[29]SA (AND ^{13}C) NMR SPECTRA OF ALL PERTRIMETHYLSILYLATED O-ACETYL AND O-BENZOYL 1,6-ANHYDRO-β-D-GLUCOPYRANOSE DERIVATIVES. A TEST OF EMPIRICAL ASSIGNMENT RULES

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All O-acetyl-1,6-anhydro-β-D-glucopyranoses and O-benzoyl-1,6-anhydro-β-D-glucopyranoses were pertrimethylsilylated. ^{29}Si and ^{13}C NMR spectra of the pertrimethylsilyl derivatives were measured and the [29]Si chemical shifts were used to test two previously described empirical assignment rules. The rule based on the shielding order must be either restricted to the order δ(Si-2) $> \delta$(Si-4) which holds for all the studied compounds or modified for each subclass of the studied compounds with the same O-substituents. The rule based on Hammett type dependence gives correct predictions for Si-3 chemical shifts. When both rules can be applied they yield identical assignments, in other cases they complement each other.

Analytical potential of ^{29}Si NMR for determination of the number of functional groups that can be trimethylsilylated is now well documented[1-5]. Further utilization of [29]Si chemical shifts for such purposes like determination of ring size[6] or steroid stereochemistry[7] require assignment of ^{29}Si NMR lines to specific silicon atoms introduced into the polyfunctional molecule by pertrimethylsilylation of the studied compound. It has been recently demonstrated[3,8-10]. that under certain conditions the exact assignments can be derived by experimental methods. They are, however, time consuming and very demanding either on the quality of NMR spectrometer[8-10] or on possibilities of preparative chemistry[3]. Therefore, empirical assignment rules, similar to those used in ^{13}C NMR spectroscopy, would be of great help if they are sufficiently reliable. Two such rules have so far been reported[11,12]: the first is based on the order of the [29]Si chemical shifts in a particular class of compounds[3,11] and the second utilizes the Hammett-type dependence of silicon shielding on polar substituent constant[12]. The chemical shift order found in a series of mono(trimethylsilyl) derivatives of O-substituted methyl β-D-xylopyranosides, δ(Si-2) $> \delta$(Si-4) $> \delta$(Si-3), permitted the assignment of silicon lines in bis(trimethylsilyl) and tris(trimethylsilyl) derivatives of this monosacharide[11], however, the order is different from that found[3] in two derivatives of α-D-glucopyranose, δ(Si-4) $> \delta$(Si-3) $> \delta$(Si-2). The Hammett-type dependence of the chemical shift of the silicon atom of the trimethylsiloxy group attached to $C_{(3)}$ skeletal carbon atom, δ(Si-3), on the sum of polar substituent constants in substituted 3-O-trimethylsilyl-1,6-anhydro-β-D-glucopyranoses permited the assignment of Si-3 line in tris(trimethylsilyl) derivative of this monosaccharide[10]. The ensuing assignment of Si-2 and Si-4 lines has been proved[9,10] to be in error.

It is therefore of interest to test the two types of empirical assignment rules on one class of compounds. The present paper represent such an attempt using all substituted O-acetyl and O-benzoyl 1,6-anhydro-β-D-glucopyranoses to which both rules can be adopted. The Si-3 chemical shifts should follow the described[10] Hammett-type dependence and it should be possible to establish the chemical shift order for this class of compounds from the chemical shifts in mono(trimethylsilyl) derivatives and use it for the assignment similarly as in ref.[11].

