much smaller in these cases than for the nitro, carbethoxy, or dimethylamino groups. The angles of twist of 37 and 49°, respectively, seem reasonable, but it is difficult to discuss the behavior of these groups in more detail since the geometry of the groups and of the conjugating orbitals is open to question.

A further significant feature of Table II is the demonstration that the resonance interaction, as reflected by σ, of a functional group with a second substituent is a variable parameter which is very sensitive to the nature of the second substituent and the reaction process in question. For this reason it is impossible to assign a single σ-value to a group which can be used successfully to correlate all reaction data through the Hammett equation, as Wepster[24] has demonstrated. Since the real value of the Hammett equation is not in correlating rate data but rather in illucidating reaction mechanisms, we feel that most applications of the Hammett equation should use only the σ-values based on the ionization constants of benzoic acids[15] and that investigators should then concentrate their efforts on analyzing the correlation or lack of correlation observed rather than defining new σ-values in an effort to obtain a straight line.

Acknowledgment.—The authors wish to thank the California Research Corporation for partial support of this work.

(24) H. von Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. trav. chim.*, **78**, 815 (1959).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Mass Spectra of O-Isopropylidene Derivatives of Pentoses and Hexoses[1,2]

BY DON C. DE JONGH AND K. BIEMANN

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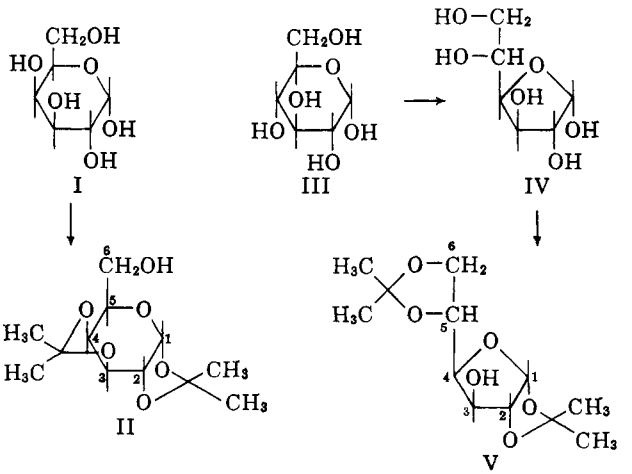
The mass spectra of O-isopropylidene derivatives of D-glucose, D-galactose, D-mannose, D-fructose, L-sorbose, L-arabinose, L-fucose, D-xylose, D-ribose, and D-lyxose are interpreted and their relationships to the stereochemistry of the parent monosaccharides are discussed. Both isotopic labeling and high resolution mass spectrometry are used to corroborate the proposed fragmentation mechanisms. As an application of the technique, the determination of the structure of a new di-O-isopropylidene derivative of D-galactose is presented.

The mass spectra of polyacetates of pentoses and hexoses,[3] of acetates of partially methylated derivatives thereof,[4] and of polymethyl ethers of monosaccharides[5] have recently been reported and interpreted. It was shown that it is possible to deduce from these spectra molecular weight and ring size of the compound, and, in the case of the O-methyl derivatives, also number and position of the methoxyl groups present in the molecules.[3,4] The spectra of these polyacetates are, however, very insensitive with respect to the stereochemistry of the molecule. This is not surprising as the only difference, for example, among the various epimeric aldohexopyranose pentacetates is the spatial relationship between substituents attached *via* a single bond to the tetrahydropyran ring. The ensuing steric repulsions—or attractions—are, however, much too weak to lead to appreciable differences in the electron-impact-induced fragmentation of the molecule and thus in the mass spectrum. The differences which can be observed are too small to permit interpretations in terms of the stereochemistry, beyond direct comparison with the spectrum of an authentic sample.

Isopropylidene derivatives appeared to be much more promising in this respect,[6] as the formation of such a bi- or tricyclic ring system is greatly dependent on the availability of *cis*-1,2- or *cis*-1,3-diol systems.[7] Thus epimers may give isopropylidene derivatives which differ in actual bonding and are no longer merely stereoisomers but structural isomers; it is the latter to which mass spectrometry is very sensitive. As a well known example, the case of D-galactose and D-glucose may be cited. While the former, in the α-pyranoid form I, has two pairs of *cis*-1,2-diol groupings and therefore forms mainly a pyranoid 1,2:3,4-di-O-isopropylidene derivative (II),[7] D-glucopyranose has only one *cis*-diol group in the α-form III (none in the β-form). The otherwise less favorable furanoid α-isomer IV, on the other hand, is capable of reacting with two moles of acetone to form 1,2:5,6-di-O-isopropylidene-D-glucofuranose (V).[7] Similarly, D-mannose forms an isomeric di-O-isopropylidene-furanose (XXV).[7]



Comparison of isomers II and V reveals that—in contrast to I and III, or their pentaacetates (–$OCOCH_3$ instead of –OH)—the covalent bonds are arranged in a very different way. Of particular importance is the C-4, C-5 bond in V, a single bond connecting two parts of the molecule. Its cleavage, especially favorable because of the strong stabilization of the resulting positive charge on either C-4 or C-5 by the adjacent oxygen atom, is mainly responsible for the great difference in the mass spectra of V and II (Fig. 1 and 2).

While a situation similar to the one present in galactose (I) exists in β-L-arabinopyranose (VI), which also

(1) Paper XVI on the Application of Mass Spectrometry to Structure Problems.

(2) Part XV: U. Renner, D. A. Prins, A. L. Burlingame, and K. Biemann, *Helv. Chim. Acta*, **46**, 2186 (1963).

(3) K. Biemann, D. C. De Jongh, and H. K. Schnoes, *J. Am. Chem. Soc.*, **85**, 1763 (1963).

(4) D. C. De Jongh and K. Biemann, *ibid.*, **86**, 2289 (1963).

(5) N. K. Kochetkov, N. S. Vulfson, O. S. Chizhov, and B. M. Zolotarev, *Dokl. Akad. Nauk SSSR*, **147**, 1369 (1962).

(6) K. Biemann, H. K. Schnoes, and J. A. McCloskey, *Chem. Ind.* (London), 448 (1963).

(7) For a discussion of these derivatives and pertinent references, see M. L. Wolfrom and A. Thompson in "The Carbohydrates," W. W. Pigman, Ed., Academic Press, Inc., New York, N. Y., 1957, pp. 236–240.

