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Isomerization in the Reaction of (Aminoalkyl)trialkoxysilanes with Carboxylic Acid Anhydrides

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Abstract—The products of the reactions of monofunctional (3-aminopropyl)triethoxysilane and (3-aminopropyl)trimethoxysilane and bifunctional [3-*N*-(2-aminoethyl)aminopropyl]trimethoxysilane with acetic and maleic anhydrides in CCl_4 at varied reagent molar ratios are studied by ^1H and ^{13}C NMR spectroscopy. It is shown that the reaction of [3-*N*-(2-aminoethyl)aminopropyl]trimethoxysilane with the above anhydrides leads to formation of diamides as mixtures of cisoid and transoid rotamers about both amide bonds. The reactions with monofunctional (aminopropyl)trialkoxysilanes give individual isomers.

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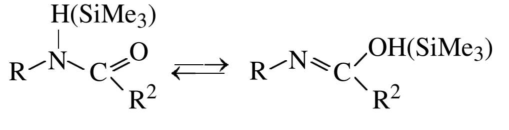
The formation of isomers about the C(O)–N bond (rotamers) in the syntheses of organic amides has been fairly well documented. An NMR study of the composition and structure of amides [1] showed that alkylamides of the general formula $RC(O)NHR^1$ [R = H, Me, Et, *i*-Bu; R^1 = Me, Et, *i*-Pr, *t*-Bu, $-CH(OOH)\cdot CH_3$, $-CH(OOH)CHR^2CH_3$. $PhCH_2$, $-CH(CH_3)Ph$] are largely present as a transoid isomer (70–100%). In the case of *N,N*-disubstituted alkylamides of the general formula $RC(O)NR^1Me$ (R = H, Me, *t*-Bu, *i*-Bu; R^1 = Et, *i*-Pr, *n*-Bu, *t*-Bu and *cyclo*-C_6H_{11}), the cisoid/transoid ratio is approximately 1 : 1, except for HC(O)NMe(*t*-Bu) which contains 89% of the transoid isomer. Obviously, such an isomer ratio is due to the steric effect of the second substituent at the nitrogen atom.

Burn et al. [2] found that the content of the transoid rotamer of formanilide depends on the concentration of the compound in $CDCl_3$ and grows from 45 to 73% as the concentration increases from 1.5 to 52.5 mol %. With other compounds [1], no definite dependence was detected for the rotamer ratio on the nature and polarity of solvents used in NMR spectroscopy and on the amide concentration in the solution.

At R^1 = H or $SiMe_3$, tautomeric isomerization is possible with migration of the hydrogen atom to oxygen:

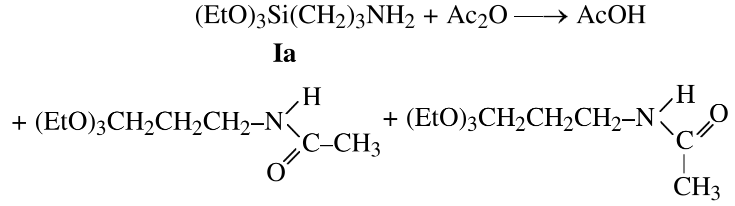


The amide form can exist as a mixture of the cisoid and transoid rotamers, as shown by ^1H NMR for *N*-trimethylsilylated formamide and acetiamide [3], and *N*-trimethylsilylanilides [4]. The ^1H NMR spectrum of *N*-trimethylsilylformanilide at 0°C displayed three signals of the trimethylsilyl group (δ 0.29, 0.18 and 0.06 ppm), two of which were assigned to rotamers about the amide bond. It was also reported that the rotation barrier about the amide bond in *N*-(trimethylsilyl)formamide is 3 kcal mol^{-1} lower than in *N*-*tert*-butylformamide [3].

The publications describing reaction of carbofunctional organisilicon amines with carboxylic acid anhydrides [5–14] include no information on their isomeric composition. Data on reaction of carboxylic acids with [3-*N*-(2-aminoethyl)aminopropyl]trimethoxysilane are practically absent from the literature.

In this connection we studied the composition and structure of products formed by reactions of monofunctional (3-aminopropyl)triethoxysilane (**Ia**) and (3-aminopropyl)trimethoxysilane (**Ib**) and bifunctional [3-*N*-(2-aminoethyl)aminopropyl]trimethoxysilane (**Ic**) with acetic and maleic anhydrides at varied molar reagent ratios. This work continues our studies reported earlier [15].

