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SELECTIVE DEUTERATION OVER RANEY NICKEL IN DEUTERIUM OXIDE: METHYL GLYCOSIDES*

STEPHEN J. ANGYAL, JOHN D. STEVENS,
School of Chemistry, University of New South Wales, Kensington, N.S.W. 2033 (Australia)

AND LÉON ODIER†
Laboratoires de Chimie, Départment de Recherche Fondamentale, Groupe Macromolécules Végétales, Centre d'Etudes Nucléaires de Grenoble, 85 X, F-38041 Grenoble (France)

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ABSTRACT

The rate of protium–deuterium exchange, catalyzed by deuterated Raney nickel in deuterium oxide, in various positions in methyl glycopyranosides and furanosides has been studied. In general, the exchange process is not highly regioselective in these compounds. However, conditions were found under which methyl β-D-fructopyranoside can be selectively labelled on C-5, methyl β-D-fructofuranoside on C-3, and methyl β-D-galactopyranoside on C-3 and C-4.

INTRODUCTION

A simple and convenient method has been described by Koch and Stuart[2,3] for the introduction of deuterium atoms into carbohydrates. They have shown that, in the presence of Raney nickel in deuterium oxide, hydrogen atoms attached to carbon atoms which also carry a free hydroxyl group undergo ready ^1H–^2H exchange. In many instances[4–7], there are considerable variations in the rate of exchange of various hydrogen atoms in the same molecule. Could cases be found in which this variation is particularly large, essentially regioselective deuteration could be achieved in one step. Our work on inositol methyl ethers has shown that this is, indeed, possible: H-6 has been selectively exchanged[1] in quebrachitol (L-2-*O*-methyl-*chiro*-inositol).

Substitution by deuterium in specific positions ("labelling") has been used extensively for the assignment of n.m.r. spectra, and for the study of reaction pathways and mechanisms, biosynthesis, and metabolism. For most of these uses, the essential feature is the ability to recognize a particular carbon or hydrogen atom; for this, it is not imperative that the labelling by deuterium be complete, nor does it matter if there are small proportions of deuterium in other positions. It is not

*Selective deuteration, Part II. For Part I, see ref. 1.
†On the staff of Université Scientifique et Médicale de Grenoble.

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possible to achieve complete selectivity of labelling by exchange over Raney nickel, unless the compound contains only one exchangeable hydrogen atom; no matter how great the difference in the rates of exchange, by the time one hydrogen atom has been almost completely exchanged, there will have been small amounts of deuterium introduced into other positions too. The simplicity and rapidity of this method, nevertheless, warrants its use; regiospecific deuteration by chemical methods is usually a long, multi-step procedure. We have set ourselves the aim of finding examples in which at least 90% of the hydrogen atoms in one or two positions are replaced, while no more than 10% of deuterium is introduced into any other position.

Free reducing sugars cannot be deuterated by this procedure, as they are reduced to alditols; derivatives in which the reducing group is protected have to be used. We have only considered derivatives that can be readily prepared in one (or, at the most, two) step(s) from the sugars, or are commercially available, and from which the free sugar can be regenerated in high yield by a simple procedure. Obviously, derivatives could be tailor-made so as to provide good selectivity in the Raney-nickel-catalyzed deuteration, but, with expenditure of that much effort, the traditional chemical procedures can just as well be used. Herein, we consider the methyl glycosides, as they are readily prepared and readily hydrolyzable derivatives.

In order to monitor the progress of exchange, both ^{1}H- and ^{13}C-n.m.r. spectra were used. The ^{13}C spectra of most of the glycosides selected are known, but the ^{1}H spectra are preferable because the integrations are more reliable. ^{13}C-N.m.r. spectra were used when the signals in the ^{1}H spectra were not well separated and, occasionally, in order to confirm the ^{1}H results. It was found that, in many instances where the ^{1}H spectra of the unsubstituted glycosides could not be satisfactorily integrated, owing to overlap of signals, the ^{1}H spectra of the acetates (and, in one case, the benzoate) proved suitable for integration.

