

Electronic Supplementary Information for “Demystifying fluorine chemical shifts: Electronic structure calculations address origins of seemingly anomalous  $^{19}\text{F}$ -NMR spectra fluorohistidine isomers and analogues”.

**Table S1:**  $^{19}\text{F}$  NMR  $\Delta$ ppm values for acid titration of 2F-(5-methyl)-imidazole and 4F-(5-methyl)-imidazole, with different methods and solvation models and both pi and tau tautomers. Here  $\Delta_a = 2\text{F}(\text{H}^+) - 2\text{F}(\tau)$ ,  $\Delta_b = 2\text{F}(\text{H}^+) - 2\text{F}(\pi)$ ,  $\Delta_c = 4\text{F}(\text{H}^+) - 4\text{F}(\tau)$  and  $\Delta_d = 4\text{F}(\text{H}^+) - 4\text{F}(\pi)$ .

Method	Solvation model	$\Delta_a$ ppm	$\Delta_b$ ppm	$\Delta_c$ ppm	$\Delta_d$ ppm
MP2/6-31++g(d)	CPCM	3.82	4.08	9.22	-2.87
BHandHLYP/6-31+g(d)	CPCM	10.28	11.23	8.93	-2.22
BHandHLYP/aug-CC-pVTZ	CPCM	10.63	11.62	9.60	-2.18
BHandHLYP/6-31+g(d)	SMD	7.46	8.49	6.40	-4.15
BHandHLYP/aug-CC-pVTZ	SMD	7.77	8.77	6.94	-4.18
B3LYP/6-31+g(d)	SMD	7.52	8.22	8.21	-2.91
B3LYP/aug-CC-pVTZ	SMD	3.82	8.22	8.92	-2.67

**Table S2:** Polarization of C-F bond in 2-fluoro imidazole analogues and 4-fluoro imidazole analogues. The charges listed here are calculated with ChelpG method on geometries obtained from BHandHLYP/6-311++g(3df,2p) using SMD water solvation model.

<b><math>\tau</math>-tautomer</b>	<b>2F-His</b>	<b>2F-MeIm</b>	<b>2F-Im</b>
<b>Fluorine (F2) ESP charge</b>	-0.264	-0.278	-0.280
<b>Carbon (C2) ESP charge</b>	0.718	0.737	0.712
<b><math>\Delta q</math></b>	0.982	1.015	0.992
<b><math>\pi</math>-tautomer</b>	<b>4F-His</b>	<b>4F-MeIm</b>	<b>4F-Im</b>
<b>Fluorine (F4) ESP charge</b>	-0.290	-0.275	-0.308
<b>Carbon (C4) ESP charge</b>	0.597	0.509	0.651
<b><math>\Delta q</math></b>	0.887	0.784	0.959

