A Theoretical Study of Substituted Stepwise Fluorinated Cyclopropanone Keto-Enol System

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MINDO-Forces calculations have been performed with complete optimization of the geometries on stepwise fluorinated cyclopropanones and their enols. Increase in the number of fluorine atoms causes destabilization of cyclopropanone. Perfluorinated enol was found to be present in substantial concentration, as was mentioned in previous work. This is supported by calculations of Gibbs free energies and isodesmic reactions. Geometrical parameters, heats of formation, electron densities, dipole moments and orbital energies (HOMO-LUMO) are reported.

Key words: Fluorinated Cyclopropanone; Keto-enol.

1. Introduction

Cyclopropanone is one of the most interesting molecules in organic chemistry [1 – 5]. Because of its unique structure and bonding characteristics, cyclopropanone has been the subject of many theoretical calculations [6 – 15]. These studies have dealt with the structure, reactions and rearrangements of strained cyclic ketones.

Cyclopropanone and its substituted precursors have never been studied as keto-enol tautomeric systems, except perfluorinated cyclopropanone [16]. This perfluorination was studied by ab initio calculations and has shown that the enol form should be present in substantial concentrations.

In the present paper the keto-enol tautomerism for the parent cyclopropanone and its enol counterpart together with stepwise fluorination, have been reinvestigated by the MINDO-Forces method [17], whereby the molecular energy of the compounds obtained from the semiempirical MINDO/3 MO [18] was completely minimized by the Murtagh-Sargent technique [19]. The derivative of the energy was calculated according to Pulay's Force method [20]. The program allows variation of the β-parameter with geometrical change in a consistent way. A full description of the program and its application is given in [17a].

2. Results and Discussion

The semiemperical MINDO-Forces method [17] was used to calculate fully optimized geometries of 11 fluorinated cyclopropanones and their enol counterparts. The structures of these compounds are shown in Figure 1. The obtained optimized geometrical parameters are given in Table 1.

2.1. *Relative Stability of the Fluorinated Cyclopropanonecyclopropenol System*

Introduction of fluorine atoms causes a change in the geometrical parameters (bond lengths and bond angles) of cyclopropanones and their enols mainly where the fluorine atom is attached (Table 1).

The calculated heats of formation and dipole moments are given in Table 2. It was found that cyclopropanone **1** has a heat of formation of -19.432 kcal/mol, while that of cyclopropenol **6** is -1.748 kcal/mol. Therefore cyclopropanone is by 17.684 kcal/mol more stable than cyclopropenol. This is confirmed by the calculated Gibbs free energy $\triangle G$, which is 17.509 kcal/mol (**1** in Table 3). This indicates that the keto-enol system is nonspontaneous, and cyclopropanone is more stable than cyclopropenol. This $\triangle G$, value will be taken as reference for determining the relative stability of fluorinated keto-enol systems.

1. Fluorocyclopropanone **2** (Fig. 1) is an unsymmetric ketone and can form the enols **7** and **8**. Enol **7** is formed by an H_1 shift from C_1 (compound **2**) which has the electron density 1.020 (Table 4), greater than that of the parent cyclopropanone **1** (0.972). So the enol formed from this side may be not favorable. This is indicated by 2. in Table 3, where

