Synthesis of A New Class of Pirkle-Type Chiral Stationary Phases on Zirconia

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Specialists in High Efficiency, Ultra-Stable Phases for HPLC.

Goal-To Make Zirconia Based Chiral Stationary Phases (CSPs)

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- Why Zirconia?
- General Synthetic Method
- Comparison of Zirconia-based CSPs with Commercial Silica-based CSPs
- Chromatographic Comparison of Different Anchors
- Stability Study of Zirconia-based CSPs
- Examples of Enantiomer Separations on Zirconia Based CSPs
- **Conclusions –Zirconia Based CSPs Have Comparable Chromatographic Performance Compared to Silica Based CSPs. Fast Chiral Separations Can Be Achieved on Nonporous Zirconia Based CSPs.**

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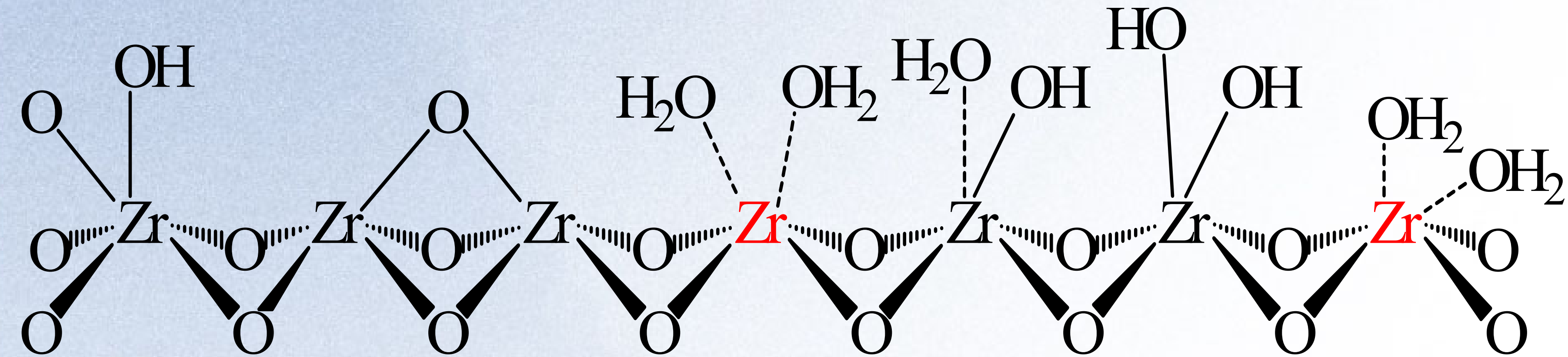
Zirconia - The difference is the surface chemistry.

Surface Chemistry of Zirconia



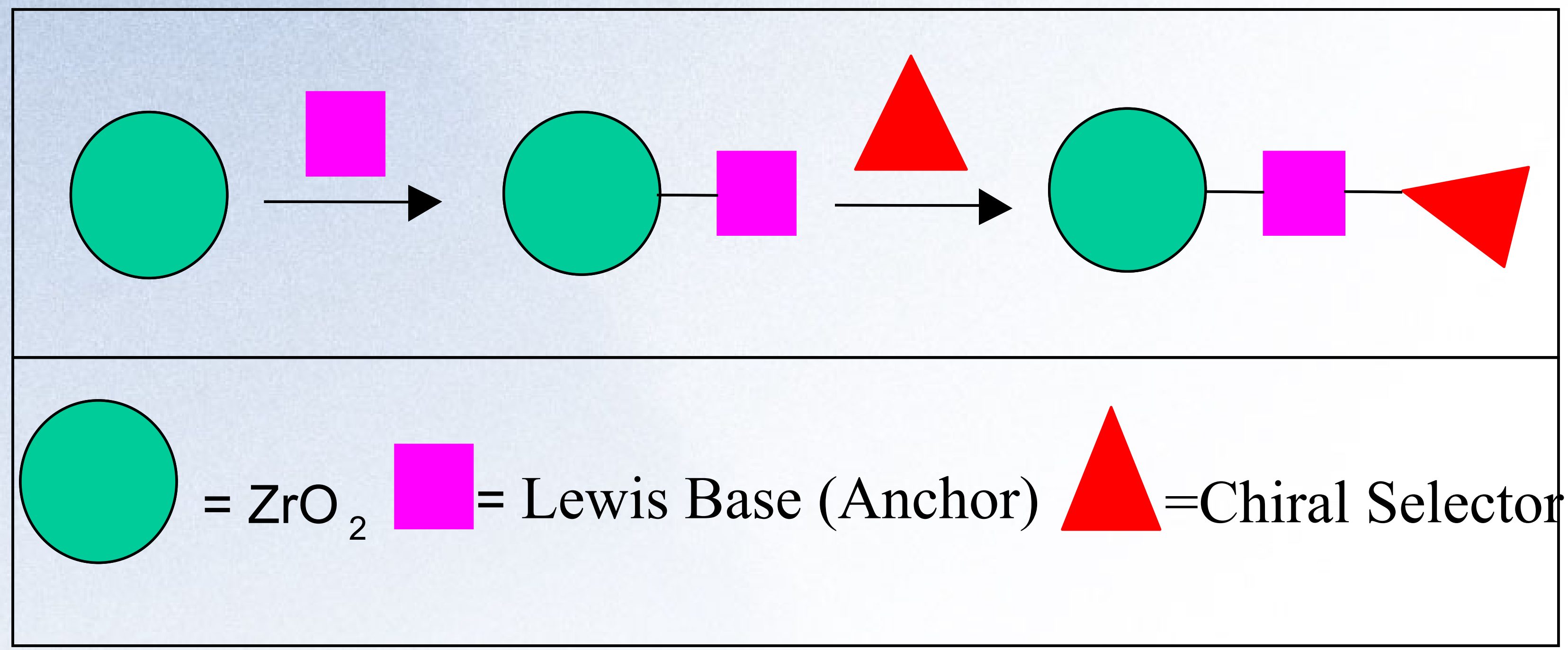
Brönsted Acid: $ZrOH + {}^{-}OH \rightleftharpoons ZrO^{-} + H_2O$

