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# Infrared and theoretical calculations in 2-halocycloheptanones conformational analysis

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# ABSTRACT

2-Halocycloheptanones (Halo = F, Cl, Br and I) were synthesized and their conformational analysis was performed through infrared spectroscopy data. The corresponding conformers geometries and energies were obtained by theoretical calculations at B3LYP/aug-cc-pVDZ level of theory in the isolated state and in solution. It was observed, by both approaches, that the conformational preferences were very sensitive to the solvent polarity, since its increase led to an increase in the population of the more polar conformer. An analysis of these conformational equilibria showed they suffer also the influence of stereoelectronic effects, like hyperconjugation and steric effects. These results were interpreted using natural bond orbital (NBO) analysis, which indicated that the electronic delocalization to the orbital  $\pi^*_{C=0}$  is directly involved in the stability increase of conformers I and II. The relative effect of the period of the halogen can also be noted, with changes in the conformational preferences and in the energies involved in the interactions of NBO.

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# 1. Introduction

The conformational study of cyclohexanones and other sixmembered rings is an important part of organic chemistry; however, higher cycloalkanones have not received as much attention, partially due to the reasonable number of conformers present in larger rings.

Conformations of cycloheptanone have been studied by molecular mechanic calculations, which have indicated that the chair/twist-chair conformations are the most stable [1]. Vibrational spectral analyses of cycloheptanone have also been carried out [2]. These analyses have shown that cycloheptanone is a molecule that presents non-rigid pseudorotation around chair/twist-chair structures.

Studies at B3LYP and CCSD(T) with 6-311+G(d,p) basis set have shown that cycloheptanone adopts a more stable asymmetric conformation [3]. In a similar way, the analysis of the radical anion of cycloheptanone through molecular mechanics calculations and ESR spectra have also shown that the asymmetric conformation of cycloheptanone is the most stable form [4].

<sup>1</sup>H and <sup>13</sup>C NMR studies of non-substituted cycloalkanones provided experimental data of chemical shifts in several solvents, and also used density functional methods (DFT) calculations, but without discuss the molecular geometry of the compounds [5].

IR analyses of the carbonyl stretching of 2-chloro- and 2bromine-cycloheptanone indicated that the C–X and C=O dipoles of the most stable conformers are not coplanar [6]. Another study with these compounds [7] using IR, UV, and dipole moment data led to the early conclusion that in nonpolar solvents the axial conformer is preferred, while in polar solvents the equatorial conformer predominates. However, the other halogens and different cycloheptanone conformations were not analyzed.

In the present work, IR spectroscopy and theoretical calculations were used to investigate the conformational preference of 2-halocycloheptanones and analyze the stereoelectronic effects involved in the conformational preference of these little investigated systems in organic physical chemistry.

# 2. Experimental and theoretical methods

### 2.1. Synthesis of the compounds

#### 2.1.1. 2-Fluorocycloheptanone (1)

Synthesized by means of direct fluorination of the corresponding ketone with 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2,2,2]octane bis-tetrafluoroborate, as described in the literature [8]. <sup>1</sup>H NMR  $\delta$  (400.13 MHz, CDCl<sub>3</sub>): 5.05 (1H, ddd); 2.56 (2H, m); 1.99 (2H, m); 1.83 (2H, m); 1.63 (4H, m). <sup>13</sup>C NMR

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 $\delta$  (100.62 MHz, CDCl<sub>3</sub>): 208.9 (d); 95.5 (d); 40.0 (s); 31.4 (d); 28.4 (s); 25.3 (d); 23.2 (s).

# 2.1.2. 2-Chlorocycloheptanone (2)

Obtained by reacting the corresponding ketone with sulfuryl chloride, as described in the literature for similar compounds [9]. <sup>1</sup>H NMR  $\delta$  (300.06 MHz, CDCl<sub>3</sub>): 4.44 (1H, dd); 2.76 (1H, m); 2.54 (1H, ddd); 2.25 (1H, dddd); 1.93 (3H, m); 1.61 (4H, m). <sup>13</sup>C NMR  $\delta$  (75.46 MHz, CDCl<sub>3</sub>): 206.5; 64.2; 40.4; 34.4; 29.1; 26.1; 24.2. IR  $\nu_{C=0}$  (cm<sup>-1</sup>): 1718.4. GC–MS: 10.441 min (145.943 *m/z*).

# 2.1.3. 2-Bromocycloheptanone (3)

Prepared from the corresponding ketone and N-bromosuccinimide (NBS) in the presence of ammonium acetate [10]. <sup>1</sup>H NMR δ (300.06 MHz, CDCl<sub>3</sub>): 4.38 (1H, dd); 2.87 (1H, ddd); 2.50 (1H, ddd); 2.37 (1H, dddd); 1.99 (3H, m); 1.76 (1H, m); 1.57 (2H, m); 1.38 (1H, m). <sup>13</sup>C NMR δ (75.46 MHz, CDCl<sub>3</sub>): 206.5; 53.9; 39.6; 34.4; 29.8; 27.0; 25.2. IR  $\nu_{C=0}$  (cm<sup>-1</sup>): 1710.7. GC–MS: 11.745 min (191.871 *m/z*).

