

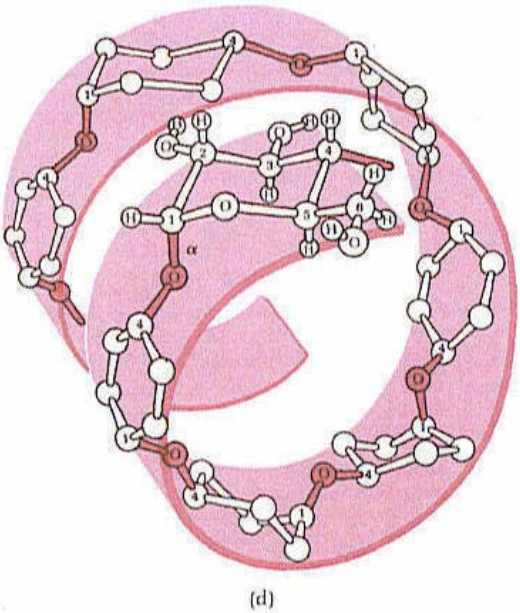
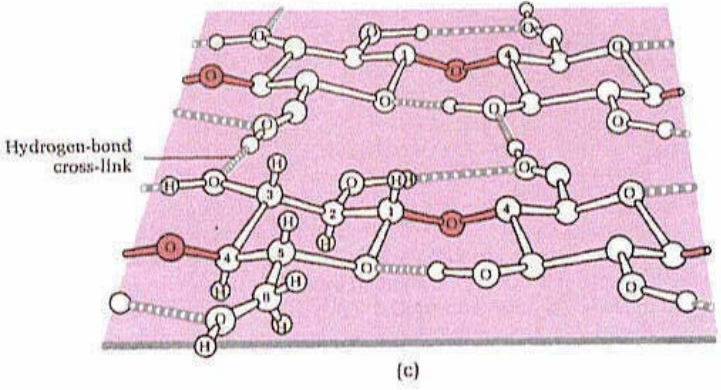
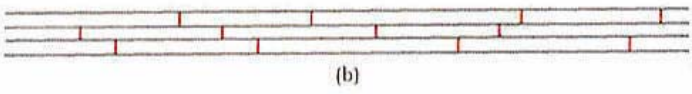
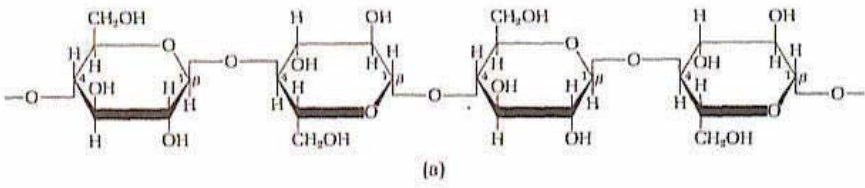
**MECHANISTIC ASPECTS OF CHIRAL  
DISCRIMINATION ON MODIFIED  
POLYSACCHARIDES STATIONARY PHASES**

Nelu Grinberg  
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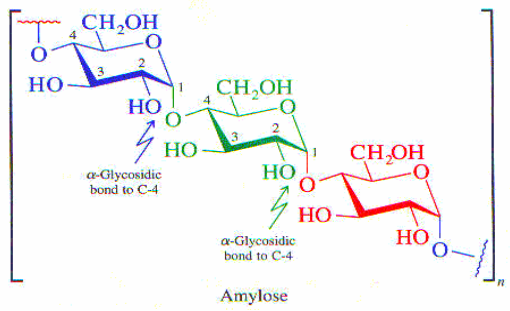
## ENANTIOSELECTIVITY IS A RESULT OF TWO TYPES OF INTERACTIONS:

- a leading interaction and,
  - a secondary interaction
- 
- The leading interaction determines the retention of the enantiomers on a particular stationary phase.
  - The secondary interaction can affect the conformation and the formation energy of the diastereomeric associates.

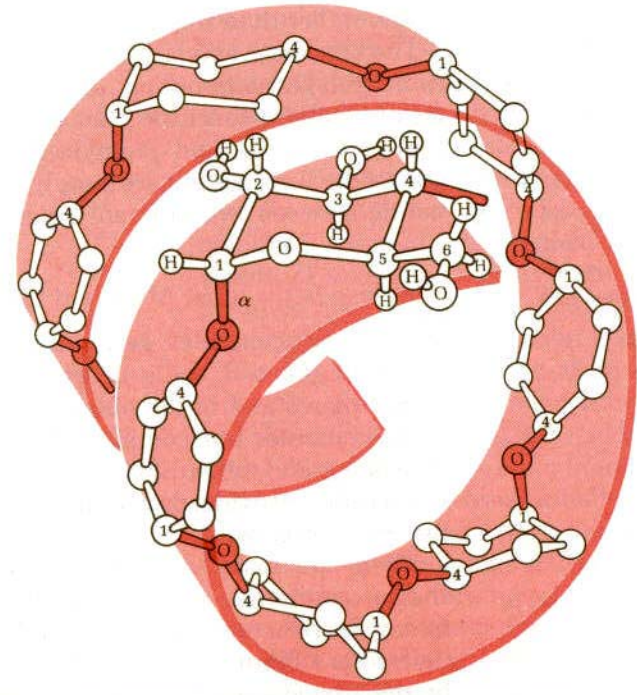
Only when the leading interactions take place and the asymmetric moieties of the two molecules are brought to close proximity, secondary interaction (e.g. van der Waals, steric hindrance, dipole-dipole, etc.) become effectively involved.



- The apparent difference in the structure of cellulose and amylose results in polymeric structures with very different properties.
- Because of their  $\beta$  linkages, D-glucose chains in cellulose assume an extended conformation and undergo side-by-side aggregation.
- Due to the geometry of their  $\alpha(1\rightarrow4)$  linkage, the main chains of D-glucose units in amylose tend to assume a coiled, helical conformation.

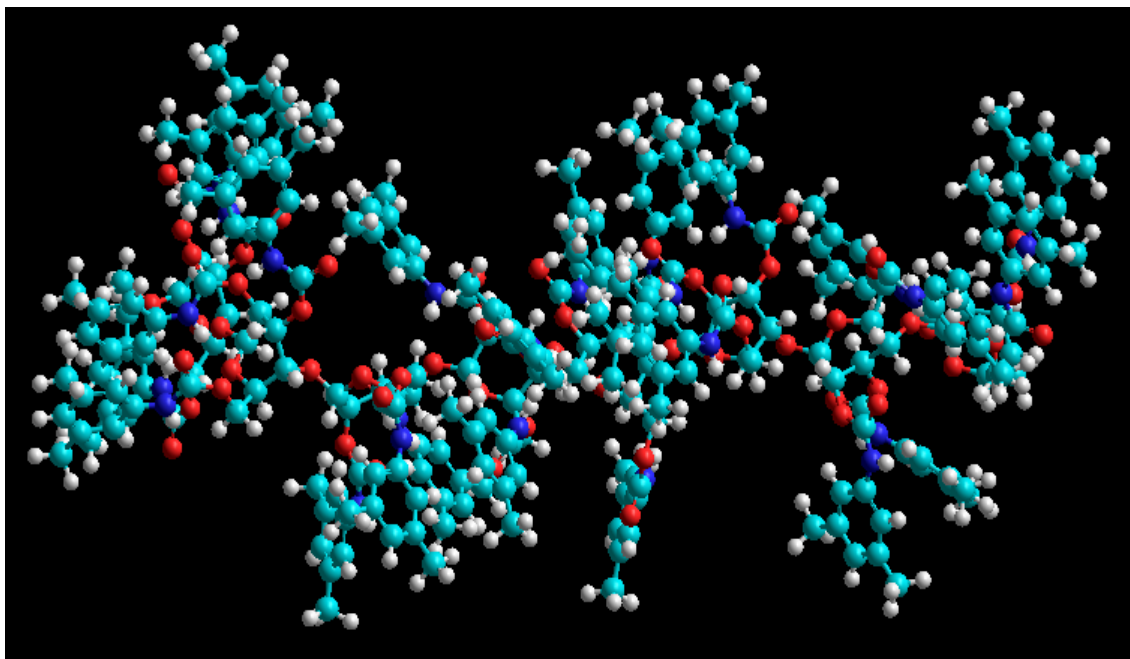


- The structure of Amylose presents an antiparallel packing of chains linked through intermolecular H-bonding.
- A large variety of helix characteristics are evident, in addition to the variability in the crystallographic unit cell dimensions.

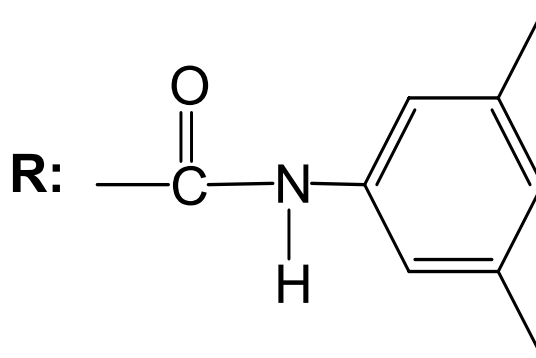
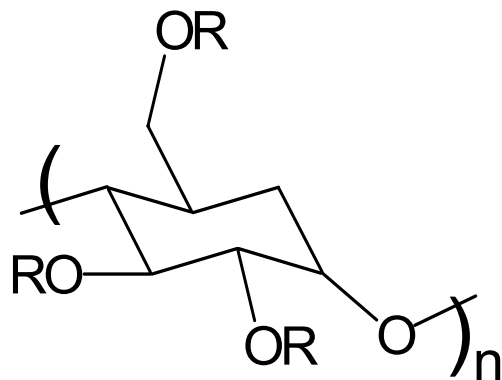


