Chiroptical Spectroscopy

Theory and Applications in Organic Chemistry

Lecture 4: Measurement of optical rotation

Masters Level Class (181 041)

Block course, october 2020

Rosenfeld equation and rotational strength

The Rosenfeld equation

$$\Delta\theta = \frac{\mathcal{N} l \mu_v}{3\hbar} \sum_{n \neq 0} \frac{\omega^2 R_{n0}}{\omega_{n0}^2 - \omega^2}$$

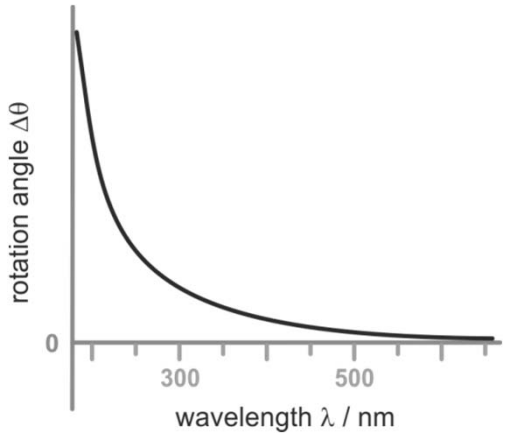
$\omega = 2\pi f$

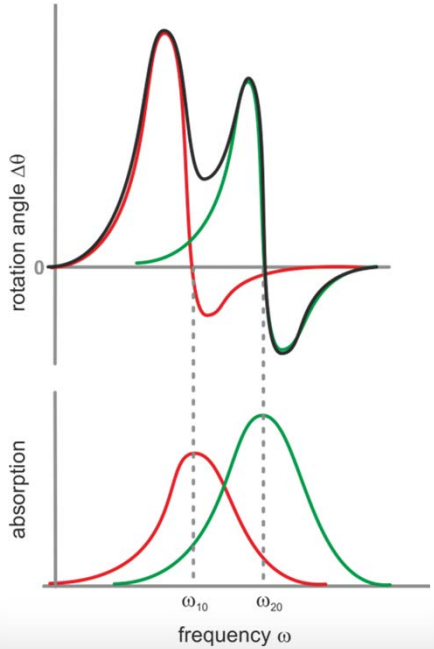
$\omega_{n0} = (E_n - E_0)/\hbar$

rotational strength of transition n←0

$$R_{n0} = Im\{\boldsymbol{\mu}_{\mathbf{0n}} \cdot \boldsymbol{m}_{\mathbf{n0}}\}$$

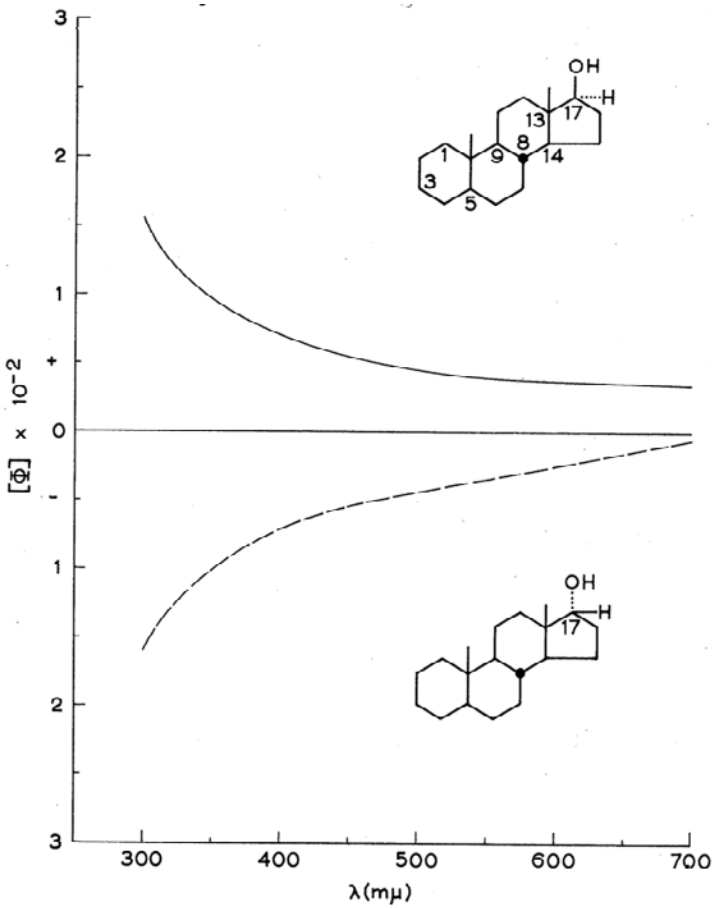
μ: electric dipole transition moment (EDTM)
m: magnetic dipole transition moment (MDTM)