#### 2.1.4. 2-Iodocycloheptanone (4)

These compounds were prepared through the formation of the lithium enolate of the corresponding ketones with LDA (lithium diisopropylamine) and subsequent reaction with molecular iodine [11]. <sup>1</sup>H NMR  $\delta$  (300.06 MHz, CDCl<sub>3</sub>): 4.57 (1H, dd); 2.95 (1H, ddd); 2.40 (2H, m); 2.05 (2H, m); 1.87 (2H, m); 1.51 (2H, m); 1.22 (1H, m). <sup>13</sup>C NMR  $\delta$  (75.46 MHz, CDCl<sub>3</sub>): 208.0; 38.4; 35.8; 32.1; 30.3; 29.0; 25.6. IR  $\nu_{C=0}$  (cm<sup>-1</sup>): 1701.0. GC–MS: 12.371 min (237.907 *m/z*).

## 2.2. Infrared experiments

Infrared analyses were performed in a BOMEN FT-IR MB-100 spectrometer using  $0.03 \text{ mol } \text{L}^{-1}$  solutions and a NaCl cell with an optical path of 0.5 mm to observe the carbonyl band in the fundamental stretching region ( $1800-1600 \text{ cm}^{-1}$ ) and a quartz cell with 1.0 cm of optical path for the first overtone region ( $3500-3300 \text{ cm}^{-1}$ ). The solutions were prepared with solvents with different polarities (CCl<sub>4</sub>, CHCl<sub>3</sub> and CH<sub>3</sub>CN) so that the effect of the medium on the conformational preference could be assessed. The spectra were acquired with 64 scans and resolution of 1 cm<sup>-1</sup>. The percentage of conformers was determined after the deconvolution of the bands in the fundamental stretching regions of the carbonyl group and in its first overtone using the program GRAMS, available in the BOMEM equipment, which utilizes Lorentzian and Gaussian functions.

#### 2.3. NMR experiments

The spectra were obtained in a Varian spectrometer, model Mercury Plus BB operating at 300.06 MHz for the hydrogen nucleus and 75.46 MHz for the carbon nucleus. A Bruker Avance III spectrometer was also used operating at 400.13 MHz and 100.62 MHz for <sup>1</sup>H and <sup>13</sup>C, respectively. Samples were prepared as solutions of 20 mg of solute in 0.7 mL of CDCl<sub>3</sub> and probe temperature around 25 °C were used. Me<sub>4</sub>Si was used as an internal reference under typical operating conditions for <sup>1</sup>H (spectrum window around 4000 Hz and number of data points equal to 32k, zero filled with 128k, to give a final digital resolution of 0.03 Hz).

## 2.4. GC-MS experiments

The chromatograms were taken in a Focus DSQ II apparatus from Thermo-Finnigan with a DB5 column (5% phenyl, 95% polydimethylsiloxane). The analyses were performed with a temperature gradient with initial temperature of 40 °C and maximum temperature of 250 °C, with the injector and the ionization source at 250 °C, a duration of 32 min, and injections of 1.0  $\mu$ L of solutions containing 1.0 mg/5.0 mL of solvent. In this case the solvent used was ethyl acetate, and the carrier gas was helium (99.999%) with a flow of 1.0 mL min<sup>-1</sup>.

# 2.5. Theoretical calculations

Theoretical calculations were performed using the software package Gaussian 03 [12]. Geometries were optimized with the density functional B3LYP [13] and the aug-cc-pVDZ [14] basis set. For the iodine atom, a mixed basis set function, LanL2DZ-ECP, was used [15]. Besides the optimization in vacuum, the compounds were also optimized in the same solvents used in the IR analysis (CCl<sub>4</sub>, CHCl<sub>3</sub>, and CH<sub>3</sub>CN) with the same level of theory of the vacuum calculations and the polarization continuum model (PCM) [16] solvation model. The optimized geometries were submitted to frequency calculations to characterize them as a minimum or transition state and to obtain the thermodynamic properties and simulate the frequencies of IR absorption.

In addition to the DFT methods, energy calculations were performed with the ab initio method MP2 [17] and the 6-311++G(3df,3dp) [18] basis set for hydrogen, carbon and oxygen atoms. For iodine atom was used the LanL2DZ-ECP basis set. These energy calculations were made both in the vacuum and in the presence of solvents, in this case employing the PCM calculation using the integral equation formalism (IEF-PCM)[19] solvation model and the description of the molecular cavity through bond's atomic radii.

