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FT-IR, FT-Raman, NMR spectra, and molecular structure investigation of C-6 fluoroalkylated pyrimidine: A combined experimental and theoretical study

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Abstract— **The FTIR and FT Raman spectra of C-6 fluoroalkylated pyrimidine were recorded in the regions 4000–400 and 3500–100 cm–1, respectively. The optimized geometry, wavenumber, and several thermodynamic properties of title compound were studied using ab initio Hartree–Fock and DFT methods with basis set 6-31G**. A complete vibrational assignment aided by the theoretical harmonic wavenumber analysis was proposed. The calculated harmonic vibrational frequencies were compared with experimental FTIR and FT Raman spectra. Based on the comparison between calculated and experimental results and the comparison with related molecules, assignments of fundamental vibrational modes were made. The X-ray geometry and experimental frequencies were compared with the results of theoretical calculations. For geometric data, good agreement between theory and experiment is obtained for the HF and B3LYP levels. In addition, 1H- and 13C-nuclear magnetic shielding constants of this compound were calculated by employing the direct implementation of the gauge including-atomic-orbital (GIAO) method at the Hartree–Fock (HF) and DFT using 6-31G** basis set.**

Keywords- C-6 fluoroalkylated pyrimidin, Optimized geometry, Hartree–Fock, Harmonic vibrational frequencies

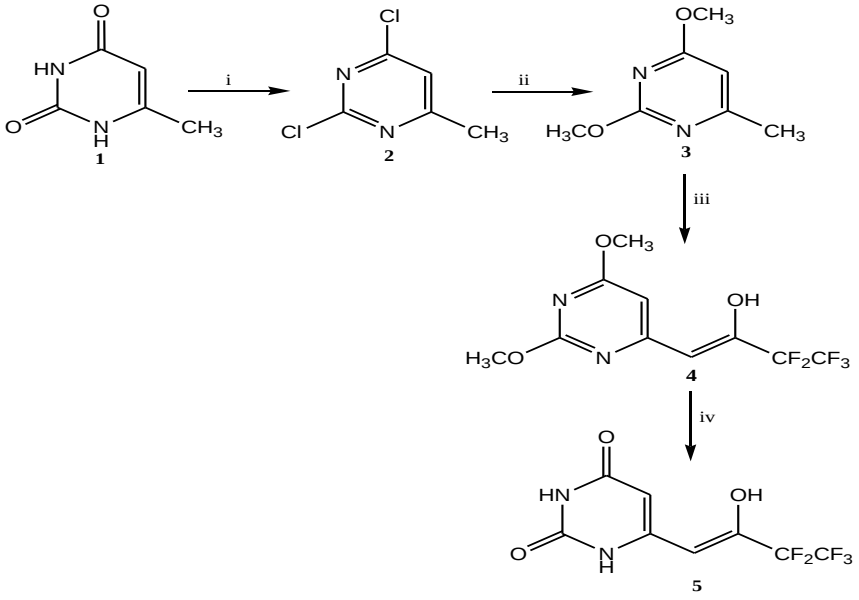
1. Introduction

Fluorine containing compounds are widely used in the synthesis of pharmaceuticals due to their favourable chemical and biological properties such as solubility and bioavailability; they enhance the lipophilicity and thus increase the rate of cell penetration and transport of drug to an active site [1]. The excellent biological activities exhibited by 6-substituted uracil derivatives provide a new emphasis to explore the chemistry and biological activities of these pyrimidine derivatives [2–7]. A large number of acyclic nucleoside analogues showed antiviral activities against herpes viruses due to their selective and efficient activation through monophosphorylation by the viral enzyme in the intact cells [8, 9]. Therefore, radiolabeling of these antiviral agents with the positron-emitting isotope 18F allows in non-invasive imaging of the viral thymidine kinase (TK) enzyme activity by means of positron- emission tomography (PET) [10,11]. Besides, the PET technique has proven to be vital in early detection of cancer and monitoring the efficacy of chemo- or radiotherapy response [12, 13]. Furthermore, we have reported that 18F-radiolabeled C-6 acyclic pyrimidine nucleosides can be

suitable candidates for the development of non-toxic PET-tracer molecules that are specifi- cally and efficiently phosphorylated by the herpes simplex virus type 1 TK [10, 11]. Fluoroalkylated pyrimidine derivatives 4 [7] and 5 were evaluated for their activity against human carcinoma cell lines. Comparison of cytostatic activities of 4 and 5 against acute lymphoblastic leukemia (Molt-4), colon carcinoma (HCT 116 and SW 620), breast carcinoma (MCF-7) and lung carcinoma (H 460) cell lines showed that demethoxylation caused the absence of inhibitory effect of novel 2,4-pyrimidinedione derivative 5. While compound 4 showed moderate activity against cell lines (IC50 = 43–76 lM), its demethoxylated structural congener showed no activity (IC50 > 100 lM).

2. Experimental

Compounds (2–5) were synthesized as illustrated in Scheme 1. Melting points were determined on a Kofler micro hot-stage apparatus (Reichert, Wien) and are uncorrected. The electron impact mass spectra were recorded with an EXTREL FT MS 2002 instrument with ionizing energy of 70 eV. 1H and 13C NMR 1D and 2D spectra were recorded on a Bruker Avance 600 MHz NMR spectrometer, operating at 150.92 MHz for the 13C resonance, and Varian Unity Inova 300 MHz NMR spectrometer. The samples of 4 and 5 were dissolved in CD3OD and DMSO-d6, respectively, and measured in 5 mm NMR tubes. The 1H, 13C and 19F NMR chemical shift values (d) are expressed in ppm and coupling constants (J) in Hz. Proton and carbon chemical shifts are referred to TMS, whereas fluorine chemical shifts are given with respect to CCl3F.



Scheme 1. Reagents and conditions: (i) POCl3; (ii) Na/MeOH; (iii) LDA, THF, ethyl pentafluoropropionate; (iv) NaI, Me3SiCl, MeCN.

