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CAPILLARY GAS CHROMATOGRAPHY OF D-MANNITOL ACETALS

CORRELATION BETWEEN STRUCTURE AND RETENTION*

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SUMMARY

Compounds obtained on acetonation of D-mannitol were studied by gas chromatography and gas chromatography–mass spectrometry. The separation of the reaction mixtures was achieved on capillary columns coated with Carbowax 20M or OV-101. Methylene unit values were determined for ten acetylated D-mannitol acetals. Correlations were found between the methylene units of the acetals and their structures on the stationary phases of different polarity. An attempt has been made to explain the relationship between the elution orders and preferred conformers of the acetals. The structures of the acetylated compounds were confirmed by mass spectrometry.

INTRODUCTION

In previous work[1] we examined O-isopropylidene and O-isopropylidene-O-acetyl derivatives of D-glucitols by capillary gas–liquid chromatography–mass spectrometry (GLC–MS). Now the same technique has been used for the study of the acetylated derivatives of D-mannitol acetals. Acetonation of D-mannitol by different methods[2–4] was reinvestigated[5–7] and the following compounds were detected and identified in the crude reaction mixtures after acetylation: 1,2:3,4:5,6-tri-O-isopropylidene-D-mannitol (A); 1,2:3,6:4,5-tri-O-isopropylidene-D-mannitol (B); 1,2:4,6-di-O-isopropylidene-3,5-di-O-acetyl-D-mannitol (D); 1,2:5,6-di-O-isopropylidene-3,4-di-O-acetyl-D-mannitol (E); 1,2:3,4-di-O-isopropylidene-5,6-di-O-acetyl-D-mannitol (F); 1,2:4,5-di-O-isopropylidene-3,6-di-O-acetyl-D-mannitol (G) 1,2:3,6-di-O-isopropylidene-4,5-di-O-acetyl-D-mannitol (H); 1,2-mono-O-isopropylidene-3,4,5,6-tetra-O-acetyl-D-mannitol (J); 3,4-mono-O-isopropylidene-1,2,5,6-tetra-O-acetyl-D-mannitol (L); 4,5-mono-O-isopropylidene-1,2,3,6-tetra-O-acetyl-D-mannitol (M). The structures of the compounds were determined by ^{13}C NMR spectroscopy[5,6]. The GLC peaks were identified by use of authentic samples. Compounds A[8], B, G and M[5], D, E and M[6], F and L[7] and J[9] were synthesized by the authors according

* The acetalation of D-mannitol, Part IV. For Part III, see ref. 7.

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to the literature. The crude reaction mixtures were acetylated before the GLC analysis with a mixture of acetic anhydride and pyridine. The separation of the compounds was optimal using capillary columns.

EXPERIMENTAL

Materials

The acetylating reagent, acetic anhydride and pyridine, was obtained from Fluka (Buchs, Switzerland). Carbowax 20M and OV-101 stationary phases were supplied by Applied Science Labs. (State College, PA, U.S.A.). The glass capillary column was prepared by the Research Laboratory for Inorganic Chemistry, Hungarian Academy of Sciences, Budapest.

GLC analysis

An HP 5830 A gas chromatograph equipped with a flame ionization detector was employed. The columns were: I, 60 ft. × 0.25 mm I.D. glass capillary coated with Carbowax 20M; II, 30 ft. × 0.25 mm I.D. coated with OV-101. In place of the original injector an all-glass injection device[10] was used. The inlet pressures for columns I and II were 10 and 18 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 rates of 1°/min and 2°/min.

GLC–MS analysis

An HP 5992 A instrument was used. The mass spectrometric 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°/min. It was connected directly to the mass spectrometer. An all-glass injection device was used[10].

Preparation of O-acetyl-O-isopropylidene derivatives

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

RESULTS AND DISCUSSION

The methylene unit (MU) values have been obtained for C_{18}–C_{30} *n*-alkanes on column I and for C_{14}–C_{21} on column II. Approximately linear relationships with time were found for successive peaks of the *n*-alkanes on the Carbowax 20 M and OV-101 capillary columns. The column temperature was programmed at 1°/min on column I and 2°/min on column II. The precision of the MU values was 0.01 unit on each column.