Calculations involving the theory of natural bonding orbitals (NBO) were made using the structures optimized in vacuum and the B3LYP/aug-cc-pVDZ level through module NBO 5.0 [20] of the Gaussian 03 program.

# 3. Results and discussion

According to molecular mechanics studies by Langley et al. [21], there are basically two conformation families for cycloheptanone: The cycloheptane ring in the chair/twist-chair conformation (C/TC) or in the boat/twist-boat conformation (B/TB) (Fig. 1).

The relative conformational energies (Table 1) for the cycloheptanone indicated the structure C/TC-2 with the carbonyl group in position two in relation to the symmetry axis C<sub>2</sub> of cycloheptane as the structure of lowest energy, but with an energy difference for the C/TC-1 structure, which has a C<sub>2</sub> symmetry of only 0.70 kcal mol<sup>-1</sup>. However, the frequency calculations characterized the latter structure as a transition state and further optimization with the halogen substituted in the  $\alpha$  position led to the more stable structure C/TC-2. The optimized and frequency calculations, in vacuum and in the solvent presence, were performed for all the ring conformations containing the halogen in position 2. These calculations showed that the conformation C/TC-2 is the most stable one. The others conformations were either less stable than or converged to C/TC-2. Considering the energy difference observed, the structure C/TC-2 of

#### Table 1

Relative conformational energies of cycloheptanone (kcal mol<sup>-1</sup>).

Conformation	E <sub>rel</sub> <sup>a</sup>	$E_{\rm rel}{}^{\rm b}$
C/TC-1 <sup>c</sup>	0.70	0.80
C/TC-2	0.00	0.00
C/TC-3	2.35	1.69
C/TC-4	2.45	2.40
B/TB	2.62	2.07

<sup>a</sup> B3LYP/aug-cc-pVDZ.

<sup>b</sup> MP2/aug-cc-pVDZ.

<sup>c</sup> Transition state.



Fig. 1. Conformations of cycloheptanone.

cycloheptanone was taken as the initial point in the optimization of 2-halocycloheptanones.

From the structure C/TC-2 of cycloheptanone, we found four non-equivalent possibilities of substitution in the  $\alpha$  position, two equatorial conformations (I and III), and two axial conformations (II and IV), as shown in Fig. 2. Some parameters obtained with the optimization and frequency calculations in vacuum, as well as the relative energy for compounds 1–4, are given in Table 2.

Besides the theoretical calculations, the IR spectra were obtained to observe the stretching behavior of the carbonyl with the variation of the solvent, and through the analytical deconvolution of the bands, to estimate the number and molar fraction of the conformers present in the solution using the intensity (absorbance) and the relative area of each band. The carbonyl band is appropriate for this type of analysis as it has a strong absorption in a relatively clear region of the IR spectrum. The region of the first overtone of the carbonyl was also analyzed to prevent the interference of Fermi's resonance on the fundamental stretching [22]. Although each conformer may has a distinct molar absorptivity for C=O absorption [23] the use of the same extinction coefficients for different conformations is very often carried out to estimate the percentages of conformers by IR at a single temperature, and this procedure is usually well accepted [24-26]. The discussion of the theoretical calculations and the IR analysis are given below, and



Fig. 2. Conformations of 2-halocycloheptanones (X = F, Cl, Br, and I).

the data obtained from the deconvolution for compounds **1–4** are given in Table 3.

# 3.1. 2-Fluorocycloheptanone (1)

The relative energy data in Table 2 indicate a preference for conformer **II** when the molecule in vacuum was considered. This conformer has the lowest dipole moment (2.28 D), and thus it is not favored in solvents with greater polarity. Conformer **I** has an intermediate dipole moment (3.47 D) and energy relative to conformer **II** of 1.69 kcal mol<sup>-1</sup>. Conformer **III** has the lowest relative energy in relation to conformer **II** in vacuum (1.27 kcal mol<sup>-1</sup>) and the highest dipole moment (4.80 D), which must favor this conformer in solvents with greater dielectric constant. Despite its greater relative energy in vacuum, conformer **IV** has a high dipole moment (4.52 D), which may favor it in polar condensed phases.

Based on the wavenumber of the calculated carbonyl stretching, it was possible to attribute the bands observed in IR spectra (Fig. 3) to the possible conformers and to estimate their respective populations in solvents with different polarities (CCl<sub>4</sub>, CHCl<sub>3</sub>, and CH<sub>3</sub>CN). In CCl<sub>4</sub>, four distinct bands were observed in the fundamental stretching but only three on the carbonyl first overtone. On the first overtone, the band with the highest wavenumber was assigned to conformer **IV**, the intermediate band to conformer **III** and the band with the greatest intensity and the lowest wavenumber to conformer **II**. In CHCl<sub>3</sub> and CH<sub>3</sub>CN these three bands were also observed both on fundamental and first overtone region.

