

# Molecular structure of *S*-ethyl thioacrylate

## Combined vibrational spectroscopic and *ab initio* SCF-MO study

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*Ab initio* 6-31G\* SCF-MO calculations have been carried out on *S*-ethyl thioacrylate [CH<sub>2</sub>=CHC(O)SCH<sub>2</sub>CH<sub>3</sub>]. Fully optimized geometries, relative stabilities, dipole moments and harmonic force fields for several conformers of this molecule have been determined and the results compared with those for similar molecules. Together with FTIR and Raman spectroscopic data, the theoretical results demonstrate that *S*-ethyl thioacrylate exists in two different conformations about the C<sub>α</sub>—C bond (the *s-cis* and *s-trans* forms, with C=C—C=O dihedral angles equal to 0° and 180°, respectively); the *s-cis* conformation being more stable than the *s-trans* form by *ca.* 6 kJ mol<sup>-1</sup> for the isolated molecule. Comparison of the experimental and theoretical vibrational spectra confirms that, as concluded from our previous study on the analogous *trans*-*S*-ethyl thiocrotonate molecule (R. Fausto, P. J. Tonge and P. R. Carey, *J. Chem. Soc., Faraday Trans.*, 1994, **90**, 3491), the presence of the *s-trans* isomer of an α,β-unsaturated thioester can be successfully monitored by the IR band at *ca.* 1170 cm<sup>-1</sup>, ascribed to the C<sub>α</sub>—C stretching mode of this form. In addition, we were also able to identify some IR bands sensitive to the conformation of the ethyl group that may be used as spectroscopic probes to study conformational equilibria associated with this internal degree of freedom in more complex *S*-ethyl thioesters.

The α,β-unsaturated acyl group, —CH=CH—C(=O)—, provides an ideal chromophoric label by which to generate the resonance Raman (RR),<sup>1,2</sup> or Raman difference,<sup>3</sup> spectra of transient enzyme–substrate complexes formed in the active site during the catalytic action of serine or cysteine proteases. In the case of the serine protease group of enzymes, where the α,β-unsaturated acyl group is covalently linked to an active site serine residue, RR spectroscopic studies have already provided important structural and mechanistic detail on key catalytic groups in the active site.<sup>2</sup> These studies are presently being extended to the cysteine protease family of enzymes, *via* intermediates of the type —CH=CH—C(=O)—S— enzyme and using Raman difference spectroscopy,<sup>4,5</sup> to investigate common as well as novel mechanistic features.

A factor which limits our interpretation of the Raman spectra of α,β-unsaturated thioesters, free in solution or bound to their target enzyme, is the paucity of information in the literature concerning the conformational and spectroscopic properties of these compounds. The present paper follows a study of *cis*- and *trans*-*S*-ethyl thiocrotonate molecules,<sup>6</sup> as part of a series whose purpose is to fill that void. In spite of their importance in a variety of biochemical systems (*e.g.* see ref. 7), simple α,β-unsaturated carbonyl thioesters have not been the object of detailed conformational and vibrational spectroscopic analysis. This may be due, in part, to compound instability and difficulties in purifying some members of this family. In addition, to the best of our knowledge, no systematic theoretical studies of this family of compounds have been undertaken until now. Thus, in the present study, the conformational preferences and vibrational properties of *S*-ethyl thioacrylate (abbreviated ETA) were studied by a combined *ab initio* SCF-MO calculations/vibrational spectroscopic approach, as a step towards the general understanding of the

conformational and vibrational properties of α,β-unsaturated thioesters.

## Experimental and computational methods

### Synthesis and equipment

*S*-Ethyl thioacrylate was synthesized by dropwise addition of acrylyl chloride to a dry solution of ethanethiol in CH<sub>2</sub>Cl<sub>2</sub>, following the general procedure described in ref. 6. Purification was undertaken by high-performance liquid chromatography (HPLC) on a silica column (Supercosil LC-SI semiprep, 25.0 cm × 10 mm, 5 μm pore) using hexane as eluent (3 ml min<sup>-1</sup>), and the purity of the sample was checked by UV and NMR spectroscopies. The Raman and FTIR spectroscopic studies were performed directly on the HPLC fractions in hexane. FTIR spectra were obtained using a Digilab FTS 40A spectrometer equipped with a DTGS (deuterated triglycine sulfate) pyroelectric detector. Data collection was performed using a demountable liquid cell equipped with KBr windows. For each spectrum, 64 scans were obtained and co-added. Raman spectra were obtained using a single monochromator, equipped with a charge-coupled device (CCD) detector and a super notch filter.<sup>8</sup> Data collection was performed using 90° sampling geometry with 300 mW 647.1 nm laser excitation. For each spectrum, 20 scans, each 10 s, were acquired and co-added.

### Computational details

The *ab initio* SCF-MO calculations were carried out with a 6-31G\* basis set<sup>9</sup> using the GAUSSIAN 92 program system<sup>10</sup> running on a DEC ALPHA 7000 computer. Molecular geometries were fully optimized by the force gradient method using Bery's algorithm.<sup>11</sup> The largest residual internal coordinate forces were always less than 3 × 10<sup>-4</sup> E<sub>h</sub> a<sub>0</sub><sup>-1</sup> or E<sub>h</sub> rad<sup>-1</sup>, for bond stretches and angle bends, respectively. The stopping criterion for the SCF iterative process required a

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density matrix convergence of less than  $10^{-8}$ . The force constants (symmetry internal coordinates) for use in the normal coordinate analysis were obtained from the *ab initio* Cartesian harmonic force constants using the program TRANSFORMER.<sup>12</sup> This program was also used to prepare the input data for the normal coordinate analysis programs used in this study (BUILD-G and VIBRAT<sup>13</sup>). The calculated force fields were scaled down in order to adjust the *ab initio* calculated wavenumbers ( $\text{cm}^{-1}$ ) to the experimental ones by using the linear equation  $\nu_{\text{scaled}} = 0.8996\nu_{\text{ab initio}} - 14.4$  previously derived for *S*-ethyl thiocrotonate.<sup>6</sup>

## Results and Discussion

### Geometries and energies

Table 1 shows the 6-31G\* energies and optimized geometries for the relevant conformers of ETA. The atom numbering is presented in Fig. 1.

