

Determining the Conformer Populations of (*R*)-(+)-3-Methylcyclopentanone Using Vibrational Absorption, Vibrational Circular Dichroism, and Specific Rotation

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Experimental mid-infrared absorption and vibrational circular dichroism (VCD) spectra of (*R*)-(+)-3-methylcyclopentanone were measured in CCl₄ solution. Theoretical absorption and VCD spectra were obtained with B3LYP functional and large basis sets, namely aug-cc-pVDZ, 6-311++G(2d,2p), and aug-cc-pVTZ. From the temperature dependent absorption spectra, ΔH° for equatorial \leftrightarrow axial equilibrium was determined to be 4.84 kJ/mol, and the ratio of percent populations of equatorial-methyl:axial-methyl conformers, to be 87:13. The populations of equatorial-methyl and axial-methyl conformers were also determined using the experimental and predicted vibrational intensities. However, the errors associated with the populations determined from infrared absorption and VCD band intensities are fairly large. Optical rotation of (+)-3-methylcyclopentanone at 589 nm was measured as a function of concentration in CCl₄, CH₃OH, and CH₃CN solvents, and intrinsic rotation was extracted therefrom. Theoretical specific rotations were predicted using the B3LYP functional and the same basis sets as those used for infrared absorption and VCD. The populations determined from predicted specific rotations and experimental intrinsic rotation are within the error ranges of those determined from infrared absorption and VCD intensities. Using the populations determined from temperature dependent absorption spectra, the predicted population weighted specific rotation for an isolated molecule is found to be larger than the observed intrinsic rotation. The incorporation of solvent influence in specific rotation calculation increased the deviation of predicted value from experimental value, indicating the need for improved models for solvent influence.

Introduction

Five-member ring compounds attracted a lot of attention because they can be found in a wide variety of natural products, such as steroids^{1,2} and alkaloids.³ Several studies on their structure have been reported before. Conformational analysis of five-member ring molecules is an interesting and challenging subject. Different methods, including electron diffraction,⁴ infrared absorbance spectroscopy,⁵ and nuclear magnetic resonance (NMR),⁶ have been used to analyze the conformations of these compounds.

In particular, cyclopentanone and substituted cyclopentanones have attracted much attention because of the interesting conformation of cyclopentanone ring. Furthermore 3-methylcyclopentanone has exhibited⁷ anticonvulsant activity, suggesting an important medicinal role for this molecule. It is not known if the conformation or absolute configuration of 3-methylcyclopentanone has any role in its anticonvulsant activity. Nevertheless, the conformations of this molecule have been a subject of research interest since very early days. Djerassi and co-workers⁸ found that the magnitude of electronic circular dichroism (ECD) of (+)-3-methylcyclopentanone increased upon lowering the temperature, indicating a conformational equilibrium at room temperature. Richardson and co-workers⁹ considered the twisted conformation with equatorial-methyl and axial-methyl group and planar conformation of (+)-3-methylcyclopentanone to explain the observed ECD using INDO molecular orbital model. Their calculations indicated that axial-methyl conformation is favored over other conformations. Li

suggested¹⁰ that the microwave spectrum of 3-methylcyclopentanone can be satisfactorily explained by the twisted conformation with the equatorial-methyl group and estimated that this conformation would have an energy at least 250 cm⁻¹ (~3 kJ/mol) lower than other conformers. More recently, the Fourier transform microwave spectrum has been reported¹¹ for 3-methylcyclopentanone, but the conformational issue was not addressed. Using experimental and ab initio predicted vibrational Raman optical activity spectra, Polavarapu et al. concluded¹² that the major features in the observed spectrum can be explained by the twisted conformation with the equatorial-methyl group. In the resonance enhanced multiphoton ionization spectrum of 3-methylcyclopentanone, Potts et al. identified¹³ both equatorial-methyl and axial-methyl conformers, with the equatorial-methyl form being dominant. Their ab initio calculations also suggested that the equatorial-methyl form is energetically favored. The equatorial-methyl conformer was also used¹⁴ to compare the predicted specific rotations for (3*R*)-methylcyclopentanone with experimental specific rotation of (+)-methylcyclopentanone. The first experimental study¹⁵ to determine the energy difference between axial-methyl and equatorial-methyl conformers of 3-methylcyclopentanone appears to be that of Kim and Baer, where they have used resonance enhanced multiphoton ionization (REMPI) spectroscopy and determined the ΔH° to be 4.98 ± 0.59 kJ/mol at 323 K. The twisted conformation with equatorial-methyl group was suggested to be more populated than that with the axial-methyl group at room temperature. These observations were supported by their ab initio calculations. 3-Methylcyclopentanone has also been used¹⁶ as one of the systems to monitor the charge-transfer reactions

