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CAPILLARY GAS CHROMATOGRAPHY OF ISOPROPYLIDENE DERIVATIVES OF D-GLUCITOL: CORRELATION BETWEEN STRUCTURE AND RETENTION

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SUMMARY

Reaction products of D-glucitol with acetone and zinc chloride were studied by gas chromatography and gas chromatography–mass spectrometry. Complete separation of the reaction mixtures was achieved on two capillary columns coated with Carbowax 20M and SE-30. The methylene unit values were determined for eleven derivatives of D-glucitol acetals. Correlations were found between the methylene units of the acetals on stationary phases of different polarities and their structures. An attempt is made to explain the relationship between the elution order and the preferred conformers of the D-glucitol acetals. The structures of all derivatives were confirmed by mass spectrometry.

INTRODUCTION

Previous gas–liquid chromatographic (GLC) investigations[1,2] of the reaction of D-glucitol with acetone and zinc chloride to form acetals revealed the presence of eleven peaks: A = 1,2:3,4:5,6-tri-; B = 1,3:2,4:5,6-tri-; C = 3,4:5,6-di; E = 2,3:5,6-di-; F_a = 1,2:3,4-di-; F_b = 1,2:5,6-di-; G = 1,3:5,6-di-; H = 1,2-mono-; J = 2,3-mono-; K = 3,4-mono- and L = 5,6-monoacetals. The structures of the compounds were established by comparison with authentic samples of acetals[3,4]. ^1H NMR and ^{13}C NMR spectroscopy were applied for the identification of compound B[5].

Before the GLC analysis, the crude reaction mixtures were acetylated with a mixture of acetic anhydride and pyridine. The separation of the reaction mixtures was achieved on a packed column, QF-1.

In the present work, a good separation of the O-isopropylidene and O-acetyl-O-isopropylidene derivatives on two capillary columns enabled us to study the behaviour of these compounds. The usefulness of GLC packed and capillary columns coupled with mass spectrometry (MS) in the analysis of sugar derivatives has been demonstrated by several authors[6–8]. Methylene unit, MU, values are reported for eleven glucitol derivatives on a polar and a non-polar phase. The structures of all derivatives were confirmed by MS.

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EXPERIMENTAL

Materials

Acetic anhydride and pyridine were obtained from Fluka (Buchs, Switzerland). Carbowax 20M and SE-30 stationary phases were supplied by Applied Science Labs. (State College, PA, U.S.A.). The glass capillary columns were prepared by The Research Laboratory for Inorganic Chemistry, Hungarian Academy of Sciences, Budapest. The reference compounds were synthesized by the authors.

GLC analysis

An HP 5830 A gas chromatograph with flame ionization detector was equipped with two columns: I, 60 ft. × 0.25 mm I.D., glass capillary coated with Carbowax 20M; II, 30 ft. × 0.25 mm I.D., coated with SE-30. In place of the original injector, an all-glass injection device[9] was used. The inlet pressures for columns I and II were 10 and 12 p.s.i., respectively. The carrier gas and make-up gas was nitrogen; inlet pressure of make-up gas, 28 p.s.i. The temperatures of the flash heater and the detector were 250°C. Separations were carried out by temperature programming at 1°C/min or at 2°C/min.

GLC–MS analysis

An HP 5992 A instrument was used. The MS conditions were: ionization beam energy, 70 eV; electron multiplier voltage, 2800 V. The glass column II was programmed from 140 to 200°C at 2°C/min. The column was connected directly to the mass spectrometer.

Preparation of O-acetyl-O-isopropylidene derivatives

About 0.1 mg of the crude acetylated material was dissolved in pyridine (100 μl) and acetic anhydride (100 μl) and was kept overnight at room temperature.

RESULTS AND DISCUSSION

The MU values were obtained with C_{20}–C_{29} *n*-alkanes on column I, and with C_{14}–C_{20} alkanes on column II. In the range studied, an approximately linear relationship with time was observed for successive *n*-alkanes on Carbowax 20M and SE-30 capillary columns. The column temperature was programmed at 1°C/min on column I and at 2°C/min on column II. The precision of the MU values was 0.01 unit on both columns.

Using the Giddings equation[11], D'Aubigné[10] has shown that the calculation of MU values is valid only if the retention temperatures are greater than 1.09 T_0. (T_0 = initial programme temperature.) This was verified at 160°C on column I and at 140°C on column II for 1,2:3,4:5,6-tri-O-isopropylidene-D-glucitol. All of the compounds gave single peaks on the columns. The MU and ΔMU values for the derivatives are listed in Table I.

Fig. 1 shows the gas chromatogram of the derivatives of D-glucitol on a Carbowax 20M glass capillary column. Fig. 2 shows the corresponding chromatogram obtained on the SE-30 glass capillary column. Three sets of peaks could be differentiated in addition to that of the starting material, hexa-O-acetyl-D-glucitol. The

TABLE I

MU AND ΔMU VALUES FOR O-ISOPROPYLIDENE AND O-ISOPROPYLIDENE-O-ACETYL DERIVATIVES OF D-GLUCITOL ON TEMPERATURE PROGRAMMED SE-30 AND CARBOWAX 20M CAPILLARY COLUMNS

Compound	*MU*		*ΔMU*
	SE-30	*Carbowax 20M*	
A	15.88	20.09	4.21
B	16.11	20.86	4.75
C	17.82	24.05	6.23
D	–	–	–
E	17.98	24.49	6.51
F_a	18.21	24.64	6.43
F_b	17.98	24.64	6.66
G	18.06	24.69	6.63
H	19.39	27.57	8.18
I	–	–	–
J	19.78	27.80	8.02
K	19.78	28.04	8.26
L	19.78	28.09	8.51

first set contains two triacetals (A and B), the second five diacetals (C to G) and the third four monoacetals (H to L). No phase was found which would separate all of the compounds in the second set (Table I), but they could be separated by using two phases.