3. Calculations Details

All the calculations were performed with the Gaussian 03W program package on a double Xeon/3.2 GHz processor with 8 GB Ram.[12] The molecular structure of the C-6 fluoroalkylated pyrimidine, in the ground state are optimized by using the Hartree-Fock (HF)[13], density functional using Becke's three-parameter hybrid method[14] with the Lee, Yang, and Parr correlation functional methods[15](B3LYP) with the standard 6-31G* [16] and 6-31+G* basis sets. The vibrational frequencies were also calculated with these methods. The frequency values computed at these levels contain known systematic errors [17]. Therefore, we have used the scaling factor values of 0.9135, 0.9163, and 0.9806 and for HF and B3LYP, respectively. We have also calculated optimal scaling factors for all investigated methods. The assignment of the calculated wave numbers

is aided by the animation option of GaussView 3.0 graphical interface for gaussian programs, which gives a visual presentation of the shape of the vibrational modes [18].

4. Results and Discussion

4.1 Geometric parameters

Calculated energies for title molecule, determined by HF and B3LYP/all basis sets are presented in Table 1. As clearly seen from the values given in Table 1, on the calculated energies, there is a little difference between basis sets for 6-311 (or 6-31), use of the basis sets of larger sizes give rise to increases in the differences between the calculated energies of the title molecule. However, when we compared the 6-31 and 6-311 basis sets the difference is large.

Table 1
Calculated energies for C-6 fluoroalkylated pyrimidine by HF and B3LYP methods

Basis sets	HF Energy (Hartree)	B3LYP Energy (Hartree)
6-311+G(d,p)	-1214.9180736	
6-311G(d,p)	-1214.8971629	
6-311G(d)	-1214.8771319	
6-31+G(d,p)	-1214.6410538	-1220.9080026
6-31G(d,p)	-1214.6083582	-1220.848366
6-31G(d)	-1214.5883907	-1220.831411

4.1. Geometric parameters

X-ray diffraction and calculated for the isolated state structures of the C-6 fluoroalkylated pyrimidine molecule with atom numbering are presented in Fig. 1.

The title compound crystallized in monoclinic space group P21/c, with the cell dimensions a = 6.9062 (4) (Å), b = 23.5039 (11) (Å), c= 9.6244 (5) (Å), β= 126.763(6) (◦) and Volume= 1251.55 (Å^3). In 4, two methoxy groups are bonded to pyrimidine ring atoms C-2 and C-4, and a 2-hydroxy-3, 3, 4, 4, 4-pentafluoro-1-butenyl moiety is bonded to the pyrimidine ring atom C-6. In this work, we performed full geometry optimization of the title compound. The main selected bond lengths and angles as well as torsion angles by HF and B3LYP methods with 6–31G (d) and 6-31+G (d) as basis set are collected in Table 1.

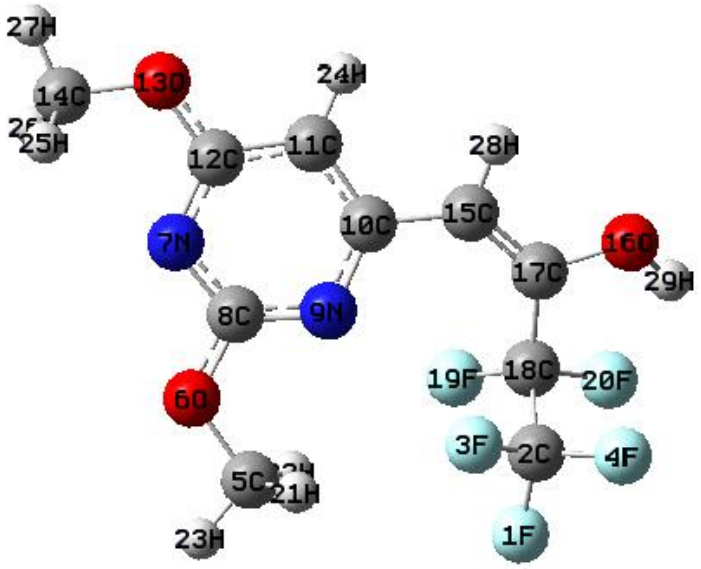


Fig. 1. Optimized molecular structure with the atomic numbering scheme for the title compound.

Table 2
Optimized and experimental Bond Lengths (Å) and Angles (deg) of the C-6 fluoroalkylated pyrimidine