The reactions of (aminoalkyl)alkoxysilanes with anhydrides were carried out in carbon tetrachloride at 20–25°C. The reaction of **Ia** with equimolar amount of acetic anhydride can lead to a mixture of the cisoid and transoid rotamers of [3-*N*-(acetamido)propyl]triethoxyilane and elimination of acetic acid:



$$(EtO)_3Si(CH_2)_3NH_2 + Ac_2O \longrightarrow AcOH + (EtO)_3CH_2CH_2CH_2\text{–}N(H)\text{–}C(=O)\text{–}CH_3 + (EtO)_3CH_2CH_2CH_2\text{–}N(H)\text{–}C(=O)\text{–}CH_3$$

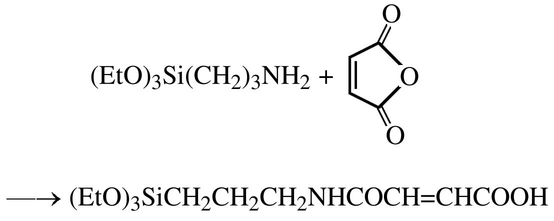
Ia

cis isomer *trans* isomer

IIa

In an analysis of the spectra of the reaction products of **Ia** with Ac_2O, by analogy with [3, 4], the formation of rotamers was determined from splitting of the signal of the acetyl group, whose chemical shift is very sensitive to conformational transformations. As shows Fig. 1, near 2 ppm there are two signals, but the downfield signal (δ 1.97 ppm) is related to acetic acid; the proton of the latter with the corresponding integral intensity is registered far downfield (δ 10.27 ppm). The CH_2N signal, too, provides no clear evidence for the presence of isomers, and as a whole it corresponds to splitting due to coupling with three protons of the neighboring CH_2 and NH groups.

The reaction of **Ia** with maleic anhydride also proceeds without side processes and leads to formation of amido acid **IIIa**:



$$\longrightarrow (EtO)_3SiCH_2CH_2CH_2NHCOCH{=}CHCOOH$$

IIIa

Like with acetic anhydride, the ^1H NMR spectrum reveals no signs of isomerism: The CH_2N group is registered as a quartet and the –CH=CH– group, as

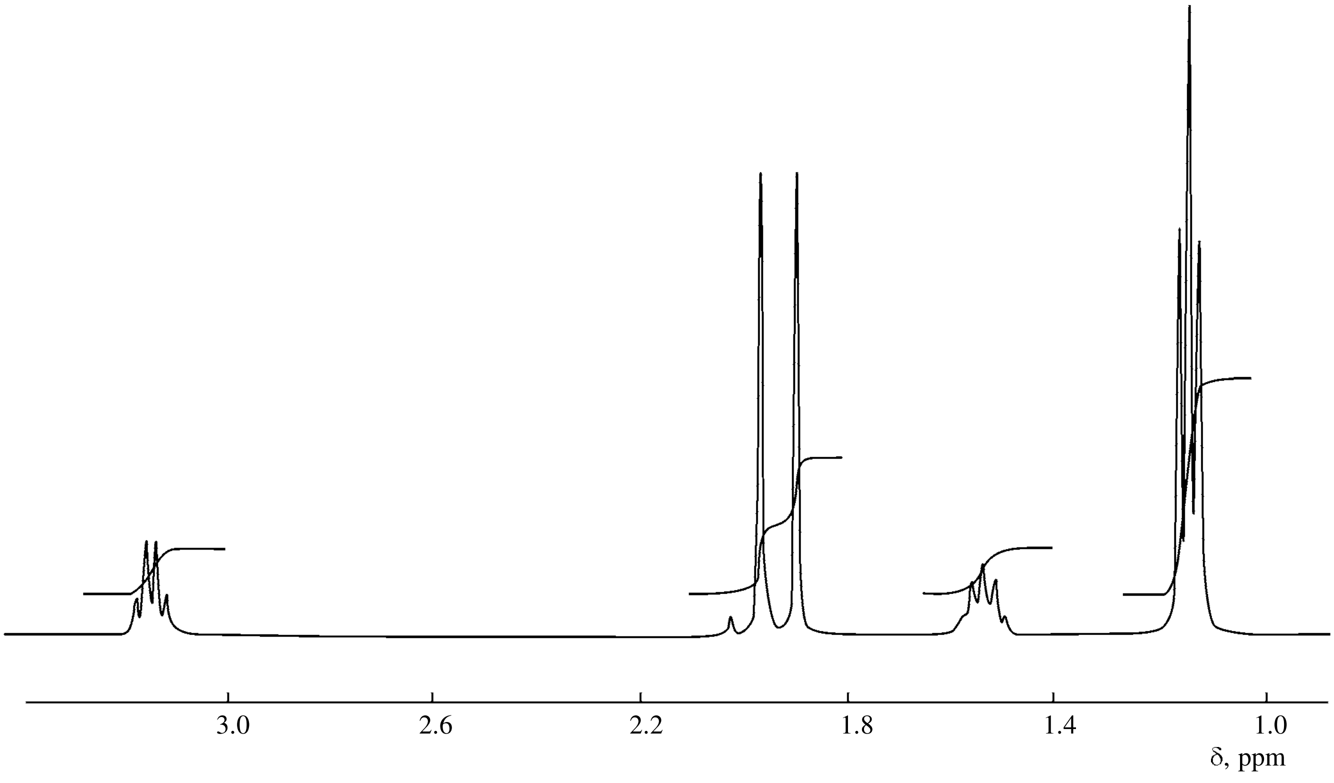


Fig. 1. Fragment ^1H NMR spectrum of compound **IIa**.

