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Structure of monosilylated benzhydroxamic acids in crystals and solutions

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Abstract

O-tert-butyldimethylsilyl (**1**) and *O-tert*-butyldiphenylsilyl (**2**) benzhydroxamates were prepared and their structure in the solid state was determined by X-ray diffraction and NMR spectroscopy (^{15}N, ^{13}C and ^{29}Si). The solution NMR spectra indicate some processes. In chloroform, both compounds isomerize to an equilibrium mixture of hydroxamic (A) and hydroximic (B or C) derivatives at room temperature. The exact structure of the hydroximic derivative could not be determined. The ratio between the isomers is affected by the solvent. In benzene solutions the hydroximic isomer is preferred whereas in acetonitrile the opposite is true. In dimethylsulfoxide the NMR lines are broad but slow heating to 80°C or above produces disilylated derivatives of the type *Z*-O^1,O^4-bis(*tert*-butyldimethylsilyl)-benzhydroximate. The changes in structure are only partially reversible, the nature of the process responsible for line broadening is not clear. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: *t*-Butyldimethylsilyl derivatives; *t*-Butyldiphenylsilyl derivatives; Benzhydroximic acid; Benzhydroxamic acid; Crystal structure; ^{1}H-NMR; ^{13}C-NMR; ^{29}Si-NMR; Chemical shifts; MAS-NMR; Rotamers; Tautomers; Solvent effects

1. Introduction

Though silyl derivatives of hydroxamic acids (HAs) were studied earlier [1–5], observation that the silyl derivatives of biologically active HAs have a potential as anticancer prodrugs [6] accelerated studies of these compounds [7]. Their advantages include the possibility of controlling drug unmasking (desilylation) and absence of toxic byproducts. Besides more common di-silyl (or fully silylated) derivatives, monosilyl derivatives of HA were reported to have been formed during the preparation of di-silylated compounds or prepared separately [6]. Mironov et al. [8] prepared the (mono) *O*-trimethylsilylbenzhydroxamate by a reaction of the parent benzhydroxamic acid with its bis(trimethylsilyl) derivative in THF. As we have shown that the disilylated derivative has hydroximic structure [9] the reaction can be written as

$$\mathrm{Ph–C(O–SiMe_3)=N–O–SiMe_3 + Ph–C(O)–NH–OH} \rightarrow 2(\mathrm{Ph–C(O)–NH–O–SiMe_3}) \quad (1)$$

The monosilylated HAs were identified by their ^{1}H-NMR spectra [3,6,8] which were not sufficiently characteristic especially when measured in solvents other than dry DMSO. Hence the claims of authors that the mono-trimethylsilyl derivative is present as only one tautomer in chloroform [6] or acetone [8] but as two tautomers (A and B) in acetone [3] cannot be taken as reliable, similar to the claim that the mono-*tert*-butyldimethylsilyl derivative is present as one conformer in chloroform [6] and that the *tert*-butyldiphenylsilyl derivative exists as a mixture of two conformers in chloroform [10]. All these studies assumed that when one tautomer was present, it had the hydroxamate structure A with the Si–O bond and not the analogous hydroximic structures B or C. Structure C as well as structures with Si–N bonds were considered unlikely.

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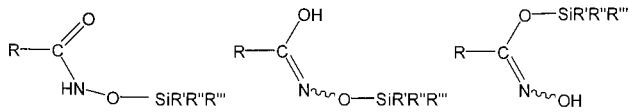

A B C

Our attempts to record conclusive ^{13}C, ^{29}Si and ^{15}N spectra of these compounds in solution failed to confirm the assumed structure [11,12]. Recent reports [10] of preparation and usage of remarkably stable *O-tert*-butyldiphenylsilyl benzhydroxamate has prompted us to reinvestigate the structure of these compounds. In the present paper, we report our findings concerning the structure and NMR spectra of mono-*tert*-butyldimethylsilyl (**1**) and mono-*tert*-butyldiphenylsilyl (**2**) derivatives of benzhydroxamic acid in solid phase and solutions.

Table 1
Crystal data and structure refinement for **1** and **2**[a]

Empirical formula	$C_{13}H_{21}NO_2Si$	$C_{23}H_{25}NO_2Si$
M_r	251.4	375.53
Crystal system	Monoclinic	Triclinic
Temperature (K)	105(2)	150(2)
Space group	$P2_1/c$	$P\bar{1}$
Unit cell dimensions		
a (Å)	6.2738(4)	9.8840(3)
b (Å)	24.714(2)	21.2770(6)
c (Å)	9.7035(6)	23.0720(6)
α (°)		62.805(2)
β (°)	108.407(3)	89.632(2)
γ (°)		77.487(1)
V (Å)^3	1427.6(2)	4189.2(2)
Z	4	8
D_{calc}, (Mg m^{-3})	1.170	1.191
$F(000)$	544	1600
Crystal size (mm^3)	$0.3\times0.2\times0.15$	$0.5\times0.22\times0.13$
Crystal description	Colorless bar	Colorless bar
2θ range for cell parameter (°)	6.64–48.2	2.18–50.08
μ (Mo–K$_\alpha$) (mm^{-1})	0.156	0.129
Index ranges	6.64–48.2; $\pm h, \pm k, \pm l$	2.18–50.08; $\pm h, \pm k, \pm l$
Number of diffractions collected	6461	42 882
Number of unique diffractions; R_{int} [a]	2235; 0.024	14 699; 0.03
Number of diffractions; $I>2\sigma(I)$	1876	9250
Number of parameters	238	989
Final R [a] indices [$I>2\sigma(I)$]	$R=0.038$, $wR_2=0.085$	$R_1=0.057$, $wR_2=0.127$
R [a] indices (all data)	$R=0.052$, $wR_2=0.092$	$R_1=0.115$, $wR_2=0.155$
w_1/w_2 [b]	0.0337/7602	0.0632/1.823
Goodness-of-fit [a] all data	1.073	1.041
$\Delta\rho$, max., min., (e Å^{-3})	0.234, −0.276	0.228, −0.333

[a] Definitions: $R_{int}=\Sigma\,|F_o^2-F_o^2(\text{mean})|/\Sigma\,F_o^2$; $R(F)=\Sigma\,||F_o|-|F_c||/\Sigma\,|F_o|$; $wR_2=[\Sigma(w(F_o^2-F_c^2)^2)/\Sigma(w(F_o^2)^2]^{1/2}$, GOF $=[\Sigma(w(F_o^2-F_c^2)^2)/(N_{refins}-N_{params})]^{1/2}$.