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between chiral Rydberg atoms and chiral molecules, although the focus was not on the conformational issues. The near-infrared (1300–800 nm) circular dichroism spectra of (*R*)-3-methylcyclopentanone were reported and analyzed.¹⁷ Molecular mechanics calculations on 3-methylcyclopentanone were also reported before.¹⁸

Vibrational spectroscopy has been widely used for conformational analysis¹⁹ of organic molecules. If vibrational bands characteristic of conformers can be identified, then the intensities of those bands as a function of temperature can be used²⁰ to determine the energy difference between conformers. The identification of characteristic conformer bands in the experimental spectra is facilitated by the availability of accurate quantum mechanical methods for predicting the vibrational properties. Despite these developments, vibrational absorption spectra have not been employed for determining the energy differences between conformers or to obtain the conformer populations of 3-methylcyclopentanone. In recent years, vibrational circular dichroism²¹ (VCD), which is analogous to electronic circular dichroism but operates in the infrared region, has emerged as a valuable tool for conformational analysis. Here the experimental VCD spectra are analyzed using the corresponding *ab initio* predicted VCD spectra. Some examples of conformational analyses using VCD have appeared in the literature,^{22,23} but quantitative estimates²² of conformer populations are lacking.

In addition to vibrational absorption and VCD, the experimental measurement and quantum theoretical prediction of specific rotation may also be used to analyze the conformer populations. The first *ab initio* prediction of specific rotation¹⁴ and subsequent developments employing density functional methods²⁴ have led to a renewed interest in the use of specific rotation for structural analyses.²⁵ The implementation of quantum mechanical methods for specific rotation calculations in both commercial software (Gaussian 03) and freeware (Dalton) programs is facilitating the wide applicability of specific rotation for structural analysis.

In the present manuscript, we use the vibrational absorption, vibrational circular dichroism, and specific rotation methods to analyze the conformers of (*R*)-(+)-3-methylcyclopentanone. Both experimental measurements and quantum theoretical predictions are presented and analyzed.

Methods

Measurements. The vibrational absorbance and vibrational circular dichroism spectra were recorded on a commercial Fourier transform VCD spectrometer Chiralir. The sample was held in a variable path length cell with BaF₂ windows. The sample concentration and path length are 1.4 M in CCl₄ and 100 μ m, respectively. The spectra were recorded with 3-h data collection time at 4 cm⁻¹ resolution. In the absorption spectrum presented here the solvent absorption was subtracted. In the presented VCD spectrum, the baseline was obtained from VCD measurement for solvent under identical conditions. Optical rotations were measured on Autopol III (in CCl₄ and CH₃OH solvents) or Autopol IV (in CH₃CN solvent) polarimeters at the sodium D line, using a 0.5 dm cell. The intrinsic rotation (specific rotation at infinite dilution) was extracted from the optical rotations at different concentrations as described in detail before.²⁶ The concentration range studied for optical rotation measurements was 0.05–0.19 M in CCl₄, 0.06–0.25 M in CH₃OH, and 0.06–0.44 M in CH₃CN.

Calculations. Geometry optimizations and VCD calculations were undertaken with the Gaussian 98 program.²⁷ The specific

rotation calculations for isolated molecules were performed using a developmental version of the DALTON program.²⁸ For density functional predictions, a B3LYP density functional available in this DALTON program was used. The basis sets used with DALTON were either available in the program library or were obtained from the EMSL library.²⁹ All specific rotation calculations reported here were based on the gauge including atomic orbitals (GIAOs, also called London orbitals) and the dynamic method.³⁰ Solvent influence on specific rotation was investigated using PCM model as implemented in the Gaussian 03 program.²⁷

Conformational Analysis from Vibrational Intensities. For molecules existing in two or more conformations, the experimental intensities of these bands, in conjunction with predicted intensities for individual conformers, can be used to determine the conformer populations as follows.²² If the experimental band intensities are represented by a column vector, $\{E\}$, predicted band intensities for different conformers by rectangular matrix \mathbf{P} , then the fractional populations of conformers, represented by column vector $\{X\}$, are related to $\{E\}$ and \mathbf{P} by

$$\begin{bmatrix} E_1 \\ E_2 \\ E_3 \\ \vdots \\ E_m \end{bmatrix} = \begin{bmatrix} P_{1,1} & P_{1,2} & \cdots & P_{1,N} \\ P_{2,1} & P_{2,2} & \cdots & P_{2,N} \\ P_{3,1} & P_{3,2} & \cdots & P_{3,N} \\ \vdots & \vdots & \ddots & \vdots \\ P_{m,1} & P_{m,2} & \cdots & P_{m,N} \end{bmatrix} \begin{bmatrix} X_1 \\ X_2 \\ \vdots \\ X_N \end{bmatrix} \quad (1a)$$

