Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

SUPPORTING INFORMATION FOR:

Photoproperties of Favipiravir and their 6-Substituted Analogues: Fluorescence Controlled through Halogen Substitution and Tautomerism

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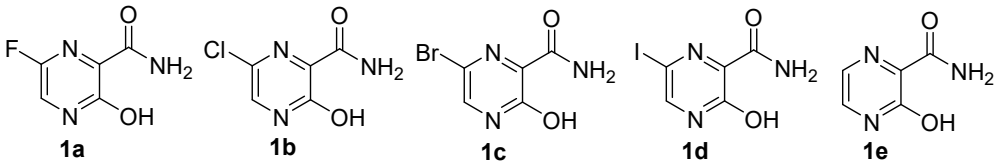
1. Experimental Data

Table S1. Absorptivity data of the 3-hydroxy-2-pyrazinecarboxamides **1a-e** in different solvents.

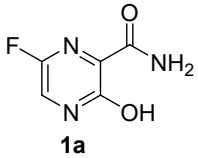


1a **1b** **1c** **1d** **1e**

Entries	Comps	H_2O	MeOH	EtOH	i-PrOH	DMSO	MeCN	*n*-hexane	DMF
1	**1a**	4723.2	4037.7	4300.5	5542.1	3935.7	1140.2	1710.4	5633.8
2	**1b**	12825	13470	6913.3	13156.2	5608.1	5731.9	989.1	-----
3	**1c**	6028.1	4078.9	5194.9	6066.6	5302.9	5230.1	1342.2	-----
4	**1d**	9137.9	5133.4	6042.2	6356.7	6936.9	---	----	----
5	**1e**	4502.1	2822.6	2346.7	2438.5	2567.4	---	---	----

[b]Molar absorptivity expressed in $M^{-1}.cm^{-1}$. Molar absorptivities were determined plotting maximum absorbance as function of pyrazine concentration. Molar absorptivities were calculated as a mean derived from three independent measurement with SD below 5%.

Table S2. Gradient plots for the quantum yield (Q.Y.) calculations for the LE state of the 6-fluoro-3-hydroxy-2-pyrazinecarboxamide **1a** in different solvents upon 360 nm.

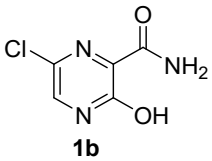


1a

Entries	Solvent	*Grad (1a)*	Q.Y. (Fl)	Q.Y. (Trp)
1	**H_20**	8870.5 ± 1.2%	~ 1.0 ± 1.6%	~ 1.0 ± 1.2%
2	**MeOH**	4970.7 ± 1.5%	0.778 ± 1.9%	0.781 ± 1.6%
3	**EtOH**	6400.1 ± 1.9%	0.960 ± 1.1%	0.971 ± 1.9%
4	**i-PrOH**	5199.6 ± 2.2%	0.789 ± 2.3%	0.782 ± 2.4%
5	**DMSO**	2001.0 ± 2.1%	0.325 ± 1.9%	0.323 ± 3.2%
6	**MeCN**	2246.1 ± 3.3%	0.332 ± 2.7%	0.329 ± 3.8%
7	**DMF**	325.2 ± 4.5%	0.051 ± 4.1%	0.051 ± 4.5%
8	***n*-Hexane**	79.9 ± 4.7%	0.012 ± 4.0%	0.012 ± 5.6%
	Grad (Fl)[a]	6263.2 ± 1.4%		
	Grad (Trp)[b]	824.6 ± 3.8%		

Gradient obtained for fluorescein[a] and tryptophan. **Notes:** Coefficient correlation were more than 0.9940 for obtaining gradient plots [Grad (1a), Grad (Fl) or Grad (Trp)]. Measurement either for the favipiravir under each solvent or for reference fluorophore were performed by triplicate. Gradients were calculated from eight to ten concentrations.

Table S3. Gradient plots for the quantum yield (Q.Y.) calculations for LE state of the 6-chloro-3-hydroxy-2-pyrazinecarboxamide **1b** in different solvents upon 360 nm.

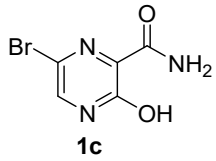


1b

Entries	Solvent	*Grad (1b)*	Q.Y. (Fl)	Q.Y. (Trp)
1	**H_20**	1061.2 ± 2.3%	0.156 ± 1.9%	0.154 ± 2.2%
2	**MeOH**	121.7 ± 2.6%	0.018 ± 2.9%	0.018 ± 2.6%
3	**EtOH**	171.9 ± 1.9%	0.025 ± 2.1%	0.025 ± 2.9%
4	**i-PrOH**	97.56 ± 2.9%	0.014 ± 3.3%	0.014 ± 3.9%
5	**DMSO**	25.3 ± 4.1%	0.004 ± 2.5%	0.004 ± 4.2%
6	**MeCN**	59.2 ± 4.3%	0.009 ± 3.6%	0.009 ± 3.8%
7	***n*-Hexane**	8.0 ± 5.3%	0.001 ± 5.0%	0.001 ± 5.6%
	Grad (Fl)[a]	6263.2 ± 1.4%		
	Grad (Trp)[b]	824.6 ± 3.8%		

Gradient obtained for fluorescein[a] and tryptophan. **Notes:** Coefficient correlation were more than 0.9940 for obtaining gradient plots [Grad (**1b**), Grad (Fl) or Grad (Trp)]. Measurement either for **1b** under each solvent or for reference fluorophore were performed by triplicate. Gradients were calculated from eight to ten concentrations.

Table S4. Gradient plots for the quantum yield (Q.Y.) calculations for the LE state of the 6-bromo-3-hydroxy-2-pyrazinecarboxamide **1c** in different solvents upon 360 nm.

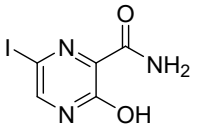


1c

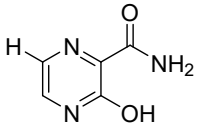
Entries	Solvent	*Grad (1b)*	Q.Y. (Fl)	Q.Y. (Trp)
1	**H_20**	615.9 ± 2.8%	0.090 ± 2.9%	0.090 ± 3.2%
2	**MeOH**	117.1 ± 2.5%	0.017 ± 3.9%	0.017 ± 3.5%
3	**EtOH**	46.19 ± 3.2%	0.007 ± 3.1%	0.007 ± 3.7%
4	**i-PrOH**	27.1 ± 3.6%	0.004 ± 3.3%	0.004 ± 3.9%
5	**DMSO**	2.1 ± 5.1%	0.0003 ± 5.5%	0.0003 ± 6.2%
6	**MeCN**	13.9 ± 5.3%	0.002 ± 4.9%	0.002 ± 4.8%
7	***n*-Hexane**	0.1 ± 5.7%	0.0001 ± 5.9%	0.0001 ± 6.6%
	Grad (Fl)[a]	6263.2 ± 1.4%		
	Grad (Trp)[b]	824.6 ± 3.8%		

Gradient obtained for fluorescein[a] and tryptophan. **Notes:** Coefficient correlation were more than 0.9940 for obtaining gradient plots [Grad (**1c**), Grad (Fl) or Grad (Trp)]. Measurement either for **1c** under each solvent or for reference fluorophore were performed by triplicate. Gradients were calculated from eight to ten concentrations.

