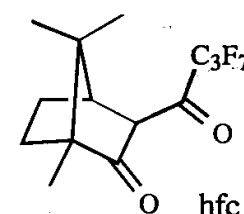
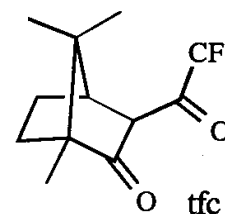
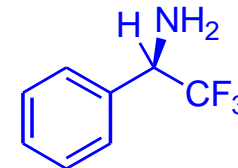
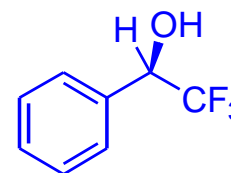


Chiral NMR

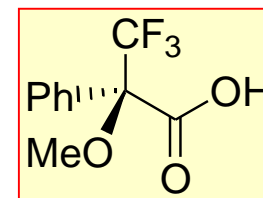
CSR Chiral Shift Reagents



CSA Chiral Solvating Agents



CDA Chiral Derivating Agents



Wenzel T. J. et al. *Tetrahedron* **2018**, 4846-4856

Risonanza Magnetica Nucleare

Essendo equivalenti per simmetria due enantiomeri danno spettri NMR identici.

Tuttavia, in presenza di un agente enantiopuro che interagisce in modo non covalente con gli enantiomeri, questi possono dare segnali anisocroni, che, se integrati separatamente, consentono la determinazione dell'ee.

In pratica, protoni enantiotopici per paragone esterno (quelli di R e di S) e indistinguibili diventano diastereotopici e differenziabili

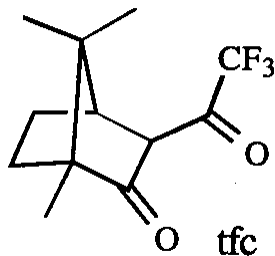
I due principali tipi di additivi chirali enantiopuri sono:

- Chiral Shift Reagents (CSR)
- Chiral Solvating Agents (CSA)

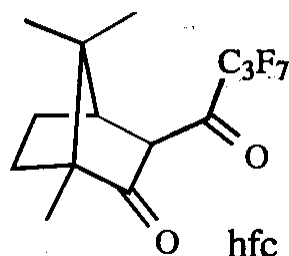
Nelle condizioni migliori il metodo ha un'accuratezza del 2%.

Chiral Shift Reagents (CSR)

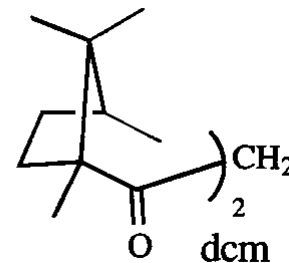
Leganti



Trifluoroacetil canfora



Eptafluorobutanoil canfora



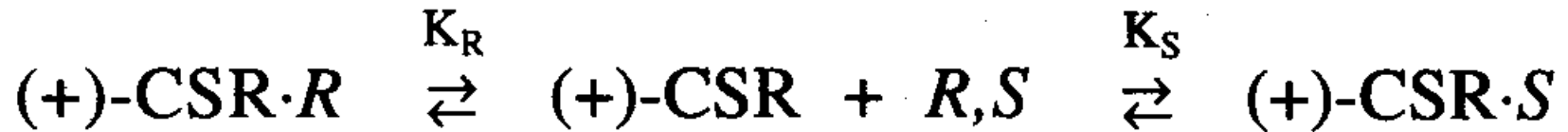
Dicanforil metano

Lantanide shift reagents: tris complessi di β -dichetonati

Complessi ottaedrici:

Europio (Eu) Praseodimio (Pr); Itterbio (Yb)

Origine dell'anisocronia indotta ($\Delta\Delta\delta$)



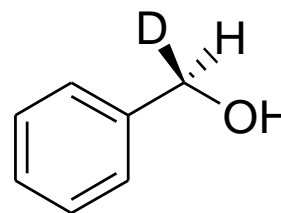
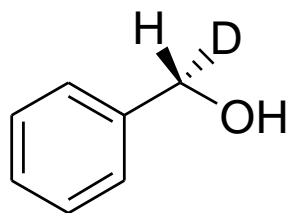
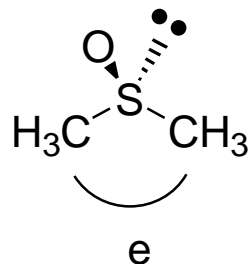
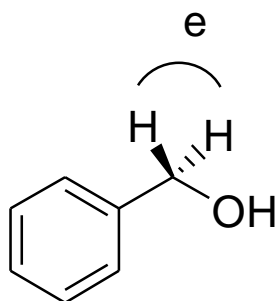
$\Delta\Delta\delta$ è dovuta a due fenomeni:

- $K_R \neq K_S$
- $(+)\text{-CSR}\cdot R$ e $(+)\text{-CSR}\cdot S$ hanno geometrie diverse

Entrambi i meccanismi sono operativi

$$K_R \neq K_S$$

Protoni enantiotopici vengono differenziati
(diventano diastereotopici)



Anche la sostituzione isotopica viene evidenziata

Cosa succede se il CSR è racemo?

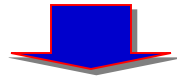
$$(+)\text{-CSR}\cdot R \xrightleftharpoons{K_R} (+)\text{-CSR} + R, S \xrightleftharpoons{K_S} (+)\text{-CSR}\cdot S$$

diventa

$$(+)\text{-CSR}\cdot R + (-)\text{-CSR}\cdot R \rightleftharpoons (\pm)\text{-CSR} + R, S \rightleftharpoons (+)\text{-CSR}\cdot S + (-)\text{-CSR}\cdot S$$

Spettro (R) = R libero + (+)-CSR·R e (-)-CSR·R

Spettro (S) = S libero + (+)-CSR·S e (-)-CSR·S



$$\Delta\Delta\delta = 0$$

Per situazioni intermedie (ee=80%)

$$(+) \text{-CSR} \cdot R + (-) \text{-CSR} \cdot R \rightleftharpoons (\pm) \text{-CSR} + R, S \rightleftharpoons (+) \text{-CSR} \cdot S + (-) \text{-CSR} \cdot S$$

Spettro (R) = R libero + (+)-CSR·R e (-)-CSR·R

Spettro (S) = S libero + (+)-CSR·S e (-)-CSR·S



Spettro (R) \neq Spettro (S)



$$\Delta\Delta\delta_{100\%} < \Delta\Delta\delta_{80\%} \neq 0$$

Lantanoidi = Acidi Hard

Basi Hard

ammine primarie > alcoli > chetoni > aldeidi > eteri > esteri > nitrili

**Sono stati anche usati con:
solfossidi, ammino acidi e complessi di transizione**

Istruzioni per l'uso:

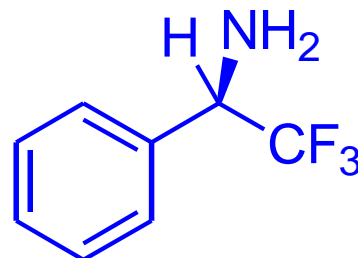
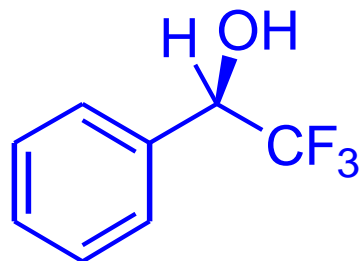
Fraser recommends the following experimental protocol [51]:

1. Try as many as four CSRs, the approximate order of capacity being $\text{Eu}(\text{dcm})_3 > \text{Pr}(\text{hfc})_3 \approx \text{Yb}(\text{hfc})_3 > \text{Eu}(\text{hfc})_3$.
2. Try changing the temperature. Lower temperature can have a substantial influence on lanthanide-induced shifts [58,61,62], while warming may sharpen lines [55].
3. If still unsuccessful, try derivatizing the ligand to make it a stronger, harder, Lewis base.

Before conducting a CSR study, the experimentalist should consult Sullivan's review for detailed experimental guidelines [50]. Briefly, the guidelines suggest: dry the substrate, the solvent, and the CSR (by sublimation if prepared fresh or over phosphorous pentoxide *in vacuo* if purchased); keep the substrate concentration low (~0.1 - 0.25 M); add the CSR (either as a solid or as a concentrated solution) in small increments, and filter the solution after each addition (the molar ratio needed for a good induced shift is rarely >1:1, and too much lanthanide can broaden lines and even cause the induced shifts to decrease); re-shim the spectrometer after the CSR is added to compensate for the presence of the paramagnetic ions, and check for paramagnetic precipitates after the sample has been spinning for several minutes. Additionally, recall (*vide supra*) that the method is usually more effective at low field.

Chiral Solvating Agents (CSA)

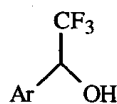
Pirkle (1966) provò l'ipotesi di Mislow (1965) che nuclidi enantiotopici potessero diventare anisocroni in un solvente chirale
(*JACS*, 1966, 88, 1837)



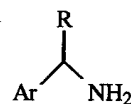
CSR vs CSA

1. **CSA sono sostanze diamagnetiche:** poiché la dinamica dei CSA e le interazioni con un soluto chirale possono essere ragionevolmente capite, spesso può essere usata per la determinazione della configurazione assoluta.
2. Negli CSA l'anisocronia tre gruppi enantiotopici è spesso dovuta alla presenza nell CSA di funzioni anisotropiche, ad esempio gruppi aromatici.
3. La variazione di chemical shift indotta è inferiore a quella fornita dai CSR e il metodo può essere utilizzato con un numero minore di composti. Un vantaggio di avere $\Delta\delta$ piccoli è che l'effetto sulla larghezza di riga del campo magnetico non è un problema.
4. Poiché CSA sono diamagnetici l'allargamento del picco non è un problema come con i CSR. Quindi è spesso possibile valutare i rapporti enantiomerici confrontando l'altezza dei picchi.

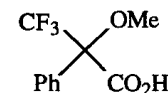
Chiral Solvating Agents



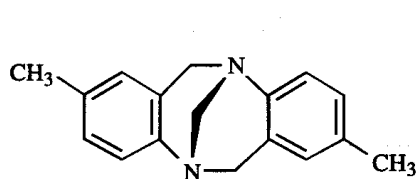
Hydroxy esters [68]
 Arylalkylamines [72]
 Amino esters [76]
 Oxiranes [79]
 Lactones [81,82]
 Phosphine oxides,
 Amineoxides,
 RS(=O)XR, X = N, O, S [86]
 Sulfoxides [87,88]



Sulfoxides [69]
 Phosphine oxides [73]
sec-Benzylic alcohols [77,78]
N-Phthalimido amino acids [80]
 2-(Aryl)carboxylic acids [83,84]
 Hydroxy esters [85]

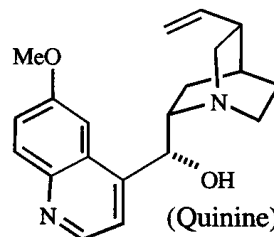


tert-Amines [70,71]
 Diamines [74,75]



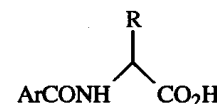
(Tröger's base)

sec- and *tert*-
 Benzylic alcohols [89]



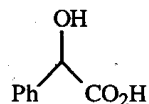
(Quinine)

Binaphthyls,
sec-Benzylic amines [90]

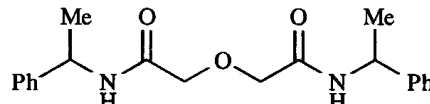


R = Ph, *i*-Bu

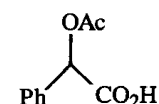
Diamines,
 Amino esters,
 Amino alcohols [74]
 Benzodiazepinones,
 Naphthamides,
 Lactones [91]



Diamines,
 Amino esters,
 Amino alcohols [74]



Amides [92]



Amines,
 Amino alcohols [93]

Chiral Solvating Agents - Meccanismo di Azione



(+)-CSA è una singola specie

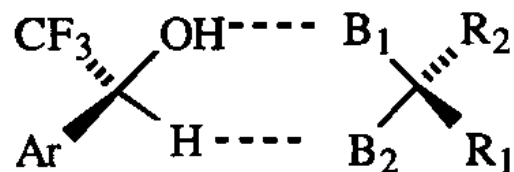
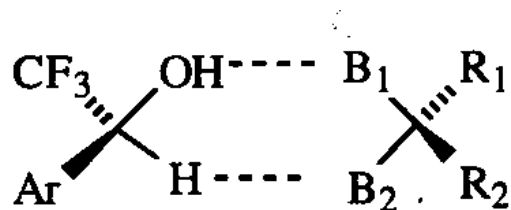
$\Delta\Delta\delta$ è dovuta a due fenomeni:

$$K_R \neq K_S$$

(+)-CSA·R e (+)-CSA·S hanno geometrie diverse

Poiché CSA sono diamagnetici possiamo usarne un eccesso con 5 equivalenti di CSA tutto il soluto è complessato

Chiral Solvating Agents - Interazioni a tre punti



Terza interazione:

$\text{Ar} - \text{R}_2$

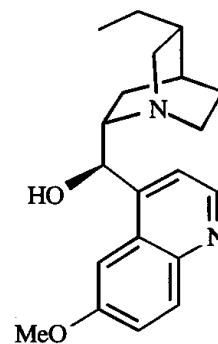
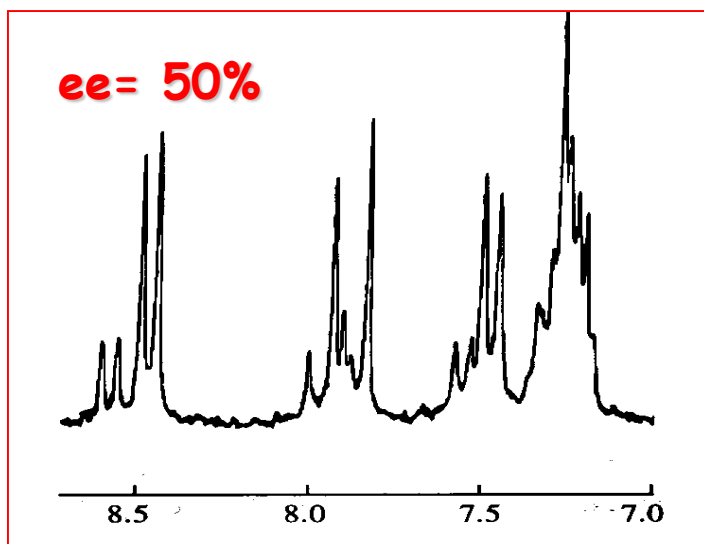
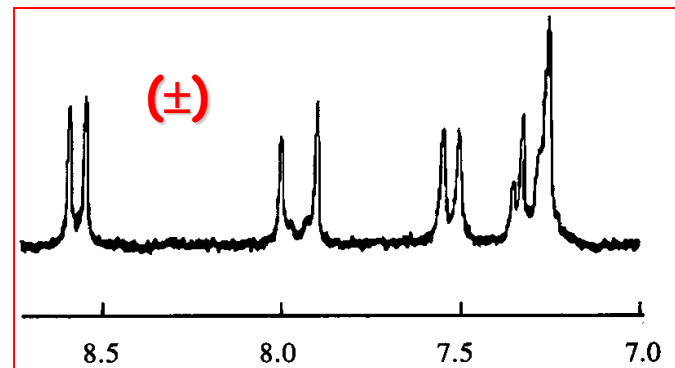
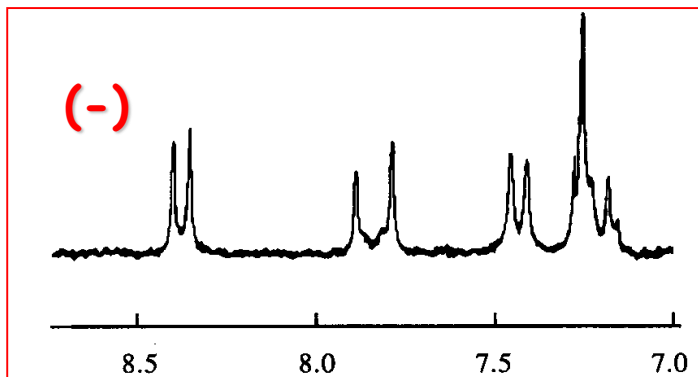
$\text{Ar} - \text{R}_1$

Nello spettro che si ottiene R_2 risuona a campi più alti a causa della schermatura dovuta all'anello aromatico.

