

Regular article

Conformations of ethyl esters versus thioesters*

Robert K. Bohn¹, Kenneth B. Wiberg²

¹ Department of Chemistry, University of Connecticut, Storrs, CT 06269-3060, USA

² Department of Chemistry, Yale University, New Haven, CT 06520-8107, USA

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Abstract. Ethyl formate and other substituted ethyl formates exist in stable *anti* and *gauche* conformations about the C–O–C–C dihedral angle, according to microwave spectroscopic studies. Similar studies of ethyl thioformates characterize stable *gauche* conformations about the corresponding C–S–C–C dihedral angle in every compound studied, but the *anti* conformation is found only in ethyl fluorothioformate and chlorothioformate. Ab initio calculations that include electron correlation via MP2 or the B3LYP density functional model have been carried out for ethyl and methyl formate and thioformate and their fluoroformate analogs. These calculations reveal that the potential energy minima at *gauche* and *anti* C–O–C–C configurations are well developed in every case. However, although the *gauche* minimum for the C–S–C–C torsional angle is clearly defined, the potential function near the *anti* C–S–C–C configuration corresponds to a potential energy plateau rather than a minimum. In the case of ethyl fluorothioformate, a modest well is predicted at the *anti* C–S–C–C configuration, in agreement with experimental results.

The pattern of stable conformations in thioesters is more complex, however. Among the ethyl thioester analogs, only ethyl fluorothioformate and chlorothioformate display both *syn-gauche* and *syn-anti* conformations like the oxoesters. Ethyl cyanothioformate and trifluorothioacetate spectra display only the *syn-gauche* conformer. The conformer which includes an *anti* configuration about the C–S–C–C dihedral angle is missing. Although *n*-propyl formate, fluoroformate, chloroformate, cyanoformate, and trifluoroacetate [4] all display mixtures of *gauche* and *anti* conformations about the C–O–C–C dihedral angle, among *n*-propyl fluorothioformate, chlorothioformate, cyanothioformate, and trifluorothioacetate, none exist in the conformation which has an *anti* configuration about the C–S–C–C dihedral angle [5]. So the *anti* C–S–C–C configuration is missing in some of the ethyl thioesters and all of the propyl thioesters while it is present in all of the oxygen ester analogs.

The focus of this work is the torsion about the C–O–C–C and C–S–C–C dihedral angles. We have carried out ab initio molecular orbital and density functional calculations exploring the C–O–C–C and C–S–C–C torsional potential functions for ethyl and methyl formate and thioformate as well as ethyl and methyl fluoroformate and fluorothioformate.

1 Introduction

The conformational properties of esters and thioesters show many similarities but also some puzzling differences. Experimental microwave spectroscopic studies of ethyl esters and thioesters [1–3] show that they exist in two stable conformations, *syn-gauche* and *syn-anti*, displayed in Fig. 1. Microwave spectra of ethyl formate [1] and ethyl fluoroformate, chloroformate, cyanoformate, and trifluoroacetate [2] display mixtures of conformers which have a *syn* configuration of the O=C–O–C dihedral angle coupled with *gauche* or *anti* configurations about the C–O–C–C dihedral angle.

2 Computational methods

The energies were calculated using Gaussian-95 [6] and the 6-311+G** basis set that is both reasonably flexible, and includes diffuse functions that are believed to be of importance in describing lone pairs [7]. Geometry optimizations were carried out with one torsional angle constrained to a given value, but all other structural parameters were allowed to vary. Both MP2 and B3LYP theoretical models were used.

3 Results and discussion

3.1 Ethyl formate

The C–O–C–C torsional potential energy curve in Fig. 2 shows a substantial (~7 kcal/mol) barrier when

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Correspondence to: K.B. Wiberg

the methyl group eclipses the carbonyl oxygen and a modest (~ 1 kcal/mol) maximum when a methylene H eclipses the carbonyl oxygen. Stable minima exist at C—O—C—C dihedral angles of $80\text{--}90^\circ$ (*gauche*) and 180° (*anti*), consistent with the experimental results [1]. The depth of the *anti* potential minimum is predicted to be 0.8 kcal/mol by the B3LYP method and 1.2 kcal/mol by MP2. In all of the calculations reported here, the B3LYP method predicts lower barriers and flatter potential energy surfaces than the MP2 method.

