

***Ab initio* SCF study of geometry and internal barriers to rotation of thiocarbamic *S*-acid and some of its derivatives**

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Dedicated to Professor L. Valko, DrSc., in honour of his 60th birthday

The *ab initio* SCF method was applied to determine the equilibrium geometry of the following thiocarbamate-containing molecules: thiocarbamic *S*-acid, *N*-methylthiocarbamic *S*-acid, *N*-vinylthiocarbamic *S*-acid, *S*-methyl thiocarbamate, *S*-methyl *N*-methylthiocarbamate, and *S*-methyl *N*-vinylthiocarbamate. Energy barriers to rotation about the C—N bond (calculated at the STO-3G level of theory) lie in the range of 50—60 kJ mol⁻¹. The structural and energetic parameters calculated were compared and discussed with the analogous data for carbamic acid and its sulfur isologues.

Применены *ab initio* расчетные методы для изучения геометрии следующих тиокарбаматную группу содержащих молекул: тиокарбаминовой *S*-кислоты, *N*-метилтиокарбаминовой *S*-кислоты, *N*-винилтиокарбаминовой *S*-кислоты, метилового эфира тиокарбаминовой *S*-кислоты, метилового эфира *N*-метилтиокарбаминовой *S*-кислоты и метилового эфира *N*-винилтиокарбаминовой *S*-кислоты. На уровне STO-3G вычисленные значения энергетических барьеров вращений вокруг C—N связи находятся в промежутке 50—60 кДж моль⁻¹. Вычисленные структурные и энергетические параметры были сравнены и дискутированы с аналогичными данными для карбаминовой кислоты и ее сульфурных изологов.

The replacement of either of the oxygen atoms of esters with sulfur profoundly modifies the abilities of such compounds to undergo enzymic and nonenzymic reactions [1]. This substitution is of biological relevance since certain esters and thiol esters can play extremely important roles in biochemical processes. The structurally related carbamate group occurs in biologically active compounds [2] such as local anaesthetics, anticonvulsants, sedatives, hypnotics, and muscle relaxants. Similarly, esters of *N*-substituted thiocarbamic *S*-acid, thiocarbamic *O*-acid and dithiocarbamic acid, respectively, show various pharmacological activities such as antibacterial, antifungal, antiviral, herbicidal, local anaesthetic, tuberculostatic, anticholinergic and antidotal [2—5].

With regard to structure, *ab initio* SCF structures have been solved for a number of carbamates [6, 7], thiocarbamate [8], and dithiocarbamates [9]. The

present paper reports on the systematic theoretical treatment of the thiocarbamic *S*-acid group. Of particular interest are details of the molecular geometries, the barriers to rotation, the hydrogen bonds and how these properties are affected by various degrees of substitution. Further, the effects of the isosteric substitution of the oxygen atoms in the carbamic acid by sulfur on the properties of the carbamate group are also examined.

Calculation method

Geometries of thiocarbamic, *N*-methylthiocarbamic, and *N*-vinylthiocarbamic *S*-acids, *S*-methyl thiocarbamate, *S*-methyl *N*-methylthiocarbamate, and *S*-methyl *N*-vinylthiocarbamate have been totally optimized using the gradient procedures contained within the program and the STO-3G (Ref. [10]) basis set. Some calculations were also carried out with the extended 3-21G basis [11]. The C_s symmetry was considered during the optimization of the geometry of the compounds studied.

The barrier to rotation about the C—N bond in each molecule was evaluated as the difference in energy between the planar equilibrium geometry and the structure optimized with the dihedral angle Φ held fixed at 90° (maximum on the potential energy curve of the rotation around the C—N bond). The atom numbering scheme used for each of the molecules studied is presented in Fig. 1.

