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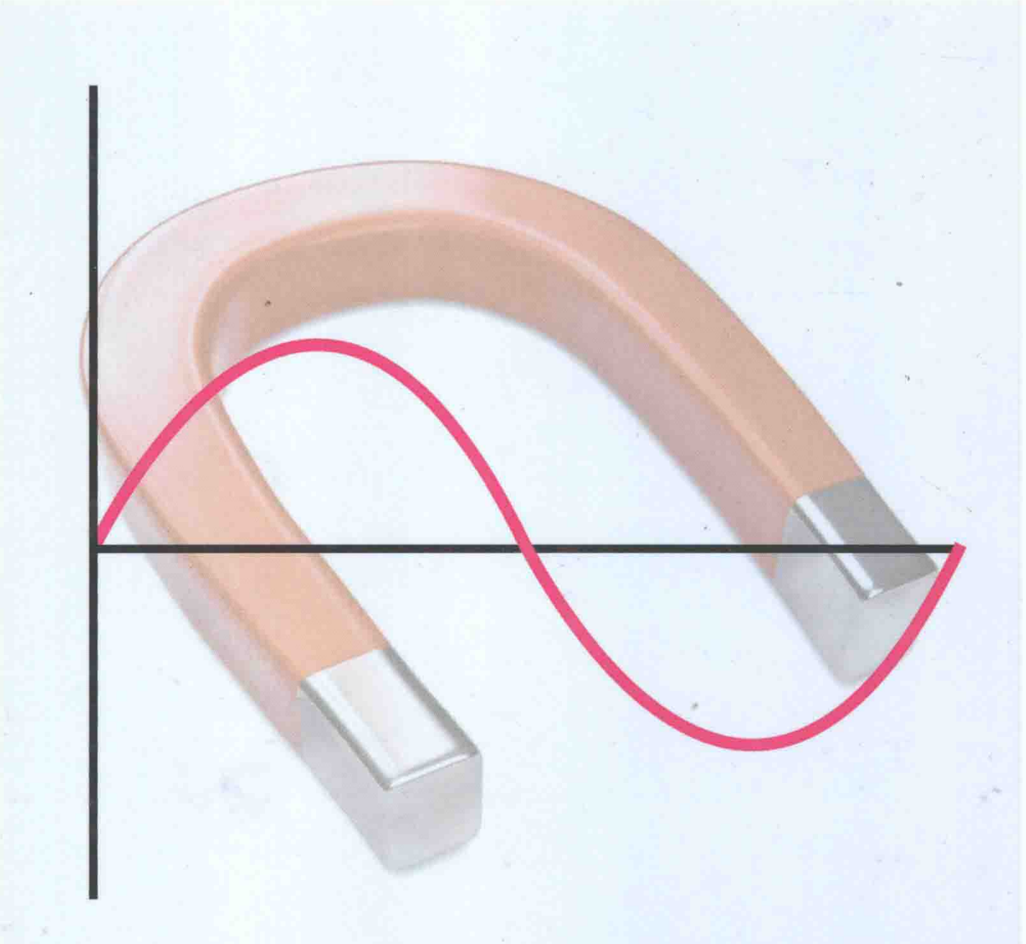
Circular Dichroism and Magnetic Circular Dichroism Spectroscopy for Organic Chemists



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RSC Publishing

ISBN: 978-1-84755-869-5

A catalogue record for this book is available from the British Library

Published by The Royal Society of Chemistry,
Thomas Graham House, Science Park, Milton Road,
Cambridge CB4 0WF, UK

Registered Charity Number 207890

For further information see our web site at www.rsc.org

Printed and bound in Great Britain by CPI Group (UK) Ltd, Croydon, CR0 4YY

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Preface

Circular dichroism (CD) and magnetic circular dichroism (MCD) spectroscopy can often provide key information about the conformations and electronic states of chromophore-containing molecules, which is required for a full understanding of the electronic structures and optical spectroscopy. Unfortunately, the theory that underpins these techniques has been largely inaccessible to many organic chemists and biochemists and only a few researchers have carried out detailed quantitative analyses of their spectral data. Until recently, a key problem that has been encountered is that relatively few molecules have been available that can be used to describe the various methods for analysing the spectral data in a clear and concise manner. This is not surprising because people who excel at spectroscopic theory usually lack the skills required to design and synthesise the molecules that would be most appropriate for describing the theory of CD and MCD spectroscopy. Most of the books that have been written on this subject have, therefore, been based on dense sets of mathematical equations and have been aimed primarily at physical chemists and physicists.

