Interaction between Asymmetric Solutes and Solvents. *N*-Lauroyl-L-valyl-t-butylamide as Stationary Phase in Gas Liquid Partition Chromatography

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Summary A powerful g.c. stationary phase for enantiomeric resolution of the *N*-trifluoroacetyl-(±)-methyl ester of α-amino-acids is reported.

THE most efficient optically active stationary phases for g.c. separation of enantiomeric α-amino-acid esters, reported so far, are dipeptide[1-5] and tripeptide[3] derivatives. It has been suggested that the high selectivity observed results from the ability of these solvents to form association complexes with the above solutes involving three hydrogen bonds in the vicinity of the chiralic centres.[3]

The *N*-acyl-L-α-aminoacylalkylamides share with the above peptides the group –NH–CO–C*H(R)–NH–CO–, which is essential for the formation of three hydrogen bonds with the solutes. It seemed, however, that the variability in certain structural features of the amides might further increase the selectivity as well as the thermal stability.

These expectations were confirmed when the behaviour of *N*-lauroyl-L-valyl-t-butylamide, m.p. <57°, $[\alpha]_D^{24}$ −21·5° (*c* 4% in $CHCl_3$), was examined. The resolution factors listed in the Table were measured at 130°. They represent the highest values reported, so far, for the resolution of α-amino-acid derivatives on asymmetric phases and are comparable with the best results obtained for the separation of the corresponding diastereomeric derivatives on symmetric phases.[6]

It is seen that for solutes RC*H(NHCOCF$_3$)CO$_2$Me, where R = Me, Pr^i, Bu^i, CH_2CH_2SMe, Bu^s, CH_2Ph, and $CH_2C_6H_4OCOCF_3$-*p*, the resolution factor, *r*, is 1·17—1·28. On the other hand, when R contains a carbonyl group in a position β or γ to the asymmetric carbon, it is seen from the Table, that with the exception of the glutamic acid derivative, the resolution factors are lower (*r* = 1·08—1·12). It can be concluded from these findings, that such hydrogen bonding acceptor groups in the R substituent compete for the formation of the selective association complex responsible for the high resolution observed. The association complexes involving the additional acceptor group of such solutes may have a smaller selectivity than the complex

Relative retention volumes[a] *and resolution factors*, r(L/D), *of* N-*trifluoroacetyl-α-amino-acid methyl esters*[b]

Alanine	D 0·105 L 0·151	1·188	Proline[c]	D 0·398 L 0·420	1·057
Valine	D 0·166 L 0·194	1·170	*O*-Trifluoroacetylserine	D 0·404 L 0·444	1·101
O-Trifluoroacetylthreonine	D 0·186 L 0·208	1·117	Aspartic acid	D 0·781 L 0·842	1·078
t-Leucine[c]	D 0·154 L 0·167	1·084	Glutamic acid	D 1·98 L 2·32	1·170
Alloisoleucine	D 0·254 L 0·301	1·186	Methionine[c]	D 2·22 L 2·70	1·215
Isoleucine	D 0·276 L 0·320	1·159	Phenylalanine	D 2·98 L 3·57	1·198
Leucine	D 0·412 L 0·528	1·280	*O*-Trifluoroacetyltyrosine[c]	D 10·78 L 13·61	1·262

[a] Reference compound n-decyl acetate: retention time 12·5 min. [b] Stainless steel capillary column 150 ft. length × 0·02 in. internal diameter, coated with *N*-lauroyl-L-valyl-t-butylamide as stationary phase, column temp. 130°, carrier gas helium—10 lb./in.[2] [c] The order of emergence was intrapolated.

formed with –C(O)–NH–C–C(O)–, or even have an effect in the opposite direction. The importance of the position of the extra carbonyl group is demonstrated by the fact that the resolution factor of glutamic ester is 1·17, which is within the range found for the neutral α-amino-acid derivatives, while that of aspartic acid is only 1·08.

The *N*-trifluoroacetylproline ester is another case where selectivity is low. Since this compound lacks a residual amidic hydrogen, its selective association complex with the solvent can contain only two hydrogen bonds.[4]

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[1] E. Gil-Av, B. Feibush, and R. Charles-Sigler, "Gas Chromatography 1966," ed. A. B. Littlewood, Institute of Petroleum, London, 1967, p. 238.
[2] E. Gil-Av and B. Feibush, *Tetrahedron Letters*, 1967, 3345.
[3] B. Feibush and E. Gil-Av, *Tetrahedron*, 1970, **26**, 1361.
[4] S. Nakaparksin, P. Birrell, E. Gil-Av, and J. Oro, *J. Chromatog. Sci.*, 1970, **8**, 177.
[5] W. Parr, J. Pleterski, C. Yang, and E. Bayer, *Adv. Chromatog.*, 1970, 277.
[6] J. W. Westley and B. Halpern, "Gas Chromatography 1968," ed. S. L. A. Harbourne, Institute of Petroleum, London, p. 119.