

Conformational enthalpies, ΔH° [axial/equatorial], of 3- and 4-methylcyclohexanone

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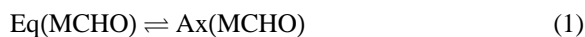
Abstract

Methylcyclohexanone exists primarily in its most stable chair form at ambient temperatures. Two chair conformers exist in which the methyl group may be either axially or equatorially oriented. The conformational energy difference between these is dominated by non-bonded interactions. Several theoretical methods were undertaken to model the conformational enthalpy, ΔH° , including molecular mechanics (MM), ab initio molecular orbital, and density functional theories (DFT). Ab initio methods include HF/6-31G*, HF/6-311G**, HF/6-311+G(3df,2p), MP2-fu/6-31G*, MP2-fu/6-31+G*, and G2(MP2) levels of theory. A hybrid theoretical model, G2(MP2,SVP), was found to give nearly identical results to G2(MP2) theory. The DFT methods included B3-LYP/6-31G*, B3-LYP/6-311+G(3df,2p), B3-PW91/6-31G*, and B3-PW91/6-311+G(3df,2p). The theoretical results are compared with recent gas-phase experimental measurements from our laboratory. The conformational energy between the more stable equatorial conformer and the less stable axial conformer has been measured by resonance-enhanced multiphoton ionization spectroscopy to be 1.55 ± 0.12 and 2.1 ± 0.2 kcal mol⁻¹ for 3- and 4-methylcyclohexanone, respectively. There is excellent agreement between these experimental values and the MM and DFT methods. A less satisfactory agreement is made for the MP2 and G2(MP2) methods. © 1997 Elsevier Science B.V.

Keywords: Conformational enthalpy; Ab initio calculations; G2(MP2); Density functional theory; Cyclohexanone; Methylcyclohexanone; Conformations

1. Introduction

Saturated six-membered ring thermochemistry has a long history. Cyclohexanone resides in the global minimum chair conformation at ambient temperatures. Within this chair conformation, a methyl group attached to the ring can be situated in either an axial or equatorial orientation, and these two structures are in rapid equilibrium.



It is well known that axial substituent orientations are less stable by about 1–2 kcal mol⁻¹ [1]. Axial methyl conformations have axial/axial steric interactions between the methyl group and hydrogen atoms that destabilize this conformation relative to the equatorial conformation, where this interaction is not present. However, in the case of axial 3-methylcyclohexanone (MCHO), interaction between the methyl and carbonyl groups leads to a van der Waals' attraction, thereby counteracting to some extent the instability of the axial orientation. The replacement of a methyl/hydrogen atom interaction with a methyl/carbonyl interaction in six-membered rings gives the

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so-called 3-methyl ketone effect [2,3]. While axial/equatorial equilibria have been studied extensively in various liquid environments, there is limited information related to experimental and theoretical gas-phase equilibria.

The free energy differences between the two methyl group orientations, ΔG° , has been measured by a variety of methods for 3-MCHO [3–10] and 4-MCHO [4,8,11]. In particular, $3s \leftarrow n$ 2 + 1 resonance-enhanced multiphoton ionization (REMPI) spectroscopy coupled with supersonically cooled samples has the ability to distinguish between axial and equatorial conformations in the gas phase [4,12–15]. The cooling rate in a supersonic expansion can effectively “freeze” out the axial and equatorial conformer equilibrium concentrations [4,13,15]. The rate of cooling, k_{cooling} , in the supersonic expansion via collisional relaxation is more rapid than axial/equatorial interconversion, k_1 or k_{-1} , so that the concentrations are frozen out in their valve temperature concentrations. For the MCHOs the experimental conditions and physical properties are such that the concentration of axial and equatorial conformations in the cold beam are representative of their concentration in the pulsed valve prior to expansion [15].

