Carbohydrate Research, 74 (1979) 7–30

BENZYLIDENE ACETAL STRUCTURAL ELUCIDATION BY N.M.R. SPECTROSCOPY: APPLICATION OF CARBON-13 N.M.R.-SPECTRAL PARAMETERS

T. BRUCE GRINDLEY AND VIJEYALAKSHMI GULASEKHARAM
Department of Chemistry, Dalhousie University, Halifax, Nova Scotia B3H 4J3 (Canada)
(Received July 14th, 1978; accepted for publication in revised form, December 20th, 1978)

ABSTRACT

The ^{13}C-n.m.r. spectra of 19 2-phenyl-1,3-dioxolane, -1,3-dioxane and -1,3-dioxopane derivatives were examined and it was found that both the ^{13}C-n.m.r. chemical shift for the acetal carbon atom and the one-bond coupling constant between the acetal carbon atom and the acetal proton had values that could be used to distinguish between acetals having different ring sizes. In addition, the presence of axial substituents at positions 4 or 6 in substituted 2-phenyl-1,3-dioxane rings and 4 or 7 in substituted 2-phenyl-1,3-dioxepane rings could be readily detected. The structures of a number of carbohydrate examples were determined by using these two parameters and also the chemical shift of the acetal proton from ^{1}H-n.m.r. spectra. The use of all three parameters made assignment of benzylidene acetal ring-size unambiguous.

INTRODUCTION

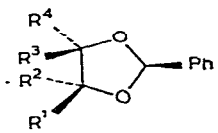
Cyclic acetals of carbohydrates are key intermediates in many synthetic routes. The most important method employed for the determination of structures of new benzylidene acetals for the last few years has been the evaluation of the ^{1}H-n.m.r. chemical shift of H-2, the proton on the acetal carbon atom, as a criterion of ring size[1]. However, there are many situations where this indicator may yield ambiguous results, particularly in fused-ring systems. Chemical methods, which often involve a number of steps such as methylation, hydrolysis of the acetal, periodate oxidation and/or comparison of the fragments with authentic samples are normally used in addition[2]. A recent publication[3] has demonstrated that certain ^{13}C-n.m.r. spectral parameters may be used to assign configurations at C-2 in 2-phenyl-1,3-dioxolane rings *cis*-fused to pyranoid sugars. In this publication, we show that ^{13}C-n.m.r. spectra provide two additional criteria of ring size and demonstrate that, in most instances, it is possible to assign unequivocally the structures of carbohydrate cyclic acetals using a combination of ^{1}H- and ^{13}C-n.m.r. spectral techniques.

To avoid lengthy descriptions we use here the terms acetal carbon atom and acetal proton to indicate the acetal carbon atom in the benzylidene ring and the proton

on that carbon atom, respectively, even when there are other acetal carbon atoms in the structure under consideration.

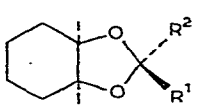
RESULTS AND DISCUSSION

Model compounds. — Structural and spectral assignment. The model compounds were synthesized conventionally from the appropriate diols and benzaldehyde and their ^{1}H- and ^{13}C-n.m.r. spectral parameters are presented in Table I. Structures and spectral parameters were assigned as follows. Assignments for the simple 2-phenyl derivatives **1**, **9**, and **14** were straightforward. *Cis*- and *trans*-4-methyl-2-phenyl-1,3-dioxolane (**2** and **3**, respectively) were obtained in unequal amounts from 1,3-propanediol; their known[1-4] proton spectra obtained for unambiguously synthesized samples[1,4,5] could be used for assignment of their ^{13}C signals. The signals for C-4 and C-5 were assigned by their appearance in off-resonance decoupled spectra.



1 $R^1 = R^2 = R^3 = R^4 = H$
2 $R^1 = Me, R^2 = R^3 = R^4 = H$
3 $R^2 = Me, R^1 = R^3 = R^4 = H$
4 $R^1 = R^3 = Me, R^2 = R^4 = H$
5 $R^1 = R^3 = H, R^2 = R^4 = Me$
6 $R^1 = R^4 = Me, R^2 = R^3 = H$

Commercial 2,3-butanediol reacted with benzaldehyde to give almost totally one acetal which, from its ^{13}C-n.m.r. spectrum, had no internal symmetry. Therefore, it was *cis,trans*-4,5-dimethyl-*r*-2-phenyl-1,3-dioxolane (**6**). Assignment of C-4 and C-5 in the spectra of **6** could not be made with certainty. Reduction of 2,3-butanedione with sodium borohydride gave a mixture of *dl* and *meso*-2,3-butanediol, as shown by the formation of three compounds on treatment of the diols with benzaldehyde and an acid; the two C_s-symmetric products from the *meso* diol were present in larger amounts. Under the equilibrium conditions[3] which our preparative conditions[4] approach, the *cis,cis* acetal (**4**) is known[4] to be formed in nearly twice the yield of the *trans,trans* isomer (**5**), and a similar observation here in conjunction with the previously assigned ^{1}H-n.m.r. spectra[4] could be used to assign the ^{13}C signals. A



7 $R^1 = Ph, R^2 = H$
8 $R^1 = H, R^2 = Ph$

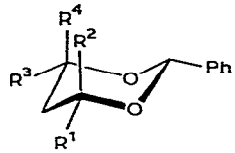
TABLE I

N.M.R.-SPECTRAL DATA[a] FOR THE MODEL COMPOUNDS

Compound	*^{1}H-n.m.r. chemical shift of H-2*	*^{13}C-n.m.r. chemical shifts (p.p.m.)*								*$^1J_{C,H}$ for C-2 (Hz)*
		C-2	*C-4*	*C-5*	*C-6*	*C-7*	*Me$_A$*	*Other Me*	*Quaternary phenyl C*	
1	5.77[b]	103.7	65.3	65.3	—	—	—	—	138.7	167.5
2	5.73[b]	104.0	73.3	71.9	—	—	18.3	—	139.0	166.6
3	5.89[b]	103.0	72.1	71.3	—	—	18.5	—	138.4	167.2
4	5.70	102.7	74.9	74.9	—	—	15.4	15.4	138.4	167.1
5	6.07	101.5	74.4	74.4	—	—	14.4	14.4	140.5	168.2
6	5.91	102.6	80.3	78.5	—	—	17.1	16.9	139.3	166.8
7[c]	5.83	103.2	74.8	74.8	—	—	—	—	139.1	167.7
8[d]	6.13	101.9	74.2	74.2	—	—	—	—	140.8	166.9
9	5.45[b]	101.4	67.0	25.9	67.0	—	—	—	138.7	160.7
10	5.44	101.0	73.0	33.0	66.7	—	21.7	—	139.2	160.4
11[e]	5.90	94.9	68.4	30.9	61.2	—	18.6	—	141.3	—
12	5.46[b]	100.6	72.6	40.4	72.6	—	21.6	—	139.4	159.7
13	5.79[b]	93.7	68.4	36.8	58.1	—	21.9	—	139.8	159.7
14	5.67[b]	100.8	65.3	29.4	29.4	65.3	—	—	140.3	164.8
15	5.72	100.2	74.6	36.4	29.4	63.4	22.6	—	140.4	163.5
16	5.70	99.3	68.3	36.4	28.6	67.2	22.6	—	140.4	165.3
17	5.50	102.4	75.8	33.6	33.6	75.8	22.7	22.7	140.7	157.0
18	5.84	93.7	70.4	33.1	33.1	70.4	19.5	19.5	139.0	163.2
19	5.75	98.4	68.0	36.4	36.0	73.7	22.6	22.6	140.6	164.0

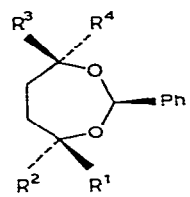
[a]On 25% solutions in chloroform-*d*, at 80 MHz for ^{1}H-n.m.r. spectra and 20 MHz for ^{13}C-n.m.r. spectra. [b]Chemical shifts in 1,4-dioxane[1] were 5.34, 5.37, 5.48, 5.05, 5.09, 5.42 and 5.26 δ for **1**, **2**, **3**, **9**, **12**, **13**, and **14** respectively. [c]The ^{13}C-n.m.r. shifts for the other carbon atoms in the cyclohexane ring were δ 28.3 and 20.7. [d]The ^{13}C-n.m.r. shifts for the other carbon atoms in the cyclohexane ring were δ 27.2 and 21.1. [e]Was not obtained in high enough concentration to be determined.

mixture of *syn*- and *anti*-2-phenyl-1,3-dioxabicyclo[4.3.0]nonane (**7** and **8**, respectively) was obtained by treating *cis*-1,2-cyclohexanediol with benzaldehyde and acid. As *cis,cis*-2,4,5-trisubstituted 1,3-dioxolanes are thermodynamically more stable[3] than their *trans,trans* isomers, it is not surprising that the *syn* isomer **7**, which gives an upfield ^{1}H-n.m.r. signal for its acetal proton at δ 5.83, is obtained in a larger amount than **8**. The proton results and the differences in signal intensity arising from the different concentrations could be used to assign the ^{13}C-n.m.r. signals of **7** and **8**. The product of the reaction of 1,3-butanediol with benzaldehyde consisted chiefly of *cis*-4-methyl-2-phenyl-1,3-dioxane (**10**), but a sufficient amount of the *trans* isomer (**11**) was present for its ^{1}H- and ^{13}C-n.m.r. spectral parameters to be obtained, with the exception of $^1J_{C,H}$ for C-2. The ^{13}C-n.m.r. spectra of *cis,cis*-4,6-dimethyl-*r*-2-phenyl-1,3-dioxane (**12**) and its *cis, trans* isomer (**13**) were assigned by comparison with the spectra of their known 2-methyl analogues[6].



