change of enthalpies (ΔH), Gibbs free energies (ΔG) and entropies (ΔS) of various tautomers,

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).

Tuoto mers	HF method				DFT method			
	6-311	6-311G (d,p)	6-311 G++	6-311 G++ (d,p)	6-311	6-311G (d,p)	6-311 G++	6-311 G++ (d,p)
K1B	-245.749694 (0.000)	-245.874199 (0.000)	-245.754696 (0.000)	-245.879607 (0.000)	-247.271050 (0.000)	-247.356878 (0.000)	-247.277702 (0.000)	-247.364207 (0.000)
E1B	-245.709010 (25.53)	-245.8450312 (18.30)	-245.7156465 (24.50)	-245.850953 (17.98)	-247.229133 (26.30)	-247.326299 (19.19)	-247.237980 (24.92)	-247.334494 (18.64)
E2B	-245.699061 (31.77)	-245.837004 (23.34)	-245.705969 (30.57)	-245.843130 (22.89)	-247.220336 (31.82)	-247.319096 (23.71)	-247.229483 (30.26)	-247.327545 (23.00)
K1G	-284.814931 (0.000)	-284.952071 (0.000)	-284.8207051 (0.000)	-284.957758 (0.000)	-286.617831 (0.000)	-286.711496 (0.000)	-286.625106 (0.000)	-286.717768 (0.000)
E1G	-284.784733 (18.95)	-284.919373 (20.52)	-284.791185 (18.52)	-284.925196 (20.43)	-286.574609 (27.12)	-286.679875 (19.84)	-286.583293 (26.24)	-286.687832 (18.78)
E2G	-284.7714842 (27.26)	-284.930064 (13.81)	-284.7782191 (26.66)	-284.935084 (14.23)	-286.586433 (19.70)	-286.689405 (13.86)	-286.594865 (18.97)	-286.697022 (13.02)
K1D	-323.8426323 (0.000)	-323.997500 (0.000)	-323.848831 (0.000)	-324.003332 (0.000)	-325.932937 (0.000)	-326.037740 (0.000)	-325.940528 (0.000)	-326.045416 (0.000)
E1D	-323.8021356 (25.41)	-323.965347 (20.17)	-323.808767 (25.14)	-323.971245 (20.13)	-325.892988 (25.06)	-326.007380 (19.05)	-325.901290 (24.62)	-326.015287 (18.90)
E2D	-323.8182080 (15.32)	-323.978236 (12.09)	-323.824399 (15.33)	-323.983787 (12.26)	-325.907155 (16.18)	-326.018988 (11.76)	-325.914973 (16.03)	-326.026424 (11.92)
K1E	-362.8641258 (0.000)	-363.037097 (0.000)	-362.870579 (0.000)	-363.042907 (0.000)	-365.242396 (0.000)	-365.358892 (0.000)	-365.250035 (0.000)	-365.366362 (0.000)
E1E	-362.8147296 (30.99)	-362.995756 (25.94)	-362.821595 (30.74)	-363.001734 (25.83)	-365.193302 (30.80)	-365.319567 (24.67)	-365.202287 (29.96)	-365.327863 (24.16)
E2E	-362.8316963 (20.35)	-363.009480 (17.33)	-362.838157 (20.34)	-363.015111 (17.44)	-365.209156 (20.86)	-365.332316 (16.67)	-365.217197 (20.60)	-365.339832 (16.65)