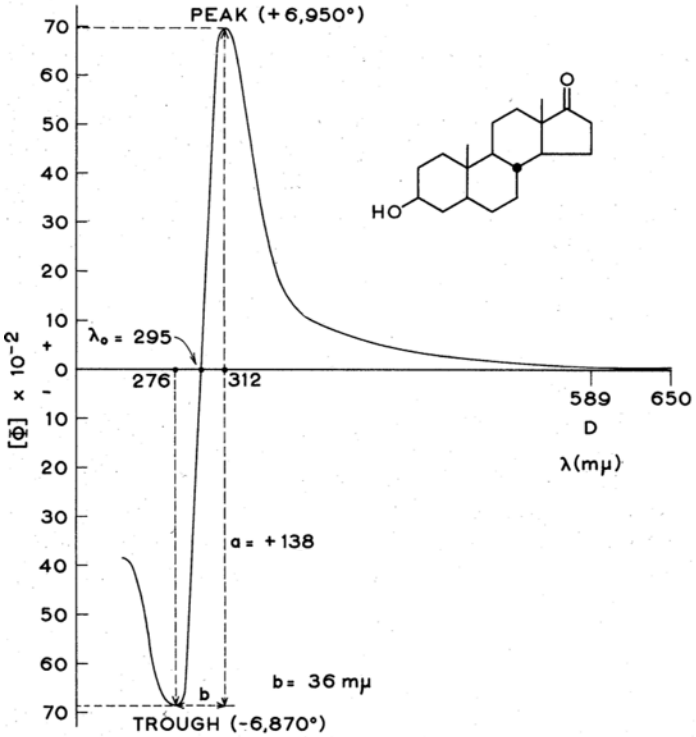


Examples for ORD curves

Normal curves / dispersion curves



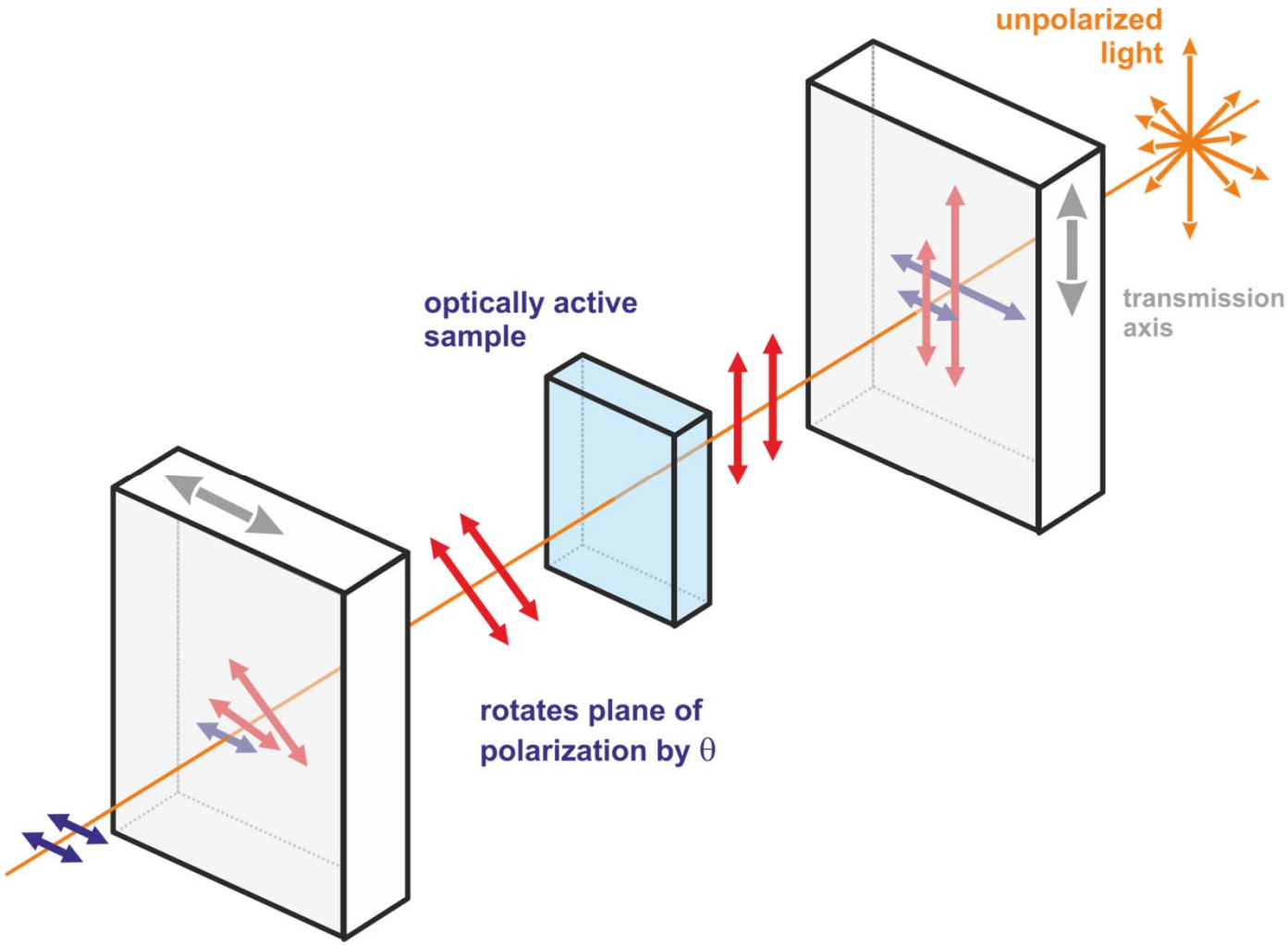
Anomaleous ORD curve



Here: Positive Cotton effect due to contribution of n→π* absorption band of carbonyl group

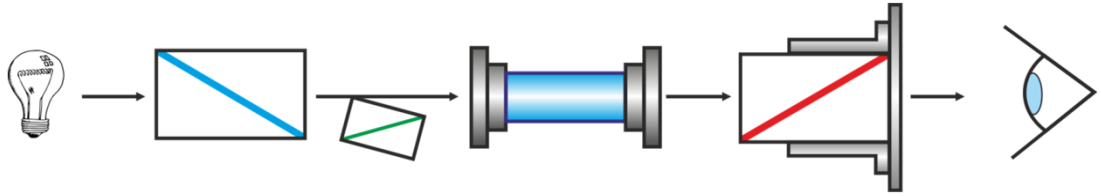
P. Crabbé, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry*, Holden-Day Publ., San Francisco, 1965

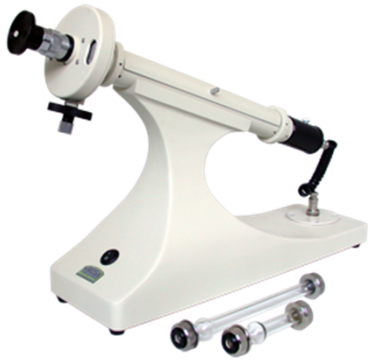
Crossed polarizers and optically active sample



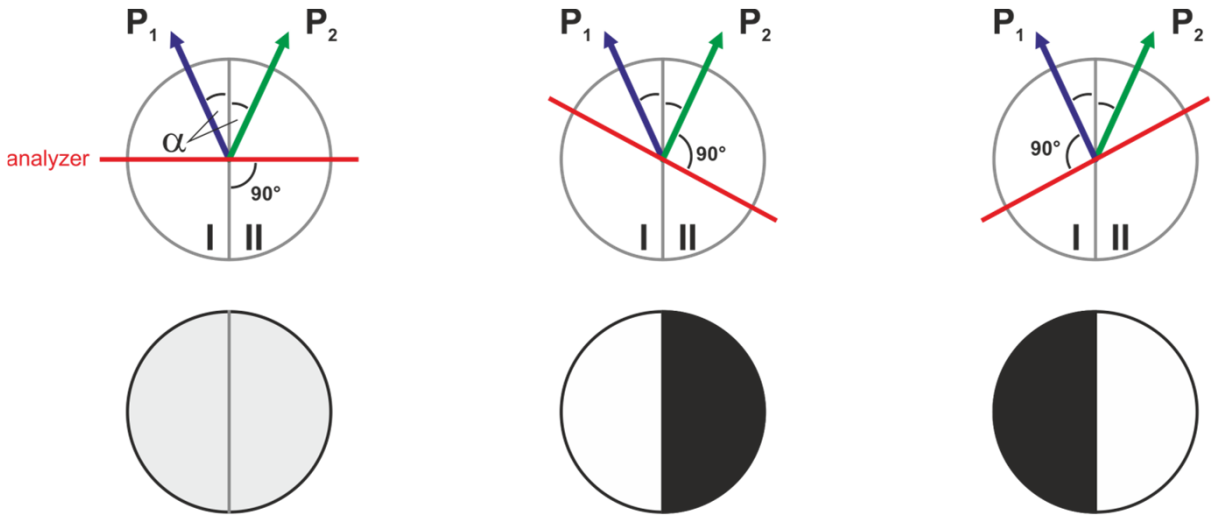
Manual polarimeter: Half-shadow devices

Lippich polarimeter





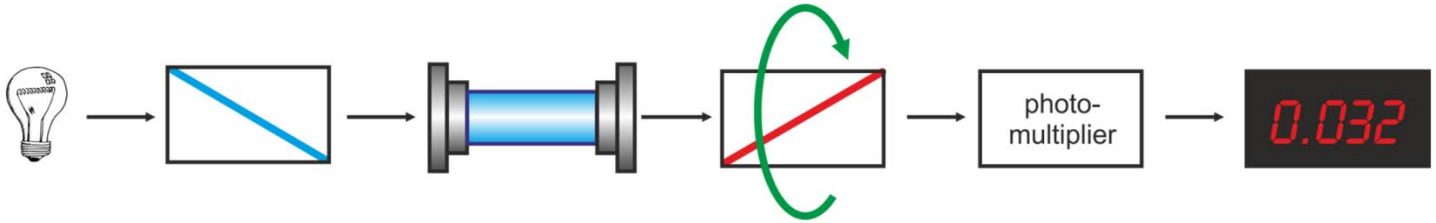
Source: Krüss Optronic Germany



Analyzer perpendicular to bisector of 2α:
Both half fields bright

Analyzer perpendicular to one of the two polarization planes:
One field max bright, one field max dark

Automatic measurement of OR



Up-to-date polarimeters

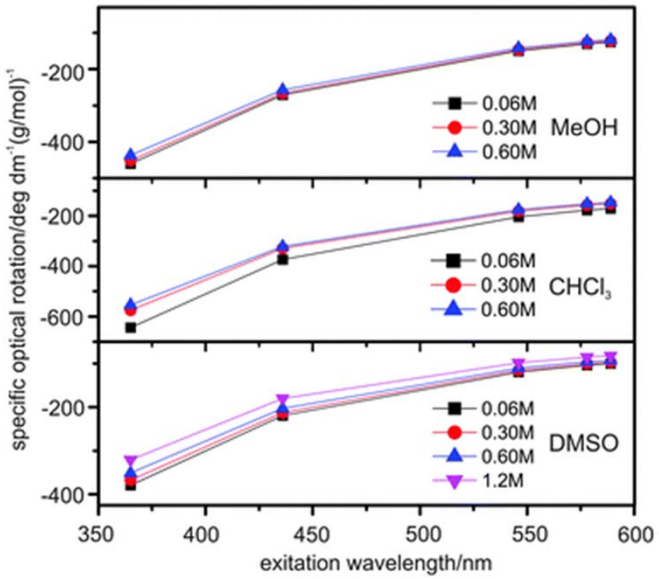
- Use LED technology
- <1s measurement time
- Range ±90°
- Accuracy 0.003°
- Reproducability 0.002°

