^{13}C-NMR STUDY OF TETROSIDES AND THEIR DERIVATIVES

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Received January 29th, 1980

^{13}C-NMR spectra of 23 tetrose derivatives were assigned. The $C_{(1)}$ resonates below 103 ppm with compounds having *cis*-arranged substituents at $C_{(1)}$ and $C_{(2)}$ and above 106 ppm with compounds having *trans*-arrangement. The carbon-13 chemical shifts are mainly influenced by the 1,2-interaction. The magnitudes of direct coupling constants $^1J(C_{(1)}, H)$ cannot be used for the determination of the anomeric configuration.

Methyl tetrosides represent the simplest model of the sugar furanose ring. A series of methyl tetrosides[1] prepared in connection with the study of the partial methylation of these compounds[2] provided rich material for the ^{1}H-NMR study. The presented paper deals with the signal assignment in their ^{13}C-NMR spectra and the discussion of the obtained data. Studied were all four methyl tetrosides *I–IV*, their peracetates and some methyl- and benzyl- derivatives as well as the 1,2-O-isopropylidene derivatives *V* and *VI*. In contrary to Ritchie and coworkers[3] who measured the spectra of methyl tetrosides in deuterium oxide, we used chloroform in which both parent compounds and their derivatives are soluble.

The assignments of $C_{(4)}$ and $C_{(1)}$-methoxyl follow directly from their multiplicity (triplet and quartet) in the off-resonance or undecoupled spectra. Signal of $C_{(1)}$ which is attached to two oxygen atoms always resonates in the lowest magnetic field. The signals of $C_{(2)}$ and $C_{(3)}$ were assigned using selective decoupling of the corresponding proton signals that have unambiguous assignment. The chemical shifts are given in Tables I and II. The signal assignments of methyl tetrosides agree well with those reported earlier[3].

In contrary to the six-membered pyranosides, it is not possible with furanosides to decide between the axial and equatorial substituents. Also the conformational mobility of the later rings is greater. Comparison of chemical shifts of all isomers shows that the relative position of the neighbour substituents plays the dominant role. *cis*-Interaction causes the steric compression which results in increased shielding

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of both carbon atoms involved. Therefore, the chemical shift of $C_{(1)}$ does not reflect the anomeric configuration but the relative position of the substituent at $C_{(2)}$. The $C_{(1)}$ atom resonates in the region 100·7 – 102·9 ppm in compounds with *cis*-arranged substituents at $C_{(1)}$ and $C_{(2)}$ (*I* and *IV*) and in the region 106·3 – 109·4 ppm in compounds having their mutual orientation *trans*-. Since both regions do not overlap, the mentioned difference is of diagnostic values. Change of the configuration at $C_{(1)}$ from *cis*- to *trans*- with respect to $C_{(2)}$ shifts the $C_{(1)}$ signal of 5·6 – 6·7 ppm downfield; the effect observed at $C_{(2)}$ is 1·5 – 3·4 ppm downfield. The changes of configuration at $C_{(2)}$ produce a more complex response reflecting also the nature of sustituents. For the similar reasons the $C_{(2)}$ signal in *III* (*trans*-orientation only) resonates in the lowest field from the whole series. The chemical shift of $C_{(3)}$ in *III* and *IV* which

TABLE I

^{13}C Chemical Shifts of Methyl Tetrosides and their Derivatives

Compound	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	OCH_3	Others
I	102·2	72·4	69·5	73·3	55·6	
Ia	100·7	71·2	68·4	69·9	55·5	170·6, 170·0 20·9, 20·7
II	108·8	75·8	70·8	72·0	55·2	
IIa	106·3	75·4	71·5	69·5	55·2	170·6, 169·6 20·5, 20·5
IIb	106·5	83·7	79·4	69·0	55·4	58·5, 58·0
IIc	106·5	85·3	70·2	72·8	55·3	58·7
III	108·7	80·2	76·4	74·1	55·1	
IIIa	106·6	81·0	76·4	70·7	54·7	170·4, 169·7 20·7, 20·7
IIIb	109·4	79·5	86·5	70·8	55·1	58·0
IIIc	106·2	88·7	73·7	74·9	54·8	57·6
IIId	106·8	89·4	81·9	70·0	54·6	71·9, 57·2
IV	102·7	78·8	76·2	71·1	55·6	
IVa	101·0	77·7	76·2	68·9	55·2	170·6, 170·4 20·7, 20·7
IVb	101·9	86·7	83·4	69·2	55·1	58·3, 57·6
IVc	101·6	86·7	81·3	69·4	55·0	72·0, 58·2
IVd	101·6	78·9	82·3	68·6	55·4	170·4, 57·4 20·7
IVe	102·9	77·3	85·9	69·6	55·5	57·3

have *trans*-mutual orientation of substituents at $C_{(2)}$ and $C_{(3)}$ are very similar. The same holds for *I* and *II* which have these substituents *cis*-oriented. These resonances are shifted upfield in the later pair. No such regularities are observed with

TABLE II

^{13}C Chemical Shifts of 1,2-Isopropylidene Derivatives

Compound	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	O—C—O	CCH_3	CCH_3	Others
V	104·9	84·7	74·8	72·7	111·5	26·4	25·9	
Va	105·4	83·0	77·2	70·6	112·1	26·7	26·2	20·9
Vb	105·5	82·5	84·3	70·0	111·6	26·9	26·3	56·9
Vc	105·6	83·0	81·9	70·4	111·6	26·8	26·2	71·2
VI	105·3	77·9	71·0	69·4	112·7	26·6	26·4	
VIa	105·1	77·2	72·1	66·5	113·2	26·5	26·5	