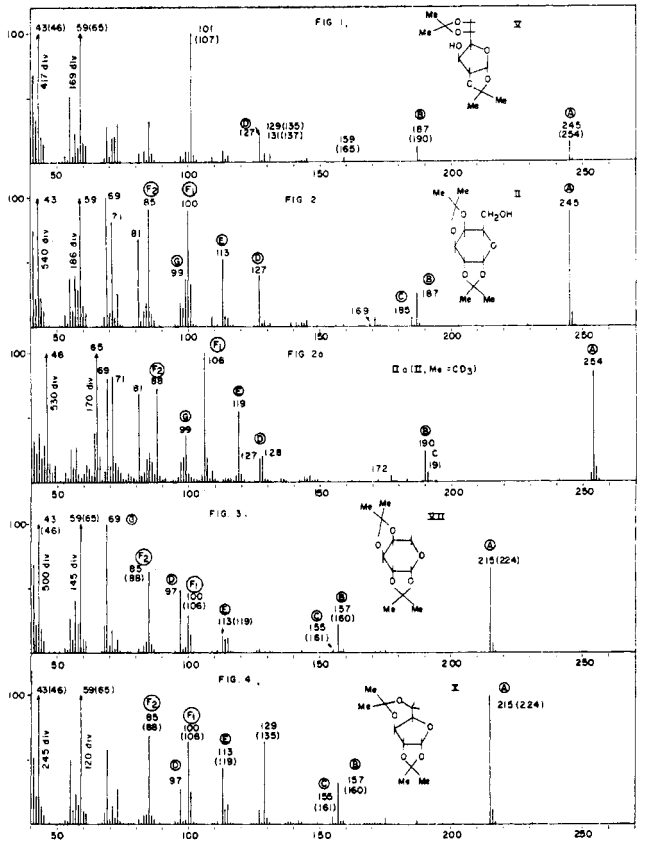


Fig. 1.—Mass spectrum of 1,2:5,6-di-O-isopropylidene-D-glucofuranose (V).

Fig. 2.—Mass spectrum of 1,2:3,4-di-O-isopropylidene-D-galactopyranose (II).

Fig. 2a.—Mass spectrum of 1,2:3,4-di-O-isopropylidene-d_{12}-D-galactopyranose (IIa).

Fig. 3. —Mass spectrum of 1,2:3,4-di-O-isopropylidene-L-arabinopyranose (VII).

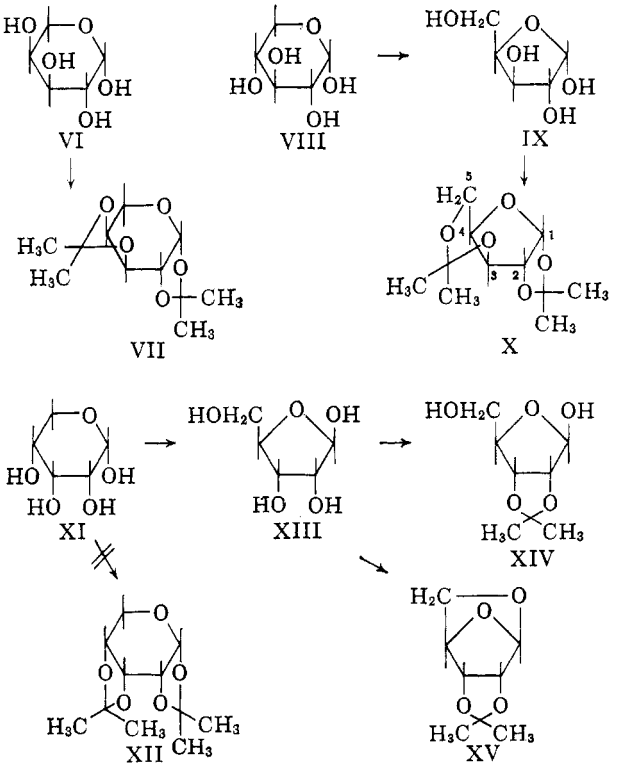
Fig. 4.—Mass spectrum of 1,2:3,5-di-O-isopropylidene-D-xylofuranose (X).

contains two 1,2-diol groupings and thus forms 1,2:3,4-di-O-isopropylidene-L-arabinopyranose (VII),[8] the epimeric α-D-xylopyranose VIII like the glucose analog III has only one 1,2-diol group. Conversion of VIII to the furanose form IX still does not lead to two 1,2-diols as in IV because of the absence of C-6 with its hydroxyl group. A di-O-isopropylidene derivative is still formed on reaction of IX with acetone, but the product (X)[9] now contains a 1,3-dioxane ring (involving C-3, C-4, and C-5) in addition to the 1,3-dioxolane ring (involving C-1 and C-2).

Finally, D-ribose (XI), while possessing two pairs of *cis* hydroxyl groups, does not form the di-O-isopropylidene derivative XII apparently because of the steric interference of the bulky *gem*-dimethyl groups. It rather forms, *via* the furanose XIII, a mono-O-isopropylidene derivative XIV[10] and an anhydro derivative thereof, XV.[10]

Thus, depending on their stereochemistry, pentoses form either pyranoid di-O-isopropylidene derivatives (*e.g.*, VII), furanoid derivatives containing one 1,3-dioxolane and one 1,3-dioxane ring (*e.g.*, X), or mono-O-isopropylidene derivatives (*e.g.*, XIV or possibly XV). All these compounds are easily distinguished mass spectrometrically as illustrated in Fig. 3–6.

(8) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 189 (1936).
(9) W. N. Haworth and C. R. Porter, *J. Chem. Soc.*, 611 (1928).
(10) P. A. Levene and E. T. Stiller, *J. Biol. Chem.*, **102**, 187 (1933).



A similar situation is found with ketohexoses which can, in principle, be considered as hydroxymethyl-substituted pentoses. D-Fructose in its pyranoid forms XVI and XVII is able to form two isomeric di-O-isopropylidene derivatives XVIII and XIX.[7] The epimeric L-sorbopyranose (XX) cannot react with two molecules of acetone but forms a di-O-isopropylidene derivative XXII *via* the furanoid form XXI. As in the similar case of 1,2:3,5-di-O-isopropylidene-D-xylofuranose (X), XXII[11] contains a six-membered 1,3-dioxane ring. The 1,2:4,6-isomer XXIII is apparently not formed; this may be due to steric interference between the 1,3-dioxolane and 1,3-dioxane rings attached to a tetrahydrofuran.

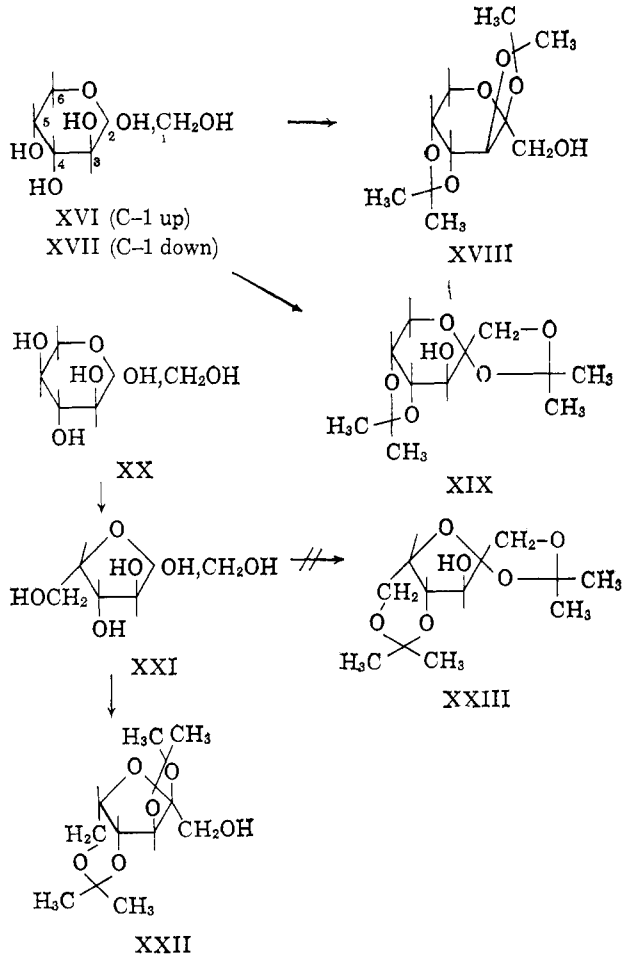
As expected on the basis of the earlier discussion, the mass spectra of XVIII, XIX, and XXII, shown in Fig. 7, 8, and 9, express these structural differences.