Nello spettro che si ottiene R_1 risuona a campi più alti a causa della schermatura dovuta all'anello aromatico.

Se la natura delle interazioni OH e H con B_1 e B_2 è nota possiamo usare questo metodo per la determinazione della configurazione assoluta.

Caso della diidrochinina



(-)-Dihydroquinine

Williams, T. *JACS* 1969, 91, 1271

Assumendo associazioni binarie, il fenomeno può essere spiegato assumendo l'esistenza dei seguenti equilibri:



Per l'enantiopuro:



Per il racemo:



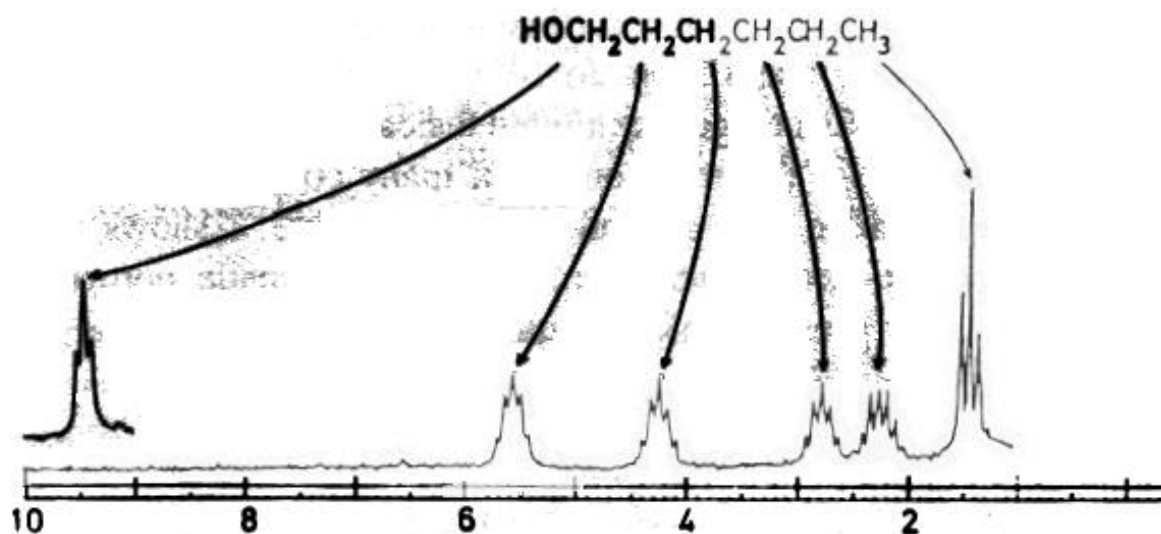
Per l'arricchito in S^* :



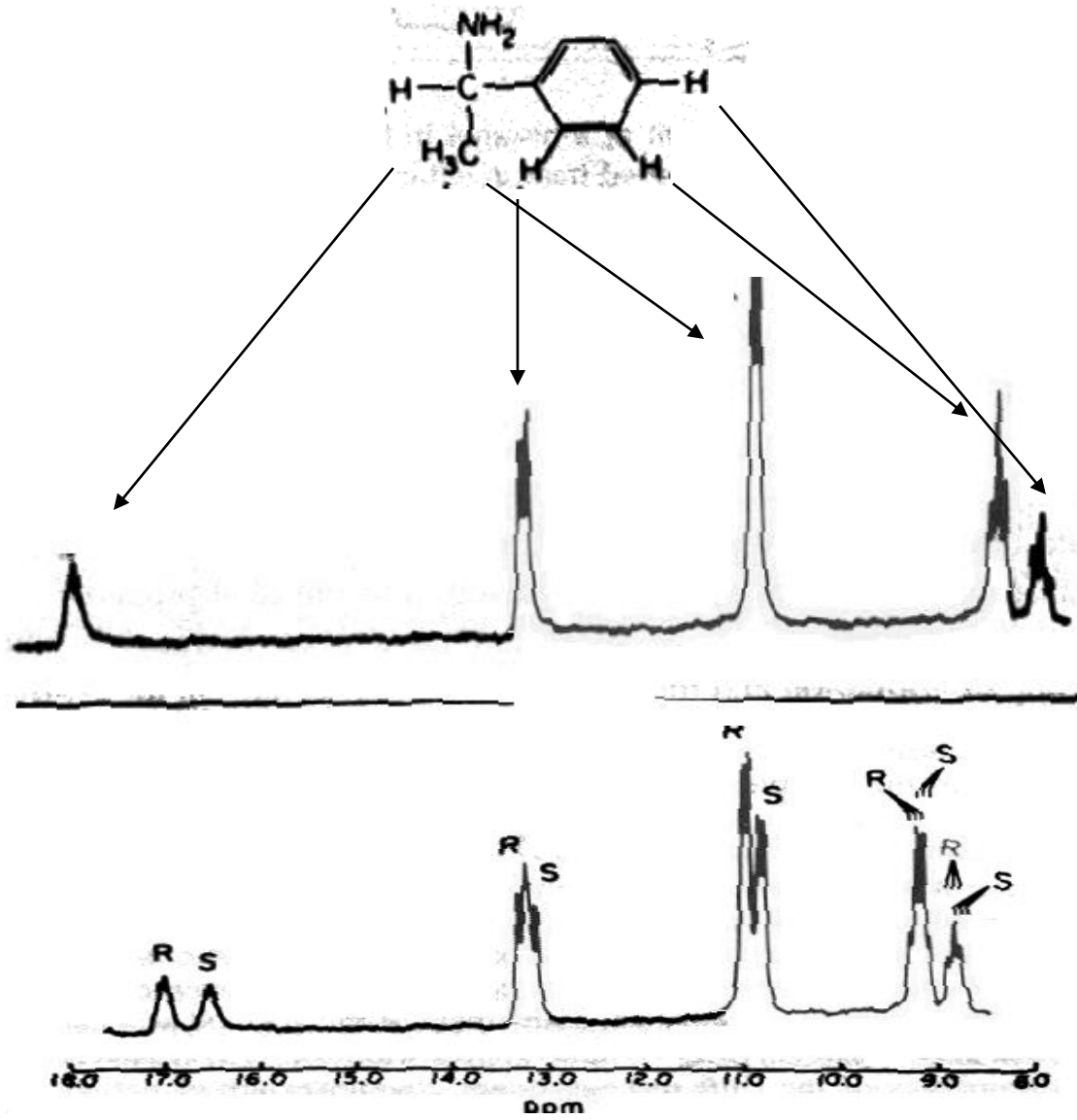
L'eccesso di S^* agisce da CSA per il racemato

Chiral Shift Reagents (CSR)

Spettro ^1H NMR (100 MHz) *n*-esano con $\text{Eu}(\text{dmp})_3$ (0.29 equiv)

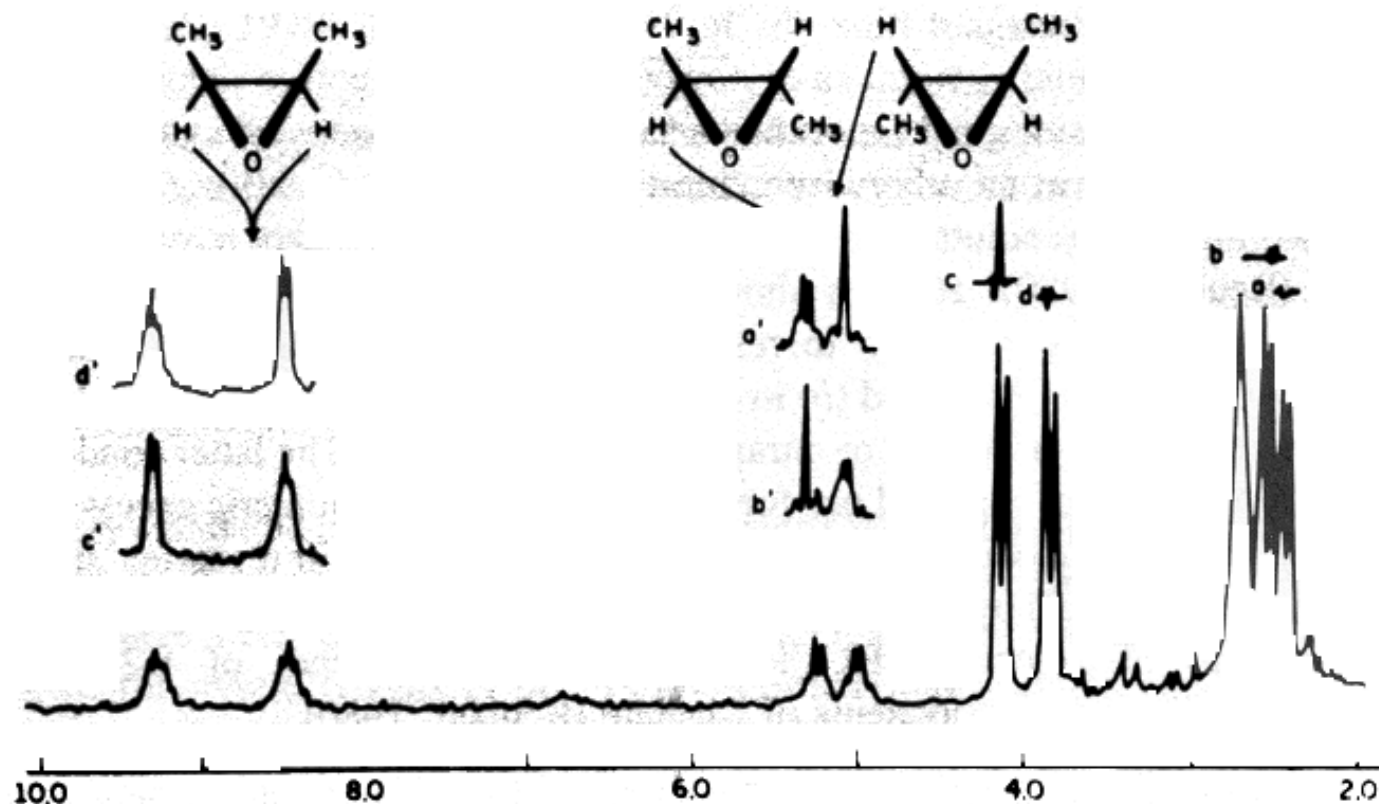


^1H NMR (100 MHz) della (S)- e (\pm)- α -fenil etil ammina con $\text{Eu}(\text{3-pivaloil-D-canfora})_3$



Assegnazione Configurazione meso e dl

meso e (R,S)-2-butene ossido



^1H NMR (100 MHz) con $\text{Eu}(\text{tfc})_3$

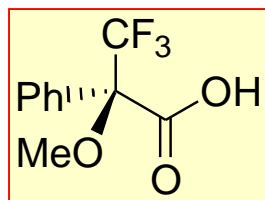
Chiral Derivating Agents (CDAs)

Trasformazione degli enantiomeri in diastereoisomeri

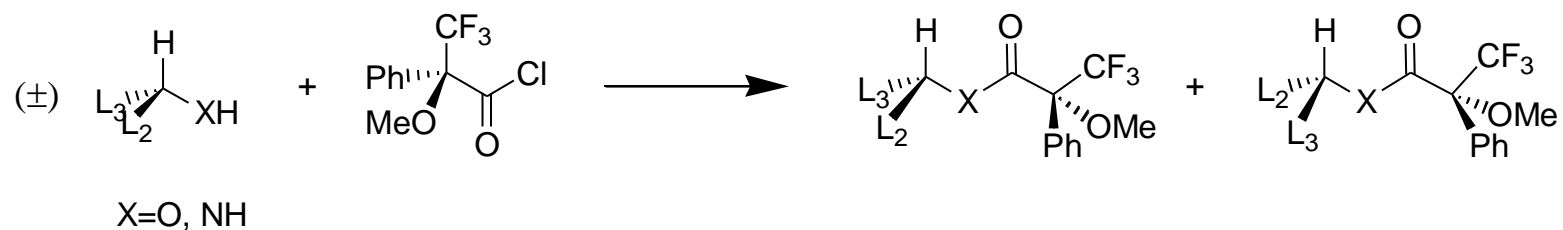
Requisiti:

1. Il CDA deve essere enantiopuro o perlomeno la sua purezza enantiomerica deve essere nota.
2. La reazione del CDA con entrambi gli enantiomeri deve essere quantitativa o perlomeno le velocità relative dei due processi devono essere note
3. Il CDA non deve racemizzare nelle condizioni di derivatizzazione o nel corso dell'analisi e le condizioni di reazioni devono essere sufficientemente blande da non far racemizzare il substrato
4. Per l'analisi NMR il CDA deve avere un gruppo funzionale che fornisce un singoletto e che risuona in zone libere dello spettro per facilitare l'integrazione. Per l'analisi HPLC il CDA deve avere un gruppo cromoforo

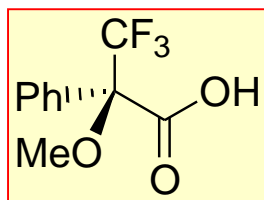
Chiral Derivating Agents (CDAs)