The MU and ΔMU values for the D-mannitol derivatives are listed in Table I. The ΔMU values, the differences between the methylene units of the compounds examined on polar and non-polar stationary phases, were used for the identification of the reaction products having one, two or three isopropylidene groups.

Figs. 1 and 2 shows GLC chromatograms of acetylated reaction mixture on the Carbowax 20M and OV-101, respectively. Three sets of peaks could be differ-

TABLE I

MU AND ΔMU VALUES FOR O-ISOPROPYLIDENE AND O-ISOPROPYLIDENE-O-ACETYL DERIVATIVES OF D-MANNITOL OBTAINED BY TEMPERATURE-PROGRAMMING ON OV-101 AND CARBOWAX 20M CAPILLARY COLUMNS

Compound	*MU*		
	OV-101	*Carbowax 20M*	*ΔMU*
A	15.79	19.85	4.06
B	16.06	20.16	4.10
D	17.60	23.77	6.17
E	17.84	24.53	6.14
F	17.93	24.27	6.34
G	18.13	25.15	7.02
H	18.27	24.56	6.33
J	19.22	27.73	8.51
L	19.61	28.13	8.52
M	19.70	28.55	8.85
O	20.33	30.84	10.51

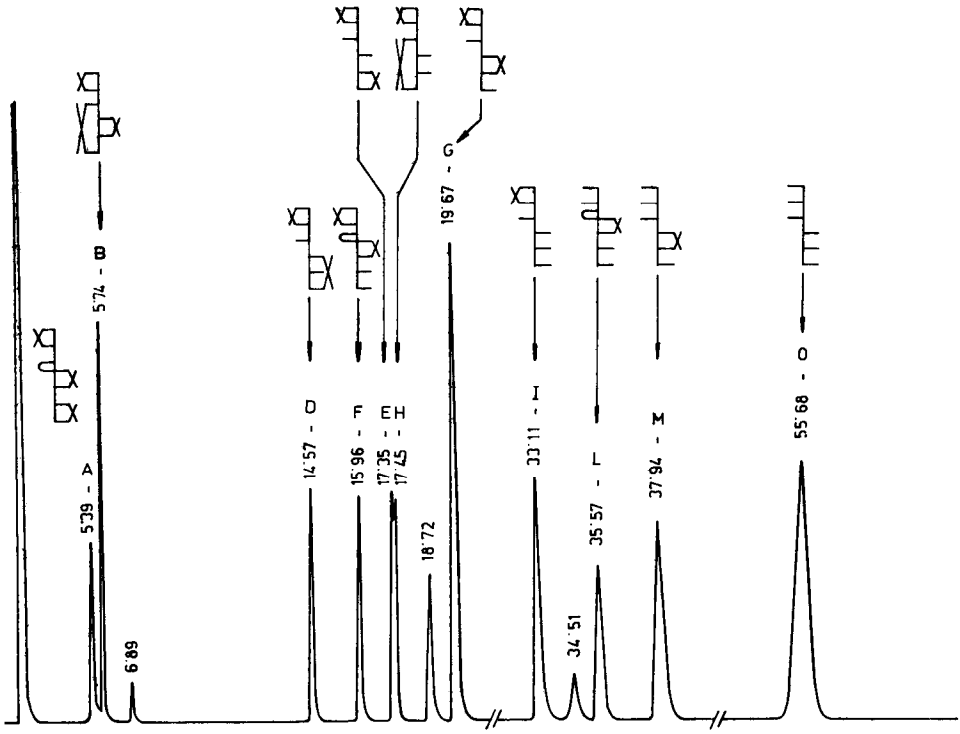

Fig. 1. GLC separation of the O-isopropylidene and O-isopropylidene-O-acetyl derivatives of D-mannitol on Carbowax 20M. The temperature was programmed from 160 to 200°C at 1°/min.

