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# Structure Determination of Strawberry Aldehyde by Broadband Microwave Spectroscopy: Conformational Stabilization by Dispersive Interactions

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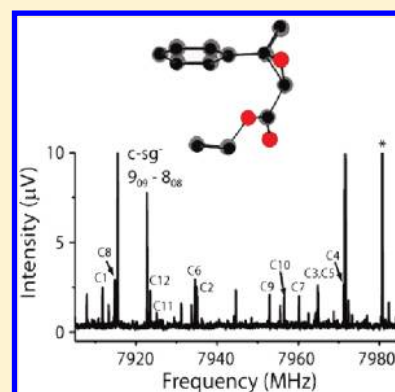
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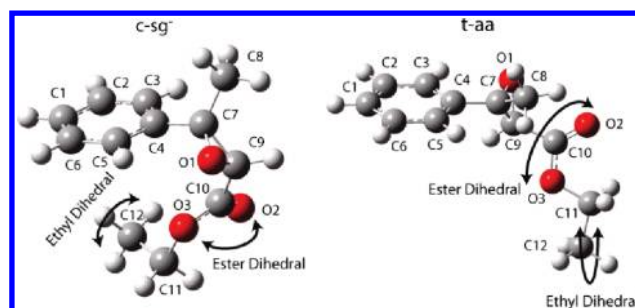
**S** Supporting Information

**ABSTRACT:** The rotational spectrum of ethyl 3-methyl-3-phenylglycidate ( $C_{12}H_{14}O_3$ , strawberry aldehyde) has been obtained with chirped-pulse Fourier transform microwave spectroscopy. The sample is a mixture of diastereomers, *cis* and *trans*, with different relative stereochemistry around the central epoxide. The spectra of five conformers of this molecule (two of *cis* and three of *trans*) have been assigned, and carbon backbone structures for the two most populated conformers (one of *cis* and one of *trans*) were determined from  $^{13}C$  isotopomers in natural abundance using the Kraitchman relations. Comparisons of experimentally determined structural data to *ab initio* calculations show that the B3LYP density functional fails to account adequately for a long-range dispersive interaction between the phenyl ring and the terminal ethyl group in *cis*-strawberry aldehyde. However, calculations performed using both MP2 and the M05-2X density functional are able to capture the effects of this interaction on the molecular geometry.

**SECTION:** Molecular Structure, Quantum Chemistry, General Theory



Gas-phase molecular spectroscopy techniques have been increasingly applied to structural studies of large molecules (defined here as having 10 or more non-hydrogen atoms), with a focus on molecules of biological interest.<sup>1–5</sup> Techniques that are sensitive to molecular shape are desirable for studying large molecules, which often have complex conformational landscapes. Molecular rotational spectroscopy in the microwave frequency region allows for precise determination of molecular moments of inertia and can be applied to any gas-phase molecule with a permanent dipole moment. Molecular structures can be determined by analyzing the rotational spectra of isotopically substituted species. From the changes in the molecular moments of inertia with isotopic substitution, atom positions can be experimentally determined by Kraitchman's equations, or a least-squares fit of internal coordinates can be performed.<sup>6</sup> Comparisons of experimentally and computationally derived molecular structures provide fundamental tests of the quality of various *ab initio* methods. Another advantage of high-resolution molecular microwave spectroscopy in pulsed jets is the ability to analyze samples that contain a rich mixture of molecular species, including conformers. As a result, rotational spectroscopy is uniquely suited to precision studies of molecular conformational structure where explicit atomic positions are determined. For example, molecular conformational preferences can be altered by crystal packing forces limiting the utility of X-ray diffraction for studying the conformational flexibility of large molecules. Conformational geometry in solution cannot be detected on the NMR time scale, and high-resolution NMR spectra are generally motionally



**Figure 1.** Two dominant conformers of strawberry aldehyde, *c-sg*<sup>−</sup> and *t-aa*. The indicated ester and ethyl dihedral angles are the two primary angles used to differentiate the 12 lowest energy conformers. In both structures, the ester dihedral involves O1, C9, C10, and O3, and the ethyl dihedral involves C10, O3, C11, and C12.