EXPERIMENTAL

Preparation and properties of starting O-acetyl and O-benzoyl 1,6-anhydro-β-D-glucopyranoses were described elsewhere[13]. Pertrimethylsilylation was achieved by different silylation reagents. The unsubstituted 1,6-anhydro-β-glucopyranose was succesfully silylated either by bis(trimethyl-silyl)acetamide (BSA) in pyridine or by a 1 : 1 mixture of hexamethyldisilazane (HMDS) and tri-methylchlorosilane (TMCS) in pyridine, or by TMCS in pyridine and formamide. Benzoyl derivatives were silylated by a mixture of BSA and TMCS either in dimethylformamide solutions or without a solvent (reaction time 15—60 min, temp. 60—80°C). Acetyl derivatives were silylat-ed by TMCS in pyridine with added formamide[14] (reaction time 5—30 min, temp. 30—50°C, products extracted by n-hexane or n-pentane). Usually about 10—50 mg of the parent compound was taken for the reaction with at least a threefold stoichiometric access of silylating reagents. Solvents and accessive reagents were removed at higher temperature and reduced pressure in a stream of dry nitrogen, purity of the products was checked by gas chromatography.

The samples were measured as 0·2—0·4M solutions in deuteriochloroform (99·5% isotopic purity, Institute of Nuclear Research, Swierk, Foland) containing 3% of hexamethyldisilane which served as a secondary reference for ^{29}Si NMR spectra ($\delta = -19·79$). The spectra were measured on a Varian XL-200 spectrometeı operating at 200 MHz for ^{1}H NMR, at 50·3 MHz for ^{13}C NMR, and at 39·7 MHz for ^{29}Si NMR. The ^{13}C FIDs were recorded with acquisition time of 1 s and 16 kHz spectral width using quadrature detection and 16 k of memory. Exponential weighting with line broadening of 3 Hz was employed with zero filling of the memory to 32 k. The lines were referenced to the central line of deuteriochloroform with $\delta = 76·99$ the relative position of this line was checked by monitoring the ^{13}C NMR line of hexamethyldisilan which should occur at $\delta = -2·49$. The ^{29}Si NMR spectra were measured by a routine INEPT technique described in detail elsewhere[15].

Heteronuclear ^{1}H—^{13}C chemical shift correlated spectrum of *1* (Fig. 1) was measured using the standard manufacturer provided software (H—1Z-version). HETCOR pulse sequence was employed that incorporated quadrature detection in both domains. 256 FIDs were acquired (each by 32 scans) with the sampling rate corresponding to the ^{13}C spectral width of 2·5 kHz, the t_1 delay time was incremented in correspondence with the ^{1}H spectral width of 1·5 kHz. The fixed delay was adjusted for $J(^1H—^{13}C) = 140$ Hz. Exponential weighting with line broaden-ing of 2·0 Hz was used in both dimensions, on 1 024 × 1 024 data matrix.

RESULTS AND DISCUSSION

^{13}C NMR *Spectra*. ^{13}C chemical shifts are given in Table I for the purpose of pos-sible future reference and to elucidate some points discussed in connection with ^{29}Si chemical shifts later. The lines in the spectrum of compound *1* were assigned unequi-