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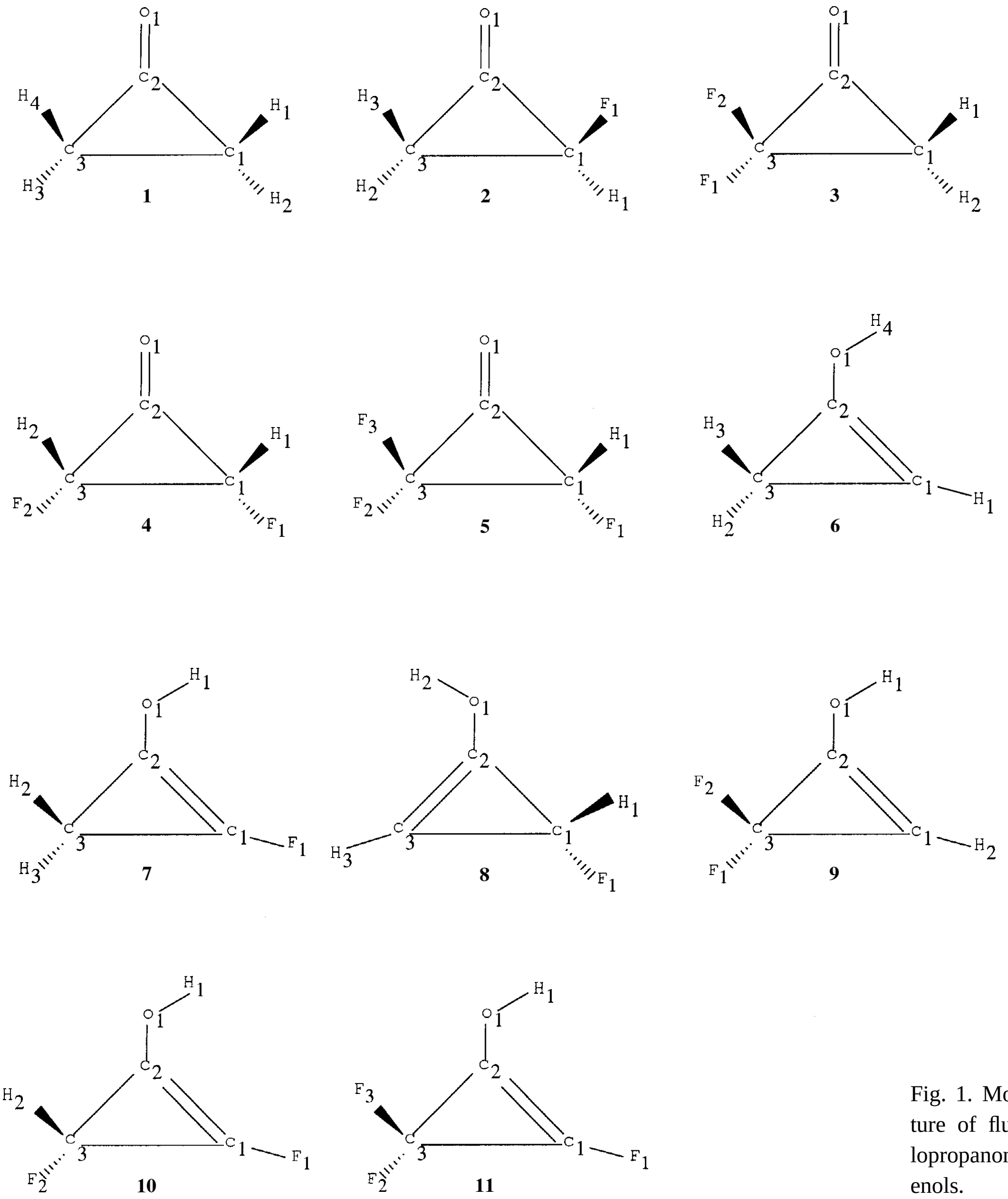


1 **2** **3** **4** **5** **6** **7** **8** **9** **10** **11**

Fig. 1. Molecular structure of fluorinated cyclopropanones and their enols.

$\triangle G = 17.303$ kcal/mol. It is almost equal to the $\triangle G$ value of the cyclopropanone-cyclopropenol transformation ($\triangle G = 17.509$ kcal/mol), which suggests that the reaction is not spontaneous and enol is unstable. The stabilization effect is also supported by using the isodesmic reaction [21–24]. A negative value for the reaction indicates a less stable, and a positive value a more stable product. It can be seen that $\triangle H_{\text{rxn(enol)}} = -4.280$ kcal/mol (2. in Table 5) is more negative than that of ketone 2 ($\triangle H_{\text{rxn(ketone)}} = -3.429$ kcal/mol, 1. in Table 5), which indicates that the enol is less stable than the ketone. The second enol (8. in Fig. 1) is formed from the shift of H_2 on C_3 (compound **2**), which has electron density 0.960 (Table 4) less (more acidic) than that of the parent cyclopropanone proton 1 (0.972). So this enol might have a relatively greater stability than the parent compound. This is indicated by 3. in Table 3 where $\Delta\triangle G = 7.241$ kcal/mol. The $\triangle G$

