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Quantum chemical study and the effect of substitution of amino group on the reactivity of 4-Aminopyridine and 3,4-Diaminopyridine by Density Functional Theory

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Abstract

Present work deals with the quantum mechanical study of the molecular structure of two well-known voltage sensitive potassium channel blockers: 4, Aminopyridine and 3, 4 Diaminopyridine. The equilibrium geometry, harmonic vibrational frequencies and HOMO-LUMO gap have been calculated by the density functional theory (DFT), employing 6-311++G (2d, 2p) as the basis set. A detailed interpretation of the infrared and Raman spectra of 4, aminopyridine and 3, 4 Diaminopyridine in terms of the potential energy distribution (P.E.D) is reported. The similarities and differences between the vibrational spectra of the two molecules studied have been highlighted. The thermodynamic calculations related to the title compounds were also performed at B3LYP/6-311++G (2d, 2p) level of theory.

Keywords: Vibrational Spectra; Density functional theory; P.E.D; HOMO-LUMO

Introduction

The compound 3,4-Diaminopyridine (3,4-DAP), a derivative of 4, Aminopyridine, is soluble in cold water and is used in the symptomatic treatment of fatigue in multiple sclerosis as well as Lambert–Eaton myasthenia syndrome. It is capable of reducing morphine-induced respiratory rate depression in doses, which did not produce signs of toridty and also used to treat downbeat nystagmus (DBN) syndrome. [1-7].

Whereas the parent compound 4-AP is used as an acetylcholine-releasing drug, in serum, saliva, and urine [8]. The pre-synaptic effects of 4-AP and 3, 4-DAP have also been investigated on rat diaphragm neuromuscular junction using intracellular recording techniques. The effects of 4-AP and 3, 4-DAP on quantal release indicates that these drugs enhance calcium entry indirectly by

blocking voltage sensitive potassium channels [9]. 4-AP is an experimental drug that may reduce symptoms in some people with multiple sclerosis, particularly those who are more sensitive to heat. 4-AP blocks potassium channels on the surface of nerve fibers and may improve conduction of electrical impulses through nerves whose protective myelin sheath has been damaged or destroyed by multiple sclerosis.

In the present communication, the molecular structure of two well-known voltage sensitive potassium channel blockers: 4, Aminopyridine and 3, 4 Diaminopyridine has been analyzed using the density functional theory. The equilibrium geometry, harmonic vibrational frequencies and HOMO-LUMO gap have been calculated by the Density Functional B3LYP method employing 6-311++G (2d, 2p) as the basis set. The detailed interpretation of the infrared and Raman spectra of 4, Aminopyridine and 3, 4 Diaminopyridine in terms of the potential energy distribution (P.E.D) has been reported. We present the Density Functional Study carried out on the 4-AP and 3, 4-DAP.

Results and Discussion

Molecular geometry and Thermodynamic properties

The optimized structure parameters and thermodynamic properties of 3,4 DAP and 4-AP are calculated by DFT/ B3LYP levels with the 6-311++G (2d, 2p) basis set are listed in Table.1 & 2, in accordance with the atom numbering scheme given in Fig. 1&2. By allowing the relaxation of all parameters, the calculations converge to optimize geometries, which correspond to true energy minima, as revealed by the lack of imaginary frequencies in the vibrational mode calculation. Subsequently, the global minimum energy obtained for structure optimization of 3, 4 DAP and 4-AP with 6-311++G (2d, 2p) basis sets is approximately -359.1208 and -303.7444 a.u. respectively for DFT/ B3LYP approaches.The energy difference between two compounds is 55.3864 a.u. This is due to the replacement of the hydrogen with NH_2 makes 3,4 DAP less stable than 4-AP. In case of 3, 4-DAP molecule has no point group symmetry in calculation of B3LYP method so this molecule have C_1 molecular symmetry. As it can see from animated view of gauss view pyrimidine ring looks like planer in case of 3, 4-DAP, some deviation occurred due to antibonding electron repulsion between nitrogen and carbon. However two Hydrogen of one amino group are bending opposite side with respect to the other two hydrogen of other amino group and also out of plane of ring (just above and below to the plane of respective ring) to reduce repulsion between hydrogen of two amino groups. However in case of 4-AP one amino group is replaced at position C_3 by hydrogen of 3,4DAP .The 4-AP look like planer and hence having Cs symmetry. The optimized bond length of 3,4 DAP of C-C in ring lies 1.389-1.406 A^0 however in case of 4-DAP C-C bond length lies some lower value than previous one 1.385-1400 A^0 this is due to bulky amino grouping case of 3,4-DAP attached to position of C3 than hydrogen in case of 4-AP. As seen in case of 3,4 DAP amino group attached with ring the N-H bond length which are not lies in the plane are different from each other e.g. bond length in between nitrogen and hydrogen which are nonplaner are N2-H3, N2-H4, and N5-H6, N5-H7 are at 1.010,1.012 A^0 and1.010, 1.007 A^0. However in case of 4-AP the two hydrogen in amino group lies in plane of ring having same bond length e.g. bond length between N2-H3, N2-H4 are1.006 A^0.