Obviously, a not so up-to-date polarimeter

Measurement of ORD

The not-so-comfy way:

Polarimeter with Hg-lamp and filters



Chiroptical properties of methyl mandelate
Xu et al. PCCP **15** (2013) 1655-1665

The comfy way (todays alternative):

It‘s simply built in to CD spectrometers

Specific rotation

Measured value: α (old Φ)

Specific rotation $[\alpha] = {}^{\alpha}/_{l \cdot c}$

Optical rotation $[\alpha]$ depends on

- wavelength (ORD)
- concentration
- solvent
- temperature

$$[\alpha]_{\lambda}^{T}\ (c, solvent)$$

unit of concentration

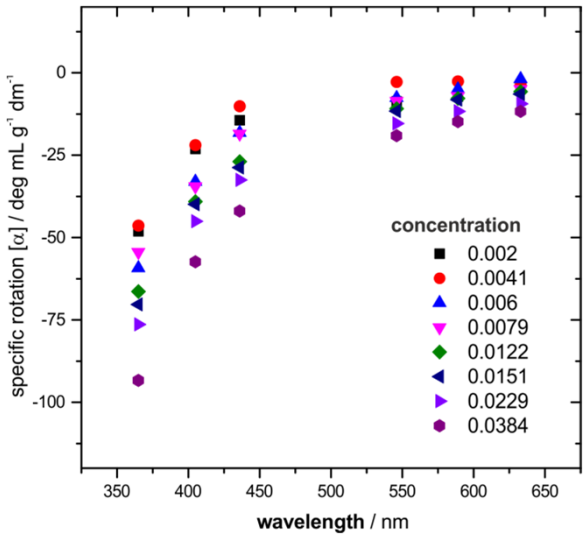
1g in 100 ml solvent
➢ c=1.0

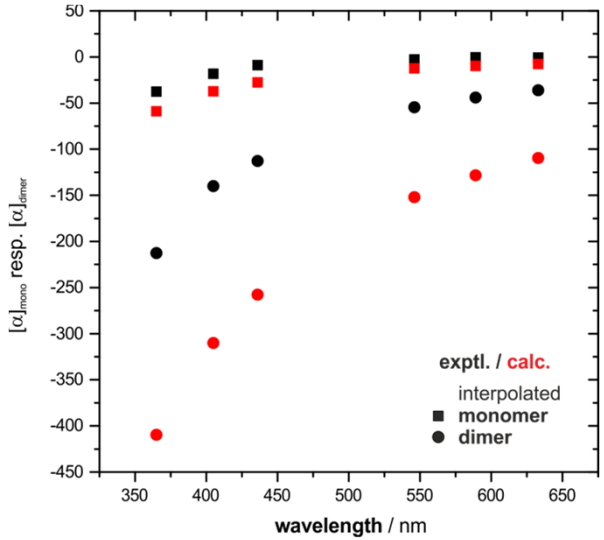
Typical notation: $[\alpha]_{D}^{25} = +28\ (c = 2.1, \mathrm{H_2O})$

$[\alpha]_{589nm}^{298} = -123\ (c = 4.0, \mathrm{CHCl_3})$

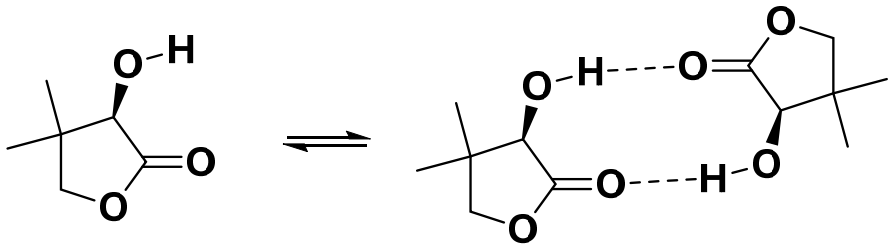
Concentration dependence of OR

Polavarapu and Covington, *Phys.Chem.Chem.Phys.* **17** (2015) 21630-21633





- Concentration dependence of ORD for α-hydroxy-β, β-dimethyl-γ-butyrolactone investigated by Polavarapu

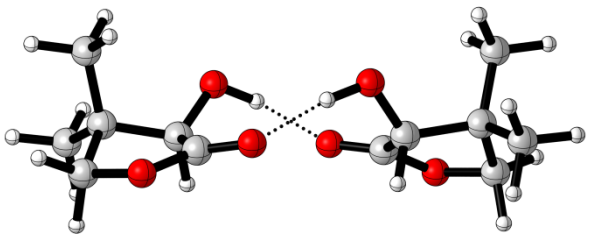


- Equilibrium can be described as

$$2M \rightleftharpoons D \implies K = c_D / c_M^2$$

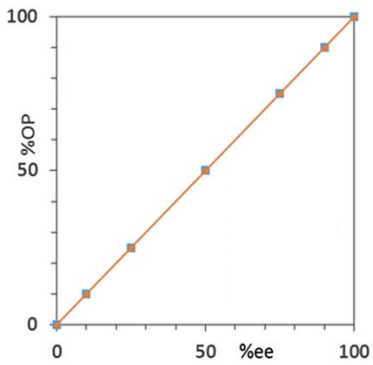
- Interpolation to 100% monomer and 100% dimer
- DFT-based calculations confirm the trend

(CAM-B3LYP/aug-cc-PVTZ)

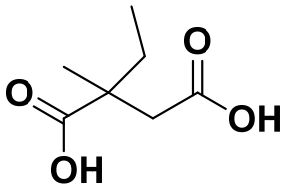


The Horeau effect

Horeau, *Tetrahedron Lett* **10** (1969) 3121-3124
Covington and Polavarapu, *Chirality* **28** (2016) 181-185



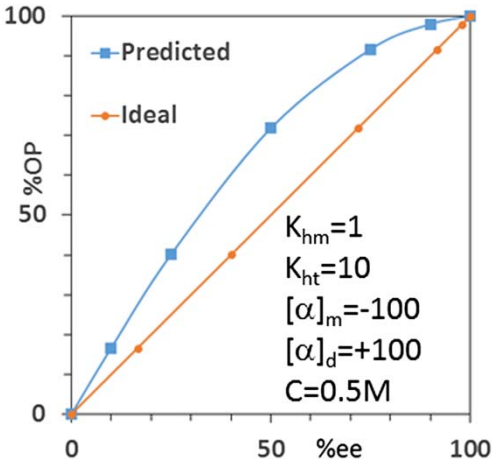
A linear correlation between SOR and the enantiomeric excess of a sample would be expected.



Horeau 1969:

OR does not reflect optical purity the succinic acid derivative

→ homo- and heterochiral dimerization possible!