Acido di Mosher

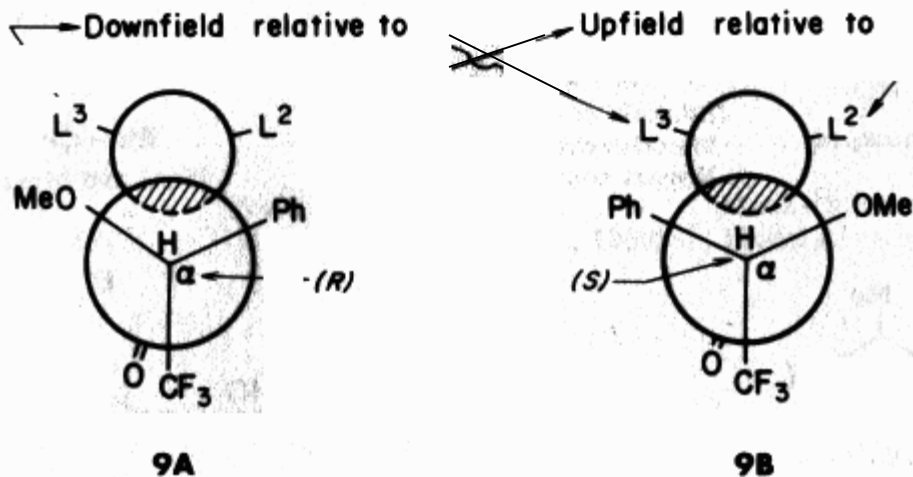
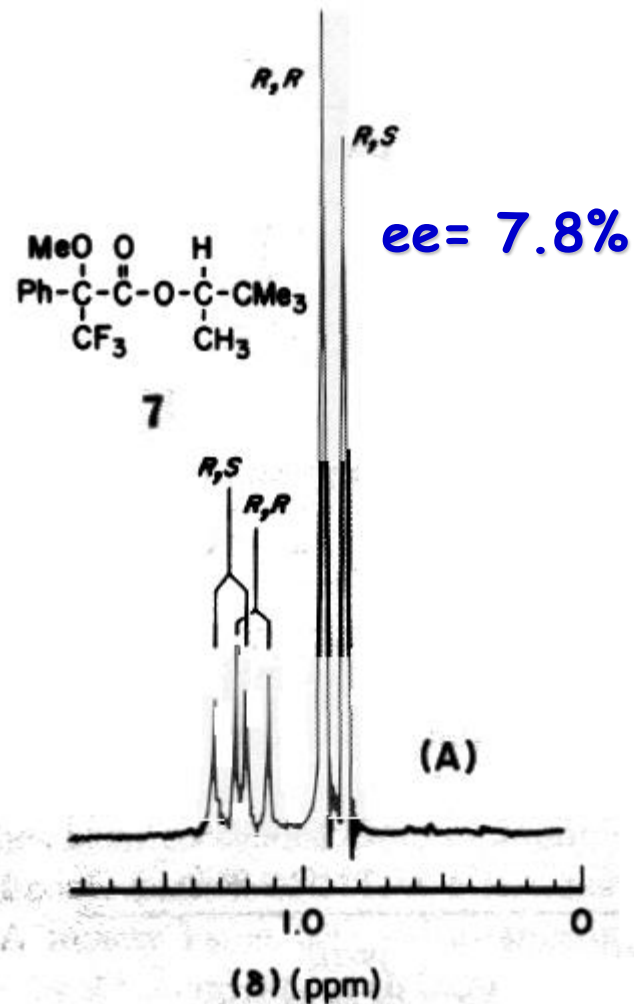
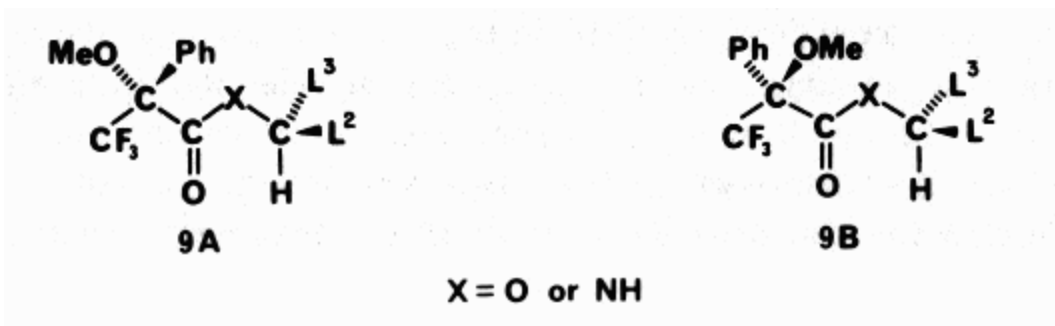


Analisi dei prodotti via NMR:

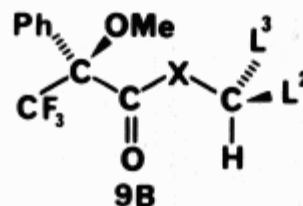
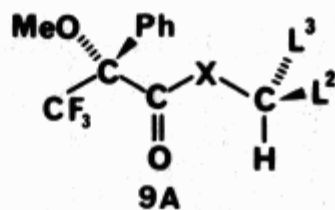


-OMe ^1H NMR; -CF₃ ^{19}F NMR

Chiral Derivating Agents (Estere di Mosher)



¹H-NMR Chemical Shift Differences for MTPA Derivatives
9A and 9B^a



X = O(NH)

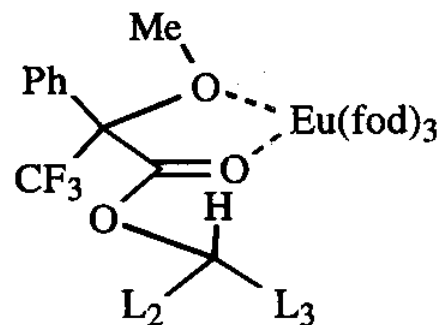
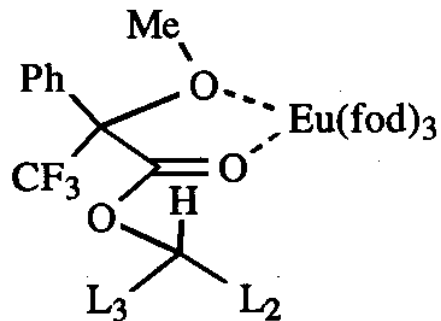
| Ligand | | Chemical shift difference $\Delta\delta$ (ppm) | |
|----------------|----------------|------------------------------------------------|----------------------------|
| L ³ | L ² | L ³ (9A - 9B) | L ² (9A - 9B) |
| Et | Me | +0.10 (+0.07) ^b | -0.13 (-0.07) ^b |
| <i>i</i> Pr | Me | +0.08 | -0.08 |
| <i>t</i> Bu | Me | +0.07 | -0.07 |
| <i>t</i> Bu | <i>n</i> Bu | +0.06 | |
| Ph | Me | | -0.06 (-0.07) ^b |
| Ph | <i>t</i> Bu | | -0.05 |
| COOMe | Me | | (-0.08) ^b |

^aData from Dale and Mosher (1973).

^bValues in parentheses are those for the MTPA amides.

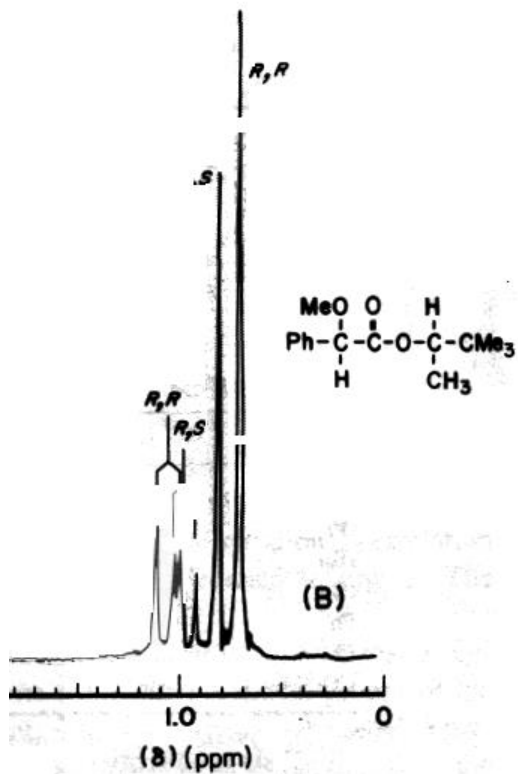
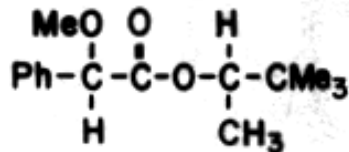
Analisi dei prodotti via NMR:

Eventualmente l'aggiunta di uno shift reagent come $\text{Eu}(\text{fod})_3$ (fod=6,6,7,7,8,8,8-heptafluoro-2,2-dimetil-3,5-ottandionato) aiuta a differenziare ulteriormente i segnali diastereoisomerici

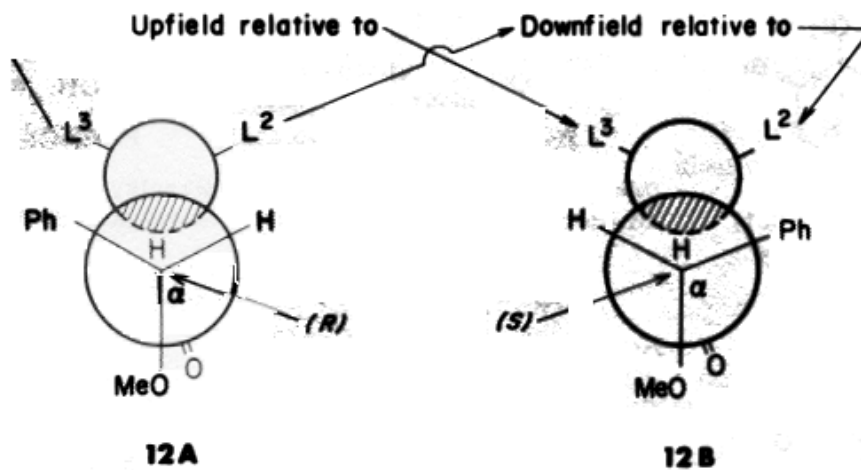


Il rapporto si determina via integrazione dei segnali

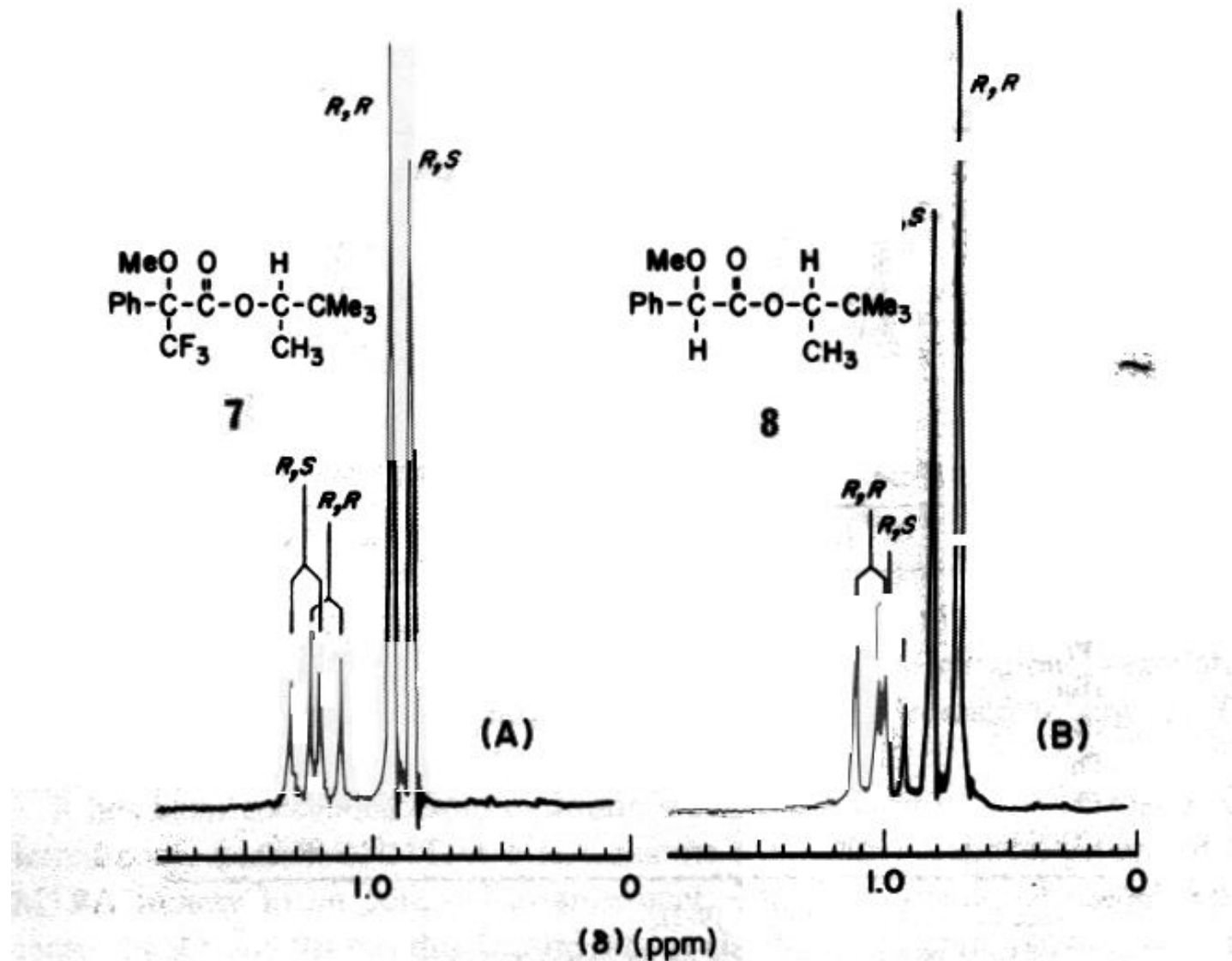
Chiral Derivating Agents (Estere acido mandelico)



$ee = 11.7\%$



Acido di Mosher vs acido mandelico



Cromatografia con fasi chirali (HPLC & GC)

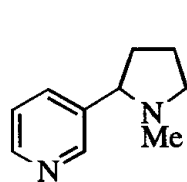
Vantaggi:

1. Non vi sono problemi di risoluzione cinetica derivanti dalla derivatizzazione con un reagente chirale enantiopuro.
2. L'ordine di eluizione di due enantiomeri può fornirci la configurazione assoluta (se nota o per serie di composti simili).
3. Elevata sensibilità dell'analisi dei rivelatori per HPLC o per GC (eventualmente si può derivatizzare l'analita).
4. Efficace separazione dei due enantiomeri grazie all'uso di tecniche ad elevata efficienza (HPLC e GC) che facilitano l'integrazione. Il metodo è particolarmente adatto per analizzare campioni ad elevato arricchimento enantiomerico.

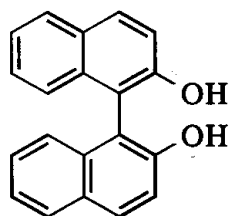
Modo d'uso:

1. Analisi del racemo e ottimizzazione della separazione
2. Confronto con un campione a configurazione nota
3. Pre-trattamento del campione da analizzare senza influenzarne le caratteristiche.

