Ab initio study of geometry and internal rotational barriers of silacarbamic acid and several derivatives

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Ab initio SCF method (STO-3G basis) has been used to determine equilibrium geometry in silacarbamic acid, methyl silacarbamate, ethyl silacarbamate, *N*-methylsilacarbamic acid, and methyl *N*-methylsilacarbamate. Rotational barriers for the rotation about the N—Si bond have been computed. At the STO-3G level, the calculated barriers lie in the range of 20—30 kJ mol^{-1} These energy barriers are progressively higher as the basis set is enlarged. The changes in gross atomic charges of silacarbamate group upon methyl substitution, resulting from the STO-3G *ab initio* calculations of silacarbamates studied, were also investigated.

Для определения равновесной геометрии силакарбаминовой кислоты, метилсилакарбамата, этилсилакарбамата, *N*-метилсилакарбаминовой кислоты и метил-*N*-метилсилакарбамата использован *ab initio* ССП метод (с базисным набором STO-3G). Рассчитаны значения вращательных барьеров для вращения вокруг связи N—Si. В рамках STO-3G рассчитанные значения находятся в промежутке 20—30 кДж моль$^{-1}$ Эти значения энергетических барьеров значительно повышаются при расширении базисного набора. Также исследуются изменения полных атомных зарядов силакарбаматной группы после метилирования, определенные с помощью STO-3G *ab initio* расчетов изучаемых силакарбаматов.

The replacement of the carbon atom in the functional group of drug with the silicon represents one of the possible isosteric substitutions leading to the considerable modification of biological activity of such compounds [1]. Isosteric groups find great application in pharmaceutical chemistry, especially in the design of new drugs [2, 3].

In connection with the investigations of the mechanism of action of local anesthetic carbamates [4], the deeper structural study of the influence of the substituents on the geometry of carbamic moiety has been performed [5, 6]. The substitution of the central carbon atom with the silicon in the carbamic acid and its derivatives can significantly influence its structural and electronic characteristics and modify the biological activity of the silicon isologues of carbamate drugs. To our knowledge, no X-ray or electron diffraction measurements of the structure of silacarbamic acid and its methyl and ethyl derivatives are available.

Therefore, the present paper brings the strength of *ab initio* calculations to bear on the problem. First the various species of silacarbamic acid were studied. The effect of progressive methyl and ethyl substitution consecutively to methyl and ethyl silacarbamate, *N*-methylsilacarbamic acid and methyl *N*-methylsilacarbamate is also investigated.

Calculation method

The geometry of silacarbamic acid, methyl and ethyl silacarbamate, *N*-methylsilacarbamic acid and methyl *N*-methylsilacarbamate has been completely optimized by using the gradient optimization method [7] and the minimal STO-3G (Ref. [8]) basis. Some calculations were also carried out with the larger 3-21G (Ref. [9]) basis. The C_s symmetry was considered during the optimization of the geometry of the compounds studied. The rotational barrier for the rotation about the N—Si bond in all molecules was determined as an energy difference between the planar equilibrium geometry and the structure with the fixed dihedral angle Φ equal to 90° The numbering of atoms for eacn compound studied is shown in Fig. 1. All calculations were performed on an EC 1045 computer at the Computing Centre of the Comenius University using the GAUSSIAN 80 program [10].

