Chiroptical Spectroscopy

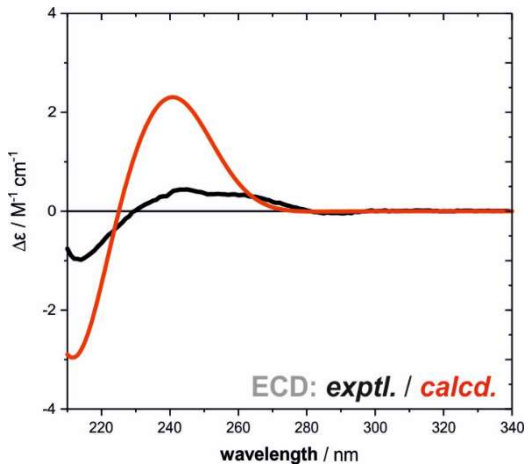
Theory and Applications in Organic Chemistry

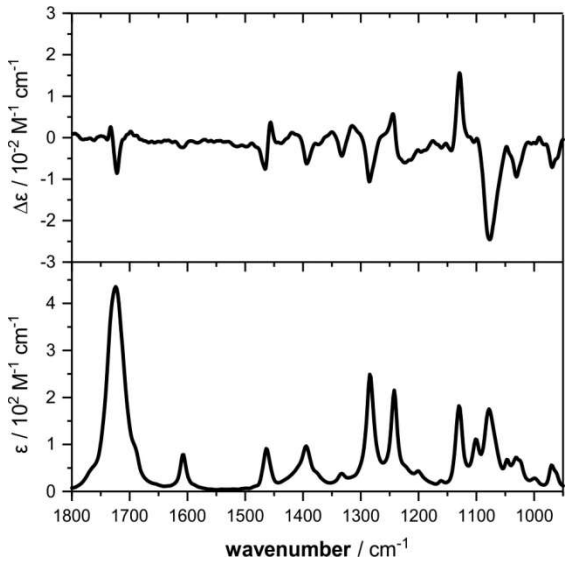
Lecture 7: Vibrational Optical Activity

Masters Level Class (181 041)

Block course, october 2020

Comparison of electronic and vibrational CD





Electronic CD

- Electronic transitions (suitable chromophore needed)
- Signal intensity: $^{I_{CD}}/_{I_{abs}} \approx 10^{-3}$

- Empirical rules available
  … but it‘s often not easy to distinguish diastereomers

- Computations need electronically excited states

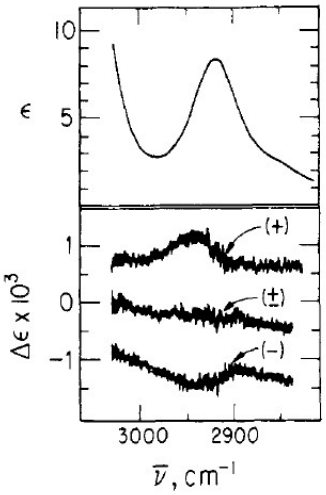
Vibrational CD

- All chiral molecules IR active
  i.e. no need for special chormophore
- Signal intensity: $^{I_{CD}}/_{I_{abs}} \approx 10^{-4} - 10^{-5}$

- Calculations very reliable, only ground state!
  … but calculations are the only way for reliable interpretation!

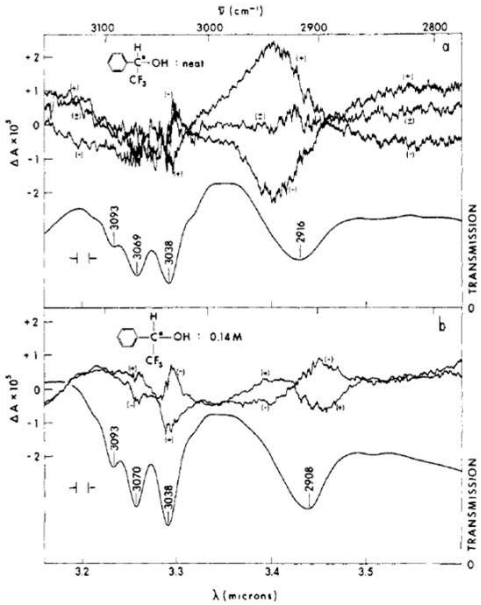
- Experimental limitation:
  Solvent absorbance and solubility

A brief history of VCD



1974:
First dispersive VCD measurements in CH/OH stretching
Holzwarth et al., *JACS* **96** (1974) 251-252

1975:
Confirmation and extension of wavelength range
Nafie, Stephens, et al., *JACS* **97** (1975) 3842-3843



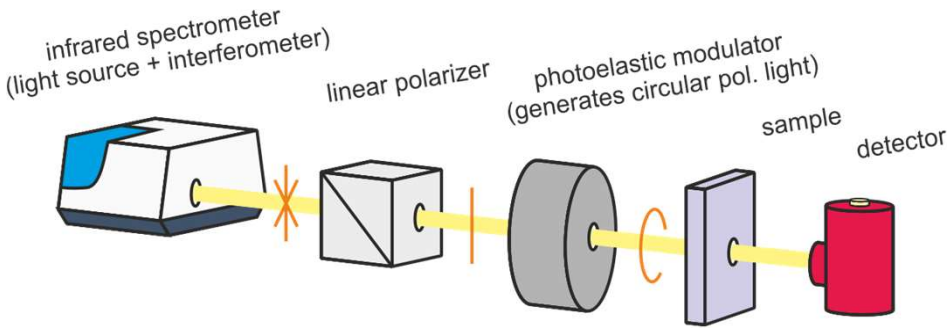
1976:
First Fourier-transform VCD (followed by mid-IR in early 80s)
Nafie, Stephens et al., *JACS* **98** (1976) 2715-2723

1983:
First attempts for a theoretical description

1985:
„The theory“ - Philip J Stephens
P.J. Stephens, *J. Phys. Chem. 89* (1985) 748-752

1994:
Implementation in Gaussian

Experimental scheme FT-VCD

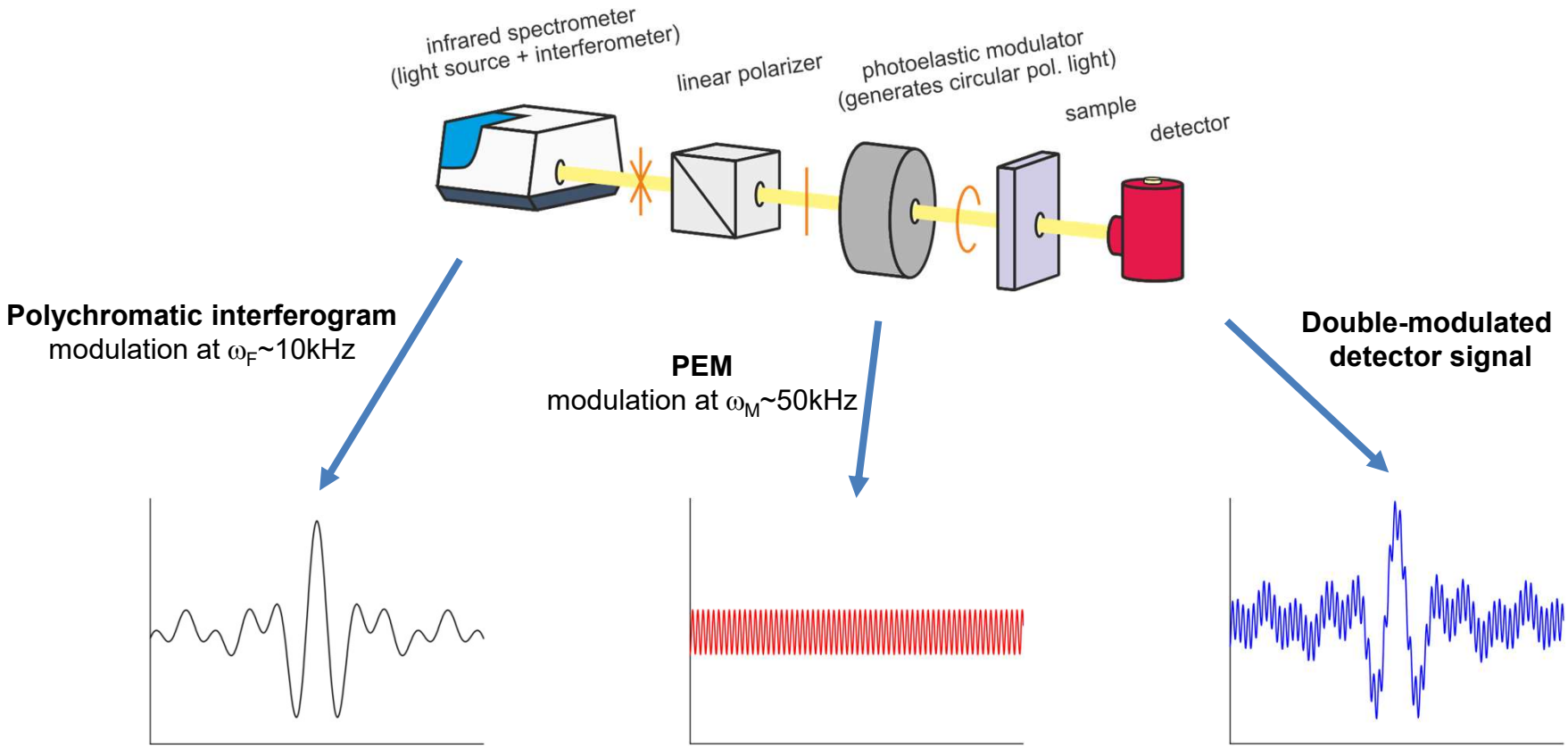


- In principle, setups for ECD and vibrational CD measurements are fairly identical.