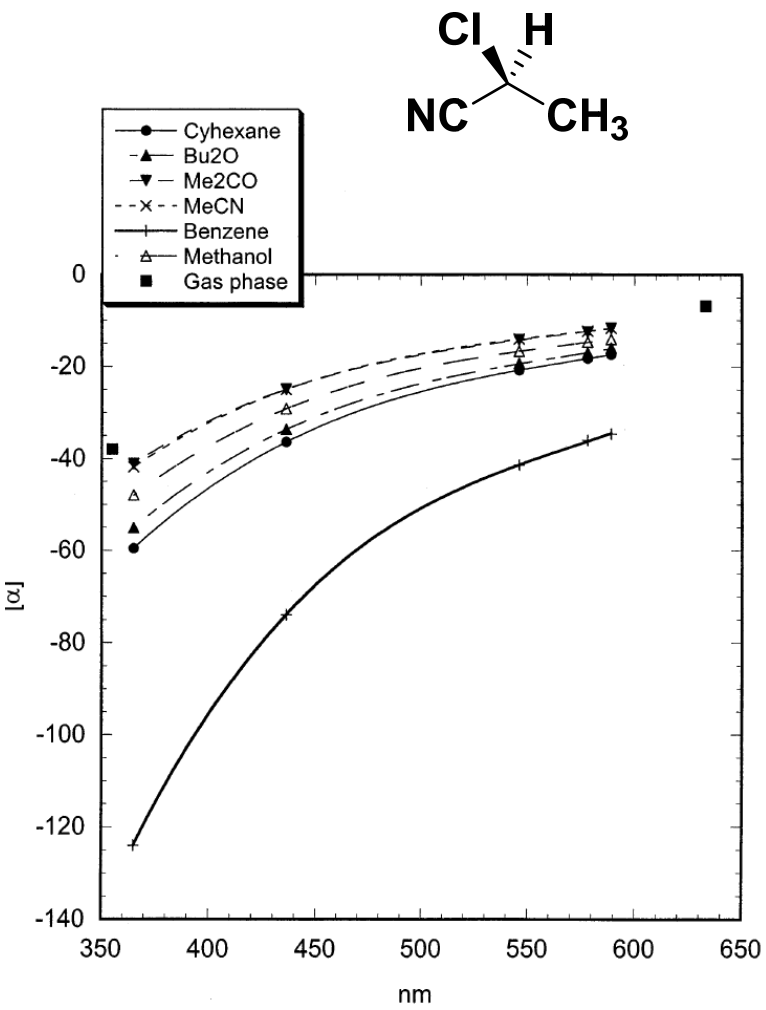
Considering simple equilibrium constants, it can be shown that Horeau effect cannot be observed if either

a) $K_{heterodimer} = 2\ K_{homodimer}$

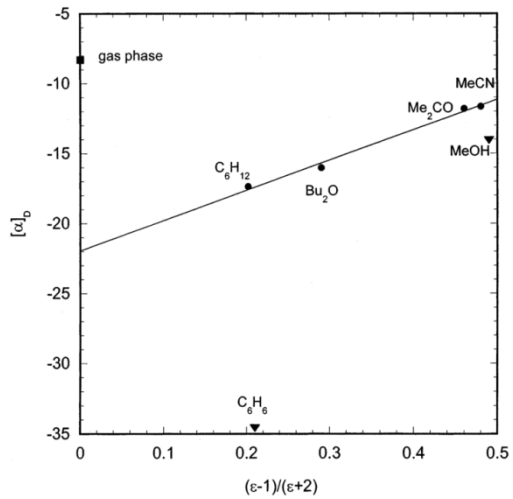
b) $SOR_{monomer} = SOR_{dimer}$

Solvent dependence of ORD

Wiberg et al. *J. Phys. Chem. A* **109** (2005) 3448-3453



- For most solvents, OR correlates approx. linearly with Onsager function $\frac{\varepsilon-1}{2\varepsilon-1}$



- Extrapolation to gas phase is not in agreement with experimental value
- Benzene: no dipole moment but large polarizability and quadrupole moments
  - ➢ Contribution larger than expected

Solvent dependence of ORD

Menger and Boyer, *J.* Org. Chem. **49** (1984) 1826-1828

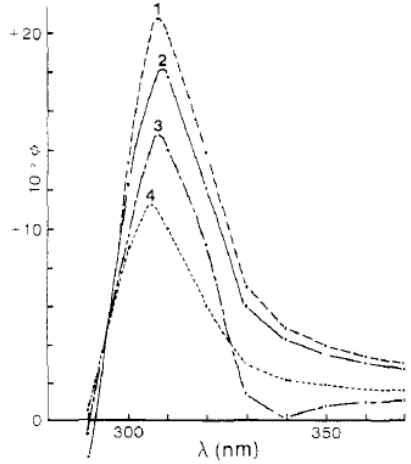


Figure 1. ORD spectra for (from top to bottom) dimethyl sulfoxide, acetonitrile, benzene, and methanol.

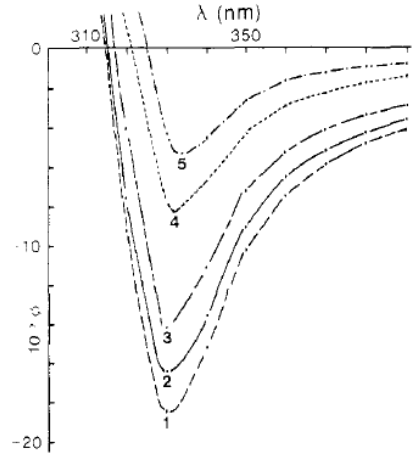
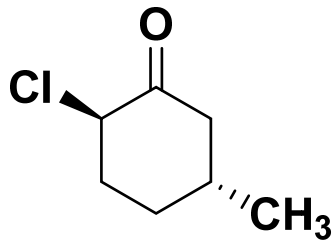


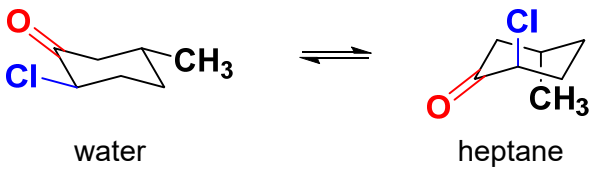
Figure 2. ORD spectra for (from bottom to top) cyclohexane, *n*-octane, carbon tetrachloride, *n*-butyl ether, and ethyl ether.

[α] at 330 nm

+680°	in DMSO
+57°	in toluene
-1819°	in cyclohexane



- Shift of conformational equilibrium:

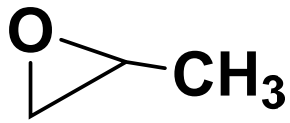


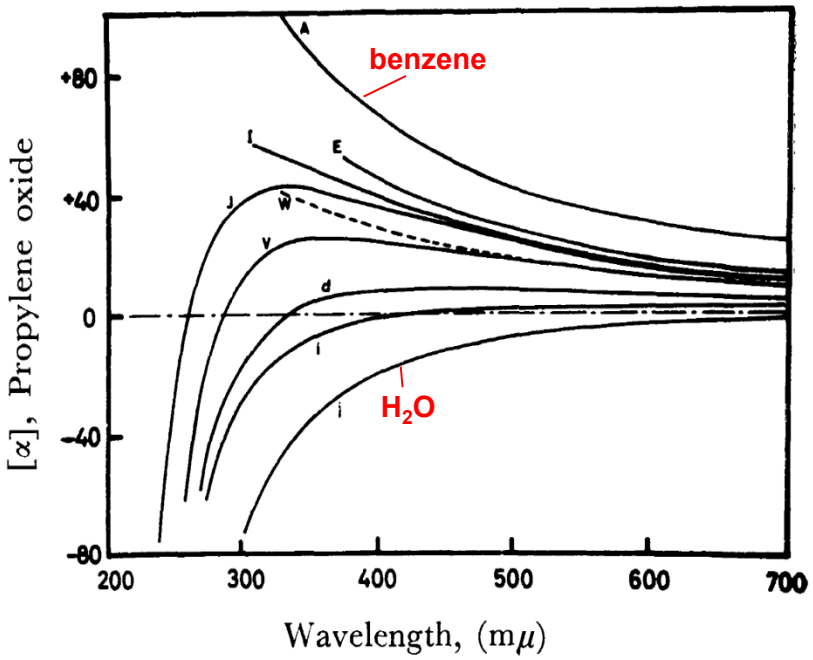
- Dipole moments less well solvate in heptane, thus they are trying to arrange as antiparallel as possible