The bond length in the ring has also shown characteristic variation but they have been small and less well pronounced as compared to the angular changes. The angular changes in benzene ring

geometry have proved to be a sensitive indicator of the interaction between the substituent and the benzene ring [10]. The bond angle in case of 4-AP C8-C10-C11 is 119.06 however bond angle in case of 3, 4 DAP C8-C9-C11 is 117.97, this is due to in case of 4-AP one amino group is replaced at position C_3 by hydrogen of 3, 4 DAP.

Table-1 Optimized geometrical parameters of 4-Aminopyridine and 3, 4-Diaminopyridine

S.No.	3,4Diaminopyridine Parameters	Calculated	4-Aminopyridine Parameters	Calculated
	Bond lengths			
1	(N1-C8)	1.3350	(N1-C5)	1.3363
2	(N1-C14)	1.3330	(N1-C11)	1.3370
3	(N2-H3)	1.0100	(N2-H3)	1.0062
4	(N2-H4)	1.0129	(N2-H4)	1.0062
5	(N2-C10)	1.4122	(N2-C8)	1.3839
6	(N5-H6)	1.0104	(C5-H6)	1.0842
7	(N5-H7)	1.0077	(C5-H7)	1.3862
8	(N5-C11)	1.3925	(C7-C8)	1.3998
9	(C8-H9)	1.0864	(C7-H13)	1.0822
10	(C8-C10)	1.3903	(C8-C9)	1.4003
11	(C10-C11)	1.4068	(C9-H10)	1.0822
12	(C11-C12)	1.3931	(C9-C11)	1.3857
13	(C12-H13)	1.0825	(C11-H12)	1.0840
14	(C12-C14)	1.3891		
15	(C14-15H)	1.0834		
	Bond angles			
16	(C8-N1-C14)	116.8565	(C5-N1-C11)	116.0857
17	(H3-N2-H4)	109.3228	(H3-N2-H4)	113.3525
18	(H3-N2-C10)	112.6432	(H3-N2-C8)	116.6777
19	(H4-N2-C10)	112.9123	(H4-N2-C8)	116.6755
20	(H6-N5-H7)	111.9069	(N1-C5-H6)	116.0959
21	(H6-N5-C11)	113.8480	(N1-C5-C7)	124.4241
22	(H7-N5-C11)	114.7301	(H6-C5-C7)	119.4800
23	(N1-C8-H9)	116.3618	(C5-C7-C8)	119.0539
24	(N1-C8-C10)	124.6009	(C5-C7-H13)	120.1847
25	(H9-C8-C10)	119.0373	(C8-C7-H13)	120.7612
26	(N2-C10-C8)	122.9391	(N2-C8-C7)	121.5141
27	(N2-C10-C11)	118.9962	(N2-C8-C9)	121.4667
28	(C8-C10-C11)	117.9798	(C7-C8-C9)	116.9659
29	(N5-C11-C10)	119.2375	(C8-C9-H10)	120.7211
30	(N5-C11-C12)	123.1512	(C8-C9-C11)	119.0631
31	(C10-C11-C12)	117.5596	(H10-C9-C11)	120.2155
32	(C11-C12-H13)	120.3283	(N1-C11-C9)	124.4071
33	(C11-C12-C14)	119.4423	(N1-C11-H12)	116.0710

34	(H13-C12-C14)	120.2222	(C9-C11-H12)	119.5217
35	(N1-C14-C12)	123.5303		
36	(N1-C14-H15)	116.5028		
37	(C12-C14-H15)	119.9659		