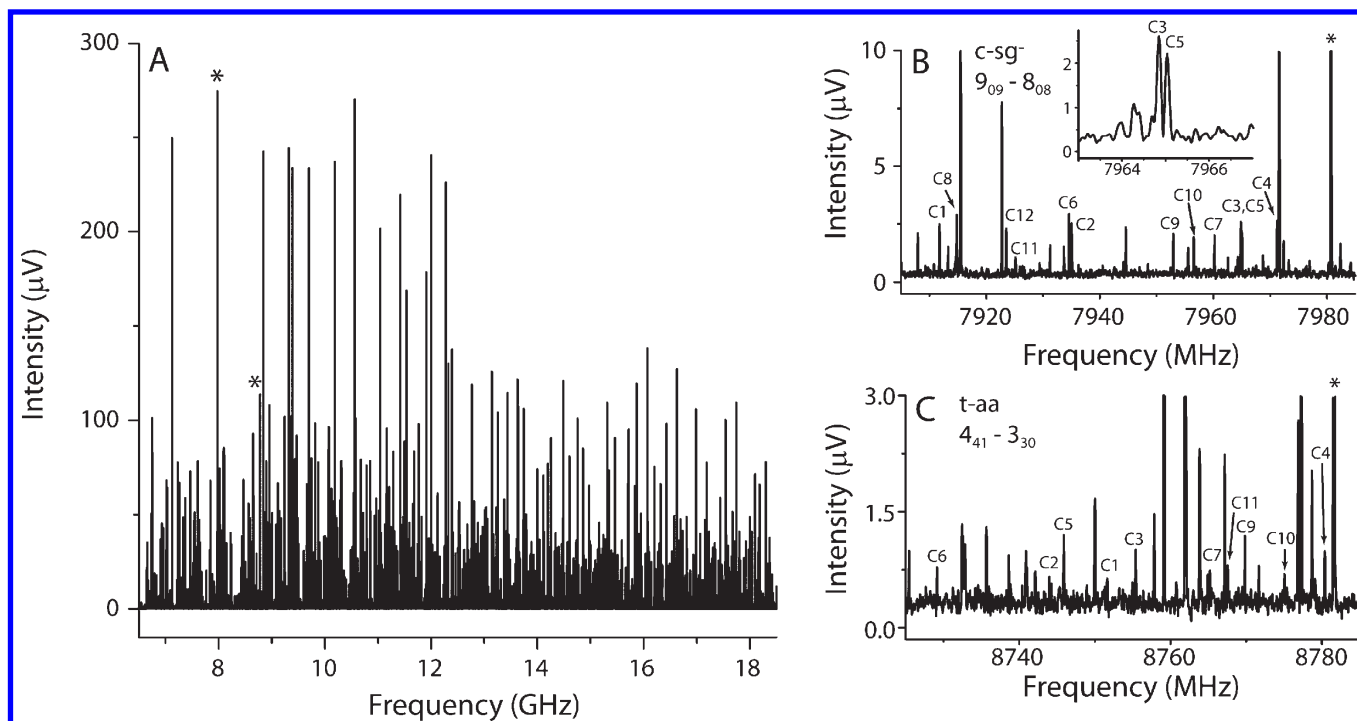
averaged. Gas-phase electron diffraction has rarely been applied to large molecules and is expected to face difficulty for the complex sample mixtures characteristic of large, flexible molecules.

Chirped-pulse Fourier transform microwave (CP-FTMW) spectroscopy in a supersonic expansion is particularly well-suited to problems of this type. In addition to being able to measure simultaneously the spectra of multiple species, this technique has

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**Figure 2.** (A) Rotational spectrum of strawberry aldehyde from 6.5 to 18.5 GHz. The noise level of this spectrum is  $\sim 0.3 \mu\text{V}$ . The two marked peaks are the  $c\text{-sg}^- 9_{09}-8_{08}$  and the  $t\text{-aa } 4_{41}-3_{30}$  transitions at 7980.75 and 8781.62 MHz, respectively. (B,C) Satellite lines of the  $^{13}\text{C}$  isotopomers of these transitions (asterisks indicate the normal species transitions that are off scale). Panel B also includes an inset of the  $^{13}\text{C}$ -3 and  $^{13}\text{C}$ -5  $c\text{-sg}^-$  transitions, showing that they are resolved in the spectrum. In panel C, the  $4_{41}-3_{30}$  transitions from the  $^{13}\text{C}$ -8 and  $^{13}\text{C}$ -12 isotopomers of the  $t\text{-aa}$  conformer are not shown in the interest of clarity because they are both located at  $\sim 60$  MHz lower frequency than those of the other isotopomers.

high sensitivity, excellent frequency accuracy, and relative intensity accuracy spanning more than four orders-of-magnitude of transition intensity.<sup>7</sup> With these qualities, it is often possible to observe singly substituted  $^{13}\text{C}$ ,  $^{15}\text{N}$ , and  $^{18}\text{O}$  isotopomers in natural abundance. Furthermore, the use of digital filtering to improve the baseline resolution of CP-FTMW spectra is crucial for structure determination from nonenriched samples, as otherwise many of the transitions from isotopomers in low natural abundance would be partially or completely obscured by transitions from the normal species isotopomer.<sup>7</sup> As such, CP-FTMW spectroscopy is capable of obtaining full heavy-atom substitution structures of sizable molecules without the need to synthesize isotopically substituted samples.

