Spectrochimica Acta Part A 75 (2010) 1605–1609

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

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

Synthesis of a new β-naphthothiazole monomethine cyanine dye for the detection of DNA in aqueous solution

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ARTICLE INFO

Article history:
Received 21 October 2009
Received in revised form 22 January 2010
Accepted 11 February 2010

Keywords:
Monomethine cyanine dyes
Ethidium bromide
DNA
Napthothiazole
Fluorescence enhancement
Intercalation

ABSTRACT

Novel monomethine cyanine dye (MC) derived from β-naphthothiazole and benzothiazole has been prepared and characterized by ^{1}H and ^{13}C NMR, FTIR, ESIMS, elemental analyses, absorption and fluorescence spectroscopy. The dye was conveniently synthesized by the condensation of two sulfate heterocyclic quaternary salts. The interaction between calf thymus DNA (ct-DNA) in tris(hydroxymethyl)aminomethane–HCl (Tris–HCl) aqueous buffer solution and MC has been studied with spectral fluorescence method. The binding constant value has been determined by fluorescence titration of MC with ct-DNA concentrations. The result obtained is consistent with an intercalative binding interaction between MC and ct-DNA. Compared with ethidium bromide (EB), MC showed a huge fluorescence enhancement upon mixing with ct-DNA.

1. Introduction

Manipulation at the molecular level of individual chemical and biological substances in solution is currently a challenging target in physics, chemistry, and biology. In particular, direct visualization of macromolecules such as DNA by staining with a suitable fluorescent dye is of great interest. Therefore, exploring new fluorescent dyes and expanding the tool box of currently available fluorescent probes for the monitoring of biological systems and processes is a challenge crucial to several research areas spanning from medical diagnostics to genomics and live cell metabolism [1]. In all these fields, new and more efficient analytical tools to characterize nucleic acids, proteins, and cells and the production of low cost, easy to manipulate systems for fast sample analysis and large-scale screening are highly required. In this rapidly developing context, fluorescent detection has become one the most exploited techniques owing to its sensitivity and noninvasiveness [2]. Conventionally, EB has been used for the detection of DNA, however its mutagenic effects pose some environmental concerns [3–5].

On the other hand, cyanine dyes are sensitive and more safe fluorescent probes and are widely used for the detection of nucleic acids [6–8]. In this way femtomoles of nucleic acids may be detected and selectively identified even in the presence of other biopolymers [9–12]. Cyanine dyes demonstrate a significant increase in fluorescence intensity upon binding to DNA [13], and the resulting high signal/noise ratio affords detection in a homogeneous medium [14–18]. The huge enhancement in fluorescence upon binding to DNA is believed to originate from the loss of mobility around the methine bridge between the two heterocyclic moieties [19]. There are three main modes of non-covalent interactions of these small molecules with DNA, intercalation, minor groove binding and electrostatic interaction of highly positively charged molecules with nucleotide phosphate backbone [14,20].

The structural differences between biological molecules results in a different modes of interaction with the same probe. Moreover, size of aromatic moiety as well as bulkiness of attached substituents and their ability to interact non-covalently with polynucleotide could also control intercalation ability as well as orientation of intercalated molecule [21,22]. Therefore, tailoring new molecular probes for the detection of biological targets is being attractive for many scientists. In a continuation of our interest in cyanine dyes suitable for the detection of DNA [23], we report here the synthesis of a new MC and its binding properties with ct-DNA.

2. Experimental

2.1. General

Ethidium bromide, calf thymus DNA of low molecular weight (1254 g/mol base pairs) and other reagents were of the highest purity available, purchased from Sigma–Aldrich Company and used as received. Solvents were of analytical grade. ^{1}H and ^{13}C

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doi:10.1016/j.saa.2010.02.026