Table-2 Calculated Thermodynamic Properties of 4-Aminopyridine and 3,4-Diaminopyridine by (B3LYP)/ 6-311++G (2d, 2p) methods

	E (Thermal) (kcalmol^{-1})		CV (cal K^{-1}mol^{-1})		S (cal K^{-1}mol^{-1})	
	4AP	3,4 DAP	4AP	3,4 DAP	4AP	3,4 DAP
Total	69.600	81.250	22.164	27.202	75.049	80.774
Translational	0.889	0.889	2.981	2.981	39.535	39.977
Rotational	0.889	0.889	2.981	2.981	26.823	27.823
Vibrational	67.822	79.472	16.203	21.241	8.691	12.974

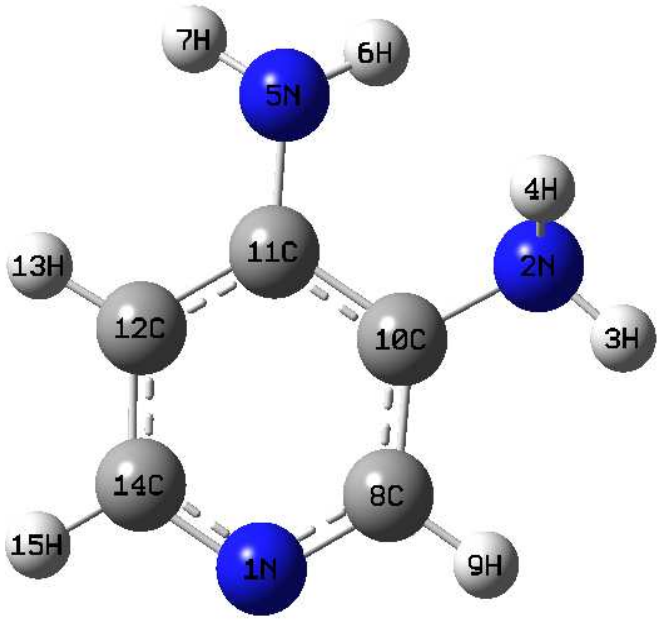

Fig 1 Molecular Structure of 3, 4 DAP

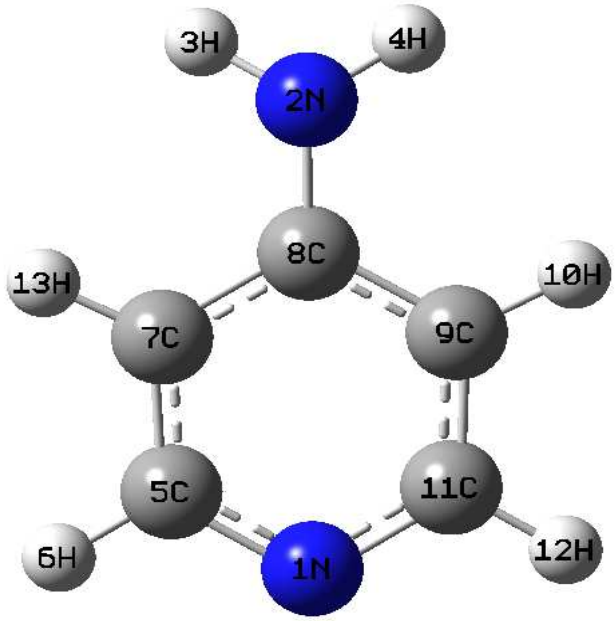

Fig 2 Molecular Structure of 4-AP

Vibrational Assignments

4-AP has 13 atoms and 33 normal modes of fundamental vibration. All the 33 fundamental vibrations are IR and Raman active. 3, 4-DAP has 15 atoms and 39 normal modes of fundamental vibrations. Here also all the 39 fundamental vibrations are IR and Raman active. Normal modes analysis provides detailed description of vibrational dynamics of the molecules in question. The detailed vibrational assignments have been analyzed by comparing the band positions and intensities observed in FTIR and FT-Raman spectra with the wave numbers and intensities obtained from the molecular modeling calculations given in Table 3 & 4.

