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Chiral Separations at Elevated Temperatures on a CHIRALPAK® IA Column

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The CHIRALPAK® IA column is found to be stable to elevated temperatures, offering an additional means of controlling chiral HPLC separations.

The effect of temperature on chiral separations is fairly well established. In general, increasing temperature increases column efficiency but decreases both retention and enantioselectivity. The decrease in selectivity will vary between compounds, and the rate of decrease depends on the difference in binding enthalpies of the enantiomers. The effect of temperature on column efficiency depends on changes in mobile-phase viscosity, diffusion rates in the stationary phase, and kinetics of dissociation. Some separations are improved using subambient temperatures if the increased selectivity is sufficient to offset the loss in column efficiency. The narrow allowed temperature range of coated polysaccharide chiral stationary phases means temperature is rarely exploited as a means of controlling separation. The CHIRALPAK® IA column is an immobilized phase, and it was expected that it would be stable at elevated temperatures.

Results

Five compounds were chromatographed on a CHIRALPAK® IA column using a methyl-*tert*-butyl ether mobile phase at 15 °C, 25 °C, 40 °C, 60 °C, and 80 °C. As expected, retention and selectivity decreased for all compounds at elevated temperatures while column efficiency improved. The net effect on resolution was a decrease with temperature for 4-benzoyloxy-2-azetidinone, devrinol, and anisoin. The loss of resolution was minor except for devrinol, which declined from 5.02 at 15 °C to 1.58 at 80 °C. Although the rate of selectivity decrease was not as dramatic for other compounds, initial selectivity was low enough that the separation collapsed with this decline. Two compounds, aminoglutethimide and α -methyl- α -phenylsuccinimide, gave increased resolution at the elevated temperatures. The resolution increase for aminoglutethimide was dramatic (5.8 \rightarrow 10.4). The separation at 80 °C was completed in 15 min compared to the 30 min required at 15 °C.

Figure 1 shows the separation of devrinol at 25 °C before and after the column was exposed to elevated temperatures. The column appears to be stable to these temperatures. Similar results were obtained for all probes.

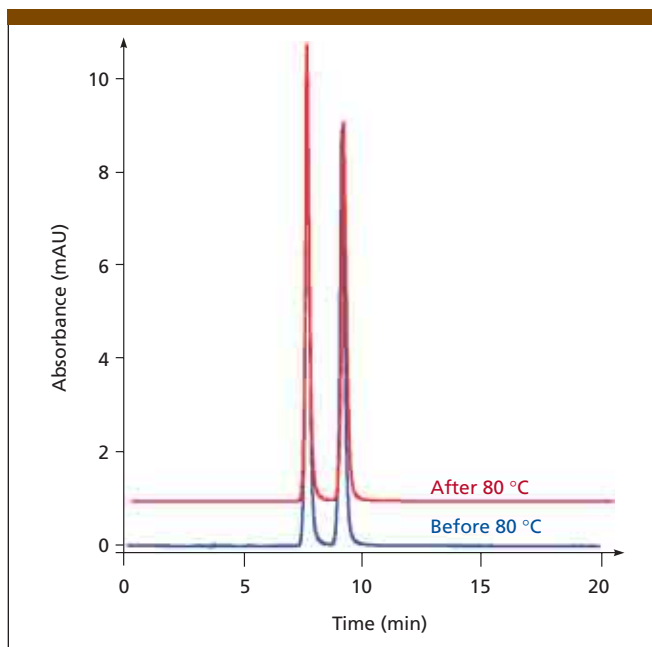


Figure 1: Separation of devrinol at 25 °C on CHIRALPAK® IA using MTBE as the mobile phase before and after exposure to 80 °C.

Conclusions

The net effects of temperature on chiral separations are specific to the compound. The CHIRALPAK® IA column appears to be stable to at least 80 °C. This expanded temperature range makes temperature a variable worth investigating.

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