ETA has three different internal degrees of freedom that can give rise to conformational isomerism: internal rotations about the  $\text{C}_\alpha\text{-C}$ ,  $\text{C-S}$  and  $\text{S-C}$  bonds. As shown in previous studies on thioesters and thioacids,<sup>14-17</sup> molecules having an *s-trans* conformation about the  $\text{O=C-S-R}$  ( $\text{R} = \text{H}$  or alkyl) axis have a much higher energy than those

adopting an *s-cis* conformation about this axis ( $\Delta E_{[s\text{-trans}(\text{C-S})\text{-}[s\text{-cis}(\text{C-S})]} > 13 \text{ kJ mol}^{-1}$ ) and thus were not considered in this study.

We have shown recently<sup>6</sup> that internal rotation about the  $\text{C}_\alpha\text{-C}$  bond in *trans-S*-ethyl thiocrotonate (*trans*-ETC) gives rise to two conformers: the *s-cis* and *s-trans* forms, with  $\text{C=C-C=O}$  dihedral angles equal to 0 and  $180^\circ$ , respectively. For the isolated molecule, the *s-cis* form was found to be *ca.*  $7 \text{ kJ mol}^{-1}$  more stable than the *s-trans* form.<sup>6</sup> In addition, these two conformers have also been found to correspond to the stable conformations about the  $\text{C=C-C=O}$  axis in the case of the analogous  $\alpha,\beta$ -unsaturated carboxylic esters and acids.<sup>18-21</sup> This general trend can be easily correlated with the increased importance of the mesomerism associated with the  $\text{C=C-C=O}$  fragment for the planar conformations, owing to a more efficient overlap of the  $p(\pi)$  orbitals.<sup>18-21</sup>



The factors that determine the relative energy of the two stable conformations have been pointed out elsewhere.<sup>18-21</sup> These are, besides the mesomerism involving the two double bonds (that was found to favour the *s-trans* conformer<sup>18,19</sup>), mesomerism within the thiocarboxylate group,

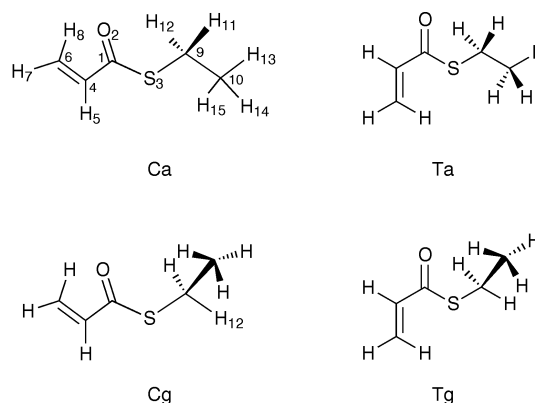


**Table 1** 6-31G\* calculated optimized geometries, energies and electric dipole moments for the relevant forms of ETA<sup>a</sup>

parameter	Cg	Ca	Tg	Ta
$\text{C}_\alpha\text{-C}$	148.97	148.99	148.92	148.89
$\text{C}=\text{O}$	119.06	119.04	119.06	119.06
$\text{C-S}$	177.94	177.82	178.57	178.45
$\text{S-C}$	181.99	182.03	182.04	182.11
$\text{C-C}$	152.46	152.55	152.42	152.57
$\text{C=C}$	132.00	131.98	131.97	131.96
$\text{C}_\alpha\text{-H}$	107.51	107.51	107.54	107.54
$\text{C}_\beta\text{-H7}$	107.46	107.46	107.47	107.47
$\text{C}_\beta\text{-H8}$	107.41	107.41	107.44	107.46
$\text{C}_\beta\text{-H11}$	108.02	108.04	107.98	108.01
$\text{C-H12}$	108.29	108.04	108.30	108.01
$\text{C-H13}$	108.62	108.48	108.62	108.49
$\text{C-H14}$	108.42	108.44	108.42	108.44
$\text{C-H15}$	108.22	108.44	108.22	108.44
$\text{C-C=O}$	123.81	123.90	120.68	120.77
$\text{O=C-S}$	122.78	122.45	121.95	121.57
$\text{C-C-S}$	113.41	113.65	117.37	117.66
$\text{C-S-C}$	101.07	100.53	100.56	99.98
$\text{S-C-C}$	113.90	109.92	114.05	109.71
$\text{C=C-C}$	120.40	120.42	126.05	126.05
$\text{H-C}_\alpha\text{-C}$	117.70	117.70	112.52	112.52
$\text{H7-C=C}$	121.49	121.51	120.66	120.69
$\text{H8-C=C}$	120.86	120.85	122.94	122.97
$\text{H11-C-S}$	107.45	108.18	107.61	108.29
$\text{H12-C-S}$	104.81	108.18	104.47	108.29
$\text{H13-C-C}$	109.65	109.47	109.61	109.46
$\text{H14-C-C}$	111.21	111.48	111.20	111.49
$\text{H15-C-C}$	110.84	111.48	110.90	111.49
$\text{C-C(=O)-S}$	179.67	180.00	179.28	180.00
$\text{O=C-S-C}$	0.86	0.00	3.09	0.00
$\text{C=C-C=O}$	-0.14	0.00	-173.93	180.00
$\text{C-S-C-C}$	80.24	180.00	79.58	180.00
$\text{H11-C-S-C}$	-43.29	58.31	-44.26	58.39
$\text{H12-C-S-C}$	-158.17	-58.31	-159.06	-58.39
$\text{H13-C-C-S}$	178.47	180.00	178.20	180.00
$\text{H14-C-C-S}$	58.80	60.56	58.55	60.57
$\text{H15-C-C-S}$	-62.20	-60.56	-62.49	-60.57
$\Delta E$	—	1.415	5.706	6.934
$ \mu $	1.010	1.021	1.674	1.733

