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Raman and Density Functional Study of the S_0 State of Phenothiazine and the Radical Cation of Phenothiazine

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Raman spectra of phenothiazine and its radical cation were obtained. Hartree−Fock (HF) and density functional theory (DFT) ab initio calculations were performed to find optimized structures and computed vibrational frequencies. The ab initio structures are compared to previously reported X-ray diffraction experimental results, and the vibrational frequencies are compared to Raman spectra given here as well as previously reported Raman spectra. We have made vibrational assignments for the observed Raman bands, based on the computed potential energy distribution (PED) and isotopic shifts. Our results indicate that the neutral phenothiazine molecule has a nonplanar structure with ∼153° dihedral angle and the radical cation has a planar (or near planar) structure with ∼180° dihedral angle.

Introduction

Phenothiazine and its derivatives have been investigated because of their interesting pharmacological activity[1−3] and their potential use in solar energy applications.[4] Phenothiazine and related compounds have significant physiological activity (mostly due to their neuroleptic properties) and can be used as tranquilizers.[5] Since phenothiazines have low ionization potentials, there have been suggestions that phenothiazine tranquilizers may be good electron donors and thus act as charge or electron transfer donors at drug receptor sites[6] and the discovery of many phenothiazine charge-transfer complexes gives some support for this idea.[7] An alternative mechanism of biological activity may involve stable radical cations of phenothiazines.[8] Even though phenothiazine by itself lacks pharmacological activity, it provides an important model and reference point for understanding the biological activity of its derivatives and related compounds such as chlorpromazine. Figure 1 presents simple diagrams of the phenothiazine, promazine, and chlorpromazine molecules.

Photoelectron spectra of phenothiazine and its derivatives indicated that the first ionization potential is N-centered, and the second ionization potential of slightly lower energy is S-centered.[9] There is only a small variation in the ionization potentials among the phenothiazine, 10-methylphenothiazine, promazine, and chlorpromazine compounds,[9] and this suggests that there is no direct relationship between the ionization potentials and the neuroleptic activity in this limited series of phenothiazines. The crystal structure of phenothiazine[10,11] shows that the molecule is folded about the N−S axis with the two planes containing the phenyl rings having a dihedral angle of 158.5°. The amount of folding increases for larger substituents on 10-substituted derivatives and chlorpromazine has a dihedral angle of 139.4°. This is consistent with molecular orbital calculations of Pullman and co-workers.[12] The phenothiazine molecule opens up upon formation of its radical cation, and the dihedral angle increases to 172° in the phenothiazine radical cation.[13] Photoionization studies[9] indicated that an increase in the dihedral angle gives better π-orbital overlap between the ring C and N atoms as well as the ring C and S atoms. Furthermore, the photoionization work[9] suggested that the amine part of phenothiazine is pyramidal in the neutral ground state and planar in the radical cation ground state. This is in agreement with the planar structure indicated by ESR spectra of the radical cation of phenothiazine.[14] A number of more recent studies have examined the photooxidation behavior of the phenothiazines and their radical cations using time-resolved laser flash photolysis experiments.[15−17] For example, time-resolved studies on the photoinduced interaction of phenothiazine and 10-methylphenothiazine with chloroalkanes[17] suggested that an electron-transfer or charge-transfer interaction takes place when the transient radical cation is present.

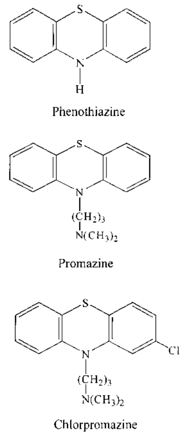

Figure 1. Simple depiction of the structures for phenothiazine, promazine, and chlorpromazine molecules.

Raman and time-resolved Raman spectroscopies can provide detailed information on the structure and dynamics of excited states and radicals which appear in photochemical reactions involving phenothiazines.[18,19] Hester and co-workers[18] have reported the resonance Raman spectra of phenothiazine, 10-methylphenothiazine, and their radical cations. They found that the skeletal deformation δ (CNC) and ring C−N stretching modes are strongly enhanced in the radical cation spectra with the frequencies shifted to higher values compared to the ground state of the parent compounds which suggests that the unpaired

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electron density in the radical cation of phenothiazine is localized on the N atom.[18] Takahashi and co-workers[19] have recently reported triplet and radical cation time-resolved resonance Raman spectra for phenothiazine and 2-chlorphenothiazine and several isotopic derivatives. They concluded that the spin density is localized on the S atom and their assignments of the C−N and C−S stretches were based on the observed isotopic shifts.

