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Distortion of Configuration of the Nitrogen Atom in 3-Trimethylsilylpropynamides

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Abstract—Analysis of the IR spectral parameters and the results of AM1 quantum-chemical calculations indicated distortion of the planar structure of the amide fragment and destabilization of the nitrogen configuration in new *N*-functionalized 3-trimethylsilylpropynamides $Me_3SiC{\equiv}CC(O)NHR$. This effect is most pronounced in *N*-hydroxy-3-trimethylsilylpropynamide upon formation of intramolecular hydrogen bond C=O···H–O.

Polyfunctional amides derived from silicon-containing acetylenic acids are important intermediate products in fine organic synthesis, specifically for the preparation of analogs of natural compounds, and they exhibit versatile biological activity [1–3]. We previously studied the molecular and electronic structure of *N*,*N*-diethyl-3-trimethyl-silylpropynamide and its heterocyclic analog [4] and found that the competition between *p*,π- and π,π-conjugation in the amide and ethynylcarbonyl fragments reduces the order of the C–N bond and hence the barrier to rotation about this bond, as compared to common carboxamides. Mass spectrometric study of *N*-aryl-3-trimethylsilylpropynamides showed that the primary fragmentation of the molecular ion involves dissociation of the amide bond with charge localization on the acyl moiety [5]. According to the IR data, the basicity of the oxygen atom in such amides is lower than in other known amides [6].

The amide fragment is characterized by very labile configuration which is sensitive to a large number of factors, including temperature, solvent, molecular environment, nonvalence interactions, and substituent effects [7, 8]. In keeping with the generally accepted views, the amide fragment is planar, and the nitrogen atom has a planar–trigonal configuration, giving rise to intramolecular resonance which may be illustrated by the following canonical structures: O=C–NH ↔ $^{-}$O–C=NH^{+}. Just the partially double character of the formally single C–N bond is responsible for the existence of N-substituted amides as *cis* and *trans* isomers [9–12]. Planar structure of the amide (thioamide) fragment has long been a matter of discussion in the literature [10, 13]. Modern physical and quantum-chemical methods provide information which not only makes the planar structure of the CONH group doubtful but also rationalizes its unusual reactivity just in terms of distortion of its planar structure and configuration of the nitrogen atom [14, 15].

In addition, the unique properties of carboxamides originate from their ability to form hydrogen bonds, which play an important role in the biochemistry of various bioorganic molecules, in particular proteins and peptides [8]. Although the effect of structural factors on the reactivity of amides was the subject of a series of publications, search for quantitative structure–property relationships [7, 16, 17], systematic analysis, and elucidation of general structural relations constitute an actual and quite difficult problem in the stereochemistry of amides. Therefore, any approach to solution of such problems is undoubtedly an important contribution to modern theoretical chemistry [18].

We have studied the molecular and electronic structure and spectral properties of new silicon-containing acetylenic carboxamides **I**–**III** [19] and previously unknown *N*-hydroxy-3-trimethylsilylpropyn-

$$Me_3Si{-}C{\equiv}C{-}CONHR$$

I–IV

I, R = C_4H_9, **II**, R = CH_2CH_2OH; **III**, R = $(CH_3)_2CCH_2OH$; **IV**, R = OH.

Table 1. Parameters of the IR spectra of N-substituted 3-trimethylsilylpropynamides **I**–**IV** (solutions in $CHCl_3$)

Comp. no.	ν(C=O)	ν(C≡C)	ν(NH)	ν(OH)
I	1650 s 1660 sh	2170	3430 s 3400 w	–
II	1640 1650	2167	3430	3480 3618
III	1660	2170	3400	3615
IV	1640 1650	2150 2170	3380 s 3400 w	3480 3530

amide (**IV**) (see Experimental) using IR spectroscopy and AM1 quantum-chemical calculations [20].

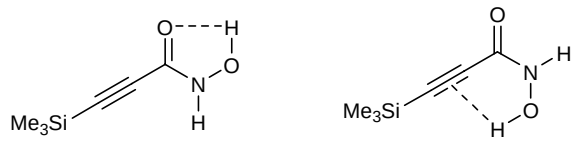
Another goal of the study was to elucidate the effect of substitution at the nitrogen atom on the configuration of the amide fragment and the role of hydrogen bonding in the structure stabilization. Amide **IV** may be regarded as a hydroxamic acid derivative; among the examined amide series, this compound represents the limiting case of replacement at the nitrogen atom (by hydroxy group directly attached thereto).

