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SEPARATION OF ALDOSE ENANTIOMERS BY GAS-LIQUID CHROMATOGRAPHY

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Pairs of enantiomers of nine aldoses were separated on gas-liquid chromatography equipped with an SE-30 capillary column as trimethylsilyl ethers after conversion of the aldoses to methyl 2-(polyhydroxyalkyl)-thiazolidine-(4R)-carboxylates using the reaction with L-cysteine methyl ester.

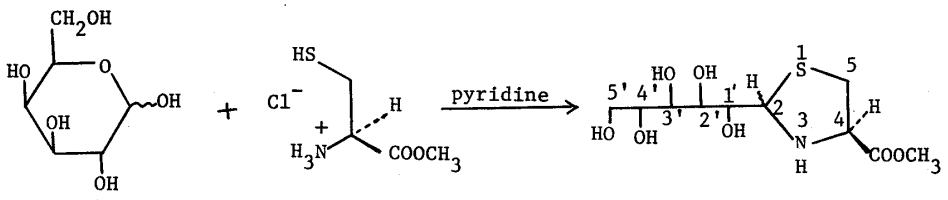
KEYWORDS ———— sugar enantiomer separation; gas-liquid chromatography; SE-30 capillary column; L-cysteine methyl ester; thiazolidine derivative; methyl 2-(polyhydroxyalkyl)-thiazolidine-(4R)-carboxylate

Several attempts have been made to separate sugar enantiomers using microgram-order samples. Some have separated enantiomers by gas-liquid chromatography (GLC) using chiral stationary phases,[1] and others have achieved separation by GLC or high performance liquid chromatography (HPLC) after introducing chiral substituents into the sugars.

The chiral sugar derivatives so far reported are, glycosides of (-)-2-butanol[2] and (+)-2-octanol,[3] bis[(+)-1-phenylethyl]dithioacetals[4] and 1-deoxy-1-α-methylbenzylaminoalditols[5] derived by the reaction of aldoses with chiral α-methylbenzylamine in the presence of sodium cyanoborohydride. Among these chiral derivatives, the last one seemed to be most prefered for sugar analysis of glycosides having several kinds of component sugars because of the commercial availability and stability of the chiral reagent, easy derivation, and simple chromatogram. Recently, this method has been effectively utilized by Kasai, et al.[6] to determine the absolute configuration (D and L) of component sugars of several glycosides. But we found this chiral derivative is still unsatisfactory in some cases for the separation of enantiomers and for the differentiation of sugars.

Bognár, et al.[7] have reported that aldoses react quantitatively with L-cysteine or its methyl ester to give thiazolidine derivatives. Their report suggested to us the applicability of these derivatives for separation of sugars and their enantiomers.

The trimethylsilyl (TMS) ethers of the thiazolidine derivatives of arabinose enantiomers were tested for separation on GLC equipped with an SE-30 capillary column. As the preliminary trial gave promising results, we examined



the reaction conditions for quantitative derivation and for GLC analysis, and have set up a nearly satisfactory analysis procedure as follows: 100 μl each of pyridine solutions of the sugar (0.04 mol/l) and L-cysteine methyl ester hydrochloride (0.06 mol/l) are mixed. After warming at 60°C for 1 h, the trimethylsilylation reagent HMDS-TMCS (150 μl) is added, and the warming at 60°C is continued for another 30 min. The precipitates are centrifuged and the supernatant (1 μl) is applied to GLC analysis. The conditions for GLC are shown in the caption of the figure. In these conditions, the enantiomers of each sugar gave a single peak and no other interfering peak was observed. As an example of separation of enantiomers, the chromatogram of the galactose derivatives is shown in the figure, and the results of the analysis of nine aldoses are summerized in the TABLE.

Fig. Separation of Galactose Enantiomers by GLC

column: WCOT SE-30 (30 m, 0.25 mm I.D.)
column temp.: 229°C. injection temp.: 252°C.
carrier gas: He (2.2 ml/min).
make-up gas flow rate: 31 ml/min.
split ratio: 40:1.

At first glance at the tR values, the absolute configurations (D or L) of the original sugar species seemed to be unrelated to the tR values. But when the tR values and the structures of the products were examined in detail, it became apparent that the configuration of C-1' significantly influenced the elution orders. The sugar derivatives which have the R-configuration at C-1' have smaller tR values than those of the counterparts, without any exception. The influence of the configuration of the other carbons could not be extracted from our data, but the small separation factors (γ) for lyxose, rhamnose and mannose suggest that separation of the enantiomers would become insufficient if C-1' and -2' had the same configuration. In the case of ribose derivatives, separation was most clear-cut although the C-1', -2' and -3' have the same configuration. It is probable that the configuration of C-3' gives some other influence on separation of enantiomers.

This method is superior to the methods hitherto reported for separation of enantiomers as the chiral derivatives in that (a) the derivation procedure is simpler and easier for getting quantitative yield of the derivative, and (b) in the ordinary GLC conditions, it effects clear separation of the enantiomers for almost all sugars examined.

TABLE. Retention Times, Separation Factors and Resolutions of TMS Ethers of Methyl 2-(Polyhydroxyalkyl)-thiazolidine-(4R)-carboxylates Derived from Aldoses

Sugars	tR		γ	Rs
	D-	L-		
Xylose	7.79(R)	8.36(S)	1.073	2.14
Arabinose	8.46(S)	7.83(R)	1.080	2.14
Lyxose	8.39(S)	8.12(R)	1.033	1.20
Ribose	8.15(R)	8.87(S)	1.088	2.27
Fucose	9.79(R)	10.63(S)	1.086	2.21
Rhamnose	9.75(S)	9.47(R)	1.030	0.93
Glucose	10.51(R)	10.96(S)	1.043	1.08
Galactose	11.12(R)	11.85(S)	1.066	1.64
Mannose	10.55(S)	10.38(R)	1.016	0.56

tR: retention time (min), γ: separation factor, Rs: resolution, R or S in the parentheses is the configuration of C-1'.

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