The titular molecule, ethyl 3-methyl-3-phenylglycidate ( $\text{C}_{12}\text{H}_{14}\text{O}_3$ , commonly referred to as strawberry aldehyde, Figure 1), contains 15 heavy atoms and possesses two chiral centers, and so conformational isomers of this molecule are either homochiral (*cis*) or heterochiral (*trans*). In the homochiral (*cis*) diastereomer of strawberry aldehyde, the terminal alkyl chain is able to interact with the phenyl ring via a through-space dispersion interaction, but in the heterochiral (*trans*) diastereomer, the molecule is insufficiently flexible for this interaction to affect substantially the molecular energy. Within each conformational family, there are 12 isomers, for a total of 24 possible conformers. On the basis of their *ab initio* calculated relative energies, only 12 of these 24 are expected to be populated in the supersonic expansion: six of *cis* and six of *trans*. These conformers are labeled  $\alpha\text{-}yz$ , where  $\alpha$  designates the stereochemistry about the epoxide (*c* or *t*),  $y$  designates the orientation of the ester oxygen with the epoxide oxygen (*s* for *syn*, *a* for *anti*), and  $z$  indicates the orientation of the terminal ethyl group (*a* for *anti*,  $g^+$  or  $g^-$  for *gauche*;  $g^+$  conformers have ethyl dihedral angles of  $\sim 80^\circ$  and  $g^-$  conformers have ethyl dihedral angles of  $\sim -80^\circ$ ).

Strawberry aldehyde was chosen for this benchmark measurement of CP-FTMW spectroscopy because it is a large molecule with a rich conformational landscape that is inexpensive, readily available, and easy to handle. Additionally, structural studies of strawberry aldehyde may be of interest to understanding olfactory response to fragrances and flavoring agents and has been the subject of a previous study relating olfactory potency to overall stereochemistry and structural modifications.<sup>8</sup>

For this molecule, a rotational spectrum from 6.5 to 18.5 GHz was obtained, with a 1000:1 signal-to-noise ratio on the most intense transition (Figure 2). This spectrum contains 8908 transitions with a signal-to-noise ratio greater than 3:1. A total of 1925 of these transitions have been assigned to the rotational spectra of 5 normal species conformers, 24  $^{13}\text{C}$  isotopomers in natural abundance (each of the 12 singly substituted isotopomers of the 2 dominant conformers), and thermal decomposition products. Rotational Hamiltonian parameters for the five assigned conformers are reported in Table 1, whereas full lists of the assigned transitions may be found in the Supporting Information.

For the two conformers for which the singly substituted  $^{13}\text{C}$  isotopologues were assigned ( $c\text{-sg}^-$  and  $t\text{-aa}$ ), Kraitchman's equations, implemented in the KRA program,<sup>9</sup> were applied to determine the coordinates of each carbon atom with respect to the molecular center-of-mass in the principal axis system. In a few cases, the substituted carbons were located near a principal axis of the molecule; for these substitutions, the coordinate was constrained to zero to avoid unphysical (imaginary) atomic coordinates. The three singly substituted  $^{18}\text{O}$  isotopomers were not assignable at the sensitivity of this spectrum. Because this analysis only determines the magnitudes of the atom positions, the signs of the coordinates must be inferred using assumptions

