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Vibrational Assignments and Electronic Structure Calculations for Chlorambucil

S. GUNASEKARAN†, S. KUMARESAN*, R. ARUN BALAJI† and G. ANAND
Faculty of Physics, Arulmigu Meenakshi Amman College of
Engineering, Vadamavandal-604 410, India
E-mail: yeskay72@yahoo.com

The Fourier transform Raman and Fourier transform infrared spectral measurements made on chlorambucil and were recorded in the solid phase. The equilibrium geometrical structure and harmonic vibrational spectra have been computed at RHF/6-31G(d,p) and B3LYP/6-31G(d,p) levels. A complete vibrational assignment aided by the theoretical harmonic frequency analysis has been proposed. The B3LYP/6-31G(d,p) geometrical parameters and frequencies of the CH_2Cl in the side chains of a cyclohexane are in good agreement with the experi-ment. The observed frequencies are used to compute the thermodynamic functions, namely, the enthalpy and entropy at temperature range 273-400 K and one atmospheric pressure.

Key Words: FTIR, FT-Raman, *ab initio*, Chlorambucil.

INTRODUCTION

Chlorambucil, a biological compound, is used as a chemotherapy drug that is given for treatment of some types of cancer. It is most commonly used to treat chronic lymphocytic leukaemia, low-grade non-Hodgkin lymphoma, Hodgkin lymphoma and ovarian cancer. Chemically, it is 4-[4-*bis*(2-chloroethyl)amino phenyl]butyric acid. It is having nitrogen mustard moiety $(ClCH_2CH_2)_2N$-, which is attached to *p*-position of the benzene nucleus of 4-phenyl butyric acid and L-phenylanin. The reactive groups in the molecule are capable of introducing alkyl groups in the molecule that perform important cellular functions. They may be acting by alkylating and cross-linking guanine and possibly other basis in deoxyribo nucleic acid there by arresting cell division[1-6]. It appears there has been no study on the structure and assignments of chlorambucil by both experimental and theoretical methods. The present work reports infrared and Raman spectral measurements and vibrational assignments for chlorambucil[7]. The assignments are aided by the *ab initio* methods, namely, RHF and B3LYP levels of theory using 6-31G(d,p) basis set. The two *ab initio* methods together have produced

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†Spectrophysics Research Laboratory, Pachaiyappa's College, Chennai-600 030, India.

a geometrical structure in agreement with the one deduced from reported literature[8]. The difference in frequencies due to two CH_2Cl groups in chlorambucil has been accounted for B3LYP more satisfactorily than the RHF. In all the normal modes arising from different coupled vibrations, the ring CH and CH_2Cl stretching vibrations have been shown pure modes; this is also true of the stretching and deformation vibrations of the CH_2Cl group.

EXPERIMENTAL

The chlorambucil sample was purchased from the Lancaster chemical company, UK and used as such for the spectral measurements. The Fourier transform infrared spectrum FT-IR of chlorambucil was recorded in the region 4000-400 cm^{-1} using Perkin-Elmer spectrophotometer equipped with He-Ne laser source, KBr beam splitter and $LiTaO_3$ detector. The sample was prepared by pressing chlorambucil with KBr into pellet form.

The FT-Raman spectrum was recorded on a Bruker IFS-66V model interferometer equipped with an FRA-106 FT-Raman accessory in the 3500-100 cm^{-1} stokes region using the 1064 nm line of an Nd:YAG laser for excitation operating at 200 mW power. The sample was packed in a glass tube of about 5 mm diameter and excited in the 180° geometry. The spectrum was measured with a total of 300 scans at the interval of ± 4 cm^{-1} and optical resolution of 0.1 cm^{-1}.

Computational details: The entire calculations were performed at Hartree-Fock (HF) and B3LYP levels on a Pentium IV/1.6 GHz personal computer using Gaussian 03W program package[9]. The optimized structural parameters were used in the vibrational frequencies calculation resulting in IR and Raman frequencies together with intensities. By combining the results of Chemcraft program[10] with symmetry considerations, vibrational frequency assignments were made with a high degree of accuracy. There is always some ambiguity in defining internal coordination. However, the defined coordinate forms complete set and matches quite well with the motions observed using the Chemcraft program.

RESULTS AND DISCUSSION

Geometrical structure: The optimized bond lengths and angles for chlorambucil at AM1, PM3, RHF/6-31G(d,p) and B3LYP/6-31G(d,p) are represented in Table-1 along with available experimental data[8]. It is seen from Table-1 and Fig. 1 that a general priority for reproducing the experimental bond lengths taken from literature, is not present among AM1 and PM3 methods. However, all bond lengths and bond angles computed with the B3LYP/6-31G(d,p) method shows excellent agreement with available experimental results when compared with AM1 and PM3 levels.