The ΔMU values, *i.e.*, the differences between the methylene units of the compounds examined on polar and non-polar stationary phases, were used for the identification of reaction products having one, two or three isopropylidene groups. In the present study we wanted to establish the elution order of the isomers and to elucidate whether the separation is due to the interactions of the dioxolane and/or dioxane ring system and of the O-acetyl groups with the stationary phases.

The first set of peaks were perfectly separated on the columns. Compound A, which contains three dioxolane rings attached to each other by single bonds, is very flexible and is believed to form a chain-like molecule (Fig. 3). This compound is eluted before compound B. The presence of two *cis* fused dioxane rings in the latter makes the molecule less flexible: its shape is disk-like (Fig. 3) as the dioxolane ring is equatorially orientated. In this case the importance of dipole forces relative to dispersion effects may be greater on a polar stationary phase. The δMU ($= MU_B^I - MU_A^I$) value is 0.77 on column I and to 0.23 ($= MU_B^{II} - MU_A^{II}$) on column II.

For the second set of peaks the retention times increase from compound C to G. Each of these isomers contains two dioxolane rings, except G which, contains one dioxolane and one dioxane ring (see Fig. 4). The cyclic acetals are symmetrically arranged in C, E and F_a. Isomers F_a and F_b could not be separated on column I, but they were separated on column II. The apolar stationary phase failed to separate isomers E and F_b. The elution order of compounds F_a and G is reversed on the stationary phases. On column II, compound G was eluted before F_a but after E and F_b. Considering isomers C and F_a (Fig. 4), it can be seen that, besides their similar structures, there is a significant conformational difference. It can be assumed that in

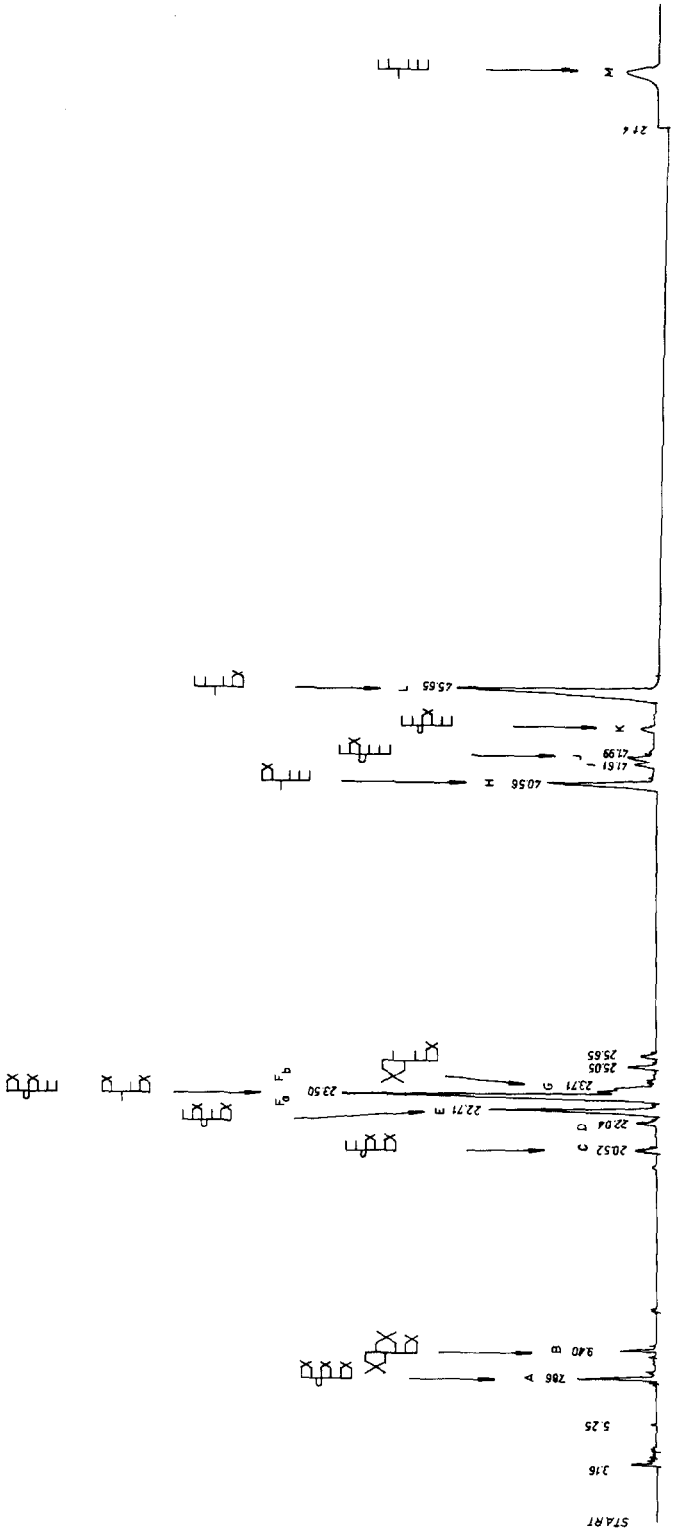

Fig. 1. GLC separation of the *O*-isopropylidene and *O*-isopropylidene-*O*-acetyl derivatives of D-glucitol on Carbowax 20M. The temperature was programmed from 160 to 200°C at 1°C/min. M = hexa-*O*-acetyl-D-glucitol.