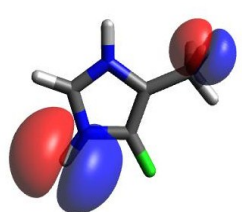
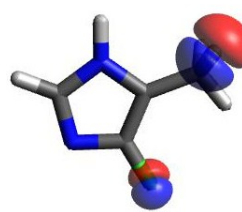
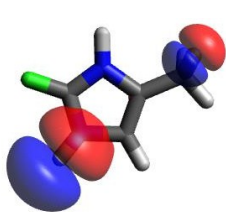
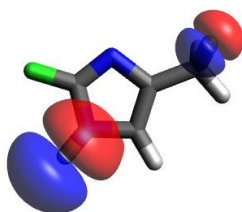
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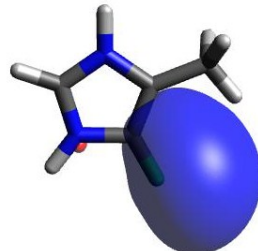
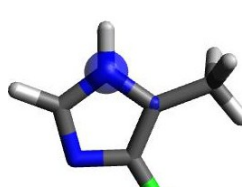
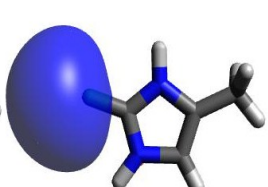
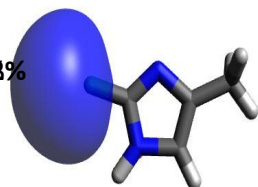
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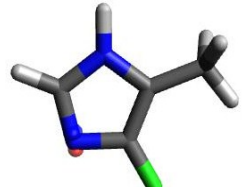
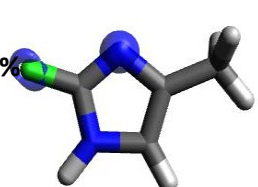
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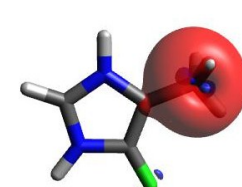