The variations of some of the bond angles as a function of C—O—C—C torsional angle are displayed in Fig. 3. These bond angles were calculated from geometry minimized structures holding only the torsional angle fixed. The MP2 and B3LYP bond angle values are very similar and the B3LYP values are shown in the figure. There is a striking similarity between the shape of the curve of the C—O—C bond angle with torsional angle in Fig. 3 and the torsional energy in Fig. 2. The C—O—C bond angle varies over a 9° range, has a maximum value when the methyl group eclipses the carbonyl oxygen, has minimum values when the α -C H atoms straddle the carbonyl oxygen, and rises slightly to an intermediate maximum when a methylene H eclipses the carbonyl oxygen. The O=C—O bond angle behaves similarly except that the range of variation is scaled down by a factor of ~ 3 . The O—C—C bond angle ranges over 15° but displays virtually no 3-fold undulation and corre-

lates inversely with the non-bonded distance between the carbonyl oxygen and the terminal carbon atom. The O—C—H_{a,b} bond angle variation shown in Fig. 3 is about 5° , with the angles largest when the methylene H atoms eclipse the carbonyl oxygen atom. It is interesting to note, however, that the O—C—H bond angle remains essentially constant over a 60° range of torsion surrounding the =O \cdots H eclipsed configuration. The variation of O—C—H bond angles with torsional angle is similar to that of the O—C—C bond angle but shifted approximately 120° in phase and scaled down by a factor of ~ 3 . The C—C—H bond angles exhibit small variations (not shown) that correlate with steric repulsion when near the carbonyl O. Variations of the other bond angles as well as bond lengths (not shown) with C—O—C—C torsion are small (but see Fig. 4).

We conclude that the form of the torsional energy is dominated by steric repulsions between the carbonyl oxygen atom and the methyl group, but the steric interactions between the carbonyl oxygen atom and the methylene H atoms may be more complex.

3.2 Ethyl thioformate

The calculated torsional energy for ethyl thioformate shown in Fig. 5 is similar to ethyl formate's potential function (Fig. 2). The major difference occurs near the *anti* 180° configuration. The B3LYP calculation predicts a potential well depth of merely 0.01 kcal/mol and the MP2 method predicts 0.08 kcal/mol. Both values are considerably smaller than their uncertainties. Therefore, the calculations suggest that although the *anti* potential energy minimum is well developed in esters, it essentially disappears in thioesters. It is interesting to note that a non-correlated calculation with a smaller basis set, HF/6-31G*, predicts a well 0.7 kcal/mol deep at the 180° configuration in ethyl thioformate, but this potential