Table S5. Gradient plots for the quantum yield (Q.Y.) calculations for the LE state of the 6-iodo-3-hydroxy-2-pyrazinecarboxamide **1d** and 3-hydroxy-2-pyrazinecarboxamide **1e** in different solvents upon 360 nm.



1c

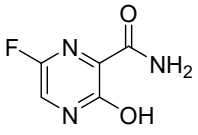


1c

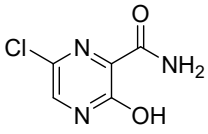
Entries	Solvent	*Grad (1b)*	Q.Y. (Fl)	Q.Y. (Trp)
1	**H_20 (1d)**	1.80 ± 4.8%	0.0003 ± 2.6%	0.0002 ± 4.1%
2	**H_20 (1e)**	21.38 ± 3.5%	0.00314 ± 3.9%	0.00311 ± 3.5%
3	**MeOH (1e)**	1.01 ± 4.3%	0.00014 ± 4.5%	0.00014 ± 3.7%
4	**EtOH (1e)**	0.93 ± 4.7%	0.00014 ± 4.9%	0.00013 ± 3.9%
5	**i-PrOH (1e)**	0.21 ± 5.1%	0.00003 ± 5.5%	0.00003 ± 6.2%
6	**DMSO (1e)**	0.00 ± 6.1%	0.0 ± 4.9%	0.00 ± 4.8%
7	**MeCN (1e)**	0.01 ± 5.7%	0.00001 ± 5.9%	0.00001 ± 6.6%
	Grad (Fl)[a]	6263.2 ± 1.4%		
	Grad (Trp)[b]	824.6 ± 3.8%		

Gradient obtained for fluorescein[a] and tryptophan. **Notes:** Coefficient correlation were more than 0.9940 for obtaining gradient plots [Grad (**1d** or **1e**), Grad (Fl) or Grad (Trp)]. Measurement either for **1d** and **1e** under each solvent or for reference fluorophore were performed by triplicate. Gradients were calculated from eight to ten concentrations.

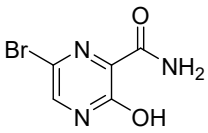
Table S6. Lifetimes (ns) for the tested 3-hydroxy-2-pyrazinecarboxamides **1a-e** with standard deviation (SD) under water solution.



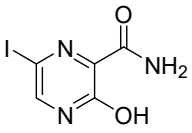
1a



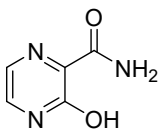
1b



1c



1d



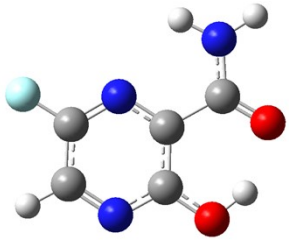
1e

	τ_1 (ns)	τ_2 (ns)	τ_3 (ns)	χ^2
1a	10.1 ± 0.03 (100%)			0.878
1b	10.2 ± 0.03 (100%)			1.00
1c	4.88 ± 0.03 (90.46%)	0.203 ± 0.04 (9.54%)		~ 1.00
1d	10.6 ± 0.06 (81.78%)	0.242 ± 0.02 (18.22%)		~ 1.00
1e	9.12 ± 0.50 (17.73%)	0.102 ± 0.09 (44.46%)	1.84 ± 0.05 (37.91%)	~ 1.00

2. Theoretical Output

2.1. Geometry optimization of ground-state of enol tautomers

2.1.1. 6-Fluoro-3-hydroxy-2-pyrazinecarboxamide **1a**



Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RM062X) = -607.532703121 A.U. after 15 cycles
Convg = 0.9306D-08 -V/T = 2.0042
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 9453 NPrTT= 30144 LenC2= 8988 LenP2D= 21935.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000245085	0.000089403	-0.000013888
2	6	-0.000046814	-0.000171404	-0.000054853
3	7	-0.000039517	0.000079359	-0.000007116
4	6	0.000098484	-0.000088514	0.000010070
5	6	-0.000121082	-0.000172310	0.000003267
6	7	0.000302047	0.000101187	0.000005407
7	1	0.000045379	0.000012589	-0.000003637
8	6	0.000104998	0.000108143	0.000170536
9	8	0.000044350	-0.000127007	-0.000058300
10	7	-0.000039350	0.000012791	-0.000042468
11	1	0.000017918	0.000011982	-0.000002129
12	1	0.000014476	0.000006909	-0.000007298
13	8	-0.000009883	0.000005108	0.000016501
14	1	-0.000182285	-0.000019968	-0.000015703
15	9	0.000056365	0.000151733	-0.000000387

Cartesian Forces: Max 0.000302047 RMS 0.000095978

Mulliken atomic charges:

1	C	0.266641
2	C	0.059600
3	N	-0.254830
4	C	0.224173
5	C	-0.103796
6	N	-0.176618
7	H	0.168075
8	C	0.379221
9	O	-0.446855
10	N	-0.472717
11	H	0.268337
12	H	0.287665
13	O	-0.393450
14	H	0.375289
15	F	-0.180735

Sum of Mulliken atomic charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

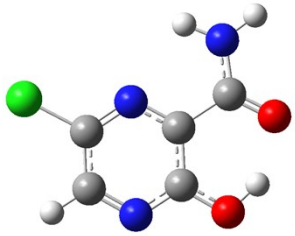
1	C	0.266641
2	C	0.059600
3	N	-0.254830
4	C	0.224173
5	C	0.064279
6	N	-0.176618
8	C	0.379221
9	O	-0.446855
10	N	0.083285
13	O	-0.018161
15	F	-0.180735

Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000

Electronic spatial extent (au): <R**2>= 1608.9173

Charge= 0.0000 electrons

2.1.2. 6-Chloro-3-hydroxy-2-pyrazinecarboxamide **1b**



Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.

Requested convergence on MAX density matrix=1.00D-06.

Requested convergence on energy=1.00D-06.

No special actions if energy rises.

SCF Done: E(RM062X) = -967.879526877 A.U. after 8 cycles
Convg = 0.3818D-08 -V/T = 2.0027
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 9730 NPrTT= 31894 LenC2= 9209 LenP2D= 22728.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000045348	0.000026638	-0.000006349
2	6	-0.000021752	-0.000016730	-0.000011246
3	7	0.000021311	-0.000012212	-0.000001444
4	6	-0.000003474	0.000030521	0.000001982
5	6	-0.000014946	-0.000074573	0.000001198
6	7	0.000054937	0.000043594	0.000001088
7	1	0.000013509	0.000021655	-0.000000931
8	6	0.000029500	0.000004619	0.000034703
9	8	-0.000005891	-0.000025551	-0.000007126
10	7	-0.000022078	-0.000015903	-0.000009544
11	1	0.000004634	0.000000127	-0.000000014
12	1	-0.000000303	-0.000002807	-0.000001386
13	8	-0.000001053	-0.000023131	0.000014295
14	1	-0.000011629	0.000011967	-0.000015198
15	17	0.000002583	0.000031787	-0.000000028

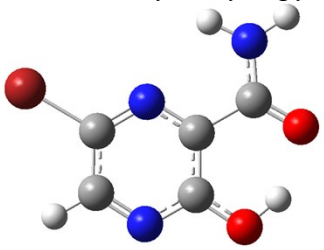
Cartesian Forces: Max 0.000074573 RMS 0.000022391

Mulliken atomic charges:

