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RESOLUTION OF ENANTIOMERS BY GAS LIQUID CHROMATOGRAPHY WITH OPTICALLY ACTIVE STATIONARY PHASES. SEPARATION ON PACKED COLUMNS

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It has been shown previously[1,2,3] that enantiomers can be resolved by gas liquid partition chromatography with optically active stationary phases. However, so far, successful separations were reported only, when using capillary columns of about 70 m length and 0.25 mm I.D. The difference in resolution factors* observed for pairs of enantiomers was, in general, in the range of 0.01 to 0.05, except in one single case where N-TFA-L-valyl-L-valine isopropyl ester (I) was used as the solvent. A difference in resolution factors as high as 0.197 was found for the enantiomers of t-butyl ester of N-TFA-alanine, with the latter stationary phase at 110°C.[4]

It was obvious that with a resolution factor of this magnitude, the use of a packed column would be sufficient for achieving good separation. However, it turned out that the stationary phase (I), when coated on Chromosorb W (5%), bled rapidly out of the column at the minimum operating temperature. A satisfactory column was obtained with N-TFA-L-valyl-L-valine cyclohexyl ester (II) which had both a lower melting point and lower volatility.

In order to illustrate the performance of such a column, we carried out the experiments described below.

N-TFA-(±)-alanine t-butyl ester was synthesized by condensation of N-TFA-alanine with isobutylene in chloroform with concentrated sulphuric acid as catalyst.[5] The crude product was chromatographed with an inactive stationary phase, and the

* Resolution factor = retention volume of the enantiomer emerging last over that of the enantiomer emerging first.

compound corresponding to the second peak was collected (shaded area Fig. 1a) and shown to be the desired amino acid ester by spectroscopic methods. The sample thus collected was then chromatographed at 100° on a 2 meter long packed column containing the optically active phase II (Fig. 1b), and two peaks were obtained. The fractions collected,which corresponded to the shaded areas on the chromatogram (Fig. 1b), gave ORD curves of opposite sign (Fig. 1c).

These experiments demonstrate clearly that resolution of enantiomers can be achieved with packed columns and that, therefore, optically active stationary phases can be used for preparative separation of enantiomers. Furthermore, for the first time,evidence has been produced for the resolution of enantiomers by G. L. C. through direct measurement of the optical rotation of the isomers separated.

It is assumed that other N-TFA-amino acid esters show equally high resolution factors on the above type of stationary phase. The reasons for the remarkable efficiency of the dipeptide derivative for the resolution of the enantiomers studied will be discussed elsewhere.

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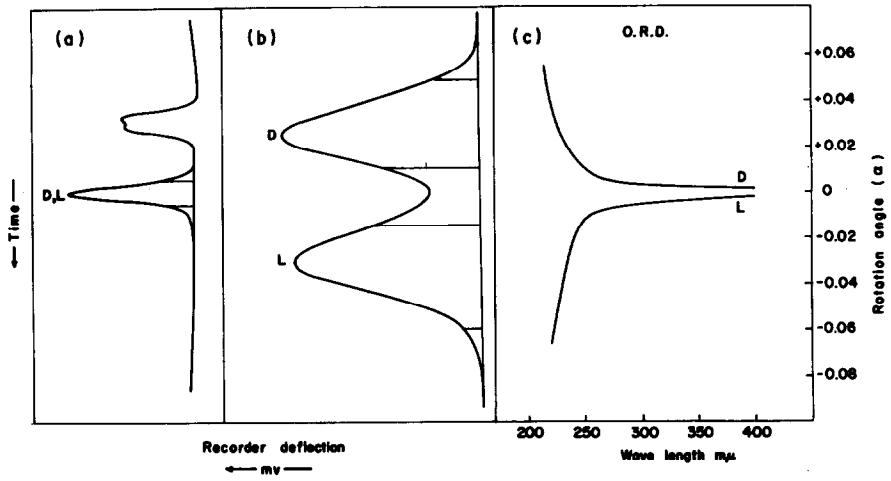

Fig. 1

Resolution of Enantiomers on a Packed Column Containing an Optically Active Stationary Phase

a. Chromatogram of impure N-TFA-(±)-alanine t-butyl ester on a 4m x 6mm I. D. column, containing 20% SE 30 on Chromosorb W; temp. 125°.

b. Chromatogram of the middle fraction (shaded area) corresponding to the second peak in (a) on a 2m x 1mm I. D. column, containing 5% N-TFA-L-val-L-valine cyclohexyl ester on Chromosorb W; temp. 100°.

c. ORD diagram of the two fractions corresponding to the shaded areas in (b). Fraction D gave curve D, and fraction L gave curve L.