In other words, the experimental intensity E_i for band i is expressed as

$$E_i = \sum_{j=1}^N P_{ij} X_j \quad \text{for } i = 1, 2, \dots, m \quad (1b)$$

where P_{ij} is the predicted intensity for band i of the j th conformer. Usually the number of vibrational bands (m), is far greater than the number of conformations (N), so the column vector of fractional populations, $\{X\}$, can be determined by regression methods, with the constraints that the sum of the fractional populations of conformers is 1 and fractional populations cannot be negative. That is,

$$\sum_{j=1}^N X_j = 1 \quad \text{and} \quad X_j \geq 0 \quad (2)$$

The integrated areas of the bands in the experimental spectra were obtained by fitting ($R^2 = 0.99$) the experimental bands to Lorentzian band shapes using the PeakFit program.³¹ The experimental band intensities in vibrational absorption spectra were expressed³² as dipole strengths (D_i) and in VCD spectra as rotational strengths (R_i) as follows:

$$D_i = \frac{0.92 \times 10^{-38}}{\nu_0} \int \epsilon(\nu) d\nu \quad (3)$$

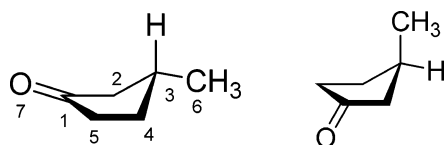
$$R_i = \frac{0.23 \times 10^{-38}}{\nu_0} \int \Delta\epsilon(\nu) d\nu \quad (4)$$

where $\epsilon(\nu)$ is the molar absorptivity (in L mol⁻¹ cm⁻¹) at frequency ν (in cm⁻¹) and ν_0 is the band center. The predicted counterparts of the experimental bands have to be identified

TABLE 1: Gibbs Energies and Populations of Conformers of (*R*)-3-Methylcyclopentanone Obtained with B3LYP Functional and Different Basis Sets

	conformer ^b	6-31G*	aug-cc-pVDZ	6-311++G(2d,2p)	aug-cc-pVTZ
enthalpy, H^a	1	-309.730654	-309.769788	-309.833518	-309.850720
	2	-309.728656	-309.767850	-309.831579	-309.848693
ΔH°		5.25 ^c	5.09 ^c	5.09 ^c	5.32 ^c
Gibbs energy, G^a	1	-309.769505	-309.808733	-309.872402	-309.889599
	2	-309.767473	-309.806761	-309.870418	-309.887524
ΔG°		5.34 ^c	5.18 ^c	5.21 ^c	5.45 ^c
percent population	1	89.6	89.0	89.1	90.0
	2	10.4	11.0	10.9	10.0

^a At 298 K, 1 atm (in atomic units). ^b 1: equatorial-methyl. 2: axial-methyl. ^c In kJ/mol (axial-equatorial).

**Figure 1.** Conformers of (*R*)-3-methylcyclopentanone: (left) equatorial-methyl; (right) axial-methyl.

and correlated one-by-one. A commercial program DataFit³³ was used for determining the fractional populations using eqs 1 and 2.

Results and Discussion

Conformers. The two major conformers of (*R*)-3-methylcyclopentanone, namely, equatorial-methyl and axial-methyl, were optimized with B3LYP functional and 6-31G*, aug-cc-pVDZ, 6-311++G(2d,2p), and aug-cc-pVTZ basis sets. The structures for the two conformers and atomic numbering are shown in Figure 1. Vibrational frequencies, absorption intensities, and rotational strengths were calculated at each of the two optimized geometries using the same functional and basis set. The Gibbs energies and population of these two conformations are listed in Table 1. The populations obtained with the three large basis sets are close to each other. Conformer 1 has about 90% population and conformer 2 has about 10% population.

Vibrational Absorption and VCD Spectra. The experimental vibrational absorption and VCD spectra of (+)-3-methylcyclopentanone were measured in CCl₄ solution. The calculated absorption and VCD spectra, obtained with all four basis sets, for (*R*)-3-methylcyclopentanone, are shown in Figure 2, along with the corresponding experimental spectra for (+)-

enantiomer. The agreement between the experimental and calculated spectra is very good except for the strongest peak (around 1150 cm⁻¹) obtained in B3LYP/aug-cc-pVDZ calculation. The B3LYP/aug-cc-pVDZ spectra show two peaks in both absorption and VCD spectra at ~1150 cm⁻¹, but the experimental spectra show only one corresponding peak.

To derive the populations from VA and VCD spectra, the correspondence between experimental and calculated bands needs to be identified. If the difference between predicted vibrational band positions of two conformers is less than 5 cm⁻¹ then they are treated as corresponding together to one experimental band. If the difference is larger than 5 cm⁻¹, then they are treated as corresponding to two separate experimental bands. We use a prime to indicate the bands coming from equatorial-methyl conformer, and a double prime to indicate the bands coming from axial-methyl conformer. The correspondence between experimental bands and B3LYP/aug-cc-pVTZ predicted peaks, following the above criterion, is summarized in Table 2 and in Figure 3. The calculations with other basis sets are provided in the Supporting Information. The numbering of bands is based on the predicted vibrational frequencies with lowest predicted vibrational frequency being band #1.

