
**APPLICATION OF ^{29}Si -NMR TO ANALYSIS
OF SILYLATED AMINO AND OTHER CARBOXYLIC ACIDS**

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^{29}Si -NMR chemical shifts are given for nine trimethylsilylated carbonfunctional carboxylic acids. Different ^{29}Si -NMR signals correspond to different silylation sites. The signals of silicon nuclei in silyl ester, alkoxysilyl, and aminosilyl groups are found in distinctly different spectral regions, so the nature of the silylation is readily apparent from the spectrum.

It was suggested¹ that measurement of ^{29}Si -NMR spectra can be useful in structure elucidation of polyfunctional compounds which are frequently prepared or isolated as trimethylsilyl derivatives. Illustrative examples were given from the field of sugar^{1,2} and steroid¹ chemistry and it was shown that structurally different sites of silylation give different ^{29}Si -NMR signals.

Since silylation is a useful technique in peptide or amino acid chemistry^{3,4} it was of interest to see if the ^{29}Si -NMR method could be of use also for this type of compounds. The same idea had occurred earlier to Bayer and coworkers⁵ who measured the ^{29}Si -NMR spectrum of N,O-bis(trimethylsilyl) derivative of trifluoroacetimidic acid and found two different signals for the two types of silicon atoms in the molecule. Literature survey⁶ indicated that the silicon atoms in Si—N—CH and Si—OC(O) groups should have also different chemical shifts but in this paper we present direct experimental results which confirm this expectation. As ^{13}C -NMR analysis of other carbonfunctional carboxylic acids is sometimes difficult^{7,8} we investigated also trimethylsilyl derivatives of some carboxylic acids bearing a hydroxy or mercapto group in the aliphatic side chain.

EXPERIMENTAL

The amino acids used were commercial products (Calbiochem, U.S.A.). Their purity was checked by paper electrophoresis at pH 2 and 5.6, by thin-layer chromatography and optical rotation

(the values found were in agreement with those in literature⁹). The silylation of substituted carboxylic acids was carried out as described in ref.³. The acids were treated with an excess of hexamethyldisilazane and a catalytic amount of ammonium sulphate in pyridine. The silylated compounds were obtained by rectification *in vacuo*, their boiling points and analyses are given in Table I. The preparation of $(\text{CH}_3)_3\text{SiSC}(\text{O})\text{CH}_3$ compound was reported earlier¹³ and N,O-bis-(trimethylsilyl) derivative of trifluoroacetic acid was supplied by Fluka A. G., Buchs. Structure of the silylated compounds was verified by their ¹H- and ¹³C-NMR spectra. The ²⁹Si-NMR spectra were measured in the FT mode with the gated decoupling to prevent nuclear Overhauser effect. Two slightly different experimental methods were employed:

A) Operating a Bruker HX 60 spectrometer at 11.919 MHz memory of 4 K was used to store the FID signal while 1.25 kHz sweep width was covered. The spectra were referenced to internal tetramethylsilane.

B) A Jeol-PFT-100 spectrometer interfaced to a Nicolet 1085 data system was employed and the spectra recorded at 19.87 MHz using 8 K memory for the FID and 2 KHz sweep width. The spectrometer was locked to ¹⁹F-NMR signal of CF₃COOH placed in a capillary. The spectra

TABLE I
Silylated Carboxylic Acids

No	Compound parent acid	B.p. °C/Torr	Calculated/ Found	
			% C	% H
I	$(\text{CH}_3)_3\text{SiNHCH}(\text{CH}_3)\text{COOSi}(\text{CH}_3)_3^a$ DL-alanine	85/12	46.31	9.93
			46.24	9.91
II	$(\text{CH}_3)_3\text{SiNHCH}(\text{CH}_2\text{C}_6\text{H}_5)\text{COOSi}(\text{CH}_3)_3$ L-phenylalanine	135/13	—	—
III	$(\text{CH}_3)_3\text{SiNHCH}(\text{CH}_2\text{OSi}(\text{CH}_3)_3)\text{COOSi}(\text{CH}_3)_3^b$ DL-serine	115/15	—	—
IV	$(\text{CH}_3)_3\text{SiNHCH}(\text{CH}(\text{CH}_3)\text{OSi}(\text{CH}_3)_3)\text{COOSi}(\text{CH}_3)_3$ DL-threonine	122/18	—	—
V	$[(\text{CH}_3)_3\text{Si}]_2\text{NCH}_2\text{COOSi}(\text{CH}_3)_3$ glycine	93/5	45.30	10.02
			44.82	9.77
VI	$(\text{CH}_3)_3\text{SiOCH}_2\text{COOSi}(\text{CH}_3)_3$ hydroxyacetic acid	77/8	43.54	9.13
VII	$(\text{CH}_3)_3\text{SiSCH}_2\text{COOSi}(\text{CH}_3)_3$ mercaptoacetic acid	45/1	37.57	7.88
			37.29	7.46
VIII	$(\text{CH}_3)_3\text{SiSC}(\text{O})\text{CH}_3$	100 ^c	—	—
IX	$\text{CF}_3\text{C}(\text{OSi}(\text{CH}_3)_3)\text{NSi}(\text{CH}_3)_3$	141.5/745 ^d	—	—

^a For an earlier preparation see ref.¹⁰; ^b for an earlier preparation see ref.¹¹; ^c *cf.*⁵, atmospheric pressure; ^d ref.¹².

were referenced to hexamethyldisiloxane contained in a separate sample. The chemical shift of $\delta = 6.78$ was found for hexamethyldisiloxane line and used in the conversion of the shifts into the δ -scale.