Brönsted Base:

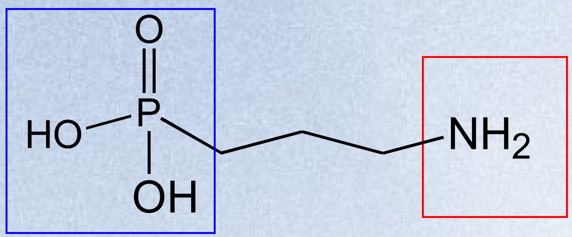
RPO_3^{2-} or Catechol

Lewis Acid: $Zr^{4+}: H_2O + R\text{-}COO^{-} \rightleftharpoons Zr^{4+}:{}^{-}OOC\text{-}R + H_2O$

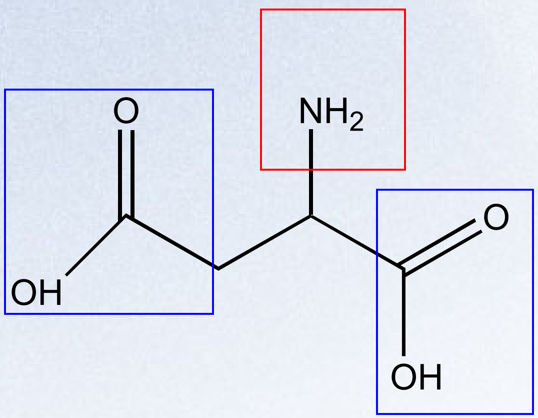
New Way to Attach Chiral Selectors to Zirconia Surface



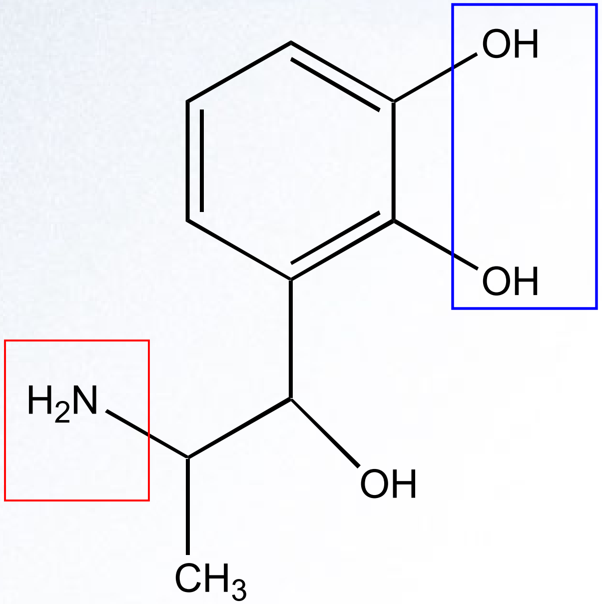
Three Anchors in This Study



APPA **(Aminopropylphosphonic acid)**



ASPA **(Aspartic acid)**



DHNP **(3,4-Dihydroxynorephedrine)**

Anchors should have two function groups: (1) A group anchoring to zirconia surface, and (2) A group bonding to Chiral selector.

Five Classes of CSPs

1. Pirkle/Brush Type CSPs
2. Polymer Based CSPs
3. Cyclodextrins Based CSPs
4. Protein Based CSPs
5. Ligand exchange CSPs

Chiral Selectors in This Study

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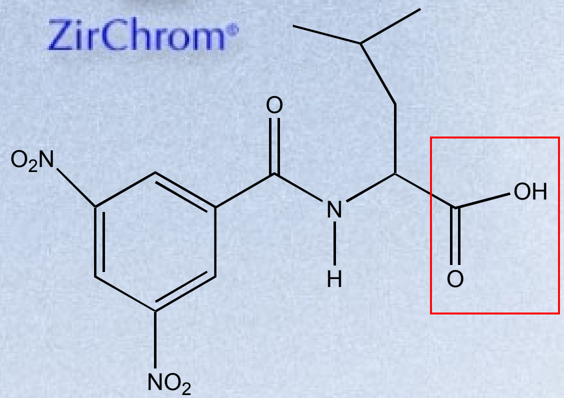
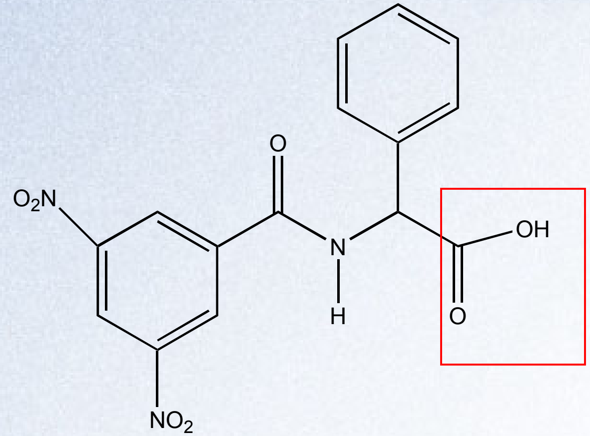
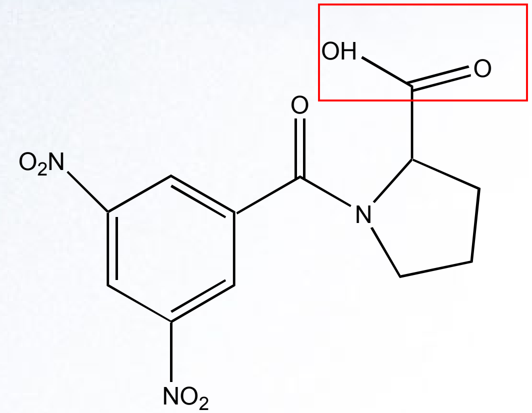