TABLE-1
GEOMETRICAL PARAMETERS OPTIMIZED FOR CHLORAMBUCIL, BOND LENGTH (Å), ANGLE (°)

Parameters	Experimental	AM1	PM3	RHF/6-31G(d,p)	B3LYP/6-31G(d,p)
Bond length					
C_1-C_2	1.511	1.494	1.507	1.511	1.567
C_1-O_5	1.228	1.234	1.218	1.225	1.251
C_1-O_6	1.359	1.364	1.354	1.383	1.426
C_2-C_3	1.526	1.514	1.520	1.536	1.559
C_2-H_{20}	1.116	1.124	1.109	1.097	1.104
C_2-H_{21}	1.115	1.122	1.109	1.097	1.106
C_3-C_4	1.528	1.517	1.522	1.540	1.567
C_3-H_{22}	1.117	1.121	1.115	1.096	1.104
C_3-H_{23}	1.115	1.123	1.108	1.096	1.104
C_4-C_7	1.499	1.488	1.495	1.527	1.542
C_4-H_{24}	1.083	1.124	1.109	1.100	1.104
C_4-H_{25}	1.083	1.123	1.110	1.100	1.104
O_6-H_{26}	0.929	0.971	0.952	0.998	1.030
C_7-C_8	1.361	1.398	1.394	1.402	1.414
C_7-C_{12}	1.362	1.399	1.397	1.399	1.415
C_8-C_9	1.354	1.391	1.389	1.391	1.407
C_8-H_{27}	1.064	1.101	1.096	1.086	1.099
C_9-C_{10}	1.367	1.409	1.399	1.411	1.418
C_9-H_{28}	1.097	1.101	1.100	1.082	1.097
C_{10}-C_{11}	1.410	1.411	1.405	1.407	1.418
C_{10}-N_{13}	1.436	1.432	1.447	1.412	1.492
C_{11}-C_{12}	1.393	1.391	1.385	1.394	1.406
C_{11}-H_{29}	1.098	1.102	1.103	1.081	1.098
C_{12}-H_{30}	1.098	1.101	1.101	1.083	1.099
N_{13}-C_{14}	1.472	1.458	1.494	1.469	1.525
N_{13}-C_{17}	1.467	1.455	1.488	1.465	1.517
C_{14}-C_{15}	1.530	1.527	1.519	1.531	1.560
C_{14}-H_{31}	1.120	1.130	1.113	1.095	1.112
C_{14}-H_{32}	1.118	1.128	1.110	1.093	1.105
C_{15}-Cl_{16}	1.176	1.755	1.775	1.087	1.105
C_{15}-H_{33}	1.111	1.116	1.111	1.087	1.105
C_{15}-H_{34}	1.110	1.116	1.107	1.529	1.562
C_{17}-C_{18}	1.529	1.526	1.517	1.104	1.114
C_{17}-H_{35}	1.122	1.131	1.114	1.091	1.105
C_{17}-H_{36}	1.119	1.128	1.113	1.089	1.106
C_{18}-Cl_{19}	1.777	1.750	1.780	1.088	1.105
C_{18}-H_{37}	1.110	1.117	1.104	1.511	1.567
C_{18}-H_{38}	1.109	1.116	1.105	1.225	1.251