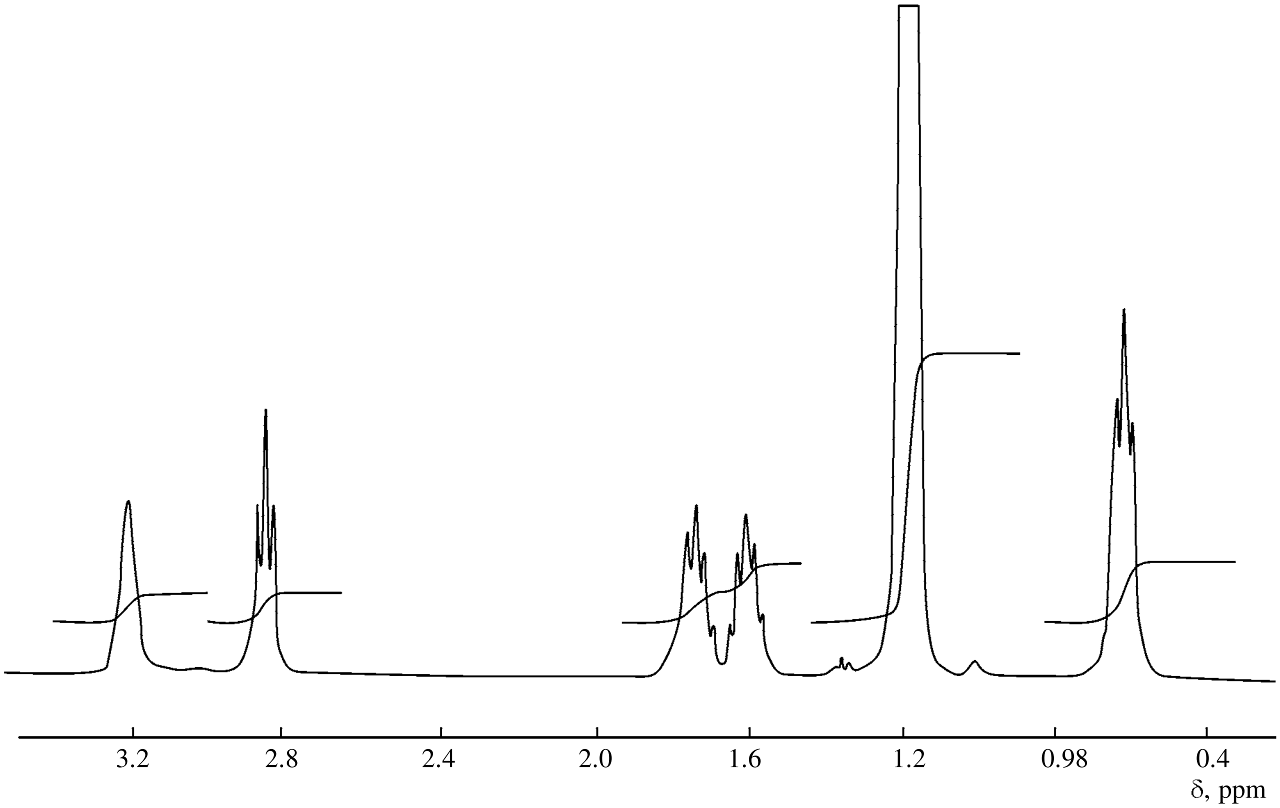


Fig. 2. Fragment ^1H NMR spectrum of compound **IVa**.

two doublets. The carboxyl proton signal is broad and appears very far downfield (δ 15.48 ppm). The absence of isomerism and the presence of the carboxyl proton signal give no evidence for the interaction of the carboxy group with the amide nitrogen, we assumed earlier [15], or this interaction is very weak.

The reaction of compound **IIIa** with aminosilane **Ia** leads to compound **III** which contains simultaneously an amide bond and ammonium group:

$$\mathbf{IIIa} + (EtO)_3SiCH_2CH_2CH_2NH_2 \longrightarrow (EtO)_3SiC^aH_2C^bH_2C^cH_2NHCOCH{=}CHCOO^-N^+H_3C^dH_2C^eH_2C^fH_2Si(OEt)_3.$$

IVa

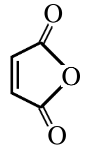
The absence of isomers in compounds **IIIa** and **IVa** allows the trimethylene CH_2 proton signals to be assigned to the amide and ammonium parts of compound **IVa** (Fig. 2). The broad signal (δ 3.21 ppm) is related to $CH_2NHC(O)$ methylene protons, while the triplet at δ 2.83 ppm, to $CH_2N^+H_3$ methylene protons. The quintet at δ 1.74 ppm probably belongs to the CH_2^b group in the amide part, while the quintet at δ 1.61 ppm, to the CH_2^c group in the ammonium part of compound **IVa**. From the integral intensity ratio, the broadened singlet at δ 7.61 ppm can be assigned to $^+NH_3$ protons and the singlet at δ 9.50 ppm, to an NHCO proton.

