

Abstract

Hinokitoil (2-Hydroxy-6-propan-2-ylcyclohepta-2,4,6-trien-1-one) was originally isolated in Taiwanese hinoki in 1936. It is structurally related to tropolone, which lacks the isopropyl substituent. Hinokitoil is a molecule being used in the medicine, beauty, and house industries particularly in oral care and treatment products. It has not been well studied. This molecule is mostly studied in Japan for studies in cancer and medical use. Hinokitoil has not been studied in gas phase but it has been studied and it has just been studied in ¹H- NMR as of today of this molecule.

To further understand the properties of hinokitoil, quantum chemical calculations were carried out using cluster computers from the Texas Advanced Computing Center (TACC) at Austin, TX to study the geometry and conformational landscape of hinokitoil. The methods and basis set used in this study are MP2 and B3LYP density functional theory (DFT) with aug-cc-pVTZ basis set. The rotational constants conformer 1 calculated from the B3LYP/aug-cc-pVTZ optimized structure are $A = 1647.99$ MHz, $B = 618.19$ MHz, $C = 498.20$ MHz. The rotational constant conformer 2 calculated from the MP2/aug-cc-pVTZ optimized structure are $A = 1,800.08$ MHz, $B = 582.98$ MHz, $C = 486.24$ MHz. These parameters will be used to guide the search and assignment of transitions for further microwave spectroscopic experimental study of hinokitoil. We anticipated that internal rotation would occur on the two methyl groups of the isopropyl group of hinokitoil, which may further perturb its rotational spectrum. We scanned the C-C-C-H dihedral angle for 36 steps with each step at 10 degrees at the B3LYP/aug-cc-pVTZ level in order to identify the stable conformation and the energy barrier of the methyl group internal rotation. Also, by calculating the γ -thujaplicin or 2-Hydroxy-5-propan-2-ylcyclohepta-2,4,6-trien-1-one able to see the energy difference of their dipole moments of the interaction within the isopropyl with the two methyl groups.