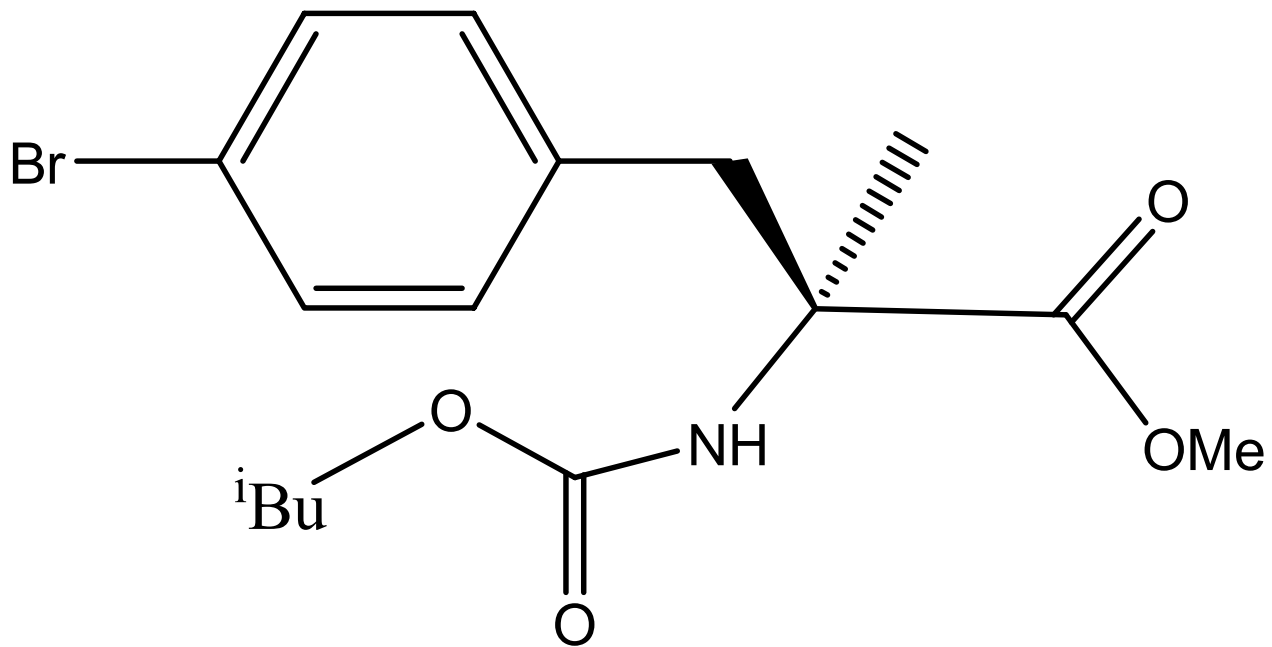
- The hydroxyl groups of Amylose can be chemically modified.
- Substitution at the hydroxyl groups disrupts the H-bonding pattern and introduces new steric interactions between the substituents depending upon the degree of substitution.

# ENERGY MINIMIZED THREE DIMENSIONAL STRUCTURE OF AMYLOSE CARBAMATE FRAGMENT CONTAINING EIGHT UNITS OF $\alpha$ -D-GLUCOSE-TRIS(PHENYL CARBAMATE)

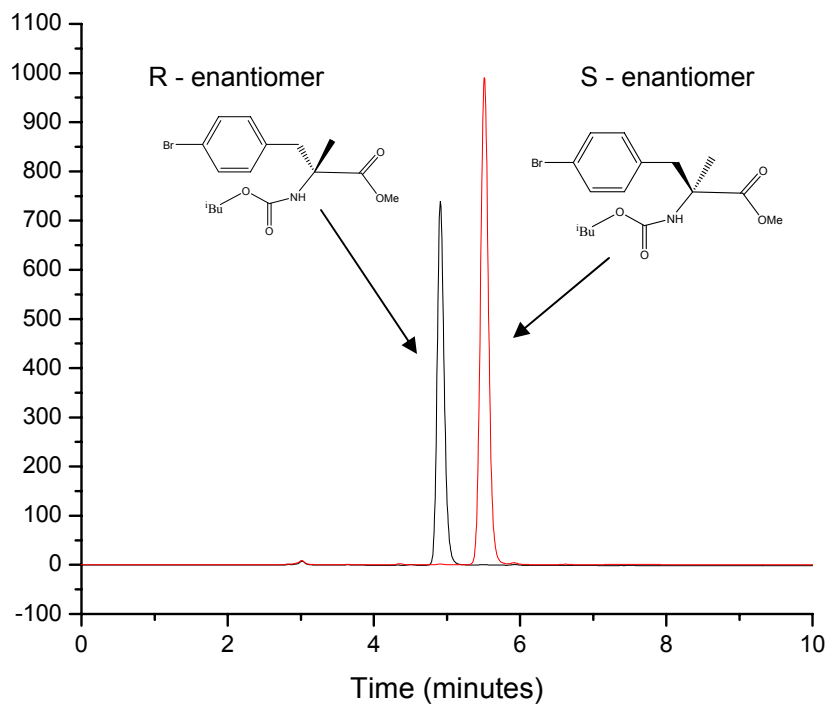
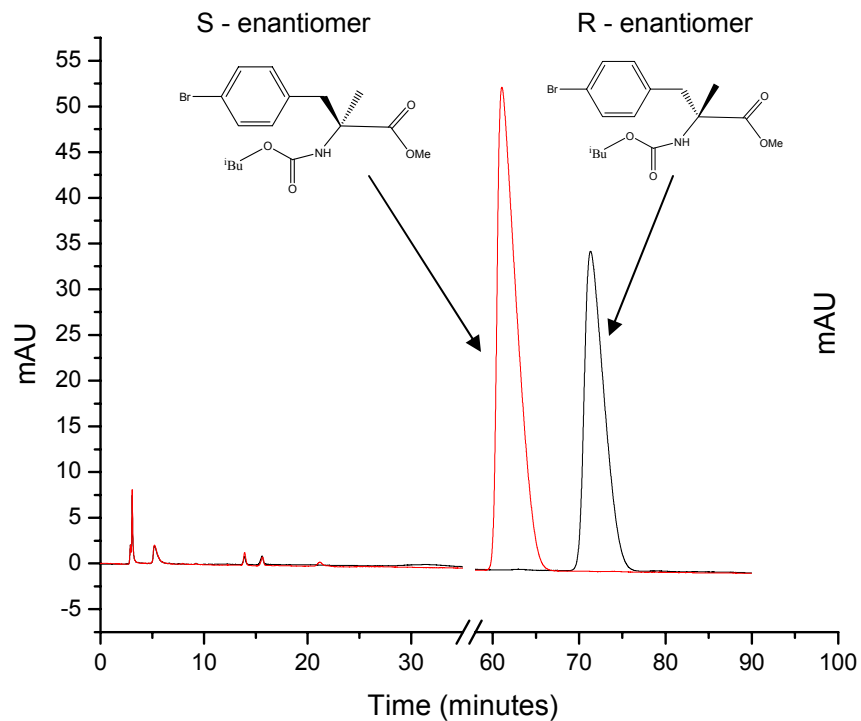


- Amylose tris-(3,5-dimethylphenyl)carbamate (ADMP) has been reported to be a left-handed fourfold (4/1) helix.

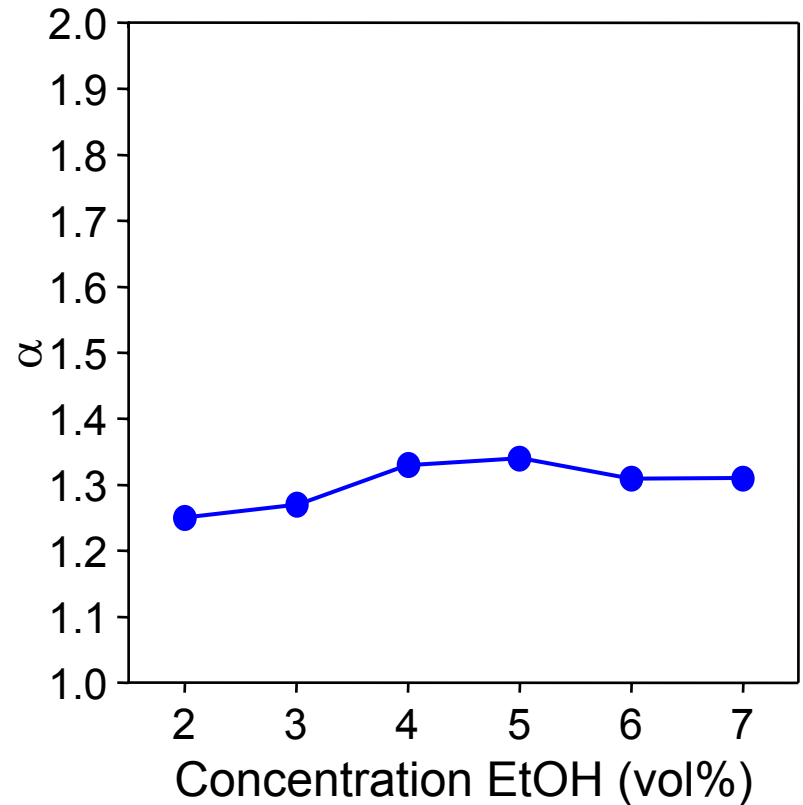
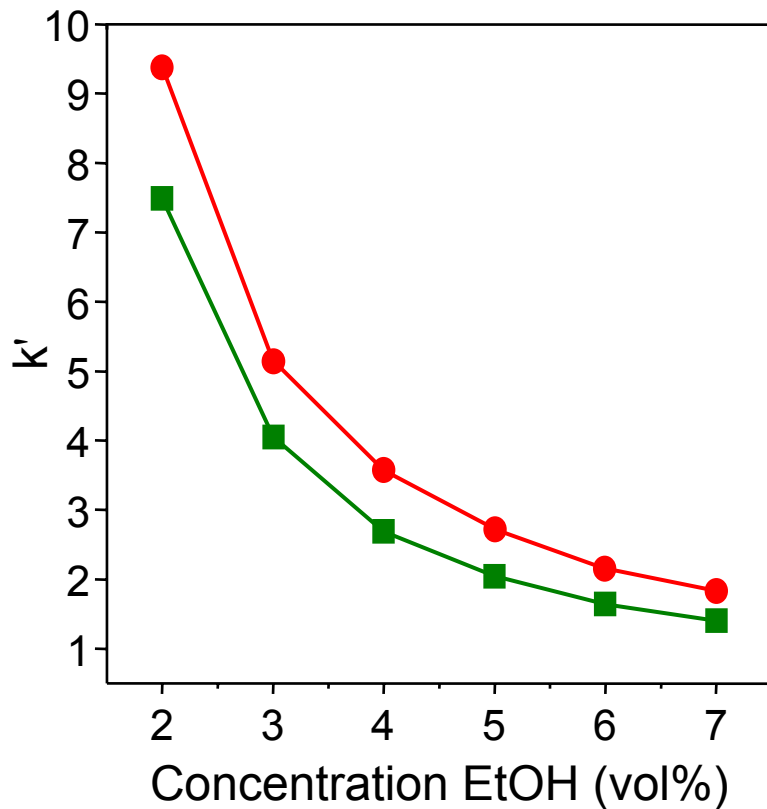




