Journal of Chromatography, 606 (1992) 288–290
Elsevier Science Publishers B.V., Amsterdam

CHROM. 24 349

Short Communication

Application of enantioselective capillary gas chromatography in lipase-catalysed transesterification reactions in organic media

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(First received February 18th, 1992; revised manuscript received May 13th, 1992)

ABSTRACT

The analysis of enantiomeric excesses of substrate and product during an enantioselective reaction can be performed easily with a chiral stationary phase based on γ-cyclodextrin. The transesterification of six related allylic alcohols to their corresponding acetates was catalysed by lipase from *Pseudomonas cepacia*.

INTRODUCTION

The determination of enantiomeric excesses is of great interest in the synthesis of enantiomerically pure pharmaceuticals. In addition to older methods such as the determination of the specific rotation, an increasing number of chiral stationary phases for gas and liquid chromatography and new chiral auxiliaries for NMR spectroscopy have been developed in recent years [1–3]. In the synthesis of enantiomerically pure compounds, the application of enzymes, especially lipases, in aqueous and organic solvents has also increased during recent years [4–8]. In our research, we investigated the enantioselective reaction of six related allylic alcohols and the influence of reaction conditions on the reaction progress and enantioselectivity [9]. The determination of enantiomeric excesses of substrate and product during the reaction was performed with a chiral stationary phase for gas chromatography (3-O-butyryl-2,6-di-O-pentyl-γ-cyclodextrin, Lipodex E) [10].

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EXPERIMENTAL

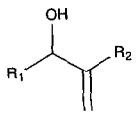
The gas chromatograph used was an HRGC 5300 Mega series (Carlo Erba) with a 30-m Pyrex glass capillary coated with 3-O-butyryl-2,6-di-O-pentyl-γ-cyclodextrin (Lipodex E, Macherey–Nagel). Analysis conditions: injector temperature, 180°C; flame ionization detector temperature, 250°C; oven temperature, see Table II, carrier gas, hydrogen 55 kPa. Samples drawn during the reaction were centrifuged to separate them from the en-

0021-9673/92/$05.00

TABLE I

STRUCTURE OF THE ALLYLIC ALCOHOLS, COMPOUNDS **1–6**

Me = Methyl; Et = ethyl; *n*-Pr = *n*-propyl; Cyh = cyclohexyl; Ph = phenyl; CN = cyano; COMe = methoxy.



Compound	R_1	R_2
1	Me	CN
2	Et	CN
3	*n*-Pr	CN
4	Cyh	CN
5	Ph	CN
6	Me	COMe

zyme. The solution was then derivatized as follows: 200 μl of dichloromethane, 50 μl of trifluoroacetic acid (TFA) anhydride and 5 μl of the reaction solution were mixed. After evaporation of solvent and excess reagent, *n*-hexane was added for the analysis.

RESULTS AND DISCUSSION

The transesterification reactions were carried out with racemic allylic alcohols (Table I), cyclohexyl acetate as acyl donor and lipase from *Pseudomonas cepacia* at 40°C (for a detailed description, see ref. 9). The results of the analysis of enantiomeric excesses of the substrate (derivatized to the TFA ester) and corresponding acetates (product) are shown in Table II, the chromatogram of the analysis of compound **1** (TFA ester) is shown in Fig. 1. In the case of compounds **1-3**, both TFA ester and

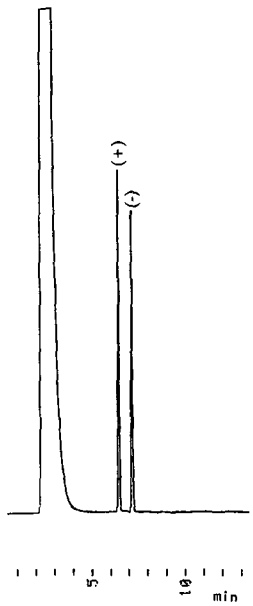


Fig. 1. Chromatogram of compound **1** (TFA ester) under the conditions described in the Experimental section with oven temperature 110°C and injection volume 0.2 μl.

TABLE II

α-VALUES, RETENTION TIMES AND ENANTIOMERIC EXCESSES OF THE SIX ALLYLIC ALCOHOLS (DETERMINED BY GC WITH LIPODEX E)

For compounds see Table I.

Compound	α-value		Retention time[a] [min (°C)]		Enantiomeric excess (%ee)		Acetate[c]
	TFA	Acetate	TFA[b]	Acetate[b]	TFA	Acetate	
1	1.118	1.258	6.23 (110)	9.13 (120)	11	98	(−)
2	1.390	1.262	7.18 (110)	11.05 (120)	5	63	(+)
3	1.428	1.238	8.33 (110)	12.90 (120)	21	75	(+)
4	1.075	–	8.34 (150)	–	9	[d]	(+)
5	–	1.023	–	19.60 (160)	8	76	(+)
6	1.147	–	10.78 (100)	–	25	86	(−)

[a] Retention time of first enantiomer.
[b] Oven temperature (isothermal).
[c] Specific rotation (determined by polarimetry).
[d] Not measured.

acetate could be separated into the enantiomers, resulting in high α-values using the enantioselective capillary gas chromatography. For compounds **4** and **6**, the separation of the acetate failed, compound **5** was only separated using the acetate.

The use of enantioselective capillary gas chromatography allows an effortless monitoring of the reaction progress. This is of great interest in the field of chemical engineering, especially for kinetic studies.

ACKNOWLEDGEMENTS

The authors thank Professor H. M. R. Hoffmann and his co-workers from the Institute of Organic Chemistry of the University of Hannover for providing them with the allylic alcohols.

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