vocally by two-dimensional heteronuclear ^{13}C—^{1}H chemical shift correlation (Fig. 1), using the assigned ^{1}H NMR spectral lines[9]. The chemical shifts in compounds *8* and *15* were assigned by a series of homo and heteronuclear decoupling experiments but because of overlap of H-2, H-4, and H-5 proton lines the assignment of the corresponding carbon atoms $C_{(2)}$, $C_{(4)}$, and $C_{(5)}$ was uncertain. The assignment for compound *8* is in agreement with that published by Ritchie and coworkers[16], the assignment given by Matsuda and Tejima[17] is at variance but it applies to a different solvent (pyridine). In the spectra of all other compounds assignments of the lines to $C_{(1)}$ and $C_{(6)}$ skeletal carbon atoms were obvious. The remaining lines were assigned on the basis of known substituent effects and comparison with the assigned spectra. These assignments must be considered tentative only. Comparison of the corresponding analogous chemical shifts reveals striking similarity of the values in monoacetyl and monobenzoyl derivatives (*e.g.* $C_{(1)}$ chemical shifts in the corresponding monoderivatives differ by less than 0·1 ppm). Similar are also the shifts in triacetyl and tribenzoyl derivatives and in 2,3- and 3,4-diacetyl and dibenzoyl
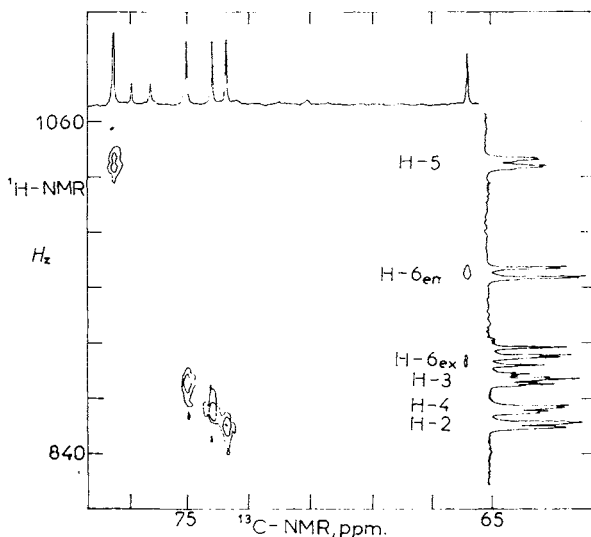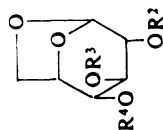

FIG. 1

Partial ^{1}H and ^{13}C NMR spectra and their correlation map obtained as a contour plot of heteronuclear shift correlated 2 D NMR spectrum of *1*. The low intensity ^{13}C NMR signals are due to deuteriochloroform. The indicated assignment of ^{1}H NMR lines was taken from ref.[9], protons are labeled by the number of their skeletal carbon atoms. ^{13}C NMR chemical shifts are in δ scale, ^{1}H NMR line positions are in Hz units relative to an arbitrary origin

TABLE I

²⁹Si and ¹³C Chemical shifts in substituted 1,6-anhydro-β-D-glucopyranose[a]

Compound	R²	R³	R⁴	Si-2[b]	Si-3[b]	Si-4[b]	$C_{(1)}$[c]	$C_{(2)}$[c]	$C_{(3)}$[c]	$C_{(4)}$[c]	$C_{(5)}$[c]	$C_{(6)}$[c]
1	SiM	SiM	SiM	18·52d	17·57d	17·78d	103·10	73·86	75·14	74·32	77·55	65·83
2	Ac	SiM	SiM	—	18·96e	18·52e	99·92	73·11f	72·21f	73·30f	77·18	65·47
3g	SiM	Ac	SiM	20·35e	—	19·67e	101·91	69·49f	74·70f	70·28f	76·64	65·01
4	SiM	SiM	Ac	19·49e	19·32e	—	103·30	73·78f	72·38f	74·76f	75·52f	66·13
5	Ac	Ac	SiM	—	—	20·38	99·01	69·48f	72·19f	69·69f	76·82	65·03
6	Ac	SiM	Ac	—	20·79	—	100·12	74·26f	69·46f	73·06f	74·33f	65·77
7g	SiM	Ac	Ac	21·03	—	—	102·18	70·86f	72·24f	69·10f	73·59	65·31
8	Ac	Ac	Ac	—	—	—	99·27	70·43f	69·70	69·22h	73·78h	65·95
9	Bz	SiM	SiM	—	19·06e	18·00c	99·90	72·77f	72·52f	72·97f	77·16	65·39
10	SiM	Bz	SiM	20·47e	—	19·88e	101·93	69·43f	74·62f	70·08f	76·63	65·05
11	SiM	SiM	Bz	18·94e	19·32e	—	103·23	73·36f	72·70f	74·62f	75·23f	65·94
12	Bz	Bz	SiM	—	—	20·00	99·02	69·39f	72·24f	69·15f	76·83	65·04
13	Bz	SiM	Bz	—	21·06	—	99·93	73·39f	69·65f	72·01f	73·97f	65·35
14	SiM	Bz	Bz	20·60	—	—	102·43	71·07f	72·49f	69·15f	73·69	65·56
15	Bz	Bz	Bz	—	—	—	99·47	70·20	69·79	69·11h	73·83	65·22