In this paper, we report an experimental and theoretical study of phenothiazine and its radical cation in the ground state in order to better understand the conformation and structure of these species. Both Hartree−Fock (HF) and density functional theory (DFT) ab initio methods were used to calculate the structures and vibrational frequencies of the neutral molecule and the radical cation of phenothiazine. The calculated vibrational frequencies are compared to previously reported Raman spectra of phenothiazine and its radical cation as well as an experimental Raman spectra reported here. The vibrational frequency changes upon formation of the radical cation from the neutral parent compound are discussed in conjunction with the calculated electronic structures. Vibrational mode assignments are reported based on the calculated PED and isotopic shifts.

Experimental Section

The experimental apparatus and methods for acquiring time-resolved resonance Raman spectra have been reported elsewhere,[20−22] so only a short description will be given here. The pump (309 nm) and probe (503 nm) excitation wavelengths were obtained from the hydrogen Raman shifted laser lines of the third harmonic of a nanosecond Nd:YAG laser. An optical delay of 15 ns was used for the time-resolved resonance Raman experiments. The pump and probe laser beams were lightly focused onto a flowing liquid sample using a near collinear geometry. The Raman scattering was collected using a back-scattering geometry and reflective optics. The Raman signal was then imaged through a depolarizer and entrance slits of a double monochromator and dispersed onto a CCD detector. The CCD signal was acquired (60 × 10 s scans) and readout to a PC computer with 10 to fifteen readouts summed together to obtain the resonance Raman spectrum. The FT-Raman spectrum of phenothiazine in the ground state was taken with a Bio-Rad FT-Raman spectrometer using 1064 nm CW excitation.

Phenothiazine samples and spectroscopic grade methanol and CCl_4 solvents were purchased from Aldrich and used as received. Sample solutions with concentrations of about 6×10^{-3} M in a 10:2 methanol:CCl_4 mixed solvent were prepared. The use of a mixed solvent system served two purposes: fluorescence of phenothiazine is quenched effectively and the radical cation of phenothiazine can be easily formed.[17]

Calculations

Density functional theory (DFT) calculations of the structures, electronic spin properties and the vibrational frequencies of phenothiazine and its radical cation were performed using the Gaussian program suites (G94 run on an IBM 9076 SP2 computer and G98W on a PC computer).[23] For comparison purposes, Hartree−Fock (HF) calculations were also done for the ground state of phenothiazine. The DFT calculations were done with Bechke's three-parameter hybrid method using the Lee−Yang−Parr correlation functional (abbreviated as B3LYP).[24] The 6-31G* split-valence polarization basis set was used. The gradients and vibrational frequencies were determined analytically, and no imaginary frequency modes were found at the optimized structures of all the species examined. The vibrational mode descriptions were made using a combination of potential energy distributions (PED) derived from the program NMODE[25] and visual inspection of the normal modes animated using the Molden program.[26] The isotopic shifts of the S-,[34] N-,[15] and D_1-substituted phenothiazines were also calculated (DFT with B3LYP at 6-31G* level) in order to assist in determining the vibrational assignments.

TABLE 1: Structural Parameters for the Ground State of the Neutral Phenothiazine Molecule Calculated Using HF and DFT Methods with a 6-31G* Basis set and a Comparison To Experimental Values Determined by X-ray Diffraction. Bond Lengths Are in angstroms and Bond Angles Are in degrees

parameters	RHF calcd	DFT/B3LYP calcd	X-ray exptl[a]
dihedral angle	151.149	152.23	158.5, 153.3[b]
C−S	1.777	1.786	1.762, 1.770[b]
C−N	1.401	1.406	1.399, 1.406[b]
C_1-C_2	1.385	1.395	1.391
C_2-C_3	1.392	1.406	1.397
C_3-C_4	1.389	1.400	1.385
C_4-C_5	1.384	1.395	1.390
C_5-C_6	1.384	1.395	1.367
C_6-C_1	1.385	1.396	1.367
N−H	0.996	1.012	1.09
C_1-H_1	1.075	1.086	0.93
C_4-H_4	1.077	1.088	0.98
C_5-H_5	1.075	1.086	1.05
C_6-H_6	1.075	1.086	0.98
C_2-S-C_8	99.072	99.603	100.9, 99.6[b]
C_3-N-C_9	120.83	121.636	124.4, 121.5[b]
C_3-N-H_{10}	113.77	113.952	114.1
C_3-C_2-S	119.31	119.743	120.9
C_2-C_3-N	120	120.31	120.2
$S-C_2-C_1$	120.602	120.128	119.6
$C_2-C_1-H_1$	119.208	119.119	122.8
$C_1-C_2-C_3$	120.008	120.009	119.2
$C_2-C_3-C_4$	119.205	119,.067	119.5
$C_3-C_4-H_4$	119.524	119.258	118.9
$C_3-C_4-C_5$	120.427	120.581	119.8
$C_4-C_5-H_5$	119.442	119.423	115.8
$C_4-C_5-C_6$	120.354	120.224	120.5
$C_5-C_6-H_6$	120.581	120.566	117