[b] Weighting scheme $w=[\sigma^2(F_o^2)+(w_1P)+w_2P]^{-1}$; $P=[\max(F_o^2,0)+2F_c^2]/3$.

2. Experimental

2.1. Synthesis

O-tert-butyldimethylsilyl benzhydroxamate (**1**) was prepared as described in Ref. [6]. Recrystallization from THF yielded white needle-like crystals with m.p. 140–142°C considerably higher than reported (lit. [6] 127–129°C). Anal. Found: C, 62.10; H, 8.61; N, 5.57. Calc. for $C_{13}H_{21}NO_2Si$: C, 62.11; H, 8.42; N, 5.57%.

O-tert-butyldiphenylsilyl benzhydroxamate (**2**) was synthesized according to the procedure described by Muri et al. [10]. The product recrystallized from a diethyl ether–hexane (1:1) mixture had m.p. 141°C (lit. [10] 138–139°C). Anal. Found: C, 73.43; H, 7.00; N, 3.74. Calc. for $C_{23}H_{25}NO_2Si$: C, 73.56; H, 6.71; N, 3.73%. Crystals for X-ray analysis were obtained by crystallization from ethanol–water, m.p. 149°C.

2.2. Structure determination — general comments

The selected crystals of **1** and **2** were mounted on glass fibers with epoxy glue. Diffraction intensities were measured on a Nonius KappaCCD difractometer with graphite monochromated Mo–K$_\alpha$ radiation ($\lambda=0.71073$ Å) and ω scans mode. An Oxford Cryostream low-temperature device was used for both measured crystals. Other details of cell data, data collection and refinement are summarized in Table 1. For compound **1** the space group $P2_1/c$ was uniquely determined from systematic absences, for triclinic compound **2** the centrosymmetric space group $P\bar{1}$ was selected and confirmed by successful structure analysis. No absorption correction was applied. The structures have been solved by direct methods (SIR-92) [13] and refined by full-matrix least-squares on weighted F^2 (SHELXL-97) [14]. Thermal ellipsoid plots were drawn by the PLATON program [15].

2.2.1. Crystal structure of *1*

The direct method solution yielded all non-hydrogen atoms, which were anisotropically refined. All hydrogen atoms were identified on the difference electron density map and isotropically refined.

2.2.2. Crystal structure of *2*

The unit cell of crystal **2** contains four symmetrically independent molecules leading into unfavorable high number of refined parameters. Therefore only hydrogen atoms bonded to nitrogen of hydroxamic moiety were localized on the difference electron density map and isotropically refined. All methyl hydrogens were attributed ideal tetrahedral geometry (C–C–H angles of 109.5°, C–H bond lengths of 0.96 Å and $U_{iso}(H)=1.2[U_{eq}(C)]$) and in this arrangement refined by being allowed to rotate freely around the pivotal C–C bond

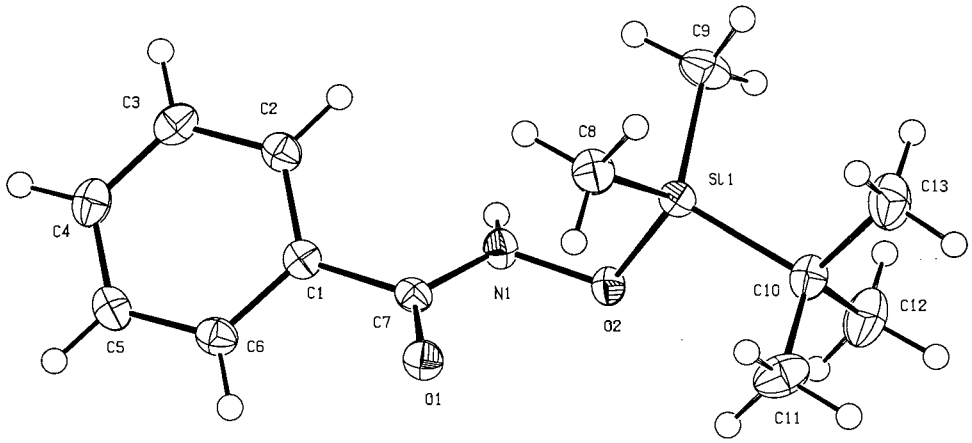

Fig. 1. Molecular structure of **1**, showing the atom labeling scheme. Thermal ellipsoids are drawn at the 50% probability level [15].

to fit the electron density maxima. Phenyl hydrogens were fixed so that the C–H bond of 0.93 Å bisects the outer C–C–C angle of the aromatic ring and $U_{iso}(H) = 1.2[U_{eq}(C)]$.

