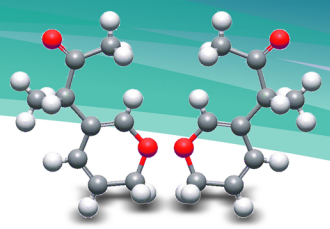
Questions & Answers About VCD
for an Organic or Medicinal Chemist



Q: What is VCD?
A: VCD is the abbreviation of infrared vibrational circular dichroism (VCD). It measures the difference in left-and-right circularly polarized infrared light.

Q: What is VCD mainly used for?
A: VCD is mainly used for the determination of absolute configuration (AC) of chiral molecules.

Q: VCD sounds like a new method, is it reliable scientifically?
A: Yes. Since early 1970's more than 1,600 papers have been published in peer-reviewed journals including JACS, JOC, Org. Lett., Anal. Chem., J. Phys. Chem., and Chirality etc. The FDA has accepted and now accepts (as far as we know) the use of VCD for determination of AC of drug molecule candidates. Major pharmaceutical companies (such as GSK, BMS, Wyeth/Pfizer, Eli Lilly, AstraZeneca and many more) have been using VCD routinely for over 10 years. Annually, close to 700 AC assignments are solved by VCD.

Q: What type of information do you need to start a VCD measurement?
A: We need the structure of your molecule to do the calculation and solubility information for sample preparation. We keep this information confidential by signing a CDA.

Q: What functional groups are needed in my molecule to measure VCD?
A: You don't need any particular functional group or atoms to perform VCD measurement. As long as your molecule is chiral with good enantiomeric excess (at least after a flash column), it is good for VCD measurement. The higher the %ee of your sample the more accurate is the measurement.

Q: How does the whole process look like experimentally?
A: Your sample is dissolved in a solvent such as CDCl3 or DMSO-d6 and the spectrum is recorded. The spectrum is processed and compared with an ab initio calculation of a chosen enantiomer. If the two spectra agree with each other, then the calculated stereochemistry is the absolute configuration of your measured sample. If your sample shows the opposite spectrum (mirror image) to the calculated, then your sample is the enantiomer of the calculated result.

Q: How much is needed for a VCD measurement?
A: Typically 5-10 mg somewhat dependant on solubility of compound.

Q: Is my sample recoverable?
A: Yes, we can recover your sample – about 90-95%.

Q: How long does it take to determine the absolute stereochemistry of a molecule?
A: The experiment takes 1 to 12 hours. The calculation takes from hours to a few days depending on the complexity of structure of your molecule and number of conformers present in solution.

Q: Can you compare VCD with X-ray crystallography?
A: Determination of AC by X-ray crystallography requires a single crystal. Only a sample in natural form, liquid or soluble solid, is needed for AC determination by VCD. You don't need to generate derivatives of your sample or separate them from other reagents or molecular species.

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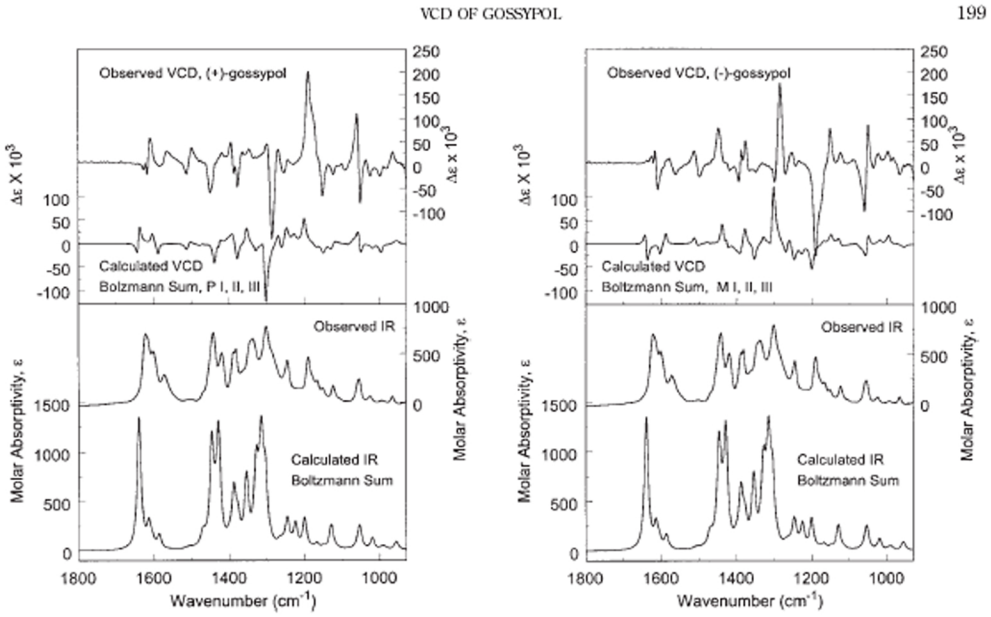
(continued)

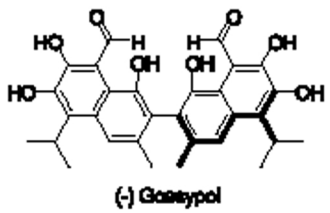
Q: What is the advantage of BioTools' VCD instrument?
A: Prof. Laurence A. Nafie, co-founder of BioTools, discovered and was first to measure the Fourier Transform-VCD. His inventions, including Dual Source for a significant increase in S/N and Dual PEM for artifact suppression are exclusively incorporated in our instrument.

Q: What kind of service is available from BioTools?
A: You provide sample and structure, and then we do the measurement and calculation. We send you a report that can be incorporated into your publication or submission to FDA. If you are from academia and want to collaborate with BioTools, please contact us.

Q: How does one contact BioTools?
A: Log on www.btools.com and find useful information there. Our phone number is 561-625-0133. In Europe, we can be reached at +447760778610.

Q: Can you provide an example for VCD measurement?
A: Illustrated here are spectra showing the AC determination of the natural oil gossypol.





"Determination of the Absolute Configuration and Solution Conformation of Gossypol by Vibrational Circular Dichroism"
by Teresa B. Freedman, Xiaolin Cao, Regina V. Oliveira, Quezia B. Cass, and Laurence A. Nafie,
Chirality, 15, 196-200, (2003)

Q: What is a good general reference for AC determination with VCD?
A: "Absolute Configuration Determination of Chiral Molecules in the Solution State Using Vibrational Circular Dichroism" by T.B. Freedman, X. Cao, R. K. Dukor and L.A. Nafie, Chirality 15, 743-758 (2003).