Experimental $\Delta G_{303\text{K}}^\circ$ values determined by 2 + 1 REMPI have been reported in the literature for 3- and 4-MCHO to be 1.62 and 2.52 kcal mol⁻¹, respectively [4]. An equilibrium constant was determined from the ratio of peak heights of the $3s \leftarrow n$ Rydberg transition origins. This earlier study made two assumptions in deriving the equilibrium constant, K_{eq} : (1) that the absorption cross-sections were equal for the two conformers and (2) that peak heights were proportional to conformer concentrations.

Rather than measuring ΔG° for the equilibrium, a more recent experiment sought to measure ΔH° [15]. The enthalpy difference can be measured from the change in the equilibrium constant with temperature through the van't Hoff equation (2):

$$\frac{d \ln(K)}{d(1/T)} = \frac{-\Delta H^\circ}{R} \quad (2)$$

Axial and equatorial concentrations (C_i) can be determined from the peak areas (A_i) in the absorption spectrum. The peaks must be scaled by the individual transition line strengths (f_i), which are a function of the laser polarization, Franck–Condon factors, and

absorption cross-sections. Thus,

$$C_i = \frac{A_i}{f_i} \quad (i = \text{eq or ax}) \quad (3)$$

Since K is the ratio of concentrations in Eq. (3), the left side of Eq. (2) can now be expressed as a sum of temperature-dependent and independent terms:

$$\frac{d}{d(1/T)}(\ln K) = \frac{d}{d(1/T)} \left(\ln F + \ln \frac{A_{\text{ax}}}{A_{\text{eq}}} \right) \quad (4)$$

Since $\ln F$ does not depend upon temperature, Eq. (4) reduces to

$$\frac{d \ln(A_{\text{ax}}/A_{\text{eq}})}{d(1/T)} = \frac{-\Delta H^\circ}{R} \quad (5)$$

In Eq. (5) A_{ax} and A_{eq} may be measured from any two convenient peaks in the $3s \leftarrow n$ absorption spectrum since they are only a function of temperature and laser power for a given set of experimental conditions. The relative peak areas were probed at various equilibrium temperatures from 303 to 473 K. By this approach, the gas-phase enthalpy of interconversion (ΔH°) between the axial and equatorial conformations of 3- and 4-MCHO have been experimentally determined to be 1.55 ± 0.12 and 2.10 ± 0.20 kcal mol⁻¹, respectively [15]. An extensive comparison with the literature has been made for 3-MCHO in our recent article [15]. The most noteworthy experiments produced ΔH° values that are 0.2 to 0.5 kcal mol⁻¹ smaller than our experimental result. There are two conflicting values of ΔH° for 4-MCHO in the literature: 1.1 kcal mol⁻¹ [8] and 1.9 kcal mol⁻¹ [11]. The conformational energy for 4-MCHO should be nearly identical to that of methylcyclohexane (MCH) since the local steric environments are similar [1]. The gas-phase conformational enthalpy of MCH has been determined to be 1.74 kcal mol⁻¹ [16], while theoretical studies have given values around 2.0 kcal mol⁻¹ [17]. Accurate conformational energies are necessary for our understanding of conformational equilibria. We have determined the ΔH° for 3- and 4-MCHO at several levels of theory here, for comparison with experiment and to gain understanding of the important factors controlling the enthalpy differences in such reactions.

2. Theoretical approach

Molecular mechanics calculations were performed

by using the MMX algorithm in the PCMODEL for Windows[™] program package [18]. MM3 calculations were carried out at the University of Georgia by N.L. Allinger [19]. The minimum energy geometries from the PCMODEL calculations were used as the starting points for the ab initio molecular orbital (MO) calculations. All of the ab initio MO and density functional calculations were carried out with GAUSSIAN94 [20] on a CRAY T-916 supercomputer.