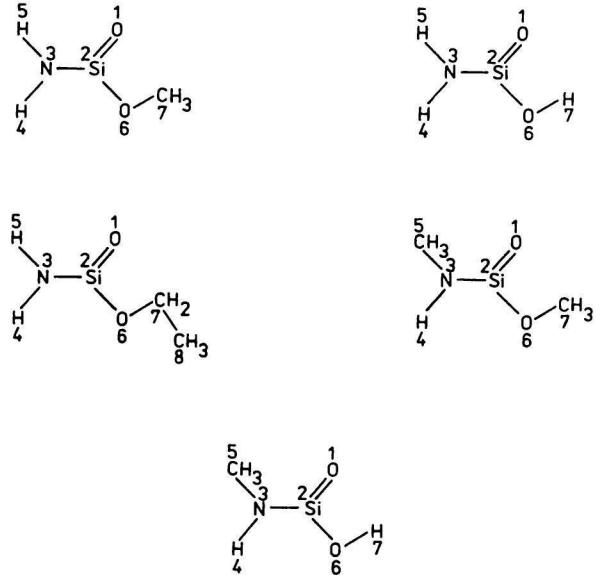

Fig. 1. Numbering scheme used for atoms. Silacarbamic acid is depicted in its *trans* configurations as are all the derivatives.

Results and discussion

Geometry

Silacarbamic acid

The hydroxyl hydrogen may adopt positions either *cis* or *trans* to the nitrogen atom. The optimized geometries of both *cis* and *trans* silacarbamic acid are presented in Table 1. We note first that the Si=O and Si—N bonds were calculated longer and the Si—O bond shorter with the 3-21G basis in comparison with the STO-3G basis set. The N—H bonds involving hydrogen atoms are approximately 1 pm longer with the minimal basis set. On the other hand, STO-3G O—H bond lengths are about 2 pm shorter than the 3-21G values. Most of the valence angles calculated appear rather insensitive to the basis set used, lying within 1° or 2° of one another. One exception is the Si—O—H angle where the basis set enlargement leads to the considerable increase in the angle (Table 1).

Table 1

Optimized bond lengths (r/pm) and angles (Θ/°) of *trans* and *cis* silacarbamic acid

Parameter	*trans*[a]			*cis*[a]		
	STO-3G	3-21G	3-21G (Φ = 90°)	STO-3G	3-21G	3-21G (Φ = 90°)
r(Si-2—O-1)	152.6	154.9	154.9	152.4	154.7	154.7
r(Si-2—N-3)	167.4	168.7	170.2	168.3	169.7	171.2
r(Si-2—O-6)	165.6	163.5	163.8	165.6	162.5	163.4
r(N-3—H-4)	101.2	99.9	99.9	101.3	99.9	100.1
r(N-3—H-5)	101.1	99.9	99.9	101.2	100.0	100.1
r(O-6—H-7)	98.3	95.8	95.9	98.4	95.4	95.7
Θ(N-3—Si-2—O-1)	129.1	128.7	128.2	126.6	126.1	127.0
Θ(Si-2—N-3—H-4)	123.6	122.8	123.2	125.8	125.5	123.3
Θ(Si-2—N-3—H-5)	123.8	122.7	123.2	122.5	121.2	123.5
Θ(N-3—Si-2—O-6)	104.6	106.2	110.8	108.2	109.8	112.0
Θ(Si-2—O-6—H-7)	108.7	127.7	126.5	110.0	138.1	131.3
$-E^{SCF}$/a. u.[b]	488.7299	492.2545	492.2414	488.7254	492.2455	492.2357

a) Relative to N atom; *b*) 1 a. u. = 2625.5 kJ mol^{-1}.

The comparison of internal geometrical parameters for *trans* and *cis* species of silacarbamic acid shows (Table 1) some differences. Both Si=O and Si—N lengths are longer in the *trans* form. The Si—O distance is, however, longer in the *cis* isomer. The transition *trans* → *cis* silacarbamic acid is manifested with the important changes in the valence angles. The angles N-3—Si-2—O-1 and

Si-2—N-3—H-5 decreased and the others increased in the *cis* form in comparison to the *trans* isomer. Larger changes in the angles N-3—Si-2—O-1, N-3—Si-2—O-6, and Si-2—O-6—H-7 are due to the steric repulsion between hydrogen atoms in the *cis* silacarbamic acid.