[a] Values are from X-ray diffraction expermental results reported in ref 10. [b] Values are from X-ray diffraction expermental results reported in ref 11.

Results and Discussion

Table 1 presents the structural parameter results of the DFT B3LYP/6-31G* and RHF/6-31G* calculations and compares them to experimental values[10,11] for the ground state of phenothiazine. The dihedral angle between the two lateral rings are 151.149° for the RHF calculations and 152.23° for the DFT calculations. The corresponding dihedral angle from X-ray diffraction experiments have values of 158.5° for the orthorhombic form and 153.3° for the monoclinic form of phenothiazine.[10,11] The calculated results are in closer agreement with the monoclinic form of phenothiazine. Both the calculated and experimental parameters indicate the ground state (S_0) of phenothiazine is folded along the N−S axis. The DFT calculations give C−C and C−H bond lengths that are 0.0059−0.016 Å longer than those of the RHF calculations. There is also a similar trend in the C−S, C−N, and N−H bond lengths. We note that the C−N and N−H bond lengths for the DFT calculations are closer to the experimental values of 1.406 and 1.09 Å than the RHF calculation results. The differences between the calculated and experimental values for the C−H bond lengths is mostly due to the relatively large 0.06 Å

TABLE 2: Structural Parameters for the Ground State of the Radical Cation of Phenothiazine Calculated using HF and DFT Methods with a 6-31G* Basis Set and a Comparison to Experimental Values Determined by X-ray Diffraction. Bond Lengths Are in angstroms and Bond Angles Are in Degrees

parameters	UHF calcd	DFT/B3LYP calcd	X-ray exptl[a]
dihedral angle	180	180	172.2
C−S	1.713	1.75	1.73
C−N	1.369	1.38	1.383
C_1−C_2	1.401	1.405	
C_2−C_3	1.401	1.42	
C_3−C_4	1.405	1.411	
C_4−C_5	1.368	1.381	
C_5−C_6	1.409	1.409	
C_6−C_1	1.363	1.385	
N−H	0.998	1.015	
C_1−H_1	1.0746	1.086	
C_4−H_4	1.075	1.087	
C_5−H_5	1.074	1.085	
C_6−H_6	1.073	1.085	
C_2−S−C_8	104.275	103.504	102.8
C_3−N−C_9	127.503	128.212	121.1
C_3−N−H_{10}	116.248	115.894	
C_3−C_2−S	122.663	122.775	
C_2−C_3−N	121.479	121.367	
S−C_2−C_1	117.246	117.653	
C_2−C_1−H_1	119.291	119.534	
C_1−C_2−C_3	120.091	119.572	
C_2−C_3−C_4	119.086	119.516	
C_3−C_4−H_4	119.442	120.619	
C_3−C_4−C_5	120.065	120.054	
C_4−C_5−H_5	119.481	119.936	
C_4−C_5−C_6	120.893	120.436	
C_5−C_6−H_6	119.998	119.736	

[a] Values are from X-ray diffraction expermental results reported in ref 13.

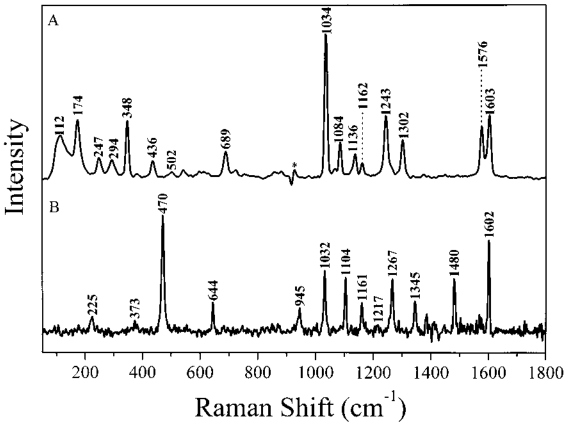

Figure 2. (A) FT-Raman spectrum obtained for neutral phenothiazine molecule in the solution phase. The spectrum has been solvent and background subtracted. The asterisk marks a solvent subtraction artifact. The larger Raman bands are labeled with the value of their Raman shift in cm^{-1}. (B) Time-resolved resonance Raman spectrum of the radical cation of phenothiazine in the solution phase. The spectrum has been solvent and background subtracted. The larger Raman bands are marked with their Raman shift wavenumber.