Parameters	Experimental	AM1	PM3	RHF/6-31G(d,p)	B3LYP/ 6-31G(d,p)
Bond angle					
C_2-C_1-O_5	128.615	129.678	129.324	126.855	127.876
C_2-C_1-O_6	114.772	113.769	115.098	110.349	109.718
C_1-C_2-C_3	111.826	111.018	111.073	111.135	111.424
C_1-C_2-H_{20}	108.784	107.319	110.917	108.099	108.755
C_1-C_2-H_{21}	109.186	109.604	108.034	108.138	108.204
O_5-C_1-O_6	117.044	116.546	115.574	122.796	122.403
C_1-O_6-H_{26}	111.912	109.714	110.059	108.157	101.860
C_3-C_2-H_{20}	110.319	110.347	110.172	111.277	110.980
C_3-C_2-H_{21}	110.590	110.630	110.616	111.358	109.927
C_2-C_3-C_4	111.823	110.537	110.929	111.639	111.778
C_2-C_3-H_{22}	109.997	109.674	110.750	108.764	109.033
C_2-C_3-H_{23}	109.773	109.607	110.173	108.862	109.446
H_{20}-C_2-H_{21}	106.764	107.813	105.886	106.646	107.423
C_4-C_3-H_{22}	109.539	109.785	109.323	110.244	109.711
C_4-C_3-H_{23}	109.809	109.934	109.966	110.225	109.416
C_3-C_4-C_7	112.638	111.608	112.327	115.204	111.910
C_3-C_4-H_{24}	109.718	109.370	109.927	108.713	109.019
C_3-C_4-H_{25}	109.782	109.363	110.136	108.698	108.969
H_{22}-C_3-H_{23}	106.546	107.242	105.561	106.976	107.352
C_7-C_4-H_{24}	109.754	109.122	110.392	108.594	109.478
C_7-C_4-H_{25}	109.334	110.095	108.161	108.657	109.554
C_4-C_7-C_8	120.853	120.708	120.280	119.391	120.888
C_4-C_7-C_{12}	120.807	120.326	120.525	123.433	120.806
H_{24}-C_4-H_{25}	106.191	107.176	105.671	106.644	107.819
C_8-C_7-C_{12}	118.765	118.961	119.175	117.167	118.295
C_7-C_8-C_9	120.894	120.681	120.529	121.878	121.131
C_7-C_8-H_{27}	120.042	119.871	120.007	119.335	119.500
C_7-C_{12}-C_{11}	121.064	120.934	120.755	121.526	120.981
C_7-C_{12}-H_{30}	119.440	119.545	118.524	120.141	119.525
C_9-C_8-H_{27}	119.104	119.447	119.464	118.785	119.369
C_8-C_9-C_{10}	120.432	120.602	120.295	120.954	120.383
C_8-C_9-H_{28}	119.112	119.224	119.352	118.487	119.398
C_{10}-C_9-H_{28}	120.576	120.174	120.353	120.554	120.219
C_9-C_{10}-C_{11}	118.861	118.498	119.198	117.117	118.654
C_9-C_{10}-N_{13}	121.686	122.743	122.934	121.434	123.593
C_{11}-C_{10}-N_{13}	119.539	118.740	117.788	121.449	117.738
C_{10}-C_{11}-C_{12}	120.247	120.323	120.046	121.331	120.552
C_{10}-C_{11}-H_{29}	120.470	119.978	120.010	119.568	119.108
C_{11}-C_{12}-H_{30}	115.886	113.684	114.827	120.633	111.049
C_{14}-N_{13}-C_{17}	117.287	113.998	118.457	121.622	111.857
N_{13}-C_{14}-H_{31}	119.401	119.697	119.943	119.008	120.326
N_{13}-C_{14}-H_{32}	119.534	119.520	120.717	118.318	119.484

Parameters	Experimental	AM1	PM3	RHF/6-31G(d,p)	B3LYP/6-31G(d,p)
N_{13}-C_{14}-H_{31}	115.717	113.458	113.144	116.946	109.740
N_{13}-C_{14}-H_{32}	111.095	112.410	109.556	109.269	110.508
N_{13}-C_{17}-C_{18}	110.264	111.447	108.848	112.358	112.564
N_{13}-C_{17}-H_{35}	110.146	107.934	111.556	108.566	107.718
N_{13}-C_{17}-H_{36}	113.276	113.208	110.178	114.995	111.409
C_{15}-C_{14}-H_{31}	110.710	111.594	111.733	109.464	113.241
C_{15}-C_{14}-H_{32}	109.005	108.693	108.786	108.907	107.856
C_{14}-C_{15}-Cl_{16}	109.465	108.844	110.219	109.904	109.442
C_{14}-C_{15}-H_{33}	109.232	108.508	110.090	109.340	108.422
C_{14}-C_{15}-H_{34}	109.095	109.931	108.258	112.627	111.025
H_{31}-C_{14}-H_{32}	111.749	111.437	111.058	112.466	111.727
Cl_{16}-C_{15}-H_{33}	112.111	111.438	111.872	107.340	108.060
Cl_{16}-C_{15}-H_{34}	106.739	107.538	106.525	111.311	109.868
H_{33}-C_{15}-H_{34}	107.931	107.003	108.859	106.069	107.367
C_{18}-C_{17}-H_{35}	107.432	106.967	108.972	109.910	108.630
C_{18}-C_{17}-H_{36}	108.987	109.870	107.764	111.678	110.077
C_{17}-C_{18}-Cl_{19}	107.787	107.127	109.326	112.870	111.958
C_{17}-C_{18}-H_{37}	109.331	108.396	110.146	107.202	108.215
C_{17}-C_{18}-H_{38}	111.868	112.617	109.580	110.921	109.224
H_{35}-C_{17}-H_{36}	109.840	108.842	110.780	126.855	127.876

