

**^{29}Si NMR CHEMICAL SHIFTS IN PERTRIMETHYLSILYLATED
1,6-ANHYDRO- β -D-GLUCOPYRANOSE DERIVATIVES.
EMPIRICAL ASSIGNMENT FROM HAMMETT TYPE DEPENDENCE
OF THE CHEMICAL SHIFTS**

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^{29}Si chemical shift of Si-3 silicon atom of the trimethylsiloxy group attached to $\text{C}_{(3)}$ carbon atom in 1,6-anhydro- β -D-glucopyranose derivatives correlates linearly with the sum of Taft polar constants σ^* of substituents R^2 and R^4 on $\text{C}_{(2)}$ and $\text{C}_{(4)}$ carbon atoms. Quality of this correlation allows assignment of Si-3 line in the spectra of derivatives containing two or three trimethylsilyl groups in the molecule. The shielding order $\delta(\text{Si-4}) < \delta(\text{Si-3})$ found in 1,6-anhydro-2,3,4-O-tris(trimethylsilyl)- β -D-glucopyranose is the same as recently found in other pyranose derivatives with the same configuration of substituents but the order is reversed by strong polar effect of the substituent in 1,6-anhydro-2-O-*p*-toluenesulphonyl-3,4-O-bis(trimethylsilyl)- β -D-glucopyranose. This finding warns against indiscriminate use of empirical assignment rules based on simple shielding order without considering possible substituent effects.

Immediately after high sensitivity of ^{29}Si chemical shifts to substituent effects was found^{1,2} in the compounds of the type $(\text{CH}_3)_3\text{SiOR}$, it has been suggested^{1,3} that this sensitivity should be utilized in structure elucidation for compounds which are easily trimethylsilylated. The obvious application to determination of the number of functional group that can be silylated has found its use in chemistry of carbohydrates^{1,3,4} and amino acids⁵ in analysis of petrol fractions⁶ and coal extracts^{7,8}.

More detailed information about the structure of polyfunctional compounds can be extracted from ^{29}Si NMR spectra only after line assignment. Assigning ^{29}Si lines has proved to be the stumbling block for wider acceptance of this method.

Exact methods of line assignment through especially designed NMR experiments are either not applicable to ^{29}Si NMR at all (*e.g.* homonuclear inadequate experiments⁹) or they are difficult to carry out and are time consuming due to low NMR sensitivity of ^{29}Si nucleus¹⁰ (*e.g.* methods of 2D NMR spectroscopy). Difficulty of these experiments stems from the isolating effect exercised by the oxygen link on ^1H - ^{29}Si coupling constants, from the lack of directly bonded hydrogen atoms, from insensitivity of ^1H chemical shifts and coupling constants in $\text{Si}(\text{CH}_3)_3$ groups to substituent effects and from other factors. Similarly, specific isotopic substitution is very tedious. Formulation of empirical assignment rules is therefore very desirable.

Nonmonotonous dependence of ^{29}Si chemical shifts on atomic charge and the concomitant

nonadditivity of substituent effects increase the danger of faulty empirical assignments in ^{29}Si NMR spectroscopy. Safe rules can be derived only for well delineated classes of compounds, e.g. for monosaccharide derivatives with the same configuration of substituents and similar average conformations. An early study of ^{29}Si NMR spectra of several pertrimethylsilylated hexopyranoses⁴ has failed to reveal logically consistent trends in the shieldings because, in our opinion, the pyranoses had different substituent configurations. When, however, two derivatives with the same substituent configuration (methyl α -D-glucopyranoside derivatives) were investigated³ and their ^{29}Si lines assigned, the two compounds were found to have the same shielding order $\delta(\text{Si-4}) < \delta(\text{Si-3})$ of the silicon atoms in trimethylsiloxy groups bonded to $\text{C}_{(4)}$ and $\text{C}_{(3)}$ carbon atoms of the pyranose ring, respectively. The same shielding order was recently found¹¹ also in a series of methyl β -D-xylopyranoside derivatives which have the same configuration of trimethylsilyl substituents as the glucopyranose derivatives³. While the assignment in the spectra of glucopyranose derivatives³ was based on a combination of specific deuteration, selective proton decoupling and use of shift reagents the assignment in the spectra of xylose derivatives¹¹ was empirical; it was based on a comparison of chemical shifts in a well chosen large series of model compounds.