[a] The chemical shifts are reported on the δ scale, approximate error ±0·02 ppm for ²⁹Si and ±0·05 ppm for ¹³C chemical shifts. Substituents: SiM = trimethylsilyl, Ac = acetate, and Bz = benzoyl. [b] The chemical shift of Si-h silicon in the substituent R^h. [c] Glucopyranose skeletal carbon atoms. [d] Assignment taken from refs[9,10]. [e] Assignment may be interchanged. [f] Assignment of labeled lines uncertain. [g] Impurity in the sample. [h] Decoupling experiments not conclusive for these lines.

derivatives but the corresponding shifts in 2,4-diacetyl and 2,4-dibenzoyl derivatives differ considerably. In analogous methyl β-D-xylopyranoside derivatives the same relations were found[18] but owing to larger flexibility of pyranose ring (without the 1,6-bridge) the differences between the ^{13}C shifts in 2,4-dibenzoyl and 2,4-diacetyl derivatives were larger and considerable differences were found also between the tribenzoate and triacetate. In the case of pertrimethylsilylated methyl-β-D-xylopyranose derivatives it was possible to perform conformational analysis on the basis of ^{1}H NMR spectral data. It was shown[18] that the chemical shift differences were connected with different conformer populations (Cl conformer populations were 68 and 62% in 2,4-dibenzoyl and 2,3,4-tribenzoyl derivatives, resp., while 78—92% in other compounds). We have attempted similar treatment of ^{1}H NMR spectra of compounds _1 – 15_ but small values of vicinal proton–proton coupling constants yielded not sufficietnly reliable results. Obviously, different conformation and steric requirements (and not polar effects) of the two substituent groups that are both large and magnetically anisotropic are responsible for the difference notes.

^{29}Si NMR _Spectra._ The chemical shifts in compounds _1, 5, 6, 7, 12, 13_ and _14_ are assigned unambiguously, assignments in all the other spectra are tentative and will be discussed below in connection with the tested empirical assignment rules.

[29]Si _shielding order._ The shielding order found for configurationally similar pertrimethylsilylated methyl-β-D-xylopyranoside derivatives (_i.e._ δ(Si-2) > δ(Si-4) > > δ(Si-3)) applies to 1,6-anhydro-β-D-glucopyranose derivatives only in a restricted form δ(Si-2) > δ(Si-4). This restricted relationship holds in the acetoxy and benzoyl series as well as in the tris(trimethylsilyl) derivative. The remaining (Si-3) silicon line does not fit into any general shielding order. One should realize that the Si-3 silicon chemical shifts are unambiguously assigned in those compounds for which differences in carbon chemical shifts have been noted. Apparently the two phenomena have the same origin discussed above. The larger mobility of the xylopyranose ring can better relieve the steric strain from the large substituent groups (giving larger differences in the carbon chemical shifts) and retain constant local spatial arrangement around each silicon atom. In the less flexibile 1,6-anhydro compounds the surroundings of each silicon atom depend much more on the nature of substituents, and the three silicon chemical shifts have different sensitivity to steric and polar influences of the substituents.

As Gale and Evans observed[19] a 1·2 ppm downfield shift of the Si-2 resonance when going from α to β anomer of a D-galactose derivative, the observed shielding order seems to be caused by configuration at $C_{(1)}$. In fact, if we assume similar 1·2 ppm anomeric shift for the Si-2 silicon and no anomeric effect on the Si-4 silicon shift (neglecting the possible effect of the 1,6-bridge) a reversed order is predicted

for α-D-glucopyranose derivatives. Such reversed order has already been reported for two derivatives[3].