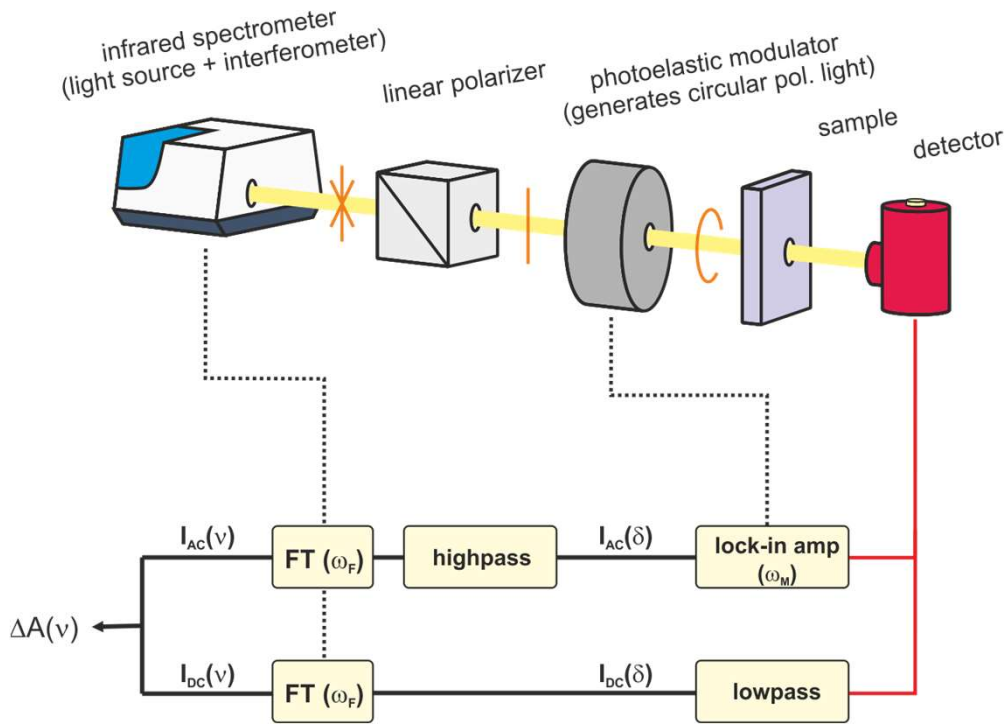
- As the signals are very small compared to parent UV/vis resp. IR, it is not possible to measure LCP and RCP light separately.

- Instead: Fast modulation between LCP and RCP

Experimental scheme FT-VCD



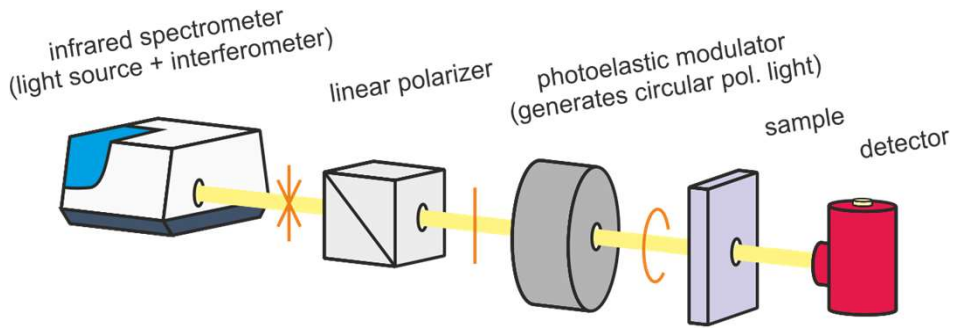
Experimental scheme FT-VCD



LIA: amplifies only those components which are modulated at reference frequency ω_M

Highpass / lowpass: electronic filters which let only high/low frequency components pass

Experimental scheme FT-VCD: Stokes-analysis



PEM induces time dependent phase shift:

$$\varphi(t) = \frac{2\pi}{\lambda} \cdot d \cdot \left[n_x(t) - n_y(t)\right]$$

Retardation phase angle:

$$\alpha_M(\tilde{\nu}) = \alpha_M^0(\tilde{\nu}) \cdot \sin(\omega_M t)$$

$$\boldsymbol{M_{PEM}} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos[\alpha_M(\tilde{\nu})] & 0 & -\sin[\alpha_M(\tilde{\nu})] \\ 0 & 0 & 1 & 0 \\ 0 & \sin[\alpha_M(\tilde{\nu})] & 0 & \cos[\alpha_M(\tilde{\nu})] \end{pmatrix}$$

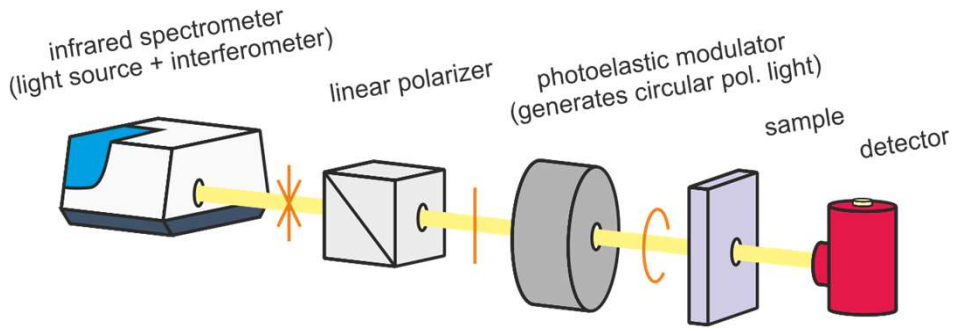
$$\boldsymbol{S_0} = \frac{I(\tilde{\nu})}{2}\begin{pmatrix} 1 \\ 1 \\ 0 \\ 0 \end{pmatrix}$$

vertically polarized light (0°)

$$\boldsymbol{S_{PEM}} = \boldsymbol{M_{PEM}}\boldsymbol{S_0} = \frac{I(\tilde{\nu})}{2}\begin{pmatrix} 1 \\ \cos[\alpha_M(\tilde{\nu})] \\ 0 \\ \sin[\alpha_M(\tilde{\nu})] \end{pmatrix}$$

… after traveling through PEM

Experimental scheme FT-VCD: Stokes-analysis



$$\boldsymbol{S_{PEM}} = \frac{I(\tilde{\nu})}{2}\begin{pmatrix} 1 \\ \cos[\alpha_M(\tilde{\nu})] \\ 0 \\ \sin[\alpha_M(\tilde{\nu})] \end{pmatrix}$$

$$\boldsymbol{M_{CDSAMPLE}} = 10^{-A(\tilde{\boldsymbol{\nu}})}\begin{pmatrix} 1 & 0 & 0 & CD \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ CD & 0 & 0 & 1 \end{pmatrix}$$

for a sample with no LD/LB/CB and *CD* = ln(10)/2 ΔA

$$\boldsymbol{S_S} = \frac{I(\tilde{\nu}) \cdot 10^{-A(\tilde{\boldsymbol{\nu}})}}{2}\begin{pmatrix} 1 + CD \cdot \sin[\alpha_M(\tilde{\nu})] \\ \cos[\alpha_M(\tilde{\nu})] \\ 0 \\ CD + \sin[\alpha_M(\tilde{\nu})] \end{pmatrix}$$

Experimental scheme FT-VCD: Stokes-analysis

$$\boldsymbol{S_S} = \frac{I(\tilde{\nu}) \cdot 10^{-A(\tilde{\nu})}}{2} \begin{pmatrix} 1 + \frac{\ln(10)}{2} \Delta A \cdot \sin[\alpha_M(\tilde{\nu})] \\ \cos[\alpha_M(\tilde{\nu})] \\ 0 \\ \frac{\ln(10)}{2} \Delta A + \sin[\alpha_M(\tilde{\nu})] \end{pmatrix} = \begin{pmatrix} I_{total} \\ I_0 - I_{90} \\ I_{45} - I_{135} \\ I_{RC} - I_{LC} \end{pmatrix}$$

At the detector, we only see the total intensity I_{total}:

alternates between -1 and +1!

$$I_D(\tilde{\nu}) = I_{DC}(\tilde{\nu}) + I_{AC}(\tilde{\nu}) = \overbrace{\frac{I(\tilde{\nu}) \cdot 10^{-A(\tilde{\nu})}}{2}}^{\boldsymbol{I_{DC}(\tilde{\nu})}} \underbrace{(1 + 1.1513 \Delta A \cdot \sin[\alpha_M(\tilde{\nu})])}_{\boldsymbol{I_{AC}(\tilde{\nu})}}$$

The absorbance spectrum simply follows from

$$A(\tilde{\nu}) = -\log_{10}\left(\frac{2 I_{DC}(\tilde{\nu})}{I_0(\tilde{\nu})}\right)$$