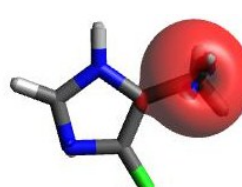
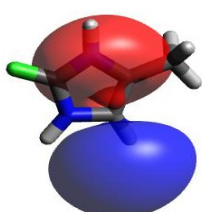
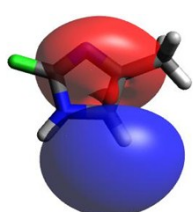
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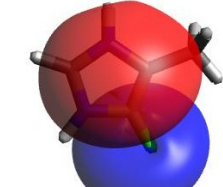
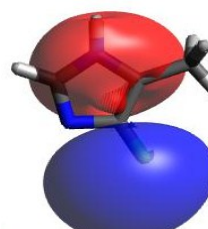
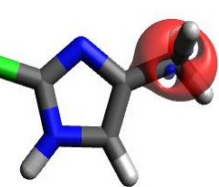
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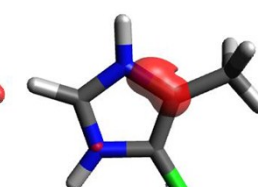
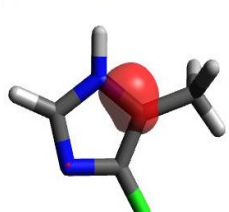
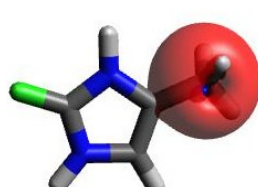
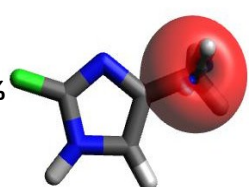
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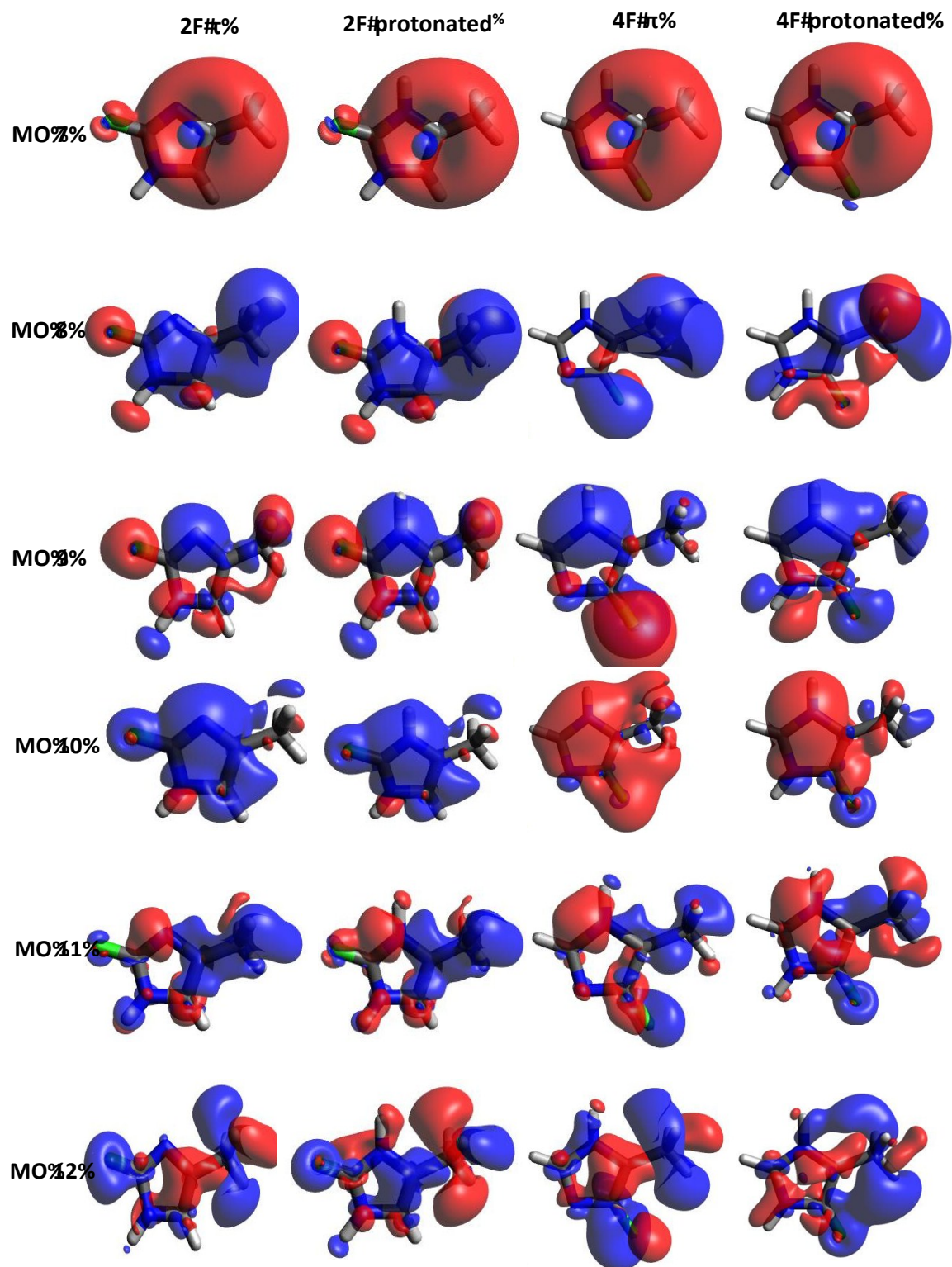


