

## Ab Initio, NBO and NICS Studies of the Decomposition ([2+2] elimination) Mechanisms of 2-Halo-2, 3-dihydropyridines

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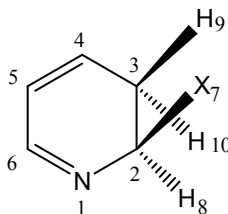
### ABSTRACT

The decomposition of 2-Fluoro-2,3-Dihydropyridine (**1**) 2-Chloro-2,3-Dihydropyridine(**3**) 2-Bromo-2,3-Dihydropyridine(**5**) to pyridine and HX(X=F, Cl, Br) was investigated using Ab initio Molecular Orbital (MO) and Density Functional Theory (DFT). This is possible for all HX elimination reactions examined here, the two pass ways as well as three or four centered transition state structures. Calculation results for the B3LYP/6-311+G\*\*, HF/6-311+G\*\*//B3LYP/6-311+G\*\* and MP2/6-311+G\*\*//B3LYP/6-311+G\*\* levels of theory for comparison of these two pass ways, showed that passing from four centered-transition state is more likely than three centered-transition state. Study on the B3LYP/6-311+G\*\* level of theory revealed that the required energy for decomposition of compound **1**, **3** and **5** to pyridine is 32.483165, 23.329822 and 19.987130 kcal mol<sup>-1</sup>, respectively. In a similar vein, these calculations were performed on HF/6-311+G\*\*//B3LYP/6-311+G\*\* and MP2/6-311+G\*\*//B3LYP/6-311+G\*\* levels of theory. Natural Bond Orbitals (NBO) population analysis and Nuclear Independent Chemical Shift (NICS) results showed that in transition state (four-membered planar structure) C-H and C-X bonds break and H-X bonds appear; besides, the results showed that reactants are non-aromatic, but elimination reaction products are aromatic.

**KEYWORDS:** Ab initio; NBO; NICS; Elimination; 2-halo-,2,3dihydropyridines.

### 1. INTRODUCTION

The decomposition mechanism of 2-halo-2,3-dihydropyridines to pyridine and HX(X=F(**1**), Cl(**3**), Br(**5**)) was investigated using Ab-initio Molecular Orbital (MO) and Density Functional Theory (DFT).[Scheme 1] The experimental study of the kinetic energy resulting from dissociation process of 2-halo-2,3-dihydropyridines, investigated by Liu [1], showed that the decomposition reaction is a unimolecular process which results from two pass ways, that is, three centered and four centered transition state. The results supported a four-membered transition state rather than a three-membered transition state structure.



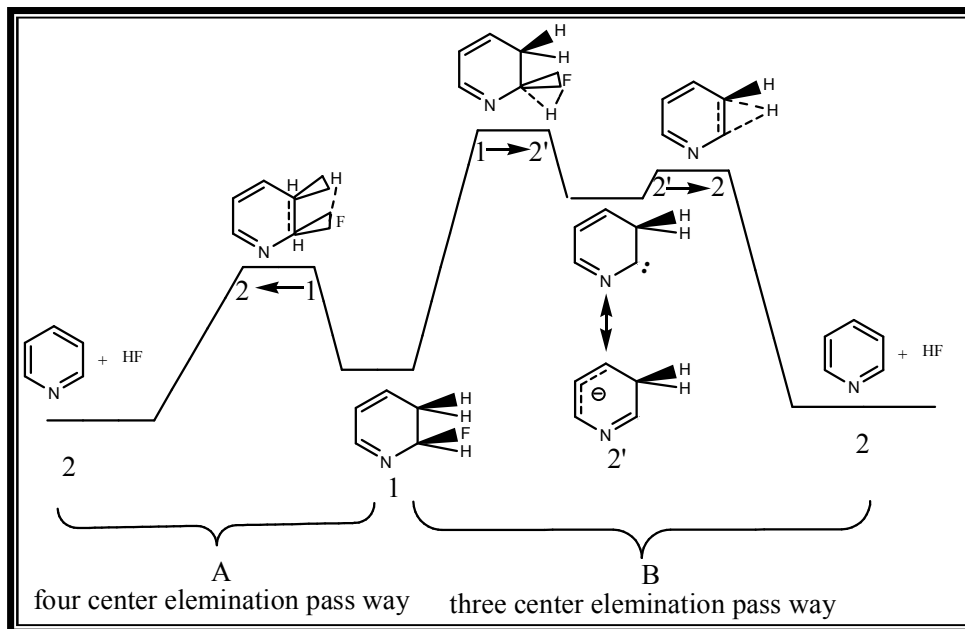
X=F: **1**, X=Cl: **3** and X=Br: **5**

[Scheme 1]