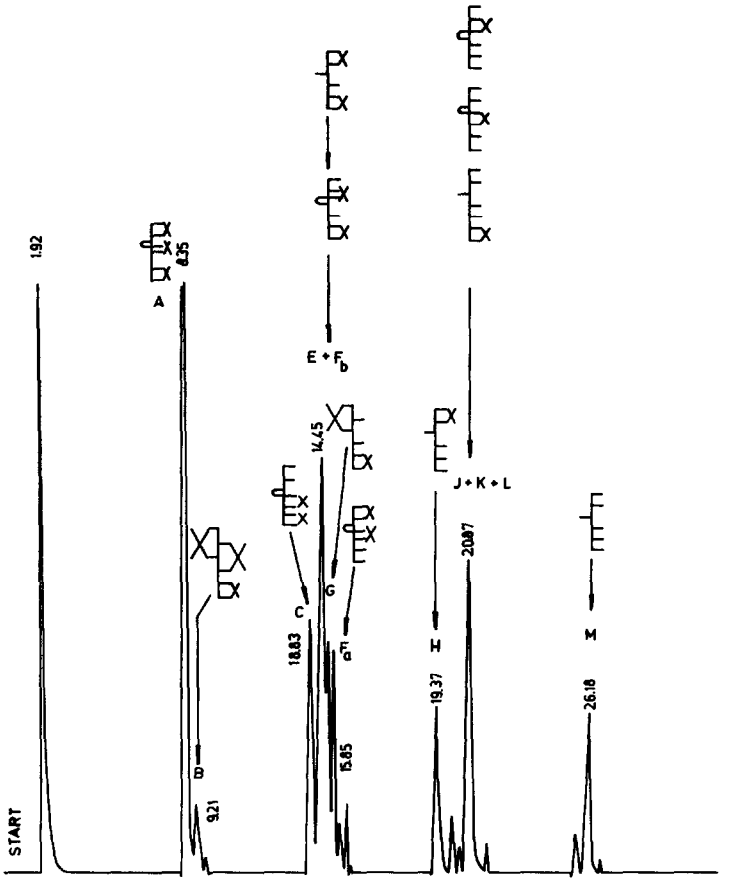

Fig. 2. GLC separation of the O-isopropylidene and O-isopropylidene-O-acetyl derivatives of D-glucitol on SE-30. The temperature was programmed from 140 to 200°C at 2°C/min.

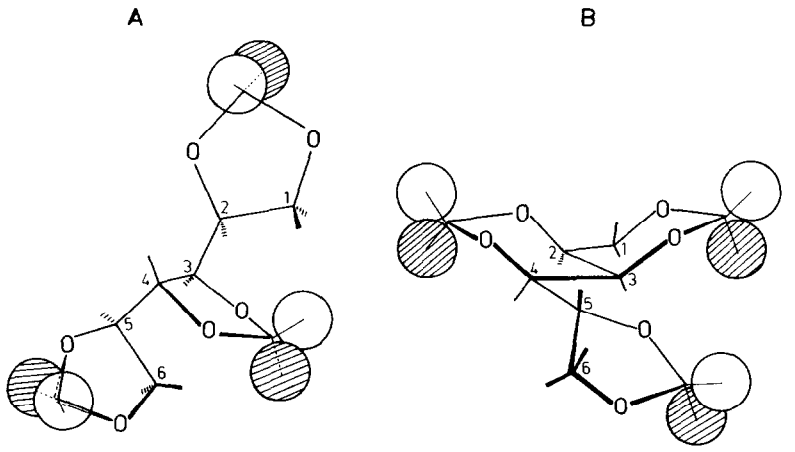

Fig. 3. The preferred conformations of compounds A and B. The filled and hatched circles refer to the two methyl groups of the isopropylidene residues which are not equivalent according to NMR investigations.

the most favourable conformation of both isomers the bulky methyl groups of the dioxolane rings point away from each other thus diminishing thereby their steric interference. It can be further assumed that the vicinal acetoxy groups will be arranged exo with respect to the dioxolane ring to which they are attached. As a consequence, the most polar primary acetoxy group at C-1 in isomer C will be more shielded by the neighbouring dioxolane ring than its counterpart at C-6 in isomer F_a which is arranged antiparallel to the neighbouring dioxolane ring. The less shielded polar group can undergo strong dipole–dipole interactions; consequently F_a will be eluted later from the polar phase than isomer C.

In compound E the two dioxolane rings are attached via a methylene group, consequently this isomer is less flexible than F_b in which the dioxolane rings are bridged by an ethyleneglycol group. The more polar, terminal acetoxy group at C-1 in isomer E is significantly shielded by the *cis*-orientated methyl group of the dioxolane ring, whereas the other acetoxy group at C-4 is shielded by both neighbouring dioxolane rings. On the contrary, in isomer F_b the two vicinal acetoxy groups at C-3 and C-4 are less hindered due to the flexibility of the chain-like arrangement, and can undergo stronger dipole–dipole interactions.

In isomer G the two acetals form a dioxane and a dioxolane ring. Previously[1], a 1,2:4,6-di-O-isopropylidene-D-glucitol structure was proposed for this isomer, which is a precursor in the formation of a new triacetal, the structure of which was presumed to correspond to 1,2:3,5:4,6-tri-O-isopropylidene-D-glucitol. Later[5,12] the structure of this compound was revised to 1,3:2,4:5,6-tri-O-isopropylidene-D-glucitol, consequently the corresponding precursor must have the 1,3:5,6-di-O-isopropylidene structure. Accordingly the acetoxy group at C-2 is directed axially and can form strong dipole–dipole interactions.