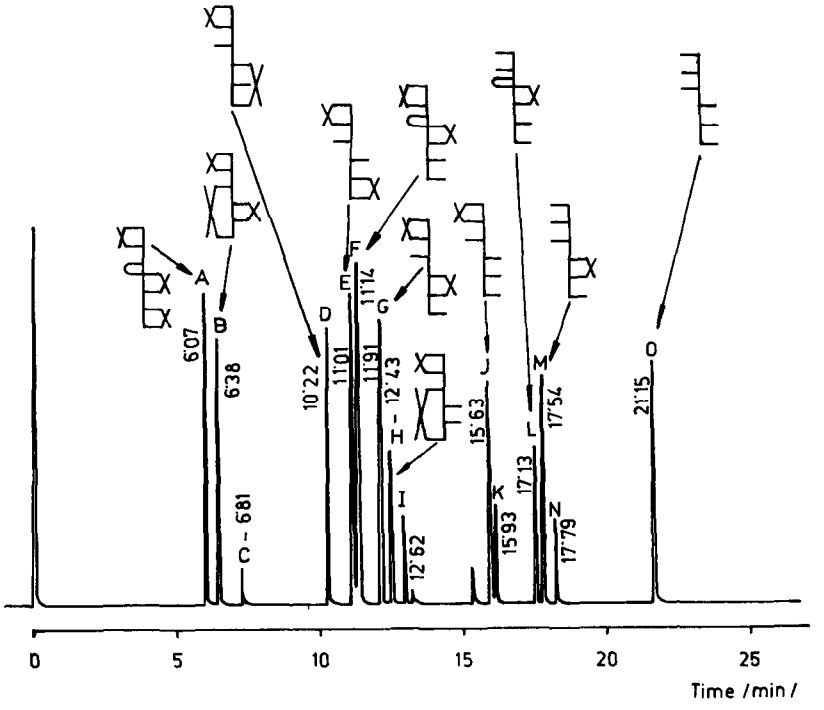

Fig. 2. GLC separation of the O-isopropylidene and O-isopropylidene-O-acetyl derivatives of D-mannitol on OV-101. The temperature was programmed from 140 to 200°C at 2°/min.

entiated besides the starting material, hexa-O-acetyl-D-mannitol (O). The first set of GLC peaks contains two triacetals, namely A and B, which were well separated on both of the columns (Table I). The preferred conformations of compounds A and B are shown in Fig. 3. Of the two triacetals, A, containing three dioxolane rings, was

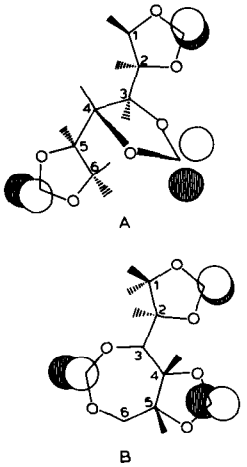

Fig. 3. The preferred conformations of compounds A and B.

eluted first. In compound B (Fig. 3), the presence of the *cis* fused dioxepane and dioxolane rings significantly diminishes the flexibility of the molecule.

The second set of GLC peaks (Figs. 1 and 2) contains five diacetals, D–H, all of which were separated on each column. The isomers E, F, and G contain two dioxolane rings, D contains one dioxolane and one dioxane ring and H contains one dioxolane and one dioxepane ring. The preferred conformations of these compounds are shown in Fig. 4. Of these five diacetals, each of which possesses two acetoxy groups, compound D was eluted first (Table I), as the acetoxy group at C-3 is flanked by the dioxolane and dioxane rings and therefore exhibits only weak dipole–dipole interactions. The elution order of compounds E–H is different on the two columns. Diacetal F, eluted on the polar stationary phase between D and E (Fig. 1), it eluted on the polar stationary phase between E and G (Fig. 2). It has two dioxolane rings linked by a C–C bond and the two polar acetoxy groups are in vicinal positions at C-5,6 (Fig. 4). These two bulky groups are bent away from the plane of the dioxolane ring, consequently the acetoxy group at C-5 becomes shielded by the neighbouring dioxolane ring and only the primary acetoxy group at C-6 can display full intermolecular interactions.

