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Application Note

► Parallel screening for chiral separation of methyl phenyl sulfoxide

Category	Chiral analysis
Matrix	
Method	HPLC
Keywords	parallel chiral screening, cellulose based chiral stationary phases, Eurocel 01, Eurocel 02
Analytes	Methyl phenyl sulfoxide
ID	**VCR1**, January 2008

Summary

With a parallel HPLC system a high throughput chiral column screening can be realized. Five different chiral column materials based on polysaccharide stationary phases were tested to find the most suitable chiral separation for methyl phenyl sulfoxide. A fast reprocess of 48 chromatograms is demonstrated and showing the overview of chiral separation with different solvent mixtures in normal phase and polar organic mode.

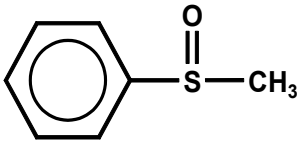
Introduction

In the absence of any good theory or empirical correlations between the types of molecules separated and any of the chiral stationary phases (CSPs) currently available, the only solution is to screen each separation problem over a number of CSPs with different solvents in order to find separation conditions. To monitor the enantioselectivity of the sulfoxidation with chloroperoxidase and hydrogen peroxide of thioanisol and related compounds a chiral HPLC method can be a useful tool [1, 2]. The first step is to find a chiral separation method with the racemic mixture of methyl phenyl sulfoxide. In case of methyl phenyl sulfoxide several polysaccharide stationary phases based on derivatized cellulose or polysaccharides of alternative selectivity were investigated.

Experimental

The traditional way to screen the CSPs is by testing each column sequentially (see Fig. 1). Different cellulose based Eurocel columns and one polysaccharide column of alternative selectivity with the dimension of 250 x 4.6 mm are used. In the parallel approach of screening (see Fig. 2) it is possible to combine up to eight different columns simultaneously. In this setup the solvent from one pump is split into 8 channels. A flow control module guarantees equal flow rates in each channel.

Chemical structures



methyl phenyl sulfoxide

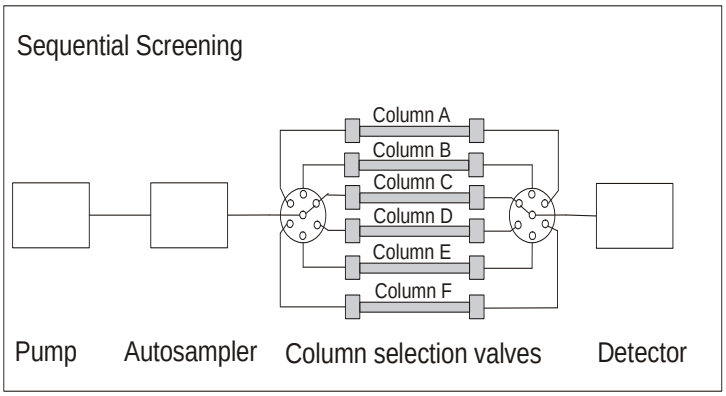


Fig. 1
Scheme for sequential chiral column screening

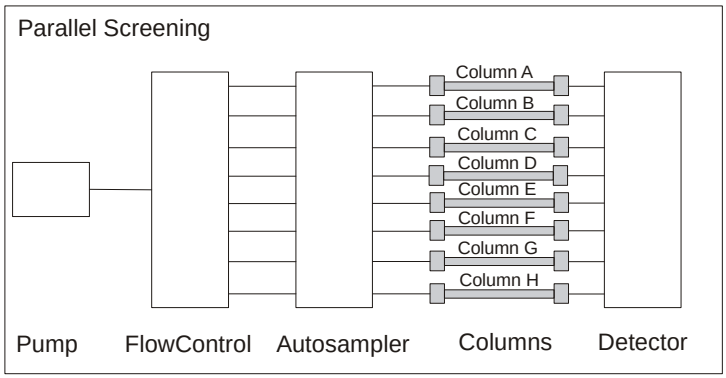


Fig. 2
Scheme for parallel chiral column screening

Method parameters

Columns (250 x 4.6 mm)	Eurocel 01 3 µm, 5 µm and 20 µm
	Eurocel 02 5 µm
	Eurocel 03 5 µm
	Eurocel 04 5 µm
	Polysaccharide phase, alt. select. 3 µm and 10 µm
Eluent A	Hexane / ethanol 90:10
Eluent B	Hexane / ethanol 75:25
Eluent C	Hexane / 2-propanol 90:10
Eluent D	Hexane / 2-propanol 75:25
Eluent E *	Ethanol
Eluent F *	Ethanol / methanol 50:50
Flow rate	1 ml/min (* 0.5 ml/min)
Injection volume	5 µl
Column temperature	Ambient
Detection	UV (diode array detector) at 210 nm
Run time	30 min

Results

In case of methyl phenyl sulfoxide 48 runs of the sequential chiral column screening can be realized in 24 hours with a programmed run time of 30 min. The same screening with parallel technique is strongly reducing the screening time. In summary the parallel screening is 8 times faster than the sequential screening. All results can be presented in 3 hours (see Fig. 3). Visual inspection of the chromatograms shows the best separation on the Eurocel 01 and Eurocel 02 column with hexane / 2-propanol mixture. The resulting parameters from the integration are used to create a hit list of separations (see table 1). It is recognizable that the two cellulose based chiral column materials with modification of benzoate (Eurocel 02) and 3,5 dimethylphenylcarbamate (Eurocel 01) are the most suitable ones. Figure 4 is showing the chiral separation of the racemic mixture with the best resolution.