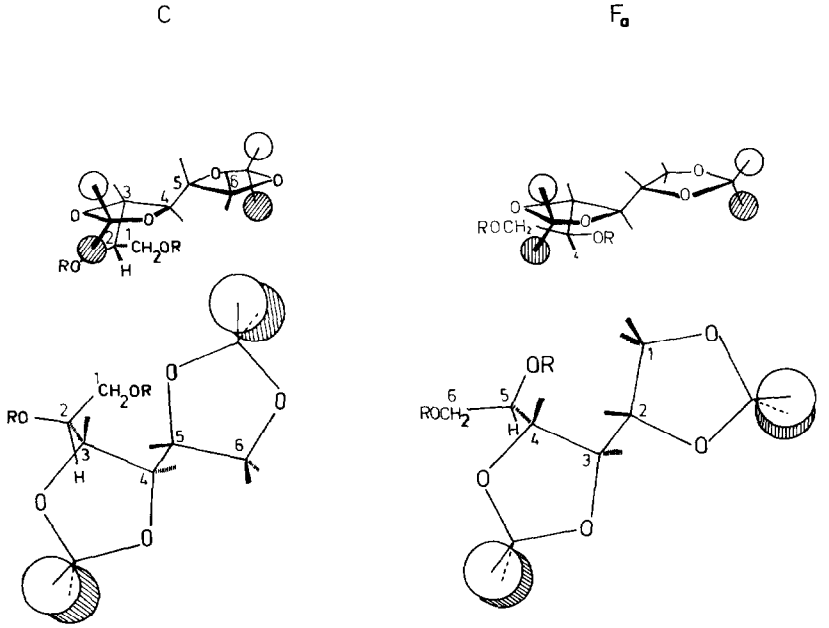

Fig. 4.

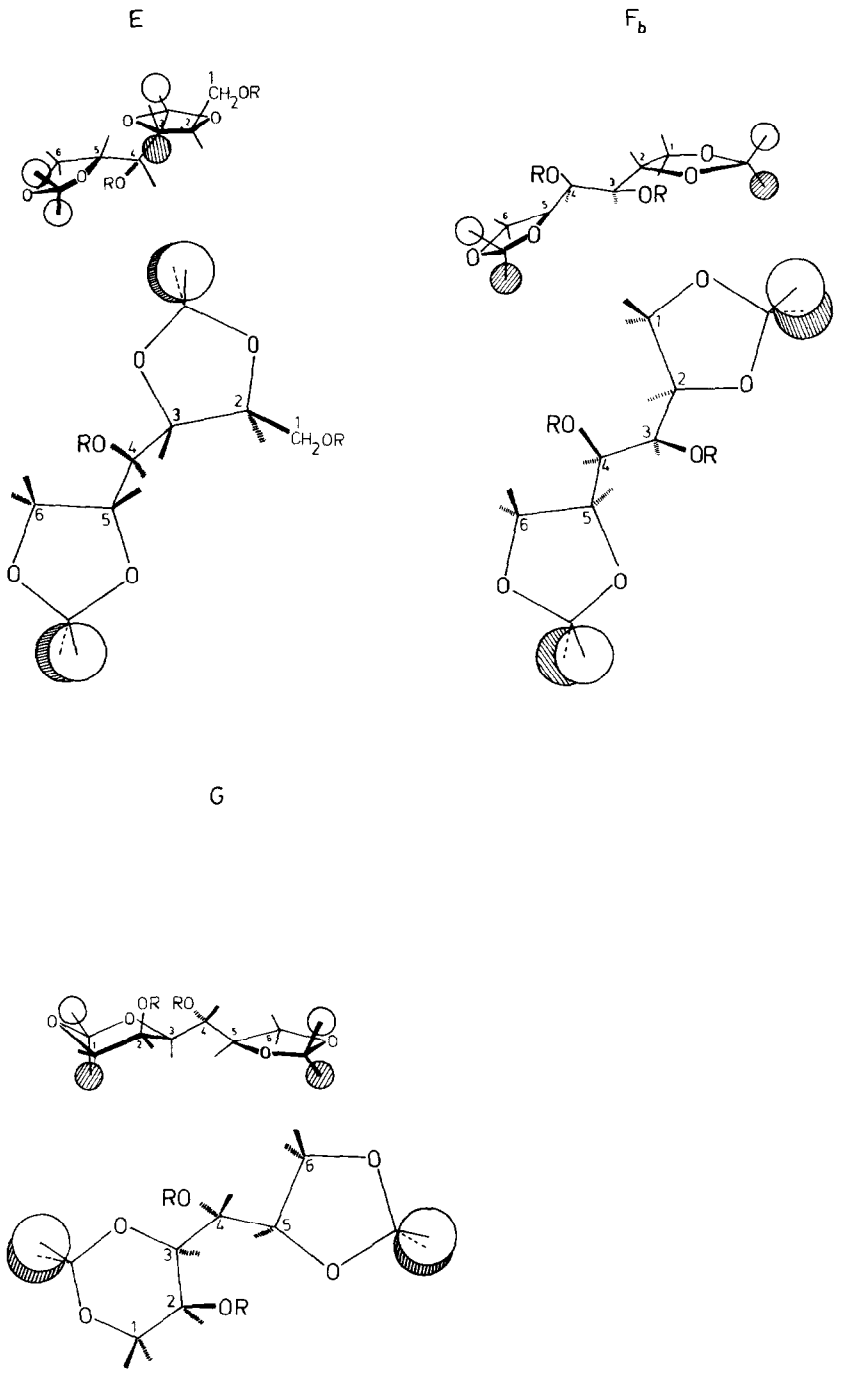

Fig. 4. The preferred conformations of compounds C, E, F_a, F_b and G (steric model and a view of the molecule from above the plane).