Table 1 contains stretching vibration frequencies of compounds **I**–**IV**, which were measured from dilute solutions in $CHCl_3$, i.e., under conditions excluding intermolecular association. The ν(NH) and ν(C=O) frequencies of compound **I** correspond to vibrations of the free groups. On the whole, these values are consistent with those found for a large number of secondary amides (3480–3400 and 1660–1700 cm^{-1}) [21]; however, they approach the lower limit of the range or even fall out from it. The absorption bands appear as doublets due to conformational *cis–trans* isomerism, and their intensity ratio indicates that the *trans* isomer predominates (3430 and 1650 cm^{-1}). Amide **I** may be used as a model for the other amides in the series under study, and its spectral properties may be taken as a starting point for analysis of their structure.

Amides **II**–**IV** are characterized by a more complex spectral pattern, as compared to **I**. The IR spectrum of amide **II** contained ν(NH) bands only from the *trans* conformer, while in the region of carbonyl absorption we observed a band at 1650 cm^{-1} from the *trans* conformer and an additional low-frequency component at 1640 cm^{-1}, which was absent in the spectrum of model amide **I**. Stretching vibrations of the hydroxy group give rise to two bands: a medium-intensity band at 3612 cm^{-1} and a band at 3480 cm^{-1}. In keeping with the generally accepted views, the presence of a low-frequency O–H band together with the absence of concentration dependence for the above bands suggest that the OH and C=O groups are involved in intramolecular hydrogen bond. Raising the temperature of solutions of amide **II** in $C_2H_2Cl_4$ to 50–100°C is accompanied by decrease in intensity of the ν(C=O) (1640 cm^{-1}) and ν(O–H) bands (3480 cm^{-1}) and simultaneous increase of the bands at 3612 and 1650 cm^{-1}, which belong to stretching vibrations of the free OH and CO groups. These data were interpreted as rupture of intramolecular hydrogen bond with participation of these groups. It should be noted that no *cis* conformer was detected under the above conditions.

Molecule **III** has a bulky substituent on the nitrogen atom, R = $C(CH_3)_2CH_2OH$. Unlike amide **I**, compound **III** showed in the IR spectra absorption bands belonging only to the *cis* conformer: ν(NH) 3400, ν(C=O) 1660 cm^{-1}, whereas absorption of the free hydroxy group was observed in the expected region (Table 1).

The IR spectrum of amide **IV** differs from those of **I**–**III** by complex character of the high-frequency absorption: ν(NH) 3380, 3400 cm^{-1} and ν(OH) 3480, 3530 cm^{-1}. However, the most interesting is that the ν(C≡C) absorption in the spectra of amides **I**–**III** appears as a single band at 2170 cm^{-1} [21], i.e., at a frequency typical of internal triple C≡C bond, while amide **IV** shows a doublet at 2150/2170 cm^{-1}. No concentration dependence was observed for the position and intensity of the ν(C≡C) and ν(OH) bands, which indicates formation of intramolecular hydrogen bond with participation of these groups. In the spectrum of a solution of **IV** in $C_2H_2Cl_4$, recorded at 80–100°C, the ν(OH) bands at 3480 and 3530 cm^{-1} decrease in intensity, the high-frequency components of the ν(C=O) bands increase in intensity, the intensity of the ν(C≡C) doublet is redistributed in favor of the high-frequency component at 2170 cm^{-1}, and a new band appears at 3620 cm^{-1} due to vibrations of free hydroxy group. These findings suggest rupture of the intramolecular hydrogen bond. Taking into account the



A **B**

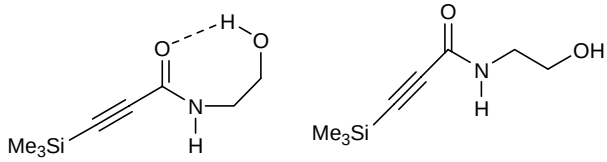
Table 2. Geometric parameters of the most favorable conformations of N-substituted 3-trimethylsilylpropynamides **I–IV**, π-orders of bonds, and pyramidalities of the amide nitrogen atom, calculated by the AM1 method

Parameter	**I** (*trans*)	**II**		**III** (*cis*)	**IV**	
		trans (**C**)	*trans* (**D**)		*trans* (**A**)	*cis* (**B**)
Bond lengths, Å:						
C–N	1.385	1.383	1.385	1.384	1.434	1.441
C=O	1.246	1.241	1.240	1.240	1.240	1.240
N–H	0.990	0.993	0.993	0.990	1.010	1.010
Bond angles, deg:						
OCN	121.99	121.74	121.81	122.03	120.53	120.40
CNH	118.34	118.72	118.80	118.70	114.05	114.30
CNC'	120.03	121.16	121.20	120.52	115.05 (CNO)	115.30 (CNO)
C'NH	116.08	117.52	117.60	117.71	107.30 (ONH)	107.62 (ONH)
Torsion angle, deg:						
OCNH	8.62	4.55	4.65	7.24	27.70	30.08
R^{π} (π-order of bonds):						
C–N	0.260	0.261	0.260	0.259	0.151	0.152
C=O	0.779	0.776	0.778	0.776	0.854	0.852
Pyramidality of nitrogen h^{N}, Å	0.040	0.063	0.063	0.056	0.262	0.262

existing donor and acceptor fragments in molecule **IV**, two modes of intramolecular hydrogen bonding can be proposed (structures **A** and **B**).