Spectral region over 2800 cm^{-1}

The bands located in the high frequency region of the spectra of 4-AP, and 3, 4-DAP are easy to identify and belong to N–H and C–H stretching modes. The NH_2 groups raise to six internal modes of vibrations viz. the symmetric stretching, the antisymmetric stretching, the symmetric deformation or the scissoring, the rocking, the wagging and torsional modes. The frequency of antisymmetric vibration is higher than that of symmetric ones. If two bond of NH in NH_2 are symmetric then these modes are satisfied empirical relation as suggested by Bellamy and Williams [11].

$$\nu_{sym} = 345.5 + 0.876\ \nu_{assym}$$

Where, ν_{sym} and ν_{assym} are wave numbers.

For 4-AP, two medium intense polarized bands due to N2–H3 symmetric stretching and N2–H4 antisymmetric stretching vibration attached to the base ring are calculated at 3451 and 3547 cm^{-1} with P.E.D. of 100% and the corresponding bands are observed at 3445(3445) and 3550(3550) cm^{-1} in the experimental IR (Raman) spectrum are having red shift of 5 cm^{-1}and blue shift of 3 cm^{-1} respectively with calculated frequency. The bands due to N2–H3 symmetric, antisymmetric

stretching vibraton and N5–H6 symmetric stretching vibration attached to the base ring are calculated at 3381, 3473 and 3411 cm^{-1} with P.E.D. of 93%, 93% and 96% and the corresponding bands are observed at 3380, 3475 and 3405 cm^{-1} in the experimental I-R spectrum are nearly superimposed to calculated data. As it can seen that N-H stretching vibration in case of 4-AP lies some higher value than 3,4-DAP this is due to attachment of two amino group at C3 and C4 position which extracts electron from ring consequently weaken bond strength between N-H in case of 3,4 –DAP more than 4-AP and hence N-H stretching vibration lies some lower value in case of 3,4-DAP than 4-AP. In the case of 3,4-DAP two medium polarized bands are observed at 3057 and 3009 cm^{-1} are assigned to the C12-H13 and C8-H9 stretching mode with P.E.D. of 91% and 99% respectively, and the corresponding bands are observed at 3050 and 3000 cm^{-1} in the I-R spectrum with a negative shift of 7 cm^{-1}, 9 cm^{-1}respectively. The bands due to C5–H6 and C9–H10 stretching vibration are calculated at 3032 and 3058 cm^{-1} with P.E.D. of 84% and 91%, respectively and the corresponding bands are observed at 3030(3030) and 3050(3060) cm^{-1} in the experimental I-R (Raman) spectrum. These are usual range of appearance for N-H and C–H stretching vibrations.

Spectral region 1750–1000 cm^{-1}

The C-C and C-N aromatic stretch known as semi-circle stretching, are may be describe as opposite quadrant of ring stretching while intervening quadrants contract .For 3,4-DAP, in middle region, the C10–C11 and C11–C12 stretches predicted at 1560 and 1554 cm^{-1} with P.E.D. of 68% and 43% respectively, are in reasonable agreement with the 1565 and 1520 cm^{-1} observed in FTIR spectra. The strong stretching vibrations of the C8-N1 band is calculated at 1254 and 1223 cm^{-1} with P.E.D. of 69% and 48% respectively, and corresponding bands are observed at 1260 and 1210 cm^{-1} in FTIR spectrum. (C10–C8–H9) and (C12–C14–H15), in plane bending modes are calculated at 1318 and 1179 cm^{-1} with P.E.D. of 68% and 49% and corresponding bands are observed at 1330 and 1185 cm^{-1} in the FTIR spectrum. Strong (H7–C5–H6) in plane bending mode is calculated at 1599 cm^{-1} with P.E.D. of 50% and corresponding band is observed given at 1590 cm^{-1} in FTIR spectrum. For 4-AP, in middle region, the C8–C9 and C9–C11 stretches predicted at 1548 and 1574 cm^{-1} with P.E.D. of 67% and 30% respectively are in reasonable agreement with the 1540 (1525) and 1560(1565) cm^{-1} observed in FTIR (Raman) spectra. With heavy substituent, the band tend to shift some what lower wave number and greater the number of subsutiuent on the ring broader the absorption region [12]. Because of one hydrogen in 4-AP replaced by heavy group named as amine in case of 3, 4-DAP so C-C stretching are shifted to some lower side of spectra in case of 3, 4 DAP. Strong (H3–N2–H4) in plane bending mode is calculated at 1604 cm^{-1} with P.E.D. of 87% and corresponding band is observed at 1605(1600) cm^{-1} in the FTIR (Raman) spectrum.