Solid state ^{13}C, ^{29}Si and ^{15}N CP MAS spectra of powdered crystals were measured on a Bruker AVANCE DSX 200 spectrometer in 4 and 7 mm spinners (the latter for ^{15}N). Lines of non-protonated carbons were identified by a NQS pulse sequence [16]. Solid state ^{29}Si- and ^{15}N-NMR spectra were externally referenced to the signal of M8Q8 ($\delta = -109.8$ ppm) and CH_3NO_2 ($\delta = 0.0$), respectively. The carbonyl peak of glycine ($\delta = 176.03$) was used as the external ^{13}C reference. All the spectra were measured with ^1H decoupling during acquisition and with cross-polarization contact time of 2 ms, relaxation delay 6 s and spinning rate 3.5 kHz. Approximately 100 transients were required for ^{13}C- and ^{29}Si-NMR spectra while 500 and 10 000 scans were needed for ^{15}N-NMR spectra of **2** and **1**, respectively.

Solution ^1H-, ^{13}C-, and ^{29}Si-NMR spectral measurements were performed on a Varian UNITY-200 spectrometer (operating at 200.04 MHz for ^1H-NMR, at 50.3 MHz for ^{13}C-NMR, and at 39.7 MHz for ^{29}Si-NMR measurements) using a 5 mm switchable probe. ^{15}N spectra were measured on a Varian UNITY 500 spectrometer (at 50.667 MHz) in a 5 mm broad-band probe. In all cases, the standard software (APT, INADEQUATE, and INEPT pulse sequences) was used. Unless indicated otherwise, the spectra were recorded in the temperature range 22–24°C. The ^{29}Si-NMR spectra were measured by the INEPT with the pulse sequence optimized [17] for TMS derivatives, i.e. for coupling to nine protons and coupling constant of 6.5 Hz. Acquisition (2.0 s) was followed by a relaxation delay of 5 s. During the acquisition period WALTZ decoupling was used and FID data (16 K) were sampled for the spectral width of 4000 Hz. Zero filling to 32 K and a mild exponential broadening were used in the data processing. The ^{29}Si $\pi/2$ pulses were at maximum 20 μs long whereas ^1H $\pi/2$ pulses were 12 μs. The ^{29}Si spectra were referenced to internal standards either to the line of HMDSS at $\delta = -19.79$ (in chloroform-*d*), -19.88 (in DMSO-d_8) or -19.56 (in benzene-d_6) or to the line of TMS at $\delta = 0.00$ (in THF-d_8). The ^{13}C-NMR spectra were measured using the spectral width of 16 000 Hz. WALTZ decoupling was applied both during acquisition (1 s) and relaxation delay (2–5 s). Zero filling to 64 K and 1–3 Hz line broadening was used in data processing. The spectra were referenced to the line of the solvent ($\delta = 76.99$, 39.70, 128.70 in chloroform-*d*, DMSO-d_8, benzene-d_6, respectively).

^{15}N-NMR spectra of non-enriched samples of high concentration were measured in a 5 mm broad-band probe using 90° excitation pulses and 1 s acquisition for the spectral width of 30 kHz. The relaxation delay varied between 5 and 60 s depending on whether the negative NOE was used or not to enhance the signal. The spectra were referenced externally to the ^{15}N-NMR line of 50% solution of nitromethane in the same deuterated solvent.

Aromatic carbon chemical shifts were assigned according to the shifts assigned for the parent benzhydroxamic acid [18] and intensity considerations.

3. Results and discussion

3.1. Crystal structures

3.1.1. Crystal structure of *1*

The molecular structure of **1** (Fig. 1) verifies proposed arrangement A on hydroxamic group with the O–Si bond. The individual bond lengths and angles are unexceptional, however similar C(O)N(H)OSi moiety was not found in the latest version of the Cambridge Structural Database [19] and therefore its selected parameters are given in Table 2. The benzene ring as

well as C(O)NO moiety are planar within ±0.007 and ±0.03 Å, respectively, with amid hydrogen displaced by 0.19(2) Å from its corresponding plane. The value of the dihedral angle subtended by the C1–C6 and C7(O1)N1O2 planes 36.9(1)° is within the range 3.5–46.1° found in benzhydroxamic acids [20], but this interval is not uniformly populated and the presented structure belongs to the group represented by values 32.1 and 35.4° in the article mentioned.

In the crystal, the molecules are connected by intermolecular –N–H···O=C– O=C–N–H···O=C–hydrogen bonds (see Table 3) into infinite chain propagating along the *c*-axis. The position of phenyl group and *tert*-butyldimethylsilyl moiety on neighboring molecules alternate along the chain and therefore no π–π interaction either within or between chains was found.

3.1.2. Crystal structure of **2**

All parameters discussed in the previous section are given in Tables 2 and 3 for four independent molecules M1–M4 of **2** numbered as shown in Fig. 2. The comparison of four molecules by fitting phenyl rings (C # 1–C # 6) of hydroxamic moiety one on other reveals that molecules M1–M3 are close to each other, whereas molecule M4 differs in the orientation of the *tert*-butyldiphenylsilyl group, which can be described as the rotation around N41–O42 bound by 180° with regard to M1 and the silicon atom Si41 is therefore moved out of the least-square plane defined by atom C41, C42, C43, C44 C45, C46 (Si-plane distances 1.834(7) Å). Similar distances for the remaining molecules are 0.399(8), 067(7) and 0.671(8) Å for M1, M2, and M3, respectively.