Experimental scheme FT-VCD: Stokes-analysis

Want more?: L . A. Nafie, Vibrational Optical Activity – Principles and Applications, Wiley 2011

The double-modulated term

$$I_{AC}(\tilde{\nu}) = \frac{I(\tilde{\nu}) \cdot 10^{-A(\tilde{\nu})}}{2}(1.1513\Delta A \cdot \sin[\alpha_M(\tilde{\nu})])$$

$$\sin[\alpha_M(\tilde{\nu})] = \sin[\alpha_M^0(\tilde{\nu})\sin(\omega_M t)]$$
$$= 2J_1[\alpha_M^0(\tilde{\nu})]\sin[\omega_M t]$$

can be expressed using odd-order Bessel functions and evaluated at ω_M as

$$I_{AC}(\tilde{\nu}) = \frac{I(\tilde{\nu}) \cdot 10^{-A(\tilde{\nu})}}{2}(1.1513\Delta A \cdot 2J_1[\alpha_M^0(\tilde{\nu})])$$

The final VCD spectrum can be obtained as

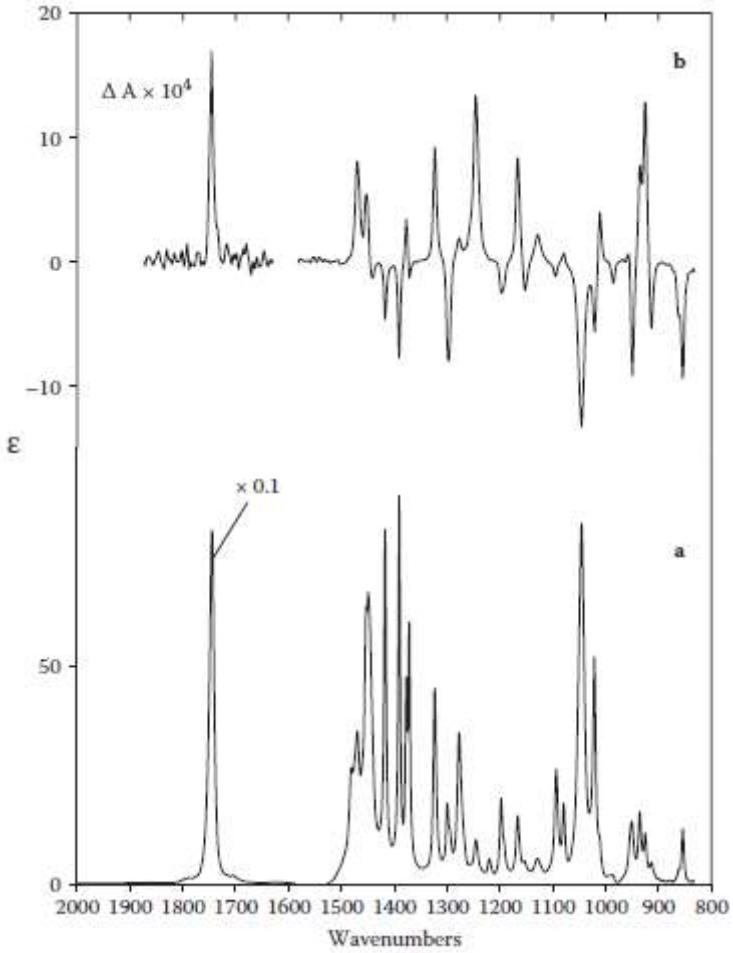
$$\Delta A(\tilde{\nu}) = \frac{1}{1.1513 \cdot 2J_1[\alpha_M^0(\tilde{\nu})]}\left(\frac{\mathrm{I_{AC}}(\tilde{\nu})}{\mathrm{I_{DC}}(\tilde{\nu})}\right)$$

Pre-factor is determined by instrument calibration!

A typical VCD spectrum

P. J. Stephens, VCD Spectr. for Organic Chemistry, CRC Press, 2012

IR (a) and VCD (b) of (+)-camphor



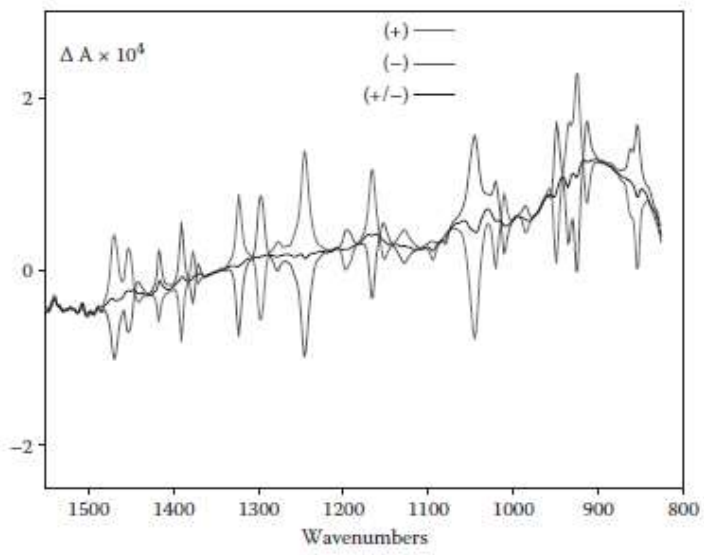
Every band in the IR spectrum will feature a corresponding VCD band

Huge intensity in IR does not necessarily mean large VCD band

- Relative intensities in IR and VCD do not correlate

Experimental considerations

P. J. Stephens, VCD Spectr. for Organic Chemistry, CRC Press, 2012



Baseline is most critical and never really straight

- Correction by subtraction of racemic sample measurement (ideal) or solvent spectrum
- Using second PEM can provide better baseline

All limitations of transmission IR spectroscopy apply:

- solvents: ideally deuterated, few IR bands such as CD_2Cl_2 / $CDCl_3$ / CCl_4, CD_3CN, DMSO-d_6, benzene-d_6
- Concentrations: 0.05 - 2 molar

  … depending on path length (15-200 µm)

  … and the IR absorbance of the molecule

Theory of VCD

rotational strength of transition n←0

$$R_{n0} = Im\{\boldsymbol{\mu_{0n}} \cdot \boldsymbol{m_{n0}}\}$$

edtm $\langle \psi_{n0} | \hat{\mu} | \psi_{n0} \rangle$

mdtm $\langle \psi_{0n} | \widehat{m} | \psi_{n0} \rangle$

For ECD: $\Psi_{g0} \rightarrow \Psi_{en}$ Excitation from electronic groundstate to electronically excited state

For VCD: $\Psi_{g0} \rightarrow \Psi_{g1}$ Excitation from vibrational groundstate to vibrationally excited state of the electronic groundstate

Theory of VCD

Born-Oppenheimer approximation:

- Cores much slower than electrons, i.e. movements happen on very different time scales
- ➢ Electron movement does not influence vibrations
- ➢ Separation of wavefunction into electronic and vibrational part: $\Psi(\vec{r},\vec{R}) = \psi(\vec{r},\vec{R})\phi(\vec{R})$

Consequences of BO approximation?

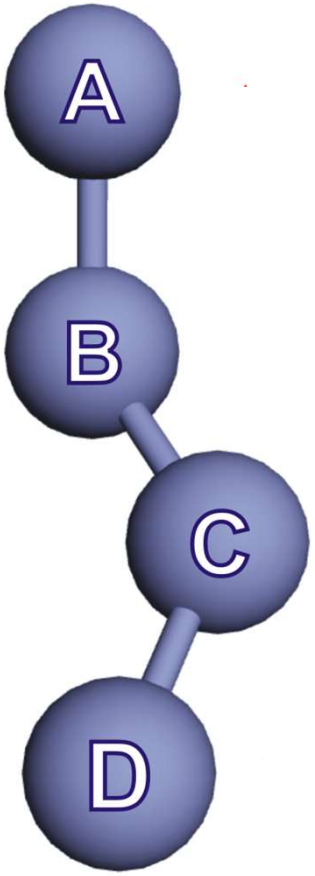
If movement of the cores does not influence any electrons, the electron density of *g0* and *g1*, the vibrational groundstate and first excited state, does not change!

