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The theoretical study of the various substitutions effect in the conversion of 3-cyclopropylmethoxy-3-chloro diazirine to various products

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Abstract

Optimized geometry and the corresponding electronic structure and thermodynamic properties of cyclopropylmethoxychlorocarbene (**cpmcc**), 3-cyclopropylmethoxy-3-chlorodiazirine and their -N2 and –CO elimination and consequent rearrangement products, cyclopropylmethoxyfluorocarbene (**cpmfc**), 3-cyclopropylmethoxy-3-fluorodiazirine and its transition state and cyclopropylmethoxyhydrocarbene (**cpmhc**), 3-cyclopropylmethoxy-3-hydrodiazirine and its transition state have been calculated using ab initio methods DFT-B3LYP with 6-311++G** basis set. The effect of substitutions was investigated on thermodynamic properties of conversion of 3-cyclopropylmethoxy-3-chloro (flouro or hydro) diazirine to different products. Also, nuclear magnetic resonance chemical shifts have been calculated for reactant, transition state and product with various substitutions.

1. Introduction

Alkoxyhalocarbenes stand at an intersection of carbene, carbocation, elimination, and substitution chemistry. Their fates are decided by several fundamental mechanisms, and we can anticipate significant contributions to mechanistic organic chemistry from an understanding of their behavior [1]. Carbenes are viewed classically as electron-deficient intermediates. However, the reactivity of carbenes is strongly influenced by the electronic properties of their substituents. If one or two heteroatoms (e.g., N, O, or S) are directly bonded to the carbene carbon atom, the electronic delocalization of the lone pair can compensate for the electronic deficiency at the carbene and could cause the nature of the carbene to change from electrophilic to nucleophilic. Carbenes can thus be divided into electrophilic carbenes, nucleophilic carbenes, and ambiphilic carbenes. The investigations showed that electronegative substitutions (e.g., Cl and F) are directly bonded to the carbene carbon atom could change the nature of the carbene from nucleophilic to electrophilic [2].

Although the most important application of electrophilic carbenes in organic synthesis is the cyclopropanation of alkenes, many monoheteroatomsubstitute electrophilic carbenes have also been used in constructing heterocyclic compounds.

The aim of this research is to study in detail the electronic structure and stability of cyclopropylmethoxychloro (flouro or hydro) carbene (**cpmxc, x**=Cl, F, H, **3**) introduced recently as a transition state in the two-step conversion of 3-cyclopropylmethoxy-3-chloro (flouro or hydro) diazirine (**2**) to cyclopropylmethyl chloride (fluoride or hydride) (**5**) during fragmentation process in the mass spectroscopy experiments [3-5].

The previous studies showed that both cis and trans forms of ROCCl generated by diazirine photolysis in cryogenic matrix [6]. Hine and Skell reported that dihalocarbenes reacted with alkoxides to form alkoxyhalocarbenes, **3**, and Skell suggested that, when *sec*- or *tert*-alcohols were used, the derived carbenes fragmented to alkyl cations with the loss of CO and X^- (eq 1, X = Cl or F). Noting the close resemblance between CO and N_2, Skell offered an analogy between reaction 1 and the decomposition of alkyldiazonium ions ($RN_2^+ \rightarrow R^+ + N_2$). [7-9].

The alkoxychlorocarbenes fragmented to alkyl chlorides, alkenes, and solvolysis products via ion pairs (**4**); Eq 1 [4-6].

$$RO^- + :CX_2 \rightarrow ROCX_2^- \xrightarrow{-X^-} RO\ddot{C}X + X^- \rightarrow R^+ + CO + X^- \qquad (1)$$

In this article, DFT-B3LYP level with 6-311++G** basis set are used to study: **cpmxc**, **3** and different products **5**, cyclobutyl chloride (fluoride or hydride) **6** and 3-butenyl chloride (fluoride or hydride) **7** (Fig. 1). At the result, for these molecules investigated optimized geometry, negative modes, and parameters of NMR, NQR and IR spectra. On the other hand, stabilities of the intermediate species [4, 5, and 10] are studied based on thermodynamic properties and the corresponding negative mode.

We studied transition state for rearrangement of carbonyl group in cpmxc and investigated the effect of substitutions on it.