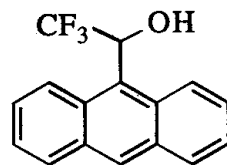
Arricchimento enantiomerico per cromatografia



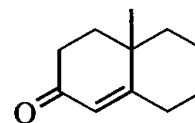
nicotine



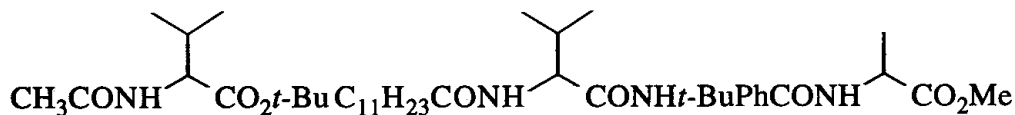
binaphthol (BINOL)



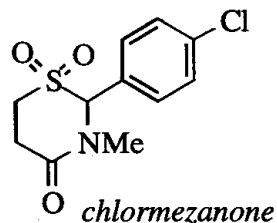
Pirkle's CSA



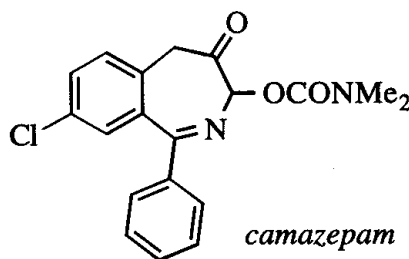
Wieland-Mischer ketone



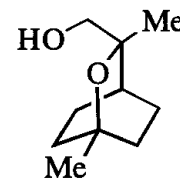
N-acetyl amino acid esters and amides



chlormezanone

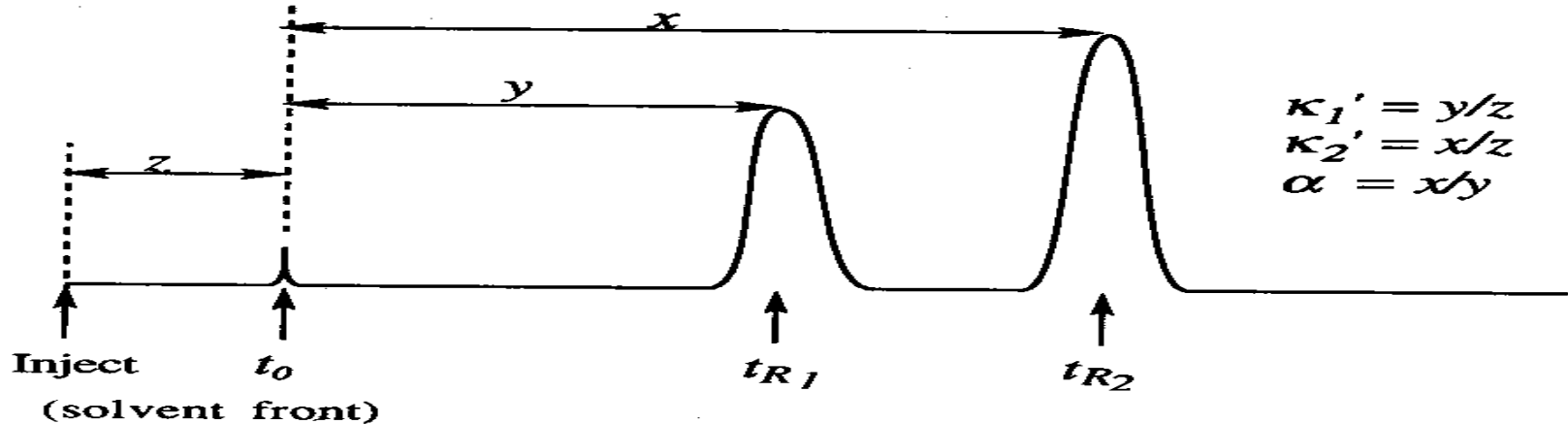


camazepam



Formazione di complessi etero e omochirali
(il fenomeno non si osserva con i composti racemici)

Cromatografia: principi base



t_0 = tempo in cui la fase mobile attraversa la colonna (nessuna interazione)

t_R = tempo di ritenzione del soluto

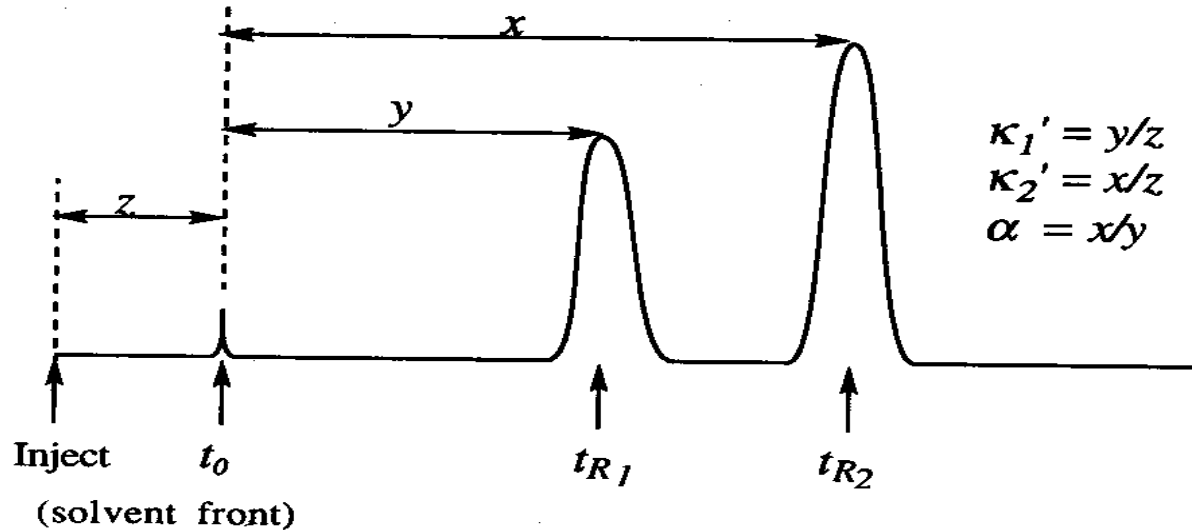
V_0 = volume morto

V_R = volume di ritenzione

κ' = rapporto di capacità = A_s/A_m

A_s = quantità di soluto nella fase stazionaria

A_m = quantità di soluto nella fase mobile



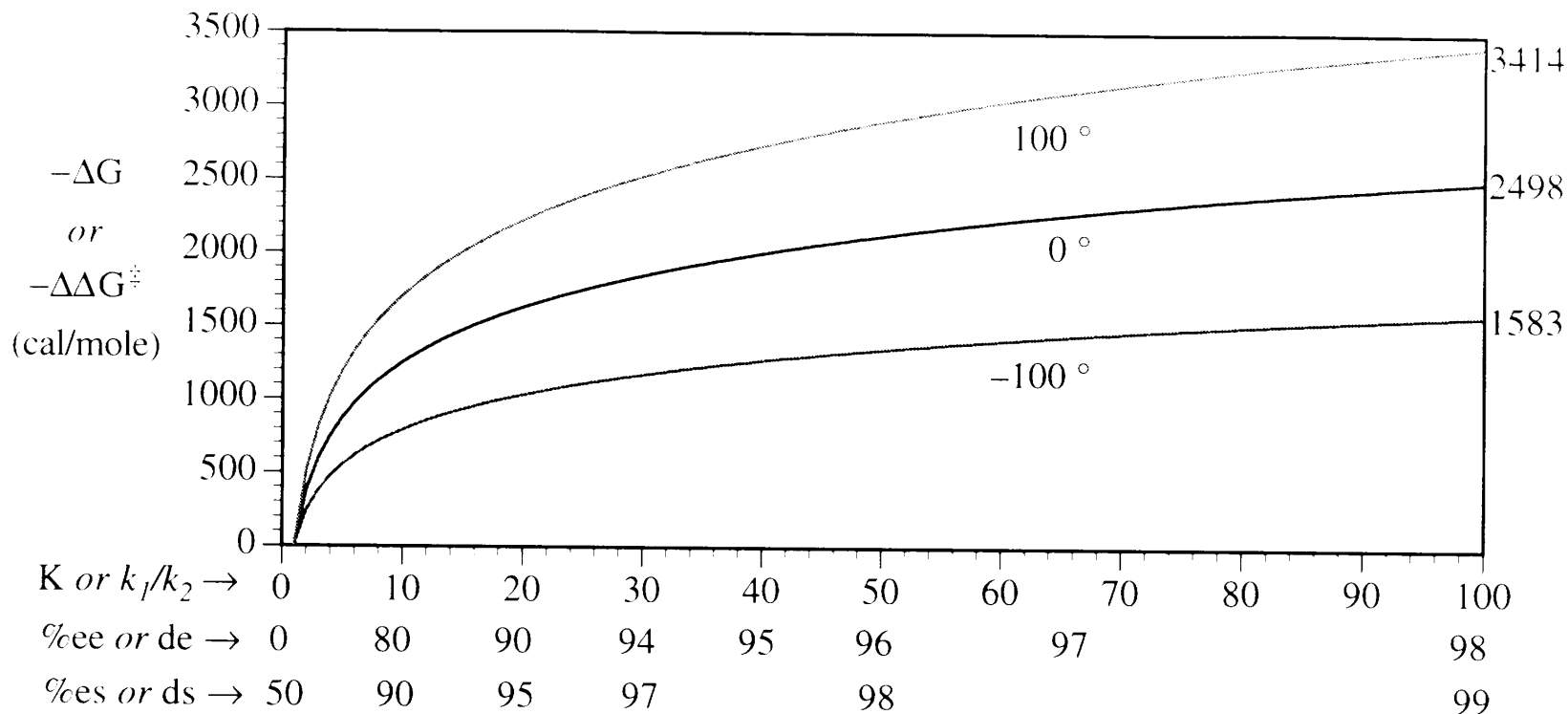
$$\text{Rapporto di capacit\`a} = \kappa' = A_s/A_m = (t_R - t_0)/t_0$$

$$\text{Fattore di separabilit\`a} = \alpha = \kappa_2' / \kappa_1' = (t_{R2} - t_0) / (t_{R1} - t_0)$$

$$\Delta\Delta G = -RT \ln \alpha \quad \alpha = e^{-\Delta\Delta G/RT}$$

$$\alpha = 1.1 (25^\circ\text{C}) \quad \Delta\Delta G = 56 \text{ cal/mol}$$

Selettività vs Energia Libera

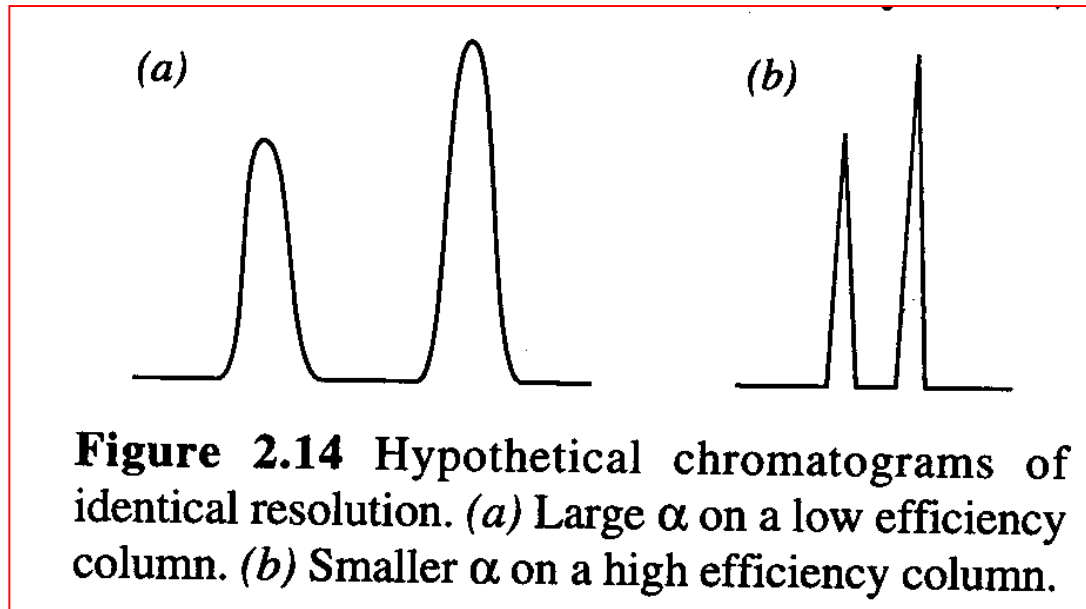


Il $\Delta\Delta G$ è significativo perché vi è un'amplificazione dell'interazione

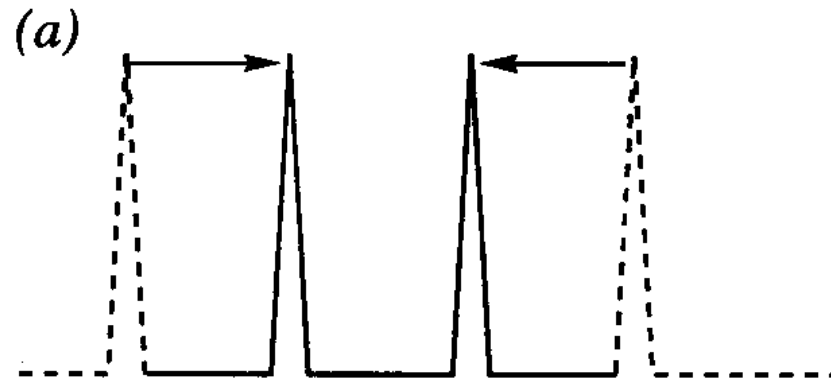
Risoluzione

$$R_s = 2(t_{R2} - t_{R1}) / (w_1 + w_2)$$

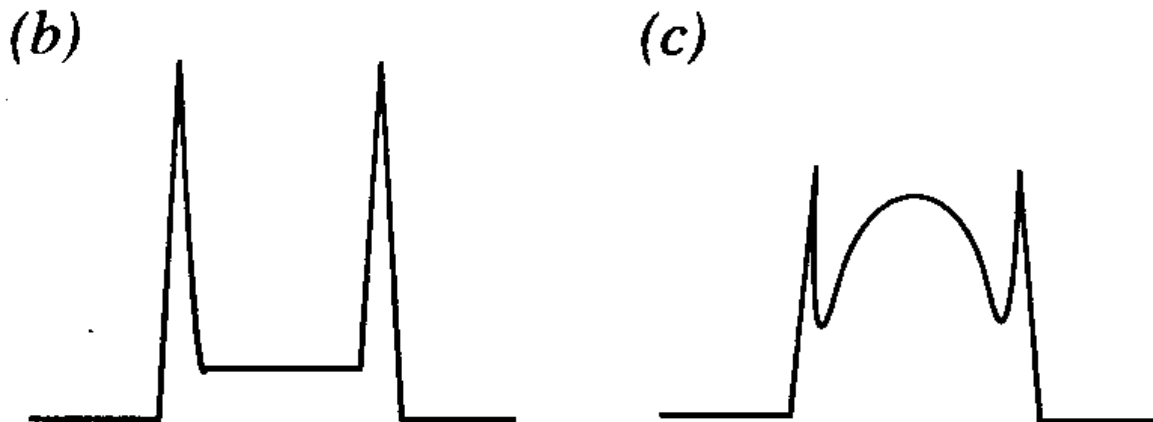
w = ampiezza



Racemizzazione della fase stazionaria



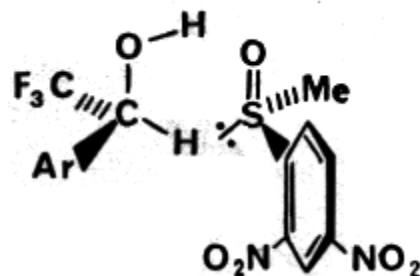
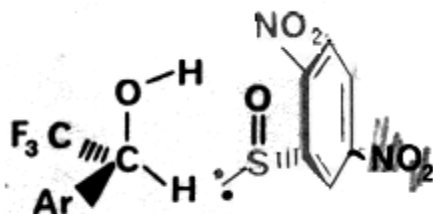
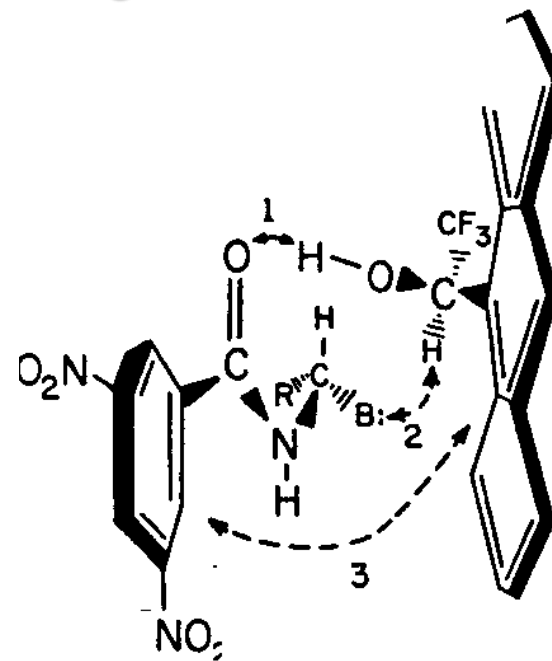
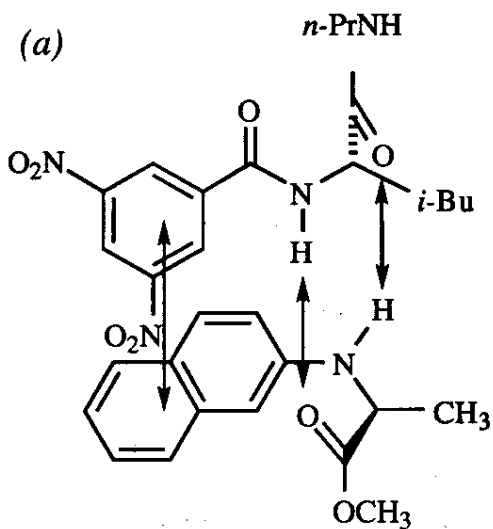
Racemizzazione dell'analita nel corso dell'analisi