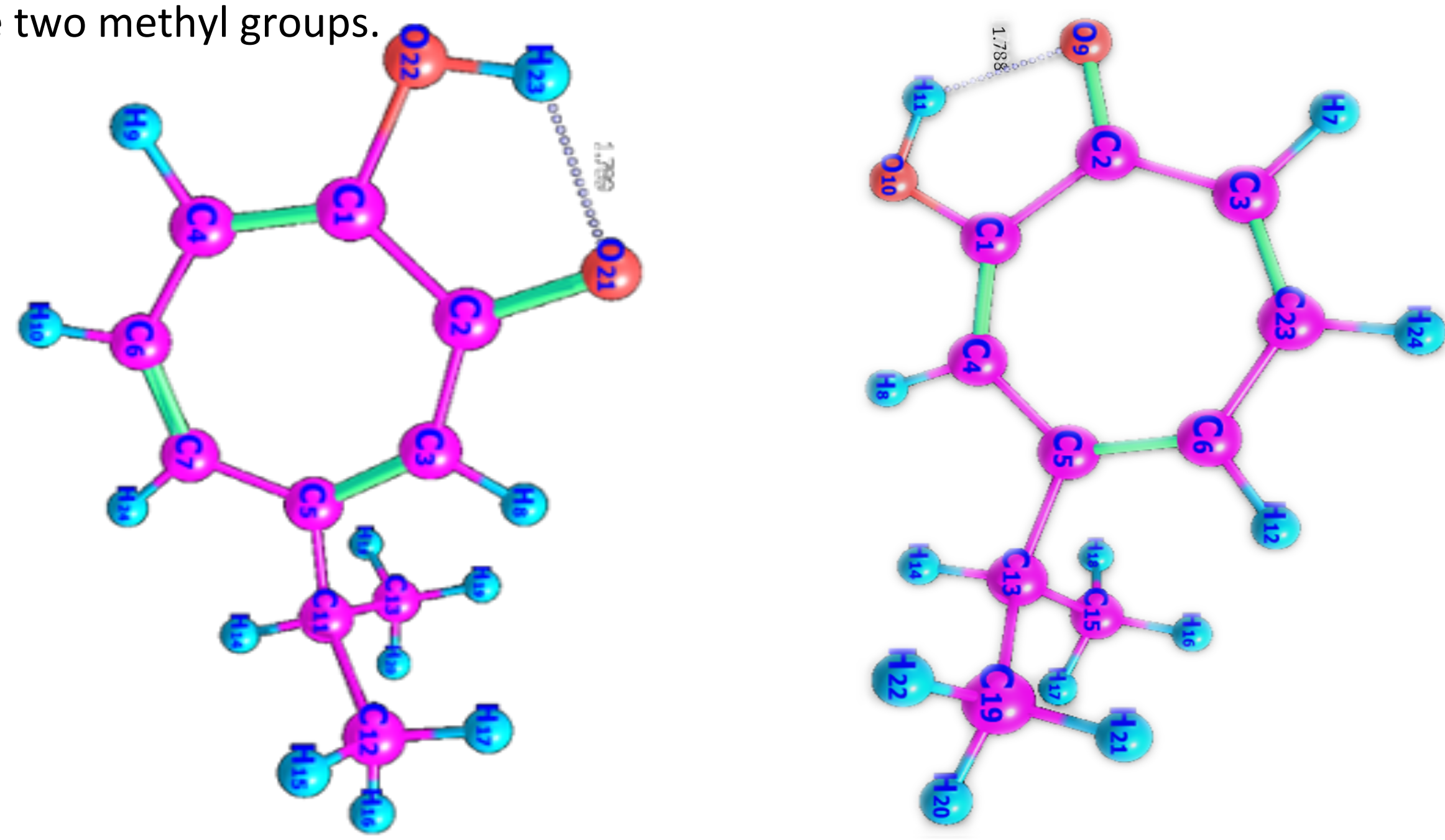


Figure 1. Calculated geometry of hinokitoil conformer 1 and conformer 2 with atomic numberings

Methodology

The Quantum calculation process used for this research was Gaussian 16 program suite. Gaussian is the computational program used for the fundamental laws of quantum mechanics by predicting the molecular energies, molecular structure and spectroscopic data thus including more advance data. Pqopher program was then used to simulate the microwave spectrum of hinokitoil to help the future experimental search. Pqopher is a program used to analyze the rotational, and vibrational spectra.

Texas Advance Computer Center (TACC) is designed and operates in the most powerful computing resources. The B3LYP functional of Density Functional Theory (DFT) was used for the calculations of the molecular structure. Two type basis sets were used. 6-31+G is the basis set of valance double zeta polarized on single or double energy on the long-range interactions and short-range interaction calculations. 6-311++G- is good to get accurate energies thus it is more expensive. In addition, the running type basis set aug-cc-pVTZ was also used. This basis places one s, one d, and one p diffuse functions on hydrogen atoms, and one d, one p, one d, and one f diffuse functions.

Results

To determine the stable conformations of hinokitoil conformer 1 along with other structural parameters and evaluate the energy barriers associated with the rotating methyl groups. Two scans along the dihedral angles $\tau_{C_7-C_5-C_{11}-C_{13}-H_{19}}$ and $\tau_{C_7-C_5-C_{11}-C_{12}-H_{16}}$ (the atom numbers are labeled of conformer 1 in figure 1) at 10° each step was run using DFT at the B3LYP/aug-cc-pVTZ level. Both scans exhibit the expected pattern for the methyl group rotation with an energy barrier of about 12.9 kJ/mol, indicating two equivalent methyl groups. The graph potential energy scan is shown in Figure 2. This energy barrier height is comparable to the reported values of several haloalkanes, as shown in Table 1. The methyl groups from the energy barrier height are comparable to the 1, 1-difluoroethane that is 13.94 (kJ/mol)

