PERTRIMETHYLSILYLATION AS A METHOD FOR IMPROVEMENT OF CHEMICAL SHIFT ADDITIVITY THROUGH CONFORMATIONAL HOMOGENIZATION. ^{1}H AND ^{13}C NMR SPECTRA OF PERTRIMETHYLSILYLATED DERIVATIVES OF METHYL β-D-XYLOPYRANOSIDES

Jan SCHRAML[a], Eva PETRÁKOVÁ[b], Otomar PIHAR[a], Ján HIRSCH[b] and Václav CHVALOVSKÝ[a]

[a] *Institute of Chemical Process Fundamentals, Czechoslovak Academy of Sciences, 165 02 Prague and*
[b] *Institute of Chemistry, Slovak Academy of Sciences, 842 38 Bratislava*

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All possible mono-, di-, and tri- O-methyl, O-benzyl, O-benzoyl, and O-acetyl derivatives of methyl β-D-xylopyranoside were fully trimethylsilylated and their ^{1}H and ^{13}C NMR spectra measured in deuteriochloroform solutions. The spectra were analysed and the chemical shifts completely assigned on the basis of decoupling experiments. The proton-proton coupling constants vary only very little throughout the series. Conformer population analysis by the method of average coupling constants shows that trimethylsilylation increases the *C1* conformer population and makes the series conformationally homogenous. Owing to this conformational homogeneity chemical shifts (both ^{1}H and ^{13}C) satisfy very well direct additivity rule. It is suggested that pertrimethylsilylation should be employed whenever deviations from chemical shift additivity are caused by conformational mobility of the investigated series of compounds and when bulky groups can stabilize one of the conformers.

It has been recognized from the onset of applications of direct additivity rules to NMR chemical shifts (for an early review see[1]) that in conformationally mobile systems the additivity rule can be valid only if either the shieldings in the conformers are not appreciably different or if the considered compounds are in the same (perhaps time averaged) conformation. Lately, however, additivity of various derivatization shifts (*e.g.* acetylation shifts) was tacitly assumed in systems in which these conditions were not necessarily met (*e.g.* monosaccharides).

We have recently shown[2] that a series of methyl β-D-xylopyranoside benzoates is (in chloroform solutions) conformationally heterogenous to the extent that the ^{13}C chemical shifts are not additive. In dimethyl sulfoxide solutions analogous acetates are conformationally homogeneous, additivity of ^{13}C chemical shifts is well satisfied[3], in chloroform solutions deviations from additivity are appreciably larger and the series of compounds is conformationally less homogeneous[4].

These results show that validity of additivity rules in nonrigid systems can be favourably influenced by a proper choice of the solvent which affects conformer populations. There is, however, another possibility; suitable substitution will affect conformations so that the conditions for additivity would be satisfied better and the precision of the calculated shifts increased. For example, substitution of pyranoso monosaccharides with *trans* configuration of neighboring OH groups by bulky substituents, which tend to assume equatorial positions, should increase populations of the conformers with the bulky substituents in the equatorial positions making thus the series of substituted compounds conformationally more homogeneous than the original series of monosaccharides without the bulky substituents. In the present paper we describe the results of such an attempt using trimethylsilyl group as the bulky substituent and a series of O-substituted methyl β-D-xylopyranosides as model compounds.

RESULTS AND DISCUSSION

^{1}H NMR *Spectra and conformation.* Results of analysis of ^{1}H NMR spectra are summarized in Table I (for numbering of compounds see Table II); details of spectral analysis and assignment are described in the Experimental.

As it is apparent from Table I all the proton–proton coupling constants vary only very little throughout the series. Considering compounds with at least one trimethylsiloxy group in the molecule the coupling constants' ranges are (exempt *16* which will be discussed later): $J_{1,2}$ = 7·0–7·9 Hz, $J_{2,3}$ = 8·4–9·6 Hz, $J_{3,4}$ = 8·0–9·4 Hz, $J_{4,5e}$ = 5·0–6·0 Hz, $J_{4,5a}$ = 8·9–10·6 Hz, and $J_{5,5}$ = −10·9 to −12·0 Hz.

Vicinal coupling constants are known to be affected both by molecular geometry and by substituent effects[5]. Effects of multiple substitution are not yet well understood and therefore the small variations in $J_{2,3}$ and $J_{3,4}$ coupling constants cannot be interpreted in detail. On the other hand, it is safe to neglect effects of remote substituents and to consider the variations in $J_{1,2}$ and $J_{4,5}$ coupling constants to be due only to changes in molecular geometry (or in conformational equilibria) and to effects of substituents R^2 and R^4, respectively.