The successful application of methods based on Density Functional Theory (DFT) has broadened the applicability of the computational methods and now represents an interesting approach for determining activation barriers and molecular energy.[2-6] The B3LYP method combines Becke's three-parameter exchange function with the correlation function of Lee and colleagues.[3,4] Therefore, in the present research, at first, two pass ways for decomposition of 2-fluoro-2,3-dihydropyridines to pyridine and HF through four-member (A) and three-member (B) transition state pass ways were compared using a DFT-B3LYP method (scheme 2). Then ab initio molecular orbital (MO),[2] DFT (B3LYP) methods[3-6] and

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NBO analysis[7–10] were performed on the basis of a two-fold aim: first, to investigate the pyrolysis reactions of 2-fluoro-2,3-dihydropyridine (**1**), 2-chloro-2,3-dihydropyridine(**3**) and 2-bromo-2,3-dihydropyridine(**5**) to pyridine and HX (X=F, Cl, Br) through four-membered transition state pass way; the second aim was to address, particularly, the arisen questions regarding these reactions.



## 2. Theoretical methods

Ab initio calculations were carried out using B3LYP/6-311+G\*\*, HF/6-311+G\*\*// B3LYP /6-311+G\*\*, and MP2/6-311+G\*\*// B3LYP /6-311+G\*\* levels of the theory with GAUSSIAN 98 package of programs [2] installed on a Pentium-PC computer with a 7300 MHz processor. Initial estimation of the structural geometry of the compound **1**, **3** and **5** were obtained by a molecular mechanic program PCMODEL (88.0) [3] and for further optimization of geometry, we used the PM3 method of the MOPAC 7.0 computer program [4,5]. The GAUSSIAN 98 package of programs was finally used to perform ab initio calculations at the B3LYP/6-311+G\*\* level. Minimum-energy molecular geometries were located by minimizing energy, with respect to all geometrical coordinates without imposing any symmetrical constraints. The nature of the stationary points for compound **1**, **3** and **5** and transition state structures were fixed by means of a number of imaginary frequencies. For minimum state structure, only real frequency values, and in the transition-state, only single imaginary frequency values were accepted [5, 6] (keyword SADDLE). These geometrical structures were reoptimized by the QST2 subroutine at the B3LYP/6-311+G\*\* level. For further optimization, TS subroutine was used. The vibrational frequencies of ground states and transition states were calculated by FREQ subroutine.

