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Empirical Determination of the operating conditions for the SMB separation of 1-phenyl-1-methyl-succinimide enantiomers

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The determination of the operating parameters for a SMB process was made empirically for a separation using 20 micron CHIRALPAK® IA™. High productivity was found using this new immobilized polysaccharide chiral stationary phase with MTBE as mobile phase.

In the course of developing methods for the separation of enantiomers, we often need to determine the operating parameters for large scale production SMB processes. The literature abounds with separations and computer simulations for compounds with simple (Langmuir) adsorption isotherms for which the parameters are easy to determine. Recently we encountered an application that required us to compare the performance of a chiral separation with two different mobile phases. One separation behaved according to a known isotherm, while the isotherm for the other set of conditions was intractably complex.

Experimental.

A SMB unit constructed in-house was used in this study. It was equipped with eight columns (10 x 1 cm), packed with CHIRALPAK IA (20 micron). The mobile phases employed were acetonitrile:2-propanol (85:15) and methyl tert-butyl ether (MTBE). The solute used in this work was 1-phenyl-1-methylsuccinimide.

Results.

A loading study was carried out using MTBE as mobile phase. The results are shown in Figure 1.

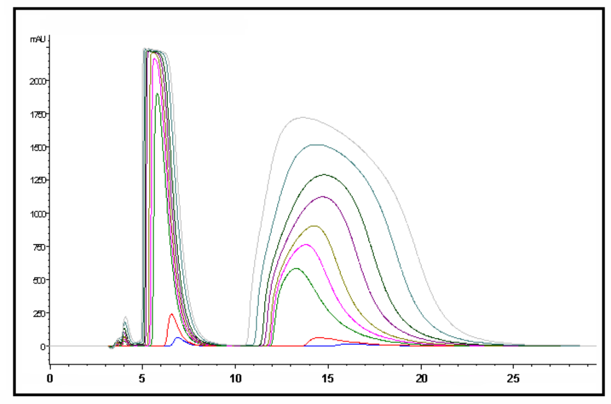

Figure 1. Loading chromatograms, MTBE mobile phase.

The isotherm equation corresponding to the elution pattern of the second component cannot easily be fitted to experimental data and so the separation was optimized empirically.

To achieve this, the Zone 2 flow rate was calculated from the elution time of the tail of the first peak and the Zone 1 flow was calculated from the elution time of the tail of the second peak, choosing arbitrarily a fixed switch time. The feed flow was increased to the point at which the second eluting component contaminated the raffinate flow. Then the extract and raffinate flows were reduced to the minimum while the switch time and feed flow were modified to adjust the extract purity and the raffinate purity respectively. Finally, the flow rates and switch time were adjusted to give the required pressure of operation, in this case 35 bar.

The separation for the acetonitrile:2-propanol mobile phase was developed more conventionally by fitting the loading data to an Ideal Adsorbed Solution Theory isotherm, calculating the operating parameters from computer simulations and then fine-tuning the conditions.

Results from the determination of productivity for the two systems with normalized operating pressure are shown in the Table.

Table. Chromatographic parameters for the two separations

	MTBE	**ACN/IPA**
		(85:15)
Viscosity (mPa.s)	0.27	0.63
Solubility (g/l)	35	70
Selectivity	3.62	6.83
P-Value (kg/kg/day)	**2.16***	**0.98**

Conclusions.

Despite the unusual isotherms observed, empirical optimization was straightforward and rapid. Although using the acetonitrile:2-propanol mobile phase gave a much higher selectivity and higher product solubility, the productivity using MTBE as the mobile phase was more than twice that in the former solvent. Part of this productivity increase was due to the difference in adsorption isotherms while part was due to the low viscosity of MTBE, which allowed a high average flow rate in the SMB unit.