Under this assumption the substituent effects are easily eliminated if we consider only the compounds with $R^2 = Si(CH_3)_3$ for $J_{1,2}$ and those with $R^4 = Si(CH_3)_3$ for $J_{4,5}$. Than the ranges of coupling constants are further narrowed: $J_{1,2}$ = 7·3 ± ± 0·3 Hz and $J_{4,5a}$ = 9·7 ± 0·4 Hz. This finding clearly demonstrates that all the compounds with trimethylsiloxy group either on $C_{(2)}$ or $C_{(4)}$ (or on both) carbon atoms have essentially the same molecular geometry. Compounds left out of our consideration have $R^2 = R^4 = Si(CH_3)_3$ (*i.e.* compounds *6*, *8*, *16*, *18*, *26*, *28*, *36*, and *38*). Some of them have coupling constants outside the indicated narrow limits ($J_{1,2}$ in *8*, *16*, *18*, *26*, and *36* and $J_{4,5a}$ in *6*, *8*, *16*, and *18*). In order to assess the effect of substituent electronegativity on these coupling constants one can use a modified

Karplus equation which Streefkerk and coworkers[6] succesfully applied to pertrimethylsilylated aldohexopyranoses:

$$J_{HH} = (6{\cdot}6 - 1{\cdot}0 \cos \varrho + 5{\cdot}6 \cos 2\varrho)(1 - \sum_i f_i \Delta X_i) . \qquad (1)$$

Here ϱ is the dihedral angle between the coupled protons, ΔX_i is the difference in electronegativity between the i-th substituent and hydrogen atom. Using maximum values of correction factors f_i and electronegativity values given in ref.[6] the maximum possible change in vicinal coupling constant can be calculated for dihedral angle $\varrho = 180°$. Replacement of the trimethylsiloxy group by an acetoxy group could decrease the vicinal coupling by as much as 0·4 Hz while substitution by methoxy group would increase the same coupling by the same amount. Obviously, this small correction for substituent electronegativity puts only $J_{1,2}$ couplings in compounds *8*, *26*, and *36* and $J_{4,5a}$ couplings in *6* and *8* within the above narrow limits. Electronegativity effects cannot explain the values of coupling constants in *16* and *18*. In the last two mentioned compounds the average molecular geometry of pyranoside skeleton must be different than in the other compounds of the series.

Making the usual assumption that the methyl β-D-xylopyranoside derivatives are present in solution in an equilibrium mixture of *C1* and *1C* conformers we can evaluate the conformer populations from the values of $J_{1,2}$ or $J_{4,5a}$ coupling constants by the method of averaged coupling constants[7]. Details of application of this method to methyl β-D-xylopyranoside derivatives were described earlier[2]; in the present work we have used the equations derived previously[2], it should be noted here that the calculations of conformer populations are only very little affected by substituent electronegativity. The *C1* conformer populations P_I calculated from $J_{1,2}$ values and P_{II} calculated from $J_{4,5a}$ values agree satisfactorily (Tables III). All the compounds are present in deuteriochloroform solutions predominantly in the *C1* form, practically all have the *C1* conformer population in the range 82–93%. The only significant exceptions are compounds *16* and *18*. Since *18* is (ref.[8]) in a twist-boat conformation in the solid state, we cannot exclude the possibility that the simple *C1* ⇌ *1C* equilibrium is not adequate for the last two mentioned compounds.

Comparison with the available[2,4] conformer populations of (not trimethylsilylated) O-acetyl and O-benzoyl methyl β-D-xylopyranosides abundantly shows that pertrimethylsilylation increases the *C1* conformer population. Since the increase is larger for precursor with lower *C1* population, pertrimethylsilylation makes the series of compounds conformationally more homogeneous as was anticipated at the beginning of the present work.

Additivity of ^{13}C *and* ^{1}H *chemical shifts.* Direct additivity of chemical shifts means the very practical and very simple rule according to which the chemical