Parameter		HF			B3LYP		Experimental
		6-31g**	6-31+g**	6-311g**	6-31g**	6-31+g**	
Bond lengths (A°)							
1	C8-N9	1.307	1.308	1.305	1.326	1.327	1.330
2	C8-N7	1.329	1.329	1.328	1.344	1.345	1.319
3	C8-O6	1.317	1.316	1.314	1.342	1.341	1.326
4	C5-O6	1.413	1.415	1.412	1.432	1.434	1.441
5	N7-C12	1.304	1.304	1.301	1.325	1.324	1.323
6	C12-O13	1.317	1.317	1.315	1.342	1.342	1.341
7	O13-C14	1.417	1.418	1.416	1.435	1.438	1.437
8	C11-C12	1.402	1.404	1.402	1.406	1.408	1.381
9	C10-C11	1.370	1.370	1.368	1.392	1.392	1.381
10	C10-N9	1.338	1.338	1.336	1.354	1.355	1.363
11	C10-C15	1.479	1.483	1.479	1.463	1.467	1.439
12	C15-C17	1.321	1.321	1.320	1.347	1.347	1.343
13	O16-C17	1.351	1.353	1.351	1.362	1.367	1.319
14	C18-F19	1.321	1.322	1.316	1.344	1.346	1.353
15	C18-F20	1.352	1.351	1.347	1.388	1.389	1.342
16	C2-F1	1.314	1.315	1.310	1.340	1.343	1.300
17	C2-F3	1.309	1.309	1.304	1.335	1.337	1.313
18	C2-F4	1.316	1.316	1.311	1.346	1.348	1.315
Bond angles (°)							
1	N7-C8-N9	127.0	126.9	127.0	127.6	127.4	126.4
2	O6-C8-N9	119.4	119.4	119.4	119.2	119.5	113.3
3	C8-O6-C5	119.1	119.5	119.3	117.3	118.0	117.6
4	O6-C8-N7	113.5	113.5	113.5	113.1	113.0	120.3
5	C8-N7-C12	115.9	116.1	116.1	115.1	115.5	115.6
6	N7-C12-O13	119.8	119.8	119.9	119.6	119.7	118.7
7	C12-O13-C14	118.9	119.2	119.0	117.2	117.7	118.1
8	O13-C12-C11	117.3	117.3	117.3	117.2	117.3	117.4
9	N7-C12-C11	122.8	122.7	122.7	123.1	122.9	123.9
10	C12-C11-C10	115.6	115.5	115.6	116.3	116.3	116.7
11	C11-C10-C15	118.4	118.5	118.2	118.2	117.5	123.7
12	C15-C10-N9	119.4	119.1	119.5	120.3	120.9	116.3
13	C11-C10-N9	122.0	122.2	122.1	121.3	121.4	120.0
14	C10-N9-C8	116.4	116.3	116.4	116.3	116.2	117.4
Torsion angles(°)							
1	C5-O6-C8-N9	-0.9	-0.7	-0.8	-0.3	-0.4	178.4
2	C14-O13-C12-N7	0.0	-0.0	-0.08	0.0	0.1	1.4
3	O16-C17-C18-F19	-157.7	-160.7	-158.5	-147.0	-150.3	178.1
4	O16-C17-C18-F20	-40.2	-43.2	-40.9	-29.6	-32.9	61.2
5	F19-C18-C2-F4	167.6	169.6	167.8	164.7	168.7	71.5

6	F19-C18-C2-F3	-72.0	-69.8	-71.7	-75.6	-71.2	-50.2
7	F19-C18-C2-F1	48.6	50.5	48.8	45.6	49.6	-168.1

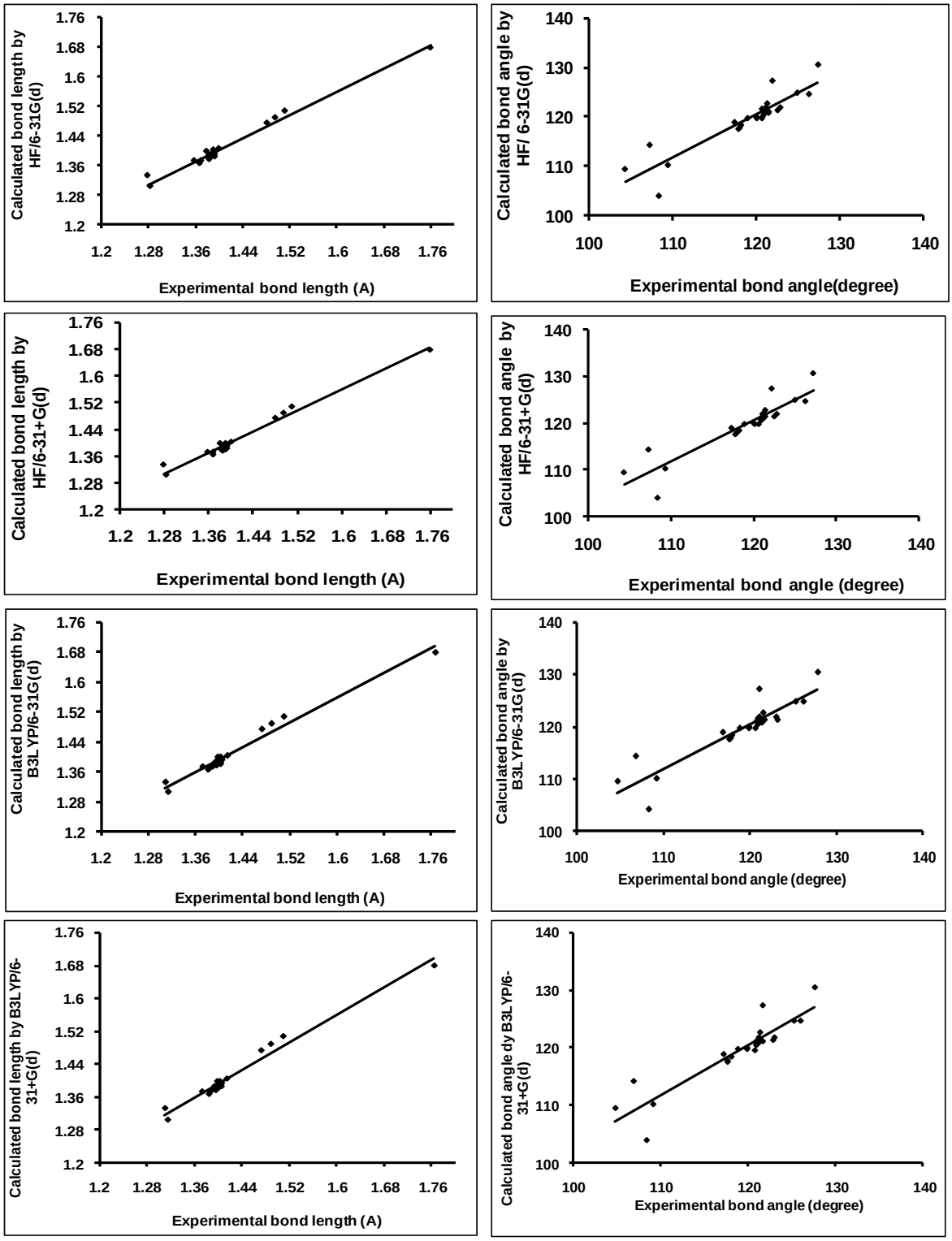


Figure 2a. Calculated bond lengths and bond angles in comparison with experimental data