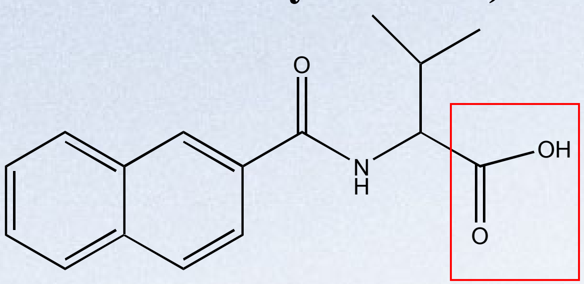
DNB-LEU (3,5-dinitro-benzoylLeucine)



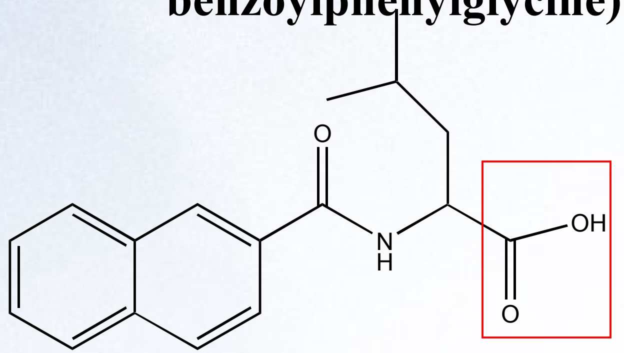
DNB-PG (3,5-dinitro-benzoylphenylglycine)



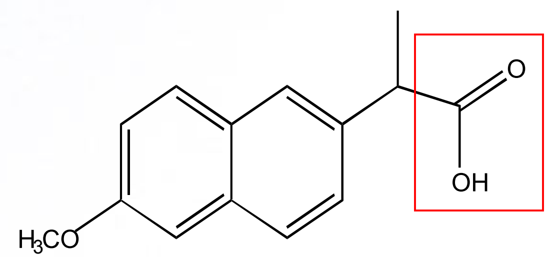
DNB-PRO (3,5-dinitro-benzoylproline)



NAP-VAL (Naphthoyl-valine)



2-NAP-LEU (2-Naphthoyl-leucine),



NAP (naproxen)

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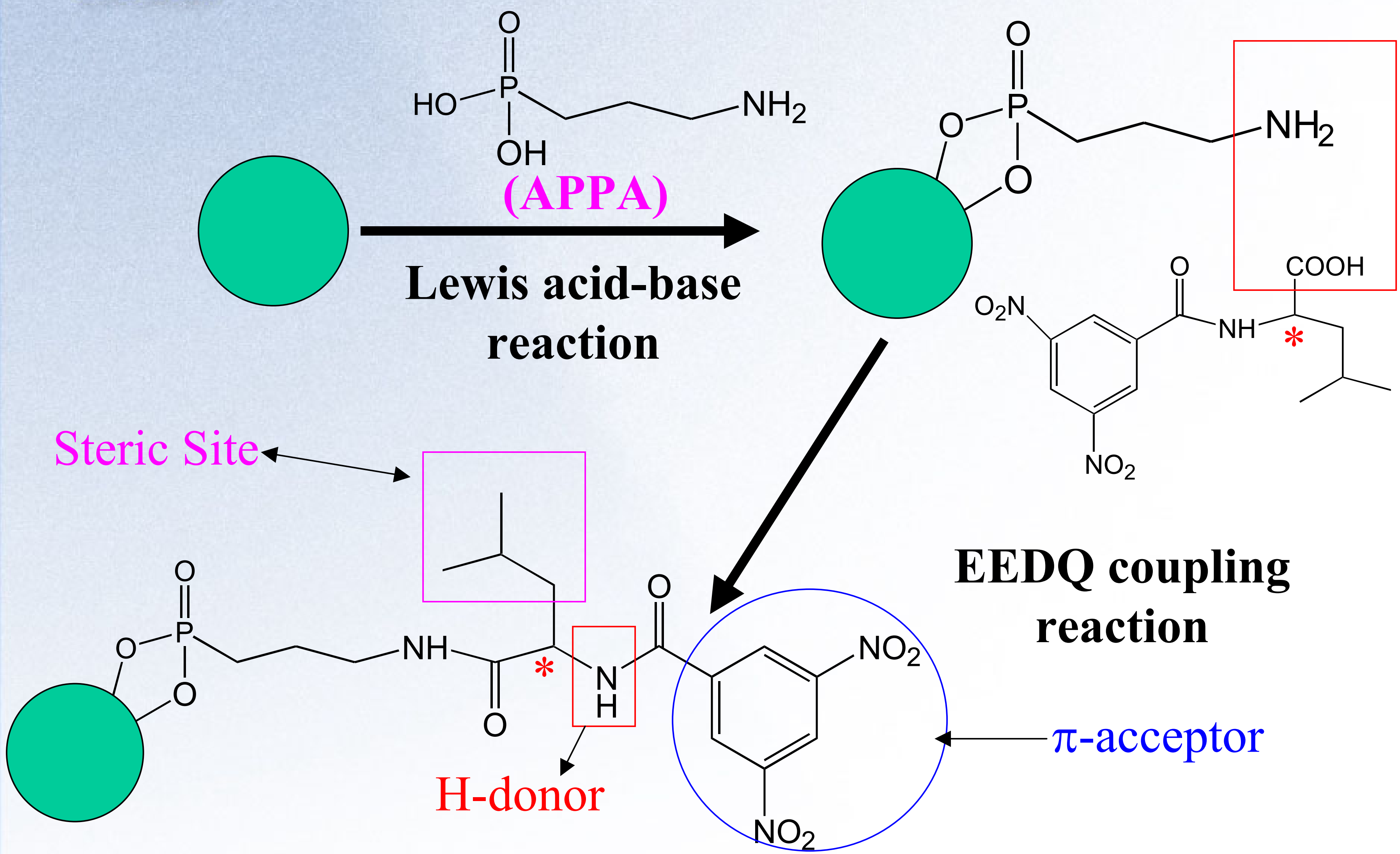
Example of Lewis Acid-Base Modified Zirconia CSPs