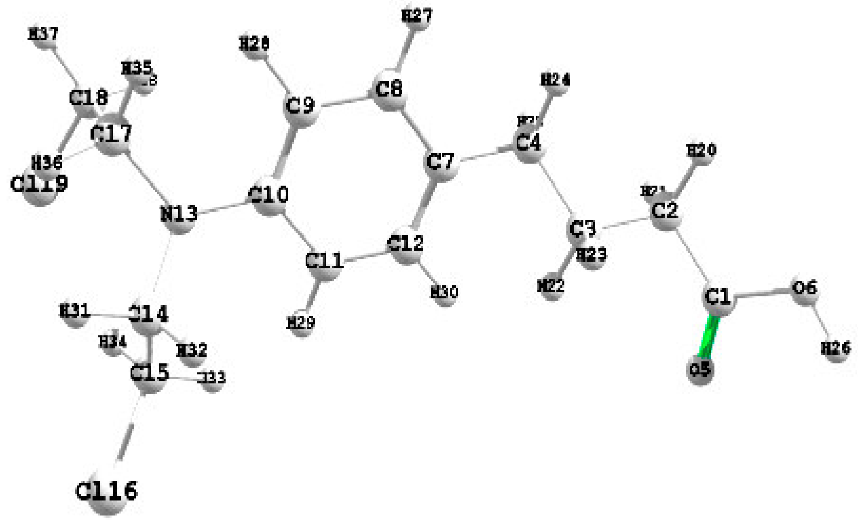


Fig. 1. Optimized structure of chlorambucil

The reduction in bond lengths is more pronounced in PM3 method compared to B3LYP/6-31G(d,p) method. The C-C bond length is slightly overestimated in both the methods where as the C-H bond length is underestimated in PM3 method and slightly overestimated in RHF/6-31G(d,p) method.

Vibrational assignments: According to the theoretical calculations, chlorambucil has a structure of C_1 point group symmetry. The molecule has 38 atoms and 108 modes of fundamental vibrations. All the 108 fundamental vibrations are active in both FT-IR and FT-Raman.

The observed FT-IR and FT-Raman frequencies for various modes of vibrations are presented in Table-2. The harmonic-vibrational frequencies calculated for chlorambucil at AM1, PM3, RHF/6-31G(d,p) and B3LYP/6-31G(d,p) have been presented in Table-3. Comparison of the frequencies calculated at AM1, PM3, RHF/6-31G(d,p) and B3LYP/6-31G(d,p) with the experimental values (Table-2) reveals the overestimation of the calculated vibrational modes due to neglect of anharmonicity in real system. The stick spectra of chlorambucil for AM1, PM3, RHF/6-31G(d,p) and B3LYP/6-31G(d,p) levels have been shown in Fig. 2.

O-H vibrations: The OH group vibrations are likely to be most sensitive to the environment, so they show pronounced shifts in the spectra of the hydrogen-bonded species. The non-hydrogen bonded or a free hydroxyl group absorbs strongly in the 3700-3550 cm^{-1} region. Intra-molecular hydrogen bonding if present in 5 or 6-membered ring system would reduce the OH stretching band[11] to 3550-3200 cm^{-1}. In the present study, a weak band was observed at 3363 cm^{-1} in FTIR for chlorambucil and was assigned to OH stretching vibration.

C-H vibrations: In aromatic compounds, C-H stretching frequencies appear in the range of 3100-3000 cm^{-1}, C-H in-plane-bending in the range of 1300-1000 cm^{-1} and C-H out-of-plane bending vibration in the range 1000-750 cm^{-1}. The vibrations assigned to aromatic C-H stretch[12,13] in the region 3061-3085 cm^{-1} are in agreement with the experimental assignment 3075 cm^{-1}. The frequency at 2977 cm^{-1} has been recorded in both infrared and Raman spectra and it is correlated with frequency calculated at 3042 and 3002 cm^{-1}. With respect to C-H out-of-plane bending vibrations, they are recorded at about 948 in FTIR and 949 cm^{-1} in FT-Raman spectrum of chlorambucil. The corresponding frequencies are calculated at 875 cm^{-1} in RHF/6-31G(d,p) and 912 cm^{-1} in B3LYP/6-31G(d,p).

CH_2 vibrations: A major coincidence of theoretical values with that of experimental evaluations is found in the asymmetric and symmetric vibrations of the methylene (-CH_2) moiety. The -CH_2 wagging mode[13,14] at 1357 cm^{-1} in B3LYP/6-31G(d,p) exactly coincides from the reported value 1350 cm^{-1}. The other vibrations namely CH_2 rocking, CH_2 symmetric bending

TABLE-2
EXPERIMENTAL FT-IR AND FT-RAMAN FREQUENCIES AND TENTATIVE ASSIGNMENTS FOR CHLORAMBUCIL (cm^{-1})