Complete optimizations were performed on the axial and equatorial geometries at the Hartree–Fock (HF) level with the 6-31G*, 6-311G**, and 6-311+G(3df,2p) basis sets. Electron-correlated calculations including core 1s electrons were performed using Møller–Plesset second-order perturbation theory (MP2-fu) with the 6-31G* and 6-31+G* basis set levels. Several variations of G2-type theory were performed on the minimized MP2 geometries [21–23]. The variations on G2 theory are those developed by Curtiss et al. [22,23] to minimize cpu time by reduced MP orders, G2(MP2), and reduced basis set requirements, G2(MP2,SVP). For G2(MP2) theory, two single-point calculations were performed on the MP2-fu/6-31G* geometry. The two single-point calculations are QCISD(T)/6-311G** and MP2-fc/6-311+G(3df,2p). For G2(MP2,SVP) theory, the basis set for the QCISD(T) calculation is reduced to 6-31G*. A third variation, G2+(MP2,SVP), was derived by adding a set of diffuse “(+)” functions to both the optimization (MP2-fu/6-31+G*) and single-point energy calculation (QCISD(T)/6-31+G*) steps. The MP2-fc/6-311+G(3df,2p) single-point calculation was also performed on the MP2-fu/6-31G* geometry. In all three cases, zero-point vibrational energies (ZPVEs) were obtained at the HF/6-31G* level from scaled (0.8929) individual frequencies [24–26]. The higher level corrections (HLC) are –0.005 Hartrees and –0.00513 Hartrees per valence pair for G2(MP2) and G2(MP2,SVP) theories, respectively. The HLC for the G2+(MP2,SVP) level was taken to be the same as that for G2(MP2,SVP) theory.

Four levels of density functional theory (DFT) were employed to calculate the enthalpy difference. Becke’s [27] three-parameter exchange functional was coupled with both Lee–Yang–Parr [28] (LYP) and Perdew–Wang [29] (PW91) correlation functionals. These in turn were coupled with each of the following basis sets: 6-31G(d) and 6-311+G(3df,2p).

The calculations with the diffuse and highly polarized basis set were important to determine the magnitude of basis set deficiencies at the 6-31G* level. The default grid, defined as having 75 radial shells and 302 angular points per shell in GAUSSIAN 94, was used as the quadrature grid in integral evaluation.

Vibrational frequencies were calculated at several levels of theory and were scaled prior to the calculation of ZPVEs, thermal enthalpies, and entropies by factors suggested by Scott and Radom [26]. ZPVEs were determined by scaling the individual frequencies by 0.8953 (HF/6-31G*), 0.9051 (HF/6-311G**), 0.9427 (MP2(fu)/6-31G*), and 0.9614 (B3LYP/6-31G*). No frequencies were determined at the HF/6-311+G(3df,2p) or MP2(fu)/6-31+G* basis levels. The vibrational part of ΔH_{298K} was determined from standard thermochemical equations by scaling the individual frequencies by 0.8905 (HF/6-31G*), 0.8951 (HF/6-311G**), 1.0084 (MP2-fu/6-31G*), and 0.9989 (B3LYP/6-31G*). These scaling factors optimize the thermal contribution at 298 K that arises mainly from low-frequency modes, thus accounting, in a single correction term, for the effects of anharmonicity. No further attempts were made to refine anharmonic contributions to the conformational enthalpies. The translational and rotational contributions were assumed to be classical ($\frac{1}{2}kT$ per degree of freedom). The entropy was also determined from statistical mechanical formulas. The vibrational part of the entropy was determined from the calculated frequencies after they had been individually scaled by 0.8978 (HF/6-31G*), 0.9021 (HF/6-311G**), and 1.0228 (MP2(fu)/6-31G*), and 1.0015 (B3LYP-6-31G*). The rotational contribution was made by using the calculated moments of inertia.

3. Results and discussion

3.1. Molecular mechanics

Molecular mechanics algorithms have progressed since their origin and are now able to predict conformational equilibrium with considerable precision [30]. The MMX algorithm in PCMODEL gives ΔH° values of 1.40 and 1.67 kcal mol⁻¹ for 3- and 4-MCHO, respectively. These are lower than the recent REMPI results by 0.1–0.4 kcal mol⁻¹. It appears that

the MMX values are not good numbers since they fall outside the range of claimed accuracy of ± 0.1 – 0.2 kcal mol⁻¹. A more recently refined algorithm, MM3 [31], gives values for ΔH° of 1.57 and 1.87 kcal mol⁻¹ for 3- and 4-MCHO, respectively. These are in better agreement with the experimental results.