9 $R^1 = R^2 = R^3 = R^4 = H$
10 $R^1 = Me, R^2 = R^3 = R^4 = H$
11 $R^2 = Me, R^1 = R^3 = R^4 = H$
12 $R^1 = R^3 = Me, R^2 = R^4 = H$
13 $R^1 = R^4 = Me, R^2 = R^3 = H$

cis-4-Methyl-2-phenyl-1,3-dioxepane (**15**) and its *trans* isomer (**16**) were produced in very similar amounts in one preparation and gave ^{13}C-n.m.r. spectra that were very similar to those of their 2-*tert*-butyl analogues[7]. In a second preparation, which presumably did not reach equilibrium, one of these (**16**) was obtained in approximately twice the amount of the other, allowing assignment of the spectral signals to the individual isomers. The analogous *tert*-butyl structures were assigned[7] from chemical-shift arguments based on the assumption that the chair conformation of 1,3-dioxepane is the most stable. Since that time, the most stable conformation



14 $R^1 = R^2 = R^3 = R^4 = H$
15 $R^1 = Me, R^2 = R^3 = R^4 = H$
16 $R^2 = Me, R^1 = R^3 = R^4 = H$
17 $R^1 = R^3 = Me, R^2 = R^4 = H$
18 $R^1 = R^3 = H, R^2 = R^4 = Me$
19 $R^1 = R^4 = Me, R^2 = R^3 = H$

of 1,3-dioxepane has been shown[8] to be a twist-chair (*TC*) and, therefore, the previous structural assignments must be reexamined. For **15** and **16**, the ^{1}H-n.m.r. chemical shifts for H-2 are very similar, as are the ^{13}C-n.m.r. chemical shifts for C-2, but the chemical shifts for C-4 and C-7 are distinctly different. C-4 and C-7 were assigned by off-resonance decoupling. In the ^{13}C-n.m.r. spectrum of **15**, the signals for C-4 and C-7 are widely separated at δ 74.6 and 63.4 respectively, whereas in that of **16**, they appear together at δ 68.3 and 67.2, respectively. These differences are used in conjunction with the results for the three 4,6-dimethyl-2-phenyl-1,3-dioxepanes (**17**, **18**, and **19**) for structural assignment. Compounds **17**, **18**, and **19** were produced from a mixture of 2,5-hexanediols obtained by reducing 2,5-hexanedione. The mixture of **17**, **18**, and **19** was partially separated by distillation into two fractions; one containing **17** and ~20% of **18**, the other containing almost pure **19**. The C_s symmetry of *cis,cis*-

4,7-dimethyl-*r*-2-phenyl-1,3-dioxepane (**17**) and its *trans,trans* isomer (**18**) readily differentiates their ^{13}C-n.m.r. spectra from those of the *cis,trans* isomer (**19**). The minor (C_s symmetric) compound (**18**) exhibited a distinctive upfield shift for C-2 of 93.7 p.p.m. This type of shift for C-2 in the 1,3-dioxane derivatives indicated that a methyl group at C-4 or C-6 was axial and, in agreement with this, examination of the chair–twist-chair pseudorotational itinerary of **18** showed that, in all fourteen *TC* conformations, one methyl group is axial. In contrast, both **17** and **19** (and **15** and **16**) had several *TC* conformations having all substituents equatorial. In addition, the ^{13}C-n.m.r. chemical shift (δ 19.5) of the methyl groups in **18** is about 3 p.p.m. upfield from that of methyl groups in **15**, **16**, **17**, and **19** and axial methyl groups at C-4 in 1,3-dioxane derivatives **11** and **13** also exhibited upfield shifts of 2–3 p.p.m. with respect to equatorial methyl groups. In compound **19**, the methyl group at C-4 is *cis* to the phenyl group, whereas that at C-7 is *trans* and very different shifts of δ 73.7 and 68.0 were observed for these two carbon atoms, with no indication that any substituents existed to any significant extent in axial disposition. In **17**, where both methyl groups are *cis* to the phenyl group and which again had an all-equatorial conformation, conformational averaging results in one shift (75.8 p.p.m.) for C-4 and C-7. Comparison of the n.m.r. parameters for **17** and **19** shows that a downfield shift for C-4 results when its substituent is *cis* to the phenyl group, whereas an upfield shift results when the substituent is *trans*. Extension of these arguments to **15** and **16** indicates that the compound giving the downfield C-4 signal at 74.6 p.p.m. is the *cis* isomer **15**, whereas the compound having the upfield signal at 68.3 p.p.m. is the *trans* isomer **16**. These chemical-shift effects, which were also observed for the *tert*-butyl analogues of **15** and **16**, are quite unusual. The cause of γ effects is presently uncertain[9,10] and so the cause of these chemical-shift differences must also be considered uncertain. However their observation should be generally useful for ^{13}C-n.m.r. spectral assignments in 1,3-dioxepanes.

Features useful for structural assignment. For the past several years, the ring size of benzylidene acetals has normally been assigned by consideration of the chemical shifts of the acetal protons in the ^{1}H-n.m.r. spectra of these compounds. For a number of model compounds as 10% solutions in 1,4-dioxane, Baggett *et al.*[1] observed that, for substituted 2-phenyl-1,3-dioxolanes, the acetal protons resonated at δ 5.34 to 5.80, whereas the corresponding signals for 2-phenyl-1,3-dioxanes appeared from δ 4.98 to 5.28 when axial substituents at 4 or 6 were not present. Comparison of the chemical shifts for the acetal protons of the model compounds measured here on 25% solutions in chloroform-*d* and by Baggett *et al.*[1] show that the present values display solvent shifts ~0.4 p.p.m. downfield from those of the earlier workers. Results here (compounds **9** and **11**) and by Baggett *et al.*[1,10] show that, when there is a axial substituent at C-4 in a 1,3-dioxane ring, the chemical shift observed is in the region expected for H-2 in 1,3-dioxolane systems. This pattern of ring substitution has been obtained in fused-ring systems[11] and could result from preparations arising under kinetic control. The 1,3-dioxepane model compounds (**14–19**) also have acetal-proton chemical shifts which, except for **17**, lie either very close to (for **14**) or inside the

1,3-dioxolane region (for **15**, **16**, **18**, and **19**). The ^{13}C-n.m.r. spectral parameters discussed next provide additional criteria that make assignment of ring size much more reliable.

Two ^{13}C-n.m.r. spectral parameters are generally useful for structural assignments of benzylidene acetals; the chemical shift of the acetal carbon and the one-bond coupling constant ($^{1}J_{C,H}$) between the acetal carbon atom and the proton bonded to that carbon atom. The signal for the acetal carbon atom for benzylidene acetals appears in a region (from 93–107 p.p.m. downfield from tetramethylsilane) that is free of all signals except that of the anomeric carbon atom in carbohydrates, and the shift of this atom can normally be readily predicted[12,13]. The chemical shift of the acetal carbon atom depends markedly on ring size. The signal for C-2 in the ^{13}C-n.m.r. spectra of 2-phenyl-1,3-dioxolane model-compounds (**1–8**), with one exception, appears from 101.9 to 104.0 p.p.m., and the carbohydrate examples considered later extend this region downfield to 105.8 p.p.m. The one exception, *trans,trans*-4,5-dimethyl-*r*-2-phenyl-1,3-dioxolane (**5**), has an upfield shift of δ 101.5 for C-2, probably because of conformational reasons. To avoid eclipsing between the adjacent methyl groups, the pseudorotational itinerary of **5** is probably dominated by conformations having one methyl group quasi-axial and the other quasi-equatorial. Methyl groups gauche to a carbon atom have much larger γ-upfield effects than do anti groups[14], and the quasi-axial methyl group is approaching a gauche relationship with C-2. When the *trans,trans* stereochemistry is present in fused-ring systems (as in *anti*-2-phenyl-1,3-dioxabicyclo[4.3.0]nonane, **8**), the shift for C-2 is slightly more downfield, and the carbohydrate examples of this type examined here are show shifts still further downfield. As there appear to be no known carbohydrate examples of either the *cis,cis* or *trans,trans* stereochemistry in a non-fused system, the observation of a shift for C-2 of greater than δ 102 is good evidence that the acetal under consideration contains a 1,3-dioxolane ring.

The model 2-phenyl-1,3-dioxane derivatives examined here exhibit ^{13}C-n.m.r. chemical shifts for C-2 in two different ranges, one from 100.6 to 101.4 p.p.m. (**9**, **10**, and **12**) and another from 93.7 to 94.9 p.p.m. (**13** and **11**, respectively). The latter two compounds have axial methyl groups at C-4 or C-6. Kellie and Riddell[6] had previously observed, for a large number of 2-methyl-1,3-dioxanes, that methyl-group substituent chemical-shift effects on C-2 from substituents at C-4, C-5, or C-6 were small ($<|1.6|$p.p.m.), except when an axial group was introduced at C-4 or C-6, whereupon an upfield shift of 9 p.p.m. was observed. This type of shift is clearly of use in structural studies. The other three compounds had shifts for C-2 that fell in a very narrow range, and other workers[3,15–17] have observed similar chemical-shift ranges in carbohydrate and other examples (total range δ 100.6–102.0) for 2-phenyl-1,3-dioxanes having equatorial substituents at C-4, C-5, or C-6 or axial substituents at C-5.

Consideration of the C-2 chemical shifts from the ^{13}C-n.m.r. spectra of 2-phenyl-1,3-dioxepane model-compounds (**14–19**) (see Table I) shows that, for this ring size, this parameter is not quite as clear an indicator of structure. For most of

these compounds (**14**, **15**, **16**, and **19**), the chemical shift of C-2 lies in a range δ 98.4–100.8, with increasingly upfield shifts on increasing substitution on C-4 and C-7. For 1,3-dioxepane, the *TC* conformation having C-2 on the C_2 axis, ($^{4,5}TC_{6,7}$ or $^{6,7}TC_{4,5}$)[17] has been observed[8] to be the most stable conformation, and calculations have suggested that the other three different types of *TC* conformations are all about 10 ($\pm$4) kJ. mol^{-1} less stable. Thus, it is likely that those compounds which can assume one of the stable *TC* conformations ($^{4,5}TC_{6,7}$ or $^{6,7}TC_{4,5}$) having all substituents equatorial will have its conformational mixture dominated by this conformation. Compounds **14**, **15**, **16**, and **19** are of this type and, in **18**, all *TC* conformations have at least one methyl group axial, and so its conformational mixture is probably dominated by the one stable *TC* conformation that has one axial methyl group. As discussed earlier, the observation of a chemical shift of δ 93.7 for C-2 and δ 19.5 for its methyl groups is in agreement with this. For **17**, both of the stable *TC* conformations, $^{4,5}TC_{6,7}$ and $^{6,7}TC_{4,5}$, have one axial methyl group, but there are other *TC* conformations that have all substituents equatorial. The downfield shifts observed for C-2, C-4 (and C-7) and the methyl carbon atom suggest that conformations having axial groups are not important for **17**. Therefore, the unusual downfield shift for C-2 in this compound is probably caused by the prevalence of different conformations in its conformational mixture. Thus, from these model compounds, substituted 2-phenyl-1,3-dioxepanes having no axial substituents at C-4 or C-7 would normally exhibit shifts for C-2 in the range δ 98.4–100.2.