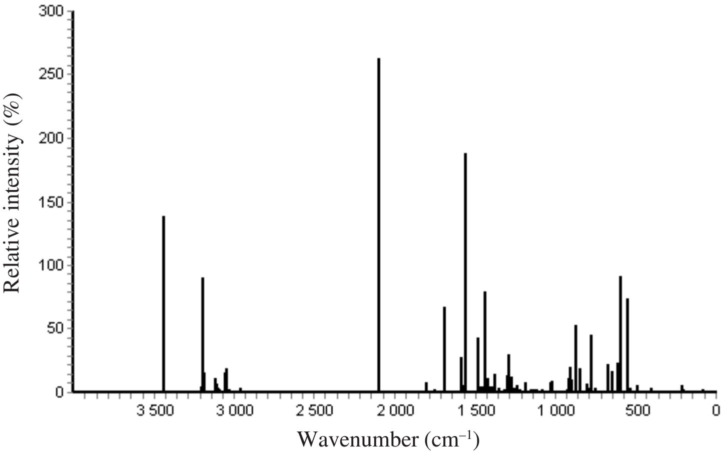
Species	FT-IR frequency and intensity	FT-Raman frequency and intensity	Vibrational assignments
a'	3360 w	3375 w	OH stretch
a'	2977 m	2977 m	CH_2 asymmetric stretch
a'	2926 w	2933 w	CH_2 symmetric stretch
a'	2915 w	2910 w	CH_2 asymmetric stretch
a'	2877 m	2884 s	CH_2 symmetric stretch
a'	1647 w	1640 w	Ring CC asymmetric stretch
a'	1626 m	1620 w	C=O stretch
a'	1555 w	1550 w	CC asymmetric stretch
a'	1518 w	1529 w	HCH asym bend
a'	1506 w	1520 w	HCH asym bend
a'	1475 w	1473 w	ring CC sym. stretch
a'	1455 w	1453 m	CC sym. stretch
a'	1418 m		HCN bend
a'	1387 w	1380 w	CH_2 wagging
a'	1361 m	1373 w	CH_2 wagging
a'	1341 s	1349 m	CN asym. stretch
a'	1308 s		CN sym. stretch
a'	1281 w		HCN bend
a'	1253 s	1265	CC stretch
a'	1225 w	1230 w	CH_2 asymmetric bend
a'	1209 w	1210 w	CH_2 asymmetric bend
a'	1192 w		CH_2 asymmetric bend
a'	1096 w	1094 s	CH_2 symmetric bend
a'	1069 s	1061 m	CH_2 symmetric bend
a'	1044 s	1040 w	CH_2 symmetric bend
a'	1034 s		CC Stretch
a'	988 s	990 w	CCN asym bend
a'	948 w	949 m	CH_2 asymmetric bend
a'	906 w	910 vw	CH_2 symmetric bend
a'	891 s	889 m	CCN bend
a'	876 s	877 s	CCN bend
a'	815 w		HCH bend
a'	701 s	700 w	CNC asym bend
a'	658 m		CCC bend
a'	640 w	642 w	CCl stretch
a'	632 vw	645 vw	CNC sym bend
a'	632 w	630 w	CCC asym. bend
a'	596 w	600 w	CCC asym. bend
a'	565 m	578 w	CCC sym bend
a'	552 s	560 w	CCl sym. stretch
a'	539 m	540 m	CCC sym bend
a'	470	475 s	CCCl bend
a'	460 w	465 m	HCCl bend
a'	435 w	438 s	CCCl bend

TABLE-3
VIBRATIONAL WAVE NUMBERS OBTAINED FOR CHLORAMBUCIL AT AM1, PM3, RHF/6-31G(d,p) and B3LYP/6-31G(d,p) (cm^{-1})