## 3. RESULTS AND DISCUSSION

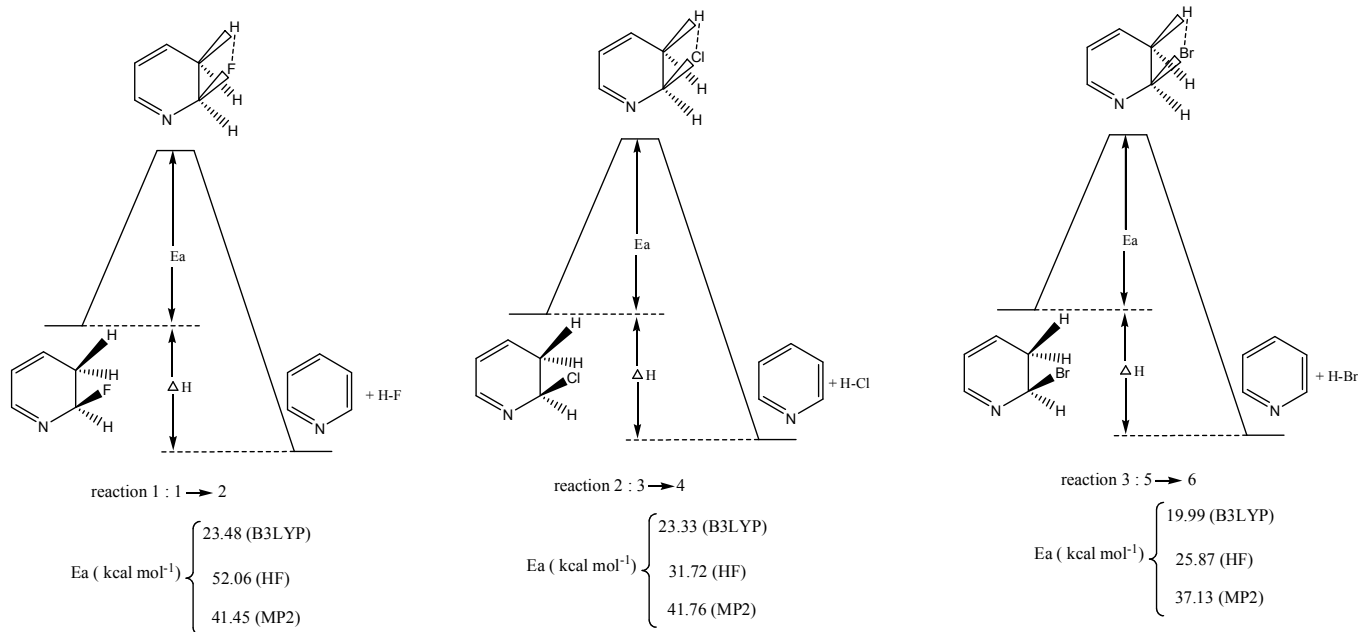
Zero point energy (*ZPE*) and total electronic ( $E_{el}$ ) energy ( $E_0 = ZPE + E_{el}$ ) for the minimum and maximum energy geometries from two path ways of the decomposition of compound **1**, **3** and **5** were calculated on the B3LYP/6-311+G\*\* level of theory. For single-point energy calculations, both HF/6-311+G\*\*// B3LYP /6-311+G\*\* and MP2/6-311+G\*\*// B3LYP /6-311+G\*\* methods were used (Table 2).

Studies on B3LYP /6-311+G\*\* level of theory show that the barrier height of the decomposition of the compound **1** to pyridine for pass way **A** (32.483165 kcal mol<sup>-1</sup>) is lower than pass way **B** (56.122345 kcal mol<sup>-1</sup>). These results justify the four-membered transition state, which are in good agreement with experimental methods. (Table 1)

Studies on the B3LYP/6-311+G\*\*, HF/6-311+G\*\*// B3LYP /6-311+G\*\*, and MP2/6-311+G\*\*// B3LYP /6-311+G\*\* of theory show that barrier height of the decomposition of the compound **1** to pyridine

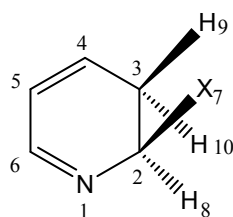
and HF (reaction 1) is 32.483165, 52.061165 and 41.448885 kcal mol<sup>-1</sup>, respectively. These calculation results for compound **2** revealed that the barrier height of reaction 2 is 23.329822, 31.720752 and 41.768282 kcal mol<sup>-1</sup>, respectively. Also, barrier height of reaction **3** is 19.987130, 25.866177 and 37.129175 kcal mol<sup>-1</sup>, respectively (see Figure 1).

It is well known that the strength of C-X bonds decreases, while the bond length increases with the size of halide atom. Lengths of the determined C-F, C-Cl and C-Br bonds were found to be 1.41, 1.86 and 2.04 Å, respectively, which is in agreement with energetic behavior and other experimental data [11,12].



*Fig 1: B3LYP, HF and MP2 energy diagram of decomposition of compounds 1,3 and 5*

C-C bond lengths in reactants are greater than transition states and products in reactions 1-3 which shows that C=C double bond is formed in products. (See table 3,4) Also, Natural Bond Orbital (NBO) data reveal that electron population of C-C bond in reactants is similar to that of the single bond but in products is similar to that of the double bond. (See table 5).



