Journal of Chromatography, 576 (1992) 179–180
Biomedical Applications
Elsevier Science Publishers B.V., Amsterdam

CHROMBIO. 6251

Discussion

Analytical studies on the chiral separation and simultaneous determination of pantothenic acid and hopantenic acid enantiomers in rat plasma by gas chromatography–mass fragmentography: a reply

E. Küsters*, C. Spöndlin and C. Eder

Chemical Research and Development, SANDOZ Pharma AG, Basle (Switzerland)

(Received November 11th, 1991)

In a recent paper by K. Banno *et al.* [1] on the enantiomeric separation of pantothenic acid and hopantenic acid, the authors introduced a derivatization method to prepare the corresponding cyclic sulphinate derivatives after derivatization with thionyl chloride (Fig. 1).

It is obvious from the molecular structure that the sulphinate contains two asymmetric centres. The second one, the chiral sulphur atom, has been introduced by the achiral thionyl chloride. The authors did not mention this asymmetric centre, which is responsible for at least two pairs of enantiomers and diastereoisomers. Based on this fact, there may be some interesting explanations regarding the reported separation of the proposed sulphinate derivative of pantothenic acid. Two of them are: (1) the published chromatogram may show the separation of diastereoisomers, owing to insufficient enantioselectivity of the chiral stationary phase; (2) the published chromatogram may show the separation of only one pair of enantiomers. In this instance the asymmetric sulphur atom has been introduced enantioselectively, an aspect of great importance for the synthesis of chiral molecules.

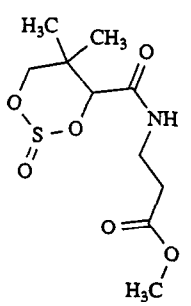

Fig. 1. Structure of pantothenic acid methyl ester after cyclic sulphination.

Both possibilities encouraged us to investigate this derivatization method further for clarification. D,L-Pantothenic and D-pantothenic acid hemicalcium salt and D,L-pantoyllactone were supplied by Sigma (St. Louis, MO, USA).

RESULTS AND DISCUSSION

We reproduced the derivatization method with pantothenic acid according to ref. 1 and chromatographed the product on a commercially available Chirasil-L-Val column. We obtained the resolution for a pair of enantiomers with

0378-4347/92/$05.00

much shorter retention time and strong tailing of the observed peaks.

Characterization of our product by ^{1}H NMR and mass spectrometry showed that we had converted pantothenic acid into pantoyllactone with *ca.* 80–90% yield. In addition, chromatography repeated with commercially available pantoyllactone as reference confirmed our previously obtained results. Methyl esterification was repeated with diazomethane and again pantoyllactone was the result. This indicates that pantoyllactone originated from the first step, release of pantothenic acid.

From our experiments it seems likely that the derivatization described by Banno *et al.* [1] belongs to a side-reaction and should be mentioned as such. To understand clearly the stereospecific aspects, it is necessary to obtain more information about the derivatization process.

REFERENCE

1 K. Banno, S. Horimoto and M. Matsuoka, *J. Chromatogr.*, 564 (1991) 1.