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	**6-311G**			**6-311G(d,p)**			**6-311G++**			**6-311G++(d,p)**		
	ΔH	**ΔG**	**ΔS**	**ΔH**	**ΔG**	**ΔS**	**ΔH**	**ΔG**	**ΔS**	**ΔH**	**ΔG**	**ΔS**
K1B $\rightleftharpoons$ E1B	25.27	25.31	-0.16	18.42	19.07	-2.15	24.32	24.38	-0.19	18.12	18.81	-2.29
K1B $\rightleftharpoons$ E2B	31.24	31.00	0.799	23.29	23.72	-1.43	29.78	29.91	0.77	22.87	23.33	-1.53
E1B $\rightleftharpoons$ E2B	5.974	5.688	0.961	4.86	4.651	0.71	5.42	5.53	0.97	4.75	4.52	0.75
K1G $\rightleftharpoons$ E1G	18.05	18.85	-2.71	20.30	20.19	0.38	17.64	18.49	-2.84	20.23	20.01	0.432
K1G $\rightleftharpoons$ E2G	26.55	26.14	1.372	13.83	13.94	-0.37	25.99	25.57	1.41	13.68	14.57	-2.98
E1G $\rightleftharpoons$ E2G	8.508	7.29	4.084	-6.47	-6.24	-0.75	8.348	7.07	4.26	-6.55	-5.53	-3.42
K1D $\rightleftharpoons$ E1D	24.55	24.38	0.55	19.77	19.83	-0.18	24.29	24.11	0.63	19.74	19.79	-0.16
K1D $\rightleftharpoons$ E2D	14.90	15.08	-0.62	11.96	12.31	-1.17	14.9	38.02	-0.56	12.12	12.45	-1.10
E1D $\rightleftharpoons$ E2D	-9.64	-9.30	-1.17	-7.81	-7.52	-0.99	-9.395	13.91	-1.19	-7.62	-7.34	-0.94
K1E $\rightleftharpoons$ E1E	30.29	29.73	1.879	25.71	25.62	0.30	30.03	29.47	1.88	25.62	25.50	0.40
K1E $\rightleftharpoons$ E2E	20.07	19.84	0.775	17.37	17.54	-0.57	20.04	19.78	0.84	17.47	17.59	-0.43
E1E $\rightleftharpoons$ E2E	-10.22	-9.89	-1.10	-8.34	-8.08	-0.87	-9.991	-9.68	-1.03	-8.15	-7.91	-0.83
DFT method												
K1B $\rightleftharpoons$ E1B	25.83	25.85	-0.042	19.12	19.52	-1.319	24.51	24.54	-0.088	18.59	18.98	-1.303
K1B $\rightleftharpoons$ E2B	31.11	30.86	0.814	23.50	23.69	-0.652	29.63	29.38	0.814	22.82	22.98	-0.563
E1B $\rightleftharpoons$ E2B	5.27	5.02	0.856	4.37	4.18	0.667	5.11	4.84	0.902	4.227	4.007	0.74
K1G $\rightleftharpoons$ E1G	25.66	26.23	-1.899	19.44	19.29	0.494	24.83	25.42	-1.99	18.86	18.08	2.588
K1G $\rightleftharpoons$ E2G	18.59	19.41	-2.776	13.68	13.74	-0.202	18.46	18.27	0.616	13.29	12.71	1.954
E1G $\rightleftharpoons$ E2G	-7.08	-6.81	-0.877	-5.76	-5.55	-0.696	-6.37	-7.14	2.606	-5.56	-5.37	-0.634
K1D $\rightleftharpoons$ E1D	24.03	23.87	0.56	18.49	18.51	-0.067	23.60	23.42	0.581	18.34	18.35	-0.056
K1D $\rightleftharpoons$ E2D	15.54	15.66	-0.41	11.46	11.73	-0.924	15.38	15.49	-0.36	11.57	11.82	-0.839
E1D $\rightleftharpoons$ E2D	-8.50	-8.21	-0.41	-7.03	-6.78	-0.924	-8.22	-7.94	-0.36	-6.76	-6.53	-0.839
K1E $\rightleftharpoons$ E1E	29.99	29.23	2.551	24.33	23.96	1.259	29.19	28.53	2.224	23.85	23.56	0.971
K1E $\rightleftharpoons$ E2E	20.37	20.12	0.862	16.54	16.58	-0.156	20.11	19.84	0.895	16.49	16.51	-0.059
E1E $\rightleftharpoons$ E2E	-9.62	-9.11	-1.689	-7.80	-7.37	-1.415	-9.08	-8.69	-1.329	-7.36	-7.05	-1.03

were studied with respect to the amide tautomer (K1) to imidol tautomers (E1&E2) equilibria and E1&E2 equilibrium are reported in Table 2. From Table 2 the change in enthalpy (ΔH) and change in free energy (ΔG) are positive in all equilibrium sates expect E1D-E2D and E1E-E2E are negative. The positive values indicate endothermic and non spontaneous process and negative values are indicating exothermic and spontaneous process respectively.

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

$$a \xleftrightarrow{K_T} b$$

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

$$K_T = e^{-(\Delta G/RT)} \qquad (3)$$

$$pK_T = \frac{\Delta G}{2.303RT} \qquad (4)$$

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 pK_T values in different basis sets. All pK_T 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 pKT was positive, equilibrium moved from right towards the left and when it was negative, equilibrium moved from left towards the right. By taking account of all these directions of displacement, we obtained………

Vibrational frequencies

The vibrational frequencies and infrared intensities were calculated with the DFT/B3LYP and HF methods. Table 7 shows the selected vibrational frequencies and their corresponding intensities of amide and imidol tautomers with DFT/B3LYP method at different basis sets.