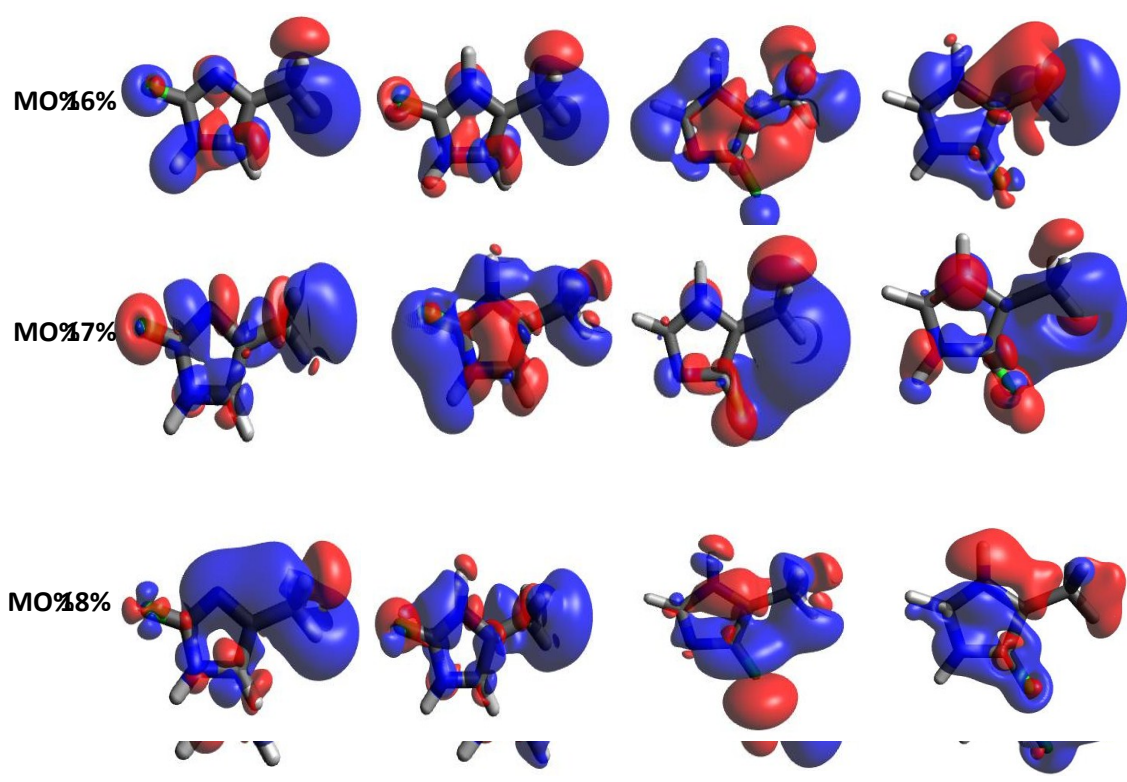
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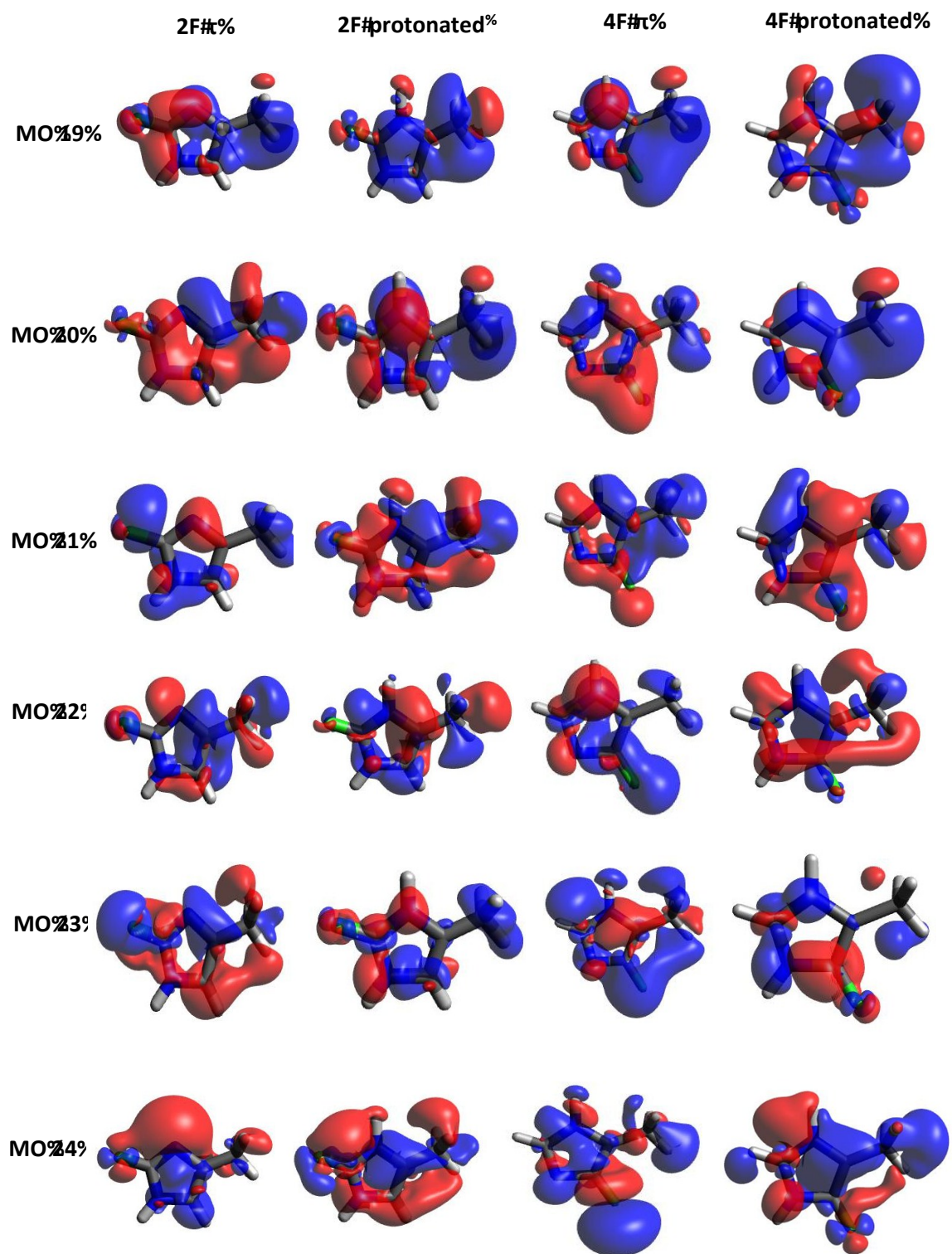