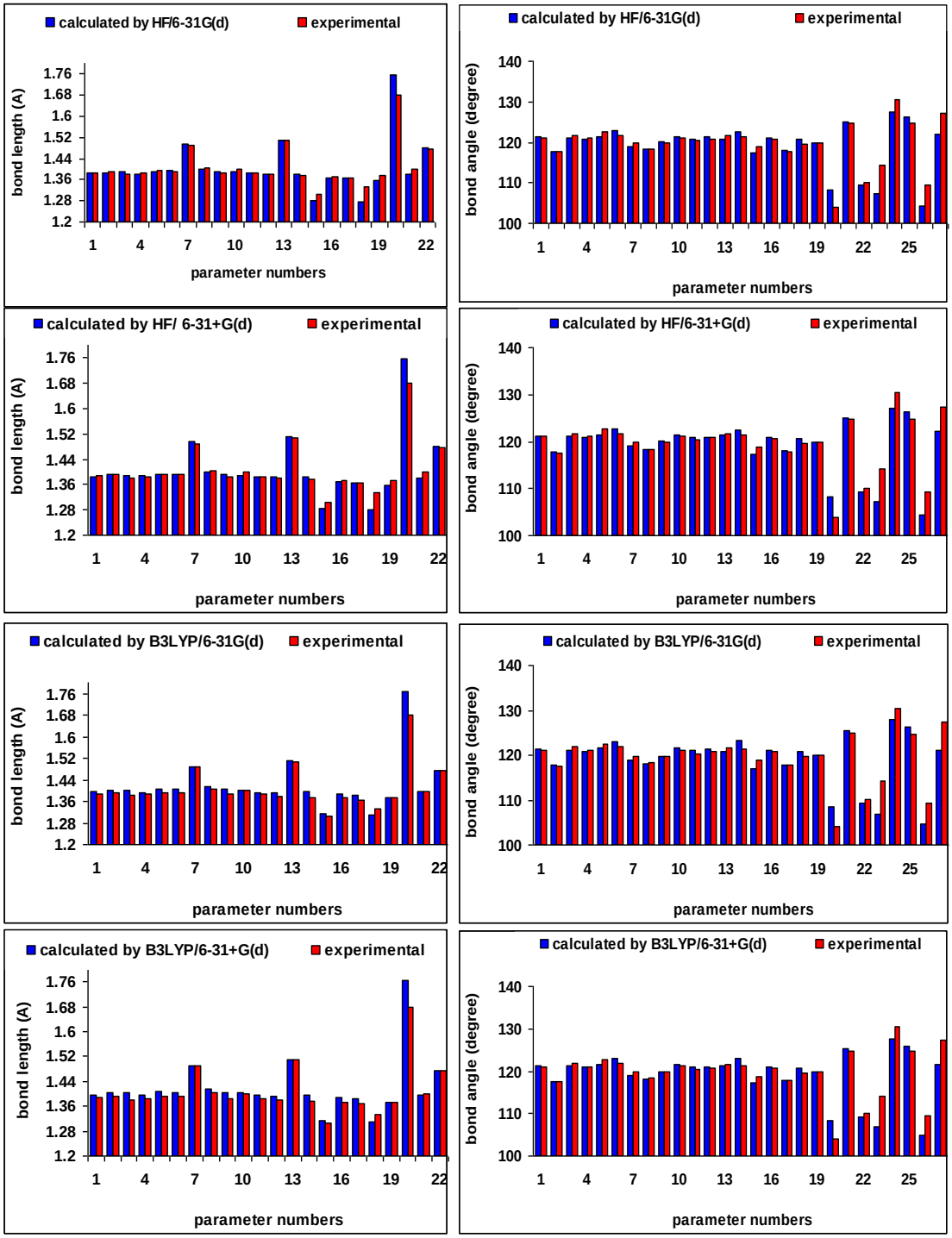


Figure 2b. Calculated bond lengths and bond angles in comparison with experimental data

As follows from this comparison, the bond lengths and angles calculated for title compound show quite good agreement with experimental values. The agreement for bond angles is not as good as that for the bond distances (figure 2a). However, owing to our calculations, DFT method correlates well for the bond length and angle in comparison to the HF method. The largest difference between experimental and calculated HF, DFT (6-31+G*) bond length and angle is about 0.079 A°, 0.086 A° (parameter number 20), -6.96° and -7.34° (parameter number 23) respectively. The results can, however, better be represented in graphical form as has been given in Figure 2b.As a result, the optimized bond lengths and angles by DFT method show the best agreement with the experimental values.

4.2. Vibrational assignments

Using the GAUSSIAN 98 program 1 [14], we first optimize the geometry of C-6 fluoroalkylated pyrimidine with the HF and B3LYP methods and 6-31G (d,p) basis set. Then, we calculate the vibrational frequencies of title compound with the same method and basis set. In order to obtain the spectroscopic signature of C-6 fluoroalkylated pyrimidine molecule, we performed a frequency calculation analysis. Calculations were made for a free molecule in vacuum, while experiments were performed for solid sample, so there are disagreements between calculated and observed vibrational wavenumbers. Experimental and theoretical Raman and Infrared spectra are shown in Figs. 2 and 3, respectively. The experimental wavenumbers are tabulated in Table 3 together with the calculated wavenumbers of studied molecule.Our results are in agreement with experiment. Title compound contains 29 atoms so that, it has 81 normal modes. For C-6 fluoroalkylated pyrimidine molecule, group the vibrational modes can be classified, O–H stretching, C=C and C–H ring stretching, C–O–C stretching, C–F stretching, C=C–H rocking, C=C–H bending, C–Br bending, C=O bending, C–C– C bending, C–C–N bending, C–N–H bending, ring bending, ring breathing, and ring torsion modes. Table 4 show the vibrational frequencies and assignments of the vibrational frequencies (cm^{-1}) of the 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol. To our knowledge, there is no complete, assigned, experimental vibrational spectrum of 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol there exists no information at all. However, several modes for title compound have been assigned and experimental frequencies measured [11]. the vibrational bands assignments have been made by using both the animation option of GaussView 3.0 graphical interface for gaussian programs. The frequency values computed at these levels contain known systematic errors. Therefore, we have used the scaling factor values of 0.9135, 0.9163 and 0.9806 for HF/6-31G*, 6-31+G* and B3LYP/6-31G*, respectively. All quoted vibrational frequencies reported along the paper are thus scaled values. Frequency changes well reflect the geometry changes.