To summarize, both compounds have the structure A of silyl benzhydroxamate and all the molecules assume *syn-periplanar* (*sp*) conformation around the C(O)–N(O) bond in the solid state. The structures of **1** and **2** resemble each other with some interesting details. The difference in the absolute value of the torsion angle C–N–O–Si between crystals **1** and **2** is in the same range as between different molecules in **2**, as well as the dihedral angles of aromatic and HA planes (Table 2). Contrary to **1**, there are more than 40 mutual positions of phenyl rings in **2** which enable some degree of π–π interactions, however, the most important contacts for molecular packing retain the same hydrogen bonding structure (Table 3), forming two infinite chains, the first from molecules M1 and M2 and the second from M3 and M4 molecules. Both chains are propagating along the *a*-axis, the length of which is close to the corresponding *c*-axis in the crystal of **1** (9.7100(9), 9.8840(3) Å for **1** and **2**, respectively). The phenyl rings are on the same side of the chains, but the chains are well shielded from the remaining space by *tert*-butyl and phenyl

Table 2
Selected bond lengths (Å), bond angles, torsion angles and dihedral angles (φ) of aromatic (C1–C6) and HA (C7(O1)N1O2) planes (°) for **1** and **2**

	1	**2**			
		Molecule 1	Molecule 2	Molecule 3	Molecule 4
Si(1)–O(2)	1.6933(14)	1.6858(19)	1.6862(19)	1.6853(19)	1.6925(19)
C(1)–C(7)	1.499(3)	1.495(4)	1.494(4)	1.489(4)	1.495(4)
C(7)–O(1)	1.234(2)	1.230(3)	1.233(3)	1.235(3)	1.236(3)
C(7)–N(1)	1.341(2)	1.335(3)	1.336(3)	1.340(3)	1.405(3)
O(1)–C(7)–N(1)	123.5(3)	122.1(3)	123.4(3)	122.1(3)	123.4(3)
O(1)–C(7)–C(1)	122.36(16)	122.0(2)	122.0(3)	122.5(2)	121.6(2)
N(1)–C(7)–C(1)	114.16(16)	115.5(2)	114.5(2)	115.4(2)	115.0(2)
C(7)–N(1)–O(2)	118.19(15)	117.9(2)	118.2(2)	118.0(2)	118.5(2)
N(1)–O(2)–Si(1)	112.96(10)	117.40(15)	115.53(15)	117.57(15)	113.76(14)
C(7)–N(1)–O(2)–Si(1)	−102.71(16)	−95.4(2)	99.5(2)	−91.9(2)	97.5(2)
φ	36.9(1)	35.1(2)	37.5(1)	30.6(2)	30.0(1)

Table 3
Hydrogen bonds for **1** and **2** (Å and °)[a]

Compound	D–H···A [a]	*d*(D–H)	*d*(H…A)	*d*(H…A)	∠(DHA)
1	N(1)–H(1)…O(1)^{i}	0.87(2)	1.97(2)	2.830(2)	173(2)
2	N(11)–H(11)…O(21)	0.86(3)	1.93(3)	2.782(3)	171(3)
2	N(21)–H(21)…O(11)^{ii}	0.90(3)	1.91(3)	2.806(3)	169(3)
2	N(31)–H(31)…O(41)	0.87(3)	1.99(3)	2.837(3)	165(3)
2	N(41)–H(41)…O(31)^{ii}	0.93(3)	1.94(3)	2.865(3)	171(2)

[a] Symmetry transformations used to generate equivalent atoms: (i) x, $-y+1/2$, $z-1/2$; (ii) $x-1$, y, z.

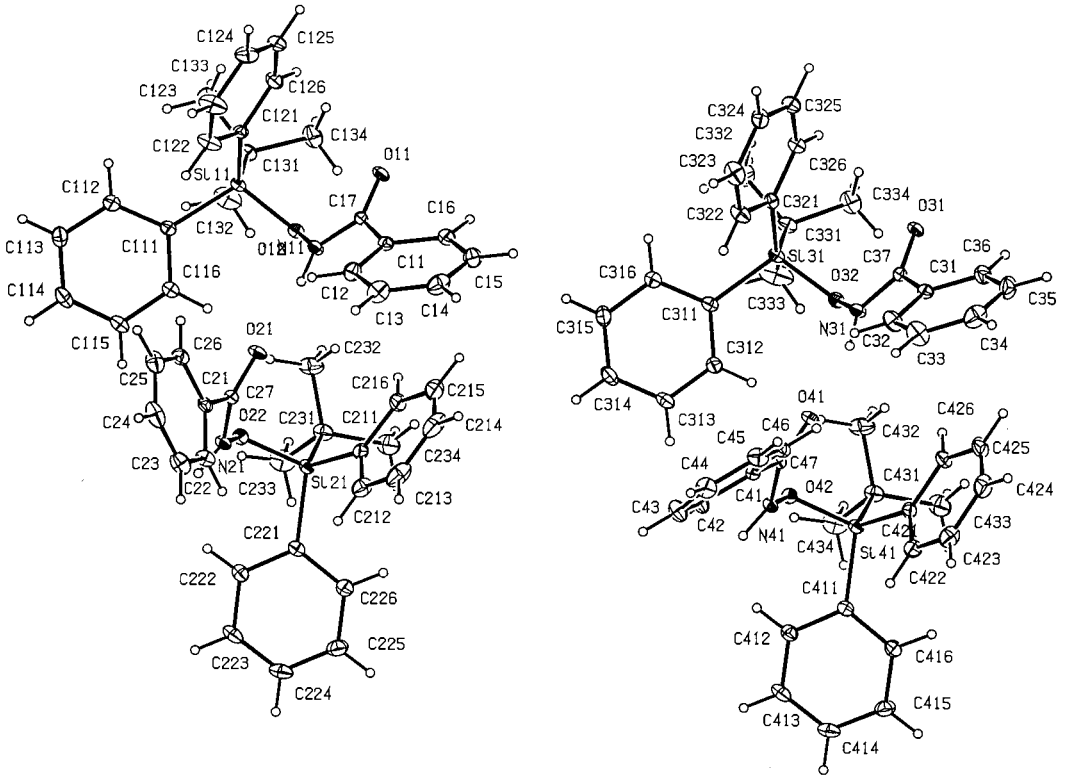

Fig. 2. Four symmetrically independent molecules of **2**. The first digit after the element name denotes the number of molecules. Thermal ellipsoids are draw at the 20% probability level for clarity of atom numbering [15].

substituents of silyl moiety (Fig. 3), thus leaving no place for a hydrolytic attack in the good agreement with stability of compound **2**.