Table 1. Optimized geometrical parameters of stepwise fluorinated cyclopropanones and their enols (see Fig. 1 for numbering).

Molecule No.	Bond	Calculated Bond Length Å	Bond Angle	Calculated Angle Degree
1	C_1-C_2	1.479	$<C_1C_2O_1$	148.9
	C_1-C_3	1.522	$<C_2C_3C_1$	62.1
	C_2-C_3	1.472	$<C_3C_1C_2$	59.2
	C_2=O_1	1.189	$<C_1C_2C_3$	58.7
	C_1-H_1	1.105	$<H_1C_1C_2$	122.0
	C_1-H_3	1.104	$<H_1C_1H_2$	107.5
			$<C_2C_3H_4$	120.5
2	C_1-C_2	1.476	$<C_1C_2C_3$	60.9
	C_2-C_3	1.489	$<C_2C_3C_1$	59.1
	C_3-C_1	1.505	$<C_3C_1C_2$	59.9
	C_2=O_1	1.186	$<C_1C_2O_1$	149.9
	C_1-F_1	1.390	$<F_1C_1C_2$	117.9
	C_1-H_1	1.104	$<F_1C_1H_1$	106.3
	C_3-H_2	1.104	$<H_1C_1C_3$	125.3
	C_3-H_3	1.106	$<C_2C_3H_3$	119.4
			$<H_3C_3H_2$	108.3
			$<C_1C_2H_2$	120.1
3	C_1-C_2	1.515	$<C_1C_2C_3$	59.9
	C_2-C_3	1.473	$<C_2C_3C_1$	61.4
	C_3-C_1	1.494	$<C_3C_1C_2$	58.6
	C_2=O_1	1.184	$<H_1C_1C_2$	120.5
	C_1-H_1	1.103	$<H_1C_1H_2$	107.7
	C_3-F_2	1.355	$<C_1C_2O_1$	149.7
			$<C_1C_3F_1$	120.0
			$<C_2C_3F_2$	120.8
			$<F_2C_3F_1$	107.9
4	C_1-C_2	1.491	$<C_1C_2C_3$	60.0
	C_2-C_3	1.489	$<C_2C_3C_1$	60.1
	C_3-C_1	1.489	$<C_3C_1C_2$	59.9
	C_2=O_1	1.183	$<H_1C_1C_2$	123.7
	C_1-H_1	1.102	$<H_1C_1F_1$	107.4
	C_1-F_1	1.391	$<C_1C_2O_1$	149.9
	C_3-F_2	1.390	$<C_1C_3F_2$	116.3
	C_3-H_2	1.102	$<C_2C_3H_2$	123.0
			$<H_2C_3F_2$	108.3
5	C_1-C_2	1.514	$<C_1C_2C_3$	59.0
	C_2-C_3	1.487	$<C_2C_3C_1$	61.4
	C_3-C_1	1.478	$<C_3C_1C_2$	59.6
	C_2=O_1	1.178	$<H_1C_1C_2$	121.7
	C_1-H_1	1.109	$<H_1C_1F_1$	106.9
	C_1-F_1	1.387	$<C_1C_2O_1$	150.4
	C_3-F_2	1.359	$<C_1C_3F_2$	117.6
	C_3-F_3	1.354	$<C_2C_3F_3$	120.6
			$<H_2C_3F_2$	120.9
			$<F_3C_3F_2$	108.9
6	C_1=C_2	1.328	$<C_1C_2C_3$	63.9
	C_2-C_3	1.477	$<C_2C_3C_1$	53.1
	C_3-C_1	1.491	$<C_3C_1C_2$	62.9
6	C_2-O_1	1.303	$<C_2O_1H_1$	109.3
	O_1-H_1	0.956	$<C_2C_1H_2$	152.8
	C_1-H_2	1.084	$<C_2C_3H_3$	123.1
