Note

Gas–liquid chromatography of trifluoroacetyl derivatives of cyclitols

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In recent years there have been widespread efforts to prepare edible mixtures of synthetic carbohydrates ("formose sugars") by polymerization of formaldehyde recovered from human metabolic wastes[1]. Such synthetic food may in time be needed on prolonged space flights and to prevent famine in overpopulated areas on earth.

Success in such efforts is highly dependent on the availability of rapid, dependable, analytical methods for complex mixtures of carbohydrates .Of the possible methods available, we find the conversion of the carbohydrates into their poly(trifluoroacetates) followed by gas–liquid chromatography[2–5] the most expedient. In our laboratory, this method has been found superior to previously reported g.l.c. methods based upon derivatization to methyl ethers[6], to polyacetates[7–10], or to the poly(trimethylsilyl) ethers[7,11,12]. The carbohydrates in normal and pathological human urines have been successfully determined by g.l.c. by utilizing the trifluoroacetates[5,13,14].

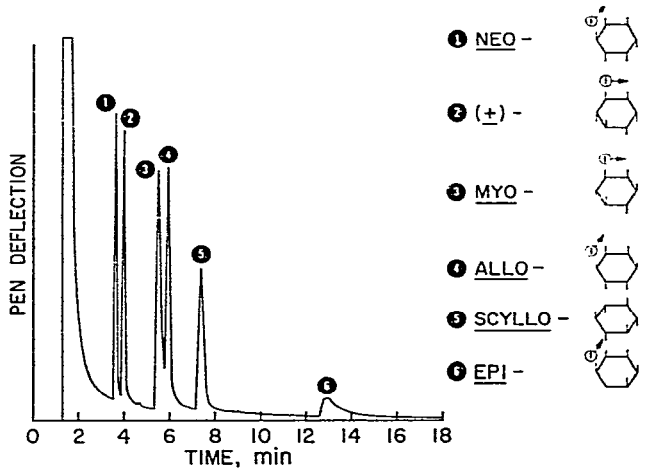

Fig. 1. G.l.c. of inositol hexakis(trifluoroacetates) on a S.C.O.T. FS-1265 column at 160°.

To demonstrate a further utility of the g.l.c. method for separating trifluoroacetates, we have applied it to a group of cyclitols and their derivatives. The diastereomeric inositols separated are listed in Table I and formulas **1–6** are depicted in Chart I. In view of the excellent separations obtained, the method was extended to other inositols and cyclitol derivatives, as listed in Table II and in Chart II where

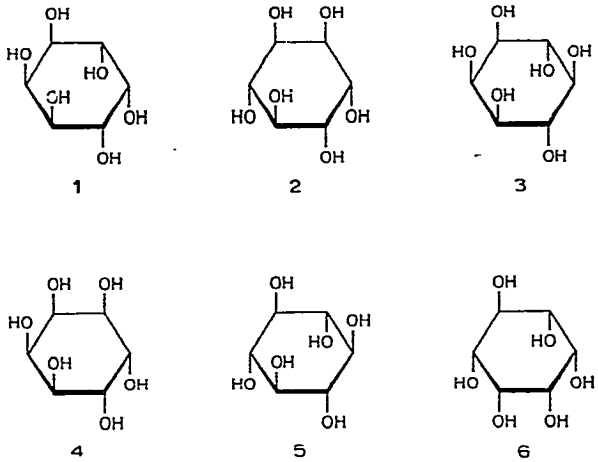

Chart I

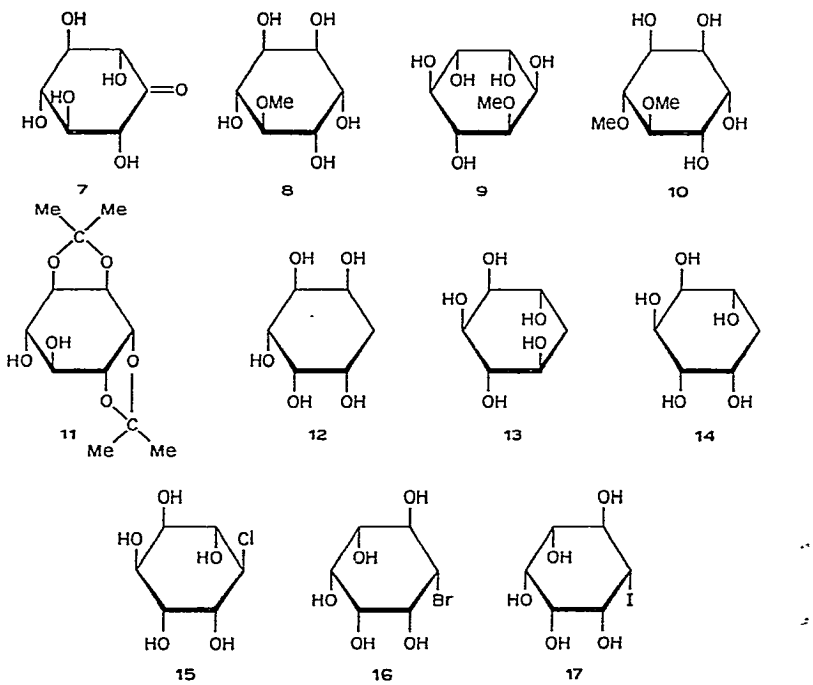

Chart II

formulas **7–17** are shown. The preparations of these cyclitols have been previously published by McCasland and are summarized in his review article[15]. A typical chromatogram is shown in Fig. 1.