Thus, we conclude that the position of methylene proton signals depends on the chemical nature of the nitrogen atom. The strongest downfield shift is characteristic of the amide nitrogen in amido acid **II** ($\Delta\delta$ = 0.85 ppm for CH_2N protons) as compared with the amine nitrogen in compound **Ia**.

Similar results were obtained with (3-aminopropyl)-trimethoxysilane (**Ib**). The ^1H NMR spectra (Table 1) showed that the products of the reactions of **Ib** with acetic and maleic anhydrides (**IIb** and **IIIb**, respectively), undergo no isomerism at the given temperature, and that the structure of their organic parts is

$$(MeO)_3Si(CH_2)_3NH_2 + Ac_2O \longrightarrow AcOH + (MeO)_3Si(CH_2)_3NHAc,$$

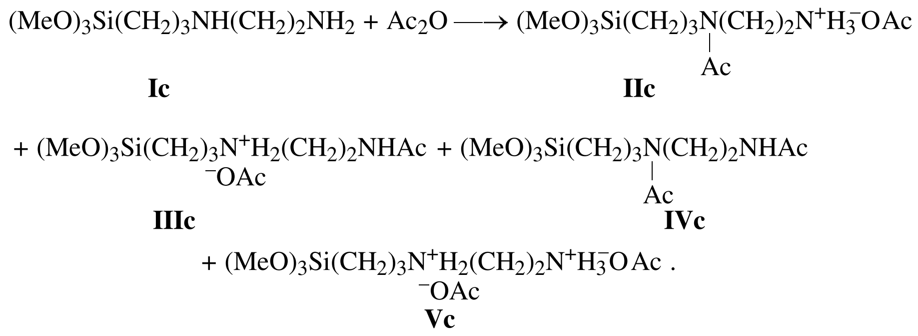
Ib **IIb**

Ib +  $\longrightarrow (MeO)_3Si(CH_2)_3NHCOCH{=}CHCOOH.$

IIIb

completely the same as the respective structures of compounds **IIa** and **IIIa**.

In the reaction of diamine **Ic** with Ac_2O, the possible number of isomeric reaction products depends on the molar ratio of the initial reagents. At a 1 : 1 molar ratio, a mixture of amides, acetates, and amidoacetates of various structure and composition can form:



$$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2 + Ac_2O \longrightarrow (MeO)_3Si(CH_2)_3\underset{\displaystyle Ac}{N}(CH_2)_2N^+H_3{}^-OAc$$

Ic **IIc**

$$+ (MeO)_3Si(CH_2)_3\underset{^-OAc}{N^+H_2}(CH_2)_2NHAc + (MeO)_3Si(CH_2)_3\underset{\displaystyle Ac}{N}(CH_2)_2NHAc$$

IIIc **IVc**

$$+ (MeO)_3Si(CH_2)_3\underset{^-OAc}{N^+H_2}(CH_2)_2N^+H_3{}^-OAc\ .$$

Vc

The acetyl group can occupy positions at the first or second nitrogen atom (structures **IIc** and **IIIc**, respectively), that is, two geometric isomers are possible. Each isomer can exist as two rotamers about the amide bond. Furthermore, double amide **IVc** and double salt **Vc** can form. Compound **IVc** includes two centers of isomerism and can exist as four isomers. Compound **Vc** should not have isomers due to the free proton exchange between the ammonium groups. Thus, at equimolar reagent ratio, nine isomers can be present in the reaction mixture.

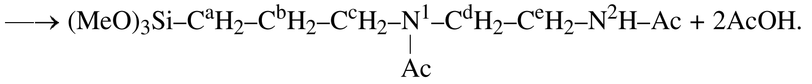
At a 1 : 2 diamine : Ac_2O molar ratio, this reaction can afford four isomers of [3-[*N*-(2-acetamidoethyl)-acetamido]propyl]trimethoxysilane (**IVc**) which has two centers of isomerism, and free acetic acid.