	C_3-H_4	1.114	$<H_4C_3H_3$	105.4
			$<H_4C_3C_1$	122.5
			$<C_1C_2O_1$	151.2
7	C_1=C_2	1.318	$<C_1C_2C_3$	62.3
	C_2-C_3	1.506	$<C_2C_3C_1$	52.6
	C_3-C_1	1.469	$<C_3C_1C_2$	65.2
	C_2-O_1	1.308	$<H_2C_3H_3$	105.6
	O_1-H_1	0.956	$<C_1C_2O_1$	153.5
	C_3-H_3	1.114	$<C_2O_1H_1$	107.9
	C_3-H_2	1.114	$<C_1C_3H_3$	123.0
	C_1-F_1	1.357	$<F_1C_1C_2$	151.1
8	C_3=C_2	1.348	$<C_3C_2C_1$	62.3
	C_2-C_3	1.463	$<C_2C_1C_3$	54.9
	C_3-C_1	1.457	$<C_1C_3C_2$	62.7
	C_1-F_1	1.388	$<F_1C_1H_1$	99.7
	C_2-O_1	1.296	$<C_3C_2O_1$	149.9
	O_1-H_2	0.956	$<C_2O_1H_2$	110.9
	C_3-H_1	1.085	$<C_2C_1H_1$	128.3
			$<C_3C_1F_1$	121.6
9	C_1=C_2	1.359	$<C_1C_2C_3$	61.1
	C_2-C_3	1.463	$<C_2C_3C_1$	55.9
	C_3-C_1	1.437	$<C_3C_1C_2$	62.9
	C_2-O_1	1.291	$<H_2C_1C_2$	149.6
	O_1-H_1	0.956	$<C_1C_2O_1$	149.0
	C_3-F_1	1.355	$<C_2O_1H_1$	111.9
			$<C_1C_3F_1$	124.7
			$<F_1C_3F_2$	99.5
10	C_1=C_2	1.337	$<C_1C_2C_3$	61.1
	C_2-C_3	1.488	$<C_2C_3C_1$	54.3
	C_3-C_1	1.442	$<C_3C_1C_2$	64.7
	C_1-F_1	1.357	$<F_1C_1C_2$	149.3
	C_2-O_1	1.302	$<C_1C_2O_1$	151.1
	O_1-H_1	0.957	$<C_2O_1H_1$	108.9
	C_3-H_2	1.108	$<C_1C_3F_2$	120.8
	C_3-F_2	1.384	$<C_2C_3H_2$	127.9
			$<H_1C_3F_2$	100.0
11	C_1=C_2	1.349	$<C_1C_2C_3$	60.6
	C_2-C_3	1.485	$<C_2C_3C_1$	55.1
	C_3-C_1	1.434	$<C_3C_1C_2$	64.4
	C_1-F_1	1.352	$<F_1C_1C_2$	148.3
	C_2-O_1	1.297	$<C_1C_2O_1$	150.6
	O_1-H_2	0.956	$<C_2O_1H_1$	110.3
	C_3-F_2	1.350	$<C_1C_3F_2$	124.5
			$<C_2C_3F_2$	124.7
			$<F_3C_3F_2$	100.4

value decreases from 17.509 kcal/mol in the parent cyclopropanone to 7.241 kcal/mol. This result is also supported by the isodesmic reaction, where $\triangle H_{\mathrm{rxn(enol)}} = -1.138$ kcal/mol (3. in Table 5) is more positive than that of the ketone ($\triangle H_{\mathrm{rxn(Ketone)}} = -3.429$ kcal/mol, 1. in Table 5) indicating that the enol is relatively more stable than the ketone.