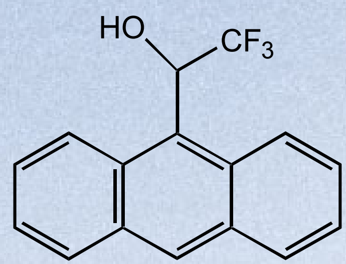


List of Zirconia and Silica CSPs Studied

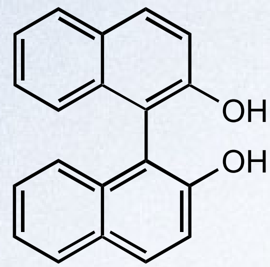
Column	CSP	Anchor
Z1	DNB-Leu	APPA
Z2	DNB-Leu	Aspartic acid
Z3	DNB-Leu	DHNP
Z4	DNB-PG	APPA
Z5	DNB-PG	Aspartic acid
Z6	DNB-PG	DHNP
Z7	DNB-Pro	DHNP
Z8	NAP-Leu	APPA
Z9	NAP-Val	DHNP
Z10	Naproxen	APPA
R1	DNB-PG	--
R2	DNB-Leu	--

Z1-Z10 **zirconia** based CSPs, R1, R2-commercialized **silica** based CSPs

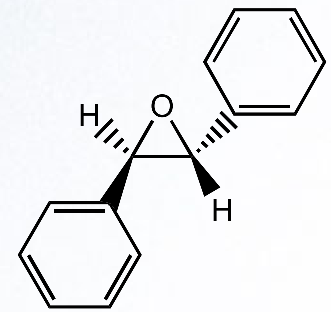
Structure of Chiral Probe Solutes Used in This Study