The two diacetals E and H differ in the sizes of the acetal rings (two dioxolane rings in E and a dioxolane and dioxepane ring in H), but in both isomers the two

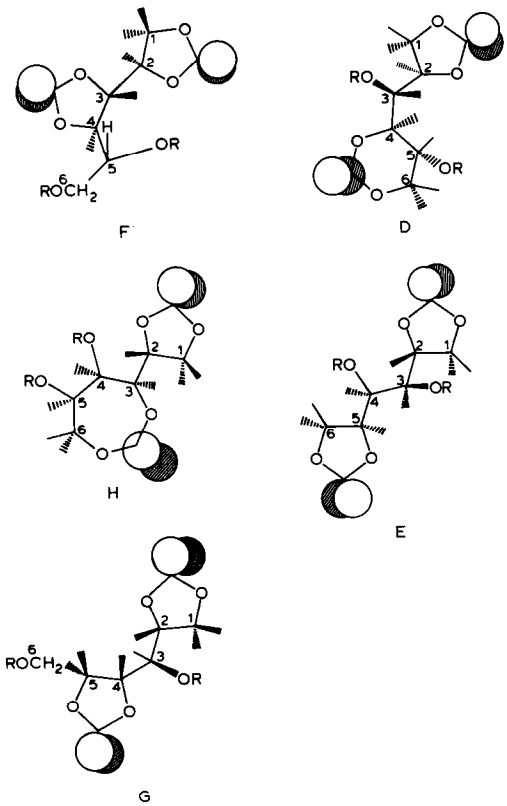

Fig. 4. Preferred conformations of compounds D–H.

acetoxy groups are located on vicinal carbon atoms and consequently can exhibit similar dipole–dipole interactions. The slightly longer retention time of H might be due to the location of these acetoxy groups on a seven membered ring, restricting their free rotation and forcing one of them to be quasi-axial. The most polar diacetal isomer G has one acetoxy group at C-3 which is similarly shielded to that of isomer D, but the other is attached to a freely rotating terminal carbon atom (C-6) and can exhibit very strong dipole–dipole interactions.

In the third set of GLC peaks (Figs. 1 and 2) the retention times of the mono-isopropylidene derivatives of D-mannitol increase from compound J to L on each stationary phase. The dominant factor for these isomers is the accessibility of the terminal (primary) acetoxy group. In compound J the dioxolane ring occupies one terminal position, consequently only one terminal acetoxy group is present. Isomers L and M both contain two terminal acetoxy groups, enhancing their retention times compared to J, but the structure of L is rather symmetrical, containing both primary acetoxy groups in *trans* positions on the central dioxolane ring. On the other hand, in isomer M these groups are in *cis* arrangements on the dioxolane ring, but that at C-1 is separated by one more carbon atom from this ring and can therefore exhibit stronger interactions.

Mass spectrometry of O-isopropylidene and O-isopropylidene-O-acetyl D-*mannitol*

The data in Table II show the variations in the relative abundances of the main fragment ions. Similar fragmentation patterns can be seen in each series of the mono-, di- and tri-O-isopropylidene derivatives. The mass spectra of compounds A and B are shown in Fig. 5. The main fragmentation pathway in the tri-O-Isopropylidene-D-mannitols is the loss of a methyl radical and neutral molecules. The terminal dioxolane ring

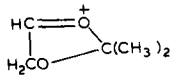

TABLE II

PARTIAL MASS SPECTRA OF D-MANNITOL ACETAL DERIVATIVES

Compound	*Base (m/z)*	*M^+ (m/z)*	*M − 15*		*Percentage abundance of peak at m/z*													
			m/z	*%*	*273*	*245*	*187*	*185*	*171*	*157*	*153*	*143*	*127*	*115*	*111*	*101*	*85*	*59*	*58*
A	143	302	287	20	–	–	–	–	5	–	–	–	2	10	26	77	38	79	15
B	59	302	287	11	–	–	–	–	4	61	–	25	–	30	20	45	21	–	–
D	101	346	331	7	12	3	4	5	11	4	52	4	11	55	59	–	32	42	–
E	101	346	331	6	13	–	–	13	13	–	58	10	10	10	55	–	22	22	3
F	101	346	331	13	8	12	46	13	13	–	50	47	40	20	53	–	86	50	7
G	101	346	331	11	19	–	–	–	15	–	71	8	8	85	66	–	36	38	4
H	85	346	331	9	12	–	32	–	–	12	56	15	47	91	71	79	–	79	15
J	101	390	375	11	3	–	–	–	–	6	60	–	6	20	25	–	9	6	–
L	85	390	375	4	4	–	25	–	6	6	65	–	52	26	44	17	–	20	3
M	115	390	375	15	–	–	8	–	4	7	65	4	4	–	15	11	15	15	4

