Chiroptical Spectroscopy
Theory and Applications in Organic Chemistry

Lecture 4: Measurement of optical rotation

Masters Level Class (181 041)
Mondays, 8.15-9.45 am, NC 02/99
Wednesdays, 10.15-11.45 am, NC 02/99
Rosenfeld equation and rotational strength

The Rosenfeld equation

$$\Delta \theta = \frac{N |\mu_v|}{3h} \sum_{\pi \neq 0} \frac{\omega^2 R_{n0}}{\omega^2 - \omega_{n0}^2}$$

$$\omega = 2\pi f$$

rotational strength of transition $n \leftrightarrow 0$

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

$\mu$: electric dipole transition moment (EDTM)

$m$: magnetic dipole transition moment (MDTM)

$$\omega_{n0} = (E_n - E_0)/\hbar$$
Examples for ORD curves

Normal curves / dispersion curves

Anomalous ORD curve

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

Crossed polarizers and optically active sample

unpolarized light
transmission axis

optically active sample

rotates plane of polarization by $\theta$
Manual polarimeter: Half-shadow devices

Lippich polarimeter

Analyzer perpendicular to bisector of $2\alpha$: Both half fields bright

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

Source: Krüss Optronic Germany
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

The comfy way (todays alternative):

It’s simply built in to CD spectrometers

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

**Measured value:** \( \alpha \) (old \( \Phi \))

**Specific rotation** \( [\alpha] = \alpha / l \cdot c \)

Optical rotation \( [\alpha] \) depends on
- wavelength (ORD)
- concentration
- solvent
- temperature

Typical notation: \( [\alpha]_{25}^{D} = +28 \) (c = 2.1, H2O)
\( [\alpha]_{298}^{298nm} = -123 \) (c = 4.0, CHCl3)
Concentration dependence of OR

- Concentration dependence of ORD for $\alpha$-hydroxy-$\beta$, $\beta$-dimethyl-$\gamma$-butyrolactone investigated by Polavarapu

- Equilibrium can be described as

$$2M \rightleftharpoons D \quad \Rightarrow K = \frac{c_D}{c_M^2}$$

- Interpolation to 100% monomer and 100% dimer

- DFT-based calculations confirm the trend

(CAM-B3LYP/aug-cc-PVTZ)
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) $K_{\text{heterodimer}} = 2 K_{\text{homodimer}}$

b) $\text{SOR}_{\text{monomer}} = \text{SOR}_{\text{dimer}}$
Solvent dependence of ORD

- 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

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

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

Detour: How to describe solvent effects in calculations?

**Implicit solvation:**
Using tiny point charges on molecular surface to simulated solvent environment with certain $\varepsilon_r$.

**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.
Attempts to calculate the ORD of PO in H₂O

- Calculations in gas phase or using implicit solvation models fail to reproduce the experimental data for PO in H₂O.

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

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

ORD of propylene oxide - rationalization

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

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

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 infinite dilution:

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

Comparison with DFT calculations:

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

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Observed</th>
<th>Calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neat</td>
<td>-25.6</td>
<td>-27</td>
</tr>
<tr>
<td>CH₂Cl₂</td>
<td>-22.4</td>
<td>-23</td>
</tr>
<tr>
<td>CHCl₃</td>
<td>+3.2</td>
<td>5</td>
</tr>
<tr>
<td>CCl₄</td>
<td>+38.5</td>
<td>43</td>
</tr>
</tbody>
</table>

*Intrinsic rotations are [α]D₀ values at zero concentration of epichlorohydrin. See the legend to Figure 1 for the equations used to derive these data.
Temperature dependence of ORD


measurements in ethylcyclohexane

(-)-Camphene

(1R)-(+) Camphor

(1R)(-) Fenchone

Chiroptical spectroscopy | Dr. C. Merten
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 ($\nu_2$ 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

\[ I(t) = I_0 \exp\left(-\frac{t}{\tau}\right) \text{ with } \tau = \frac{n}{c} \cdot \frac{l}{1-R+X+\alpha l} \]
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.
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
Take home messages

For the daily work in organic chemistry:

- OR depends on $\lambda$, $T$, $c$, 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 crucial
  - Thus, calculations for gas phase OR must include vibrational corrections
## Outline of the lecture

<table>
<thead>
<tr>
<th>Dates</th>
<th>Topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>09.04.</td>
<td>Introduction</td>
</tr>
<tr>
<td>✓ 11.04.</td>
<td>Polarization of light</td>
</tr>
<tr>
<td>✓ 16.04.</td>
<td>Theoretical basis of optical activity</td>
</tr>
<tr>
<td>✓ 18.04.</td>
<td>Optical rotation</td>
</tr>
<tr>
<td>23.04.</td>
<td>Circular dichroism</td>
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<tr>
<td>25.04.</td>
<td>Circular dichroism</td>
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<tr>
<td>07.05.</td>
<td>Vibrational optical activity</td>
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<tr>
<td>14.05.</td>
<td>Vibrational optical activity</td>
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<td>18.06.</td>
<td>applications</td>
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<td>20.06.</td>
<td>applications</td>
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Wednesdays 10.15-11.45 am