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Conformational Study of 3-Methyltetrahydropyran by (2+1) Resonance-Enhanced Multiphoton Ionization Spectroscopy

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The conformational enthalpy ($\Delta H°$) of 3-methyltetrahydropyran (3-MTHP) has been measured by (2+1) resonance-enhanced multiphoton ionization (REMPI) spectroscopy. The measured value (1.60 ± 0.12 kcal/mol) is in good agreement with results from ab initio calculations but somewhat higher than the $\Delta H°$ values predicted by molecular mechanics calculations. Under our supersonic expansion conditions, vibration cooling of the axial and equatorial conformers of 3-MTHP was observed to be faster than interconversion between them up to the highest temperature investigated (383 K). The measurement of $\Delta G°$ between the conformers shows that oscillator strengths for the 3s ← n transition of the conformers are different from each other. A molecular mechanics calculation demonstrates that the interconversion barrier of 11 kcal/mol from the equatorial chair to the axial chair form in 3-MTHP is close to that in tetrahydropyran and cyclohexane.

I. Introduction

Studies on structures and energetics of saturated cyclic organic molecules such as cyclohexane, cyclohexanone, tetrahydropyran, etc. have a long history.[1−3] In the case of substituted six-membered ring compounds, two chair conformations dominate the room temperature sample, the lower energy equatorial and the higher energy axial forms. The energy difference between the two conformers comes mainly from the repulsive steric interaction between the axial methyl and hydrogen groups, an interaction that is largely absent in the case of the equatorial conformer. Nuclear magnetic resonance (NMR) spectroscopy has been a standard tool for measuring free energy difference ($\Delta G°$) between the two conformers.[1,4] A drawback of this method for some molecules is that the measurement needs to be carried out at a sufficiently low temperature to prevent the NMR peaks associated with the two conformers from coalescing. This shifts the equilibrium to the more stable conformer and consequently the signal from the high-energy conformer diminishes, making it difficult to detect it in cases where the enthalpy difference is large.

The use of (2+1) resonance-enhanced multiphoton ionization (REMPI) spectroscopy has permitted us to study the 3s ← n or 3s ← σ transitions in various methyl and ethyl substituted cyclohexanones, cyclohexanes, and tetrayhdropyrans, and to distinguish the various isomers on the basis of their REMPI spectra.[5−8] The 3s Rydberg state, which lies between 48 000 and 56 000 cm^{-1} above the highest occupied molecular orbital (HOMO) of these molecules, is the lowest unoccupied molecular orbital (LUMO) for the tetrahydropyrans and cyclohexanes, and the (LUMO + 1) state for ketones. On the basis of more than 60 mono-, di-, trimethyl substituted forms studied, it is known that the transition energy is very sensitive to the location and orientation of the methyl group, which permits the identification of various conformations such as the axial form on the basis of their spectra.[5−8]

Recently, we have also measured enthalpy differences ($\Delta H°$) between gas-phase conformers by monitoring their population at temperatures between 300 and 480 K and constructing van't Hoff plots.[9,10] This was done by heating the nozzle of a pulsed valve used to supersonically cool the sample prior to analysis by REMPI. The sample is cooled so rapidly in the supersonic expansion that the relative concentrations of the two conformers remained what they were in the valve prior to expansion. In view of the fact that thermodynamic quantities such as $\Delta G°$ and $\Delta H°$ of molecules in the liquid phase are affected by the characteristics of the solvent used, it is of interest to obtain gas-phase energies in order to understand better the solvation process for various conformations.