TABLE II

PARTIAL MASS SPECTRA OF O-ISOPROPYLIDENE AND O-ISOPROPYLIDENE-O-ACETYL DERIVATIVES

Compound	*Base (m/z)*	*M^+ (m/z)*	*M − 15*		*m/z 273 (%)*	*m/z 245 (%)*	*m/z 187 (%)*	*m/z 169 (%)*	*m/z 153 (%)*	*m/z 127 (%)*	*m/z 115 (%)*	*m/z 101 (%)*	*m/z 85 (%)*
			m/z	*%*									
A	143	302	287	37	–	–	–	61	–	–	11	94	35
B	59	302	287	25	–	–	–	16	–	–	25	100	67
C	101	346	331	29	12	10	17	–	59	44	17	–	83
E	153	346	331	31	27	–	–	–	–	10	92	97	36
F_a	101	346	331	12	23	–	–	–	68	6	14	–	17
F_b	101	346	331	29	14	11	43	–	71	35	14	–	64
G	101	346	331	15	20	–	1.4	–	58	6	11	–	18
H	101	390	375	21	14	–	–	–	50	–	7	–	21
J	153	390	375	53	18	–	29	–	–	41	35	24	77
K	153	390	375	27	15	–	28	–	–	49	29	27	93
L	101	390	375	18	8	–	2	–	64	2	18	–	14

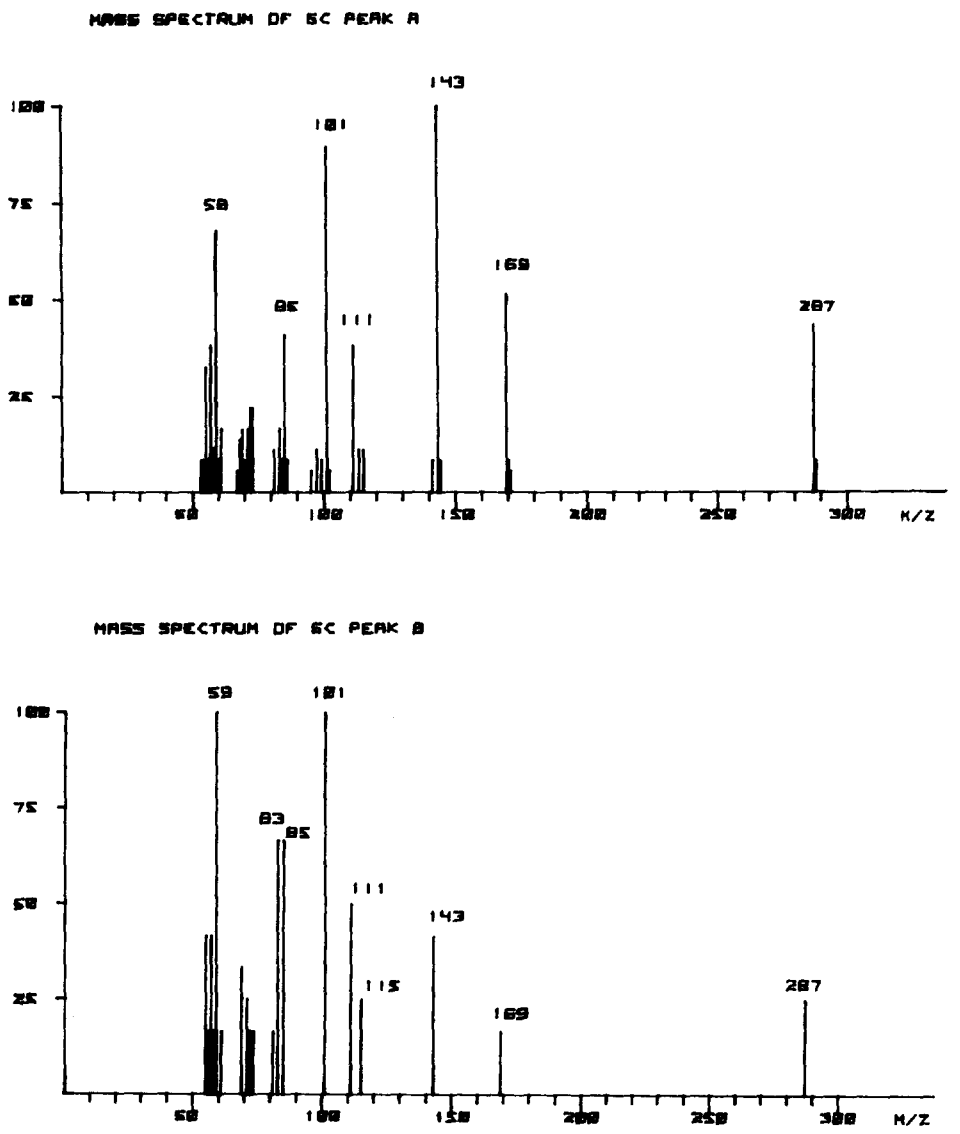

Fig. 5. The mass spectra of compounds A and B.

In the third set of peaks the retention of the monoisopropylidene derivatives of D-glucitol increases from compound H to L on the polar stationary phase. The apolar phase failed to separate all of the isomers. It is proposed that in isomer H the acetoxy groups are *trans-trans-cis* orientated at C-3, C-4 and C-5, while in isomer L the same groups at C-2, C-3 and C-4 are *cis* orientated; thus the interaction of the latter with the polar phase is enhanced. Compound J has a shorter retention time than K. It is supposed that the interactions between the bulky terminal $-CH_2OAc$ (Ac = acetyl) groups decrease the polarity of molecule J much more than of K.