In BO approximation:

$$\langle \phi_{0g} | \hat{m} | \phi_{g0} \rangle = 0$$

Circumventing the limitations of BO: Partial charge models

Here: Electronic ring current model
Nafie and Freedman, *J. Mol. Struc.* **224** (1990) 121-132

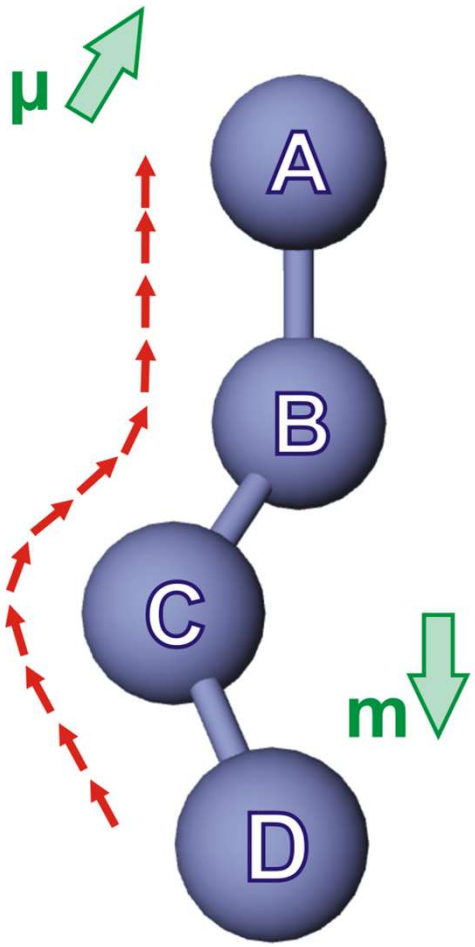


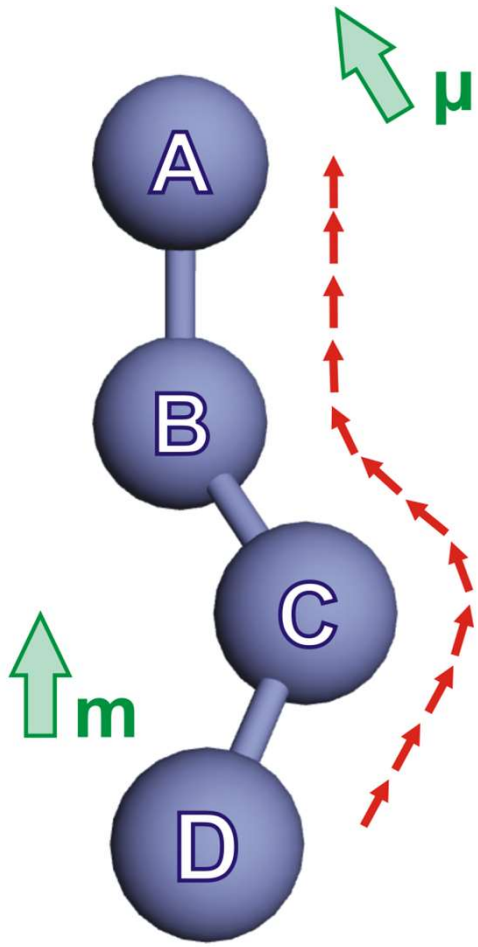
Rotational strength (= VCD intensity)

$$R = \mathrm{Im}[\langle 0|\boldsymbol{\mu}|1\rangle\langle 1|\boldsymbol{m}|0\rangle] = |\mu| \cdot |m| \cdot \cos\xi$$

$\angle(\mu, m) > 0 \;\Rightarrow$ positive VCD

Circumventing the limitations of BO: Partial charge models





$\angle(\mu, m) < 0 \;\Rightarrow$ negative VCD

$\angle(\mu, m) > 0 \;\Rightarrow$ positive VCD

Circumventing the limitations of BO

Vibronic coupling theory (VCT)

by Freedman and Nafie, *J. Chem. Phys.* **78** (1983) 7108

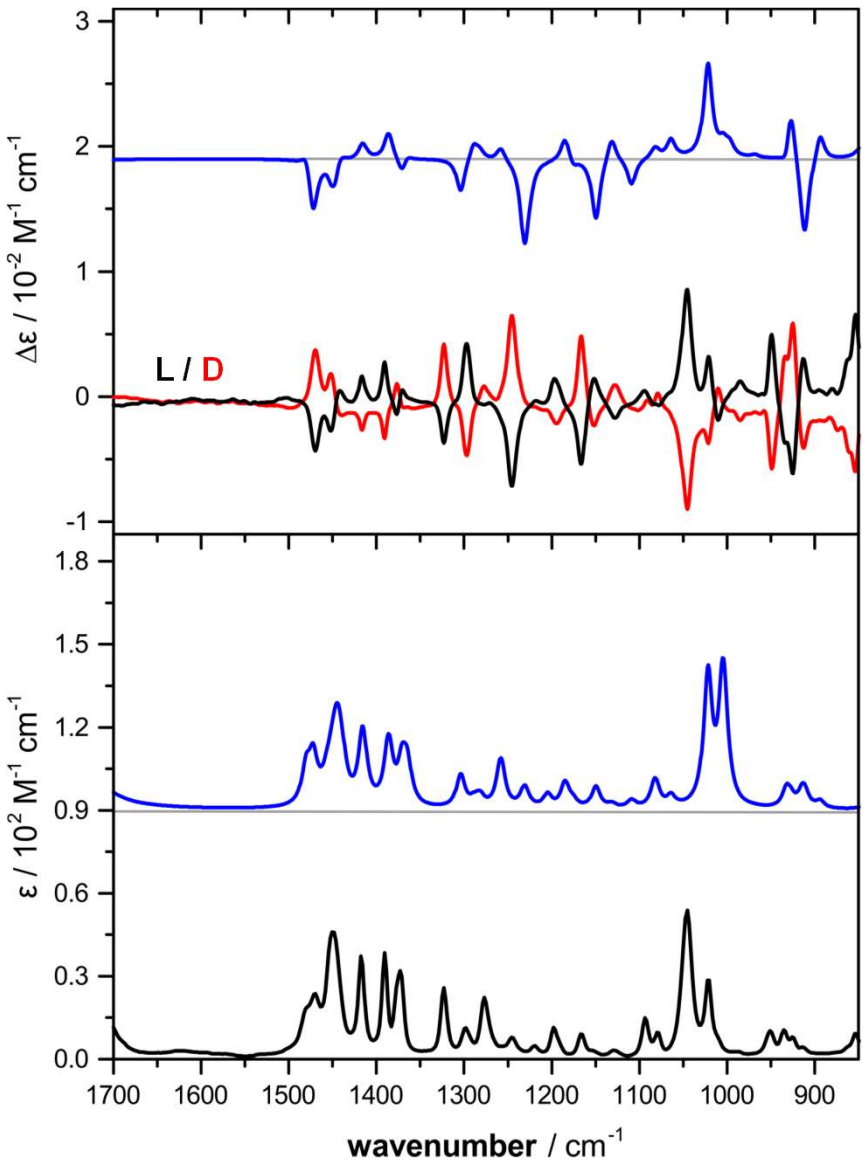
- ➢ Includes terms which take into account movement of electrons
- Pro: First ab initio theory for VCD
- Con: Knowledge (read: calculation) of electronic states necessary

Magnetic field perturbation theory (MPT)

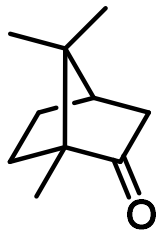
by Stephens, *J. Phys. Chem.* **89** (1985) 748-752

- ➢ Taking into account the electron movement by perturbation theoretical considerations
- Pro: Easy to implement in computer code, available in Gaussian since 1994