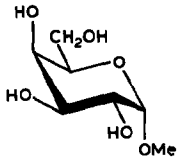
Methyl pyranosides. — Previous work[6] and the study of inositols[1] have shown that, in the six-membered ring-system, equatorial hydrogen atoms exchange more rapidly than axial ones, hydrogen atoms *syn*-axial to a hydroxyl group exchange slowly, and those *syn*-axial with a methoxyl group, even slower. A neighboring methoxyl group hinders the exchange, the extent of the hindrance being dependent on the relative configurations. If there is no hydroxyl group on a neighboring carbon atom, or if it is antiperiplanar to the hydrogen atom, exchange is very slow.

Armed with this knowledge, a methyl glycoside in which selective deuteration is likely to occur can be chosen. We chose methyl α-D-galactopyranoside (**1**), in which H-4 is equatorial, and H-2 and H-3 are *syn*-axial with oxygen atoms; the hydrogen atoms on C-6, which lack neighboring hydroxyl groups, always exchange slowly in pyranosides. The exchange was not, however, as selective as expected (see Table I); although H-4 exchanges rapidly, there was also considerable exchange of H-2; the *syn*-axial hydroxyl group (in contrast to the *syn*-axial methoxyl group) does not slow down this exchange sufficiently. Closely similar results were

obtained with methyl α-D-fucopyranoside. The lower homomorph, methyl β-D-arabinopyranoside, showed different behavior: after reaction for 1 h, only 3% of hydrogen remained on C-4, but 31% on C-3, and 73% on C-2. This glycoside in solution is a mixture of the $^4C_1$ (**2a**) and the $^1C_4$ (**2b**) conformational forms; whereas in the latter H-4 would exchange the most rapidly, in the former H-4 is hindered by a *syn*-axial hydroxyl group, H-2 (though to a lesser extent) by the neighboring methoxyl group, and only H-3 is unhindered.

The homomorphous ketoside, methyl β-D-fructopyranoside (**3**), however, showed satisfactory selectivity. In this compound, H-3 is hindered not only by the *syn*-axial OH-5 but also by the neighboring hydroxymethyl group; H-5 is the only hydrogen atom that exchanges rapidly. In this way, fructose can be readily labelled on C-5. The method is less successful, however, with other pyranosides.

The rate of exchange is controlled not only by *syn*-axial groups but also by the presence and the anomeric configuration of the methoxyl group. Being a bulky neighboring group that is not adsorbed on the catalyst, the methoxyl group hinders the exchange of H-2. This hindrance is much greater when the methoxyl group is *cis* than when it is *trans* to H-2. An equatorial methoxyl group exerts greater hindrance than an axial one, because exchange of H-2 requires adsorption by both H-2 and OH-2 on the catalyst surface, and the equatorial methoxyl group is *gauche* to both, whatever the configuration of C-2. It is thus found that exchange of H-2 in methyl α-D-glucopyranoside (OMe *trans* and *ax*) is almost as fast as that of the unhindered H-4; in methyl β-D-mannopyranoside (OMe *trans* and *eq*), H-2 ex-



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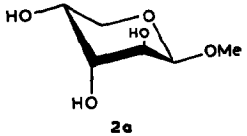

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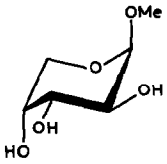

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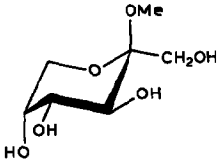

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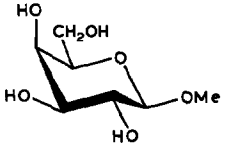

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TABLE I

HYDROGEN (EQUIV.) FOUND IN VARIOUS POSITIONS OF METHYL PYRANOSIDES AFTER EXCHANGE[a]