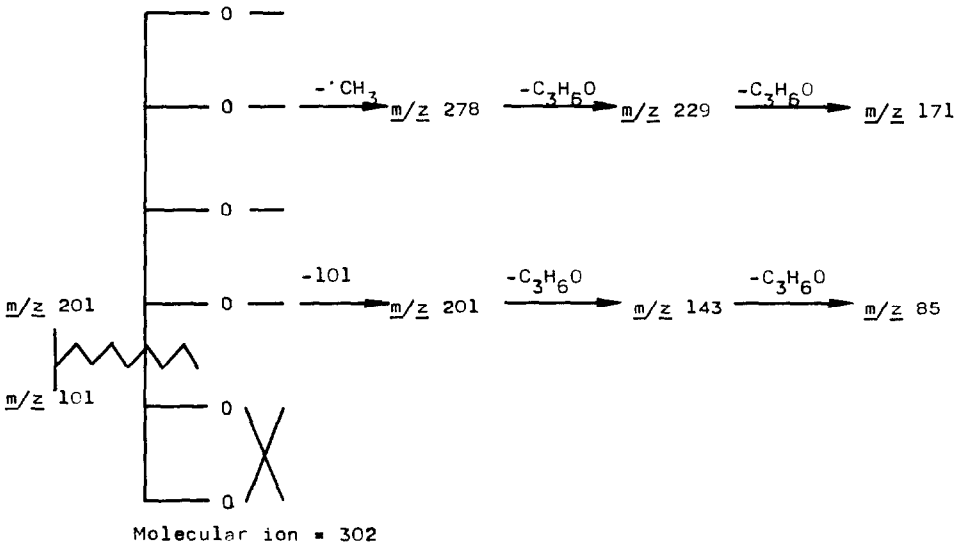

Fig. 6. The main fragmentation of tri-O-isopropylidene D-glucitols.

The mass spectral data for the O-isopropylidene and O-isopropylidene-O-acetyl derivatives of D-glucitol are listed in Table II. Similar fragmentation patterns are exhibited by each series of the mono-, di- and tri-O-isopropylidene derivatives. The fragment ion of highest mass, M − 15, is formed by loss of a methyl radical from an isopropylidene group. The mass spectra of compounds A and B are shown in Fig. 5, and their main fragmentation pattern is depicted in Fig. 6. The ion at *m/z* 143 (201 − C_3H_6O) gives rise to a large signal in the spectrum of A, but to a less intense signal in the spectrum of B. The base peak in the spectrum of B is at *m/z* 59.

The mass spectra of compounds C to G are shown in Fig. 7. Characteristic ions occur at *m/z* 273 (M − $\cdot CH_3$ − C_3H_6O) in the spectra of C, E, F_a, F_b and G, at *m/z* 245 (M − 101) in the spectra of C and F_b. The ion at *m/z* 153 (M − $\cdot CH_3$ − C_3H_6 − $2CH_3COOH$) is abundant in the spectra of C, E, F_a, F_b and G. Large differences in the relative abundances of the ion at *m/z* 143 [M − $\cdot CH(OOCCH_3)CH_2OOCCH_3$ − C_3H_6O] are observed in the spectra of C, E, F_a, F_b and G. This ion is more abundant in the spectra of compounds C and F_b having terminal di-OAc groups. The ion at *m/z* 85 [M − $\cdot CH(OOCCH_3)CH_2OOCCH_3$ − $2C_3H_6O$] in the spectrum of F_b is very abundant, but of lower intensity in the spectra of F_a and G. The ion at *m/z* 187 (M − 101 − C_3H_6O) gives a large signal in the spectrum of F_b, while it is not present or only of very low abundance in those of F_a and G. The ion at *m/z* 201 [M − $\cdot CH(OOCCH_3)CH_2OOCCH_3$] is not observed in the spectra of C and F_b, but that at *m/z* 143, assumed to be due to the loss of acetone from the ion at *m/z* 201, is abundant. The different stereochemistries of these molecules may be the reason for the varying extents of loss of acetic acid from the ion at *m/z* 245, which gives rise to an abundant peak at *m/z* 185 only in the spectrum of C. A characteristic of the fragmentation patterns of the mono- and diisopropylidene derivatives investigated is that after the loss of a radical most of the ions are formed by elimination of the neutral molecules acetone, acetic acid and ketene in various combinations.