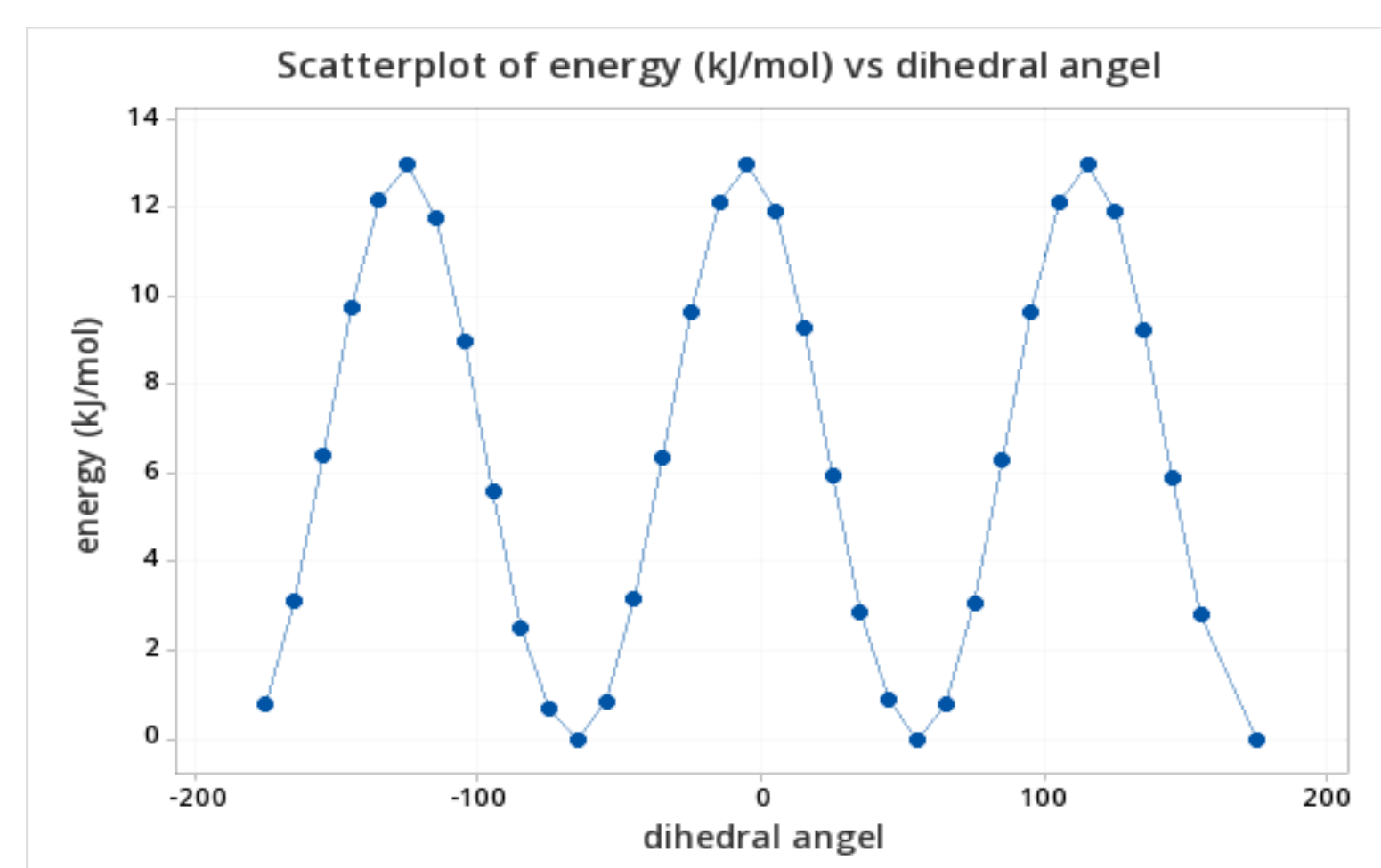
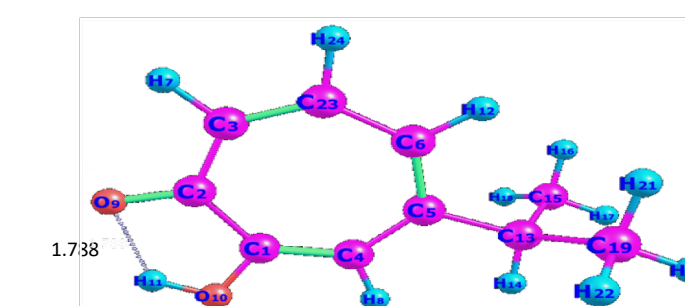
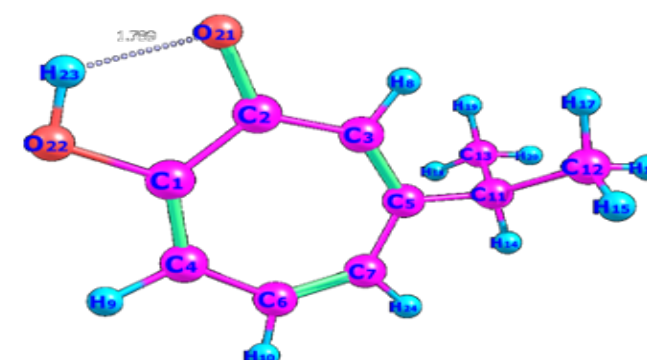