A second ^{13}C-n.m.r. parameter, the one-bond coupling constant ($^1J_{C,H}$) between the acetal carbon atom and protons in benzylidene acetals, provides a third criterion for determination of ring size, and this is probably the most reliable of the three. In 2-phenyl-1,3-dioxolane model-compounds, $^1J_{C,H}$ for C-2 has values ranging from 166.6 to 168.2 Hz, and the carbohydrate examples extend this range to 170.5 Hz. In the ^{13}C-n.m.r. spectra of 2-phenyl-1,3-dioxanes recorded here, including compound **13**, which has an axial methyl group, the $^1J_{C,H}$ value for C-2 was observed to range from 159.7 to 161.8 Hz. A value of 158 Hz had previously been observed for *trans*-5-*tert*-butyl-2-phenyl-1,3-dioxane[17]. Clearly, this parameter is more diagnostic than either the ^{13}C or ^{1}H chemical-shift observations for choosing between 1,3-dioxane- and 1,3-dioxolane-containing structures. In all of the 2-phenyl-1,3-dioxane derivatives studied here, the phenyl group is equatorial, and 2-phenyl-1,3-dioxane derivatives prepared for synthetic purposes, either under acidic conditions or from a diol, α,α-dibromotoluene, and pyridine[19], are conveniently obtained only with the phenyl group equatorial. However, 2-phenyl-1,3-dioxane derivatives having an axial phenyl group (which may be prepared together with their equatorial isomers from the appropriate diol with sodium hydride and α,α-dichlorotoluene *N*,*N*-dimethylformamide[20]), would be expected to have a $^1J_{C,H}$ value of about 166 Hz, as two derivatives of 1,3-dioxane having predominantly one chair conformation present in solution (the 5-*tert*-butyl and *cis*-4,6-dimethyl derivatives), both have two different $^1J_{C,H}$ values for the acetal carbon ($\sim$158 and 166 Hz[17]), and as $^1J_{C,H}$ values for acetal carbon atoms are little affected by phenyl substitution[17]. For all of the 2-phenyl-

1,3-dioxepanes except **17**, the $^1J_{C,H}$ value for C-2 lies in a narrow range (163.5–165.3 Hz) intermediate between ranges observed for the 5- and 6-membered cyclic acetals, but distinctly different. However, for **17**, the compound that did not adopt the most stable *TC* conformation, the $^1J_{C,H}$ value for C-2 is 157.0 Hz, markedly different than that of the others. Compounds containing 2-phenyl-1,3-dioxepane rings having conformations like **17** are clearly marked as having unusual properties, as **17** has a ^{1}H shift for H-2 in the 1,3-dioxane range, a ^{13}C shift for C-2 in the 1,3-dioxolane range, and a $^1J_{C,H}$ value lower than that of any of the other compounds studied here. Despite the significantly longer recording times required to determine one-bond carbon–hydrogen coupling constants for C-2, the magnitudes of these parameters obviously provide additional structural evidence.

A possible fourth indicator of ring size in benzylidene acetals, the ^{13}C-n.m.r. chemical shift of the quaternary phenyl carbon atom, may also be considered, and these values are also recorded in Table I. Careful study of these data indicates that this value is related to some extent to ring size, but other factors must also be important. The small range observed, and the fact that there is considerable overlapping between the values obtained from compounds having different ring sizes, precludes its use as a diagnostic tool for the determination of ring size. It can however, be used for the determination of configuration in 2-phenyl-1,3-dioxolanes[3].

Application to carbohydrate derivatives. — Acetals from galactose diethyl dithioacetal. 5-*O*-Methyl-D-galactose was required in connection with a program[21] to determine the relative stabilities of septanose sugars. Consideration of the stereochemistry of the hydroxyl groups of D-galactose diethyl dithioacetal in conjunction with the Hann–Hudson rules[22] suggested that the major product of benzylidenation should be the 2,3:4,6-di-benzylidene acetal. The 2,3:4,5- and 2,5:3,4-dibenzylidene

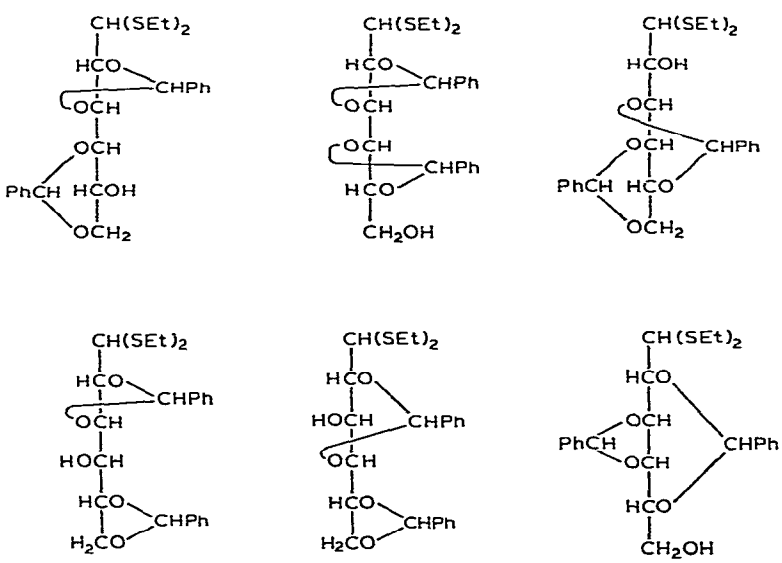
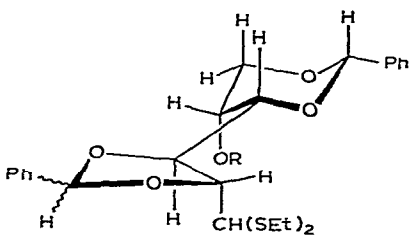


Chart I. Possible products of the benzylidenation of D-galactose diethyl dithioacetal.

acetals shown here (Chart I) are also probable products, as methylenation of galactose derivatives having positions 2, 3, 4, and 5 unsubstituted yielded the analogous *O*-methylene isomers[23]. Other less likely possibilities are the 3,5:4,6-, 2,4:5,6-, and 2,3:5,6-dibenzylidene acetals. The many different types of acetals possible makes this system suitable for testing the use of ^{13}C-n.m.r. parameters as structural guides.

Treatment of D-galactose diethyl dithioacetal (**20**) with benzaldehyde and zinc chloride for 6 h at room temperature gave a complex mixture, mainly dibenzylidene acetals, as suggested by t.l.c. The mixture was resolved chromatographically into 4 homogeneous components plus fractions containing overlapping components. ^{1}H-N.m.r. spectra showed that three of these homogeneous components were pure compounds (**23**, **24**, and **25**), and the fourth, the fastest moving on t.l.c. contained two compounds (**21** and **22**). This latter fraction could be further separated by chromatography give pure **21** and a mixture of **21** and **22**.

The ^{1}H- and ^{13}C-n.m.r. spectral parameters for these compounds necessary for assignment of benzylidene-ring size are shown in Table II; other data are given in Table III. Consideration of the acetal-proton chemical shifts alone suggests that compounds **21** and **24** probably contain 1,3-dioxane and 1,3-dioxolane ring systems, whereas **22**, **23**, and **25** contain two 1,3-dioxolane rings. However, a number of other possibilities exist. For instance, either 2,4- or 3,5-*O*-benzylidene groups would have 1,3-dioxane rings having axial substituents, which would give low-field shifts for the acetal proton. If 1,3-dioxepane fused-ring systems analogous to the *O*-methylene derivatives[21] are considered, from the ^{1}H-n.m.r. chemical shifts, **25** could constitute a 2,5:3,4- or a 3,6:4,5-substituted combination, whereas **24** could be a 2,5:4,6 combination. However, consideration of the ^{13}C-n.m.r. spectral results immediately remove any ambiguity from the assignment of ring sizes. Compounds **21** and **24** each have one acetal carbon atom having both a chemical shift and a one-bond carbon–hydrogen coupling constant in the 1,3-dioxolane range, plus one acetal carbon atom having a chemical shift and a $^{1}J_{C,H}$ value in the 1,3-dioxane region. The values for this latter acetal carbon atom are not compatible with a 1,3-dioxepane ring. As **21** and **24** contain both five- and six-membered rings, only two structures are possible, the 2,4:5,6- and 2,3:4,6-dibenzylidene acetals. The 2,4-benzylidene acetal would require one axial substituent at either C-4 or C-6 in its 1,3-dioxane ring. As shown by the model compounds, the chemical shift for the acetal carbon atom in the



21 and **24** R = H
26 and **27** R = Ac

TABLE II

N.M.R. PARAMETERS[a] OF DIAGNOSTIC VALUE FROM CARBOHYDRATE EXAMPLES

Compound	*^{1}H-N.m.r. chemical shifts[b] for benzylidene protons (p.p.m.)*			*^{13}C-N.m.r. chemical shifts (p.p.m.)*						*$^1J_{C,H}$ for benzylidene carbon atoms (Hz)*		
				Benzylidene carbon atoms			*Quaternary phenyl carbon atoms*					
	1	*2*	*3*	*1*	*2*	*3*	*1*	*2*	*3*	*1*	*2*	*3*
21	6.15	5.56		104.6	101.3		137.9	138.0		170.1	161.8	
22	6.11[c]	6.01[c]		104.6[c]	104.1[c]		137.0	137.5		170.5[d]	170.5[d]	
23	6.00[c]	6.10[c]		105.0[c]	104.5[c]		138.4	138.8		168.8[d]	168.8[d]	
24	5.89	5.58		104.5	101.4		137.1	137.7		168.2	161.8	
25	5.94[c]	5.98[c]		104.6[c]	104.2[c]		137.7	139.2		168.7[d]	168.7[d]	
28	5.93	5.71		103.8	105.8		136.5	136.2		168.5	166.7	
29	5.76	5.81		102.3	103.9		135.9	136.3		168.7	167.7	
30	5.75	6.41		104.2	104.0		138.9	136.3		168.0[d]	168.0[d]	
31	6.24	5.81		102.2	104.6		136.0	138.2		168.9	170.1	
32	6.22	6.39		103.9	104.6		139.0	138.2		167.2	170.1	
33	5.55[c]	5.85	5.49[c]	101.0[c]	99.4	100.9[c]	137.6	137.9	137.6	160.7[d]	170.5	160.7[d]
34	6.04, 5.95, 5.76, 5.71, 5.44			105.8[c], 105.3[c], 104.8, 104.0, 102.4, 100.9, 100.5			138.5, 136.5, 136.3, 135.9					

[a]In chloroform-*d*. [b]Recorded at 60 or 80 MHz. [c]Signals could not be definitely assigned to a particular ring. [d]Signals overlapped when coupled. [e]May be a signal for C-1.

