Synthesis of Asymmetric Cyanine Dyes in Solid State

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Perspective

Cyanine Dyes (CD) are a type of organic molecule utilised in a variety of applications, including photography and bioimaging. High molar extinction coefficients up to 105 L mol-1cm-1 and absorption spectra spanning from 500 nm to 1000 nm are the most well-known properties of CDs, which can be fine-tuned by lengthening the length of the central methylene bridge or altering the terminal heterocycles. New synthetic approaches, such as microwave-assisted and solid-phase procedures, have been developed in recent decades to address the limitations of traditional synthetic processes. While the microwave method lowers the time that reagents and products are exposed to thermal deterioration, the solid-phase method allows for simpler synthetic methods, which results in higher yields and easier product purification. The current study provides a thorough examination of solid-phase methods for the synthesis of asymmetrical CDs, as well as a critical assessment of the differences between the currently available solid-state methodologies. Cyanine Dyes (CD) are an organic functional dye with a chemical structure in which two nitrogen atoms are joined by a single or multiple methane group to generate a delocalized system with an odd number of atoms. The total structure is entirely conjugated, with electrons delocalized along the entire molecular backbone and the positive charge on the nitrogen, resulting in CDs that can be described as a resonance hybrid of two configurations. The conjugated carbon bridge plays an important structural role in the photophysical characteristics of CDs, causing a bathochromic shift of roughly 100 nm with each addition of a methylene unit. By adjusting the length of the Polymethine Bridge, cyanines can cover a substantial portion of the visible spectrum. These peculiar characteristics, combined with remarkable molar extinction coefficients of 1.5-3 x 105 L mol-1cm-1, made CDs one of the most researched classes of chromophores for a variety of applications including photography, sensors, fluorescence imaging, data storage, nucleic acid labelling, medicine, and dyessensitised solar cells. The length of the chain between the two nitrogen atoms is used to name CDs in general. Mono-, tri-, penta-, and heptamethine are the dyes having one, three, five, and seven methine units, respectively. However, an additional classification based on the chemical structure of the nitrogen-containing groups is frequently described. Streptocyanines are cyanines without any terminal heterocyclic groups, hemicyanines are cyanines with only one terminal heterocycle, and closed chain cyanines are cyanines with two heterocycles at the chain edges. The nature of heterocyclic structures such as indole, benzoindole, benzoxazole, benzothiazole, benzoselenazole, quinaldine, and lepidine is utilised to further subclassify them. The nature of the two terminal groups not only distinguishes the CDs, but also influences the entire dye's electrical behaviour. The dye exhibits an even electron density distribution when the terminal moieties on the edges of the polymethine chain are identical, and these cyanines are called symmetrical. When the termini differ from one another, however, the CDs are described as asymmetrical. In both circumstances, the heterocyclic precursors must have a methyl group in or position to the nitrogen atom, which increases methyl acidity when quaternized. Except for monomethine cyanines, the most frequent synthesis technique for symmetrical CDs is to combine two equivalents of quaternary ammonium salts with the polymethine chain linker in a one-pot procedure. The general reaction mechanism entails multiple steps, beginning with (I) enhanced deprotonation at the methyl group of the quaternary ammonium salt, resulting in the creation of a nucleophilic methylene unit by a base (e.g. triethylamine, pyridine, acetate salts). The active methylene attacks the dianilide-based linker, producing a new carbon-carbon bond, and (ii) promotes electronic rearrangement, releasing a secondary amine as a leaving group. The hemicyanine with a complete

conjugated structure is formed after a last proton extraction (iv) by a base. The hemicyanine is then treated with another equivalent of the quaternary salt in the same chemical pathway (v and vi) to produce the final symmetrical colour. Precursors include orthoesters for trimethine bridges, malondialdehydes and their dianilide-based derivatives for pentamethine scaffolds, glutaconaldehyde dianilide, and Vilsmeier-Haack reagent for heptamethine dyes, and glutaconaldehyde dianilide and Vilsmeier-Haack reagent for heptamethine dye Unsymmetrical colours can also be synthesised using this method. Despite this, because symmetrical analogues are created concurrently, asymmetrical dyes are often produced in poor yields and need difficult purification. Unsymmetrical CDs can be accessible using various approaches based on the polymethine bridge length to circumvent the limits imposed by the one-pot synthesis procedure. Cyanines' history dates back more than a century and it has been studied and employed in a variety of scientific domains and applications over the years. Nonetheless, this dye family's synthetic process and, more importantly, purifying protocols have slowed, if not hampered, their preparation and availability on the market. Organic chemists are now having difficulty synthesising asymmetrical CDs and isolating them from the symmetrical side product. The methodology of solid-phase syntheses has been investigated in the creation of asymmetrical CDs, initially on the most basic and tiny derivatives, and more recently, on water soluble heptamethine analogues. In general, these methods allow for higher yields and higher purity rates of the finished chemical than traditional methods. Furthermore, the primary benefit is from the relatively simple purification techniques necessary to separate the desired product from impurities with significant structural similarity. It is easy to predict that synthetic procedures that reduce the use of organic solvents, waste, and reaction time while improving product yields and reducing reaction time will become increasingly important in the coming decades, driven by the goal of a more sustainable and environmentally friendly economy and lifestyle.