Our aim in writing this book is to try to rectify this situation by summarising the different types of CD and MCD spectra and by describing in detail the qualitative and quantitative methods that can be used to analyse the spectral data. Over the last two decades we have successfully synthesised a series of molecules which are ideal for illustrating key points related to the theory of CD and MCD spectroscopy, and we are confident that the time is finally ripe to write a book which will provide the key practical knowledge required to use the CD and MCD techniques to their full potential. In the first chapter, we will provide an introduction to the most important aspects of the theory of electronic absorption, CD and MCD spectroscopy. The important aspects of electronic absorption spectroscopy are described first, since absorption spectra are usually recorded and analysed during any study of the CD and MCD spectra because the spectral bands in each case arise from the same set of transitions. The content is aimed primarily at a reader who already possesses a

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first year undergraduate level of understanding of physical chemistry. In the case of small chromophores, the lowest energy electric dipole allowed transitions are often aligned along the direction of the permament dipole moment of the molecule. Transitions of this type are often ideally suited for analysis by CD spectroscopy, since both the electric and magnetic dipole transition moments are well defined in terms of their alignment and can play a key role in generating CD intensity based on several different intensity mechanisms, which will be described in detail. MCD spectra are obtained by placing a magnet in the sample compartment of a CD spectrometer. MCD spectroscopy provides key information about the degeneracy of ground and excited states which cannot easily be derived from the electronic absorption spectrum alone.

In Chapters 2 and 3, we present key information about two of the most widely used analytical approaches that have been reported to date, which could probably be viewed as core knowledge for organic chemists and biochemists who want to become active in this field. Our hope is that in many instances researchers who are new to the field will find that the examples provided can serve as a useful template for analysing their own data. In Chapter 2, the most well known empirical rules for analysing CD spectra, which have been developed over the past 50 years, are described. Although theoreticians have described detailed mathematical rationales for these, there is usually no need to study their research in detail to be able to derive key information about the conformation or configuration of certain specific types of chiral system, such as ketones and substituted benzene rings. The key is to learn how the empirical rules have been applied successfully by earlier researchers and to be fully aware of any exceptions to the rules which have been reported. In Chapter 3, we describe a wide range of examples of the use of exciton coupling theory in the conformational analysis of natural and synthetic dimers, oligomers and polymers. The sign sequence observed in the CD spectra of excition couplets has been found to be related to the relative alignments of the interacting chromophores in space.

In Chapters 4 to 8 more specialised types of analysis are examined. In chapter 4, the use of cyclodextrin inclusion compounds to study the CD spectra of guest molecules trapped in the central cavity is described in detail. Host-guest complexes with clearly defined geometries are readily formed in solution, which enables the analysis of the alignment of band polarisations at wavelengths as short as 200 nm even in the absence of single crystals. The focus in Chapter 5 shifts over to the CD spectroscopy of inorganic complexes based either on the π-system transitions of the ligand or on the $d \rightarrow d$ transitions of the central metal. In recent years the incorporation of 1,1'-binaphthyl (BINAP) moieties has been used to study the asymmetric synthesis of porphyrinoids, since BINAP provides a well defined asymmetric field, which interacts with the porphyrinoid π-system in a manner that can be readily predicted. This research is described in detail in Chapter 6. Although CD spectra can often be readily analysed in conceptual terms based on the theory which describes various intensity mechanisms, in some cases this is not possible and the analysis of the system has to depend almost entirely on theoretical calculations. Molecules with intrinsic chirality are best suited to this approach. Several examples are described in detail in Chapter 7. The results of these calculations have to be treated with caution, however, for reasons that are described in detail. In Chapter 8, the CD spectroscopy of biomolecules will be described. Since large proteins contain many chromophores, which lie at various distances from each other in a wide range of alignments, the quantitative analysis of these spectra is usually not possible, but the CD technique can still be used to derive qualitative information and has been widely applied on this basis.

In Chapter 9, representative examples of the use of MCD spectroscopy are described. Many of the examples revolve around the study of porphyrin complexes, since the technique has been particularly widely utilised in this context. The theory of MCD spectroscopy can be challenging for many organic chemists, because it revolves around the application of molecular orbital theory to conceptualise the structure and bonding of chromophores, rather than the valence bond theory approach that tends to be used in organic chemistry. In Chapter 10, we describe how Michl's perimeter model, a molecular bonding theory approach, can be used a molecular bonding theory approach can be used to analyse the MCD spectra of aromatic and antiaromatic π-systems.