In addition, it should be noted that the spectra of O-isopropylidene derivatives are most suitable for the determination of the molecular weight of carbohydrates as the loss of one of the methyl groups from the 2,2-dimethyl-1,3-dioxolane or 1,3-dioxane ring gives rise to an abundant fragment of mass M − 15, because of the exceptional stabilization of the tertiary carbonium ion by two neighboring ether oxygens (see discussion of fragment A, below).

The presence of the many ether oxygens leads to a noticeable "M + 1" peak due to ion–molecule collisions, if the spectrum is determined with a sufficiently high sample pressure. As in simple ethers,[12] this peak can be taken as an indication of the molecular weight, which is one mass unit less. While too small to be shown on the scale of Fig. 1–9, the "M + 1" peak is easily recognized on the original record.

It now remains to discuss and interpret the spectra of di-O-isopropylidenealdopyranoses (*e.g.*, II and VII), di-O-isopropylidenealdofuranoses (*e.g.*, V and X), di-O-isopropylideneketopyranoses (*e.g.*, XVIII and XIX), di-O-isopropylideneketofuranoses (*e.g.*, XXII), and mono-O-isopropylidenefuranoses (*e.g.*, XIV and XV)

(11) T. Reichstein and A. Grüssner, *Helv. Chim. Acta*, **17**, 311 (1934).
(12) F. W. McLafferty, *Anal. Chem.*, **29**, 1782 (1957).



in greater detail to support the general statements made above.

For a confirmation of the proposed fragmentation processes, the spectra of some of the key compounds (II, V, XVIII, and XIX) have been determined not only with a conventional mass spectrometer (CEC 21-103C) but, in addition, with a double-focusing instrument (CEC 21-110) of very high resolving power, permitting determination of the mass of an ion with an accuracy of 1 part in 10^5 or better.[13] The elemental compositions of fragments mentioned below are derived from the accurate mass found (the value is given in parentheses, along with the deviation, in *milli*-mass units, from the theoretical mass of a particle of that elemental composition). Particularly in the lower mass range (<100) many peaks are resolved into multiplets, but unless mentioned otherwise, the fragment in question is the most abundant one.

Some of the fragmentation processes are the same for all these various derivatives, particularly those involving only the 1,3-dioxolane ring (*e.g.*, the above-mentioned loss of methyl and the further loss of the elements of acetone and/or acetic acid). These processes will be discussed with the first group, namely, di-O-isopropylidenehexopyranoses, while the cleavages characteristic for a particular group shall be outlined later.[14]

This discussion may also provide the basis for the possible extension of this work on common monosaccharides of known structure to the eventual use of the technique in the characterization or determination of

(13) We are indebted to Drs. P. Bommer and W. McMurray for these spectra.

(14) For a general discussion of the fragmentation of organic molecules in the mass spectrometer, see K. Biemann "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, particularly Chapter 3.

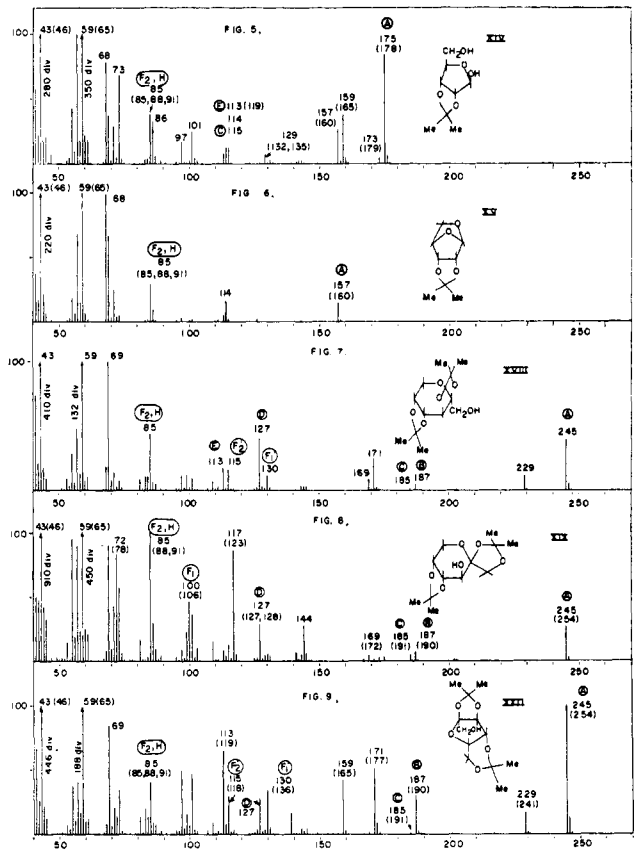


Fig. 5.—Mass spectrum of 2,3-O-isopropylidene-D-ribofuranose (XIV).

Fig. 6.—Mass spectrum of 2,3-O-isopropylidene-1,5-anhydro-D-ribofuranose (XV).

Fig. 7.—Mass spectrum of 2,3:4,5-di-O-isopropylidene-D-fructopyranose (XVIII).

Fig. 8.—Mass spectrum of 1,2:4,5-di-O-isopropylidene-D-fructopyranose (XIX).

Fig. 9.—Mass spectrum of 1,2:4,6-di-O-isopropylidene-L-sorbofuranose (XXII).

the structure of new carbohydrates or other derivatives (*e.g.*, alkylation or deoxygenation products) of known ones.

In this connection it is worth noting that isopropylidene derivatives are particularly well suited to gas chromatographic separation and purification[15]; this technique has been used in our work to isolate these derivatives on a small scale. As it was considered important for any practical application to be able to use very small amounts of the original carbohydrate, a technique for the derivatization of about 1 mg. was devised. Most of the compounds to be discussed were prepared in this manner. The technique was also very convenient for the preparation of the deuterioisopropylidene derivatives[16] used here to confirm the proposed fragmentation mechanisms but which should also prove valuable in the mass spectrometric determination of the structure of new sugars.