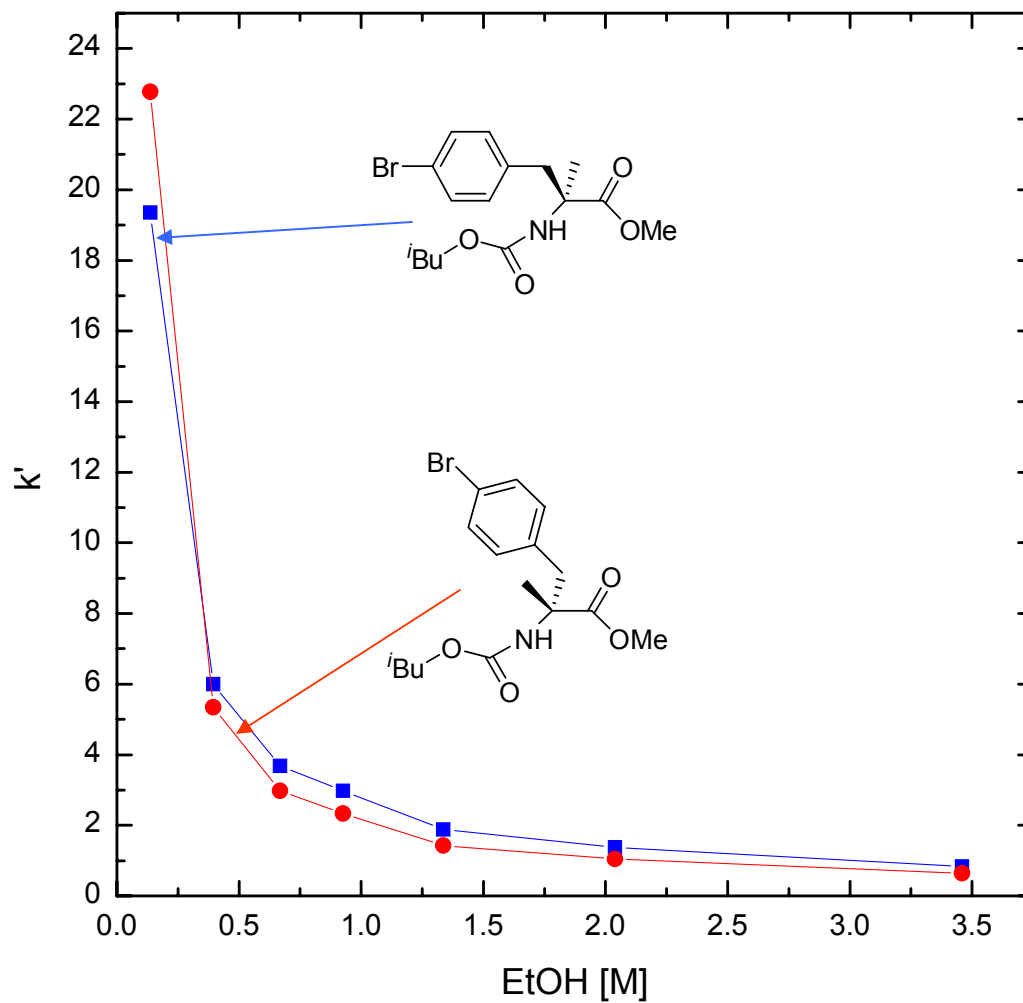
# EFFECT OF THE AMOUNT OF ETHANOL ON THE SEPARATION



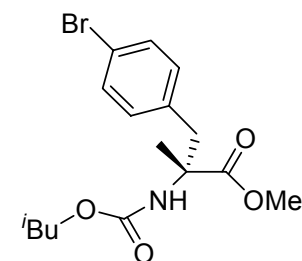
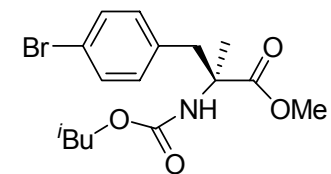
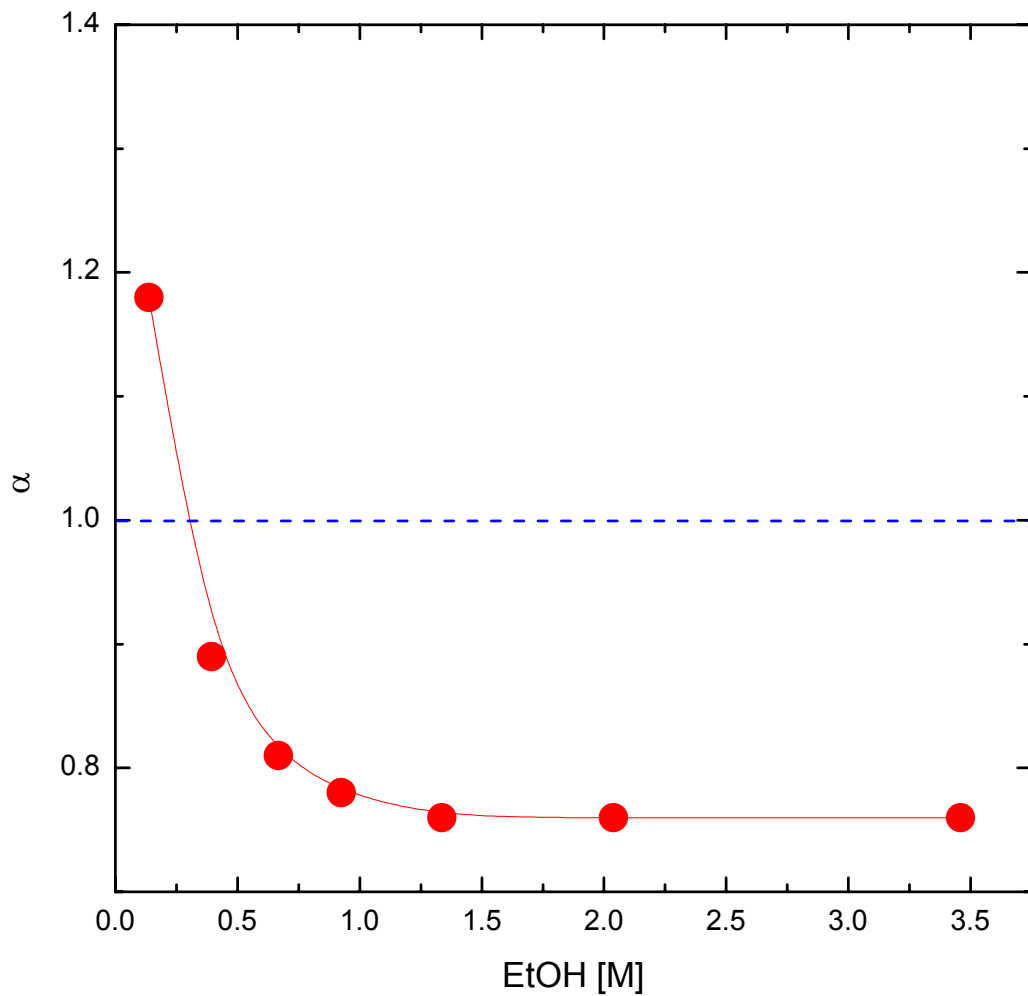
# INFLUENCE OF ETHANOL CONCENTRATION ON $k'$ AND $\alpha$



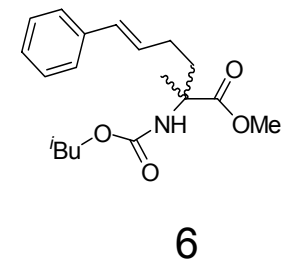
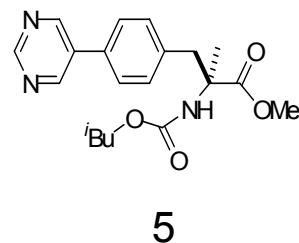
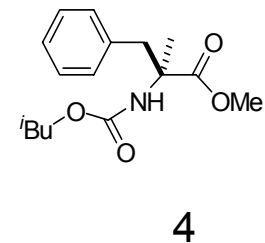
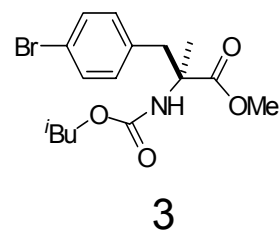
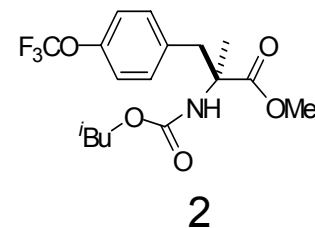
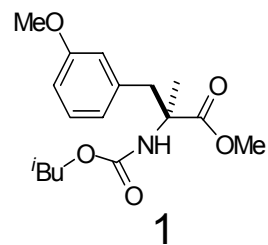
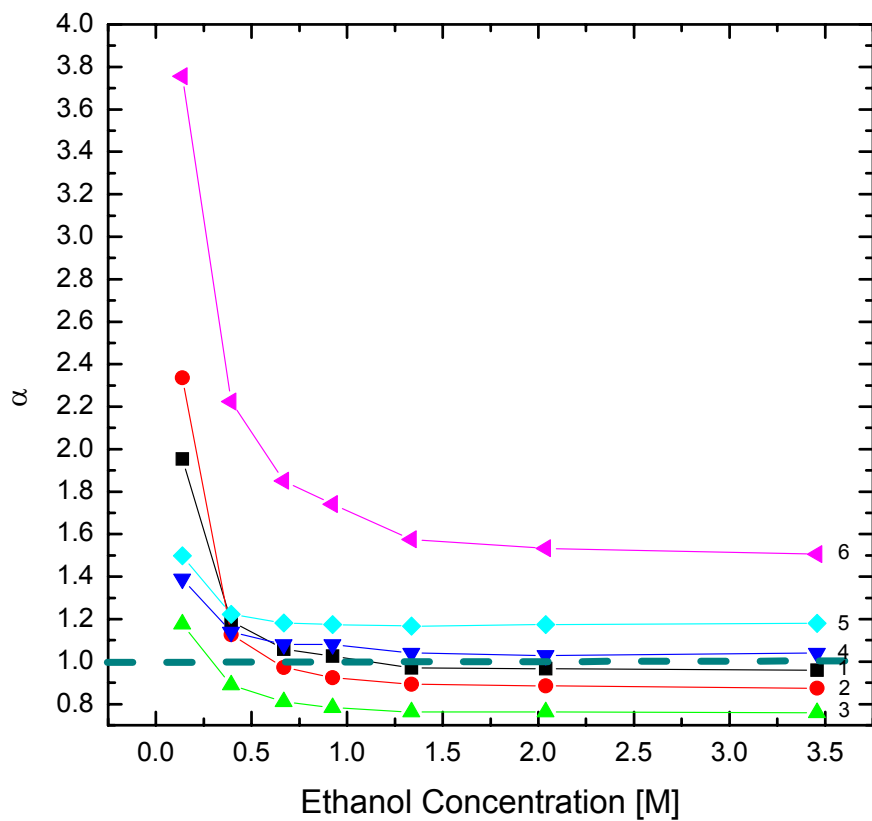
# INFLUENCE OF EtOH CONCENTRATION ON $k'$