<sup>a</sup> Bond lengths in pm, angles in degrees, energies in  $\text{kJ mol}^{-1}$ , dipole moments in Debye; see Fig. 1 for atom numbering. <sup>b</sup> Energies relative to the most stable conformer; the total energy for the most stable form is  $-666.3559832 E_h$ .

and steric and electrostatic repulsions between the vinyl moiety and the O or S atoms (both favouring the *s-cis* form<sup>18,19</sup>). In the case of ETA, the *s-trans* conformation about the  $\text{C=C-C=O}$  axis is found to be *ca.*  $5.6 \text{ kJ mol}^{-1}$  higher in energy than the *s-cis* form ( $\Delta E_{\text{Tg-Cg}} = 5.706 \text{ kJ mol}^{-1}$ ;  $\Delta E_{\text{Ta-Ca}} = 5.519 \text{ kJ mol}^{-1}$ ; see Table 1). The slightly smaller  $\Delta E_{\text{Tg-Cg}}$  values found for ETA when compared with the previously reported data for *trans*-ETC<sup>6</sup> result from a delicate balance between the above mentioned factors: (i) the presence of the electron releasing  $\beta$ -methyl substituent in *trans*-ETC leads to an increased importance of the mesomerism within the  $\text{C=C-C=O}$  moiety, thus giving rise to an additional stabilization of the *s-trans* forms relative to the most stable *s-cis* conformers (this gives rise to longer  $\text{C=C}$  and shorter  $\text{C}_\alpha\text{-C}$  bond lengths in *trans*-ETC<sup>6</sup> by 0.4 and 0.5 pm, respectively, when compared with those bond lengths in ETA); (ii) since the mesomerism associated with the  $\text{C=C-C=O}$  fragment competes with the mesomerism within the thiocarboxylic group, the latter effect is less important in *trans*-ETC than in ETA (consequently, the  $\text{C-S}$  bond is longer in *trans*-ETC<sup>6</sup>



**Fig. 1** Numbering of atoms for the relevant conformers of ETA

than in ETA by 0.4 pm), and it also contributes to a slight additional stabilization in *trans*-ETC of the *s-trans* conformers; (iii) the dominating effect is, however, the electrostatic destabilizing repulsions between the more positively charged  $\beta$ -methyl substituent and the slightly positive thioester sulfur atom<sup>22,23</sup> in *s-trans trans*-ETC when compared with the vinyl-S electrostatic repulsion in *s-trans* ETA, thus leading to the observed relative values of  $\Delta E_{T-C}$ .

The greater importance of the mesomerism involving the two double bonds in the *s-trans* conformers [Tg and Ta (see Fig. 1)] when compared with the *s-cis* forms (Cg and Ca) gives rise to the shorter  $C_\alpha-C$  bond lengths calculated for the *s-trans* forms (see Table 1). On the other hand, the  $C=C$  bond lengths are predicted to be very similar in all conformers, indicating that the structural consequences of the mesomeric effect are, for this bond, compensated by the more important steric and electrostatic repulsions between the vinyl moiety and the S atom in the *s-trans* forms, when compared to the vinyl-O steric interaction which is operating in the *s-cis* conformers.

The fundamental importance of the vinyl-S and vinyl-O steric or electrostatic repulsions to the conformational preferences of the  $C=C-C=O$  axis in ETA is reinforced by the calculated changes in the structural parameters associated with the *s-cis*  $\rightarrow$  *s-trans* isomerization (see Table 1). Thus the  $C-C-S$ ,  $C=C-C$  and  $H8-C=C$  angles increase considerably (ca. 4.0, 5.5 and 2.0°, respectively), whereas the  $C-C=O$ ,  $O=C-S$ ,  $H-C_\alpha-C$ ,  $H-C_\alpha=C$ ,  $H7-C=C$  and  $H8-C-H7$  angles decrease to compensate those changes. In turn, no significant changes are observed in the bond lengths, which usually are mainly determined by electronic effects.<sup>13-17</sup>

Besides the forms resulting from internal rotation about the  $C_\alpha-C$  axis, ETA may also exist in two different-by-symmetry stable conformations differing in the relative orientation of the terminal methyl group of the  $SCH_2CH_3$  fragment. As was previously found for *trans*-ETC,<sup>6</sup> the most stable of these conformations in the studied molecule is a doubly degenerate conformational state (point group  $C_1$  at equilibrium), corresponding to  $C1-S-C-C$  axes of ca.  $\pm 80^\circ$  (*gauche* forms). The second conformer is the  $C_s$  symmetric *anti* form ( $C1-S-C-C$  dihedral angle equal to  $180^\circ$ ), which is ca. 1.4 kJ mol<sup>-1</sup> less stable than the *gauche* conformation. The fact that the preferred conformations assumed by the  $C-S-C-C$  axis are not significantly affected by the conformation of the acyl fragment follows the same pattern observed for *trans*-ETC<sup>6</sup> and is in consonance with our previous studies on ethyl dithioacetate and ethyl dithiopropionate,<sup>22,23</sup> where the conformational preferences of this axis (in particular its tendency to adopt *gauche* conformations) have been analysed in detail. The main structural changes associated with the *anti*  $\rightarrow$  *gauche* rotamerization occur in the  $C10-C-S$ ,  $H11-C-S$  and  $H12-C-S$  angles (i.e., those angles involving the atoms directly affected by the internal rotation), which increase by ca. 4° and decrease by ca. 1 and 4°, respectively. Indeed, these changes follow the general trends reported in previous studies on ethyl dithioesters.<sup>22,23</sup>