3.2. *Ab initio* Hartree–Fock calculations

It seems too much to ask of an *ab initio* molecular orbital calculation to yield values with accuracy of ± 0.1 kcal mol⁻¹ since feasible calculations on molecules of this size are good to only ± 2 kcal mol⁻¹. On the other hand, the cancellation of errors between the calculated energies for axial and equatorial methyl groups in cyclohexanone should be significantly better than in most chemical reactions. Since *ab initio* MO calculations depend upon cancellation of errors, it could be hoped that this would work in our favor here.

The top of Table 1 shows the results from the HF calculations. An interesting observation is that the ΔE is slightly smaller for HF/6-311G** than for HF/6-31G*. However, with the HF/6-311+G(3df,2p) basis set the ΔE increases by over 0.1 kcal mol⁻¹. The variance in ΔE s for the HF calculations is of the order of 0.2 kcal mol⁻¹, and is greater for 3-MCHO (0.21 kcal mol⁻¹) than for 4-MCHO (0.15 kcal mol⁻¹). The addition of “+” diffuse functions may be

responsible for this ΔE increase. The diffuse functions lead to a minimized structure with a slightly longer carbonyl/methyl distance. However, there is also a relaxation of the C–C bond distances on the ring, leading to a slightly longer and flatter chair for the axial conformations. While there is an attraction between the methyl and carbonyl groups in axial-3-MCHO, we do not know where on this van der Waals’ surface the minimized structure resides. Small changes in geometry in either direction may increase or decrease the conformational energy on the van der Waals’ surface. However, this relatively small energy contribution to the total energy may pale when compared with the much larger bond and torsion potentials of the ring. While we note that the ΔE increase is greater for 3-MCHO than for 4-MCHO, we cannot attribute this difference to the physical structure or non-bonded interaction potentials. Furthermore, these calculations do not include electron correlation, the effects of which are certainly important in these long-range interactions.

The MP2 calculations are also shown in Table 1. The magnitude of the ΔE has *decreased* by over 0.6 kcal mol⁻¹ compared with the HF calculations. Why does the addition of electron correlation decrease ΔE ? It is possible that higher levels of electron correlation may be needed to converge this contribution to the overall energy. It is also possible that larger basis sets are needed at the correlated levels.

Table 1

Calculations on 3- and 4-methylcyclohexanone axial and equatorial conformations. Energy units are Hartrees and energy differences are kcal mol⁻¹

Theoretical method	3-methylcyclohexanone			4-methylcyclohexanone		
	Axial	Equatorial	ΔE	Axial	Equatorial	ΔE
HF/6-31G*	-346.939066	-346.941715	1.66	-346.938169	-346.941483	2.08
HF/6-311G**	-347.023011	-347.025525	1.58	-347.022092	-347.025299	2.01
HF/6-311+G(3df,2p)	-347.054011	-347.056856	1.79	-347.053181	-347.056617	2.16
MP2 Electron Correlation						
MP2(fu)/6-31G*	-348.059762	-348.061177	0.89	-348.058476	-348.060873	1.50
MP2(fu)/6-31+G*	-348.079670	-348.081525	1.16	-348.078472	-348.081173	1.70
Density functional theory						
B3-LYP/6-31G*	-349.204068	-349.206495	1.52	-349.203215	-349.206209	1.88
B3-LYP/6-311+G(3df,2p)	-349.325947	-349.328505	1.61	-349.325203	-349.328191	1.87
B3-PW91/6-31G*	-349.078876	-349.081232	1.48	-349.078049	-349.080946	1.82
B3-PW91/6-311+G(3df,2p)	-349.192303	-349.194719	1.52	-349.191567	-349.194423	1.79

The energy difference for the basis with the diffuse functions (MP2/6-31+G*) increases the ΔE by 0.27 and 0.20 kcal mol⁻¹ over the MP2/6-31G* calculations for both 3- and 4-MCHO, respectively. Thus, the ΔE is sensitive to choice of basis set at the MP2 level of theory. While it is not feasible for us to optimize structures at higher levels of theory, we have performed several single-point energies on both the MP2/6-31G* and MP2/6-31+G* optimized geometries consistent with those necessary to compute G2 chemical energies.