The deconvolution data shown in Table 3 indicate that conformer II is preferred in CCl<sub>4</sub>, corresponding to 50% of the equilibrium. As the medium polarity increases, the population of conformer II decreases to 21% and 5% in CHCl<sub>3</sub> and CH<sub>3</sub>CN, respectively, while the population of III increases to 35%, 60%, and 75% in CCl<sub>4</sub>, CHCl<sub>3</sub>, and CH<sub>3</sub>CN, respectively. The percentage of IV also increases with the increase in the medium polarity.

#### 3.2. 2-Chlorocycloheptanone (2)

According to the analysis of the dipole moment data and the relative energy of the conformers of **2**, conformer **II** is expected to occur in a significant amount in apolar solvents, but to decrease as the polarity of the medium increases, as it has the lowest dipole moment (2.68 D). Conformer **I** has an intermediate dipole moment (3.78 D) and the lowest energy in vacuum and probably has a significant population in the different solvents. Despite the highest

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Parameters calculated at the B3LYP/aug-cc-pVDZ level (LanL2DZ-ECP for iodine) for	1-4.
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Compound	Conformer	Parameters						
		$\theta_{X-C-C=0}^{a}$	ω <sub>X-C2-C1</sub> <sup>b</sup>	<i>r</i> <sub>C−X</sub> <sup>c</sup> (Å)	$\mu^{\mathrm{d}}(\mathrm{D})$	$v_{c=0}^{e} (cm^{-1})$	$I \upsilon_{C=0} f(km mol^{-1})$	$E_{\rm rel}^{\rm g}$ (kcal mol <sup>-1</sup> )
1	I	110.31	106.56	1.419	3.47	1777.46	153.7	1.69
	II	-150.05	110.05	1.416	2.28	1767.76	165.3	0.00
	III	-17.04	108.86	1.397	4.80	1784.93	179.7	1.27
	IV	-12.62	108.80	1.399	4.52	1789.85	169.9	1.84
2	I	99.03	106.50	1.839	3.78	1735.88	161.2	0.00
	II	-133.08	111.07	1.840	2.68	1721.04	175.3	0.11
	III	-29.25	110.37	1.818	4.70	1749.14	140.1	1.46
	IV	-16.00	110.38	1.820	4.54	1749.86	140.7	1.96
3	I	97.55	106.19	2.004	3.80	1729.73	160.9	0.00
	II	-128.10	110.82	2.006	2.83	1715.56	177.5	0.55
	III	-33.27	110.44	1.981	4.62	1747.06	129.1	2.13
	IV	-21.13	110.32	1.987	4.50	1744.43	132.9	2.64
4	I	95.54	106.38	2.217	3.66	1757.56	166.9	0.00
	II	-117.92	109.77	2.222	3.06	1742.60	184.0	0.99
	III	-38.04	110.65	2.192	4.30	1779.17	125.8	2.87

<sup>a</sup>  $\theta_{X-C-C=0}$  dihedral angles between the halogen and carbonyl oxygen.

<sup>b</sup>  $\omega_{X-C2-C1}$  angles between the halogen and carbon 1.

<sup>c</sup>  $r_{C-X}$  bond length of the carbon-halogen.

<sup>d</sup>  $\mu$  dipole moment.

<sup>e</sup>  $v_{C=0}$  carbonyl frequency.

<sup>f</sup>  $Iv_{C=0}$  carbonyl frequency intensity.

<sup>g</sup> Relative energy of the conformers.

energy of conformer **III**, its dipole moment is high enough (4.70 D) to give significant percentages in solvents with moderate and high polarities. Due to the greater energy of **IV** and its high dipole moment (4.54 D), it should have a considerable percentage only in more polar solvents.

The IR analysis of **2** through the deconvolution of the carbonyl stretching bands in the fundamental and the first overtones (Fig. 4) indicated three bands in  $CCl_4$  and  $CHCl_3$  (a and b, respectively). The band with the lowest wavenumber was assigned to conformer **II**, the most intense band, of intermediate frequency, to the more stable conformer **II**. In  $CH_3CN$ , a fourth band with the highest wavenumber was assigned to conformer was estimated based on the intensities and the relative areas of each band in the IR spectra (Table 3).

In relation to the effect of the solvent, there was a decrease in the percentage of **II** in equilibrium as the medium polarity increased, while the percentage of **III** increased until it became the main conformer in  $CH_3CN$ . Conformer **I** predominated in  $CCl_4$ , and  $CHCl_3$ 

but was the second in  $CH_3CN$ . In the last solvent, the population of conformer **IV** was similar to that of **II**. The analysis in the first overtone of carbonyl revealed the same behavior as the analysis of the fundamental stretching.