The calculated electric dipole moments of the *s-trans* conformers of ETA are larger than those of the *s-cis* forms (Table 1). This result can be understood by considering the closer proximity of the overall positively charged  $H_2C=$  to the negatively charged carbonyl oxygen in the *s-cis* conformers. On the other hand, the electric dipole moments associated with an *anti* or *gauche*  $C-S-C-C$  axis are very similar. Thus, it can be predicted that the relative population about the *s-cis/s-trans*  $C=C-C=O$  axis will be sensitive to the polarity of the solvent, while the *gauche/anti*  $C-S-C-C$  axis population ratio will not vary significantly upon changing the solvent polarity.

In summary, ETA exists in four different conformational states differing by the relative orientation of the  $C=C-C=O$

and  $C-S-C-C$  axes: besides the most stable *s-cis* conformers about the  $C=C-C=O$  axis [Ca and Cg (Fig. 1)], two higher energy forms having the  $C=C-C=O$  axis in the *s-trans* conformation also participate in the conformational equilibrium [the Ta and Tg conformers (Fig. 1)]. The structural parameters (bond lengths and, in particular, bond angles) of the different conformers studied are strongly influenced by the presence of either the strong repulsive steric and electrostatic interactions between the vinyl group and the sulfur atom (in the *s-trans*  $C=C-C=O$  conformers) or those involving the vinyl group and the carbonyl oxygen atom. Finally, considering the relative values of the dipole moments of the various conformers, the calculations indicate that solvent variation may be used successfully to change the  $C=C-C=O$  *s-cis/s-trans* relative populations, but does not provide a useful way to modify significantly the *anti/gauche*  $C-S-C-C$  conformational equilibrium.

### Vibrational studies

ETA has 39 fundamental vibrations. In the case of the symmetric ( $C_s$ ) conformers (Ca, Ta), the normal modes will span the irreducible representations  $25A' + 14A''$ , while those of non-symmetric *gauche* forms (Cg and Tg,  $C_1$  point group) belong to the  $A$  symmetry species. Hence, all vibrations are active in both Raman and IR.

As mentioned in the Experimental and computational methods section, calculated spectra were obtained from the 6-31G\* *ab initio* wavefunctions at the equilibrium geometries

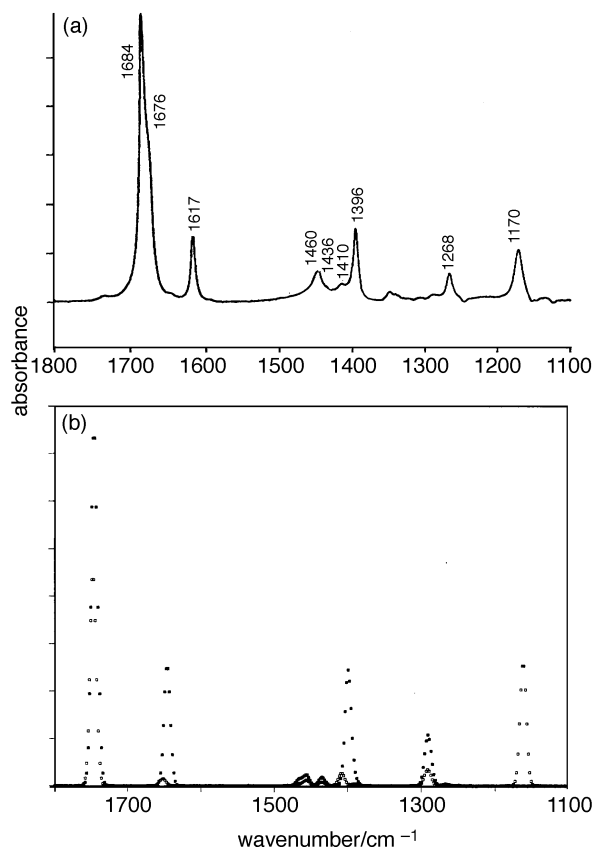
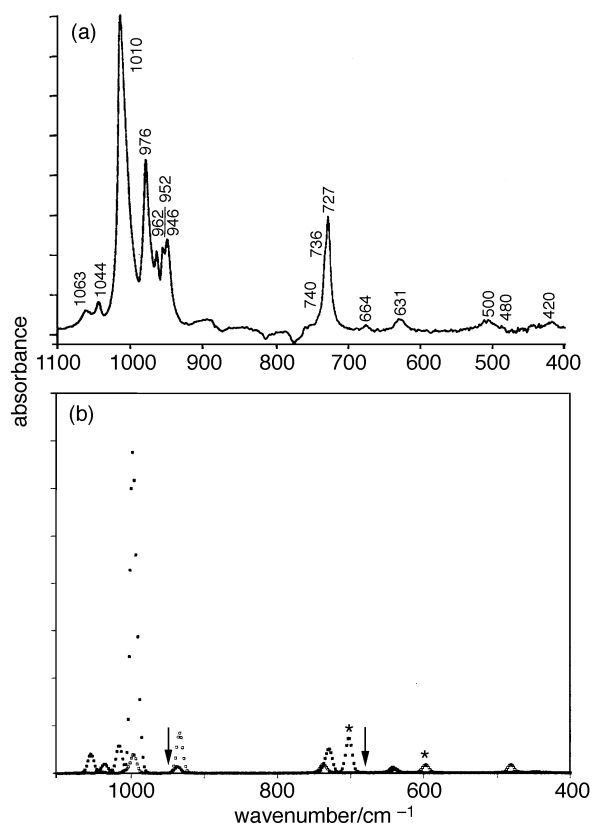


