

Conformational and configurational studies on diastereoisomeric methyl (methyl 3,4-*O*-benzylidene- α - and - β -D-galactopyranosid)-uronates

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Received 14 August 1974

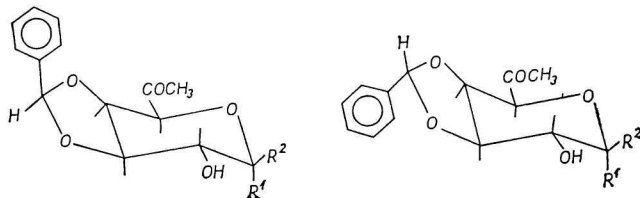
Proton magnetic resonance and circular dichroism spectra for two pairs of diastereoisomeric methyl (methyl 3,4-*O*-benzylidene- α - and - β -D-galactopyranosid)uronates and carbon magnetic resonance spectra for the diastereoisomeric title α anomers were measured. From the p.m.r. coupling constants, chemical shifts, and Cotton effects conformation and configuration for the compounds under investigation was determined. The possibility of the deformation of the tetrahydropyran ring containing a dioxolane fused ring is also discussed.

Были измерены спектры ядерного магнитного резонанса диастереомерных пар метил (метил-3,4-*O*-бензилиден- α - и - β -D-галактопиранозид)уроната. На основе констант, спин-спиновой связи химических сдвигов и эффектов Коттона, полученных измерением CD кривых, определялась структура отдельных изомеров. Одновременно обсуждается возможность деформирования пиранового кольца присоединением диоксоланового кольца в положении C-3 и C-4.

The deformation of the energetically favoured chair conformation of the tetrahydropyran ring (C1, 1C) induced by dioxolane fused ring systems has been investigated by numerous authors [1–6].

Although considerable effort has been devoted to the clarification of the effect of a dioxolane fused ring systems upon the chair conformation, the effect of a bulky planar *exo* and *endo* substituents on the benzylic carbon upon the conformation of the tetrahydropyran ring has not yet been fully understood.

To be able to assign a configuration to diastereoisomeric methyl (methyl 3,4-*O*-benzylidene- α - and - β -D-galactopyranosid)uronates and examine the possible de-



I. $R^1 = \text{OCH}_3$, $R^2 = \text{H}$; II. $R^1 = \text{OCH}_3$, $R^2 = \text{H}$; III. $R^1 = \text{H}$, $R^2 = \text{OCH}_3$;
IV. $R^1 = \text{H}$, $R^2 = \text{OCH}_3$.

Scheme 1

formation of the tetrahydropyran sugar ring in these systems, p.m.r. and c.d. spectra of *I*–*IV* (see Scheme 1 where the assignment of the configuration to the individual substances is based on the results of this work), and c.m.r. spectra of *I* and *II* have been studied.

Experimental

The p.m.r. spectra were measured in the frequency sweep mode at 80 MHz and 25°C using a Tesla BS 487 B spectrometer. Chloroform-*d*, acetone-*d*₆, and pyridine (Merek, A.G., Darmstadt) were used as solvents and tetramethylsilane as the internal standard. The concentration of the solutions was ~10% (w/v). The spectra were recorded at a sweep width of 100 Hz. The chemical shifts, given in δ , were either read directly from the spectra or measured electronically using a frequency counter Tesla BM 455 E with an accuracy of ± 0.005 p.p.m. The proton-signal assignment was done by the INDOR technique.

The chemical shifts and the coupling constants were calculated by iteration using the LAOCOON 3 program [7] on a CDC 3300 computer. When the calculations were completed the theoretical spectra of the five-spin system (H-1–H-5) were drawn using the PMR PLOT program (Lorentz's curve-shape), with a half-line width of 0.9 Hz. The theoretical spectra were in a good agreement with those recorded. After five iterations the probable error of parameters was below 0.05 Hz and the RMS error was below 0.06 Hz.