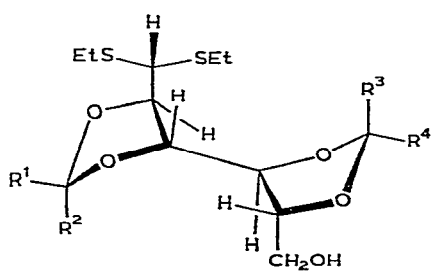
TABLE III

^{13}C-N.M.R. CHEMICAL SHIFTS FOR THE REMAINING CARBON ATOMS[a,b] (p.p.m.)

Compound	*C-1*	*C-2*	*C 3*	*C 4*	*C-5*	*C-6*	*SCH_2CH_3 groups*			
							CH_2		*CH_3*	
20[c]	55.0	71.9	70.3[d]	70.1[d]	69.7[d]	63.5	24.8	25.5	14.3	14.3
21	54.2	84.2	80.9	77.8	63.3	72.4	24.5	25.4	14.4	14.6
22	53.3	83.0	80.7[d]	80.1[d]	78.5	63.1	24.7	25.3	14.4	14.4
23	53.9	84.7	82.2	80.3	78.6	63.0	25.3	23.9	14.7	14.7
24	53.4	84.1	79.9	76.9	63.4	72.4	24.8	25.5	14.3	14.3
25	53.1	84.5	80.9[d]	79.6[d]	78.3	62.4	25.0	25.6	14.4	14.4
28	106.2	81.7, 82.6, 82.8, 85.6			65.1, 65.2,					
		85.7, 87.0, 87.3, 87.4			65.4					
29	96.0	71.5[d]	70.9	71.8[d]	60.1					
30	96.5	71.6[d]	71.4	69.8[d]	61.5					
31	96.1	72.8[d]	69.8	72.5[d]	61.5					
32	96.6	70.7[d]	70.2	72.5[d]	62.5					
33	69.4[d,e]	60.9	82.5[d]	82.2[d]	66.2	69.2[d,e]				
34	105.8[f],	81.4, 81.6, 82.7, 86.2,			71.7, 72,0,					
	105.3	87.1, 87.4, 88.1, 88.2,			75.5, 77.1,					
		88.5			78.7					

[a]At 20 MHz. [b]In chloroform-*d* except when indicated. [c]In dimethyl sulfoxide-d_6. [d]Assignments may be interchanged. [e]These two carbons appeared as triplets in the off-resonance decoupled spectrum. [f]One of these could be caused by an acetal carbon atom.

2,4-benzylidene acetal would be expected to be about δ 93–95. The chemical-shift values for acetal carbon atoms in **21** and **24** are δ 101.3 and 104.6 and δ 101.4 and 104.5 respectively, which indicate that these two compounds are the two 2,3:4,6-dibenzylidene acetals having different configurations in the 1,3-dioxolane ring. The other three compounds (**22**, **23**, and **25**) all have values for the two diagnostic ^{13}C-n.m.r. spectral parameters that can only arise from two 1,3-dioxolane acetal rings; 1,3-dioxepane-containing structures would not give these results. Clearly, the use



22 or 23 $R^1 = R^3 = Ph, R^2 = R^4 = H$
23 or 22 $R^2 = R^4 = Ph, R^1 = R^3 = H$
25 $R^1 = R^4 = Ph, R^2 = R^3 = H$

of all three n.m.r.-spectral parameters for the assignment of ring size remove any possible ambiguity.

The precise structures of **22**, **23**, and **25** were established by consideration of their ^{13}C-n.m.r., off-resonance-decoupled spectra. In the spectra of these compounds, the primary (C-6) carbon resonances were readily identified as triplets at 63.0, 62.4, and 63.1 p.p.m. respectively, all slightly upfield from the position (63.5 p.p.m.) where C-6 resonates in D-galactose diethyl dithioacetal (**20**). This similarity of chemical shifts could arise only if O-6 were unsubstituted in **22**, **23**, and **25**, and therefore these compounds must be three of the four possible 2,3:4,5-dibenzylidene diastereomers. In both **21** and **24**, C-6 resonates at δ 72.4, consistent with an additional β effect arising from substitution on O-6.

Confirmation of the 2,3:4,6-dibenzylidene structures of **21** and **24** was obtained from the 220-MHz ^{1}H-n.m.r. spectra in both chloroform-*d* and benzene-d_6 of the acetates of **21** and **24** (**26** and **27**, respectively). In all of the spectra of **26** and **27** (see Table IV), all signals were assigned without ambiguity and the similarity of the spectra of these two compounds (see Fig. 1) strongly support the contention that they are stereoisomers and not structural isomers. Because of this similarity, only one spectrum will be discussed. In the spectrum of **27** in chloroform-*d*, the two H-6 signals could be readily identified as widely separated quartets at δ 4.11 and 4.42 from the size of their geminal coupling-constant, 12.9 Hz. The wide chemical-shift separation of the two H-6 signals is typical of axial and equatorial protons at C-4 in 1,3-dioxane rings (see ref. 15, for instance). The two H-6 signals were narrowly coupled (*J* values

TABLE IV

^{1}H-N.M.R.-SPECTRAL PARAMETERS FOR THE TWO DIASTEREOMERIC 5-*O*-ACETYL-2,3:4,6-DI-*O*-BENZYLIDENE-D-GALACTOSE DIETHYL DITHIOACETALS[a] (**26** AND **27**)

Compound	*Solvent*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6 eq*	*H-6 ax*
Chemical shifts[a]								
26	Chloroform-*d*	4.08	4.59	4.65	3.97	4.91	4.40	4.05
27	Chloroform-*d*	3.96	4.63	4.59	4.18	4.92	4.42	4.11
26	Benzene-d_6	4.15	4.80	4.98	3.67	4.99	4.27	3.43
27	Benzene-d_6	4.14	4.78	4.89	3.73	4.89	4.38	3.59
Compound	*Solvent*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6\ eq}$	$J_{5,6\ ax}$	$J_{6,6}$
Coupling constants[b]								
26	Chloroform-*d*	4.4	4.5	8.8	1.8	1.3	1.5	12.9
27	Chloroform-*d*	2.8	5.3	8.4	1.6	1.2	1.0	12.9
26	Benzene-d_6	4.2	4.9	9.2	1.9	1.2	1.4	13.0
27	Benzene-d_6	3.0	5.5	8.9	1.7	1.3	1.4	12.9

[a]In p.p.m. downfield from Me_4Si at 220 MHz. [b]Obtained from a first-order analysis of 220-MHz spectra.

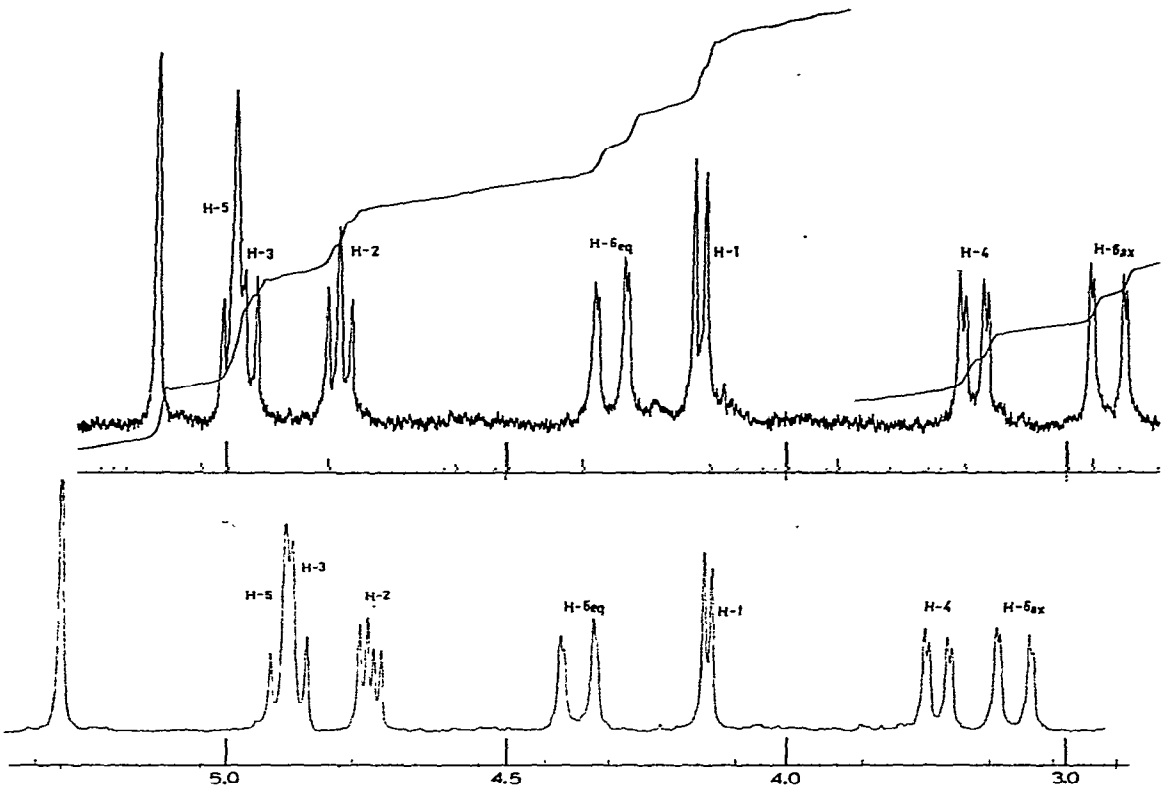
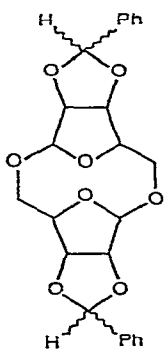


Fig. 1. Part of the ^{1}H-n.m.r. spectra of the two diastereomers of 5-*O*-acetyl-2,3:4,6-di-*O*-benzylidene-D-galactose diethyl dithioacetal in benzene-d_6 at 220 MHz: **26** at top; **27** at bottom. The signal on the left of both spectra is caused by the benzylidene H of 1,3-dioxane.