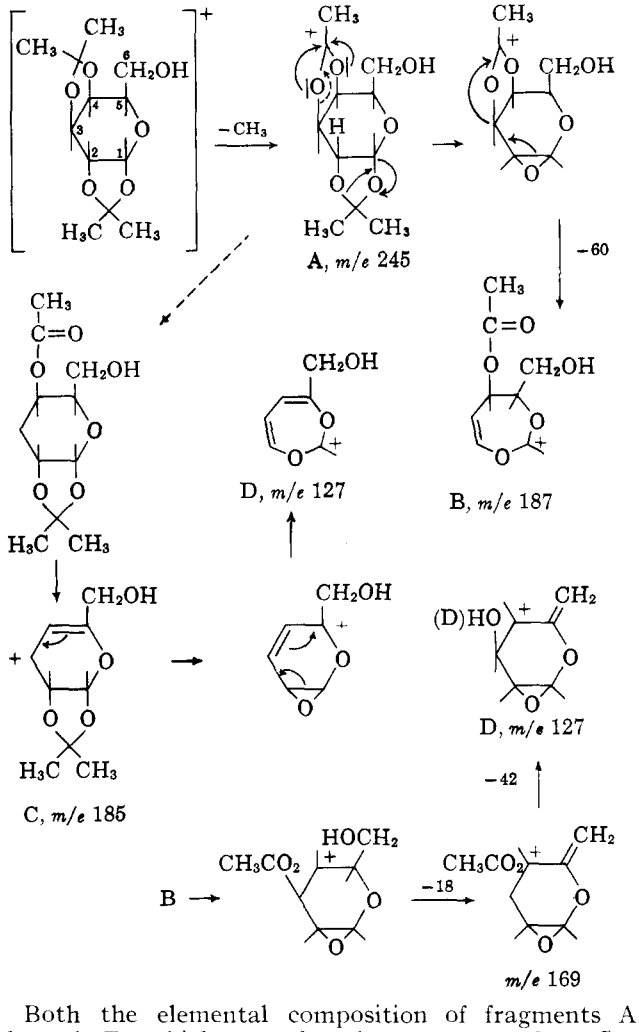
(15) H. W. Kircher in "Methods in Carbohydrate Chemistry," Vol. I, R. L. Whistler and M. L. Wolfrom, Ed., Academic Press, Inc., New York, N. Y., 1962, p. 13.

(16) Addition of the letter "a" to the formula number refers to the derivative prepared using acetone-d_6. Thus IIa is di-O-isopropylidene-d_{12}-D-galactopyranose, and XIVa is mono-O-isopropylidene-d_6-D-ribofuranose. Only the spectrum of IIa is shown (Fig. 2a) as an illustration of the changes in the spectrum due to deuterium labeling. The numbers shown in parentheses in Fig. 1, 3–6, 8, 9 are the *m/e* values of the corresponding peak in the spectrum of the deuterium-labeled analog, unless their mass remains unchanged.

Di-O-isopropylidene Derivatives. Aldopyranoses.—As a typical representative of this group, the mass spectrum of 1,2:3,4-di-O-isopropylidene-D-galactopyranose (II) is shown in Fig. 2 along with its d_{12}-analog (IIa, Fig. 2a). The more important peaks in the higher mass range are found at *m/e* 245 (M − 15, fragment A), 187 (M − 15 − 58, fragment B), 185 (M − 15 − 60, fragment C), and 127 (M − 15 − 58 − 60, fragment D). These fragments are formed by the consecutive loss of parts or all of the two O-isopropylidene groups and are thus found in all di-O-isopropylidene derivatives.

Fragment A arises by loss of a methyl group from the molecular ion as discussed above. The resulting ion of *m/e* 245, the exceptional abundance of which is due to the stabilization of the positive charge by one of the two neighboring oxygen atoms, further loses either acetic acid or acetone, or both (see Scheme I), leading to fragments B (*m/e* 187), C (*m/e* 185), and D (*m/e* 127). The available data do not permit a distinction between the loss of a methyl group from the 1,2-O-isopropylidene group and the loss of methyl from the analogous grouping attached to C-3 and C-4, the process shown in Scheme I.

SCHEME I

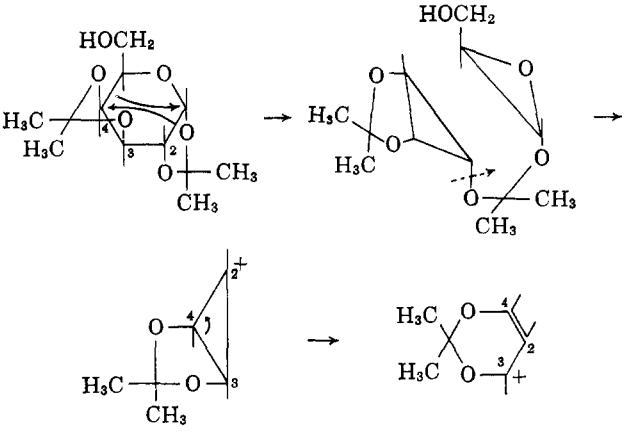


Both the elemental composition of fragments A through D, which were found to correspond to $C_{11}H_{17}O_6$ (found 245.1027; +0.3), $C_8H_{11}O_5$ (found 187.0602; −0.4), $C_9H_{13}O_4$ (found 185.0808; −0.5), and $C_6H_7O_3$ (found 127.0404; +0.9) as well as the mass spectrum (Fig. 2a) of the d_{12}-analog IIa is in agreement with the proposed fragmentation path. Figure 2a exhibits the corresponding peaks at *m/e* 254 (245 + 9), 191 (185 + 6), and 190 (187 + 3). The last-mentioned peak confirms that the loss of 58 mass units involves the elimination of acetone without participation of any one of the hydrogen atoms of the methyl groups, therefore justifying writing the ion of mass 185 as an epoxide, a structural element also known in carbohydrate derivatives (1,2-anhydro-sugars, such as "Brigl's anhydride").[17,18]

The rather low intensity of *m/e* 185, as contrasted to *m/e* 187, seems to indicate that loss of acetone is favored over loss of acetic acid from ion A. Further decomposition of either one of these fragments leads to mass 127, which may be written as a dioxacycloheptatriene ion (D). The formation of the fragment of mass 127, seems, however, to be more complex because in the deuterated derivative IIa it is found equally distributed over mass 127 and 128, indicating that, in part, one deuterium atom present in the methyl groups is retained. This can be rationalized assuming a second path for the elimination of the elements of acetic acid from fragment B involving the loss of water to give $C_8H_9O_4$ (found 169.0491; −1.0) and ketene.

It should be noted that the elimination of acetone on the one hand and of acetic acid on the other must involve two different 1,3-dioxolane rings, and fragments of type B and D are thus not formed from mono-O-isopropylidene derivatives (*e.g.*, XIV and XV, Fig. 5 and 6).

The fragment of mass 113 has the elemental composition $C_6H_9O_2$ (found 113.0606; +0.4) and shifts to *m/e* 119 in the deuterated analog IIa. Fragment E is in agreement with these facts.

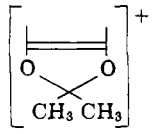


Fragment E would thus be analogous to a fragment quite abundant in the spectra of the acetates and methyl ethers of carbohydrates and which has been interpreted to contain C-2, C-3, and C-4, retaining two substituents (*m/e* 157 in the pentaacetates of I and III, for example).[3,4]

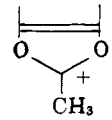
A fragment of mass 100 seems to be common not only to di-O-isopropylidene derivatives of aldopyranoses but to all compounds containing two dioxolane or dioxane moieties attached to pyranose or furanose rings. Both the elemental composition of this species, $C_5H_8O_2$ (found 100.0516; −0.8), and the shift to mass 106 in the deuterated analog are consistent with structure F_1 of this fragment which may lose one of the methyl groups to give ion F_2, $C_4H_5O_2$ (found 85.0284; −0.5); the latter can be derived also from the $(M - 15)^+$ ion directly. Exceptions are the fructose and sorbose derivatives XVIII and XXII where this peak is found at mass 130 (Fig. 9) because of the CH_2OH group attached to this moiety. The spectrum (Fig. 1) of the glucose derivative V also lacks comparatively intense peaks of *m/e* 85 and *m/e* 100, most probably because of the predominance of another fragmentation process,

(17) P. Brigl, *Z. physiol. Chem.*, **122**, 245 (1922).
(18) See also ref. 7, pp. 220-225.

namely, cleavage of the C-4, C-5 bond (resulting in the intense fragment of mass 101).