TABLE I

^{1}H NMR data on substituted methyl β-D-xylopyranosides

Compound[a]	Chemical shifts[b]								Coupling constants[c]					
	CH_3Si		H-1	H-2	H-3	H-4	H_e-5	H_a-5	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{5,5}$
1	0·14	0·13[d]	4·02	3·25	3·37	3·53	3·80	3·13	7·32	8·6	8·4	5·0	10·0	−11·4
2	0·14	0·11	4·19	4·79	3·54	3·64	3·85	3·17	7·93	9·0	8·0	5·0	9·8	−11·4
3	0·09		4·13	3·36	4·93	3·69	3·81	3·26	7·52	9·4	9·1	5·3	9·9	−10·9
4	0·14	0·13	4·07	3·34	3·61	4·72	4·04	3·14	7·20	8·6	8·8	5·4	9·6	−11·4
5	0·17		4·34	4·83	5·01	3·80	3·87	3·29	7·57	9·6	8·4	5·5[e]	9·3	−12·0[e]
6	0·11		4·28	4·84	3·78	4·79	4·12	3·22	7·11	8·7	8·4	5·1	8·9	−11·7
7	0·10		4·18	3·48	5·07	4·90	4·04	3·31	7·21	9·0	9·2	5·3	9·6	−11·5
8	—		4·40	4·91	5·17	4·95	4·13	3·37	6·71	8·5	8·5	5·0	8·7	−11·5
12	0·15	−0·12	4·37	5·07	3·70	3·71	3·91	3·25	7·81	9·0	8·5	5·0	9·8	−11·5
13	−0·01	−0·03	4·21	3·53	5·22	3·84	3·86	3·34	7·57	8·8	8·8	5·0	9·0	−11·0
14	0·16	0·05	4·15	3·44	3·81	5·07	4·11	3·31	7·17	8·5[e]	8·5[e]	5·3	9·3	−11·5
15	0·15		4·55	5·29	5·49	4·01	3·99	3·46	7·30	9·4	8·0	5·4	10·0	−12·0
16[f]	−0·01		4·58	5·16	4·17	5·15	4·29	3·53	6·07	7·3	7·6	4·4	7·8	−11·9
17	0·13		4·33	3·71	5·57	5·24	4·30	3·48	7·05	8·8	9·4[e]	5·6	9·8[e]	−11·3[e]
18	—		4·73	5·39	5·78	5·31	4·43	3·70	5·61	7·5	7·5	4·4	7·2	−12·0
22	0·14	0·11	4·20	3·15	3·47	3·58	3·80	3·13	7·69	8·7	8·0[d]	4·9	9·9	−11·4
23	0·11	0·10	4·06	3·42	3·30	3·69	3·78	3·18	7·33	8·7	8·4	6·0	9·7	−11·3
24	0·15	0·14	4·00	3·27	3·50	3·36	3·78	3·09	7·54	8·4	8·0	4·9	10·0	−11·3
25	0·13		4·25	3·32	3·42	3·75	3·80	3·19	7·32	9·0	9·0	5·5	10·0	−11·0
26	0·12		4·18	3·18	3·63	3·43	3·83	3·12	7·69	8·8	8·7	5·0	10·1	−11·4
27	0·14		4·08	3·48	3·44	3·56	3·91	3·20	7·3[g]	9·2	9·0	4·8	9·8	−11·3
28	—		4·25	3·35	3·57	3·61	3·93	3·21	7·47	9·1	9·0	4·8	9·8	−11·4

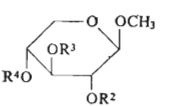
TABLE I
(*Continued*)

Compound[a]	Chemical shifts[b]								Coupling constants[c]					
	CH_3Si		H-1	H-2	H-3	H-4	H_e-5	H_a-5	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{5,5}$
32	0·15	0·13	4·10	2·83	3·36	3·55	3·77	3·11	7·69	8·9	8·7	5·2	10·1	−11·4
33	0·14		4·03	3·29	2·97	3·59[h]	3·74	3·15	7·46	8·8	8·6	5·4	10·1	−11·1
34	0·14	0·13	4·01	3·27	3·40	3·12	4·03	3·09	7·32	8·6	8·7	5·6	10·6	−11·3
35	0·14		4·12	2·93	3·03	3·61	3·75	3·14	7·33	9·0	8·5	5·5	9·9	−11·6
36	0·15		4·09	2·85	3·49[h]	3·16	4·00	3·08	7·78	8·9	8·5	5·6	9·8	−11·6
37	0·14		4·04	3·32	3·05	3·23	4·00	3·12	7·57	9·1	8·6	5·5	9·9	−11·7
38	—		4·14	2·97	3·13	3·26	3·99	3·14	7·33	9·1	8·3	4·4	9·7	−11·4

[a] For numbering of the compounds see Table II. [b] Chemical shifts in δ-scale, approximate error ±0·01 ppm. Protons numbered as the skeletal carbon atoms, indices *a* and *e* refer to axial and equatorial protons, resp. [c] Coupling constants in *Hz*, approximate error ±0·1 Hz but $J_{1,2}$ ± ± 0·08 Hz, [d] Doubled intensity. [e] Due to overlap error ±1 Hz. [f] The spectrum is strongly concentration and solvent dependent. [g] Due to virtual coupling error ±0·1 Hz. [h] Due to overlap error ±0·04 ppm.