Table 3
Calculated wave numbers for 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol using HF/6-31G (d,p) level [a]

Mode No.	Assignments	Wave number		IR	Red	Force	Raman
		Unscaled	Scaled	Inten.	mass	const.	active
ν1	νO-H		3776.4	2.03E+02	1.0663	10.9398	123.213
ν2	νC-H	80	3088.3	1.84E-01	1.0955	7.5164	78.5033
ν3	νC-H		3038.6	2.74E+00	1.0898	7.2385	62.6614
ν4	νCH3 asym.		3008.7	3.46E+01	1.1090	7.2217	111.346
ν5	νCH3 asym.		3006.0	3.74E+01	1.1088	7.2075	97.0444
ν6	νCH3 asym.		2996.5	3.54E+01	1.1084	7.1599	37.1515
ν7	νCH3 asym.	75	2996.1	2.24E+01	1.1080	7.1553	37.5282
ν8	νCH3 sym.		2919.2	2.69E+01	1.0294	6.3103	230.774
ν9	νCH3 sym.		2919.0	6.33E+01	1.0293	6.3093	12.4748
ν10	νC=C		1744.9	1.33E+02	8.1829	17.9233	409.728
ν11	νN=C-N+N=C-C		1622.2	7.21E+02	9.5158	18.0156	71.9046
ν12	νN=C-N+N=C-C	70	1615.6	6.04E+02	7.9363	14.9025	11.0823
ν13	δCH3		1515.2	1.37E+02	2.655	4.3863	6.3392
ν14	δCH3		1493.0	1.02E+02	1.8946	3.0380	1.7956

ν15	CH2 Scis.		1477.8	2.01E+01	1.0740	1.6875	7.6965
ν16	CH2 Scis.		1476.4	3.49E+01	1.0659	1.6716	11.8649
ν17	CH2 Scis.	65	1471.2	4.44E+00	1.0472	1.6305	18.7360
ν18	CH2 Scis.		1468.7	4.84E+00	1.0466	1.6241	23.6196
ν19	δCH3		1451.9	2.60E+01	2.2669	3.4377	54.0201
ν20	δCH3		1425.1	3.73E+01	1.9747	2.8851	6.6621
ν21	δCH3		1403.6	4.32E+02	2.2074	3.1284	2.8293
ν22	νC-C+δCH3		1390.8	3.19E+02	7.8873	10.9763	2.3893
ν23	δCH3	59	1378.7	2.89E+02	4.4913	6.1418	20.6273
ν24	νC-F		1290.1	2.51E+02	8.6342	10.3378	1.6776
ν25	νC-F+		1286.3	8.78E+01	4.4431	5.2884	3.7805
ν26	δOHC+δHCC		1260.3	4.22E+02	3.9411	4.5036	2.1817
ν27	δOHC		1247.1	7.69E+01	1.5957	1.7855	20.6926
ν28	δOHC+δHCC		1229.1	6.02E+01	2.7275	2.9644	4.7112
ν29	δCH3		1216.2	1.41E+02	3.4252	3.6446	1.5527
ν30	δCH3		1209.0	1.00E+02	2.1373	2.2474	3.8358
ν31			1196.6	3.37E+01	2.2027	2.2690	11.0451
ν32	Twist.CH2	50	1168.6	1.65E+00	1.2686	1.2462	2.8008
ν33	Twist.CH2		1165.9	2.67E+00	1.2666	1.2387	4.2792
ν34	δHCCCH	48	1156.2	4.88E+02	2.6375	2.5365	21.5917
ν35	Twist.CH2+νC-O-C		1136.9	8.74E+01	3.9266	3.6514	5.2255
ν36	δHCC	46	1123.9	6.76E+01	3.2958	2.9950	6.2706
ν37	δHCC+νC-O-C	45	1066.0	4.80E+01	3.3864	2.7684	6.4909
ν38	νCF2-CF3		1039.7	1.80E+02	8.3798	6.5170	3.2654
ν39	ν O-CH3	43	1001.1	1.25E+01	6.4287	4.6353	8.5273
ν40	Ring breathing	42	986.0	1.36E+01	9.4009	6.5754	24.0424

[a] Harmonic frequencies (in cm^{-1}), IR intensities (km mol^{-1}), reduced masses (amu) and force constants (m dyn A^{o-1}). ν, stretching; δ, in-plane bending; γ, out-of-plane bending; ω, wagging; a, asymmetric, s, symmetric; ρ, rocking; Twist., twisting; Scis., scissorings; τ, torsion.

Continue to table 3

Mode No.	Assignments	Wave number Unscaled	Scaled	IR Inten.	Red mass	Force const.	Raman active
ν41	ν O-CH3		950.6	4.60E+01	5.7471	3.7365	5.8948
ν42	γCH	40	913.4	4.43E+01	1.5796	0.9482	30.221
ν43	γCHRing+γCH		845.3	6.57E+01	2.6198	1.3467	0.4842
ν44	γNCN+γCHRing		815.7	4.41E+00	2.8058	1.3431	0.5442
ν45	νCF3+δHCC	37	761.7	1.95E+01	10.4333	4.3555	2.8073
ν46			746.6	3.66E+01	6.8215	2.7353	2.8385
ν47	τHCCRing		723.8	5.39E+00	3.6438	1.3735	0.1356
ν48	τHCCO		708.1	1.86E+01	6.0399	2.1788	2.4276
ν49	τOCC		686.1	1.34E+00	7.4232	2.5139	3.2817
ν50	τHCC		666.0	2.19E+01	5.3089	1.6940	9.5228
ν51			608.8	3.95E+00	10.9707	2.9256	1.9774
ν52	γCCCRing	30	594.6	6.28E+00	6.3370	1.6121	2.9471
ν53	γFCF		572.1	3.38E+00	10.1020	2.3791	3.4975
ν54	γCCC		539.1	4.64E+00	9.7015	2.0287	2.6836
ν55	γCCC		513.5	9.38E+00	8.9137	1.6909	0.8974
ν56	γ CO-CH3		504.6	4.20E+00	8.5885	1.5732	4.5415