ORD of propylene oxide

Table 1. Specific rotation of (R)-propylene oxide in various solvents

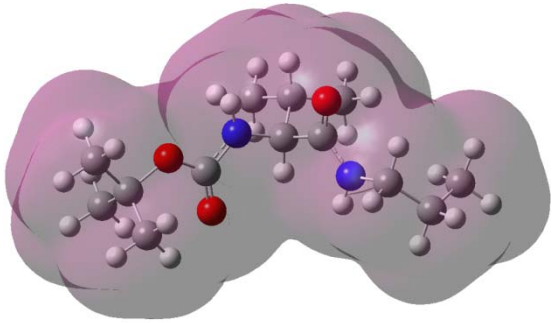
	Solvent	$[\alpha]_D$	$\frac{3[\alpha]_D}{n_D^2+2}$
A	Benzene	30.6	21.6
B	*N,N*-Dimethylaniline	29.0	19.6
C	Anisole	26.4	18.4
D	Tetrachloroethylene	20.1	14.1
E	Carbon disulfide	19.4	12.5
F	Chlorobenzene	19.4	13.5
G	Carbon tetrachloride	18.7	13.6
H	Hexamethylphosphoric triamide	18.4	13.4
I	Pyridine	18.1	12.7
J	*p*-Dioxane	18.0	13.4
K	*o*-Nitroanisole	17.7	12.0
L	Diethyl ether	17.0	13.3
M	Triethylamine	17.0	12.9
N	Nitrobenzene	16.4	11.2
O	Methylene iodide	15.6	9.3
P	*n*-Pentane	14.3	11.2
Q	*N*-Methylacetamide	14.1	10.5
R	Tetrahydrofuran	13.7	10.3
S	Ethyl acetate	13.1	10.1
T	*N,N*-Dimethylformamide	12.9	9.6
U	Dimethylsulfoxide	12.8	9.2
V	Cyclohexane	11.9	8.8
W	Aniline	11.9	7.9
X	Benzonitrile	9.4	6.5
Y	Chloroform	8.5	6.2
Z	Acetone	8.2	6.4
a	Ethanol	7.9	6.2
b	Cyclohexanone	7.9	5.8
d	Methanol	7.2	5.7
e	Acetonitrile	6.0	4.7
f	1,2-Dichloroethane	5.8	4.3
g	Methylene chloride	5.5	4.1
h	Nitromethane	5.0	3.8
i	Acetic acid	2.0	1.5
j	Water	−4.3	−3.4





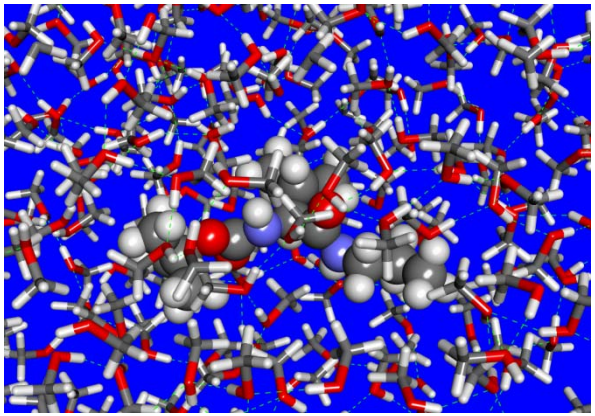
Kumata et al. *Bull. Chem. Soc. Jpn.* **43** (1970) 3920-3921

Detour: How to describe solvent effects in calculations?



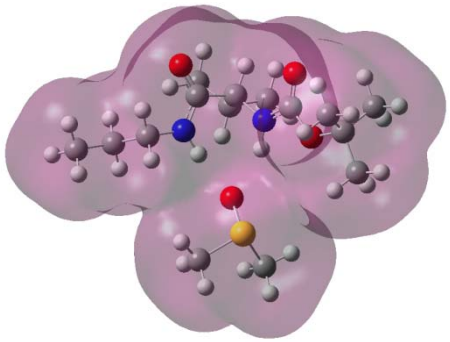
Implicit solvation:

Using tiny point charges on molecular surface to simulated solvent environment with certain ε_r



Molecular dynamics:

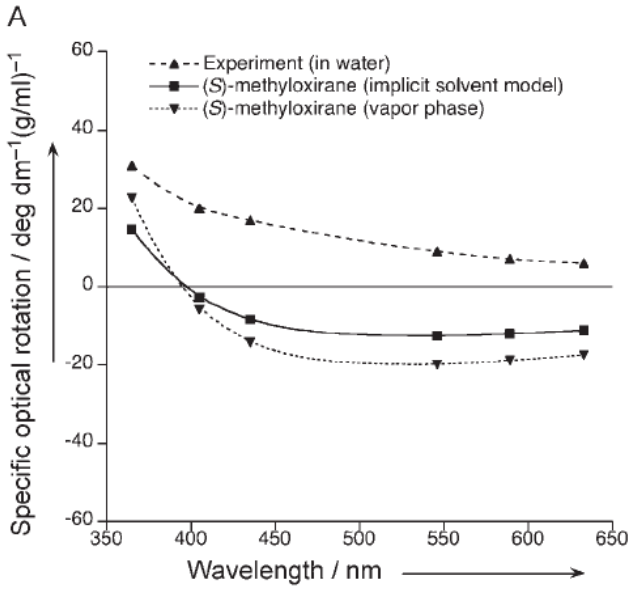
Immerse solute in pool of actual solvent molecules and simulated the dynamical behaviour

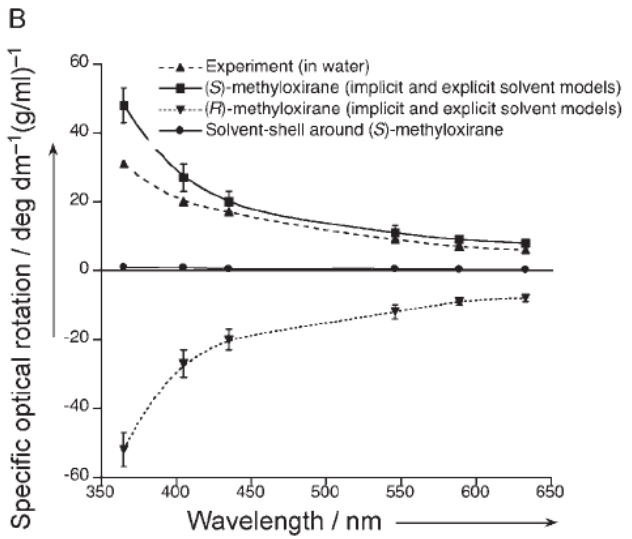


Supermolecule approach:

Few solvent molecules describe important explicit solute-solvent contacts; system treated with implicit solvent model

ORD of propylene oxide - rationalization



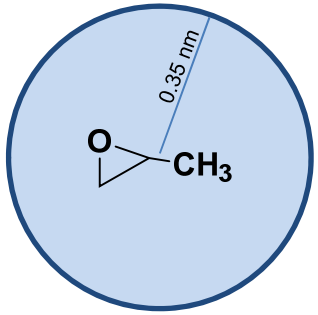


Attempts to calculate the ORD of PO in H_2O

- Calculations in gas phase or using implicit solvation models fail to reproduce the experimental data for PO in H_2O.