TABLE II

^{13}C NMR chemical shifts of substituted methyl β-D-xylopyranosides[a]



Compound[b]	R^2	R^3	R^4	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	CH_3O[c]	CH_3Si	
1	SiM	SiM	SiM	105·11	75·73	78·42	71·31	66·07	56·81	1·00	0·80 0·32
2	Ac	SiM	SiM	102·51	73·57	75·83	71·26	66·08	56·49	0·53	0·20
3	SiM	Ac	SiM	104·94	73·28	77·53	68·93	66·22	57·23	0·23	−0·21
4	SiM	SiM	Ac	104·96	75·52	75·22	72·40	62·41	56·81	0·58	
5	Ac	Ac	SiM	102·14	71·53	75·19	68·81	66·08	56·79	−0·14	
6	Ac	SiM	Ac	101·96	73·15	72·20	72·05	62·10	56·38	0·24	
7	SiM	Ac	Ac	104·79	72·87	74·60	69·25	62·59	57·20	0·17	
8	Ac	Ac	Ac	101·58	70·74	71·46	68·94	61·98	56·62	—	
12	Bz	SiM	SiM	102·63	74·16	76·02	71·35	66·11	56·60	0·55	0·27
13	SiM	Bz	SiM	105·07	73·53	78·20	69·10	66·35	57·29	0·17	−0·07
14	SiM	SiM	Bz	105·01	75·60	75·49	72·75	62·55	56·83	0·66	
15	Bz	Bz	SiM	102·40	71·54	75·07	69·11	66·12	56·90	−0·13	
16	Bz	SiM	Bz	101·54	73·14	71·33	72·03	61·25	56·33	0·07	
17	SiM	Bz	Bz	104·92	73·11	74·66	69·96	62·64	57·28	0·14	
18	Bz	Bz	Bz	101·25	70·41[d]	70·55	69·34[d]	61·38	56·59	—	
22	Bn	SiM	SiM	105·51	82·22	77·37[d]	71·45[d]	66·05	56·97	0·77	0·25
23	SiM	Bn	SiM	105·26	75·39	85·54	70·96	66·30	56·98	0·51	0·15
24	SiM	SiM	Bn	105·06	75·82	77·52	78·43	63·81	56·86	0·79	0·70
25	Bn	Bn	SiM	105·37	81·97	84·52	71·20	66·21	56·96	0·15	
26	Bn	SiM	Bn	105·33	82·25	76·58	78·41	63·81	56·95	0·64	
27	SiM	Bn	Bn	105·20	75·48	84·87	77·77	64·02	57·04	0·55	
28	Bn	Bn	Bn	105·26	81·95	83·66	77·89	63·89	56·96	—	
32	Me	SiM	SiM	105·36	83·75	77·52	71·25	66·03	56·81	0·58	0·16
33	SiM	Me	SiM	105·23	75·22	87·45	70·92	66·29	57·06	0·41	0·09
34	SiM	SiM	Me	105·18	75·69	77·44	80·04	63·09	56·93	0·59	
35	Me	Me	SiM	105·03	83·51[d]	86·48[d]	70·97	66·18	56·88	0·08	
36	Me	SiM	Me	105·13	83·83	76·93	80·14	63·34	56·92	0·44	
37	SiM	Me	Me	105·12	75·11[d]	86·49	79·47[d]	63·46	57·05	0·36	
38	Me	Me	Me	104·71	83·18[d]	85·02[d]	79·35[d]	63·08	56·76	—	

[a] Chemical shifts in δ scale, approximate error ±0·02 ppm. Measured in $CDCl_3$ solutions. Substituents: Ac = acetate, Bn = benzyl, Bz = benzoyl, Me = methyl and SiM = trimethylsilyl. [b] Compounds *1*—*8* numbered consecutively, numbers *9*—*11*, *19*—*21*, *29*—*31* omitted in order to stress relations between the compounds. [c] Methoxy group on $C_{(1)}$ carbon atom. [d] The labeled lines in the row could not be assigned by the selective decoupling experiments.

shift δ of a given nucleus in a molecule can be expressed as

$$\delta = \delta_0 + \sum_i \Delta_i , \qquad (2)$$

where δ_0 is the chemical shift of the corresponding nucleus in a parent or reference compound. Contributions Δ_i are assigned to substituents which differentiate the given molecule from the molecule of the parent compound. The contributions Δ_i will be called derivatization chemical shifts (DCS) here for the reasons explained elsewhere[2].