In this work, we measured the enthalpy difference ($\Delta H°$) between axial and equatorial 3-methyltetrahydropyrans (3-MTHP) using (2+1) REMPI spectroscopy in the gas phase. This is compared with results from theoretical calculations. The latter are used to determine the possible temperature dependence of $\Delta H°$ for this reaction. In addition, we tried simulating a conversion path between the axial and equatorial conformers with a molecular mechanics method. Since the experiment involves cooling the sample in a supersonic molecular beam, the population ratio of the two conformers may change during supersonic expansion, an effect that depends on competition between the vibrational relaxation rates of the conformers and the rate of interconversion between them. This effect is also reflected in a curved van't Hoff plot. Finally, we address the use of spectroscopic peak intensities for determining the population ratio. The validity of this approach depends on the assumption that the oscillator strengths of the transition in the axial and equatorial conformations are the same. The validity of this assumption is investigated by comparing $\Delta G°$ ($= -RT \ln K_{\mathrm{eq}}$) measured directly from the experiment with ab initio results.

II. Experimental Approach

Details of the experimental scheme have been described elsewhere.[9,10] Frequency doubling of a dye laser light or mixing of 1064 nm and a dye laser lights makes a linearly polarized UV light of wavelength 380−395 nm, which is used to obtain (2+1) REMPI spectra of 3s ← n transition of 3-MTHP. The

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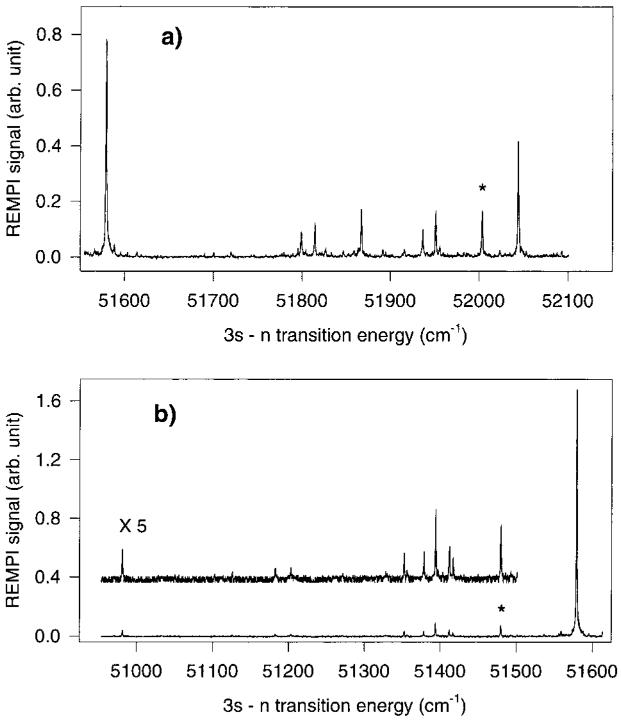


Figure 1. (2+1) REMPI spectra of equatorial (a) and axial (b) conformers of 3-methyltetrahydropyran. The peak at 51579 cm^{-1} in Figure 1b is the transition origin of the equatorial form. The (*) peaks were used for a van't Hoff plot.

UV light is focused into a time-of-flight mass spectrometer by a 30 cm focal length lens where it is intersected by molecular beam. The typical energy of the UV light was 1.5−2 mJ/pulse.

The molecular beam of argon and 3-MTHP with a seed ratio of ~1% was generated from a pulsed valve (Iota One, General Valve) with a 500 μm nozzle orifice. Electrons from REMPI of the molecules were detected by a set of chevron multichannel plates and were monitored as a function of the input UV wavelength. An OMEGA temperature controller (CN76000) controlled the temperature of the molecular beam valve. At each temperature for obtaining REMPI spectra, the valve was allowed to equilibrate for at least 30 min before data collection. Between 6 and 10 REMPI spectra were collected at each temperature.

3-MTHP with 97% stated purity was purchased from Aldrich and was used without further purification.