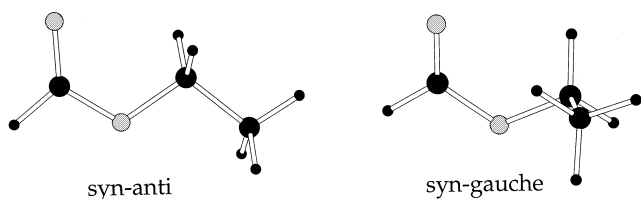


Fig. 1. Conformations of ethyl esters

Fig. 2. Ethyl formate: potential energy vs torsional angle C—O—C—C

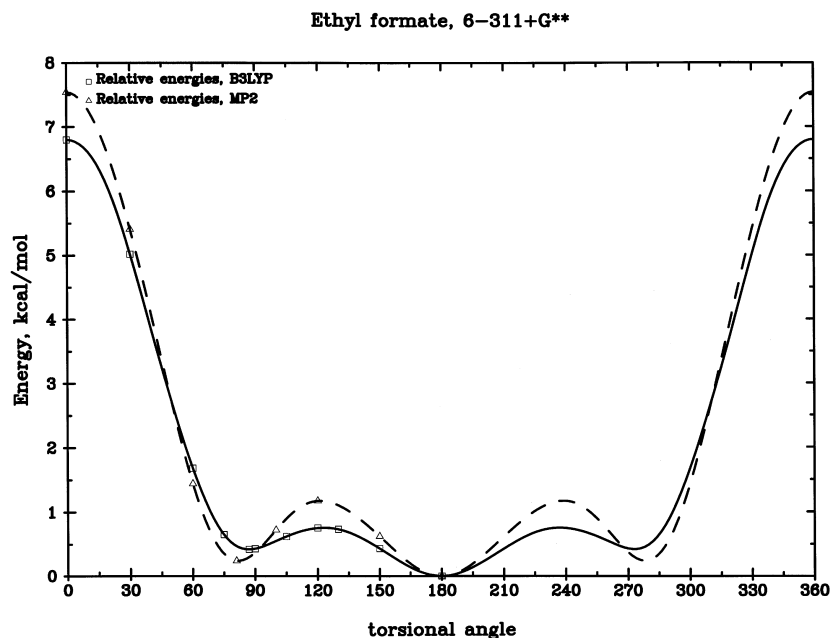


Fig. 3. Ethyl formate: variation of bond angles with torsional angle

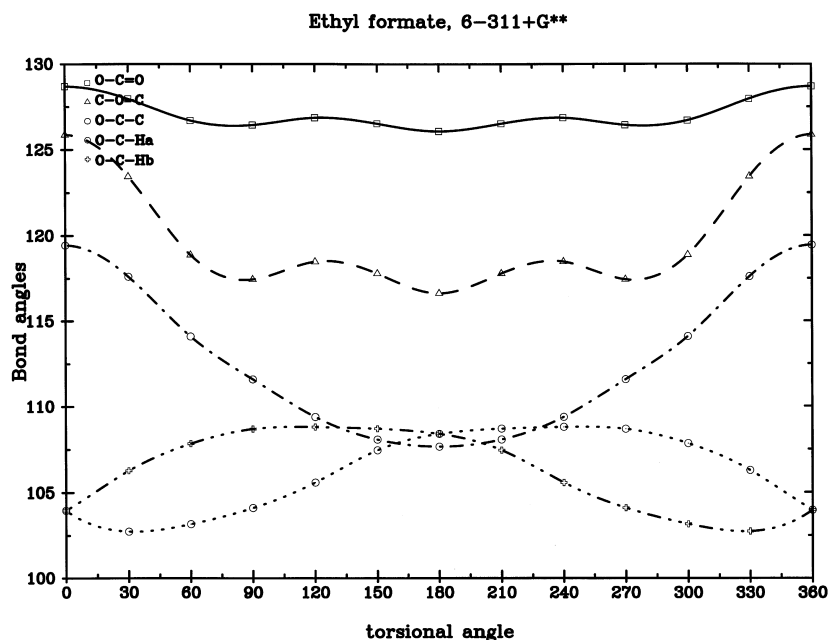
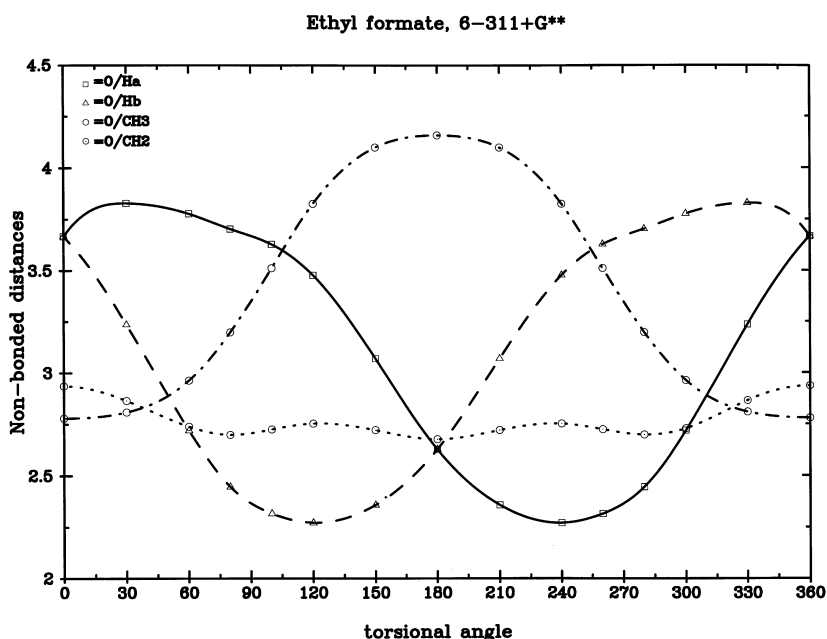