3.2. Solid state NMR spectra

The solid state NMR spectra (Table 4) of the compounds **1** and **2** indicate, independently on the X-ray structure, that the two compounds have essentially the same structure and that it is the structure A. The strongest points of evidence are ^{15}N, ^{29}Si and $^{13}C(C{=}O)$ chemical shifts, the remaining ^{13}C chemical shifts are given for the sake of complete structure identification. The ^{15}N chemical shifts are close to that found in the parent benzhydroxamic acid, both in the solid state ($\delta = -216.1$) and in the DMSO solution ($\delta = -215.1$). The ^{15}N chemical shift of structure B would be expected somewhere around -80 to -90, as signals of benzhydroximic derivatives are found in that region [9,12]. Similarly, the highest frequency ^{13}C chemical shifts in Table 4 are close to solution $^{13}C(C{=}O)$ chemical shifts of HA which occur in the region of 162–165 ppm, while those of hydroximic structures $^{13}C(C{=}N)$ occur at $\delta = 151–153$ ppm [9,12]. The ^{29}Si chemical shift of **1** is definitely the shift of silicon from the RR′R″Si–O– grouping [21]. The shift in **2** falls into the region where the interpretation is not that straightforward. However, as the difference in $\delta(^{29}Si)$ values between the two compounds corresponds to the change in the substituents bonded to the silicon atom (e.g. in $PhCH_2$-*O*-$SiMe_2Bu^t$ the shift is $\delta(^{29}Si) = 20.47$ while it is $\delta(^{29}Si) = -3.20$ in $PhCH_2$-*O*-$SiPh_2Bu^t$), the ^{29}Si chemical shift agrees with the proposed structure. Obviously, solid state NMR can be used to establish hydroxamic or hydroximic structure when the crystals are difficult to prepare and the compounds decompose in solutions.

3.3. NMR spectra and structure in solutions

The appearance of the spectra of compounds **1** and **2** depends on the solvent used, on the concentration and on the thermal history of the solution in a striking manner. Depending on these conditions we could identify besides the products of the expected (and found in the solid state) structure A, also derivatives of hydroximic structure both mono and disilylated. Since measurements of the decisive ^{15}N-NMR spectra is time consuming only chloroform and dimethylsulfoxide solutions were studied in detail, and solutions in other solvents (benzene and tetrahydrofuran) were studied only briefly.

3.4. Chloroform-d solutions

^{13}C-NMR spectra of **2** (both in 0.06 and 0.3 M solutions in dry chloroform-*d*) agree fully with the data given in the supplementary material of Ref. [10], namely all lines appear in pairs (their intensity ratio varying around 1:1 with sample temperature). Our ^{1}H-NMR spectra contain two singlet lines at 8.31 and 7.94 ppm (OH or NH protons, the chemical shift and linewidth depend on sample concentration and measuring conditions; the two lines might be broadened in non-dry and/or acidic conditions and so overlooked in the spectrum), in addition to the lines listed in Ref. [10]. The ^{1}H-NMR spectra measured at a higher field (500 MHz) also show two non-equivalent CH_3 groups (with the chemical shift difference of only 0.004 ppm). The appearance of paired lines in ^{1}H- and ^{13}C-NMR spectra was attributed to the presence of two rotamers in the solution [10]. In ^{29}Si-NMR spectra (Table 5) we also see two lines. The small chemical shift differences (less than 1 ppm) between the paired ^{13}C lines in majority of pairs supports the idea of two conformers, the large difference between the two shifts of CNO carbons (8.0 ppm) is, however, suspect. The decisive results come from

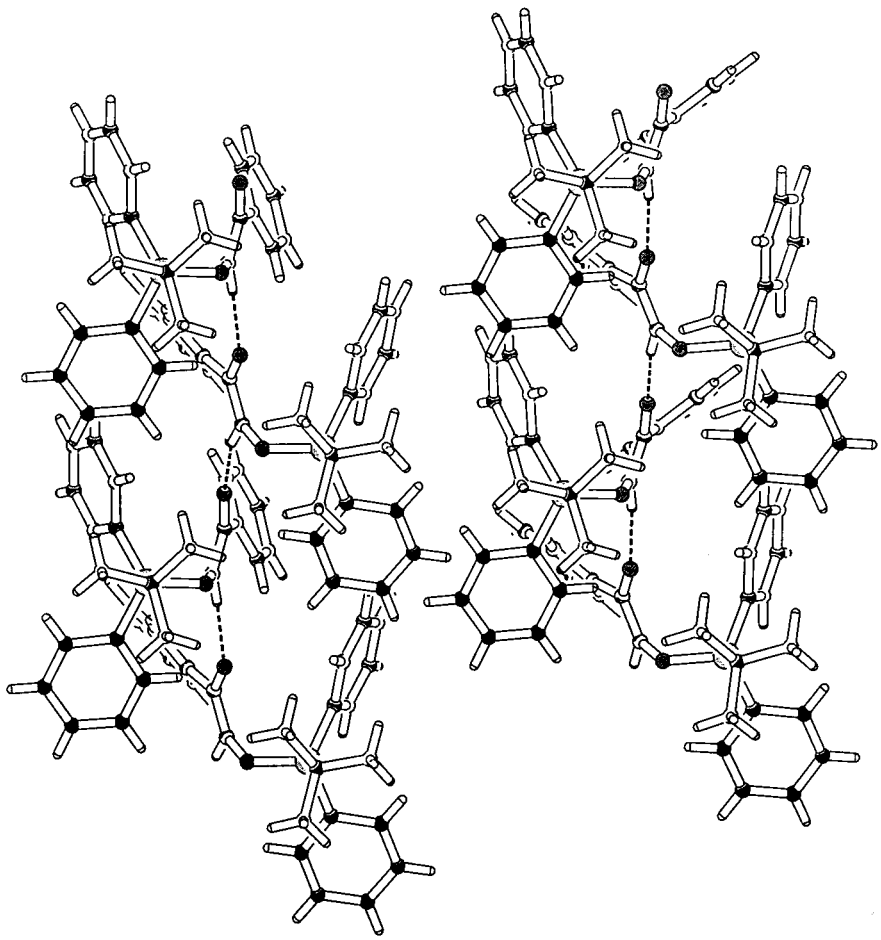

Fig. 3. System of hydrogen bonds N–H···O=C forming two chains in the crystal of **2** [15].