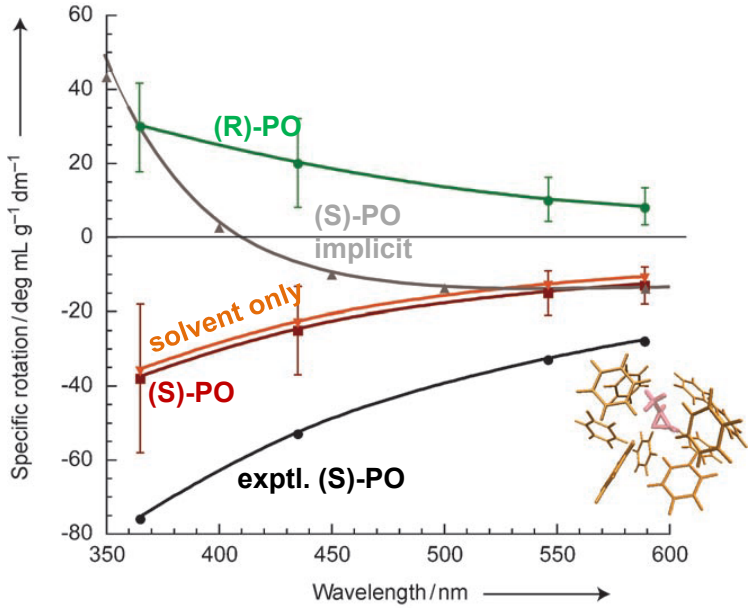
- Considering the solvent shell of 0.35 nm thickness explicitly provides a fairly reasonable agreement of theroetical values with the experimental data

- Removal of solute from solute-solvent cluster: no optical activity of the solvation shell



Mukhopadhyay et al. ChemPhysChem **7** (2006) 2483-2486

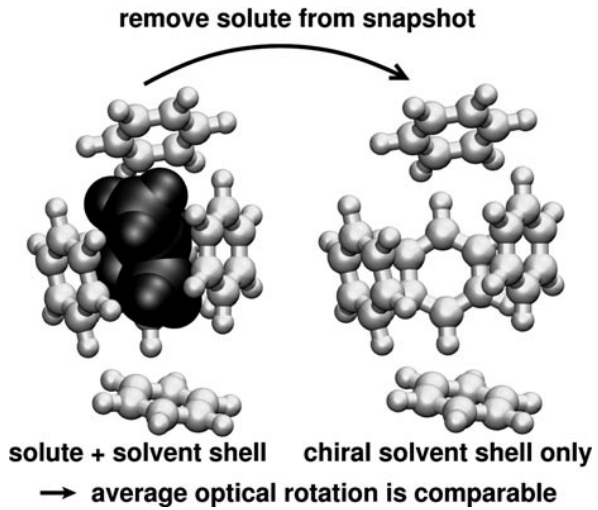
ORD of propylene oxide - rationalization



Mukhopadhyay et al. *Angew. Chem.* **119** (2007) 6570 –6572

Attempts to calculate the ORD of PO in benzene

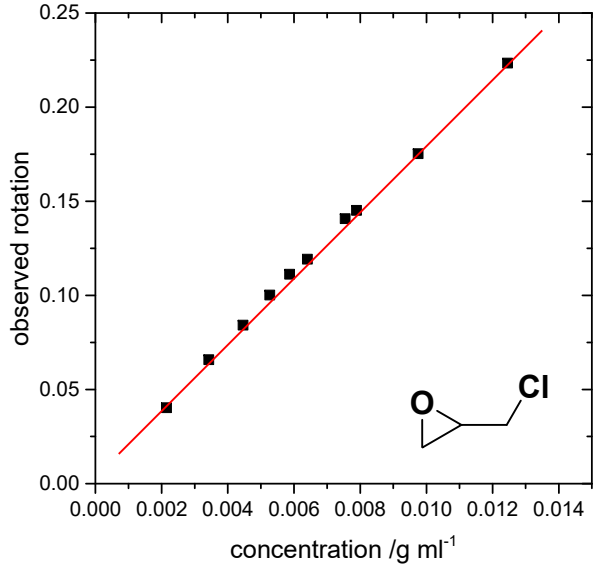
- Calculations using implicit solvation model fails to reproduce the experimental data for PO in benzene
- Immersing PO in benzene (MD simulation) and calculating the ORD for ~1000 snapshots at least yields same trend as experiment

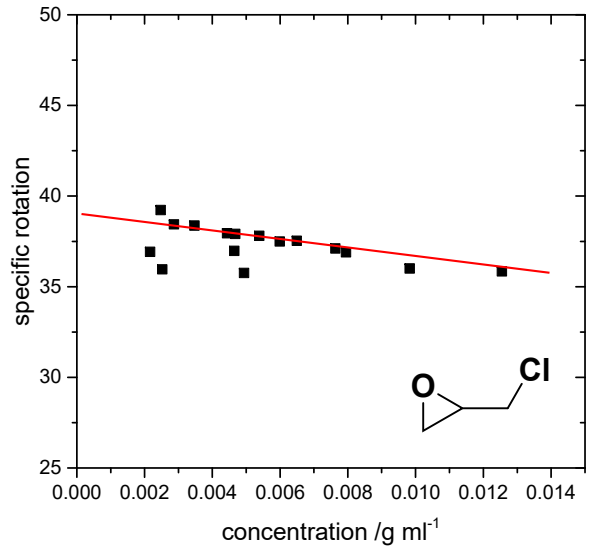


Angew. Chem. Int. Ed. **46** (2007) 7738 – 7740

- Chiral arrangement of solvent environment is key contributor to calculated OR values (orange line).

Solvent dependence of ORD





It has been recommended to determine the intrinsic OR by interpolation to inifte dilution:

Polavarapu et al., Chirality **15** (2003) S143-S149

TABLE 1. Intrinsic rotations, $\{\alpha\}_D$, of (R)-(–)-epichlorohydrin[a]

Solvent	Intrinsic rotation
CH_3OH	–32.8 ± 0.6
CH_2Cl_2	–22.4 ± 0.1
$CHCl_3$	+3.2 ± 1.5
CCl_4	+38.5 ± 0.3

[a]Intrinsic rotations are $[\alpha]_D$ values at zero concentration of epichlorohydrin. See the legend to Figure 1 for the equations used to derive these data.

Comparison with DFT calculations:

(B3LYP / aug-cc-pVTZ / PCM, conformer weighted average)

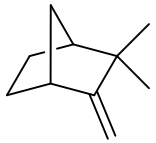
	Observed	Calc.
Neat	-25.6	-27
CH_2Cl_2	-22.4	-23
$CHCl_3$	+3.2	5
CCl_4	+38.5	43