[Scheme 3]

In order to understand the reason for the lower barrier height of reaction 3 in comparison with reactions 1 and 2, natural charge distribution (from NBO calculations) for the ground state structures of compounds 1, 3, 5 and the transition state structures of reactions 1-3 has been carried out. Consequently, for such a drastic change in the charge distribution of halide and hydrogen atoms in the transition state structures of reactions 1, 2 and 3, the formation of the transition structure of reaction 3 is more favorable than reaction 1 and 2 because of the larger variation of the charge distribution of the Br atom in the transition state structure of reaction 3. According to the Natural charge distribution results, the hydrogen atom charge in the ground state structure of compound **5** and **6** is 0.17609 and 0.18256 respectively, while in the transition state structure of reaction 3 it is 0.20551. (See Table 6)

Value of C2-C3-H9-X7 dihedral angles in transition state shows the planar structure for transition state. This form is the best structure for H-X dissociation. Internal dihedral angles in the heterocyclic structures of reactants and products reveal that reactants are non-planar (non-aromatic) while products are planar and aromatic. (See table 4) Natural Bond Orbital (NBO) population analysis and Nuclear Independent Chemical Shift (NICS) [13] results are in good agreement with calculated structural parameters.

The NBO analysis of donor-acceptor interactions shows that the resonance energies of  $\pi_{C2-C3} \rightarrow \pi^*_{C4-C5}$  and  $\pi_{C2-C3} \rightarrow \pi^*_{N1-C6}$  for electron delocalization in pyridine as product are 22.74 and 17.22 kcal mol<sup>-1</sup>, respectively. These electronic transitions disappear in reactant; therefore C-C bond in reactant is a single bond.

Nuclear Independent Chemical Shift (NICS) results at GIAO/B3LYP/6-311+G\*\* level of the theory reveal that pyridine cycle is aromatic while all reactants are non-aromatic.

NICS values for ring center, as well as 0.5 and 1 angstrom upper than the ring center are 2.578, 0.306 and -1.325 for compound 1 and -7.126, -9.454 and -10.213 for compound 2 (pyridine), respectively. (See table 7)

Table1: Calculated B3LYP/6-311+G\*\* total Energy ( $E$ ), Zero-Point Energies  $ZPE$ , and Relative Energies for the energy minima structures of compounds 1, 2, 2' and transition structures for two reaction pass ways (Scheme 2).

Pass way	Geometry	$ZPE$	$E_d$	$E_0$	$\Delta E_0$
A	1	0.102700	-348.799821	-348.697121	<b>0.000000</b> (0.000000) <sup>b</sup>
	2	0.101302	-348.855846	-348.754544	<b>-0.057423</b> (-36.032932) <sup>b</sup>
	[1→2]#	0.096742	-348.742097	-348.645355	<b>0.051766</b> (32.483165) <sup>b</sup>
B	[1→2']#	0.095229	-348.702912	-348.607683	<b>0.089438</b> (56.122345) <sup>b</sup>
	2'	0.096298	-348.715791	-348.619493	<b>0.077628</b> (48.71157) <sup>b</sup>
	[2'→2]#	0.095025	-348.713241	-348.618216	<b>0.078905</b> (49.512887) <sup>b</sup>

<sup>b</sup> Numbers in parenthesis are the corresponding  $\Delta E$  values in kcalmol<sup>-1</sup>

Table2: Calculated Total Energy ( $E$ ), Zero-Point Energy  $ZPE$ , and Relative Energy  $\Delta E$  ( $E_h$  in Hartree) for the energy minima structures of compounds 1-6 and transition structures of reactions 1-3