F_1, m/e 100

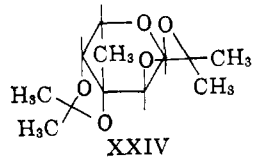


F_2, m/e 85

It is of interest to note that mono-O-isopropylidene derivatives do not exhibit a prominent peak at m/e 100 but one at m/e 85 (see Fig. 5 and 6). This is attributed to the facile loss of one methyl group (M − 15), a species which cannot fragment further to give the ion of mass 100 (F_1) but only of mass 85 (F_2).

There are two prominent peaks in the lower mass range, namely at m/e 43 and 59, which are common to all O-isopropylidene derivatives. The former corresponds to C_2H_3O and the latter to C_3H_7O; they contain one and two methyl groups, respectively, from the O-isopropylidene moiety as evidenced by the shift to m/e 46 and 65 in the mass spectra of the compounds prepared with acetone-d_6. The formation of mass 59 involves the elimination of acetone and one additional hydrogen atom as protonated acetone, a positive ion of high stability. It finds its analogy in the fragments of mass 103 (protonated acetic anhydride) in the spectra of the polyacetates of carbohydrates.[3] The ion of mass 43 results from the loss of CH_3CO^+ from an acetoxyl group formed during the fragmentations outlined in Scheme I.

Other ions in the region of mass 60 to 100 in the mass spectra of the pyranose derivatives must involve a complex fragmentation of the molecule to form relatively stable ions. To those belong the peaks at m/e 99 ($C_5H_7O_2$: found 99.0444; −0.1), 83, and 69 in the mass spectra, respectively, of II, the L-fucose derivative XXIV,[19] and VII which can be written as substituted



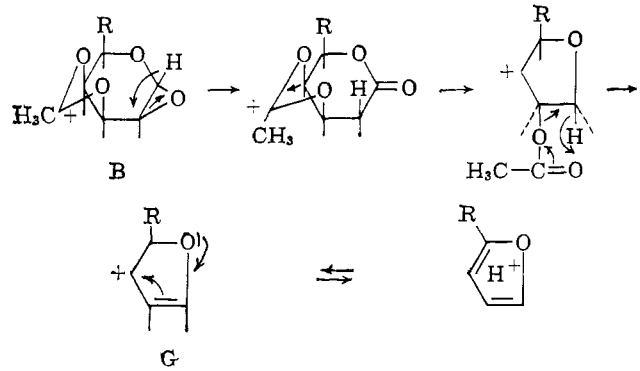
XXIV

dihydrofuryl ions (G) or protonated furanes (R = H, m/e 69; R = CH_3, m/e 83; R = CH_2OH, m/e 99). The comparatively low intensity of the peak at mass 99 in the spectrum of II (Fig. 2) may be due to further fragmentation involving the elimination of water, carbon monoxide, or formaldehyde leading to the species of mass 81 (C_5H_5O: found 81.0343; +0.3), 71 (C_4H_7O: found 71.0488; −0.8), and 69 (C_4H_5O: found 69.0337; −0.3). The corresponding peaks in the spectra of VII (Fig. 3) and XXIV are absent, as these processes require the oxygen atom at C-6.

The spectra of the d_{12}-analogs permit the conclusion that none of the methyl groups of the isopropylidene moieties, nor any hydrogen atoms thereof, are retained in these fragments (no shift to higher masses), but specific ^{13}C and ^{18}O labeling would be required to deduce the source of all atoms therein. A plausible, but still speculative, mechanism would involve a hydride shift, loss of carbon monoxide and acetic acid from fragment B.

Otherwise the spectra of the di-O-isopropylidenepyranoses, *e.g.*, the derivatives L-arabinose (VII) and L-fucose (XXIV), are rather similar to the spectrum of II, with the exception that the fragments containing C-5 are found 16 (CH_3 *vs.* CH_2OH) and 30 (H *vs.* CH_2OH) mass units lower.

(19) K. Freudenberg and K. Raschig, *Chem. Ber.*, **60**, 1633 (1927).

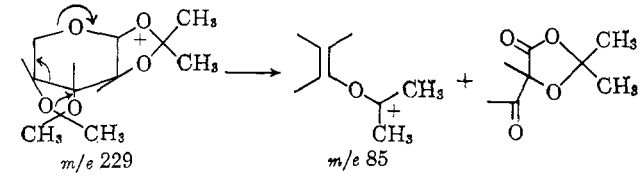


B

G

Ketopyranoses.—Of the two isomeric di-O-isopropylidene derivatives of fructose, namely, 2,3:4,5-di-O-isopropylidene-D-fructopyranose (XVIII)[7] and 1,2:4,5-di-O-isopropylidene-D-fructopyranose (XIX),[7] the former, XVIII, differs from the galactose derivative II, aside from the absolute stereochemistry, mainly in the attachment of the CH_2OH group. It is located at a ketal-carbon atom (C-2) in XVIII, whereas it is attached to a less highly substituted ether carbon atom in II. While the similarity in the gross structure of the two compounds gives rise to fragments of the same mass in both compounds (compare Fig. 2 and 7) the intensity of many of these peaks is quite different if the formation of the fragment involves rupture of a bond at or near the CH_2OH group. Thus the loss of this group, leading to a $C_{11}H_{17}O_5$ ion (found 229.1068; −0.7) is appreciable (in contrast to II). It is followed by further loss of the elements of acetone to give a fragment $C_8H_{11}O_4$ (found 171.0660; +0.3).

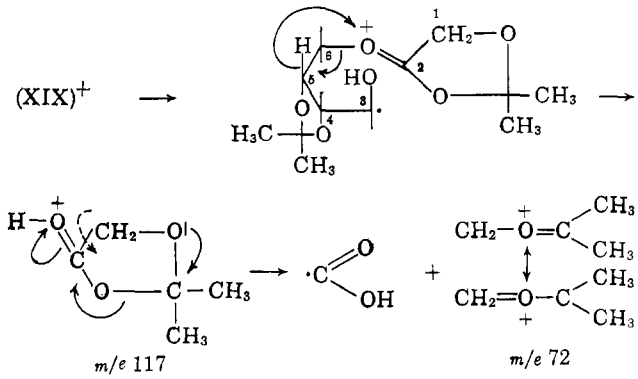
On the other hand, retention of the CH_2OH group at the 2,3-O-isopropylidene moiety gives rise to peak F_1 at m/e 130 ($C_6H_{10}O_3$ found 130.0636; +0.6) rather than m/e 100, as in II (fragment F_1). The low intensity of the peak at mass 100 and the high abundance of the ion of mass 85 seem to indicate that in di-O-isopropylidene derivatives the former is mainly derived from the dioxolane ring adjacent to the tetrahydropyran oxygen, while the ion of mass 85 comes to a considerable extent from the M − 15 fragment. It should be pointed out that the peak at mass 85 can be resolved into a doublet, namely C_5H_9O and $C_4H_5O_2$, but the latter one (fragment F_2) is in all cases by far the more abundant one. The species C_5H_9O seems to be responsible for the partial shift of the peak of mass 85 to m/e 91 in the d_{12}-analog XIXa (most of the species, however, shift to mass 88) indicating that two methyl groups derived from acetone are retained in this minor fragment of mass 85. An attractive mechanism for its formation involves fragmentation of the species of mass 229



m/e 229 m/e 85

The mass spectrum of isomer XIX (Fig. 8) differs markedly from the spectrum of XVIII due to the variation in the attachment of one of the dioxolane rings. The most pronounced differences are the absence of the peak at mass 229 in Fig. 8 because in XIX the CH_2OH group of fructose is not free but part of a ring, and the presence of rather intense peaks at m/e 117 and m/e 72 which, in turn, are absent in all other O-isopropylidene derivatives. Both fragments, mass 117 and 72, are believed to contain the dioxolane ring at-