1.4 and 1.7 Hz) to the most downfield skeletal proton signal, that of H-5 at δ 4.92, which was also narrowly coupled to H-4 (J 1.6 Hz) at δ 4.18. The galactose stereochemistry requires the 4,6-*O*-benzylidene ring to have O-5 in axial orientation, and therefore H-5 has gauche relationships with H-4, H-6eq and H-6ax. A calculation[24] of the values of $J_{4,5}$, $J_{5,6eq}$, and $J_{5,6ax}$ expected on the basis of substituent electronegativities (if torsional angles of 60° are assumed) gave 1.0, 2.0, and 1.0 Hz, respectively, similar to the observed values. A second calculation[24], which used a Karplus relationship to relate the calculated to the experimental coupling-constants, yielded torsional angles of 51°, 66°, and 54° for the torsional angles H-4–C-4–C-5–H-5, H-5–C-5–C-6–H-6eq, and H-5–C-5–C-6–H-6ax respectively, which are approximately the magnitudes expected for these angles, as 1,3-dioxane rings are known to be flattened in this region[25]. Any structure lacking a 4,6-*O*-benzylidene ring is extremely unlikely to have such a combination of small coupling-constants. The downfield position of the H-5 signal indicates that it is geminal to the acetoxyl group, and therefore provides additional support for the 2,3:4,6-di-*O*-benzylidene structure. The other assignments follow routinely (see Table IV).

The foregoing structural determination showed that the seemingly complex reaction-mixture consisted chiefly of two types of di-*O*-benzylidene acetals. The percentage composition of each component, expressed as a fraction of the amount of the di-*O*-benzylidene mixture isolated, is as follows: **21**, 27%; **22**, 9%; **23**, 10%; **24**, 39%; and **25**, 15%. Compounds **21** and **24** the 2,3:4,6-di-benzylidene acetals, make up the major proportion of the product (66%), in agreement with the Hann–Hudson rules. As the relative amounts of the dibenzylidene products as observed by t.l.c. over a period from two h to three days appear to be approximately constant, it is probable that the mixture isolated was close to an equilibrium mixture. It is therefore somewhat surprising that only three of the four possible 2,3:4,5-di-*O*-benzylidene isomers were produced in sufficient quantities to be isolated. Models suggest that the diastereomer having the two phenyl groups *cis* to the larger remaining portions of the molecule, that is, the *S,S* diastereomer, would have a considerable decrease in its rotational freedom and would therefore be disfavoured in an equilibrium on steric and entropic grounds. The diastereomer having the *R,R* configuration would have least hindrance to internal rotation and also appears to be the most extended in models. The diastereomer (**25**) having the lowest R_F value was isolated in the largest amount of the 2,3:4,5-di-benzylidene acetals and is therefore tentatively assigned the *R,R* configuration. Zinner and Thielebeule[22] isolated two of the three possible 2,3:4,5 chemically different stereoisomers (2 *meso* and one *dl* pair) in 93% overall yield from the benzylidenation of 1,6-di-*O*-benzoylgalactitol and it was later shown[1] that the missing isomer was one of the *meso* ones. The preponderant stereoisomer[1,22] was also a *meso* compound, and as the *meso* compounds have the phenyl groups either both *cis* or both *trans* to the larger groups on the 1,3-dioxolane rings, this result is in agreement with our tentative conclusion.

trans,trans-4,5-Dialkyl-r-2-phenyl-1,3-dioxolanes. The ^{13}C-n.m.r. chemical shift of C-2 from *trans,trans*-4,5-dimethyl-2-phenyl-1,3-dioxolane (**5**) fell in the region where 2-phenyl-1,3-dioxanes absorb, and this factor could cause difficulty in structural assignment. Consideration of both the H-2 chemical shift in the ^{1}H-n.m.r. spectra



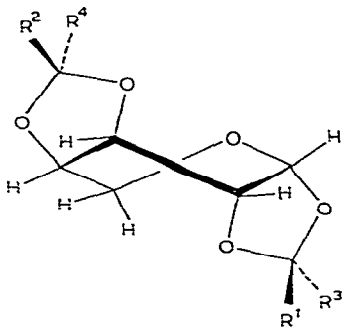
28

and $^{1}J_{C,H}$ should clarify this problem, but we present here n.m.r.-spectral parameters of several carbohydrate examples of different types to verify that this is so.

Di-(2,3-*O*-benzylidene-β-D-ribofuranose) 1,5′:1′,5-dianhydride (**28**), because of the possibility of stereoisomerism in its benzylidene rings, can exist in three diastereomeric forms, the *syn,syn*, the *anti,anti*, and the *syn,anti*. The sample examined[27] probably contained all three stereoisomers, as shown by the three signals observed for the C-5 and C-5′ carbon atoms. These carbons are homotopic in the *syn,syn* and *anti,anti* isomers by virtue of their C_2 symmetry, but diastereotopic in the *syn,anti* isomer, and so, in theory, four signals should be observed for these carbon atoms. However, it seems more likely that there is signal overlap than that one isomer was not obtained. Three signals were observed (at δ 106.2, 105.8, and 103.8) in the region of the ^{13}C-n.m.r. spectrum of **28** where acetal carbon atoms absorb, and the lowfield signal was considerably more intense than the other two, of which the signal at δ 103.8 was the more intense. The signal at δ 106.2 may be assigned to the anomeric carbon atoms in all isomers on the basis of its chemical shift[13], its large intensity, and the observation that, as expected[28], it has a much larger one-bond coupling constant (178.0 Hz) than the acetal carbon atoms. The observation by ^{1}H-n.m.r. spectroscopy that the *anti* configuration is present to a greater extent allows assignment of the ^{13}C-signal at δ 103.8 to this configuration and the signal at δ 105.8 to the *syn* configuration; as in our model compounds, the *anti* isomer has an upfield shift. Not surprisingly, the effect of a change in configuration in one benzylidene ring is not transmitted through the three intervening rings to the second benzylidene ring. As the shifts for the acetal carbon atom in both configurations are more downfield than those in the corresponding model compounds, 2-phenyl-1,3-dioxolane rings fused 2,3- to a furanose ring are readily identified from their ^{13}C-n.m.r. spectra.

As benzylidenation of galactose yields as the major product a 1,2:3,4-dibenzylidene acetal[29], benzylidenation of arabinose should give the analogous product, which would provide an example wherein a benzylidene acetal is fused to a pyranose ring. One di-*O*-benzylidene-L-arabinose isomer was previously known[30], although its structure had not been determined. Benzylidenation of arabinose under forcing conditions gave the known isomer (**29**), which crystallized from the product mixture, and a second (**30**) that crystallized from the mother liquors. Chromatography of the remaining syrup allowed isolation of a fraction containing two more isomers (**31** and **32**) in equal amounts, from which a third pure crystalline isomer (**31**) was obtained by fractional recrystallization. The spectral parameters of the four isomers (**29**, **30**, **31**, and **32**) are presented in Tables II and III. In the ^{13}C-n.m.r. spectral region where acetal carbons absorb, all four compounds have a signal near 96 p.p.m., which is close to the shift of the anomeric carbon atom in methyl β-L-arabinopyranoside[13]. The observation of large values for $^{1}J_{C,H}$ for this carbon atom (180.6, 179.9, 182.1, and 182.1 Hz for **29**, **30**, **31**, and **32**, respectively), confirmed the assignment of this signal to the anomeric carbon atom. The other signals in this region are all inside the range expected for 1,3-dioxolane rings, as are the values for $^{1}J_{C,H}$ and the chemical shifts of the benzylidene protons. Therefore, these compounds (**29**–**32**) are the four

possible 1,2:3,4-di-*O*-benzylidene-β-L-arabinopyranosides. The vicinal proton coupling-constants derived from ^{1}H-n.m.r. spectra of **29** to **31** are very similar to those observed for 1,2:3,4-di-*O*-isopropylidene-β-L-arabinopyranose, and thus these



29 $R^1 = R^2 = H, R^3 = R^4 = Ph$
30 $R^2 = R^3 = H, R^1 = R^4 = Ph$
31 $R^1 = R^4 = H, R^2 = R^3 = Ph$
32 $R^3 = R^4 = H, R^1 = R^2 = Ph$

compounds probably also exist in a skew conformation[31]. Assignment of the configurations at the acetal carbon atoms of the individual isomers may be performed by using the observation[8] that the ^{1}H-n.m.r. chemical shifts for the acetal carbon atom in *syn* isomers are upfield from those in *anti* isomers and by assuming that a change in chemical shift of C-1 by 0.5 p.p.m. is caused by a change in configuration in the 1,2-*O*-benzylidene ring. Thus compound **29** is the *syn,syn* diastereomer, as it has two upfield values for the acetal-proton chemical shifts. In compound **30**, one of these shifts has changed, as has the chemical shift for C-1. This latter change suggests that the ring whose configuration has changed is the 1,2-*O*-benzylidene ring, and thus **30** would be the *anti,syn* stereoisomer. In **29**, the chemical shifts for the acetal carbon atoms are δ 103.9 and 102.3, whereas in **30**, they are δ 104.2 and 104.0. The upfield shift of 102.3 in **29** (having *syn* stereochemistry in the benzylidene ring) is probably caused by the ring oxygen atom, which is in the γ position with respect to this carbon atom. The γ substituent effects by first-row heteroatoms are known to be larger than those of carbon atoms[9]. Consideration of all of the spectral data shows that the following assignments are consistent with all the data: for the chemical shift of the acetal proton, values of δ 5.75 or 5.76, ~6.40, 5.81, and ~6.23 are caused respectively by *syn* and *anti* configurations in a 1,2-*O*-benzylidene ring and by *syn* and *anti* configurations in a 3,4-*O*-benzylidene ring; for the chemical shift of the acetal carbon atom, values of ~102.25, ~103.95, ~104.05, ~104.55 p.p.m. are caused respectively by *syn* and *anti* configurations in a 3,4-*O*-benzylidene ring. The shifts for C-1 and for the quaternary carbon atom may be assigned in a similarly consistent fashion. Thus, the remaining two isomers have the *syn,anti* (**31**) and *anti,anti* (**32**) configurations. Assignment of C-3 could be made for all spectra by selective, hetero-

nuclear decoupling as H-3 appears downfield from H-2 and H-4 in the spectra of all isomers. The signals for C-2 and C-4 could not be definitely assigned.

The mass spectra of compounds **29**, **30**, and **31** are very similar and may be readily interpreted as arising from fragmentation patterns related to those observed for other benzylidene acetals[32] and for 1,2:3,4-di-*O*-isopropylidene-L-arabinose[33]. The intensities of all peaks were very similar in the mass spectra of **29** and **31**, but in **30**, although the same ions were present, the intensities observed were different. Compounds **29** and **31** have the same configuration (*syn*) in the 1,2-*O*-benzylidene ring, whereas in **30**, this ring has the *anti* stereochemistry. A possible explanation of the intensity differences is that, for the benzylidene rings in each of these compounds, the favored site of initial fragmentation is in the 1,2-*O*-benzylidene ring.