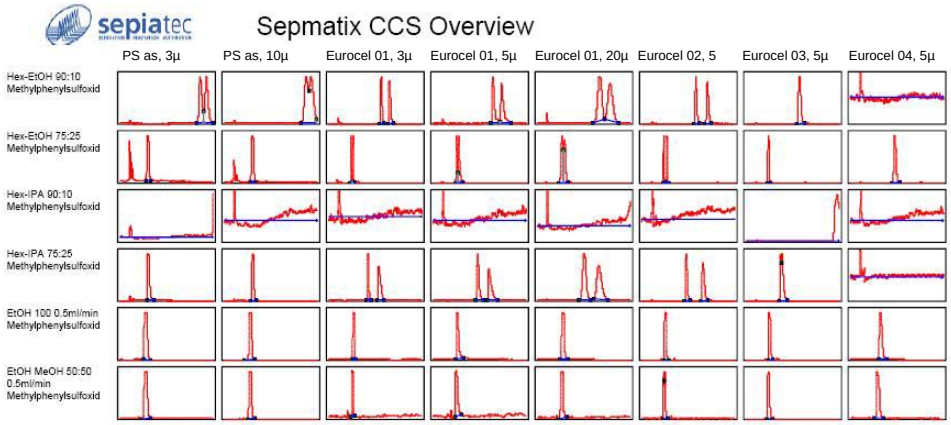


Fig. 3

Chromatogram overview of all 48 runs for methyl phenyl sulfoxide

No.	Column type	Eluent	t_{R1} [min]	t_{R2} [min]	Selectivity
1	Eurocel 02, 5 µm	Hex-IPA 75:25	14.32	19.68	1.42
2	Eurocel 02, 5 µm	Hex-EtOH 90:10	17.42	21.10	1.23
3	Eurocel 01, 3 µm	Hex-IPA 75:25	12.72	16.17	1.30
4	Eurocel 01, 3 µm	Hex-EtOH 90:10	16.95	19.55	1.17

Table 1

Hit list of chiral separation for methyl phenyl sulfoxide

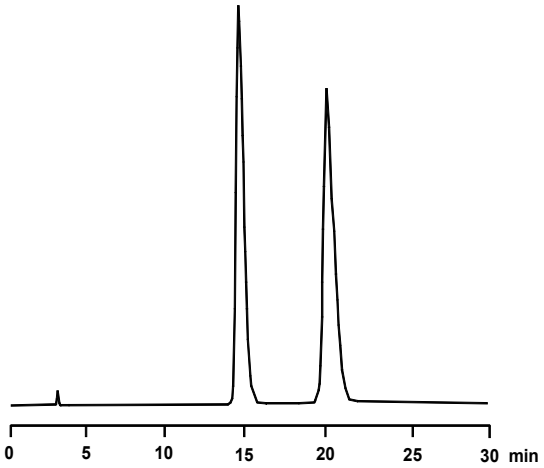


Fig. 4

Chiral separation of methyl phenyl sulfoxide with Eurocel 02 (5 µm) in normal phase mode (Hex-IPA 75:25)

Conclusion

With the availability of more stationary phases for the separation of chiral samples, enhancing the throughput of column screening is a key issue for a thorough test of possible combinations. With parallel HPLC systems the process can be speeded up. Thus the influence of other parameters and more solvents can also be investigated in shorter time. With the Chiral Column Screening Wizard Software it is possible to reprocess up to 80 chromatograms (10 sepmatix runs) in a few minutes. The racemic mixture of methyl phenyl sulfoxide can be separated with Eurocel 01 and Eurocel 02 column types in normal phase mode with different selectivity. In this case the cellulose based column material with benzoate and 3,5 dimethylphenylcarbamate modification can used for monitoring the enantioselectivity of the sulfoxidation of methyl phenyl sulfoxide.

References

[1] M.P.J. van Deurzen, I.J. Remkes, F. van Rantwijk, R.A.Sheldon; J. of Molecular Catalysis A: Chemical 117 (1997) 329-337
[2] S. Colonna, N. Gaggero, L. Casella, G. Carrera, P. Pasta; Tetrahedron: Asymmetry Vol.3, No. 1 pp. 95-106 (1992)

Physical properties of recommended columns

Knauer Eurocel chiral columns are designed to cover a majority of chiral applications. They are based on a high quality spherical silica matrix with a derivatized cellulose coating.

Stationary phase	Eurocel 01	Eurocel 02	Eurocel 03	Eurocel 04
USP code	L40			
Pore size	<- 1000 A ->			
Avail. particle sizes	<- 3 µm, 5 µm, 10 µm, 20 µm ->			
Shape	<- spherical ->			
Dimensions	<- 250 x 4.6 mm ->			
Order number	25EM370ECG	25EM390ECJ	25EM400ECJ	25EM480ECJ

Recommended instrumentation

The sequential screening system was assembled with the following modules:

Description	Order No.
Smartline Pump 1000, incl. 10 ml pump head	A50303
Smartline Autosampler 3950	A5005-1
Smartline Oven 4050	A5300
Smartline Manager 5000 with degasser and LPG	A5313
Smartline Detector 2800 PDA	A5250
Smartline Solvent Selection Valve	A1490
Smartline Switching Valve for column selection (2x)	A1488
ChromGate Software	A1493
ChromGate PDA License	A1460

The parallel screening system shown above is assembled from the following modules:

Description	Order No.
Smartline 1000 Pump, incl. 10 ml pump head	A50303
Solvent Selection Rack- 6 solvents, Sepiatec	upon request
Sepmatix 8x FlowControl, Sepiatec	upon request
Sepmatix 8x Autosampler, Sepiatec	upon request
Sepmatix 8x DADetector, Sepiatec	upon request

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