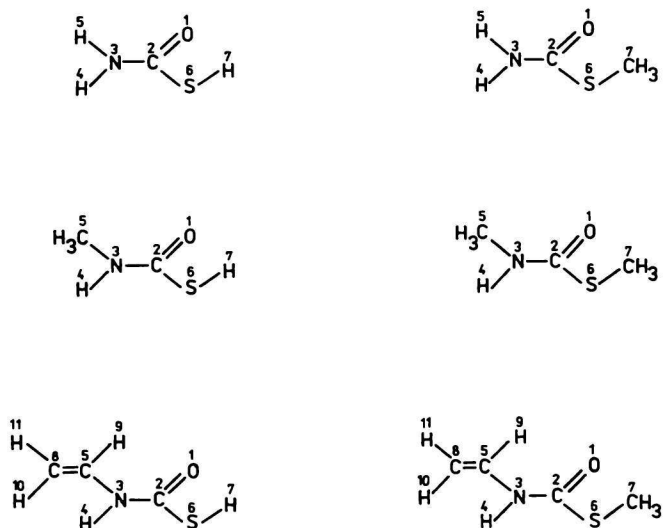


Fig. 1. Numbering scheme used for atoms. Thiocarbamic *S*-acids are depicted in their *trans* configurations as are all the esters.

Ab initio calculations were carried out with the aid of the GAUSSIAN 80 package of computer codes [12].

Results and discussion

Geometry

The optimized geometries of the thiocarbamic, *N*-methylthiocarbamic, and *N*-vinylthiocarbamic *S*-acids are summarized in Table 1. The thiol hydrogen may adopt positions either *trans* or *cis* to the nitrogen atom. The geometry of both isomers of the acids studied was optimized. The comparison of internal geometrical parameters for *trans* and *cis* species of thiocarbamic *S*-acid shows (Table 1) some differences. Both C-2—N-3 and C-2—S-6 lengths are longer in the *cis* form. Most prominent of the angular changes are increases of 1–5° in $\Theta(\text{C-2—N-3—H-4})$, $\Theta(\text{N-3—C-2—S-6})$, and $\Theta(\text{C-2—S-6—H-7})$, all of which may be attributed to steric repulsion between H-4 and the thiocarboxylic hydrogen in the *cis* geometry.

In order to illustrate the effects upon the geometry of bond rotation, the geometries optimized for thiocarbamic *S*-acid with the dihedral angle $\Phi(\text{H-4—N-3—C-2—O-1}) = 90^\circ$ have also been listed in Table 1. Those conformers represent the transition state for the rotation about the C—N bond. The disruption of the conjugation between the C—N and C=O bonds in the orthogonal structures is in both cases accompanied by the considerable lengthening of the central C—N bond (4.9 and 4.6 pm, respectively) and shortening in the C=O bond (0.9 pm). As to the bond angles, the most marked changes are observed for the C-2—N-3—H-4, C-2—N-3—H-5, and C-2—S-6—H-7 angles, respectively.

The effect of basis set extension on the computed internal parameters of *trans* and *cis* thiocarbamic *S*-acids was also studied (Table 1). The O-1—C-2 and C-2—N-3 lengths were calculated shorter and C-2—S-6 and S-6—H-7 distances longer with the 3-21G basis than with the STO-3G one. Most of the bond angles appear rather insensitive to the basis set, lying within 1° or 2° of one another. One exception is the N-3—C-2—O-1 angle where the basis set enlargement leads to the considerable increase in the angle (Table 1).

The replacing of one N—H hydrogen by methyl and vinyl groups, respectively, has only slight effect on the geometry of the thiocarbamate group. The only appreciable change is a reduction in C-2—N-3—H-4 angle by some 3°. The N-3—C-5 distance was calculated much shorter (4.3 pm) in the vinyl derivative than for the methyl substituent. In addition to the *trans* conformers of *N*-methylthiocarbamic and *N*-vinylthiocarbamic *S*-acid, respectively, illustrated