1	C	0.269531
2	C	0.056571
3	N	-0.254927
4	C	0.070037
5	C	-0.078877
6	N	-0.180941
7	H	0.169075
8	C	0.380336
9	O	-0.446345
10	N	-0.471582
11	H	0.268480
12	H	0.288254
13	O	-0.389277
14	H	0.376557
15	Cl	-0.056891

Sum of Mulliken atomic charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms:
1 C 0.269531
2 C 0.056571
3 N -0.254927
4 C 0.070037
5 C 0.090198
6 N -0.180941
8 C 0.380336
9 O -0.446345
10 N 0.085152
13 O -0.012720
15 Cl -0.056891
Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000
Electronic spatial extent (au): <R**2>= 2032.2104
Charge= 0.0000 electrons

2.1.3. 6-Bromo-3-hydroxy-2-pyrazinecarboxamide **1c**



Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RM062X) = -3081.87247924 A.U. after 15 cycles
Convg = 0.8553D-08 -V/T = 2.0018
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 10153 NPrTT= 35014 LenC2= 9582 LenP2D= 24404.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000087097	0.000048909	-0.000007303
2	6	-0.000073377	-0.000086929	-0.000015674
3	7	0.000021648	0.000054584	-0.000002209
4	6	-0.000002737	0.000048777	0.000002859

5	6	-0.000009231	-0.000002485	0.000001305
6	7	0.000110657	0.000014469	0.000001536
7	1	0.000014142	0.000051968	-0.000001119
8	6	0.000076877	-0.000007471	0.000049349
9	8	0.000013519	-0.000080662	-0.000012961
10	7	-0.000030940	-0.000027188	-0.000012663
11	1	-0.000002820	-0.000031421	-0.000000470
12	1	-0.000019189	-0.000015464	-0.000001996
13	8	0.000034076	-0.000023523	0.000014835
14	1	-0.000015973	0.000014850	-0.000015417
15	35	-0.000029555	0.000041584	-0.000000072

Cartesian Forces: Max 0.000110657 RMS 0.000039013

Mulliken atomic charges:

1	C	0.272182
2	C	0.058462
3	N	-0.260077
4	C	0.078046
5	C	-0.077013
6	N	-0.179190
7	H	0.174175
8	C	0.380898
9	O	-0.446926
10	N	-0.471987
11	H	0.268685
12	H	0.288195
13	O	-0.387619
14	H	0.376745
15	Br	-0.074577

Sum of Mulliken atomic charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

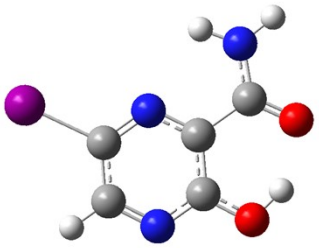
1	C	0.272182
2	C	0.058462
3	N	-0.260077
4	C	0.078046
5	C	0.097162
6	N	-0.179190
8	C	0.380898
9	O	-0.446926
10	N	0.084894
13	O	-0.010874
15	Br	-0.074577

Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000

Electronic spatial extent (au): <R**2>= 2698.6689

Charge= 0.0000 electrons

2.1.4. 6-Iodo-3-hydroxy-2-pyrazinecarboxamide **1d**



Optimization:

SCF Done: E(RM062X) = -805.307041384 A.U. after 8 cycles
Convg = 0.5542D-08 -V/T = 2.3011
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 10153 NPrTT= 32907 LenC2= 9588 LenP2D= 23494.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000023447	0.000020777	-0.000005473
2	6	-0.000055024	-0.000025186	-0.000004628
3	7	-0.000000317	0.000001063	-0.000000591
4	6	0.000007717	0.000036742	0.000000637
5	6	-0.000009362	-0.000008690	0.000000857
6	7	0.000036448	-0.000028482	0.000000500
7	1	0.000007048	0.000002066	-0.000000496
8	6	0.000061092	0.000013772	0.000015191
9	8	-0.000000862	-0.000045437	-0.000000249
10	7	-0.000023311	-0.000004536	-0.000004612
11	1	0.000006700	0.000011362	0.000000136
12	1	0.000003788	0.000005418	-0.000000352
13	8	0.000010869	-0.000018127	0.000013881
14	1	-0.000039891	0.000031701	-0.000014790
15	53	0.000018551	0.000007557	-0.000000011

Cartesian Forces: Max 0.000061092 RMS 0.000020732

Mulliken atomic charges:

1	C	0.276468
2	C	0.054796
3	N	-0.279104
4	C	0.086251
5	C	-0.089001
6	N	-0.177329
7	H	0.177328
8	C	0.378686
9	O	-0.447024
10	N	-0.471890
11	H	0.268404
12	H	0.288041
13	O	-0.387488
14	H	0.376777
15	I	-0.054914

Sum of Mulliken atomic charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

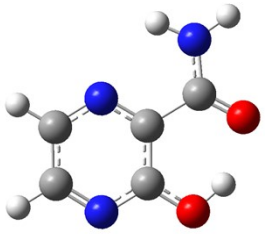
1	C	0.276468
2	C	0.054796
3	N	-0.279104
4	C	0.086251
5	C	0.088327
6	N	-0.177329
8	C	0.378686
9	O	-0.447024
10	N	0.084555
13	O	-0.010711
15	I	-0.054914

Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000

Electronic spatial extent (au): <R**2>= 2706.9816

Charge= 0.0000 electrons

2.1.5. 3-Hydroxy-2-pyrazinecarboxamide **1e**



Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.

Requested convergence on MAX density matrix=1.00D-06.

Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RM062X) = -508.276769054 A.U. after 15 cycles
Convg = 0.6113D-08 -V/T = 2.0044
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 8515 NPrTT= 26800 LenC2= 8222 LenP2D= 20139.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000140870	-0.000081276	0.000008430
2	6	-0.000098137	0.000120400	-0.000012924
3	7	-0.000004626	-0.000118085	0.000004358
4	6	0.000096446	0.000011407	-0.000004180
5	6	-0.000045809	0.000001836	0.000000025
6	7	-0.000014870	-0.000045274	-0.000002291
7	1	0.000015018	-0.000007070	-0.000000407
8	6	-0.000104879	0.000209569	0.000031485
9	8	0.000040176	-0.000111288	-0.000006093
10	7	0.000048804	-0.000063679	-0.000015444
11	1	-0.000046180	0.000007836	0.000002848
12	1	0.000002191	0.000012074	0.000000281
13	8	0.000016807	0.000105156	0.000009209
14	1	-0.000052807	-0.000051075	-0.000016058
15	1	0.000006996	0.000009468	0.000000762

Cartesian Forces: Max 0.000209569 RMS 0.000062378

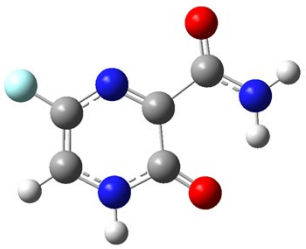
Mulliken atomic charges:

1	C	0.272035
2	C	0.052881
3	N	-0.273008
4	C	-0.106598
5	C	-0.042507
6	N	-0.192020
7	H	0.152976
8	C	0.375042
9	O	-0.449885
10	N	-0.471380
11	H	0.265982
12	H	0.284315
13	O	-0.392398
14	H	0.375065