Thus, our experimental data for compound **IV** indicated a combination of two equally probable modes of intramolecular hydrogen bonding of a rare type (**B**) which involves π-system of the triple C≡C bond [21, 22]. Insofar as the intramolecular hydrogen bond in amide **II** is formed with participation of only C=O and O–H groups, the band at 3480 cm^{-1} in the IR spectrum of **IV** should be assigned to stretching vibrations of associated hydroxy group in structure **A**, and that located at 3530 cm^{-1}, to the H-bonded hydroxy group in structure **B**. However, the ν(NH) frequencies in the spectrum of amide **IV** remain unusual, for they almost do not change while transformations of the other band occur.

In order to reliably determine the molecular and electronic structure of amides **I–IV**, rationalize their unusual spectral patterns, and substantiate conformational assignments and modes of intramolecular hydrogen bonding, we performed AM1 calculations of their molecules with full geometry optimization. Table 2 contains geometric parameters of the most favorable conformations, which are characterized by the minimal enthalpies of formation. According to the AM1 calculations, the most thermodynamically stable form of amide **I** has a *trans* configuration. The *cis* isomer of hydroxy amide **II** was also found to be unfavorable: apart from H-bonded structure **C**, the second stable (with respect to the energy of formation) conformer has extended structure **D** with *trans* configuration about the C–N bond:

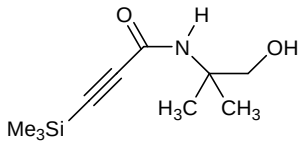


C **D**

A shortened intramolecular O···H contact was found in structure **C**. The O···H distance is 2.348 Å, which is shorter than the sum of the van der Waals radii. The calculated energy of intramolecular hydrogen bond is 1.9 kcal/mol, and the experimental Δ*H* value (determined from the temperature dependence of the optical densities of the corresponding IR absorption bands) is 2.2 kcal/mol. Although hydrogen bonding is classed with weak interactions, quasicyclic conformation **C** is more stable than sterically unstrained extended conformation **D** just due to intramolecular hydrogen

bonding. Thus the spectral behavior of **II** is very consistent with the results of AM1 calculations.

The only stable conformation of amide **III** having a bulky substituent on the nitrogen is that with *cis* structure of the amide fragment; the energy minimum corresponds to the following structure:



The calculation revealed no shortened intramolecular contacts in molecule **III**. Two conformations, **A** and **B** (both with intramolecular hydrogen bonds) were found to be equally probable from the viewpoint of thermodynamics. The shortened intramolecular C=O···H contact in **III** was estimated at 2.58 Å.

The torsion angles OCNH in molecules of amides **I**–**III** (Table 2) suggest that the amide fragment therein is nonplanar within 9–5°, while the corresponding angle in molecule **IV** ranges from 27 to 30°. A similar distortion of planar structure of the amide fragment was observed while studying the structure of *N*,*N*-diethyl-3-trimethylsilil-2-propynamide and its heterocyclic analog, where analogous torsion angles were 12–8° [4]. The NH stretching vibration frequency is known to be strongly sensitive to *p*,π-conjugation which depends mostly on the planarity of the amide fragment; therefore, this parameters may be regarded as an indicator of the nitrogen atom configuration in amides. With the above in mind, it becomes clear why the ν(NH) frequencies in the IR spectra of amides **I**–**IV** change so strongly, depending on their stereochemical structure.

Insofar as the main factor determining specific properties of the amide is hybridization (*p* character) of the lone electron pair on the nitrogen atom (which is related to the bond angles at the nitrogen atom and degree of its pyramidality), we thought it reasonable to compare these parameters. The sum of the bond angles Σ_N at the nitrogen atom in the series of compounds **I**–**IV** is lower than the corresponding value typical of common amides [13–15]. The difference is the largest for hydroxy amide **IV**, for which Σ_N is as low as 336°; this value approaches that typical of an ideal tetrahedral structure (328.2°). The calculated heights of the nitrogen pyramid (h^N) in amides **I**–**IV** are given in Table 2. It is seen that amide **IV** is characterized by the greatest h^N value. In combination with Σ_N, these data indicate that the configuration of the nitrogen atom in **I**–**III** is appreciably distorted toward greater pyramidality, as compared to *N*-methylacetamide [4]. The degree of pyramidality of the nitrogen atom in **IV** is so high that its lone electron pair is essentially rehybridized toward sp^3 configuration. As a result, the amide *p*,π-conjugation is broken, and the ν(NH) frequency in the IR spectrum is strongly reduced (especially for amide **IV**). Rupture of *p*,π-conjugation in the amide fragment is also confirmed by considerable elongation of the amide C–N bond (up to 1.44 Å in molecule **IV**) and N–H bond (up to 1.01 Å; Table 2). For comparison, the C–N bond length in *N*-methylacetamide is 1.368 Å [23].