The c.m.r. spectra (for CDCl₃ solutions) were obtained using a Varian CFT-20 spectrometer. The impulse interval was 0.51 sec and the number of accumulated spectra was 93 000.

The c.d. spectra were measured on a Jouan spectrometer, Model 185, at room temperature using spectral grade methanol and 1–5 mm cells.

Compounds under investigation were prepared as described before [8] and showed the following physical constants: *I* – m.p. 140–140.5°C, $[\alpha]_D^{28} - 5^\circ$ ($c=1$, chloroform); *II* – m.p. 117–118°C, $[\alpha]_D^{28} + 103^\circ$ ($c=1$, chloroform); *III* – m.p. 154–155°C, $[\alpha]_D^{25} - 73^\circ$ ($c=1$, methanol); *IV* – m.p. 132–134°C, $[\alpha]_D^{25} + 19^\circ$ ($c=1$, methanol).

Results and discussion

In agreement with [5] from the proton magnetic resonance spectral data of the investigated compounds (Table 1) it can be seen that, regardless the solvent used in the measurements, the benzylic proton in an *endo* configuration (*exo*-phenyl isomers) is relatively more deshielded than that in an *exo* position (*endo*-phenyl isomer), and consequently it resonates at lower field.

Examining the Dreiding models it became clear that the *endo*-phenyl ring in *I* and *III* is located closely to H-2. Therefore, it may be expected that due to the effect of the phenyl ring this proton is more or less shielded and will resonate at lower or higher field. The data in Table 1 show, however, that the observed H-2 chemical shifts for *I* and *II* are almost identical. It is known that the sign and the magnitude of the shielding effect of a phenyl ring depends upon the values of Z and ρ coordinates of the proton under examination. The calculations [9] for the models of *I* and *III* showed that even such a mutual position of the phenyl ring and the H-2 proton is possible at which the shielding contribution of the phenyl ring is negligible. This explains the almost identical chemical shifts of the H-2 protons in *I* and *II*.

Table 1

The p.m.r. chemical shifts and first-order coupling constants for I-IV

Com- pound	Solvent	Chemical shift ^a δ , p.p.m.										Coupling constants ^a J /Hz			
		H-1	H-2	H-3	H-4	H-5	2'-H	2'- Φ	-OCH ₃	OCH ₃	OH	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
I	(CD ₃) ₂ CO	4.75d	3.86q	4.41t	4.60q	4.74d	5.87s	7.35m	3.71	3.44	2.80	3.7	6.	6.6	2.6
II	(CD ₃) ₂ CO	4.80d	3.87m	4.52m	4.55m	4.64m	6.07s	7.36s	3.69	3.41	2.79	3.6	6.7	5.8	2.8
I	CDCl ₃	4.90d	4.02q	4.46q	4.62q	4.73d	5.84s	7.35m	3.79	3.51	2.75	3.8	5.3	6.7	2.4
II	CDCl ₃	4.98d	4.08m	4.5 m ^b	4.6 m ^b	4.7 m ^b	6.21s	7.35s	3.78	3.50	2.63	3.8	<i>b</i>	<i>b</i>	<i>b</i>
I	C ₅ H ₅ N	5.20d	4.35m	4.87m	4.87m	5.09m	6.03s		3.79	3.59	<i>d</i>	3.4	6.5	6.9	2.4
II	C ₅ H ₅ N	5.28d	4.40q	5.03q	4.86q	5.00d	6.29s		3.73	3.54	<i>d</i>	3.4	7.3	5.4	2.6
III	CDCl ₃	4.16d	3.60q	4.26q	4.52q	4.47d	5.93s	7.35m	3.87	3.53	2.60	7.7	6.7	5.5	
IV	CDCl ₃	4.20d	3.81m	4.33		4.56 ^b	6.13s	7.34s	3.80	3.58	2.62	7.6	<i>b</i>	<i>b</i>	<i>b</i>

Peak multiplicities: s — singlet, d — doublet, t — triplet, q — quartet, m — multiplet.

a) Value calculated using LAOCOON 3 program.

b) Proton-signal assignment could not be made accurately.

c) Region overlapped with the signals of the solvent.

d) Measured with the addition of D₂O.