15 H 0.149500
Sum of Mulliken atomic charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms:
1 C 0.272035
2 C 0.052881
3 N -0.273008
4 C 0.042902
5 C 0.110469
6 N -0.192020
8 C 0.375042
9 O -0.449885
10 N 0.078917
13 O -0.017333
Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000
Electronic spatial extent (au): <R**2>= 1275.8697
Charge= 0.0000 electrons

2.2. Geometry optimization of ground-state of keto tautomers

2.2.1. 6-Fluoro-3-oxo-3,4-dihydropyrazine-2-carboxamide **1a**



Optimization:
Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RM062X) = -607.511392262 A.U. after 16 cycles
Convg = 0.7899D-08 -V/T = 2.0042
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 9453 NPrTT= 30144 LenC2= 8962 LenP2D= 21828.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000102824	0.000044201	0.000009611

2	6	0.000020126	0.000001305	-0.000001924
3	7	-0.000035998	-0.000019843	-0.000000384
4	6	0.000019191	-0.000044218	-0.000002389
5	6	-0.000010227	0.000006436	-0.000000145
6	7	0.000077711	-0.000025843	-0.000003528
7	1	-0.000005172	-0.000043615	0.000000365
8	6	-0.000007907	0.000003765	0.000011491
9	8	-0.000006998	0.000024570	-0.000005202
10	7	0.000015127	0.000043849	-0.000004589
11	1	0.000008771	0.000027331	0.000000644
12	1	0.000003102	0.000014373	-0.000000905
13	8	0.000070513	-0.000038634	-0.000004153
14	1	0.000003988	-0.000009643	0.000000549
15	9	-0.000049403	0.000015966	0.000000559

Cartesian Forces: Max 0.000102824 RMS 0.000029527

Mulliken atomic charges:

1	C	0.325006
2	C	-0.037513
3	N	-0.092412
4	C	0.230189
5	C	-0.059198
6	N	-0.235976
7	H	0.184342
8	C	0.281975
9	O	-0.322982
10	N	-0.489396
11	H	0.256647
12	H	0.300330
13	O	-0.430466
14	H	0.266397
15	F	-0.176944

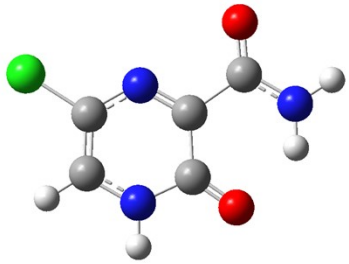
Sum of Mulliken atomic charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.325006
2	C	-0.037513
3	N	-0.092412
4	C	0.230189
5	C	0.125144
6	N	0.030421
8	C	0.281975
9	O	-0.322982
10	N	0.067581
13	O	-0.430466
15	F	-0.176944

Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000
Electronic spatial extent (au): <R**2>= 1641.6712
Charge= 0.0000 electrons

2.2.2. 6-Chloro-3-oxo-3,4-dihydropyrazine-2-carboxamide **1b**



Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RM062X) = -967.859397254 A.U. after 16 cycles
Convg = 0.6093D-08 -V/T = 2.0027
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 9730 NPrTT= 31894 LenC2= 9180 LenP2D= 22598.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000119154	-0.000024373	-0.000029431
2	6	-0.000022144	0.000024909	0.000062628
3	7	0.000093165	-0.000141300	0.000004533
4	6	-0.000035776	0.000228457	-0.000009041
5	6	-0.000015272	-0.000089561	0.000002882
6	7	0.000099495	0.000008067	0.000003939
7	1	-0.000006182	-0.000016595	0.000001611
8	6	0.000025489	0.000014315	-0.000165156
9	8	-0.000001896	0.000008637	0.000067837
10	7	-0.000096888	-0.000033914	0.000037078
11	1	-0.000014209	-0.000014772	0.000000159
12	1	-0.000019714	-0.000005052	0.000011369
13	8	0.000135650	0.000071065	0.000011639
14	1	-0.000027696	0.000013759	0.000000047
15	17	0.000005133	-0.000043643	-0.000000095

Cartesian Forces: Max 0.000228457 RMS 0.000065597

Mulliken atomic charges:

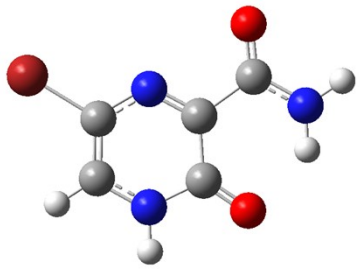
1	C	0.327313
2	C	-0.048573
3	N	-0.093157
4	C	0.072663
5	C	-0.024592
6	N	-0.238195
7	H	0.183404
8	C	0.283896
9	O	-0.322095
10	N	-0.490183
11	H	0.256697
12	H	0.299244
13	O	-0.423707
14	H	0.266062
15	Cl	-0.048778

Sum of Mulliken atomic charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.327313
2	C	-0.048573
3	N	-0.093157
4	C	0.072663
5	C	0.158813
6	N	0.027867
8	C	0.283896
9	O	-0.322095
10	N	0.065758
13	O	-0.423707
15	Cl	-0.048778

Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000
Electronic spatial extent (au): <R**2>= 2066.1953
Charge= 0.0000 electrons

2.2.3. 6-Bromo-3-oxo-3,4-dihydropyrazine-2-carboxamide **1c**



Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.

SCF Done: E(RM062X) = -3081.85249999 A.U. after 8 cycles
Convg = 0.8183D-08 -V/T = 2.0018
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 10153 NPrTT= 35014 LenC2= 9559 LenP2D= 24293.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000098913	-0.000027526	0.000008207
2	6	-0.000001167	0.000045085	-0.000001529
3	7	-0.000005985	-0.000030878	0.000001074
4	6	0.000061612	-0.000017783	-0.000001427
5	6	-0.000042535	0.000079248	-0.000000727
6	7	0.000088363	-0.000040146	-0.000002440
7	1	0.000004809	0.000008539	0.000000384
8	6	0.000041564	-0.000011183	0.000000333
9	8	-0.000009568	-0.000019216	0.000000230
10	7	-0.000018009	-0.000004918	-0.000001868
11	1	-0.000003771	-0.000021808	0.000000475
12	1	-0.000013234	-0.000012685	0.000000426
13	8	0.000027446	0.000006958	-0.000003423
14	1	-0.000022517	0.000023442	0.000000316
15	35	-0.000008094	0.000022870	-0.000000032

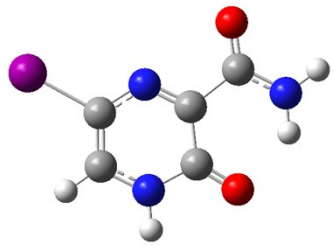
Cartesian Forces: Max 0.000098913 RMS 0.000030299

Mulliken atomic charges:

1	C	0.327696
2	C	-0.042847
3	N	-0.100637
4	C	0.071629
5	C	-0.013588
6	N	-0.237031
7	H	0.188194
8	C	0.281980
9	O	-0.322274
10	N	-0.490449
11	H	0.256777
12	H	0.299144
13	O	-0.422040
14	H	0.266200
15	Br	-0.062753

Sum of Mulliken atomic charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms:
1 C 0.327696
2 C -0.042847
3 N -0.100637
4 C 0.071629
5 C 0.174606
6 N 0.029168
8 C 0.281980
9 O -0.322274
10 N 0.065472
13 O -0.422040
15 Br -0.062753
Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000
Electronic spatial extent (au): <R**2>= 2731.8166
Charge= 0.0000 electrons