Because of necessity we use compound *1* as a reference. The DCS values that will be derived therefore represent contributions due to the replacement of trimethylsiloxy group by either acetoxy or benzoyloxy or methoxy or benzoxy groups. Two methods are in general use for evaluation of the DCS values. If the series of compounds is small, δ_0 is taken to be equal to the corresponding δ value in the reference compound and the DCS values are obtained from monosubstituted compounds as $\Delta_i = \delta_i - \delta_0$. Validity of Eq. (2) is then tested on multiply substituted compounds. Data given

TABLE III

Estimates of *C1* conformer populations *P* in substituted methyl β-D-xylopyranosides[a]

Compound[b]	P_I[c]	P_{II}[d]	Average	Compound[b]	P_I[c]	P_{II}[d]	Average
1	0·89	0·88	0·89 ± 0·01	*22*	0·94	0·87	0·90 ± 0·04
2	0·98	0·86	0·92 ± 0·06	*23*	0·89	0·85	0·87 ± 0·02
3	0·92	0·87	0·90 ± 0·03	*24*	0·92	0·88	0·90 ± 0·02
4	0·87	0·84	0·86 ± 0·02	*25*	0·89	0·88	0·89 ± 0·01
5	0·92	0·81	0·87 ± 0·06	*26*	0·94	0·90	0·92 ± 0·02
6	0·86	0·77	0·82 ± 0·05	*27*	0·89	0·86	0·87 ± 0·02
7	0·87	0·84	0·86 ± 0·02	*28*	0·91	0·86	0·88 ± 0·03
8	0·80	0·75	0·78 ± 0·03	*32*	0·94	0·90	0·92 ± 0·02
12	0·96	0·86	0·91 ± 0·05	*33*	0·91	0·90	0·90 ± 0·01
13	0·92	0·78	0·85 ± 0·07	*34*	0·89	0·97	0·93 ± 0·04
14	0·87	0·81	0·84 ± 0·03	*35*	0·89	0·87	0·88 ± 0·01
15	0·89	0·88	0·89 ± 0·01	*36*	0·95	0·86	0·91 ± 0·04
16	0·71	0·66	0·68 ± 0·03	*37*	0·92	0·87	0·90 ± 0·03
17	0·85	0·86	0·86 ± 0·01	*38*	0·89	0·85	0·87 ± 0·02
18	0·65	0·59	0·62 ± 0·03				

[a] Conformer populations *P* in mole fractions. [b] For numbering of the compounds see Table II. [c] Calculated from Eq. $J_{1,2} = 8{\cdot}1P_I + 1{\cdot}0\ (1 - P_I)$. [d] Calculated from Eq. $J_{4,5a} = 11{\cdot}1P_{II} + 1{\cdot}5\ (1 - P_{II})$.

TABLE IV

^{13}C DCS values for O-acetylation, O-benzoylation, O-benzylation, and O-methylation of methyl 2,3,4-tris-O-trimethylsilyl-β-D-xylopyranoside and the calculated chemical shifts[a,b]

Compound	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$
2[a]	−2·60	−2·16	−2·59	−0·05	+0·01
3[a]	−0·17	−2·45	−0·89	−2·38	+0·15
4[a]	−0·15	−0·21	−3·20	+1·09	−3·66
5[b]	102·34	71·12	74·94	68·88	66·23
	(+0·10)	(−0·41)	(−0·25)	(+0·07)	(+0·15)
6[b]	102·36	73·36	72·63	72·35	62·42
	(+0·40)	(+0·21)	(+0·43)	(+0·30)	(+0·32)
7[b]	104·79	73·07	74·33	70·02	62·56
	(+0·00)	(+0·20)	(−0·27)	(+0·77)	(−0·03)
8[b]	102·19	70·91	71·74	69·97	62·57
	(+0·61)	(+0·17)	(+0·28)	(+1·03)	(+0·59)
12[a]	−2·48	−1·57	−2·40	+0·04	+0·04
13[a]	−0·04	−2·20	−0·22	−2·21	+0·28
14[a]	−0·10	−0·13	−2·93	+1·44	−3·52
15[b]	102·59	71·96	75·80	69·14	66·39
	(+0·19)	(+0·42)	(+0·73)	(+0·03)	(+0·27)
16[b]	102·53	74·03	73·09	72·79	62·59
	(+0·99)	(+0·89)	(+1·76)	(+0·76)	(+1·34)
17[b]	104·97	73·40	75·27	70·54	62·83
	(+0·05)	(+0·29)	(+0·61)	(+0·58)	(+0·19)
18[b]	102·49	71·83	72·87	70·58	62·87
	(+1·19)	(+1·43)	(+2·27)	(+1·28)	(+1·47)
22[a]	+0·39	+6·49	−1·05	+0·14	−0·02
23[a]	+0·15	−0·34	+7·12	−0·35	+0·23
24[a]	−0·05	+0·09	−0·90	+7·12	−2·26
25[b]	105·66	81·88	84·49	71·10	66·32
	(+0·29)	(−0·09)	(−0·03)	(−0·10)	(+0·11)
26[b]	105·45	82·31	76·47	78·57	63·79
	(+0·12)	(+0·06)	(−0·11)	(+0·16)	(−0·02)
27[b]	105·21	75·48	84·64	78·08	64·04
	(+0·01)	(0·00)	(−0·23)	(+0·31)	(+0·02)
28[b]	105·60	81·97	83·59	78·22	64·02
	(+0·34)	(+0·02)	(−0·07)	(+0·33)	(+0·13)
32[a]	+0·25	+8·02	−0·90	−0·06	−0·04
33[a]	+0·12	−0·51	+9·03	−0·39	+0·22
34[a]	+0·10	−0·01	−0·95	+8·76	−2·95
35[b]	105·48	83·24	86·55	70·86	66·25
	(+0·45)	(−0·27)	(+0·07)	(−0·11)	(+0·07)
36[b]	105·46	83·74	76·57	80·01	63·08
	(+0·33)	(−0·09)	(−0·36)	(−0·13)	(−0·26)