Table 1. ^1H chemical shifts in the reaction systems involving compounds **Ia** or **Ib**

Reaction systems and compounds	Chemical shift, δ, ppm							
	$SiCH_2$	$CH_2CH_2CH_2$	CH_2N	NH_n	CH_3CH_2O	CH_2CH_2O	COOH	*R*COOH
$(EtO)_3Si(CH_2)_3NH_2$	0.45 t	1.37 quintet	2.51 t	1.05 s	1.05 t	3.64 q		
$(EtO)_3Si(CH_2)_3NH_2$ + AcOH	0.56 t	1.66 quintet	2.72 t	8.21 s	1.13 t	3.72 q		1.81 s
$(EtO)_3Si(CH_2)_3NH_2$ + Ac_2O	0.54 t	1.54 quintet	3.14 q	6.36 s	1.14 t	3.73 q	10.27	1.90 s 1.97 s
$(EtO)_3Si(CH_2)_3NH_2$ + MA	0.62 t	1.68 quintet	3.32 q	8.56 s	1.13 t	3.77 q	15.48	6.24 d 6.48 d
$(MeO)_3Si(CH_2)_3NH_2$ + Ac_2O	0.48 t	1.44 quintet	3.03 q	6.77 s	3.39 s CH_3O		10.74	1.82 s 1.88 s
$(MeO)_3Si(CH_2)_3NH_2$ + MA	0.57 t	1.62 quintet	3.26 q	8.63 s	3.46 s CH_3O		16.92	6.21 d 6.54 d

$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2 + 2Ac_2O$

Ic



$$\longrightarrow (MeO)_3Si{-}C^aH_2{-}C^bH_2{-}C^cH_2{-}\underset{\displaystyle Ac}{\underset{|}{N^1}}{-}C^dH_2{-}C^eH_2{-}N^2H{-}Ac + 2AcOH.$$

IVc

The ^1H NMR spectrum of the reaction product of **Ic** with Ac_2O at a 1:2 molar ratio shows five acetyl signals (δ 1.80, 1.83, 1.89, 1.94, and 1.96 ppm), one of which belongs to acetic acid. The ^{13}C NMR spectrum of compound **IV** also confirms the presence in the reaction mixture of four isomers: It contains four signals of the carbonyl group (δ_C 171.4–172.2 ppm) and four signals of the $CH_3C(O)$ group (δ_C 20.6–22.2 ppm). Note that each carbon atom in the trimethylene bridge gives two signals. This fact suggests that that the chemical shift of the trimethylene carbon signals is affected by the conformation of the amide bond of the nearest nitrogen atom. The NCH_2CH_2N methylene carbons are registered as four signals, rather than eight expected, two signals for each isomer.

The ^{13}C NMR spectrum allows estimation of the conformer ratio for different amide groups. The integral intensity ratio of the $^{13}C(a)$, $^{13}C(c)$, $^{13}C(d)$, and $^{13}C(e)$ signals of the isomers (Fig. 3) gives evidence showing that the conformer ratio varies from 1:3 to 1:4 and is equal for both nitrogen atoms (Fig. 3a).

It has been shown on an example of *N,N*-dibutylformamide [16] that the signal of the α-carbon atom in the cisoid position to the carbonyl oxygen is shifted upfield from that of the transoid carbon atom. This fact suggests that C^e (δ_C 44.64 ppm) is cisoid and C^d (δ_C 51.17 ppm) is transoid to the carbonyl group. Consequently, the signals at δ_C 47.82 and 47.19 ppm relate to transoid-C^e and cisoid-C^d (Fig. 3a). Hence, the preferable molecular conformation of **Vc** is [*trans*-3-[*cis*-*N*-(2-acetamidoethyl)acetamido]propyl]trimethoxysilane.

Thus, the reaction of diamine **Ic** with two molecules of acetic anhydride leads to formation of the maximum number of possible isomers.

The ^1H NMR spectrum of the reaction mixture of **Ic** and Ac_2O in a 1:1 molar ratio is more complicated and does not allow judging about the number of isomers, because the acetyl spectral region which is in the most informative in this case contains overlapping signals. However, the ^{13}C NMR spectrum attests the presence of practically all isomers: The carbonyl region contains nine peaks, eight of which belong to the acetamido groups (δ_C 170.3–171.5 ppm) and one to the acetoxy anion (δ_C 177.4 ppm). The acetoxy carbonyl carbon signal of the reaction product of the diamine with acetic acid falls in the same region (δ_C 177.5 ppm) (Tables 2 and 3).

Table 2. ^1H chemical shifts in the reaction systems involving compound **Ic**

Reaction mixtures and compounds	Chemical shift, δ, ppm							
	$SiCH_2$	$CH_2CH_2CH_2$	CH_2N	NCH_2	CH_2N	MH_n	*R*COOH	CH_3O
$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2$	0.35 t	1.29 quintet	2.46 t	2.34 t	2.30 t	0.81 s		3.25 s
$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2$ + Ac_2O	0.29 t 0.36 t	1.39 m 1.49 quintet	2.59 m 2.75 t	3.05 m	3.14 m	7.28 s 7.57 s 8.33 s 9.57 s	1.81 s	3.28 s
$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2$ + $2Ac_2O$	0.45 t	1.54 m	3.14	3.26 m	3.34 m	7.01 s 7.17 s 7.26 s	10.9 s	2.08 s
$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2$ + MA	0.49 quintet 0.61 quintet	1.56 quintet 1.72 m	2.78 t 2.93 t	3.11	3.50	8.25 s 8.93 s 9.62 s 10.75 s	5.80–6.20 m	3.50 s
$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2$ + 2MA	0.55 t	1.66 quintet	3.34 t	3.63		8.49 s	6.19–6.75 m	3.53 s