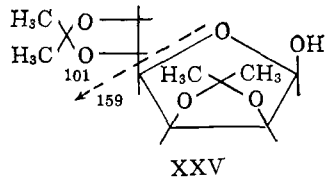
tached to C-2 or parts thereof. The genesis of the fragment of mass 117 ($C_5H_9O_3$: found 117.0557; +0.6) most probably involves the cleavage of the C-2, C-3 bond, followed by rearrangement of hydrogen from C-5 to the tetrahydropyran oxygen with simultaneous cleavage of the C-5,O bond



m/e 117 *m/e* 72

The shift of this peak to mass 123 in the d_{12}-analog XIXa is in agreement with this proposal. The species of mass 72 (C_4H_8O: found 72.0585; +1.0) must involve C-1 and the three carbons of acetone, as it shifts to *m/e* 78 in XIXa, and is probably formed by the elimination of CO_2H from mass 117 (broken arrow). The fragment of mass 144 corresponds to elimination of two molecules of acetone from the molecular ion.

Aldofuranoses.—The di-O-isopropylidene derivatives (V and XXV)[7] of glucofuranose and mannofuranose have very similar spectra (*e.g.*, Fig. 1 for V) which differ, however, greatly from those of aldopyranoses, as mentioned above.



XXV

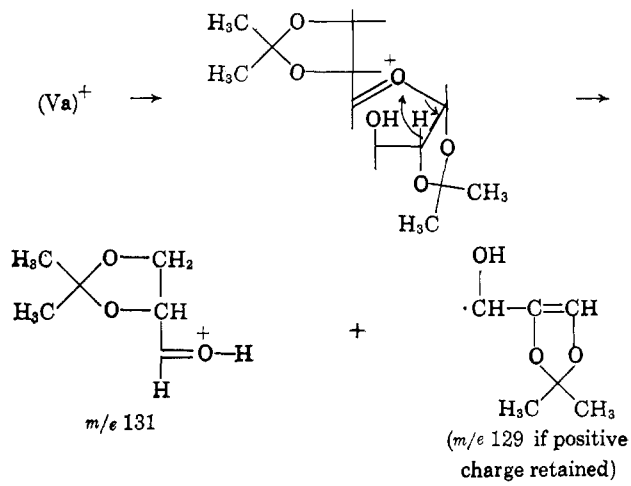
The most characteristic fragmentation process is the rupture of the C-4, C-5 bond resulting in a positive charge next to a ketal oxygen. The elemental composition of this fragment, $C_5H_9O_2$ (found 101.0604; +0.2), and its shift to *m/e* 107 in the d_{12}-analog Va support this assignment.

The fragments A, B, C, and D, typical for di-O-isopropylidene derivatives as discussed earlier, are also present but in reduced relative intensity, because of the competitive cleavage of the C-4, C-5 bond.

The pair of peaks at *m/e* 129 and 131 seem to represent the two halves of the molecule with loss or addition of a hydrogen as deduced from the elemental composition, $C_6H_9O_3$ (found 129.0560; +0.9) and $C_6H_{11}O_3$ (found 131.0711; +0.3), respectively, and the shift to *m/e* 135 and 137 in the spectrum of the d_{12}-analog Va.

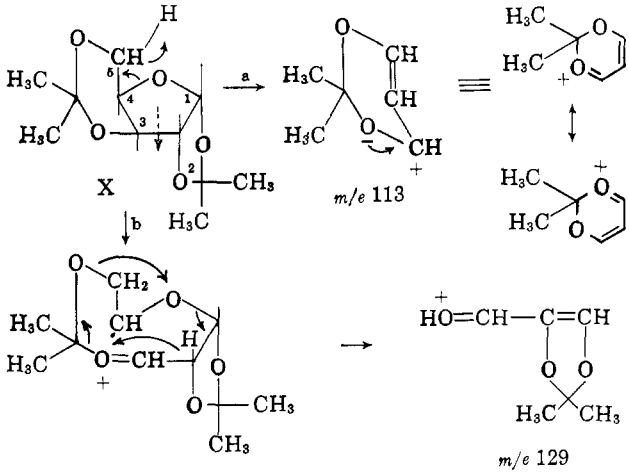
While the spectra of V and XXV are, in general, very similar, XXV has a more intense M − 17 peak due to the attachment of OH to C-1 rather than to C-3.

As outlined earlier, xylose, like glucose and mannose, can form a di-O-isopropylidene derivative (X) only in its furanoid form, but the absence of C-6 necessitates the formation of a 1,3-dioxane ring involving C-3, C-4, and C-5. The absence in X of a single bond connecting two parts of the molecule (C-4, C-5 in V and XXV) leads to a spectrum (Fig. 4) radically different from those of the hexofuranose derivatives (*e.g.*, Fig. 1) but resembles more those of the other di-O-isopropylidene derivatives, with intense fragments A



m/e 131 (*m/e* 129 if positive charge retained)

(*m/e* 215), B (*m/e* 157), C (*m/e* 155), D (*m/e* 97), F_1 (*m/e* 100), F_2 (*m/e* 85), and *m/e* 59 and 43. Significant are the peaks at *m/e* 113 and *m/e* 129, both of which shift six mass units in the d_{12}-analog Xa but only the latter is found 30 mass units higher (CH_2OH *vs.* H) in the sorbose derivative XXII (Fig. 9), which exhibits peaks at *m/e* 113 and 159. On the basis of these facts the formation of these ions may be represented as



X *m/e* 113 *m/e* 129

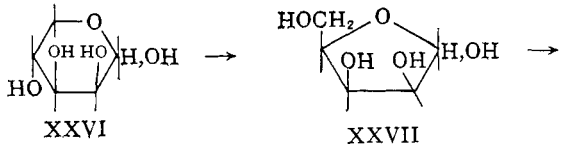
Admittedly, path b is rather involved, but it consists of reasonable steps leading to a fragment whose structural elements agree with the requirements of the spectra (two methyl groups derived from acetone and retention of C-1, which carries the CH_2OH group in XXII).

Ketofuranoses.—The only representative of this group investigated is the sorbose derivative XXII, the spectrum of which was discussed above along with the aldopentofuranose derivative X. Compound XXII differs from X mainly in the additional CH_2OH group (aside from the different stereochemistry) and this is borne out by the pronounced loss of 31 mass units leading to the peak at *m/e* 229, a fragment that easily loses 58 mass units resulting in the peak at *m/e* 171. Both processes have been discussed earlier in connection with XVIII (Fig. 7) which contains a similar structural entity.