Method	B3LYP/6-311+G**				HF/6-311+G**// B3LYP /6-311+G**			MP2/6-311+G**// B3LYP /6-311+G**		
	$ZPE$ $ZPE$	$E_{el}$	$E_0$	$\Delta E_0$	$E_{el}$	$E_0$	$\Delta E_0$	$E_{el}$	$E_0$	$\Delta E_0$
1	0.102700	-348.799821	-348.697121	0.000000 (0.000000) <sup>b</sup>	-346.773413	-346.670713	0.000000 (0.000000) <sup>b</sup>	-347.848522	-347.745822	0.000000 (0.000000) <sup>b</sup>
2	0.101302	-348.855846	-348.754544	-0.057423 (-36.032932) <sup>b</sup>	-346.820286	-346.718984	-0.048271 (-30.290052) <sup>b</sup>	-347.908072	-347.806770	-0.060948 (-38.244870) <sup>b</sup>
[1→2]#	0.096742	-348.742097	-348.645355	0.051766 (32.483165) <sup>b</sup>	-346.684489	-346.587747	0.082966 (52.061165) <sup>b</sup>	-347.776510	-347.679768	0.066054 (41.448885) <sup>b</sup>
3	0.101278	-709.152944	-709.051666	0.000000 (0.000000) <sup>b</sup>	-706.814266	-706.712988	0.000000 (0.000000) <sup>b</sup>	-707.828031	-707.726744	0.000000 (0.000000) <sup>b</sup>
4	0.97565	-709.201269	-709.103704	-0.052038 (-32.653840) <sup>b</sup>	-706.854866	-706.757301	-0.044313 (-27.806407) <sup>b</sup>	-707.896223	-707.771658	-0.044914 (-28.183535) <sup>b</sup>
[3→4]#	0.096312	-709.110799	-709.014487	0.037179 (23.329822) <sup>b</sup>	-706.758749	-706.662437	0.050551 (31.720752) <sup>b</sup>	-707.756493	-707.660181	0.066563 (41.768282) <sup>b</sup>
5	0.1100669	-2823.074587	-2822.973918	0.000000 (0.000000) <sup>b</sup>	-2819.675180	-2819.574511	0.000000 (0.000000) <sup>b</sup>	-2820.675690	-2820.575021	0.000000 (0.000000) <sup>b</sup>
6	0.098679	-2823.121571	-2823.022892	-0.048974 (-30.731185) <sup>b</sup>	-2819.718522	-2819.61.984	-0.045332 (-28.445830) <sup>b</sup>	-2820.713512	-2820.614833	-0.039812 (-24.982030) <sup>b</sup>
[5→6]#	0.095993	-2823.038059	-2822.942066	0.031852 (19.987130) <sup>b</sup>	-2819.629283	-2819.533290	0.041221 (25.8661775) <sup>b</sup>	-2820.611844	-2820.515851	0.059170 (37.129175) <sup>b</sup>

Table 3: selected B3LYP/6-31+G\*\* calculated bond lengths in angstrom for the energy minima structures of compounds **1,2,2'** and transition structures of reactions in scheme 2.

Bonds	Path way A [1→2]			Path way B [1'→2']		
	1	2	---	1.963	---	---
C <sub>2</sub> -X <sub>7</sub>	1.413	1.952	---	1.963	---	---
C <sub>3</sub> -H <sub>9</sub>	1.094	1.217	---	1.088	1.089	1.086
C <sub>2</sub> -H <sub>8</sub>	1.096	---	---	2.328	---	---
C <sub>2</sub> -C <sub>3</sub>	1.526	1.475	1.391	1.493	1.505	1.726

Table 4: selected B3LYP/6-31+G\*\* calculated bond lengths in angstrom for the energy minima structures of compounds **1-6** and transition structures of reactions 1-3

Bonds	1		2		3		4		5		6	
	1	[1→2]	2	---	3	[3→4]	4	---	5	[5→6]	6	---
C <sub>2</sub> -X <sub>7</sub>	1.413	---	1.952	---	1.860	---	2.637	---	2.045	---	2.835	---
C <sub>3</sub> -H <sub>9</sub>	1.094	---	1.217	---	1.092	---	1.162	---	1.091	---	1.157	---
C <sub>2</sub> -C <sub>3</sub>	1.526	---	1.475	---	1.391	---	1.526	---	1.476	---	1.391	---

Table 5: selected B3LYP/6-31+G\*\* calculated bond populations for the energy minima structures of compounds **1-6** and transition structures of reactions 1-3