Pyranoside	*T* (°)	*t (min)*	*H-2*	*H-3*	*H-4*	*H-6*$_R$	*H-6*$_S$	*Anal. method*[b]	*Ref. to n.m.r.*
α-D-Gluco-	100	10	0.45	0.88	0.56	0.92	1.00	^{1}H (Ac) in $CDCl_3$	12
β-D-Gluco-	100	12	0.87	0	0.46	0.74	0.90	^{1}H (Ac) in $CDCl_3$	12
α-D-Galacto-	85	25	0.75	1.00	0.15	1.00	1.00	^{1}H (Ac) in $CDCl_3$	12
	90	95	0.30	0.80	<0.02		1.50		
—, 6-deoxy-	100	8	0.50	1.00	0.12		3.00	^{1}H (Ac) in $CDCl_3$	this work
β-D-Galacto-	100	10	0.92	0.14	0.08	1.00	1.00	^{1}H (Ac) in $CDCl_3$	12
	100	25	0.87	0	0		0.81[c]	^{13}C in D_2O	13
α-D-Manno-	100	12	0.2	0.5	0.15	0.50	0.77	^{1}H in D_2O	14
β-D-Manno-	60	60	0.44	~0.05	0.77		0.82[c]	^{13}C, ^{1}H in D_2O	13,15
α-D-Talo-	85	15	0.4	0.9	0.2		2.00	^{13}C in D_2O	16
β-D-Fructo-[d]	100	60	—	>0.96	>0.96	1.00	1.00	^{13}C, ^{1}H in D_2O	17,18
α-D-Xylo-[e]	reflux		0.48	0.73	0.23			^{1}H (Ac) in C_6D_6	this work
β-D-Xylo-[e]	reflux		0.94	0.22	0.50			^{1}H (Bz) in C_6D_6	19
β-D-Arabino-[e]	reflux		0.73	0.31	0.03			^{1}H (Ac) in C_6D_6	this work
β-D-Ribo-[e]	reflux		0.51	0.16	0.07			^{1}H (Ac) in $(CD_3)_2CO$	19

[a]In all cases, except the β-fructoside (see footnote *d*), H-1 and H-5 were assumed, and found, to be 1.00. [b] ^{1}H (Ac) means n.m.r. spectrum of the acetate; ^{1}H (Bz), the spectrum of the benzoate. [c]Equivalent of molecules containing two hydrogen atoms in that position. [d]H-1 and H-1′ were >0.96; H-5 was 0. [e]The compound was recrystallized before recording the n.m.r. spectrum.

changes less rapidly than the unhindered H-3 but more rapidly than H-4, which is affected by a *syn*-axial interaction; in methyl α-D-mannopyranoside (OMe *cis* and *ax*), H-2 exchanges about as slowly as H-4, which is *syn*-axial with O-2; and in methyl β-D-glucopyranoside (OMe *cis* and *eq*) the exchange of H-2 is very slow[6]. Because H-2 is hindered by both O-4 and the methoxyl group in methyl β-D-galactopyranoside (**4**), this compound can be labelled at both C-3 and C-4 without substantial deuteration in other positions.

The behavior of several methyl pyranosides is shown in Table I. Methyl α-D-glucopyranoside had already been studied by Balza and Perlin[6]; our results are in agreement with theirs (allowing for the fact that they designated the H-6 atoms erroneously). The behavior of the α- and β-D-xylopyranosides is analogous to that of the glucopyranosides. Methyl β-D-ribopyranoside is a conformational mixture: in the $^4C_1$ form, H-2 is hindered, but in the $^1C_4$ form, it is H-3 and, to a lesser extent, H-2. As a result, the rate of exchange is H-4 > H-3 > H-2, the difference between them being insufficient to cause selectivity.

Although the hydrogen atoms on C-6 exchange slowly, in prolonged experiments there is considerable introduction of deuterium into these positions. ^{1}H-N.m.r. spectra show that, in the glucosides and the mannosides, H-6_R exchanges more rapidly than H-6_S; in the galactosides, this information was not available, as the two H-6 signals overlap, and ^{13}C spectra do not provide this information. When one of the hydrogen atoms is replaced by deuterium, the signal of C-6 becomes a triplet, owing to coupling with deuterium; the area under this triplet does not give an accurate measure of the amount of hydrogen remaining[8] on C-6. When both of these hydrogen atoms are replaced, the signal practically disappears. When exchange is partial, the signal in the original position indicates only the proportion of molecules that still have two hydrogen atoms attached to C-6; this is the figure shown in the Tables.

