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Conformational and vibrational analysis of *S*-(2-methoxyphenyl)-4-substituted-benzenecarbothioates, using X-ray, infrared and Raman spectroscopy and theoretical calculations

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Abstract

Structural and conformational properties of *S*-(2-methoxyphenyl) 4-nitrobenzenecarbothioate (**I**), *S*-(2-methoxyphenyl) 4-chlorobenzenecarbothioate (**II**) and *S*-(2-methoxyphenyl) 4-methylbenzenecarbothioate (**III**) are analyzed using data of two new structures obtained from X-ray diffraction, vibrational data and theoretical calculations. According to chemical quantum calculations, the synperiplanar and +anticlinal forms were found as the first and second more stable conformations, respectively, for the title compounds. The geometric parameters and normal modes of vibration have been calculated using a density functional theory method (B3LYP) and the 6-31+G** basis set. The calculated parameters are in good agreement with the corresponding X-ray diffraction values. The combined experimental and theoretical approach allows a consistent assignment for most of the fundamental modes.

Keywords: X-ray structure; Thiol esters; Structural analysis; Vibrational analysis; DFT

1. Introduction

Our interest in the conformational and vibrational properties of thiol ester compounds of the type XC(O)SY is in part due to the antiviral activity against HIV-1 virus [1,2], and because of their structural connection with biological systems such as acetyl coenzyme A and malonyl coenzyme A. The thiol ester compounds may act as intermediary metabolites of carboxilate-containing drugs. In fact, many steroidal anti-inflammatory agents may form *S*-acyl-coA thiol esters *in vivo*. In general, *S*-acyl-coA and reduced glutathione GSH play an important role against free radicals and are emerging as potentially significant intermediates in the metabolism of acidic drugs. These thiol esters may represent latent drug forms that may be reactivated *via* hydrolysis [3].

Furthermore, it has been broadly reported that thiol esters (sulfenyl carbonyl compounds) possess planar configurations around the δ(C(O)—SY) dihedral angle, with the possibility of conformational equilibria between synperiplanar ($\delta(C(O)—SY)=0°$) and antiperiplanar ($\delta(C(O)—SY)=180°$) conformations (see Fig. 1). It has been observed that

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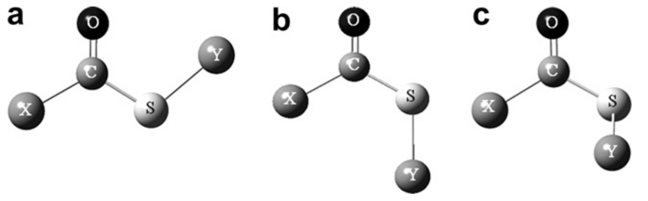


Fig. 1. Synperiplanar (a), antiperiplanar (b) and +anticlinal (c) forms for sulfenyl carbonyl compounds.

the synperiplanar form is the most stable conformation for both organic and inorganic molecules [4].

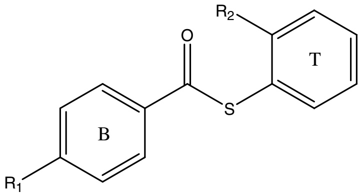
In this paper we report the crystal structures of *S*-(2-methoxyphenyl)-4-nitrobenzenecarbothioate (**I**) and *S*-(2-methoxyphenyl)-4-chlorobenzenecarbothioate (**II**), while the crystal structure of *S*-(2-methoxyphenyl)-4-methylbenzenecarbothioate (**III**) is included for the sake of comparison [5].

The geometric parameters and vibrational frequencies for compounds **I**–**IV** (see Fig. 2) have been calculated using the B3LYP/6-31+G** level of approximation. Linked with this analysis we report a comparative study of the infrared and Raman spectra of the compounds **I**–**III**. The calculated spectra afford a basis for the assignments of the experimental infrared and Raman bands. The comparison between theoretical and experimental parameters assists in the determination of intra- or inter-molecular interactions of the free molecules or in the packed molecules, respectively.

