Pais, L.S., Loureiro, J.M., and Rodrigues, A.E.

Separation of Enantiomers of a Chiral Epoxide by Simulated Moving Bed Chromatography

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PREP '98

1998 International Symposium,
Exhibit & Workshops on

Preparative Chromatography,

Ion Exchange,

Adsorption / Desorption Processes,

and Related Techniques

May 31 – June 3, 1998
Georgetown University Conference Center
Washington, DC, USA

PREP '98
— Program —

MONDAY, JUNE 1
— Meeting Location: Grand Ballroom G —

8:00 am **Registration & Exhibits Open**

8:55 am **Opening Remarks**

CHAIR: DR. FIROZ ANTIA

9:00 am (L-101) **Continuous Chromatographic Separation of Fine Chemicals Through Simulated Moving Beds**—M. Mazzotti, MASSIMO MORBIDELLI, ETH Zurich, Zurich, SWITZERLAND

9:20 am (L-102) **Optimal Design of a Nine Zone SMB for the Separation of Glucose from Acids from Biomass Hydrolyzate**—ZIDU MA, N.-H. L. Wang, R. Wooley*, *National Renewable Energy Lab.; Purdue University, West Lafayette, IN USA

9:40 am (L-103) **Aspects of the Optimization of Preparative Enantioselective Separations**—GEOFFREY B. COX, O. Dapremont, T. Murakami, C. Suteu, Chiral Technologies Europe, Illkirch, FRANCE

10:00 am (L-104) **Separation of Enantiomers of a Chiral Epoxide by Simulated Moving Bed Chromatography**—L.S. Pais, J.M. Loureiro and ALÍRIO E. RODRIGUES, University of Porto, Porto Codex, PORTUGAL

10:20 am (L-105) **SMB Processing: Escape from the High-Cost Box**—BRUCE W. PYNNONEN, Dow Chemical, Midland, MI USA

10:40 am **BREAK** sponsored by BTR-Separations in Exhibit Area

dimensions and packing material properties have to be reached in order to minimize the cost contribution of the packing media. The impact of these considerations on the design of enantioselective separations is discussed.

L-104

SEPARATION OF ENANTIOMERS OF A CHIRAL EPOXIDE BY SIMULATED MOVING BED CHROMATOGRAPHY. Luís S. Pais, José M. Loureiro and Alírio E. Rodrigues, Laboratory of Separation and Reaction Engineering, Faculty of Engineering, University of Porto, Rua dos Bragas, 4099 Porto Codex, PORTUGAL
The simulated moving bed (SMB) technology is receiving an increasing interest as an alternative technique for the production of fine chemicals and pharmaceuticals. Recent works proved the efficiency of this technology at lab scale, and first industrial applications have been mentioned. Following the new regulations regarding the approval of new pharmaceutical drugs, SMB chromatographic separation systems have been developed in order to obtain single enantiomer drugs. In this work, the separation of the enantiomers of a chiral epoxide (1a,2,7,7a-tetrahydro-3-methoxynaphth-(2,3b)-oxirane) is considered[1,2]. This separation was carried out experimentally in a SMB pilot unit (*Licosep 12-26*, developed by *Novasep*), using cellulose triacetate as stationary phase and methanol as eluent. Experimental adsorption equilibrium data is reported. A linear driving force model[3] is used as a prediction and optimization tool for the operation of this SMB chromatographic system. References: [1]Nicoud, R.-M., G. Fuchs, E. Kusters, F. Antia, R. Reuille, E. Schmid, "Preparative Scale Enantioseparation of a Chiral Epoxide - A Comparison of Liquid Chromatography and Simulated Moving-Bed Adsorption Technology" in *3rd International Symposium on Chiral Discrimination*, Tubigen (1992). [2]Rodrigues, A.E., Z. P. Lu, J.M. Loureiro, L.S. Pais, "Separation of Enantiomers of 1a,2,7,7a-tetrahydro-3-methoxynaphth-2(2,3b)-oxirane by liquid chromatography: laboratory-scale elution chromatography and modelling of simulated moving bed," *J. Chromatog. A*, 702, 223 (1995). [3]Pais, L.S., J.M. Loureiro, A.E. Rodrigues, "Separation of 1,1'-Bi-2-Naphthol Enantiomers by Continuous Chromatography in Simulated Moving Bed, " *Chem. Eng. Sci.*, 52, 245 (1997).

L-105

SMB PROCESSING: ESCAPE FROM THE HIGH-COST BOX. Bruce Pynnonen, The Dow Chemical Company, Midland, MI USA
The prime objectives of analytical chromatography are compact equipment, complete peak separation, speed, accuracy, precision, sensitivity, and minimum sample waste. Processing versus analyzing compounds via chromatography is much simpler, yet much more complex. The objective of chromatography as a manufacturing process step is to minimize cost. Constraints of GMP, product purity, product recovery, etc., are givens and are irrelevant since the costs of achieving these are incorporated as components of the objective function to be minimized, the cost. When process designers assume the truths derived from the assumptions and boundary constraints appropriate to the regime of analytical chromatography, process chromatography is *the expensive operation of last resort.* Keys to unlock the invisible door of the high cost box will be presented using a real separation and its associated costs as an example.

L-106

CHIRAL SEPARATIONS IN LARGE SCALE. Gregor Mann, Schering AG, VT-Prep Chromatography, D-13342 Berlin, GERMANY
Chiral separations carried out by HPLC are growing in their importance. The demand on it might be explained through the fact that the pharmaceutical industry is dealing more than in the previous years with chiral drug substances. The acceptance of racemic drugs has become very low. Different to normal and reversed phase HPLC the chromatographer should pay much more attention on the surface chemistry. Bleeding stability is rather important as well. In order to avoid bleeding effects the number of suitable solvents is, different to normal and reversed phase, strongly restricted. However, due to its complexity the design of a chiral separation process is not a trivial task. This will be illustrated by two different chiral separations processed in larger scale. Much more than in other separation modes chiral separations are in use for two total different targets: Achieving a short-cut in needed development time, in purpose switching later on to more economic other separation methods. The other target is to establish finally a production separation method carried out by PHPLC. Chiral PHPLC is, in general, much more cost intensive than regular PHPLC. This creates an environment, that leads finally - often - to the SMB-technology.