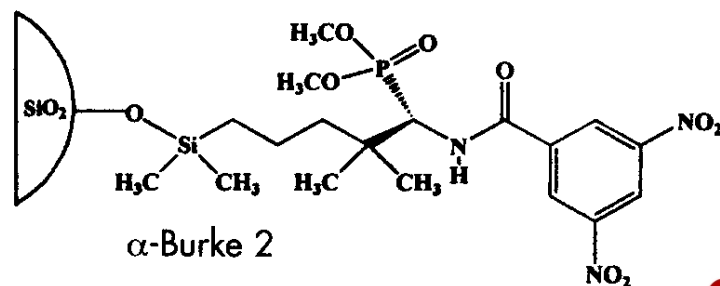
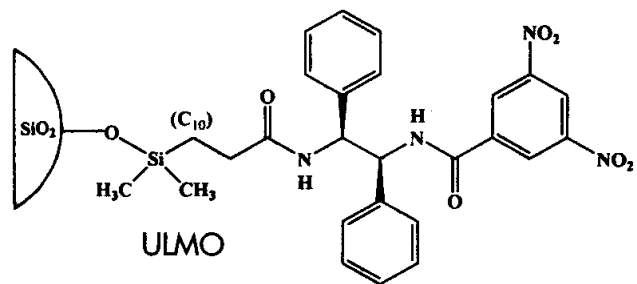
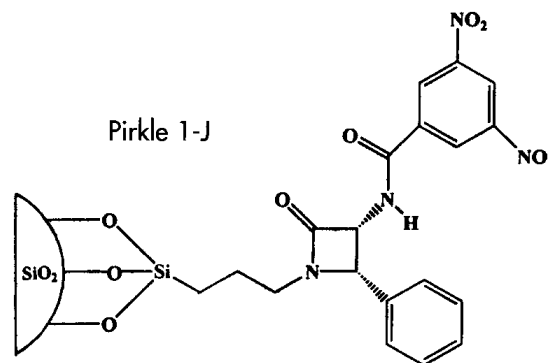
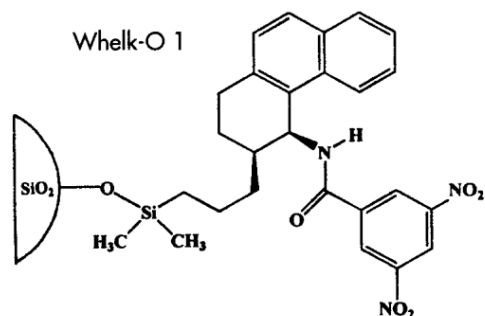
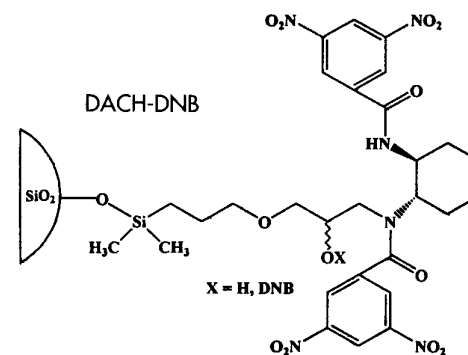
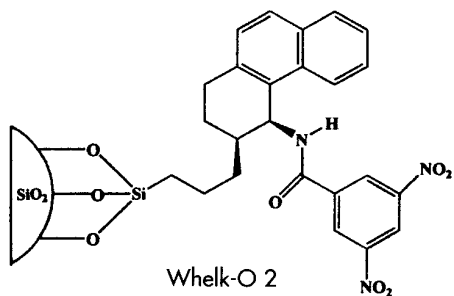
Meccanismo di azione - interazione a tre punti

$\Delta\Delta G$ molto piccoli (ca 50 cal/mol)!

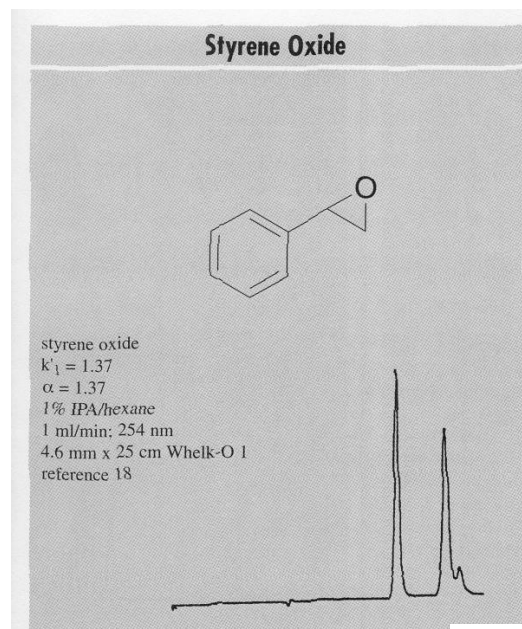
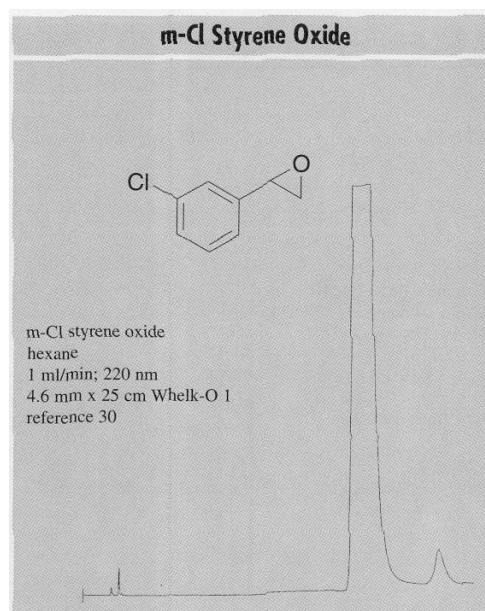
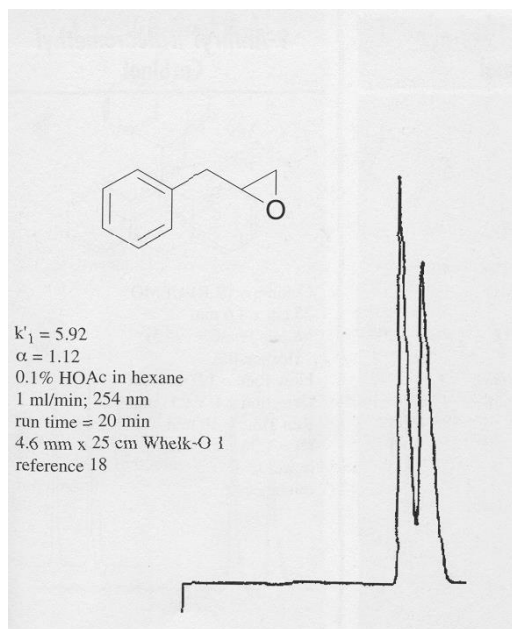
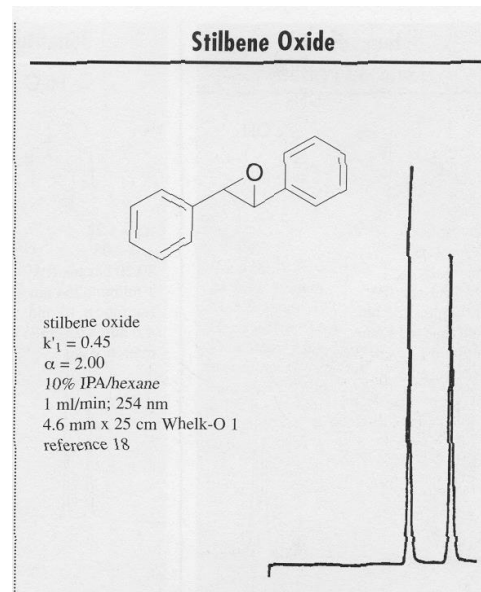
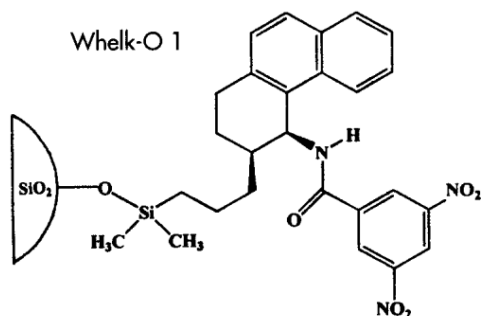
Legami ad idrogeno, interazione $\pi-\pi$



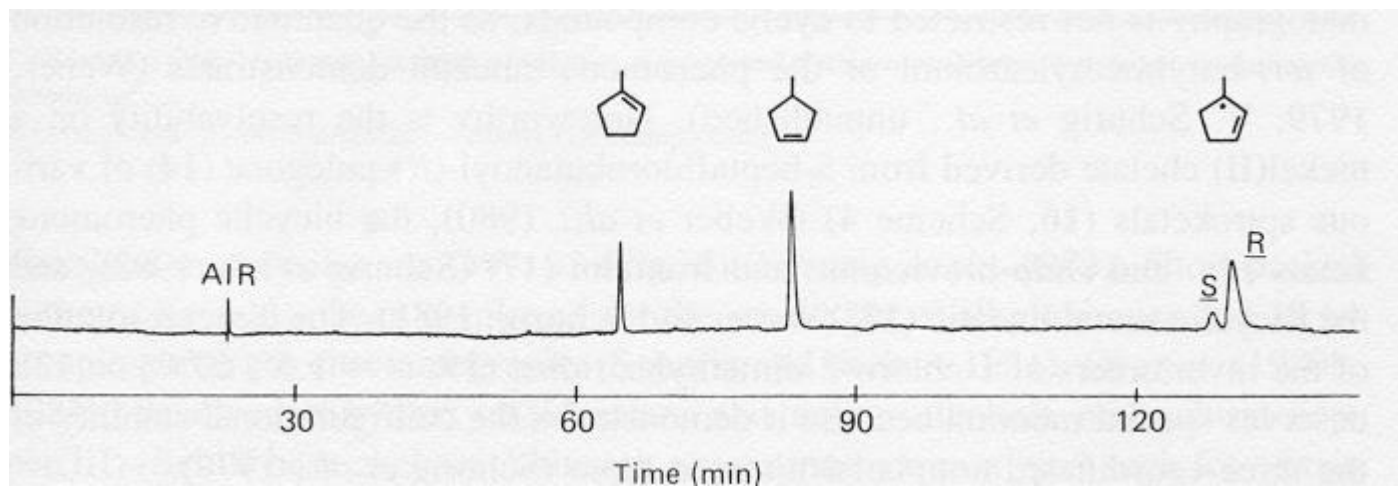
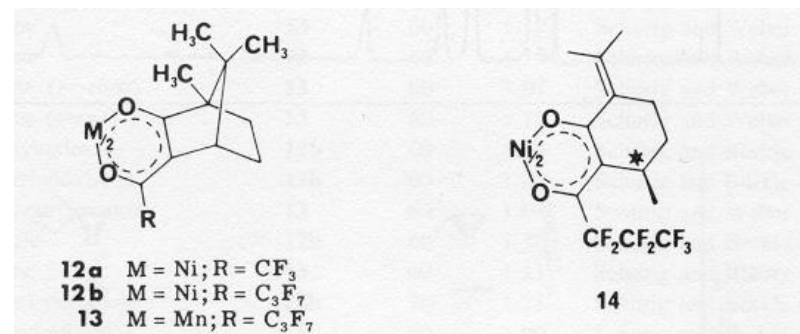
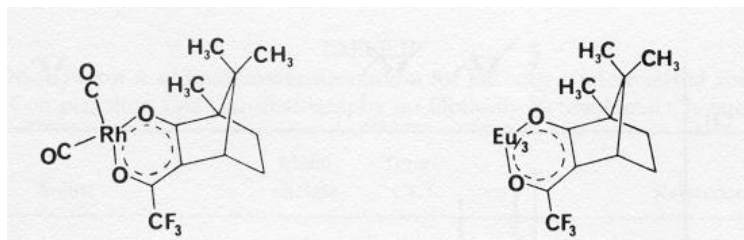
Colonne chirali HPLC tipo Pirkle



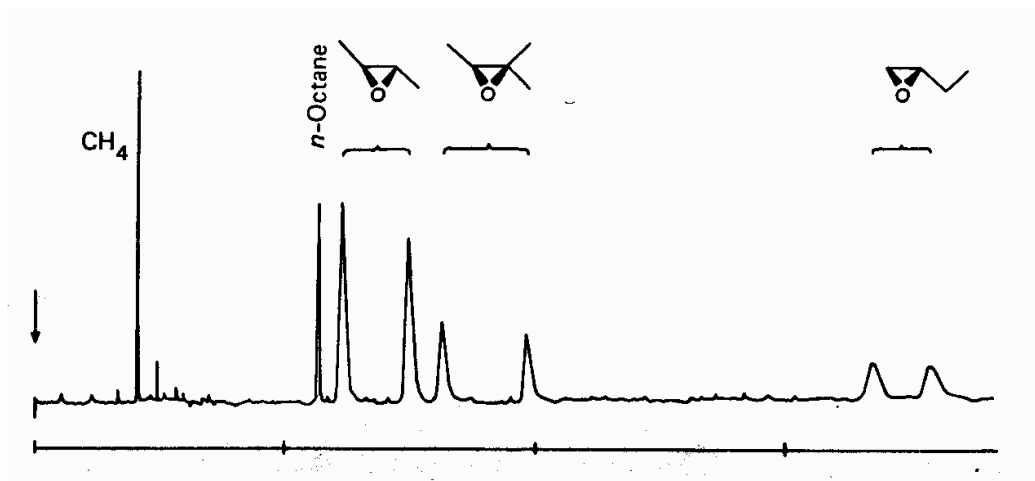
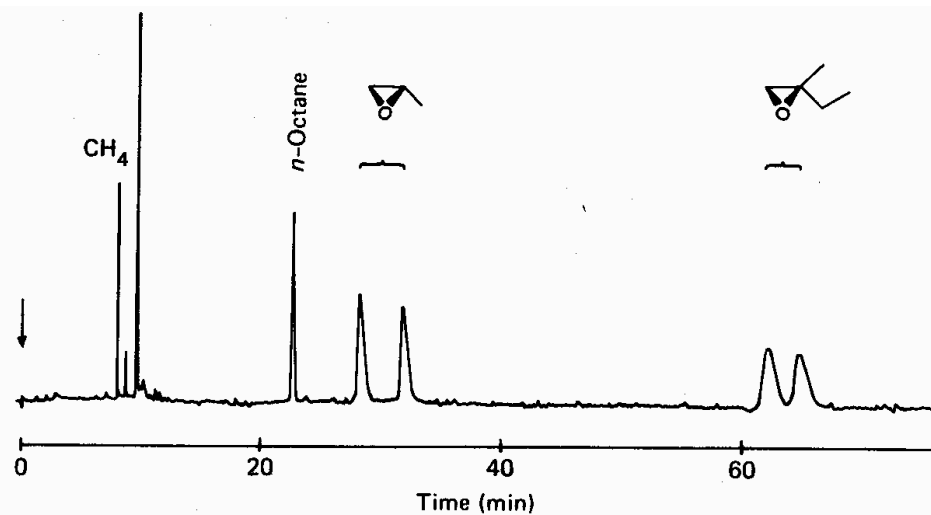
Colonne chirali HPLC tipo Pirkle