uncertainty of the experimental values.[10] The 1.084 Å C−H bond length given by Bell and co-workers[11] for the monoclinic form of phenothiazine is in better agreement with the calculated values. Hartree−Fock methods are thought to give C−H bond lengths for closed shell molecules that are ~0.01 Å too short.[27] The bond angles calculated for both DFT and RHF calculations are generally very similar to one another. However, the C−S−C (99.603°) and C−N−C (121.636°) from the DFT calculations agree better with the experimental values of Bell and co-workers[11] for the monoclinic form of phenothiazine.

Table 2 gives the structural parameters for the radical cation of phenothiazine obtained from the DFT (HF/DF) and UHF calculations and compares them to X-ray diffraction experimental values.[13] Both types of calculations yield a nearly planar structure for the radical cation with a dihedral angle of 180° while the experimental dihedral angle is 172.2°.[13] This discrepancy is most likely due to the different molecular system examined in the experimental study (the phenothiazine-nickel-(tfd)$_2$ complex).[13] The radical cation of phenothiazine in the phenothiazine-nickel(tfd)$_2$ complex is very likely noticeably perturbed by the nearby nickel(tfd)$_2$ part of the complex which gives rise to a noticeably different configuration for the radical cation part of the complex compared to a free radical cation of phenothiazine. The shape of the first ionization band in a photoelectron study[9] suggested that the amine part of the phenothiazine molecule is pyramidal in the neutral ground state and planar in the ground state of the radical cation. Similarly, the radical cations of phenothiazine were found to have a nearly planar structure as determined from electron-spin-resonance (esr) experiments.[14] The results of the photoelectron and esr experiments on free radical cations of phenothiazine are consistent with the results of our calculations that indicate the radical cation has a planar (or nearly planar) structure in its ground state. Comparison of the DFT calculated bond distances with those of the UHF calculated ones in Table 2 display similar trends as the DFT and RHF calculated results for the phenothiazine molecule (shown in Table 1).

We have examined the electronic states of the phenothiazine radical cation and found that the HOMO is a bonding π-orbital and the LUMO is an antibonding π-orbital. The DFT calculated C−S and C−N bond lengths (1.75 and 1.38 Å respectively) for the radical cation are noticeably shorter than those found for the DFT results for the phenothiazine molecule (1.786 and 1.406 Å, respectively) and this implies that the HOMO is bonding with respect to the C−S and C−N bonds. Similarly, the C−S−C and C−N−C angles increase significantly in the radical cation (103.504° and 128.212°, respectively) compared to the phenothiazine molecule (99.603° and 121.636°, respectively).

Figure 2A displays the FT-Raman spectrum of phenothiazine in the ground state. Table 3 shows the RHF and DFT/B3LYP calculated vibrational frequencies for phenothiazine and a comparison to the vibrational frequencies observed in our FT-Raman spectrum (Figure 1A). Table 3 also lists the DFT/B3LYP calculated isotopic shifts for S-,^{34} N-,^{15} and D$_1$-substituted phenothiazine and a comparison to the experimental isotopic shifts reported by Takahashi and co-workers.[19] The RHF calculated vibrational frequencies have been uniformly scaled by 0.893 in Table 3. Even with scaling, the RHF calculated vibrational frequencies do not agree very well at higher frequencies (except for the two ring C−C stretches ~1600 cm^{-1}) but are comparable to experimental values in the lower frequency region. In contrast, the DFT/B3LYP calculated vibrational frequencies show reasonable agreement with the experimental values without any scaling. Similar results have been observed in other comparisons of HF and DFT ab initio calculations in other molecular systems.[27,28]