3.3. Gaussian-2 theory

A series of G2(MP2)-type calculations was performed which extends the electron correlation contribution to effectively fourth order with partial contributions from higher orders in the QCISD(T) step of the calculation. G2 and G2(MP2) theory are comparable methods for obtaining accurate heats of atomization for a wide variety of simple molecules [22,24]. G2(MP2) theory effectively calculates energies at the QCISD(T)/6-311+G(3df,2p) level of theory. The results of the G2(MP2) calculations are

given in Tables 2 and 3. There is negligible improvement in the ΔE over MP2 theory. This is troubling considering the sophisticated level of this theory.

The effects of basis set requirements at the G2(MP2) level of theory was determined from the calculation of G2(MP2,SVP) energies which requests that single-point energies at the QCISD(T) level of theory be done at the 6-31G* basis set. There are only marginal differences in the calculated ΔH° values, showing that the reduced basis set approximation may be used with good precision in this case. Furthermore, the supposition that G2(MP2,SVP) theory may be good on medium-sized molecules is thus verified [23].

The effects of diffuse functions was also determined, by performing the initial optimization at MP2-fu/6-31+G* and the single point at the QCISD(T)/6-31+G* and MP2/6-311+G(3df,2p) levels of theory. From Tables 2 and 3 it is observed that the G2+(MP2,SVP) enthalpy differences are again negligibly different from the G2(MP2) values. While it appears that the diffuse functions are responsible for increasing the ΔE at the HF and MP2 levels, they do not make an appreciable difference to the energy at the G2 + (MP2,SVP) level of theory.

Table 2

G2(MP2)-type calculations on 3-methylcyclohexanone axial and equatorial conformations. Energies in units of Hartrees and energy differences in kcal mol⁻¹

Theoretical method	Axial	Equatorial	ΔE	ΔH_{0K}	ΔH_{298K}
Optimized					
HF/6-31G*//HF/6-31G*ZPVE [ν scaled 0.8929]	0.172069	0.171823	0.15		
MP2-full/6-31G*//MP2-full/6-31G*	-348.059762	-348.061177	0.89		
MP2-full/6-31+G*//MP2-full/6-31+G*	-348.079670	-348.081525	1.16		
Single point calculations on MP2(fu)/6-31G* geometry					
MP2(fc)/6-311G**	-348.246929	-348.248002	0.67		
MP2(fc)/6-311+G(3df,2p)	-348.460916	-348.462169	0.79		
QCISD(T)/6-31G*	-348.133129	-348.134825	1.06		
QCISD(T)/6-311G**	-348.368725	-348.370009	0.81		
Single point calculations on MP2(fu)/6-31+G* geometry					
MP2(fc)/6-311+G(3df,2p)	-348.460685	-348.461988	0.82		
QCISD(T)/6-31+G*	-348.153298	-348.155403	1.32		
G2(MP2) Energies ^a					
G2(MP2)	-348.525643	-348.527354		1.07	1.03
G2(MP2,SVP)	-348.480204	-348.481984		1.12	1.08
G2+(MP2,SVP)	-348.480233	-348.482032		1.13	1.09

^a See text for calculation of G2(MP2) energies.