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

HF method								
Equilibrium	**6-311G**		**6-311G(d,p)**		**6-311G++**		**6-311G++(d,p)**	
	K_T	**pK_T**	**K_T**	**pK_T**	**K_T**	**pK_T**	**K_T**	**pK_T**
K1B $\rightleftharpoons$ E1B	2.79×10^{-19}	18.56	1.05×10^{-14}	13.98	1.34×10^{-18}	17.87	1.62×10^{-14}	13.79
K1B $\rightleftharpoons$ E2B	1.88×10^{-23}	22.73	4.07×10^{-18}	17.39	1.18×10^{-22}	21.93	7.88×10^{-18}	17.10
E1B $\rightleftharpoons$ E2B	6.76×10^{-5}	4.17	3.89×10^{-4}	3.41	8.78×10^{-5}	4.06	4.82×10^{-4}	3.32
K1G $\rightleftharpoons$ E1G	1.52×10^{-14}	13.82	1.57×10^{-15}	14.80	2.78×10^{-14}	13.56	1.84×10^{-15}	14.74
K1G $\rightleftharpoons$ E2G	6.86×10^{-20}	19.16	5.99×10^{-11}	10.22	1.80×10^{-19}	18.75	2.08×10^{-11}	10.68
E1G $\rightleftharpoons$ E2G	4.53×10^{-6}	5.34	3.81×10^{4}	-4.58	6.49×10^{-6}	5.19	1.13×10^{4}	-4.05
K1D $\rightleftharpoons$ E1D	1.34×10^{-18}	17.87	2.90×10^{-15}	14.54	2.11×10^{-18}	17.68	3.10×10^{-15}	14.51
K1D $\rightleftharpoons$ E2D	8.80×10^{-12}	11.06	9.45×10^{-10}	9.02	1.34×10^{-28}	27.87	7.46×10^{-10}	9.13
E1D $\rightleftharpoons$ E2D	6.58×10^{6}	-6.82	3.26×10^{5}	-5.51	6.35×10^{-11}	10.20	2.40×10^{5}	-5.38
K1E $\rightleftharpoons$ E1E	1.60×10^{-22}	21.80	1.64×10^{-19}	18.78	2.48×10^{-22}	21.60	2.02×10^{-19}	18.69
K1E $\rightleftharpoons$ E2E	2.85×10^{-15}	14.54	1.38×10^{-13}	12.86	3.16×10^{-15}	14.50	1.27×10^{-13}	12.90
E1E $\rightleftharpoons$ E2E	1.78×10	-7.25	8.41×10^{5}	-5.92	1.25×10^{7}	-7.10	6.29×10^{5}	-5.80
DFT method								
K1B $\rightleftharpoons$ E1B	2.79×10^{-19}	18.55	4.89×10^{-15}	14.31	1.02×10^{-18}	17.99	1.22×10^{-14}	13.91
K1B $\rightleftharpoons$ E2B	1.88×10^{-23}	22.72	4.29×10^{-18}	17.37	2.89×10^{-22}	21.54	1.42×10^{-17}	16.85
E1B $\rightleftharpoons$ E2B	6.76×10^{-5}	4.16	8.62×10^{-4}	3.06	2.83×10^{-4}	3.55	1.15×10^{-3}	2.94
K1G $\rightleftharpoons$ E1G	1.52×10^{-14}	13.81	7.21×10^{-15}	14.14	2.31×10^{-1}	18.64	5.56×10^{-14}	13.25
K1G $\rightleftharpoons$ E2G	6.86×10^{-20}	19.16	8.45×10^{-11}	10.07	4.04×10^{-14}	13.39	4.81×10^{-10}	9.32
E1G $\rightleftharpoons$ E2G	4.53×10^{-6}	5.34	1.17×10^{4}	-4.07	1.72×10^{5}	-5.23	8.65×10^{3}	-3.94
K1D $\rightleftharpoons$ E1D	1.34×10^{-18}	17.87	2.69×10^{-14}	13.57	$6. \times 10^{-18}$	17.17	3.53×10^{-14}	13.45
K1D $\rightleftharpoons$ E2D	8.80×10^{-12}	11.05	2.51×10^{-9}	8.60	4.41×10^{-12}	11.36	2.16×10^{-9}	8.67
E1D $\rightleftharpoons$ E2D	6.58×10^{6}	-6.81	9.34×10^{4}	-4.97	6.62×10^{5}	-5.82	6.13×10^{4}	-4.79
K1E $\rightleftharpoons$ E1E	1.60×10^{-22}	21.79	2.72×10^{-18}	17.57	1.21×10^{-21}	20.92	5.34×10^{-18}	17.27
K1E $\rightleftharpoons$ E2E	2.85×10^{-15}	14.54	6.99×10^{-13}	12.15	2.85×10^{-15}	14.54	7.88×10^{-13}	12.10
E1E $\rightleftharpoons$ E2E	1.78×10^{7}	-7.25	2.52×10^{5}	-5.40	2.35×10^{6}	-6.37	1.47×10^{5}	-5.17