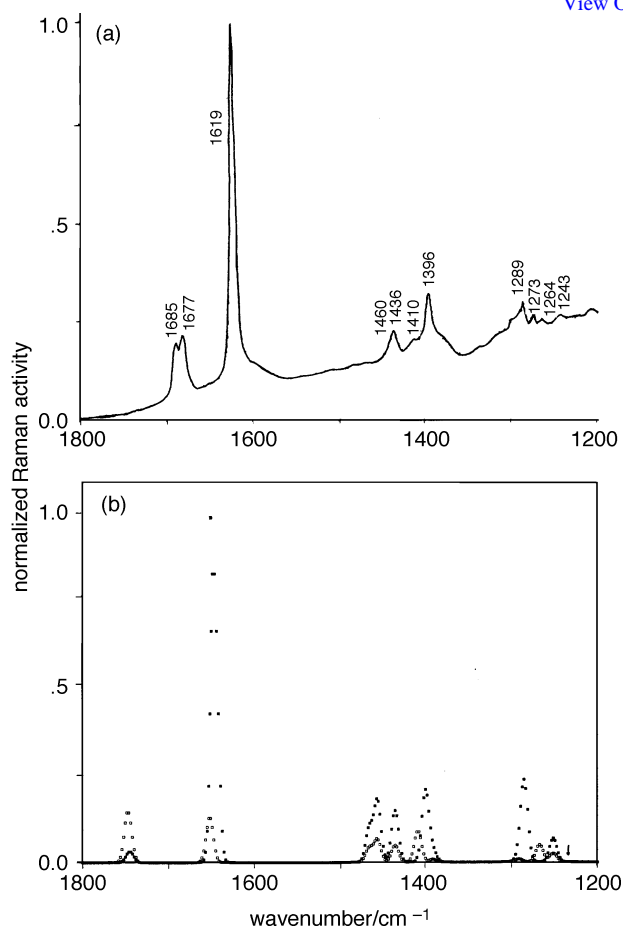
Fig. 2 FTIR spectrum (1100–1800 cm<sup>-1</sup> region) of ETA (a) in hexane solution at room temperature and (b) 6-31G\* calculated IR spectrum (Cg and Tg scaled frequencies): ■ Cg; □ Tg. The calculated intensities of the bands due to the *s-trans* conformer are multiplied by the factor 1/2.25 (see text). In this spectral region, the calculated spectra of the *anti* conformers (Ca and Ta) superimpose so closely to those of the corresponding most stable *gauche* forms (Cg and Tg) that no bands exclusively due to these conformers are predicted to occur in the observed spectrum.

of the various conformers considered, and then scaled down in order to reproduce the experimental wavenumbers ( $\text{cm}^{-1}$ ) by using the linear relationship  $\nu_{\text{scaled}} = 0.8996\nu_{\text{ab initio}} - 14.4$  previously derived for *S*-ethyl thiocrotonate.<sup>6</sup> Table 2 summarizes the vibrational results of this study (additional tables containing full details of the normal coordinate analysis calculations are available from the corresponding author). The experimental and calculated spectra are presented in Fig. 2–4.

The FTIR spectrum of ETA in hexane solution (Fig. 2 and 3) is dominated by the intense bands at 1684 and 1010  $\text{cm}^{-1}$ , the first band showing a shoulder in its low wavenumber wing (1676  $\text{cm}^{-1}$ ). These two intense bands are easily assigned to the  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}_\alpha-\text{C})$  stretching modes of the more stable *s-cis* conformers, in agreement with the theoretical results (Table 2). It should be noted, however, that the calculations predict that the  $\nu(\text{C}_\alpha-\text{C})$  band should be the most intense IR band, while in the observed spectrum this band is less intense than, for instance, that originating from the carbonyl stretching mode. Indeed, the results seem to indicate that the  $\nu(\text{C}_\alpha-\text{C})$  fundamental in the *s-cis* conformers (or at least in the most stable Cg form) interacts by Fermi resonance with the combination mode involving the relatively intense  $\nu(\text{C}-\text{S})$  and  $\delta(\text{S}-\text{C}-\text{C})$  vibrations, whose fundamentals occur at 727  $\text{cm}^{-1}$  and *ca.* 300  $\text{cm}^{-1}$ . The second component of the expected Fermi resonance doublet is here considered to be the band appearing at 976  $\text{cm}^{-1}$  [that has also a contribution to



**Fig. 3** FTIR spectrum (400–1100  $\text{cm}^{-1}$  region) of ETA (a) in hexane solution at room temperature and (b) 6-31G\* calculated IR spectrum (Cg and Tg scaled frequencies); ■ Cg; □ Tg. The calculated intensities of the bands due to the *s-trans* conformer are multiplied by the factor 1/2.25 (see text). In this spectral region, the *anti* forms give rise to observable bands at 664  $\text{cm}^{-1}$  and 960  $\text{cm}^{-1}$ ; the calculated (scaled) bands appear (Ca; Ta) at (664; 666  $\text{cm}^{-1}$ ) and (943; 943  $\text{cm}^{-1}$ ), respectively, and their positions are indicated by the two vertical arrows (↓). Note also the appreciable frequency underestimation by the calculations of the  $\nu(\text{C}-\text{S})$  bands (noted by the symbol \*) and the absence in the calculated spectrum of the band at *ca.* 976  $\text{cm}^{-1}$  that corresponds to the second band of the Fermi doublet associated with the  $\nu(\text{C}_\alpha-\text{C})$  mode of the Cg and Ca conformers (see text).