Comparison experiment and theory



VCD spectra of L- and D-camphor show good mirror image quality



Calculation yields dipole strength and rotational strength as line spectra

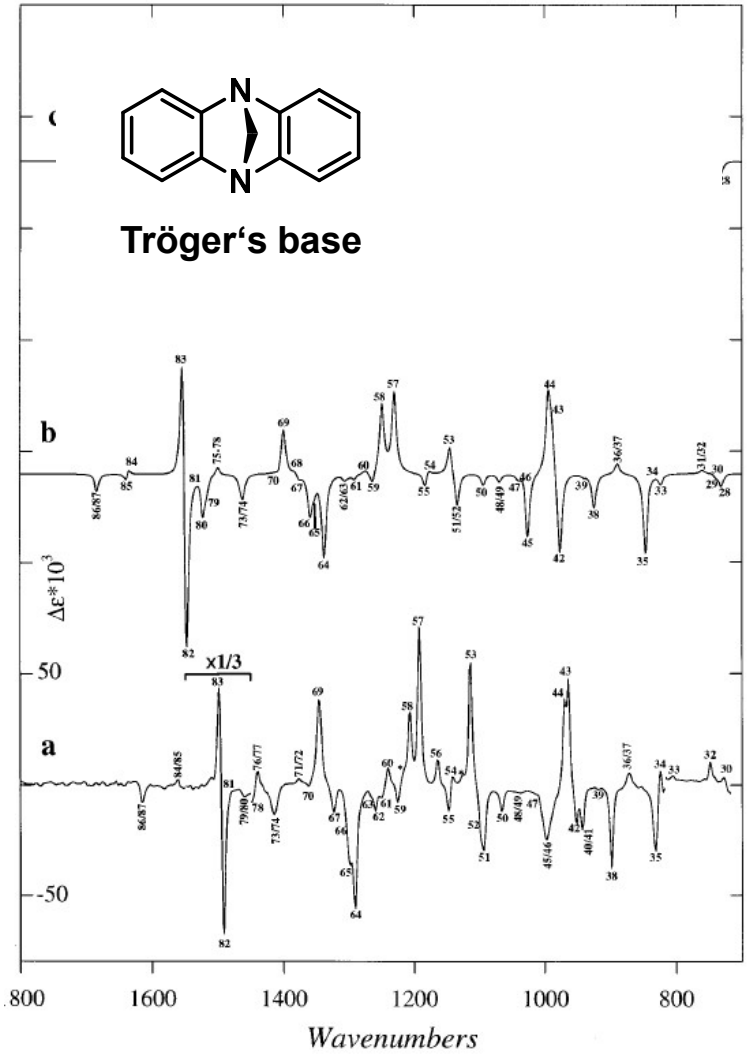
- Pair of frequency and intensity

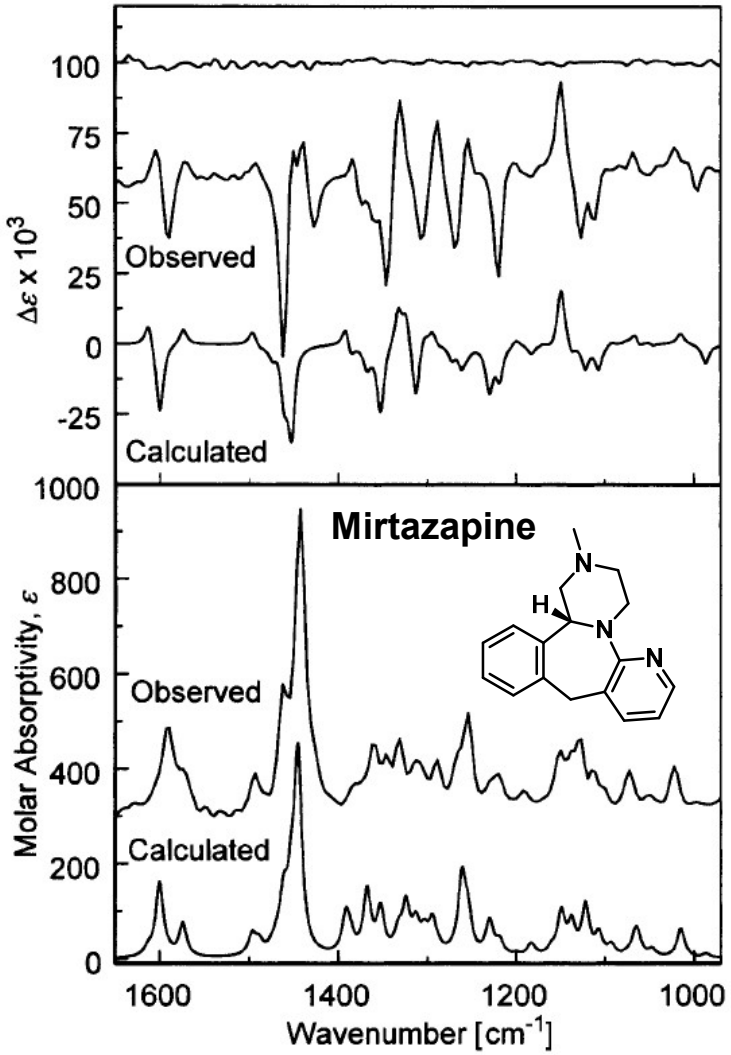
Assignment of Lorentzian band shape to simulate spectrum (typical 6 cm^{-1} HWHH)

Typically, calculated frequencies need to be scaled by 0.985-0.95 to account for incorrections due to harmonic approximations.

Some other simple (=rigid) examples

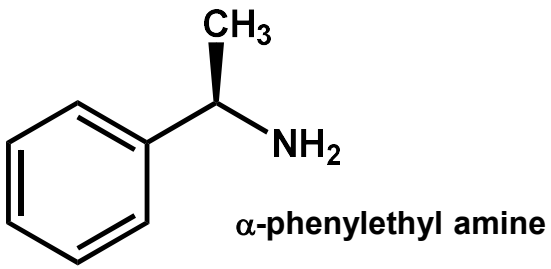
A. Aamouche, F. J. Devlin, P. J. Stephens, *J. Am. Chem. Soc.* **2000**, *122*, 2346-2354
T. B. Freedman, et al., *Helv. Chim. Acta* **2002**, *85*, 1160



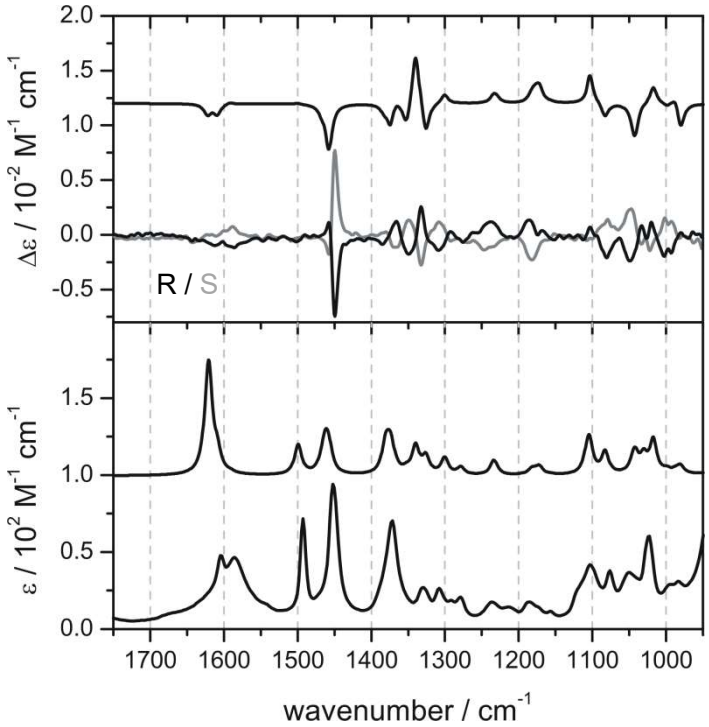


Taking into account conformational preferences

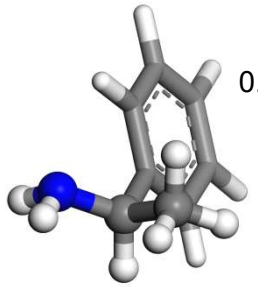
C. Merten, M. Amkreutz, A. Hartwig. *Chirality* **22** (2010) 754-761



α-phenylethyl amine

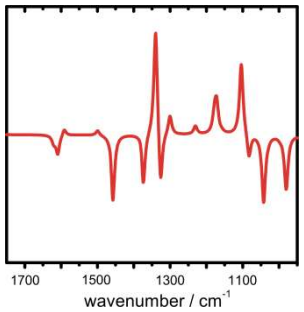


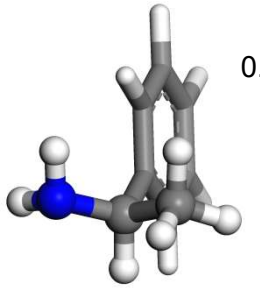
Theo: B3LYP / aug-cc-pVTZ, gas phase, 4 cm^{-1} HWHH
Exp.: 3M in $CDCl_3$, 25 µm pathlength