ν57	τHCCO	25	461.5	2.17E+01	8.4777	1.2992	0.9303
ν58	δCO-CH3+		452.6	1.02E+01	5.6853	0.8379	1.3544
ν59	τ CF2-CF3		389.5	2.01E+00	11.1976	1.2224	1.1785
ν60	δOH		366.4	1.72E+01	6.9138	0.6679	0.7109
ν61	τHOCC		346.5	1.44E+00	5.7380	0.4958	1.6075
ν62	δOH	20	330.0	1.69E+02	1.2669	0.0993	4.4160
ν63	τHOCC		314.4	1.94E+01	5.5123	0.3922	0.9091
ν64	ωCF2+δFCC		285.5	3.06E+00	12.3249	0.7230	2.7623
ν65	δCO-CH3		272.7	5.83E+00	4.6132	0.2469	2.6270
ν66	γ CO-CH3		260.1	5.68E+00	6.1939	0.3015	0.8966
ν67	Twist. CF2+γ CO-CH3	15	256.6	2.96E+00	7.3096	0.3463	0.7923
ν68	δ CH3+τRing		239.2	8.65E-01	3.0778	0.1268	2.0642
ν69	γ OH+τ CF3		212.3	6.21E+00	10.4287	0.3382	0.0853
ν70	δ CH3		190.	2.24E+00	1.7640	0.0461	1.1403
ν71	δ CH3		188.8	5.47E-01	2.1877	0.0561	0.5819
ν72	δ CO-CH3	10	179.1	5.46E+00	3.3440	0.0772	0.5273
ν73	δ CH3		166.9	4.79E-01	1.2814	0.0257	0.5089
ν74	τ COH		144.3	6.36E-01	9.3960	0.1408	0.5282
ν75	γ CO-CH3		109.2	8.39E-01	4.5643	0.0392	1.8202
ν76	γ CO-CH3		104.9	7.21E+00	3.7033	0.0294	0.3384
ν77	δ CH3		90.1	1.29E-01	5.8740	0.0343	0.8262
ν78	δ OH+δ CH3		67.2	1.90E+00	5.1335	0.0167	0.4930
ν79	δ CF3+δ CH3		54.9	2.78E-01	10.9351	0.0237	0.1264
ν80	δ CF3		37.0	3.44E-02	13.5457	0.0134	0.1706
ν81			14.0	4.71E-02	6.6030	0.0009	1.7649

Harmonic frequencies (in cm^{-1}), IR intensities (km mol^{-1}), reduced masses (amu) and force constants (m dyn A^{o-1}). ν, stretching; δ, in-plane bending; γ, out-of-plane bending; ω, wagging; a, asymmetric, s, symmetric; ρ, rocking; Twist., twisting; Scis., scissorings; τ, torsion.

The simulated scaled and unscaled IR and Raman spectrum obtained from HF/6-31G (d,p) is presented in Figures 4. From the calculated frequencies the higher intensities correspond NH2 wagging, N27-C29 stretching. The strongest bands at 1703.93 cm^{-1} have been assigned to the C=N stretching groups modes. Raman ring C-H symmetry, asymmetry stretching and the symmetrical stretching in CH_3 (CH_3 sym. stretch) modes have dominate intensities.

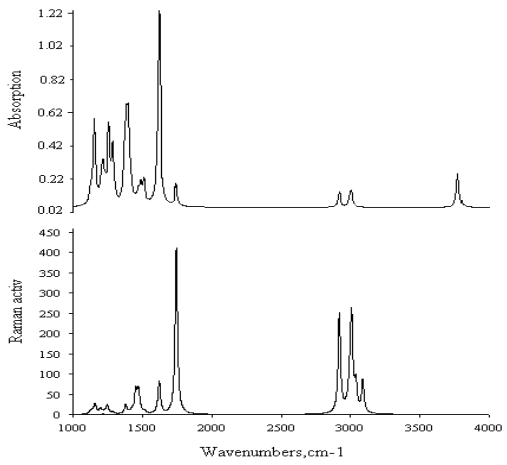


Figure 4. Comparison theoretical Raman and Infrared spectra of C-6 fluoroalkylated pyrimidine computed at HF/6-31G (d,p) level.

Raman spectroscopy requires a change in polarisability, thus is more sensitive to the non-polar motions of the molecule while Infrared spectroscopy requires a change in dipole moment thus is sensitive to the polar motions of the molecule. These two techniques provide information on the heavy atom motions of the molecule, for example νC=C, νC=N.
The very strong bands at 1744.934 cm^{-1} in FT-IR (1714 cm^{-1}, FT-Raman) and 1783 cm^{-1} in FT-IR (1783 cm^{-1}, FT-Raman) spectra were assigned as asymmetric and symmetric C=O stretching vibration, respectively. The theoretically computed values (1764 and 1709 cm^{-1}, B3LYP) show very good agreement with experimental results. The HF method calculated νC=O frequencies higher than the B3LYP method

4.2a C–NH2 vibrations: The molecule under investigation possesses only one NH2 group and hence one expects one symmetric and one asymmetric N–H stretching vibrations in NH2 group. In all the primary aromatic amines, the N–H stretching frequency occurs in the region 3300–3500 cm^{-1}[19]. Hence, the weak bands in IR spectrum were located at 3515.68 and 3418.52 cm^{-1} assigned to N–H asymmetric and symmetric stretching vibrations, respectively in NH2 group. The computed –NH2 scissoring vibration at 1697.27 cm^{-1} in HF/6-31G* is in agreement with the expected experimental value at