**Fig. 4** Raman spectrum (1200–1800  $\text{cm}^{-1}$  region) of ETA (a) in hexane solution at room temperature and (b) 6-31G\* calculated Raman spectrum (Cg and Tg scaled frequencies); ■ Cg; □ Tg. The calculated intensities of the bands due to the *s-trans* conformer are multiplied by the factor 1/2.25 (see text). The *anti* forms give rise to observable band at 1243  $\text{cm}^{-1}$ ; the corresponding calculated (scaled) band at *ca.* 1232  $\text{cm}^{-1}$  (see Table 2) is indicated by the vertical arrow (↓).

its total intensity from the  $\gamma(\text{C}_\alpha-\text{H})$  fundamental vibration from the *s-cis* conformers; see Table 2].

Apart from the forementioned point, the general agreement between the calculated and experimental IR spectra of ETA (both frequencies and intensities) is remarkable (see Fig. 2 and 3, and Table 2). As the energy differences between the various conformers of this compound are predicted to be small, all conformers are present in significant amounts at room temperature and thus, they must contribute to the observed spectrum. Assuming a Boltzmann distribution, and taking into consideration the relative conformational energies obtained theoretically (see Table 1) as well as the fact that the *gauche* conformers are by symmetry doubly degenerate forms; the expected relative conformational populations (%) at room temperature can be easily calculated, yielding Cg : Ca : Tg : Ta = 71 : 20 : 7 : 2. Thus, forms Cg and Ca must provide the main contributions to the bands observed. However, in general, the calculated spectra of forms differing in the relative orientation of the C–S–C–C axis do not differ very much, and thus only a few bands could be ascribed to individual conformers differing in the relative orientation of this axis. In fact, with a few exceptions, all modes which are predicted to occur at significantly different frequencies in the *gauche* and *anti* C–S–C–C conformers have frequencies nearly coincident with those of different modes, and have been ascribed to bands which also have contributions from these latter vibrations [exceptions are the  $\nu(\text{C}-\text{C})$  and  $\nu(\text{S}-\text{C})$