Methyl furanosides. — The exchange reaction of the methyl tetrosides and pentosides had been investigated by Wu *et al.*[7]; in many instances, they established the order of the reaction rates within each glycoside. They found one case in which the exchange was selective: in methyl α-D-threofuranoside, H-3 was exchanged to the extent of >85%, with little exchange at other positions.

The steric interactions that affect the rate of catalytic exchange in the furanosides differ from those operating in the pyranosides. From our results (see Table II) and those of Wu *et al.*[7], the following conclusions may be drawn for the methyl pentosides. (*i*) Exchange of H-2 is slow if it is *cis* to the methoxyl group. Being *cis* to the sidechain has a small retarding effect also. (*ii*) The exchange of H-3 is also slowed down, although not to the same extent, if it is *cis* to the methoxyl group. This appears to be a *quasi-syn*-axial effect. (*iii*) The hydrogen atoms of the hydroxymethyl group in pentofuranosides react more rapidly than those in the pyranosides, presumably because the greater flexibility of the five-membered ring allows them to assume conformations more favorable for adsorption on the catalyst surface. In those cases where both H-2 and H-3 exchange slowly, the hydrogen

TABLE II

HYDROGEN (EQUIV.) FOUND IN VARIOUS POSITIONS OF METHYL FURANOSIDES AFTER EXCHANGE[a]

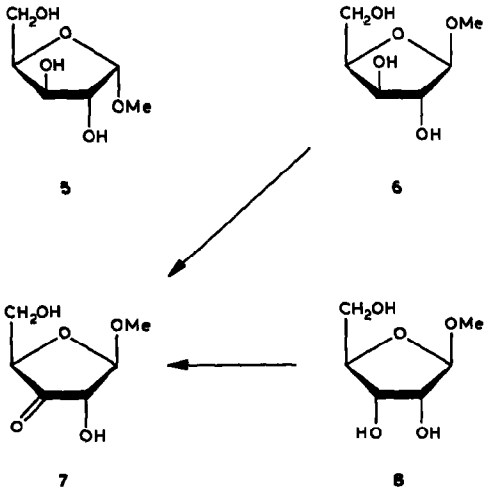
Furanoside	*T* (°)	*t (min)*	*H-2*	*H-3*	*H-4*	*H-5*$_R$	*H-5*$_S$	*H-6*$_R$	*H-6*$_S$	*Anal. method*[b]	*Ref. to n.m.r.*
β-D-Gluco-	85	8	1.00	0.32	0.63	0.79		0.54	0.61	^{1}H	20
α-D-Altro-	80	30	0.93	0.86	1.00	0.80		0.80	0.65	^{1}H	20
β-D-Altro-	100	90	0.32	0.87	1.00	0.73		~0.40		^{1}H, ^{13}C	20, this work
β-D-Allo-	100	90	0.73	0	1.00	0.28			0.04[c]	^{13}C	21
β-D-Fructo-[d]	80	20		0.25	0.94	1.00		1.95[e]	1.00	^{1}H	this work
	80	40		0.05	0.88	1.00		1.84[e]	0.92	^{1}H	
	80	60		0.02	0.81	1.00		1.60[e]	0.73	^{1}H	
α-D-Arabino-	100	25	0.80	0.50	1.00	0.68	0.84			^{1}H	22
β-D-Arabino-	100	25	0.24	0.92	1.00	0.88	0.88			^{1}H	22
α-D-Xylo-	100	90	0.22	0.51	0.89?		0.64[c]			^{13}C	21
β-D-Xylo-	100	15	1.00	0.71	0.87	0.95	0.95			^{1}H	20
	100	100	0.66	0	0	0.32	0.40			^{1}H	
α-D-Lyxo-	100	90	0.81	0.59	1.00		0.29[c]			^{13}C	21
α-D-Ribo-	100	30	0.65	0.75	1.00		0.80[c]			^{13}C	21
β-D-Ribo-	100	60	>0.66	0.62	<1.00	0.46	0.23			^{1}H	20
	100	360	0.77	0.49	0.88	0	0			^{1}H (Ac)	this work