TABLE I

RELATIVE G.L.C. RETENTION TIMES OF HEXATHRIFLUOROACETATES OF INOSITOL DIASTEREOMERS

Configuration	*Compound no.*	*Relative retention time*[a]
meso (123/456)	("*neo*", **1**)	0.84
D (124/356)	("(+)-*chiro*", **2**)	1.00
meso (1235/46)	("*myo*", **3**)	1.53
meso (1234/56)	("*allo*", **4**)	1.68
meso (135/246)	("*scyllo*", **5**)	2.21
meso (12345/6)	("*epi*", **6**)	4.09

[a]The actual retention time for (+)-*chiro*-inositol was 2.76 min.

TABLE II

RELATIVE G.L.C. RETENTION TIMES OF POLYTRIFLUOROACETATES OF CERTAIN CYCLITOL DERIVATIVES

Configuration	*Structure and compound no.*	*Relative retention time*[a]
meso (246/35)	2,3,4,5,6-pentahydroxyclyclohexanone (**7**)	0.56
D (124/356)	(+)-*chiro*-inositol (**2**)	1.00
D (124/356)	3-*O*-methyl-(+)-*chiro*-inositol (**8**)	1.24
L (124/356)	2-*O*-methyl-(−)-*chiro*-inositol (**9**)	1.24
D (124/356)	3,4-di-*O*-methyl-(+)-*chiro*-inositol (**10**)	1.15
D (124/356)	1,2;5,6-di-*O*-isopropylidene-(+)-*chiro*-inositol (**11**)	1.99
D (123/45)	1,2,3,4,5-cyclohexanepentol ("(+)-*talo*-quercitol", **12**)	1.76
L (134/25)	1,2,3,4,5-cyclohexanepentol ("(+)-*proto*-quercitol", **13**)	1.76
D (125/34)	1,2,3,4,5-cyclohexanepentol "(−)-*galacto*-quercitol", **14**)	2.14
DL (125/346)	3-chloro-3-deoxy-(−)-*chiro*-inositol (**15**)	1.10
DL (12346/5)	DL-5-bromo-5-deoxy-*allo-inositol* (**16**)	7.33
DL (12346/6)	DL-5-iodo-5-deoxy-*allo*-inositol (**17**)	9.73

[a]The actual retention time for (+)-*chiro*-inositol was 2.76 min.

It appears that this method will be useful for measuring the ratio of stereoisomers (or structural isomers) obtained in reactions of cyclitols. For example, it was possible to determine the ratio of *scyllo* and *myo*-inositol formed by the reduction of a pentahydroxycyclohexanone ("*scyllo*-inosose", **7**).

EXPERIMENTAL

A 5-mg sample of each cyclitol was added to a solution consisting of 10 ml of trifluoroacetic anhydride, 2.0 g of sodium trifluoroacetate, and 10 ml of reagent-grade acetonitrile. The solution was kept for 1 h at 25–30°.

G.l.c. was conducted by injecting a 1.0-μl sample of the resulting solution at an injector temperature of 185°. The instrument was a Perkin–Elmer Model 900 gas chromatograph, equipped with a flame-ionization detector (temperature was 190°C). The column was an open tubular (S. C. O. T.) FS-1265 column, 50 ft by 0.02 in. The column temperature was 160° and the carrier gas was nitrogen (4 ml/min).

scyllo-Inositol and *myo*-inositol were prepared by reduction of 10 mg of *scyllo*-inosose with 10 mg of sodium borohydride in 0.5 ml of water.

RESULTS AND DISCUSSION

The results were obtained by treating the carbohydrate mixture (with or without preliminary reduction of carbonyl groups with sodium borohydride) in acetonitrile with trifluoroacetic anhydride containing sodium trifluoroacetate. The acylation proceeds in a short time at 25 or 35°, giving a clear solution. G.l.c. analysis of a sample of the solution is rapid and convenient, a low column-temperature can be used, and the resolution is excellent. This solvent was previously used by Vilkas *et al.*[4].

The mixture of inositols (Chart I) was easily separated; each compound gave a single peak. The order of retention times (Table I) was in general agreement with those reported by Ueno *et al.*[3] who used formamide as a derivatizing solvent, and a similar column.

The relative retention-times of the derivatives given in Table II is based upon (+)-inositol as a reference standard. The *chiro*-inositol monomethyl ethers **8** and **9** could not be separated under the conditions used; neither could the cyclohexanepentol diastereomers **12** and **13**. These were the exceptions rather than the rule.

Also, a sample, supposedly consisting of the pure *chiro*-inositol dimethyl ether, **10**, was found actually to contain appreciable amounts of the corresponding diisopropylidene acetal and of the monomethyl ether diacetal.

The trifluoroacetate derivatives should also be well suited to preparative g.l.c., as they are readily hydrolyzed to regenerate the parent cyclitols.

Efforts to predict or explain the retention times in terms of the structures, configurations, and conformations have as yet not been successful. The unusually long retention-times of the halocyclohexanepentols (see Table II) are of interest.

ACKNOWLEDGMENT

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