AstraZeneca Void Volume Study

Column Void Study by Daniel C. Hill Performed September 2007

The purpose of this experiment is to determine if the column void present in Thomson SINGLE StEP Columns Patented affects the separation efficiency. In this example the column void was left empty in two experiments and filled with sand in a separate experiment. The results clearly show there is little difference between the three runs.

Procedure: The sample used in this experiment originated from a somewhat inefficient palladium catalyzed coupling reaction between an aryl bromide and N-methylpiperizine: the two major peaks observed were starting bromide and coupled product. Dry columns were equilibrated with hexane prior to use. Approximately 200 mg of the solid reaction product isolated from the reaction was loaded onto a 4g Thomson column dissolved in ~1 mL of dichloromethane. The column was eluted with hexane for 1 minute, ramped to 10% EtOAc/Hexane over 1 minute and kept at 10% EtOAc/Hexanes for 4 minutes. The column was ramped to 90% EtOAc/Hexane over 9 minutes and kept at 90% EtOAc/Hexanes for 2.5 minutes. Detect peaks @ 254 nm, fraction collection volume = 16 mL. The three chromatograms show the results obtained.

Figure 1 - Column void left empty. Thomson2 - 4 g; equilibration time 1 min 56 seconds @ 30 mL/min. Loaded 200.2 mg solid mixture, run flow rate 10 mL/min

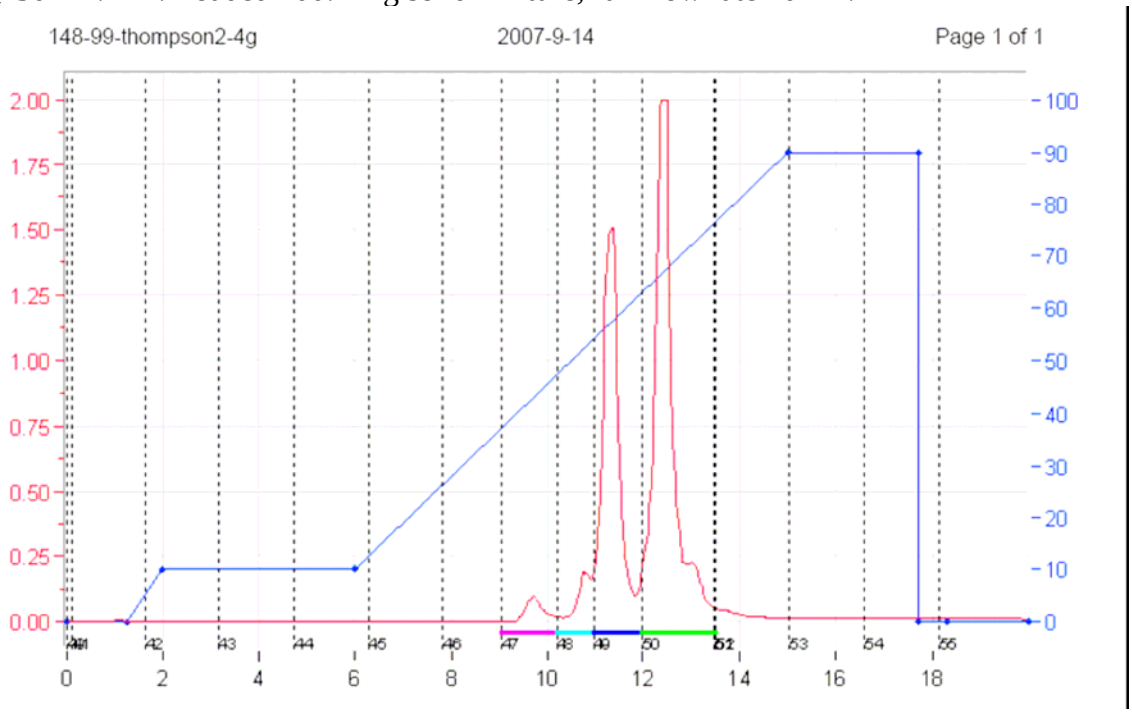

Figure 2 - Column void filled with sand. Thomson3 - 4 gs; equilibration time 2 min 5 seconds @ 30 mL/min. Loaded 204.4 mg solid, run flow rate 10 mL/min.
(void @ top of column filled with sand/hexane)

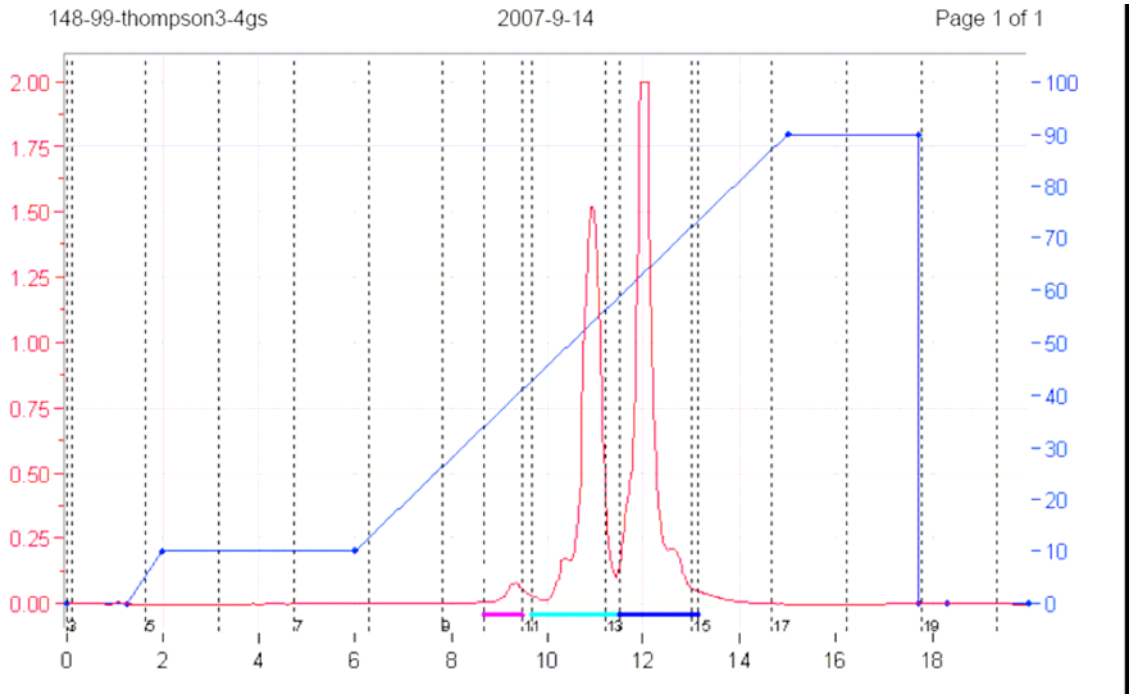

Figure 3 - Column void left empty. Thomson4 - 4 g; equilibration time 2 min 15 seconds @ 30 mL/min. Loaded 202.6 mg solid, run flow rate 10 mL/min.