Table 4
Solid state chemical shifts in compounds **1** and **2** [a]

Compound	^{13}C								^{29}Si	^{15}N
	C=O	C_{arom}				CH_3	C	MeSi		
1	167.3	134.5	132.0	128.4		26.8	17.8	−6.7	31.7	−213.8
2	164 [b]	136.8	131.6	128.9	127.4	27.7	19.1		8.0	−212.5

[a] Chemical shifts in δ scale, ^{13}C relative to external glycin ($\delta = 176.03$), ^{29}Si relative to external M_8Q_8 ($\delta = -109.8$) and ^{15}N relative to external CH_3NO_2 ($\delta = 0.0$).

[b] Broad peak.

Table 5
Chemical shifts of compounds **1** and **2** in solutions [a]

Compound	^{13}C								^{1}H			^{29}Si	^{15}N
	O–C–N	C–1	C–2/6 [b]	C–3/5 [b]	C–4	CH_3	C	MeSi	NH/OH	CH_3	MeSi		
*Chloroform solution of **1***													
1A [c]	167.59	130.67	126.94	128.68	131.86	25.87	18.27	−5.62	8.28	1.01	0.26	33.71	– [d]
1BC [e]	158.56	129.11	125.73	128.24	132.21	26.06	18.27	−5.23	8.16	1.01	0.26	29.55	– [d]
*Chloroform solution of **2***													
2A [c]	166.88	128.91	[f]	[f]	[f]	26.78	19.21	–	7.94	1.19	–	6.44	−213.9 [g]
2BC [e]	158.86	132.28	[f]	[f]	[f]	27.27	19.60	–	8.31	1.19	–	2.23	−83.7
*Dimethylsulfoxide solution of **1** after heat treatment*													
1A	165.54	132.91	127.29	128.56	131.52	25.94	18.19	−5.25	11.34	0.96	0.17	31.84	−211.7 [h]
1D	152.88	133.03 [b]	125.93	[i]	131.28	26.40	18.80	−3.22	–	0.84	0.26	28.50	−79.6
						25.94	18.58	−4.86		0.96	0.19	24.60	
3	164.40	132.45 [b]	127.09	[i]	[i]	–	–	–	11.25	–	–	–	−215.8
									9.05				
*Dimethylsulfoxide solution of **2** after slow heat treatment*													
2A	166.69	[j]	[j]	[j]	[j]	27.03	19.34	–	11.39	1.12	–	3.73	−209.7
2D	151.67	[j]	[j]	[j]	[j]	26.39	18.85	–	–	0.75		2.43	–
						27.03	19.92			0.96		−3.20	
*Dimethylsulfoxide solution of **2** after fast heat treatment*													
2A	166.62	[k]	[k]	[k]	[k]	27.01	19.34	–	11.51	1.21	–	3.90	−209.7 [l]
2BC	157.11	[k]	[k]	[k]	[k]	26.40	19.34	–	11.06	1.06	–	0.13	−89.2

[a] Chemical shifts in δ scale, for the references see Section 2, measurements at 22°C, C–1 through C–4 denotes aromatic carbon atoms of benzhydroxamic group.
[b] Tentative assignment, it may be reversed.
[c] The more abundant mixture component.
[d] Not measurable or not measured.
[e] The less abundant mixture component.
[f] Other unassigned lines: 135.67, 135.32, 133.13, 131.64, 131.39, 130.47, 129.79, 128.47, 128.18, 127.91, 127.63, 126.89, 125.86.
[g] Coupling to NH proton $^{1}J(^{15}N–^{1}H) = 94.1$ Hz.
[h] Coupling to NH proton $^{1}J(^{15}N–^{1}H) = 98.1$ Hz.
[i] Other lines not assigned.
[j] Unassigned aromatic carbon lines (relative intensity) 135.62 (10), 134.91(1), 134.63(1), 134.31(1), 132.96(1), 132.74(1) 132.26(4, broad), 131.45(4, broad), 130.13(6), 128.48(10), 127.73(20), 127.3(2, broad), 127.0(2, broad).
[k] Unassigned aromatic carbon lines (relative intensity) 135.65 (10), 134.91(1), 134.63(1), 134.31(1), 132.82(4, broad), 132.23(6, broad),131.48(4, broad), 130.14(6), 128.48(10), 127.73(20), 127.27(6, broad), 127.03(1)).
[l] Coupling to NH proton $^{1}J(^{15}N–^{1}H) = 96.1$ Hz.

^{15}N-NMR. Comparison with the above-mentioned data on NMR spectra of benzhydroxamic acid derivatives clearly shows that the major component has the structure of HA derivative A (compound **2A**) while the minor component has either B or C hydroximic structure (compound **2BC**). At present, we are not in a position to distinguish between the structures B and C and to determine the geometry on the double bond C=N (*E* or *Z* isomers).