0.0 kcal/mol

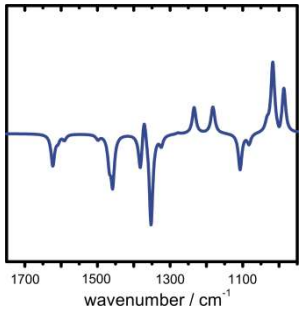
64 %

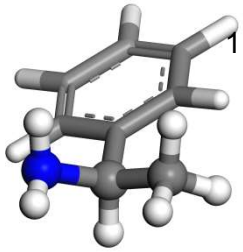




0.4 kcal/mol

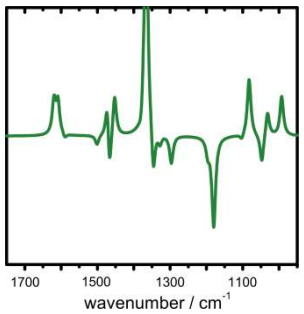
33 %





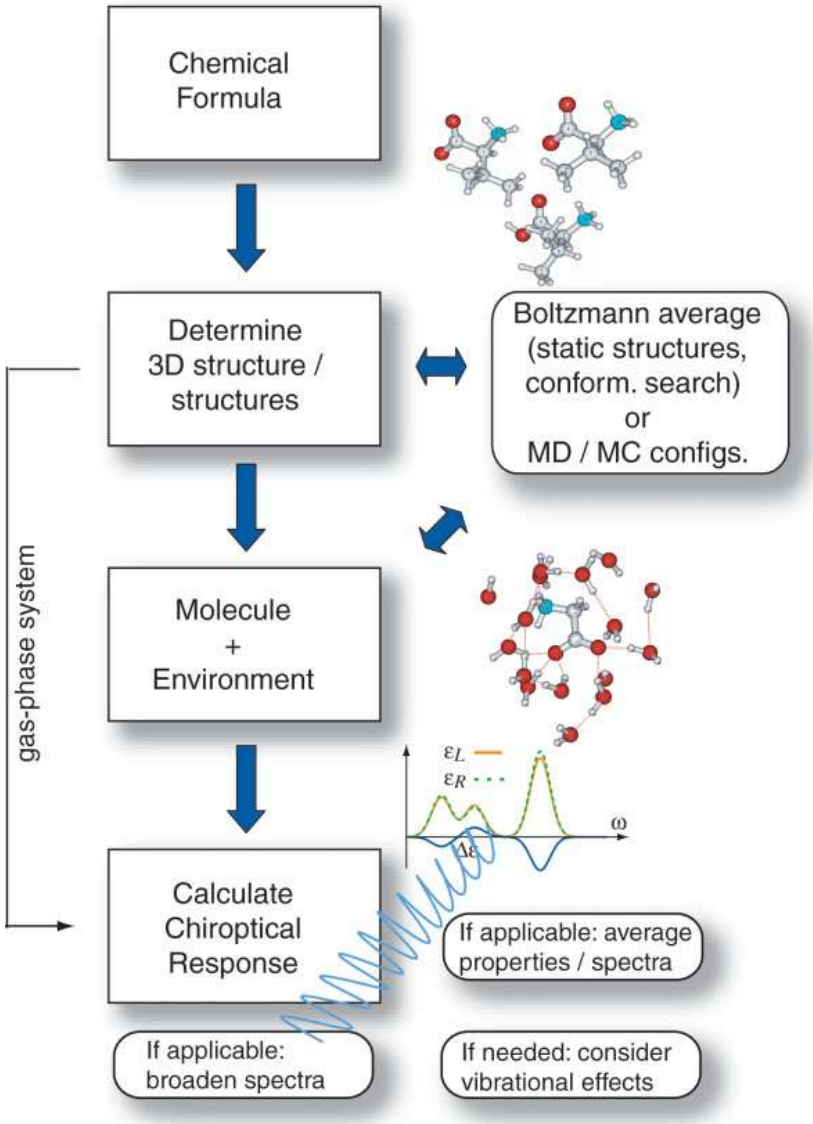
1.9 kcal/mol

3 %



Computing VCD spectra

J. Autschbach, *Chirality* **21** (2009) E116-E152
G. Pescitelli, T. Bruhn, *Chirality* **28** (2016) 466–474



If the molecules can adopt many different conformations, their individual spectra need to be averaged using Boltzmann statistics:

$$p = \frac{e^{-kT\Delta E_n}}{\sum_n e^{-kT\Delta E_n}}$$

Important:

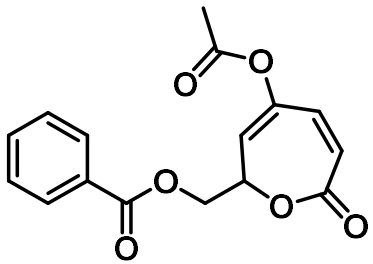
Getting good single conformer energies ΔE!

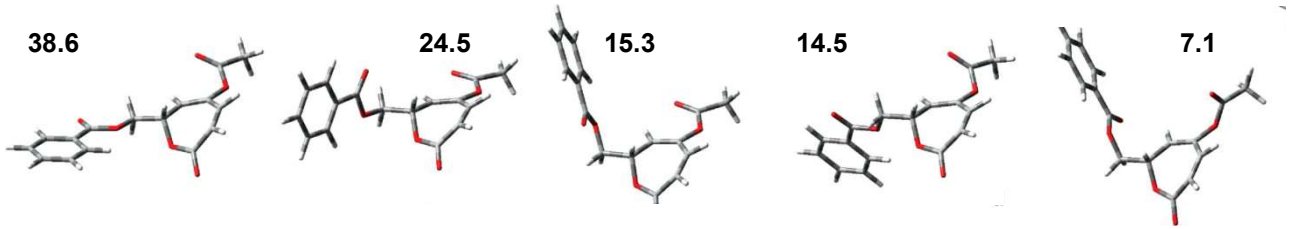
Note:

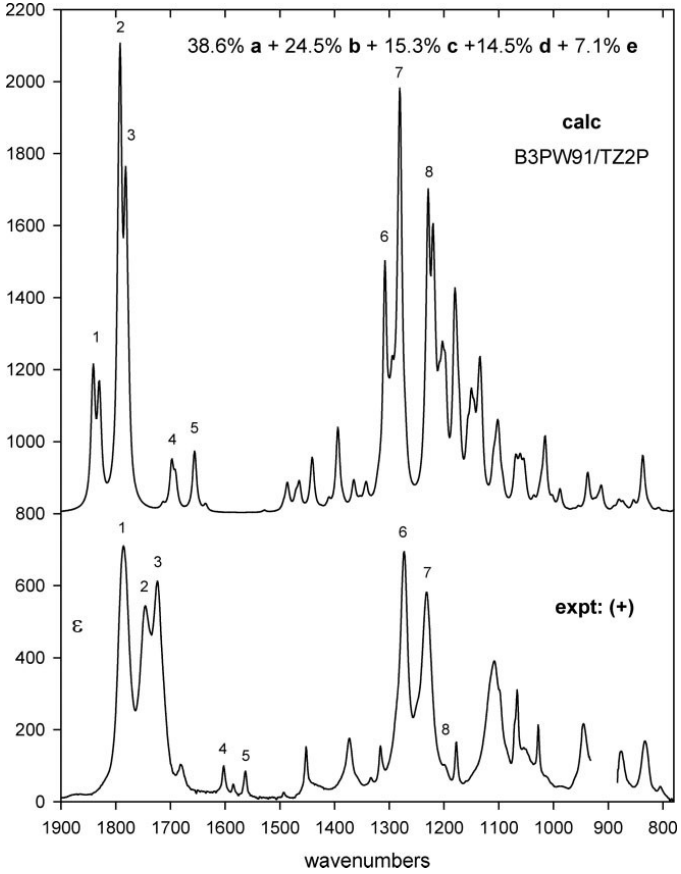
Computed excitation energies often too high, therefore energy axis often empirically scaled to allow better comparison!