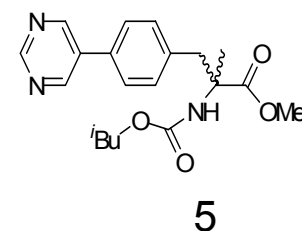
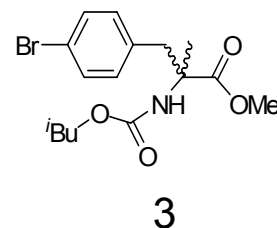
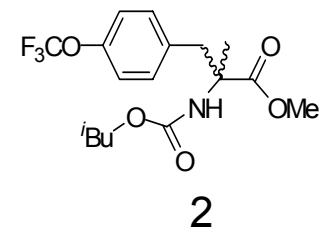
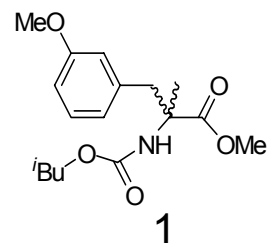
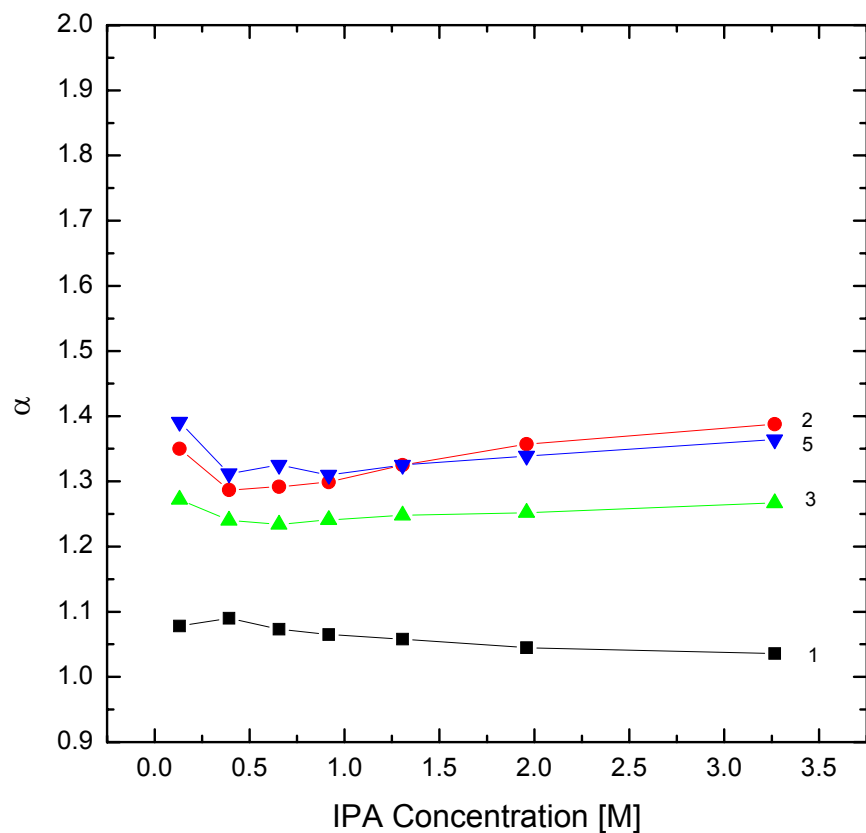
# INFLUENCE OF EtOH CONCENTRATION ON $\alpha$



# INFLUENCE OF ETHANOL CONCENTRATION ON SELECTIVITY $\alpha$



# INFLUENCE OF IPA CONCENTRATION ON $\alpha$



# WHAT IS VCD?

- VCD is an extension of electronic CD (ECD) into the infrared (IR) region of electromagnetic spectrum.
- Is a form of differential absorption spectroscopy arising from the preferential absorption of left and right circularly polarized infrared radiation by mirror image stereoisomers:

$$\Delta A = A_L - A_R$$

# WHAT IS VCD?

- VCD and IR involve the same vibrational transitions.
- VCD combines the rich structural information inherent in an IR spectrum with the chiroptical specificity exhibited by mirror-image stereoisomers.
- VCD is capable of characterizing both a molecule's absolute configuration and its natural solution phase conformational state.

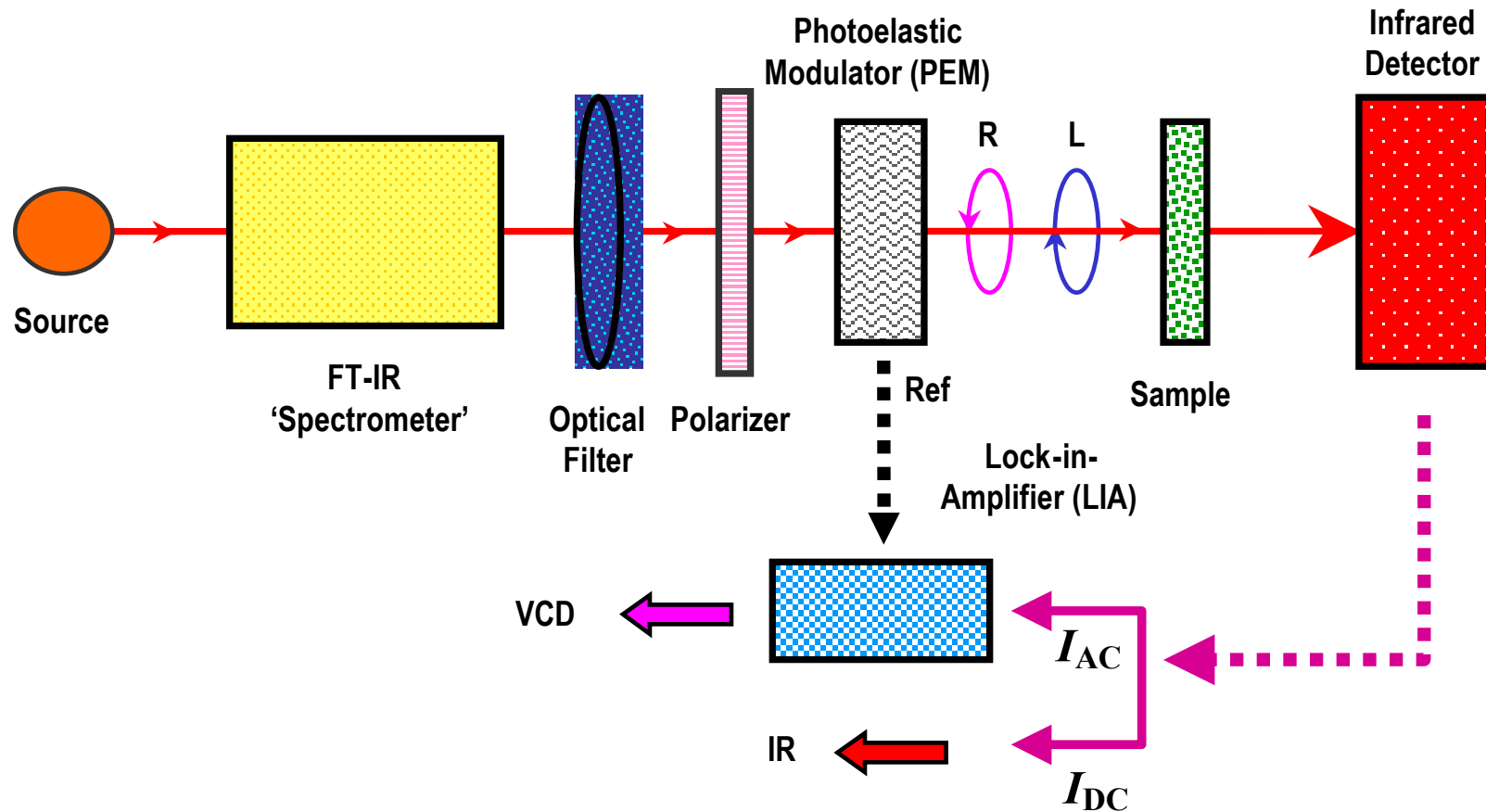
# ADVANTAGES OF VCD SPECTROSCOPY

- VCD is well suited for stereochemical analysis.
- Vibrational transitions occur 100-1000 times faster than most bond rotation.
- Allows the absorption process to occur at a faster rate than the interconversion of conformation.