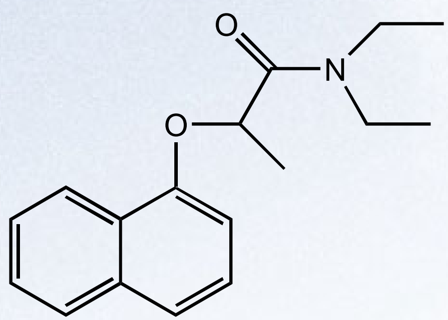
Trifluoroanthryl Ethanol



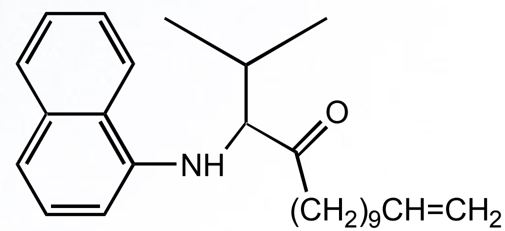
1,1'-bi-2-naphthol



Trans-stilbene oxide

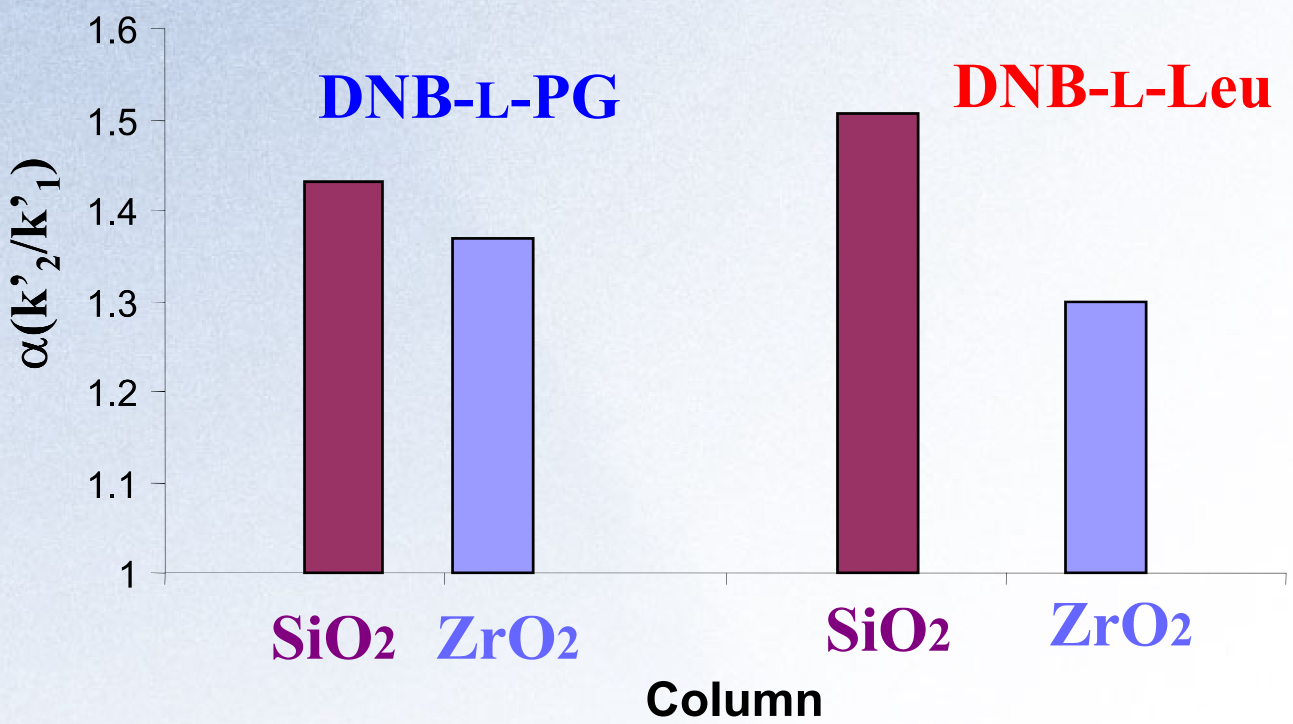


Napropamide



1-naphthyl leucine ester

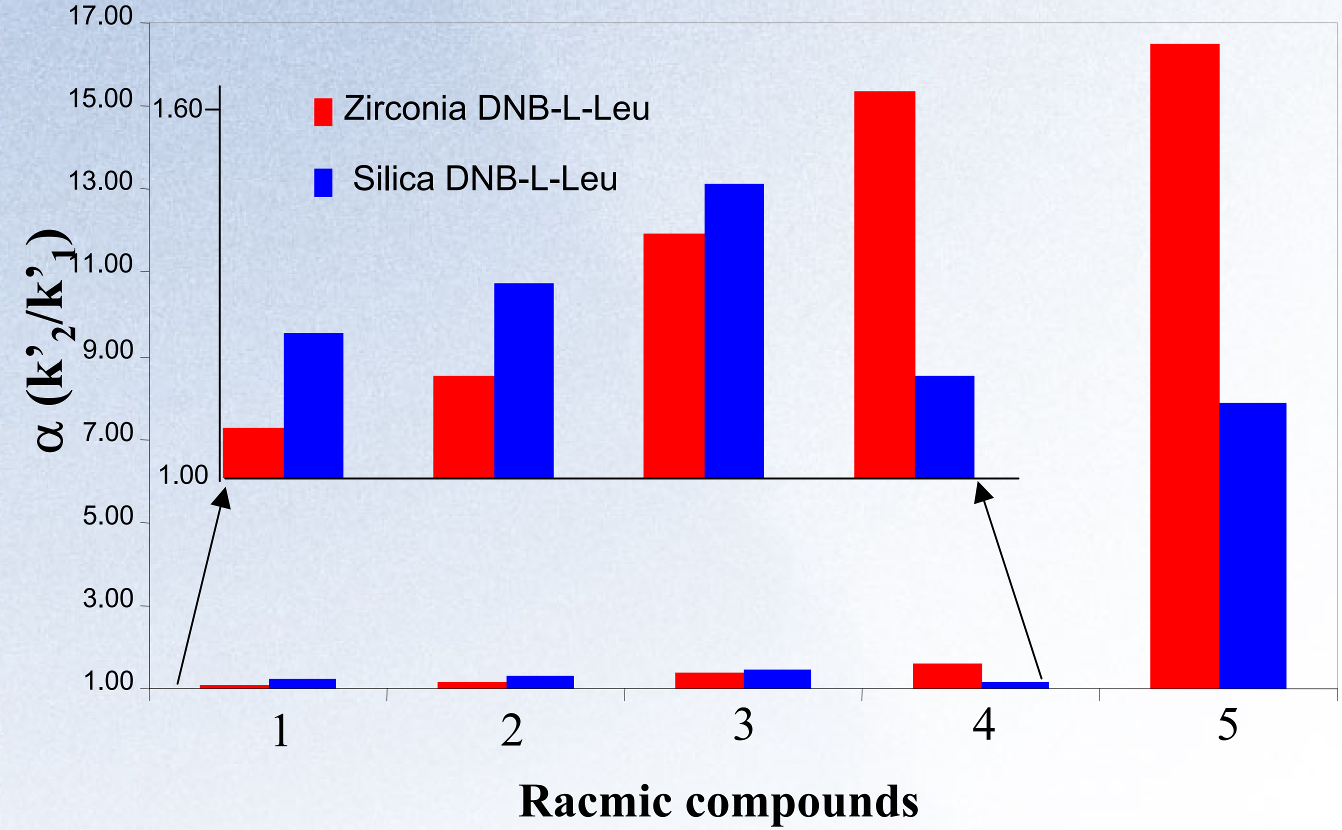
Chromatographic Comparison of Zirconia- and Silica-CSPs



Probe solute: Trifluoroanthryl ethanol

Conclusion: Zirconia based CSPs performed quite well.

Direct Comparison of DNB-L-LEU Zirconia and Silica Based CSPs



1 trans-stibene oxide
2 1,1'-bi-2-naphthol
3 trifluoranthyl ethanol
4 napropamide
5 1-naphthyl leucine ester

Much better separations for napropamide and 1-naphthyl leucine ester are obtained on zirconia-based CSPs.