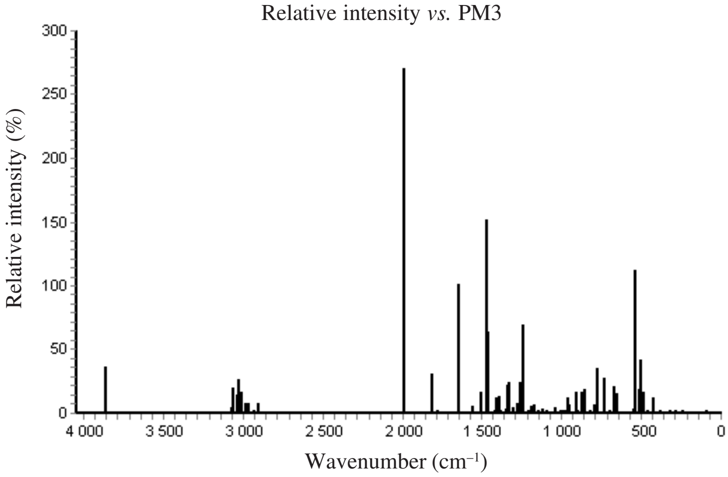
AM1	PM3	RHF/6-31G(d,p)	B3LYP/6-31G(d,p)	Assignments
421	417	432	418	C-C-C / C-N-C out-of-plane bend
441	452	438	430	N-C-C bend
482	473	498	459	C-C-H / C-C-C out-of-plane bend
524	493	502	479	C-N-C bend
539	498	530	512	C-N-C bend
580	529	551	569	C-O-H out-of-plane bend
597	540	571	588	C-O-H/O-C-O out-of-plane bend
634	580	614	606	CCl stretch
663	640	624	646	C-O-H out-of-plane bend
675	651	663	672	O-H out-of-plane bend
737	655	664	731	Ring deformation
769	687	679	770	C-CH_2 / C-C-H out-of-plane bend
776	725	723	779	C-CCl bend
791	764	737	788	Ring C-C-H out-of-plane bend
837	781	775	822	CH_2 wagging
864	809	782	845	C-CH_2 out-of-plane bend
884	844	815	862	C-CH_2 out-of-plane bend
894	861	846	879	C-C-H out-of-plane bend
907	887	851	899	Ring C-H out-of-plane bend
914	893	875	910	C-H out-of-plane bend
983	944	887	912	C-H out-of-plane bend
990	952	899	925	CH_2 sym. stretch/ C-O-H bend
1007	971	934	1003	CH_2 wagging
1013	979	978	1014	Ring C-H out-of-plane bend
1022	992	993	1028	C-H out-of-plane bend
1073	992	1000	1039	Ring C-C-H out-of-plane bend
1087	1028	1022	1075	Ring C-C-H bend
1102	1048	1035	1093	CH_2 out-of-plane bend
1120	1057	1038	1105	CH_2 out-of-plane bend
1124	1068	1053	1113	CH_2 out-of-plane bend
1137	1078	1056	1122	CH_2 in-plane bend
1170	1098	1081	1126	CH_2 in-plane bend
1183	1104	1110	1137	CH_2 in-plane bend
1196	1106	1113	1177	Ring C-C-H bend
1206	1116	1142	1184	Ring C-C-H bend
1208	1126	1181	1204	Ring C-C-H bend
1220	1132	1207	1241	CH_2 rocking
1224	1147	1224	1243	CH_2 rocking
1227	1148	1230	1263	Ring C-C-H bend
1229	1158	1259	1284	N-C-H in-plane-bend/CH_2 rocking
1247	1175	1264	1302	C-C-H in-plane-bend
1259	1199	1272	1306	CH_2 wagging

AM1	PM3	RHF/6-31G(d,p)	B3LYP/6-31G(d,p)	Assignments
1279	1215	1280	1326	CH_2 wagging
1283	1234	1286	1333	CH_2 wagging
1305	1237	1318	1357	CH_2 wagging
1328	1249	1325	1374	CH_2 wagging
1340	1264	1343	1381	CH_2 rocking
1366	1289	1354	1390	CH_2 wagging
1369	1294	1361	1407	C-C-H in-plane-bend/CH_2 wagging
1377	1322	1373	1422	CH_2 wagging
1378	1323	1383	1424	CH_2 wagging
1379	1330	1388	1441	CH_2 wagging
1381	1339	1412	1482	CH_2 scissoring
1391	1373	1419	1484	C-O-H bend/CH_2 scissoring
1398	1376	1422	1492	CH_2 out-of-plane bend
1400	1380	1433	1520	CH_2 wagging
1409	1383	1473	1527	CH_2 rocking/C-C-H bend
1430	1396	1515	1615	CH_2 symmetric bend
1439	1400	1523	1622	CH_2 symmetric bend
1454	1408	1534	1630	CH_2 symmetric bend
1474	1447	1537	1640	C-C stretch
1548	1458	1538	1646	CH_2 symmetric bend
1556	1492	1554	1652	CH_2 symmetric bend
1571	1546	1561	1658	CH_2 symmetric bend
1680	1633	1571	1680	CH_2 rocking/C-C-H bend
1743	1770	1595	1703	C-C stretch/ C-C-C bend
1791	1806	1647	1750	C=O stretch
2086	1978	1783	1878	C-OH bend
2952	2891	2981	3268	CH_2 asymmetric stretch
2959	2910	3023	3292	CH_2 asymmetric stretch
3002	2917	3047	3329	CH_2 asymmetric stretch
3015	2940	3061	3336	CH_2 asymmetric stretch
3025	2953	3067	3341	CH_2 asymmetric stretch
3032	2955	3075	3349	CH_2 asymmetric stretch
3034	2968	3088	3352	CH_2 asymmetric stretch
3042	2978	3120	3429	CH stretch
3042	3002	3121	3432	CH stretch
3076	3006	3130	3435	CH stretch
3087	3016	3148	3445	CH stretch
3093	3018	3152	3448	CH stretch
3097	3021	3177	3452	CH stretch
3103	3022	3200	3460	CH stretch
3175	3024	3214	3462	CH_2 asymmetric stretch
3178	3027	3223	3469	CH stretch
3184	3055	3227	3471	CH stretch
3189	3061	3236	3477	CH_2 asymmetric stretch
3429	3852	3471	3685	OH- stretch