Since the exact assignment procedures[9,10] are difficult and tedious to apply to the studied class of compounds with small vicinal and large long-range proton-proton couplings[20] and with considerable ^{1}H chemical shift overlap, the remaining silicon chemical shifts were assigned according to their shielding order. The assignment

TABLE II

^{29}Si DCS Values for O-acetylation and O-benzoylation of 2,3,4-tris-O-trimethylsilyl-1,6-anhydro-
-β-D-glucopyranose[a]

	DCS[b]	Si-2[c]	Si-3[c]	Si-4[c]
	Ac^2	—	1·39	0·74
	Ac^3	1·83	—	1·89
	Ac^4	0·97	1·75	—
	Bz^2	—	1·49	0·22
	Br^3	1·95	—	2·10
	Bz^4	0·42	1·75	—

[a] The ^{29}Si DCS values were calculated as the difference between the corresponding chemical shifts in mono-O-derivatives and in compound *1*. All values are in ppm. [b] The DCS values of substituent R^n; for substituent designations see Table I. [c] The DCS experienced by the Si-n silicon atom of the trimethylsiloxy group bonded to the $C_{(n)}$ skeletal carbon atom.

TABLE III

^{29}Si Chemical shifts calculated for di-O-derivatives of 2,3,4-tris-O-trimethylsilyl-1,6-anhydro-
-β-D-glucopyranose[a]

Compound[b]	Si-2	Si-3	Si-4
5	—	—	20·41 (+0·03)
6	—	20·71 (−0·08)	—
7	21·32 (+0·29)	—	—
12	—	—	20·10 (+0·10)
13	—	20·81 (−0·25)	—
14	20·89 (+0·29)	—	—

[a] Chemical shifts calculated by adding the appropriate DCS values to the chemical shift in compound *1*. The values in parentheses are the differences between the calculated and experimental chemical shifts. [b] For numbering of compounds see Table I.

for compounds *3* and *10* appears safe as it is based on the above general shielding order, other chemical shifts were assigned according to the order observed in the narow subclass of the compounds with exactly assigned shifts and with the same O-substituents (*i.e.*, the order δ(Si-2) > δ(Si-3) > δ(Si-4) was assumed for all acetoxy and δ(Si-2) > δ(Si-4) > δ(Si-3) for all benzoyl derivatives). In consequence, additivity of derivatization chemical shifts[11] (DCS) is well satisfied by the silicon chemical shifts as demonstrated by the data in Tables II and III.

Hammett-type dependence. The reported[12] correlation of the Si-3 silicon chemical shifts with the sum of Taft polar substituent constants $(\sigma^*(R^2) + \sigma^*(R^4))$ can be used to predict the chemical shifts in the compounds *2, 4, 6, 9,* and *11* (compound *13* was utilized in deriving the correlation). According to this correlation the Si-3 chemical shifts should be: δ(Si-3) = 18·97 ± 0·35 in compounds *2* and *4*, δ(Si-3) = = 20·41 ± 0·31 in compound *6* and δ(Si-3) = 19·29 ± 0·34 in compounds *9* and *11*. Comparison with experimental data (Table I) shows that the correlation gives good predictions as with the exception of compound *6* the experimental shifts are found within the indicated 90% confidence limits of the predicted values. In the compound *6* the difference between the prediction and experiment exceeds the confidence limit by 0·07 ppm which is only three times experimental error of a single measurement. The chemical shifts assigned according to these predictions agree with the assignment made above on the basis of the shielding order.

CONCLUSION

The two tested empirical assignment rules and chemical shift additivity are valid for ^{29}Si chemical shifts in the studied class of compounds though the general rule based on the shielding order must be either restricted in order to hold for all the compounds or modified to hold in subclasses of compounds with the same substituents. When both rules can be applied they yield identical assignments, in other cases they complement each other.

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