Another fairly convincing proof for weakening of conjugation in the CONH fragment of compounds **I**–**IV** may be π-orders (R^π) of the C–N and C=O bonds (Table 2). Considerably reduced R^π values for the C–N bonds in amides **I**–**IV** relative to *N*-methylacetamide (R^π = 0.35) indicate a weak interaction between the nitrogen lone electron pair and the carbonyl group. By contrast, the π-orders of the carbonyl group are increased up to a value of 0.854.

It should be emphasized that formation of intramolecular hydrogen bond usually makes the H-bonded ring more planar, as it was shown with a large number of various compounds [8, 21]. However, the torsion angles in amide **IV** give rise to nonplanar *zygo* forms of the five-membered H-bonded ring with pronounced pyramidality of the nitrogen atom.

According to the calculations, the NH hydrogen atom in amide **IV** is characterized by the greatest (among the examined amides) positive charge, +0.23 a.u., which is likely to be responsible for the increased strength of intramolecular hydrogen bond formed therein. The corresponding value for amides **I**–**III** is +0.19 a.u.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR double-beam spectrometer from solutions in $CHCl_3$ and $C_2H_2Cl_4$; cells with a layer thickness of 0.01 to 0.5 cm were used. The temperature dependences were measured with the aid of a Carl Zeiss Jena temperature-controlling unit equipped with a calibrated thermocouple. The experimental error in the determination of the ν(C=O) and ν(C–N) frequencies was ±1 cm^{-1}, and in the determination of ν(NH) and ν(OH), 2 cm^{-1}. The temperature was maintained with

an accuracy of ±0.5°C. The experimental enthalpies of formation were determined by the van't Hoff procedure [23] from the temperature dependences of the optical densities at frequencies corresponding to C=O, OH, and C≡C groups involved in hydrogen bond formation. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DPX-400 spectrometer in DMSO-d_6 using cyclohexane as internal reference.

Quantum-chemical calculations were performed with full geometry optimization. For preliminary optimization, the MM+ molecular mechanics procedure was used. The initial files were prepared, and the results were visualized, with the aid of HyperChem graphical interface [24]. The geometric parameters were optimized with account taken of data available from the Cambridge Structural Database [25].

***N*-Hydroxy-3-trimethylsilylpropynamide (IV)**. A mixture of 0.5 g (7.2 mmol) of powdered hydroxylamine hydrochloride, 1.54 g (12 mmol) of hexamethyldisilazane, and 0.01 mol % of saccharin was heated for 1 h at 100–130°C. Excess hexamethyldisilazane was removed under reduced pressure, the residue was dissolved in 15 ml of diethyl ether, and a solution of 0.58 g (3.6 mmol) of 3-trimethylsilylpropynoyl chloride in 10 ml of diethyl ether was added over a period of 15 min at room temperature. The mixture was stirred for 1 h, decomposed with 5% hydrochloric acid, and extracted with diethyl ether. The extract was dried over $MgSO_4$, and the solvent was removed to isolate 0.48 g (86%) of amide **IV** with mp 119–121°C. ^{1}H NMR spectrum, δ, ppm: 0.249 s (9H, Me_3Si-*Z*), 0.246 s (9H, Me_3Si-*E*), 9.25 br.s (1H, NH-*Z*), 7.56 br.s (1H, NH-*E*), 11.21 br.s (1H, OH-*Z*), 8.01 br.s (1H, OH-*E*); *E*/*Z* ratio 1:3. ^{13}C NMR spectrum, δ_C, ppm: 0.27 (Me_3Si-*Z*), 0.32 (Me_3Si-*E*), 92.61 (Si**C**≡C-*Z*), 90.24 (Si**C**≡C-*E*), 97.81 (SiC≡**C**-*Z*), 100.36 (SiC≡**C**-*E*), 150.43 (C=O-*Z*), 154.41 (C=O-*E*). Found, %: C 45.72; H 7.65; N 8.56; Si 17.21. $C_6H_{11}NO_2Si$. Calculated, %: C 45.83; H 7.05; N 8.91; Si 17.86.

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