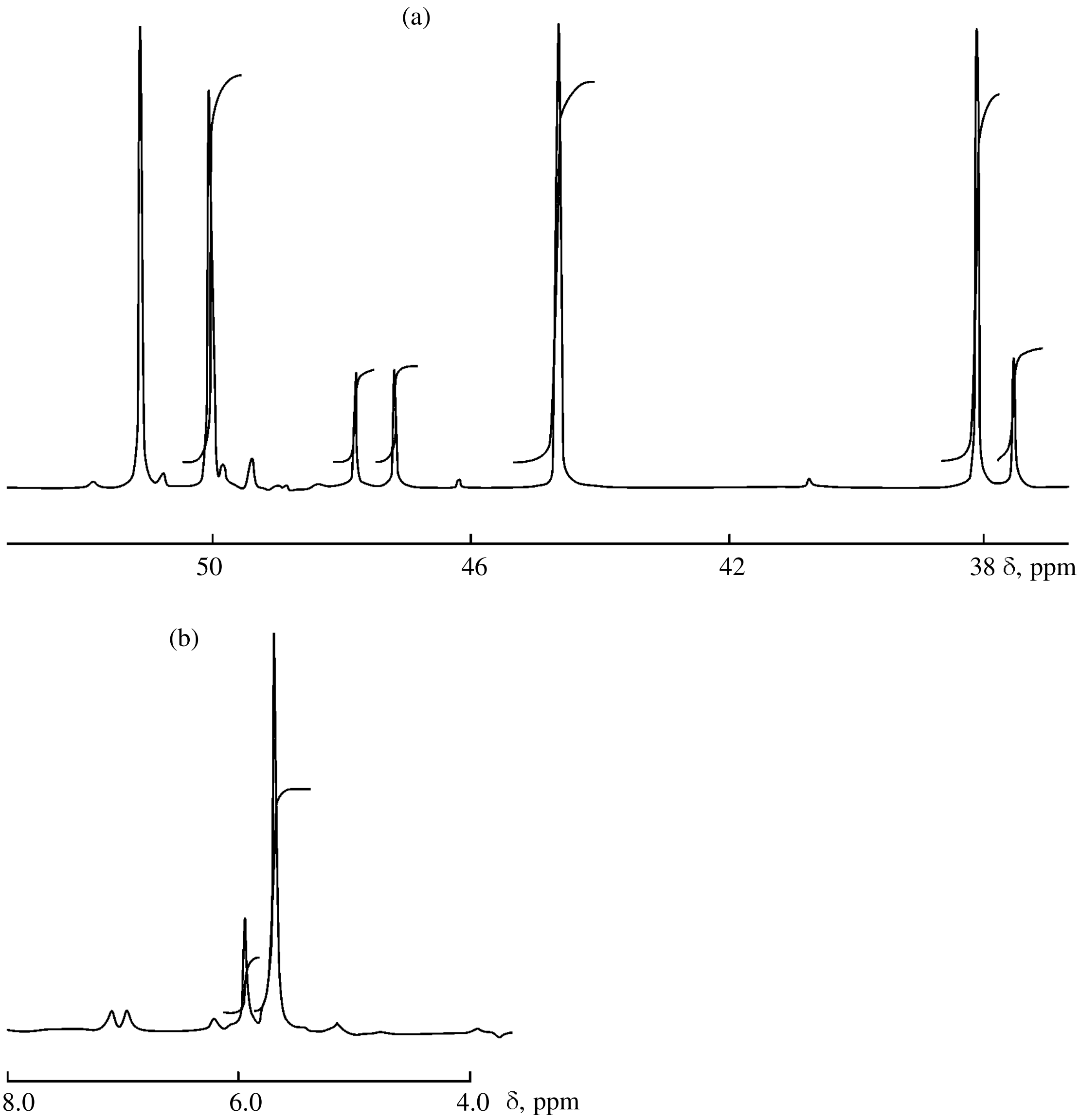
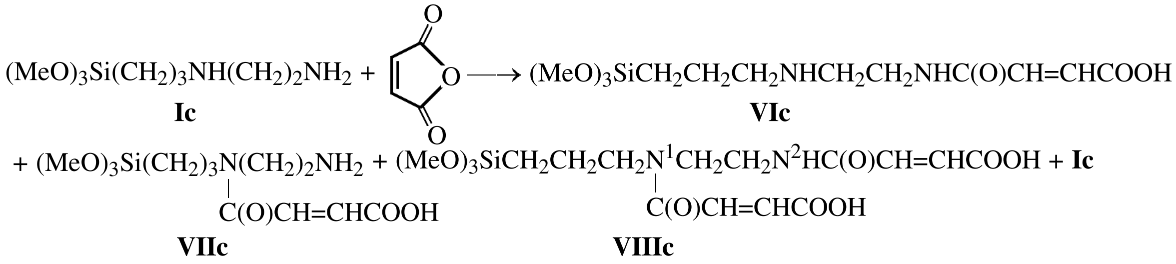


Fig. 3. Fragment ^{13}C NMR spectrum of compound **IVc** for the (a) $NC^dH_2C^eH_2N$ and NC^cH_2 and (b) SiC^aH_2 groups.