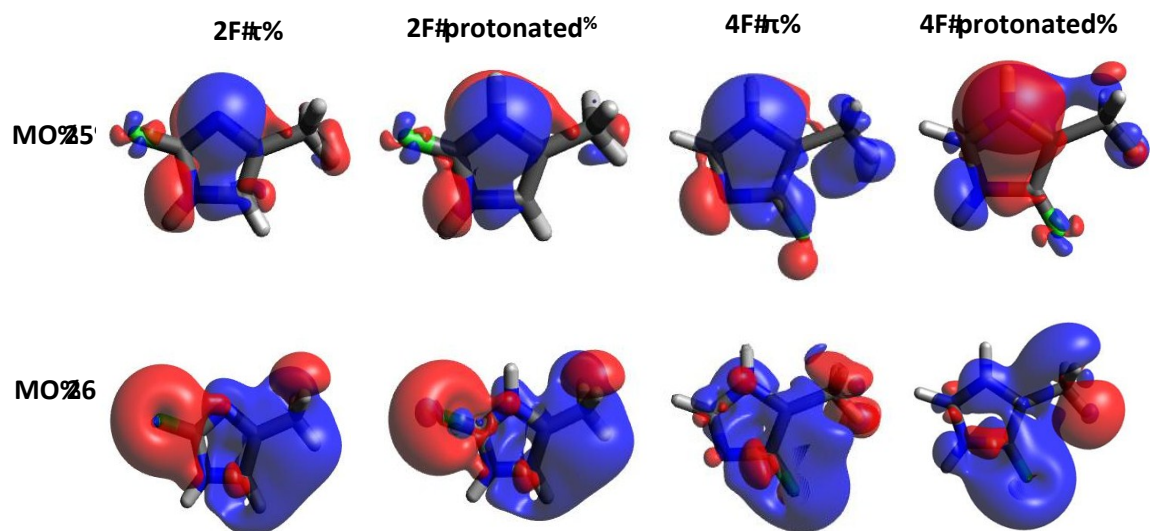
MO6%











**Figure S1:** 2F- and 4F-(5-methyl)-imidazole and –imidazolium molecular orbitals (MOs) with BHandHLYP/6-311++G(3df,2p) method

### Computational Methods: Energies (in Hartree) and geometries

All data presented below come from frequency calculation output, using the following method (command line):

#freq BHandHLYP/6-311++g(3df,2p) SCRF=(smd,solvent=water)

#### 2F-histidine (zwitterionic, $\tau$ -form):

Sum of electronic and thermal Free Energies= -647.811993 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	2.969487	0.127724	-0.105555
2	6	0	1.483660	-0.115520	-0.381304
3	1	0	1.259157	0.157045	-1.401344
4	6	0	0.613678	0.681607	0.584792
5	1	0	0.816916	0.339678	1.595863
6	1	0	0.918595	1.716648	0.526309
7	6	0	-0.839896	0.589411	0.294192
8	6	0	-1.714070	1.581136	0.028023
9	1	0	-1.595598	2.639900	-0.039738
10	6	0	-2.712618	-0.329684	-0.010413
11	9	0	-3.681265	-1.192283	-0.136245
12	7	0	-2.933868	0.968719	-0.164441
13	1	0	-3.812837	1.402848	-0.366751
14	7	0	-1.496639	-0.633062	0.265409
15	8	0	3.411414	1.224880	-0.474167
16	8	0	3.590242	-0.774372	0.477760
17	1	0	1.654813	-1.916070	0.591498
18	1	0	0.188618	-1.723025	-0.166332
19	1	0	1.555654	-2.086252	-1.027710
20	7	0	1.192131	-1.565991	-0.239930