Substrati non funzionalizzati: analisi GC

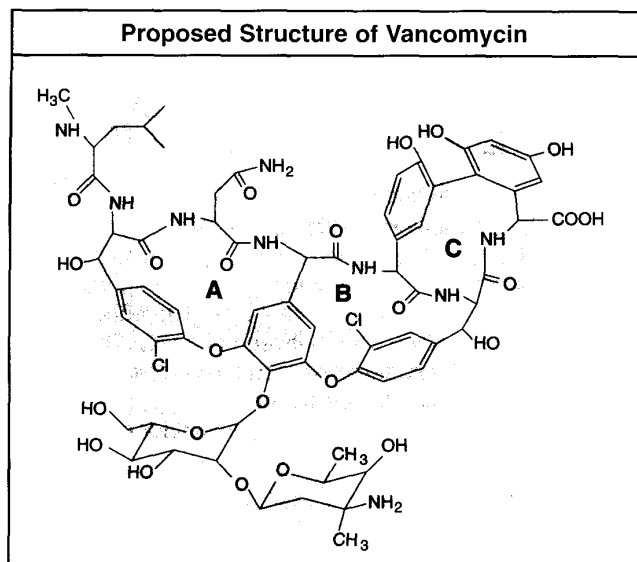


Substrati non funzionalizzati



Colonne HPLC CHIROBIOTIC

CHIROBIOTIC V

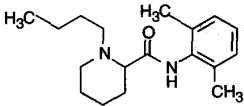
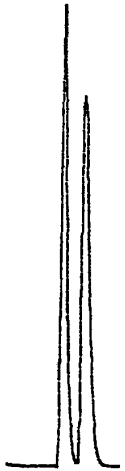
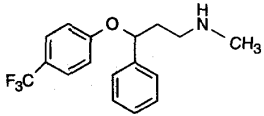
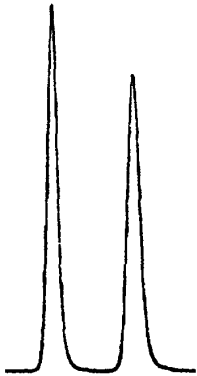
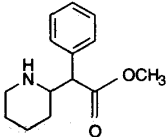
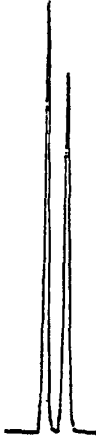


CHIROBIOTIC V is based on the covalent bonding of the amphoteric glycopeptide Vancomycin to a high purity, spherical silica gel through multiple linkages while retaining the essential components for chiral recognition. This phase has 18 chiral centers surrounding three cavities. Five aromatic groups bridge these cavities and hydrogen donor and acceptor sites are available around these ring structures. Chiral anionic and cationic groups are also present. CHIROBIOTIC phases have been proven to be stable in a variety of mobile phase conditions. Statistically, the reversed phase mode has been most successful on this phase (50%), followed by the polar organic mode which uses normal phase type solvent (40%) and, finally, in much smaller numbers, the typical normal phase mode (10%).

Possono essere usati in tre diversi tipi di modalità:

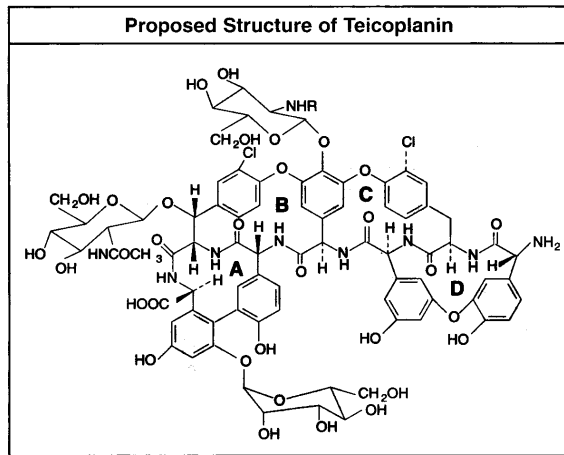
Modalità inversa
Modalità organica polare
Modalità normale

CHIROBIOTIC V

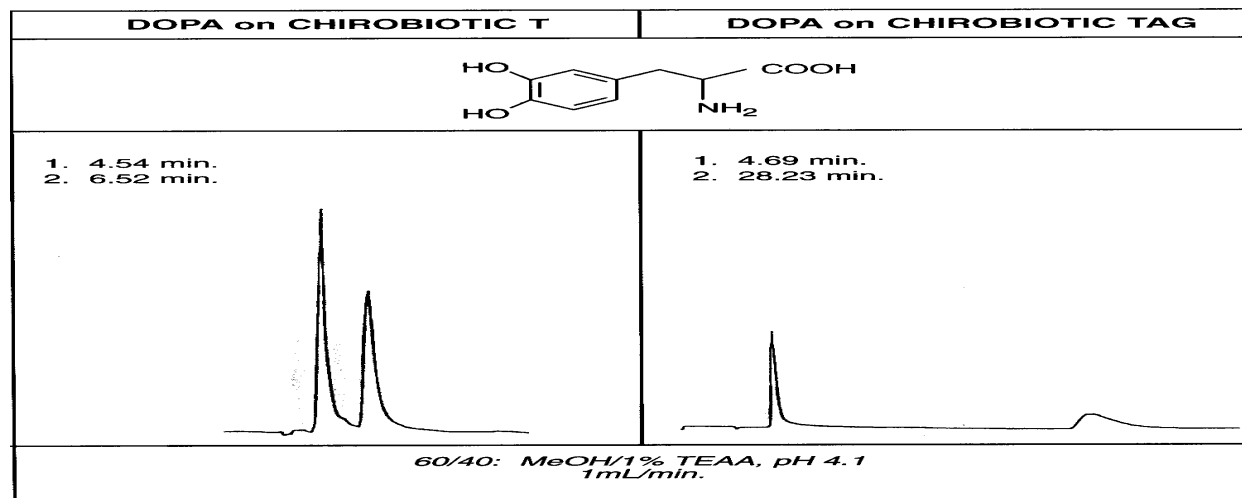
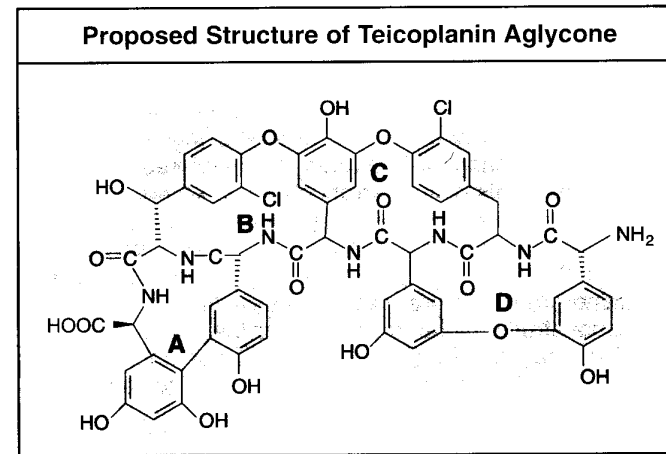
| Bupivacaine | Fluoxetine | Methylphenidate (Ritalin) |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <div style="text-align: center;">  </div> <p>1. 6.4 min. 2. 7.1 min.</p> <div style="text-align: center;">  </div> | <div style="text-align: center;">  </div> <p>1. 18.7 min. 2. 23.4 min.</p> <div style="text-align: center;">  </div> | <div style="text-align: center;">  </div> <p>1. 4.5 min. 2. 5.2 min.</p> <div style="text-align: center;">  </div> |
| <p style="text-align: center;"> CHIROBIOTIC V 95/5: MeOH/1.0% TEAA pH 4.1 1.0 mL/min. </p> | <p style="text-align: center;"> CHIROBIOTIC V 90/10: EtOH/20mM NH₄NO₄, pH 4 0.2 mL/min. </p> | <p style="text-align: center;"> CHIROBIOTIC V 95/5: MeOH/1.0% TEAA pH 4.1 2.0 mL/min. </p> |

Colonne HPLC - CHIROBIOTIC

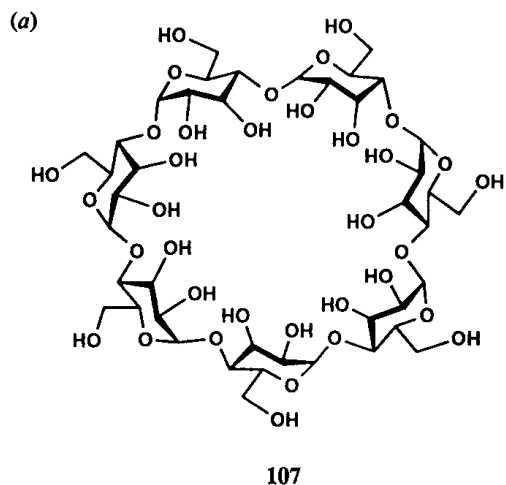
CHIROBIOTIC T



CHIROBIOTIC TAG



analisi GC: colonne chirali Chiraldex



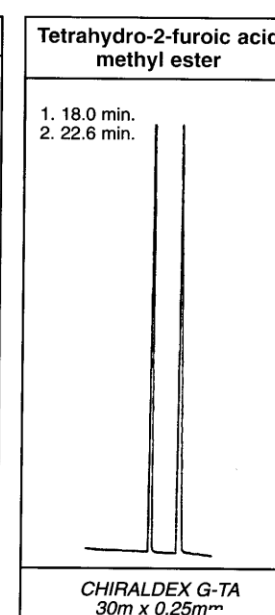
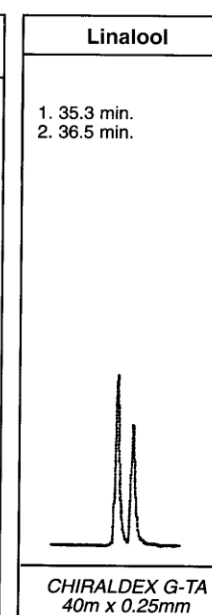
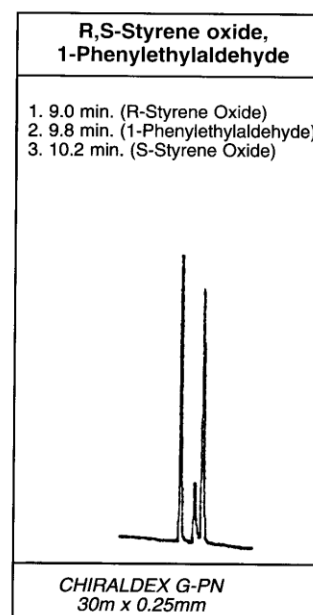
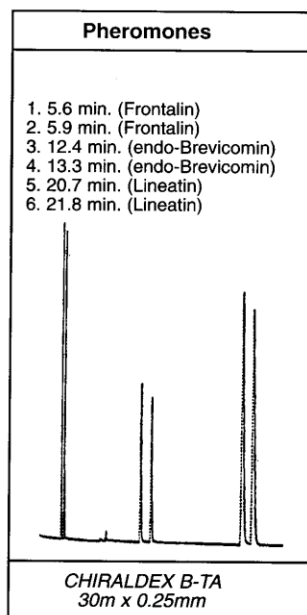
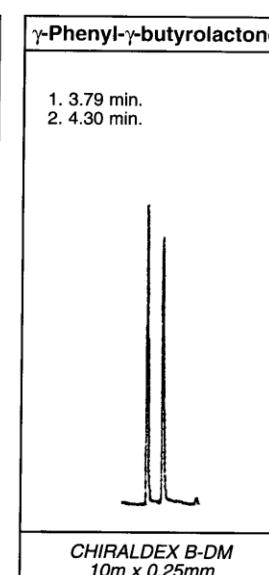
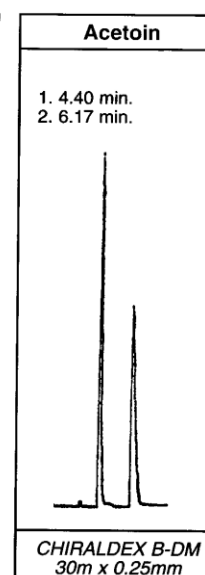
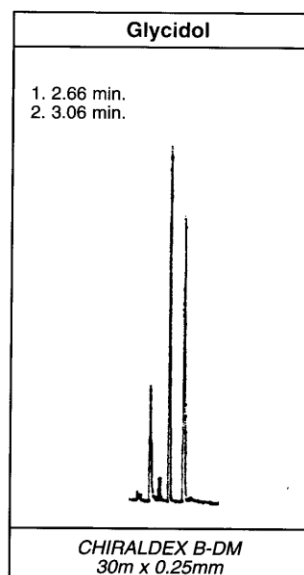
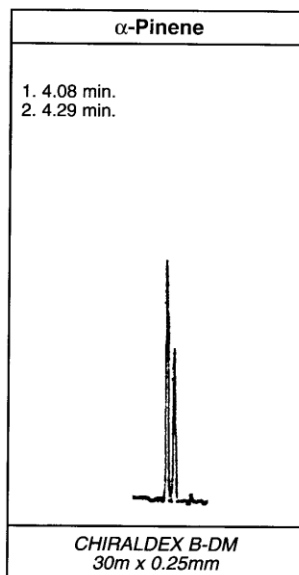
β -Cyclodextrin (β -CD; cycloheptaamylose)