Fig. 4. Ethyl formate: variation of selected non-bonded distances with torsional angle



minimum disappears with larger basis sets and inclusion of electron correlation.

The calculated variations of various bond angles with torsional angles in ethyl thioformate are shown in Fig. 6. As in the oxygen case, there is a striking similarity between the curve of the C—S—C bond angle (Fig. 6) and the torsional energy (Fig. 5) with C—S—C—C torsion. The C—S—C bond angle appears to respond to steric repulsion as the methyl group and the methylene H atoms eclipse the carbonyl oxygen, and varies over a 9° range. A similar effect is shown by the variation of the O=C—S bond angle with torsion. In the thiol compound, the range of variation is down by a factor of ~ 2 from the C—S—C variation. The S—C—C

bond angle shows a nearly 1-fold variation (range $\sim 9^\circ$) with torsion, which correlates inversely with the non-bonded carbonyl oxygen to methyl carbon distance.

The curves of the S—C—H bond angles versus torsion (Fig. 6) are rather different than the curves of the corresponding O—C—H bond angles (Fig. 3). It is interesting to note that the closest approach of the carbonyl O atom and methylene H atoms during torsion is 2.27 Å in both ethyl formate (Fig. 4) and ethyl thioformate (Fig. 7). This occurs even though the C—S—C group has approximately 0.4 Å longer bond lengths and a 16° smaller bond angle than the C—O—C group. In the formate, the O—C—H bond angles increase as the torsional angle of minimum separation approaches, but