2.2.4. 6-Iodo-3-oxo-3,4-dihydropyrazine-2-carboxamide **1d**



Optimization:
SCF Done: E(RM062X) = -805.287656878 A.U. after 9 cycles
Convg = 0.3500D-08 -V/T = 2.3010
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 10153 NPrTT= 32907 LenC2= 9556 LenP2D= 23357.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
***** Axes restored to original set *****

Center Atomic Forces (Hartrees/Bohr)
Number Number X Y Z
---
1 6 -0.000153146 -0.000132413 -0.000030304

2	6	-0.000047725	0.000104404	0.000035921
3	7	-0.000014674	-0.000091612	0.000000877
4	6	0.000133152	0.000001350	-0.000003096
5	6	-0.000110947	0.000122847	0.000003667
6	7	0.000194370	-0.000060757	0.000006232
7	1	0.000011326	-0.000000078	-0.000000342
8	6	0.000108093	0.000022045	-0.000084272
9	8	-0.000022091	-0.000052137	0.000035120
10	7	-0.000096143	-0.000022396	0.000018018
11	1	-0.000004668	-0.000037636	0.000000460
12	1	-0.000022037	-0.000010350	0.000006539
13	8	0.000084596	0.000103308	0.000012195
14	1	-0.000050515	0.000038245	-0.000000374
15	53	-0.000009592	0.000015180	-0.000000641

Cartesian Forces: Max 0.000194370 RMS 0.000068304

Mulliken atomic charges:

1	C	0.329594
2	C	-0.045975
3	N	-0.119363
4	C	0.074406
5	C	-0.023060
6	N	-0.235649
7	H	0.191447
8	C	0.278941
9	O	-0.322954
10	N	-0.491341
11	H	0.256463
12	H	0.298982
13	O	-0.421484
14	H	0.265572
15	I	-0.035579

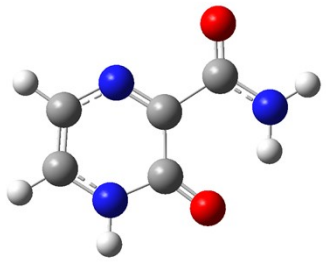
Sum of Mulliken atomic charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.329594
2	C	-0.045975
3	N	-0.119363
4	C	0.074406
5	C	0.168387
6	N	0.029922
8	C	0.278941
9	O	-0.322954
10	N	0.064104
13	O	-0.421484
15	I	-0.035579

Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000
Electronic spatial extent (au): <R**2>= 2738.9354
Charge= 0.0000 electrons

2.2.5. 3-Oxo-3,4-dihydropyrazine-2-carboxamide **1e**



Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RM062X) = -508.260432843 A.U. after 9 cycles
Convg = 0.8008D-08 -V/T = 2.0043
1 Symmetry operations used in ECPInt.
ECPInt: NShTT= 8515 NPrTT= 26800 LenC2= 8195 LenP2D= 20023.
LDataN: DoStor=T MaxTD1= 7 Len= 274
Calling FoFJK, ICntrl= 2127 FMM=F ISym2X=0 I1Cent= 0 IOpClX= 0 NMat=1 NMatS=1 NMatT=0.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000097958	-0.000054582	0.000050965
2	6	-0.000054631	-0.000017865	-0.000031570
3	7	-0.000010621	-0.000006297	0.000012403
4	6	0.000044856	-0.000010555	0.000009834
5	6	0.000030003	0.000022680	-0.000012548
6	7	-0.000110550	-0.000011262	-0.000002087
7	1	0.000003053	-0.000012846	0.000000838
8	6	0.000010204	0.000375716	-0.000062139
9	8	0.000044672	-0.000190150	0.000030781
10	7	-0.000035266	-0.000154459	0.000020604
11	1	0.000008147	-0.000004123	-0.000003064
12	1	-0.000002597	0.000005858	0.000007596
13	8	-0.000007554	0.000053035	-0.000018767
14	1	-0.000028441	0.000002198	-0.000002287
15	1	0.000010766	0.000002652	-0.000000559

Cartesian Forces: Max 0.000375716 RMS 0.000074567

Mulliken atomic charges:

1	C	0.332922
2	C	-0.049734
3	N	-0.110145
4	C	-0.115280
5	C	0.012596
6	N	-0.245527
7	H	0.171538
8	C	0.279689
9	O	-0.328769
10	N	-0.492744
11	H	0.253896
12	H	0.297976
13	O	-0.427427
14	H	0.159518
15	H	0.261492

Sum of Mulliken atomic charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.332922
2	C	-0.049734
3	N	-0.110145
4	C	0.044238
5	C	0.184134
6	N	0.015964
8	C	0.279689
9	O	-0.328769
10	N	0.059127
13	O	-0.427427

Sum of Mulliken charges with hydrogens summed into heavy atoms = 0.00000
Electronic spatial extent (au): <R**2>= 1309.7913
Charge= 0.0000 electrons

2.3. **Geometry optimization of excited-state of enol tautomers**

2.3.1. 6-Fluoro-3-hydroxy-2-pyrazinecarboxamide **1a**

Optimization:
Keep R1 ints in memory in canonical form, NReq=151357516.

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RB3LYP) = -607.471351372 A.U. after 8 cycles
NFock= 8 Conv=0.75D-08 -V/T= 2.0088
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.61D-01 ExpMax= 7.00D+03 ExpMxC= 1.05D+03 IAcc=3 IRadAn= 5 AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 12 185
NBasis= 185 NAE= 40 NBE= 40 NFC= 11 NFV= 0
NROrb= 174 NOA= 29 NOB= 29 NVA= 145 NVB= 145
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000004962	-0.000006153	-0.000003665
2	6	0.000019368	0.000021845	-0.000000994
3	7	-0.000016508	-0.000016214	0.000000712
4	6	0.000007916	0.000009900	0.000003486
5	6	0.000018010	-0.000004995	0.000010195
6	7	-0.000005093	0.000005336	-0.000000712
7	1	0.000004110	-0.000013280	0.000000781
8	6	-0.000024241	-0.000006138	-0.000013632
9	7	0.000003495	0.000008191	0.000009212
10	1	0.000000083	0.000000224	-0.000002742
11	1	-0.000001148	-0.000001182	0.000003933
12	8	-0.000001594	-0.000009445	0.000001007
13	8	-0.000006185	0.000019652	-0.000009282
14	1	-0.000001958	-0.000009357	0.000000243
15	9	-0.000001217	0.000001616	0.000001458

Cartesian Forces: Max 0.000024241 RMS 0.000009478

Mulliken atomic charges:

1	C	0.041748
2	C	0.518419
3	N	-0.440224
4	C	0.205995
5	C	0.530264
6	N	-0.477308
7	H	0.143028
8	C	0.551726
9	N	-0.621788

10 H 0.289949
11 H 0.287558
12 O -0.542082
13 O -0.557349
14 H 0.338907
15 F -0.268842
Sum of Mulliken charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms:
1 C 0.184776
2 C 0.518419
3 N -0.440224
4 C 0.205995
5 C 0.530264
6 N -0.477308
8 C 0.551726
9 N -0.044281
12 O -0.542082
13 O -0.218442
15 F -0.268842