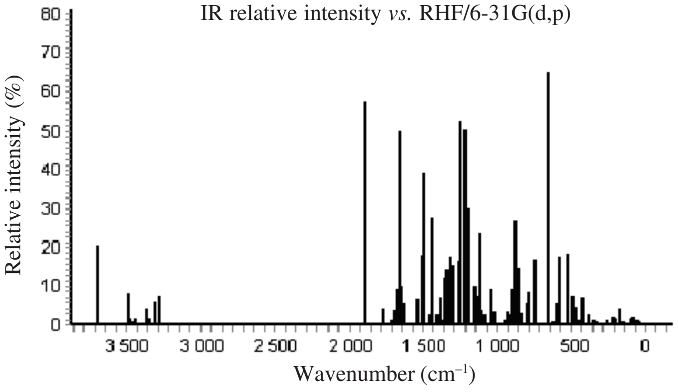
IR relative intensity *vs.* AM1



Relative intensity *vs.* PM3



IR relative intensity *vs.* RHF/6-31G(d,p)



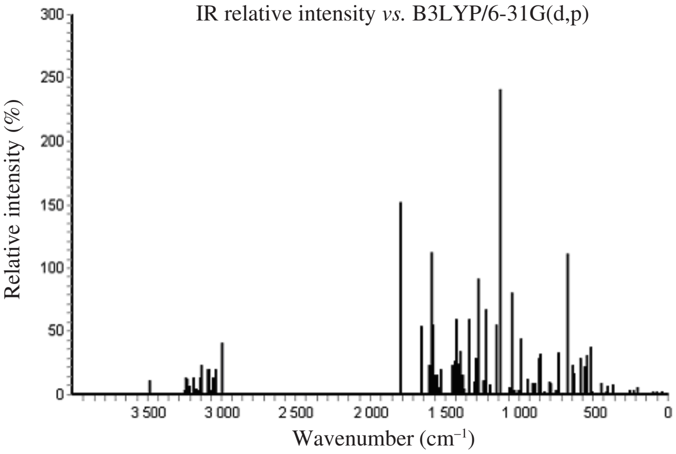


Fig. 2. Comparison of corrected frequencies in cm^{-1} normalized IR intensities at each level of calculations considered

whose theoretically predicted values at 1340 cm^{-1} in AM1 and 1343 cm^{-1} in RHF/6-31G(d,p), 1183 cm^{-1} in AM1 and 1137 cm^{-1} in B3LYP/6-31G(d,p) also coincide exactly with experimentally observed values of 1361 and 1192 cm^{-1}, respectively.

C-C vibrations: The C-C aromatic stretch, known as semi-circle stretching predicted at 1474 cm^{-1} in AM1, 1537 cm^{-1} in RHF and 1640 cm^{-1} in B3LYP/6-31G(d,p) are in excellent agreement with experimental observations of both in FTIR and FT-Raman spectra. The ring deformation[15] at 737 in AM1, 664 in RHF/6-31G(d,p) and 731 in B3LYP/6-31G(d,p) methods coincides satisfactorily with the medium band at 658 cm^{-1} and sharp band at 891 cm^{-1} both in FT-IR spectrum. The theoretically calculated C-C-C out-of-plane bending modes around 430 cm^{-1} have been found to be consistent with the recorded spectral values.

C-Cl vibrations: The vibrations belonging to the bond between the ring and the halogen atoms are worth to discuss here, since mixing of vibrations are possible due to the lowering of the molecular symmetry and the presence of heavy atoms on the periphery of the molecule[16]. But in the present work, the side chain C-Cl bonding was present. The assignments of C-Cl stretching and deformation vibrations have been made by comparison with similar molecules like the halogen substituted benzene derivatives[17]. Mooney[18,19] assigned vibrations of C-X group (X = Cl, Br, I) in the frequency range of 1129-480 cm^{-1}. The FTIR spectrum of chlorambucil the strong band at 552 cm^{-1} is assigned to C-Cl stretching vibration. The theoretical wavenumber of C-Cl stretching vibration coupled with C-C-Cl stretching vibration 634 cm^{-1} in AM1 and 614 cm^{-1} in RHF/6-31G(d,p) coincides well with the experimental values.

Thermodynamic properties: In the study of chemical kinetics and chemical equilibrium, knowledge of the thermodynamic functions is of great importance. The direct experimental measurements of these quantities are usually tedious and may not be reliable. The calculated vibrational frequencies of chlorambucil molecules by semi-empirical methods were utilized to determine the thermodynamical properties due to vibrational contributions such as enthalpy and specific heat capacity in the temperature range 273-400 K at one atmospheric pressure under the usual approximation of molecules being rigid rotator harmonic oscillator. In the present work, we have computed the vibrational contribution to thermodynamic functions alone, by using the standard expressions as given by Colthup[20]. The calculated values of the vibrational contribution to the thermodynamic functions (H_{vib} and Cv_{vib}) for chlorambucil by (AM1 and PM3) are given in Table-4. The computed thermodynamic functions are plotted as a function of temperature and presented in Fig. 3. The enthalpy represents the total energy stored in a system. When a system brought from liquid to vapour state, the enthalpy of the system increases. Similar trend is reflected in specific heat of the molecule as the temperature increases (Fig. 3). It is evident from Table-4 and Fig. 3 that the heat capacity decreases with the increase in temperature.