[a]In all cases, H-1 was found to be 1.00. [b]In deuterium oxide, exept for methyl β-D-ribofuranoside triacetate ($CDCl_3$). [c]Equivalent of molecules containing two hydrogen atoms in that position. [d]Less than the usual amount of catalyst was used in this instance (0.5 mL of nickel for 100 mg of glycoside in 5 mL of deuterium oxide). [e]This figure is the sum of H-1′ and H-6$_R$ (since the signals overlap); H-1′ exchanges slowly, but more rapidly than H-1. After 60 min, H-1 has decreased to 0.95.

atoms on C-5 are the ones that react the most rapidly. The two methylene hydrogen atoms exchange at similar rates.

Thus, in methyl α-D-xylofuranoside (**5**), H-2 exchanges most rapidly; in methyl β-D-xylofuranoside (**6**), H-3 exchanges most readily; and, in methyl α-D-lyxofuranoside and β-D-ribofuranoside, one of the hydrogen atoms on C-5 exchanges more rapidly than any other one. Balza *et al.*[4] noted that, in methyl α-D-mannofuranoside, H-2 exchanges more slowly than H-3, H-5, or the two H-6 atoms.

In methyl α-D-arabinofuranoside, H-3 exchanges most rapidly, in the β anomer, H-2. Similarly, in the homomorphous α-D-fructofuranoside, H-4 exchanges most rapidly; in the β anomer, H-3. This example shows that, although a neighboring, *cis* methoxyl group greatly hinders the exchange, a neighboring *cis* hydroxymethyl group does so only slightly. In the fructosides, considerable exchange occurs on C-6, but very little on C-1; the latter seems to be hindered by the neighboring methoxyl group. (Overlapping of signals prevents integration of the ^{1}H-n.m.r. spectrum of methyl α-D-fructofuranoside, but it is clear that there is little deuterium, after exchange, on C-1, C-3, or C-5.) In most instances, the difference in reaction rates is insufficient to give rise to specific labelling, but methyl β-D-fructofuranoside is selectively deuterated on C-3, and the labelling of methyl β-D-arabinofuranoside comes close to being selective.



In methyl β-D-xylofuranoside (**6**) and β-D-glucofuranoside, H-3 exchanges the fastest, but H-4 also exchanges rapidly. Exchange of a hydrogen atom on a carbon atom not bearing a free hydroxyl group was not encountered in Koch and Stuart's work[2–4], but was first observed by Wu *et al.*[7]. They clearly established the configuration required for such exchange: for H-4 to react, OH-2 must be *cis* and the anomeric methoxyl group *trans*. Methyl α-D-threoside, β-D-xyloside, and β-D-

glucoside have the required configuration. We consider that this exchange occurs *via* enolization. The 3-keto group formed on the catalyst surface by dehydrogenation will enolize towards C-4 if the resulting enol has a configuration readily adsorbed on the surface. The double bond is, of course, well adsorbed; if OH-2 faces the catalyst, it provides another point of adsorption; but the methoxyl group must be on the other side, or it would hinder adsorption of the almost planar molecule. This proposed mechanism is supported by the fact that, in all cases, H-4 exchanges more slowly than H-3. Moreover, such exchange has not been observed among the pyranosides; ketonic groups in five-membered rings are known to enolize more readily than those in six-membered rings.

Barker and co-workers[7] rejected the reaction course *via* the enol, arguing that 3-epimeric sugars would yield the same 3-ulose and hence the same enol, and would therefore give the same products in the same proportion, whereas they do not. Certainly, the same ketone would be formed from the β-xylofuranoside and the β-ribofuranoside; but, at the moment when it is formed, it would be adsorbed by the catalyst on different sides. When the glycosid-3-ulose **7** is formed from the xyloside **6**, it is adsorbed on its lower (α) side, and it could readily rearrange to the enol while on the catalyst surface, because the enol is readily adsorbed. When the glycosid-3-ulose is formed from the D-ribose (**8**), it is adsorbed on its upper (β) side (a less comfortable fit, and hence the reaction is slower), and enolization would not occur on the catalyst surface as easily, because the enol would be poorly adsorbed, with its hydroxyl group away from the surface and the methoxyl group protruding into it. Thus, in methyl β-D-ribofuranoside, H-4 exchanges very slowly, and in methyl β-D-allofuranoside, although it has the required configuration and H-3 exchanges rapidly, H-4 does not react. It is possible that the slow exchange of H-4 occurring in methyl β-D-erythrofuranoside is the result of epimerization at C-3, exchange *via* the enol, and another epimerization on C-3. Wu *et al.*[7] showed that these epimerizations occur readily.