The DFT/B3LYP calculations indicate the ring C−C stretch modes are at 1632 and 1641 cm^{-1} the experimental bands at 1576 and 1603 cm^{-1} can be easily assigned to these two modes. This agrees with previous assignments of both Hester[18] and Takahashi.[19] The ring C−C stretch vibrational mode is assigned to the 1491 cm^{-1} experimental band (1510 cm^{-1} DFT/B3LYP band), and the central ring chair deformation mode is assigned

TABLE 3: Vibrational Frequencies of the Neutral Phenothiazine Molecule Calculated Using HF and DFT/B3LYP Methods with a 6-31G* Basis Set. Calculated Frequencies Are Compared to Experimental Values where Available

				S^{34} substitution		N^{15}substitution	D_1 substitution	
approximate description	calcd RHF	calcd DFT	exptl[a]	DFT	exptl[b]	DFT	DFT	exptl[b]
central ring def[c] (out of plane butterfly like mode)	55	56						
ring def. (out of plane)	117	119	112 m[d]					
central ring boat def	157	163	174 s					
HCCH wag	233	242	247 m					
CSC wag	244	251	294 m	1.5				
central ring chair def	333	346	348 s	1.2				
CSC bend	419	436	436 m	5.7	4			
CSC bend + CNC wag	494	506	502 w	4	2	1.5	6	
N−H bend (out of plane)	557	568	542 w			3.7	13	
ring def	582	609	596 vw			2		
N−H bend (out of plane) + CCC bend	652	677				2.2	17	
ring def	671	695	689 m	2	1			
ring def (out of plane)	724	734	723 w					
C−H bend (out of plane)	752	759						
C−H bend (out of plane) N−H bend (out of plane)	829	866	857 w			6.3	7	
CCC bend + CNC bend	848	894	882 w			7.8	30	
C−H bend (out of plane)	863	927						
C−H bend (out of plane)	947	966	976 vw					
Ring breathing	1013	1062	1034 vs					
CSC sym stretch	1059	1096	1084 m	1	1			
C−H bend	1106	1151	1136 m					
C−H bend	1114	1164	1162 w					
C−H bend	1185	1194						
CNC sym stretch	1212	1274	1243 s			3.5	6	4
CNC asym stretch	1246	1296				4.8	13	
central ring chair def	1270	1357	1302 m				2	2
ring CC stretch	1401	1452				2		
ring CC stretch	1455	1510	1491 vw			4	5	
N−H bend	1500	1550				3.5	16	
ring CC stretch	1582	1632	1576 s				1	1
ring CC stretch	1592	1641	1603 s				2	1
C−H stretch	2981	3173						
C−H stretch	2997	3192						
C−H stretch	3006	3201						
C−H stretch	3020	3215						
N−H stretch	3426	3586				8	370	

[a] This work. [b] Values from experimental data reported in ref 19. [c] def = deformation. wag = wagging. sym = symmetric. asym = asymmetric. [d] Experiment intensity description: vs = very strong, s = strong, m = medium, w = weak, vw = very weak.

to the experimental 1302 cm^{-1} band. The C−N−C symmetric stretch vibrational mode is attributed to the 1243 cm^{-1} experimental Raman band. The DFT/B3LYP calculated isotopic shifts upon D_1 substitution for the three ring C−C stretch modes and the C−N−C symmetric stretch vibrational mode show good agreement with the observed experimental isotopic shifts of Takahashi[19] and give additional support for these assignments. The experimental 1084 cm^{-1} band is assigned to the C−S−C symmetric stretch vibrational mode (DFT calculated frequency of 1096 cm^{-1}), and the isotopic shift upon S^{34} substitution exhibits good agreement between the DFT calculated and experimental values.[19] The experimental 641, 502, and 436 cm^{-1} bands are assigned to the ring deformation mode, the C−S−C bend plus C−N−C wag mode and the C−S−C bend mode, respectively, and the isotopic shift upon S^{34} substitution show good agreement between the experimental and DFT calculated values.[19] The other experimentally observed Raman bands are assigned based on the DFT calculated vibrational frequencies and their assignments are listed in Table 3. For future reference, we have also calculated the isotopic shifts for N^{15} substitution and these are also shown in Table 3. The DFT calculated internal coordinate contributions to the normal modes assigned to the 23 experimentally observed Raman bands are available upon request. We note that our assignment of the 436 cm^{-1} experimental Raman band to the C−S−C bend mode is somewhat different than those previously reported (ring C−S stretch[19] or C−N−C bend[18]).