Fig. 5. Ethyl thioformate: potential energy vs torsional angle C—S—C—C

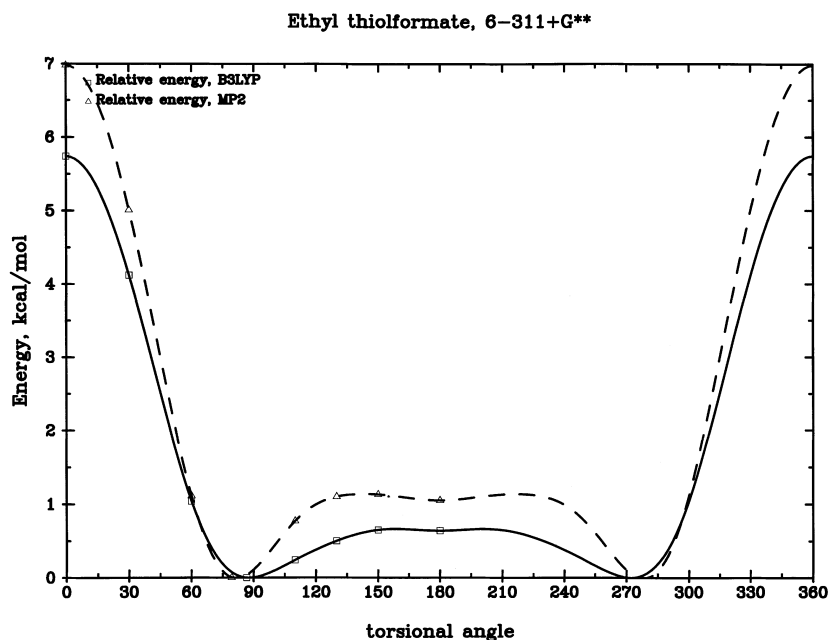
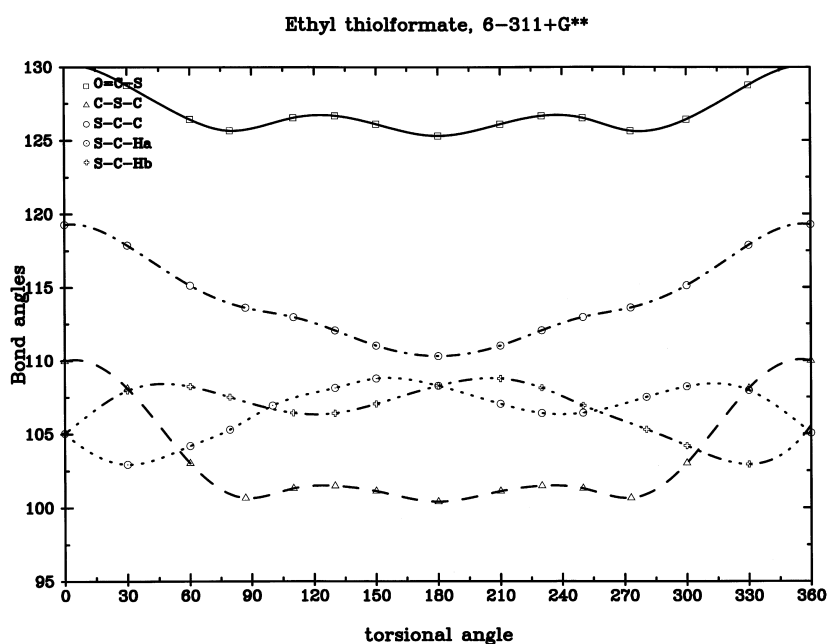


Fig. 6. Ethyl thioformate: variation of bond angles with torsional angle



then remain essentially constant over about a 60° range surrounding the torsional angle of closest approach. In the thioformate, the S—C—H bond angles are calculated to decrease in that torsional region and achieve the 2.27 Å non-bonded distance. This suggests a weak $=O \cdots H-C$ hydrogen bond at this configuration. It should be noted that the O—C—C and O—C—H (or S—C—C and S—C—H) bond angles are not independent, but that a change of one bond angle implies a change of hybridization at the central atom affecting the remaining bond angles.

There are a number of examples of $=O \cdots H-C$ hydrogen bonds, especially when the carbon is substituted by an electronegative atom [8] and the $O \cdots H$ distances are generally on the order of 2.2–2.5 Å. Intramolecular

examples of such hydrogen bonds are known even when the carbon is attached to only other carbons and hydrogens, and in the case of nonanolactone the distance is 2.34 Å [9].

The theoretical calculations agree with the experimental evidence of stable *anti* and *gauche* conformations about the C—O—C—C torsional angle and the disappearance of the *anti* potential energy minimum about the C—S—C—C angle.

3.3 Ethyl fluoroformate and ethyl fluorothioformate

Experiments reveal the existence of *anti* conformers about the C—S—C—C dihedral angle in the cases of

Fig. 7. Ethyl thioformate: variation of selected non-bonded distances with torsional angle