The methyl hexofuranosides are unsuitable for specific deuteration, because the hydrogen atoms on C-5 and C-6 exchange readily, each having a hydroxyl neighbor. In methyl α-D-altrofuranoside, where H-2 and H-3 exchange slowly, the hydrogen atoms in the sidechain react the most rapidly. Interestingly, in methyl β-D-allofuranoside, H-3 is the most rapidly exchanging hydrogen atom, and H-2 exchanges slowly. Wu *et al.*[7] found, and we have confirmed, that, in the homomorphous β-D-riboside, H-2 and H-3 exchange at similar rates. Possibly, OH-5 of the D-alloside assists in the adsorption of H-3 and OH-3.

Sucrose reacts as expected from the behavior of its components: H-3 of the D-glucosyl and H-4 of the D-fructosyl moiety exchange slowly (see Table III); H-2 and H-4 of the D-glucosyl and H-3 of the D-fructosyl group exchange rapidly. Hydrolysis of sucrose thus exchanged would give D-glucose labelled on C-2 and C-4.

To summarize, the methyl glycosides are not particularly suitable derivatives for selective deuteration. Only three useful examples were found: methyl β-D-

TABLE III

HYDROGEN (EQUIV.) FOUND IN VARIOUS POSITIONS IN SUCROSE AFTER EXCHANGE[a,b]

t (min)	*H-2*	*H-3*	*H-4*	*H-3'*	*H-4'*	CH_2[c]
10	0.77	1.00	0.75	0.63	0.95	0.96
30	0.62	0.97	0.57	0.47	0.93	0.94
60	0.36	0.95	0.33	0.19	0.90	0.80
240	0.11	0.89	0.10	0.05	0.84	0.59

[a]Determined from the ^{1}H-n.m.r. spectra of the acetate in deuteriobenzene[23]; H-1, H-5, and H-5' were taken as 1.00. [b]After refluxing for the given period, the sucrose was recrystallized, and acetylated, and the acetate recrystallized. [c]The spectrum does not allow separate integration of each hydrogen atom of the methylene groups, but indicates, qualitatively, that most of the deuterium is on C-6' and very little on C-1'. This would be expected by analogy with the behavior of the relevant D-glucoside and D-fructoside.

fructopyranoside can be thus labelled on C-5, methyl β-D-fructofuranoside on C-3, and methyl β-D-galactopyranoside on C-3 and C-4. During the short periods used in our reactions, there was little isomerization: the signals of epimers were rarely seen in the n.m.r. spectra of the products after exchange, and, even then, in very small proportions only. Nevertheless, for the purpose of producing labelled compounds, it is imperative that the exchanged product be recrystallized, or purified by chromatography. We have done that only with methyl α- and β-D-xylopyranoside, β-D-arabinopyranoside, β-D-ribopyranoside, and sucrose; for purposes of a general survey, the n.m.r. spectra of the crude products of the exchange reaction gave sufficient information.

It must be reemphasized[1] that the extent of deuterium exchange by this method is not reproducible. Because the catalyst is stored under a solvent (deuterium oxide), it cannot be weighed accurately, and its amount may vary from one experiment to another; its activity is affected by age; and, as the reaction is heterogeneous, its rate will depend on the method and rate of stirring, which is not rigorously controlled. The relative extent of deuterium exchange in different positions is, of course, reproducible. It is recommended that, for a certain extent of exchange, an experiment be made over a shorter time than shown herein, and an aliquot be tested by filtering off the catalyst and recording the ^{1}H- or ^{13}C-n.m.r. spectrum; according to the result, the deuteration may then be continued[4]; this was done with methyl β-D-fructofuranoside, and the result (see Table II) shows that useful deuteration on C-3 can be achieved.