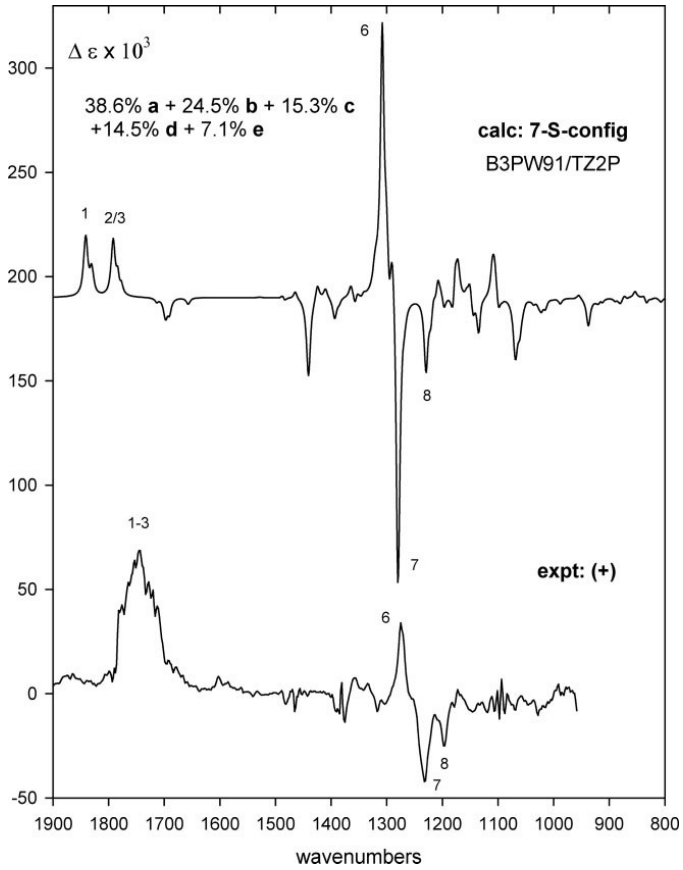
Typical AC-determination

Devlin et al., *Chirality* **21** (2009) S48–S53





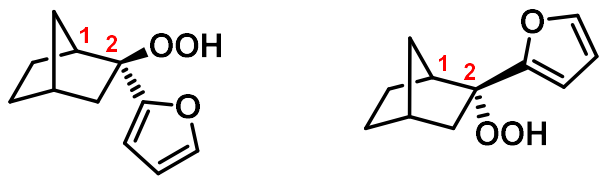


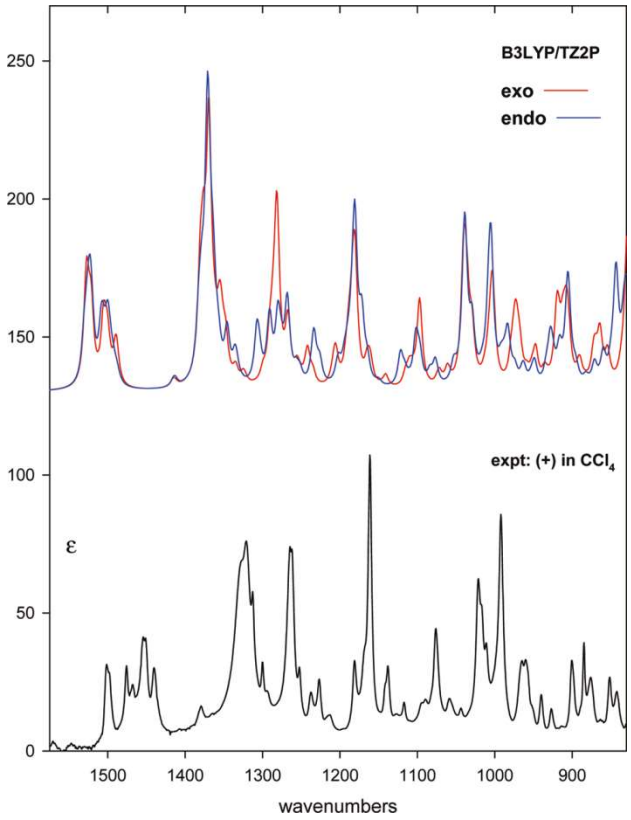


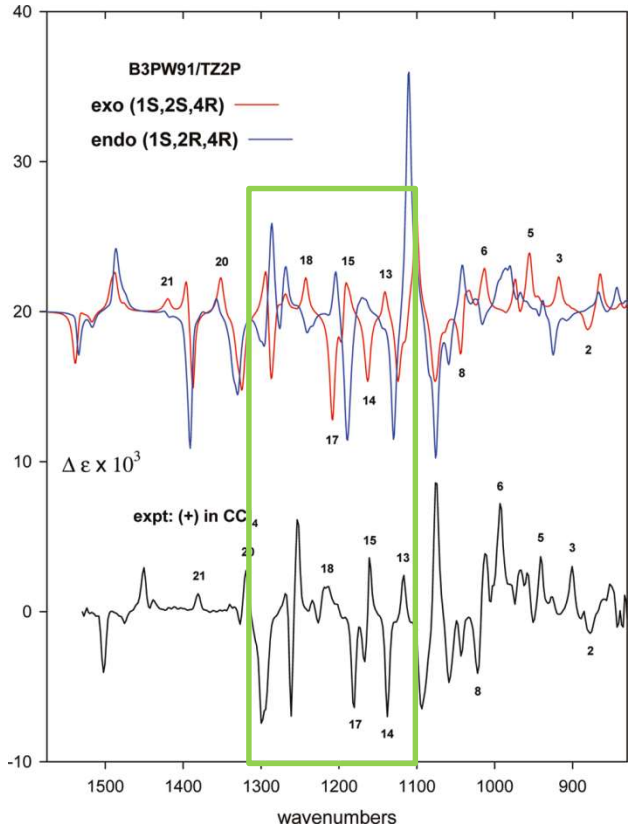
Distinguishing diastereomers

Lattanzi, *J. Org. Chem.* 2010, **75**, 2179–2188

Diastereomers can often be distinguished using VCD, as at least some of the spectral features show mirror image relationsship between them





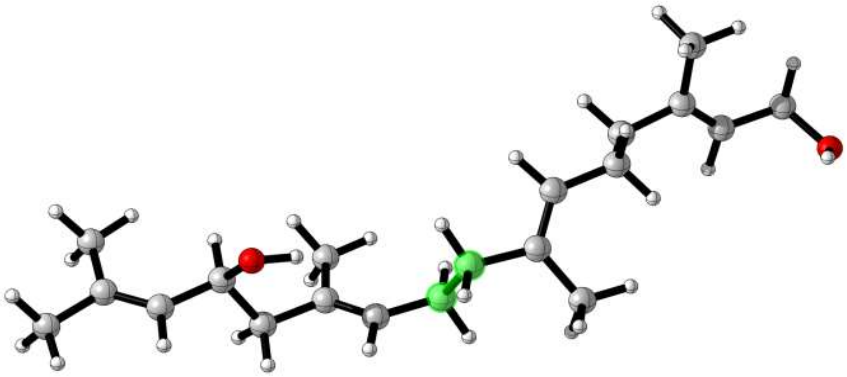


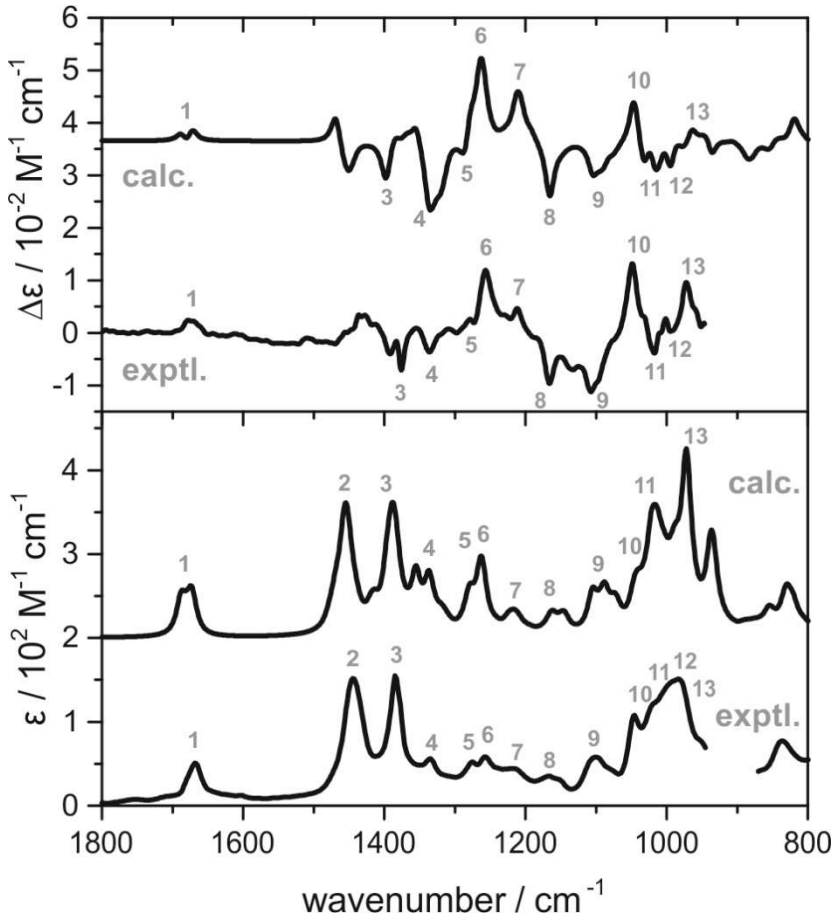
Quite challenging: linear diterpenes

C. Merten et al., *Chem Comm.*, **51** (2015) 16217-16220

Challenges:

- Oily substance which does not crystallize
- Highly unfunctionalized
- Only small amounts
- Highly flexible (>1000 conformers)

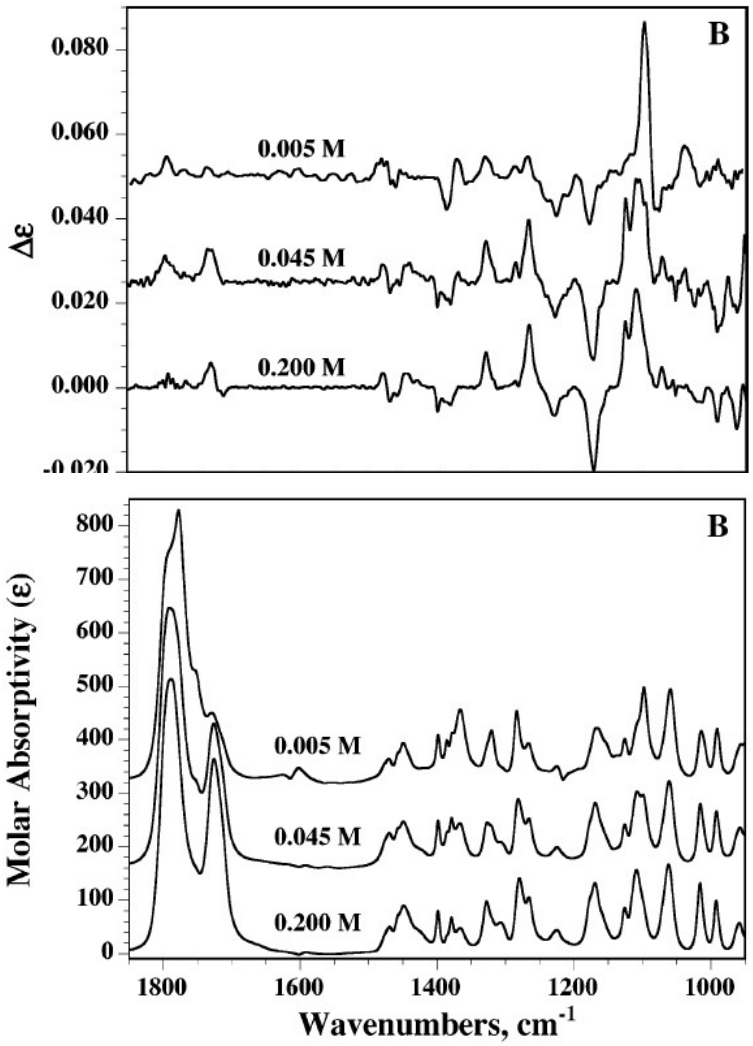


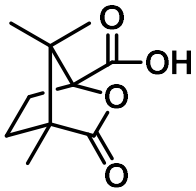


0.5 M in CDCl3 // B3LYP/6-311++G(2d,p)/scrf(chloroform)

Concentration dependence

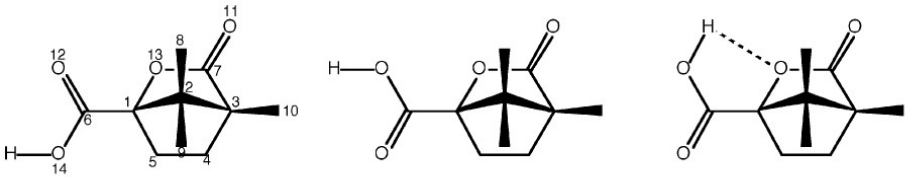
Buffeteau et al., *J. Phys. Chem. A* **2007**, *111*, 1045-1051