TABLE IV
(*Continued*)

Compound	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$
37[b]	105·33 (+0·21)	75·21 (+0·10)	86·50 (+0·02)	79·68 (+0·21)	63·34 (−0·12)
38[b]	105·58 (+0·87)	83·23 (+0·05)	85·60 (+0·58)	79·62 (+0·27)	63·30 (+0·22)

[a] DCS values calculated by subtracting the corresponding chemical shift in the parent compound *1* from that in the derivative. [b] The chemical shift calculated as the sum of the corresponding chemical shift in the parent compound *1* and of the appropriate DCS values. Values in parentheses are the differences between the experimental and calculated chemical shifts

in Tables IV and V summarize results of such treatment of ^{13}C and ^{1}H chemical shifts in compounds *1*–*38*.

The second method is applicable only to sufficiently large series of compounds. It employs multidimensional regression analysis to find the "best" δ_0 and Δ_i values. The best values are those which lead to the smallest sum of squared differences between calculated and experimental chemical shifts. Since the summation includes reference compound, mono and multiple substituted compounds, the "best" values are not necessarily equal to those determined by the first method. The extent to which Eq. (2) is satisfied is apparent from statistical tests.

The second method which considers all the measured chemical shifts in the reference, in mono and multiple substituted compounds to be of equal importance should be prefered for the DCS additivity in cases which involve large or bulky substituents in the reference compound. Despite this, to the best of our knowledge, the second method has not yet been applied to chemical shifts in carbohydrates. Data in Tables VI and VII are the results of the first such treatment.

As it is apparent from Tables IV–VII the DCS additivity is well satisfied for both ^{1}H and ^{13}C chemical shifts in the investigated series of *29* compounds irrespective of the method of data treatment. Significant deviations are found only in compounds (*8*, *16*, and *18*) with different conformer populations. It appears that the deviations of the calculated chemical shifts are proportional to the decrease in the *C1* conformer population.

Comparison with the available tests[2,4] of ^{13}C chemical shift additivity in (not silylated) O-acetyl and O-benzoyl derivatives of methyl β-D-xylopyranoside shows that pertrimethylsilylation improves the precision of the DCS additivity. The above results demonstrate that this improvement is due to trimethylsilyl group making

TABLE V

^{1}H DCS values for O-acetylation, O-benzoylation, O-benzylation and O-methylation of methyl 2,3,4-tris-O-trimethylsilyl-β-D-xylopyranoside and the calculated chemical shifts[a,b]