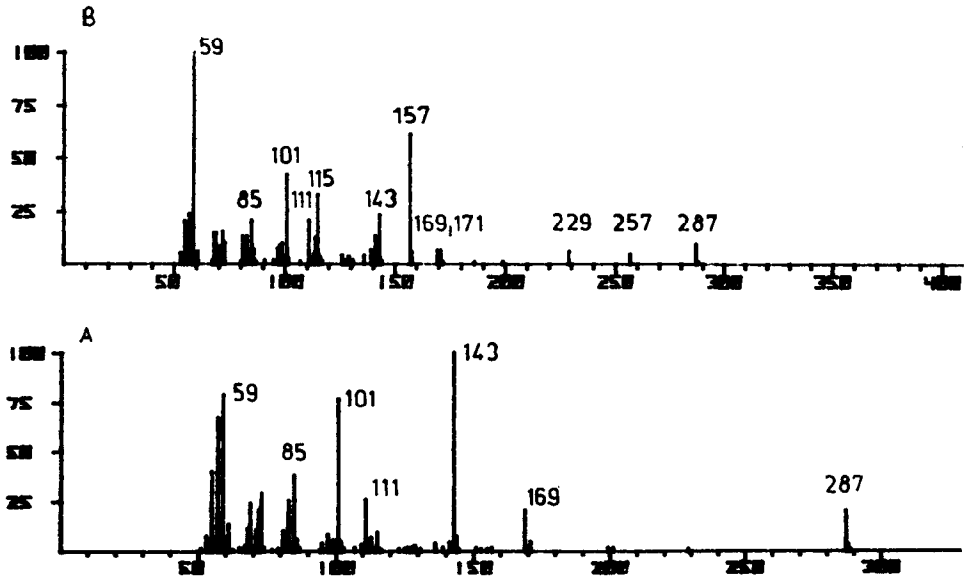

Fig. 5. The mass spectra of compounds A and B.

appears at *m/z* 101 with an intensity of 77% for A (which contains two terminal dioxane rings), while for B this value is only 45%. The ions at *m/z* 171 ($M-{}^{\bullet}CH_3-2\ CH_3H_6O$) and *m/z* 85 ($M-101-\ C_3H_6O$) show two main fragmentation pathways. The base peak is at *m/z* 143 ($M-101-C_3H_6O$) in the spectrum of A, and at *m/z* 59 as that of B. The ion at *m/z* 157 is very abundant in the spectrum of B; the same fragment has an intensity of 12% for compound H. The fragment ions at *m/z* 59 and 157 demonstrate the structural similarity between these two compounds. The fragment ion observed at the highest mass ($M-15$), formed by the loss of a methyl radical from an isopropylidene group, can be found in all of the spectra.

The mass spectra of compounds D–H are shown in Fig. 6. Characteristic ions occur at *m/z* 273 ($M-{}^{\bullet}CH_3-C_3H_6O$) in the spectra of D–H, at *m/z* 245 ($M-101$) in those of D and F and at *m/z* 153 ($M-{}^{\bullet}CH_3-C_3H_6O-2\ CH_3CO_2H$) in those pectra of D, E, F, G and H. The ion at *m/z* 143 ($M-{}^{\bullet}CH(O_2CCH_3)-C_3H_6O$) is abundant in the spectrum of F, indicating the presence of terminal vicinal diacetoxy groups in the molecule, and less abundant in the spectra of D, E, G and H. The ion at *m/z* 187 ($M-101-C_3H_6O$) gives an intense signal in the spectra of H and F, but is absent in that of G.