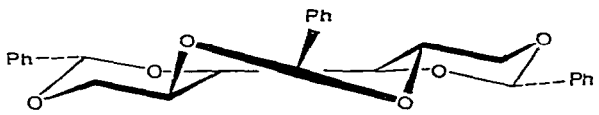
1,2:3,4-Di-*O*-benzylidene-D-galactopyranose was obtained as a mixture of isomers[11] that showed signals in its ^{1}H-n.m.r. spectrum in 1,3-dioxane having shifts of δ 5.32, 5.38, 5.79, and 5.98, and in the integrated ratio of 3:3:0.5:1.0, respectively. As the values recorded here in chloroform-*d* have a downfield solvent-shift of 0.4 p.p.m., the values of δ 5.72, 5.78, 6.10, and 6.38 correspond quite closely to the values obtained for arabinose. As for the arabinose derivatives, the *syn,syn* isomer appears to preponderate in the product mixture.

In the isomers **29–32**, the signal for the acetal carbon atom in the benzylidene rings having the *syn* configuration appears upfield from that having the *anti* configuration, in contrast to previous observations. Support for the foregoing assignment made on the basis of the ^{1}H chemical shifts may be obtained from the shift of the quaternary phenyl carbon atoms. The signal for this atom in the model compounds **4** and **5** is more upfield in the *cis* isomer **4** by 2.1 p.p.m. Comparison of these shifts in compounds **29** and **32** (in which both rings have the same stereochemistry, either both *syn* or both *anti*) shows that the signals for these carbon atoms in **29** appear upfield of the same signals for **32** by about the same difference as in the model compounds.

Neszmélyi *et al.* have recently[3] examined the ^{13}C-n.m.r. spectra of a large number of compounds containing 2-phenyl-1,3-dioxolane rings *cis*-fused at positions 2 and 3, and 3 and 4 of pyranoid sugars and have demonstrated that, for this type of system, the difference in chemical shift between the signal for the acetal carbon and the quaternary carbon atom on the phenyl ring is indicative of configuration. They suggest that differences of >35.4 p.p.m. and <33.8 indicate *anti* and *syn* isomers, respectively. The corresponding differences obtained from the arabinose derivatives examined here fall within these ranges, even for the signals obtained from carbon atoms in the 1,2-benzylidene rings, but the other compounds considered in this publication that can be classified as *trans,trans* or *cis,cis* disubstituted 2-phenyl-1,3-dioxolanes (**4** and **5**, **7** and **8**, and **28**) do not. For all of these compounds, the difference is smaller for the *cis,cis* or *syn* isomer than for the *trans,trans* or *anti* isomer (30.4 and 32.7 p.p.m. for **28**, 35.7 and 39.0 for **4** and **5**, respectively, and 35.9 and 38.8 p.p.m. for **7** and **8**, respectively). The previous authors[3] suggested that application of their criterion allowed assignment of configuration even if only a single isomer were avail-

able. Present results show that this is true only if it is known that the 1,3-dioxolane ring is fused to a pyranoid ring.

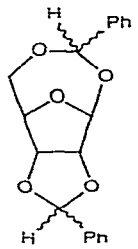
1,3-Dioxepane examples. The n.m.r.-spectral parameters of one of the 2-phenyl-1,3-dioxepane model compounds, **15**, were such that there could be difficulty in structural assignment of this type of acetal. Few carbohydrate 2-phenyl-1,3-dioxepane derivatives are known, but presented here are the spectral parameters of two of them. Tri-*O*-benzylidene-D-mannitol (**33**) has recently[34] been shown to have the 1,3:2,5:4,6



33

constitution. The ^{1}H-n.m.r. spectrum of **33** showed peaks for the acetal protons at δ 5.85, 5.55, and 5.49, which could be initially interpreted as being consistent with the presence of two 1,3-dioxane rings plus either a 1,3-dioxolane or a 1,3-dioxepane ring. The ^{13}C-n.m.r. spectrum of **33** is consistent only with the latter structure. The chemical shift for the one benzylidene carbon atom having a shift outside the 2-phenyl-1,3-dioxane range is δ 99.2, which is what would be expected for a 1,3-dioxepane ring. The chemical shifts of the skeletal carbon atoms provide additional support for this structure. These signals could be assigned by off-resonance decoupling, whereupon the primary carbon atoms resonated as triplets. The signals for C-2 and C-5 appear widely separated at δ 60.9 and 66.2, as do C-4 and C-7 in the comparable model compound **19**. Comparable separations are not observed for other ring sizes. The values of $^1J_{C,H}$ for the benzylidene carbon atom in the 1,3-dioxepane ring is unusually large (170.5 Hz), which may be caused by the considerable strain[35] in the favored *TC* conformation of this 1,3-dioxepane ring.

1,5:2,3-Di-*O*-benzylidene-D-ribofuranose (**34**) was obtained as a mixture[27] by benzylidenation of D-ribose at room temperature[34]. Its ^{1}H-n.m.r. spectrum shows



34

signals in the benzylidene proton region at δ 6.04, 5.95, 5.76, 5.74, 5.71, and 5.44 with relative peak heights of 20, 14, 66, 71, 7 and 8, respectively. The acetal region of the ^{13}C-n.m.r. spectrum is more complex because C-1 also appears in it (C-1 in **28** absorbed at δ 106.2) and signals were observed at δ 105.8, 105.3, 104.8, 104.0,

102.3, 100.9, and 100.5, with relative peak heights of 19, 33, 12, 8, 9, 23, and 15, respectively. Because of the complexity of this region, $^{1}J_{C,H}$ values could not be measured. Total assignment of these data was impossible, but the data do provide some evidence about structure. The major signals in the ^{1}H-n.m.r. spectra are only compatible with 1,3-dioxolane or 1,3-dioxepane rings or 1,3-dioxane rings having axial substituents at C-4 or C-6. The latter type of structure is immediately ruled out by the absence of a ^{13}C-n.m.r. signal at 93 or 94 p.p.m. The shifts in the ^{13}C-n.m.r. spectra ranging from δ 105.8 to 104.0 can only be assigned to acetal carbons in 1,3-dioxolane rings, and the shift at δ 102.3 probably also arises from this type of ring. However, because of the proton evidence, the signals at δ 100.9 and 100.5 must be caused by acetal carbon atoms in the fused 1,3-dioxepane ring. Clearly, the use of more than one n.m.r. parameter provides considerable structural information even in such very complex situations as in **34**.

SUMMARY

In Table V are listed the ranges observed for those n.m.r. parameters of use for the determination of structures of benzylidene acetals. As these ranges were derived from spectra measured in chloroform-*d*, caution must be observed if these ranges are applied to spectra measured in other solvents, particularly if the ranges for the proton chemical-shifts are being considered. Application of all three parameters presented here should allow assignment of the structure of a particular benzylidene acetal to one of the five classes listed in Table V. Although structures containing 2-phenyl-1,3-dioxane rings having the phenyl group axial have been prepared[20] by base-catalyzed benzylidenation of partially protected sugars, this type of isomer has not been considered here because these conditions are not used preparatively for the synthesis of *O*-benzylidene protecting groups spanning β diols.

TABLE V

SUMMARY OF THE N.M.R. PARAMETERS USEFUL FOR STRUCTURAL ASSIGNMENTS OF BENZYLIDENE ACETALS

Class of compound	*^{1}H-N.m.r. shift of H-2 (δ, p.p.m.)*	*^{13}C-N.m.r. shift of C-2 (δ, p.p.m.)*	*$^{1}J_{C,H}$ for C-2 (Hz)*	*Number of present examples*
1,3-Dioxolanes	5.71–6.41	101.9–105.8[a]	166.6–170.5	31
Normal 1,3-dioxanes	5.44–5.58	100.6–101.4	159.7–161.8	9
1,3-Dioxanes with axial groups at C-4 or C-6	5.79–5.90	93.7– 94.9	159.7	2
Normal 1,3-dioxepanes	5.70–5.95[b]	98.4–100.2[b]	163.2–165.3[c]	4
1,3-Dioxepanes with axial groups at C-4 or C-7	5.84	93.7	163.2	1

[a]The one exception is discussed in the text. [b]One exception became of conformational factors: see text. [c]One exception.

EXPERIMENTAL

General methods. — Melting points were determined by using a Reichert melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter at 23 ± 3° in chloroform. ^{1}H-N.m.r. spectra were recorded at 60, 80, or 220 MHz on Varian T-60, CFT-20, or HR-220 spectrometers in chloroform-*d* with tetramethylsilane as an internal standard, unless otherwise stated. ^{13}C-N.m.r. spectra were recorded at 20 MHz on a Varian CFT-20 spectrometer with 8000 data points. Chemical shifts were obtained from spectra recorded using 66° pulses, 0.5-sec pulse-intervals and internal tetramethylsilane as reference. Chemical-shift assignments in Table II not specifically mentioned in the discussion were made by using standard chemical-shift effects and are internally consistent. Variation in shifts from different samples of the same compound was ±0.05 p.p.m. Coupling constants were obtained from spectra recorded with 90° pulses, with gated decoupling and acquisition times between 2.5 and 4.1 sec. The error is estimated to be ±0.5 Hz. Selective heteronuclear and homonuclear decoupling was performed with a Wavetek Model 171 frequency synthesizer. Mass spectra were obtained with a CEC 21-104 mass spectrometer operating at 70-eV ionizing voltage. T.l.c. was performed on 0.25-mm thick Brinkmann Silica Gel G/uv-254 glass plates cut to be approximately 7 cm long. Plates were developed by spraying with 2% ceric sulfate solution in M sulfuric acid and then heating the plates for a few min at 150°. Eluent systems used were: *A*, 4:1 (v/v) petroleum ether (30–80°)–ethyl acetate; *B*, 6:1 (v/v) petroleum ether (30–80°)–ethyl acetate; and *C*, 9:1 (v/v) benzene–ethyl acetate.

