

Berger Minigram – Analytical & Small Scale Prep (Nov 2005)



- Analytical columns: 250mm x 4.6mm (4ml/min, 100bar, 35°C)
 - Chiral: AD-H, AS-H, OJ-H, OJ-H, IA, I C, CHI-TBB
 - Achiral: pyridine, cyano, diol, silica
- Prep columns: 250mm x 10mm (9.99ml/min, 100 bar, 35°C)
- Screen solvents: MeOH, EtOH, IPA, MeCN/MeOH 90/10, EtOH/MeOH 50/50, BuOH

Berger Multigram III – Large Scale Prep (Oct 2007)



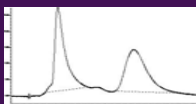
- Bulk tank 3.73m x 1.91m (1680kg CO₂)
- Flow: 0-400ml./min.
- Columns: 150mm x 20mm cyano
 - 250mm x 20mm AD-H, AS-H, OJ-H, OD-H,
 - 250mm x 30mm diol, silica, pyridine, chiralpak IC

Comparisons of SFC with HPLC

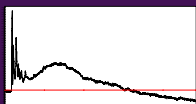
In addition to SFC's advantages of speed, reduced evaporation times, low cost of CO₂, green technology, it complements HPLC often giving separations seemingly intractable by HPLC and other techniques

Example 1 SFC Vs. HPLC

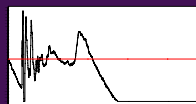
20µm Chiralpak AS
iso-Hexane/EtOH 50/50



5µm Chiralpak AS-H
CO₂/EtOH 60/40

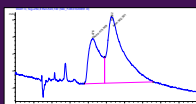


5µm Chiralpak AS-H
CO₂/EtOH/isopropylamine 60/40/0.2

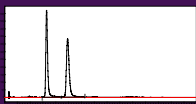


•Most compounds for a particular project gave poor SFC results using the amylose columns which had given good separation by HPLC

5µm Chiralcel OD-H
iso-Hexane/EtOH 50/50



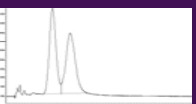
5µm Chiralcel OD-H
CO₂/EtOH 80/20



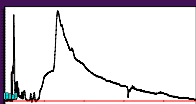
•Most compounds from this project gave no/little separation by HPLC using Chiralcel OD-H but very good separation with OD-H by SFC

Example 2 SFC Vs. HPLC – Addition of modifiers

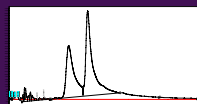
20µm Chiralpak AD
iso-Hexane/EtOH 40/60



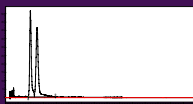
5µm Chiralpak AD-H
CO₂/EtOH 60/40



5µm Chiralpak AD-H
CO₂/EtOH/isopropylamine 60/40/0.2



5µm Chiralcel OD-H
CO₂/EtOH 80/20



- No base was required for HPLC
- Addition of base was essential for SFC using Chiralpak AD-H but not for Chiralcel OD-H

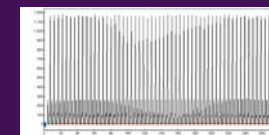
Example 3 SFC Vs. HPLC for large scale prep

A precursor to a final compound was found to contain a major impurity (approx 10%) even after large Scale prep HPLC. Within the Separation Science Group at Alderley Park large scale preps are usually carried out directly after method development by TLC, however, even after investigating an extensive range of solvent systems no separation of the impurity could be detected. An initial SFC screen gave excellent separations on all 4 achiral columns with all 6 solvent systems (10%) with short run times

	MeOH	EtOH	IPA	MeCN/MeOH 90/10	EtOH/MeOH 50/50	Bu-1-OH	
Pyridine							Analytical column/ solvent screening
Cyano							
Diol							
Silica							



Single injection



60 stacked injections

Approximately 31gms were chromatographed in 404 injections.
First eluted peak (impurity) (> 99.9%)

Second eluted peak (desired compound) 23.6gms (>99.9%)

Prep Conditions

Column: 5µm Diol 250mm x 30mm
Eluent: CO₂/MeOH 90/10
Flow: 120ml/min
Sample Conc: 25.44mg/ml in MeCN/
MeOH + sonication
Inj vol: 3.75ml