Also, to better understand bonding and electronic structure in **cpmxc** (x=F, Cl, H) isotropic and anisotropic NMR chemical shieldings have been calculated for the ^{13}C nuclei in reactant, transition state and products.

2. Computations

The fully optimized geometries and the corresponding electronic structures, vibrational frequencies and thermochemical properties of compounds **2** to **7** (Fig. 1) have been calculated using ab initio density function theory (DFT) using Becke's three-parameter hybrid functional combined with the Lee-Yang-Parr correlation functional (B3LYP) level of theory with 6-311++G** basis set [11,12]. All ab initio calculations were performed using GAUSSIAN 98 package [13]. Furthermore, electron spin density distribution over the entire molecule and NMR chemical shielding for all nuclei of the compound have been calculated based on the optimized geometry.

3. Results and discussion

3.1. Structural analysis

The optimized geometrical parameters obtained for **cpmxc** with different substituents are tabulated in Table 1. These data Results show that transient species **3** is formed from one cyclopropyl group with a tetrahedral structure around the C_2 carbene center. Similar to other known carbenes, the carbene bonds in **cpmxc** (x=F, Cl and H) are non-linear.

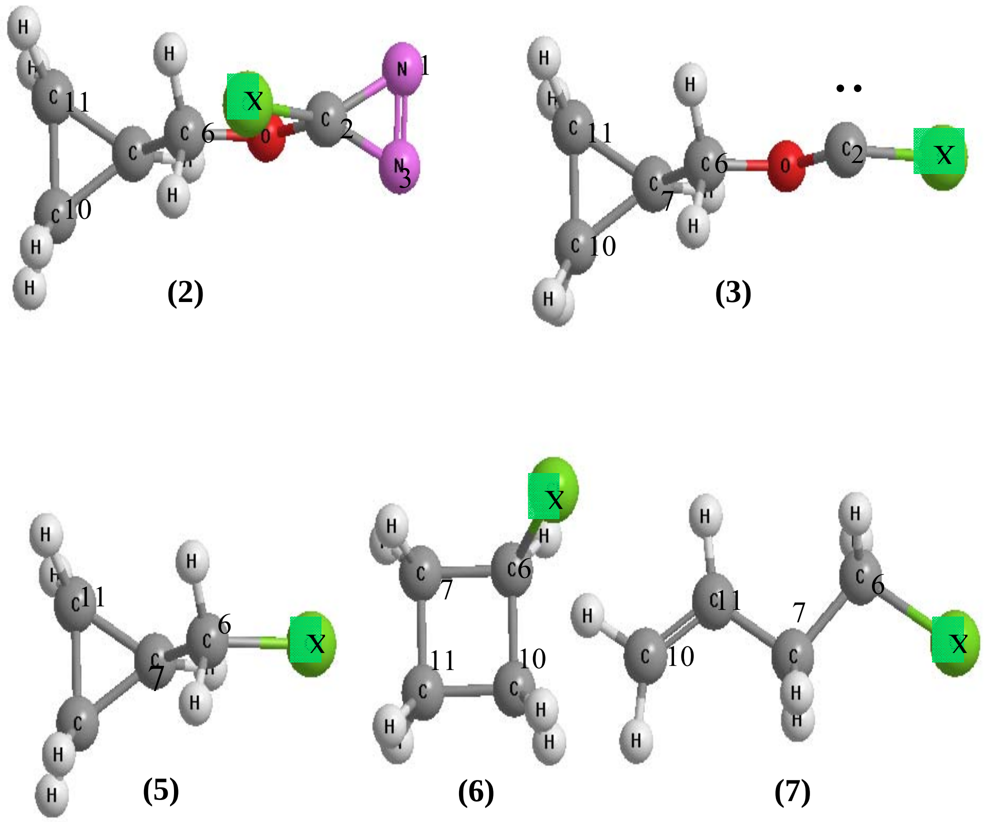
The investigations showed that C2-O bond length is shorter and C6-O bond length is longer in **cpmxc** with more electronegative substituent.

Transition state structures of **cpmxc** (x=Cl, F and H) have been found and optimized by B3LYP/6-311++G** level of theory. Results show that **cpmxc** have one imaginary frequency and thus one negative mode. Existence of a single negative mode shows that **cpmxc** have a first order saddle point which requires a single product.