In the present study another route for empirical assignment will be attempted using derivatives of 1,6-anhydro- β -D-glucopyranose as models with the same configuration of substituents as in previously studied compounds^{3,11} but with additional rigidity due to 1,6-bridge which eliminates problems associated with conformational equilibrium.

RESULTS AND DISCUSSION

The present new attempt stems from the established¹² linear correlation between ^{29}Si chemical shifts and Taft polar substituent constants σ^* . The correlation described for a general class of compounds of the type $(\text{CH}_3)_3\text{SiOR}$ does not predict chemical shifts with accuracy sufficient for assignment purposes. It is reasonable to expect, however, that much more precise predictions can be made if analogous correlation is derived for a narrow class of closely related compounds with the same structure in the vicinity of the silicon atom. This assumption is verified here on the chemical shifts of Si-3 silicon (the silicon atoms are numbered as the skeletal carbon atoms to which the corresponding trimethylsiloxy groups are attached) in 1,6-anhydro- β -D-glucopyranose derivatives given in Table I.

Silicon-29 chemical shifts in compounds 1–3 (i.e. in 2-O-*p*-toluenesulphonyl derivatives) correlate linearly with Taft polar constants of substituents R^4 similarly as do the shifts in compounds 3–5 (i.e. compounds with $\text{R}^2 = \text{R}^4$). Owing to the presence of different substituents R^2 the two correlations are different. However, they can be united if the chemical shifts in 1–5 are correlated with the sum of polar constants of substituents R^2 and R^4 . Least-square treatment gives correlation

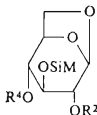
$$\delta(\text{Si-3}) = 18.476 + 0.5872 \sum \sigma^* \quad (1)$$

with correlation coefficient $r = 0.997$ for 5 experimental points. The correlation is significant at 5% level, symmetrical 90% confidence limits are ± 0.263 for the intercept and ± 0.0614 for the slope.

This correlation can be used for assignment of ^{29}Si lines with sufficiently different chemical shifts. For example the two lines observed in the spectrum of compound 6 have the shifts $\delta = 18.54$ and 19.81 ; calculation according Eq. (1) for Si-3 line predicts the shift $\delta(\text{Si-3}) = 20.0 \pm 0.3$ (90% confidence limit). Since the latter of the observed lines lies within the confidence limits of the predicted shift (Fig. 1) and since the former line is sufficiently remote (in fact deviation of 1.5 ppm is beyond 99% confidence limits which are ± 1.0 ppm), the former line must be assigned to Si-4 and the latter to Si-3 silicon atoms as given in Table I. Similarly, calculation predicts $\delta(\text{Si-3}) = 17.5 \pm 0.4$ for compound 7. There are, however, two lines (Fig. 1) in the experimental spectrum with the shifts within the limits of the prediction ($\delta = 17.57$ and 17.78). We assign rather arbitrarily the line which is closer

TABLE I

^{29}Si NMR Chemical shifts in trimethylsilylated derivatives of 1,6-anhydro- β -D-glucopyranose



Compound	(R ²) ^a	(R ⁴) ^a	$\delta(\text{Si-3})^b$	$\sigma^*(\text{R}^2)^c$	$\sigma^*(\text{R}^4)^c$
1	Ts	Me	20.67	3.43 ^d	0.000 ^e
2	Ts	Bn	20.53	3.43 ^d	0.215 ^e
3	Ts	Ts	22.47	3.43 ^d	3.43 ^d
4	Bn	Bn	18.68	0.215 ^e	0.215 ^e
5	Bz	Bz	21.05	2.20 ^f	2.20 ^f
6	Ts	SiM	19.81 ^g	3.43 ^d	-0.81 ^h
7	SiM	SiM	17.57 ⁱ	-0.81 ^h	-0.81 ^h
8 ^j	Ts	-j	18.70	3.43 ^d	

^a Substituent abbreviations: Ts = *p*-toluenesulphonyl, Me = methyl, Bn = benzyl, Bz = benzoyl, and SiM-trimethylsilyl. ^b Chemical shifts in δ scale, approximate error ± 0.02 ppm, for the assignment see the text. ^c Polar constants σ^* of the substituents R, ^d Estimated¹³ as $\sigma^* = 6.23\sigma_1$, σ_1 from ref.¹⁴. ^e Value taken from ref.¹⁵. ^f Value taken from ref.¹⁶. ^g $\delta(\text{Si-4}) = 18.54$. ^h Value taken from ref.¹² ⁱ $\delta(\text{Si-2}) = 17.78$, $\delta(\text{Si-4}) = 18.52$. ^j 1,6-anhydro-4-deoxy-2-O-*p*-toluenesulphonyl-3-O-trimethylsilyl- β -D-glucopyranose.

to the prediction to Si-3 silicon nucleus. The third line is again sufficiently remote; since it has practically the same chemical shift as Si-4 line in compound 6 and because Si-4 line can be affected only very little by R^2 substituents which differentiate compounds 6 and 7, the third line in 7 can be safely assigned to Si-4 silicon. The remaining line is hence assigned to Si-2.