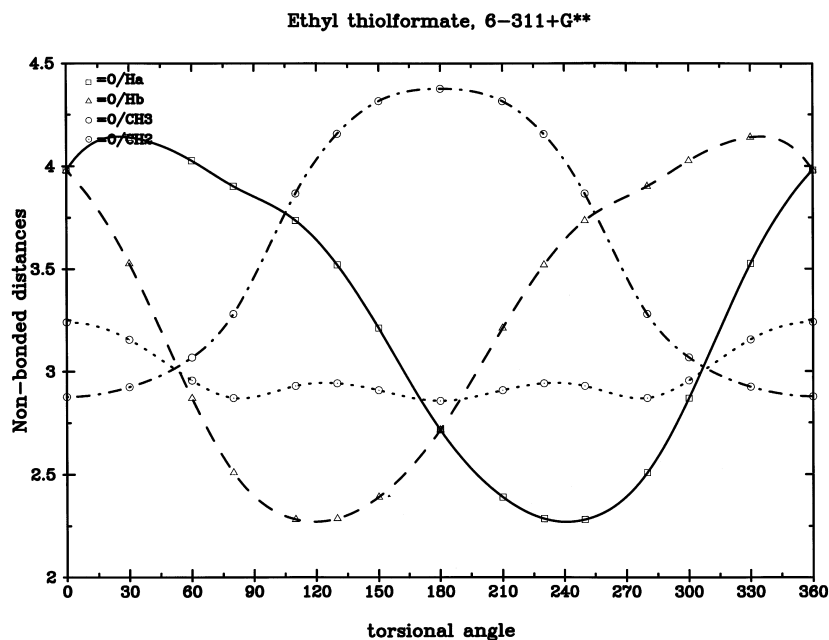
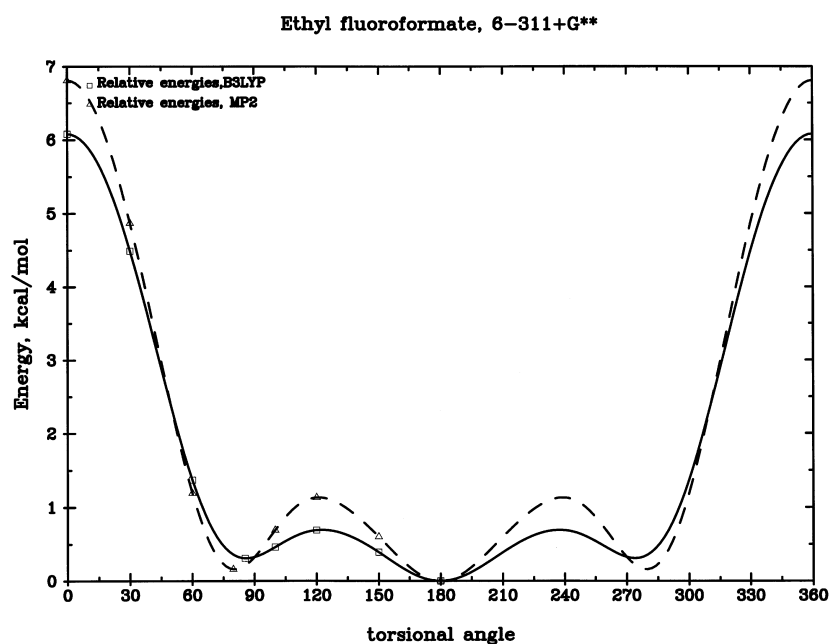