# 3.3. 2-Bromocycloheptanone (3)

The theoretical calculations of **3** revealed a greater preference for conformer **I** than that observed for **2**. Again, conformer **II** had the lowest dipole moment (2.83 D) and conformers **III** and **IV**, the highest values (4.62 and 4.50 D, respectively). However, the relative energy of conformer **I** for the latter two increased, mainly for **IV** (from 1.96 to 2.64 kcal mol<sup>-1</sup> in **2** and **3**, respectively), which probably does not have a significant population in equilibrium in the condensed phases.

The deconvolution (Fig. 5) gave two bands in  $CCl_4$ ; the one with the highest wavenumber was attributed to conformer I, and that with the lowest intensity and wavenumber to conformer II. In CHCl<sub>3</sub> and CH<sub>3</sub>CN, a third band with a wavenumber higher than

Table 3

Percentage of conformers for 1–4 obtained from the average between the relative intensities and areas of the fundamental and first overtone carbonyl stretching in the IR spectra in selected solvents.

Compound	Conformer	$v_{ ext{c=0}}$ fundamental			$v_{c=0}$ overtone			
		CCl <sub>4</sub>	CHCl <sub>3</sub>	CH <sub>3</sub> CN	CCl <sub>4</sub>	CHCl <sub>3</sub>	CH <sub>3</sub> CN	
1	I	5						
	II	50	21	5	61	22		
	III	35	60	75	27	61		
	IV	10	19	20	12	17		
2	I	55	51	36	54	51	36	
	II	32	19	10	32	21	11	
	III	13	30	41	14	28	42	
	IV			13			11	
3	I	86	72	70	79	71	68	
	II	14	18	12	21	18	19	
	III		10	18		11	19	
4	I	81	79	78	75	76		
	II	16	21	15	18	14		
	III	3		7	7	10		



Fig. 3. Carbonyl absorption band in the IR spectrum of 2-fluorcycloheptanone (1) in (a) CCl<sub>4</sub>, (a') CCl<sub>4</sub> (first overtone), (b) CHCl<sub>3</sub>, (b') CHCl<sub>3</sub> (first overtone), and (c) CH<sub>3</sub>CN.

that of conformer I was observed and attributed to conformer III. This band was relatively less intense than that of conformer II in CHCl<sub>3</sub> but stronger than in CH<sub>3</sub>CN, as expected, due to the greater dipole moment of III. Conformer I predominated in all the analyzed solvents with estimated populations of 86%, 72%, and 70% in CCl<sub>4</sub>, CHCl<sub>3</sub>, and CH<sub>3</sub>CN, respectively. Again, the results obtained in the analysis of the fundamental stretching and of the first overtone of carbonyl agreed.

# 3.4. 2-Iodocycloheptanone (4)

For this compound, the optimization calculations resulted in only three conformers, with conformer I being the most stable. In this case, the dipole moment of conformer II (3.06 D) is close to that of I (3.66 D), but the difference in energy between them (0.99 kcal mol<sup>-1</sup>) is greater than in the case of compounds 2 and 3, like the difference in energy for conformer III (2.87 kcal mol<sup>-1</sup>),

which was also greater. However, the high dipole moment of **III** (4.30 D) suggests that in more polar solvents, a small fraction of this conformer must be favored.

The analysis of the deconvolution (Fig. 6) of the fundamental stretching of carbonyl for **4** indicated a clear preference for one of the conformers. CCl<sub>4</sub> showed three bands. The band with the lowest wavenumber was assigned to conformer **II**, the strongest band and of intermediate wavenumber, to conformer **I**, and the band of lowest intensity and highest wavenumber to conformer **III**. In CHCl<sub>3</sub>, the band relative to **III** was observed only in the first overtone. The data in Table 3 show that the population of **I** remains stable, while that of **III** slightly increases as that of **II** decreases.

The preference for conformer I was even more pronounced in compound **4** than in **2** and **3**. In contrast, for conformer II, it had a smaller decrease in relation to observed in **2** and **3**. This is related to the greater dipole moment of II in compound **4** in relation to the other compounds.



Fig. 4. Carbonyl absorption band in the IR spectrum of 2-chlorocycloheptanone (2) in (a) CCl<sub>4</sub>, (a') CCl<sub>4</sub> (first overtone), (b) CHCl<sub>3</sub>, (b') CHCl<sub>3</sub> (first overtone), (c) CH<sub>3</sub>CN and (c') CH<sub>3</sub>CN (first overtone).

#### 3.5. Solvation calculations

The parameters of comparison with the data obtained in IR analysis were obtained through solvation calculations for the three solvents used. Energy calculation at a higher level also was performed and the results are given in Table 4.