Stability of Zirconia-based DNB-L-LEU

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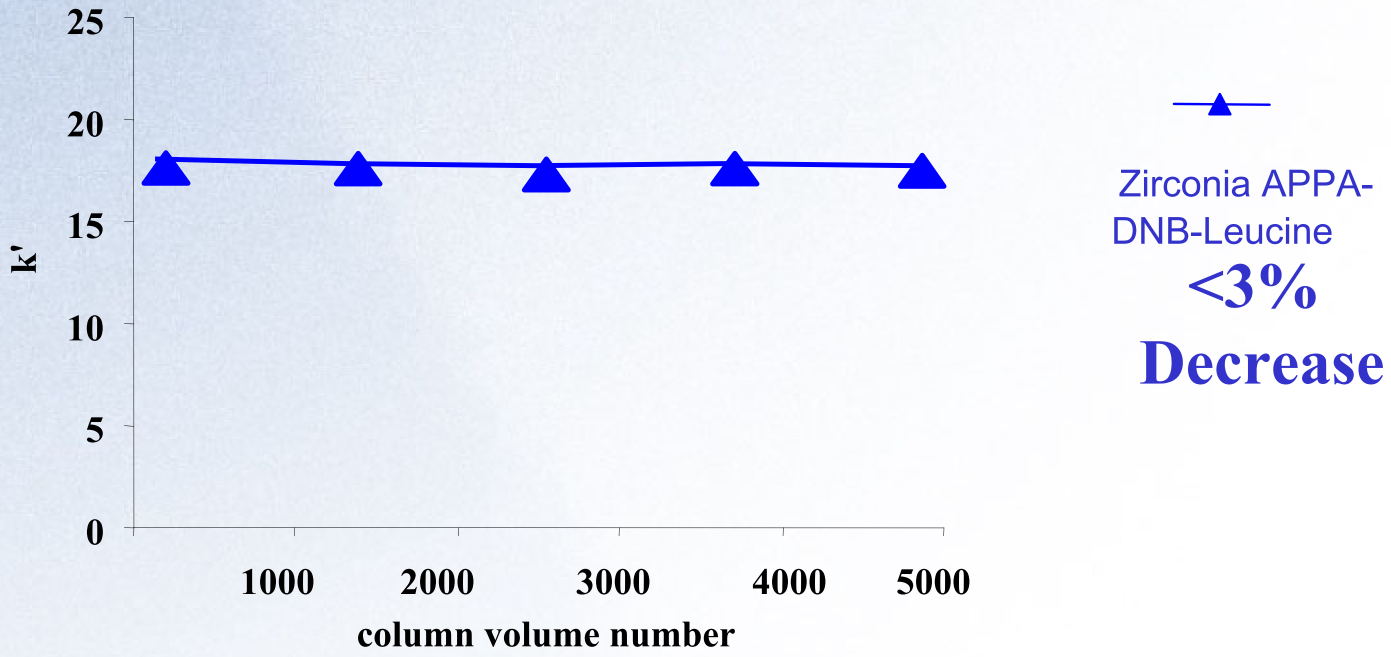
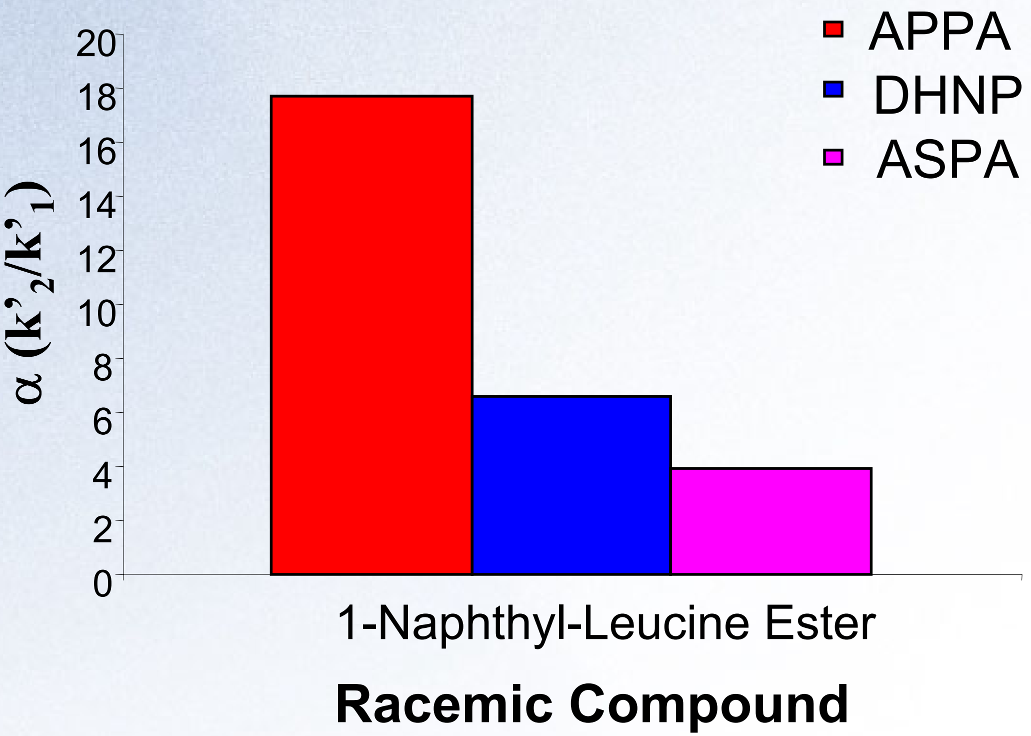
Retention Factor Stability for S-Napthylleucine ester



Flush Solvent: 49.5/49.5/1 Hexane/IPA/TFA

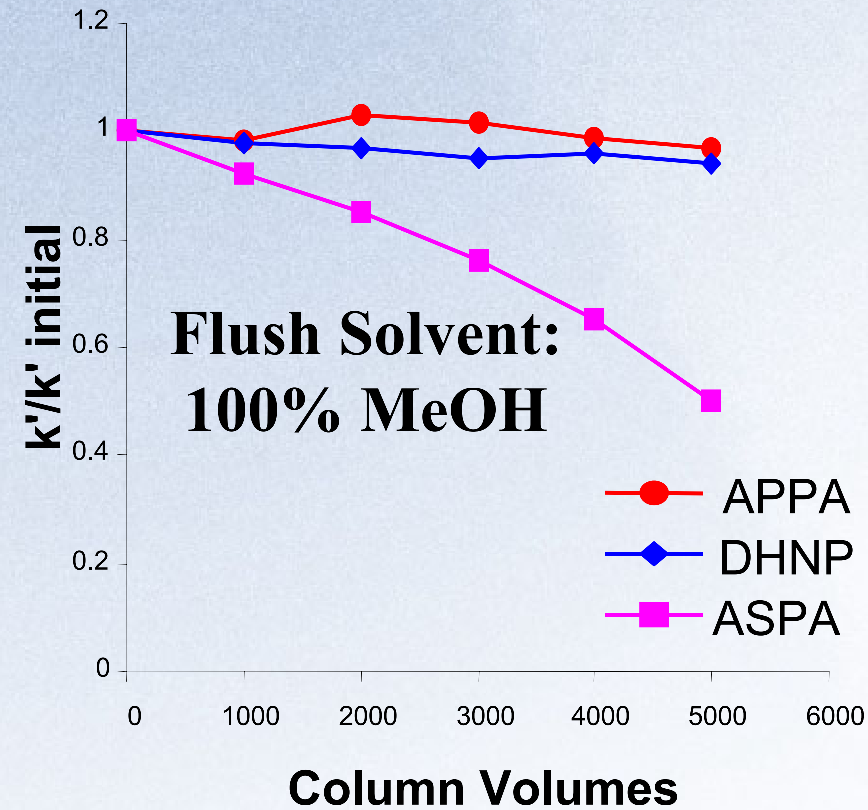
Zirconia-based CSP is a very stable CSP.