Besides, the carbon signals of each CH_2 group in the trimethylene fragment is registered as six peaks, providing evidence for the assumption that the $13C^{a–c}$ chemical shifts are affected exclusively by the conformation of the amide bond of the nearest nitrogen atom. For example, the C^a atom of the $SiCH_2$ group in compounds **IIc** and **IVc** should give 2 signals, while that in compounds **IIIc** and **Vc**, one signal, i.e. a total of six signals should be observed.

In the reaction of diamine **Ic** with maleic anhydride, the number of possible reaction products should also be defined by the molar ratio of the reagents. At an equimolar ratio, the reaction mixture can contain compounds **VIc** and **VIIc**, diamido diacid **VIIIc**, and parent diamine **Ic**:



$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2$ + $\longrightarrow$ $(MeO)_3SiCH_2CH_2CH_2NHCH_2CH_2NHC(O)CH{=}CHCOOH$

Ic **VIc**

+ $(MeO)_3Si(CH_2)_3N(CH_2)_2NH_2$ + $(MeO)_3SiCH_2CH_2CH_2N^1CH_2CH_2N^2HC(O)CH{=}CHCOOH$ + **Ic**

$C(O)CH{=}CHCOOH$ $C(O)CH{=}CHCOOH$

VIIc **VIIIc**

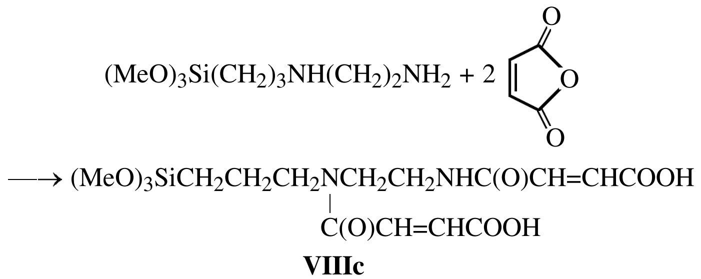
Table 3. ^{13}C chemical shifts in the reaction systems involving compound **Ic**

Reaction mixtures and compounds	Chemical shift, δ, ppm							
	Si*C*H$_2$	CH$_2$*C*H$_2$CH$_2$	*C*H$_2$N	N*C*H$_2$*C*H$_2$N	RCOOH	*C*H$_3$C(O)N	*C*(O)N	CH$_3$O
$(MeO)_3Si(CH_2)_3NH\cdot(CH_2)_2NH_2$	6.16	22.67	41.37	51.89, 51.93				49.77
$(MeO)_3Si(CH_2)_3NH\cdot(CH_2)_2NH_2$ + Ac_2O	5.77, 6.03, 6.09, 7.20, 7.24, 7.41	19.50, 19.78, 19.92, 20.23, 20.33, 20.71	35.68, 35.76, 36.08, 36.94, 37.67, 38.44	44.67, 46.03, 46.83, 47.03, 47.20, 47.25, 47.68, 50.23, 50.29, 51.27, 49.67	CH$_3$*C*O 177.38 *C*H$_3$CO 23.19	20.87, 20.94, 22.30, 22.56	170.33, 170.49, 170.56, 170.84, 171.03, 171.10, 171.52	49.43, 49.84, 50.06, 50.12
$(MeO)_3Si(CH_2)_3NH\cdot(CH_2)_2NH_2$ + $2Ac_2O$	5.70, 5.96	20.20, 20.34	37.55, 38.14	44.64, 47.19, 47.82, 51.17	CH$_3$*C*O 174.18 *C*H$_3$CO 21.57	20.58, 20.66, 22.09, 22.21	171.38, 171.49, 171.57, 172.19	50.07, 50.13
$(MeO)_3Si(CH_2)_3NH\cdot(CH_2)_2NH_2$ + 2MA	5.70, 6.12	20.09, 21.70	37.35	49.82, 49.94, 50.66, 51.85	CH=CH 128.03, 131.95, 134.17, 135.08	*C*(O)NCH$_2$=CH$_2$*C*OOH 165.74, 165.98, 166.31, 166.48, 166.72, 166.83, 167.16, 168.11		50.54, 52.39

The neutral reaction of the reaction mixture indicates that the carboxy groups of the formed amidoacids react with residual amino groups to form both intra- and intermolecular ammonium salts.