Figure 2B presents a time-resolved resonance Raman spectrum of the radical cation of phenothiazine. Table 4 lists a comparison of the UHF and DFT/B3LYP ab initio calculated vibrational frequencies with the experimental Raman band frequencies for the radical cation of phenothiazine. Since the UHF and DFT/B3LYP ab initio calculations gave a planar optimized structure for the radical cation of phenothiazine, we have used C_{2v} symmetry in interpreting the transient resonance Raman spectra. Takahashi and co-workers[19] reported eleven bands at 473, 646, 684, 946, 1032, 1102, 1164, 1262, 1341, 1485, and 1602 cm^{-1} in their 517 nm resonance Raman spectrum and tentatively assigned three bands based on isotopic shift data. Our 503 nm spectrum shown in Figure 2B agrees well with Takahashi and co-workers[19] spectrum above 400 cm^{-1} except that we do not observe the 684 cm^{-1} band (this could be due to the different excitation wavelengths used in the two experiments). We observe two additional bands at 225 and 373 cm^{-1} in the resonance Raman spectrum of the radical cation of phenothiazine. The DFT/B3LYP calculated vibrational frequencies agree well with the experimental vibrational frequencies we observe (see Table 4) for the radical cation of phenothiazine. The DFT/B3LYP calculated vibrational frequencies are unscaled and better fit the experimental frequencies than the scaled UHF

TABLE 4. Vibrational Frequencies of the Radical Cation of Phenothiazine Calculated Using HF and DFT/B3LYP Methods with a 6-31G* Basis Set. Calculated Frequencies Are Compared to Experimental Values where Available

				S^{34} substituted		N^{15} substituted	D_1 substituted	
approximate description	calcd UHF	calcd DFT	exptl[a]	DFT	exptl[b]	DFT	DFT	exptl[b]
A_1 N−H stretch	3427	3565				8	327	
C−H stretch	3041	3238						
C−H asym stretch	3031	3226						
C−H stretch	3023	3199						
ring C−C stretch	1580	1621	1602 s[d]					
ring C−C stretch	1473	1531						
ring C−C stretch	1430	1489	1480 w					
ring def. (in plane)	1268	1318	1345 m					
C−N−C sym[c] stretch	1283	1290	1267 s			4	5	5
C−H bend	1156	1212						
C−H bend	1134	1187	1161 m					
C−S−C sym. stretch	1085	1114	1104 s	1.2	2			
ring def. (ring breathing)	996	1060	1032 s	1	1			
CCC bend + CNC bend	831	858				7.9		
CCC bend	666	691				1.2		
CNC bend + CCC bend	626	658	644 m			4	4	3
CSC bend	467	476	470 s	6	7	1	1	3
central ring def. (in plane)	349	360						
central ring def.	225	220	225 w	1				
A_2								
C−H bend (out of plane)	1010	1011						
C−H bend (out of plane)	851	868						
C−H bend (out of plane)	759	776						
C−H bend (out of plane)	690	712						
central ring def. (out of plane)	486	502					28	
CCC wag	435	449						
ring def. (out of plane)	107	107						
B_1								
N−H bend (out of plane)	564	653				3.3	51	
CSC wag	182	179		1.4				
central ring def. (butterfly like mode)	58	55						
B_2 C−H stretch	3015	3212						
ring C−C stretch + N-H bend	1554	1550					45	
C−H bend	1391	1470						
C−N asym. stretch	1330	1390				3.4	24	
C−H bend	1199	1264						
C−H bend	1168	1207	1217 vw					
C−H bend	1104	1162						
C−H bend	1033	1083						
CSC bend asym. stretch + CCC bend	686	706		3.3				
ring def.	581	607				2		
central ring def.	425	445						
central ring def.	368	385	373 vw			1		

[a] This work. [b] Values from experimental data reported in ref 19. [c] def = deformation. wag = wagging. sym = symmetric. asym = asymmetric. [d] Experiment intensity description: vs = very strong, s = strong, m = medium, w = weak, vw = very weak.

calculated vibrational frequencies for the radical cation and this is similar to what we observed for the neutral phenothiazine molecule.