2. 3,3-Difluorocyclopropanone compound **3** (Fig. 1) has one possibility of enol formation. The enol that might be formed is enol **9** (Fig. 1), resulting from

Table 2. Calculated δH_f (kcal/mol) and μ (Debye) of fluorinated Cyclopropanones and Cyclopropenols (see Figure 1 for numbering).

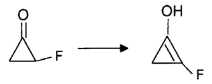
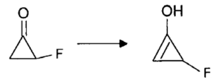
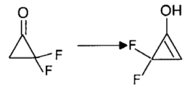
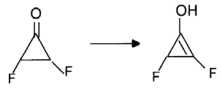
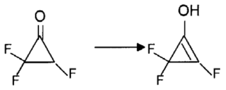
Compd. #	$\triangle H_f$	μ	Compd. #	$\triangle H_f$	μ
1	−19.432	2.075	7	−52.204	1.280
2	−69.632	3.363	8	−62.122	3.112
3	−128.618	2.458	9	−124.362	4.200
4	−119.698	0.431	10	−111.989	2.561
5	−175.685	1.909	11	−173.669	3.334
6	−1.748	1.450			

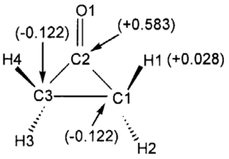
an H_1 shift on C_1. The electron density for this proton is 0.929 (compound **3** in Table 4), which is less than that of the parent cyclopropanone proton (0.972). So this enol may have a relatively greater stability than the parent compound. This is supported by thermodynamic calculations in Table 3, 4. where $\triangle G = 3.898$ kcal/mol is less than that of the parent ($\triangle G = 17.509$ kcal/mol). This suggests that the two fluorine atoms destabilized the ketone. i.e increase the stability of the enol. This is also supported by the isodesmic reaction, where $\triangle H_{\text{rxn(enol)}} = 2.018$ kcal/mol (5. in Table 5) is more positive than that of the ketone ($\triangle H_{\text{rxn(ketone)}} = -5.593$ kcal/mol, 4. in Table 5), indicating that the enol is relatively more stable than the ketone.

3. 1,3-Difluorocyclopropanone compound **4** is a symmetrical ketone (Fig. 1). The possible enol formed is compound **10**. The $\triangle G$ value is calculated to be 7.521 kcal/mol (5. in Table 3), which is less than that of the parent keto – enol transformation ($\triangle G = 17.509$) indicating the increase in the enol stability.

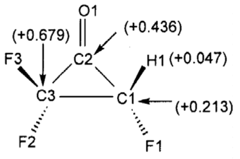
4. 1,3,3-Trifluorocyclopropanone (perfluorination) compound **5** (Fig. 1) has one possibility of enol formation. The enol formed is compound **11** resulting from H_1 shift on C_1. The electron density of H_1 in ketone **5** is 0.953 (Table 4), which is less than that of the parent cyclopropanone (0.972). So the enol formation may have a higher relative stability than the parent. This is indicated by 6. in Table 3, where $\triangle G = 1.401$ kcal/mol is less than the parent ($\triangle G = 17.509$ kcal/mol). This indicates that the enol becomes relatively more stable. This result is also supported by the isodesmic reactions, where $\triangle H_{\text{rxn(enol)}} = -1.719$ kcal/mol (9. in Table 5) is more positive than that of the ketone ($\triangle H_{\text{rxn(ketone)}} = -8.312$ kcal/mol, 8. in Table 5). This suggests an increase in the relative stability of the enol, but both enol and ketone are still unstable. The stability of enol is a result of the destabilization of ketone. This result agrees with previous work on trifluorocyclopropanone (perfluorination) [16].

Table 3. Gibbs free energy for fluorinated cyclopropanones and cyclopropenols.