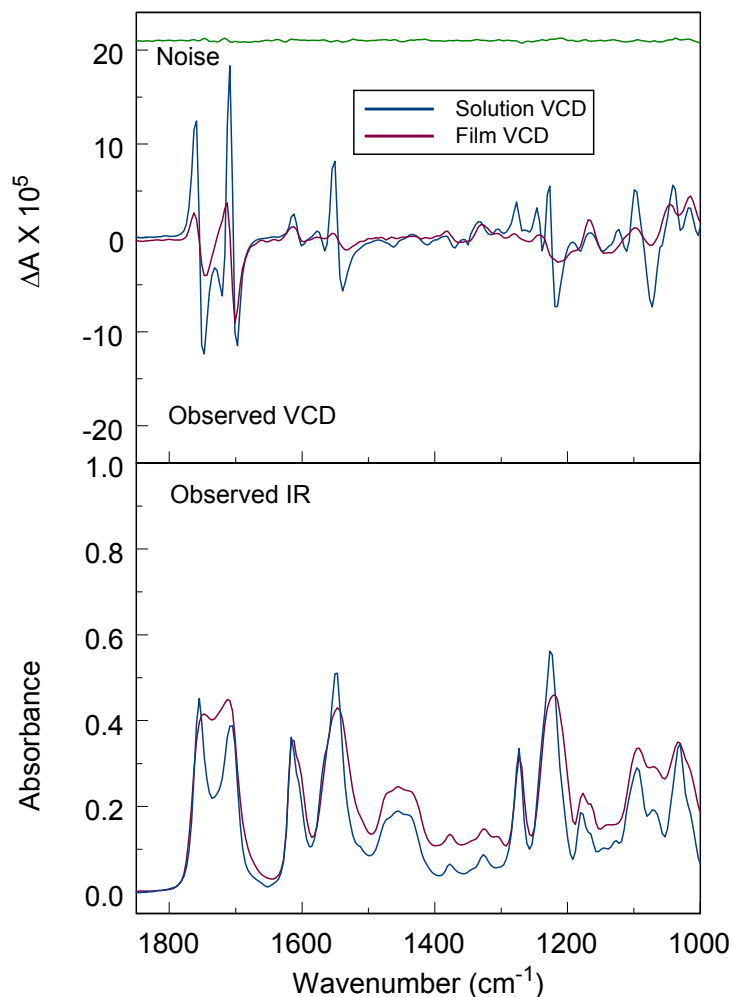
# ADVANTAGES OF VCD SPECTROSCOPY

- VCD and IR spectra represent a superposition of discrete absorption spectra, individually determined by the structure of major conformation.
- The spectra are a combination of weighted distribution of relative population of these conformations.

# Chiral *IR* FT-VCD Instrumental Layout

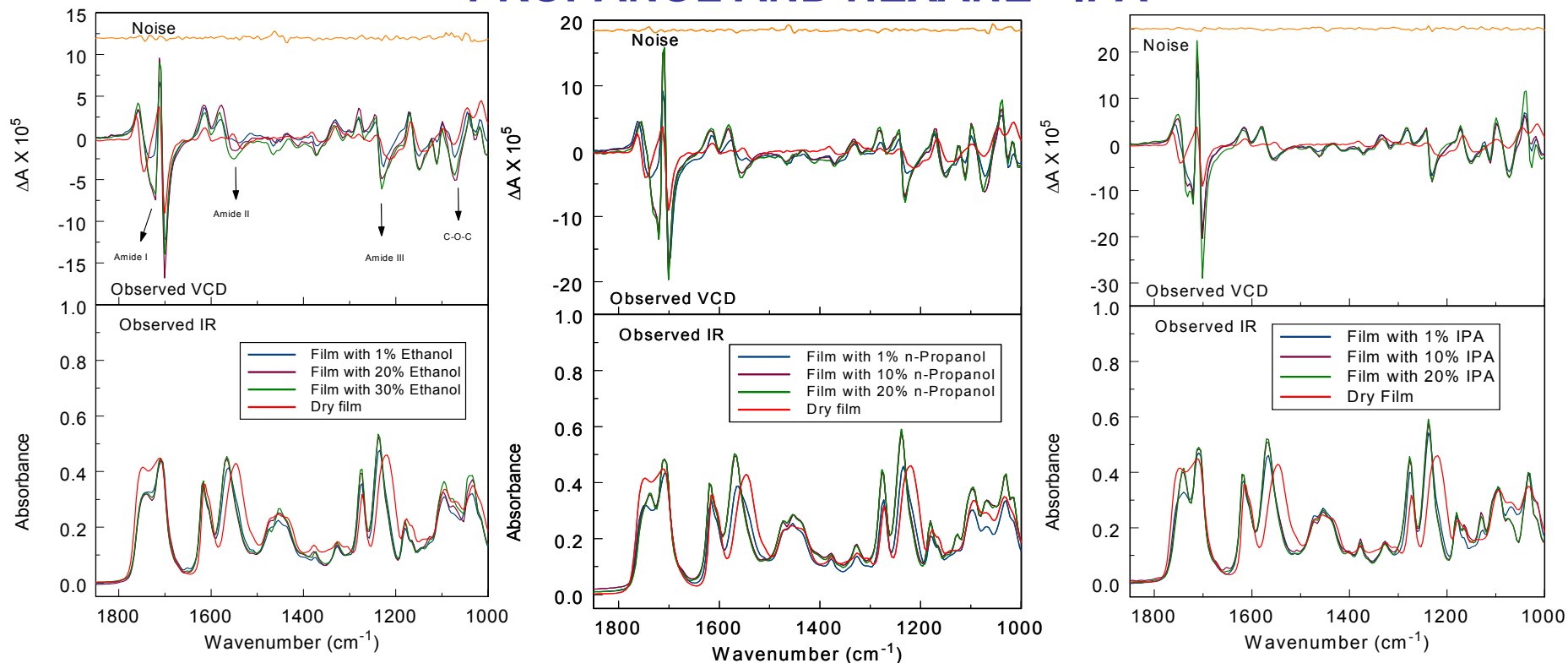


# VCD AND IR SPECTRA OF ADMPC IN $\text{CD}_2\text{Cl}_2$ SOLUTION AND DRY FILM

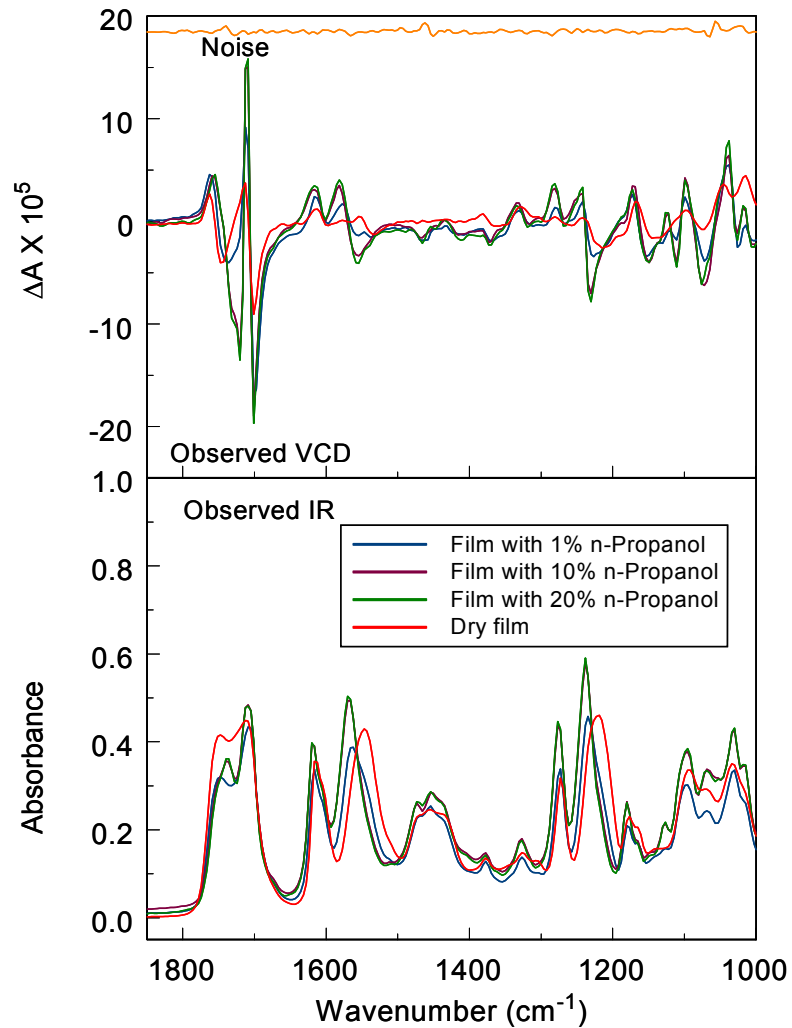
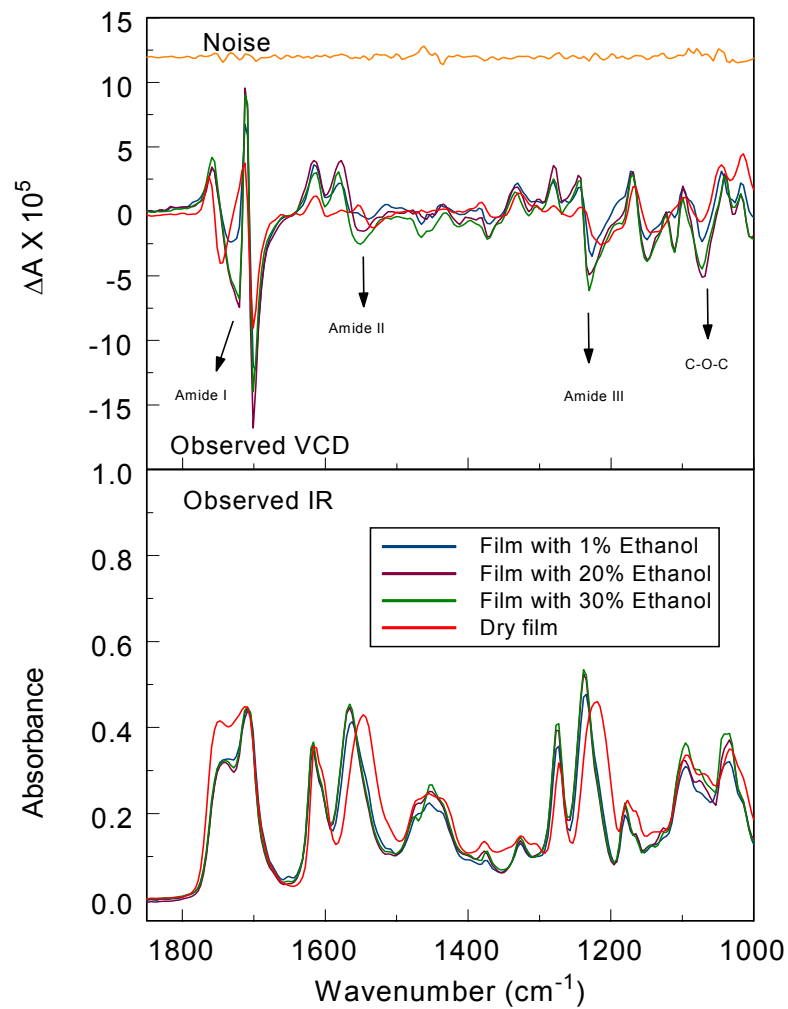


- The Amide I ( $\text{C}=\text{O}$  coupled with  $-\text{NH}$ ) presents in dry film two distinct couplets (+-, +-) – left handed helix and two types of  $\text{C}=\text{O}$  groups (weakly – **Type I ( $1740 \text{ cm}^{-1}$ )** - and strongly bounded – **Type II ( $1710 \text{ cm}^{-1}$ )** - to the neighboring  $-\text{NH}$ ).
- In solution Amide I presents three distinct coupling (+-, -, +); The band at  $1740 \text{ cm}^{-1}$  (weakly bonded  $\text{C}=\text{O}$ ) splits in two new bands – **Type I' and I''**.
- The  $\text{C}=\text{C}$  from the aromatic group ( $1610 \text{ cm}^{-1}$ ) shows broadening of the bands in dry film compared to solution.
- The Amide II ( $1560 \text{ cm}^{-1}$ ) shows that the solution spectra has higher VCD intensity than in dry film.
- The VCD of Amide III ( $1226 \text{ cm}^{-1}$ ) and the  $\text{C}-\text{O}-\text{C}$  group ( $1070 \text{ cm}^{-1}$ ) corresponding to the glycosidic group showed increased intensity in solution than in dry film.