Compound	H-1	H-2	H-3	H-4	H-5	H-5
2[a]	+0·17	+1·54	+0·17	+0·11	+0·05	+0·04
3[a]	+0·11	+0·11	+1·56	+0·16	+0·01	+0·13
4[a]	+0·05	+0·09	+0·24	+1·19	+0·24	+0·01
5[b]	4·30	4·90	5·10	3·80	3·86	3·30
	(+0·04)	(−0·07)	(−0·09)	(0·0)	(+0·01)	(−0·01)
6[b]	4·24	4·88	3·78	4·83	4·09	3·18
	(+0·04)	(−0·04)	(0·0)	(−0·04)	(+0·03)	(+0·04)
7[b]	4·18	3·45	5·17	4·88	4·05	3·27
	(0·0)	(+0·03)	(−0·10)	(+0·02)	(−0·01)	(+0·04)
8[b]	4·35	4·99	5·34	4·99	4·10	3·31
	(+0·05)	(−0·08)	(−0·17)	(−0·04)	(+0·03)	(+0·06)
12[a]	+0·35	+1·82	+0·33	+0·18	+0·11	+0·12
13[a]	+0·19	+0·28	+1·85	+0·31	+0·06	+0·21
14[a]	+0·13	+0·19	+0·44	+1·54	+0·31	+0·18
15[b]	4·56	5·29	5·49	4·01	3·99	3·46
	(−0·01)	(−0·06)	(−0·06)	(−0·01)	(+0·02)	(0·0)
16[b]	4·50	5·26	4·14	5·25	4·22	3·43
	(+0·08)	(−0·10)	(+0·03)	(−0·10)	(+0·07)	(+0·10)
17[b]	4·34	3·72	5·66	5·38	4·17	3·52
	(−0·01)	(−0·01)	(−0·09)	(−0·14)	(+0·13)	(−0·04)
18[b]	4·69	5·54	5·99	5·56	4·28	3·64
	(+0·04)	(−0·15)	(−0·21)	(−0·25)	(+0·15)	(+0·06)
22[a]	+0·18	−0·10	+0·10	+0·05	0·0	0·0
23[a]	+0·04	+0·17	−0·07	+0·16	−0·02	+0·05
24[a]	−0·02	+0·02	+0·13	−0·17	−0·02	−0·04
25[b]	4·24	3·32	3·40	3·74	3·78	3·18
	(+0·01)	(0·0)	(+0·02)	(+0·01)	(+0·02)	(+0·01)
26[b]	4·18	3·17	3·60	3·41	3·78	3·09
	(0·0)	(+0·01)	(+0·03)	(+0·02)	(+0·05)	(+0·03)
27[b]	4·04	3·44	3·43	3·52	3·76	3·14
	(+0·04)	(+0·04)	(+0·01)	(+0·04)	(+0·15)	(+0·06)
28[b]	4·22	3·34	3·53	3·57	3·76	3·14
	(+0·03)	(+0·01)	(+0·04)	(+0·04)	(+0·17)	(+0·07)
32[a]	+0·08	−0·42	−0·01	+0·02	−0·03	−0·02
33[a]	+0·01	+0·04	−0·40	+0·06	−0·06	+0·02
34[a]	−0·01	+0·02	+0·03	−0·41	+0·23	−0·04
35[b]	4·11	2·87	2·96	3·61	3·71	3·13
	(+0·01)	(+0·06)	(+0·07)	(0·0)	(+0·04)	(+0·01)
36[b]	4·09	2·85	3·39	3·14	4·00	3·07
	(0·0)	(+0·01)	(+0·10)	(+0·02)	(0·0)	(+0·01)

TABLE V
(*Continued*)

Compound	H-1	H-2	H-3	H-4	H-5	H-5
37[b]	4·02 (+0·02)	3·31 (+0·01)	3·00 (+0·05)	3·18 (+0·05)	3·97 (+0·03)	3·11 (+0·01)
38[b]	4·10 (+0·04)	2·89 (+0·08)	2·99 (+0·14)	3·20 (+0·06)	3·94 (+0·05)	3·09 (+0·05)

[a] DCS values calculated by subtracting the corresponding chemical shift in the parent compound *1* from that in the derivative. [b] The chemical shift calculated as the sum of the corresponding chemical shift in the parent compound *1* and of the appropriate DCS values. Values in parentheses are the differences between the experimental and calculated chemical shifts.

TABLE VI
Multidimensional regression analysis of ^{13}C chemical shifts

DCS[a]	$C_{(1)}$[b]	$C_{(2)}$[b]	$C_{(3)}$[b]	$C_{(4)}$[b]	$C_{(5)}$[b]
Ac^2	−2·978	−2·163	−2·891	−0·221	−0·309
Ac^3	−0·348	−2·445	−0·841	−2·786	0·006
Ac^4	−0·428	−0·518	−3·491	0·569	−3·889
Bz^2	−3·069	−2·084	−3·314	−0·309	−0·621
Bz^3	−0·159	−2·414	−0·559	−2·469	0·194
Bz^4	−0·619	−0·579	−3·784	0·815	−4·141
Bn^2	0·102	6·413	−1·218	0·019	−0·164
Bn^3	−0·088	−0·386	7·012	−0·546	0·066
Bn^4	−0·208	−0·031	−0·968	6·794	−2·379
Me^2	−0·149	8·051	−1·048	−0·119	−0·166
Me^3	−0·219	−0·574	8·697	−0·619	0·024
Me^4	−0·194	−0·179	−1·083	8·525	−2·996
δ_0[c]	105·414	75·893	78·728	71·594	66·310
σ[d]	0·994	0·999	0·999	0·999	0·995
SD[e]	0·151	0·157	0·256	0·160	0·184

[a] The DCS values associated with the replacement of trimethylsilyl group in *1* by the indicated substituent in the position denoted by the superscript. For substituent designations see Table II. All values are in ppm units. [b] The DCS values for the given carbon atom[c]. Defined in Eq. (*2*). [d] Multiple regression correlation coefficient. [e] Standard deviation of the calculated chemical shift.

the series of compounds conformationally more homogeneous. Since trimethylsilyl group should have similar effects in other series of conformationally nonrigid compounds with equatorial functional groups in the more stable conformer, pertrimethylsilylation appears to be a general method for improving precision of the DCS additivity in such series.