4.2b Methyl group vibrations: The title compound 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol, possesses one CH_3 group attached to the benzene ring. There are nine fundamentals one can expect to CH_3 group, namely the symmetrical stretching in CH_3 (CH_3 sym. stretch) and asymmetrical stretching (in plane hydrogen stretching mode); the symmetrical (CH_3 sym. deform) and asymmetrical (CH_3 asym. deform) deformation modes; the in-plane rocking, out-of-plane rocking, twisting and bending modes. For the methyl compounds, the stretching mode appears in the range of 2825–2870 cm^{-1}, lower in magnitude compared to its value in CH_3 compounds (2860–2935 cm^{-1}), whereas the two asymmetric modes for both the types of compounds lie in the same region of 2998–2925 cm^{-1}. The FTIR bands at 2998 and 2925 cm^{-1} and FT-Raman band at 2851 and 2739 cm^{-1} represent the asymmetric and symmetric CH3 stretching vibrations of the methyl group of 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol.

4.2c C=N, C–N vibrations: The identification of C–N vibrations is a difficult task, since the mixing of vibrations is possible in this region. However, by using both the animation option of GaussView 3.0 graphical interface for gaussian programs the C–N vibrations identified. Silverstein [19] assigned C–N stretching absorption in the region 1382–1266 cm^{-1} for aromatic amines. The IR bands appearing at 1510 and 1441 cm^{-1} are assigned to νC=N vibrations and 1374 and 1209 cm^{-1} are assigned to νC–N vibrations with the δCH for the title compound.

4.2d C-S, S–H vibrations: The IR bands appearing at 2697.98 and 1047.82 cm^{-1} are assigned to νS-H vibrations and 945.74 and 161.52 cm^{-1} are assigned to S-H in plane bending vibrations with the out plane for the title compound.

4.3 VCD Spectra

Vibrational Circular Dichroism (VCD) spectroscopy in the Near Infrared (NIR) range was successfully tried long time ago [20], in one case even earlier than the more known and used VCD spectroscopy in the IR range. More recently some advancement has been achieved in developing new instrumentation, based either on dispersive or Fourier transform interferometric technologies [21, 22]. The usability of the NIR-VCD data needs though a parallel advancement in the interpretation of the spectra. Such an interpretation is hampered by many factors, among which two are of utmost importance: the enormous number of modes that may in principle contribute to the overtone regions and the essential role played by anharmonic terms in determining both the wave functions and the functional form of the electric and magnetic dipole moment operators. Necessarily one

has to resort to some kind of approximations. The optical activity of asymmetric molecules is explained when a plane polarized radiation passes through an active medium. The plane of the emergent plane polarized radiation rotates by an angle. The plane polarized beam can be considered as a superposition of two oppositely rotating circularly polarized component. The absorbance coefficient is defined as, $\Delta\varepsilon = \varepsilon_R - \varepsilon_L$[23]. Simulated VCD and absorption spectra of the 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol are plotted in Figure 5. These simulations were obtained with HF/6-31G (d) level calculation.

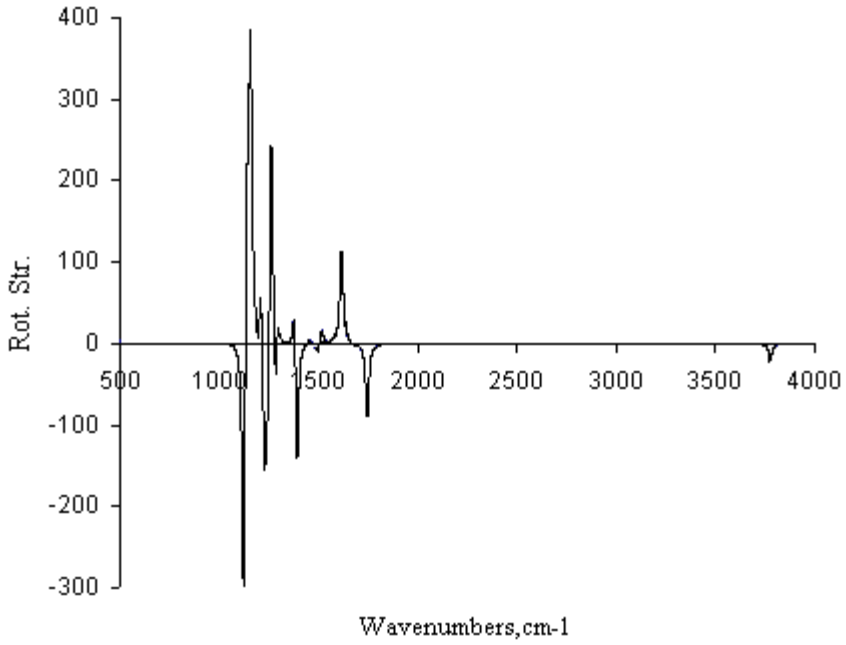


Figure 5. Comparison of a) scaled and b) unscaled computed VCD spectra of the 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol at HF/6-31G (d) level

4.4 ^{1}H and ^{13}C NMR

^{1}H and ^{13}C NMR 1D and 2D spectra were recorded on a Bruker Avance 600 MHz NMR spectrometer, operating at 150.92 MHz for the 13C resonance, and Varian Unity Inova 300 MHz NMR spectrometer. The samples of 4 and 5 were dissolved in CD3OD and DMSO-d6, respectively, and measured in 5 mm NMR tubes. The ^{1}H, ^{13}C and ^{19}F NMR chemical shift values (d) are expressed in ppm and coupling constants (J) in Hz. Proton and carbon chemical shifts are referred to TMS, whereas fluorine chemical shifts are given with respect to CCl3F. The sample temperature was set at 298 K and controlled to approximately ±0.5 K. 1H NMR measurements were performed under the following spectral and processing conditions: 4.0 kHz sweep width, 90_ pulse (11 ls), 2 s relaxation delay, 32 K time domain, zero filling to 64 K and line broadening of 0.5 Hz. 2D NMR spectra: NOESY: 4096 (x2) _ 256 (x1) data points, 16 scans per FID, 32 dummy scans, a pulse delay of 2 s, with mixing time of 150 ms, 4.0 kHz (x2) _ 4.0 kHz (x1) spectral width, transformed after multiplication with a sine-bell squared filter shifted by π/ 2 in both x2 and x1 to give 4 K _ 1 K matrix.