Model 1,3-dioxane and 1,3-dioxolane compounds. — These compounds were prepared by boiling under reflux the appropriate diol with an equivalent amount of

TABLE VI

PHYSICAL PROPERTIES OF MODEL COMPOUNDS AND KNOWN CARBOHYDRATE EXAMPLES

Compound	*Present work b.p. (deg./mm Hg)*	*Lit. b.p. (deg./mm Hg)*	*Ref.*	*Compound*	*Present work b.p. (deg./mm Hg)*	*Lit. b.p. (deg./mm Hg)*	*Ref.*
1	116–120/5	106–107/11	38	**12**	86–87/0.7	126/12	42
2	98–100/2.5	83–85/4	39	**13**	88/0.66	115/10	42
3	98–100/2.5	83–85/4	39	**14**	115/5	135/14	19
4	64–66/0.2	86/0.1	4	**15**	84/1		
5	64–66/0.2	86/0.1	4	**16**	84/1		
6	94/2	119/19	40	**17**	96/0.75	85/0.15	40
7	116–119/0.55	150–155/12	41	**18**	96/0.75	85/0.15	40
8	116–119/0.55	150–155/12	41	**19**	82/0.5	85/0.15	44
9	116–120/5	115/12	42	**28**[a]	200–201	197–198	45
10	107–108/2	134–135/18	42	**33**[a]	219–220	223–224	34
11	107–108/2	73/0.2	43	**34**[a]	92–94	89–91	27

[a]m.p.

benzaldehyde and either benzene or toluene and some dry Rexyn 101 (H^+ form) cation-exchange resin in a device for azeotropic removal of water until the theoretical amount of water had been removed. The mixture was then filtered and the product distilled from the filtrate. Most alcohols were obtained commercially. 2,4-Pentanediol was obtained as a mixture of *dl* and *meso* isomers by reduction of 2,5-pentanedione with sodium borohydride[35]. 2,3-Butanediol, 1,4-pentanediol, and 2,5-hexanediol were similarly produced by reduction of the appropriate ketones with sodium borohydride. Where mixtures were obtained, fractionation of the benzylidene acetals was performed by distillation through a concentric-tube column. The properties of these compounds are listed in Table VI.

Benzylidenation of D-*galactose diethyl dithioacetal.* — Dried D-galactose diethyl dithioacetal (10 g) was mechanically stirred for 6 h at ~25° with benzaldehyde (120 mL) and zinc chloride (25 g, freshly fused and powdered under dry nitrogen) and the mixture was then added to ice–water (500 mL) containing sodium hydrogencarbonate. This mixture was extracted with chloroform (3 × 200 mL) and the combined extracts were washed with water (100 mL), dried (magnesium sulfate), and evaporated to a yellow syrup (16.8 g) which, by t.l.c. (solvent *A*), was a complex mixture. The syrup was fractionated by column chromatography on silica gel (800 g, column 188 × 4.6 cm) with solvent *B* as eluent. A few unidentified minor components were collected first (total 0.15 g), and then fraction **a** (3.269 g, R_F 0.44 in *A*), a mixture of **a** and **23** (0.556 g), **23** (0.316 g, R_F 0.39 in *A*) a mixture of **23** and **24** (0.722 g), **24** (3.501 g, R_F 0.34 in *A*), and **25** (1.526 g, R_F 0.29 in *A*). ^{1}H-N.m.r. spectroscopy showed that fraction **a** was a mixture and part of it (1.4 g) was further resolved by column chromatography on silica gel (120 g) with 14:1 (v/v) benzene–ethyl acetate as eluent to give pure **21** (0.743 g, R_F 0.56 in *C*) and a mixture of **21** and **22** (0.505 g), in the ratio of ~2:3 as measured by ^{1}H-n.m.r. spectroscopy. Compound **22** had R_F 0.47 in solvent *C*.

The following $[\alpha]_D^{26}$ values were obtained: **21**, +11.3° (*c* 0.8); **23**, −54.2° (*c* 1.0); **25**, −43.1° (*c* 1.2); and **26**, +41.1° (*c* 0.8). Compound **25** crystallized and was recrystallized from ethanol–water, m.p. 110–112°.

Anal. Calc. for $C_{24}H_{30}O_5S_2$: C, 62.3; H, 6.5; S, 13.9. Found: C, 62.3; H, 6.5; S, 13.9.

The reaction was repeated at room temperature with identical molar ratios and was monitored by t.l.c. (solvent *A*) from 2 h to 3 days (when observation was stopped). Qualitatively, the mixture of dibenzylidenated products appeared at all times to contain the same components in similar amounts as obtained after isolation as already described. At 0°, the reaction was significantly slower, but the product ratios did not alter markedly.

*5-O-Acetyl-2,3:4,6-di-O-benzylidene-*D-*galactose diethyl dithioacetal* (**27**). — Compound **24** (35 mg) in dry pyridine (1.5 mL) and acetic anhydride (0.5 mL) was stirred overnight at room temperature, and then poured into ice–water (30 mL). The mixture was extracted with ether (2 × 25 mL) and the ether extracts were combined, washed with saturated cupric sulfate solution (3 × 25 mL), saturated sodium

hydrogencarbonate solution (3 × 25 mL), and water (2 × 20 mL), dried, and evaporated to give **27** (27 mg, 71%) as a syrup; ^{1}H-n.m.r. spectrum in chloroform-*d* at 220 MHz: δ ~1.14, 1.25 (2t, 6H, *J* 7 Hz SCH_2CH_3, 2.10 (s, 3H, ac), 2.57–2.83 (m, 4H, SCH_2CH_3 protons), 7.55–7.24 (m, 10H, aromatic protons); in benzene-d_6 at 220 MHz; δ 1.03, 1.06 (2t, 6H, *J* 7 Hz, SCH_2CH_3), 1.60 (s, 3H, ac), 2.50–2.80 (complex m, 4H, SCH_2CH_3), 7.07–7.18 (m, 6H, meta and para protons), 7.60 (d, *J* 7 Hz, 2H, 2 ortho protons), and 7.70 (d, 2H, *J* 7 Hz, 2 ortho protons in a different ring).

*5-O-Acetyl-2,3:4,6-di-O-benzylidene-*D*-galactose diethyl dithioacetal* (**26**). — Compound **21** (90 mg) was stirred with pyridine (1.5 mL) and acetic anhydride (1.0 mL) for 3.5 h at room temperature and then poured into ice–water (30 mL). Isolation as for **27** gave **26** as a syrup (67 mg, 72%); ^{1}H-n.m.r. spectrum in chloroform-*d* at 220 MHz: δ 1.10, 1.20 (2t, 6H, SCH_2CH_3), 2.20 (s, 3H), 2.50–2.75 (complex m, 4H, SCH_2CH_3), 7.47 (m, 10H, aromatic protons); in benzene-d_6 at 220 MHz: δ 1.01, 1.04 (2t, 6H, *J* 7 Hz, SCH_2CH_3 protons), 1.67 (s, 3H), 2.54 (q, 2H, SCH_2CH_3 protons), ~2.54–2.79 (complex m, 2H, SCH_2CH_3, AB part of ABX_3 pattern), 6.92 (narrow m, 6H, meta and para protons), and 7.56 (d, *J* 7 Hz, 4 ortho protons).

Benzylidenation of L*-arabinose.* — L-Arabinose (209, 0.125 m) was suspended in toluene (200 mL), and then benzaldehyde (34.6 g, 2.2 eq) and a few crystals of *p*-toluenesulfonic acid were added. The mixture was boiled under reflux in an apparatus for the azeotopic removal of water until about 2 equiv had been removed. The solution was cooled, washed with aqueous sodium hydrogencarbonate solution (2 × 51 mL), and then dried (magnesium sulfate) and evaporated. The resulting syrup crystallized on dilution with ethanol. The crystals were recrystallized twice from ethanol to give feathery crystals of **29**, yield 3.5 g, m.p. 152–154°, $[\alpha]_D^{23}$ +3.1° (*c* 1.0, chloroform) [lit.[26] m.p. 154°, $[\alpha]_D$ +26.8° (methanol);] ^{1}H-n.m.r. spectrum in chloroform-*d* at 80 MHz: δ 7.62–7.27 (complex m, 10H, phenyl H), 5.71 (d, 1H, $J_{1,2}$ 5.2 Hz, H-1), 4.63 (d of d, 1H, $J_{2,3}$ 2.4, $J_{3,4}$ 8.2 Hz, H-3), 4.33 (d of d, 1H, H-2), 4.21 (broadened d, 1H, H-4), and 3.87 [AB part of apparent ABX pattern, 2H, $J_{5,5'}$ 12.8 Hz (obtained from decoupled spectra), H-5,5']. The coupling constants given are from a first-order analysis. Assignments were confirmed by irradiation at δ 5.71 and 4.63. Mass-spectral data: *m/e* 327 (M + 1, 4%), 326 (M^+, 20%), 325 (M^+ − 1, 25%), 249 (M^+ − 7, 1%), 220 (M^+ − 106, 12%), 219 (M^+ + 107, 3%) 161 (M^+ − 165, 6%), 148 (28%), 114 (11%), 107 (16%), 106 (18%), and 105 (100%). The peaks at *m/e* 325, 249, 320, and 219 are the typical b_1, c_1, e_1 and b_2 fragmentation-ions from benzylidene acetals[32], whereas the peaks at *m/e* 161 and 148 result from processes of the G_1^1, and H_1^1, and H_1^3 types, respectively[33], similar to the patterns from 1,2:3,4-di-*O*-isopropylidene-L-arabinose[33].

The mother liquors gave a second crystalline product (**30**) that was recrystallized from chloroform–ethanol to give needles, m.p. 138–140, $[\alpha]_D^{23}$ −71.7° (*c* 1.2, chloroform); 80 MHz ^{1}H-n.m.r. spectrum in chloroform-*d*: δ 7.60–7.27 (complex m, 10H, phenyl H), ~5.75 (1H, overlapped with acetal signals, H-1), 4.64 (d of d, 1H, $J_{2,3}$ 2.3 Hz, $J_{3,4}$ 8.0 Hz, H-3), 4.35–4.23 (complex m, 2H, H-2 and H-4), and 3.93 (broad-

ened s, 2H, H-5,5'). Irradiation at δ 5.75 did not affect the signal at δ 4.64. Mass-spectral data: *m/e* 327 (0.5%), 326 (M^+, 3%), 325 (9%), 249 (1%), 221 (4%), 220 (21%), 219 (3%), 148 (10%), 107 (12%), 106 (14%), and 105 (100%).