In contrast, **1** has a limited solubility in chloroform (approximately 0.35 M solution at 22°C) and only one broad (20.8 Hz) line is seen in the ^{29}Si-NMR spectrum ($\delta = 33.52$) of the saturated solution. We could not detect any ^{15}N-NMR signal in this solution. In the ^{13}C-NMR spectrum some lines are narrow (e.g. lines of *tert*-butyl group and of some aromatic carbons) while others are broad (e.g. the lines of CNO and some aromatic carbons). Increasing sample temperature (to 40–50°C) further broadens the broad lines (both ^{29}Si and ^{13}C). On the other hand, decreasing solute concentration (below 0.1 M) makes lines narrower and leads to the appearance of new weak lines. Despite the absence of ^{15}N-NMR data for this solution, it seems rather safe to conclude on the basis of the comparison of ^{29}Si- and ^{13}C-NMR results for compounds **1** and **2**, that also in dilute chloroform solutions of **1** the major component has structure A (**1A**) and the minor one either B or C (**1BC**). The described changes with concentration and temperature can be explained by an exchange process between the two structures that is faster in the concentrated solution but does not reach coalescence under conditions that could be employed.

3.5. Dimethylsulfoxide-d_6 solutions

^{29}Si-NMR spectra usually have narrow lines (less than 1 Hz), even diluted (less than 0.1 M) samples of **1** and **2** have, however, spectral linewidths larger than 4 Hz. Heating of the samples had surprising effects that are described here for concentrated solutions (0.5 M or

higher) in which ^{15}N-NMR spectra could also be measured.

^{29}Si-NMR spectra of **1** measured at different temperatures are shown in Fig. 4. The 8 Hz broad line at $\delta = 31.8$ visible in the spectrum of native **1** (i.e. before any thermal treatment of the solution) is not an instrumental artifact. With increasing temperature this line broadens and at 80°C and two new narrow (1 Hz) ^{29}Si lines appear ($\delta = 28.5$ and 24.63), their intensity increases further with temperature at the expense of the intensity of the original broad line. At 100°C the combined integral of the two narrow lines takes 60% of all the ^{29}Si signals. Cooling down does not restore the native situation completely. The two narrow lines remain present but constitute only 20% of the total ^{29}Si signal and the major line at $\delta = 31.8$ also becomes narrow (1.6 Hz). The repeated heating cycle is, however, reversible: e.g. the line at $\delta = 31.8$ becomes broad and intensities of the two lines increase at 80°C. The temperature dependence of the ^{29}Si-NMR spectra is paralleled in the ^{15}N-NMR spectra. The line seen in the native sample at $\delta = -211.7$ is 18 Hz broad; its chemical shift confirms the hydroxamic structure (A) of **1**. At 50°C, no line could be detected supposedly because it became too broad. The sample which went through the thermal cycle had three lines at $\delta = -215.7$, -211.7, and -79.6 in an approximate ratio 10:1:1.

Using GC–MS analysis of the measured mixture and NMR spectra of an authentic sample of *Z*-O^1,O^4-bis(-*tert*-butyldimethylsilyl)benzhydroximate (**1D**) [11] we have proved that the two narrow ^{29}Si lines are due to this compound which is formed through the reversed reaction (1) under these conditions. The presence of all three compounds occurring in reaction (1) in the thermally treated solution is obvious from the ^{13}C- and ^{15}N-NMR spectra of the C–N moiety ($\delta(^{13}C) = 165.54$,