Table 1: The optimized Bond lengths and angles computed at DFT-B3LYP/6-311++G** levels of theory for intermediate 3 (**cpmxc**) with various substitutions (x=Cl, F and H). The number of atoms is according to Fig. 1.

Substitutions	Cl	F	H
Parameters	[a]m=1	m=1	m=1
R (C2-O)	1.282	1.293	1.295
R (C2-X)	1.801	1.339	1.116
R (C6-O)	1.481	1.468	1.470
R (C6-C2)	1.495	1.517	1.497
R (C6-H)	1.091	1.090	1.092
R (C3-C1)	1.505	1.509	1.506
R (C3-H)	1.083	1.083	1.083
∠O-C2-X	106.208	104.691	102.483
∠C6-O-C2	115.638	115.478	116.875
∠C2-O-C6-C7	-113.144	-179.593	-113.164
∠C6-O-C2-X	179.283	179.991	179.310
Stability energy	-730.157	-369.806	-270.505

[a] Multiplicity of carbene



(2) (3) (5) (6) (7)

Fig. 1: The optimized structures of cyclopropylmethoxychloro (flouro and hydro) carbene (cpmxc) (3), reactant (2) and its CO elimination products (5, 6, 7).

3.2. NMR Spectra

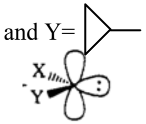
NMR Spectrum of molecule of cyclopropylmethoxychloro (fluoro and hydro) carbene (**cpmxc**) also has been studied with B3LYP/6-311++G** method.

The trends in the principal components of the chemical shift tensor extracted from NMR data were consistent with the structures determined by ab initio computations. To better understand bonding and electronic structure in **cpmxc** (x=F, Cl, H) isotropic and anisotropic NMR chemical shieldings have been calculated for the ^{13}C nuclei using GIAO method for the optimized structure of intermediate **cpmxc** at B3LYP level of theory using 6-311++G** basis set and the results tabulated in Table 3. To convert σ_{ii} to chemical shift, δ_{ii}, TMS was chosen as the reference. $\delta_{ii} = \sigma_{ii,r} - \sigma_{ii,s}$, where the subscripts “r” and “s” refer to the reference and sample, respectively. The results show that to increasing the electronegativity of the atoms bond to 2C (Fig 1) [H (2.2), Cl (3.16) and F (3.98)], electron density at the carbon nucleus should be depleted in the same order and thereby generate a chemical shift trend opposite to what is observed in Table 2. On the basis of Ramsey's theory of nuclear magnetic shielding, the shielding of a nucleus can be separated into two main contributions, the diamagnetic shielding (σ^d) and the paramagnetic shielding (σ^p) [14, 15]. The diamagnetic shielding contribution describes the shielding of the nucleus from the external magnetic field by the surrounding electrons that induce a magnetic field opposite to the external one. The paramagnetic shielding contribution is a perturbation of the electron density currents that generally causes a decrease in the absolute shielding. In other words, the paramagnetic contribution, usually negative, is typically responsible for observed changes in chemical shifts for a given nucleus. Since paramagnetic shielding, a reflection of the mixing of ground and excited states is increased by more electronegative substituent. The results of Table 3 show that the HOMO-LUMO energy gap in carbene increases with more electronegative substituent, therefore a smaller contribution to the paramagnetic shielding is expected to produce a more upfield resonance. Other explanation for the order of δ_{iso} for these compounds based on their π-back-bonding capacity lead to predictions consistent with the observed δ_{iso} trend.

The investigation of the results in Table 2 shows that δ_{nn} values describe the shape of an ellipsoid in three dimensions in the principal axis system of the chemical shift tensor. This shape is related to the topology of the electronic wave function at the site of the nucleus and can therefore lead to details about chemical bonding. The difference between δ_{nn} values for particular site is a strong function of the symmetry and structure of the bonding environment.

Table 2: The calculated Chemical Shielding Tensors and [a]chemical shifts of 2C (Fig. 1) atom B3LYP/6-311++G** in **cpmxc**. Also HOMO-LUMO energy gap and important bonding length and angle are showed.