2.3.2. 6-Chloro-3-hydroxy-2-pyrazinecarboxamide **1b**

Optimization:
Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RB3LYP) = -967.830318312 A.U. after 8 cycles
NFock= 8 Conv=0.97D-08 -V/T= 2.0063
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.43D-01 ExpMax= 2.52D+04 ExpMxC= 3.78D+03 IAcc=3 IRadAn= 5
AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 16 189
NBasis= 189 NAE= 44 NBE= 44 NFC= 15 NFV= 0
NROrb= 174 NOA= 29 NOB= 29 NVA= 145 NVB= 145
Keep R1, R2, and R3 ints in memory in canonical form, NReq=524366177.
***** Axes restored to original set *****

Center Atomic Forces (Hartrees/Bohr)

Number	Number	X	Y	Z
1	6	-0.000026171	0.000054286	-0.000000221
2	6	-0.000004003	-0.000067811	-0.000001875
3	7	0.000030698	0.000018881	-0.000008025
4	6	-0.000012131	-0.000021531	-0.000027406
5	6	-0.000026003	0.000024439	-0.000014513
6	7	0.000042945	-0.000032659	0.000006054
7	1	0.000005297	-0.000013109	-0.000000627
8	6	0.000000814	0.000027051	0.000130563
9	7	0.000001945	-0.000004634	-0.000041245
10	1	-0.000007698	0.000014667	-0.000003789
11	1	-0.000000482	0.000003166	-0.000003087
12	8	-0.000015346	0.000000772	-0.000040645
13	8	0.000012421	-0.000019460	0.000002747
14	1	0.000009028	0.000017325	0.000001278
15	17	-0.000011314	-0.000001384	0.000000791

Cartesian Forces: Max 0.000130563 RMS 0.000029198

Mulliken atomic charges:

1	C	0.113406
2	C	0.102149
3	N	-0.395394
4	C	0.204513
5	C	0.533408
6	N	-0.477929
7	H	0.147306
8	C	0.553367
9	N	-0.621820
10	H	0.290803
11	H	0.287084
12	O	-0.540129
13	O	-0.553569
14	H	0.339586
15	Cl	0.017220

Sum of Mulliken charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.260713
2	C	0.102149
3	N	-0.395394
4	C	0.204513
5	C	0.533408
6	N	-0.477929
8	C	0.553367
9	N	-0.043934

12 O -0.540129
13 O -0.213984
15 Cl 0.017220
Electronic spatial extent (au): <R**2>= 2087.5049
Charge= 0.0000 electrons

2.3.3. 6-Bromo-3-hydroxy-2-pyrazinecarboxamide **1c**

Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RB3LYP) = -3079.33847134 A.U. after 9 cycles
NFock= 9 Conv=0.47D-08 -V/T= 2.0066
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.43D-01 ExpMax= 5.74D+05 ExpMxC= 5.74D+03 IAcc=3 IRadAn= 5 AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 25 200
NBasis= 200 NAE= 53 NBE= 53 NFC= 24 NFV= 0
NROrb= 176 NOA= 29 NOB= 29 NVA= 147 NVB= 147
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000002263	0.000022392	-0.000005153
2	6	0.000004733	-0.000000595	-0.000006191
3	7	-0.000005395	0.000003477	-0.000000446
4	6	0.000000771	-0.000000503	-0.000004506
5	6	0.000012369	0.000008023	0.000017665
6	7	-0.000003211	-0.000002421	-0.000000718
7	1	0.000002326	-0.000005363	0.000001128
8	6	-0.000010779	-0.000021868	0.000003810
9	7	-0.000000544	0.000010997	0.000002391
10	1	0.000005608	-0.000006438	-0.000004888
11	1	0.000000732	-0.000008522	0.000000719
12	8	0.000003746	-0.000008929	-0.000000096
13	8	-0.000008028	0.000015795	-0.000005225

14	1	-0.000004055	-0.000013369	-0.000001808
15	35	0.000003991	0.000007325	0.000003318

Cartesian Forces: Max 0.000022392 RMS 0.000007970

Mulliken atomic charges:

1	C	0.103253
2	C	0.240136
3	N	-0.422103
4	C	0.206243
5	C	0.532990
6	N	-0.479897
7	H	0.146828
8	C	0.551809
9	N	-0.621931
10	H	0.290672
11	H	0.286787
12	O	-0.540314
13	O	-0.553426
14	H	0.339485
15	Br	-0.080532

Sum of Mulliken charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms

1	C	0.250081
2	C	0.240136
3	N	-0.422103
4	C	0.206243
5	C	0.532990
6	N	-0.479897
8	C	0.551809
9	N	-0.044472
12	O	-0.540314
13	O	-0.213941
15	Br	-0.080532

Electronic spatial extent (au): <R**2>= 2769.1645

Charge= 0.0000 electrons

2.3.4. 6-Iodo-3-hydroxy-2-pyrazinecarboxamide **1d**

Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.

Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
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Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
SCF Done: E(RB3LYP) = -519.001715230 A.U. after 9 cycles
NFock= 9 Conv=0.57D-08 -V/T= 2.0232
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.05D-01 ExpMax= 5.48D+03 ExpMxC= 8.25D+02 IAcc=3 IRadAn= 5 AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000047202	0.000031792	-0.000000384
2	6	0.000001962	-0.000003795	-0.000000254
3	7	0.000029786	-0.000009233	0.000000457
4	6	-0.000024889	0.000014686	0.000000042
5	6	-0.000020925	-0.000011809	0.000001340
6	7	0.000046036	0.000002251	0.000000040
7	1	-0.000000384	0.000001614	-0.000000146
8	6	0.000010763	-0.000001583	0.000001709
9	7	0.000003080	-0.000008181	-0.000011735
10	1	0.000002269	-0.000002306	0.000005052
11	1	-0.000000764	-0.000009259	0.000004261
12	8	-0.000000353	-0.000002266	-0.000000070
13	8	0.000005111	-0.000016817	-0.000000766
14	1	-0.000006300	0.000007881	0.000000231
15	53	0.000001807	0.000007026	0.000000224

Cartesian Forces: Max 0.000047202 RMS 0.000013918

Mulliken atomic charges:

1	C	0.140350
2	C	-0.173741
3	N	-0.261778
4	C	0.141121
5	C	0.461378
6	N	-0.394745
7	H	0.143580
8	C	0.491045
9	N	-0.583976
10	H	0.290287
11	H	0.284111
12	O	-0.503331
13	O	-0.527520
14	H	0.339539
15	I	0.153679

Sum of Mulliken charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.283930
2	C	-0.173741
3	N	-0.261778
4	C	0.141121
5	C	0.461378
6	N	-0.394745
8	C	0.491045
9	N	-0.009577
12	O	-0.503331
13	O	-0.187981
15	I	0.153679

Electronic spatial extent (au): <R**2>= 2371.7718

Charge= 0.0000 electrons

2.3.5. 3-Hydroxy-2-pyrazinecarboxamide **1e**

Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.

Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RB3LYP) = -508.236371772 A.U. after 8 cycles
NFock= 8 Conv=0.88D-08 -V/T= 2.0093
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.61D-01 ExpMax= 5.48D+03 ExpMxC= 8.25D+02 IAcc=3 IRadAn= 5 AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 11 175
NBasis= 175 NAE= 36 NBE= 36 NFC= 10 NFV= 0
NROrb= 165 NOA= 26 NOB= 26 NVA= 139 NVB= 139
Keep R1, R2, and R3 ints in memory in canonical form, NReq=392782533.