# COMPARISON OF VCD AND IR SPECTRA IN DRY FILM AND FILM EQUILIBRATED WITH HEXANE-ETHANOL, HEXANE – n-PROPANOL AND HEXANE - IPA



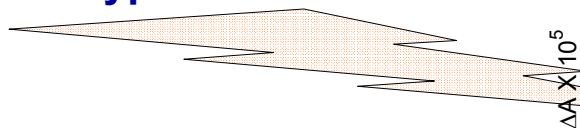
- Increasing the concentration of n-alcohols in hexane - enhanced intensity – a higher order of structure organization in the presence of n-alcohols compared to the dry film.
- **Type I** C=O – red shift; **Type II** no shift but enhanced VCD intensity.
- **Amide II** and **Amide III** had a blue shift in the presence of alcohols studied.
- Increasing the amount of alcohol increases the shift and the band intensity – break up of H-bond between the C=O and NH of the amylose at the expense of the formation of new H-bond between the amylose and the alcohol molecules.



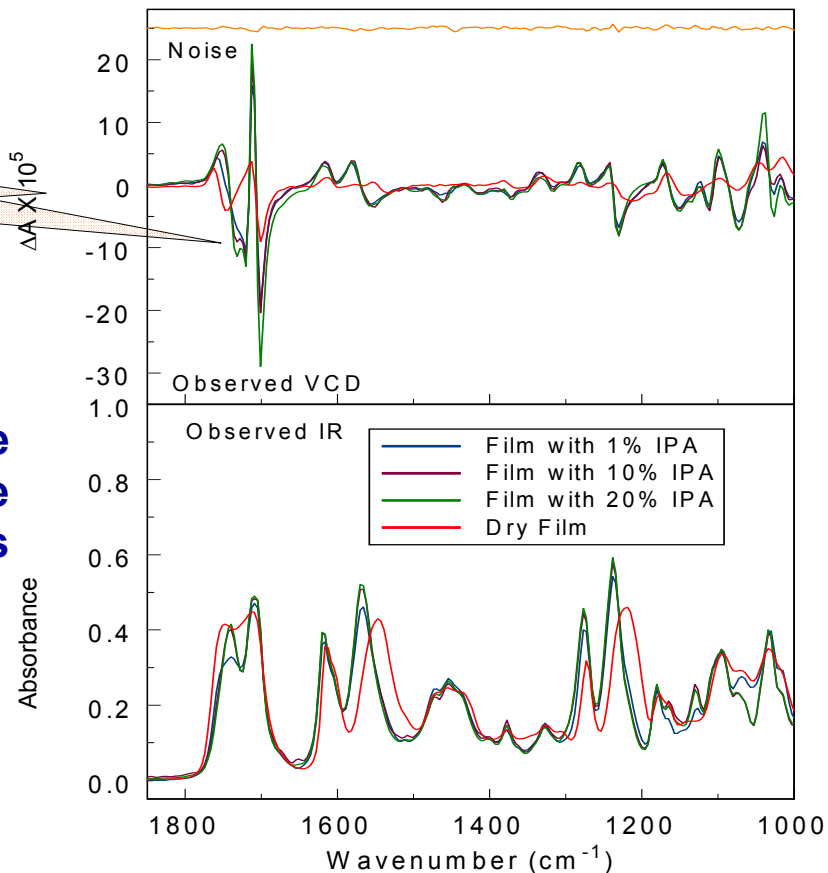
**Increasing the concentration of n-alcohol led to the appearance of a new shoulder in the first negative VCD band of ADMPC ( $\sim 1730 \text{ cm}^{-1}$ ) corresponding to the Type I'.**

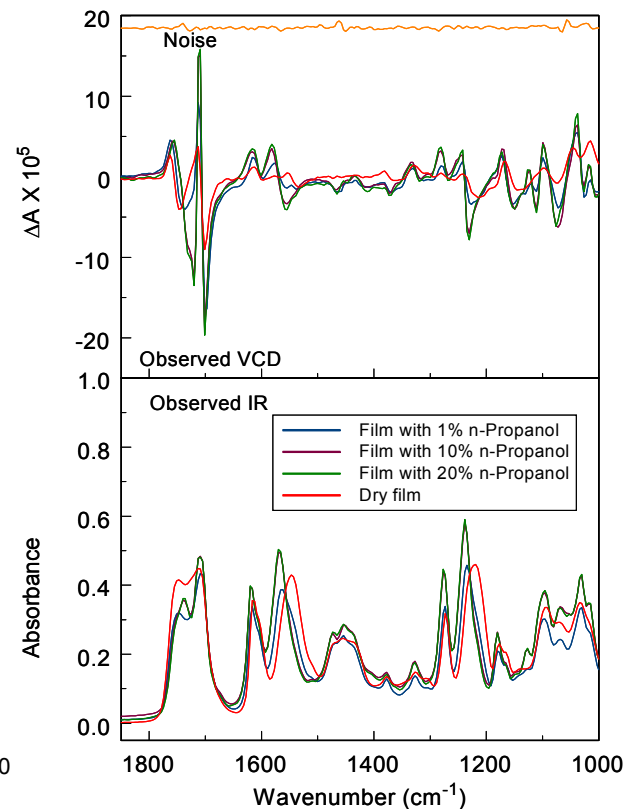
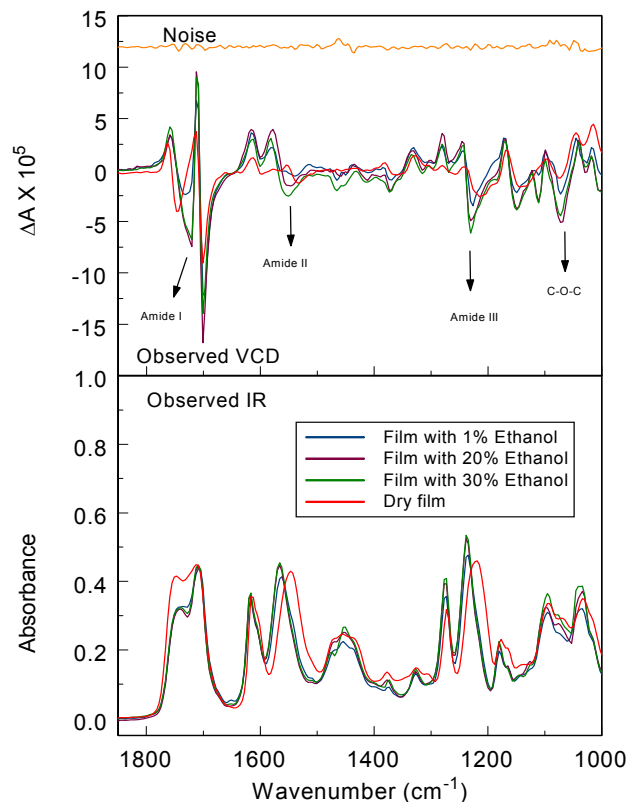
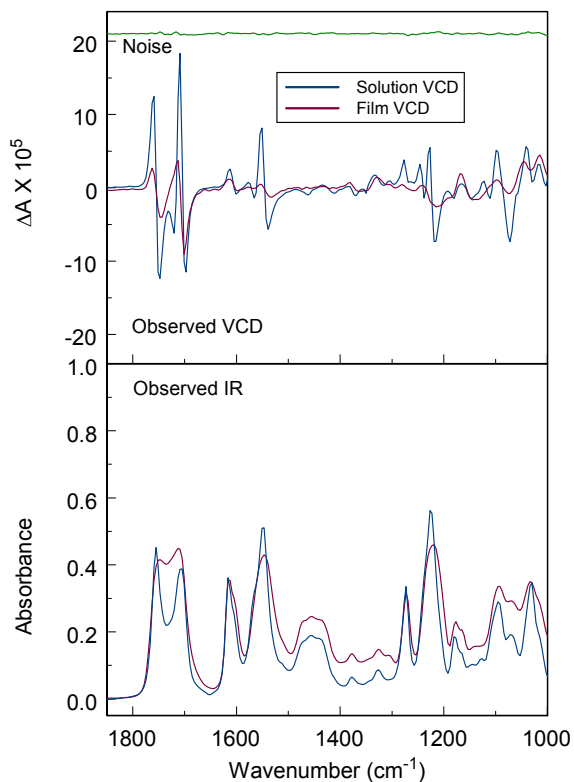
# COMPARISON OF VCD AND IR SPECTRA IN DRY FILM AND FILM EQUILIBRATED WITH HEXANE-ISOPROPANOL

The appearance of Type I' C=O



Type I' increases in intensity with the increase of alcohol concentration, while Type I'' remain unchanged – Type I' is more involved in H-bonding than Type I''.