Spectral region 1000–450 cm^{-1}

For 3, 4-DAP, as expected, the ring torsion modes along with out of plane bending modes appear in the observed low frequency range. The ring torsion and out of plane ring bend; all of them appear in the 1000-450 cm^{-1} frequency range. The experimental modes 570 [(H6-N5-H7) out of plane bending modes] and 854 cm^{-1} [(C14–N1–C8) out of plane bending modes] are well matched with modes at 560 and 850 cm^{-1} respectively. For 4-AP, the theoretical modes 528 (C8-NH_2, out of plane bending mode) & 795(ring breathing) and 660 cm^{-1} [(C9–C11–N1) out of plane bending modes] with appropriate P.E.D. are well matched with modes at 535(540) & 795(-) and 665(670) cm^{-1} in FTIR (Raman) spectrum. On comparing the computed and the

experimental frequencies of 3, 4-DAP and 4-AP, one can conclude that accurate results could be achieved with scaled DFT (B3LYP).

Table-3 Comparison of the observed and calculated Vibrational spectra of 3, 4-Diamino pyridine with B3LYP/6-311++G (2d, 2p)

B3LYP (CALC.)	I-R (INT.)	I-R (EXP.)	VIBRATIONAL ASSIGNMENTS WITH P.E.D. [%]
178	1.0206	-	Ring Tors.
218	17.010	-	Ring Tors.
272	2.1268	-	γ (H3-N2-H4)[80]
291	0.7182	-	w (C11-NH_2)[88]
415	2.3905	413(sh)	(C11-NH_2) twist [64]
425	16.698	425(sh)	(C11-NH_2) twist [64]
431	12.976	430(sh)	γ (H6-N5-H7)[87]
519	6.8175	520(sh)	β (C10-C11-C12)[61]
570	41.632	560(w)	γ (H6-N5-H7)[69]
595	2.2499	600(m)	Ring breathing
646	221.73	650(sh)	γ (H7-N5-H6)[70]
725	79.734	725(w)	γ (H3-N2-H4)[73]
757	30.469	760(vw)	ν_s (C10-C11)[51] + β (C12-C14-N1)[10]
774	123.42	775(sh)	γ (H3-N2-H4)[61]
800	49.678	805(sh)	Ring breathing
854	32.202	850(m)	γ (C14-N1-C8)[57]
889	10.747	885(m)	w (C8-H9)
933	0.5887	930(vw)	w (C14-H15)
1023	2.5337	1025(w)	β (H6-N5-C11)[45]
1064	1.1287	1050(sh)	β (H6-N5-C11)[45] + β (C10-C8-N1)[15]
1086	4.3576	1085(sh)	β (H6-N5-C11)[52] + ν_{as} (C8-C10)[11]
1179	21.619	1185(m)	γ (C12-C14-H15)[49] + β (H9-C8-N1)[11]
1223	28.252	1210(sh)	ν_s (C8-N1)[48] + β(C8-C10-C11)[21]
1254	47.903	1260(s)	ν_s (C8-N1)[69] + γ (C11-C12-H13)[10]
1289	28.545	1285(m)	ν_{as} (C11-C12)[55] + γ (C10-C8-H9)[16] + γ (H6-N5-C11)[11]
1318	1.7028	1330(m)	β (C10-C8-H9)[68] + β (C12-C11-N5)[16]
1408	22.531	1410(sh)	β (C11-C10-N2)[21] + β (N1-C14-H15)[16] + β (C11-C12-H13)[14]
1480	72.080	1465(s)	β (H9-C8-N1)[41] + ν_{as} (C14-N1)[17] + ν_{as} (C11-C12)[12]
1554	31.792	1520(vs)	ν_{as} (C11-C12)[43] + γ (H3-N2-H4)[21] + β(C14-C12-H13)[11]
1560	31.374	1565(sh)	ν_s (C10-C11)[68]
1599	135.14	1590(s)	β (H7-N5-H6)[50] + ν_{as} (C11-C12)[18]
1605	28.265	1600(sh)	β (H3-N2-H4)[70]
3009	33.959	3000(m)	ν_s (C8-H9)[99]
3037	10.862	3040(sh)	ν_{as} (C14-H15)[91]
3057	20.209	3050(m)	ν_s (C12-H13)[91]
3381	4.1125	3380(sh)	ν_s (N2-H4)[93]
3411	16.073	3405(sh)	ν_s (N5-H6)[96]
3473	15.144	3475(sh)	ν_{as} (N2-H3)[93]
3509	22.779	3510(sh)	ν_s (N5-H7)[96]