The solvation calculations presented the same tendency observed in the IR analysis. For **1**, the most stable conformer in vacuum and in  $CCl_4$  was **II**, while in  $CHCl_3$  and  $CH_3CN$ , conformer **III** was more stable, with an increase in the relative energy of **II** with the increase in the medium polarity. The relative energy of conformer **I** was the highest in the solvation calculations of **1**, which indicates that this conformer does not contribute effectively to the equilibrium of this compound.

For **2–4**, conformer **I** was the most stable in all solvents, with the exception of **2** in CH<sub>3</sub>CN, in which conformer **III** was calculated with only 0.05 kcal mol<sup>-1</sup> more stable than **I**. The difference in energy for

conformer **II** increased with the increase in the medium polarity, which can be explained by the smaller dipole moment of **II** in relation to the other conformers. The difference in energy of conformers **III** and **IV** regarding conformer **I** decreased with the increase in the polarity of the medium, which also agreed with the difference in dipole moment between them.

#### 3.6. Conformational preference

It has been suggested that the orbital interaction  $\eta_X \rightarrow \pi^*_{C=0}$  is important in the conformational preference of 2-halocyclohexanones [27–30] and that the overlapping of these orbitals increases as the volume of halogen and the proximity in energy of the orbitals  $\eta_X$  and  $\pi^*_{C=0}$  increase. For the cyclohexanones, this interaction is greater for the axial conformer than for the equatorial one and increases in the order F < Cl < Br < I, according to the difference in axial-equatorial energy of these



Fig. 5. Carbonyl absorption band in the IR spectrum of 2-bromocycloheptanone (3) in (a) CCl<sub>4</sub>, (a') CCl<sub>4</sub> (first overtone), (b) CHCl<sub>3</sub>, (b') CHCl<sub>3</sub> (first overtone), and (c) CH<sub>3</sub>CN and (c') CH<sub>3</sub>CN (first overtone).

compounds, which in the vapor phase is 0.45, 1.05, 1.50, and  $1.90 \text{ kcal mol}^{-1}$ , respectively [31].

To investigate these orbital interactions, second-order perturbation theory analyses were performed with software NBO 5.0 of Gaussian 03. This type of calculation describes the chemical structure of a molecule based on the bonds between two atoms and lone pairs in a way very similar to the Lewis structures and allows analyzing charge transfers of bonding orbitals to antibonding orbitals, as well as the associated energetic implications. The main orbital interactions observed for 2-halocycloheptanones are shown in Table 5. These orbital interactions have a stabilizing character and the greater the interaction energy, the greater the resulting stabilizing effect.

The main interactions observed were  $\eta_X \rightarrow \pi^*_{C=0}$  and  $\sigma_{C-X} \rightarrow \pi^*_{C=0}$ . These interactions increase with the increase in the halogen volume, in a way similar to that reported for

2-halocyclohexanones. The interaction  $\eta_X \rightarrow \pi^*_{C=0}$  was observed only in conformers I and II in 2-halocycloheptanones, and the interaction  $\sigma_{C-X} \rightarrow \pi^*_{C=0}$  was far more pronounced in these same conformers, which contributed to the lower energy of conformer I and II observed in the calculations with the molecules in the vacuum. With the increase in halogen, these interactions in conformers III and IV were also observed, although with lower intensity than those observed for conformers I and II. For compound 1, the effect of the volume of the substituent was still important, as the calculations show that conformer II is the most stable in vacuum.

The greater energy of interaction observed for conformers **I** and **II** can be understood based on the geometry of each conformer, in which the position of the substituent is important for an appropriate overlapping of orbitals to occur. The closer to  $180^{\circ}$  or  $0^{\circ}$  the angle between the orbitals involved is, the better the



Fig. 6. Carbonyl absorption band in the IR spectrum of 2-iodocycloheptanone (4) in (a) CCl4, (a') CCl4 (first overtone), (b) CHCl3, (b') CHCl3 (first overtone), and (c) CH3CN.

#### Table 4

Percentage of conformers for 1-4<sup>a</sup> calculated in different media.