An important diagnostical phenomenon here is the fact that the aromatic protons of *I* and *III* appear in their p.m.r. spectra as multiplets and those of *II* and *IV* appear as singlets. From the Dreiding models it again could be observed that the phenyl ring in *I* and *III* is located closely to H-2 proton which hinders the free rotation around the benzylic linkage and results in a lower degree of equivalency among the aromatic protons. This nonequivalency among the aromatic protons in the case of the derivatives *I* and *III* explains their appearance in their p.m.r. spectra as multiplets (Table 1).

These results are supported by the values of chemical shifts of phenyl-1-carbons of *I* and *II* in their c.m.r. spectra (136.7 and 138.5 p.p.m. for *I* and *II*, respectively). The differences appear to be due to increased perturbation in the *endo*-phenyl isomer *I* resulting in increased shielding of the phenyl-1-carbon. For the carbons of the tetrahydropyran ring, unfortunately, the differences in their chemical shifts were found to be too small to be significant for drawing any conclusions as far as the deformation of this arrangement is concerned.

The p.m.r. data of *III* and *IV* were used for the configurational assignment in an analogous manner. Hence, the β anomer *III* is assumed to be the *endo*-phenyl and the β anomer *IV* the *exo*-phenyl isomer.

Circular dichroism measurements of *I*–*IV* also confirm the different position of the benzene ring in the dioxolane arrangement. The c.d. spectra of *I* and *III* showed weak negative ($\Delta\epsilon_{215} = -0.65$ and $\Delta\epsilon_{216} = -0.73$, respectively) and of *II* and *IV* intense positive ($\Delta\epsilon_{213} = 4.76$ and $\Delta\epsilon_{213} = 4.43$, respectively) Cotton effects. From the position and the intensity of the absorption band at 215 nm ($\log \epsilon$ 3.70) it follows that it corresponds to the 1L_a band of the benzenoid chromophore. In the region of 1L_a band of the benzene chromophore also the $n-\pi^*$ band of the methoxycarbonyl group is present. Compounds *I* and *III* (*endo*-phenyl isomers) show weak positive Cotton effects of equal intensity ($\Delta\epsilon_{226} = 0.05$) corresponding to the $n-\pi^*$ transition. The weak Cotton effects of the *exo*-phenyl isomers *II* and *IV* corresponding to this transition are not observed as these are overlapped by very strong positive chiroptical bands of the 1L_a transition of the benzene chromophore.

Applying the Karplus' equation as modified by Abraham *et al.* [10] for the calculation of the dihedral angles the following approximate values were obtained: $\Phi_{1,2} = 46-47^\circ$, $\Phi_{2,3} = 140-147^\circ$, $\Phi_{3,4} = 23-25^\circ$, $\Phi_{4,5} = 53-54^\circ$ for *I*, and $\Phi_{1,2} = 45-47^\circ$, $\Phi_{2,3} = 148-153^\circ$, $\Phi_{3,4} = 31-35^\circ$, $\Phi_{4,5} = 51-53^\circ$ for *II*. These values are in a good agreement with those obtained from Dreiding models *i.e.* 50° (H_1-H_2), 150° (H_2-H_3), 25° (H_3-H_4), and 43° (H_4-H_5), and they confirm the chair (C1) conformation for *I* and *II* (and analogically also for *III* and *IV*) suggesting that the dioxolane fused ring system does not result in the deformation of the tetrahydropyran ring to such an extent as to affect its original C1 conformation.

Acknowledgements. The authors wish to thank Dr T. Wirthlin from Varian A.G. (Zug, Switzerland) Research Laboratories for c.m.r. and S. Bystrický for c.d. measurements. They are also grateful to the management of the Institute of Organic Chemistry and Biochemistry, Prague, for allowing them to use their equipment for the latter measurements.

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Translated by P. Kováč