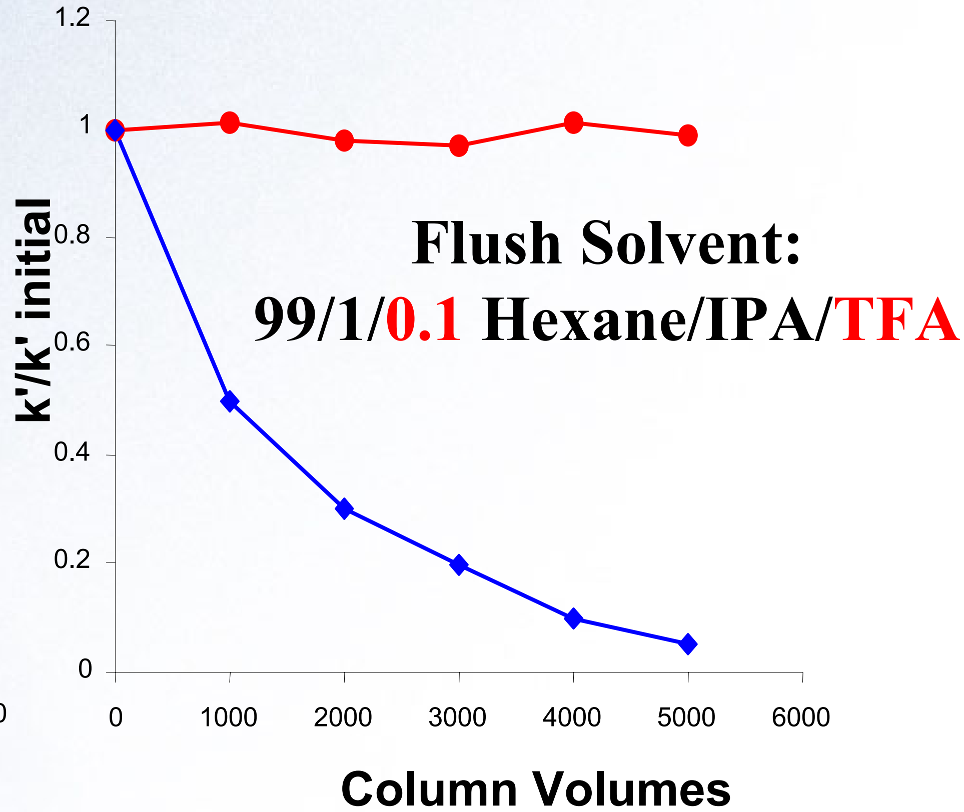
Chromatographic Comparison of Differently Anchored Zirconia-based DNB-L-LEU



Different anchors show different selectivity.

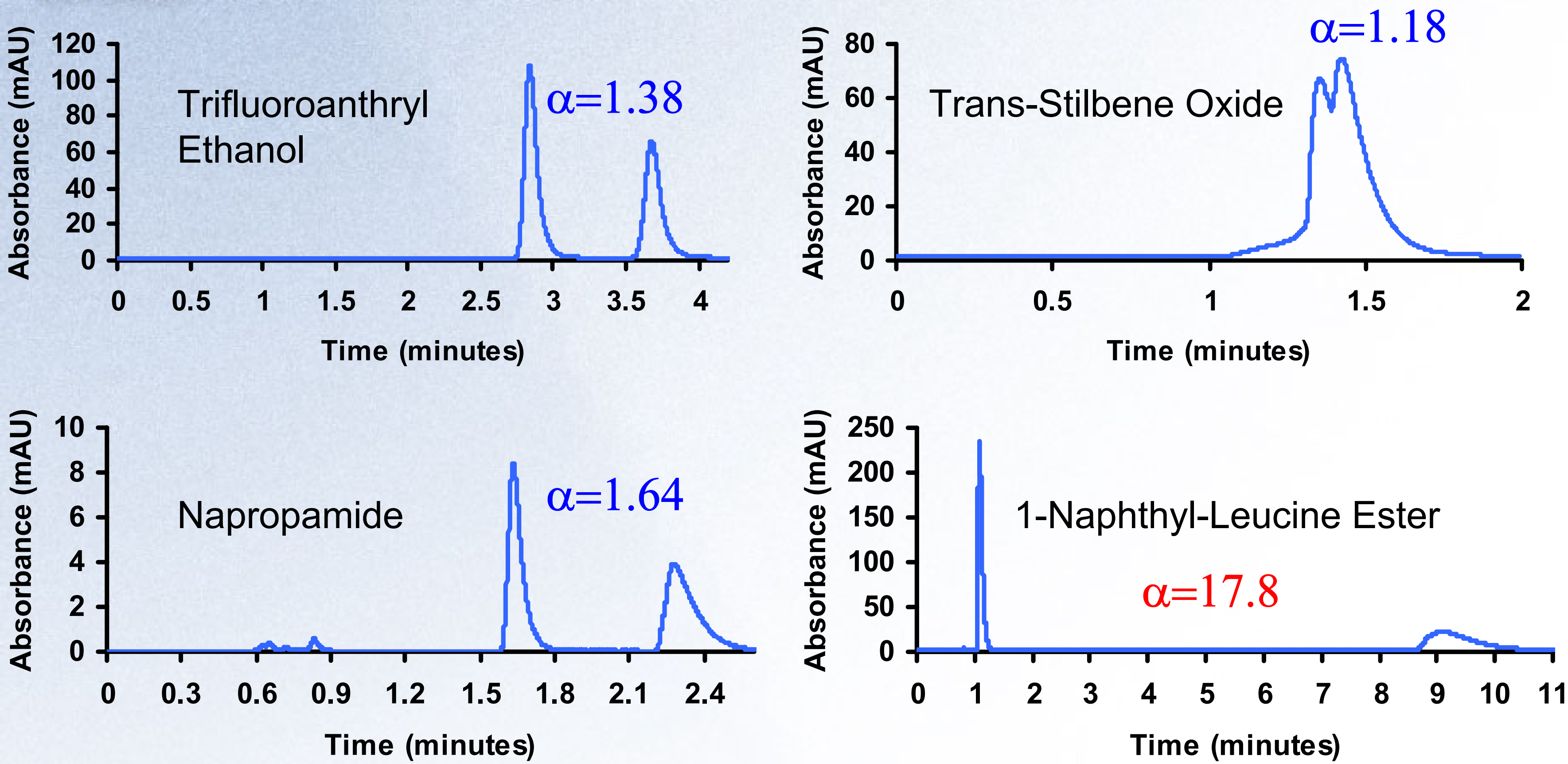
Stability Comparison of Differently Anchored Zirconia-Based DNB-L-LEU