A preliminary survey of polysaccharides indicates that deuteration is possible by this method. Perlin and co-workers[4] found no exchange of the hydrogen atoms of soluble starch by the Koch–Stuart technique, but, when the reaction is prolonged to 48 hours, a substantial diminution of the C-2 signal[9] at δ 73 was observed, with no other changes occurring in the ^{13}C-n.m.r. spectrum. In dextran, as shown by the ^{13}C-n.m.r. spectrum[10], H-2, H-3, and H-4 all exchange slowly.

EXPERIMENTAL

The methyl glycosides were synthesized during several previous studies (see for example, ref. 20); their identity and purity were checked by their n.m.r. spectra. Deuterium exchange over the catalyst was conducted as described by Koch and Stuart[3]. Commercial Raney nickel (W. R. Grace & Co., No. 2800 Raney Active Nickel Catalyst) was used; kept in the refrigerator under water, this catalyst retained its activity for at least three years. After completion of the exchange, the reaction mixture was filtered, the filtrate evaporated, the residue dissolved in deuterium oxide, and the n.m.r. spectrum recorded. If the spectrum of the acetate was required, the residue was acetylated with acetic anhydride and pyridine, and the product isolated in the usual way.

N.m.r. spectra were recorded with a Cameca 250 spectrometer in Grenoble, and with a Jeol JNM-FX-100 or a Bruker CXP-300 spectrometer in Sydney, using the solvents indicated in the Tables.

^{1}H-N.m.r. spectra. — The spectra of the methyl aldopyranosides[15] and the methyl aldofuranosides[20] have been recorded, but those of the methyl fructofuranosides are described here for the first time: *methyl β-D-fructofuranoside* (D_2O): δ 4.17 (d, $J_{3,4}$ 8.0 Hz, H-3), 4.05 (dd, $J_{4,5}$ 7.3 Hz, H-4), 3.87 (dt, $J_{5,6R}$ 7.0, $J_{5,6S}$ 3.9 Hz, H-5), 3.81 (dd, $J_{6R,6S}$ −12.0 Hz, H-6_S), 3.72 (d, $J_{1,1'}$ −12.2 Hz, H-1), 3.65 (dd, H-6_R), 3.65 (d, H-1′), and 3.32 (s, OMe); *R* and *S* were assigned by analogy with methyl β-D-arabinofuranoside[7] (compare also with the spectrum of sucrose[11]); *methyl α-D-fructofuranoside* (D_2O): δ 4.11 (d, $J_{3,4}$ 2.5 Hz, H-3), 3.97 (m, H-4,5), 3.83 (dd, $J_{6R,6S}$ −12.2, $J_{5,6S}$ 3.2 Hz, H-6_S), 3.79 (d, $J_{1,1'}$ −12.4 Hz, H-1), 3.70 ($J_{5,6R}$ 5.8 Hz, H-6_R), 3.68 (d, H-1′), and 3.33 (s, OMe). The couplings of H-6_R and H-6_S could be observed only after the signal of H-4 had been removed by replacing H-4 with deuterium; *R* and *S* were assigned by analogy with methyl α-D-arabinofuranoside[7].