***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000004779	-0.000035158	-0.000000915
2	6	-0.000015173	0.000012492	0.000000473
3	7	0.000026334	-0.000027931	-0.000001647
4	6	-0.000022818	0.000030199	-0.000028705
5	6	-0.000000056	-0.000021461	-0.000029924
6	7	0.000021013	0.000030221	0.000010193
7	1	-0.000000933	0.000001595	-0.000000978
8	1	0.000009401	-0.000000777	0.000000766
9	6	0.000032855	-0.000012884	0.000154559
10	7	-0.000011247	0.000021966	-0.000044775
11	1	0.000001871	-0.000000981	-0.000002529
12	1	0.000000175	0.000003500	0.000003502
13	8	-0.000030048	-0.000014779	-0.000060081
14	8	-0.000019190	0.000011882	-0.000000558
15	1	0.000003037	0.000002117	0.000000617

Cartesian Forces: Max 0.000154559 RMS 0.000030304

Mulliken atomic charges:

1	C	0.085243
2	C	0.095379
3	N	-0.405078
4	C	0.203672
5	C	0.531999
6	N	-0.486188
7	H	0.125550

8 H 0.117944
9 C 0.550699
10 N -0.622885
11 H 0.287309
12 H 0.284868
13 O -0.547607
14 O -0.556238
15 H 0.335332
Sum of Mulliken charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms
1 C 0.210793
2 C 0.213323
3 N -0.405078
4 C 0.203672
5 C 0.531999
6 N -0.486188
9 C 0.550699
10 N -0.050708
13 O -0.547607
14 O -0.220905
Electronic spatial extent (au): <R**2>= 1303.0307
Charge= 0.0000 electrons

2.4. **Geometry optimization of ground-state of keto tautomers**

2.4.1. 6-Fluoro-3-oxo-3,4-dihydropyrazine-2-carboxamide **1a**

Optimization:
Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RB3LYP) = -607.468369319 A.U. after 10 cycles
NFock= 10 Conv=0.90D-08 -V/T= 2.0088
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.61D-01 ExpMax= 7.00D+03 ExpMxC= 1.05D+03 IAcc=3 IRadAn= 5 AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 12 185

NBasis= 185 NAE= 40 NBE= 40 NFC= 11 NFV= 0
NROrb= 174 NOA= 29 NOB= 29 NVA= 145 NVB= 145
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000372668	-0.000136865	0.000003928
2	6	-0.000055793	0.000028959	-0.000005915
3	7	0.000129036	0.000066629	-0.000005916
4	6	-0.000079057	-0.000157122	-0.000026059
5	6	-0.000230202	-0.000608919	-0.000085089
6	7	0.000219886	0.000089004	0.000020451
7	1	0.000035101	0.000051277	-0.000001775
8	6	0.000491834	-0.000353110	0.000212442
9	7	-0.000076120	-0.000561173	-0.000069970
10	1	0.000025200	-0.000098806	-0.000007245
11	1	-0.000316287	0.000443919	0.000017047
12	8	-0.000268862	0.000792400	-0.000076652
13	8	0.000325357	0.000353048	0.000016570
14	1	-0.000001724	0.000034511	0.000004712
15	9	0.000174300	0.000056249	0.000003470

Cartesian Forces: Max 0.000792400 RMS 0.000245977

Mulliken atomic charges:

1	C	0.084301
2	C	0.506019
3	N	-0.428719
4	C	0.153911
5	C	0.616810
6	N	-0.526802
7	H	0.163618
8	C	0.560167
9	N	-0.626698
10	H	0.277917
11	H	0.321676
12	O	-0.555984
13	O	-0.578407
14	H	0.301714
15	F	-0.269523

Sum of Mulliken charges = 0.00000
Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.247919
2	C	0.506019
3	N	-0.428719

4 C 0.153911
5 C 0.616810
6 N -0.225088
8 C 0.560167
9 N -0.027106
12 O -0.555984
13 O -0.578407
15 F -0.269523
Electronic spatial extent (au): <R**2>= 1639.5702
Charge= 0.0000 electrons

2.2.2. 6-Chloro-3-oxo-3,4-dihydropyrazine-2-carboxamide **1b**

Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RB3LYP) = -967.828856262 A.U. after 9 cycles
NFock= 9 Conv=0.86D-08 -V/T= 2.0063
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.43D-01 ExpMax= 2.52D+04 ExpMxC= 3.78D+03 IAcc=3 IRadAn= 5 AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 16 189
NBasis= 189 NAE= 44 NBE= 44 NFC= 15 NFV= 0
NROrb= 174 NOA= 29 NOB= 29 NVA= 145 NVB= 145
Keep R1, R2, and R3 ints in memory in canonical form, NReq=563693793.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000044966	-0.000057398	-0.000002944
2	6	-0.000023931	0.000002132	0.000003518
3	7	0.000063526	0.000029148	-0.000009688
4	6	-0.000077145	-0.000010653	-0.000035933
5	6	-0.000033983	0.000010524	0.000025486
6	7	0.000059990	0.000027604	-0.000007906

7	1	0.000007252	0.000008657	-0.000000821
8	6	0.000038741	0.000087056	0.000118843
9	7	-0.000007024	-0.000029904	-0.000038813
10	1	0.000007451	0.000013288	-0.000004416
11	1	-0.000002341	0.000015650	0.000003288
12	8	-0.000002049	-0.000093764	-0.000039180
13	8	0.000020115	0.000001357	-0.000014563
14	1	-0.000011732	-0.000006580	0.000002639
15	17	0.000006094	0.000002884	0.000000490

Cartesian Forces: Max 0.000118843 RMS 0.000037138

Mulliken atomic charges:

1	C	0.161915
2	C	0.077647
3	N	-0.387386
4	C	0.152744
5	C	0.617226
6	N	-0.526737
7	H	0.167877
8	C	0.561467
9	N	-0.625155
10	H	0.279281
11	H	0.318130
12	O	-0.553911
13	O	-0.571355
14	H	0.301602
15	Cl	0.026653

Sum of Mulliken charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.329792
2	C	0.077647
3	N	-0.387386
4	C	0.152744
5	C	0.617226
6	N	-0.225135
8	C	0.561467
9	N	-0.027744
12	O	-0.553911
13	O	-0.571355
15	Cl	0.026653

Electronic spatial extent (au): <R**2>= 2081.5291

Charge= 0.0000 electrons

2.2.3. 6-Bromo-3-oxo-3,4-dihydropyrazine-2-carboxamide **1c**

Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.
Requested convergence on MAX density matrix=1.00D-06.
Requested convergence on energy=1.00D-06.
No special actions if energy rises.
SCF Done: E(RB3LYP) = -3079.33724029 A.U. after 8 cycles
NFock= 8 Conv=0.94D-08 -V/T= 2.0066
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.43D-01 ExpMax= 5.74D+05 ExpMxC= 5.74D+03 IAcc=3 IRadAn= 5
AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 25 200
NBasis= 200 NAE= 53 NBE= 53 NFC= 24 NFV= 0
NROrb= 176 NOA= 29 NOB= 29 NVA= 147 NVB= 147
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000065943	-0.000051460	-0.000008097
2	6	0.000031688	0.000007785	0.000010664
3	7	0.000075554	0.000034152	-0.000011742
4	6	-0.000062277	-0.000005449	-0.000042169
5	6	-0.000085875	-0.000009209	0.000105380
6	7	0.000063212	0.000023539	-0.000027029
7	1	0.000013531	0.000008229	-0.000000499
8	6	0.000025947	0.000089027	0.000046864
9	7	-0.000006397	-0.000056159	-0.000016515
10	1	0.000004883	0.000009683	-0.000002517
11	1	-0.000001604	0.000046404	-0.000000346
12	8	-0.000012278	-0.000095842	-0.000012340
13	8	0.000047730	0.000006360	-0.000041443
14	1	-0.000011413	-0.000002682	0.000000899
15	35	-0.000016756	-0.000004378	-0.000001110