Rotational constants (GHZ): 2.5128416 0.4435697 0.3905306

Standard basis: 6-311++G(3df,2p) (5D, 7F)



## 2F-histidine (zwitterionic, $\pi$ -form):

Sum of electronic and thermal Free Energies= -647.809993 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	2.060744	-0.971818	0.007240
2	6	0	1.647883	0.470355	-0.326486
3	1	0	1.273847	0.469458	-1.341873
4	6	0	0.620283	1.096334	0.615418
5	1	0	0.849277	0.800765	1.634165
6	1	0	0.719372	2.173890	0.567206
7	6	0	-0.792125	0.787885	0.282696
8	6	0	-1.846371	1.595310	0.035764
9	1	0	-1.866265	2.663988	0.022946
10	6	0	-2.577680	-0.358254	-0.105670
11	9	0	-3.332625	-1.412613	-0.275761
12	7	0	-2.986101	0.851897	-0.209015
13	7	0	-1.290932	-0.491917	0.194037
14	8	0	3.264703	-1.240892	-0.106715
15	8	0	1.153445	-1.752593	0.330893
16	1	0	2.723241	2.179599	-0.830532
17	1	0	3.179022	1.519280	0.602292
18	1	0	3.624190	0.786244	-0.783968
19	7	0	2.875235	1.306913	-0.341296
20	1	0	-0.718045	-1.318960	0.258343

Rotational constants (GHZ): 1.9570109 0.5378401 0.4361949

Standard basis: 6-311++G(3df,2p) (5D, 7F)

## 4F-histidine (zwitterionic, $\tau$ -form):

Sum of electronic and thermal Free Energies= -647.803872 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	2.776432	0.389688	-0.104530
2	6	0	1.381465	-0.182588	-0.364443
3	1	0	1.111311	0.000938	-1.394042
4	6	0	0.344067	0.427172	0.569831
5	1	0	0.605724	0.171724	1.593213
6	1	0	0.409800	1.502103	0.482008
7	6	0	-1.043380	-0.007537	0.265534
8	6	0	-2.143607	0.733014	0.040880
9	6	0	-2.682635	-1.347118	-0.116218
10	7	0	-3.182695	-0.101536	-0.198338
11	1	0	-4.130449	0.159435	-0.390958
12	7	0	-1.413085	-1.333453	0.160851
13	8	0	2.935362	1.578871	-0.414669
14	8	0	3.615635	-0.371165	0.401225
15	1	0	1.905482	-1.879260	0.675771
16	1	0	0.456616	-2.018830	-0.128310
17	1	0	1.904393	-2.107068	-0.937969
18	7	0	1.409820	-1.657057	-0.179300
19	9	0	-2.319540	2.032647	0.027232
20	1	0	-3.287332	-2.215969	-0.266073

Rotational constants (GHZ): 1.9788549 0.5182190 0.4242283  
Standard basis: 6-311++G(3df,2p) (5D, 7F)

**4F-histidine (zwitterionic,  $\pi$ -form):**

Sum of electronic and thermal Free Energies= -647.809568 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	2.253077	-0.713724	-0.023311
2	6	0	1.438601	0.559509	-0.301460
3	1	0	1.112382	0.508420	-1.331967
4	6	0	0.245251	0.801845	0.619154
5	1	0	0.529154	0.557656	1.637801
6	1	0	0.011817	1.859594	0.601927
7	6	0	-0.994860	0.087042	0.233836
8	6	0	-2.248351	0.528084	-0.011363
9	6	0	-2.384508	-1.540948	-0.224615
10	7	0	-3.115590	-0.454827	-0.289923
11	7	0	-1.118741	-1.270249	0.091931
12	8	0	3.483674	-0.611524	-0.133710
13	8	0	1.615213	-1.740133	0.250793
14	1	0	1.996550	2.523426	-0.708240
15	1	0	2.529276	1.981785	0.746190
16	1	0	3.259434	1.446394	-0.613297
17	7	0	2.365253	1.718336	-0.218802
18	1	0	-0.330893	-1.892774	0.156344
19	9	0	-2.659368	1.786632	0.015622
20	1	0	-2.736210	-2.534606	-0.401905