Overlapping of signals in the ^{1}H-n.m.r. spectra of methyl glycosides often prevents reliable integration. In such cases, we used the spectra of the acetates. The ^{1}H-n.m.r. spectra of acetylated methyl glycosides are widely scattered in the literature, and are difficult to locate. Those we have not found are described here: *methyl α-L-fucopyranoside triacetate* ($CDCl_3$): δ 5.36 (dd, $J_{2,3}$ 10.4, $J_{3,4}$ 3.3 Hz, H-3), 5.30 (dd, $J_{4,5}$ 1.0 Hz, H-4), 5.15 (dd, $J_{1,2}$ 3.4 Hz, H-2), 4.95 (d, H-1), 4.14 (broad q, $J_{5,6}$ 6.3 Hz, H-5), 3.40 (s, OMe), 2.17, 2.09, 1.97 (s, Ac), and 1.16 (d, H-6); *methyl α-D-xylopyranoside triacetate* (C_6D_6): δ 5.87 (dd, $J_{2,3}$ 10.19, $J_{3,4}$ 9.47 Hz, H-3), 5.15 (ddd, $J_{4,5R}$ 6.06, $J_{4,5S}$ 10.78 Hz, H-4), 5.03 (dd, $J_{1,2}$ 3.57 Hz, H-2), 4.86 (d, H-1), 3.645 (dd, $J_{5R,5S}$ −10.79 Hz, H-5_R), 3.44 (t, H-5_S), 2.94 (s, OMe), 1.72, 1.63, and 1.605 (s, Ac); *methyl β-D-arabinopyranoside triacetate* (C_6H_6): δ 5.69 (dd, $J_{2,3}$ 10.86, $J_{3,4}$ 3.42 Hz, H-3), 5.57 (dd, $J_{1,2}$ 3.43 Hz, H-2), 5.42 (ddd, $J_{4,5}$ 1.44, $J_{4,5'}$ 1.98 Hz, H-4), 5.05 (d, H-1), 3.39 and 3.345 (AB part of ABX system, $J_{5,5'}$ −13.00 Hz, H-5,5′), 2.96 (s, OMe), 1.75, 1.655, and 1.65 (s, Ac); and *methyl β-D-ribofuranoside triacetate* ($CDCl_3$): δ 5.33 (dd, $J_{2,3}$ 4.86, $J_{3,4}$ 6.72 Hz, H-3), 5.23 (dd,

$J_{1,2}$ 0.95 Hz, H-2), 4.90 (d, H-1), 4.37 (dd, $J_{4,5S}$ 3.70, $J_{5R,5S}$ −11.42 Hz, H-5_S), 4.30 (ddd, $J_{4,5R}$ 5.49 Hz, H-4), 4.10 (dd, H-5_R), 3.38 (s, OMe), 2.11, 2.10, and 2.06 (s, Ac). In the spectrum of methyl β-D-ribofuranoside, the signals of H-2 and H-4 overlap[7]; in that of its triacetate, the H-5_S and H-4 signals are too close for integration; however, addition of a small amount of Eu(fod)$_3$ (Pierce Chemicals Co.) causes an upfield shift that completely separates these signals.

The spectrum of methyl β-D-glucopyranoside tetraacetate has been described by Izumi[12]; however, we found that his assignments of the signals of H-3 and H-4 need to be interchanged. The triplet at δ 5.18 disappears on deuteration, and the doublet of doublets at 4.96 (H-2) and the triplet at 5.08 both become doublets; Hence, the signal at δ 5.18 must be that of H-3. This assignment was confirmed by the ^{13}C-n.m.r. spectrum.

The hydrogen atoms on C-6 of most of the hexosides were assigned as *R* or *S* by consideration of their coupling constants[24–26]; this could not be done for the α- and β-D-galactopyranosides owing to overlap of the H-6 signals. The H-5 signals in the spectra of the methyl pentofuranosides had already been assigned by Wu *et al.*[7].

^{13}C-N.m.r. spectra. — All of the spectra we used, except those of the altrofuranosides, were found in the review by Bock and Pedersen[27]; *methyl α-D-altrofuranoside* (D_2O): δ 109.0 (C-1), 81.4 (C-2), 77.2 (C-3), 84.9 (C-4), 72.2 (C-5). 63.1 (C-6), and 55.5 (Me), assigned by analogy with α-D-altrofuranose and methyl α-D-arabinofuranoside[27]; *methyl β-D-altrofuranoside* (D_2O): δ 102.9 (C-1), 77.4 (C-2), 76.5 (C-3), 81.9 (C-4), 73.9 (C-5), 63.3 (C-6), and 55.9 (Me), assigned by analogy with β-D-altrofuranose and methyl β-D-arabinofuranoside[27].

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NOTE ADDED IN PROOF

In a recent paper [*Tetrahedron Lett.*, 27 (1986) 415–418], E. A. Cioffi and J. H. Prestegard suggested that ultrasonic irradiation provides particularly favourable conditions for the Raney-nickel-catalyzed deuteration.

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