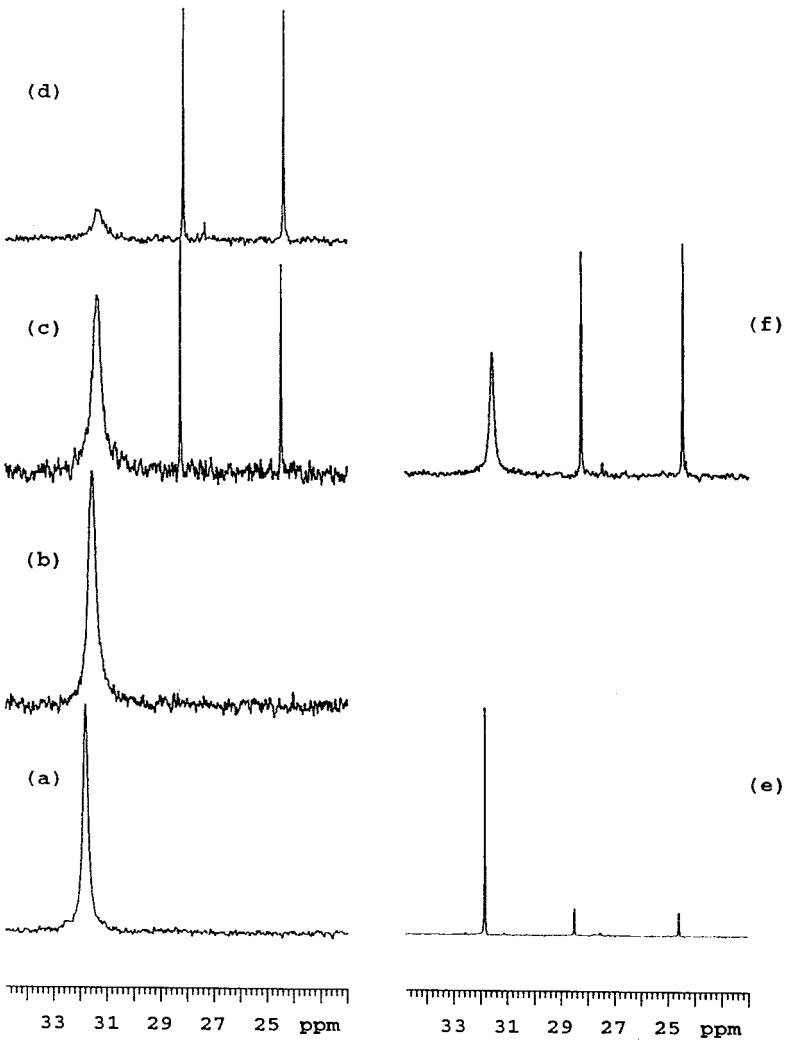

Fig. 4. Temperature dependence of ^{29}Si-NMR spectra of **1** in dimethylsulfoxide-d_6 solution (0.6 M solution, external ^{29}Si referencing, spectra measured by INEPT, intensity normalized to the same height of the most intense line, 136 transients, relaxation delay 5.0 s, line broadening 1.0 Hz): (a) native solution at 295°K; (b) native solution at 333°K; (c) native solution at 353°K; (d) native solution at 373°K; (e) heat treated solution at 295°K; and (f) heat treated solution at 353°K.

152.88, and 164.40; $\delta(^{15}N)$: = −211.7, −79.6, and −215.7 for **1A**, **1D**, and benzhydroxamic acid, respectively). Probably, formation of free benzhydroxamic acid increases the exchange rate of the process responsible for the broadening of the line at $\delta = 31.8$ at 22°C. The nature of this process, and why that line broadens with increasing temperature in the presence of the acid remains unclear.

Native dimethylsulfoxide solutions of **2** contain only two broad signals in the ratio 6:1 both in the ^{29}Si-NMR spectra ($\delta = 3.80$, 5 Hz broad, and $\delta = -0.07$, 20 Hz broad) and ^{1}H-NMR spectra of NH/OH protons ($\delta =$ 11.39 and 10.96). In ^{15}N-NMR spectra we could see only one line at: $\delta = -209.7$ (with linewidth of 12.7 Hz and $^{1}J(^{1}H–^{15}N) = 96.1$ Hz), obviously, the line is due to the structure which is more abundant in the solution. When the sample went through the heating stages slowly, we could not see any ^{29}Si signal and only one broad line at $\delta = 11.17$ in the ^{1}H-NMR spectrum at 60°C. At 100°C, we could detect one ^{29}Si line at $\delta =$ 2.31 (line 15 Hz broad, externally referenced) and one ^{1}H line at $\delta = 10.90$ (15 Hz broad). Cooling this solution produced ^{29}Si-NMR spectra similar in appearance to the spectra of **1**, except for its different ratio (25:1:1) and that the main line remains broad and all three lines have different chemical shifts in agreement with the different substituents on the silicon atom. In analogy with the similar solution of **1**, these shifts indicate formation of disilylated product *Z*-O^{1},O^{4}-bis(*tert*-butyldiphenylsilyl)-benzhydroximate (**2D**) under these conditions. When an identical sample is heated fast directly to 100°C and then cooled down, the cooled down solution produces ^{29}Si- and ^{15}N-NMR spectra, each containing only two lines in the 4:1 ratio. Obviously, the major product is **2** with structure A (**2A**) and the minor one has either B or C (**2BC**) hydroximic structure, where again we are not able to differentiate between structures B and C.

3.6. Tetrahydrofuran-d_8 solutions

The spectra of **1** contain two sets of lines; in concentrated solutions the lines are broad and the ratio of the two components is roughly 3:1. In dilute solutions the ratio is 3:2, the lines are about 20-times narrower (0.5 Hz in the ^{29}Si-NMR spectra) but the chemical shifts are not different ($\delta = 30.17$ and 27.21). Since ^{15}N-NMR spectra (of concentrated solutions) show two lines at $\delta = -213.7$ and -84.7 we conclude that in this solvent **1** is present as a mixture of **1A** (major) and **1BC** (minor component) similar to that in the chloroform solution. The spectra of **2** also indicate the presence of two components but in the ratio 4:1. The chemical shifts ($\delta(^{29}Si) = 1.09$ and 3.79 and $\delta(^{13}C–N) = 158.65$ and 167.60) indicate that the major component has the structure of **2BC** and the **2A** structure is the minor component under these circumstances.

3.7. Benzene-d_6 solutions

Compound **1** has a very limited solubility in this solvent; the ^{29}Si chemical shift ($\delta = 29.63$) and ^{13}C chemical shift of C–N carbon ($\delta = 159.53$) suggest that the compound is present in this solvent solely in structure **1BC**. The ^{29}Si-NMR spectrum of **2** exhibits two lines with $\delta = 2.99$ and 5.74 in a 5:2 ratio. These values together with the ^{13}C shifts of C–N carbons ($\delta =$ 160.19 and 156.81) indicate that **2** is present in structures **2BC** and **2A** similar to that in the chloroform solution except for the preference of the **2BC** isomer (the ratio of these isomers of **2** is reversed in acetonitrile solutions, $\delta = 1.69$ and 5.33 in 1:2 ratio).

4. Conclusions

Though the studied monosilylated benzhydroxamic acids have in the solid state, structure A of silyl hydroxamates, on dissolving in chloroform they spontaneously form an equilibrium mixture of hydroxamic (A) and hydroximic derivatives (B or C) (and not a mixture of conformers of A as assumed before). The ratio of hydroxamic–hydroximic isomers is close to 1:1 in solutions of **2** and 5:1 in solutions of **1** in chloroform. In other solvents (tetrahydrofuran, benzene, acetonitrile) the ratios are different. In imethylsulfoxide, the NMR lines of hydroxamic isomers A are broad, heating leads to the formation of hydroximic isomers BC or to a disilylated product (D) of the type *Z*-O^{1},O^{4}-bis(*tert*-butyldimethylsilyl)-benzhydroximate, depending on the experimental conditions.

5. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 154242 and 154243 for compounds **1** and **2**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www:http://www.ccdc.cam.ac.uk).

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