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

C=O								
	6-311		**6-311G(d,p)**		**6-311++G**		**6-311G ++G(d,p)**	
	Frequency	**intensity**	**Frequency**	**intensity**	**Frequency**	**intensity**	**Frequency**	**intensity**
K1B	1776.55	496.96	1881.66	572.04	1751.05	594.16	1854.86	678.54
K1G	1712.91	398.4	1813.22	455.97	1684.96	482.8	1781.82	558.00
K1D	1677.19	319.24	1769.86	391.74	1651.72	381.58	1742.66	472.86
K1E	1675.29	323.1	1765.55	393.0	1650.09	387.6	1738.02	472.9
N-H								
K1B	3633.19	14.70	3600.48	18.71	3627.28	18.61	3599.98	24.71
K1G	3644.91	21.69	3629.46	28.15	3637.36	25.13	3630.06	34.69
K1D	3589.05	12.16	3590.00	18.33	3584.78	15.29	3589.81	23.10

K1E	3597.97	13.79	3609.30	22.52	3594.50	17.07	3608.10	27.08
C=N								
E1B	1636.63	251.4	1708.71	271.08	1626.04	255.6	1698.84	282.47
E2B	1674.23	139.02	1729.92	159.94	1666.45	162.5	1723.38	182.53
E1G	1725.16	149.38	1759.32	170.33	1716.89	172.13	1751.41	189.48
E2G	1693.35	227.10	1736.13	256.48	1679.59	232.52	1727.60	266.12
E1D	1748.53	165.98	1780.38	178.88	1742.18	184.96	1773.04	194.57
E2D	1723.00	222.84	1759.27	246.03	1715.78	225.81	1751.18	255.24
E1E	1719.21	174.9	1752.06	195.6	1714.74	195.6	1746.58	212.0
E2E	1724.47	239.2	1754.37	270.6	1718.84	243.3	1747.89	278.7
O-H								
E1B	3639.32	33.33	3752.09	54.23	3631.88	38.93	3754.93	63.32
E2B	3715.29	58.35	3845.95	85.38	3710.22	65.00	3847.24	95.71
E1G	3701.62	41.05	3846.13	63.91	3698.38	44.74	3846.20	70.93
E2G	3648.87	30.03	3762.55	48.13	3642.95	33.85	3767.19	55.96
E1D	3683.77	26.51	3837.12	47.05	3681.22	27.64	3837.15	51.87
E2D	3630.30	20.28	3747.66	36.87	3627.45	23.54	3753.05	43.73
E1E	3704.49	28.72	3852.59	51.22	3699.03	30.03	3851.05	55.95
E2E	3632.94	23.32	3750.39	40.51	3628.64	26.44	3754.51	47.59

C=O vibrations

The carbonyl stretching frequency is very sensitive to the factors that disturb the nature of the carbonyl group and its precise frequency is characteristic of the type of the carbonyl compound being studied. Particularly detailed correlations have been made for the carbonyl bond stretching frequency. The carbon oxygen double bond is formed by the pπ–pπ bonding between carbon and oxygen. Because of the different electronegativities of carbon and oxygen atoms, the bonding electrons are not equally distributed between the two atoms. The position of the C=O stretching vibration is very sensitive to various factors such as the physical state, electronic effects by substituents, ring strains, etc. Consideration of these factors provides further information about the environment of the C=O group. The carbonyl stretching generally occurs as a strong absorption in the region from 1730 to 1645 cm^{-1}. Accordingly, in the present investigation, the peaks identified at 1880 and 1650 cm^{-1} have been assigned to C=O stretching vibrations for all ring size lactams. The C=O stretching vibrations are different for different basis sets because of the effect of polarization and diffusion functions include the basis set.

O-H vibrations

In the studied tautomers, the frequencies of the OH stretching vibrations are the most sensitive to intermolecular interactions and can be used as a sensitive probe for studying hydrogen bonding or self-association. As shown in Tables 6, the OH stretching vibration is observed at 3754 – 3851 cm^{-1} in E1 tautomers and 3851-3753 cm^{-1} in E2 tautomers respectively at largest basis set 6-311G++(d,p). It should be noted that in the vapor phase the OH stretching vibrations are observed at higher frequencies. The calculated harmonic OH stretching frequencies are overestimated, since these vibrations are known to be strongly anharmonic. In addition we have calculated the C=N and N-H stretching vibrations which are different in different basis sets.

Conclusion

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 pK_T were negative that determinate the privileged direction of equilibrium. The vibrational frequencies and infrared intensities were calculated with the DFT/B3LYP and HF methods. However, the assignments made during the present investigation can be put on a greater confidence level because these are visualized in three dimensions using a Gaussview program.

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