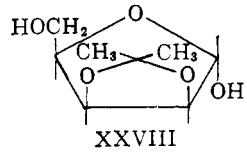
Mono-O-isopropylidene Derivatives. Aldofuranoses.—For reasons discussed at the outset of this paper, some of the pentoses, such as ribose (XI and XIII) and lyxose (XXVI and XXVII), react only with one mole of acetone to form a mono-O-isopropylidene derivative, such as XIV[10] and XXVIII,[20] respectively. This is reflected in the molecular weight, deducible from the M − 15 peak found at *m/e* 175 in the spectrum of XIV

(20) R. Schaffner, *J. Research Natl. Bur. Standards*, **65A**, 507 (1961).

(Fig. 5) and of XXVIII, in contrast to the derivatives (VII and X) of arabinose and xylose (Fig. 3 and 4, respectively) in which the corresponding peak is at *m/e* 215 (indicating a mol. wt. of 230).



XXVI XXVII

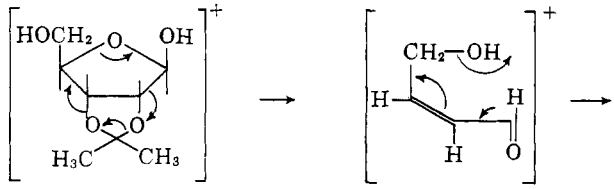


XXVIII

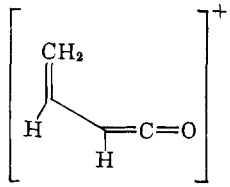
Those of the fragments A through F, common for all di-O-isopropylidene derivatives, which require one intact O-isopropylidene group in the M − 15 species cannot be found in mono-O-isopropylidene derivatives. Thus fragments B and D cannot be formed because their genesis (see Scheme I) requires the loss of CH_3-$COCH_3$ from a species (A or C) that has previously lost a methyl group from one O-isopropylidene moiety. For similar reasons, ion F_1 of mass 100 cannot be formed either. The presence of a free hydroxyl group in XIV and XXVIII permits elimination of water as an alternative, leading to the peaks at *m/e* 157 (M − 15 − 18) and *m/e* 97 (M − 15 − 60 − 18).

Loss of the substituents (CH_2OH and OH, respectively) at the α-carbons of the tetrahydrofuran ring is a significant process, leading to the peaks at *m/e* 173 and 159. Elimination of acetone from the latter gives rise to the ion of mass 101.

The rather intense peaks at *m/e* 86 and 68 are interpreted as (*m/e* 68 could isomerize to a furan ion)



XIV *m/e* 86

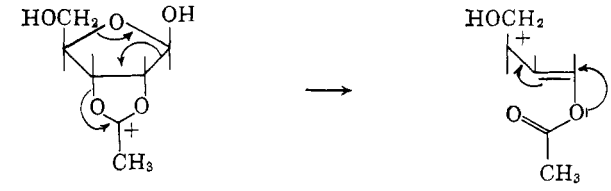


m/e 68

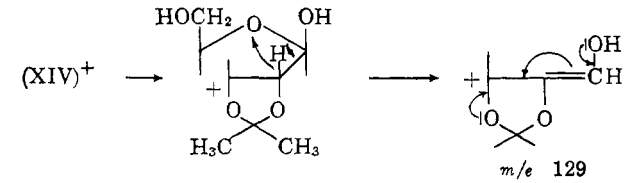
The mass spectrum of XIVa, the d_6-analog of XIV, is in agreement with the postulated fragmentation processes. The peak at *m/e* 85 shifts partly to *m/e* 88 and 91, partly it remains at *m/e* 85 which must be an oxygenated dihydrofuryl ion.

The peak at *m/e* 129 consists of two isomeric ions, one of which contains one (*m/e* 132 in XIVa) and the other two methyl groups (*m/e* 135 in XIVa) of the O-isopropylidene grouping. The latter is probably due to a fragment analogous to the peak at *m/e* 129 in the spectra of aldofuranose derivatives (*e.g.*, V). That part which shifts to *m/e* 132 is thought to be formed from the M − 15 fragment.

The spectrum (Fig. 6) of 2,3-O-isopropylidene-1,5-anhydro-D-ribofuranose (XV) is still simpler than the one of XIV. The molecular weight of 172 (157 + 15) points to a mono-O-isopropylideneanhydropentose.

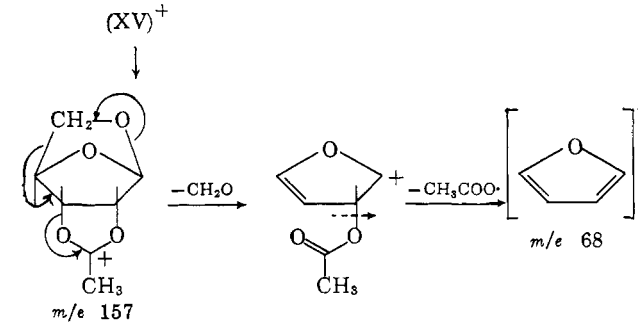


M-15 *m/e* 129 (132 in XIVa)



m/e 129 (135 in XIVa)

The peaks at *m/e* 157 (M − 15), 114 (M − 58), 85 (F_2), 59, and 43 are due to fragmentation processes discussed earlier. The formation of the ion of *m/e* 68 must involve the loss of the "anhydro-bridge" and the isopropylidene group, possibly by further fragmentation of the M − 15 species



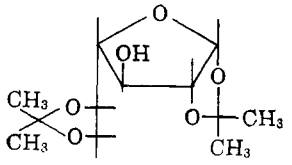
m/e 157 *m/e* 68

The discussion of mass spectra presented above indicates the kind and magnitude of information that can be deduced from the spectrum of the product of the reaction of a monosaccharide with acetone under ketalization conditions. To reach conclusions of this type by conventional means would require more-or-less elaborate chemical transformation or degradation of the O-isopropylidene derivative and would thus consume much more time and material. The mass spectra of such derivatives may therefore be useful in the characterization or structure determination of carbohydrates.

The elucidation of the structure of an as yet unreported di-O-isopropylidene derivative of D-galactose may serve as an illustration of the use of this technique. While the crude product obtained on treatment of D-galactose with acetone, anhydrous cupric sulfate, and 0.5% sulfuric acid at room temperature is reported[21] to yield only 1,2:3,4-di-O-isopropylidene-D-galactopyranose (II), gas chromatography indicates the presence of another product (less than 3%). If the reaction is, however, carried out at elevated temperature and in the absence of mineral acid (see Experimental), the minor product is formed in a much larger amount (about 20%). The mass spectrum of this material is practically identical with the spectrum (Fig. 1) of the 1,2:5,6-di-O-isopropylidene-D-glucofuranose derivative V; the new compound must thus be 1,2:5,6-di-O-isopropylidene-D-galactofuranose (XXIX).

While this compound was obtained in this case from pure D-galactose, as further established by the formation of almost pure II under the slightly different conditions of Levene and Meyer,[21] all other epimeric 1,2:-

(21) P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, **92**, 257 (1931).