No		ΔG (kcal/mol)
1.		17.509
2.		17.303
3.		7.241
4.		3.898
5.		7.521
6.		1.401

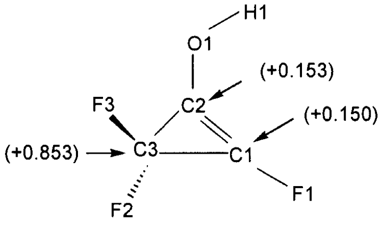


1



5

The calculated charge distribution in 2H-perfluorocyclopropanone **5**, obtained from the electron density (Table 4), may give a plausible explanation for its destabilization. The calculated charge at the α-carbons (C1, C3) is more positive in ketone **5** than ketone **1**. The positive charge adjacent to carbonyl is destabilizing due to the electrostatic repulsion between the α-carbons and the carbonyl carbon. Therefore this repulsion might be responsible for the destabilization of 5. The hydrogen H1 becomes more acidic (+0.047) in ketone **5** than in ketone **1** (+0.028). Increasing the acidity of this hydrogen H1 is likely to be important for easy enolization.



11

Compd.	C_1	C_2	C_3	O_1	H_1	H_2	H_3	H_4	F_1	F_2	F_3
1	4.122	3.417	4.120	6.456	0.972	0.972	0.971	0.971			
2	3.698	3.472	4.179	6.415	1.020	0.960	0.935		7.320		
3	4.224	3.519	3.274	6.372	0.929	0.929			7.376	7.376	
4	3.749	3.526	3.747	6.373	0.984	0.985			7.318	7.318	
5	3.787	3.564	3.321	6.330	0.953				7.285	7.385	7.345
6	4.252	3.671	3.895	6.397	0.749	0.927	1.055	1.055			
7	4.269	3.702	3.498	6.378	0.746	0.927	0.913		7.427		
8	3.927	3.810	3.789	6.376	1.038	0.747	1.038		7.278		
9	4.310	3.737	3.115	6.362	0.742	0.848			7.418	7.418	
10	3.812	3.821	3.532	6.364	0.737	1.050			7.270	7.415	
11	3.850	3.847	3.147	6.354	0.730				7.259	7.407	7.407

Table 4. Calculated electron density of fluorinated cyclopropanones and cyclopropenols (see Fig. 1 for numbering).

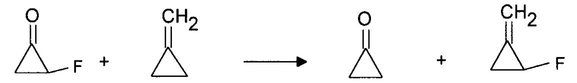
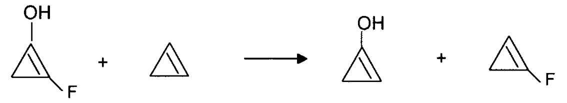
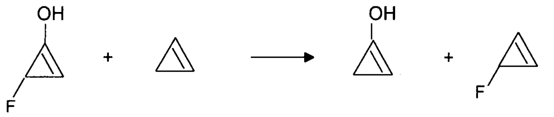
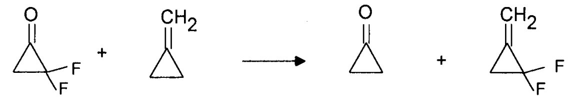
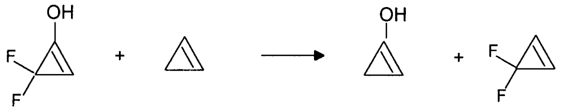
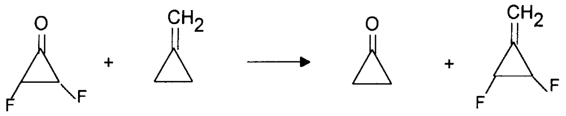
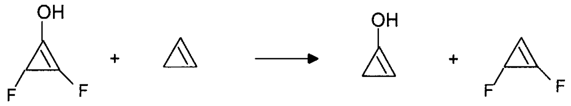
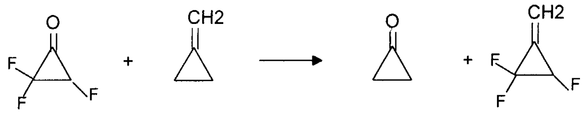
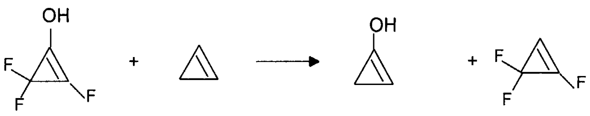
	Isodesmic reaction	$\triangle H_{rxn}$
1.		−3.429
2.		−4.280
3.		−1.138
4.		−5.593
5.		2.018
6.		−2.832
7.		−2.811
8.		−8.312
9.		−1.719