In order to determine the effect of the bond rotation on the geometrical parameters, the equilibrium geometries of the orthogonal conformers of *trans* and *cis* silacarbamic acid (the dihedral angle H-4—N-3—Si-2—O-1 = 90°) are also shown in Table 1. Those conformers represent the transition state for the rotation about the N—Si bond. The disruption of the conjugation between Si—N and Si=O bonds in the orthogonal structures is in both cases accompanied by the lengthening of the central Si—N bond and the increase of the N-3—Si-2—O-6 angle. The other internal parameters do not change noticeably upon rotation.

Our calculations suppose (Table 1) that the *trans* form is more stable than the *cis* isomer. This is consistent with the similar calculations for carbamic acid [5] and thiocarbamic acid [11]. The higher stability of the *trans* silacarbamic acid may be ascribed to the existence of an intramolecular hydrogen bond in this isomer. The energy difference between *cis* and *trans* forms may be considered as the energy of that intramolecular hydrogen bond. The value of 23.5 kJ mol^{-1} has been found from the 3-21G calculations. However, in comparison with the carbamic acid [5] ($E_{cis} - E_{trans} = 44.7$ kJ mol^{-1}, the 3-21G//3-21G calculation) this H-bond is substantially weaker.

Methyl and ethyl silacarbamate

The optimized geometries of methyl and ethyl silacarbamate are given in Table 2. According to our results for the silacarbamic acid, the *trans* orientation about the Si—O bond is used for these esters, *i.e.* dihedral angle N-3—Si-2—O-6—C-7 = 180°. The supposition of lowest energy for the *trans* form has been also confirmed by our STO-3G calculations for methyl silacarbamate, in which the *trans* geometry was found to be 30.4 kJ mol^{-1} more stable.

The overall comparison of calculated geometries for the methyl and ethyl silacarbamate (Table 2) shows that the geometrical parameters are nearly identical to one another. The methyl (or ethyl) substitution of *trans* silacarbamic acid brings a slight lengthening of the Si-2—N-3 and Si-2—O-6 bonds (by 0.1 and 0.3 pm, respectively) and decrease of the N-3—Si-2—O-6 valence angle (Tables 1 and 2).

The 90° rotation about the Si—N bond is accompanied by the significant lengthening of this bond in both methyl and ethyl silacarbamate. The bonds Si=O and Si—N are slightly shorter and the angle N-3—Si-2—O-6 is considerably larger (4.6°) in the orthogonal conformers (Table 2).

Table 2

STO-3G optimized bond lengths (r/pm) and angles (Θ/°) of methyl and ethyl silacarbamate

Parameter	Methyl silacarbamate		Ethyl silacarbamate	
	Planar	Orthogonal	Planar	Orthogonal
r(Si-2—O-1)	152.5	151.3	152.5	151.3
r(Si-2—N-3)	167.5	168.8	167.5	168.9
r(Si-2—O-6)	165.9	165.7	165.9	165.7
r(N-3—H-4)	101.2	101.1	101.2	101.1
r(N-3—H-5)	101.1	101.1	101.2	101.1
r(O-6—C-7)	142.6	142.6	142.8	142.8
r(C-7—H)	109.5	109.5	109.8	109.8
r(C-7—C-8)			154.5	154.5
r(C-8—H)			108.6	108.6
Θ(N-3—Si-2—O-1)	129.1	129.1	128.8	128.8
Θ(N-3—Si-2—O-6)	103.7	108.3	103.9	108.5
Θ(Si-2—N-3—H-4)	123.6	123.9	123.7	123.9
Θ(Si-2—N-3—H-5)	123.7	123.9	123.7	123.9
Θ(Si-2—O-6—C-7)	116.2	116.2	116.5	116.6
Θ(O-6—C-7—H)	111.4	111.4	111.7	111.7
Θ(O-6—C-7—C-8)			108.8	108.8
Θ(C-7—C-8—H)			110.3	110.3
$-E^{SCF}$/a. u.	527.3095	527.2986	565.8936	565.8826