The bands 18' and 18'' are of special significance because they originate from equatorial-methyl and axial-methyl conformers, respectively, and are well separated from each other (unlike other bands of these conformers). The vibrational origins of these two bands involve the 3-methyl group, which has different orientations in the two conformers. The 18' band originates from the C–C bond stretch between the 3-methyl group and ring deformation. The 18'' band originates from the –CH₃ wag and ring deformation. These two bands serve as conformer markers.

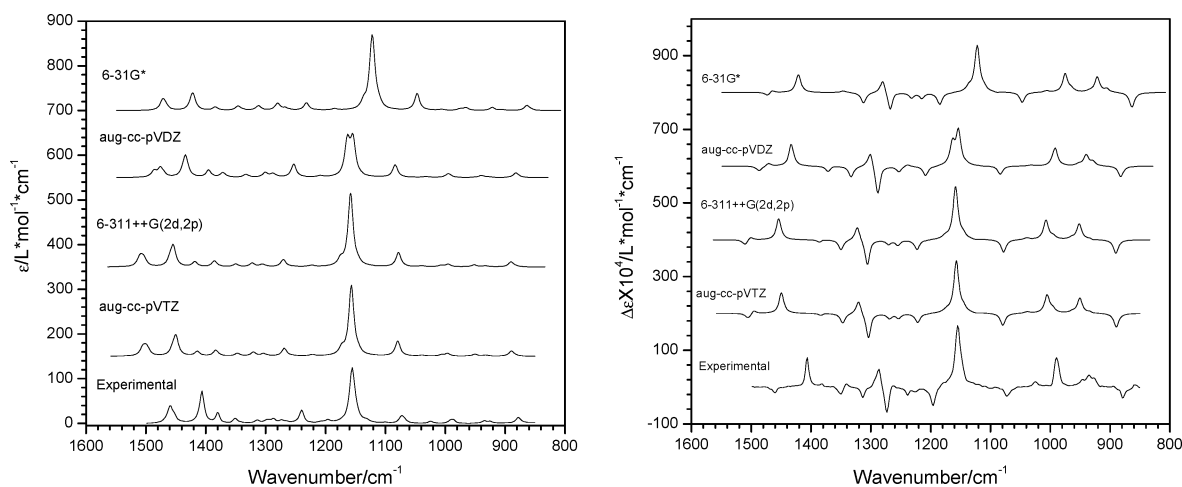
**Figure 2.** Experimental (bottom trace) and predicted (top four traces) spectra of (*R*)-(+)-3-methylcyclopentanone: (left panel) absorption spectra; (right panel) VCD spectra. 6-31G* frequencies were scaled with 0.9613; aug-cc-pVDZ, 6-311++G(2d,2p) and aug-cc-pVTZ frequencies were not scaled.

TABLE 2: Frequencies,^a Dipole Strengths,^b and Rotational Strengths^c of (R)-(+)-3-Methylcyclopentanone

no.	experimental			B3LYP/aug-cc-pVTZ					
	ν_i	D_i	R_i	equatorial-methyl			axial-methyl		
	ν_i	D_i	R_i	ν_i	D_i	R_i	ν_i	D_i	R_i
13''	873	3.3					883	21.2	0.1
13'	878	18.4	-10.1	890	20.6	-16.8			
14	925	5.9	6.6	933	3.3	2.4	931	7.7	-12.4
15'	935	7.8	8.8	951	7.3	17.3			
15''	946		5.5				963	3.1	16.1
16	988	14.6	24.9	996	8.8	4.7	996	2.2	-5.4
17				1005	4.2	20.7	1006	6.2	-11.5
18''	1024	5.4	4.0				1039	28.3	14.4
18'	1072	23.2	-7.8	1079	49.8	-12.3			
19''							1124	4.4	-7.0
19'	1148	17.7	9.2	1145	8.4	4.1			
20	1155	138.5	41.6	1157	195.5	50.7	1155	232.1	-14.4
21	1161	10.5	5.2	1173	20.1	2.0	1178	7.4	5.1
22''							1205	0.9	-3.5
22'	1196	6.0	-13.2	1222	3.6	-8.1			
23''	1205	0.9					1229	3.8	-3.3
23'	1226		-2.8	1254	0.8	-4.1			
24	1240	28.5	-4.7	1269	21.1	-3.8	1271	6.9	-2.5
25''	1264		2.6				1298	9.8	14.5
25'	1272	5.0	-16.6	1304	5.8	-21.7			
26	1287	7.4	12.3	1320	10.2	11.0	1323	2.8	5.0
27	1314	4.1	-6.4	1347	6.4	-7.7	1348	6.8	-1.9
28	1350	7.2	-4.8	1383	14.7	-1.7	1378	7.5	4.4
29	1380	17.6	1.0	1414	9.8	-0.2	1414	16.0	1.0
30	1407	65.8	14.5	1450	40.3	16.1	1450	53.6	-1.2
31				1455	13.3	-0.6	1455	6.9	-3.7
32	1453	14.3		1496	5.2	2.4	1498	16.1	2.7
33				1499	14.7	-0.2	1500	6.0	-4.3
34	1460	33.7	-3.6	1505	18.1	-3.0	1508	13.3	-5.2

^a Frequencies, ν_i , in cm^{-1} . ^b Dipole strengths, D_i , in $10^{-40} \text{ esu}^2 \text{ cm}^2$.