III. Results and Discussion

a. Experimental Results. Figure 1 shows the (2+1) REMPI spectra of $3s \leftarrow n$ transitions of the equatorial methyl and axial methyl conformers of 3-methyltetrahydropyran (3-MTHP). The peaks in Figure 1b at 50 982 and 51 579 cm^{-1} are the (0, 0) transition origins of the axial and equatorial forms, respectively, which were assigned by Cornish and Baer.[7] Between these two wavelengths are a number of vibronic peaks associated with the axial conformer. The spectrum of the equatorial conformation is shown in Figure 1a. The vibronic peaks of particular importance for this paper at 51 479.5 and 52 003.5 cm^{-1} are marked with an asterisk. These peaks are associated with the axial and equatorial conformations, respectively. Care was taken to ensure that the peak at 51 479.5 cm^{-1} is really due the axial conformation and is not due to a hot band of the equatorial conformer. This was established by noting that the relative peak intensities were identical as the backing pressure was varied. At lower backing pressure, the cooling in the molecular beam is less effective so that hot bands begin to show up. However, the two peaks in question retained their relative intensities, and thus the peak with an asterisk to the red of the equatorial transition origin is not a hot band. In fact, all of the peaks to the red of the equatorial origin in Figure 1b are due to the axial conformation.

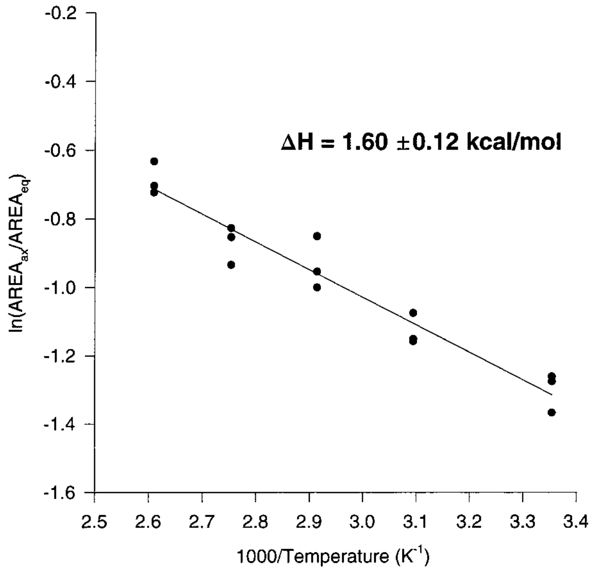


Figure 2. van't Hoff plot of 3-methyltetrahydropyran from the relative peak areas of axial and equatorial conformations in the $3s \leftarrow n$ (2+1) REMPI spectra. Each point in the plot is the experimental data.

At a given temperature, the axial and equatorial forms of 3-MTHP are in equilibrium expressed by

$$\text{Eq(3-MTHP)} \rightleftharpoons \text{Ax(3-MTHP)}$$

in which the equilibrium constant is given by $K_{\text{eq}} = [\text{Ax}]/[\text{Eq}]$. The van't Hoff equation (eq 1) shows the temperature dependence of the equilibrium constant, in which

$$\ln K_{\text{eq}} = -\frac{\Delta H^\circ}{R}\frac{1}{T} + \text{constant} \tag{1}$$

R is the gas constant and ΔH° is the enthalpy difference between the axial and equatorial conformations. The ΔH° can be determined from the slope of a plot of $\ln K_{\text{eq}}$ vs T^{-1}.

The ratio of the peak areas associated with the peaks referenced by the asterisks in Figure 1 was used to determine the K_{eq}. These peaks were chosen because they have similar REMPI intensities so that they can be measured with the same detection sensitivity. In addition, there are no neighboring peaks around them, which makes it easier to measure the peak areas. The ratio of the peak areas is equal to the equilibrium constant only under the assumption that the transition probabilities for REMPI signal are the same for the axial and equatorial conformations. However, by measuring this ratio at several temperatures and plotting the data as eq 1, variations in the transition probability cancel out [they are incorporated in the constant in eq 1].

A van't Hoff plot for 3-MTHP is shown in Figure 2. From the slope of this linear plot, the calculated ΔH° is 1.60 ± 0.12 kcal/mol. In general, enthalpy differences are temperature dependent and a van't Hoff plot may show curvature. In the case of 3-MTHP, however, the ab initio calculations of ΔH° show in Table 1 that in the temperature range between 298 and 383 K, ΔH° remains essentially constant within the experimental uncertainty of the present data.