XXIX

5,6-di-O-isopropylidenehexofuranoses could easily be excluded also on the basis of the optical rotation of the hydrolysis product. The rotation of a solution of XXIX after hydrolysis with 0.1 *N* hydrochloric acid was in agreement only with the equilibrium value of D-galactose which is quite different from all other hexoses, the stereochemistry of which could permit the formation of a 1,2:5,6-di-O-isopropylidenehexofuranose. Furthermore, the melting point of XXIX differs from that of V and XXV. Thus the second di-O-isopropylidene-D-galactose has structure XXIX.

Experimental

Mass Spectra.—The spectra were determined with a CEC 21-103C mass spectrometer, equipped with a heated stainless steel inlet system operated at 170°; ionizing potential 70 e.v., ionizing current 50 μamp., temperature of the ion source 250°. The sample (~0.5–1.0 mg.) was sublimed from a glass tube into the reservoir (3 l.).

High resolution spectra were determined[13] with a CEC 21-110 double focusing mass spectrometer, equipped with a glass inlet system operated at 200°; ionizing current 250 μamp., ionizing potential 150 e.v.

1,2:4,5-Di-O-isopropylidene-d_{12}-D-fructopyranose (XIX).—D-Fructose (170 mg.) was dissolved in deuterium oxide to replace the hydroxyl protons with deuterium. After evaporation of the excess deuterium oxide, the residue was converted to the di-O-isopropylidene derivative[22] using acetone-d_6 in place of acetone. The product had m.p. 115–120° which was undepressed on admixture of authentic, nondeuterated material (lit.[22] 119.5°). The mass spectra of the product when purified either by recrystallization or by gas chromatography (3% SE-30, 165°) were identical, thus proving that no changes occur on gas chromatographic separation.

1,2:5,6-Di-O-isopropylidene-d_{12}-D-glucofuranose (V).—D-Glucose (100 mg.) was similarly converted to D-glucose-O-d_6; the di-O-isopropylidene derivative was prepared[23] by treating this with acetone-d_6; m.p. 109–110° (reported[24] for unlabeled material, 109–110°).

1,2:3,4-Di-O-isopropylidene-D-galactopyranose (II), 1,2:5,6-Di-O-isopropylidene-D-galactofuranose (XXIX), and Their d_{12}-Analogs IIa and XXIXa.—A mixture of 10 mg. of D-galactose, 50 mg. of cupric sulfate, and 0.8 ml. of acetone was sealed in an ampoule and heated on a steam bath for 18 hr. The acetone layer was separated and made slightly basic with potassium carbonate. After evaporation of the excess acetone, the residue was shown by gas chromatography (Apiezon L, 200°) to consist of two components (ratio 4:1), in addition to traces of acetone and its self-condensation products. Both components were collected; the mass spectrum of the larger fraction was found to be identical with the spectrum of 1,2:3,4-di-O-isopropylidene-D-galactopyranose (II) prepared by the method of Levene and Meyer[21] (by this procedure only a trace, less than 3%, of the second component is detectable by gas chromatography). The smaller, slower-moving fraction was a solid, m.p. 97.5–98.5°; it has been assigned the structure 1,2:5,6-di-O-isopropylidene-D-galactofuranose (XXIX) for reasons discussed above.

Samples of both di-O-isopropylidene-D-galactoses (II and XXIX) were each dissolved in 1.00 ml. of 0.1 *N* hydrochloric acid and hydrolyzed for 2 hr. at 100°. The optical rotations of the resulting solutions were measured: D-galactose from derivative II, $[\alpha]^{32}D$ +78° (0.1 *N* HCl, *c* 0.55) and D-galactose from derivative XXIX, $[\alpha]^{32}D$ +75° (0.1 *N* HCl, *c* 0.19); lit. $^{25}[\alpha]^{32}D$ +77.4° (H_2O, *c* 11.4).

1,2:3,4-Di-O-isopropylidene-L-arabinopyranose (VII) and its d_{12}-analog, m.p. 40.0° (reported[26] for nonlabeled material, 42°); **2,3:4,6-di-O-isopropylidene-L-sorbofuranose (XXII)** and its d_{12}-analog; **1,2:3,4-di-O-isopropylidene-L-fucopyranose (XXIV)**; **1,2:3,5-di-O-isopropylidene-D-xylofuranose (X)** (prepared on 1 mg. of D-xylose) and its d_{12}-analog; **2,3-O-isopropylidene-D-ribofuranose (XIV)**, **2,3-O-isopropylidene-1,5-anhydro-D-ribofuranose (XV)** and their d_6-analogs; and **2,3-O-isopropylidene-α-D-lyxofuranose (XXVIII)** were prepared by the procedure described above for D-galactose and purified by gas chromatography (3% SE-30, 130–160°).

Acknowledgment.—We are indebted to Prof. R. U. Lemieux for compounds XIX, XVIII, and V. This investigation was supported by research grants (RG-5474 and RG-9352) of the National Institutes of Health, Public Health Service.

(22) H. O. L. Fischer and C. Taube, *Chem. Ber.*, **60B**, 485 (1927).

(23) D. J. Bell, *J. Chem. Soc.*, 1874 (1935).

(24) E. Fischer and C. Rund, *Chem. Ber.*, **49**, 88 (1916).

(25) Rindell, *Neue Ztschr. Rübenzuckerind.*, **4**, 166 (1880); *cf.* "Beilstein," Band 31, p. 298.

(26) P. A. Levene and R. S. Tipson, *J. Biol. Chem.*, **115**, 731 (1936).

[CONTRIBUTION FROM LIFE SCIENCES RESEARCH, STANFORD RESEARCH INSTITUTE, MENLO PARK, CALIF.]

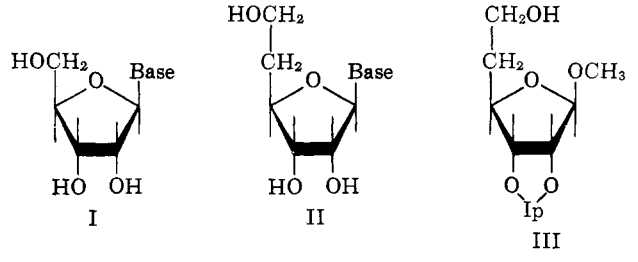
Formation and Hydroboration of an Olefinic Sugar[1]

BY HENRI ARZOUMANIAN, EDWARD M. ACTON,[2] AND LEON GOODMAN

RECEIVED AUGUST 9, 1963

The tosylate VI of methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-allofuranoside (IV) on base-catalyzed elimination afforded the furanose propenyl ether VII, rather than the desired terminal olefin VIII. Hydroboration of VII occurred from the less hindered side to form methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-gulofuranoside (IX), identical with an authentic sample prepared by inverting the rhamnofuranoside tosylate (XI).

The D-ribofuranose moieties I in RNA are connected in this important polymer through a series of 3′,5′-phosphate linkages. If the homologous 5-deoxy-D-allofuranose bases II could be incorporated into nucleic acids, these would probably be linked by 3′,6′-phosphate bonds with attendant changes in the nucleic acid geometry. As a first step in the preparation of II, we were interested in devising a synthesis of hitherto unreported 5-deoxy-D-allose, and this paper reports some efforts in that direction.



I II III

A logical point of departure for the work was the known[3,4] 6-deoxy-D-allose derivative IV, whose con-

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. SA-43-ph-1892. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

(2) To whom reprint requests should be sent.

(3) E. J. Reist, L. Goodman, R. R. Spencer, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 3962 (1958).

(4) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 169 (1936).