Fig. 8. Ethyl fluoroformate: potential energy vs torsional angle C—O—C—C



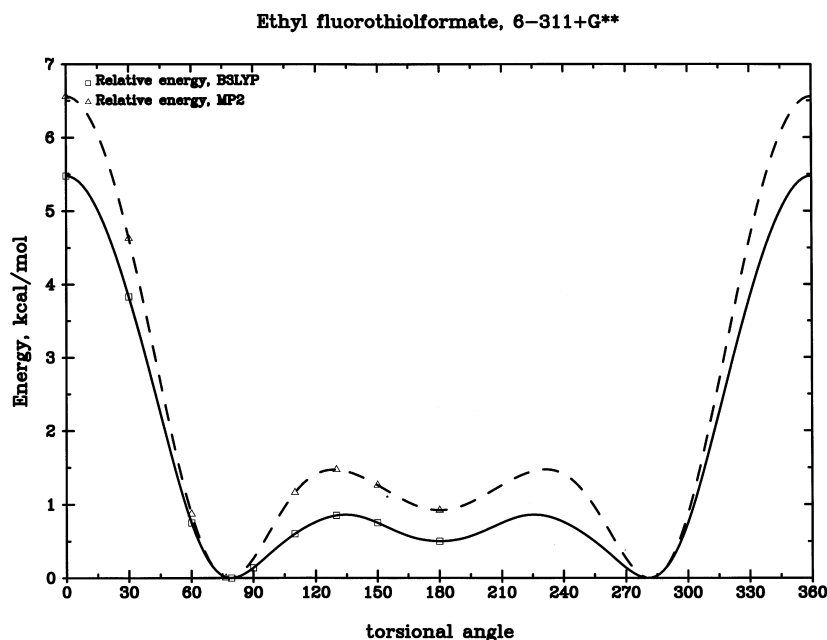
ethyl fluorothioformate and chlorothioformate. MP2 and B3LYP calculations were carried out for ethyl fluoroformate and ethyl fluorothioformate to test the effect of fluorine substitution in the acid fragment. The C—O—C—C torsional potential energy function was calculated for ethyl fluoroformate and is shown in Fig. 8. It is essentially identical to that of ethyl formate (Fig. 2). Substitution by fluorine has no significant qualitative nor quantitative effect on the torsional potential function. There is a small but significant effect of fluorine substitution on the C—S—C—C torsional potential energy function of ethyl fluorothioformate shown in Fig. 9, however. A shallow 0.6 kcal/mol minimum develops at the *anti* configuration which was just a flat plateau in the thioformate. This

conformation lies 0.9 kcal/mol higher in energy than the *gauche* conformation. This result is consistent with the experimental observation of *gauche* and *anti* conformers in ethyl fluorothioformate and chlorothioformate. Experimentally, the *anti* configuration is absent in the cyanothioformate or the trifluorothioacetate. No calculations were carried out on these derivatives.

3.4 Methyl formate, thioformate, fluoroformate, and fluorothioformate

The C—O—C—C torsional potential function of ethyl formate shown in Fig. 2 has the appearance of a large

Fig. 9. Ethyl fluorothiolfornate: potential energy vs torsional angle C—S—C—C



steric repulsion barrier from carbonyl oxygen \cdots methyl group repulsions and smaller contributions from carbonyl oxygen \cdots H(methylene) repulsions. We noted above, however, that the relationship between the O—C—H and S—C—H bond angles and torsional angle is not as simple as implied by a purely repulsive interaction. MP2/6-311+G** and B3LYP/6-311+G** calculations were carried out on methyl formate, fluoroformate, thiolformate, and fluorothiolfornate to determine the 3-fold barrier to rotation of the methyl group. In methyl formate the barrier is 1.4 kcal/mol (0.8 kcal/mol in the B3LYP calculation) and the ground state has the methyl H atoms straddling the carbonyl oxygen. This barrier is the same as the small barriers calculated in ethyl formate. The O—C—H bond angles are largest when the H eclipses the carbonyl oxygen, but the bond angle remains essentially constant over a 120° range surrounding the eclipsed position, which again corresponds to a minimum =O \cdots H distance of 2.27 Å. MP2/6-311+G** calculations for methyl fluoroformate predict a 1.3 kcal/mol methyl torsional barrier, 0.1 kcal/mol smaller than the calculated value for methyl formate.

In methyl thiolformate the MP2 calculation predicts a 3-fold barrier of only 0.5 kcal/mol, with the methyl hydrogens straddling the carbonyl oxygen in the ground state. The B3LYP calculation yields a barrier below 0.1 kcal/mol. The minimum =O \cdots H distance is again 2.26 Å. In any case, the 3-fold barrier is predicted to be smaller in methyl thioesters than in oxoesters. The variation of the S—C—H bond angles with torsion show similar complex behavior as occurred in the ethyl analog. As a methylene H atom approaches the configuration where it is eclipsed with the carbonyl oxygen, the angle decreases and achieves that 2.28 Å favorable hydrogen bonded distance. MP2/6-311+G** calculations for methyl fluorothiolfornate predict a 1.0 kcal/mol methyl barrier, 0.5 kcal/mol larger than that calculated