N-Methylated derivatives

The effect of replacing NH hydrogen in both silacarbamic acid and methyl silacarbamate is shown in Table 3. *N*-Methylation of silacarbamic acid brings about lengthening of the Si-2—N-3 and Si-2—O-6 bonds. As to the bond angles, the Si-2—N-3—H-4 and O-1—Si-2—N-3 angles exhibit the highest changes (Tables 1 and 3). Comparison of the methyl *N*-methylsilacarbamate (Table 3) with the methyl silacarbamate in Table 2 indicates subtle changes in geometry caused by single methyl substitution. Both the Si-2—N-3 and N-3—H-4 lengths were calculated longer (0.6 and 0.4 pm) and the angles O-1—Si-2—N-3 and Si-2—N-3—H-4 lower than in the methyl silacarbamate.

In the case of methyl *N*-methylsilacarbamate it is also reasonable, in addition to the *trans* conformer illustrated in Fig. 1, to presume the existence of structure in which the *O*-methyl group is *cis*-oriented with respect to the nitrogen. Optimization of this structure yielded a conformer which is only by 0.4 kJ mol^{-1} less stable. Based on the energies computed for these two most stable conformers, the equilibrium distribution 51 : 49 has been calculated (at 298.2 K). Then both *trans* and *cis* structures of *N*-methylsilacarbamate are present with practically

Table 3

STO-3G optimized bond lengths (r/pm) and angles (Θ/°) of *N*-methylsilacarbamic acid and methyl *N*-methylsilacarbamate

Parameter	*N*-Methylsilacarbamic acid		Methyl *N*-methylsilacarbamate	
	Planar	Orthogonal	Planar	Orthogonal
r(Si-2—O-1)	152.6	151.4	152.5	151.4
r(Si-2—N-3)	168.1	169.6	168.1	169.6
r(Si-2—O-6)	165.7	165.5	165.9	165.7
r(N-3—H-4)	101.6	101.4	101.6	101.4
r(N-3—C-5)	146.4	146.4	146.4	146.4
r(O-6—C-7)			142.6	142.6
r(O-6—H)	98.3	98.4		
r(C-5—H)	109.2	109.2	109.2	109.2
r(C-7—H)			109.5	109.5
Θ(O-1—Si-2—N-3)	128.7	129.0	128.9	129.1
Θ(Si-2—N-3—H-4)	120.9	121.1	120.8	121.1
Θ(Si-2—N-3—C-5)	125.8	126.2	125.8	126.2
Θ(N-3—Si-2—O-6)	104.4	109.0	103.6	108.2
Θ(Si-2—O-6—C-7)			116.1	116.2
Θ(Si-2—O-6—H)	108.6	108.3		
Θ(N-3—C-5—H)	111.2	111.4	111.2	111.4
Θ(O-6—C-7—H)			111.3	111.4
$-E^{SCF}$/a. u.	527.3062	527.2939	565.8859	565.8738

the same probability. Much higher energy difference (5.7 kJ mol^{-1}, the 3-21G//3-21G calculation) between *trans* and *cis* conformers has been found [5] for the structurally related methyl *N*-methylcarbamate.

Internal rotational barriers

In Table 4 the calculated rotational barriers for rotation about the central Si—N bond in silacarbamates studied are given. The absolute values of calculated rotational barriers depend on both the basis set used and the way of calculations. Generally, with increasing size of the basis set increases also the height of the calculated barrier in the silacarbamic acid. The absolute values of the barriers calculated using rigid rotor approximation [5] (values in parentheses in Table 4) represent the upper limit of rotational barrier. This value decreases by complete relaxation of all internal coordinates for both planar and orthogonal species of silacarbamates investigated.