α , β e γ - ciclodestrine funzionalizzate

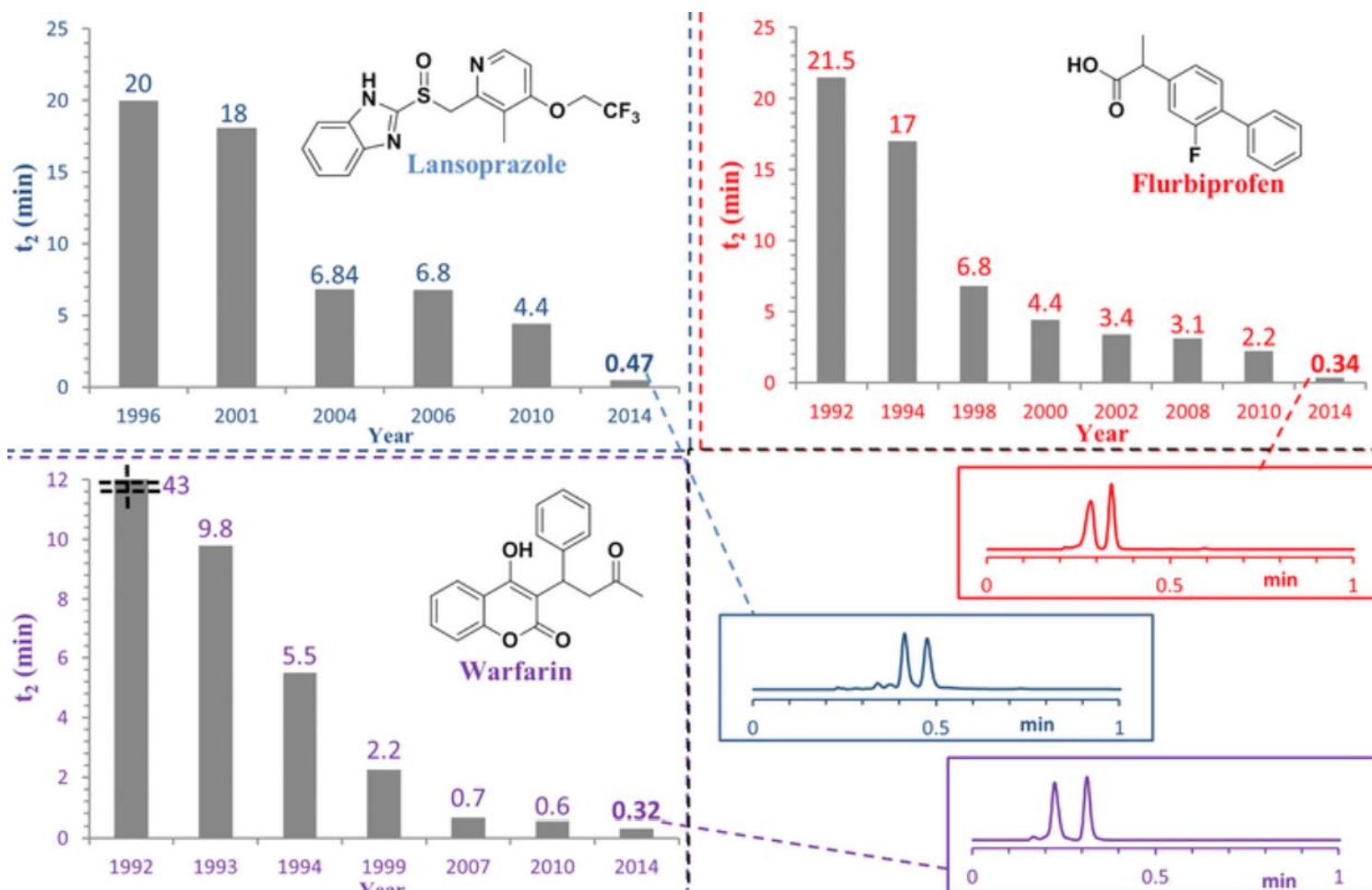
colonne chirali ChiralDEX

| DESIGNATION | DERIVATIVE | TYPICAL COMPOUNDS SEPARATED |
|----------------|-----------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| CHIRALDEX A-PH | α -cyclodextrin, Permethylated Hydroxypropyl | Smaller linear and saturated amines, alcohols, esters, epoxides. |
| CHIRALDEX B-PH | β -cyclodextrin, Permethylated Hydroxypropyl | Most structural types of compounds including linear and cyclic amines and alcohols, lactones, amino alcohols, sugars, bicyclics, epoxides, haloalkanes, aromatic and cyclic hydrocarbons, and more. Very useful for hydrocarbons. |
| CHIRALDEX G-PH | γ -cyclodextrin, Permethylated Hydroxypropyl | Cyclic and bicyclic diols and other larger compounds including steroids and carbohydrates. |
| CHIRALDEX A-DA | α -cyclodextrin, Dialkylated | Smaller cyclic and aromatic amines, alcohols and epoxides. |
| CHIRALDEX B-DA | β -cyclodextrin, Dialkylated | Heterocyclics, some multi-ring lactones, aromatic amines, sugars, certain amino acid derivatives, bicyclics, epoxides. |
| CHIRALDEX G-DA | γ -cyclodextrin, Dialkylated | Aromatic amines containing 2 or more rings, large cyclic diols, some heterocyclics, multi-ring compounds or compounds with bulky substituents. |
| CHIRALDEX A-TA | α -cyclodextrin, Trifluoroacetylated | Smaller epoxides and alcohols, amino alcohols, amino alkanes, diols. |
| CHIRALDEX B-TA | β -cyclodextrin, Trifluoroacetylated | Broad range alkyl alcohols, halo acid esters, amino alkanes, amino acid derivatives, halocycloalkanes, certain lactones, diols, alkyl halides, furan and pyran derivatives. |
| CHIRALDEX G-TA | γ -cyclodextrin, Trifluoroacetylated | Chiral alcohols, diols, polyols, hydrocarbons, lactones, amino alcohols, halocarboxylic acid esters, homologous series, furan, pyran derivatives, epoxides, glycidyl analogs and haloepihydrins. |
| CHIRALDEX G-PN | γ -cyclodextrin, Propionylated | Epoxides, secondary amines, higher alcohols >C ₄ , esters, lactones, diols. Good alternate for G-TA but not as broad selectivity. |
| CHIRALDEX G-BP | γ -cyclodextrin, Butyrylated | Amino acids, certain primary amines and furans. |
| CHIRALDEX B-PM | β -cyclodextrin, Permethylated | Acids, alcohols, barbitals, diols, epoxides, esters, hydrocarbons, ketones, lactones and terpenes. |
| CHIRALDEX B-DM | β -cyclodextrin, Dimethylated | Aromatic alcohols, short chain alcohols \leq C ₆ , amines, amino alcohols, epoxides, cyclic ketones, diols, aromatic acids and esters (many of these underivatized). |
| CHIRALDEX G-DM | γ -cyclodextrin, Dimethylated | Aromatic alcohols >C ₅ , polar amines and bulky amines. Aromatic amines, halogenated aliphatic acids and derivatized long chain diols. |

Applicazioni colonne gc Chiraldex



The race to the shortest chromatogram

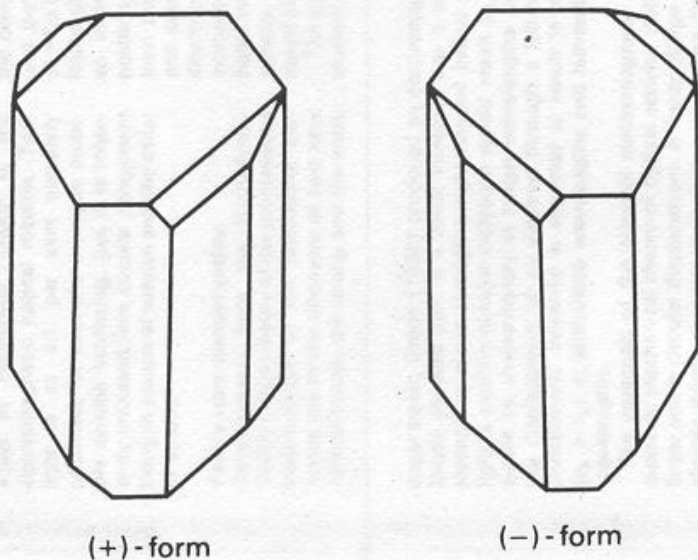


A. Ciogli, O.H. Ismail, G. Mazzocanti, C. Villani, F. Gasparrini *J. Separation Science* **2018**, 1307

X-Ray: Absolute Structure of Chiral Compounds

How to correlate microscopic absolute configurations to macroscopic properties such as the sign of the optical rotation of polarised light. Emil Fischer: relative system; assign 'D' configuration to (+) Glyceraldehyde.

Example of a Macroscopic Property

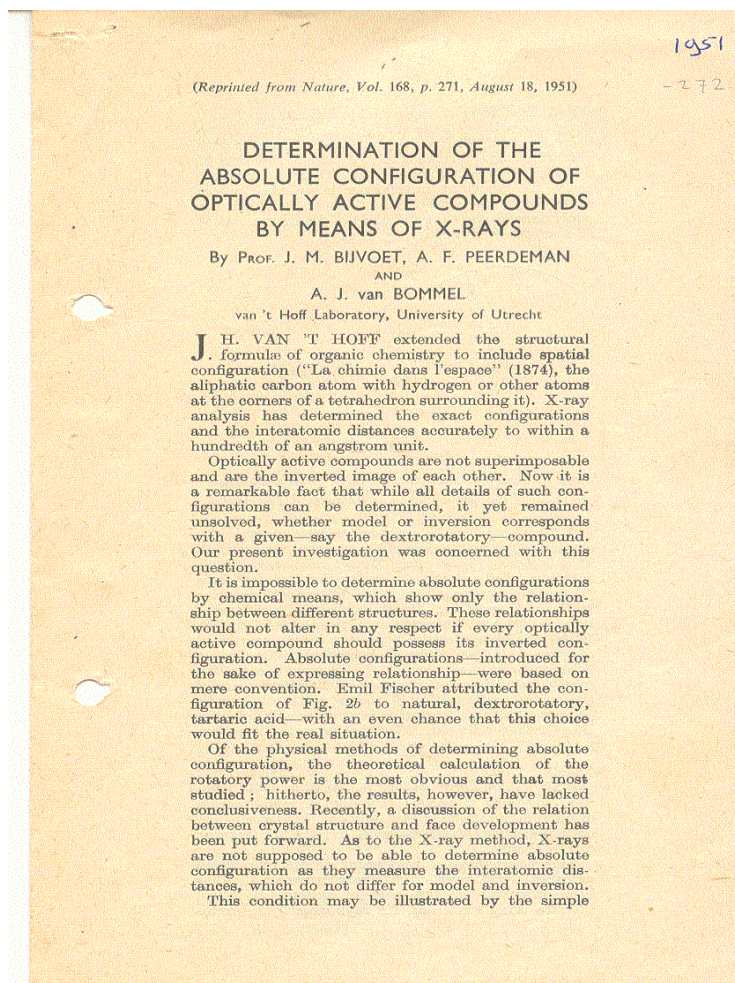


Sodium ammonium tartrate



X-Ray: Absolute Structure of Chiral Compounds

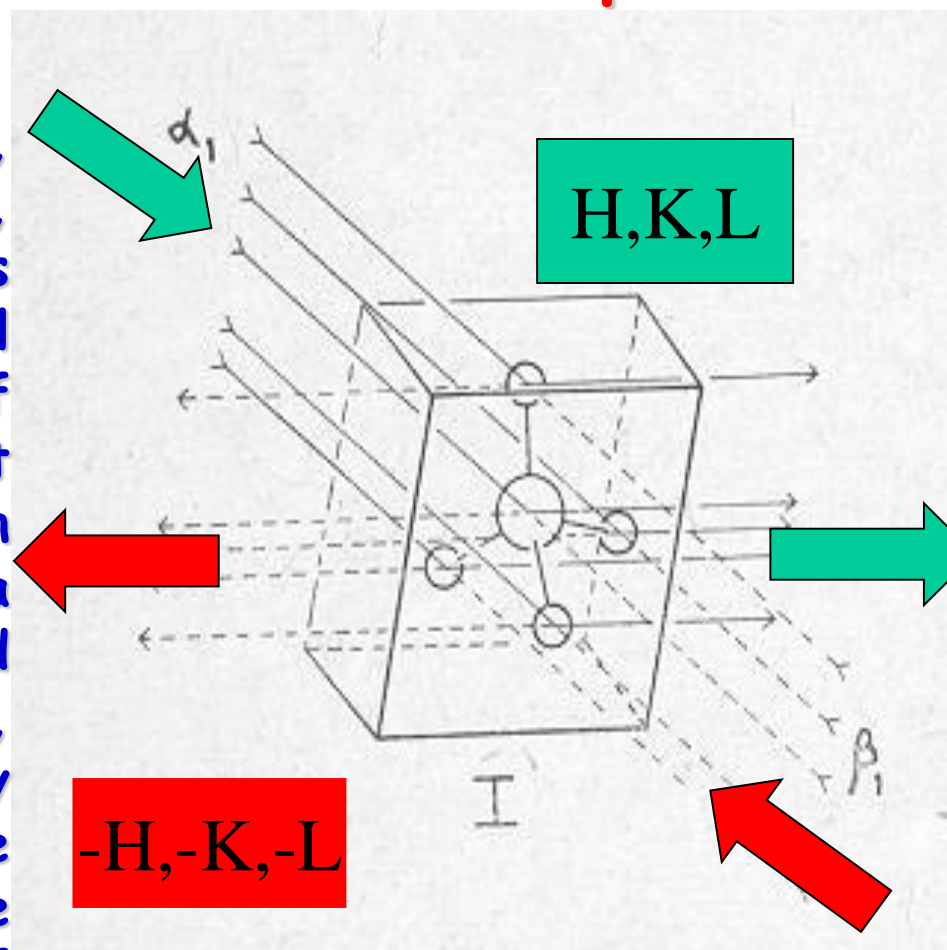
Bijvoet used Anomalous Dispersion (Resonant Scattering) to Solve the Absolute Structure Problem around 1950.



Prof. Dr. J.M. Bijvoet

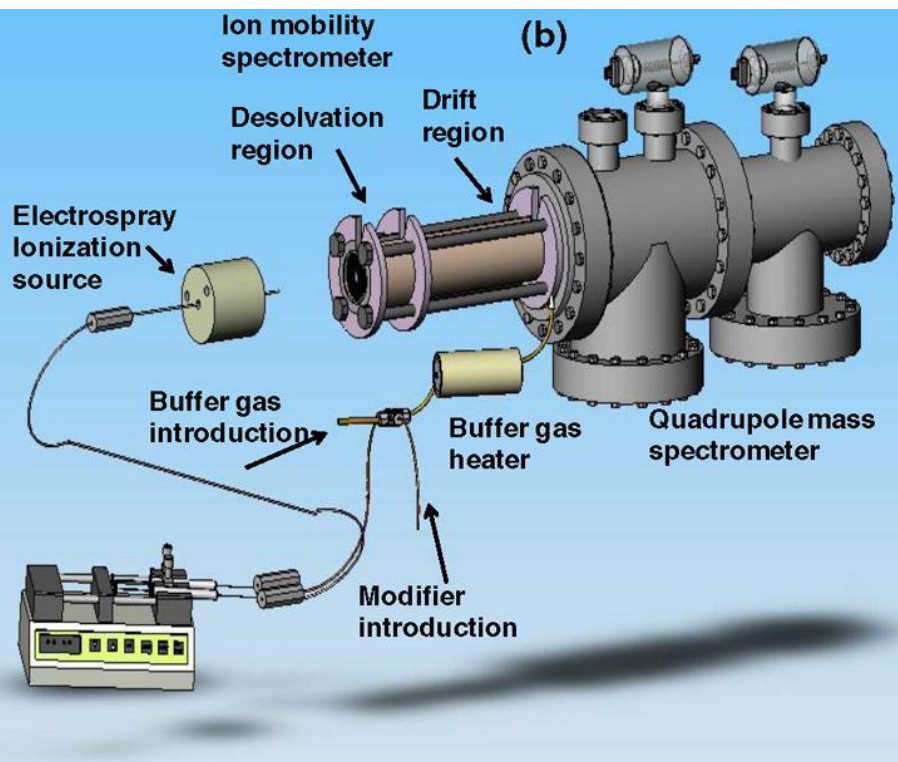
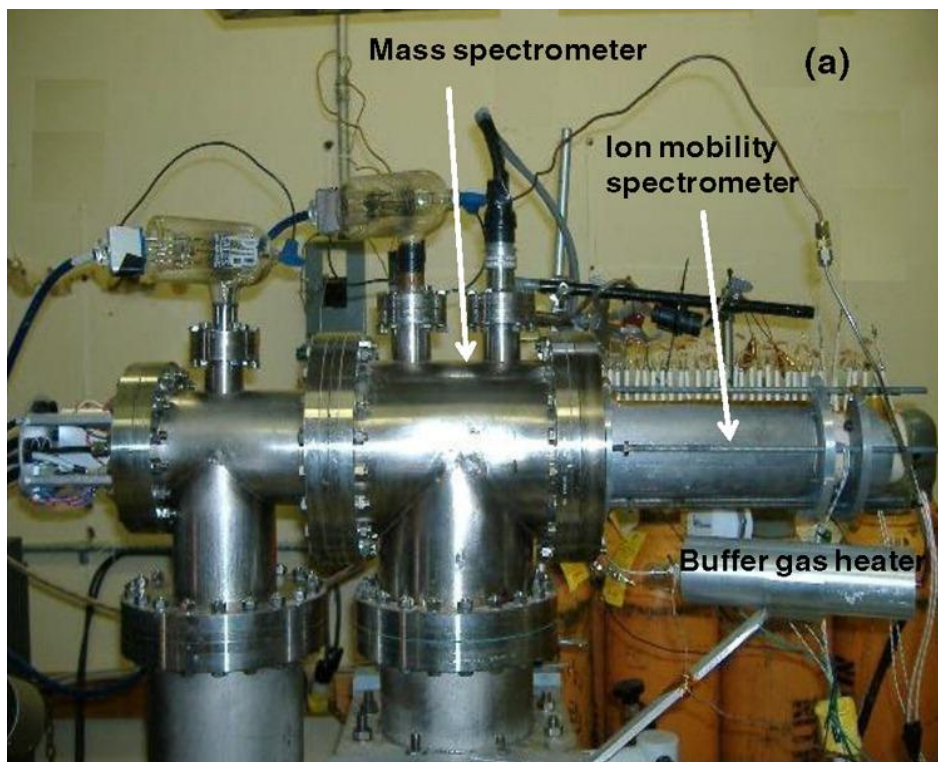
X-Ray: Absolute Structure of Chiral Compounds

The couple of reflections h, k, l , and $\bar{h}, \bar{k}, \bar{l}$ is called a Friedel pair, or Bijvoet pair. Their intensities are equal either if the crystal structure is centrosymmetric or if there is no resonant scattering, but differ otherwise. Friedel's law then does not hold. For crystals with a non-centrosymmetric structure and significant resonant scattering, equivalent reflections generated by the symmetry operations of the point group of the crystal have intensities different from those of equivalent reflections generated by the introduction of an additional inversion centre in normal scattering.