Table 3

G2(MP2)-type calculations on 4-methylcyclohexanone axial and equatorial conformations. Energies in units of Hartrees and energy differences in kcal mol⁻¹

Theoretical method	Axial	Equatorial	ΔE	ΔH_{0K}	ΔH_{298K}
Optimized					
HF/6-31G*/HF/6-31G*					
ZPVE [ν scaled 0.8929]	0.172089	0.171820	0.17		
MP2-full/6-31G*/MP2-full/6-31G*	-348.058476	-348.060873	1.50		
MP2-full/6-31+G*/MP2-full/6-31+G*	-348.078470	-348.081173	1.70		
Single point calculations on MP2(fu)/6-31G* geometry					
MP2(fc)/6-311G**	-348.245684	-348.247597	1.20		
MP2(fc)/6-311+G(3df,2p)	-348.459788	-348.461795	1.26		
QCISD(T)/6-31G*	-348.132086	-348.134565	1.55		
QCISD(T)/6-311G**	-348.367656	-348.369641	1.25		
Single point calculations on MP2(fu)/6-31+G* geometry					
MP2(fc)/6-311+G(3df,2p)	-348.459582	-348.461610	1.27		
QCISD(T)/6-31+G*	-348.152271	-348.155082	1.76		
G2(MP2) Energies ^a					
G2(MP2)	-348.524671	-348.527019		1.47	1.43
G2(MP2,SVP)	-348.479300	-348.481657		1.48	1.44
G2+(MP2,SVP)	-348.479284	-348.481689		1.51	1.47

^a See text for calculation of G2(MP2) energies.

The lack of significant change between the three G2(MP2) theories and MP2 theory is troubling. There is little change in the calculated ΔE with respect to basis set and estimated convergence is likely to be not more than ± 0.2 kcal mol⁻¹. However, the contribution from electron correlation may not yet be sufficiently converged. G2(MP2) calculations give effective total energies at the QCISD(T)/6-311+G(3df,2p) level of theory. However, G2(MP2) formalism requires that two of the single-point energies be computed at MP2 theory. The errors from MP2 theory then become additive in G2(MP2) theory. In this case, there appears to be a serious underestimation of the conformational energy by MP2 theory and hence by G2(MP2) theory. It would be too costly at present to explore this phenomenon by performing higher level calculations.

3.4. Density functional theory

A different sort of approach to understanding electron-correlation contributions can be done through density functional theory. Becke's three-parameter exchange functional was coupled with the LYP and

PW91 correlation functionals and the 6-31G* and 6-311+G(3df,2p) basis sets. The results in Table 1 show that the total energies are nearly 1 Hartree lower than those of MP2 theory and G2(MP2) theory. The axial/equatorial ΔE values are determined to be between 1.48 and 1.61 kcal mol⁻¹ for 3-MCHO and between 1.79 and 1.88 kcal mol⁻¹ for 4-MCHO. The DFT ΔE s are smaller than the HF calculations by roughly 0.2 kcal mol⁻¹ but are 0.5 kcal mol⁻¹ larger than the MP2 or G2(MP2) calculations. The ΔE values calculated with the PW91 correlation functional are a bit smaller than those calculated with the LYP functional. The differences in ΔE between basis sets are less than ± 0.1 kcal mol⁻¹, indicating that basis set convergence is probably adequate at the 6-31G* basis set.

3.5. Zero-point vibrational energies, thermal enthalpies and entropies

The ZPVEs for HF/6-31G*, HF/6-311G**, MP2/6-31G*, and B3-LYP/6-31G* can be found in Table 4. The $\Delta ZPVE$ s are all roughly the same and can be approximated as 0.17 kcal mol⁻¹ for both 3- and 4-MCHO. Thermal enthalpies for each molecule are

Table 4

Zero-point vibrational energies, thermal enthalpies, and entropies of 3- and 4-methylcyclohexanone