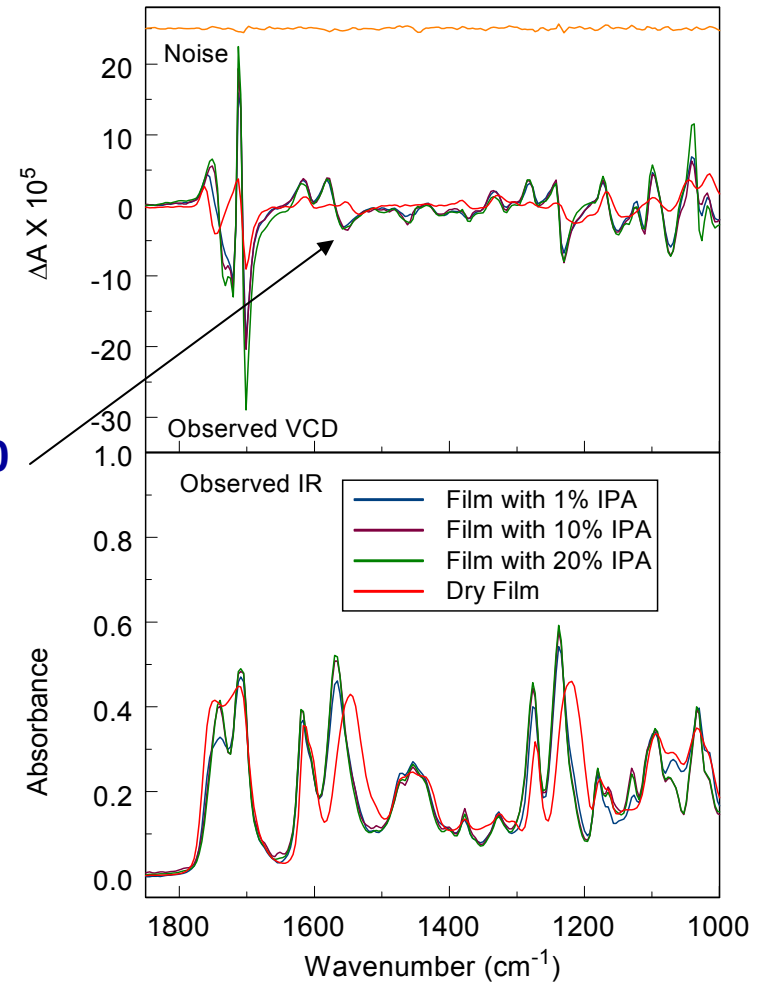




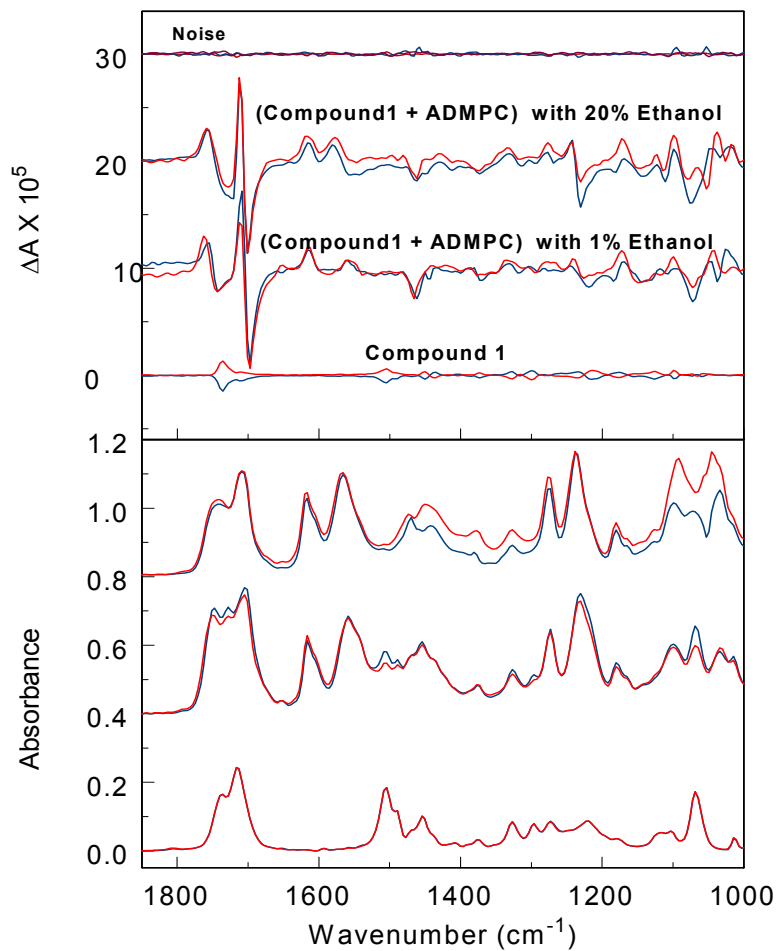
- The Amide II VCD bands of the film and methylene chloride solution presents a small positive small, small negative, followed by a big positive big negative band – two types of NH groups.
- H- bonds are broadly distributed between C=O and NH groups.
- In the present of n-alcohol, the VCD band at  $\sim 1560 \text{ cm}^{-1}$  starts decreasing in intensity, eventually switching sign from positive to negative upon increasing the concentration of n-alcohols.
- The negative band at  $\sim 1540 \text{ cm}^{-1}$  becomes a shoulder upon increasing the concentration of n-alcohols.
- Such behavior indicates that ADMPC undergoes an alcohol induced conformational change

# COMPARISON OF VCD AND IR SPECTRA IN DRY FILM AND FILME EQUILIBRATED WITH HEXANE-ISOPROPANOL

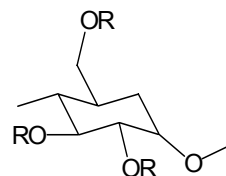
In the presence of isopropanol, this change from positive to negative of the band at 1560  $\text{cm}^{-1}$  is more drastic.



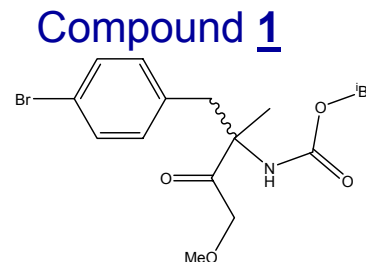
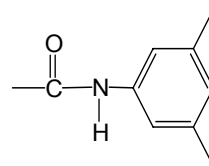
# INFLUENCE OF ETHANOL CONCENTRATION ON THE INTERACTION OF THE TWO ENANTIOMERS OF COMPOUND 1 WITH ADMPC



Blue trace R – enantiomer  
Red trace S - enantiomer

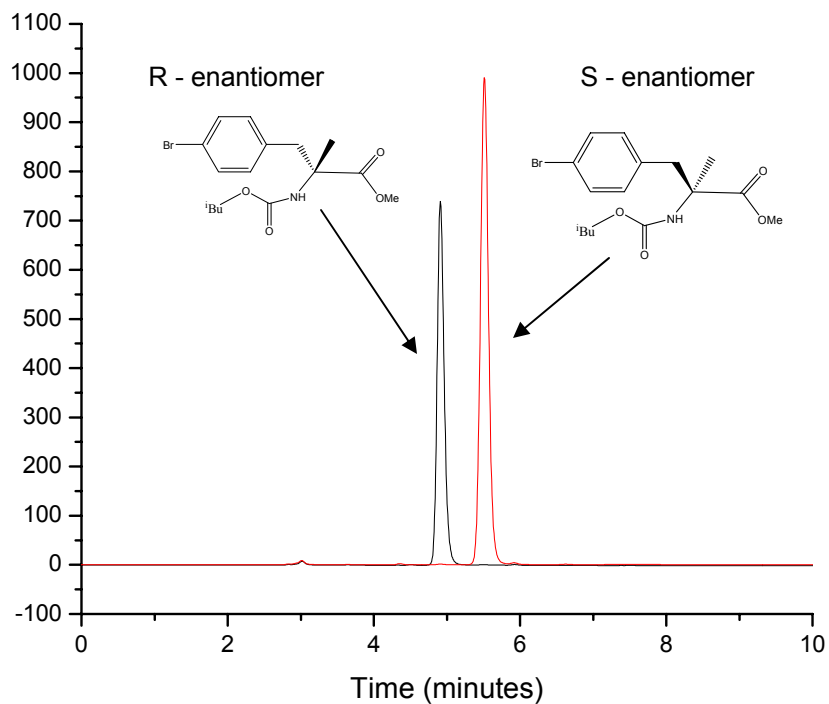
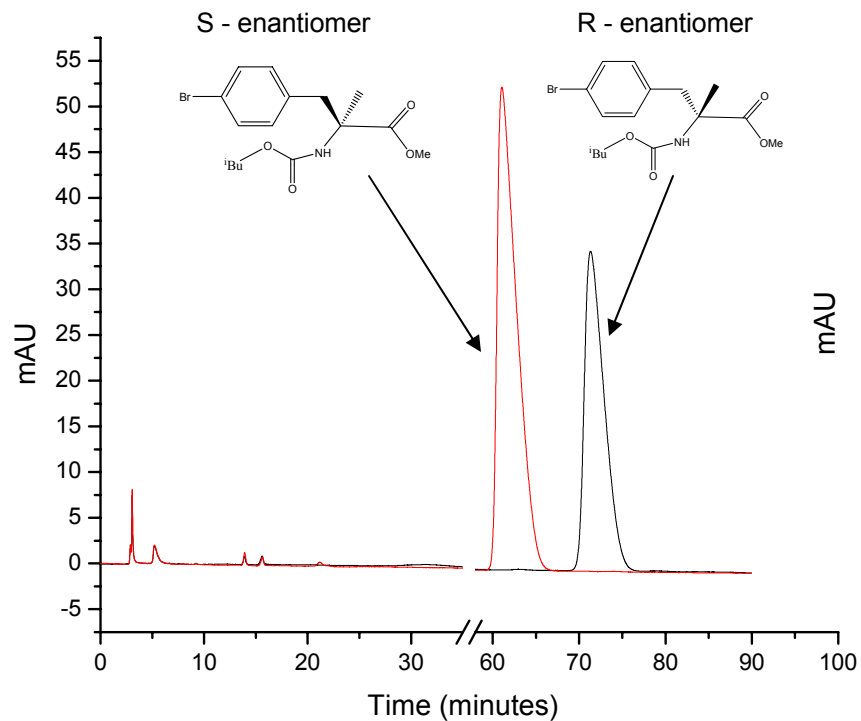