**Table 1. Rotational S-Reduction Hamiltonian Parameters for the Five Assigned Conformers of Strawberry Aldehyde**

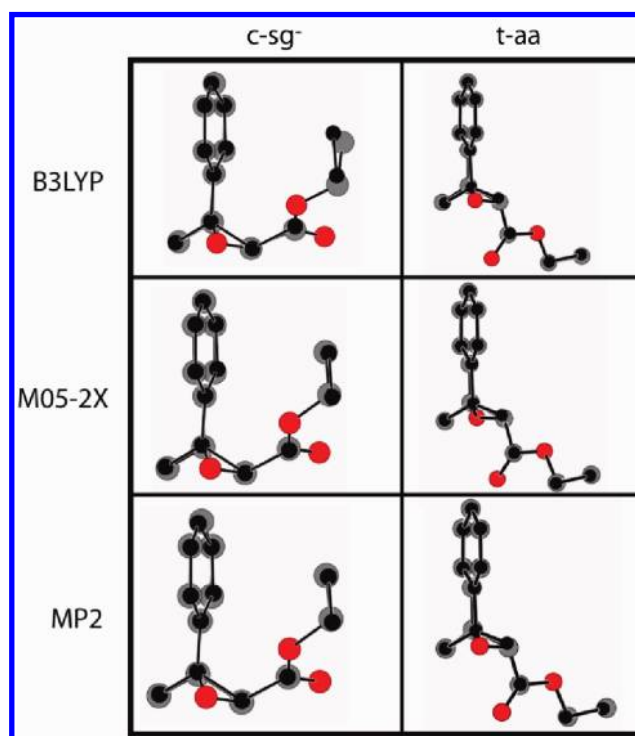
	c-sg <sup>−</sup>	c-ag <sup>+</sup>	t-aa	t-ag <sup>−</sup>	t-ag <sup>+</sup>
A (MHz)	728.09520(17)	723.14170(25)	1214.7279(4)	1460.5230(11)	1330.9492(7)
B (MHz)	628.69170(12)	581.41140(18)	287.76660(8)	275.045860(20)	293.48150(12)
C (MHz)	429.84840(20)	421.96270(28)	269.46240(7)	269.61760(19)	281.86590(13)
D <sub>J</sub> (kHz)	0.0808(7)	0.3430(9)	0.01740(7)	0.01080(28)	0.01720(13)
D <sub>JK</sub> (kHz)	−0.1070(18)	−0.863(4)	−0.0770(10)	−0.050(3)	−0.0820(17)
D <sub>K</sub> (kHz)	0.0900(24)	0.656(5)	0.820(10)	1.350(23)	0.950(20)
d <sub>1</sub> (Hz)	−25.6(7)	−119.3(8)	−3.410(29)	−0.91(5)	−3.14(4)
d <sub>2</sub> (Hz)	2.3(4)	8.6(4)	0.800(11)	0.700(19)	−0.750(18)
no. lines	280	229	256	138	193
max J	16	16	30	28	28
max K <sub>a</sub>	12	10	6	6	5
rms (kHz)	12.9	13.7	11.2	14.5	15.6

about atomic connectivity. In Figure 3, the substitution structures of these conformers are compared to ab initio calculated structures using density functional theory (using both the B3LYP and M05-2X functionals) and MP2 methods.

Limitations of the Kraitchman analysis have been previously discussed for both small and very large coordinates.<sup>10</sup> Therefore, we also performed least-squares fits of most heavy-atom internal coordinates using the STRFIT program,<sup>9</sup> fixing the remaining internal coordinates to ab initio values at an M05-2X/6-311++G(d,p) level of theory. The Kraitchman analysis and the least-squares fitting routine produced similar structures: a root-mean-square deviation of  $\sim 0.1$  Å is observed in the coordinates of the carbon atoms in the principal axis system. Given the similarity of the structures, only the substitution structure is shown in Figure 3. A similar overlay based on the output of the STRFIT program, a description of the STRFIT fitting process, and tables of the fit internal coordinates are presented in the Supporting Information.

In the B3LYP calculated structure of the c-sg<sup>−</sup> conformer, the ethyl chain at the end of the molecule (C11–C12) is  $\sim 0.5$  Å farther from the phenyl ring than in the experimental structure. The M05-2X and MP2 calculated structures agree with the experimental structure (rms atom position deviations between theory and experiment of 0.08 and 0.15 Å for M05-2X and MP2, respectively; the rms deviation for B3LYP is 0.38 Å). Meanwhile, for the t-aa conformer, where a long-range interaction between the phenyl ring and the terminal alkyl chain is not present, all three calculated structures agree with the experimentally determined structure (rms atom position deviations between theory and experiment of 0.15, 0.06, and 0.11 Å for B3LYP, M05-2X, and MP2, respectively).

The primary difference between the B3LYP and M05-2X functionals is that the latter was specifically designed to account for long-range dispersive interactions.<sup>11–13</sup> Because of the relatively close approach of the terminal alkyl chain to the phenyl ring in the cis conformers, the interaction between these groups plays an important role in the relative conformer energies and interconformer barrier heights. In the trans conformers, on the other hand, these two groups are well-separated and so interactions between them do not significantly affect the potential energy surface. In support of these observations, we note that the B3LYP functional has previously been shown to describe poorly systems with these kinds of interactions,<sup>14–16</sup> and recent reports suggest that M05-2X performs markedly better than B3LYP on systems where dispersion is important.<sup>17–19</sup>



**Figure 3.** Renderings of the carbon substitution structures (black circles) of the c-sg<sup>−</sup> and t-aa conformers of strawberry aldehyde compared with calculated atom positions (carbon in gray, oxygen in red) at the B3LYP/6-311++G(d,p) (top), M05-2X/6-311++G(d,p) (middle), and MP2/6-31+G(d) (bottom) levels of theory. The calculated atom positions have diameter 0.7 Å, whereas the substitution coordinates have diameter 0.45 Å.