^c Rotational strengths, R_i , in $10^{-44} \text{ esu}^2 \text{ cm}^2$.

Experimental Determination of Conformer Populations.

In the following discussion, results obtained from three different approaches to determine the conformer populations will be presented. These are based on (1) temperature dependent vibrational absorption band intensities, (2) regression analysis of experimental and DFT predicted vibrational band intensities, and (3) analysis of experimental intrinsic rotation and DFT predicted specific rotations.

(1) *Temperature Dependent Vibrational Absorption Band Intensities.* If the vibrational absorption bands due to individual conformers can be identified, then the temperature dependence of their experimental intensities can be used to obtain ΔH° . The bands 18' and 18'', assigned to the equatorial-methyl and axial-methyl conformers, are appropriate for this purpose because they are isolated and separated from each other. To avoid the problems associated with solvent interference in the infrared absorption spectra, we have investigated the temperature dependent spectra for neat liquid sample (Figure 4). The areas of bands 18' and 18'', as a function of temperature were used for preparing the van't Hoff plot (see Figure 5). From this plot, ΔH° is found to be $4.84 \pm 0.08 \text{ kJ/mol}$. This value is very close to the value of $4.98 \pm 0.59 \text{ kJ/mol}$ obtained¹⁵ from REMPI spectra of a gas phase sample. Because the ΔH° values obtained in the gas phase¹⁵ and the present liquid phase measurements for methylcyclopentanone are the same (within experimental uncertainties), it is reasonable to assume that this ΔH° value will apply for liquid solution in CCl_4 as well. The predicted ΔH° values (Table 1) at 298 K in the current B3LYP calculations with aug-cc-pVDZ, 6-311++G(2d,2p), and aug-cc-pVTZ basis sets for isolated molecule are very close to the experimental values. The entropy term, $T\Delta S^\circ$ at room temperature is negligible compared to ΔH° , as can be inferred from

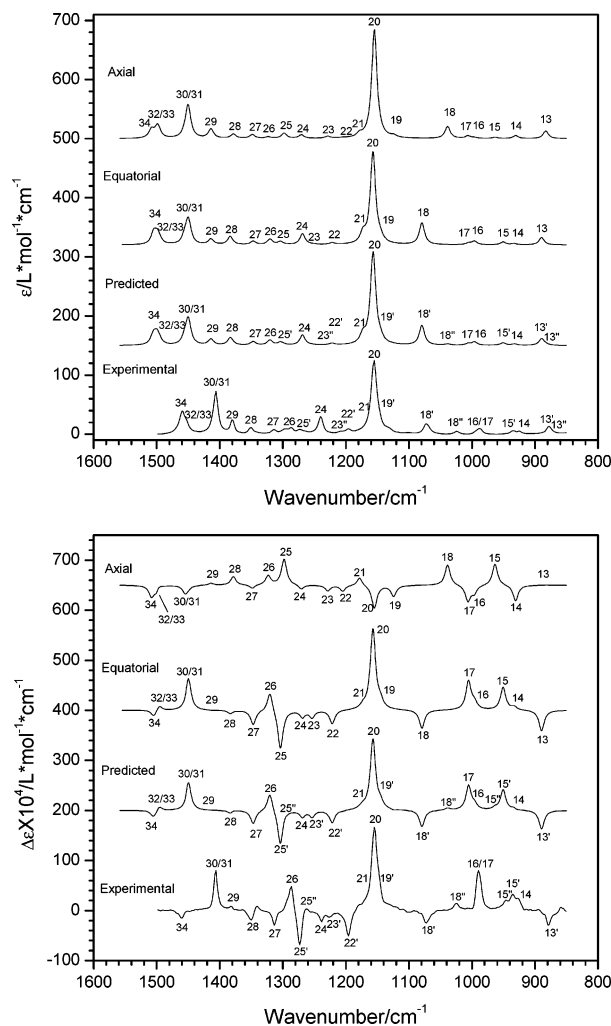


Figure 3. Correlation between the predicted spectra obtained at B3LYP/aug-cc-pVTZ level and the experimental spectra: (top panel) absorption spectra; (bottom panel) VCD spectra.