The experimental and calculated values for ^{1}H, ^{13}C and ^{19}F NMR are shown in Tables 3-5. As in Fig. 1, the studied molecule shows teen different carbon atoms, which is consistent with the structure on the basis of molecular asymmetry. ^{13}C and ^{1}H chemical shift values (with respect to TMS) have been calculated for the optimized structures of the title compound and compared to the experimental chemical shift values. As can be seen in Fig. 1, molecular structure of the title compound includes pyrimidine ring. This ring includes nitrogen atoms which show electronegative property. On the other side, oxygen atoms show more electronegative property than nitrogen and carbon atoms. Therefore, the chemical shift values of C12, C10 and C8 have been

observed at 171.331 ppm , 165.456 ppm and 162.018 ppm calculated (with respect to TMS) by using HF method and 165.11 , 155.19, 160.62 by using B3LYP method (in Table 4). Similarly, other carbon peaks of C5, C14, (O–CH3) are observed at 49.882, 48.90 ppm and 53.533, 52.22 ppm calculated by using HF and B3LYP methods, respectively.

As can be seen from Tables 3, 4 and 5 there is a good agreement between experimental and theoretical chemical shift results for the title compound.

Table 3

Experimental and theoretical, ^{13}C NMR isotropic chemical shifts (with respect to TMS) of C-6 fluoroalkylated pyrimidine by HF and DFT (B3LYP) methods.

Atomic specific	^{13}C chemical shifts		Experimental[a]
	HF/6-31G(d,p)[a]	B3LYP/6-31G(d,p)[a]	
C1: C2	106.336	124.887	120.27
C2: C5	49.882	53.533	
C3: C8	162.018	160.62	162.71
C4: C10	165.456	155.19	163.59
C5: C11	95.678	99.501	96.15
C6: C12	171.331	165.11	173.71
C7: C17	142.057	141.85	167.63
C8: C18	102.151	117.06	110.49
C9: C 14	48.90	52.22	
C10:C 15	114.14	110.07	

[a] All values in ppm

Table 4

Experimental and theoretical, ^{1}H NMR isotropic chemical shifts (with respect to TMS) of C-6 fluoroalkylated pyrimidine by HF and DFT (B3LYP) methods.

Atomic specific	^{1}H chemical shifts		Expt.[11]
	HF/6-31G(d,P)[a]	B3LYP/6-31G(d,P)[a]	
H1:(H 21,22,23)	3.79, 3.75, 3.72	3.90, 3.96, 3.68	4.01
H2:(H 24)	6.13	5.98	6.32
H3:(H 25,26,27)	3.83,3.84, 3.67	3.95, 3.96, 3.59	4.07
H4:(H 28)	6.62	6.13	6.47
H5:(H 29)	3.57	4.90	

[a] All values in ppm

Table 5

Experimental and theoretical, ^{19}F NMR isotropic chemical shifts (with respect to CCl3F) of C-6 fluoroalkylated pyrimidine by HF and DFT (B3LYP) methods.

Atomic specific	HF		B3LYP		Expt.[11]
	6-31G(d,P)[a]	6-31G+(d,P)	6-31G(d,P)[a]	6-31G+(d,P)	
F 1	-64.55(16.64)	-56.244(24.95)	-104.51 (23.32)	-97.88(16.69)	-81.19
F 3	-57.81 (23.38)	-50.932(30.26)	-94.48(13.28)	-89.66(8.47)	-81.19
F 4	-59.39 (21.8)	-51.313(29.88)	-97.34 (16.15)	-91.09(9.90)	-81.19
F 19	-98.79 (21.58)	-89.291(31.08)	-137.17 (16.80)	-127.59(7.22)	-120.37
F 20	-105.01 (15.36)	-92.391(27.98)	-143.74 (23.37)	-131.57(11.2)	-120.37

[a] All values in ppm

Changes in values from the corresponding experimental are given in parentheses.

4.5 Thermodynamic properties

The calculated thermodynamic parameters are presented in table 6. Scale factors have been recommended [26] for an accurate prediction in determining the zero-point vibrational energies. The variation in the thermodynamic parameters seems to be insignificant.

Table 6. Calculated dipole moments (D. Mom), zero-point vibrational energy (ZPV) (kcal/mol), thermal energy (E thermal; kcal/mol) and Rotational constants (GHZ) for 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol definitions of theory levels

Theory levels	D. Mom	ZPV	E (Thermal)	Rotational constants		
HF/6-31G(d)	4.867	178.77	188.764	0.331	0.323	0.187
B3LYP/6-31G(d)	4.708	166.08	176.783	0.329	0.322	0.184

5. Conclusions

The results of the study lead to the following conclusions:
(i) The ground state geometries were optimized using the HF and B3LYP methods with the 6-31G (d), 6-31+G (d) basis set and geometries reported within the limits of accuracy of available experimental data. The bond lengths and angles calculated for title compound show quite good agreement with experimental values. The agreement for bond angles is not as good as that for the bond distances.(ii) The frequency assignments performed for the first time from FTIR and FT-Raman spectra recorded were for 2-(4-methyl-2-biphenyl)-4-amino-1,2,4-triazole-3-thiol.(iii) Mulliken charges of dacarbazine at different levels were calculated and the results discussed.(iv) calculated NMR chemical shifts and thermodynamic properties at HF and B3LYP/6-31G(d) levels of 2-(4-methyl-2-biphenyl)-4-amino-1, 2, 4-triazole-3-thiol were discussed and reported.

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