Cartesian Forces: Max 0.000105380 RMS 0.000040972

Mulliken atomic charges:

1	C	0.151749
2	C	0.216707
3	N	-0.413738
4	C	0.153464
5	C	0.616946
6	N	-0.529002
7	H	0.166962
8	C	0.560033
9	N	-0.625219
10	H	0.279079
11	H	0.317814
12	O	-0.554301
13	O	-0.571240
14	H	0.301094
15	Br	-0.070346

Sum of Mulliken charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms:

1	C	0.318711
2	C	0.216707
3	N	-0.413738
4	C	0.153464
5	C	0.616946
6	N	-0.227909
8	C	0.560033
9	N	-0.028326
12	O	-0.554301
13	O	-0.571240
15	Br	-0.070346

Electronic spatial extent (au): <R**2>= 2764.1986

Charge= 0.0000 electrons

2.2.4. 6-Iodo-3-oxo-3,4-dihydropyrazine-2-carboxamide **1d**

Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.

Requested convergence on MAX density matrix=1.00D-06.

Requested convergence on energy=1.00D-06.

No special actions if energy rises.

Defaulting to unpruned grid for atomic number 53.

Defaulting to unpruned grid for atomic number 53.

Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
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Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
Defaulting to unpruned grid for atomic number 53.
SCF Done: E(RB3LYP) = -519.000481027 A.U. after 10 cycles
NFock= 10 Conv=0.59D-08 -V/T= 2.0231
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.05D-01 ExpMax= 5.48D+03 ExpMxC= 8.25D+02 IAcc=3 IRadAn= 5
AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 11 168
NBasis= 168 NAE= 39 NBE= 39 NFC= 10 NFV= 0
NROrb= 158 NOA= 29 NOB= 29 NVA= 129 NVB= 129
Keep R1, R2, and R3 ints in memory in canonical form, NReq=340119789.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000057794	-0.000030720	-0.000013102
2	6	-0.000050063	0.000011586	0.000014547
3	7	-0.000094036	0.000040028	-0.000018674
4	6	0.000070286	-0.000008674	-0.000079282
5	6	0.000081186	-0.000006618	0.000176569
6	7	-0.000056878	0.000022345	-0.000044745
7	1	-0.000025002	0.000018541	-0.000001249
8	6	-0.000015302	0.000140151	0.000112465
9	7	0.000015476	-0.000055364	-0.000041177
10	1	0.000001302	0.000001373	-0.000004929
11	1	0.000000351	0.000027912	0.000007915
12	8	0.000035838	-0.000152703	-0.000034378
13	8	-0.000045169	-0.000018465	-0.000076700
14	1	0.000003392	0.000002330	0.000002838
15	53	0.000020826	0.000008281	-0.000000097

Cartesian Forces: Max 0.000176569 RMS 0.000057134

Mulliken atomic charges:

1	C	0.196340
2	C	-0.204996
3	N	-0.255363
4	C	0.089253
5	C	0.538909
6	N	-0.473345
7	H	0.162751
8	C	0.492925
9	N	-0.587486
10	H	0.279015
11	H	0.312953
12	O	-0.512679
13	O	-0.518292
14	H	0.302229
15	I	0.177785

Sum of Mulliken charges = 0.00000

Mulliken charges with hydrogens summed into heavy atoms

1	C	0.359091
2	C	-0.204996
3	N	-0.255363
4	C	0.089253
5	C	0.538909
6	N	-0.171116
8	C	0.492925
9	N	0.004482
12	O	-0.512679
13	O	-0.518292
15	I	0.177785

Electronic spatial extent (au): <R**2>= 2368.8532

Charge= 0.0000 electrons

2.2.5. 3-Oxo-3,4-dihydropyrazine-2-carboxamide **1e**

Optimization:

Requested convergence on RMS density matrix=1.00D-08 within 128 cycles.

Requested convergence on MAX density matrix=1.00D-06.

Requested convergence on energy=1.00D-06.

No special actions if energy rises.
SCF Done: E(RB3LYP) = -508.238379402 A.U. after 9 cycles
NFock= 9 Conv=0.76D-08 -V/T= 2.0093
DoSCS=F DFT=T ScalE2(SS,OS)= 1.000000 1.000000
ExpMin= 1.61D-01 ExpMax= 5.48D+03 ExpMxC= 8.25D+02 IAcc=3 IRadAn= 5 AccDes= 0.00D+00
HarFok: IExCor= 205 AccDes= 0.00D+00 IRadAn= 5 IDoV=-2 UseB2=F ITyADJ=14
ICtDFT= 12500011 ScaDFX= 1.000000 1.000000 1.000000 1.000000
Range of M.O.s used for correlation: 11 175
NBasis= 175 NAE= 36 NBE= 36 NFC= 10 NFV= 0
NROrb= 165 NOA= 26 NOB= 26 NVA= 139 NVB= 139
Keep R1, R2, and R3 ints in memory in canonical form, NReq=428567813.
***** Axes restored to original set *****

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000045188	-0.000063054	0.000008556
2	6	-0.000043594	-0.000006747	-0.000006934
3	7	0.000014411	0.000058417	0.000005149
4	6	0.000034586	-0.000024525	0.000013911
5	6	0.000017788	-0.000030880	-0.000129685
6	7	-0.000021362	0.000047088	0.000030706
7	1	-0.000003949	0.000026837	-0.000000202
8	1	0.000018090	0.000002849	0.000000113
9	6	0.000022085	0.000055588	0.000086770
10	7	-0.000021132	-0.000020632	-0.000025008
11	1	-0.000000103	-0.000006829	-0.000001679
12	1	0.000020629	0.000035428	-0.000000016
13	8	-0.000054404	-0.000092595	-0.000032411
14	8	-0.000026187	0.000016049	0.000050081
15	1	-0.000002046	0.000003006	0.000000648

Cartesian Forces: Max 0.000129685 RMS 0.000038552

Mulliken atomic charges:

1	C	0.133452
2	C	0.073046
3	N	-0.400728
4	C	0.155373
5	C	0.612172
6	N	-0.527178
7	H	0.147579
8	H	0.125672
9	C	0.558798
10	N	-0.626562

```
  11  H    0.275268
  12  H    0.316873
  13  O   -0.562070
  14  O   -0.576570
  15  H    0.294875
Sum of Mulliken charges =   0.00000
Mulliken charges with hydrogens summed into heavy atoms:
   1  C    0.281031
   2  C    0.198718
   3  N   -0.400728
   4  C    0.155373
   5  C    0.612172
   6  N   -0.232303
   9  C    0.558798
  10  N   -0.034421
  13  O   -0.562070
  14  O   -0.576570
Electronic spatial extent (au):  <R**2>=           1294.9345
Charge=              0.0000 electrons
```