Amylose Carbamate

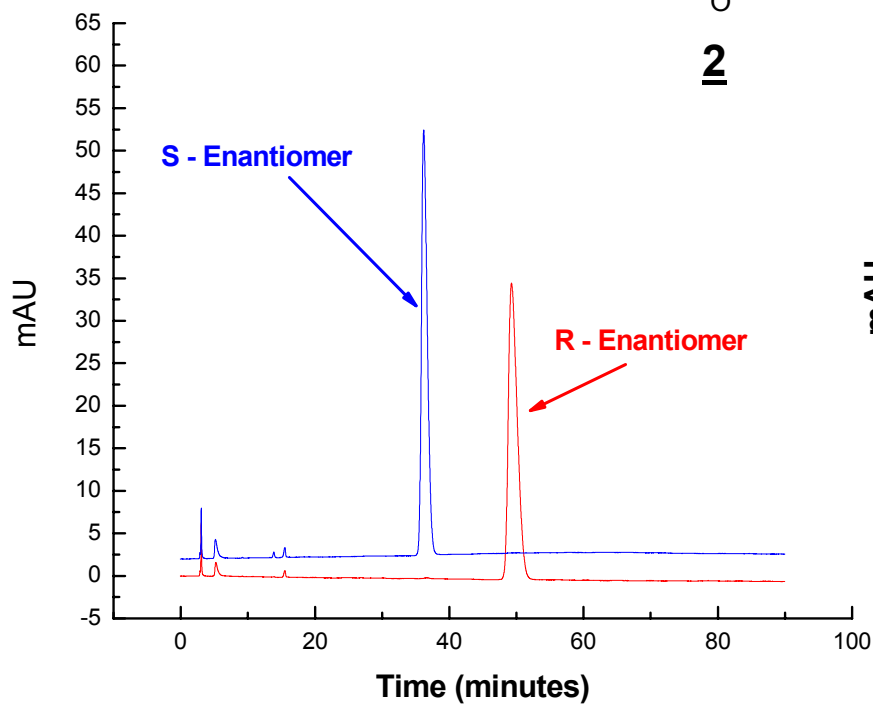
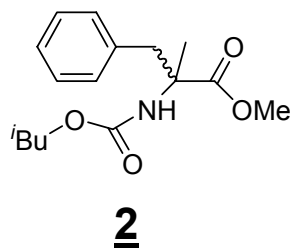


- At 1% ethanol the positive band at  $\sim 1710 \text{ cm}^{-1}$  (strongly bonded C=O) shows  $\sim 60\%$  stronger intensity for the (R) enantiomer compared to (S) enantiomer – Stronger interaction of (R) enantiomer relative to (S). Addition of 20% ethanol produces an equalizing effect – both enantiomer interact the same.
- At 20% ethanol the negative band centered at  $\sim 1740 \text{ cm}^{-1}$  shows a red shift indicating that (S) enantiomer interacts stronger than (R).
- The aromatic region located at  $\sim 1612 \text{ cm}^{-1}$  shows upon increasing the concentration of ethanol from 1% to 20% a shift for the (S) enantiomer compared to (R) enantiomer. Such shift is due to the enhanced  $\pi-\pi$  interaction upon increasing the polarity of the solvent.
- The C-O-C region located at  $1070 \text{ cm}^{-1}$  shows a split for the (S) enantiomer upon increasing the concentration of ethanol.
- Addition of ethanol produced a swelling of ADMPC favoring an inclusion in the polymer cavities.

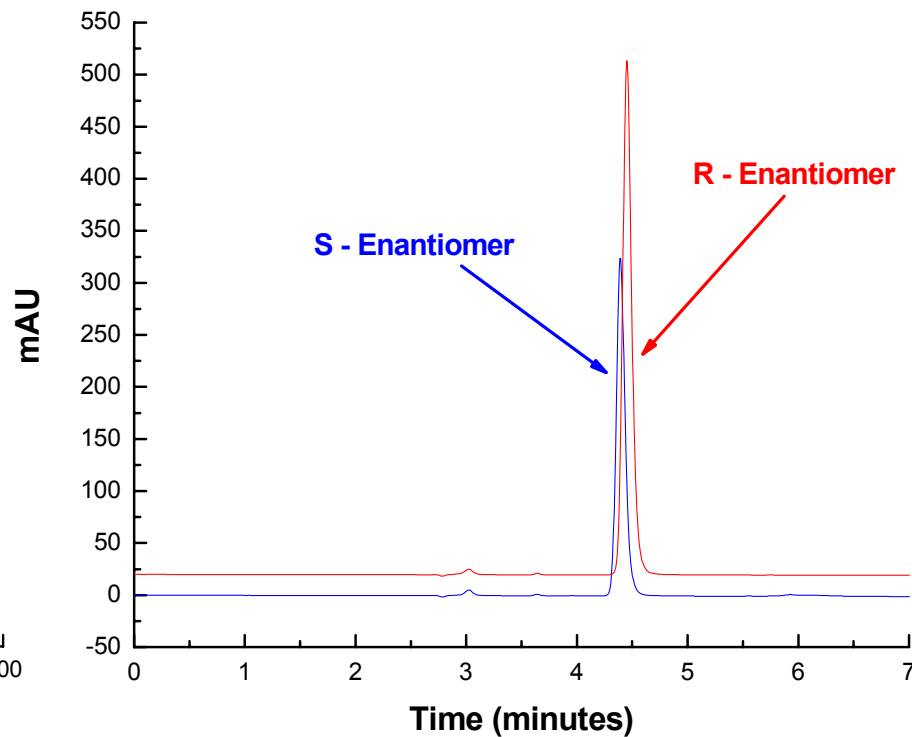
# EFFECT OF THE AMOUNT OF ETHANOL ON THE SEPARATION



# EFFECT OF THE AMOUNT OF ETHANOL ON THE SEPARATION OF COMPOUND 2

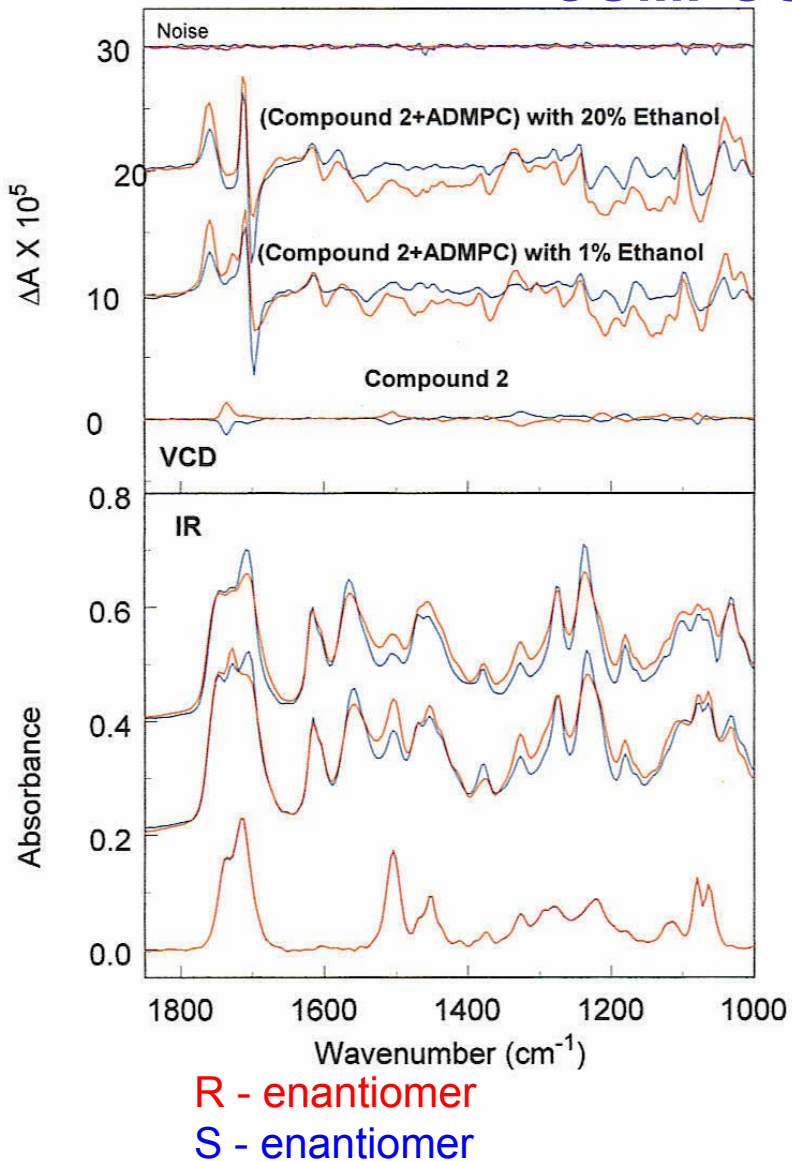
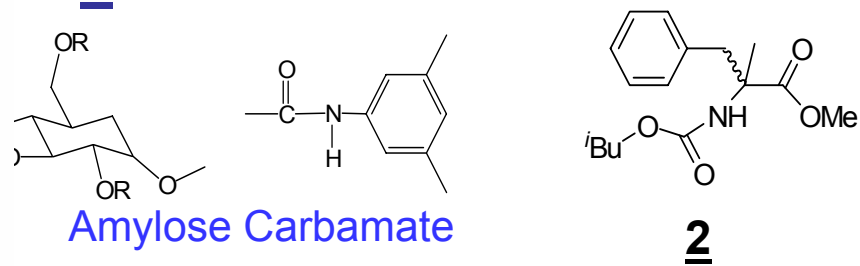


Mobile Phase: 99/1 Hexanes/EtOH



Mobile Phase: 80/20 Hexanes/EtOH

# INFLUENCE OF ETHANOL CONCENTRATION ON THE INTERACTION OF THE TWO ENANTIOMERS OF COMPOUND 2 WITH ADMPC



- In the Amide I and aromatic region of the VCD spectra there is no shift with the increase of the amount of ethanol – both enantiomers have similar interactions with ADMPC.
- In the Amide II region there is a red shift of the R enantiomer relative to S upon increasing the concentration of ethanol in hexane.
- In the C-O-C region, increasing the amount of ethanol produces an increase in the intensity of the negative band for R – enantiomer relative to S.
- R enantiomer interacts stronger with ADMPC compared to S enantiomer.

# **ACKNOWLEDGEMENTS**

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**Dr. Heewon Lee                  Jing Wang**

**Dr. Xufeng Sun**

**Chiral Technologies**