EXPERIMENTAL

Syntheses. Preparation and properties of methyl β-D-xylopyranosides partially O-substituted by acetyl, benzoyl, methyl, and benzyl groups were described earlier[2,9–15]. Their trimethylsilylations yielded the compounds investigated here. Compounds *1*, *3*, *5*, *7*, *22*, *27*, *28*, *32*, *33*, *35*, *34*, and *37*, were prepared by trimethylsilylation in a heterogenous mixture of formamide — trimethylchlorsilane — hexane containing catalytic amount of pyridine[16]. All the remaining compounds were trimethylsilylated by an excess (20%) of bis(trimethylsilyl)acetamide in pyridine. After the compounds were dissolved the reaction was left to proceed for 15 minutes at 60°C

TABLE VII

Multidimensional regression analysis of ^{1}H chemical shifts

DCS[a]	H-1[b]	H-2[b]	H-3[b]	H-4[b]	H-5e[b]	H-5a[b]
Ac^2	0·204	1·488	0·141	0·080	0·086	0·057
Ac^3	0·124	0·093	1·481	0·160	0·026	0·147
Ac^4	0·064	0·088	0·206	1·170	0·266	0·052
Bz^2	0·383	1·757	0·309	0·147	0·139	0·174
Bz^3	0·178	0·262	1·769	0·257	0·119	0·194
Bz^4	0·163	0·152	0·404	1·442	0·394	0·214
Bn^2	0·184	−0·113	0·105	0·043	0·021	0·016
Bn^3	0·064	0·172	−0·075	0·163	0·051	0·081
Bn^4	−0·001	0·027	0·130	−0·162	0·066	0·001
Me^2	0·090	−0·404	0·027	0·010	−0·001	0·001
Me^3	0·030	0·060	−0·387	0·065	−0·016	0·041
Me^4	0·005	0·010	0·057	−0·394	0·254	−0·019
δ_0[c]	4·004	3·264	3·390	3·549	3·760	3·106
r[d]	0·998	1·000	0·999	0·999	0·992	0·994
SD[e]	0·012	0·023	0·035	0·029	0·022	0·017

[a] The DCS values associated with the replacement of trimethylsilyl group in *1* by the indicated substituent in the position denoted by the superscript. For substituent designations see Table II. All values are in ppm units. [b] The DCS values for the given hydrogen atom. [c] Defined in Eq. (*2*). [d] Multiple regression correlation coefficient. [e] Standard deviation of the calculated chemical shift.

Solvents and the silylating agents were removed by blowing a stream of dry nitrogen through the samples at an elevated temperature and reduced pressure (80°C, 1 333 Pa). The yields varied within 80–95%.

Spectral measurements. ^1H and ^{13}C NMR spectra were measured under exactly the same conditions as described previously[2] for other methyl β-D-xylopyranoside derivatives. Special precautions were undertaken to prevent sample decomposition by moisture; NMR tubes were closed by septum caps. All solvents were dried over activated molecular sieve (Fischer Scientific 5A). Homonuclear decoupling $^1H-\{^1H\}$ lead in all cases to unambiguous assignment of proton chemical shifts, the only possible source of errors was overlapp of methine proton signals with the strong methyl proton line. With the exception of cases noted in the Table I all spectra were of the first order. The analysis was confirmed by spectral simulation by LAOCOON program which was a part of spectrometer software. The few strongly coupled subspectra were analysed by manual readjustment of the parameters until a satisfactory agreement between experimental and simulated spectra was achieved. Since the values of $J_{1,2}$ coupling constants could be read directly from the spectra, their precision is higher than that of the other coupling constants. The most of ^{13}C chemical shifts could be assigned unequivocally by selective heteronuclear decoupling experiments. Only in compounds *22*, *35*, *37*, and *38* small differences in proton chemical shifts of two protons and large proton–carbon coupling constants precluded assignments within the pairs of the lines. In these cases, that assignment of the two lines was adopted which lead to a smaller sum of deviations from additivity.

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