RESULTS AND DISCUSSION

The experimental results are summarized in Table II. It is clear from the data that the ^{29}Si signals of silylated amino-, hydroxy- and mercapto-substituted carboxylic acids are found in three different non-overlapping spectral regions: 3.0–8.2, 15.0 to 19.7, and 22.0–25.5 ppm (δ -scale).

In the first region (3.0–8.2 ppm) the line of the silicon nucleus in trimethylsilyl-amino group is found; when a primary amino group is monosilylated the signal occurs in a narrow range 3.0–4.2, silicon nuclei in N,N-bis(trimethylsilyl)amino group resonate around $\delta = 8$. According to other measurements^{14,15} the lines of trimethylsilylated secondary amines can be found between 2.15 and 7.42 ppm. The present data, though limited, also show that the silicon shielding in compounds of the type $(\text{CH}_3)_3\text{Si}-\text{NH}-\text{CH}(\text{COOR}')\text{CH}_2\text{R}$ is sensitive to the nature of the substituent R. The sensitivity is not, however, greater than that in compounds of the type $(\text{CH}_3)_3\text{Si}-\text{CH}_2-\text{CH}_2-\text{CH}_2\text{R}$ as one might expect on the grounds of similar properties of Si–N and Si–O bonds and of the larger sensitivity of the silicon

TABLE II
 ^{29}Si -NMR Chemical Shifts $\delta(^{29}\text{Si})$

Compound	Si–N	Si–O–CH	Si–OC(=O)	Si–S	Method ^a
I	3.02	—	23.14	—	A
II	3.68	—	23.13	—	B
III	4.03	17.45	23.01	—	B
IV	4.13	15.12	22.39	—	B
V	8.19	—	22.78	—	A
VI	—	19.66	24.14	—	B
VII	—	—	—	25.29 25.39	A B
VIII	—	—	—	22.42	A
IX	–2.43	—	24.48 ^b	—	B

^a The chemical shifts are in δ -scale (ppm units relative to tetramethylsilane line, shifts to lower field are positive). For the description of the method of measurements see Experimental. ^b The line of SiOC=N silicon nucleus.

shielding in compounds containing Si—O—C—R than in those containing Si—C—R fragments¹. This conclusion follows from a comparison of the shifts in compounds *I—V* with those in trimethylpropylsilane $\delta = 0.7$ (ref.¹⁶), trimethylbutylsilane $\delta = 0.6$ (ref.¹⁶), 3-trimethylsilylpropan-1-ol $\delta = 1.7$ (ref.¹⁶), and 1-trimethylsilyl-3-phenylpropane $\delta = 1.1$ (ref.¹⁷). Smaller variation of the chemical shifts of silicon atom bonded to a nitrogen atom than that bonded to an oxygen atom was noticed in a study of silazanes¹⁸, but it is possible that in the studied compounds the COOR' group reduces the sensitivity of the silicon shift to substituent effects. Similar attenuation of substituent effects has been reported¹⁹. The variation in the silicon shielding in compounds *I—IV* is such that it can be described as increasing deshielding with the increasing size of the substituent R. The same trend was described^{20,21} for the compounds of the type $(\text{CH}_3)_3\text{SiOR}$ and it was attributed to steric interactions²¹.

The range 15.0–19.7 ppm contains signals from $(\text{CH}_3)_3\text{Si—O—CH}$ groups. Compounds with such groupings are now being intensively studied^{1,16,20,21}. The published correlation²⁰ allows one to estimate from the silicon shift the value of σ^* constant of the substituent R in compounds of the type $(\text{CH}_3)_3\text{SiOR}$, but the estimate is very approximative to be utilized analytically. As noted above for Si—N silicon shielding, the trend in the silicon shielding in Si—O—CH groups confirms the reported²¹ deshielding with increasing bulkiness of the substituent R. Unfortunately, more direct conclusion about the structure of the substituent R cannot be made on the basis of this shift alone for it depends not only on the number but also on the nature of the atoms in γ positions with respect to the silicon atom^{1,21}.

Silicon chemical shifts of $(\text{CH}_3)_3\text{SiOC(O)}$ groups, which are found in the third range of δ (22.0–25.5 ppm), have been studied in some detail^{22,23}. The established correlations of the shifts with the pK_A values of the parent acids⁹ are too approximate to be utilized for an estimation of these constants. Also the shifts in carboxylic acids vary only so little that they cannot be analytically utilized. With regard to literature values^{22,23} the range in which the signals of this type of silicon nuclei might occur should be extended up to $\delta = 32$.

In the spectrum of trimethylsilyl trimethylsilylthioacetate (*VII*) the signals of the two types of silicon nuclei overlap. As the line of the isolated trimethylsilylthio ether group is found²⁴ at $\delta = 14.95$ (in $(\text{CH}_3)_3\text{SiSC}_2\text{H}_5$) the diamagnetic shift observed in *VII* for this type of silicon nucleus is apparently due to the proximity of the carboxylic group. Obviously, the presence of sulphur containing groups in similar positions can complicate the application of ²⁹Si-NMR spectroscopy to unknown substances. Another limitation arises from the small shifts for the signals of trimethylsilyl esters caused by a modification of the carboxylic group (compare compounds *VIII* and *IX*). The high-field shift of the silicon nucleus in $(\text{CH}_3)_3\text{SiN}$ group in *IX* is outside of the discussed three ranges but similar shifts were found for silicon atoms attached to doubly-bonded nitrogen atoms²⁵.

Despite of limited and somewhat fragmentary character of this study the results convincingly show that the chemical shifts of ^{29}Si atoms in trimethylsilyl groups reflect the position of this group in the molecule of trimethylsilylated acid. The presence of amino or hydroxy group can be detected unequivocally, some difficulties may arise in the case of mercapto groups.

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