The shielding order $\delta(\text{Si-4}) < \delta(\text{Si-3})$ found here for pertrimethylsilylated-1,6-anhydro- β -D-glucopyranose is the same as found in pertrimethylsilylated methyl α -D-glucopyranoside³ and methyl β -D-xylopyranoside¹¹ which all have the same configuration — but not conformation — of substituents on $C_{(2)}$, $C_{(3)}$, and $C_{(4)}$

TABLE II

¹³C NMR Chemical shifts in trimethylsilylated derivatives of 1,6-anhydro- β -D-glucopyranose^a

Compound ^b	C ₍₁₎	C ₍₂₎	C ₍₃₎	C ₍₄₎	C ₍₅₎	C ₍₆₎	CH ₃ Si
1	99.34	77.86	68.88	81.00	73.48	65.28	-0.30
2	99.26	77.85	69.29	74.12	71.30	65.24	-0.30
3	99.17	77.53	69.38	75.93	73.90	65.06	-0.58
4	100.76	79.61	70.68	79.24	74.44	65.68	-0.02
5	99.82	73.86	69.55	73.27	71.88	65.25	-0.22
6	99.22	77.38	72.14	72.53	76.79	65.21	0.03, -0.10
7	103.10	74.32	75.14	73.86	77.55	65.83	0.42, 0.16, 0.07
8	98.96	77.19	64.46	33.69	71.15	67.13	-0.42

^a Chemical shifts in δ scale, approximate error ± 0.02 ppm. Assignment only on the basis of off-resonance decoupling and analogy with the data of ref.²⁵. ^b For numbering of the compounds see Table I.

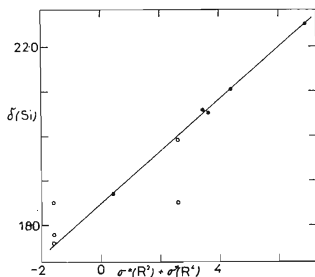


FIG. 1

Correlation of Si-3 chemical shifts, $\delta(\text{Si-3})$, with the sum of polar constants of substituents R^2 and R^4 . Solid line is the least-squares fit of the full points, open points are unassigned chemical shifts in compounds 6 and 7)

carbon atoms of pyranose skeleton. (Derivatives of 1,6-anhydro- β -D-glucopyranose adopt a slightly distorted conformation ${}^1\text{C}_4(\text{D})$ and not the conformation $\text{B}_{0,3}$ as given by mistake in Ref.¹). This shielding order seems to be in a qualitative agreement with the diamagnetic steric effects observed on silicon chemical shift in similar situations^{17,18}. The fact that the relative shielding of Si-2 silicon is in all three classes of compounds different reflects the differences between these compounds. Obviously, of the three silicon atoms the Si-2 shift should be most sensitive to substitution and configuration at $\text{C}_{(1)}$ carbon atom.

Danger of making faulty assignment on the basis of simple shielding order rules without considering possible substituent effects which may alter the order can be demonstrated on compound **6** in which the strong polar substituent R^2 induces order $\delta(\text{Si-3}) < \delta(\text{Si-4})$. From this point of view empirical assignment rules based on Hammett-type dependences like Eq. (1) are superior to the rules based on the shielding order.

EXPERIMENTAL

Preparation of the compounds **1**–**8**. All the investigated compounds were prepared by trimethylsilylation of the corresponding hydroxy derivatives which were prepared earlier^{9,19–24}. Hydroxy derivatives (0.2 g) were dissolved in pyridine (5 ml) and silylated by an excess of hexamethyldisilazane (2 ml) with trimethylchlorosilane (1 ml). The reaction was carried for one hour under stirring. Formed salts were filtered off and the solvent removed by distillation under vacuum. The remaining traces of pyridine were removed by dissolving the samples in tetrachloromethane which was after another filtration distilled off. Identity of the samples was checked by ^{13}C NMR spectroscopy. The data are summarized in Table II.