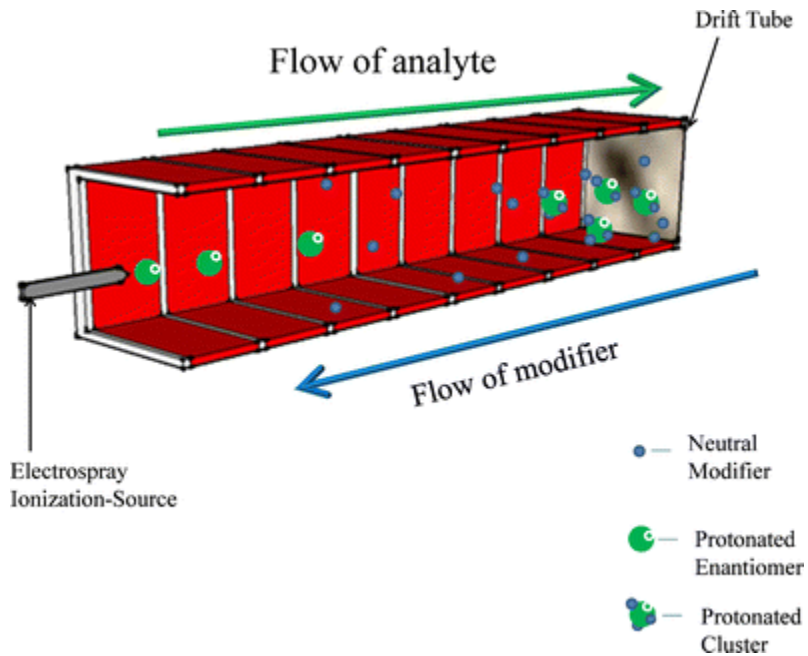
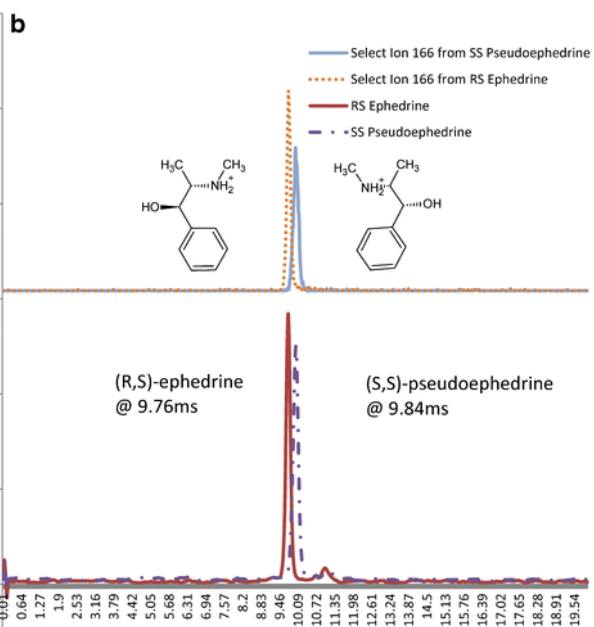
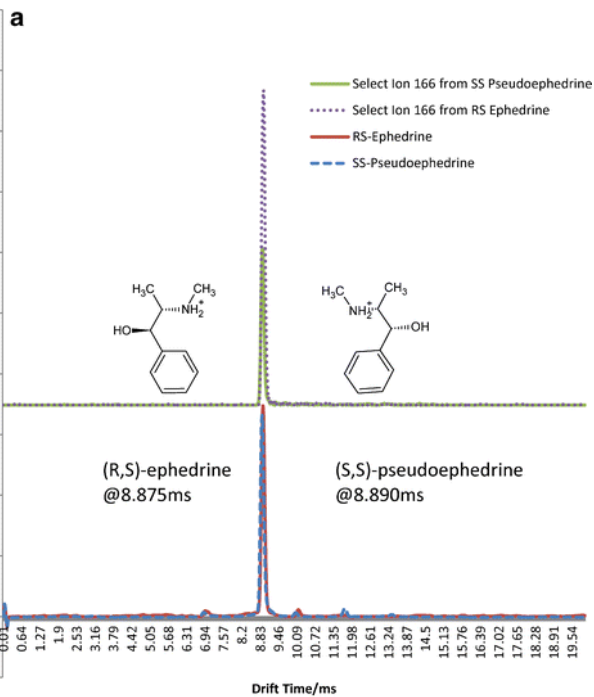
Friedel Pair of Reflections

Mass Spectrometry. Chiral Ion Mobility



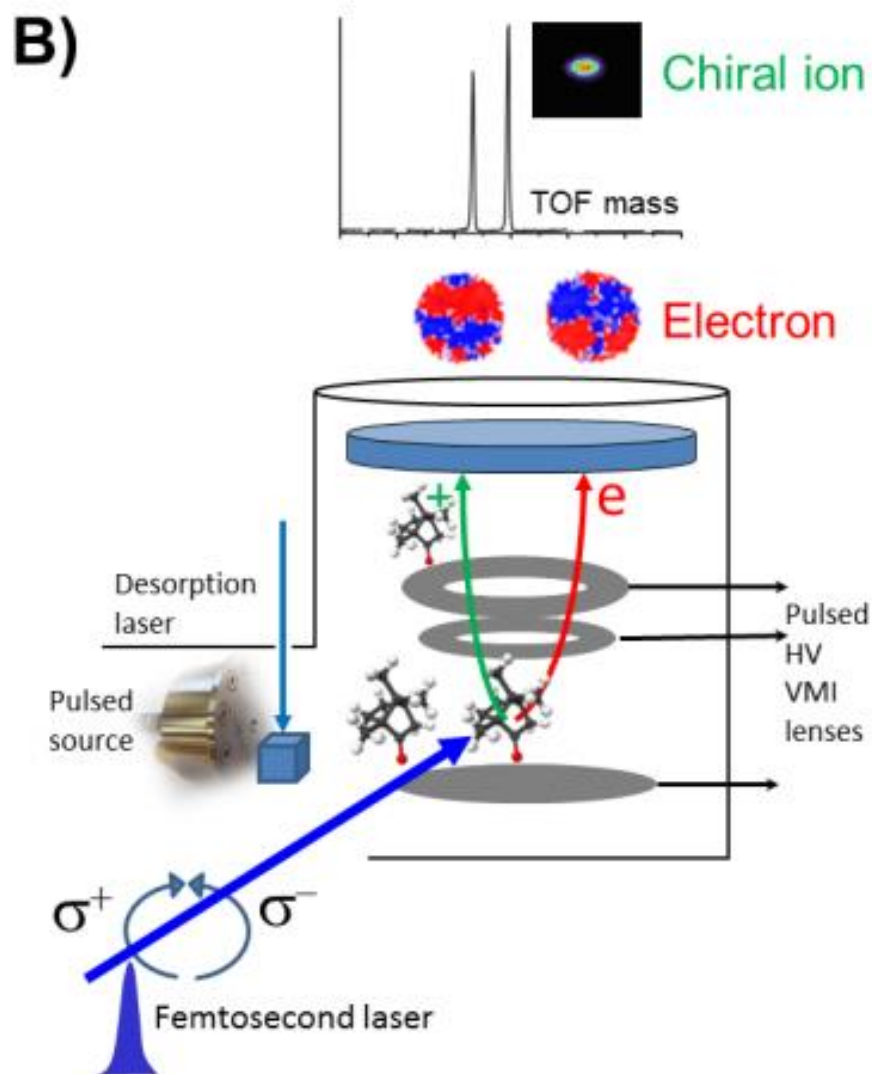
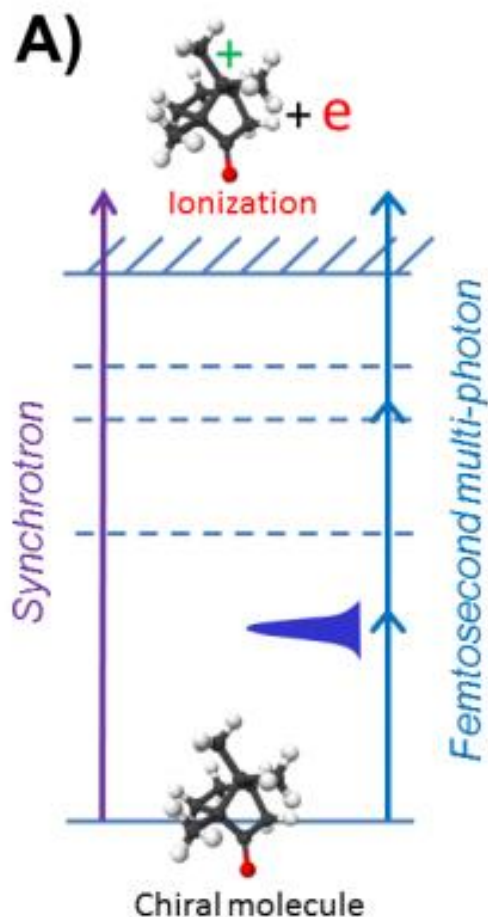
Bijvoet used Anomalous Dispersion (Resonant Scattering) to Solve the Absolute Structure Problem around 1950

Chiral Ion Mobility

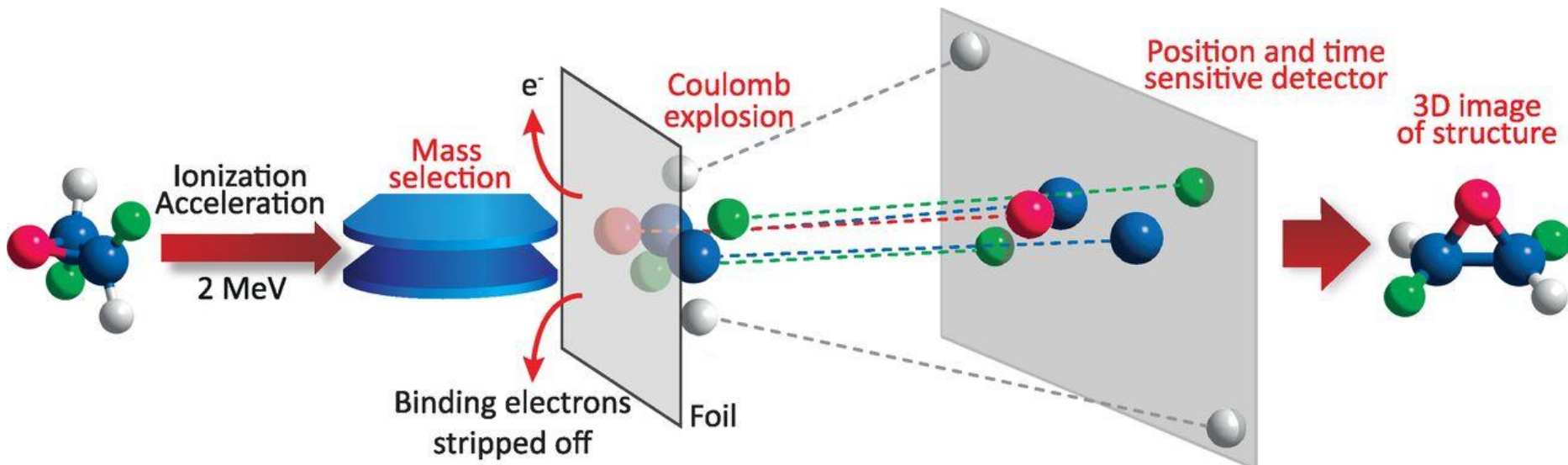


Nature Chem 2014, 281

Photo-electron circular dichroism,

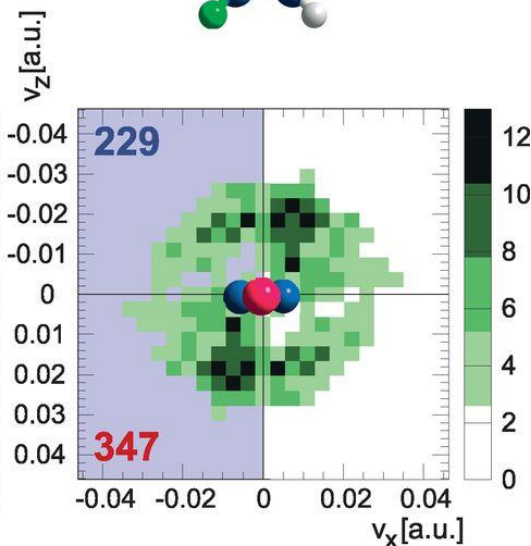
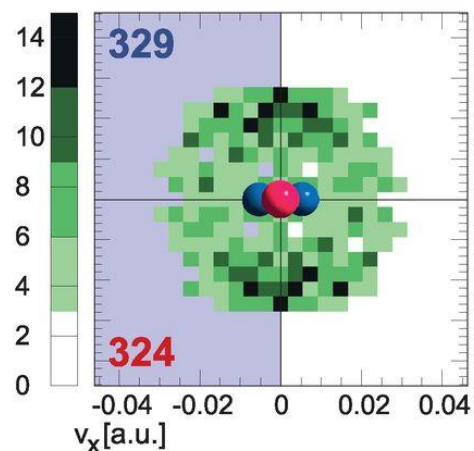
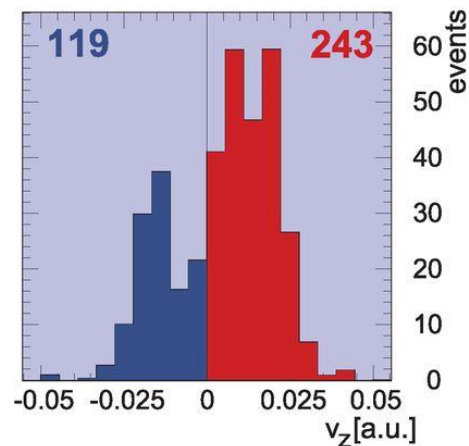
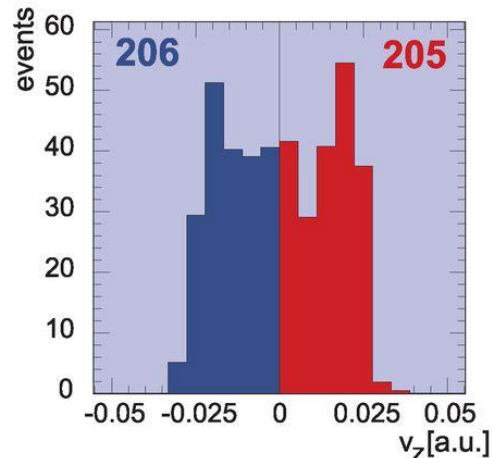


Coulomb Explosion



A Racemic oxirane

Enantiopure oxirane

**B** Positions of D's**C** Background-subtracted projections**D** Identification of enantiomer