Figure 2. Scans of the dihedral angles $\tau(C_6-C_7-C_{23}-O_{24})$ and $\tau(C_6-C_7-C_{23}-O_{24})$ at 10° each step for the two methyl groups of isopropyl group.



Molecule	V_3 (kJ/mol)
1,1-difluoroethane	13.94
Ethyl Fluoride	14.07
Ethyl Chloride	15.13
Ethyl Iodide	15.20
Ethyl Bromide(79Br)	15.32
1,2-dichloroethane	17.89
1,1-dichloroethane	17.90
1-chloro-1,1-difluoroethane	18.48

Table 1. Comparison of the energy barriers of methyl rotors in some haloalkanes

	Conformer 1		Conformer 2	
	B3LYP	MP2	B3LYP	MP2
A (MHz)	1,647.99	1,664.52	1,789.35	1,800.08
B (MHz)	618.19	628.63	580.22	582.98
C (MHz)	498.20	490.37	484.22	486.24
μ_a (Debye)	2.8	3.2	4.4	4.4
μ_b (Debye)	3.1	2.9	1.0	1.1
μ_c (Debye)	0.0	0.3	0.0	0.00
μ (Debye)	4.2	4.3	4.5	4.6
Energy (kJ/mol)	0	0	0.13	-0.39

Table 2. Rotational constants, dipole moments and relative energies for hinokitoil conformers 1 and 2. The basis set used was aug-cc-pVTZ.

The structure of hinokitoil can also be considered as adding an isopropyl group to tropolone. Tropolone is known to undergo intramolecular proton tunneling in which the hydrogen atom tunnels between the two oxygen atoms. This proton tunneling can be interpreted with a double minimum potential resulting from the C_{2v} symmetry of the transition state. Adding the asymmetric isopropyl group will break the symmetry. But the substituted position of the isopropyl group is relatively far from the tunneling proton. It would be interesting to see if the proton tunneling with still exist and if so, how it is affected by the substitution. To that end, we also calculated the structure resulting from the tautomerization (conformer 2). Both conformers were further optimized at B3LYP/aug-cc-pVTZ and MP2/aug-cc-pVTZ levels. The calculated rotational constants, dipole moments, and relative energies of conformer 1 and 2 are listed in Table 2. Based on our calculations, both conformers have similar dissociation energies, suggesting the possibility of observing both experimentally. The microwave spectrum of hinokitoil will feature a-type and b-type rotational transitions. Using the calculated rotational constants and dipole moments, the microwave spectrum of hinokitoil was simulated using the Pqopher program to guide the experimental search. The simulated rotational spectra are shown in Figure 3.