Theoretical method	3-methylcyclohexanone					4-methylcyclohexanone				
	Axial	Equatorial	ΔE (kcal mol ⁻¹)	$\Delta H_{298}-H_0$ (kcal mol ⁻¹)	ΔS_{298} (e.u.)	Axial	Equatorial	ΔE (kcal mol ⁻¹)	$\Delta H_{298}-H_0$ (kcal mol ⁻¹)	ΔS_{298} (e.u.)
HF/6-31G*	0.172532	0.172285	0.16	-0.04	-0.31	0.172551	0.172282	0.17	-0.04	-0.32
HF/6-311G**	0.172421	0.172131	0.18	-0.05	-0.38	0.172442	0.172132	0.20	-0.05	-0.35
MP2(fu)/6-31G*	0.173561	0.173298	0.16	-0.05	-0.46	0.173577	0.173304	0.17	-0.06	-0.41
B3-LYP/6-31G*	0.173228	0.172940	0.18	-0.05	-0.36	0.173129	0.172870	0.16	-0.04	-0.35

also roughly equal, contributing -0.05 kcal mol⁻¹ at 298 K. We can now compare the recent REMPI experimental results with the calculated ΔH_{298K}° values. It is important to note that the enthalpy difference is a function of temperature and that direct comparison with experiment may not always be possible. The REMPI experiment gave 1.55 ± 0.12 and 2.10 ± 0.20 kcal mol⁻¹ for 3- and 4-MCHO, respectively, assuming only a small temperature dependence (within 90% confidence levels of the van't Hoff regression) over the temperature range from 303 to 473 K. The calculated thermal enthalpy $H_{473K} - H_{0K}$ is -0.06 kcal mol⁻¹ or roughly 0.01 kcal mol⁻¹ different from the 298 K values. In the case of MCHOs, the REMPI experimental results may be directly compared with the calculated ΔH_{298K}° . We find that the ΔH_{298K}° values for the HF calculations agree quite well with the experimental values (1.70 – 1.91 kcal mol⁻¹ for 3-MCHO and 2.13 – 2.28 kcal mol⁻¹ for 4-MCHO). MP2 and G2(MP2) theories predict ΔH_{298K}° to be roughly 0.5 kcal mol⁻¹ lower than the REMPI experimental result. Density functional theories agree the best with experiment (1.60 – 1.73 kcal mol⁻¹ for 3-MCHO and 1.91 – 2.00 kcal mol⁻¹ for 4-MCHO).

The conformational entropy difference, ΔS° , was determined at several levels of theory and the results are shown in Table 4. The entropy difference is small and negative but not nominally zero as has been found for substituted cyclohexanes [32]. Cornish and Baer [4] experimentally determined ΔG_{303K}° for both 3- and 4-MCHO by 2+1 REMPI spectroscopy. Their reported values are 1.62 and 2.52 kcal mol⁻¹ for 3- and 4-MCHO, respectively. We can use the calculated ΔS° to obtain ΔG° for comparison with this experimental measurement. Using ΔH° of 1.55 kcal mol⁻¹ for 3-MCHO, we find that ΔG° is 1.64 – 1.69 kcal

mol⁻¹ which is in excellent agreement with 1.62 kcal mol⁻¹ reported by Cornish and Baer. Using ΔH° of 2.10 kcal mol⁻¹ for 4-MCHO we find that ΔG° is 2.20 to 2.22 kcal mol⁻¹, which is roughly 0.3 kcal mol⁻¹ lower than the value of 2.52 kcal mol⁻¹ determined by Cornish and Baer. Considering the approximations made in their measurement, there is excellent agreement between our numbers.

4. Conclusions

The MM3 molecular mechanics and DFT values agree very well with the experiment. The ab initio calculations, however, are inconclusive. The DFT calculations give values for ΔH_{298K}° about 0.2 kcal mol⁻¹ less than the HF calculated conformational enthalpies and 0.5 kcal mol⁻¹ greater than the MP2 and G2(MP2) values. We cannot offer any explanation for the poor performance of G2(MP2) theory for modeling this enthalpy difference. There is good agreement between the ΔG_{303K}° reported by Cornish and Baer and that determined here for 3-MCHO. The agreement is less satisfactory for 4-MCHO; however, considering the assumptions made in their study, the disagreement is less conspicuous.

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