NMR Measurements. The compounds were measured in approximately 0.5M solutions in deuteriochloroform (Merck, Uvasol) to which 5% (V/V) of hexamethyldisilane (PCR) were added to serve as a secondary ^{29}Si NMR reference with $\delta = -19.79$. The solvent was dried over molecular sieves, NMR tubes were either sealed or closed by septum caps to prevent decomposition by moisture. The spectra were measured on a Varian XL-200 spectrometer operating for ^{29}Si NMR at 39.7 MHz and at 50.3 MHz for ^{13}C NMR. All the spectra were measured at probe temperature of approximately 23°C. ^{29}Si NMR spectra were measured with gated decoupling of protons in order to suppress negative Overhauser effect. Acquisition time was 1 s, delay between consecutive scans 15 s. Spectral width of 3 kHz with zero-filling to 16 k assured experimental error in chemical shifts smaller than ± 0.02 ppm. ^{13}C NMR spectra were measured with noise decoupling.

REFERENCES

1. Schraml J., Pola J., Jancke H., Engelhardt G., Černý M., Chvalovský V.: This Journal **41**, 360 (1976).
2. Schraml J., Koehler P., Licht K., Engelhardt G.: J. Organometal. Chem. **121**, C 1 (1976).
3. Haines A. H., Harris R. K., Rao R. C.: Org. Magn. Resonance **9**, 432 (1977).
4. Gale D. J., Haines A. H., Harris R. K.: Org. Magn. Resonance **7**, 635 (1975).

5. Schraml J., Pola J., Chvalovský V., Marsmann H. C., Bláha K.: *This Journal* **42**, 1165 (1977).
6. Schraml J., Pihar O., Chvalovský V.: Unpublished results.
7. Rose K. D., Scouten C. G.: *ATP Conf. Proc. Chem. Phys. Coal Util.* p. 82–100 (1980); *Chem. Abstr.* **95**, 8677 V (1981).
8. Schraml J., Pihar O., Hájek M., Chvalovský V.: Unpublished results.
9. Bax A., Freeman R., Kempell S. P.: *J. Amer. Chem. Soc.* **102**, 4849 (1980).
10. Levy G. C., Cargioli J. D. in the book: *Nuclear Magnetic Resonance Spectroscopy of Nuclei Other Than Protons* (T. Axenrod, G. A. Webb, Eds) p. 251. Wiley, New York 1974.
11. Schraml J., Petráková E., Pihar O., Hirsch J., Chvalovský V.: *Org. Magn. Resonance*, in press.
12. Schraml J., Chvalovský V., Mägi M., Lippmaa E.: *This Journal* **46**, 377 (1981).
13. Charton M.: *J. Org. Chem.* **29**, 1222 (1964).
14. Meyers C., Cremonini B., Maioli L.: *J. Amer. Chem. Soc.* **86**, 2944 (1964).
15. Taft R. W. jr in the book: *Steric Effects in Organic Chemistry* (M. S. Newman, Ed.) Wiley, New York 1956.
16. Kashik T. V., Prokopen B. V., Atavin A. S., Mirskova A. N., Alert M. L., Pilkevich S. G., Ponomareva C. M.: *Zh. Org. Khim.* **7**, 1582 (1971).
17. Schraml J., Včelák J., Chvalovský V., Engelhardt G., Jancke H., Vodička L., Hlavatý J.: *This Journal* **43**, 3179 (1978).
18. Buděšinský M., Trnka T., Černý M.: *This Journal* **44**, 1949 (1979).
19. Zemplén G., Csűrös Z., Angyal S.: *Ber. Dent. Chem. Gr.* **70**, 1848 (1937).
20. Černý M., Gut. V., Pacák J.: *This Journal* **26**, 2542 (1961).
21. Černý M., Pacák J.: *This Journal* **27**, 94 (1962).
22. Černý M., Pacák J., Staněk J. jr: *This Journal* **30**, 1151 (1965).
23. Carlson L. S.: *J. Org. Chem.* **30**, 3953 (1965).
24. Černý M., Kalvoda L., Pacák J.: *This Journal* **33**, 1143 (1968).
25. Gullyev N., Shmyrina A. Ya., Sviridov A. F., Shashkov A. S., Chozkov O. S.: *Bioorg. Khim.* **3**, 50 (1977).

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