The sensitivity of the spectrum was not high enough to observe the <sup>13</sup>C isotopomers of the other three assigned conformers. Structural assignments of these conformers were therefore derived from a correlation of observed rotational constants and relative *a*, *b*, and *c*-type transition intensities to ab initio values of these parameters for local minima. Tables 2 and 3 show these comparisons. Qualitative agreement of relative transition intensities, coupled to close agreement between calculated and experimental rotational constants (with the notable exception of B3LYP values in the cis conformations), confirm the assignments of the remaining conformers.

Two-dimensional relaxed potential energy surfaces, presented in Figure 4, offer insight into the effect of the dispersive interaction

Table 2. Calculated and Experimental Rotational Constants for the Assigned *cis* Conformers

conformer	method <sup>a</sup>	A (MHz)	B (MHz)	C (MHz)	Normalized transition intensity <sup>b</sup>		
					<i>a</i> -type	<i>b</i> -type	<i>c</i> -type
c-sg <sup>−</sup>	experiment	728.09520(17)	628.69170(12)	429.84840(20)	0.85	0.15	0
	B3LYP	726.6	576.7	403.6	0.65	0.35	0
	M05-2X	735.8	637.2	436.0	0.91	0.09	0
	MP2	727.0	634.7	434.4	0.93	0.06	0.01
c-ag <sup>+</sup>	experiment	723.14170(25)	581.41140(18)	421.96270(28)	0	0.08	0.92
	B3LYP	772.8	476.8	374.8	0.05	0.08	0.87
	M05-2X	720.6	612.7	436.5	0	0.13	0.87
	MP2	712.2	604.5	431.2	0	0.12	0.88

<sup>a</sup> B3LYP and M05-2X calculations were performed with a 6-311++G(d,p) basis set, whereas the MP2 calculations were performed with a 6-31+G(d) basis set. <sup>b</sup> Calculated transition intensities are determined assuming quadratic scaling of intensity with dipole moment.

Table 3. Calculated and Experimental Rotational Constants for the Assigned *trans* Conformers

conformer	method <sup>a</sup>	A (MHz)	B (MHz)	C (MHz)	normalized transition intensity <sup>b</sup>		
					<i>a</i> -type	<i>b</i> -type	<i>c</i> -type
t-aa	experiment	1214.7279(4)	287.76660(8)	269.46240(7)	0	0.86	0.14
	B3LYP	1214.2	285.3	264.2	0	0.92	0.08
	M05-2X	1225.4	288.8	270.9	0	0.88	0.12
	MP2	1215.5	291.8	265.5	0	0.96	0.04
t-ag <sup>−</sup>	experiment	1460.5230(11)	275.04860(20)	269.61760(19)	0	0.71	0.29
	B3LYP	1442.8	272.6	265.1	0	0.84	0.16
	M05-2X	1484.7	276.3	270.9	0	0.45	0.55
	MP2	1459.8	277.8	266.7	0.01	0.94	0.05
t-ag <sup>+</sup>	Experiment	1330.9492(7)	293.48150(12)	281.86590(13)	0	0.94	0.06
	B3LYP	1317.5	289.4	274.6	0	0.99	0.01
	M05-2X	1344.0	293.7	284.2	0	0.93	0.07
	MP2	1337.1	298.2	277.7	0.01	0.98	0.01

<sup>a</sup> B3LYP and M05-2X calculations were performed with a 6-311++G(d,p) basis set, while the MP2 calculations were performed with a 6-31+G(d) basis set. <sup>b</sup> Calculated transition intensities are determined assuming quadratic scaling of intensity with dipole moment.