The loss of acetic acid from ion at *m/z* 245 gives rise to a less intense signal at *m/z* 185 ($245-CH_3CO_2H$) only in the spectra of D–F. The ion at *m/z* 111 ($M-{}^{\bullet}CH_3-C_3H_6O-CH_2CO-2\ CH_3CO_2H$) is abundant in the spectra of D–H. The ion at *m/z* 85 [$M-{}^{\bullet}CH(O_2CCH_3)-2\ C_3H_6O$] in the spectra of F and H (base peak) is very abundant, while it can be found with a lower intensity in the spectra of D, E and G. The ion at *m/z* 115 [$M-101-{}^{\bullet}CH(O_2CCH_3)-C_3H_6O$] is abundant in the spectra of G and H. It is a characteristic of the fragmentation of the diisopropylidene derivatives investigated that after the loss of a radical most of the ions are

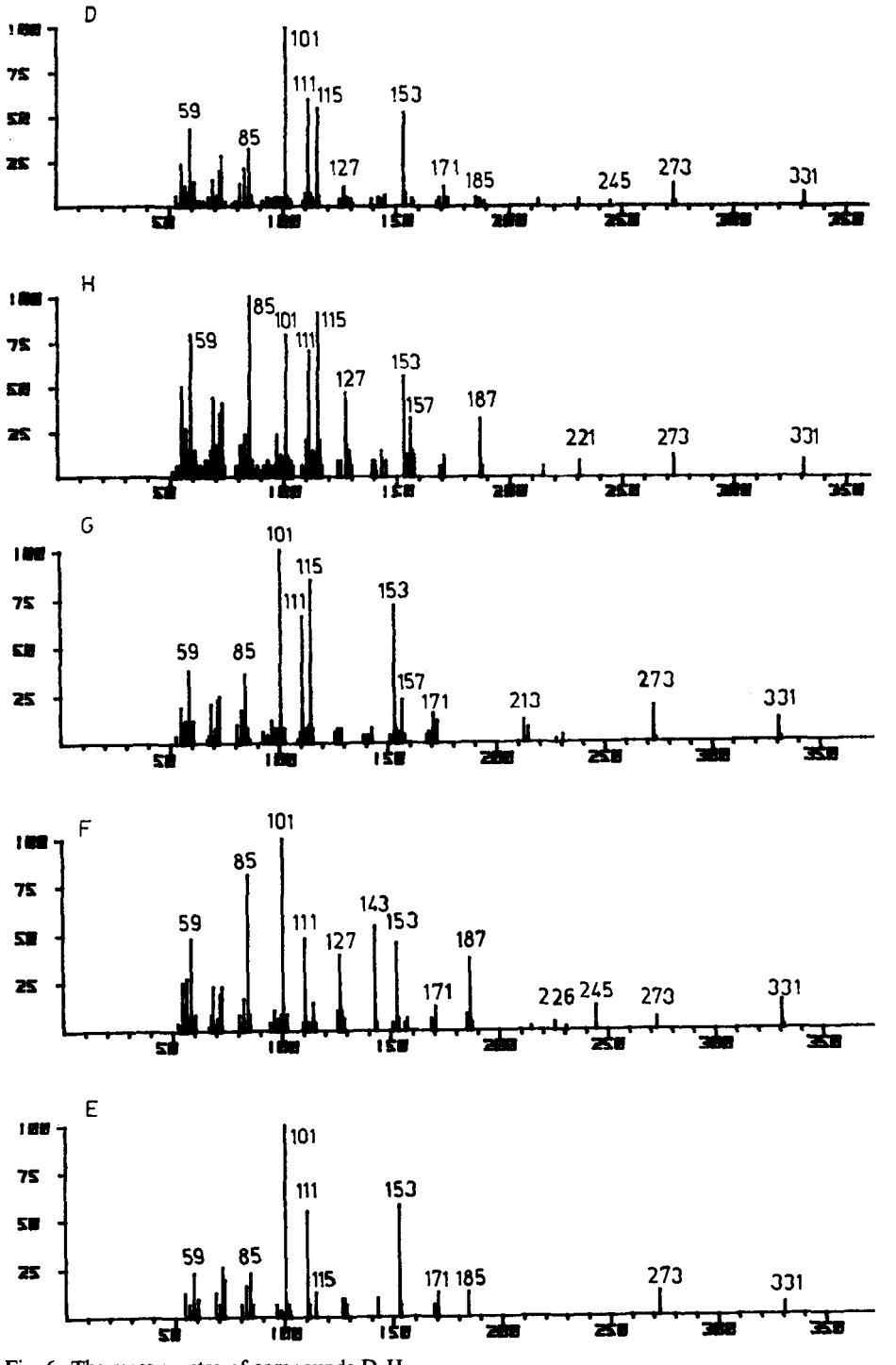

Fig. 6. The mass spectra of compounds D–H.