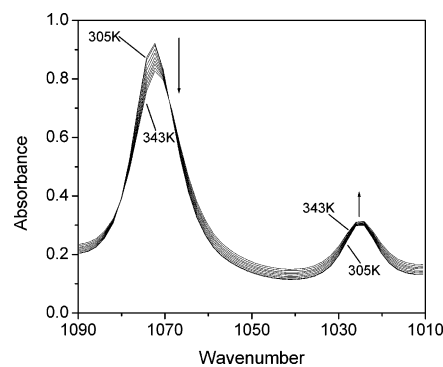


Figure 4. Temperature dependent absorption spectra between 305 and 343 K at ~ 5 deg intervals of liquid (+)-3-methylcyclopentanone. The absorption bands at 1072 and 1024 cm^{-1} are assigned to equatorial and axial conformations, respectively, of 3-methylcyclopentanone and are labeled as 18' and 18'' in the text and Table 2. Arrows indicate the direction of intensity change.

$\Delta G^\circ \sim \Delta H^\circ$ in Table 1. Then the experimental ΔH° value gives the populations as 87% for equatorial-methyl and 13% for axial-methyl conformers, with error estimated at less than 1%.

(2) *Regression Analysis of Experimental and DFT Predicted Vibrational Band Intensities.* The calculated vibrational dipole strengths and rotational strengths from the largest basis set used in this study, B3LYP/aug-cc-pVTZ, are considered to be most accurate. Using the ratio of intensities for 18' and 18'' bands

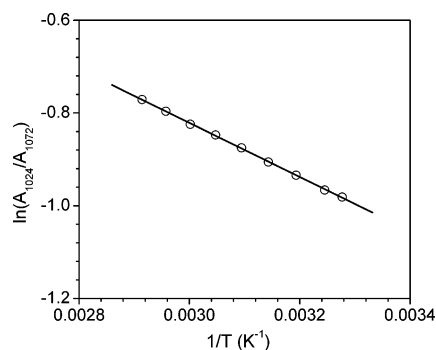


Figure 5. van't Hoff plot obtained from the integrated areas of 1072 and 1024 cm^{-1} bands assigned to equatorial-methyl and axial-methyl conformations, respectively, at different temperatures. The circles represent the experimental data points and the solid line represents the equation, $\ln(A_{1024}/A_{1072}) = -582.7/T + 0.927$. ΔH° derived from the slope is 4.84 ± 0.08 kJ/mol.

TABLE 3: Population (X_e) of Equatorial-Methyl Conformer of (*R*)-(+)-3-Methylcyclopentanone Determined from Absorbance and VCD Spectra

quantity ^a	absorbance		VCD	
	normal ^b	modified ^c	normal ^b	modified ^c
k	0.74 ± 0.10	0.77 ± 0.08	0.93 ± 0.30	1.00 ± 0.30
X_e	0.89 ± 0.36	0.79 ± 0.37	0.91 ± 0.21	0.94 ± 0.22
R^2	0.903	0.943	0.928	0.950

^a k is the correction factor used to account for errors in concentration and path length; X_e is the fractional population of equatorial-methyl conformer; R^2 is the goodness of fit (1 for perfect fit). ^b With correspondence between experimental and predicted bands as in Table 2. ^c Correspondence in Table 2 modified with peaks 19', 20, and 21 combined together as one peak.

obtained in this B3LYP/aug-cc-pVTZ calculation, the observed ratio for the corresponding experimental bands yields the population ratio of equatorial-methyl to axial-methyl conformer as 71:29 from absorption and 70:30 from VCD. However, this is based on only one each of the many vibrational bands of the two conformers. If the predicted intensities happen to be in error for one or both of these two bands, then the conclusion on populations will be in error as well. To avoid such a possibility, one has to consider as many vibrational bands as possible in the analysis. For using all vibrational bands possible in the analysis, we used eqs 1–3 with the correspondence between experimental bands and calculated peaks, as shown in Figure 3 and Table 2. Although several options have been attempted in the least-squares fitting between observed and calculated intensities, only two different options will be presented and discussed here: (a) treating bands 19', 20, and 21 together as one band or (b) treating the bands 19', 20, and 21 as separate bands. The results are shown in Table 3.

Judging from the correlation coefficient, R^2 , the fit that combined the bands 19', 20, and 21 together is preferred. Irrespective of the option used, the error in the population determined from absorption band intensities is larger than that in the population determined from VCD intensities. This observation is consistent with that noted earlier for a single conformer molecule 3-chloro-1-butyne,²² that the deviations between calculated and experimental intensities is larger for absorption than that for VCD. In addition, the larger error in the population determined from absorption band intensities (than that determined from VCD band intensities) of 3-methylcyclopentanone may also arise from the similarity of the absorbance spectra predicted for equatorial-methyl and axial-methyl conformers. When the spectra of the two conformers are similar, it

will be difficult to distinguish between the populations of individual conformers and the precision in the regression method will be lower. The differences between the VCD spectra of the equatorial-methyl and axial-methyl conformers are substantial, thereby making the population determination from VCD spectra more accurate. Note that the population predicted from intensities of 18' and 18'' alone (vide supra) is within the error range in the populations predicted from full spectra.