Compound	Conformer	B3LYP/aug-cc-pVDZ				MP2/6-311++G(3df,3dp)			
		Vacuum	CCl <sub>4</sub>	CHCl <sub>3</sub>	CH <sub>3</sub> CN	Vacuum	CCl <sub>4</sub>	CHCl <sub>3</sub>	CH <sub>3</sub> CN
1	I	4.7	4.4	3.0	0.9	2.1	2.2	1.6	0.6
	II	82.0	55.5	25.3	5.6	95.0	74.3	44.3	15.1
	III	9.6	30.7	55.7	78.3	2.2	9.6	24.1	36.9
	IV	3.7	9.4	16.0	15.2	0.7	13.9	30.0	47.4
2	I	51.2	51.4	47.0	36.7	51.7	55.9	51.8	36.7
	II	42.5	32.0	17.7	8.5	43.7	32.6	23.9	12.9
	III	4.4	12.3	27.4	40.0	2.0	5.1	10.4	20.4
	IV	1.9	4.3	7.9	14.8	2.6	6.4	13.9	30.0
3	I	69.7	74.4	71.7	64.1	82.1	83.9	82.1	73.9
	II	27.6	19.6	16.5	11.9	15.4	10.9	7.9	5.4
	III	1.9	4.3	8.7	17.8	1.3	2.8	5.2	9.9
	IV	0.8	1.7	3.1	6.2	1.2	2.4	4.8	10.8
4	I	83.6	83.2	76.8	87.9	91.4	92.9	94.1	94.3
	II	15.7	15.7	21.7	9.0	7.7	5.9	4.6	3.6
	III	0.7	1.1	1.5	3.1	0.9	1.2	1.3	2.1

<sup>a</sup> LanL2DZ-ECP for iodine.

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Main NBO orbit	A ain NBO orbital interactions energies (kcal mol <sup>-1</sup> ) and $\pi^*_{C=0}$ occupancy calculated at the B3LYP/aug-cc-pVDZ level (LanL2DZ-ECP for iodine) for 1–4.									
Compound	Conformer	Orbital intera	Occupancy $\pi^*_{C=0}$							
		$\eta_X \rightarrow \pi^*_{C=0}$	$\sigma_{C-X} \rightarrow \pi^*_{C=0}$	$\sigma_{C-X} \rightarrow \sigma^*_{C=0}$	$\sigma_{C=0} \rightarrow \sigma^*_{C-X}$	$\pi_{C=0} \rightarrow \sigma^*_{C-X}$	$\eta_0 \rightarrow \sigma^*_{C-X}$	Σ		
1	I	2.02	1.92	0.75	-	3.87	-	8.56	0.0683	
	II	0.66	0.62	1.59	0.82	1.62	1.71	7.02	0.0775	
	III	-	-	-	-	-	-	0	0.0809	
	IV	-	-	-	-	-	-	0	0.0783	
2	I	2.55	4.61	0.54	-	3.71	-	11.41	0.0839	
	II	1.30	2.37	1.65	0.77	3.03	1.34	10.46	0.0799	
	III	-	0.52	-	-	-	-	0.52	0.0782	
	IV	-	-	-	-	-	-	0	0.0772	
3	I	2.41	6.20	-	-	3.79	-	12.40	0.0924	
	II	1.37	3.56	1.67	0.75	3.47	1.30	12.12	0.0846	
	III	-	0.86	-	-	0.51	-	1.37	0.0788	
	IV	-	0.66	-	-	-	-	0.66	0.0785	
4	I	2.08	9.30	_	_	3.28	_	14.66	0.1043	
	II	1.51	6.71	1.44	0.60	3.61	1.05	14.92	0.0960	
	III	-	1.70	-	-	0.56	-	2.23	0.0814	

overlapping. For **I** and **II**, the dihedral angle (Table 2) between the halogen and the oxygen of the carbonyl is favorable to the orbital overlapping, while for **III** and **IV**, this interaction is not favored (Fig. 7). The occupancy data of orbital  $\pi^*_{C=0}$  were also analyzed (Table 5) and demonstrated the same tendency observed in the orbital interaction energies. The largest the occupancy of  $\pi^*_{C=0}$  the bigger the electronic delocalization (hyperconjugation) to this orbital.

Table 5

To evaluate the importance of the interactions involving the orbital  $\pi^*_{C=0}$ , NBO calculations were performed without this orbital so that the energy obtained for the molecule did not include the electronic delocalization for this orbital. The differences in energy between conformers are given in Table 6. These calculations indicate that the interactions involving the  $\pi^*_{C=0}$  orbital are actually important for the stabilization of conformers I and II, mainly for compounds 2–4. In these compounds, with the removal of only the  $\pi^*_{\rm C=O}$  orbital, conformer II became more stable, but had reduced energy in relation to conformers III and IV. Without the  $\pi^*_{C=O}$ , conformers III and IV became more stable than conformer I. However, with the increase in the size of the halogen, the energy difference between  ${\bf I}$  and  ${\bf II}$  becomes smaller. As a result, the calculations of the deletion of the  $\pi^*_{C=0}$  orbital indicated that this orbital is directly involved in the greater stability observed for conformer I in 2-4.

Another factor that was evaluated was the exchange energy [32,33] of each conformer, whose energy has a destabilizing character. The energy of these interactions is given in Table 7. The analysis of these data indicates that conformer I has the greatest exchange energy, which indicates a greater destabilizing effect.

Table 6

Relative energy (kcal mol<sup>-1</sup>) before and after deletion of the  $\pi^*_{C=0}$  orbital calculated at the B3LYP/aug-cc-pVDZ level (LanL2DZ-ECP for iodine) for **1–4**.