**Table 2** Experimental frequencies and calculated frequencies and intensities for ETA<sup>a</sup>

approximate description	calculated												experimental <sup>b</sup>					
	Cg				Ca				Tg				Ta				IR	Raman
	<i>ab initio</i>	scaled	<i>I</i> <sub>(00)</sub>	<i>I</i> <sub>(Raman)</sub>	<i>ab initio</i>	scaled	<i>I</i> <sub>(00)</sub>	<i>I</i> <sub>(Raman)</sub>	<i>ab initio</i>	scaled	<i>I</i> <sub>(00)</sub>	<i>I</i> <sub>(Raman)</sub>	<i>ab initio</i>	scaled	<i>I</i> <sub>(00)</sub>	<i>I</i> <sub>(Raman)</sub>		
$\nu(\text{=CH}_2)_{\text{as}}$	A	3445	3085	3.2	68.5	3444	3084	3.2	69.4	3431	3072	10.2	59.3	3434	3075	11.4	66.5	
$\nu(\text{C-H})$	A'	3381	3027	3.9	75.1	3380	3026	4.3	76.4	3382	3028	4.2	125.9	3382	3028	4.1	133.6	
$\nu(\text{=CH}_2)_{\text{s}}$	A'	3352	3001	10.4	72.2	3352	3001	10.7	73.3	3346	2996	4.6	82.2	3351	3000	4.3	74.4	
$\nu(\text{CH}_2)_{\text{as}}$	A''	3326	2978	13.3	21.9	3329	2980	15.0	32.9	3329	2980	11.0	24.6	3332	2983	14.4	35.0	
$\nu(\text{CH}_2)_{\text{as}}$	A''	3303	2957	15.8	61.8	3280	2936	21.7	80.7	3304	2958	17.3	57.5	3280	2936	22.3	75.6	
$\nu(\text{CH}_2)_{\text{as}}$	A'	3273	2930	36.1	95.5	3283	2939	43.8	91.7	3272	2929	35.5	92.3	3284	2940	43.4	86.2	
$\nu(\text{CH}_2)_{\text{s}}$	A'	3211	2874	38.3	124.2	3213	2876	33.0	120.3	3211	2874	37.7	123.6	3213	2876	31.1	117.9	
$\nu(\text{C=O})$	A'	1956	1745	200.4	3.9	1958	1747	219.8	3.9	1958	1747	296.9	45.7	1959	1748	315.0	46.2	
$\nu(\text{C=C})$	A'	1847	1647	67.5	104.0	1848	1648	65.4	103.8	1854	1653	10.6	40.0	1854	1653	11.2	38.5	
$\delta(\text{CH}_2)_{\text{as}}$	A''	1636	1457	5.8	21.6	1640	1461	6.6	23.1	1636	1457	6.7	19.9	1640	1461	6.6	22.4	
$\delta(\text{CH}_2)_{\text{s}}$	A'	1612	1436	4.7	18.2	1629	1451	7.5	13.8	1612	1436	6.1	16.2	1629	1451	7.3	14.0	
$\delta(\text{=CH}_2)$	A'	1572	1400	64.4	25.1	1572	1400	62.1	27.4	1582	1409	18.1	27.4	1583	1410	17.5	26.2	
$\delta(\text{CH}_2)_{\text{s}}$	A'	1562	1391	3.5	3.6	1567	1395	4.8	2.5	1562	1391	3.6	3.6	1567	1395	2.2	4.7	
$\omega(\text{CH}_2)$	A'	1452	1292	27.6	1.3	1450	1290	12.4	10.7	1452	1292	22.6	2.3	1446	1286	23.1	1.6	
$\delta(\text{C-H})$	A'	1446	1286	1.7	28.3	1442	1283	19.9	21.0	1426	1268	3.6	14.5	1426	1268	2.3	14.0	
$\tau(\text{CH}_2)$	A'	1408	1252	0.2	8.3	1384	1231	<0.1	8.6	1408	1252	0.2	6.4	1385	1232	<0.1	8.1	
$\omega(\text{=CH}_2)$	A'	1190	1056	21.5	10.6	1186	1053	22.9	7.9	1054	934	109.3	1.0	1053	933	106.0	2.3	
$\gamma(\text{CH}_2)$	A'	1173	1041	0.6	4.2	1169	1037	22.7	2.9	1172	1040	2.4	4.3	1174	1042	4.6	6.3	
$\gamma(\text{CH}_2)$	A''	1169	1037	10.0	0.7	1164	1033	0.4	4.7	1178	1045	2.7	4.4	1164	1033	0.3	4.9	
$\gamma(\text{=CH}_2)$	A''	1147	1017	31.4	3.4	1146	1017	31.4	3.6	1124	997	53.1	0.4	1123	996	55.8	0.3	
$\nu(\text{C-C})$	A'	1123	996	353.2	1.1	1126	999	347.5	2.3	1309	1163	173.0	8.1	1309	1163	189.4	8.8	
$\nu(\text{C}_s\text{-H})$	A''	1115	989	23.1	1.5	1115	989	23.1	1.5	1137	1008	7.1	3.4	1135	1007	4.3	3.4	
$\nu(\text{C-C})$	A'	1058	937	7.3	7.2	1064	943	9.2	8.4	1059	938	2.2	7.0	1064	943	2.8	5.6	
$\gamma(\text{CH}_2)$	A''	834	736	7.0	2.8	851	751	0.1	0.1	831	733	3.7	2.1	854	754	0.2	0.9	
$\tau(\text{C=C})$	A''	828	730	23.7	6.8	829	731	31.7	8.5	838	739	22.7	8.4	835	737	26.7	8.7	
$\nu(\text{C-S})$	A'	798	703	39.0	2.5	802	707	37.7	4.8	681	598	21.9	16.1	695	611	32.6	8.0	
$\nu(\text{S-C})$	A'	727	640	3.5	23.6	754	664	2.7	21.4	631	643	15.4	14.8	756	666	3.7	21.5	
$\delta(\text{O=C-S})$	A'	545	476	0.8	3.2	564	493	0.2	2.0	552	482	21.8	1.1	542	473	21.8	2.7	
$\delta(\text{C=O})$	A''	538	470	0.5	4.5	537	469	0.5	4.3	485	422	1.0	5.2	486	423	0.4	5.4	
$\delta(\text{C=C}_s\text{-C})$	A'	423	366	314	8.5	328	281	1.9	6.6	371	319	3.7	0.6	345	296	2.1	2.5	
$\delta(\text{S-C-C})$	A'	365	314	8.5	2.6	328	281	1.9	6.6	371	319	3.7	0.6	345	296	2.1	2.5	
$\delta(\text{C-C=O})$	A'	307	262	3.8	0.7	293	249	4.5	0.6	245	206	2.0	3.2	259	219	4.4	4.5	
$\tau(\text{C-C})$	A''	262	221	1.4	0.2	265	224	0.2	<0.1	298	254	3.7	0.9	265	219	0.2	0.1	
$\delta(\text{C-S-C})$	A'	182	149	3.1	1.3	137	109	3.3	1.1	193	159	3.4	0.7	146	117	3.6	1.1	
$\tau(\text{C}_s\text{-C})$	A''	118	92	0.3	5.2	87	64	3.6	2.3	122	95	3.1	2.6	32	14	1.4	2.1	
$\tau(\text{S-C})$	A''	96	72	1.7	1.5	48	29	0.7	2.1	100	76	0.4	1.8	61	40	<0.1	1.5	
$\tau(\text{C-S})$	A''	69	48	3.8	3.3	125	98	2.0	4.5	32	14	1.8	3.7	131	103	4.2	2.8	

<sup>a</sup> Frequencies in  $\text{cm}^{-1}$ , IR intensities in  $\text{km mol}^{-1}$ , Raman scattering activities in  $\text{\AA}^4 \text{u}^{-1}$ ,  $\nu$ , Bond stretching;  $\delta$ , bending;  $\gamma$ , rocking;  $\omega$ , wagging;  $\tau$ , torsion. Calculated frequencies have been scaled using the linear equation  $\nu_{\text{scaled}} = 0.8996\nu_{\text{ab initio}} - 14.4$ . <sup>b</sup> When different bands are assigned to the same mode in different conformers, the ones originated in the less stable *anti* or *s-trans* conformers are marked with the symbols # or \*, respectively. <sup>c</sup> The  $\nu(\text{C}_s\text{-C})$  mode in the *s-cis* conformers gives rise to a Fermi resonance doublet (see text).