Table 1. Methyl group torsional barriers in formates and thioformates

X	Esters		Thioesters	
	V_3 (cal/mol)	Ref.	V_3 (cal/mol)	Ref.
H	1140 (3)	10	>2500 (est.)	16
F	1080 (30)	11	917 (2)	17
Cl	1224 (1)	12	890 (20)	18
CN	1170 (30)	11	705 (20)	19
N ₃	1060 (30)	13		
CH ₃	1215 (30)	11		
CH ₂ OH	1130 (30)	14		
CH=CH ₂	1220 (30)	11		
C≡CH	1266 (30)	11		
NH—NH ₂	980 (30)	15		

for methyl thiolformate. As was seen above in ethyl esters, fluorine substitution has little effect on torsions in esters, but increases torsional barriers in thioesters.

Experimentally known 3-fold barriers in methyl esters and thioesters are shown in Table 1. Our MP2 calculations are in good agreement with the observed barriers, 1140 cal/mol for methyl formate [10] and 1080 cal/mol for methyl fluoroformate [11], with calculated values of 1400 and 1310 cal/mol, respectively. In methyl fluorothiolfornate, our MP2/6-311+G** calculated barrier, 1.0 kcal/mol, agrees with the observed value, 917 cal/mol [17]. The barriers in the substituted formates all have similar values in the range 1–1.2 kcal/mol. The experimental barriers for thiolformates are smaller than in the formates, with the glaring exception of methyl thiolformate. In that study the authors searched for, but failed to find, tunneling splittings from methyl internal rotation in the microwave spectrum [16] They had to choose whether the barrier was so large that the splittings were unresolved, or so small that their spectral search was not large enough to include the split com-

ponent of the rotational transition. They chose the former option, an apparently unlucky choice. The 2.5 kcal/mol lower limit was calculated from the minimum resolution of the Stark microwave spectrometer employed.

Our calculations and almost all the experimental results are consistent with a smaller V_3 barrier in methyl thioesters than methyl oxoesters. The authors have initiated experimental studies to determine the torsional barrier in methyl thioformate.

4 Conclusions

MP2/6-311+G** molecular orbital and B3LYP/6-311+G** density functional calculations have been carried out for ethyl and methyl formate, thioformate, fluoroformate, and fluorothioformate, focusing upon the torsional C—O—C—C/H and C—S—C—C/H potential functions. In ethyl formate, conformational minima are predicted at *gauche* and *anti* configurations, in agreement with experimental results. Substitution of a fluorine into the acid group has negligible effects. In ethyl thioformate, the potential minimum at the *anti* configuration essentially disappears and becomes a broad potential plateau. However, in this compound, substitution of a fluorine into the acid group produces a small potential minimum at the *anti* configuration, again in agreement with experiment.

The torsional potential functions in the ethyl compounds are dominated by steric repulsion between the carbonyl oxygen and the methyl group. The lesser maxima when methylene H atoms eclipse the carbonyl oxygen can also be rationalized by steric repulsion, but the O—C—H and S—C—H bond angle variations with torsion suggest a weak hydrogen bond between the methylene H atoms and the carbonyl oxygen at a distance of 2.27 Å.

The MP2 method predicts torsional barriers in methyl formate and fluoroformate which are in very good agreement with experiment, and fluorine substitution decreases the barrier very slightly. The method predicts a lower barrier in thioesters, a prediction generally consistent with experimentally determined barriers with the exception of methyl thioformate. The authors plan to experimentally investigate this compound. The MP2 method predicts a torsional barrier in methyl fluorothioformate which also agrees well with experiment and which is larger than in the non-fluorinated compound. As

in the case of the ethyl compounds, fluorine substitution in the acid group markedly increased the torsional barrier about the S—C(alkyl) bond but causes a very small decrease in the O—C(alkyl) torsional barrier.

In general, with the same basis set, the MP2 molecular orbital method calculates higher potential barriers than the B3LYP method. The MP2 values correlate with experimental values better than the B3LYP values.

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