The experimental 1602 and 1480 cm^{-1} bands are assigned to ring C−C stretch vibrational modes (DFT calculated 1621 and 1489 cm^{-1}, respectively). The experimental 1345 cm^{-1} band is assigned to the in plane ring deformation mode (DFT calculated 1318 cm^{-1}). The observed 1267 cm^{-1} band is assigned to the C−N−C symmetric stretch (DFT calculated 1290 cm^{-1}), and the excellent agreement between the calculated and experimental isotopic shift upon D_1 (e.g. N−H becomes N−D) substitution provides further support for this assignment. The observed 1161 cm^{-1} band is assigned to a C−H bend vibrational mode (DFT calculated 1187 cm^{-1}). The experimental Raman bands at 1104, 1032, and 470 cm^{-1} are assigned to the C−S−C symmetric stretch, the ring deformation (ring breathing), and C−S−C bend modes, respectively (with DFT calculated values of 1114, 1060, and 476 cm^{-1}). These assignments are also supported by the good agreement between the calculated and experimental isotopic shifts upon S^{34} substitution shown in Table 4. The observed 644 cm^{-1} Raman band is assigned to a C−N−C bend plus C−C−C bend vibrational mode (DFT calculated value of 658 cm^{-1}) which is further supported by the good agreement between the calculated and experimental isotopic shift upon D_1 (N−H becomes N−D) substitution given in Table 4. The observed 373 and 225 cm^{-1} Raman bands are assigned to central ring deformation modes (DFT calculated values of 385 and 220 cm^{-1}, respectively). We have also assigned the experimental 945 cm^{-1} band to the first overtone of the 471 cm^{-1} mode, and this is consistent with Takahashi's assignment.[19] We note that our assignment of the 471 cm^{-1} Raman band to the C−S−C bend is slightly different from previous assignments to the C−S stretch.[19] The DFT calculated internal coordinate contributions to the normal modes assigned to the 12 experimental Raman bands of the radical cation that we observe in our spectrum shown in Figure 2B are available upon request.

For future reference we have also calculated the DFT/B3LYP isotopic shifts expected upon N^{15} substitution. Inspection of Table 4 shows that some of the DFT calculated isotopic shifts upon D_1 substitution (N−H becomes N−D) are quite large for the A_2 central ring mode (28 cm^{-1} shift), the B_1 out of plane N−H bend (51 cm^{-1} shift), the B_2 ring C−C stretch plus N−H bend (45 cm^{-1} shift), and the C−N asymmetric stretch (24 cm^{-1} shift). If these bands and their shifts could be observed in higher signal-to-noise Raman and/or IR spectra of the radical cation of phenothiazine, this would help test the accuracy of using DFT/B3LYP calculations to predict experimental isotopic shifts as well as test the accuracy of the planar optimized structure we have found for our present calculations.

Comparison of the Raman spectra of the neutral phenothiazine molecule with its radical cation in the S_0 ground state shows that a number of Raman bands increase their vibrational frequencies. The C−S−C bend, the C−S−C symmetric stretch, and the C−N−C symmetric stretch Raman bands increase from 436, 1084, and 1243 cm^{-1} in the neutral molecule to 470 cm^{-1} (a 34 cm^{-1} shift), 1104 cm^{-1} (a 20 cm^{-1} shift), and 1267 cm^{-1} (a 24 cm^{-1} shift) in the radical cation. This suggests that the bond orders of the C−S and C−N bonds increase upon formation of the radical cation from the neutral molecule and the C−S and C−N bonds will be somewhat shorter in the radical cation than in the neutral molecule for phenothiazine. This is consistent with the both the HF and DFT calculations and X-ray experimental results (see Tables 1 and 2). The dihedral angle of the radical cation is 180° for the DFT calculations or 172° for the experimental X-ray study of the phenothiazine radical cation−nickel(tfd)$_2$ complex compared to 152.23° (DFT calculation) to 153.3° (exptl) in the neutral molecule of phenothiazine. Inspection of Tables 3 and 4 shows that the phenyl C−C stretch, ring breathing, and C−H bend modes do not change their frequencies much upon formation of the radical cation from the neutral phenothiazine molecule. This suggests that the dihedral angle change upon formation of the radical cation leads to better π-orbital overlap between the ring C and N atoms, as well as the ring C and S atoms, to give larger aromatic resonance stabilization of the radical cation structure which affects mainly the C−S and C−N bonds electron density compared to the two phenyl rings. Figure 3 shows the DFT calculated electron density (+0.05 contours) for the HOMO of the radical cation. Our results suggests that the HOMO of the radical cation is a π-bonding orbital strongly localized on the S and N atoms. Figure 4 also shows the LUMO electron density given by the DFT calculations, and this appears to be mainly antibonding π*-orbital in character.