TABLE-4 Comparison of the observed and calculated Vibrational spectra of 4-Amino pyridine with B3LYP/6-311++G (2d, 2p)

B3LYP (CALC.)	I-R (INT.)	EXP. FREQ. I-R (RAMAN)	RAMAN ACTIVITY	VIBRATIONAL ASSIGNMENTS WITH P.E.D. [%]
209	1.4447	-(220)	0.2150	γ (C8-NH_2) [83]
337	14.045	-(-)	0.0167	Ring Tors.
372	0.8911	-(-)	1.0489	Ring Tors.
381	0.0598	-(-)	0.0797	Ring Breathing
475	283.46	475(-)	1.5150	γ (C8-NH_2) [85]
513	5.2678	510(525)	4.9012	β(C11-C9-C8)[52]+β(C11-N1-C5)[14]
528	42.270	535(540)	2.7377	γ (C8-NH_2) [64]
660	0.0111	665(670)	4.4306	γ (C9-C11-N1)[86]
721	0.1988	720(735)	0.2039	Ring Breathing
795	50.525	795(-)	1.8392	Ring Breathing
810	0.0420	815(820)	0.4258	Ring Breathing
820	19.142	825(850)	25.206	β (C11-N1-C5)[65] + ν_s (C8-C9)[15]
933	0.0794	935(-)	0.2419	Ring Breathing
962	0.0016	960(955)	0.0111	Ring Breathing
969	17.380	985(995)	26.677	Ring Bend
1028	0.0027	1015(-)	0.0361	(C8-NH_2) twist [50] +ν_{as} (C7-C8)[23]
1044	0.1050	1050(1050)	4.3293	β(C7-C5-N1)[44]+β(H13-C7-C8)[26]+ ν_{as} (C5-N1)[11]
1092	0.0385	1090(-)	0.2279	β(H10-C9-C11)[42]+ν_{as}(C5-C7)[23] + γ (H3-N2-C8)[21]
1199	25.972	1190(-)	7.9782	γ (H12-C11-C9)[63] + ν_{as} (C5-N1)[20]
1246	11.975	1240(1230)	10.096	Ring Stretch
1275	45.951	1275(1270)	11.447	ν_s (C8-N2)[59] + β(H6-C5-C7)[13]
1333	0.1312	1335(1335)	0.9040	β (H5-C5-N1)[81]
1410	12.220	1430(1435)	1.8409	γ (H10-C9-C8)[42] + ν_{as} (C5-C7)[40]
1477	32.973	1465(-)	4.9495	γ(H12-C11-C9)[58] + β (C9-C8-N2)[15]
1548	31.797	1540(1525)	1.0414	ν_{as} (C8-C9)[67]
1574	153.34	1560(1565)	15.802	ν_s(C9-C11)[30]+β(H10-C9-C8)[22] +ν_{as} (C5-N1)[14]
1604	149.74	1605(1600)	12.990	(H3-N2-H4) scissoring [87]
3032	22.319	3030(3030)	114.40	ν_s (C5-H6)[84]
3034	13.099	3035(3035)	57.260	ν_s (C11-H12)[78]
3058	30.217	3050(3060)	15.555	ν_{as} (C9-H10)[91]
3060	3.5535	3080(-)	288.45	ν_s (C7-H13)[85]
3451	28.835	3445(3445)	186.58	ν_s (N2-H3)[100]
3547	22.673	3550(3550)	54.139	ν_{as} (N2-H4)[100]

Abbreviations:

w-weak; vs.-very strong; s-strong; m-middle; sh-shoulder;ν: stretching; ν_s: symmetric stretching ν_{as}: asymmetric stretching, *β*: -in plane bending; *γ:* out of plane bending, τ: torsion, F.C.: force constant.