Abbreviations

[3,3]PCP	[3,3]paracyclophane
acac	acetylacetonate
Ara	arabinose
BINAP	1,1'-binaphthyl
bipy	2,2'-bipyridyl
B3LYP	Becke 3-parameter (exchange), Lee, Yang and Parr (correlation)
CAM–B3LYP	Coulomb attenuated method B3LYP
CBD	cyclobutadiene
CD	circular dichroism
CI	configuration interaction
con.	consignate
Cp	cyclopentadiene
CyD	cyclodextrin
dis.	dissignate
DFT	density functional theory
DNA	deoxyribonucleic acid
edtm	electric dipole transition moment
en	ethylenediamine
EPR	electron paramagnetic resonance
Fc	ferrocene
Gal	galactose
Glu	glucose
HPLC	high-performance liquid chromatography
ICD	induced circular dichroism
LCAO	linear combination of atomic orbitals
lcp	left circularly polarised
LMCT	ligand to metal charge transfer
Lys	lysine

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Man	mannose
MCD	magnetic circular dichroism
mdtm	magnetic dipole transition moment
MO	molecular orbital
MORD	magnetic optical rotatory dispersion
MLCT	metal to ligand charge transfer
MW	molecular weight
NMR	nuclear magnetic resonance
OAM	orbital angular momentum
OBz	benzoate
ORD	optical rotatory dispersion
Pc	phthalocyanine
phen	*o*-phenanthroline
rcp	right circularly polarised
RNA	ribonucleic acid
SCF-CI-DV	self consistent field–configuration interaction–dipole velocity
SCF-PPP-CI	self-consistent field Pariser-Parr-Pople configuration interaction
SM	spectroscopic moment
TD-DFT	time dependent–density functional theory
TFA	trifluoroacetic acid
TZVP	triple zeta valence plus polarisation
VTVF	variable temperature variable field
x–c	exchange–correlation
Xyl	xylose
ZFS	zero field splitting

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CHAPTER 1

Theory of Optical Spectroscopy

1.1 Electronic Absorption Spectroscopy

Optical spectroscopy is based ultimately on the interaction between atoms or molecules and incident electromagnetic radiation. In the 1860s, a Scottish physicist called James Clerk Maxwell first postulated that an oscillating electric field generates an oscillating magnetic field and *vice versa*. A propagating sinusoidal electromagnetic wave can be formed on this basis, with electric and magnetic fields oscillating perpendicular to one another and to the direction of propagation. Electromagnetic radiation exhibits both wave properties and particle properties and was described successfully by Albert Einstein in quantum mechanical terms as a particle, referred to as a photon (hν), which has no mass or charge. At longer wavelengths in the IR region ($>$1000 nm) the interaction between the atomic nuclei and the oscillating electric and magnetic fields typically results in molecular vibrations, which can be studied by infrared spectroscopy. At shorter wavelengths the heavier nuclei can no longer oscillate significantly, but the surrounding cloud of electron density can still be polarised in the direction of the oscillating electron field, resulting in an electronic transition from a groundstate electron configuration to an excited state. UV-visible absorption spectroscopy can be used to derive key information about the electronic structures of molecules on this basis, while techniques such as fluorescence spectroscopy can be used to derive information from the manner in which the molecule returns to its groundstate configuration.

As shown in Figure 1.1, molecular orbital theory can be used to describe this electronic excitation on the basis of the transfer of an electron from an occupied molecular orbital to an unoccupied molecular orbital. The energy difference between the ground and excited states (ΔE) is proportional to the frequency of the absorbed electromagnetic radiation (ν):

$$\Delta E = \mathrm{h}\nu = \mathrm{hc}/\lambda \tag{1.1}$$

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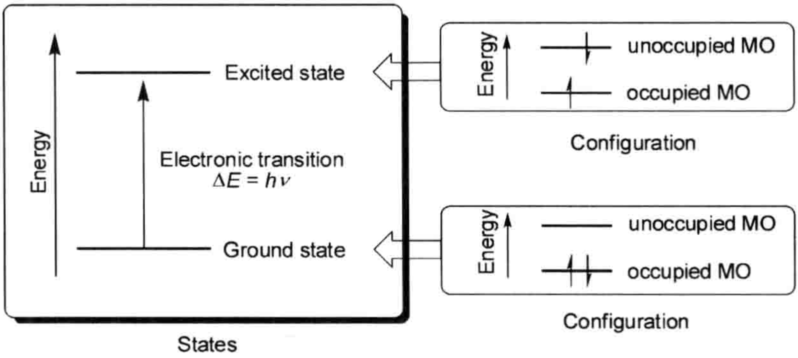