Table 1

Optimized bond lengths (r /pm) and angles (Θ /°) of the studied compounds

Parameter	<i>trans</i> NH ₂ C(O)SH ^a			<i>cis</i> NH ₂ C(O)SH ^a			<i>trans</i> CH ₃ NHC(O)SH ^a	<i>trans</i> CH ₂ CHNHC(O)SH ^a
	STO-3G	3-21G	3-21G ($\Phi = 90^\circ$)	STO-3G	3-21G	3-21G ($\Phi = 90^\circ$)	STO-3G	STO-3G
$r(\text{O-1—C-2})$	121.9	120.2	119.3	121.9	120.0	119.1	121.9	121.8
$r(\text{C-2—N-3})$	140.7	134.1	139.0	141.3	134.6	139.2	141.0	142.1
$r(\text{N-3—H-4})$	101.4	99.5	99.7	101.3	99.3	99.7	101.7	101.9
$r(\text{N-3—H-5})$	101.5	99.9	99.7	101.5	99.9	99.7	—	—
$r(\text{N-3—C-5})$	—	—	—	—	—	—	146.3	142.0
$r(\text{C-2—S-6})$	179.0	187.6	186.8	179.5	187.9	188.0	179.1	178.8
$r(\text{S-6—H-7})$	133.0	134.8	135.1	133.0	135.1	134.7	133.0	133.0
$r(\text{C-5—H-9})$	—	—	—	—	—	—	—	108.6
$r(\text{C-5—C-8})$	—	—	—	—	—	—	—	131.2
$r(\text{C-8—H-10})$	—	—	—	—	—	—	—	107.9
$r(\text{C-8—H-11})$	—	—	—	—	—	—	—	107.8
$r(\text{C-5—H})$	—	—	—	—	—	—	109.1	—
$\Theta(\text{N-3—C-2—O-1})$	123.1	127.1	127.9	121.8	126.2	127.5	123.3	122.9
$\Theta(\text{C-2—N-3—H-4})$	122.0	122.6	120.4	123.4	123.9	120.4	119.3	119.0
$\Theta(\text{C-2—N-3—H-5})$	119.6	118.5	120.3	118.8	117.7	120.3	—	—
$\Theta(\text{C-2—N-3—C-5})$	—	—	—	—	—	—	122.4	122.5
$\Theta(\text{N-3—C-2—S-6})$	112.1	111.1	111.4	115.5	115.0	114.8	112.0	111.9
$\Theta(\text{C-2—S-6—H-7})$	94.2	94.9	97.5	95.7	99.8	97.3	94.2	94.1
$\Theta(\text{N-3—C-5—H-9})$	—	—	—	—	—	—	—	112.4
$\Theta(\text{N-3—C-5—C-8})$	—	—	—	—	—	—	—	124.9
$\Theta(\text{C-5—C-8—H-10})$	—	—	—	—	—	—	—	122.2
$\Theta(\text{C-5—C-8—H-11})$	—	—	—	—	—	—	—	120.9
$\Theta(\text{N-3—C-5—H})$	—	—	—	—	—	—	110.3	—
$-E^{\text{SCF}}/\text{a.u.}^b$	559.8796	563.5450	563.5160	559.8747	563.5379	563.5122	598.4595	635.8266

a) Relative to N atom; b) 1 a.u. = 2625.5 kJ mol⁻¹.

Table 2

Hydrogen bond energies (kJ mol⁻¹) in some isosteric derivatives of carbamic acid

Compound	NH ₂ COOH	NH ₂ C(S)OH	NH ₂ CSSH	NH ₂ C(O)SH
3-21G//3-21G	44.7	53.3	18.6	18.7

in Fig. 1, it is also reasonable to presume a structure in which the NH group hydrogen is *cis*-oriented with respect to the oxygen atom (the dihedral angle $\Phi(\text{H-4-N-3-C-2-O-1}) = 0^\circ$). Optimization of the latter structures, however, yielded conformers higher in energy than the *trans* geometry by 6.8 and 5.6 kJ mol⁻¹ for *N*-methyl and *N*-vinyl derivatives, respectively.