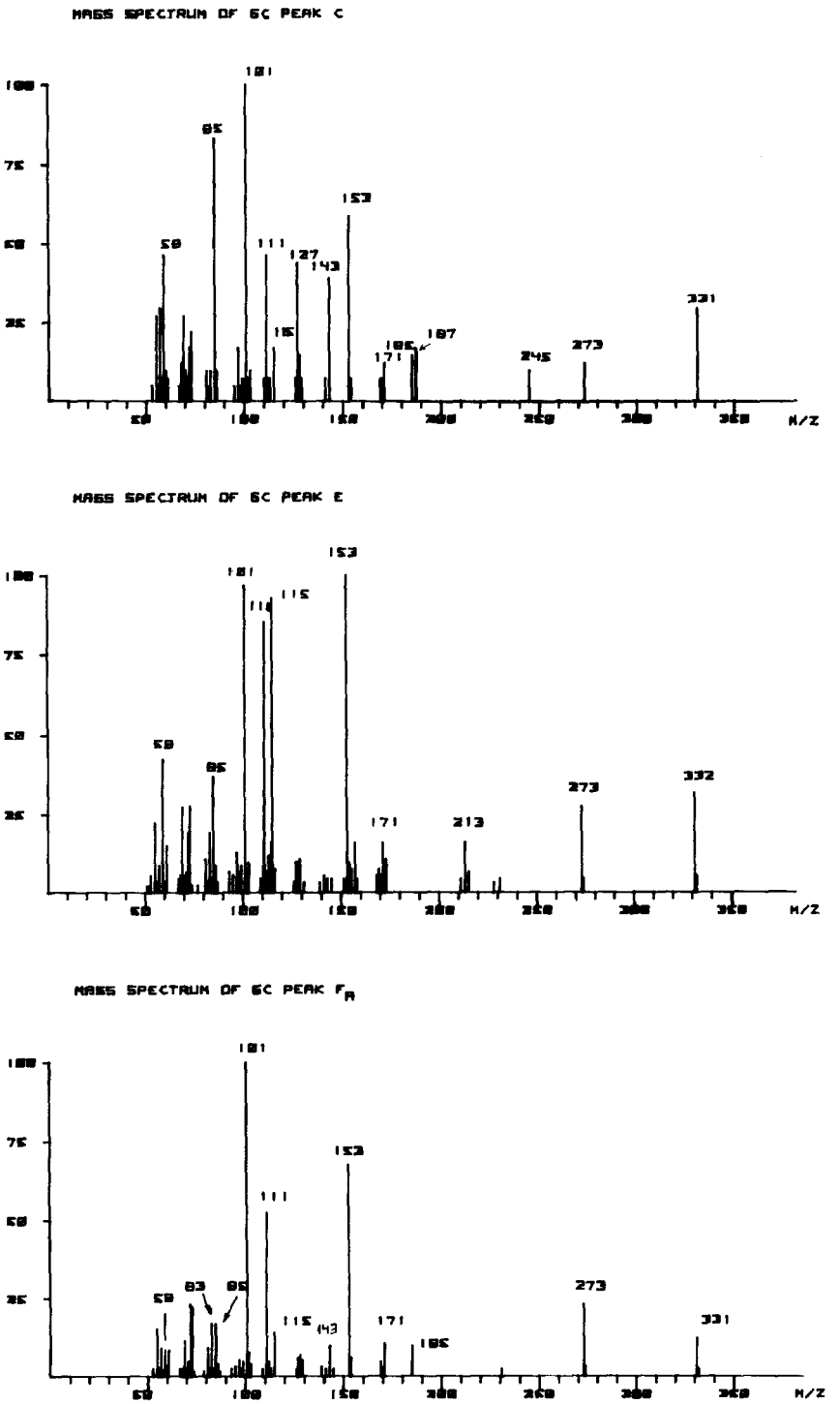

Fig. 7.

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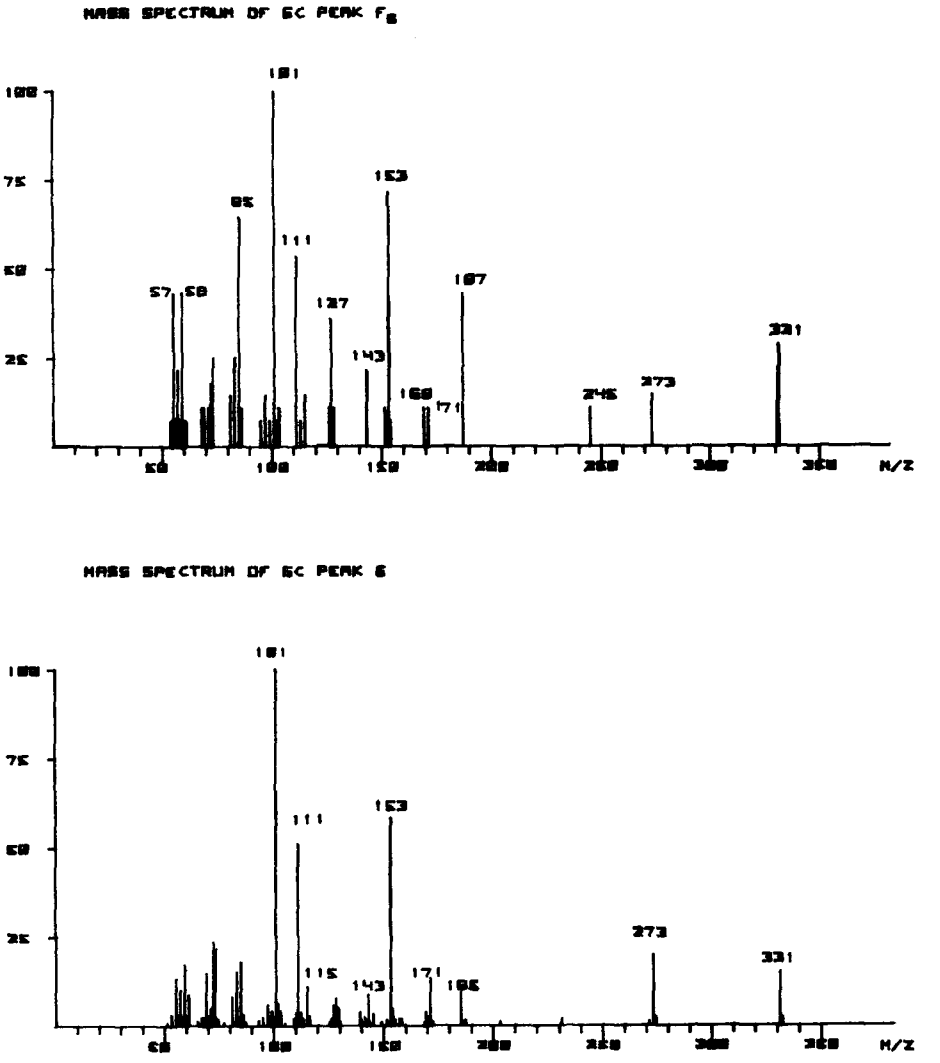

Fig. 7. The mass spectra of compounds C, E, F_a, F_b and G.

The mass spectra of the monoisopropylidene-tetra-O-acetyl derivatives of compounds H to L are shown in Fig. 8. For compounds H and L the ion at m/z 101 is the base peak, and the ion at m/z 153 is less abundant than in the spectra of J and K where it forms the base peak. The ion at m/z 187 (245 − C_3H_6O) is abundant in the spectra of J and K but less abundant in those of H and L. The different spectra reflect the different stereochemistries of these molecules.