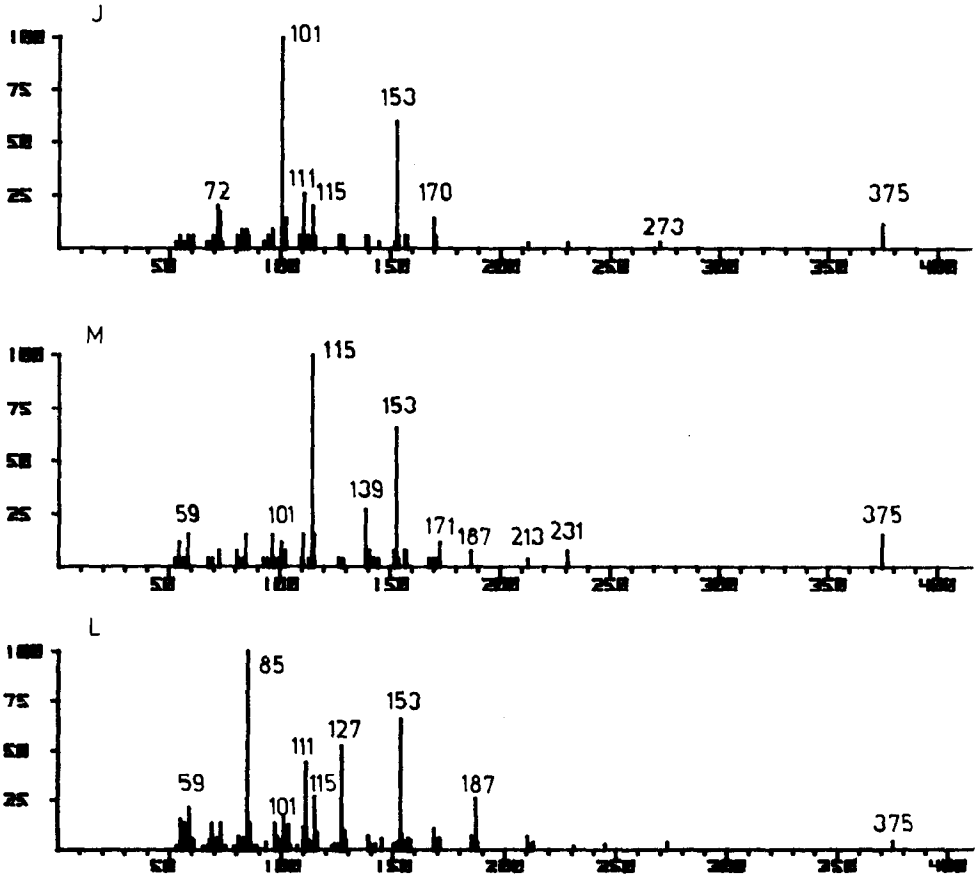

Fig. 7. The mass spectra of compounds J, L and M.

formed by elimination of the neutral molecules acetone, acetic acid and ketene in various combinations.

The same fragmentation can be found in the monoisopropylidene derivatives J, L and M (Fig. 7). The base peaks are at *m/z* 101 (J), 85 (L) and 115 (M). The ion at *m/z* 153 ($M - {}^{\bullet}CH_3 - 3\ CH_3CO_2H - CH_2CO$) is abundant in all three spectra. The ion at *m/z* 127 [$M - {}^{\bullet}CHO_2CCH_3(CH_2O_2CCH_3) - C_3H_6O - CH_3CO_2H$] is abundant in the spectrum of L, less abundant in those of J and M. The different stereochemistries of these molecules is reflected in differences in the loss of acetic acid.

Considering all the acetylated D-mannitol acetals, the variations in the relative abundances of the main fragment ions reflect the different configurations. The molecule size, shape and ring systems and the dipole–dipole interactions between the molecules and the stationary phases all contribute to the separation mechanism on these stationary phases. With the help of the MU and ΔMU values, the number of isopropylidene groups in a reaction mixture can be established immediately.

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