Results

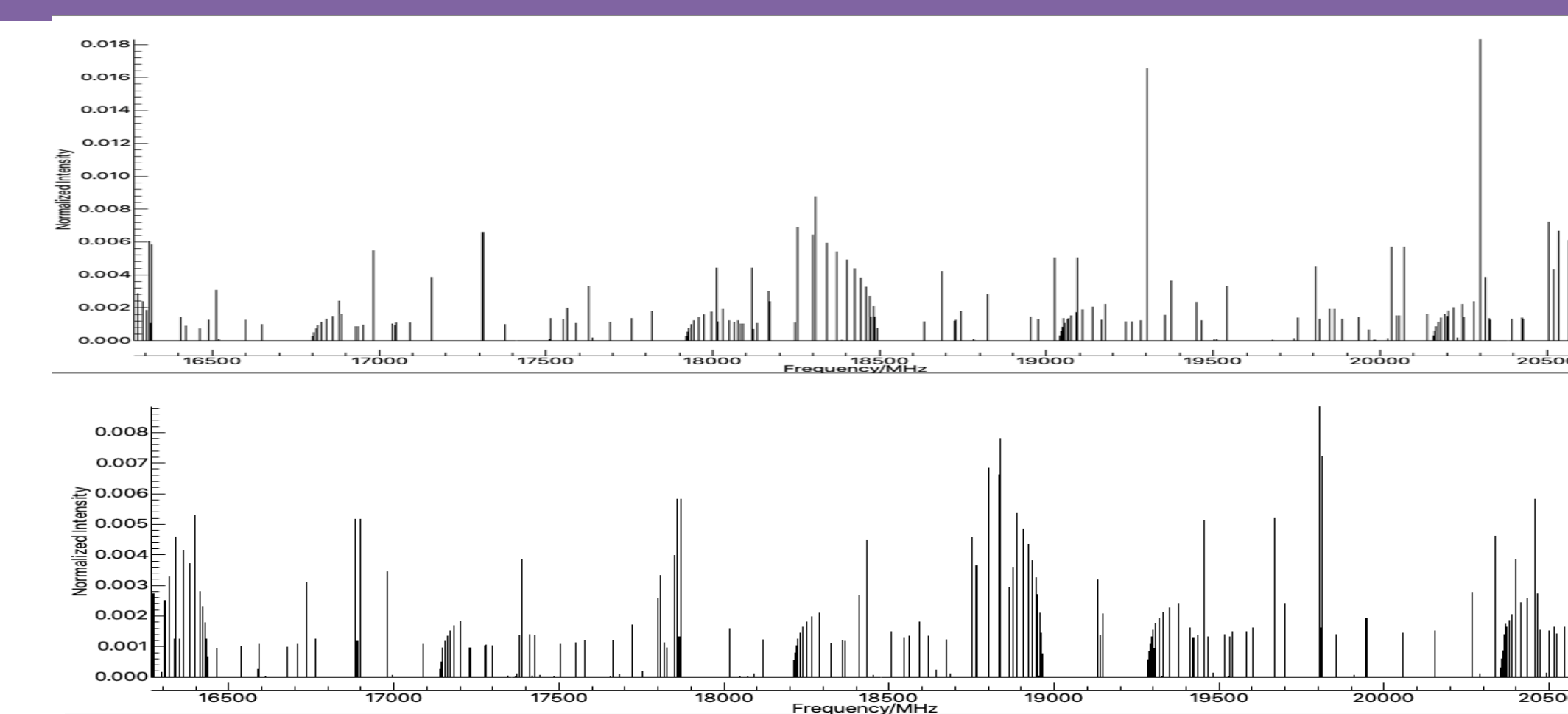


Figure 3. The simulated rotational spectrum of Hinokitoil conformers 1 and 2

We will use the UTRGV microwave spectrometer to measure the rotational spectrum of hinokitoil.



Figure 4. BrightSpec chirped-pulse microwave spectroscopy at UTRGV (18-26 GHz)

Summary

We report the quantum chemical calculations of hinokitoil. The structures of the two conformers from tautomerization were calculated. The rotational constants, dipole moments, and their relative energies were reported. The energy differences of the two conformers were calculated to be relatively small, suggesting possible experimental observation of both conformers. The energy barriers of the internal rotations of the two methyl groups of the isopropyl group were evaluated through potential energy scans. The energy barriers were calculated to be 12.9 kJ/mol, comparable to that of 1,1-difluoroethane.

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