Our calculations suppose (Table 1) that the *trans* form (dihedral angle $\Phi(\text{N-3-C-2-S-6-H-7}) = 180^\circ$) is more stable than the *cis* isomer. For the higher stability of the *trans* structure in comparison with the *cis* one, the intramolecular hydrogen bond S—H...O is mainly responsible. The 3-21G energies of such hydrogen bonds, calculated as the energy difference between *cis* and *trans* isomers, are contained in Table 2. For reasons of comparison the hydrogen bonds of the corresponding oxygen and sulfur isologues (taken from papers [6–9]) are also shown in this table. The proton donor hydroxyl group forms with both proton acceptor atoms (the oxygen and sulfur) substantially stronger intramolecular hydrogen bonds than the thiol group. This corresponds to the observation that the O—H groups form stronger hydrogen bonds as compared with the S—H groups [13].

The optimized geometries of *S*-methyl thiocarbamate, *S*-methyl *N*-methylthiocarbamate and *S*-methyl *N*-vinylthiocarbamate are given in Table 3. In keeping with results for the acids the *trans* orientation about the C—S bond is used for these esters, *i.e.* $\Phi(\text{N-3-C-2-S-6-C-7}) = 180^\circ$. The carbonyl C=O group and the NH group of the thiocarbamate moiety may adopt both *cis* or *trans* positions. As our calculations have shown the *trans* forms (the dihedral angle $\Phi(\text{O-1-C-2-N-3-H-4}) = 180^\circ$) are by 7.3 and 6.2 kJ mol⁻¹ more stable (for methyl and vinyl substituents, respectively). Comparison with *trans* thiocarbamic *S*-acid in Table 1 indicates that the esterification does not essentially affect the bond lengths and angles. The replacing of one N—H hydrogen by methyl and vinyl groups results in more marked changes of the geometry of thiocarbamate group. The lengths C-2—N-3 and N-3—H-4 are predicted to be slightly elongated (by about 0.3–1.5 pm) and the angle C-2—N-3—H-4 reduced by some 3° (Table 3) by the comparison with the unsubstituted thiocarbamic *S*-acid (Table 1).

Table 3

STO-3G optimized bond lengths (r/pm) and angles ($\theta/^\circ$) of *S*-methyl thiocarbamate, *S*-methyl *N*-methylthiocarbamate, and *S*-methyl *N*-vinylthiocarbamate

Parameter	$\text{NH}_2\text{C}(\text{O})\text{SCH}_3$	$\text{CH}_3\text{NHC}(\text{O})\text{SCH}_3$	$\text{CH}_2\text{CHNHC}(\text{O})\text{SCH}_3$
$r(\text{O}-1-\text{C}-2)$	121.9	121.9	121.8
$r(\text{C}-2-\text{N}-3)$	140.8	141.1	142.2
$r(\text{N}-3-\text{H}-4)$	101.4	101.7	101.8
$r(\text{N}-3-\text{H}-5)$	101.5	—	—
$r(\text{N}-3-\text{C}-5)$	—	146.2	142.0
$r(\text{C}-2-\text{S}-6)$	179.0	179.1	178.8
$r(\text{S}-6-\text{C}-7)$	179.8	179.8	179.9
$r(\text{C}-5-\text{H})$	—	109.1	—
$r(\text{C}-7-\text{H})$	108.6	108.6	108.6
$r(\text{C}-5-\text{H}-9)$	—	—	108.6
$r(\text{C}-5-\text{C}-8)$	—	—	131.2
$r(\text{C}-8-\text{H}-10)$	—	—	107.9
$r(\text{C}-8-\text{H}-11)$	—	—	107.7
$\theta(\text{N}-3-\text{C}-2-\text{O}-1)$	122.9	123.2	122.7
$\theta(\text{C}-2-\text{N}-3-\text{H}-4)$	121.9	119.3	119.0
$\theta(\text{C}-2-\text{N}-3-\text{H}-5)$	119.8	—	—
$\theta(\text{C}-2-\text{N}-3-\text{C}-5)$	—	122.5	122.5
$\theta(\text{N}-3-\text{C}-2-\text{S}-6)$	111.8	111.7	111.7
$\theta(\text{C}-2-\text{S}-6-\text{C}-7)$	97.7	97.7	97.7
$\theta(\text{S}-6-\text{C}-7-\text{H})$	110.6	110.4	110.5
$\theta(\text{N}-3-\text{C}-5-\text{H})$	—	110.6	—
$\theta(\text{N}-3-\text{C}-5-\text{H}-9)$	—	—	112.4
$\theta(\text{N}-3-\text{C}-5-\text{C}-8)$	—	—	124.9
$\theta(\text{C}-5-\text{C}-8-\text{H}-10)$	—	—	122.2
$\theta(\text{C}-5-\text{C}-8-\text{H}-11)$	—	—	120.9
$-E^{\text{SCF}}/\text{a.u.}^a$	568.4655	637.0454	674.4127