The remaining syrup showed 3 spots on t.l.c. in solvent *A*, R_F values 0.61, 0.53 and 0.50, and **30** and **29** had R_F values similar to the latter two. Column chromatography of part of this syrup (5.5 g) on silica gel (250 g, column 101 × 2 cm), separated the mixture into one homogeneous component (2.6 g, R_F 0.61), plus overlapping fractions and fractions containing **29** and **30**. This homogeneous component was shown by ^{1}H- and ^{13}C-n.m.r. spectroscopy to be a mixture of two compounds (**31** and **32**) in equal amounts, from which **31** could be selectively crystallized from chloroform–ethanol. Two more crystallizations from chloroform–ethanol gave pure **31** as clear prisms, m.p. 128–130°, $[\alpha]_D^{23}$ −35.1° (*c* 1.2, chloroform); 80-MHz ^{1}H-n.m.r. spectrum in chloroform-*d*: δ 7.52–7.34 (complex m, 10H, phenyl H), 5.74 (d, 1H, $J_{1,2}$ 5.2 Hz, H-1), 4.75 (d of d, 1H, $J_{2,3}$ 2.6 Hz, $J_{3,4}$ 7.7 Hz, H-3), 4.43 (d of d, 1H, H-2), 4.37 (broadened d obscured by H-2 in undecoupled spectra, H-4), and 3.94 (AB part of apparent ABX pattern, 2H, $J_{5,5'}$ 13.0 Hz, $\Delta\nu$ = 0.17 p.p.m. from decoupled spectra, H-5,5'). Assignments were confirmed by decoupling. Mass-spectral data: *m/e* 327 (6%), 326 (M^+, 27%), 325 (29%), 249 (2%), 220 (11%), 219 (4%), 161 (6%), 148 (31%), 114 (11%), 107 (17%), 106 (17%), and 105 (100%).

ACKNOWLEDGMENTS

The authors thank the National Research Council of Canada for financial support of this work and Mr. Munjal Parikh for technical assistance. They also thank the Atlantic Regional Laboratories of the National Research Council of Canada for use of the polarimeter, and the Canadian 220-MHz NMR Centre for determining ^{1}H-n.m.r. spectra. Dr. W. A. Szarek kindly provided samples of **28** and **34**. They also thank Dr. J. F. Stoddart and M. Pinto for discussions.

REFERENCES

1 N. Baggett, K. W. Buck, A. B. Foster, M. H. Randall, and J. M. Webber, *J. Chem. Soc.*, (1965) 3394–3400.
2 See, for instance, D. J. J. Potgieter and D. L. MacDonald, *J. Org. Chem.*, 26 (1961) 3934–3938; M. L. Wolfrom and G. G. Parekh, *Carbohydr. Res.*, 11 (1969) 547–557; H. Zinner, B. Richard, M. Blessmann, and M. Schlutt, *Carbohydr. Res.*, 2 (1966) 197–203; D. J. Brecknell, R. M. Carman, J. J. Kibby, and L. T. Nicholas, *Aust. J. Chem.*, 26 (1976) 1859–1863.
3 A. Neszmélyi, A. Lipták, and P. Nánási, *Carbohydr. Res.*, 58 (1977) C7–C9.
4 W. E. Willy, G. Binsch, and E. L. Eliel, *J. Am. Chem. Soc.*, 92 (1970) 5394–5402.
5 O. J. Triggle and B. Belleau, *Can. J. Chem.*, 40 (1962) 1201–1215.
6 G. M. Kellie and F. G. Riddell, *J. Chem. Soc., B*, (1971) 1030–1034.
7 M. H. Gianni, J. Saavedra, and J. Savoy, *J. Org. Chem.*, 38 (1973) 3971–3975.
8 D. F. Bocian and H. L. Strauss, *J. Am. Chem. Soc.*, 99 (1977) 2866–2876; 2876–2882.
9 E. L. Eliel, W. F. Bailey, L. O. Kopp, R. L. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, M. W. Buch, E. Wenkert, F. M. Schell, and D. W. Cochran, *J. Am. Chem. Soc.*, 97 (1975) 322–330; T. P. Forrest and J. G. K. Webb, *Org. Magn. Reson.*, in press.

10 H. BEIERBECK AND J. K. SAUNDERS, *Can. J. Chem.*, 54 (1976) 2985–2995; D. G. GORENSTEIN, *J. Am. Chem. Soc.*, 99 (1977) 2254–2258.
11 N. BAGGETT, K. W. BUCK, A. B. FOSTER, AND J. M. WEBBER, *J. Chem. Soc.*, (1965) 3401–3407.
12 D. E. DORMAN AND J. D. ROBERTS, *J. Am. Chem. Soc.*, 92 (1970) 1355–1361; A. S. PERLIN, B. CASU, AND H. J. KOCH, *Can. J. Chem.*, 48 (1970) 2596–2606.
13 R. G. S. RITCHIE, N. CYR, B. KORSCH, H. J. KOCH, AND A. S. PERLIN, *Can. J. Chem.*, 53 (1975) 1424–1433.
14 F. W. WEHRLI AND T. WIRTHIN, *Interpretation of Carbon-13 NMR Spectra*, Heyden, London, 1976, p. 38.
15 E. CONWAY, R. D. GUTHRIE, S. D. GERO, G. LUKACS, AND A.-M. SEPULCHRE, *J. Chem. Soc. Perkin Trans. 2*, (1974) 542–546; A. J. JONES, E. L. ELIEL, D. M. GRANT, M. C. KNOBBER, AND W. E. BAILEY, *J. Am. Chem. Soc.*, 93 (1971) 4772–4777.
16 V. P. LEZINA, A. U. STEPANYANTS, F. A. ALIMIRZOEV, S. S. ZLOTSKII, AND D. L. RAKHMANKULOV, *Izv. Akad. Nauk SSSR*, (1976) 792–798.
17 K. BOCK AND L. WIEBE, *Acta Chem. Scand.*, 27 (1973) 2676–2678.
18 See J. F. STODDART, *Stereochemistry of Carbohydrates*, Wiley–Interscience, New York, 1971, pp. 102–108, 198–199.
19 P. J. GAREGG AND C.-G. SWAHN, *Acta Chem. Scand.*, 26 (1972) 3895–3901.
20 N. BAGGETT, J. M. DUXBURY, A. B. FOSTER, AND J. M. WEBBER, *Carbohydr. Res.*, 1 (1965) 22–30.
21 D. B. TULSHIAN, M.Sc. Thesis, Dalhousie University, 1977; V. GULASEKHARAM AND T. B. GRINDLEY, *Chem. Commun.*, (1978) 1073–1074.
22 R. M. HANN AND C. S. HUDSON, *J. Am. Chem. Soc.*, 66 (1944) 1909–1912; A. T. NESS, R. M. HANN, AND C. S. HUDSON, *ibid.*, 70 (1948) 765–770; S. A. BARKER AND E. J. BOURNE, *Adv. Carbohydr. Chem.*, 7 (1952) 137–207.
23 I. J. BURDEN AND J. F. STODDART, *J. Chem. Soc. Perkin Trans. 1*, (1975) 666–674.
24 T. P. FORREST, *J. Am. Chem. Soc.*, 97 (1975) 2628–2830; *Org. Magn. Reson.*, 6 (1974) 355–357.
25 A. J. DE KOK AND C. ROMERS, *Recl. Trav. Chim.*, 89 (1970) 313–320.
26 H. ZINNER AND W. THIELEBEULE, *Chem. Ber.*, 93 (1960) 2791–2803.
27 T. B. GRINDLEY AND W. A. SZAREK, *Carbohydr. Res.*, 25 (1972) 187–195.
28 K. BOCK AND C. PEDERSEN, *Acta Chem. Scand., Ser. B*, 29 (1975) 258–264; *J. Chem. Soc. Perkin Trans. 2*, (1974) 293–297; F. R. TARAVEL AND P. J. A. VOTTERO, *Tetrahedron Lett.*, (1975) 2341–2344.
29 J. PACÁK AND M. ČERNÝ, *Collect. Czech. Chem. Commun.*, 26 (1961) 2212–2216; 28 (1963) 541–544.
30 (a) W. ALBERDA VAN EKENSTEIN AND J. J. BLANSKMA, *Recl. Trav. Chim.*, 25 (1906) 153–161; (b) M. OLDHAM AND J. HONEYMAN, *J. Chem. Soc.*, (1946) 986–989.
31 C. CONE AND L. HOUGH, *Carbohydr. Res.*, 1 (1965) 1–9.
32 O. S. CHIZHOV, L. S. GOLOVKINA, AND N. S. WULFSON, *Carbohydr. Res.*, 6 (1968) 143–149; J. MITERA, V. KUBELKA, A. ZOBACOUA, AND J. JARÝ, *Collect. Czech. Chem. Commun.*, 37 (1972) 3744–3748.
33 D. C. DEJONGH AND K. BIEMANN, *J. Am. Chem. Soc.*, 86 (1964) 67–74; N. K. KOCHETKOV AND D. S. CHIZHOV, *Adv. Carbohydr. Chem.*, 21 (1966) 39–93.
34 D. J. BRECKNELL, R. M. CARMAN, AND J. J. KIBBY, *Aust. J. Chem.*, 29 (1976) 1749–1760.
35 T. B. GRINDLEY, J. F. STODDART, AND W. A. SZAREK, *J. Chem. Soc., B*, (1969) 172–175; 623–626.
36 G. R. BARKER AND J. W. SPOORS, *J. Chem. Soc.*, (1956) 1192–1195.
37 H. YONEMOTO, *Yakugaku Zasshi*, 79 (1959) 143–150, *Chem. Abstr.*, 53 (1959) 13168g; see also J. G. PRITCHARD AND R. L. VOLIMER, *J. Org. Chem.*, 28 (1963) 1545–1549.
38 A. RIECHE, E. SCHMITZ, AND E. BEYER, *Chem. Ber.*, 91 (1958) 1935–1941.
39 C. PIANTADOSI, C. E. ANDERSON, E. A. BRECHT, AND C. L. YARBRO, *J. Am. Chem. Soc.*, 80 (1958) 6613–6617.
40 D. GAGNAIRE AND J. B. ROBERT, *Bull. Soc. Chim. Fr.*, (1965) 3646–3650.
41 A. RIECHE, E. SCHMITZ, W. SCHADE, AND E. BEYER, *Chem. Ber.*, 94 (1961) 2926–2932.
42 J. KOVAŘ, J. STEFFKOVA, AND J. JARÝ, *Collect. Czech. Chem. Commun.*, 30 (1965) 2793–2800.
43 E. L. ELIEL AND F. W. NADER, *J. Am. Chem. Soc.*, 92 (1970) 584–590.
44 R. M. MUNAVU AND H. H. SZMANT, *Tetrahedron Lett.*, (1975) 4543–4546.
45 H. B. WOOD, JR., H. W. DIEHL, AND H. G. FLETCHER, JR., *J. Am. Chem. Soc.*, 78 (1956) 4715–4717.