TABLE 1: Measured and Calculated $\Delta H°$ and $\Delta G°$ for 3-Methyltetrahydropyran

method	$\Delta H°$ (kcal/mol)			$\Delta S°$ (cal/mol·K)		$\Delta G°$ (kcal/mol)	
	0 K	298 K	383 K	298 K	383 K	298 K	383 K
MMX		1.26					
MM3		1.27					
HF/6-31G*	1.61	1.57	1.56	−0.348	−0.386	1.67	1.71
MP2/6-31G**	1.70	1.65	1.64	−0.380	−0.426	1.76	1.80
B3LYP/6-31G*	1.61	1.55	1.53	−0.459	−0.511	1.69	1.73
REMPI exp.		1.60 ± 0.12				1.17 ± 0.18[a]	
REMPI exp.[b]						1.49[a]	
liquid phase NMR exp.[c]						1.44 ± 0.04	

[a] Determined from the ratio of the two origin peaks. [b] From Cornish and Baer.[7] [c] From Eliel et al.[26] at 173 K.

The deviation from the linearity of the plot can also arise if interconversion between the axial and equatorial conformers takes place during the supersonic expansion. Higher energy conformers such as the axial conformation here, have been reported by many groups.[11−18] However, it is not obvious from those studies whether the higher energy forms isomerize to the lower energy conformation during the courses of the supersonic expansion or whether the final relative concentrations of the isomers are the same as they were at the valve temperature. If isomerization takes place during the expansion, the effective temperature will be less than it was in the valve. As a result, the van't Hoff plot will exhibit curvature with a reduced slope at higher temperatures. Whether or not isomerization takes place depends on its rate, which in turn is strongly affected by the activation energy. Whereas the barrier for interconversion in the case of the 3- and 4-methyl cyclohexanones was on the order of 4−5 kcal/mol,[1,2,9,10] according to the molecular mechanics calculations which will be shown later in this section, the barrier from the axial chair to the equatorial chair form of 3-MTHP is about 10 kcal/mol. Similar van't Hoff plots for the cyclic ketones were linear thereby showing that the isomerization rate is slower than the vibrational relaxation rate.[9,10] Because of the considerably higher barrier in the case of the THPs, we do not expect to observe any depletion of the axial population during the course of the expansion. Indeed, we see none, as evidenced by the straight van't Hoff plot in Figure 2.

b. Calculated Energies and Barrier Heights. The experimentally determined $\Delta H°$ is compared with results from molecular mechanics and ab initio calculations in Table 1. The molecular mechanics calculations were done with PCMODEL.[19] The GAUSSIAN calculations[20] were carried out at various levels indicated in Table 1. Vibrational frequencies from the Gaussian calculations were scaled before calculations of zero-point vibrational energies, thermal enthalpies, and entropies by factors recommended by Scott and Radom.[21]

The present experimental value is in excellent agreement with the ab initio calculations with and without electron correlation and also agrees with the density functional calculation. On the other hand, the MMX and MM3 calculations give lower values, as in the cases of 3-methylcyclohexanone, 4-methylcyclohexanone, and 4-ethylcyclohexanone.[9,10] We do not know why molecular mechanics calculations systematically produce lower values at this time.

c. $\Delta G°$ from Experiment and Theory. Equation 2 shows the relation between $\Delta G°$ and the equilibrium constant K_{eq}

$$\Delta G° = -RT \ln K_{eq} = -RT \ln\left(\frac{P_{eq}}{P_{ax}}\right) = -RT \ln\left(\frac{O_{ax}}{O_{eq}}\frac{S_{eq}}{S_{ax}}\right) \quad (2)$$

where P_{eq} and P_{ax} are populations, O_{eq} and O_{ax} REMPI cross sections, and S_{eq} and S_{ax} REMPI signals of the equatorial and axial conformers from the present experiment, respectively. If one assumes that the REMPI cross sections (O_{eq}, O_{ax}) for the equatorial and axial forms are the same, $\Delta G°$ can be directly deduced from the REMPI signal ratio of the two transition origin peaks at 50 982 and 51 579 cm^{-1} in Figure 1. In so doing, we assume that origin peak is representative of the integrated intensity of the whole spectrum.