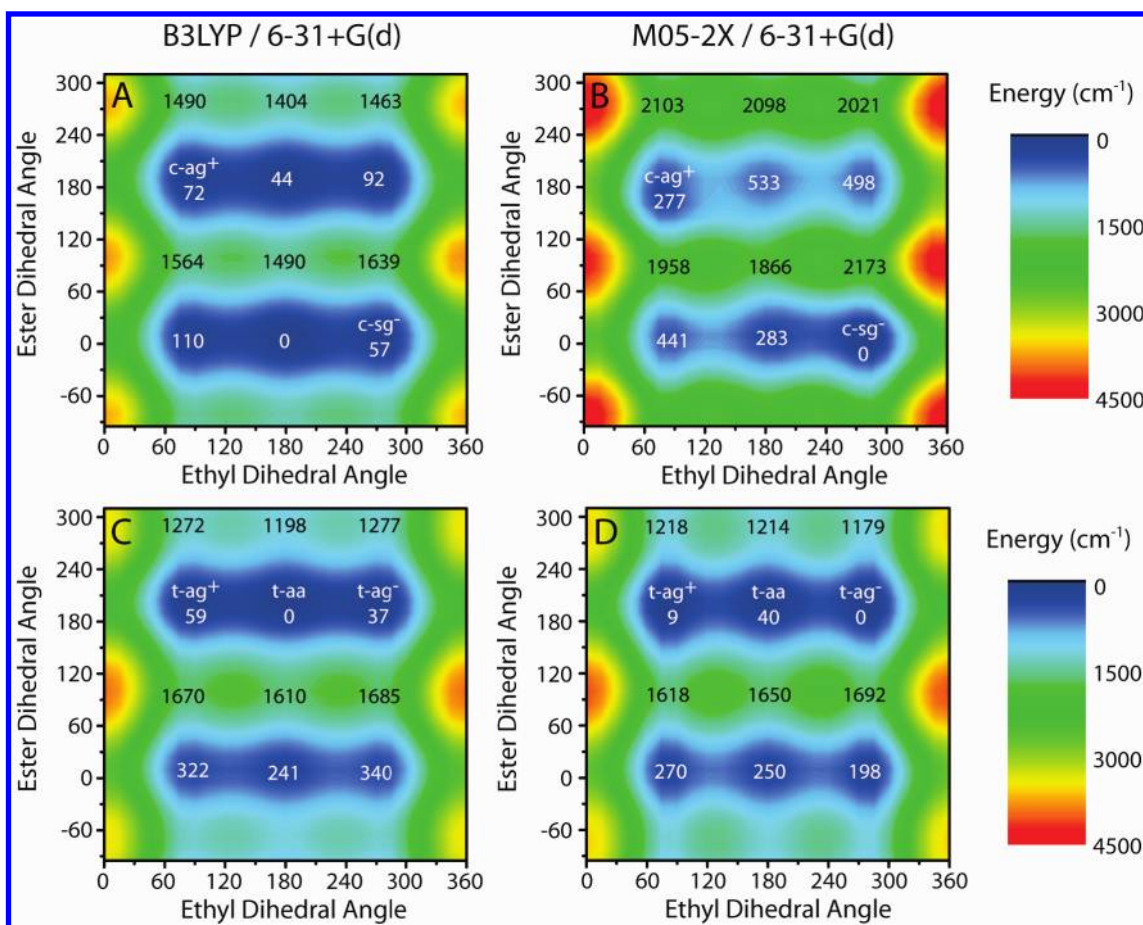
on the structure and interconformer dynamics of strawberry aldehyde. In these surfaces, calculated using both the B3LYP and M05-2X functionals, the ester and ethyl dihedral angles were fixed to points on a grid (15° spacing), whereas the rest of the structure was allowed to relax to its lowest-energy configuration. To reduce computation time, these calculations were performed with a 6-31+G(d) basis set and so should be viewed as qualitative.

On the basis of their calculated relative energies, all 12 conformers are expected to have substantial populations in thermal equilibrium at 120 °C, the sample temperature before the supersonic expansion, but cooling in the pulsed jet causes some of the conformers to relax to lower-energy minima, depending on the barriers to relaxation.<sup>20</sup> The 2D potential energy surfaces reveal clear differences in the relative energies and barrier heights for conformers depending on the calculation method. On the B3LYP/6-31+G(d) surface, the two observed *cis* conformers have intermediate relative energies, and so other conformers should have been present at higher abundances than the two observed if this surface were correct. The M05-2X surface calculates that the two observed *cis* conformers, in which the methyl group is oriented facing the phenyl ring, are stabilized relative to the others with the same ester dihedral angle. It has a higher barrier to changing the ester dihedral angle than the B3LYP surface (by roughly 500 cm<sup>−1</sup>), which makes it more

likely to trap molecules in a particular ester configuration, with conformational cooling only occurring in the relatively low barrier ethyl dihedral coordinate. Our observation of only two *cis* conformers is in better agreement with the M05-2X surface than with the B3LYP surface. For the *trans* conformers, the M05-2X and B3LYP surfaces are qualitatively similar.

A chirped-pulse Fourier transform microwave spectrometer was used to obtain the rotational spectrum of strawberry aldehyde (C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>) in a supersonic expansion. Analysis of the spectrum resulted in the assignment of five conformers of strawberry aldehyde, two of *cis*, and three of *trans*. Strawberry aldehyde is sufficiently flexible that intramolecular interactions between functional groups on the molecule are present. In this situation, the B3LYP density functional adequately described the conformers of *trans*-strawberry aldehyde but did not properly handle the *cis* conformers, whose energies and interconversion barriers are strongly influenced by a long-range interaction between an alkyl group and a phenyl ring. This is demonstrated by an experimental heavy-atom structure using assignments of each singly substituted <sup>13</sup>C isotopomer of the most populated conformers to derive atom positions. The M05-2X density functional as well as MP2 methods appropriately treated the intramolecular interaction in the conformers of *cis*, and excellent agreement between calculated and experimental structures was