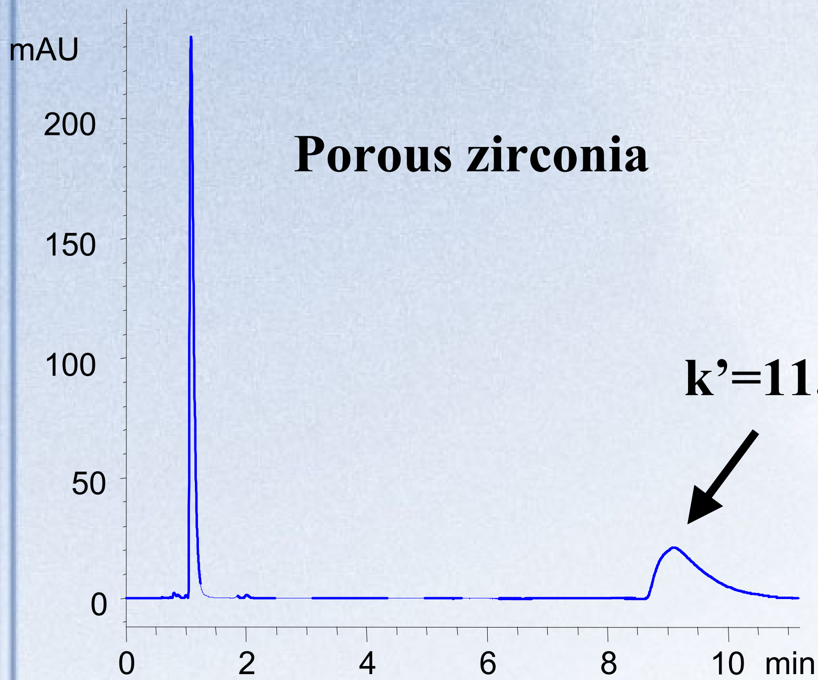
Test solute: trifluoranthryl ethanol. Note that the retention factor ratio is for the less retained isomer.

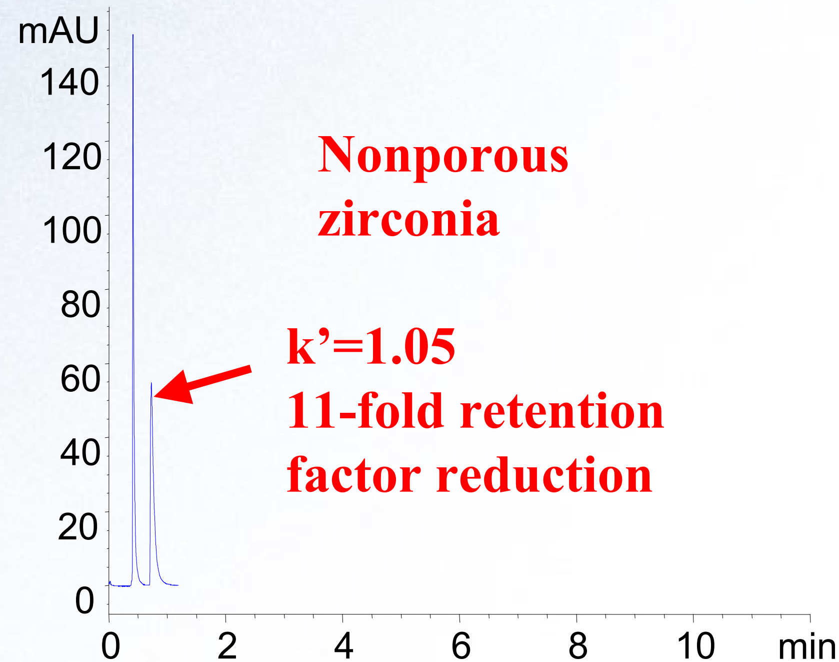
Enantiomer Separations on DNB-L-LEU Modified Zirconia Phase Anchored via APPA



Selected Chromatograms of Chiral Compounds on Zirconia Based DNB-L-LEU Anchored with APPA.

Fast Chiral Separation on Nonporous Zirconia-based DNB-L-Leu





Chiral compounds on nonporous and porous zirconia-based DNB-L-Leu anchored with APPA. Chromatographic conditions: mobile phase 99/1Hexane/IPA, probe solute: (±)1-naphthyl leucine ester.

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Conclusions

- Flexible attachment chemistry.
- APPA is the best anchor in terms of column stability.
- Zirconia based CSPs have comparable chromatographic performance compared to the commercial silica based CSPs for a wide range of chiral compounds.
- Fast Separation can be achieved on nonporous zirconia based CSPs.
- Acknowledgement: National Institutes of Health Grant # 1 R43 HL070334-01.