HOMO-LUMO GAP

The HOMO-LUMO gap in 3, 4 DAP is calculated to be 8.6 ev and 5.9 ev in case of 4 AP. The electron withdrawing amino group at both the Meta and Para positions and one amino group at

Para position in case of 3, 4 DAP and of 4AP respectively may be responsible for the lower activity in the former than the later. Furthermore it is also reported in the literature that in the context of their role in multiple sclerosis, 3, 4 DAP has been reported to provide similar improvements in symptoms but its penetration into the brain is very small as compared to 4-AP. The inability of 3, 4-DAP to reach the brain is due to its large HOMO-LUMO band gap as compared to 4-AP. One clinical trial showed that 3, 4-DAP was less effective than 4-AP and produced more side effects such as nausea and abdominal pain [13].

Material and Methods

The experimental and computational methods are given in this section to analyze 3, 4-DAP and 4-AP.

Experimental

The FTIR and FT-Raman spectra of 4-AP was taken from the Sigma-Aldrich chemicals with a stated purity of greater than 98% in condensed phase [14-15]. The FTIR spectra of 3, 4-DAP was obtained from Prof. Ulli Englert. The observed FTIR and FT-Raman spectra of 4-AP are shown in Fig 3 & 4 and FTIR spectra of 3, 4-DAP is shown in Fig. 5.