Analysis of the ^{1}H NMR spectra does not allow determining the number of isomers. However, the splitting patterns and chemical shifts of the proton signals of the trimethylene fragment attest the presence of both the amide and ammonium forms of N^1. In the ^{1}H NMR spectrum (Fig. 4), the SiCH$_2$ and C–CH$_2$–C signals are doubled (δ 0.49, 0.61 and δ 1.56, 1.72 ppm, respectively). The higher intensity of the downfield signals related to amide N^1 provide evidence to show that the predominant reaction route is acylation of the secondary amino group by maleic anhydride with subsequent formation of an ammonium salt with a primary amino group. The shapes of the ≡SiCH$_2$– (two quartets or, probably, overlapping triplets) and C–CH$_2$–C (complex multiplets) signals suggest *cis–trans* isomerism about the amide bond in the reaction products.

The formation of the cisoid and transoid isomers about the amide bond is confirmed by the ^{1}H and ^{13}C NMR spectra of the reaction product of the diamine with two molecules of maleic anhydride. The reaction mixture can contain four isomers, because the product has two centers of isomerism about the amide bond.



$$(MeO)_3Si(CH_2)_3NH(CH_2)_2NH_2 + 2\,(\text{maleic anhydride}) \longrightarrow (MeO)_3SiCH_2CH_2CH_2\underset{\displaystyle C(O)CH{=}CHCOOH}{\underset{|}{N}}CH_2CH_2NHC(O)CH{=}CHCOOH$$

VIIIc

The presence of all possible isomers is confirmed by the observation of eight carbonyl carbon signals in the ^{13}C NMR spectrum of compound **VIIIc** (Table 3).

Thus, unlike (aminopropyl)trialkoxysilanes **Ia** and **Ib**, diamine **Ic** reacts with acetic and maleic anhydrides to form a mixture of cisoid and transoid isomers

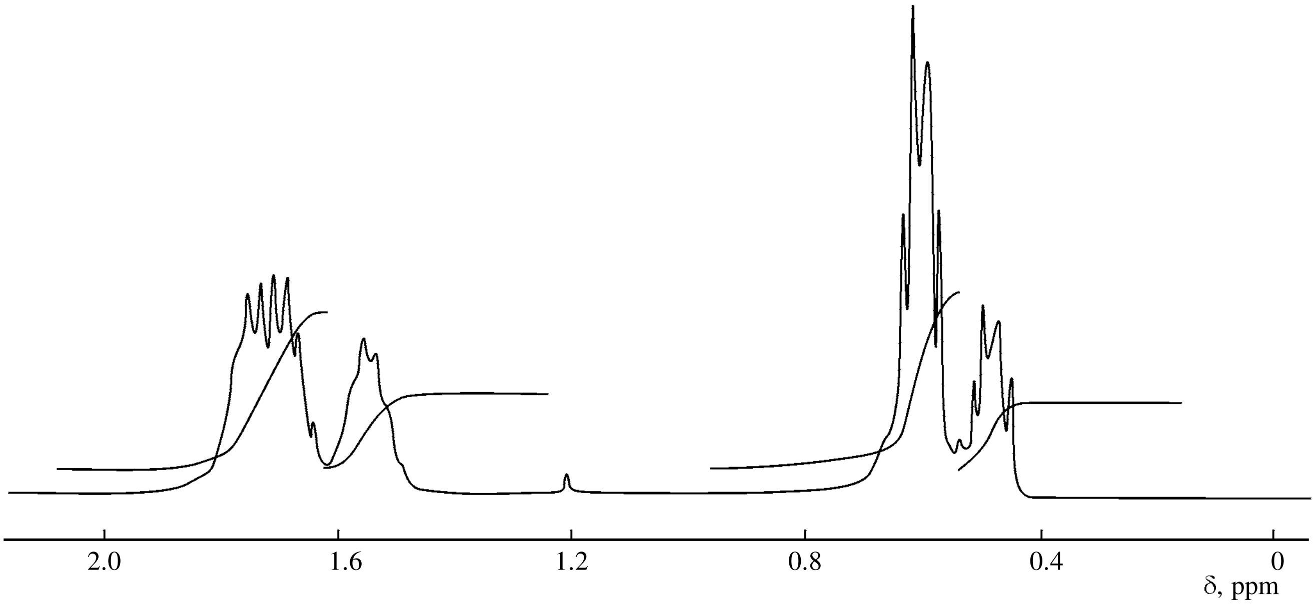


Fig. 4. Fragment ^{1}H NMR spectrum of compound **VIIIc**.

about both amide bonds. The resulting data are rather unexpected, since, according to published data, isomer formation is more probable with primary amines **Ia** and **Ib**.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were registered on a Bruker AM-360 instrument (360 MHz) at 300 K, solvent $CDCl_3$. Syntheses were performed according to the procedures described in [15], solvent CCl_4.

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