Selected Bonds	Occupancy		
	Reactant	Transition state	Product
C2 - F7	1.99138(σ)	---	---
C2 - C3	1.98728(σ)	1.97453(σ)	<b>1.98359(σ) &amp; 1.62613(π)</b>
C3 - H9	1.96601(σ)	1.73093(σ)	---
C2 - C17	1.97525(σ)	-	-
C2 - C3	1.98679(σ)	1.98144(σ)	<b>1.98294(σ) &amp; 1.62466(π)</b>
C3 - H9	1.96969(σ)	1.81076(σ)	-
C2 - Br7	1.96539(σ)	-	-
C2 - C3	1.98692(σ)	1.98287(σ)	<b>1.98168(σ) &amp; 1.61583(π)</b>
C3 - H9	1.97024(σ)	1.82613(δ)	-

Table 6: selected B3LYP/6-31+G\*\* calculated atomic charge for the energy minima structures of compounds **1-6** and transition structures of reactions 1-3

Selected Atoms	Natural Charge		
	Reactant	Transition state	Product
C2	0.38037	0.32237	<b>0.07606</b>
C3	-0.48304	-0.58277	<b>-0.23664</b>
F7	-0.40662	-0.60808	<b>-0.61743</b>
H9	0.23811	0.43980	<b>0.54577</b>
C2	0.00349	0.27010	<b>0.07874</b>
C3	-0.47078	-0.60459	<b>-0.23430</b>
CL	-0.10312	-0.58830	<b>-0.40526</b>
H9	0.23903	0.37972	<b>0.29838</b>
C2	-0.04059	0.25871	<b>0.10339</b>
C3	-0.47540	-0.60555	<b>-0.22419</b>
Br	-0.06727	-0.56061	<b>-0.68430</b>
H9	0.24001	0.36393	<b>0.37970</b>

Table 7: calculated NICS values at GIAO/B3LYP/6-311+G\*\* and Magnetic susceptibilities at CSGT/B3LYP/6-311+G\*\* level of the theory for the energy minima structures of compounds **1-6** and transition structures of reactions 1-3

compounds	X=F			X=Cl			X=Br		
	1	1→2	2	3	3→4	4	5	5→6	6
NICS(0)	2.578	0.114	-7.126	2.537	4.962	-7.316	2.682	7.369	<b>-7.877</b>
NICS(0.5)	0.306	-3.930	-9.454	0.834	0.475	-9.619	0.908	2.588	<b>-9.929</b>
NICS(1)	-1.325	-6.063	-10.213	-1.711	-3.101	-10.317	-2.743	-1.746	<b>-10.348</b>
χ	<b>-46.098</b>	<b>-44.41</b>	<b>-58.58</b>	<b>-58.096</b>	<b>-41.77</b>	<b>-74.89</b>	<b>-67.253</b>	<b>-41.65</b>	<b>-88.26</b>

#### 4. Conclusion

Ab initio HF, MP2, and B3LYP density functional-theory calculations provide a picture from structural, energetic, and natural charge distributions points of view for the decomposition mechanism of compound **1**, **3** and **5** to pyridine and HX(X=F, Cl, Br). B3LYP/6-311+G\*\*// B3LYP/6-311+G\*\*, HF/6-311+G\*\*// B3LYP /6-311+G\*\*, and MP2/6-311+G\*\*// B3LYP /6-311+G\*\* results reveal a lower barrier height for reaction 3 than that of reactions 1 and 2. These results are justified by natural charge distribution values, calculated structural parameters and NBO results analysis in the ground-state structure of compounds **1,3** and **5** and transition state structures of reactions 1– 3. NBO analysis reveals that resonance energy in products is greater than reactants. Therefore, the number of conjugated  $\pi$  bond increases in products.

Also, NICS results show that reactants are non-aromatic but products are aromatic compounds.

Consequently, the calculated data could be considered as fairly acceptable and useful information from the QSAR point of view in the corresponding organic compounds which are further confirmed by the corresponding energetic and structural results generated by the NBO analysis and NICS results.

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