stretching modes of the *anti* forms, ascribed to the bands at  $962\text{ cm}^{-1}$  and  $664\text{ cm}^{-1}$ , respectively; the  $\delta(\text{CH}_2)$  bending mode of the *gauche* forms ( $1436\text{ cm}^{-1}$ ); and the low intensity Raman doublet of bands is  $1264\text{ cm}^{-1}$  and  $1243\text{ cm}^{-1}$ , ascribed to the  $\nu(\text{CH}_2)$  vibration in *gauche* and *anti* forms, respectively]. On the other hand, the calculations predict that the *s-trans* forms about the  $\text{C}=\text{C}=\text{O}$  axis are spectroscopically distinct from the corresponding *s-cis* conformers (Table 2). Indeed, comparison of calculated and observed IR spectra shown in Fig. 2 and 3 shows that bands at  $1676$ ,  $1410$ ,  $1170$  and  $946\text{ cm}^{-1}$  must be respectively assigned to the  $\nu(\text{C}=\text{O})$ ,  $\delta(\text{=CH}_2)$ ,  $\nu(\text{C}_\alpha-\text{C})$  and  $\omega(\text{=CH}_2)$  vibrations in the *s-trans* conformers. The *s-trans*  $\nu(\text{C}_\alpha-\text{C})$  stretching band at *ca.*  $1170\text{ cm}^{-1}$  is of note, as it corresponds to a very intense band appearing in a 'clean' spectral region (see Fig. 3). Indeed, this result gives further support to the conclusion presented in our previous study on *trans*-ETC,<sup>6</sup> where it is stressed that this band may be used as a probe of the presence of *s-trans* conformers of  $\alpha,\beta$ -unsaturated thioesters in more complex situations (for example, in enzyme active sites), since it is not expected that the  $\nu(\text{C}_\alpha-\text{C})$  stretching mode will change much in frequency within this family of molecules.

Both the experimental Raman and IR spectra obtained in hexane solution are fitted well by the calculations when the calculated spectra of *s-cis* and *s-trans* conformers are added with the *s-trans* spectra multiplied by a factor of  $1/2.25$  (Fig. 2–4). Assuming a Boltzman population distribution, the (*s-trans*)–(*s-cis*) energy difference may be estimated to be *ca.*  $2.0\text{ kJ mol}^{-1}$ . Although this estimation may have a substantial error considering that intrinsic band intensities may be significantly different in the isolated molecule situation and for the solution phases, the magnitude of the differences in energy found is large enough to enable us to conclude that the experimental data point to a considerably smaller energy difference between the two stable conformations about the  $\text{C}=\text{C}=\text{O}$  axis for ETA in solution than for the isolated molecule (*ca.*  $6\text{ kJ mol}^{-1}$ ). Note that this result follows the same trend as that previously reported for *trans*-ETC, where the influence of the polarity of the solvent on the conformational equilibrium was analysed and it was found that, as expected, more polar solvents tend to stabilize the more polar *s-trans* conformers.<sup>6</sup>

Also, as was found for *trans*-ETC, the experimental frequencies of  $\nu(\text{C}=\text{C})$  and  $\nu(\text{C}=\text{O})$  in ETA are significantly smaller than the calculated (scaled) values, pointing to an increased polarity of these bonds (less double bond character) owing to intermolecular interactions with the solvent. As expected, the red shift in frequency is considerably more pronounced for  $\nu(\text{C}=\text{O})$  than for  $\nu(\text{C}=\text{C})$  and, for the same mode, for the more polar *s-trans* conformers (Table 2). A solvent dependent effect can also be observed for  $\nu(\text{C}-\text{S})$  in both conformers, but this time leading to a blue shift. The observed increase of the frequency of this mode is also more pronounced for the more polar *s-trans* forms [ $\Delta\nu(\text{C}-\text{S})_{(\text{obs}-\text{calc})}$   $30\text{ cm}^{-1}$  in *s-trans* forms *vs.* *ca.*  $20\text{ cm}^{-1}$  in *s-cis* conformers].

Finally, it is also interesting to note that, as for other thioesters,<sup>22,23</sup> in ETA  $\nu(\text{S}-\text{C})$  is an essentially pure mode whichever conformer is considered [however, in the *gauche* forms this coordinate mixes somewhat with one of the  $\gamma(\text{CH}_3)$  rocking coordinates], while both  $\nu(\text{C}_\alpha-\text{C})$  and  $\nu(\text{C}-\text{S})$  are considerably mixed modes. Particularly relevant is the fact that  $\nu(\text{C}-\text{S})$  reduces its frequency by *ca.*  $100\text{ cm}^{-1}$  in going from the *s-cis* to the *s-trans*  $\text{C}=\text{C}=\text{O}$  axis conformation (*i.e.*, *s-cis*  $\rightarrow$  *s-trans* isomerization about the  $\text{C}_\alpha-\text{C}$  axis leads to a weakening of the  $\text{C}-\text{S}$  bond), since this result may be important to the analysis of the  $\alpha,\beta$ -unsaturated thioacyl-enzyme vibrational data.<sup>3–5</sup> The importance of this result is

underlined by the fact that the  $\text{C}-\text{S}$  bond is the catalytically relevant bond that undergoes cleavage during the deacylation step of the catalytic reaction,<sup>3–5</sup> as well as because the structural data do not reflect very clearly such a weakening of the  $\text{C}-\text{S}$  bond length upon conformation change (as discussed before, the changes with conformation of the relevant intramolecular interactions, which determine the bond lengths in the two stable conformations, partially compensate each other, leading to a  $\text{C}-\text{S}$  bond length in the *s-trans* form that is larger than in the *s-cis* conformer by only *ca.*  $0.4\text{ pm}$ ; Table 1).

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