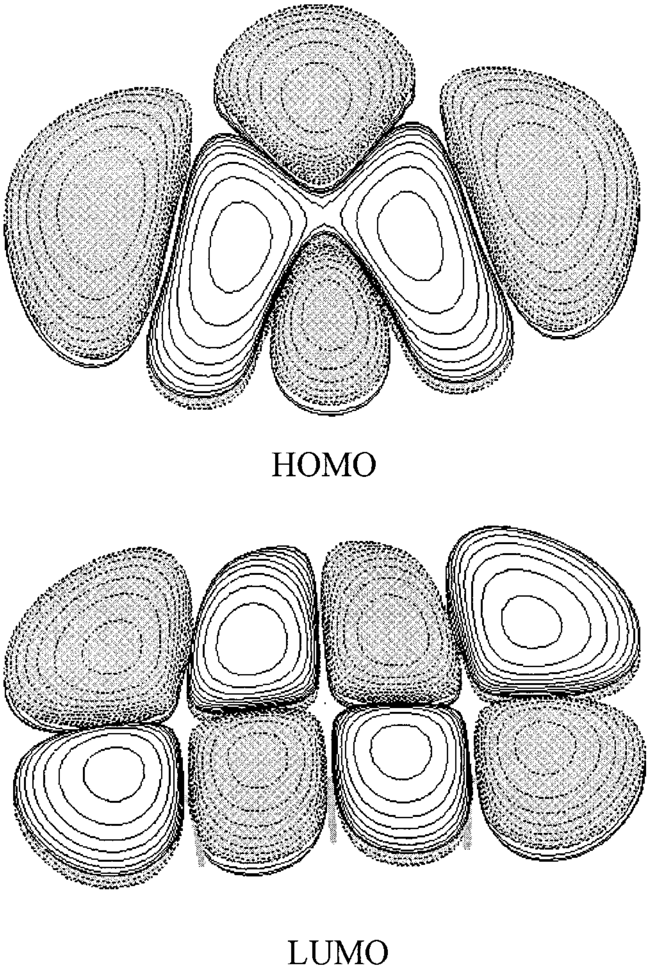

Figure 3. DFT calculated HOMO and LUMO electron density for the radical cation of phenothiazine. The contour number is ± 0.05.

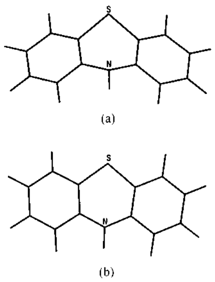

Figure 4. Diagram of the DFT calculated geometries of the nonplanar neutral phenothiazine molecule and the planar phenothiazine radical cation.

We have obtained time-resolved resonance Raman spectra of the ground state radical cation of phenothiazine where the radical cation was generated photochemically and an FT-Raman spectrum of the ground state of the neutral phenothiazine molecule. We have also reported the results of HF and DFT ab initio calculations to elucidate the structure and vibrational assignments of the ground state (S_0) radical cation and neutral molecule of phenothiazine. We have assigned all of the experimentally observed Raman bands for both the neutral molecule and radical cation based on the DFT calculations and a comparison of the calculated (this work) and experimental isotopic shifts upon S^{34} or D_1 substitution where available from previously reported Raman spectra.[19] Our results indicate that the neutral phenothiazine molecule has a nonplanar structure with ∼153° dihedral angle while the radical cation has a planar (or near planar) structure with ∼180° dihedral angle. Figure 4 presents a simple depiction of the DFT calculated geometries for the neutral phenothiazine molecule (Figure 4a) and the radical cation (Figure 4b). The C−S−C bend, C−S−C symmetric stretch, and the C−N−C symmetric stretch Raman bands increase in frequency upon formation of the radical cation from the neutral phenothiazine molecule. This suggests the C−N and C−S bonds become stronger in the radical cation and is consistent with the more planar structure of the radical cation that would give better π-orbital overlap between the ring C and N, as well as the ring C and S atoms, and increased aromatic resonance stabilization. Our present work provides a reference point to which Raman and density functional studies of pharmacological active derivatives such as promazine and chloropromazine can be compared to better understand the structural details of the neutral parent molecules and their radical cations. The amount of folding increases for larger substituents on 10-substituted derivatives; for example, chlorpromazine has a dihedral angle of 139.4°. The variation of the dihedral angle in the structures of phenothiazine and related derivatives such as promazine and chloropromazine and their radical cations may play an important role in the differing degrees of pharmacological activity and toxicity that they display. We are currently working on time-resolved resonance Raman spectroscopy of promazine and chloropromazine in order to better elucidate their structures, and these results will be reported later.

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