[1]X	[2]σ_{11}	σ_{22}	σ_{33}	σ_{iso}	$\Delta\sigma$	δ_{11}	δ_{22}	δ_{33}	δiso	$\Delta\delta$	[3]ΔE(ev)	R (C2-X)	R (C2-O)	∠O-C2-X
F	-433.06	8.75	33.13	-130.39	245.29	613.706	171.9402	157.7293	314.4585	-235.094	0.2183	1.339	1.293	104.691
Cl	-552.61	-55.87	25.30	-194.39	329.55	733.2559	236.559	165.5582	378.4577	-319.349	0.1855	1.800	1.282	106.208
H	-929.21	-67.50	65.66	-310.35	564.01	1109.85	248.1824	125.2046	494.4123	-553.812	0.1611	1.116	1.295	102.483

Structure of singlet carbine, X=F, Cl, H and Y=  CH_2O

[1] X= The various substitutions in **cpmxc**.

[2] Calculated σ_{iso}, σ_{11}, σ_{22}, σ_{33} and $\Delta\sigma$ values in ppm.

[3]ΔE=HOMO-LUMO Gap energy.

[a] To convert σ_{ii} of ^{13}C to chemical shifts, $\delta_{ii,}$ TMS was chosen as the reference, $\delta_{ii} = \sigma_{ii,r} - \sigma_{ii,s}$, where the subscripts "r" and "s" refer to the reference and sample, respectively.

δ_{11} and δ_{33} correspond to the minimum and maximum values of the chemical shift or the minimum and maximum electron density along orthogonal directions in the principal axis system of the chemical shift tensor. With regard to the structure of carbene which has both an empty p-orbital and lone electron pair, it is most likely that the 11 direction lies along the symmetry axis of the empty p-orbital whereas the 33 direction involves the hybrid orbital containing the lone electron pair. The structure of carbene indicates essentially zero electron density along the 11 direction. Therefore, one would expect δ_{11} for cpmxc to tend toward the bare nucleus value. The large value for δ_{11}, coupled with its variation in the order smallest to largest in sequence X=F<Cl<H can be explained by back-bonding.

3.3. Thermochemistry

Thermodynamic properties of conversion of 3-cyclopropylmethoxy-3-chloro (flouro and hydro) diazirine to different products (Eq. 1) have been computed and summarized in Table 3.

The results show that formation of 4-cloro (flouro and hydro) -1-buten (**7**) is thermochemically most favored. Also, the results show that **cpmfc** transition state was converted faster than **cpmhc** and **cpmcc** to products and process of conversion reactant to product is more spontaneous. In the formation reaction of the products, entropy increases and enthalpy decreases. Therefore these reactions are favored from both energetic and entropic points of view.

Table 3. The thermochemical properties calculated in temperature of 298K for conversion of 3-cyclopropyl methoxy-3-chloro diazirine to different products (Eq. 1) for example $\Delta H_{reaction}$, $\Delta G_{reaction}$ and $\Delta S_{reaction}$ by DFT-B3LYP/6-311++G** levels.

substituent		(Cl)			(F)			(H)	
Thermodynamic Functions → Reactions ↓	ΔH (kJ/mol)	ΔS (J/mol K)	ΔG (kJ/mol)	ΔH (kJ/mol)	ΔS (J/mol K)	ΔG (kJ/mol)	ΔH (kJ/mol)	ΔS (J/mol K)	ΔG (kJ/mol)
2 → 5	-19.63	339.83	-120.95	-22.40	333.72	-121.88	-20.02	339.10	-121.12
2 → 6	-18.57	332.53	-117.72	-19.54	329.80	-117.87	-20.21	325.84	-117.35
2 → 7	-23.40	342.61	-125.55	-26.24	334.01	-125.82	-23.83	340.40	-125.32

4. Conclusion

The obtained geometries using the ab initio method predict that **cpmxc** is a stable intermediate with a first-order saddle point (having only one negative mode). The chemical shift of carbene carbon atom decreases to increasing the electronegativity of the atoms bond to this carbon atom owing to formation of π-back-bonding. The large value for δ_{11}, coupled with its variation in the order smallest to largest in sequence X=F<Cl<H can be explained by back-bonding. Also, the results show that **cpmfc** transition state was converted faster than **cpmhc** and **cpmcc** to products and process of conversion of reactant to product is more spontaneous. In the formation reaction of the products, entropy increases and enthalpy decreases. Therefore these reactions are favored from both energetic and entropic points of view.

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