Nevertheless, the errors estimated in the populations, obtained from full spectra, are fairly large, as already pointed out for 3-chloro-1-butyne.²² This observation can be attributed to the deviation of the predicted dipole and rotational strengths from the corresponding experimental values, even at the very high levels of calculations employed.

(3) *Analysis of Experimental Intrinsic Rotation and DFT Predicted Specific Rotations.* The optical rotation of (+)-3-methylcyclopentanone was measured at 589 nm in CCl_4 , CH_3OH , and CH_3CN solvents as a function of concentration. These data are provided as supporting material. The specific rotation at infinite dilution, known as intrinsic rotation,²⁶ was deduced from these data. The intrinsic rotation, $\{\alpha\}_D$ was obtained as 150.3 ± 0.2 in CCl_4 , 138.9 ± 0.3 in CH_3OH , and 144.9 ± 0.4 in CH_3CN . The specific rotations for equatorial-methyl and axial-methyl conformers were calculated at 589 nm using B3LYP functional and different basis sets (Table 4). With these calculated specific rotations the populations can be estimated using $\{\alpha\}_D = [\alpha]_{D,e} p_e + [\alpha]_{D,a} p_a$, where $\{\alpha\}_D$ is the experimental intrinsic rotation and $[\alpha]_{D,e}$ and $[\alpha]_{D,a}$ are the predicted specific rotations for equatorial-methyl and axial-methyl conformers and p_e and p_a are the percent populations of equatorial-methyl and axial-methyl conformers (with the constraint that $p_e + p_a$ is 100%). The populations determined in this manner, using four different basis sets, are shown in Table 4. Among the three large basis set calculations, the values obtained in B3LYP/aug-cc-pVDZ and B3LYP/6-311++G(2d,2p) calculations are almost the same, whereas those obtained in B3LYP/aug-cc-pVTZ calculation are only slightly different. The average populations obtained from three large basis set calculations (namely, 77.9% for equatorial-methyl and 22.1 for axial-methyl) are within the error ranges of those predicted (Table 3) from absorption and VCD spectra.

Approaching this analysis from a different viewpoint, if the conformer populations are known, then it would be useful to determine the errors in the predicted specific rotations by comparing the population weighted specific rotation with the experimental intrinsic rotation. If we take the populations of conformers determined from temperature dependent absorption intensities of liquid sample (87:13 for equatorial:axial, vide supra), which are the same as those obtained from the REMPI spectrum of the gas phase sample,¹⁵ as accurate populations, then the population weighted values are 209, 209, and 202, respectively, in B3LYP/aug-cc-pVDZ, B3LYP/6-311++G(2d,2p), and B3LYP/aug-cc-pVTZ calculations, with an average value of 207. The experimental intrinsic rotation in CCl_4 is 150. The difference in these two values suggests that the specific rotations predicted with large basis sets for (*R*)-3-methylcyclopentanone are overestimated by $\sim 38\%$. The population weighted specific rotation obtained in a smaller B3LYP/6-31G* calculation is 180, which is much closer to the experimental rotation.

To investigate if the larger difference obtained in the three large basis set calculations is due to the absence of solvent influence in the predicted specific rotation, we have repeated the specific rotation calculations in the presence of CCl_4 , CH_3OH , and CH_3CN solvents using the PCM model incorporated

TABLE 4: Specific Rotations Predicted with B3LYP Functional and Populations Determined There from Using Experimental Intrinsic Rotation for (*R*)-(+)-3-Methylcyclopentanone

basis set	equatorial-methyl				axial-methyl			
	predicted [α] _D	percent population in			predicted [α] _D	percent population in		
		CCl ₄	CH ₃ OH	CH ₃ CN		CCl ₄	CH ₃ OH	CH ₃ CN
6-31G*	247.7	81.3	79.2	80.3	−274.3	18.7	20.8	19.7
aug-cc-pVDZ	291.2 (311.7 ^a , 300.3 ^b , 302.2 ^c)	77.6	75.8	76.8	−339.1 (−361.0 ^a , −343.4 ^b , −344.0 ^c)	22.4	24.2	23.2
6-311++G(2d,2p)	291.5	77.6	75.8	76.7	−338.2	22.4	24.2	23.3
aug-cc-pVTZ	280.9	78.5	76.6	77.6	−325.2	21.5	23.4	22.4
Average ^d	288 ± 6	77.9 ± 0.5	76.1 ± 0.5	77.0 ± 0.5	−334 ± 8	22.1 ± 0.5	23.9 ± 0.5	23.0 ± 0.5