Compound	Conformer	E <sub>rel</sub> (kcal mol <sup>-1</sup> )				
		Before Deletion	After Deletion			
1	I	1.69	4.26			
	II	0.00	0.00			
	III	1.27	1.57			
	IV	1.84	2.12			
2	I	0.00	2.86			
	II	0.11	0.00			
	III	1.46	0.81			
	IV	1.96	1.46			
3	I	0.00	2.50			
	II	0.55	0.00			
	III	2.13	0.40			
	IV	2.64	0.91			
4	I	0.00	0.14			
	II	0.99	0.00			
	III	2.87	2.82			

For **1**, conformer **IV** has the lowest exchange energy, while for **2** and **3**, it is conformer **II**, and for **4**, it is conformer **III**. Despite the greater exchange energy observed for conformer **I**, the stabilizing effect afforded by the interactions involving the  $\pi^*_{C=0}$  orbital compensates the destabilizing effect of the exchange energy, which justifies the lower stability of this conformer after the deletion of the  $\pi^*_{C=0}$  orbital. The preference for conformer **II** after



**Fig. 7.**  $\sigma_{C-X}$  and  $\pi^*_{C=0}$  orbital representation for 2-halocycloheptanones.

Main exchange or	rbital interactions en	ergies (kcal mol <sup>-1</sup> ) cal	culated at the B3LYP/a	ug-cc-pVDZ level	(LanL2DZ-ECP for ic	odine) for <b>1–4</b> .						
Compound	Conformer	Orbital interactio	Orbital interaction									
		$\sigma_{C-X} \rightarrow \pi_{C=0}$	$\sigma_{C-X} \rightarrow \sigma_{C=0}$	$\eta_X \to \eta_0$	$\eta_{\rm X} \rightarrow \pi_{\rm C=0}$	$\eta_{\rm X} \rightarrow \sigma_{\rm C=0}$	$\eta_0 \rightarrow \sigma_{C-X}$	Σ				
1	I	3.29	-	-	0.72	-	-	4.01				
	II	1.04	1.33	-	-	-	-	2.37				
Main exchange orbi	III	-	0.59	0.52	-	-	0.96	2.07				
	IV	-	0.63	-	-	-	1.01	1.64				
2	I	5.01	-	-	1.15	-	-	6.16				
	II	2.68	1.31	-	-	-	-	3.99				
	III	1.01	0.60	0.70	0.59	-	1.23	4.13				
	IV	-	0.84	1.49	-	0.58	1.49	4.40				
3	I	5.77	-	-	1.06	-	-	6.83				
	II	3.37	0.97	-	-	-	-	4.34				
	III	1.36	0.79	0.58	0.68	-	1.39	4.80				
	IV	0.63	1.11	1.36	-	0.61	1.75	5.46				
4	I	6.26	-	_	0.95	_	_	7.21				
	II	4.57	0.76	-	-	-	-	5.33				
	III	1.76	0.83	-	0.75	_	1.18	4.52				

the deletions can also be attributed to the small exchange energy observed for this conformer.

# 4. Conclusion

For 1, the IR analysis and the theoretical calculations indicated the preference for conformer II in more apolar media, while the increase in the solvent polarity favored conformer III, which has a greater dipole moment. The preference of compound 2 in apolar media was for conformer I, with an increase in the percentage of III in the equilibrium with the increase in the polarity of the medium until this conformer became the most stable in CH<sub>3</sub>CN. For **3**, the preference for conformer **I** was greater than in **2**, and although the percentage of III increased with the medium polarity, it was smaller than the percentage of I. For 4, the preference for I was more pronounced, indicating that the increase in the volume of the substituted halogen favors I in the equilibrium of the 2-halocycloheptanones and that the increase in the polarity of the medium starts to contribute less to the conformational preference, as the more polar conformers start to have higher relative energy in relation to the more stable conformer with the increase in the halogen.

The preference observed in the vacuum can be understood based on the orbital interactions involving  $\pi^*_{C=0}$  orbital, mainly the  $\eta_X \to \pi^*_{C=0}$  and  $\sigma_{C-X} \to \pi^*_{C=0}$  interactions. These interactions increase with the increase in the halogen, according to the capacity of each substituent to act as a sigma electron donor. However, the halogen volume also influences the repulsion interactions, as the steric interactions also do. In **1**, even with the greater stabilizing effect observed in **I**, conformer **II** was the most stable, which can be justified by the smaller exchange energy observed in this conformer. For **2–4**, even though conformer **II** has a smaller exchange energy, the contribution of the stabilizing effect of the  $\sigma_{C-X} \to \pi^*_{C=0}$  interaction compensates the greater destabilizing effects present in **I**.

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# Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.saa.2012.03.027.

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