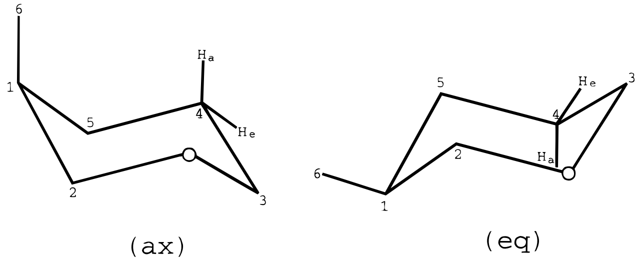
The measured $\Delta G°$ at 298 K in this way is 1.17 ± 0.18 kcal/mol. There is clearly a large discrepancy between this experimental value and the ab initio values in Table 1, which indicates that for these data O_{eq} does not equal O_{ax}. We have considerable confidence in the calculated $\Delta G°$ values, because (a) the experimental and calculated $\Delta H°$ values agree and (b) the calculated $\Delta S°$ values are small and negative. A slightly negative $\Delta S°$ is expected because the higher energy axial conformer is expected to be "tighter", i.e., to have higher vibrational frequencies. Some years ago, Cornish and Baer[7] using a similar experimental approach reported a $\Delta G°$ for 3-MTHP at 303 K of 1.49 kcal/mol, which is closer to the theoretical values, but still too low. The major difference between that study and the present one is that circularly polarized laser light was used rather than the linearly polarized light in this work. In their study, Cornish and Baer reported Ω values for the axial and equatorial transition origins of 3-MTHP. The Ω values, which are the ratio of peak intensities under circular and linear laser polarization, were found to be $\Omega_{ax} = 0.14$ and $\Omega_{eq} = 0.18$. The difference in the Ω values leads to a derived $\Delta G°$ that is 0.15 kcal/mol higher for circularly polarized light. More importantly, it points out that the transition probabilities for the axial and equatorial conformations are not the same and that they depend on how the experiment is done. In simple molecules, the Ω values are related to the molecular symmetry.[22−25] However, the Ω values are difficult to predict for nonsymmetric molecules such as 3-MTHP.[6]

Eliel and co-workers obtained a $\Delta G°$ of 1.44 kcal/mol at 173 K from an NMR experiment in which 3-MTHP was dissolved in CD_2Cl_2.[26] $\Delta G°$ in the liquid phase is different from that in the gas phase mainly because the difference in $\Delta H°$ between the liquid and gas phase.[1] That is, the difference in the $\Delta S°$ is generally small. The difference in the $\Delta H°$ is reflected in the different heats of vaporization of the conformational isomers. In the case of mono- or dimethyl substituted cyclohexanes, enthalpy differences in the gas phase are usually 0.2−0.3 kcal/mol larger than those in the liquid phase.[1,4,27] This trend is consistent with the results here.

It has been shown that the $\Delta H°$ in the liquid phase depends on characteristics of the solvent used. For example, if cyclohexane has electron withdrawing groups such as Cl or polar groups such as OCH_3, the $\Delta H°$ between axial and equatorial conformers changes by as much as 0.3 kcal/mol when polar solvents such as $CFCl_3$ and $CHFCl_2$ are used.[28]

d. Geometry of the Conformations and the Transition States. Table 2 shows some of the bond parameters from

TABLE 2: Optimized Geometries of the Two Conformers of 3-MTHP at the MP2/6-31G Level**



parameters[a]	axial form	equatorial form
$\angle C_6C_1C_5$	112.5726°	112.1659°
$\angle C_6C_1C_2$	110.7592°	111.1234°
$\angle C_1C_5C_4$	111.1942°	110.7846°
$\angle C_1C_2O$	111.4717°	112.2221°
$\angle C_5C_4H_a$	110.5400°	109.8260°
$l\ (C_1{-}C_6)$	1.5263 Å	1.5235 Å
$l\ (C_4{-}H_a)$	1.0911 Å	1.0921 Å
$l\ (C_4{-}H_e)$	1.0927 Å	1.0927 Å

[a] ∠, bond angle; *l*, bond length.