**Figure 4.** Relaxed potential energy surfaces in two dihedral angles for the (A,B) cis and (C,D) trans families of strawberry aldehyde conformers, calculated at the (A,C) B3LYP/6-31G+(d) and the (B,D) M05-2X/6-31+G(d) levels of theory. Potential wells corresponding to observed conformers are labeled with their conformer designations. The ester and ethyl dihedrals are as shown in Figure 1. Numbers on the plot indicate the energies (in inverse centimeters) of different conformers and of interconformer transition states along the ester dihedral coordinate, relative to the most stable conformer on each surface.

observed. This molecule demonstrates some of the difficulties that will become more commonplace as high-resolution spectroscopies are used to study ever-larger systems. As molecules increase in size, they have a larger number of populated conformers, and some fraction of these conformers will almost certainly be stabilized by intramolecular interactions that are poorly treated by the theoretical methods currently in use by experimentalists. The CP-FTMW technique, which provides sensitivity sufficient to obtain heavy atom molecular structures from samples in natural abundance with low sample consumption, will be essential in allowing experimental results to inform the development of new theoretical methods.

## EXPERIMENTAL METHODS

A sample of ethyl 3-methyl-3-phenylglycidate (strawberry aldehyde,  $C_{12}H_{14}O_3$ ) was obtained from Sigma-Aldrich ( $\geq 98\%$  purity, equal mixture of isomers) and used without further purification.

The rotational spectrum of strawberry aldehyde was measured from 6.5 to 18.5 GHz with a CP-FTMW spectrometer. A detailed discussion of the operating principles of this spectrometer may be found in ref 7. For the spectra shown here, ten FID signals were collected per valve pulse and two heated reservoir nozzles were used, allowing a given signal-to-noise ratio to be achieved

with a factor of 40 less sample consumption that would be required with a single nozzle, single FID per pulse approach. The conditions for the supersonic expansion were a reservoir temperature of 120 °C (monitored via a calibrated thermistor) and a backing pressure of 1 atm with a mixed He/Ne carrier gas (30:70 He/Ne ratio, “first run neon”). The spectrum is the Fourier transform of 929 000 FIDs, each with a 20  $\mu$ s duration; after the application of a Kaiser-Bessel window function, the transitions have a fwhm of 120 kHz. It was acquired in 42.6 h of continuous averaging and consumed  $\sim 400$  mg of sample; the spectrometer repetition rate is currently limited by the data throughput of the oscilloscope.

After acquisition, the frequency-domain spectrum was initially plotted and analyzed with JB95, a graphical user interface for working with broadband molecular spectra.<sup>21</sup> Final fitting was performed with the SPFIT/SPCAT program suite;<sup>22</sup> transition frequencies for the final fits were determined by interpolating the spectrum to a frequency resolution of 2 kHz with a cubic spline. All rotational spectra were fit using a Watson S-reduction Hamiltonian.

All ab initio calculations were performed using Gaussian 03 revision E.01<sup>23</sup> on a desktop computer. Calculations were performed with several basis sets using both density functional (B3LYP and M05-2X) and wave-function-based (MP2) methods; calculation details are provided in the text where appropriate.

## ■ ASSOCIATED CONTENT

**S Supporting Information.** Rotational constants of  $^{13}\text{C}$  isotopologues, ab initio relative energies of the different conformers, results from both Kraitichman analysis and least-squares fitting methods, and line lists of assigned transitions. This material is available free of charge via the Internet at <http://pubs.acs.org/>.