Figure 1.1 Energy diagram showing an electronic transition.

where h is the Planck constant ($h = 6.626 \times 10^{34}$ J s), and c and λ denote the velocity of light ($c = 2.998 \times 10^{8}$ m s^{-1}) and the wavelength, respectively. Especially in the context of organic molecules, absorption in a particular region of the spectrum is often characteristic of a transition that is associated primarily with a particular type of bond or structural unit within a molecule. These structural units are usually referred to as chromophores. In the context of saturated organic molecules, wavelengths much shorter than 200 nm are required to cause electronic transitions. Since the conventional use of UV-visible absorption spectrometers under an air atmosphere tends to be limited to 200 nm, owing to strong absorption by oxygen and ozone formation at shorter wavelengths, electronic absorption spectroscopy is applied primarily to the π-systems of organic molecules and inorganic metal complexes, which absorb strongly at wavelengths >200 nm, with a particularly strong focus on aromatic and heteroaromatic cyclic compounds.

The interaction of UV or visible region light (typically 200–750 nm) with a molecule or complex can result in an electronic excitation from one molecular orbital to another, resulting in a transition from the groundstate electronic configuration to an excited state, Figure 1.1. This inherently results in a rearrangement of the electron density of a molecule. Since the size of molecules and complexes will typically be a few orders of magnitude smaller than the wavelength of UV-visible light, the electric field induces an oscillating electric dipole moment upon absorption of a photon. An electric dipole transition moment (edtm), $\boldsymbol{\mu}$, can be defined for each transition, which describes the net linear displacement of charge during a transition. The initial point of this vector is set to the centre of gravity of the molecule, and the square of the transition dipole moment is proportional to the intensity of the electronic transition. If a transition is dipole forbidden, $\boldsymbol{\mu} = 0$, while a transition is said to be allowed if $\boldsymbol{\mu} > 0$. The direction in which $\boldsymbol{\mu}$ is aligned determines the polarisation of the associated spectral band with respect to the x-, y- and z-axes. It should be noted that edtms are different from static electric dipole moments (also known as permanent dipole moments), which describe the polarisation of charge in a

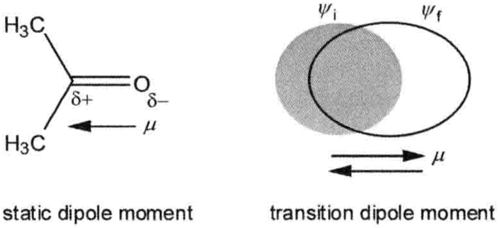

Figure 1.2 An illustration of a static dipole moment (left) and an electric transition dipole moment (right). The grey and white circles indicate electron distributions of the groundstate and an excited state.

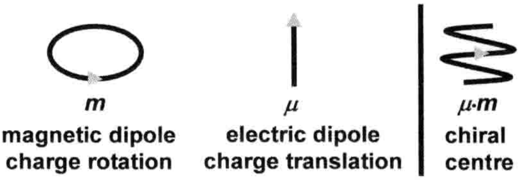

Figure 1.3 The origin of chirality, based on the combined effect of electronic and magnetic transition moments.

molecule in the groundstate, Figure 1.2. The direction of a static dipole moment can be determined definitively on the basis of the molecular structure. In contrast, since a transition dipole has an oscillating property, the choice of the sense of a transition dipole moment is arbitrary and depends on the phase of the wavefunctions. A magnetic dipole transition moment (mdtm), $\boldsymbol{m}$, can also be defined for each electronic transition, which describes the net circulation of charge during a transition, Figure 1.3. The edtms are usually the dominant factor in coupling the groundstate with excited states within UV-visible absorption spectroscopy, since they tend to be *ca.* five orders of magnitude stronger than magnetic dipole moments. It should be noted that this is not the case during the quantitative analysis of CD spectral data, since the intensity mechanism is based on an interaction between electric and magnetic dipole transition moments. Sections 2.2 and 5.2 describe the analyses of carbonyl $n \rightarrow \pi^*$ transitions in organic molecules and the $d \rightarrow d$ transitions of transition metal complexes, which are magnetic dipole allowed but electric dipole forbidden.

Group theory can be used to determine whether transitions are electric dipole and magnetic dipole allowed or forbidden and the polarisation of the spectral bands, which arise in the UV-visible absorption spectrum based on the value of the transition moment integral:

$$\int \psi_1 \boldsymbol{\mu} \psi_2 \mathrm{d}\tau \qquad (1.2)$$