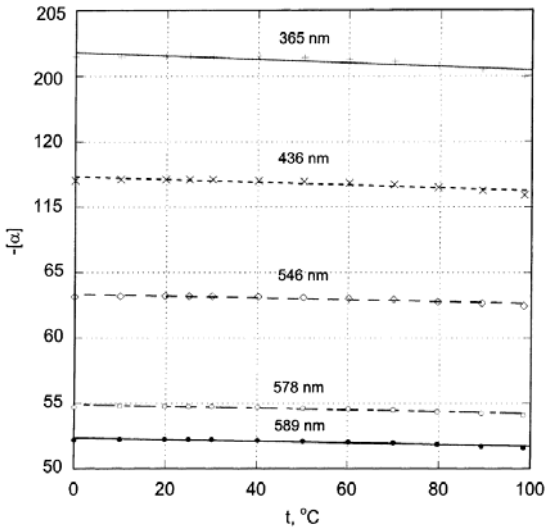
Temperature dependence of ORD

Wiberg et al. *J. Phys. Chem. A* **108** (2004) 5559-5563

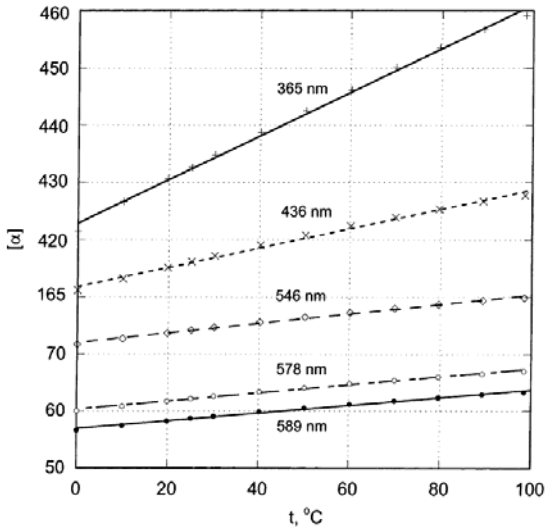
measurements in ethylcyclohexane

(-)-Camphene

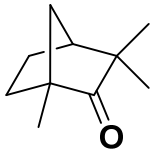


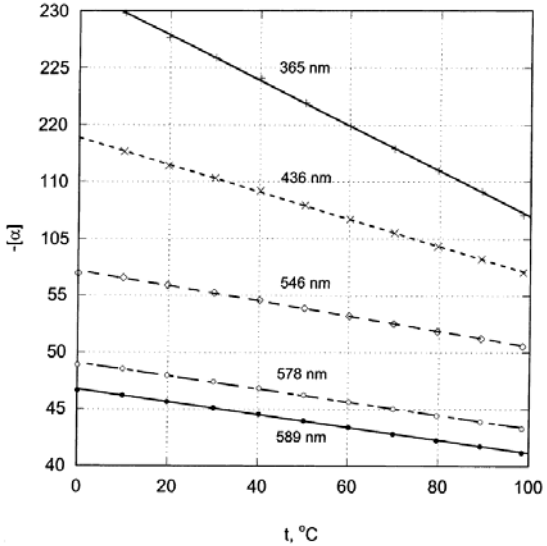


(1R)-(+)-Camphor



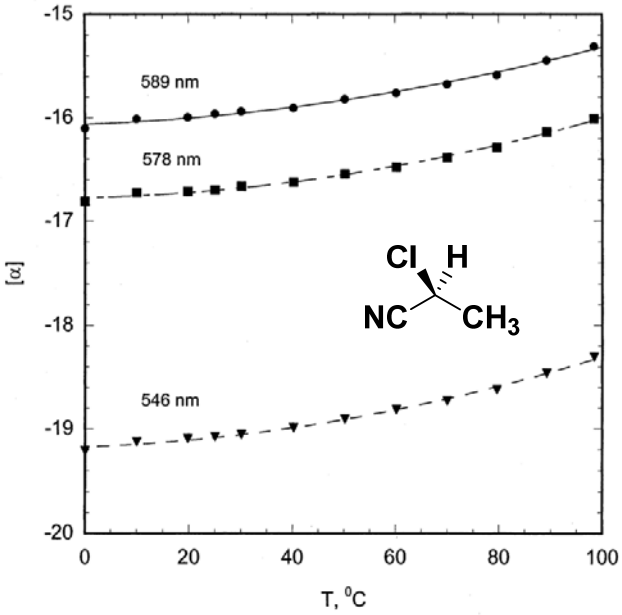
(1R)-(-)-Fenchone





Temperature dependence of ORD

Wiberg et al. *J. Phys. Chem. A* **109** (2005) 3448-3453



Even 2-chloropropionitrile shows T-dependence!

Reasons excluded:

- aggregation
- density changes

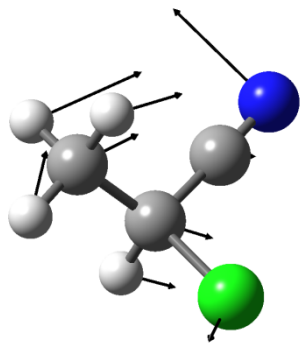
Only possible conformational change:
methyl group rotation

… but it‘s symmetric, i.e. $|\Delta x| \rightarrow |\Delta \alpha|$!

Vibrational degrees of freedom:

Displacement along vibration modes might have influence?

Indeed, temperature dependence can be traced back to one specific vibrational mode (ν_2 224 cm^{-1})!

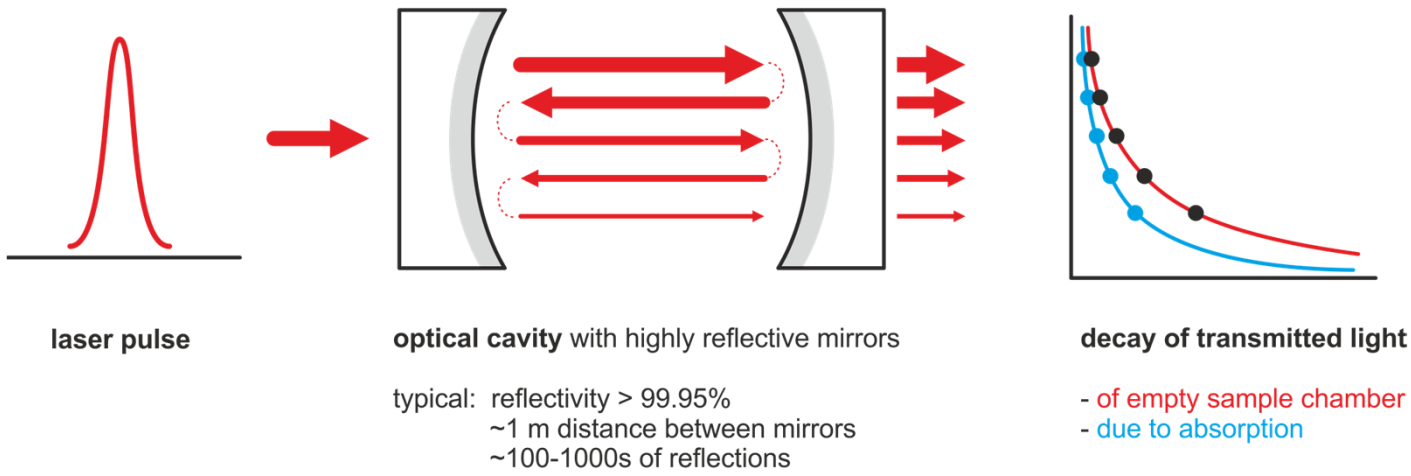


Cavity ring down spectroscopy

Gas phase has intrinsically low optical density

- Not much material in the light beam
- Huge inaccuracies due to experimental noise

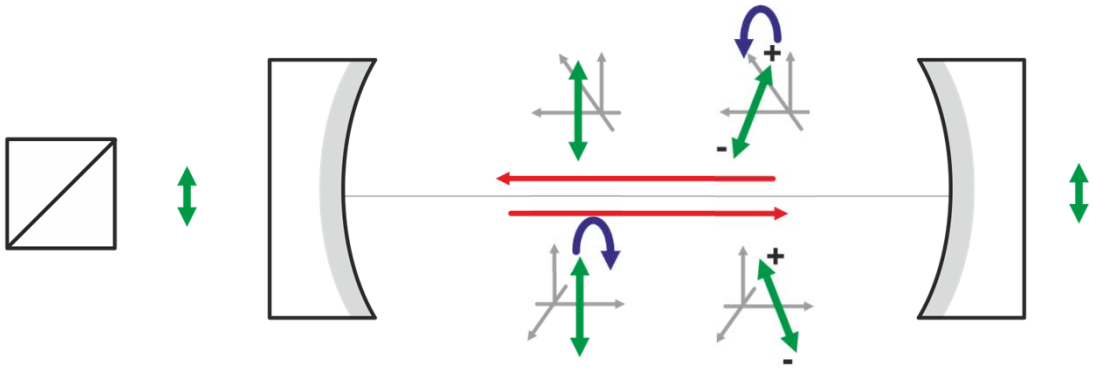
Concept: Install mirrors and have light beam bounce back and forth



$$I(t) = I_0 \exp(-t/\tau) \text{ with } \tau = \frac{n}{c} \cdot \frac{l}{1-R+X+al}$$

Cavity ring down polarimetry

Wouldn‘t it work to just use linearly polarized light between the cavity mirrors?