2. Experimental

Compounds **I**, **II** and **III** have been obtained according to preparation procedures reported in the literature [5]. Infrared spectra of the compounds **I**, **II** and **III** in KBr pellets were measured between 4000 and 400 cm^{-1} (2 cm^{-1} resolution) with a Thermo-Nicolet IR200 FT-IR spectrometer. Raman spectra between 3500 and 150 cm^{-1} were recorded using a FT Bruker IFS85 spectrometer (spectral resolution 4 cm^{-1}). The 1064-nm radiation line of a Nd/YAG laser was used for excitation. The samples were handled in Pyrex capillaries at room temperature.

Colorless crystals from **I** and **II** have been obtained by slow evaporation from a tetrahydrofuran solution. Single crystal X-ray diffraction data were collected on an Enraf-Nonius CAD4 diffractometer (graphite monochromatic CuKα radiation, $\lambda = 1.54184$ Å) with EXPRESS [6] and reduced with XCAD4 [7]. Both data were corrected for absorption with PLATON [8]. The structures were solved by direct and Fourier methods with SHELXS [9] and its non-H atoms were refined by full-matrix least-squares with SHELXL [10]. The hydrogen atoms of both substances were positioned stereo-chemically and refined with the riding model. The methyl H-atom positions were optimized by treating them as rigid groups which were allowed to rotate around the corresponding C—C bonds during the refinement. As expected, they converged to staggered positions. Crystal data and structure refinement parameters for compounds **I** and **II** are summarized in Table 1. Fig. 3 shows ORTEP [11] drawings of these molecules. CIF files coded CCDC 617494 and CCDC 617493 contain the supplementary crystallographic data of both compounds. These data can be obtained free of charge upon request.



Compound	R$_1$	R$_2$
I	NO$_2$	OCH$_3$
II	Cl	OCH$_3$
III	CH$_3$	OCH$_3$
IV	H	H

Fig. 2. Studied compounds and classification of aromatic rings as B (benzoate) and T (thiophenyl) used in the vibrational assignment (Table 3).

Quantum chemical calculations were carried out with GAUSSIAN 98 [12] program package, implemented on a personal computer. The potential curves for internal rotation around the C1—S and S—C21 bonds were calculated for compounds **I**–**IV** employing the HF/6-31G approximation with structure optimizations for the torsional angles performed in steps of 30° except near the minimum where the optimizations were performed in steps of 10°.

The geometric structures for the more stable conformers were subsequently calculated at the B3LYP/6-31+G** level of approximation and the same method was used to determine the vibration mode frequencies of all **I**–**III** free molecules. Assignment of vibration modes was obtained by visual inspection of atomic displacement vectors.

The calculations were performed for molecules in vacuum and therefore environmental effects were not considered.

3. Results and discussion

3.1. Crystal structure analysis

For the synperiplanar rotamer of sulfenyl carbonyl compounds (Fig. 1) a value of 0° would be expected for the dihedral angle δ(C(O)—SY) according to the reported study on the conformational transferability of sulfenyl carbonyl compounds [13]. Values of 1.04°, 3.56° and 4.50° were found from the crystal structures of **I**, **II** and **III**, respectively. These results are in agreement with corresponding values reported in the literature for the torsional angle of *S*,*S*-[sulfonylbis(1,4-phenylene)]di(thiobenzoate) [14].

The bond distances between S and C1, 1.778(2) Å for (**I**), 1.778(3) Å for (**II**) and 1.789(3) Å for (**III**), are longer than those between S and C21, 1.766(2) Å for (**I**), 1.760(3) Å for (**II**) and 1.772(3) Å for (**III**), and are in agreement with the crystal structural data of *S*,*S*-[sulfonylbis(1,4-phenylene)]di(thiobenzoate) [14]. The opposite, however, has been observed in the crystalline structure of a similar compound where both phenyl groups are substituted in the *para* position [15]. In both bonds the hybridization of the C atom is sp^2. This family can not be compared with other thiol esters of the type XC(O)SR where R is an alkyl group. The S—C bond distance is dependent on the hybridization of the