CONCLUSIONS

The observed retentions of the O-isopropylidene and O-acetyl-O-isopropyli-

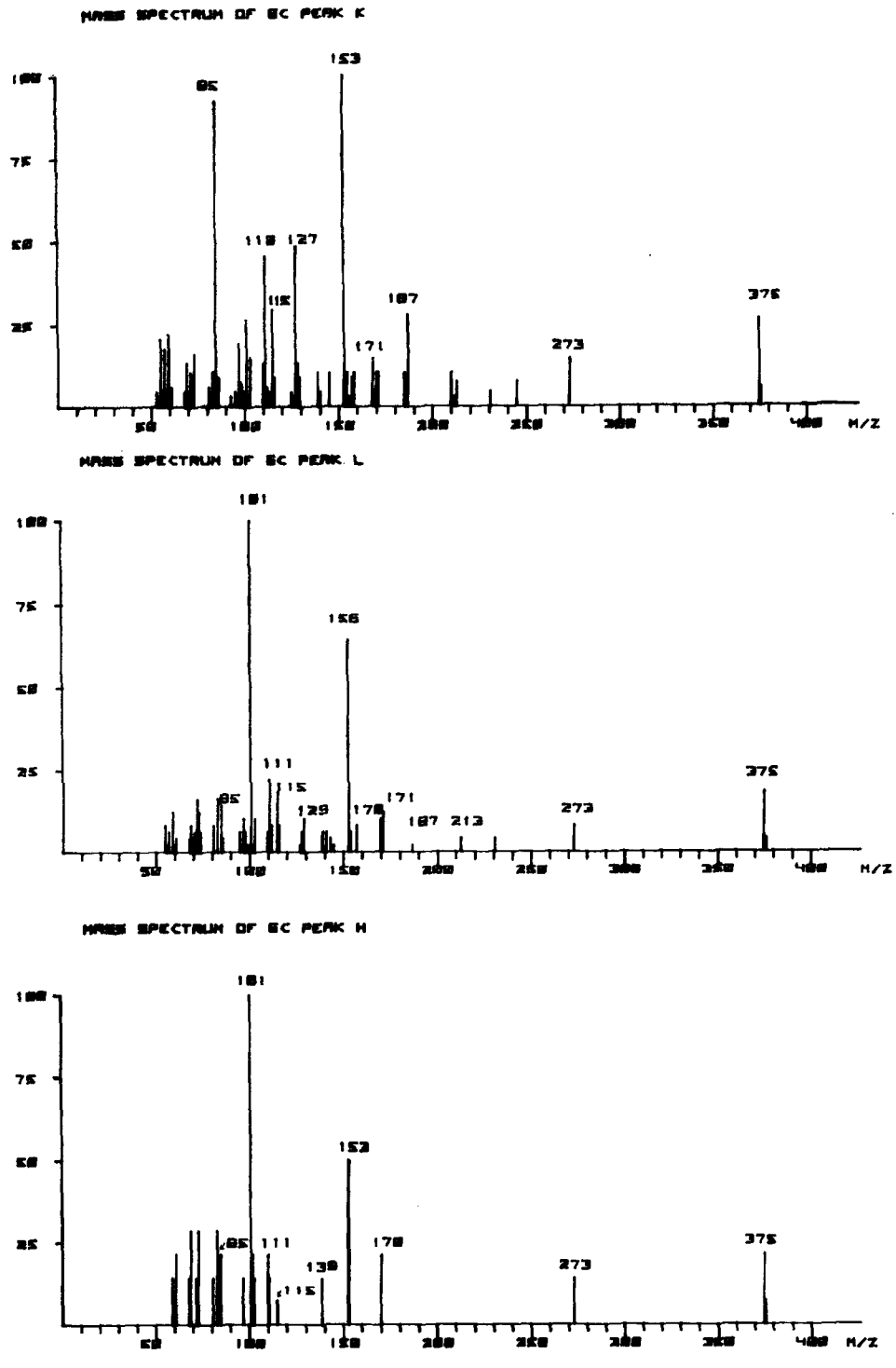

Fig. 8.

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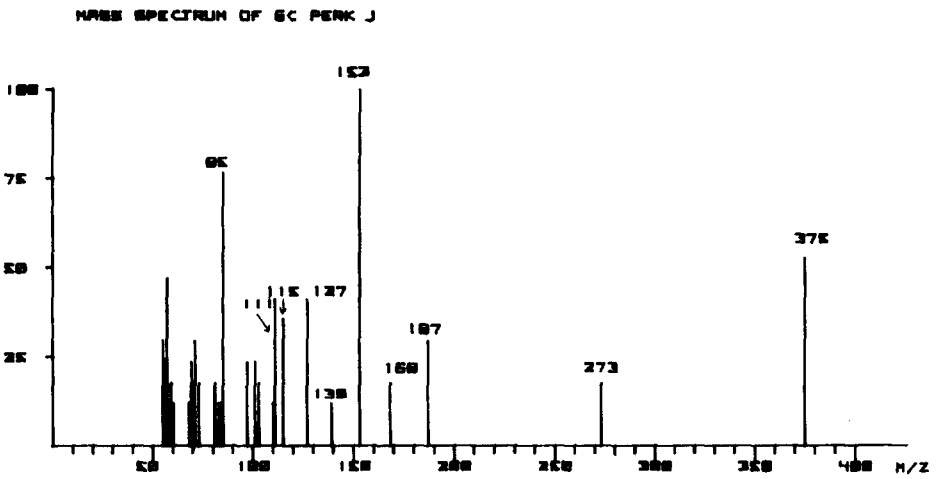

Fig. 8. The mass spectra of compounds H, J, K and L.

dene derivatives of sugar isomers on the stationary phases examined arose from a combination of different effects:

(1) The molecular size, shape and flexibility, as well as non-bonded interactions of the London type

(2) The polarity of molecules with dioxolane and dioxane ring systems

(3) The interactions between the functional groups of the compounds and the stationary phase, dipole–dipole interactions

Correlations were found between the MU values and the structures of mono-, di- and tri-O-isopropylidene-D-glucitol derivatives. An attempt has been made to correlate the retention times of the isomers with their preferred conformations.

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