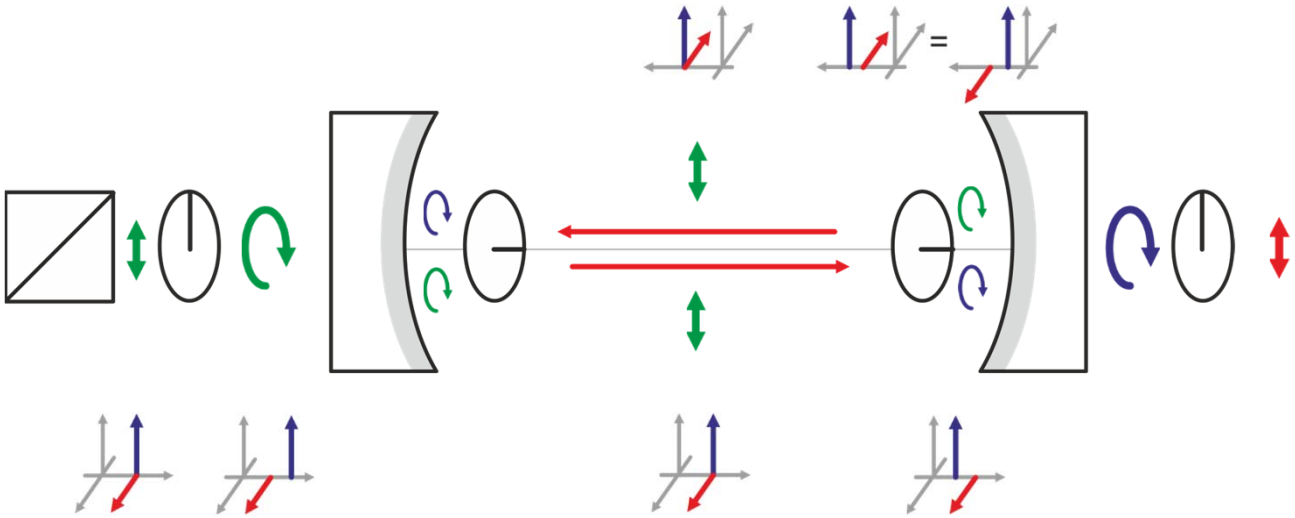


No:

Linearly polarized light would leave the cavity unaltered even in the presence of an optically active vapor, as the reflection on the mirror inverts the coordinate system and thus the polarization state of the linearly polarized light beam.

Cavity ring down polarimetry

The trick: Use of circularly polarized light and quarterwave plates to recover correct linear polarization state after reflection.



Afterwards: Analysis of the linear polarization state of the exiting light beam.

Cavity ring down polarimetry

T. Müller, K. B. Wiberg, P. H. Vaccaro J. Phys. Chem. A **2000**, *104*, 5959-5968

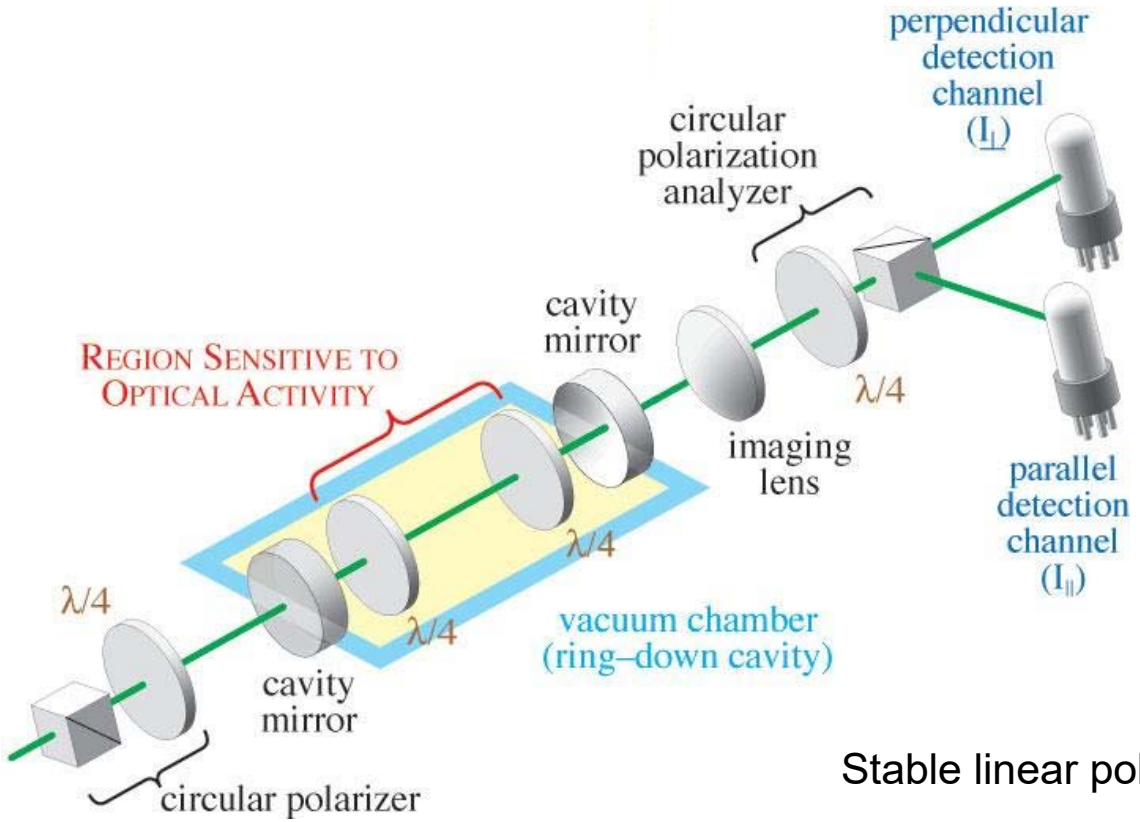


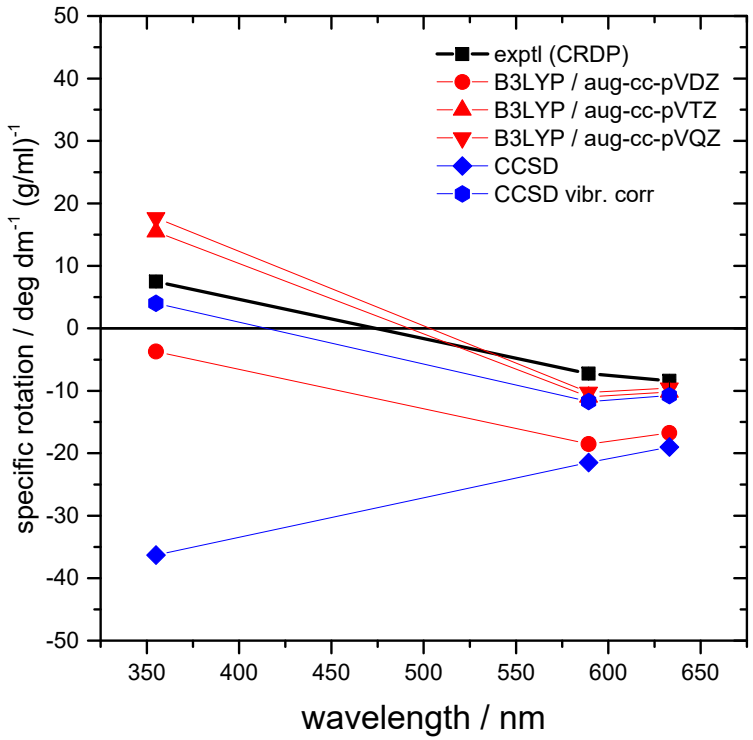
Figure: Vaccaro group website

Stable linear polarization can be achieved by combination of mirrors and quarterwave plates

Not so convenient:

For each wavelength, the optics need to be changed and re-calibrated!

OR of propylene oxide in gas phase



Theoretical prediction should get better, the better a theory describes the excitation energies and transition moments

- Use coupled cluster calculations rather than DFT

Even if perturbations from environment are ignored, quantitative prediction is difficult

Kogsted et al., *JACS* **128** (2006) 976-982

Kogsted et al., *Chem. Phys. Lett.* **401** (2005) 385-392

Take home messages

For the daily work in organic chemistry:

- OR depends on λ, T, c, solvent
- Solvent can even change sign of OR

From the physical chemical and theoretical perspective:

- Intrinsic optical rotation (the one we calculate) must be determined by interpolation to infinite dilution

- Gas phase OR measurements reveal that even then torsional motions can become crutial
  - ➢ Thus, calculations for gas phase OR must include vibrational corrections

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