TABLE III

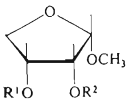
Coupling Constants $^1J_{(^{13}C-H)}$

Compound[a]	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$
I	175·8	152·8	156·3	148·9
Ia	174·6	150·8	159·9	152·6
II	170·9	152·0	152·6	148·9
IIa	172·2	155·0	156·3	152·3
IIb	170·9	146·5	146·5	145·3
IIc	170·9	149·4	152·6	145·9
III	174·6	153·2	152·6	149·2
IIIa	173·3	158·7	152·0	150·9
IIIb	169·7	151·4	148·9	148·9
IIIc	171·5	152·6	152·6	148·3
IIId	170·9	149·5	146·5	148·4
IV	173·3	150·5	150·2	149·5
IVa	175·8	153·2	156·9	149·7
IVb	172·1	144·0	153·8	148·9
IVc	170·9	152·6	150·1	[b]
IVd	175·8	153·8	145·4	148·9
IVe	177·7	150·8	148·3	148·3

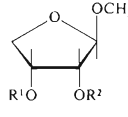
[a] In the OCH_3 group was ^1J = 141·6—144·0 Hz; [b] not determined.

$C_{(4)}$. The largest chemical shift of $C_{(4)}$ among the studied hydroxy- and acetoxy-derivatives was found in *III* and the lowest one in *IV*. However, the interpretation of this phenomenon is not clear.

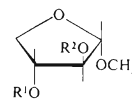
Values of the direct coupling constants $^1J_{(^{13}C-H)}$ (Table III) shows that their magnitude for $C_{(1)}$ (169·7 – 177·7 Hz) cannot be used to distinguish between the α- and β-anomers in the way used for pyranoses[4,5] and some furanoses[6]. This is a consequence of the difficulty with the definition of the conformation of tetroses and therefore uncertain relative orientation of the $C_{(1)}$—H bond with respect to the lone electron pairs of the oxygen atoms in its neighbourhood. Owing to the strong signal overlap in the undecoupled spectra and to the second-order effects associated with low carbon-13 observing frequency, the geminal and vicinal coupling constants $^2J_{C-C-H}$ and $^3J_{C-C-C-H}$ were observed in several cases only. Therefore, they remained uninterpreted. Substituent effects due to methylation of the hydroxyl group were in the studied series +8·5 to 10·1 ppm at the α-carbon and −1·5 to −2·8 ppm at the β-carbon, respectively. Our data do not differ much from the literature values[7–10]. The asymmetry of the chemical shift effects suggests that probably some change of conformation takes place. The effects due to acetylation, benzoylation and benzylation derivable from the Table I have also usual values[11].



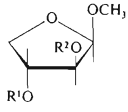
I; $R^1 = R^2 = H$
Ia; $R^1 = R^2 = COCH_3$



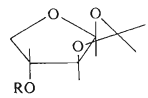
II; $R^1 = R^2 = H$
IIa; $R^1 = R^2 = COCH_3$
IIb; $R^1 = R^2 = CH_3$
IIc; $R^1 = H$, $R^2 = CH_3$



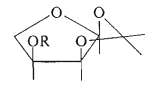
III; $R^1 = R^2 = H$
IIIa; $R^1 = R^2 = COCH_3$
IIIb; $R^1 = H$, $R^2 = CH_3$
IIIc; $R^1 = CH_3$, $R^2 = H$
IIId; $R^1 = Bn$, $R^2 = H$



IV; $R^1 = R^2 = H$
IVa; $R^1 = R^2 = COCH_3$
IVb; $R^1 = R^2 = CH_3$
IVc; $R^1 = CH_3$, $R^2 = H$
IVd; $R^1 = CH_3$, $R^2 = COCH_3$
IVe; $R^1 = Bn$, $R^2 = CH_3$



V; R = H
Va, R = OCH_3
Vb; R = CH_3
Vc; R = $CH_2C_6H_5$



VI; R = H
VIa; R = Bz

Comparison of 1,2-O-isopropylidene derivatives *V* and *VI* (Table II) shows that $C_{(2)}$ and $C_{(3)}$ resonate in the higher field in the *erythro*-compound, which can be explained by *cis*-2,3-interactions. However, the differences in $C_{(4)}$ chemical shifts suggest possible conformational changes. The chemical shift differences of the isopropylidene methyls also point to this direction. They amount 0·5–0·6 ppm (^{13}C) and 0·15–0·17 ppm (^{1}H) in the *threo*-series and 0·0–0·2 ppm (^{13}C) and 0·19–0·21 ppm (^{1}H) in the *erythro*-series. It is possible that after accumulation of more data this effect could find an application similar to the $\Delta\delta$-criterion used with 2',3'-isopropylidene derivatives of ribofuranosyl nucleotides[12–15].

EXPERIMENTAL

^{13}C-NMR spectra were measured on a Jeol FX-60 NMR spectrometer (15·036 MHz) in FT mode in deuteriochloroform at 25°C. Chemical shifts are given in the δ-scale referenced to tetramethylsilane (internal standard) with accuracy $\pm$0·08 ppm. They were calculated from the digitally obtained address differences. To improve the signal to noise ratio, the accumulated free induction decays were multiplied by an exponential causing additional line broadening of 1·6 Hz. Undecoupled ^{13}C-NMR spectra were obtained using the "gated decoupling" method (decoupler off during the acquisition)[16]; digital resolution in this experiment was 0·6 Hz.

Preparation and physical constants of the studied compounds are described elsewhere[1,2].

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Translated by the author (P. S.).