Coordination Chemistry Reviews 318 (2016) 1–15

Contents lists available at ScienceDirect

Coordination Chemistry Reviews

journal homepage: www.elsevier.com/locate/ccr

Review

Optically active BODIPYs

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Contents

ARTICLE INFO

Article history:
Received 28 December 2015
Accepted 28 March 2016
Available online 1 April 2016

Keywords:
BODIPY
Chirality
Circular dichroism
Circularly polarized luminescence

ABSTRACT

This review highlights and summarizes various optically active BODIPY molecules and describes the analysis of their circular dichroism (CD) and circularly polarized luminescence (CPL) spectroscopy, to provide a platform for the rational design of novel optically active BODIPY structures and the development of new chiroptical applications. Possible future research directions are also discussed.

1. Introduction

Chirality is one of the most fascinating phenomena that is commonly observed in nature, and is of interest to physicists, chemists and biologists [1]. Chiral molecules have two possible structures that are non-superimposable mirror images of each other, due to the absence of a center of symmetry or mirror plane. The two forms are called enantiomers (from the Greek word for opposite) or optical isomers, because they rotate plane-polarized light either to the left or right. A large number of molecules produced by natural organisms display a specific chiral handedness, since the response of an organism to a particular molecule depends on how it fits a specific site on a receptor molecule [2]. Chirality is increasingly important in synthetic chemical research, especially in the design of pharmaceuticals, since usually only one enantiomer is active in its intended receptor [2]. This in turn has encouraged the development of suitable instrumentation for the synthesis, separation and detection of synthetic chiral molecules [2,3].

Since the emergence in the 1960s of photoelastic modulators, which can generate alternating beams of left and right circularly

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Abbreviations: BODIPY, boron dipyrromethene difluoride; B3LYP, Becke 3-Parameter (Exchange), Lee, Yang and Parr; CD, circular dichroism; CPL, circularly polarized luminescence; DCM, dichloromethane; DMF, dimethylformamide; DPEDA, 1,2-diphenyl-1,2-ethanodiamine; edtm, electric dipole transition moment; mdtm, magnetic dipole transition moment; ICD, induced circular dichroism; ECCD, exciton coupling circular dichroism; UV, ultraviolet.

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http://dx.doi.org/10.1016/j.ccr.2016.03.015
0010-8545/

polarized (lcp and rcp) light from an incident plane polarized beam, circular dichroism (CD) spectroscopy has been the main spectroscopic tool for studying the ground-state electronic structures of chiral molecules. A CD signal represents the differential absorbance of beams of equally intense lcp and rcp light, i.e., $\Delta A = A_L \times A_R$, where A_L and A_R are the absorbance values for the lcp and rcp beams, respectively [4]. In recent years, circularly polarized luminescence (CPL) spectroscopy has been emerging as a powerful tool for probing the excited-state electronic structures of chiral molecules [5], based on the differential spontaneous emission of lcp and rcp light, i.e., $\Delta I = I_L - I_R$, where I_L and I_R denote the intensity of lcp and rcp luminescence from a chiral fluorophore. Until recently, this field has been dominated by lanthanide complexes, since they exhibit high CPL dissymmetry [6,7]. In recent years, however, there has been growing interest in the synthesis of organic molecules that are capable of emitting CPL due to their potential applications in optoelectronic devices [8–11].

Boron-dipyrromethene (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene, BDP or BODIPY) dyes have been the focus of considerable research interest in recent decades due to their structural versatility and excellent spectroscopic properties, such as their intense absorption and emission bands, which can be fine-tuned through facile structural modifications to lie anywhere from the blue portion of the visible to near infrared region, as well as their excellent photostability and high solubility in commonly used organic solvents of differing polarities (Fig. 1) [12–17]. Since most BODIPYs are planar and achiral, they do not exhibit CD and CPL signals. When chiral substituents are covalently linked to the BODIPY core to form extrinsically active dyes, or the structure is modified so that it is intrinsically chiral, CD and CPL signals are observed, however. In recent decades, BODIPYs have been studied extensively for use in a wide range of applications, such as chemosensors, biological labels, dye lasers, photodynamic therapy and optoelectronic devices [13–16]. Since chirality sometimes plays an important role in this regard and could inspire the development of other applications, a considerable number of optically active BODIPYs have been investigated in recent years. There are very few detailed analyses of the chiroptical properties, however, and CPL spectroscopy studies are particularly rare.