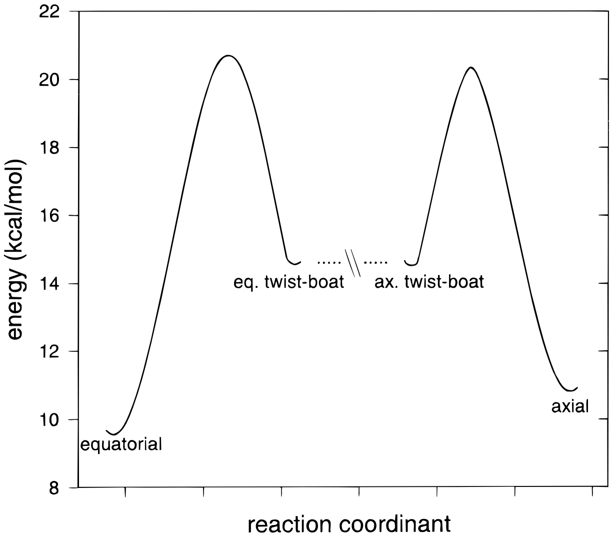


Figure 3. Conversion path between axial and equatorial conformers of 3-methyltetrahydropyran obtained by MMX calculation.

optimized geometries of the two chair conformers of 3-MTHP calculated at the MP2/6-31G** level. The calculation shows that the $\angle C_6C_1C_5$, $\angle C_1C_5C_4$, and $\angle C_5C_4H_a$ angles in the axial conformer are larger than they are in the equatorial form. It is reasonable to think that these changes are caused by steric interaction between C_6 group and H_a atom, making the axial conformer unstable with respect to the equatorial one.

A molecular mechanics calculation was carried out to simulate the path of the conversion between the axial and equatorial forms. We assumed that transformation from the chair form to the twist-boat gives the transition state.[10,29] The dihedral angles $\angle OC_2C_1C_5$ and $\angle OC_3C_4C_5$ in Table 2 were changed from the chair form values to the twist-boat form values. Figure 3 shows that the barrier between the equatorial chair and the equatorial twist-boat is ~11 kcal/mol which is close to the chair−chair inversion barrier in tetrahydropyran (10.3 kcal/mol)[30] and similar to the barrier in cyclohexane (10.7−11.5 kcal/mol).[31,32] These are much higher than the barrier (~4 kcal/mol) in cyclohexanone.[1,2,9,10] The difference is undoubtedly due to 120° bond angle in the keto group which makes the cyclic ketones more planar and thus reduces the energy required to reach the partly planar half-chair transition state. Inspection of the geometry shows that the transition state from the axial chair to the axial twist-boat form is similar to a half-chair form. The conversion between the equatorial and axial twist-boat forms was not calculated here, but the relative energy of the transition state(s) connecting them is not expected to exceed that of the half-chair transition state.[1,2,29] In reality, the conversion coordinate between the two chair forms may be a function of dihedral torsions and bending and stretching motions. A theoretical description of the simultaneous changes of all degrees of freedom is beyond the scope of this work.

IV. Conclusion

We have measured the $\Delta H°$ between the two chair conformers of 3-methyltetrahydropyran by measuring REMPI signals from the conformers and plotting them as a function of temperature. The van't Hoff plot is linear which shows that we can assume that, in the temperature range 298−383 K, $\Delta H°$ is constant and vibrational cooling of the conformers during supersonic expansion is faster than interconversion between them. The measured $\Delta H°$ is in good agreement with the ab initio calculation results. From the direct $\Delta G°$ measurement, we conclude that oscillator strengths for 3s − n transition of the conformers are not the same. The molecular mechanics calculation shows that the conversion barrier between the equatorial chair and axial chair form is close to the barrier in cyclohexane and tetrahydropyran.

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