^a Specific rotations calculated with CCl₄ solvent influence using PCM model. ^b Specific rotations calculated with CH₃OH solvent influence using PCM model. ^c Specific rotations calculated with CH₃CN solvent influence using PCM model. ^d Average values were obtained from the aug-cc-pVDZ, 6-311++G(2d,2p), and aug-cc-pVTZ calculations

TABLE 5: Comparison of B3LYP Predicted Specific Rotations for (*R*)-(+)-3-Chloro-1-butyne with and without Solvent Influence

	without solvent ^b	with solvent	
		CCl ₄	CH ₃ OH
6-31G*	26.8	37.0	36.6
aug-cc-pVDZ	32.8	41.2	41.8
6-311++G(2d,2p)	28.3	44.3	40.7
aug-cc-pVTZ	28.6	42.9	39.2
average ^a	30 ± 2	43 ± 2	41 ± 1
obsd ^b intrinsic rotation in CCl ₄	28.4 ± 0.2		
obsd ^b intrinsic rotation in CH ₃ OH	29.0 ± 0.3		

^a The average of three large basis set (aug-cc-pVDZ, 6-311++G(2d,2p), aug-cc-pVTZ) predictions. ^b From ref 22.

in the Gaussian 03 program. Because the specific rotations obtained in the absence of solvent influence with different large basis sets are very close to each other, we investigated the solvent influence with only one of the three large basis sets used in this investigation. The geometries were re-optimized and specific rotation calculated using B3LYP functional and aug-cc-pVDZ basis set by incorporating the solvent influence. The specific rotations predicted in the presence of CCl₄ solvent influence (see Table 4) are +311.7 and −361.0, respectively for equatorial-methyl and axial-methyl conformers, whose magnitudes are larger than those (+291.2 and −339.1) predicted for the isolated molecule. The predicted population weighted specific rotation in B3LYP/aug-cc-pVDZ calculation with CCl₄ solvent influence is 224 (as opposed to 209 for isolated molecule), which is ~50% larger than the experimental value. Thus the deviation of the calculated value from experimental value is even larger when CCl₄ solvent influence is included.

Similar observations are obtained with CH₃OH and CH₃CN solvents. The specific rotations predicted in the presence of CH₃OH (or CH₃CN) solvent influence (see Table 4) are +300.3 (or +302.2) and −343.4 (or −344.0), respectively, for equatorial-methyl and axial-methyl conformers, whose magnitudes are larger than +291.2 and −339.1 predicted for the isolated molecule. The predicted population weighted specific rotation in B3LYP/aug-cc-pVDZ calculation with CH₃OH (or CH₃CN) solvent influence is 217 (or 218), as opposed to 209 for the isolated molecule. The experimental intrinsic rotations obtained in CH₃OH and CH₃CN are 138.9 and 144.9, respectively.

These observations are consistent with those found for a single conformer molecule (*R*)-(+)-3-chloro-1-butyne. In the case of (*R*)-(+)-3-chloro-1-butyne (see Table 5), the predicted specific rotation for an isolated molecule is in good quantitative agreement with experimental intrinsic rotation obtained in CCl₄ and CH₃OH solvents, but when solvent influence (CCl₄ or CH₃-

OH) is included with PCM model, the predicted value is overestimated by ~50%. Thus the current observations for 3-methylcyclopentanone and 3-chloro-1-butyne, contradict previously reported³⁴ conclusions that the PCM model improves the agreement between predicted and experimental specific rotations in CH₃OH and CH₃CN solvents. More theoretical developments appear needed to correctly model the solvent influence on specific rotation.

Conclusions

The conformer populations of (*R*)-(+)-3-methylcyclopentanone are determined using experimental and predicted vibrational absorption spectra, VCD spectra, and specific rotation. The temperature dependent absorption spectra of liquid 3-methylcyclopentanone provided ΔH° for equatorial-axial equilibrium, which is in good agreement with that determined for gas phase molecules, and populations as 87% equatorial-methyl and 13% axial-methyl. On the other hand, the populations determined from experimental and predicted vibrational intensities are associated with large errors because the predicted vibrational intensities even with large basis sets are not sufficiently close to the experimental intensities. The predicted specific rotations for individual conformers and the observed intrinsic rotation yield conformer populations within the error ranges associated with the populations obtained from predicted and experimental vibrational intensities. Using the populations determined from temperature dependent absorption spectra, the predicted population weighted specific rotation for isolated molecules is found to be larger than the experimental value in CCl₄, CH₃OH, and CH₃CN solvents. This deviation is further increased when solvent influence is included in the calculations, indicating the need for better theoretical models for incorporating solvent influence on specific rotation.

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Supporting Information Available: Tables of dihedral angles, Cartesian coordinates in the optimized structures, predicted vibrational frequencies, dipole strengths, rotational strengths for the two conformers of (*R*)-3-methylcyclopentanone, and their correlation with corresponding experimental quantities and a figure showing the concentration dependence of optical rotation and specific rotation for (+)-3-methylcyclopentanone. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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