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## ■ REFERENCES

- (1) Brenner, V.; Piuze, F.; Dimicoli, I.; Tardivel, B.; Mons, M. Spectroscopic Evidence for the Formation of Helical Structures in Gas-Phase Short Peptide Chains. *J. Phys. Chem. A* **2007**, *111*, 7347–7354.
- (2) Cocinero, E. J.; Stanca-Kaposta, E. C.; Gamblin, D. P.; Davis, B. G.; Simons, J. P. Peptide Secondary Structures in the Gas Phase: Consensus Motif of N-Linked Glycoproteins. *J. Am. Chem. Soc.* **2009**, *131*, 1282–1287.
- (3) Stearns, J. A.; Seaiby, C.; Boyarkin, O. V.; Rizzo, T. R. Spectroscopy and Conformational Preferences of Gas-Phase Helices. *Phys. Chem. Chem. Phys.* **2009**, *11*, 125–132.
- (4) Alvarez-Valtierra, L.; Yi, J. T.; Pratt, D. W. Lifetime Broadening in the Rotationally Resolved Electronic Spectra of Dibenzothiophene, 2,5-Diphenylfuran, and 2,5-Diphenyl-1,3,4-oxadiazole in the Gas Phase. Intersystem Crossing Dynamics in the Statistical Limit. *J. Phys. Chem. A* **2009**, *113*, 2261–2267.
- (5) Alonso, J. L.; Sanz, M. E.; López, J. C.; Cortijo, V. Conformational Behavior of Norphedrine, Ephedrine, and Pseudoephedrine. *J. Am. Chem. Soc.* **2009**, *131*, 4320–4326.
- (6) Gordy, W.; Cook, R. L. *Microwave Molecular Spectra*; John Wiley and Sons: New York, 1984.
- (7) Brown, G. G.; Dian, B. C.; Douglass, K. O.; Geyer, S. M.; Shipman, S. T.; Pate, B. H. A Broadband Fourier Transform Microwave Spectrometer Based on Chirped Pulse Excitation. *Rev. Sci. Instrum.* **2008**, *79*, 053103.
- (8) Tekin, A. R.; Karaman, H. Odor Thresholds of Some Derivatives of Strawberry Aldehyde. *Chem. Senses* **1992**, *17*, 795–799.
- (9) Kisiel, Z. *PROSPE, Programs for ROTational SPECTroscopy*. <http://info.ifpan.edu.pl/~kisiel/prospe.htm> (accessed April 27, 2009).
- (10) Demaison, J.; Rudolph, H. D. When Is the Substitution Structure Not Reliable? *J. Mol. Spectrosc.* **2002**, *215*, 78–84.
- (11) Zhao, Y.; Truhlar, D. G. A Density Functional That Accounts for Medium-Range Correlation Energies in Organic Chemistry. *Org. Lett.* **2006**, *8*, 5753–5755.
- (12) Zhao, Y.; Schultz, N. E.; Truhlar, D. G. Design of Density Functionals by Combining the Method of Constraint Satisfaction with Parameterization for Thermochemistry. *J. Chem. Theory Comput.* **2006**, *2*, 364–382.
- (13) Zhao, Y.; Truhlar, D. G. Assessment of Model Chemistries for Noncovalent Interactions. *J. Chem. Theory Comput.* **2006**, *2*, 1009–1018.
- (14) Restrepo, A. A.; Bohn, R. K. Alkyl Chains with CN and CCH Substituents Prefer Gauche Conformations. *J. Mol. Struct.* **2007**, *833*, 189–186.
- (15) Wodrich, M. D.; Corminboeuf, C.; Schleyer, P. R. Systematic Errors in Computed Alkane Energies Using B3LYP and Other Popular DFT Functionals. *Org. Lett.* **2006**, *8*, 3631–3634.
- (16) Holroyd, L. F.; van Mourik, T. Insufficient Description of Dispersion in B3LYP and Large Basis Set Superposition Errors in MP2 Calculations Can Hide Peptide Conformers. *Chem. Phys. Lett.* **2007**, *442*, 42–46.
- (17) James, W. H., III; Baquero, E. E.; Shubert, V. A.; Choi, S. H.; Gellman, S. H.; Zwier, T. S. Single-Conformation and Diastereomer Specific Ultraviolet and Infrared Spectroscopy of Model Synthetic Foldamers:  $\alpha/\beta$ -Peptides. *J. Am. Chem. Soc.* **2009**, *131*, 6574–6590.
- (18) Barone, V.; Biczysko, M.; Pavone, M. The Role of Dispersion Correction to DFT for Modelling Weakly Bound Molecular Complexes in the Ground and Excited Electronic States. *Chem. Phys.* **2008**, *346*, 247–256.
- (19) Pietra, F. Why Colchicine Does Not Show Mutarotation. With M05–2X Density Functional in the Realm of Tricky Natural Products. *J. Phys. Org. Chem.* **2007**, *20*, 1102–1107.
- (20) Ruoff, R. S.; Klotz, T. D.; Emilsson, T.; Gutowsky, H. S. Relaxation of Conformers and Isomers in Seeded Supersonic Jets of Inert Gases. *J. Chem. Phys.* **1990**, *93*, 3142.
- (21) Plusquellic, D. F.; Suenram, R. D.; Maté, B.; Jensen, J. O.; Samuels, A. C. The Conformational Structures and Dipole Moments of Ethyl Sulfide in the Gas Phase. *J. Chem. Phys.* **2001**, *115*, 3057. The JB95 spectral fitting program can be downloaded from the following web address: <http://www.nist.gov/pml/div685/grp08/jb95.cfm>.
- (22) Pickett, H. M. The Fitting and Prediction of Vibration-Rotation Spectra with Spin Interactions. *J. Mol. Spectrosc.* **1991**, *148*, 371–377. The CALPGM suite of programs can be downloaded from the following web address: <http://spec.jpl.nasa.gov>.
- (23) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision E.01; Gaussian, Inc.: Wallingford, CT, 2004.