a) 1 a.u. = 2625.5 kJ mol⁻¹.

Internal barriers to rotation

Barriers to the hindered rotation about the central C—N bond in the substituted derivatives of thiocarbamic *S*-acid studied are reported in Table 4. In order to determine the influence of the isosteric substitution of sulfur for oxygen in thiocarbamic *O*-acid and dithiocarbamic acid on the internal barriers to rotation the energy barriers for those compounds are also contained in Table 4.

A considerably higher barrier to rotation emerges for the *trans* form of thiocarbamic *S*-acid (Table 4). The esterification has negligible effect on the

Table 4

Calculated barriers to rotation (kJ mol^{-1})

Compound	STO-3G//STO-3G	3-21G//3-21G
NH_2COOH^a	57.1	88.6
$\text{NH}_2\text{C(O)SH}^a$	58.0	76.2
$\text{NH}_2\text{C(S)OH}^a$	76.4	125.2
NH_2CSSH^a	76.8	114.2
$\text{NH}_2\text{C(O)SH}^b$	49.5	67.6
$\text{NH}_2\text{C(O)SCH}_3$	57.6	
$\text{CH}_3\text{NHC(O)SH}^a$	62.3	
$\text{CH}_2\text{CHNHC(O)SH}^a$	54.7	
$\text{CH}_3\text{NHC(O)SCH}_3$	61.8	
$\text{CH}_2\text{CHNHC(O)SCH}_3$	54.2	

a) *trans* conformer; b) *cis* conformer.

height of barrier to rotation in the *trans* thiocarbamic S-acid. On the other hand, a significant increase up to 5 kJ mol^{-1} is associated with methyl substitution on the N atom. The methyl group, by means of its hyperconjugation effect, stabilizes the planar conformation in comparison with the orthogonal structure. If instead of a methyl group, a vinyl group is bounded to the nitrogen, the barrier height decreases by some 4 kJ mol^{-1} . The decrease of barrier to rotation in vinyl derivatives is obviously due to the weakening of conjugation between the C—N and C=O bonds. This was also reflected in the computed C—N distance. This distance was calculated about 1.5 pm longer in the vinyl derivatives than in the thiocarbamic S-acid (Tables 1 and 3).

The comparison of the barrier to rotation for the carbamic acid and its thio-substituted isologues shows some differences. The structures containing the —NHC=O fragment possess lower energy barriers than the corresponding thio derivatives —NHC=S (Table 4). The replacement of the oxygen of the hydroxyl group for sulfur in thiocarbamic S-acid has much smaller effect on the computed height of the barrier to rotation. Comparing the two basis sets, extension of the basis set leads to an enlargement in the computed barrier. However, the calculations of the compounds investigated were carried out (due to the limited operating capacity of EC 1045 computer system applied) using unpolarized STO-3G basis set and the inclusion of *d*-polarization functions for sulfur may greatly improve the accuracy of the energy barriers predictions.

Direct measurement of hindered rotation about the N—C bond in carbamates and their sulfur isologues is particularly difficult, with the results highly sensitive to the experimental conditions, methods used, and procedures for data interpretation [14—21]. Published values of the activation enthalpy for rotation

of carbamates and thiocarbamates are also very high (45–95 kJ mol⁻¹). Our calculated barriers to rotation using the extended 3-21G basis set are somewhat higher (Table 4), however, the direct comparison is very difficult because theoretical barriers correspond to the vapour state and experimental to the condensed phase. Of particular relevance would be a measurement of the barrier to rotation in the gas phase.

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