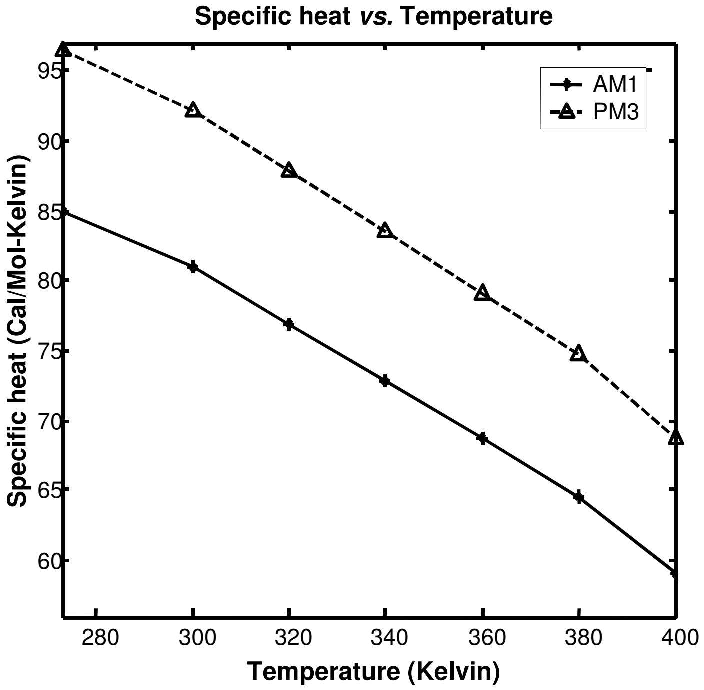


Fig. 3a. Variation of specific heat with temperature

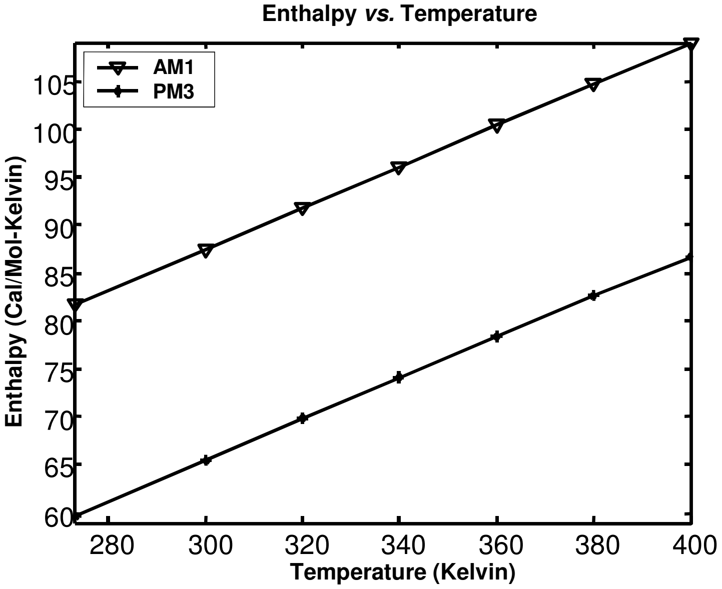


Fig. 3b. Variation of enthalpy of specific heat with temperature

TABLE-4
VIBRATIONAL CONTRIBUTIONS TO ENTHALPY AND SPECIFIC HEAT CAPACITY WITH TEMPERATURE FOR CHLORAMBUCIL

Temp. (Kelvin)	AM1		PM3	
	Enthalpy (Cal/mol-Kelvin)	Specific heat (Cal/mol-Kelvin)	Enthalpy (Cal/mol-Kelvin)	Specific heat (Cal/mol-Kelvin)
273	81.680	84.931	59.707	96.513
300	87.508	80.967	65.557	92.173
320	91.809	76.928	69.894	87.821
340	96.098	72.835	74.197	83.460
360	100.377	68.714	78.436	79.093
380	104.645	64.597	82.587	74.723
400	108.899	59.104	86.633	68.821

Conclusion

Attempts have been made in the present work for proper frequency assignments for the compound chlorambucil from FTIR and FT-Raman spectra. The equilibrium geometries and harmonic frequencies of chlorambucil were determined using semi-empirical methods. The difference between the observed and wavenumber 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. Further, the thermodynamical properties like enthalpy, specific heat shows variations with temperature were studied. Therefore, the assignments made at density functional methods with only reasonable deviations from the experimental values seem to be correct.

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