Rotational constants (GHZ): 1.8483307 0.5761774 0.4523899

Standard basis: 6-311++G(3df,2p) (5D, 7F)

### 2F-(5-methyl)-imidazole(zwitterionic, $\tau$ -form):

Sum of electronic and thermal Free Energies= -364.653544 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	7	0	0.002130	-0.950300	0.000001
2	7	0	0.811842	1.093873	-0.000002
3	6	0	-1.049221	-0.045332	0.000000
4	6	0	-2.460480	-0.493187	-0.000001
5	6	0	-0.564130	1.214192	-0.000003
6	6	0	1.049747	-0.211184	0.000000
7	1	0	-2.680177	-1.096465	0.874027
8	1	0	-3.127195	0.359000	-0.000005
9	1	0	-2.680174	-1.096473	-0.874024
10	1	0	-1.046733	2.166492	-0.000008
11	9	0	2.276278	-0.661095	0.000003
12	1	0	1.494470	1.825357	0.000019

Rotational constants (GHZ): 7.1447376 2.1146359 1.6480868  
Standard basis: 6-311++G(3df,2p) (5D, 7F)

**2F-(5-methyl)-imidazole(zwitterionic,  $\pi$ -form):**

Sum of electronic and thermal Free Energies= -364.653776 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	7	0	0.033030	-0.842574	-0.000008
2	7	0	0.859825	1.195562	0.000010
3	6	0	-1.056581	0.005221	-0.000001
4	6	0	-2.451857	-0.483290	0.000004
5	6	0	-0.525315	1.245679	-0.000006
6	6	0	1.109379	-0.058847	0.000001
7	1	0	0.026441	-1.843172	-0.000023
8	1	0	-2.660223	-1.088104	0.875562
9	1	0	-3.129512	0.359355	-0.000008
10	1	0	-2.660220	-1.088127	-0.875539
11	1	0	-1.046319	2.178881	-0.000008
12	9	0	2.307343	-0.582480	0.000002

Rotational constants (GHZ): 7.2148116 2.1002679 1.6430652  
Standard basis: 6-311++G(3df,2p) (5D, 7F)

**4F-(5-methyl)-imidazole(zwitterionic,  $\tau$ -form):**

Sum of electronic and thermal Free Energies= -364.644504 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	7	0	0.214894	-1.489037	0.000003
2	7	0	1.440384	0.326775	0.000000
3	6	0	-0.631550	-0.400665	0.000001
4	6	0	-2.107608	-0.512170	0.000000
5	6	0	0.138886	0.702157	0.000000
6	6	0	1.426690	-1.019172	-0.000005
7	1	0	-2.458843	-1.046694	0.875513
8	1	0	-2.564212	0.468962	-0.000036
9	1	0	-2.458836	-1.046754	-0.875479
10	1	0	2.239224	0.929846	0.000033
11	9	0	-0.181055	1.978421	-0.000002
12	1	0	2.326696	-1.596224	-0.000008

Rotational constants (GHZ): 3.7011083 3.4875494 1.8155098

Standard basis: 6-311++G(3df,2p) (5D, 7F)

**4F-(5-methyl)-imidazole(zwitterionic,  $\pi$ -form):**

Sum of electronic and thermal Free Energies= -364.654333 (Hartree)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	7	0	0.396303	-1.356796	0.000132
2	7	0	1.463972	0.553624	-0.000027
3	6	0	-0.582892	-0.393072	0.000031
4	6	0	-2.035060	-0.670546	0.000033
5	6	0	0.136000	0.749298	-0.000070
6	6	0	1.586211	-0.747797	0.000113
7	1	0	0.245350	-2.346033	0.000209
8	1	0	-2.330614	-1.236324	0.876445
9	1	0	-2.586254	0.259622	-0.000084
10	1	0	-2.330577	-1.236522	-0.876265
11	1	0	2.509315	-1.286731	0.000187
12	9	0	-0.350522	1.982321	-0.000208

Rotational constants (GHZ): 3.7136609 3.4888587 1.8189207

Standard basis: 6-311++G(3df,2p) (5D, 7F)