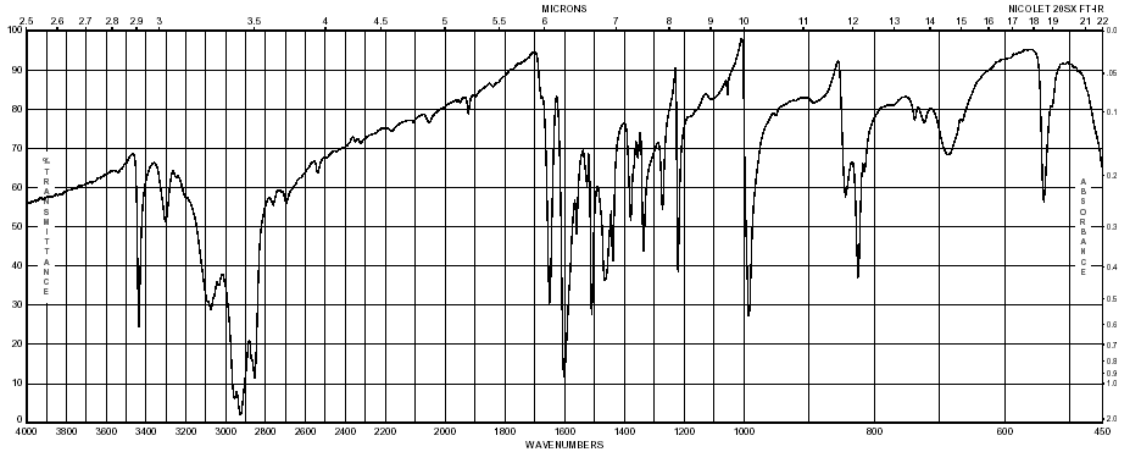

Fig 3 FTIR spectra of 4-AP

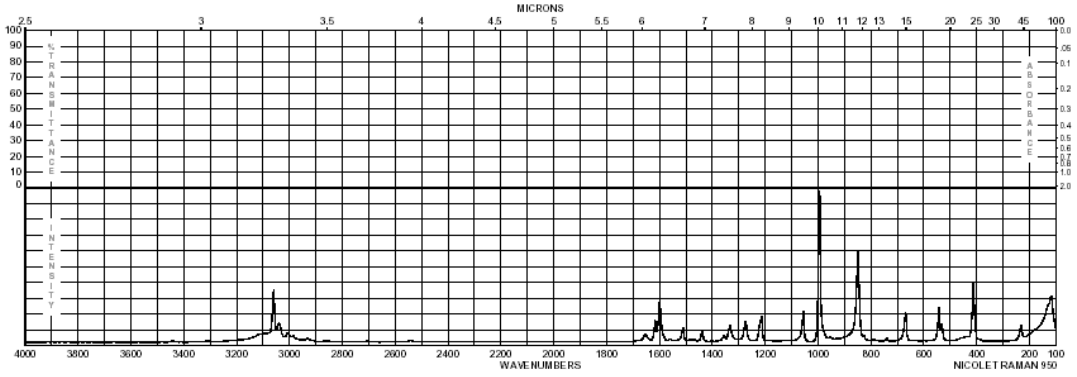

Fig 4 FT-Raman spectra of 4-AP

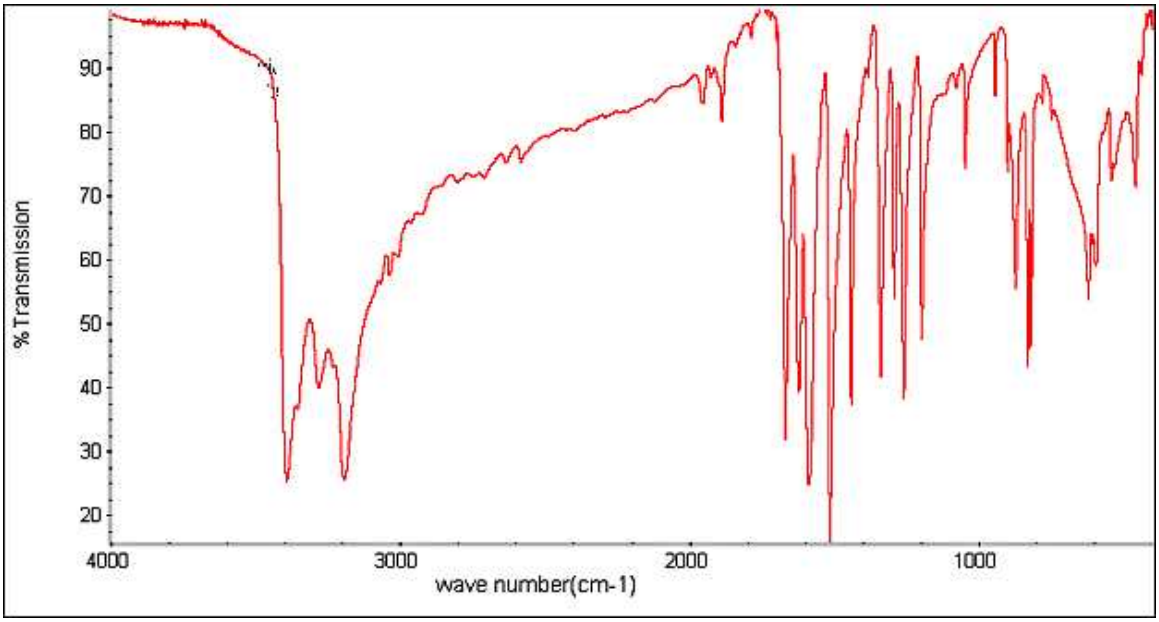

Fig 5 FTIR spectra of 3, 4 DAP

Computational details

Initial geometry was generated from standard geometrical parameters and was minimized without any constraint in the potential energy surface. The gradient corrected Density Functional Theory (DFT) [16] with the three-parameter hybrid functional (B3) [17] for the exchange part and the Lee-Yang-Parr (LYP) correlation function [18] has been employed for the computation of molecular structure, vibrational frequencies, HOMO-LUMO, and energies of the optimized structures, using GAUSSIAN 98 [19]. The calculated vibrational frequencies have also been scaled by a factor of 0.963 [20]. By combining the results of the GAUSSVIEW'S program [21] with symmetry considerations, vibrational frequency assignments were made with a high degree of accuracy. The infrared and Raman spectra were analyzed in terms of the PED contributions using the VEDA program [22].

Conclusion

Attempts have been made in the present work for the proper frequency assignments for 4-AP and 3, 4-DAP from the FTIR and FT-Raman spectra. The equilibrium geometries and harmonic frequencies of 4-AP and 3, 4-DAP were determined and analysed at DFT level of theory utilizing 6-311++G (2d, 2p) as the basis set. The vibrational frequency calculation proved that both structures are stable (no imaginary frequency). The difference between the observed and scaled wave number values of most of the fundamentals is very small. Any discrepancy noted between the observed and the calculated frequencies may be due to the fact that the calculations have been actually done on a single molecule in the gaseous state contrary to the experimental values recorded in the presence of intermolecular interactions. The P.E.D. contribution to each of the observed frequency shows the reliability and accuracy of the normal mode analysis.

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