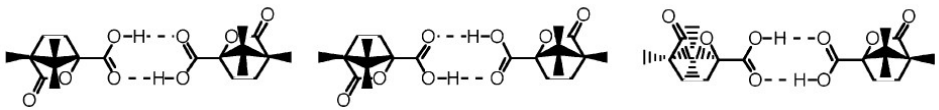
Camphanic acid

Monomers



1a **1b** **1c**

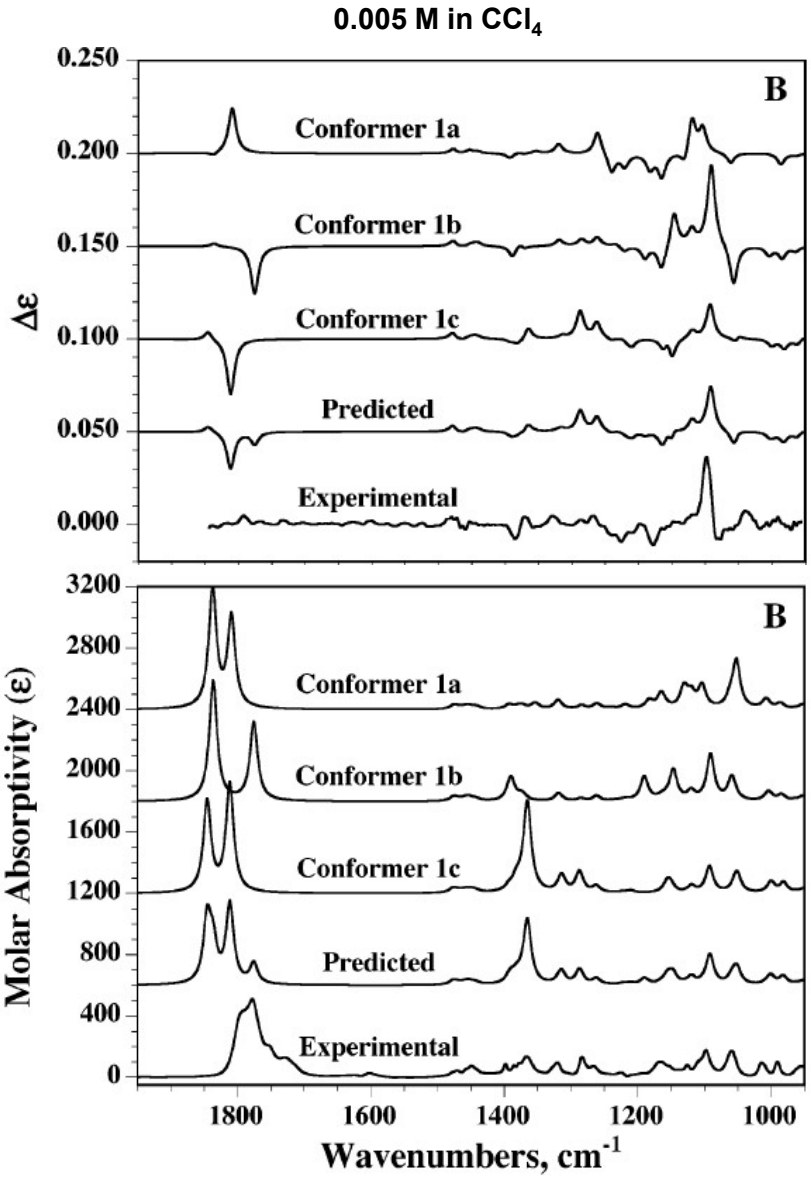
Dimers

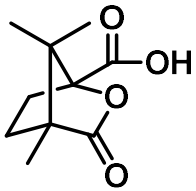


1aa **1bb** **1ab**

Concentration dependence

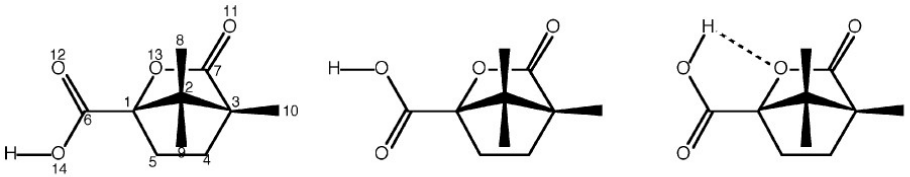
Buffeteau et al., *J. Phys. Chem. A* **2007**, *111*, 1045-1051





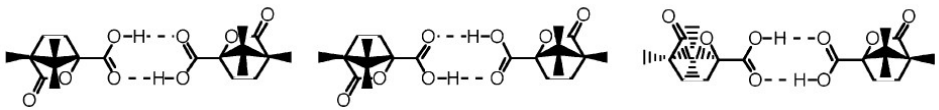
Camphanic acid

Monomers



1a **1b** **1c**

Dimers

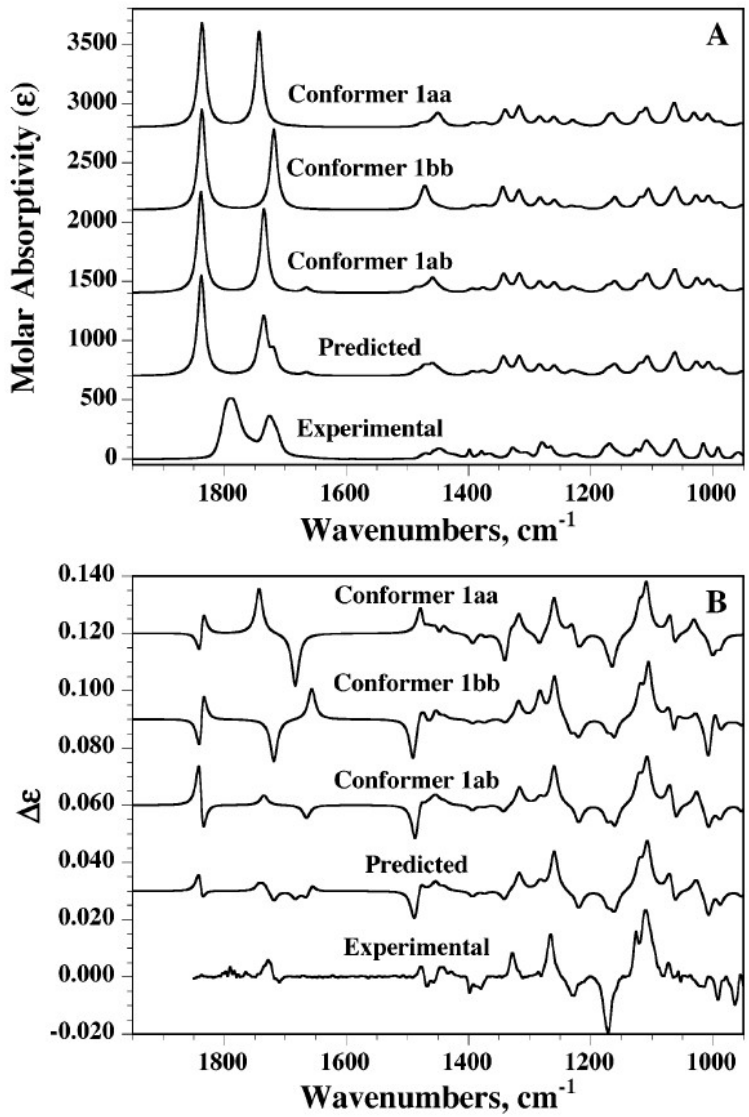


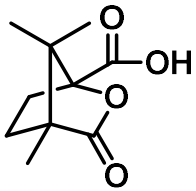
1aa **1bb** **1ab**

Concentration dependence

Buffeteau et al., *J. Phys. Chem. A* **2007**, *111*, 1045-1051

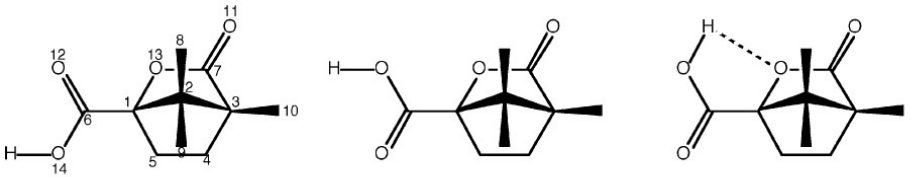
0.2 M in CCl_4





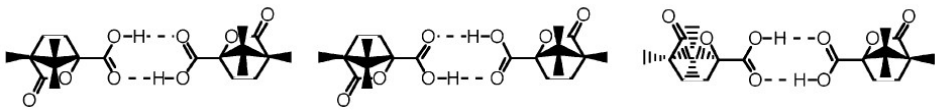
Camphanic acid

Monomers



1a **1b** **1c**

Dimers



1aa **1bb** **1ab**

Outline of the lecture

	Dates	topics	
✓	Monday	Introduction	
✓		Polarization of light	
✓	Tuesday	Theoretical basis of optical activity	
✓		Optical rotation	
✓	Wednesday	Circular dichroism	
✓		Circular dichroism	
✓	Thursday	Vibrational optical activity	
		Vibrational optical activity	
	Oct 22?	applications	your part
	Oct 29?	applications	your part