In this review, the directly relevant fundamental aspects of CD and CPL theory are first briefly introduced, and a series of BODIPY systems are then analyzed on this basis to provide examples of how the theory should be applied. The review focuses primarily on the electronic CD spectroscopy in the 300–800 nm region and the chiral BODIPYs are divided into three groups according to their differing structures. Firstly, BODIPYs that contain chiral carbon atoms, secondly those BODIPYs that are linked with optically active aromatic molecules, and thirdly BODIPYs that are axially-chiral or have a stereogenic center at the tetrahedral boron atom. Particular attention is paid to the analysis of CD spectra containing exciton coupling systems. The main goal of this review is to highlight and summarize the synthesis of different types of chiral BODIPY structures and outline their CD and CPL spectroscopy, since this should help to provide a platform for the rational design of novel structures and the development of new chiroptical applications. Where appropriate, systems that are of interest from a CD analysis standpoint are described even if their CD spectra have not been analyzed or reported in a BODIPY context. This review focuses on providing synthetic chemists with a fundamental insight into the design of optically-active BODIPYs in a manner that can facilitate their future applications in optoelectronic devices and as biological sensors.

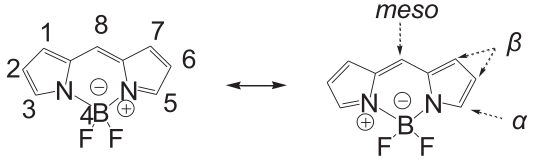

Fig. 1. The BODIPY fluorophore and its IUPAC numbering system. The 8-position is often referred to as the *meso*-carbon, while the 3,5-positions on the one hand, and the 2,6- and 1,7-positions on the other, are sometimes referred to as the α- and β-carbons, respectively, based on their relative proximity to the pyrrole nitrogens. Delocalized resonance structures of BODIPY are provided with the formal charges indicated.

2. Basic concepts and theory

2.1. BODIPY dyes

In the absence of structural modifications that introduce significant charge transfer character, the theoretical calculations of BODIPY dyes have consistently predicted that the lowest-lying $S_0 \rightarrow S_1$ excitation is almost exclusively associated with the HOMO → LUMO transition of the π-system. Since symmetrically-substituted BODIPYs belong to the C_{2v} point group, the electric dipole transition moments (edtms) of allowed transitions are polarized either parallel or perpendicular to the main C_2 axis of symmetry [18]. The a_2 HOMO has a short-axis nodal plane passing through the boron atom, while the b_2 LUMO has a nodal plane that is aligned with the long-axis [12,19]. The transition density calculated by means of semi-empirical calculations displays significant amplitudes on the pyrrole rings, leading to a large transition dipole, μ_{ag}. According to the quantitative evaluation of the electro-optical absorption measurements and semi-empirical calculations, the transition dipole direction is aligned perpendicular to the ground-state dipole moment and parallel to the long-axis of the molecule (Fig. 2) [18]. Since the dipole difference density $\Delta\mu$ is aligned with the short-axis, only small differences are anticipated between the excited- and ground-state dipole moments. This, along with the relatively rigid structures that result from difluoroboron coordination, explains the weak influence of solvent polarity and the coordination environment on the spectral properties observed for most BODIPY dyes [18].

2.2. Circular dichroism

Since CD is defined as the difference in the absorbance of lcp and rcp light, the obvious starting point for analyzing a CD spectrum is the electronic absorption spectrum. When BODIPYs are excited by electromagnetic radiation, an electron is excited from an occupied

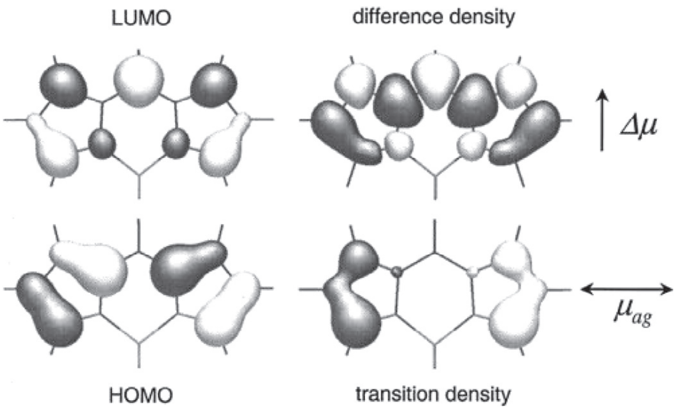

Fig. 2. The calculated HOMO, LUMO, difference density and transition density of 1,3,5,7-tetramethyl-BODIPY. The CNDO/S method was used, assuming an AM1 optimized geometry. [Reprinted with permission from ref. [18]. Copyright © 2001 American Chemical Society.]