In the planar *cis* conformation of silacarbamic acid the hydrogens of amino and hydroxy groups come into close contact with each other giving rise to the

Table 4

Calculated rotational barriers[a] (kJ mol^{-1})

Compound	STO-3G//STO-3G	3-21G//3-21G
NH_2SiO_2H[b]	29.4 (33.2)	34.5 (38.6)
NH_2SiO_2H[c]	21.1 (23.3)	25.9 (29.1)
$NH_2SiO_2CH_3$	28.7 (32.7)	
$NH_2SiO_2C_2H_5$	28.9 (32.8)	
$(CH_3)NHSiO_2H$	32.2 (36.5)	
$(CH_3)NHSiO_2CH_3$	32.8 (36.0)	

a) Parentheses contain barriers computed using rigid rotor approximation; *b*) *trans* conformer; *c*) *cis* conformer.

repulsion energy term. This term depends on both the Si-2—N-3 bond length and the dihedral angle Φ. The net result of this repulsion in planar structure is substantial decrease of computed barrier. The height of that barrier in *cis* silacarbamic acid is about 20—30 % lower (Table 4) than that found in the *trans* form. The alkyl substitution has, generally, small effect on the height of rotational barrier in the *trans* silacarbamic acid. Replacing the silacarbonyl hydrogen of acid by a methyl or ethyl group lowers the barrier by only 0.7—0.9 kJ mol^{-1} On the other hand, more significant increase up to 3.4 kJ mol^{-1} was found in the *N*-methyl-substituted derivatives.

Much higher energy barrier (88.6 kJ mol^{-1}) has been found from the 3-21G calculations of the *trans* carbamic acid [5]. Then the substitution of the carbamate carbon atom by the silicon destabilizes the planar conformer in comparison with the orthogonal.

Mulliken population analysis

In order to study the effect of substitution on the distribution of electronic charge inside of the silacarbamate group, we report (Table 5) also the gross atomic charges of silacarbamate moiety. The charges are evaluated for most stable structures using the STO-3G basis set.

The O-1 oxygen atom of silacarbamic acid becomes less negatively charged in alkyl-substituted derivatives. At the same time the electron density on the silicon atom in the *N*-methyl acid slightly decreases and in the other alkyl--substituted derivatives it increases. The electron density on the nitrogen atom is practically the same in methyl and ethyl silacarbamates. Its value, however, considerably decreases as the carbon atoms are attached to this atom in *N*-methyl-substituted compounds. The negative charge on the ester O-6 oxygen is lower in esters in comparison with acids. The carbon atom attached to O-6

carries the negative charge of $-0.07\ e$ if a methyl group is present and the positive charge (0.01 *e*) in case of the ethyl group. The hydrogens bound to the nitrogen are more acidic than the hydroxyl hydrogen of acids.

Table 5

Atomic Mulliken charges (*Q*/*e*) computed with STO-3G basis set

Compound	O-1	Si-2	N-3	O-6	H-4	H—C-5	H—C-7
NH_2SiO_2H[a]	−0.533	1.130	−0.640	−0.469	0.174	0.172	0.169
$NH_2SiO_2CH_3$	−0.528	1.145	−0.639	−0.429	0.175	0.172	−0.070
$NH_2SiO_2C_2H_5$	−0.529	1.141	−0.639	−0.434	0.174	0.172	0.011
$(CH_3)NHCO_2H$	−0.532	1.126	−0.563	−0.468	0.168	−0.081	0.170
$(CH_3)NHCO_2CH_3$	−0.527	1.139	−0.562	−0.429	0.170	−0.081	−0.070
NH_2SiO_2H (*cis*)	−0.521	1.135	−0.643	−0.463	0.161	0.172	0.162

a) All molecules are in the *trans* conformation with the exception of the last.

The comparison of electronic charges of *trans* and *cis* silacarbamic acid (the first and last rows of Table 5) shows that the oxygen atoms have higher negative charge in the *trans* form. Similarly, the H-7 hydrogen atom loses the electron density in comparison with the *cis* conformer. Since such electron redistribution is typical for the formation of hydrogen bonds [12], the changes found in the electron density of the O-6—H-7 and O-1 atoms in the *trans* and *cis* silacarbamic acid confirmed the existence of such hydrogen bond in the *trans* conformer.

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