Table 5. Evaluation of substituent effects on cyclopropanones and cyclopropenols via isodesmic reactions.

In the case of enol **11**, the electrostatic forces between the two positive α-carbons (C1, C3) and the carbonyl carbon (C1) are less repulsive than those in ketone **5**. Thus the enol form is favored over the ketone form in a similar explanation to that given in previous work on 2H-Perfluorocyclobutanone and 2H-Perfluorocyclopentanone [25, 26].

Table 6. Calculated HOMO and LUMO (eV) of fluorinated cyclopropanones and cyclopropenols. (see Figure 1 for numbering).

Compd.	HOMO	LUMO	Gap
1	−10.178	0.593	10.771
2	−10.592	0.104	10.696
3	−11.012	−0.308	10.704
4	−10.984	−0.363	10.621
5	−11.377	−0.734	10.643
6	−9.170	1.010	10.492
7	−9.482	0.439	9.921
8	−9.801	0.417	10.218
9	−10.372	−0.136	10.236
10	−10.071	−0.129	9.942
11	−10.565	−0.647	9.918

2.2. The Dipole Moment of Fluorinated Cyclopropanones and their Enols

Stepwise fluorination affects the dipole moment of ketones and their enols as shown in Table 2. Introduction of a fluorine atom into cyclopropanone increases the dipole moment from 2.075 Debye (**1** without fluorination) to 3.363 Debye (**2** with fluorination). This is due to the presence of the fluorine atom near the carbonyl group. It is shown from **4** that the two fluorine atoms decrease the dipole moment to 0.431 Debye. This is because the resultant of the two fluorine atoms and the carbonyl group are in opposite direction. But when the two fluorine atoms are at the same carbon atom (compound **3**), the dipole moment is greater than that in compound **4**. Compound **5** shows that the dipole moment is greater than that in compound **4**, since the resultant of the three fluorine atoms has constructive direction with the carbonyl group. Similarly the changes in the dipole moments of the fluorinated cyclopropenols can be explained.

2.3. HOMO-LUMO of Fluorinated Cyclopropanones and their Enols

The introduction of fluorine atoms into cyclopropanones and their enols affect their orbital energies (HOMO and LUMO) compared with their parent compounds.

In the case of fluorinated ketones (compounds **2** – **5**, Table 6), an increase in the number of fluorine atoms causes a decrease in the energy gaps, but not steadily. This depends on the geometry of the compound.

Same trends are observed in the case of fluorinated enols (compounds **7** – **11**, Table 6). This decrease in the energy gaps suggests a destabilization of ketone and enol.

In the case of the perfluorination of ketone **1** (Table 6), the energy gap decreases from 10.771 ev (compound **1**, without perfluorination) to 10.643 ev (compound **5**, with perfluorination), suggesting a destabilization of the ketone.

Also, in the case of perfluorination of enol **6**, the energy gap decreases from 10.492 ev (compound **6**, without perfluorination) to 9.918 ev (compound **11**, with perfluorination), suggesting a destabilization of the enol too. Thus both enol and ketone are still unstable, which was mentioned in previous work [16].

3. Conclusion

It can be concluded that cyclopropanone is more stable than cyclopropenol by 17.684 kcal/mol. This stability of cyclopropanone was found to decrease on fluorination. Perfluorinated enol was found to be present in substantial concentration. These results were confirmed by Gibbs free energy calculations, isodesmic reactions and orbital energies.

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